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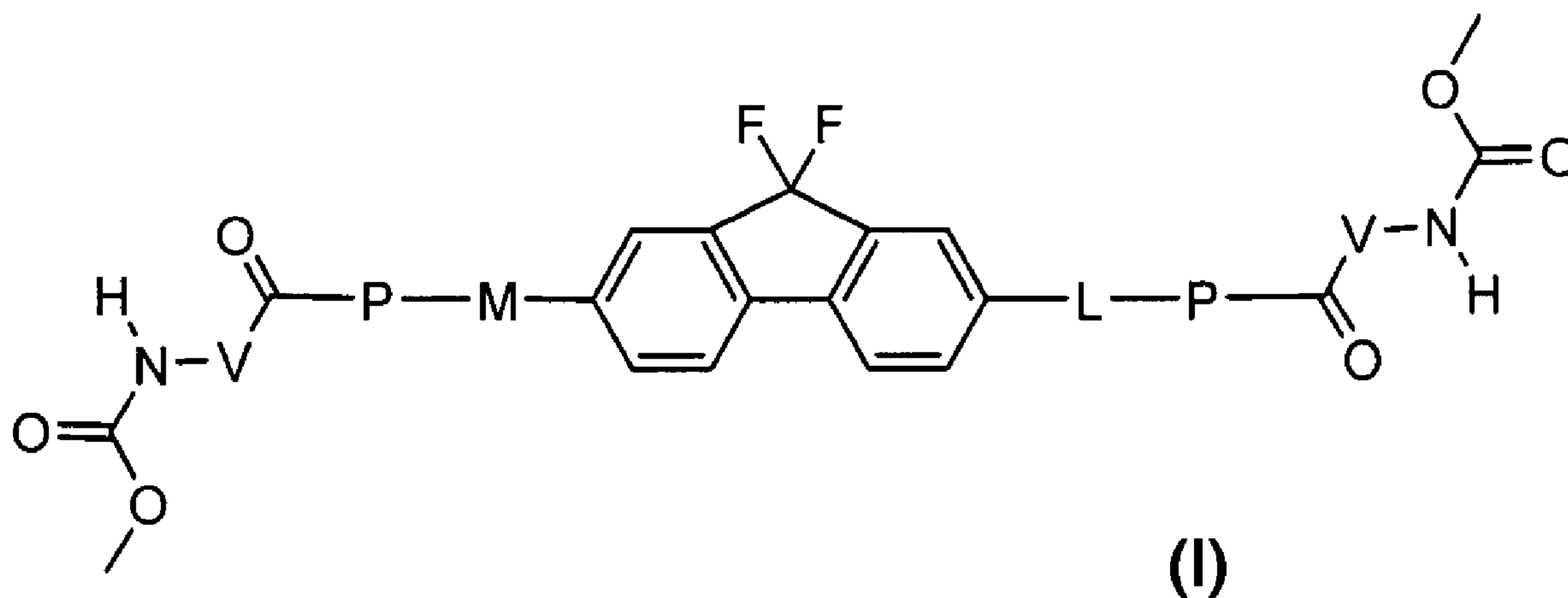
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(54) Titre : COMPOSES ANTIVIRAUX
 (54) Title: ANTIVIRAL COMPOUNDS



(57) Abrégé/Abstract:

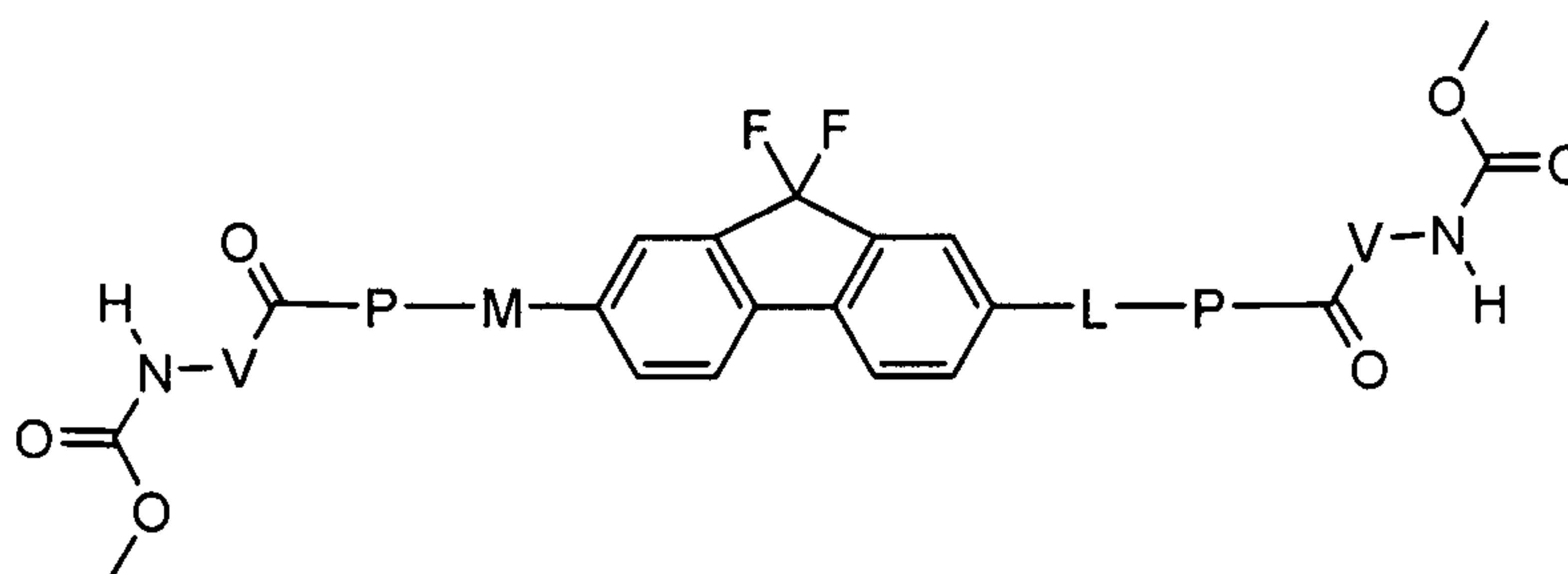
The invention relates to anti-viral compounds, compositions containing such compounds, and therapeutic uses of such compounds, as well as to processes and intermediates useful for preparing such compounds. Representative compounds include compounds of formula I: (see formula I)

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ABSTRACT

The invention relates to anti-viral compounds, compositions containing such compounds, and therapeutic uses of such compounds, as well as to processes and intermediates useful for preparing such compounds. Representative compounds include compounds of formula I:



DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3
CONTENANT LES PAGES 1 À 435

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 3
CONTAINING PAGES 1 TO 435

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NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

The present invention also provides for a method of treating disorders associated with hepatitis C, said method comprising administering to an individual a pharmaceutical composition which comprises a therapeutically effective amount of a compound of the invention.

The present invention also provides a method of inhibiting HCV, comprising administering to a mammal afflicted with a condition associated with HCV activity, an amount of a compound of the invention, effective to inhibit HCV.

The present invention also provides a compound of the invention for use in medical therapy (preferably for use in inhibiting HCV activity or treating a condition associated with HCV activity), as well as the use of a compound of the invention for the manufacture of a medicament useful for inhibiting HCV or the treatment of a condition associated with HCV activity in a mammal.

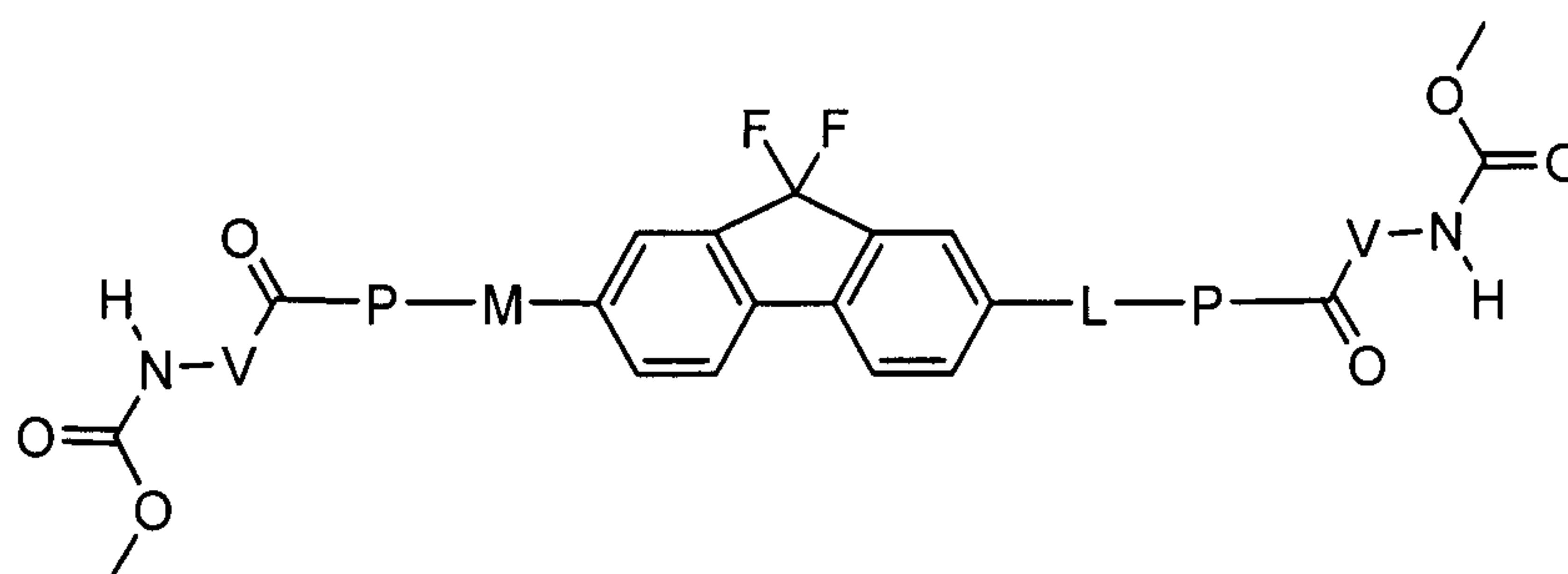
The present invention also provides synthetic processes and novel intermediates disclosed herein which are useful for preparing compounds of the invention. Some of the compounds of the invention are useful to prepare other compounds of the invention.

In another aspect the invention provides a compound of formula I, or a pharmaceutically acceptable salt or prodrug thereof, for use in the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.

In another aspect the invention provides a method of inhibiting HCV activity in a sample comprising treating the sample with a compound of the invention.

In one embodiment the invention provides a compound having improved inhibitory or pharmacokinetic properties, including enhanced activity against development of viral resistance, improved oral bioavailability, greater potency (for example, in inhibiting HCV activity) or extended effective half-life *in vivo*. Certain compounds of the invention may have fewer side effects, less complicated dosing schedules, or be orally active.

In another aspect, the invention provides a compound of formula:



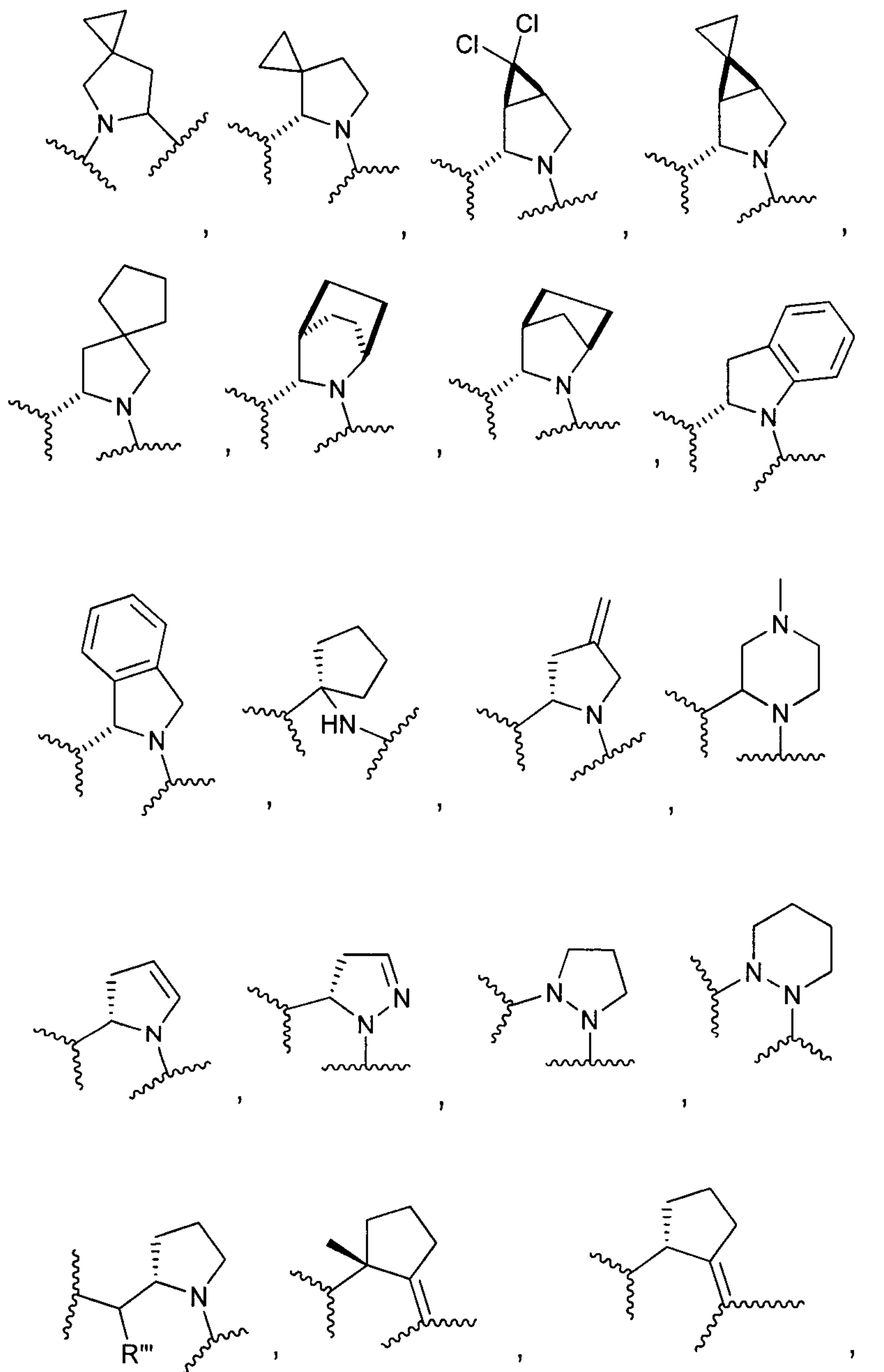
wherein:

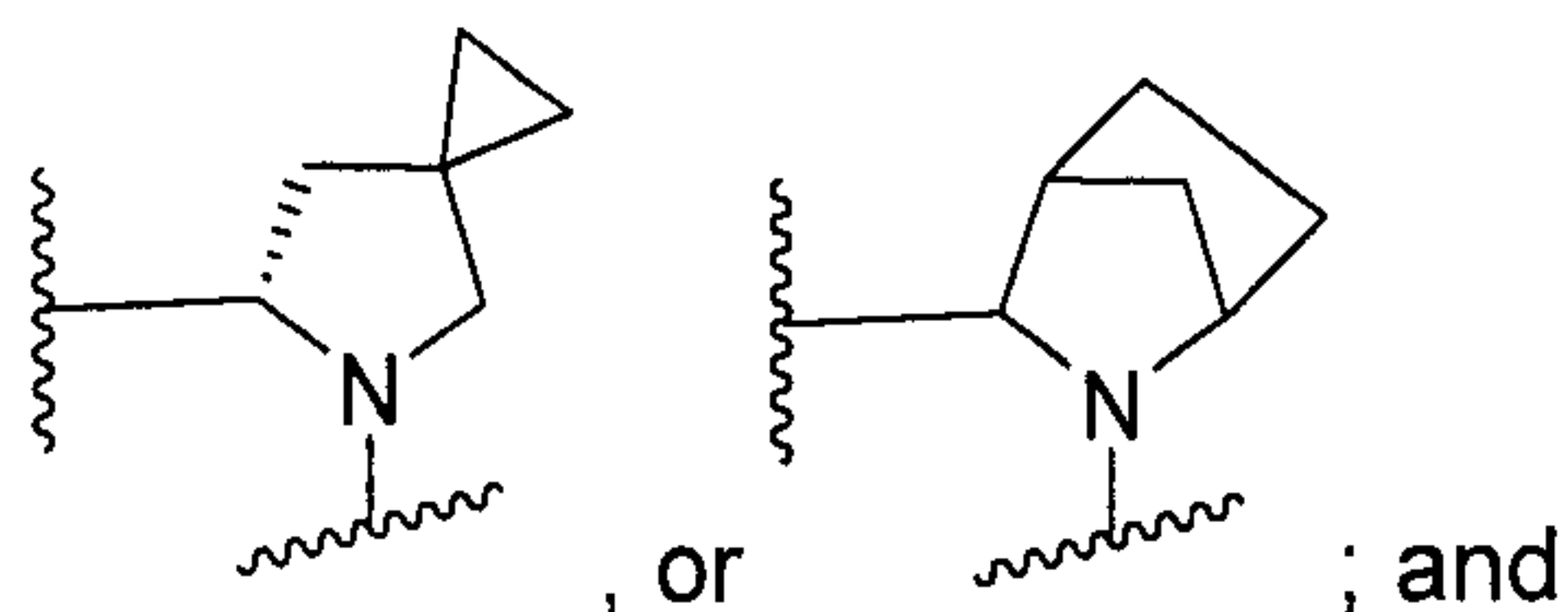
each V is independently alkyl;

L is benzimidazolyl;

M is a 5-membered heteroaryl ring;

each P is independently:

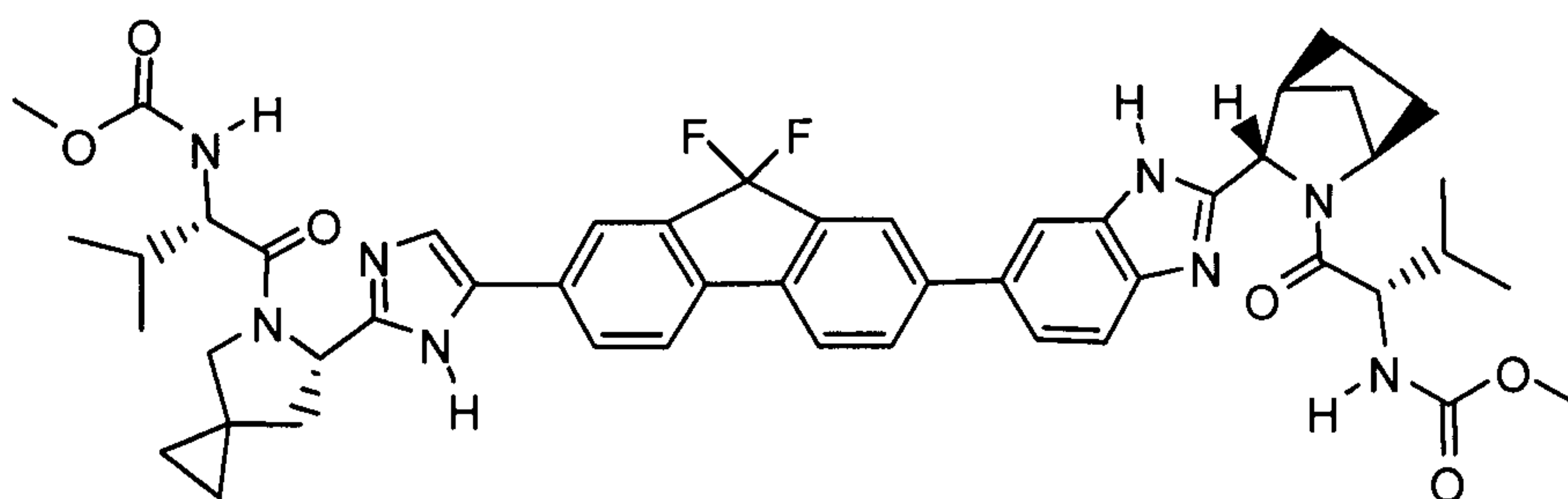




R^{'''} is hydrogen or methyl;

or a pharmaceutically acceptable salt thereof.

In another aspect, the invention provides a compound of formula:



In another aspect, the invention provides a pharmaceutical composition comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

In another aspect, the invention provides the use of a compound or a pharmaceutically acceptable salt thereof as defined herein for medical therapy.

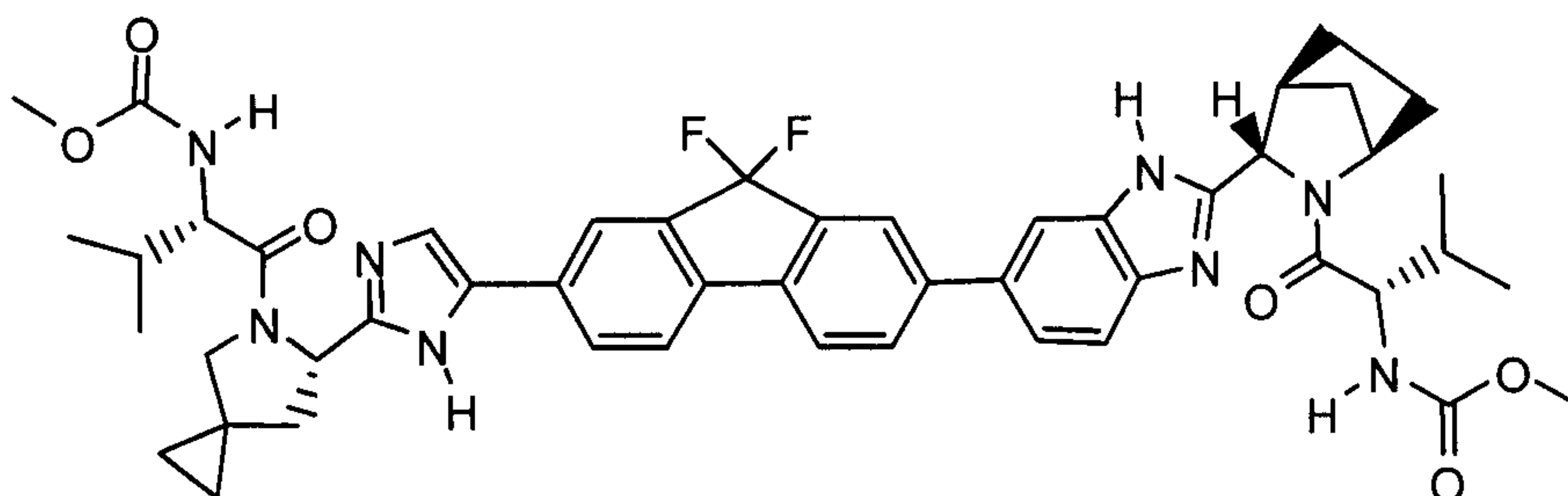
In another aspect, the invention provides the use of a compound or a pharmaceutically acceptable salt thereof as defined herein in the preparation of a medicament for medical therapy.

In another aspect, the invention provides the use of a compound or a pharmaceutically acceptable salt thereof or a composition as defined herein for the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.

In another aspect, the invention provides the use of a compound or a pharmaceutically acceptable salt thereof as defined herein in the preparation of a

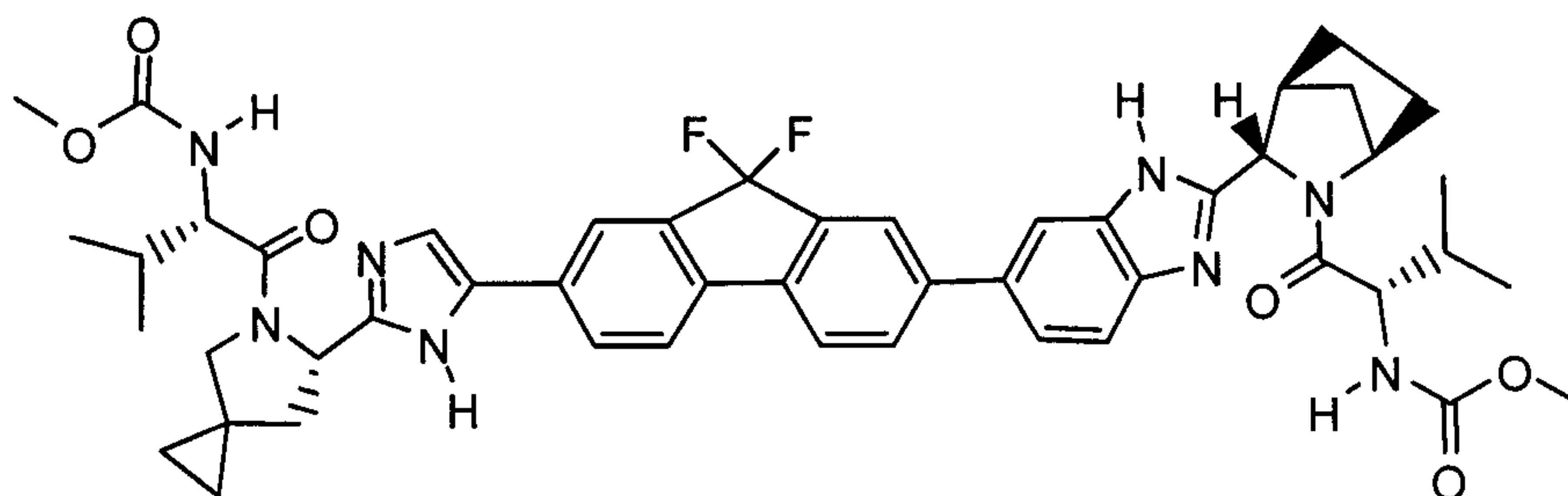
medicament for the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.

In another aspect, the invention provides a compound of formula:



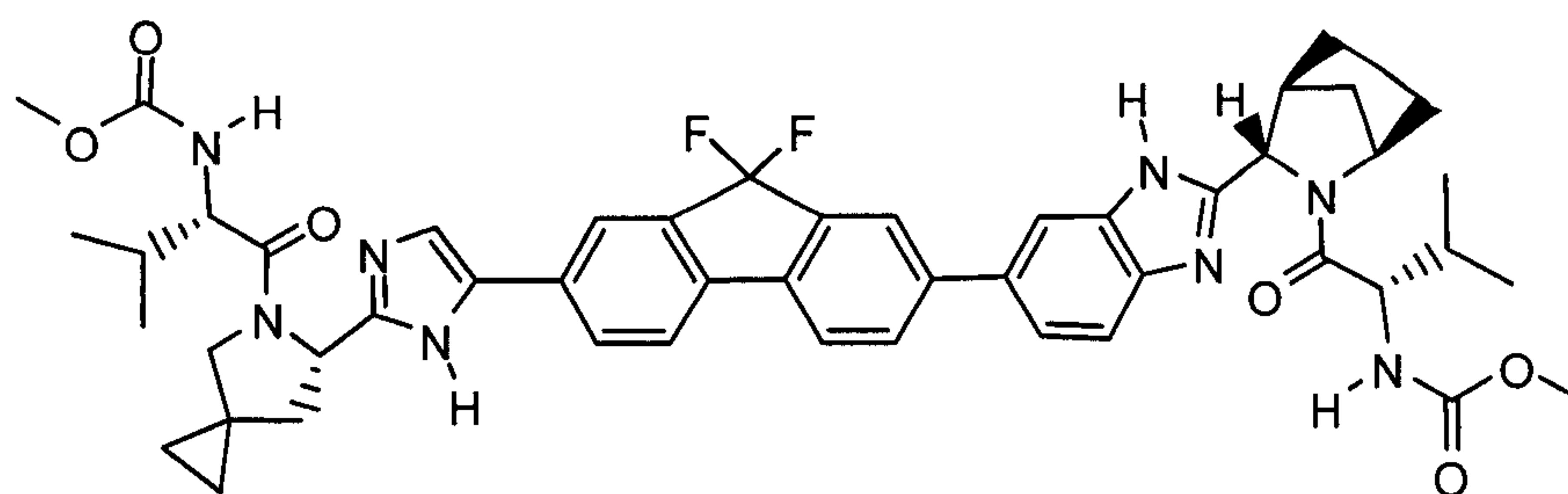
for use in the prophylactic or therapeutic treatment of hepatitis C.

In another aspect, the invention provides the use of a compound of formula:



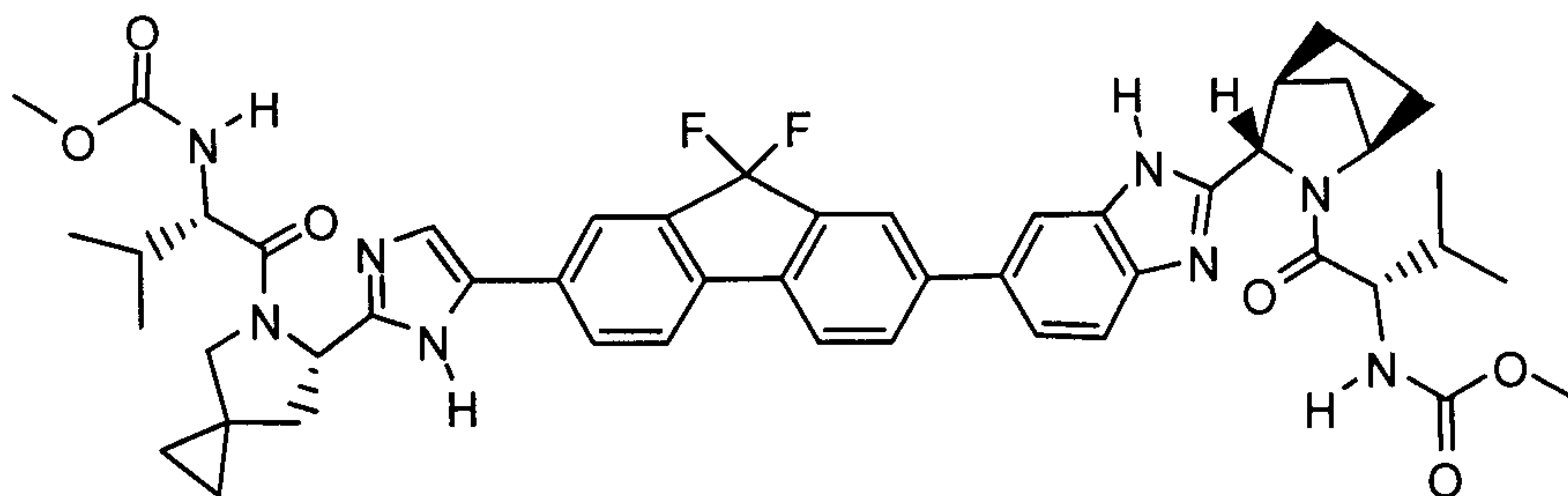
for the prophylactic or therapeutic treatment of hepatitis C.

In another aspect, the invention provides the use of a compound of formula:



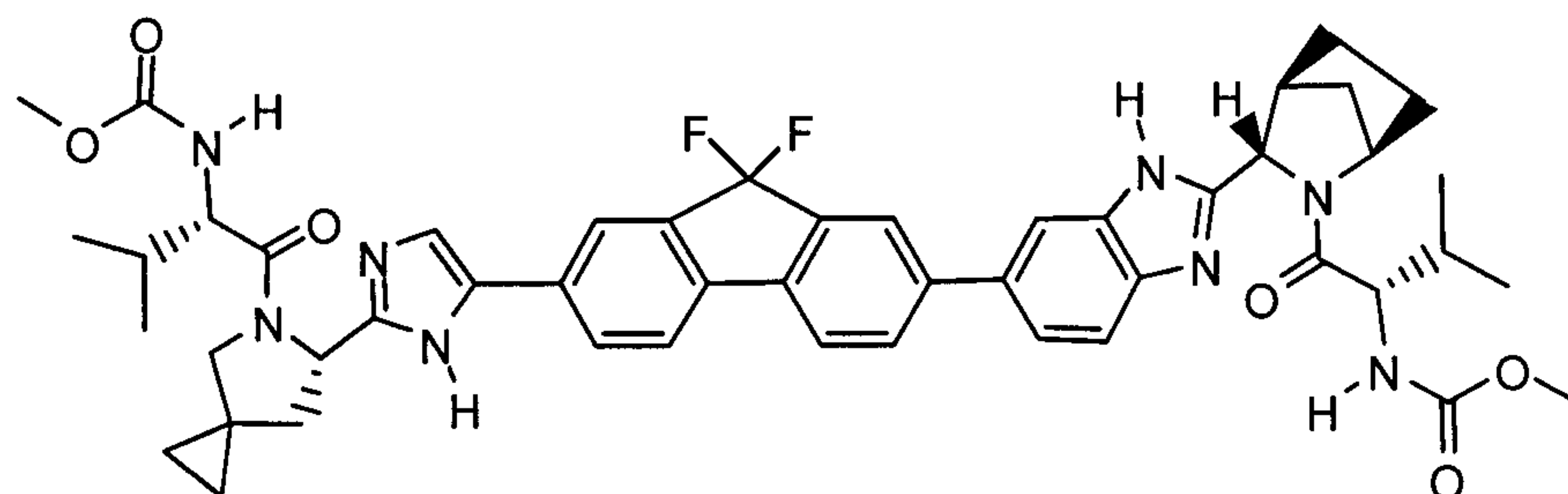
in the preparation of a medicament for the prophylactic or therapeutic treatment of hepatitis C.

In another aspect, the invention provides a compound of formula:



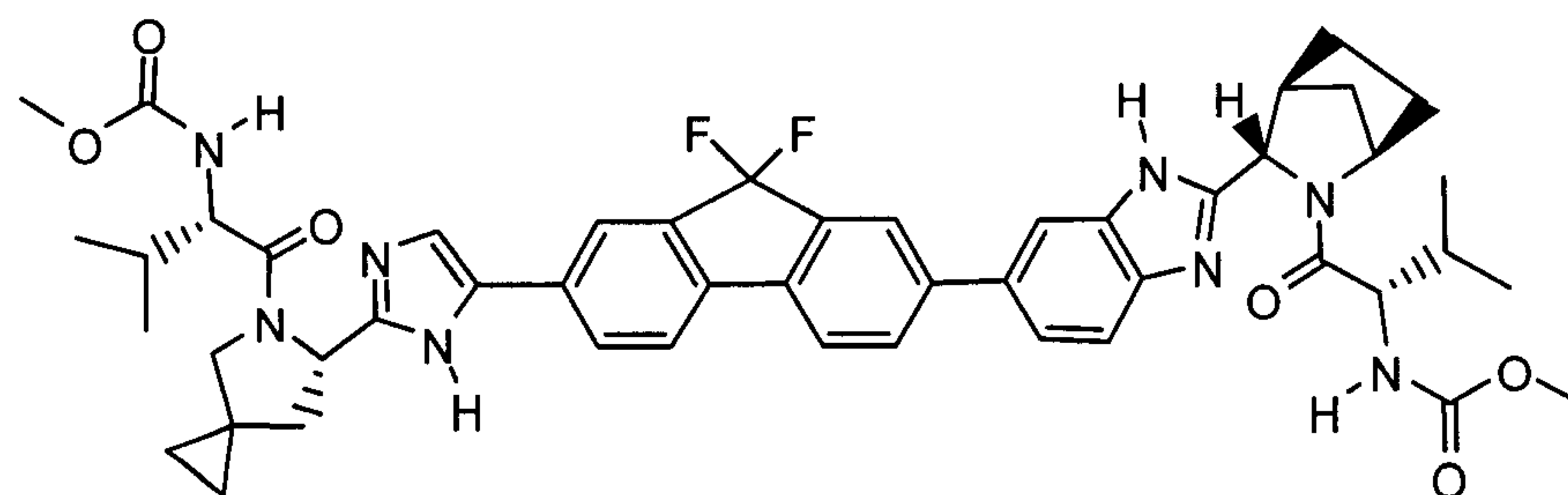
for use in the treatment of hepatitis C.

In another aspect, the invention provides the use of a compound of formula:



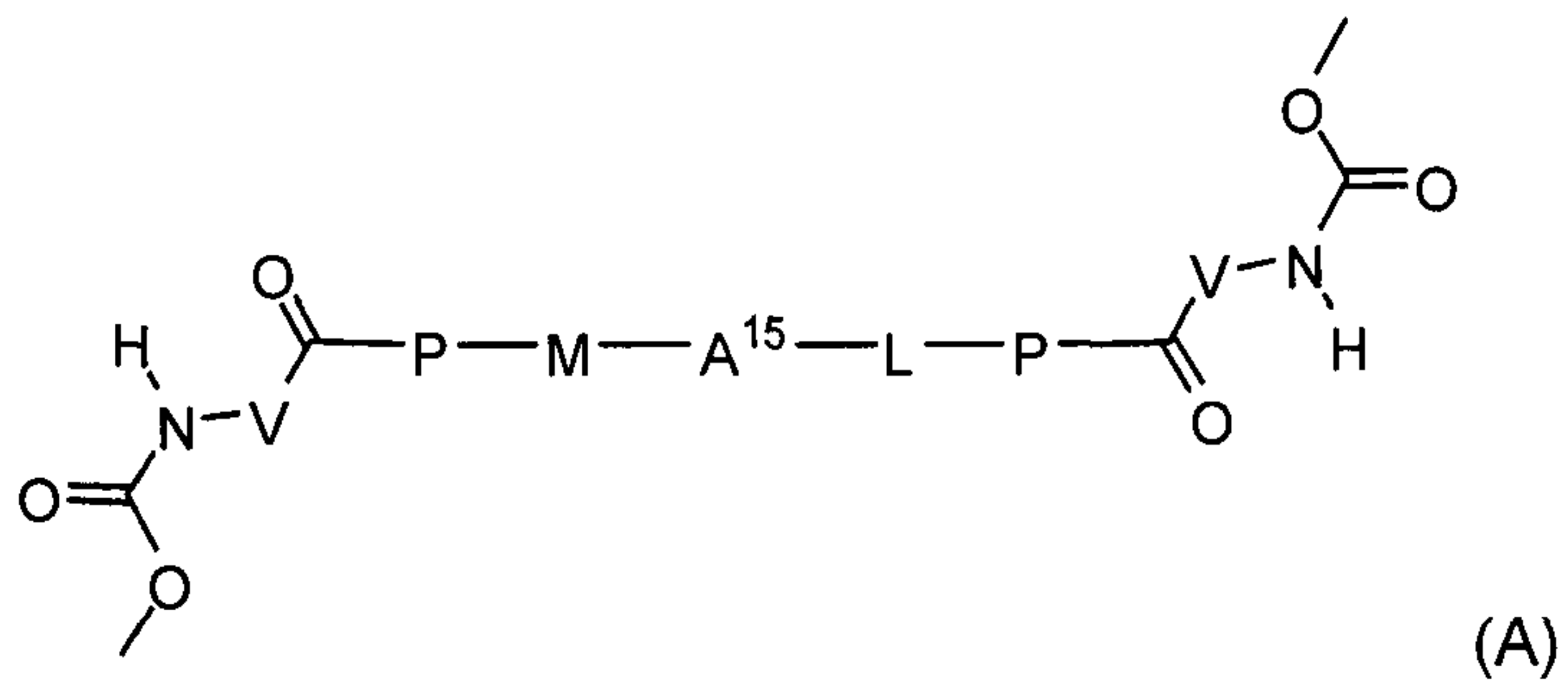
for treatment of hepatitis C.

In another aspect, the invention provides the use of a compound of formula:

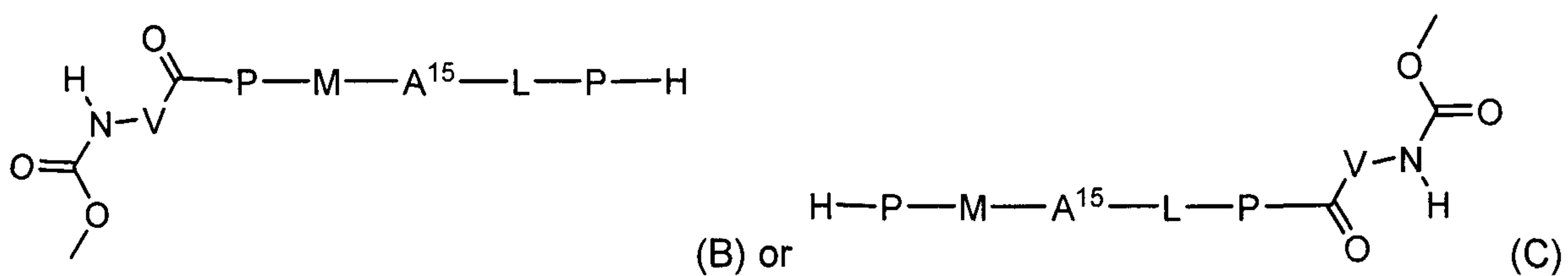


in the preparation of a medicament for the treatment of hepatitis C.

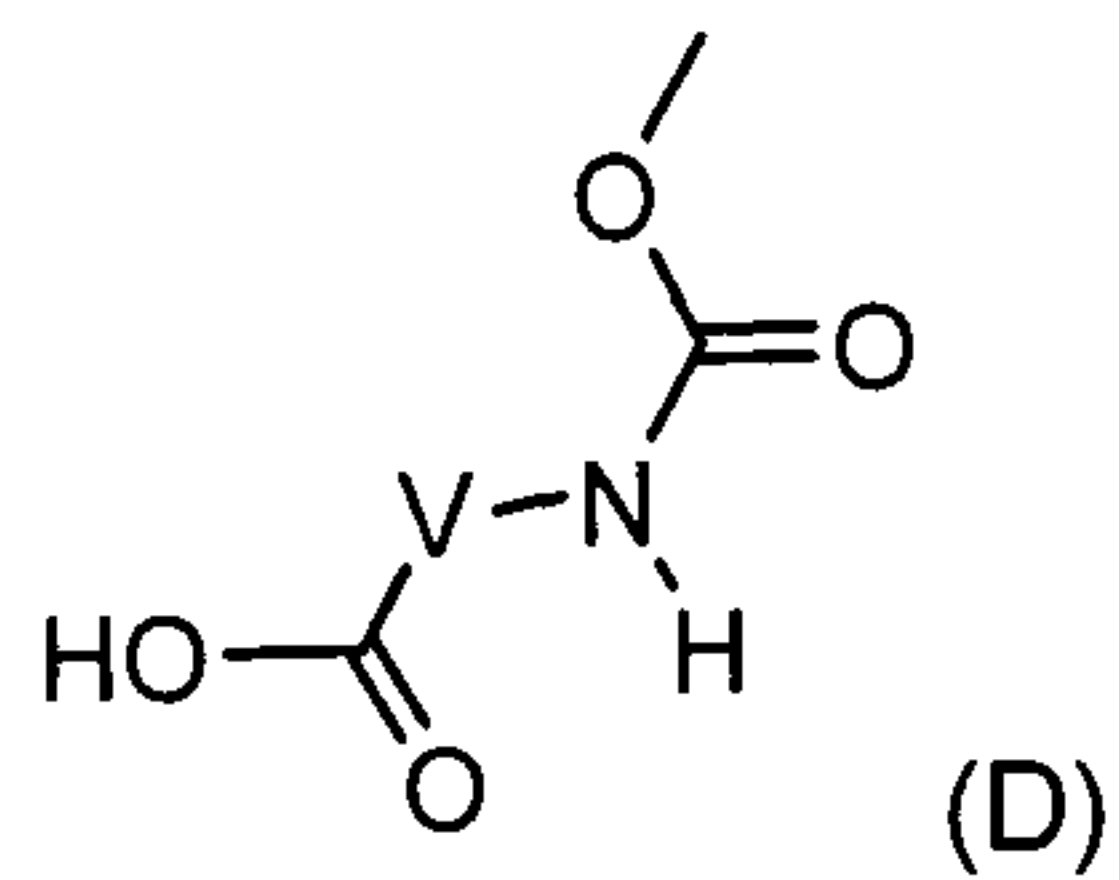
In another aspect, the invention provides a method for preparing a compound of formula (A):



comprising contacting a compound of formula (B) or (C):



with a compound of formula (D):



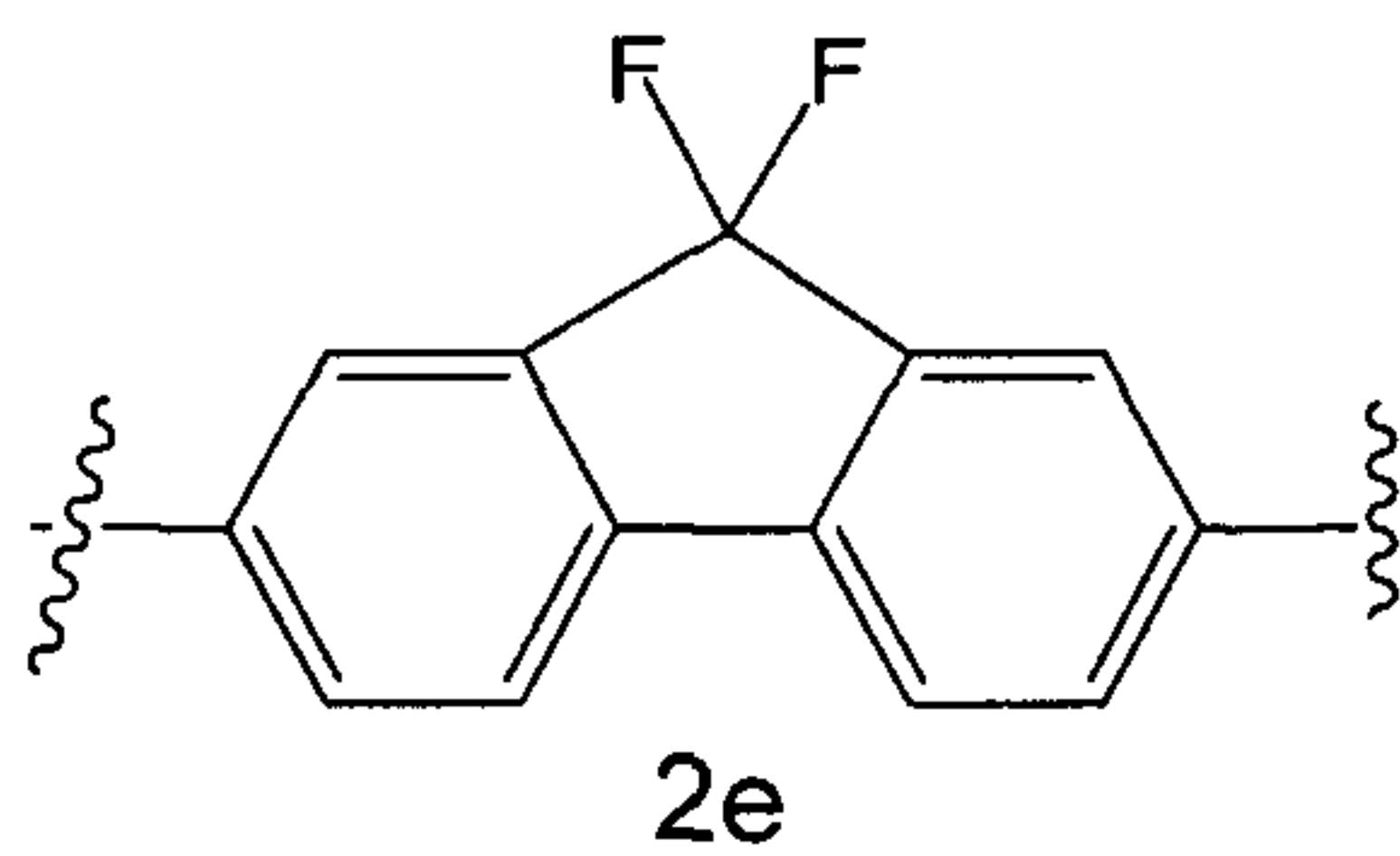
to yield a compound of formula (A), wherein:

V is alkyl;

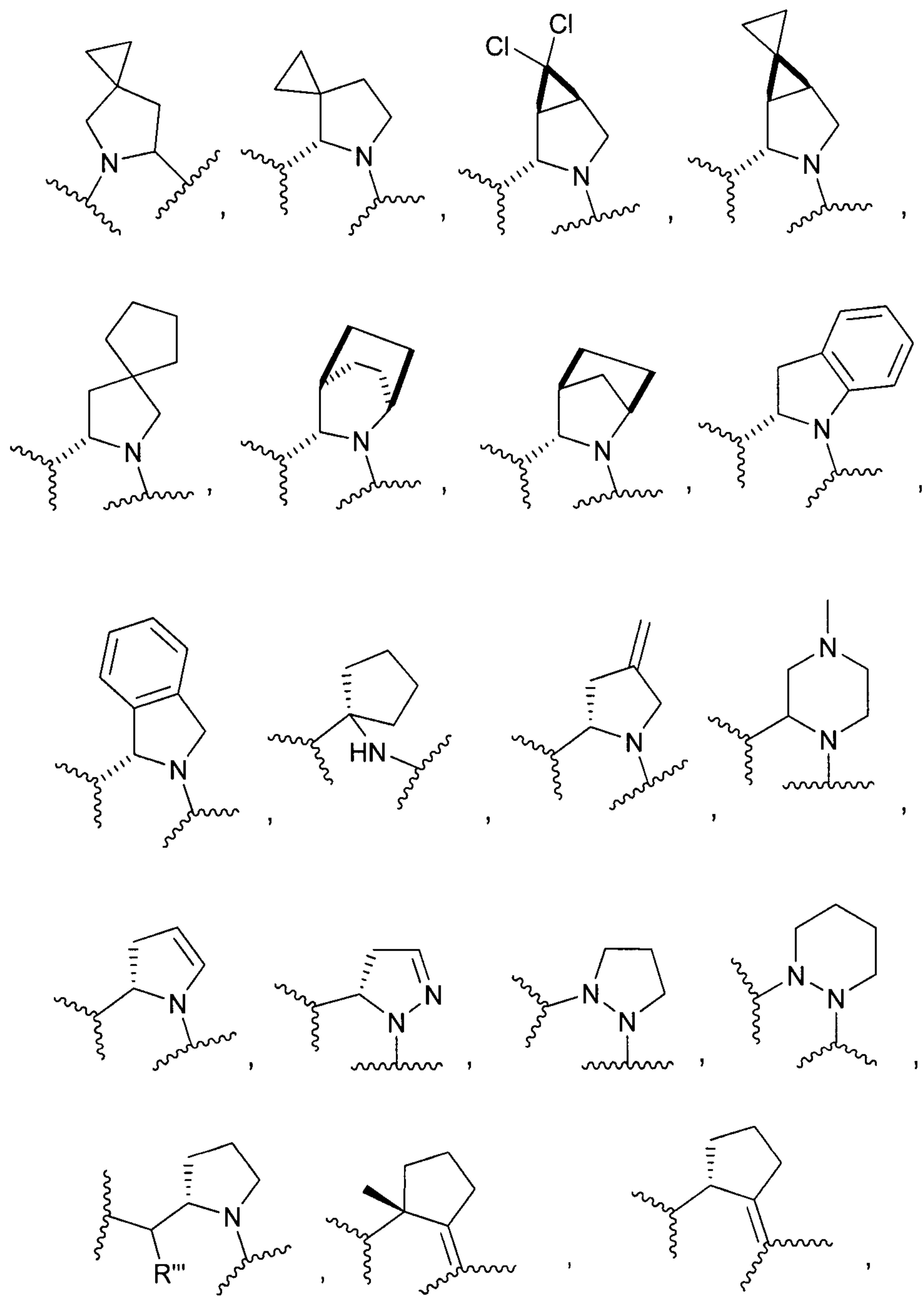
L is benzimidazolyl;

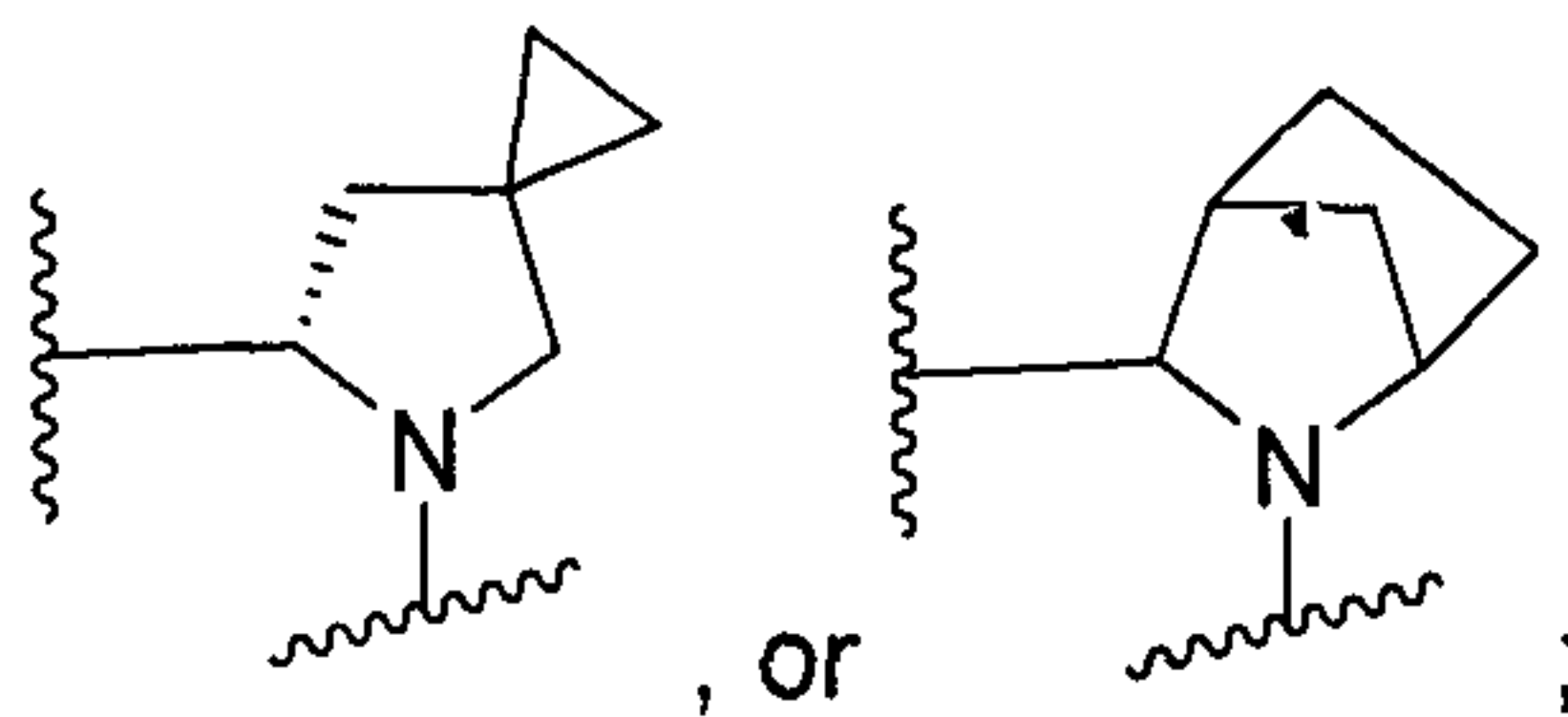
M is a 5-membered heteroaryl ring;

A¹⁵ is:



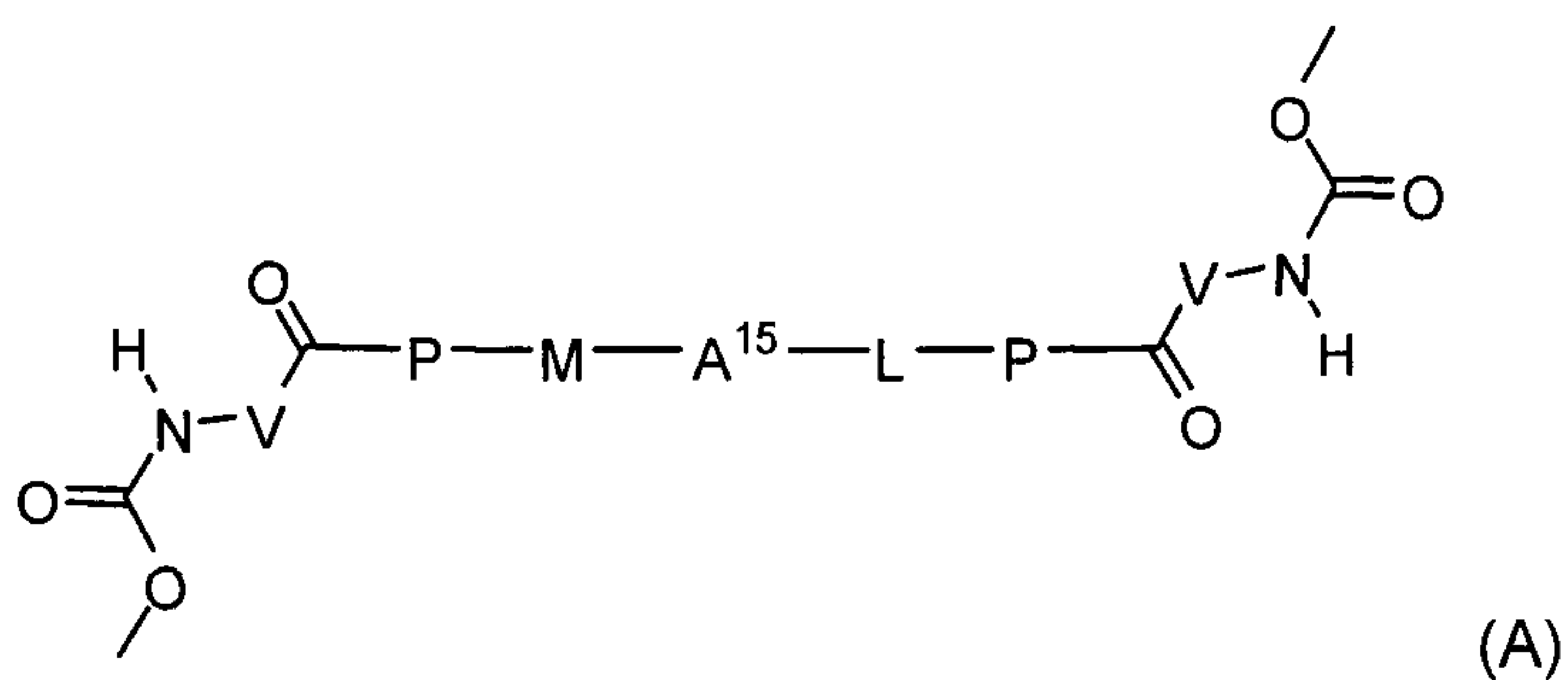
each P is independently:



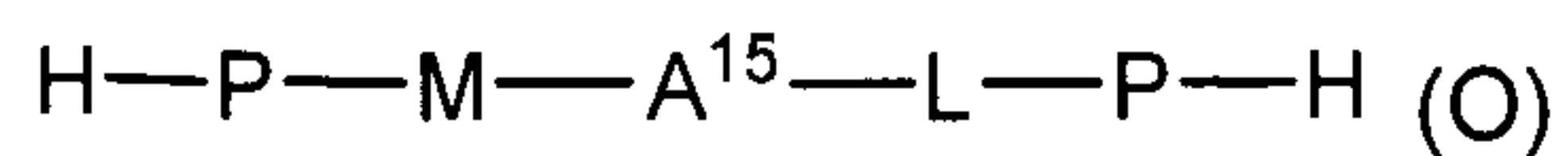


and R''' is hydrogen or alkyl.

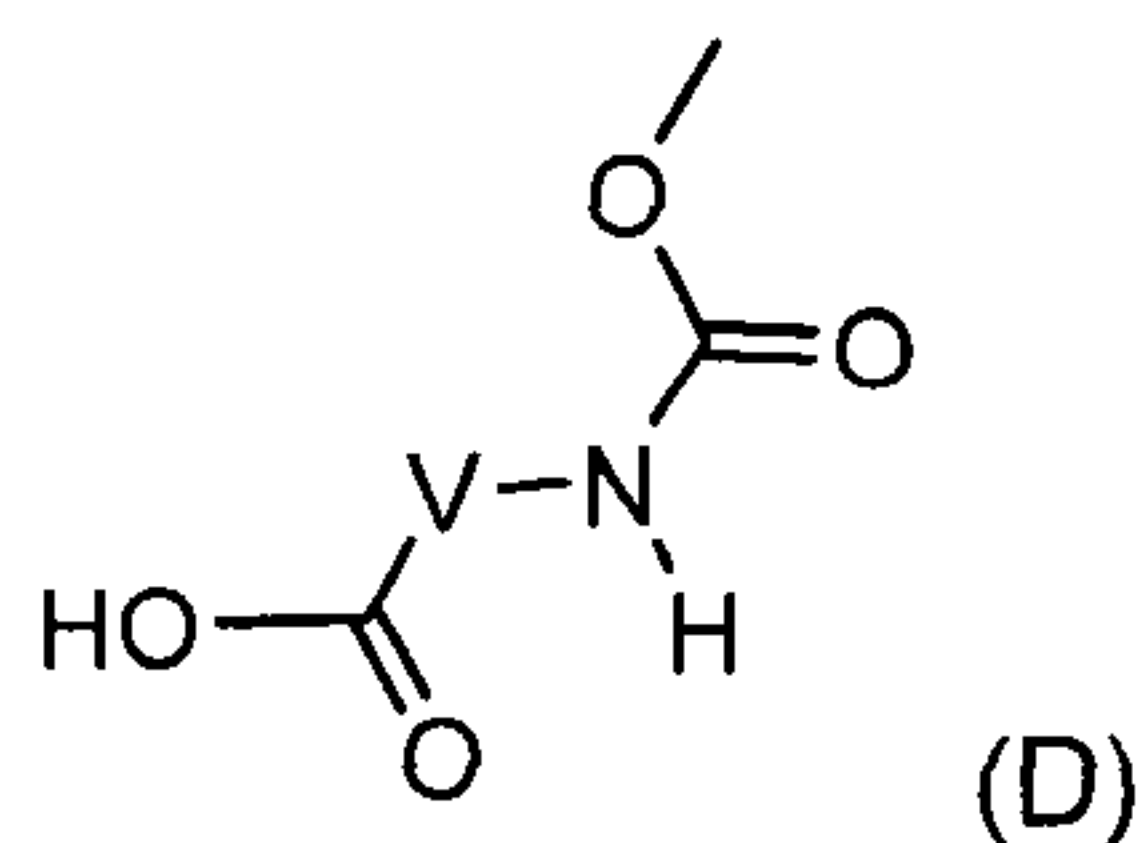
In another aspect, the invention provides a method for preparing a compound of formula (A):



comprising contacting a compound of formula (O):



with at least two equivalents of a compound of formula (D):

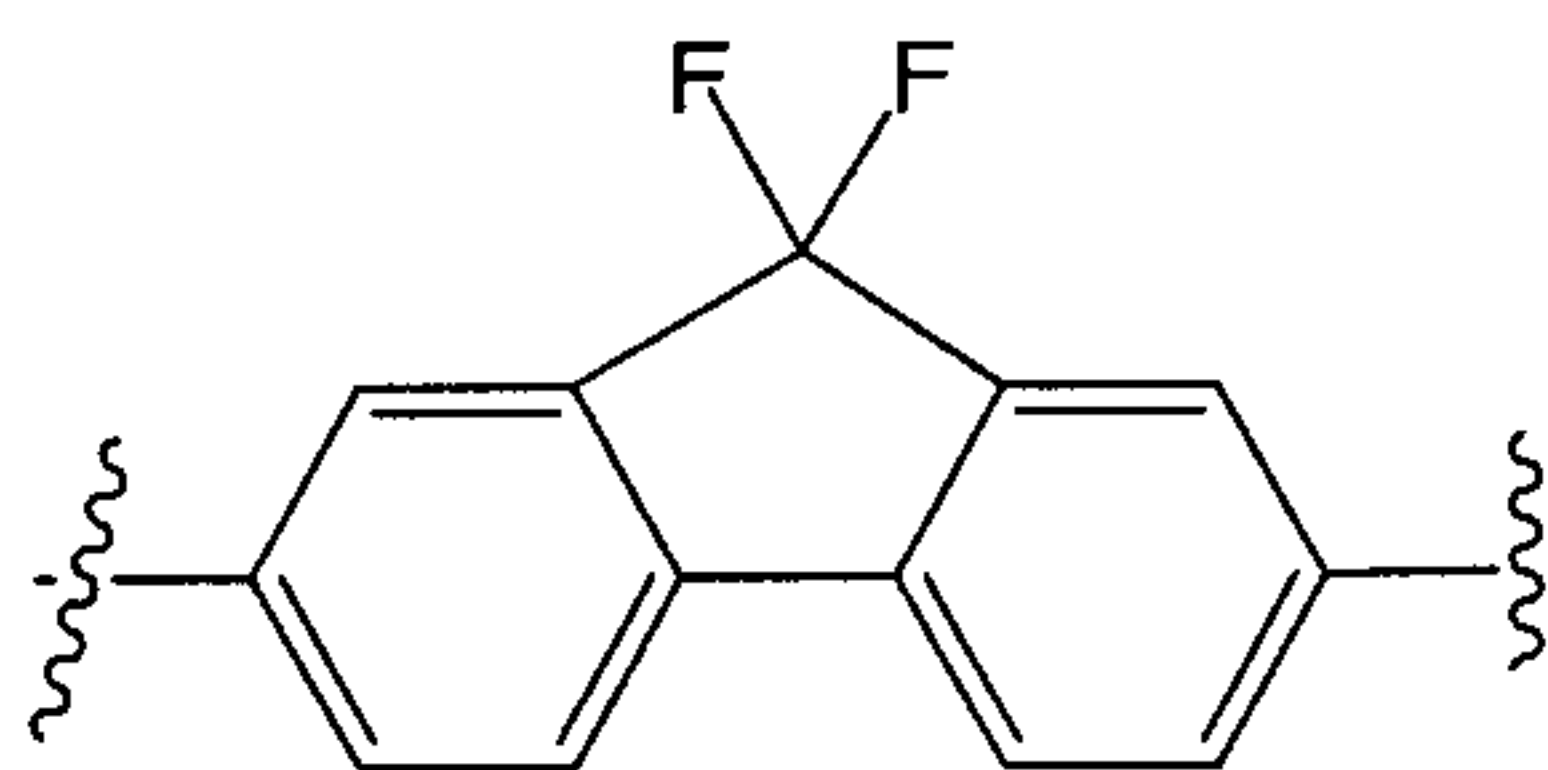


to yield a compound of formula (A), wherein:

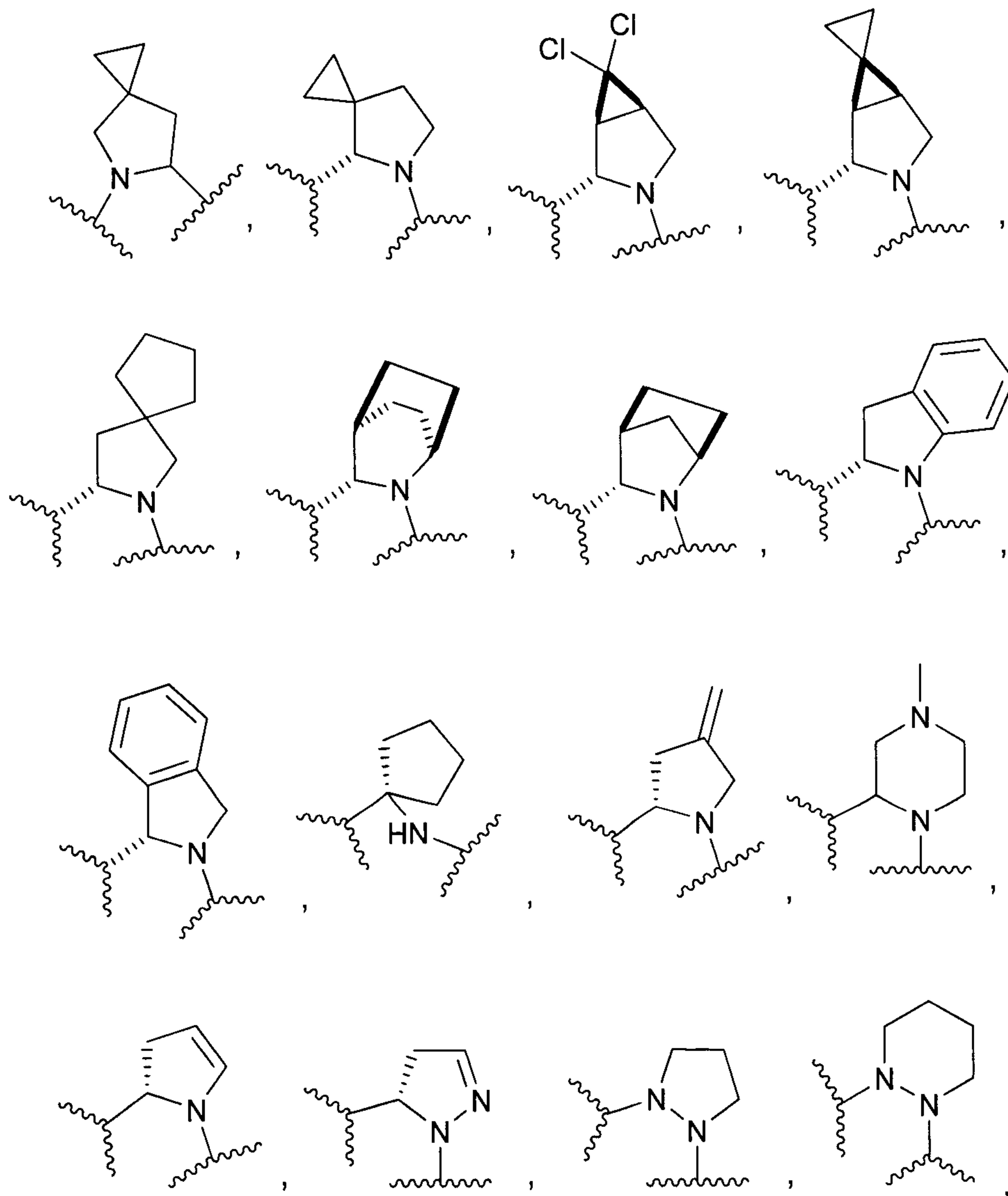
V is alkyl;

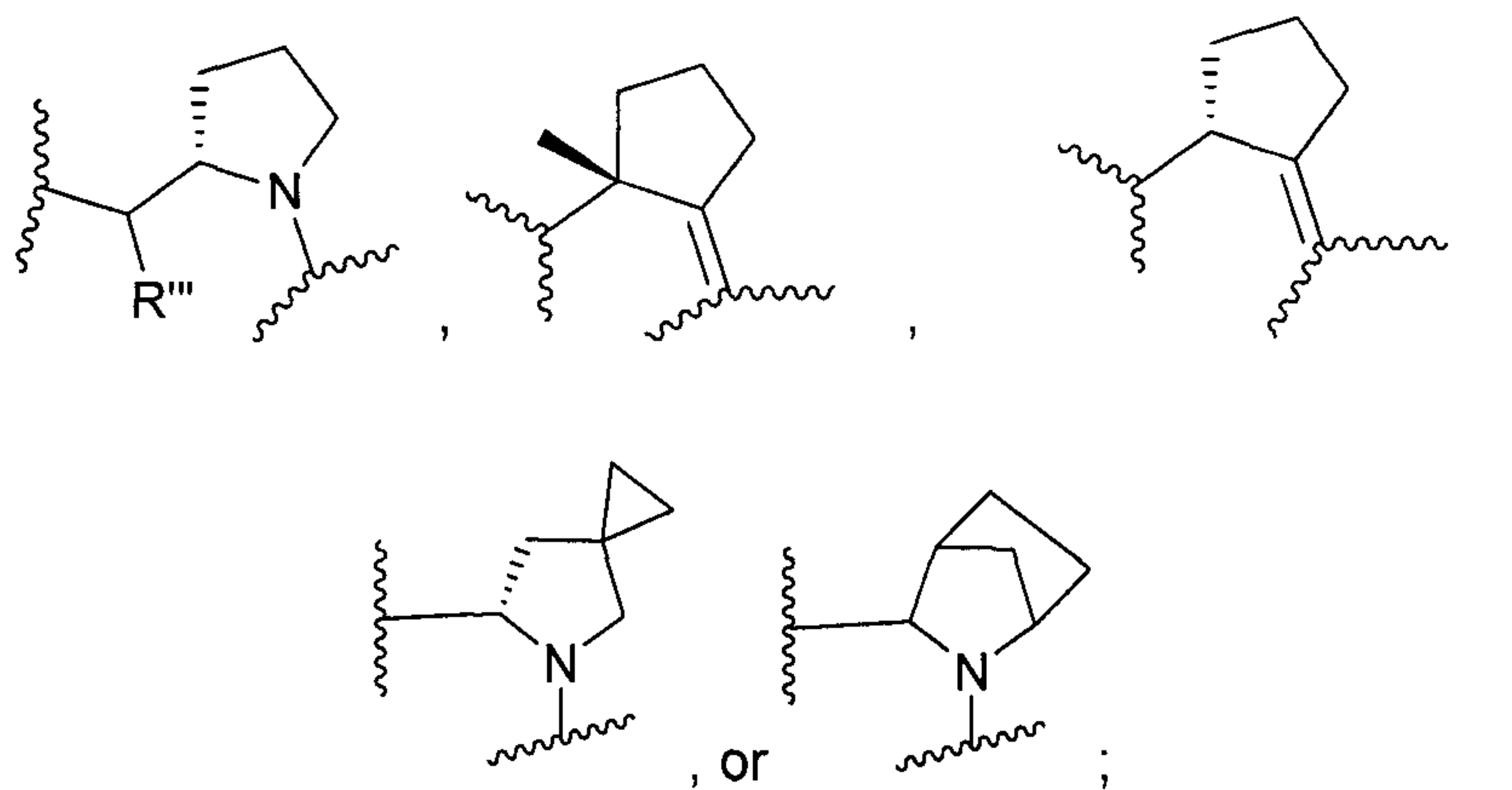
L is benzimidazolyl;

M is a 5-membered heteroaryl ring;

A¹⁵ is:

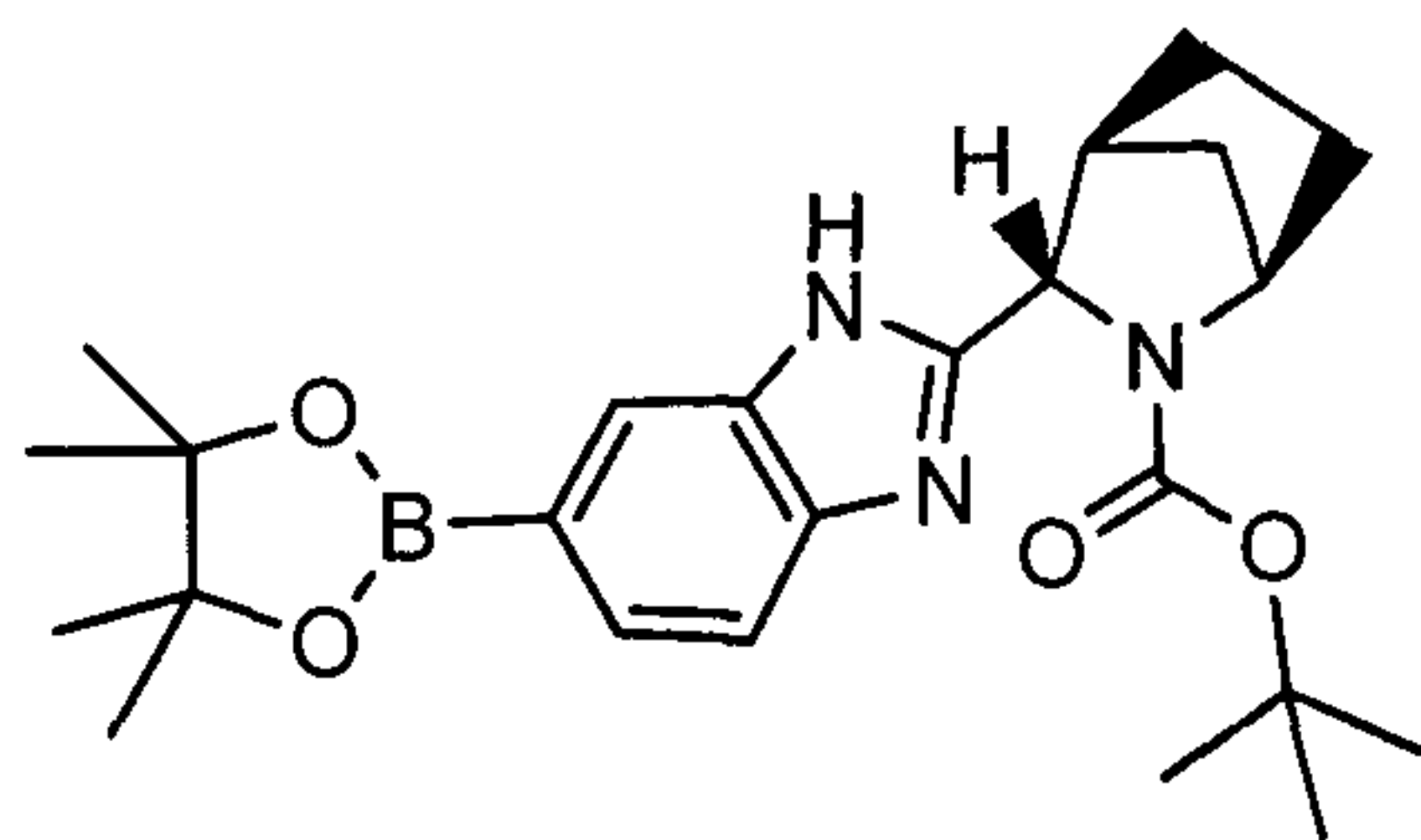
each P is independently:



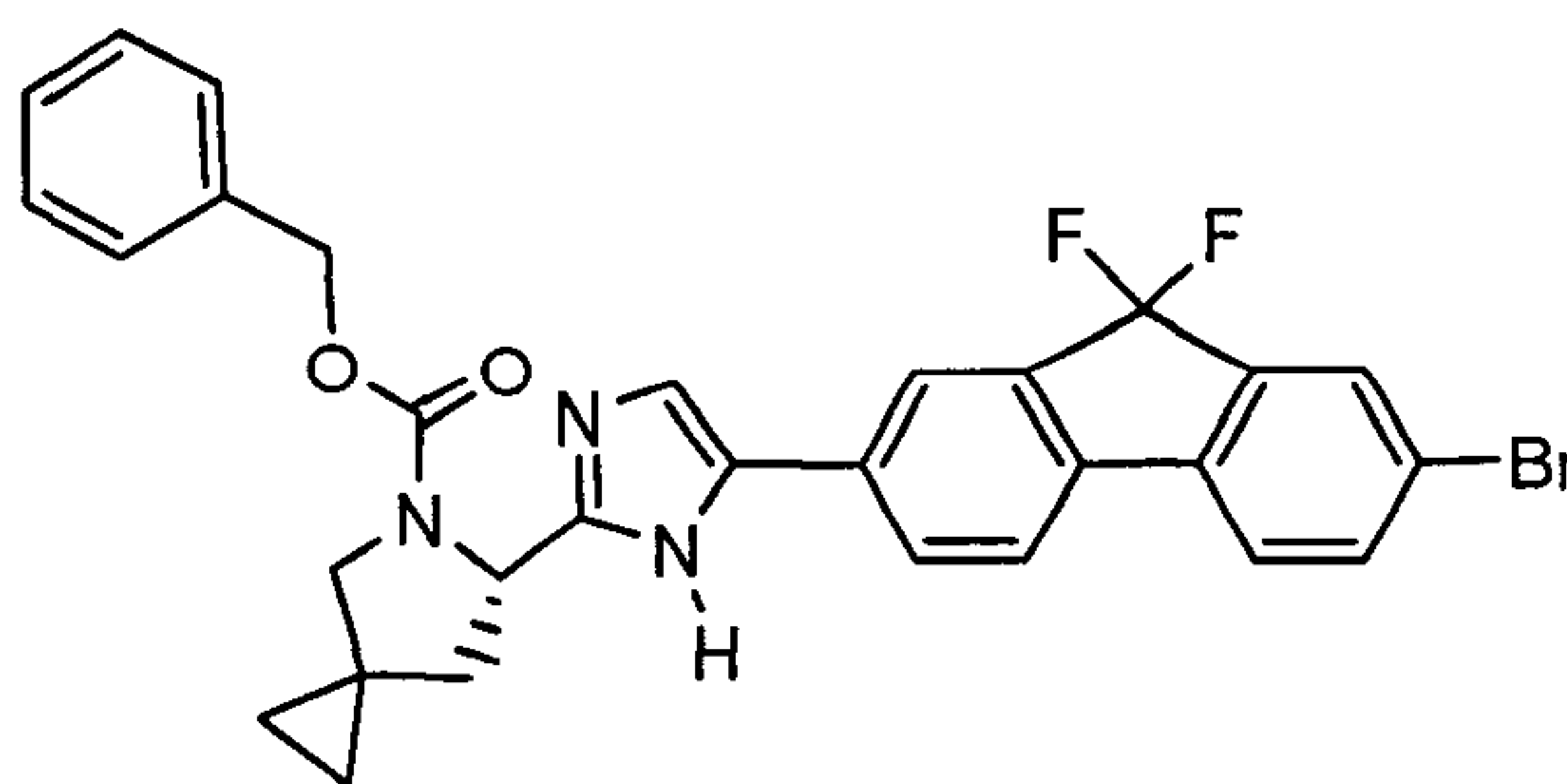


and R''' is hydrogen or alkyl.

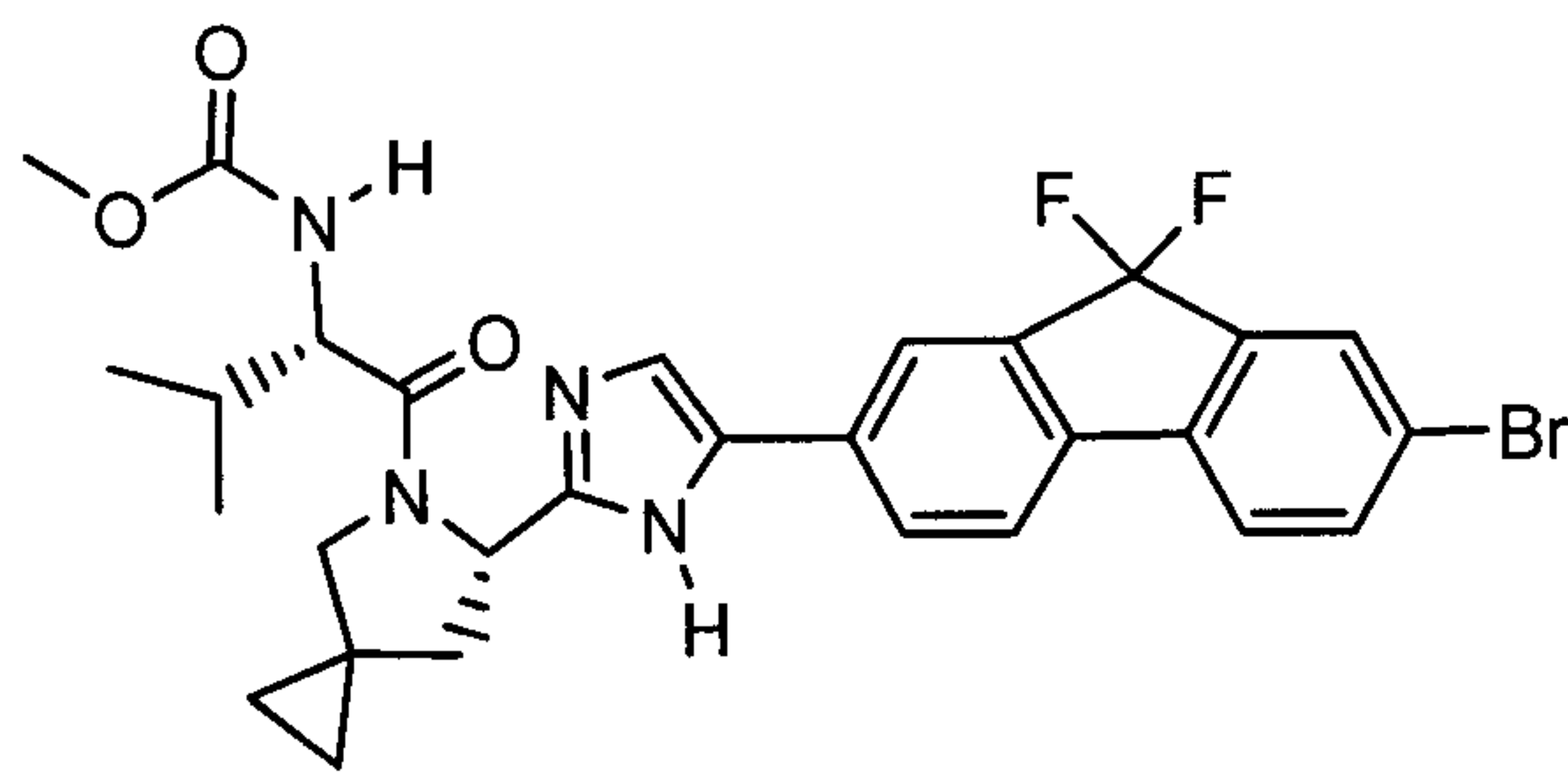
In another aspect, the invention provides a compound of formula:



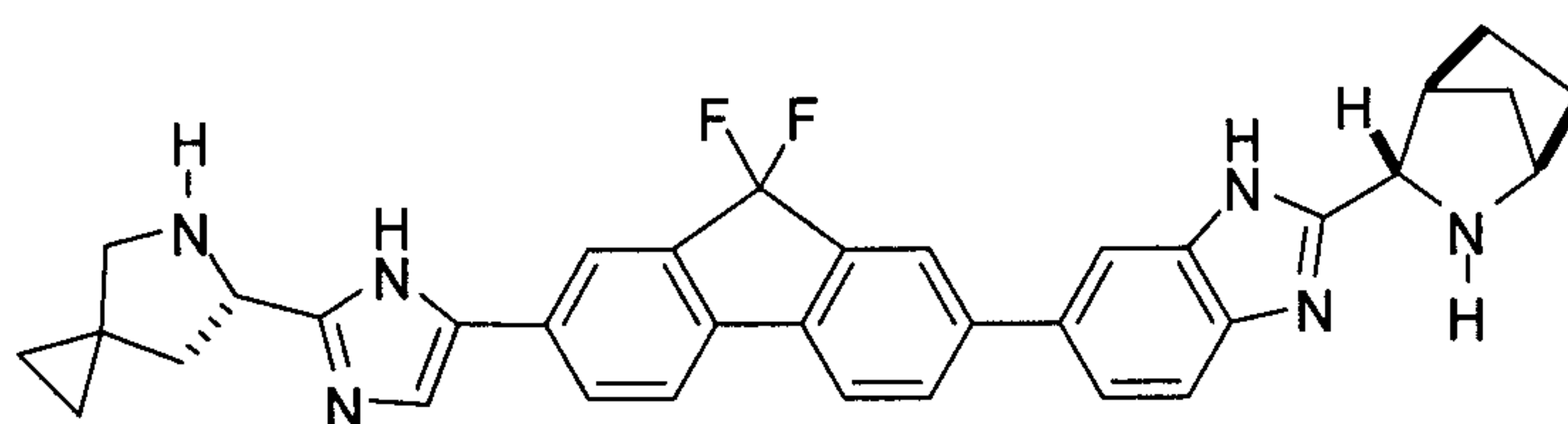
In another aspect, the invention provides a compound of formula:



In another aspect, the invention provides a compound of formula:



In another aspect, the invention provides a compound of formula:



DETAILED DESCRIPTION OF THE INVENTION

Reference will now be made in detail to certain embodiments of the invention, examples of which are illustrated in the accompanying structures and formulas. While the invention will be described in conjunction with the enumerated embodiments, it will be understood that they are not intended to limit the invention to those embodiments. On the contrary, the invention is intended to cover all alternatives, modifications, and equivalents, which may be included within the scope of the present invention as defined by the embodiments.

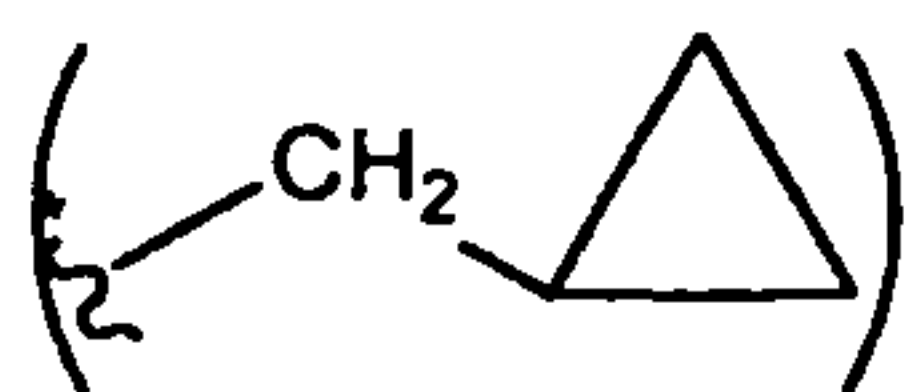
Compounds of the Invention

The compounds of the invention exclude compounds heretofore known. However, it is within the invention to use compounds that previously were not known to have antiviral properties for antiviral purposes (e.g. to produce an anti-viral effect in an animal). With respect to the United States, the compounds or compositions herein exclude compounds that are anticipated under 35 USC §102 or that are obvious under 35 USC §103.

Whenever a compound described herein is substituted with more than one of the same designated group, e.g., "R¹" or "A³", then it will be understood that the groups may be the same or different, i.e., each group is independently selected.

"Absent" – Some groups are defined such that they can be absent. When a group is absent it becomes a bond connector. The two groups that would otherwise be connected to that absent group are connected to each other through a bond. For example, when W is absent, M is bonded to M.

"Alkyl" is C₁-C₁₈ hydrocarbon containing normal, secondary, tertiary or cyclic carbon atoms. Examples are methyl (Me, -CH₃), ethyl (Et, -CH₂CH₃), 1-propyl (n-Pr, n-propyl, -CH₂CH₂CH₃), 2-propyl (i-Pr, i-propyl, -CH(CH₃)₂), 1-butyl (n-Bu, n-butyl, -CH₂CH₂CH₂CH₃), 2-butyl (s-Bu, s-butyl, -CH(CH₃)CH₂CH₃), 2-methyl-1-propyl (i-Bu, i-butyl, -CH₂CH(CH₃)₂), 2-butyl (s-Bu, s-butyl, -CH(CH₃)CH₂CH₃), 2-methyl-2-propyl (t-Bu, t-butyl, -C(CH₃)₃), 1-pentyl (n-pentyl, -CH₂CH₂CH₂CH₂CH₃), 2-pentyl (-CH(CH₃)CH₂CH₂CH₃), 3-pentyl (-CH(CH₂CH₃)₂), 2-methyl-2-butyl (-C(CH₃)₂CH₂CH₃), 3-methyl-2-butyl (-CH(CH₃)CH(CH₃)₂), 3-methyl-1-butyl (-CH₂CH₂CH(CH₃)₂), 2-methyl-1-butyl (-CH₂CH(CH₃)CH₂CH₃), 1-hexyl (-CH₂CH₂CH₂CH₂CH₂CH₃), 2-hexyl (-CH(CH₃)CH₂CH₂CH₂CH₃), 3-hexyl (-CH(CH₂CH₃)(CH₂CH₂CH₃)), 2-methyl-2-pentyl (-C(CH₃)₂CH₂CH₂CH₃), 3-methyl-2-pentyl (-CH(CH₃)CH(CH₃)CH₂CH₃), 4-methyl-2-pentyl (-CH(CH₃)CH₂CH(CH₃)₂), 3-methyl-3-pentyl (-C(CH₃)(CH₂CH₃)₂), 2-methyl-3-pentyl (-CH(CH₂CH₃)CH(CH₃)₂), 2,3-dimethyl-2-butyl (-C(CH₃)₂CH(CH₃)₂), 3,3-dimethyl-2-butyl (-CH(CH₃)C(CH₃)₃), and cyclopropylmethyl



"Alkenyl" is C₂-C₁₈ hydrocarbon containing normal, secondary, tertiary or cyclic carbon atoms with at least one site of unsaturation, i.e. a carbon-carbon, *sp*² double bond. Examples include, but are not limited to, ethylene or vinyl (-CH=CH₂), allyl (-CH₂CH=CH₂), cyclopentenyl (-C₅H₇), and 5-hexenyl (-CH₂CH₂CH₂CH₂CH=CH₂).

“Alkynyl” is C₂-C₁₈ hydrocarbon containing normal, secondary, tertiary or cyclic carbon atoms with at least one site of unsaturation, *i.e.* a carbon-carbon, *sp* triple bond. Examples include, but are not limited to, acetylenic (-C≡CH) and propargyl (-CH₂C≡CH).

“Alkylene” refers to a saturated, branched or straight chain or cyclic hydrocarbon radical of 1-18 carbon atoms, and having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of a parent alkane. Typical alkylene radicals include, but are not limited to, methylene (-CH₂-), 1,2-ethyl (-CH₂CH₂-), 1,3-propyl (-CH₂CH₂CH₂-), 1,4-butyl (-CH₂CH₂CH₂CH₂-), and the like.

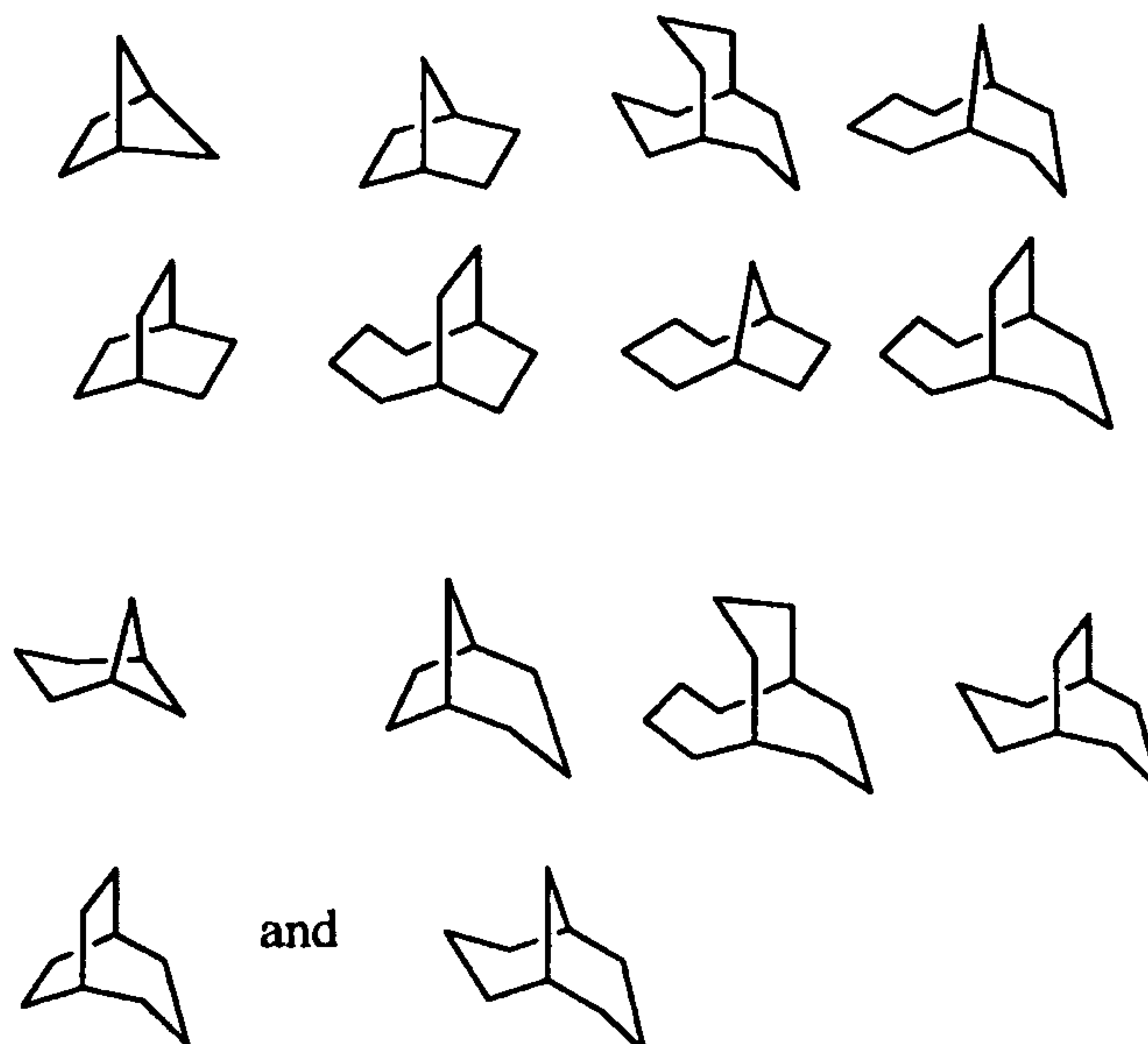
“Alkenylene” refers to an unsaturated, branched or straight chain or cyclic hydrocarbon radical of 2-18 carbon atoms, and having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of a parent alkene. Typical alkenylene radicals include, but are not limited to, 1,2-ethylene (-CH=CH-).

“Alkynylene” refers to an unsaturated, branched or straight chain or cyclic hydrocarbon radical of 2-18 carbon atoms, and having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of a parent alkyne. Typical alkynylene radicals include, but are not limited to, acetylene (-C≡C-), propargyl (-CH₂C≡C-), and 4-pentynyl (-CH₂CH₂CH₂C≡CH).

“Aryl” means a monovalent aromatic hydrocarbon radical of 6-20 carbon atoms derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Typical aryl groups include, but are not limited to, radicals derived from benzene, substituted benzene, naphthalene, anthracene, biphenyl, and the like.

“Arylalkyl” refers to an acyclic alkyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or *sp*³ carbon atom, is replaced with an aryl radical. Typical arylalkyl groups include, but are not limited to, benzyl, 2-phenylethan-1-yl, naphthylmethyl, 2-naphthylethan-1-yl, naphthobenzyl, 2-naphthophenylethan-1-yl and the like. The arylalkyl group comprises 6 to 20 carbon atoms, *e.g.*, the alkyl moiety, including alkanyl, alkenyl or alkynyl groups, of the arylalkyl group is 1 to 6 carbon atoms and the aryl moiety is 5 to 14 carbon atoms.

The term “polycarbocycle” refers to a saturated or unsaturated polycyclic ring system having from about 6 to about 25 carbon atoms and having two or more rings (*e.g.* 2, 3, 4, or 5 rings). The rings can be fused and/or bridged to form the polycyclic ring system. For example, the term includes bicyclo [4,5], [5,5], [5,6] or [6,6] ring systems, as well as the following bridged ring systems:



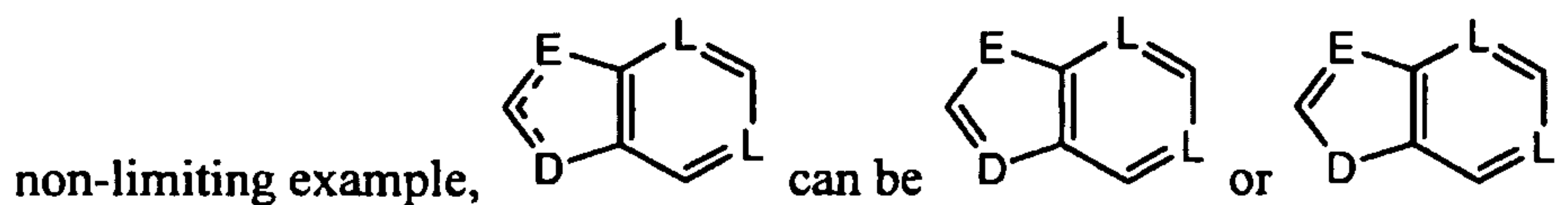
(i.e., [2.1.1], [2.2.1], [3.3.3], [4.3.1], [2.2.2], [4.2.2], [4.2.1], [4.3.2], [3.1.1], [3.2.1], [4.3.3], [3.3.2], [3.2.2] and [3.3.1] polycyclic rings, respectively) that can be linked to the remainder of the compound of formula (I) through any synthetically feasible position. Like the other polycarbocycles, these representative bicyclo and fused ring systems can optionally comprise one or more double bonds in the ring system.

The term “polyheterocycle” refers to a polycarbocycle as defined herein, wherein one or more carbon atoms is replaced with a heteroatom (e.g., O, S, S(O), S(O)₂, N⁺(O⁻)R_x, or NR_x); wherein each R_x is independently H, (C1-10)alkyl, (C2-10)alkenyl, (C2-10)alkynyl, (C1-10)alkanoyl, S(O)₂NR_nR_p, S(O)₂R_x, or (C1-10)alkoxy, wherein each (C1-10)alkyl, (C2-10)alkenyl, (C2-10)alkynyl, (C1-10)alkanoyl, and (C1-10)alkoxy is optionally substituted with one or more halo).

“Substituted alkyl”, “substituted aryl”, and “substituted arylalkyl” mean alkyl, aryl, and arylalkyl respectively, in which one or more hydrogen atoms are each independently replaced with a non-hydrogen substituent. Typical substituents include, but are not limited to: halo (e.g. F, Cl, Br, I), -R, -OR, -SR, -NR₂, -CF₃, -CCl₃, -OCF₃, -CN, -NO₂, -N(R)C(=O)R, -C(=O)R, -OC(=O)R, -C(O)OR, -C(=O)NRR, -S(=O)R, -S(=O)₂OR, -S(=O)₂R, -OS(=O)₂OR, -S(=O)₂NRR, and each R is independently -H, alkyl, aryl, arylalkyl, or heterocycle. Alkylene, alkenylene, and alkynylene groups may also be similarly substituted.

The term “optionally substituted” in reference to a particular moiety of the compound of formula I, (e.g., an optionally substituted aryl group) refers to a moiety having 0, 1, 2, or more substituents.

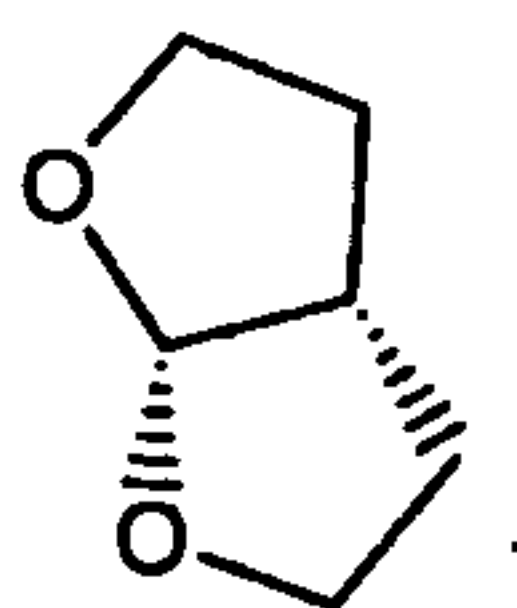
The symbol “-----” in a ring structure means that a bond is a single or double bond. In a



“Haloalkyl” as used herein includes an alkyl group substituted with one or more halogens (e.g. F, Cl, Br, or I). Representative examples of haloalkyl include trifluoromethyl, 2,2,2-trifluoroethyl, and 2,2,2-trifluoro-1-(trifluoromethyl)ethyl.

“Heterocycle” as used herein includes by way of example and not limitation these heterocycles described in Paquette, Leo A.; Principles of Modern Heterocyclic Chemistry (W.A. Benjamin, New York, 1968), particularly Chapters 1, 3, 4, 6, 7, and 9; The Chemistry of Heterocyclic Compounds, A Series of Monographs (John Wiley & Sons, New York, 1950 to present), in particular Volumes 13, 14, 16, 19, and 28; and *J. Am. Chem. Soc.* (1960) 82:5566. In one specific embodiment of the invention “heterocycle” includes a “carbocycle” as defined herein, wherein one or more (e.g. 1, 2, 3, or 4) carbon atoms have been replaced with a heteroatom (e.g. O, N, or S).

Examples of heterocycles include by way of example and not limitation pyridyl, dihydropyridyl, tetrahydropyridyl (piperidyl), thiazolyl, tetrahydrothiophenyl, sulfur oxidized tetrahydrothiophenyl, pyrimidinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, tetrazolyl, benzofuranyl, thianaphthalenyl, indolyl, indolenyl, quinolinyl, isoquinolinyl, benzimidazolyl, piperidinyl, 4-piperidonyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolinyl, tetrahydrofuranyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, octahydroisoquinolinyl, azocinyl, triazinyl, 6H-1,2,5-thiadiazinyl, 2H,6H-1,5,2-dithiazinyl, thienyl, thianthrenyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxathinyl, 2H-pyrrolyl, isothiazolyl, isoxazolyl, pyrazinyl, pyridazinyl, indolizinyl, isoindolyl, 3H-indolyl, 1H-indazolyl, purinyl, 4H-quinolizinyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, 4H-carbazolyl, carbazolyl, β -carbolinyl, phenanthridinyl, acridinyl, pyrimidinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, furazanyl, phenoxazinyl, isochromanyl, chromanyl, imidazolidinyl, imidazolynyl, pyrazolidinyl, pyrazolynyl, piperazinyl, indolynyl, isoindolynyl, quinuclidinyl, morpholynyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolynyl, isatinoyl, and bis-tetrahydrofuranyl:



By way of example and not limitation, carbon bonded heterocycles are bonded at position 2, 3, 4, 5, or 6 of a pyridine, position 3, 4, 5, or 6 of a pyridazine, position 2, 4, 5, or 6 of a pyrimidine, position 2, 3, 5, or 6 of a pyrazine, position 2, 3, 4, or 5 of a furan, tetrahydrofuran, thiofuran, thiophene, pyrrole or tetrahydropyrrole, position 2, 4, or 5 of an oxazole, imidazole or thiazole, position 3, 4, or 5 of an isoxazole, pyrazole, or isothiazole, position 2 or 3 of an aziridine, position 2, 3, or 4 of an azetidine, position 2, 3, 4, 5, 6, 7, or 8 of a quinoline or position 1, 3, 4, 5, 6, 7, or 8 of an isoquinoline. Still more typically, carbon bonded heterocycles include 2-pyridyl, 3-pyridyl, 4-pyridyl, 5-pyridyl, 6-pyridyl, 3-pyridazinyl, 4-pyridazinyl, 5-pyridazinyl, 6-pyridazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 2-pyrazinyl, 3-pyrazinyl, 5-pyrazinyl, 6-pyrazinyl, 2-thiazolyl, 4-thiazolyl, or 5-thiazolyl.

By way of example and not limitation, nitrogen bonded heterocycles are bonded at position 1 of an aziridine, azetidine, pyrrole, pyrrolidine, 2-pyrroline, 3-pyrroline, imidazole, imidazolidine, 2-imidazoline, 3-imidazoline, pyrazole, pyrazoline, 2-pyrazoline, 3-pyrazoline, piperidine, piperazine, indole, indoline, 1H-indazole, position 2 of a isoindole, or isoindoline, position 4 of a morpholine, and position 9 of a carbazole, or β -carboline. Still more typically, nitrogen bonded heterocycles include 1-aziridyl, 1-azetetyl, 1-pyrrolyl, 1-imidazolyl, 1-pyrazolyl, and 1-piperidinyl.

“Carbocycle” refers to a saturated, unsaturated or aromatic ring having up to about 25 carbon atoms. Typically, a carbocycle has about 3 to 7 carbon atoms as a monocycle, about 7 to 12 carbon atoms as a bicycle, and up to about 25 carbon atoms as a polycycle. Monocyclic carbocycles typically have 3 to 6 ring atoms, still more typically 5 or 6 ring atoms. Bicyclic carbocycles typically have 7 to 12 ring atoms, *e.g.*, arranged as a bicyclo [4,5], [5,5], [5,6] or [6,6] system, or 9 or 10 ring atoms arranged as a bicyclo [5,6] or [6,6] system. The term carbocycle includes “cycloalkyl” which is a saturated or unsaturated carbocycle. Examples of monocyclic carbocycles include cyclopropyl, cyclobutyl, cyclopentyl, 1-cyclopent-1-enyl, 1-cyclopent-2-enyl, 1-cyclopent-3-enyl, cyclohexyl, 1-cyclohex-1-enyl, 1-cyclohex-2-enyl, 1-cyclohex-3-enyl, phenyl, spiryl and naphthyl.

The term “chiral” refers to molecules which have the property of non-superimposability of the mirror image partner, while the term “achiral” refers to molecules which are superimposable on their mirror image partner.

The term “stereoisomers” refers to compounds which have identical chemical constitution, but differ with regard to the arrangement of the atoms or groups in space.

“Diastereomer” refers to a stereoisomer with two or more centers of chirality and whose molecules are not mirror images of one another. Diastereomers have different physical

properties, *e.g.*, melting points, boiling points, spectral properties, and reactivities. Mixtures of diastereomers may separate under high resolution analytical procedures such as electrophoresis and chromatography.

“Enantiomers” refer to two stereoisomers of a compound which are non-superimposable mirror images of one another.

The term “treatment” or “treating,” to the extent it relates to a disease or condition includes preventing the disease or condition from occurring, inhibiting the disease or condition, eliminating the disease or condition, and/or relieving one or more symptoms of the disease or condition.

Stereochemical definitions and conventions used herein generally follow S. P. Parker, Ed., McGraw-Hill Dictionary of Chemical Terms (1984) McGraw-Hill Book Company, New York; and Eliel, E. and Wilen, S., Stereochemistry of Organic Compounds (1994) John Wiley & Sons, Inc., New York. Many organic compounds exist in optically active forms, *i.e.*, they have the ability to rotate the plane of plane-polarized light. In describing an optically active compound, the prefixes (D and L) or (R and S) are used to denote the absolute configuration of the molecule about its chiral center(s). The prefixes d and l or (+) and (-) are employed to designate the sign of rotation of plane-polarized light by the compound, with (-) or l meaning that the compound is levorotatory. A compound prefixed with (+) or d is dextrorotatory. For a given chemical structure, these stereoisomers are identical except that they are mirror images of one another. A specific stereoisomer may also be referred to as an enantiomer, and a mixture of such isomers is often called an enantiomeric mixture. A 50:50 mixture of enantiomers is referred to as a racemic mixture or a racemate, which may occur where there has been no stereoselection or stereospecificity in a chemical reaction or process. The terms “racemic mixture” and “racemate” refer to an equimolar mixture of two enantiomeric species, devoid of optical activity. The invention includes all stereoisomers of the compounds described herein.

Specific Definitions for Groups A⁰, M⁰, W⁰, L⁰, P⁰, J⁰, T⁰, V⁰, Z⁰, E⁰, and R⁹⁰

For the groups A⁰, M⁰, W⁰, L⁰, P⁰, J⁰, T⁰, V⁰, Z⁰, E⁰, and R⁹⁰ the following definitions apply. These definitions also apply for all other A, M, W, L, P, J, T, B, V, Z, E, and R⁹ groups unless those groups are otherwise defined herein.

Unless stated otherwise, all aryl, cycloalkyl, and heterocyclyl groups of the present disclosure may be substituted as described in each of their respective definitions. For example, the aryl part of an arylalkyl group may be substituted as described in the definition of the term 'aryl'.

The term "alkenyl," as used herein, refers to a straight or branched chain group of two to six carbon atoms containing at least one carbon-carbon double bond.

The term "alkenyloxy," as used herein, refers to an alkenyl group attached to the parent molecular moiety through an oxygen atom.

The term "alkenyloxycarbonyl," as used herein, refers to an alkenyloxy group attached to the parent molecular moiety through a carbonyl group.

The term "alkoxy," as used herein, refers to an alkyl group attached to the parent molecular moiety through an oxygen atom.

The term "alkoxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three alkoxy groups.

The term "alkoxyalkylcarbonyl," as used herein, refers to an alkoxyalkyl group attached to the parent molecular moiety through a carbonyl group.

The term "alkoxycarbonyl," as used herein, refers to an alkoxy group attached to the parent molecular moiety through a carbonyl group.

The term "alkoxycarbonylalkyl," as used herein, refers to an alkyl group substituted with one, two, or three alkoxycarbonyl groups.

The term "alkyl," as used herein, refers to a group derived from a straight or branched chain saturated hydrocarbon containing from one to six carbon atoms.

The term "alkylcarbonyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a carbonyl group.

The term "alkylcarbonylalkyl," as used herein, refers to an alkyl group substituted with one, two, or three alkylcarbonyl groups.

The term "alkylcarbonyloxy," as used herein, refers to an alkylcarbonyl group attached to the parent molecular moiety through an oxygen atom.

The term "alkylsulfanyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a sulfur atom.

The term "alkylsulfonyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a sulfonyl group.

The term "aryl," as used herein, refers to a phenyl group, or a bicyclic fused ring system wherein one or both of the rings is a phenyl group. Bicyclic fused ring systems consist of a phenyl group fused to a four- to six-membered aromatic or non-aromatic carbocyclic ring. The aryl groups of the present disclosure can be attached to the parent molecular moiety through any substitutable carbon atom in the group. Representative examples of aryl groups include, but are not limited to, indanyl, indenyl, naphthyl, phenyl, and tetrahydronaphthyl. The aryl groups of the present disclosure are optionally substituted with one, two, three, four, or five substituents

independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, a second aryl group, arylalkoxy, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyl carbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the aryl carbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclyl carbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro.

The term "arylalkenyl," as used herein, refers to an alkenyl group substituted with one, two, or three aryl groups.

The term "arylalkoxy," as used herein, refers to an aryl group attached to the parent molecular moiety through an alkoxy group.

The term "arylalkoxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three arylalkoxy groups.

The term "arylalkoxyalkyl carbonyl," as used herein, refers to an arylalkoxyalkyl group attached to the parent molecular moiety through a carbonyl group.

The term "arylalkoxycarbonyl," as used herein, refers to an arylalkoxy group attached to the parent molecular moiety through a carbonyl group.

The term "arylalkyl," as used herein, refers to an alkyl group substituted with one, two, or three aryl groups. The alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyl carbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy, and $-NR^c R^d$, wherein the heterocyclyl is further optionally substituted with one or two substituents independently selected from alkoxy, alkyl, unsubstituted aryl, unsubstituted arylalkoxy, unsubstituted arylalkoxycarbonyl, halo, haloalkoxy, haloalkyl, hydroxy, and $-NR^X R^Y$;

The term "arylalkyl carbonyl," as used herein, refers to an arylalkyl group attached to the parent molecular moiety through a carbonyl group.

The term "aryl carbonyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a carbonyl group.

The term "aryloxy," as used herein, refers to an aryl group attached to the parent molecular moiety through an oxygen atom.

The term "aryloxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three aryloxy groups.

The term "aryloxycarbonyl," as used herein, refers to an aryloxy group attached to the parent molecular moiety through a carbonyl group.

The term "arylsulfanyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a sulfur atom.

The term "arylsulfonyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a sulfonyl group.

The terms "Cap" and "cap" as used herein, refer to the group which is placed on the nitrogen atom of the terminal nitrogen-containing ring. It should be understood that "Cap" or "cap" can refer to the reagent used to append the group to the terminal nitrogen-containing ring or to the fragment in the final product.

The term "carbonyl," as used herein, refers to $-C(=O)-$.

The term "carboxy," as used herein, refers to $-CO_2H$.

The term "cyano," as used herein, refers to $-CN$.

The term "cyanoalkyl" as used herein, refers to an alkyl group having at least one $-CN$ substituent.

The term "cycloalkyl," as used herein, refers to a saturated monocyclic, hydrocarbon ring system having three to seven carbon atoms and zero heteroatoms. Representative examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclopentyl, and cyclohexyl. The cycloalkyl groups of the present disclosure are optionally substituted with one, two, three, four, or five substituents independently selected from alkoxy, alkyl, aryl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy, hydroxyalkyl, nitro, and $-NR^xR^y$ wherein the aryl and the heterocyclyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, hydroxy, and nitro.

The term "(cycloalkyl)alkenyl," as used herein, refers to an alkenyl group substituted with one, two, or three cycloalkyl groups.

The term "(cycloalkyl)alkyl," as used herein, refers to an alkyl group substituted with one, two, or three cycloalkyl groups. The alkyl part of the (cycloalkyl)alkyl is further optionally substituted with one or two groups independently selected from hydroxy and $-NR^cR^d$.

The term "cycloalkyloxy," as used herein, refers to a cycloalkyl group attached to the parent molecular moiety through an oxygen atom.

The term "cycloalkyloxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three cycloalkyloxy groups.

The term "cycloalkylsulfonyl," as used herein, refers to a cycloalkyl group attached to the parent molecular moiety through a sulfonyl group.

The term "formyl," as used herein, refers to -CHO.

The terms "halo" and "halogen," as used herein, refer to F, Cl, Br, or I.

The term "haloalkoxy," as used herein, refers to a haloalkyl group attached to the parent molecular moiety through an oxygen atom.

The term "haloalkoxycarbonyl," as used herein, refers to a haloalkoxy group attached to the parent molecular moiety through a carbonyl group.

The term "haloalkyl," as used herein, refers to an alkyl group substituted by one, two, three, or four halogen atoms.

The term "haloalkylsulfanyl," as used herein, refers to a haloalkyl group attached to the parent molecular moiety through a sulfur atom.

The term "heterocyclyl," as used herein, refers to a four-, five-, six-, or seven-membered ring containing one, two, three, or four heteroatoms independently selected from nitrogen, oxygen, and sulfur. The four-membered ring has zero double bonds, the five-membered ring has zero to two double bonds, and the six- and seven-membered rings have zero to three double bonds. The term "heterocyclyl" also includes bicyclic groups in which the heterocyclyl ring is fused to another monocyclic heterocyclyl group, or a four- to six-membered aromatic or non-aromatic carbocyclic ring; as well as bridged bicyclic groups such as 7-azabicyclo[2.2.1]hept-7-yl, 2-azabicyclo[2.2.2]oc-2-tyl, and 2-azabicyclo[2.2.2]oc-3-tyl. The heterocyclyl groups of the present disclosure can be attached to the parent molecular moiety through any carbon atom or nitrogen atom in the group. Examples of heterocyclyl groups include, but are not limited to, benzothienyl, furyl, imidazolyl, indolinyl, indolyl, isothiazolyl, isoxazolyl, morpholinyl, oxazolyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrrolidinyl, pyrrolopyridinyl, pyrrolyl, thiazolyl, thienyl, thiomorpholinyl, 7-azabicyclo[2.2.1]hept-7-yl, 2-azabicyclo[2.2.2]oc-2-tyl, and 2-azabicyclo[2.2.2]oc-3-tyl. The heterocyclyl groups of the present disclosure are optionally substituted with one, two, three, four, or five substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aryl, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclyl carbonyl, hydroxy, hydroxyalkyl, nitro, -NR^XR^Y, -(NR^XR^Y)alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl, the aryl part of the aryl carbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclyl carbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro.

The term "heterocyclalkenyl," as used herein, refers to an alkenyl group substituted with one, two, or three heterocycl groups.

The term "heterocyclalkoxy," as used herein, refers to a heterocycl group attached to the parent molecular moiety through an alkoxy group.

The term "heterocyclalkoxycarbonyl," as used herein, refers to a heterocyclalkoxy group attached to the parent molecular moiety through a carbonyl group.

The term "heterocyclalkyl," as used herein, refers to an alkyl group substituted with one, two, or three heterocycl groups. The alkyl part of the heterocyclalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylcarbonyloxy, aryl, halo, haloalkoxy, haloalkyl, hydroxy, and $-NR^cR^d$, wherein the aryl is further optionally substituted with one or two substituents independently selected from alkoxy, alkyl, unsubstituted aryl, unsubstituted arylalkoxy, unsubstituted arylalkoxycarbonyl, halo, haloalkoxy, haloalkyl, hydroxy, and $-NR^xR^y$.

The term "heterocyclalkylcarbonyl," as used herein, refers to a heterocyclalkyl group attached to the parent molecular moiety through a carbonyl group.

The term "heterocyclcarbonyl," as used herein, refers to a heterocycl group attached to the parent molecular moiety through a carbonyl group.

The term "heterocycloxy," as used herein, refers to a heterocycl group attached to the parent molecular moiety through an oxygen atom.

The term "heterocycloxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three heterocycloxy groups.

The term "heterocycloxy carbonyl," as used herein, refers to a heterocycloxy group attached to the parent molecular moiety through a carbonyl group.

The term "hydroxy," as used herein, refers to $-OH$.

The term "hydroxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three hydroxy groups.

The term "hydroxyalkylcarbonyl," as used herein, refers to a hydroxyalkyl group attached to the parent molecular moiety through a carbonyl group.

The term "nitro," as used herein, refers to $-NO_2$.

The term " $-NR^aR^b$," as used herein, refers to two groups, R^a and R^b , which are attached to the parent molecular moiety through a nitrogen atom. R^a and R^b are independently selected from hydrogen, alkenyl, and alkyl.

The term " (NR^aR^b) alkyl," as used herein, refers to an alkyl group substituted with one, two, or three $-NR^aR^b$ groups.

The term " (NR^aR^b) carbonyl," as used herein, refers to an $-NR^aR^b$ group attached to the parent molecular moiety through a carbonyl group.

The term " $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$," as used herein, refers to two groups, R^{c} and R^{d} , which are attached to the parent molecular moiety through a nitrogen atom. R^{c} and R^{d} are independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, $(\text{NR}^{\text{e}}\text{R}^{\text{f}})\text{alkyl}$, $(\text{NR}^{\text{e}}\text{R}^{\text{f}})\text{alkylcarbonyl}$, $(\text{NR}^{\text{e}}\text{R}^{\text{f}})\text{carbonyl}$, $(\text{NR}^{\text{e}}\text{R}^{\text{f}})\text{sulfonyl}$, $-\text{C}(\text{NCN})\text{OR}'$, and $-\text{C}(\text{NCN})\text{NR}^{\text{x}}\text{R}^{\text{y}}$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-\text{NR}^{\text{e}}\text{R}^{\text{f}}$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro.

The term " $(\text{NR}^{\text{c}}\text{R}^{\text{d}})\text{alkenyl}$," as used herein, refers to an alkenyl group substituted with one, two, or three $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$ groups.

The term " $(\text{NR}^{\text{c}}\text{R}^{\text{d}})\text{alkyl}$," as used herein, refers to an alkyl group substituted with one, two, or three $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$ groups. The alkyl part of the $(\text{NR}^{\text{c}}\text{R}^{\text{d}})\text{alkyl}$ is further optionally substituted with one or two additional groups selected from alkoxy, alkoxyalkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, arylalkoxyalkylcarbonyl, carboxy, heterocyclyl, heterocyclylcarbonyl, hydroxy, and $(\text{NR}^{\text{e}}\text{R}^{\text{f}})\text{carbonyl}$; wherein the heterocyclyl is further optionally substituted with one, two, three, four, or five substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro.

The term " $(\text{NR}^{\text{c}}\text{R}^{\text{d}})\text{carbonyl}$," as used herein, refers to an $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$ group attached to the parent molecular moiety through a carbonyl group.

The term " $-\text{NR}^{\text{e}}\text{R}^{\text{f}}$," as used herein, refers to two groups, R^{e} and R^{f} , which are attached to the parent molecular moiety through a nitrogen atom. R^{e} and R^{f} are independently selected from hydrogen, alkyl, unsubstituted aryl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted (cycloalkyl)alkyl, unsubstituted heterocyclyl, unsubstituted heterocyclylalkyl, $(\text{NR}^{\text{x}}\text{R}^{\text{y}})\text{alkyl}$, and $(\text{NR}^{\text{x}}\text{R}^{\text{y}})\text{carbonyl}$.

The term "(NR^eR^f)alkyl," as used herein, refers to an alkyl group substituted with one, two, or three -NR^eR^f groups.

The term "(NR^eR^f)alkylcarbonyl," as used herein, refers to an (NR^eR^f)alkyl group attached to the parent molecular moiety through a carbonyl group.

The term "(NR^eR^f)carbonyl," as used herein, refers to an -NR^eR^f group attached to the parent molecular moiety through a carbonyl group.

The term "(NR^eR^f)sulfonyl," as used herein, refers to an -NR^eR^f group attached to the parent molecular moiety through a sulfonyl group.

The term "-NR^xR^y," as used herein, refers to two groups, R^x and R^y, which are attached to the parent molecular moiety through a nitrogen atom. R^x and R^y are independently selected from hydrogen, alkoxy carbonyl, alkyl, alkylcarbonyl, unsubstituted aryl, unsubstituted arylalkoxy carbonyl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted heterocyclyl, and (NR^xR^y)carbonyl, wherein R^x and R^y are independently selected from hydrogen and alkyl.

The term "(NR^xR^y)alkyl," as used herein, refers to an alkyl group substituted with one, two, or three -NR^xR^y groups.

The term "oxo," as used herein, refers to =O.

The term "sulfonyl," as used herein, refers to -SO₂-.

The term "trialkylsilyl," as used herein, refers to -SiR₃, wherein R is alkyl. The R groups may be the same or different

The term "trialkylsilylalkyl," as used herein, refers to an alkyl group substituted with one, two, or three trialkylsilyl groups.

The term "trialkylsilylalkoxy," as used herein, refers to a trialkylsilylalkyl group attached to the parent molecular moiety through an oxygen atom.

The term "trialkylsilylalkoxyalkyl," as used herein, refers to an alkyl group substituted with one, two, or three trialkylsilylalkoxy groups.

Prodrugs

The term "prodrug" as used herein refers to any compound that when administered to a biological system generates a compound of the invention that inhibits HCV activity ("the active inhibitory compound"). The compound may be formed from the prodrug as a result of: (i) spontaneous chemical reaction(s), (ii) enzyme catalyzed chemical reaction(s), (iii) photolysis, and/or (iv) metabolic chemical reaction(s).

"Prodrug moiety" refers to a labile functional group which separates from the active inhibitory compound during metabolism, systemically, inside a cell, by hydrolysis, enzymatic

cleavage, or by some other process (Bundgaard, Hans, "Design and Application of Prodrugs" in A Textbook of Drug Design and Development (1991), P. Krosgaard-Larsen and H. Bundgaard, Eds. Harwood Academic Publishers, pp. 113-191). Enzymes which are capable of an enzymatic activation mechanism with the prodrug compounds of the invention include, but are not limited to, amidases, esterases, microbial enzymes, phospholipases, cholinesterases, and phosphatases. Prodrug moieties can serve to enhance solubility, absorption and lipophilicity to optimize drug delivery, bioavailability and efficacy. A prodrug moiety may include an active metabolite or drug itself.

Exemplary prodrug moieties include the hydrolytically sensitive or labile acyloxymethyl esters $-\text{CH}_2\text{OC}(=\text{O})\text{R}^{99}$ and acyloxymethyl carbonates $-\text{CH}_2\text{OC}(=\text{O})\text{OR}^{99}$ where R^{99} is C_1-C_6 alkyl, C_1-C_6 substituted alkyl, C_6-C_{20} aryl or C_6-C_{20} substituted aryl. The acyloxyalkyl ester was first used as a prodrug strategy for carboxylic acids and then applied to phosphates and phosphonates by Farquhar et al. (1983) *J. Pharm. Sci.* 72: 324; also US Patent Nos. 4816570, 4968788, 5663159 and 5792756. Subsequently, the acyloxyalkyl ester was used to deliver phosphonic acids across cell membranes and to enhance oral bioavailability. A close variant of the acyloxyalkyl ester, the alkoxycarbonyloxyalkyl ester (carbonate), may also enhance oral bioavailability as a prodrug moiety in the compounds of the combinations of the invention. An exemplary acyloxymethyl ester is pivaloyloxymethoxy, (POM) $-\text{CH}_2\text{OC}(=\text{O})\text{C}(\text{CH}_3)_3$. An exemplary acyloxymethyl carbonate prodrug moiety is pivaloyloxymethylcarbonate (POC) $-\text{CH}_2\text{OC}(=\text{O})\text{OC}(\text{CH}_3)_3$.

Aryl esters of phosphorus groups, especially phenyl esters, are reported to enhance oral bioavailability (De Lombaert et al. (1994) *J. Med. Chem.* 37: 498). Phenyl esters containing a carboxylic ester ortho to a phosphate have also been described (Khamnei and Torrence, (1996) *J. Med. Chem.* 39:4109-4115). Benzyl esters are reported to generate parent phosphonic acids. In some cases, substituents at the *ortho*- or *para*- position may accelerate the hydrolysis. Benzyl analogs with an acylated phenol or an alkylated phenol may generate the phenolic compound through the action of enzymes, *e.g.*, esterases, oxidases, etc., which in turn undergoes cleavage at the benzylic C-O bond to generate phosphoric acid and a quinone methide intermediate. Examples of this class of prodrugs are described by Mitchell et al. (1992) *J. Chem. Soc. Perkin Trans. II* 2345; Glazier WO 91/19721. Still other benzylic prodrugs have been described containing a carboxylic ester-containing group attached to the benzylic methylene (Glazier WO 91/19721). Thio-containing prodrugs are reported to be useful for the intracellular delivery of phosphonate drugs. These proesters contain an ethylthio group in which the thiol group is either esterified with an acyl group or combined with another thiol group to form a disulfide. Deesterification or reduction of the disulfide generates the free thio intermediate

which subsequently breaks down to the phosphoric acid and episulfide (Puech et al. (1993) *Antiviral Res.*, 22: 155-174; Benzaria et al. (1996) *J. Med. Chem.* 39: 4958).

Protecting Groups

In the context of the present invention, protecting groups include prodrug moieties and chemical protecting groups.

“Protecting group” refers to a moiety of a compound that masks or alters the properties of a functional group or the properties of the compound as a whole. Chemical protecting groups and strategies for protection/deprotection are well known in the art. *See e.g.*, Protective Groups in Organic Chemistry, Theodora W. Greene, John Wiley & Sons, Inc., New York, 1991.

Protecting groups are often utilized to mask the reactivity of certain functional groups, to assist in the efficiency of desired chemical reactions, *e.g.*, making and breaking chemical bonds in an ordered and planned fashion. Protection of functional groups of a compound alters other physical properties besides the reactivity of the protected functional group, such as the polarity, lipophilicity (hydrophobicity), and other properties which can be measured by common analytical tools. Chemically protected intermediates may themselves be biologically active or inactive.

Protected compounds may also exhibit altered, and in some cases, optimized properties *in vitro* and *in vivo*, such as passage through cellular membranes and resistance to enzymatic degradation or sequestration. In this role, protected compounds with intended therapeutic effects may be referred to as prodrugs. Another function of a protecting group is to convert the parental drug into a prodrug, whereby the parental drug is released upon conversion of the prodrug *in vivo*. Because active prodrugs may be absorbed more effectively than the parental drug, prodrugs may possess greater potency *in vivo* than the parental drug. Protecting groups are removed either *in vitro*, in the instance of chemical intermediates, or *in vivo*, in the case of prodrugs. With chemical intermediates, it is not particularly important that the resulting products after deprotection, *e.g.*, alcohols, be physiologically acceptable, although in general it is more desirable if the products are pharmacologically innocuous.

Protecting groups are available, commonly known and used, and are optionally used to prevent side reactions with the protected group during synthetic procedures, *i.e.* routes or methods to prepare the compounds of the invention. For the most part the decision as to which groups to protect, when to do so, and the nature of the chemical protecting group “PG” will be dependent upon the chemistry of the reaction to be protected against (*e.g.*, acidic, basic, oxidative, reductive or other conditions) and the intended direction of the synthesis. PGs do not need to be, and generally are not, the same if the compound is substituted with multiple PG. In

general, PG will be used to protect functional groups such as carboxyl, hydroxyl, thio, or amino groups and to thus prevent side reactions or to otherwise facilitate the synthetic efficiency. The order of deprotection to yield free deprotected groups is dependent upon the intended direction of the synthesis and the reaction conditions to be encountered, and may occur in any order as determined by the artisan.

Various functional groups of the compounds of the invention may be protected. For example, protecting groups for –OH groups (whether hydroxyl, carboxylic acid, phosphonic acid, or other functions) include “ether- or ester-forming groups”. Ether- or ester-forming groups are capable of functioning as chemical protecting groups in the synthetic schemes set forth herein. However, some hydroxyl and thio protecting groups are neither ether- nor ester-forming groups, as will be understood by those skilled in the art, and are included with amides, discussed below.

A very large number of hydroxyl protecting groups and amide-forming groups and corresponding chemical cleavage reactions are described in Protective Groups in Organic Synthesis, Theodora W. Greene (John Wiley & Sons, Inc., New York, 1991, ISBN 0-471-62301-6) (“Greene”). See also Kocienski, Philip J.; Protecting Groups (Georg Thieme Verlag Stuttgart, New York, 1994), which can be referred to. In particular Chapter 1, Protecting Groups: An Overview, pages 1-20, Chapter 2, Hydroxyl Protecting Groups, pages 21-94, Chapter 3, Diol Protecting Groups, pages 95-117, Chapter 4, Carboxyl Protecting Groups, pages 118-154, Chapter 5, Carbonyl Protecting Groups, pages 155-184. For protecting groups for carboxylic acid, phosphonic acid, phosphonate, sulfonic acid and other protecting groups for acids see Greene as set forth below.

By way of example and not limitation, R^1 , R^3 , R^{A1} , R^{A3} , and X^A are recursive substituents in certain embodiments. Typically, each of these may independently occur 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0, times in a given embodiment. More typically, each of these may independently occur 12 or fewer times in a given embodiment. Whenever a compound described herein is substituted with more than one of the same designated group, e.g., “ R^1 ” or “ R^3 ”, then it will be understood that the groups may be the same or different, i.e., each group is independently selected. Wavy lines indicate the site of covalent bond attachments to the adjoining groups, moieties, or atoms.

In one embodiment of the invention, the compound is in an isolated and purified form. Generally, the term “isolated and purified” means that the compound is substantially free from biological materials (e.g. blood, tissue, cells, etc.). In one specific embodiment of the invention, the term means that the compound or conjugate of the invention is at least about 50 wt.% free from biological materials; in another specific embodiment, the term means that the compound or

conjugate of the invention is at least about 75 wt.% free from biological materials; in another specific embodiment, the term means that the compound or conjugate of the invention is at least about 90 wt.% free from biological materials; in another specific embodiment, the term means that the compound or conjugate of the invention is at least about 98 wt.% free from biological materials; and in another embodiment, the term means that the compound or conjugate of the invention is at least about 99 wt.% free from biological materials. In another specific embodiment, the invention provides a compound or conjugate of the invention that has been synthetically prepared (e.g., *ex vivo*).

Stereoisomers

The compounds of the invention may have chiral centers, e.g., chiral carbon or phosphorus atoms. The compounds of the invention thus include racemic mixtures of all stereoisomers, including enantiomers, diastereomers, and atropisomers. In addition, the compounds of the invention include enriched or resolved optical isomers at any or all asymmetric, chiral atoms. In other words, the chiral centers apparent from the depictions are provided as the chiral isomers or racemic mixtures. Both racemic and diastereomeric mixtures, as well as the individual optical isomers isolated or synthesized, substantially free of their enantiomeric or diastereomeric partners, are all within the scope of the invention. The racemic mixtures are separated into their individual, substantially optically pure isomers through well-known techniques such as, for example, the separation of diastereomeric salts formed with optically active adjuncts, e.g., acids or bases followed by conversion back to the optically active substances. In most instances, the desired optical isomer is synthesized by means of stereospecific reactions, beginning with the appropriate stereoisomer of the desired starting material.

The compounds of the invention can also exist as tautomeric isomers in certain cases. Although only one delocalized resonance structure may be depicted, all such forms are contemplated within the scope of the invention. For example, ene-amine tautomers can exist for purine, pyrimidine, imidazole, guanidine, amidine, and tetrazole systems and all their possible tautomeric forms are within the scope of the invention.

Salts and Hydrates

Examples of physiologically acceptable salts of the compounds of the invention include salts derived from an appropriate base, such as an alkali metal (for example, sodium), an alkaline earth metal (for example, magnesium), ammonium and NX_4^+ (wherein X is $\text{C}_1\text{-C}_4$ alkyl). Physiologically acceptable salts of a hydrogen atom or an amino group include salts of organic carboxylic acids such as acetic, benzoic, lactic, fumaric, tartaric, maleic, malonic, malic,

isethionic, lactobionic and succinic acids; organic sulfonic acids, such as methanesulfonic, ethanesulfonic, benzenesulfonic and p-toluenesulfonic acids; and inorganic acids, such as hydrochloric, sulfuric, phosphoric and sulfamic acids. Physiologically acceptable salts of a compound of a hydroxy group include the anion of said compound in combination with a suitable cation such as Na^+ and NX_4^+ (wherein X is independently selected from H or a $\text{C}_1\text{-C}_4$ alkyl group).

For therapeutic use, salts of active ingredients of the compounds of the invention will typically be physiologically acceptable, *i.e.* they will be salts derived from a physiologically acceptable acid or base. However, salts of acids or bases which are not physiologically acceptable may also find use, for example, in the preparation or purification of a physiologically acceptable compound. All salts, whether or not derived from a physiologically acceptable acid or base, are within the scope of the present invention.

Metal salts typically are prepared by reacting the metal hydroxide with a compound of this invention. Examples of metal salts which are prepared in this way are salts containing Li^+ , Na^+ , and K^+ . A less soluble metal salt can be precipitated from the solution of a more soluble salt by addition of the suitable metal compound.

In addition, salts may be formed from acid addition of certain organic and inorganic acids, *e.g.*, HCl, HBr, H_2SO_4 , H_3PO_4 or organic sulfonic acids, to basic centers, typically amines, or to acidic groups. Finally, it is to be understood that the compositions herein comprise compounds of the invention in their un-ionized, as well as zwitterionic form, and combinations with stoichiometric amounts of water as in hydrates.

Also included within the scope of this invention are the salts of the parental compounds with one or more amino acids. Any of the natural or unnatural amino acids are suitable, especially the naturally-occurring amino acids found as protein components, although the amino acid typically is one bearing a side chain with a basic or acidic group, *e.g.*, lysine, arginine or glutamic acid, or a neutral group such as glycine, serine, threonine, alanine, isoleucine, or leucine.

Methods of Inhibition of HCV

Another aspect of the invention relates to methods of inhibiting the activity of HCV comprising the step of treating a sample suspected of containing HCV with a compound or composition of the invention.

Compounds of the invention may act as inhibitors of HCV, as intermediates for such inhibitors or have other utilities as described below. The inhibitors will generally bind to locations on the surface or in a cavity of the liver. Compounds binding in the liver may bind

with varying degrees of reversibility. Those compounds binding substantially irreversibly are ideal candidates for use in this method of the invention. Once labeled, the substantially irreversibly binding compounds are useful as probes for the detection of HCV. Accordingly, the invention relates to methods of detecting NS3 in a sample suspected of containing HCV comprising the steps of: treating a sample suspected of containing HCV with a composition comprising a compound of the invention bound to a label; and observing the effect of the sample on the activity of the label. Suitable labels are well known in the diagnostics field and include stable free radicals, fluorophores, radioisotopes, enzymes, chemiluminescent groups and chromogens. The compounds herein are labeled in conventional fashion using functional groups such as hydroxyl or amino. In one embodiment the invention provides a compound of formula (I) that comprises or that is bound or linked to one or more detectable labels. Within the context of the invention samples suspected of containing HCV include natural or man-made materials such as living organisms; tissue or cell cultures; biological samples such as biological material samples (blood, serum, urine, cerebrospinal fluid, tears, sputum, saliva, tissue samples, and the like); laboratory samples; food, water, or air samples; bioproduct samples such as extracts of cells, particularly recombinant cells synthesizing a desired glycoprotein; and the like. Typically the sample will be suspected of containing HCV. Samples can be contained in any medium including water and organic solvent/water mixtures. Samples include living organisms such as humans, and man made materials such as cell cultures.

The treating step of the invention comprises adding the compound of the invention to the sample or it comprises adding a precursor of the composition to the sample. The addition step comprises any method of administration as described above.

If desired, the activity of HCV after application of the compound can be observed by any method including direct and indirect methods of detecting HCV activity. Quantitative, qualitative, and semiquantitative methods of determining HCV activity are all contemplated. Typically one of the screening methods described above are applied, however, any other method such as observation of the physiological properties of a living organism are also applicable.

Many organisms contain HCV. The compounds of this invention are useful in the treatment or prophylaxis of conditions associated with HCV activation in animals or in man.

However, in screening compounds capable of inhibiting HCV activity it should be kept in mind that the results of enzyme assays may not always correlate with cell culture assays. Thus, a cell based assay should typically be the primary screening tool.

Pharmaceutical Formulations

The compounds of this invention are formulated with conventional carriers and

excipients, which will be selected in accord with ordinary practice. Tablets will contain excipients, glidants, fillers, binders and the like. Aqueous formulations are prepared in sterile form, and when intended for delivery by other than oral administration generally will be isotonic. All formulations will optionally contain excipients such as those set forth in the Handbook of Pharmaceutical Excipients (1986). Excipients include ascorbic acid and other antioxidants, chelating agents such as EDTA, carbohydrates such as dextrin, hydroxyalkylcellulose, hydroxyalkylmethylcellulose, stearic acid and the like. The pH of the formulations ranges from about 3 to about 11, but is ordinarily about 7 to 10.

While it is possible for the active ingredients to be administered alone it may be preferable to present them as pharmaceutical formulations. The formulations, both for veterinary and for human use, of the invention comprise at least one active ingredient, as above defined, together with one or more acceptable carriers therefor and optionally other therapeutic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and physiologically innocuous to the recipient thereof.

The formulations include those suitable for the foregoing administration routes. The formulations may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. Techniques and formulations generally are found in Remington's Pharmaceutical Sciences (Mack Publishing Co., Easton, PA). Such methods include the step of bringing into association the active ingredient with the carrier which constitutes one or more accessory ingredients. In general the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

Formulations of the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution or a suspension in an aqueous or non-aqueous liquid; or as an oil-in-water liquid emulsion or a water-in-oil liquid emulsion. The active ingredient may also be administered as a bolus, electuary or paste.

A tablet is made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as a powder or granules, optionally mixed with a binder, lubricant, inert diluent, preservative, surface active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered active ingredient moistened with an inert liquid diluent. The tablets may optionally be coated or scored and optionally are formulated so as to provide slow or controlled release of the active ingredient therefrom.

For administration to the eye or other external tissues *e.g.*, mouth and skin, the formulations are preferably applied as a topical ointment or cream containing the active ingredient(s) in an amount of, for example, 0.075 to 20% w/w (including active ingredient(s) in a range between 0.1% and 20% in increments of 0.1% w/w such as 0.6% w/w, 0.7% w/w, etc.), preferably 0.2 to 15% w/w and most preferably 0.5 to 10% w/w. When formulated in an ointment, the active ingredients may be employed with either a paraffinic or a water-miscible ointment base. Alternatively, the active ingredients may be formulated in a cream with an oil-in-water cream base.

If desired, the aqueous phase of the cream base may include, for example, at least 30% w/w of a polyhydric alcohol, *i.e.* an alcohol having two or more hydroxyl groups such as propylene glycol, butane 1,3-diol, mannitol, sorbitol, glycerol and polyethylene glycol (including PEG 400) and mixtures thereof. The topical formulations may desirably include a compound which enhances absorption or penetration of the active ingredient through the skin or other affected areas. Examples of such dermal penetration enhancers include dimethyl sulphoxide and related analogs.

The oily phase of the emulsions of this invention may be constituted from known ingredients in a known manner. While the phase may comprise merely an emulsifier (otherwise known as an emulgent), it desirably comprises a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier which acts as a stabilizer. It is also preferred to include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base which forms the oily dispersed phase of the cream formulations.

Emulgents and emulsion stabilizers suitable for use in the formulation of the invention include Tween[®] 60, Span[®] 80, cetostearyl alcohol, benzyl alcohol, myristyl alcohol, glyceryl mono-stearate and sodium lauryl sulfate.

The choice of suitable oils or fats for the formulation is based on achieving the desired cosmetic properties. The cream should preferably be a non-greasy, non-staining and washable product with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters known as Crodamol CAP may be used, the last three being preferred esters. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils are used.

Pharmaceutical formulations according to the present invention comprise one or more compounds of the invention together with one or more pharmaceutically acceptable carriers or excipients and optionally other therapeutic agents. Pharmaceutical formulations containing the active ingredient may be in any form suitable for the intended method of administration. When used for oral use for example, tablets, troches, lozenges, aqueous or oil suspensions, dispersible powders or granules, emulsions, hard or soft capsules, syrups or elixirs may be prepared. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents including sweetening agents, flavoring agents, coloring agents and preserving agents, in order to provide a palatable preparation. Tablets containing the active ingredient in admixture with non-toxic pharmaceutically acceptable excipient which are suitable for manufacture of tablets are acceptable. These excipients may be, for example, inert diluents, such as calcium or sodium carbonate, lactose, lactose monohydrate, croscarmellose sodium, povidone, calcium or sodium phosphate; granulating and disintegrating agents, such as maize starch, or alginic acid; binding agents, such as cellulose, microcrystalline cellulose, starch, gelatin or acacia; and lubricating agents, such as magnesium stearate, stearic acid or talc. Tablets may be uncoated or may be coated by known techniques including microencapsulation to delay disintegration and adsorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate alone or with a wax may be employed.

Formulations for oral use may be also presented as hard gelatin capsules where the active ingredient is mixed with an inert solid diluent, for example calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, such as peanut oil, liquid paraffin or olive oil.

Aqueous suspensions of the invention contain the active materials in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients include a suspending agent, such as sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia, and dispersing or wetting agents such as a naturally occurring phosphatide (*e.g.*, lecithin), a condensation product of an alkylene oxide with a fatty acid (*e.g.*, polyoxyethylene stearate), a condensation product of ethylene oxide with a long chain aliphatic alcohol (*e.g.*, heptadecaethyleneoxycetanol), a condensation product of ethylene oxide with a partial ester derived from a fatty acid and a hexitol anhydride (*e.g.*, polyoxyethylene sorbitan monooleate). The aqueous suspension may also contain one or more preservatives such as ethyl or n-propyl p-

hydroxy-benzoate, one or more coloring agents, one or more flavoring agents and one or more sweetening agents, such as sucrose or saccharin.

Oil suspensions may be formulated by suspending the active ingredient in a vegetable oil, such as arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oral suspensions may contain a thickening agent, such as beeswax, hard paraffin or cetyl alcohol. Sweetening agents, such as those set forth above, and flavoring agents may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an antioxidant such as ascorbic acid.

Dispersible powders and granules of the invention suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, a suspending agent, and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those disclosed above. Additional excipients, for example sweetening, flavoring and coloring agents, may also be present.

The pharmaceutical compositions of the invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, such as olive oil or arachis oil, a mineral oil, such as liquid paraffin, or a mixture of these. Suitable emulsifying agents include naturally-occurring gums, such as gum acacia and gum tragacanth, naturally occurring phosphatides, such as soybean lecithin, esters or partial esters derived from fatty acids and hexitol anhydrides, such as sorbitan monooleate, and condensation products of these partial esters with ethylene oxide, such as polyoxyethylene sorbitan monooleate. The emulsion may also contain sweetening and flavoring agents. Syrups and elixirs may be formulated with sweetening agents, such as glycerol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, a flavoring or a coloring agent.

The pharmaceutical compositions of the invention may be in the form of a sterile injectable preparation, such as a sterile injectable aqueous or oleaginous suspension. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, such as a solution in 1,3-butane-diol or prepared as a lyophilized powder. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile fixed oils may conventionally be employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid may likewise be used in the preparation of injectables.

The amount of active ingredient that may be combined with the carrier material to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. For example, a time-release formulation intended for oral administration to humans may contain approximately 1 to 1000 mg of active material compounded with an appropriate and convenient amount of carrier material which may vary from about 5 to about 95% of the total compositions (weight:weight). The pharmaceutical composition can be prepared to provide easily measurable amounts for administration. For example, an aqueous solution intended for intravenous infusion may contain from about 3 to 500 μg of the active ingredient per milliliter of solution in order that infusion of a suitable volume at a rate of about 30 mL/hr can occur.

Formulations suitable for administration to the eye include eye drops wherein the active ingredient is dissolved or suspended in a suitable carrier, especially an aqueous solvent for the active ingredient. The active ingredient is preferably present in such formulations in a concentration of 0.5 to 20%, advantageously 0.5 to 10% particularly about 1.5% w/w.

Formulations suitable for topical administration in the mouth include lozenges comprising the active ingredient in a flavored basis, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert basis such as gelatin and glycerin, or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

Formulations for rectal administration may be presented as a suppository with a suitable base comprising for example cocoa butter or a salicylate.

Formulations suitable for intrapulmonary or nasal administration have a particle size for example in the range of 0.1 to 500 microns (including particle sizes in a range between 0.1 and 500 microns in increments microns such as 0.5, 1, 30 microns, 35 microns, etc.), which is administered by rapid inhalation through the nasal passage or by inhalation through the mouth so as to reach the alveolar sacs. Suitable formulations include aqueous or oily solutions of the active ingredient. Formulations suitable for aerosol or dry powder administration may be prepared according to conventional methods and may be delivered with other therapeutic agents such as compounds heretofore used in the treatment or prophylaxis of conditions associated with HCV activity.

Formulations suitable for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or spray formulations containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes

which render the formulation isotonic with the blood of the intended recipient; and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening agents.

The formulations are presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze-dried (lyophilized) condition requiring only the addition of the sterile liquid carrier, for example water for injection, immediately prior to use. Extemporaneous injection solutions and suspensions are prepared from sterile powders, granules and tablets of the kind previously described. Preferred unit dosage formulations are those containing a daily dose or unit daily sub-dose, as herein above recited, or an appropriate fraction thereof, of the active ingredient.

It should be understood that in addition to the ingredients particularly mentioned above the formulations of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example those suitable for oral administration may include flavoring agents.

The invention further provides veterinary compositions comprising at least one active ingredient as above defined together with a veterinary carrier therefor.

Veterinary carriers are materials useful for the purpose of administering the composition and may be solid, liquid or gaseous materials which are otherwise inert or acceptable in the veterinary art and are compatible with the active ingredient. These veterinary compositions may be administered orally, parenterally or by any other desired route.

Compounds of the invention can also be formulated to provide controlled release of the active ingredient to allow less frequent dosing or to improve the pharmacokinetic or toxicity profile of the active ingredient. Accordingly, the invention also provides compositions comprising one or more compounds of the invention formulated for sustained or controlled release.

Effective dose of active ingredient depends at least on the nature of the condition being treated, toxicity, whether the compound is being used prophylactically (lower doses), the method of delivery, and the pharmaceutical formulation, and will be determined by the clinician using conventional dose escalation studies.

Routes of Administration

One or more compounds of the invention (herein referred to as the active ingredients) are administered by any route appropriate to the condition to be treated. Suitable routes include oral, rectal, nasal, topical (including buccal and sublingual), vaginal and parenteral (including subcutaneous, intramuscular, intravenous, intradermal, intrathecal and epidural), and the like. It will be appreciated that the preferred route may vary with for example the condition of the

recipient. An advantage of the compounds of this invention is that they are orally bioavailable and can be dosed orally.

HCV Combination Therapy

In another embodiment, non-limiting examples of suitable combinations include combinations of one or more compounds of the present invention with one or more interferons, ribavirin or its analogs, HCV NS3 protease inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, nucleoside or nucleotide inhibitors of HCV NS5B polymerase, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophilin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers, and other drugs for treating HCV.

More specifically, one or more compounds of the present invention may be combined with one or more compounds selected from the group consisting of

1) interferons, *e.g.*, pegylated rIFN-alpha 2b (PEG-Intron), pegylated rIFN-alpha 2a (Pegasys), rIFN-alpha 2b (Intron A), rIFN-alpha 2a (Roferon-A), interferon alpha (MOR-22, OPC-18, Alfaferone, Alfanative, Multiferon, subalin), interferon alfacon-1 (Infergen), interferon alpha-n1 (Wellferon), interferon alpha-n3 (Alferon), interferon-beta (Avonex, DL-8234), interferon-omega (omega DUROS, Biomed 510), albinterferon alpha-2b (Albuferon), IFN alpha-2b XL, BLX-883 (Locteron), DA-3021, glycosylated interferon alpha-2b (AVI-005), PEG-Infergen, PEGylated interferon lambda-1 (PEGylated IL-29), and belerofon,

2) ribavirin and its analogs, *e.g.*, ribavirin (Rebetol, Copegus), and taribavirin (Viramidine),

3) HCV NS3 protease inhibitors, *e.g.*, boceprevir (SCH-503034, SCH-7), telaprevir (VX-950), TMC435350, BI-1335, BI-1230, MK-7009, VBY-376, VX-500, GS-9256, GS-9451, BMS-790052, BMS-605339, PHX-1766, AS-101, YH-5258, YH5530, YH5531, and ITMN-191,

4) alpha-glucosidase 1 inhibitors, *e.g.*, celgosivir (MX-3253), Miglitol, and UT-231B,

5) hepatoprotectants, *e.g.*, emericasan (IDN-6556), ME-3738, GS-9450 (LB-84451), silibinin, and MitoQ,

6) nucleoside or nucleotide inhibitors of HCV NS5B polymerase, *e.g.*, R1626, R7128 (R4048), IDX184, IDX-102, BCX-4678, valopicitabine (NM-283), and MK-0608,

7) non-nucleoside inhibitors of HCV NS5B polymerase, *e.g.*, PF-868554, VCH-759, VCH-916, JTK-652, MK-3281, GS-9190, VBY-708, VCH-222, A848837, ANA-598, GL60667, GL59728, A-63890, A-48773, A-48547, BC-2329, VCH-796 (nesbuvir), GSK625433, BILN-1941, XTL-2125, and GS-9190,

- 8) HCV NS5A inhibitors, *e.g.*, AZD-2836 (A-831), BMS-790052, and A-689,
- 9) TLR-7 agonists, *e.g.*, imiquimod, 852A, GS-9524, ANA-773, ANA-975, AZD-8848 (DSP-3025), and SM-360320,
- 10) cyclophilin inhibitors, *e.g.*, DEBIO-025, SCY-635, and NIM811,
- 11) HCV IRES inhibitors, *e.g.*, MCI-067,
- 12) pharmacokinetic enhancers, *e.g.*, BAS-100, SPI-452, PF-4194477, TMC-41629, GS-9350, GS-9585, and roxythromycin,
- 13) other drugs for treating HCV, *e.g.*, thymosin alpha 1 (Zadaxin), nitazoxanide (Alinea, NTZ), BIVN-401 (virostat), PYN-17 (altirex), KPE02003002, actilon (CPG-10101), GS-9525, KRN-7000, civacir, GI-5005, XTL-6865, BIT225, PTX-111, ITX2865, TT-033i, ANA 971, NOV-205, tarvacin, EHC-18, VGX-410C, EMZ-702, AVI 4065, BMS-650032, BMS-791325, Bavituximab, MDX-1106 (ONO-4538), Oglufanide, and VX-497 (merimepodib).

In yet another embodiment, the present application discloses pharmaceutical compositions comprising a compound of the present invention, or a pharmaceutically acceptable salt, solvate, and/or ester thereof, in combination with at least one additional therapeutic agent, and a pharmaceutically acceptable carrier or excipient.

According to the present invention, the therapeutic agent used in combination with the compound of the present invention can be any agent having a therapeutic effect when used in combination with the compound of the present invention. For example, the therapeutic agent used in combination with the compound of the present invention can be interferons, ribavirin analogs, NS3 protease inhibitors, NS5b polymerase inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, non-nucleoside inhibitors of HCV, and other drugs for treating HCV.

In another embodiment, the present application provides pharmaceutical compositions comprising a compound of the present invention, or a pharmaceutically acceptable salt, solvate, and/or ester thereof, in combination with at least one additional therapeutic agent selected from the group consisting of pegylated rIFN-alpha 2b, pegylated rIFN-alpha 2a, rIFN-alpha 2b, IFN alpha-2b XL, rIFN-alpha 2a, consensus IFN alpha, infergen, rebif, locteron, AVI-005, PEG-infergen, pegylated IFN-beta, oral interferon alpha, feron, reaferon, intermax alpha, r-IFN-beta, infergen + actimmune, IFN-omega with DUROS, albuferon, rebetol, copegus, levovirin, VX-497, viraclidine (taribavirin), A-831, A-689, NM-283, valopicitabine, R1626, PSI-6130 (R1656), HCV-796, BILB 1941, MK-0608, NM-107, R7128, VCH-759, PF-868554, GSK625433, XTL-2125, SCH-503034 (SCH-7), VX-950 (Telaprevir), ITMN-191, and BILN-2065, MX-3253 (celgosivir), UT-231B, IDN-6556, ME 3738, MitoQ, and LB-84451, benzimidazole derivatives, benzo-1,2,4-thiadiazine derivatives, and phenylalanine derivatives, zadaxin, nitazoxanide (alinea), BIVN-401 (virostat), DEBIO-025, VGX-410C, EMZ-702, AVI

4065, bavituximab, oglufanide, PYN-17, KPE02003002, actilon (CPG-10101), KRN-7000, civacir, GI-5005, ANA-975 (isatoribine), XTL-6865, ANA 971, NOV-205, tarvacin, EHC-18, and NIM811 and a pharmaceutically acceptable carrier or excipient.

In yet another embodiment, the present application provides a combination pharmaceutical agent comprising:

- a) a first pharmaceutical composition comprising a compound of the present invention, or a pharmaceutically acceptable salt, solvate, or ester thereof; and
- b) a second pharmaceutical composition comprising at least one additional therapeutic agent selected from the group consisting of HIV protease inhibiting compounds, HIV non-nucleoside inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, interferons, ribavirin analogs, NS3 protease inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, non-nucleoside inhibitors of HCV, and other drugs for treating HCV, and combinations thereof.

Combinations of the compounds of formula I and additional active therapeutic agents may be selected to treat patients infected with HCV and other conditions such as HIV infections. Accordingly, the compounds of formula I may be combined with one or more compounds useful in treating HIV, for example HIV protease inhibiting compounds, non-nucleoside inhibitors of HIV reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, interferons, ribavirin analogs, NS3 protease inhibitors, NS5b polymerase inhibitors, alpha-glucosidase 1 inhibitors, hepatoprotectants, non-nucleoside inhibitors of HCV, and other drugs for treating HCV.

More specifically, one or more compounds of the present invention may be combined with one or more compounds selected from the group consisting of 1) HIV protease inhibitors, *e.g.*, amprenavir, atazanavir, fosamprenavir, indinavir, lopinavir, ritonavir, lopinavir + ritonavir, nelfinavir, saquinavir, tipranavir, brecanavir, darunavir, TMC-126, TMC-114, mozenavir (DMP-450), JE-2147 (AG1776), AG1859, DG35, L-756423, RO0334649, KNI-272, DPC-681, DPC-684, and GW640385X, DG17, PPL-100, 2) a HIV non-nucleoside inhibitor of reverse transcriptase, *e.g.*, capravirine, emivirine, delaviridine, efavirenz, nevirapine, (+) calanolide A, etravirine, GW5634, DPC-083, DPC-961, DPC-963, MIV-150, and TMC-120, TMC-278 (rilpivirine), efavirenz, BILR 355 BS, VRX 840773, UK-453,061, RDEA806, 3) a HIV nucleoside inhibitor of reverse transcriptase, *e.g.*, zidovudine, emtricitabine, didanosine, stavudine, zalcitabine, lamivudine, abacavir, amdoxovir, elvucitabine, alovudine, MIV-210, racivir (\pm -FTC), D-d4FC, emtricitabine, phosphazide, fozivudine tidoxil, fosalvudine tidoxil,

apricitibine (AVX754), amdoxovir, KP-1461, abacavir + lamivudine, abacavir + lamivudine + zidovudine, zidovudine + lamivudine, 4) a HIV nucleotide inhibitor of reverse transcriptase, *e.g.*, tenofovir, tenofovir disoproxil fumarate + emtricitabine, tenofovir disoproxil fumarate + emtricitabine + efavirenz, and adefovir, 5) a HIV integrase inhibitor, *e.g.*, curcumin, derivatives of curcumin, chicoric acid, derivatives of chicoric acid, 3,5-dicaffeoylquinic acid, derivatives of 3,5-dicaffeoylquinic acid, aurintricarboxylic acid, derivatives of aurintricarboxylic acid, caffeic acid phenethyl ester, derivatives of caffeic acid phenethyl ester, tyrphostin, derivatives of tyrphostin, quercetin, derivatives of quercetin, S-1360, zintevir (AR-177), L-870812, and L-870810, MK-0518 (raltegravir), BMS-707035, MK-2048, BA-011, BMS-538158, GSK364735C, 6) a gp41 inhibitor, *e.g.*, enfuvirtide, sifuvirtide, FB006M, TRI-1144, SPC3, DES6, Locus gp41, CovX, and REP 9, 7) a CXCR4 inhibitor, *e.g.*, AMD-070, 8) an entry inhibitor, *e.g.*, SP01A, TNX-355, 9) a gp120 inhibitor, *e.g.*, BMS-488043 and BlockAide/CR, 10) a G6PD and NADH-oxidase inhibitor, *e.g.*, immunitin, 10) a CCR5 inhibitor, *e.g.*, aplaviroc, vicriviroc, INCB9471, PRO-140, INCB15050, PF-232798, CCR5mAb004, and maraviroc, 11) an interferon, *e.g.*, pegylated rIFN-alpha 2b, pegylated rIFN-alpha 2a, rIFN-alpha 2b, IFN alpha-2b XL, rIFN-alpha 2a, consensus IFN alpha, infergen, rebif, locteron, AVI-005, PEG-infergen, pegylated IFN-beta, oral interferon alpha, feron, reaferon, intermax alpha, r-IFN-beta, infergen + actimmune, IFN-omega with DUROS, and albuferon, 12) ribavirin analogs, *e.g.*, rebetol, copegus, levovirin, VX-497, and viramidine (taribavirin) 13) NS5a inhibitors, *e.g.*, A-831, A-689, and BMS-790052, 14) NS5b polymerase inhibitors, *e.g.*, NM-283, valopicitabine, R1626, PSI-6130 (R1656), HCV-796, BILB 1941, MK-0608, NM-107, R7128, VCH-759, PF-868554, GSK625433, and XTL-2125, 15) NS3 protease inhibitors, *e.g.*, SCH-503034 (SCH-7), VX-950 (Telaprevir), ITMN-191, and BILN-2065, 16) alpha-glucosidase 1 inhibitors, *e.g.*, MX-3253 (celgosivir) and UT-231B, 17) hepatoprotectants, *e.g.*, IDN-6556, ME 3738, MitoQ, and LB-84451, 18) non-nucleoside inhibitors of HCV, *e.g.*, benzimidazole derivatives, benzo-1,2,4-thiadiazine derivatives, and phenylalanine derivatives, 19) other drugs for treating Hepatitis C, *e.g.*, zadaxin, nitazoxanide (alinea), BIVN-401 (virostat), DEBIO-025, VGX-410C, EMZ-702, AVI 4065, bavituximab, oglufanide, PYN-17, KPE02003002, actilon (CPG-10101), KRN-7000, civacir, GI-5005, ANA-975 (isatoribine), XTL-6865, ANA 971, NOV-205, tarvacin, EHC-18, and NIM811, 19) pharmacokinetic enhancers, *e.g.*, BAS-100 and SPI452, 20) RNase H inhibitors, *e.g.*, ODN-93 and ODN-112, 21) other anti-HIV agents, *e.g.*, VGV-1, PA-457 (bevirimat), ampligen, HRG214, cytolin, polymun, VGX-410, KD247, AMZ 0026, CYT 99007, A-221 HIV, BAY 50-4798, MDX010 (iplimumab), PBS119, ALG889, and PA-1050040.

Metabolites of the Compounds of the Invention

Also falling within the scope of this invention are the *in vivo* metabolic products of the compounds described herein. Such products may result for example from the oxidation, reduction, hydrolysis, amidation, esterification and the like of the administered compound, primarily due to enzymatic processes. Accordingly, the invention includes compounds produced by a process comprising contacting a compound of this invention with a mammal for a period of time sufficient to yield a metabolic product thereof. Such products typically are identified by preparing a radiolabelled (*e.g.*, C¹⁴ or H³) compound of the invention, administering it parenterally in a detectable dose (*e.g.*, greater than about 0.5 mg/kg) to an animal such as rat, mouse, guinea pig, monkey, or to man, allowing sufficient time for metabolism to occur (typically about 30 seconds to 30 hours) and isolating its conversion products from the urine, blood or other biological samples. These products are easily isolated since they are labeled (others are isolated by the use of antibodies capable of binding epitopes surviving in the metabolite). The metabolite structures are determined in conventional fashion, *e.g.*, by MS or NMR analysis. In general, analysis of metabolites is done in the same way as conventional drug metabolism studies well-known to those skilled in the art. The conversion products, so long as they are not otherwise found *in vivo*, are useful in diagnostic assays for therapeutic dosing of the compounds of the invention even if they possess no HCV –inhibitory activity of their own.

Methods for determining stability of compounds in surrogate gastrointestinal secretions are known.

Compounds of formula (I)

In one embodiment the invention provides a compound of formula (I):



wherein:

Y is –L-L-, –M-W-M- or Y^y;

J is T-P-, -P-T or -J^m;

W is a bond or –W^r-;

L is –M-A-, -A-M-, or –Lⁿ;

T is R⁹-Z-, -Z-R⁹, or –T^p;

R⁹ is E-V-, or –V-E, or –R^{9q};

each A is selected from –A^s;

each M is selected from –M^t;

each P is selected from –P^u;

each Z is selected from $-Z^v$;
 each V is selected from $-V^w$;
 each E is selected from $-E^x$;
 each m is 1
 each n is 0, 1, 2, 3, 4, 5, 6, 7, 9, or 10;
 each p is 1, 2, 3, 4, 5, 6, 7, or 8;
 each q is 0, 1, 2, or 3;
 each r is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20;
 each s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 21;
 each t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11;
 each u is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19;
 each v is 0, 1, 2, 3, 4, 5, or 6;
 each w is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24;
 each x is 0, 1, 2, 3, 4, 5, 6, or 7;
 each y is 0, 1, or 2 ;

wherein the sum of m, n, p, q, r, s, t, u, v, w, x, and y is not 0; P is connected to M, L, or Y^y ; A is connected to A or L; M is connected to P or J; Z is connected to P; V is connected to Z; and when W is a bond M is connected to M;

each Y^1 is independently:

a fused nine-ring system with up to thirty-five atoms that may be fully aromatic or partially saturated and contains atoms selected from C, N, O, and S and which ring system is optionally substituted with one or more groups independently selected from H, oxo, R^{A1} and R^{A3} ;

each Y^2 is independently:

a fused five to eight ring system with up to thirty-two atoms that may be fully aromatic or partially saturated and contains atoms selected from C, N, O, and S and which ring system is optionally substituted with one or more groups independently selected from H, oxo, R^{A1} and R^{A3} ;

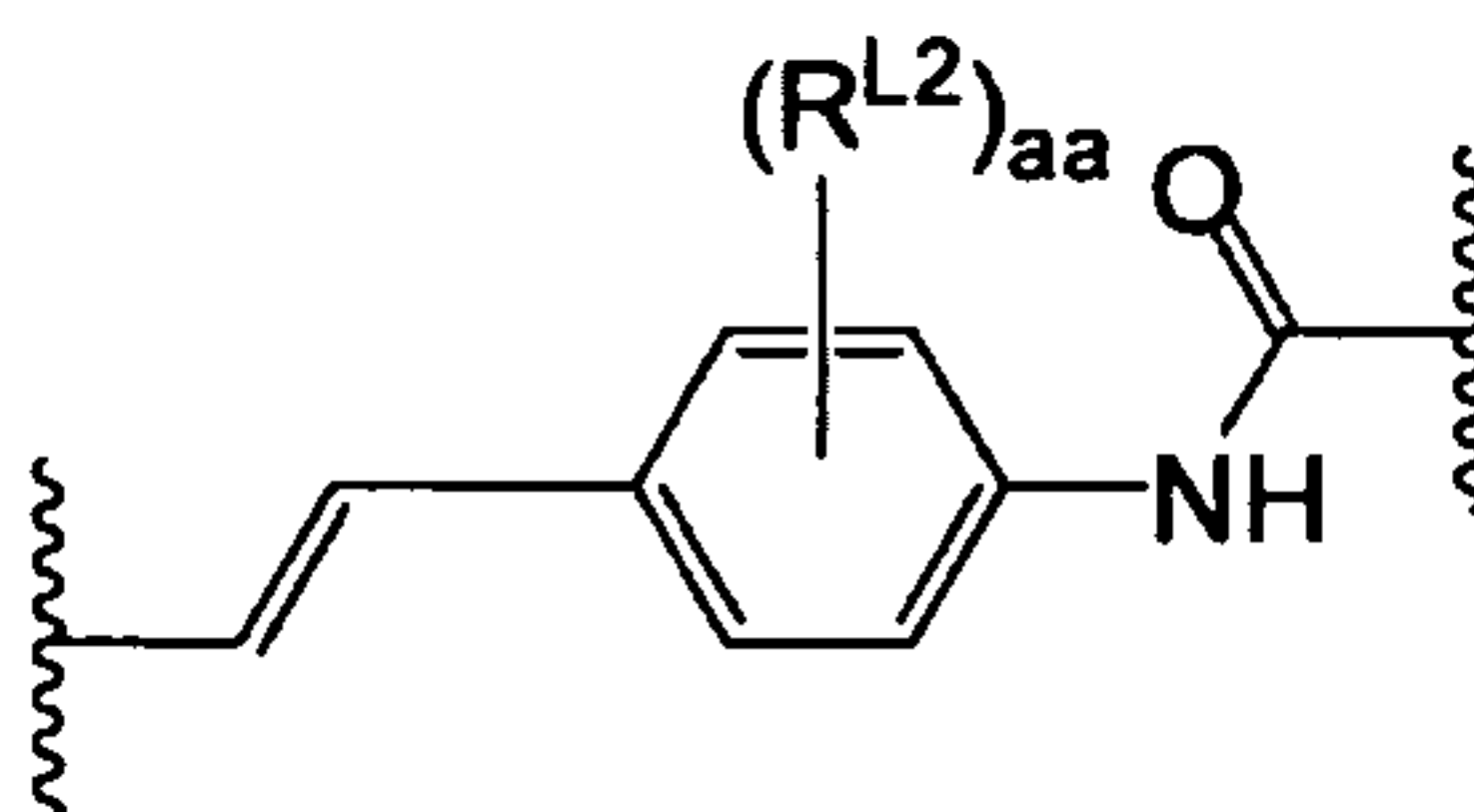
each J^1 is independently a fused bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is substituted with one or more $-N(R^{L7})C(=O)OR^{L7}$, and that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$,

$-\text{C}(\text{O})\text{OR}^{\text{L}7}$, $-\text{C}(\text{=O})\text{NR}^{\text{L}7}$, $-\text{S}(\text{=O})\text{R}^{\text{L}7}$, $-\text{S}(\text{=O})_2\text{OR}^{\text{L}7}$, $-\text{S}(\text{=O})_2\text{R}^{\text{L}7}$, $-\text{OS}(\text{=O})_2\text{OR}^{\text{L}7}$, $-\text{S}(\text{=O})_2\text{NR}^{\text{L}7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-\text{NR}^{\text{a}}\text{R}^{\text{b}}$, $(\text{NR}^{\text{a}}\text{R}^{\text{b}})\text{alkyl}$, and $(\text{NR}^{\text{a}}\text{R}^{\text{b}})\text{carbonyl}$;

each $\text{R}^{\text{L}7}$ is independently $-\text{H}$, alkyl, aryl, arylalkyl, or heterocycle;

R^{a} and R^{b} are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^0 is independently:

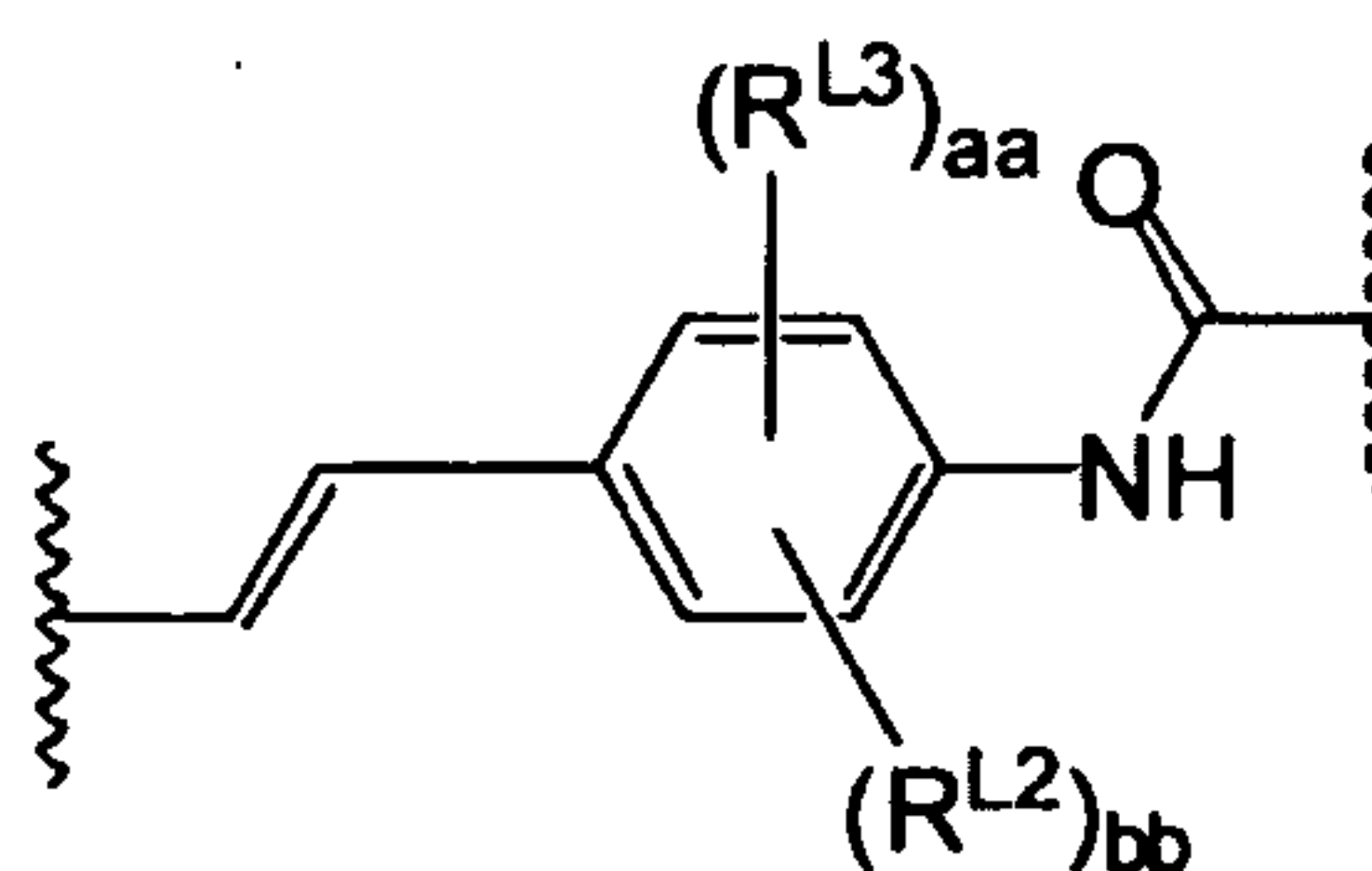


wherein:

each $\text{R}^{\text{L}2}$ is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl; and

each aa is independently 1, 2, 3, or 4;

each L^1 is independently:



wherein:

each $\text{R}^{\text{L}2}$ is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl;

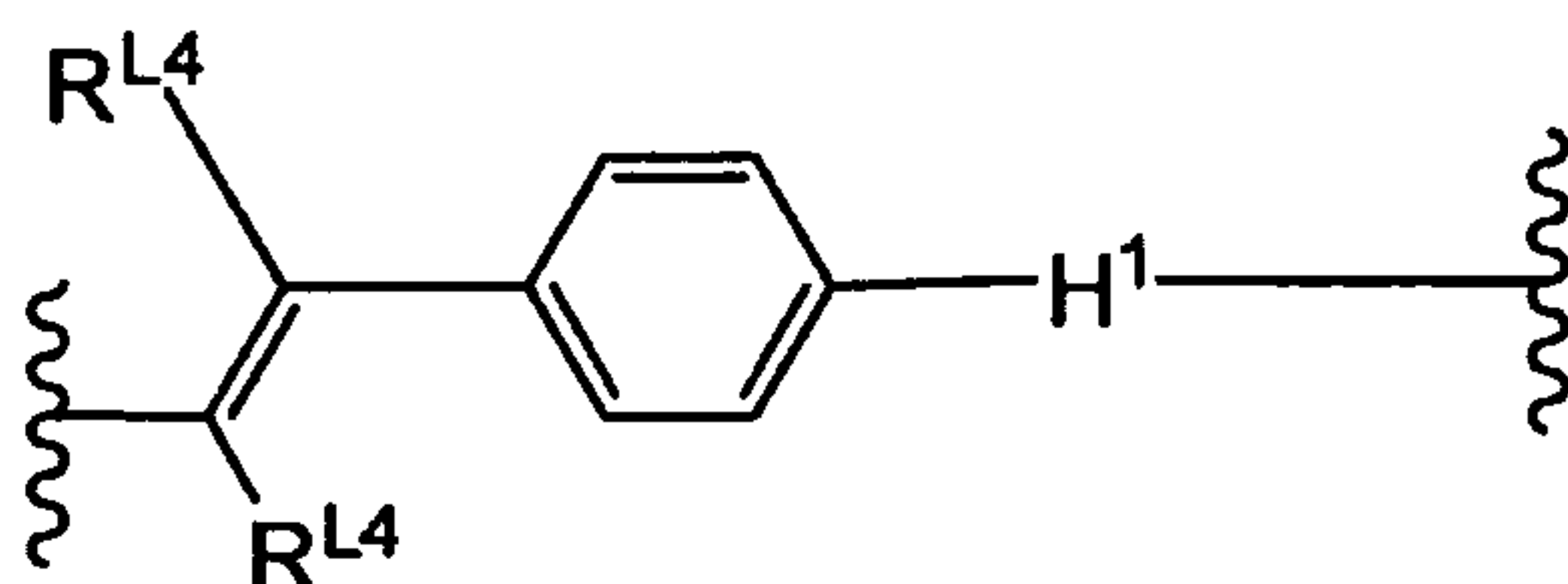
each $\text{R}^{\text{L}3}$ is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-\text{alkylSO}_2\text{R}^4$, haloalkoxy, cyanoalkyl, $\text{NR}^4\text{SO}_2\text{R}^4$, cycloalkyl, (halo)cycloalkyl, heterocycle,

(cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each bb is 0, 1, 2, 3, or 4; each aa is 1, 2, 3, or 4; and the sum of bb and aa is 1, 2, 3, or 4;

each L^2 is independently:



wherein:

the phenyl ring shown in L^2 is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{L4} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl; and

each H^1 is a 5 membered saturated, partially unsaturated, or aromatic ring comprising one or more heteroatoms;

each L^3 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl,

(halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁴ is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁵ is independently a -CR=CR-fused bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R is independently selected from H or alkyl;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁶ is independently a -CR=CR-fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy,

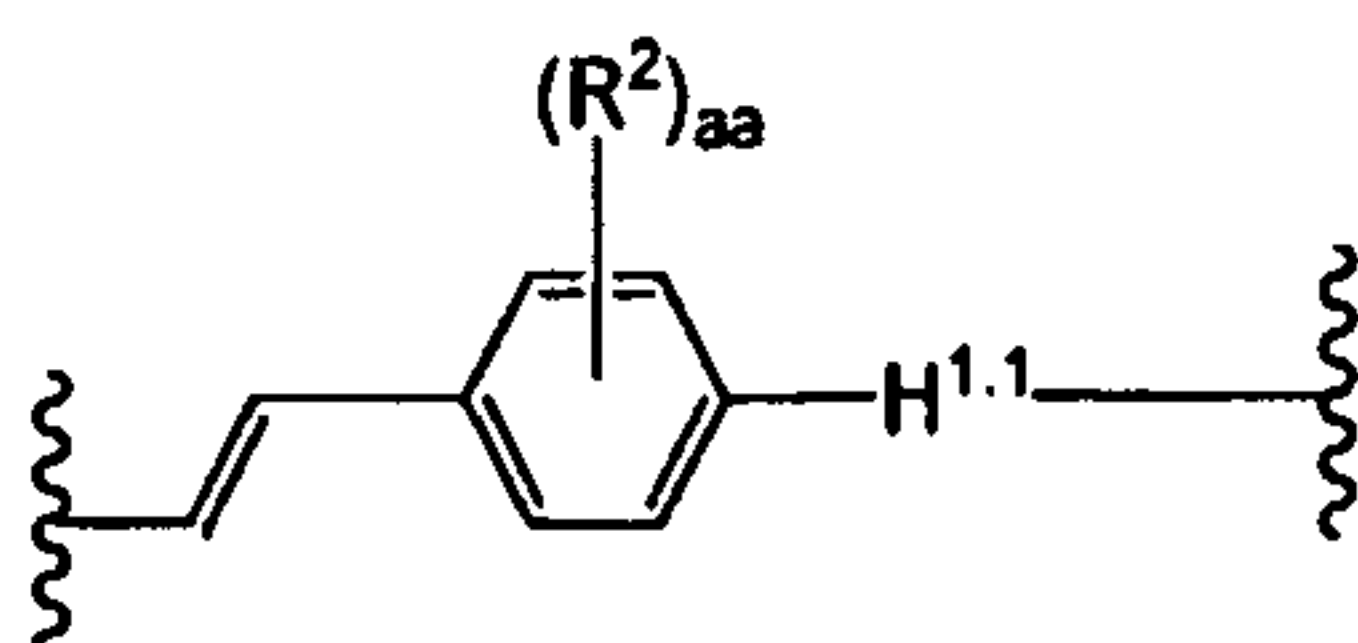
formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R is independently selected from H or alkyl;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^7 is independently:



wherein:

each $H^{1.1}$ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^2 ;

each R^2 is independently selected from halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-N(R^{L7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, and $-S(=O)_2NR^{L7}$;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle; and

each aa is independently 1, 2, 3, or 4;

each L^9 is independently a fused-tetracyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^{10} is independently a fused-pentacyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^{11} is independently a six-ring fused saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each R^9 is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylcarbonylalkyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, aryloxyalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, cycloalkyloxyalkyl, haloalkyl, heterocyclyl, heterocyclylalkenyl, heterocyclylalkoxy, heterocyclylalkyl, heterocycliloxyalkyl, hydroxyalkyl, $-NR^cR^d$, (NR^cR^d) alkenyl, (NR^cR^d) alkyl, and (NR^cR^d) carbonyl;

R^c and R^d are independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxy carbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl,

heterocyclalkoxycarbonyl, heterocyclalkyl, heterocyclalkylcarbonyl, heterocyclcarbonyl, heterocyclloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f)alkyl, (NR^eR^f)alkylcarbonyl, (NR^eR^f)carbonyl, (NR^eR^f)sulfonyl, -C(NCN)OR', and -C(NCN)NR^XR^Y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclalkyl, and the heterocyclalkylcarbonyl are further optionally substituted with one -NR^eR^f group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocycl, and the heterocycl part of the heterocyclalkoxycarbonyl, the heterocyclalkyl, the heterocyclalkylcarbonyl, the heterocyclcarbonyl, and the heterocyclloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

R^X and R^Y are independently selected from hydrogen, alkoxycarbonyl, alkyl, alkylcarbonyl, unsubstituted aryl, unsubstituted arylalkoxycarbonyl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted heterocycl, and (NR^XR^Y)carbonyl, wherein R^X and R^Y are independently selected from hydrogen and alkyl;

each R⁹¹ is independently -N(R^{9a})-NHC(=O)O-R^{9b}, wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl, arylalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclalkyl, heterocycl, heterocyclcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and wherein arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylcarbonyloxy, halo, haloalkoxy, haloalkyl, heterocycl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocycl, heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^XR^Y, - (NR^XR^Y)alkyl, oxo, and -P(O)OR₂, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocycl, and the heterocycl part of the heterocyclalkyl and the

heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

each R^{9^2} is independently $-N(R^{9a})-NHC(=O)NR^{9b}$; wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxy carbonylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylcarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

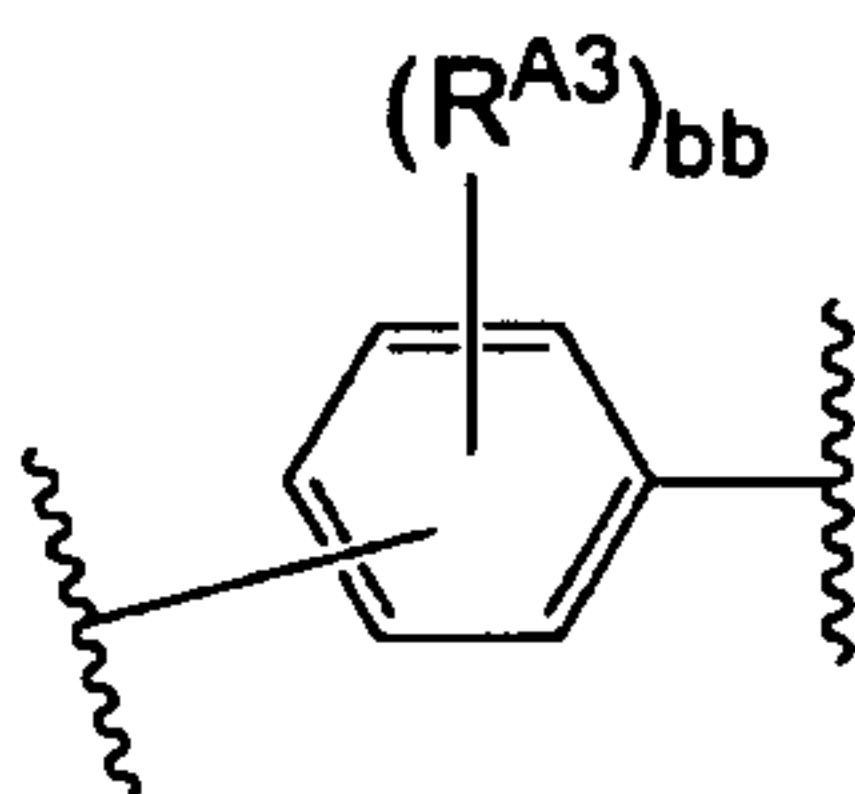
each R^{9^3} is independently $-N(R^{9a})-NHC(=O)R^{9b}$, wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl; and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylcarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein

the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocycl group, and the heterocycl part of the heterocyclalkyl and the heterocyclcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

each A^0 is independently:



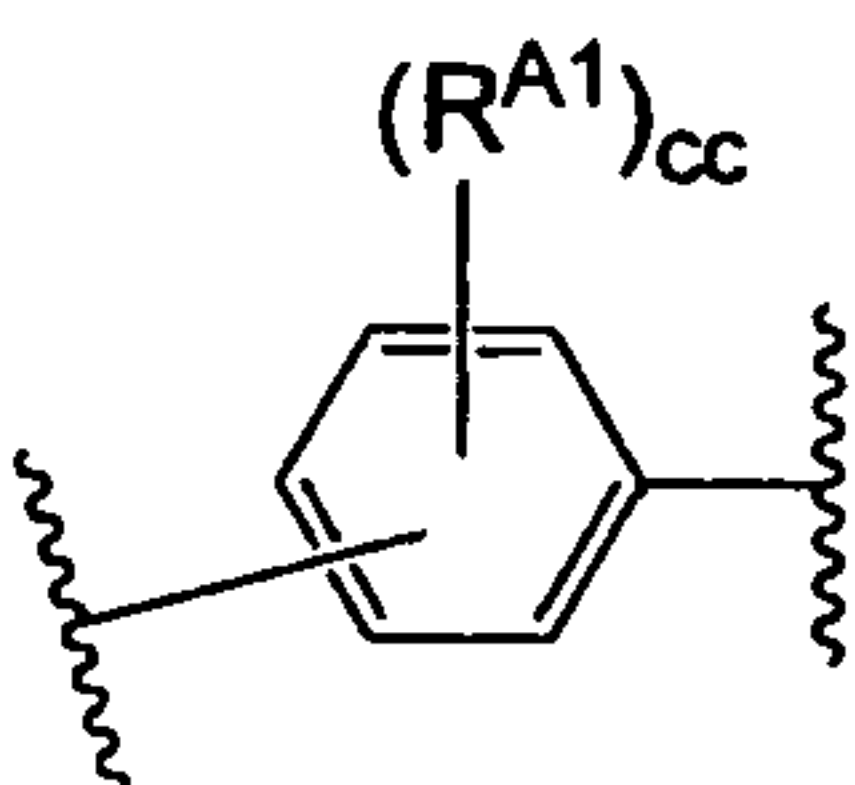
wherein:

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocycl, and heterocyclalkyl; and each

bb is independently 0, 1, 2, 3, or 4; or

each A^0 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is optionally substituted with 1, 2, 3, or 4 R^{A3} groups;

each A^1 is independently:



wherein:

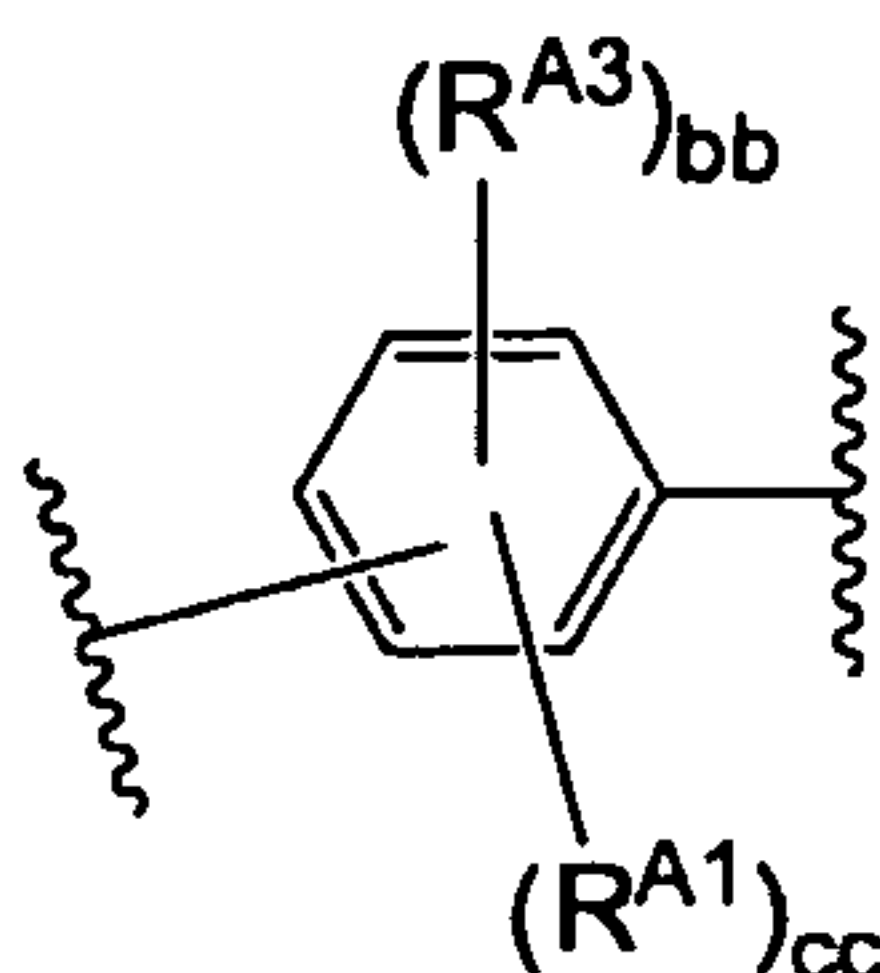
each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl,

(heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each cc is independently 1, 2, 3, or 4

each A^2 is independently:



wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , -alkyl SO_2R^4 , haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

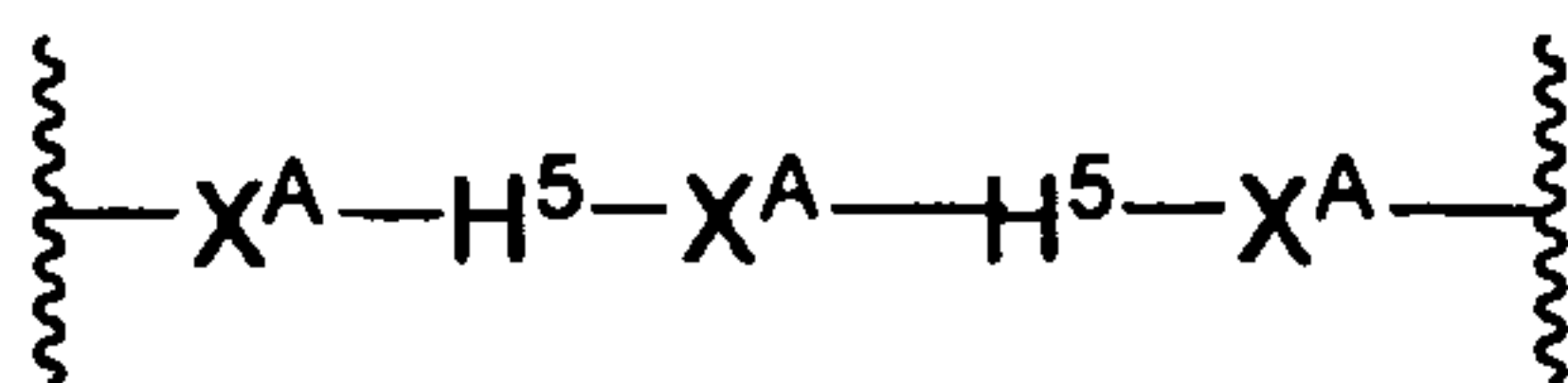
each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is 0, 1, 2, 3, or 4; each cc is 1, 2, 3, or 4; and the sum of bb and cc is 1, 2, 3, or 4;

each A^3 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is substituted with one or more R^{A1} groups, and which ring is optionally substituted with one or more R^{A3} groups;

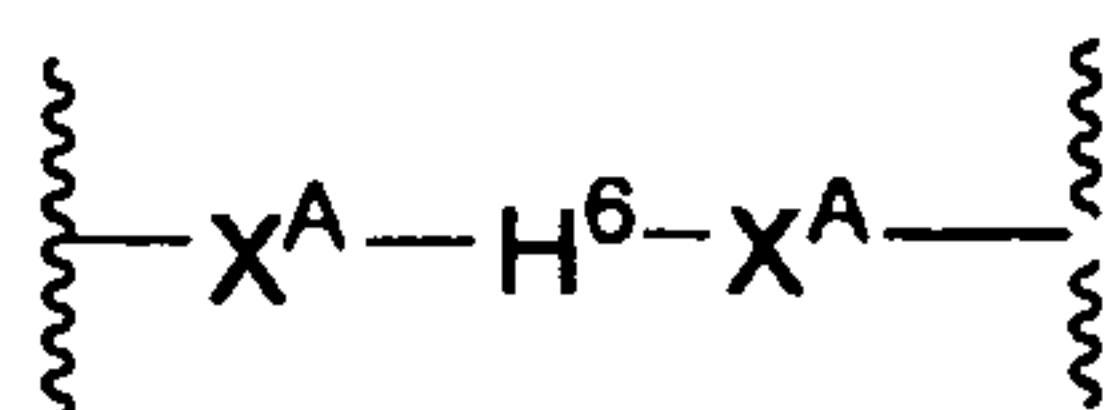
each A^4 is independently:



wherein:

each H^5 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^5 is optionally substituted with one or more groups independently selected from $\text{R}^{\text{A}1}$ and $\text{R}^{\text{A}3}$; and each X^{A} is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

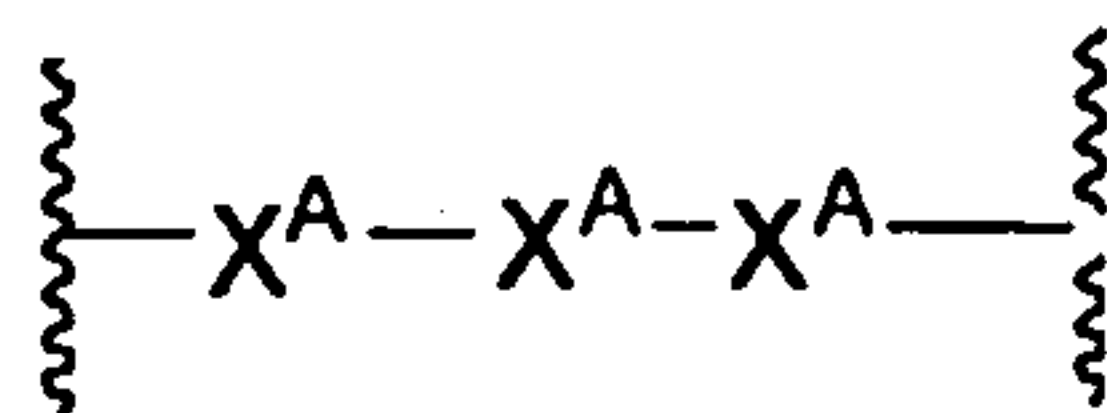
each A^5 is independently:



wherein:

each H^6 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^6 is optionally substituted with one or more groups independently selected from $\text{R}^{\text{A}1}$ and $\text{R}^{\text{A}3}$; and each X^{A} is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent; provided that at least one X^{A} is present and each R is independently selected from H or alkyl;

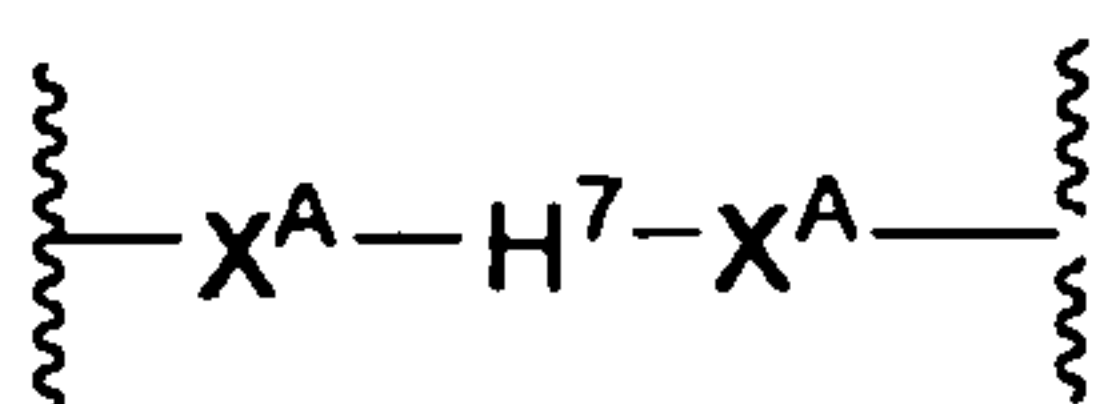
each A^6 is independently:



wherein:

each X^{A} is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, allenyl, alkynyl, or absent; provided that at least one X^{A} is present and each R is independently selected from H or alkyl;

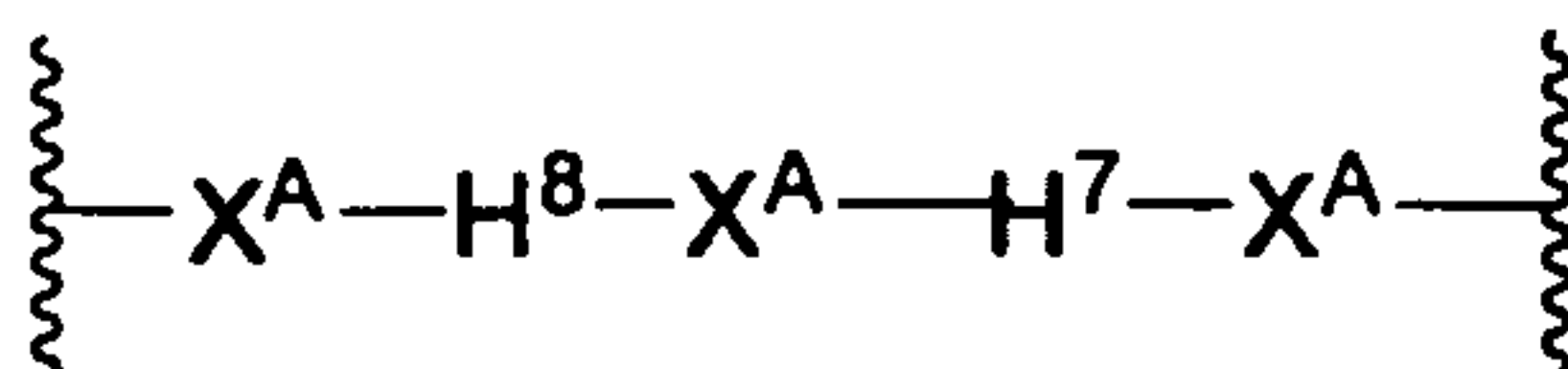
each A^7 is independently:



wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent; and each R is independently selected from H or alkyl;

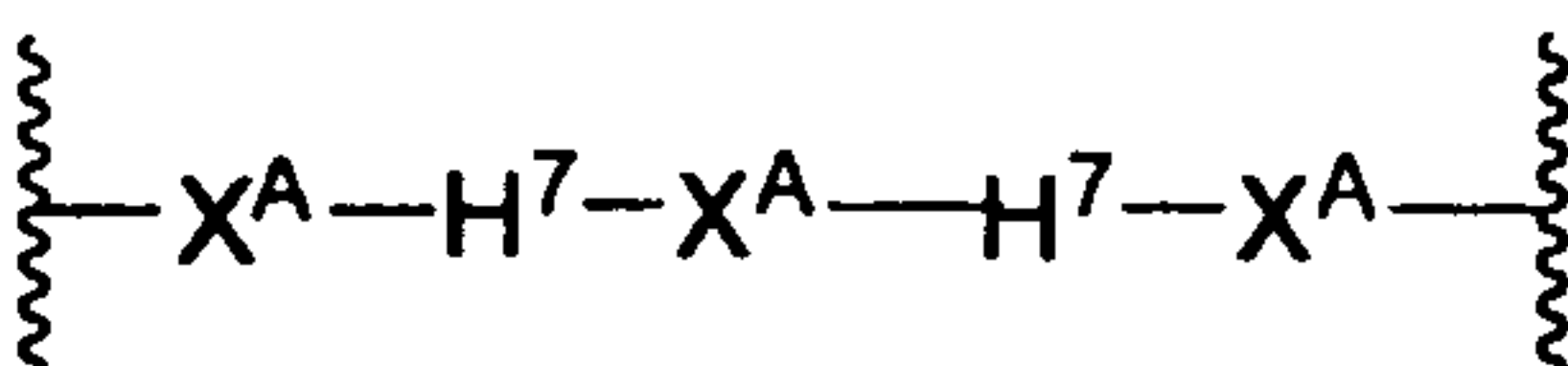
each A⁸ is independently:



wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

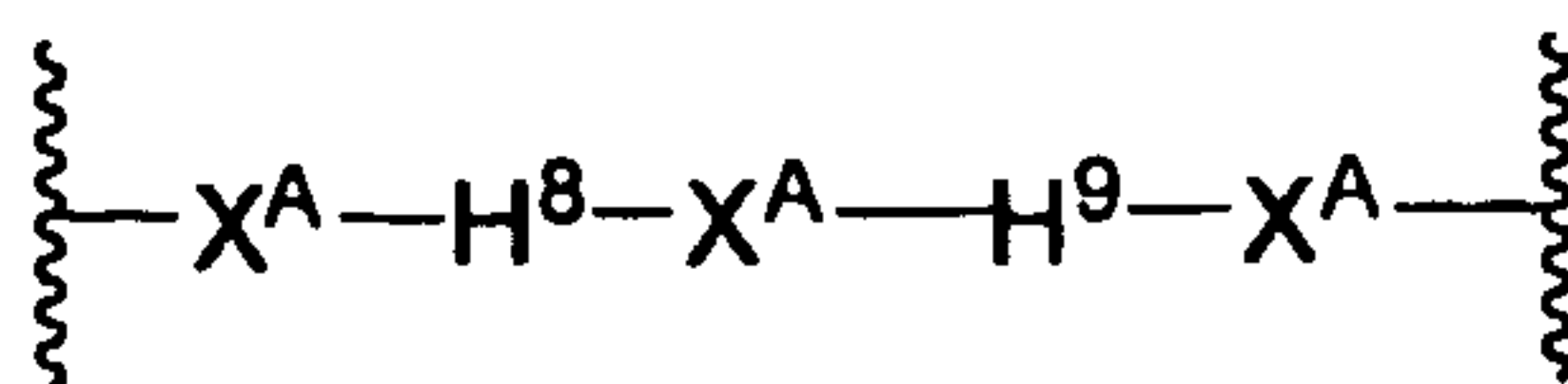
each A⁹ is independently:



wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁰ is independently:



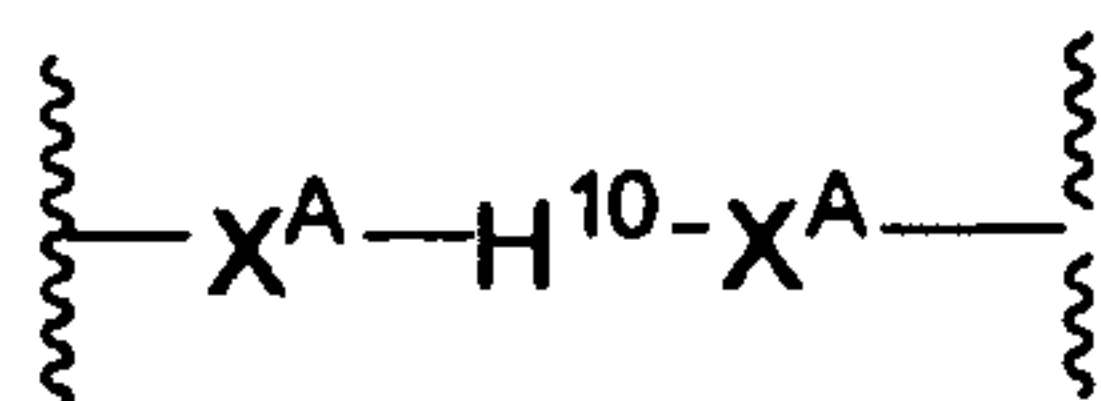
wherein:

each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each H⁹ is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹¹ is independently:



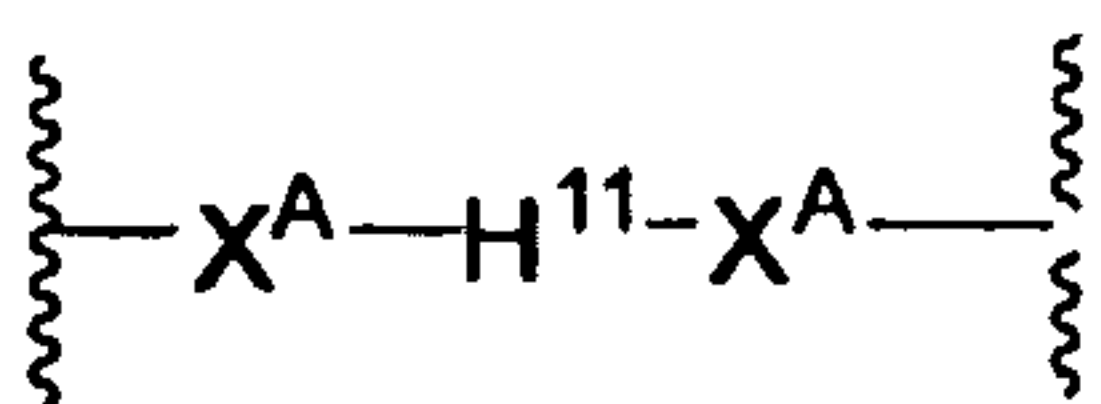
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H¹⁰ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that is optionally fused to an aryl, which H¹⁰ is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl

each A¹² is independently:



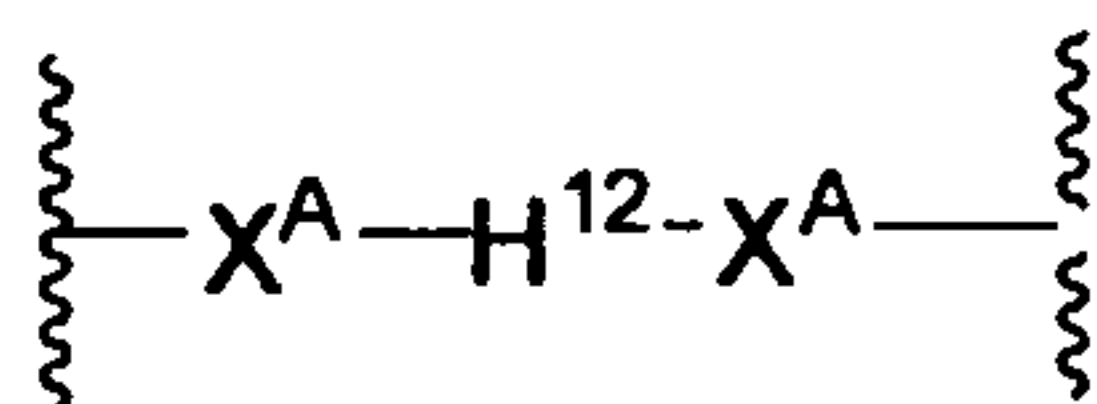
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H¹¹ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms that is optionally fused to an aryl, which H¹¹ is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

each A¹³ is independently:

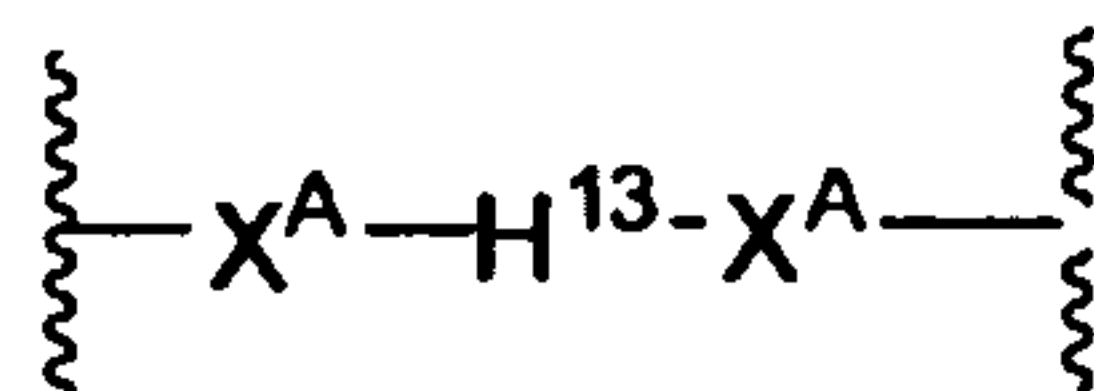


wherein:

each H¹² is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁴ is independently:

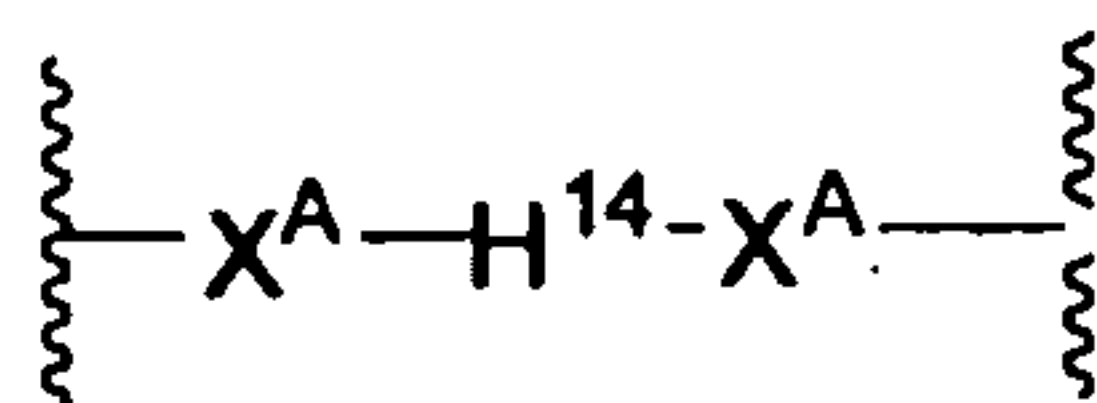


wherein:

each H¹³ is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{15} is independently:

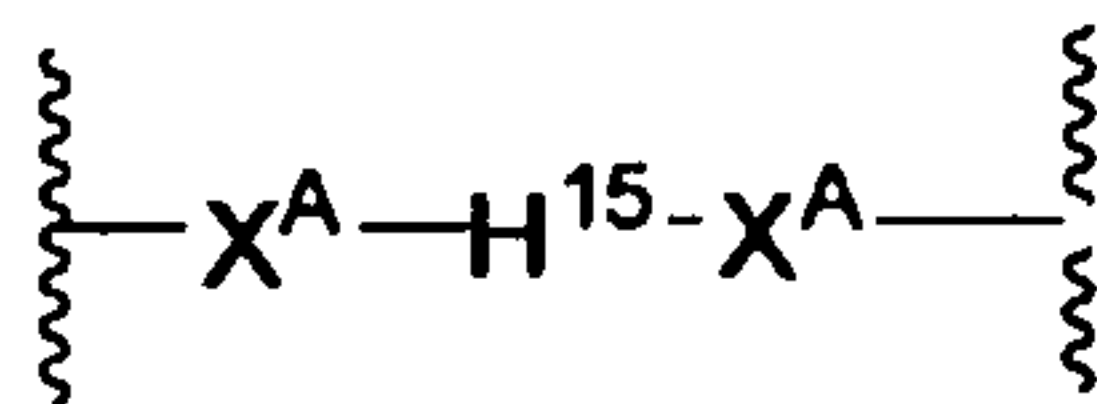


wherein:

each H^{14} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{16} is independently:

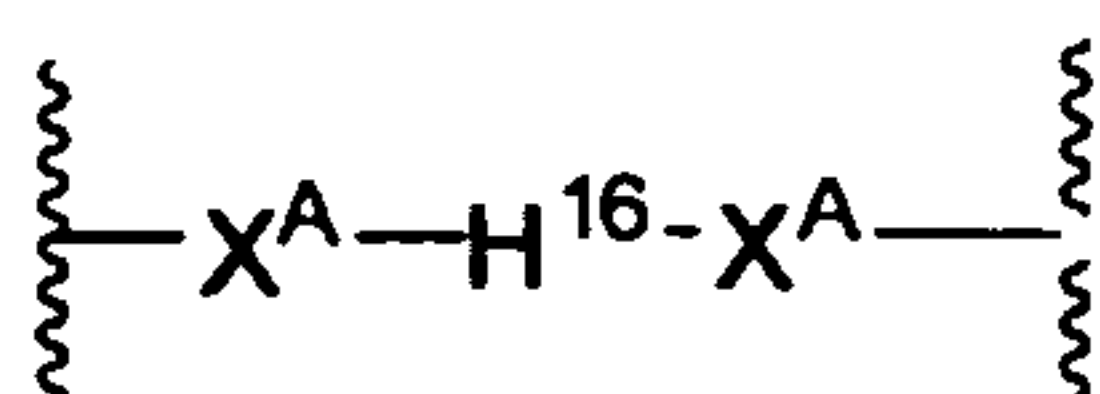


wherein:

each H^{15} is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{17} is independently:

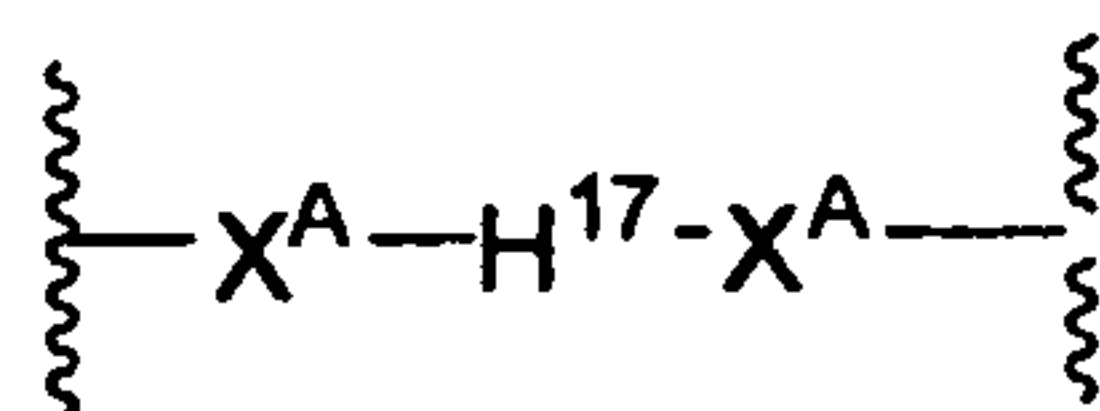


wherein:

each H¹⁶ is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁸ is independently:

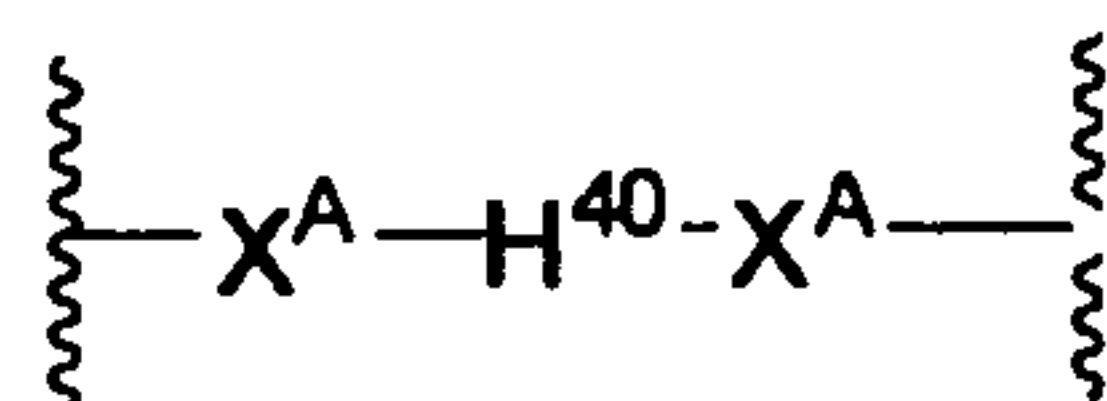


wherein:

each H¹⁷ is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A²¹ is independently:



wherein:

each H⁴⁰ is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

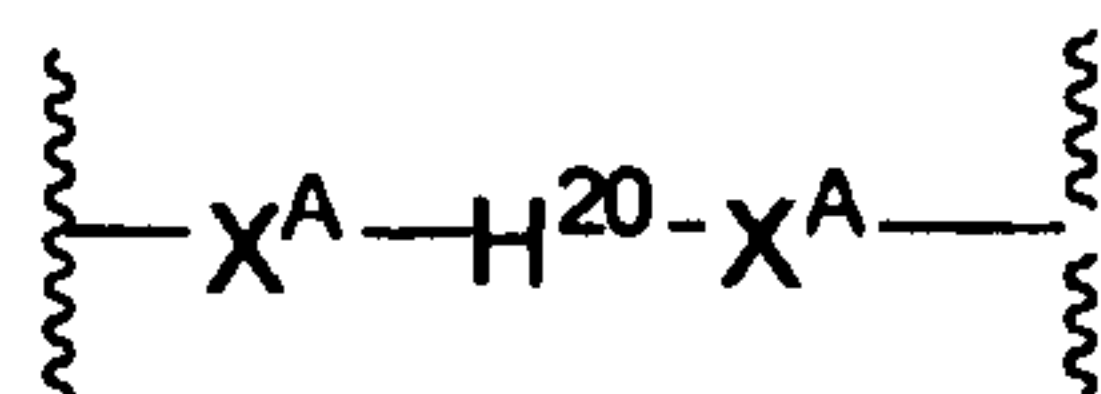
each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^1 is independently $-X^A-$:

wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

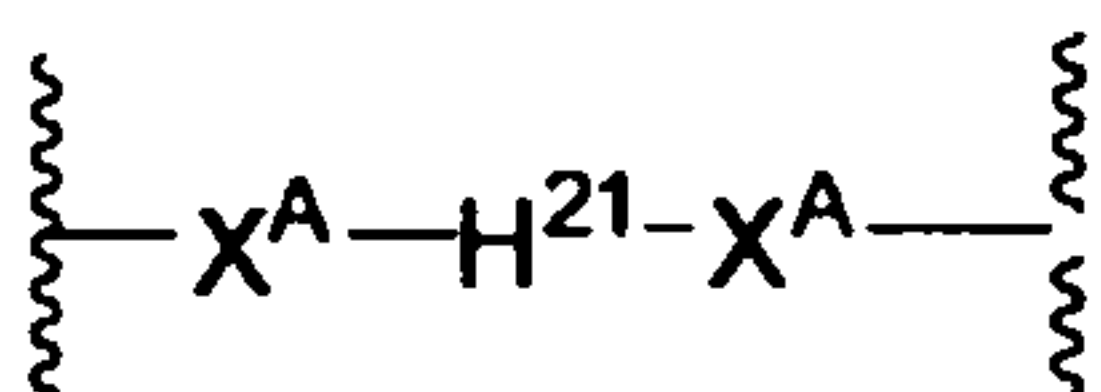
each W^2 is independently:



wherein:

each H^{20} is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^3 is independently:

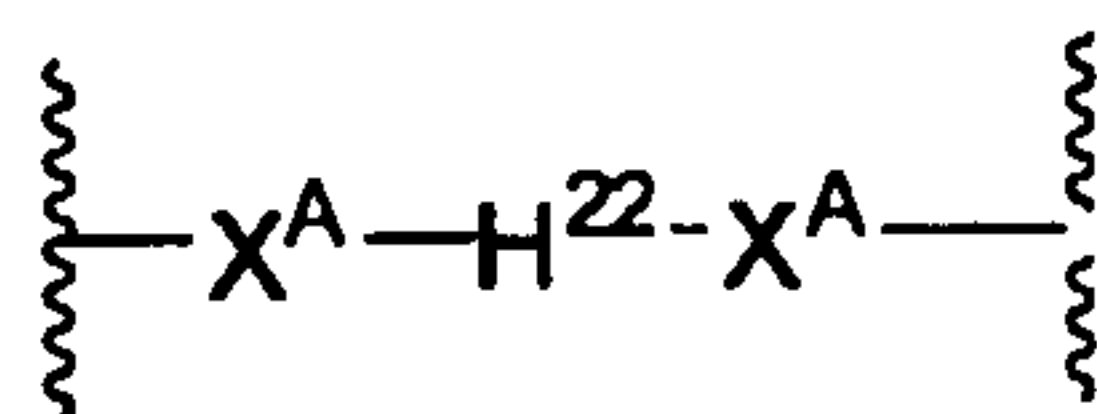


wherein:

each H^{21} is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^4 is independently:

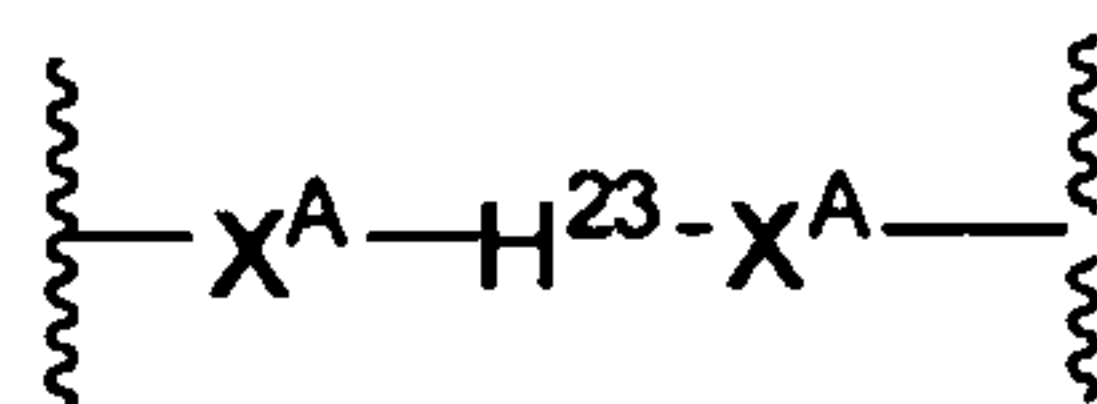


wherein:

each H²² is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W⁵ is independently:

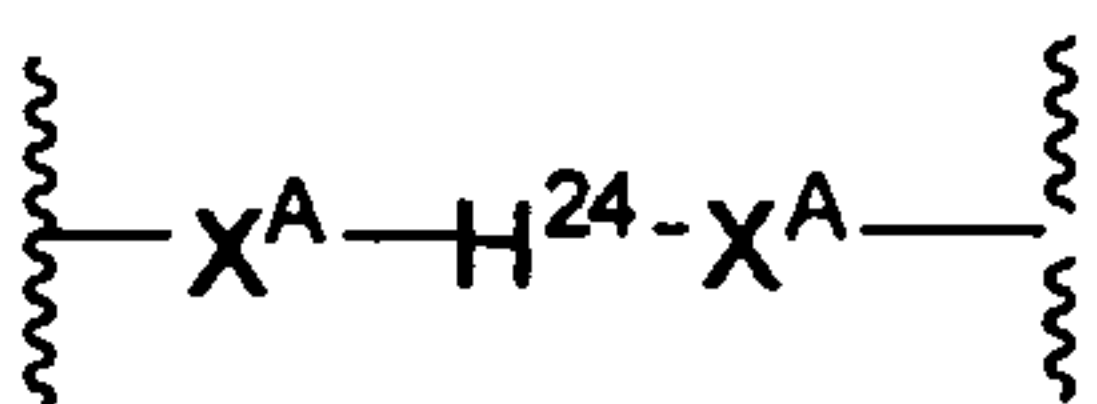


wherein:

each H²³ is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W⁶ is independently:

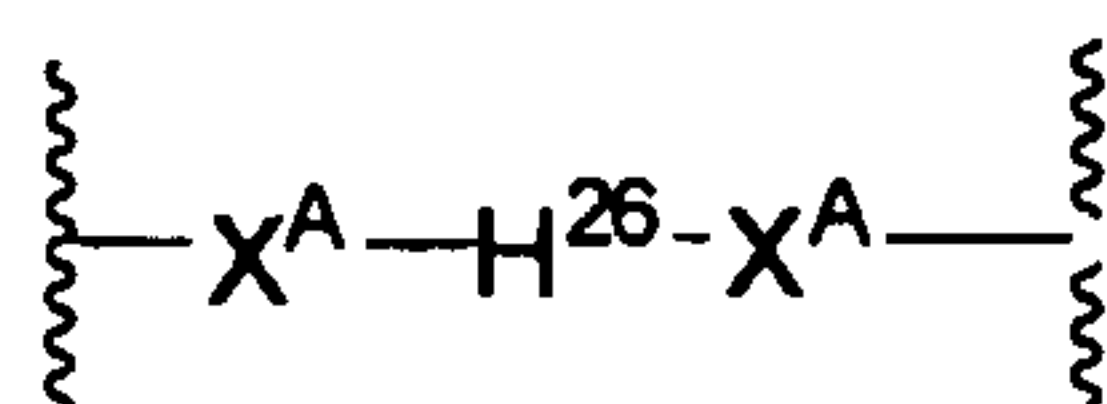


wherein:

each H²⁴ is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle, which is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^7 is independently:

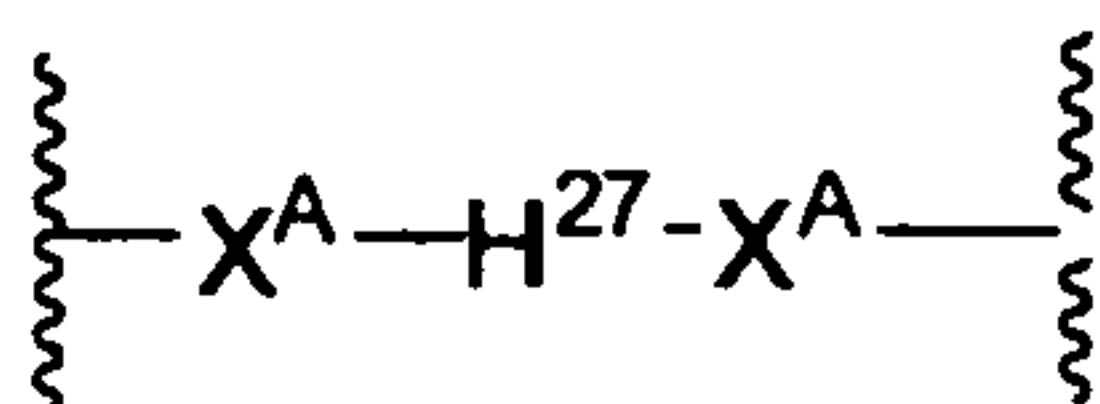


wherein:

each H^{26} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^8 is independently:

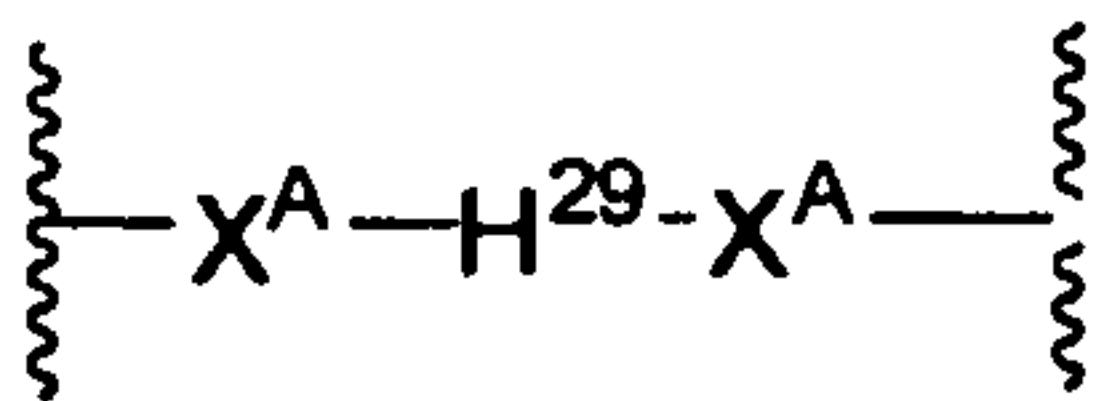


wherein:

each H^{27} is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^9 is independently:



wherein:

each H²⁹ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W¹⁰ is independently -H³⁰=C=H³¹-

wherein each of -H³⁰ and H³¹ is independently a saturated 6-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W¹¹ is independently -H³²=C=H³³-

wherein each of -H³² and H³³ is independently a saturated 5-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W¹² is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each W¹³ is independently a phenyl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each W¹⁴ is independently a 5 or 6 membered heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each W¹⁵ is independently a fused unsaturated, partially unsaturated or saturated tetracyclic carbocyclic ring, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3};

each W¹⁶ is independently a fused unsaturated, partially unsaturated or saturated tetracyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3};

each W¹⁷ is independently a fused unsaturated, partially unsaturated or saturated pentacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3};

each W^{18} is independently a fused unsaturated, partially unsaturated or saturated pentacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{19} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

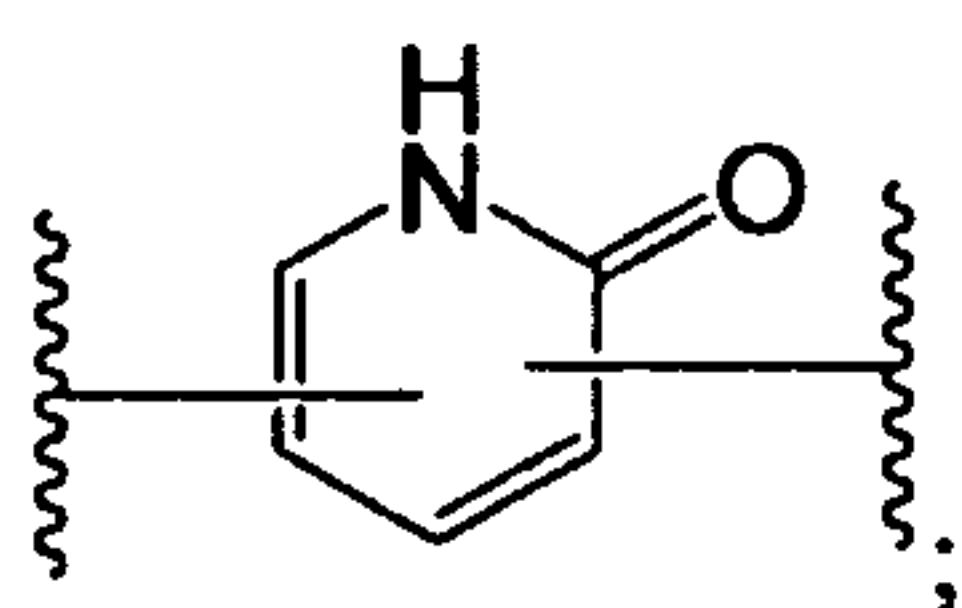
each W^{20} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each M^0 is independently a five membered heteroaryl group optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, haloalkyl, (NR^aR^b) carbonyl and trialkylsilylalkoxyalkyl;

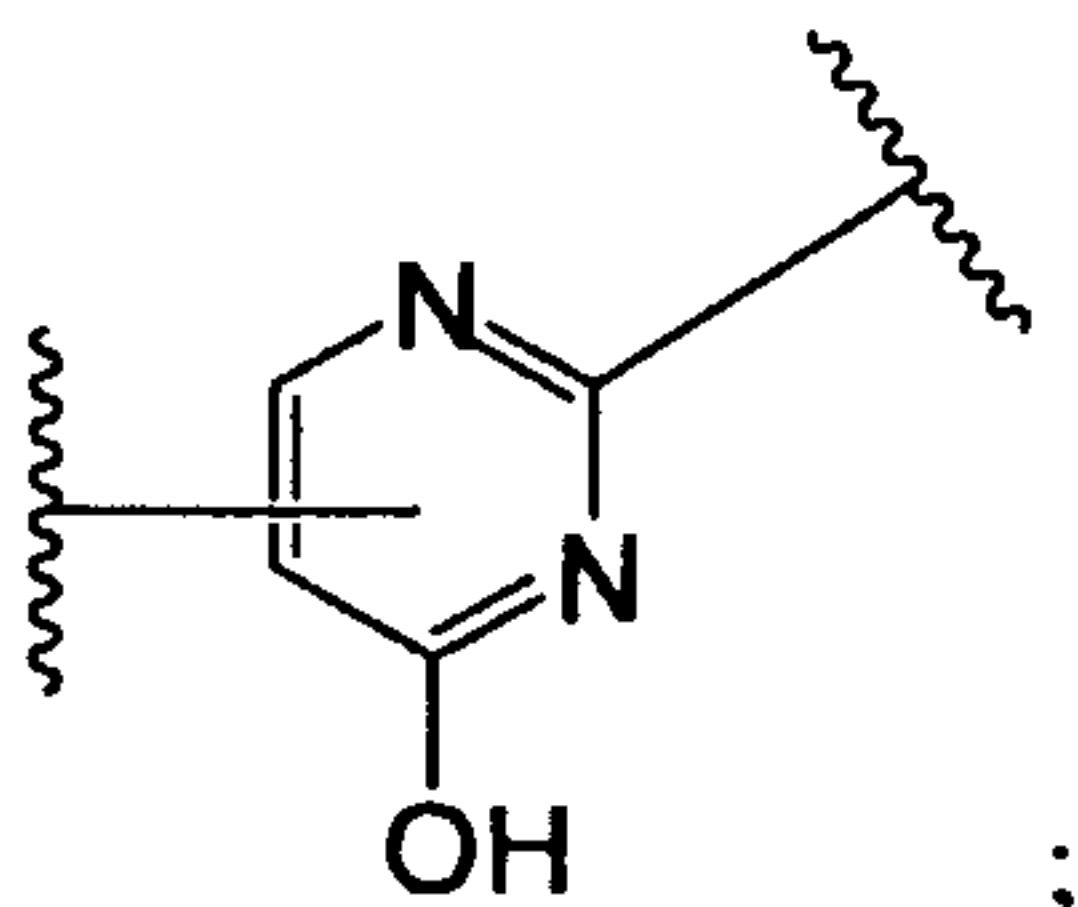
each M^1 is independently selected from $-C(=O)NH-$, $-C(=O)NH-C(R^M)_2-$, $-NHC(=O)-$, $-C(R^M)_2NHC(=O)-$, $-NHC(=O)NR^M-$, $-NHC(=O)O-$; wherein each R^M is independently selected from H and alkyl;

each M^2 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

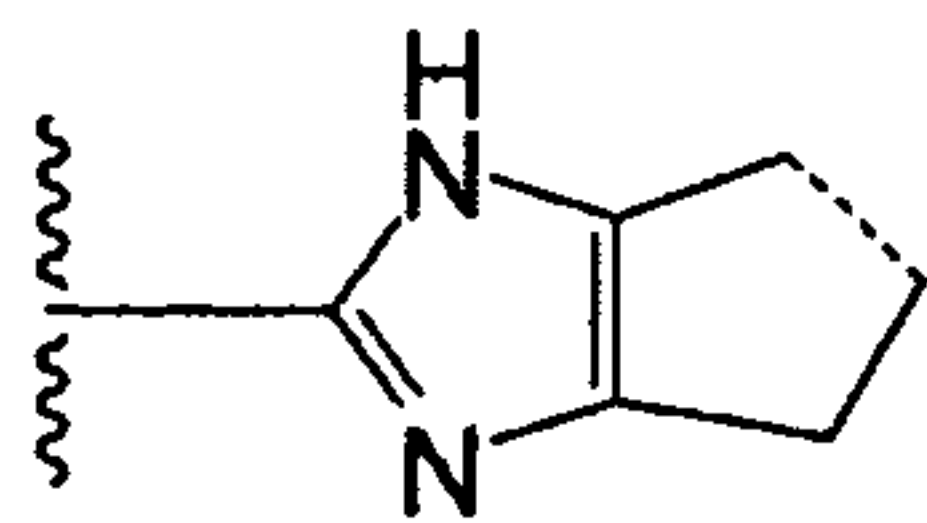
each M^3 is independently:



each M^4 is independently:



each M^5 is independently:



wherein the bond designated with --- is fused to a ring defined for P;

each M^6 is independently a bicyclic bridged ring system comprising 5-15 atoms wherein at least one of the atoms is a heteroatom;

each M^7 is independently a pyrid-di-yl;

each M^8 is independently partially saturated or a saturated five-membered ring that comprises one or more heteroatoms and that is optionally substituted with one or two oxo;

each M^9 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^{P11} ;

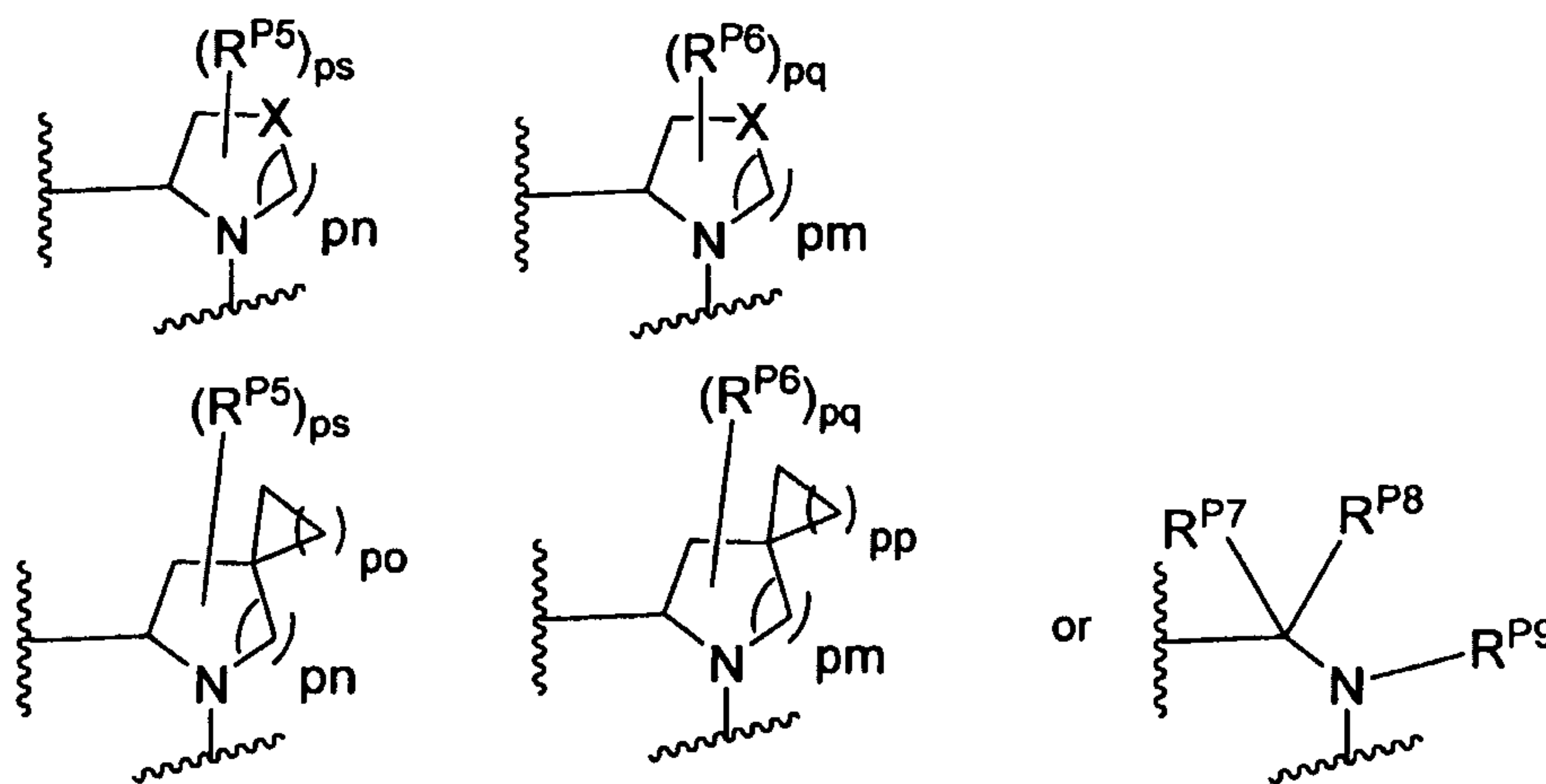
each M^{10} is independently a five membered heteroaryl group substituted with at least one alkoxy, cycloalkyl, cyano, alkylsulfonyl, arylsulfonyl, NR^hR^h , (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cycloalkoxy, heterocyclyl, alkoxyalkyl, cycloalkoxyalkyl, (NR^hR^h) alkyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, and sulfonylalkyl; and wherein the five membered ring is also optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxycarbonyl, carboxy, haloalkyl, and (NR^aR^b) carbonyl;

each M^{11} is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo, halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$; each R^{M7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each M^{12} is independently a fused-pentacyclic, hexacyclic, or heptacyclic partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$;

each R^{M7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each P^0 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

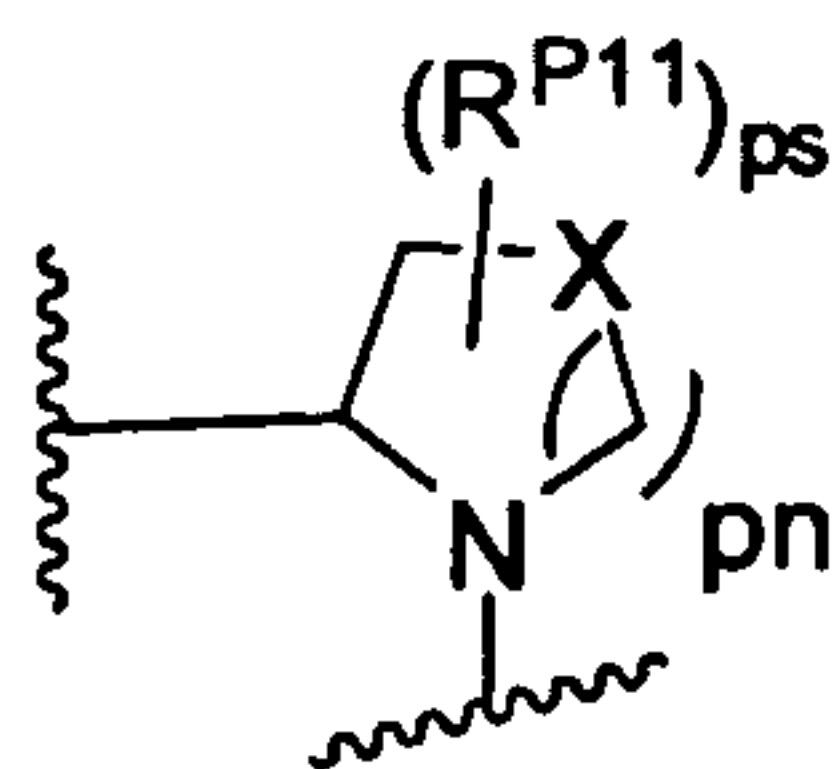
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^1 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

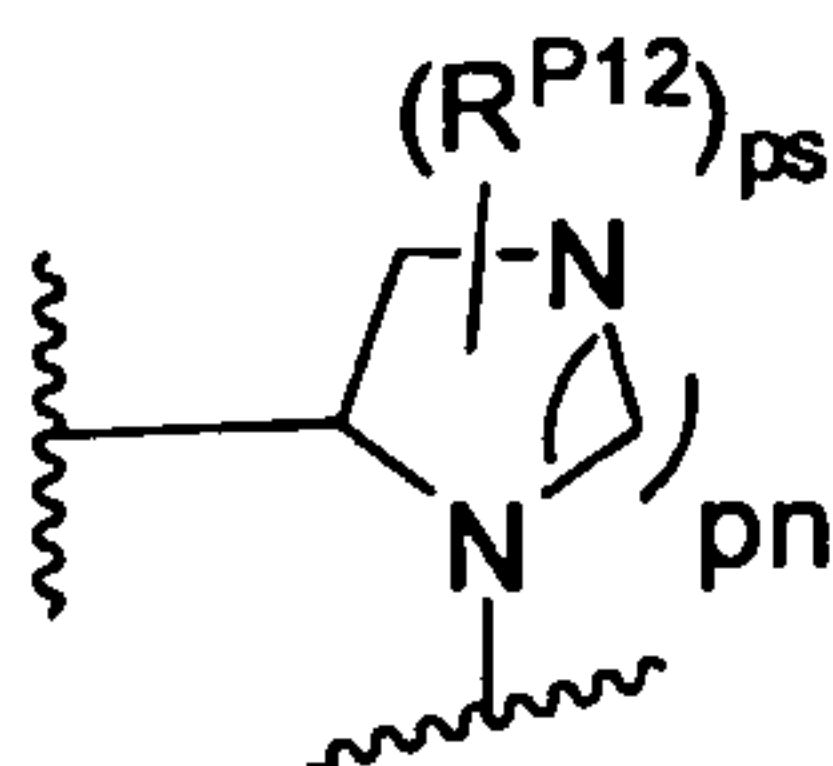
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^ha) lkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy,

haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P² is independently:



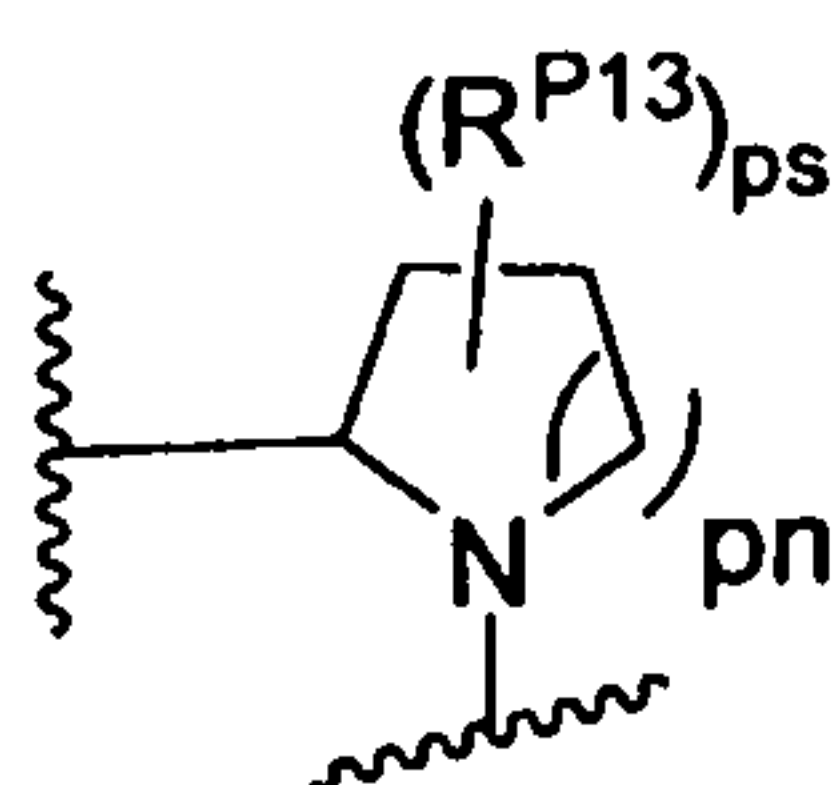
wherein:

each R^{P12} is independently selected from R^{P5}, R^{P11}, -C(=O)OR^h, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P³ is independently a ring of the formula:



wherein:

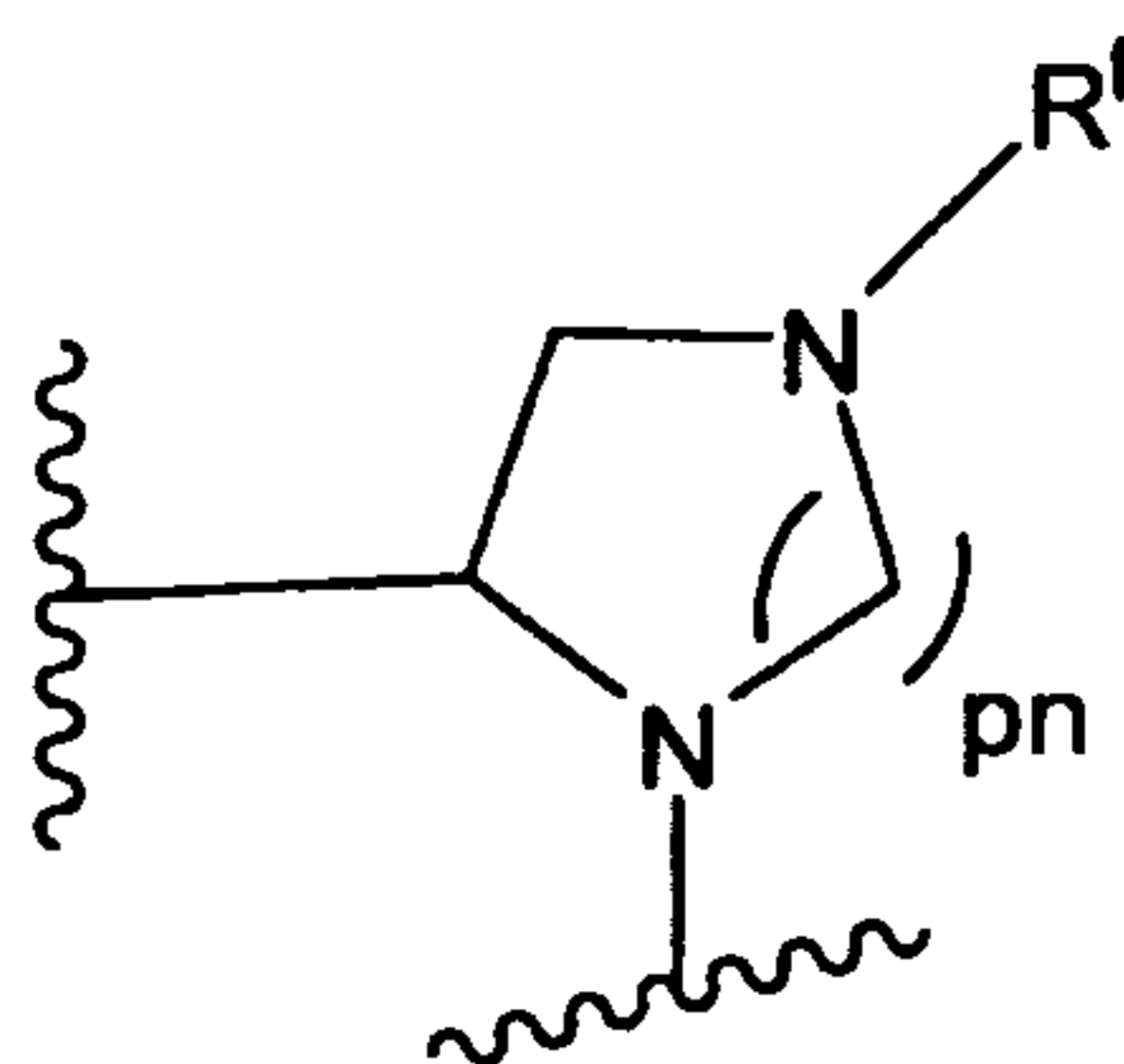
the ring is substituted with one or more oxo group;

each R^{P13} is independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^4 is independently a ring of the formula:



wherein:

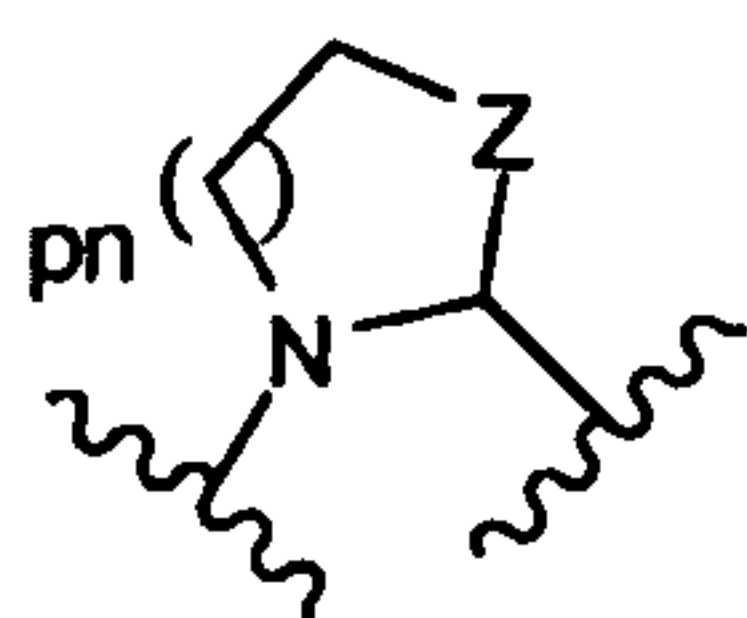
the ring is optionally substituted with one or more groups R^{P14} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P14} that are attached to the same carbon

when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^5 is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

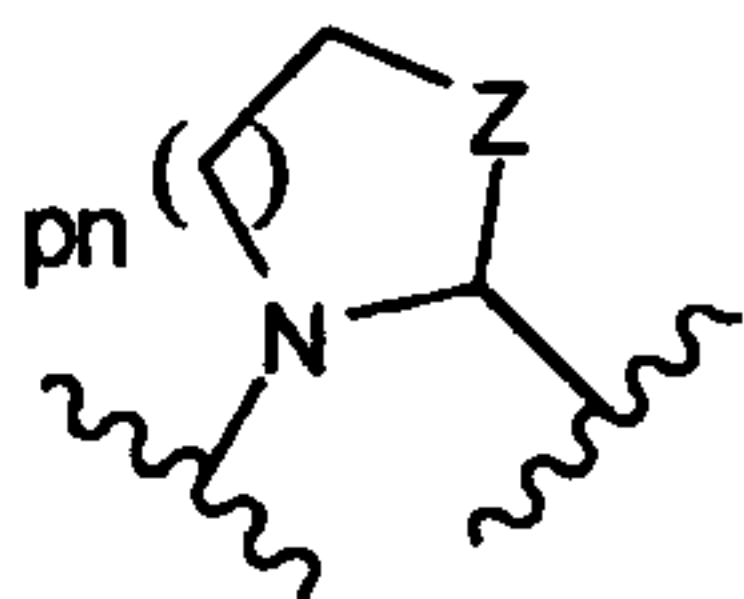
pn is 0, 1, or 2;

Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^6 is independently a ring of the formula:



wherein:

the ring is substituted with one or more oxo and is optionally substituted with one or more groups R^{P16} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

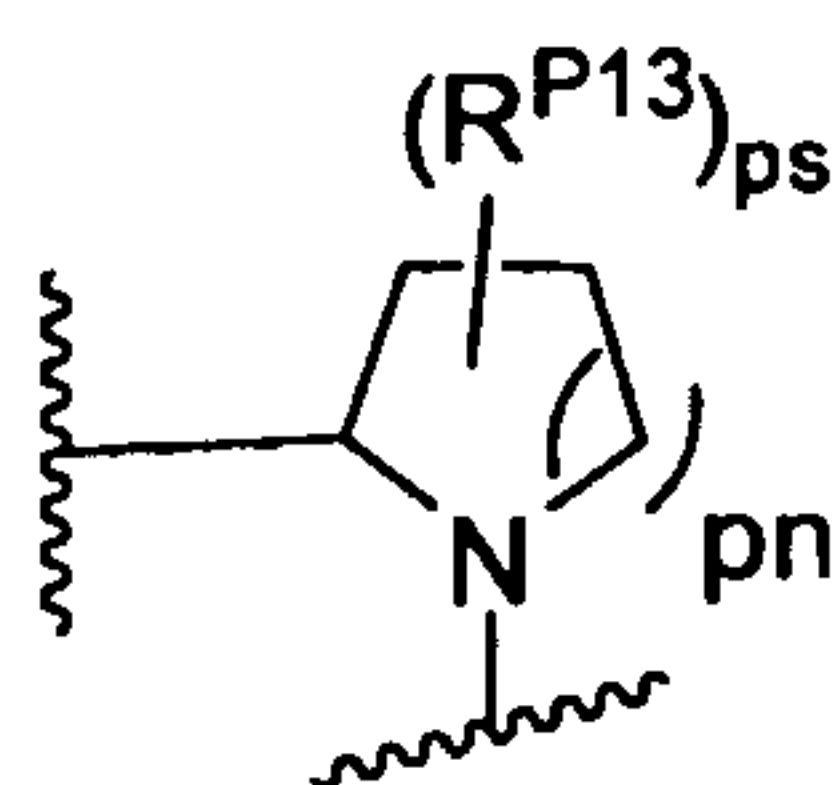
Z is O, S, S(=O), S(=O)₂, or NR^f ;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:



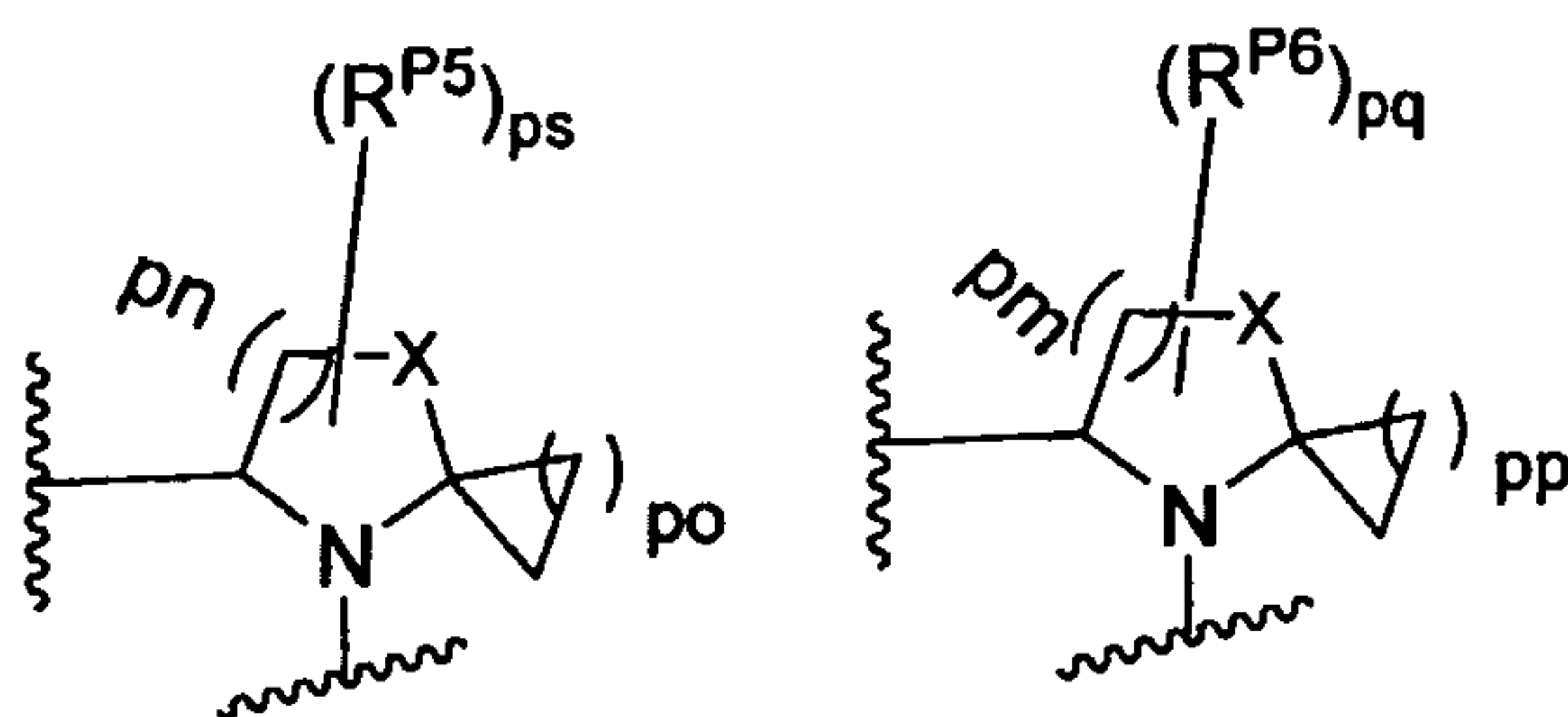
wherein:

ps is 2, 3, 4, 5, or 6;

pn is 0, 1 or 2;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused

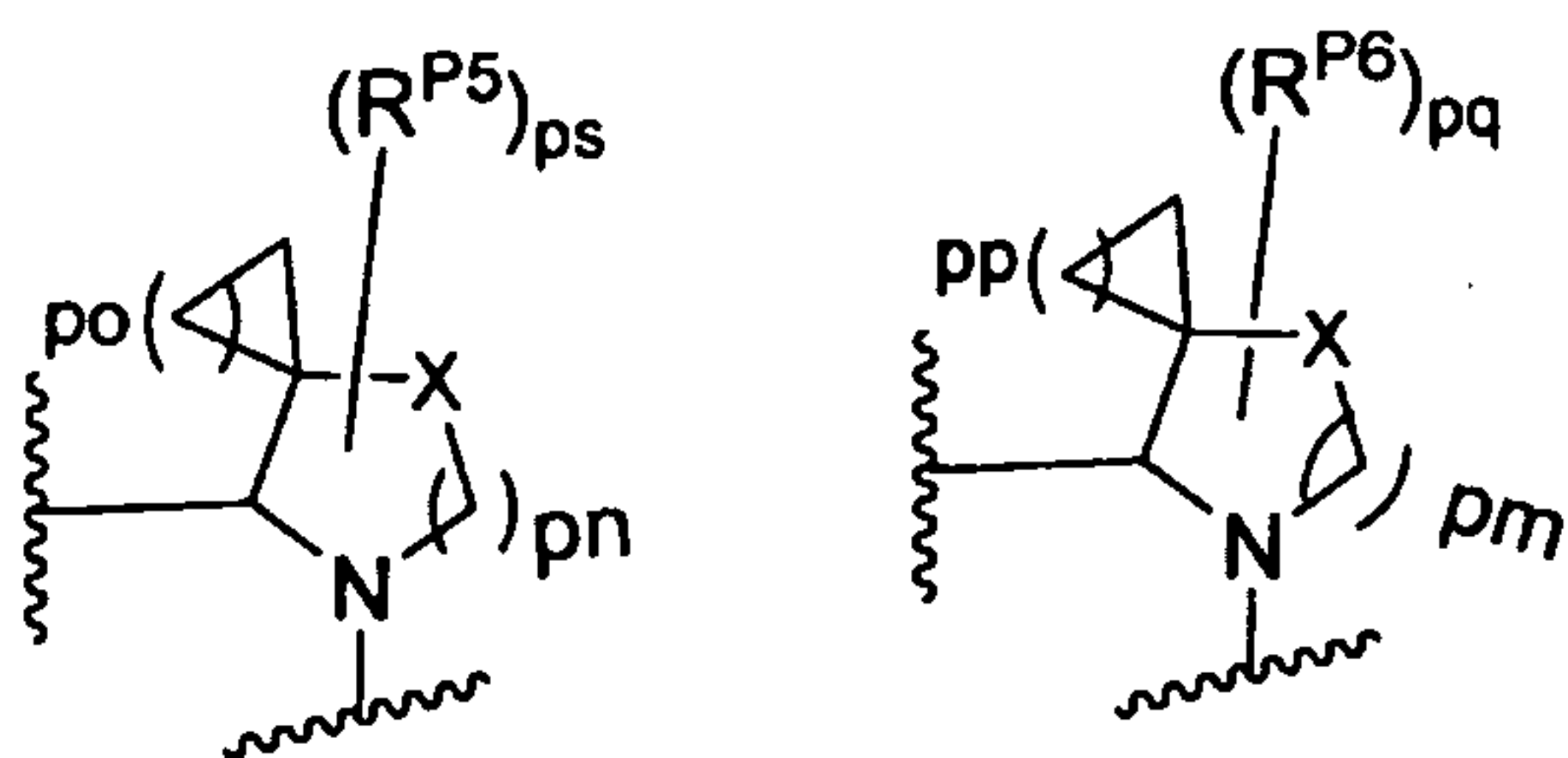
three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{11} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

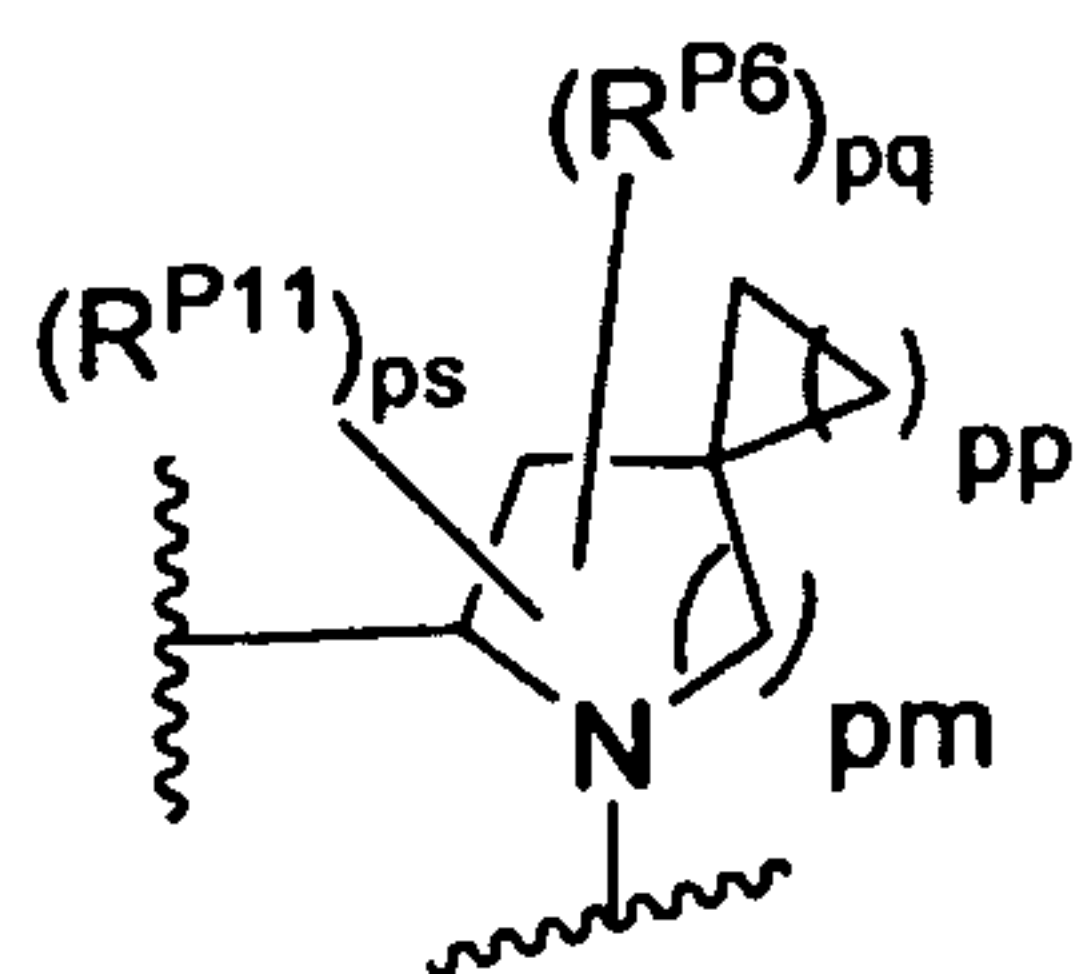
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{12} is independently:



wherein:

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

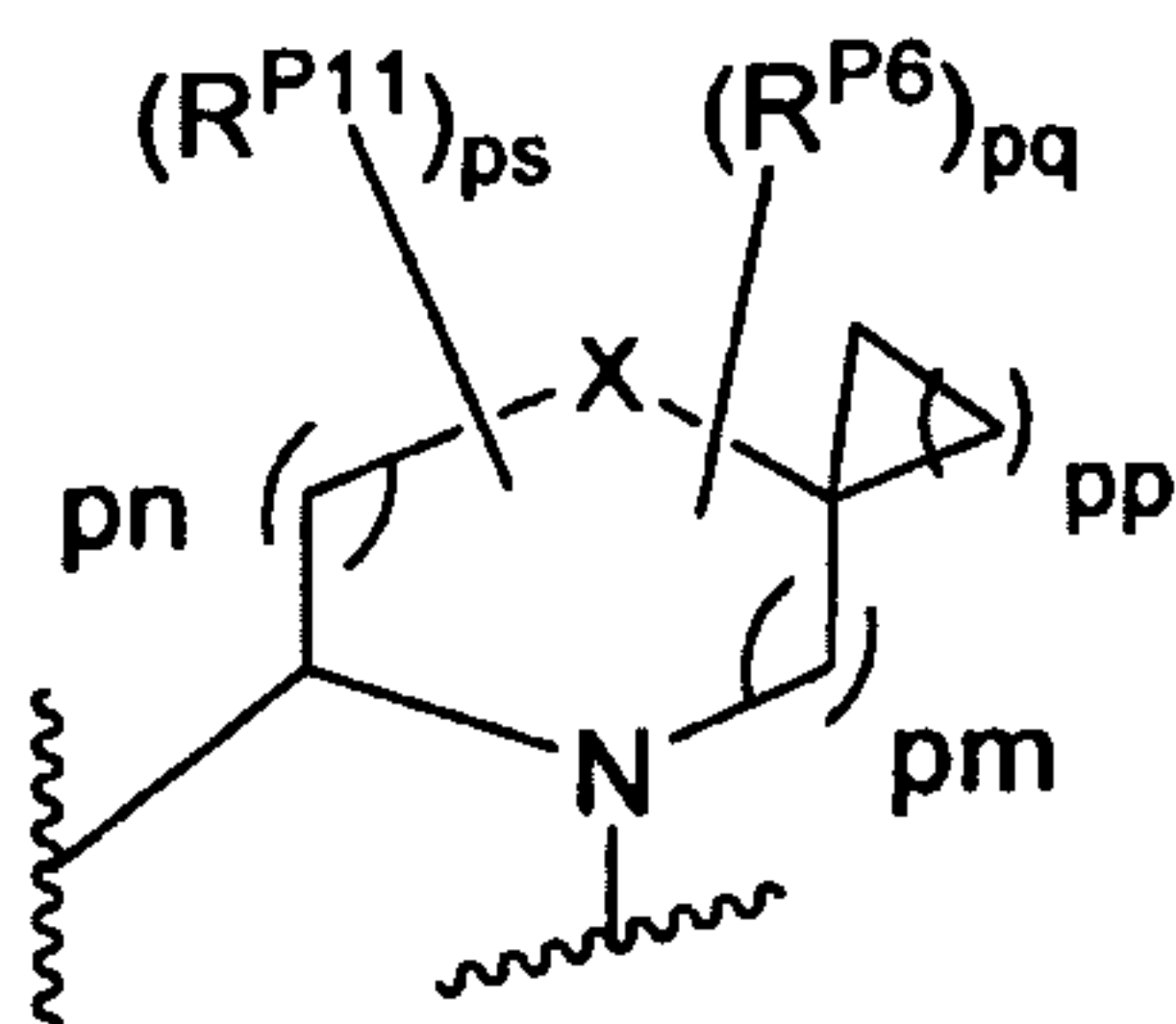
pp is independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$; and the remaining R^{P11} are independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{13} is independently:



wherein:

X is selected from O, S, S(O), SO₂, or NR^h;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2 but the sum of pn and pm is greater than zero;

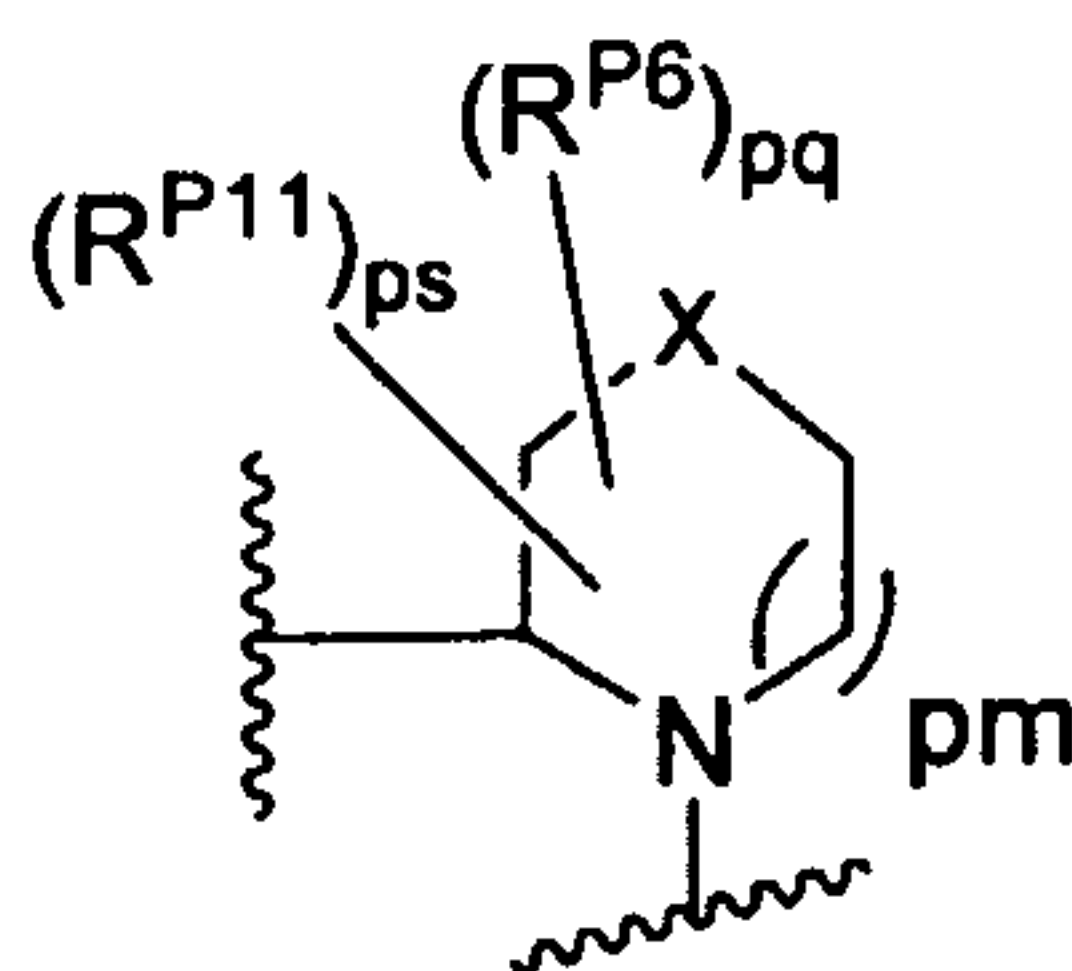
pp are independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^h$, (NR^{hh}R^h)alkyl, (NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$, R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{14} is independently:



wherein:

the ring is substituted with one or more oxo group;

X is NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

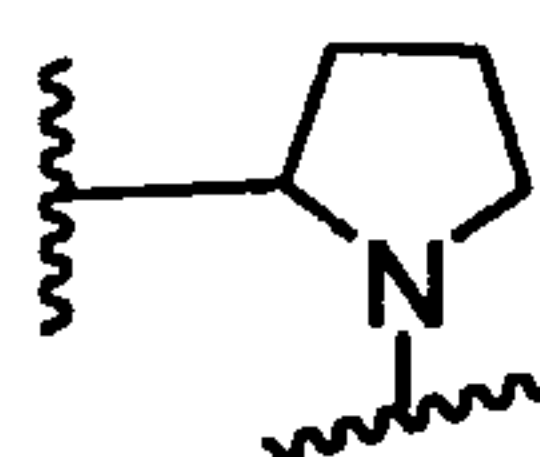
pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

ps is 1, 2, 3, or 4;

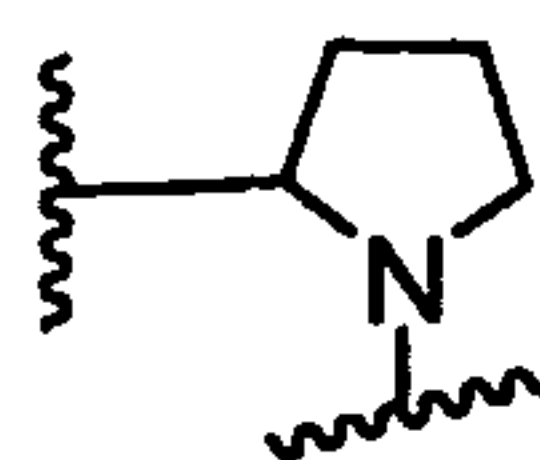
R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy aryloxyalkyloxy, heteroaryloxyakyloxy, heterocyclooxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{15} is:



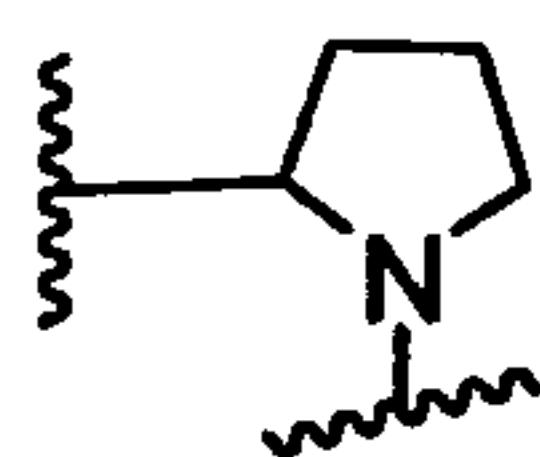
which is substituted with one or two groups independently selected from alkoxyalkyl, haloalkoxyalkyl, alkylsulfonyl, alkylsulfonylalkyl, cyanoalkyl, and cycloalkylalkyl;

each P^{16} is:



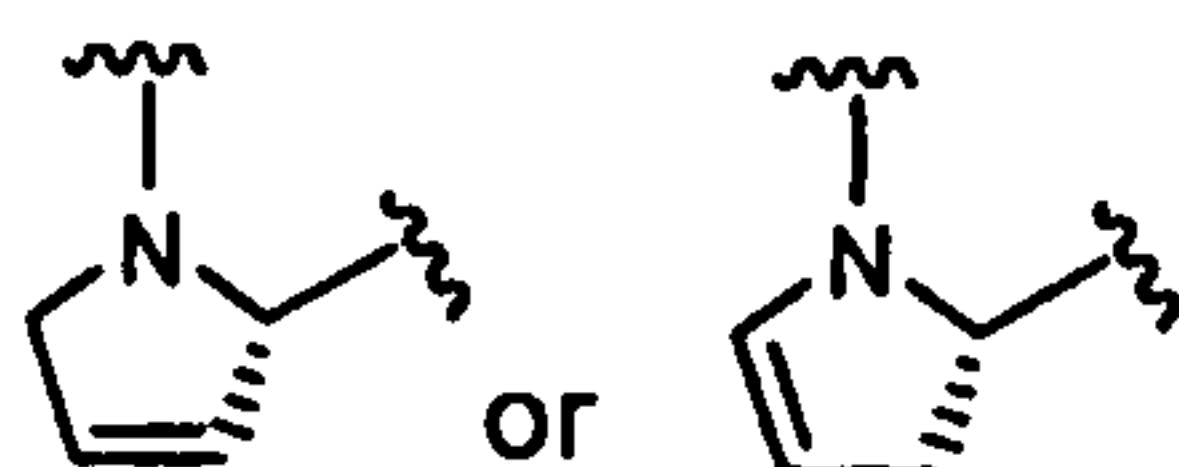
which is substituted with methylene;

each P^{17} is:



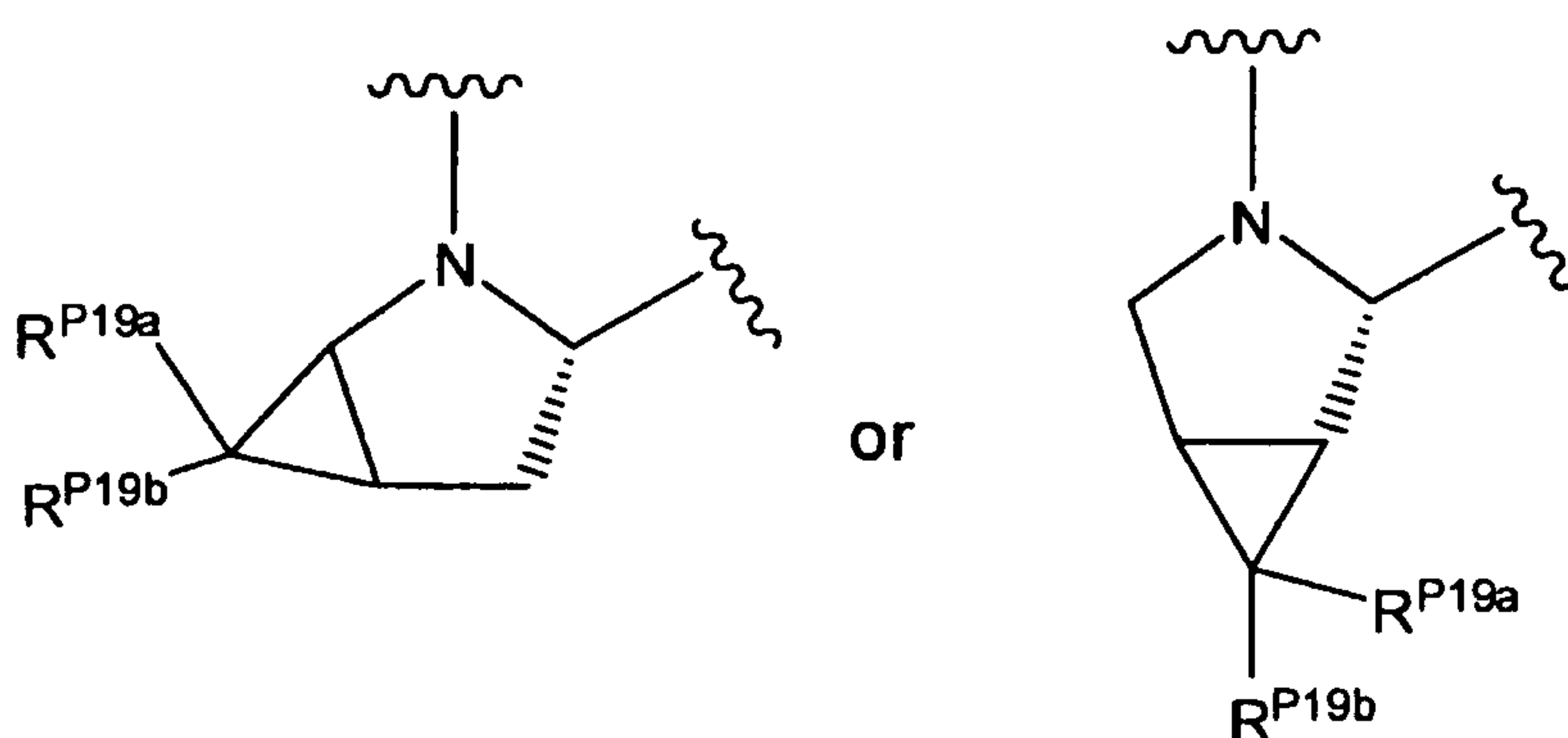
which is substituted with one or two groups independently selected from alkenyl, alkynyl, cycloalkyl, cycloalkylalkenyl, and cycloalkylalkynyl;

each P^{18} is:



which is optionally substituted with one or two groups independently selected from halo, alkyl, alkoxyalkyl, haloalkyl, cycloalkyl, and cycloalkylalkyl;

each P^{19} is:



wherein each R^{P19a} is independently selected from H and halo; and each R^{P19b} is independently selected from halo;

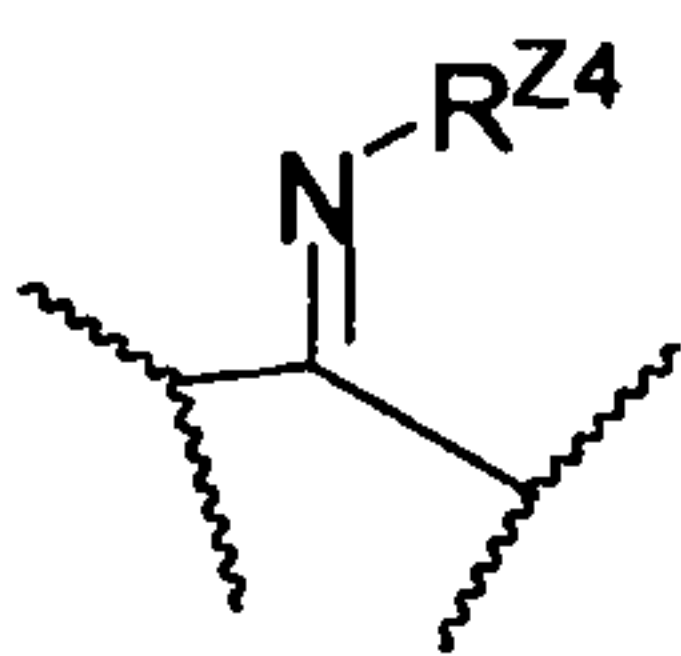
each $-Z^0-$ is $-C(=O)-$ or $-C(=S)-$;

each $-Z^1-$ is independently a bond, or $-C(R^{Z1})_2-$; wherein each R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each $-Z^2-$ is independently saturated or partially unsaturated (C_3-C_8)cycloalkyl that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

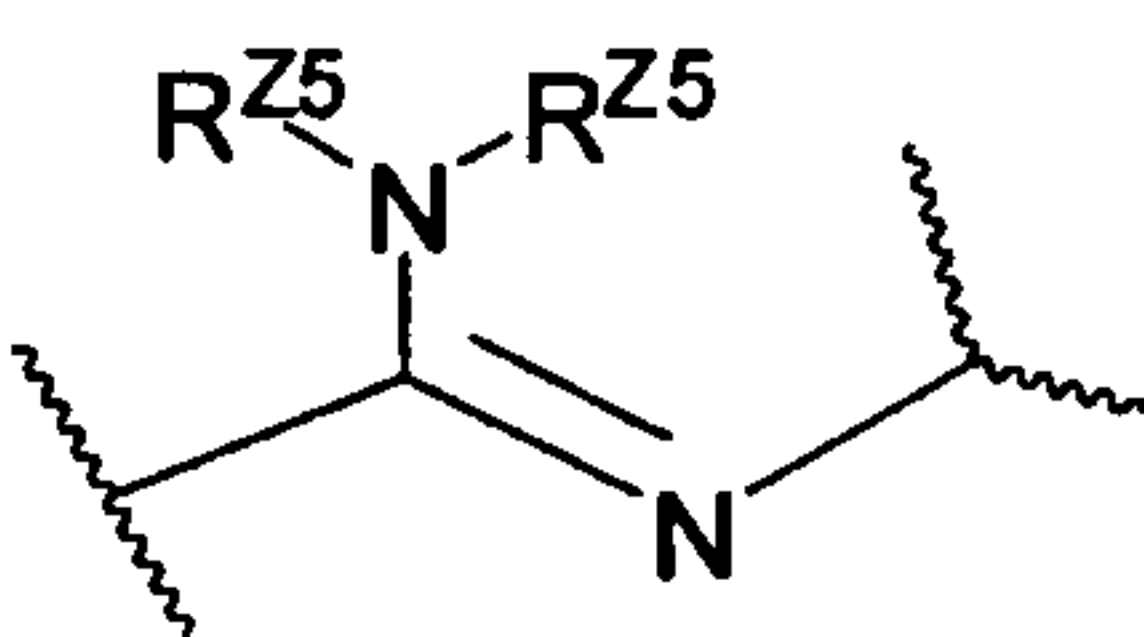
each $-Z^3-$ is independently saturated, partially unsaturated, or aromatic 4-8 membered heterocyclic or heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^4-$ is independently:



wherein each R^{Z4} is independently H, alkyl, cyano, aryl, or heteroaryl;

each $-Z^5-$ is independently:



wherein each R^{Z5} is independently H, alkyl, cyano, aryl, or heteroaryl; or two R^{Z5} s together with the nitrogen to which they are attached form a 4-8 membered heterocyclic ring that is optionally substituted with one or more oxo and with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^6-$ is independently $-C(R^{Z1})-$ and is doublebonded to a carbocyclic P; wherein R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f) alkyl, (NR^eR^f) alkylcarbonyl, (NR^eR^f) carbonyl, (NR^eR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^XR^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^eR^f$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the

heterocyclylcarbonyl, and the heterocyclyloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each E^1 is independently $-OC(=O)NR^{E^c}R^{E^f}$ wherein each R^{E^c} and R^{E^f} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclyloxycarbonyl, hydroxyalkylcarbonyl, (NR^{E^f}) alkyl, (NR^{E^f}) alkylcarbonyl, (NR^{E^f}) carbonyl, (NR^{E^f}) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^X R^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^{E^f}$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclyloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; or wherein R^{E^c} and R^{E^f} , together with the nitrogen atom to which they are attached, form a heterocycle;

each E^2 is independently $-NR^a R^b$, wherein R^a is haloalkyl and R^b is H, alkyl, alkoxycarbonyl or haloalkyl;

each E^3 is independently $-NR^{E^c}R^{E3a}$, wherein R^{E3a} is (C_3-C_6) cycloalkyloxycarbonyl;

each E^4 is independently $-OC(=O)OR^{E4a}$, wherein R^{E4a} is cycloalkyl, aryl, or alkyl;

each E^5 is independently $-NR^{E^c}S(=O)_2OR^{E5a}$, wherein R^{E5a} is cycloalkyl, aryl or alkyl;

each E^6 is independently $-NR^{E^c}S(=O)_2R^{E6a}$, wherein R^{E6a} is cycloalkyl, aryl, or alkyl;

each E^7 is independently $-NR^{E^c}OR^{E7a}$, wherein R^{E7a} is cycloalkyl, aryl, alkyl, haloalkyl, cycloalkylalkyl or heteroaryl;

each V^0 is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxyalkylcarbonylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclalkyl, heterocyclalkylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyloxy, halo, haloalkoxy, haloalkyl, heterocycl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkylcarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocycl, heterocyclalkyl, heterocyclalkylcarbonyl, hydroxy, hydroxyalkyl, nitro,

$-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocycl, and the heterocycl part of the heterocyclalkyl and the heterocyclalkylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; and the heterocycl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkylcarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocycl group, heterocyclalkyl, heterocyclalkylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocycl group, and the heterocycl part of the heterocyclalkyl and the heterocyclalkylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; wherein R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^6 is independently arylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^7 is independently heterocyclosulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^8 is independently spirocycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^9 is independently spirocycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{10} is independently fusedbicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{11} is independently fusedbicycliccycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{12} is independently bridged-bicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{13} is independently bridged-bicyclic-cycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{14} is independently aryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{15} is independently arylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O^-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{16} is independently cycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{17} is independently cycloalkylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{18} is independently heterocyclooxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{19} is independently heterocycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{20} is independently heteroaryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{21} is independently heteroarylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{22} is independently cycloalkenylalkyl;

each V^{23} is independently arylalkyl, wherein the aryl is substituted with one or more groups independently selected from cycloalkyl, alkenyl, cycloalkylalkyl, cyanoalkyl, cycloalkoxy, hydroxyalkoxy, $-C(=O)NR^XR^Y$, $S(=O)_2NR^XR^Y$, alkylsulfanyl, alkylsulfonyl, haloalkylsulfanyl,

haloalkylsulfonyl, alkylsulfonylalkyl, alkylsulfonylalkyl, arylsulfanyl, arylsulfonyl, alkoxyalkoxy, alkynyl, aryloxy, heteroaryloxy, alkylsulfonylamino;

R^X and R^Y are independently selected from hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, unsubstituted aryl, unsubstituted arylalkoxy carbonyl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted heterocyclyl, and $(NR^X R^Y)$ carbonyl, wherein R^X and R^Y are independently selected from hydrogen and alkyl;

each V^{24} is independently heterocycloalkyl, wherein the heterocycle is substituted with one or more groups independently selected from cycloalkyl, alkenyl, cycloalkylalkyl, cyanoalkyl, cycloalkoxy, hydroxyalkoxy, $-C(=O)NR^X R^Y$, $S(=O)_2 NR^X R^Y$, alkylsulfanyl, alkylsulfonyl, haloalkylsulfanyl, haloalkylsulfonyl, alkylsulfonylalkyl, alkylsulfonylalkyl, arylsulfanyl, arylsulfonyl, alkoxyalkoxy, alkynyl, aryloxy, heteroaryloxy, alkylsulfonylamino;

R^X and R^Y are independently selected from hydrogen, alkoxy carbonyl, alkyl, alkyl carbonyl, unsubstituted aryl, unsubstituted arylalkoxy carbonyl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted heterocyclyl, and $(NR^X R^Y)$ carbonyl, wherein R^X and R^Y are independently selected from hydrogen and alkyl;

each T^1 is independently a spiro, branched or fused bicycloalkyl;

each T^2 is independently aryl;

each T^3 is independently heteroaryl;

each T^4 is independently arylalkyl;

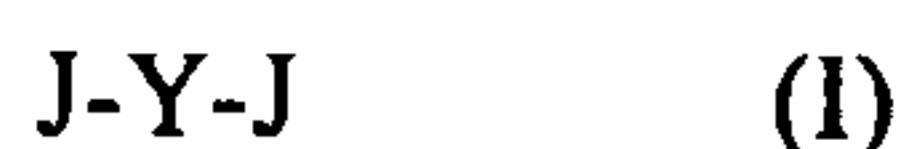
each T^5 is independently haloalkyl;

each T^6 is independently heteroarylalkyl;

each T^7 is independently heterocycle; and

each T^8 is independently heterocycloalkyl.

In another specific embodiment the invention provides a compound of formula (I):



wherein:

Y is $-L-L-$, $-M-W-M-$ or Y^y ;

J is $T-P-$, $-P-T$ or $-J^m$;

W is a bond or $-W^r$;

L is $-M-A-$, $-A-M-$, or $-L^n$;

T is R^9-Z- , $-Z-R^9$, or $-T^p$;

R⁹ is E-V-, or -V-E, or -R^{9q};
 each A is selected from -A^s;
 each M is selected from -M^t;
 each P is selected from -P^u;
 each Z is selected from -Z^v;
 each V is selected from -V^w;
 each E is selected from -E^x;
 each m is 1;
 each n is 0, 1, 2, 3, 4, 5, 6, 7, 9, or 10;
 each p is 1, 2, 3, 4, 5, 6, 7, or 8;
 each q is 0, 1, 2, or 3;
 each r is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20;
 each s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 21;
 each t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11;
 each u is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, or 14;
 each v is 0, 1, 2, 3, 4, 5, or 6;
 each w is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21;
 each x is 0 or 1;
 each y is 0, 1, or 2;

wherein the sum of m, n, p, q, r, s, t, u, v, w, x, and y is not 0; P is connected to M, L, or Y^y; A is connected to A or L; M is connected to P or J; Z is connected to P; V is connected to Z; and when W is a bond M is connected to M;

each Y¹ is independently:

a fused nine-ring system with up to thirty-five atoms that may be fully aromatic or partially saturated and contains atoms selected from C, N, O, and S, and which ring system is optionally substituted with one or more groups independently selected from H, oxo, R^{A1} and R^{A3};

each Y² is independently:

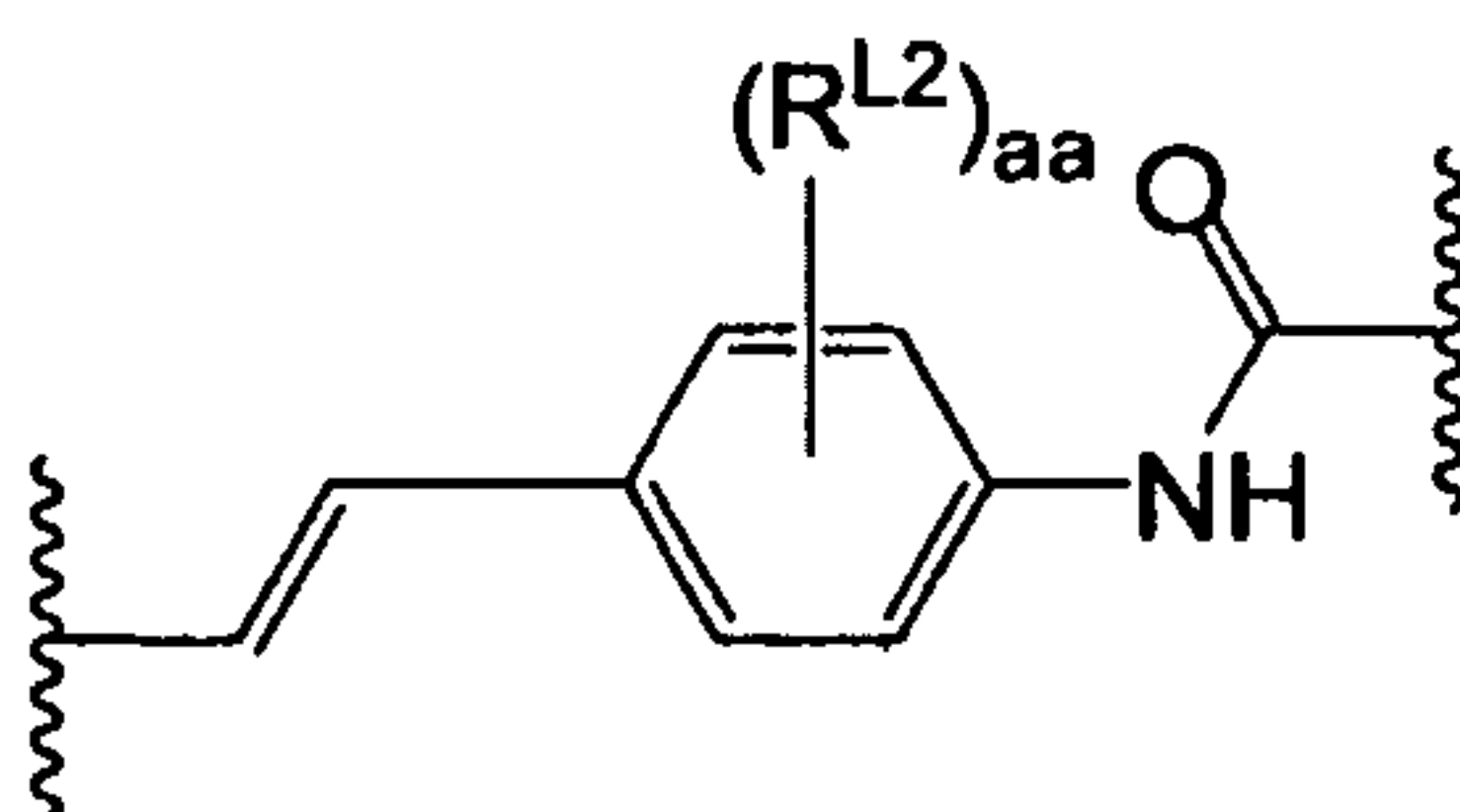
a fused five to eight ring system with up to thirty-two atoms that may be fully aromatic or partially saturated and contains atoms selected from C, N, O, and S, and which ring system is optionally substituted with one or more groups independently selected from H, oxo, R^{A1} and R^{A3};

each J^1 is independently a fused bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is substituted with one or more $-N(R^{L7})C(=O)OR^{L7}$, and that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^0 is independently:

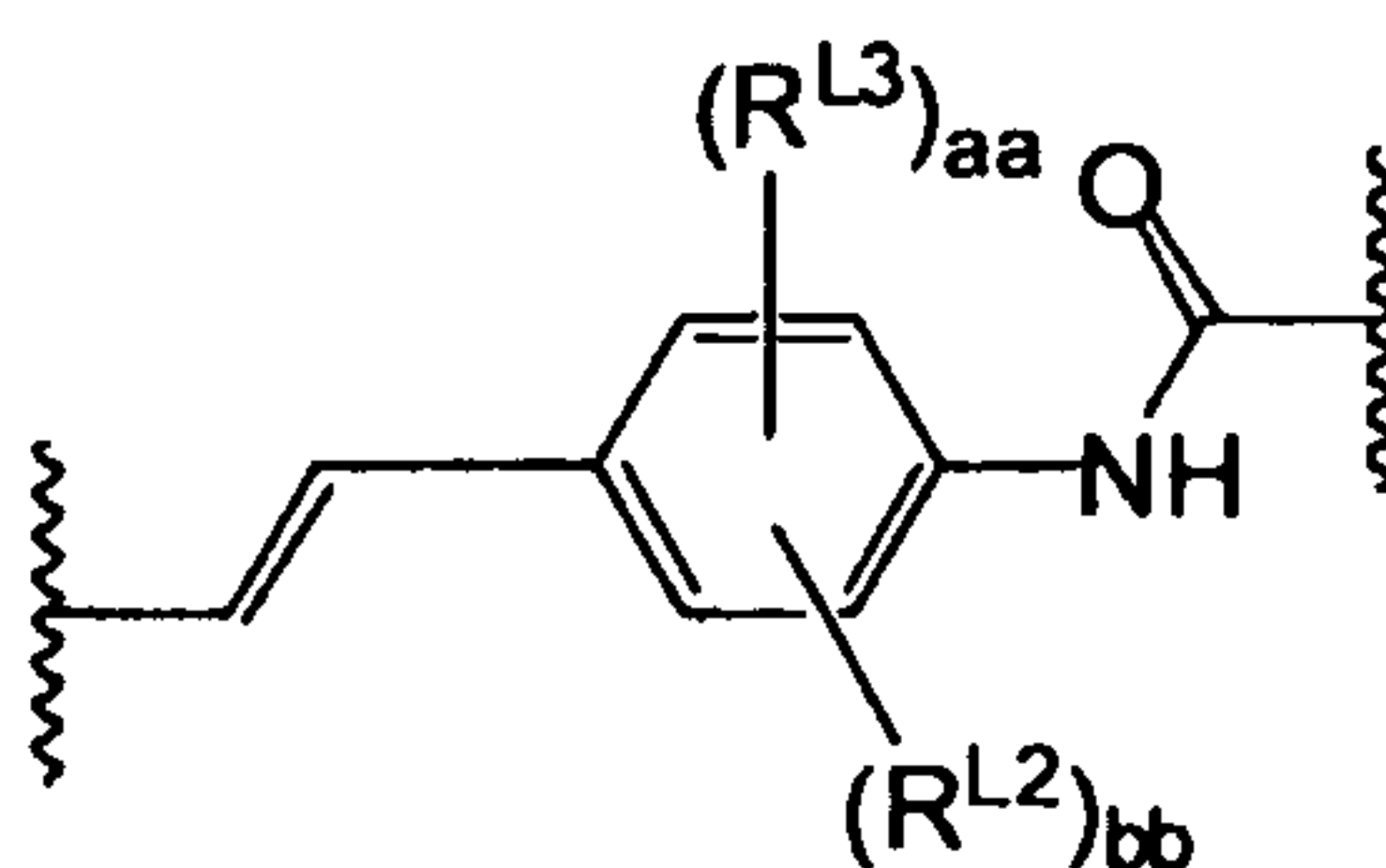


wherein:

each R^{L2} is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl; and

each aa is independently 1, 2, 3, or 4;

each L^1 is independently:



wherein:

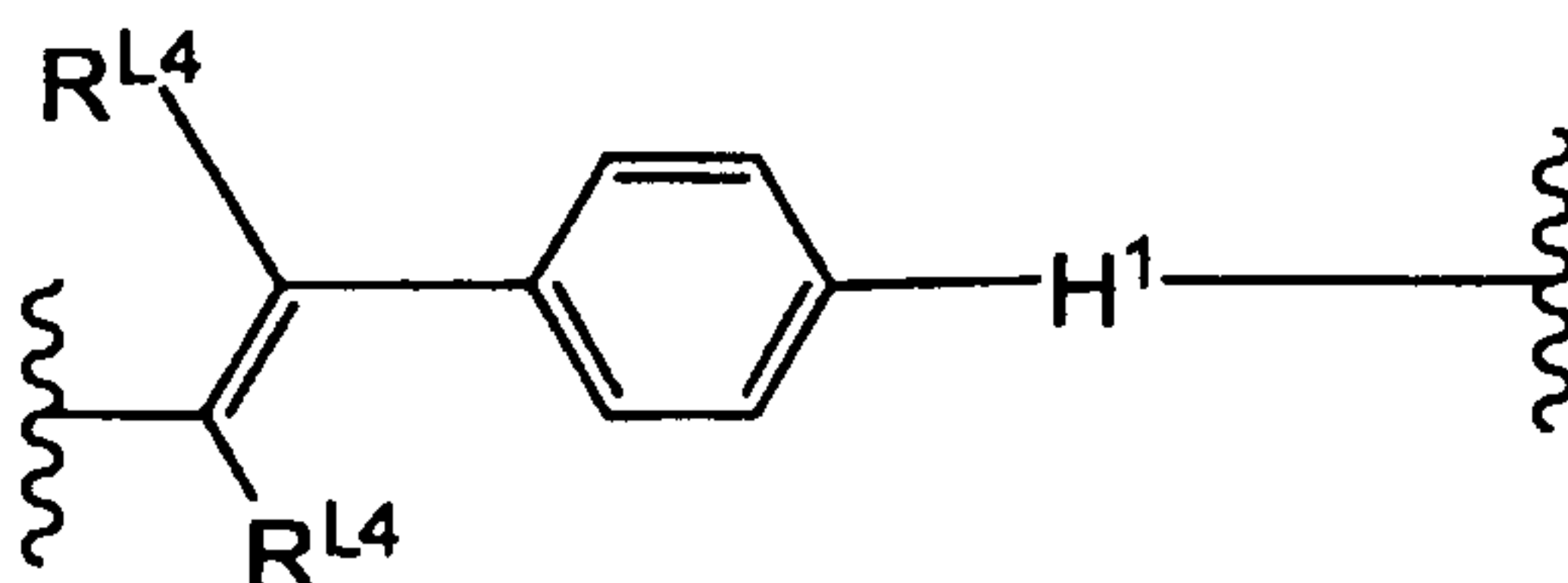
each R^{L2} is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl;

each R^{L3} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each bb is 0, 1, 2, 3, or 4; each aa is 1, 2, 3, or 4; and the sum of bb and aa is 1, 2, 3, or 4;

each L^2 is independently:



wherein:

the phenyl ring shown in L^2 is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, $(NR^aR^b)alkyl$, $(NR^aR^b)carbonyl$, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{L4} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl; and

each H^1 is a 5 membered saturated, partially unsaturated, or aromatic ring comprising one or more heteroatoms;

each L³ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁴ is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁵ is independently a -CR=CR-fusedbicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R is independently selected from H or alkyl;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

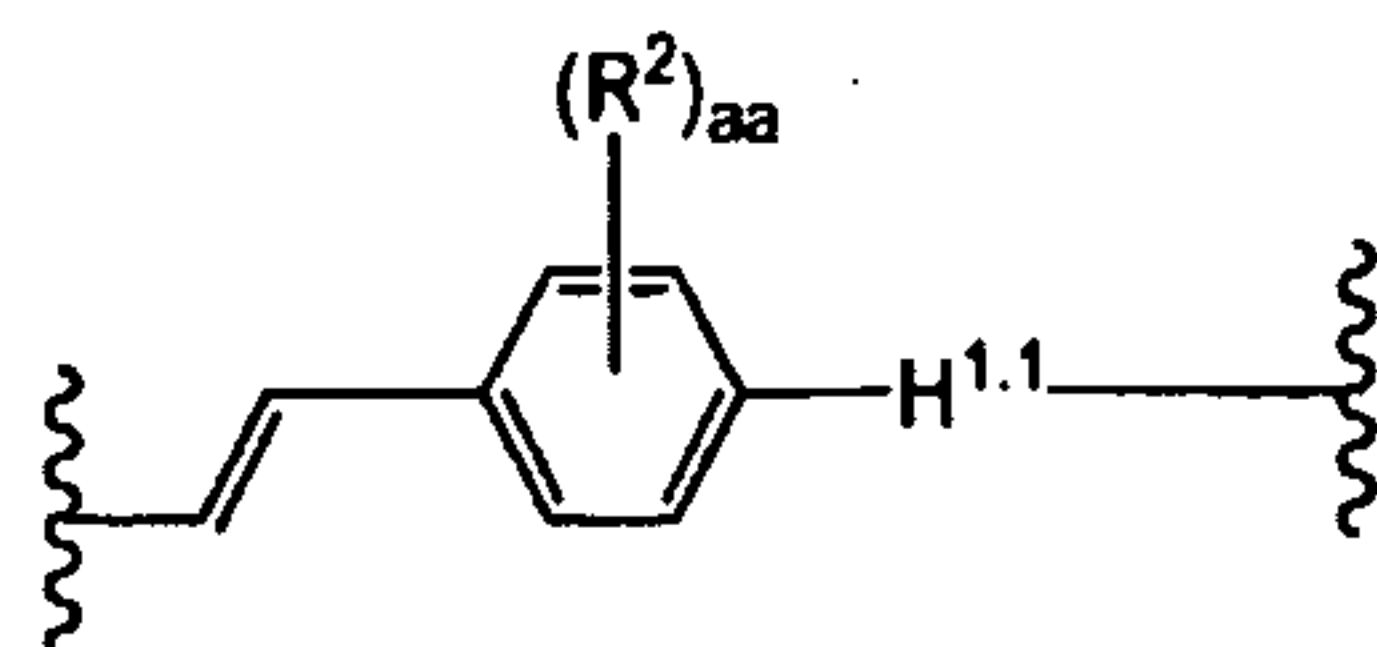
each L^6 is independently a $-CR=CR-$ fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R is independently selected from H or alkyl;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^7 is independently:



wherein:

each $H^{1.1}$ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^2 ;

each R^2 is independently selected from halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-N(R^{L7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, and $-S(=O)_2NR^{L7}$;

each R^{L7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle; and

each aa is independently 1, 2, 3, or 4;

each L^9 is independently a fused-tetracyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^{10} is independently a fused-pentacyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^{11} is independently a six-ring fused saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, $-S(=O)_2NR^{L7}$, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each R⁹⁰ is independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, aryloxyalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, cycloalkyloxyalkyl, haloalkyl, heterocyclyl, heterocyclylalkenyl, heterocyclylalkoxy, heterocyclylalkyl, heterocycliloxyalkyl, hydroxyalkyl, -NR^cR^d, (NR^cR^d)alkenyl, (NR^cR^d)alkyl, and (NR^cR^d)carbonyl;

R^c and R^d are independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocycliloxyalkyl, hydroxyalkylcarbonyl, (NR^eR^f)alkyl, (NR^eR^f)alkylcarbonyl, (NR^eR^f)carbonyl, (NR^eR^f)sulfonyl, -C(NCN)OR', and -C(NCN)NR^xR^y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one -NR^eR^f group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocycliloxyalkyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

R^x and R^y are independently selected from hydrogen, alkoxycarbonyl, alkyl, alkylcarbonyl, unsubstituted aryl, unsubstituted arylalkoxycarbonyl, unsubstituted arylalkyl, unsubstituted cycloalkyl, unsubstituted heterocyclyl, and (NR^xR^y)carbonyl, wherein R^x and R^y are independently selected from hydrogen and alkyl;

each R⁹¹ is independently -N(R^{9a})-NHC(=O)O-R^{9b}, wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl, aryloxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups

independently selected from alkoxy, alkylocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyacetyl, alkyl, alkylacetyl, a second aryl group, arylalkoxy, arylalkyl, arylacetyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylacetyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylacetyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylacetyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyacetyl, alkyl, alkylacetyl, aryl, arylalkyl, arylacetyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylacetyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylacetyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylacetyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

each R^{92} is independently $-N(R^{9a})-NHC(=O)NR^{9b} 2$; wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylacetylalkyl, alkoxyacetylalkyl, alkylsulfanylalkyl, arylalkoxyalkylacetylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylacetylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, a second aryl group, arylalkoxy, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyl carbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the aryl carbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclyl carbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aryl, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclyl carbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the aryl carbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclyl carbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

each R^{9^3} is independently $-N(R^{9a})-NHC(=O)R^{9b}$, wherein each R^{9a} is independently arylalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkoxy, halocycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkoxy, alkylSO₂alkyl, cycloalkylalkylSO₂alkyl, cyanoalkyl, haloalkyl cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkyl carbonylalkyl, alkoxy carbonylalkyl, alkylsulfanylalkyl, arylalkoxyalkyl carbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclyl carbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from H or alkyl;

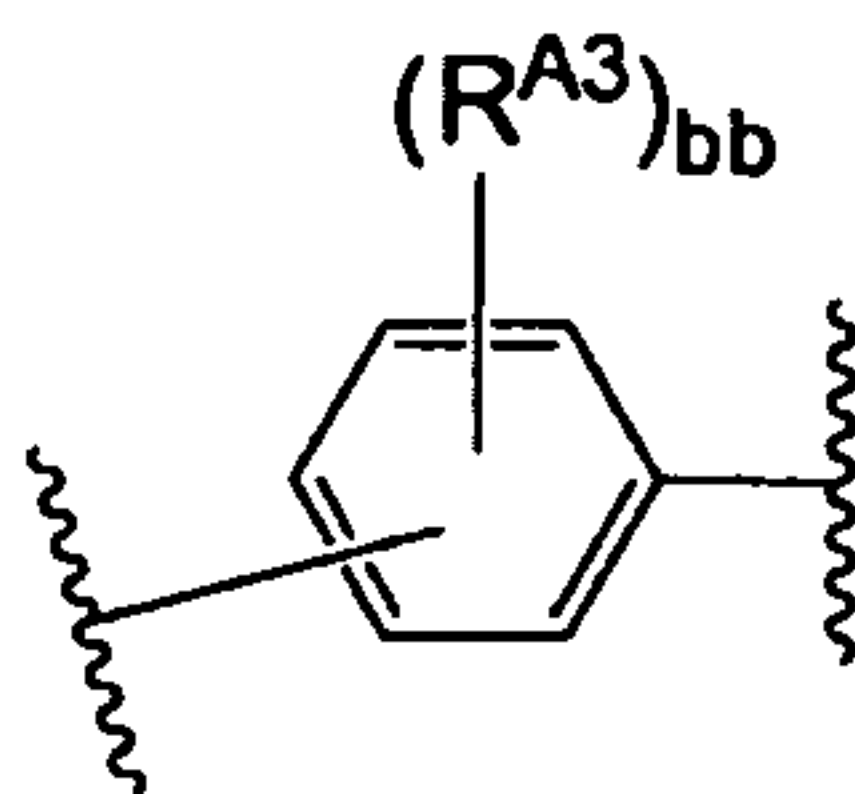
and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkoxy carbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, a second aryl group, arylalkoxy, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl,

heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)alkyl$, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocycl, and the heterocycl part of the heterocyclalkyl and the heterocyclcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocycl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocycl group, heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)alkyl$, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocycl group, and the heterocycl part of the heterocyclalkyl and the heterocyclcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; R^{9b} is independently H, alkyl, aryl, haloalkyl, or arylalkyl;

each A^0 is independently:



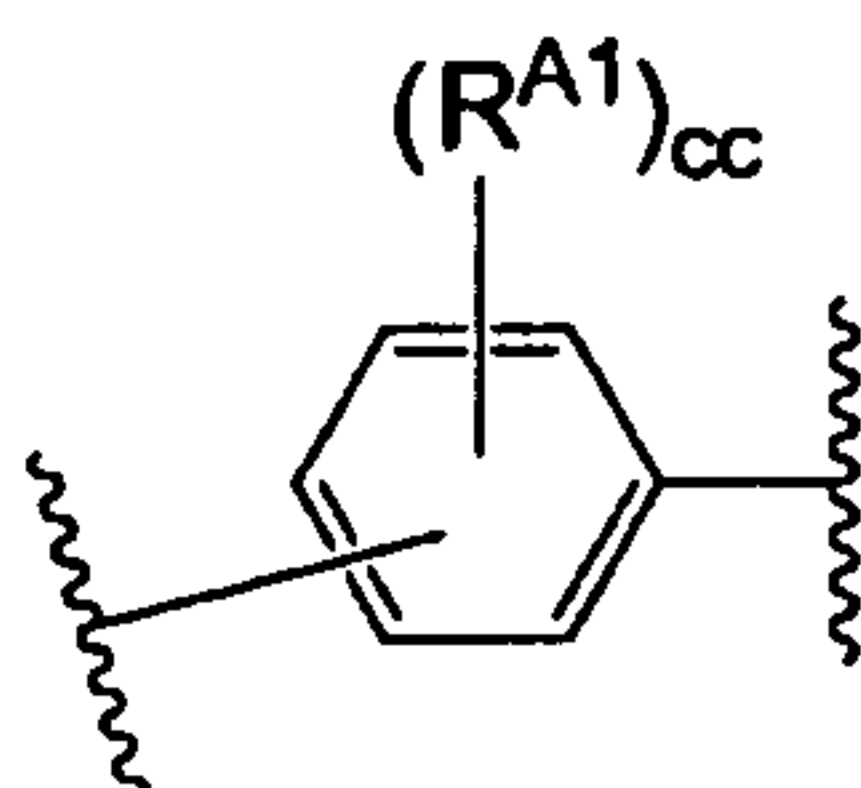
wherein:

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^a R^b$, $(NR^a R^b)alkyl$, and $(NR^a R^b)carbonyl$; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocycl, and heterocyclalkyl; and each

bb is independently 0, 1, 2, 3, or 4; or

each A^0 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is optionally substituted with 1, 2, 3, or 4 R^{A3} groups;

each A^1 is independently:



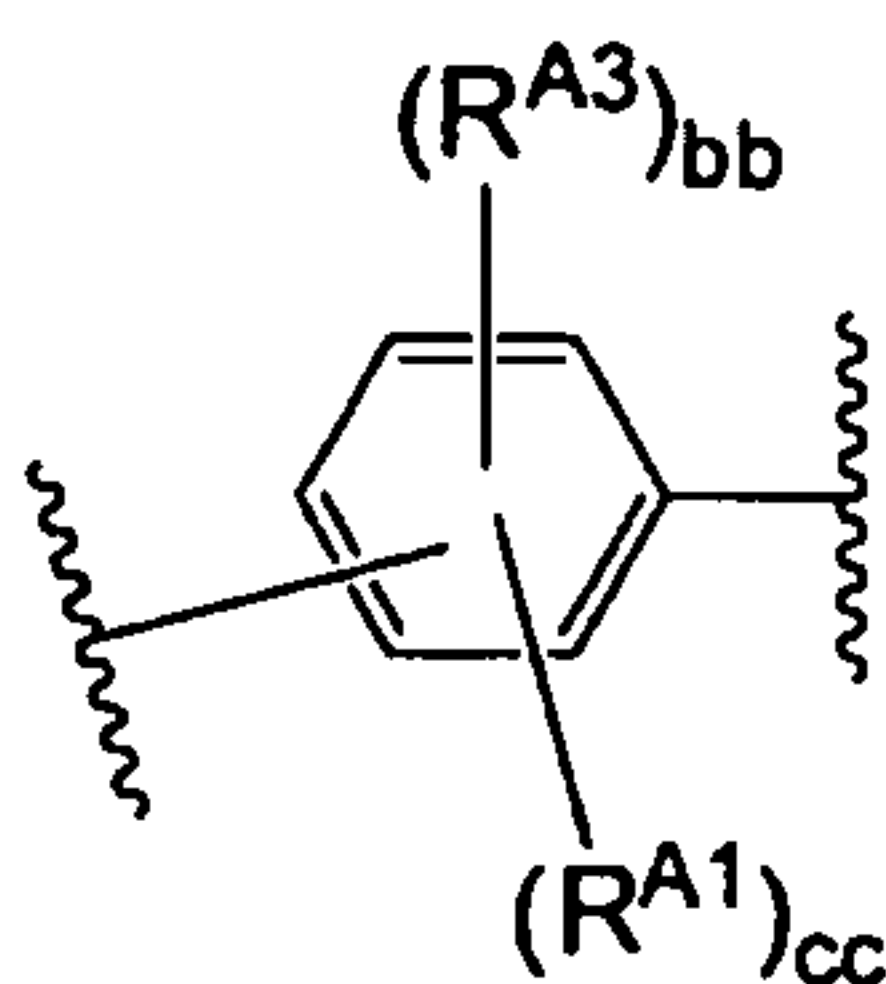
wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each cc is independently 1, 2, 3, or 4;

each A^2 is independently:



wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, $(NR^aR^b)alkyl$, and $(NR^aR^b)carbonyl$; R^a and R^b are each independently selected from the group

consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

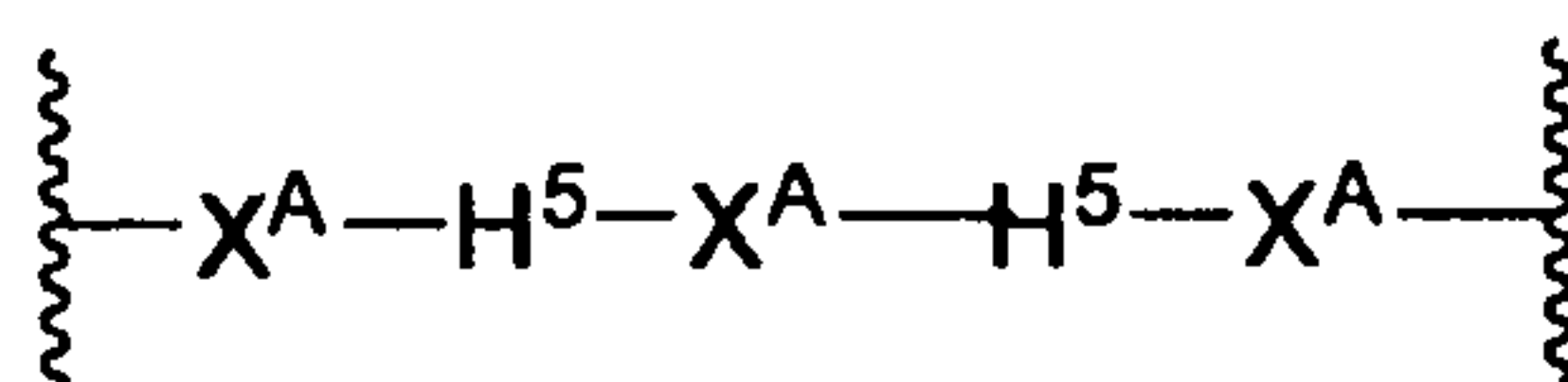
each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is 0, 1, 2, 3, or 4; each cc is 1, 2, 3, or 4; and the sum of bb and cc is 1, 2, 3, or 4;

each A^3 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is substituted with one or more R^{A1} groups, and which ring is optionally substituted with one or more R^{A3} groups;

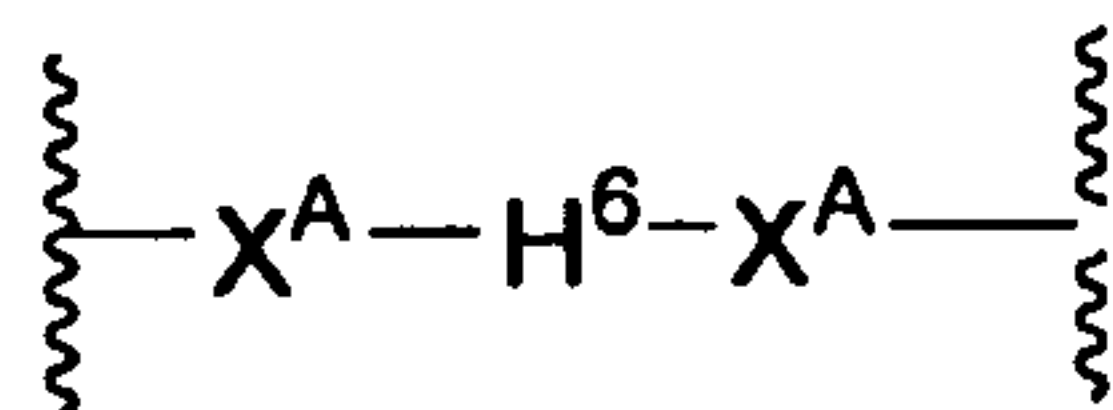
each A^4 is independently:



wherein:

each H^5 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^5 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

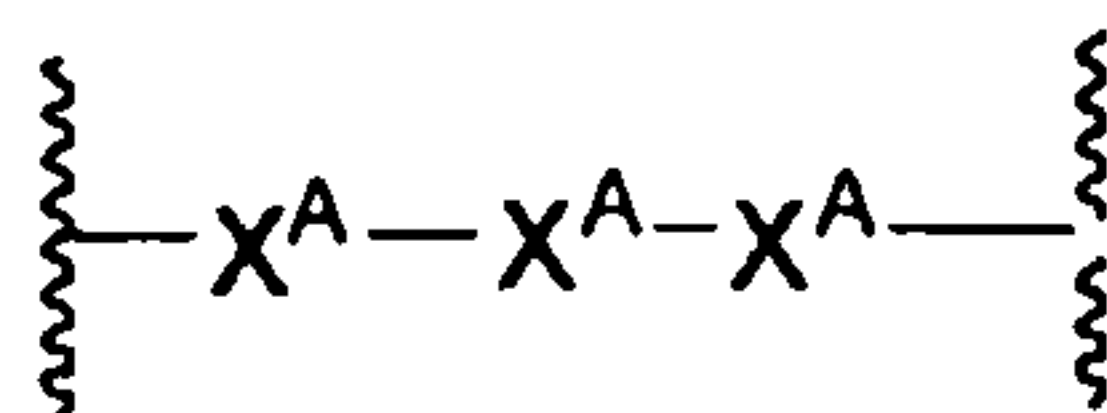
each A^5 is independently:



wherein:

each H^6 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^6 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent; provided that at least one X^A is present and each R is independently selected from H or alkyl;

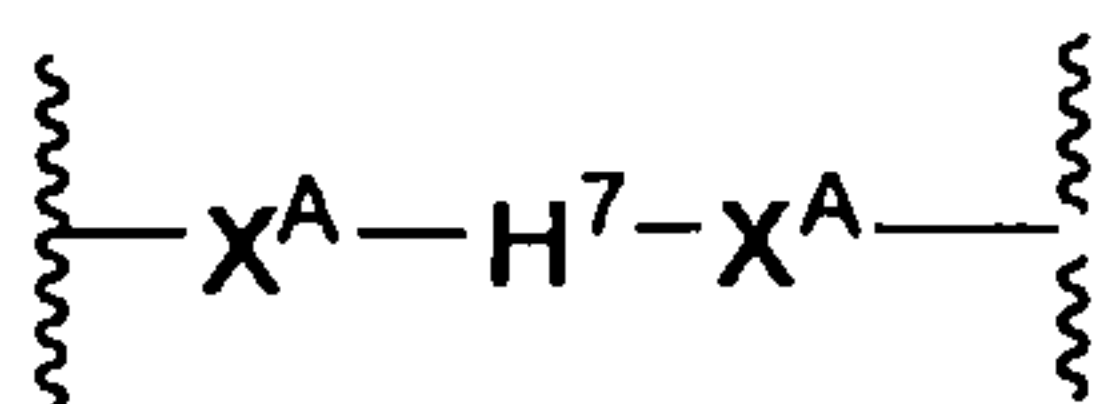
each A⁶ is independently:



wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, allenyl, alkynyl, or absent; provided that at least one X^A is present and each R is independently selected from H or alkyl;

each A⁷ is independently:

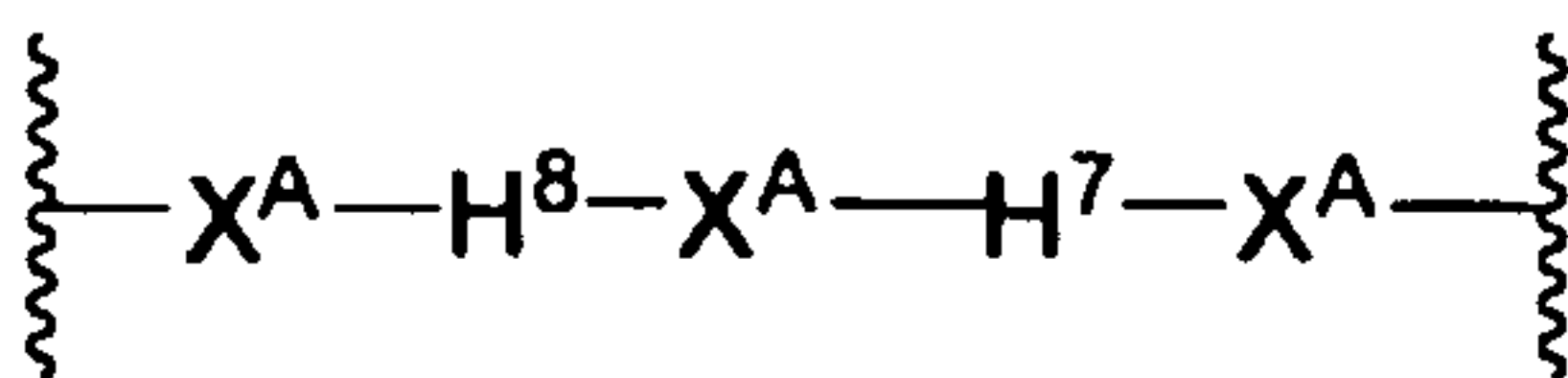


wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A⁸ is independently:



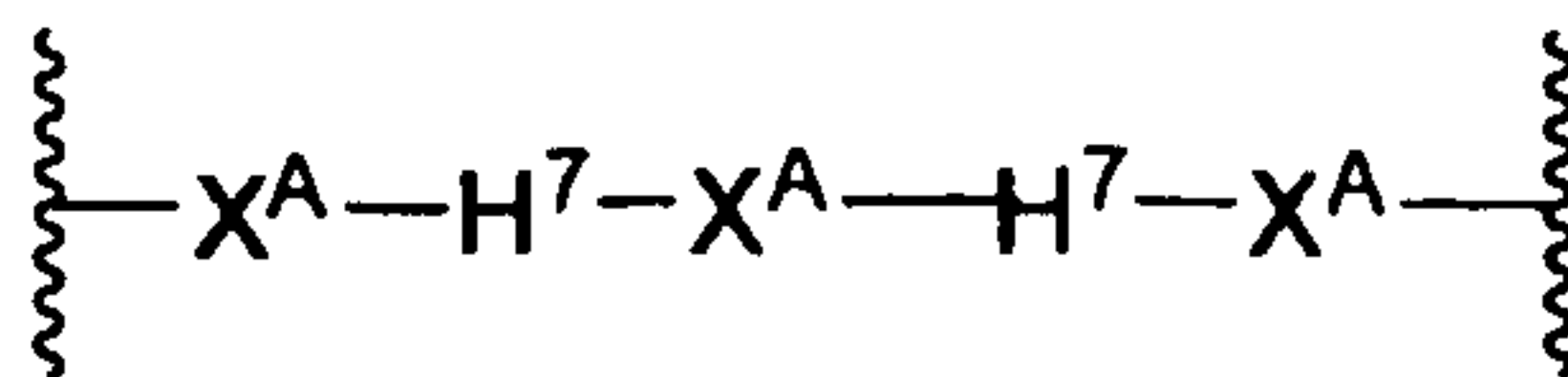
wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

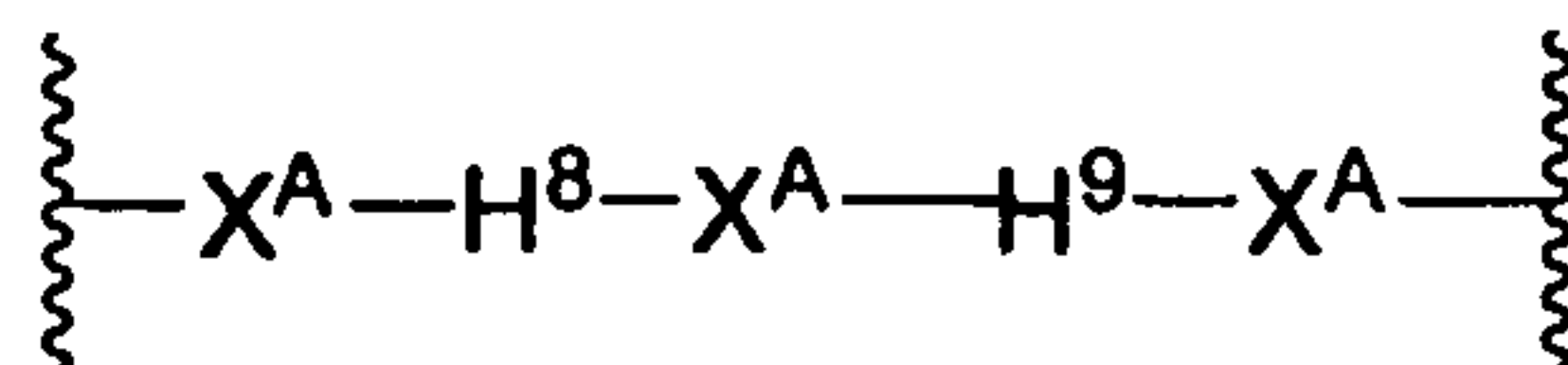
each A⁹ is independently:



wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

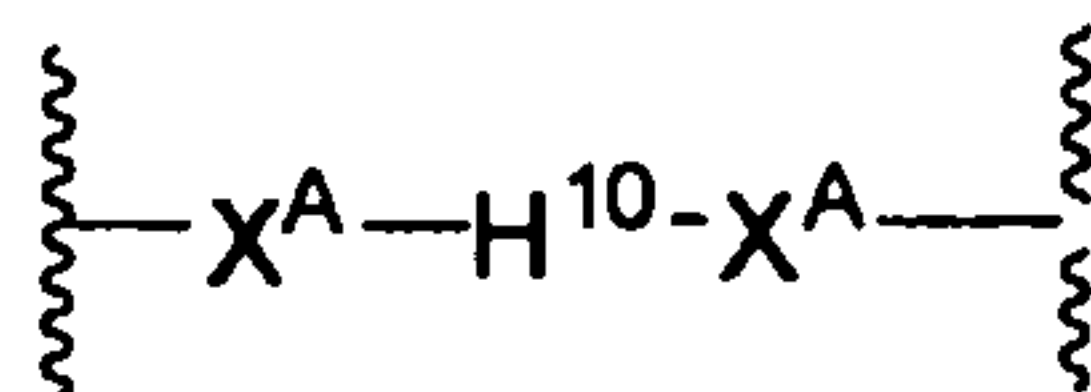
each A¹⁰ is independently:



wherein:

each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; each H⁹ is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹¹ is independently:



wherein:

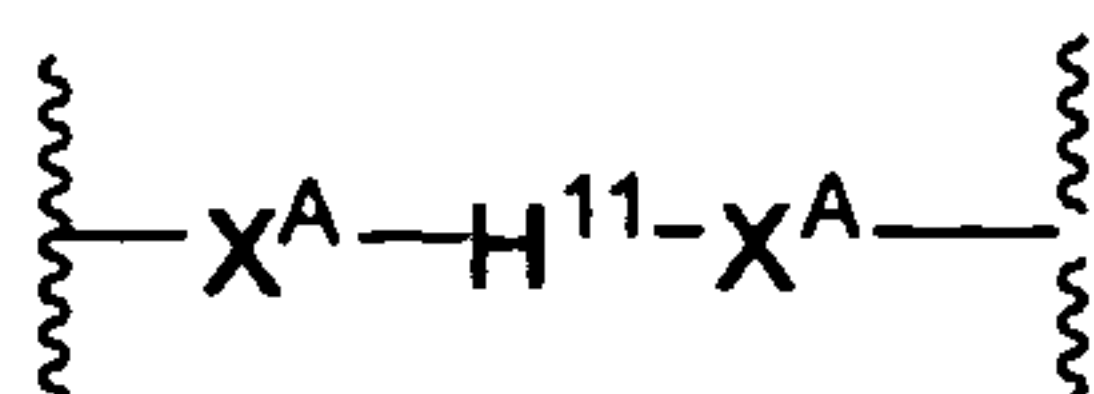
each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H¹⁰ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that is optionally fused to an aryl, which H¹⁰ is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl,

alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each A^{12} is independently:



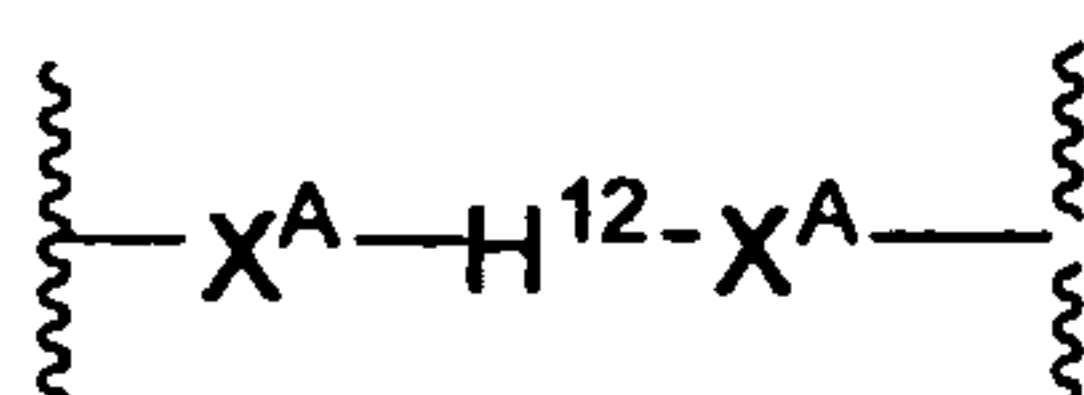
wherein:

each X^A is independently O, NR, SO, SO_2 , C(=O), $NRC(=O)$, $C(=O)NR$, $CR=CR$, $NRC(=O)NR$, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H^{11} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms that is optionally fused to an aryl, which H^{11} is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

each A^{13} is independently:

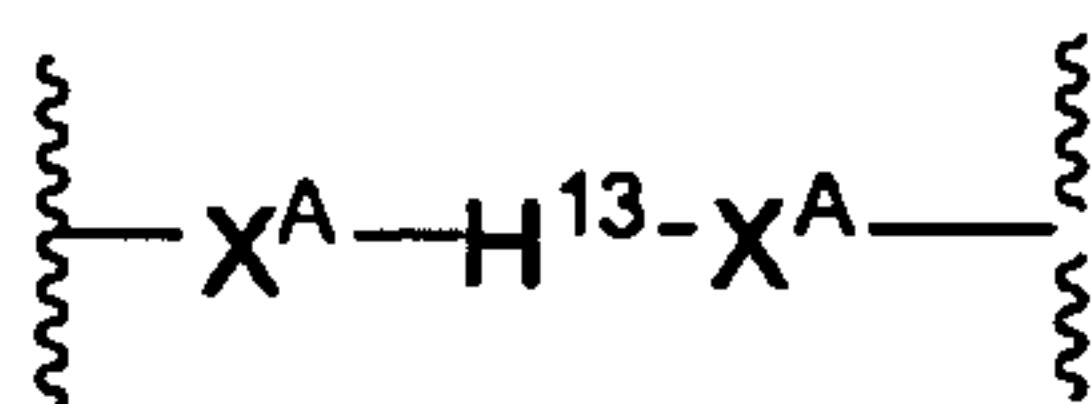


wherein:

each H^{12} is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{14} is independently:

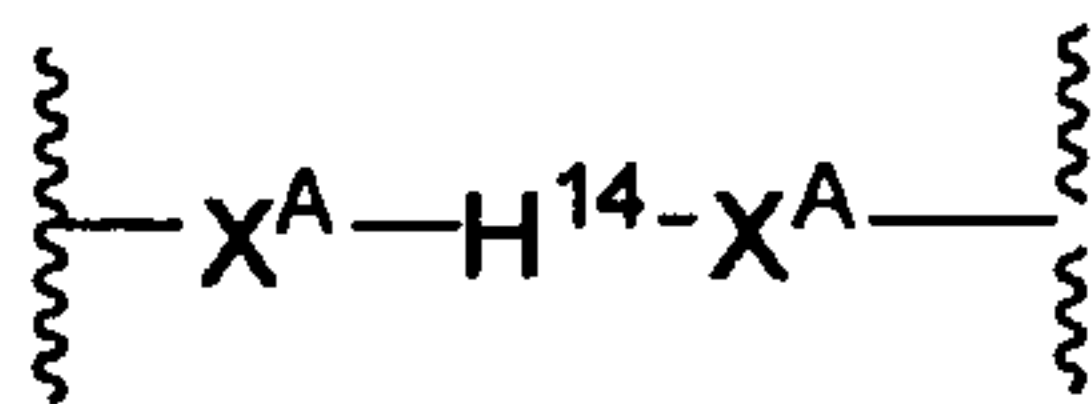


wherein:

each H^{13} is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{15} is independently:

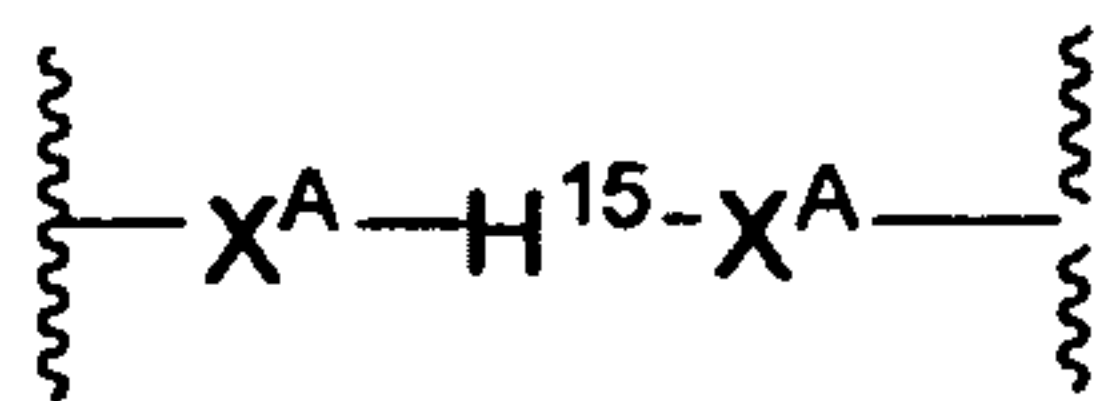


wherein:

each H^{14} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{16} is independently:

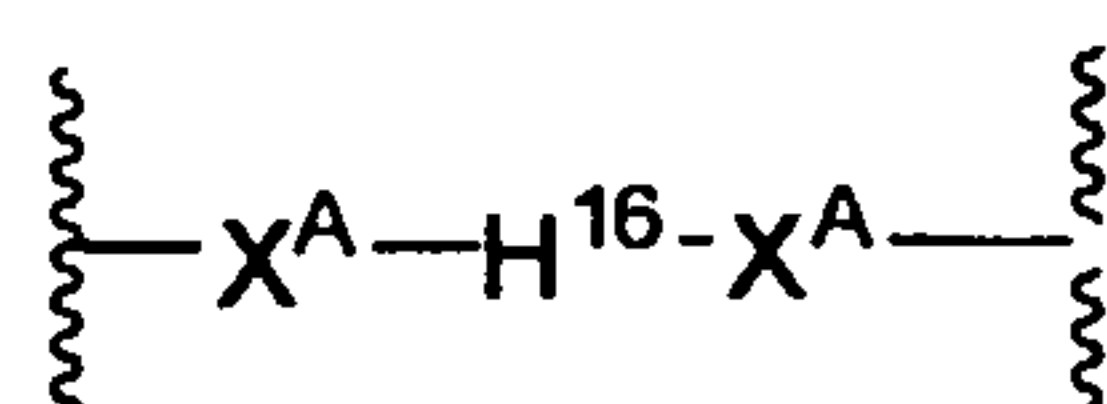


wherein:

each H¹⁵ is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁷ is independently:

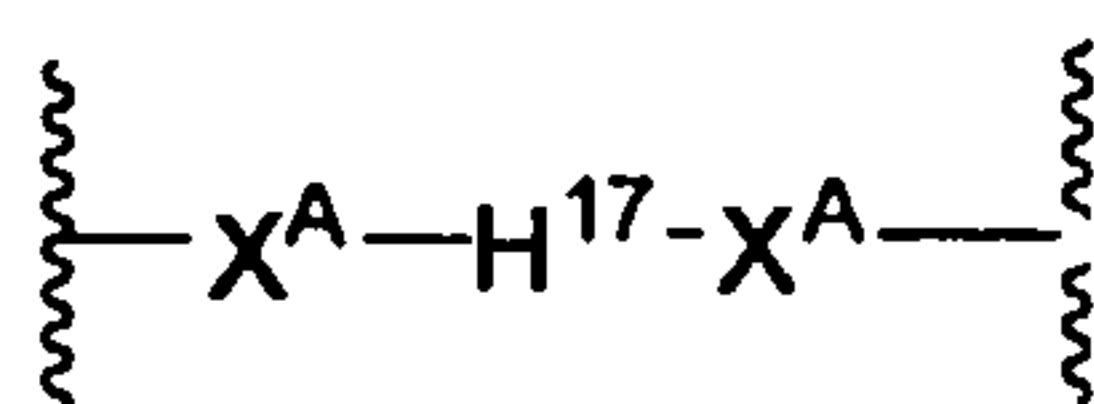


wherein:

each H¹⁶ is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁸ is independently:

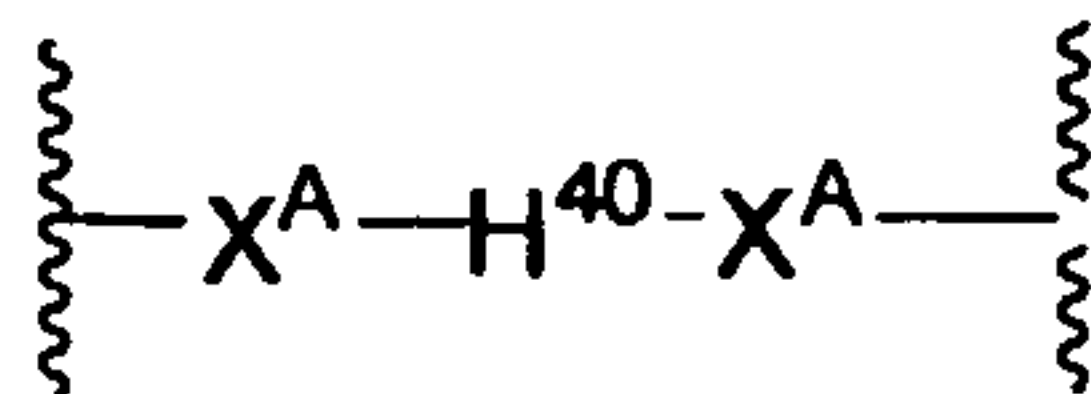


wherein:

each H¹⁷ is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A²¹ is independently:



wherein:

each H⁴⁰ is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

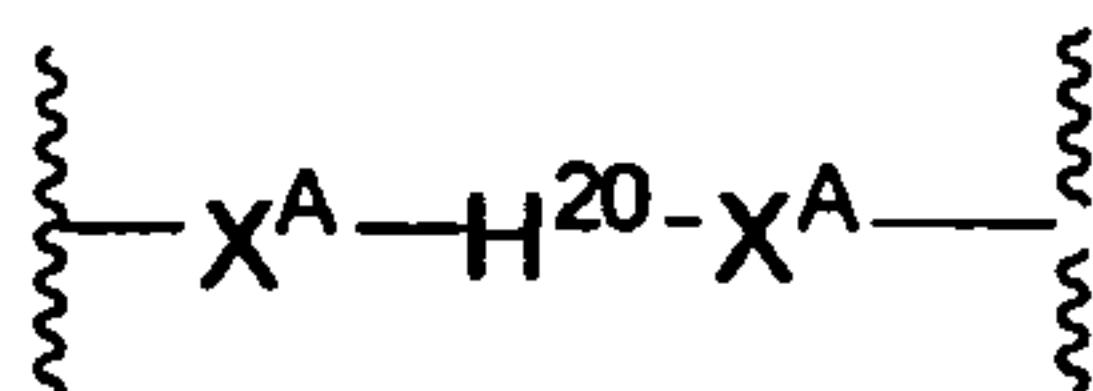
each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W¹ is independently -X^A-:

wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W² is independently:

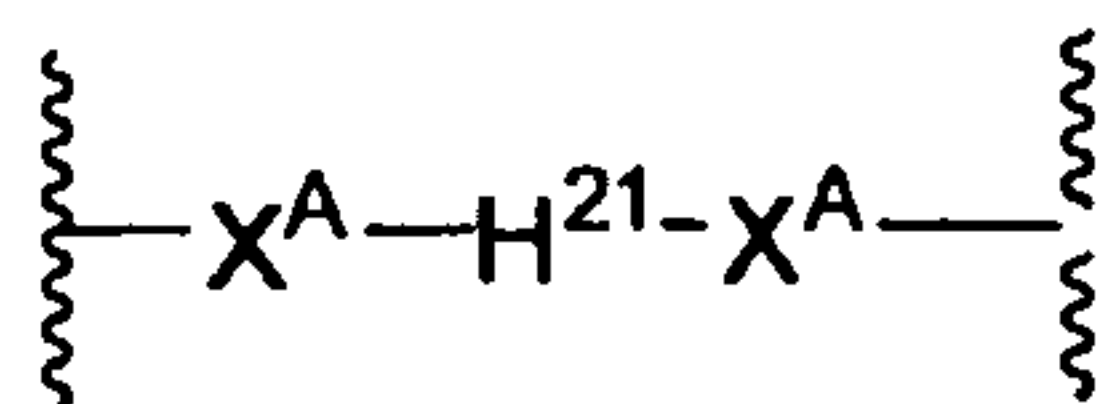


wherein:

each H²⁰ is independently is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W³ is independently:

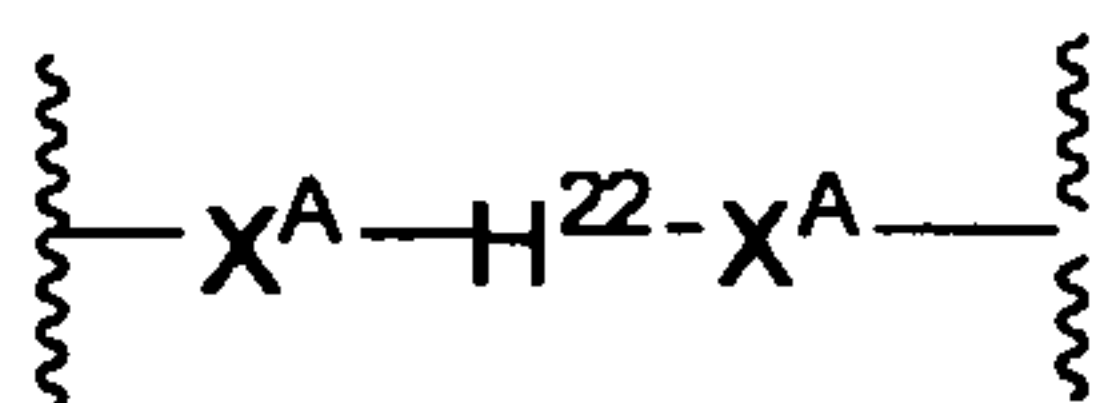


wherein:

each H^{21} is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^{A} is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^{4} is independently:

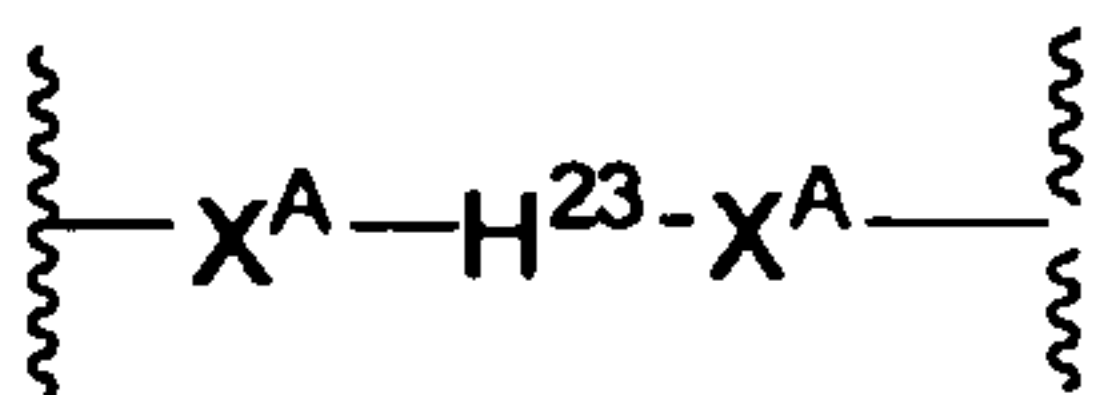


wherein:

each H^{22} is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^{A} is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^{5} is independently:

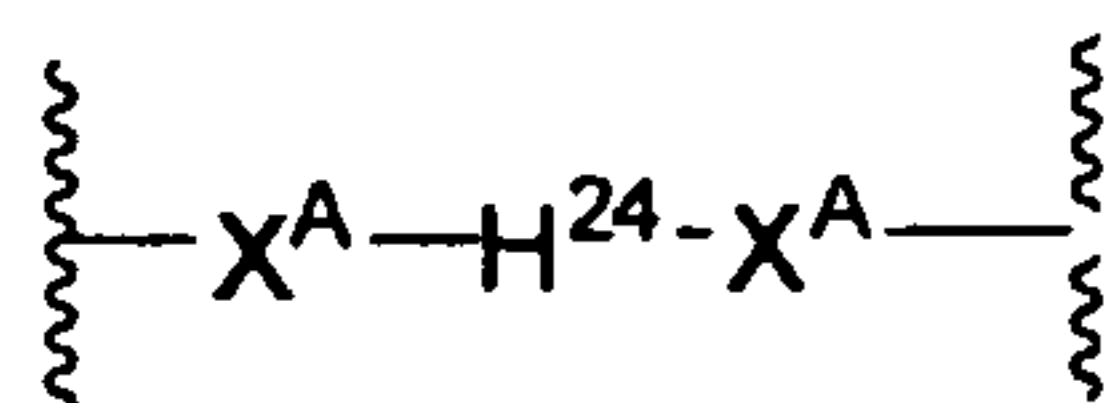


wherein:

each H^{23} is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^6 is independently:

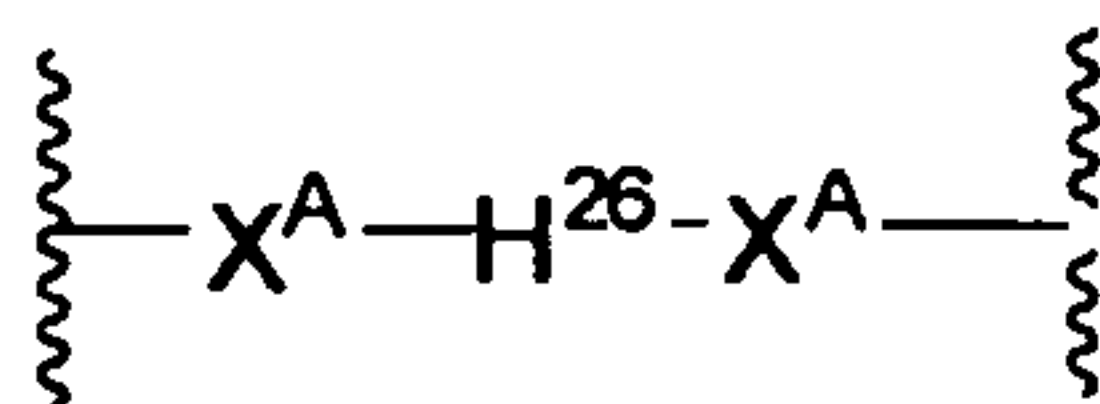


wherein:

each H^{24} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^7 is independently:

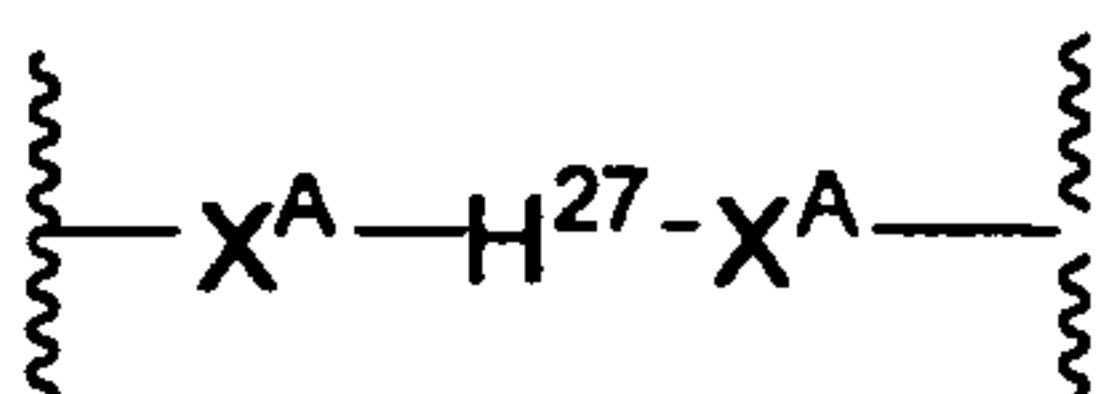


wherein:

each H^{26} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^8 is independently:

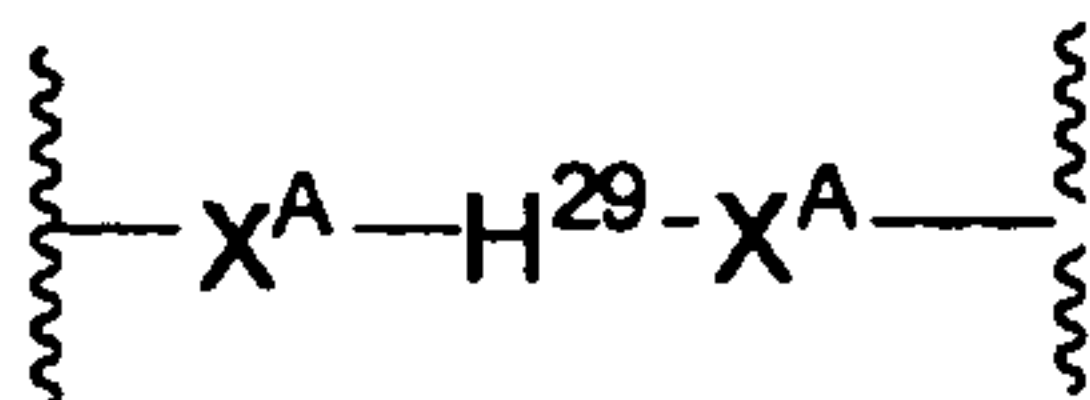


wherein:

each H^{27} is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^9 is independently:



wherein:

each H^{29} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^{10} is independently $-H^{30}=C=H^{31}-$

wherein each of $-H^{30}$ and H^{31} is independently a saturated 6-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W^{11} is independently $-H^{32}=C=H^{33}-$

wherein each of $-H^{32}$ and H^{33} is independently a saturated 5-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W^{12} is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{13} is independently a phenyl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{14} is independently a 5 or 6 membered heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{15} is independently a fused unsaturated, partially unsaturated or saturated tetracyclic carbocyclic ring, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{16} is independently a fused unsaturated, partially unsaturated or saturated tetracyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{17} is independently a fused unsaturated, partially unsaturated or saturated pentacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{18} is independently a fused unsaturated, partially unsaturated or saturated pentacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{19} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

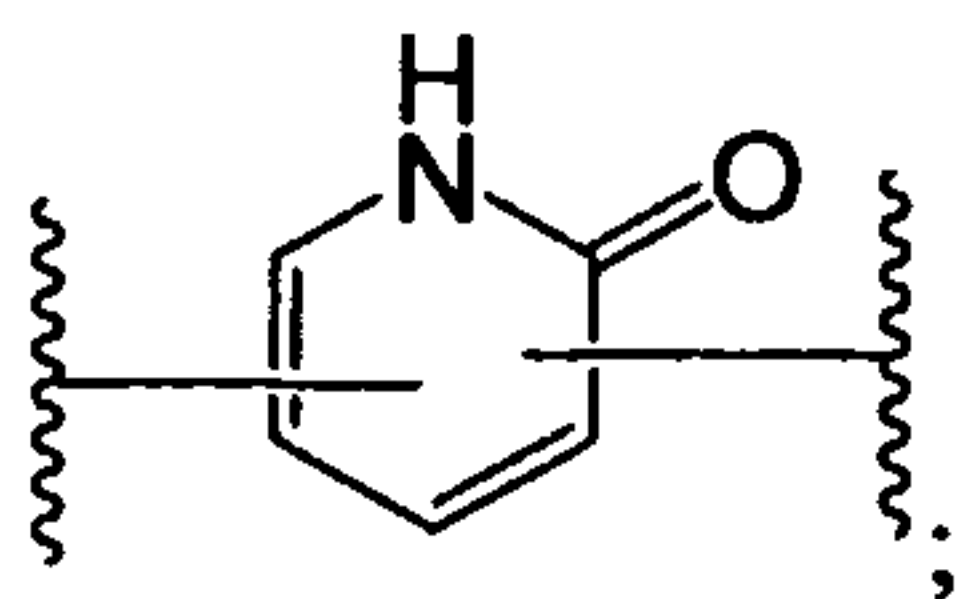
each W^{20} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each M^0 is independently a five membered heteroaryl group optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, haloalkyl, (NR^aR^b) carbonyl and trialkylsilylalkoxyalkyl;

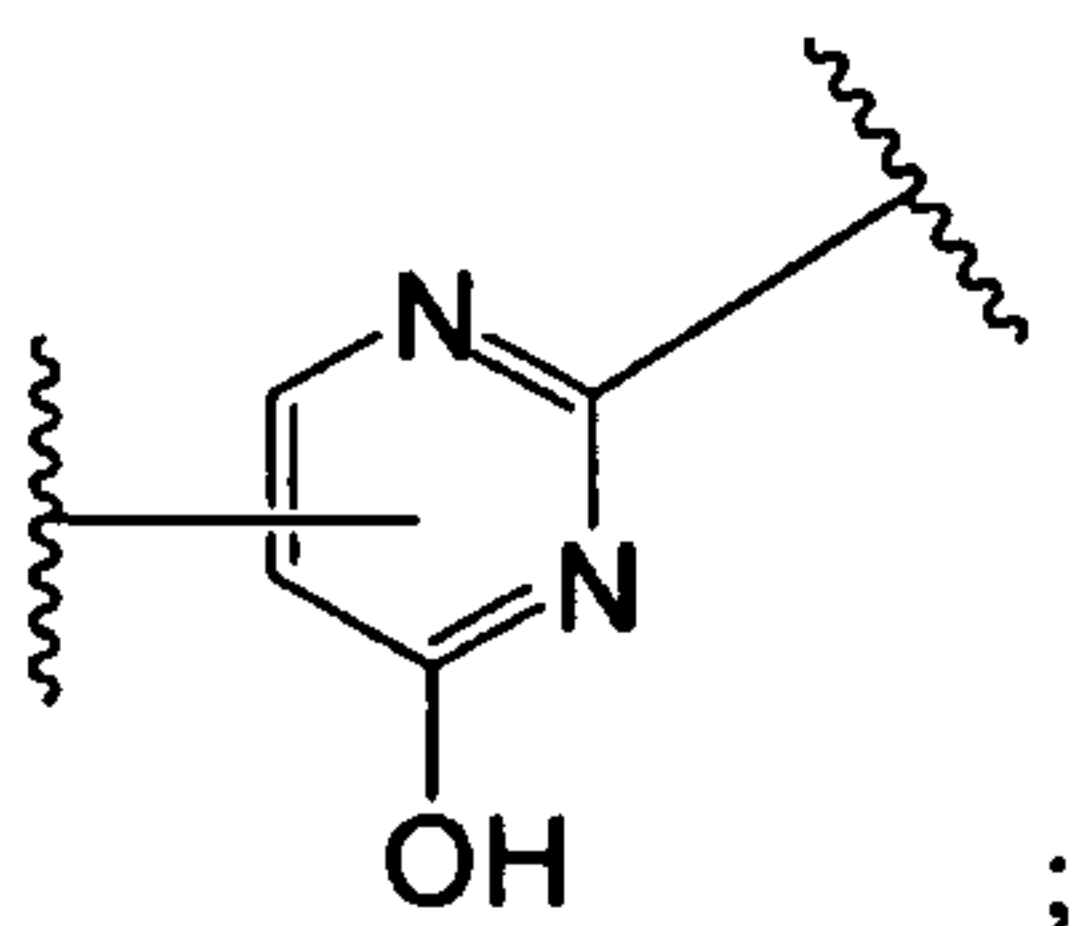
each M^1 is independently selected from $-C(=O)NH-$, $-C(=O)NH-C(R^M)_2-$, $-NHC(=O)-$, $-C(R^M)_2NHC(=O)-$, $-NHC(=O)NR^M-$, $-NHC(=O)O-$; wherein each R^M is independently selected from H and alkyl;

each M^2 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

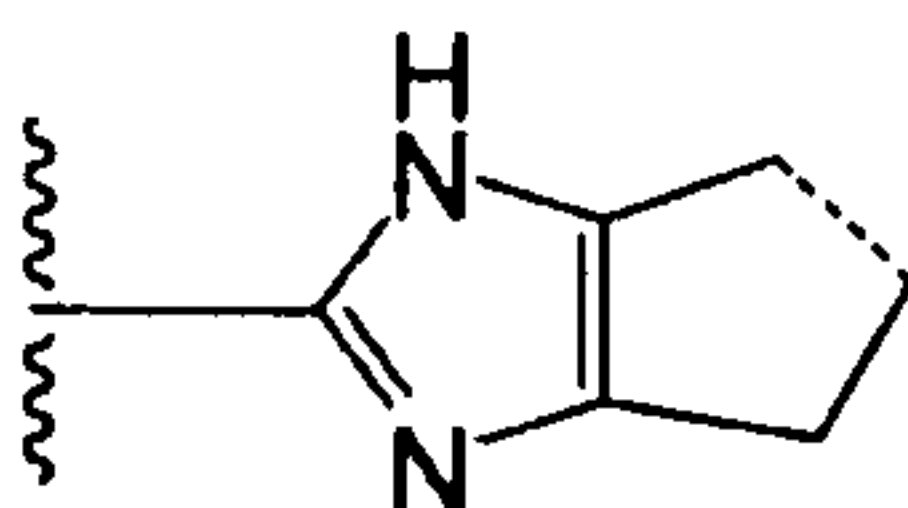
each M^3 is independently:



each M^4 is independently:



each M^5 is independently:



wherein the bond designated with --- is fused to a ring defined for P;

each M^6 is independently a bicyclic bridged ring system comprising 5-15 atoms wherein at least one of the atoms is a heteroatom;

each M^7 is independently a pyrid-di-yl;

each M^8 is independently partially saturated or a saturated five-membered ring that comprises one or more heteroatoms and that is optionally substituted with one or two oxo;

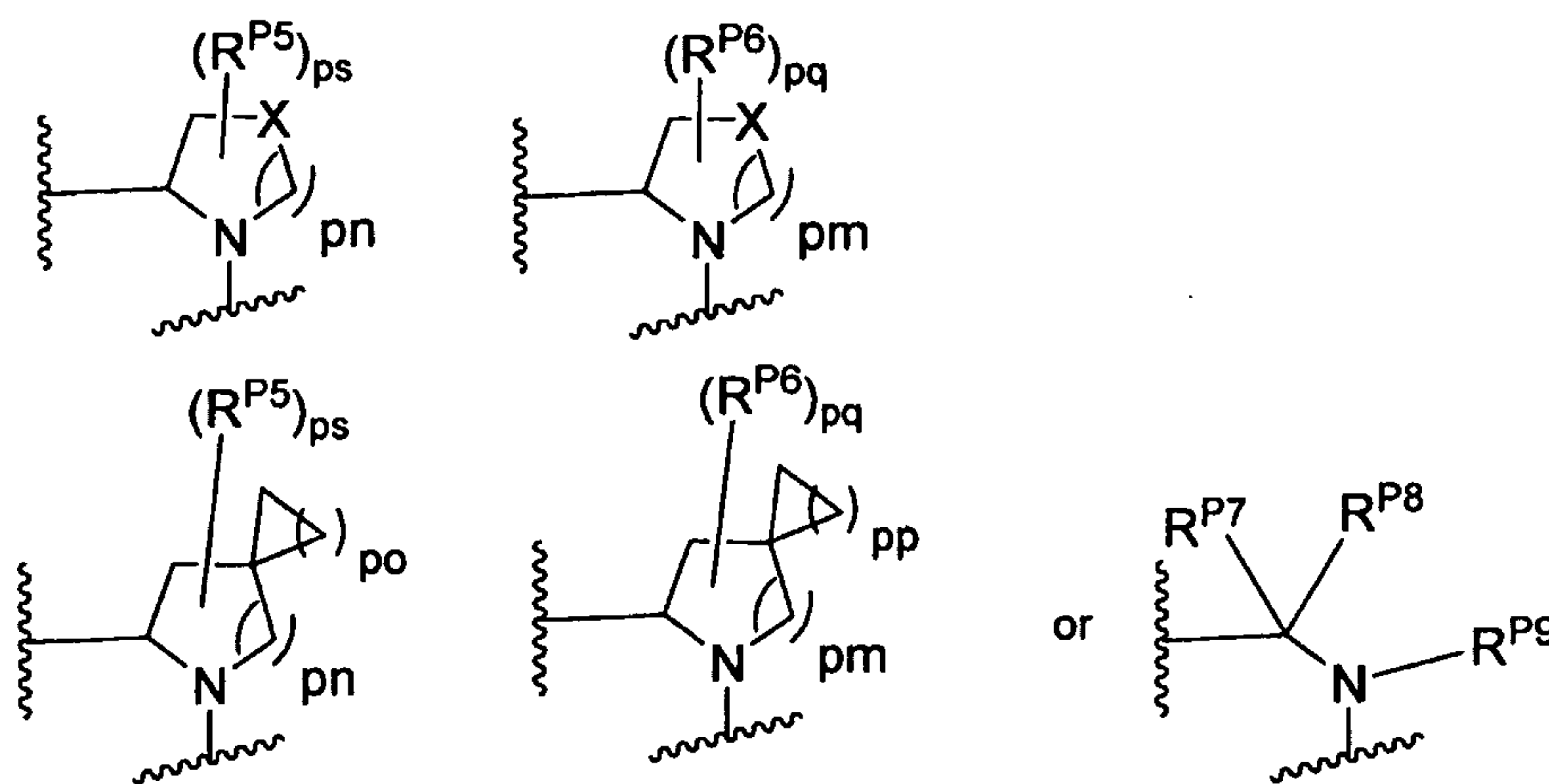
each M^9 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^{P11} ;

each M^{10} is independently a five membered heteroaryl group;

each M^{11} is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo, halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$;

each R^{M7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

each P^0 is independently:



wherein:

X is selected from O , S , $S(O)$, SO_2 , CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

provided that when pn or pm is 0 , X is selected from CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H , alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0 , 1 , 2 , 3 , or 4 ;

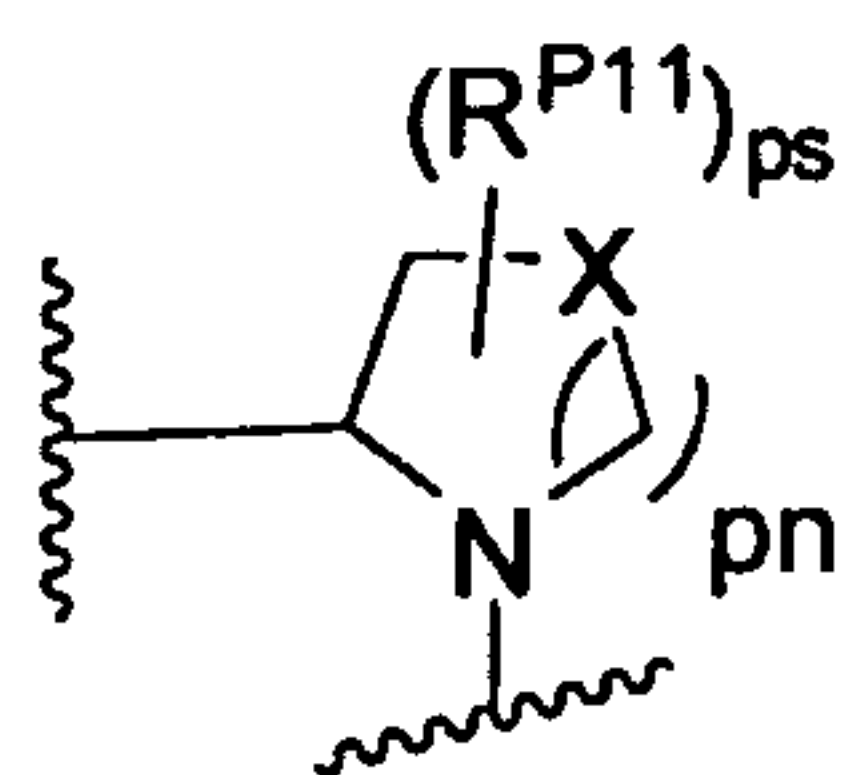
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^1 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

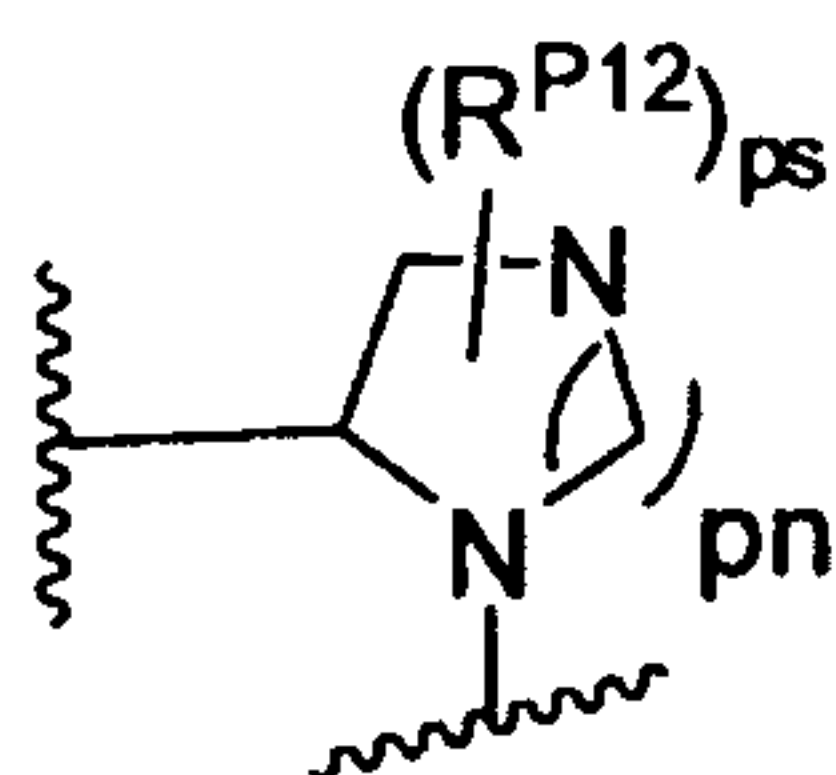
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl,

(NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P² is independently:



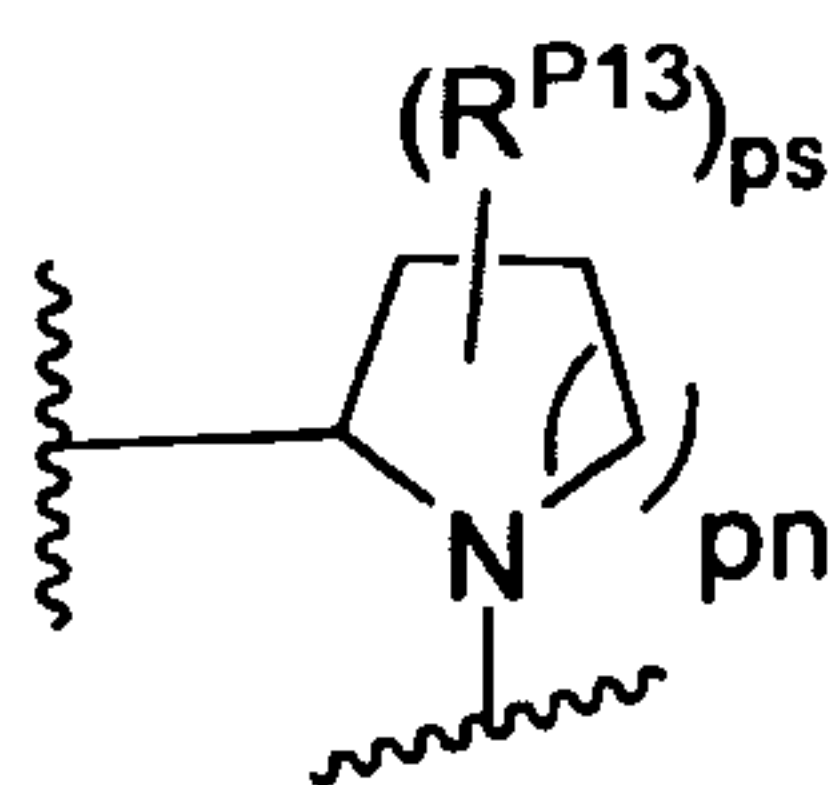
wherein:

each R^{P12} is independently selected from R^{P5}, R^{P11}, -C(=O)OR^h, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P³ is independently a ring of the formula:



wherein:

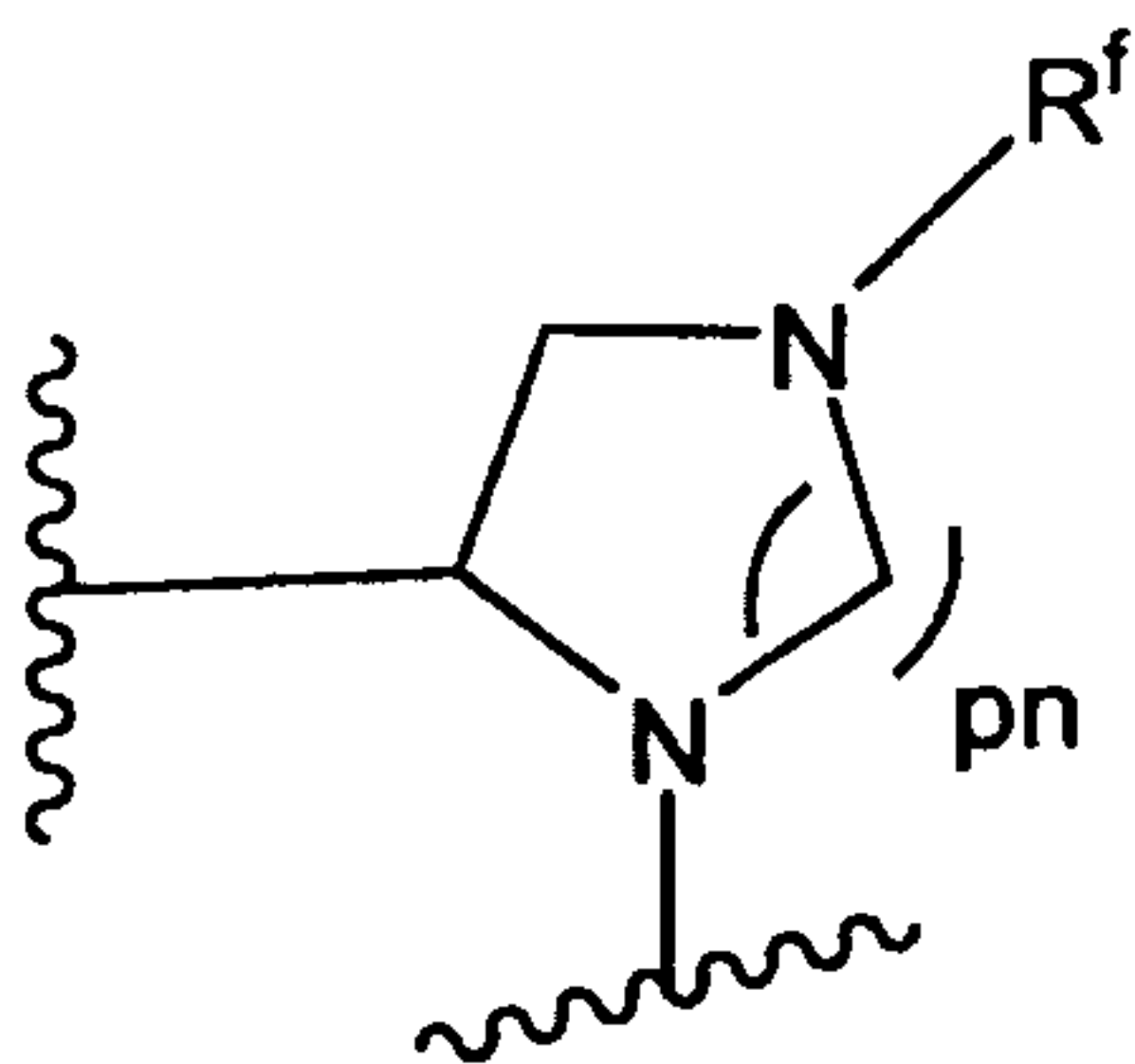
the ring is substituted with one or more oxo group;

each R^{P13} is independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^4 is independently a ring of the formula:



wherein:

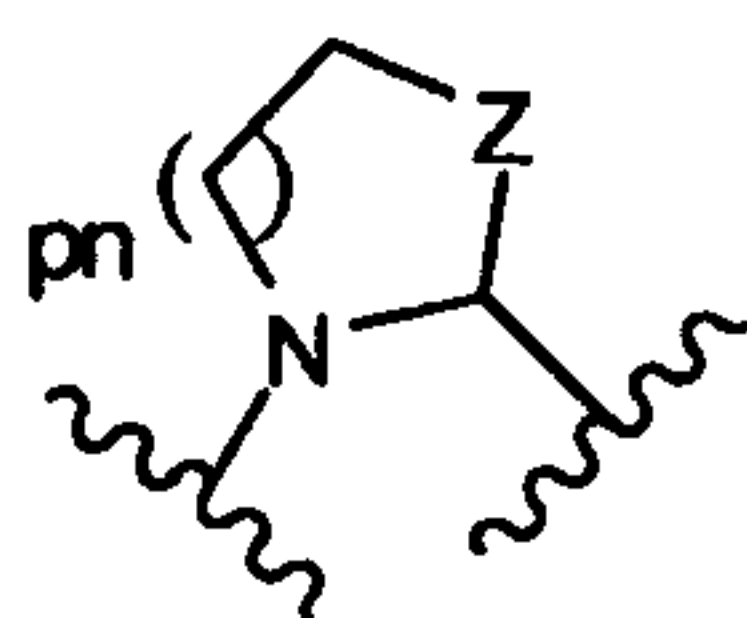
the ring is optionally substituted with one or more groups R^{P14} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P14} that are attached to the same carbon

when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^5 is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

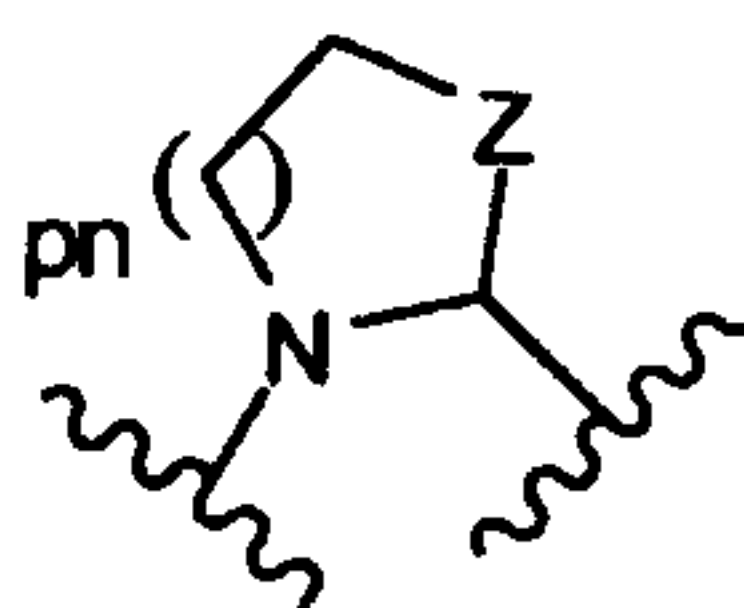
pn is 0, 1, or 2;

Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^6 is independently a ring of the formula:



wherein:

the ring is substituted with one or more oxo and is optionally substituted with one or more groups R^{P16} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

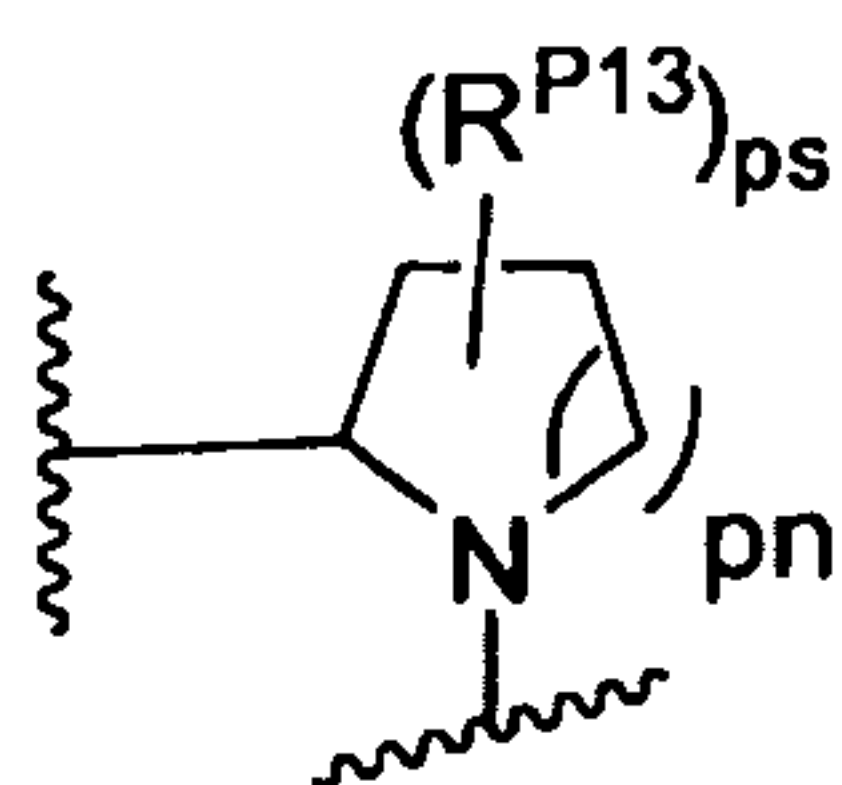
Z is O, S, S(=O), S(=O)₂, or NR^f ;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:



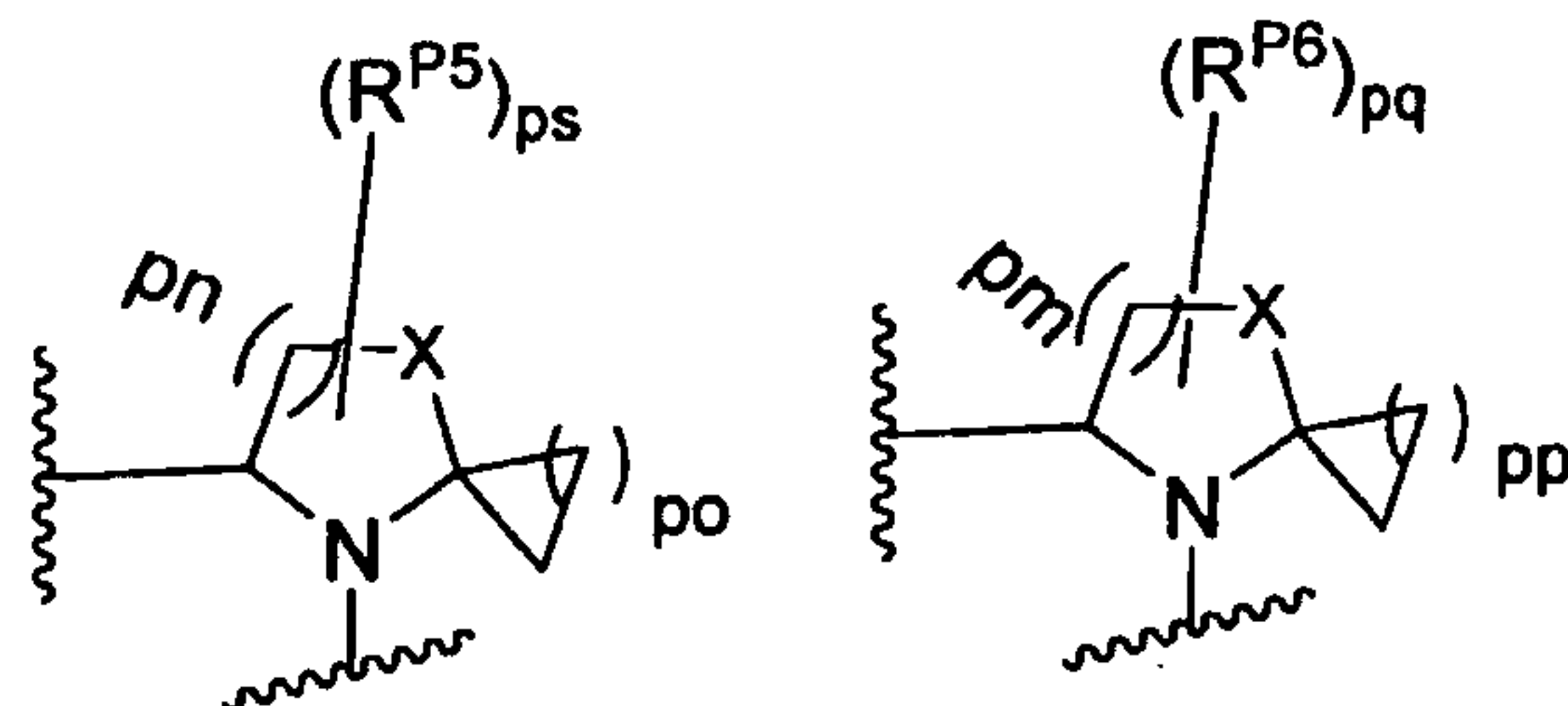
wherein:

ps is 2, 3, 4, 5, or 6;

pn is 0, 1, or 2;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused

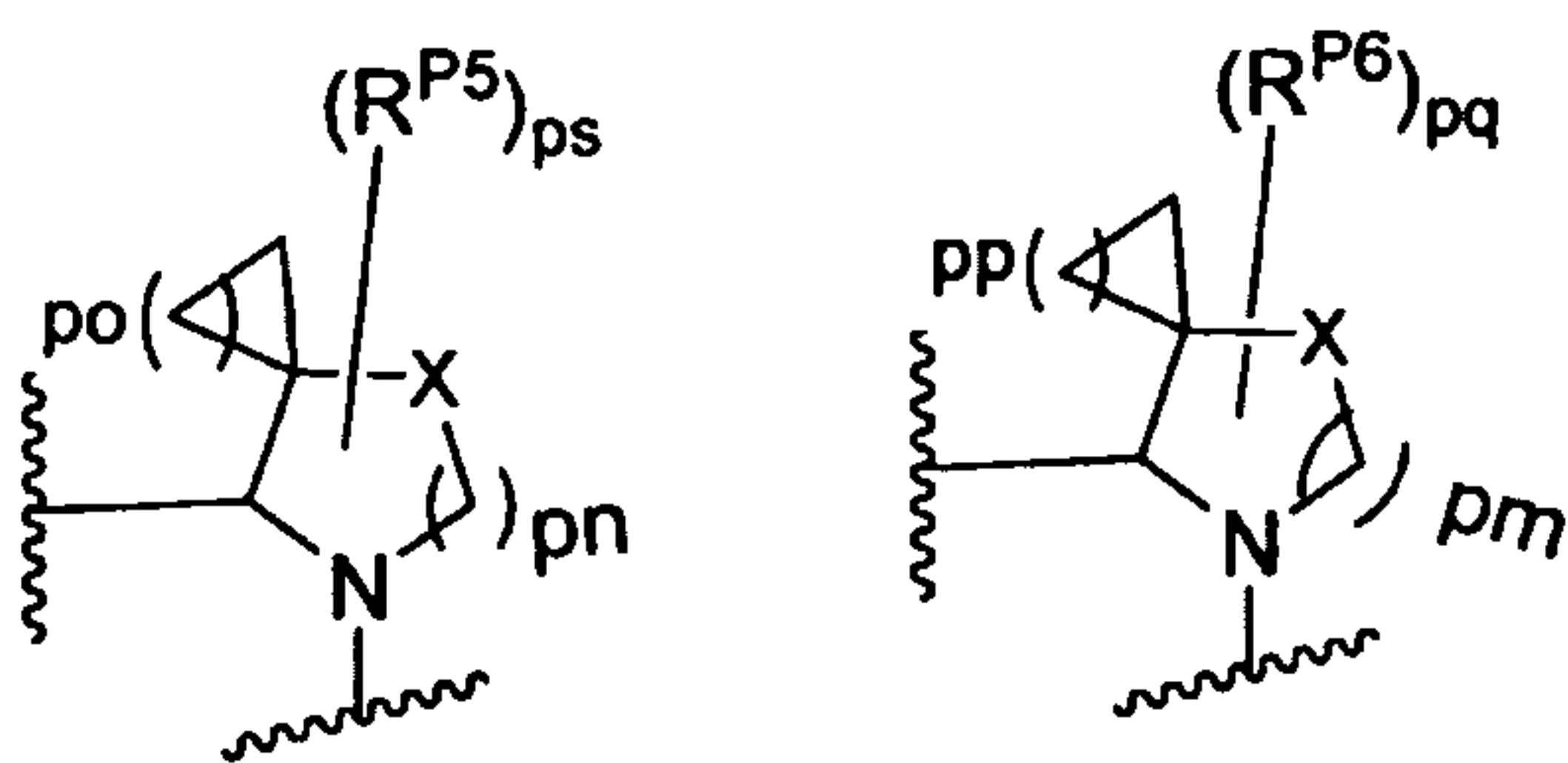
three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{11} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

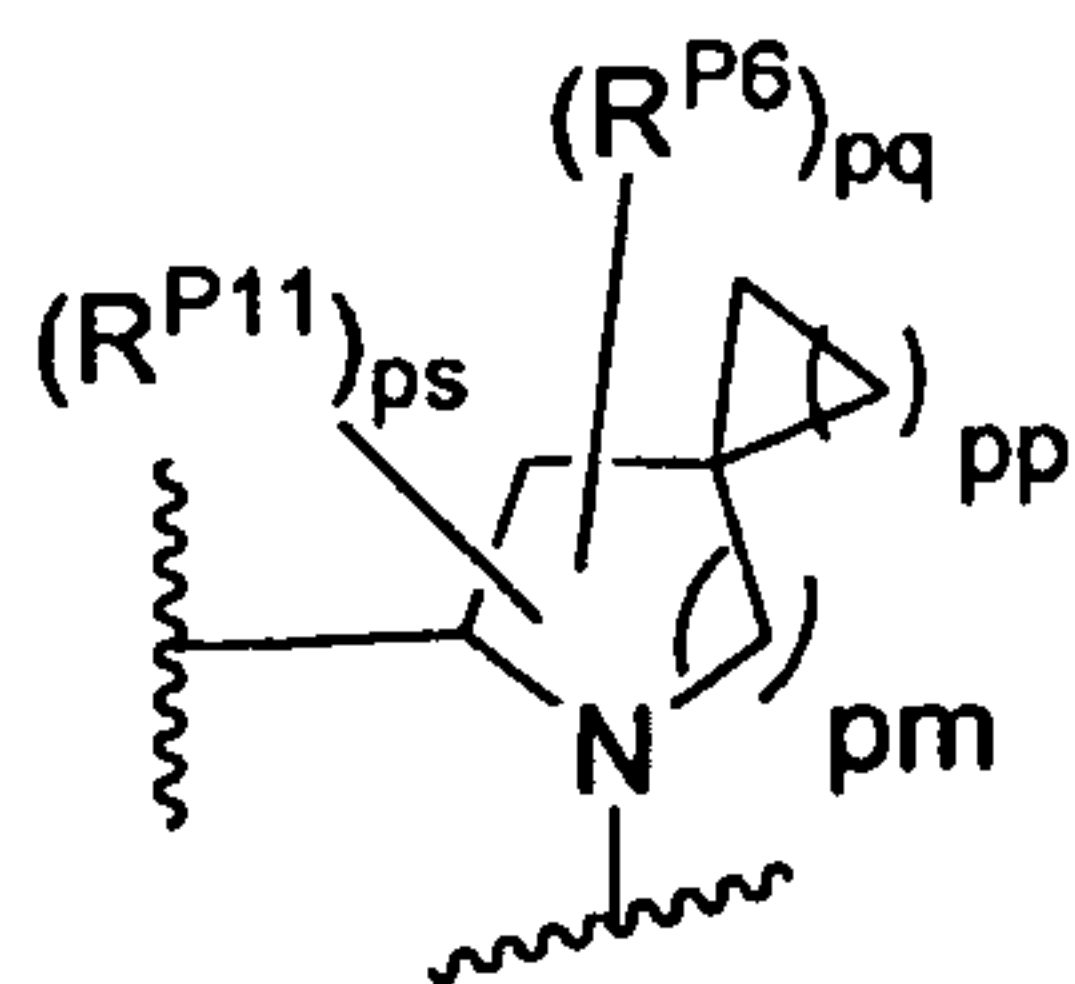
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{12} is independently:



wherein:

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

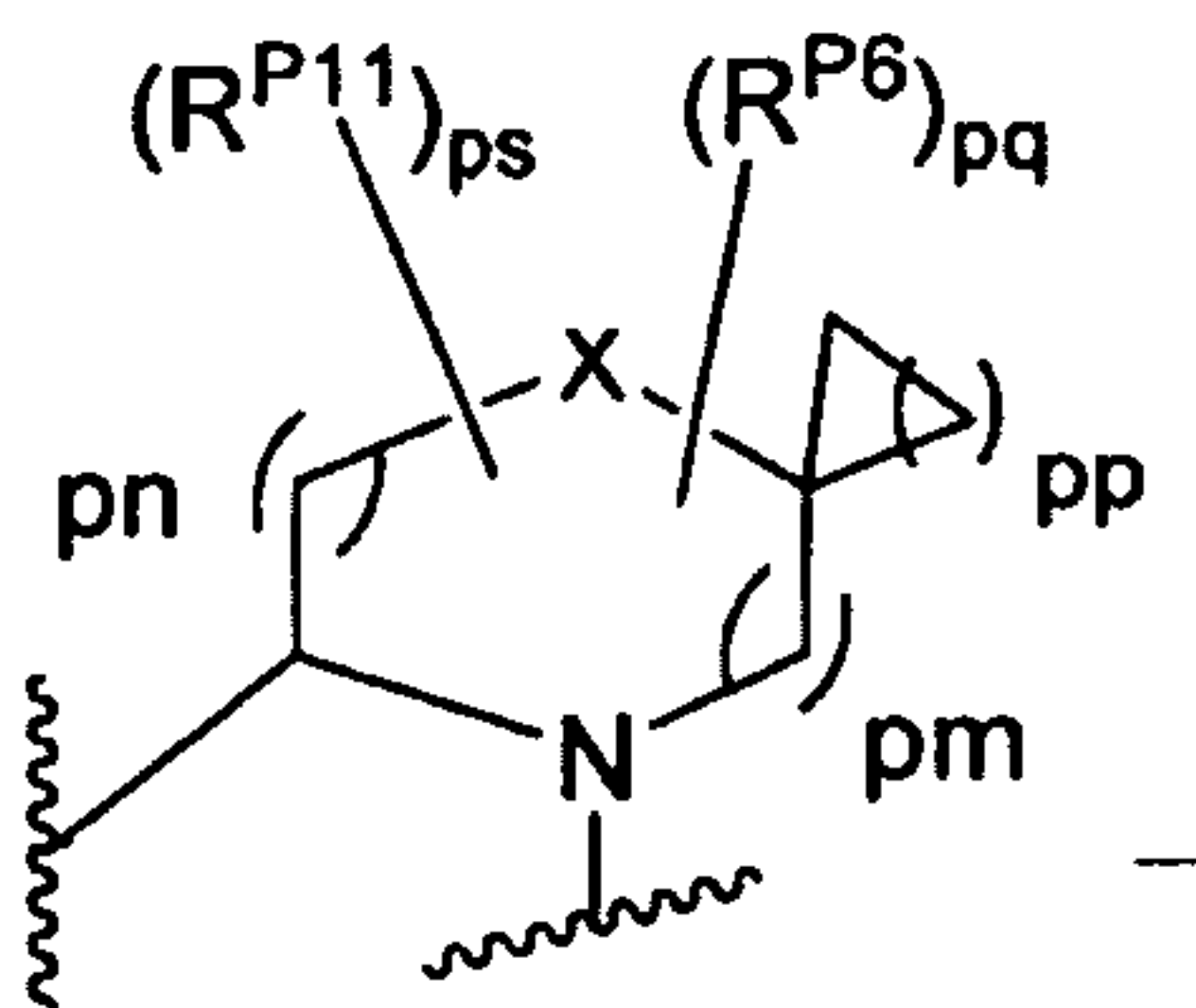
pp is independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^{hh}) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^{hh}) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $NR^{hh}R^h$ sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^{hh}R^h$; and the remaining R^{P11} are independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^h)$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, $(NR^{hh}R^h)$ alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{13} is independently:



wherein:

X is selected from O, S, S(O), SO₂, or NR^h;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2 but the sum of pn and pm is greater than zero;

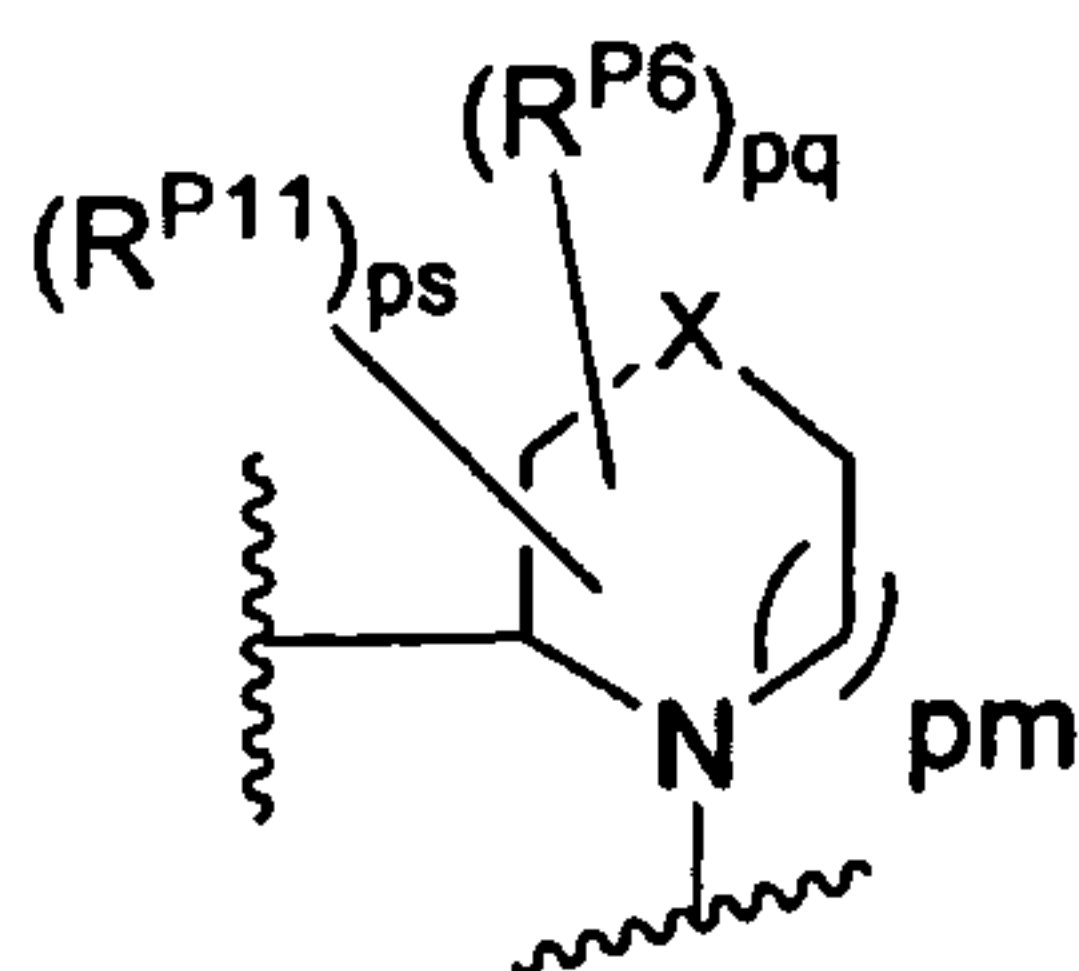
pp are independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, -NR^{hh}R^h, (NR^{hh}R^h)alkyl, (NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h)sulfonyl, heteroarylsulfonyl, -S(=O)₂R^h, -C(=O)R^h, -C(=O)NR^hR^h, R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P¹⁴ is independently:



wherein:

the ring is substituted with one or more oxo group;

X is NR^f;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, -S(=O)₂NR^hR^h, -S(=O)₂R^h, C(=O)R^h, C(=O)OR^h, -C(=O)NR^hR^h; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

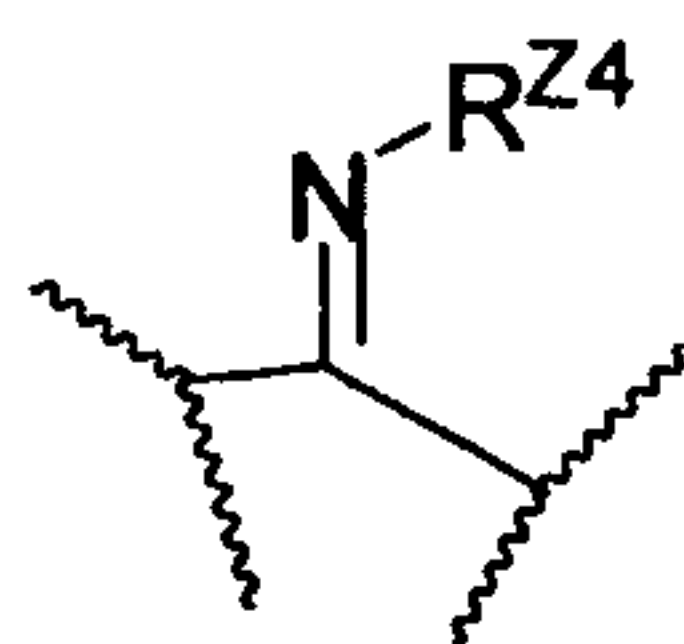
each $-Z^0-$ is $-C(=O)-$ or $-C(=S)-$;

each $-Z^1-$ is independently a bond, or $-C(R^{Z1})_2-$; wherein each R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each $-Z^2-$ is independently saturated or partially unsaturated (C_3-C_8) cycloalkyl that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

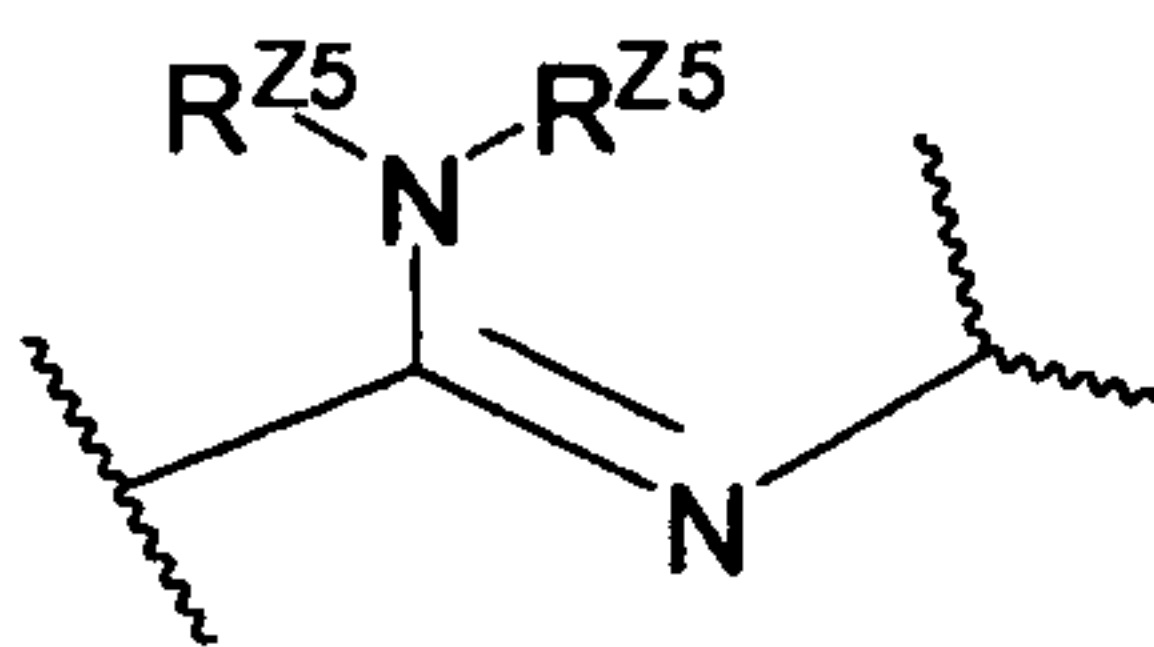
each $-Z^3-$ is independently saturated, partially unsaturated, or aromatic 4-8 membered heterocyclic or heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^4-$ is independently:



wherein each R^{Z4} is independently H, alkyl, cyano, aryl, or heteroaryl;

each $-Z^5-$ is independently:



wherein each R^{Z5} is independently H, alkyl, cyano, aryl, or heteroaryl; or two R^{Z5} s together with the nitrogen to which they are attached form a 4-8 membered heterocyclic ring that is optionally substituted with one or more oxo and with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^6-$ is independently $-C(R^{Z1})-$ and is doublebonded to a carbocyclic P; wherein R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f) alkyl, (NR^eR^f) alkylcarbonyl, (NR^eR^f) carbonyl, (NR^eR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^XR^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^eR^f$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each E^1 is independently $-OC(=O)NR^{Ec}R^{Ef}$ wherein each R^{Ec} and R^{Ef} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl,

alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f)alkyl, (NR^eR^f)alkylcarbonyl, (NR^eR^f)carbonyl, (NR^eR^f)sulfonyl, -C(NCN)OR', and -C(NCN)NR^xR^y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one -NR^eR^f group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; or wherein R^{ee} and R^{ef}, together with the nitrogen atom to which they are attached, form a heterocycle;

each V⁰ is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^xR^y, - (NR^xR^y)alkyl, oxo, and -P(O)OR₂, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^6 is independently arylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^7 is independently heterocyclosulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^8 is independently spirocycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^9 is independently spirocycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{10} is independently fusedbicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{11} is independently fusedbicycliccycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{12} is independently bridged-bicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{13} is independently bridged-bicyclic-cycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{14} is independently aryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{15} is independently arylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{16} is independently cycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{17} is independently cycloalkylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{18} is independently heterocyclooxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{19} is independently heterocycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{20} is independently heteroaryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{21} is independently heteroarylalkylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each T^1 is independently a spiro, branched or fused bicycloalkyl;

each T^2 is independently aryl;

each T^3 is independently heteroaryl;

each T^4 is independently arylalkyl;

each T^5 is independently haloalkyl;

each T^6 is independently heteroarylalkyl;

each T^7 is independently heterocycle; and

each T^8 is independently heterocyclealkyl.

In another specific embodiment the invention provides a compound of formula (I) which comprises M^0-W-M^0 , M^0-W-M^9 , M^9-W-M^0 , or M^9-W-M^9 , $M^{10}-W-M^0$, M^0-W-M^{10} , $M^{10}-W-M^9$, M^9-W-M^{10} , or $M^{10}-W-M^{10}$.

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^2 .

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^8 .

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^{15} .

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^{16} .

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^{18} .

In another specific embodiment the invention provides a compound of formula (I) which comprises $M^0-A-A-M^0$, $M^0-A-A-M^9$, $M^9-A-A-M^0$, or $M^9-A-A-M^9$, $M^{10}-A-A-M^0$, $M^0-A-A-M^{10}$, $M^{10}-A-A-M^9$, $M^9-A-A-M^{10}$, or $M^{10}-A-A-M^{10}$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^0-A^0-$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^0-A^5-$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^0-A^{13}-$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^{13}-A^{13}-$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^0-A^{11}-$.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A-A-$ is $-A^{13}-A^6-$.

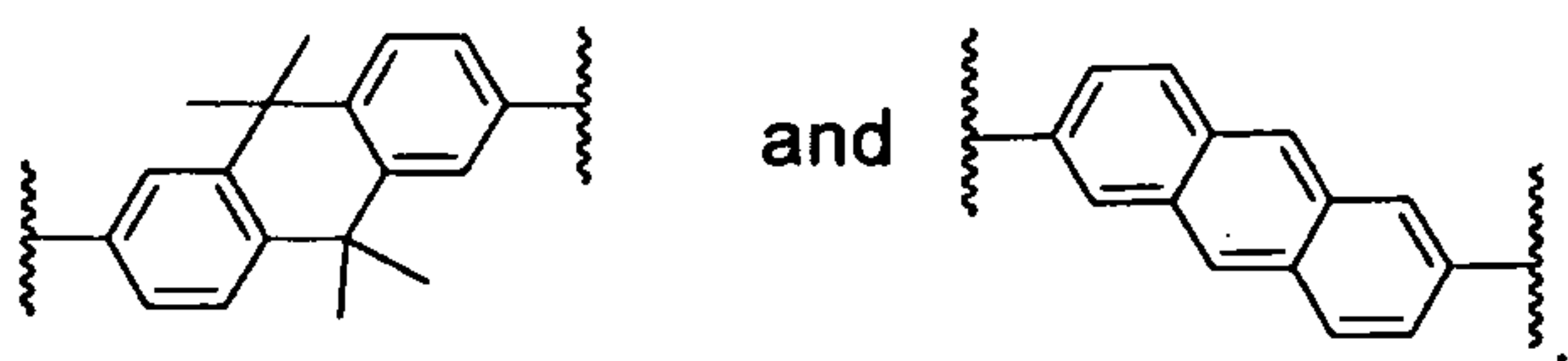
In another specific embodiment the invention provides a compound of formula (I) wherein W is W^6 .

In another specific embodiment the invention provides a compound of formula (I) wherein each X^A is absent where it is allowed to be absent.

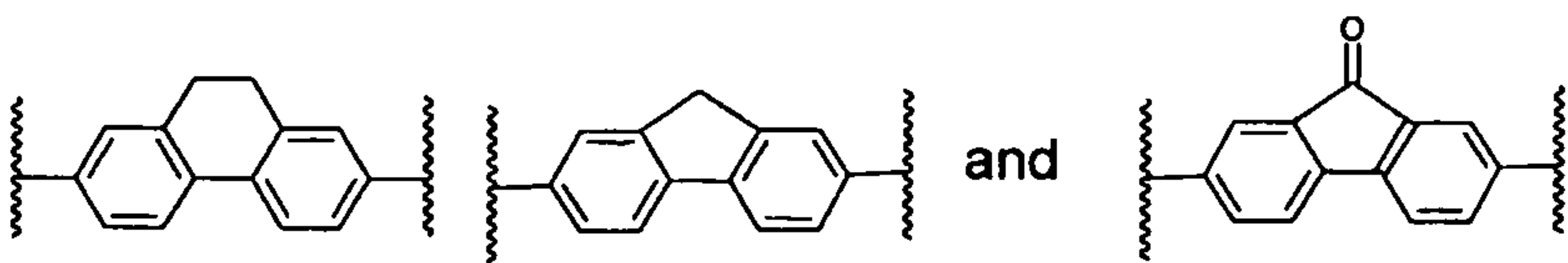
In another specific embodiment the invention provides a compound of formula (I) wherein one or two X^A are present and X^A is alkynyl.

In another specific embodiment the invention provides a compound of formula (I) wherein one or two X^A are present and X^A is alkenyl.

In another specific embodiment the invention provides a compound of formula (I) wherein W^6 is selected from:

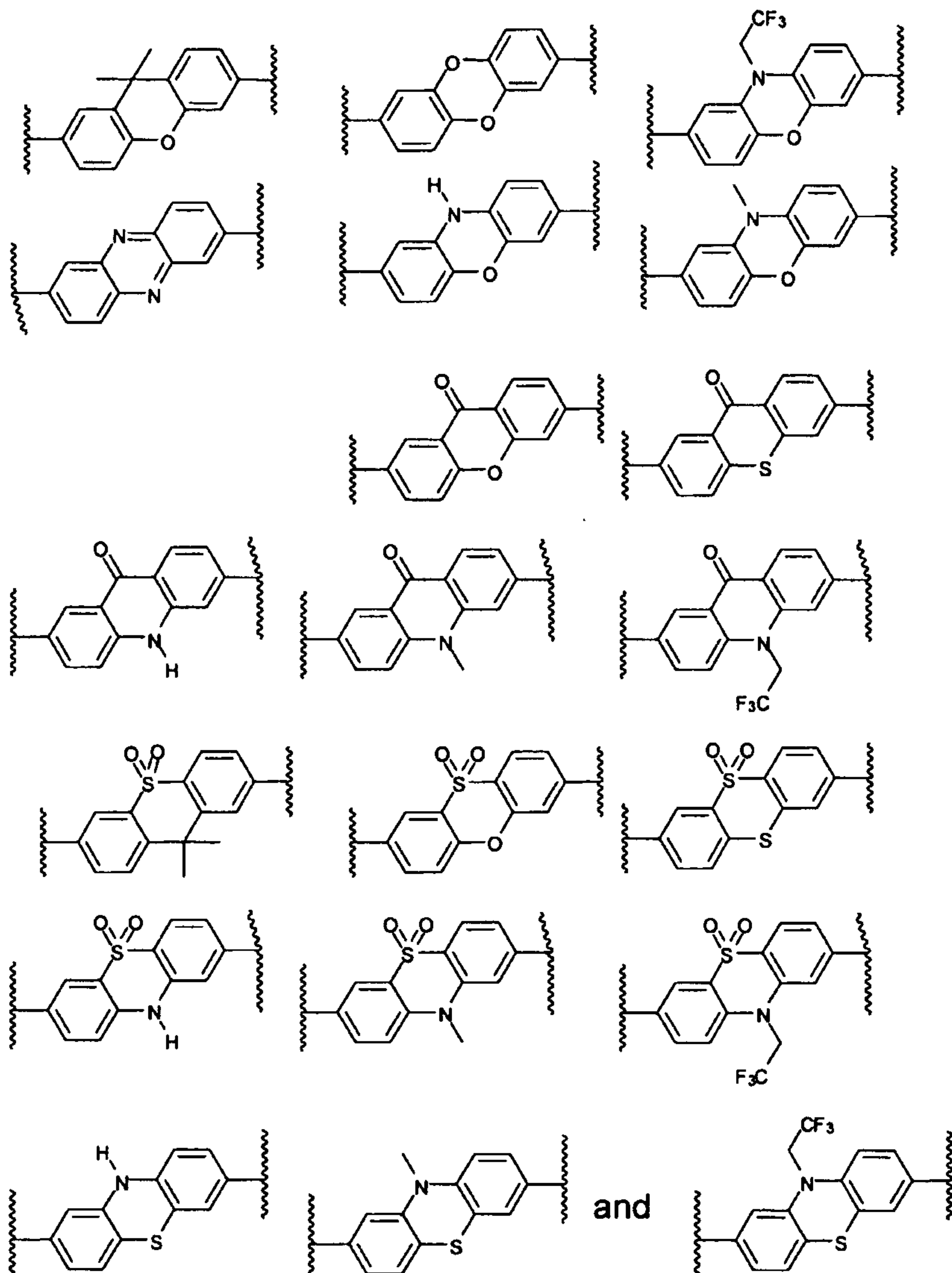


In another specific embodiment the invention provides a compound of formula (I) wherein W^6 is selected from:

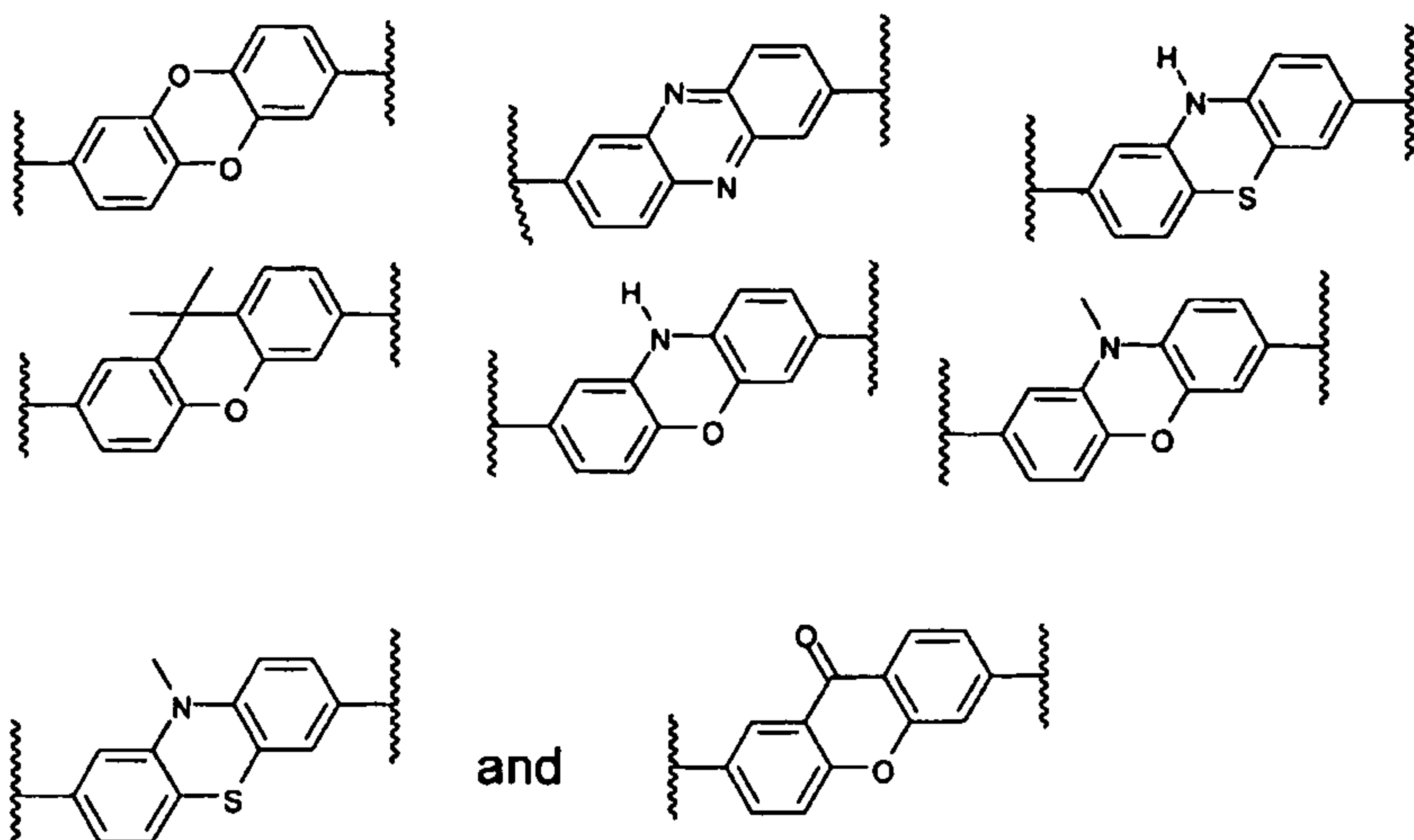


In another specific embodiment the invention provides a compound of formula (I) wherein W is W⁸.

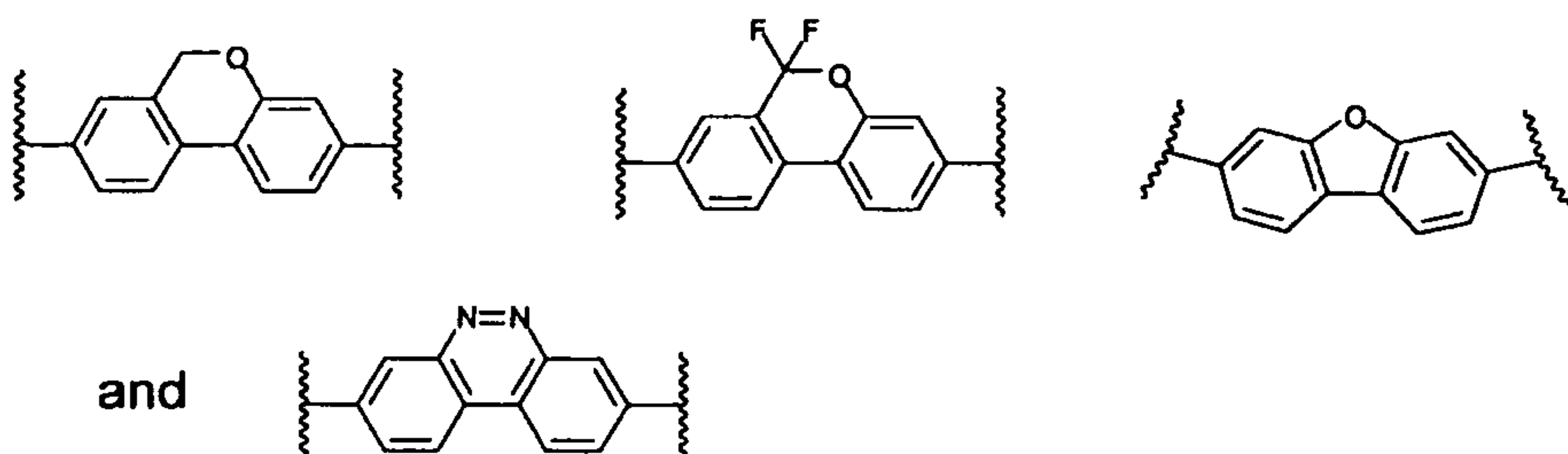
In another specific embodiment the invention provides a compound of formula (I) wherein W⁸ is selected from:



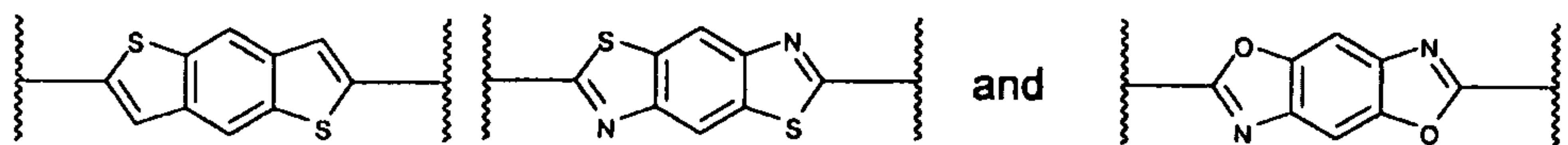
In another specific embodiment the invention provides a compound of formula (I) wherein W⁸ is selected from:



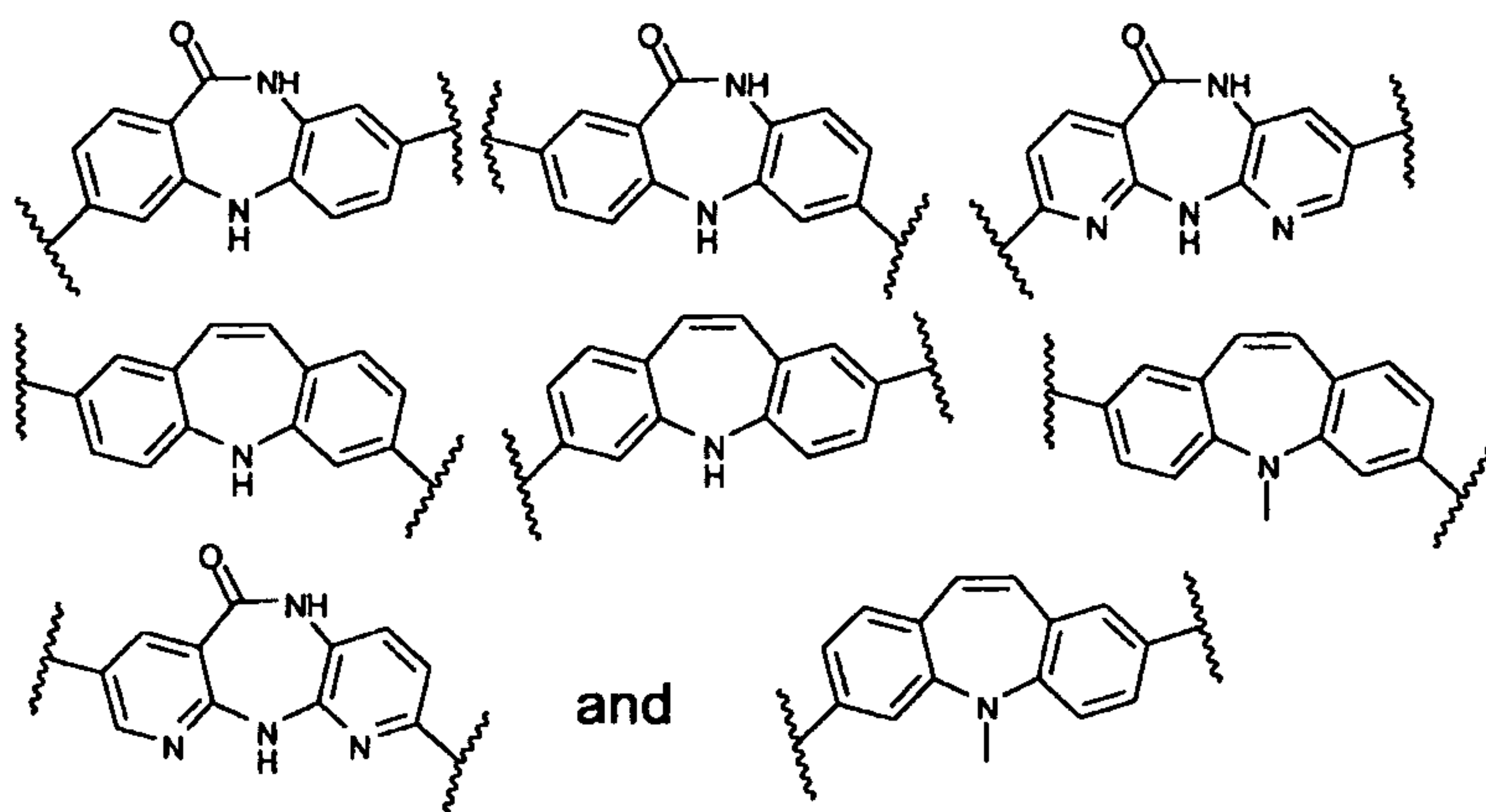
In another specific embodiment the invention provides a compound of formula (I) W^8 is selected from:



In another specific embodiment the invention provides a compound of formula (I) W^8 is selected from:

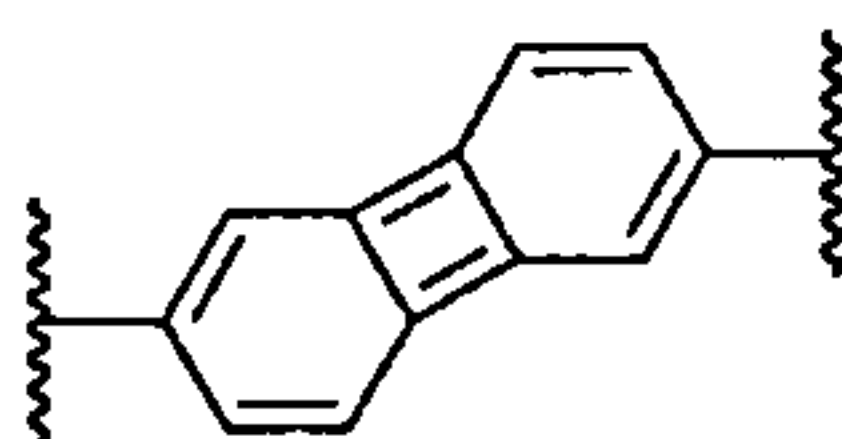


In another specific embodiment the invention provides a compound of formula (I) wherein W^8 is selected from:



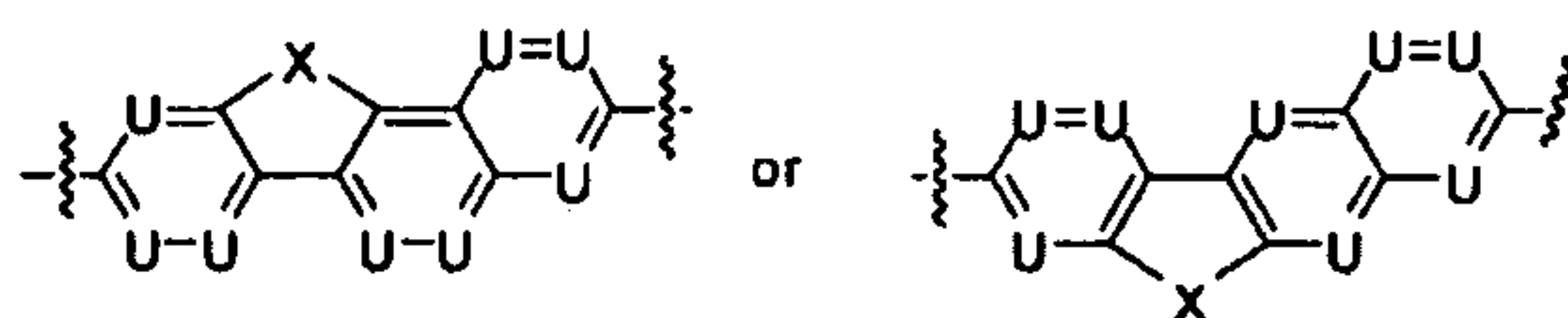
In another specific embodiment the invention provides a compound of formula (I) wherein W is W⁸ that is unsubstituted.

In another specific embodiment the invention provides a compound of formula (I) wherein W¹² is:



In another specific embodiment the invention provides a compound of formula (I) wherein W is W¹⁵ or W¹⁶.

In another specific embodiment the invention provides a compound of formula (I) wherein W is a ring system of formula:



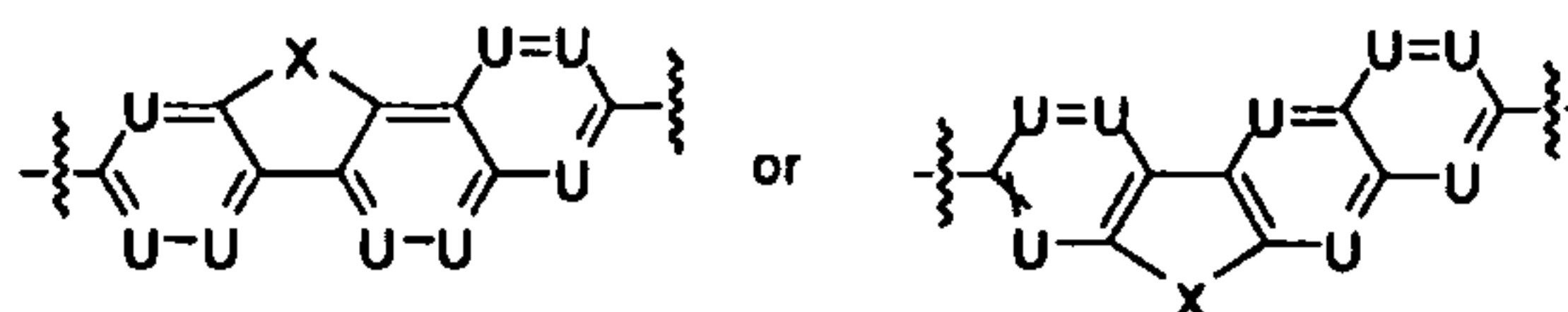
wherein :

U is CH or N; and

X is -CH₂-, -C(=O)-, -CH₂CH₂-, -CH₂CH₂CH₂-, or -CH=CH-;

wherein the ring system is optionally substituted with one or more R^{A1} or R^{A3}.

In another specific embodiment the invention provides a compound of formula (I) wherein W is a ring system of formula:



wherein :

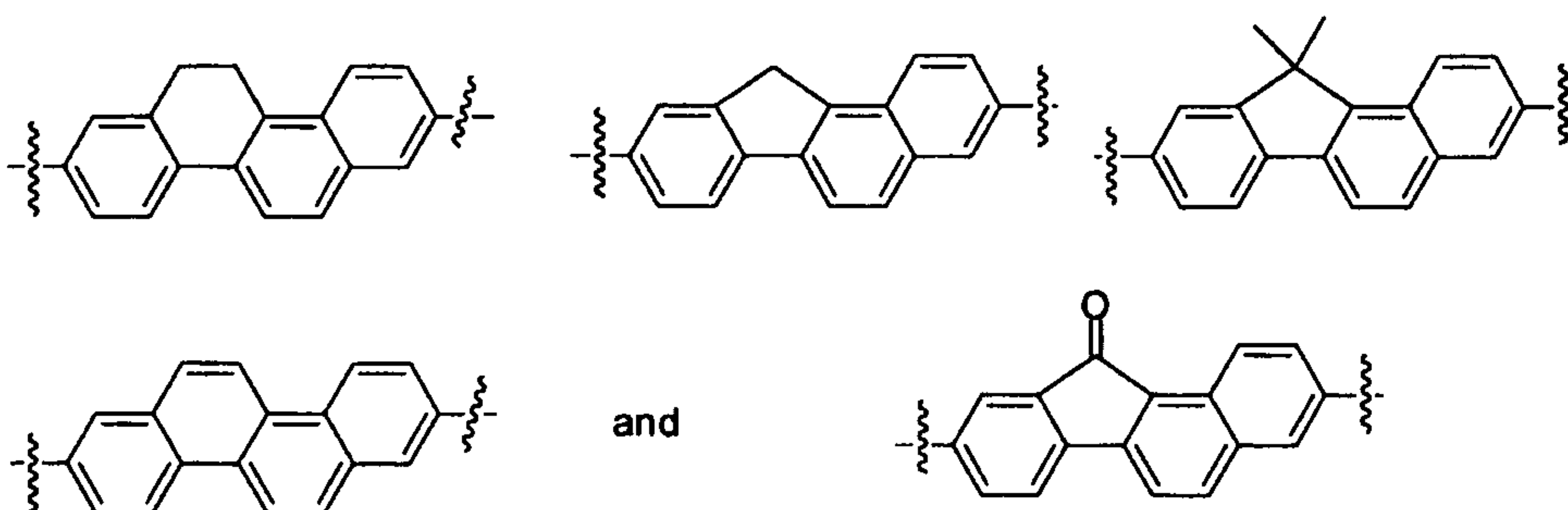
U is CH or N; and

X is $-OCH_2-$, $-CH_2O-$, $-CH_2OCH_2-$, or CF_2 ;

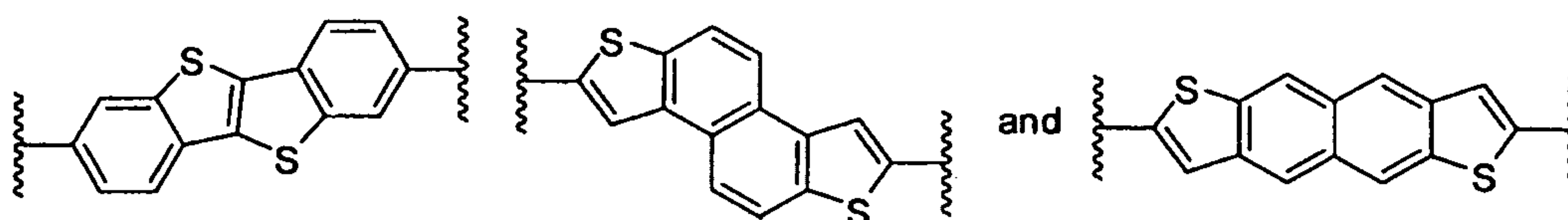
wherein the ring system is optionally substituted with one or more R^{A1} or R^{A3} .

In another specific embodiment the invention provides a compound of formula (I) wherein W is W^{15} .

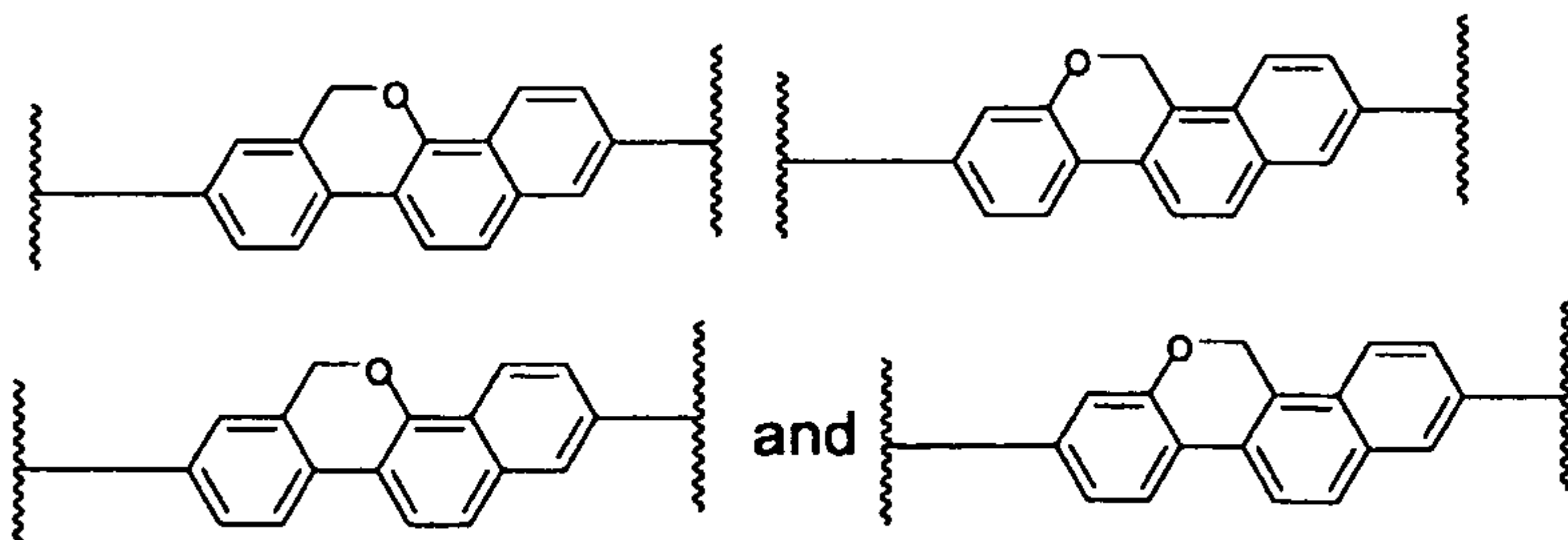
In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:



In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:

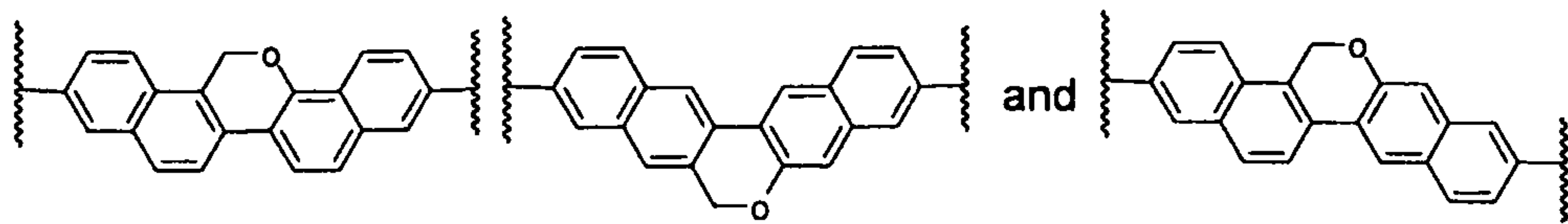


In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:

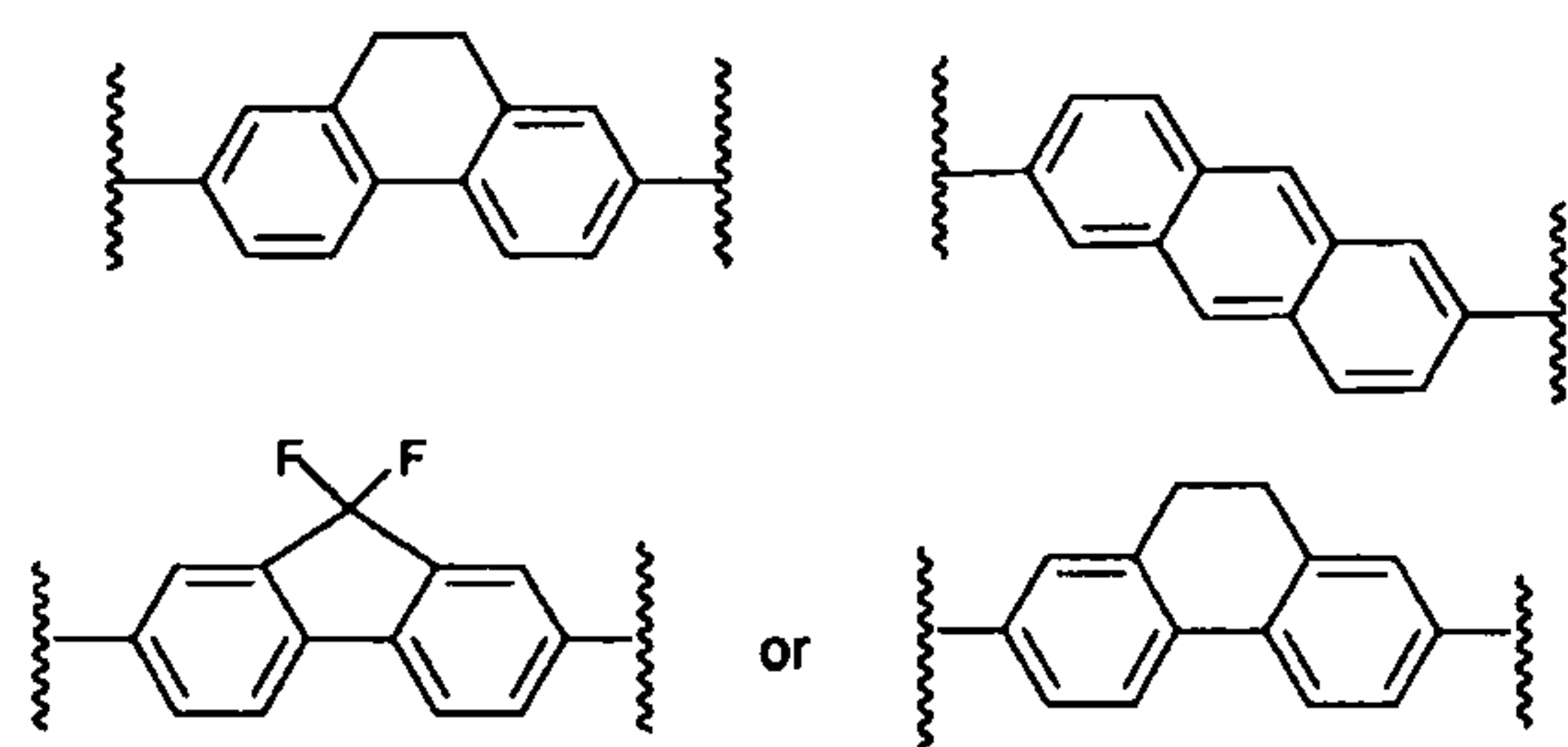


In another specific embodiment the invention provides a compound of formula (I) wherein W is W^{18} .

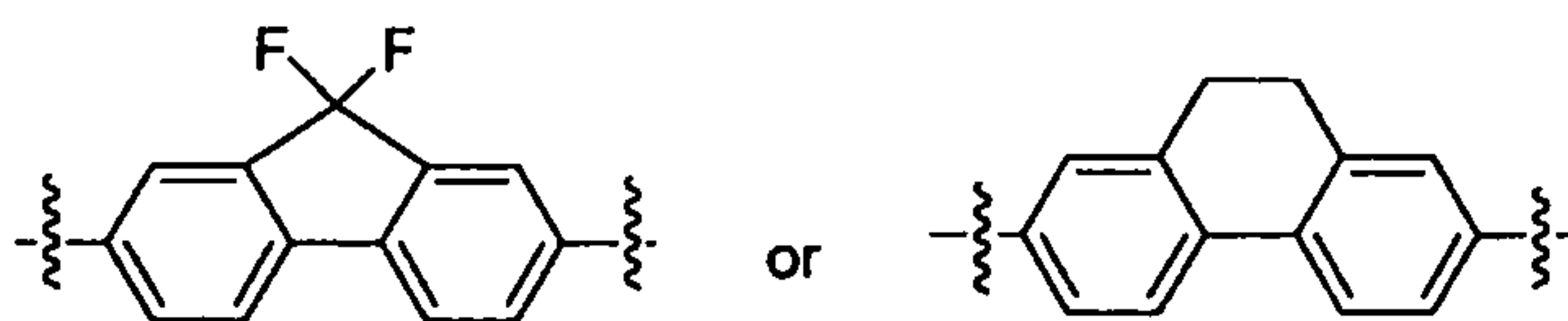
In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:



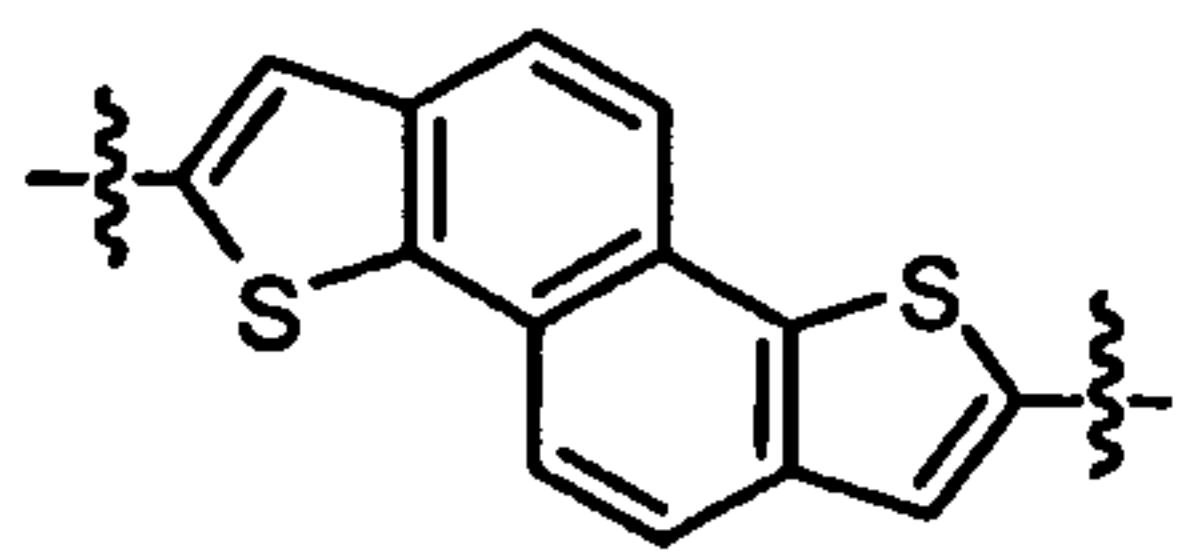
In another specific embodiment of the invention W is



In another specific embodiment of the invention W is

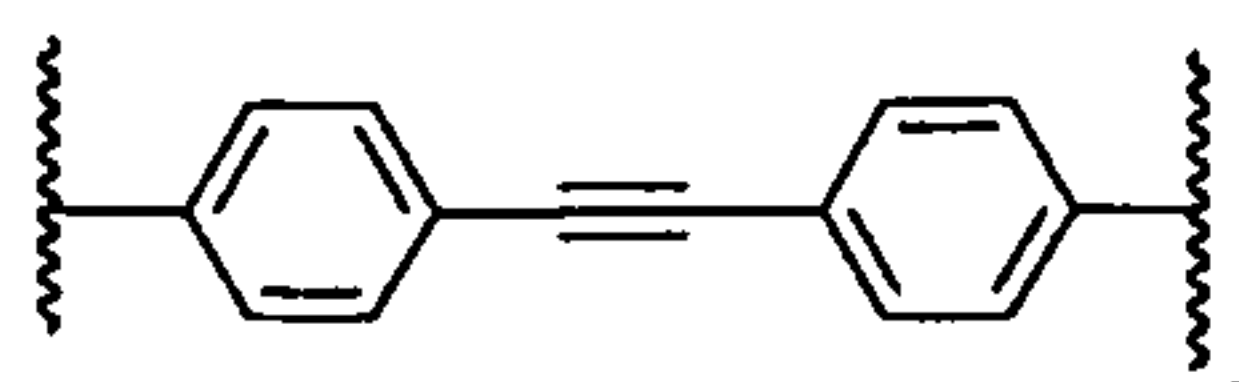


In another specific embodiment of the invention W is



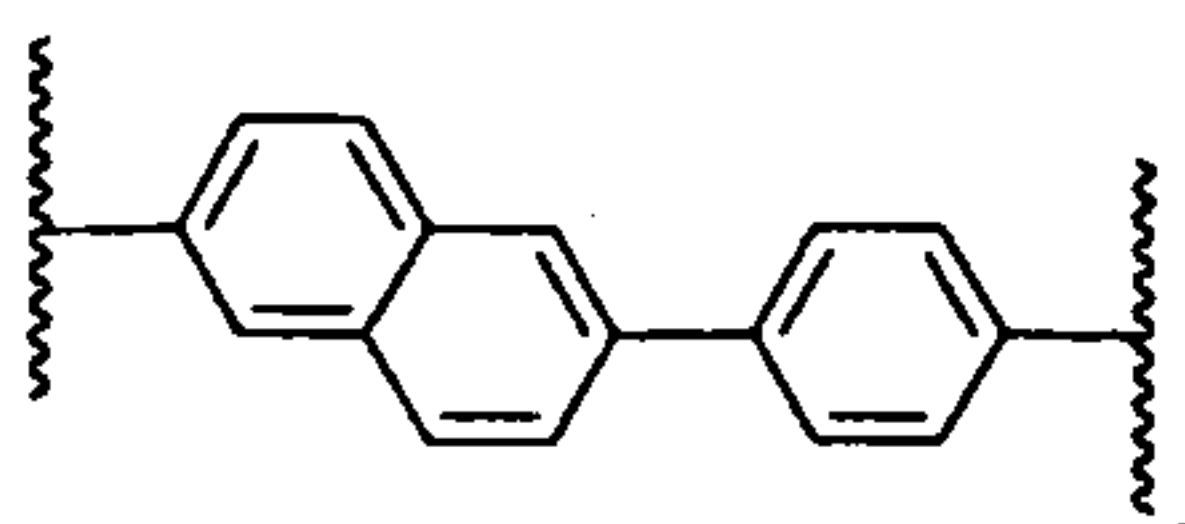
In another specific embodiment the invention provides a compound of formula (I) wherein one A is A⁰ and one A is A⁵, wherein one X^A in the A⁵ is absent and the other X^A in the A⁵ is alkynyl.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A^0-A^5-$ has the following structure:



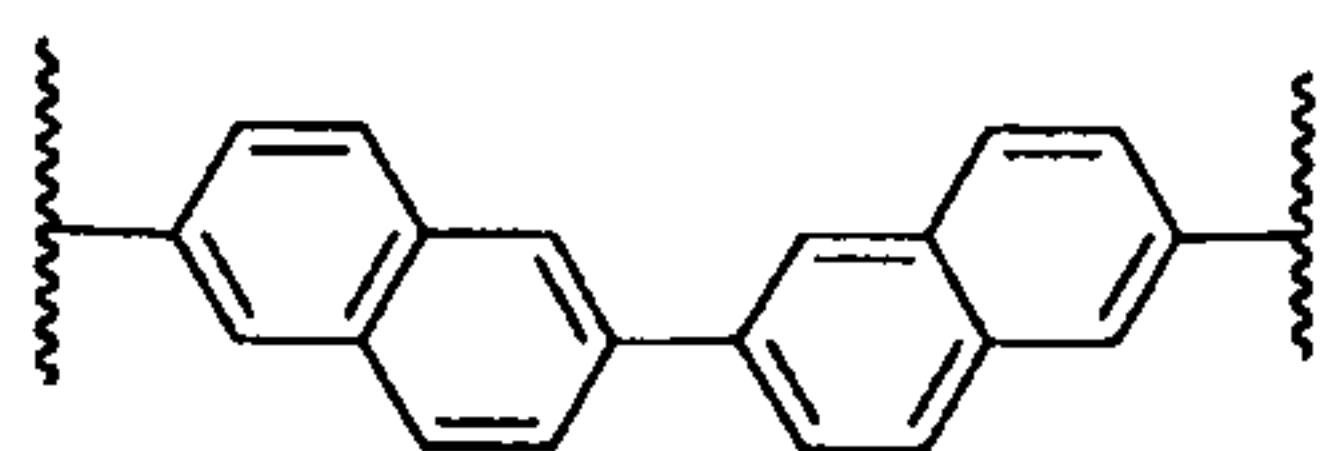
In another specific embodiment the invention provides a compound of formula (I) wherein one A is A^0 and one A is A^{13} , wherein both X^A in the A^{13} are absent.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A^0-A^{13}-$ has the following structure:



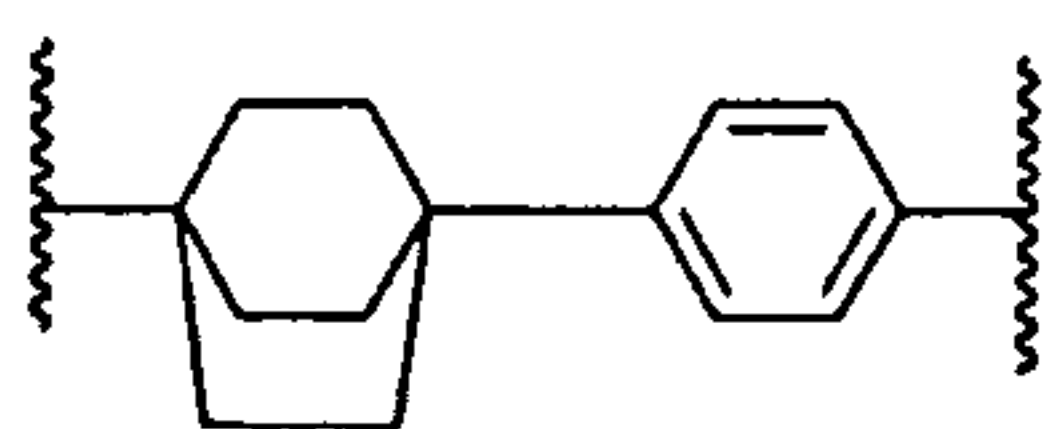
In another specific embodiment the invention provides a compound of formula (I) that comprises $A^{13}-A^{13}$, wherein all X^A in both A^{13} are absent.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A^{13}-A^{13}-$ has the following structure:



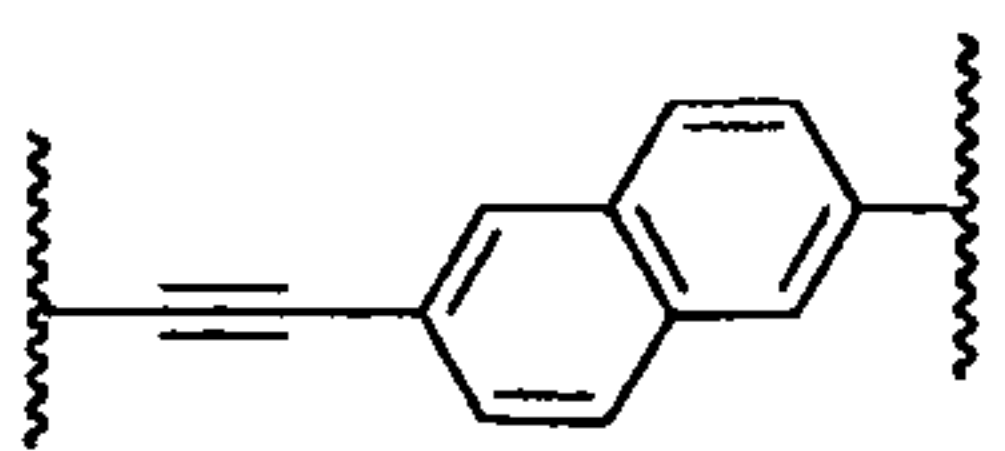
In another specific embodiment the invention provides a compound of formula (I) that comprises A^0-A^{11} wherein all X^A in both the A^0 and the A^{11} , are absent or alkynyl.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A^0-A^{11}-$ has the following structure:



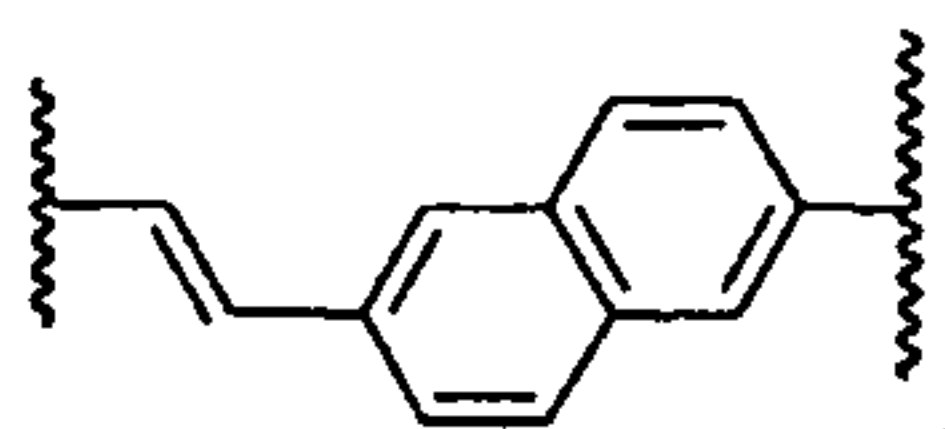
In another specific embodiment the invention provides a compound of formula (I) that comprises one A^{13} and one A^6 wherein all X^A in the A^{13} are bonds.

In another specific embodiment the invention provides a compound of formula (I) wherein $-A^{13}-A^6-$ has the following structure:



In another specific embodiment the invention provides a compound of formula (I) wherein W is W^2 and within the W^2 one X^A is absent and one X^A is $RC=CR$ and each R is independently selected from H or alkyl.

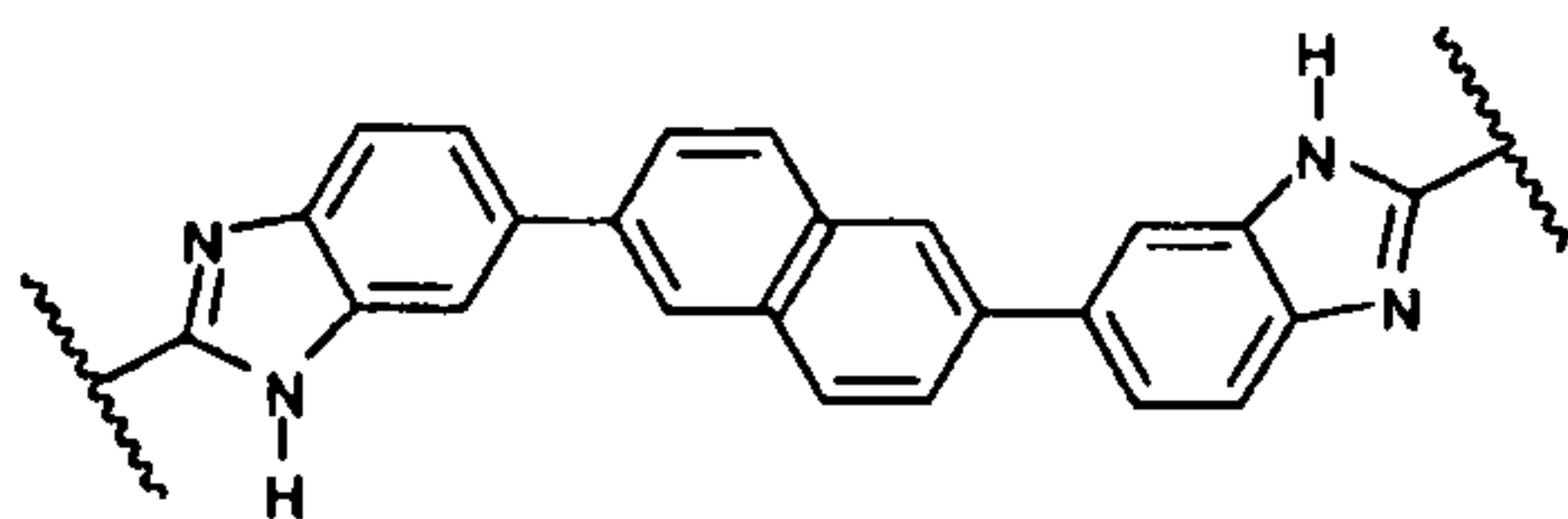
In another specific embodiment the invention provides a compound of formula (I) wherein W^2 has the following structure:



In another specific embodiment the invention provides a compound of formula (I) wherein W is W^2 and within the W^2 one X^A is absent and one X^A is selected from absent, alkynyl, or $RC=CR$ and each R is independently selected from H or alkyl; and M is selected from M^0 or M^9 .

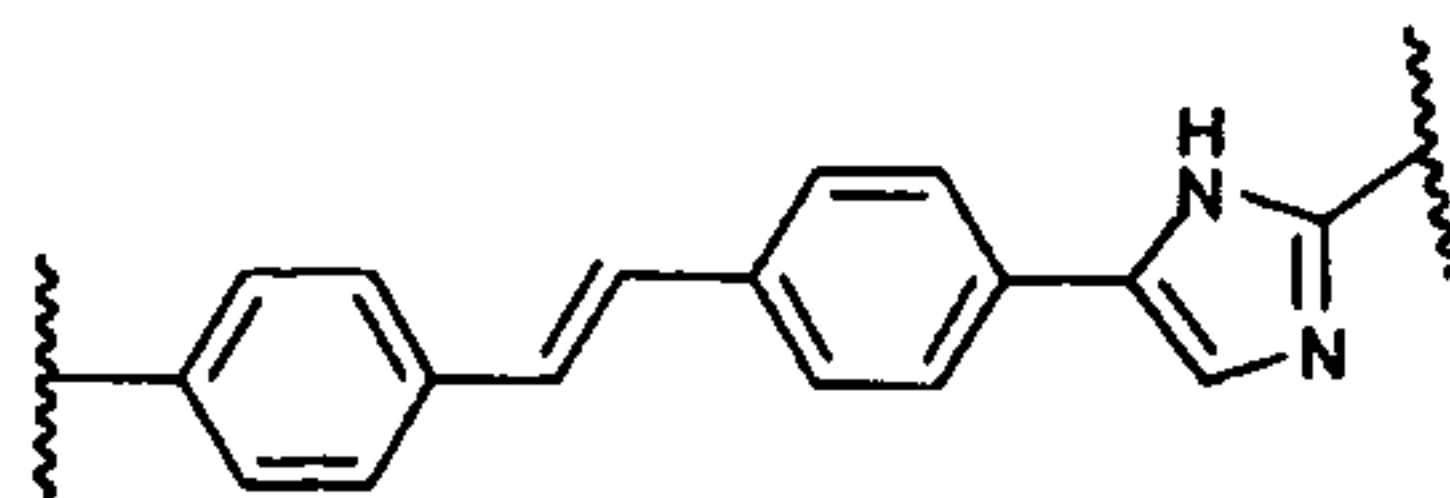
In another specific embodiment the invention provides a compound of formula (I) wherein M^0 is imidazolyl and M^9 is benzimidazolyl.

In another specific embodiment the invention provides a compound of formula (I) that comprises a group $M^9-W^2-M^9$. In another specific embodiment the invention provides a compound of formula (I) wherein the group $M^9-W^2-M^9$ has the following structure:



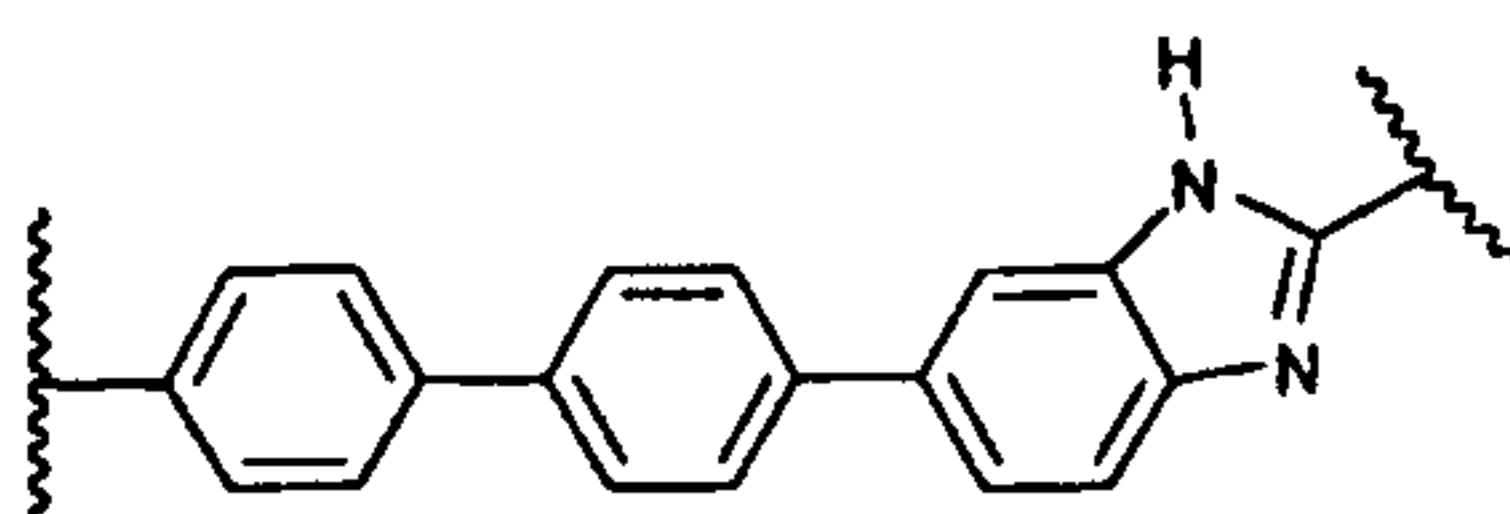
In another specific embodiment the invention provides a compound of formula (I) wherein A is A^0 and L is L^2 .

In another specific embodiment the invention provides a compound of formula (I) wherein A^0-L^2 has the following structure:

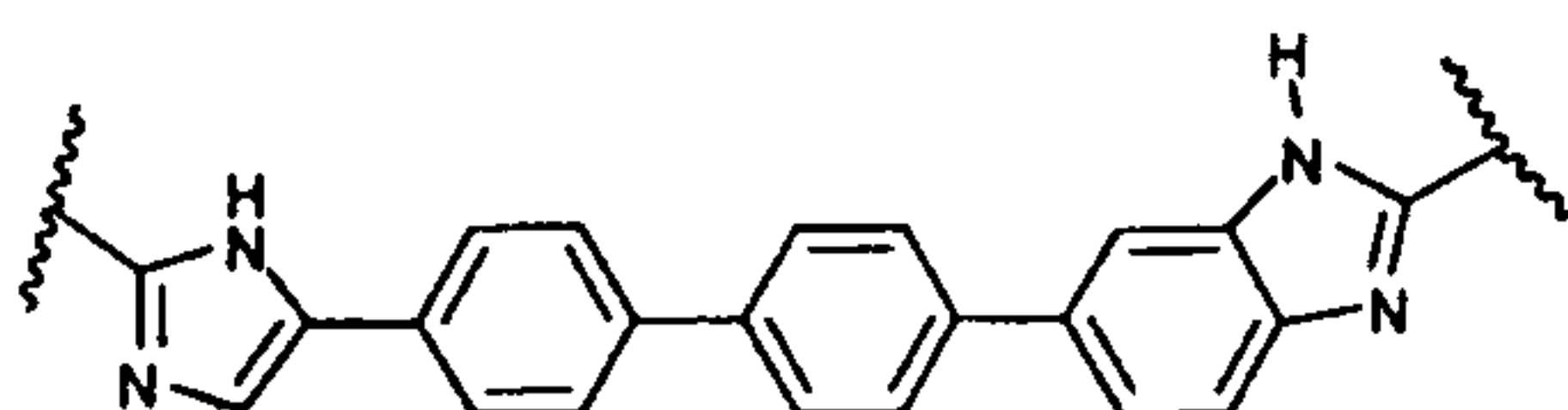


In another specific embodiment the invention provides a compound of formula (I) that comprises two A^0 and one M is M^9 .

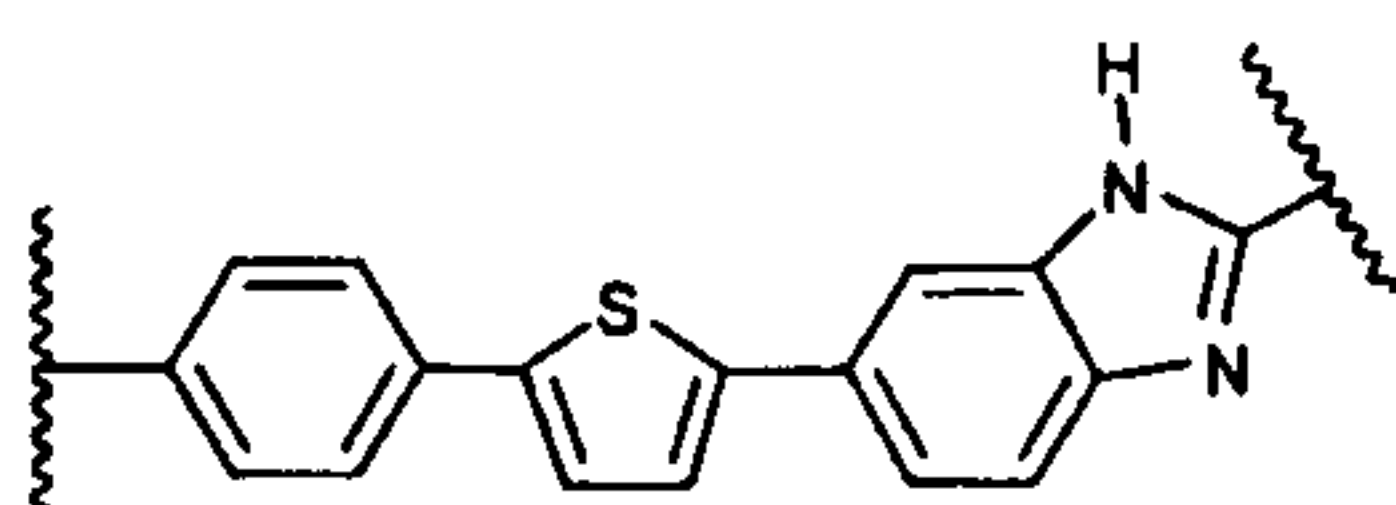
In another specific embodiment the invention provides a compound of formula (I) that comprises two A^0 and one M is M^0 and another M is M^9 . In another specific embodiment the invention provides a compound of formula (I) wherein $A^0-A^0-M^9$ has the following structure:



In another specific embodiment the invention provides a compound of formula (I) that comprises $M^0-A^0-A^0-M^9$. In another specific embodiment the invention provides a compound of formula (I) wherein $M^0-A^0-A^0-M^9$ has the following structure:



In another specific embodiment the invention provides a compound of formula (I) that comprises $A^0-A^7-M^9$. In another specific embodiment the invention provides a compound of formula (I) wherein $A^0-A^7-M^9$ has the following structure:



In another specific embodiment the invention provides a compound of formula (I) that comprises one or two M and each M is M^0 .

In another specific embodiment the invention provides a compound of formula (I) that comprises one or two M and each M is imidazolyl.

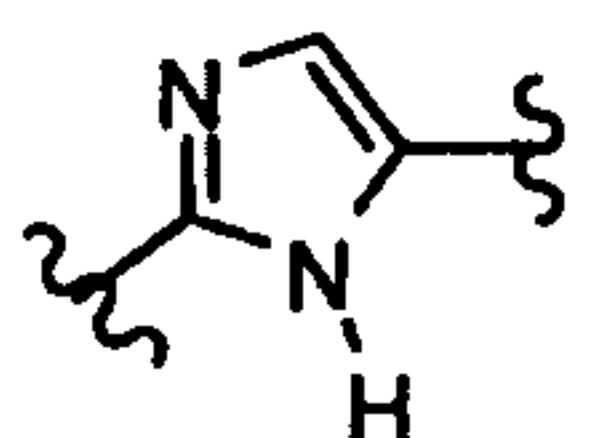
In another specific embodiment the invention provides a compound of formula (I) that comprises one or two M and each M is M^9 .

In another specific embodiment the invention provides a compound of formula (I) that comprises one or two M and each M is benzimidazolyl.

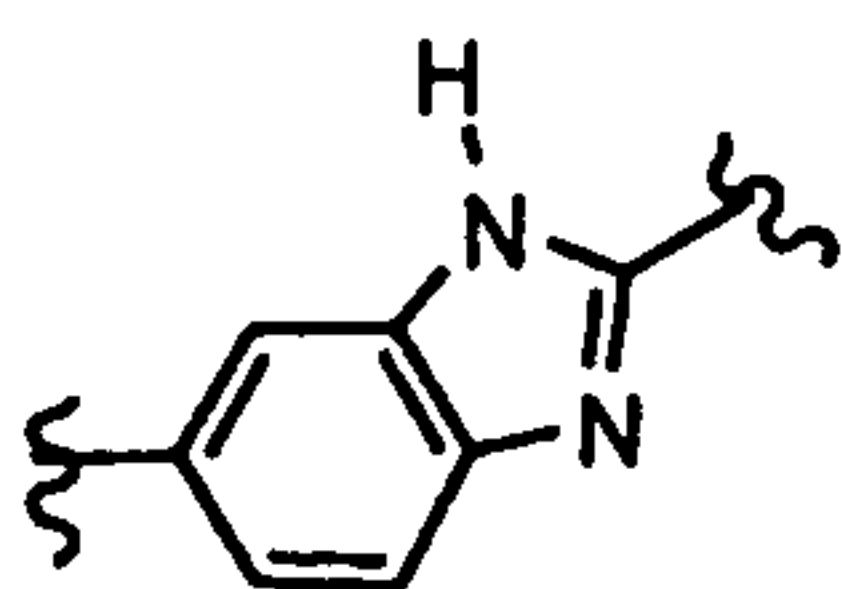
In another specific embodiment the invention provides a compound of formula (I) that comprises two M wherein one M is M^0 and one M is M^9 .

In another specific embodiment the invention provides a compound of formula (I) that comprises two M wherein one M is imidazolyl and one M is benzimidazolyl.

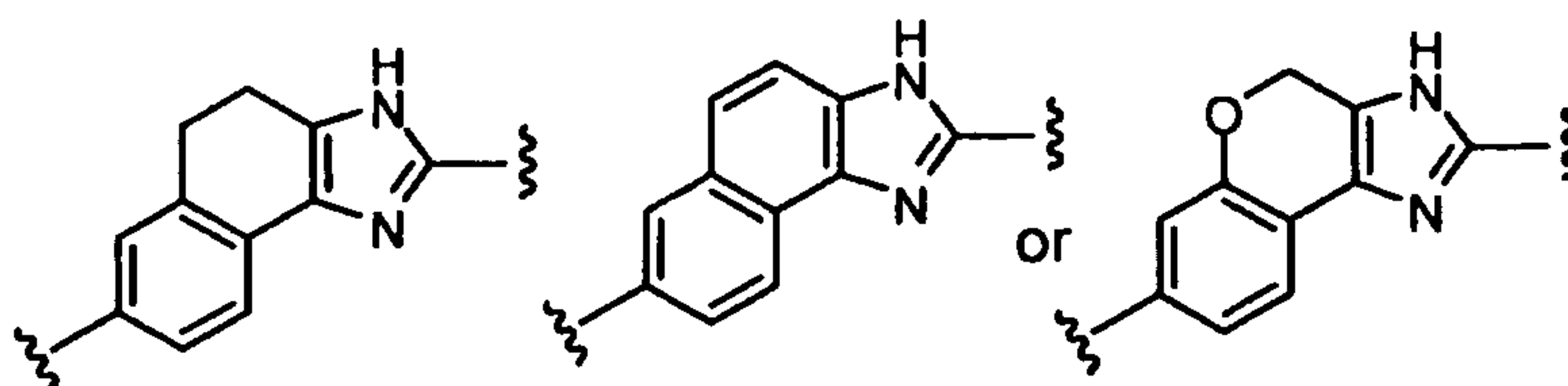
In another specific embodiment of the invention M^0 is :



In another specific embodiment of the invention M^9 is :



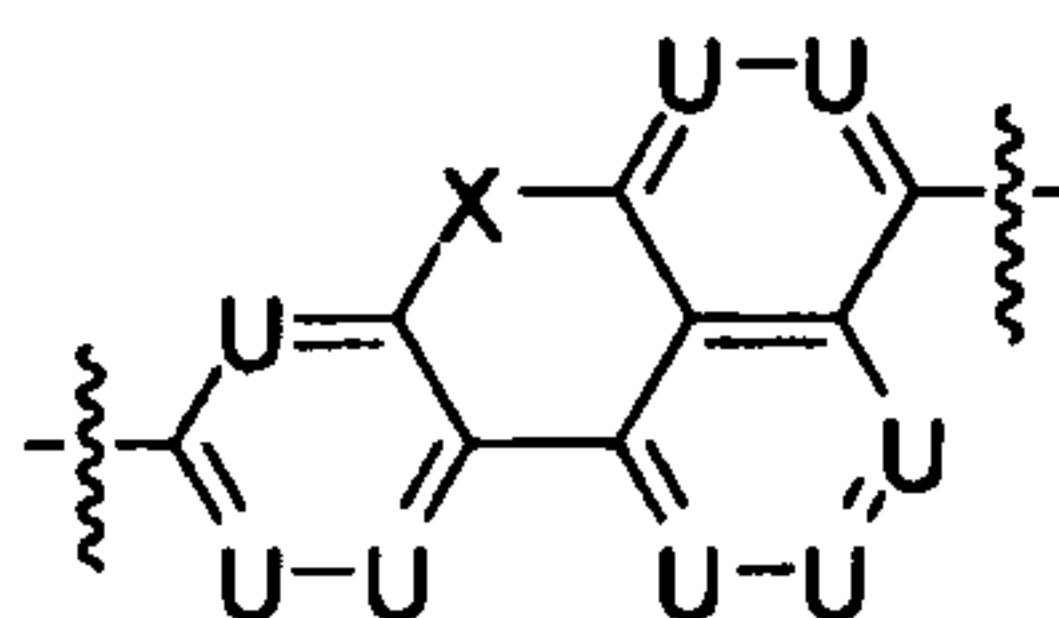
In another specific embodiment of the invention M is M^{11} and is:



In another specific embodiment the invention provides a compound of formula (I) that comprises one or two L wherein each L is L^3 .

In another specific embodiment the invention provides a compound of formula (I) that comprises one or two L wherein each L is benzimidazolyl.

In another specific embodiment the invention provides a compound of formula (I) wherein W is a ring system of formula:



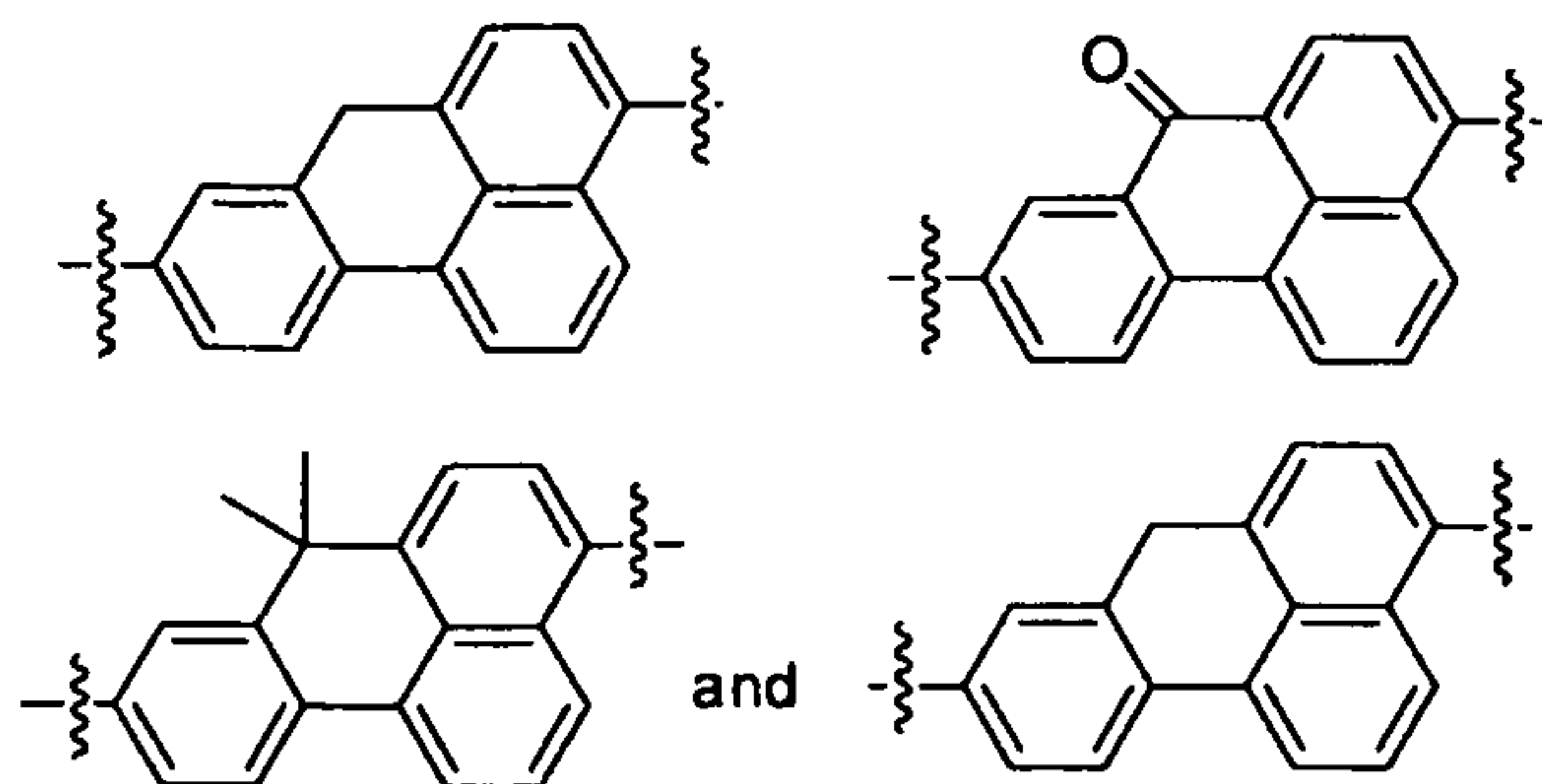
wherein :

U is CH or N ; and

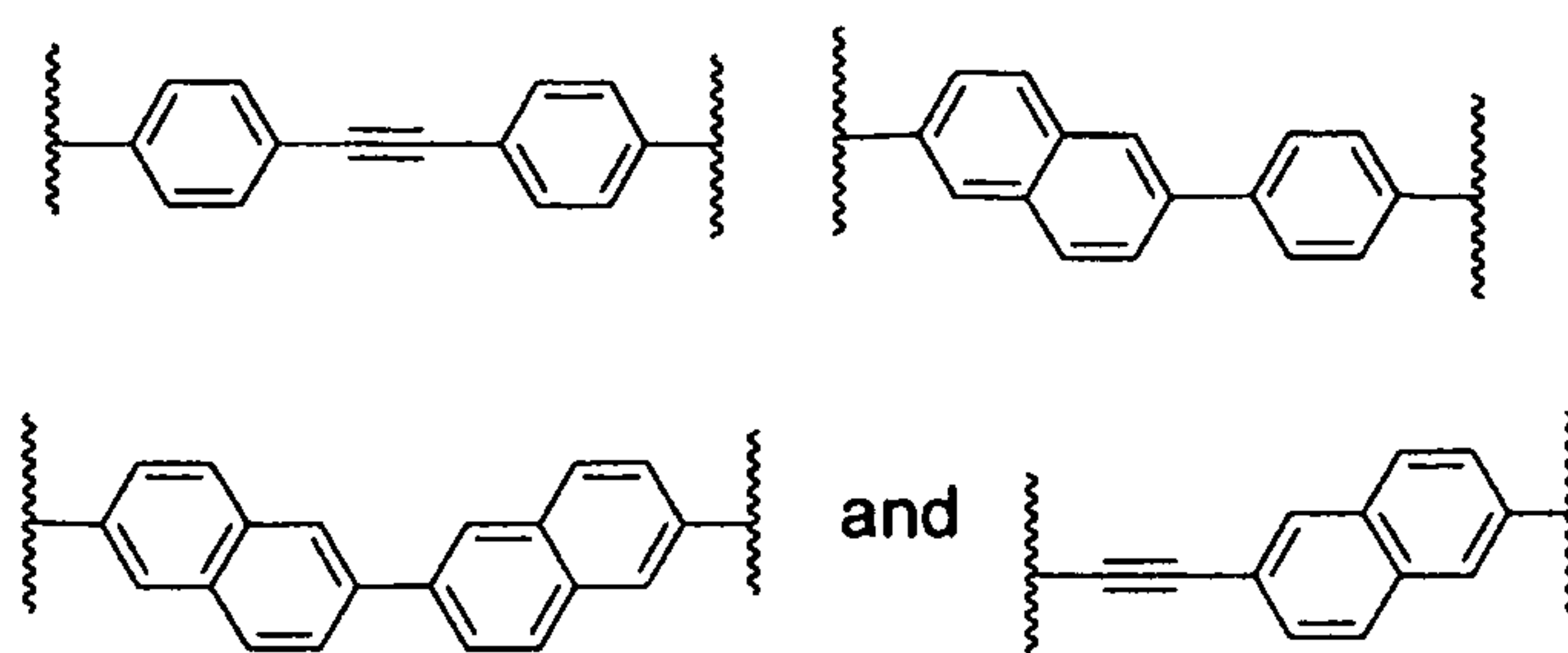
X is $-CH_2-$, $-C(=O)-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, or $-CH=CH-$;

wherein the ring system is optionally substituted with one or more R^{A1} or R^{A3} .

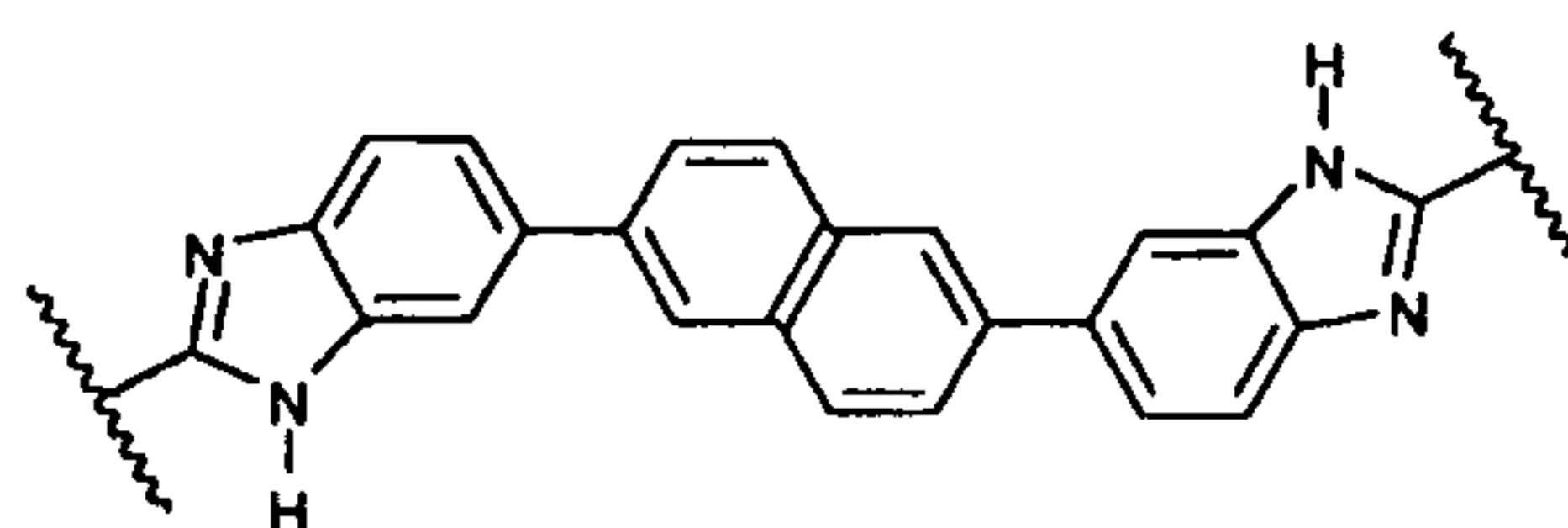
In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:



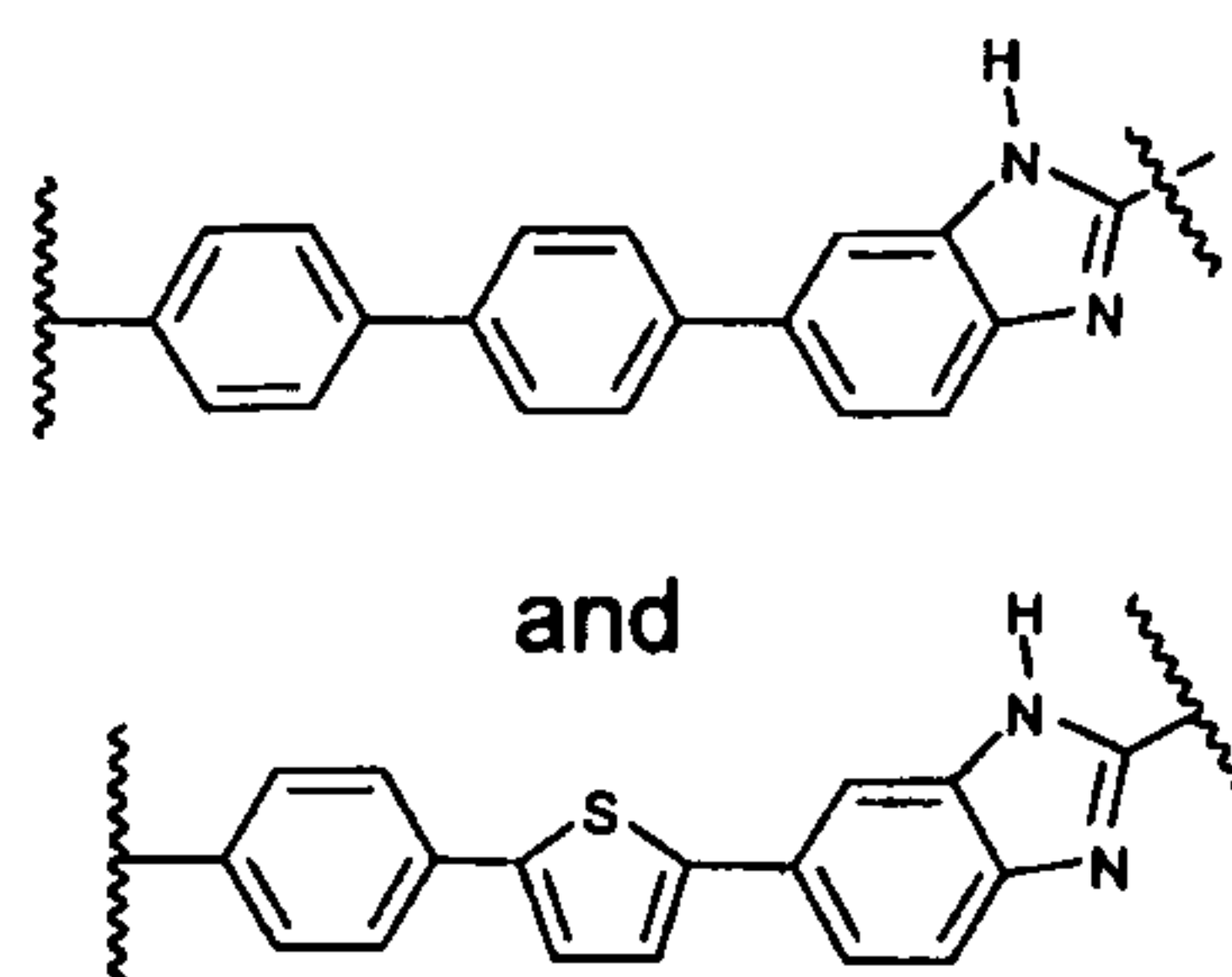
In another specific embodiment the invention provides a compound of formula (I) wherein A-A is selected from:



In another specific embodiment the invention provides a compound of formula (I) wherein M-W-M is:



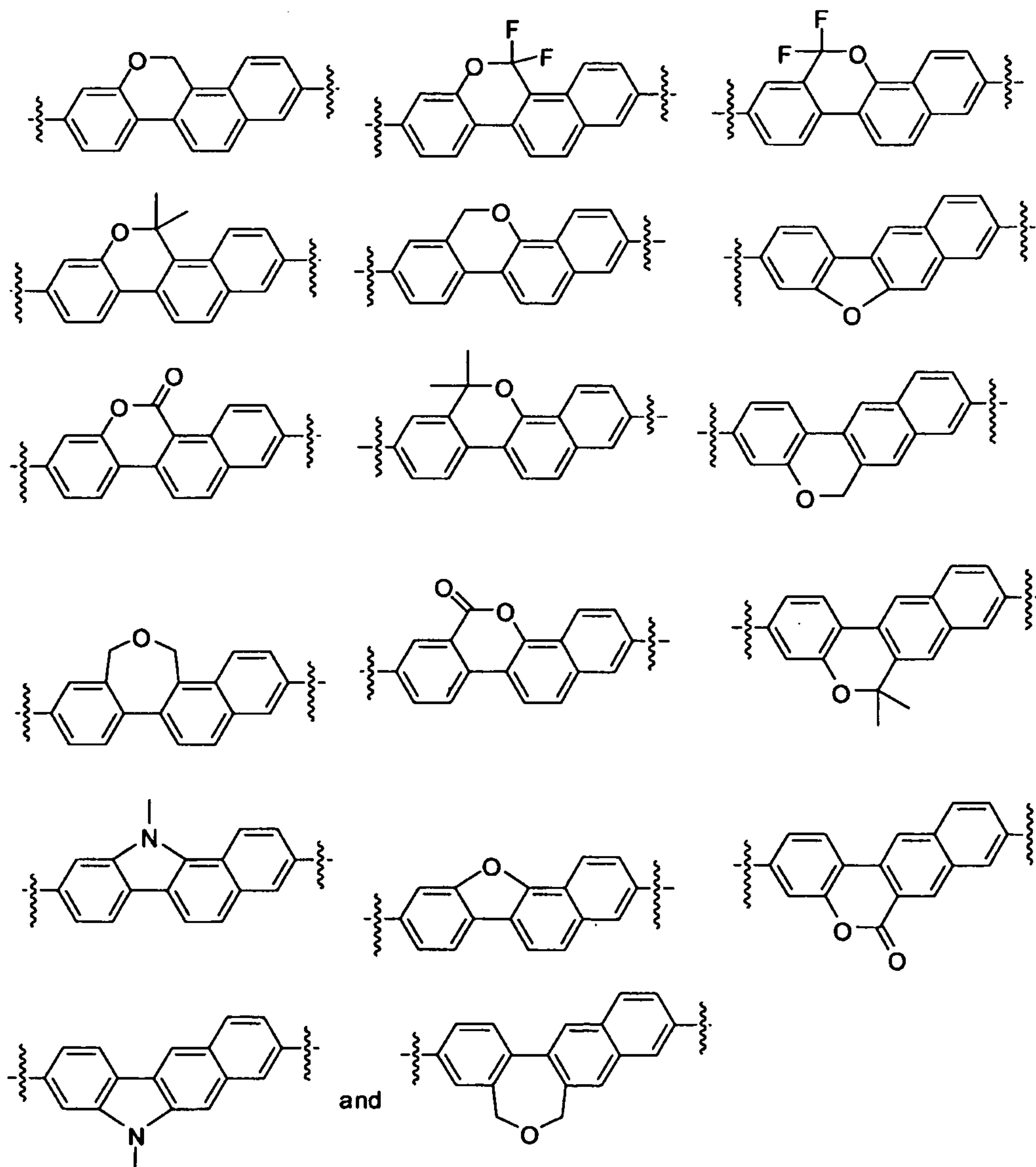
In another specific embodiment the invention provides a compound of formula (I) wherein -A-L- is selected from:



In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-A-L-P-Z-V-E.

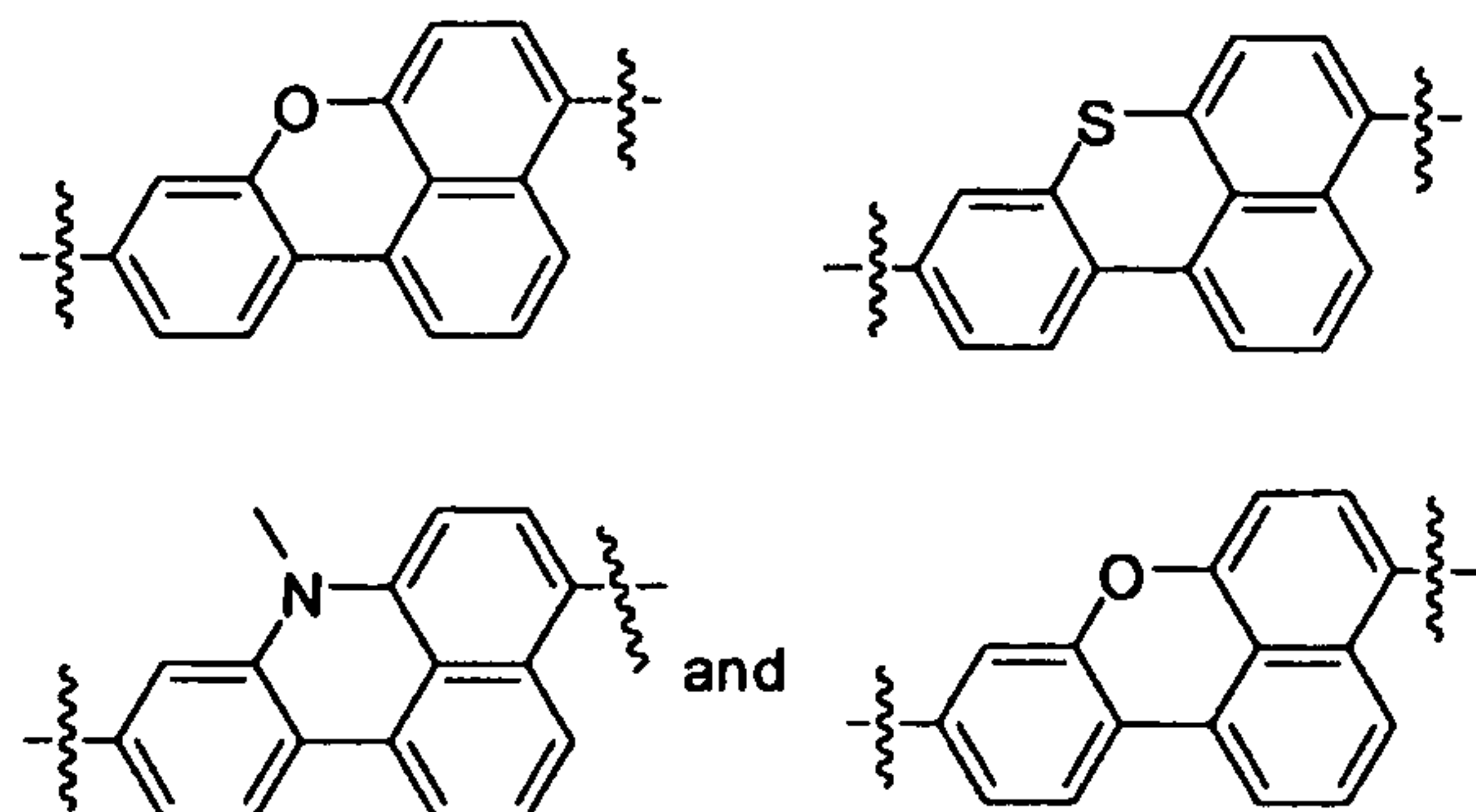
In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-A-Lⁿ-P-Z-V-E.

In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:



In another specific embodiment the invention provides a compound of formula (I) wherein W is W¹⁷.

In another specific embodiment the invention provides a compound of formula (I) wherein W is selected from:



In another specific embodiment the invention provides a compound of formula (I) that has the formula J-M-W-M-J.

In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-W-M- P-Z-V-E.

In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-A-A-M-P-Z-V-E.

In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-A-L-P-Z-V-E.

In another specific embodiment the invention provides a compound of formula (I) that has the formula E-V-Z-P-M-A-Lⁿ-P-Z-V-E.

In another specific embodiment the invention provides a compound of formula (I) wherein -M-W-M- is selected from M⁰-W-M⁰, M⁰-W-M⁹, M⁹-W-M⁰, and M⁹-W-M⁹.

In another specific embodiment the invention provides a compound of formula (I) wherein -M-W-M- is selected from M¹⁰-W-M⁰, M⁰-W-M¹⁰, M¹⁰-W-M⁹, M⁹-W-M¹⁰, and M¹⁰-W-M¹⁰.

In another specific embodiment the invention provides a compound of formula (I) wherein -M-A-A-M- is selected from M⁰-A-A-M⁰, M⁰-A-A-M⁹, M⁹-A-A-M⁰, and M⁹-A-A-M⁹.

In another specific embodiment the invention provides a compound of formula (I) wherein -M-W-M- is selected from M¹⁰-A-A-M⁰, M⁰-A-A-M¹⁰, M¹⁰-A-A-M⁹, M⁹-A-A-M¹⁰, and M¹⁰-A-A-M¹⁰.

In another specific embodiment the invention provides a compound of formula (I) wherein each E is E⁰.

In another specific embodiment the invention provides a compound of formula (I) wherein each E is -NHC(=O)Oalkyl.

In another specific embodiment the invention provides a compound of formula (I) wherein each E is methoxycarbonylamino.

In another specific embodiment the invention provides a compound of formula (I) wherein each V is V^0 .

In another specific embodiment the invention provides a compound of formula (I) wherein each V is alkyl.

In another specific embodiment the invention provides a compound of formula (I) wherein each V is isopropyl.

In another specific embodiment the invention provides a compound of formula (I) wherein each V is V^2 .

In another specific embodiment the invention provides a compound of formula (I) wherein each V is haloalkyl.

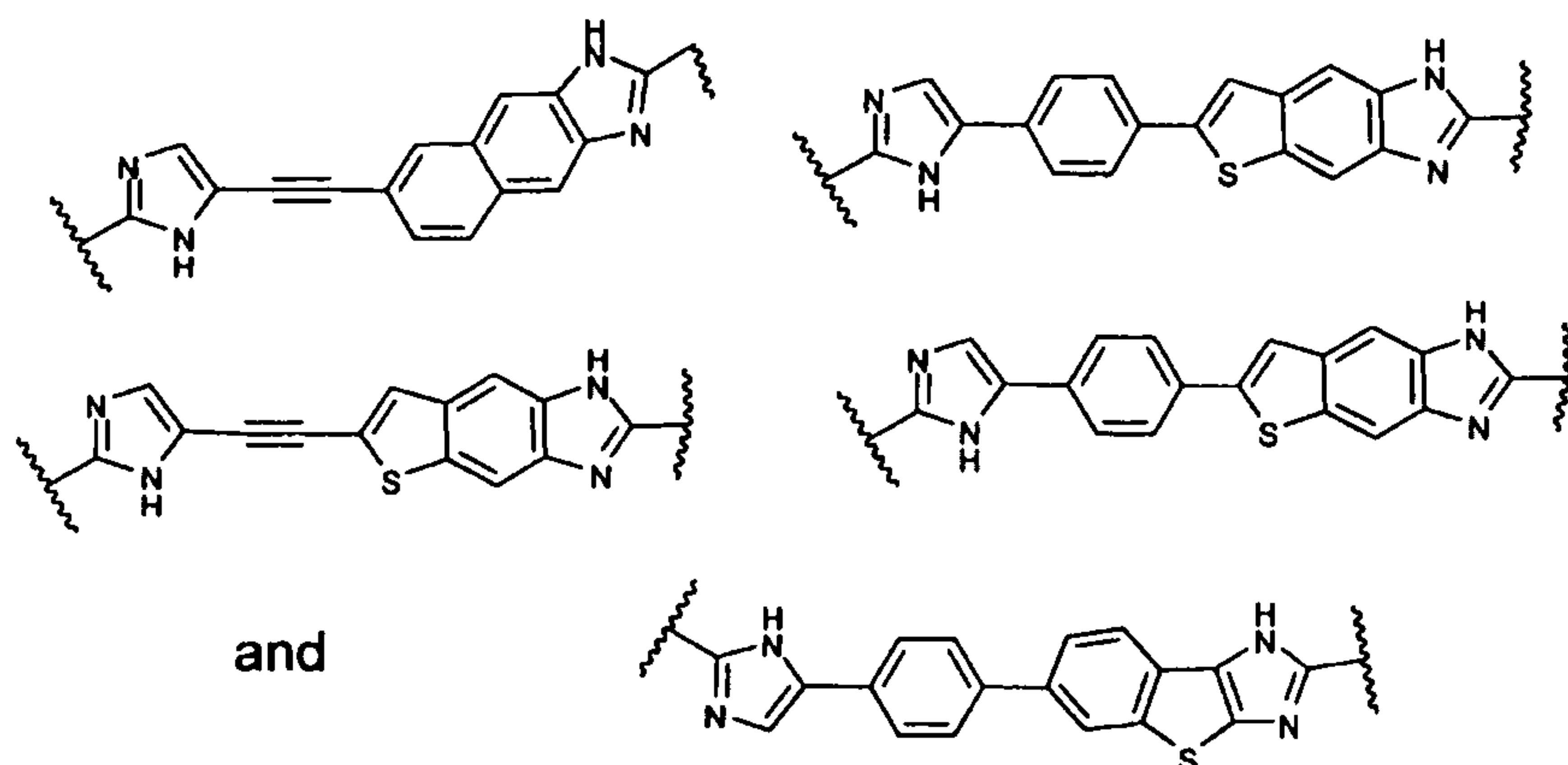
In another specific embodiment the invention provides a compound of formula (I) wherein each Z is Z^0 .

In another specific embodiment the invention provides a compound of formula (I) wherein each Z is $-C(=O)-$.

In another specific embodiment the invention provides a compound of formula (I) wherein each M is independently a 5-membered heteroaryl ring.

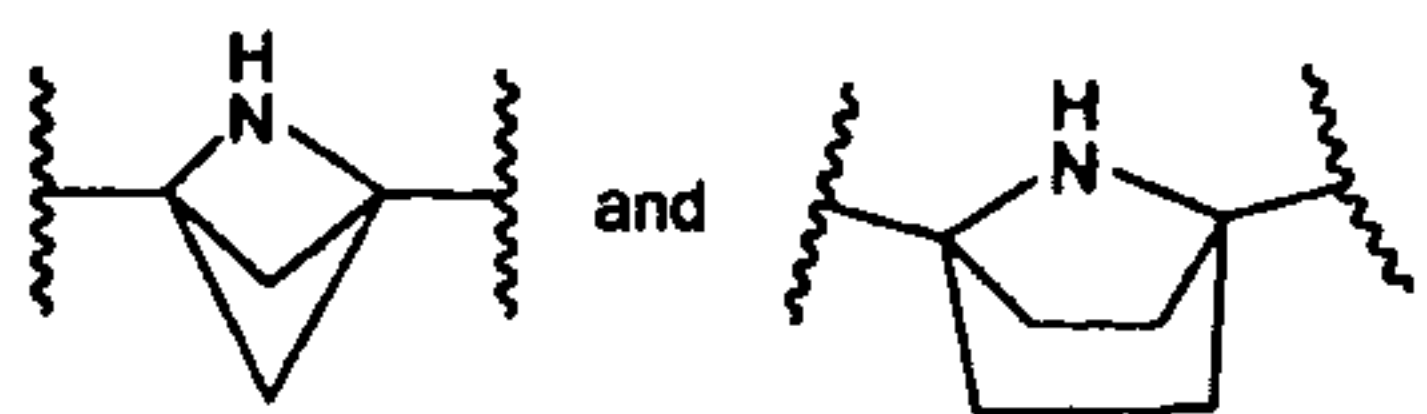
In another specific embodiment the invention provides a compound of formula (I) wherein each M is 2,4-imidazoldiyl.

In another specific embodiment the invention provides a compound of formula (I) wherein -M-A-L- is selected from:



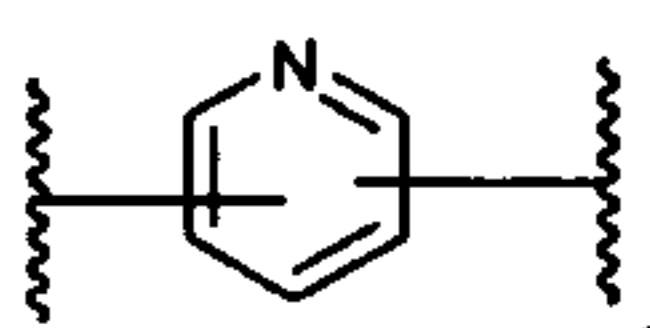
In another specific embodiment the invention provides a compound of formula (I) wherein M is M^6 .

In another specific embodiment the invention provides a compound of formula (I) wherein M is selected from:



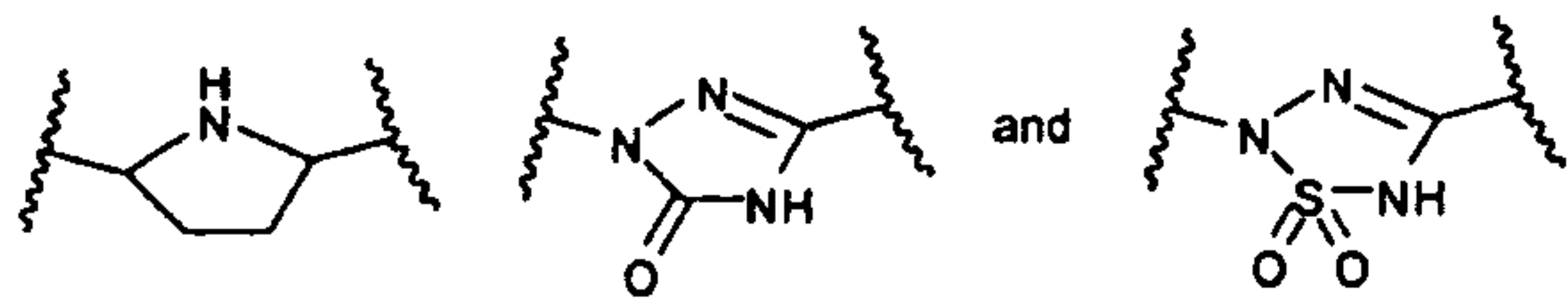
In another specific embodiment the invention provides a compound of formula (I) wherein M is M⁷.

In another specific embodiment the invention provides a compound of formula (I) wherein M is:



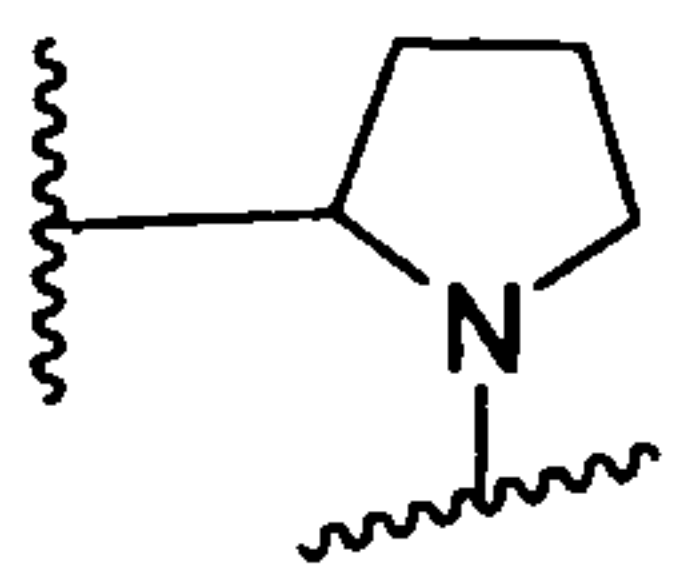
In another specific embodiment the invention provides a compound of formula (I) wherein M is M⁸.

In another specific embodiment the invention provides a compound of formula (I) wherein M is:

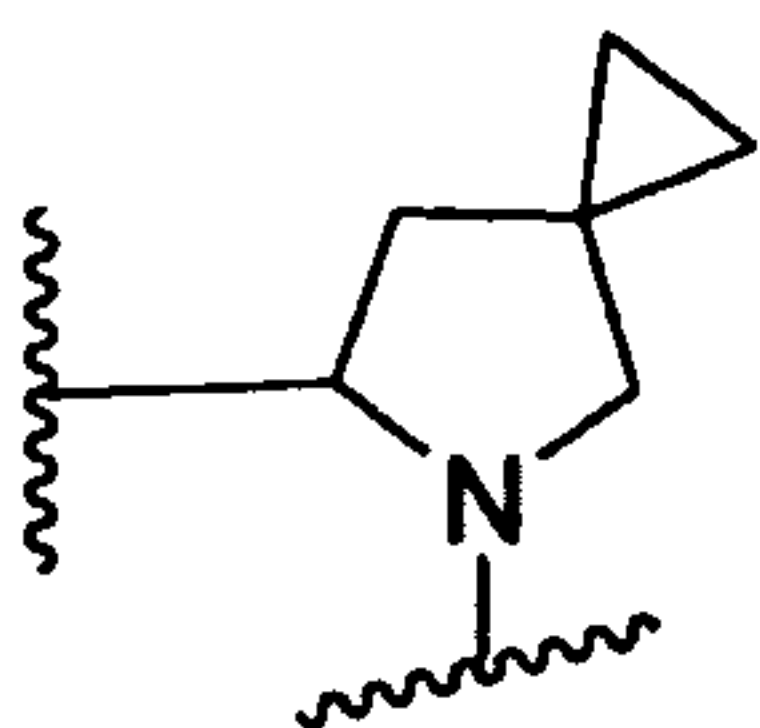


In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁰.

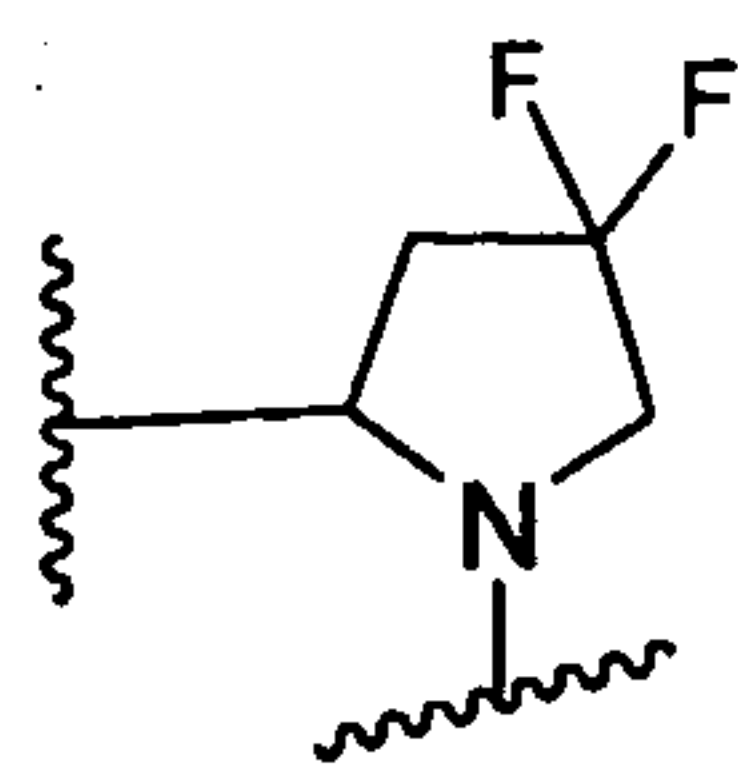
In another specific embodiment the invention provides a compound of formula (I) wherein P is



In another specific embodiment the invention provides a compound of formula (I) wherein P is:



In another specific embodiment the invention provides a compound of formula (I) wherein P is



In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P².

In another specific embodiment the invention provides a compound of formula (I) wherein P is P²; and pn is 1.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P²; pn is 1; and R^{P12} is independently selected from alkylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, -C(=O)R^h, -C(=O)NR^hR^h, -C(=O)OR^h, and haloalkyl.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P³; pn is 1 and ps is zero.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁵.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁵; pn is 1; and Z is O, S, S(=O), S(=O)₂, or NR^f.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁵; pn is 1; and Z is O, or S.

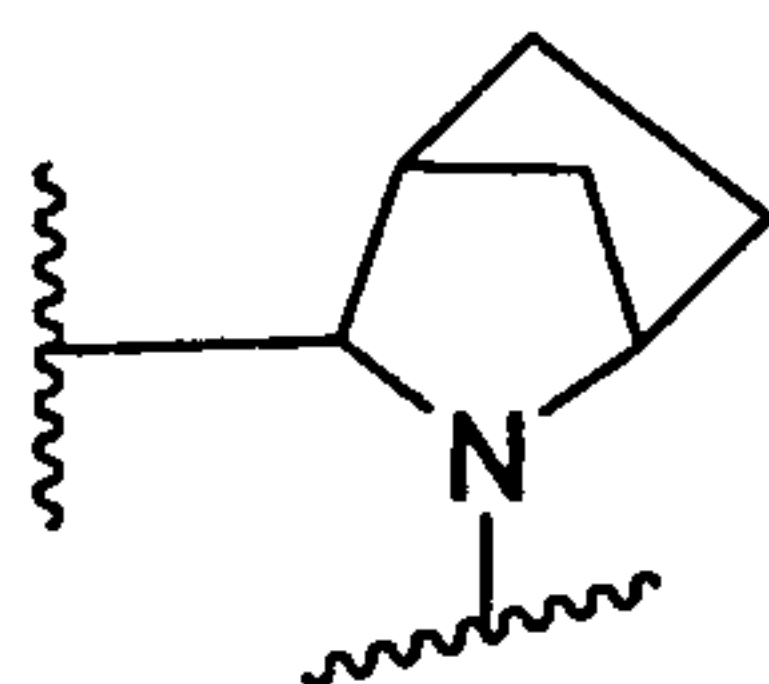
In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁶.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁶; pn is 1; and Z is O, S, S(=O), S(=O)₂, or NR^f.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁷ wherein P⁷ is a [2.2.1] or a [2.2.2] ring system.

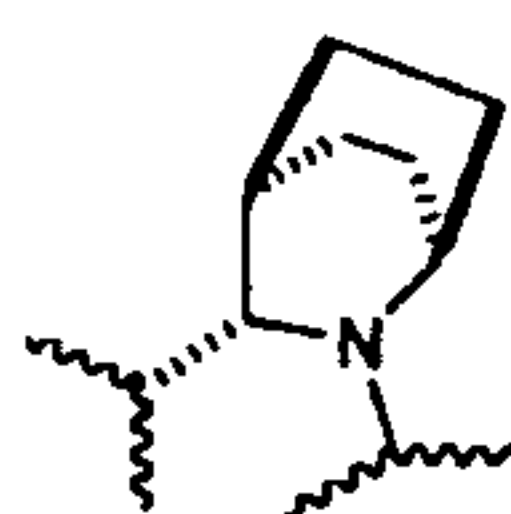
In another specific embodiment the invention provides a compound of formula (I) wherein P is P⁷ wherein P⁷ is a [2.2.1] ring system.

In another specific embodiment the invention provides a compound of formula (I) wherein P is



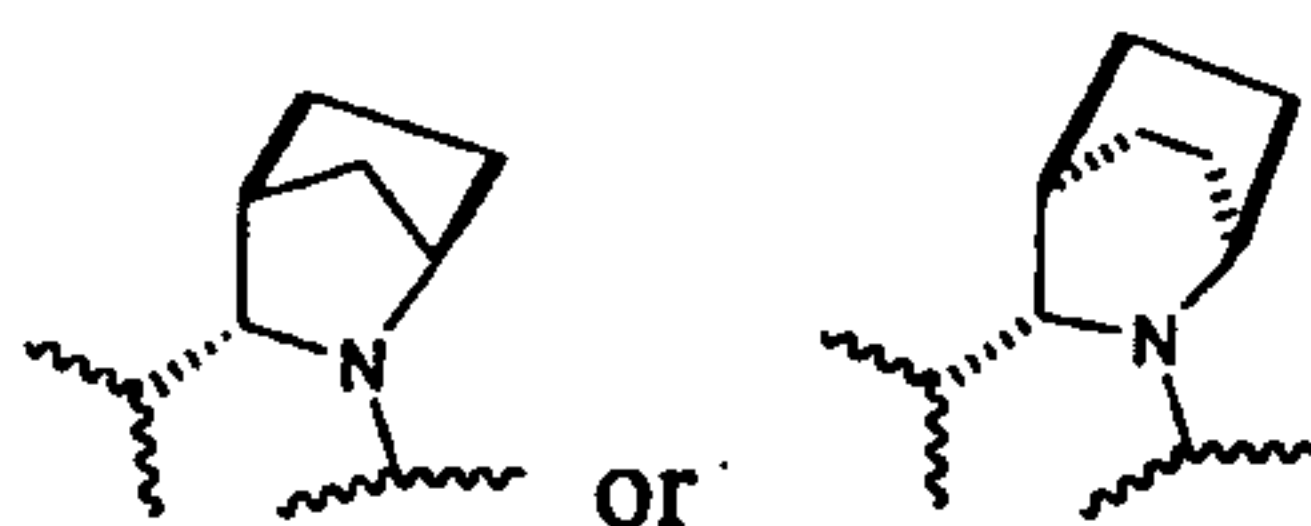
optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} .

In another specific embodiment the invention provides a compound of formula (I) wherein P is



optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} .

In another specific embodiment the invention provides a compound of formula (I) wherein P is



optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} .

In another specific embodiment the invention provides a compound of formula (I) wherein P is P^8 .

In another specific embodiment the invention provides a compound of formula (I) wherein P is P^8 ; and pn is 1.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P^8 ; pn is 1; and ps is 2.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P^{10} .

In another specific embodiment the invention provides a compound of formula (I) wherein P is P^{10} ; pn is 1; and X is O, S, S(=O), S(=O)₂, CHR^{P10}, or CH(R^{P10})₂.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹⁰; pn is 1; po is 1; and X is O, S, S(=O), S(=O)₂, CHR^{P10}, or CH(R^{P10})₂.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹⁰; pn is 1; po is 1; ps is 0; and X is O, S, S(=O), S(=O)₂, CHR^{P10}, or CH(R^{P10})₂.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹¹.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹¹; pn is 1; po is 1; ps is 0; and X is O, S, S(=O), S(=O)₂, CHR^{P10}, or CH(R^{P10})₂.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹².

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹²; pm is 1; and pp is 1.

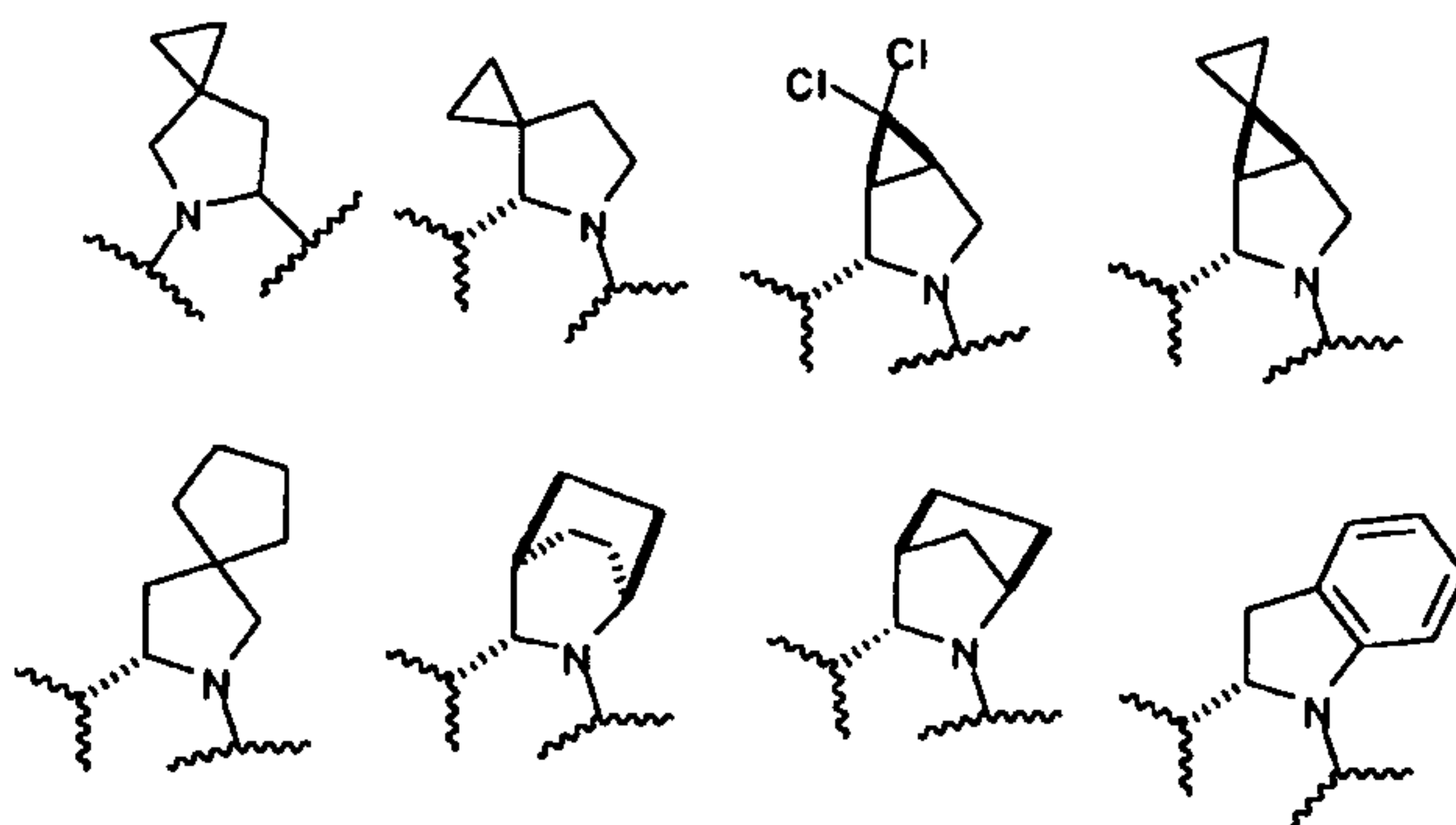
In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹³.

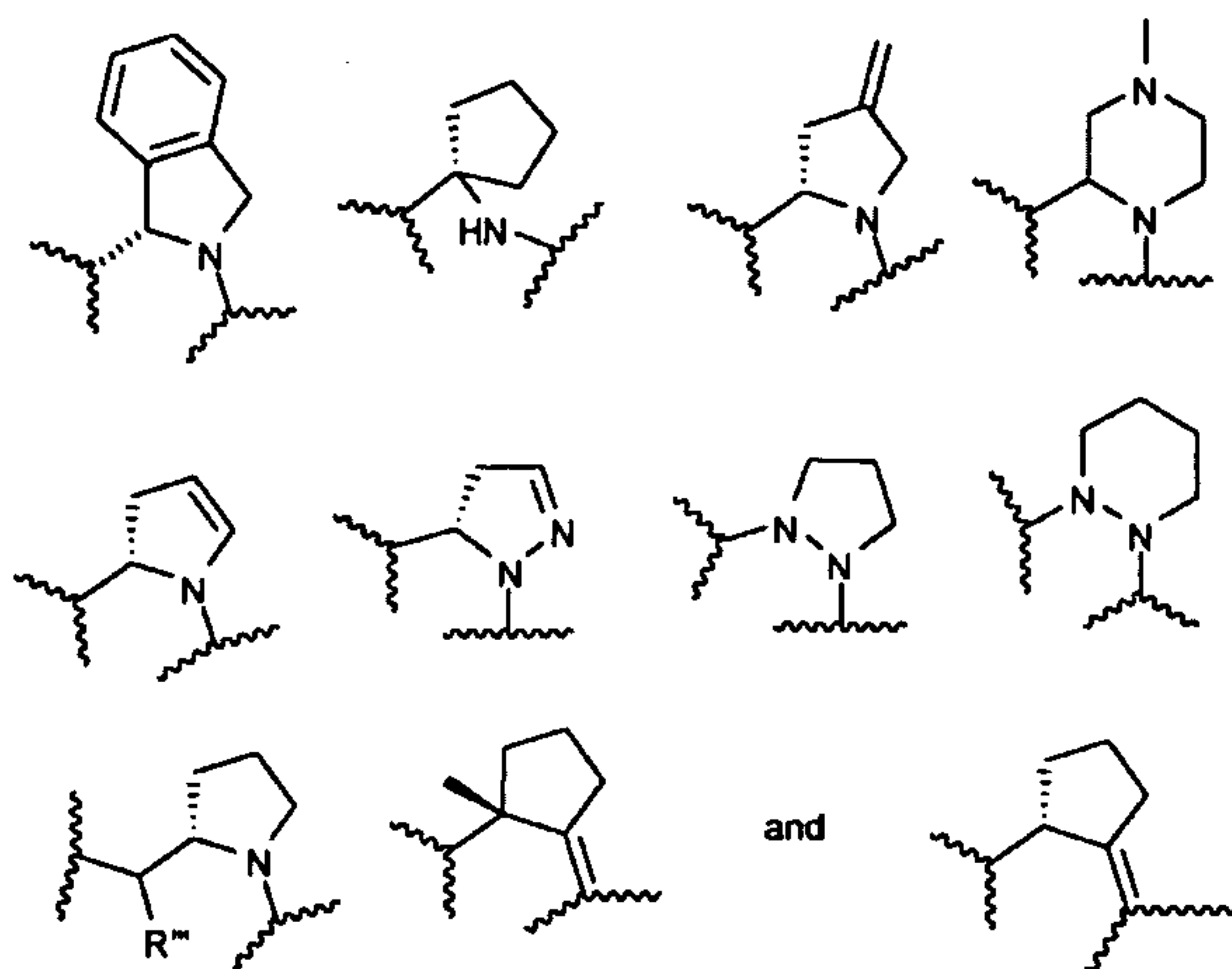
In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹³; pm is 1; pn is 0; ps is 0; pp is 1; pq is 0; and X is O, S, or S(=O)₂.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹⁴.

In another specific embodiment the invention provides a compound of formula (I) wherein P is P¹⁴; pm is 0; and pq is 0.

In another specific embodiment the invention provides a compound of formula (I) wherein P is selected from:





In another specific embodiment the invention provides a compound of formula (I) having a formula selected from:

T-P-Y-P-T; T-P-Y-J; J-Y-J; T-P-Y-P-Z-R₉; R₉-Z-P-Y-P-Z-R₉; J-Y-P-Z-R₉; T-P-Y-P-Z-V-E; E-V-Z-P-Y-P-Z-V-E; J-Y-P-Z-V-E; T-P-L-L-P-T; T-P-L-L-J; J-L-L-J; T-P-L-L-P-Z-R₉; R₉-Z-P-L-L-P-Z-R₉; J-L-L-P-Z-R₉; T-P-L-L-P-Z-V-E; E-V-Z-P-L-L-P-Z-V-E; J-L-L-P-Z-V-E; T-P-M-A-L-P-T; T-P-M-A-L-J; J-M-A-L-J; T-P-M-A-L-P-Z-R₉; R₉-Z-P-M-A-L-P-Z-R₉; J-M-A-L-P-Z-R₉; L-P-M-A-L-P-Z-V-E; E-V-Z-P-M-A-L-P-Z-V-E; J-M-A-L-P-Z-V-E; T-B-A-L-P-T; T-B-A-L-J; T-B-A-L-P-Z-R₉; R₉-Z-B-A-L-P-Z-R₉; T-B-A-L-P-Z-V-E; E-V-Z-B-A-L-P-Z-V-E; T-P-M-A-A-M-P-T; T-P-M-A-A-M-J; J-M-A-A-M-J; T-P-M-A-A-M-P-Z-R₉; R₉-Z-P-M-A-A-M-P-Z-R₉; J-M-A-A-M-P-Z-R₉; T-P-M-A-A-M-P-Z-V-E; E-V-Z-P-M-A-A-M-P-Z-V-E; J-M-A-A-M-P-Z-V-E; T-B-A-A-M-P-T; T-B-A-A-M-J; T-B-A-A-M-P-Z-R₉; R₉-Z-B-A-A-M-P-Z-R₉; T-B-A-A-M-P-Z-V-E; E-V-Z-B-A-A-M-P-Z-V-E; T-P-M-A-A-B-T; T-P-M-A-A-B-Z-R₉; R₉-Z-P-M-A-A-B-Z-R₉; J-M-A-A-B-Z-R₉; T-P-M-A-A-B-Z-V-E; E-V-Z-P-M-A-A-B-Z-V-E; J-M-A-A-B-Z-V-E; T-B-A-A-B-T; T-B-A-A-B-Z-R₉; R₉-Z-B-A-A-B-Z-R₉; T-B-A-A-B-Z-V-E; E-V-Z-B-A-A-B-Z-V-E; T-P-M-W-M-P-T; T-P-M-W-M-J; J-M-W-M-J; T-P-M-W-M-P-Z-R₉; R₉-Z-P-M-W-M-P-Z-R₉; J-M-W-M-P-Z-R₉; T-P-M-W-M-P-Z-V-E; E-V-Z-P-M-W-M-P-Z-V-E; J-M-W-M-P-Z-V-E; T-B-W-M-P-T; T-B-W-M-J; T-B-W-M-P-Z-R₉; R₉-Z-B-W-M-P-Z-R₉; T-B-W-M-P-Z-V-E; E-V-Z-B-W-M-P-Z-V-E; T-P-M-W-B-T; T-P-M-W-B-Z-R₉; R₉-Z-P-M-W-B-Z-R₉; J-M-W-B-Z-R₉; T-P-M-W-B-Z-V-E; E-V-Z-P-M-W-B-Z-V-E; J-M-W-B-Z-V-E; T-B-W-B-T; T-B-W-B-Z-R₉; R₉-Z-B-W-B-Z-R₉; T-B-W-B-Z-V-E; E-V-Z-B-W-B-Z-V-E; T-P-M-M-P-T; T-P-M-M-J; J-M-M-J; T-P-M-M-P-Z-R₉; R₉-Z-P-M-M-P-Z-R₉; J-M-M-P-Z-R₉; T-P-M-M-P-Z-V-E; E-V-Z-P-M-M-P-Z-V-E; J-M-M-P-Z-V-E; T-B-M-P-T; T-B-M-J; T-B-M-P-Z-R₉; R₉-Z-B-M-P-Z-R₉; T-B-M-P-Z-V-E; E-V-Z-B-M-P-Z-V-E; T-P-M-B-T; T-P-M-B-Z-R₉; R₉-Z-P-M-B-Z-R₉; J-M-B-Z-R₉; T-P-M-

B-Z-V-E; E-V-Z-P-M-B-Z-V-E; J-M-B-Z-V-E; T-B-B-T; T-B-B-Z-R9; R9-Z-B-B-Z-R9; and T-B-B-Z-V-E; E-V-Z-B-B-Z-V-E; or a pharmaceutically acceptable salt thereof.

In another specific embodiment the invention provides a compound of formula (I) having a formula selected from:

T-P-Y-P-T; T-P-Y-J; J-Y-J; T-P-Y-P-Z-R9; R9-Z-P-Y-P-Z-R9; J-Y-P-Z-R9; T-P-Y-P-Z-V-E; E-V-Z-P-Y-P-Z-V-E; J-Y-P-Z-V-E; R9-Z-P-Y-P-Z-V-E; T-P-L-L-P-T; T-P-L-L-J; J-L-L-J; T-P-L-L-P-Z-R9; R9-Z-P-L-L-P-Z-R9; J-L-L-P-Z-R9; T-P-L-L-P-Z-V-E; E-V-Z-P-L-L-P-Z-V-E; J-L-L-P-Z-V-E; R9-Z-P-L-L-P-Z-V-E; T-P-M-A-L-P-T; T-P-M-A-L-J; J-M-A-L-J; T-P-M-A-L-P-Z-R9; R9-Z-P-M-A-L-P-Z-R9; J-M-A-L-P-Z-R9; T-P-M-A-L-P-Z-V-E; E-V-Z-P-M-A-L-P-Z-V-E; J-M-A-L-P-Z-V-E; J-M-A-L-P-T; R9-Z-P-M-A-L-J; R9-Z-P-M-A-L-P-T; R9-Z-P-M-A-L-P-Z-V-E; E-V-Z-P-M-A-L-J; E-V-Z-P-M-A-L-P-T; E-V-Z-P-M-A-L-P-Z-R9; T-P-M-A-A-M-P-T; T-P-M-A-A-M-J; J-M-A-A-M-J; T-P-M-A-A-M-P-Z-R9; R9-Z-P-M-A-A-M-P-Z-R9; J-M-A-A-M-P-Z-R9; T-P-M-A-A-M-P-Z-V-E; E-V-Z-P-M-A-A-M-P-Z-V-E; J-M-A-A-M-P-Z-V-E; R9-Z-P-M-A-A-M-P-Z-V-E; T-P-M-W-M-P-T; T-P-M-W-M-J; J-M-W-M-J; T-P-M-W-M-P-Z-R9; R9-Z-P-M-W-M-P-Z-R9; J-M-W-M-P-Z-R9; T-P-M-W-M-P-Z-V-E; E-V-Z-P-M-W-M-P-Z-V-E; J-M-W-M-P-Z-V-E; R9-Z-P-M-W-M-P-Z-V-E; T-P-M-M-P-T; T-P-M-M-J; J-M-M-J; T-P-M-M-P-Z-R9; R9-Z-P-M-M-P-Z-R9; J-M-M-P-Z-R9; T-P-M-M-P-Z-V-E; E-V-Z-P-M-M-P-Z-V-E; J-M-M-P-Z-V-E; R9-Z-P-M-M-P-Z-V-E; or a pharmaceutically acceptable salt thereof.

In another specific embodiment the invention provides a compound of formula (I) having a formula selected from:

T^p-P^u-Y^y-P^u-T^p; T^p-P^u-Y^y-J^m; J^m-Y^y-J^m; T^p-P^u-Y^y-P^u-Z^v-R9^q; R9^q-Z^v-P^u-Y^y-P^u-Z^v-R9^q; J^m-Y^y-P^u-Z^v-R9^q; T^p-P^u-Y^y-P^u-Z^v-V^w-E^x; E^x-V^w-Z^v-P^u-Y^y-P^u-Z^v-V^w-E^x; J^m-Y^y-P^u-Z^v-V^w-E^x; R9^q-Z^v-P^u-Y^y-P^u-Z^v-V^w-E^x; T^p-P^u-Lⁿ-Lⁿ-P^u-T^p; T^p-P^u-Lⁿ-Lⁿ-J^m; J^m-Lⁿ-Lⁿ-J^m; T^p-P^u-Lⁿ-Lⁿ-P^u-Z^v-R9^q; R9^q-Z^v-P^u-Lⁿ-Lⁿ-P^u-Z^v-R9^q; J^m-Lⁿ-Lⁿ-P^u-Z^v-R9^q; T^p-P^u-Lⁿ-Lⁿ-P^u-Z^v-V^w-E^x; E^x-V^w-Z^v-P^u-Lⁿ-Lⁿ-P^u-Z^v-V^w-E^x; J^m-Lⁿ-Lⁿ-P^u-Z^v-V^w-E^x; R9^q-Z^v-P^u-Lⁿ-Lⁿ-P^u-Z^v-V^w-E^x; T^p-P^u-M^t-A^s-Lⁿ-P^u-T^p; T^p-P^u-M^t-A^s-Lⁿ-J^m; J^m-M^t-A^s-Lⁿ-J^m; T^p-P^u-M^t-A^s-Lⁿ-P^u-Z^v-R9^q; R9^q-Z^v-P^u-M^t-A^s-Lⁿ-P^u-Z^v-R9^q; J^m-M^t-A^s-Lⁿ-P^u-Z^v-R9^q; T^p-P^u-M^t-A^s-Lⁿ-P^u-Z^v-V^w-E^x; E^x-V^w-Z^v-P^u-M^t-A^s-Lⁿ-P^u-Z^v-V^w-E^x; J^m-M^t-A^s-Lⁿ-P^u-Z^v-V^w-E^x; J^m-M^t-A^s-Lⁿ-P^u-T^p; R9^q-Z^v-P^u-M^t-A^s-Lⁿ-J^m; R9^q-Z^v-P^u-M^t-A^s-Lⁿ-P^u-T^p; R9^q-Z^v-P^u-M^t-A^s-Lⁿ-P^u-Z^v-V^w-E^x; E^x-V^w-Z^v-P^u-M^t-A^s-Lⁿ-J^m; E^x-V^w-Z^v-P^u-M^t-A^s-Lⁿ-P^u-T^p; E^x-V^w-Z^v-P^u-M^t-A^s-Lⁿ-P^u-Z^v-R9^q; T^p-P^u-M^t-A^s-A^s-M^t-P^u-T^p; T^p-P^u-M^t-A^s-A^s-M^t-J^m; J^m-M^t-A^s-A^s-M^t-J^m; T^p-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-R9^q; R9^q-Z^v-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-R9^q; J^m-M^t-A^s-A^s-M^t-P^u-Z^v-R9^q; T^p-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-V^w-E^x; E^x-V^w-Z^v-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-V^w-E^x; J^m-M^t-A^s-A^s-M^t-P^u-Z^v-V^w-E^x; R9^q-Z^v-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-V^w-E^x; T^p-P^u-M^t-W^r-M^t-P^u-T^p; T^p-P^u-M^t-W^r-M^t-J^m; J^m-M^t-W^r-M^t-J^m; T^p-P^u-M^t-W^r-M^t-P^u-Z^v-R9^q; R9^q-Z^v-P^u-M^t-W^r-M^t-P^u-Z^v-R9^q; J^m-M^t-W^r-M^t-P^u-Z^v-R9^q;

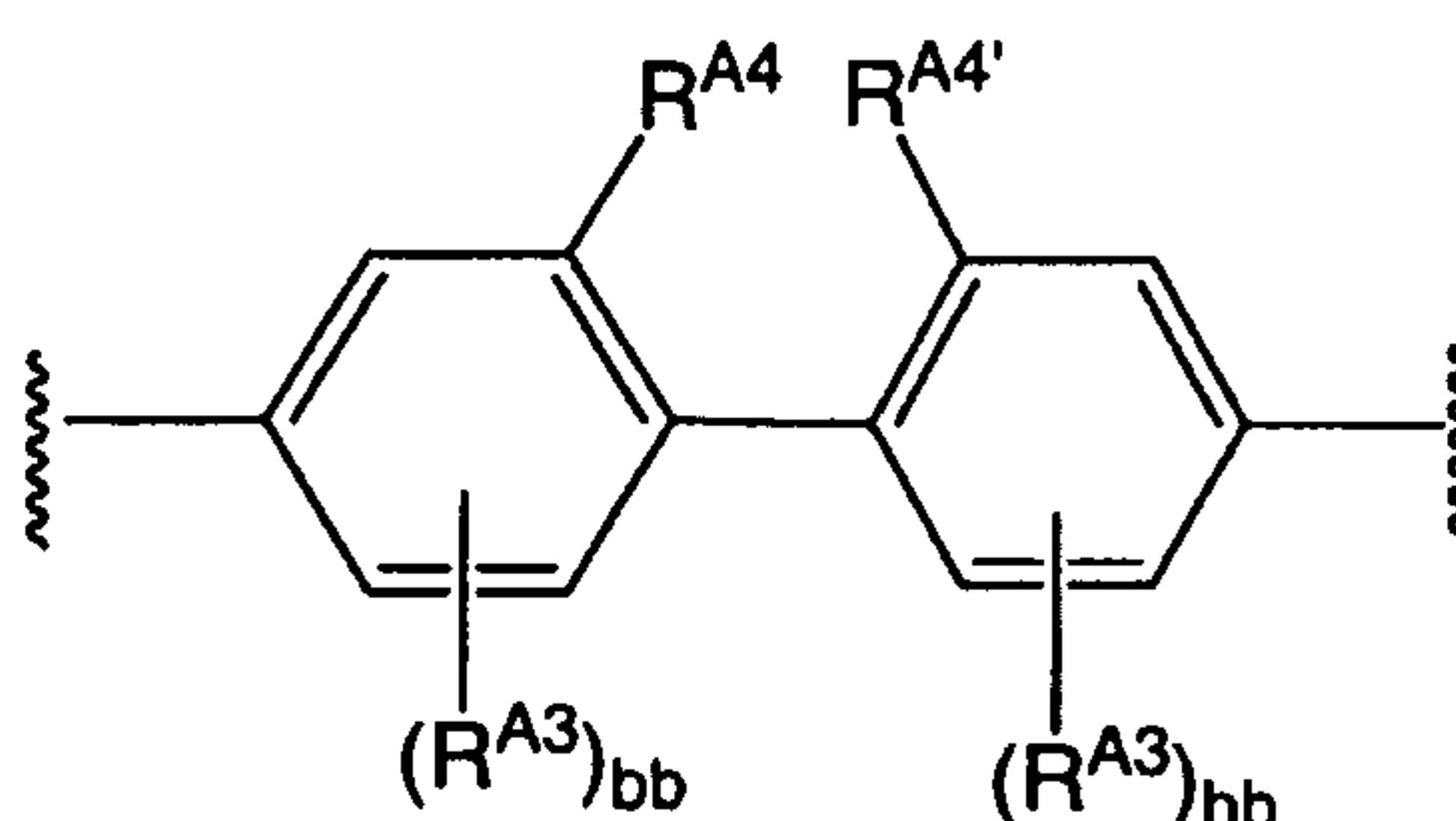
$T^p-P^u-M^l-W^r-M^l-P^u-Z^v-V^w-E^x$; $E^x-V^w-Z^v-P^u-M^l-W^r-M^l-P^u-Z^v-V^w-E^x$; $J^m-M^l-W^r-M^l-P^u-Z^v-V^w-E^x$; $R9^q-Z^v-P^u-M^l-W^r-M^l-P^u-Z^v-V^w-E^x$; $T^p-P^u-M^l-M^l-P^u-T^p$; $T^p-P^u-M^l-M^l-J^m$; $J^m-M^l-M^l-J^m$; $T^p-P^u-M^l-M^l-P^u-Z^v-R9^q$; $R9^q-Z^v-P^u-M^l-M^l-P^u-Z^v-R9^q$; $J^m-M^l-M^l-P^u-Z^v-R9^q$; $T^p-P^u-M^l-M^l-P^u-Z^v-V^w-E^x$; $E^x-V^w-Z^v-P^u-M^l-M^l-P^u-Z^v-V^w-E^x$; $J^m-M^l-M^l-P^u-Z^v-V^w-E^x$; $R9^q-Z^v-P^u-M^l-M^l-P^u-Z^v-V^w-E^x$ or a pharmaceutically acceptable salt thereof.

In another specific embodiment of the invention s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20, or 21.

In another specific embodiment of the invention r is 1, 2, 3, 4, 5, 6, 8, 13, 14, 15, 16, 17, 18, 19, or 20.

In another specific embodiment the invention provides a compound which is a prodrug or a pharmaceutically acceptable salt of a compound of formula (I).

In one specific embodiment the invention provides a compound of formula (I) wherein W is not a group of the following formula:



wherein:

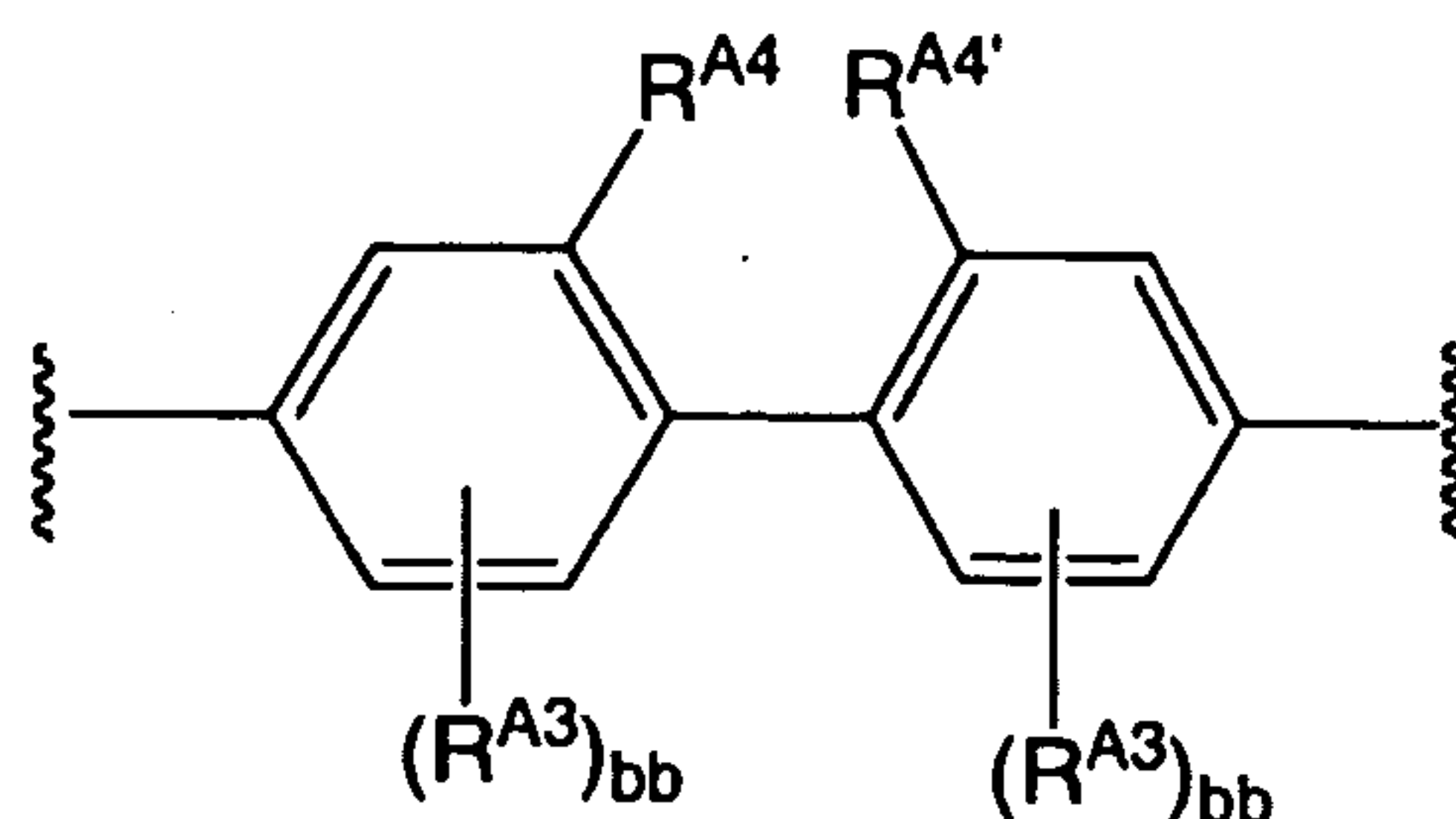
each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is independently 0, 1, 2, or 3; and

R^{A4} and $R^{A4'}$, together with the atoms to which they are attached, form a five- to eight-membered unsaturated ring optionally containing one or two heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein the five- to eight-membered unsaturated ring is optionally substituted with one, two or three substituents independently selected from R^{A3} , oxo and a spirocycle.

In one specific embodiment the invention, the sum of m , n , p , q , s , t , u , v , w , x , and y is not 0 when W is a group of the following formula:



wherein:

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is independently 0, 1, 2, or 3; and

R^{A4} and $R^{A4'}$, together with the atoms to which they are attached, form a five- to eight-membered unsaturated ring optionally containing one or two heteroatoms independently selected from nitrogen, oxygen, and sulfur; wherein the five- to eight-membered unsaturated ring is optionally substituted with one, two or three substituents independently selected from R^{A3} , oxo and a spirocycle.

In one embodiment when M comprises an imidazole ring it is connected to P through the 2-position.

In one embodiment when M or L comprises a benzimidazole it is connected to P through the 2-position.

Compounds of formula (Ia)

In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ia):



wherein:

W is a bond or $-W^r-$;

each M is selected from $-M^t$;

each P is selected from $-P^u$;

each Z is selected from $-Z^v$;

each V is selected from $-V^w$;

each E is selected from $-E^x$;

each r is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20;

each t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11;

each u is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, or 14;

each v is 0, 1, 2, 3, 4, 5, or 6;

each w is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21;

each x is 0 or 1 ;

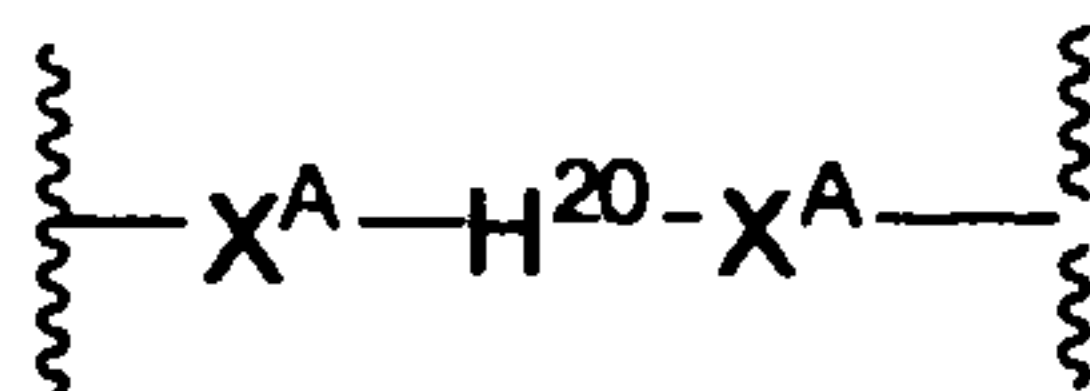
wherein the sum of r, t, u, v, w, and x is not 0;

each W^1 is independently $-X^A-$:

wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^2 is independently:

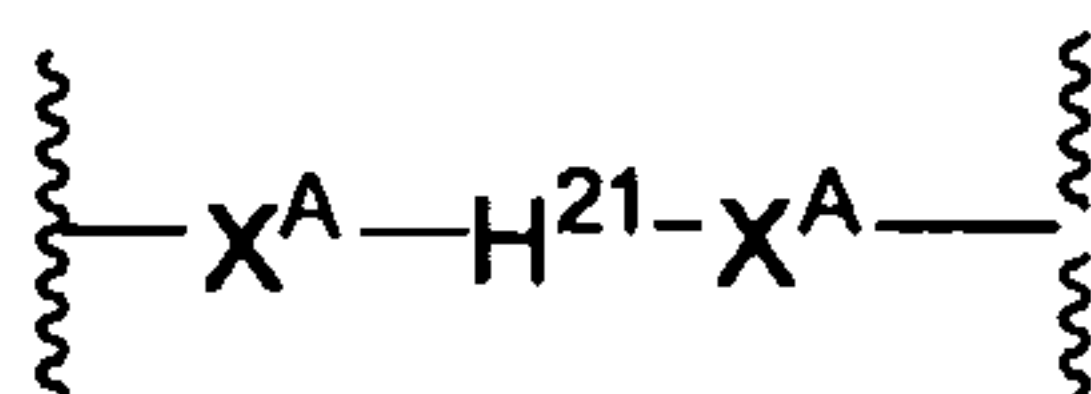


wherein:

each H^{20} is independently is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^3 is independently:

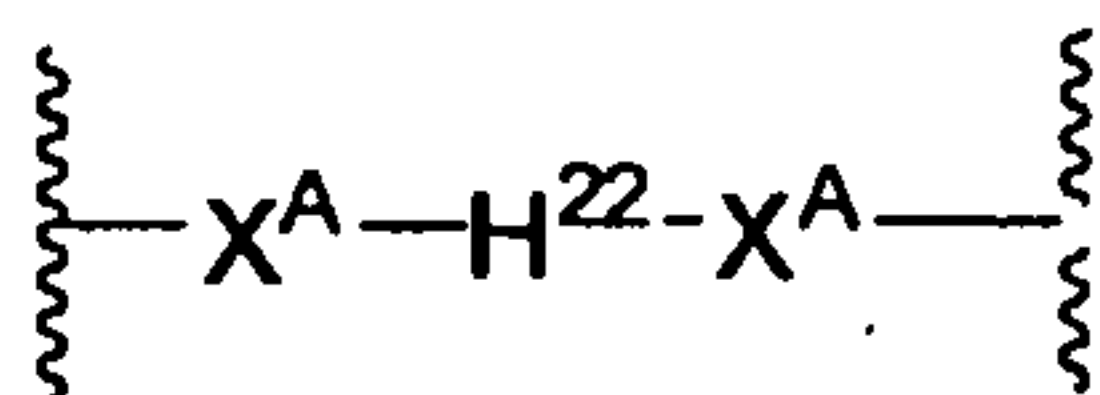


wherein:

each H^{21} is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^4 is independently:

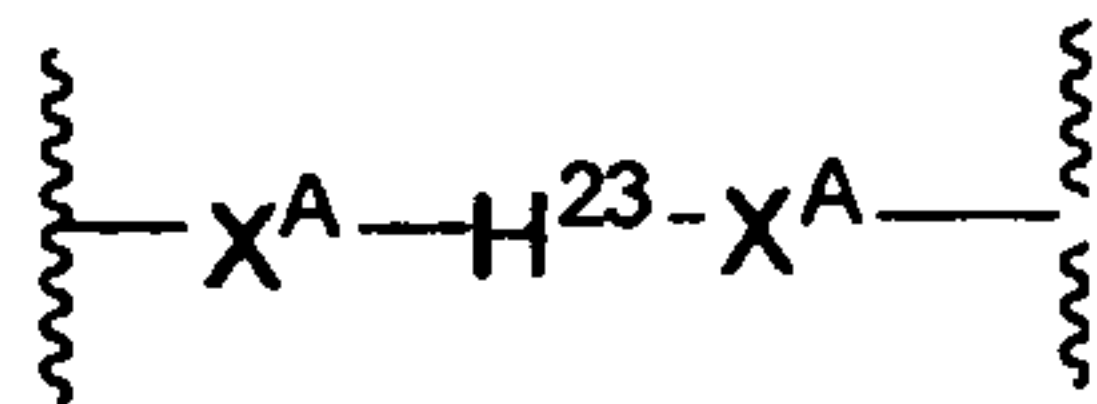


wherein:

each H^{22} is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^5 is independently:

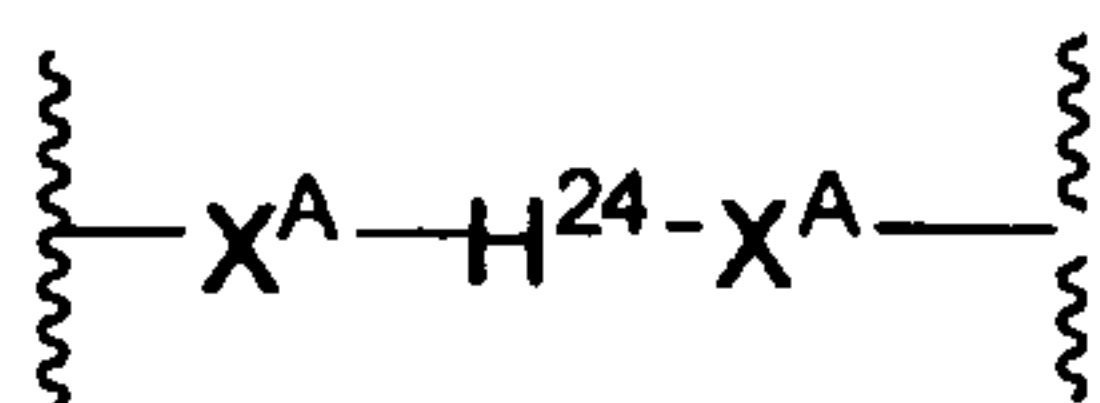


wherein:

each H^{23} is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^6 is independently:

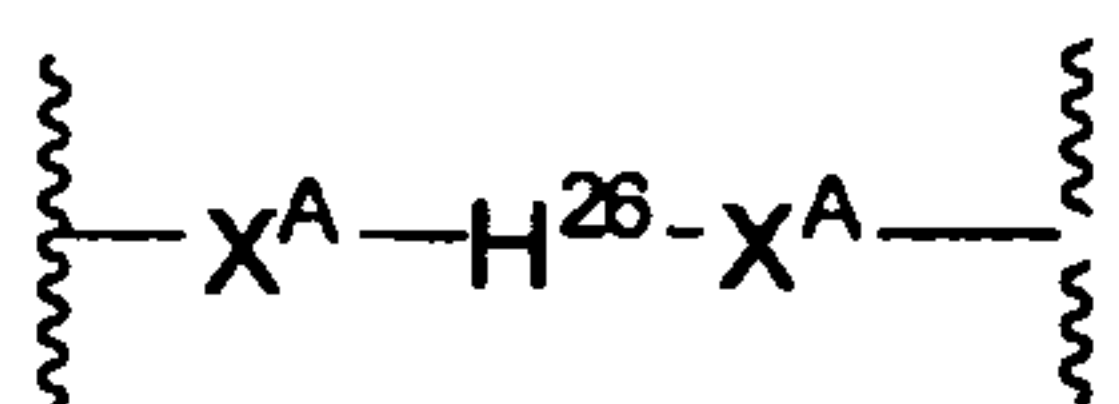


wherein:

each H^{24} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^7 is independently:

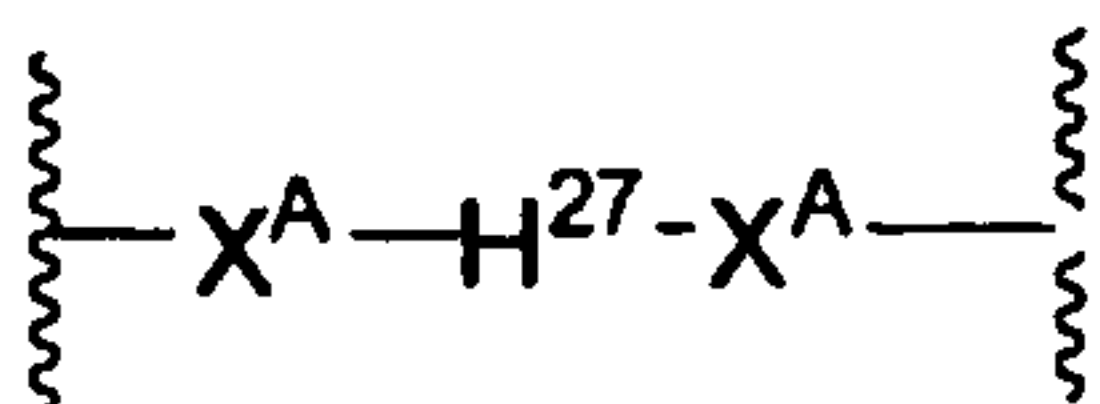


wherein:

each H^{26} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^8 is independently:

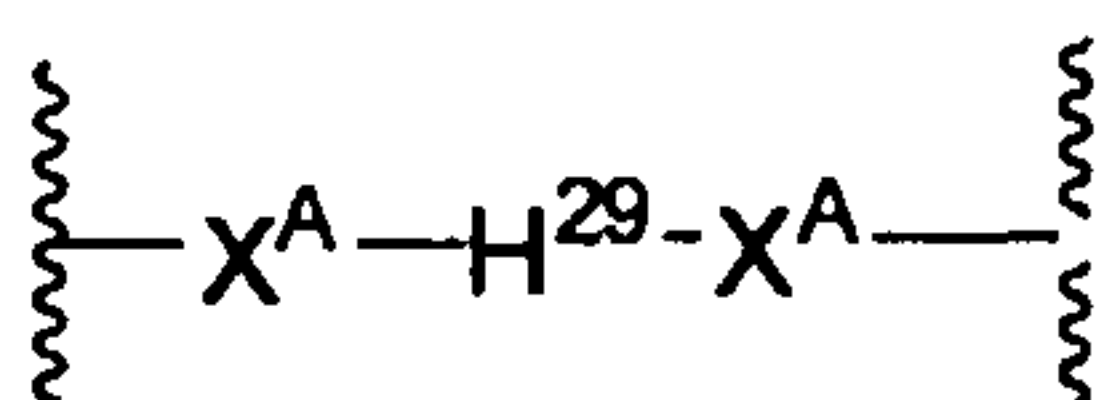


wherein:

each H^{27} is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^9 is independently:



wherein:

each H^{29} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each W^{10} is independently $-H^{30}=C=H^{31}-$

wherein each of $-H^{30}$ and H^{31} is independently a saturated 6-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W^{11} is independently $-H^{32}=C=H^{33}-$

wherein each of $-H^{32}$ and H^{33} is independently a saturated 5-membered heterocyclic ring comprising one or more heteroatoms, which ring is optionally substituted with oxo;

each W^{12} is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{13} is independently a phenyl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{14} is independently a 5 or 6 membered heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each W^{15} is independently a fused unsaturated, partially unsaturated or saturated tetracyclic carbocyclic ring, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{16} is independently a fused unsaturated, partially unsaturated or saturated tetracyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{17} is independently a fused unsaturated, partially unsaturated or saturated pentacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{18} is independently a fused unsaturated, partially unsaturated or saturated pentacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each W^{19} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic carbocyclic ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

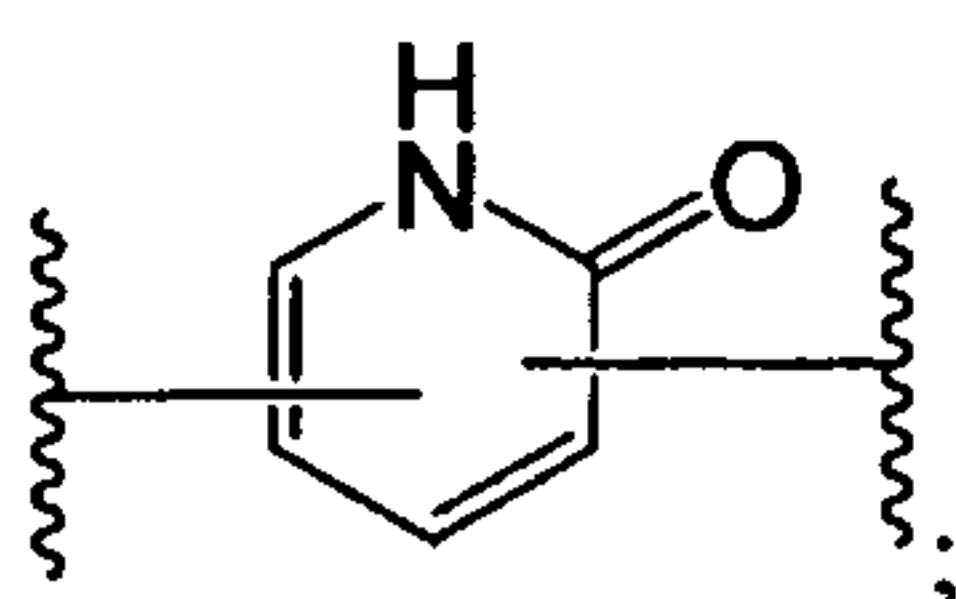
each W^{20} is independently a fused unsaturated, partially unsaturated or saturated hexacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each M^0 is independently a five membered heteroaryl group optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, haloalkyl, (NR^aR^b) carbonyl and trialkylsilylalkoxyalkyl;

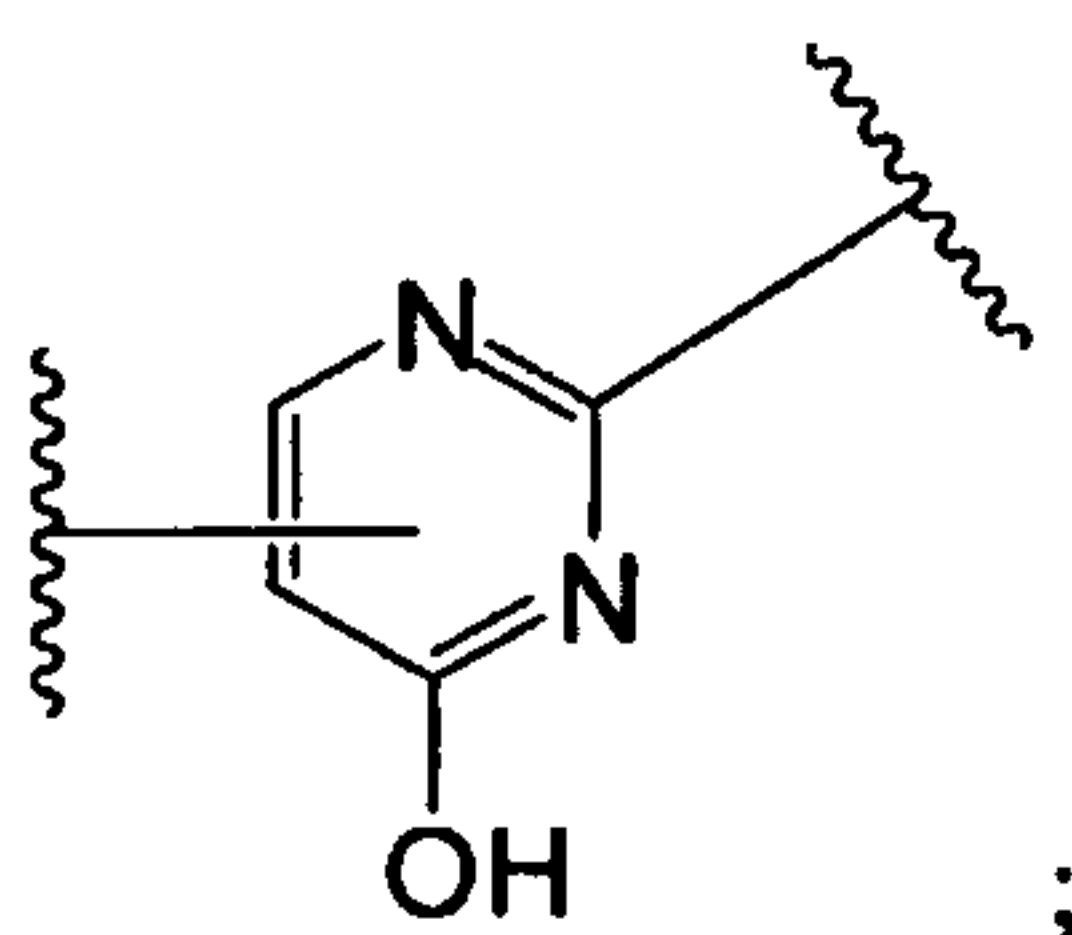
each M^1 is independently selected from $-C(=O)NH-$, $-C(=O)NH-C(R^M)_2-$, $-NHC(=O)-$, $-C(R^M)_2NHC(=O)-$, $-NHC(=O)NR^M-$, $-NHC(=O)O-$; wherein each R^M is independently selected from H and alkyl;

each M^2 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

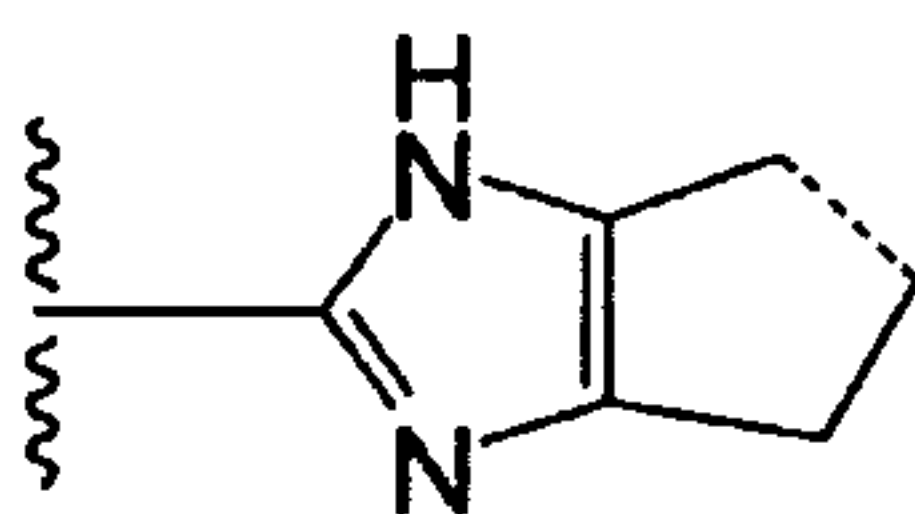
each M^3 is independently:



each M^4 is independently:



each M^5 is independently:



wherein the bond designated with --- is fused to a ring defined for P;

each M^6 is independently a bicyclic bridged ring system comprising 5-15 atoms wherein at least one of the atoms is a heteroatom;

each M^7 is independently a pyrid-di-yl;

each M^8 is independently partially saturated or a saturated five-membered ring that comprises one or more heteroatoms and that is optionally substituted with one or two oxo;

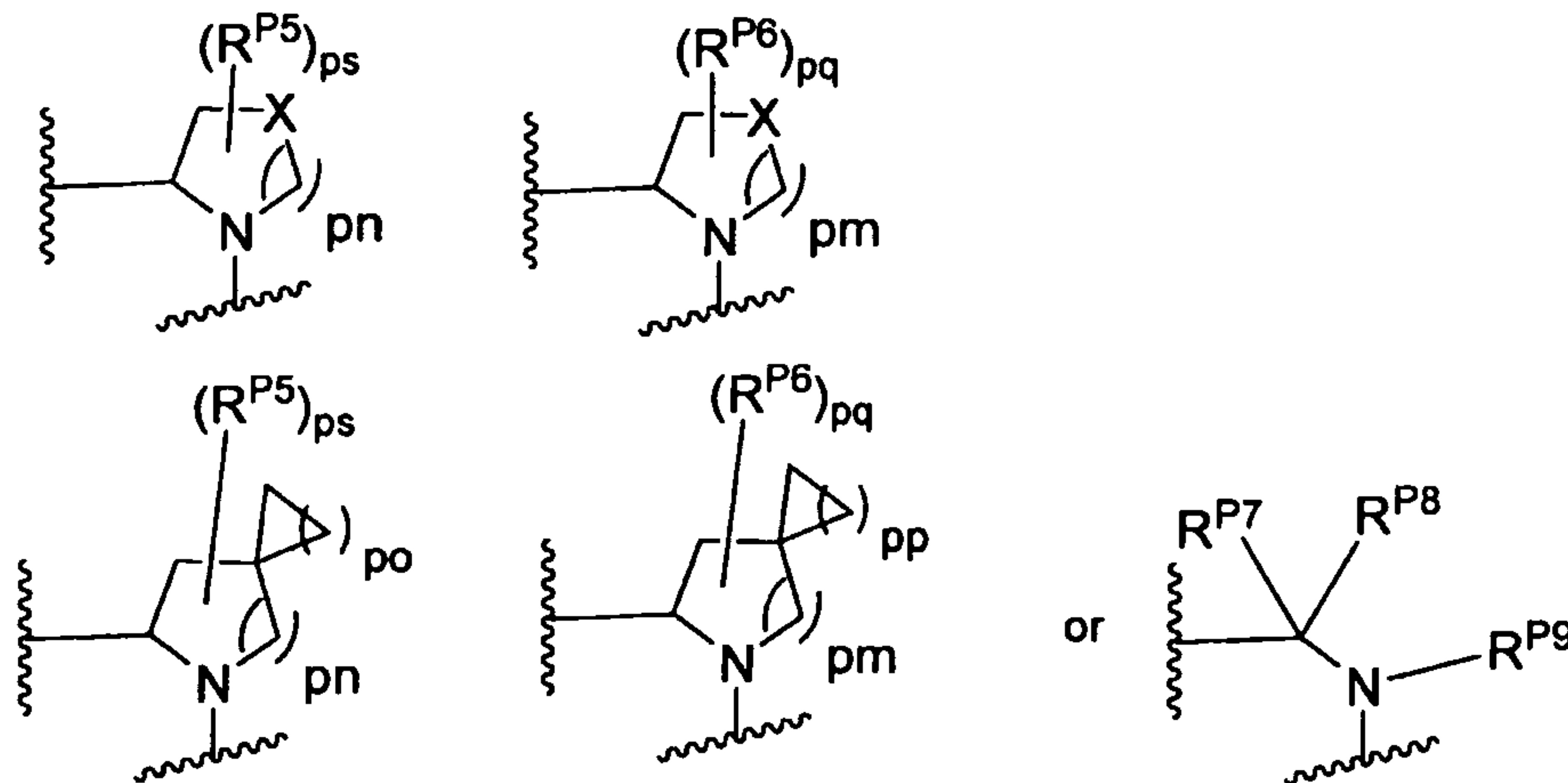
each M^9 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^{P11} ;

each M^{10} is independently a five membered heteroaryl group;

each M^{11} is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$;

each R^{M7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each P^0 is independently:



wherein:

X is selected from O, S, S(O), SO_2 , CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

provided that when pn or pm is O, X is selected from CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

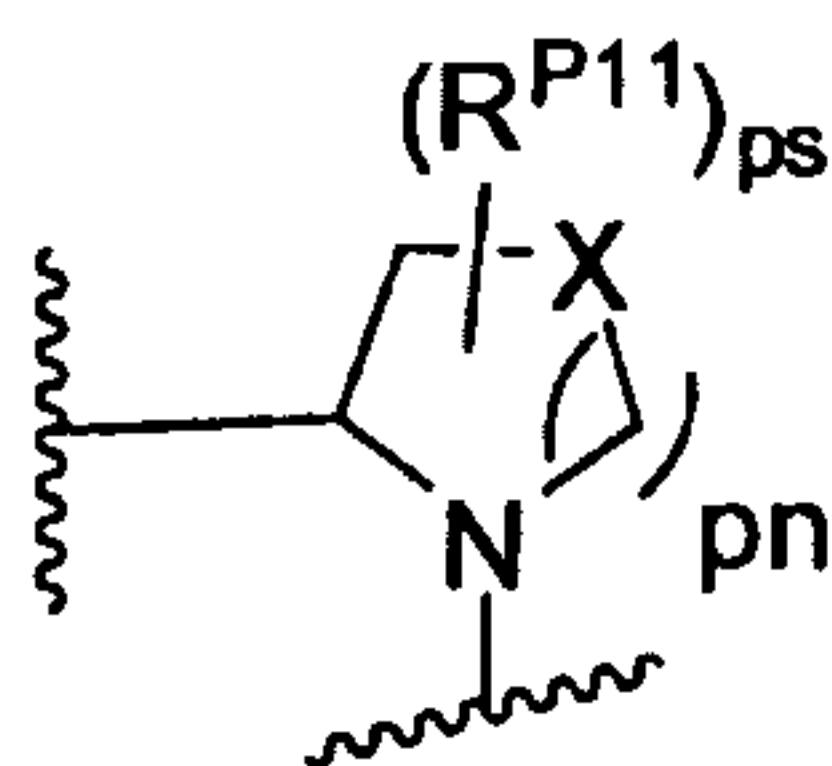
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^1 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

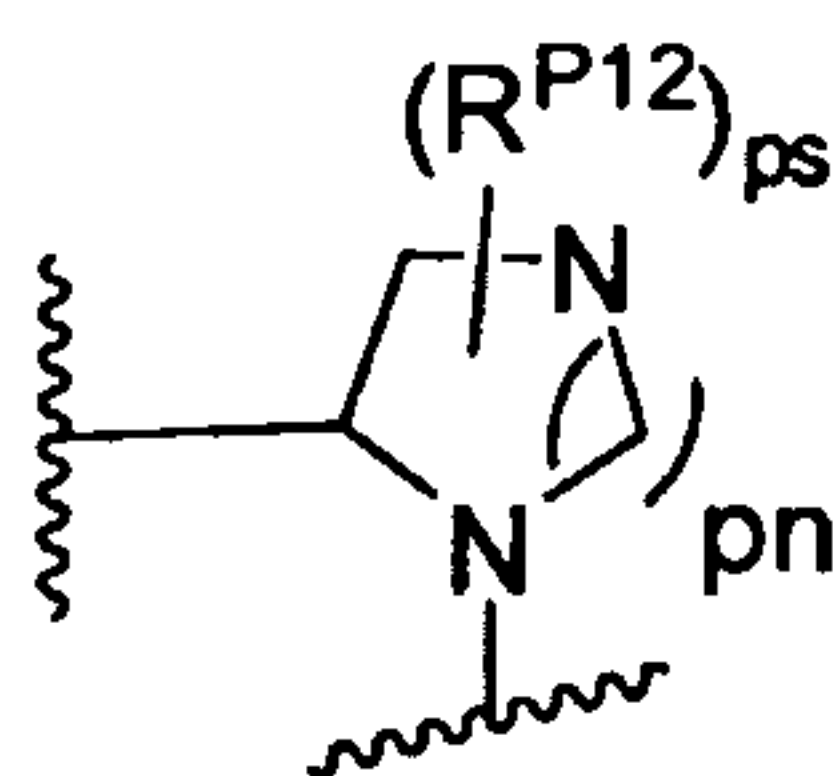
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl,

haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$; and the remaining R^{P11} are independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^2 is independently:



wherein:

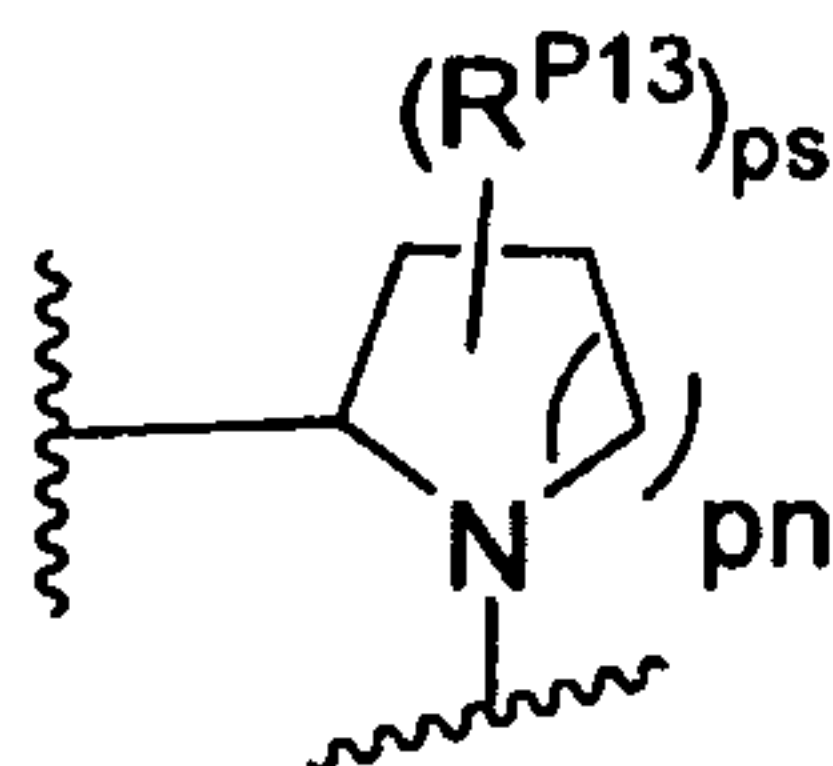
each R^{P12} is independently selected from R^{P5} , R^{P11} , $-C(=O)OR^h$, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^3 is independently a ring of the formula:



wherein:

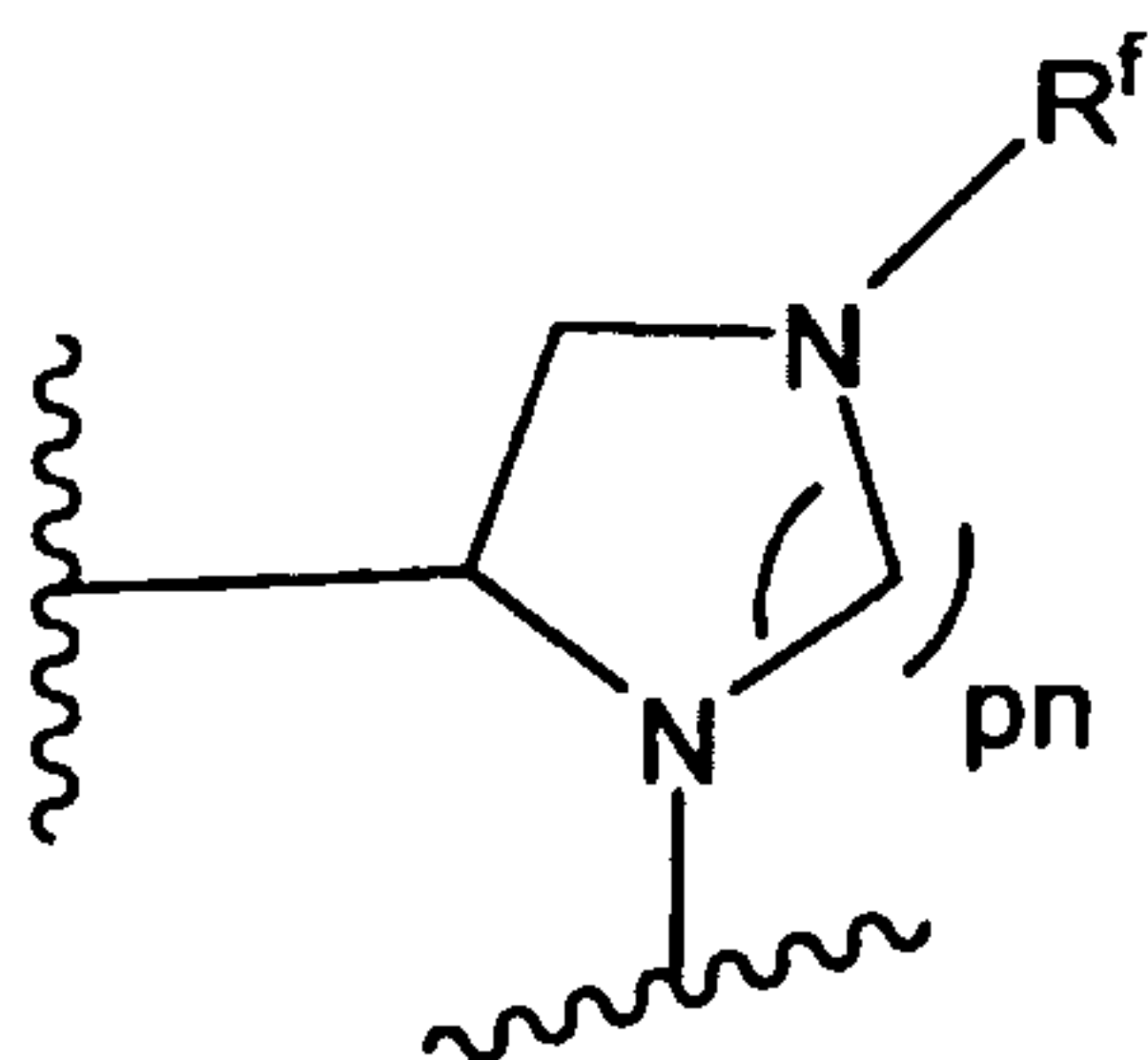
the ring is substituted with one or more oxo group;

each R^{P13} is independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^4 is independently a ring of the formula:



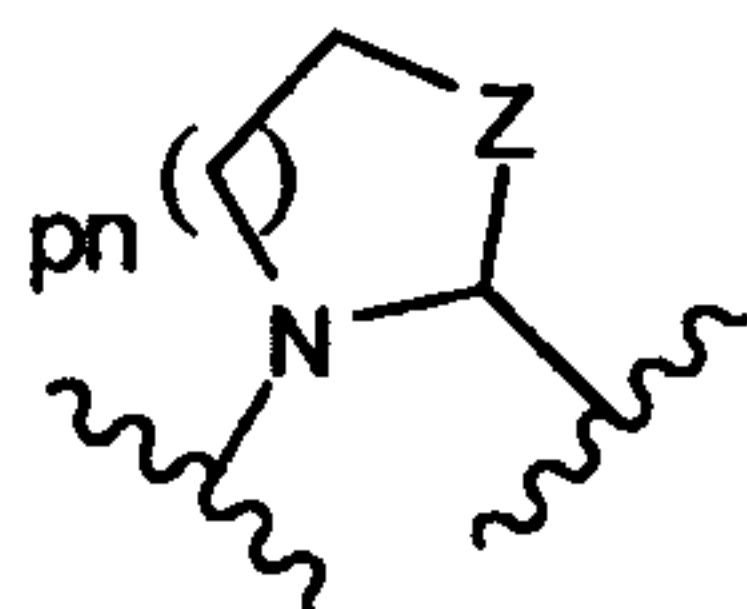
wherein:

the ring is optionally substituted with one or more groups R^{P14} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P14} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^5 is independently a ring of the formula:



wherein:

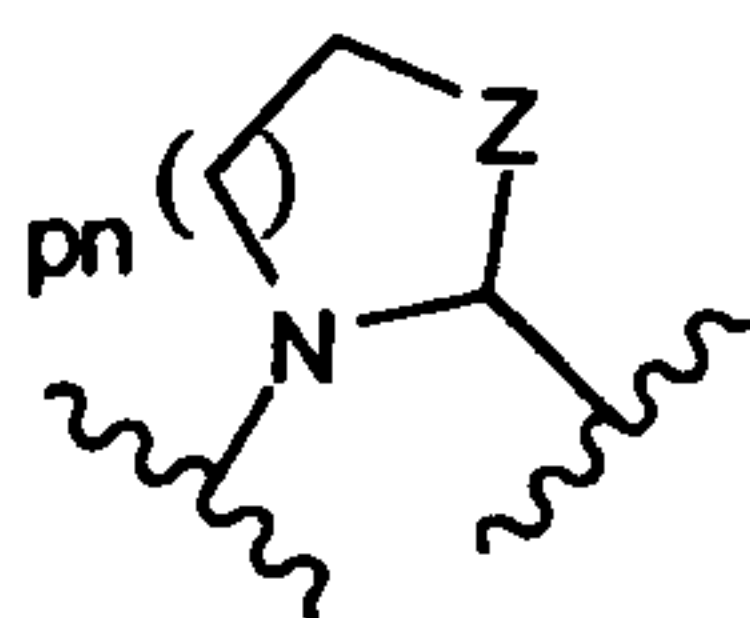
the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^6 is independently a ring of the formula:



wherein:

the ring is substituted with one or more oxo and is optionally substituted with one or more groups R^{P16} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

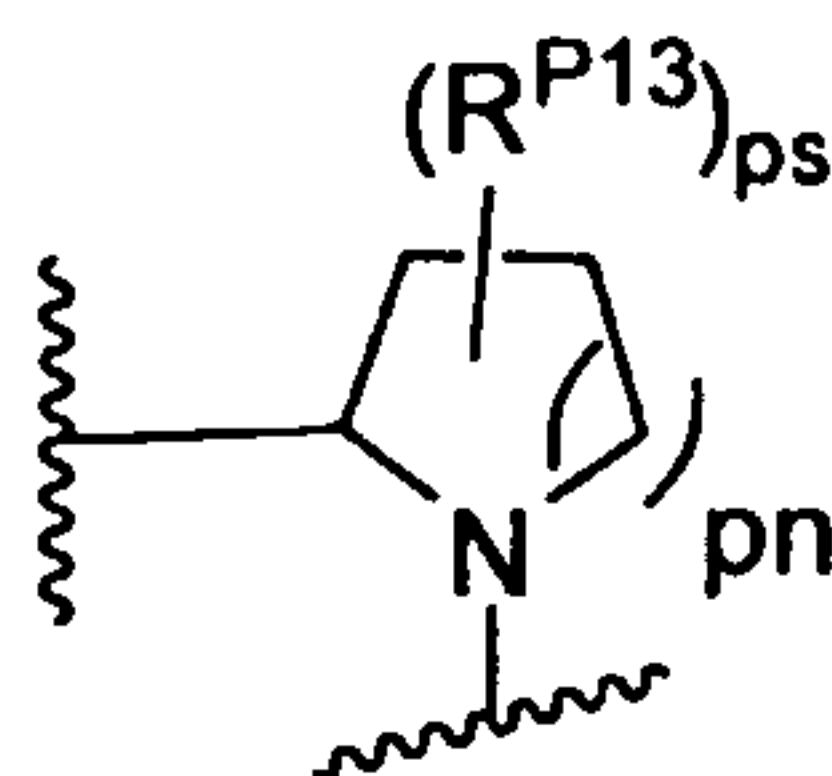
Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:

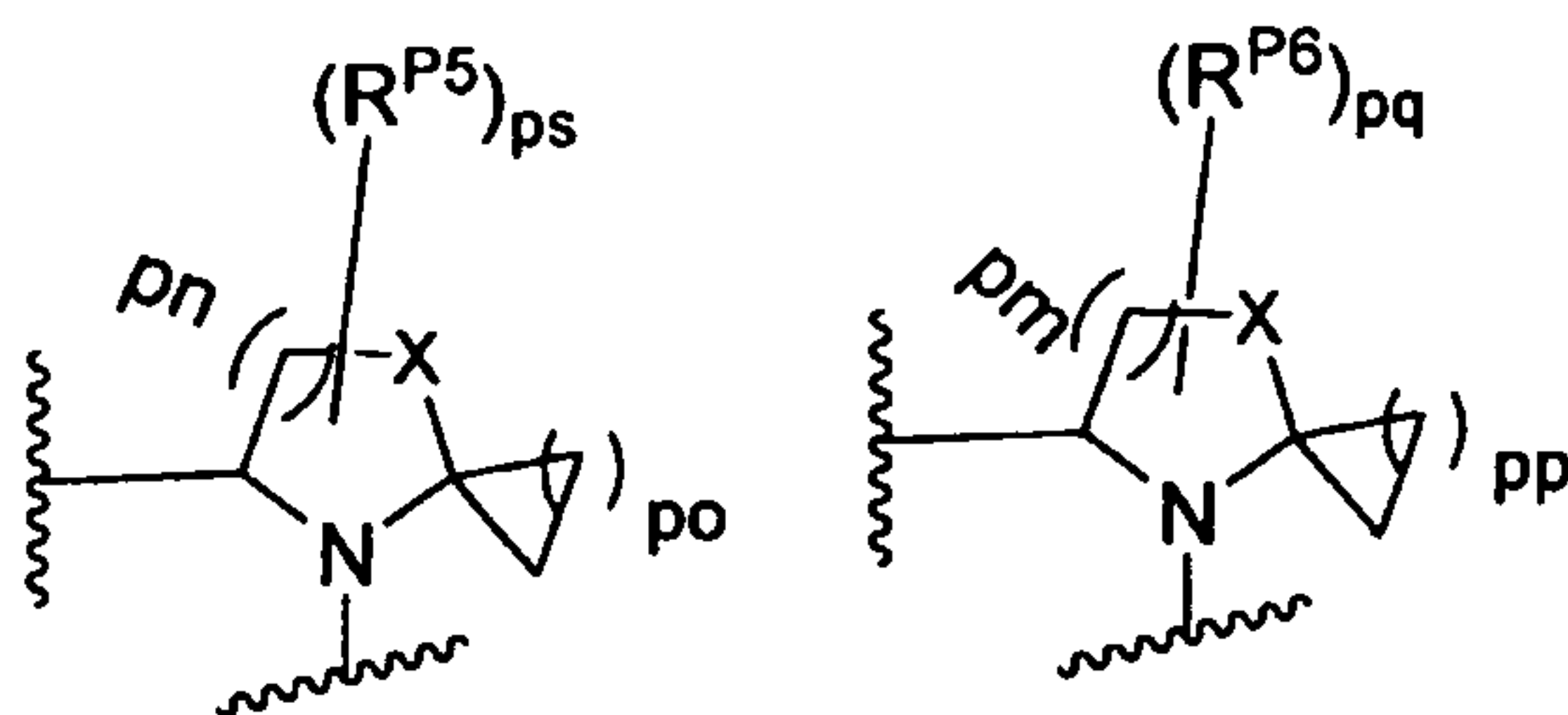


wherein:

ps is 2, 3, 4, 5, or 6;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

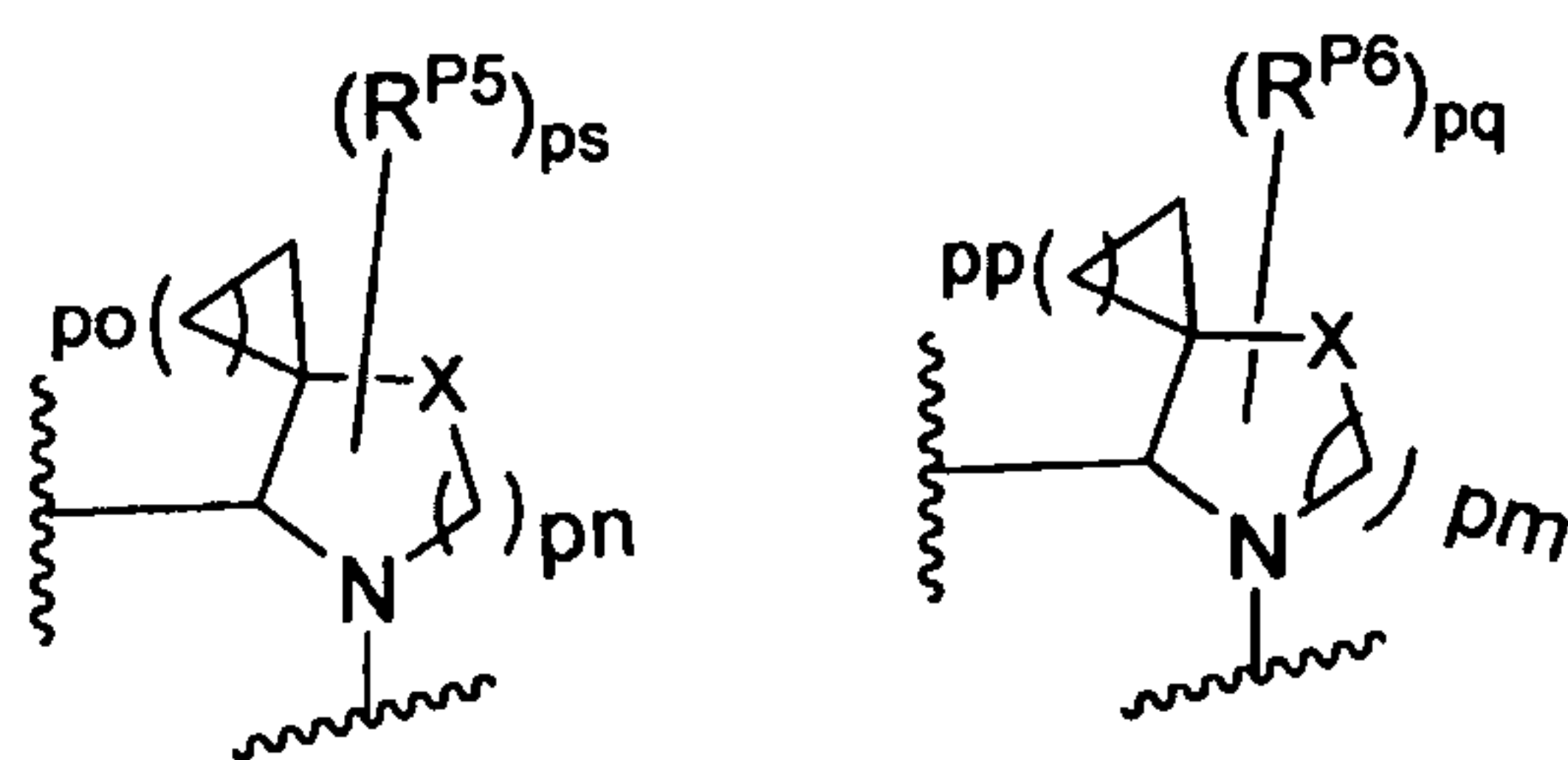
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{11} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

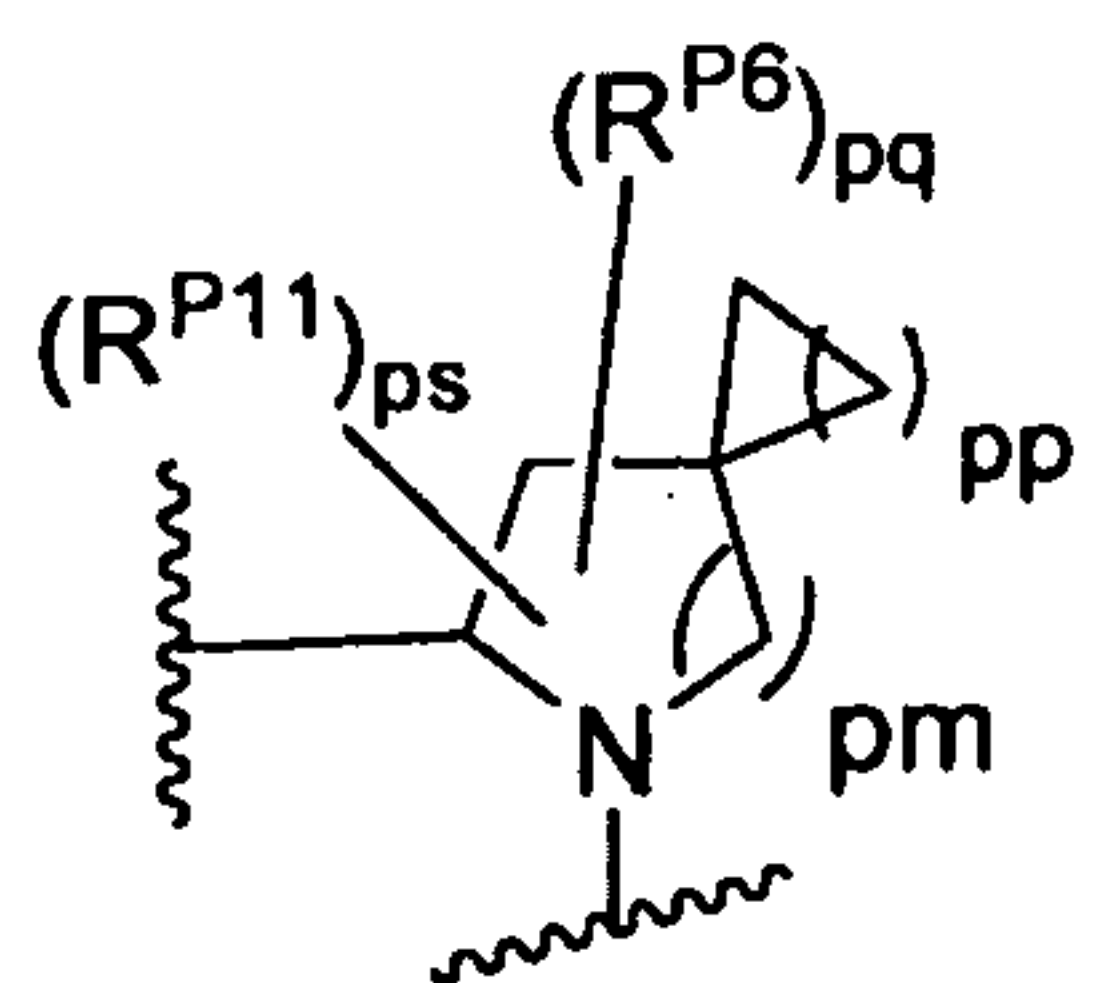
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P^{12} is independently:



wherein:

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

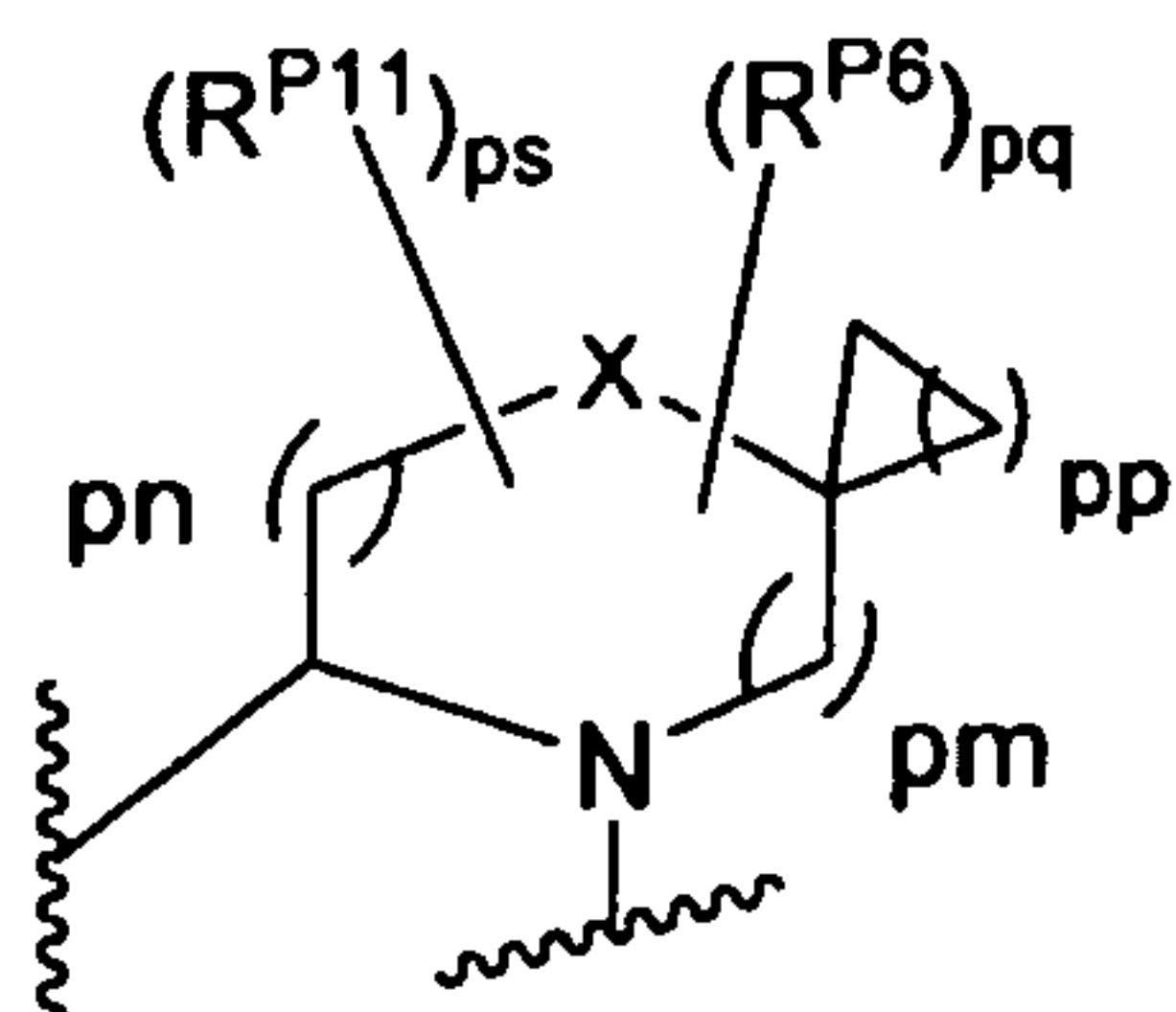
pp is independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^{hh}) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^{hh}) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $(NR^{hh}R^h)$ sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^{hh}R^h$; and the remaining R^{P11} are independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^h)$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, $(NR^{hh}R^h)$ alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{13} is independently:



wherein:

X is selected from O, S, S(O), SO₂, or NR^h;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2 but the sum of pn and pm is greater than zero;

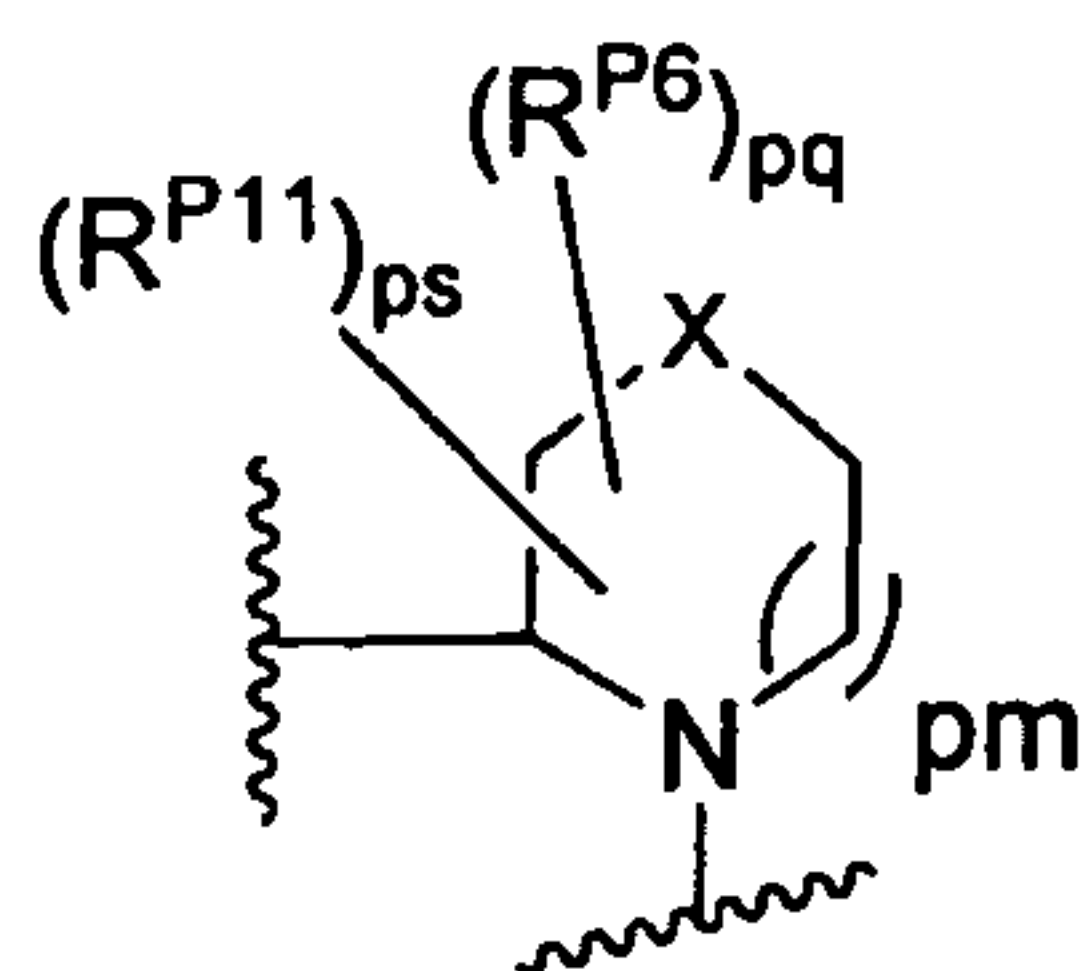
pp are independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, (NR^{hh}R^h)alkyl, (NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-\text{S}(=\text{O})_2\text{R}^h$, $-\text{C}(=\text{O})\text{R}^h$, $-\text{C}(=\text{O})\text{NR}^h\text{R}^h$, $\text{R}^{\text{P}5}$, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{14} is independently:



wherein:

the ring is substituted with one or more oxo group;

X is NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-\text{S}(=\text{O})_2\text{NR}^h\text{R}^h$, $-\text{S}(=\text{O})_2\text{R}^h$, $\text{C}(=\text{O})\text{R}^h$, $\text{C}(=\text{O})\text{OR}^h$, $-\text{C}(=\text{O})\text{NR}^h\text{R}^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each $\text{R}^{\text{P}6}$ is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-\text{NR}^{\text{P}a}\text{R}^{\text{P}b}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

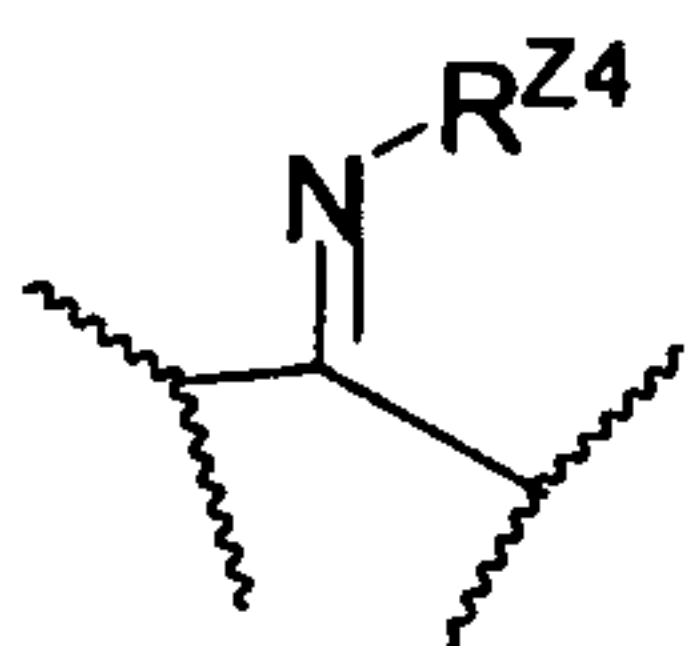
each $-Z^0-$ is $-C(=O)-$ or $-C(=S)-$;

each $-Z^1-$ is independently a bond, or $-C(R^{Z1})_2-$; wherein each R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each $-Z^2-$ is independently saturated or partially unsaturated (C_3-C_8) cycloalkyl that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

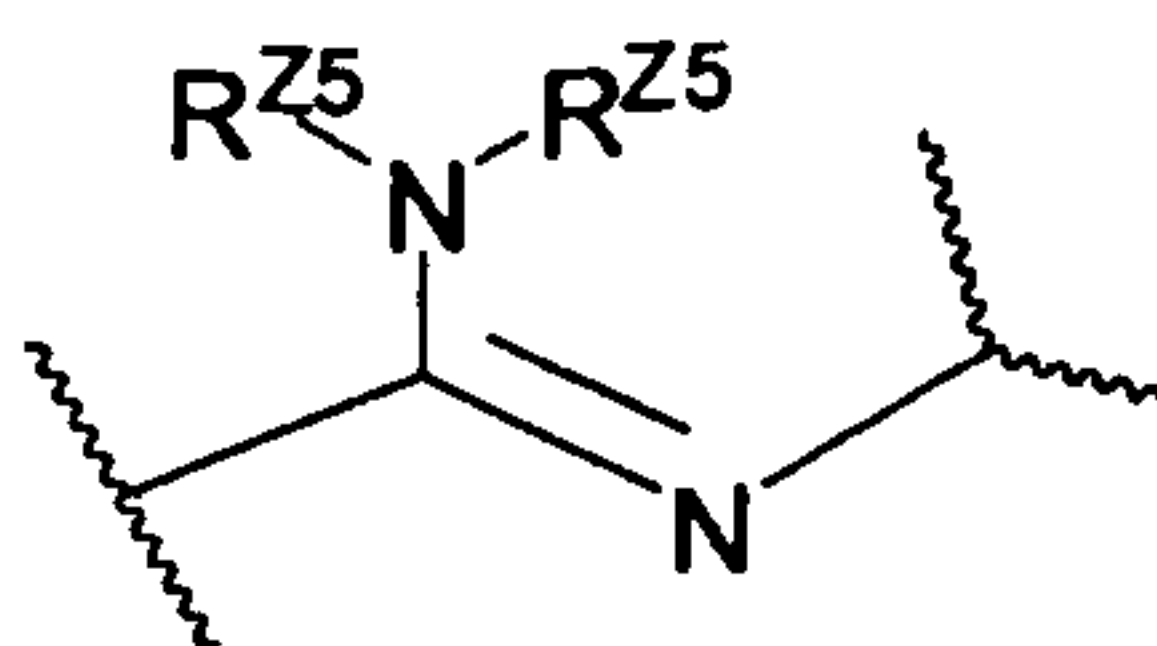
each $-Z^3-$ is independently saturated, partially unsaturated, or aromatic 4-8 membered heterocyclic or heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^4-$ is independently:



wherein each R^{Z4} is independently H, alkyl, cyano, aryl, or heteroaryl;

each $-Z^5-$ is independently:



wherein each R^{Z5} is independently H, alkyl, cyano, aryl, or heteroaryl; or two R^{Z5} s together with the nitrogen to which they are attached form a 4-8 membered heterocyclic ring that is optionally substituted with one or more oxo and with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^6-$ is independently $-C(R^{Z1})-$ and is doublebonded to P; wherein R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^f) alkyl, (NR^f) alkylcarbonyl, (NR^f) carbonyl, (NR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^X R^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^f$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each E^1 is independently $-OC(=O)NR^{Ee}R^{Ef}$ wherein each R^{Ee} and R^{Ef} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl,

formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f)alkyl, (NR^eR^f)alkylcarbonyl, (NR^eR^f)carbonyl, (NR^eR^f)sulfonyl, -C(NCN)OR', and -C(NCN)NR^XR^Y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one -NR^eR^f group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; or wherein R^{Ec} and R^{Ef}, together with the nitrogen atom to which they are attached, form a heterocycle;

each V⁰ is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxyalkylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^XR^Y, - (NR^XR^Y)alkyl, oxo, and -P(O)OR₂, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group,

heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocycl group, and the heterocycl part of the heterocyclalkyl and the heterocyclcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^6 is independently arylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle,

heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^7 is independently heterocyclosulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^8 is independently spirocycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^9 is independently spirocycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{10} is independently fusedbicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{11} is independently fusedbicycliccycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{12} is independently bridged-bicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{13} is independently bridged-bicyclic-cycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy,

cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{14} is independently aryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{15} is independently arylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{16} is independently cycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{17} is independently cycloalkylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{18} is independently heterocyclooxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{19} is independently heterocycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{20} is independently heteroaryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle,

heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl; and

each V^{21} is independently heteroarylalkylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention r is 1, 2, 3, 4, 5, 6, 8, 13, 14, 15, 16, 17, 18, 19, or 20.

In another specific embodiment of the invention W is W^2 .

In another specific embodiment of the invention W is W^4 .

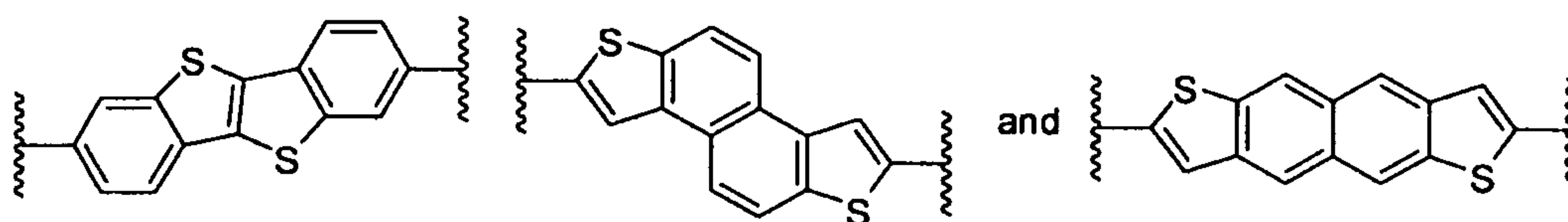
In another specific embodiment of the invention W is W^8 .

In another specific embodiment of the invention W is W^6 .

In another specific embodiment of the invention W is W^{15} .

In another specific embodiment of the invention W is W^{16} .

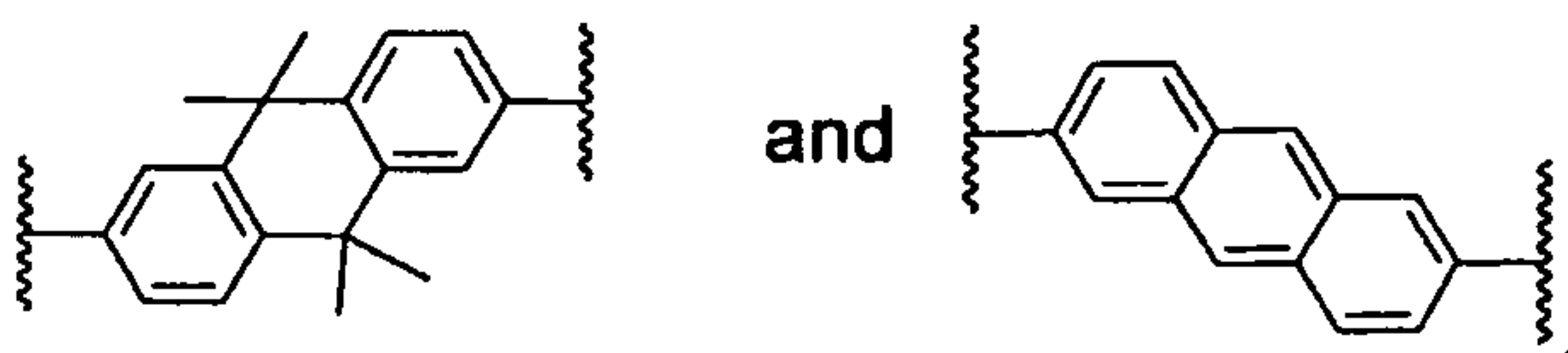
In another specific embodiment of the invention W^{16} is selected from:



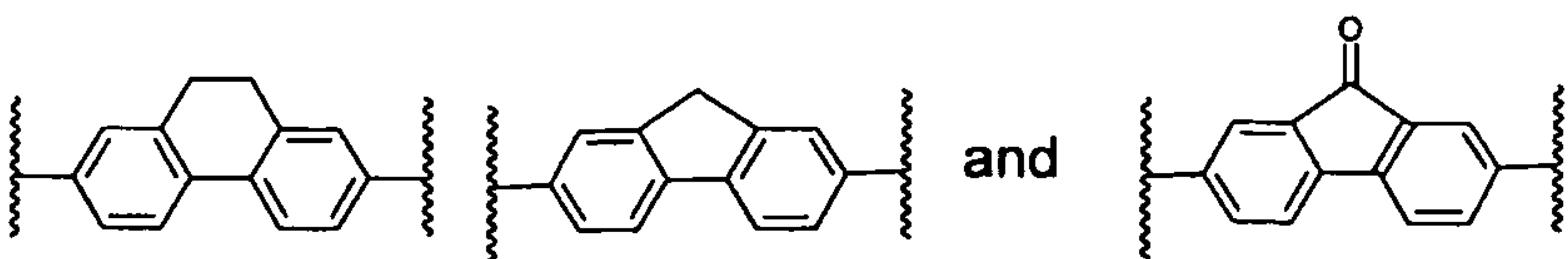
In another specific embodiment of the invention W is W^{17} .

In another specific embodiment of the invention W is W^{18} .

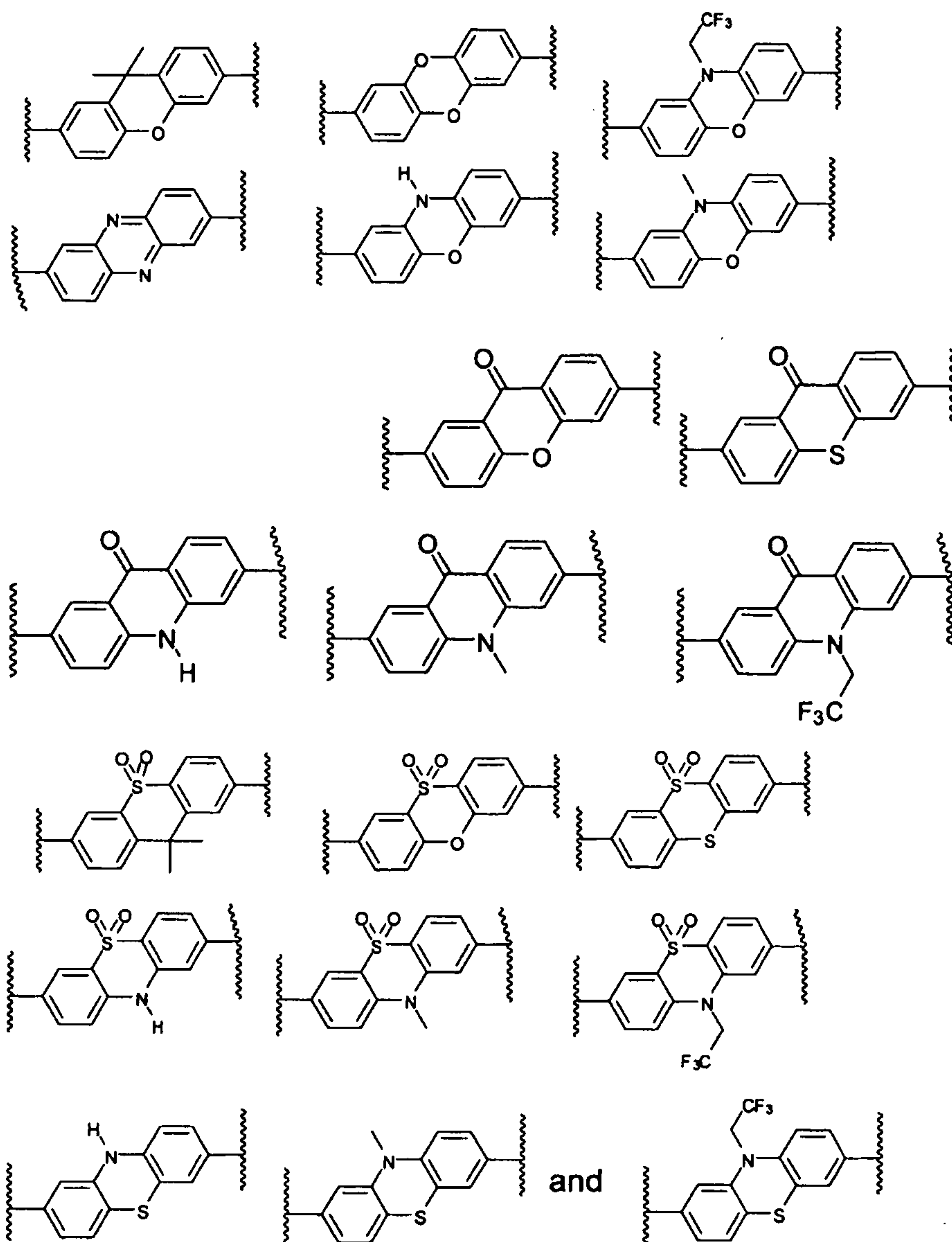
In another specific embodiment of the invention W^6 is selected from:



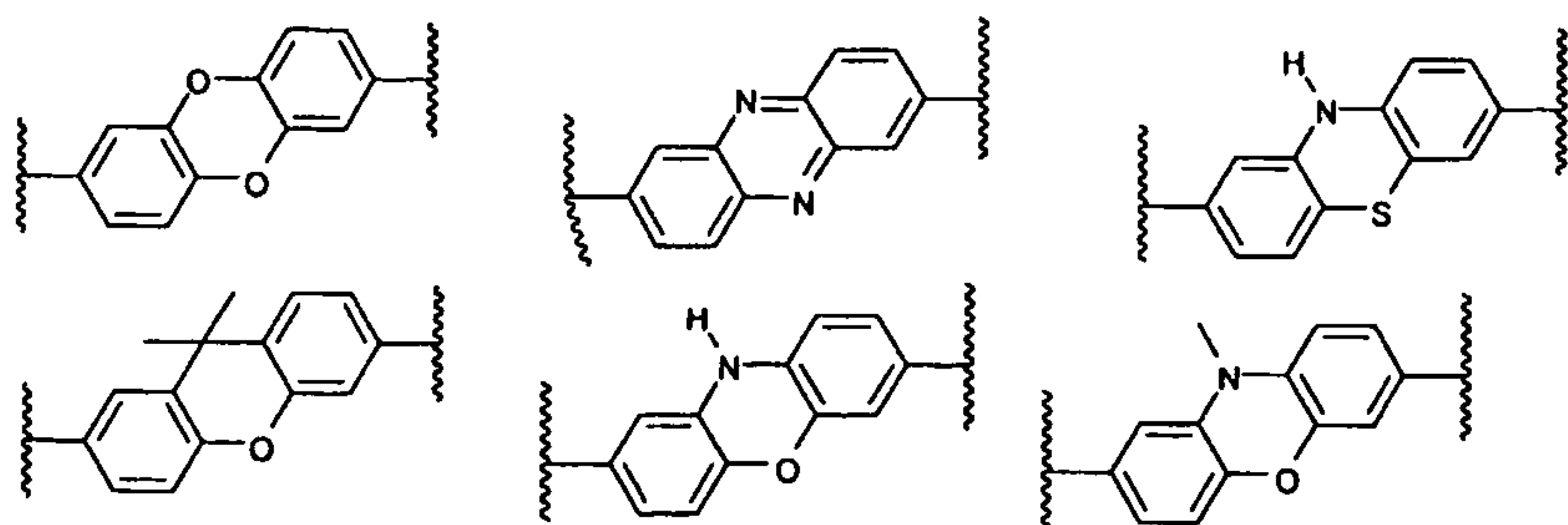
In another specific embodiment of the invention W^6 is selected from:



In another specific embodiment of the invention W⁸ is selected from:

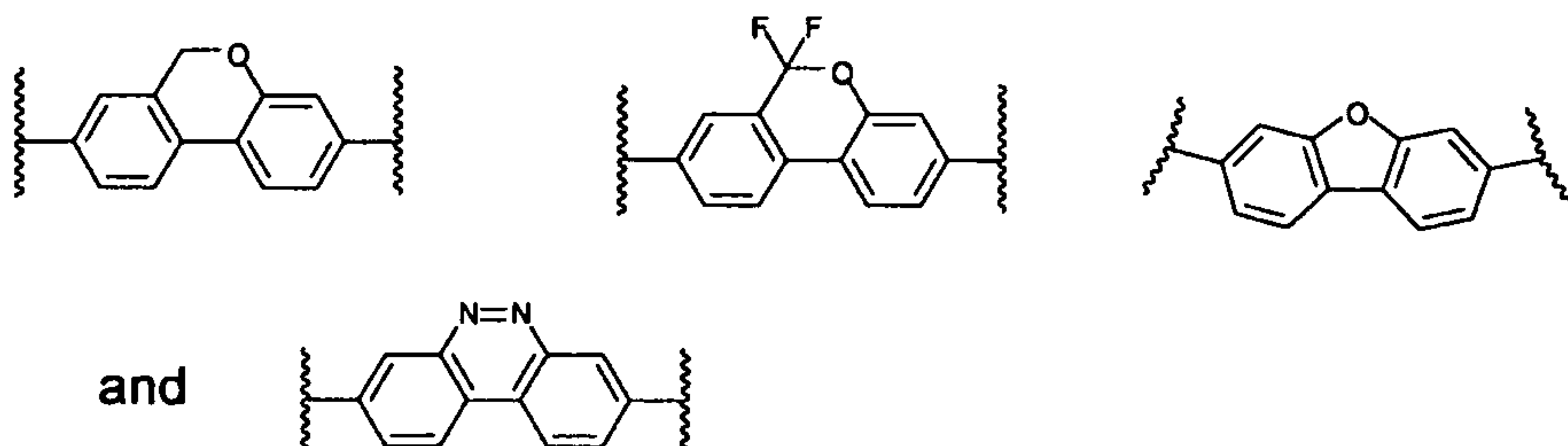


In another specific embodiment of the invention W⁸ is selected from:

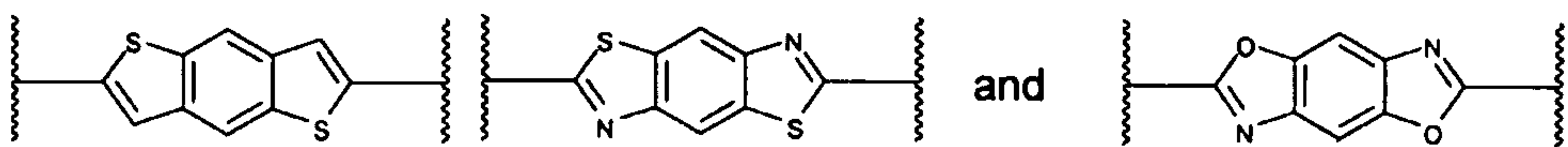




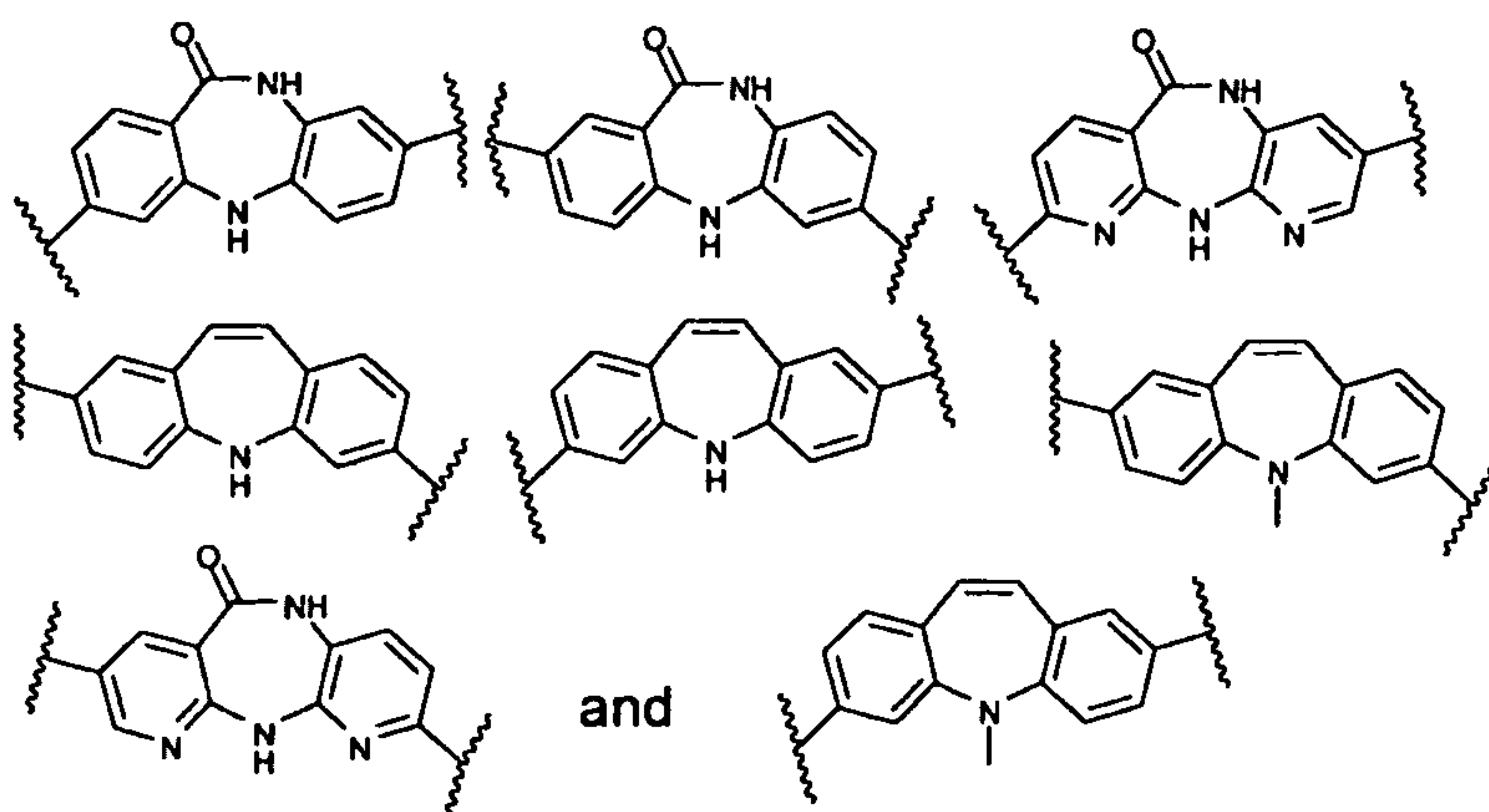
In another specific embodiment of the invention W^8 is selected from:



In another specific embodiment of the invention W^8 is selected from:

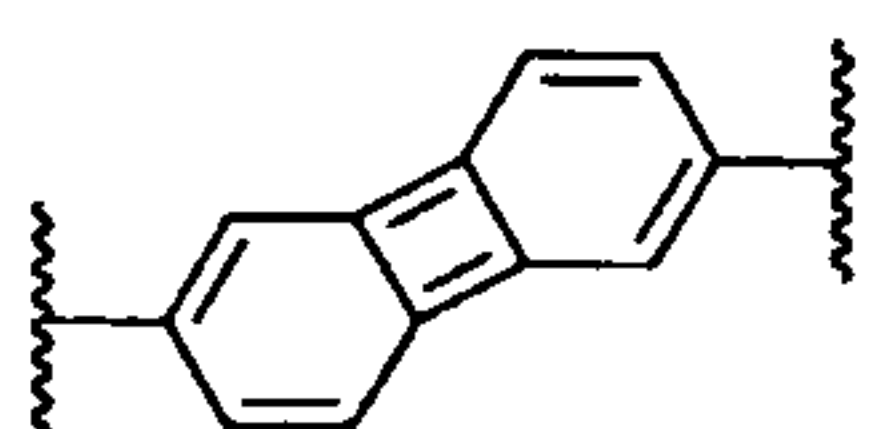


In another specific embodiment of the invention W^8 is selected from:



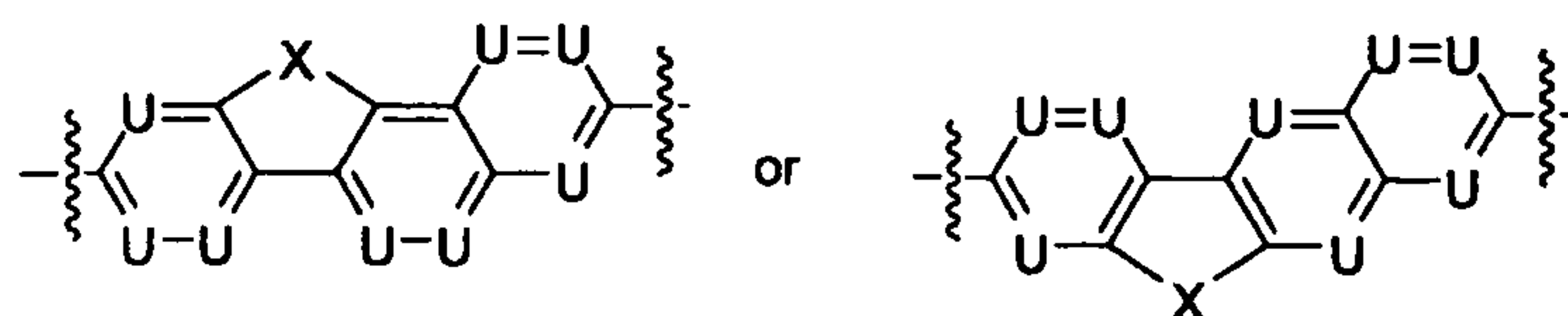
In another specific embodiment of the invention W is W^8 that is unsubstituted.

In another specific embodiment of the invention W^{12} is:



In another specific embodiment of the invention W is W^{15} or W^{16} .

In another specific embodiment of the invention W is a ring system of formula:



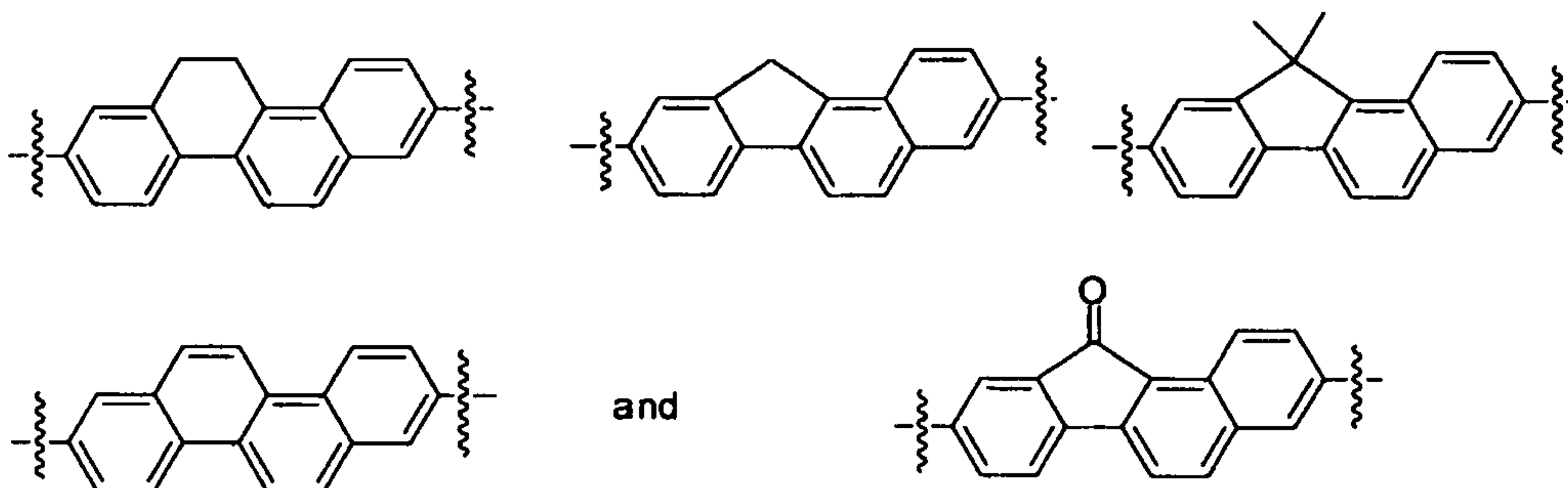
wherein :

U is CH or N; and

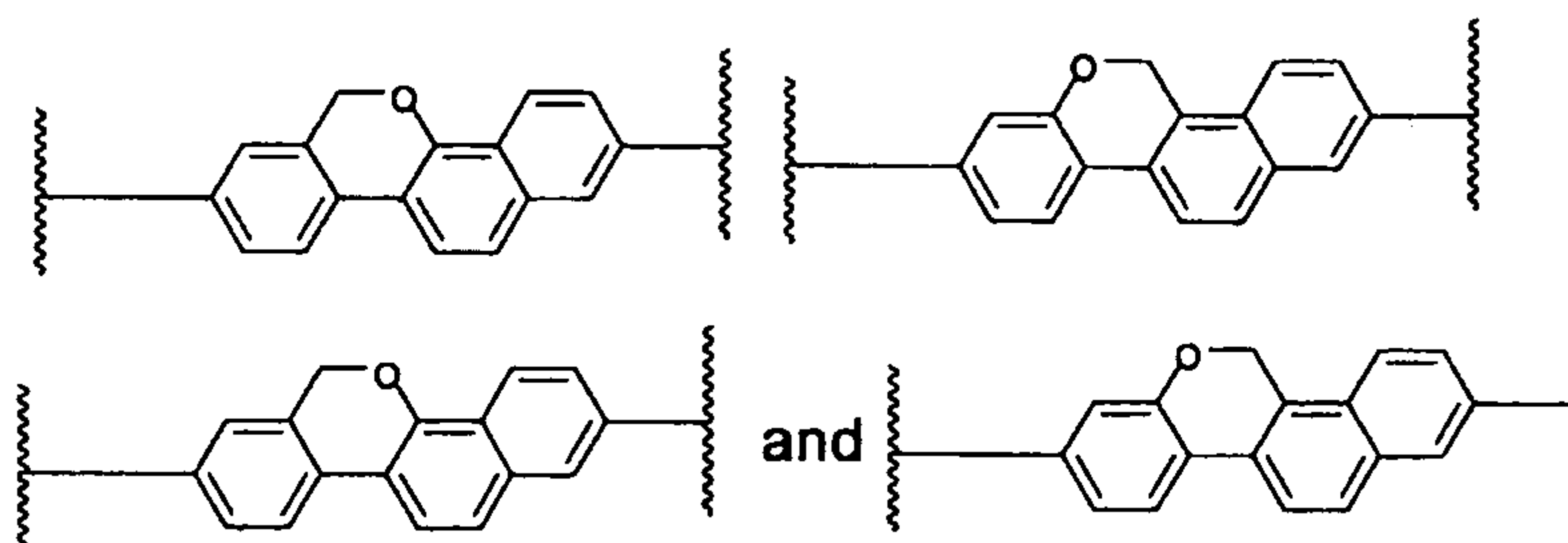
X is $-\text{CH}_2-$, $-\text{C}(=\text{O})-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, or $-\text{CH}=\text{CH}-$;

wherein the ring system is optionally substituted with one or more R^{A1} or R^{A3} .

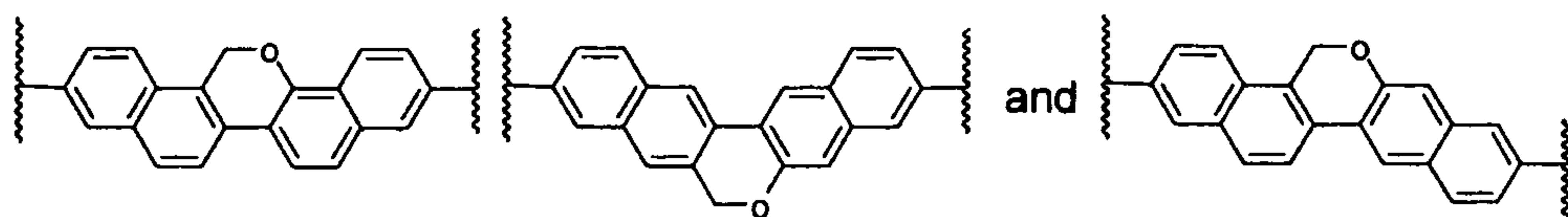
In another specific embodiment of the invention W is selected from:



In another specific embodiment of the invention W is selected from:

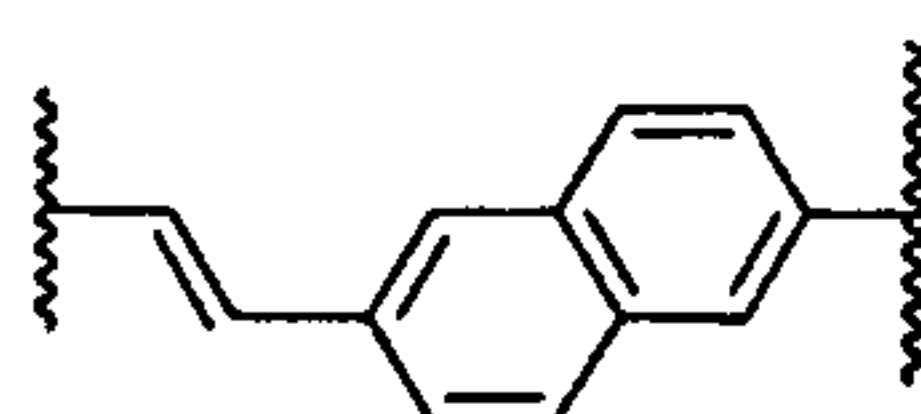


In another specific embodiment of the invention W is selected from:



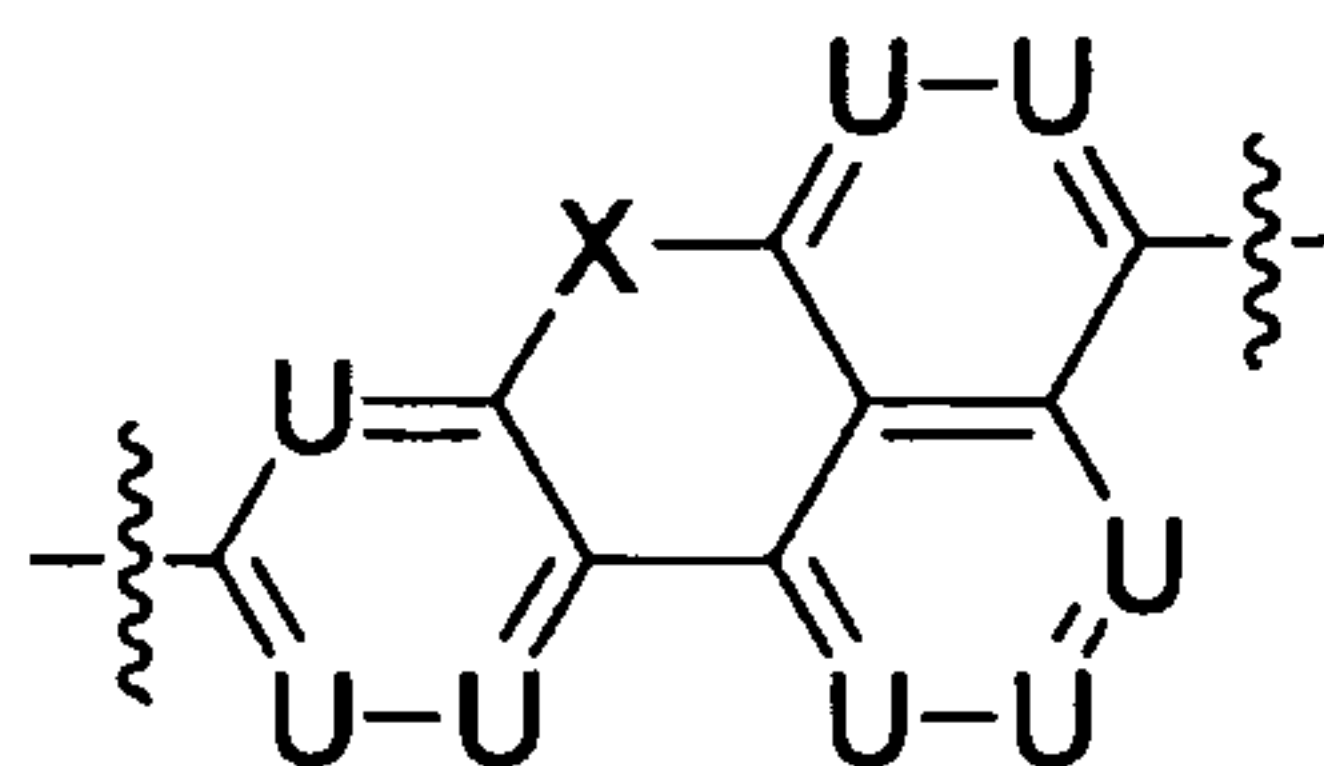
In another specific embodiment of the invention W is W^2 and within the W^2 one X^{A} is absent and one X^{A} is $\text{RC}=\text{CR}$ and each R is independently selected from H or alkyl.

In another specific embodiment of the invention W^2 has the following structure:



In another specific embodiment of the invention W is W^2 and within the W^2 one X^A is absent and one X^A is selected from absent, alkynyl, or $RC=CR$ and each R is independently selected from H or alkyl; and M is selected from M^0 or M^9 .

In another specific embodiment of the invention W is a ring system of formula:



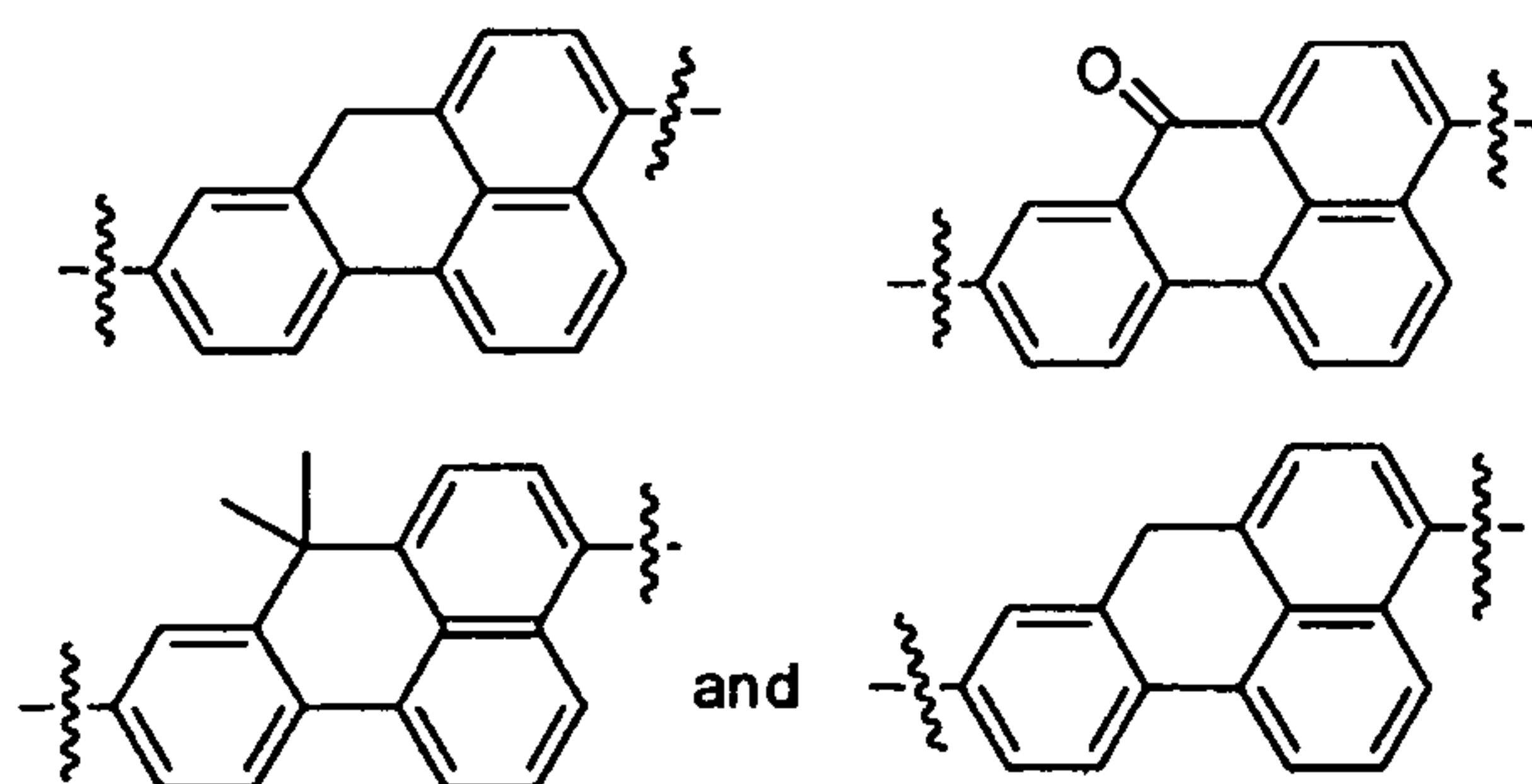
wherein :

U is CH or N; and

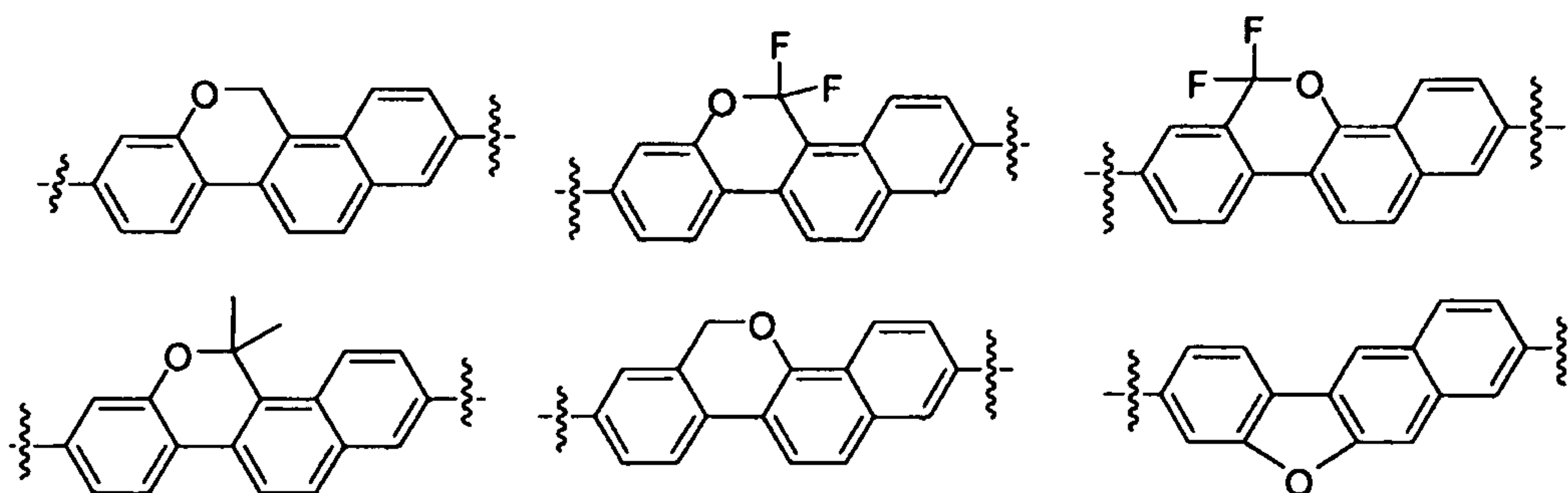
X is $-CH_2-$, $-C(=O)-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, or $-CH=CH-$;

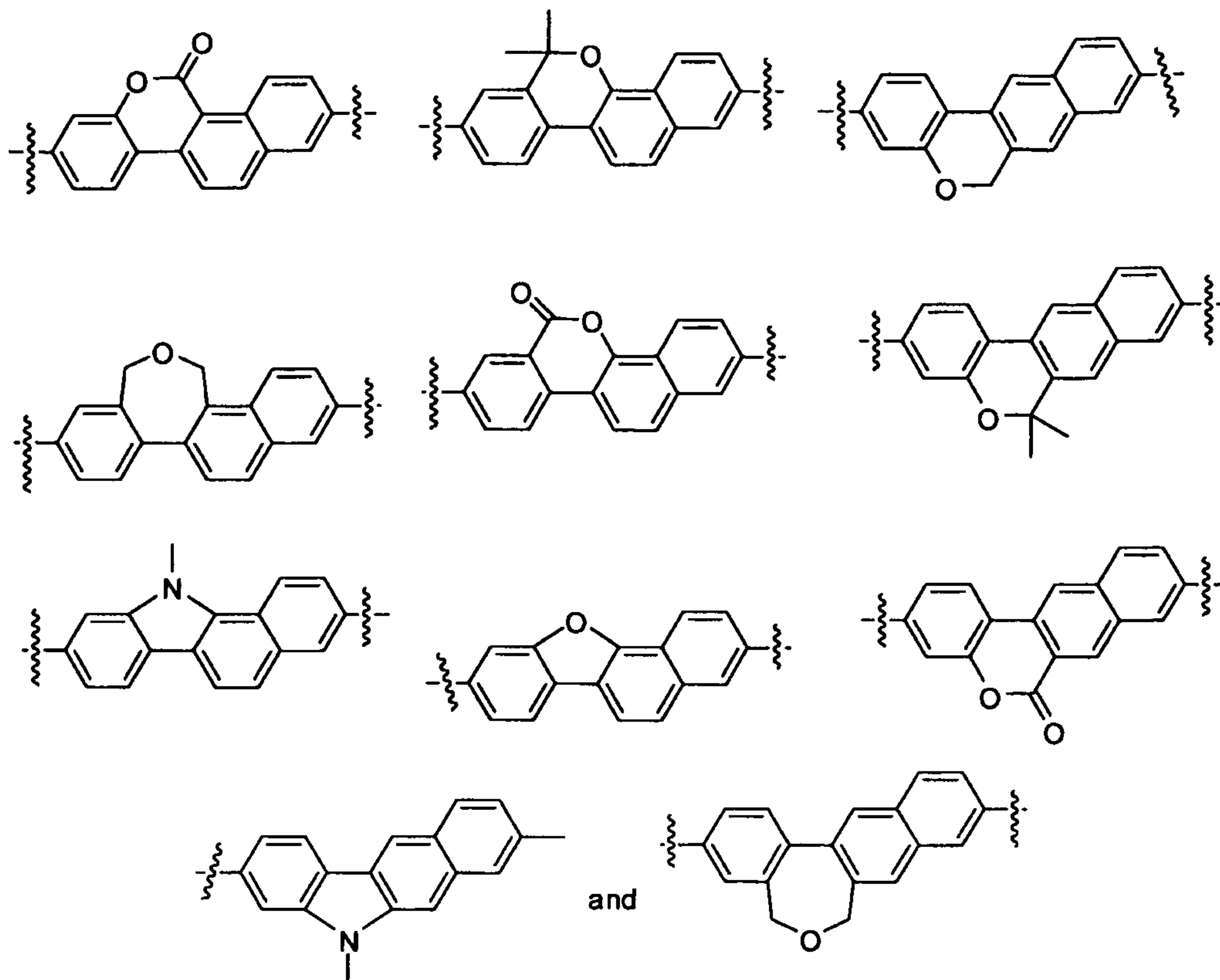
wherein the ring system is optionally substituted with one or more R^{A1} or R^{A3} .

In another specific embodiment of the invention W is selected from:

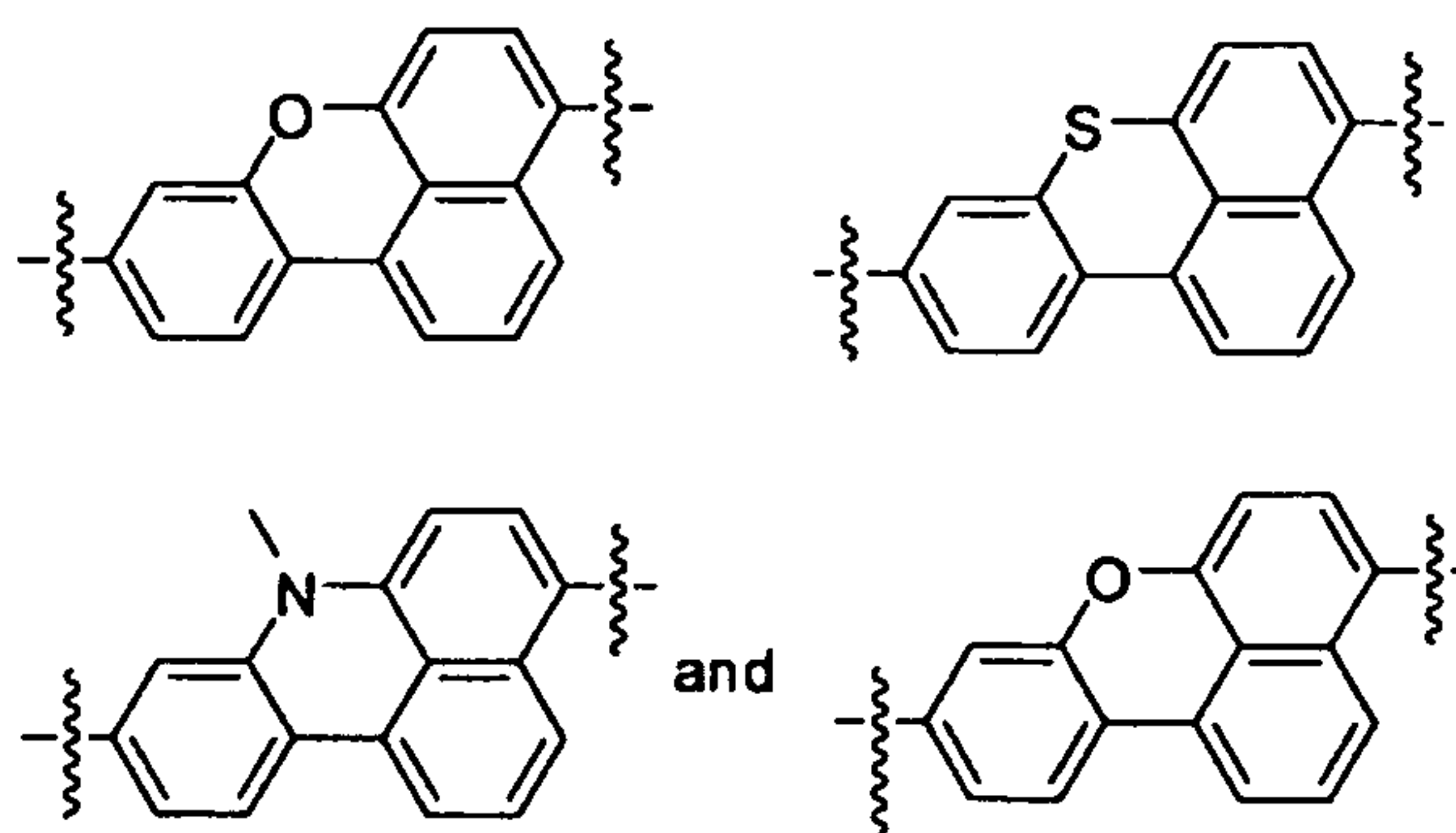


In another specific embodiment of the invention W is selected from:

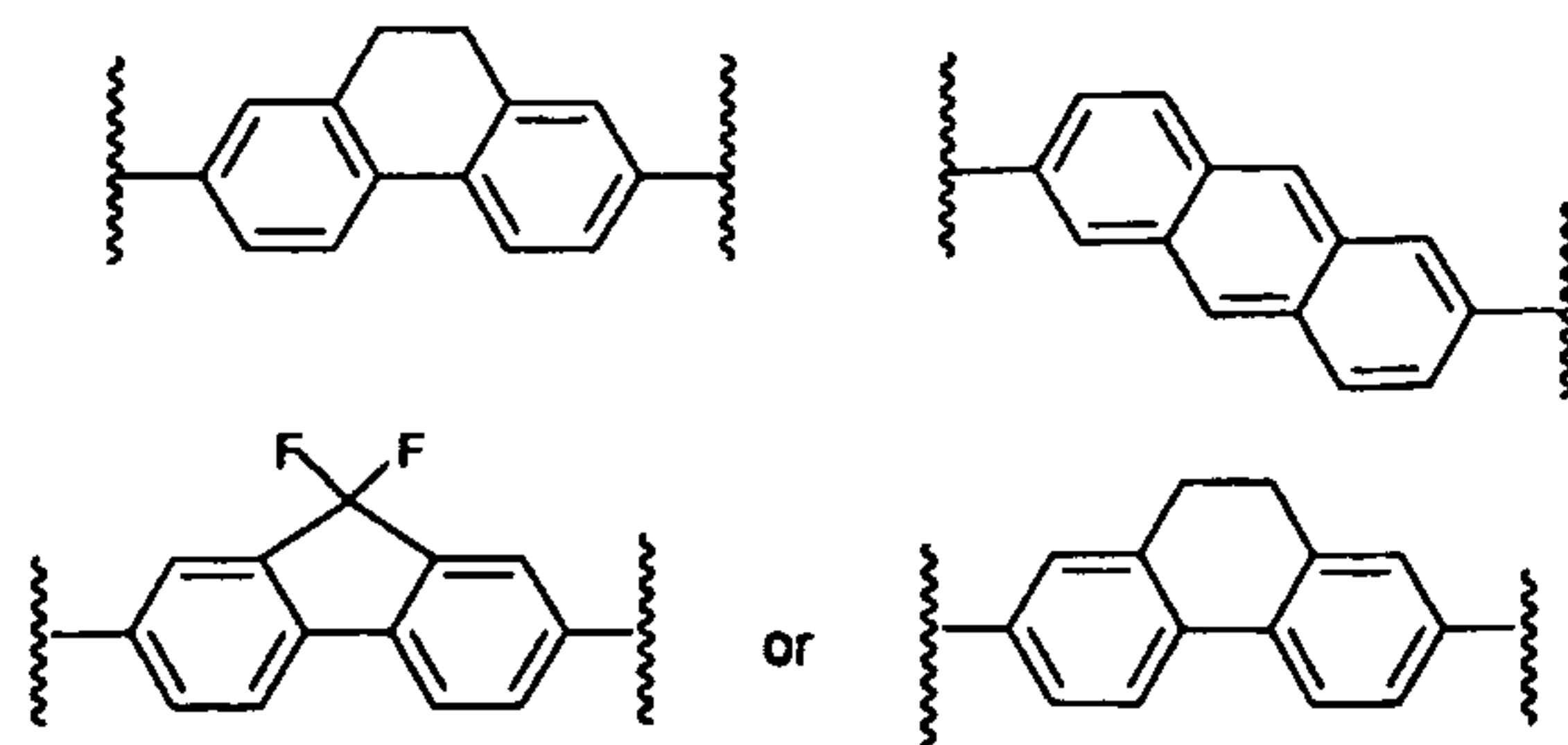




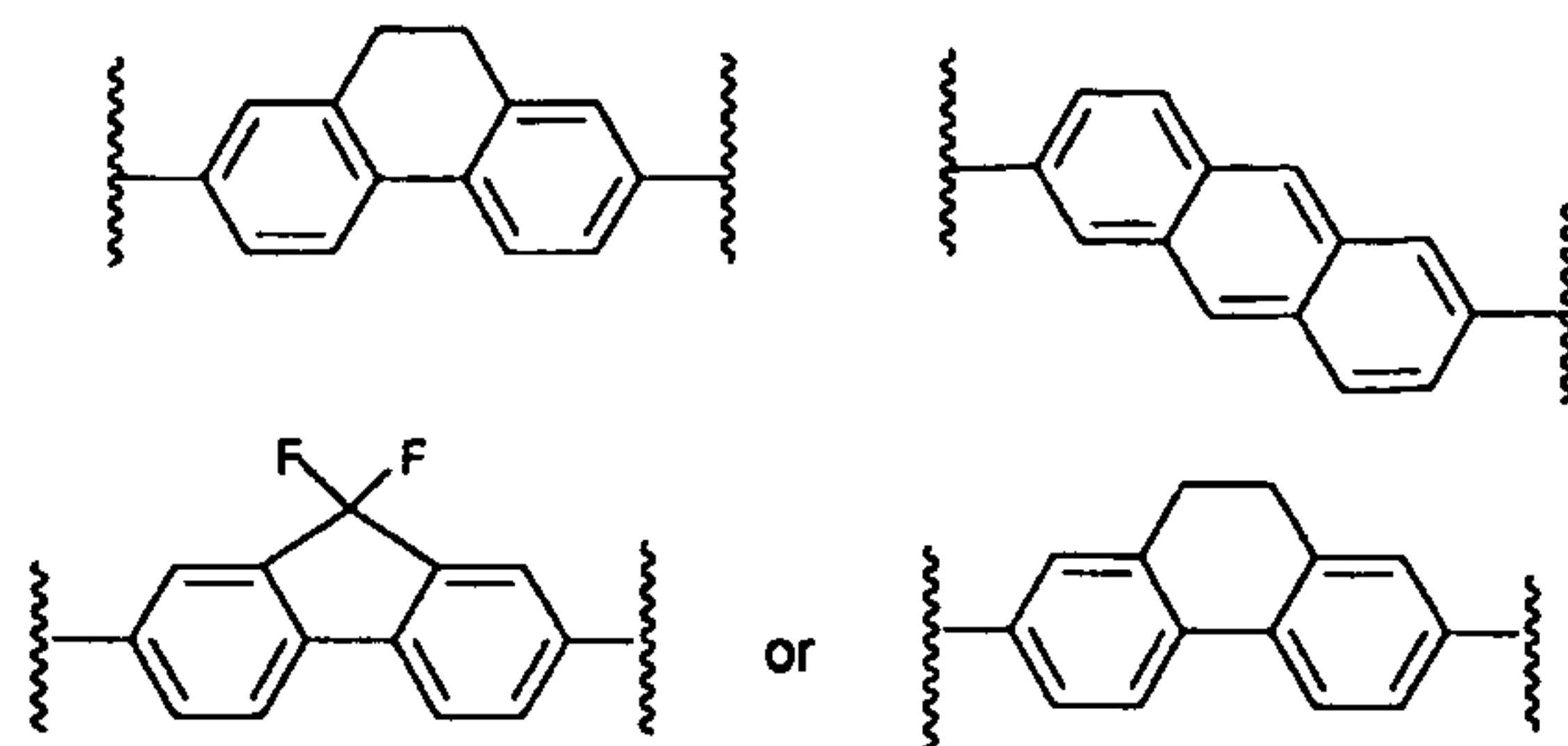
In another specific embodiment of the invention W is selected from:



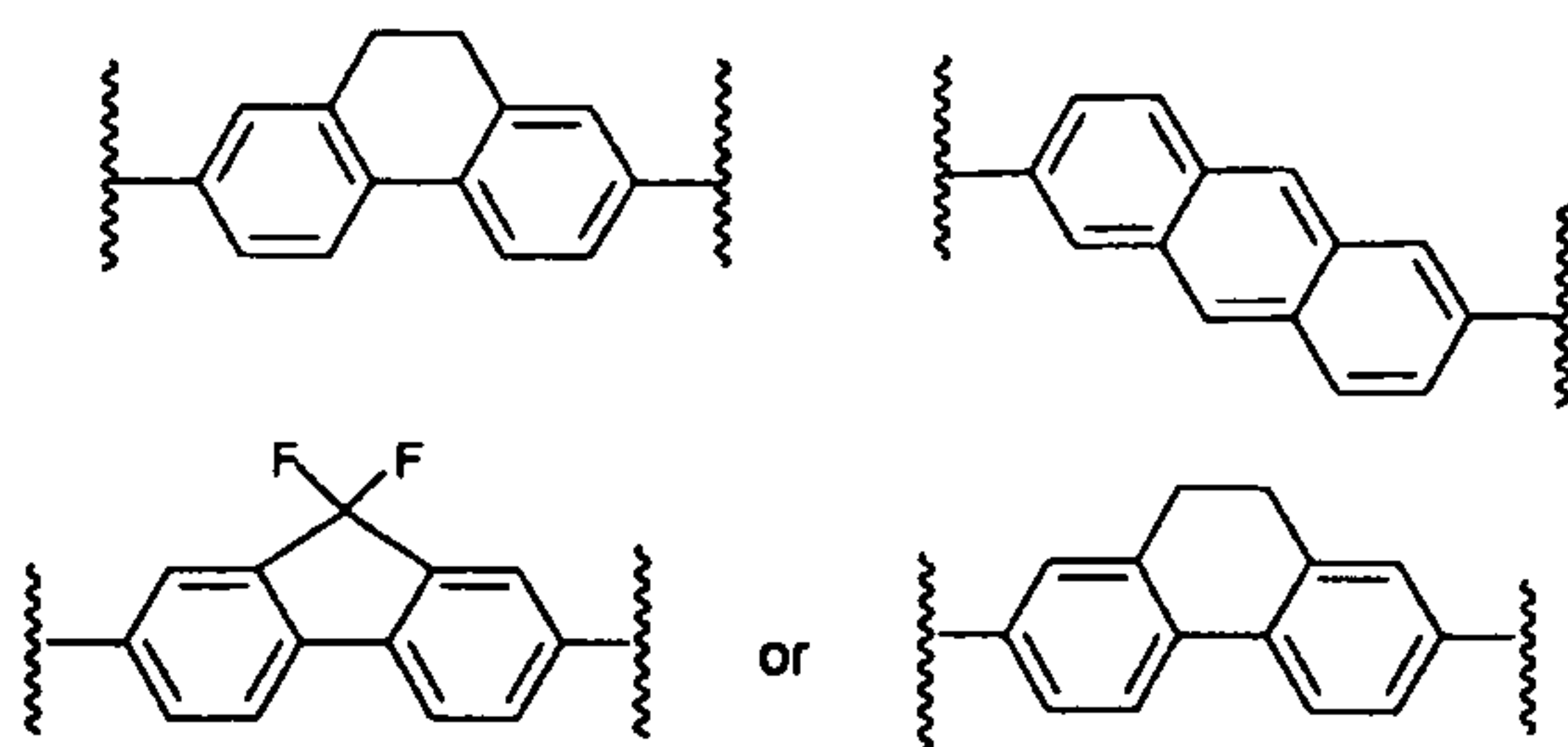
In another specific embodiment of the invention W is



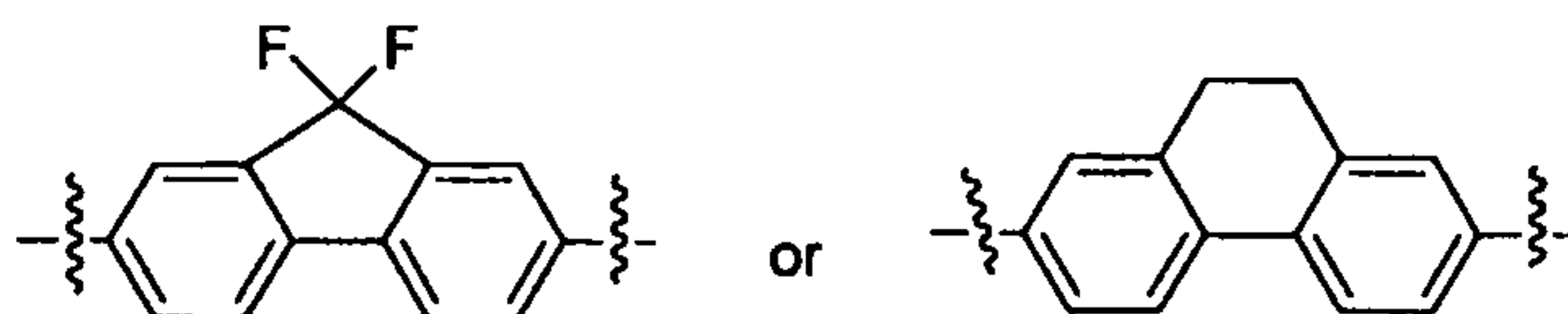
In another specific embodiment of the invention W is



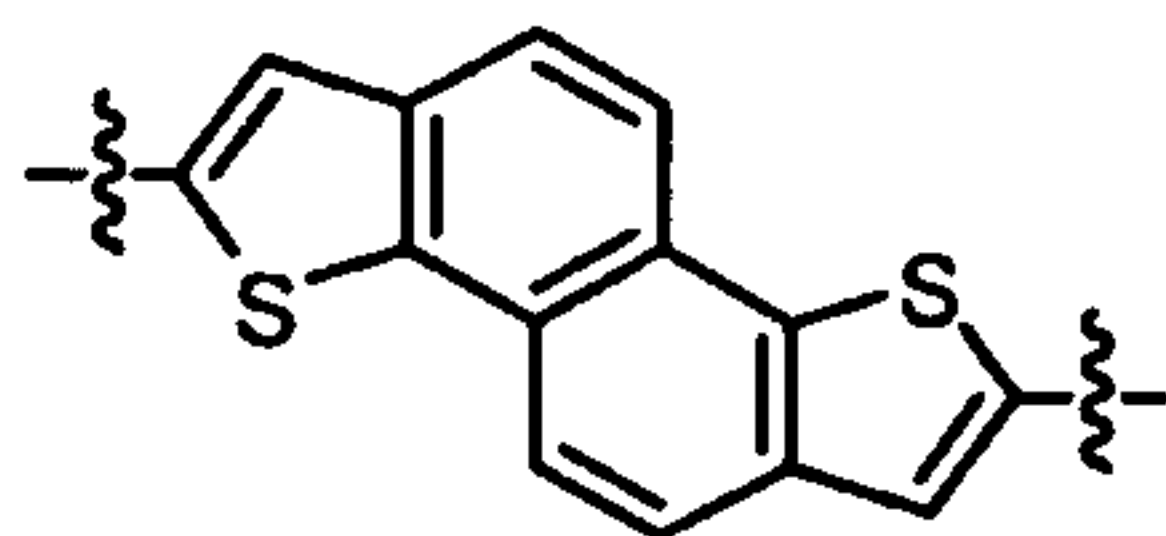
In another specific embodiment of the invention W is



In another specific embodiment of the invention W is



In another specific embodiment of the invention W is



In another specific embodiment of the invention each X^A within W is absent.

In another specific embodiment of the invention t is 0, 9, 10, or 11.

In another specific embodiment of the invention M^0 is imidazolyl and M^9 is benzimidazolyl.

In another specific embodiment of the invention the compound of formula (Ia) comprises a group $M^9-W^2-M^9$.

In another specific embodiment of the invention M is M^0 .

In another specific embodiment of the invention M is imidazolyl.

In another specific embodiment of the invention M is M^9 .

In another specific embodiment of the invention each M is benzimidazolyl.

In another specific embodiment of the invention one M is M^0 and one M is M^9 .

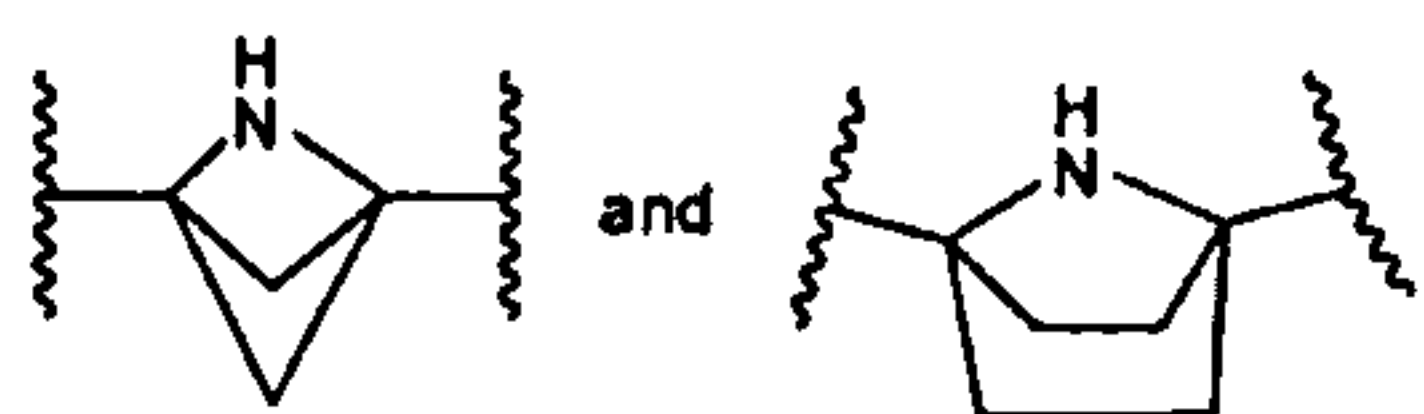
In another specific embodiment of the invention one M is imidazolyl and one M is benzimidazolyl.

In another specific embodiment of the invention each M is independently a 5-membered heteroaryl ring.

In another specific embodiment of the invention each M is 2,4-imidazoldiyl.

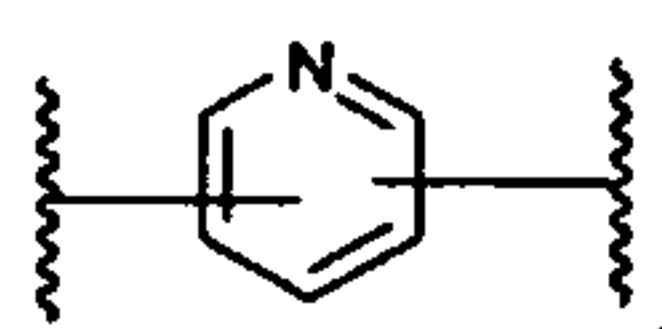
In another specific embodiment of the invention M is M^6 .

In another specific embodiment of the invention M is selected from:



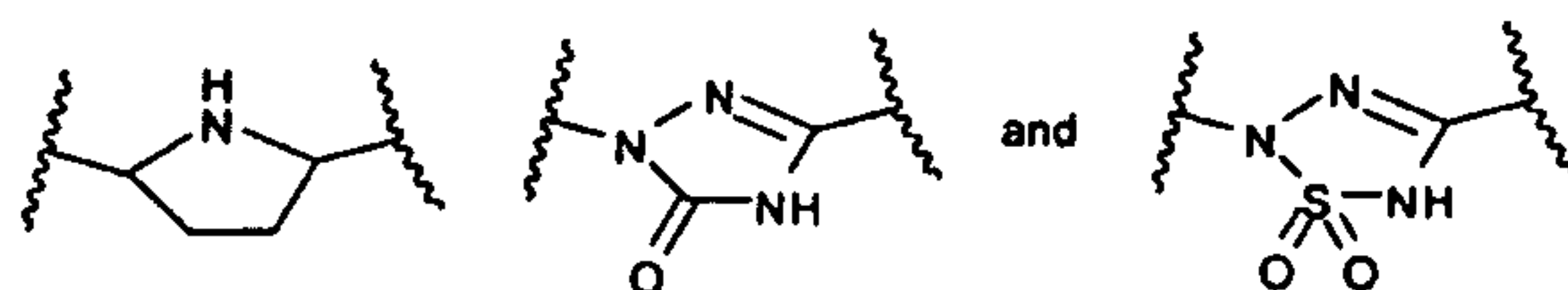
In another specific embodiment of the invention M is M^7 .

In another specific embodiment of the invention M is:

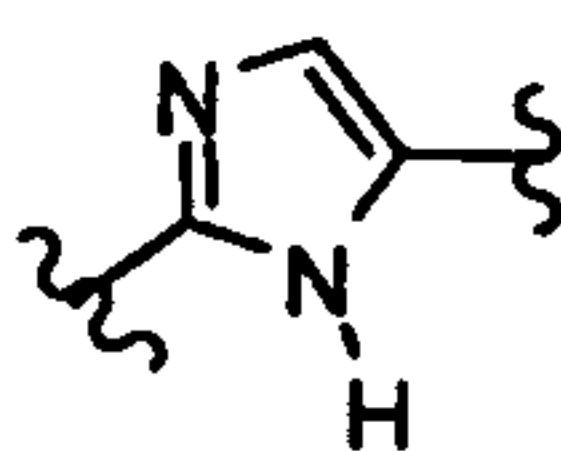


In another specific embodiment of the invention M is M^8 .

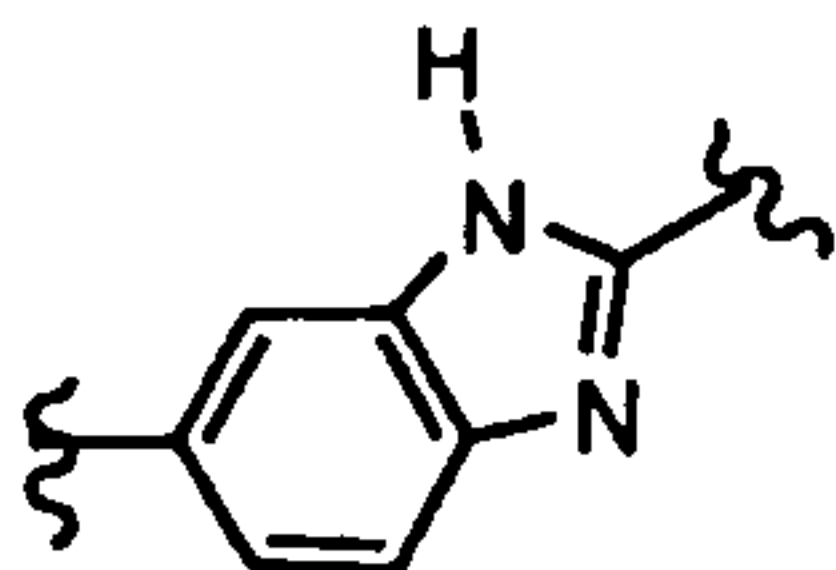
In another specific embodiment of the invention M is:



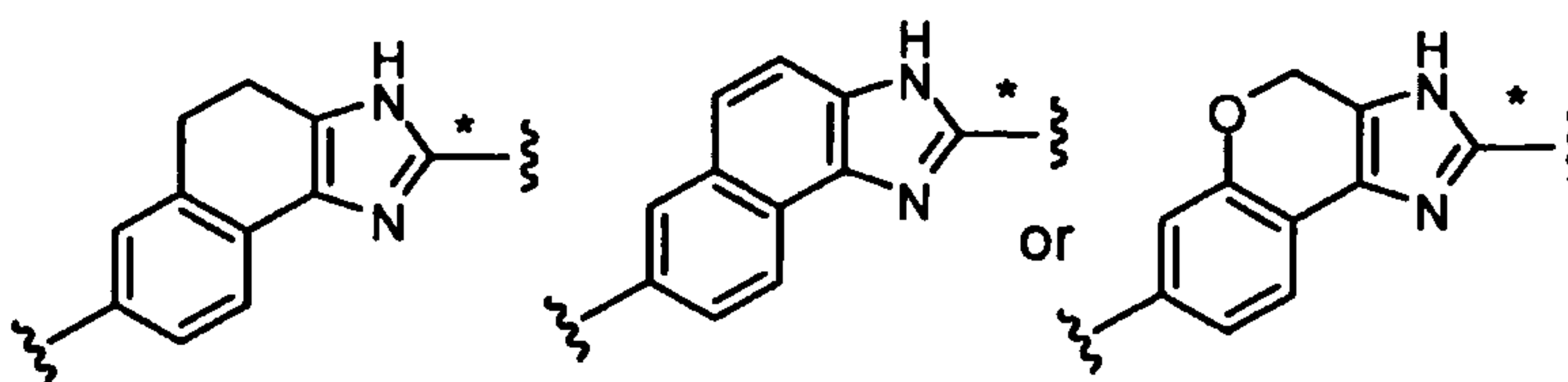
In another specific embodiment of the invention M^0 is:



In another specific embodiment of the invention M^9 is :



In another specific embodiment of the invention M is M^{11} and is:



wherein * designates the site of connection to P.

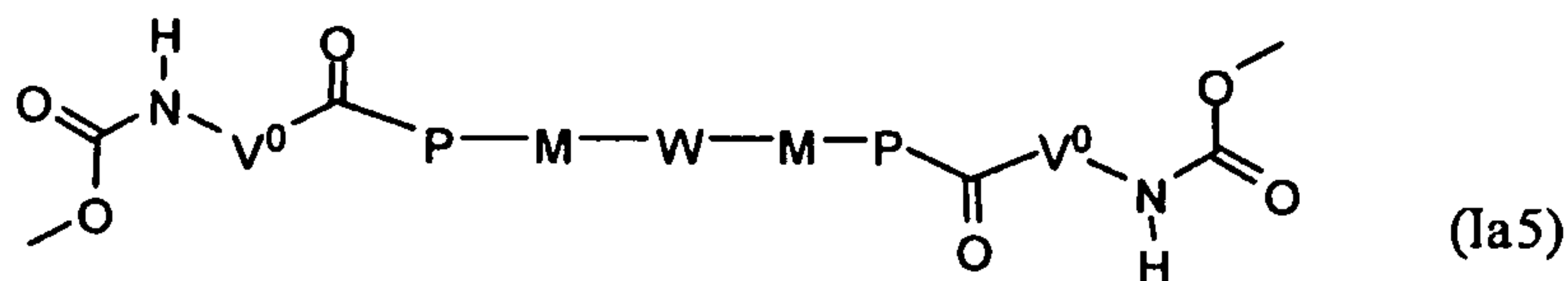
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia1): E-V-Z-P- M^0 - W^6 - M^9 -P-Z-V-E (Ia1).

In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia2): E^0 - V^0 - Z^0 -P- M^0 - W^6 - M^9 -P- Z^0 - V^0 - E^0 (Ia2)

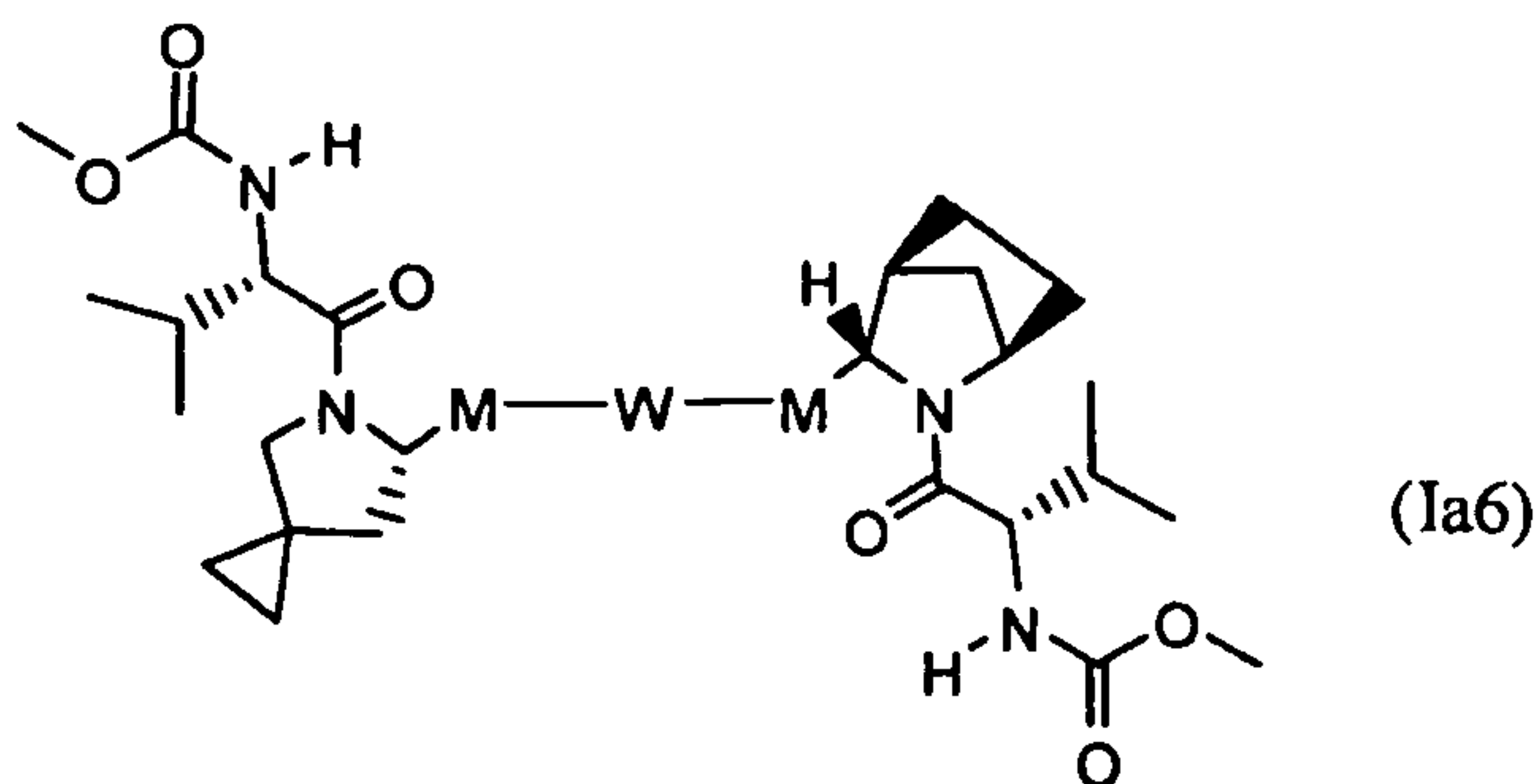
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia3): E-V-Z- P^0 - M^0 - W^6 - M^9 - P^7 -Z-V-E (Ia3).

In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia4): E^0 - V^0 - Z^0 - P^0 - M^0 - W^6 - M^9 - P^7 - Z^0 - V^0 - E^0 (Ia4).

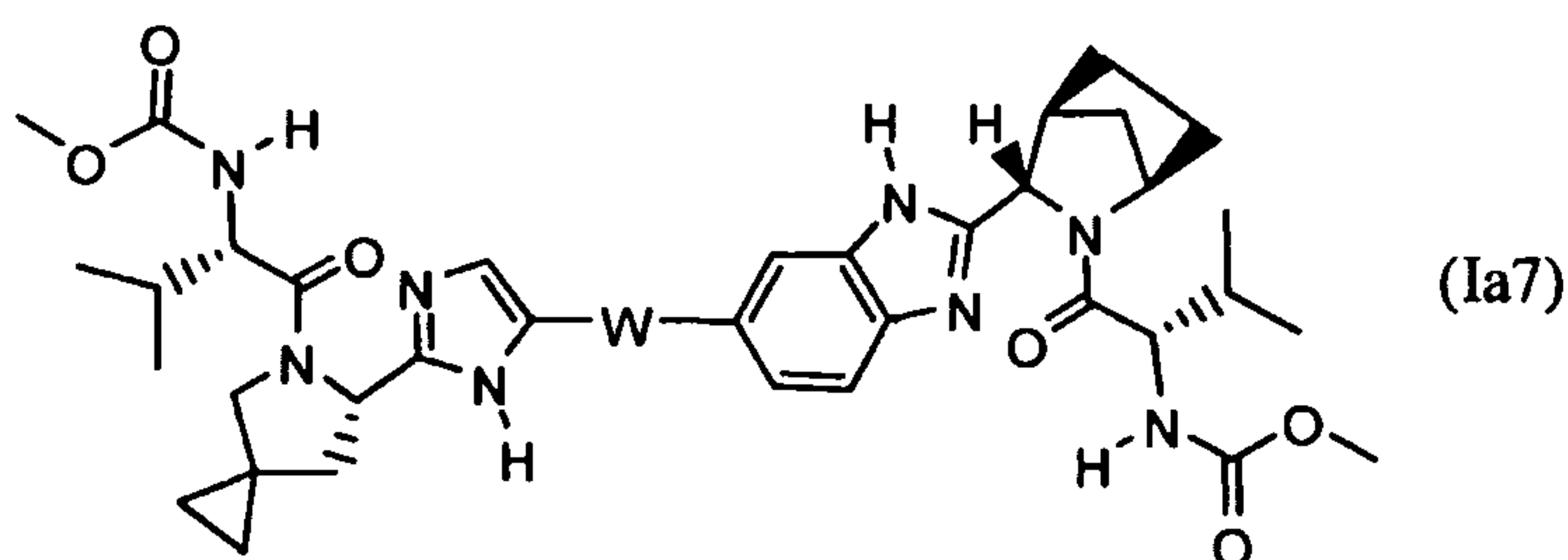
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia5):



In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia6):



In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia7):



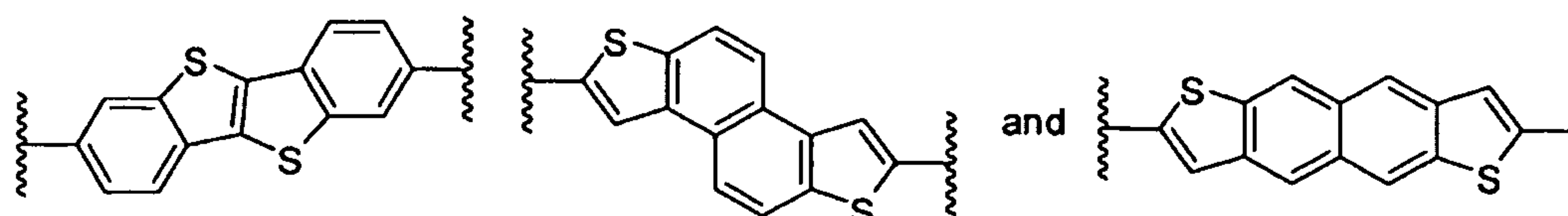
In another specific embodiment the invention provides a compound of formula (Ia5), (Ia6) or (Ia7), wherein W is W².

In another specific embodiment the invention provides a compound of formula (Ia5), (Ia6) or (Ia7), wherein W is W⁶.

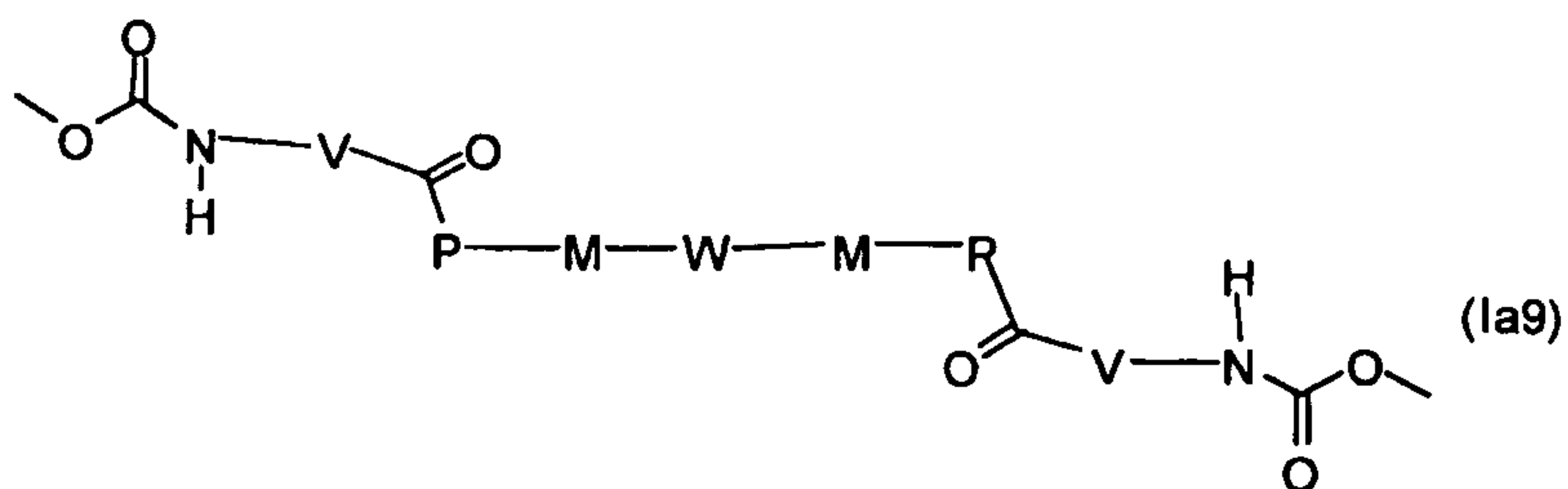
In another specific embodiment the invention provides a compound of formula (Ia5), (Ia6) or (Ia7), wherein W is W⁸.

In another specific embodiment the invention provides a compound of formula (Ia5), (Ia6) or (Ia7), wherein W is W¹⁶.

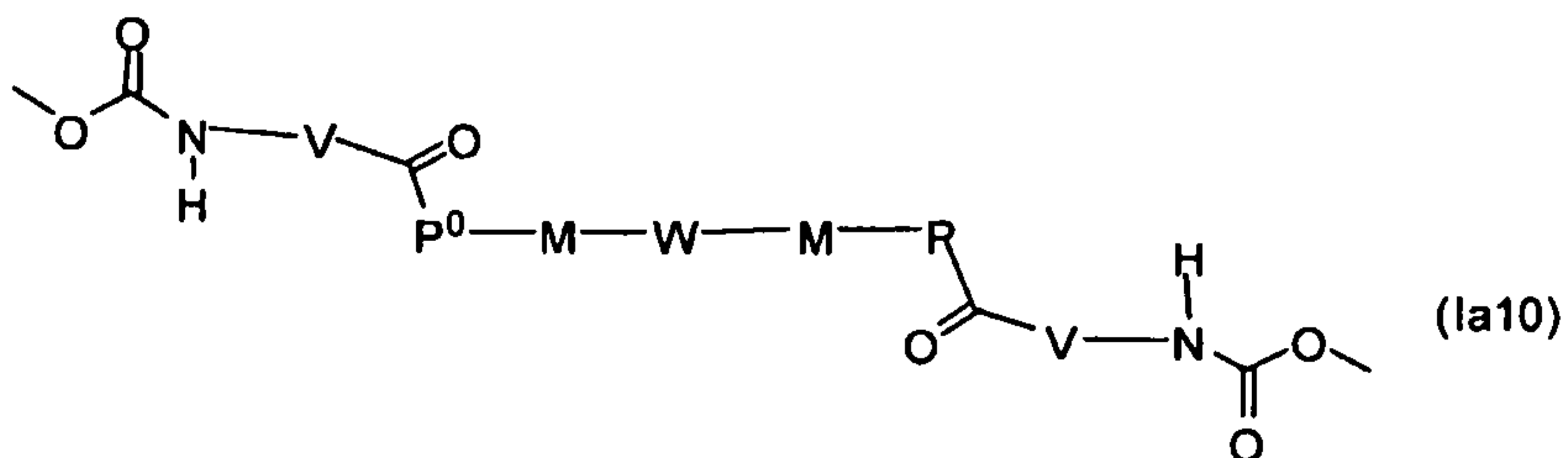
In another specific embodiment the invention provides a compound of formula (Ia5), (Ia6) or (Ia7), wherein W¹⁶ is selected from:



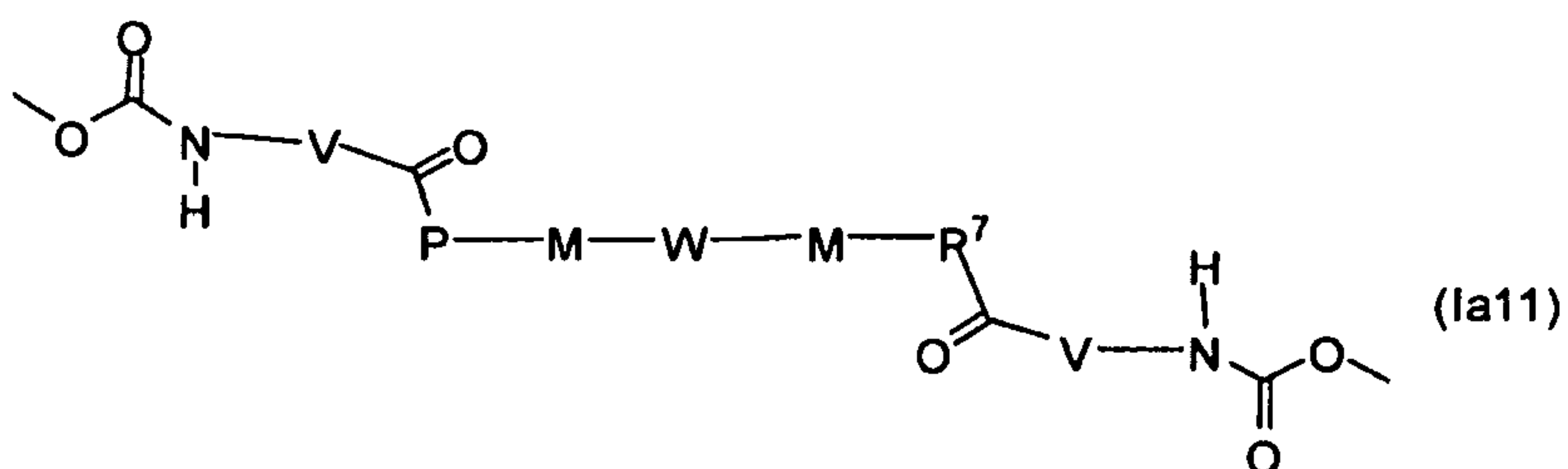
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia9):



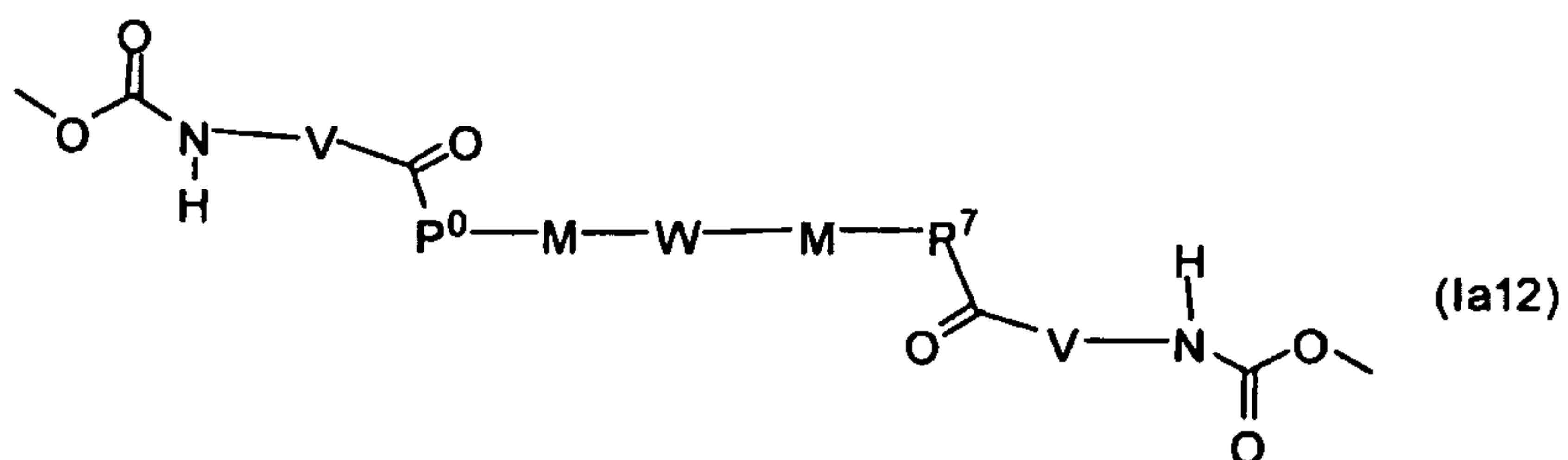
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia10):



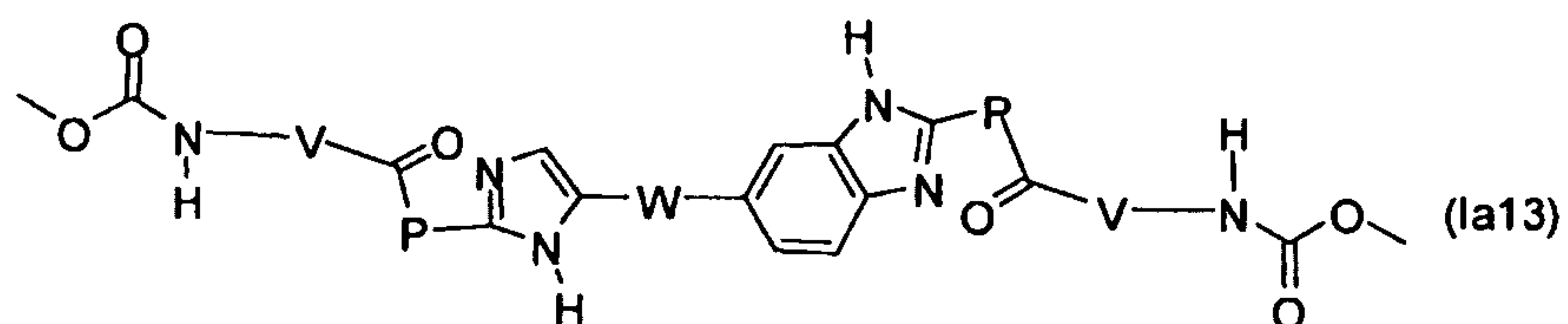
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia11):



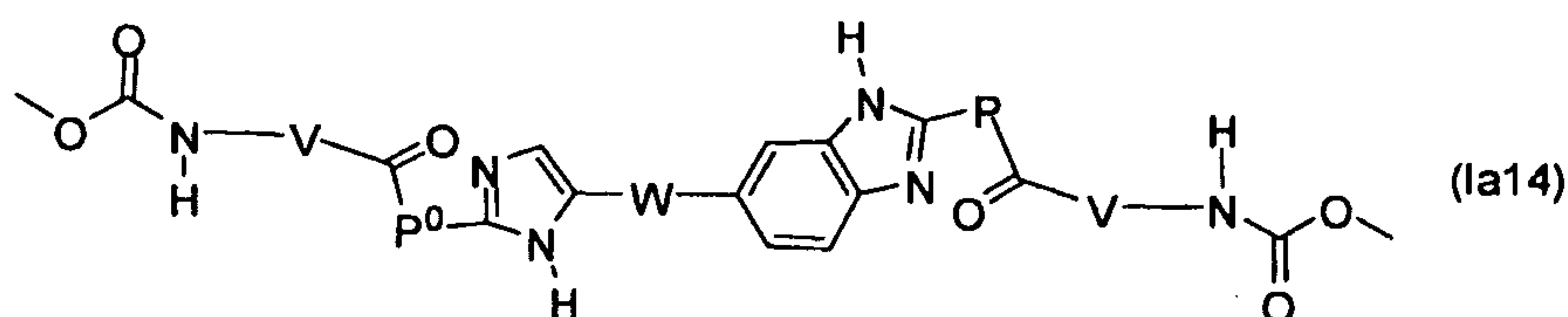
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia12):



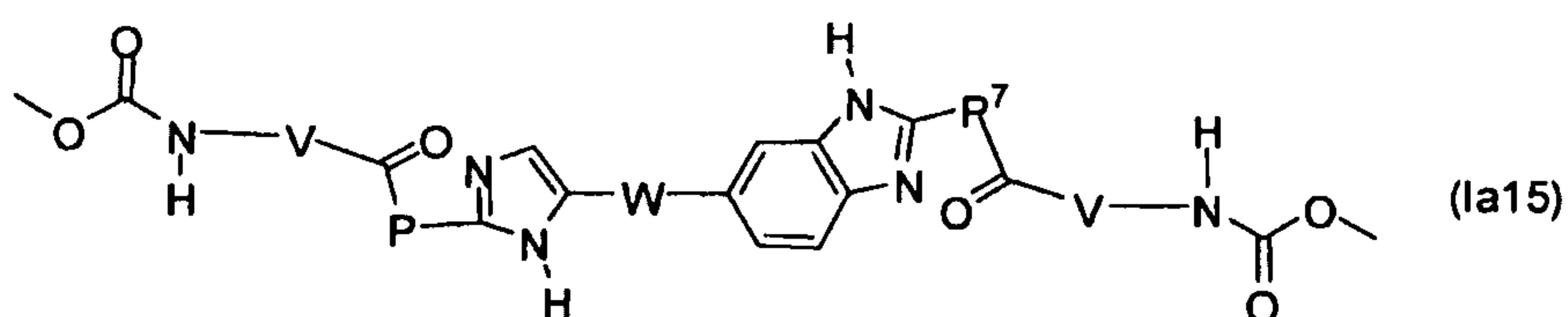
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia13):



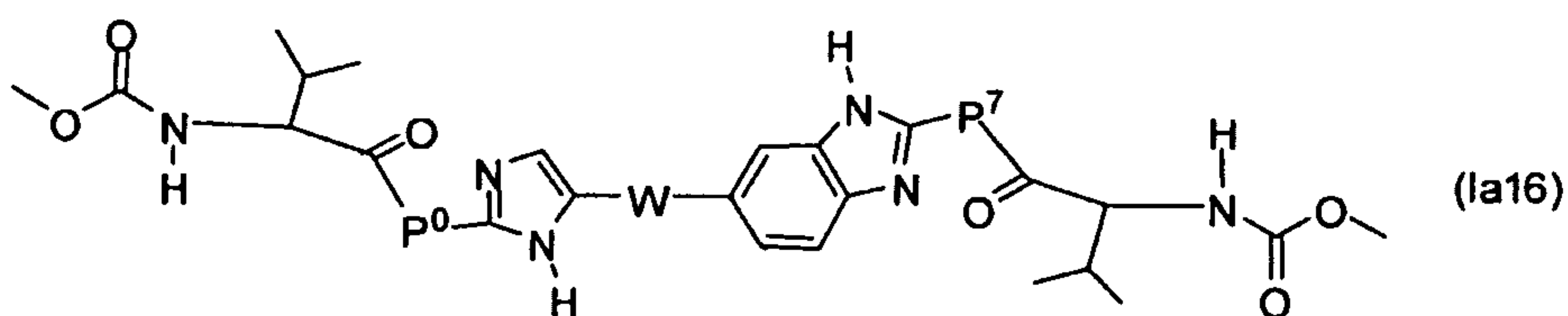
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia14):



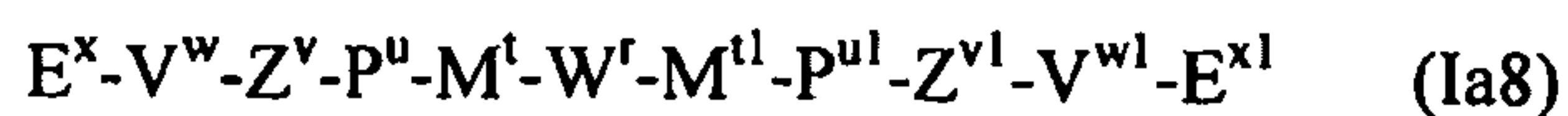
In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia15):



In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula (Ia16):



In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8):

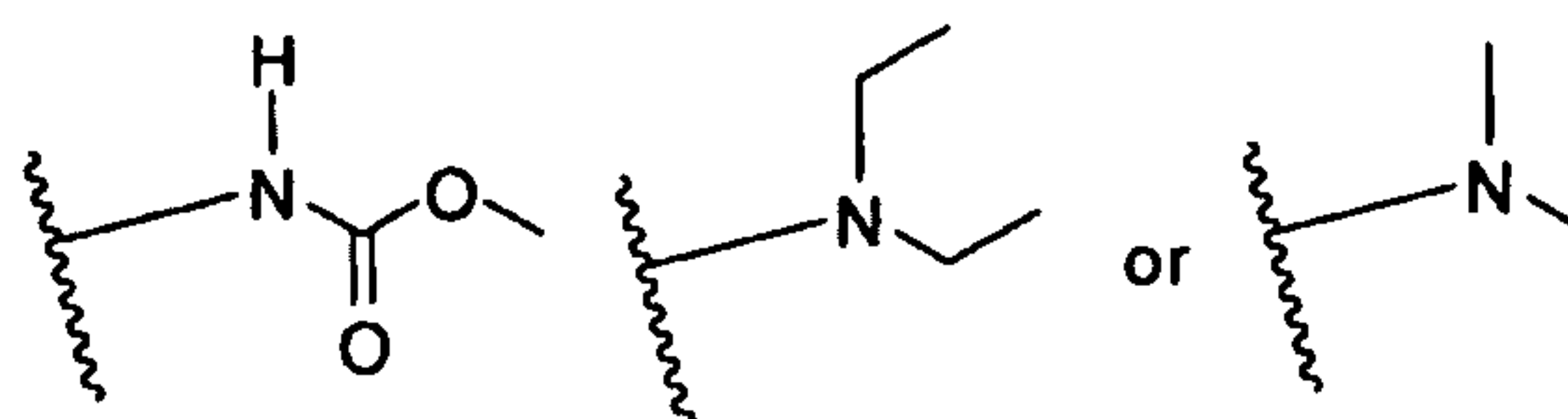


wherein:

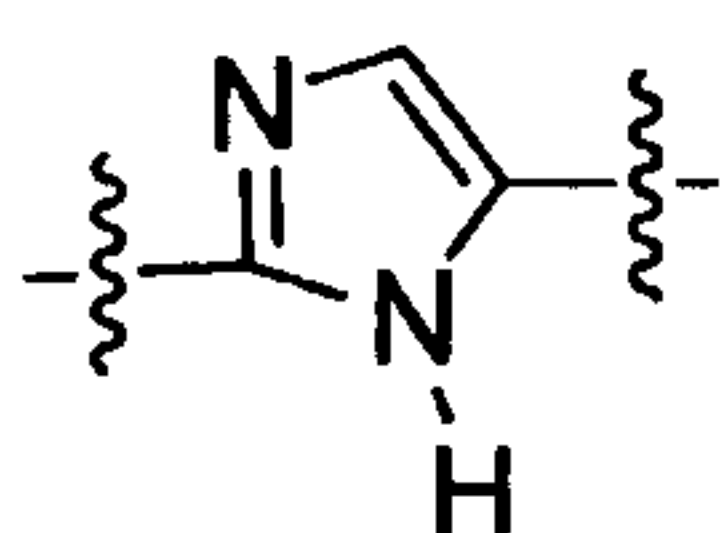
r is 2, 4, 6, 8, or 16; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 0, 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 0, 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

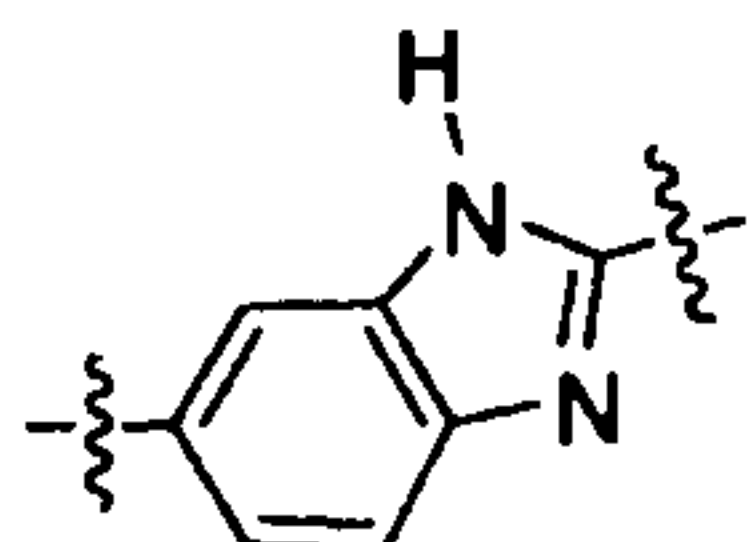
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein E⁰ is:



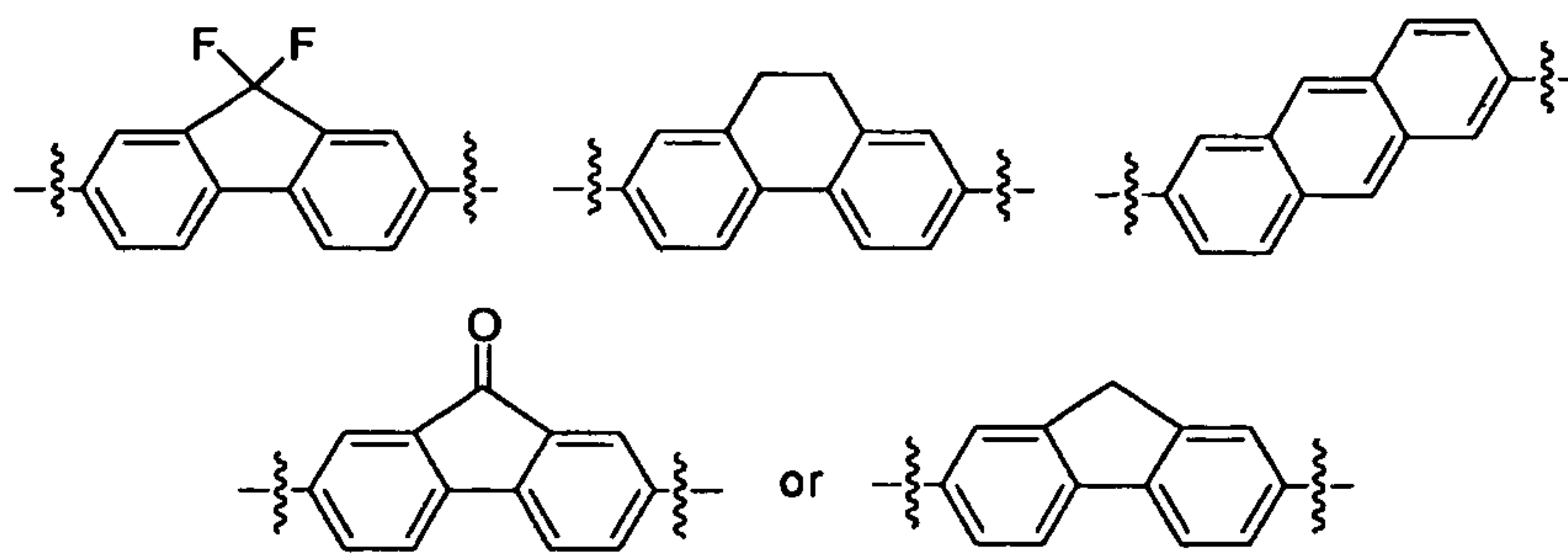
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein M⁰ is:



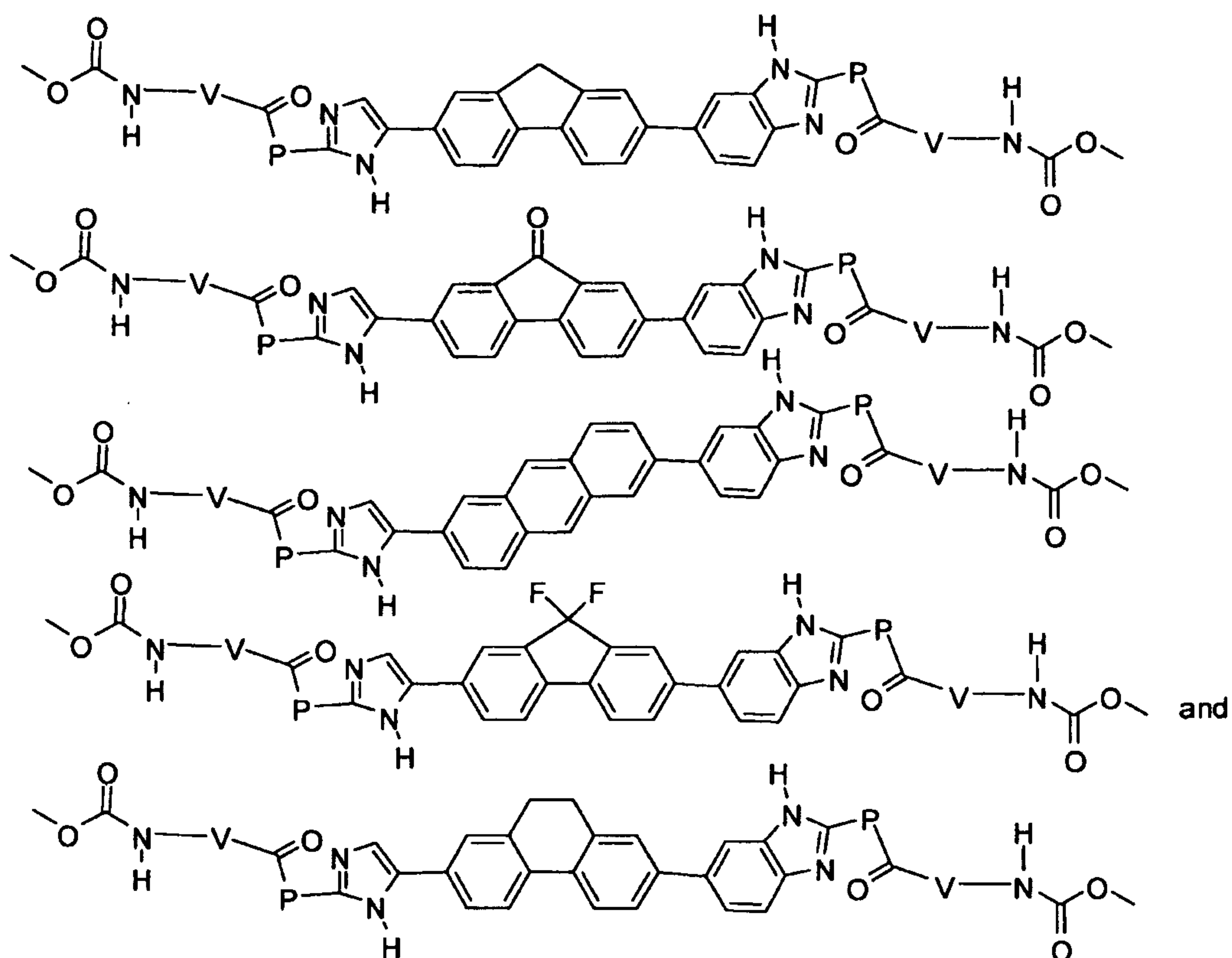
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein M⁹ is:



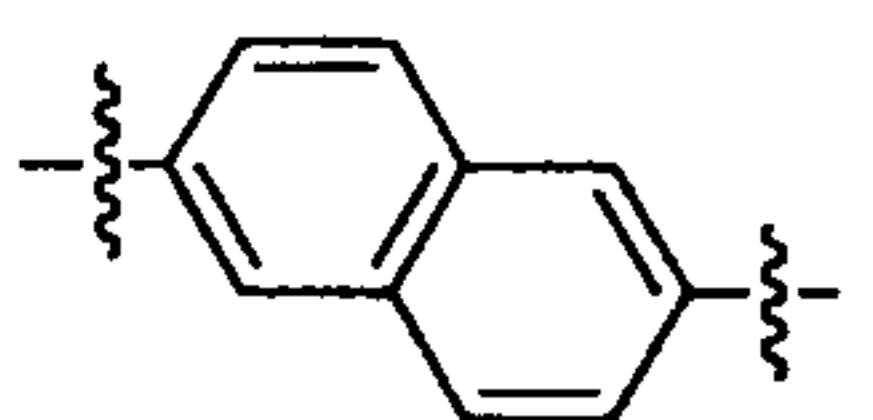
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 6 and W⁶ is:



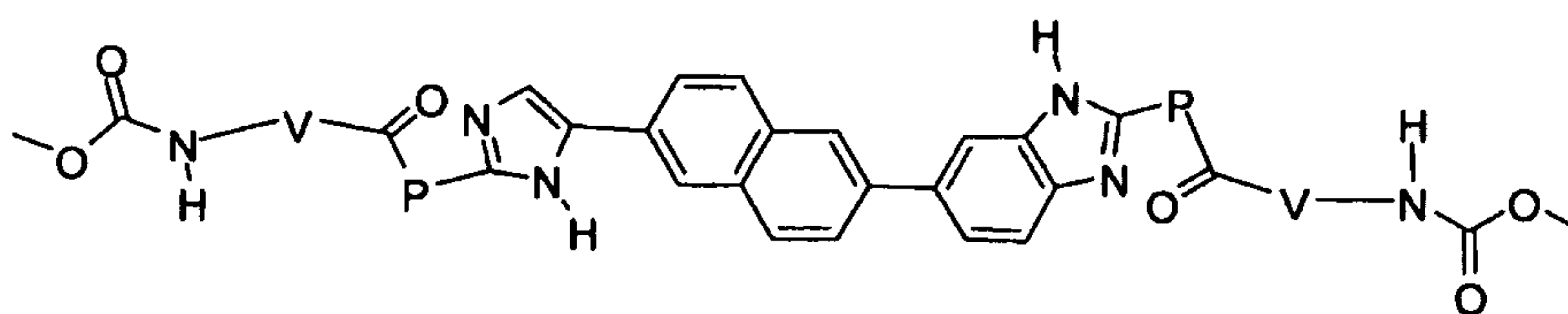
In one embodiment of the invention, the compound of formula (Ia) which is selected from:



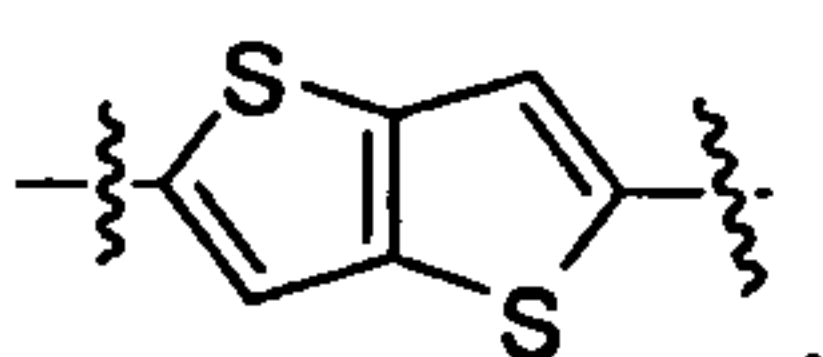
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 2 and W^2 is:



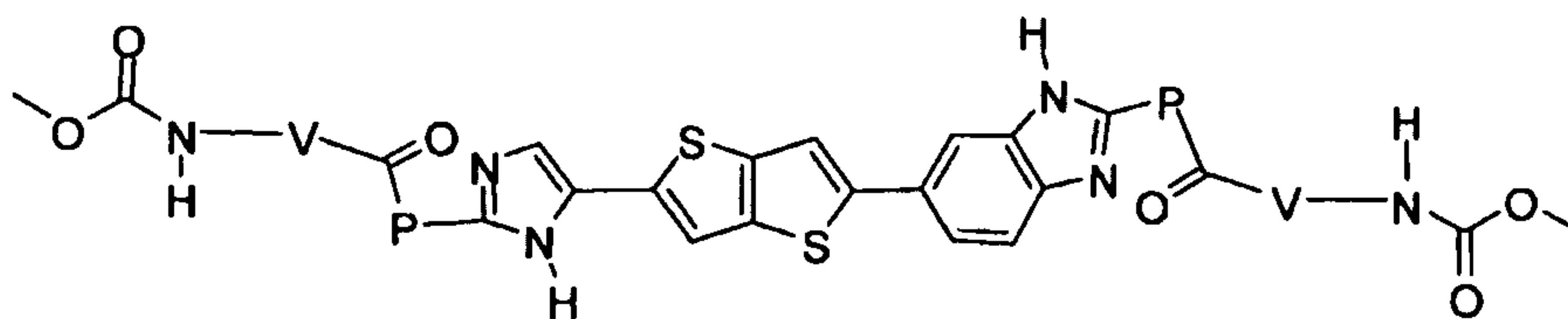
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is:



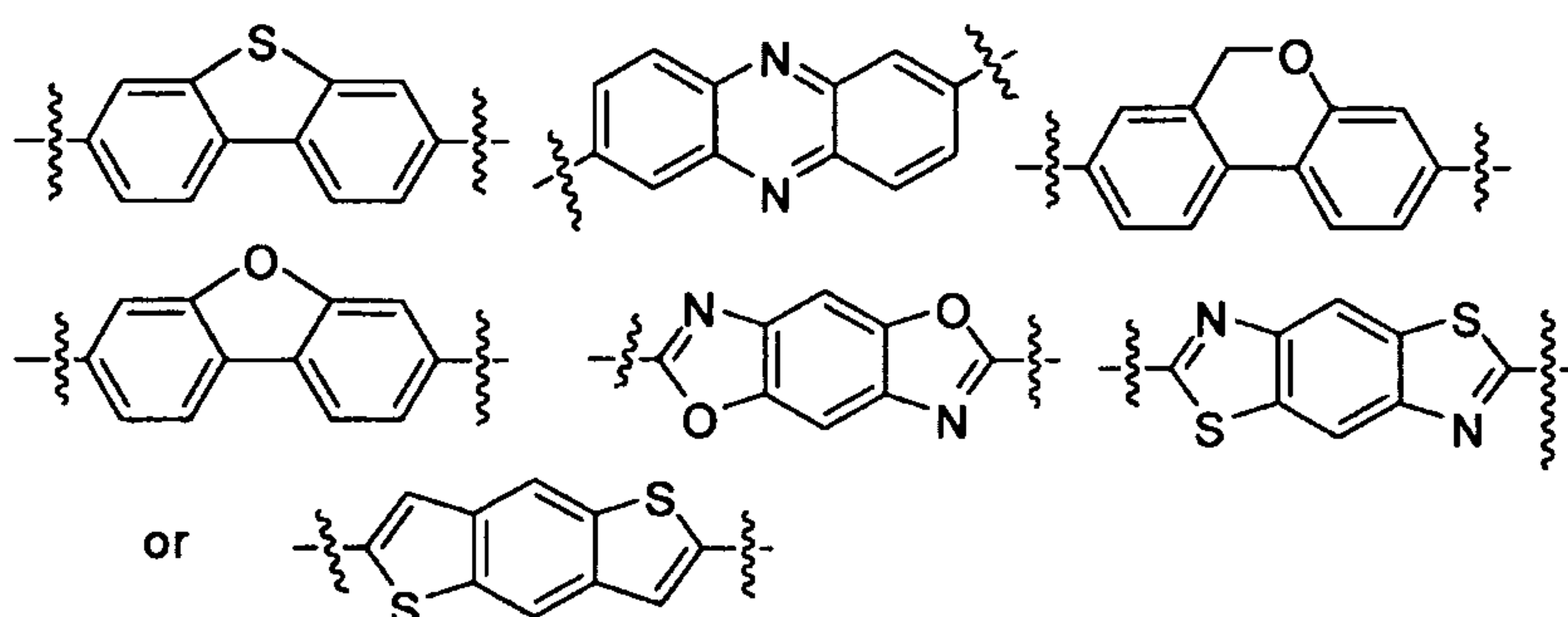
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 4 and W^4 is:



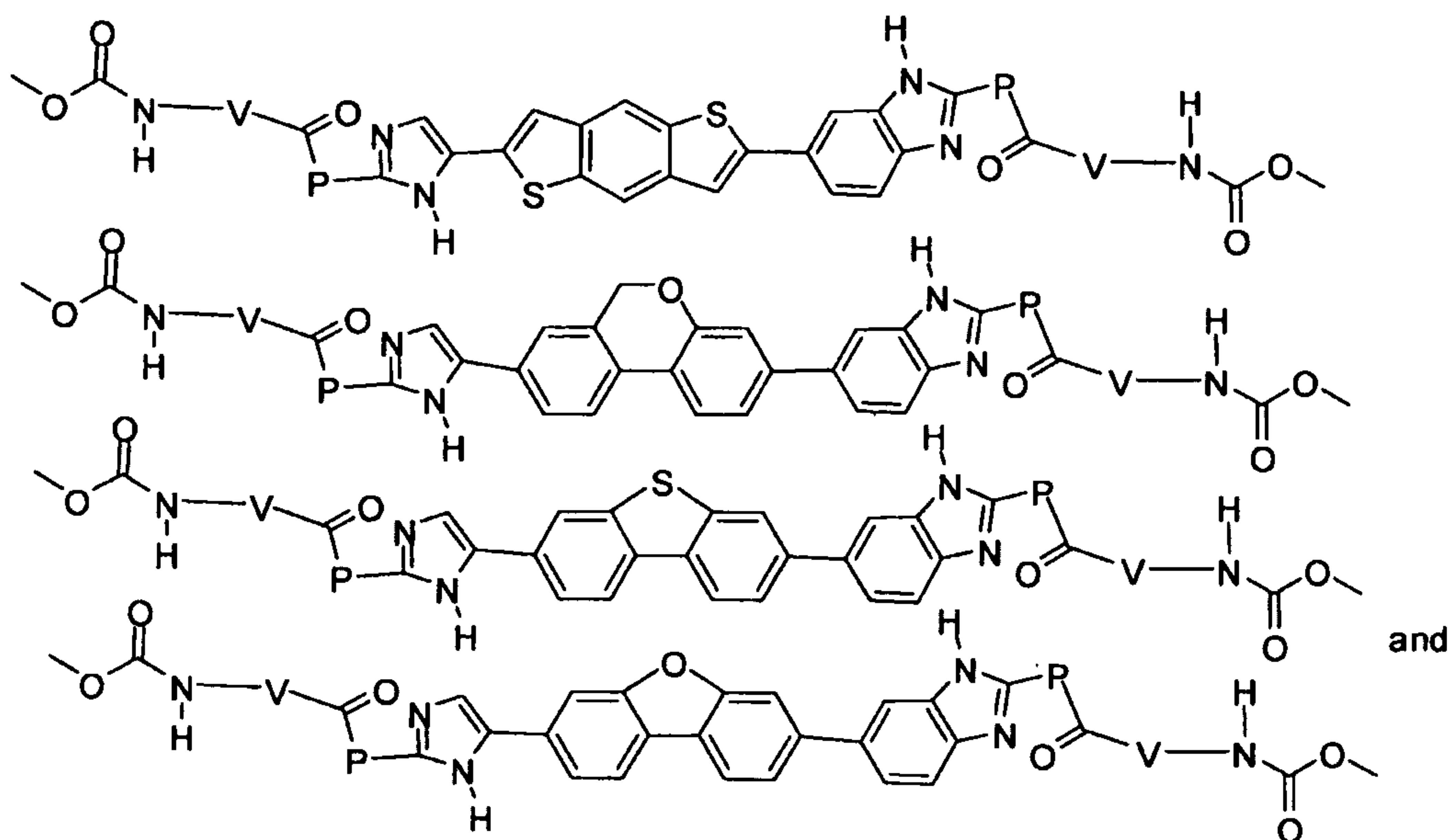
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is:



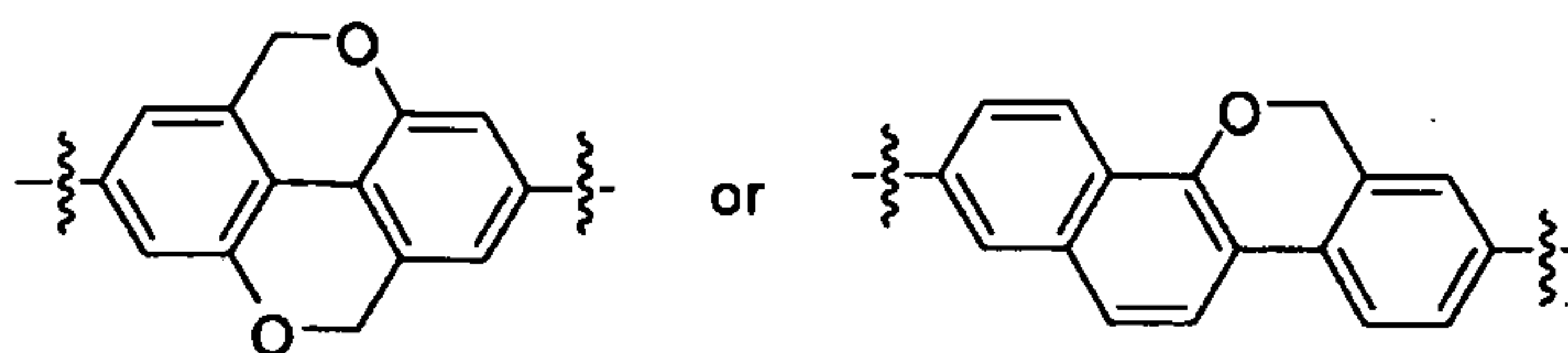
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 8 and W⁸ is:



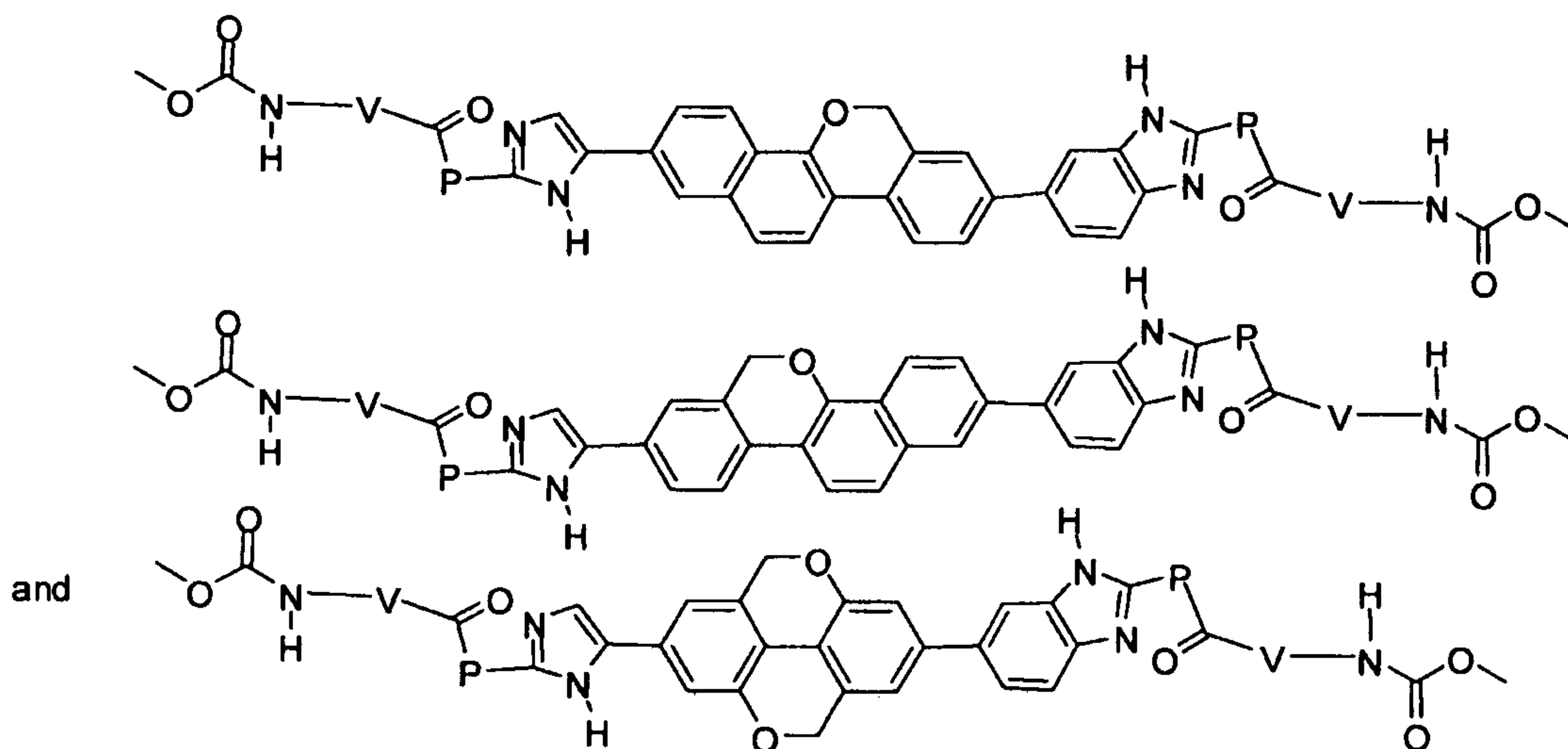
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:



In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 16 and W¹⁶ is:



In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:



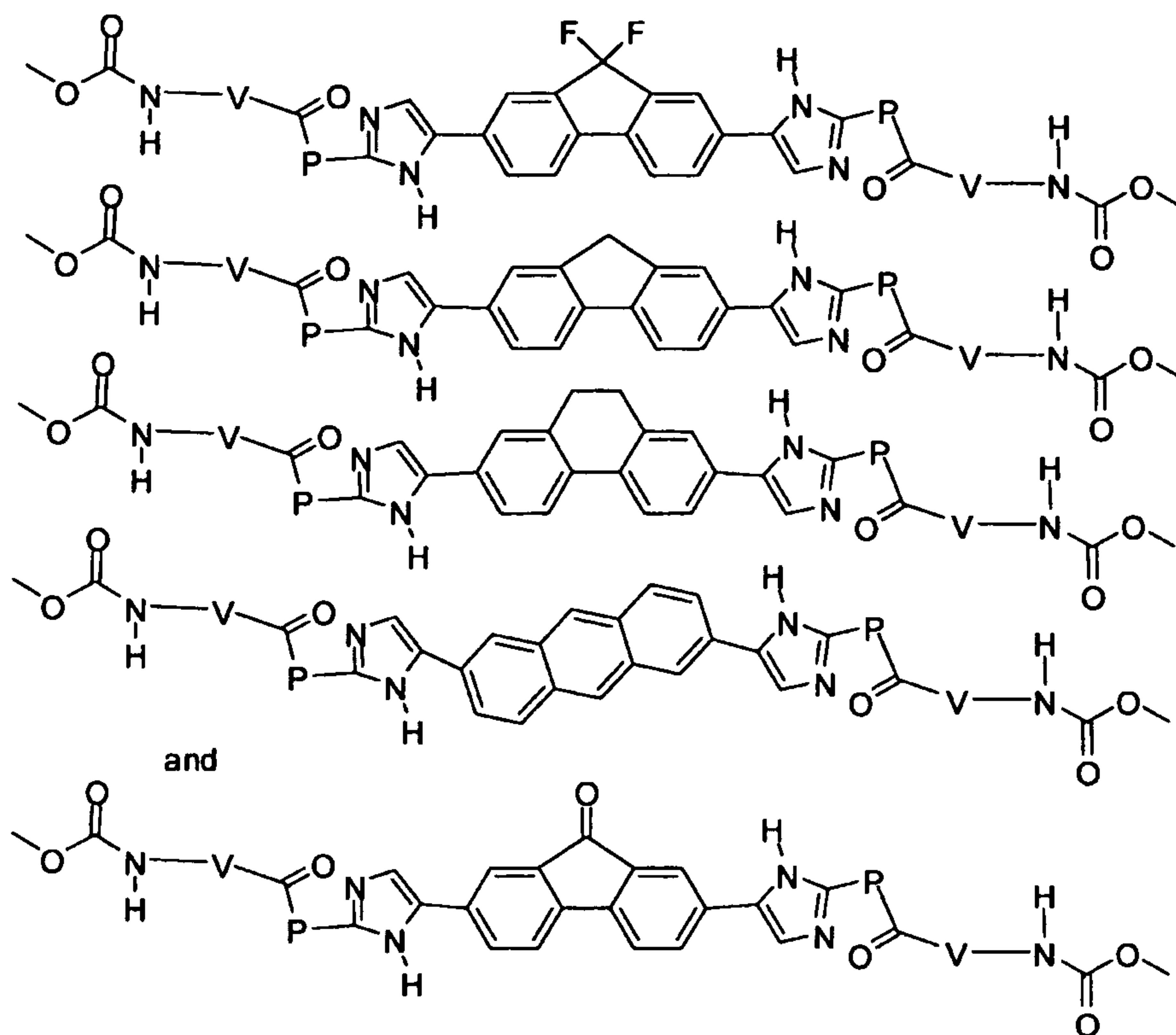
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6, or 8; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 0, 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6, or 8; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 0, 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

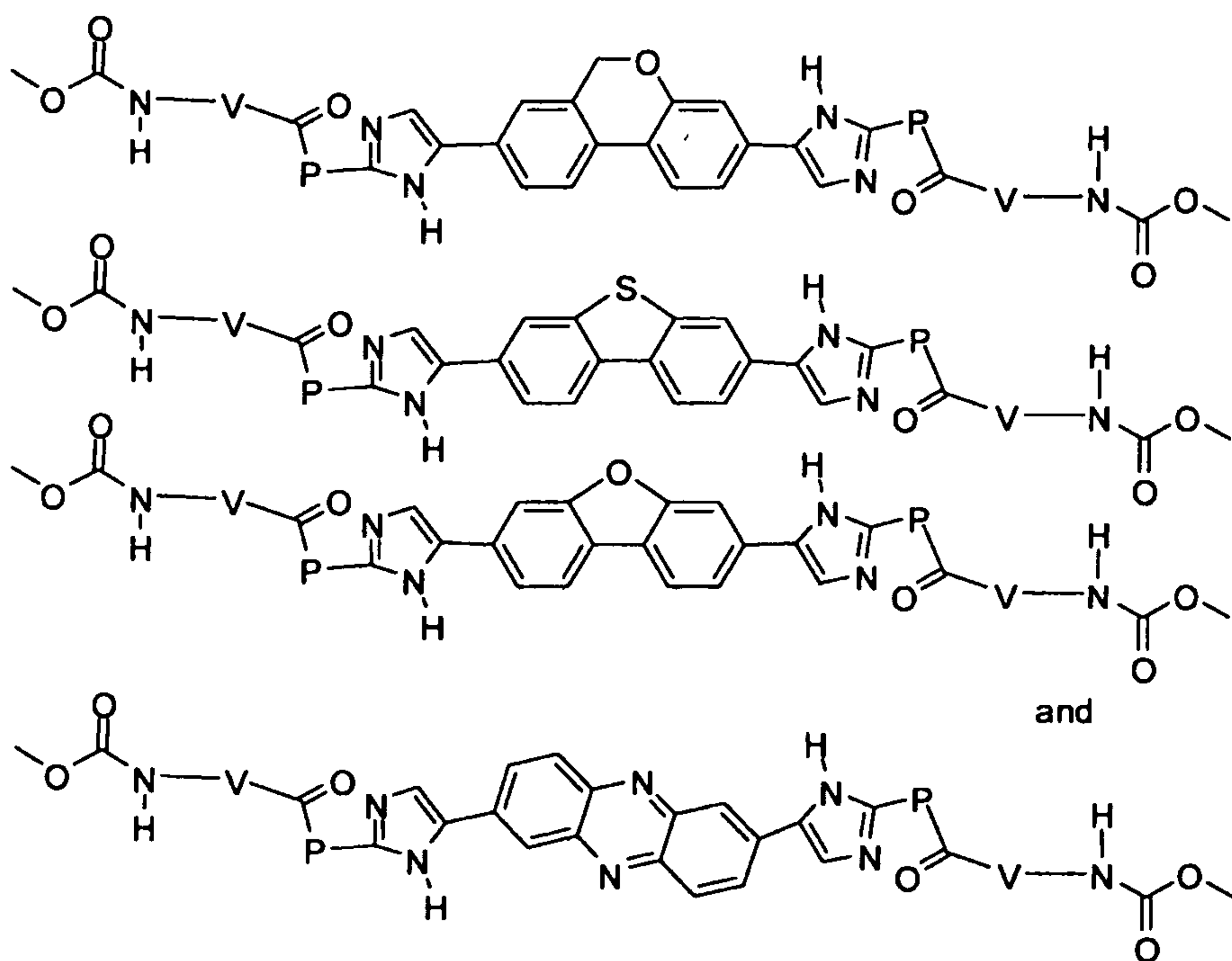
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6, or 8; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6, or 8; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 1, 2, 3, 4, or 5; x is 0; t1 is 9; u1 is 1, 3, 5, 7, 8, 10, or 11; v1 is 0; w1 is 0, 1, 2, 3, 4, or 5; and x1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:

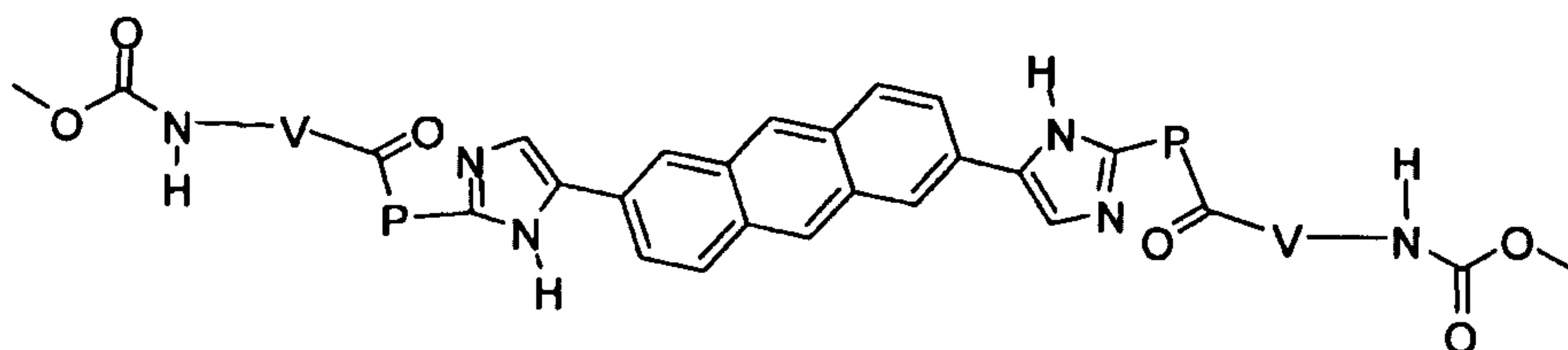


In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:

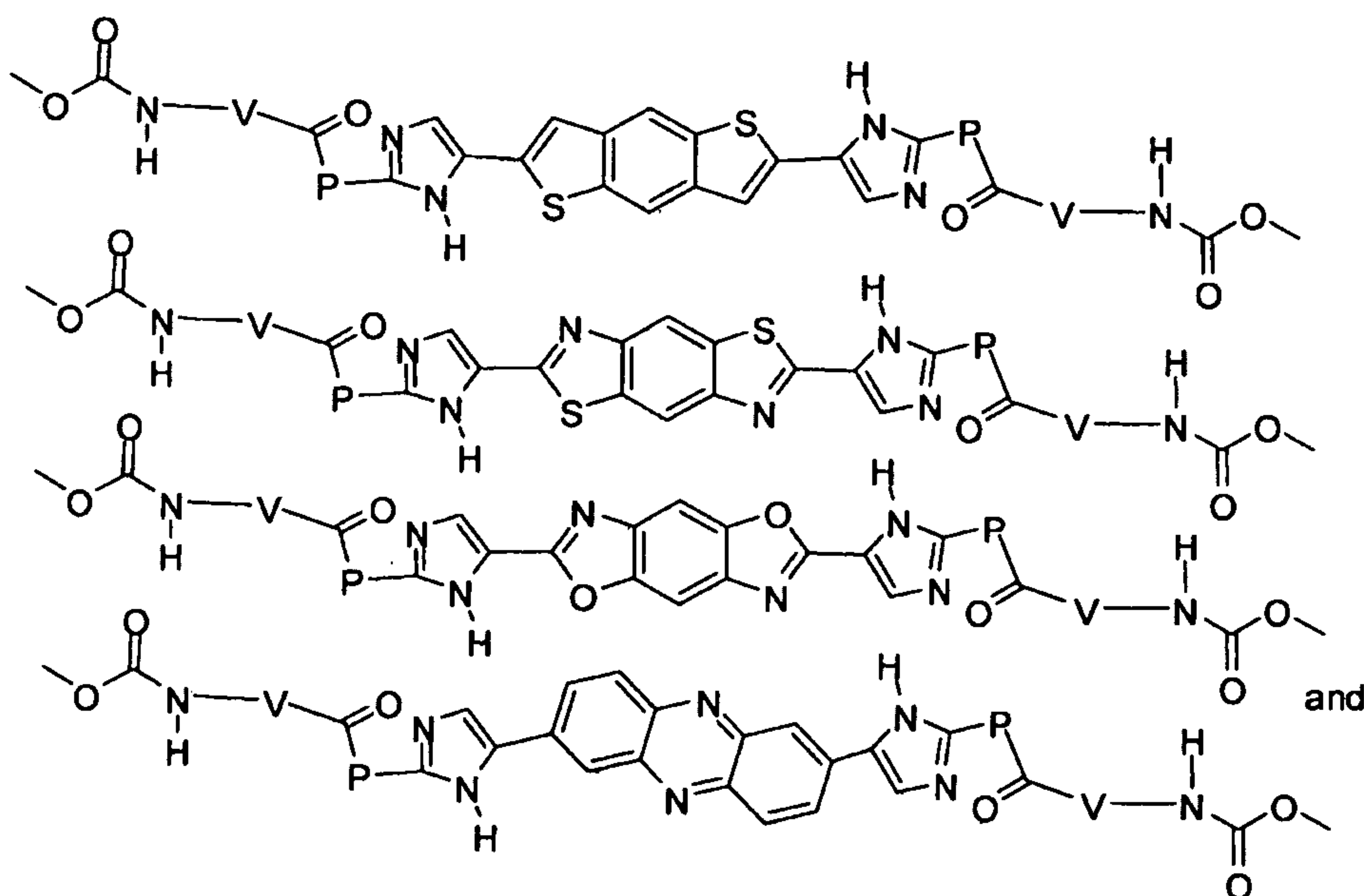


In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 6, or 8; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t_1 is 0 or 10; u_1 is 1, 3, 5, 7, 8, 10, or 11; v_1 is 0; w_1 is 0, 1, 2, 3, 4, or 5; and x_1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which has the formula:

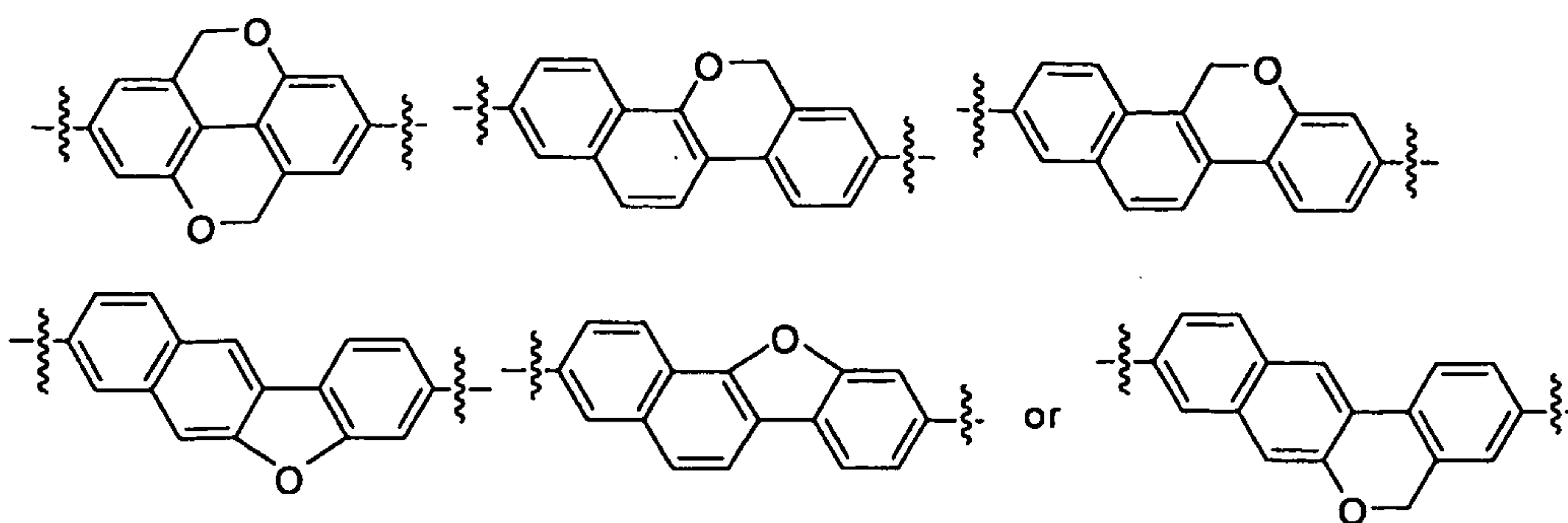


In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:

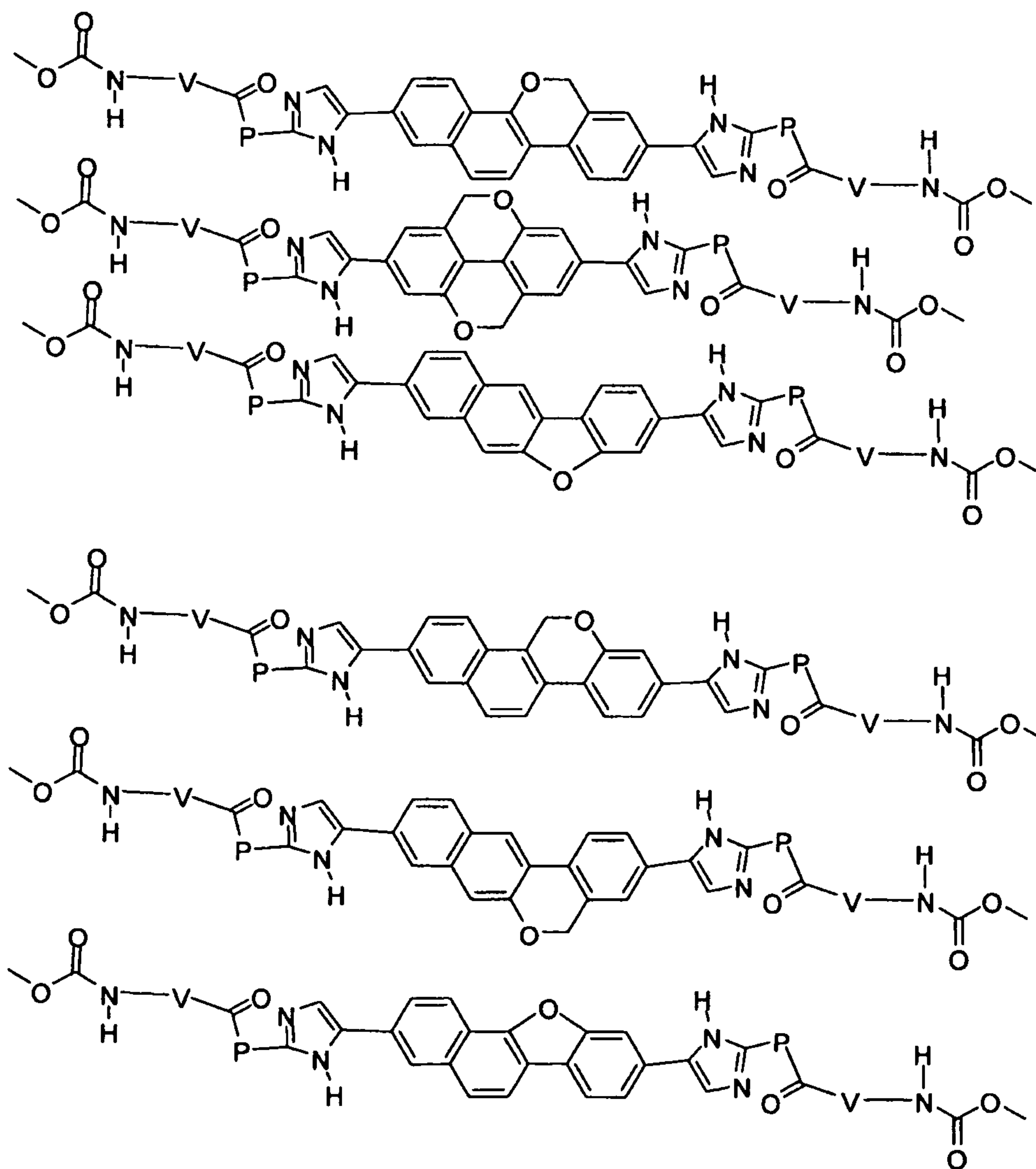


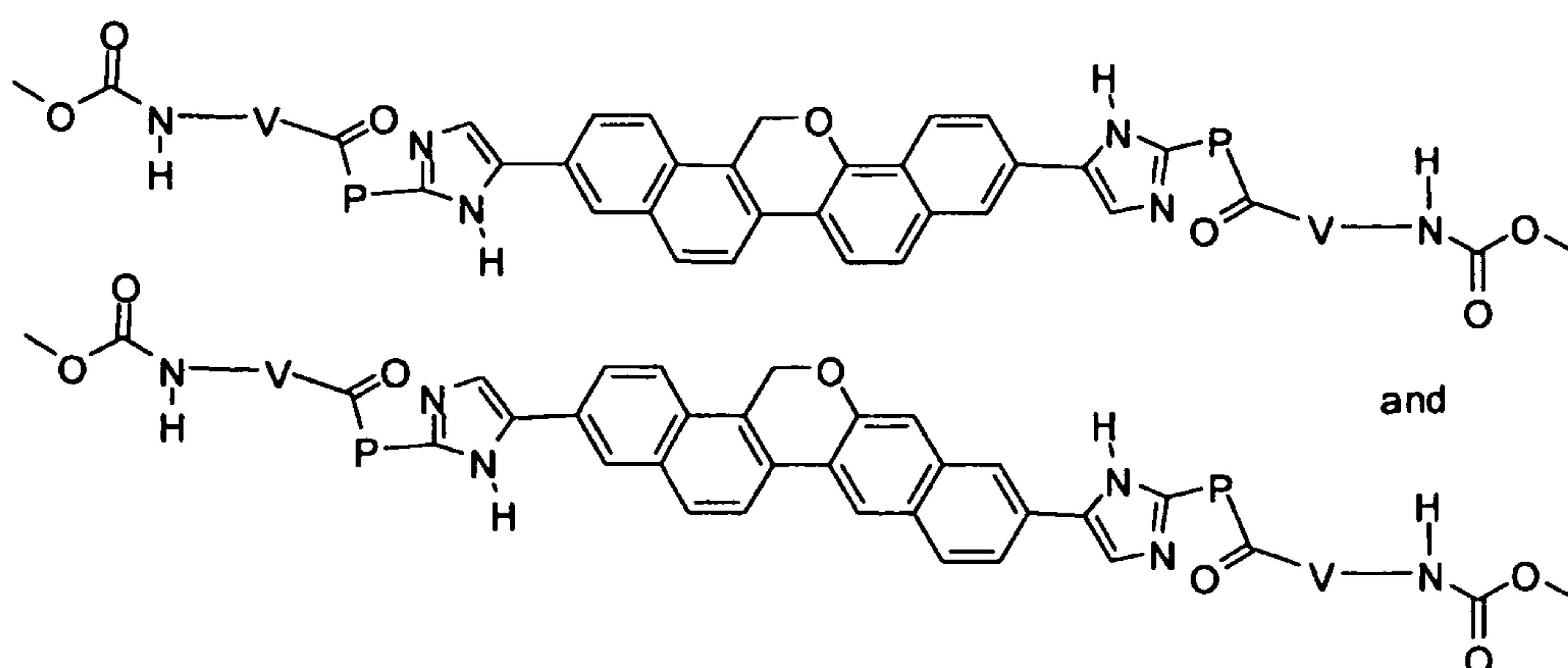
In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein: r is 16 or 18; t is 0 or 10; u is 0, 1, 3, 5, 7, 8, 10, or 11; v is 0; w is 0, 1, 2, 3, 4, or 5; x is 0; t_1 is 0 or 10; u_1 is 0, 1, 3, 5, 7, 8, 10, or 11; v_1 is 0; w_1 is 0, 1, 2, 3, 4, or 5; and x_1 is 0.

In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 16 and W^{16} is:

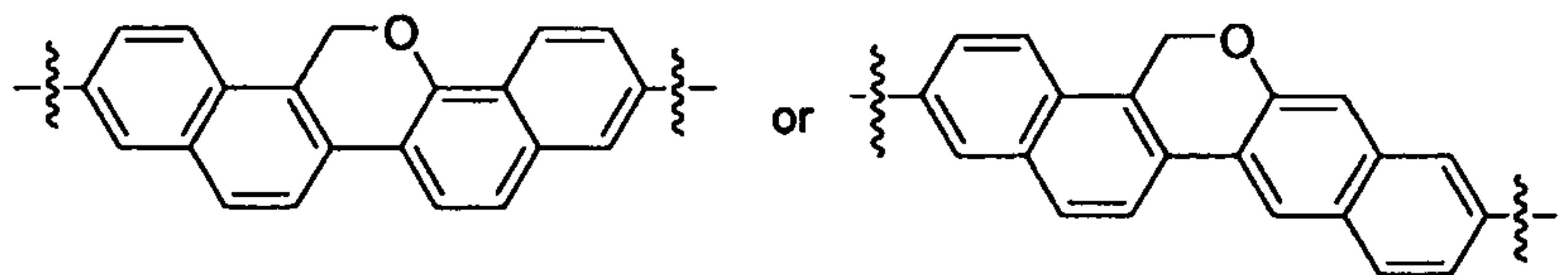


In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) which is selected from:





In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia8) wherein r is 18 and W^{18} is:



In one embodiment of the invention, the compound of formula (Ia) is a compound of formula (Ia17):



wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11;

each w is independently 0, 1, 2, 3, 4, or 5;

t is 0, 9, 10, or 11;

W^1 is a bond;

M^{12} is a fused unsaturated, partially unsaturated or saturated hexacyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ;

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

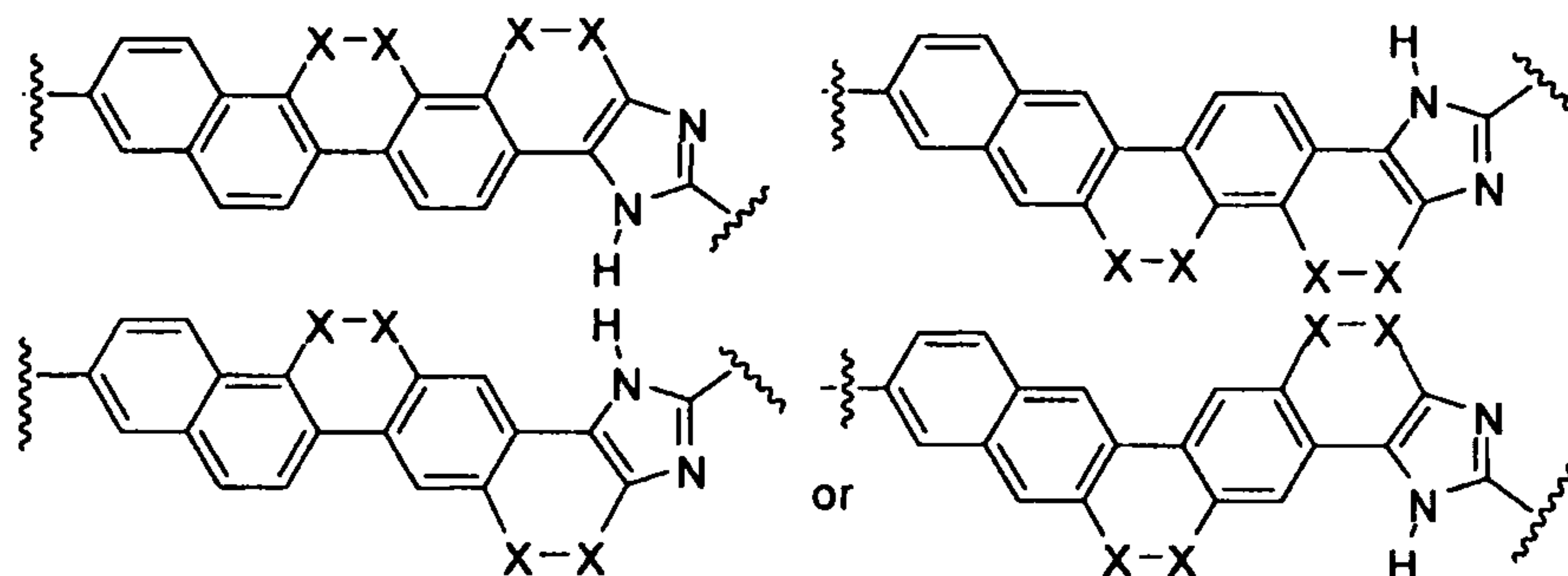
each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, $(NR^aR^b)alkyl$, and $(NR^aR^b)carbonyl$; R^a and R^b are each independently selected from the group

consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

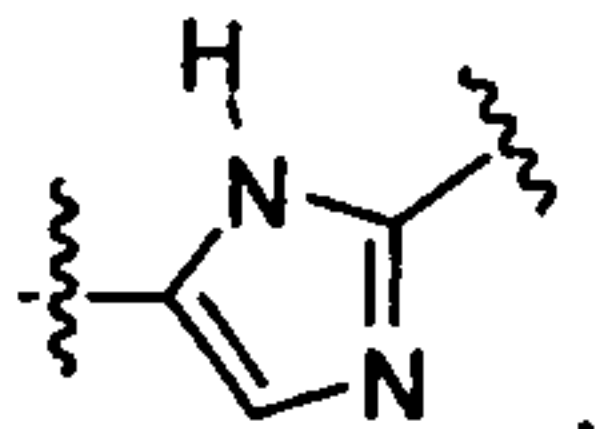
R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl.

In one embodiment the invention provides a compound of formula (Ia17) wherein M^{12} is:

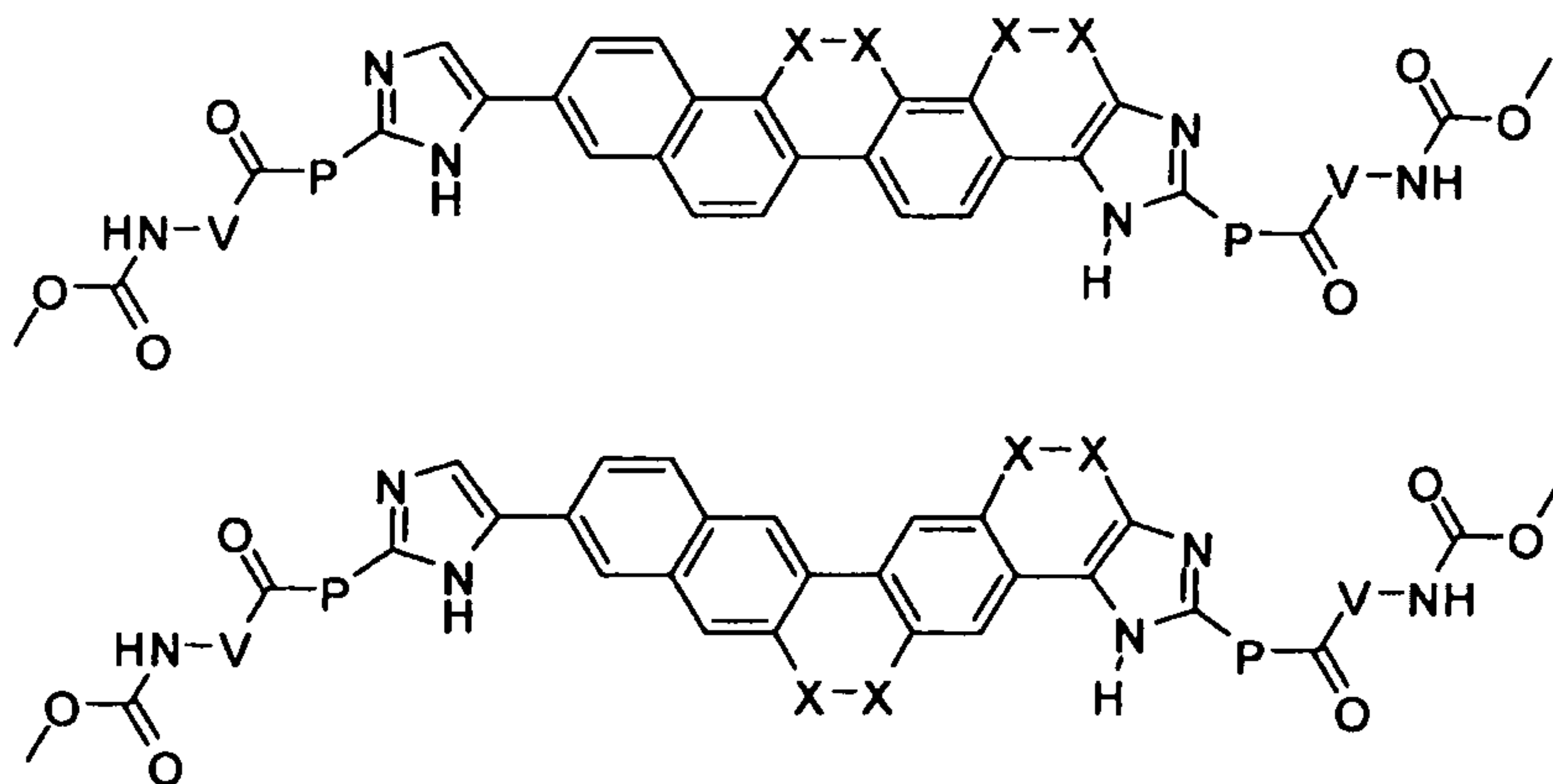


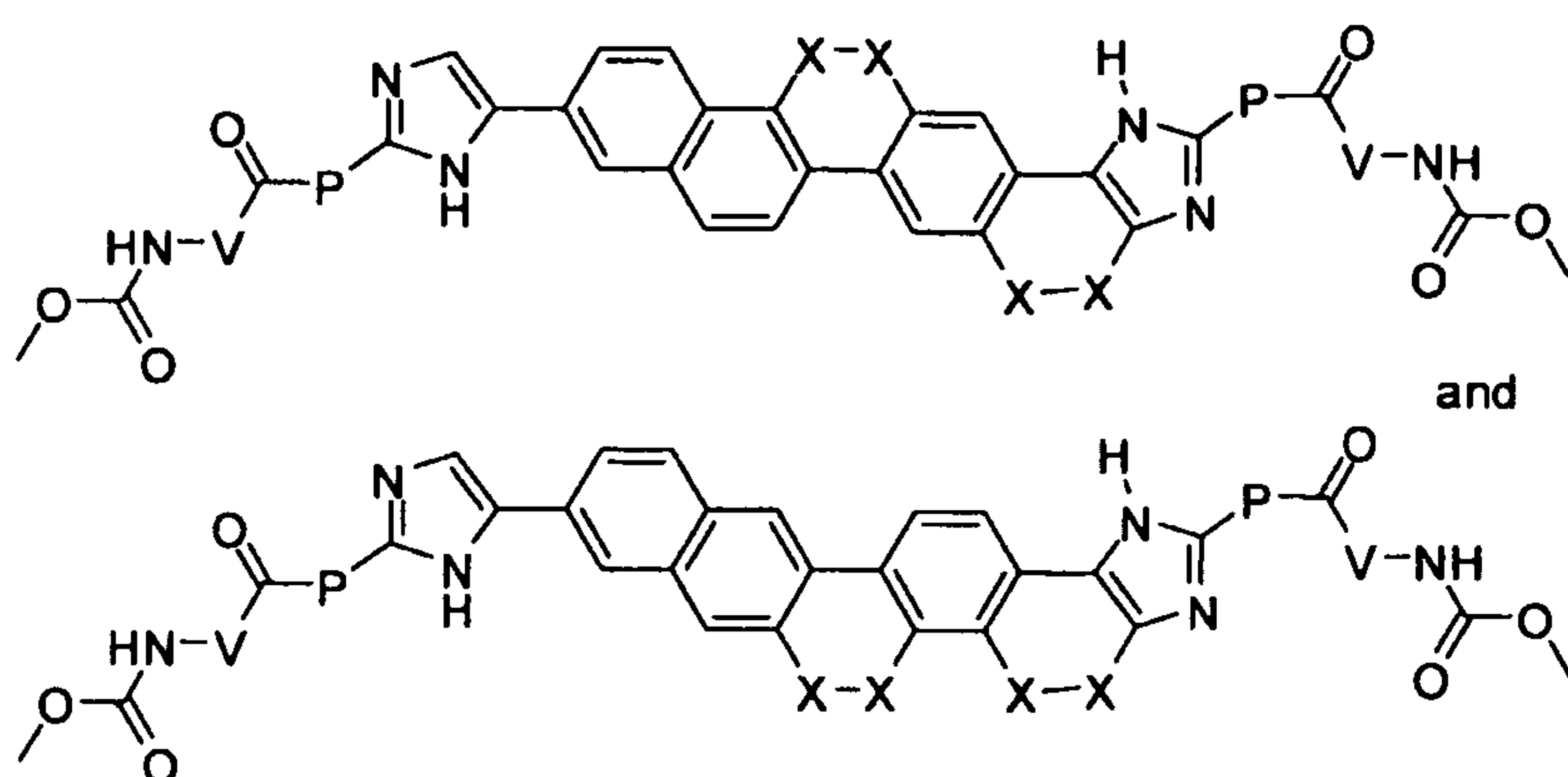
wherein X-X is selected from O, CH_2 , $CH=CH$, CH_2-CH_2 , CH_2-O , $O-CH_2$, $CH_2-CH_2-CH_2$, and CH_2-O-CH_2 .

In one embodiment the invention provides a compound of formula (Ia17) wherein M^0 is:



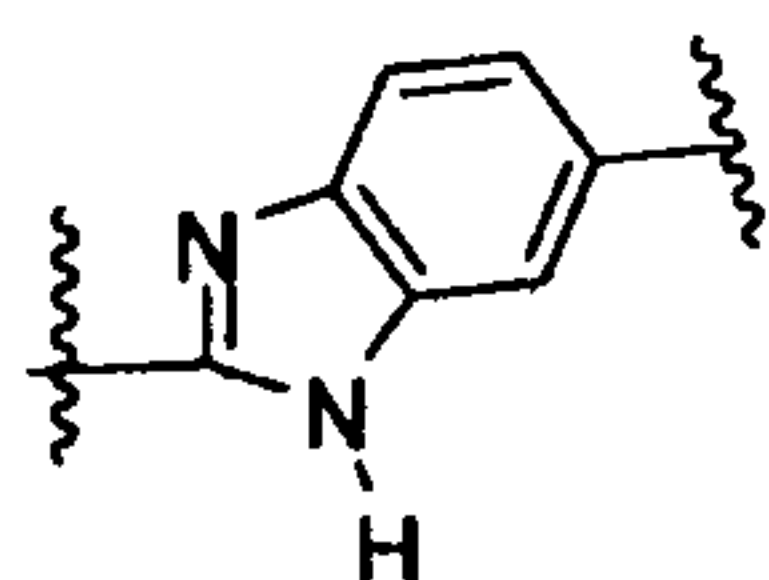
In one embodiment the invention provides a compound of formula (Ia17) which is selected from:



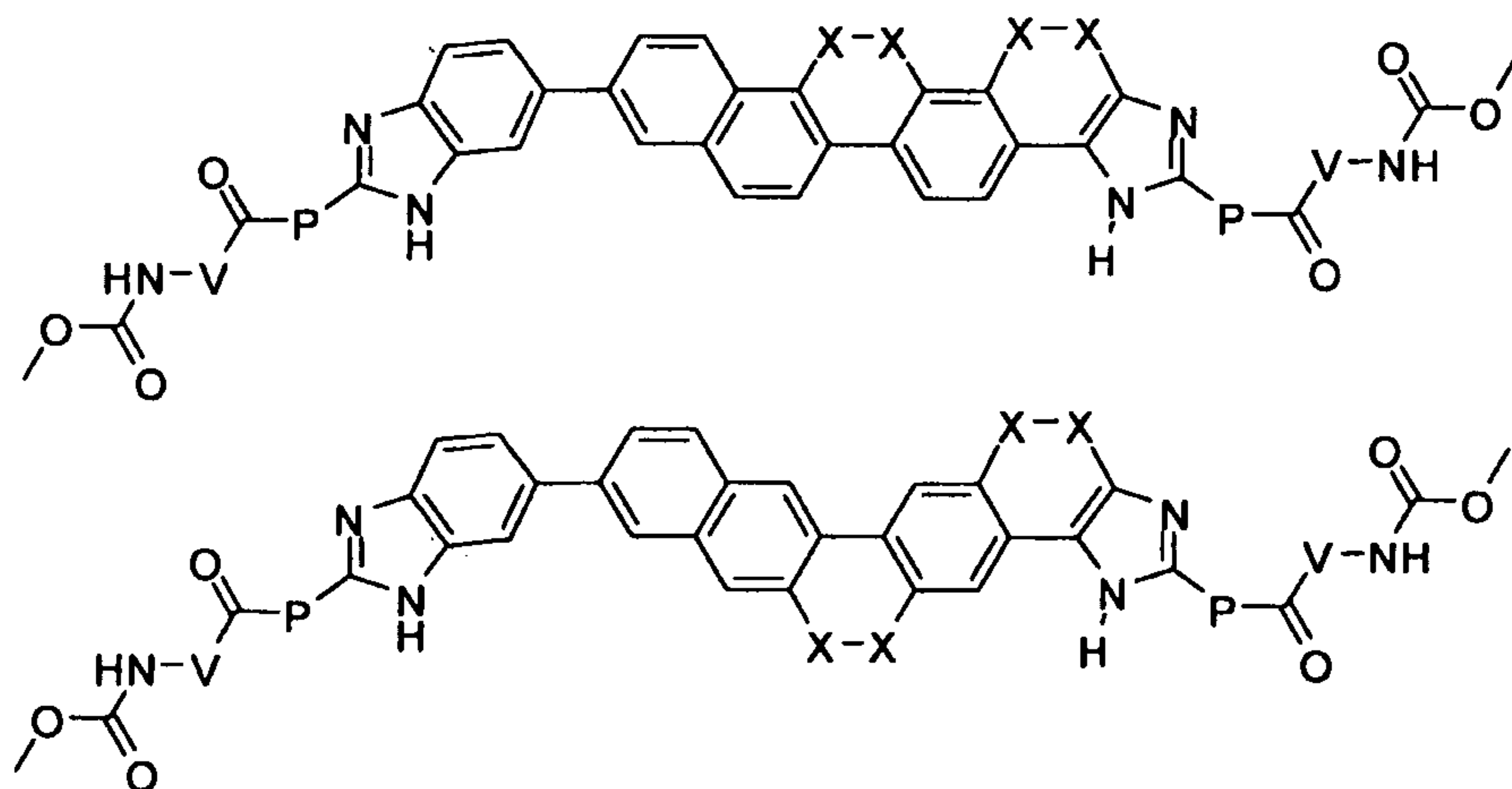


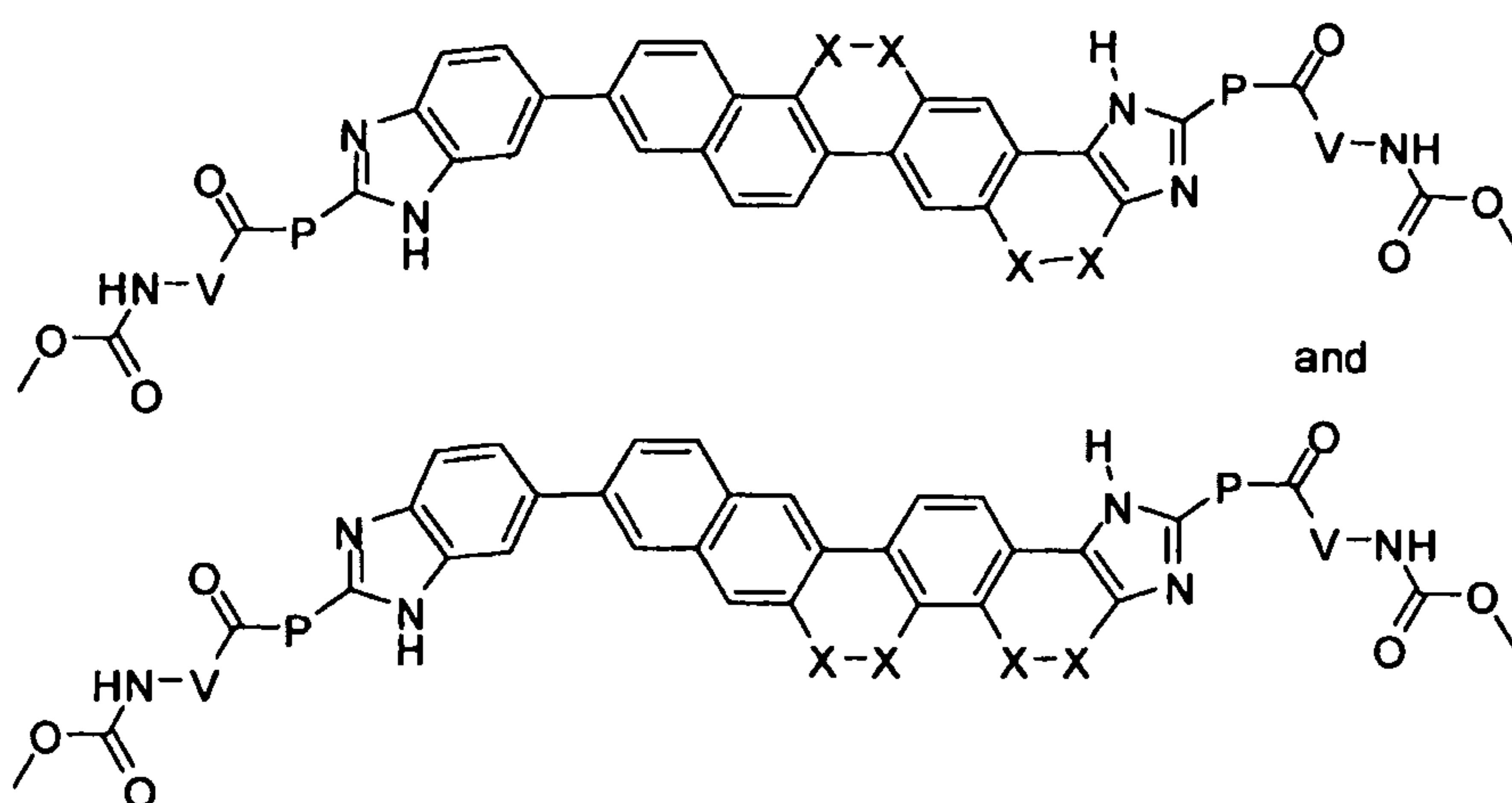
wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ia17) wherein M⁹ is:



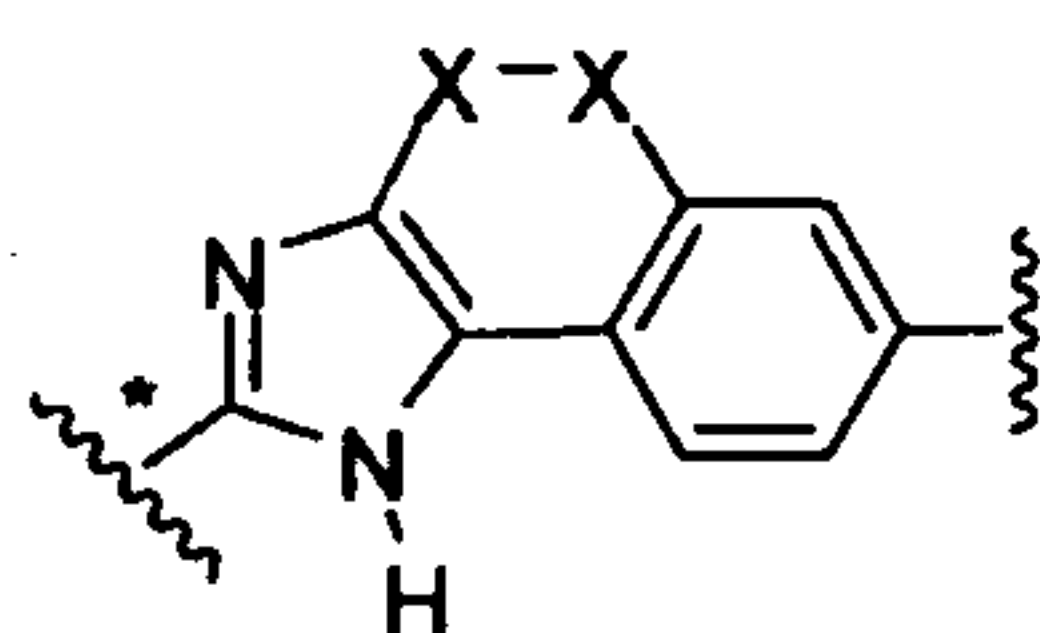
In one embodiment the invention provides a compound of formula (Ia17) which is selected from:





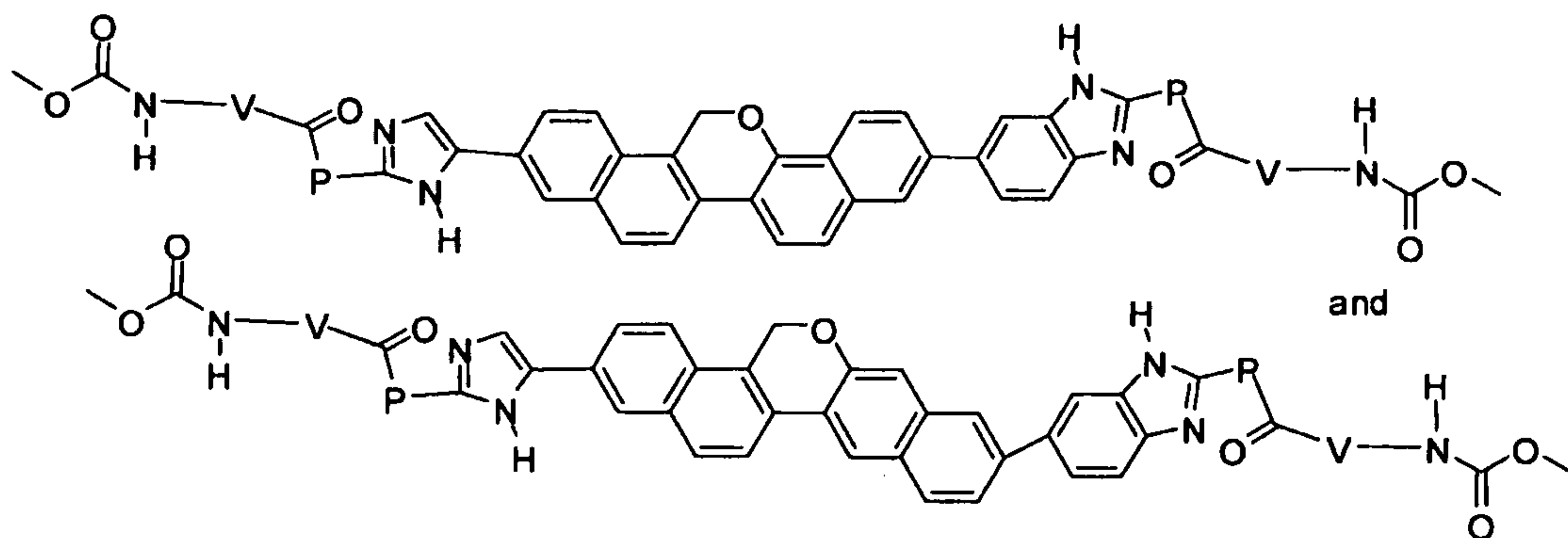
wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ia17) wherein M¹¹ is:

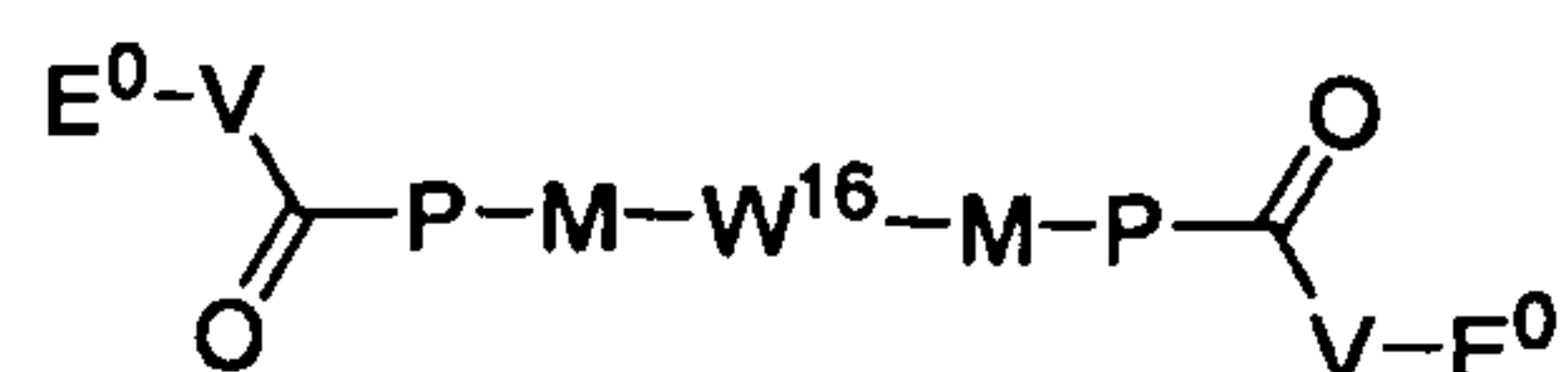


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; and wherein * designates the site of connection to P.

In one embodiment of the invention, the compound of formula (Ia) is selected from:



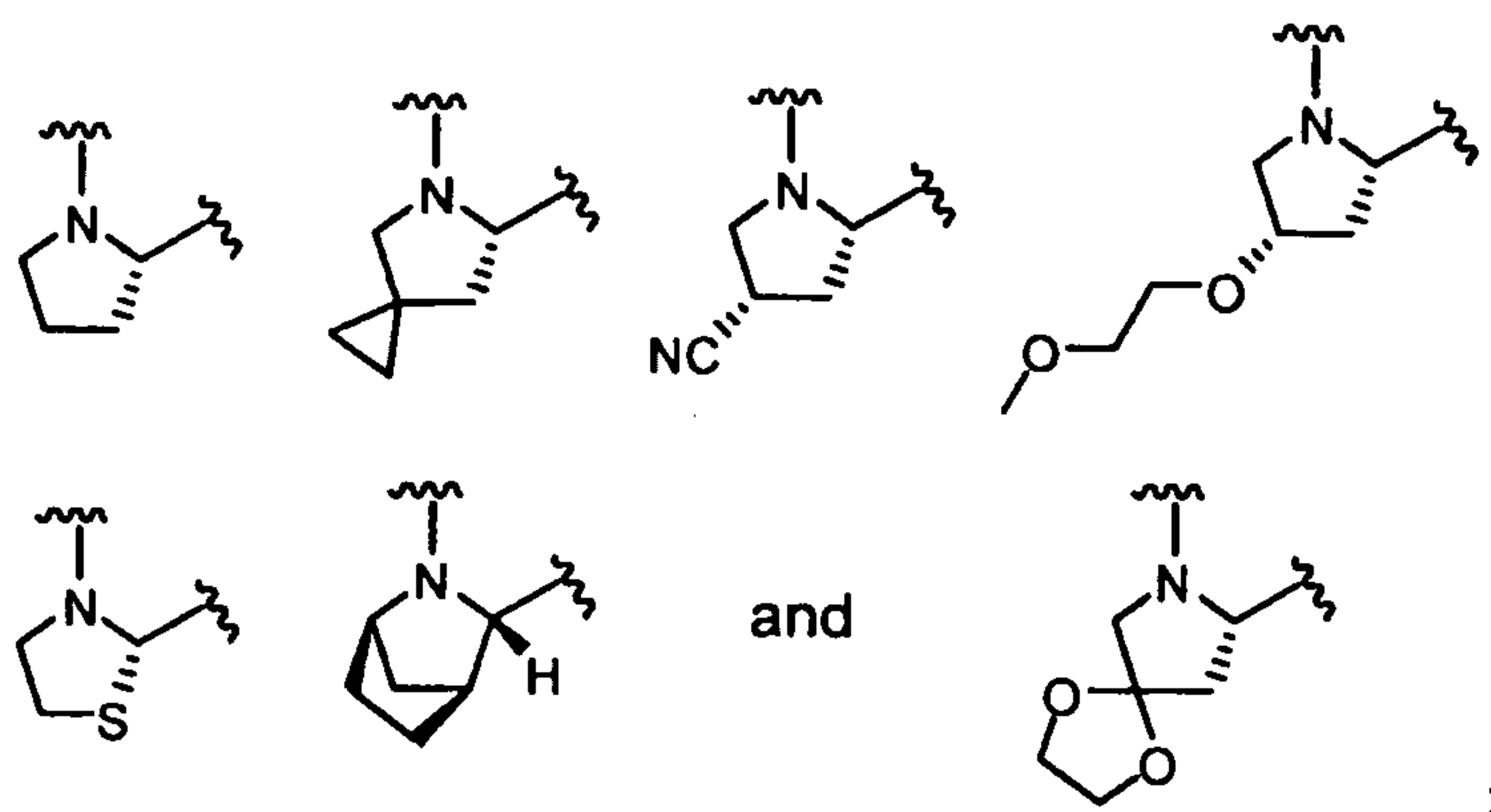
In one embodiment the invention provides a compound of formula (Ia18):



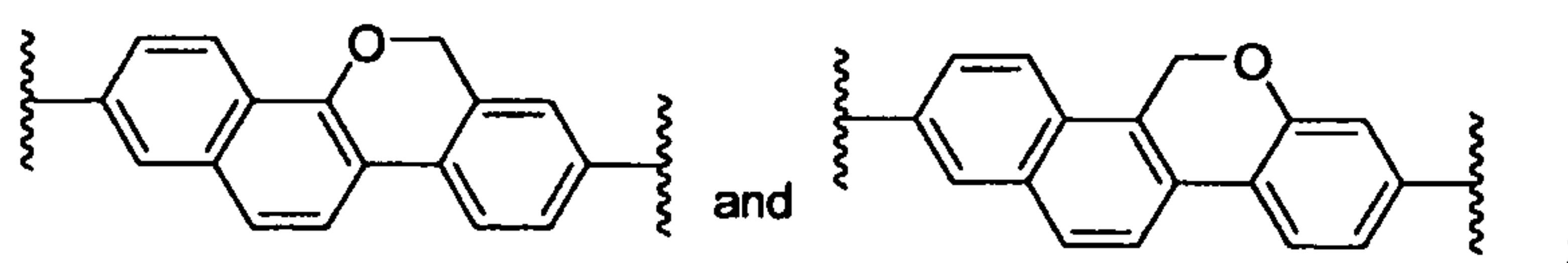
(Ia18)

wherein:

each P is independently selected from:

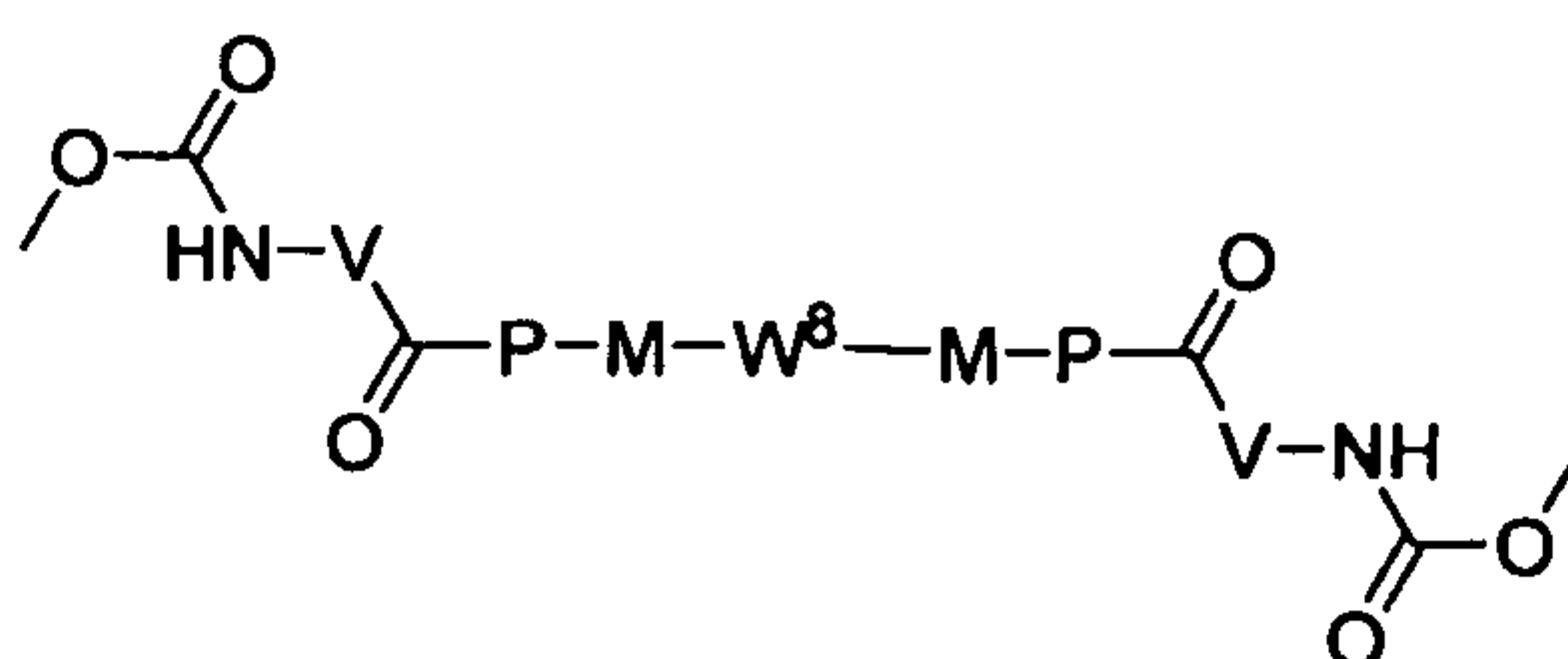


each M is independently M^0 , M^9 , or M^{10} ; and
 W^{16} is selected from:



or a pharmaceutically acceptable salts or prodrug thereof.

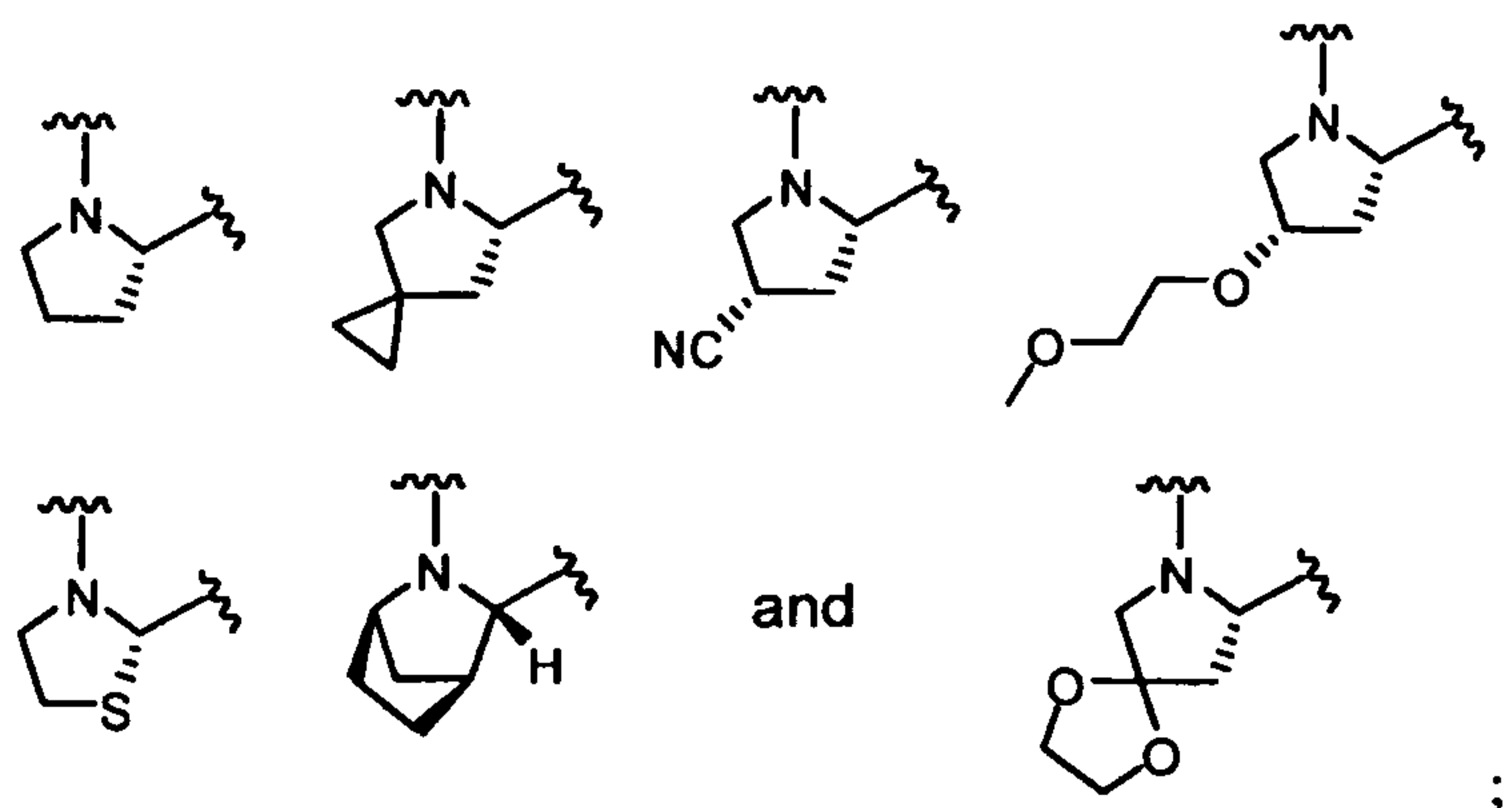
In one embodiment the invention provides a compound of formula (Ia19):



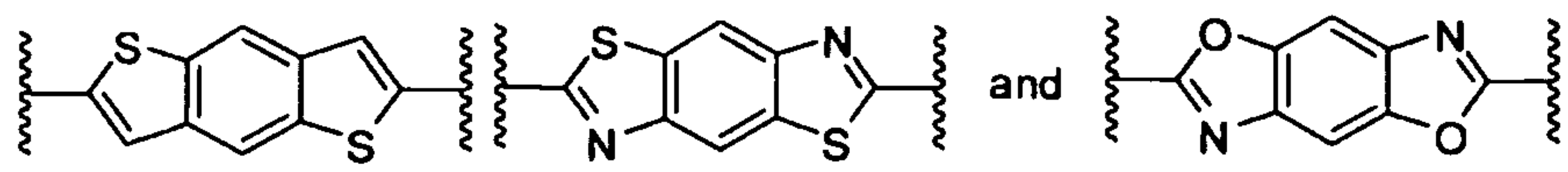
(Ia19)

wherein:

each P is independently selected from:



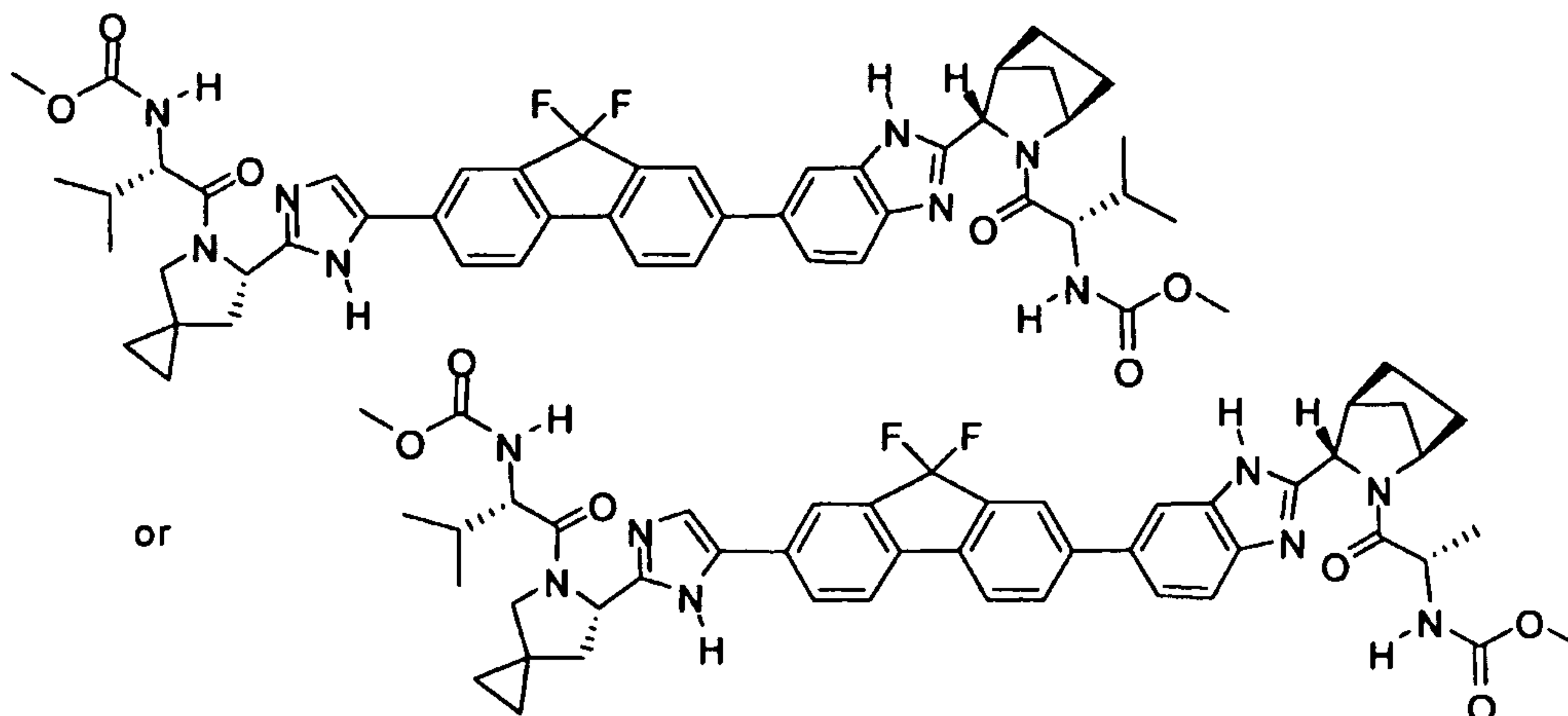
each M is independently M^0 , M^9 , or M^{10} ; and
 W^8 is selected from:



or a pharmaceutically acceptable salts or prodrug thereof.

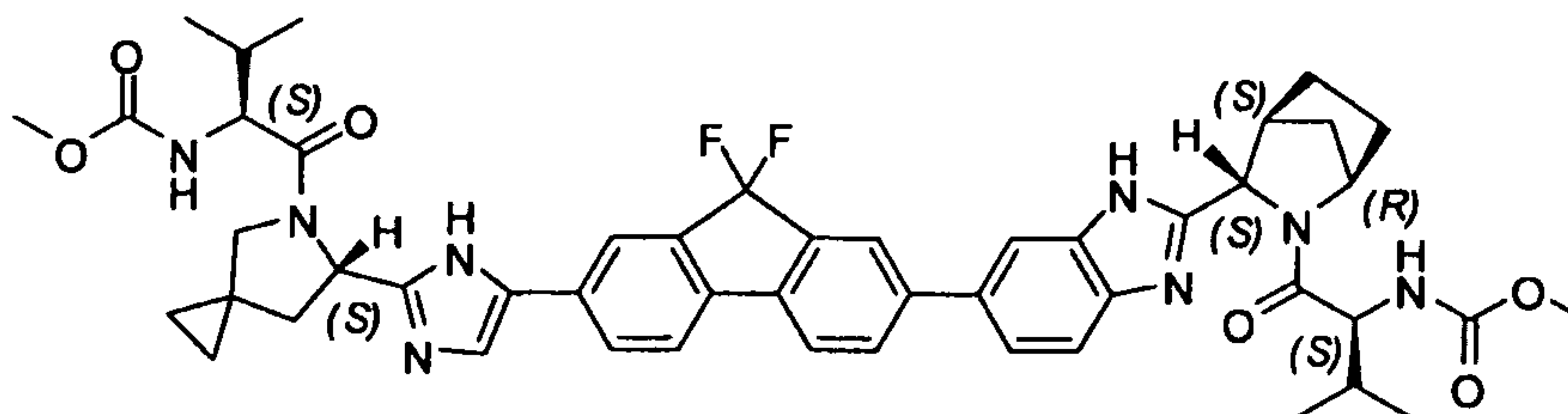
In one embodiment the invention provides a compound of formula (Ia18) or (Ia19) wherein each E^0 is methoxycarbonylamino.

In another specific embodiment of the invention the compound of formula (Ia) is:



or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ia) is:



or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula: $R^9-Z-P-M-W-M-P-Z-R^9$.

In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula: $R^9-Z-P-M^0-W^6-M^9-P-Z-R^9$.

In another specific embodiment of the invention the compound of formula (Ia) is a compound of formula: $R^9-Z-P^0-M^0-W^6-M^9-P^7-Z-R^9$.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of t , u , v , w , and x is not 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r , t , u , v , w , and x are other than 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r , t , u , v , w , and x are other than 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w, and x are other than 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least five of r, t, u, v, w, and x are other than 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, t, u, v, w or x are not zero and at least one t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, and 11.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, t, u, v, w and x are not zero and at least two of the non-zero groups are not the same letter (for example, one w and two u's can be non zero, but just having two u's being non-zero and the remaining r, t, v, w, and x values all zero is not acceptable).

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w or x are not zero and at least four of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of t, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of r, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and at least one t is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r, and at least one t and at least one u are all not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u, w and t are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, u, and w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least r and both u are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u, v, w and x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one of u and or w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u and or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two u are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both t are 9 and r is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 15, 16, 17, 18, 19, or 20.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r is 1, 13, or 14; one t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11; and the other t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, or 11.

In another specific embodiment the invention provides a compound of formula (Ia) wherein one t is 0; the other t is 11; and r is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 17, 18, 19, or 20.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r is 13; one t is 0; and the other t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r is 13; one t is 11; and the other t is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both t are 11; and W is not a bond, or r is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20.

In another specific embodiment the invention provides a compound of formula (Ia) wherein, when W is a bond or W¹ is absent, then one t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 and the other t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

In another specific embodiment the invention provides a compound of formula (Ia) wherein when W is W^r and r is 6 or 8 then at least one t is not 0.

In another specific embodiment the invention provides a compound of formula (Ia) wherein when both t are 0, then r is 1, 2, 3, 4, 5, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one of t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, t, u, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, t, u, w or x are not zero and at least one t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, t, u, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r, t, u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least three of r, t, u, v, w or x are not zero and at least three of the non-zero groups are not in the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least four of r, t, u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of t, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of r, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and at least one t is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein r, and at least one t, and at least one u are all not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u, w and t are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, u, and w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of r, u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least r and both u are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ia) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Ia) wherein both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Ia35): $E^x-V^w-Z^v-P^u-M^9-W^r-M^9-P^u-Z^v-V^w-E^x$ (Ia35) wherein r is 1, 13, or 14.

In another specific embodiment the invention provides a compound of formula (Ia) wherein for a compound of formula (Ia35) at least one of u, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least two of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least three of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least four of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment of the invention for a compound of formula (Ia35) at least three of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia35) at least three of u, v, w or x are not zero and at least three of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia35) at least four of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia35) the sum of u, v, w and x is not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least one of u, or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least two of u, or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least one u is not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) both u are not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least one u is not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) both of u are not zero.

In another specific embodiment of the invention for a compound of formula (Ia35) at least one of w is not zero.

I In another specific embodiment of the invention for a compound of formula (Ia35) both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Ia36): $E^x-V^w-Z^y-P^u-M^0-W^{13}-M^{11}-P^u-Z^y-V^w-E^x$ (Ia36).

In another specific embodiment of the invention for a compound of formula (Ia36) at least one of u, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least two of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least three of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least four of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment of the invention for a compound of formula (Ia36) at least three of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia36) at least three of u, v, w or x are not zero and at least three of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia36) at least four of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia36) the sum of u, v, w and x is not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least one of u or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least two of u or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least one u is not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) both u are not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least one u is not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) both of u are not zero.

In another specific embodiment of the invention for a compound of formula (Ia36) at least one of w is not zero.

I In another specific embodiment of the invention for a compound of formula (Ia36) both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Ia37): $E^x-V^w-Z^v-P^u-M^{11}-M^{11}-P^u-Z^v-V^w-E^x$ (Ia37).

In another specific embodiment of the invention for a compound of formula (Ia37) at least one of u, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least two of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least three of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least four of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment of the invention for a compound of formula (Ia37) at least three of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia37) at least three of u, v, w or x are not zero and at least three of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia37) at least four of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia37) the sum of u, v, w and x is not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least one of u, or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least two of u, or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least one u is not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) both u are not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least one u is not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) both of u are not zero.

In another specific embodiment of the invention for a compound of formula (Ia37) at least one of w is not zero.

I In another specific embodiment of the invention for a compound of formula (Ia37) both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Ia38): $E^x-V^w-Z^v-P^u-M^0-W^r-M^0-P^u-Z^v-V^w-E^x$ (Ia38) wherein r is 6 or 8.

In another specific embodiment of the invention for a compound of formula (Ia38) at least one of u, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least two of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least three of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least four of u, v, w or x are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment of the invention for a compound of formula (Ia38) at least three of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia38) at least three of u, v, w or x are not zero and at least three of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia38) at least four of u, v, w or x are not zero and at least two of the non-zero groups are not in the same letter.

In another specific embodiment of the invention for a compound of formula (Ia38) the sum of u, v, w and x is not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least one of u, or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least two of u or w are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least one u is not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) both u are not zero, and at least one w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least one u is not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) both of u are not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) at least one of w is not zero.

In another specific embodiment of the invention for a compound of formula (Ia38) both w are not zero.

Compounds of formula (Ib)

In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib):



wherein:

L is $-L^n$;

each A is selected from $-A^s$;

each M is selected from $-M^t$;

each P is selected from $-P^u$;

each Z is selected from $-Z^v$;

each V is selected from $-V^w$;

each E is selected from $-E^x$;

each n is 0, 1, 2, 3, 4, 5, 6, 7, 9, or 10;

each s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 21;

each t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11;

each u is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, or 14;

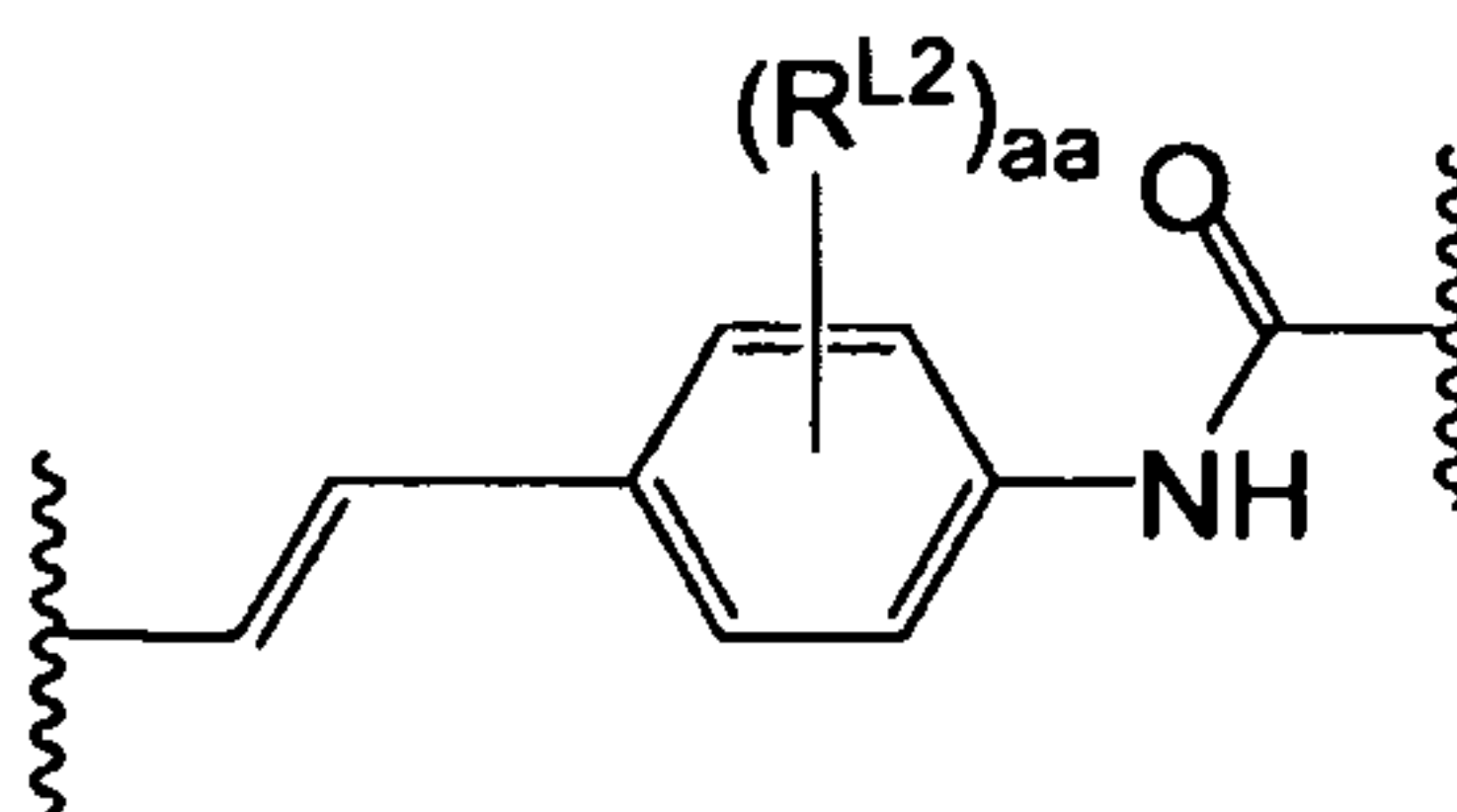
each v is 0, 1, 2, 3, 4, 5, or 6;

each w is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21;

each x is 0 or 1 ;

wherein the sum of n, s, t, u, v, w, and x is not 0;

each L^0 is independently:

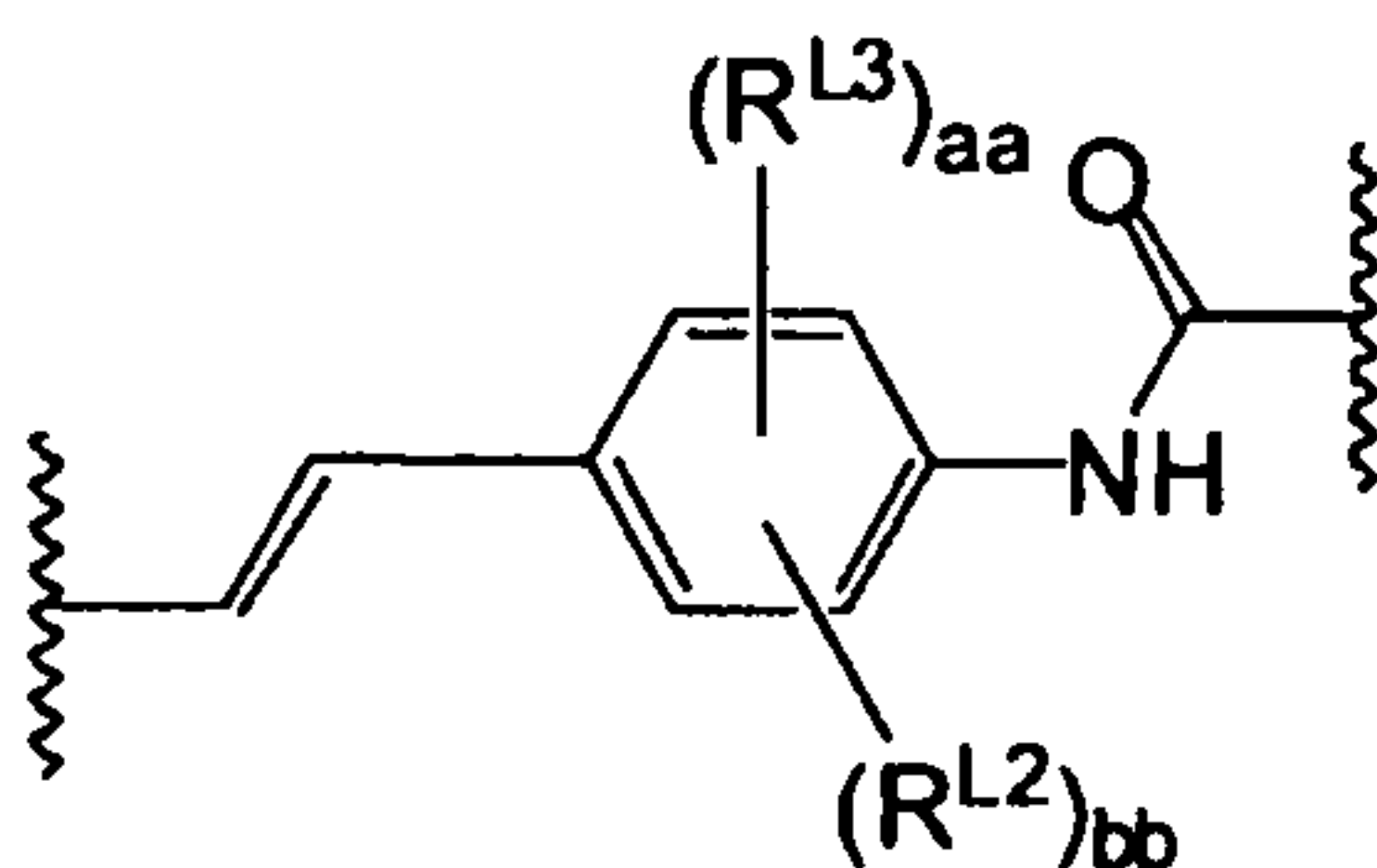


wherein:

each R^{L2} is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl; and

each aa is independently 1, 2, 3, or 4;

each L¹ is independently:



wherein:

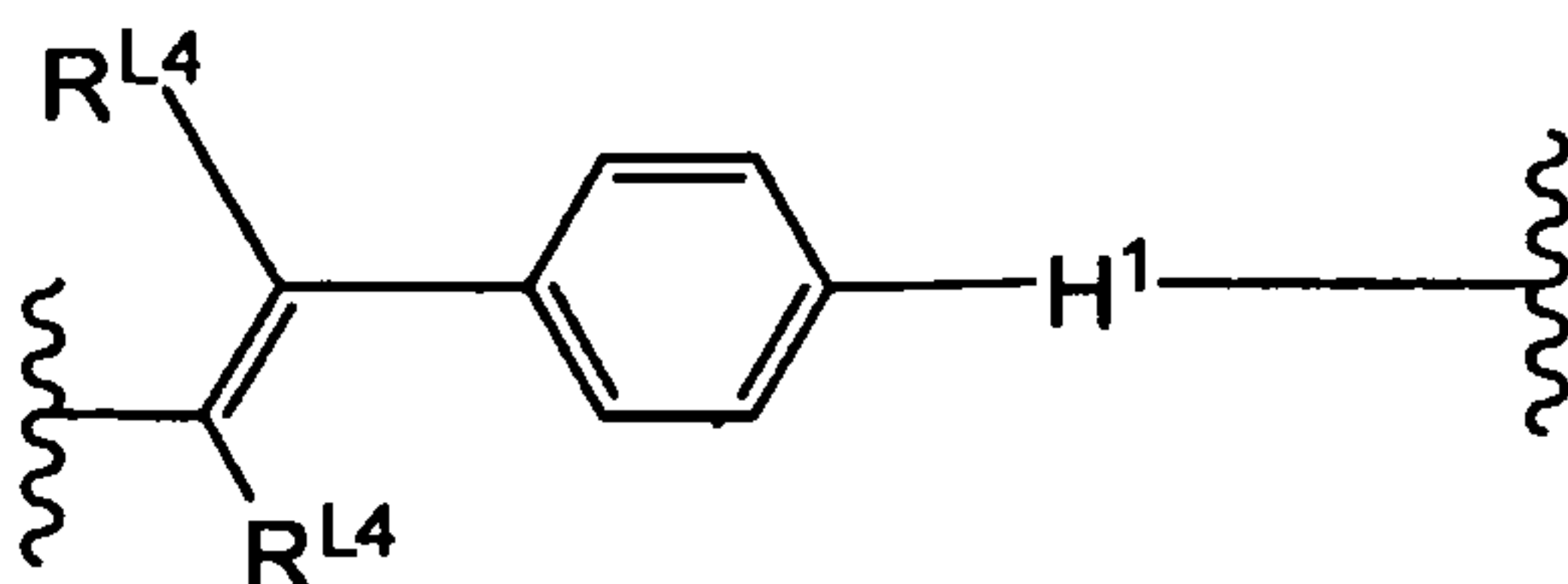
each R^{L2} is independently selected from hydrogen, alkenyl, alkoxy, alkyl, halo, and haloalkyl;

each R^{L3} is independently selected from cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each bb is 0, 1, 2, 3, or 4; each aa is 1, 2, 3, or 4; and the sum of bb and aa is 1, 2, 3, or 4;

each L² is independently:



wherein:

the phenyl ring shown in L² is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{L4} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl; and

each H¹ is a 5 membered saturated, partially unsaturated, or aromatic ring comprising one or more heteroatoms;

each L³ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁴ is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁵ is independently a -CR=CR-fused bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy,

formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

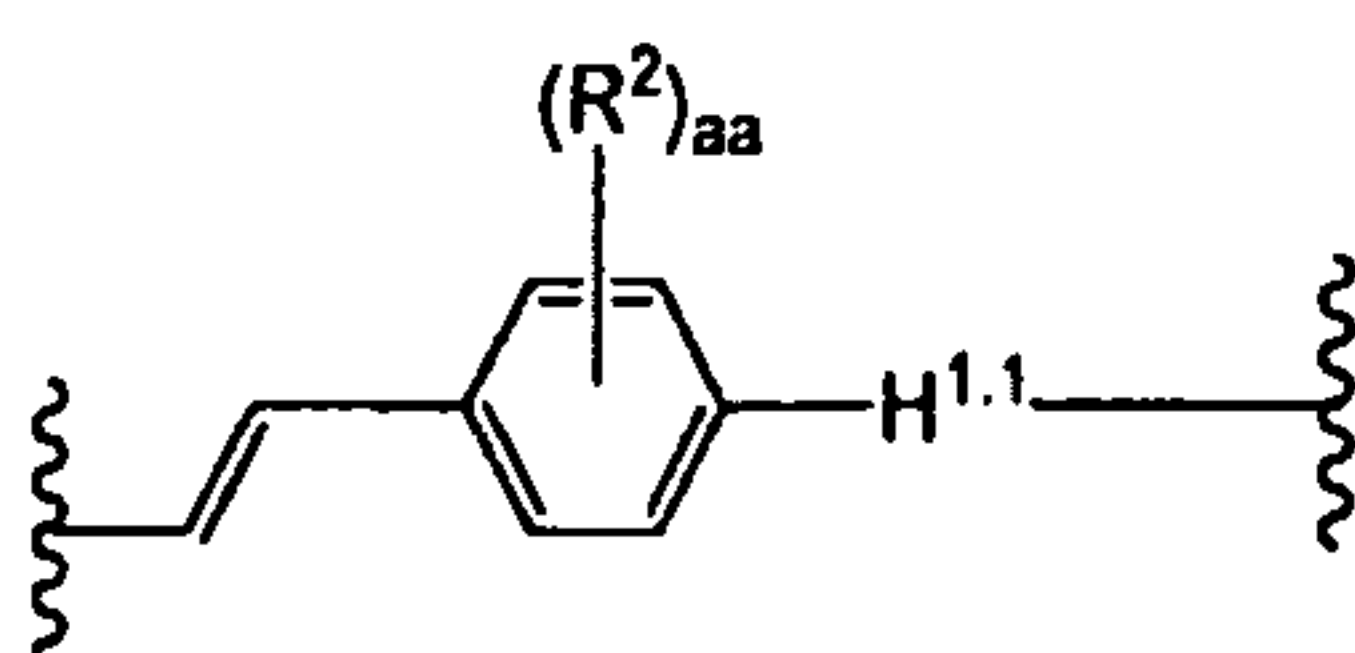
R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^6 is independently a $-CR=CR-$ fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, (NR^aR^b) carbonyl, cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L^7 is independently:



wherein:

each $H^{1.1}$ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^2 ;

each R^2 is independently selected from halo, $-R^{L7}$, $-OR^{L7}$, $-SR^{L7}$, $-N(R^{L7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{L7})C(=O)R^{L7}$, $-C(=O)R^{L7}$, $-OC(=O)R^{L7}$, $-C(O)OR^{L7}$, $-C(=O)NR^{L7}$, $-S(=O)R^{L7}$, $-S(=O)_2OR^{L7}$, $-S(=O)_2R^{L7}$, $-OS(=O)_2OR^{L7}$, and $-S(=O)_2NR^{L7}$;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle; and
 each aa is independently 1, 2, 3, or 4;

each L⁹ is independently a fused-tetracyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, -R^{L7}, -OR^{L7}, -SR^{L7}, -CF₃, -CCl₃, -OCF₃, -CN, -NO₂, -N(R^{L7})C(=O)R^{L7}, -C(=O)R^{L7}, -OC(=O)R^{L7}, -C(O)OR^{L7}, -C(=O)NR^{L7}, -S(=O)R^{L7}, -S(=O)₂OR^{L7}, -S(=O)₂R^{L7}, -OS(=O)₂OR^{L7}, -S(=O)₂NR^{L7}, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L¹⁰ is independently a fused-pentacyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, -R^{L7}, -OR^{L7}, -SR^{L7}, -CF₃, -CCl₃, -OCF₃, -CN, -NO₂, -N(R^{L7})C(=O)R^{L7}, -C(=O)R^{L7}, -OC(=O)R^{L7}, -C(O)OR^{L7}, -C(=O)NR^{L7}, -S(=O)R^{L7}, -S(=O)₂OR^{L7}, -S(=O)₂R^{L7}, -OS(=O)₂OR^{L7}, -S(=O)₂NR^{L7}, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

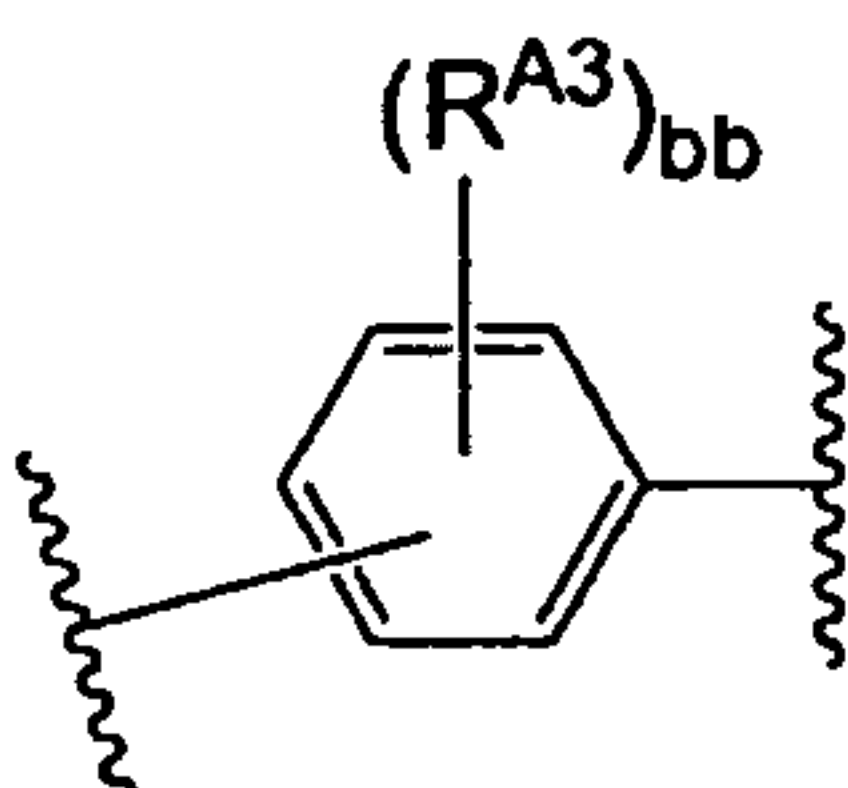
R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L¹¹ is independently a six-ring fused saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, -R^{L7}, -OR^{L7}, -SR^{L7}, -CF₃, -CCl₃, -OCF₃, -CN, -NO₂, -N(R^{L7})C(=O)R^{L7}, -C(=O)R^{L7}, -OC(=O)R^{L7}, -C(O)OR^{L7}, -C(=O)NR^{L7}, -S(=O)R^{L7}, -S(=O)₂OR^{L7}, -S(=O)₂R^{L7}, -OS(=O)₂OR^{L7}, -S(=O)₂NR^{L7}, alkoxyalkyl, arylalkoxycarbonyl, halo, haloalkyl, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each A^0 is independently:



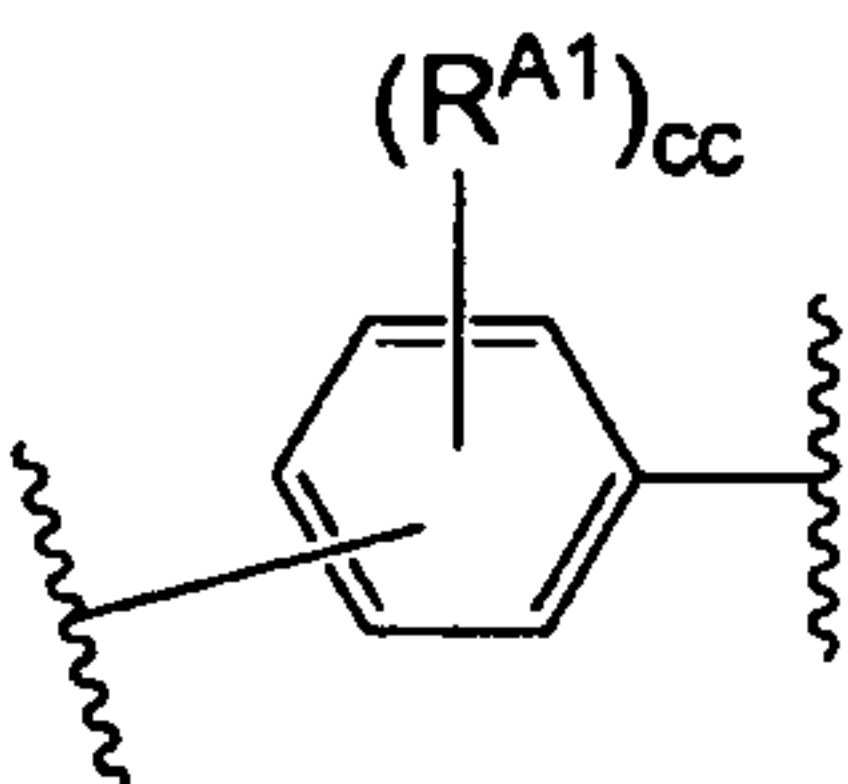
wherein:

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl; and each

bb is independently 0, 1, 2, 3, or 4; or

each A^0 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is optionally substituted with 1, 2, 3, or 4 R^{A3} groups;

each A^1 is independently:



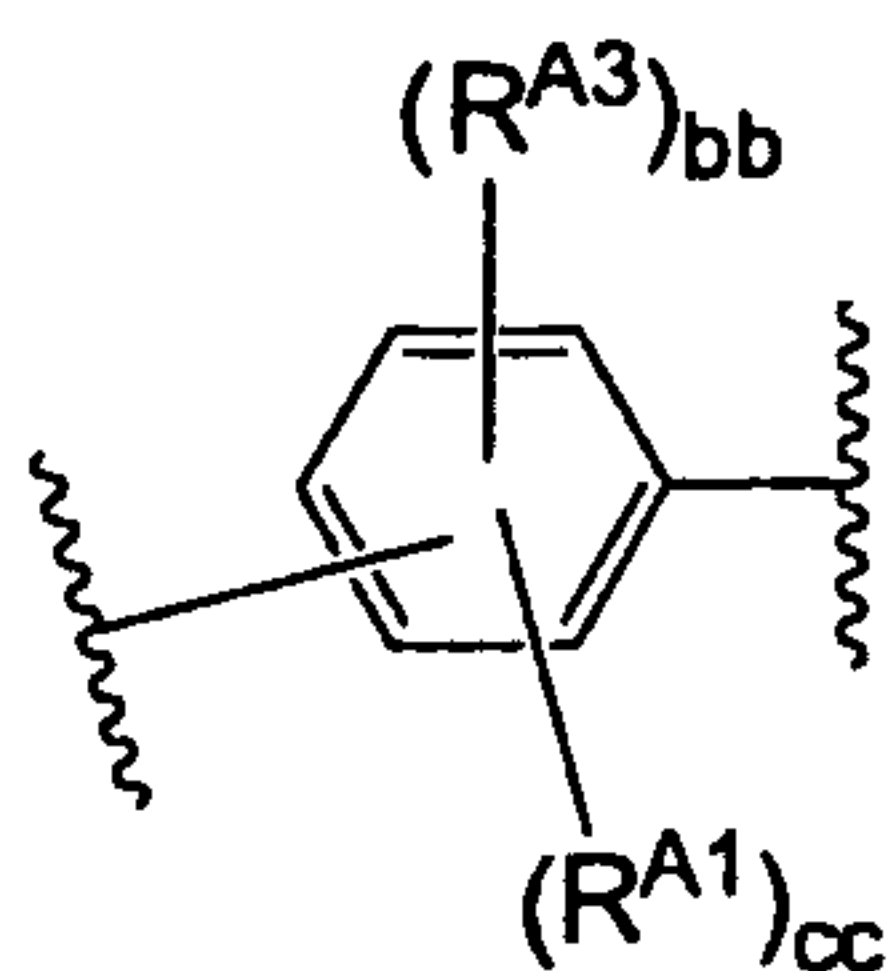
wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each cc is independently 1, 2, 3, or 4

each A^2 is independently:



wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , -alkyl SO_2R^4 , haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

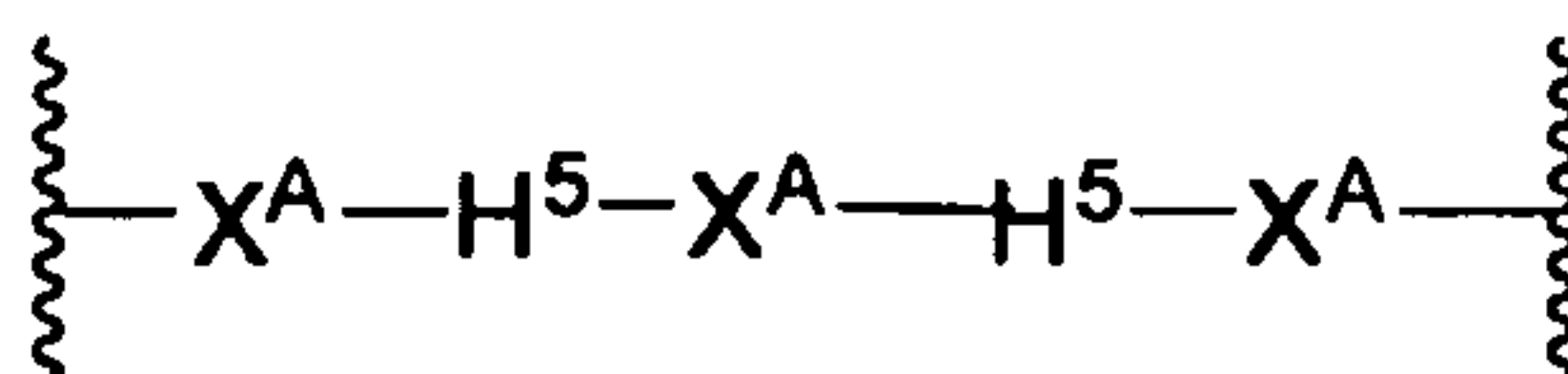
each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is 0, 1, 2, 3, or 4; each cc is 1, 2, 3, or 4; and the sum of bb and cc is 1, 2, 3, or 4;

each A^3 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is substituted with one or more R^{A1} groups, and which ring is optionally substituted with one or more R^{A3} groups;

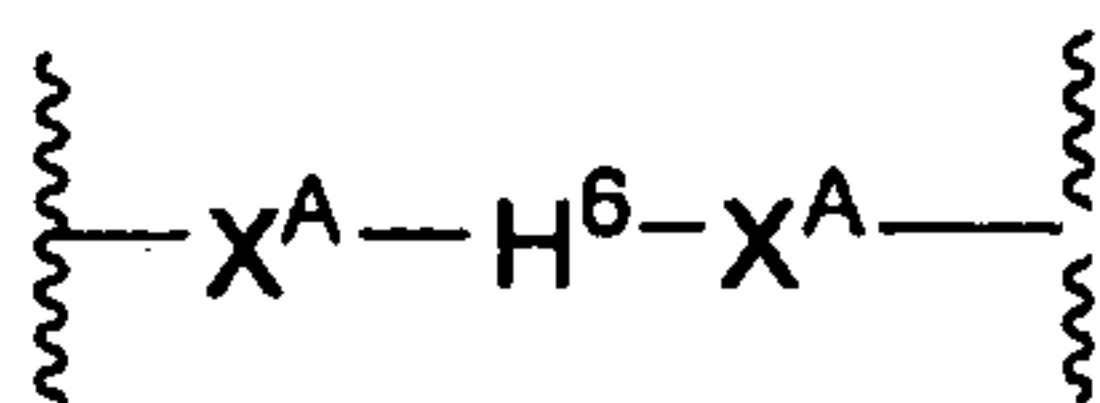
each A^4 is independently:



wherein:

each H⁵ is independently a phenyl ring or a six-membered heteroaromatic ring, which H⁵ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

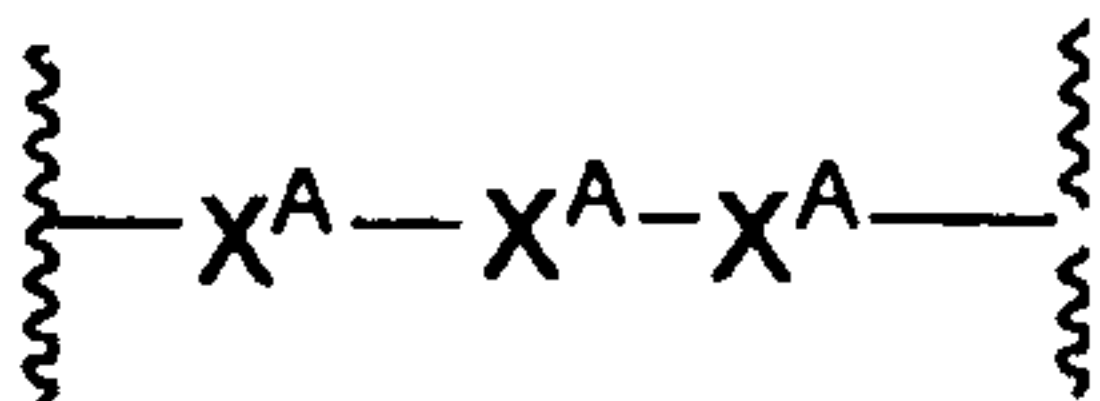
each A⁵ is independently:



wherein:

each H⁶ is independently a phenyl ring or a six-membered heteroaromatic ring, which H⁶ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent; provided that at least one X^A is present and each R is independently selected from H or alkyl;

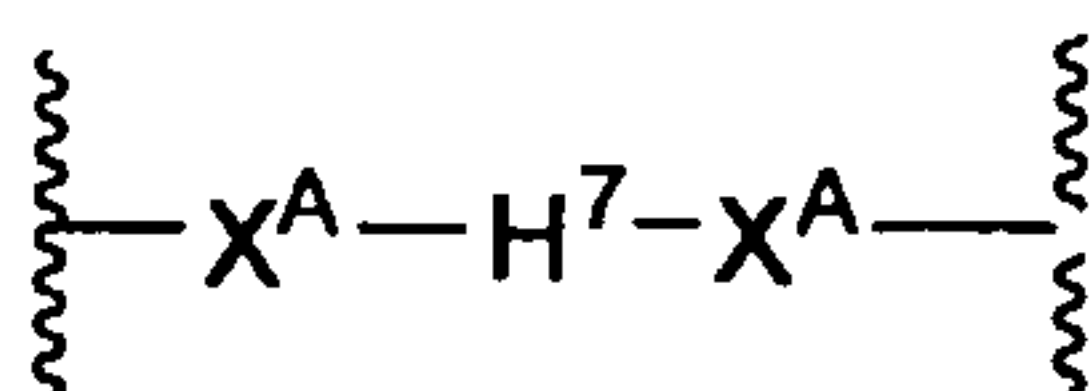
each A⁶ is independently:



wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, allenyl, alkynyl, or absent; provided that at least one X^A is present and each R is independently selected from H or alkyl;

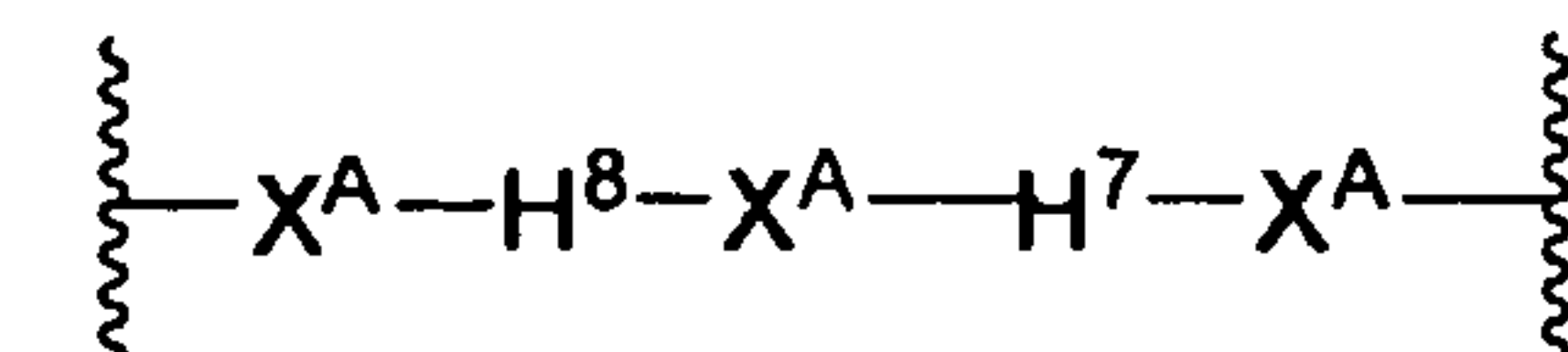
each A⁷ is independently:



wherein:

each H^7 is independently a five-membered heteroaromatic ring, which H^7 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

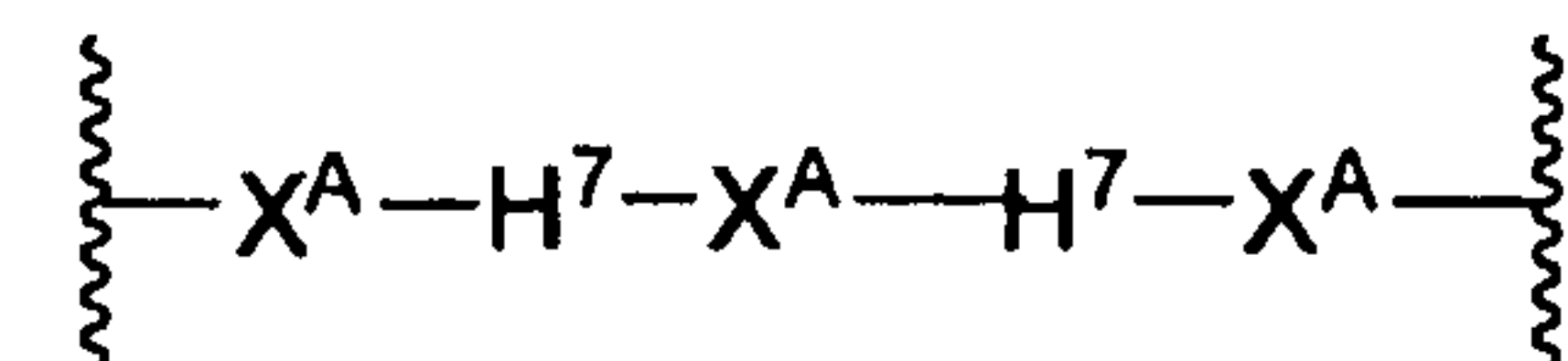
each A^8 is independently:



wherein:

each H^7 is independently a five-membered heteroaromatic ring, which H^7 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; each H^8 is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

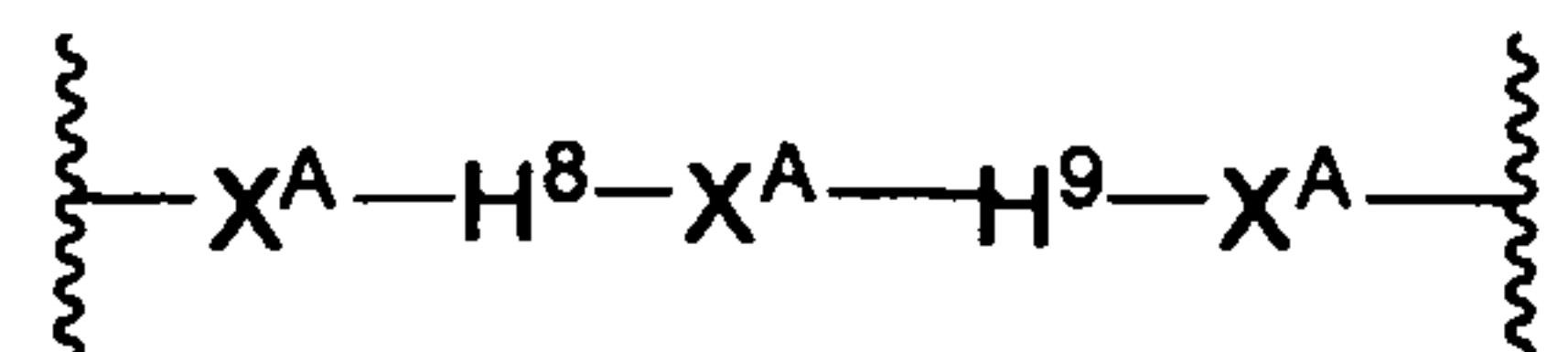
each A^9 is independently:



wherein:

each H^7 is independently a five-membered heteroaromatic ring, which H^7 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A^{10} is independently:



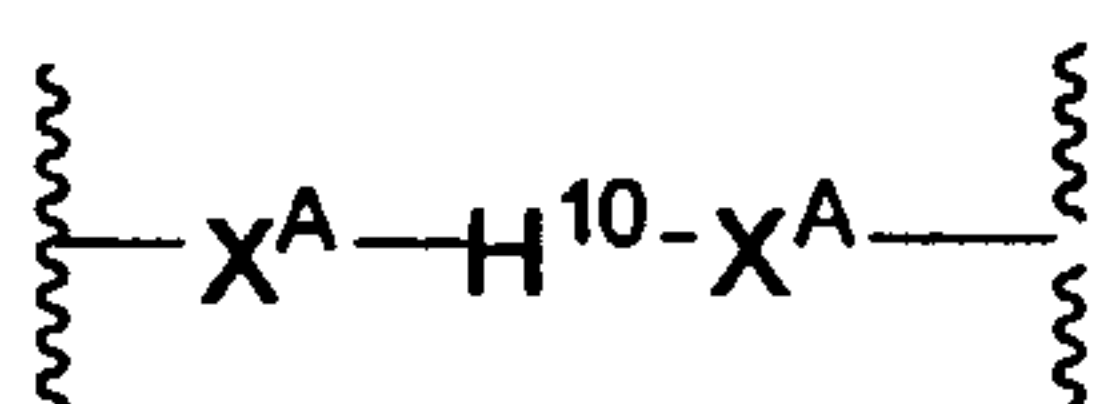
wherein:

each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each H⁹ is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹¹ is independently:



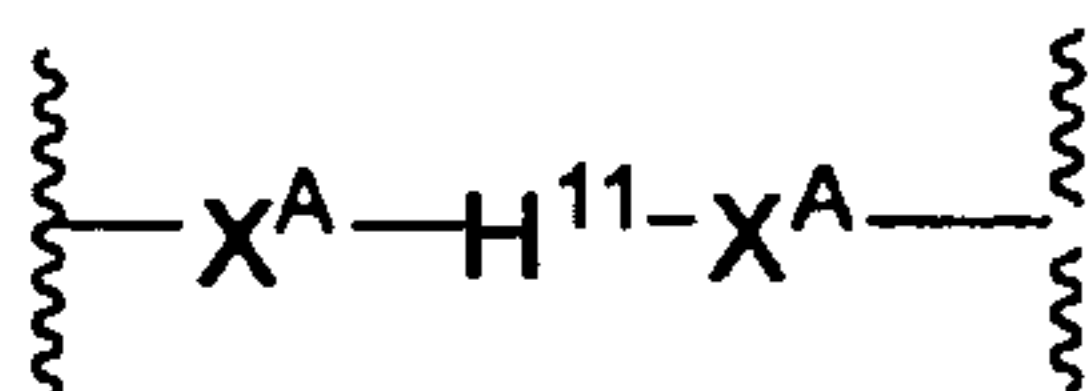
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H¹⁰ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that is optionally fused to an aryl, which H¹⁰ is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl

each A¹² is independently:



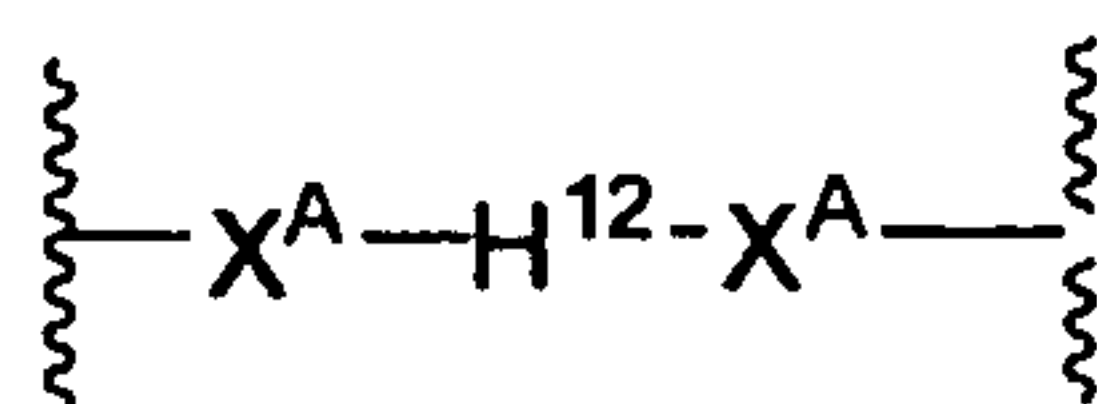
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each H¹¹ is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms that is optionally fused to an aryl, which H¹¹ is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

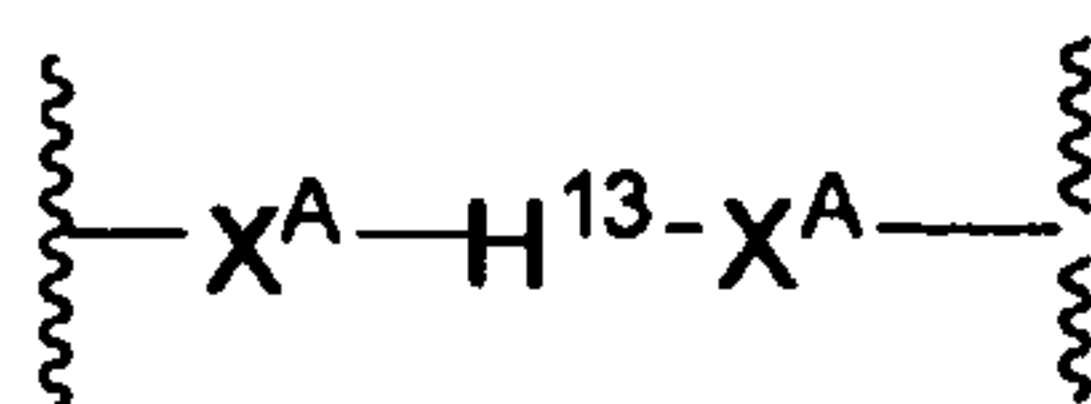
each A¹³ is independently:



wherein:

each H¹² is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R¹ and R³; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

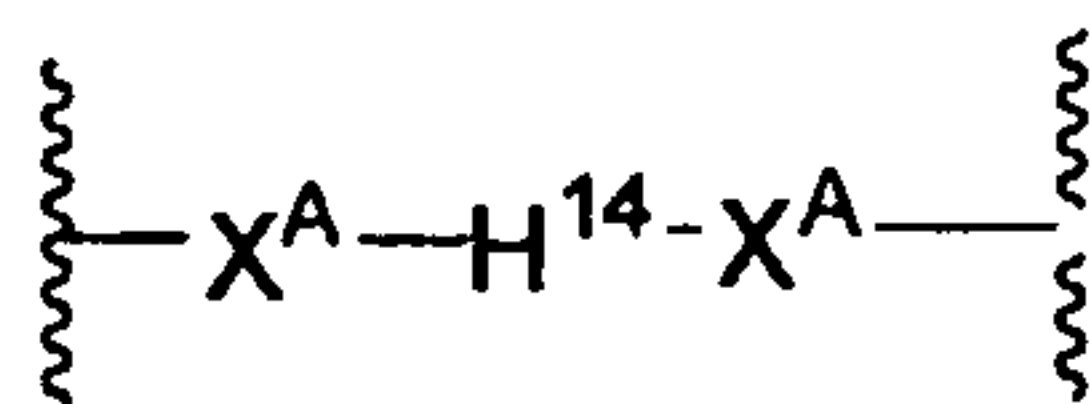
each A¹⁴ is independently:



wherein:

each H¹³ is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁵ is independently:

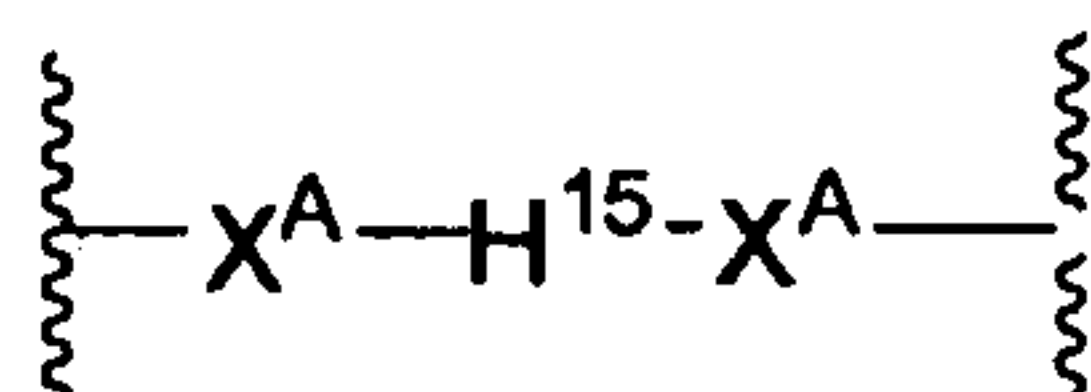


wherein:

each H¹⁴ is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁶ is independently:

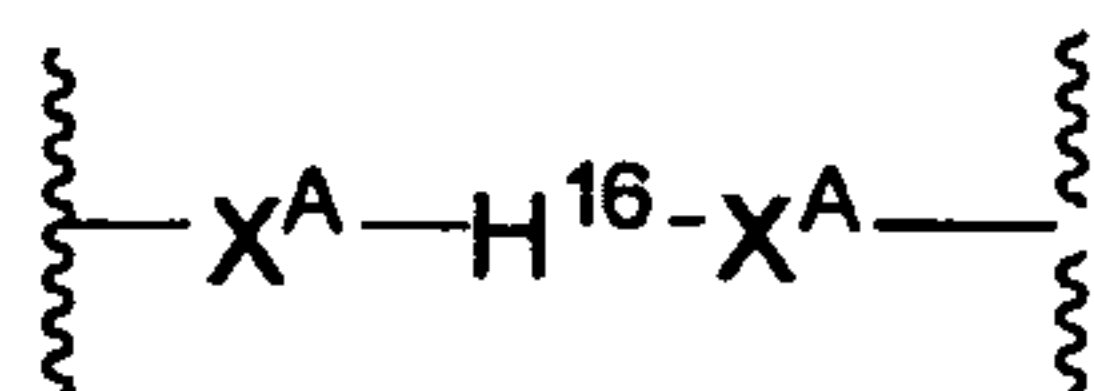


wherein:

each H¹⁵ is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each A¹⁷ is independently:



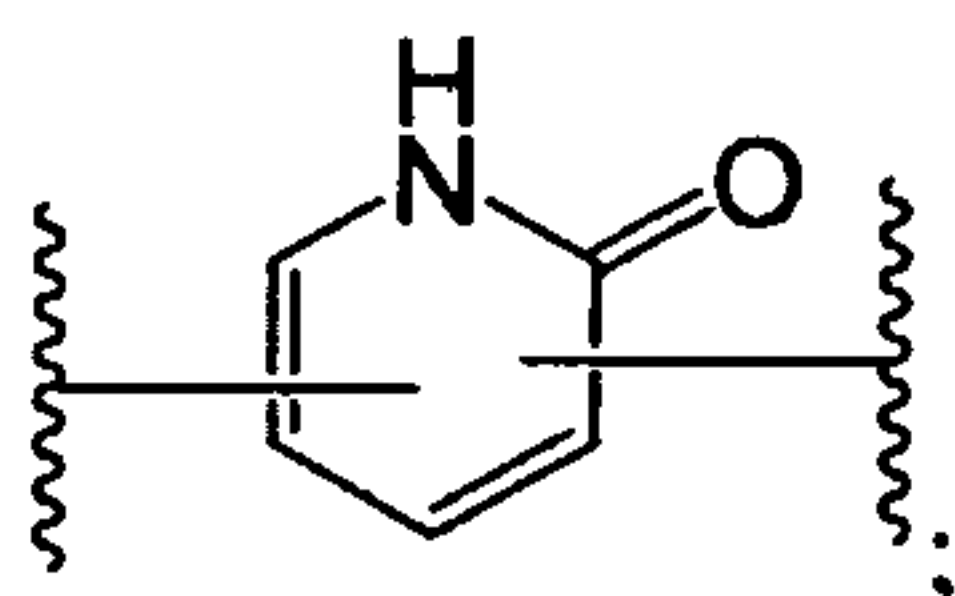
wherein:

each M^0 is independently a five membered heteroaryl group optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, haloalkyl, (NR^aR^b) carbonyl and trialkylsilylalkoxyalkyl;

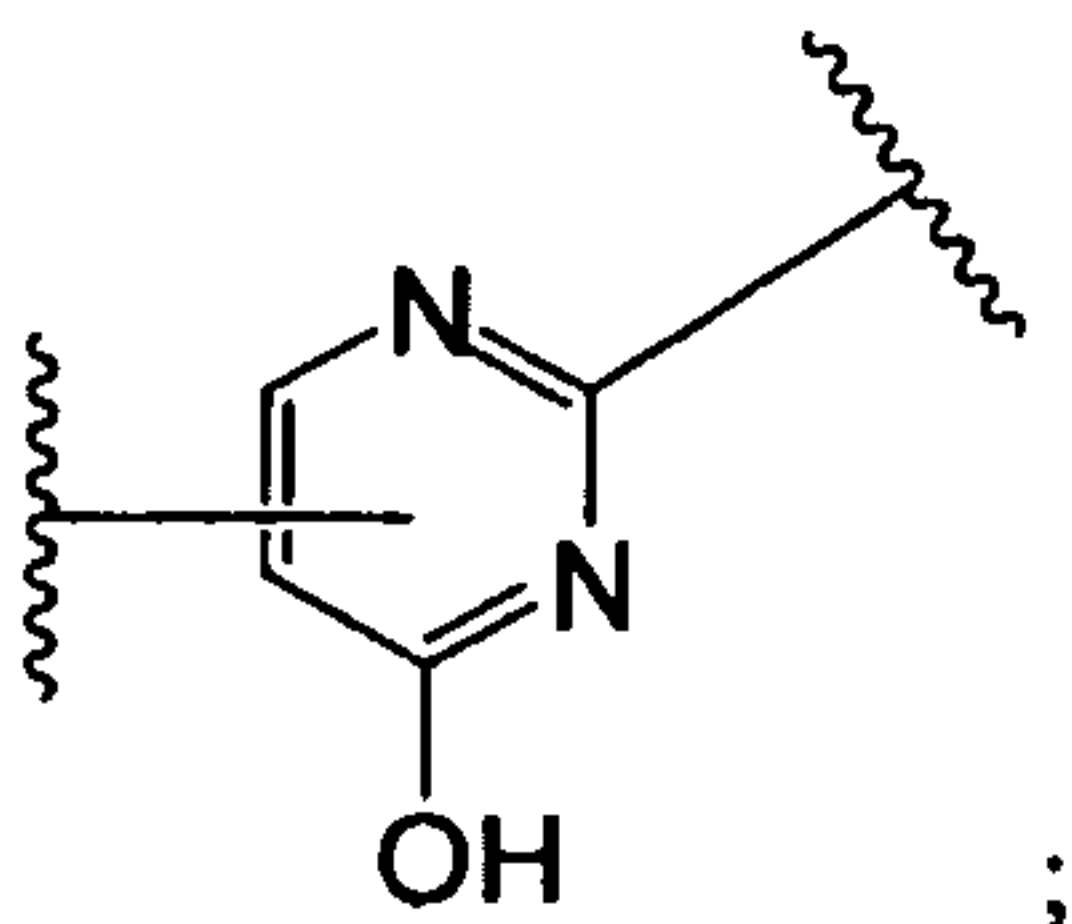
each M^1 is independently selected from $-C(=O)NH-$, $-C(=O)NH-C(R^M)_2-$, $-NHC(=O)-$, $-C(R^M)_2NHC(=O)-$, $-NHC(=O)NR^M-$, $-NHC(=O)O-$; wherein each R^M is independently selected from H and alkyl;

each M^2 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

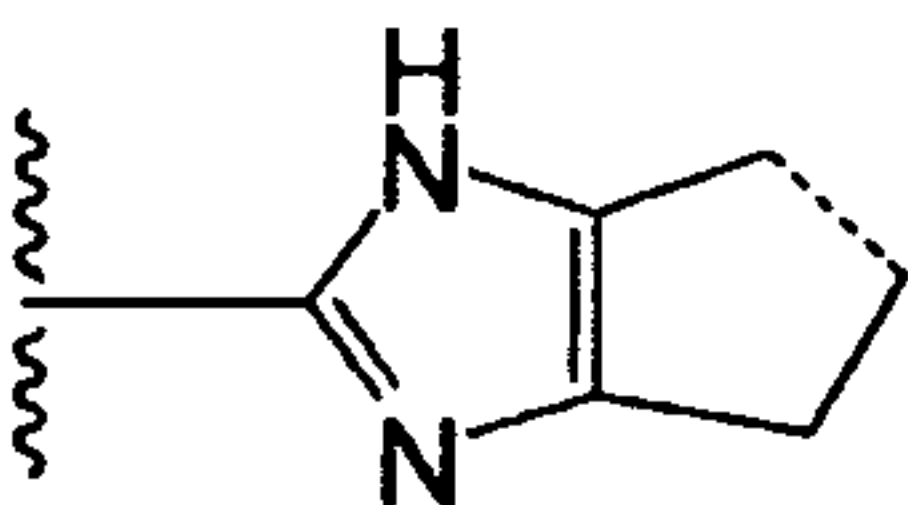
each M^3 is independently:



each M^4 is independently:



each M^5 is independently:



wherein the bond designated with --- is fused to a ring defined for P;

each M^6 is independently a bicyclic bridged ring system comprising 5-15 atoms wherein at least one of the atoms is a heteroatom;

each M^7 is independently a pyrid-di-yl;

each M^8 is independently partially saturated or a saturated five-membered ring that comprises one or more heteroatoms and that is optionally substituted with one or two oxo;

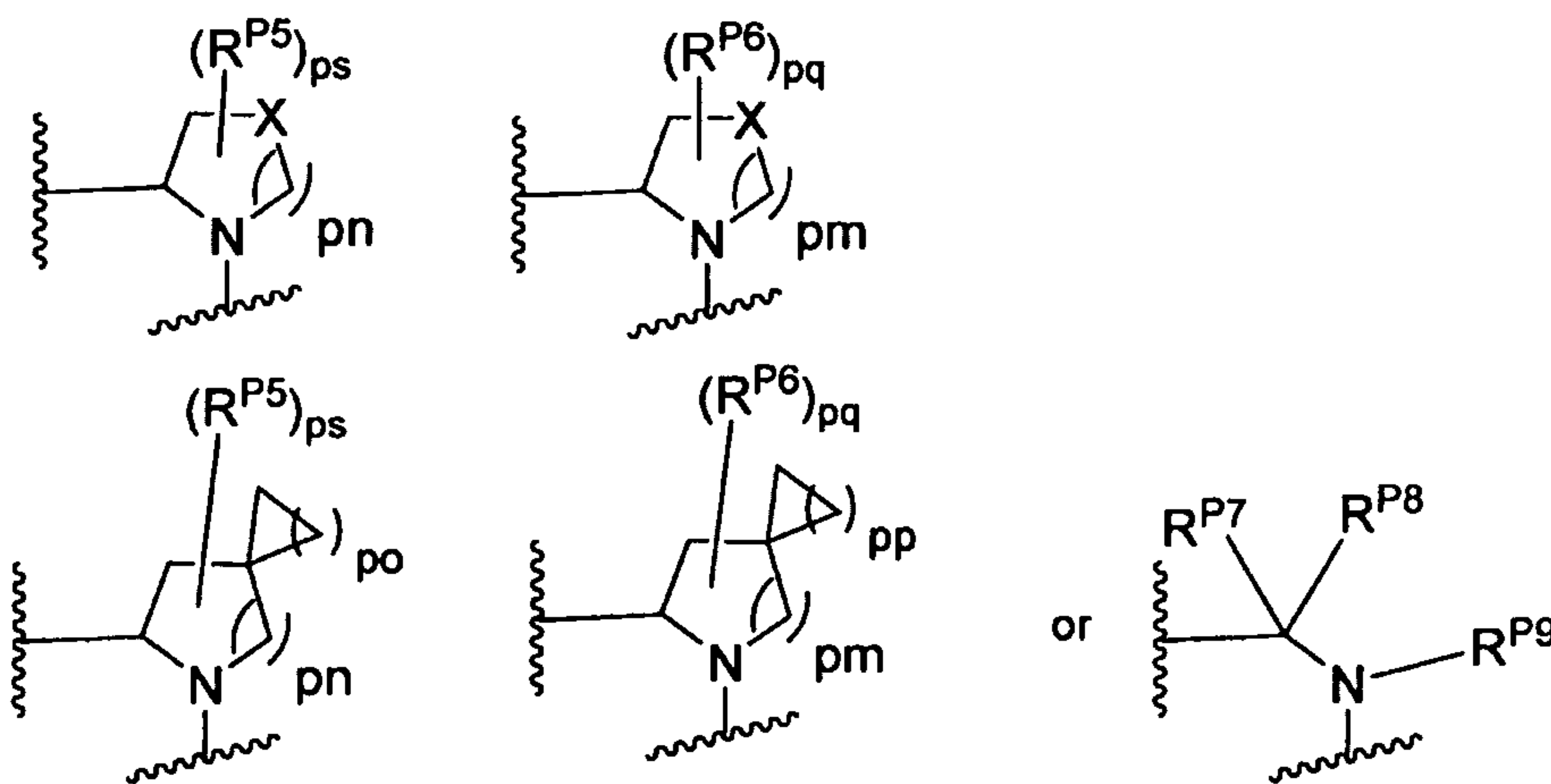
each M^9 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^{P11} ;

each M^{10} is independently a five membered heteroaryl group;

each M^{11} is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$;

each R^{M7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

each P^0 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-

to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

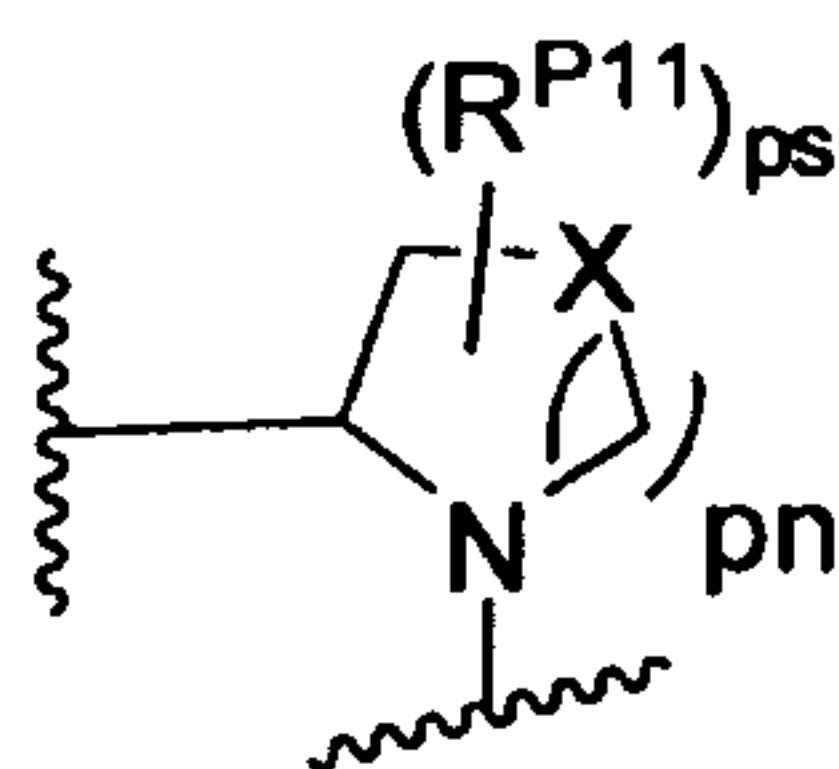
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^l is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

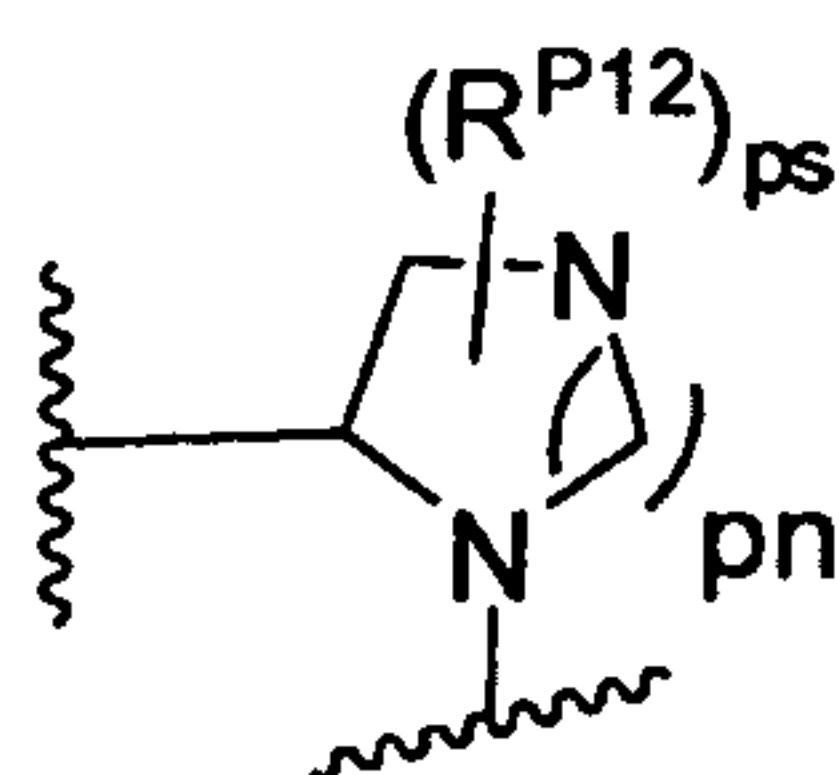
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl,

(NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h)sulfonyl, heteroarylsulfonyl, -S(=O)₂R^h, -C(=O)R^h, -C(=O)NR^hR^h; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P² is independently:



wherein:

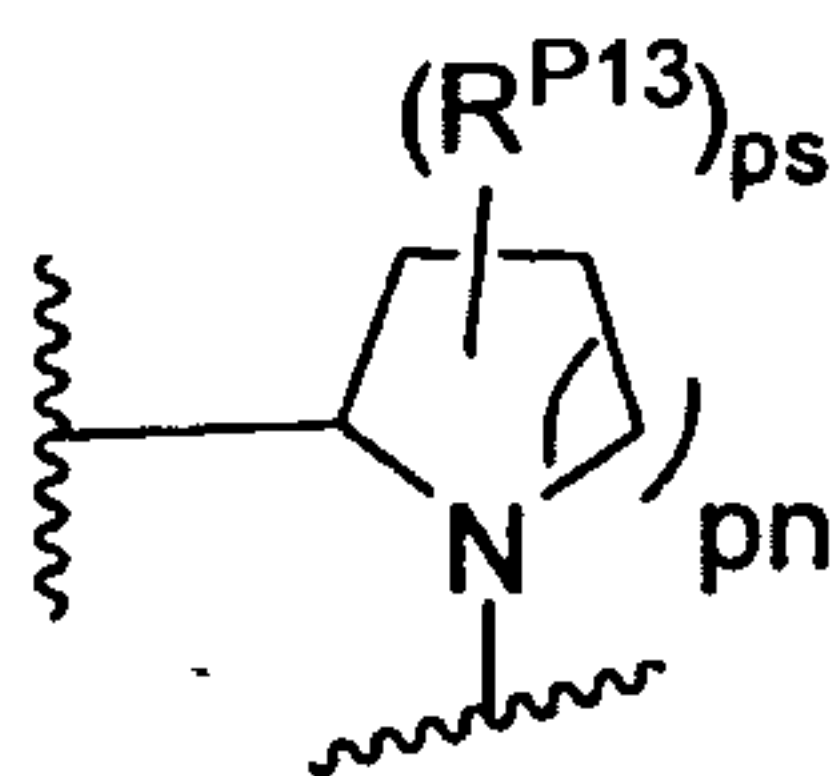
each R^{P12} is independently selected from R^{P5}, R^{P11}, -C(=O)OR^h, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H,

alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^3 is independently a ring of the formula:



wherein:

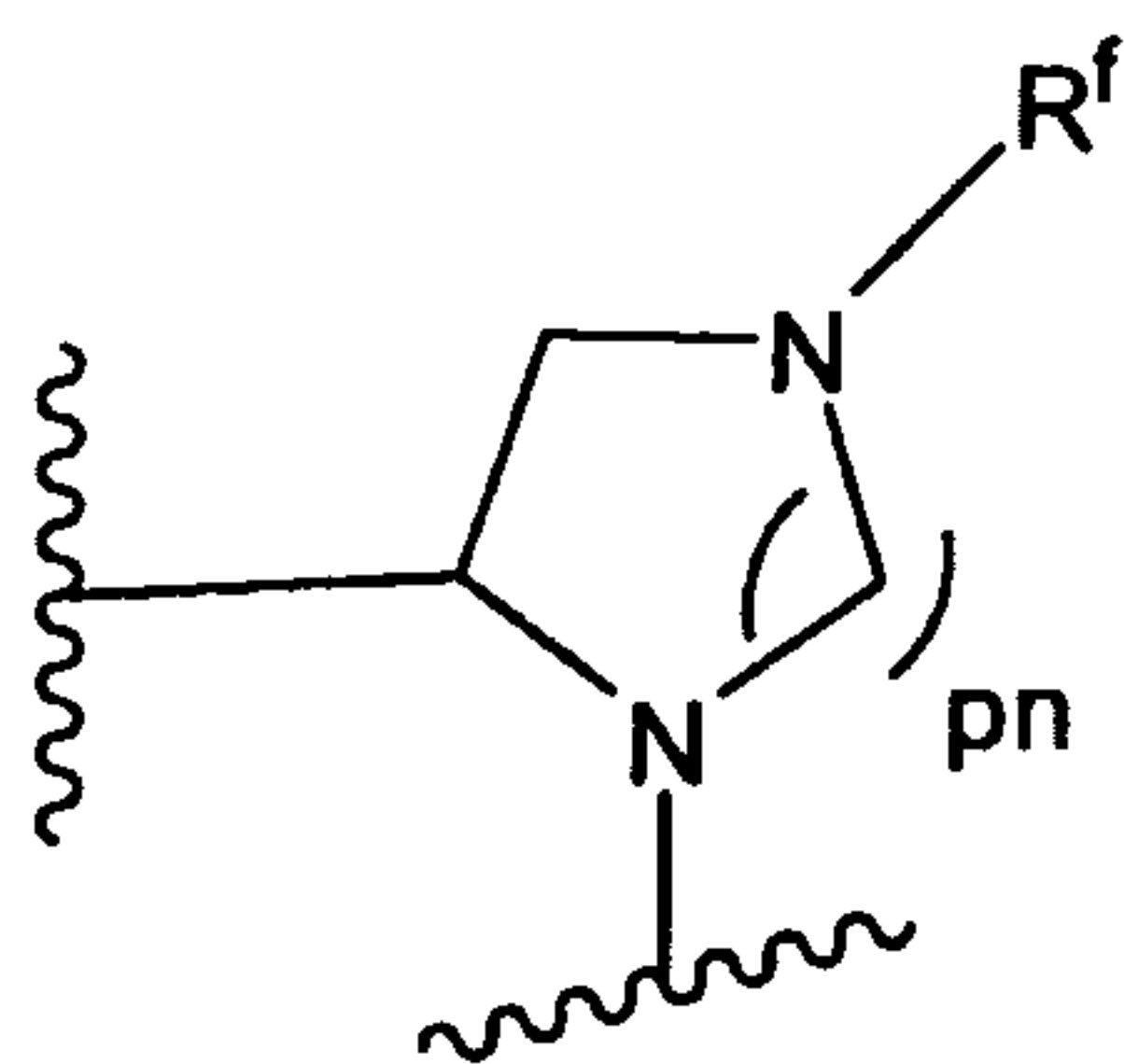
the ring is substituted with one or more oxo group;

each R^{P13} is independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^4 is independently a ring of the formula:



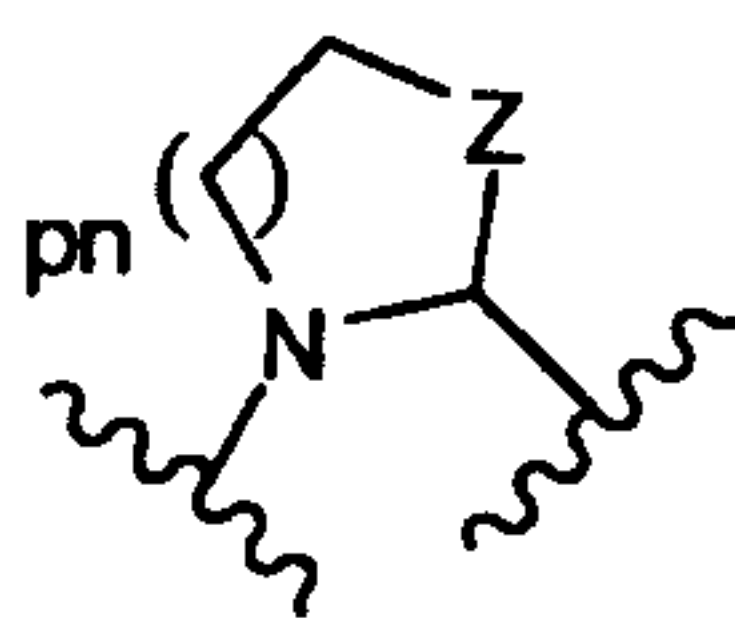
wherein:

the ring is optionally substituted with one or more groups R^{P14} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P14} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^5 is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an

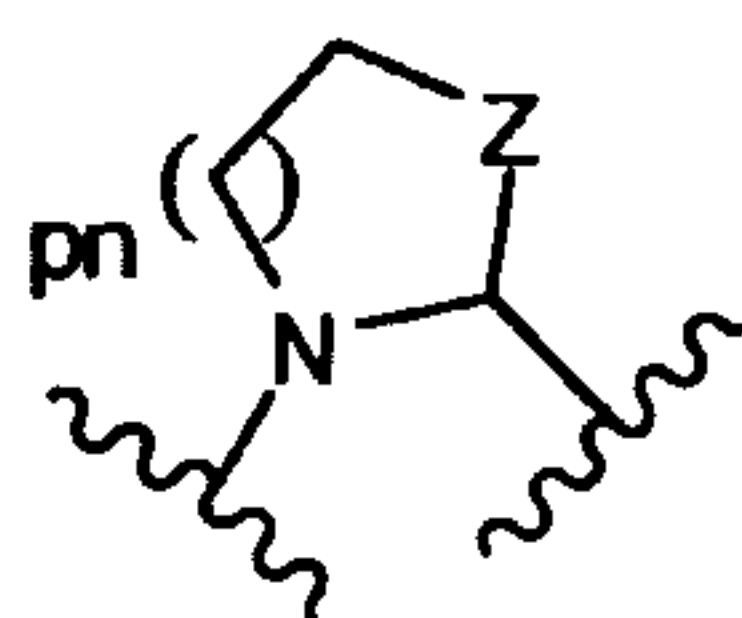
adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

Z is O, S, S(=O), S(=O)₂, or NR^f;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, -S(=O)₂NR^hR^h, -S(=O)₂R^h, C(=O)R^h, C(=O)OR^h, -C(=O)NR^hR^h; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P⁶ is independently a ring of the formula:



wherein:

the ring is substituted with one or more oxo and is optionally substituted with one or more groups R^{P16} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

Z is O, S, S(=O), S(=O)₂, or NR^f;

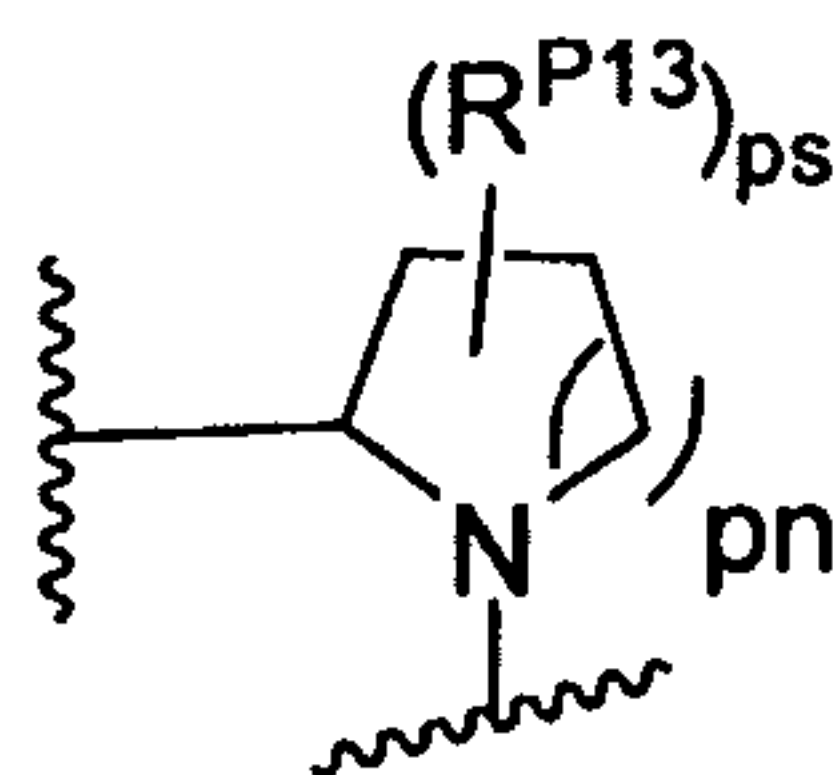
pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, -S(=O)₂NR^hR^h, -S(=O)₂R^h, C(=O)R^h, C(=O)OR^h, -C(=O)NR^hR^h; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:

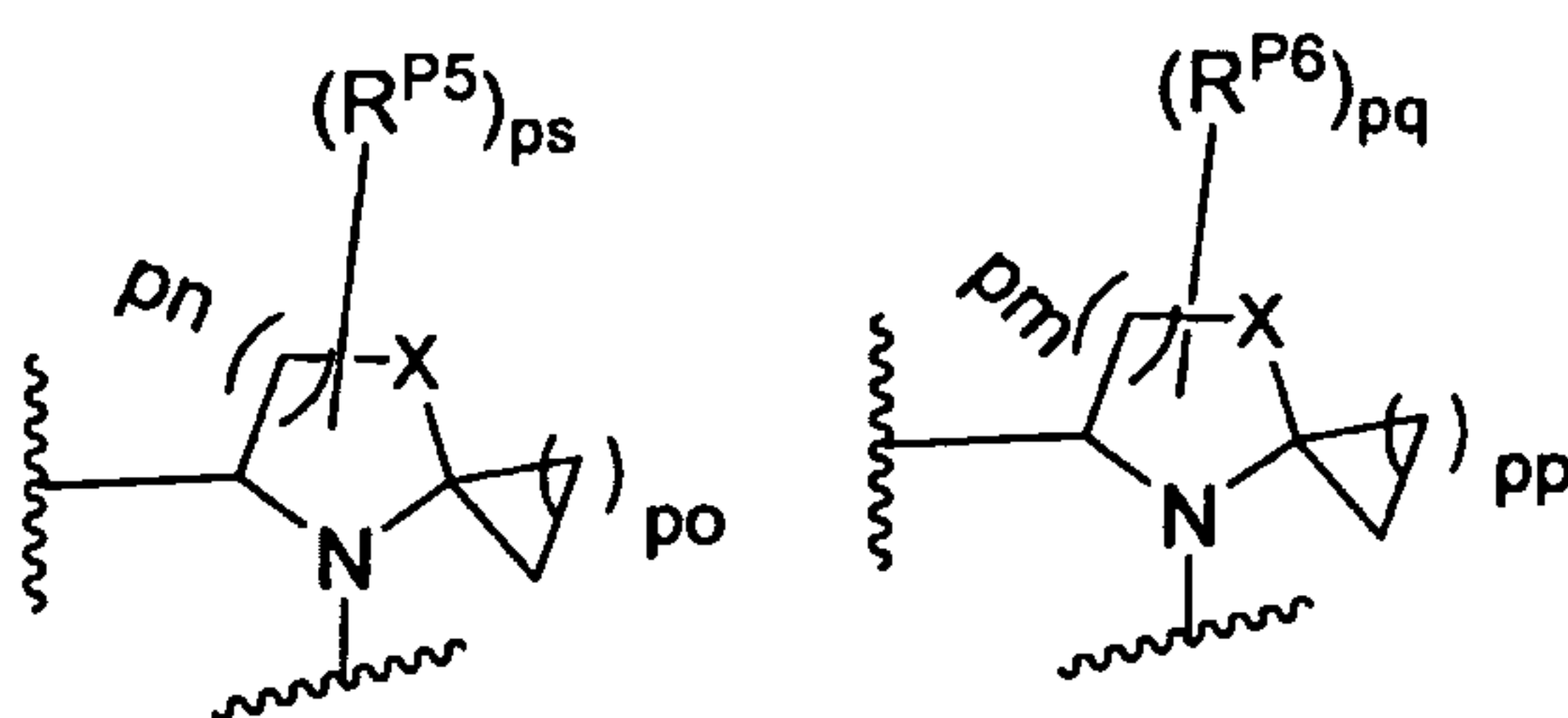


wherein:

ps is 2, 3, 4, 5, or 6;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

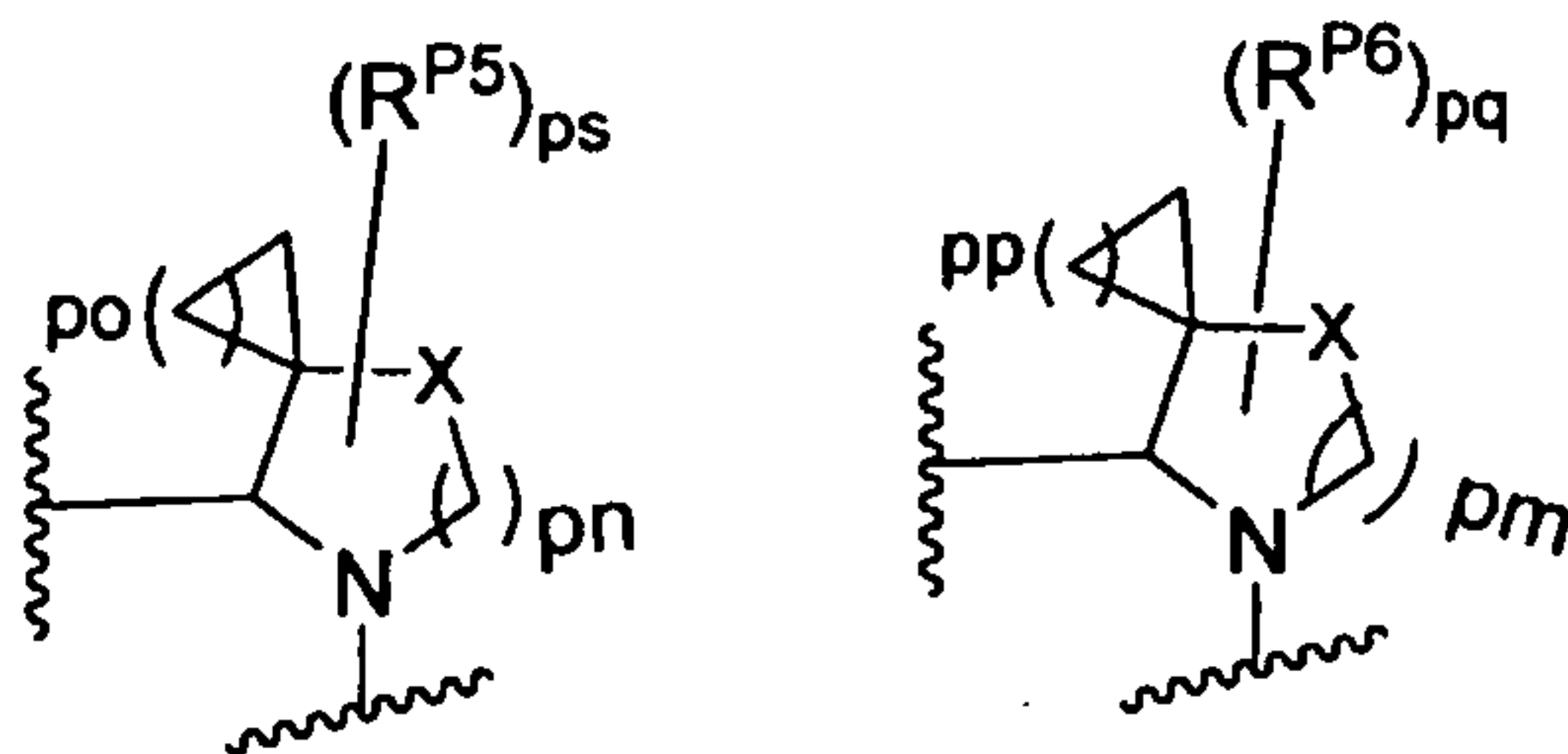
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P¹¹ is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

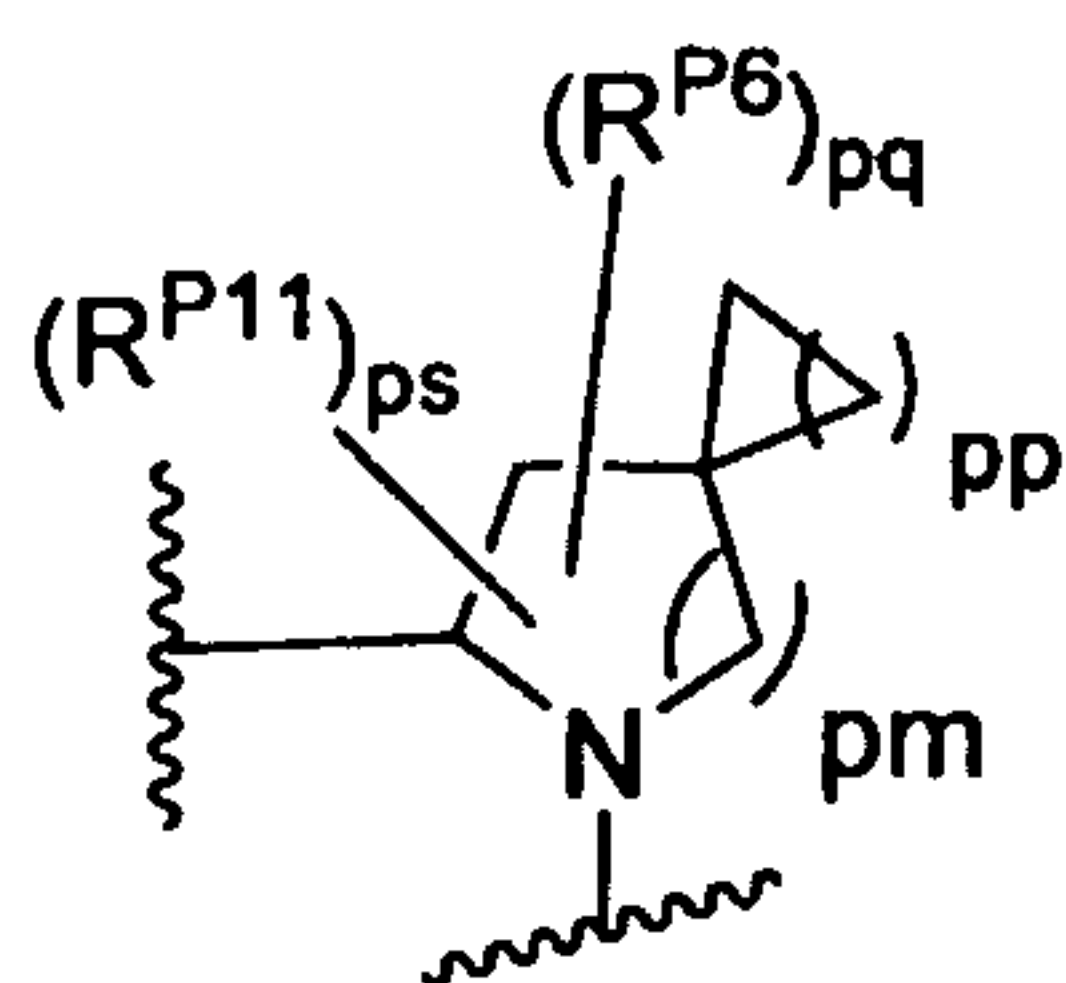
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P¹² is independently:



wherein:

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

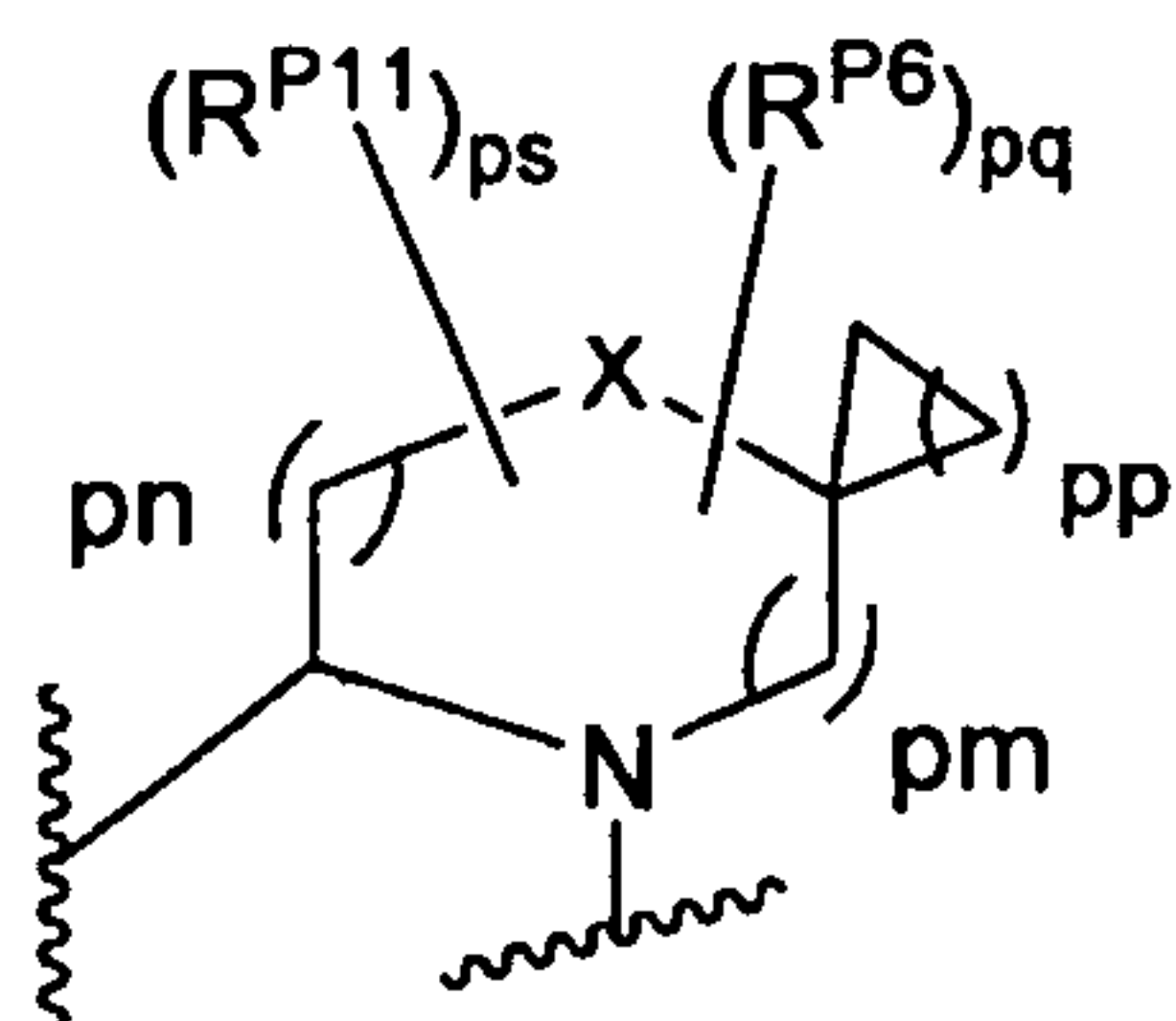
pp is independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, -NR^{hh}R^h, (NR^{hh}R^h)alkyl, (NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h)sulfonyl, heteroarylsulfonyl, -S(=O)₂R^h, -C(=O)R^h, -C(=O)NR^hR^h; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy,

heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{13} is independently:



wherein:

X is selected from O, S, S(O), SO₂, or NR^h ;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2 but the sum of pn and pm is greater than zero;

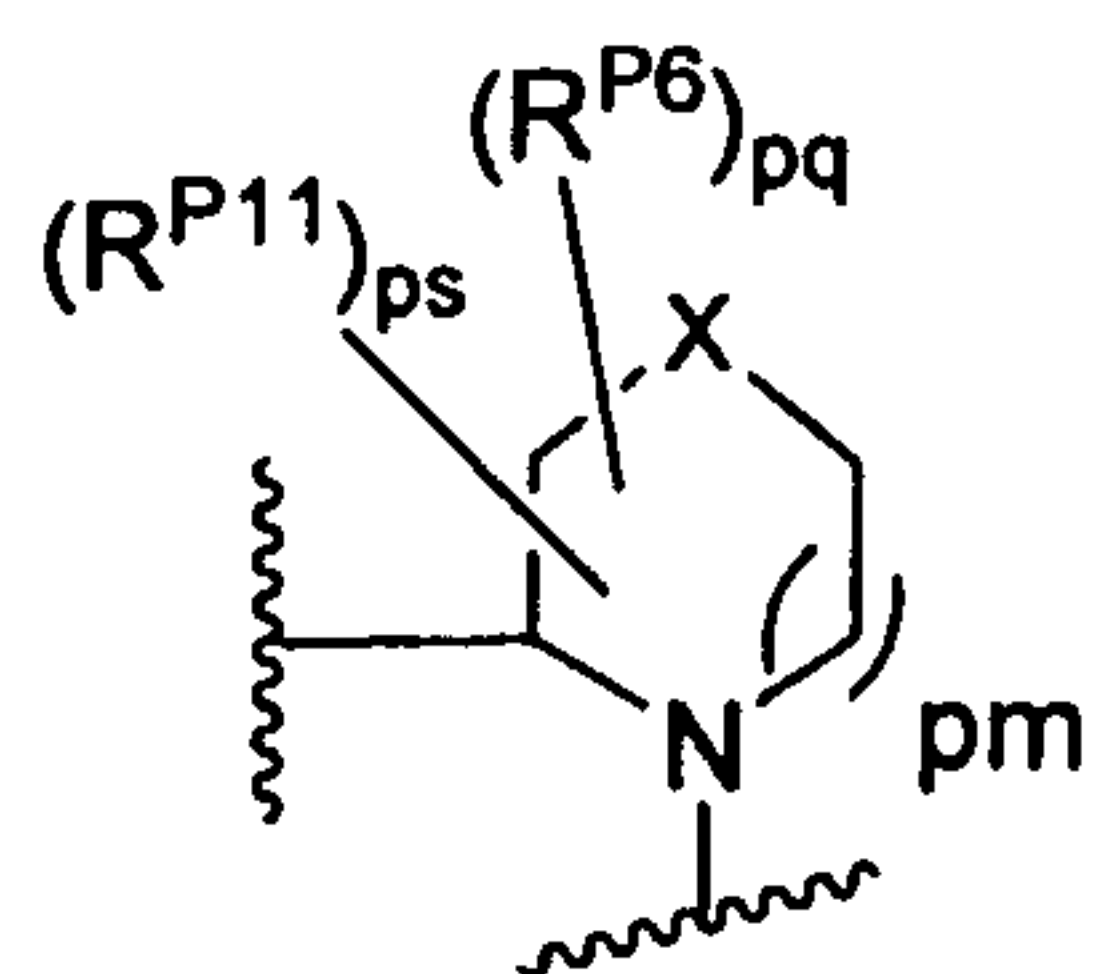
pp are independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$, R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{14} is independently:



wherein:

the ring is substituted with one or more oxo group;

X is NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

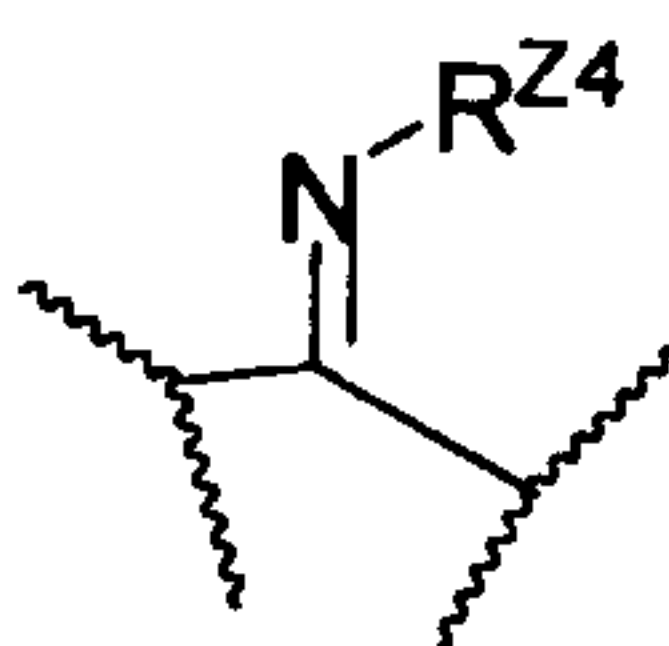
each $-Z^0-$ is $-C(=O)-$ or $-C(=S)-$;

each $-Z^1-$ is independently a bond, or $-C(R^{Z1})_2-$; wherein each R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each $-Z^2-$ is independently saturated or partially unsaturated (C_3-C_8)cycloalkyl that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

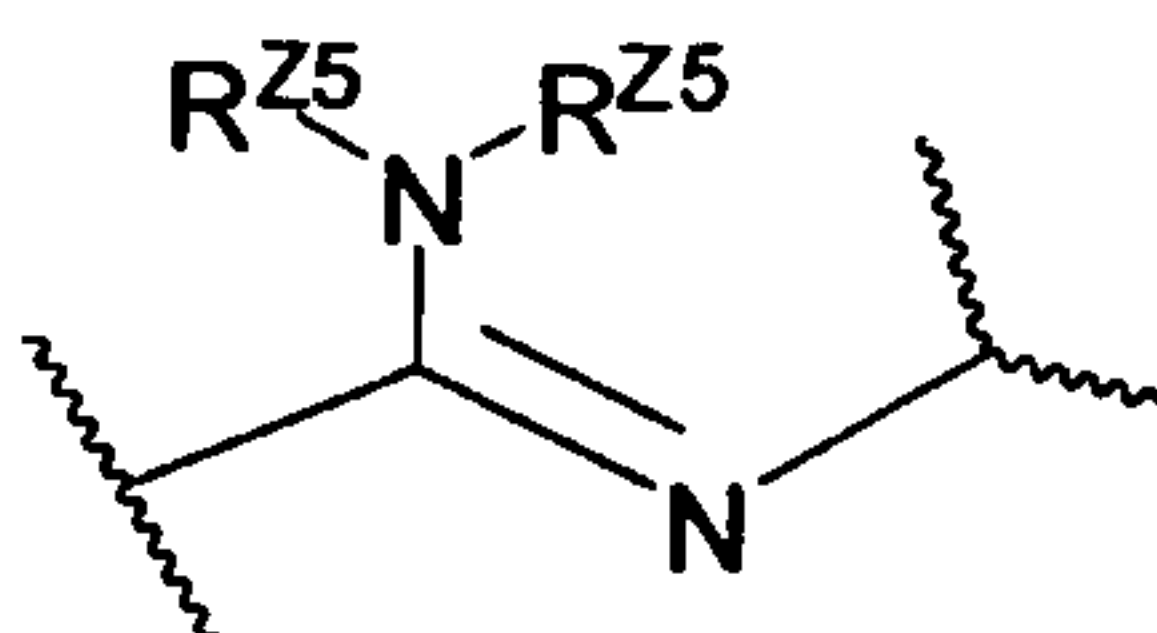
each $-Z^3-$ is independently saturated, partially unsaturated, or aromatic 4-8 membered heterocyclic or heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^4-$ is independently:



wherein each R^{Z4} is independently H, alkyl, cyano, aryl, or heteroaryl;

each $-Z^5-$ is independently:



wherein each R^{Z5} is independently H, alkyl, cyano, aryl, or heteroaryl; or two R^{Z5} s together with the nitrogen to which they are attached form a 4-8 membered heterocyclic ring that is optionally substituted with one or more oxo and with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^6-$ is independently $-C(R^{Z1})-$ and is doublebonded to P; wherein R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^{Ef}) alkyl, (NR^{Ef}) alkylcarbonyl, (NR^{Ef}) carbonyl, (NR^{Ef}) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^XR^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^{Ef}$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each E¹ is independently -OC(=O)NR^{E^c}R^{E^f} wherein each R^{E^c} and R^{E^f} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^{E^f})alkyl, (NR^{E^f})alkylcarbonyl, (NR^{E^f})carbonyl, (NR^{E^f})sulfonyl, -C(NCN)OR', and -C(NCN)NR^XR^Y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one -NR^{E^f} group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; or wherein R^{E^c} and R^{E^f}, together with the nitrogen atom to which they are attached, form a heterocycle;

each V⁰ is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl, aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^XR^Y, - (NR^XR^Y)alkyl, oxo, and -P(O)OR₂, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the

heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NRaRbC(=O)O-$; Ra and Rb are each independently selected from hydrogen, alkenyl, and alkyl;

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle,

heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^6 is independently arylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^7 is independently heterocyclosulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^8 is independently spirocycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^9 is independently spirocycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{10} is independently fusedbicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{11} is independently fusedbicycliccycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{12} is independently bridged-bicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl,

heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{13} is independently bridged-bicyclic-cycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{14} is independently aryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{15} is independently arylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{16} is independently cycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{17} is independently cycloalkylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{18} is independently heterocycloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{19} is independently heterocycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl,

heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{20} is independently heteroaryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl; and

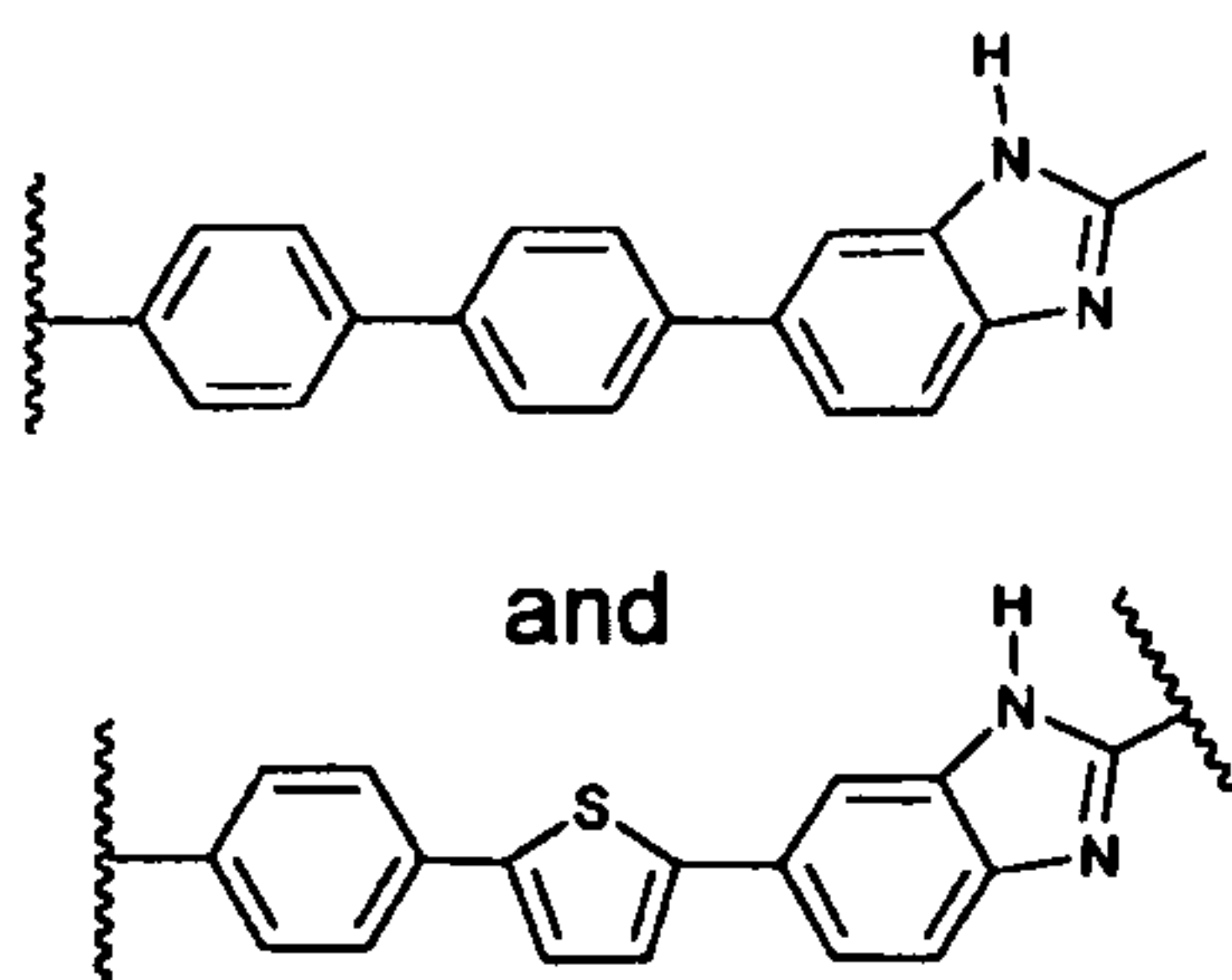
each V^{21} is independently heteroarylalkylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

or a pharmaceutically acceptable salt, or prodrug thereof.

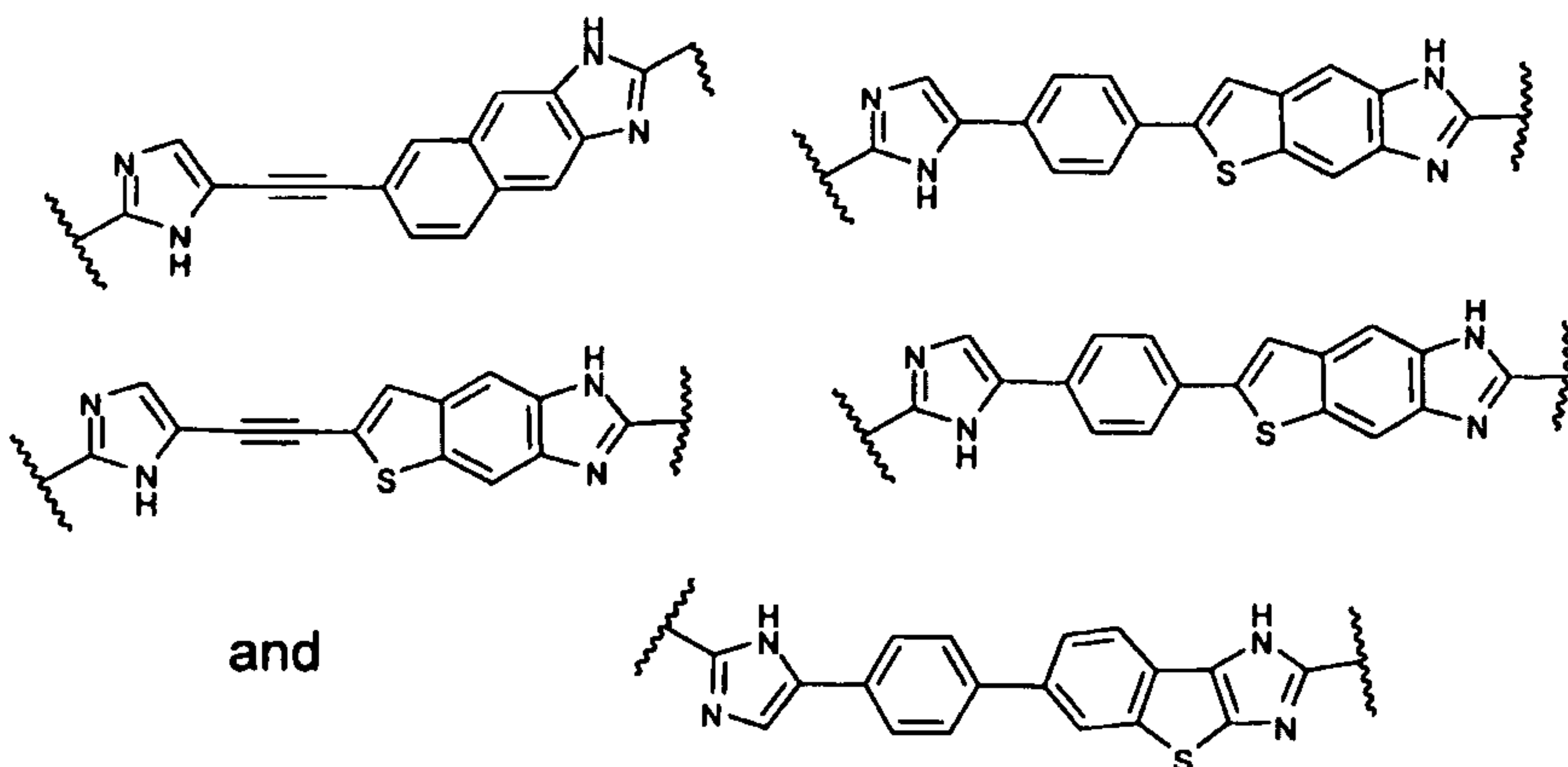
In another specific embodiment of the invention L is L^3 .

In another specific embodiment of the invention L is benzimidazolyl.

In another specific embodiment of the invention -A-L- is selected from:



In another specific embodiment of the invention -M-A-L- is selected from:



optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} .

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib1): $E^0-V^0-Z^0-P-M-A^{15}-L-P-Z^0-V^0-E^0$ (Ib1).

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib2): $E^0-V^0-Z^0-P-M-A^{15}-L^3-P-Z^0-V^0-E^0$ (Ib2).

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib3): $E^0-V^0-Z^0-P-M^0-A^{15}-L^3-P-Z^0-V^0-E^0$ (Ib3).

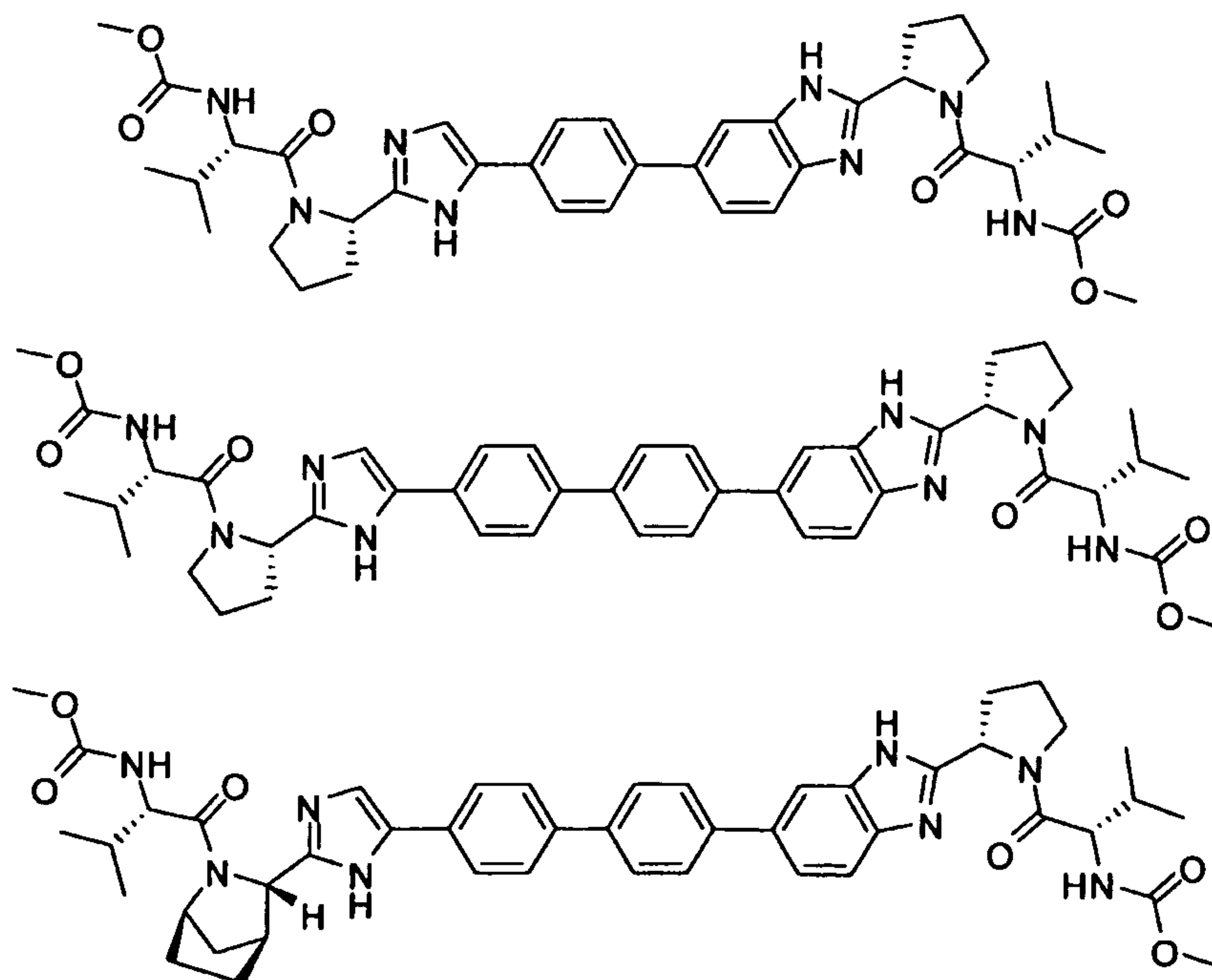
In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib4): $E^0-V^0-Z^0-P-M-A^{16}-L-P-Z^0-V^0-E^0$ (Ib4).

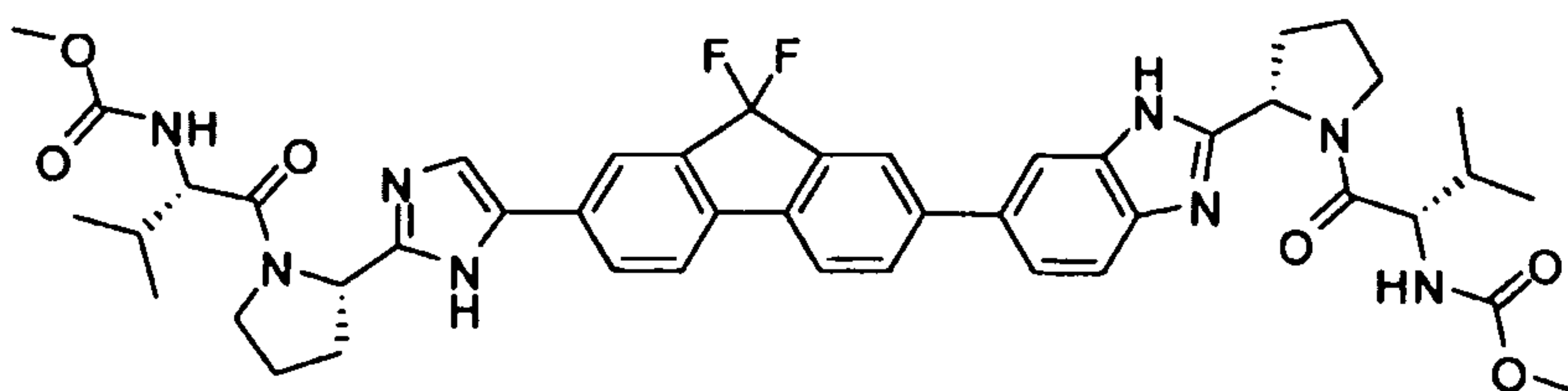
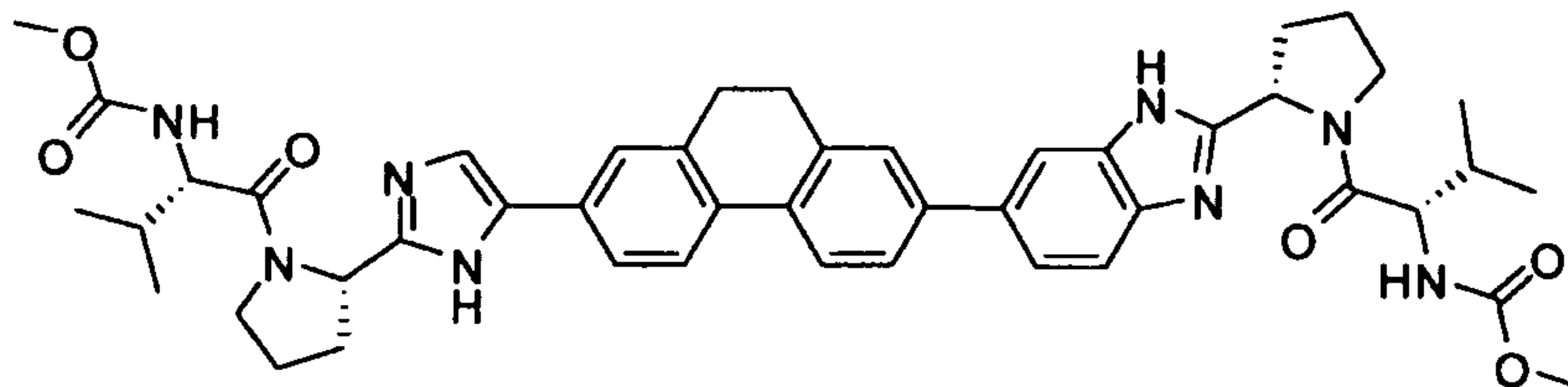
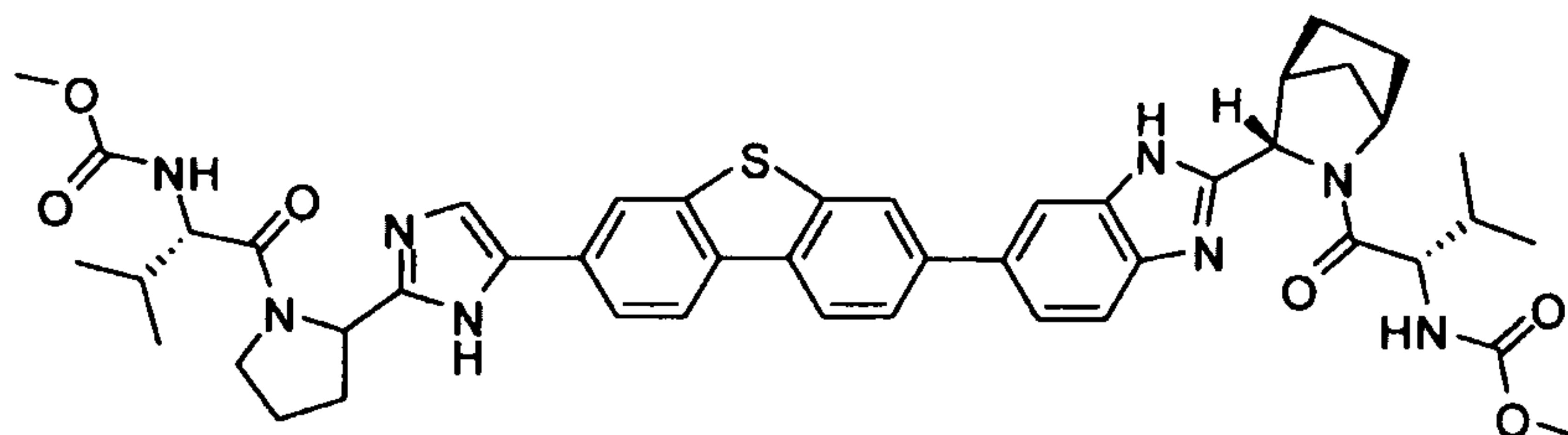
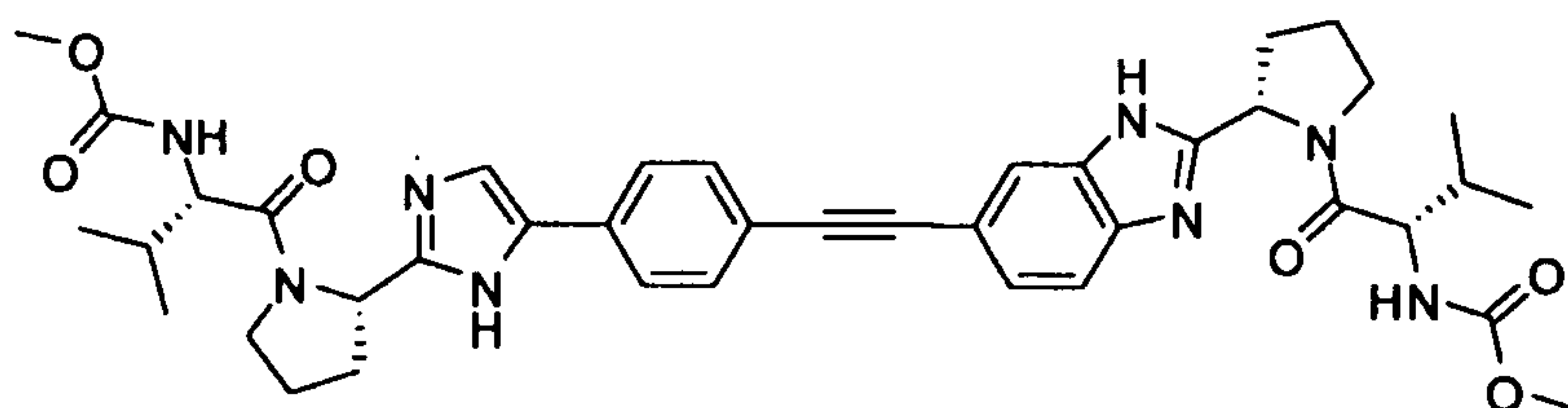
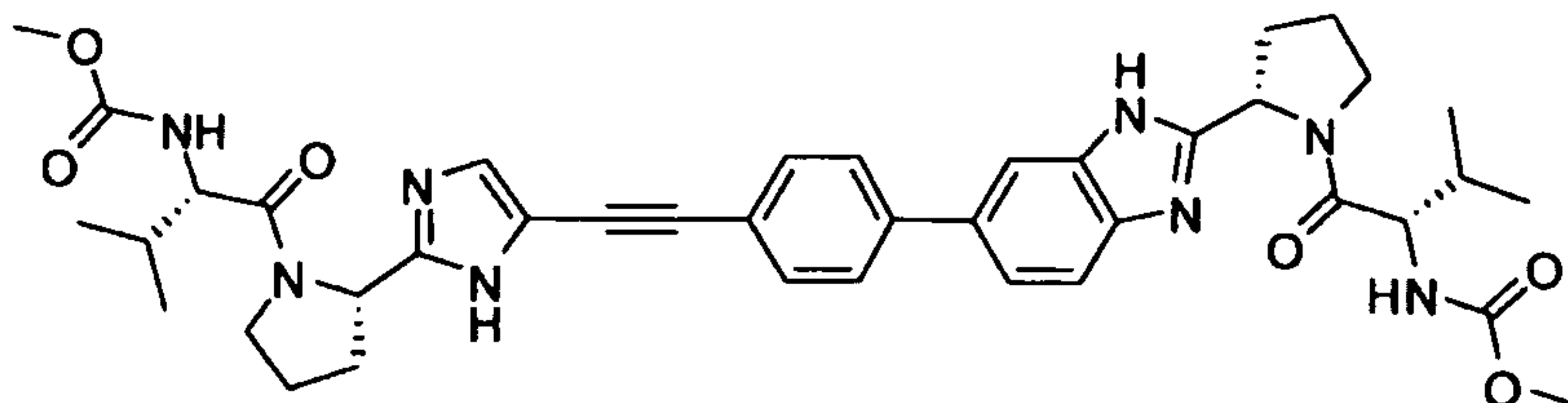
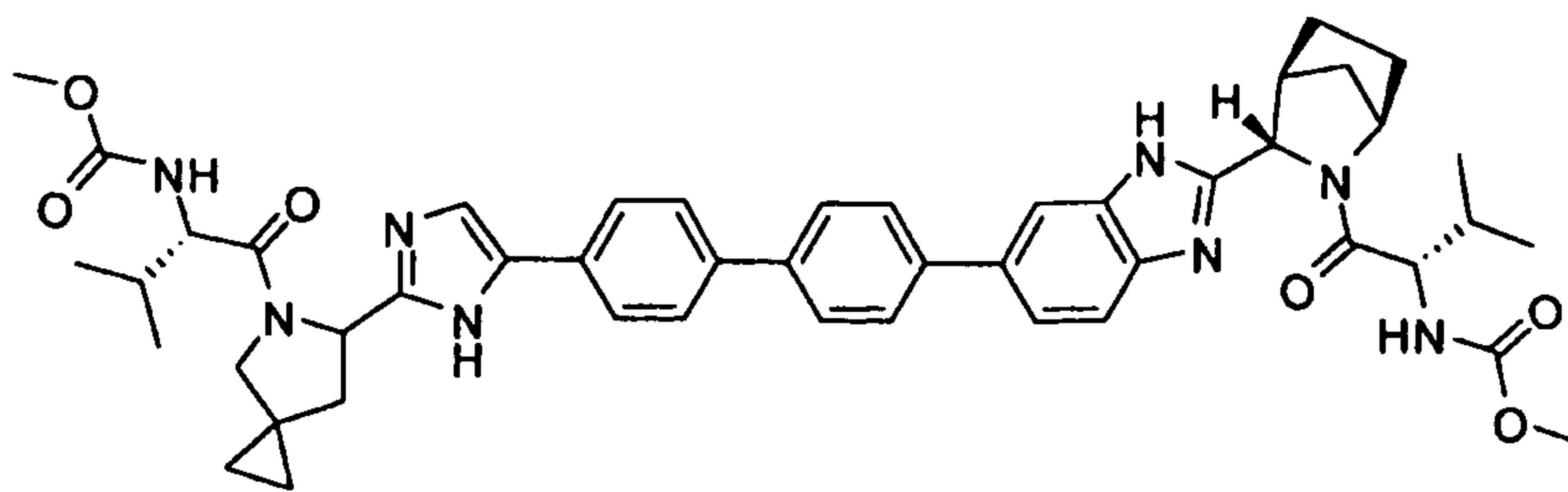
In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib5): $E^0-V^0-Z^0-P-M-A^{16}-L^3-P-Z^0-V^0-E^0$ (Ib5).

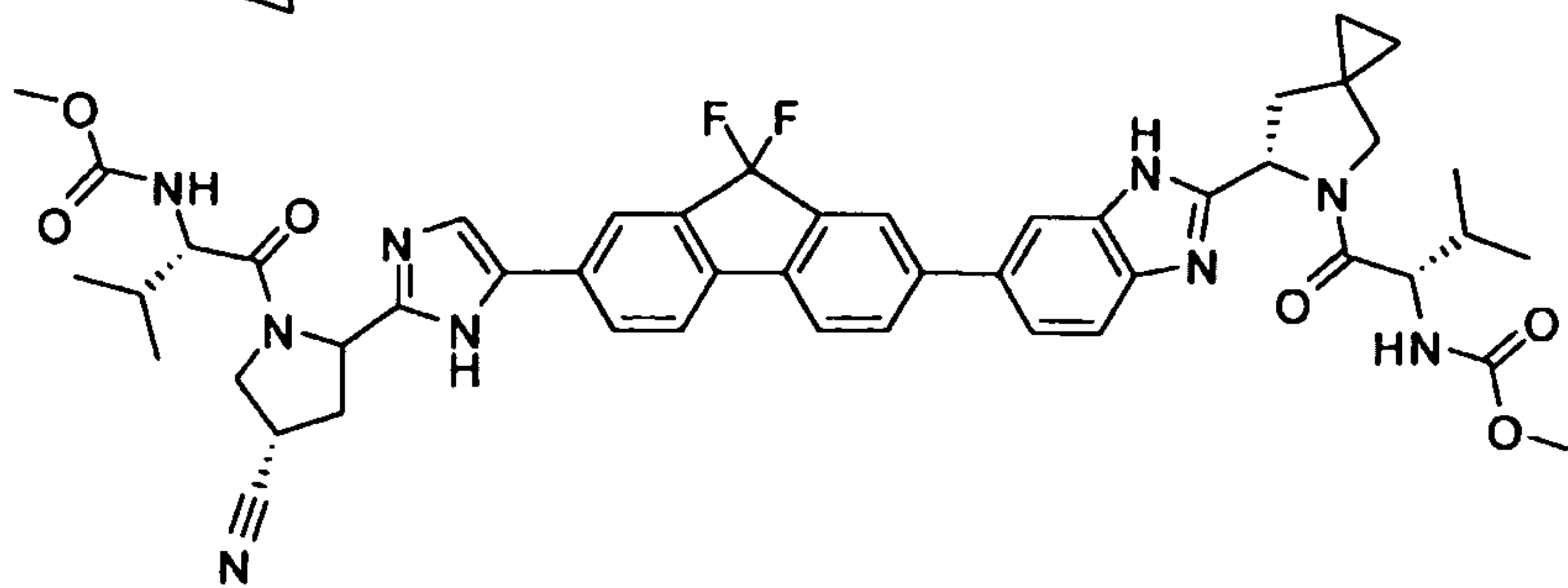
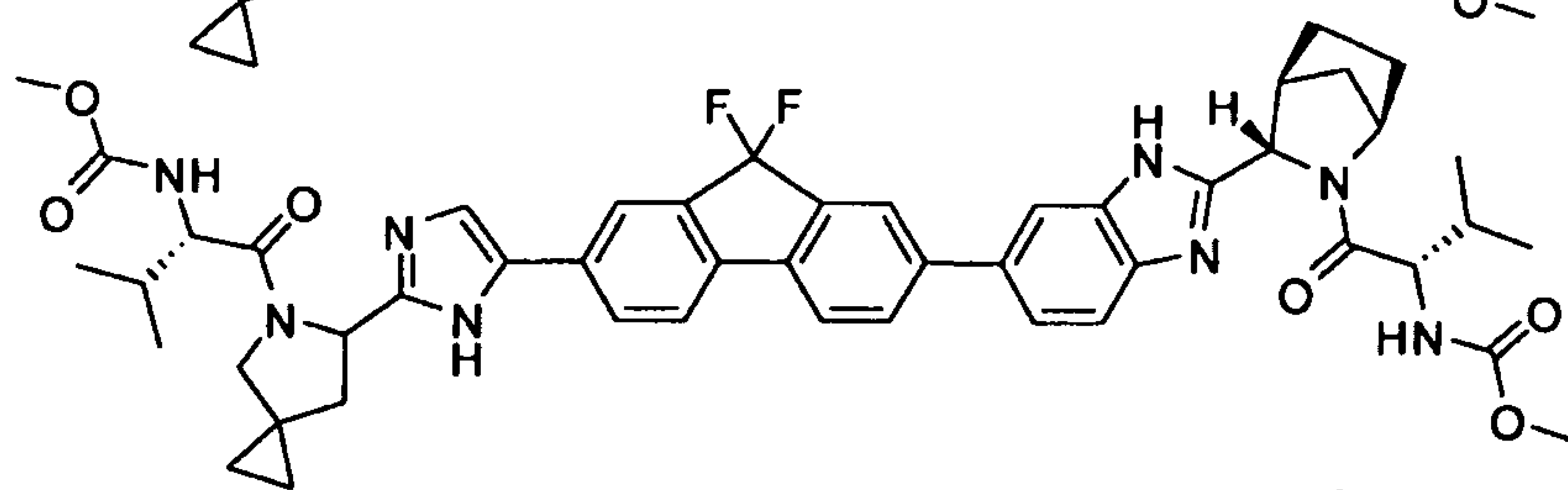
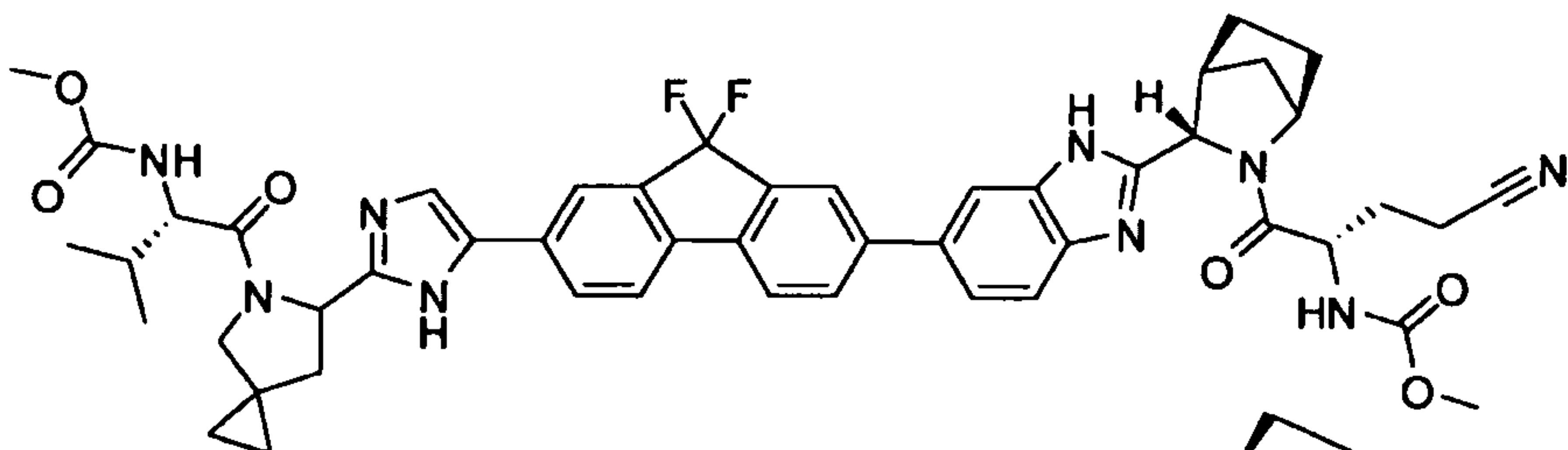
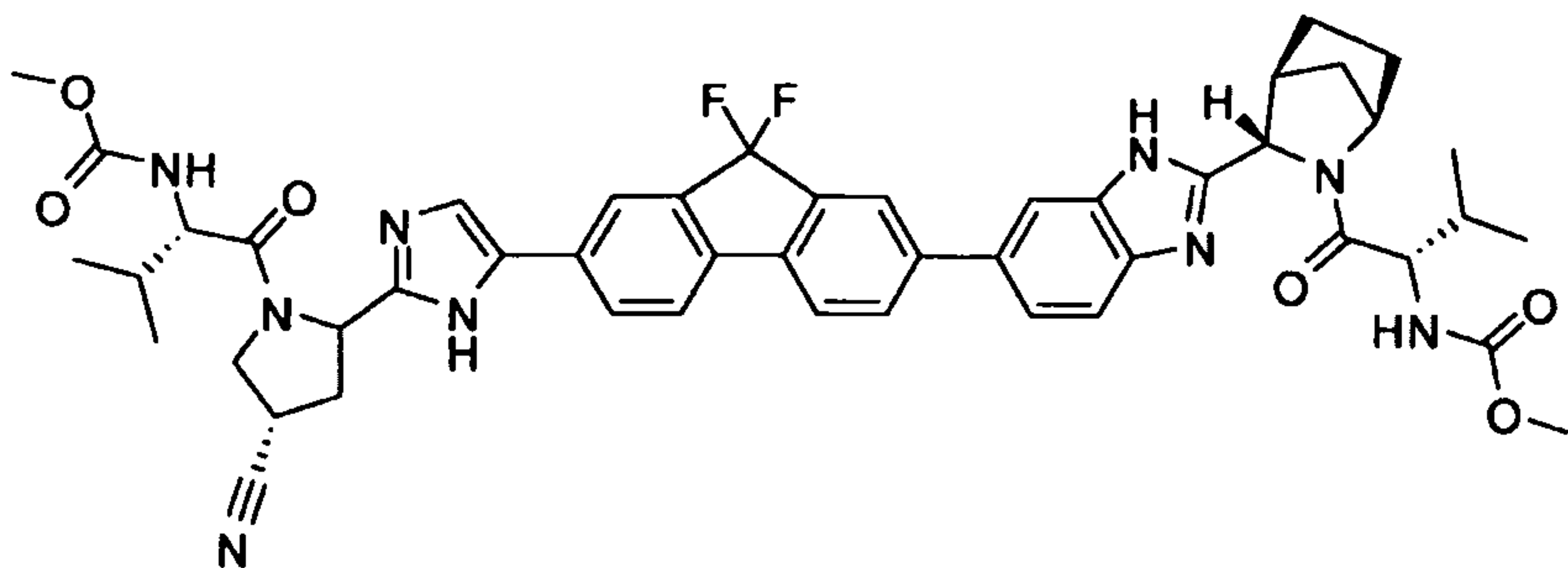
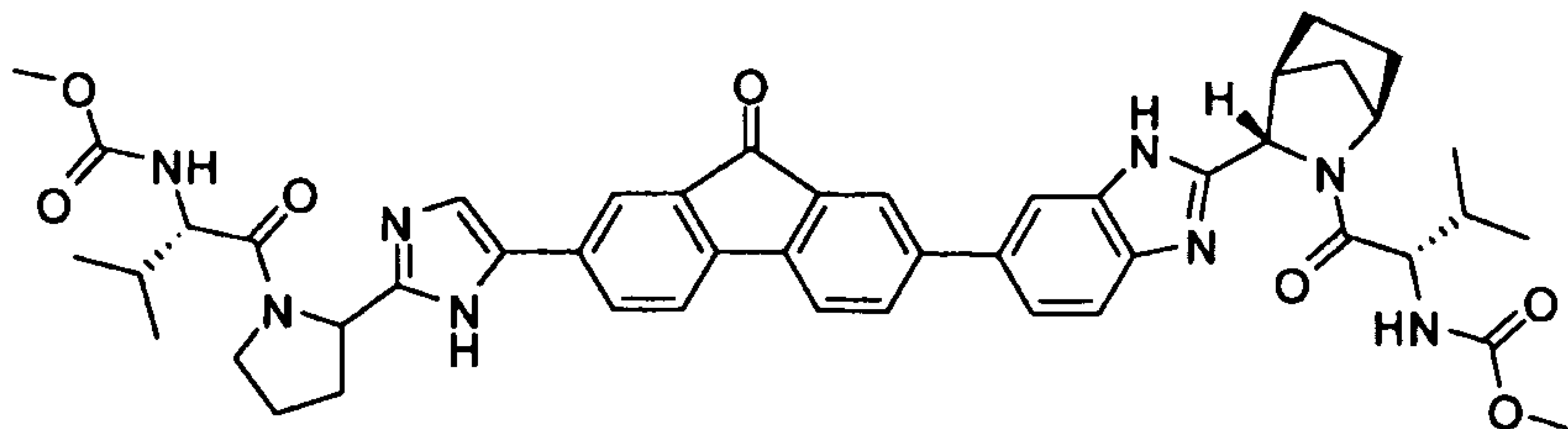
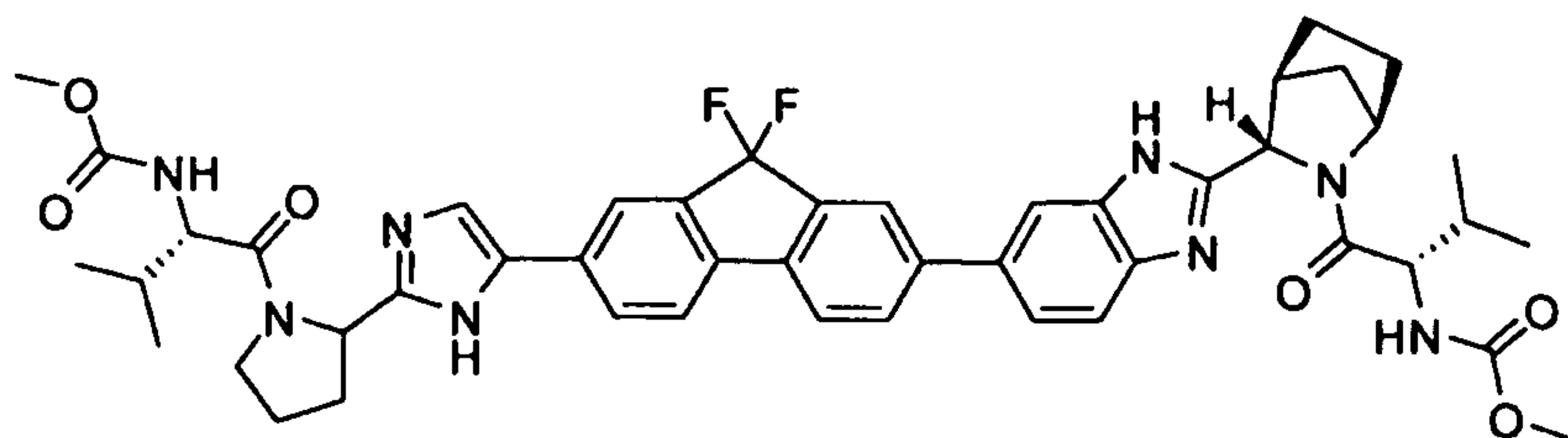
In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib6): $E^0-V^0-Z^0-P-M^0-A^{16}-L^3-P-Z^0-V^0-E^0$ (Ib6).

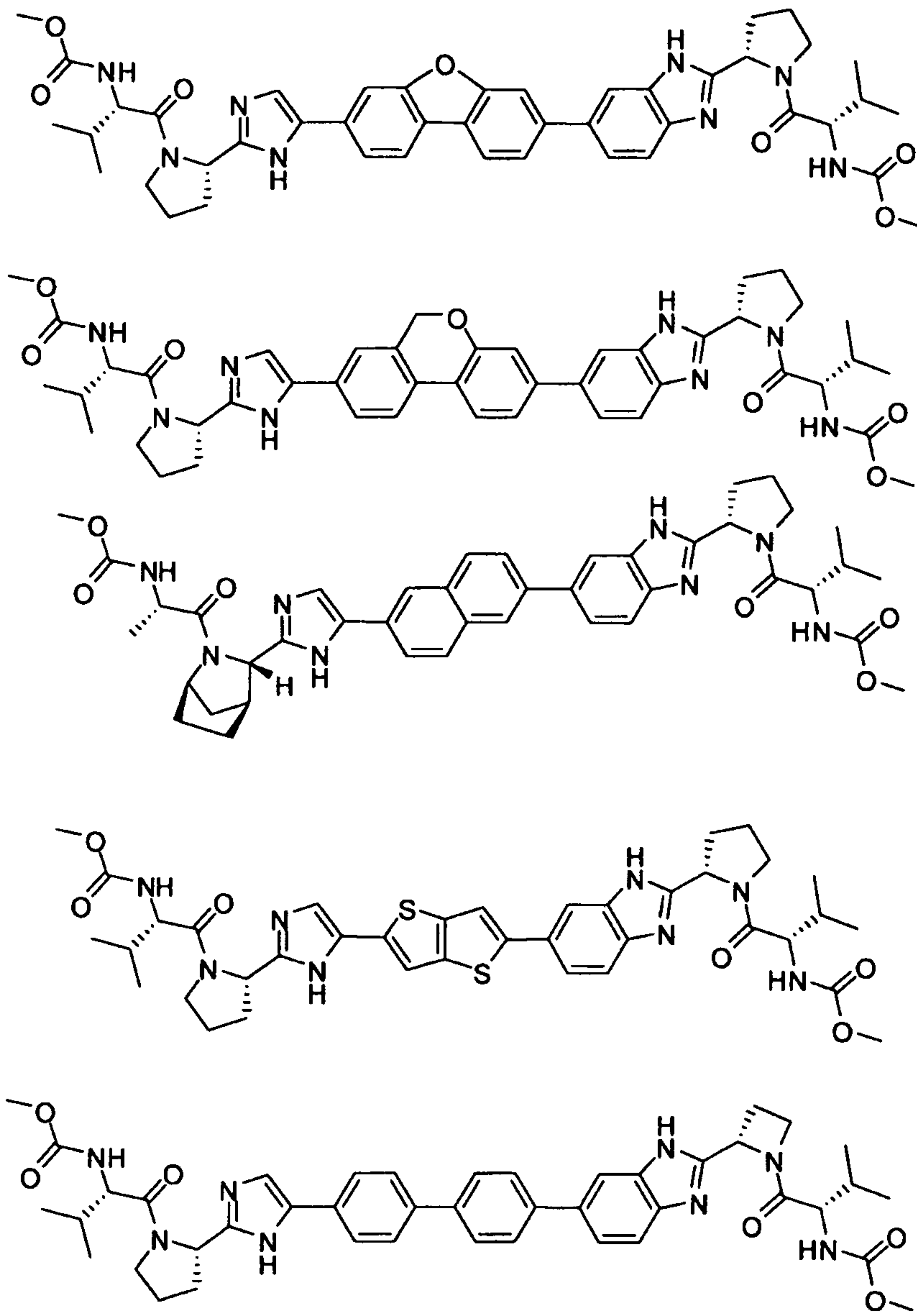
In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib7): $E^0-V^0-Z^0-P-M^0-A^{16}-L^3-P-Z^0-V^0-E^0$ (Ib7).

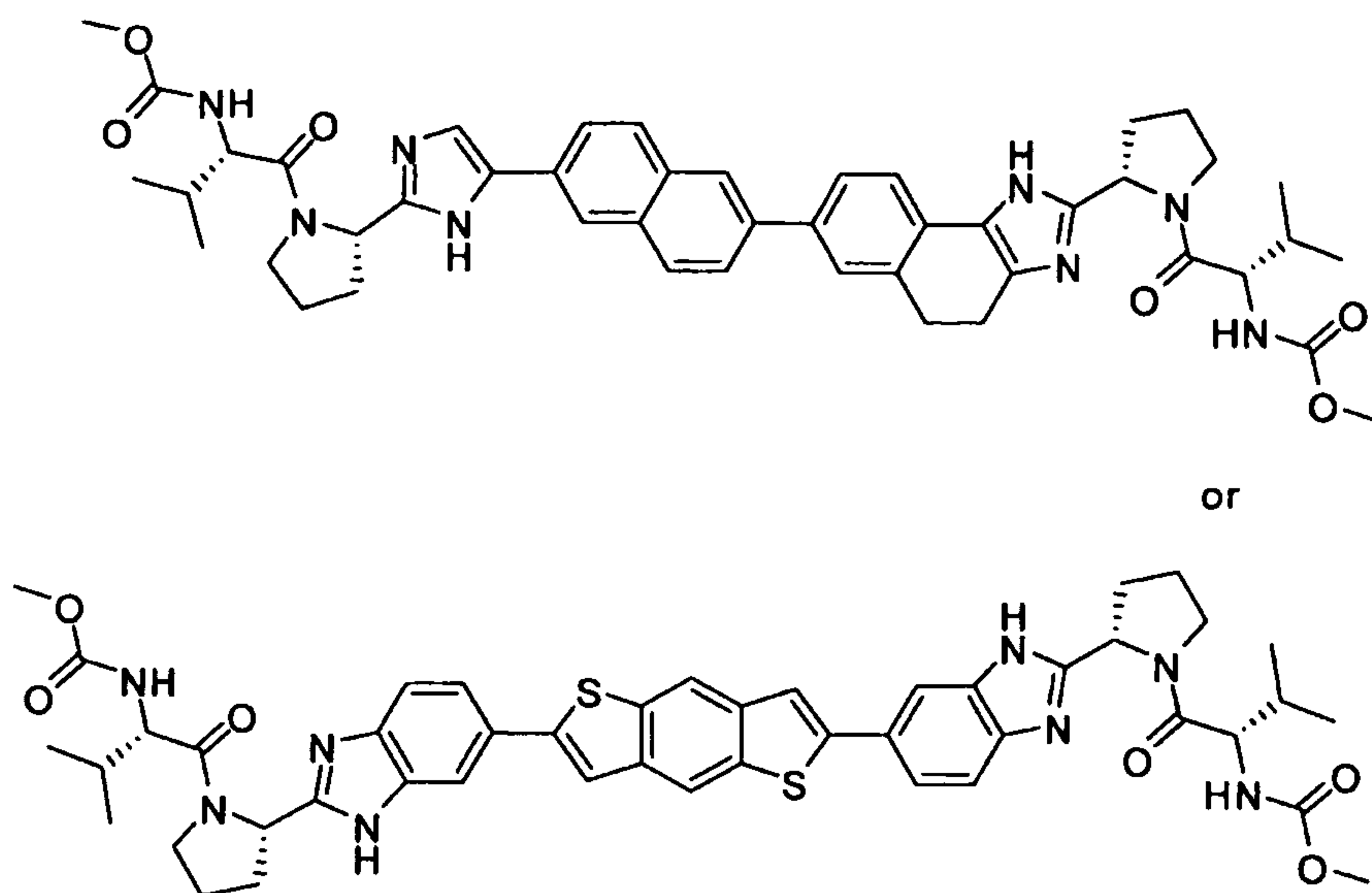
In another specific embodiment of the invention the compound of formula (Ib) is:









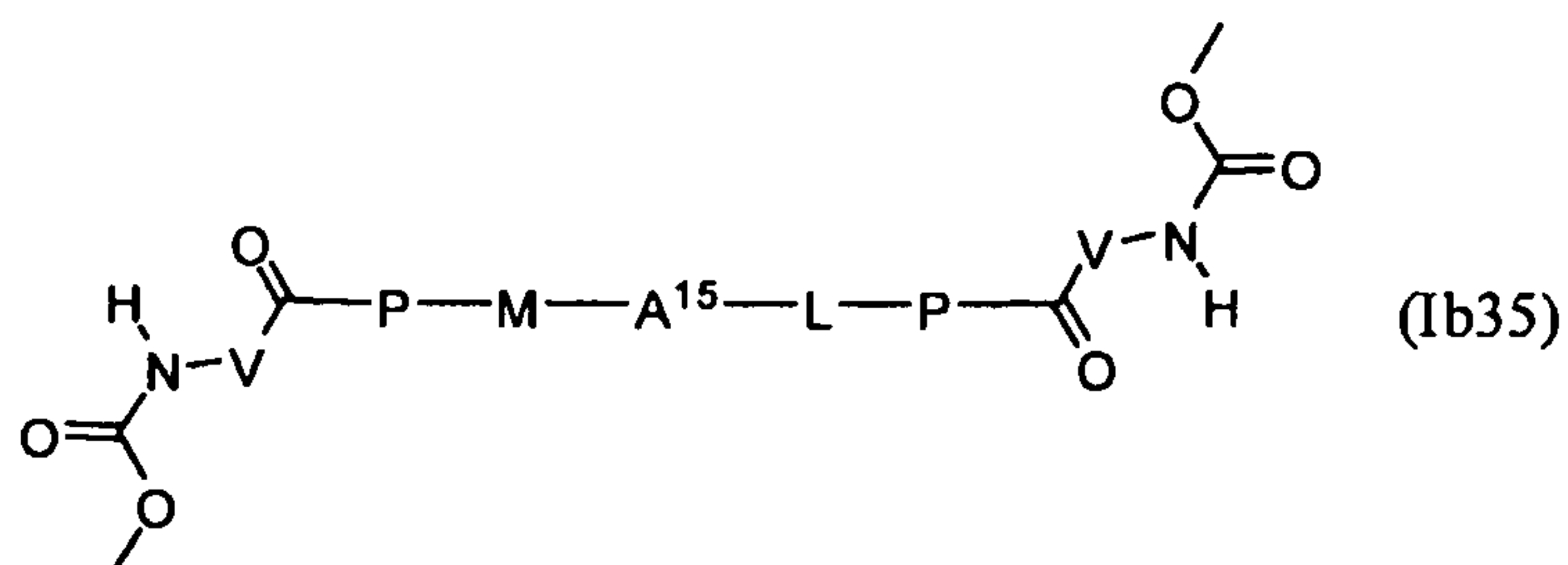


or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib60): $E^0-V-Z^0-P-M-A^{15}-L-P-Z^0-V-E^0$ (Ib60).

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib61): $E^0-V-Z^0-P-M-A^{16}-L-P-Z^0-V-E^0$ (Ib61).

In another specific embodiment the invention provides a compound of formula (Ib35):



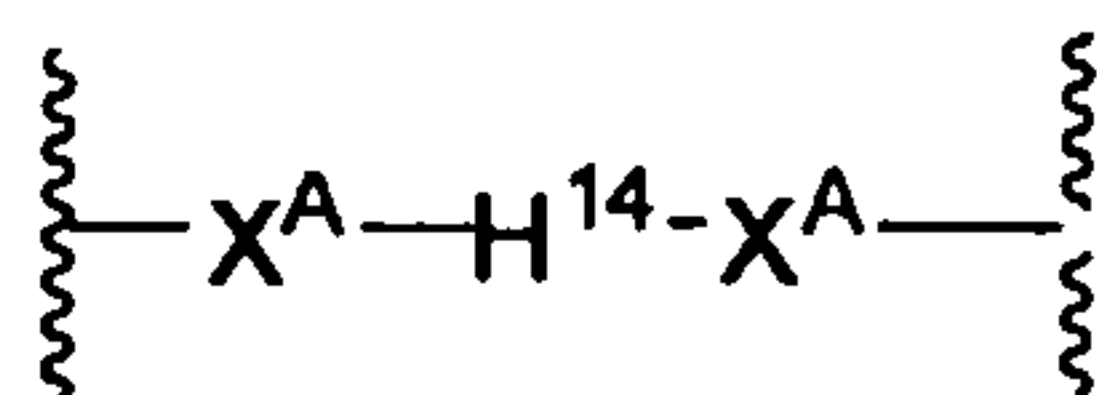
wherein:

V is alkyl;

L is benzimidazolyl;

M is a 5-membered heteroaryl ring;

A^{15} is:



each H^{14} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

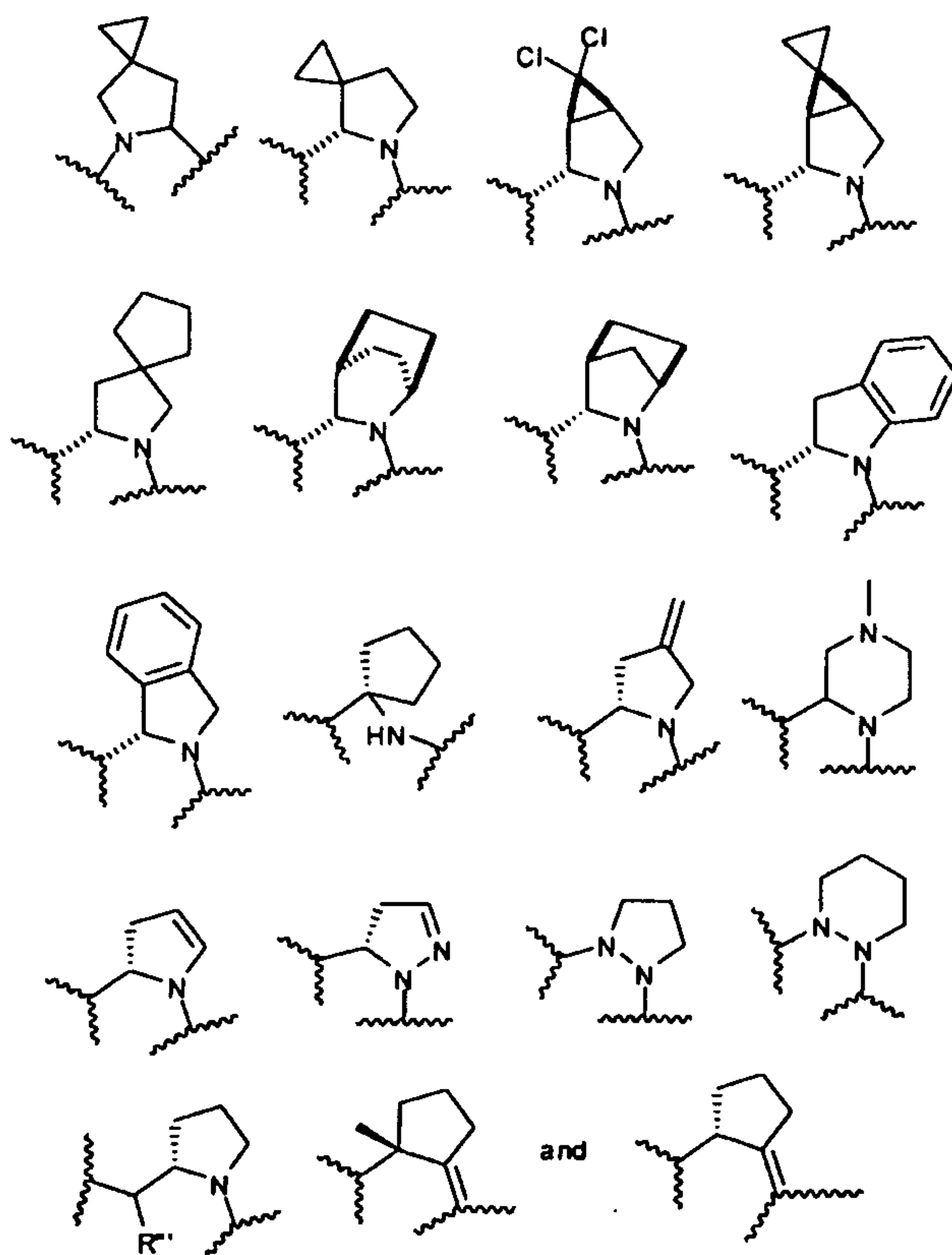
each X^A is independently O, NR, SO, SO_2 , C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , -alkyl SO_2R^4 , haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

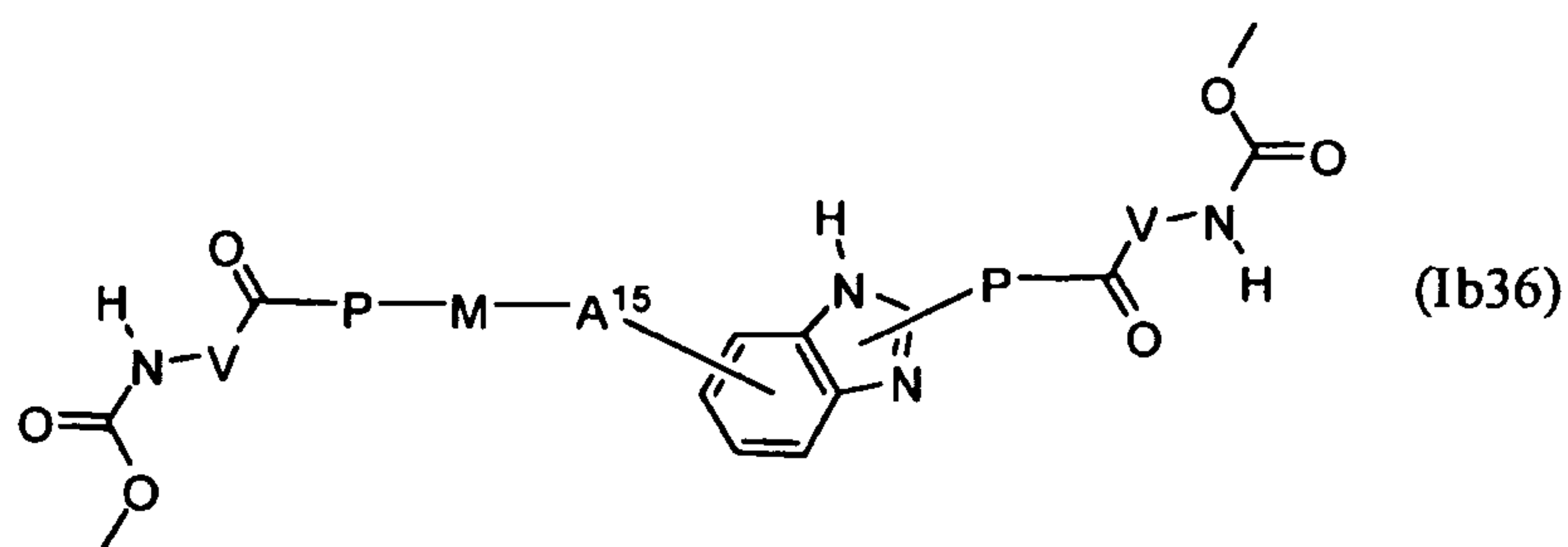
each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

each P is independently selected from:



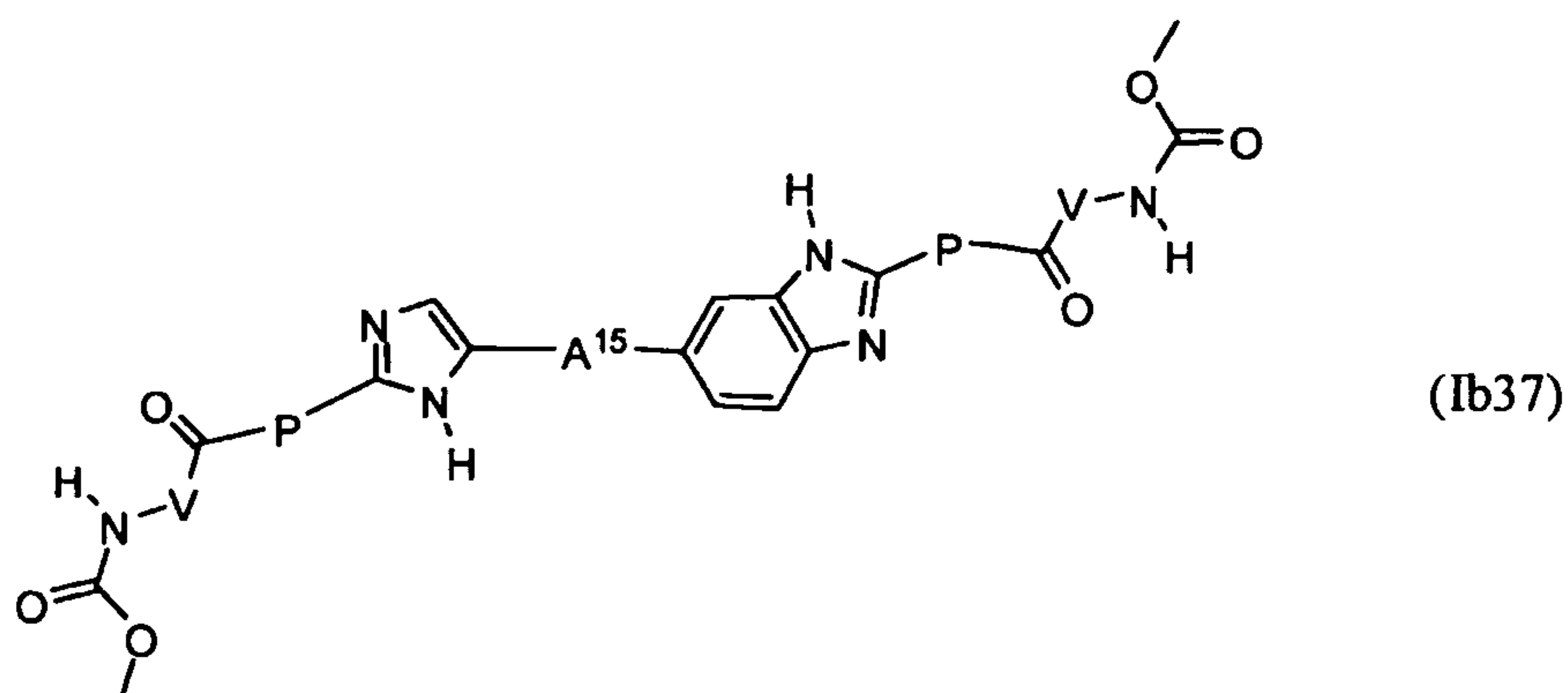
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib36):



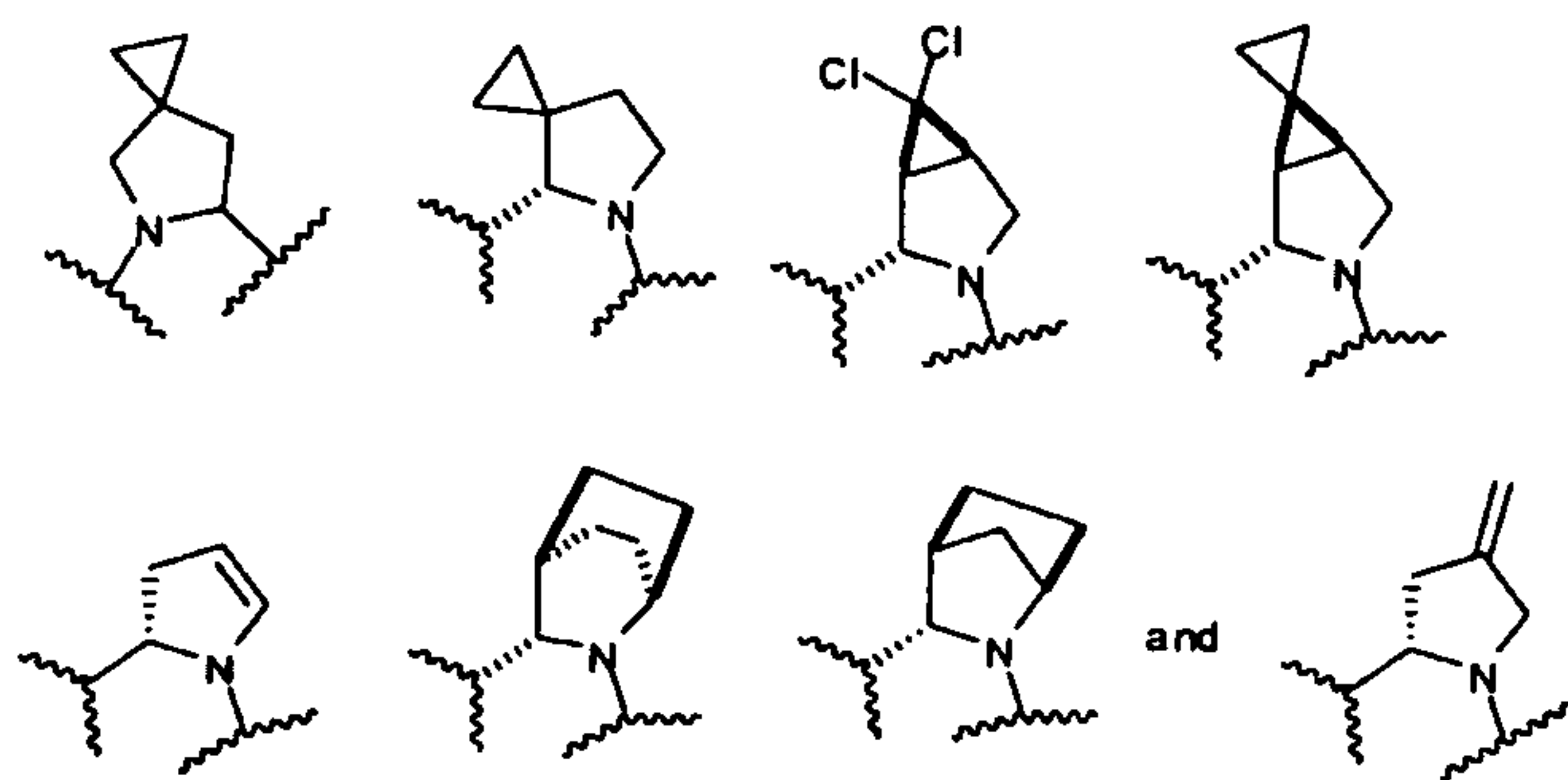
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib37):



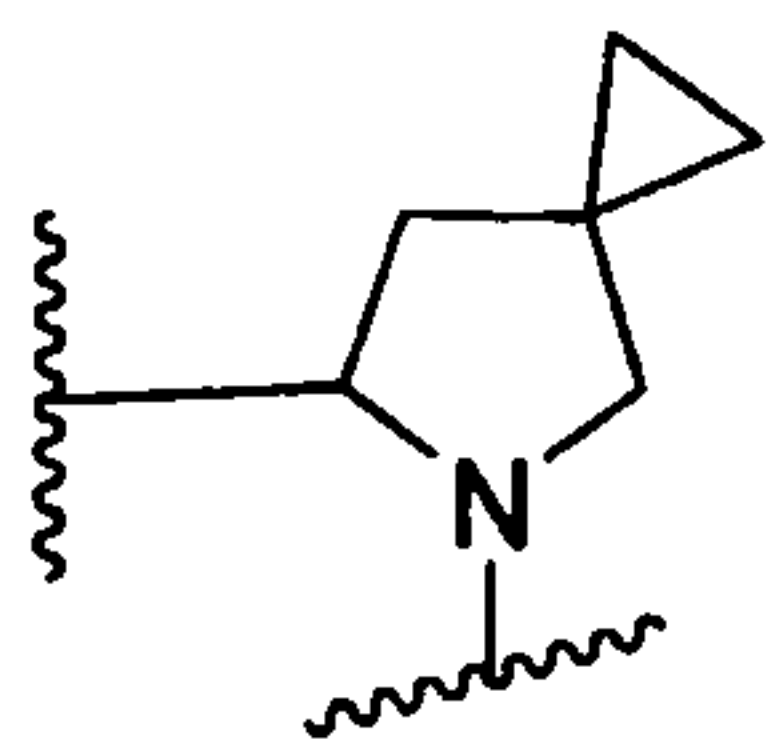
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), or (Ib37) wherein P is selected from:

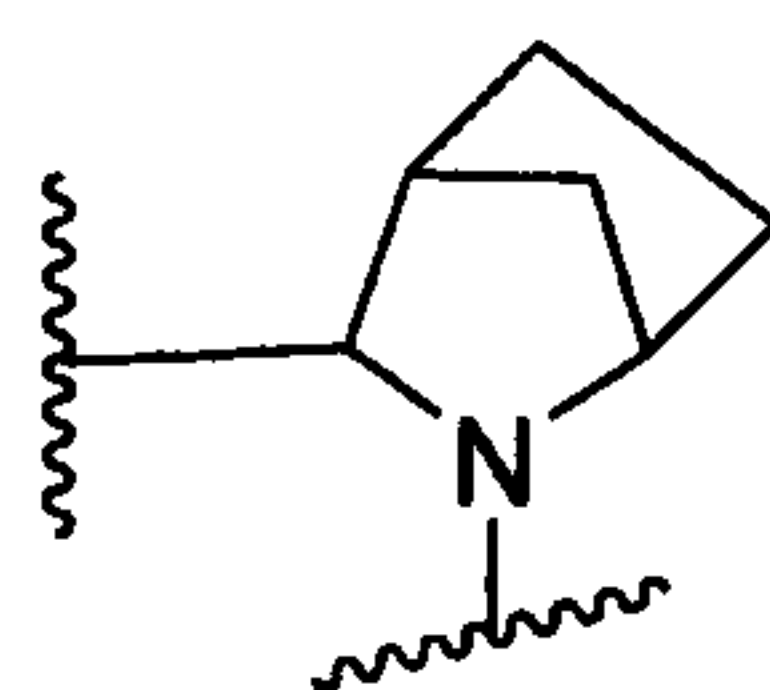


In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), or (Ib37):

wherein P is:



In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), or (Ib37): wherein P is:

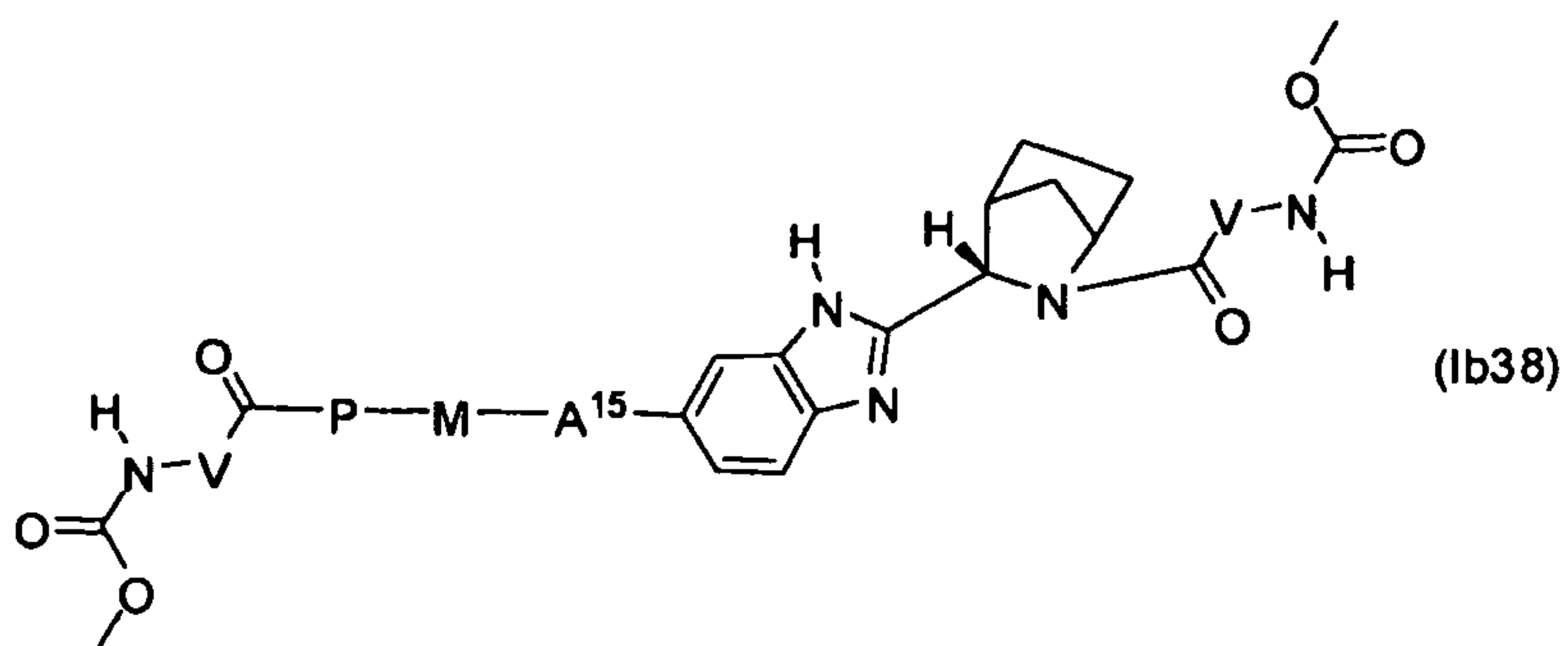


optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

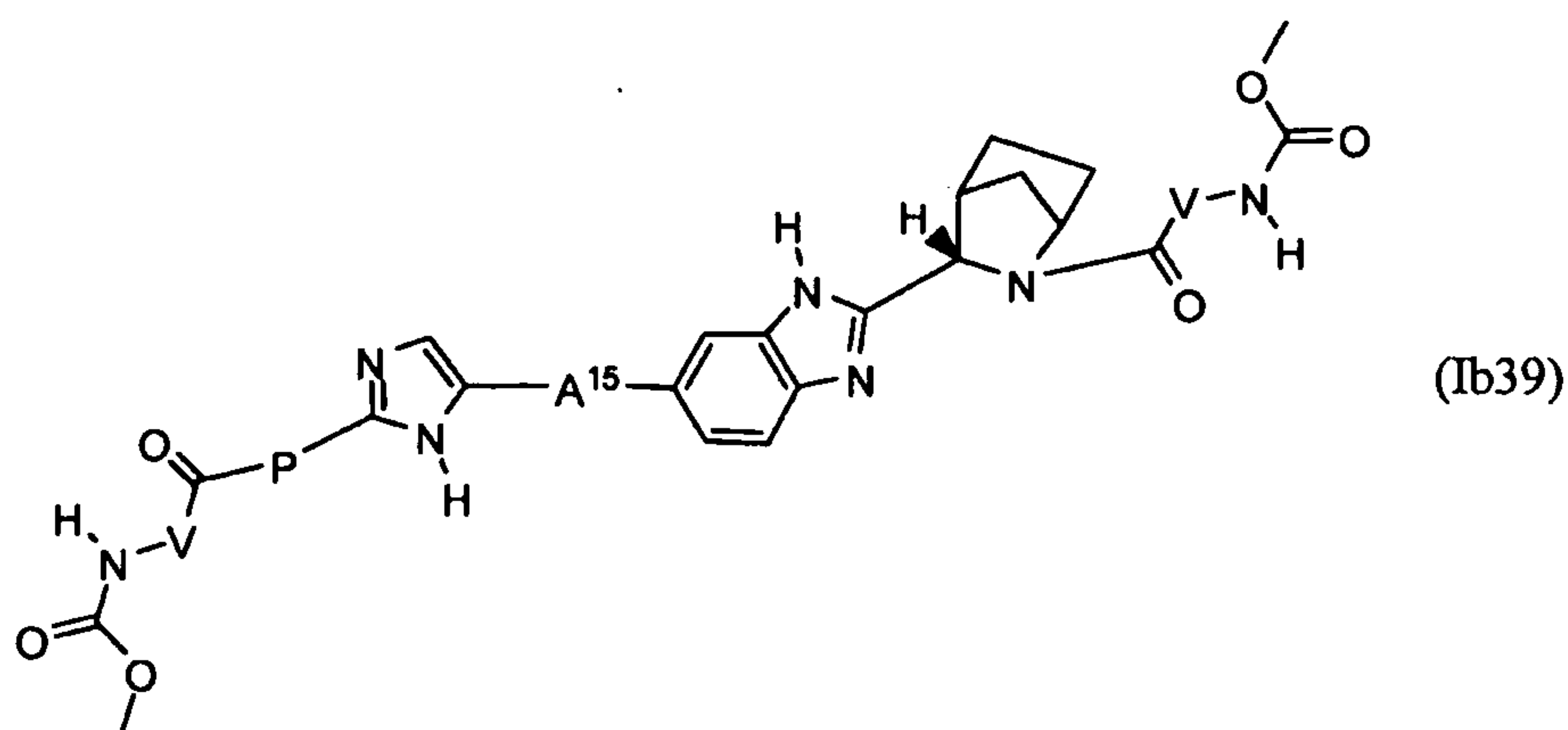
each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^{hh})$ sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, $(NR^{hh}R^{hh})$ alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^{hh}$, $(NR^{hh}R^{hh})$ alkyl, $(NR^{hh}R^{hh})$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $(NR^{hh}R^{hh})$ sulfonyl, heteroarylsulfonyl, and $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^{hh}$.

In another specific embodiment the invention provides a compound of formula (Ib38):



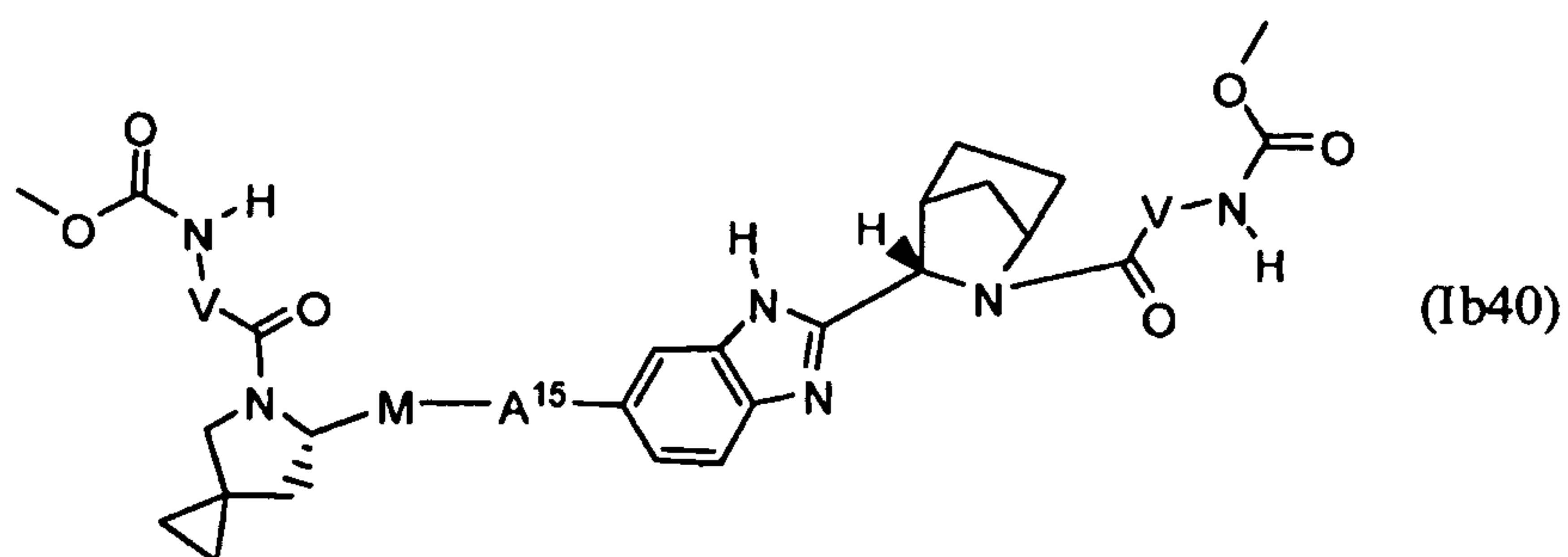
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib39):



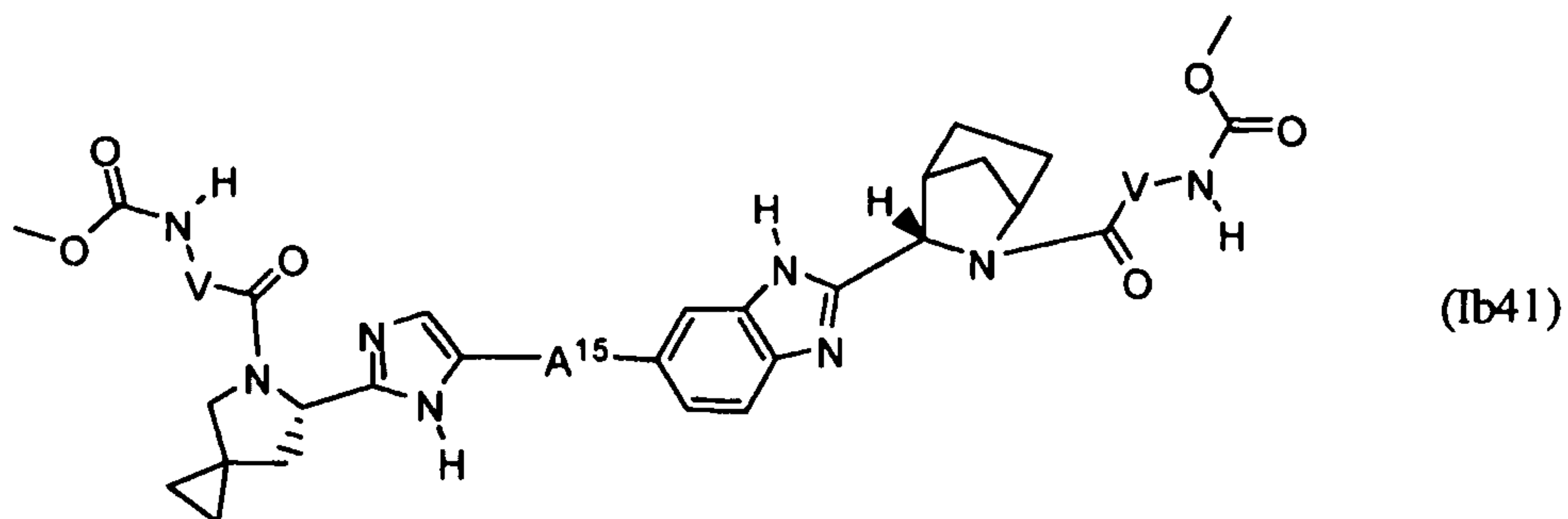
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib40):



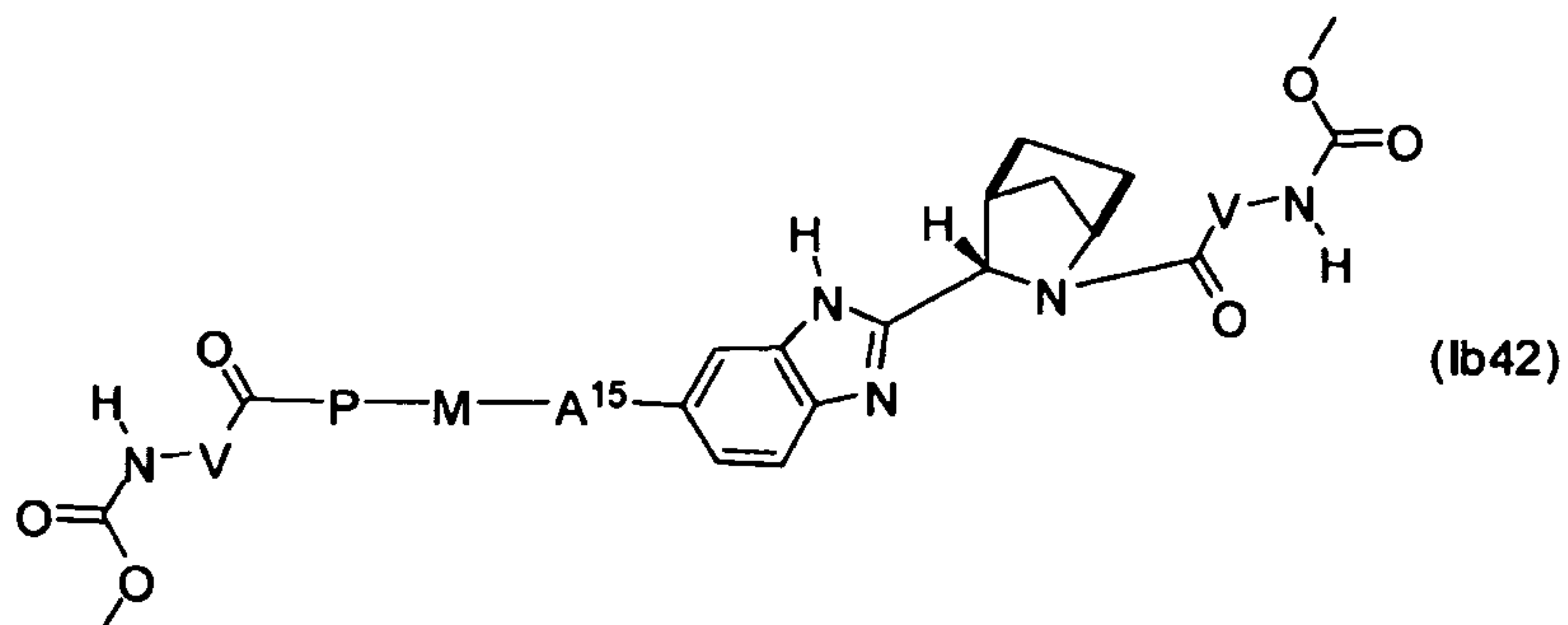
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib41):



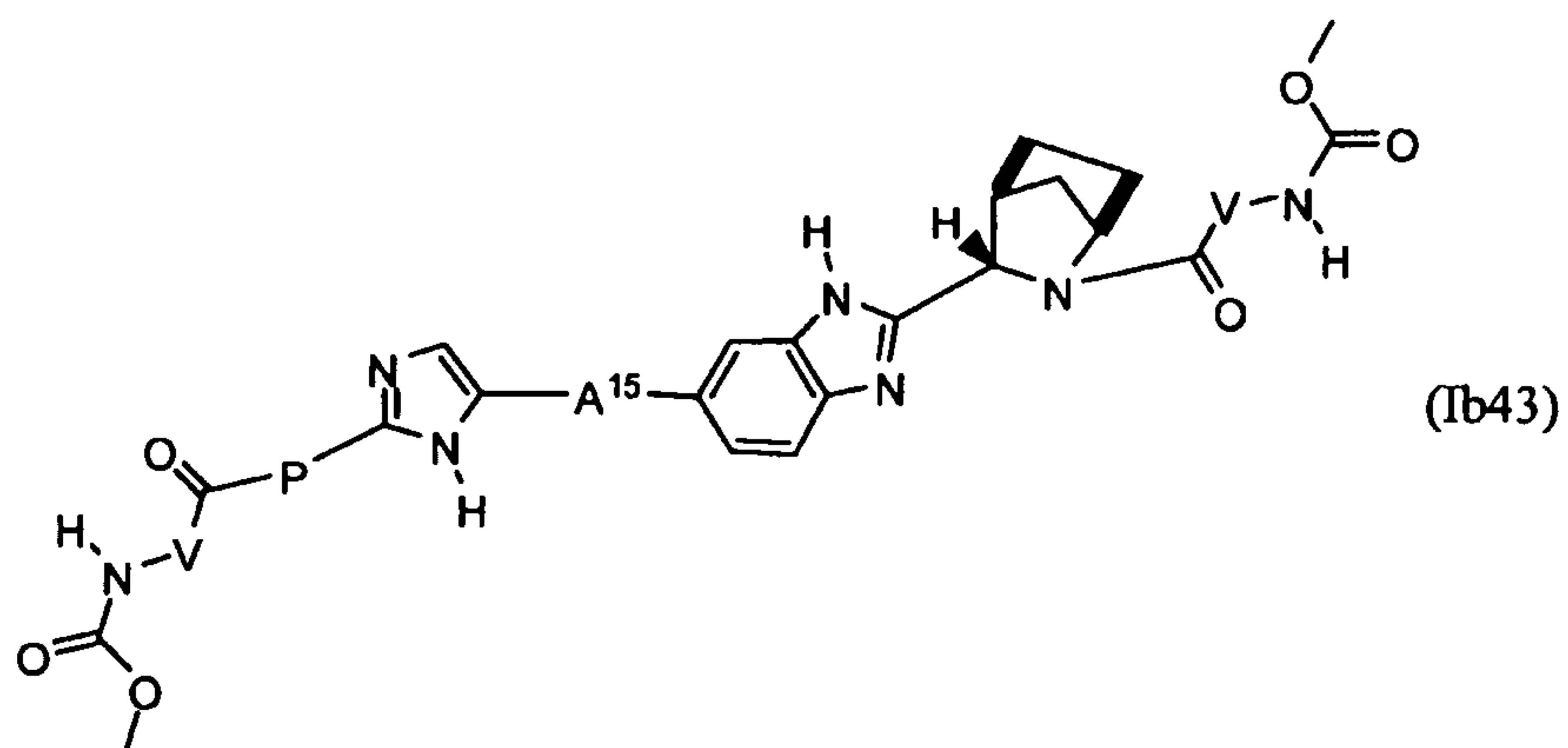
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib42):



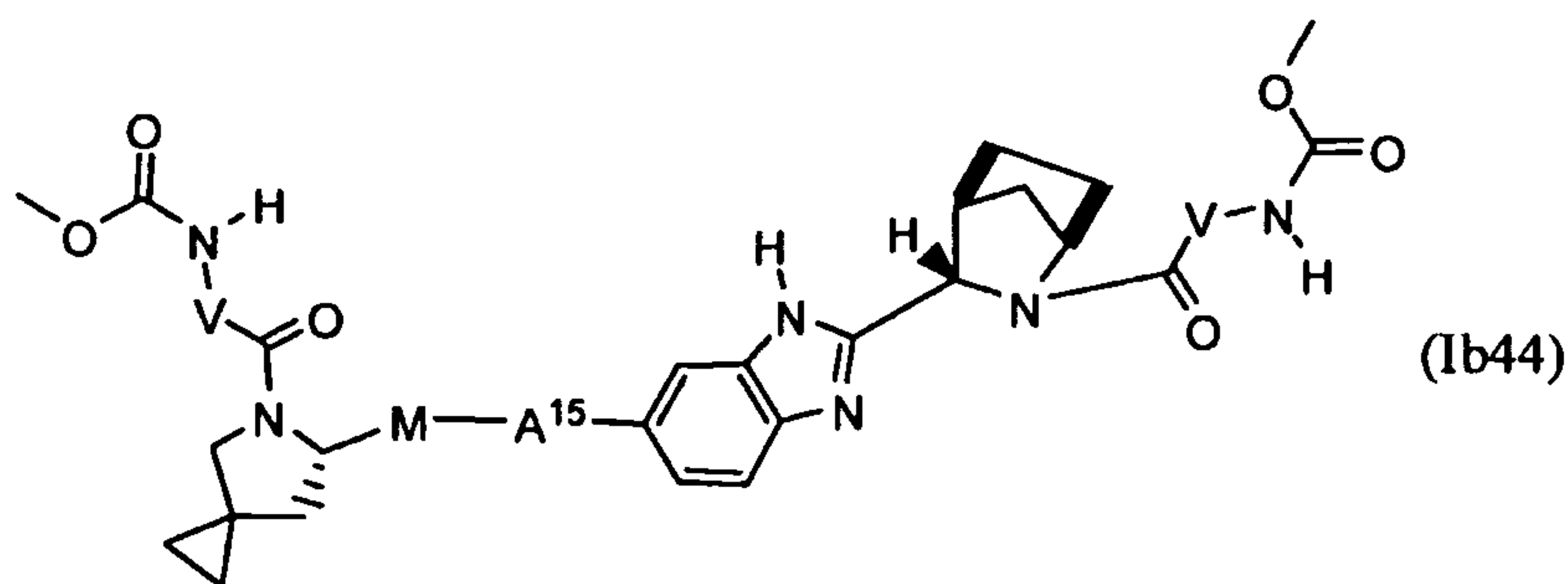
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib43):



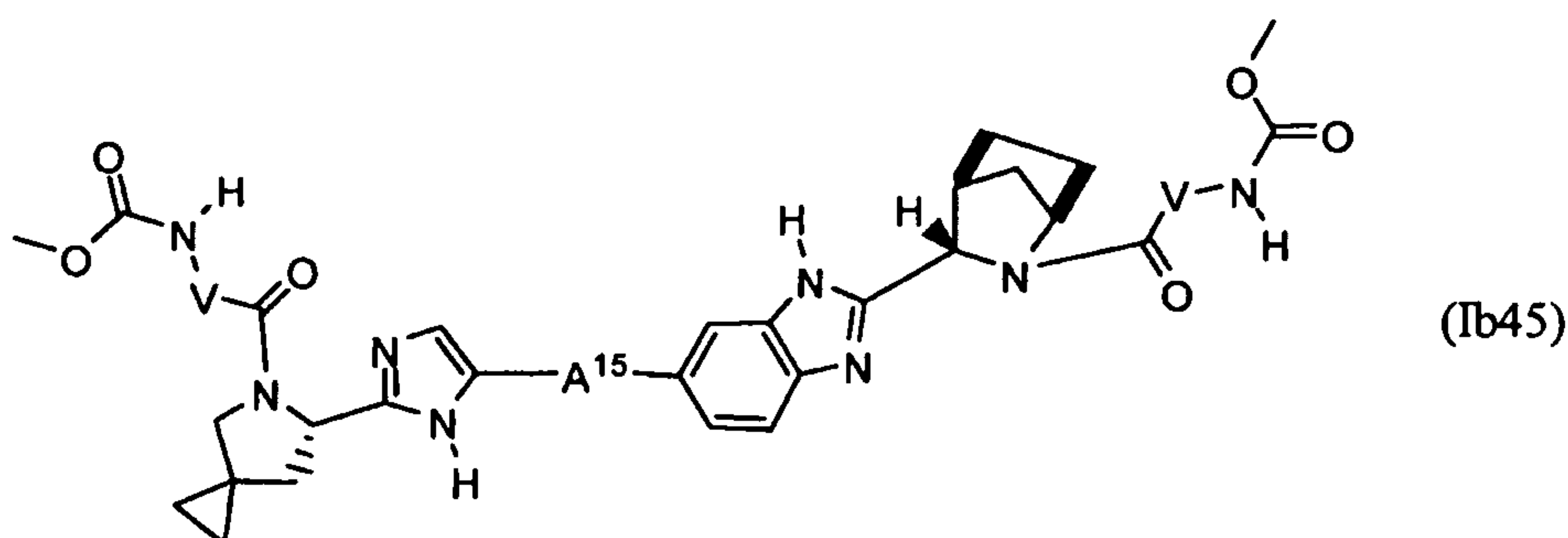
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib44):



or a pharmaceutically acceptable salt, or prodrug thereof.

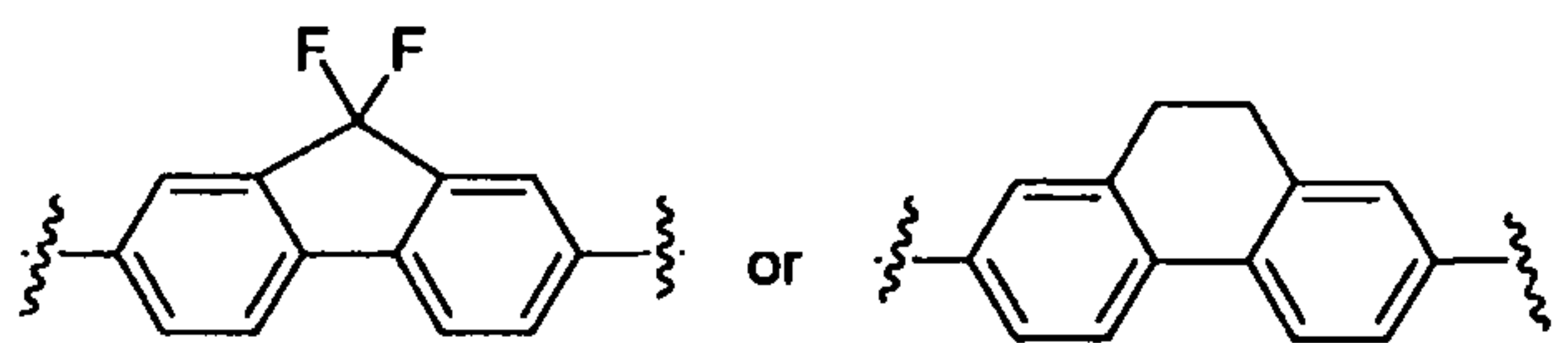
In another specific embodiment the invention provides a compound of formula (Ib45):



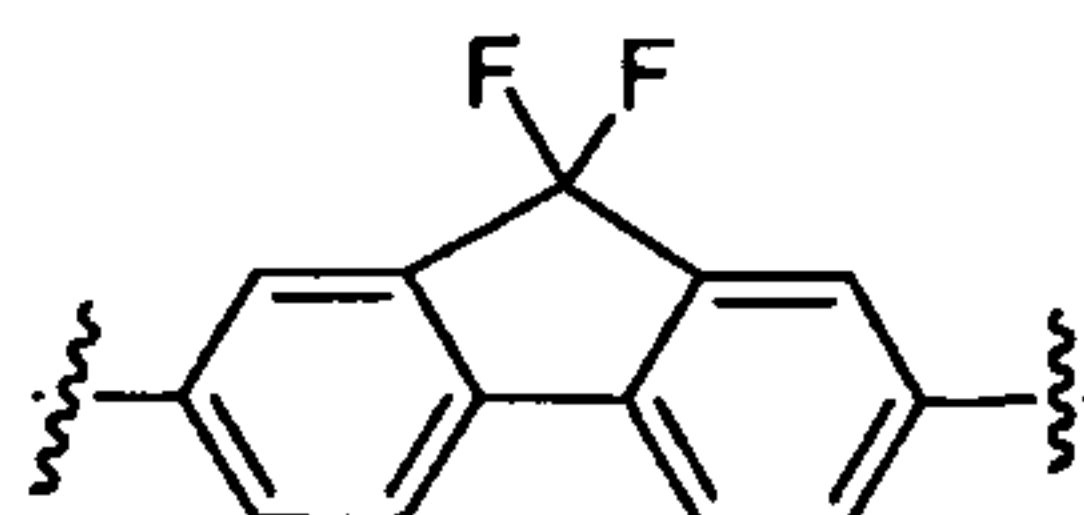
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), (Ib37), (Ib38), (Ib39), (Ib40), (Ib41), (Ib42), (Ib43), (Ib44), or (Ib45) wherein each X^A that is allowed to be absent is absent.

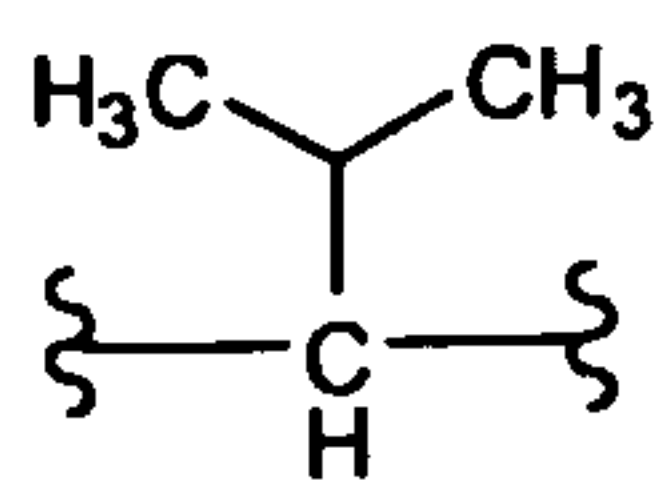
In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), (Ib37), (Ib38), (Ib39), (Ib40), (Ib41), (Ib42), (Ib43), (Ib44), or (Ib45) wherein A^{15} is selected from:



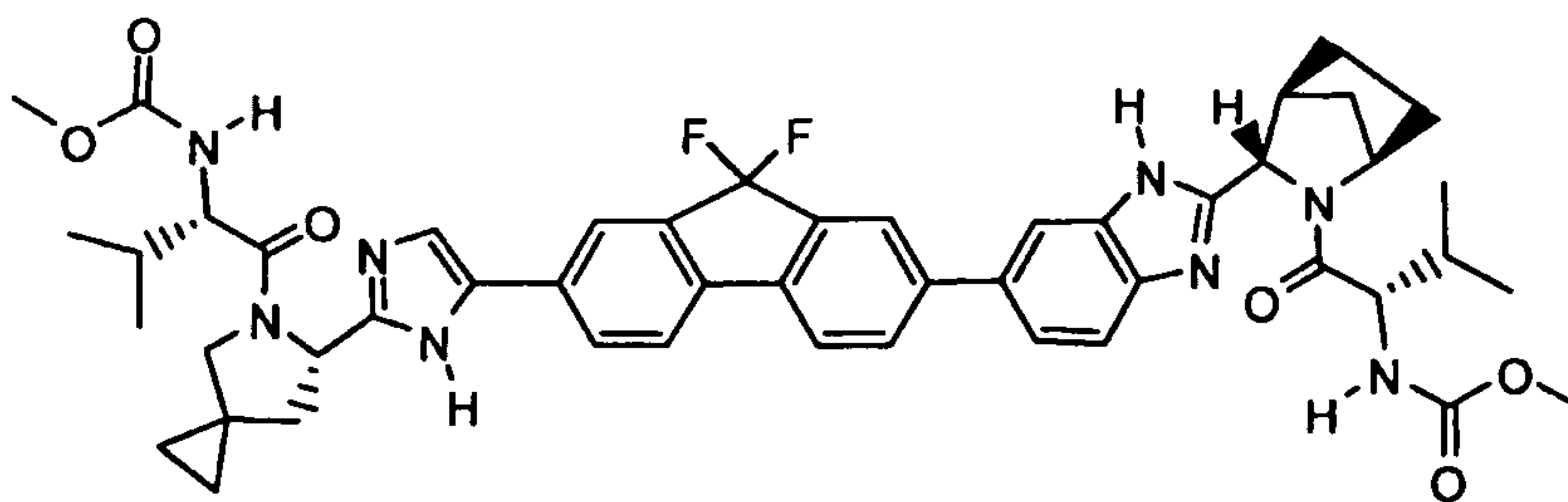
In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), (Ib37), (Ib38), (Ib39), (Ib40), (Ib41), (Ib42), (Ib43), (Ib44), or (Ib45) wherein A^{15} is selected from:



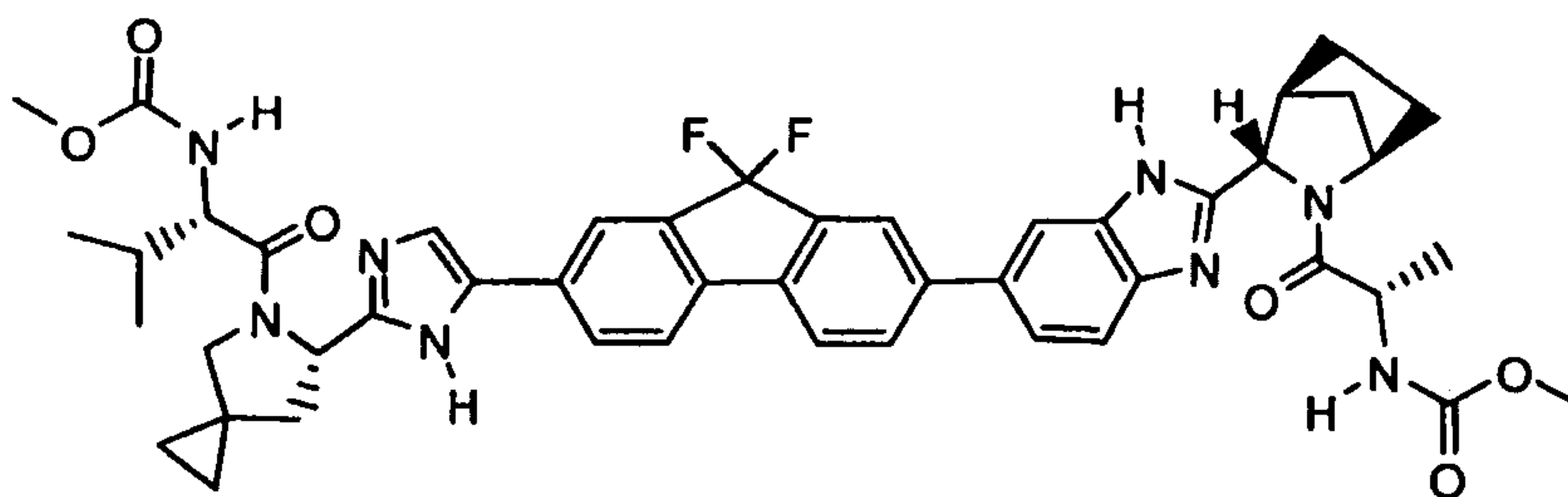
In another specific embodiment the invention provides a compound of formula (Ib35), (Ib36), (Ib37), (Ib38), (Ib39), (Ib40), (Ib41), (Ib42), (Ib43), (Ib44), or (Ib45) wherein each V is:



In another specific embodiment the invention provides a compound which is:

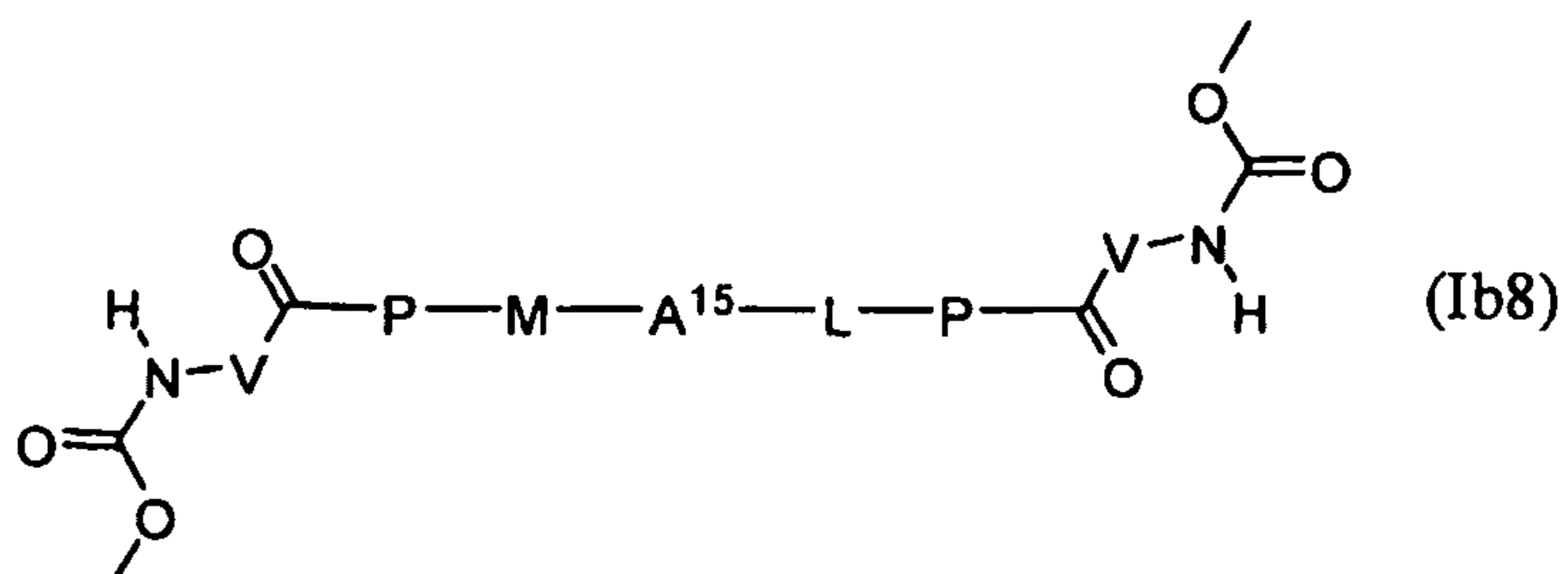


or



or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib8)



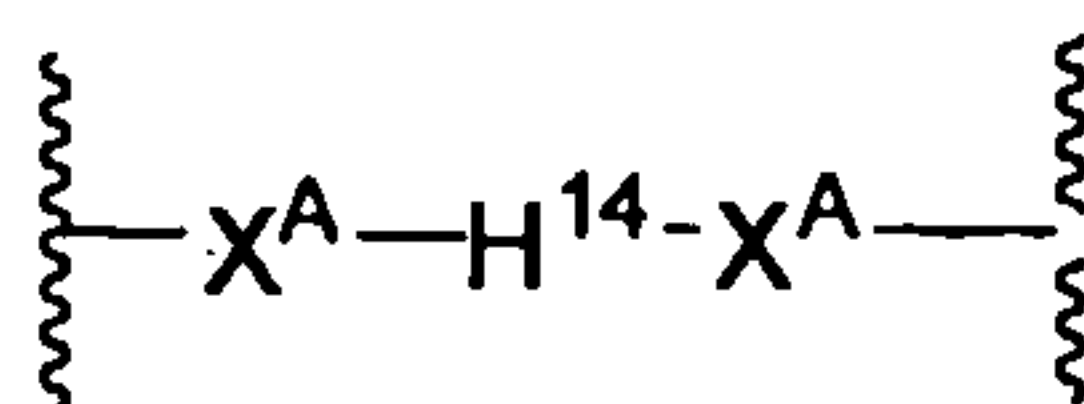
wherein:

V is alkyl;

L is benzimidazolyl;

M is a 5-membered heteroaryl ring;

A¹⁵ is:



each H^{14} is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from $\text{R}^{\text{A}1}$ and $\text{R}^{\text{A}3}$; and

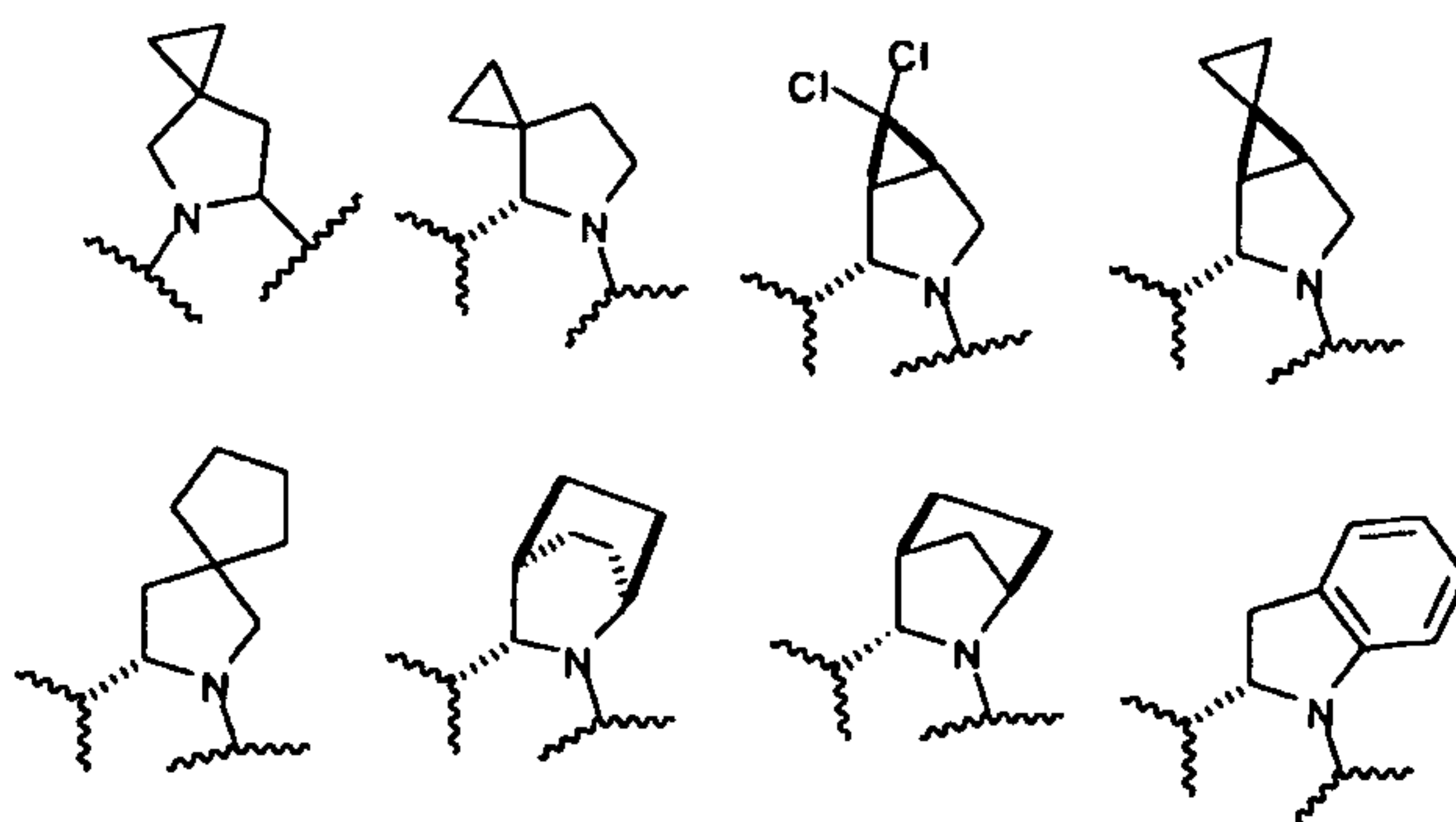
each X^{A} is independently O, NR, SO, SO_2 , C(=O), $\text{NRC}(=\text{O})$, $\text{C}(=\text{O})\text{NR}$, $\text{CR}=\text{CR}$, $\text{NRC}(=\text{O})\text{NR}$, allenyl, alkynyl, or absent and each R is independently selected from H or alkyl;

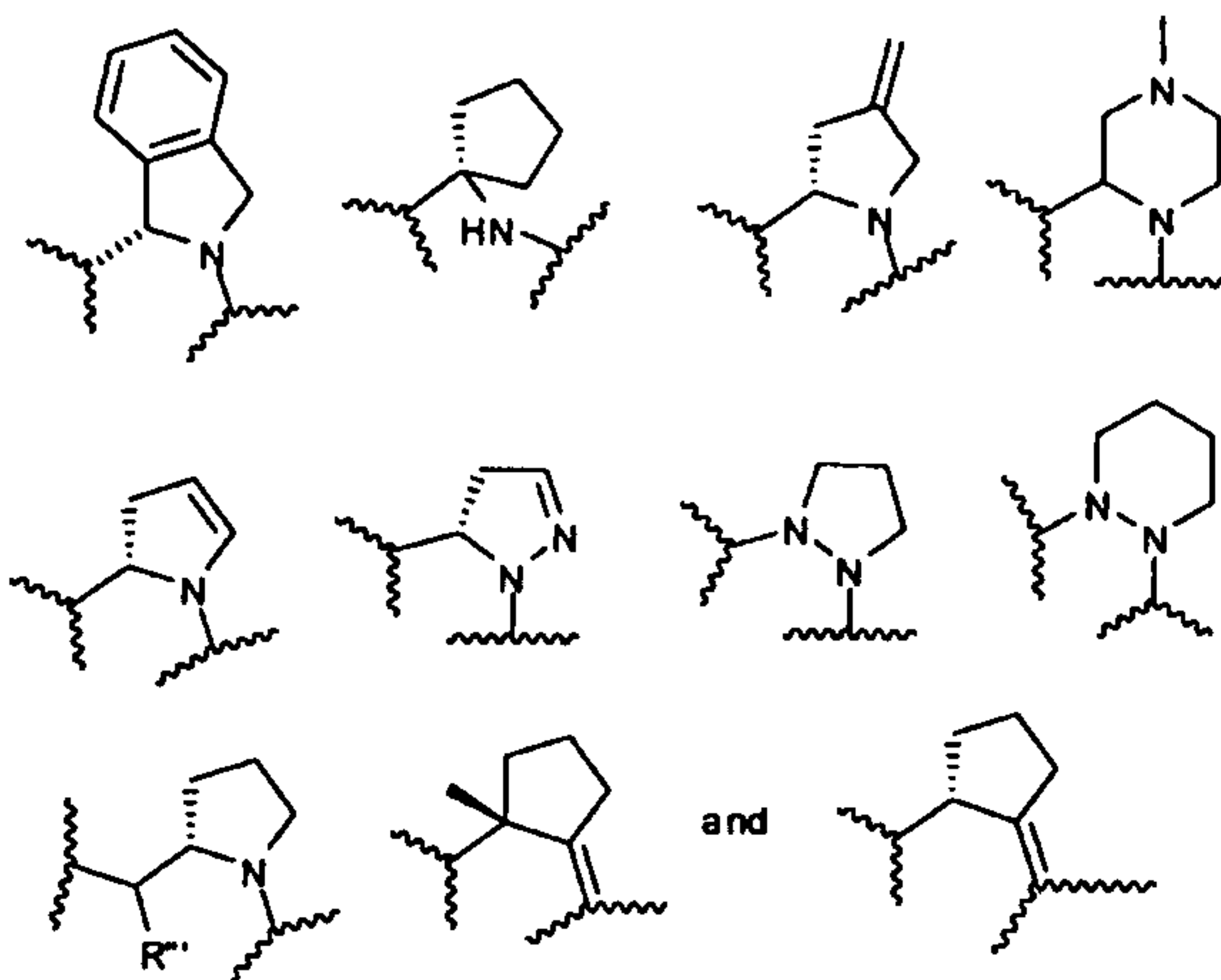
each $\text{R}^{\text{A}1}$ is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , -alkyl SO_2R^4 , haloalkoxy, cyanoalkyl, $\text{NR}^4\text{SO}_2\text{R}^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each $\text{R}^{\text{A}3}$ is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-\text{NR}^{\text{a}}\text{R}^{\text{b}}$, $(\text{NR}^{\text{a}}\text{R}^{\text{b}})\text{alkyl}$, and $(\text{NR}^{\text{a}}\text{R}^{\text{b}})\text{carbonyl}$; R^{a} and R^{b} are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

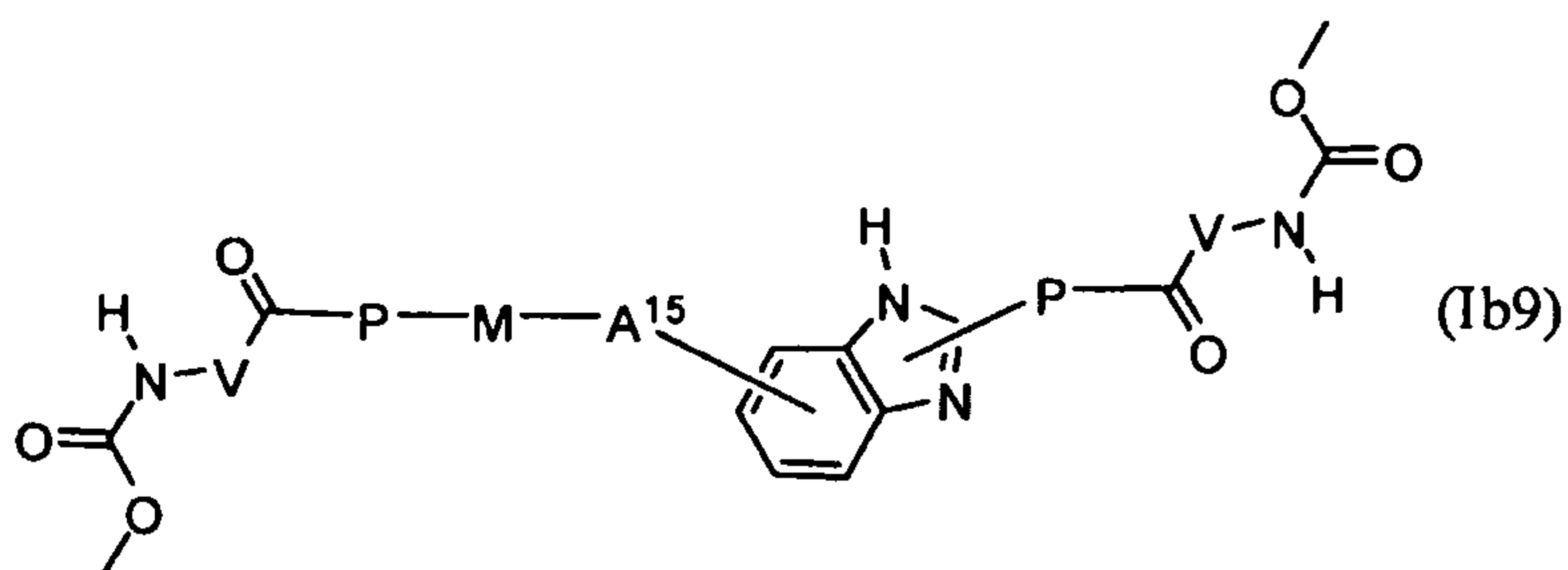
P is selected from:





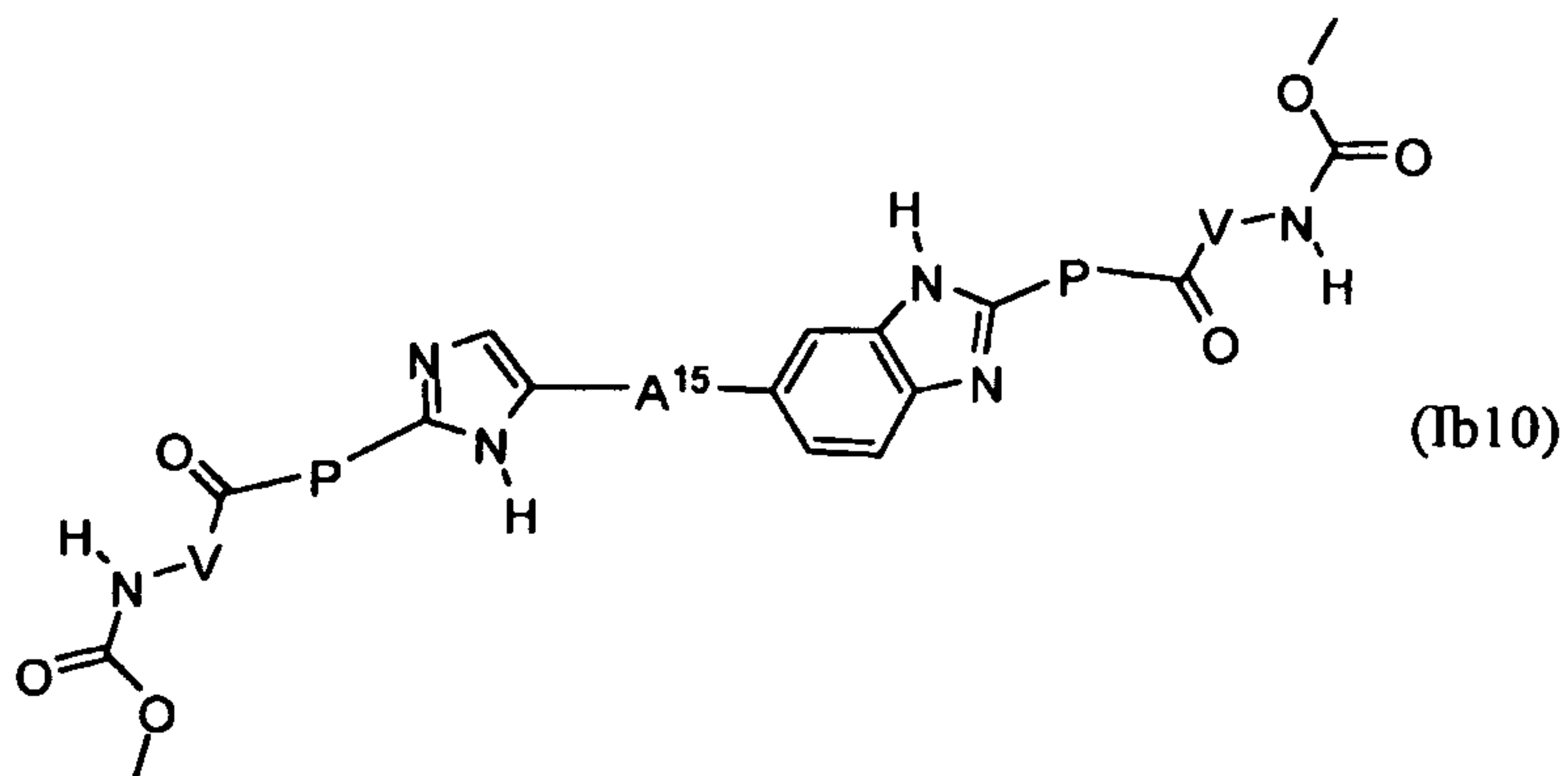
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib9):



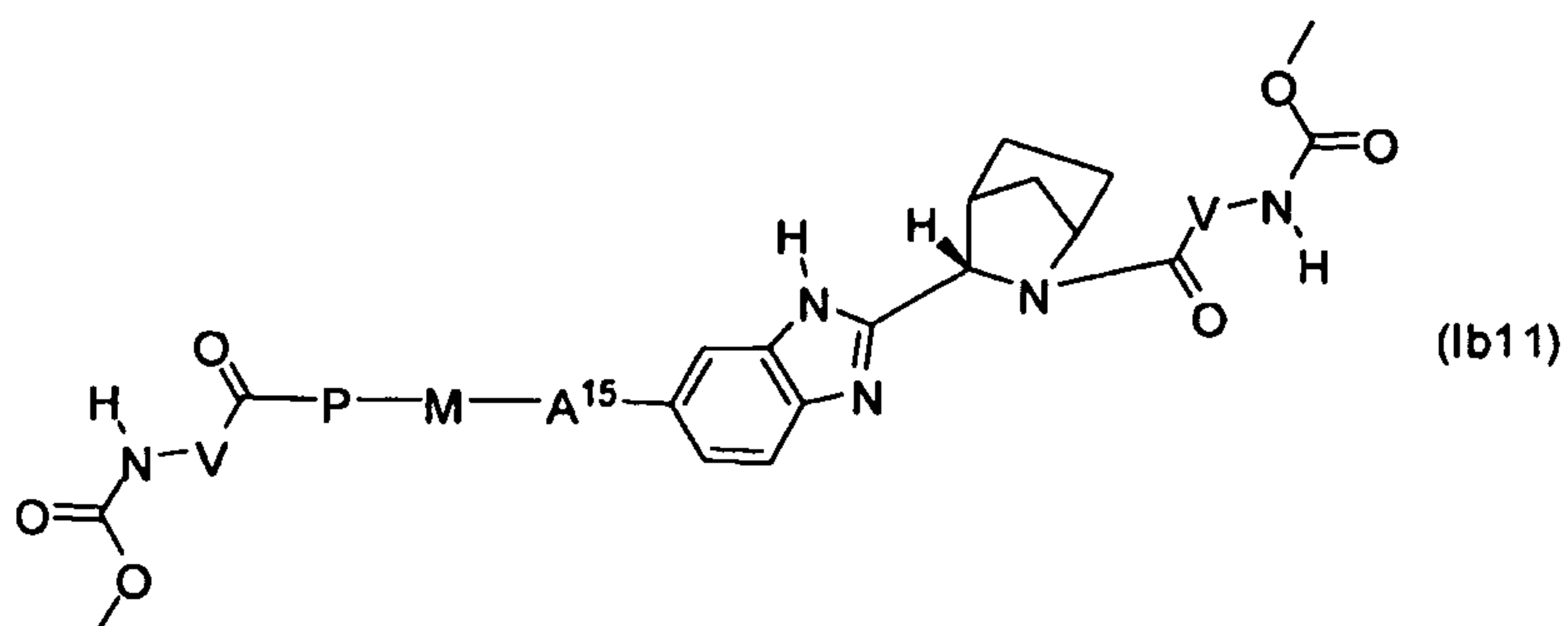
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib10):



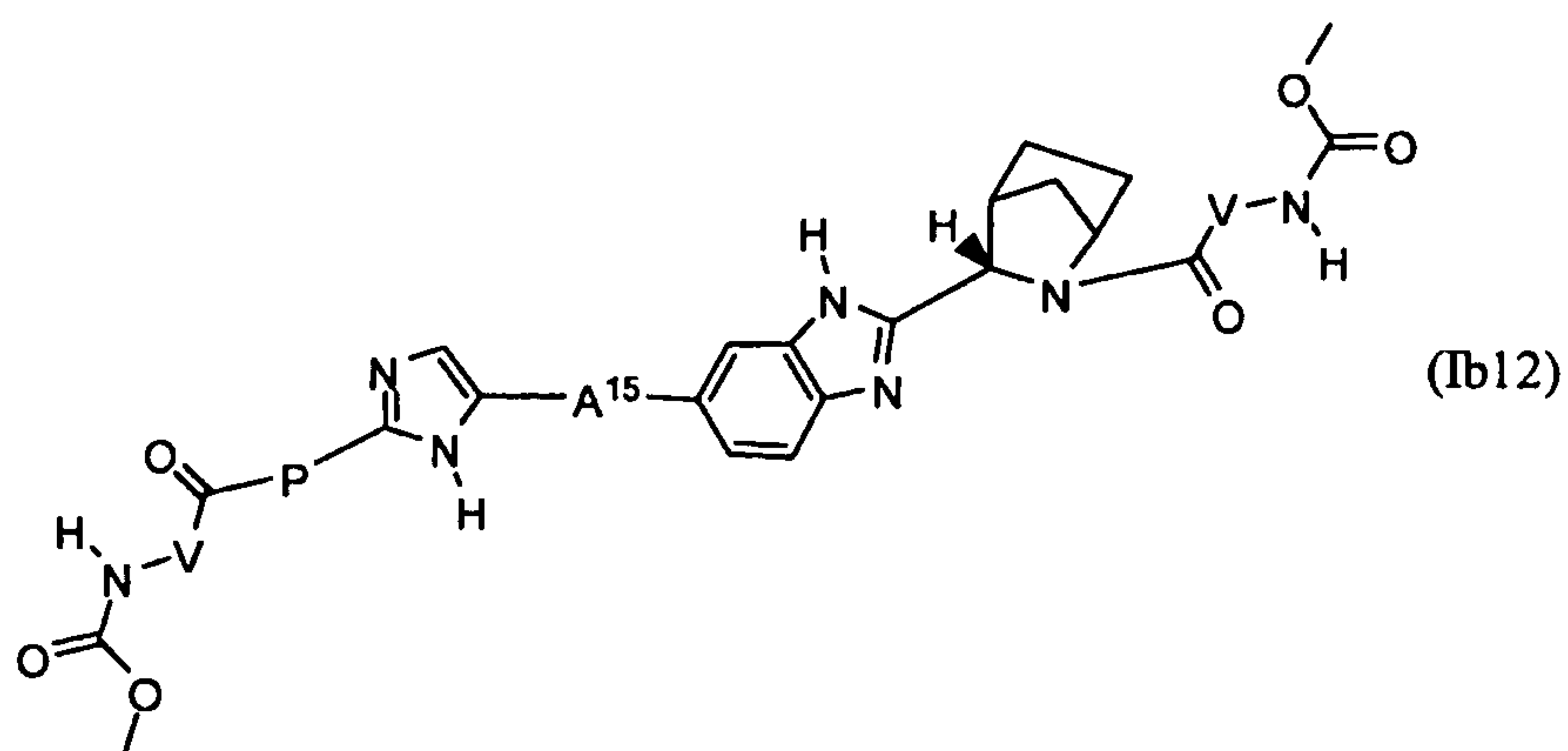
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib11):



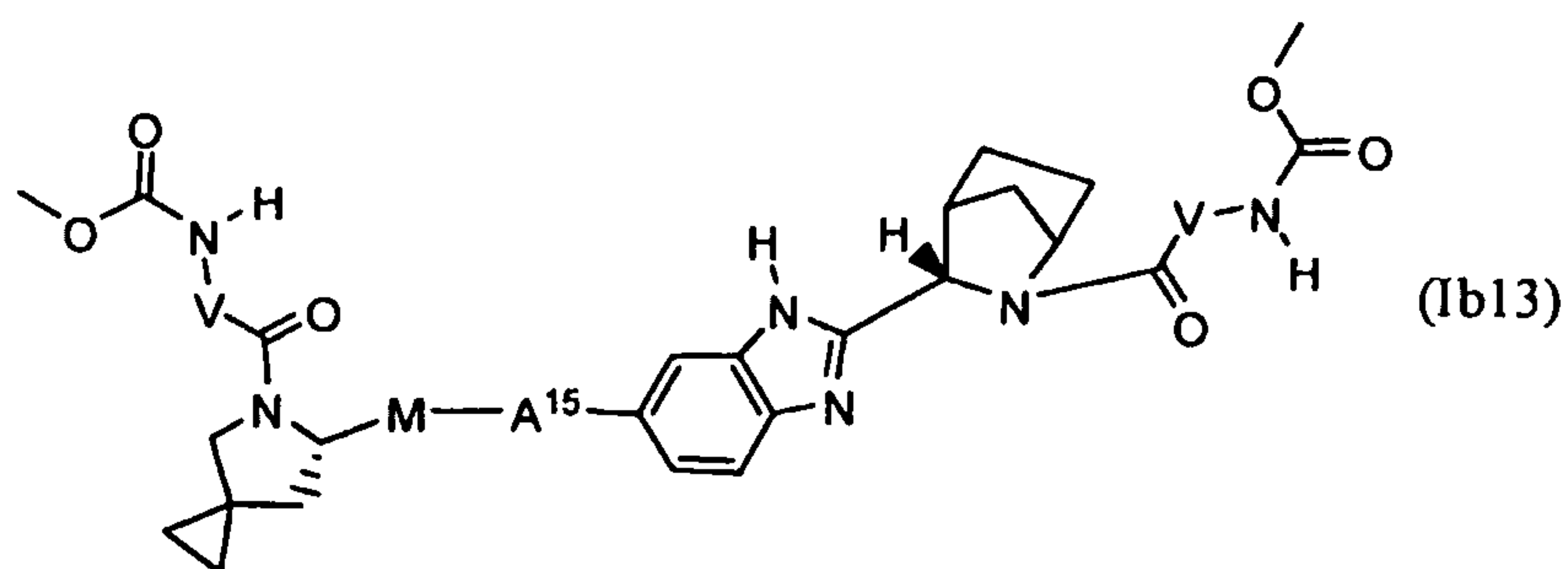
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib12):



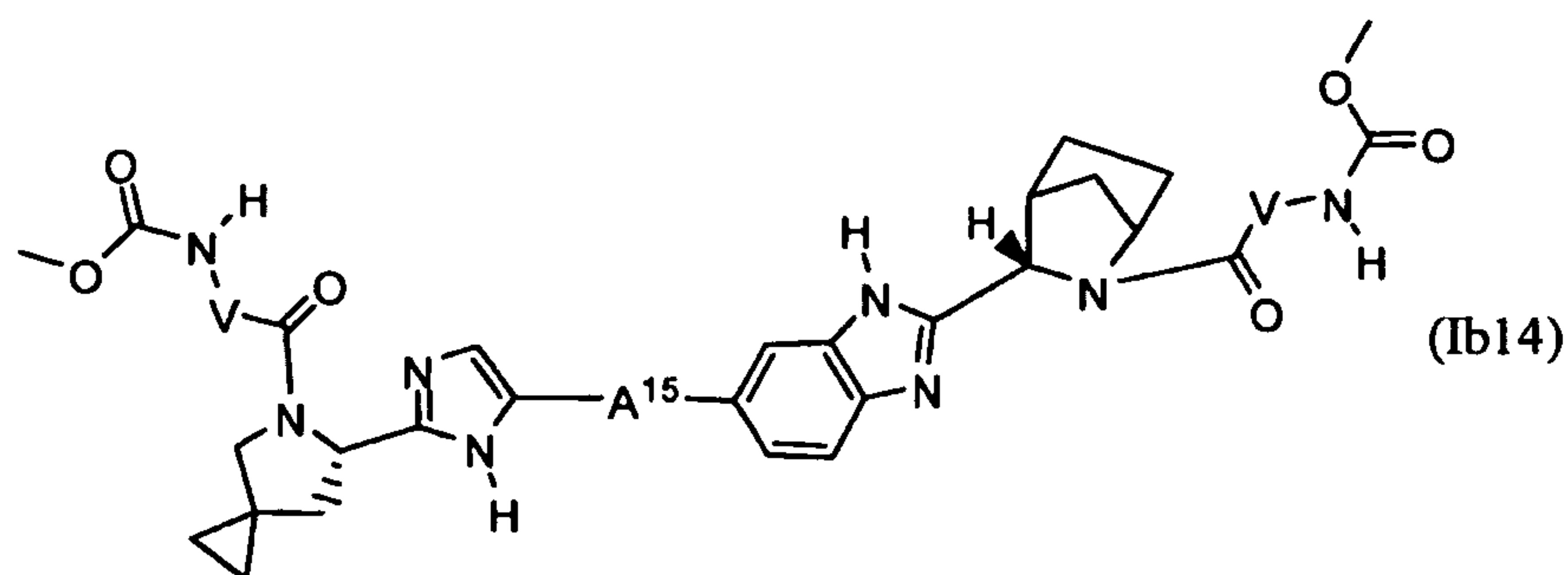
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib13):



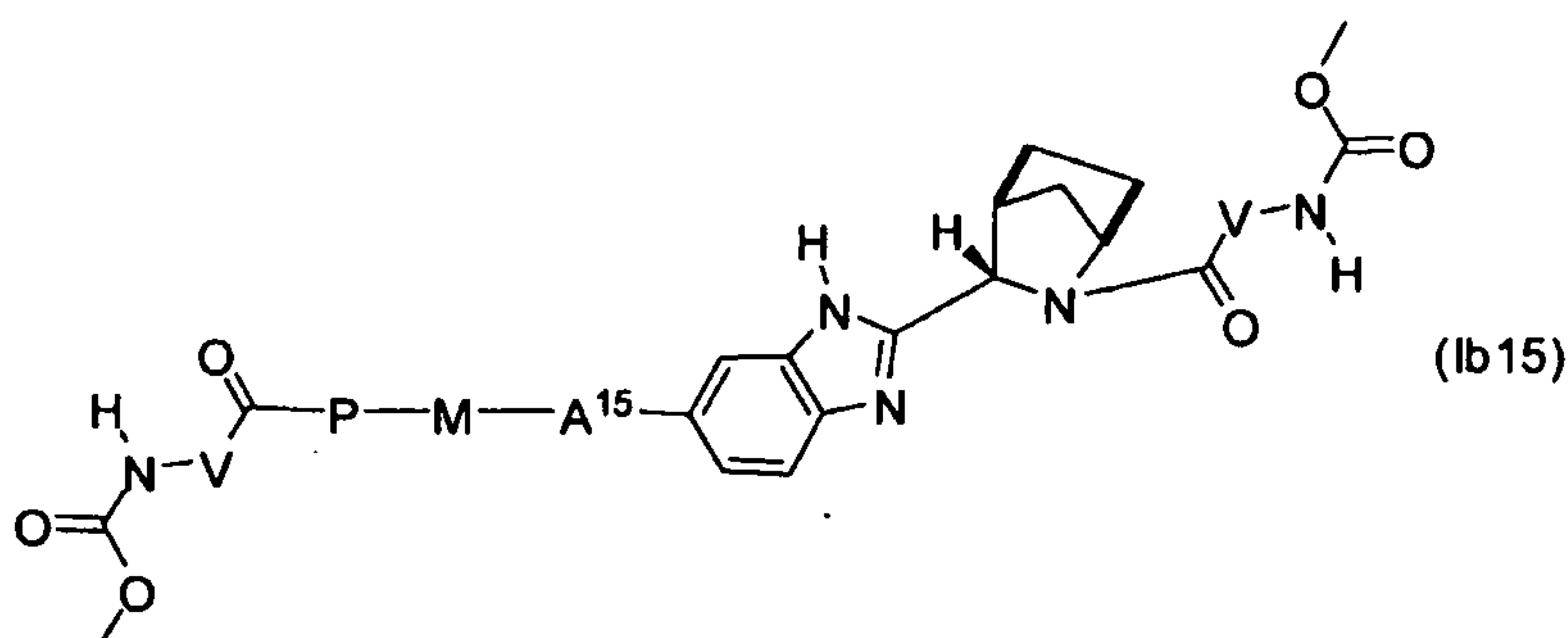
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib14):



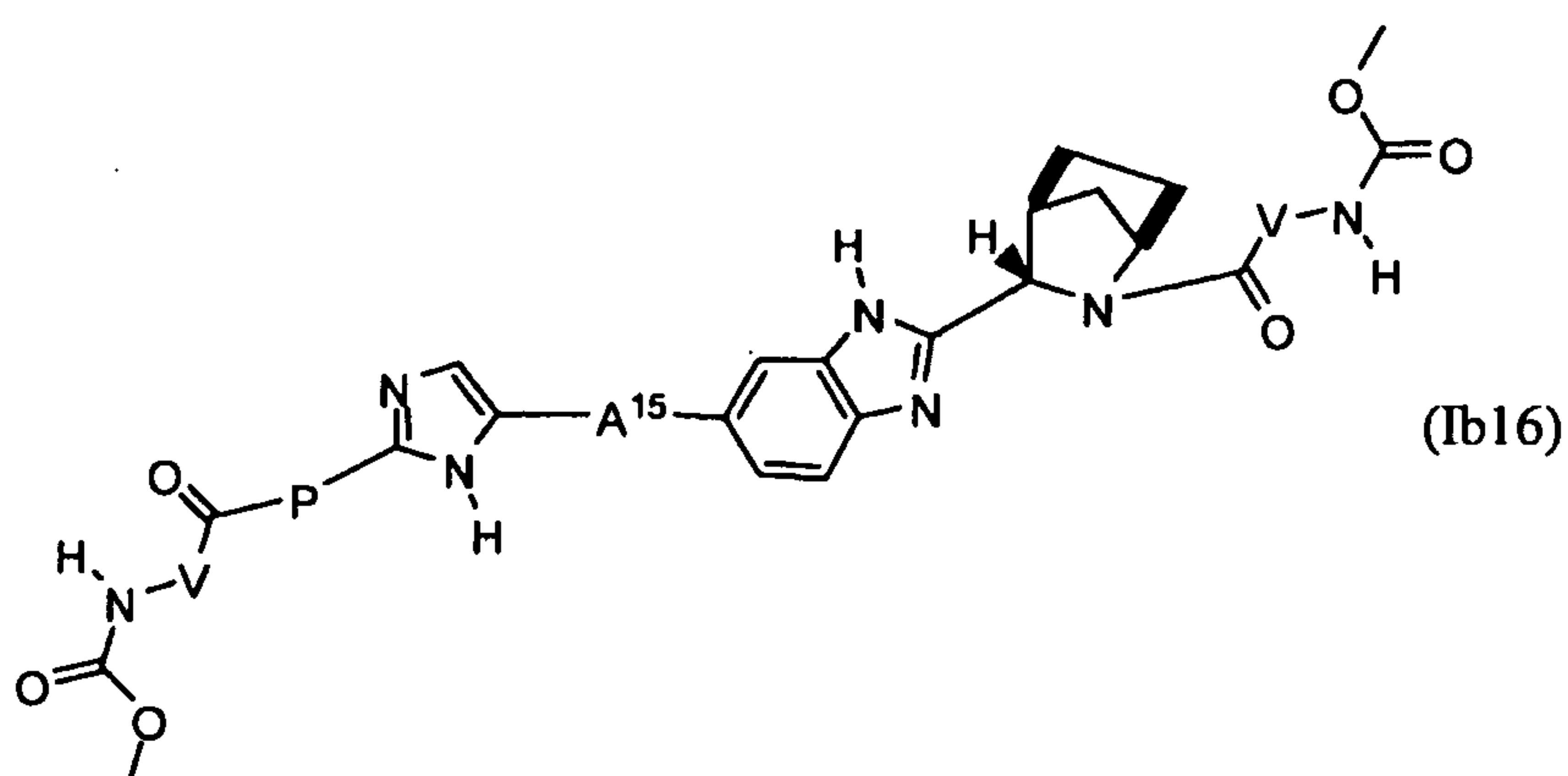
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib15):



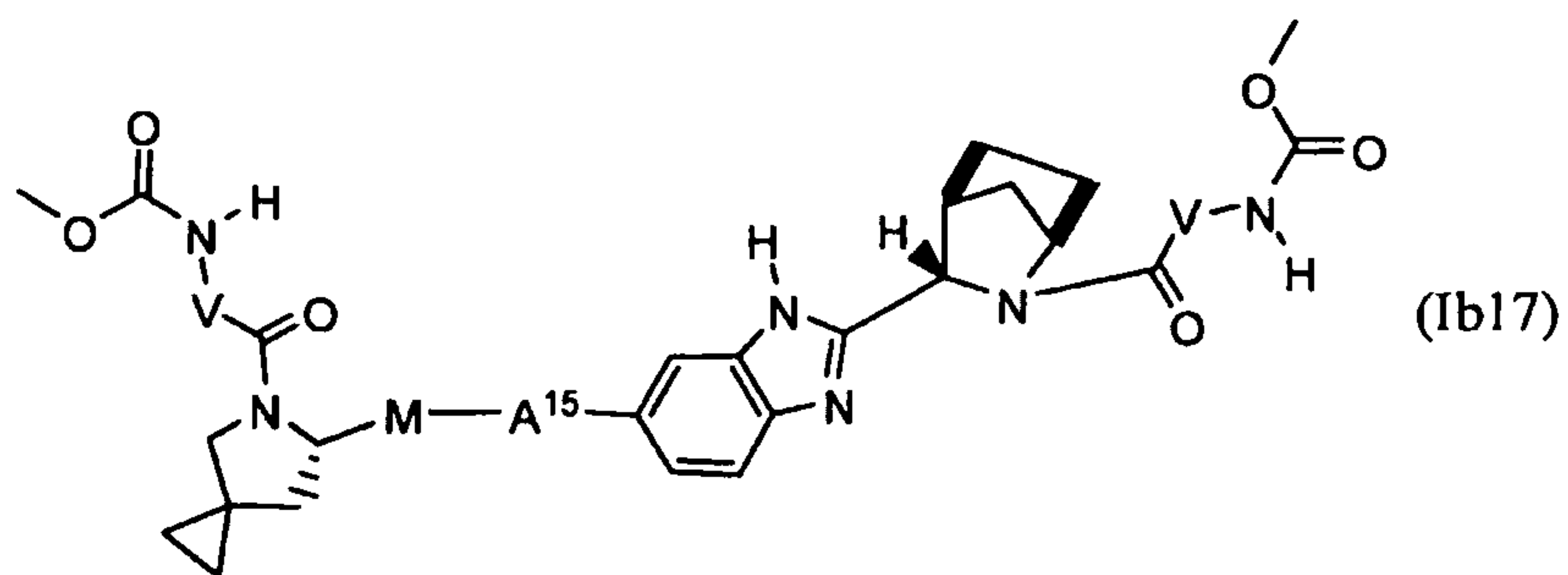
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib16):



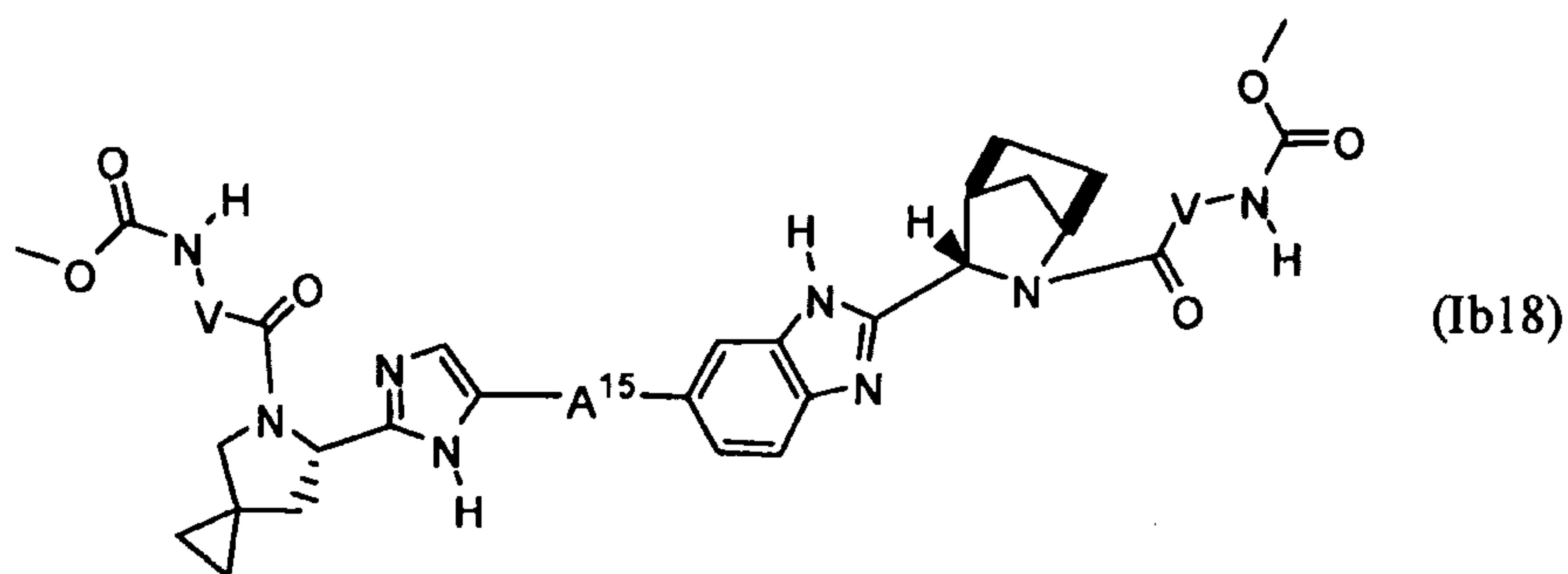
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib17):



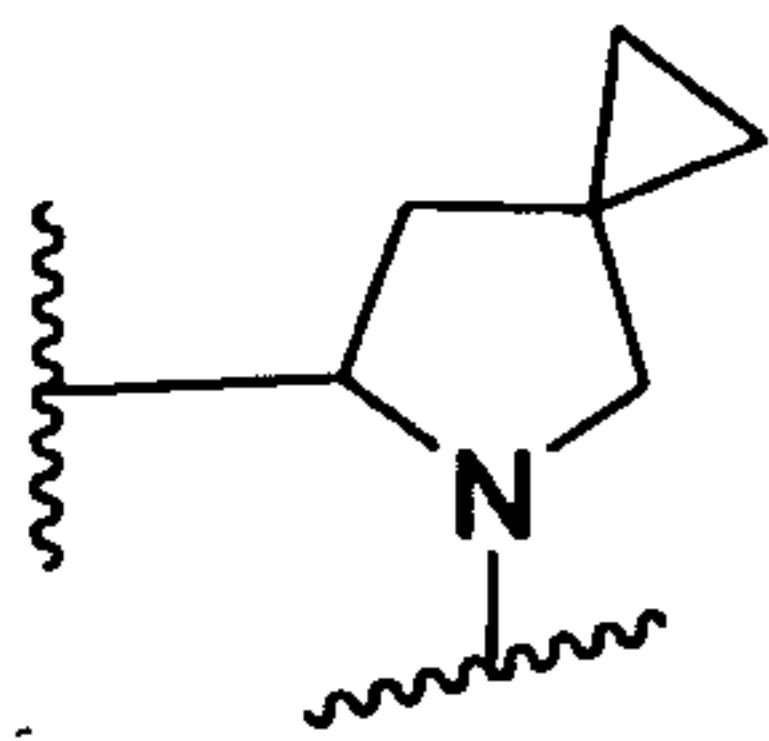
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula (Ib18):

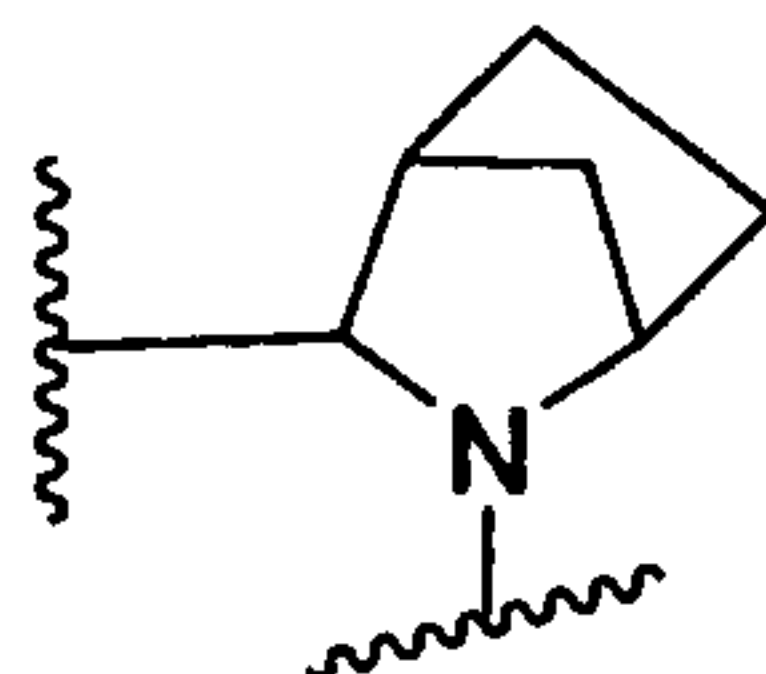


or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of formula (Ib) wherein P is



In another specific embodiment the invention provides a compound of formula (Ib) wherein P is

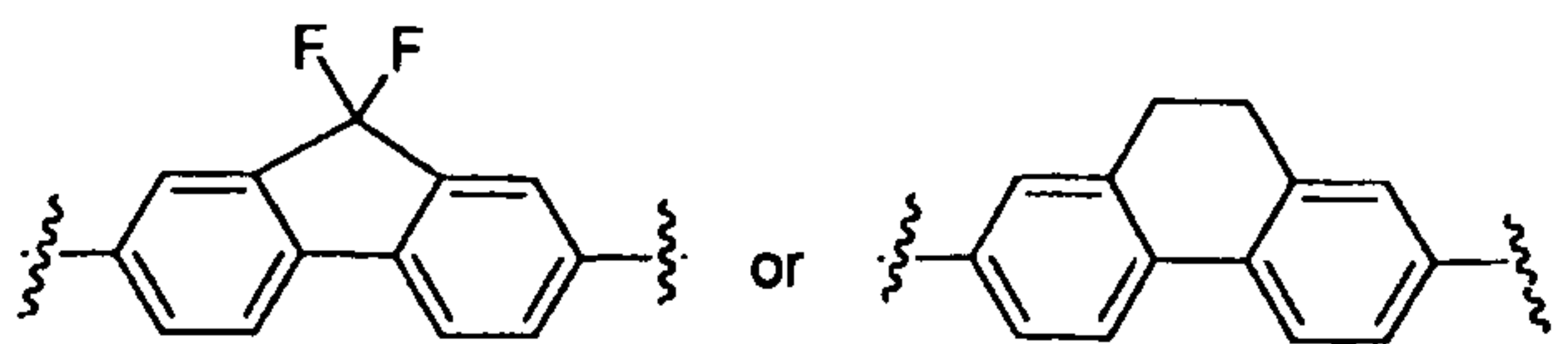


optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ; each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

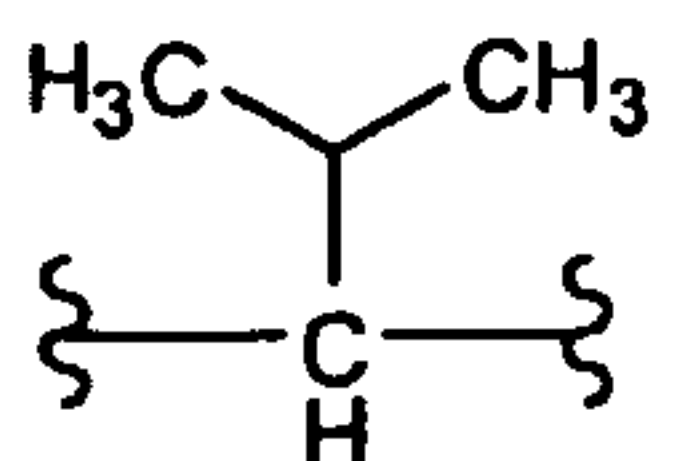
each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^{hh}) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^{hh}) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^{hh}$, $(NR^{hh}R^{hh})$ alkyl, $(NR^{hh}R^{hh})$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $(NR^{hh}R^{hh})$ sulfonyl, heteroarylsulfonyl, and $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^{hh}R^{hh}$.

In another specific embodiment the invention provides a compound of formula (Ib) wherein each X^A that is allowed to be absent is absent.

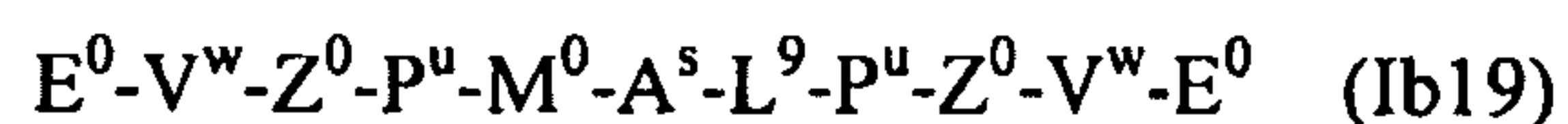
In another specific embodiment the invention provides a compound of formula (Ib) wherein A^{15} is selected from:



In another specific embodiment the invention provides a compound of formula (Ib) wherein each V is:



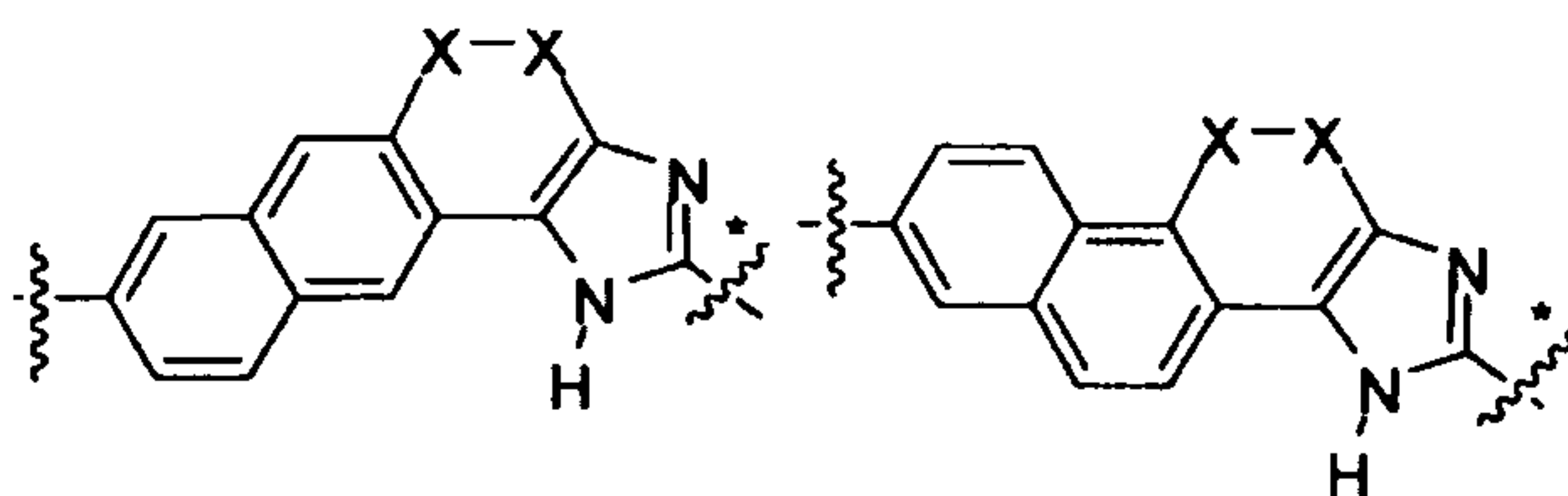
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib19):



wherein:

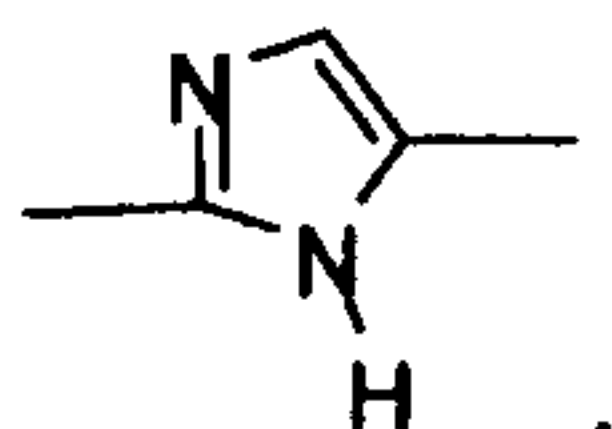
each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each w is independently 0, 1, 2, 3, 4, or 5; and each s is 0, 6, 13, or 14.

In one embodiment the invention provides a compound of formula (Ib19) wherein L^9 is:

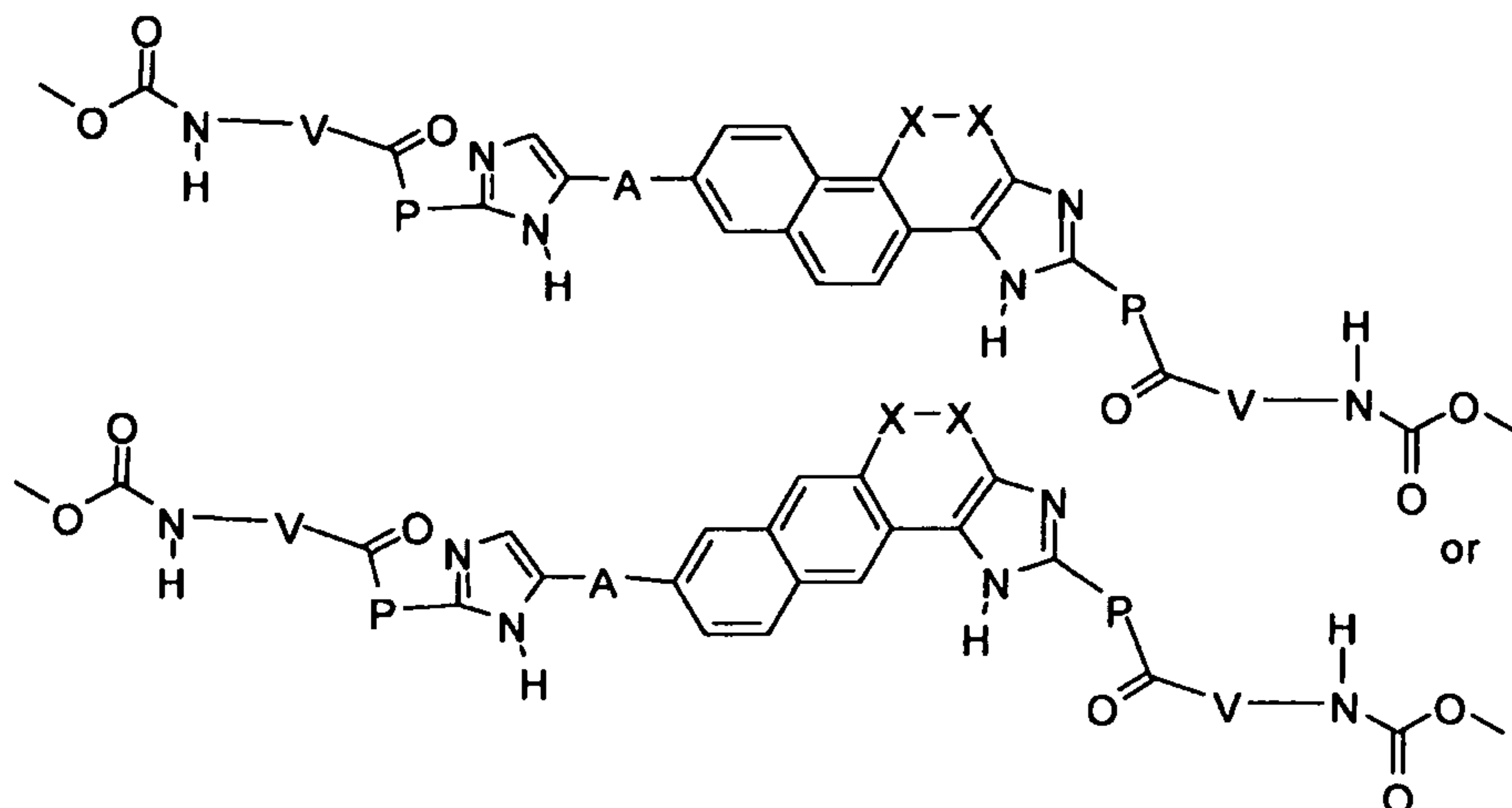


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; wherein * designates the site of connection to P.

In one embodiment the invention provides a compound of formula (Ib19) wherein M^0 is:



In one embodiment the invention provides a compound of formula (Ib19) which is:

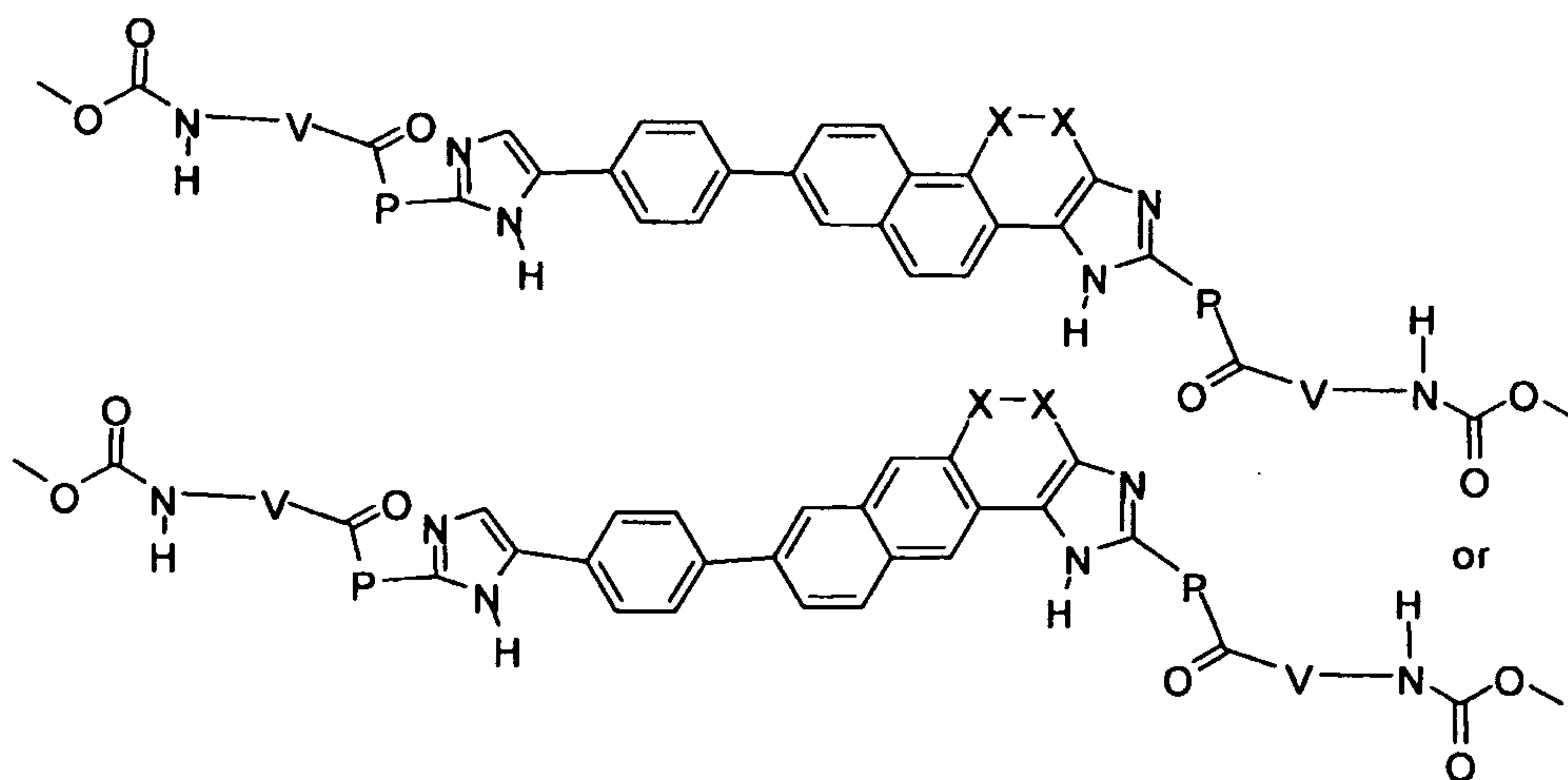


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib19) wherein A⁰ is:

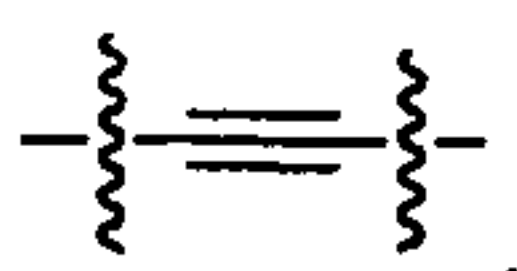


In one embodiment the invention provides a compound of formula (Ib19) which is:

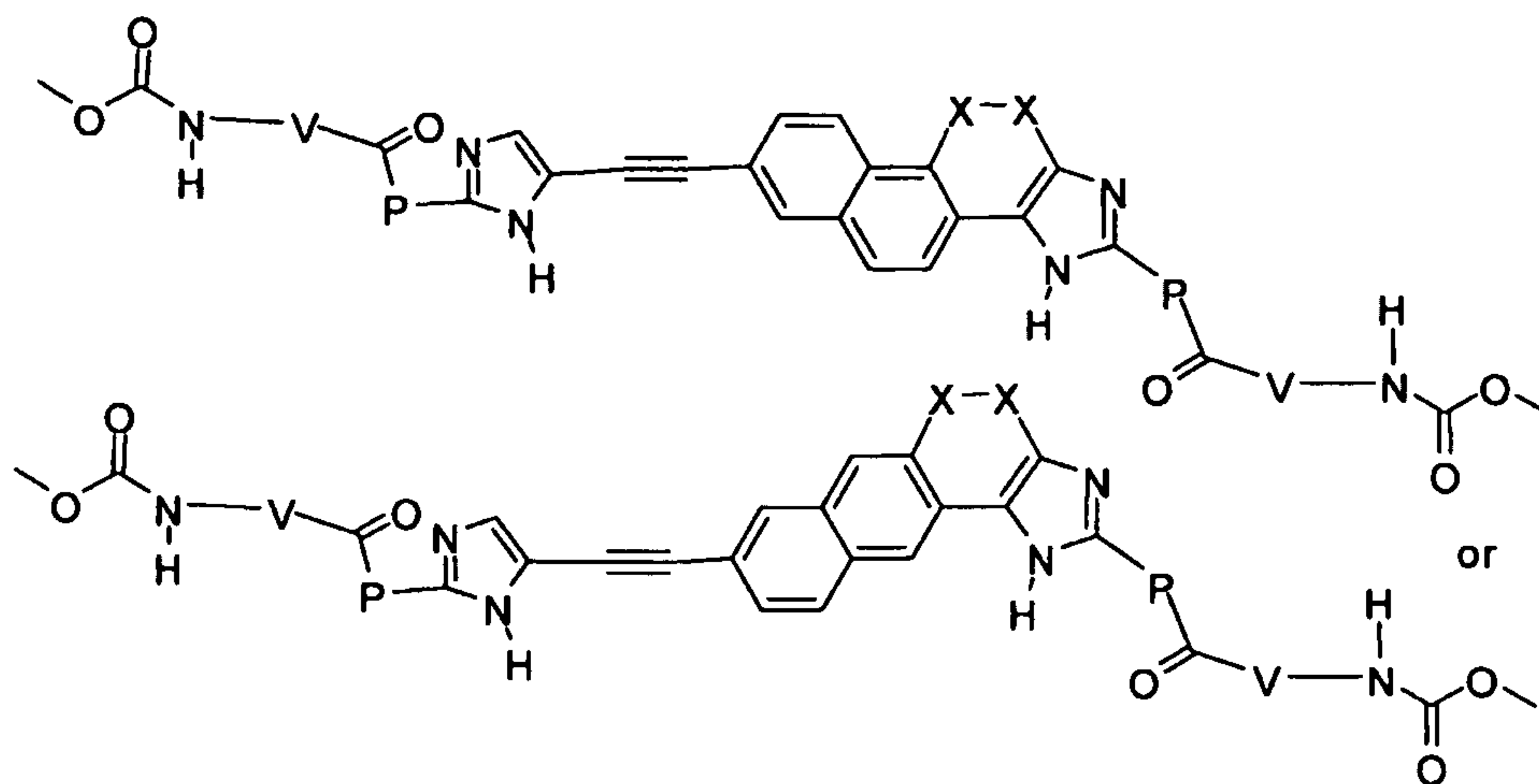


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib19) wherein A⁶ is:

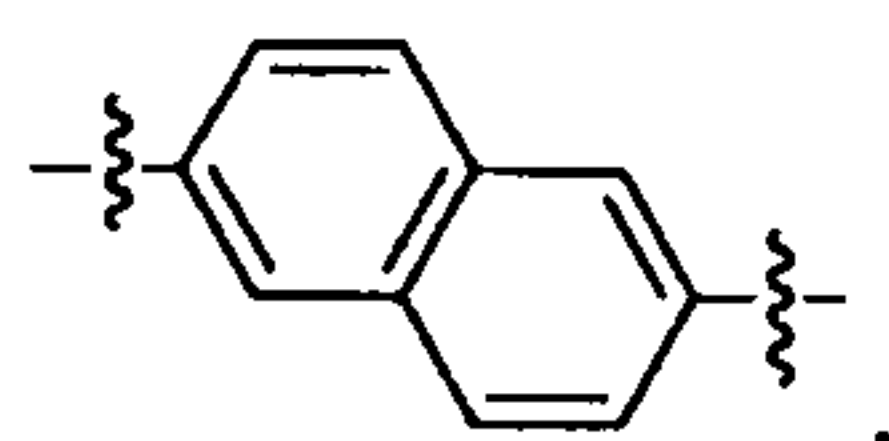


In one embodiment the invention provides a compound of formula (Ib19) which is:

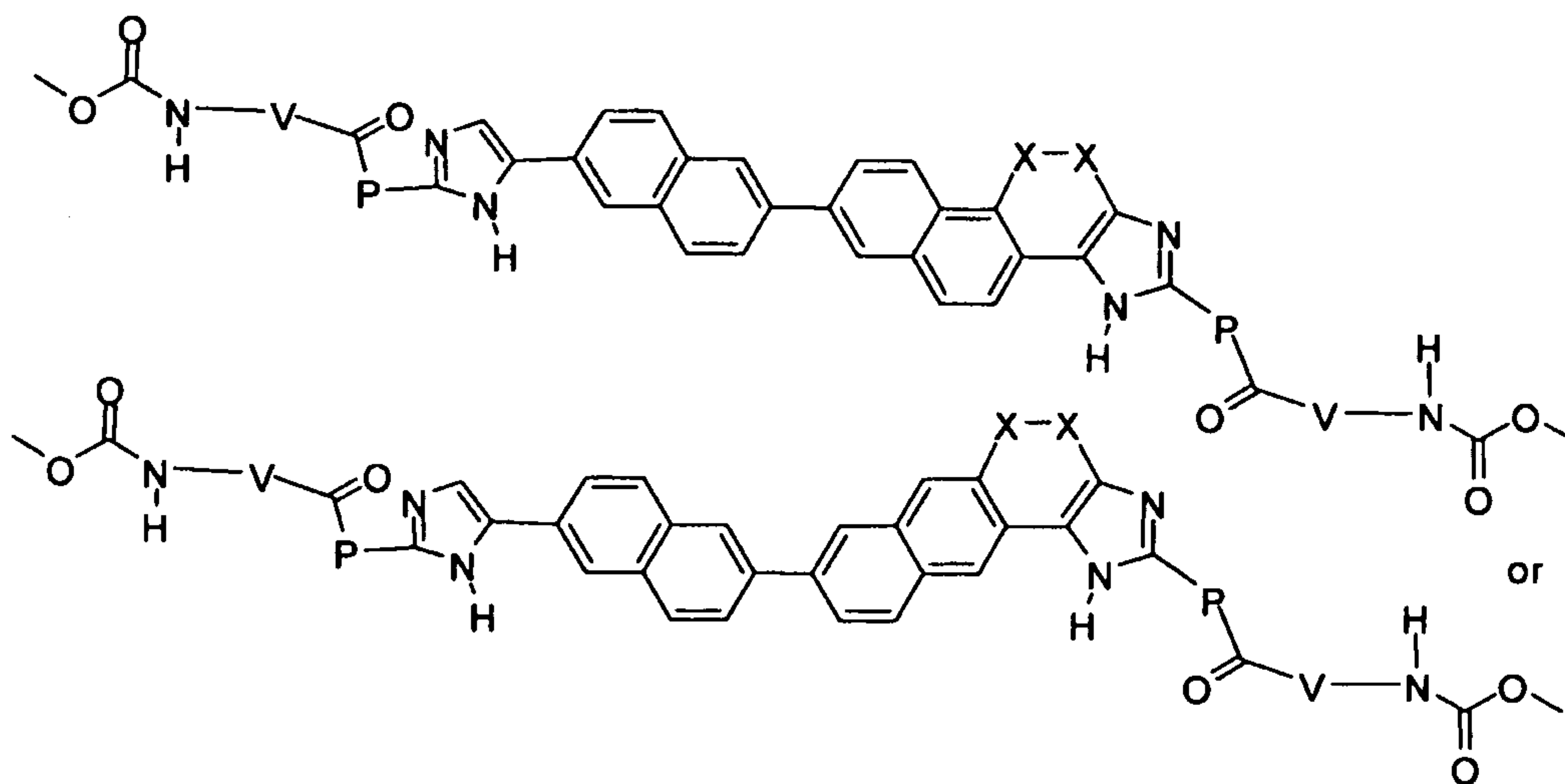


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib19) wherein A^{13} is:

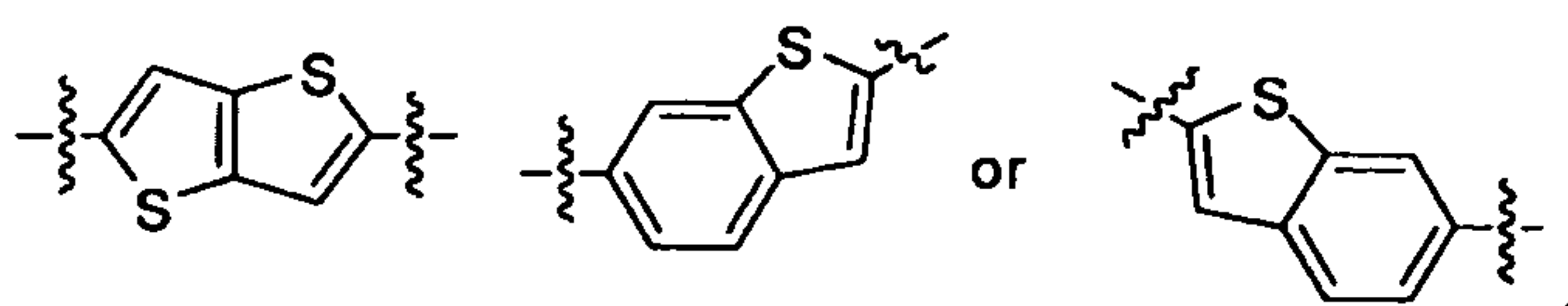


In one embodiment the invention provides a compound of formula (Ib19) which is:

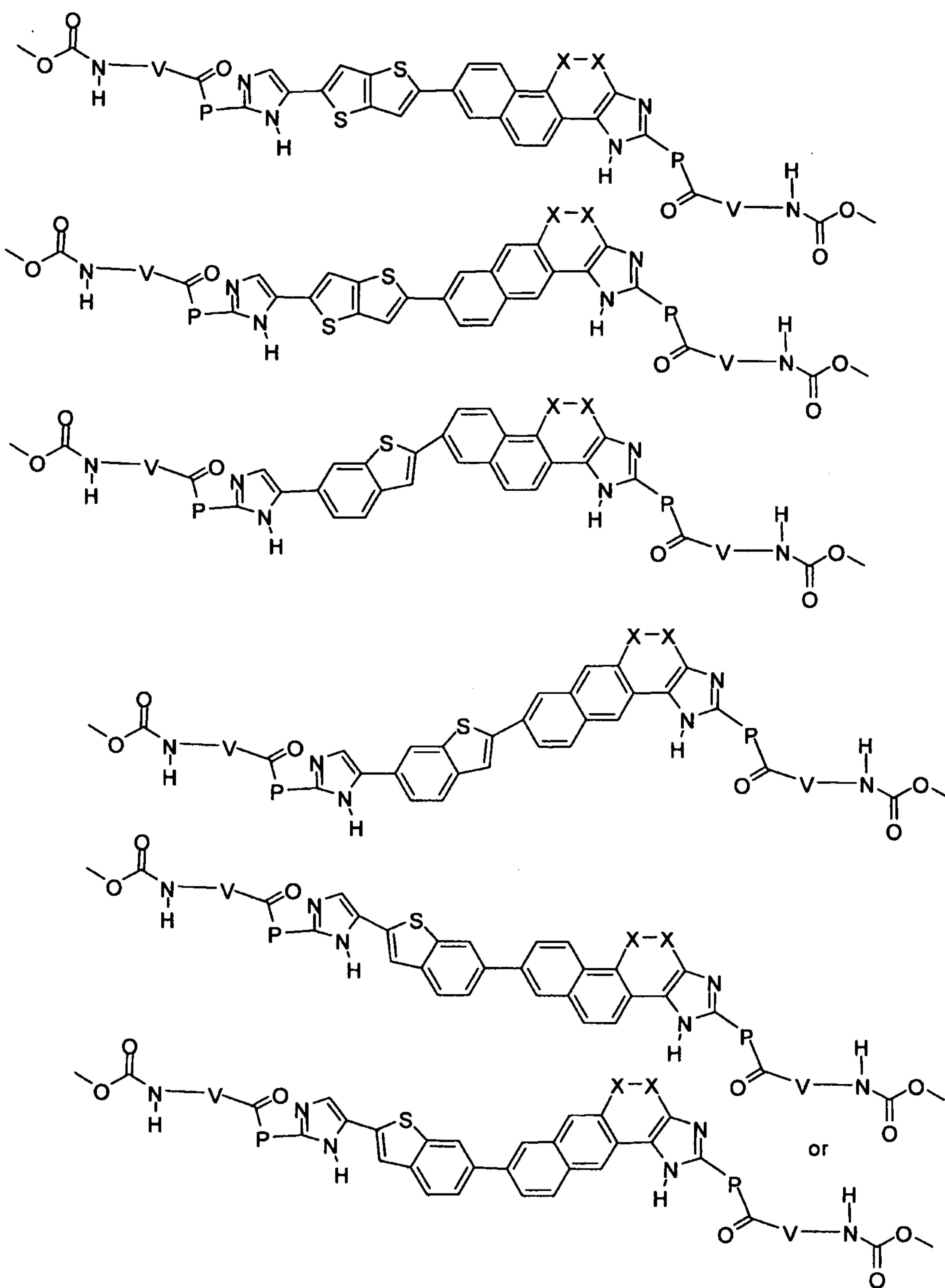


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib19) wherein A^{14} is:

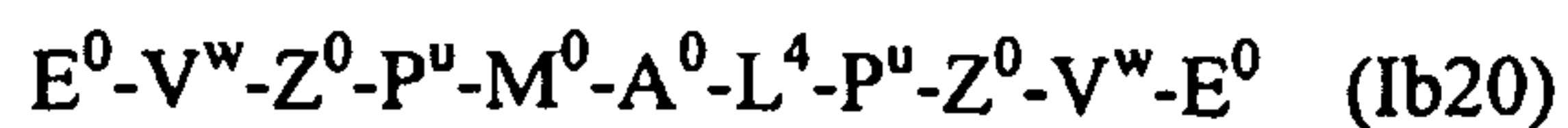


In one embodiment the invention provides a compound of formula (Ib19) which is:



or a pharmaceutically acceptable salt, or prodrug thereof.

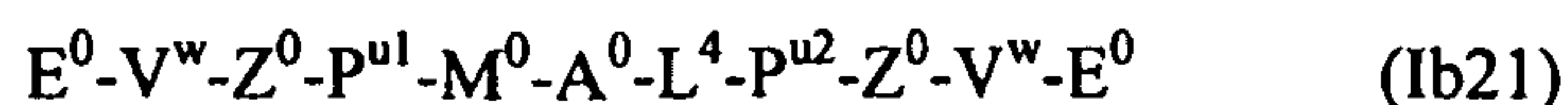
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib20):



wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; and each w is independently 0, 1, 2, 3, 4, or 5.

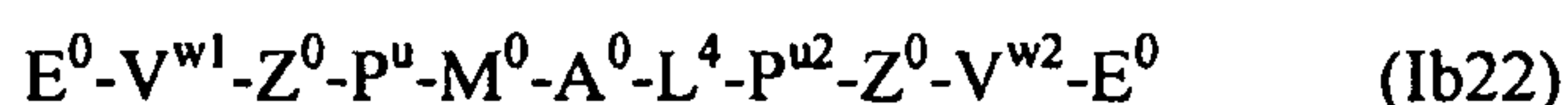
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib21):



wherein:

each u1 is 1, 3, 5, 7, 8, 10, or 11; u2 is 0, 1, 3, 5, 7, 8, 10, or 11; and each w is independently 0, 1, 2, 3, 4, or 5.

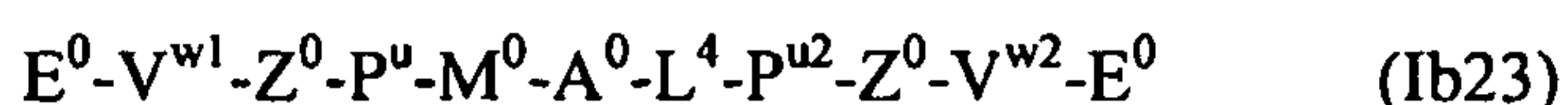
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib22):



wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each u2 is independently 0, 1, 3, 5, 7, 8, 10, or 11; w1 is independently 0, 1, 2, 3, 4, or 5; and each w2 is independently 1, 2, 3, 4, or 5.

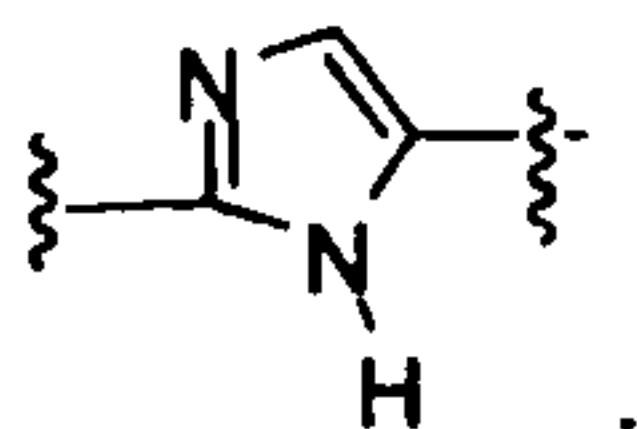
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib23):



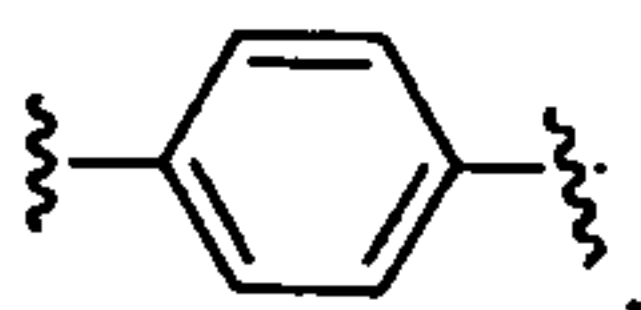
wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each u2 is independently 0, 1, 3, 5, 7, 8, 10, or 11; w1 is independently 1, 2, 3, 4, or 5; and each w2 is independently 0, 1, 2, 3, 4, or 5.

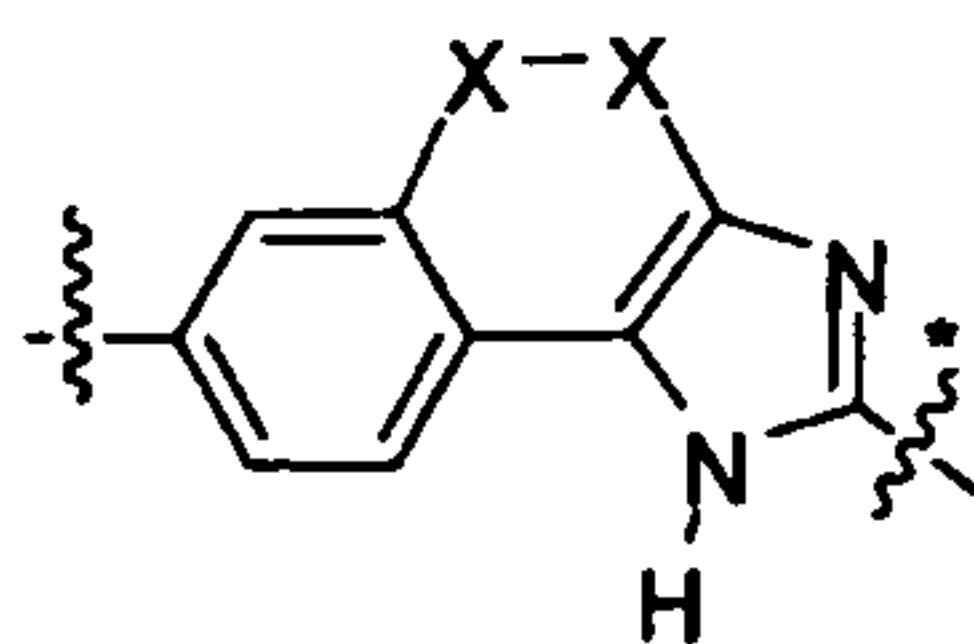
In one embodiment the invention provides a compound of formula (Ib20)-(Ib23) wherein M^0 is:



In one embodiment the invention provides a compound of formula (Ib20)-(Ib23) wherein A^0 is:

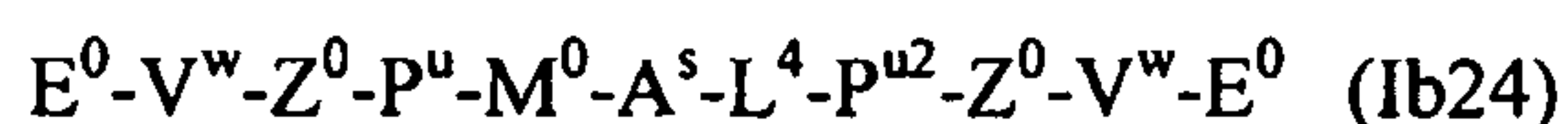


In one embodiment the invention provides a compound of formula (Ib20)-(Ib23) wherein L^4 is:



wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; and wherein * designates the site of connection to P.

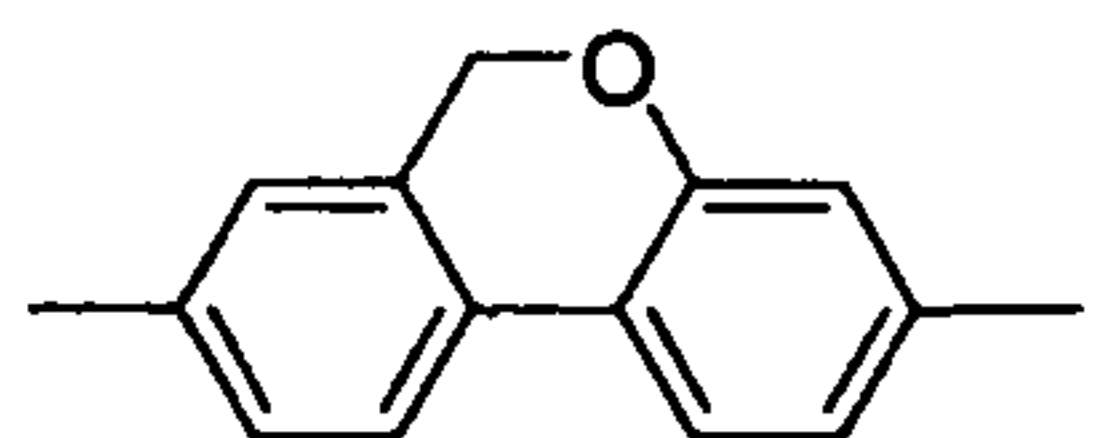
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ib24):



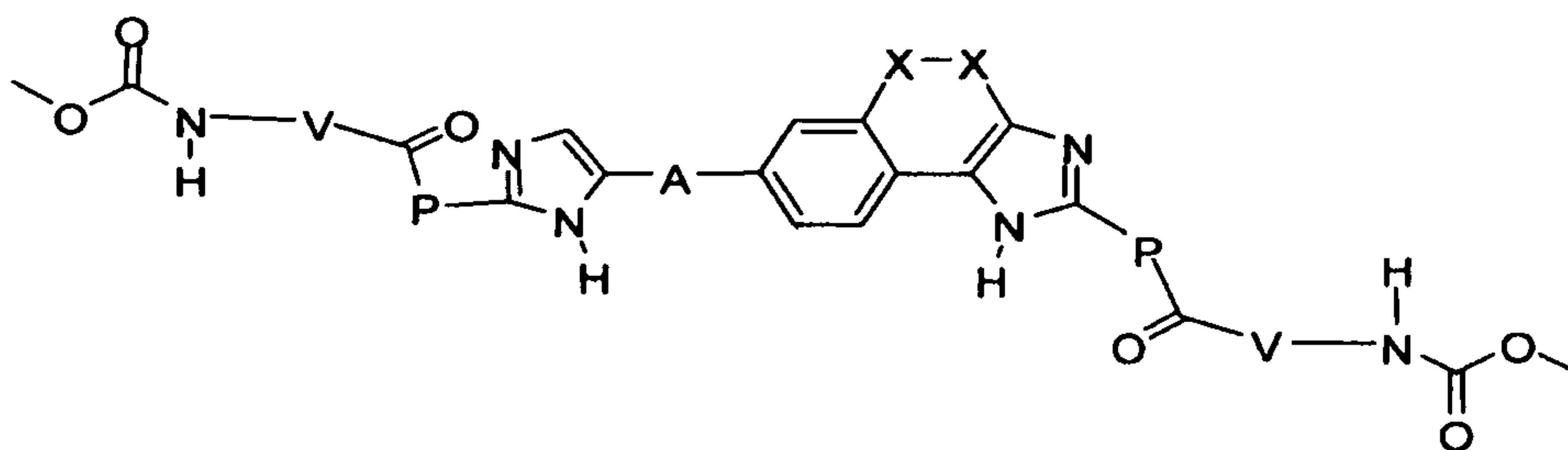
wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each u₂ is independently 0, 1, 3, 5, 7, 8, 10, or 11; each w is independently 0, 1, 2, 3, 4, or 5; and s is 5, 6, 13, 14, 15, or 16.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 16 and A¹⁶ is:

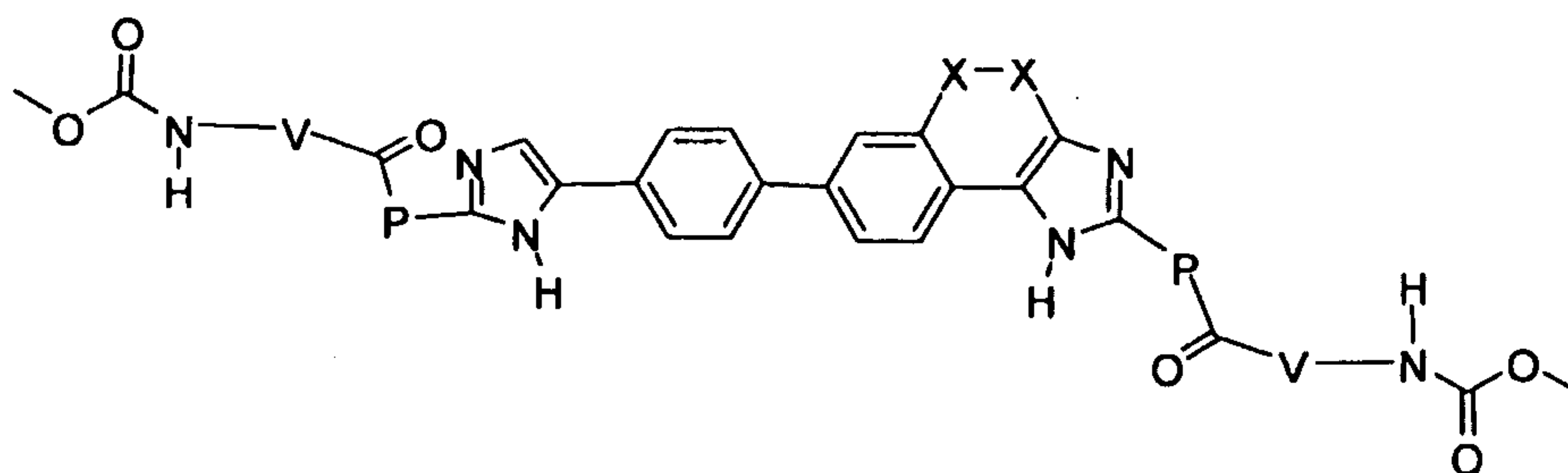


In one embodiment the invention provides a compound of formula:



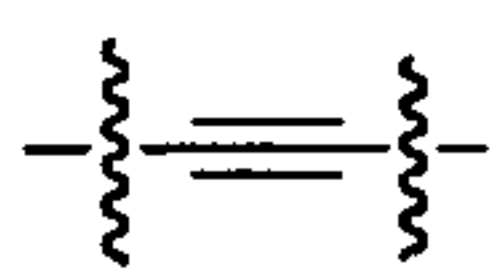
wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; and A is A⁰; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula:

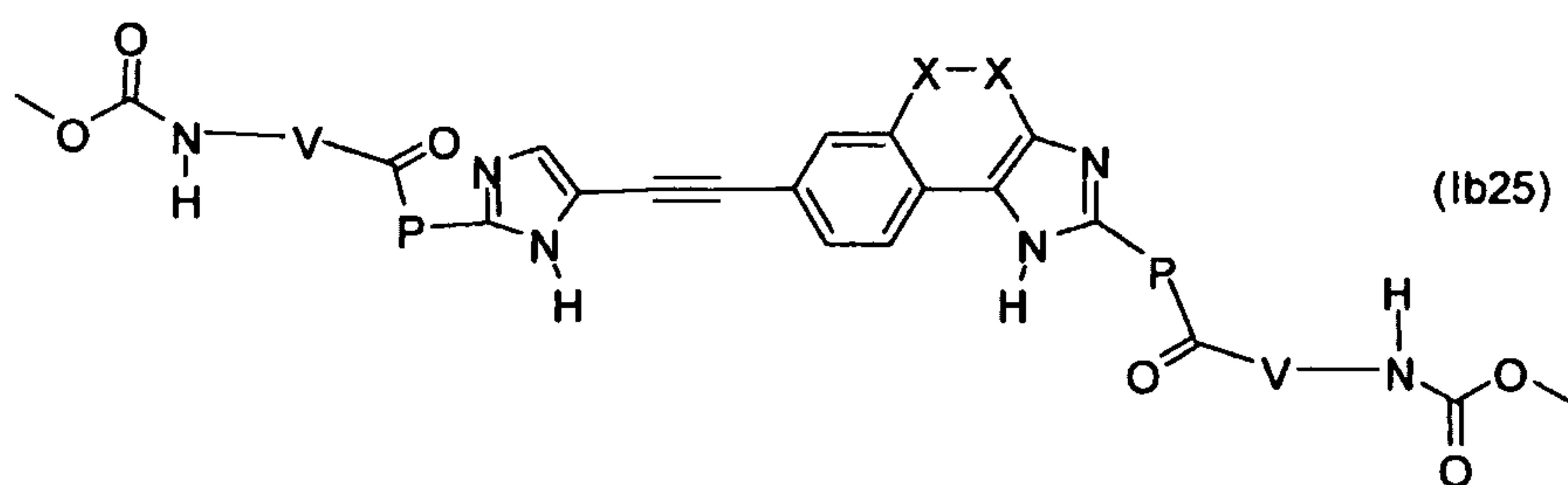


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 6 and A⁶ is:

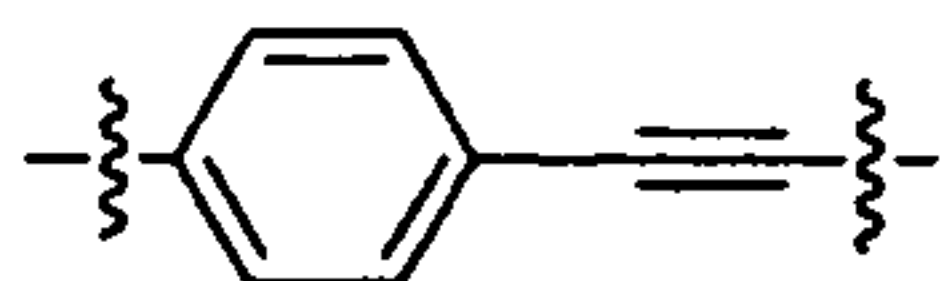


In one embodiment the invention provides a compound of formula (Ib25):

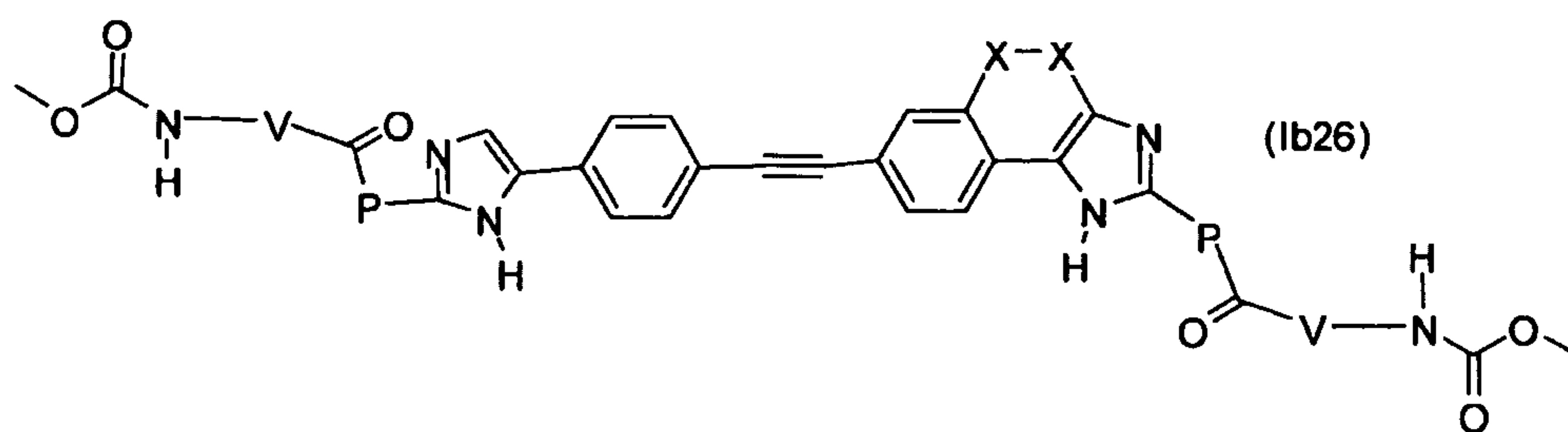


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 5 and A⁵ is:

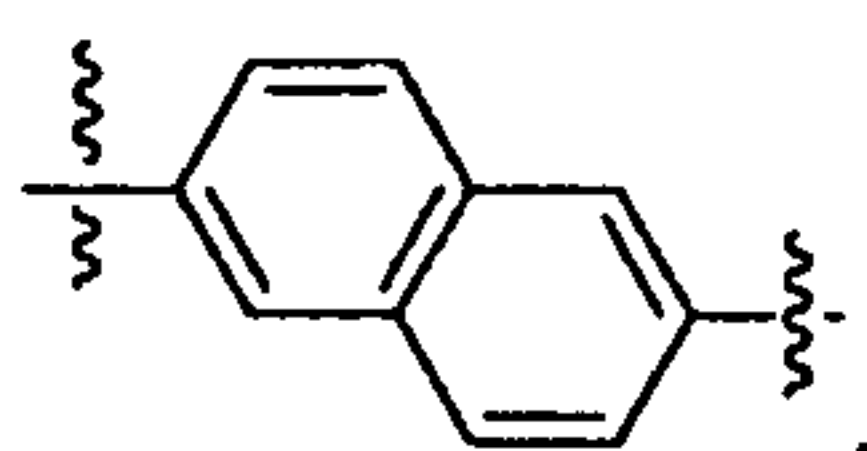


In one embodiment the invention provides a compound of formula (Ib26):

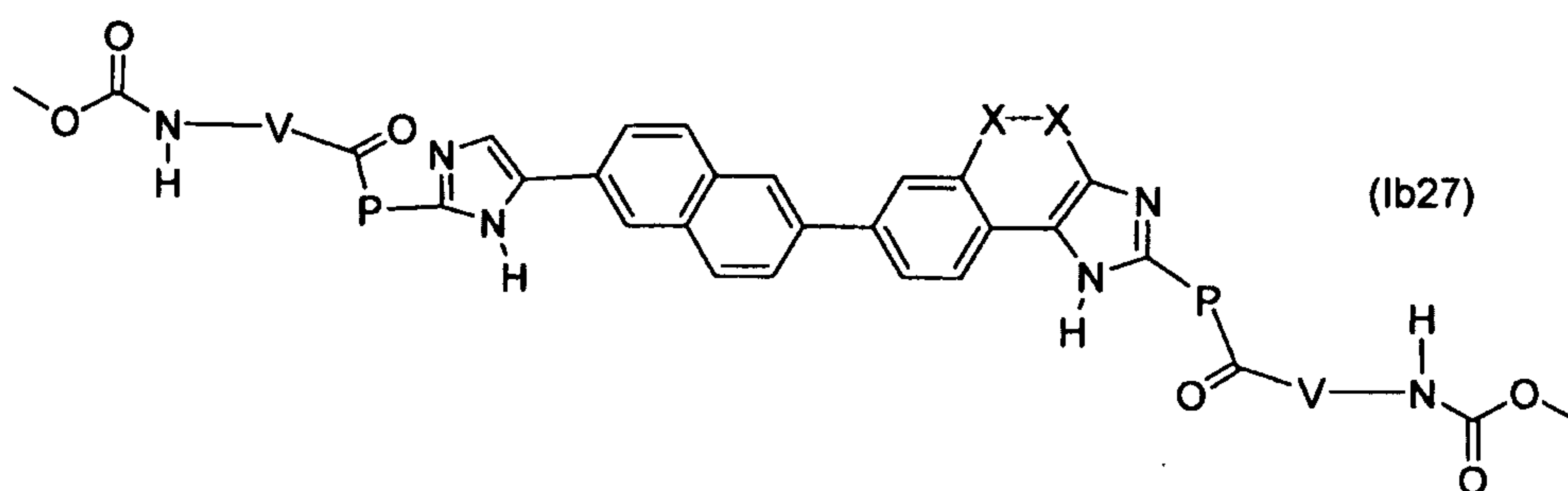


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 13 and A¹³ is:

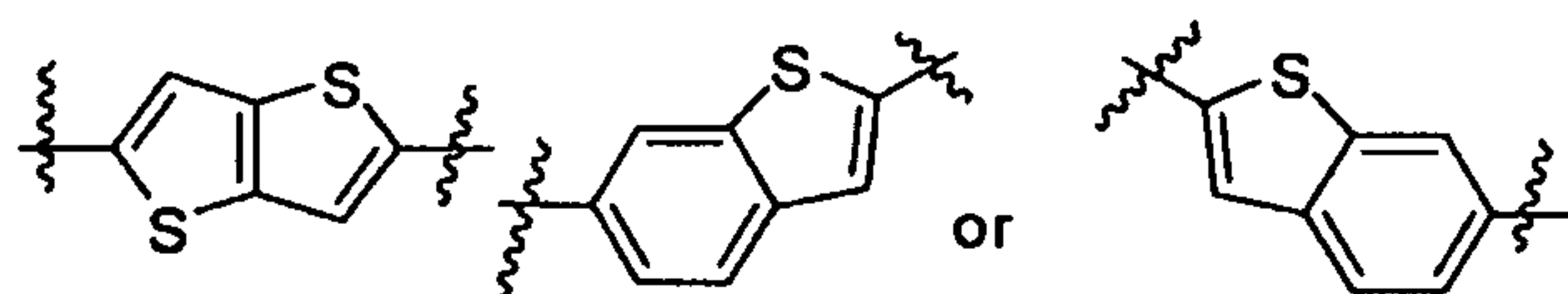


In one embodiment the invention provides a compound of formula (Ib27):

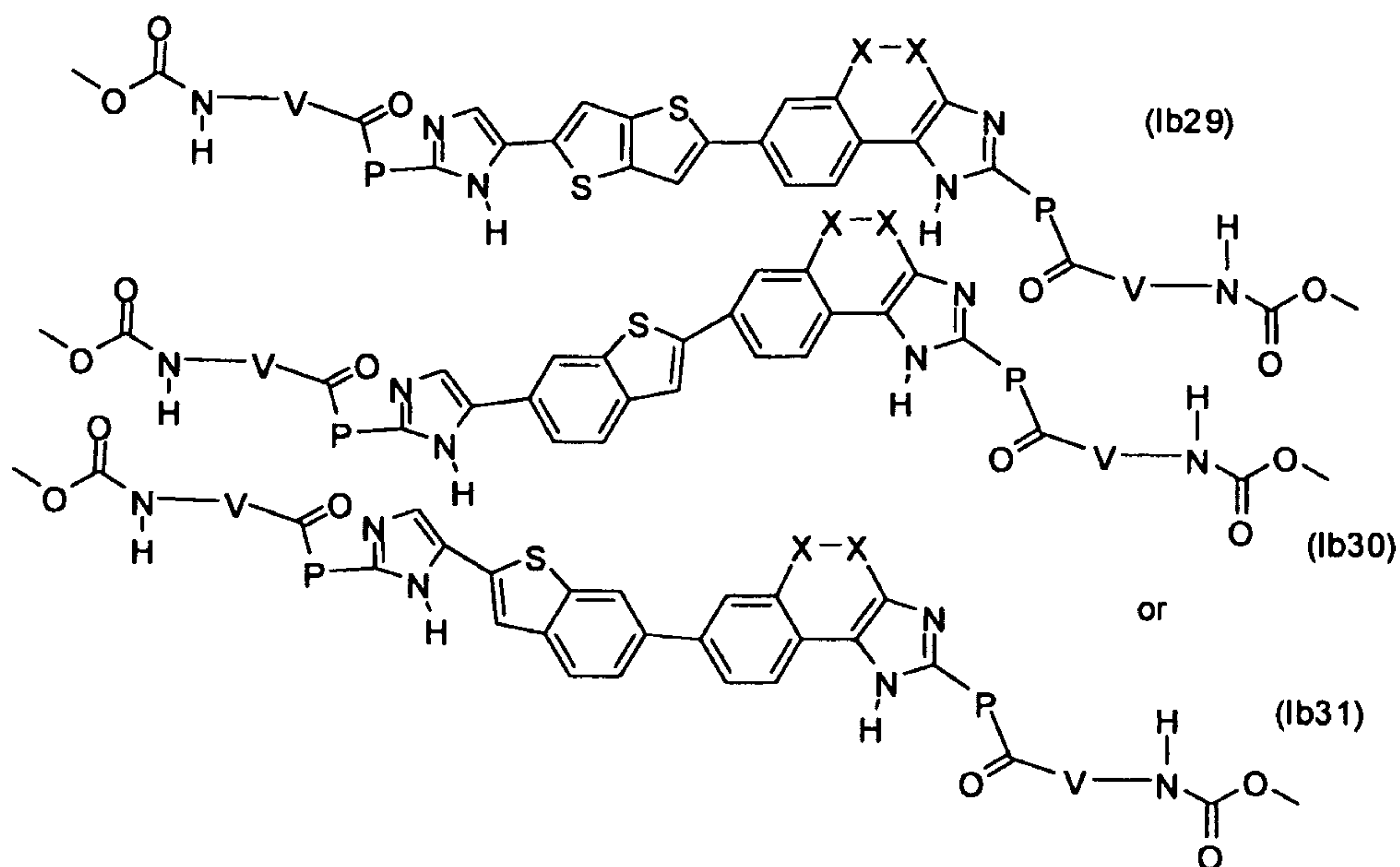


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 14 and A¹⁴ is:

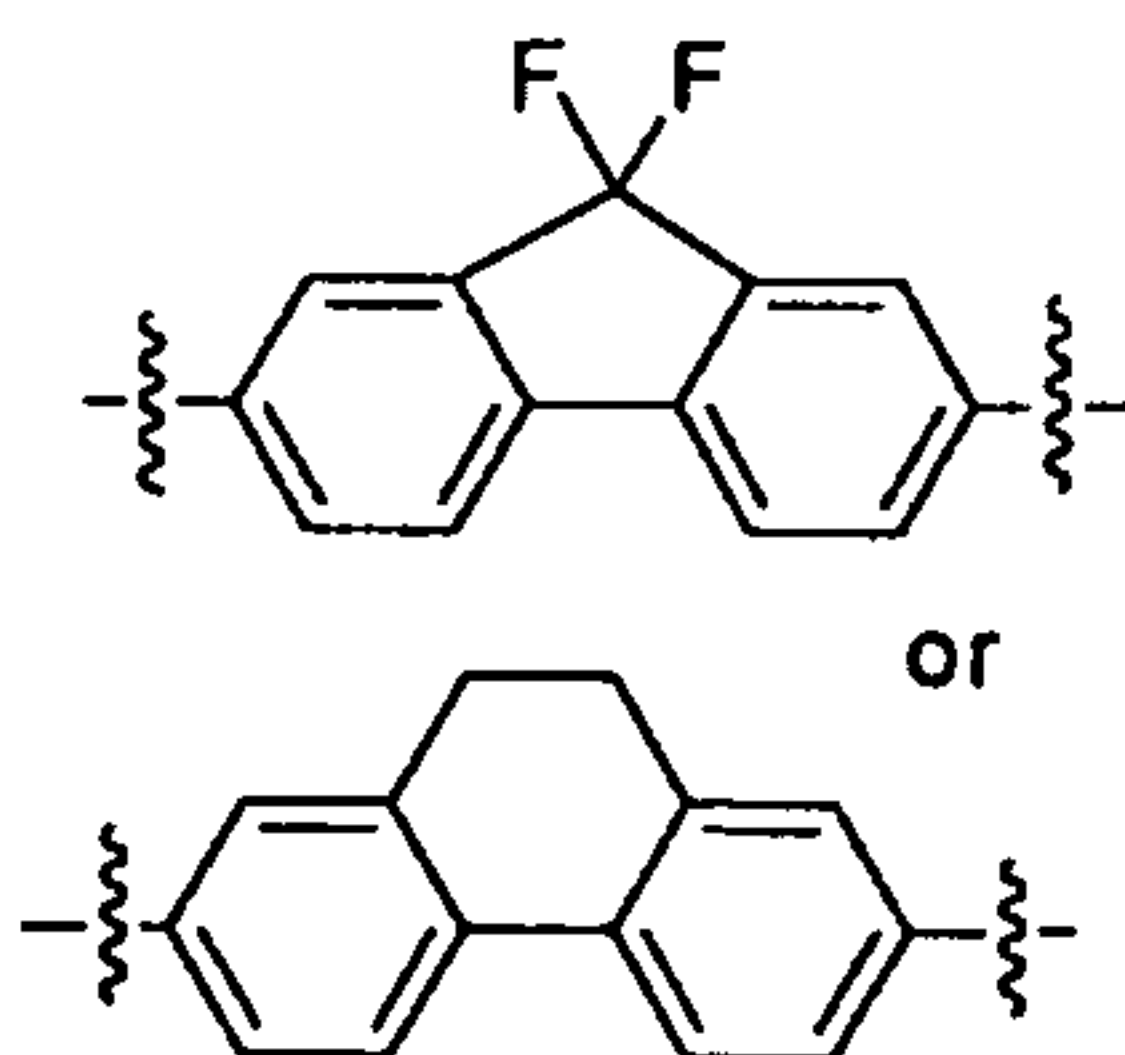


In one embodiment the invention provides a compound of formula:

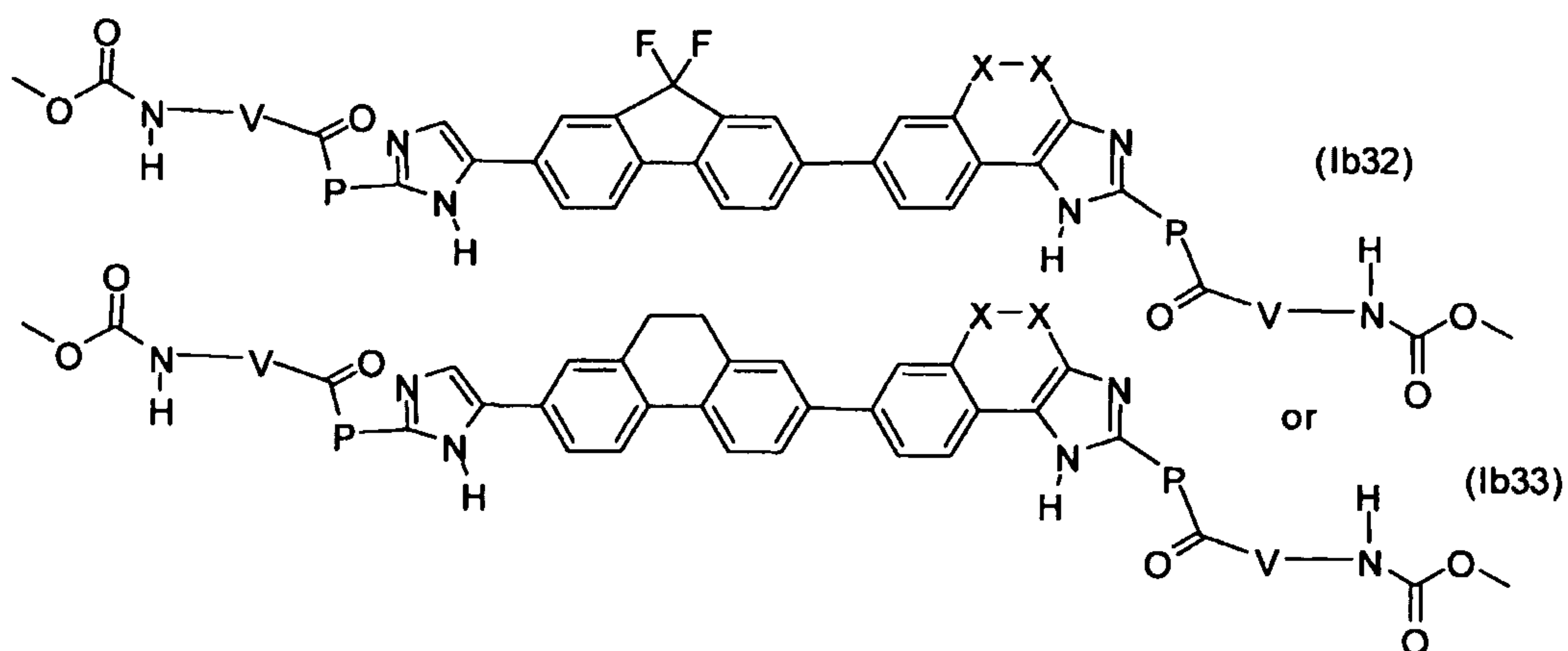


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib24) wherein s is 15 and A¹⁵ is:

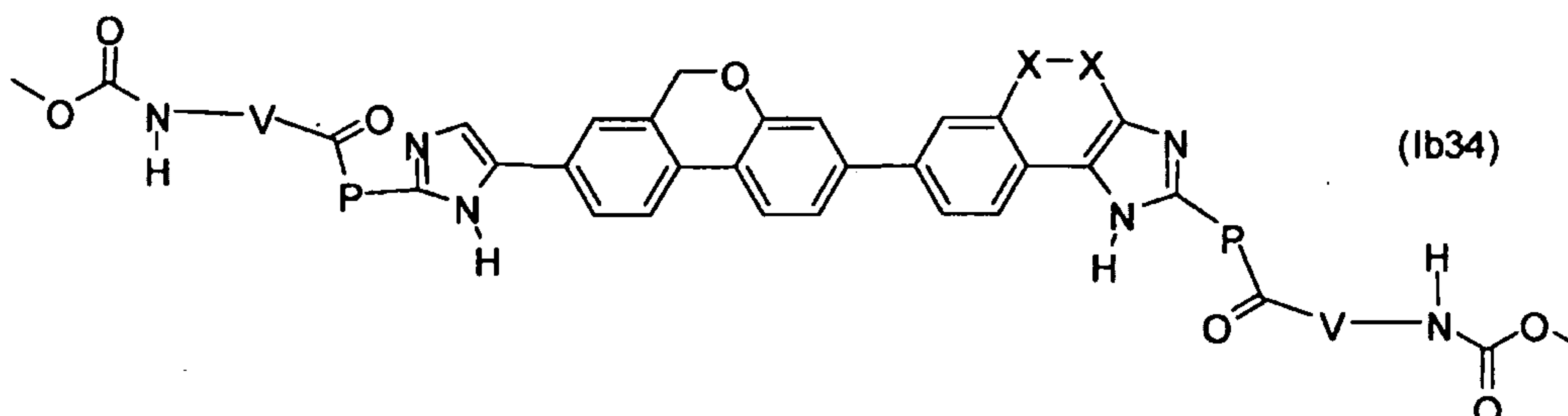


In one embodiment the invention provides a compound of formula:



wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ib34):



wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M-A¹⁵-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M-A¹⁵-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M⁰-A¹⁵-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M-A¹⁶-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M-A¹⁶-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M⁰-A¹⁶-L³-P-Z-R⁹.

In another specific embodiment of the invention the compound of formula (Ib) is a compound of formula: R⁹-Z-P-M⁹-A¹⁶-L³-P-Z-R⁹.

In another specific embodiment the invention provides a compound of the following formula (Ib50): E^x-V^w-Z^v-P^u-M^t-A^s-Lⁿ-P^u-Z^v-V^w-E^x (Ib50) wherein the sum of t, s, n, u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of n, s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least three of n, s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of n, s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least three of n, s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least three of n, s, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least four of n, s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least four of n, s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least four of n, s, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least four of n, s, t, u, v, w or x are not zero and at least four of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein the sum of n, t, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein the sum of s, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein s, and at least one t, and at least one u are all not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of u, w and t are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of s, u, and w are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of s, u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least s and both u are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least one of u, or w is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of u are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein at least two of w are not zero.

In another specific embodiment the invention provides a compound of formula (Ib50) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 0 or 10; n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 21.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 0 or 10; n is 0, 1, 2, 4, 5, 6, 7, 8, 9, or 10; and s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 21.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 9; n is 3; and s is 3, 4, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 21.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 0, 1, 2, 4, 5, 6, 7, 8, 9, 10, or 11; n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and s is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 21.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 0; n is 0, 1, 2, 3, 5, 6, 7, 8, 9, or 10; and s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 20.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein t is 1, 2, 4, 5, 6, 7, 8, 9, 10, or 11; n is 4; and s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 21.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least one of u , v , w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of n , s , t , u , v , w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least three of n , s , t , u , v , w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of n , s , t , u , v , w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least three of n , s , t , u , v , w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least three of n , s , t , u , v , w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least four of n , s , t , u , v , w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least four of n , s , t , u , v , w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least four of n , s , t , u , v , w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least four of n , s , t , u , v , w or x are not zero and at least four of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein the sum of n , t , u , v , w or x is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein the sum of s , u , v , w or x is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein s, and at least one t, and at least one u are all not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of u, w and t are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of s, u, and w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of s, u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least s and both u are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least one of u, or w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of u are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein at least two of w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib50) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the following formula (Ib51): $E^x-V^w-Z^v-P^u-M^9-A^s-L^3-P^u-Z^v-V^w-E^x$ (Ib51) wherein s is 0, 1, 2, 5, 6, or 7.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least two of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least three of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least four of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least three of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least three of u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least four of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least one of u, or w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib51) wherein both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Ib52): $E^x-V^w-Z^v-P^u-M^0-A^0-L^4-P^u-Z^v-V^w-E^x$ (Ib52).

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least two of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least three of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least four of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least three of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least three of u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least four of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least one of u, or w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ib52) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of the formula (Ib52) wherein both w are not zero.

Compounds of formula (Ic)

In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ic):



wherein:

each A is selected from $-A^s$;

each M is selected from $-M^t$;

each P is selected from $-P^u$;

each Z is selected from $-Z^v$;

each V is selected from $-V^w$;

each E is selected from $-E^x$;

each s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21;

each t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11;

each u is 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, or 14;

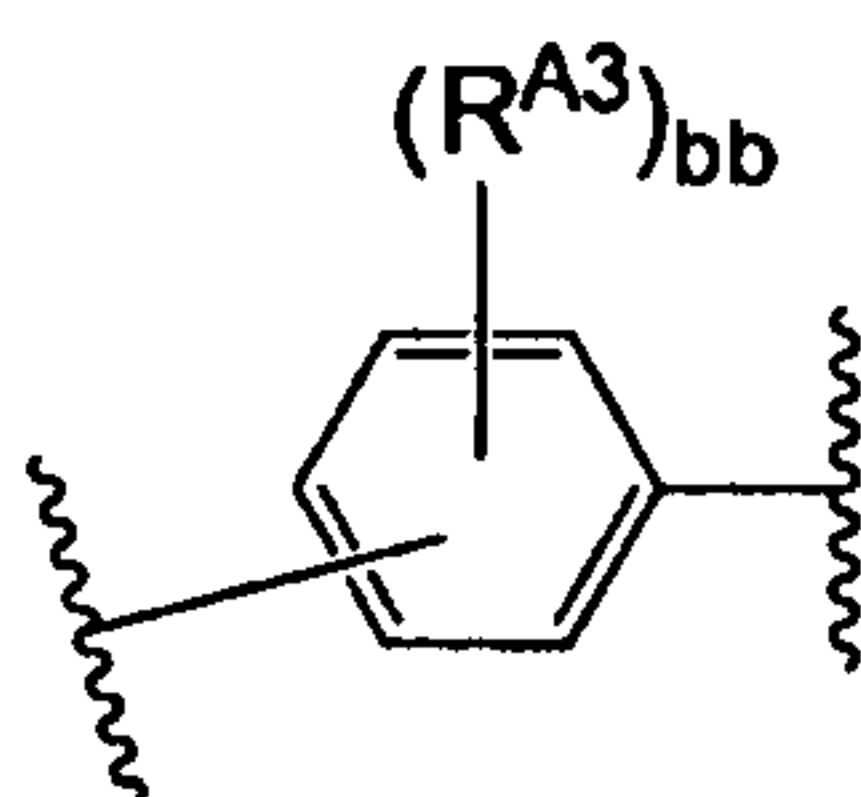
each v is 0, 1, 2, 3, 4, 5, or 6;

each w is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21;

each x is 0 or 1;

wherein the sum of s, t, u, v, w, and x is not 0;

each A^0 is independently:



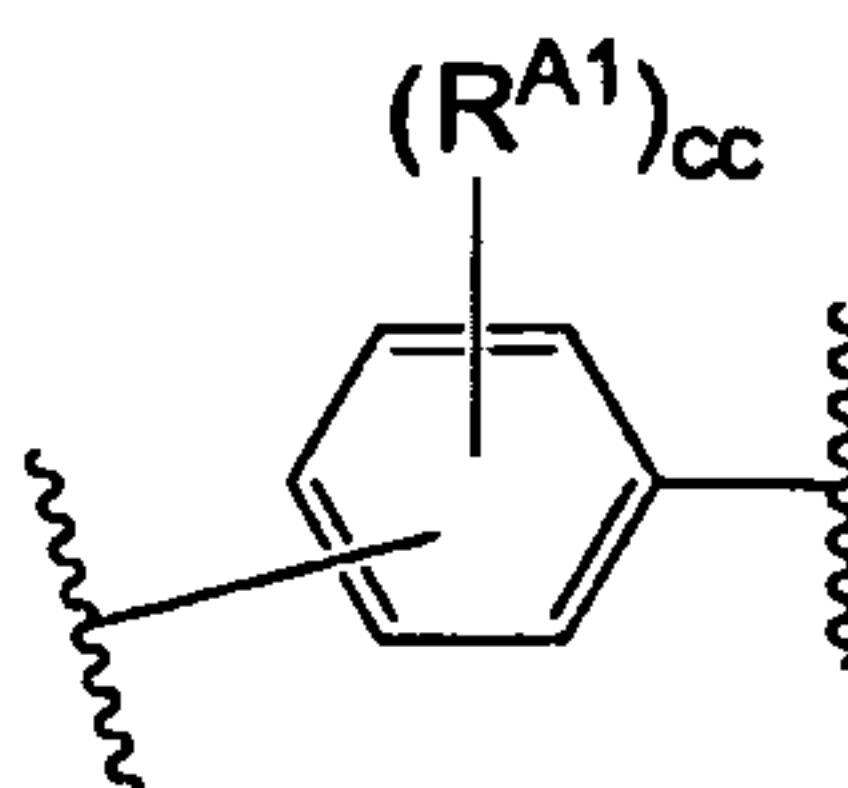
wherein:

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl; and each

bb is independently 0, 1, 2, 3, or 4; or

each A^0 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is optionally substituted with 1, 2, 3, or 4 R^{A3} groups;

each A^1 is independently:



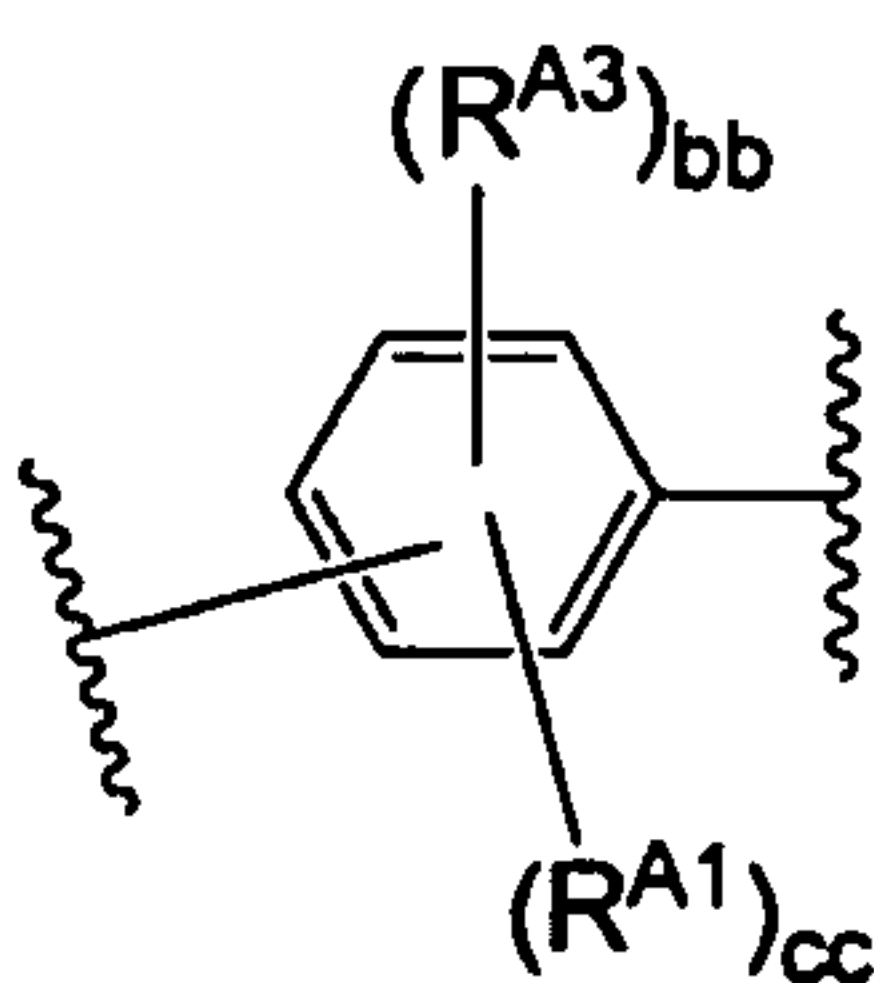
wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

each cc is independently 1, 2, 3, or 4;

each A^2 is independently:



wherein:

each R^{A1} is independently selected from cyano, nitro, SOR^4 , SO_2R^4 , $-alkylSO_2R^4$, haloalkoxy, cyanoalkyl, $NR^4SO_2R^4$, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, $(NR^aR^b)alkyl$, and $(NR^aR^b)carbonyl$; R^a and R^b are each independently selected from the group

consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

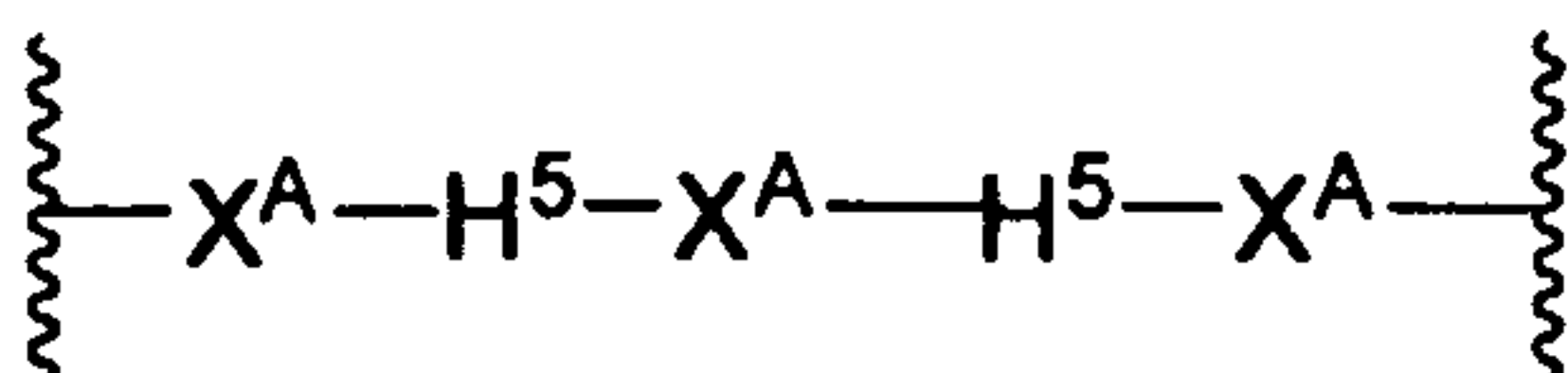
each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each bb is 0, 1, 2, 3, or 4; each cc is 1, 2, 3, or 4; and the sum of bb and cc is 1, 2, 3, or 4;

each A^3 is independently a six-membered heteroaromatic ring containing one, two, or three nitrogen atoms, which ring is substituted with one or more R^{A1} groups, and which ring is optionally substituted with one or more R^{A3} groups;

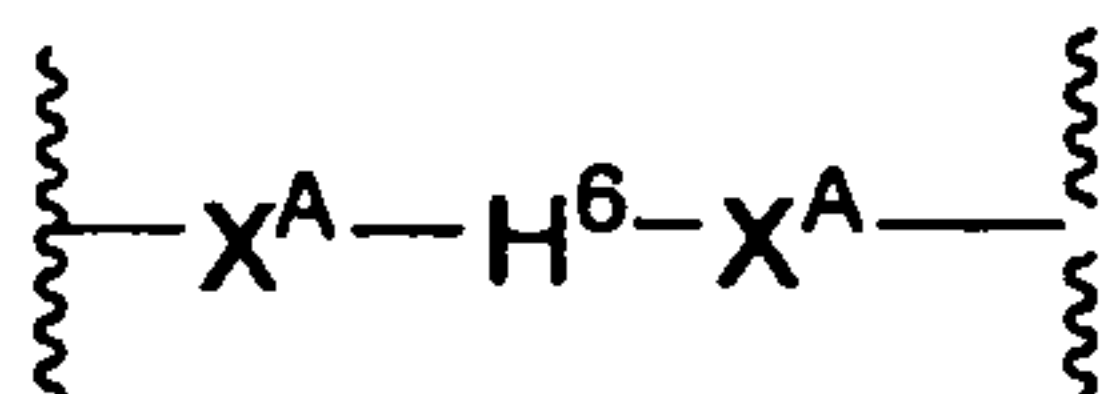
each A^4 is independently:



wherein:

each H^5 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^5 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent

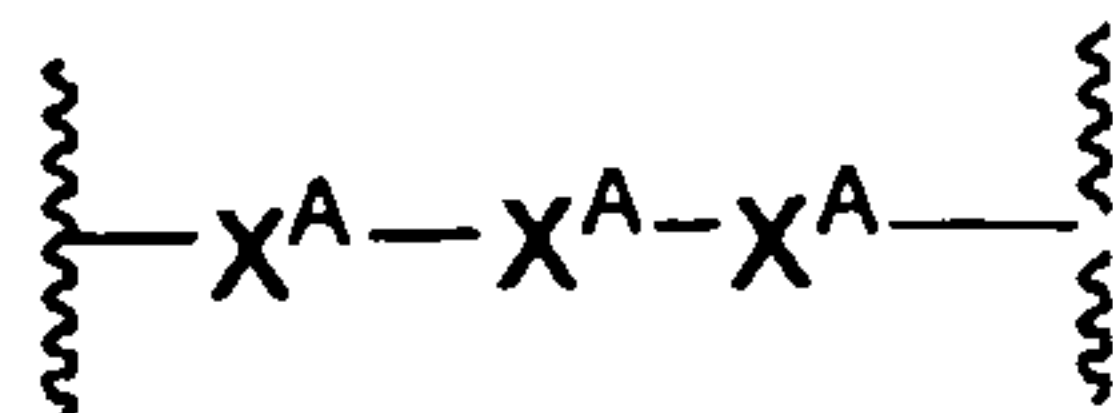
each A^5 is independently:



wherein:

each H^6 is independently a phenyl ring or a six-membered heteroaromatic ring, which H^6 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent; provided that at least one X^A is present;

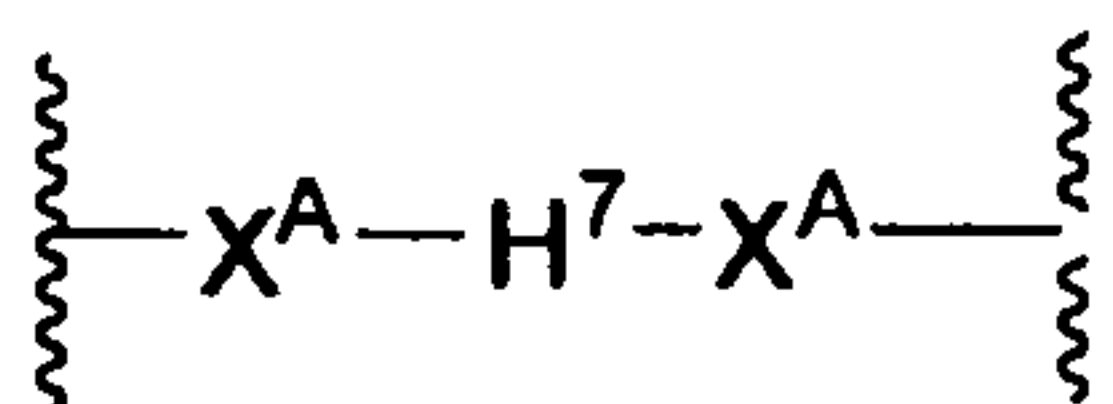
each A⁶ is independently:



wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, allenyl, alkynyl, or absent; provided that at least one X^A is present;

each A⁷ is independently:

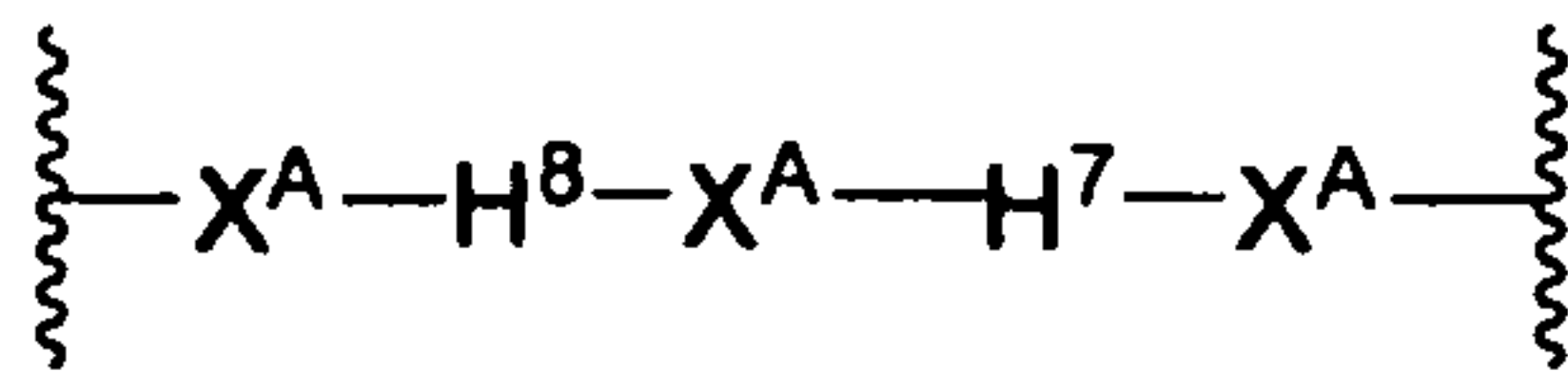


wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A⁸ is independently:



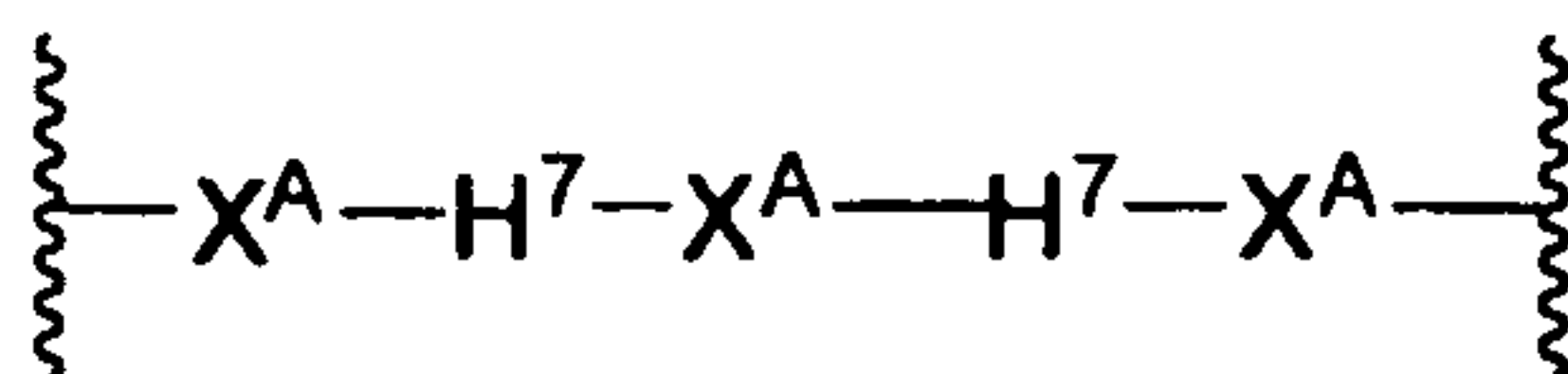
wherein:

each H⁷ is independently a five-membered heteroaromatic ring, which H⁷ is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3};

each H⁸ is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A^9 is independently:

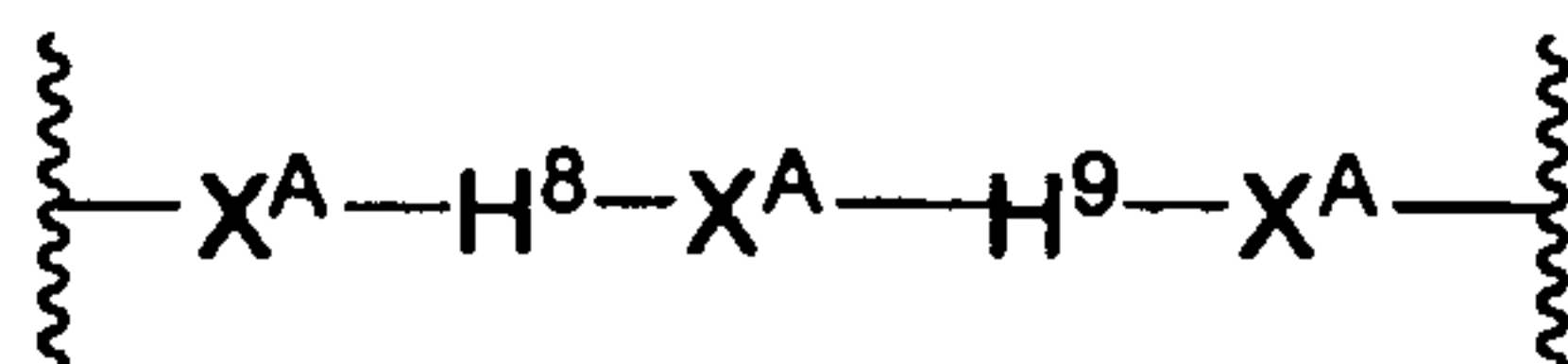


wherein:

each H^7 is independently a five-membered heteroaromatic ring, which H^7 is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A^{10} is independently:



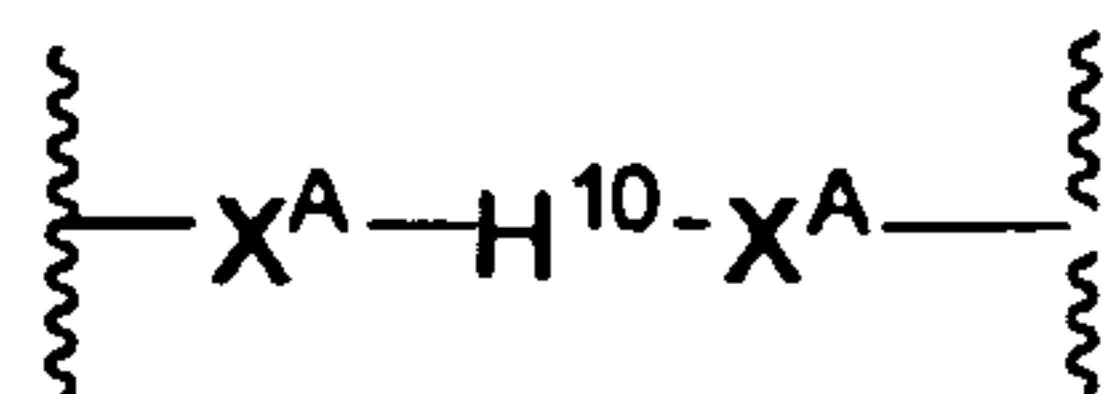
wherein:

each H^8 is independently a phenyl ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each H^9 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent

each A^{11} is independently:



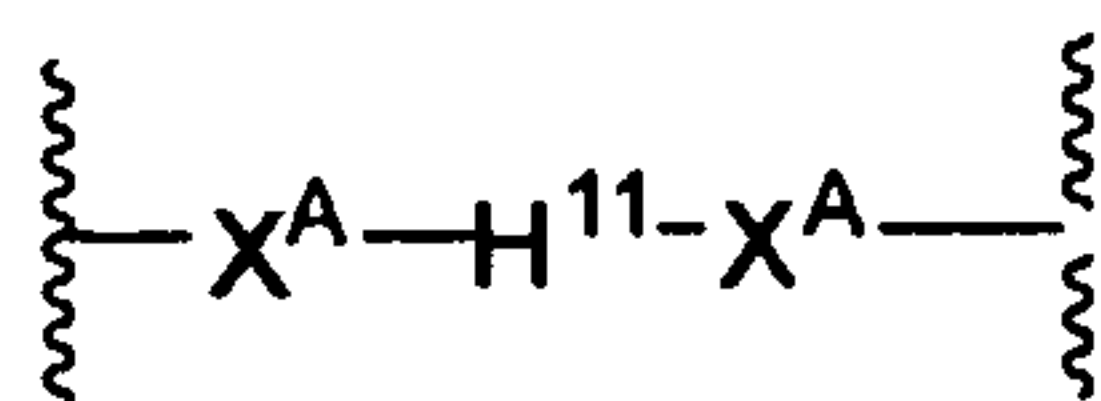
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each H^{10} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that is optionally fused to an aryl, which H^{10} is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl

each A¹² is independently:



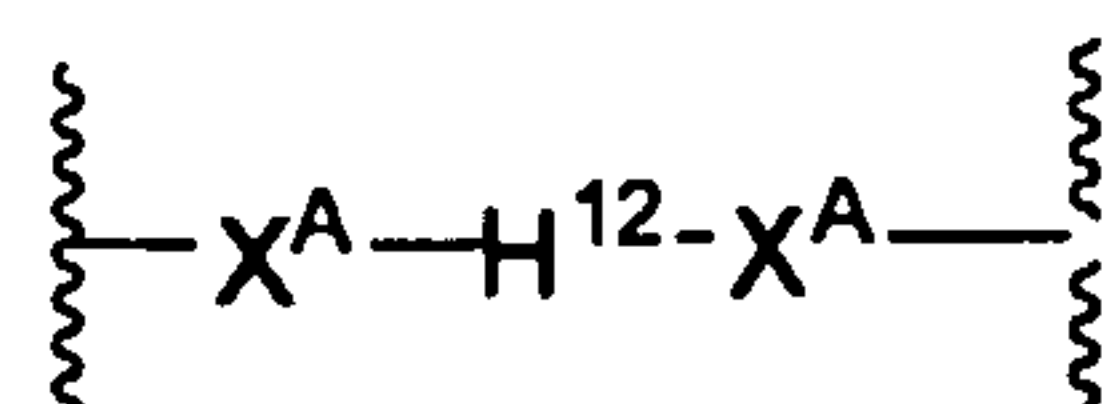
wherein:

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each H^{11} is independently a 5-15 carbon unsaturated, partially unsaturated or saturated bicyclic ring system that contains one or more heteroatoms that is optionally fused to an aryl, which H^{11} is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, and (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo; and

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and

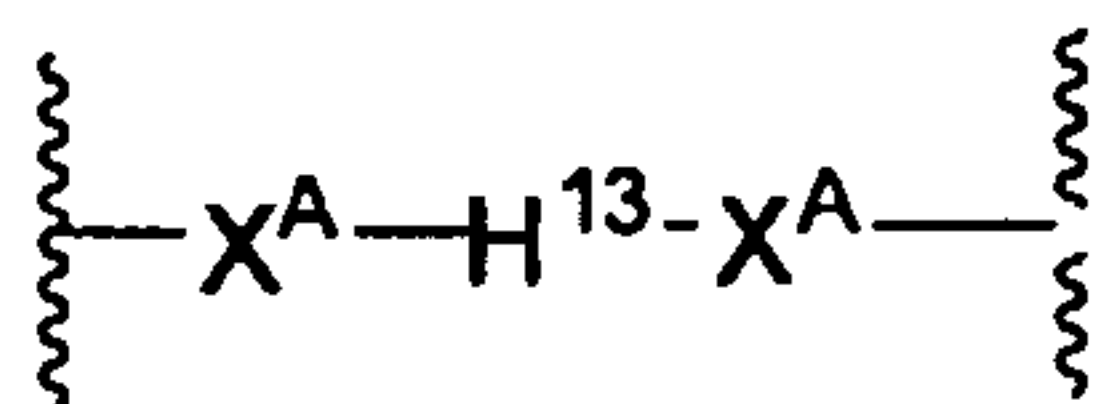
each A¹³ is independently:



wherein:

each H¹² is independently a fused aromatic bicyclic carbocycle, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and
 each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

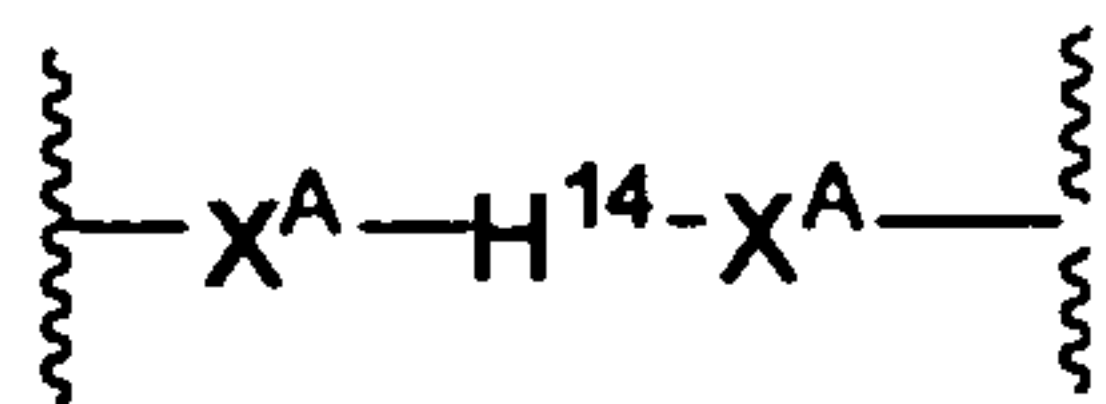
each A¹⁴ is independently:



wherein:

each H¹³ is independently a fused aromatic bicyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and
 each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

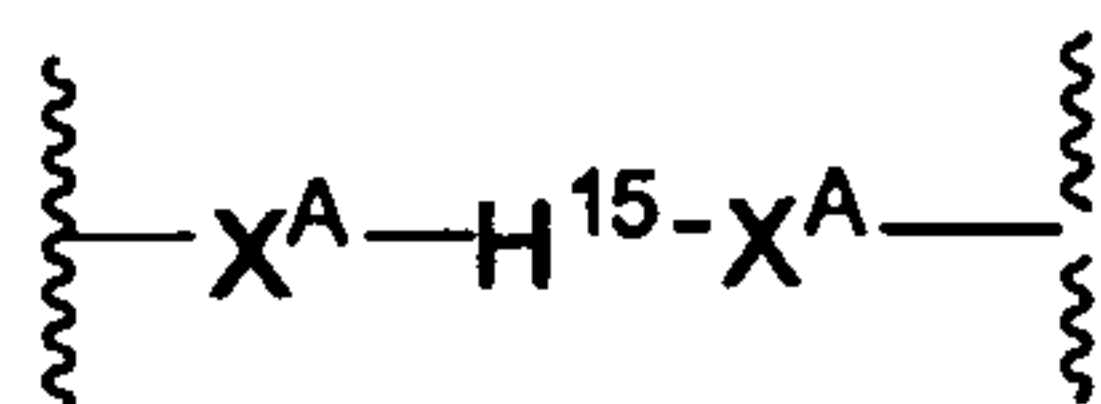
each A¹⁵ is independently:



wherein:

each H¹⁴ is independently a fused unsaturated, partially unsaturated or saturated tricyclic carbocycle which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and
 each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A¹⁶ is independently:

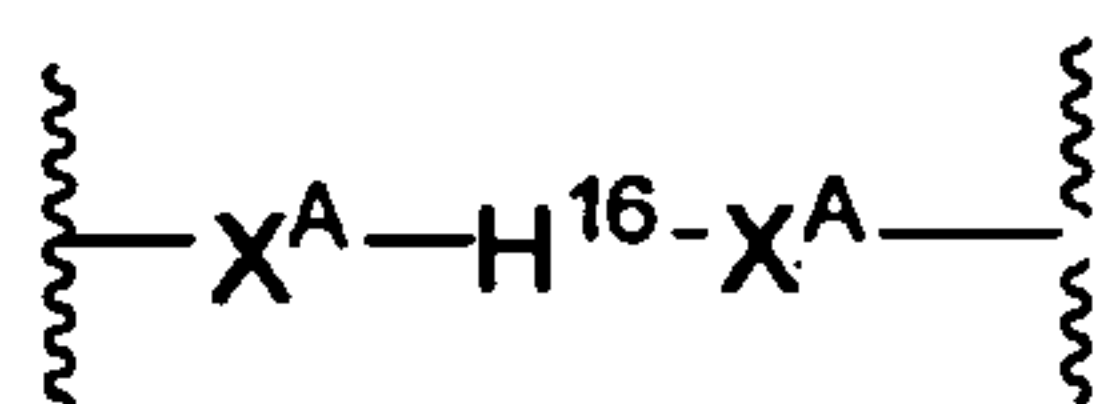


wherein:

each H¹⁵ is independently a fused unsaturated, partially unsaturated or saturated tricyclic heterocycle that comprises at least one heteroatom in the ring system, which ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A¹⁷ is independently:

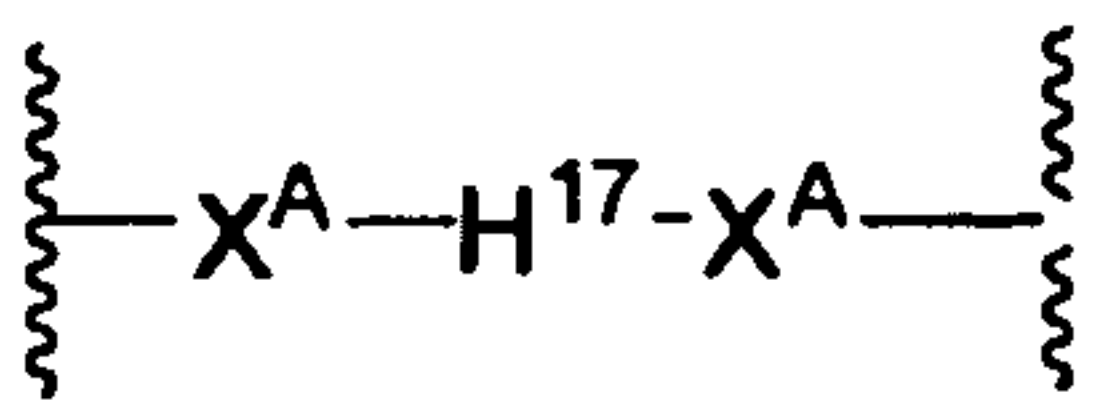


wherein:

each H¹⁶ is independently a fused bicyclic carbocyclic ring system wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3}; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A¹⁸ is independently:

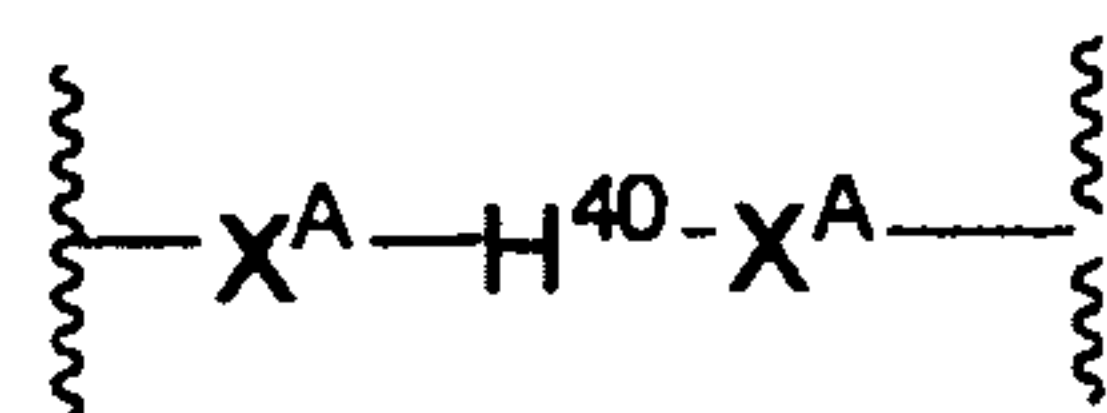


wherein:

each H^{17} is independently a fused bicyclic ring system comprising at least one heteroatom, wherein one ring is aromatic and another ring is partially or fully saturated, which ring system is optionally substituted with one or more groups independently selected from oxo, R^{A1} and R^{A3} ; and

each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each A^{21} is independently:



wherein:

each H^{40} is independently an anti-aromatic monocyclic or fused carbocyclic ring system, which carbocyclic ring system is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ; and

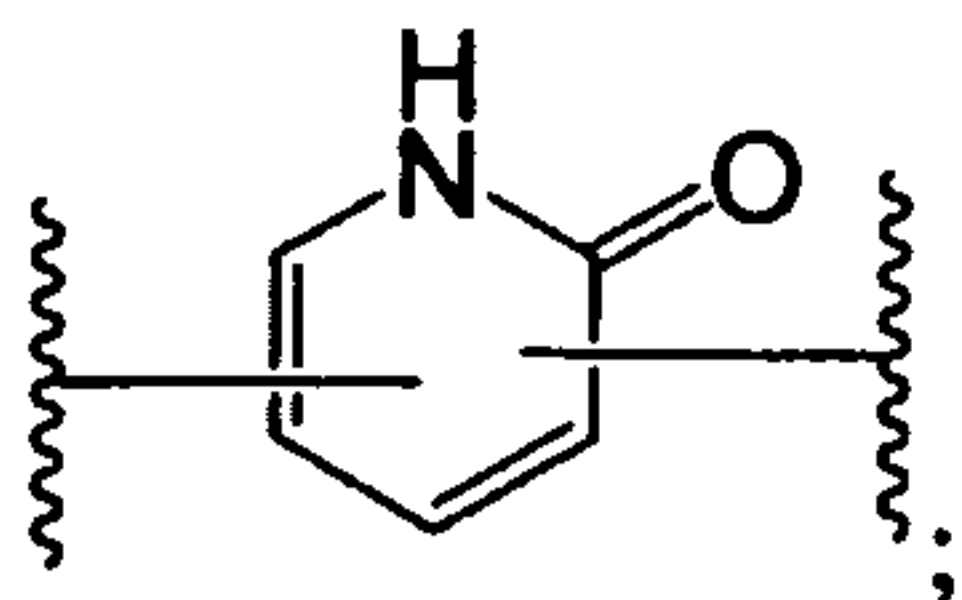
each X^A is independently O, NR, SO, SO₂, C(=O), NRC(=O), C(=O)NR, CR=CR, NRC(=O)NR, allenyl, alkynyl, or absent;

each M^0 is independently a five membered heteroaryl group optionally substituted with one or more alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, haloalkyl, (NR^aR^b) carbonyl and trialkylsilylalkoxyalkyl;

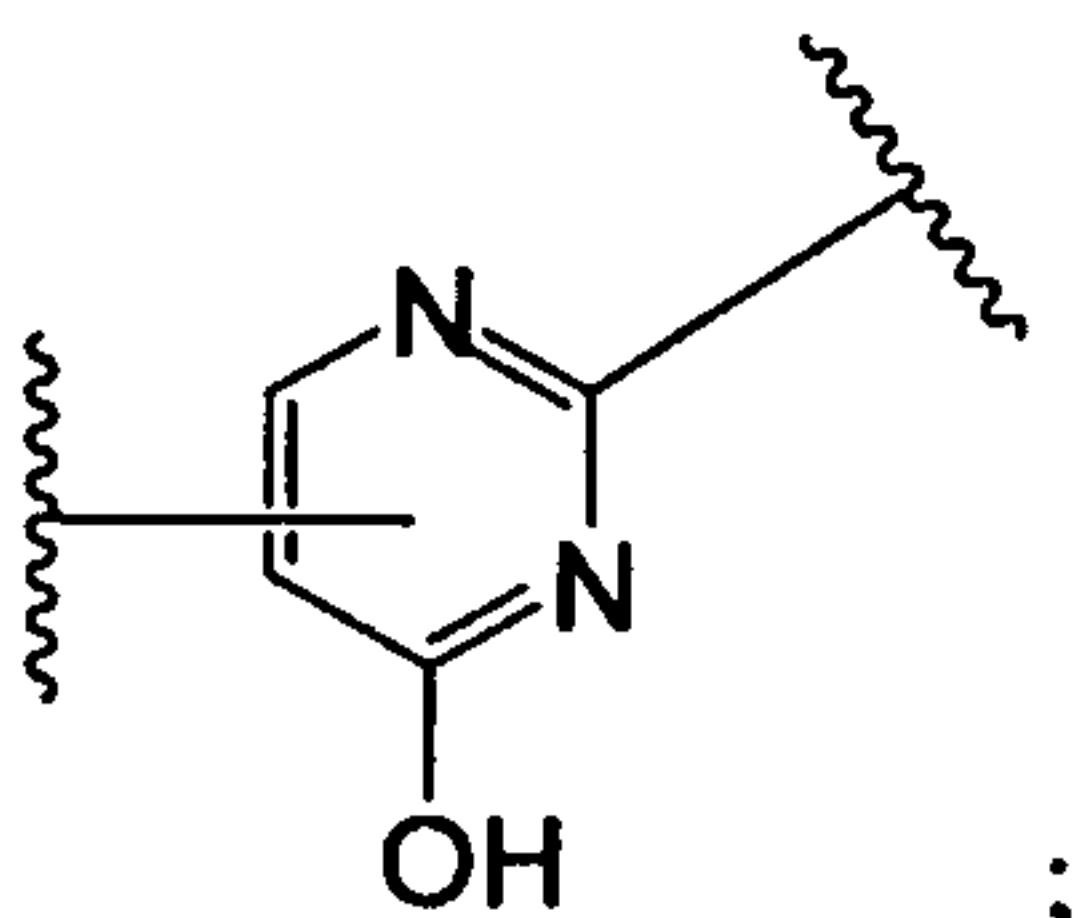
each M^1 is independently selected from $-C(=O)NH-$, $-C(=O)NH-C(R^M)_2-$, $-NHC(=O)-$, $-C(R^M)_2NHC(=O)-$, $-NHC(=O)NR^M-$, $-NHC(=O)O-$; wherein each R^M is independently selected from H and alkyl;

each M^2 is independently a six-membered heteroaromatic ring, which is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

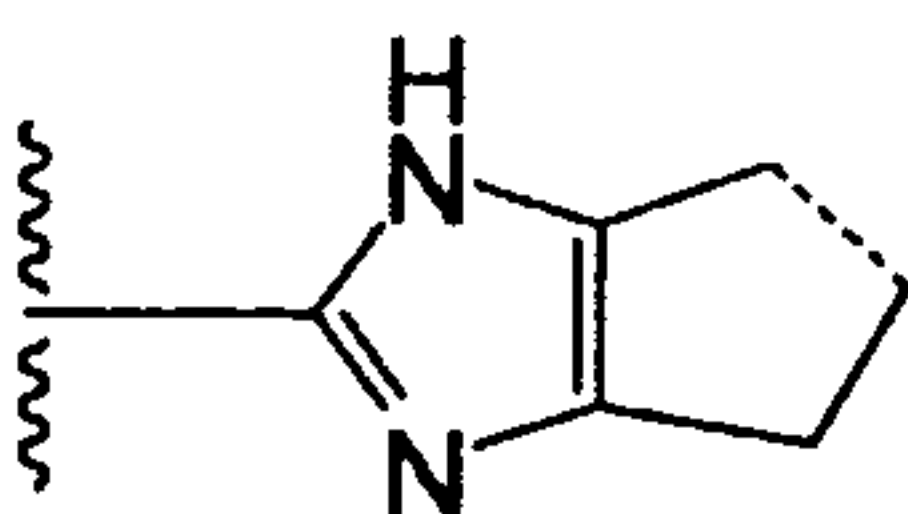
each M^3 is independently:



each M^4 is independently:



each M^5 is independently:



wherein the bond designated with --- is fused to a ring defined for P;

each M^6 is independently a bicyclic bridged ring system comprising 5-15 atoms wherein at least one of the atoms is a heteroatom;

each M^7 is independently a pyrid-di-yl;

each M^8 is independently partially saturated or a saturated five-membered ring that comprises one or more heteroatoms and that is optionally substituted with one or two oxo;

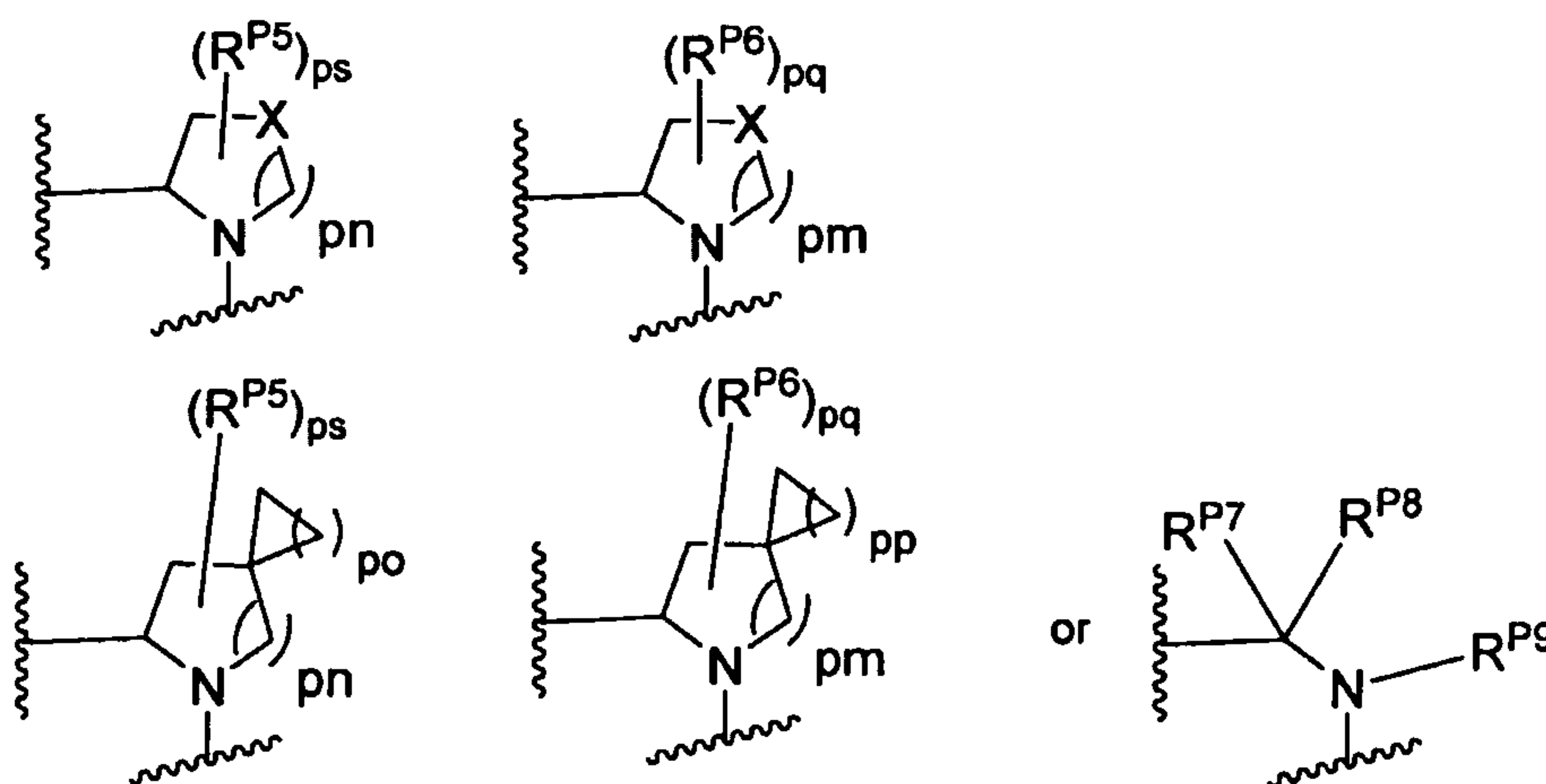
each M^9 is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more R^{P11} ;

each M^{10} is independently a five membered heteroaryl group;

each M^{11} is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more oxo halo, $-R^{M7}$, $-OR^{M7}$, $-SR^{M7}$, $-N(R^{M7})_2$, $-CF_3$, $-CCl_3$, $-OCF_3$, $-CN$, $-NO_2$, $-N(R^{M7})C(=O)R^{M7}$, $-C(=O)R^{M7}$, $-OC(=O)R^{M7}$, $-C(O)OR^{M7}$, $-C(=O)NR^{M7}$, $-S(=O)R^{M7}$, $-S(=O)_2OR^{M7}$, $-S(=O)_2R^{M7}$, $-OS(=O)_2OR^{M7}$, or $-S(=O)_2NR^{M7}$;

each R^{M7} is independently $-H$, alkyl, aryl, arylalkyl, or heterocycle;

each P^0 is independently:



wherein:

X is selected from O , S , $S(O)$, SO_2 , CH_2 , CHR^{P10} , and $C(R^{P10})_2$;
provided that when pn or pm is 0, X is selected from CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H , alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

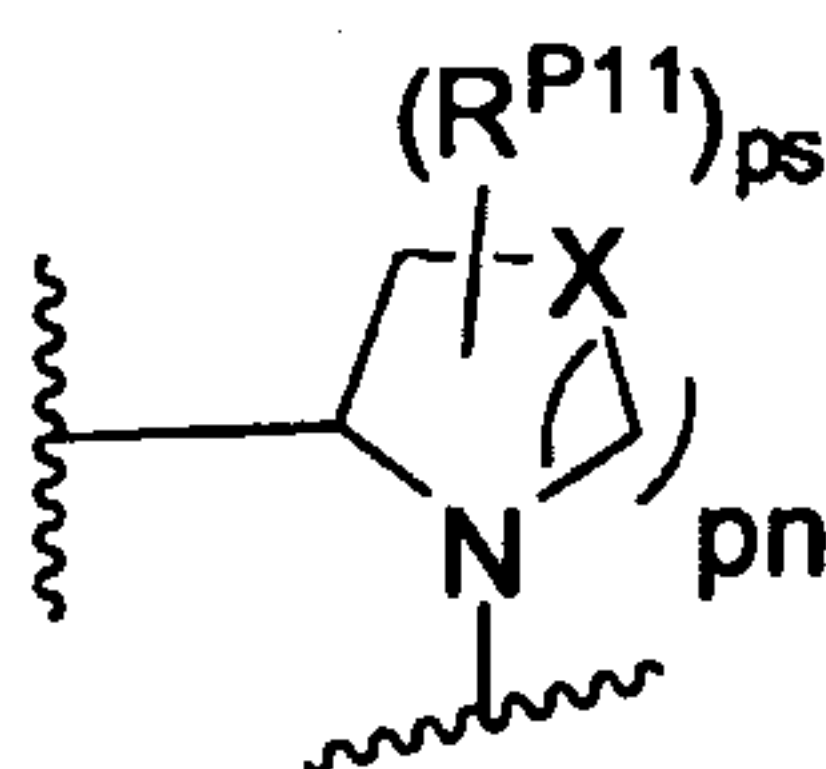
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^1 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂; provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

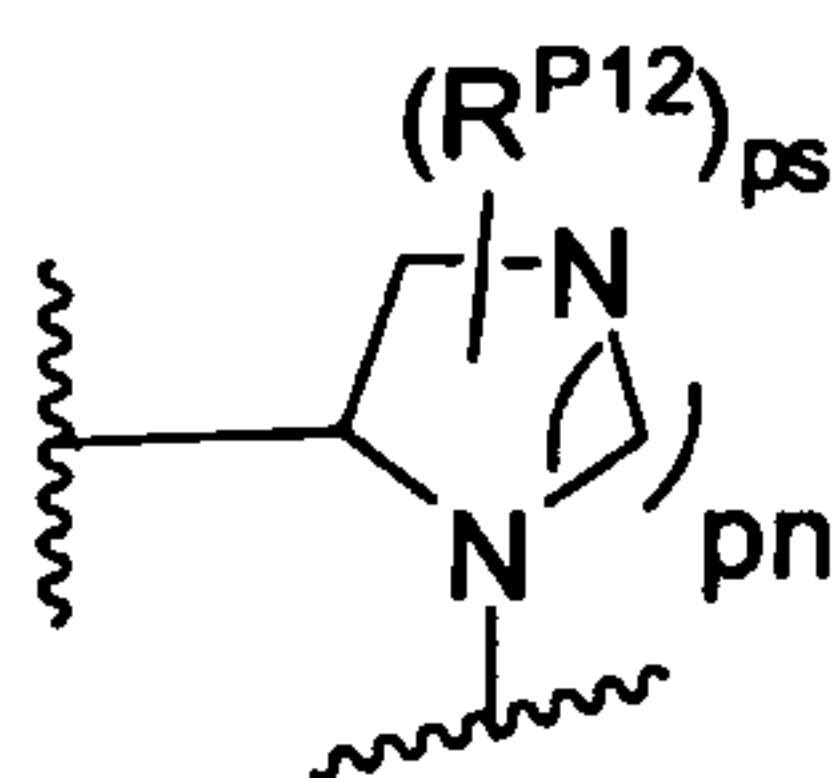
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h) alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h) sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^hR^h$; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy,

haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P² is independently:



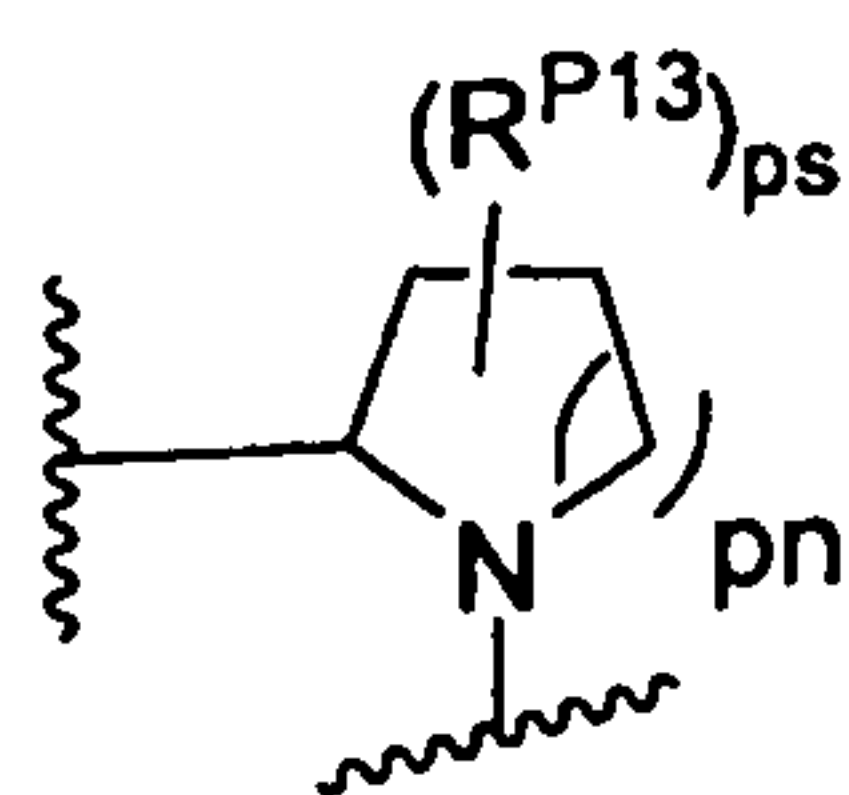
wherein:

each R^{P12} is independently selected from R^{P5}, R^{P11}, -C(=O)OR^h, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P³ is independently a ring of the formula:



wherein:

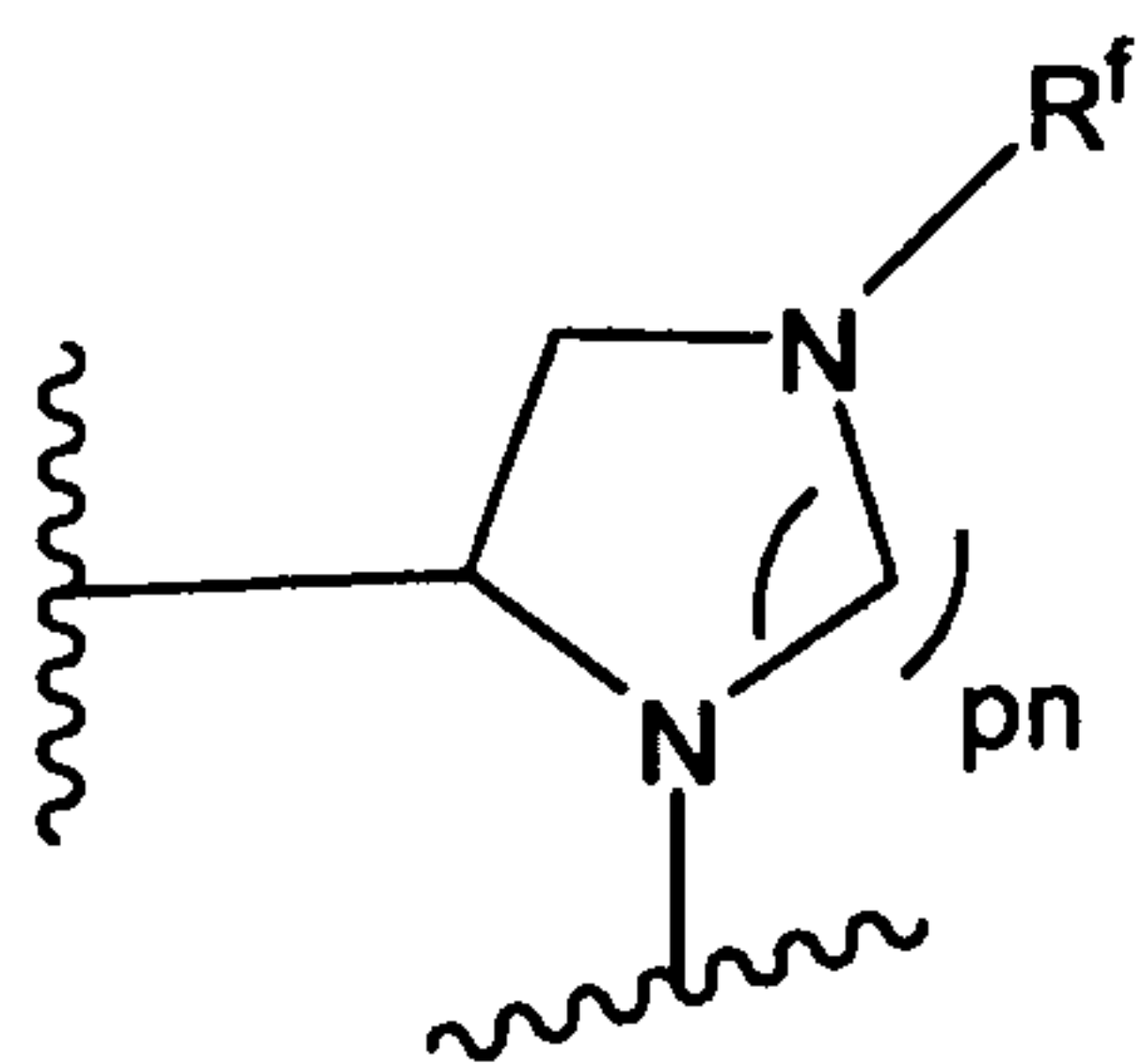
the ring is substituted with one or more oxo groups;

each R^{P13} is independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^4 is independently a ring of the formula:



wherein:

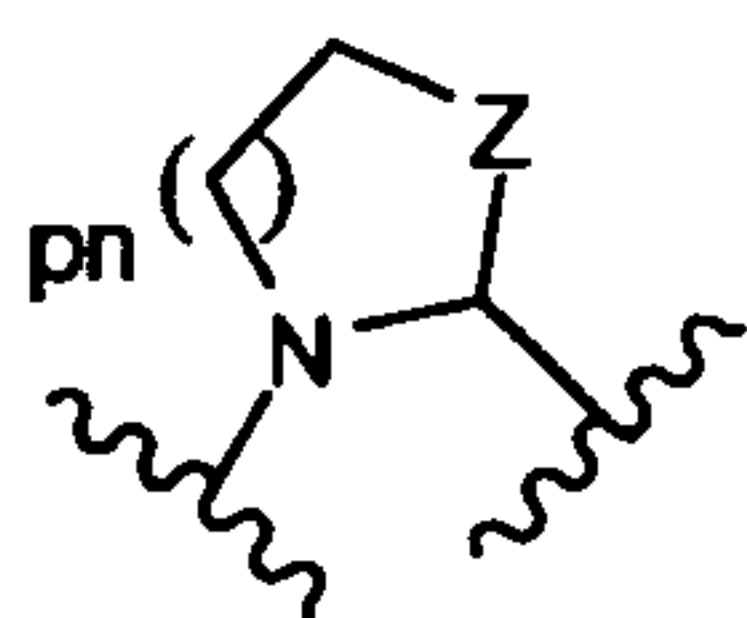
the ring is optionally substituted with one or more groups R^{P14} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P14} that are attached to the same carbon

when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^5 is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

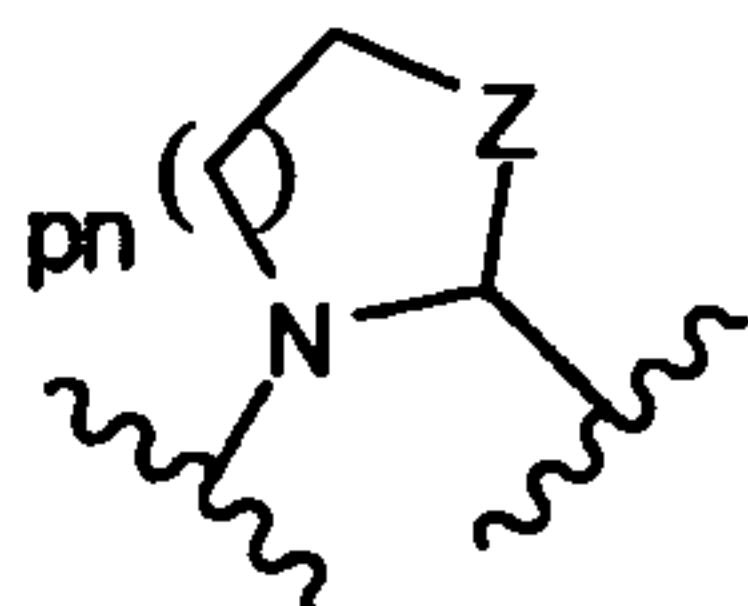
pn is 0, 1, or 2;

Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^6 is independently a ring of the formula:



wherein:

the ring is substituted with one or more oxo and is optionally substituted with one or more groups R^{P16} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

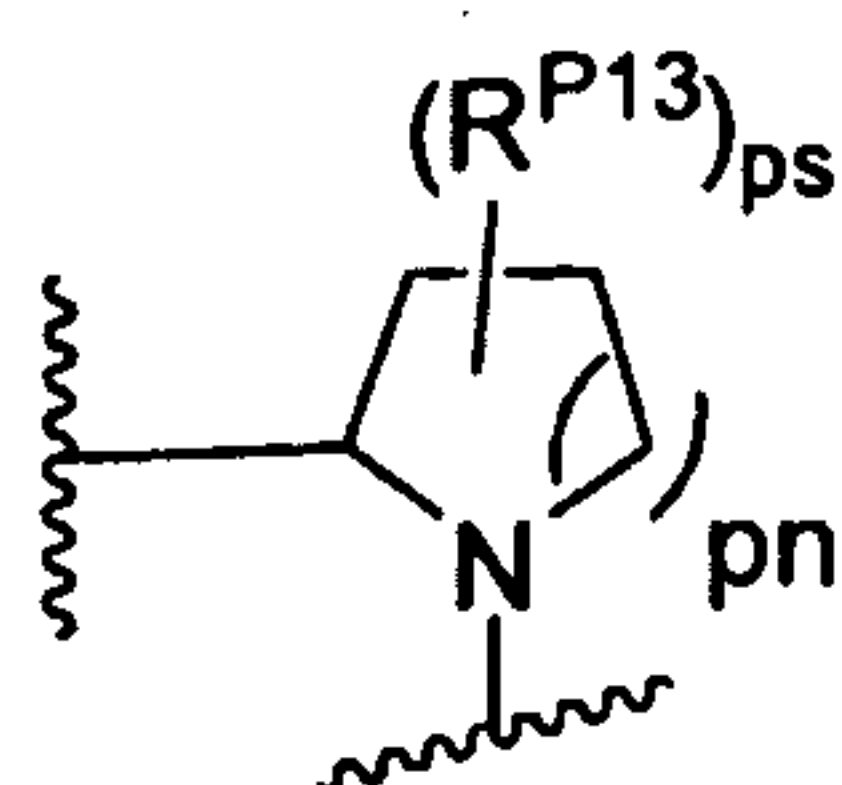
Z is O, S, S(=O), S(=O)₂, or NR^f ;

pn is 0, 1, or 2;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:



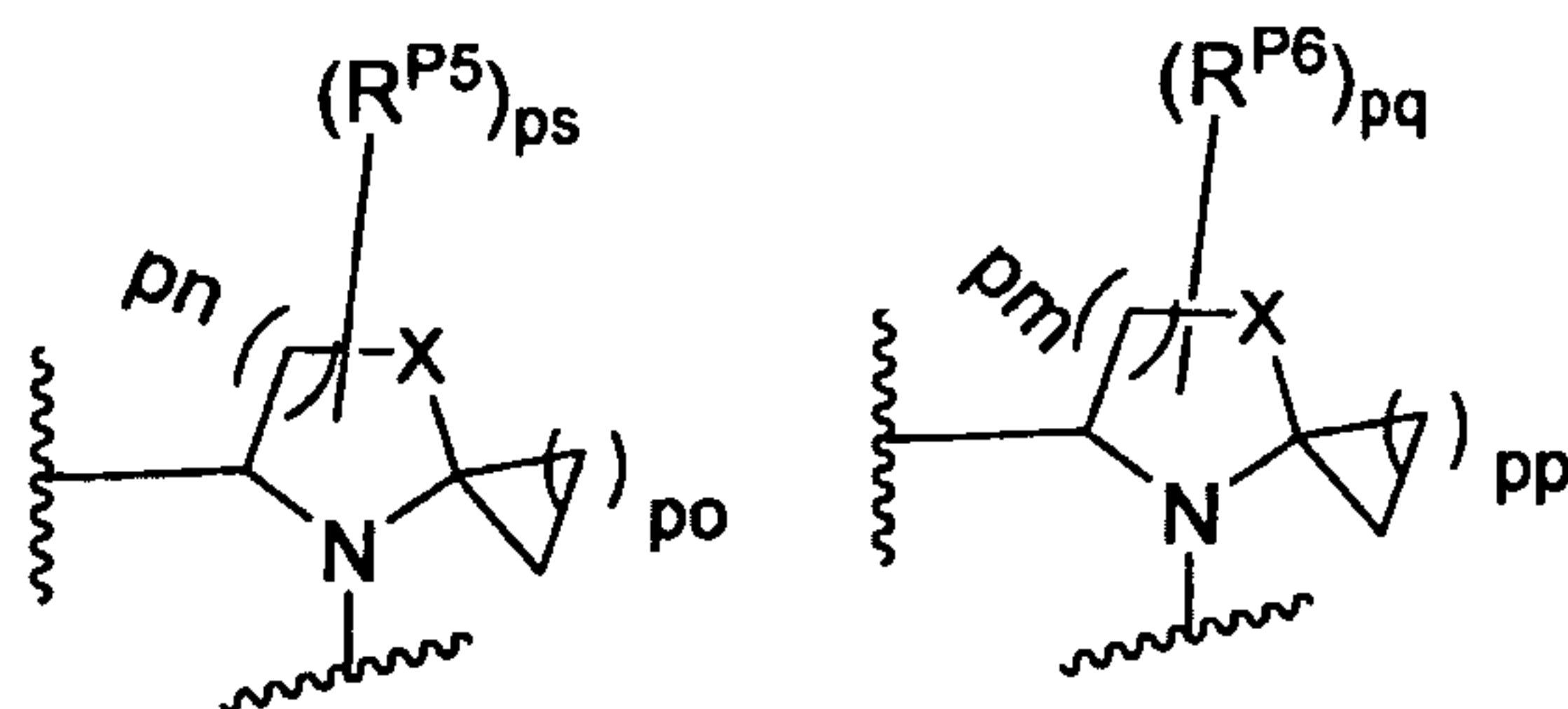
wherein:

ps is 2, 3, 4, 5, or 6;

pn is 0, 1 or 2;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused

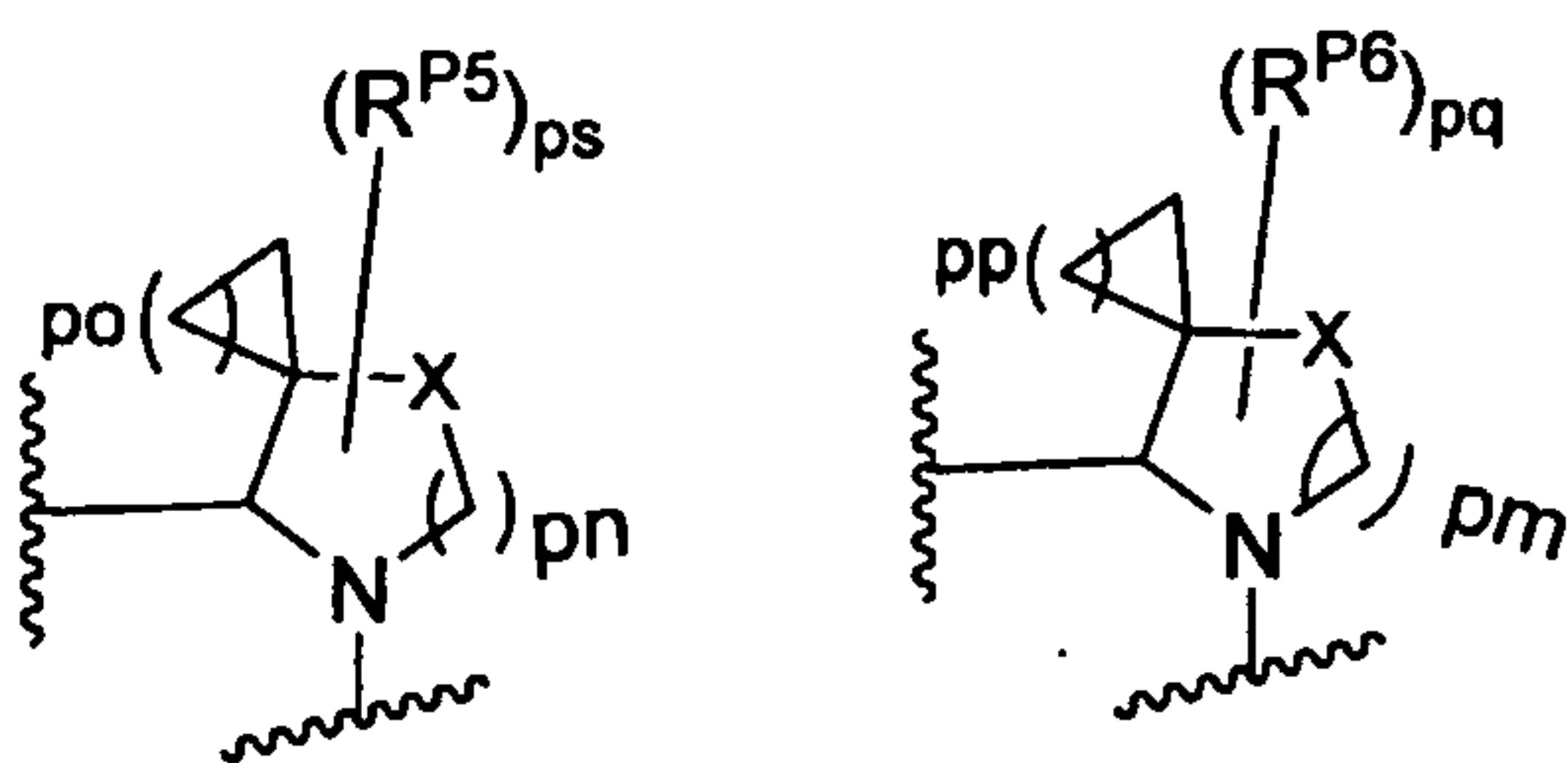
three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P¹¹ is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

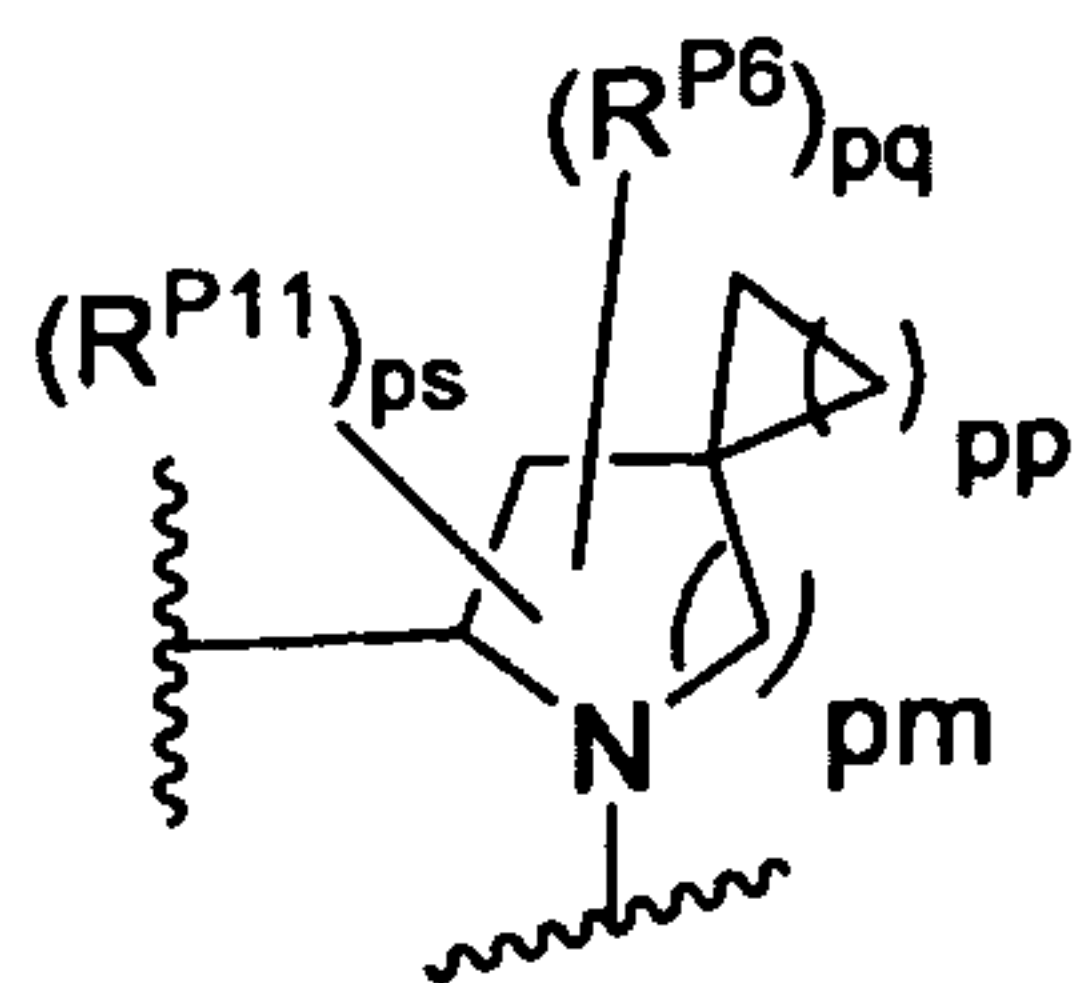
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each P¹² is independently:



wherein:

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

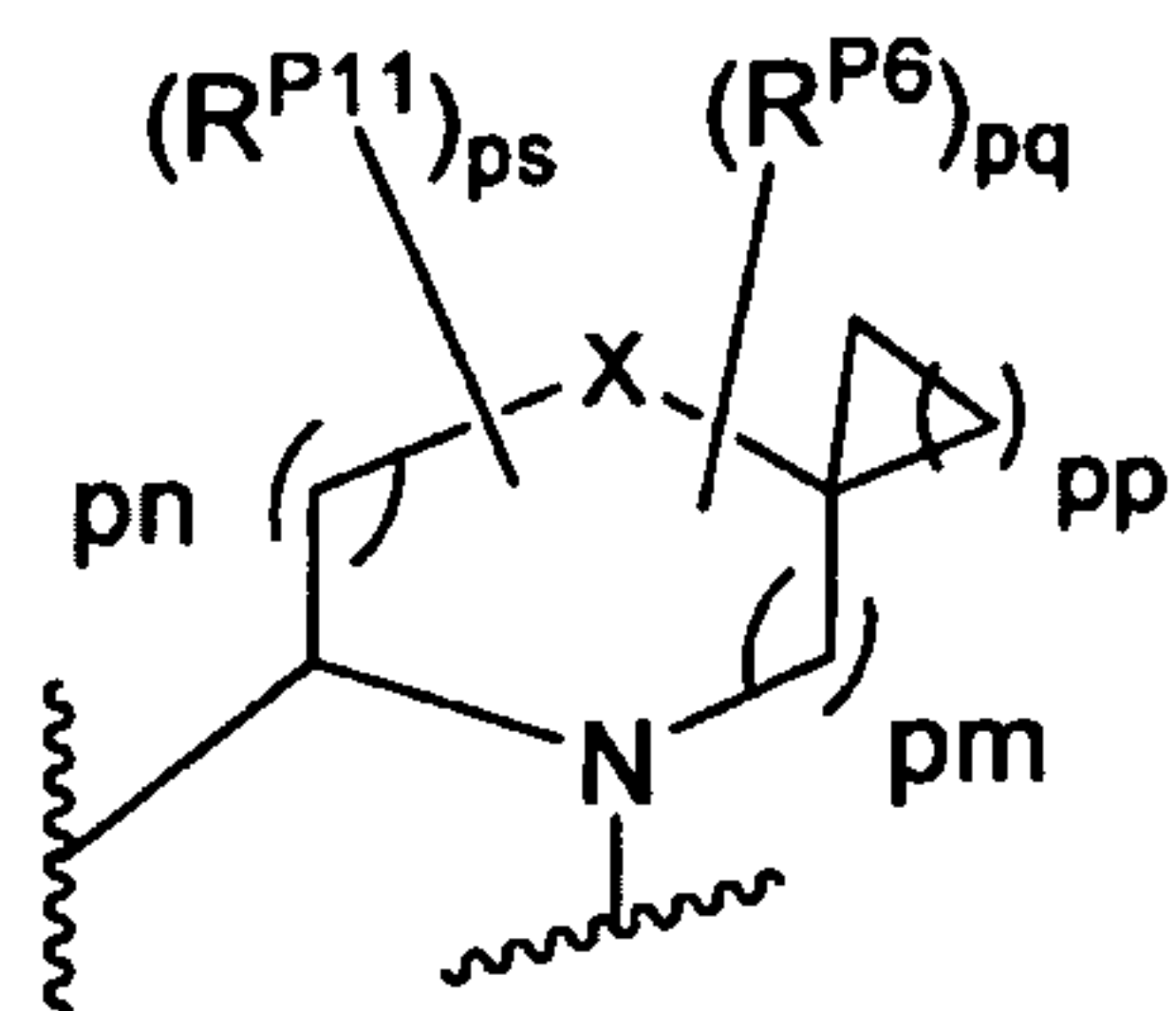
pp is independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^h)$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, $(NR^{hh}R^h)$ alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $(NR^{hh}R^h)$ sulfonyl, heteroarylsulfonyl, $-S(=O)_2R^h$, $-C(=O)R^h$, $-C(=O)NR^{hh}R^h$; and the remaining R^{P11} are independently selected from R^{P5} , cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^h)$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, $(NR^{hh}R^h)$ alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{13} is independently:



wherein:

X is selected from O, S, S(O), SO₂, or NR^h;

each R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2 but the sum of pn and pm is greater than zero;

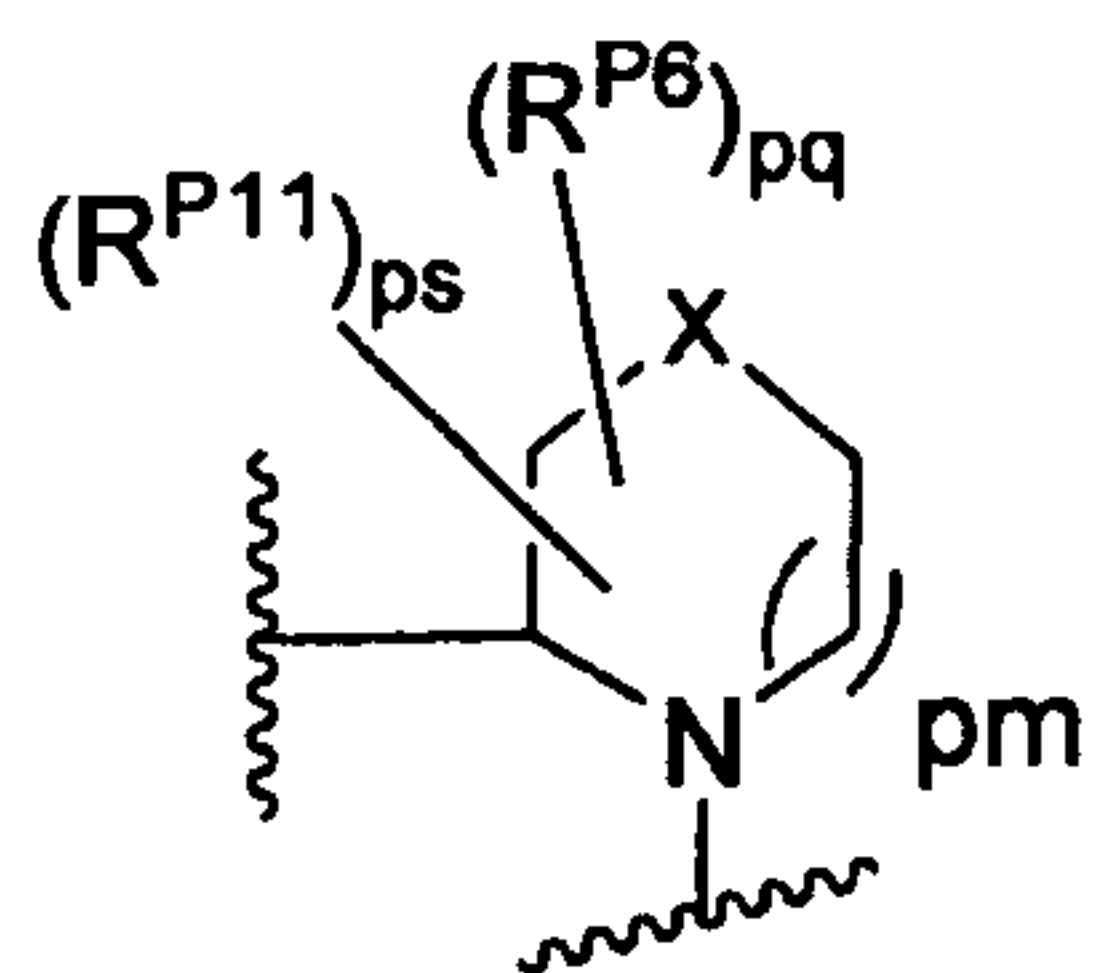
pp are independently 1, 2, or 3;

ps is 1, 2, 3, or 4;

each R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, $(NR^{hh}R^h)$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, $(NR^{hh}R^h)$ alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^h$, $(NR^{hh}R^h)$ alkyl, $(NR^{hh}R^h)$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, sulfonylalkyl, $(\text{NR}^{\text{h}}\text{R}^{\text{h}})$ sulfonyl, heteroarylsulfonyl, $-\text{S}(=\text{O})_2\text{R}^{\text{h}}$, $-\text{C}(=\text{O})\text{R}^{\text{h}}$, $-\text{C}(=\text{O})\text{NR}^{\text{h}}\text{R}^{\text{h}}$, $\text{R}^{\text{P}5}$, cyano, alkylsulfonyl, arylsulfonyl, $(\text{NR}^{\text{h}}\text{R}^{\text{h}})$ sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, $(\text{NR}^{\text{h}}\text{R}^{\text{h}})$ alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^{h} is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^{h} groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^{14} is independently:



wherein:

the ring is substituted with one or more oxo group;

X is NR^{f} ;

each R^{f} is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-\text{S}(=\text{O})_2\text{NR}^{\text{h}}\text{R}^{\text{h}}$, $-\text{S}(=\text{O})_2\text{R}^{\text{h}}$, $\text{C}(=\text{O})\text{R}^{\text{h}}$, $\text{C}(=\text{O})\text{OR}^{\text{h}}$, $-\text{C}(=\text{O})\text{NR}^{\text{h}}\text{R}^{\text{h}}$; each R^{h} is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^{h} groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each $\text{R}^{\text{P}6}$ is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-\text{NR}^{\text{Pa}}\text{R}^{\text{Pb}}$, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq is independently 0, 1, 2, 3, or 4;

pm is independently 0, 1, or 2;

ps is 1, 2, 3, or 4;

R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h) sulfonyl, heterocyclylsulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, NR^hR^h alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

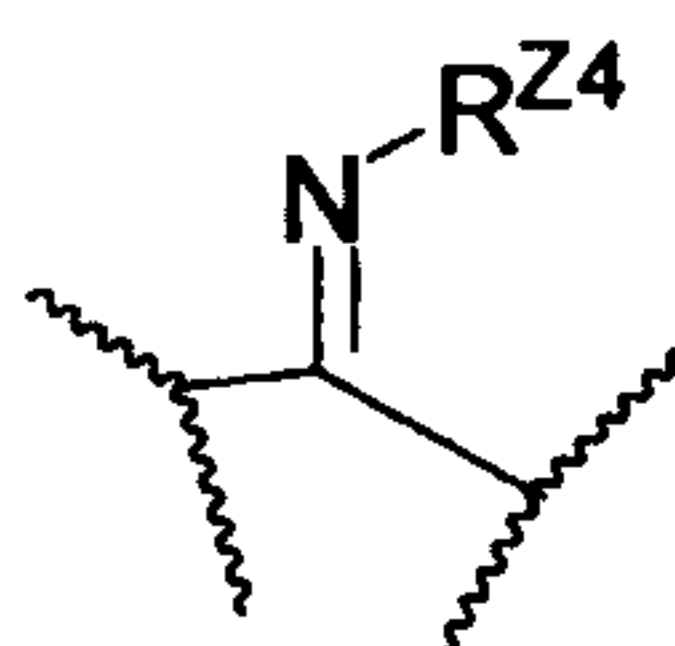
each $-Z^0-$ is $-C(=O)-$ or $-C(=S)-$;

each $-Z^1-$ is independently a bond, or $-C(R^{Z1})_2-$; wherein each R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each $-Z^2-$ is independently saturated or partially unsaturated (C_3-C_8)cycloalkyl that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

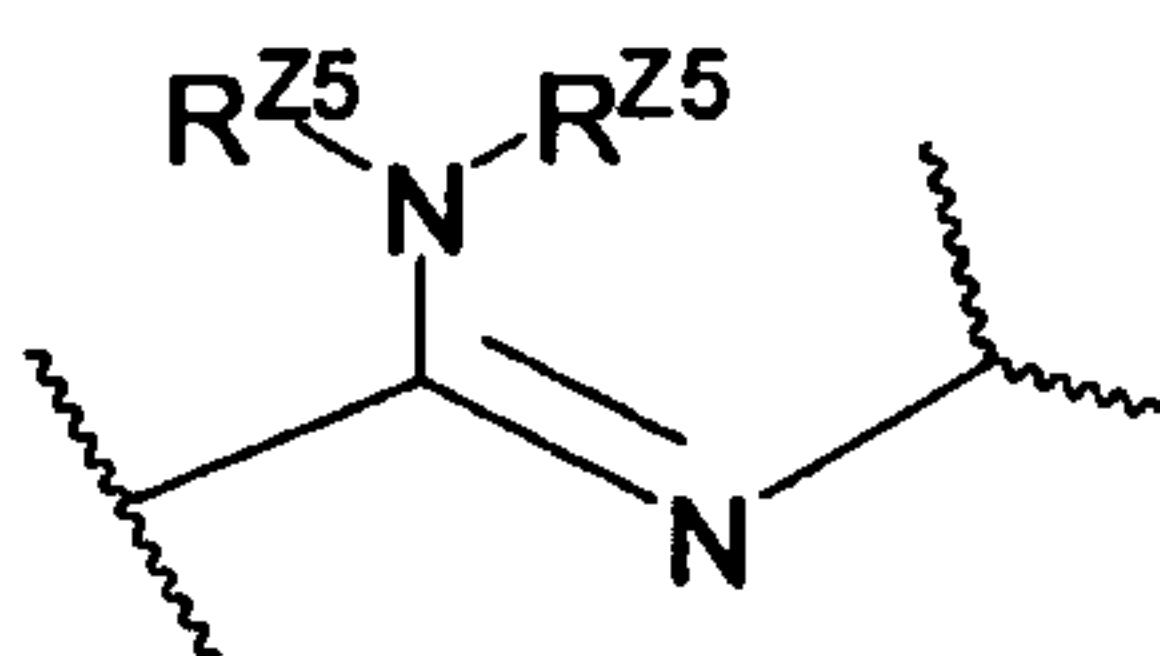
each $-Z^3-$ is independently saturated, partially unsaturated, or aromatic 4-8 membered heterocyclic or heteroaryl ring that is optionally substituted with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^4-$ is independently:



wherein each R^{Z4} is independently H, alkyl, cyano, aryl, or heteroaryl;

each $-Z^5-$ is independently:



wherein each R^{Z5} is independently H, alkyl, cyano, aryl, or heteroaryl; or two R^{Z5} s together with the nitrogen to which they are attached form a 4-8 membered heterocyclic ring that is optionally substituted with one or more oxo and with one or more groups independently selected from R^{A1} and R^{A3} ;

each $-Z^6-$ is independently $-C(R^{Z1})-$ and is doublebonded to P; wherein R^{Z1} is independently H, alkyl, haloalkyl, or halo;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^fR^f) alkyl, (NR^fR^f) alkylcarbonyl, (NR^fR^f) carbonyl, (NR^fR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^X R^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^fR^f$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each E^1 is independently $-OC(=O)NR^{Ec}R^{Ef}$ wherein each R^{Ec} and R^{Ef} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl,

arylalkylcarbonyl, arylcarbonyl, aryloxy carbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f)alkyl, (NR^eR^f)alkylcarbonyl, (NR^eR^f)carbonyl, (NR^eR^f)sulfonyl, -C(NCN)OR', and -C(NCN)NR^xR^y, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one -NR^eR^f group; and wherein the aryl, the aryl part of the aryloxy carbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxy carbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; or wherein R^{Ec} and R^{Ef}, together with the nitrogen atom to which they are attached, form a heterocycle;

each V⁰ is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxy carbonylalkyl, alkylsulfonylalkyl, aryloxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl, wherein each R is independently selected from hydrogen and alkyl;

and wherein arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^xR^y, - (NR^xR^y)alkyl, oxo, and -P(O)OR₂, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, alkyl carbonyl, aryl, arylalkyl, aryl carbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclyl carbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the aryl carbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclyl carbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NRaRbC(=O)O-$; Ra and Rb are each independently selected from hydrogen, alkenyl, and alkyl;

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va} R^{Vb} C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^6 is independently arylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^7 is independently heterocyclosulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^8 is independently spirocycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^9 is independently spirocycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{10} is independently fusedbicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{11} is independently fusedbicycliccycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{12} is independently bridged-bicycliccycloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{13} is independently bridged-bicyclic-cycloalkylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{14} is independently aryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{15} is independently arylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{16} is independently cycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{17} is independently cycloalkylalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{18} is independently heterocyclooxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{19} is independently heterocycloalkyloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^{20} is independently heteroaryloxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl; and

each V^{21} is independently heteroarylalkylalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl.

In another specific embodiment of the invention the compound of formula (Ic) comprises: $M^0-A-A-M^0$, $M^0-A-A-M^9$, $M^9-A-A-M^0$, or $M^9-A-A-M^9$, $M^{10}-A-A-M^0$, $M^0-A-A-M^{10}$, $M^{10}-A-A-M^9$, $M^9-A-A-M^{10}$, or $M^{10}-A-A-M^{10}$.

In another specific embodiment of the invention $-A-A-$ is $-A^0-A^5-$.

In another specific embodiment of the invention $-A-A-$ is $-A^0-A^{13}-$.

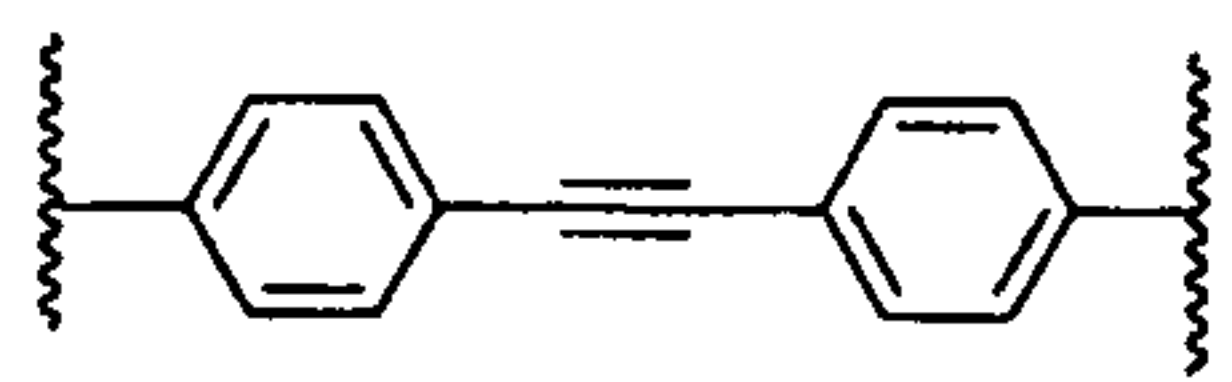
In another specific embodiment of the invention $-A-A-$ is $-A^{13}-A^{13}-$.

In another specific embodiment of the invention $-A-A-$ is $-A^0-A^{11}-$.

In another specific embodiment of the invention $-A-A-$ is $-A^{13}-A^6-$.

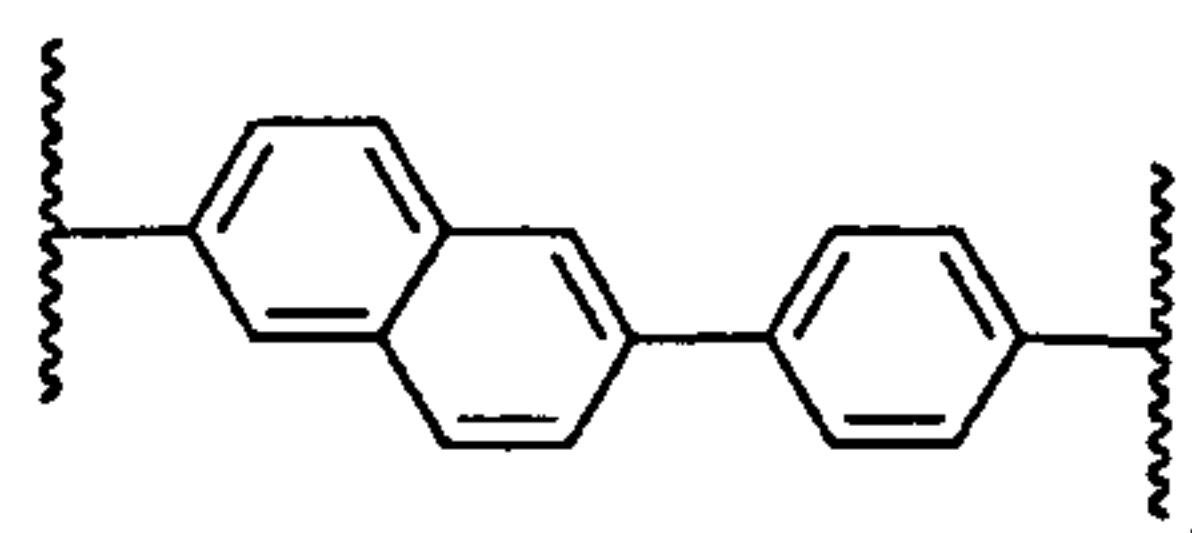
In another specific embodiment of the invention one A is A^0 and one A is A^5 , wherein one X^A in the A^5 is absent and the other X^A in the A^5 is alkynyl.

In another specific embodiment of the invention $-A^0-A^5-$ has the following structure:



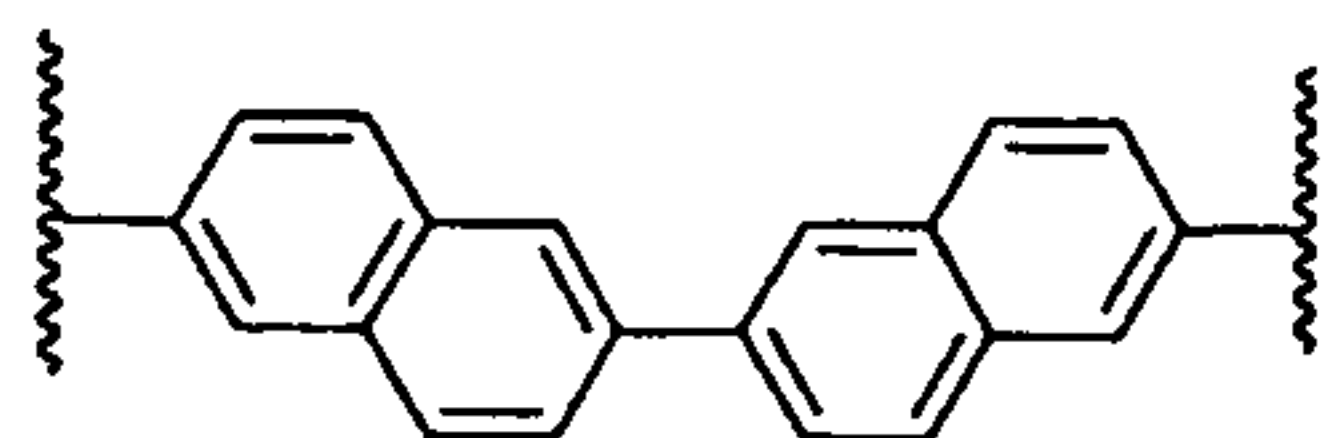
In another specific embodiment of the invention one A is A^0 and one A is A^{13} , wherein both X^A in the A^{13} are absent.

In another specific embodiment of the invention $-A^0-A^{13}-$ has the following structure:



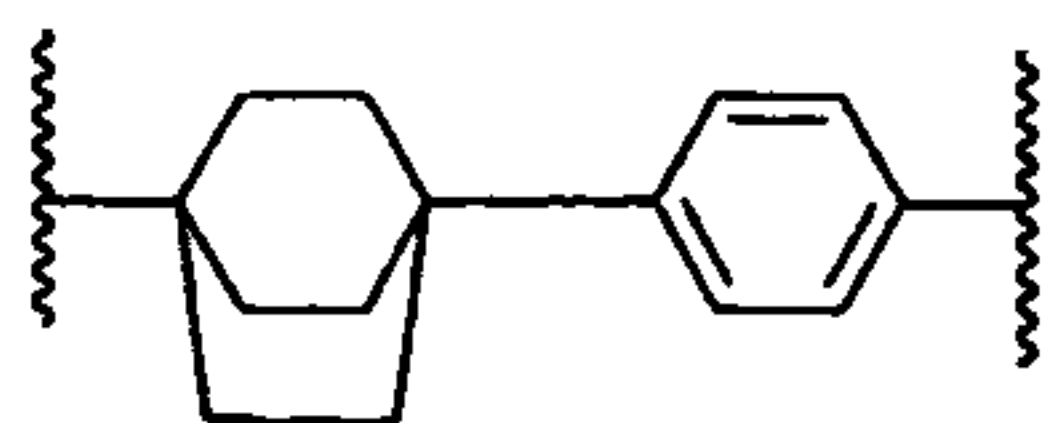
In another specific embodiment of the invention $A-A$ is $A^{13}-A^{13}$, wherein all X^A in both A^{13} are absent.

In another specific embodiment of the invention $-A^{13}-A^{13}-$ has the following structure:



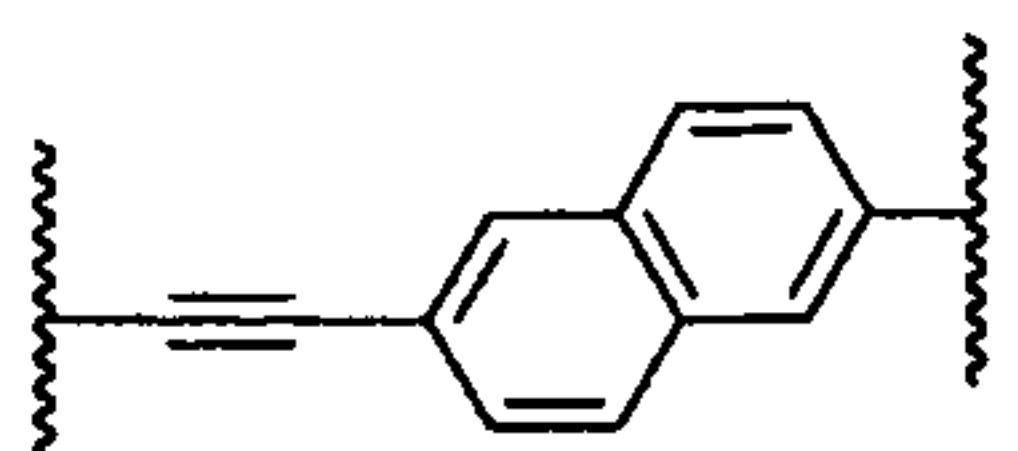
In another specific embodiment of the invention A-A- is A⁰-A¹¹ wherein all X^A in both the A⁰ and the A¹¹, are absent or alkynyl.

In another specific embodiment of the invention -A⁰-A¹¹- has the following structure:



In another specific embodiment of the invention the compound of formula (Ic) comprises one A¹³ and one A⁶ wherein all X^A in the A¹³ are absent.

In another specific embodiment of the invention -A¹³-A⁶- has the following structure:

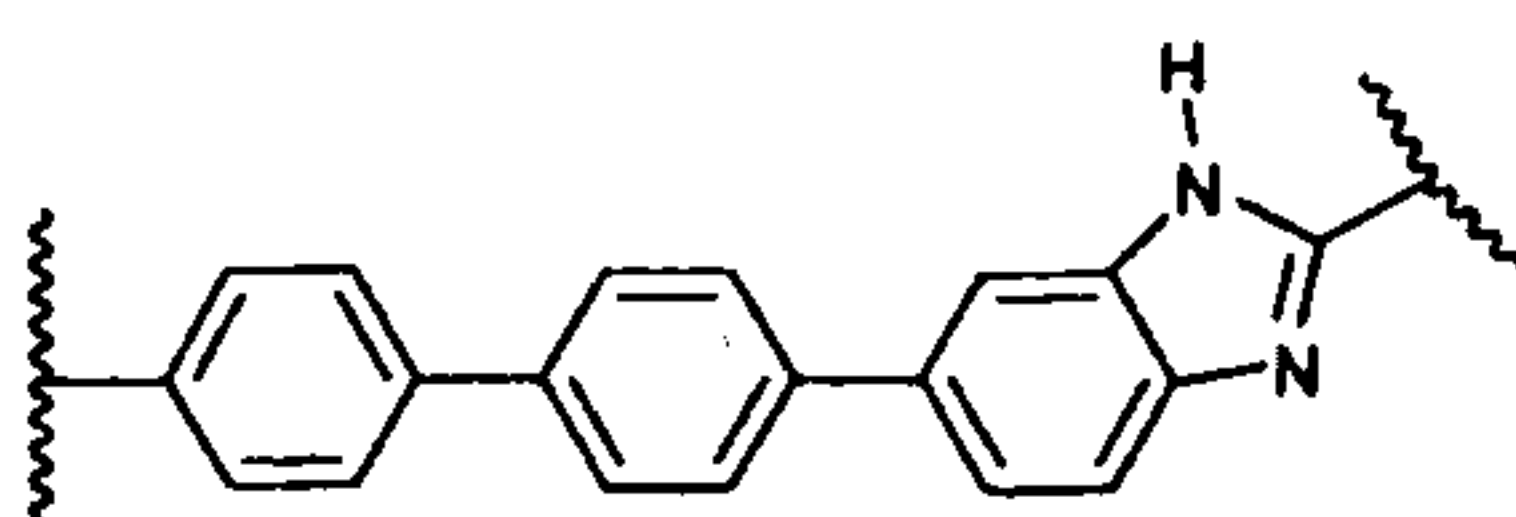


In another specific embodiment of the invention M⁰ is imidazolyl and M⁹ is benzimidazolyl.

In another specific embodiment of the invention the compound of formula (Ic) comprises two A⁰ and one M is M⁹.

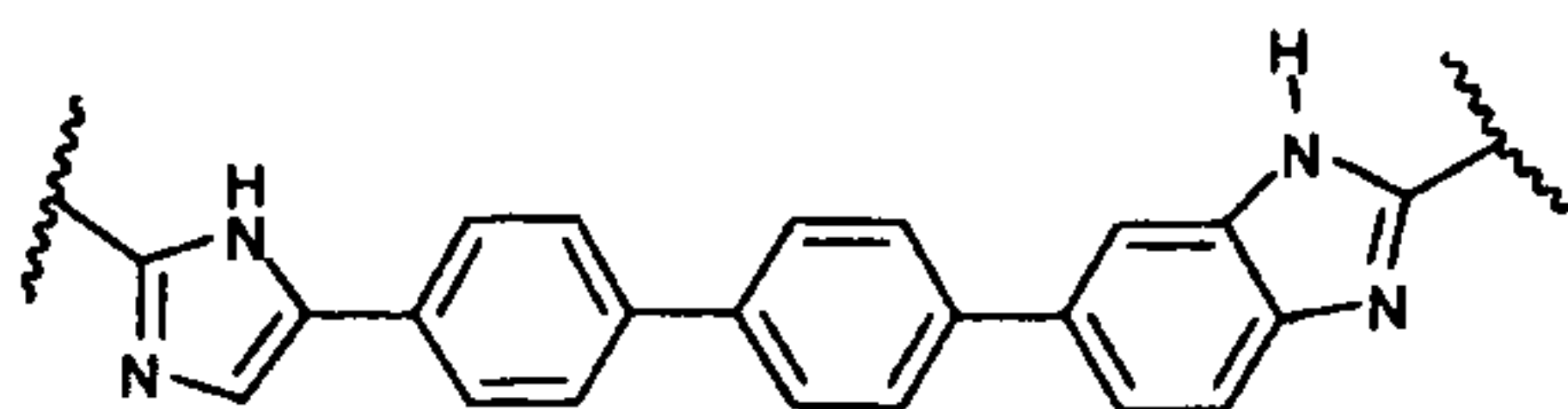
In another specific embodiment of the invention the compound of formula (Ic) comprises two A⁰ and one M is M⁰ and another M is M⁹.

In another specific embodiment of the invention the compound of formula (Ic) comprises A⁰-A⁰-M⁹ which has the following structure:



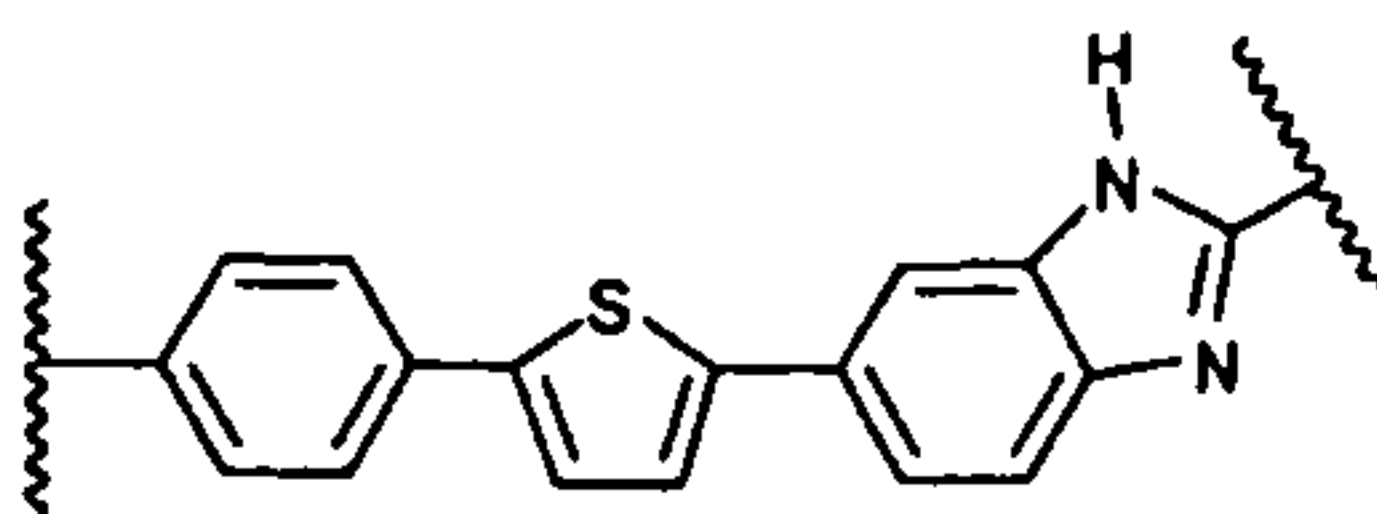
In another specific embodiment of the invention the compound of formula (Ic) comprises M⁰-A⁰-A⁰-M⁹.

In another specific embodiment of the invention M⁰-A⁰-A⁰-M⁹ has the following structure:



In another specific embodiment of the invention the compound of formula (Ic) comprises A⁰-A⁷-M⁹.

In another specific embodiment of the invention A⁰-A⁷-M⁹ has the following structure:



In another specific embodiment of the invention the compound of formula (Ic) comprises one or two M and each M is M^0 .

In another specific embodiment of the invention the compound of formula (Ic) comprises one or two M and each M is imidazolyl.

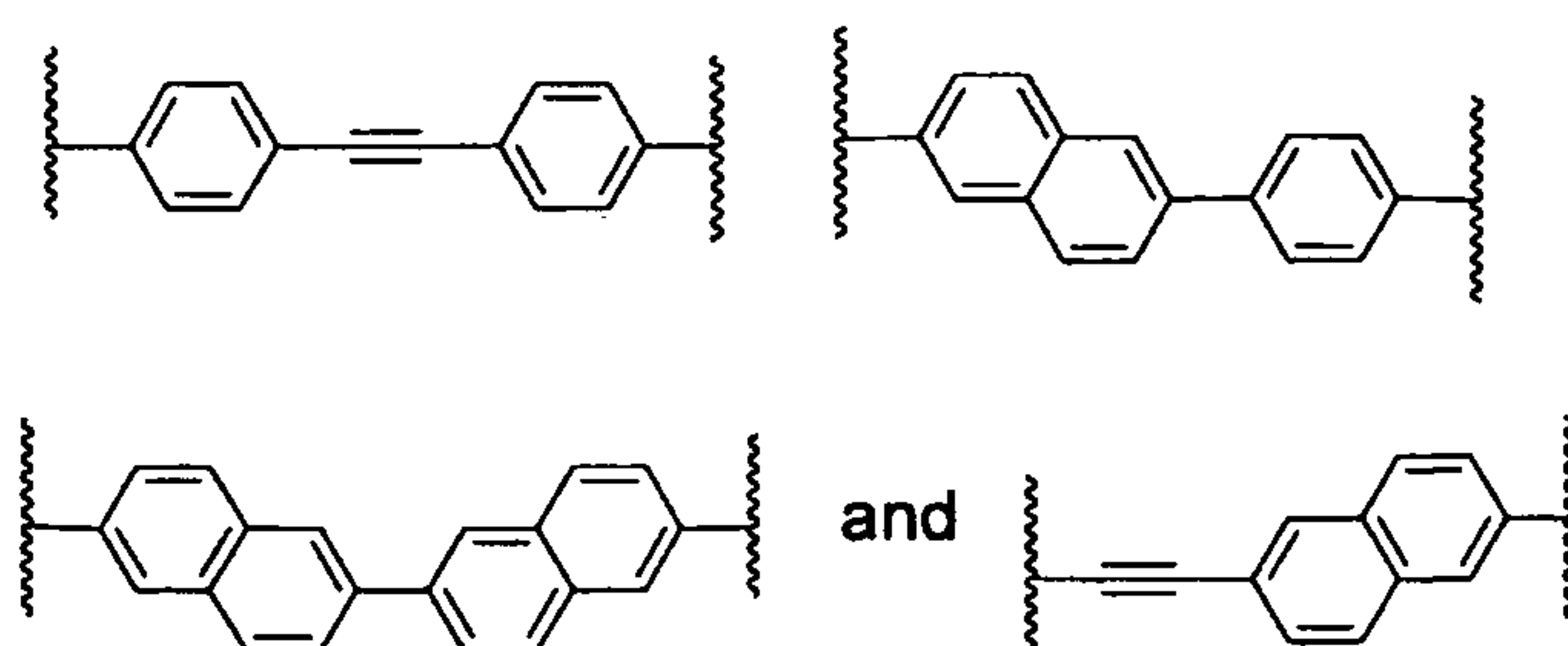
In another specific embodiment of the invention the compound of formula (Ic) comprises one or two M and each M is M^9 .

In another specific embodiment of the invention the compound of formula (Ic) comprises one or two M and each M is benzimidazolyl.

In another specific embodiment of the invention the compound of formula (Ic) comprises two M wherein one M is M^0 and one M is M^9 .

In another specific embodiment of the invention the compound of formula (Ic) comprises two M wherein one M is imidazolyl and one M is benzimidazolyl.

In another specific embodiment of the invention A-A is selected from:



In another specific embodiment of the invention $-M-A-A-M-$ is selected from $M^0-A-A-M^0$, $M^0-A-A-M^9$, $M^9-A-A-M^0$, and $M^9-A-A-M^9$.

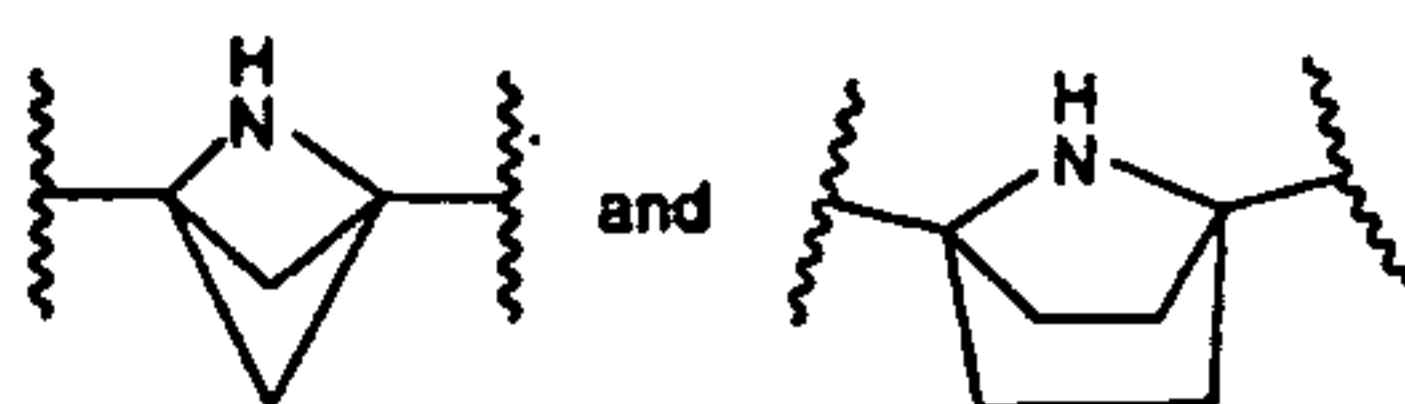
In another specific embodiment of the invention the compound of formula (Ic) $M-A-A-M$ is selected from $M^{10}-A-A-M^0$, $M^0-A-A-M^{10}$, $M^{10}-A-A-M^9$, $M^9-A-A-M^{10}$, and $M^{10}-A-A-M^{10}$.

In another specific embodiment of the invention each M is independently a 5-membered heteroaryl ring.

In another specific embodiment of the invention each M is 2,4-imidazoldiyl.

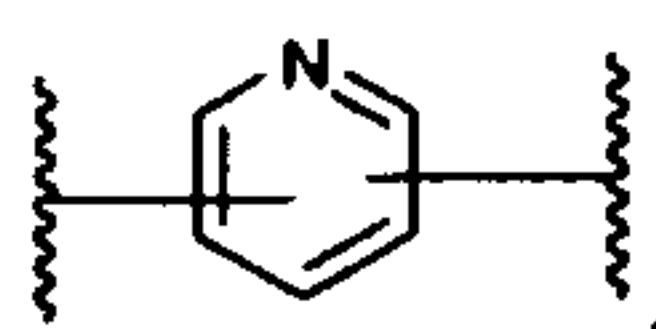
In another specific embodiment of the invention M is M^6 .

In another specific embodiment of the invention M is selected from:



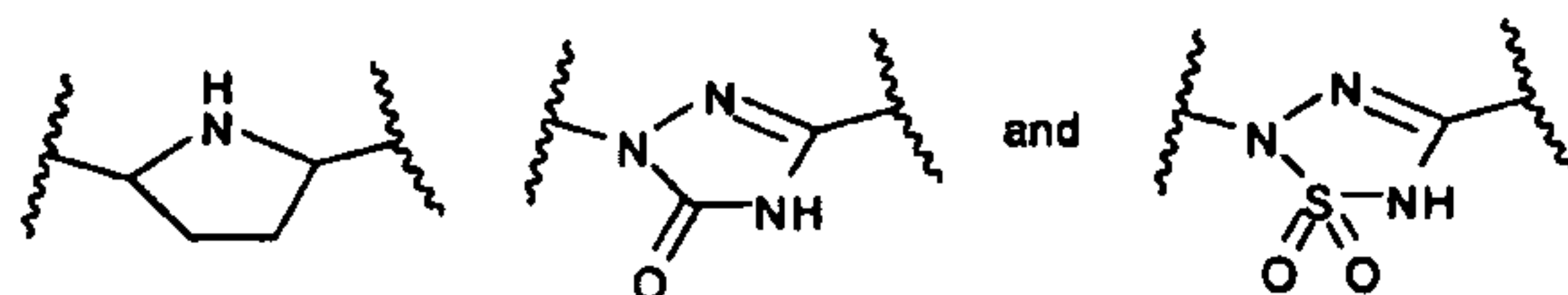
In another specific embodiment of the invention M is M⁷.

In another specific embodiment of the invention M is:

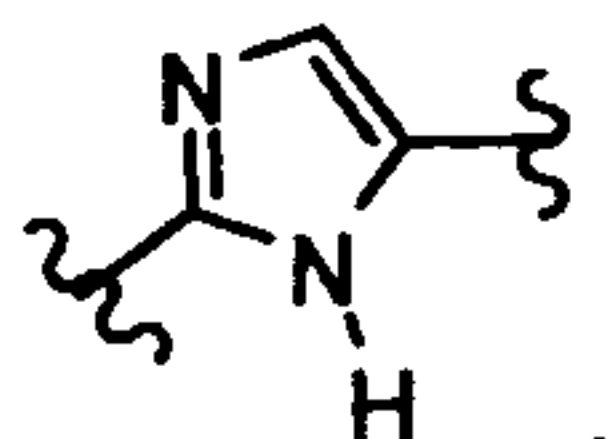


In another specific embodiment of the invention M is M⁸.

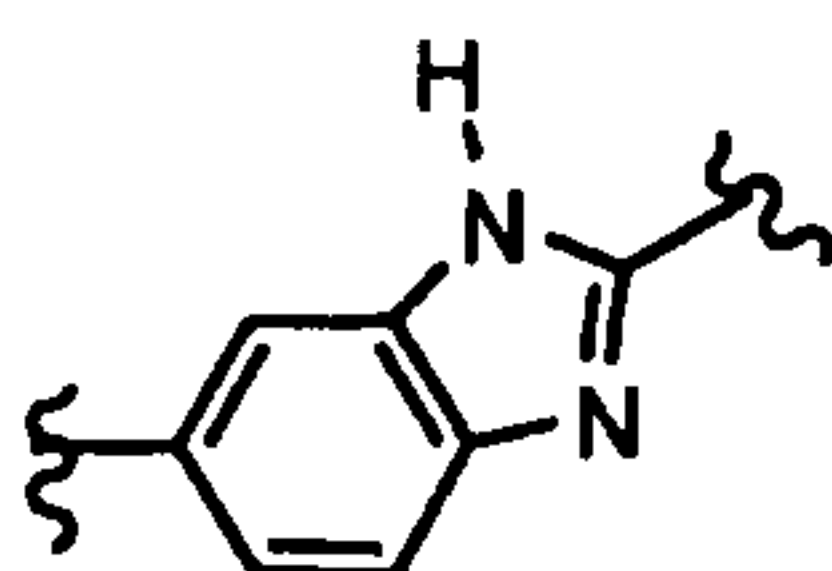
In another specific embodiment of the invention M is selected from the group consisting of:



In another specific embodiment of the invention M⁰ is:



In another specific embodiment of the invention M is M⁹ which is:



In another specific embodiment of the invention the sum of s, t, u, v, w, and x is not 0;

In another specific embodiment of the invention at least two of s, t, u, v, w, and x are other than 0.

In another specific embodiment of the invention at least three of s, t, u, v, w, and x are other than 0.

In another specific embodiment of the invention at least four of s, t, u, v, w, and x are other than 0.

In another specific embodiment of the invention at least five of s, t, u, v, w, and x are other than 0.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic1): $E^0-V^0-Z^0-P-M^0-A^{13}-A^6-M-P-Z^0-V^0-E^0$ (Ic1) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic2): $E^0-V^0-Z^0-P-M^9-A^{13}-A^6-M-P-Z^0-V^0-E^0$ (Ic2) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic3): $E^0-V^0-Z^0-P-M^{10}-A^{13}-A^6-M-P-Z^0-V^0-E^0$ (Ic3) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic4): $E^0-V^0-Z^0-P-M^{11}-A^{13}-A^6-M-P-Z^0-V^0-E^0$ (Ic4) or a pharmaceutically acceptable salt, or prodrug thereof.

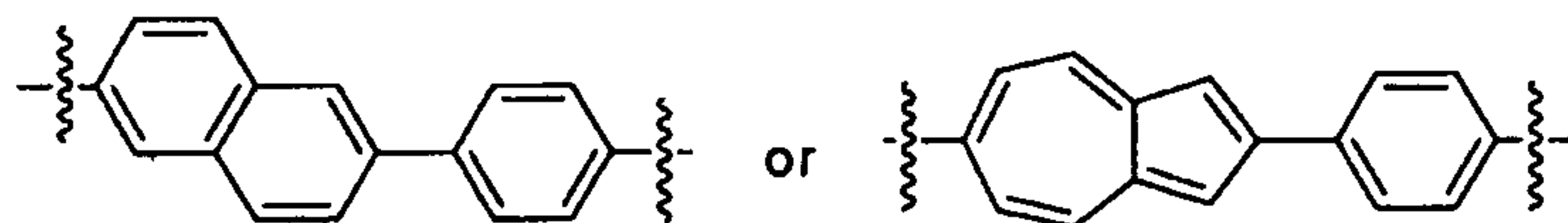
In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic5): $E^0-V^0-Z^0-P-M^0-A^{13}-A^0-M-P-Z^0-V^0-E^0$ (Ic5) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic6): $E^0-V^0-Z^0-P-M^9-A^{13}-A^0-M-P-Z^0-V^0-E^0$ (Ic6) or a pharmaceutically acceptable salt, or prodrug thereof.

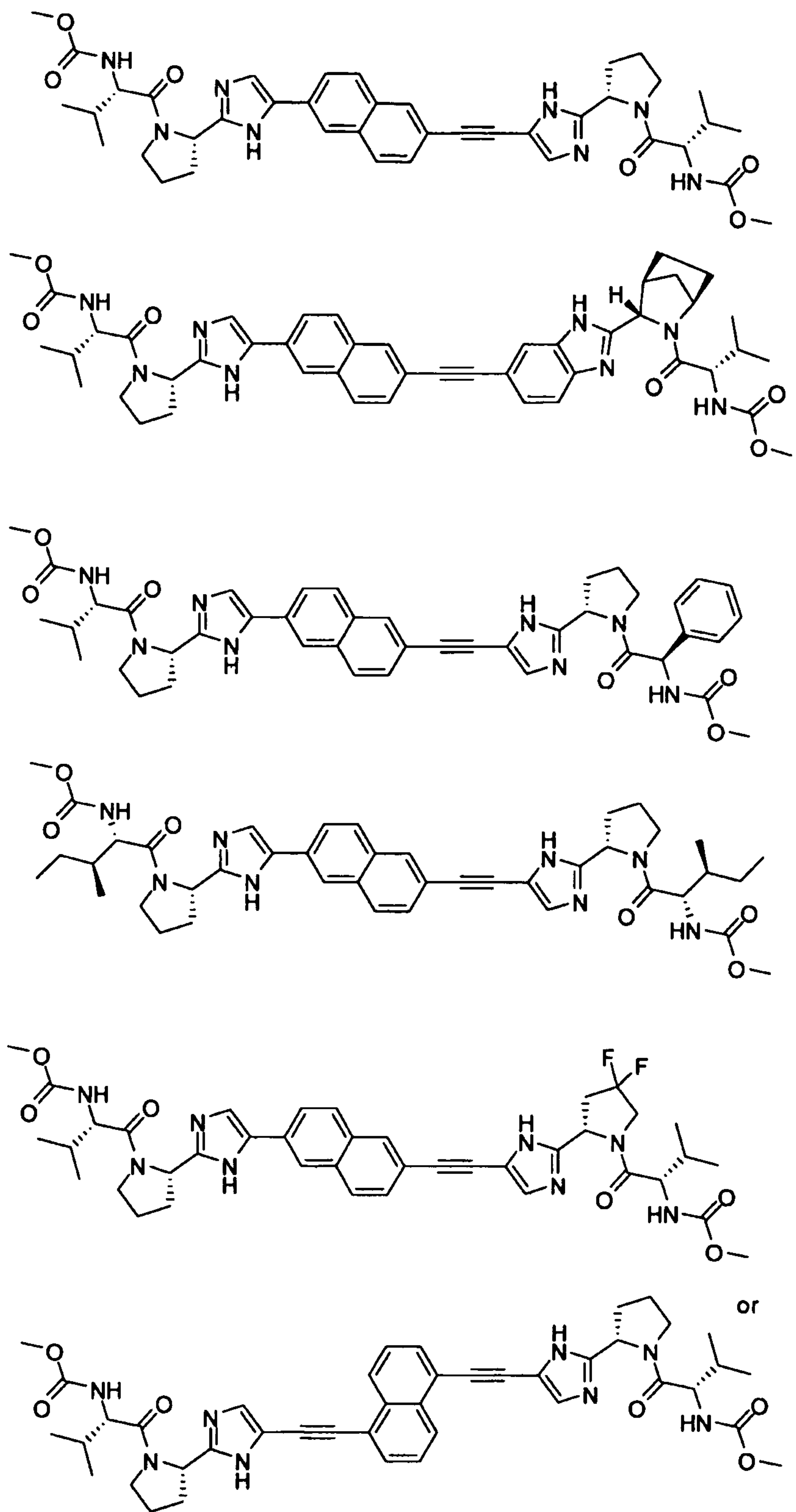
In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic7): $E^0-V^0-Z^0-P-M^{10}-A^{13}-A^0-M-P-Z^0-V^0-E^0$ (Ic7) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic8): $E^0-V^0-Z^0-P-M^{11}-A^{13}-A^0-M-P-Z^0-V^0-E^0$ (Ic8) or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention $A^{13}-A^0$ is:

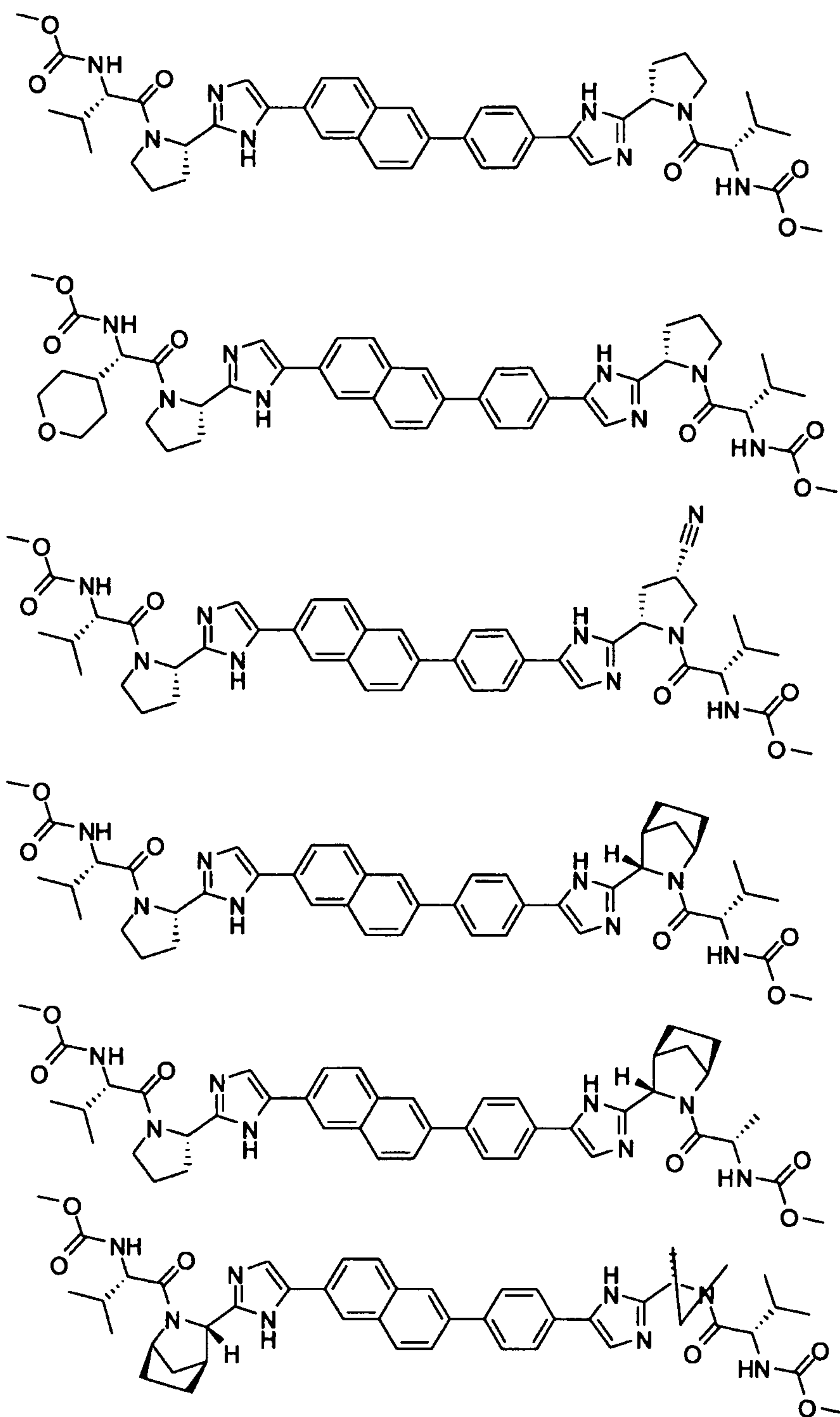


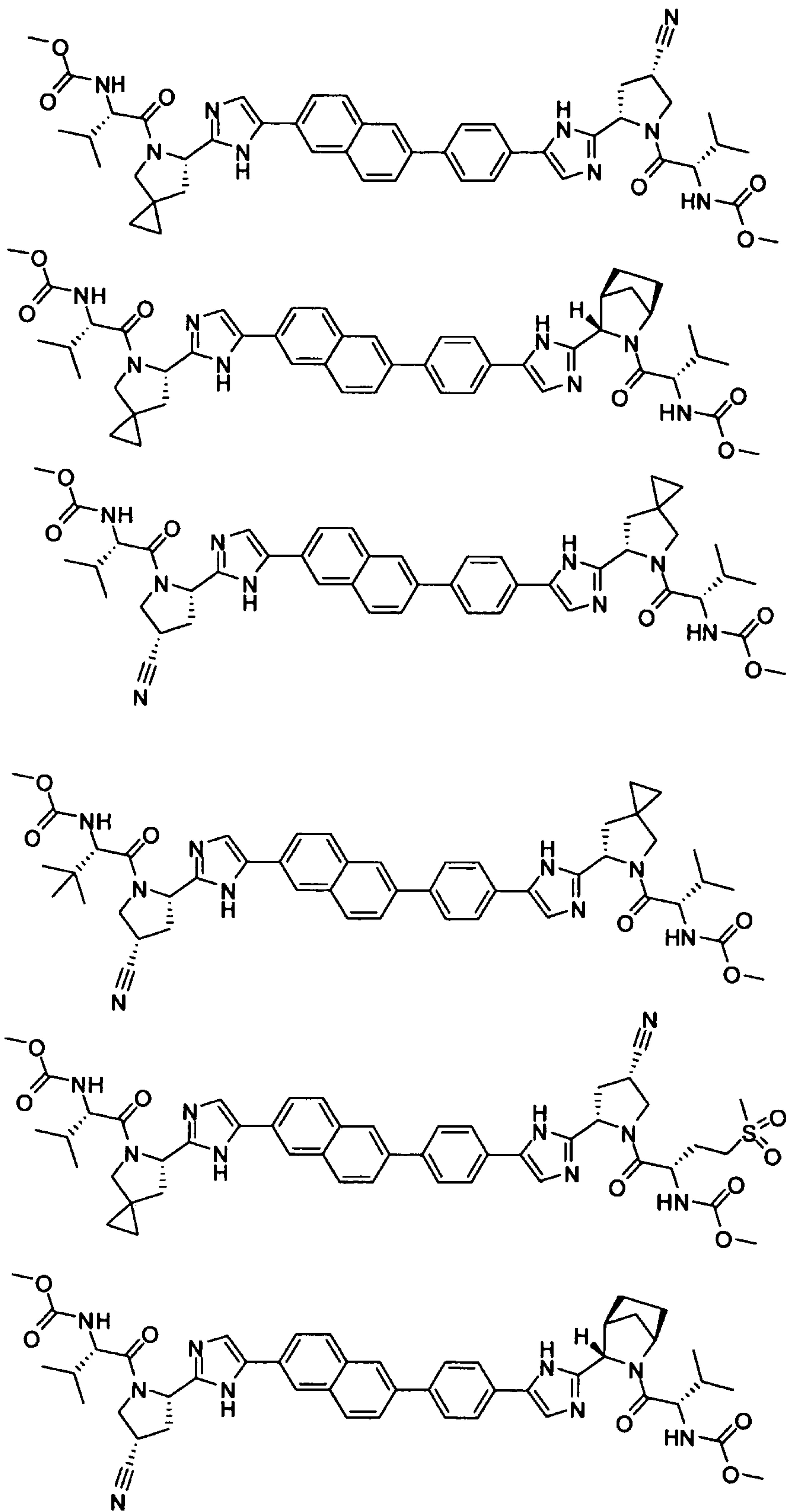
In another specific embodiment of the invention the compound of formula (Ic) is:

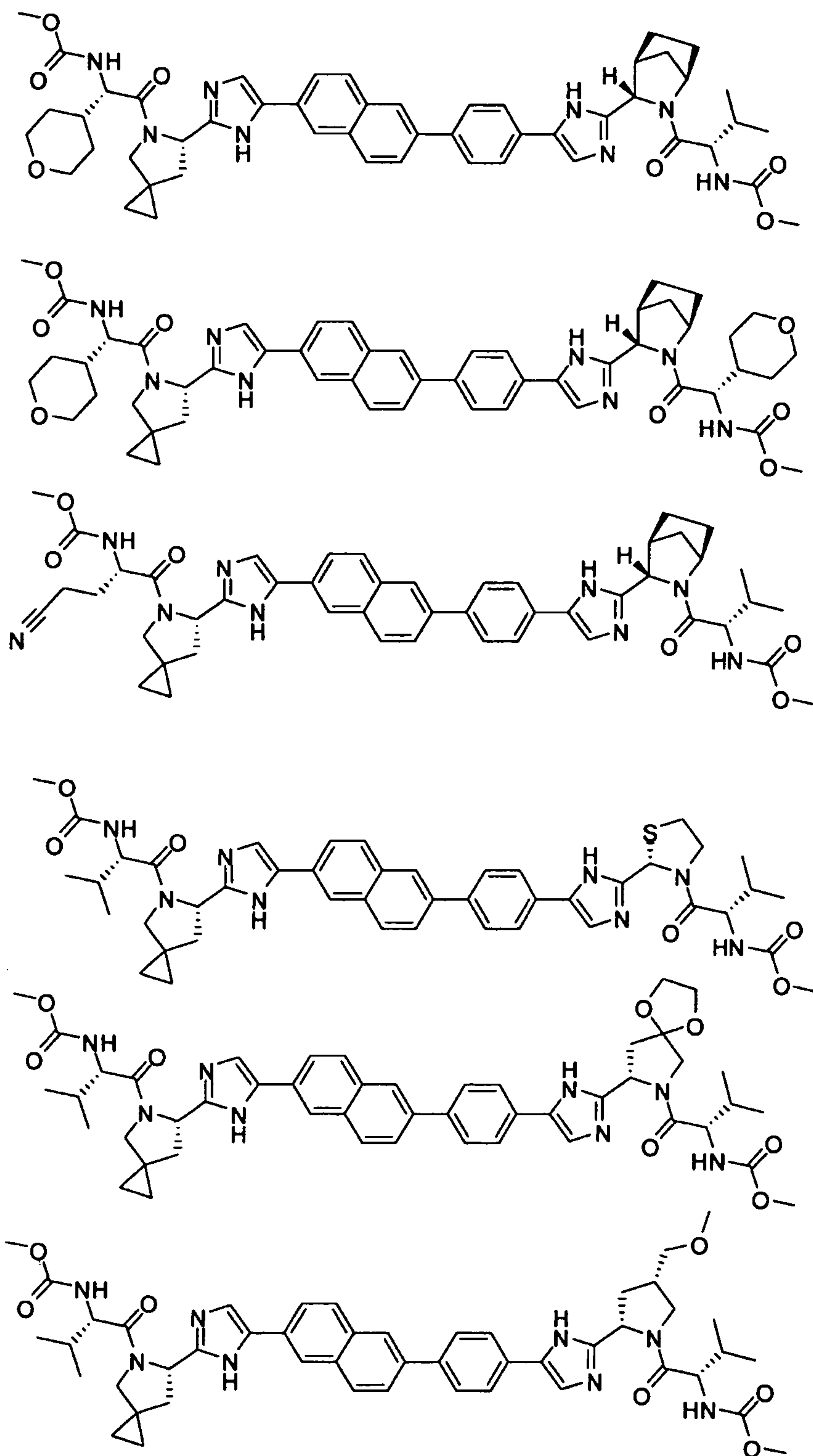


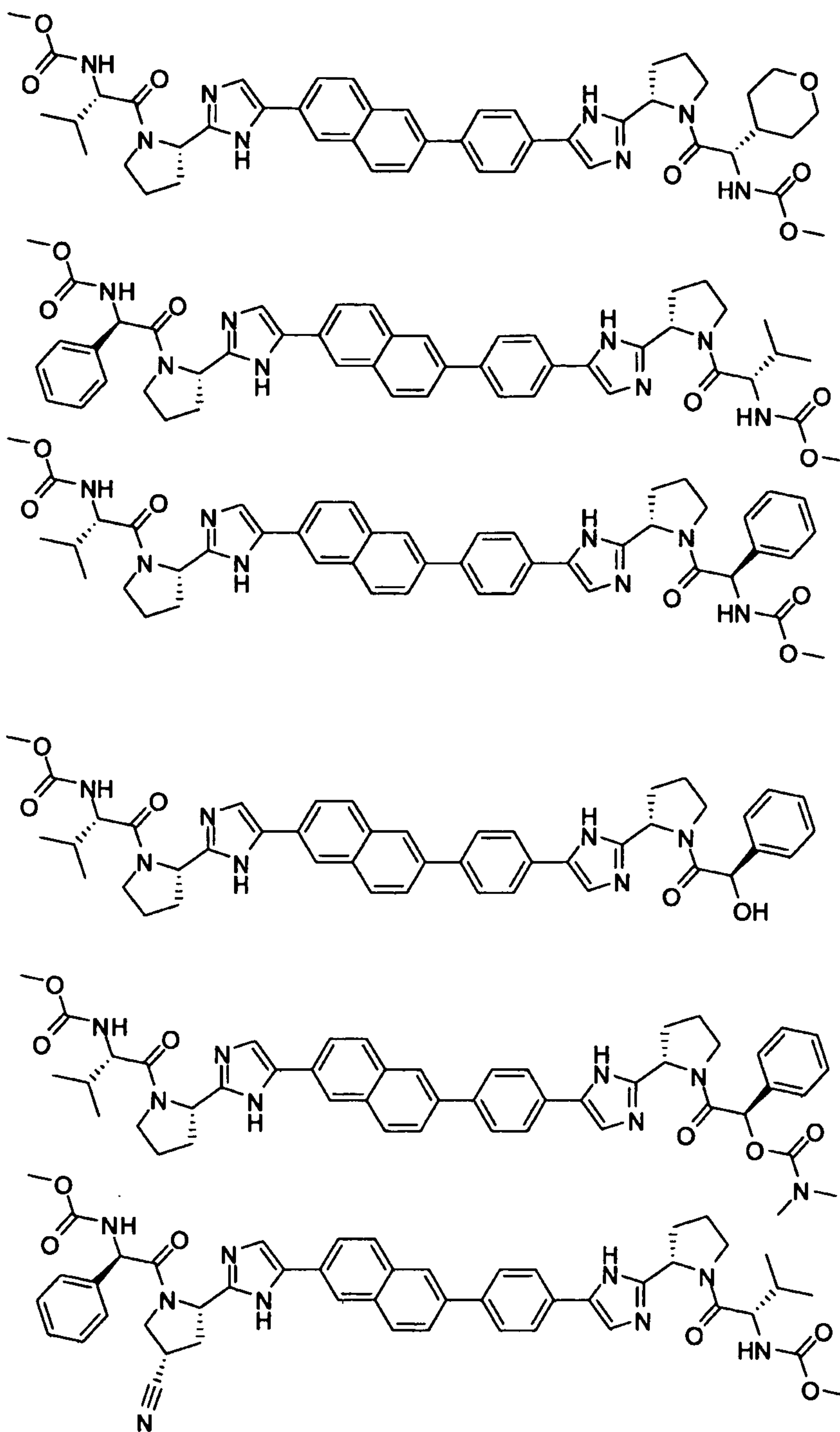
or a pharmaceutically acceptable salt, or prodrug thereof.

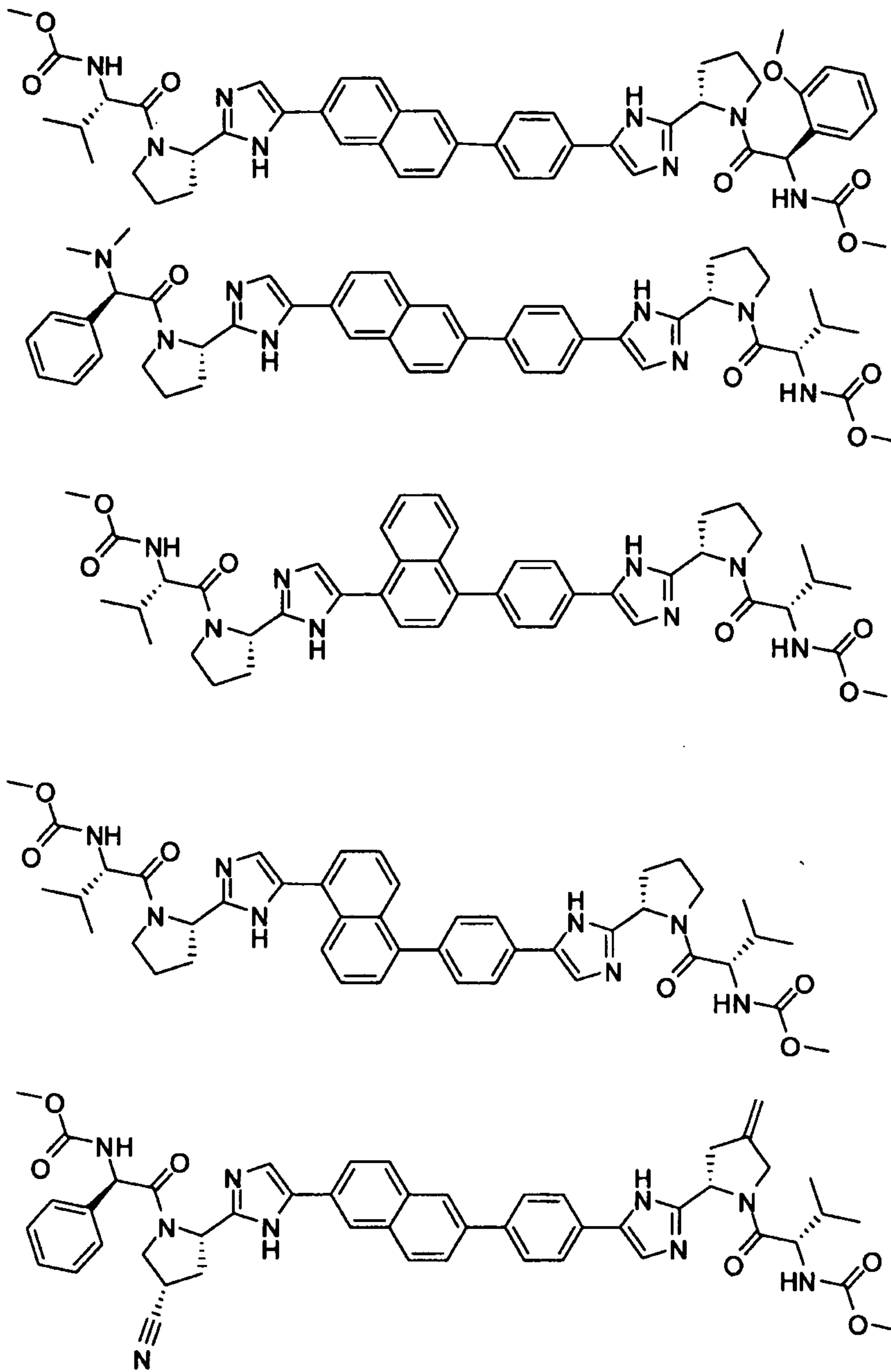
In another specific embodiment of the invention the compound of formula (Ic) is:

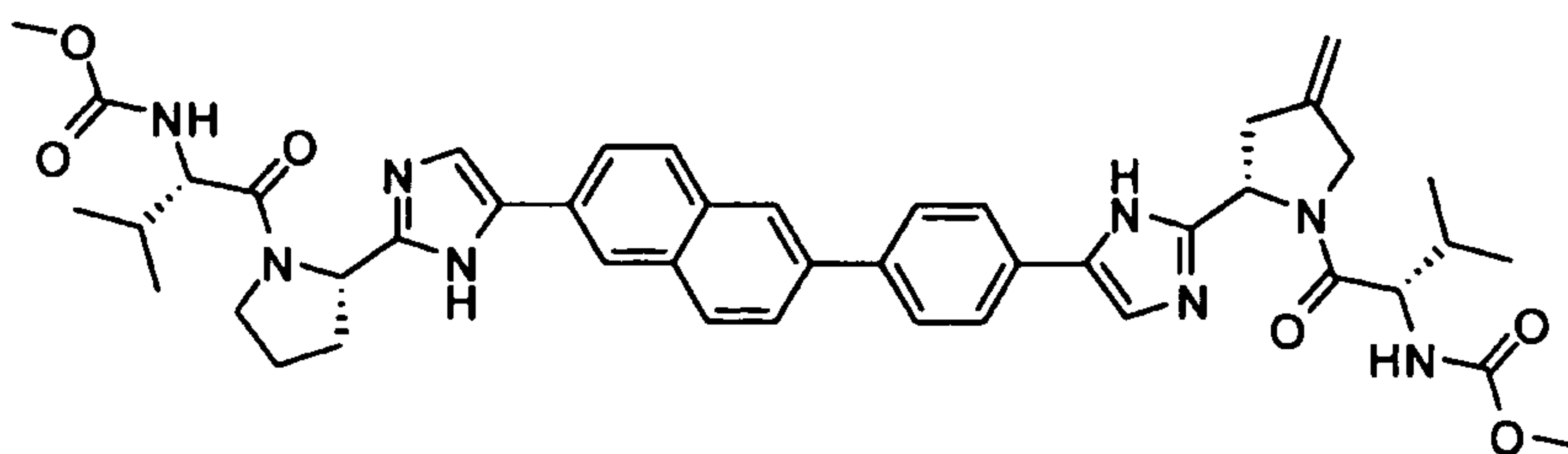




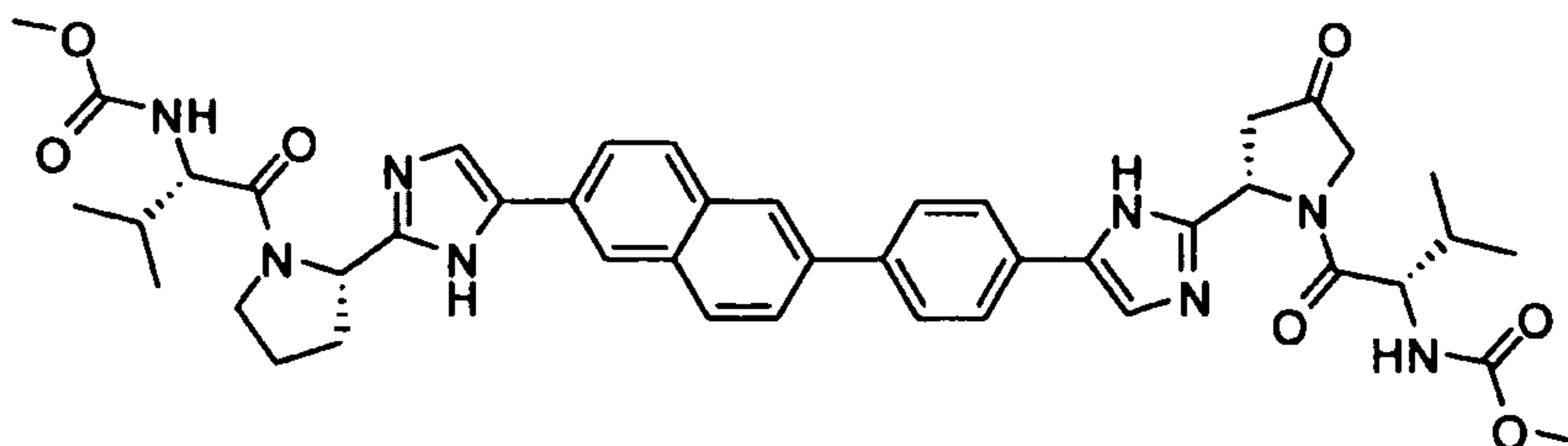






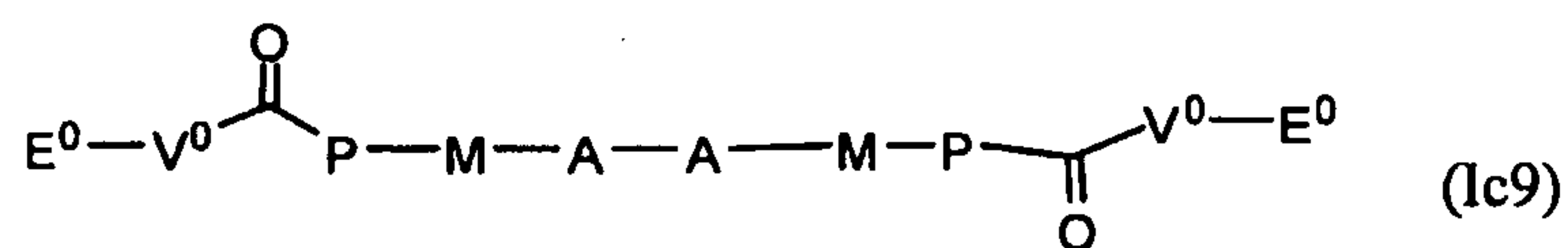


or



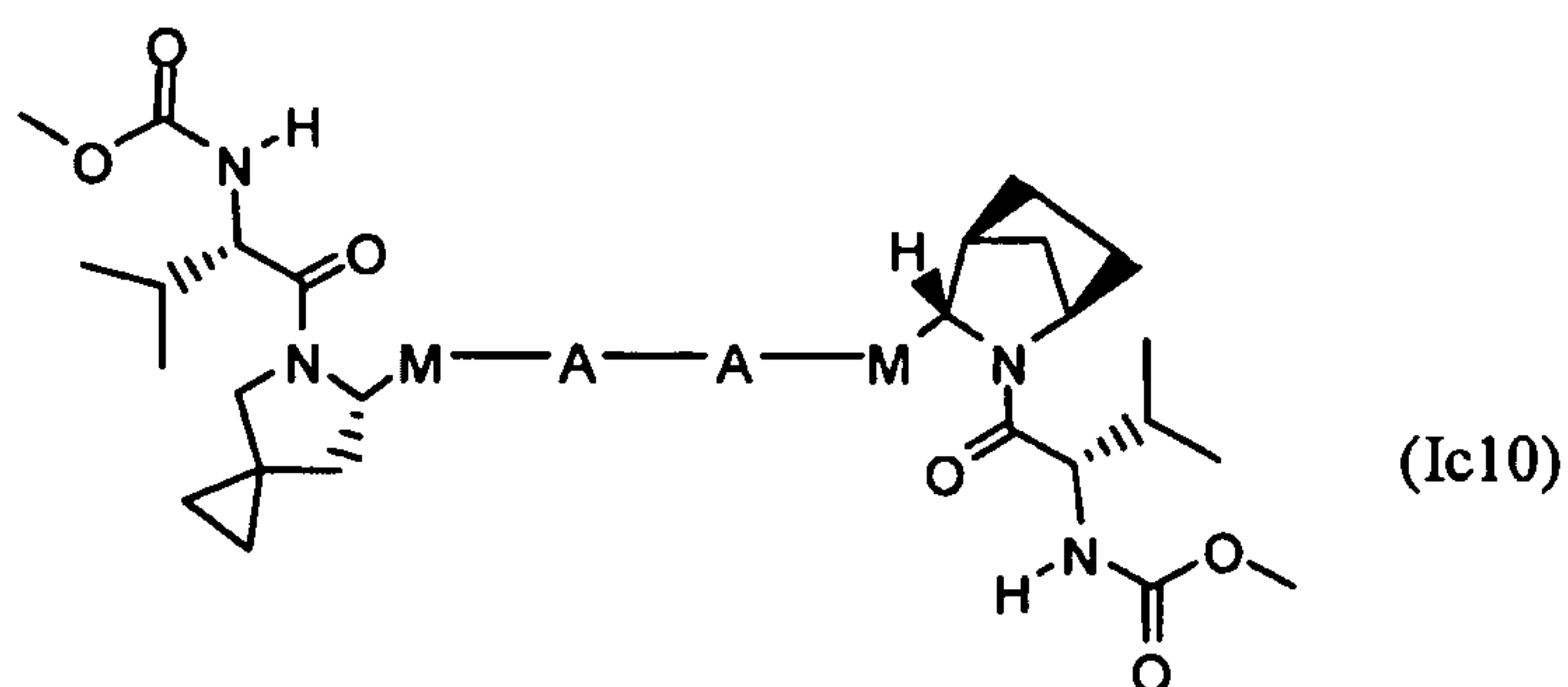
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic9):



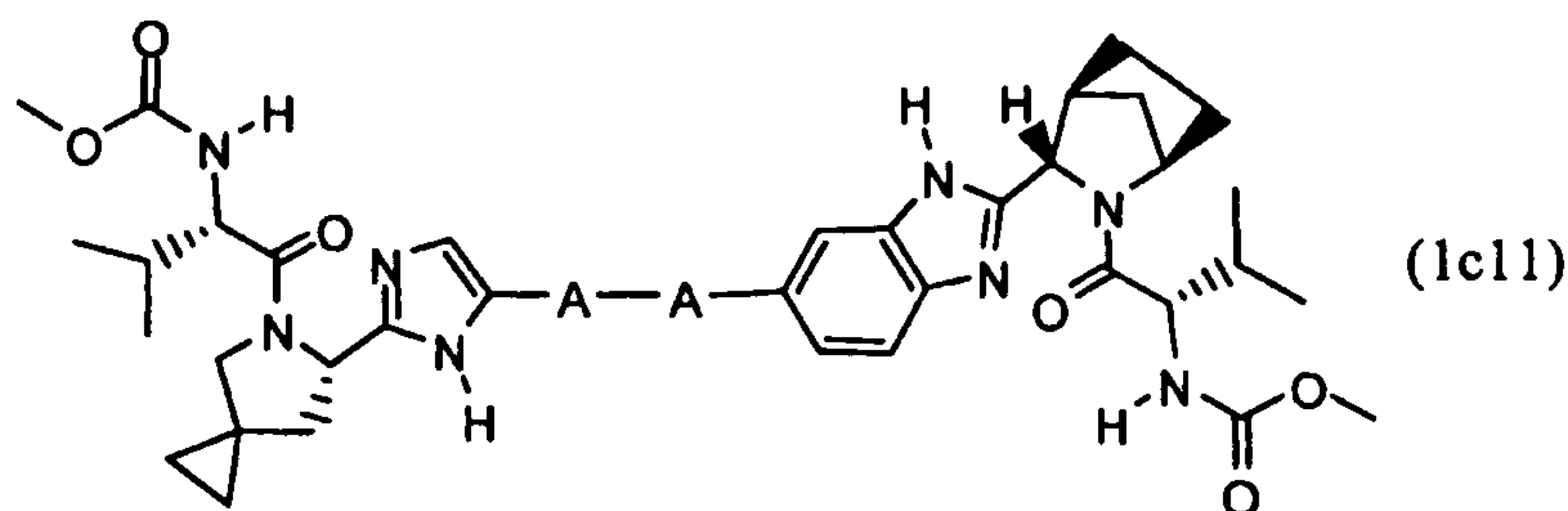
or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic10):



or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic11):

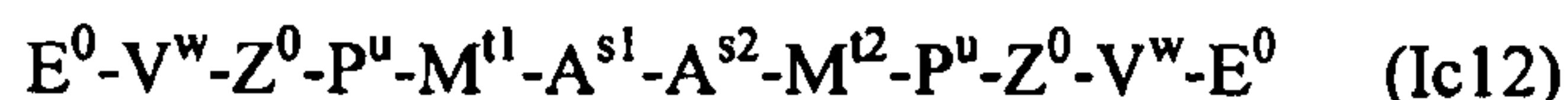


or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic9), (Ic10), or (Ic11) wherein -A-A- is -A¹³-A⁶-.

In another specific embodiment of the invention the compound of formula (Ic) is a compound of formula (Ic9), (Ic10), or (Ic11) wherein -A-A- is -A¹³-A⁰-.

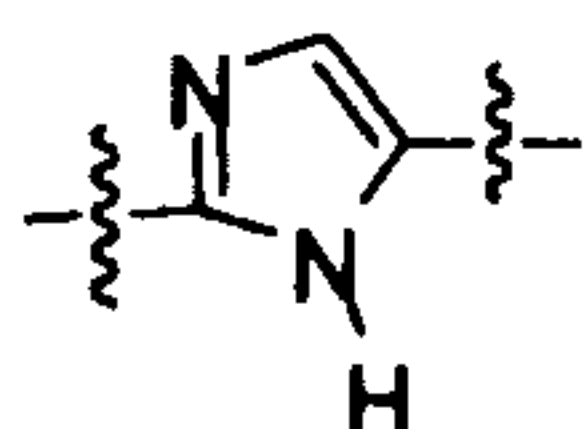
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ic12):



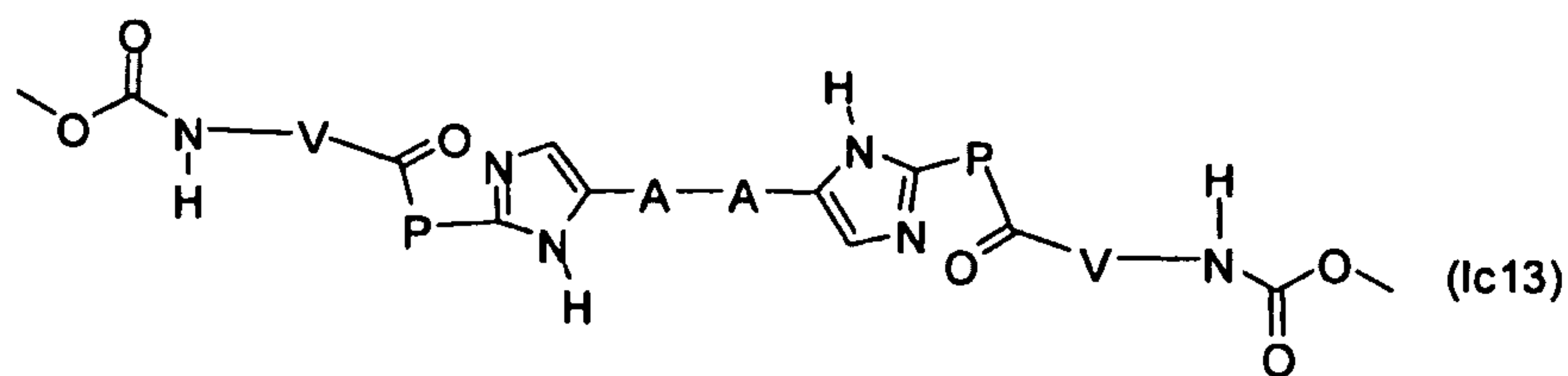
or a pharmaceutically acceptable salt, or prodrug thereof, wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each w is independently 0, 1, 2, 3, 4, or 5; each t1 is 0 or 10; each t2 is 0 or 10; each s1 is 4, 5, 6, 13, 14, 15, or 16; and each s2 is 0, 4, or 13.

In one embodiment the invention provides a compound of formula (Ic12) wherein M⁰ is:

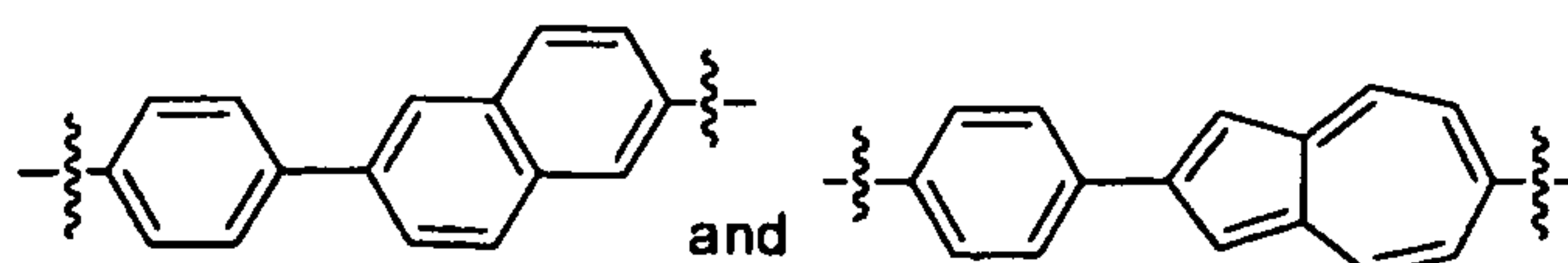


In one embodiment the invention provides a compound of formula (Ic13)

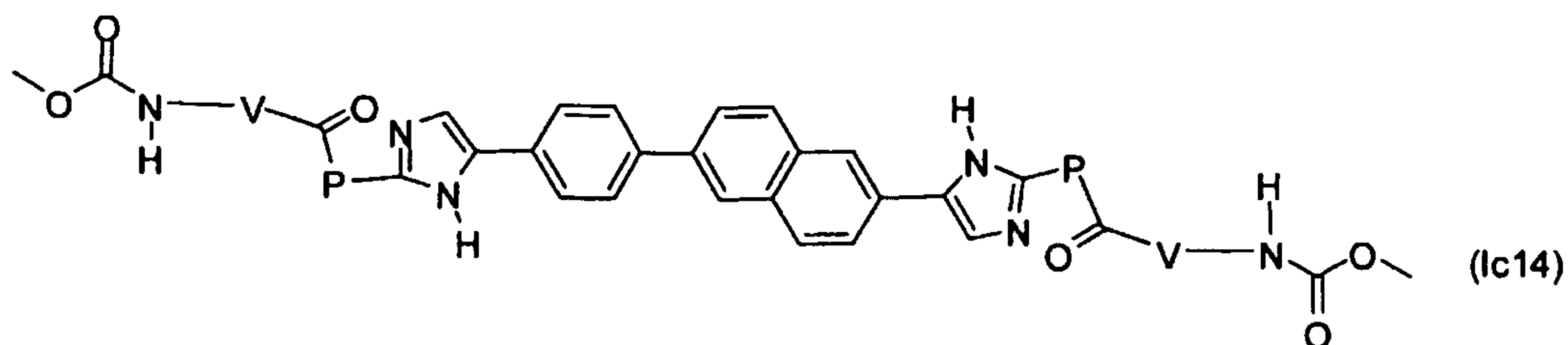


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A⁰-A¹³ and is selected from:

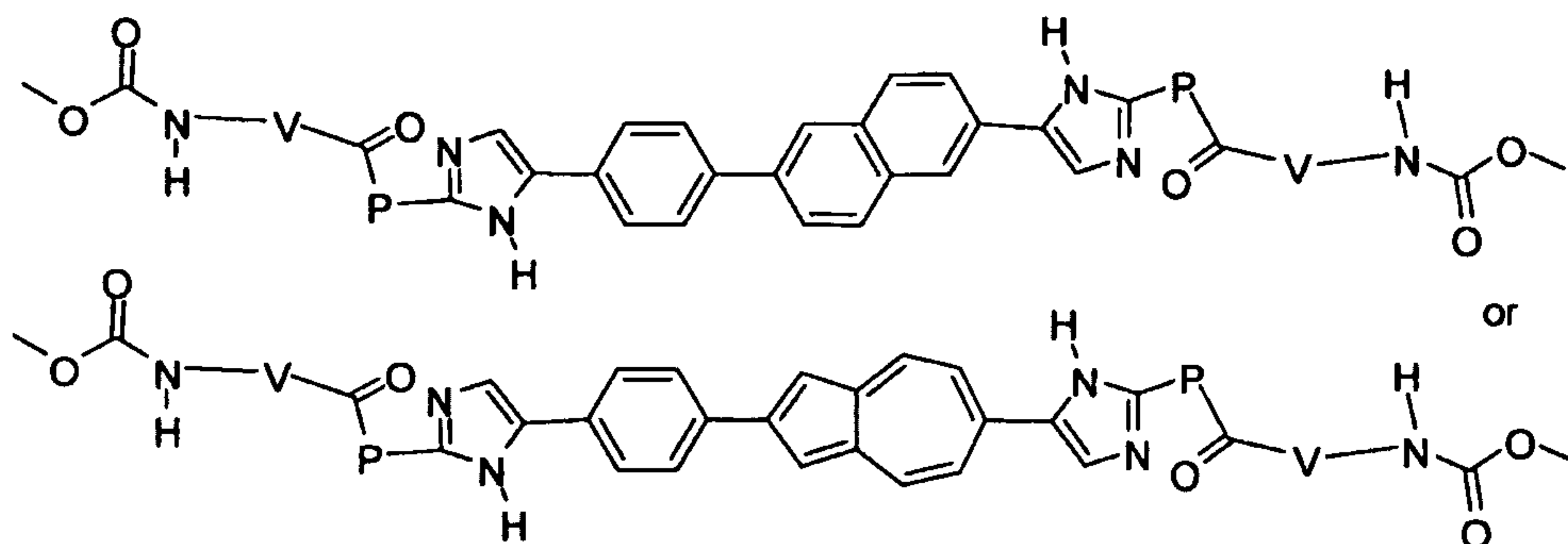


In one embodiment the invention provides a compound of formula (Ic14)



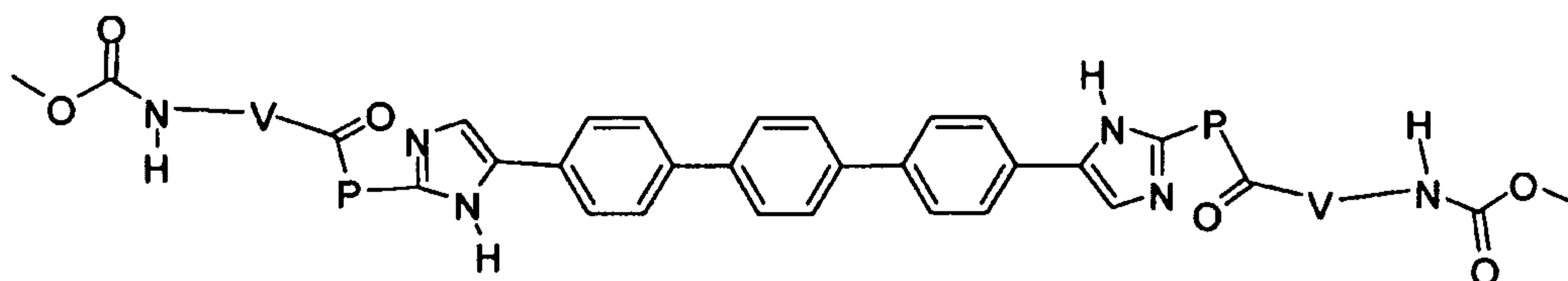
or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic12) which is:



or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic12) which is:

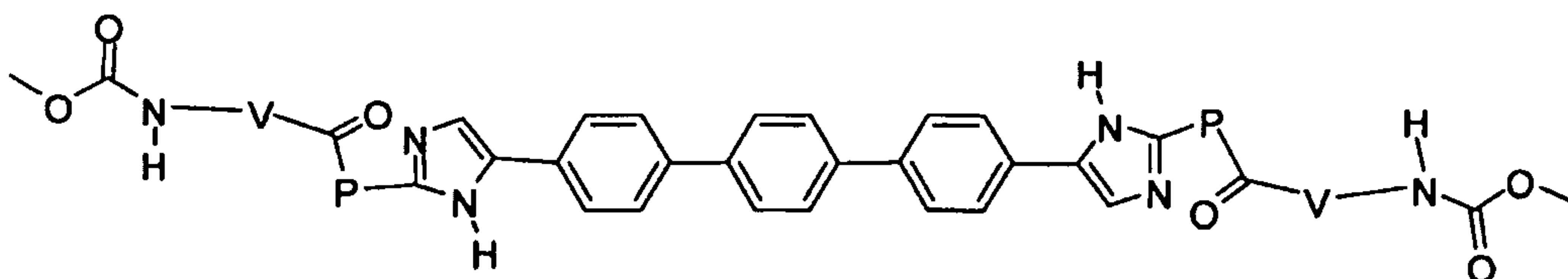


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A⁰-A⁴ and is:

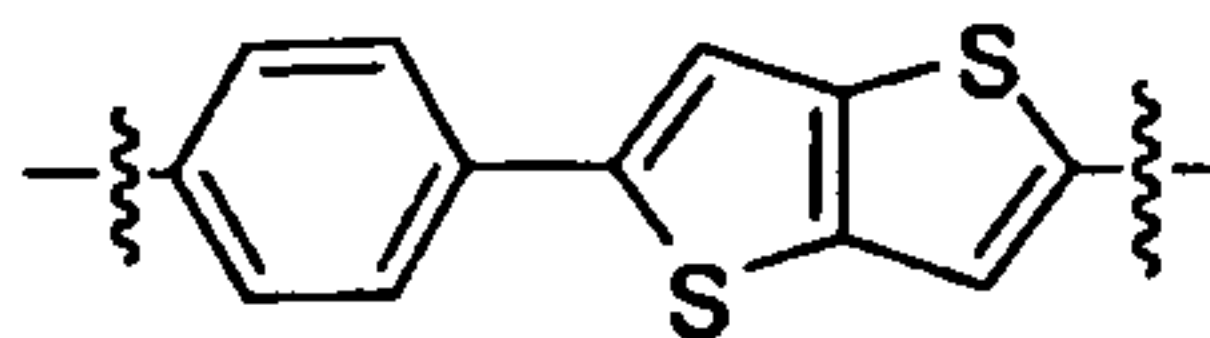


In one embodiment the invention provides a compound of formula (Ic12) which is:

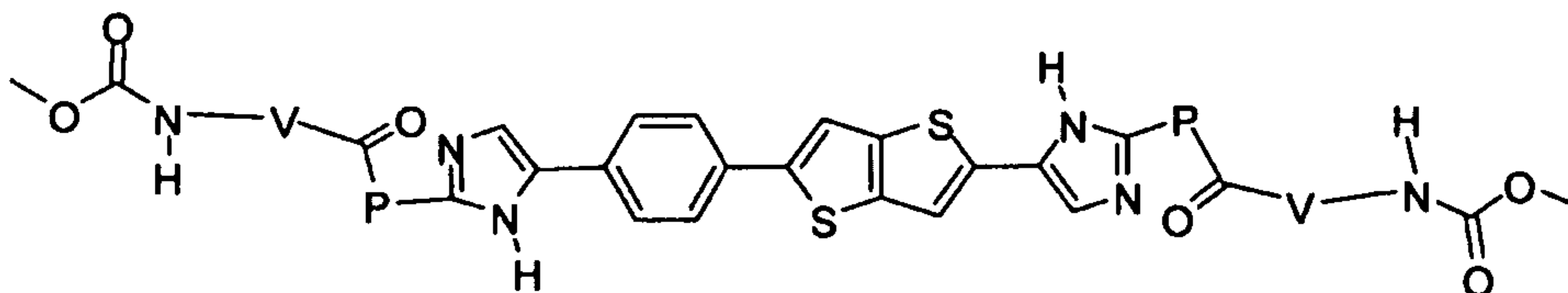


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A⁰-A¹⁴ and is:

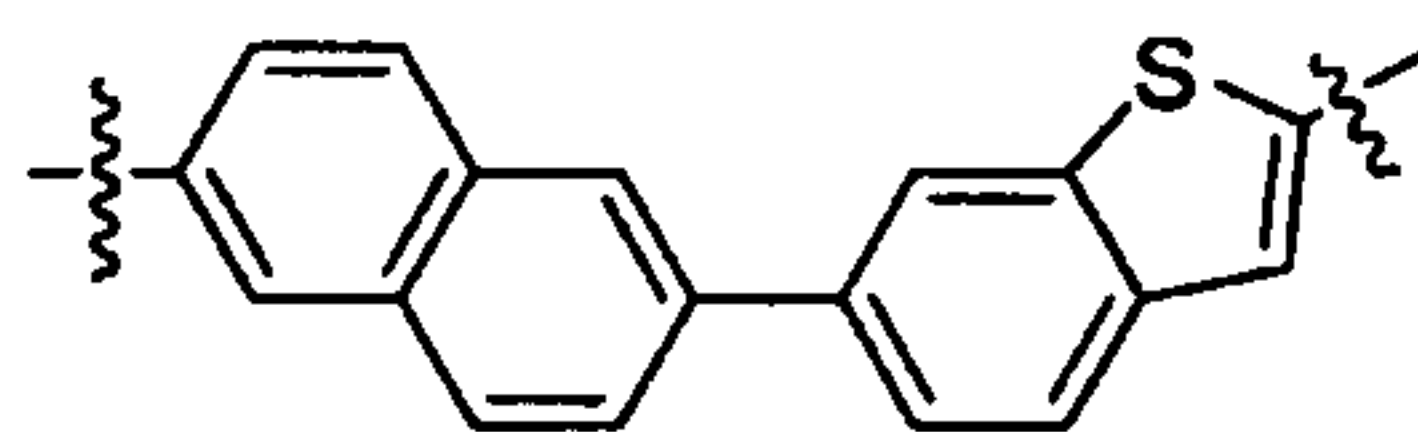


In one embodiment the invention provides a compound of formula (Ic12) which is:

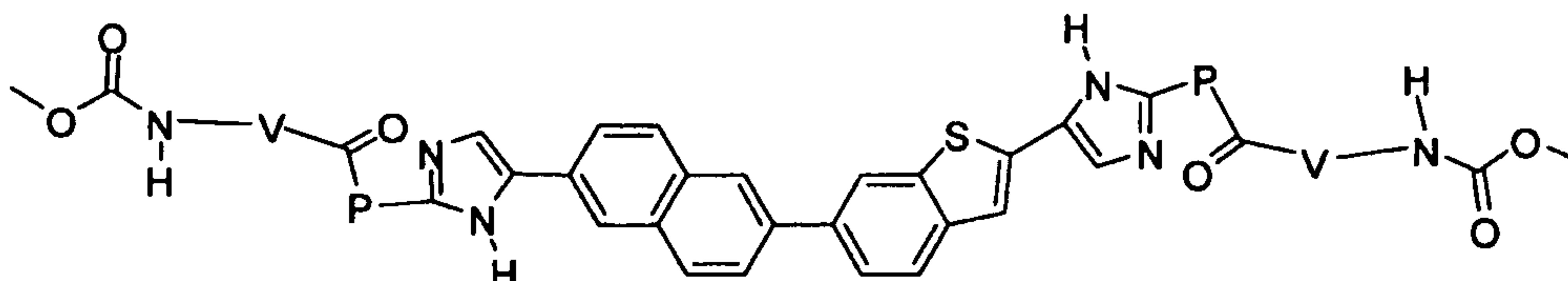


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹³-A¹⁴ and is:

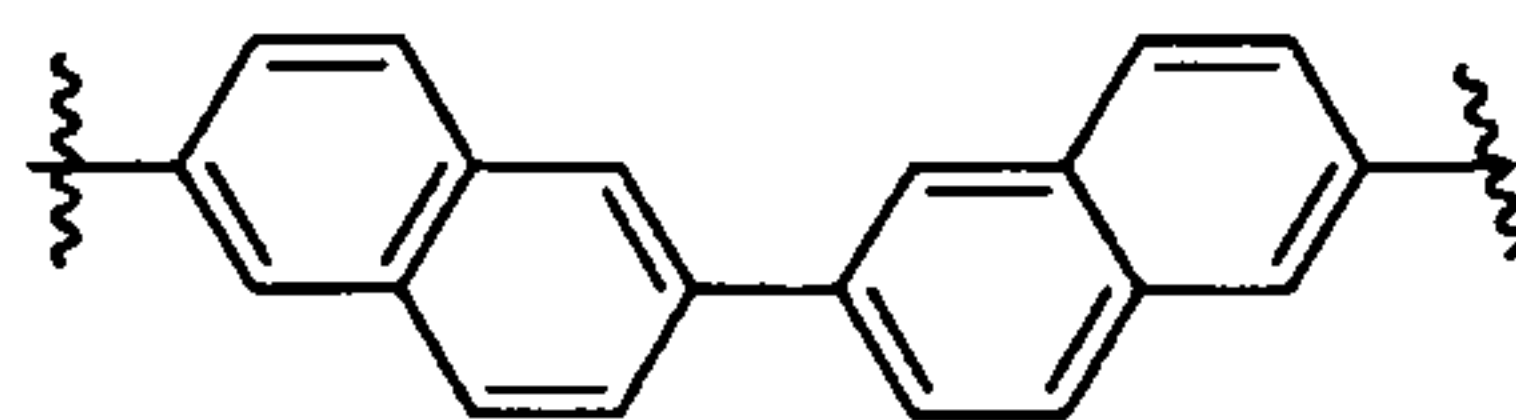


In one embodiment the invention provides a compound of formula (Ic12) which is:

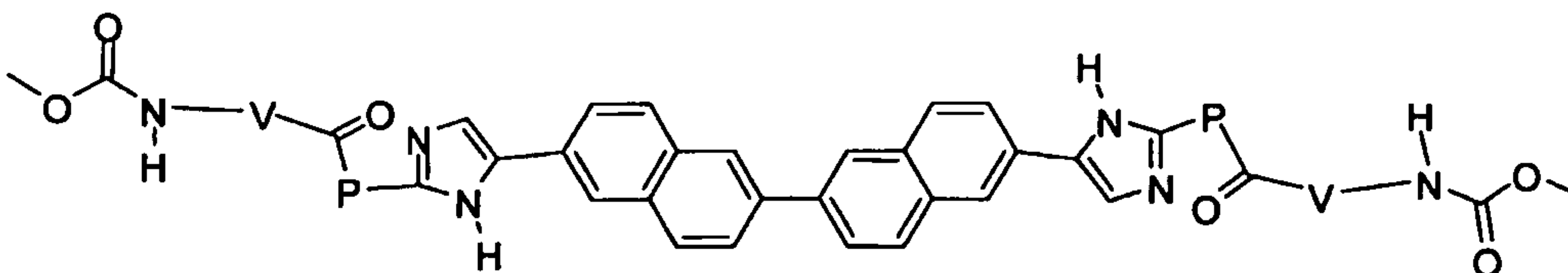


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹³-A¹³ and is:

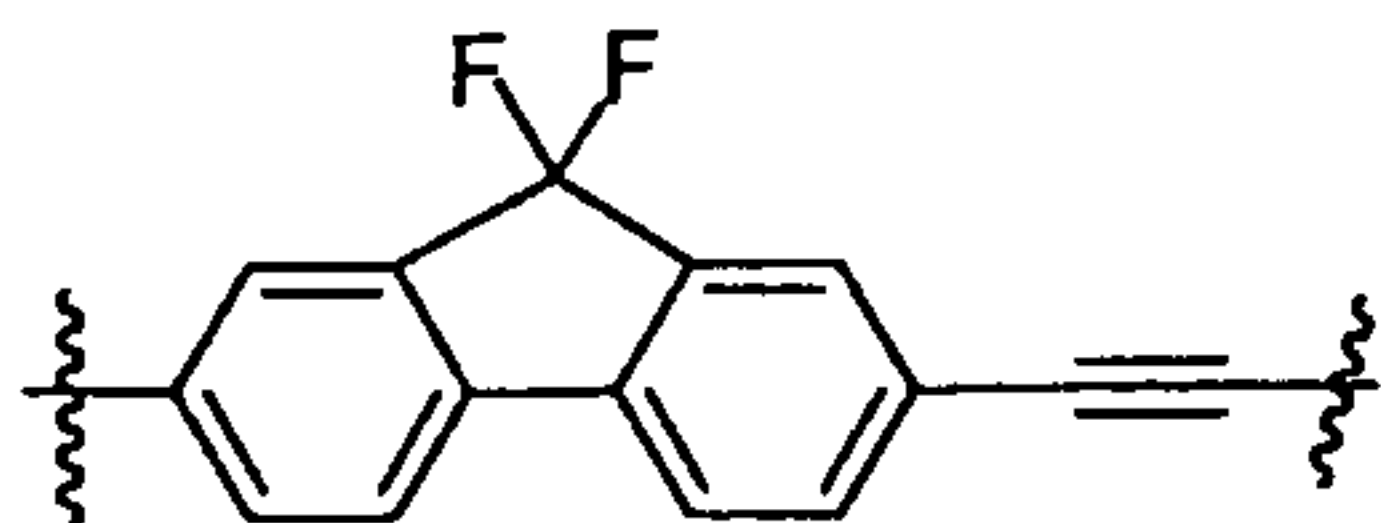


In one embodiment the invention provides a compound of formula (Ic12) which is:

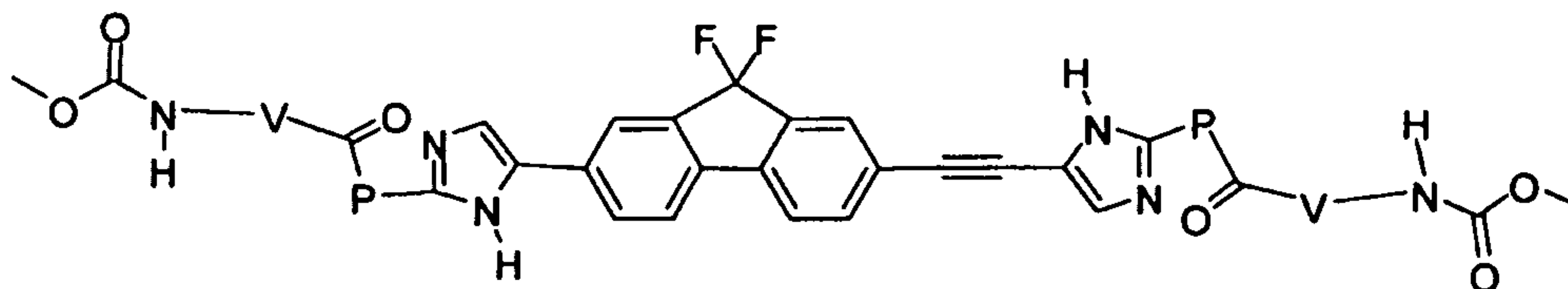


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹⁵-A⁶ and is:

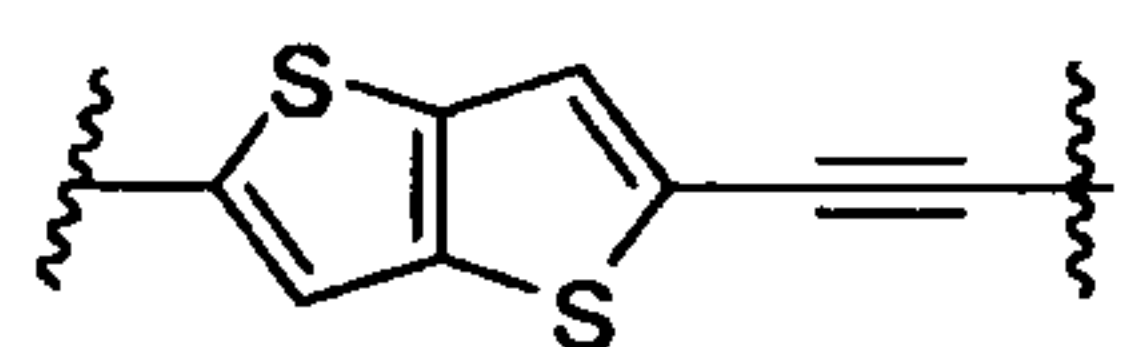


In one embodiment the invention provides a compound of formula (Ic12) which is:

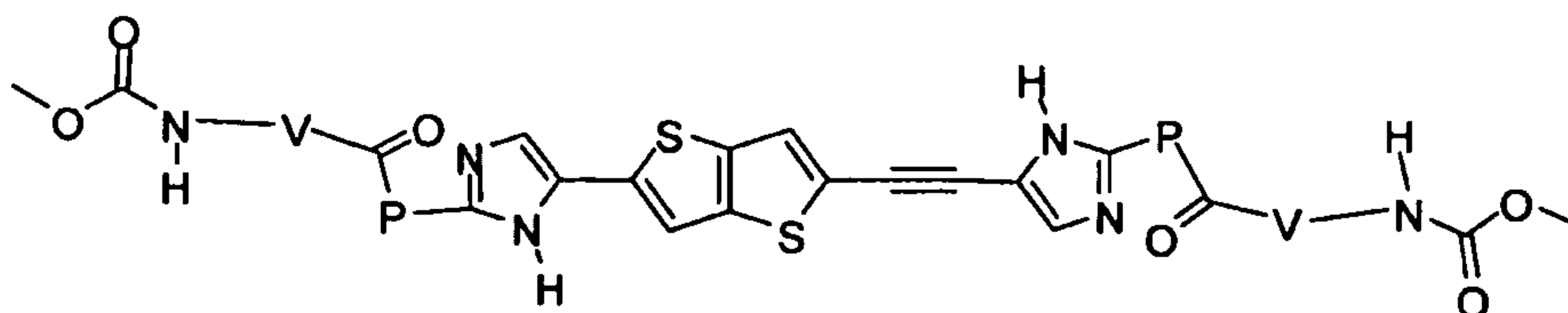


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹⁴-A⁶ and is:

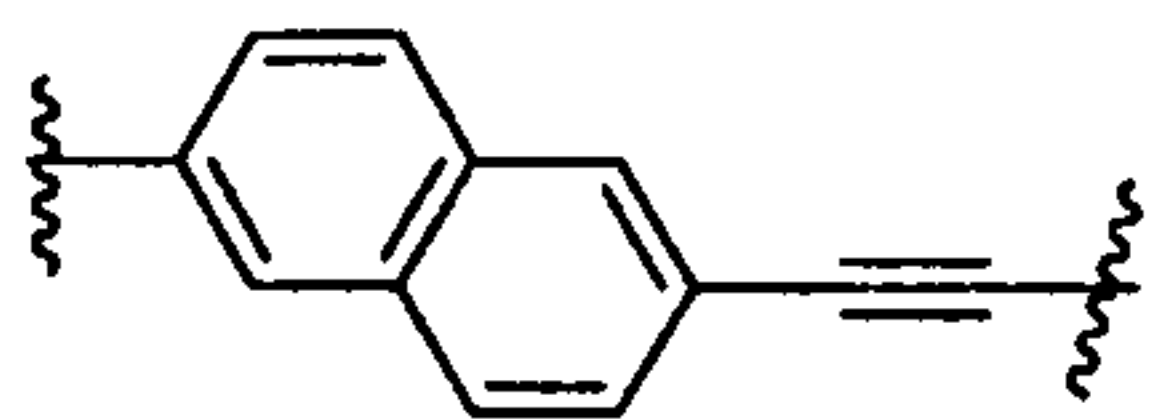


In one embodiment the invention provides a compound of formula (Ic12) which is:

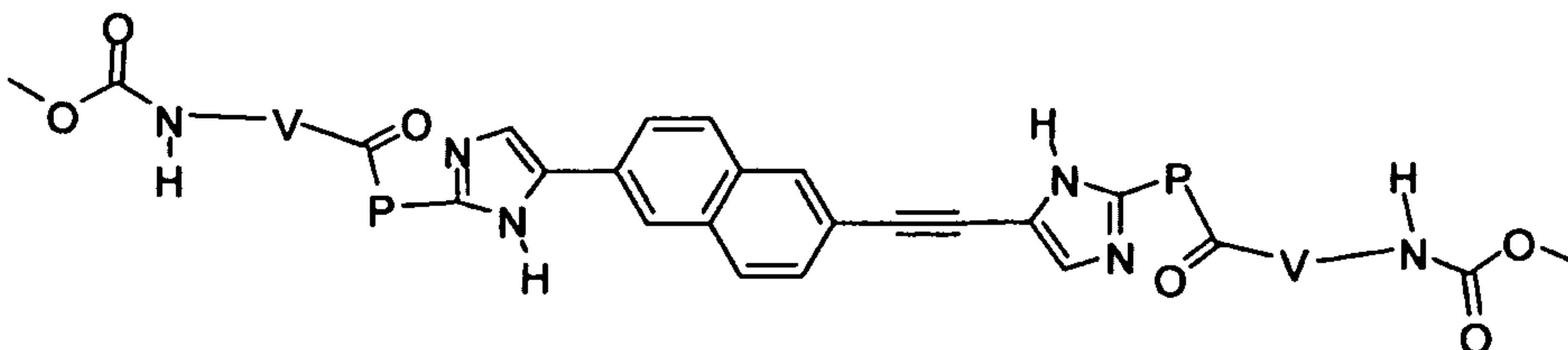


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹³-A⁶ and is:

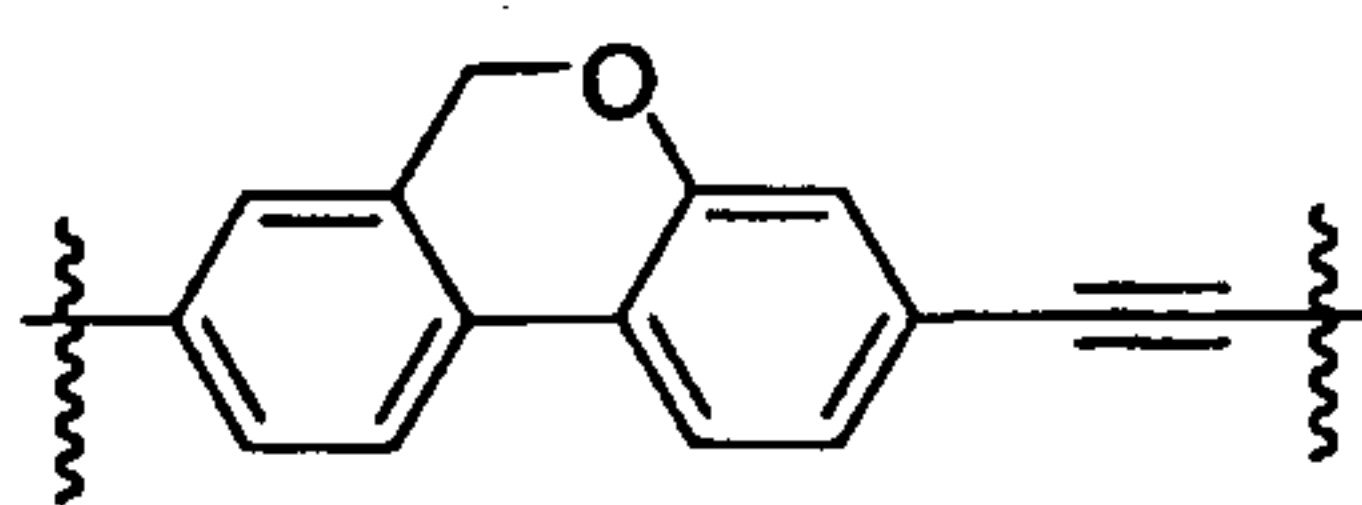


In one embodiment the invention provides a compound of formula (Ic12) which is:

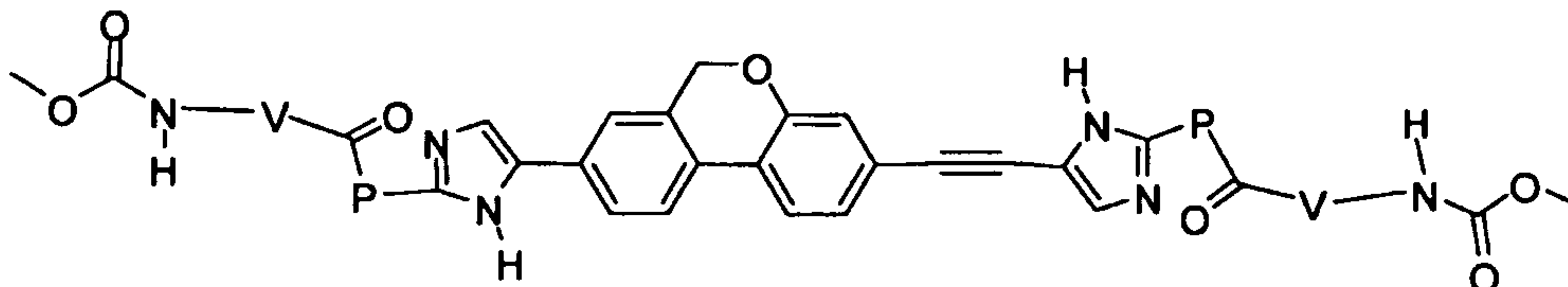


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A¹⁶-A⁶ and is:

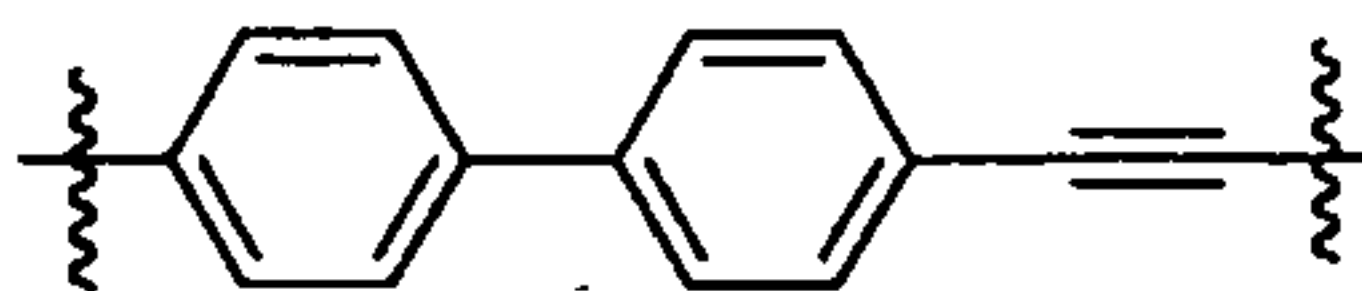


In one embodiment the invention provides a compound of formula (Ic12) which is:

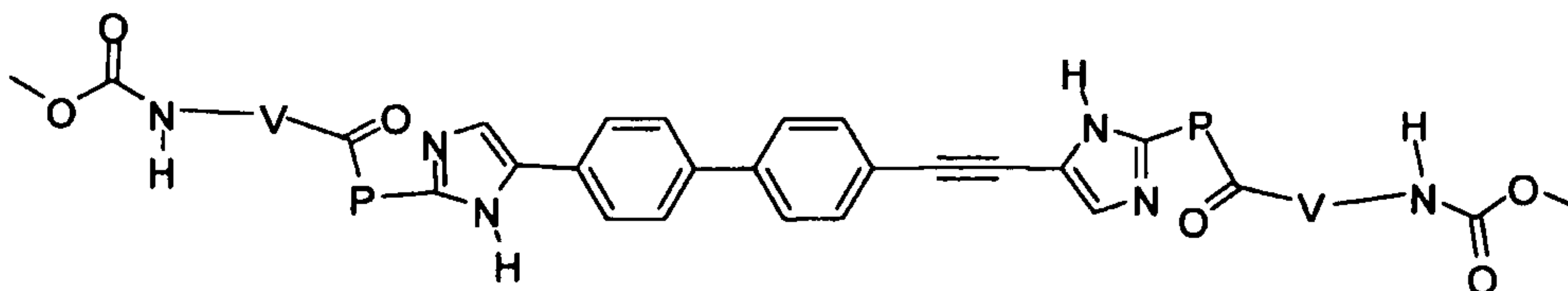


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A⁰-A⁵ and is:

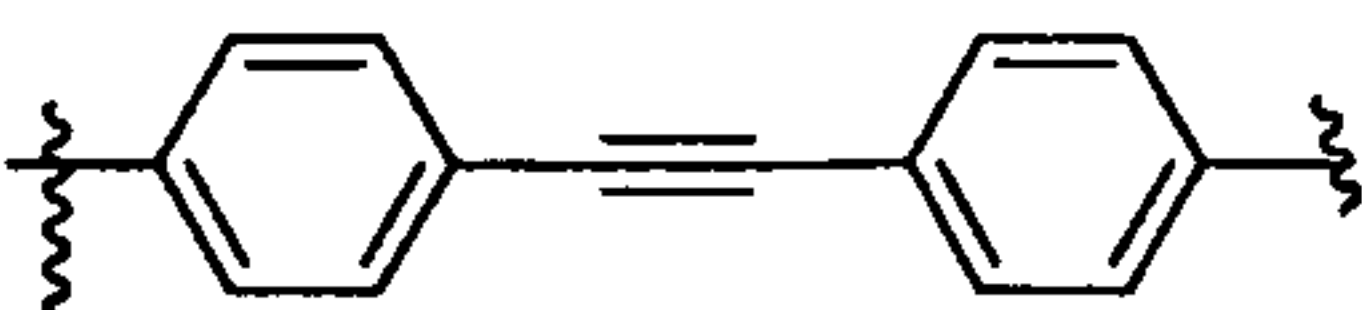


In one embodiment the invention provides a compound of formula (Ic12) which is:

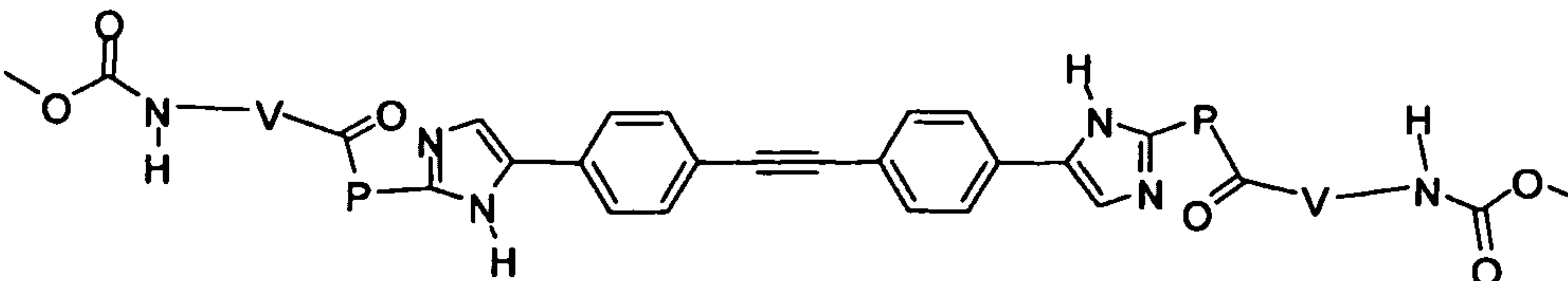


or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic13) wherein A-A is A⁰-A⁵ and is:

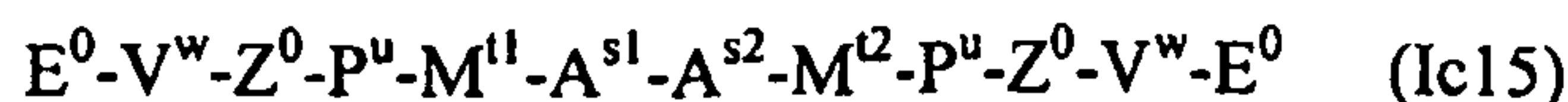


In one embodiment the invention provides a compound of formula (Ic12) which is:



or a pharmaceutically acceptable salt, or prodrug thereof.

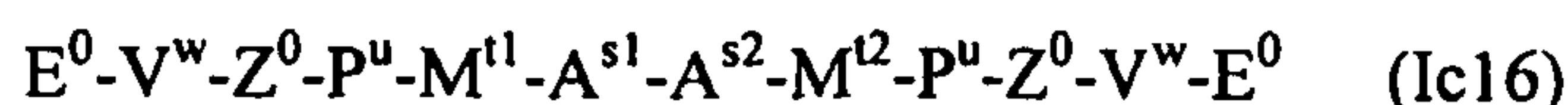
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ic15):



or a pharmaceutically acceptable salt, or prodrug thereof, wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each w is independently 0, 1, 2, 3, 4, or 5; each t1 is 0, 10, or 13; t2 is 9; s1 is 4, 5, 6, 13, 14, 15, or 16; and s2 is 0, 4, or 13.

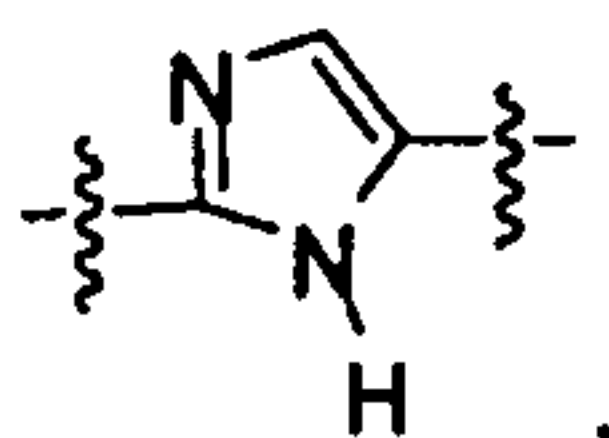
In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ic16):



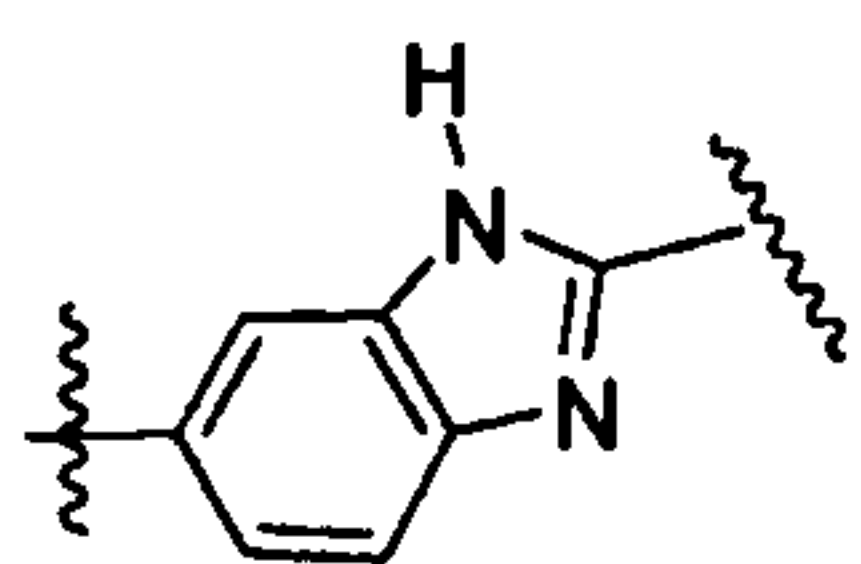
or a pharmaceutically acceptable salt, or prodrug thereof, wherein:

each u is independently 0, 1, 3, 5, 7, 8, 10, or 11; each w is independently 0, 1, 2, 3, 4, or 5; each t1 is 9; t2 is 0, 10, or 13; s1 is 4, 5, 6, 13, 14, 15, or 16; and s2 is 0, 4, or 13.

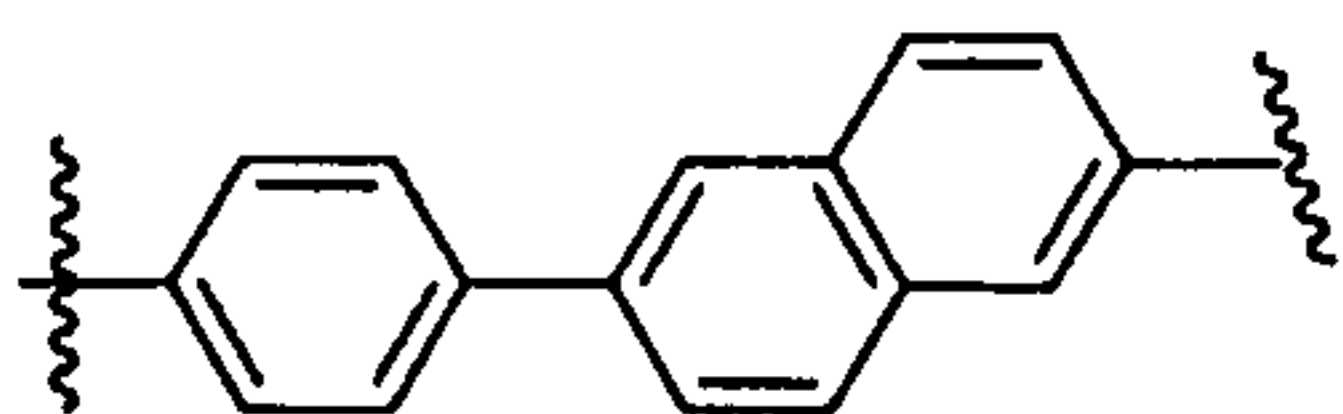
In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein M^0 is:



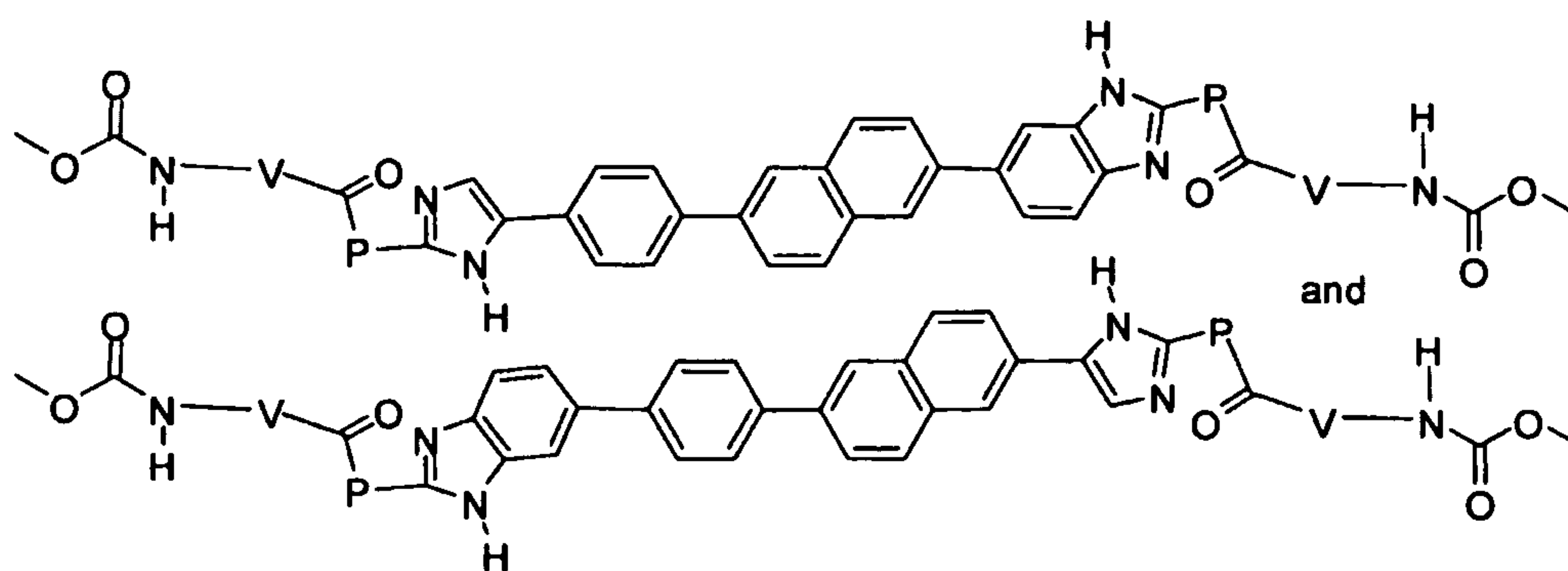
In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein M^9 is:



In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A^0-A^{13} and is:

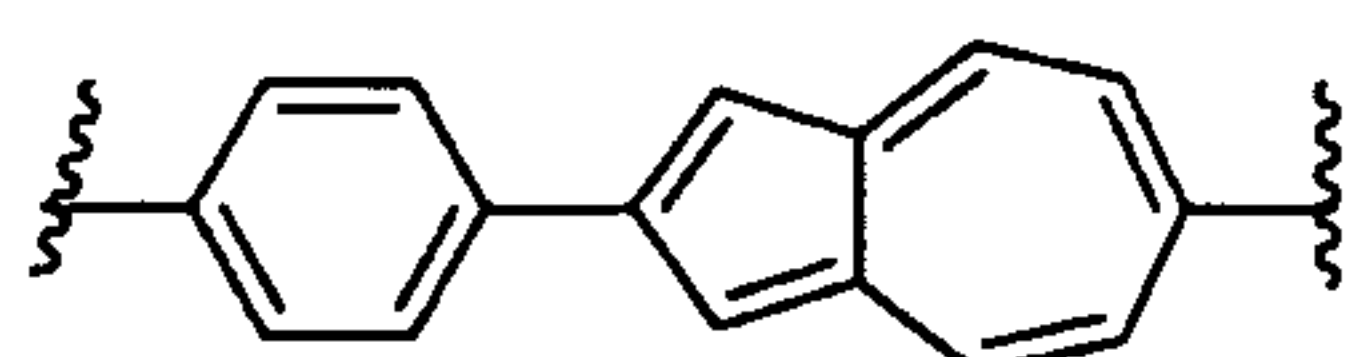


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

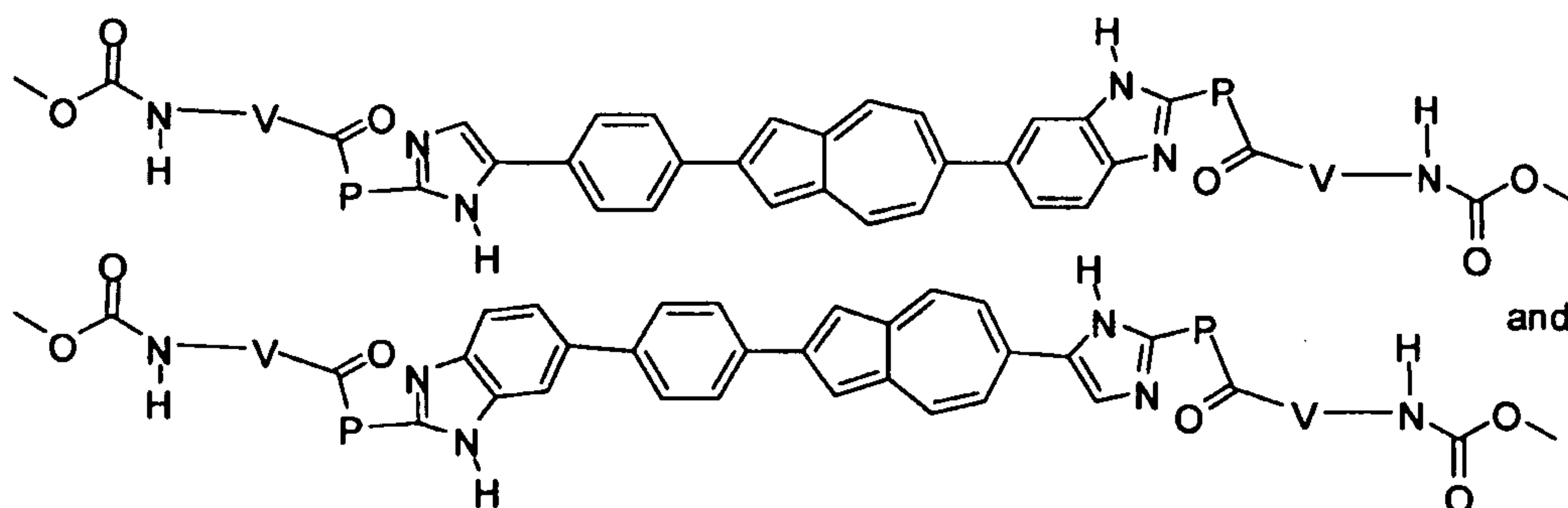


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A^0-A^{13} and is:

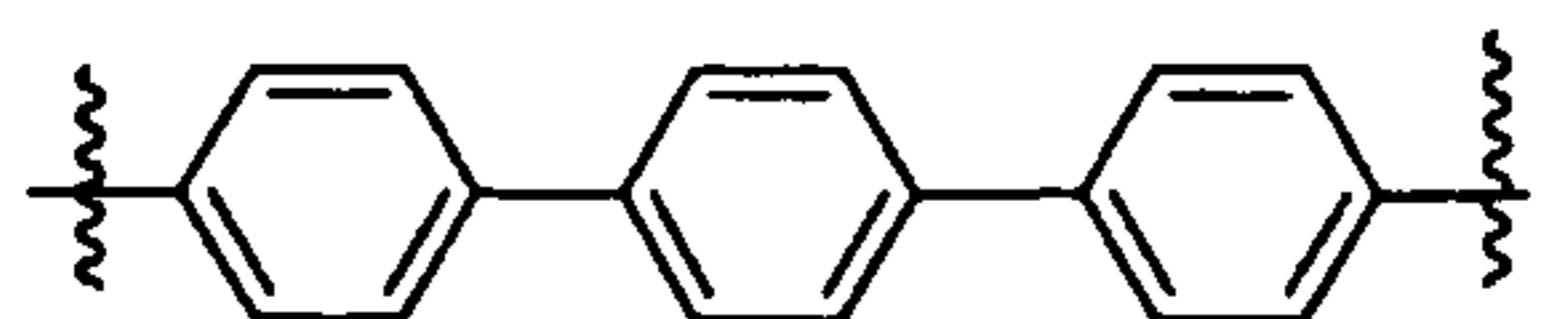


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

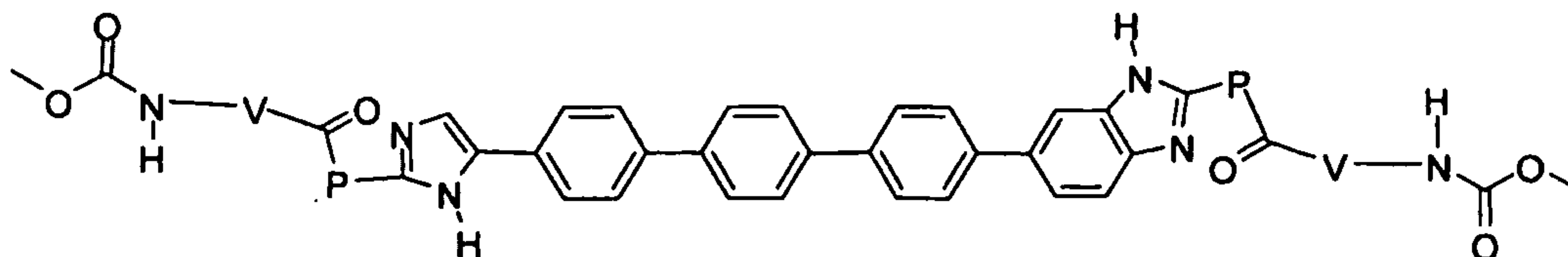


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A^0-A^4 and is:

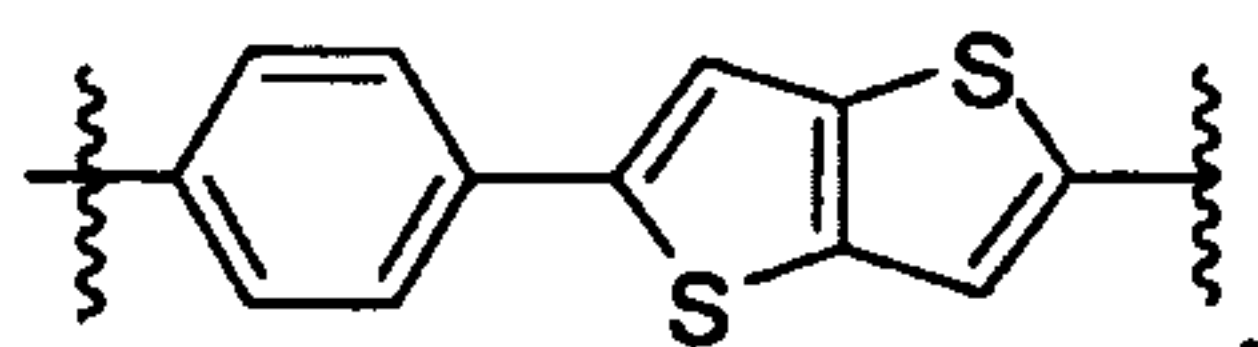


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16):

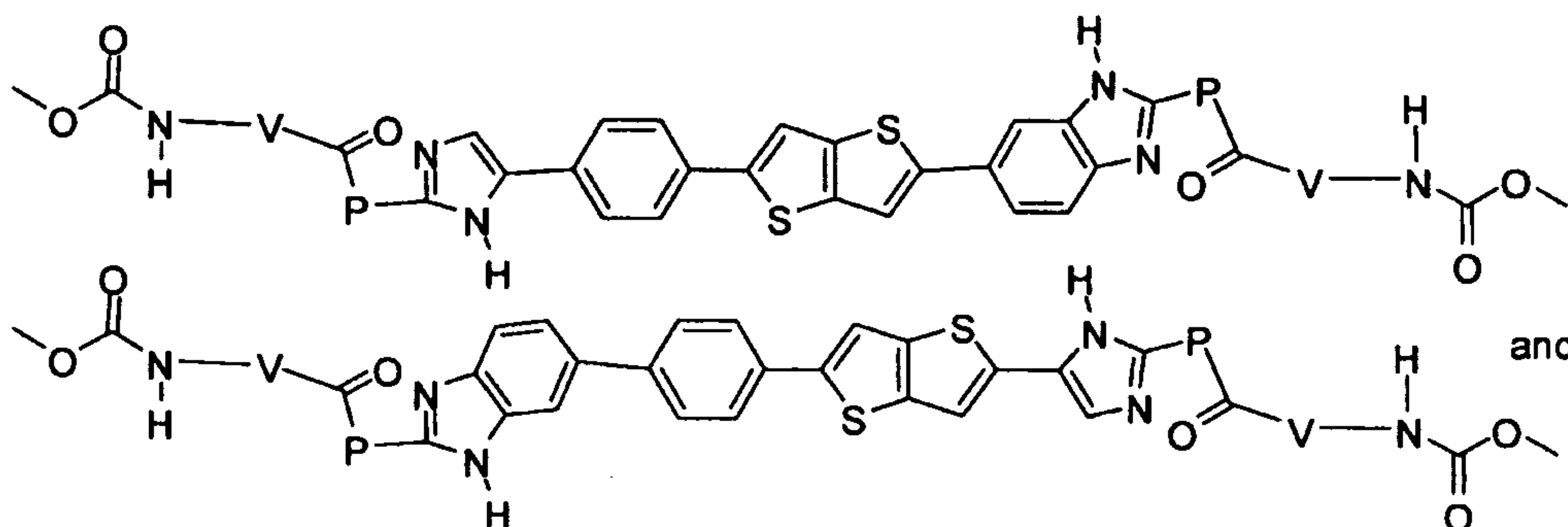


or a pharmaceutically acceptable salt or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A⁰-A⁴ and is:

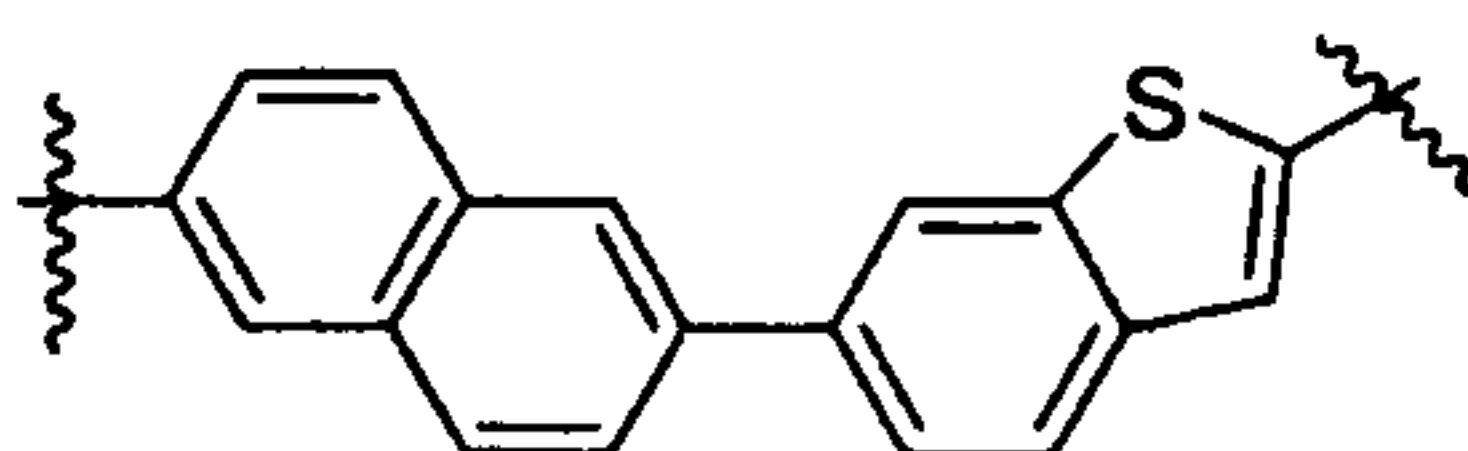


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

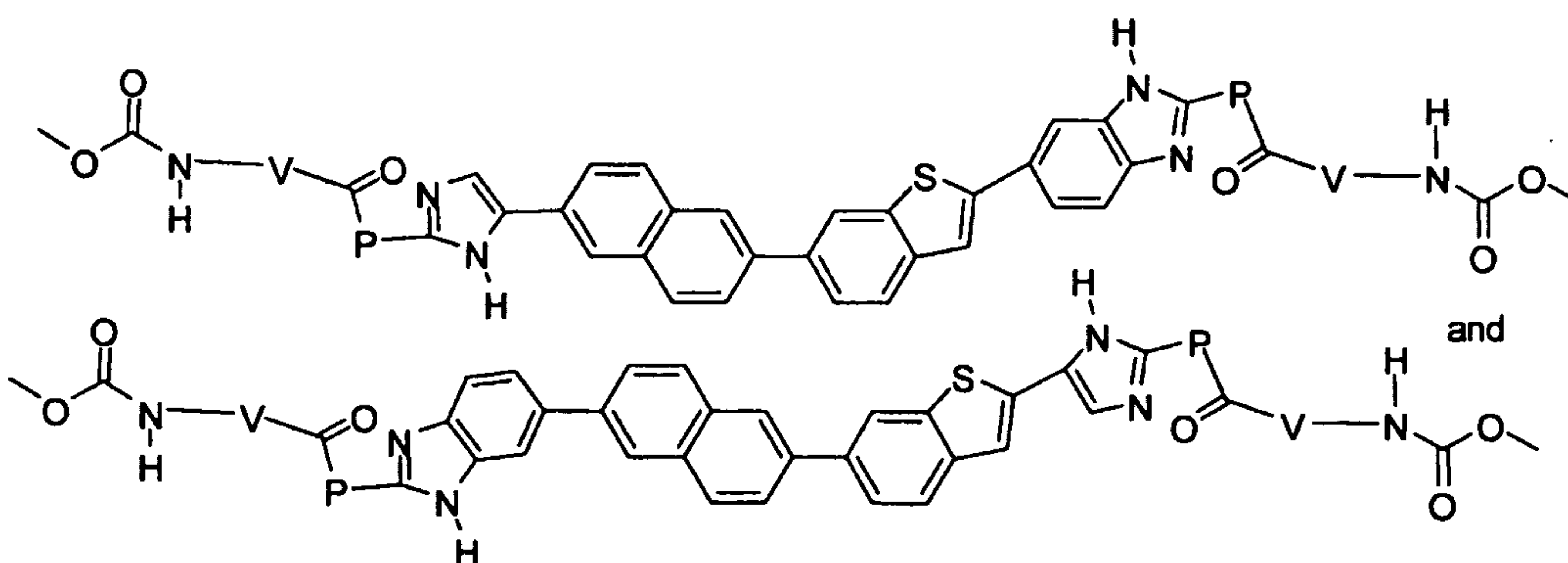


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹³-A¹⁴ and is:

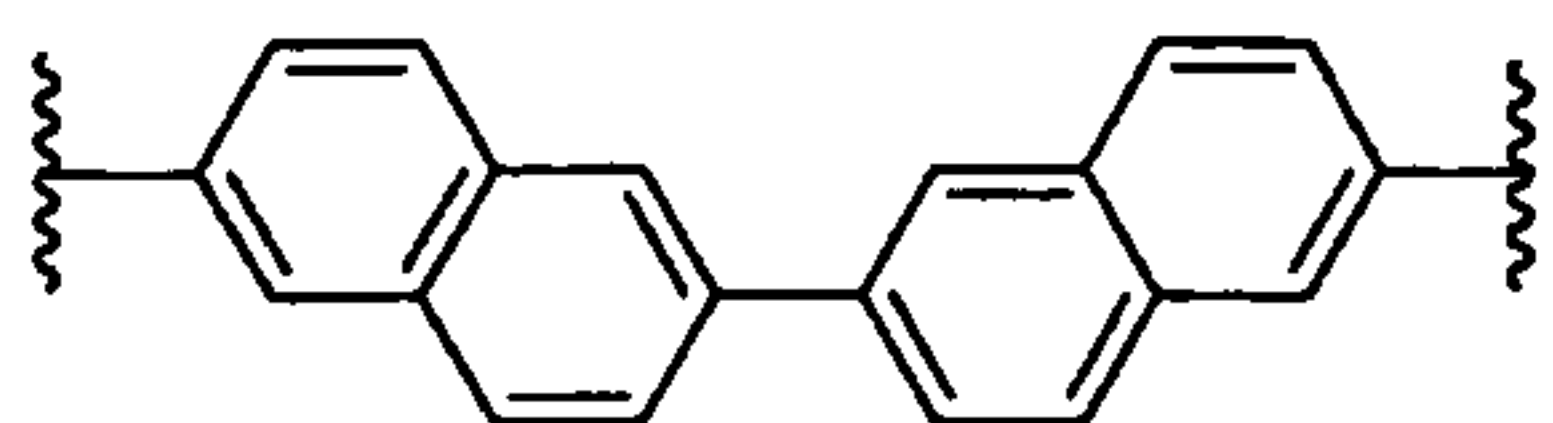


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

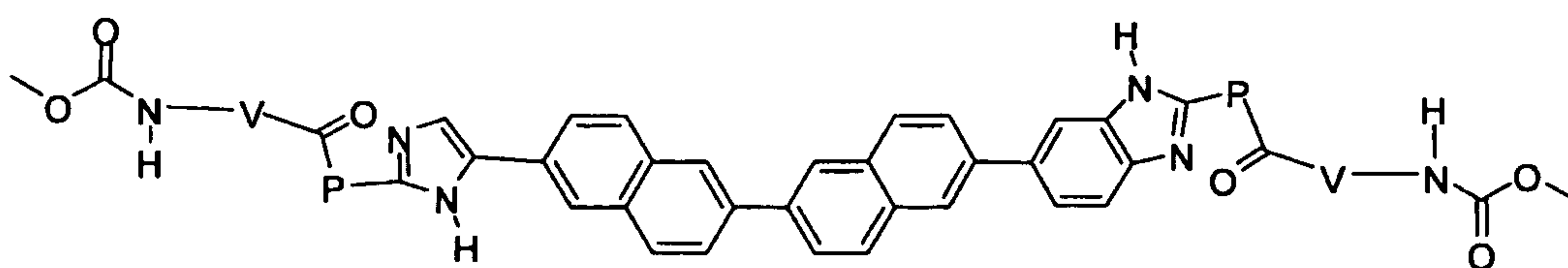


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹³-A¹³ and is:

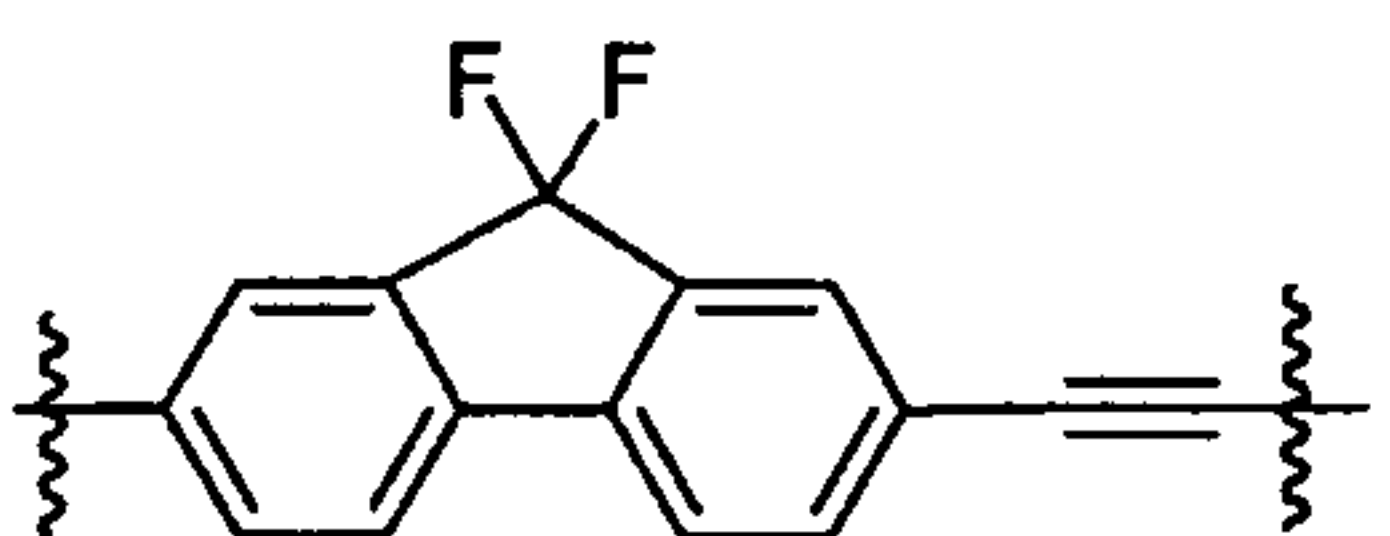


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16):

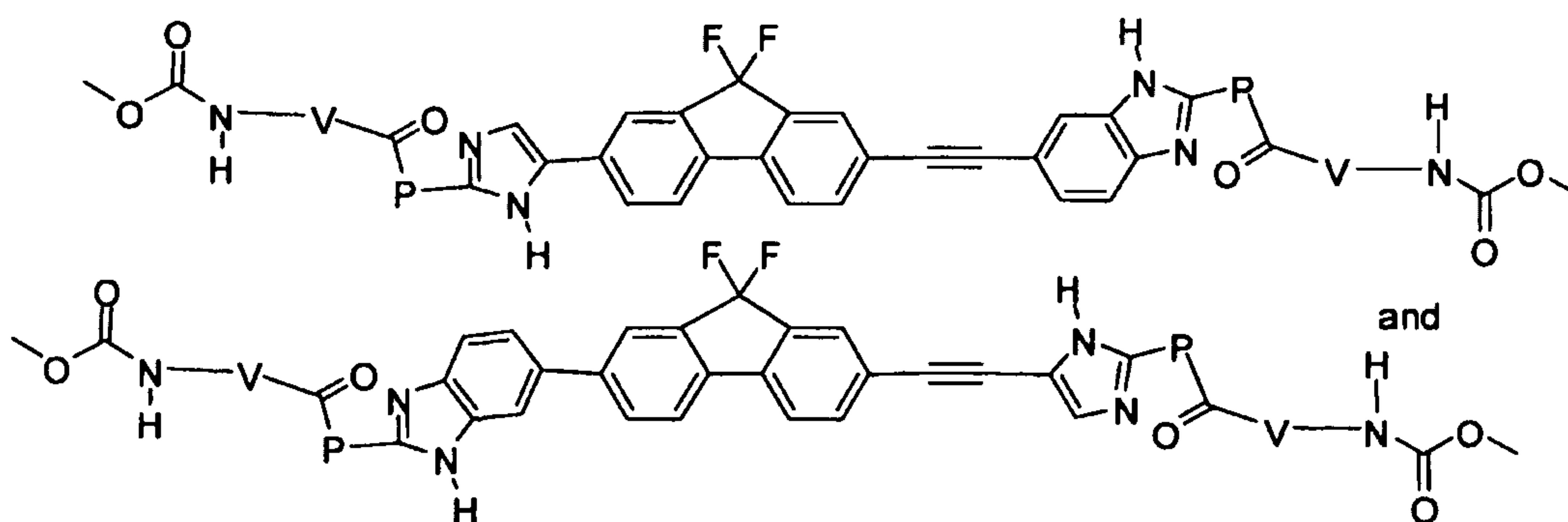


or a pharmaceutically acceptable salt or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹⁵-A⁶ and is:



In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

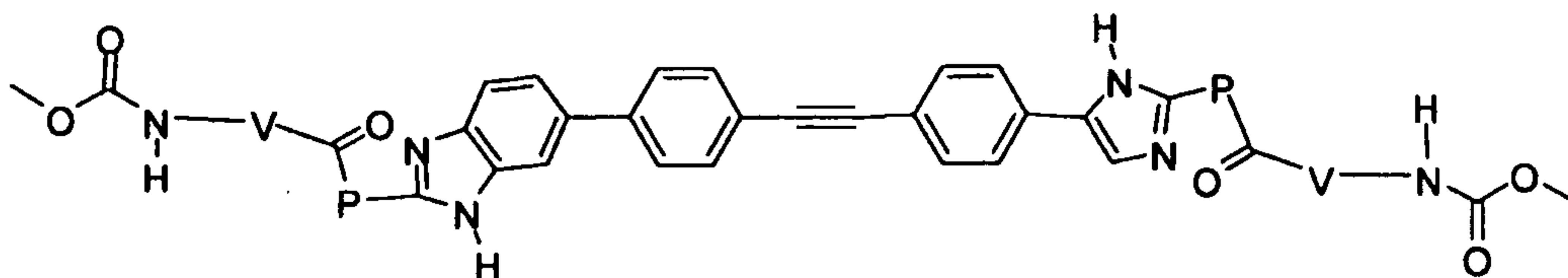


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A⁰-A⁵ and is:

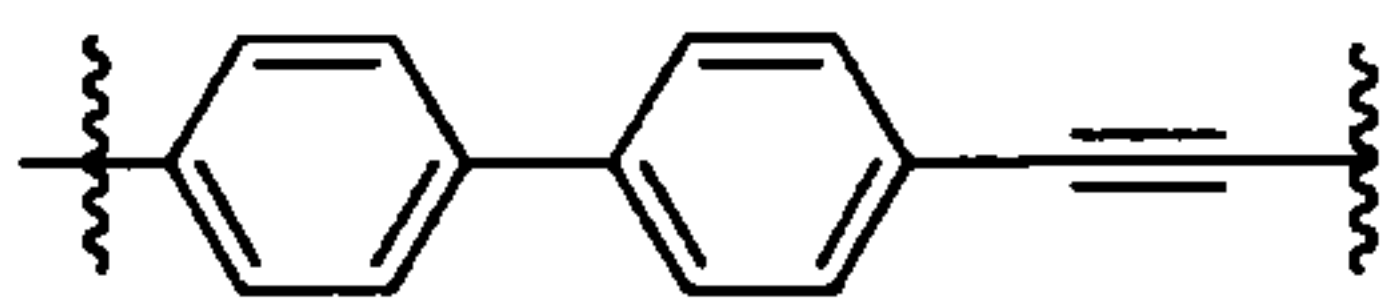


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16):

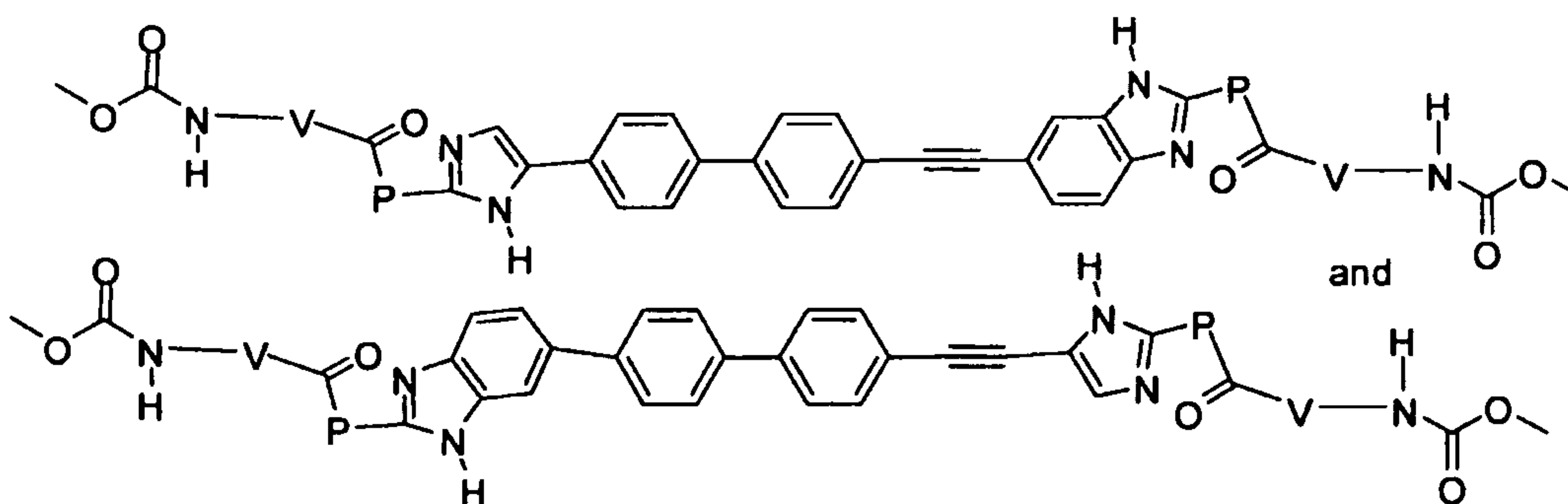


or a pharmaceutically acceptable salt or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A⁰-A⁵ and is:

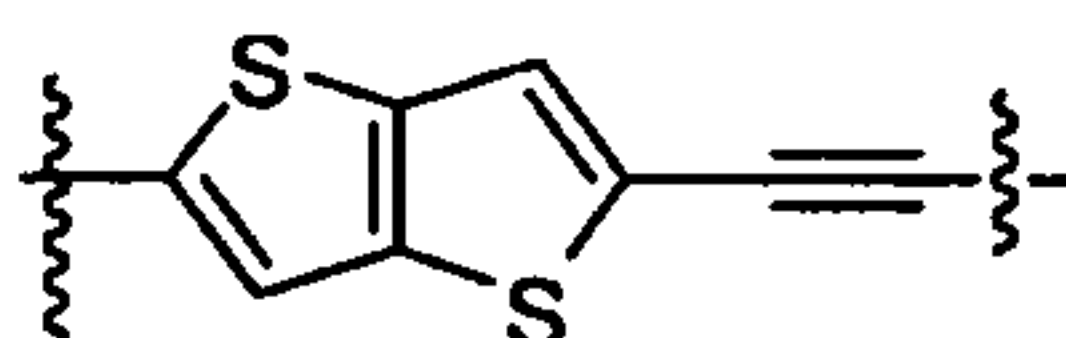


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

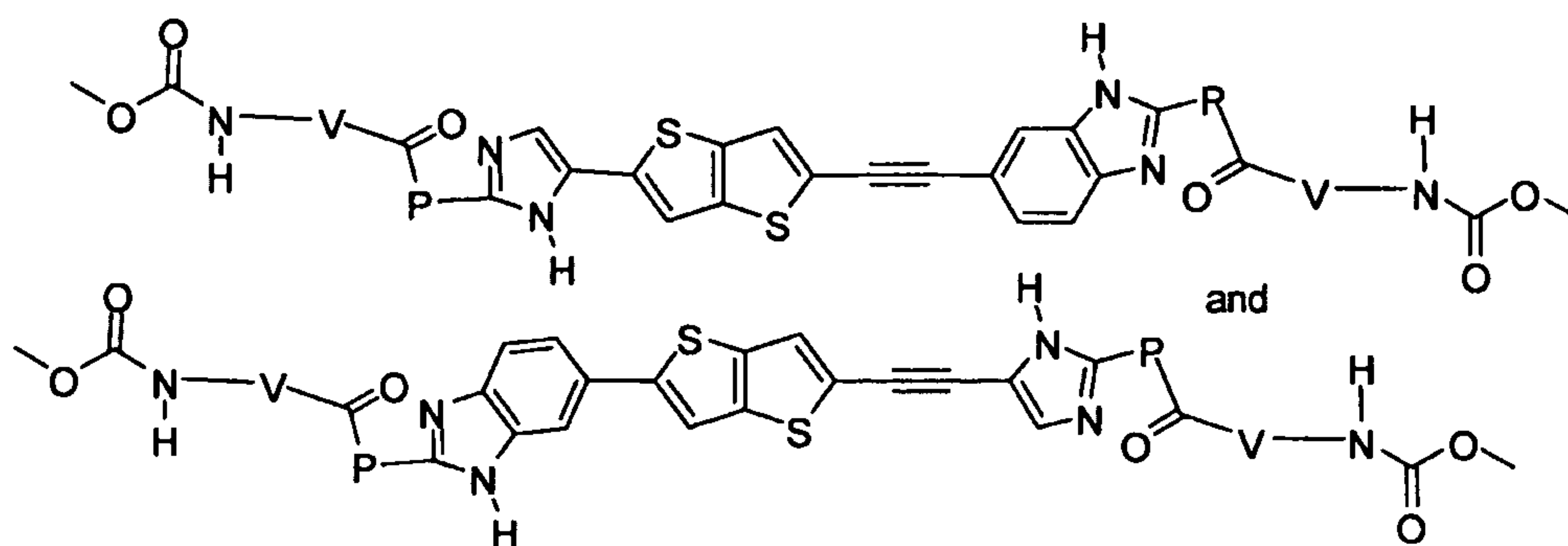


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹⁴-A⁶ and is:

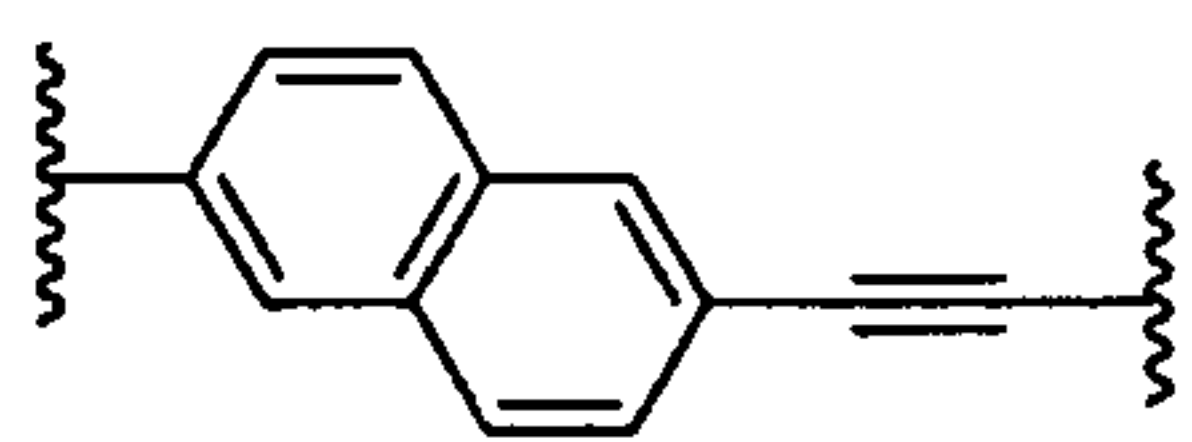


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

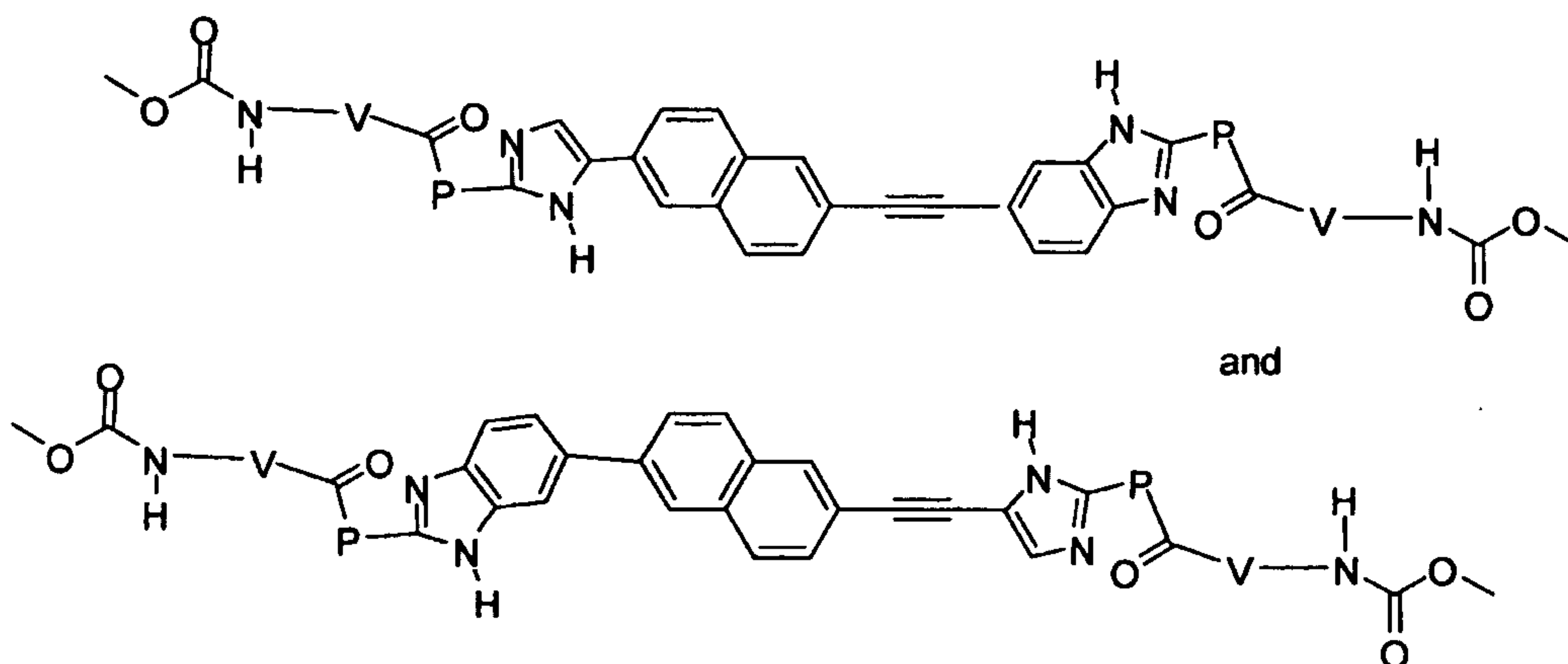


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹³-A⁶ and is:

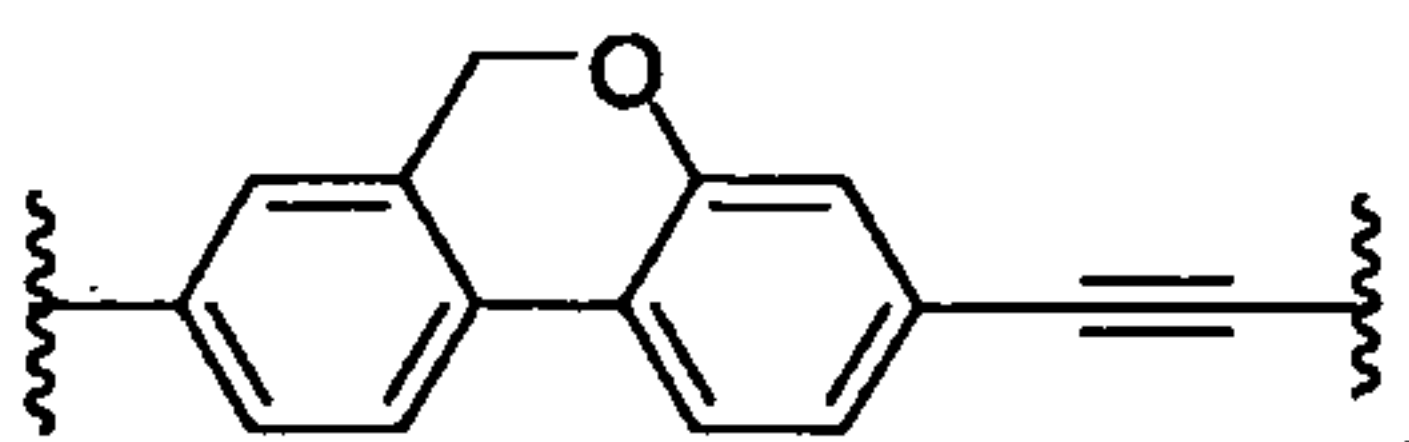


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

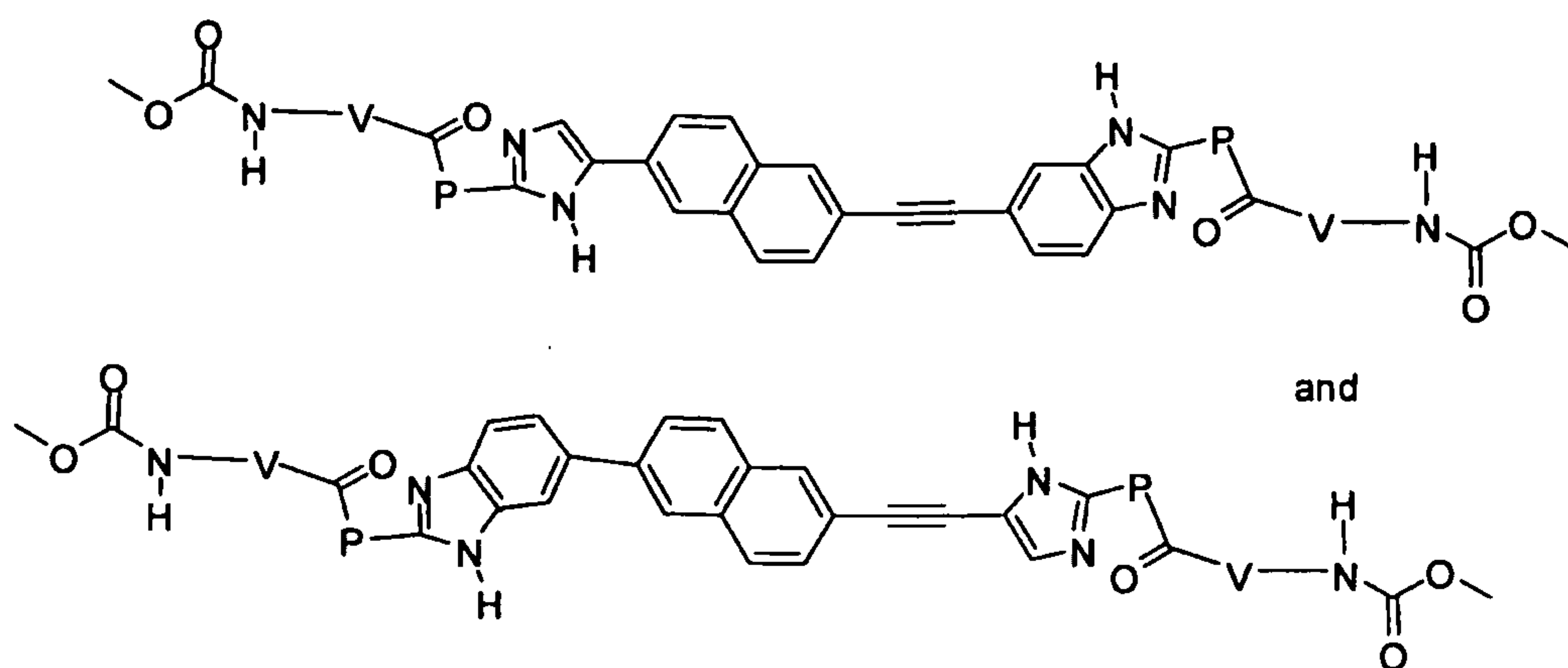


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) wherein A-A is A¹⁶-A⁶ and is:

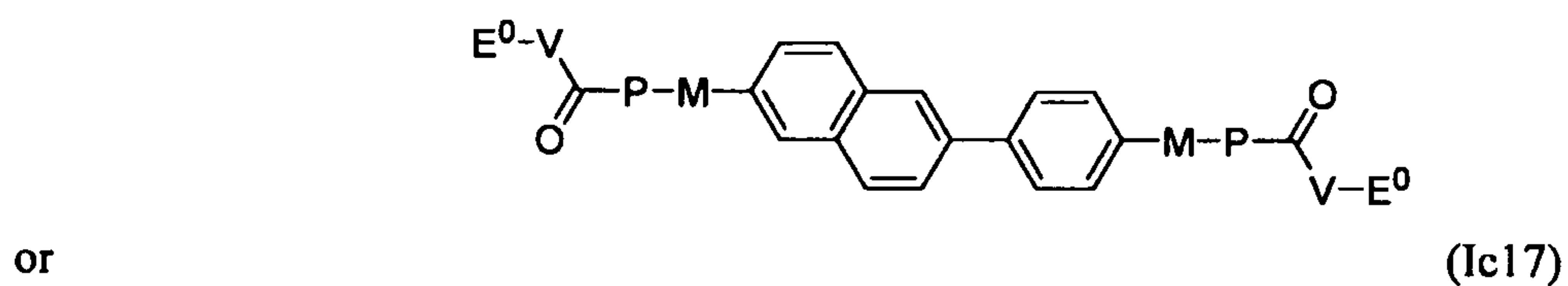


In one embodiment the invention provides a compound of formula (Ic15) or (Ic16) which is selected from:

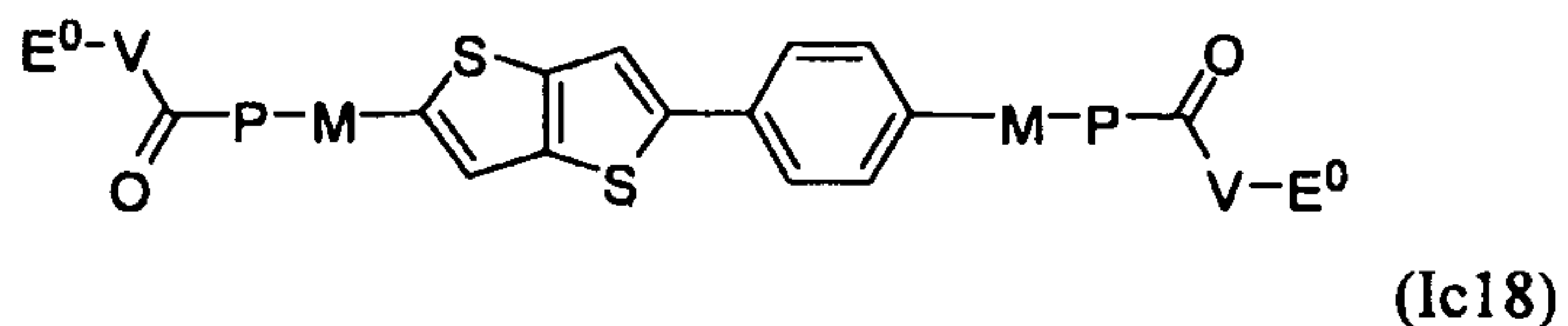


and pharmaceutically acceptable salts and prodrugs thereof.

In one embodiment the invention provides a compound of formula (Ic17) or (Ic18)

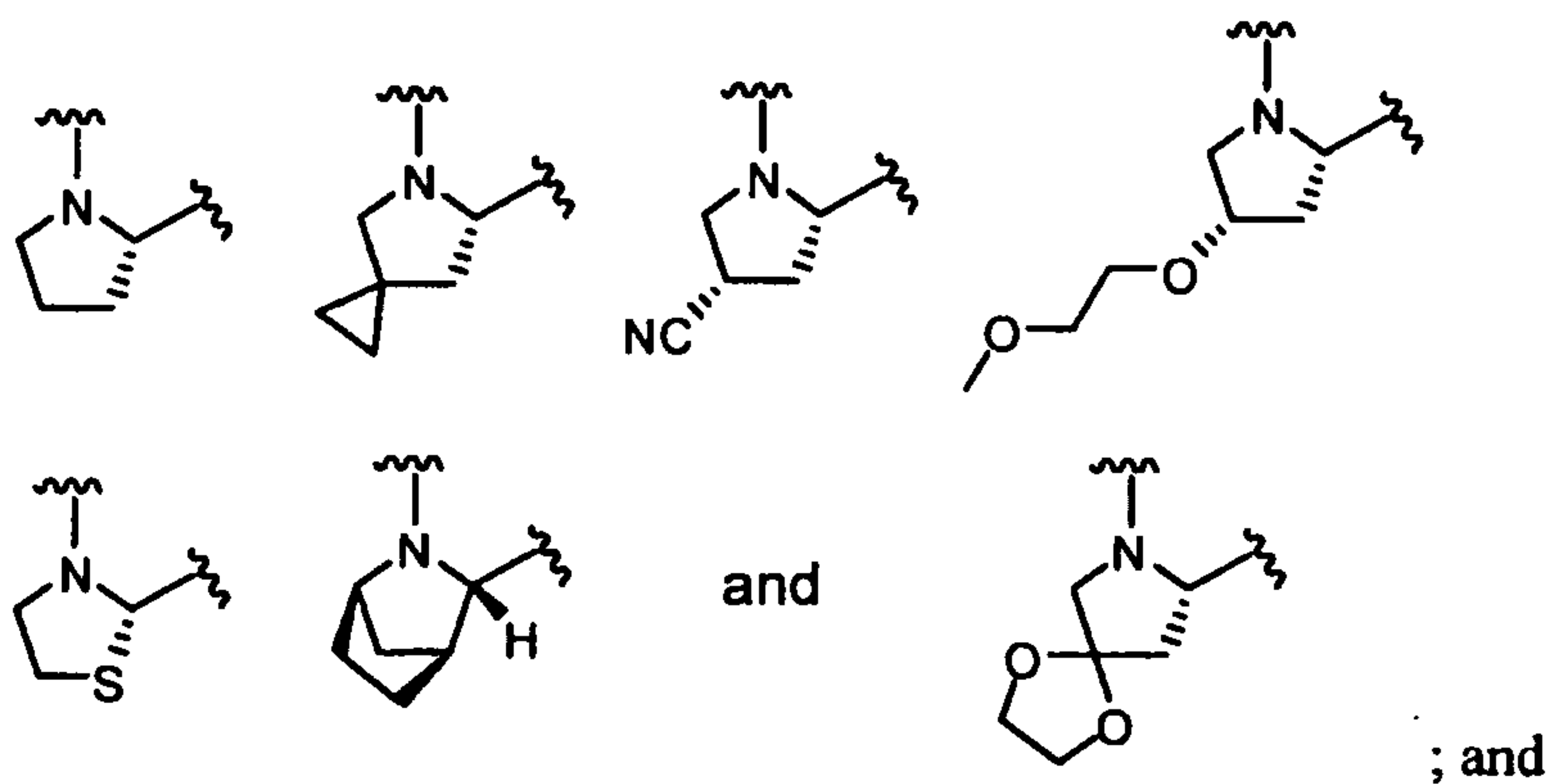


or



wherein:

each P is independently selected from:



each M is independently M^0 , M^9 , or M^{10} ;

or a pharmaceutically acceptable salts or prodrug thereof.

In one embodiment the invention provides a compound of formula (Ic17) or (Ic18) wherein each E^0 is methoxycarbonylamino.

In one embodiment the invention provides a compound of formula (Ic17) or (Ic18) wherein at least one E^0 is $-NR^{Ec}R^{Ed}$ wherein R^{Ec} is H, alkyl or cycloalkyl and R^{Ed} is heterocycle.

In another specific embodiment the invention provides a compound of the following formula (Ic30): $E^x-V^w-Z^v-P^u-M^t-A^s-A^s-M^t-P^u-Z^v-V^w-E^x$ (Ic30) wherein at least two of s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one of u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one t is 0 or 10.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein both t are 9; one s is 0; and one s is 0, 1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein both t are 9; one s is 1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21; and one s is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of s, t, u, v, w or x are not zero and at least one t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least three of s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least three of s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least three of s, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least four of s, t, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least four of s, t, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least four of s, t, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least four of s, t, u, v, w or x are not zero and at least four of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein the sum of t, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein the sum of s, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein s, and at least one t, and at least one u are all not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of u, w and t are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of s, u, and w are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of s, u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least s and both u are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one of u, or w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of u or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of u are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein at least two of w are not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein both t are 9; one s is 0; and one s is 0,1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12,13, 14, 15, 16, 17, 18, 19, 20, or 21.

In another specific embodiment the invention provides a compound of formula (Ic30) wherein both t are 9; one s is 1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12,13, 14, 15, 16, 17, 18, 19, 20, or 21; and one s is 0,1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12,13, 14, 15, 16, 17, 18, 19, 20, or 21.

In another specific embodiment the invention provides a compound of the following formula (Ic31): $E^x-V^w-Z^v-P^u-M^9-A^s-A^s-M^9-P^u-Z^v-V^w-E^x$ (Ic31) wherein one s is 0 or 6 and one s is 6.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least two of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least three of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least four of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least three of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least three of u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least four of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least one of u or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least two of u or w are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least one u is not zero.

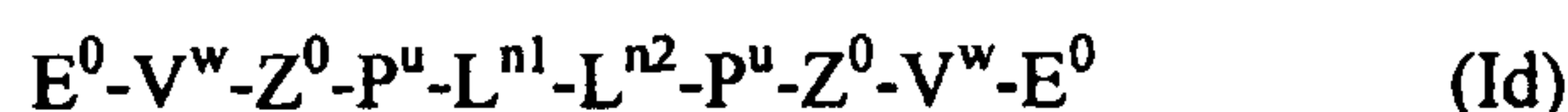
In another specific embodiment the invention provides a compound of formula (Ic31) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Ic31) wherein both w are not zero.

Compounds of formula (Id)

In one embodiment of the invention, the compound of formula (I) is a compound of formula (Id):



wherein:

n1 is 3, 4, or 9;

n2 is 9;

each u is 0, 1, 3, 5, 7, 8, 10, or 11;

each w is 0, 1, 2, 3, 4, or 5;

each L³ is independently a fused-bicyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl,

(halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁴ is independently a fused-tricyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkyl, arylalkoxy carbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, (NR^aR^b)carbonyl, cyano, nitro, SOR⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl, (heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

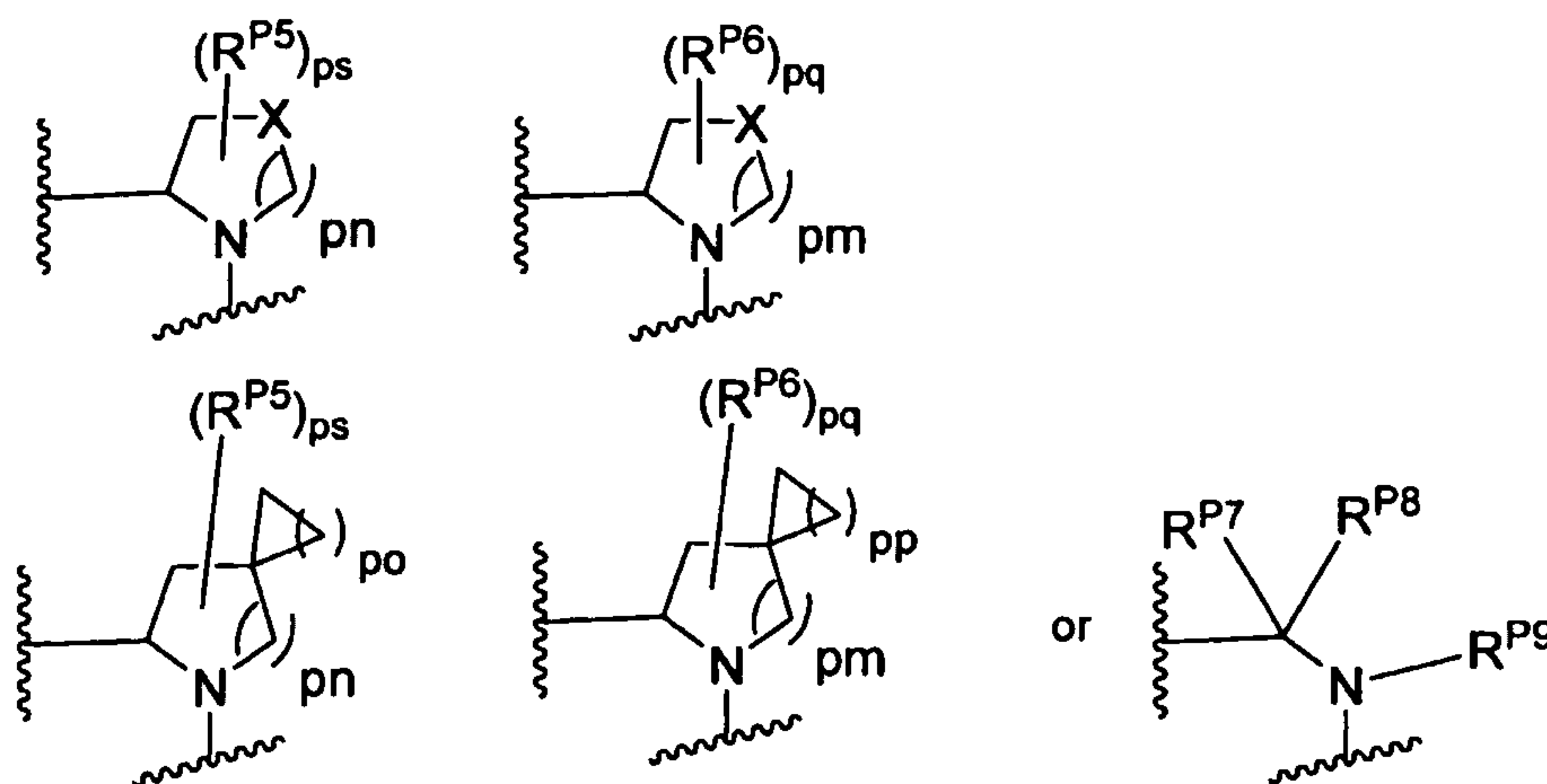
each R⁴ is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl; and R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each L⁹ is independently a fused-tetracyclic saturated, partially unsaturated, or aromatic heterocyclic ring system that is optionally substituted with one or more groups independently selected from oxo, halo, -R^{L7}, -OR^{L7}, -SR^{L7}, -CF₃, -CCl₃, -OCF₃, -CN, -NO₂, -N(R^{L7})C(=O)R^{L7}, -C(=O)R^{L7}, -OC(=O)R^{L7}, -C(O)OR^{L7}, -C(=O)NR^{L7}, -S(=O)R^{L7}, -S(=O)₂OR^{L7}, -S(=O)₂R^{L7}, -OS(=O)₂OR^{L7}, -S(=O)₂NR^{L7}, alkoxyalkyl, arylalkoxy carbonyl, halo, haloalkyl, hydroxyalkyl, -NR^aR^b, (NR^aR^b)alkyl, and (NR^aR^b)carbonyl;

each R^{L7} is independently -H, alkyl, aryl, arylalkyl, or heterocycle;

R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each P⁰ is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
 provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

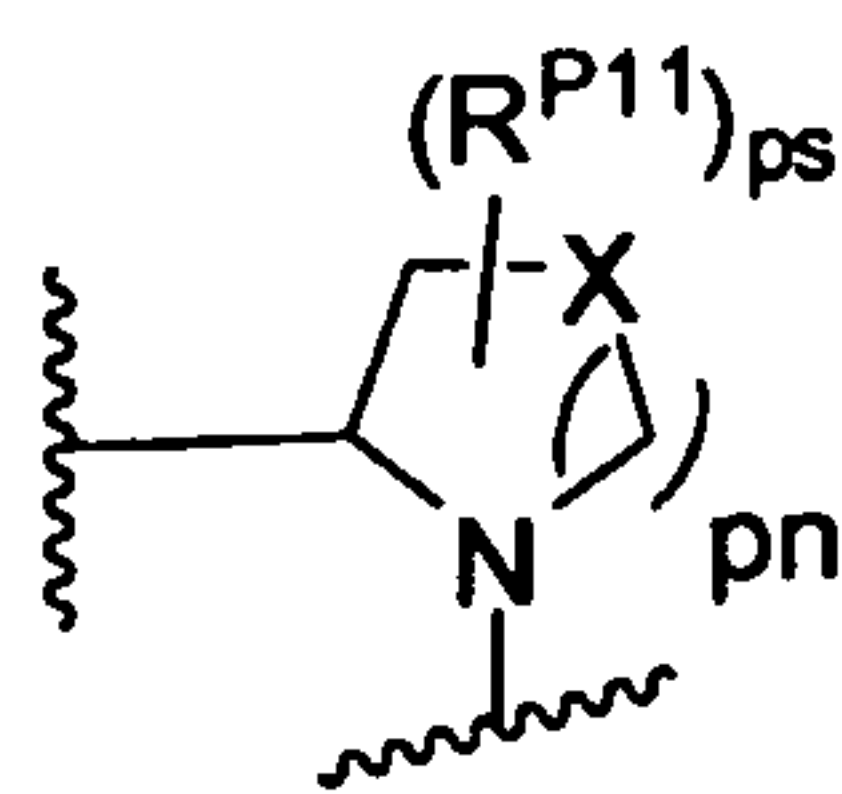
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and (NR^{Pa}R^{Pb})alkyl; or R^{P7} and R^{P8}, together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz}, O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^l is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

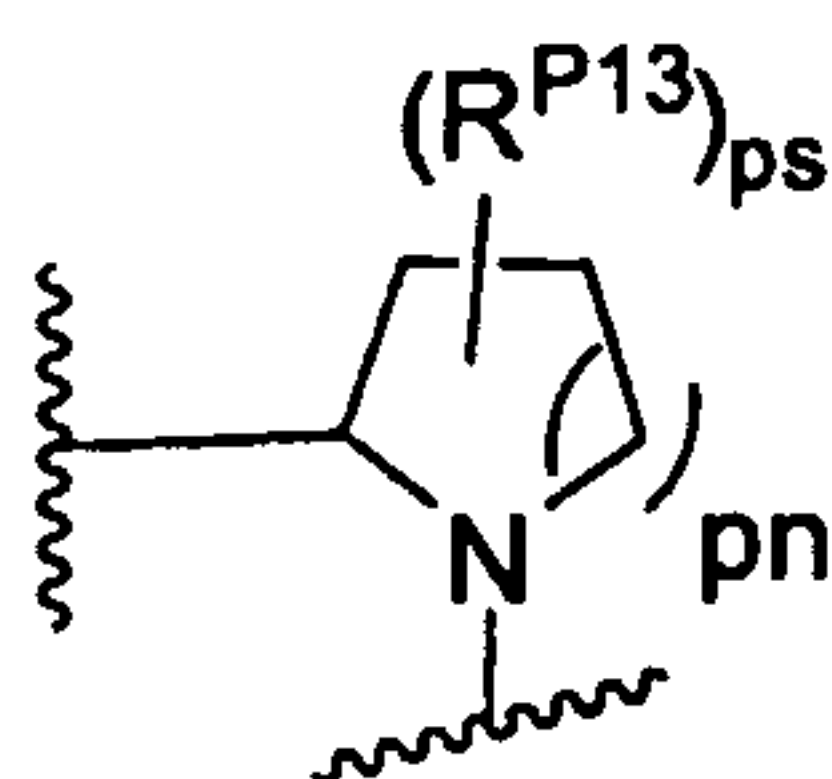
each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl, -NR^{hh}R^h, (NR^{hh}R^h)alkyl, (NR^{hh}R^h)carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h)sulfonyl, heteroarylsulfonyl, -S(=O)₂R^h, -C(=O)R^h, -C(=O)NR^hR^h; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P³ is independently a ring of the formula:



wherein:

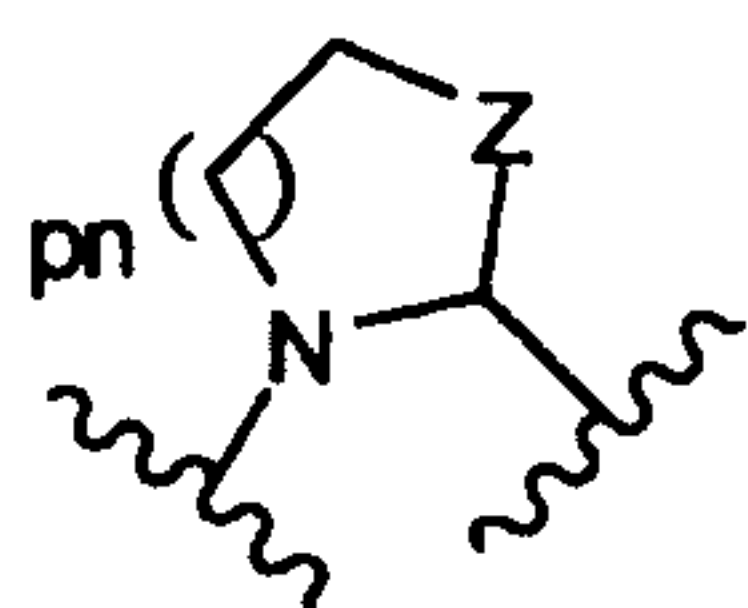
the ring is substituted with one or more oxo groups;

each R^{P13} is independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkoxy, haloalkoxyalkoxy, cycloalkoxyalkoxy, aryloxyalkoxy, heteroaryloxyalkoxy, heterocycloxyalkoxy, (NR^hR^h)alkoxy, cyanoalkoxy, cyanocycloalkoxy, cycloalkoxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P⁵ is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one

or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

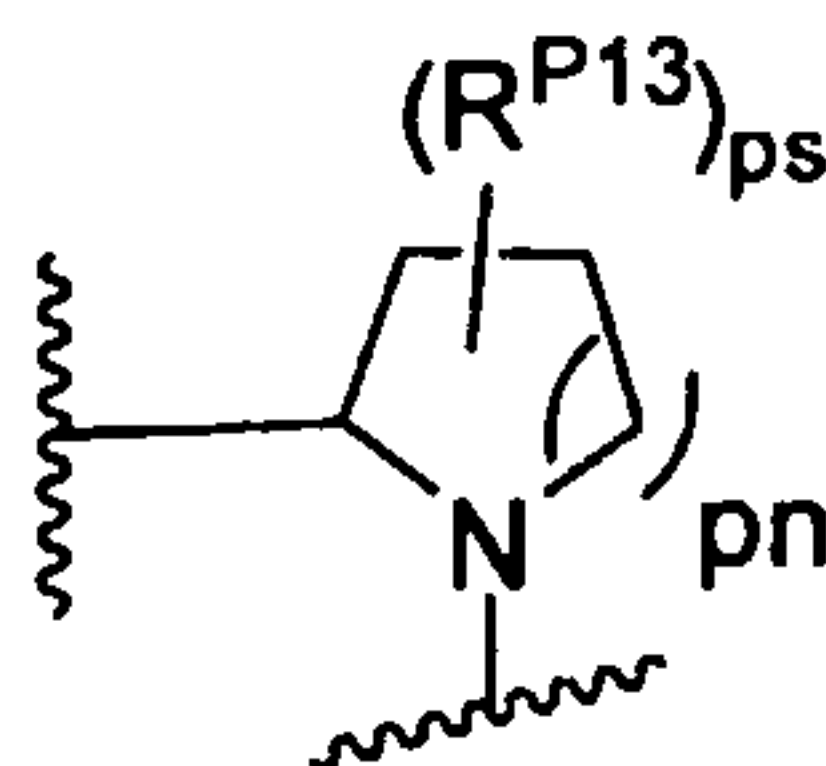
pn is 0, 1, or 2;

Z is O, S, S(=O), S(=O)₂, or NR^f;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, -S(=O)₂NR^hR^h, -S(=O)₂R^h, C(=O)R^h, C(=O)OR^h, -C(=O)NR^hR^h; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P⁷ is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11};

each P⁸ is independently a ring of the formula:

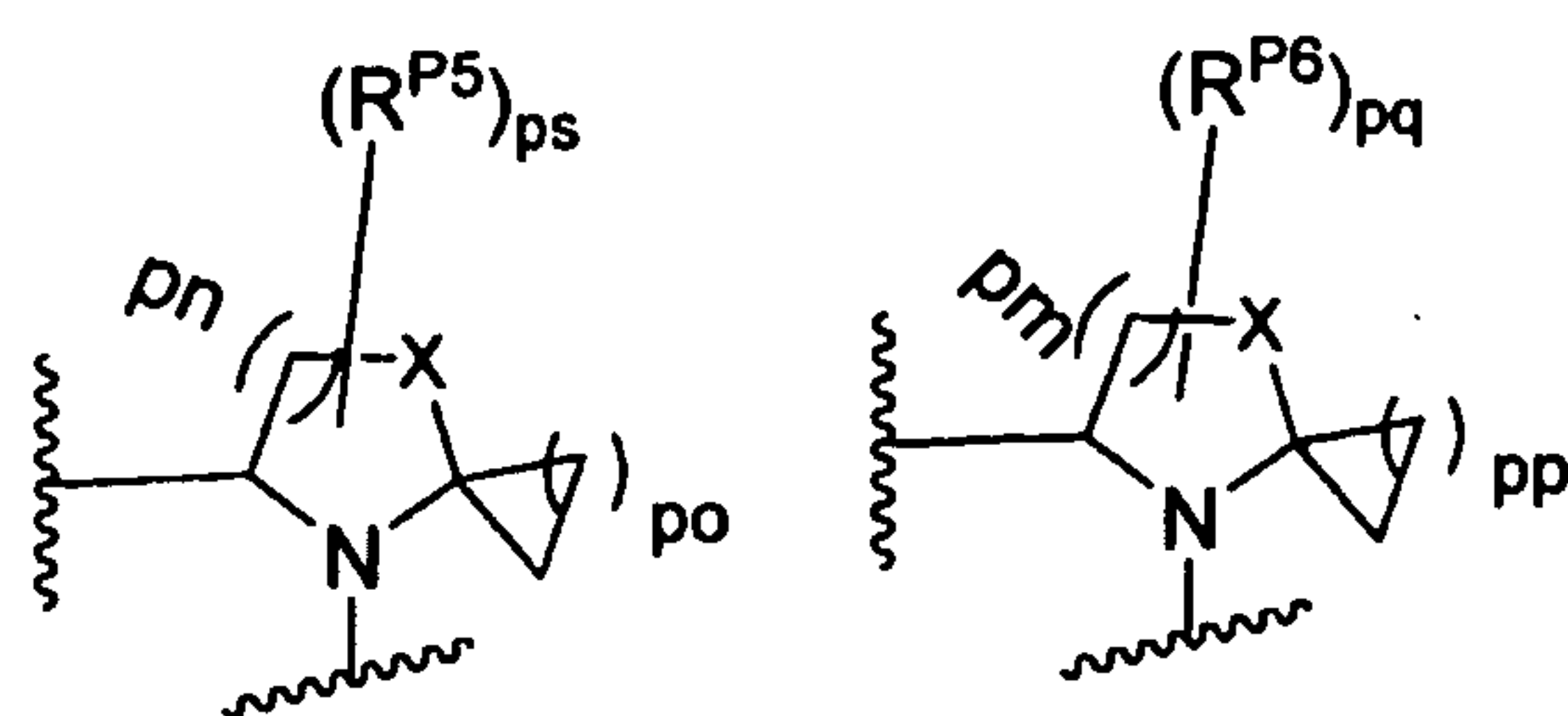


wherein:

ps is 2, 3, 4, 5, or 6;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three-to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

X is selected from O , S , $S(O)$, SO_2 , CH_2 , CHR^{P10} , and $C(R^{P10})_2$;
provided that when pn or pm is 0 , X is selected from CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

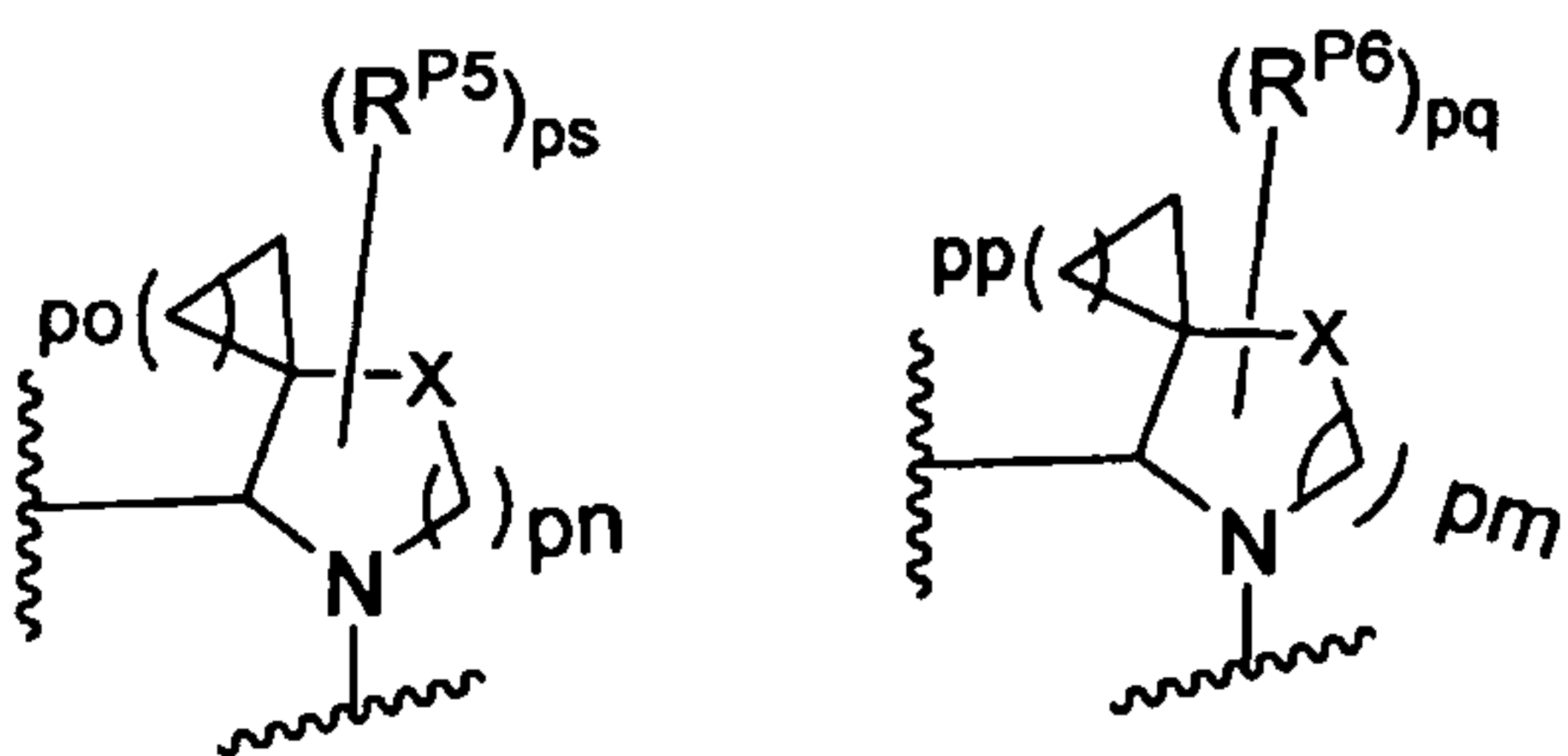
each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0 , 1 , 2 , 3 , or 4 ;

pm and pn are independently 0 , 1 , or 2 ;

po and pp are independently 1 , 2 , or 3 ;

each P^{11} is independently:



wherein:

X is selected from O , S , $S(O)$, SO_2 , CH_2 , CHR^{P10} , and $C(R^{P10})_2$;
provided that when pn or pm is 0 , X is selected from CH_2 , CHR^{P10} , and $C(R^{P10})_2$;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;

pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

each $-Z^0$ is $-C(=O)-$ or $-C(=S)-$;

each E^0 is independently $-NR^{Ec}R^{Ed}$ wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl, heterocyclylloxycarbonyl, hydroxyalkylcarbonyl, (NR^f) alkyl, (NR^f) alkylcarbonyl, (NR^f) carbonyl, (NR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^X R^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclylalkyl, and the heterocyclylalkylcarbonyl are further optionally substituted with one $-NR^f$ group; and wherein the aryl, the aryl part of the arylalkoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxycarbonyl, and the arylsulfonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkoxycarbonyl, the heterocyclylalkyl, the heterocyclylalkylcarbonyl, the heterocyclylcarbonyl, and the heterocyclylloxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^0 is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxycarbonylalkyl, alkylsulfanylalkyl,

aryalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclylalkyl, heterocyclylcarbonylalkyl, hydroxyalkyl, NRRCOalkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $-(NR^X R^Y)$ alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocyclyl, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^X R^Y$, $(NR^X R^Y)$ alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclylalkyl are unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle,

heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

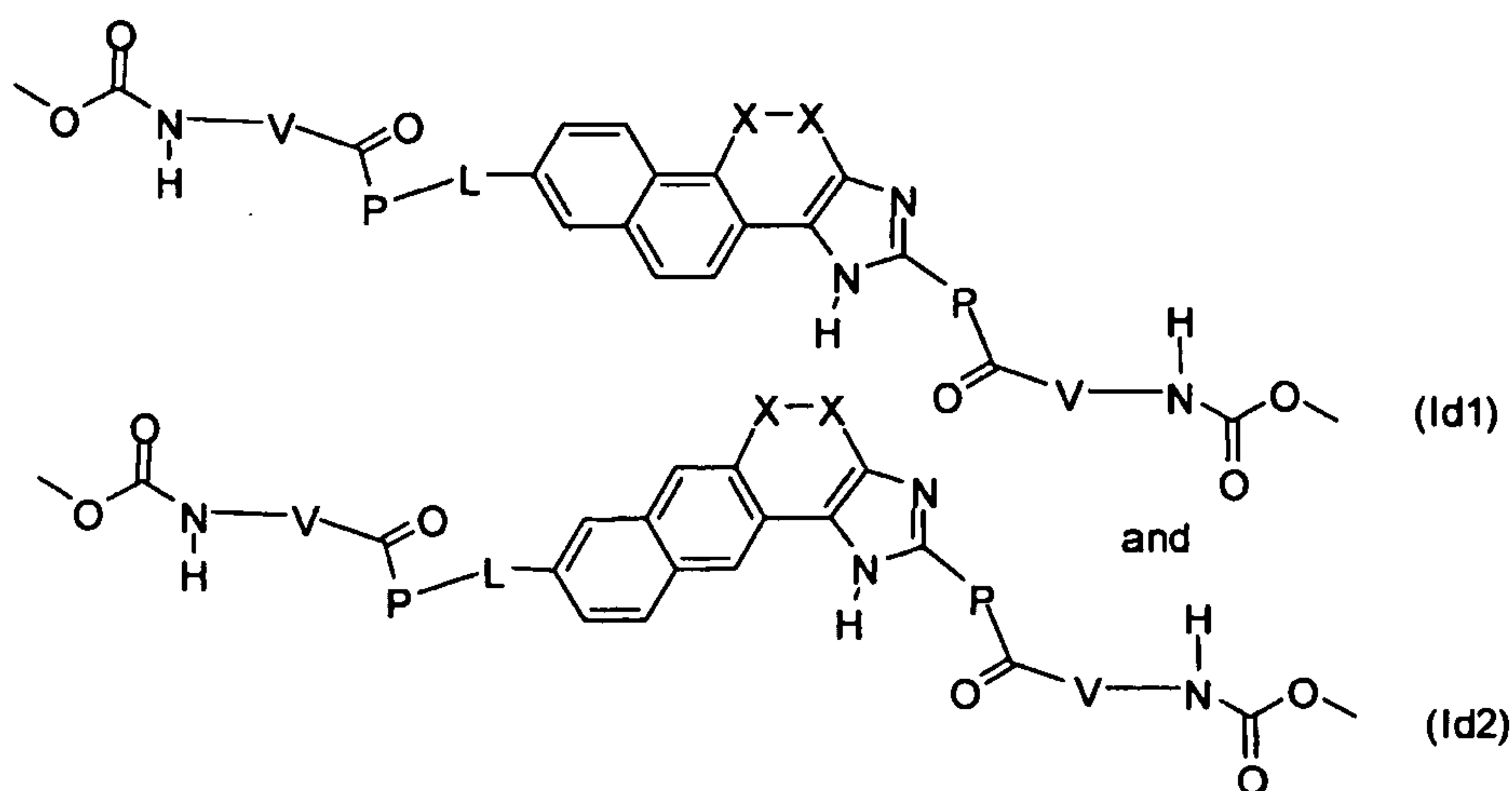
each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano; and

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{a}}\text{R}^{\text{b}}\text{C}(=\text{O})\text{O}-$; R^{a} and R^{b} are each independently selected from hydrogen, alkenyl, and alkyl; and

each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl.

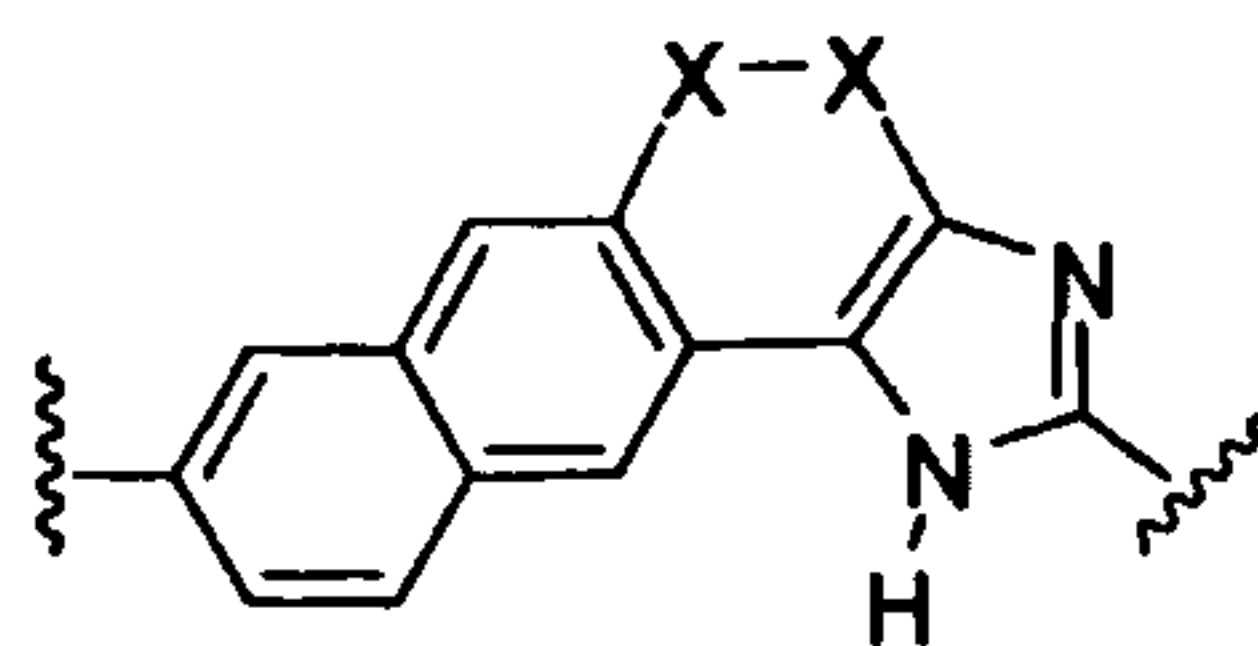
In one embodiment the invention provides a compound of formula (Id) wherein each L is benzimidazolyl.

In one embodiment the invention provides a compound of formula (Id1) or (Id2) which is selected from:

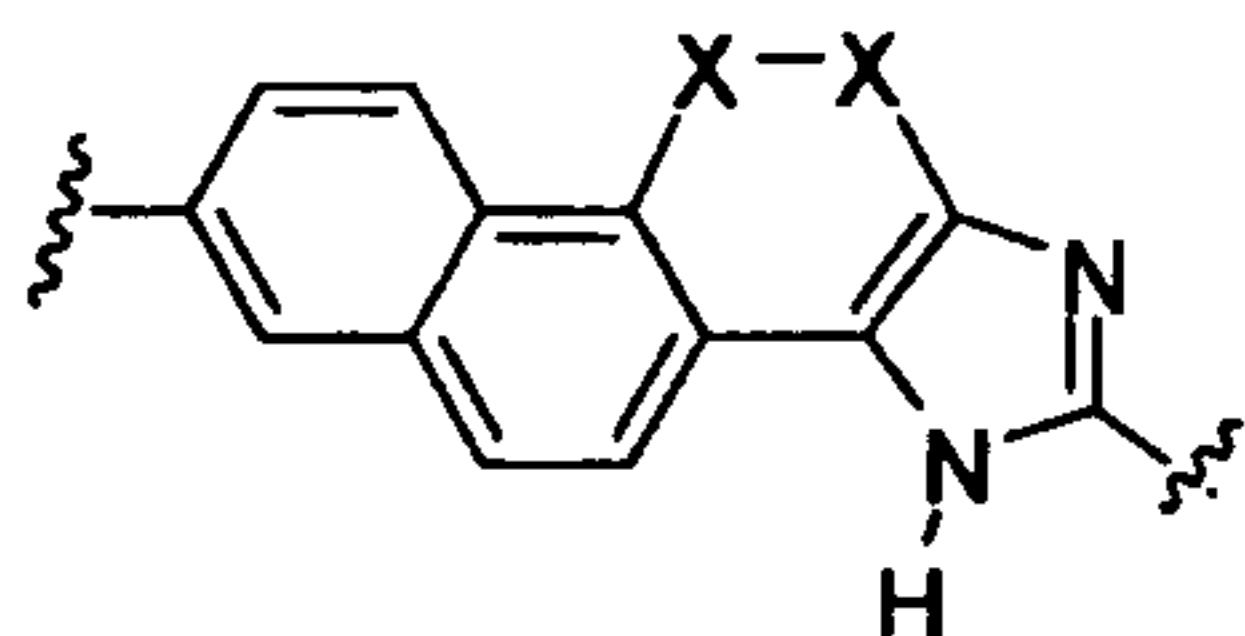


wherein X-X is selected from O, CH_2 , $\text{CH}=\text{CH}$, $\text{CH}_2\text{-CH}_2$, $\text{CH}_2\text{-O}$, O-CH_2 , $\text{CH}_2\text{-CH}_2\text{-CH}_2$, and $\text{CH}_2\text{-O-CH}_2$; or a pharmaceutically acceptable salt, or prodrug thereof.

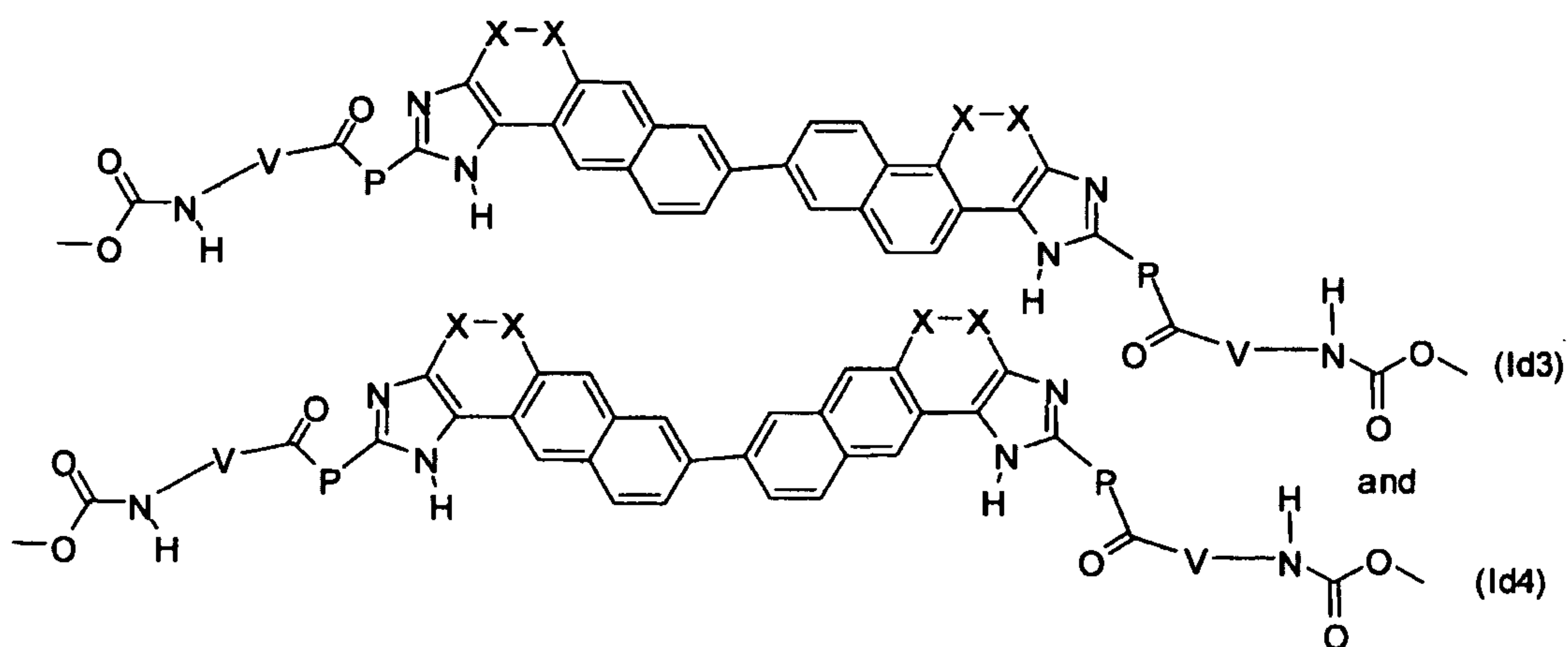
In one embodiment the invention provides a compound of formula (Id) wherein L^9 is:



In one embodiment the invention provides a compound of formula (Id) wherein L^9 is:

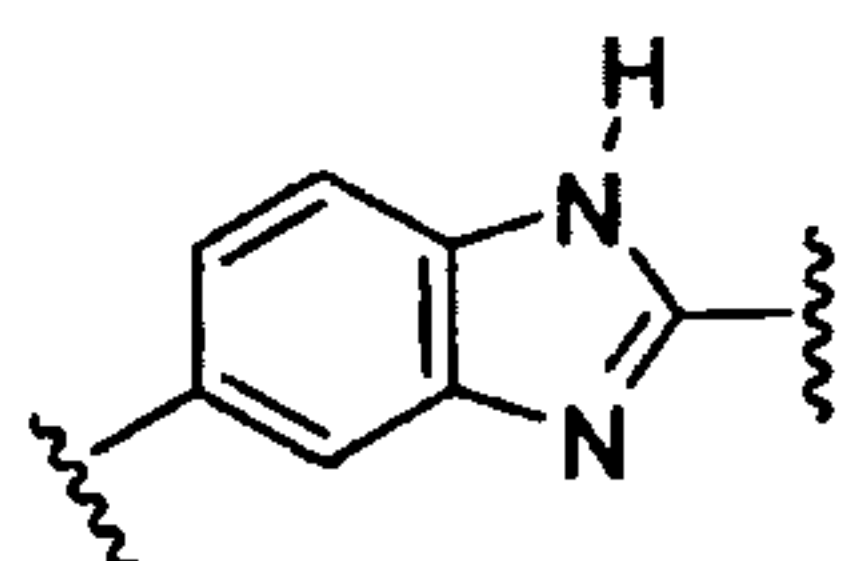


In one embodiment the invention provides a compound of formula (Id3) or (Id4) which is selected from:

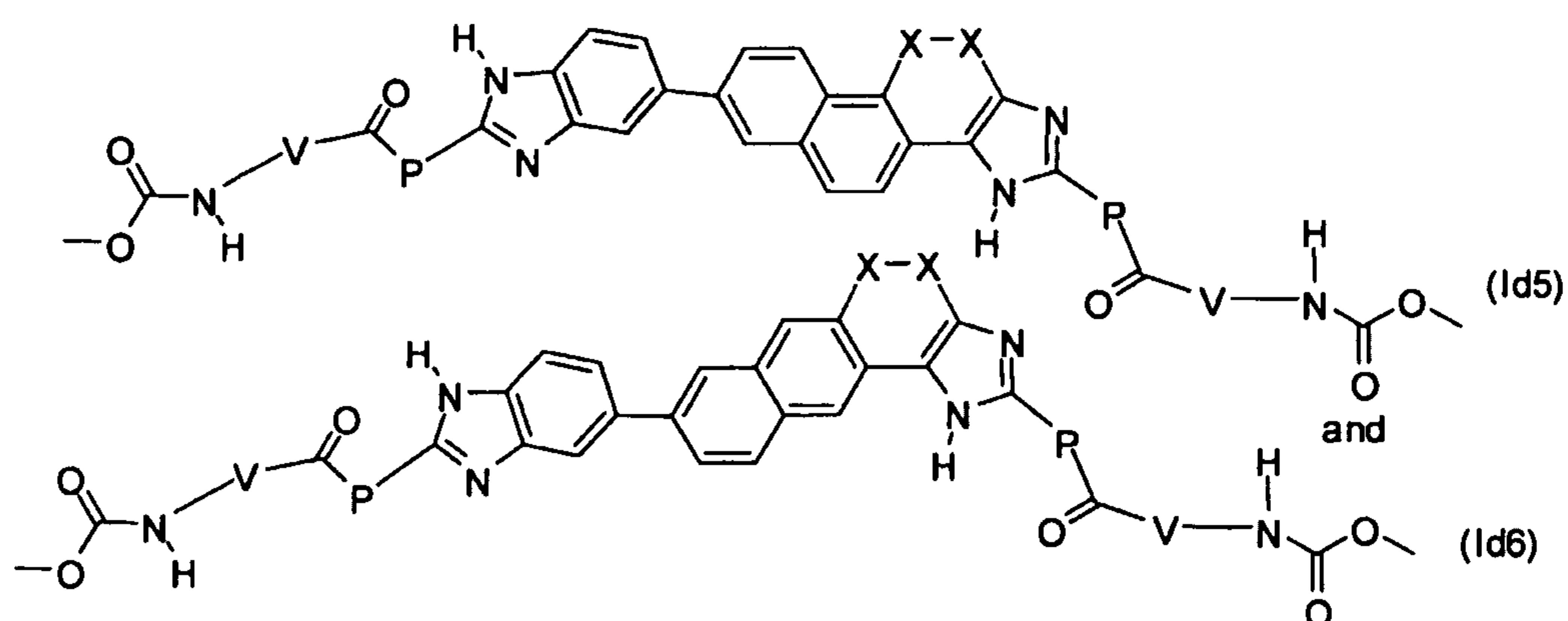


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Id) wherein L^3 is:

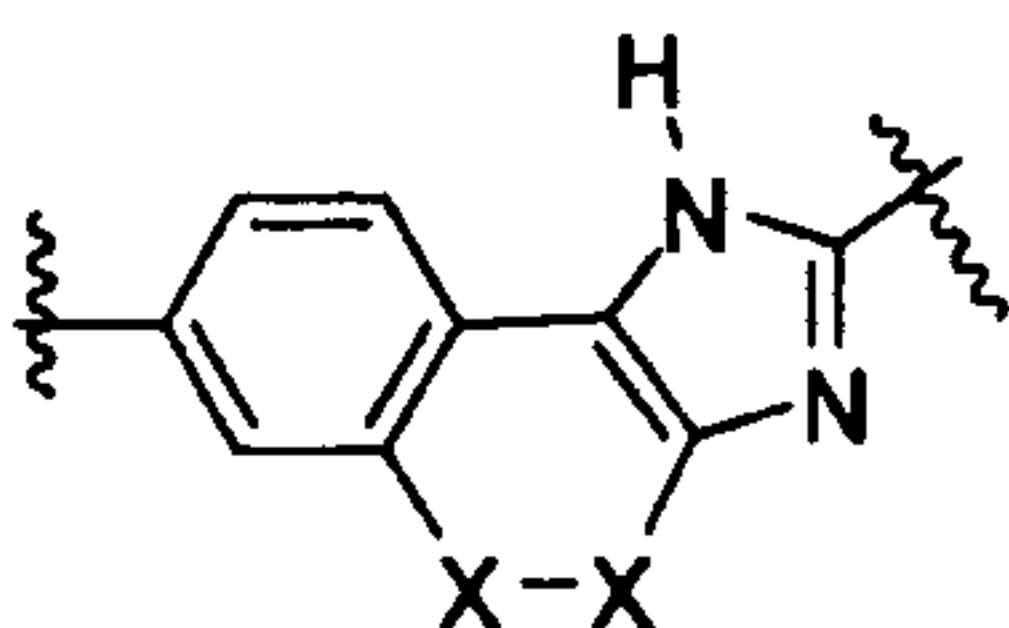


In one embodiment the invention provides a compound of formula (Id5) or (Id6) which is selected from:

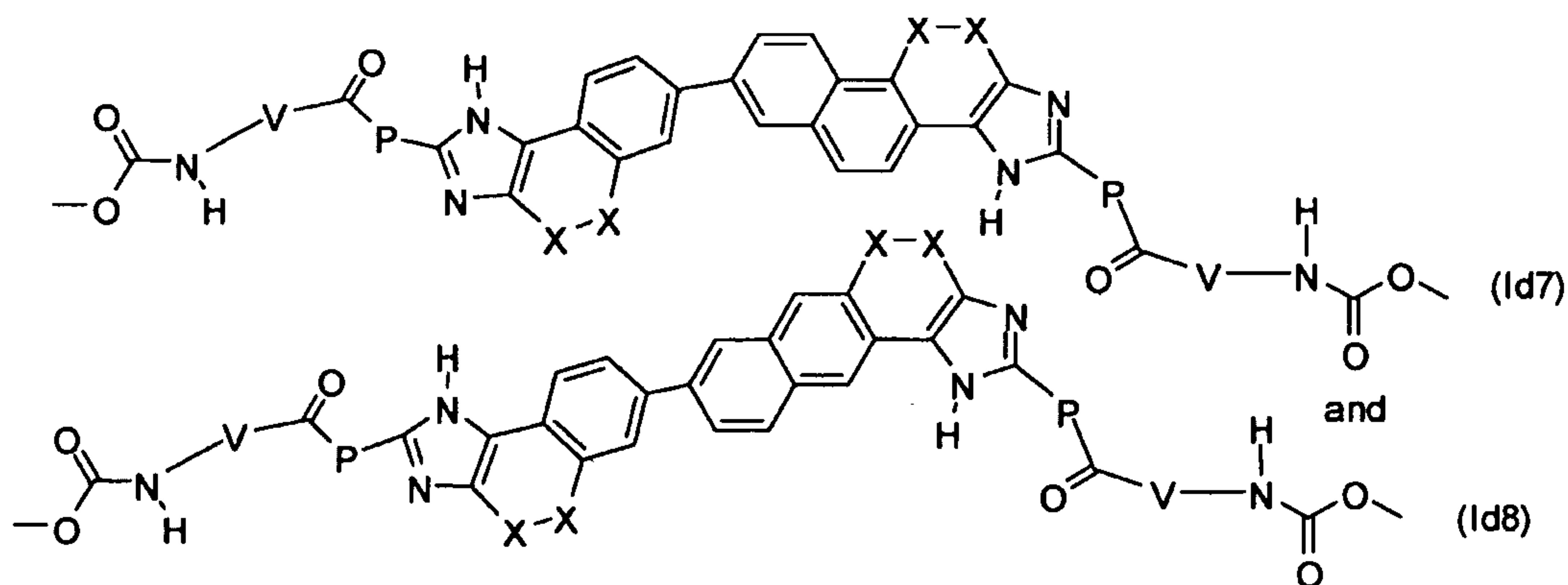


wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In one embodiment the invention provides a compound of formula (Id) wherein L⁴ is:



In one embodiment the invention provides a compound of formula (Id5) or (Id6) which is selected from:



wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

In another specific embodiment the invention provides a compound of the following formula (Id30): $E^x-V^w-Z^v-P^u-L^n-L^n-P^u-Z^v-V^w-E^x$ (Id30); wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein one n is 0, 1, 2, 4, 5, 6, 7, 8, 9, or 10; and one n is 1, 2, 3, 5, 6, 7, 8, 9, or 10.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of n, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of n, u, v, w or x are not zero and at least one n is selected from 0, 1, 2, 4, 5, 6, 7, 8, and 10

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of n, u, v, w or x are not zero and at least one n is selected from 0, 1, 2, 3, 5, 6, 7, 8, and 10

Wherein at least three of n, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of n, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least three of n, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least three of n, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least four of n, u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least four of n, u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least four of n, u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least four of n, u, v, w or x are not zero and at least four of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein the sum of n, u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein the sum of u, v, w or x is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least one n, and at least one u are all not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u, w and n are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u, and w are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u, and w are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least w and both u are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least one of u, or w is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of u are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein at least two of w are not zero.

In another specific embodiment the invention provides a compound of formula (Id30) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of the following formula (Id31): $E^x-V^w-Z^v-P^u-L^3-L^3-P^u-Z^v-V^w-E^x$ (Id31).

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least two of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least three of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least four of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least three of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least three of u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least four of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id31) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least one of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least one u is not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Id31) wherein both w are not zero.

In another specific embodiment the invention provides a compound of the following formula (Id32): $E^x-V^w-Z^y-P^u-L^4-L^4-P^u-Z^y-V^w-E^x$ (Id32).

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least one of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least two of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least three of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least four of u, v, w or x are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least two u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least three of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least three of u, v, w or x are not zero and at least three of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least four of u, v, w or x are not zero and at least two of the non-zero groups are not the same letter.

In another specific embodiment the invention provides a compound of formula (Id32) wherein the sum of u, v, w and x is not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least one of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least two of u, or w are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least one u is not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein both u are not zero, and at least one w is not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least one u is not zero.

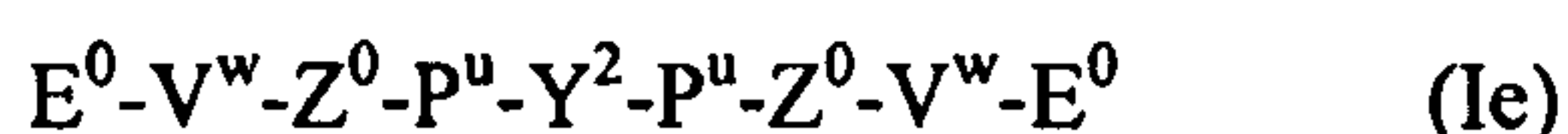
In another specific embodiment the invention provides a compound of formula (Id32) wherein both of u are not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein at least one of w is not zero.

In another specific embodiment the invention provides a compound of formula (Id32) wherein both w are not zero.

Compounds of formula (Ie)

In one embodiment of the invention, the compound of formula (I) is a compound of formula (Ie):



wherein:

each u is 0, 1, 3, 5, 7, 8, 10, or 11;

each w is 0, 1, 2, 3, 4, or 5;

each Y² is independently:

a fused five to eight ring system with up to thirty-two atoms that may be fully aromatic or partially saturated and contains atoms selected from C, N, O, S, SO₂, SO and which ring system is optionally substituted with one or more groups independently selected from H, oxo, R^{A1} and R^{A3};

each R^{A1} is independently selected from cyano, nitro, SO₂R⁴, SO₂R⁴, -alkylSO₂R⁴, haloalkoxy, cyanoalkyl, NR⁴SO₂R⁴, cycloalkyl, (halo)cycloalkyl, heterocycle, (cycloalkyl)alkyl,

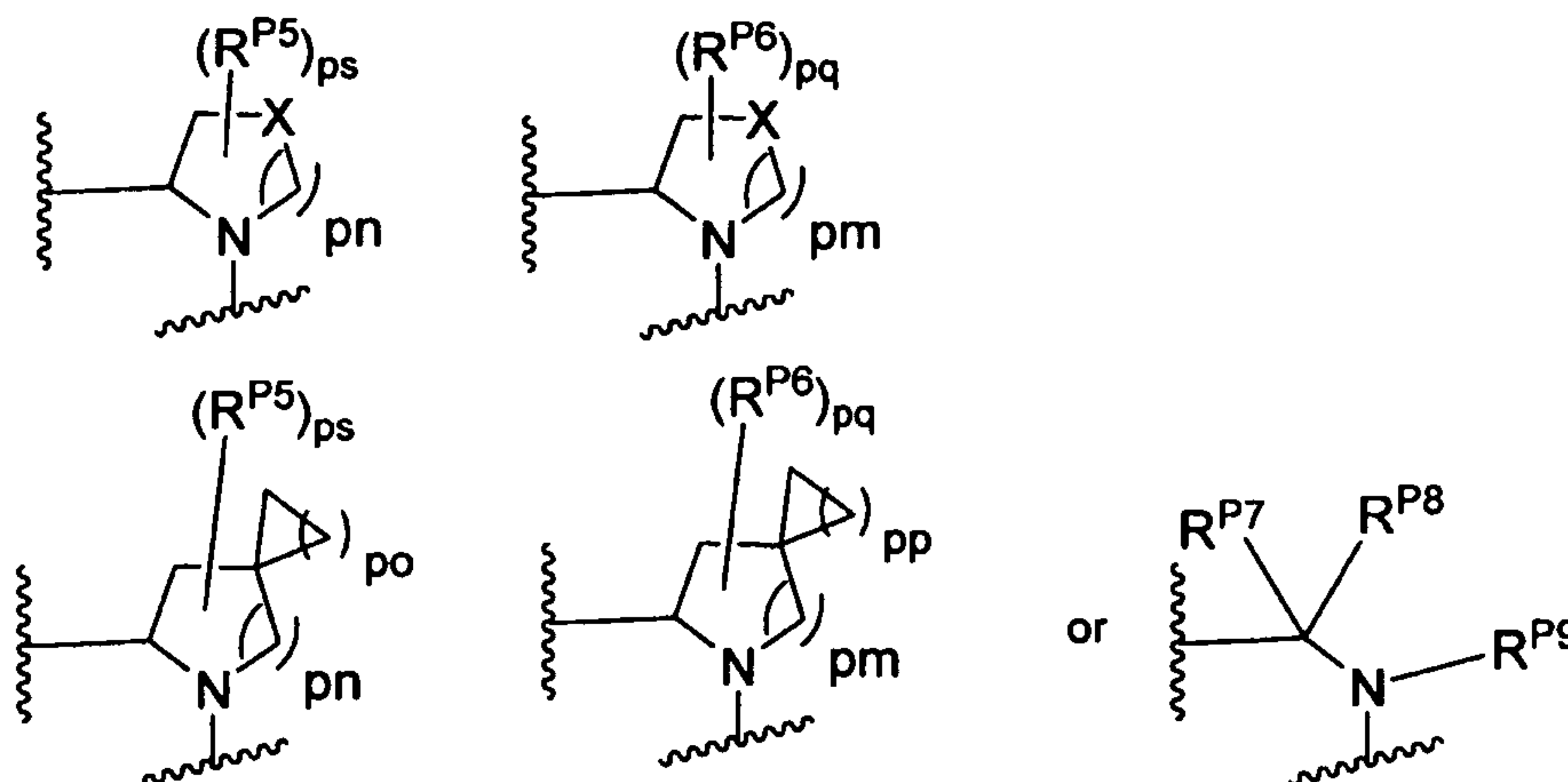
(heterocycle)alkyl, wherein each alkyl, heterocycle and cycloalkyl is optionally substituted with one or more halo;

each R^{A3} is independently selected from alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, arylalkoxycarbonyl, carboxy, formyl, halo, haloalkyl, hydroxy, hydroxyalkyl, $-NR^aR^b$, (NR^aR^b) alkyl, and (NR^aR^b) carbonyl; R^a and R^b are each independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each R^4 is independently selected from H, alkyl, haloalkyl, aryl, and arylalkyl;

R^a and R^b are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylalkylcarbonyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, and heterocyclylalkyl;

each P^0 is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; R^{Pa} and R^{Pb} are each independently

H, alkyl, aryl, or arylalkyl; or R^{Pa} and R^{Pb} taken together with the atom to which they are attached form a heterocycle;

pq and ps are independently 0, 1, 2, 3, or 4;

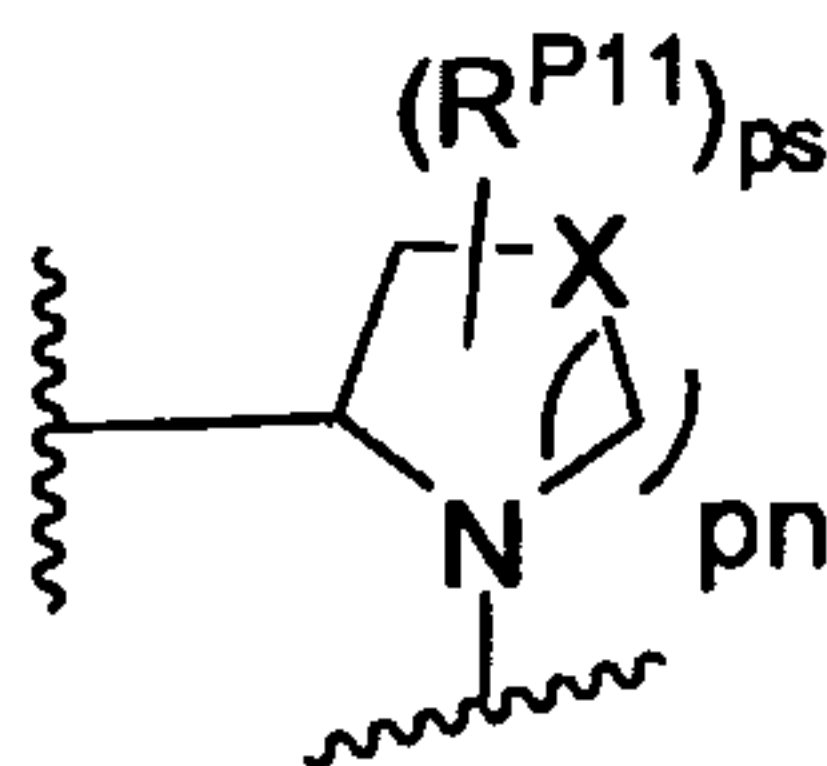
pm and pn are independently 0, 1, or 2;

po and pp are independently 1, 2, or 3;

R^{P7} and R^{P8} are each independently selected from hydrogen, alkenyl, alkoxyalkyl, alkyl, haloalkyl, and $(NR^{Pa}R^{Pb})$ alkyl; or R^{P7} and R^{P8} , together with the carbon atom to which they are attached, form a five or six membered saturated ring optionally containing one or two heteroatoms selected from NR^{Pz} , O, and S; wherein R^{Pz} is selected from hydrogen and alkyl;

R^{P9} is selected from hydrogen and alkyl;

each P^l is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;

provided that when pn is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

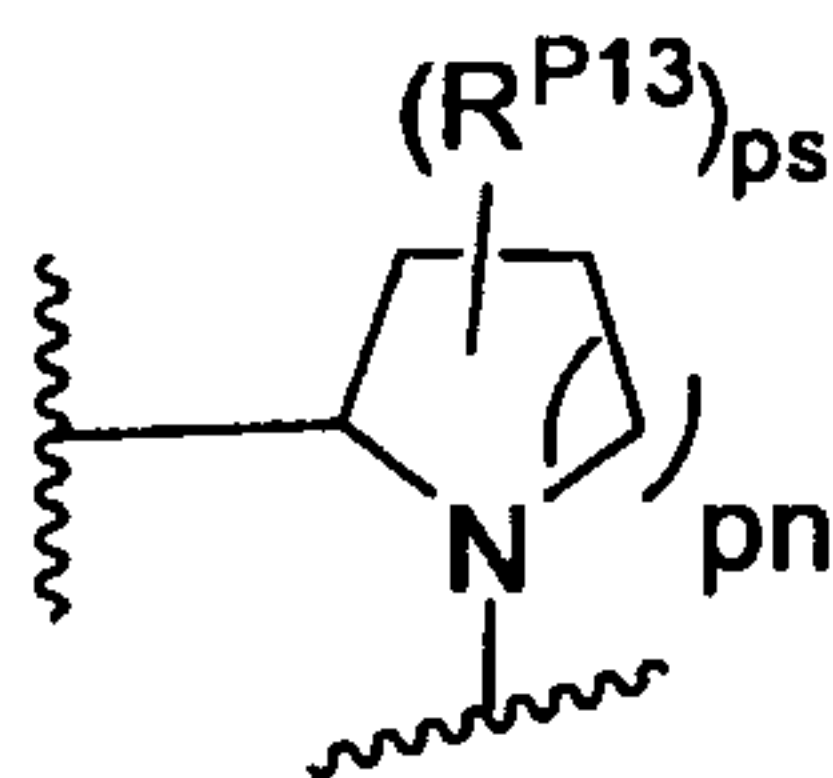
at least one R^{P11} is independently selected from cyano, alkylsulfonyl, arylsulfonyl, (NR^{hh}) sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^{hh}) alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl, $-NR^{hh}R^{hh}$, $(NR^{hh}R^{hh})$ alkyl, $(NR^{hh}R^{hh})$ carbonyl, wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring; wherein each R^{hh} is independently aryl, arylalkyl, heterocycle, heterocycloxy, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl,

haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, (NR^hR^h)sulfonyl, heteroarylsulfonyl, -S(=O)₂R^h, -C(=O)R^h, -C(=O)NR^hR^h; and the remaining R^{P11} are independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P³ is independently a ring of the formula:



wherein:

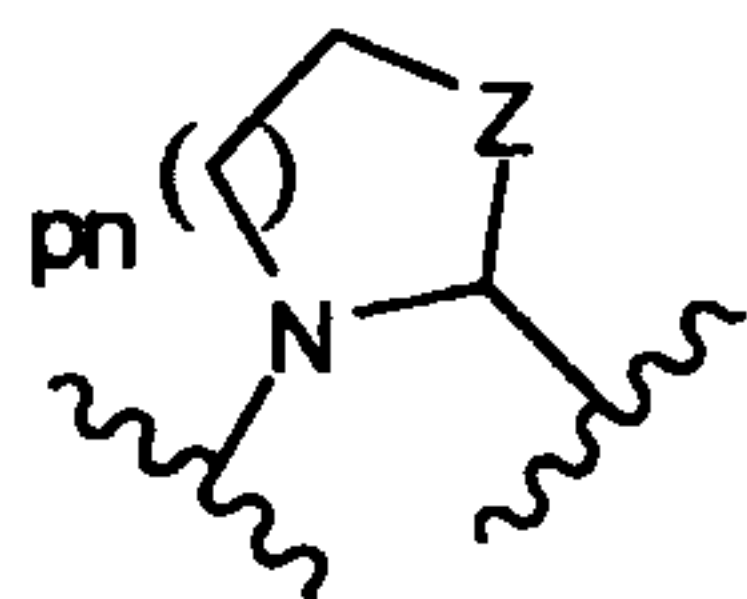
the ring is substituted with one or more oxo group;

each R^{P13} is independently selected from R^{P5}, cyano, alkylsulfonyl, arylsulfonyl, (NR^hR^h)sulfonyl, heterocyclisulfonyl, heteroarylsulfonyl, haloalkoxy, alkoxyalkyloxy, haloalkoxyalkyloxy, cycloalkoxyalkyloxy, aryloxyalkyloxy, heteroaryloxyalkyloxy, heterocycloxyalkyloxy, (NR^hR^h)alkyloxy, cyanoalkoxy, cyanocycloalkyloxy, cycloalkyloxy, oxo, heterocyclyl; wherein each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; and when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

ps is 0, 1, 2, 3, or 4;

pn is 0, 1, or 2;

each P^5 is independently a ring of the formula:



wherein:

the ring is optionally substituted with one or more groups R^{P15} that are independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; and where two groups R^{P15} that are attached to the same carbon when taken together with the carbon to which they are attached can form a 3-6 membered carbocyclic or heterocyclic ring;

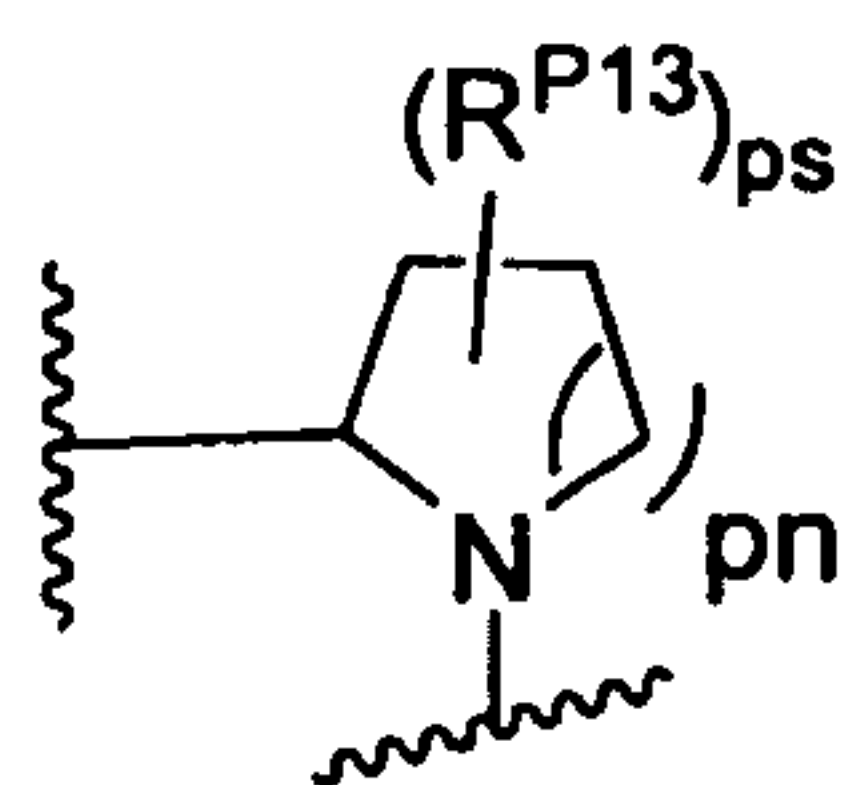
pn is 0, 1, or 2;

Z is O, S, $S(=O)$, $S(=O)_2$, or NR^f ;

each R^f is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl, $-S(=O)_2NR^hR^h$, $-S(=O)_2R^h$, $C(=O)R^h$, $C(=O)OR^h$, $-C(=O)NR^hR^h$; each R^h is independently -H, alkyl, alkoxyamino, aryl, arylalkyl, heterocycle, heterocycloxy, alkenyl, alkenyloxy, alkynyl, alkoxyalkyl, haloalkyl, cyanoalkyl, haloalkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, sulfonylalkyl; or when two R^h groups are present then they may come together with the atoms to which they are bound to form a 4-15 membered heterocyclic ring;

each P^7 is a bridged 5-15 membered bicyclic heterocyclic ring that is attached to the remainder of the compound of formula I through one N-link and through one C-link; wherein the ring is optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} ;

each P^8 is independently a ring of the formula:

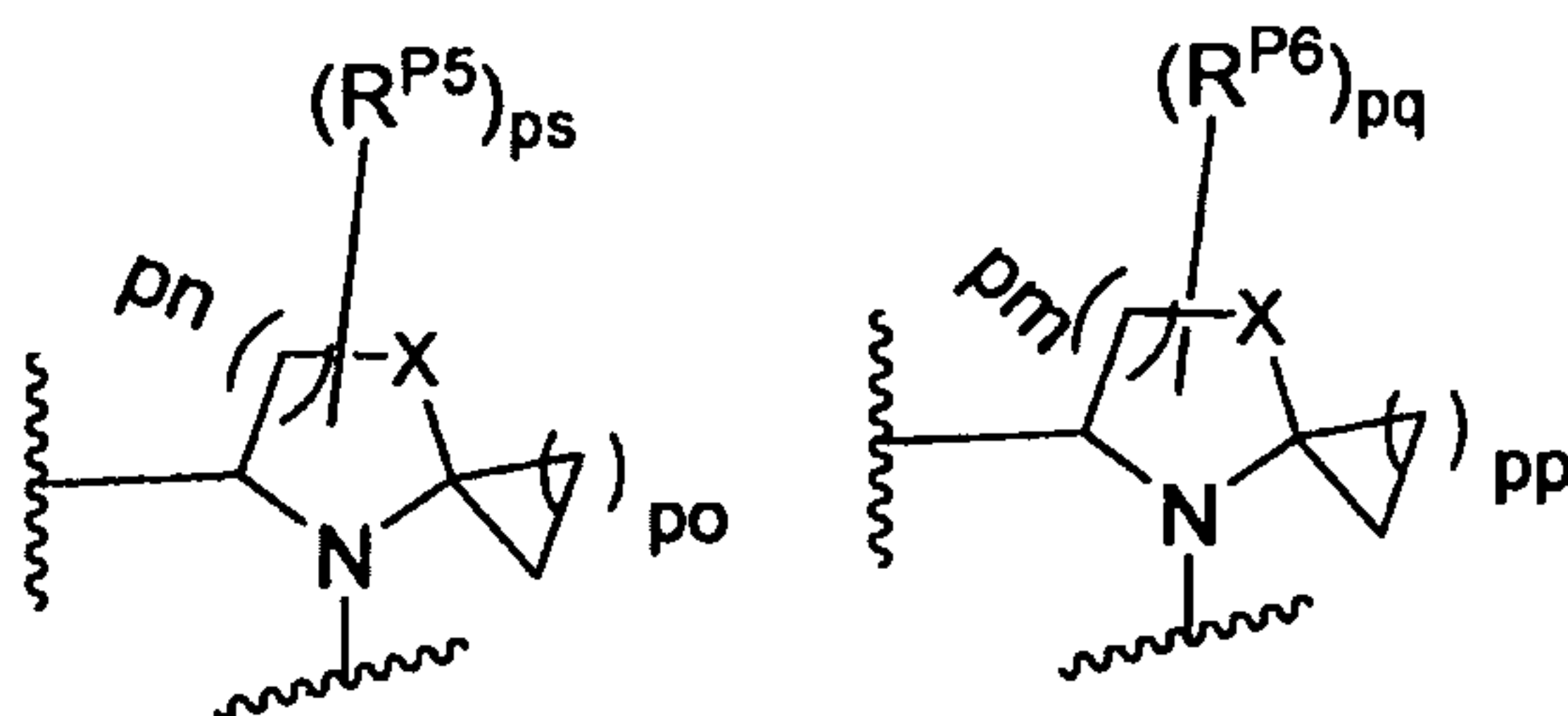


wherein:

ps is 2, 3, 4, 5, or 6;

each R^{P13} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups; where in at least one case two groups R^{P13} that are attached to the same carbon are taken together with the carbon to which they are attached and form a 4-6 membered heterocyclic ring;

each P^{10} is independently:



wherein:

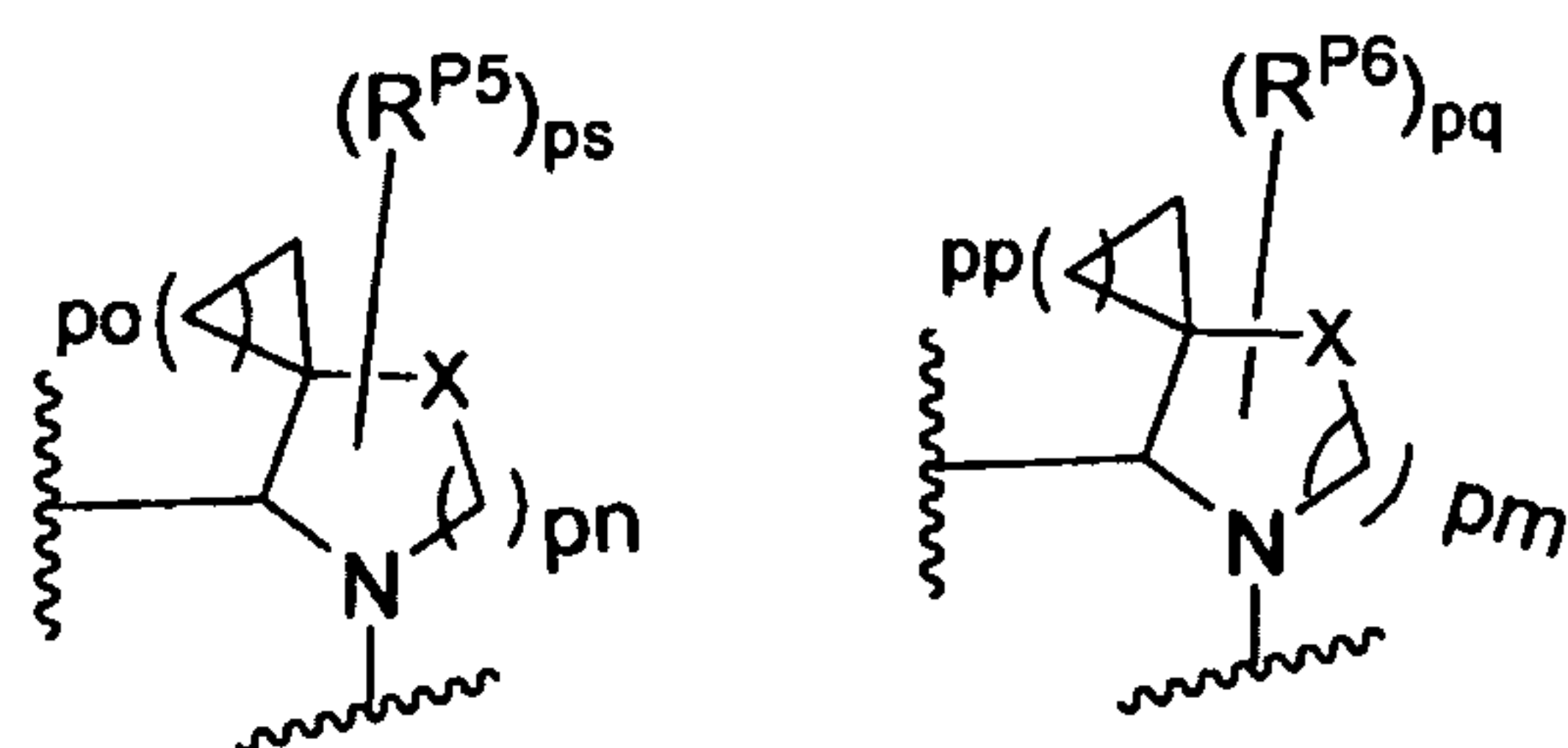
X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and $-NR^{Pa}R^{Pb}$, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;
 pm and pn are independently 0, 1, or 2;
 po and pp are independently 1, 2, or 3;

each P^{11} is independently:



wherein:

X is selected from O, S, S(O), SO₂, CH₂, CHR^{P10}, and C(R^{P10})₂;
 provided that when pn or pm is 0, X is selected from CH₂, CHR^{P10}, and C(R^{P10})₂;

each R^{P10} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

each R^{P5} and R^{P6} is independently selected from alkoxy, alkyl, aryl, halo, haloalkyl, hydroxy, and -NR^{Pa}R^{Pb}, wherein the alkyl can optionally form a fused three- to six-membered ring with an adjacent carbon atom, wherein the three- to six-membered ring is optionally substituted with one or two alkyl groups;

pq and ps are independently 0, 1, 2, 3, or 4;
 pm and pn are independently 0, 1, or 2;
 po and pp are independently 1, 2, or 3;

each -Z⁰- is -C(=O)- or -C(=S)-;

each E⁰ is independently -NR^{Ec}R^{Ed} wherein

R^{Ec} and R^{Ed} are each independently selected from hydrogen, alkenyloxycarbonyl, alkoxyalkylcarbonyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfonyl, aryl, arylalkoxycarbonyl, arylalkyl, arylalkylcarbonyl, arylcarbonyl, aryloxycarbonyl, arylsulfonyl, cycloalkyl, cycloalkylsulfonyl, formyl, haloalkoxycarbonyl, heterocyclyl, heterocyclylalkoxycarbonyl, heterocyclylalkyl, heterocyclylalkylcarbonyl, heterocyclylcarbonyl,

heterocycloxyoxycarbonyl, hydroxyalkylcarbonyl, (NR^eR^f) alkyl, (NR^eR^f) alkylcarbonyl, (NR^eR^f) carbonyl, (NR^eR^f) sulfonyl, $-C(NCN)OR'$, and $-C(NCN)NR^XR^Y$, wherein R' is selected from alkyl and unsubstituted phenyl, and wherein the alkyl part of the arylalkyl, the arylalkylcarbonyl, the heterocyclalkyl, and the heterocyclalkylcarbonyl are further optionally substituted with one $-NR^eR^f$ group; and wherein the aryl, the aryl part of the arylalkoxyoxycarbonyl, the arylalkyl, the arylalkylcarbonyl, the arylcarbonyl, the aryloxyoxycarbonyl, and the arylsulfonyl, the heterocycl, and the heterocycl part of the heterocyclalkoxyoxycarbonyl, the heterocyclalkyl, the heterocyclalkylcarbonyl, the heterocyclcarbonyl, and the heterocycloxyoxycarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^0 is independently H, alkyl, arylalkyl, alkenyl, CO, cycloalkylalkyl, cycloalkyl, alkoxyalkyl, alkoxyalkylcarbonylalkyl, alkoxyoxycarbonylalkyl, alkylsulfonylalkyl, arylalkoxyalkylcarbonylalkyl, carboxyalkyl, heterocyclalkyl, heterocyclcarbonylalkyl, hydroxyalkyl, $NRRCO$ alkyl;

and where in arylalkyl the alkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkyoxycarbonyloxy, halo, haloalkoxy, haloalkyl, heterocycl, hydroxy;

and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyoxycarbonyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocycl, heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^XR^Y$, (NR^XR^Y) alkyl, oxo, and $-P(O)OR_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the arylalkyl and the heterocyclalkyl are unsubstituted and wherein the second aryl group, the aryl part of the arylalkyl, the aryl part of the arylcarbonyl, the heterocycl, and the heterocycl part of the heterocyclalkyl and the heterocyclcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

and the heterocycl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyoxycarbonyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second heterocycl group, heterocyclalkyl, heterocyclcarbonyl, hydroxy, hydroxyalkyl, nitro, $-NR^XR^Y$, (NR^XR^Y) alkyl, and oxo, wherein the alkyl part of the arylalkyl and the heterocyclalkyl are

unsubstituted and wherein the aryl, the aryl part of the arylalkyl; the aryl part of the arylcarbonyl, the second heterocyclyl group, and the heterocyclyl part of the heterocyclylalkyl and the heterocyclylcarbonyl are further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro;

each V^1 is independently cyanoalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

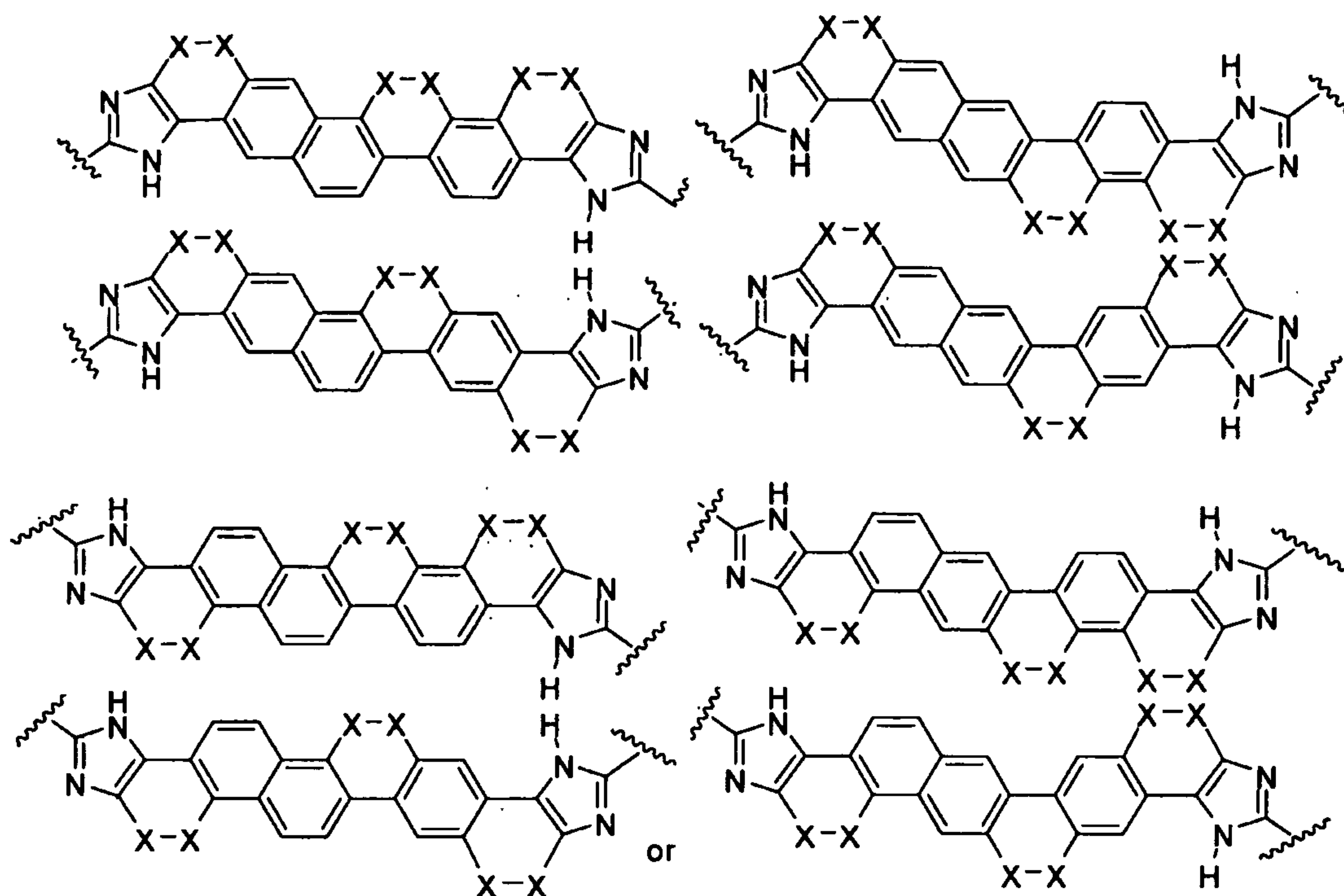
each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

each V^3 is independently alkyl, which is substituted with one or more oxo, and which is optionally substituted with one or more groups independently selected from cycloalkyl, halo, aryl, alkenyl, and cyano;

each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^aR^bC(=O)O-$; R^a and R^b are each independently selected from hydrogen, alkenyl, and alkyl; and

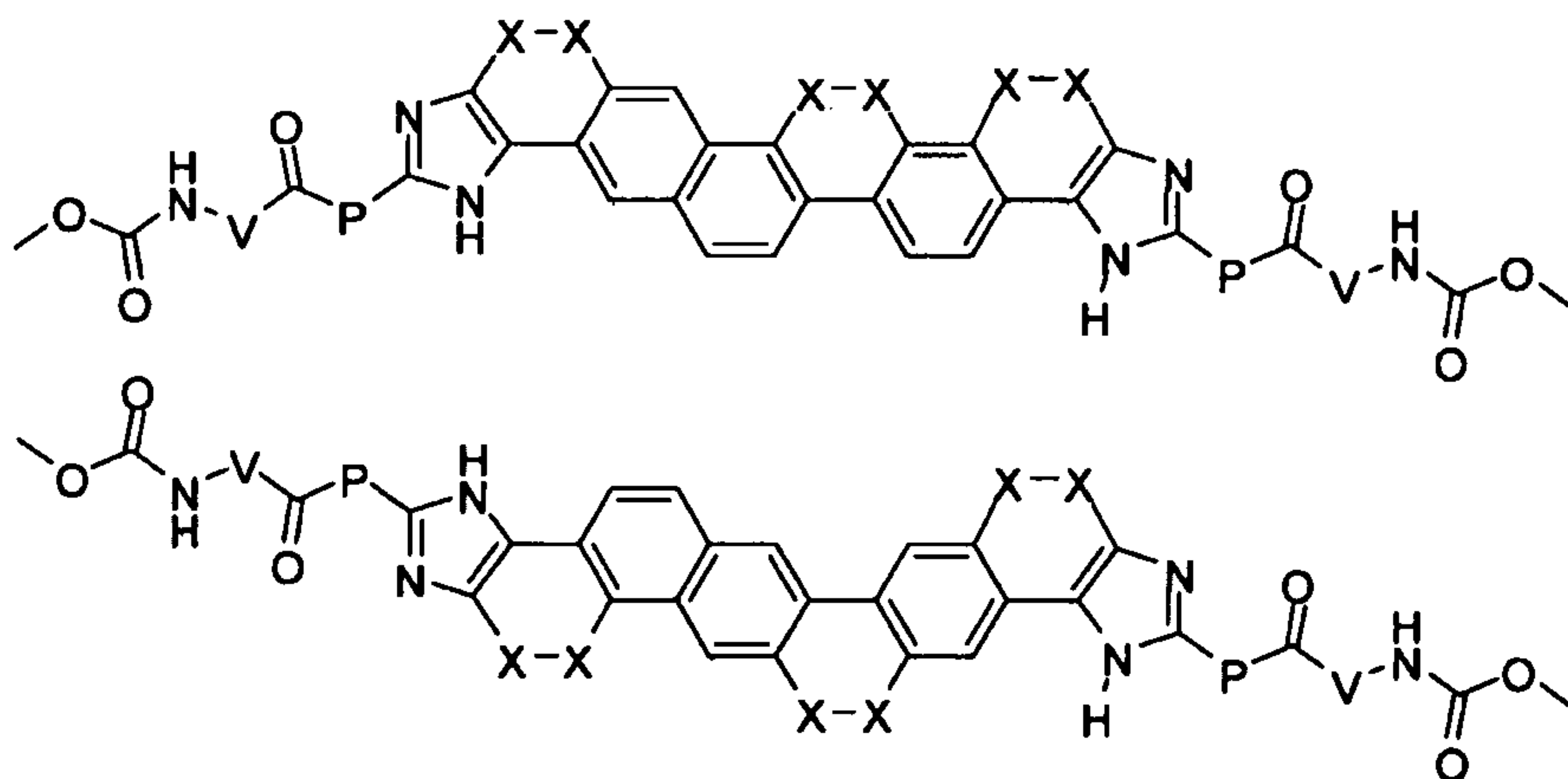
each V^5 is independently alkylsulfonylalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, heterocycle, heteroaryl, hydroxy, and $NR^{Va}R^{Vb}C(=O)O-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl;

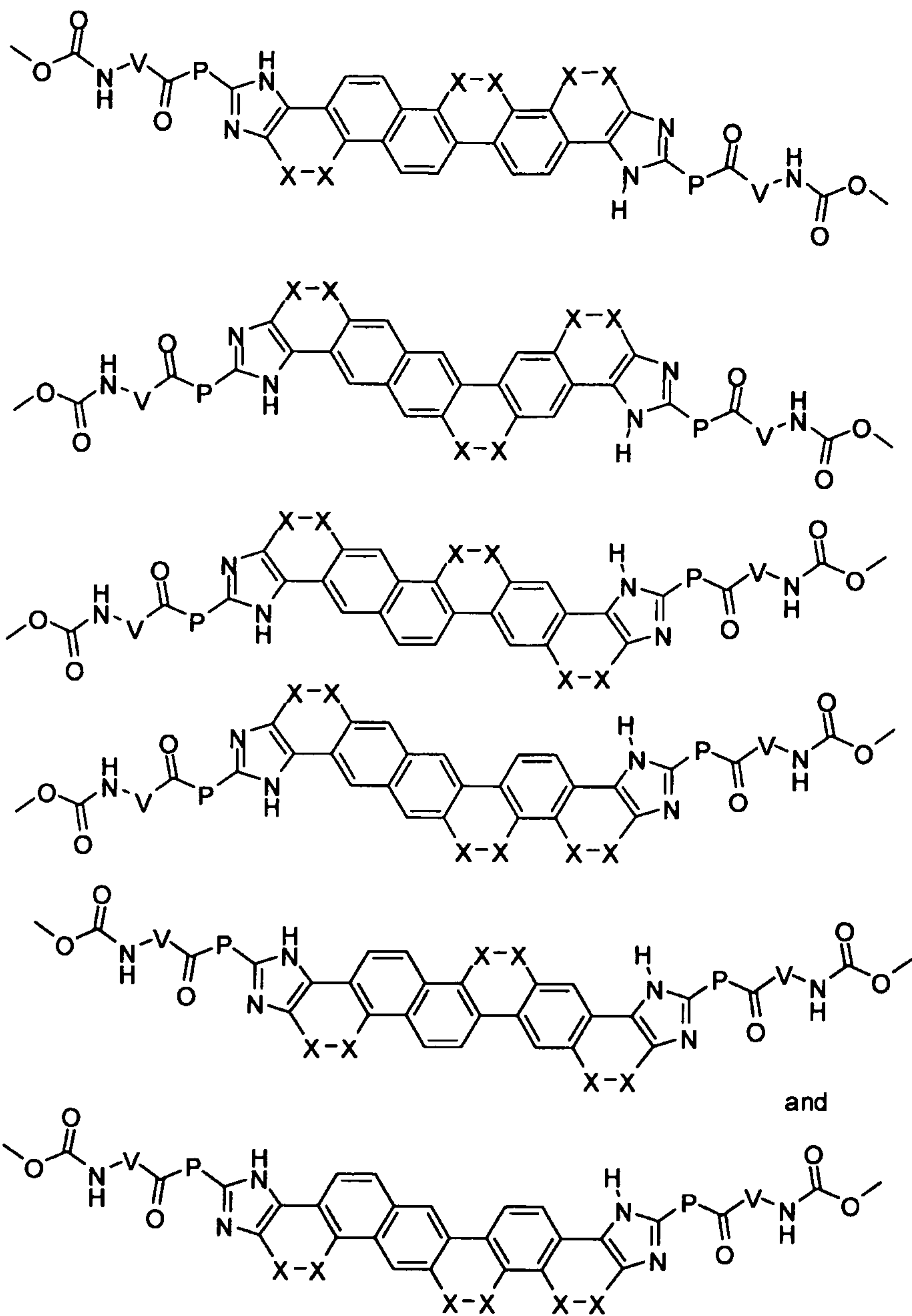
In one embodiment the invention provides a compound of formula (Ie) wherein Y^2 is:



wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂.

In one embodiment the invention provides a compound of formula (Ie) which is selected from:





wherein X-X is selected from O, CH₂, CH=CH, CH₂-CH₂, CH₂-O, O-CH₂, CH₂-CH₂-CH₂, and CH₂-O-CH₂; or a pharmaceutically acceptable salt, or prodrug thereof.

Specific values for E, P, V, and Z

In another specific embodiment of the invention each E is E⁰.

In another specific embodiment of the invention each E is -NHC(=O)Oalkyl.

In another specific embodiment of the invention E⁰ is methoxycarbonylamino.

In one embodiment the invention E⁰ is -NH₂, alkylamino or dialkylamino.

In one embodiment the invention E⁰ is cycloalkylamino or cycloalkyl(alkyl)amino, or dicycloalkylamino.

In one embodiment the invention E⁰ is heterocyclyl.

In one embodiment the invention E⁰ is heterocyclylamino where the amino is optionally substituted with alkyl.

In one embodiment the invention provides a compound of formula (I) wherein at least one E⁰ is -NR^{Ec}R^{Ed} wherein R^{Ec} is H and R^{Ed} is methoxycarbonyl.

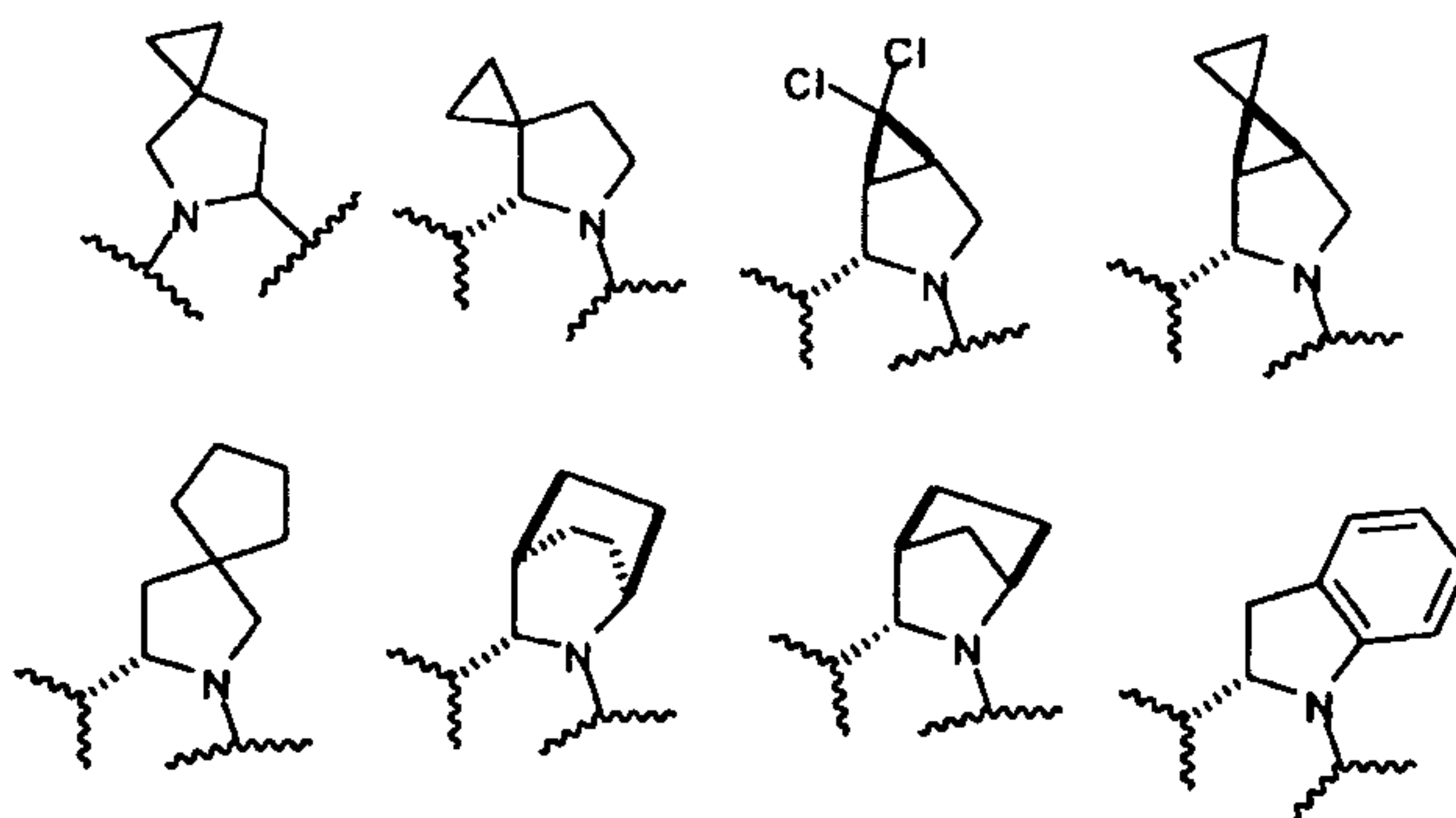
In one embodiment the invention provides a compound of formula (I) wherein at least one E⁰ is -NR^{Ec}R^{Ed} wherein R^{Ec} is H or alkyl and R^{Ed} is H or alkyl.

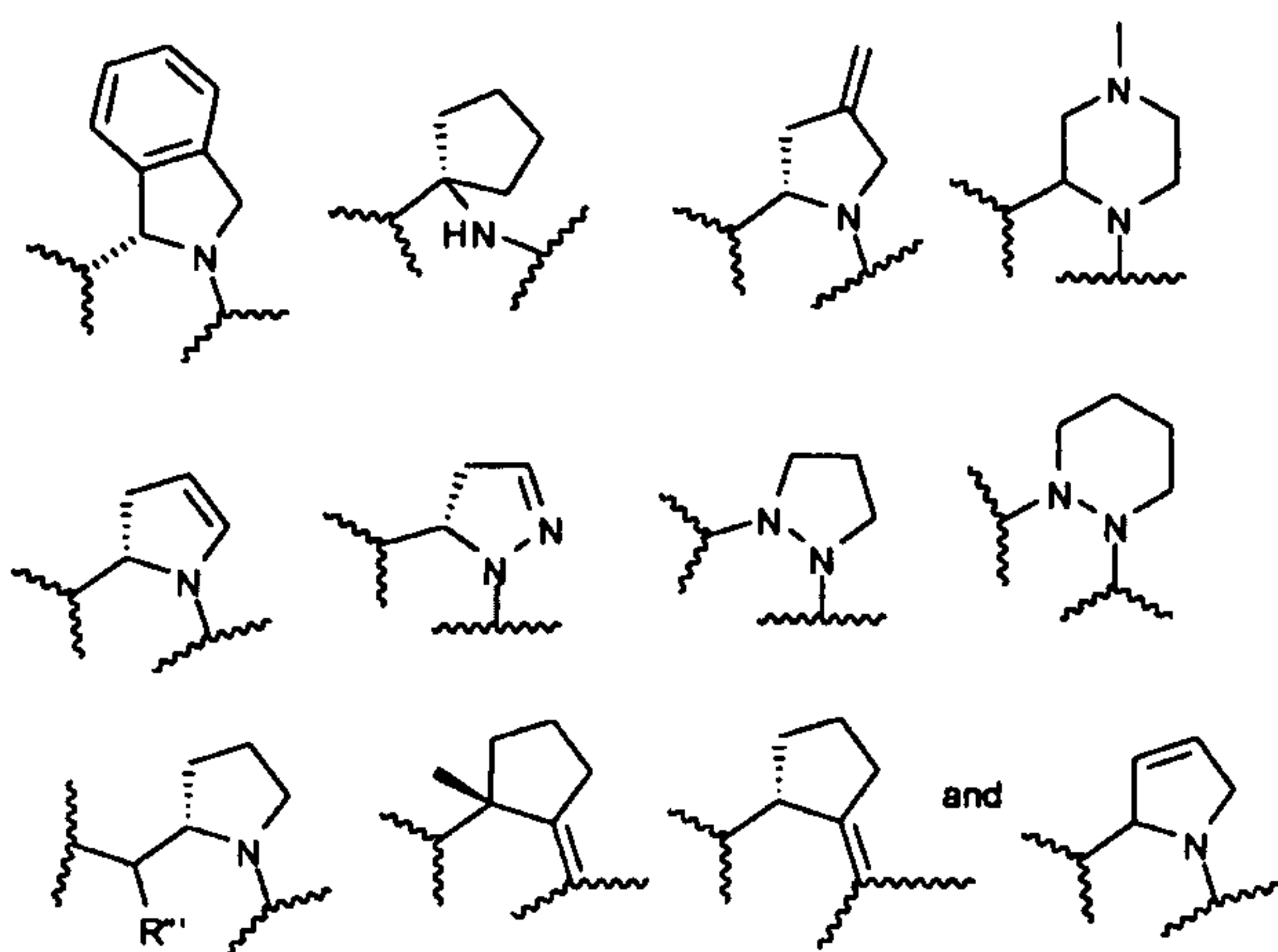
In one embodiment the invention provides a compound of formula (I) wherein at least one E⁰ is -NR^{Ec}R^{Ed} wherein R^{Ec} is H, alkyl or cycloalkyl and R^{Ed} is cycloalkyl.

In one embodiment the invention provides a compound of formula (I) wherein at least one E⁰ is an N-linked heterocyclyl.

In one embodiment the invention provides a compound of formula (I) wherein at least one E⁰ is -NR^{Ec}R^{Ed} wherein R^{Ec} is H, alkyl, or cycloalkyl; and R^{Ed} is heterocycle.

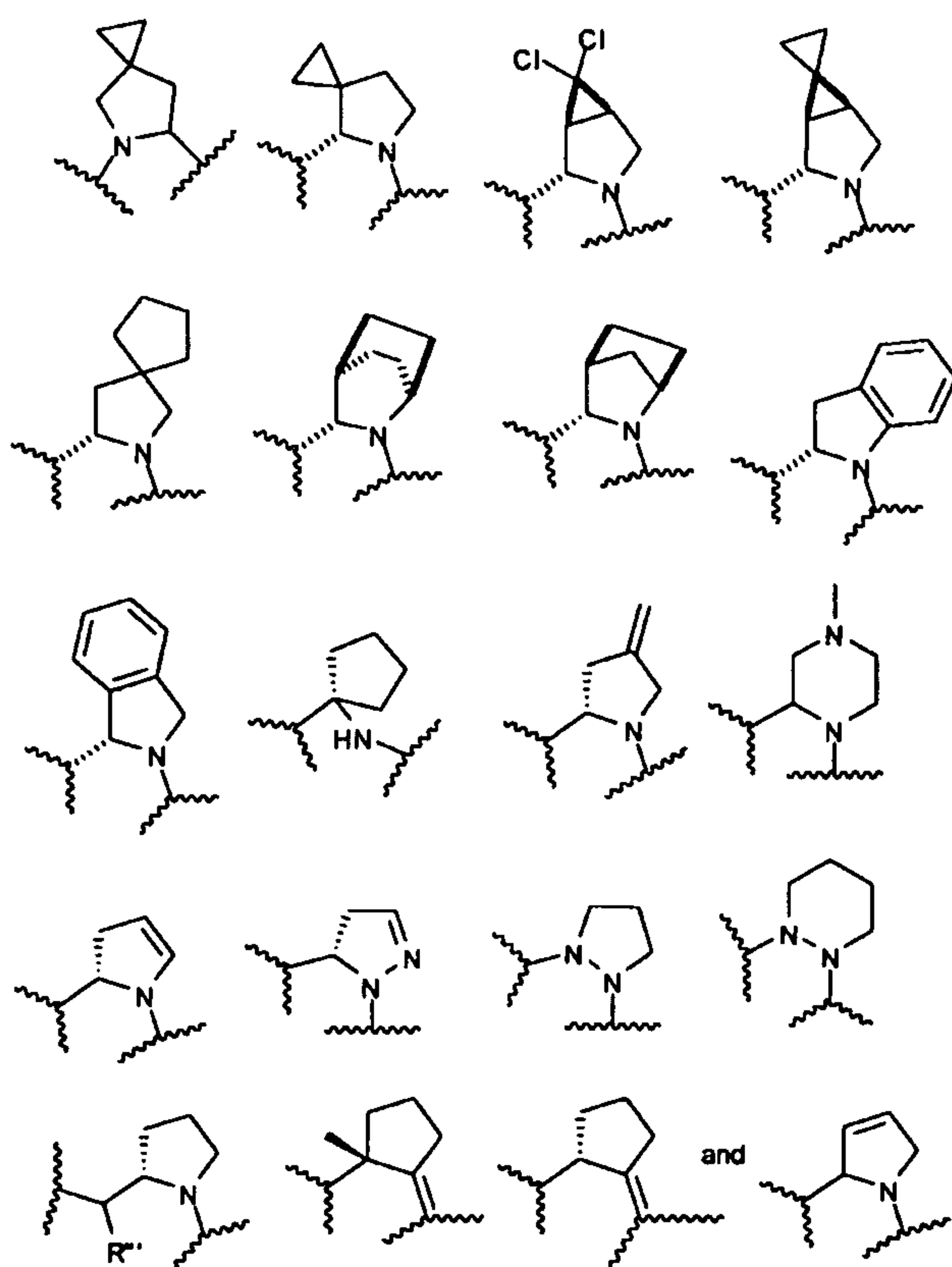
In another specific embodiment of the invention P is selected from:





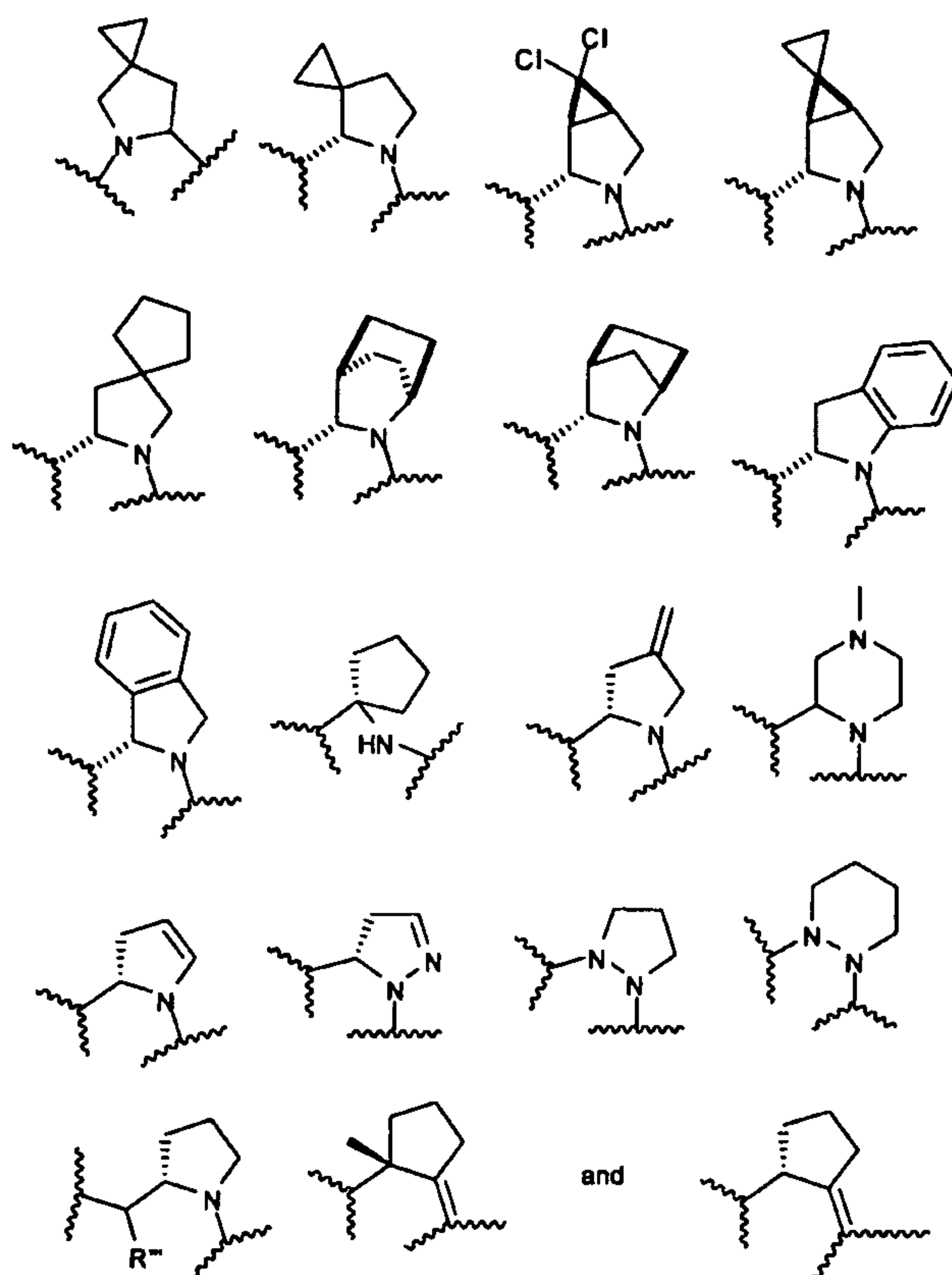
wherein R''' is hydrogen or methyl.

In another specific embodiment of the invention P is selected from



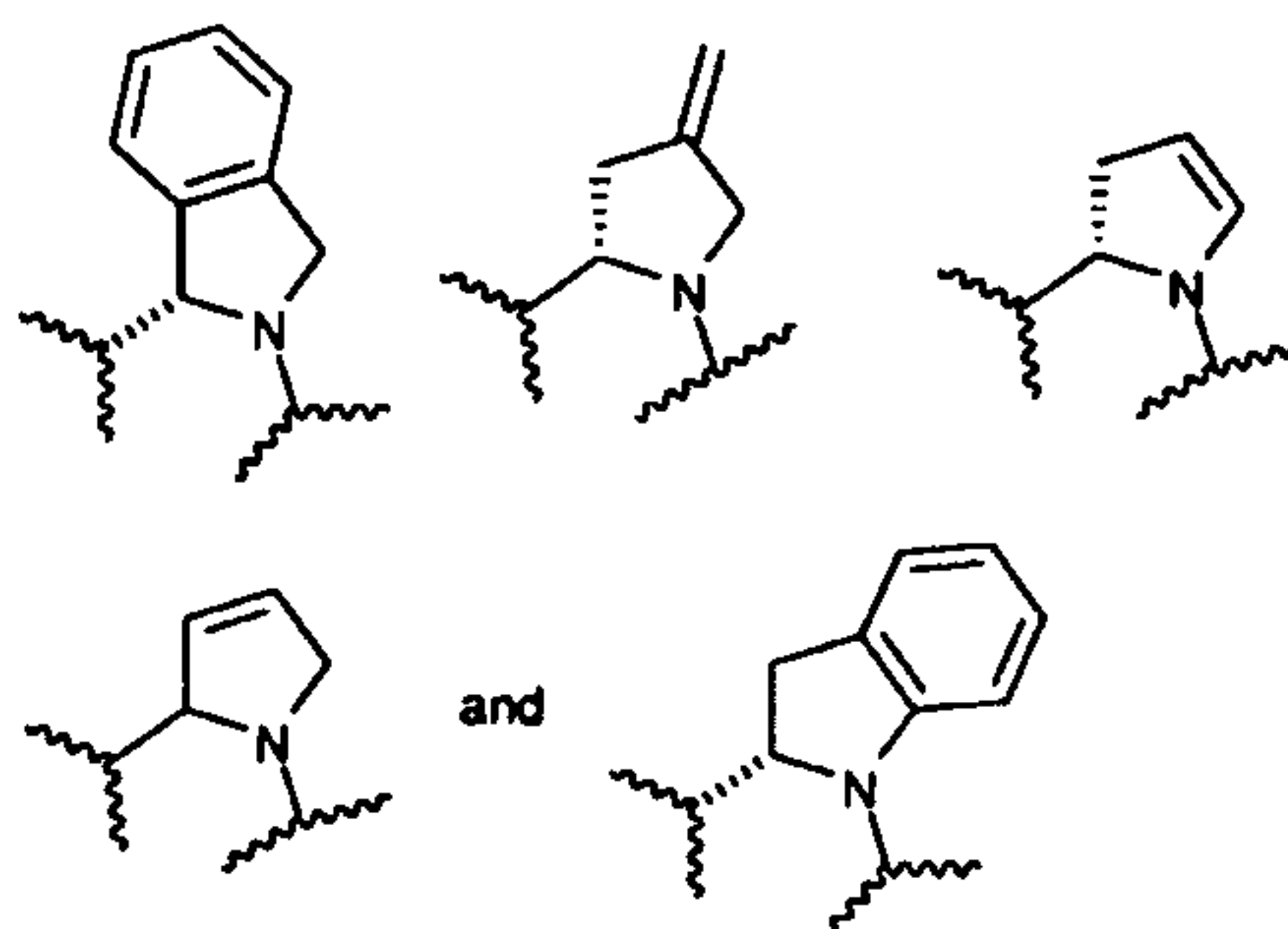
and another P is P⁰.

In another specific embodiment of the invention P is selected from



wherein R'' is hydrogen or methyl; and another P is P⁰.

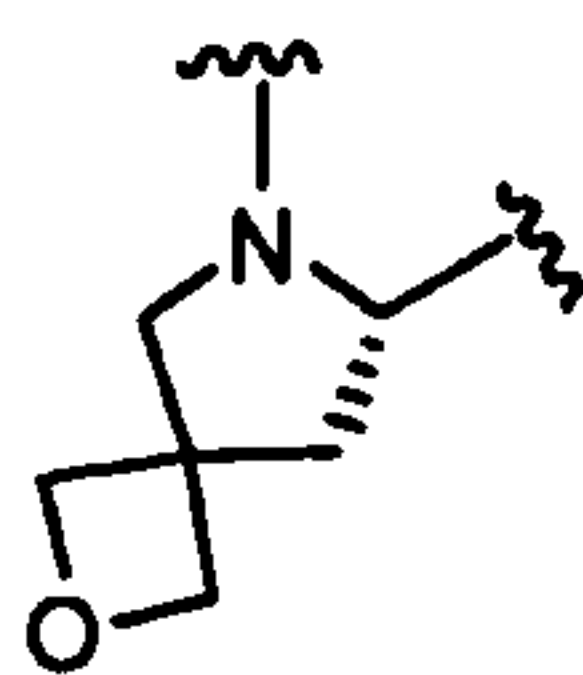
In another specific embodiment of the invention P is selected from:



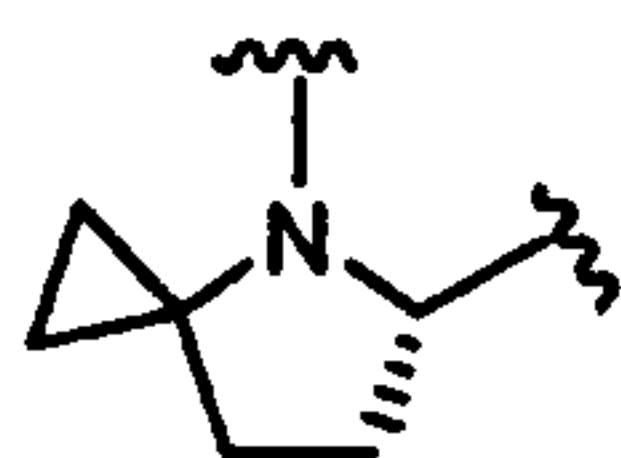
In another specific embodiment of the invention at least one P is P⁷ and is:



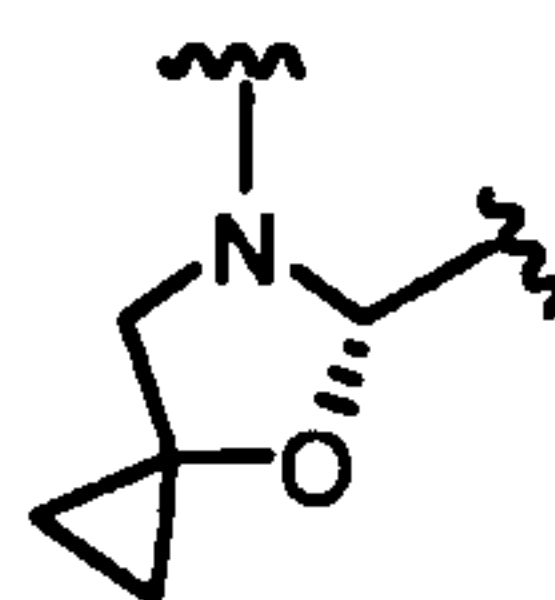
In another specific embodiment of the invention at least one P is P⁸ and is:



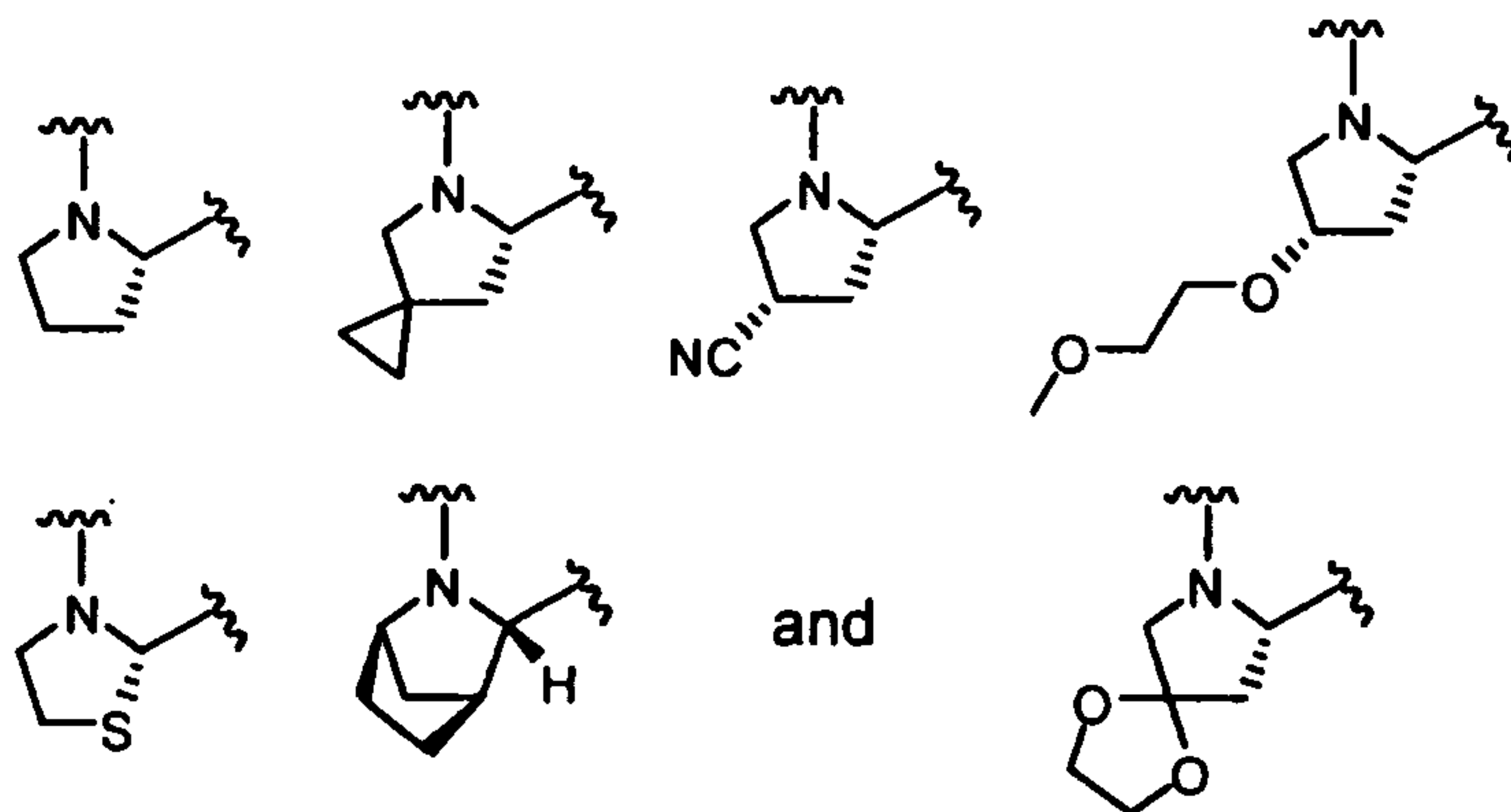
In another specific embodiment of the invention P is P¹⁰ and is:



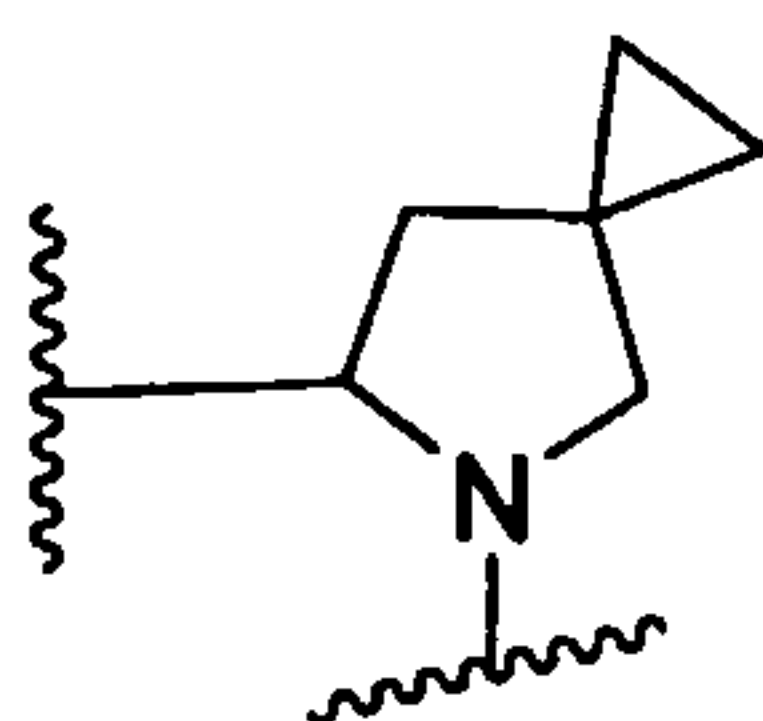
In another specific embodiment of the invention P is P¹¹ and is:



In another specific embodiment of the invention each P is independently selected from:

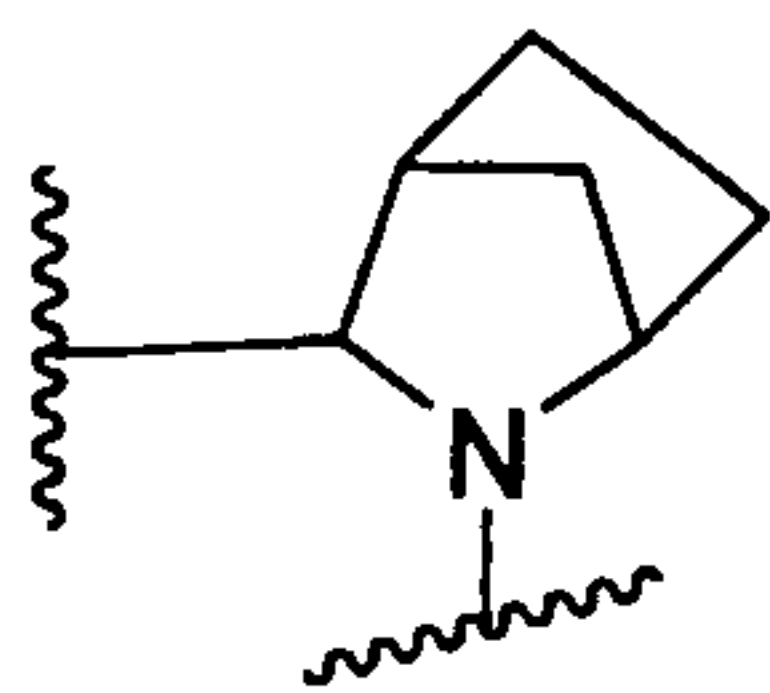


In another specific embodiment of the invention P⁰ is



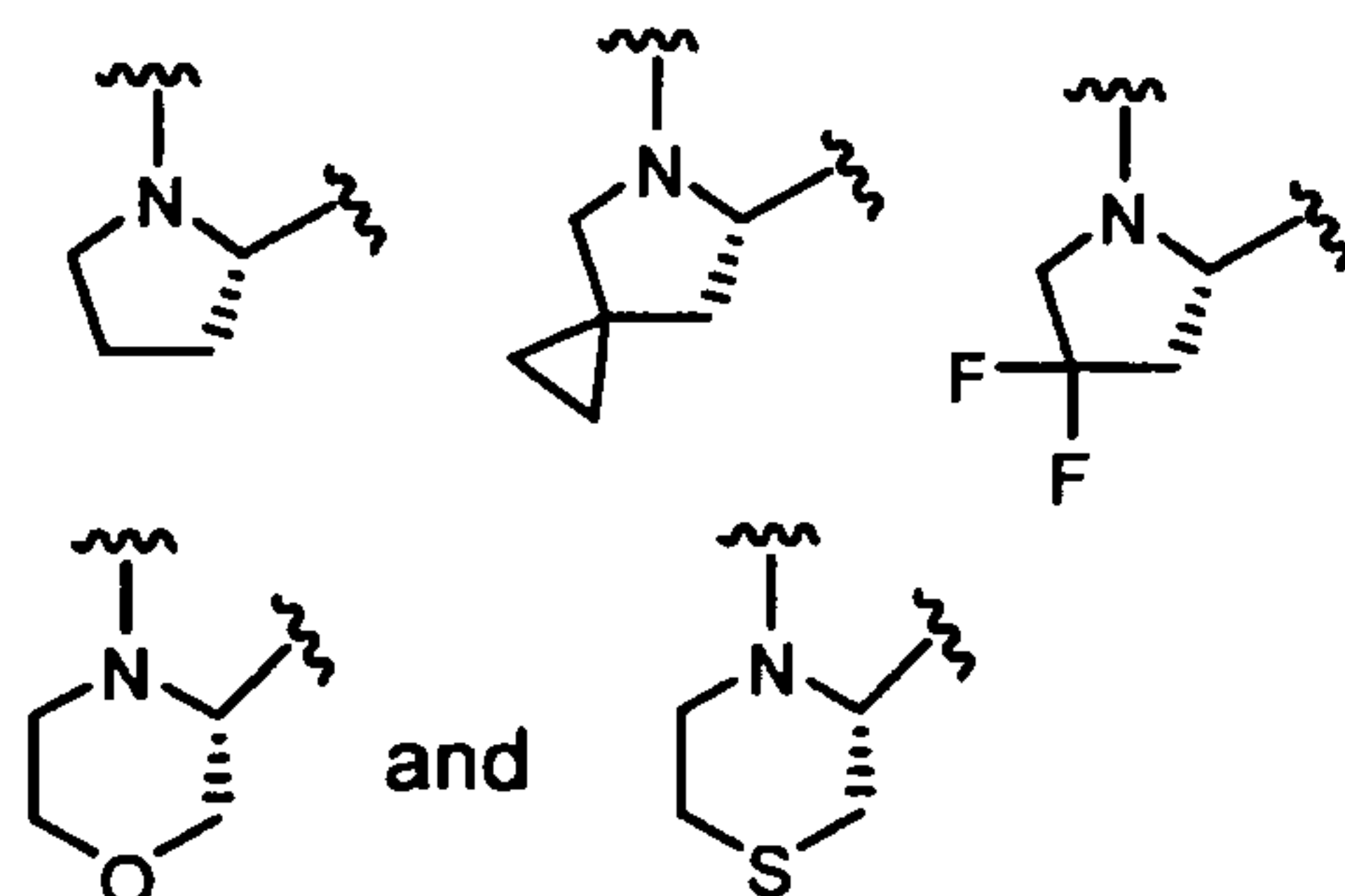
In another specific embodiment of the invention P^7 is a [2.2.1] or a [2.2.2] ring system.

In another specific embodiment of the invention P^7 is

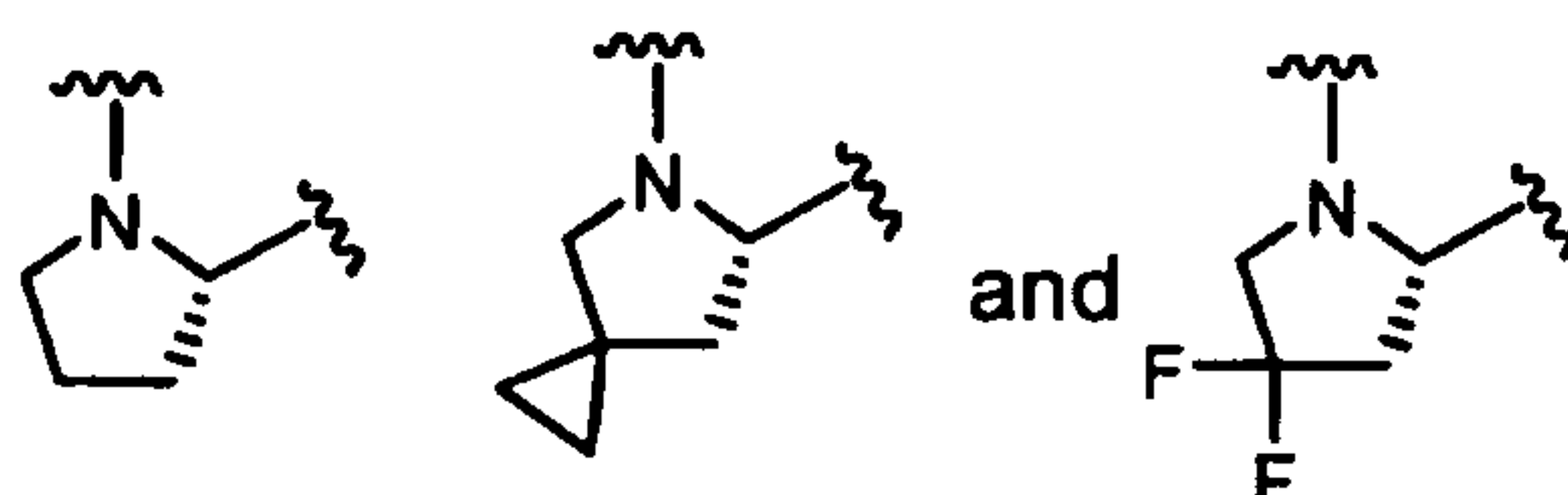


optionally substituted with one or more groups independently selected from R^{P6} and R^{P11} .

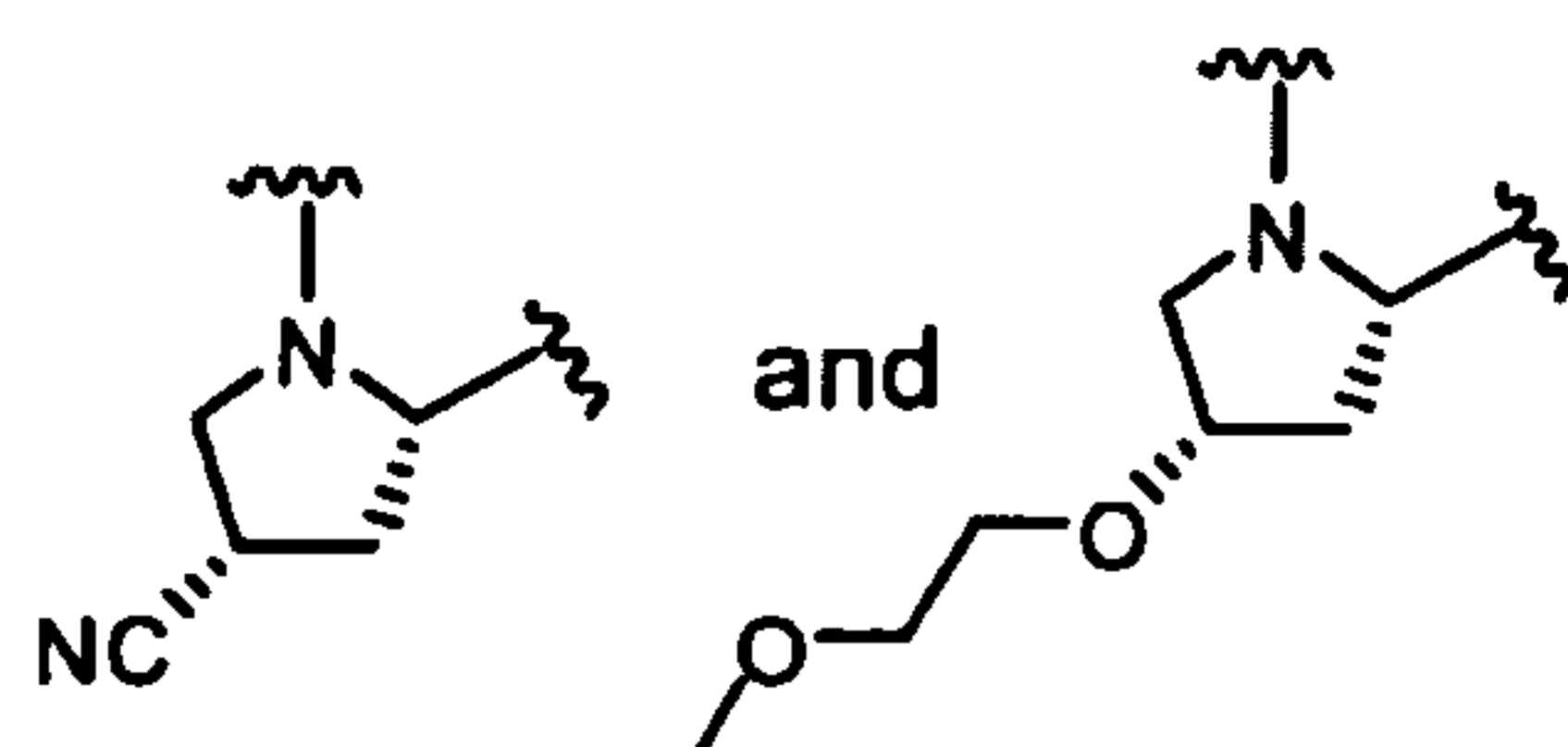
In another specific embodiment of the invention P is selected from:



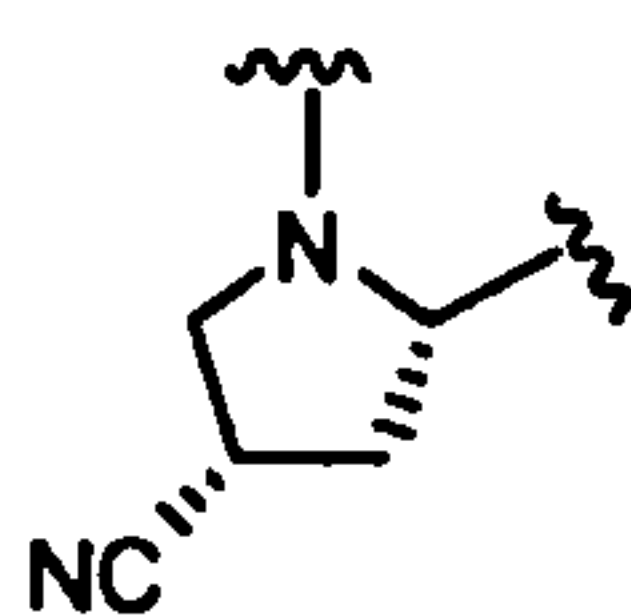
In another specific embodiment of the invention P is selected from:



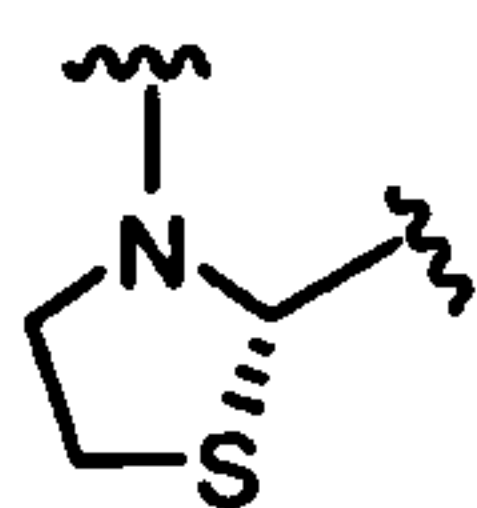
In another specific embodiment of the invention P is selected from:



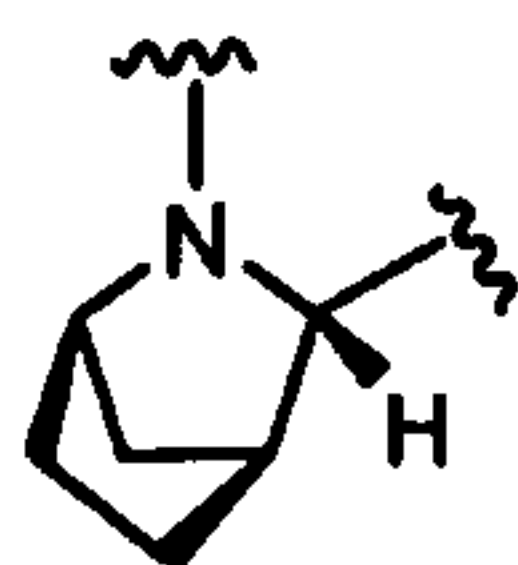
In another specific embodiment of the invention P is:



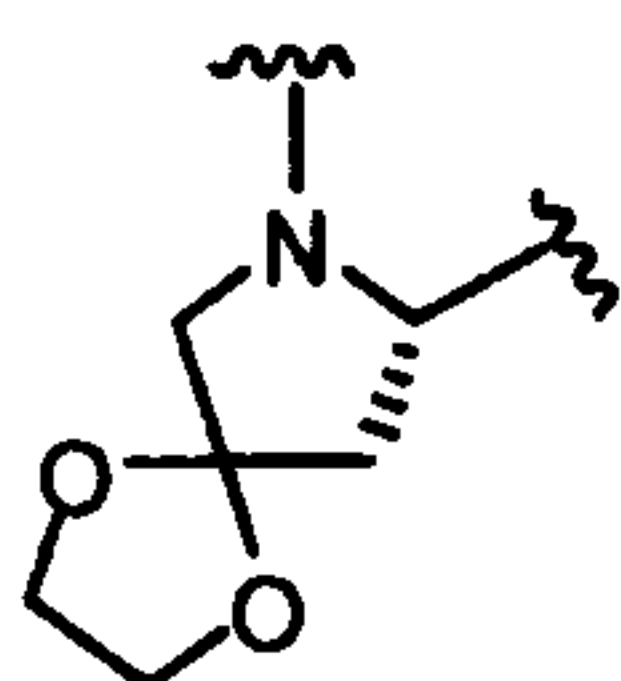
In another specific embodiment of the invention P is:



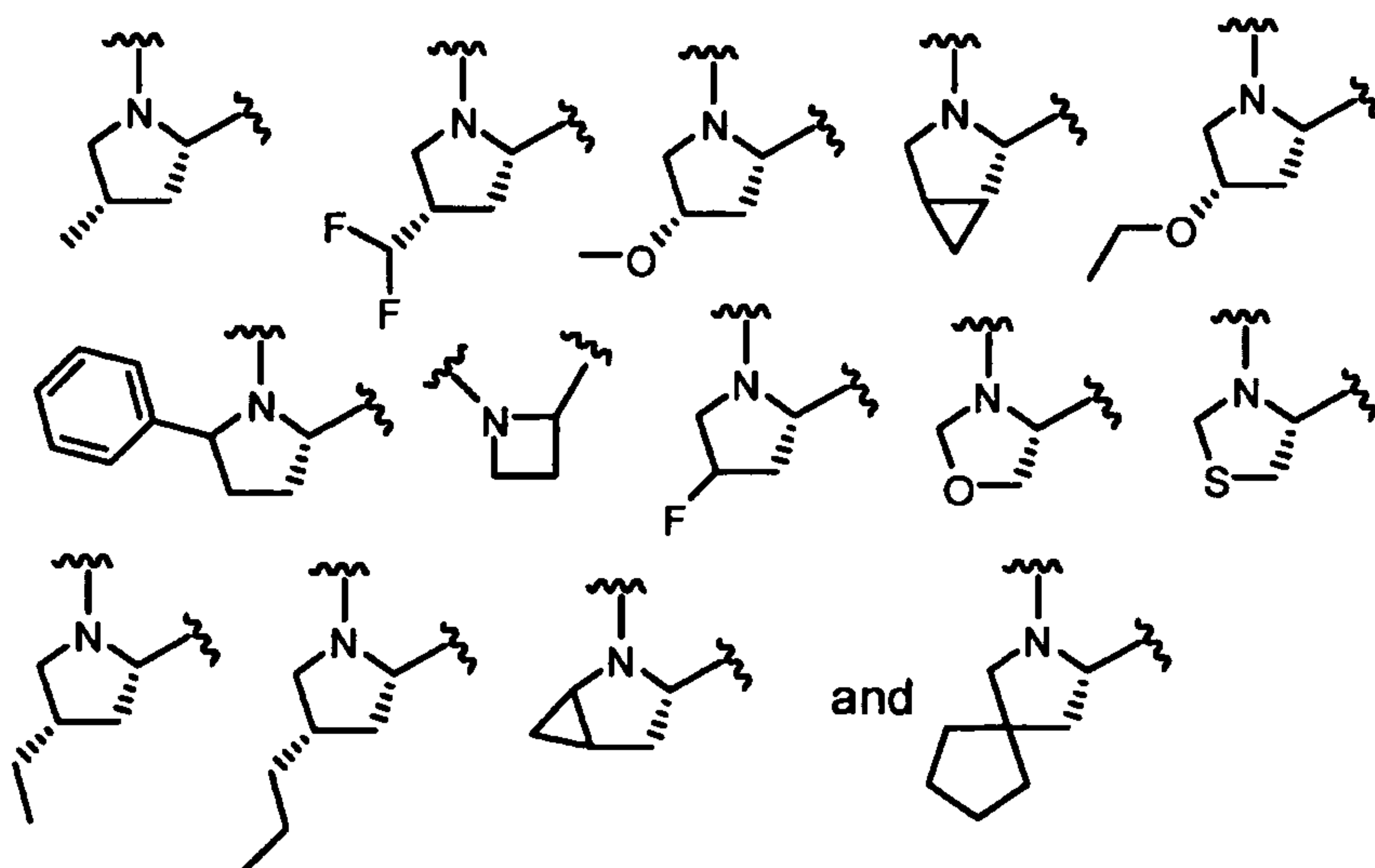
In another specific embodiment of the invention P is:



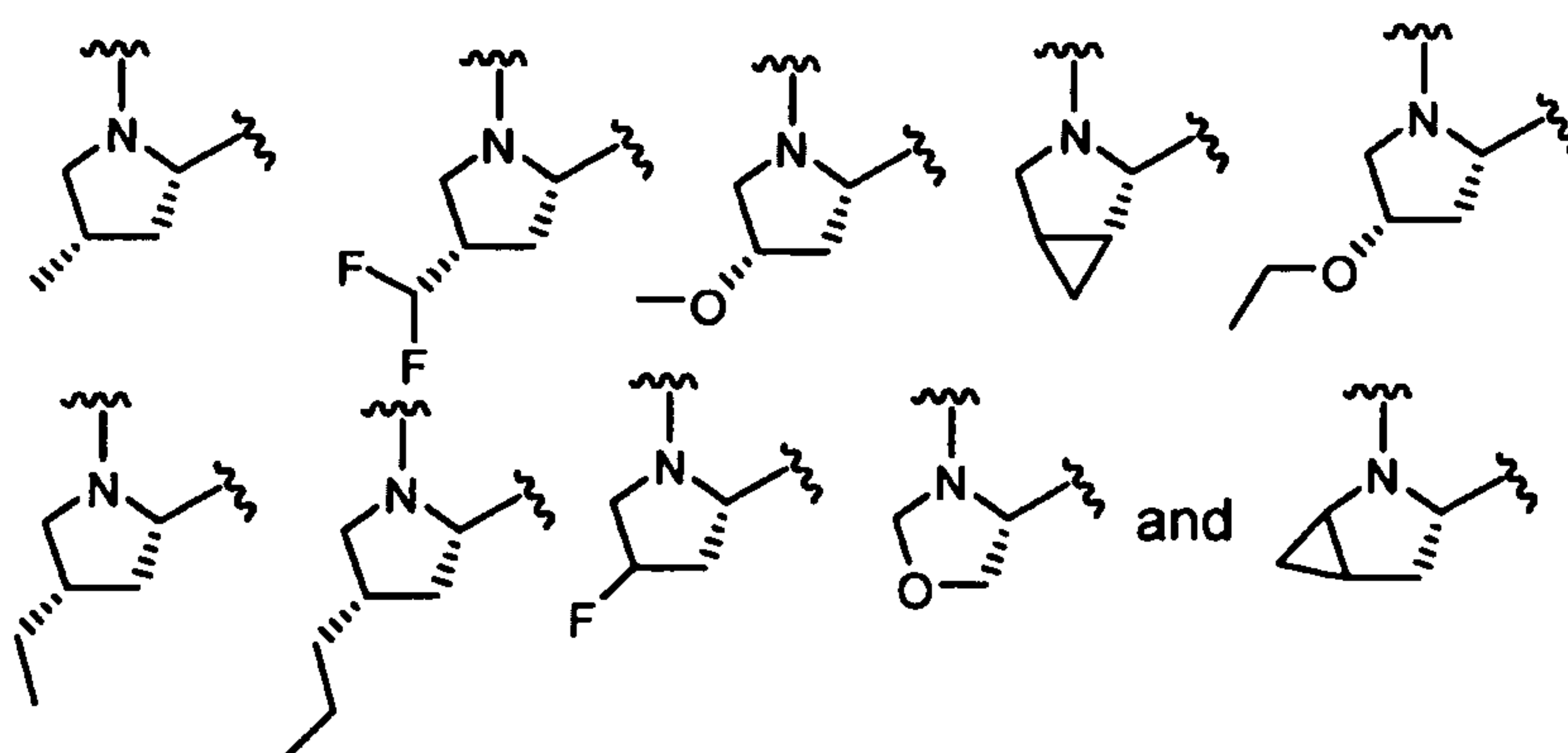
In another specific embodiment of the invention P is:



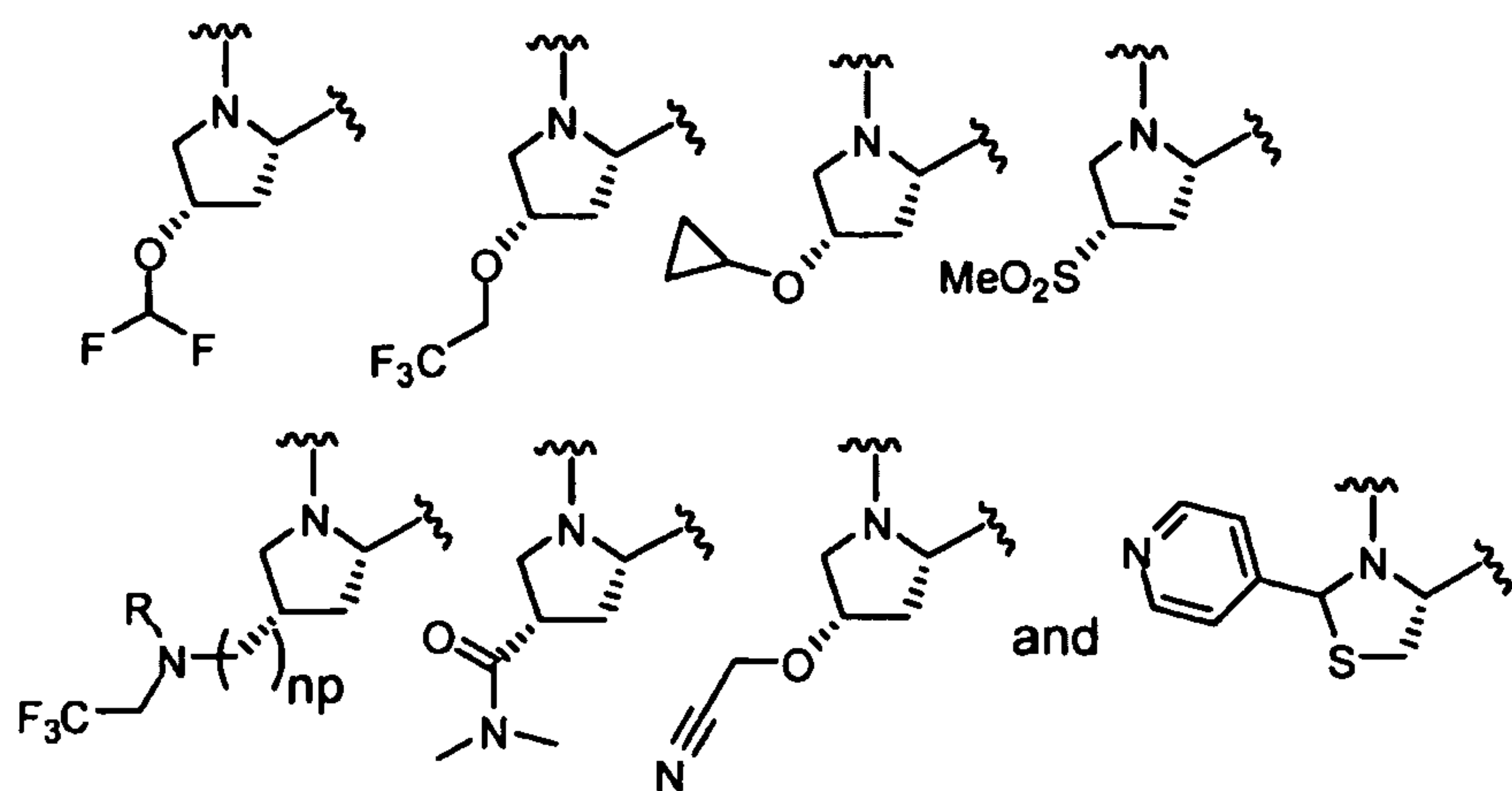
In another specific embodiment of the invention P is selected from:



In another specific embodiment of the invention P is selected from:

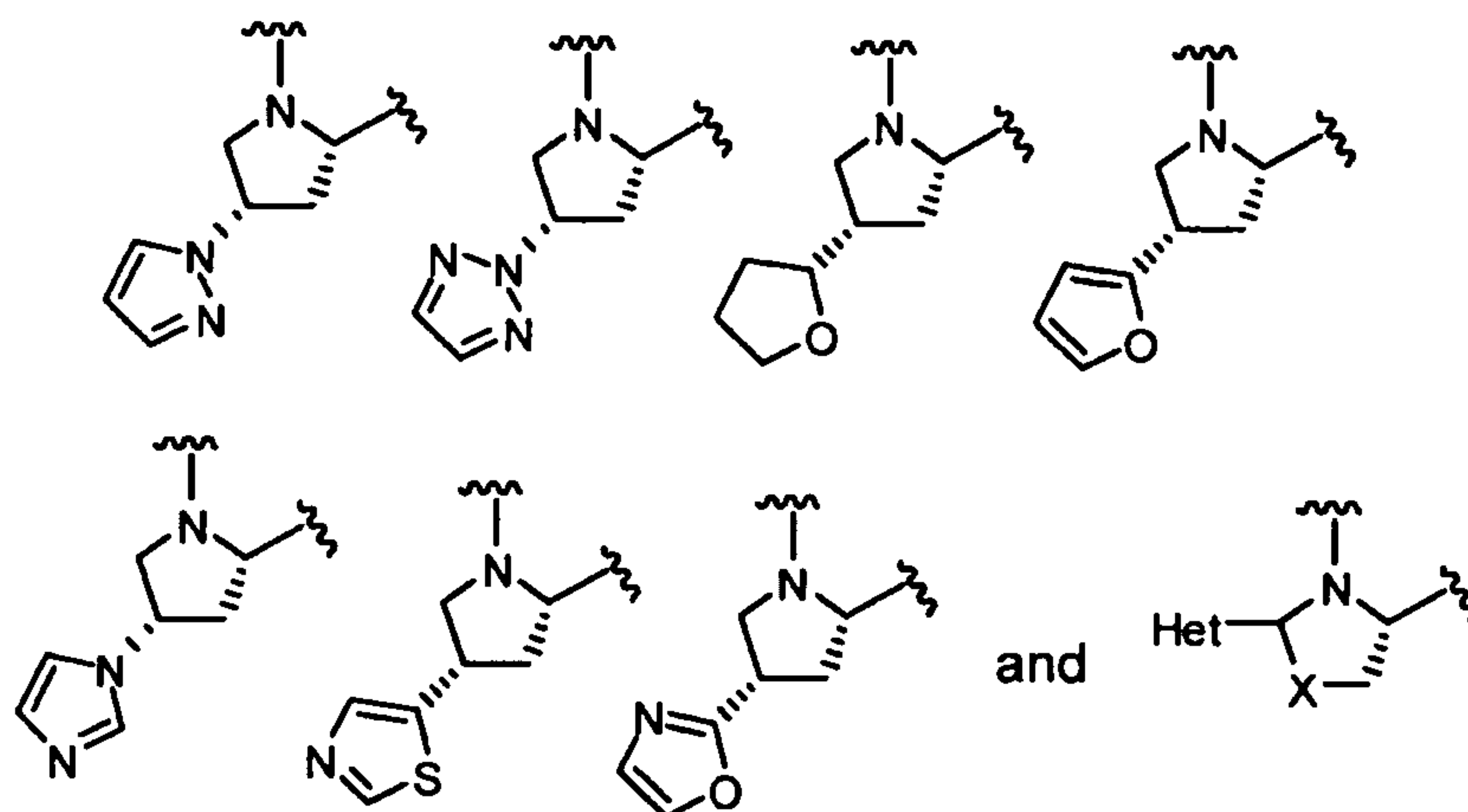


In another specific embodiment of the invention P is selected from:



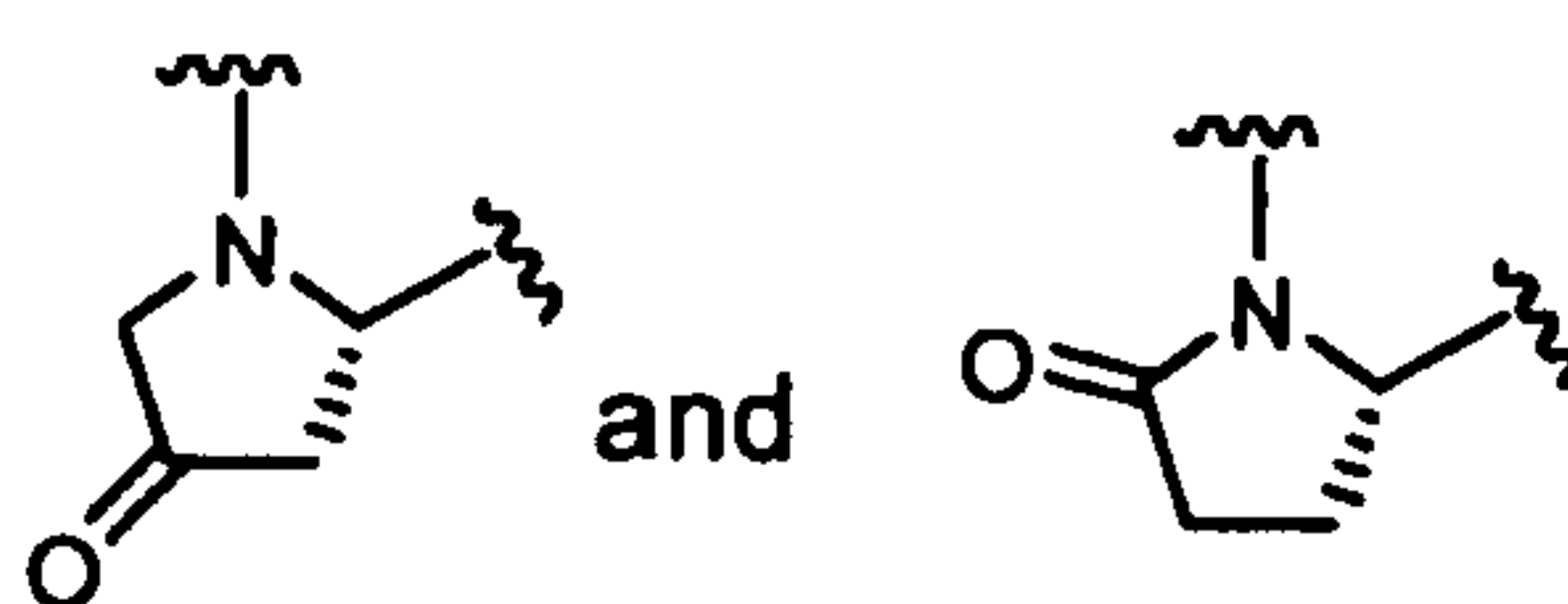
wherein R is hydrogen or methyl and np is 0 or 1.

In another specific embodiment of the invention P is selected from:

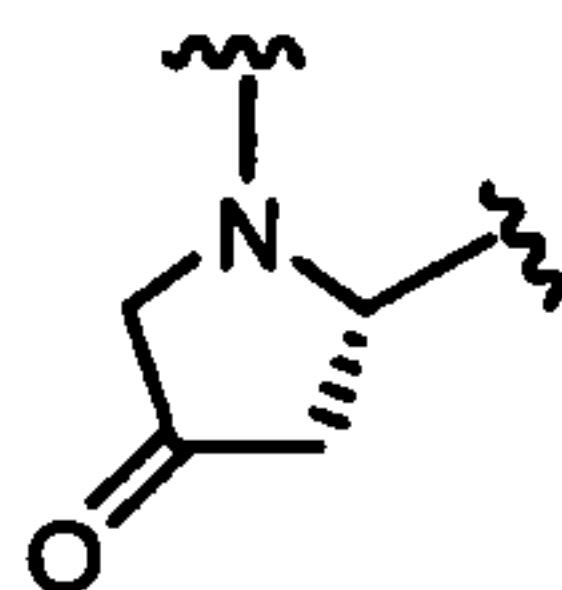


wherein X is O or S; and Het is a heterocycle.

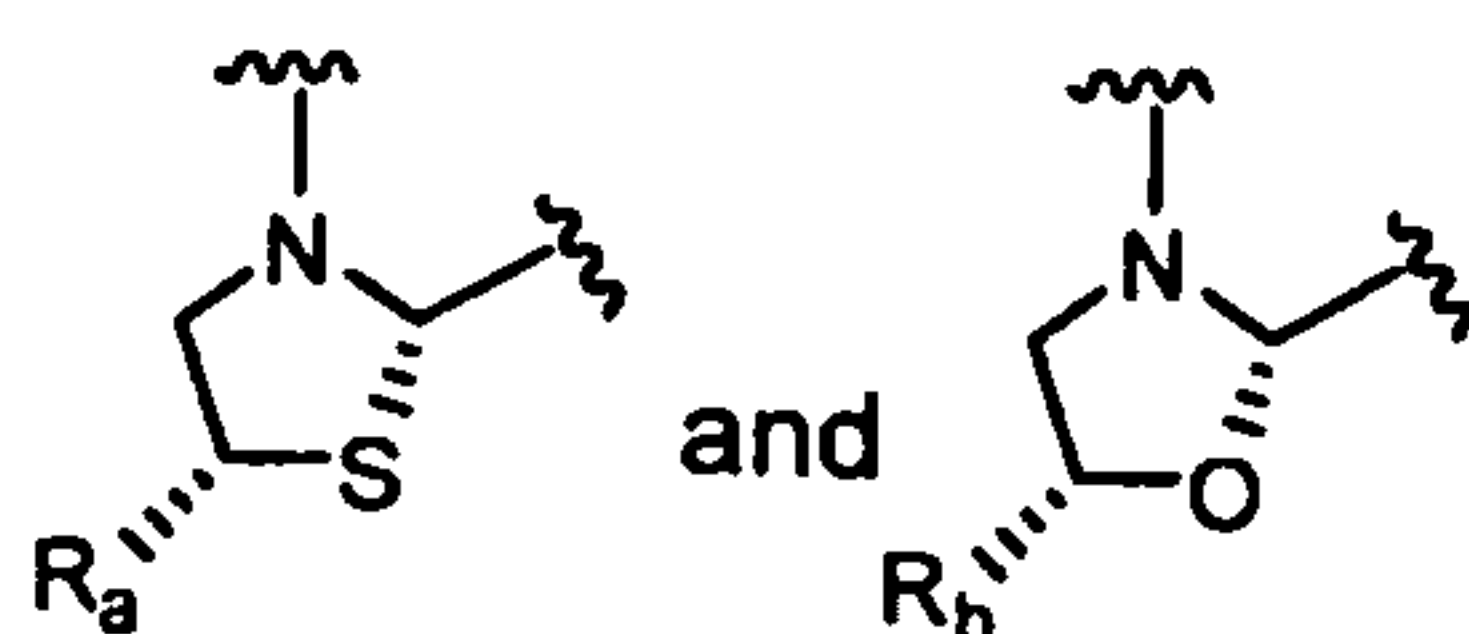
In another specific embodiment of the invention P is selected from:



In another specific embodiment of the invention P is:

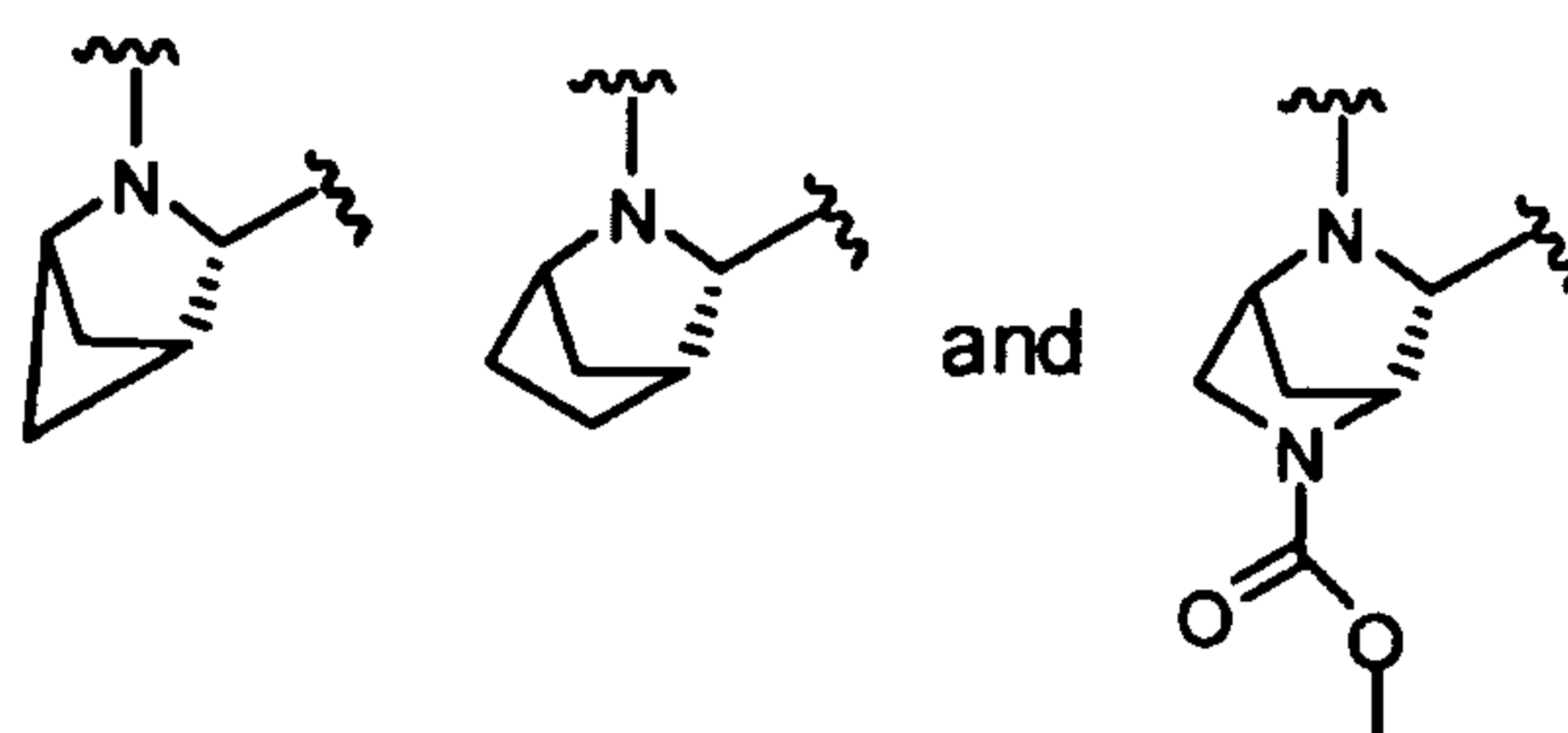


In another specific embodiment of the invention P is selected from:

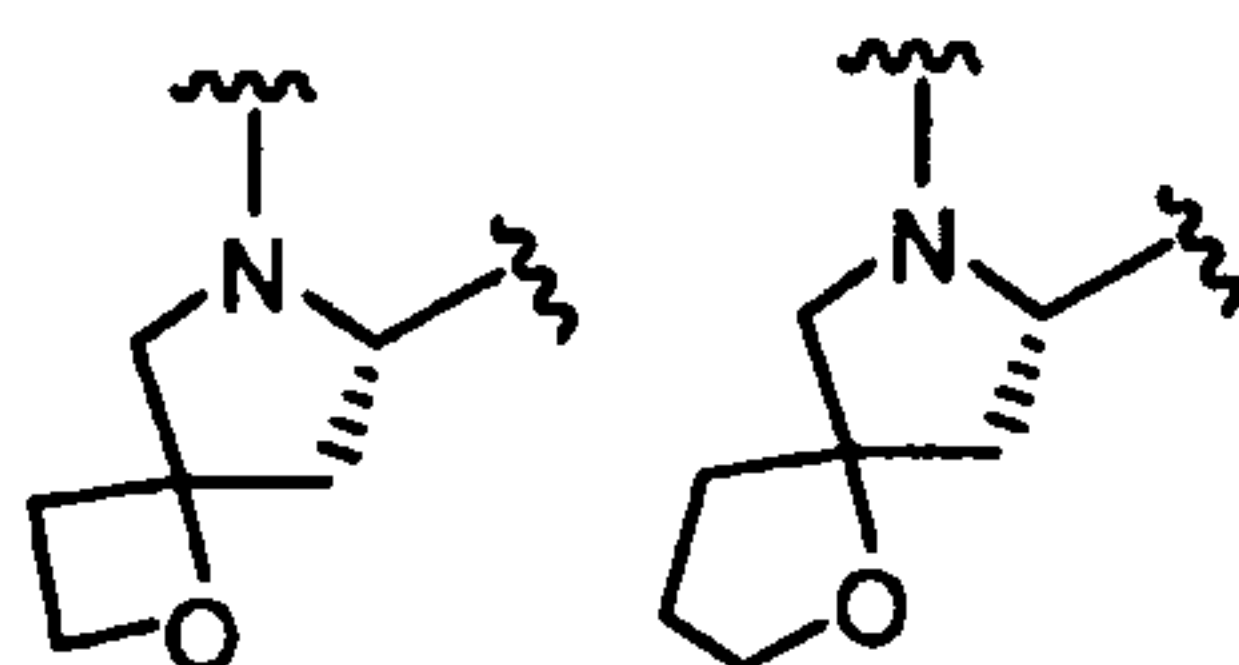


wherein R_a is hydrogen or methyl and R_b is methyl, or ethyl.

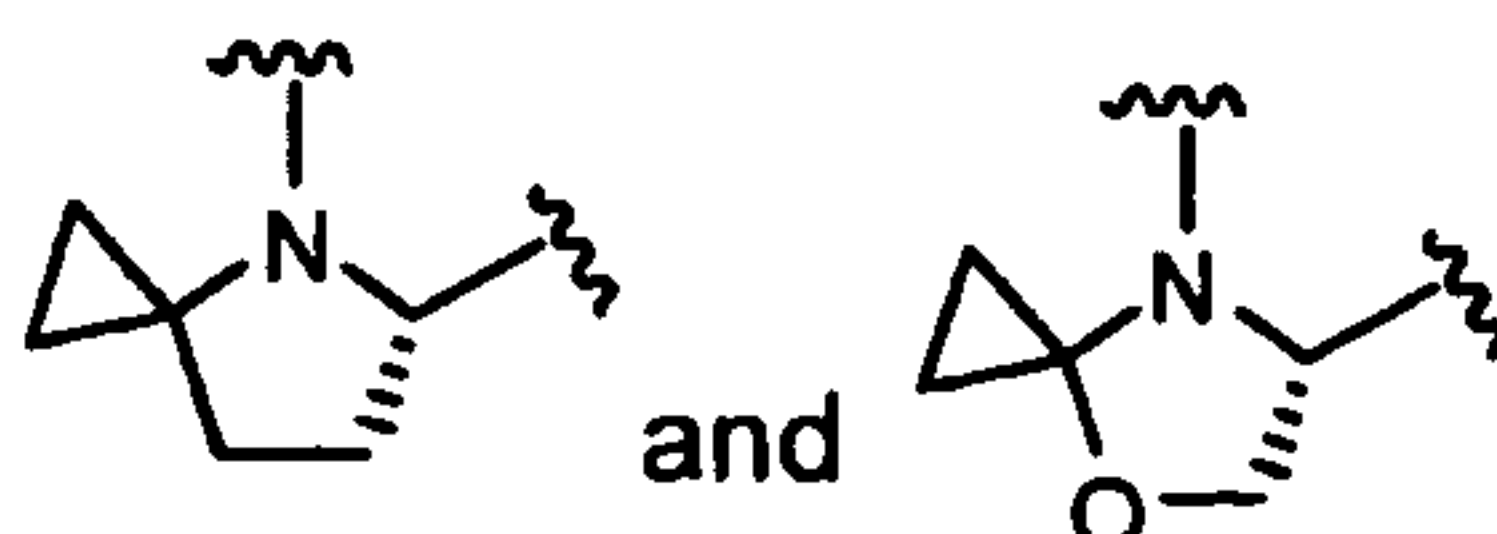
In another specific embodiment of the invention P is selected from:



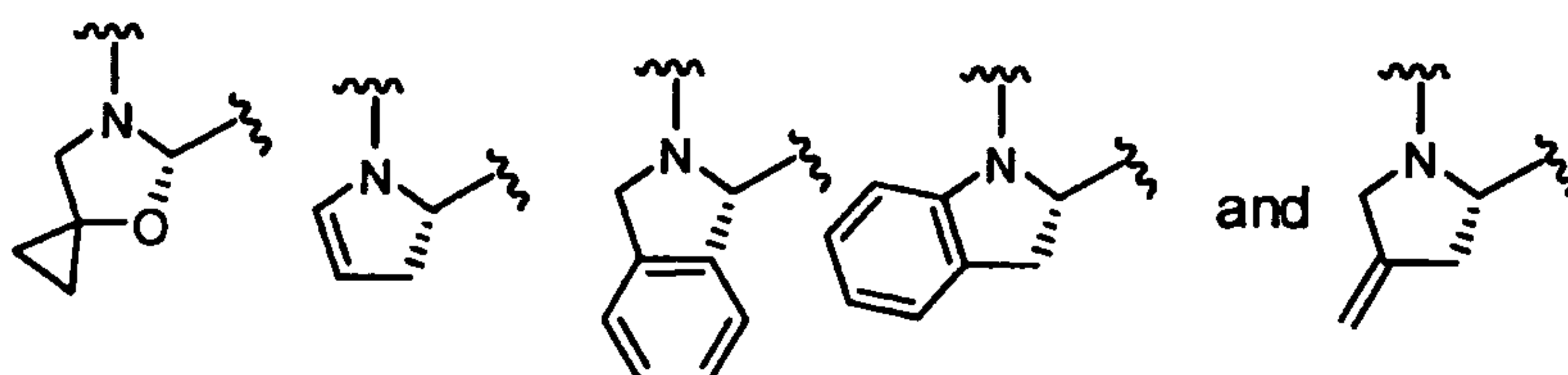
In another specific embodiment of the invention P is selected from:



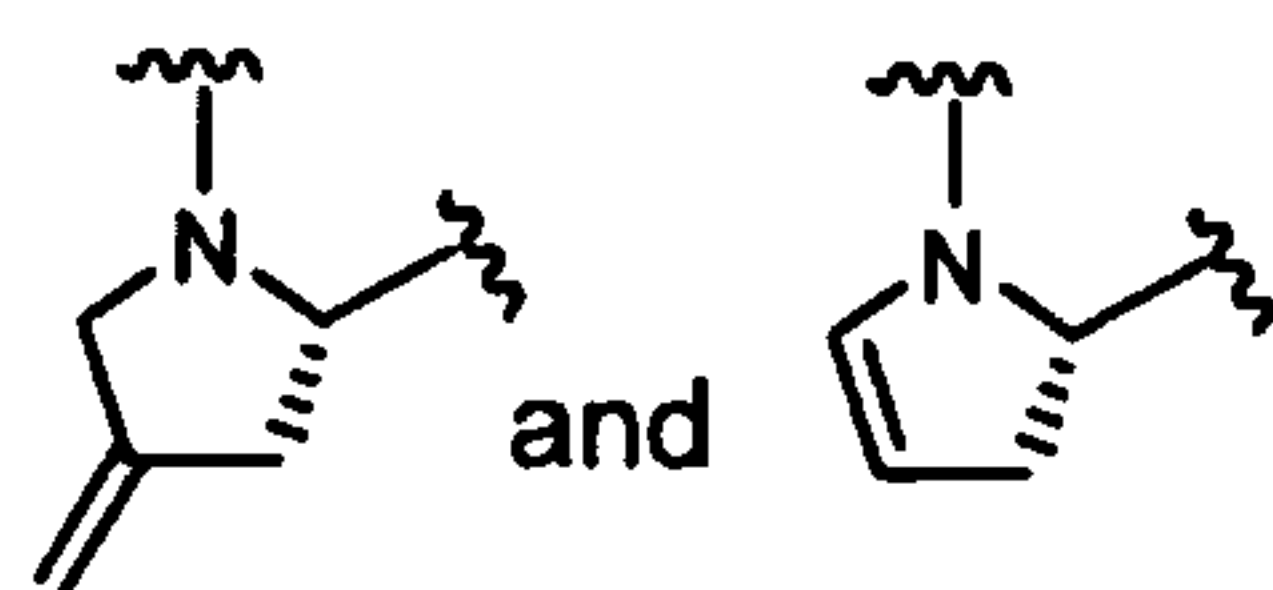
In another specific embodiment of the invention P is selected from:



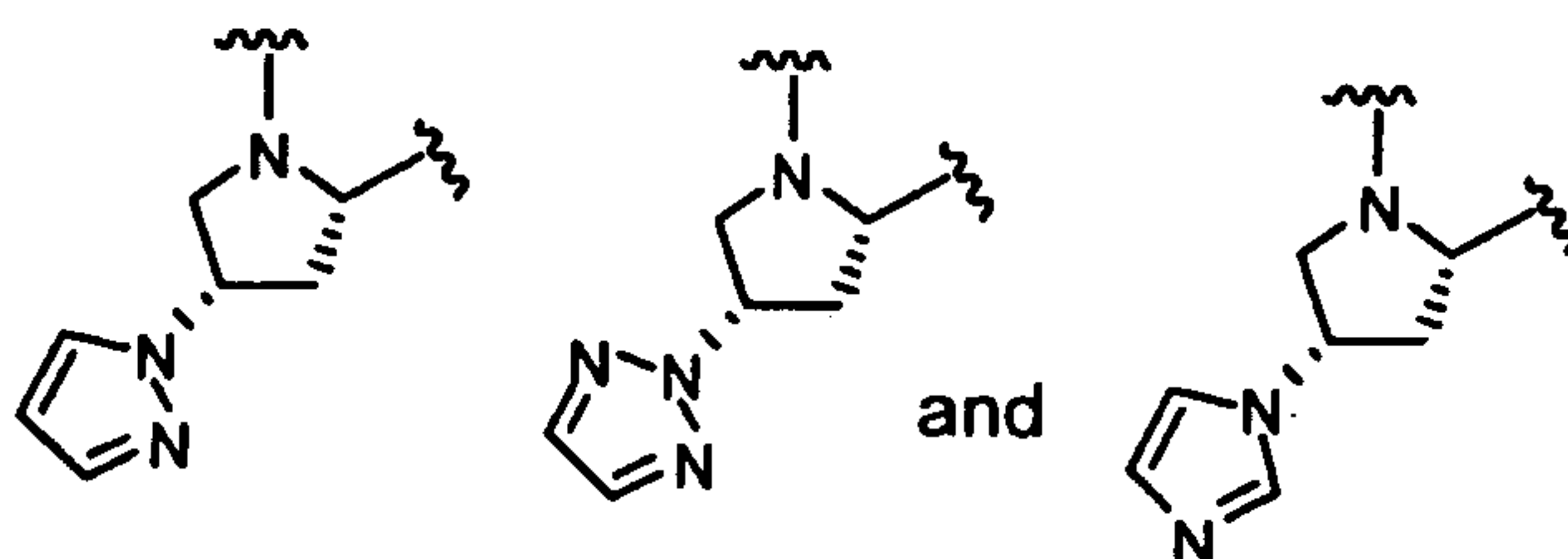
In another specific embodiment of the invention P is selected from:



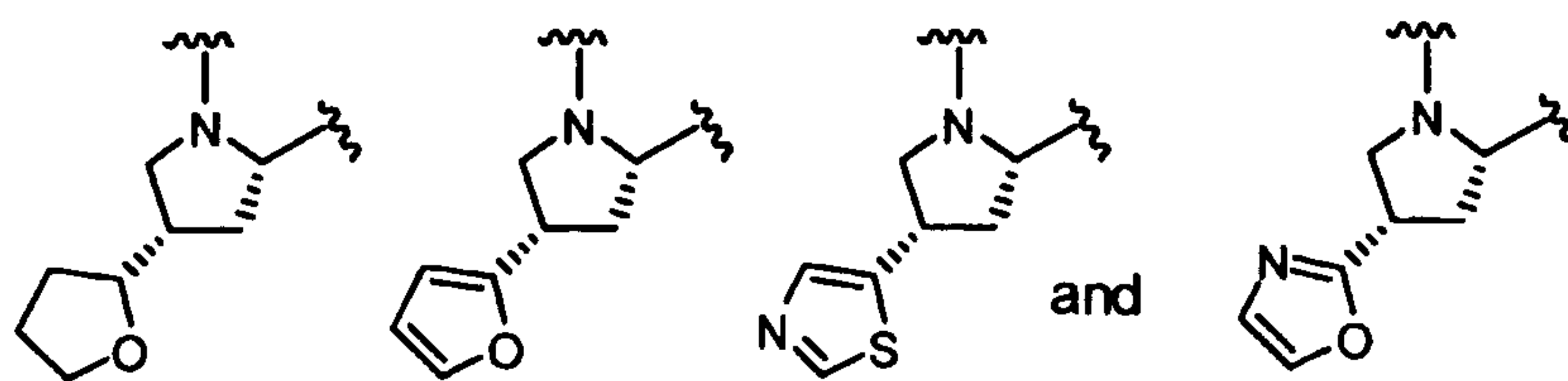
In another specific embodiment of the invention P is selected from:



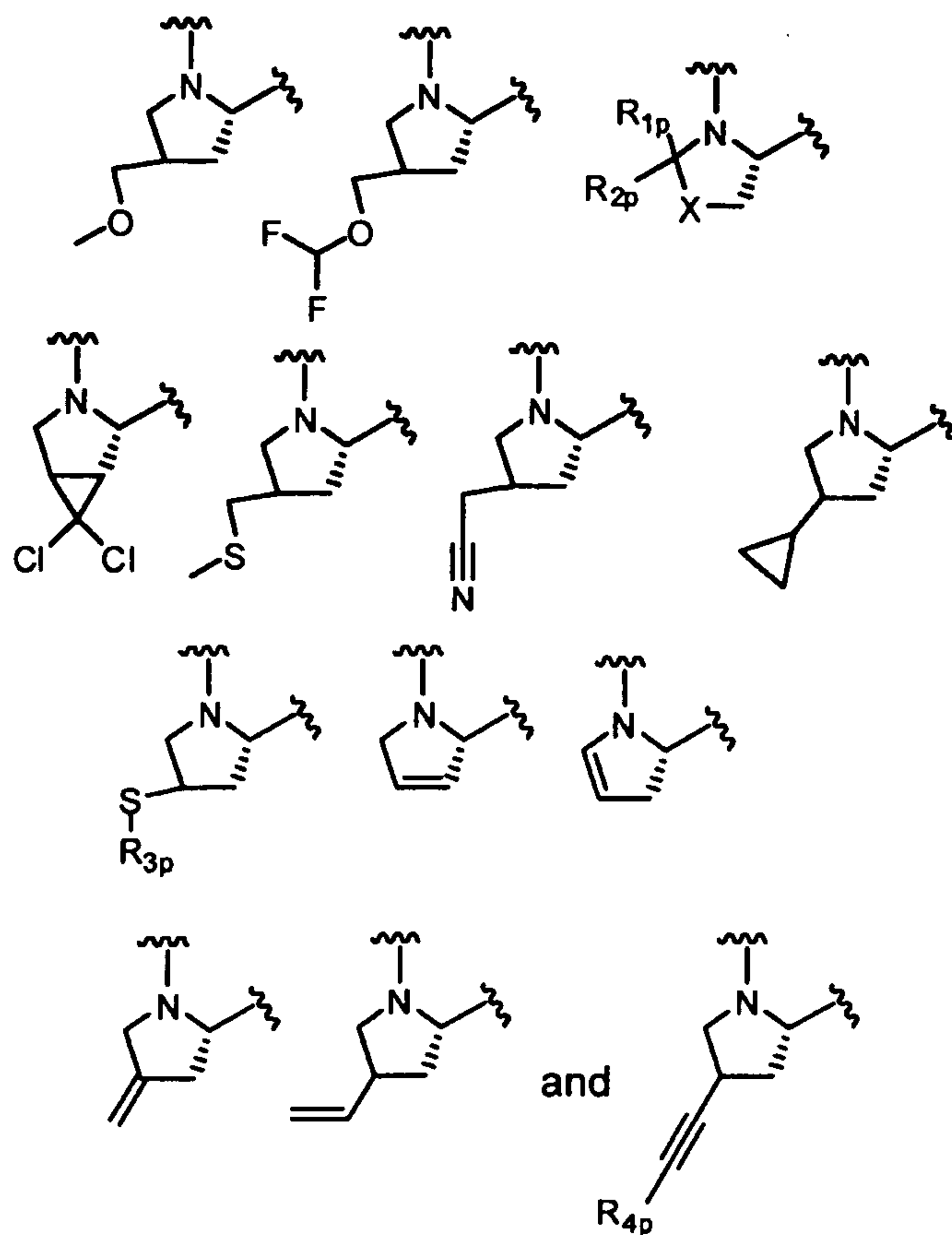
In another specific embodiment of the invention P is selected from:



In another specific embodiment of the invention P is selected from:

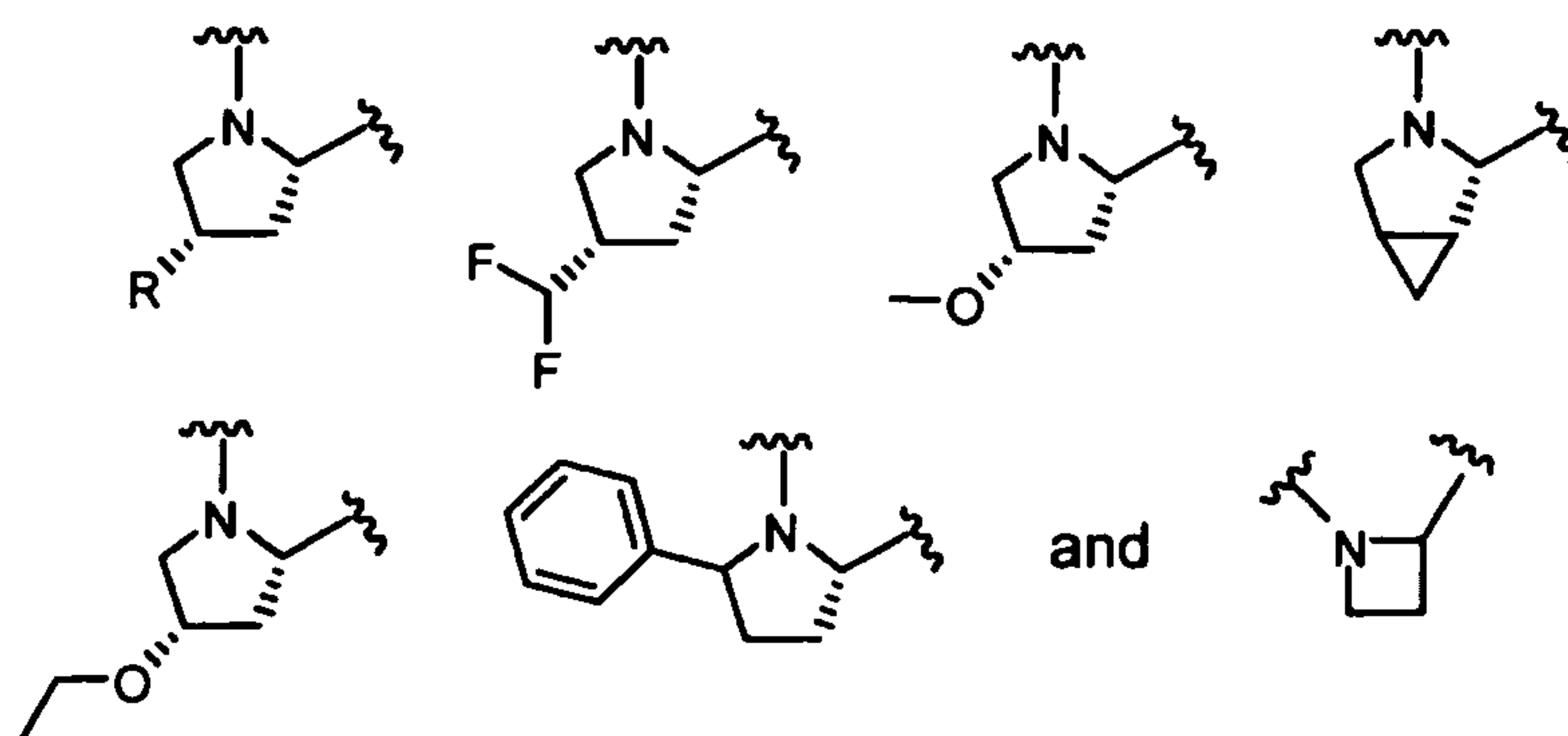


In another specific embodiment of the invention P is selected from:



wherein X is O or S; R_{1p} and R_{2p} are carbon linked and when taken together form a 4-6 membered heterocycle; R_{3p} is alkyl or cycloalkyl; and R_{4p} is hydrogen, methyl, or cyclopropyl.

In another specific embodiment of the invention P is P^0 and is selected from:



wherein R is alkyl.

In another specific embodiment of the invention when P is a divalent group that is linked through a nitrogen of P and through a carbon of P, it is the nitrogen of P that is connected to Z.

In another specific embodiment of the invention each V is V^0 .

In another specific embodiment of the invention each V is alkyl.

In another specific embodiment of the invention each V is isopropyl.

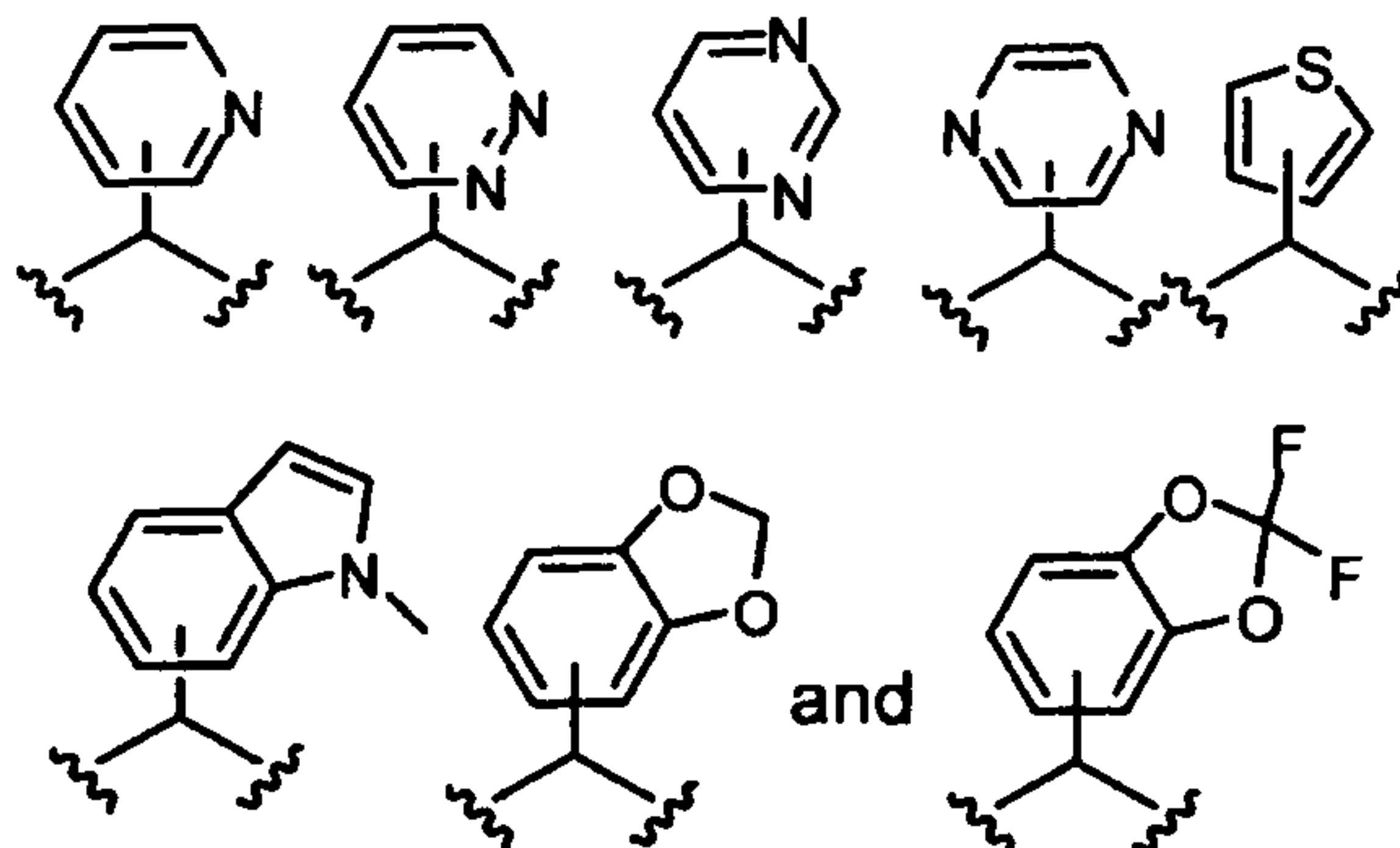
In another specific embodiment of the invention each V is isobutyl.

In another specific embodiment of the invention each V is V^2 .

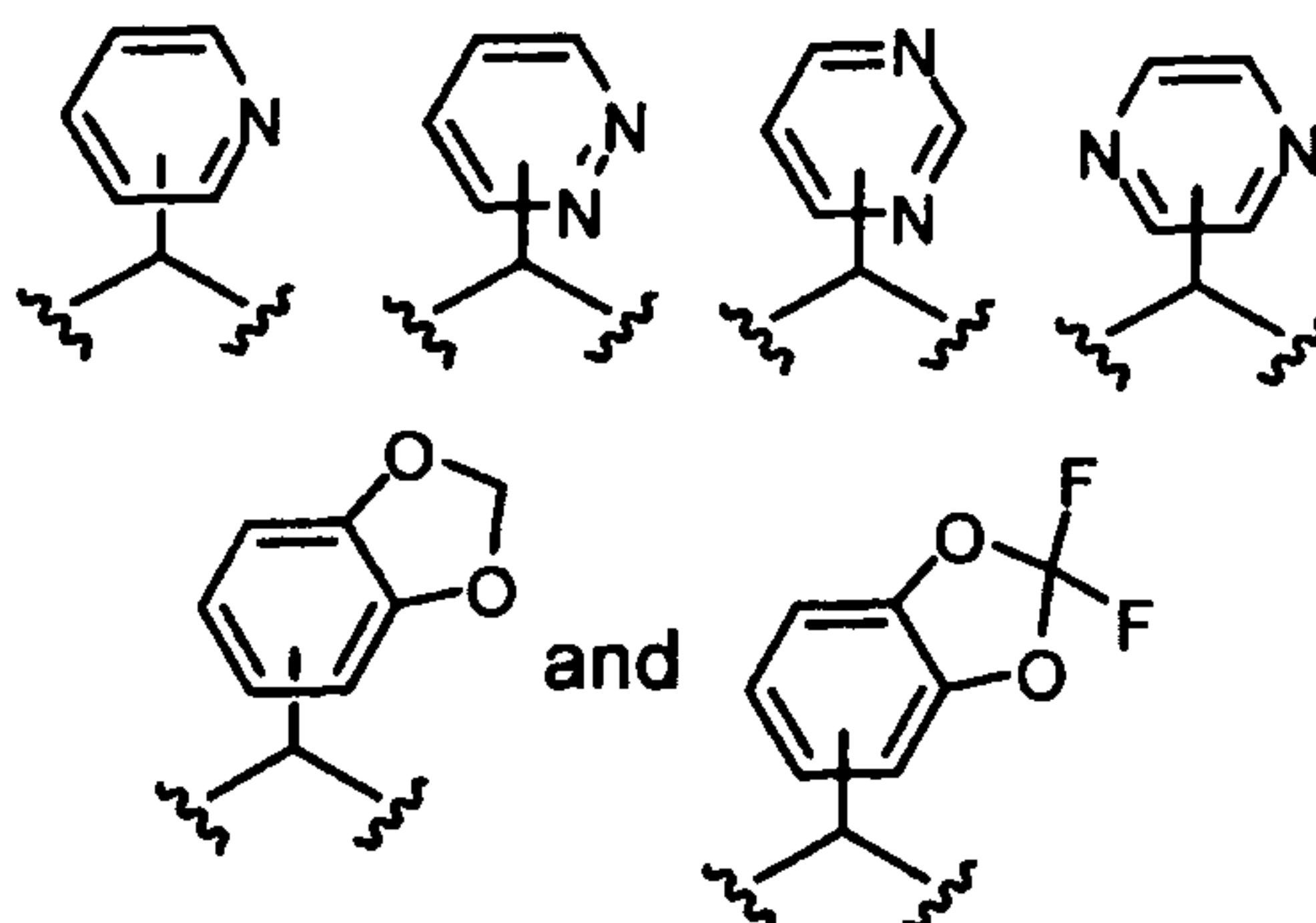
In another specific embodiment of the invention each V is haloalkyl.

In another specific embodiment of the invention each V is independently selected from V^0 , V^1 , V^2 , V^3 , V^4 , and V^5 .

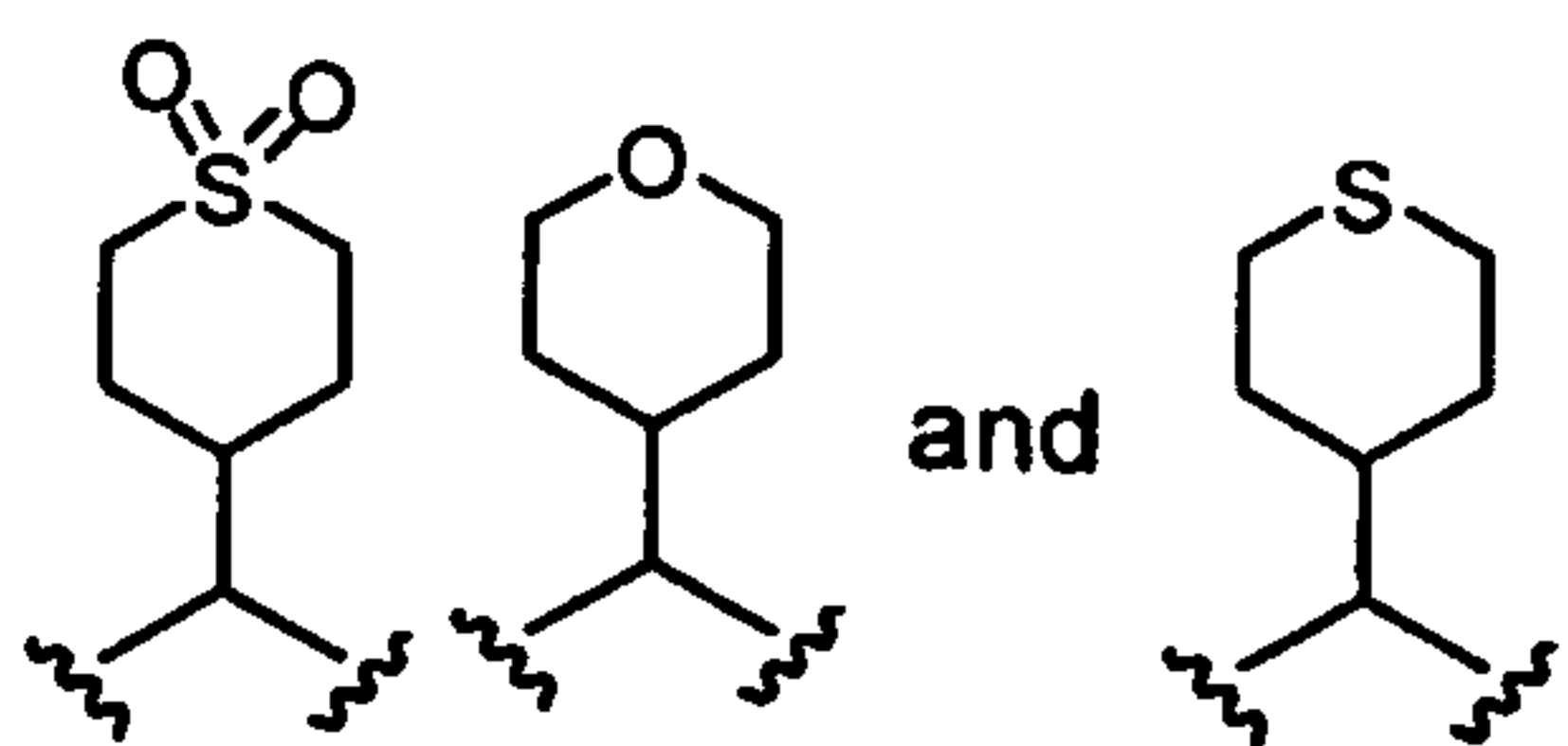
In another specific embodiment of the invention at least one V is selected from:



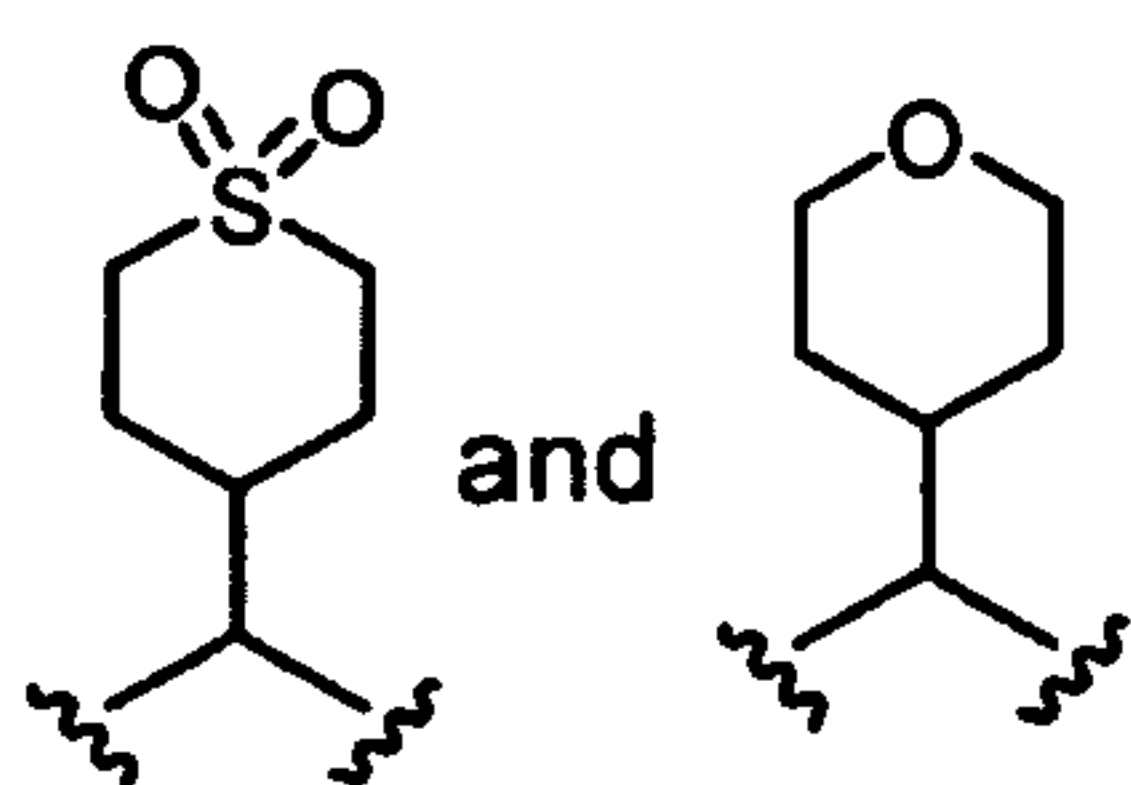
In another specific embodiment of the invention at least one V is selected from:



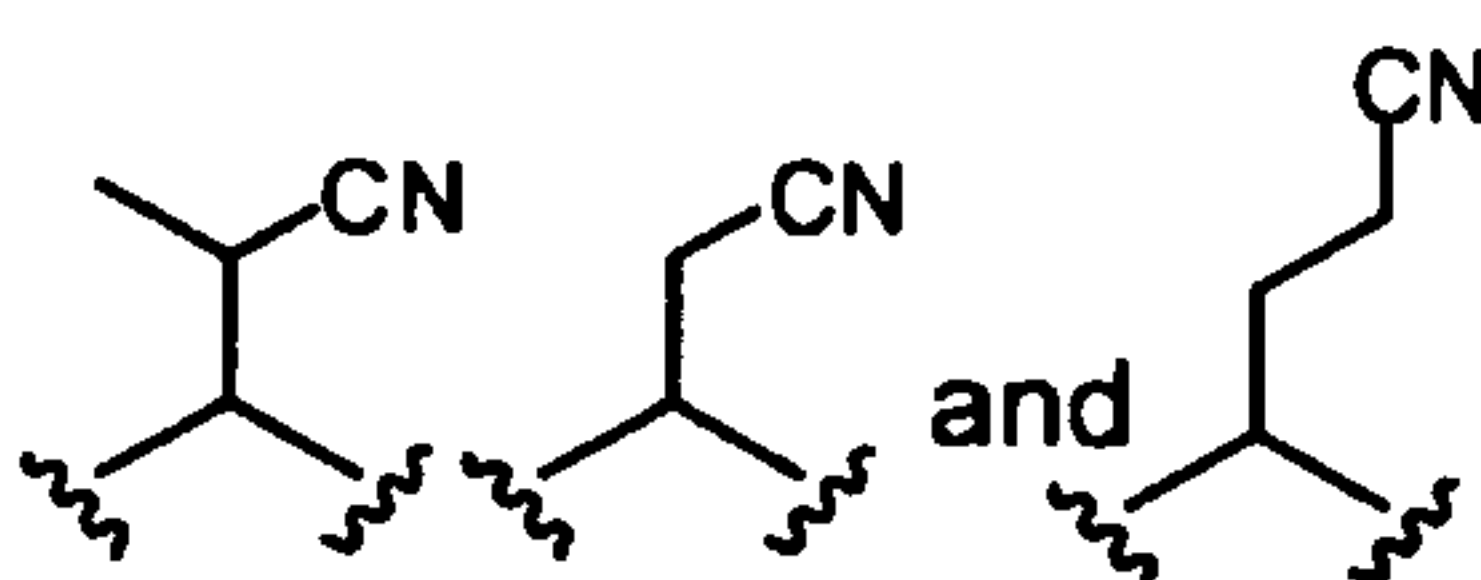
In another specific embodiment of the invention at least one V is selected from:



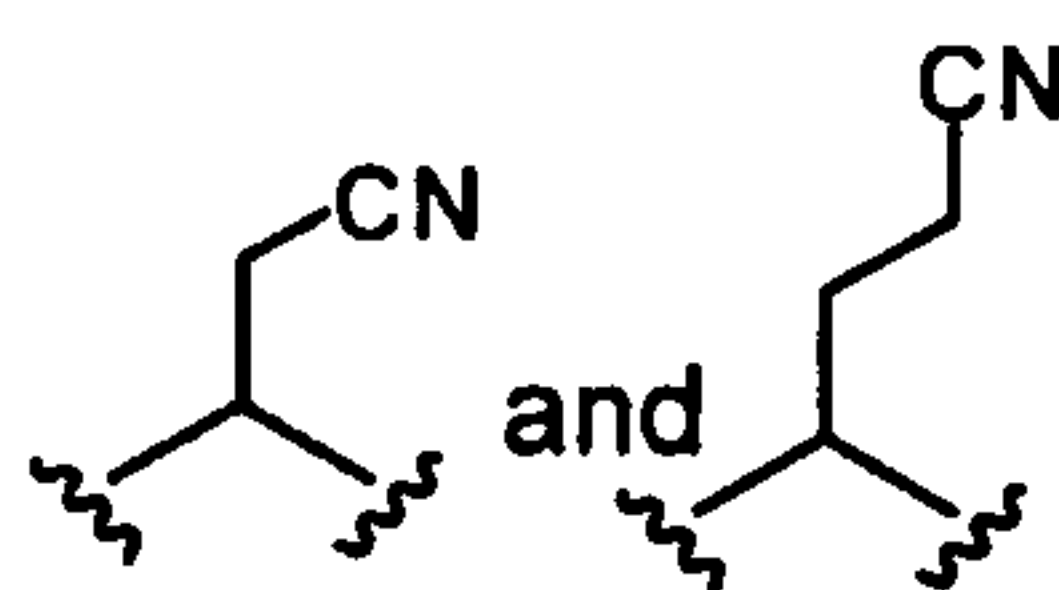
In another specific embodiment of the invention at least one V is selected from:



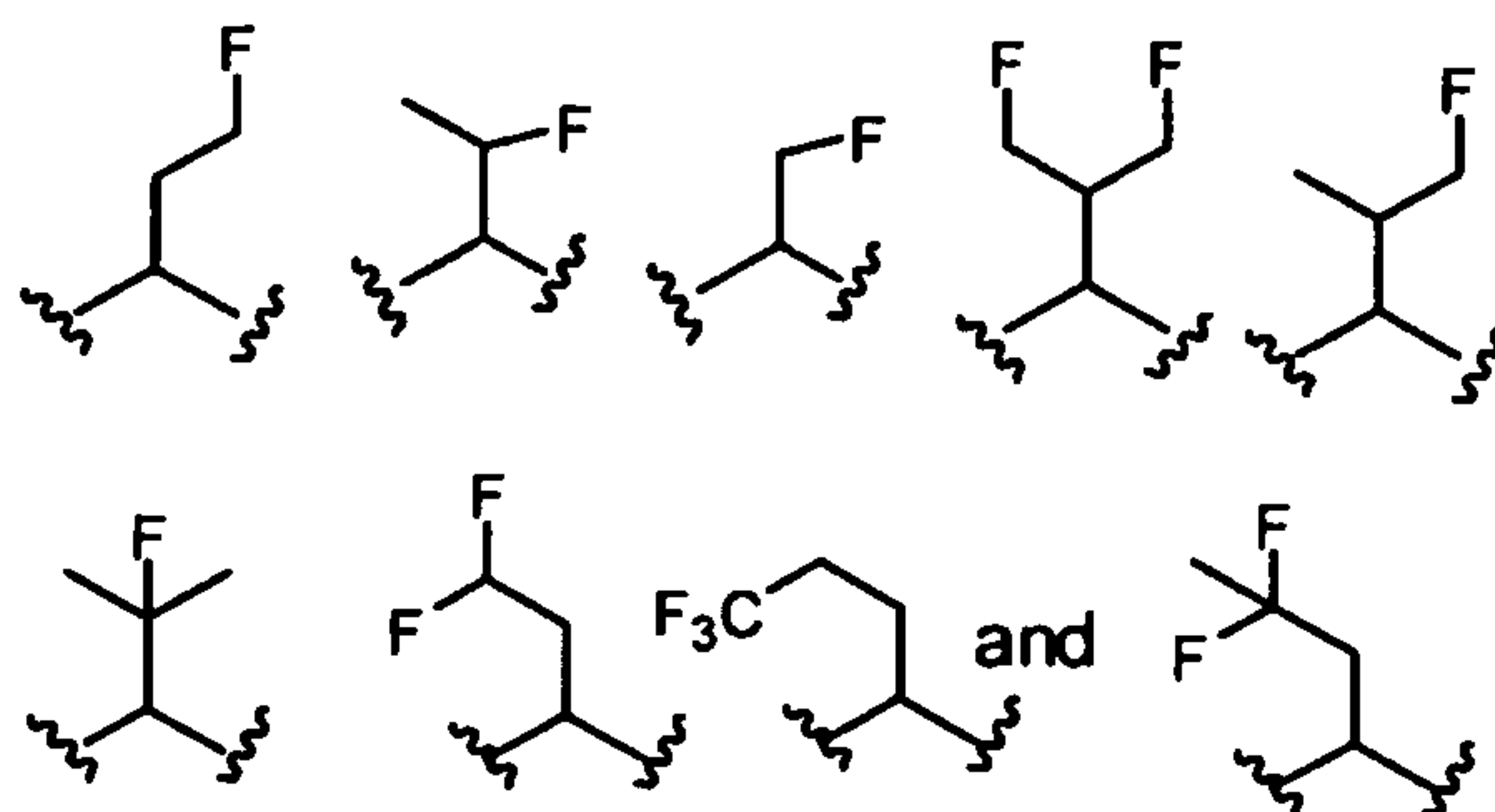
In another specific embodiment of the invention at least one V is selected from:



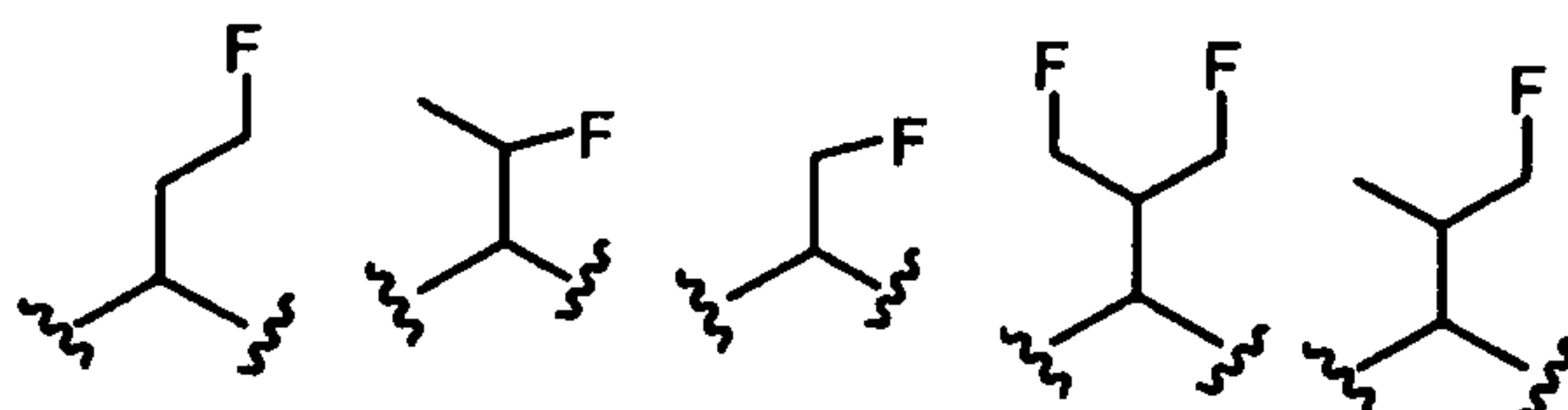
In another specific embodiment of the invention at least one V is selected from:

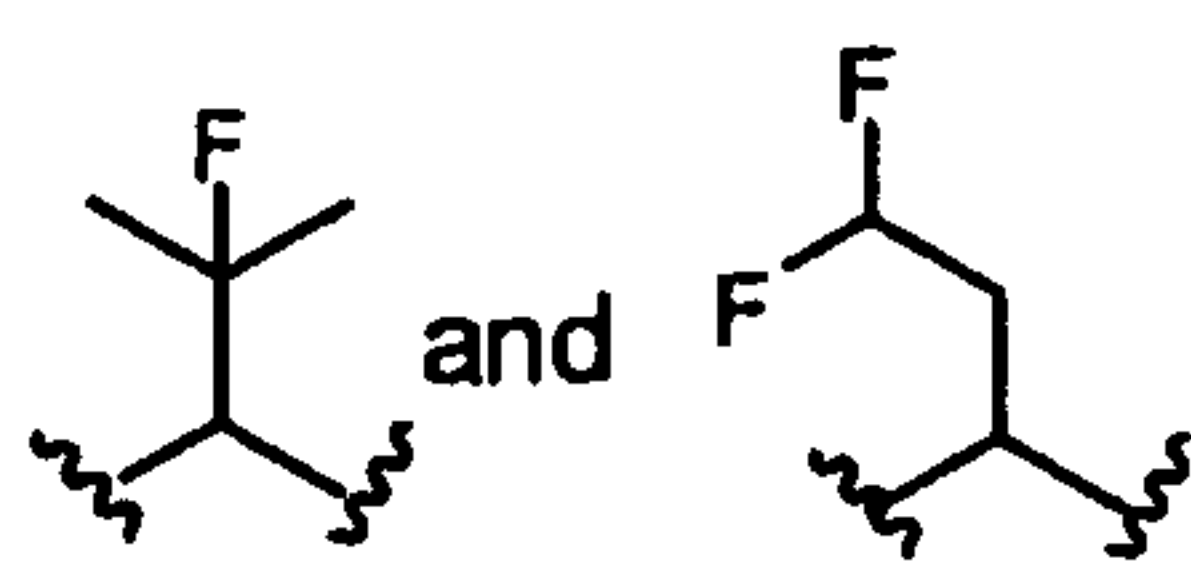


In another specific embodiment of the invention at least one V is selected from:

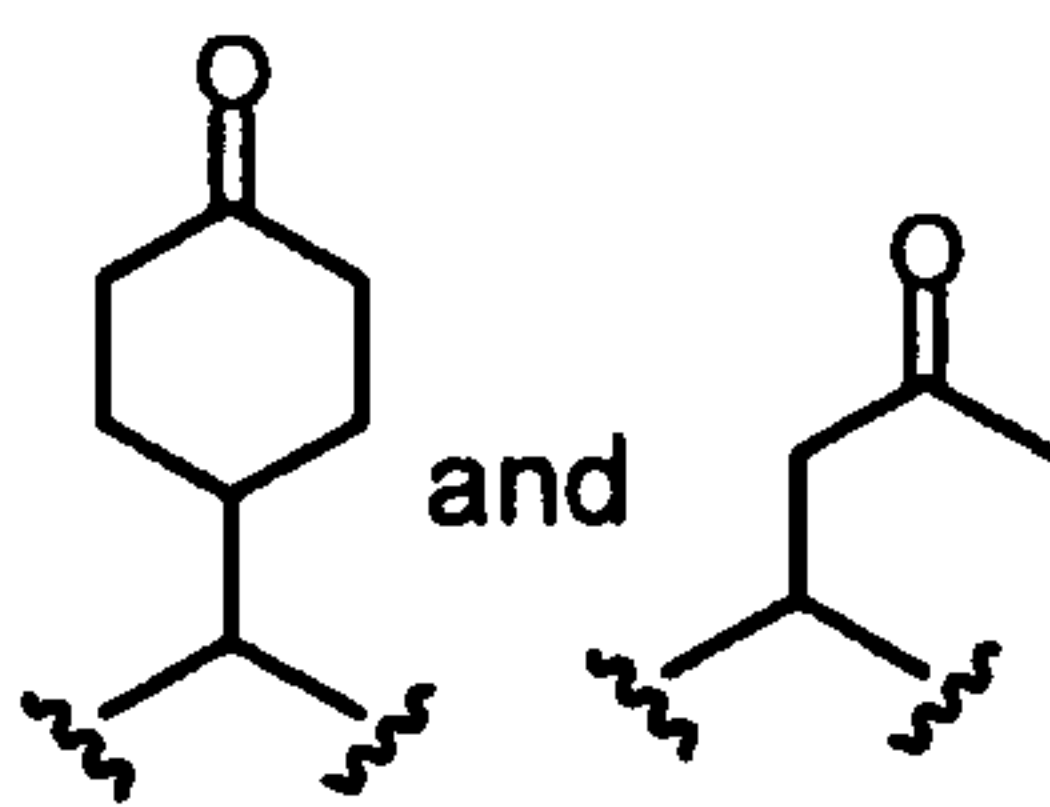


In another specific embodiment of the invention at least one V is selected from:

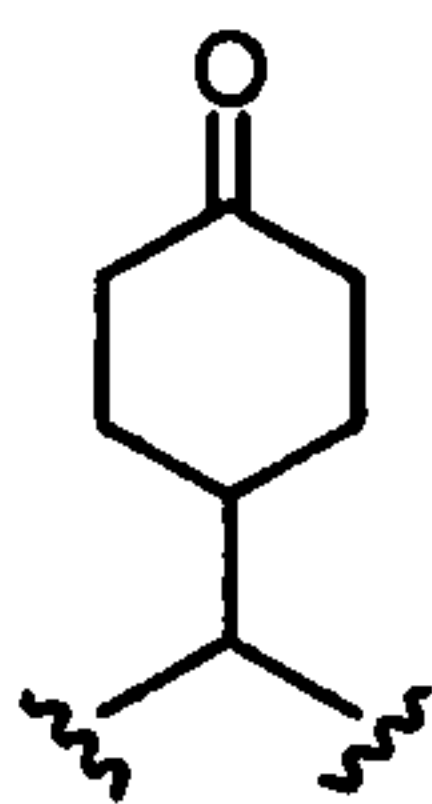




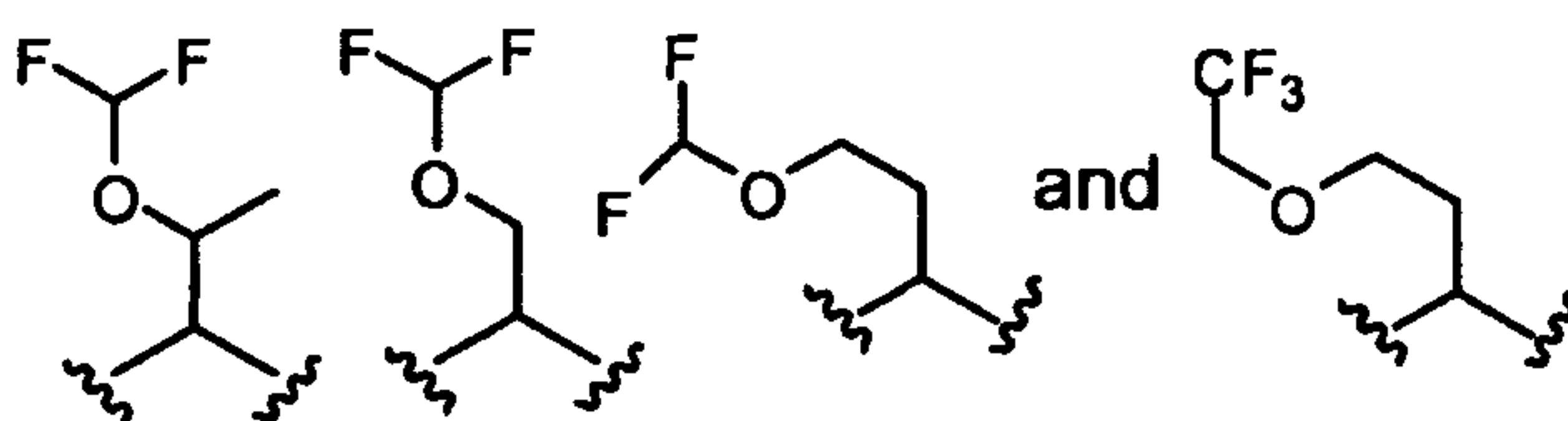
In another specific embodiment of the invention at least one V is selected from:



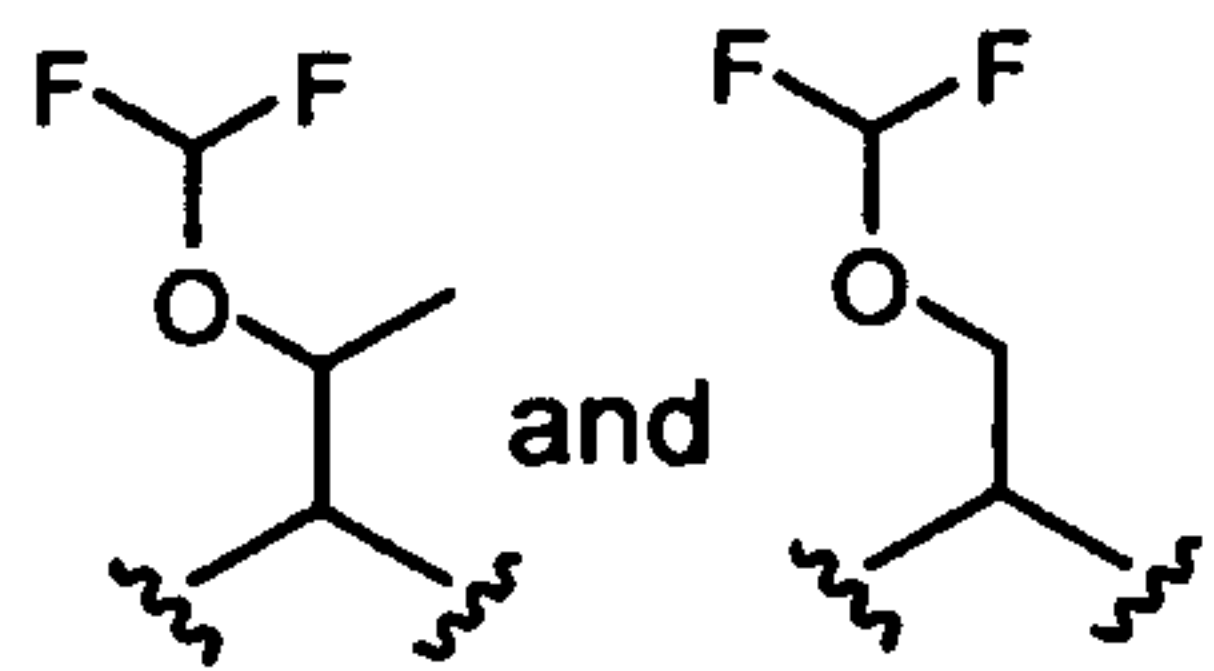
In another specific embodiment of the invention at least one V is:



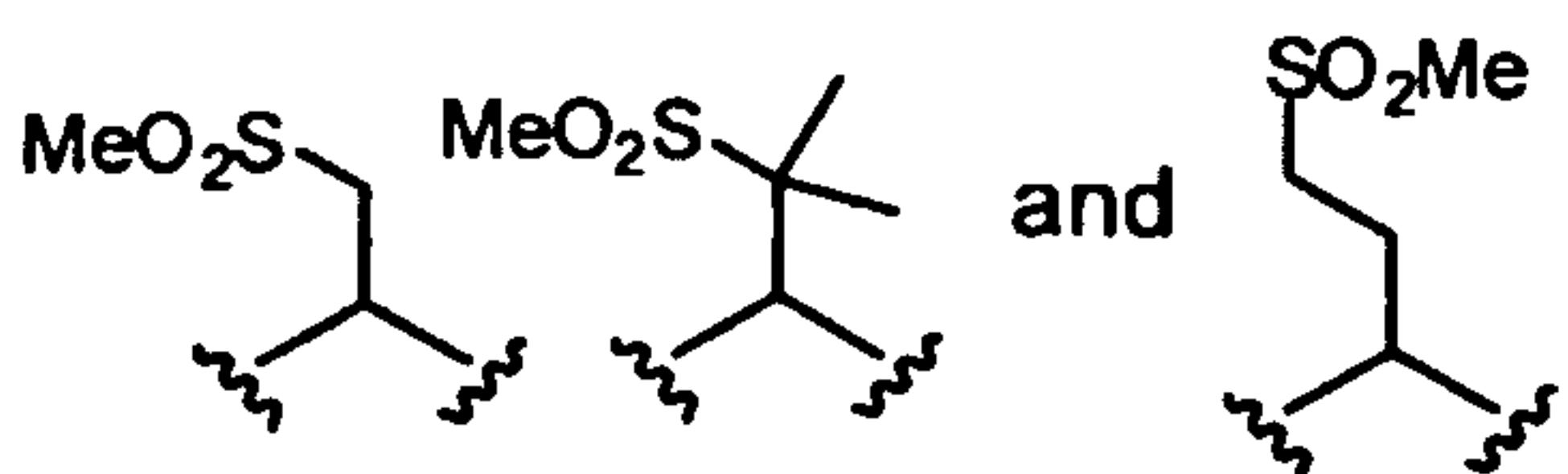
In another specific embodiment of the invention at least one V is selected from:



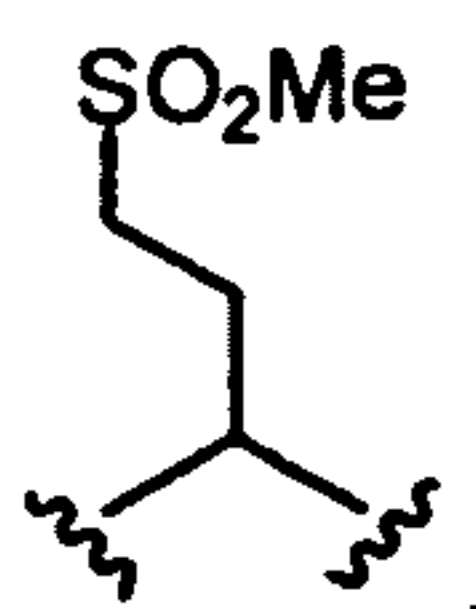
In another specific embodiment of the invention at least one V is selected from:



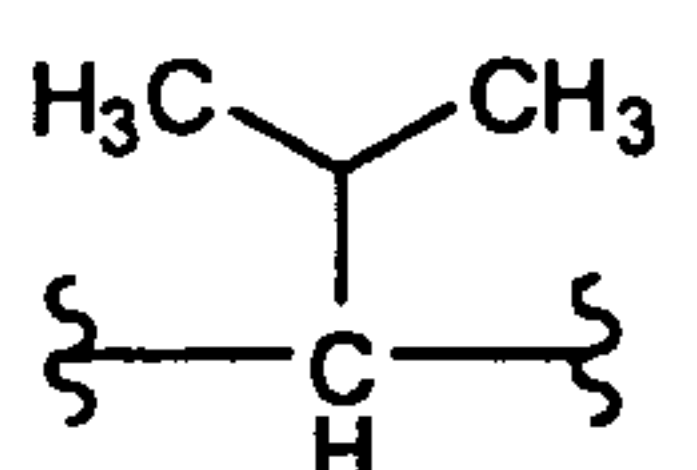
In another specific embodiment of the invention at least one V is selected from:



In another specific embodiment of the invention at least one V is:



In another specific embodiment of the invention each V is:



In another specific embodiment of the invention each V^2 is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl; and each V^4 is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, hydroxy, and $\text{NR}^{\text{Va}}\text{R}^{\text{Vb}}\text{C}(=\text{O})\text{O}-$; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl.

In another specific embodiment of the invention each V^0 is independently arylalkyl or heterocyclylalkyl, wherein arylalkyl can be substituted with up to three aryl groups, and the alkyl part of the arylalkyl is further optionally substituted with one or two additional groups independently selected from alkoxy, alkylocarbonyloxy, halo, haloalkoxy, haloalkyl, heterocyclyl, hydroxy; and the aryl part can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkyl, alkyl, alkylcarbonyl, a second aryl group, arylalkoxy, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, $-\text{NR}^{\text{X}}\text{R}^{\text{Y}}$, $-(\text{NR}^{\text{X}}\text{R}^{\text{Y}})\text{alkyl}$, oxo, and $-\text{P}(\text{O})\text{OR}_2$, wherein each R is independently selected from hydrogen and alkyl; and wherein the alkyl part of the heterocyclylalkyl is further optionally substituted with one, two, or three substituents independently selected from alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, and nitro; and the heterocyclyl can be substituted with 1, 2, 3, 4, or 5 substituents independently selected from alkoxy, alkoxyalkyl, alkoxyalkyl, alkyl, alkylcarbonyl, aryl, arylalkyl, arylcarbonyl, cyano, halo, haloalkoxy, haloalkyl, a second

heterocyclyl group, heterocyclylalkyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, nitro, -NR^XR^Y, -(NR^XR^Y)alkyl, and oxo.

In another specific embodiment the invention each V is isobutyl.

In another specific embodiment the invention at least one V is isobutyl.

In another specific embodiment the invention at least one V is phenylmethyl where the Z and E groups are each connected to the methyl group (i.e. -CH(Ph)-).

In another specific embodiment the invention at least one V is V⁰ and at least one V⁰ is phenylmethyl where the Z and E groups are each connected to the methyl group and the phenyl can be substituted as described in the description for the V⁰ aryl group.

In another specific embodiment the invention at least one V⁰ is arylmethyl where the Z and E groups are each connected to the methyl group and the aryl can be substituted as described in the description for the V⁰ aryl group.

In another specific embodiment the invention at least one V is V⁰ and at least one V⁰ is heterocyclymethyl where the Z and E groups are each connected to the methyl group.

In another specific embodiment the invention at least one V is V⁰ and at least one V⁰ is heterocyclymethyl where the Z and E groups are each connected to the methyl group and the heterocyclyl group can be substituted as described in the description for the V⁰ heterocyclyl group.

In another specific embodiment the invention each V² is independently haloalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, hydroxy, and NR^{Va}R^{Vb}C(=O)O-; R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl.

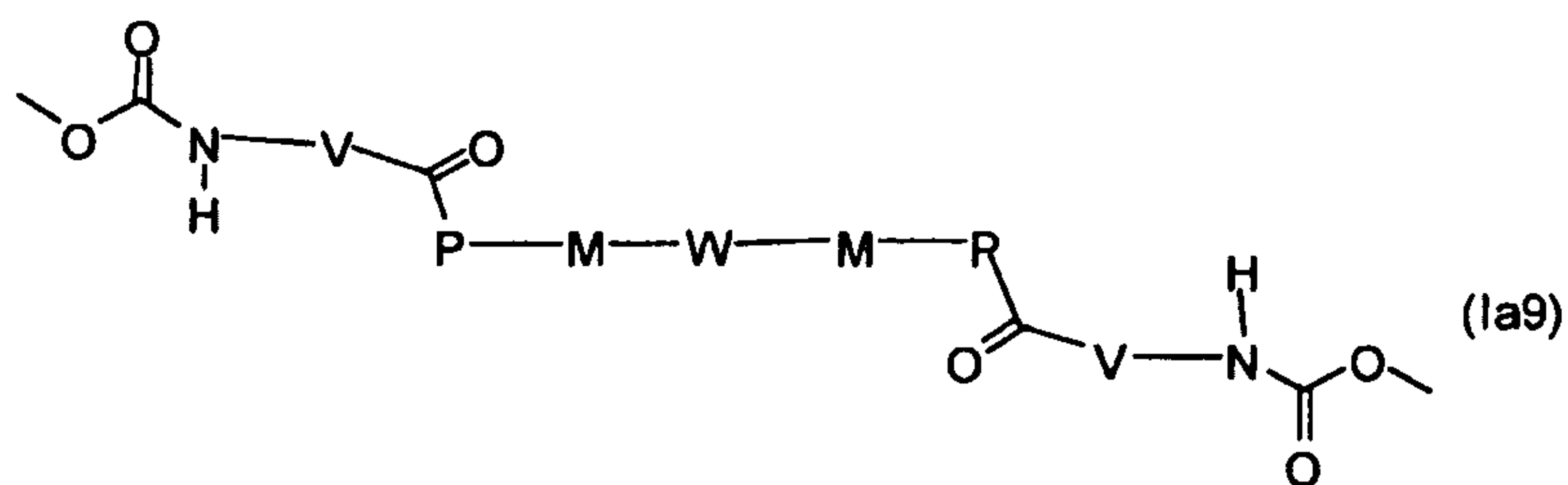
In another specific embodiment the invention each V⁴ is independently haloalkoxyalkyl, which is optionally substituted with one or more groups independently selected from cycloalkyl, alkoxy, haloalkoxy, cycloalkenyl, hydroxy, and NR^{Va}R^{Vb}C(=O)O-; wherein R^{Va} and R^{Vb} are each independently selected from hydrogen, alkenyl, and alkyl.

In another specific embodiment of the invention each Z is Z⁰.

In another specific embodiment of the invention each Z is -C(=O)-.

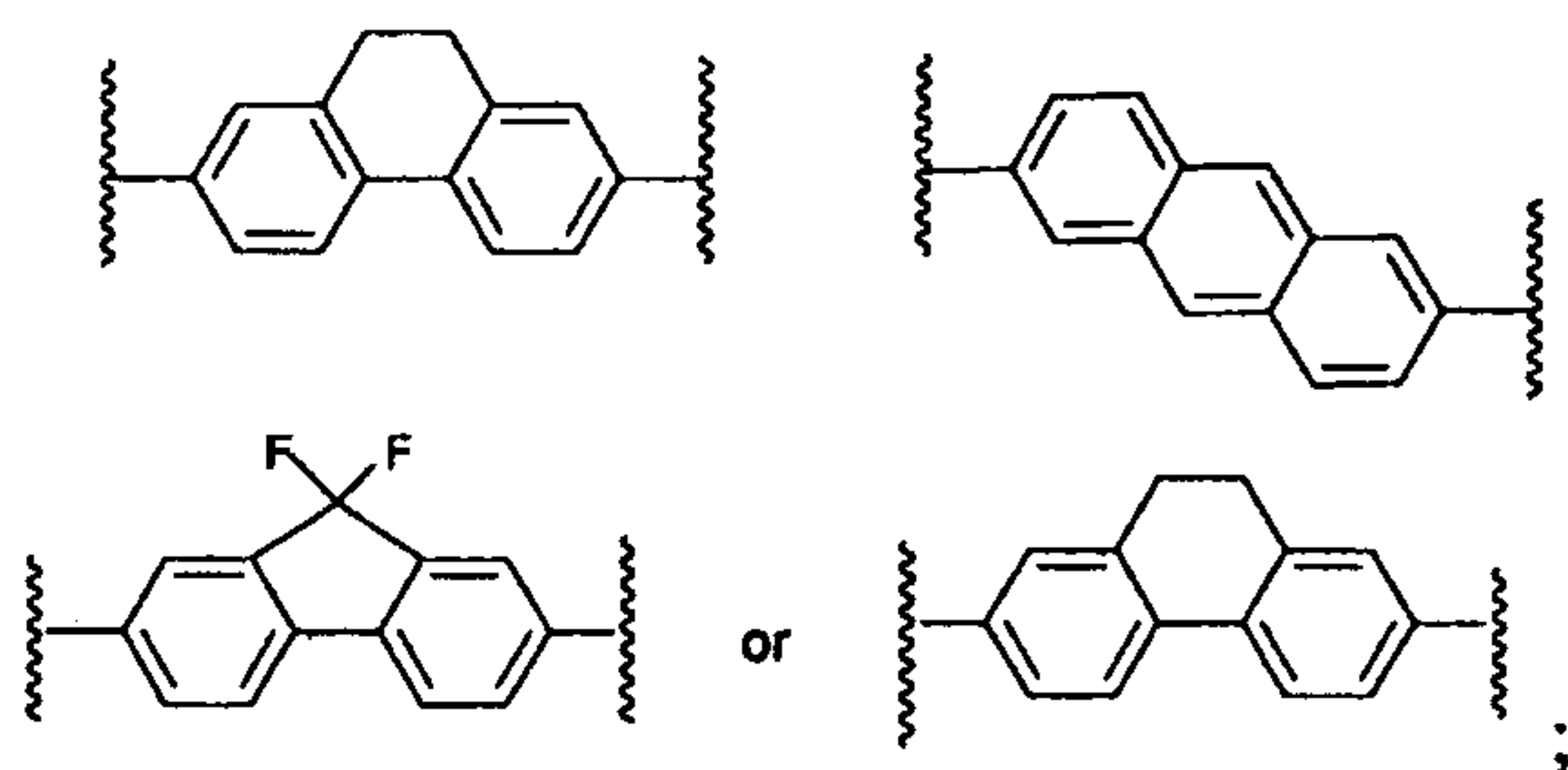
For the compounds of formula (I) described herein, including the compounds of formulae (Ia), (Ib), (Ic), (Id), and (Ie), any of the above specific values or embodiments for the variables E, P, V, and Z, can be applied. Thus, the invention also includes specific embodiments wherein one or more of the specific values or embodiments for J, T, P, W, L, M, A, R⁹, E, P, V, and Z described herein are combined with one of formulae (Ia), (Ib), (Ic), (Id), and (Ie), to provide a sub-set of compounds that represents a specific embodiment of the invention.

For example, by selecting a compound of formula (Ia9) above, along with specific values for P, M, W, and V identified herein, one can identify a specific embodiment the invention which is a compound of formula (Ia9):



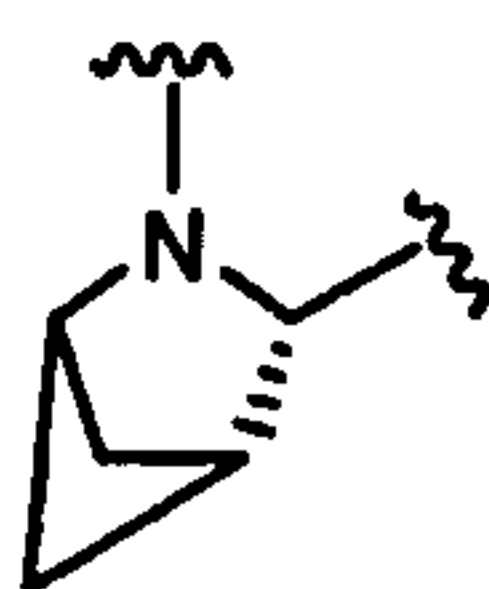
wherein:

W is

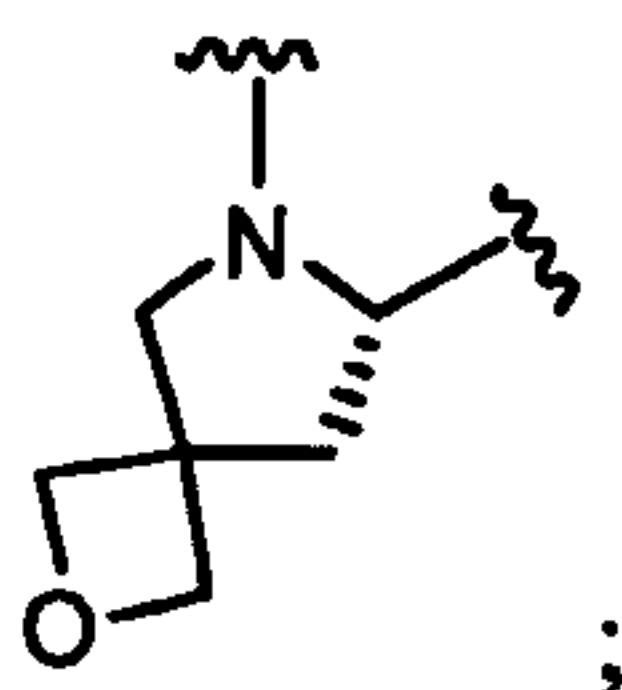


one M is imidazolyl and one M is benzimidazolyl;

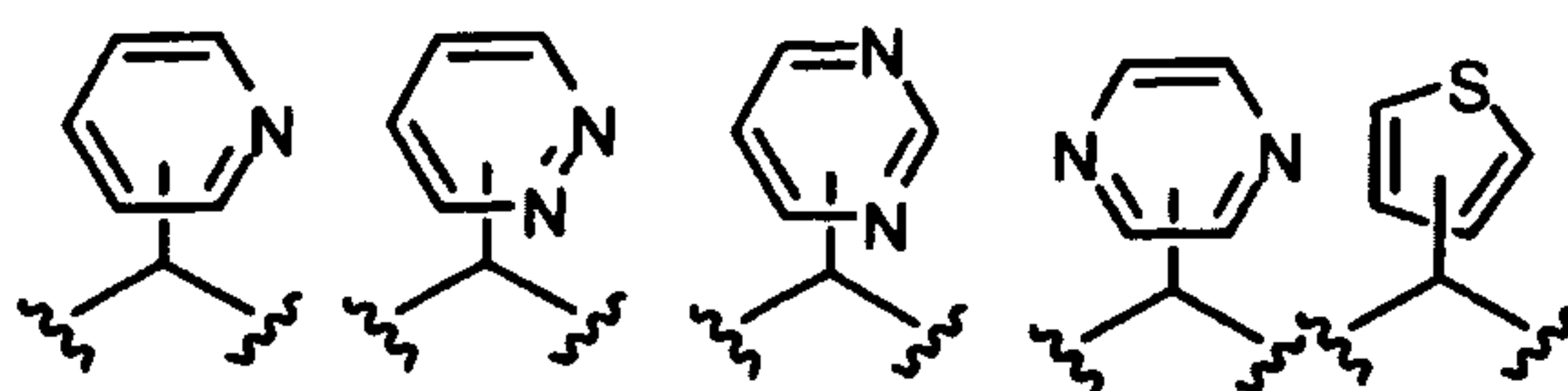
one P is P⁷ and is:

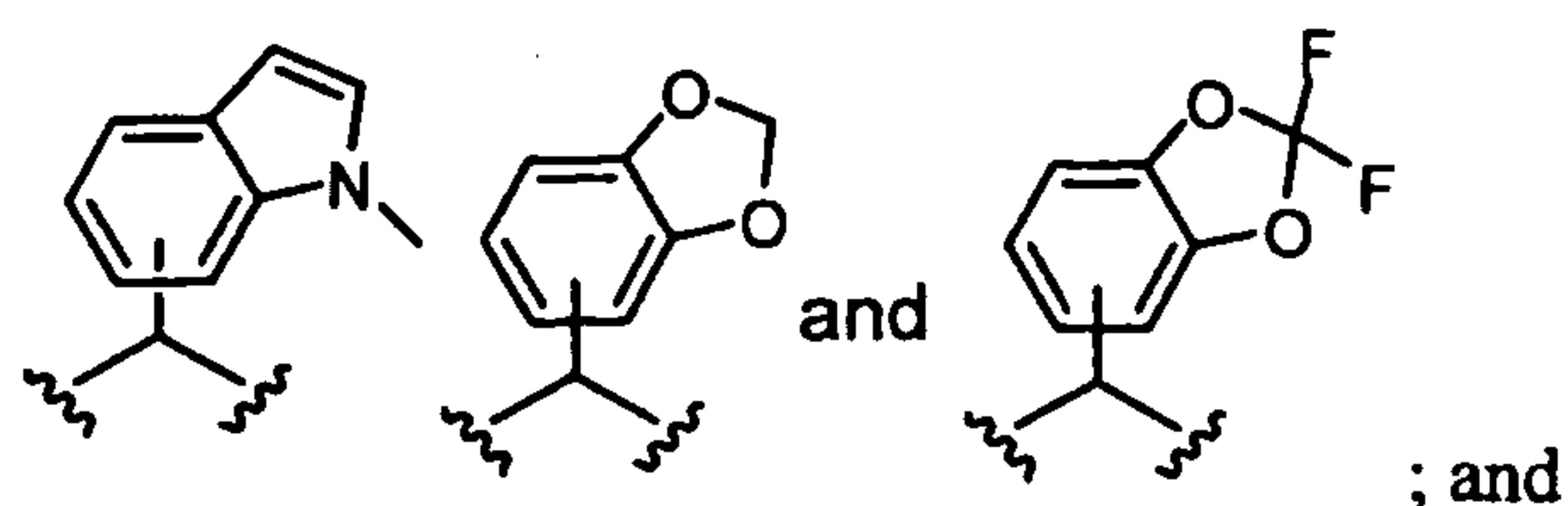


one P is P⁸ and is:

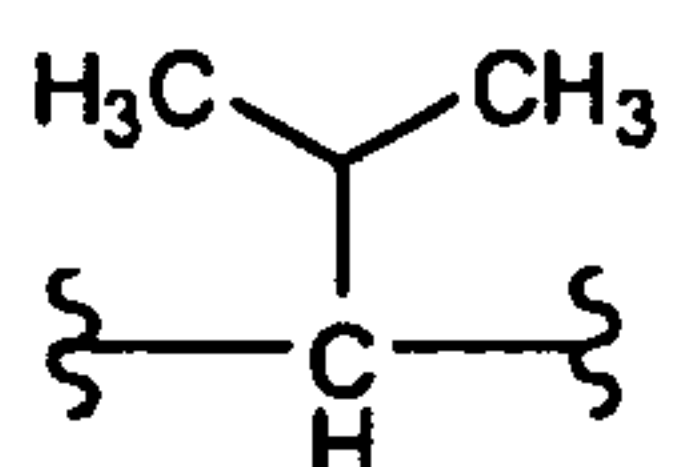


one V is selected from:





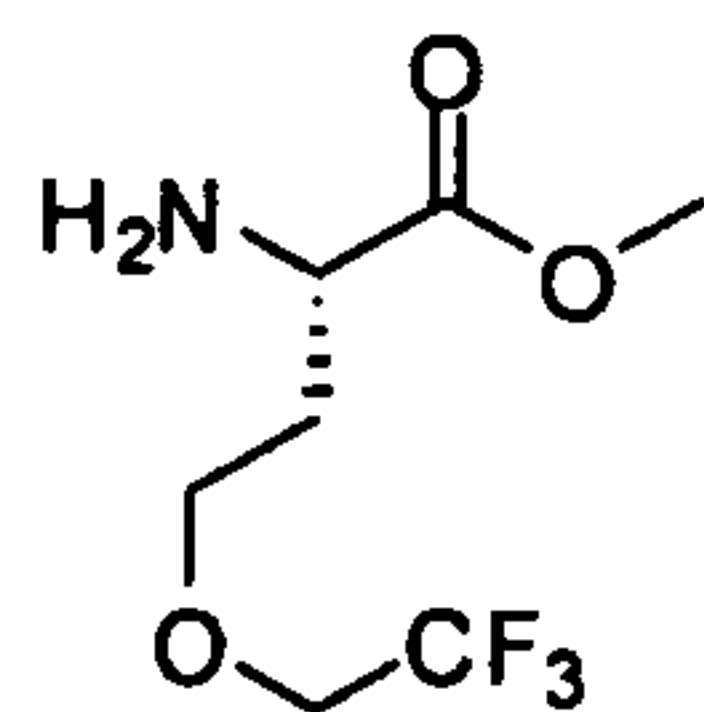
one V is:



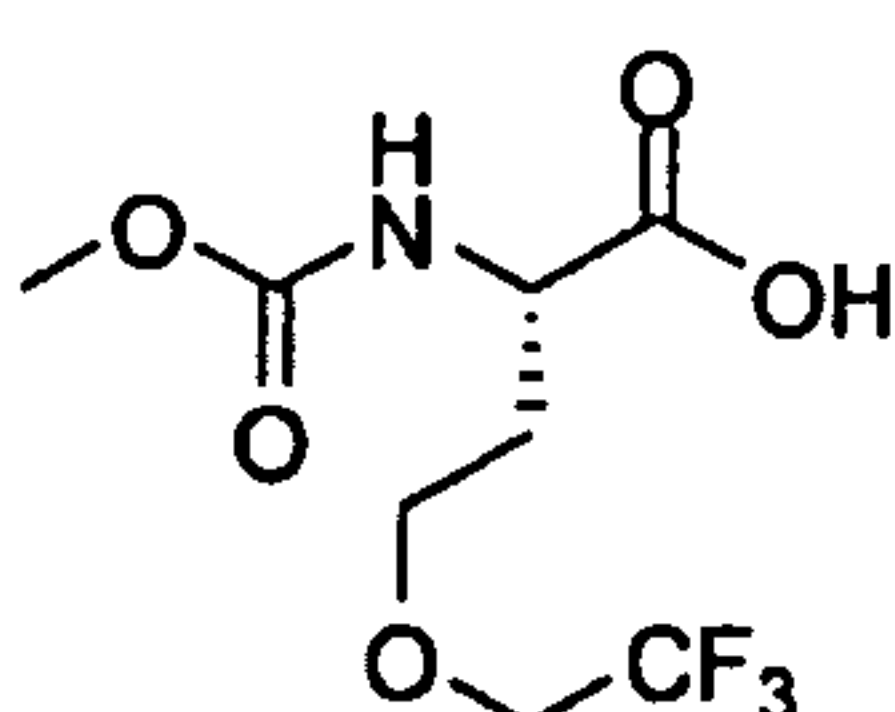
The invention provides all such combinations as specific embodiments of the invention.

Synthetic Intermediates

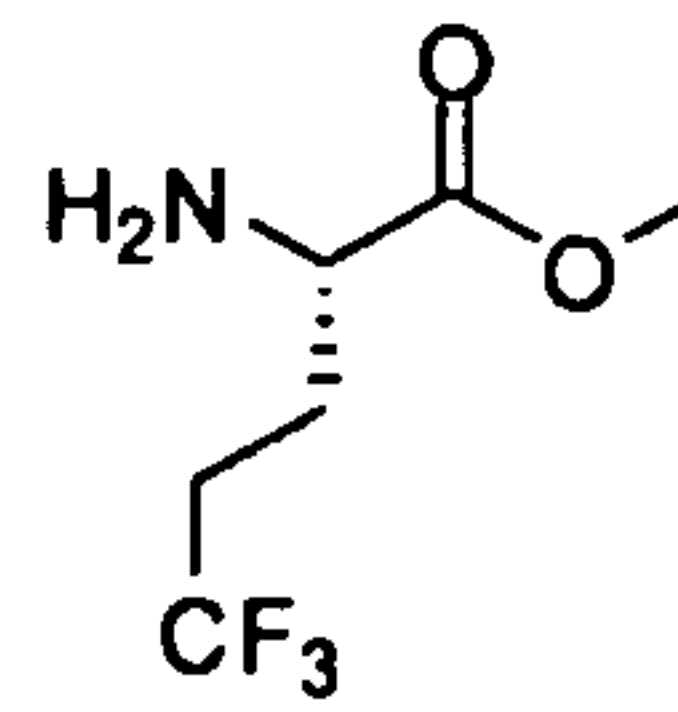
The invention also provides synthetic processes and novel synthetic intermediates disclosed herein. For example, the invention provides the following specific intermediate compounds that are useful for preparing compounds of formula (I):



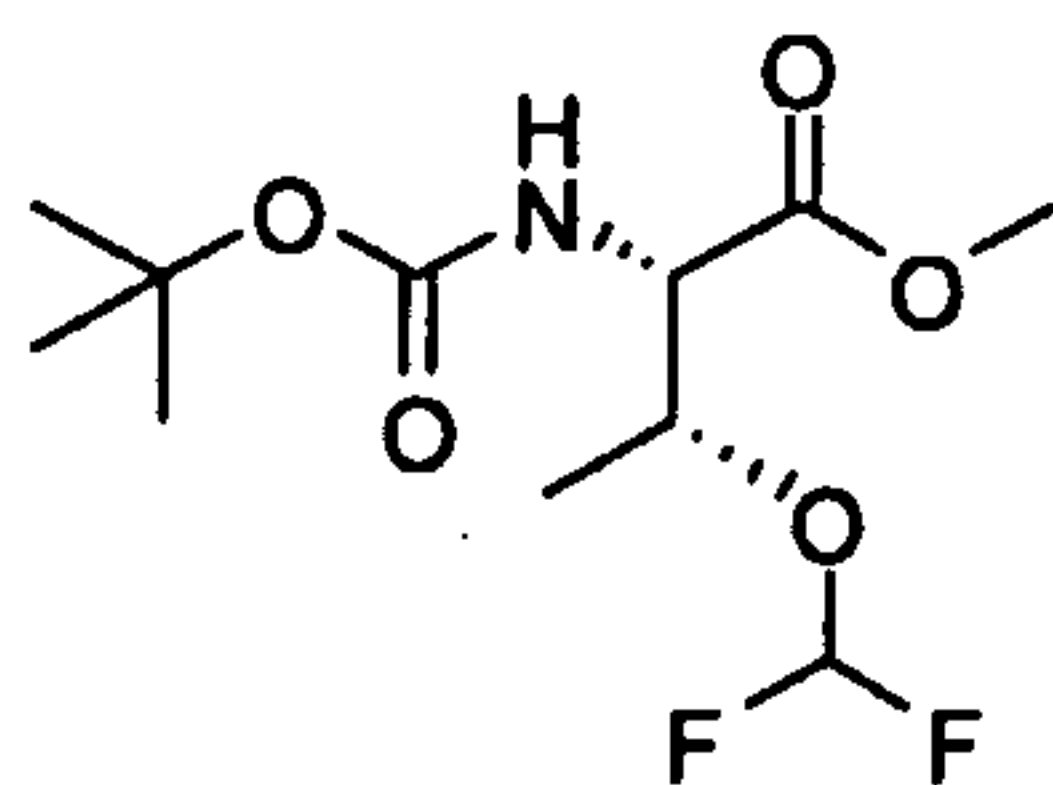
2-Amino-4-(2,2,2-trifluoro-ethoxy)-butyric acid methyl ester



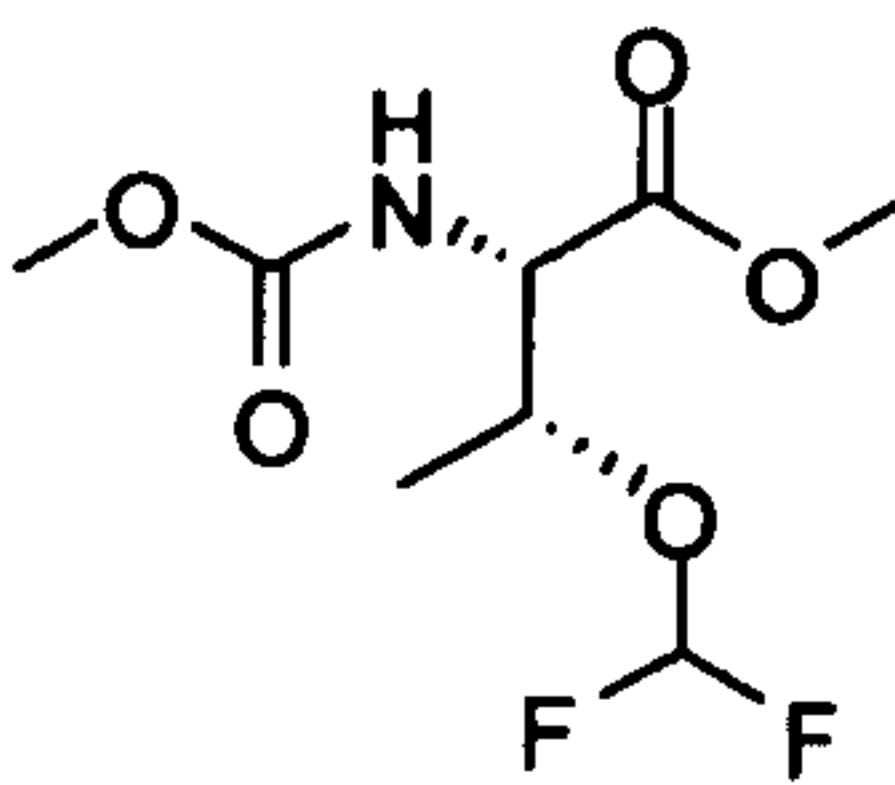
2-Methoxycarbonylamino-4-(2,2,2-trifluoro-ethoxy)-butyric acid



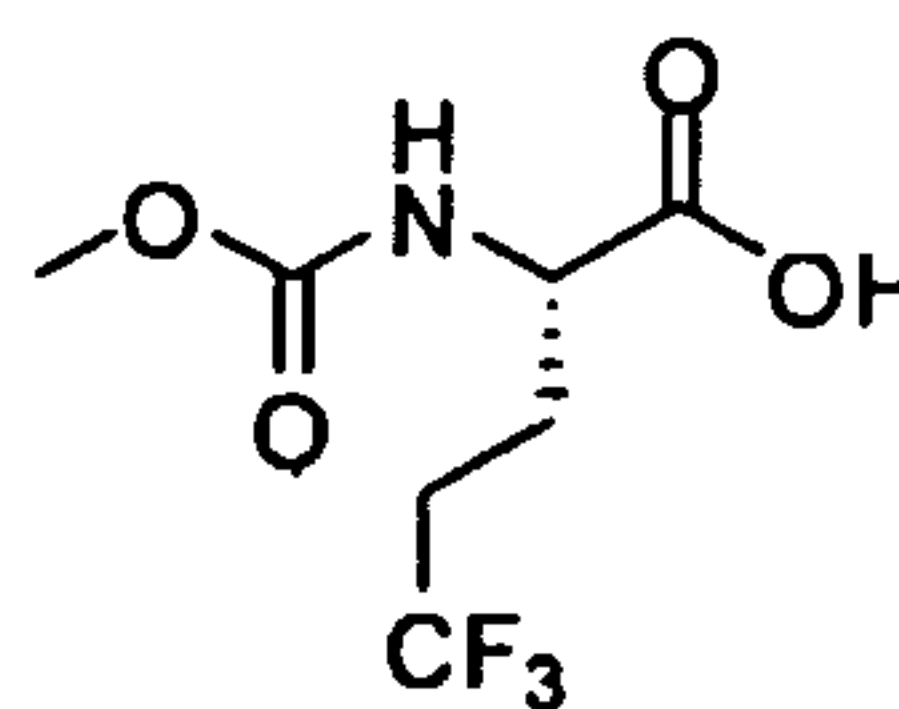
2-Amino-5,5,5-trifluoropentanoic acid methyl ester



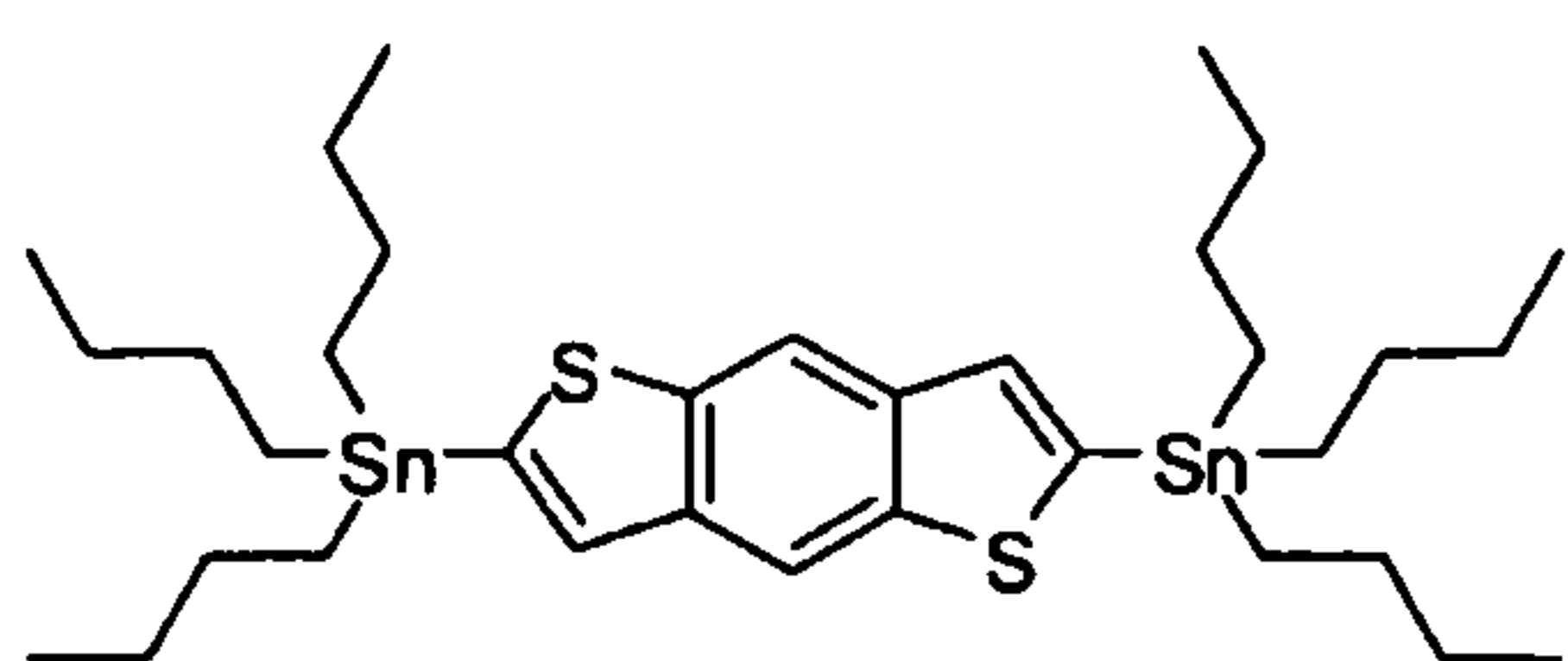
2-*tert*-Butoxycarbonylamino-3-difluoromethoxy-butylric acid methyl ester



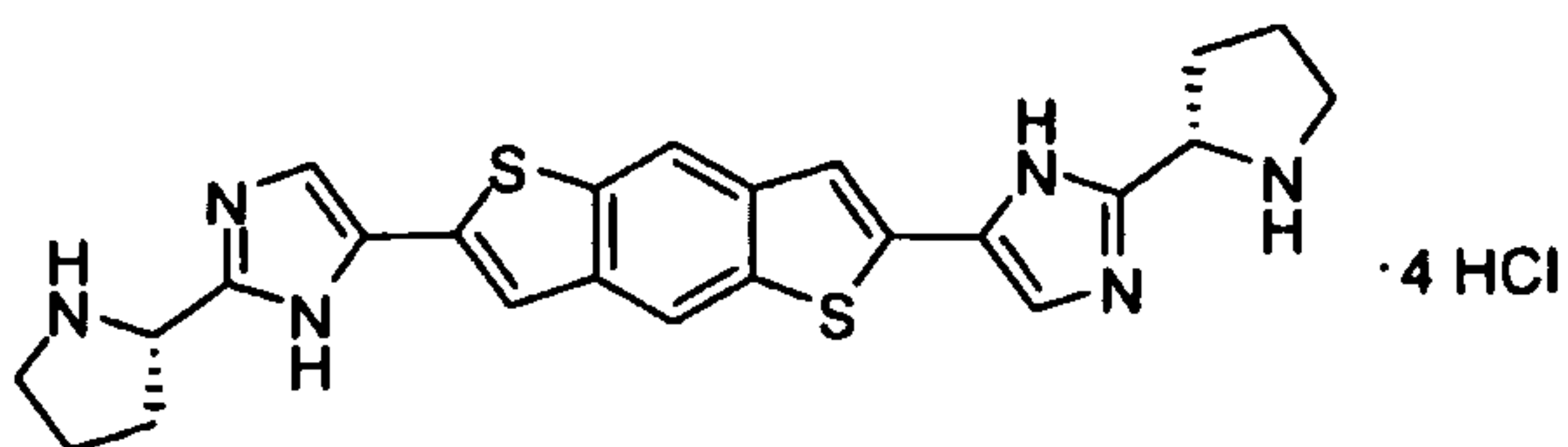
3-Difluoromethoxy-2-methoxycarbonylamino-butylric acid methyl ester



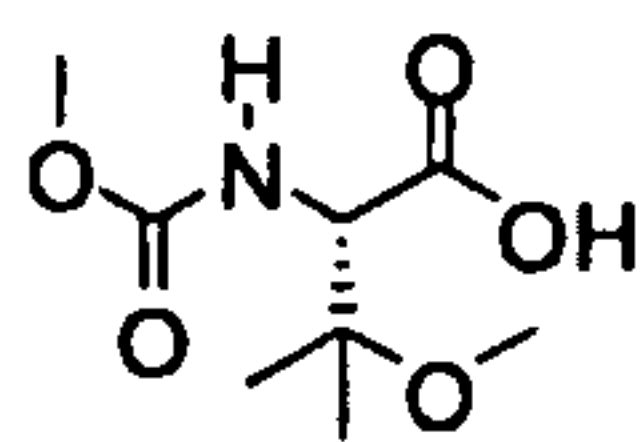
5,5,5-Trifluoro-2-methoxycarbonylamino-pentanoic acid



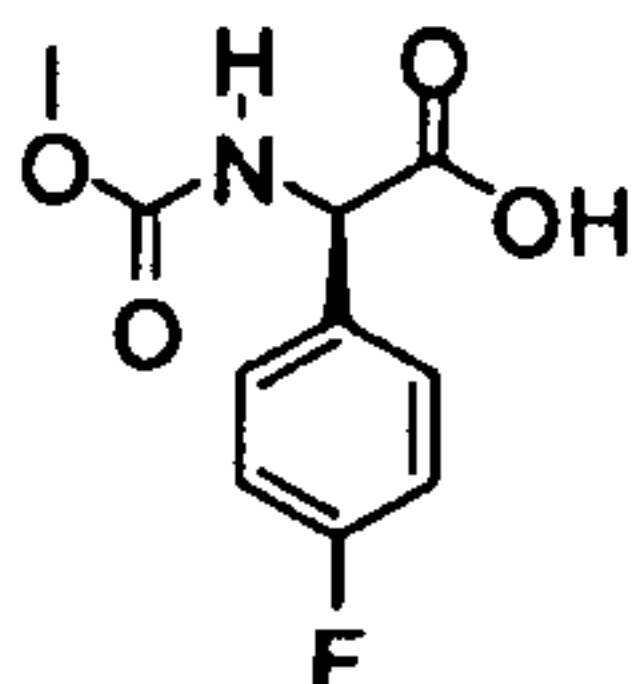
2,6-bis(tri-*n*-butylstannyl)-
benzo[1,2-*b*:4,5-*b'*]dithiophene



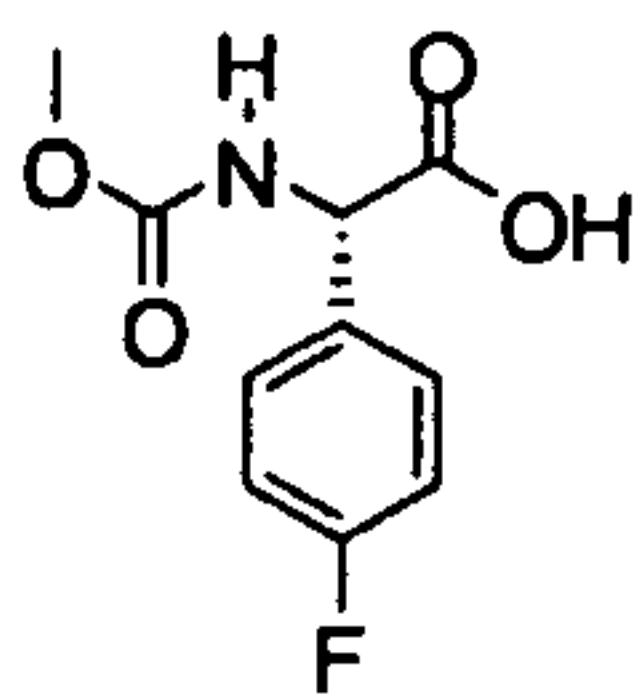
2-[5-(6-{2-[pyrrolidin-2-yl]-3*H*-imidazol-4-yl}-
benzo[1,2-*b*:4,5-*b'*]dithiophene-2-yl)-1*H*-imidazol-2-yl]-
pyrrolidine tetrahydrochloride



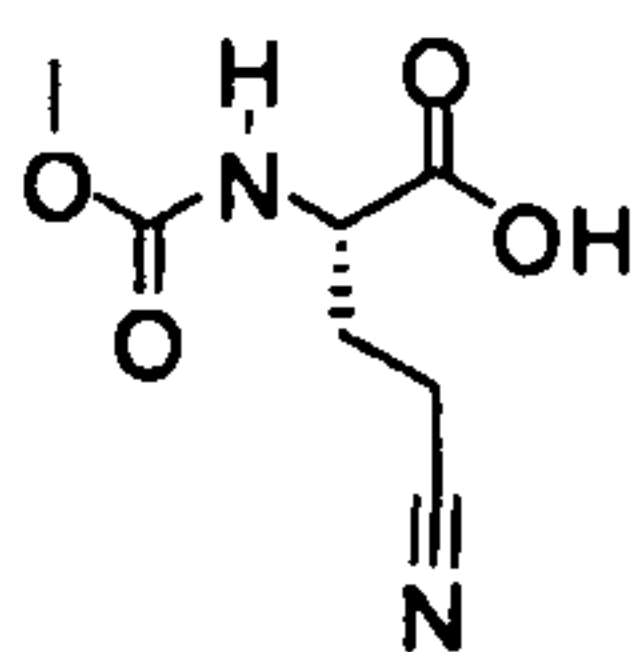
(*S*)-3-Methoxy-2-methoxycarbonylamino-
3-methylbutyric acid



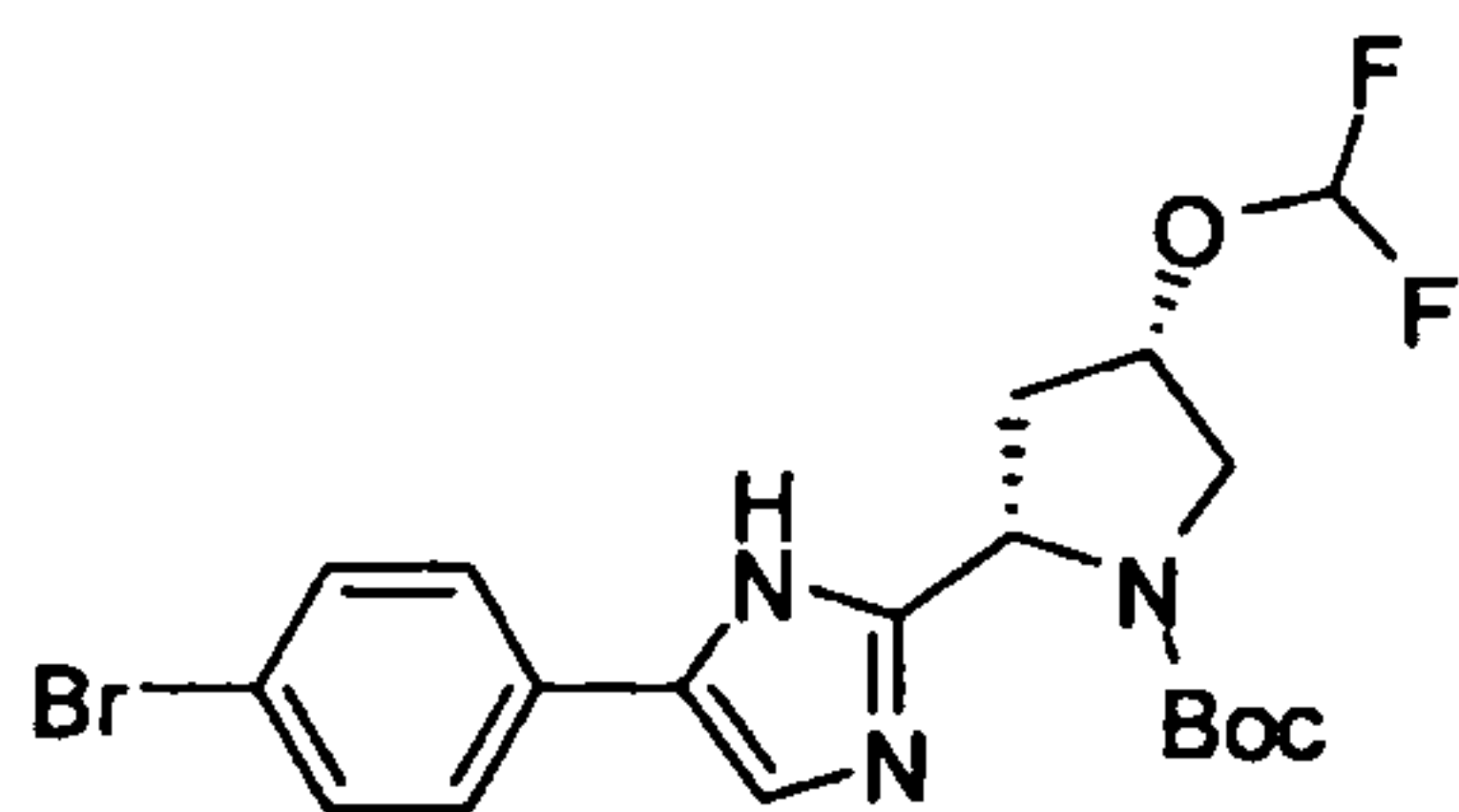
(*R*)-(4-Fluoro-phenyl)-
methoxycarbonylamino-acetic acid



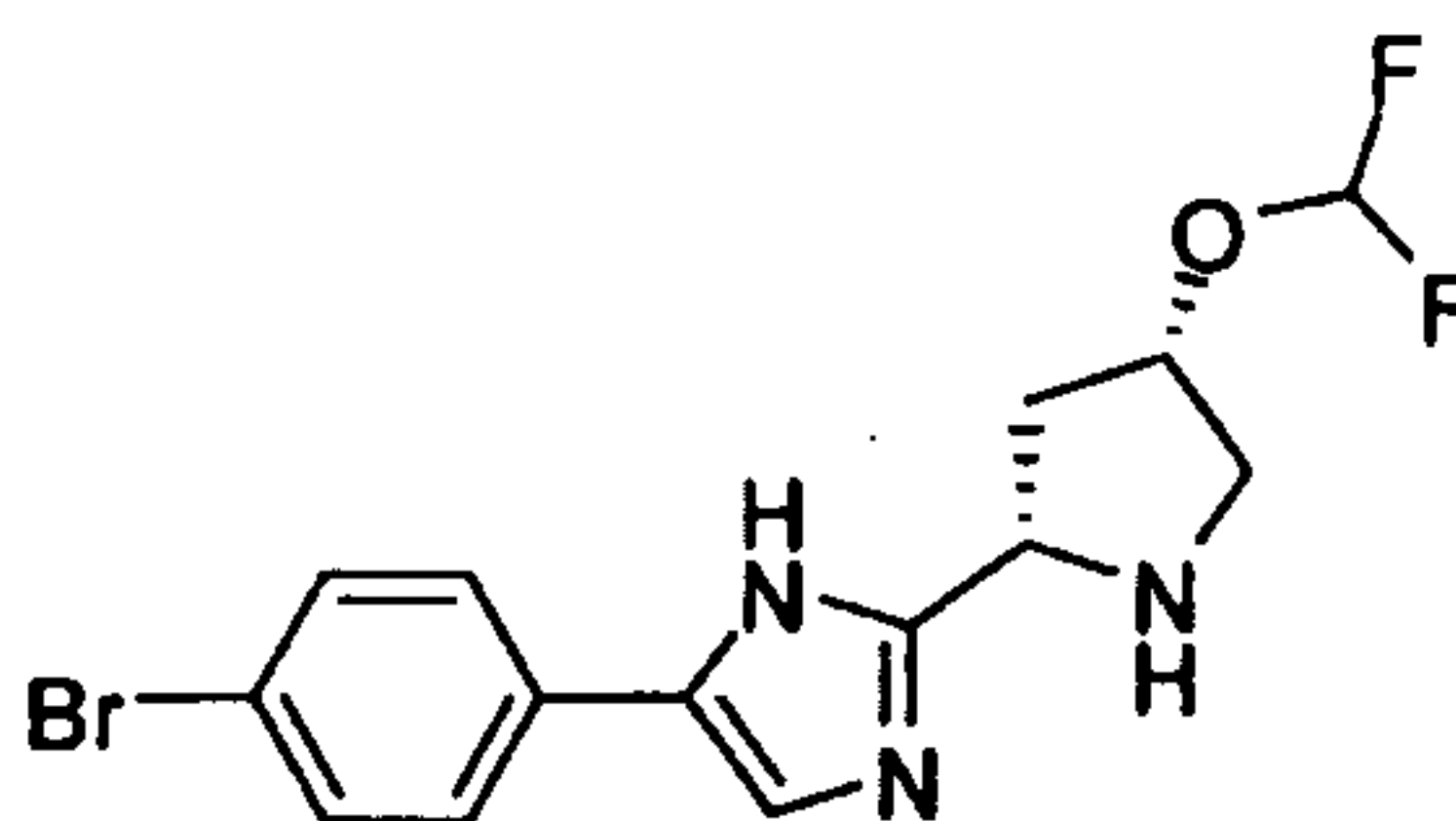
(*S*)-(4-Fluoro-phenyl)-
methoxycarbonylamino-acetic acid



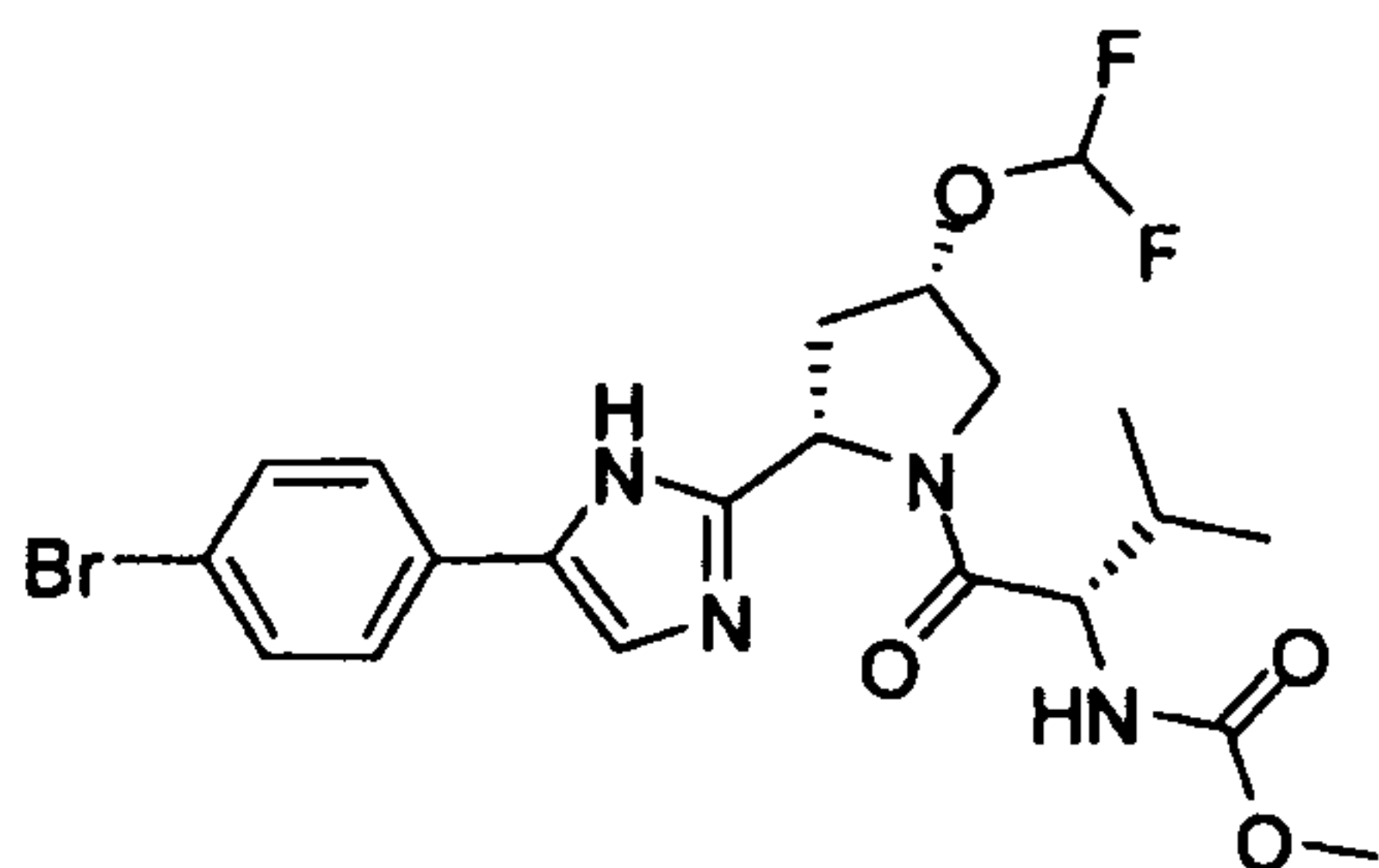
(*S*)-4-Cyano-2-methoxycarbonyl-
aminobutyric acid



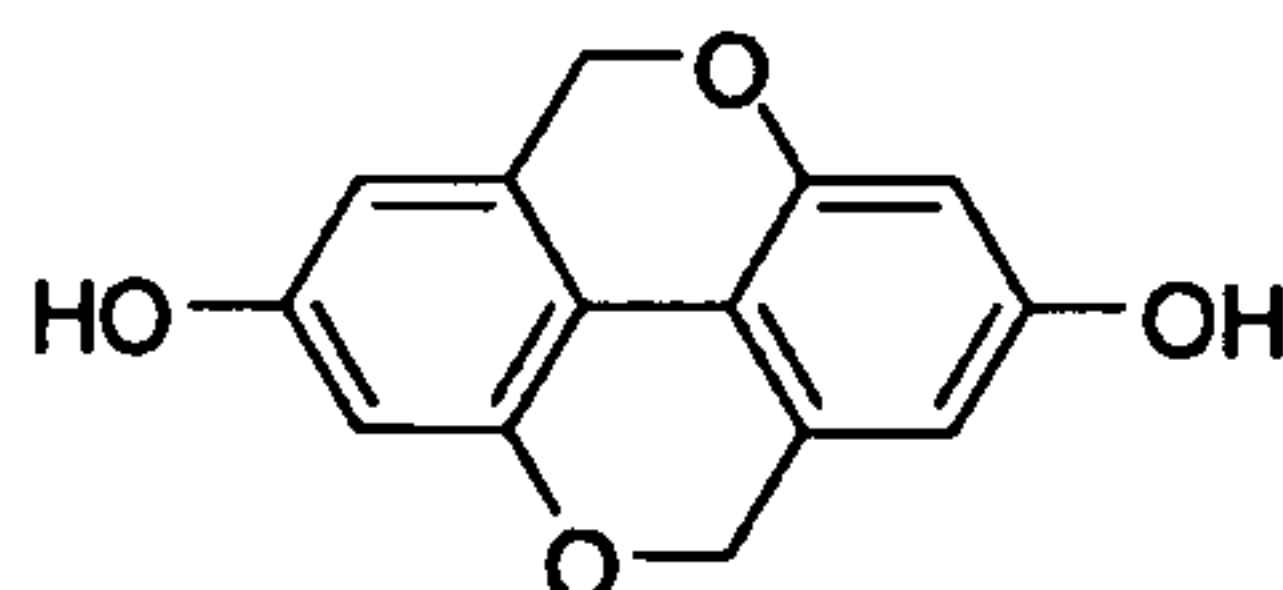
2-[5-(4-Bromo-phenyl)-1*H*-imidazol-
2-yl]-4-difluoromethoxy-pyrrolidine-
1-carboxylic acid *tert*-butyl ester



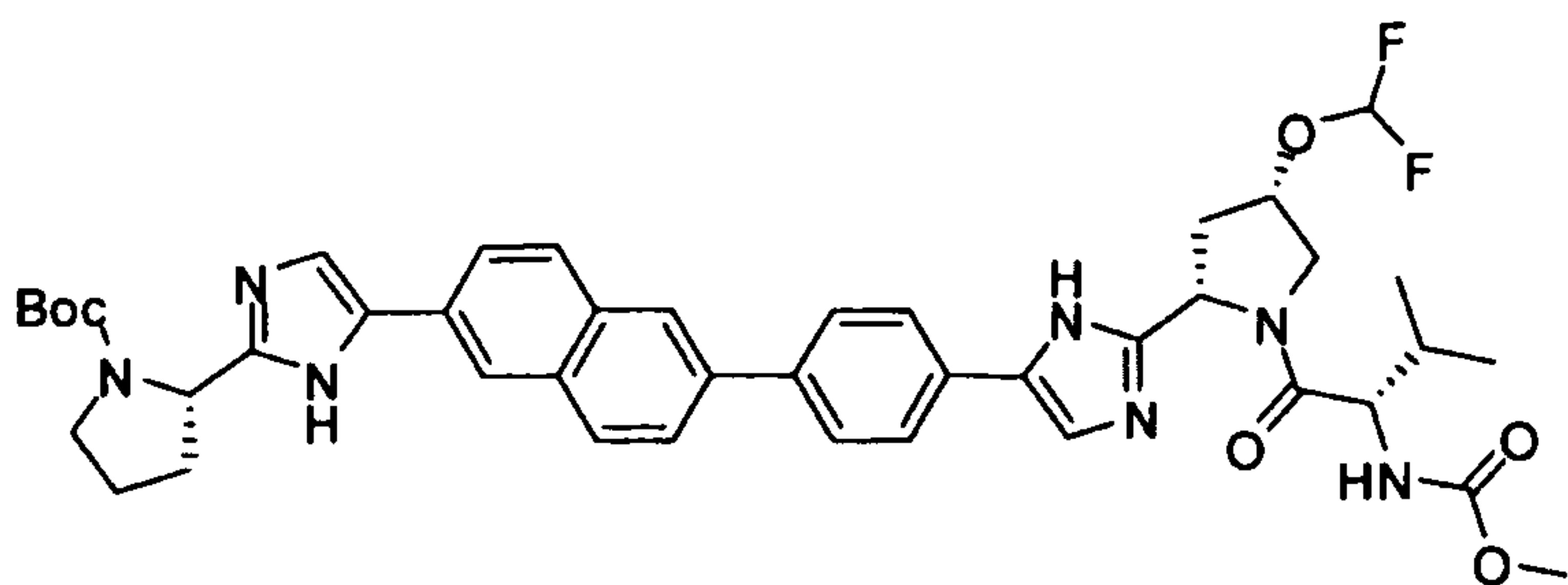
5-(4-Bromo-phenyl)-2-(4-difluoromethoxy-
pyrrolidin-2-yl)-1*H*-imidazole



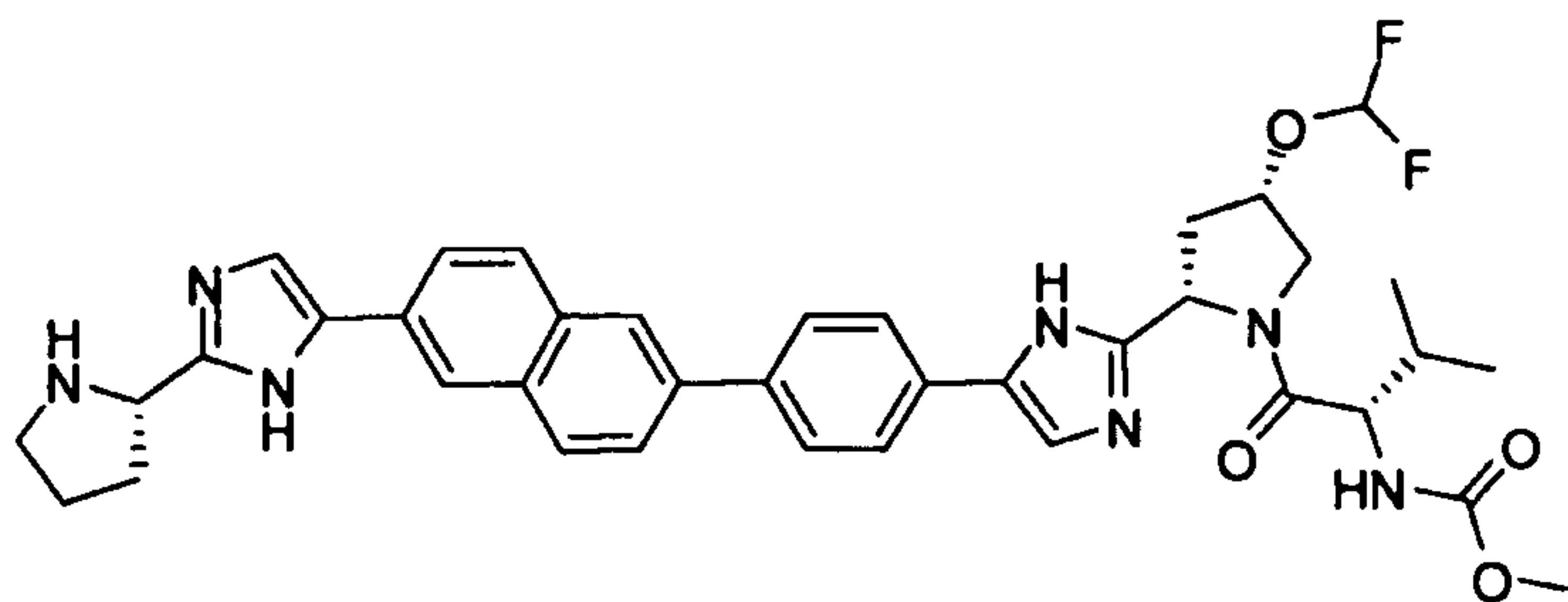
(1-{2-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-
4-difluoromethoxy-pyrrolidine-1-carbonyl}-2-
methyl-propyl)-carbamic acid methyl ester



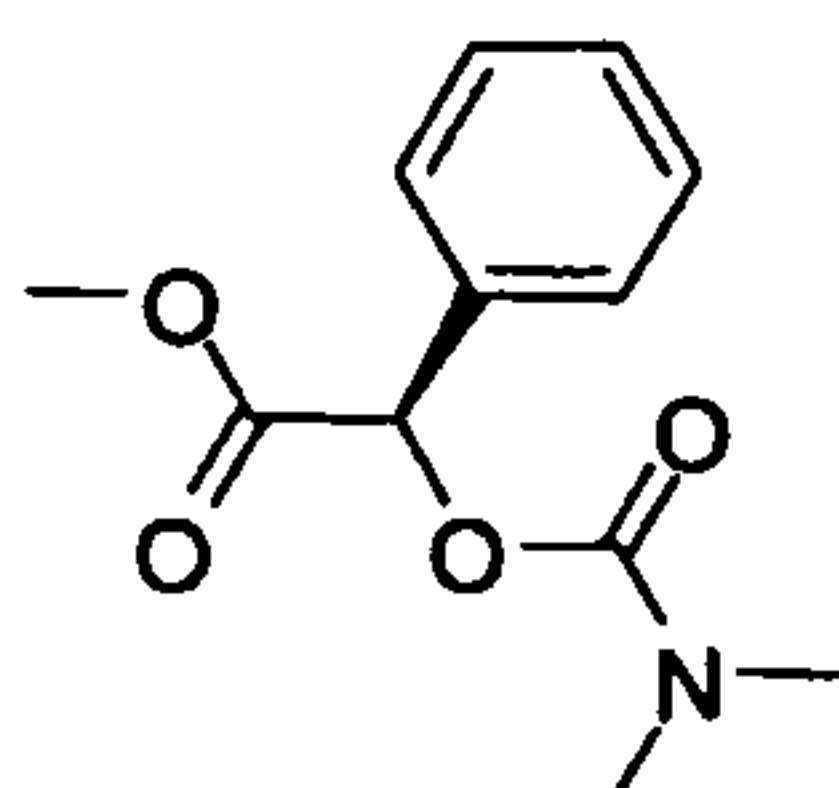
5,10-Dihydro-chromeno
[5,4,3-*cde*]chromene-2,7-diol



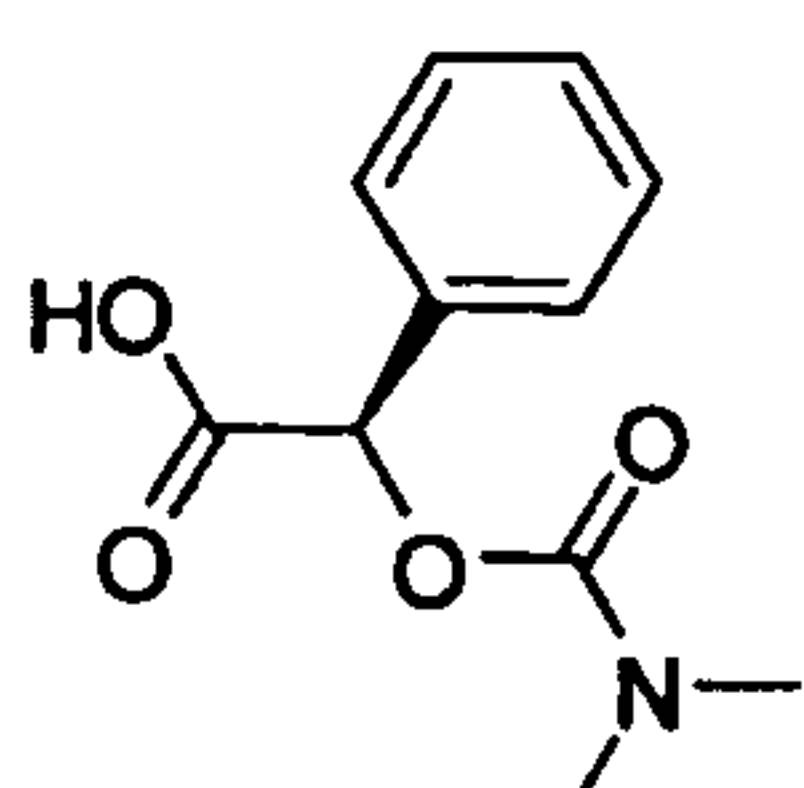
2-{5-[6-(4-{2-[4-Difluoromethoxy-1-(2-methoxycarbonylamino-3-methyl-butyl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-phenyl)-naphthalen-2-yl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester



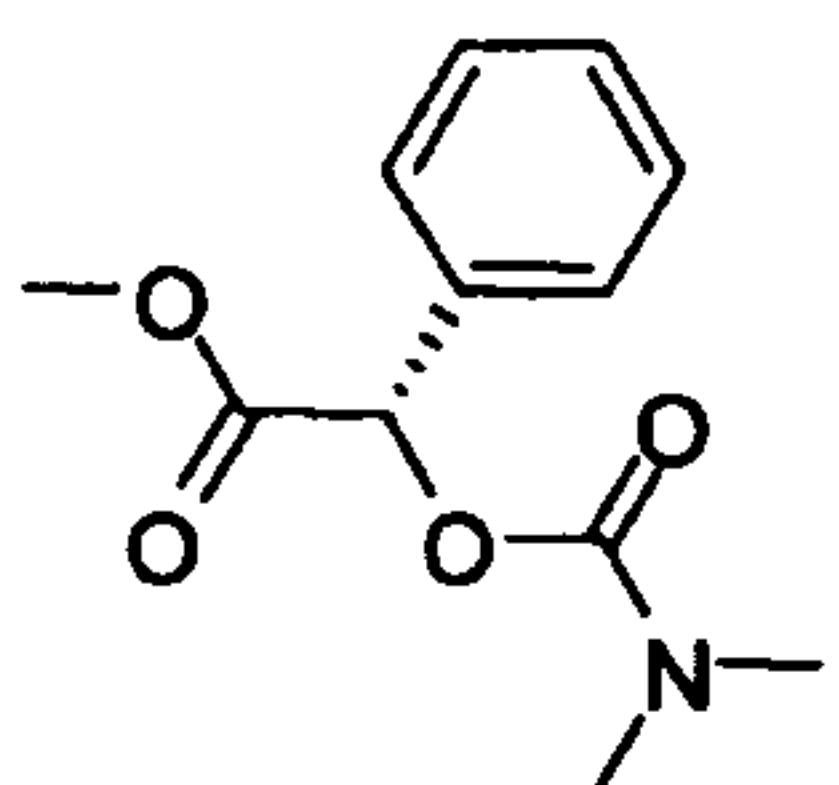
{1-[4-Difluoromethoxy-2-(5-[4-[6-(2-pyrrolidin-2-yl)-3H-imidazol-4-yl]-naphthalen-2-yl]-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl]-2-methyl-propyl}-carbamic acid methyl ester



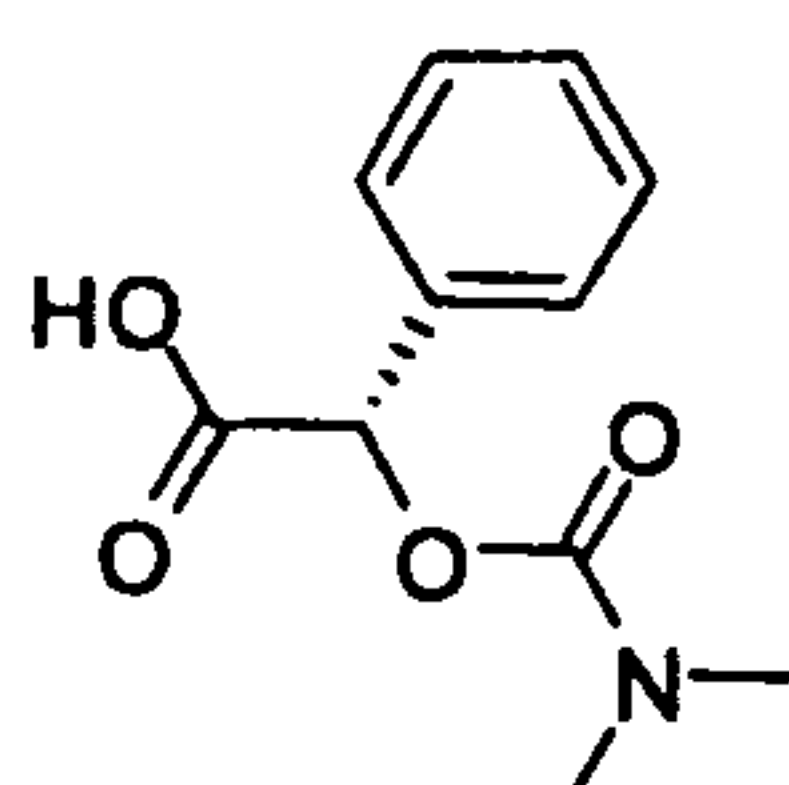
Dimethylcarbamoyloxy-phenyl-acetic acid methyl ester



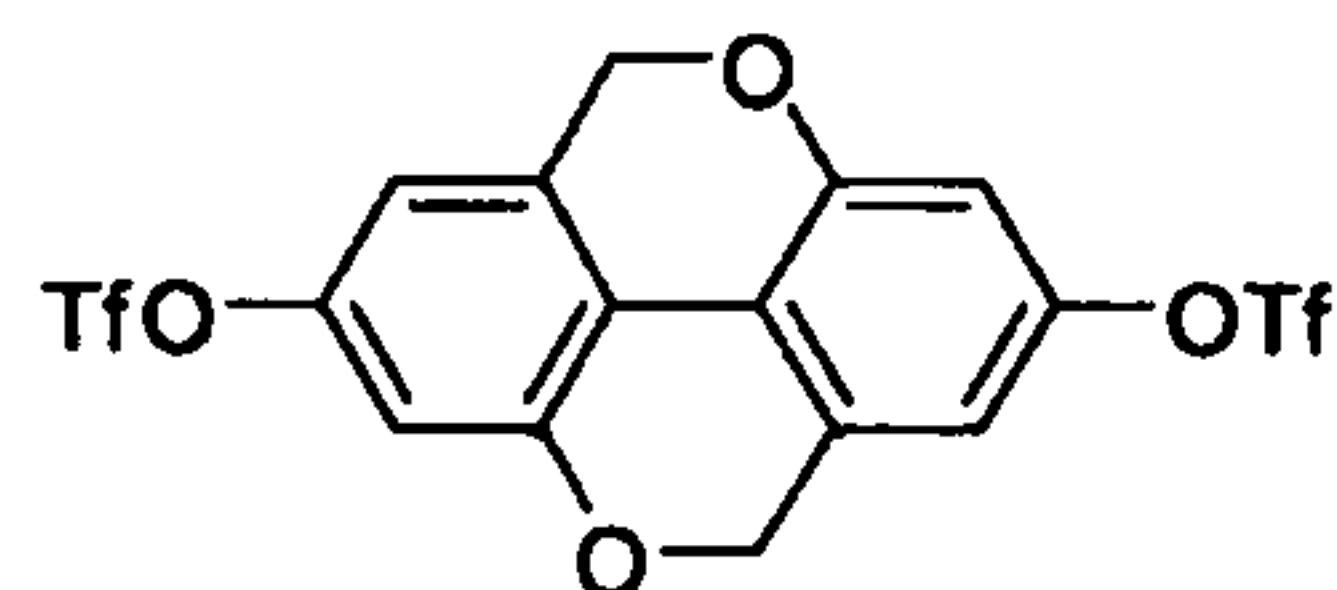
Dimethylcarbamoyloxy-phenyl-acetic acid



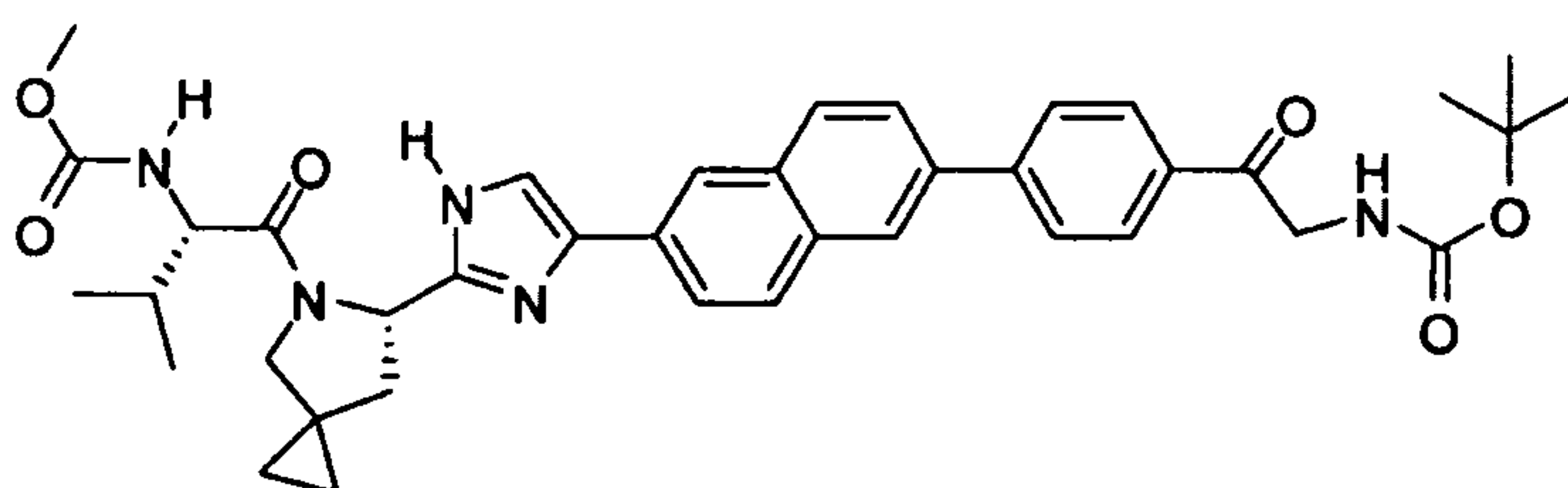
Dimethylcarbamoyloxy-phenyl-acetic acid methyl ester



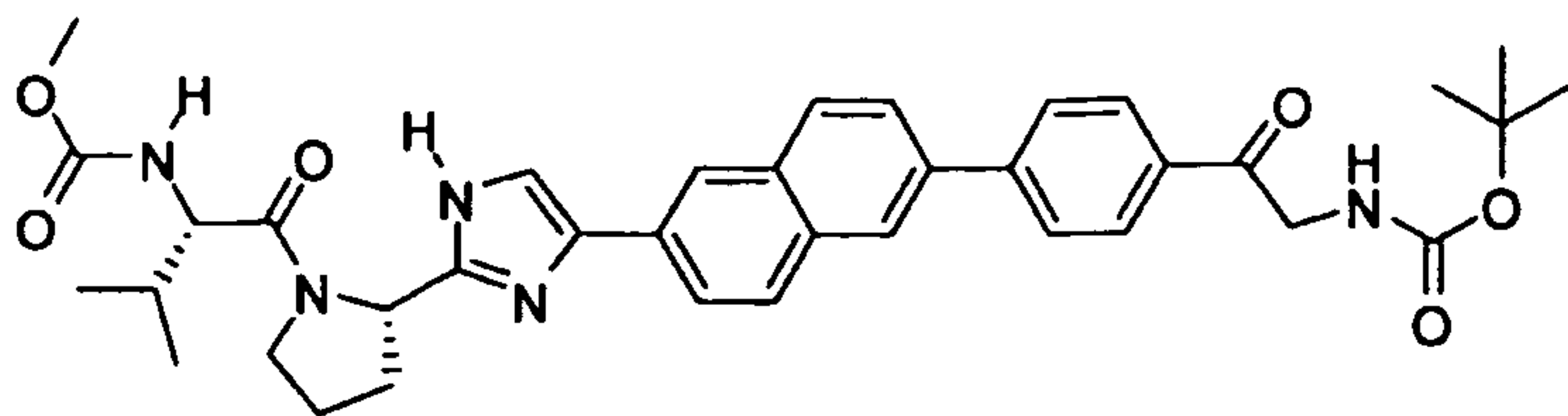
Dimethylcarbamoyloxy-phenyl-acetic acid



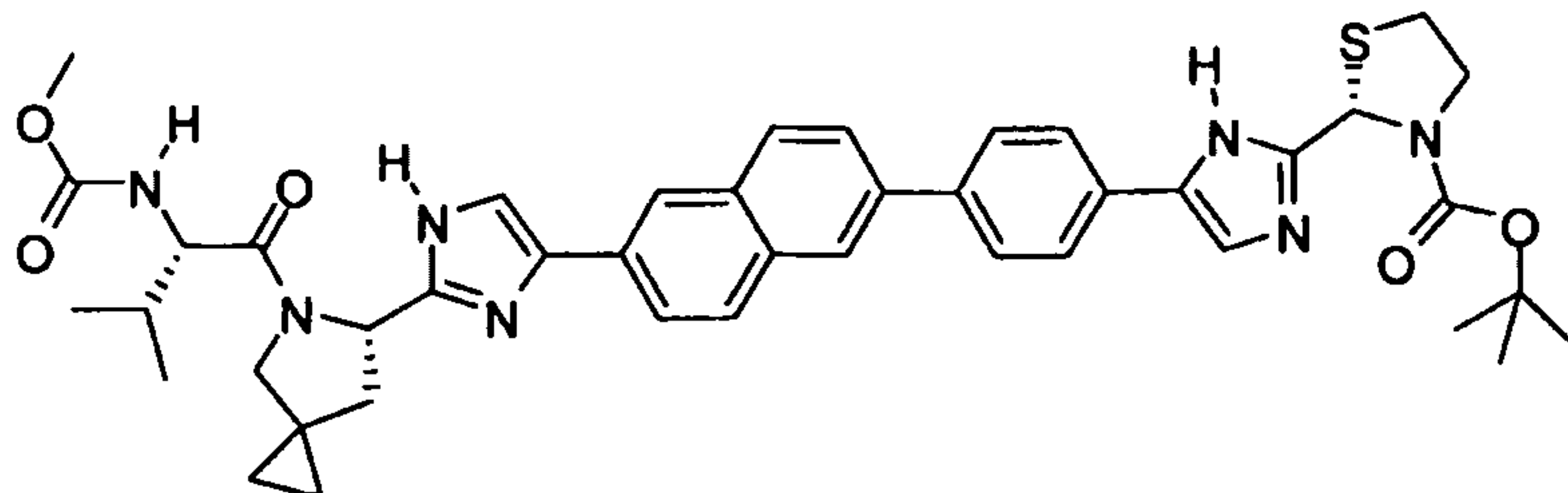
Trifluoro-methanesulfonic acid 7-trifluoro methanesulfonyloxy-5,10-dihydro-chromeno[5,4,3-cde]chromen-2-yl ester



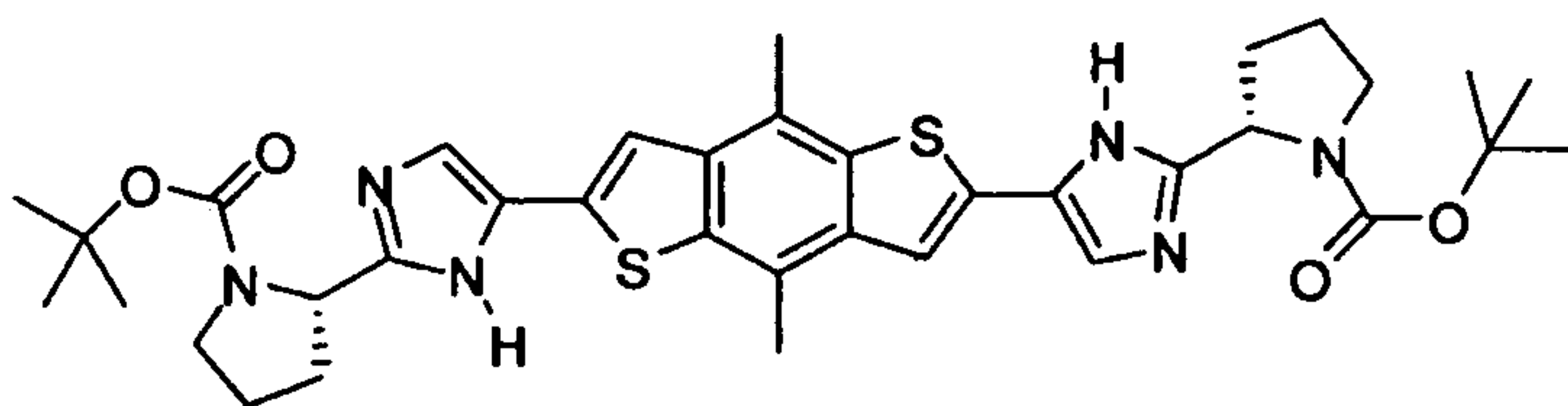
{1-[6-(4-[6-[4-(2-*tert*-Butoxycarbonylamino-acetyl)-phenyl]-naphthalen-2-yl]-1H-imidazol-2-yl)-5-aza-spiro[2.4]heptane-5-carbonyl]-2-methyl-propyl}-carbamic acid methyl ester



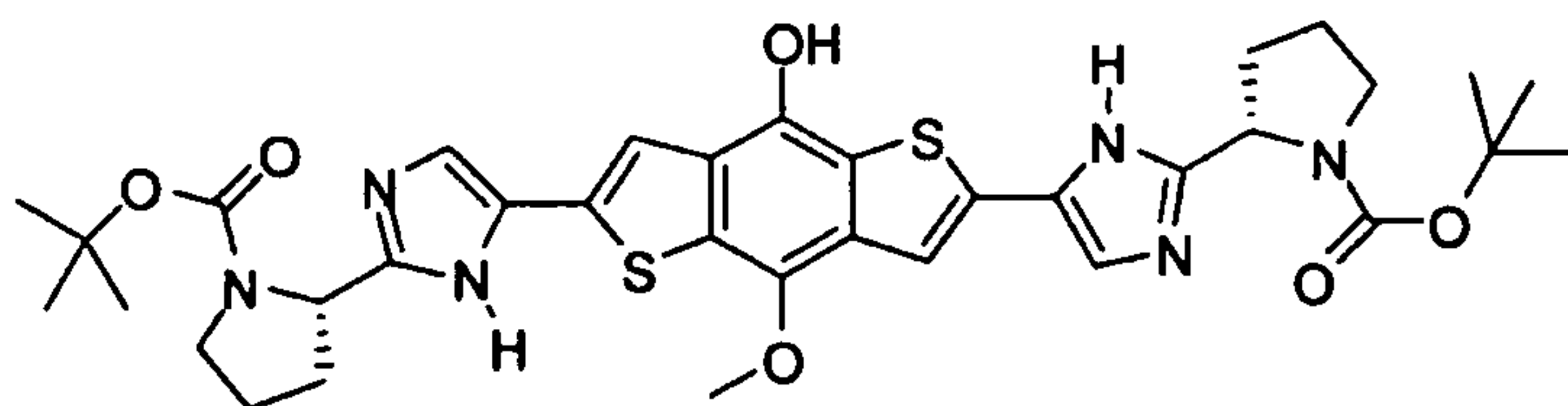
{1-[2-(4-[6-[4-(2-*tert*-Butoxycarbonylamino-acetyl)-phenyl]-naphthalen-2-yl)-1*H*-imidazol-2-yl]-pyrrolidine-1-carbonyl]-2-methyl-propyl}-carbamic acid methyl ester



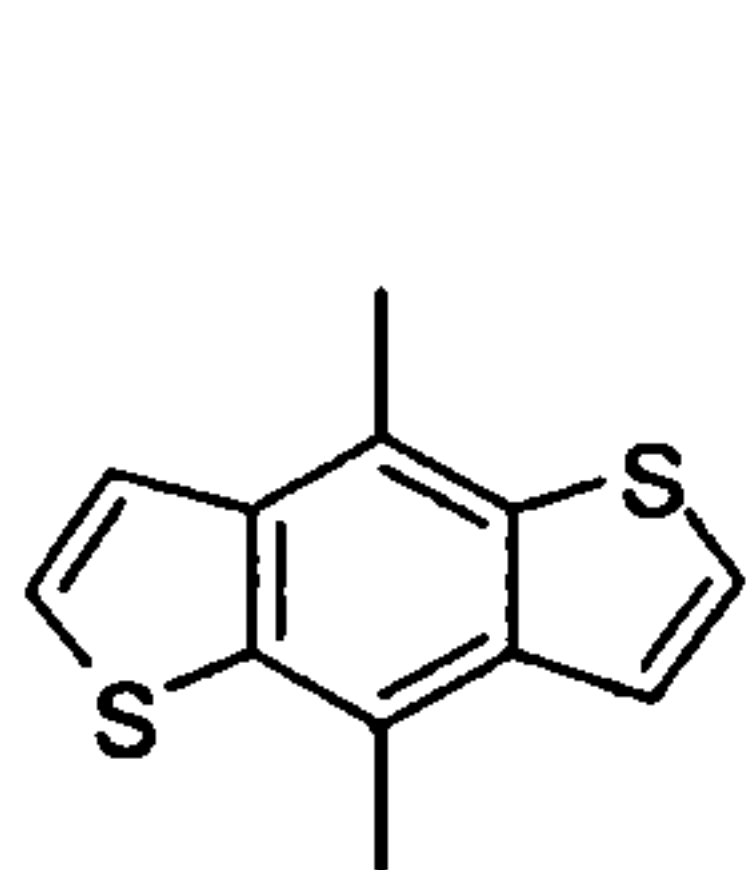
2-[5-[4-(6-[2-[5-(2-Methoxycarbonylamino-3-methyl-butyl)-5-aza-spiro[2.4]hept-6-yl]-1*H*-imidazol-4-yl)-naphthalen-2-yl]-phenyl]-1*H*-imidazol-2-yl]-thiazolidine-3-carboxylic acid *tert*-butyl ester



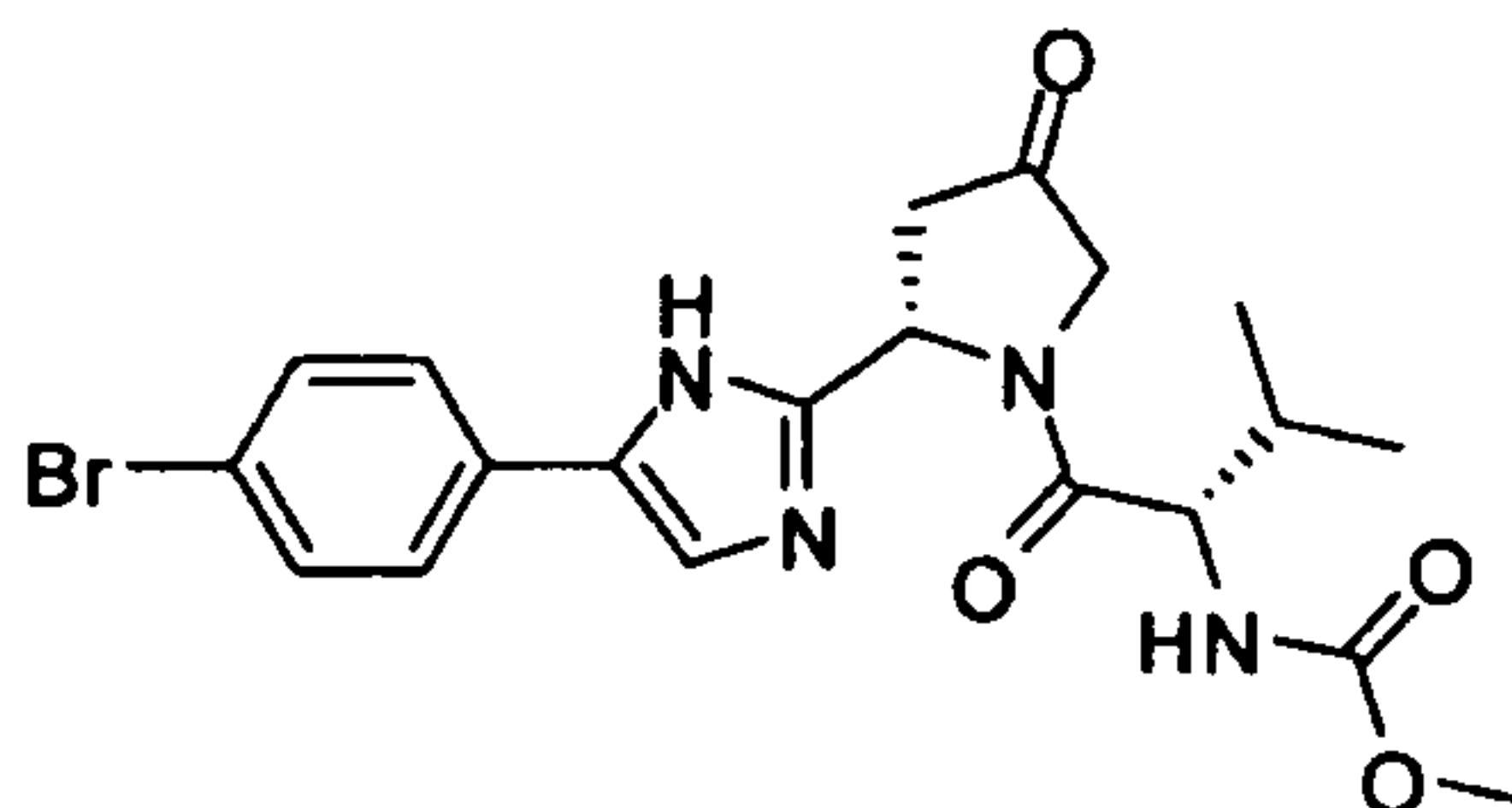
1-[2-[5-(6-[2-[1-carbamic acid *tert.* buty ester-pyrrolidin-2-yl]-3*H*-imidazol-4-yl]-4,8-dimethyl-1,5-dithia-*s*-indacen-2-yl)-1*H*-imidazol-2-yl]-pyrrolidine-1-carbamic acid *tert.*butyl ester



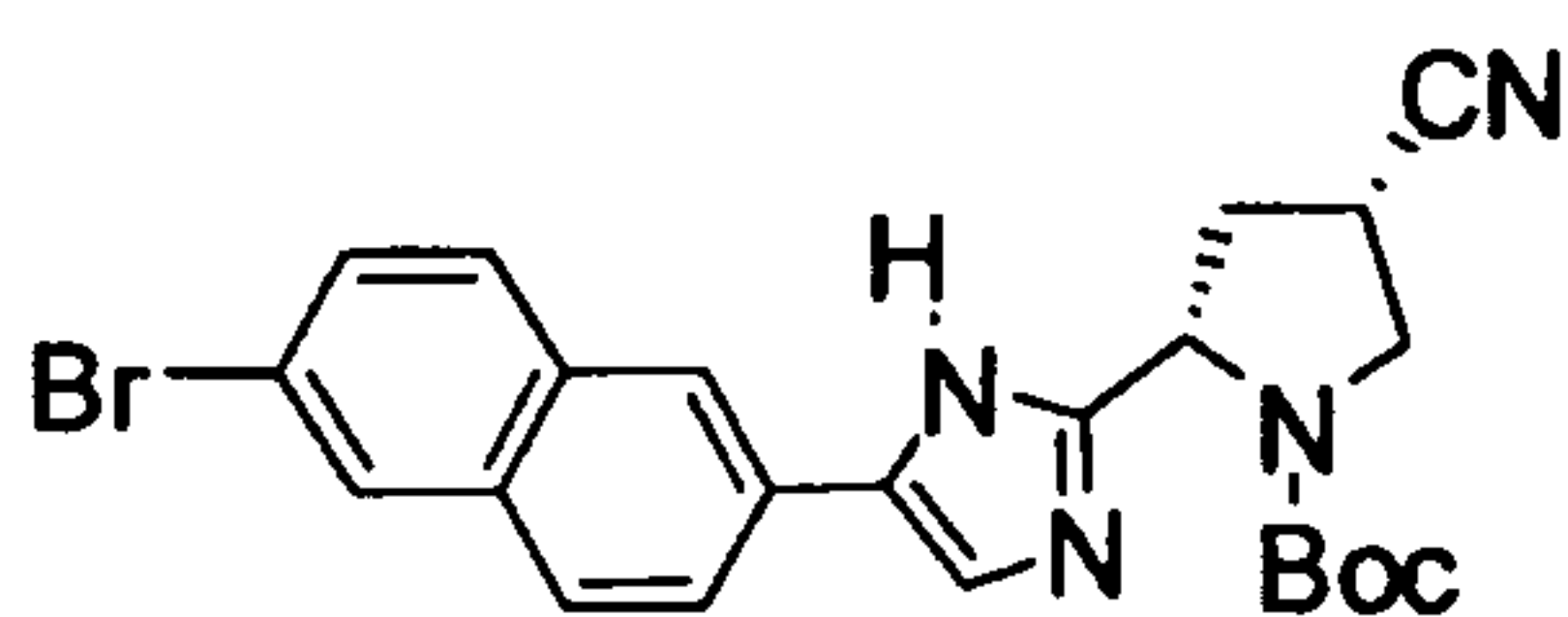
1-[2-[5-(6-[2-[1-carbamic acid *tert.* buty ester-pyrrolidin-2-yl]-3*H*-imidazol-4-yl]-4,8-dimethoxy-1,5-dithia-*s*-indacen-2-yl)-1*H*-imidazol-2-yl]-pyrrolidine-1-carbamic acid *tert.*butyl ester



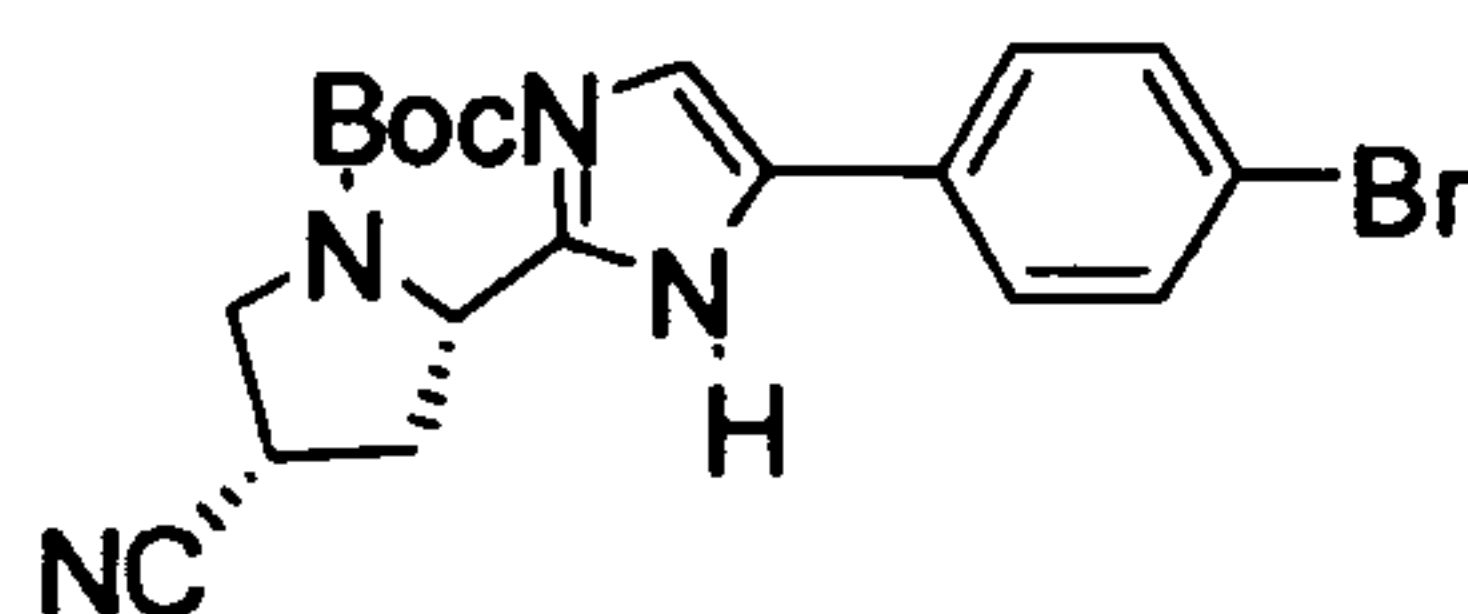
4,8-Dimethyl-1,5-dithia-*s*-indacene



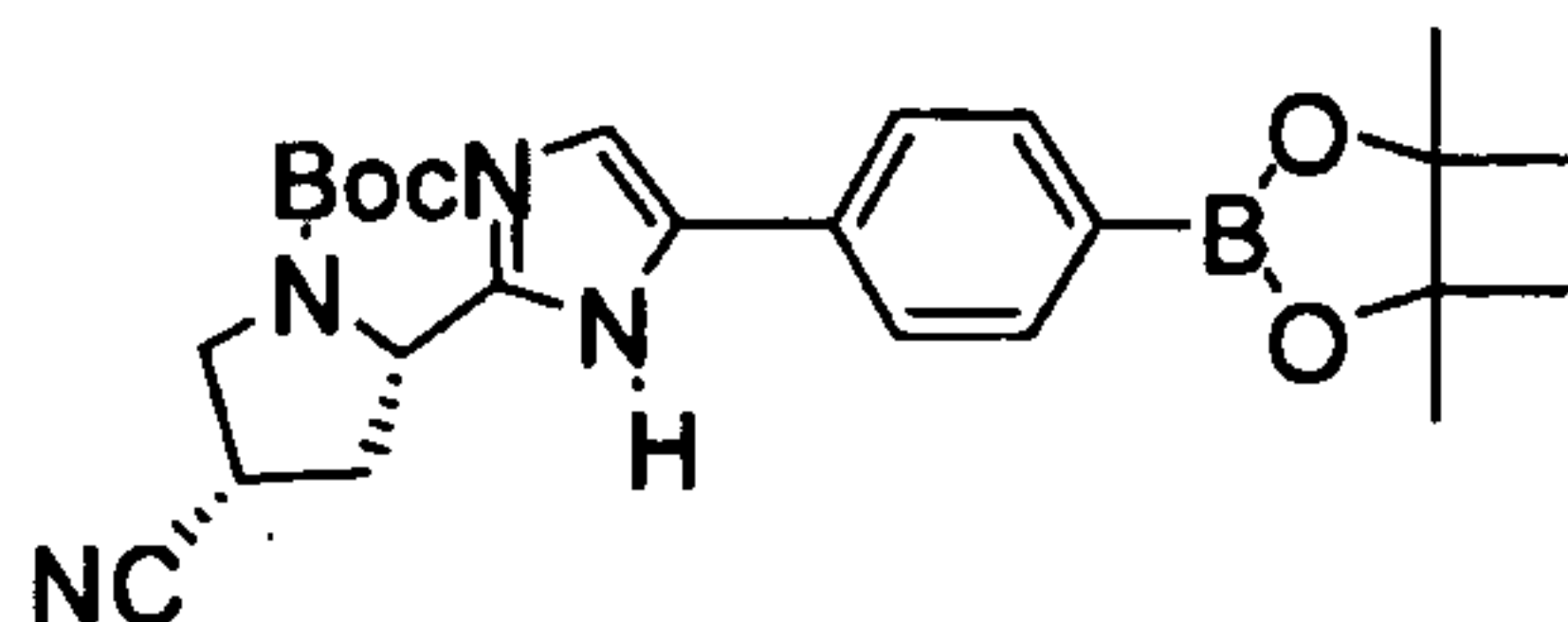
(1-[2-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-4-oxo-pyrrolidine-1-carbonyl]-2-methyl-propyl)-carbamic acid methyl ester



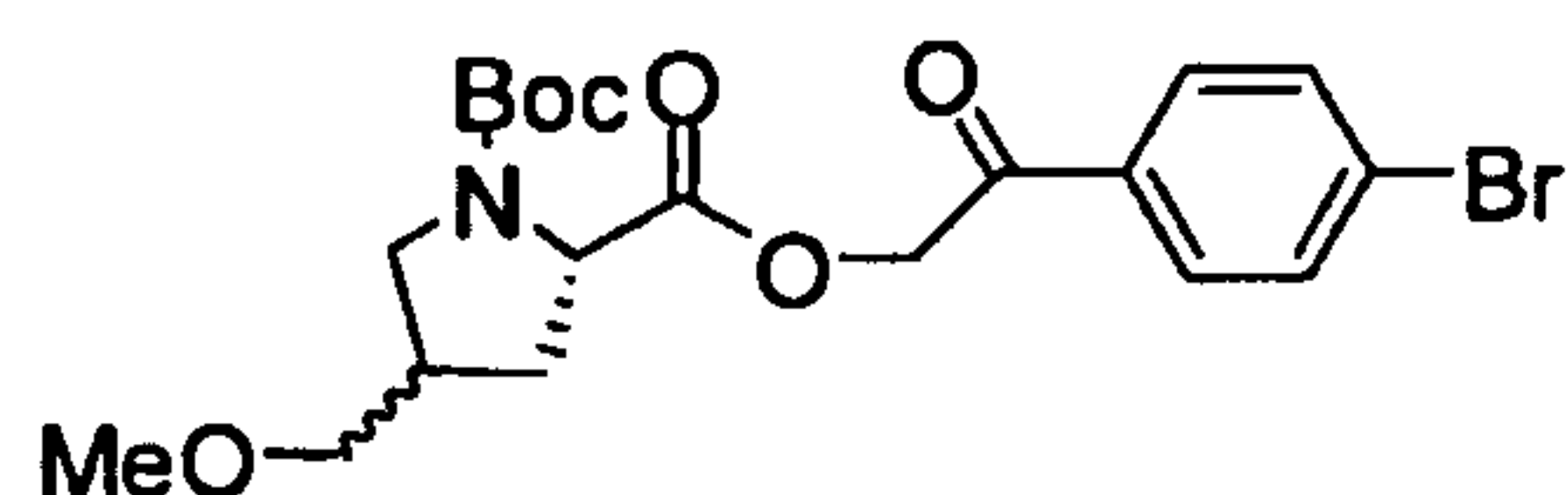
2-[5-(6-Bromo-naphthalen-2-yl)-1*H*-imidazol-2-yl]-4-cyano-pyrrolidine-1-carboxylic acid *tert*-butyl ester



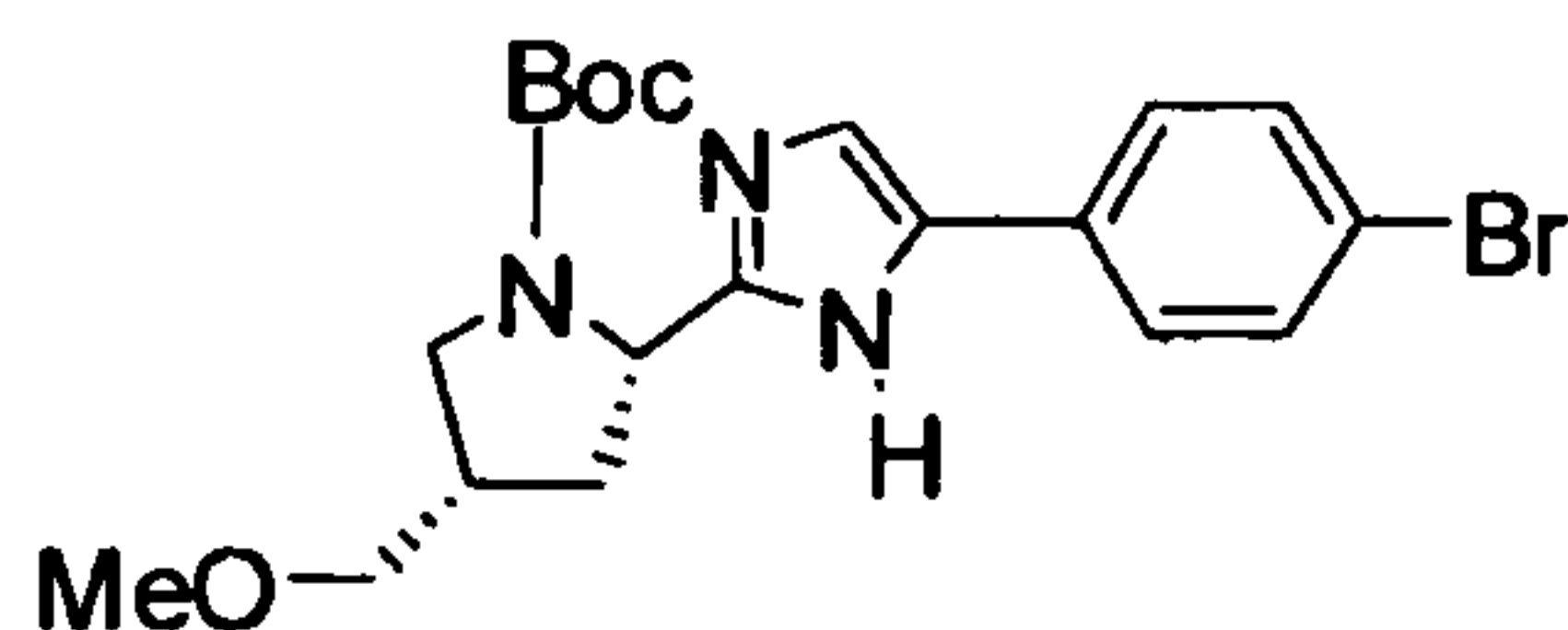
2-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-4-cyano-pyrrolidine-1-carboxylic acid *tert*-butyl ester



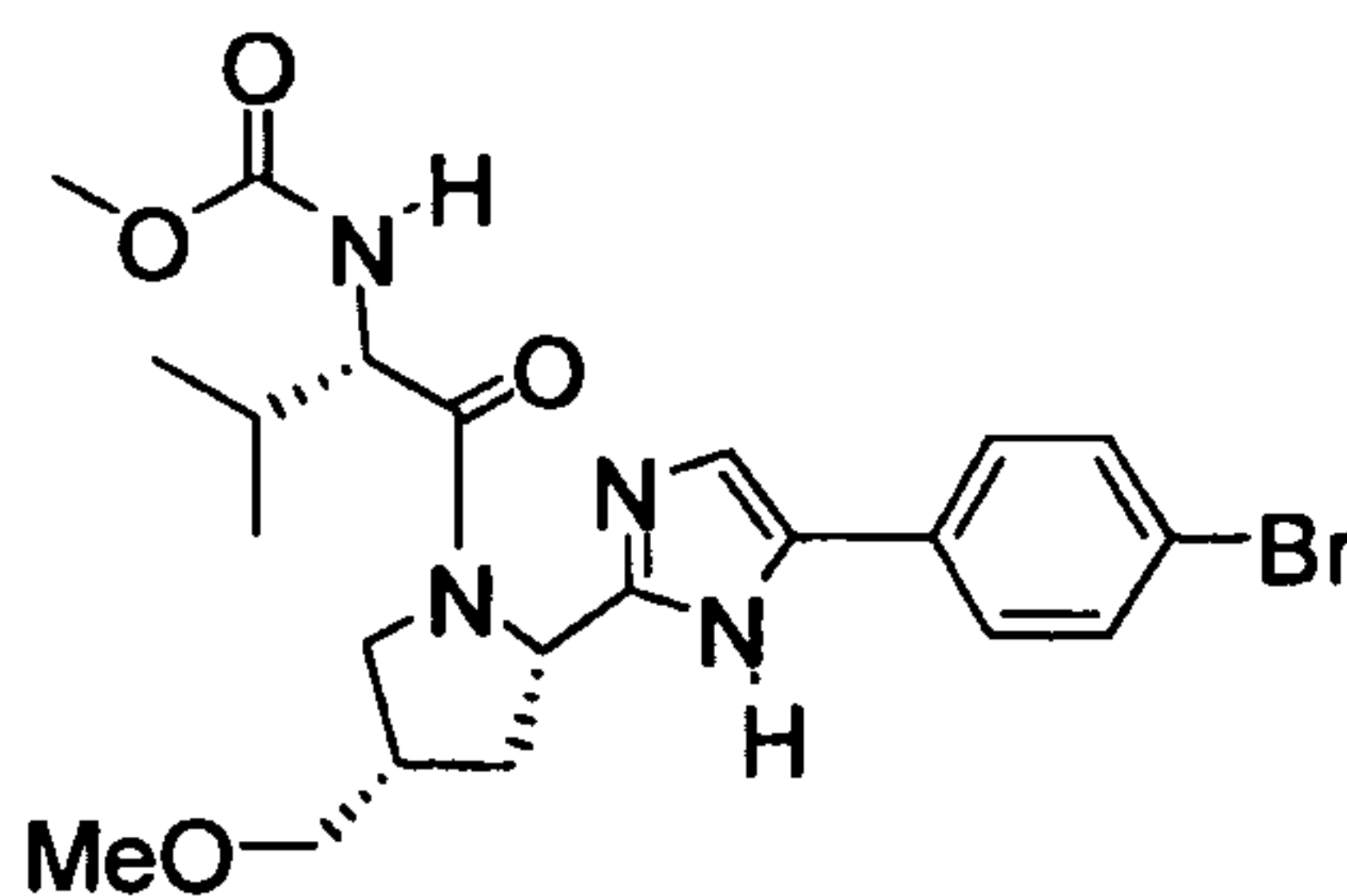
4-Cyano-2-[5-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-phenyl]-1*H*-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester



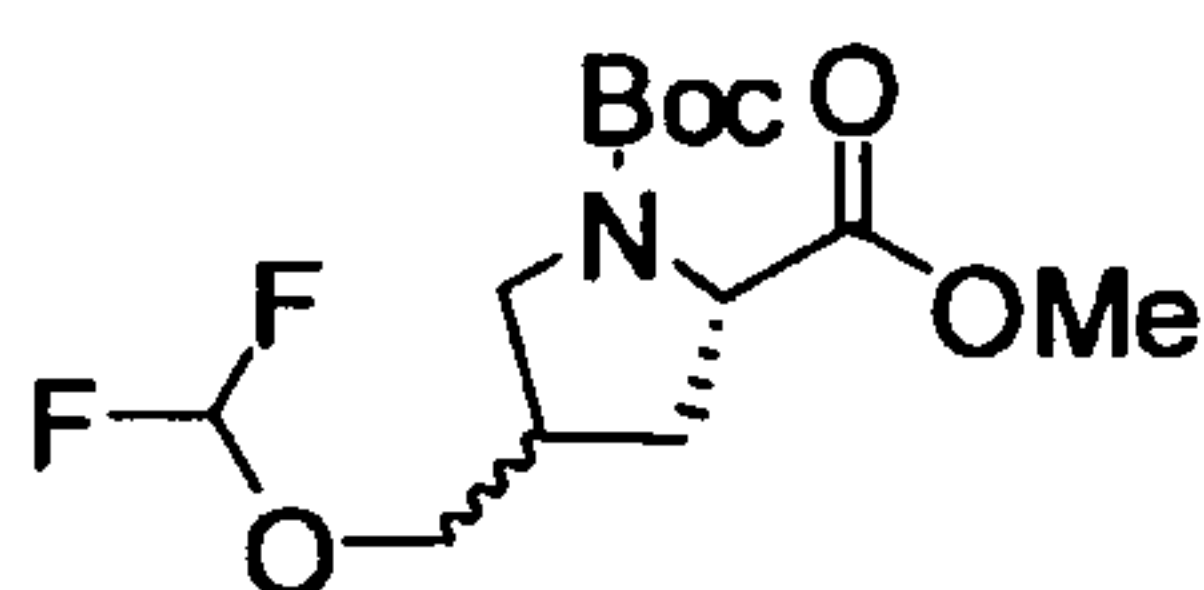
4-Methoxymethyl-pyrrolidine-1,2-dicarboxylic acid 2-[2-(4-bromophenyl)-2-oxo-ethyl] ester 1-*tert*-butyl ester



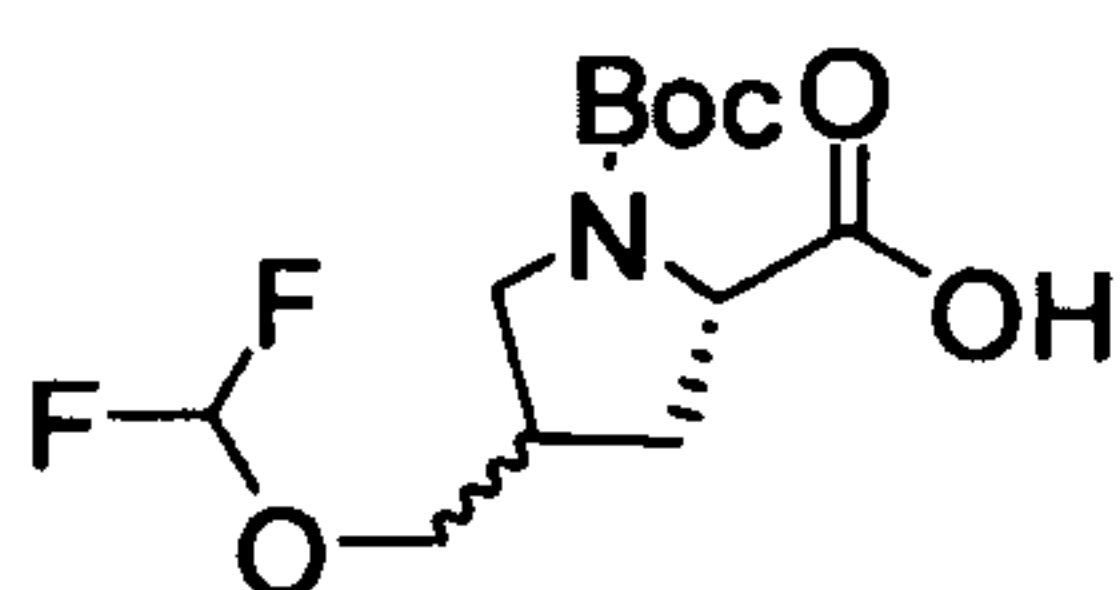
2-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-4-methoxymethyl-pyrrolidine-1-carboxylic acid *tert*-butyl ester



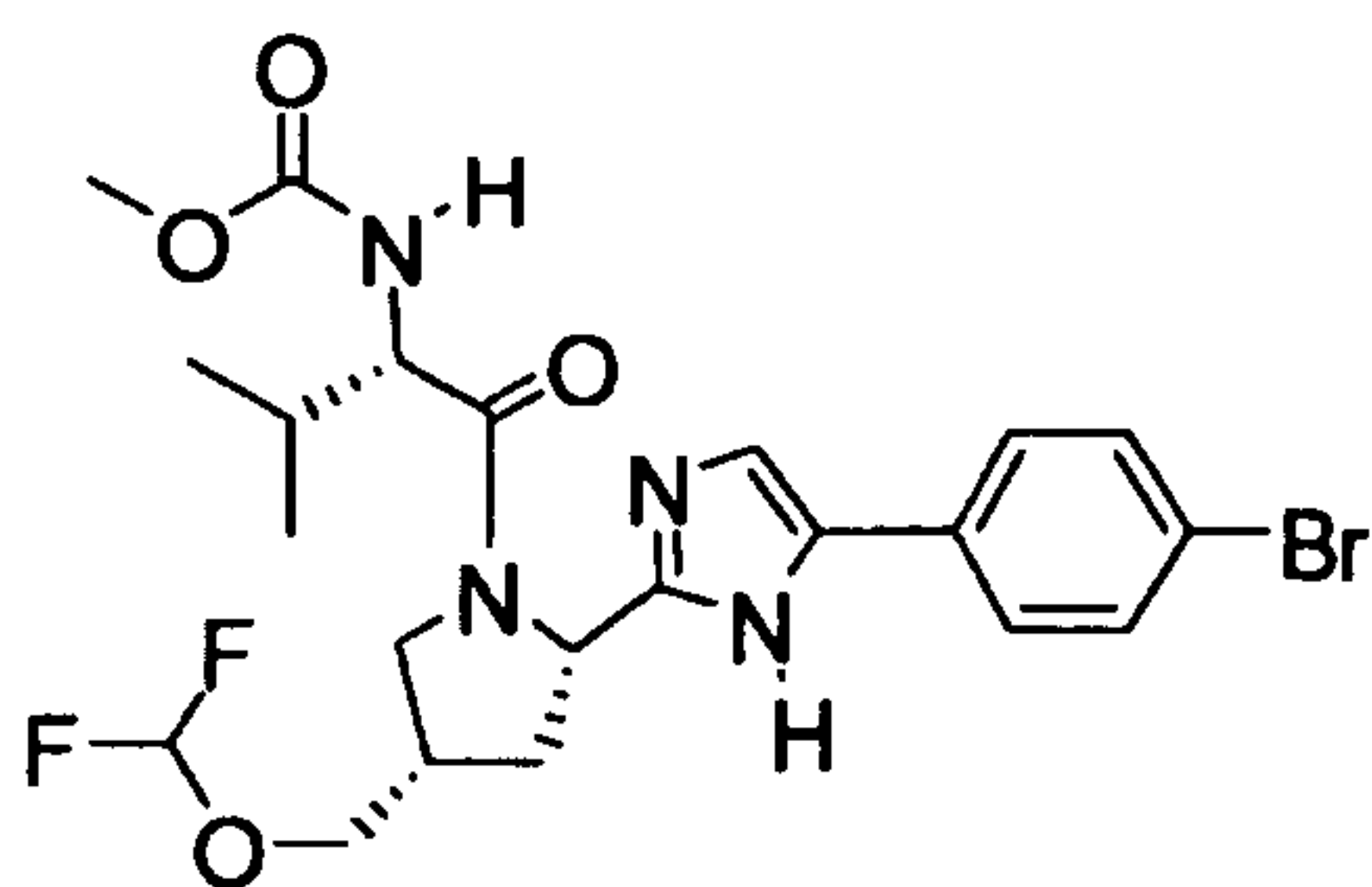
(1-{2-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-4-methoxymethyl-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester



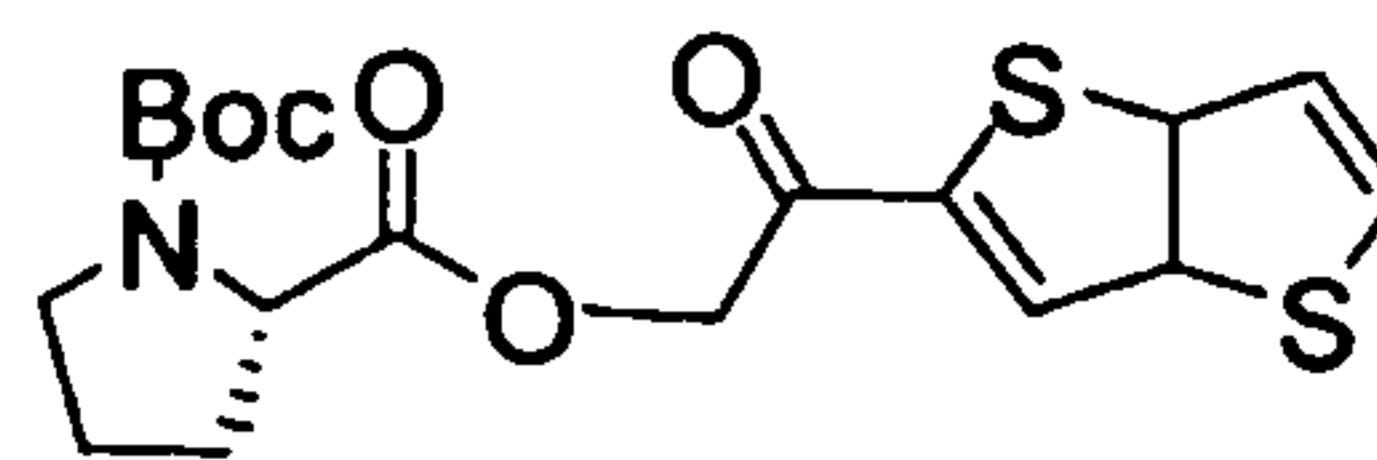
4-Difluoromethoxymethyl-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester



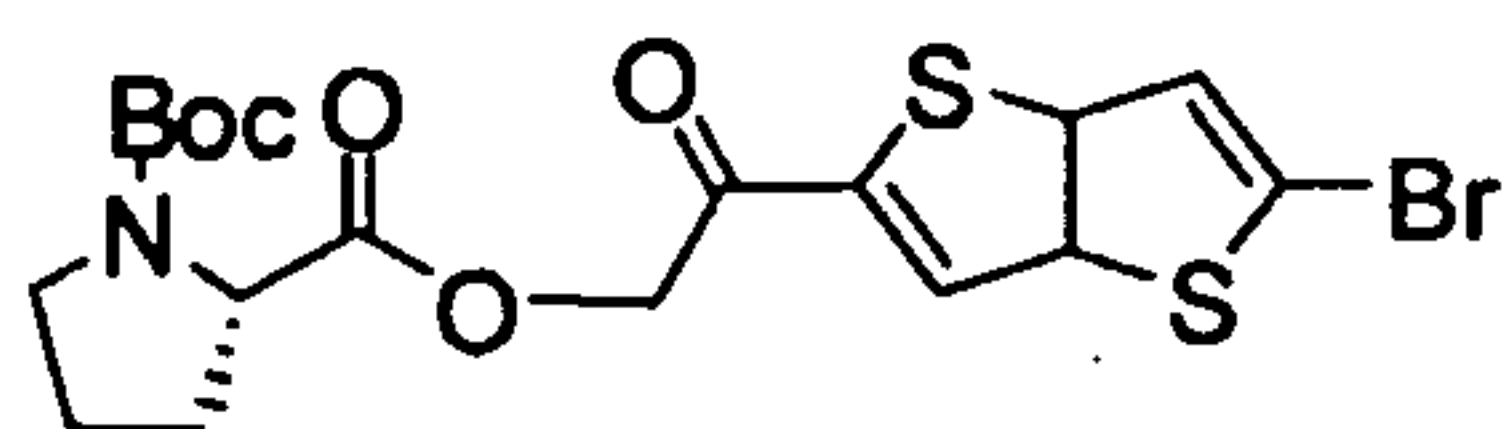
4-Difluoromethoxymethyl-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester



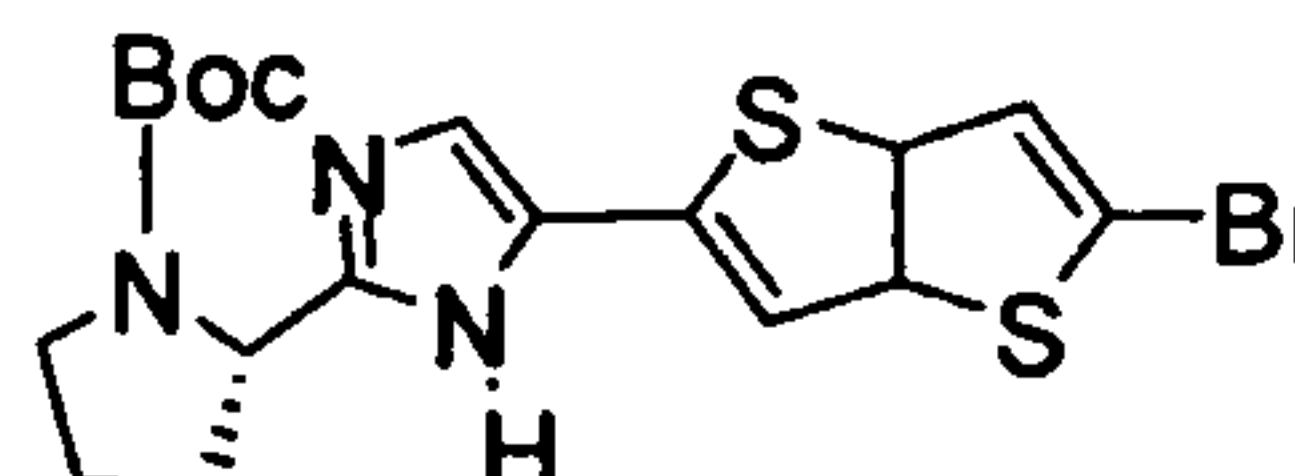
(1-{2-[5-(4-Bromo-phenyl)-1H-imidazol-2-yl]-4-difluoromethoxymethyl-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester



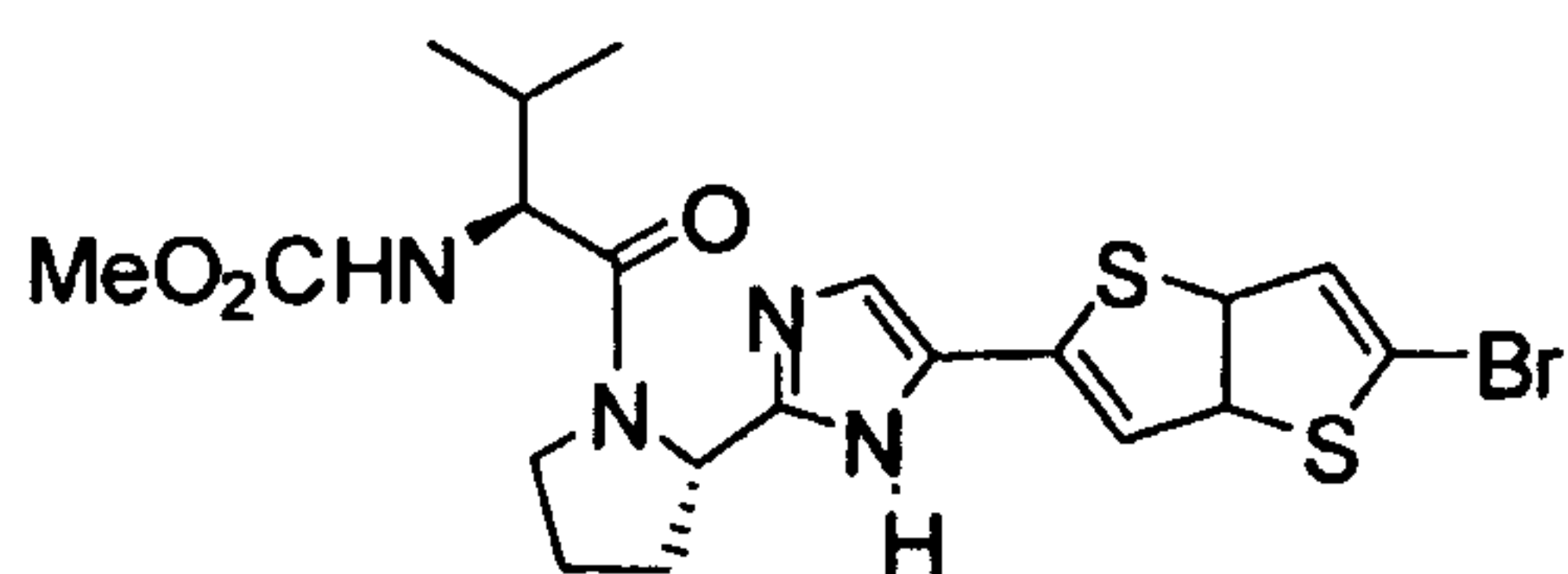
Pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-[2-(3a,6a-dihydro-thieno[3,2-*b*]thiophen-2-yl)-2-oxo-ethyl] ester



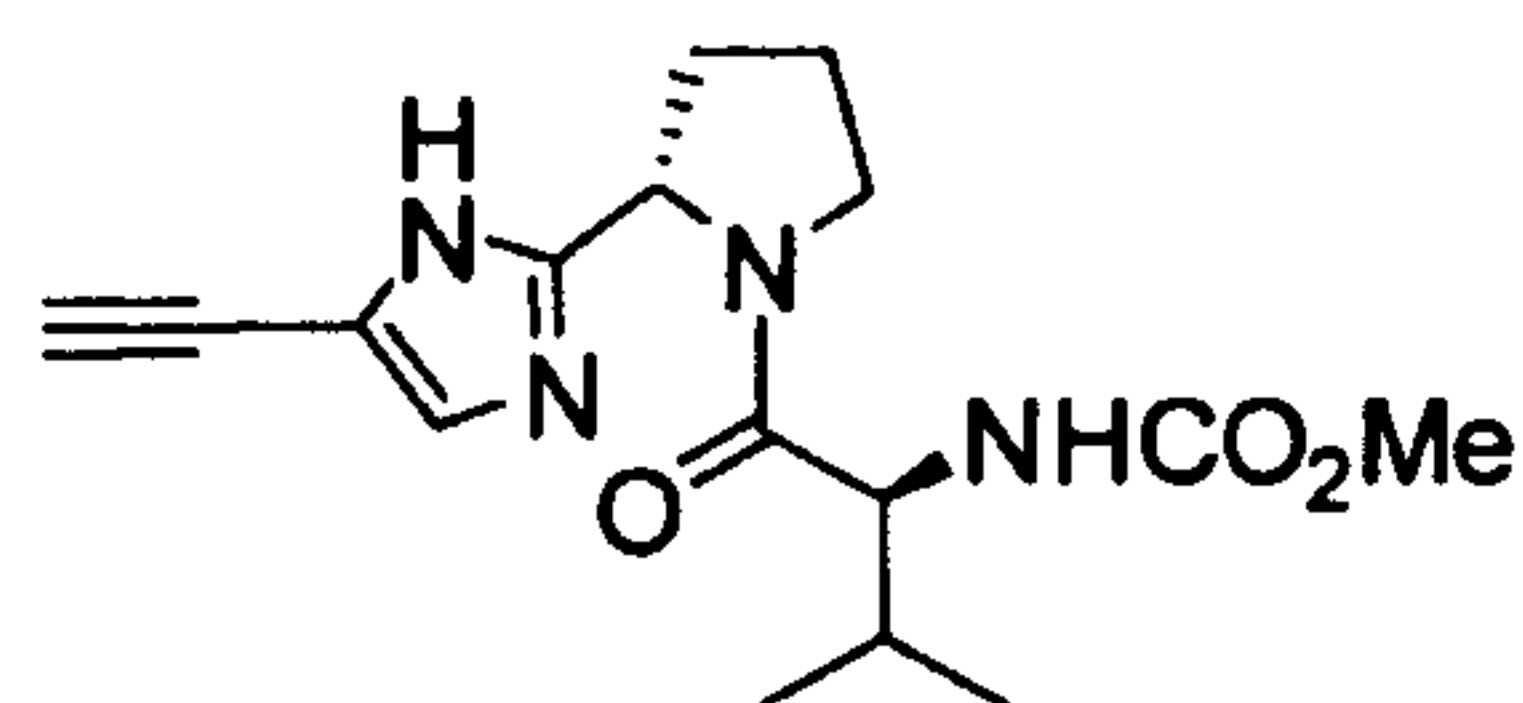
Pyrrolidine-1,2-dicarboxylic acid 2-[2-(5-bromo-3a,6a-dihydro-thieno[3,2-*b*]thiophen-2-yl)-2-oxo-ethyl] ester 1-*tert*-butyl ester



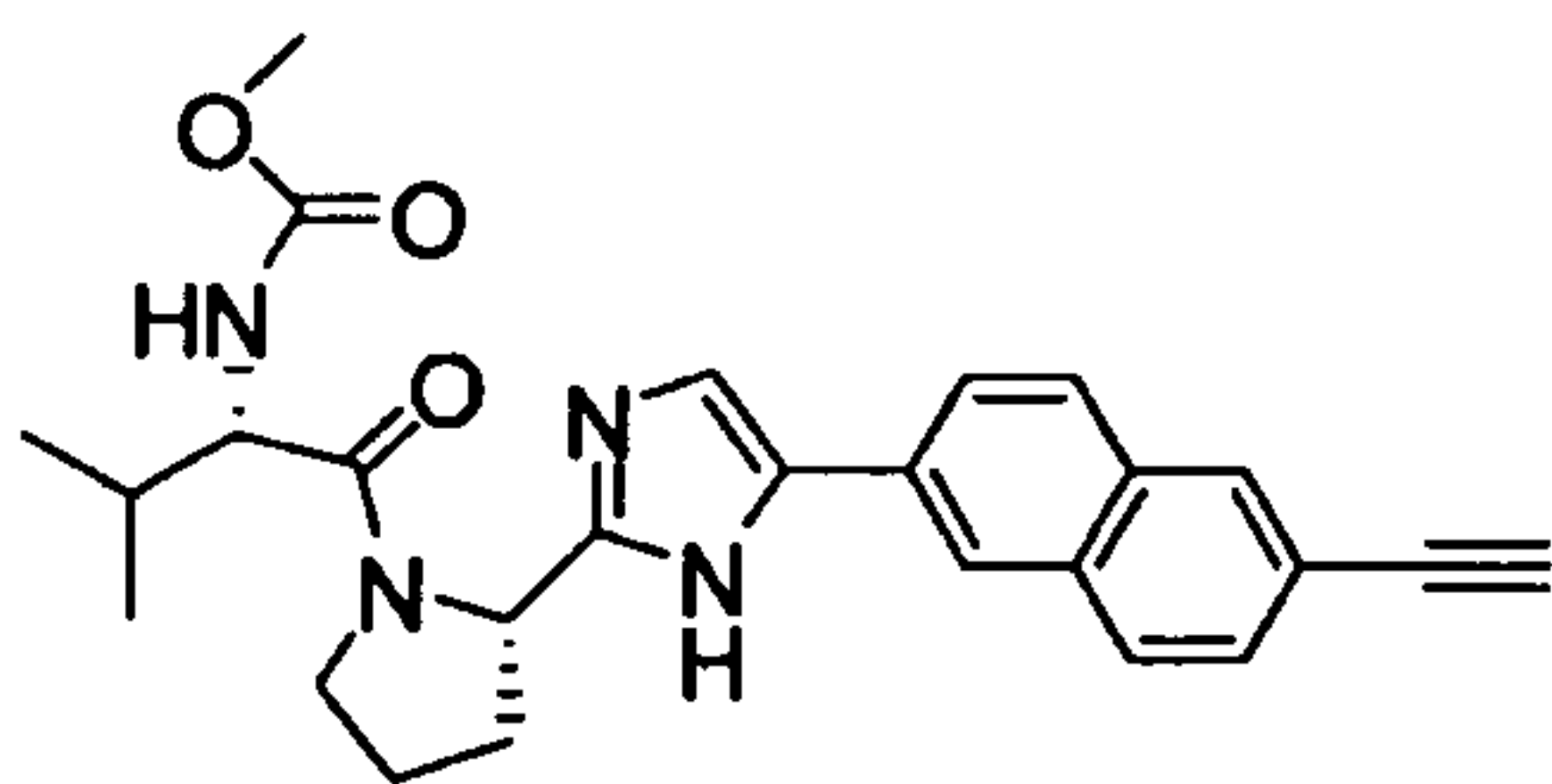
2-[5-(5-Bromo-3a,6a-dihydro-thieno[3,2-*b*]thiophen-2-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester



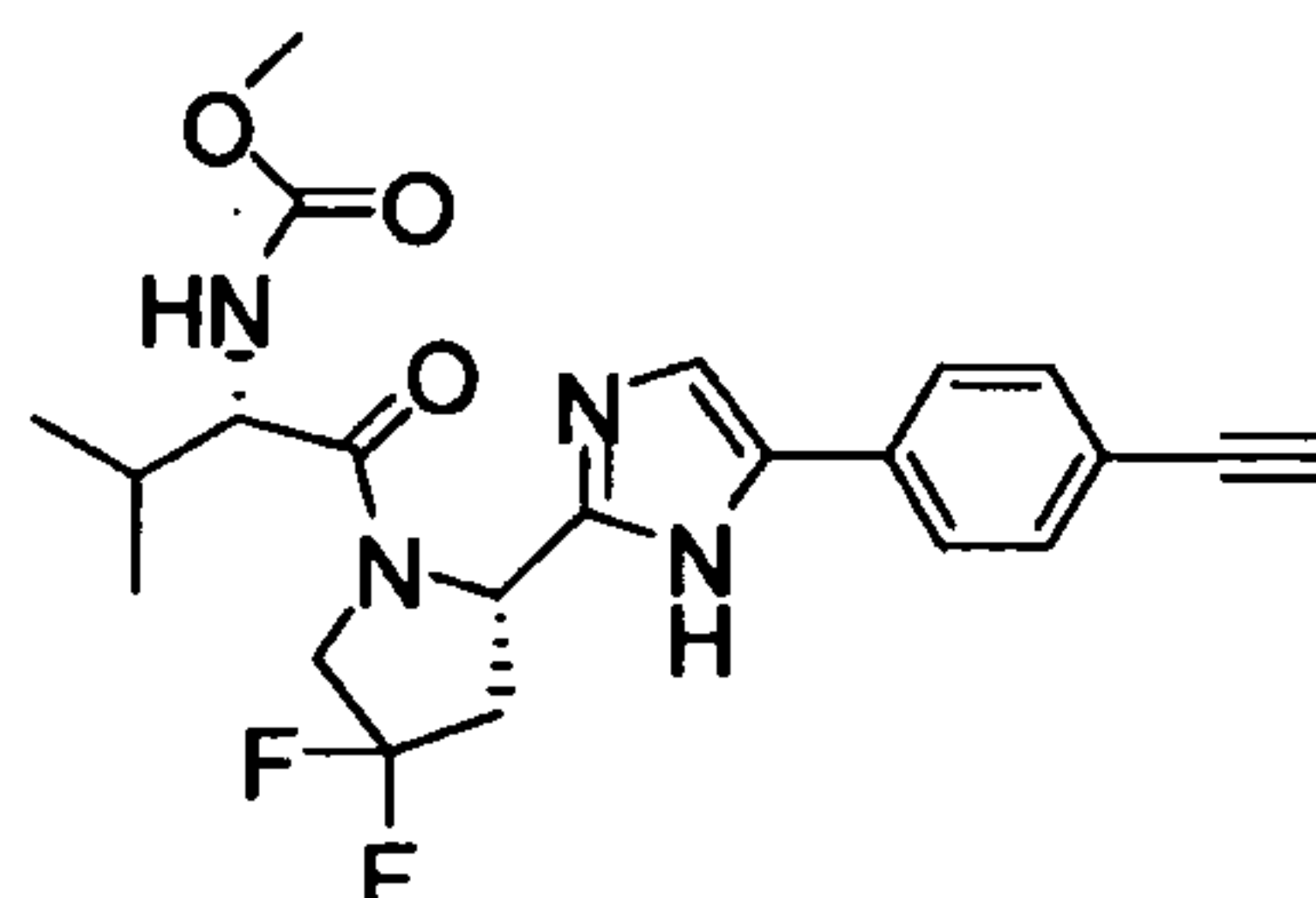
(1-{2-[5-(5-Bromo-3a,6a-dihydro-thieno[3,2-*b*]thiophen-2-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester



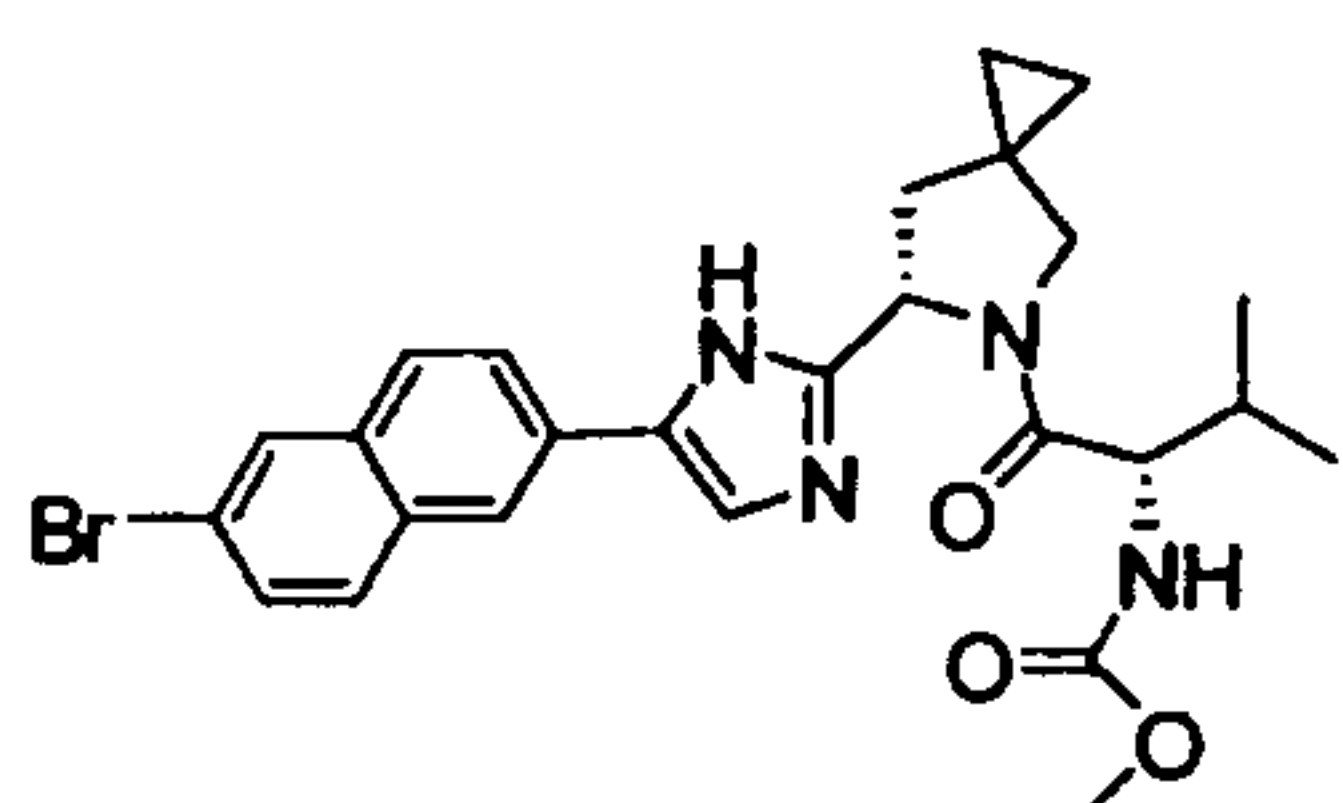
{1-[2-(5-Ethynyl-1H-imidazol-2-yl)-pyrrolidine-1-carbonyl]-2-methyl-propyl}-carbamic acid methyl ester



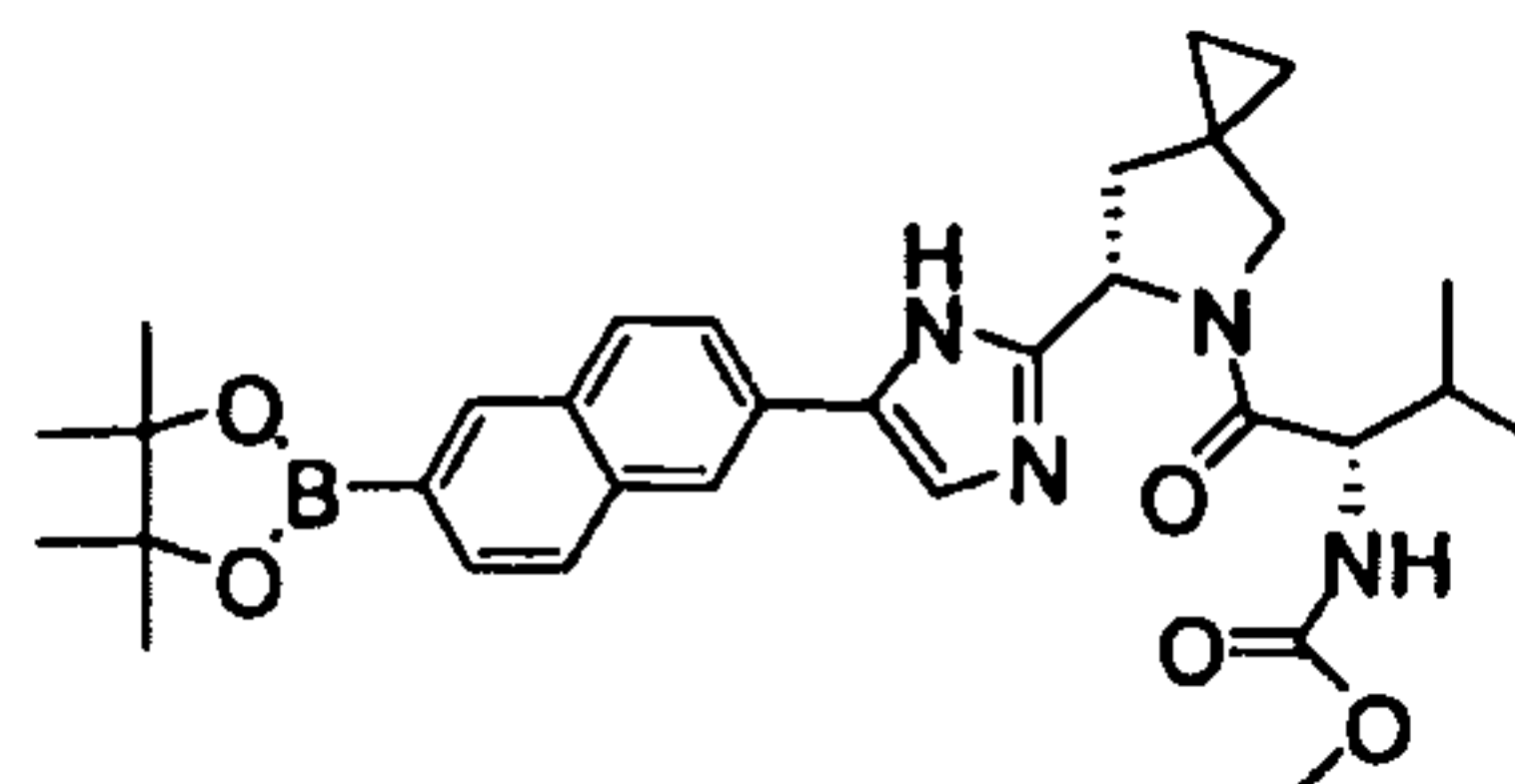
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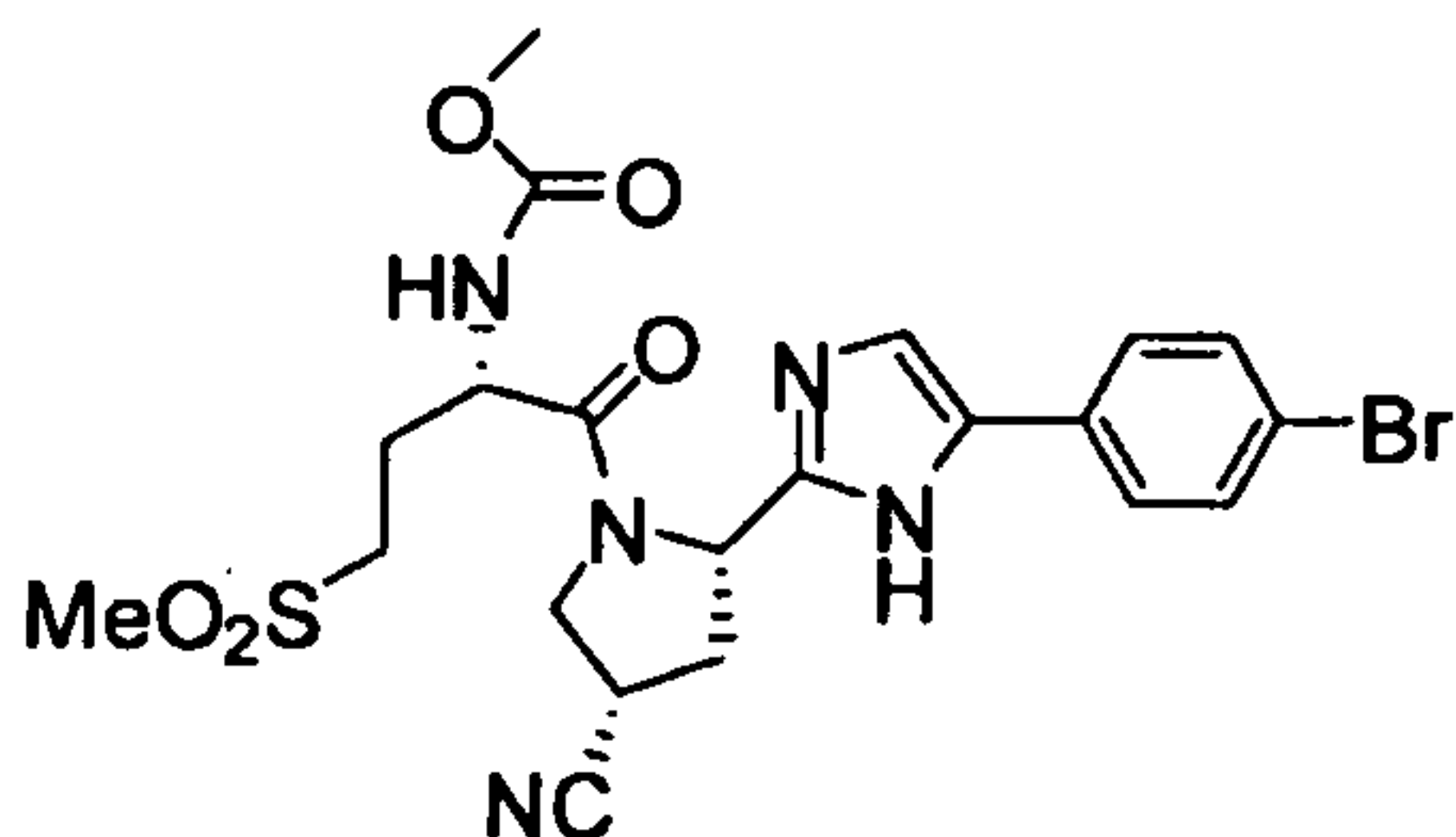
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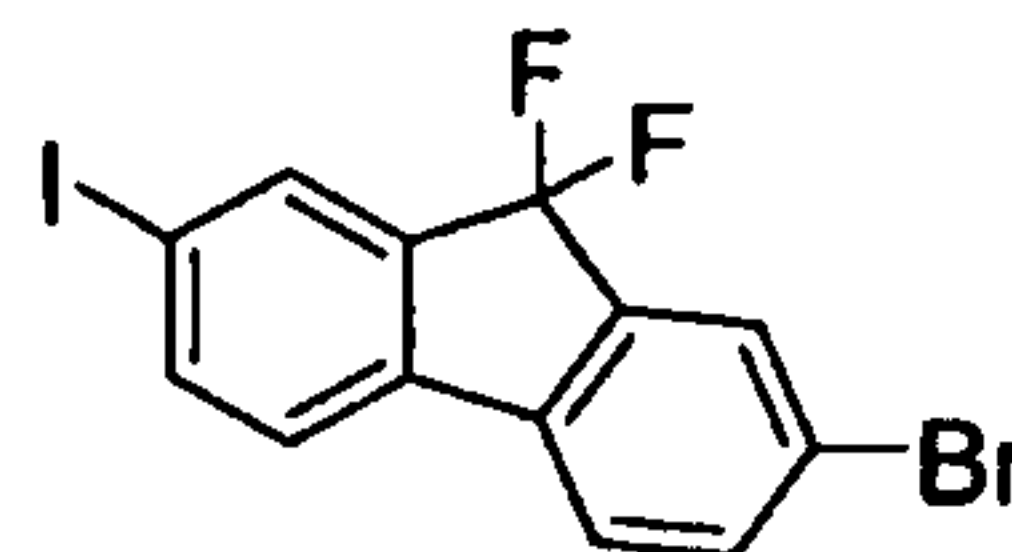
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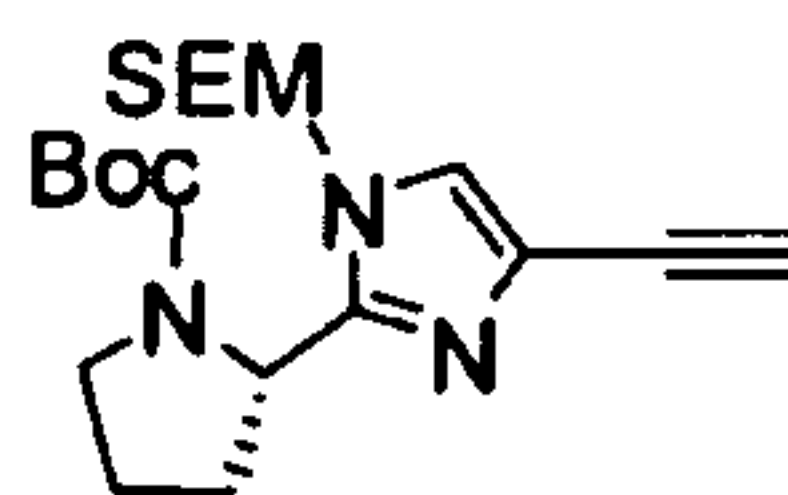
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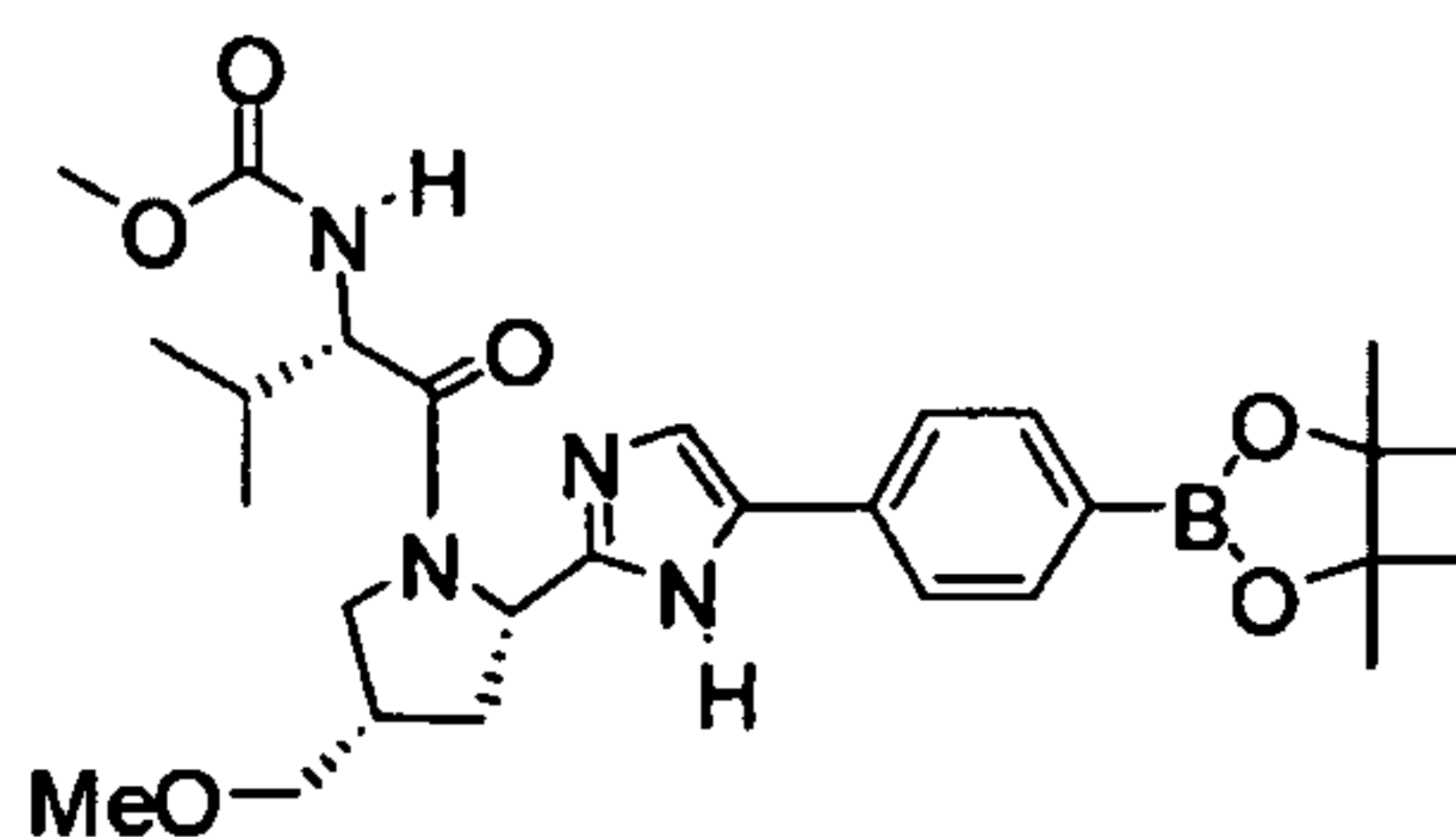
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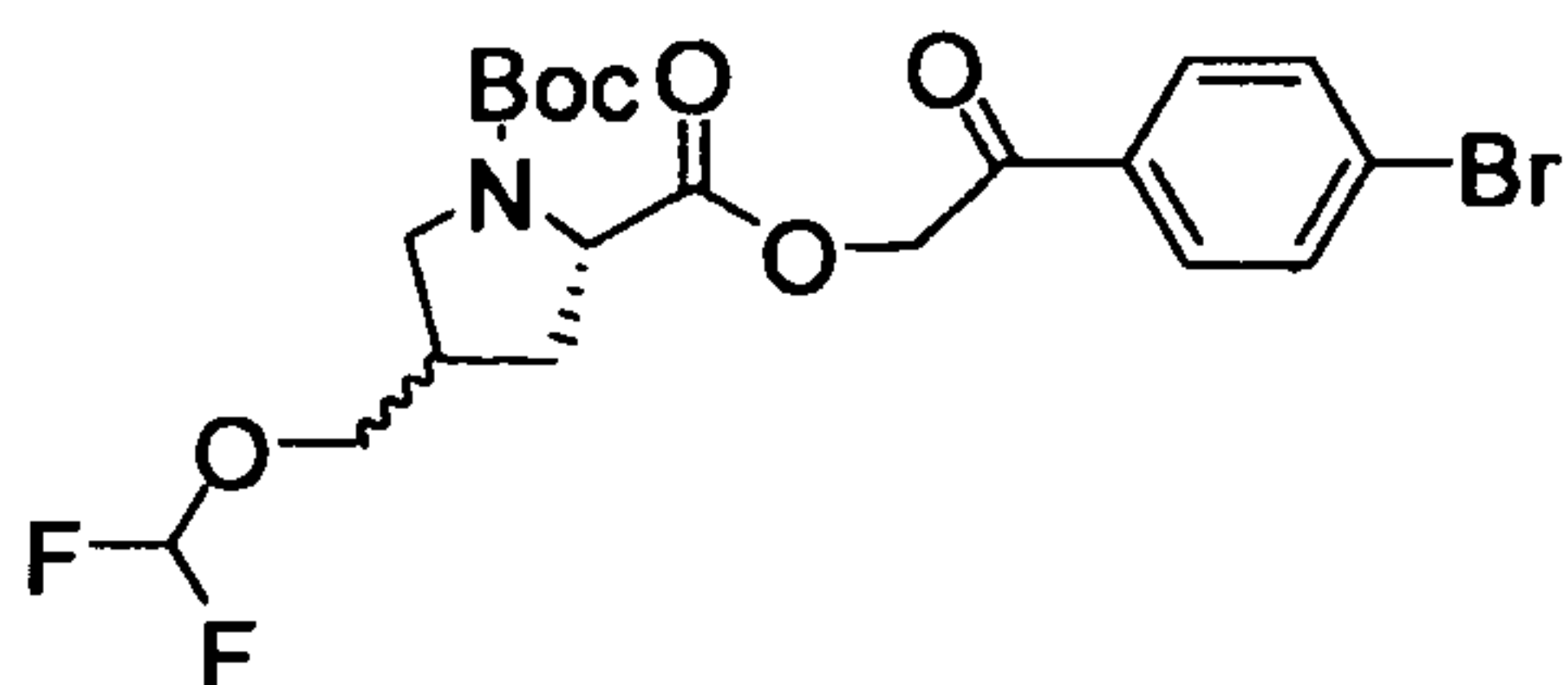
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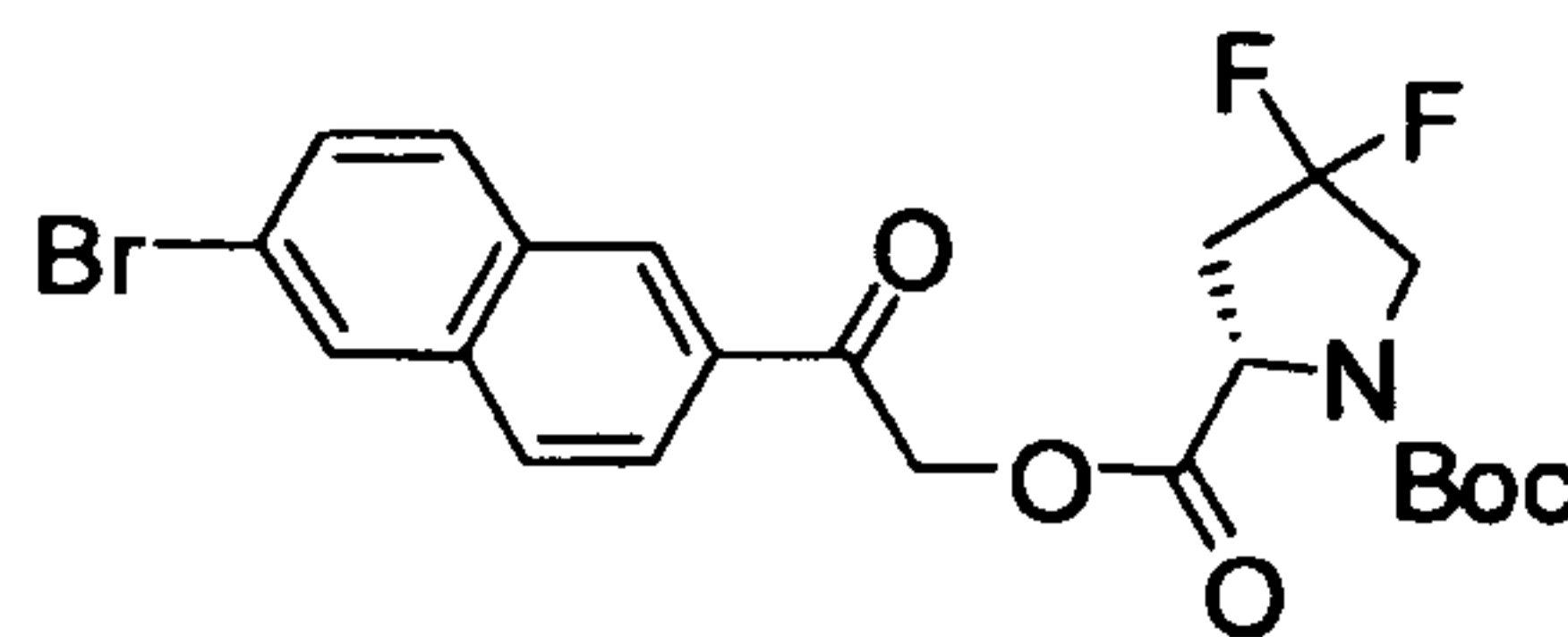
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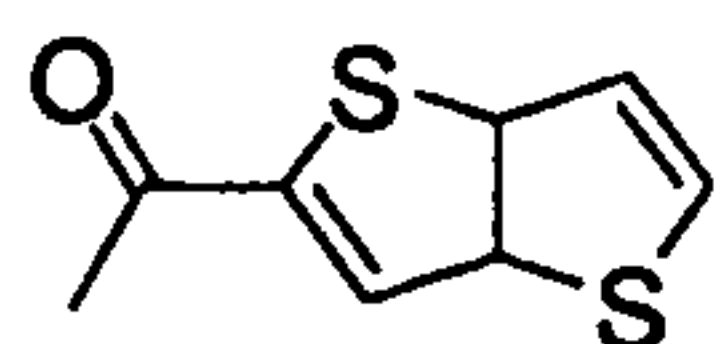
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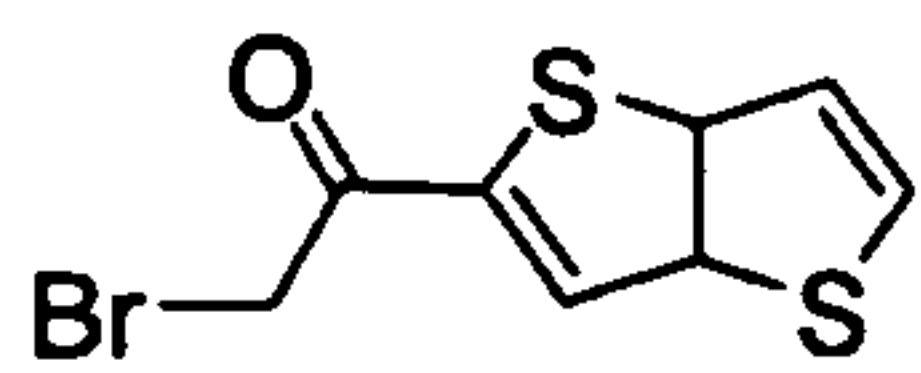
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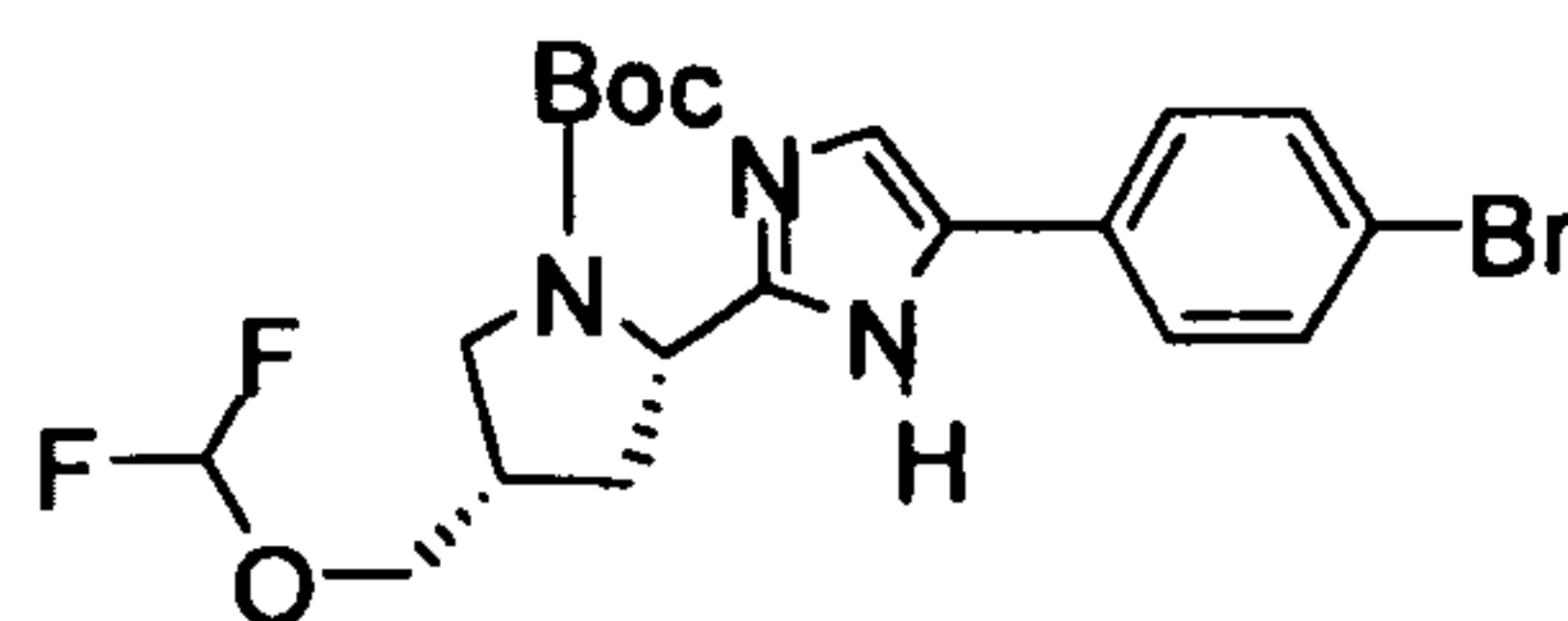
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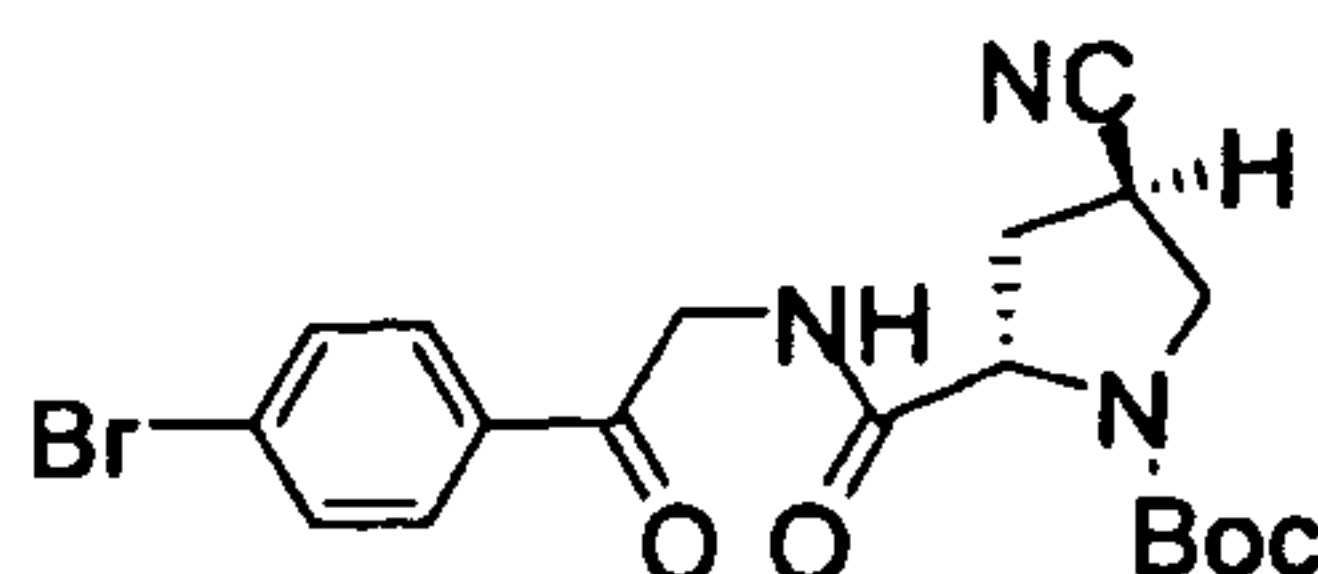
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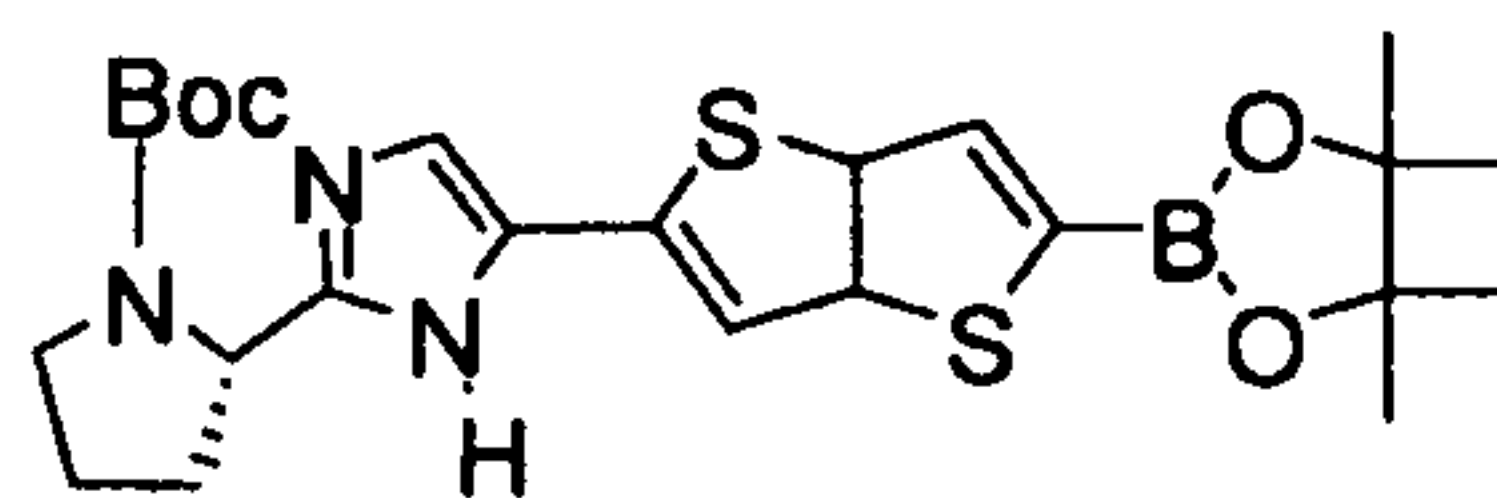
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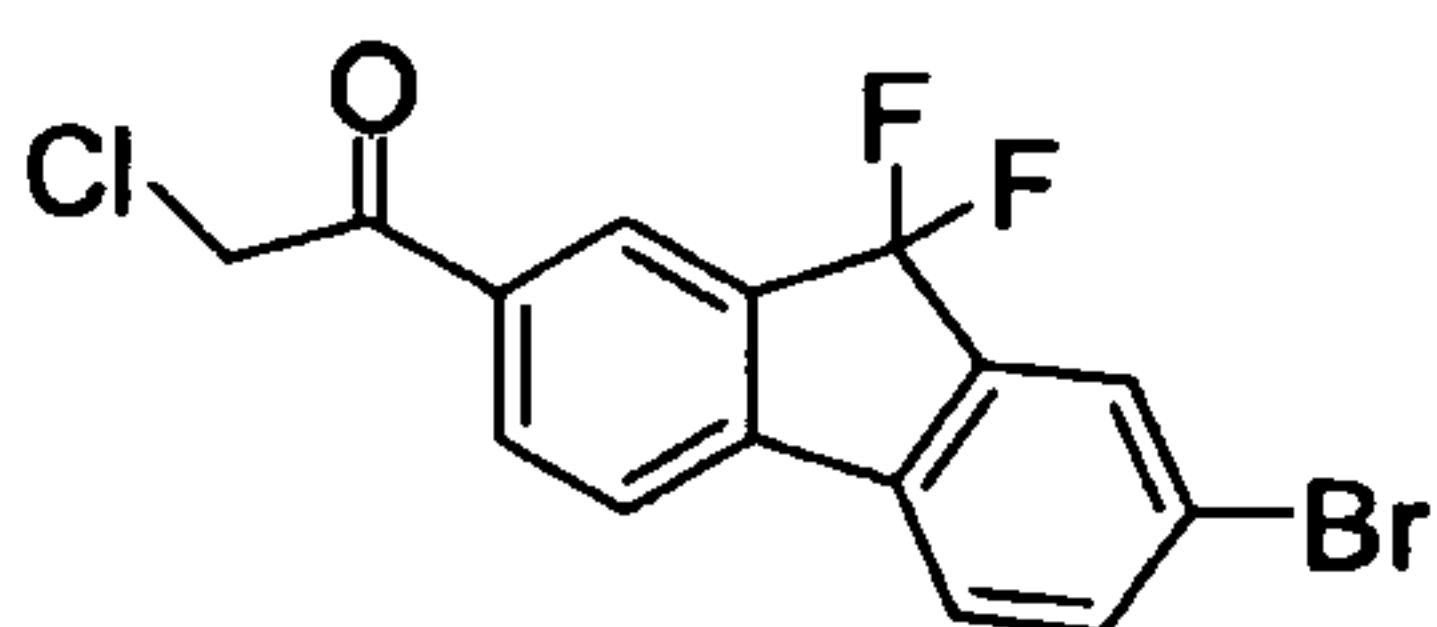
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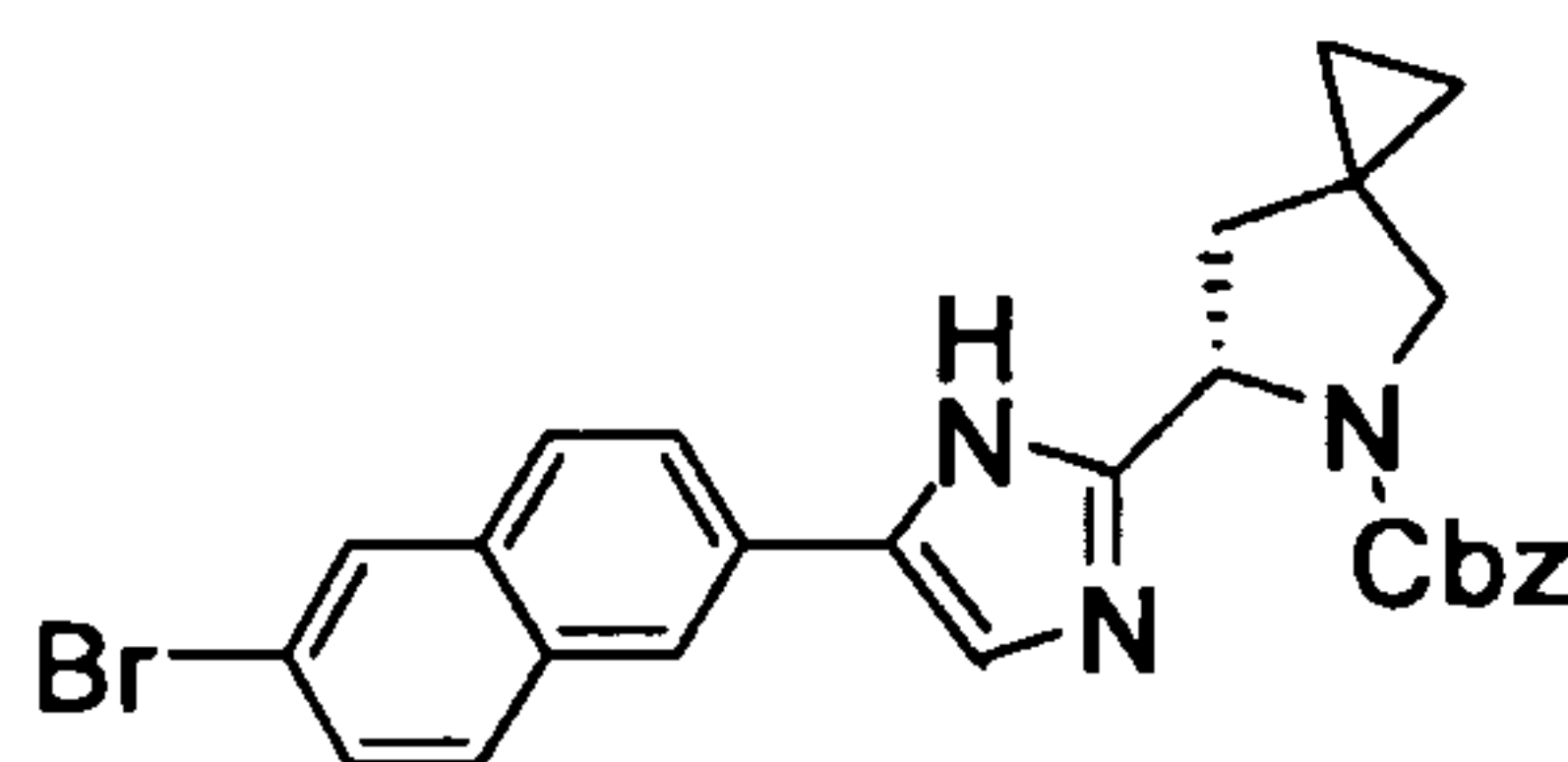
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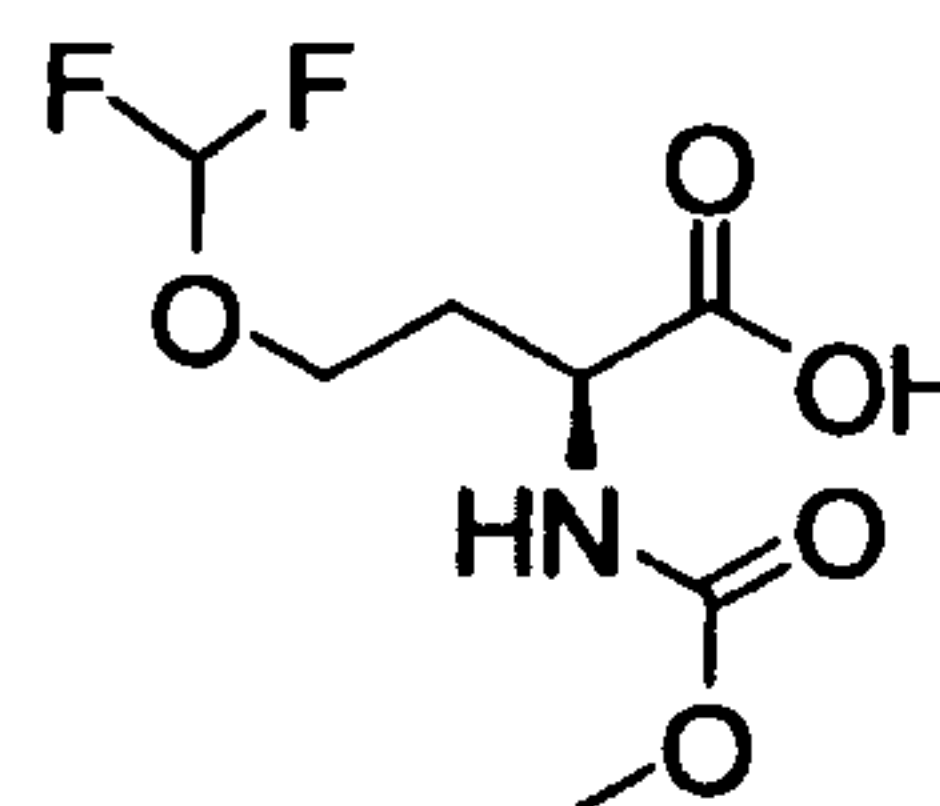
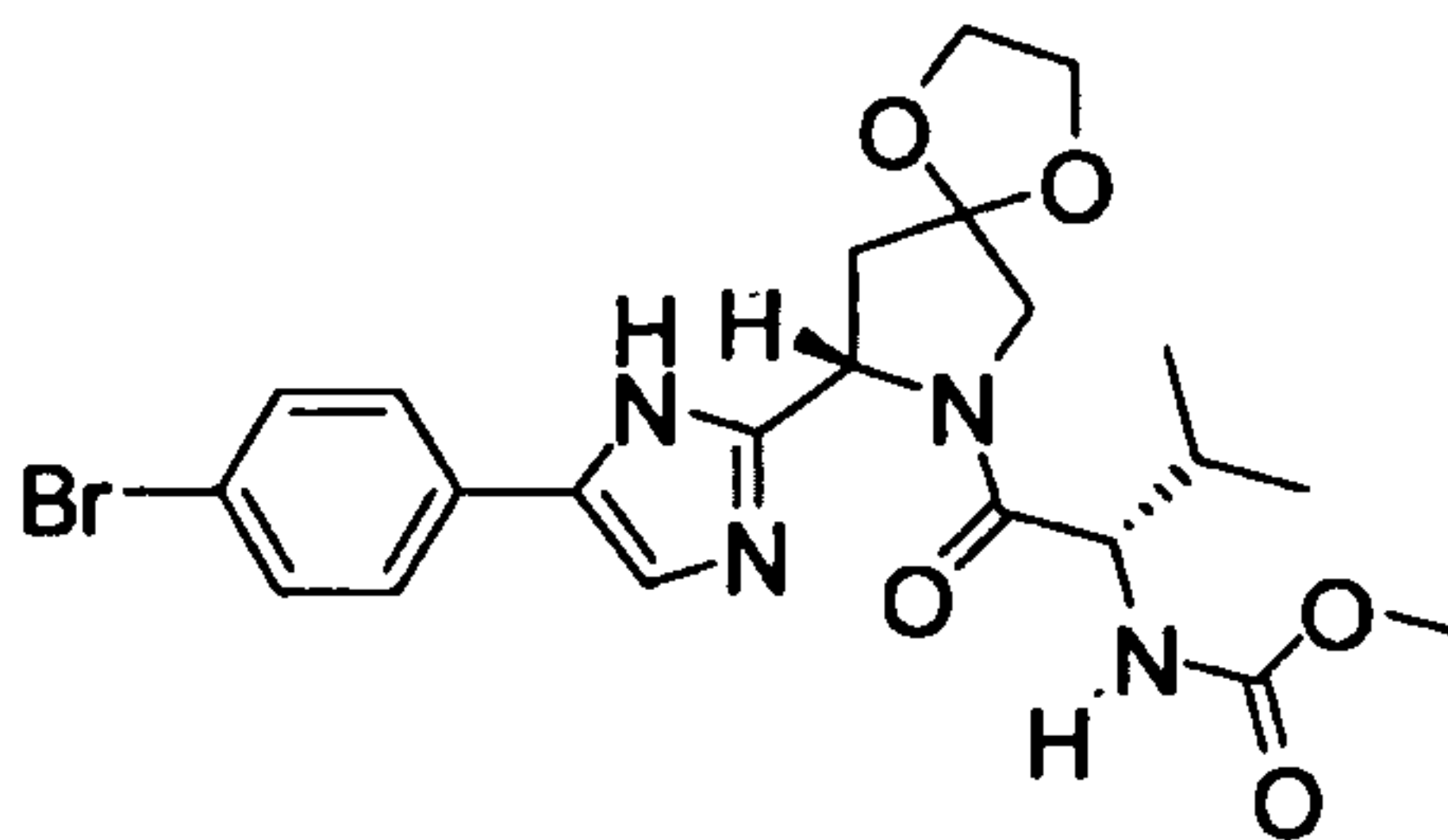
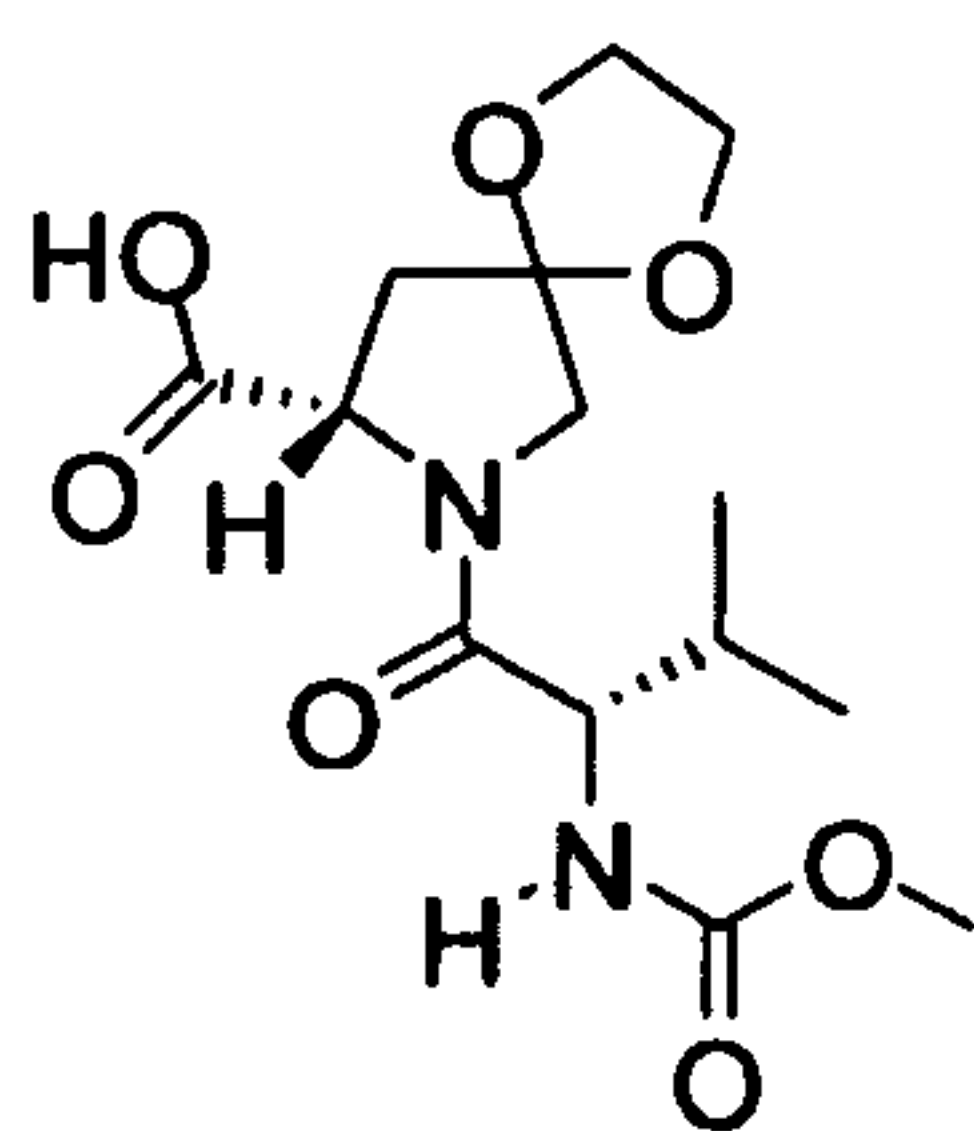
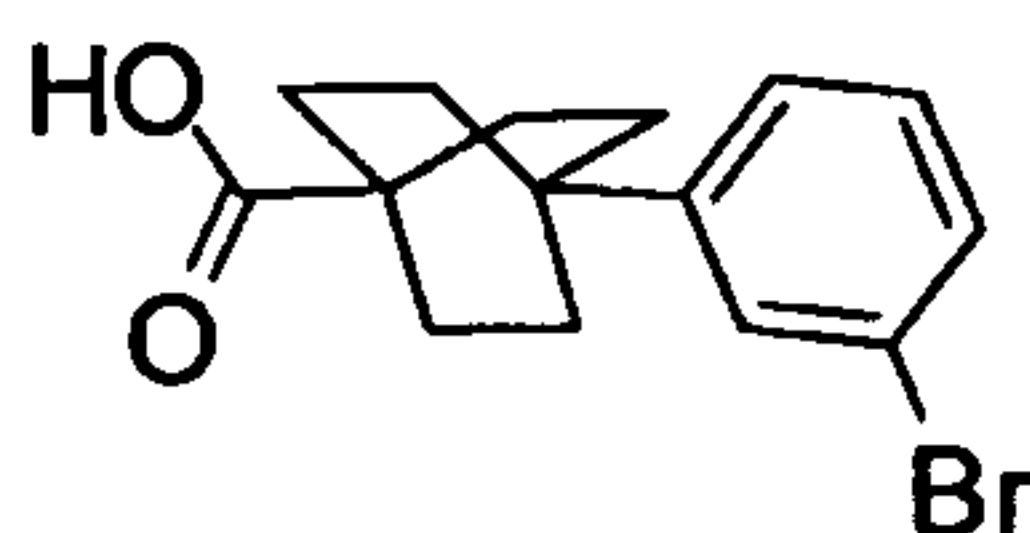
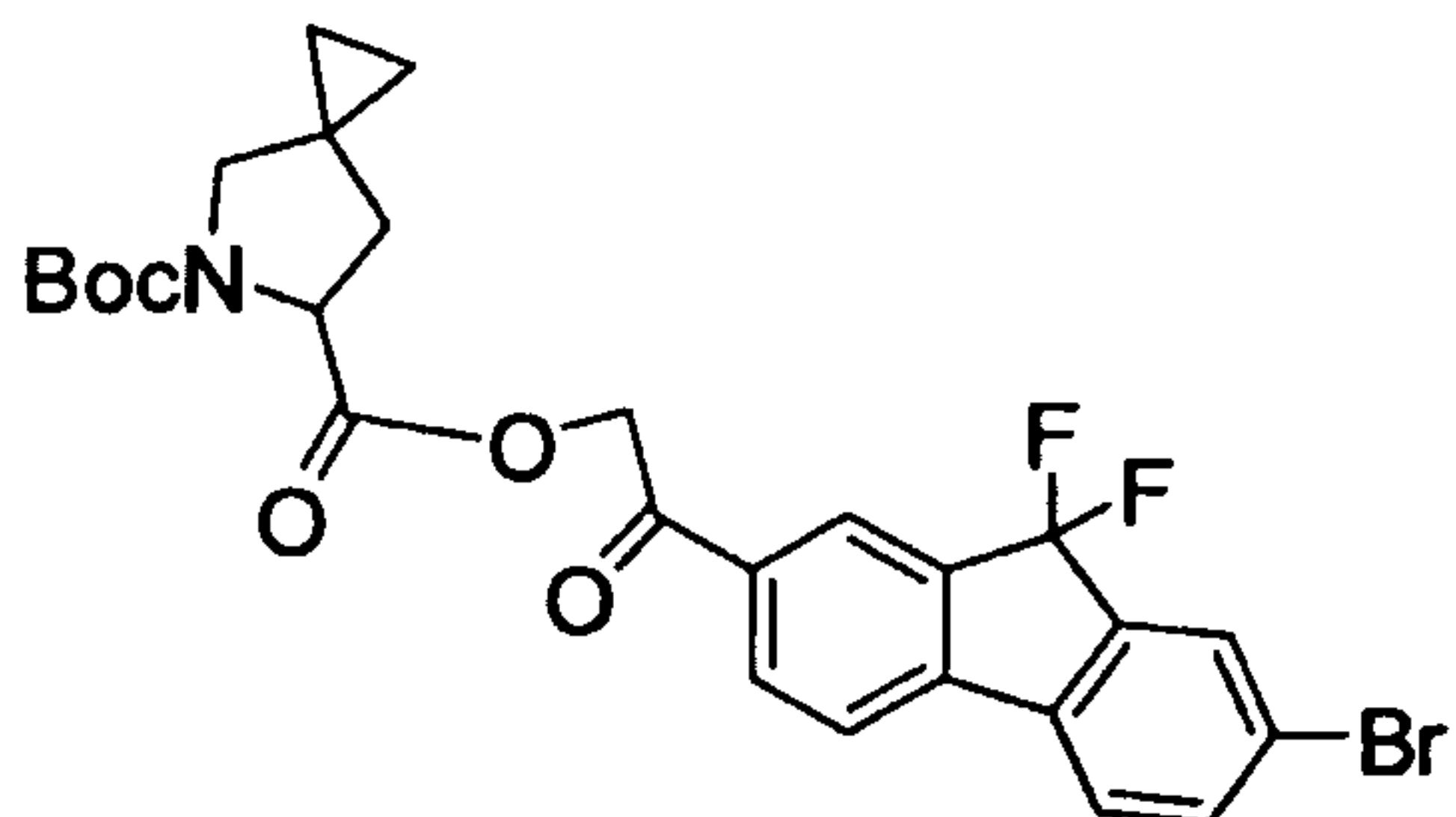
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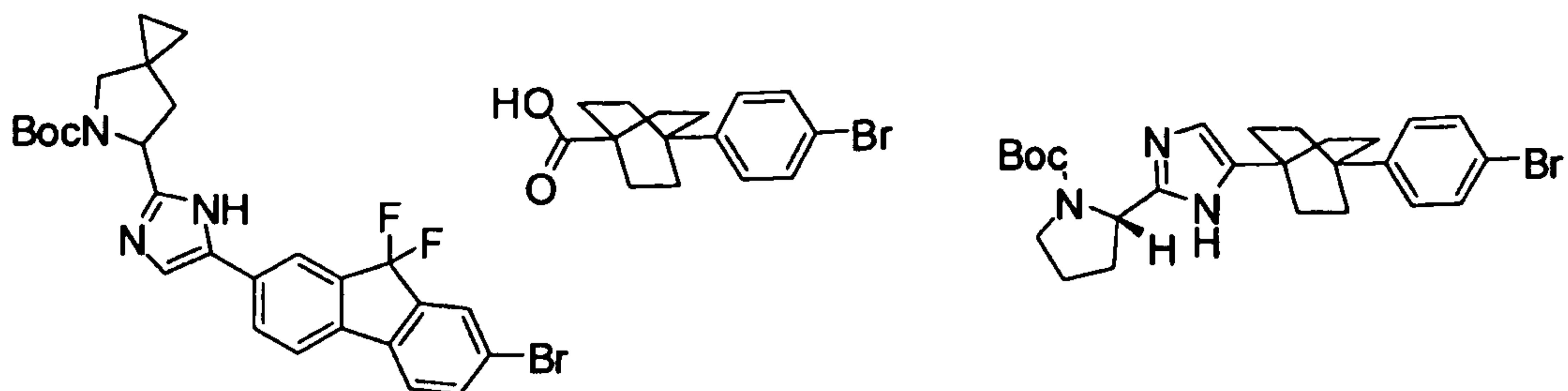


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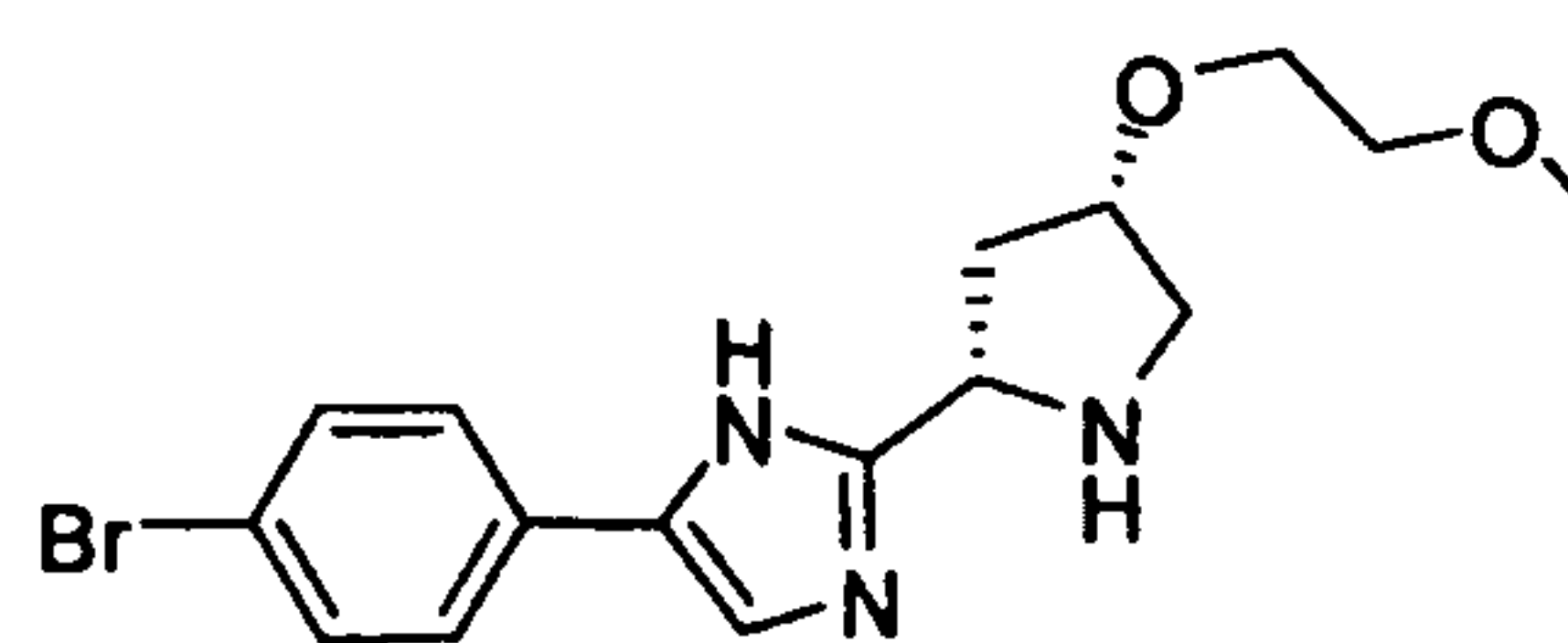


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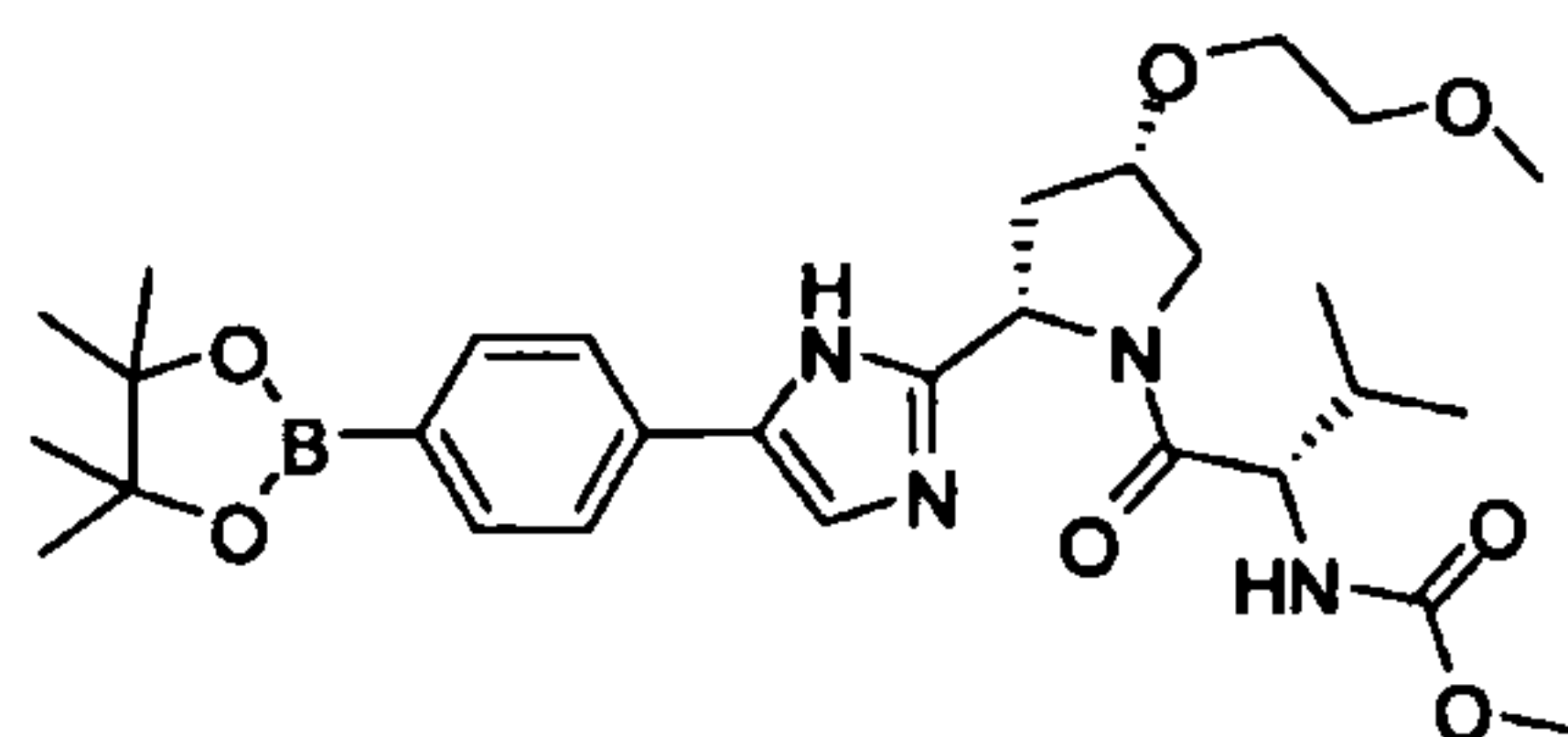




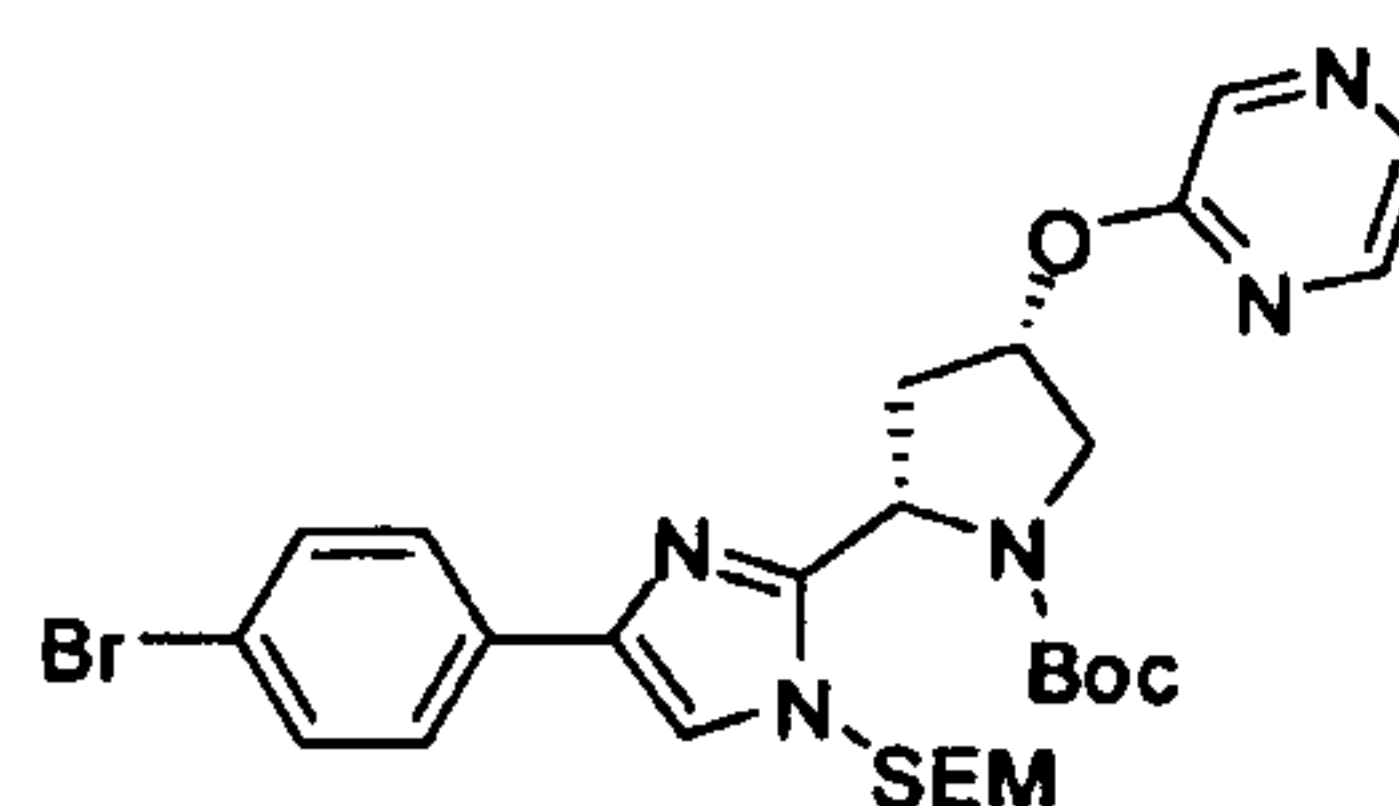
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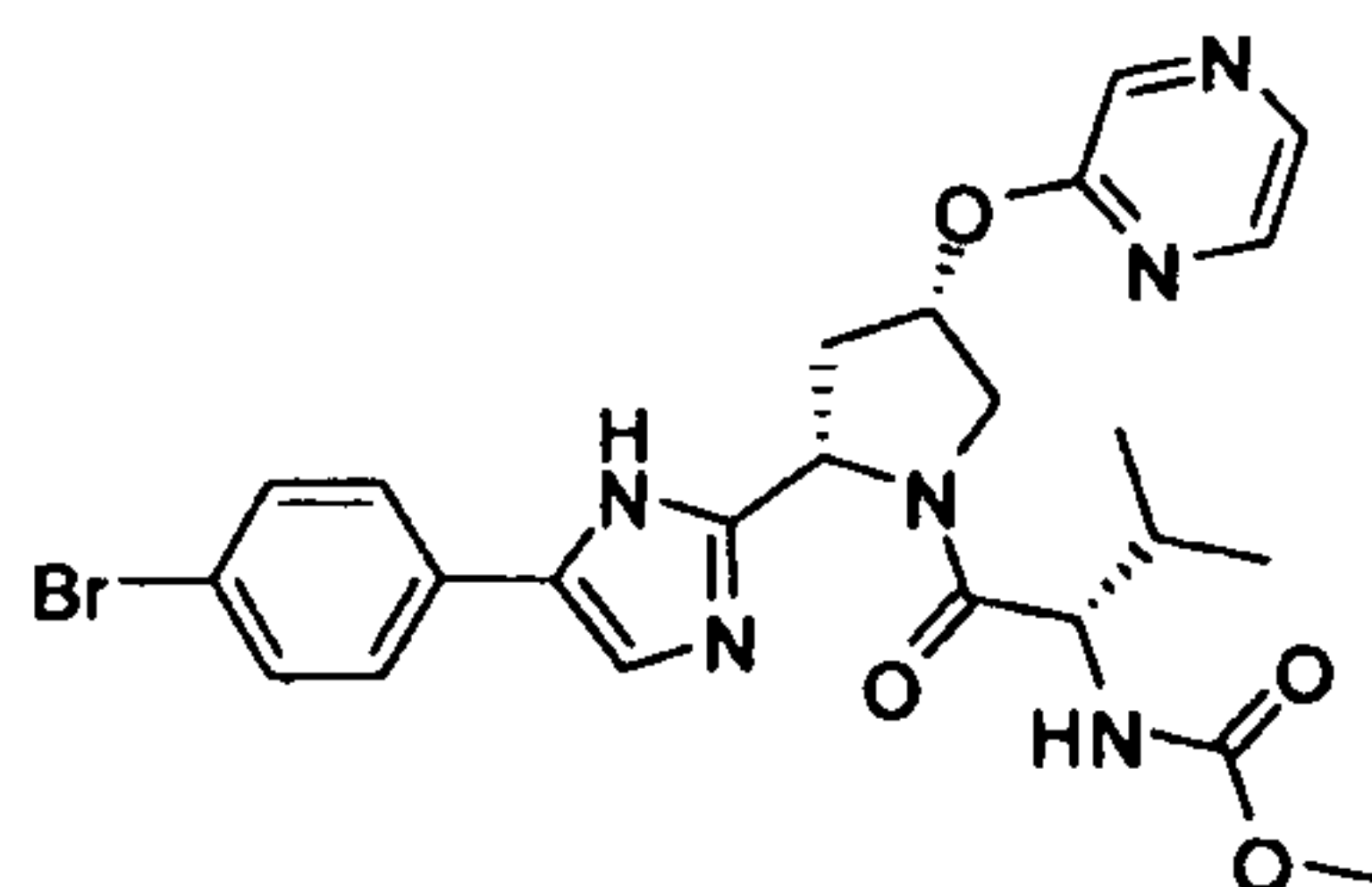
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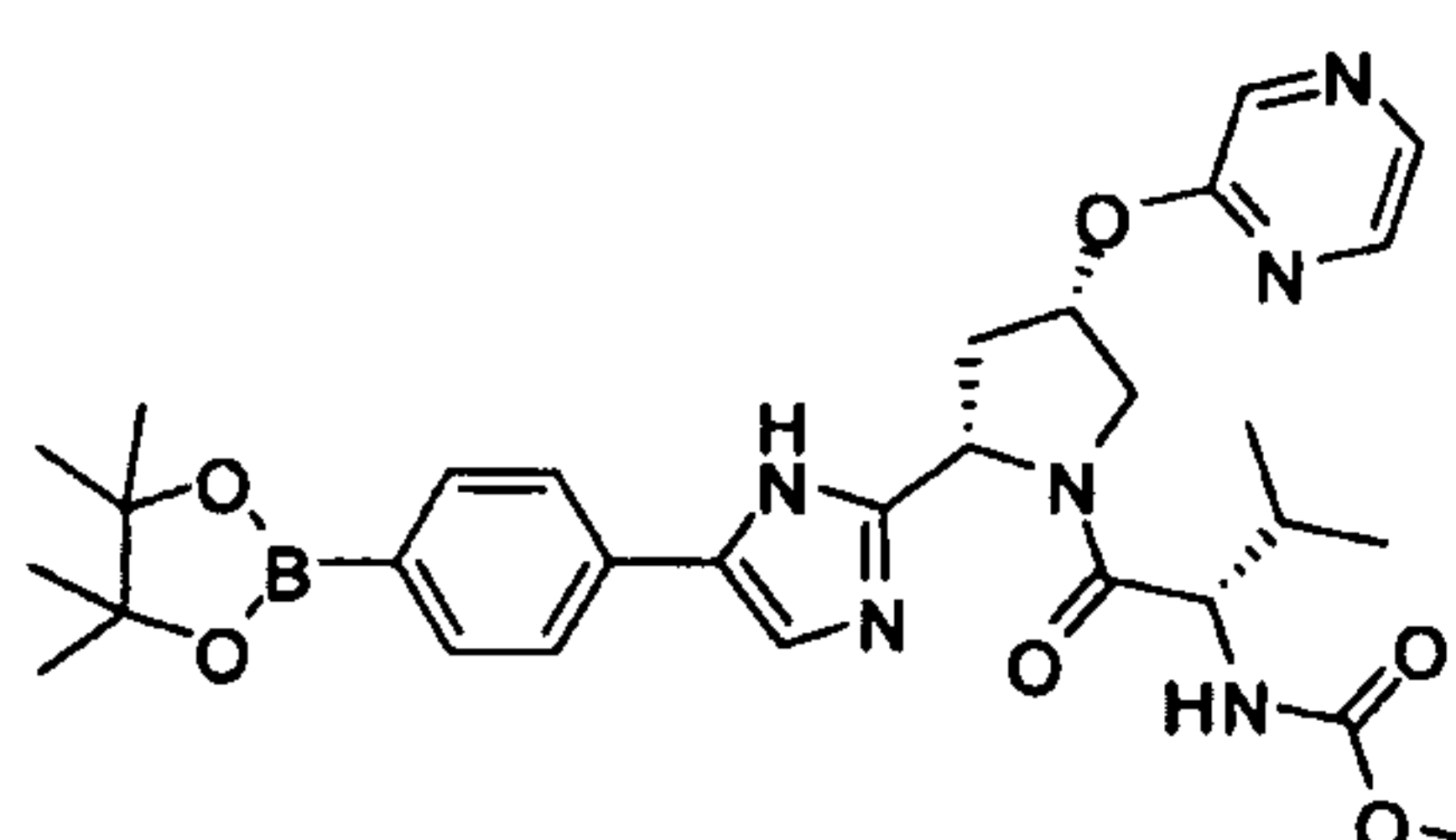
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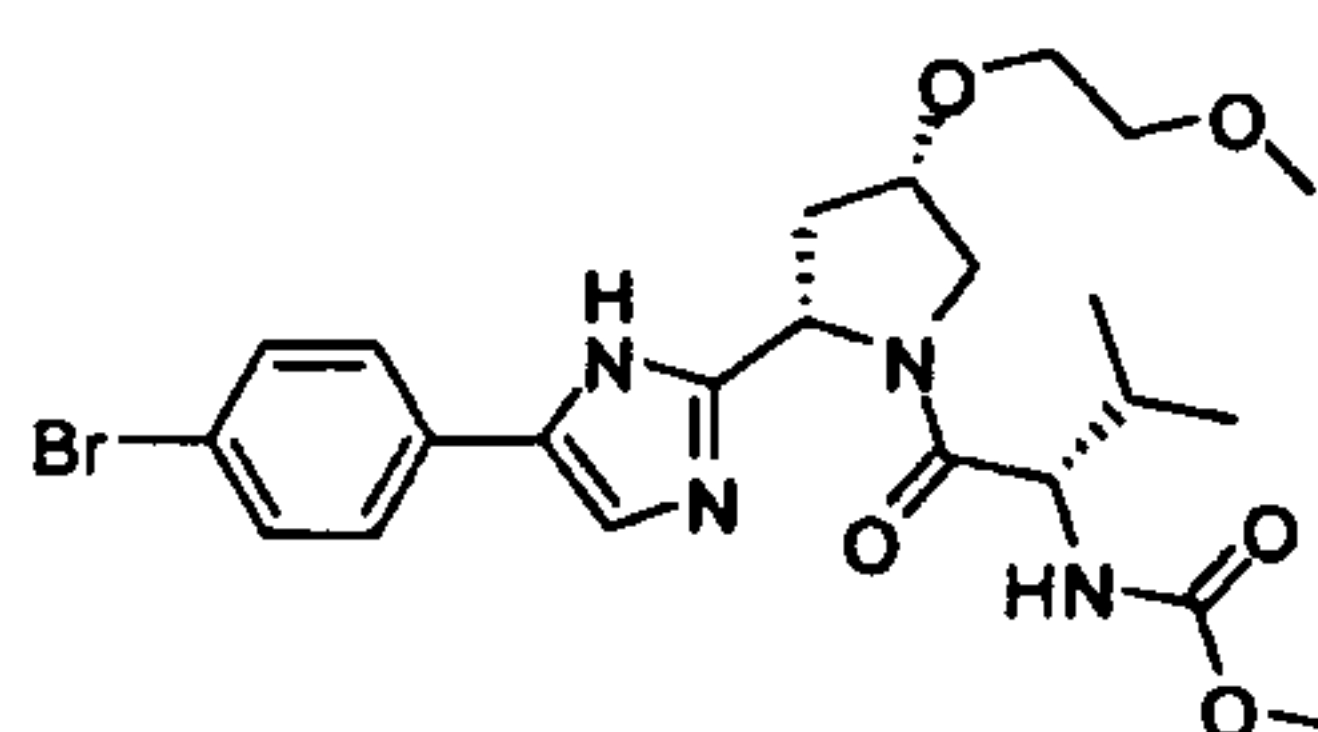
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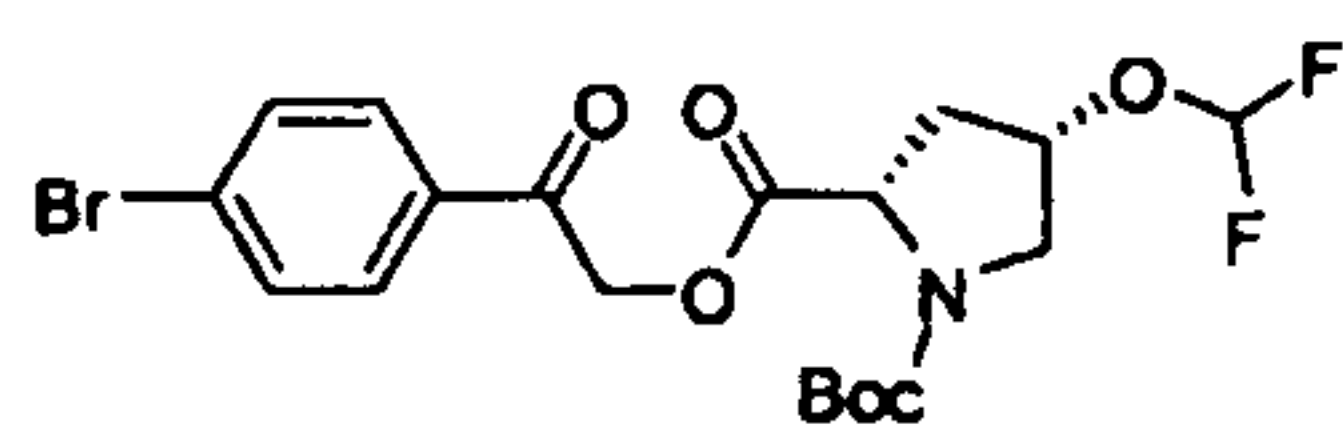
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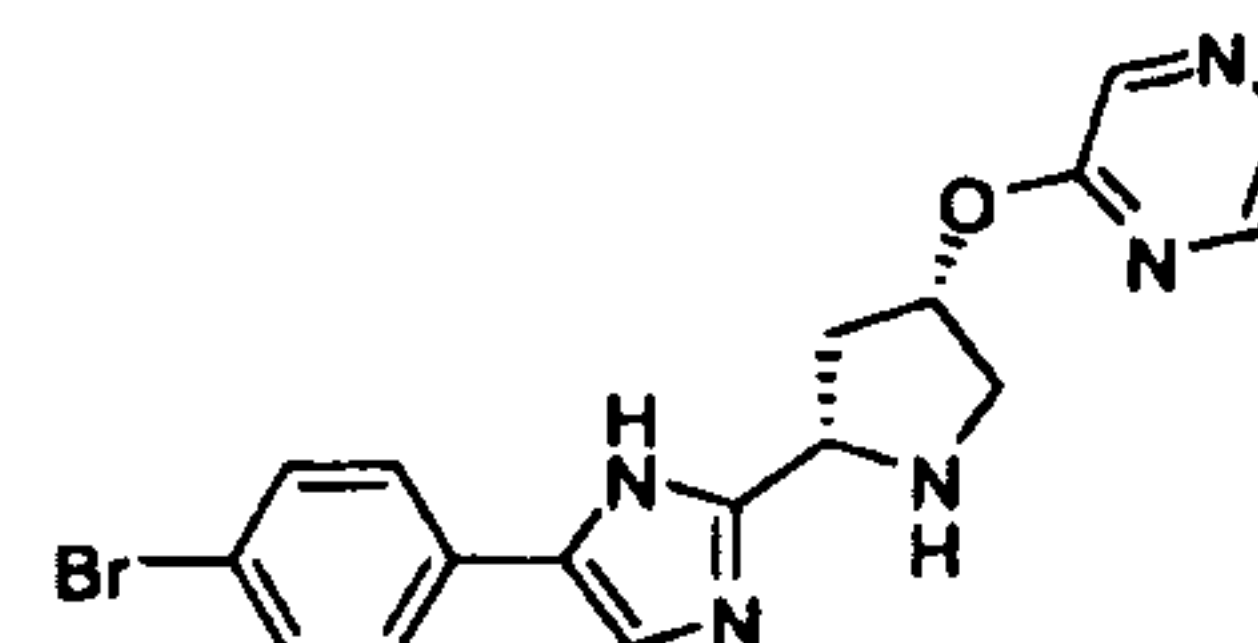
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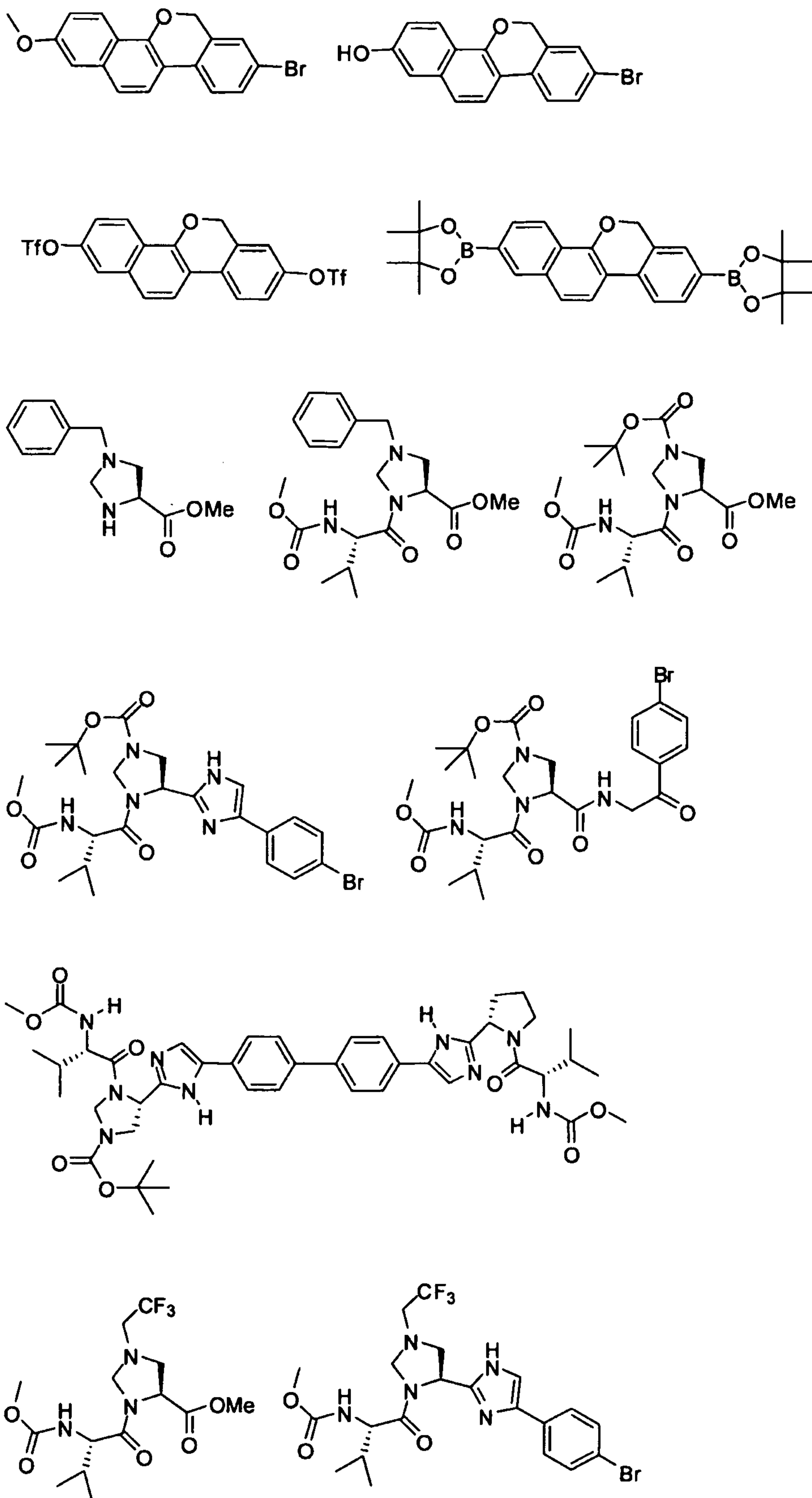
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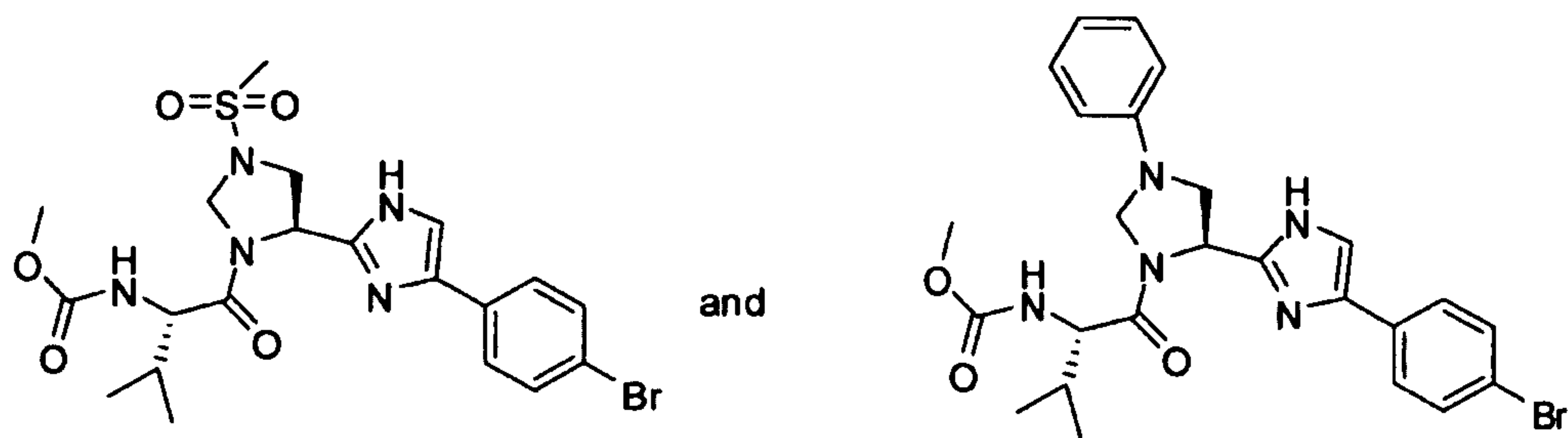


4-Difluoromethoxy-pyrrolidine-1,2-dicarboxylic acid 2-[2-(4-bromo-phenyl)-2-oxo-ethyl] ester 1-*tert*-butyl ester



2-[5-[5-(4-Bromo-phenyl)-1*H*-imidazol-2-yl]-pyrrolidin-3-yloxy]-pyrazine





Exemplary Methods of Making the Compounds of the Invention.

The invention also relates to methods of making the compositions of the invention. The compositions are prepared by any of the applicable techniques of organic synthesis. Many such techniques are well known in the art. However, many of the known techniques are elaborated in Compendium of Organic Synthetic Methods (John Wiley & Sons, New York), Vol. 1, Ian T. Harrison and Shuyen Harrison, 1971; Vol. 2, Ian T. Harrison and Shuyen Harrison, 1974; Vol. 3, Louis S. Hegedus and Leroy Wade, 1977; Vol. 4, Leroy G. Wade, Jr., 1980; Vol. 5, Leroy G. Wade, Jr., 1984; and Vol. 6, Michael B. Smith; as well as March, J., Advanced Organic Chemistry, Third Edition, (John Wiley & Sons, New York, 1985), Comprehensive Organic Synthesis. Selectivity, Strategy & Efficiency in Modern Organic Chemistry. In 9 Volumes, Barry M. Trost, Editor-in-Chief (Pergamon Press, New York, 1993 printing). Other methods suitable for preparing compounds of the invention are described in International Patent Application Publication Number WO 2006/020276.

A number of exemplary methods for the preparation of the compositions of the invention are provided in the schemes and examples below. These methods are intended to illustrate the nature of such preparations and are not intended to limit the scope of applicable methods.

Generally, the reaction conditions such as temperature, reaction time, solvents, work-up procedures, and the like, will be those common in the art for the particular reaction to be performed. The cited reference material, together with material cited therein, contains detailed descriptions of such conditions. Typically the temperatures will be -100°C to 200°C, solvents will be aprotic or protic, and reaction times will be 10 seconds to 10 days. Work-up typically consists of quenching any unreacted reagents followed by partition between a water/organic layer system (extraction) and separating the layer containing the product.

Oxidation and reduction reactions are typically carried out at temperatures near room temperature (about 20°C), although for metal hydride reductions frequently the temperature is reduced to 0°C to -100°C, solvents are typically aprotic for reductions and may be either protic or aprotic for oxidations. Reaction times are adjusted to achieve desired conversions.

Condensation reactions are typically carried out at temperatures near room temperature, although for non-equilibrating, kinetically controlled condensations reduced temperatures (0°C to -100°C) are also common. Solvents can be either protic (common in equilibrating reactions) or aprotic (common in kinetically controlled reactions).

Standard synthetic techniques such as azeotropic removal of reaction by-products and use of anhydrous reaction conditions (*e.g.*, inert gas environments) are common in the art and will be applied when applicable.

The terms “treated”, “treating”, “treatment”, and the like, when used in connection with a chemical synthetic operation, mean contacting, mixing, reacting, allowing to react, bringing into contact, and other terms common in the art for indicating that one or more chemical entities is treated in such a manner as to convert it to one or more other chemical entities. This means that “treating compound one with compound two” is synonymous with “allowing compound one to react with compound two”, “contacting compound one with compound two”, “reacting compound one with compound two”, and other expressions common in the art of organic synthesis for reasonably indicating that compound one was “treated”, “reacted”, “allowed to react”, etc., with compound two. For example, treating indicates the reasonable and usual manner in which organic chemicals are allowed to react. Normal concentrations (0.01M to 10M, typically 0.1M to 1M), temperatures (-100°C to 250°C, typically -78°C to 150°C, more typically -78°C to 100°C, still more typically 0°C to 100°C), reaction vessels (typically glass, plastic, metal), solvents, pressures, atmospheres (typically air for oxygen and water insensitive reactions or nitrogen or argon for oxygen or water sensitive), etc., are intended unless otherwise indicated. The knowledge of similar reactions known in the art of organic synthesis is used in selecting the conditions and apparatus for “treating” in a given process. In particular, one of ordinary skill in the art of organic synthesis selects conditions and apparatus reasonably expected to successfully carry out the chemical reactions of the described processes based on the knowledge in the art.

Modifications of each of the exemplary schemes and in the Examples (hereafter “exemplary schemes”) leads to various analogs of the specific exemplary materials produce. The above-cited citations describing suitable methods of organic synthesis are applicable to such modifications.

In each of the exemplary schemes it may be advantageous to separate reaction products from one another and/or from starting materials. The desired products of each step or series of steps is separated and/or purified (hereinafter separated) to the desired degree of homogeneity by the techniques common in the art. Typically such separations involve multiphase extraction, crystallization from a solvent or solvent mixture, distillation, sublimation, or chromatography.

Chromatography can involve any number of methods including, for example: reverse-phase and normal phase; size exclusion; ion exchange; high, medium, and low pressure liquid chromatography methods and apparatus; small scale analytical; simulated moving bed (SMB) and preparative thin or thick layer chromatography, as well as techniques of small scale thin layer and flash chromatography.

Another class of separation methods involves treatment of a mixture with a reagent selected to bind to or render otherwise separable a desired product, unreacted starting material, reaction by product, or the like. Such reagents include adsorbents or absorbents such as activated carbon, molecular sieves, ion exchange media, or the like. Alternatively, the reagents can be acids in the case of a basic material, bases in the case of an acidic material, binding reagents such as antibodies, binding proteins, selective chelators such as crown ethers, liquid/liquid ion extraction reagents (LIX), or the like.

Selection of appropriate methods of separation depends on the nature of the materials involved. For example, boiling point, and molecular weight in distillation and sublimation, presence or absence of polar functional groups in chromatography, stability of materials in acidic and basic media in multiphase extraction, and the like. One skilled in the art will apply techniques most likely to achieve the desired separation.

A single stereoisomer, *e.g.*, an enantiomer, substantially free of its stereoisomer may be obtained by resolution of the racemic mixture using a method such as formation of diastereomers using optically active resolving agents (Stereochemistry of Carbon Compounds, (1962) by E. L. Eliel, McGraw Hill; Lochmuller, C. H., (1975) *J. Chromatogr.*, 113, 3) 283-302). Racemic mixtures of chiral compounds of the invention can be separated and isolated by any suitable method, including: (1) formation of ionic, diastereomeric salts with chiral compounds and separation by fractional crystallization or other methods, (2) formation of diastereomeric compounds with chiral derivatizing reagents, separation of the diastereomers, and conversion to the pure stereoisomers, and (3) separation of the substantially pure or enriched stereoisomers directly under chiral conditions.

Under method (1), diastereomeric salts can be formed by reaction of enantiomerically pure chiral bases such as brucine, quinine, ephedrine, strychnine, α -methyl- β -phenylethylamine (amphetamine), and the like with asymmetric compounds bearing acidic functionality, such as carboxylic acid and sulfonic acid. The diastereomeric salts may be induced to separate by fractional crystallization or ionic chromatography. For separation of the optical isomers of amino compounds, addition of chiral carboxylic or sulfonic acids, such as camphorsulfonic acid, tartaric acid, mandelic acid, or lactic acid can result in formation of the diastereomeric salts.

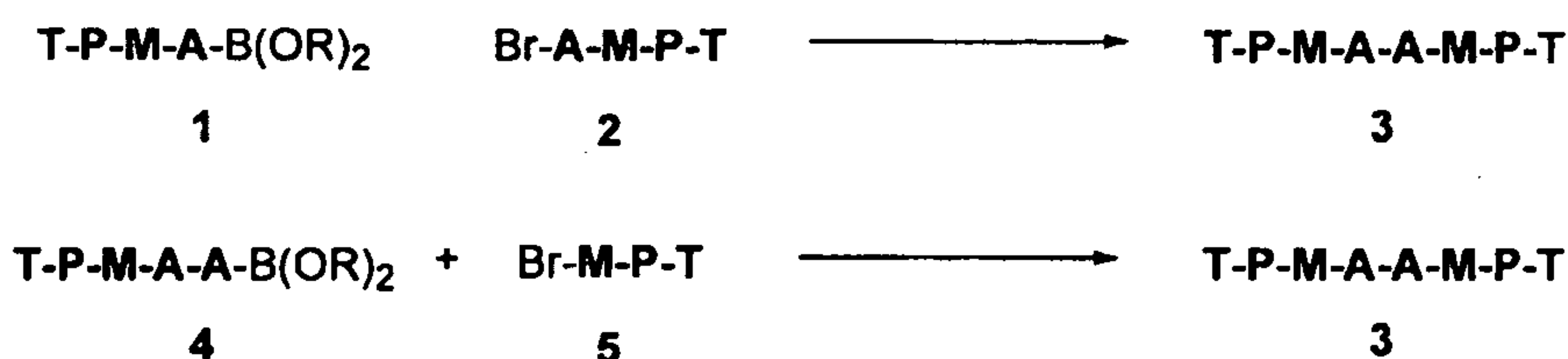
Alternatively, by method (2), the substrate to be resolved is reacted with one enantiomer of a chiral compound to form a diastereomeric pair (Eliel, E. and Wilen, S. (1994) Stereochemistry of Organic Compounds, John Wiley & Sons, Inc., p. 322). Diastereomeric compounds can be formed by reacting asymmetric compounds with enantiomerically pure chiral derivatizing reagents, such as menthyl derivatives, followed by separation of the diastereomers and hydrolysis to yield the free, enantiomerically enriched substrate. A method of determining optical purity involves making chiral esters, such as a menthyl ester, *e.g.*, (-) menthyl chloroformate in the presence of base, or Mosher ester, α -methoxy- α -(trifluoromethyl)phenyl acetate (Jacob III. (1982) *J. Org. Chem.* 47:4165), of the racemic mixture, and analyzing the NMR spectrum for the presence of the two atropisomeric diastereomers. Stable diastereomers of atropisomeric compounds can be separated and isolated by normal- and reverse-phase chromatography following methods for separation of atropisomeric naphthyl-isoquinolines (Hoye, T., WO 96/15111). By method (3), a racemic mixture of two enantiomers can be separated by chromatography using a chiral stationary phase (Chiral Liquid Chromatography (1989) W. J. Lough, Ed. Chapman and Hall, New York; Okamoto, (1990) *J. of Chromatogr.* 513:375-378). Enriched or purified enantiomers can be distinguished by methods used to distinguish other chiral molecules with asymmetric carbon atoms, such as optical rotation and circular dichroism.

Schemes and Examples

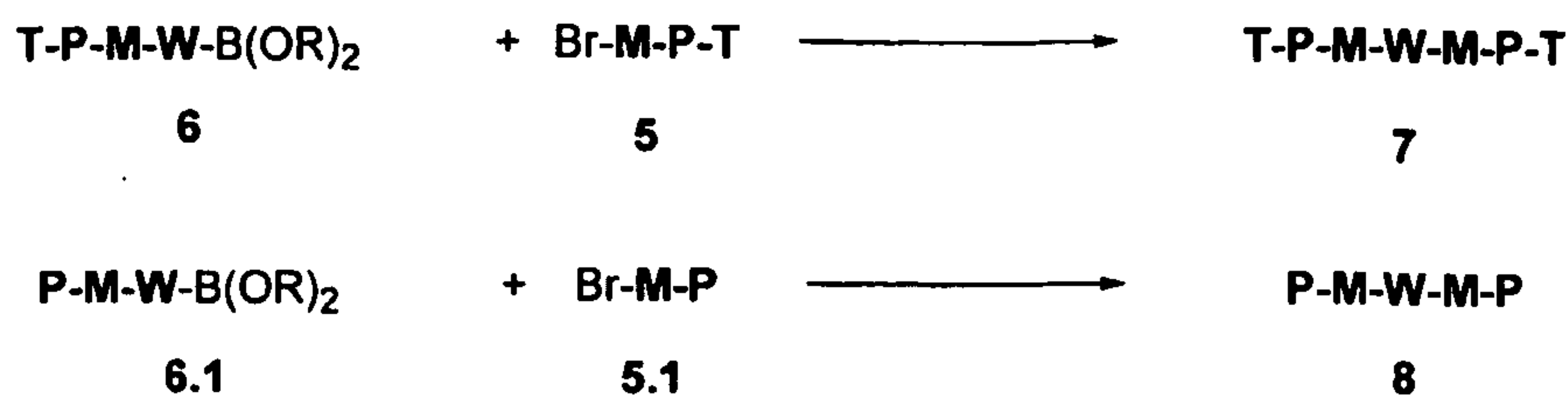
General aspects of these exemplary methods are described below and in the Examples. Each of the products of the following processes is optionally separated, isolated, and/or purified prior to its use in subsequent processes.

A number of exemplary methods for the preparation of compounds of the invention are provided herein, for example, in the Examples hereinbelow. These methods are intended to illustrate the nature of such preparations are not intended to limit the scope of applicable methods. Certain compounds of the invention can be used as intermediates for the preparation of other compounds of the invention. In the exemplary methods described herein, the fragment E-V- can also be written as R9-. Subsequently, the fragment E-V-Z- or R9-Z- can be written as T-. The fragments E-V-Z-P, R9-Z-P-, or T-P- can all be written as J-.

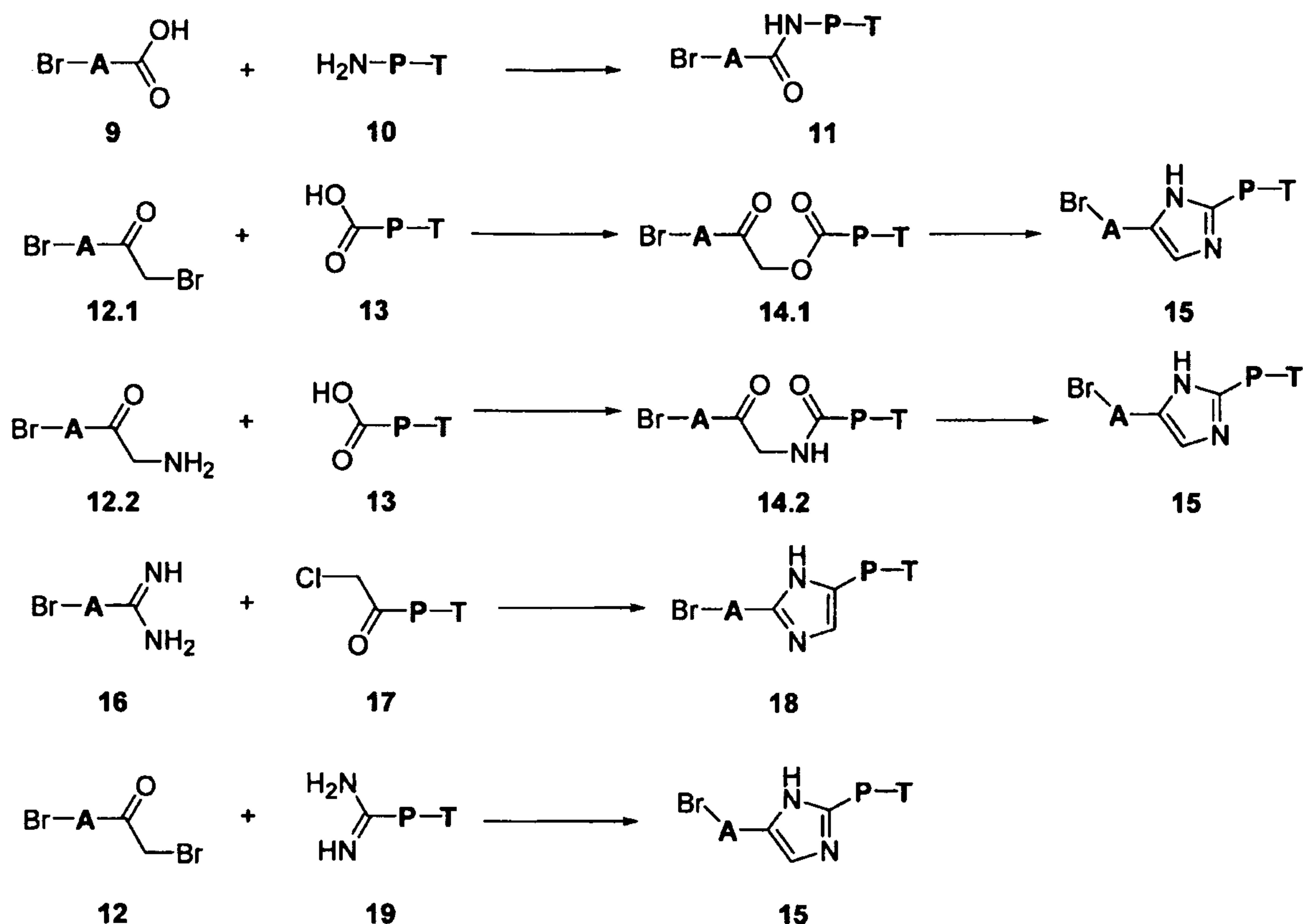
Scheme 1: Representative synthesis of T-P-M-A-A-M-P-T



Scheme 1 shows a general synthesis of the T-P-M-A-A-M-P-T molecule of the invention, wherein transition metal-mediated cross-coupling reaction is utilized to construct the A-A bond and/or A-M bond. For illustrative purposes, the Suzuki reaction is employed to couple a Br-M-P-T and an (RO)₂B-A-A-M-P-T intermediate or a Br-A-M-P-T and a (RO)₂B-A-M-P-T intermediate. Boronic ester 1 (or 4) is coupled with an appropriate coupling partner (e.g. arylbromide 2 or 5) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 3. Palladium mediated cross-coupling reactions that enable the A-A bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

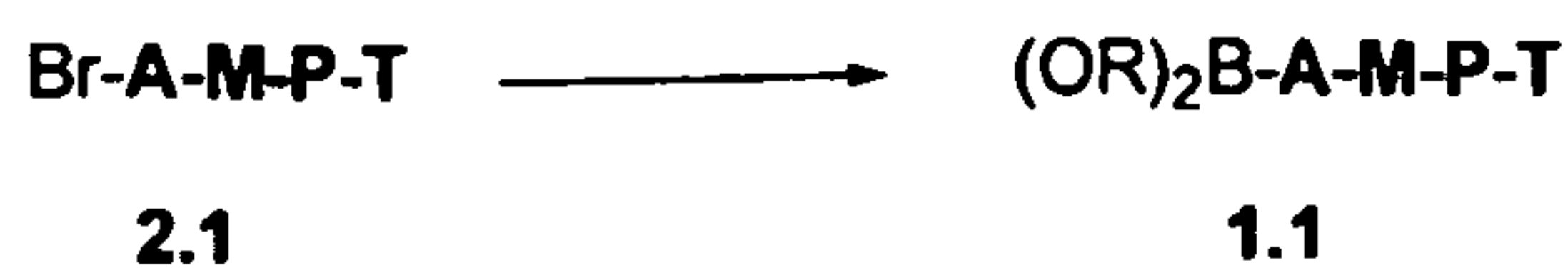
Scheme 1a: Representative synthesis of T-P-M-W-M-P-T

Scheme 1a shows a general synthesis of the T-P-M-W-M-P-T molecule and the P-M-W-M-P molecule of the invention, wherein transition metal-mediated cross-coupling reaction is utilized to construct the W-M bond. For illustrative purposes, the Suzuki reaction is employed to couple a Br-M-P-T and a (RO)₂B-W-M-P-T intermediate or a Br-M-P-PG to a (RO)₂B-W-M-P-PG intermediate. Boronic ester **6** (or **6.1**) is coupled with an appropriate coupling partner (e.g. arylbromide **5** or **5.1**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford **7** and **8**. Palladium mediated cross-coupling reactions that enable the A-A bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

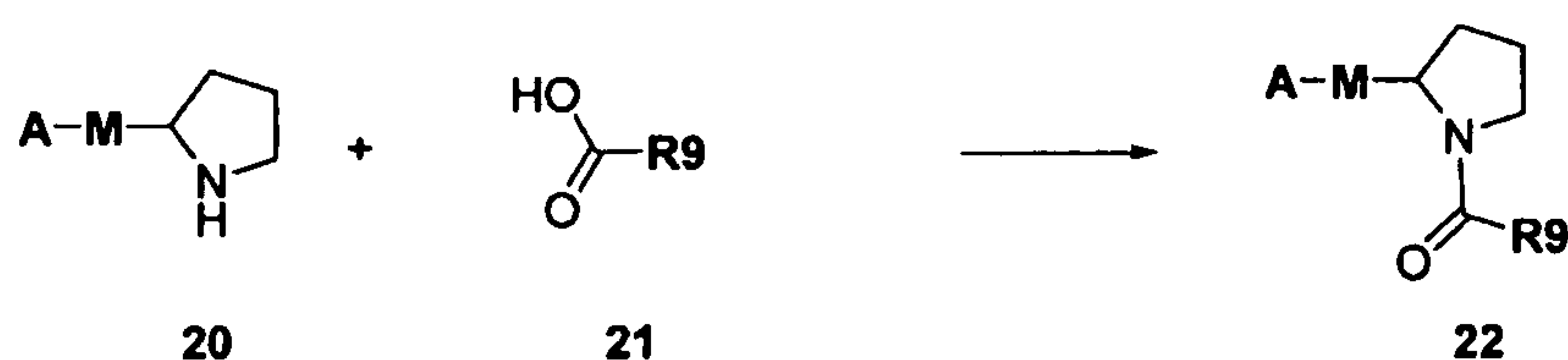
Scheme 2: Representative synthesis of A-M-P-T

Scheme 2 shows a general synthesis of an A-M-P-T molecule of the invention wherein, for illustrative purposes, M is an amide or an imidazole. Coupling of amine 10 with acid 9 is accomplished using a peptide coupling reagent (e.g. HATU) to afford amide containing 11. The acid 13 is coupled with an α -haloketone, such as α -bromoketone 12.1, under basic conditions (e.g. Et₃N) to afford 14.1. Alternatively, the acid 13 is coupled with an α -aminoketone 12.2, under amide formation conditions (e.g. EDC, Et₃N) to afford 14.2. Reaction of 14.1 or 14.2 with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing molecule Br-A-M-P-T.

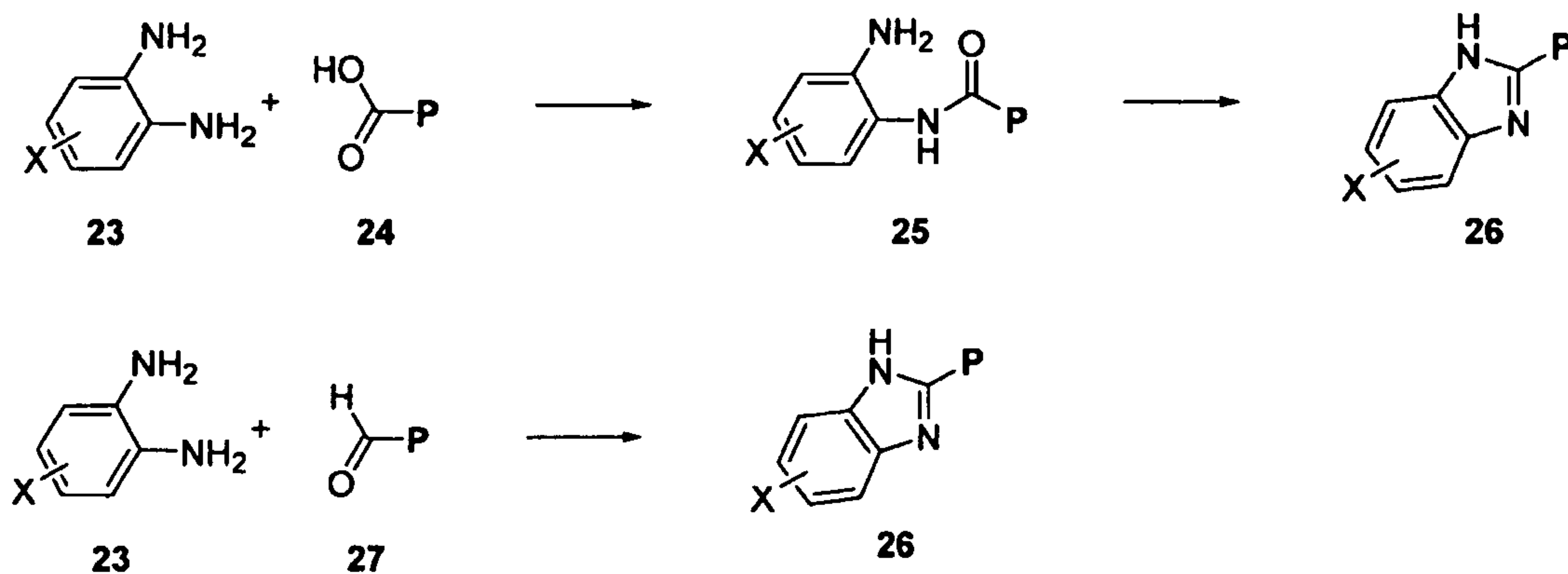
The benzamidine 16 is coupled with an α -haloketone such as α -chloroketone 17 under basic conditions such as K₂CO₃ to afford the imidazole containing molecule Br-A-M-P-T 18. A-M-P-T 15 can be prepared analogously.

Scheme 3: Representative synthesis of A-M-P-T

Scheme 3 shows a general synthesis of an A-M-P-T molecule of the invention wherein borate or boronic acid **1.1** can be synthesized from bromide **2.1**.

Scheme 4: Representative synthesis of A-M-P-Z-R9

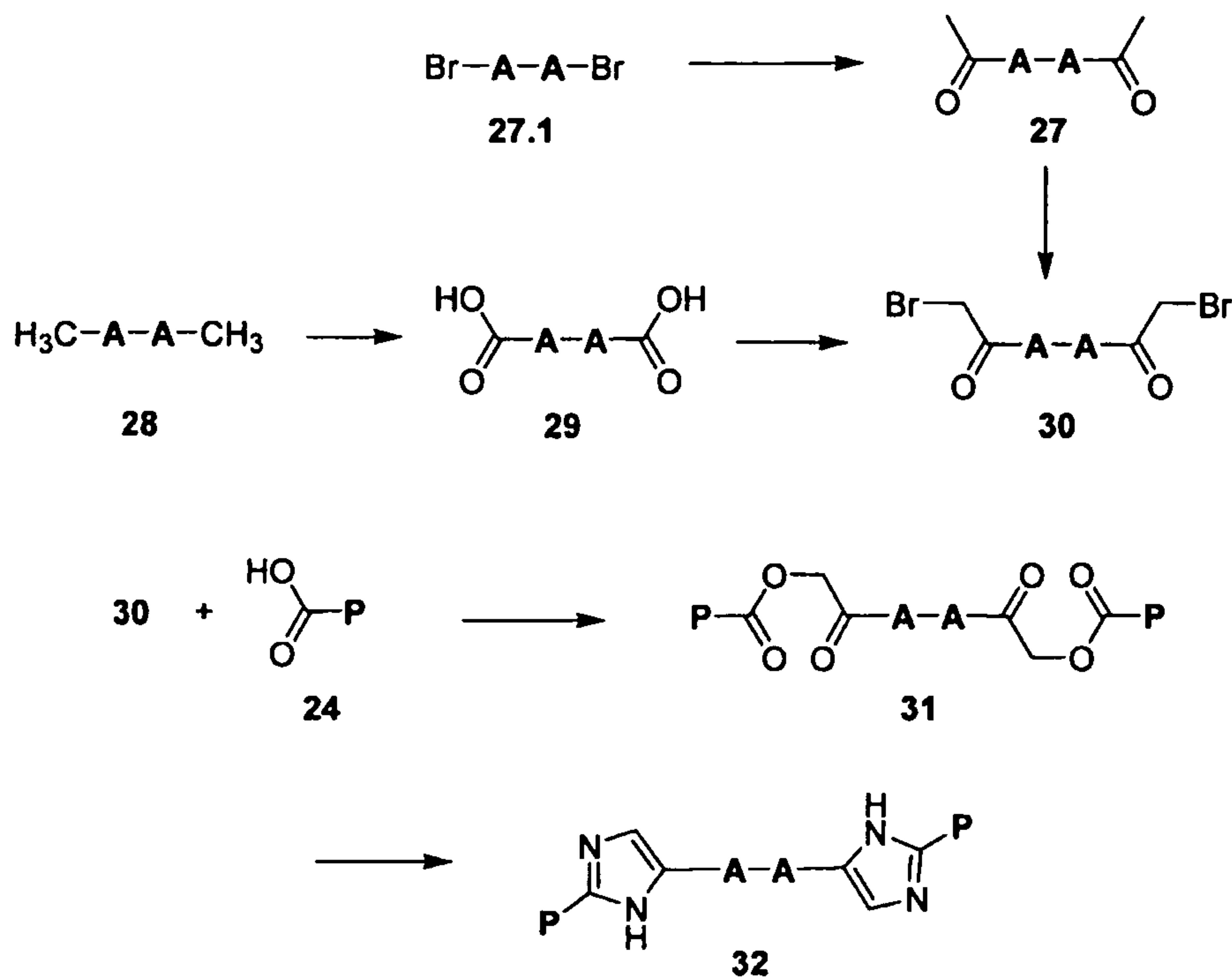
Scheme 4 shows a general synthesis of an A-M-P-Z-R9 fragment of the invention wherein, for illustrative purposes, P = pyrrolidine and Z = carbonyl. Coupling of amine **20** with acid **21** is accomplished using a peptide coupling reagent (e.g. HATU) to afford **22**.

Scheme 5: Representative synthesis of L-P

Scheme 5 shows a general synthesis of an L-P molecule of the invention wherein, for illustrative purposes, L = benzimidazole. The acid **24** is coupled with **23** using a peptide coupling reagent such as HATU to afford **25**. Heating in solvent (such as refluxing ethanol) affords L-P fragment **26**.

Alternatively, the L-P fragment **26** is obtained by reaction of diamine (such as **23**) and carbonyl compound (such as aldehyde **27**) in a solvent under heating conditions (e.g. ethanol under microwave irradiation).

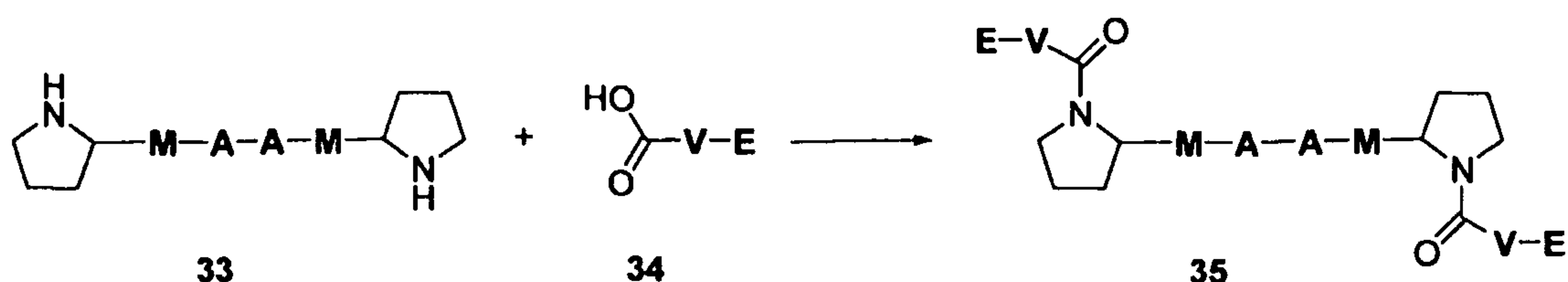
Scheme 6: Representative synthesis of P-M-A-A-M-P fragment



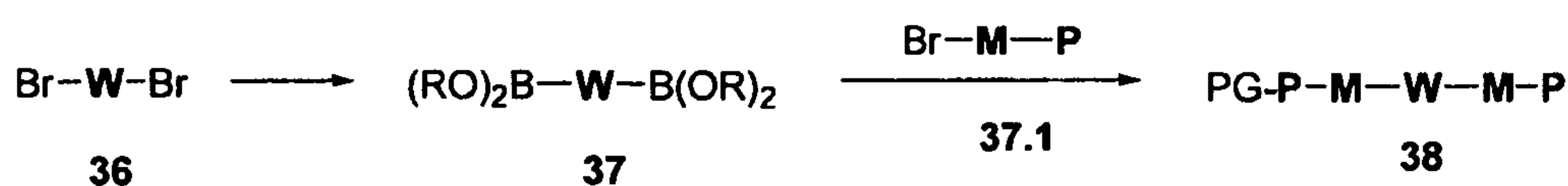
Scheme 6 shows a general synthesis of P-M-A-A-M-P molecule of the invention wherein, for illustrative purposes, M = imidazole. For example, the diketone **27** is converted to **30** using bromine. Compound **27** can be commercially available or can be prepared from dibromide **27.1** through coupling with a vinyltin reagent such as tributyl(ethoxyvinyl)stannane with palladium. Coupling of **30** with acid **24** under basic conditions such as diisopropylethylamine affords diester **31**. Imidazole formation is accomplished by treatment of **31** with ammonium acetate to provide the imidazole containing molecule P-M-A-A-M-P.

Alternatively, bromide **30** can be synthesized from **28**. The methyl compound **28** can be converted to the corresponding diacid **29** using potassium permanganate as oxidant.

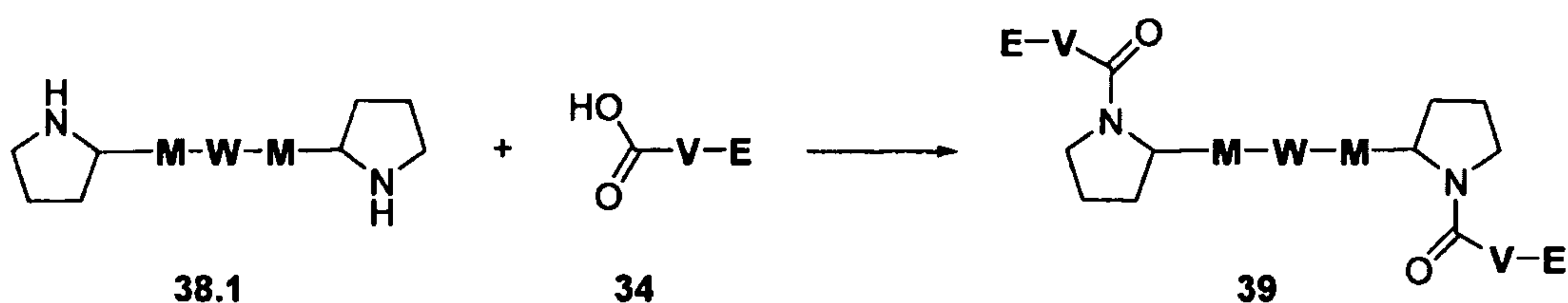
Conversion of **29** to **30** can be accomplished by a multi-step reaction, first treatment of **29** with oxalyl chloride, then by trimethylsilyl diazomethane, then with hydrobromic acid to afford compound **30**.

Scheme 7: Representative synthesis of E-V-P-M-A-A-M-P-V-E

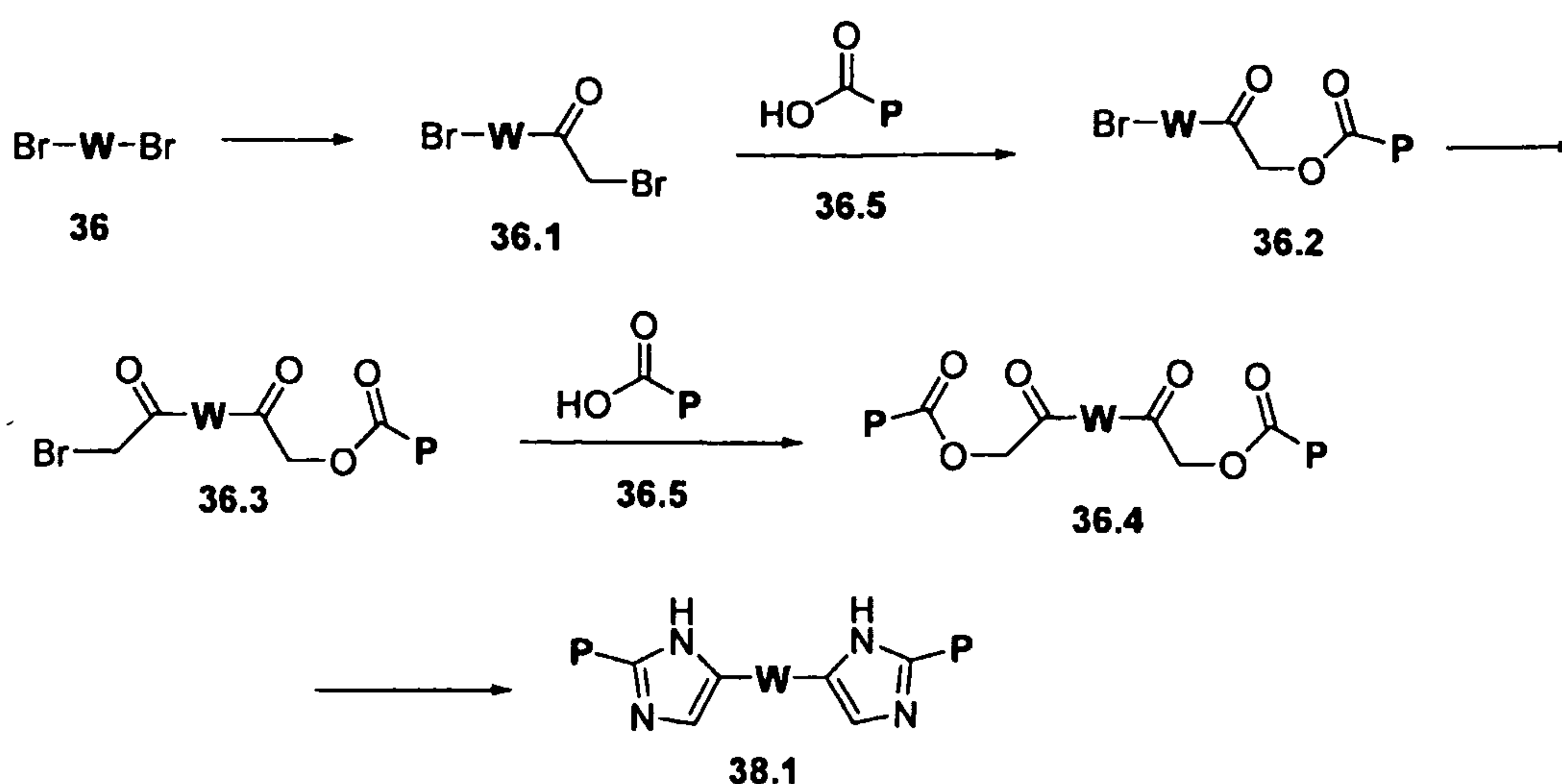
Scheme 7 shows a general synthesis of an E-V-P-M-A-A-M-P-V-E molecule of the invention wherein, for illustrative purposes, P = pyrrolidine and Z = carbonyl. Coupling of amine 33 with acid 34 is accomplished using a peptide coupling reagent, such as HATU, to afford 35.

Scheme 8: Representative synthesis of P-M-W-M-P

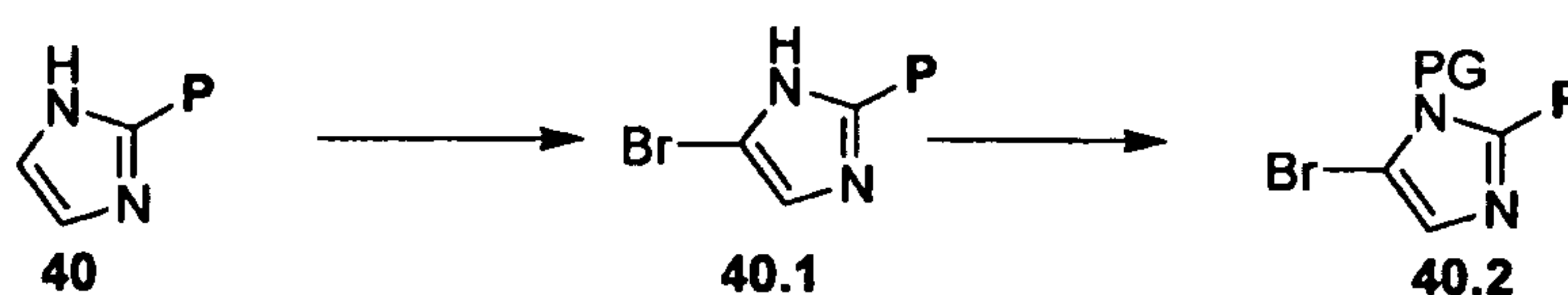
Scheme 8 shows a general synthesis of P-M-W-M-P molecule of the invention wherein, for illustrative purposes, W = polycyclic. Conversion of 36 to 37 was accomplished using transition metal-mediated reactions. Diboronate ester or acid 37 is coupled with a suitable reaction partner, such as bromide 37.1 using Suzuki coupling conditions to afford 38.

Scheme 9: Representative synthesis of E-V-P-M-W-M-P-V-E

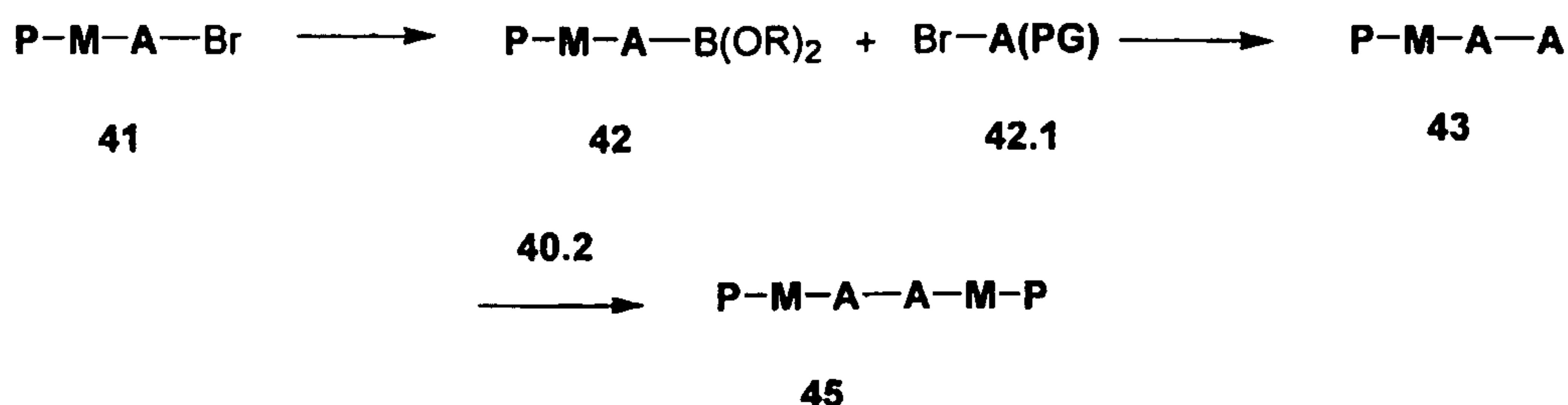
Scheme 9 shows a general synthesis of an E-V-P-M-W-M-P-V-E molecule of the invention wherein, for illustrative purposes, P = pyrrolidine and Z = carbonyl. Coupling of amine 38.1 with acid 34 is accomplished using a peptide coupling reagent, such as HATU, to afford 39.

Scheme 9a: Representative synthesis of P-M-W-M-P

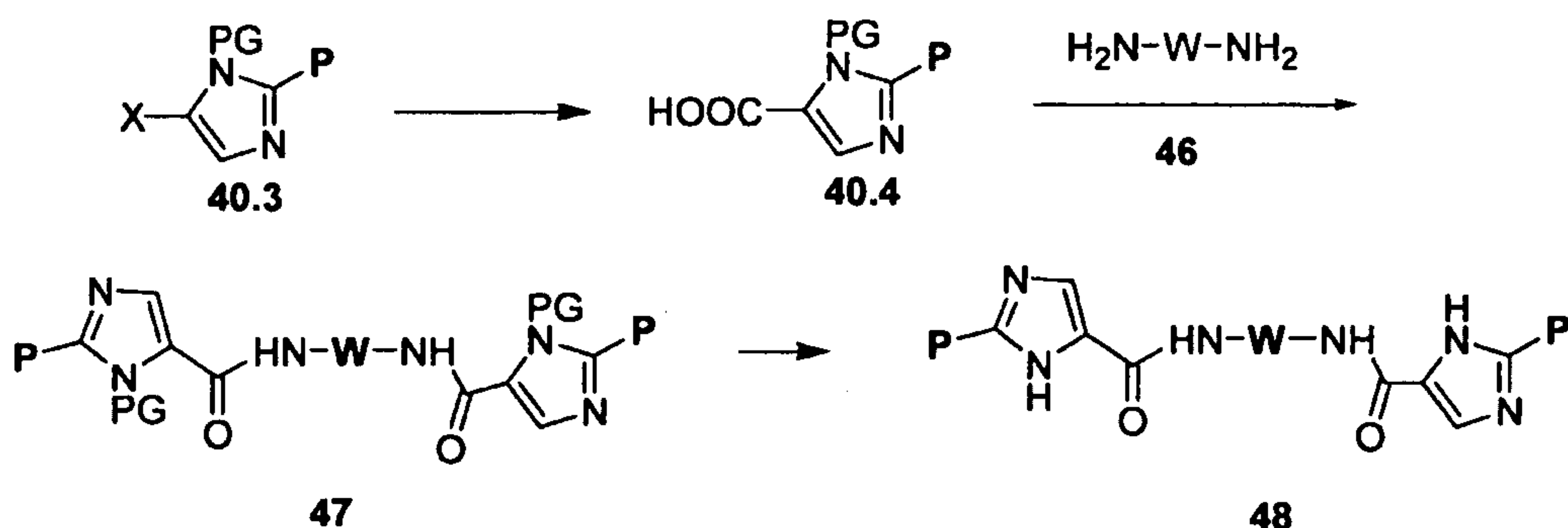
Scheme 9a shows a general synthesis of a P-M-W-M-P molecule of the invention wherein, for illustrative purposes, M = imidazole, W = polycyclic. The compound 36 was coupled with a vinyltin reagent such as tributyl(ethoxyvinyl)stannane with palladium, followed by bromination and hydrolysis with NBS and water, to give bromoketone 36.1. The reaction between bromide 36.1 and a carboxylic acid (36.5) under basic condition generated ester 36.2. Following the same reaction sequence, compound 36.2 was converted to diester 36.4. Conversion of 36.4 to 38.1 was accomplished with ammonia reagents such as ammonium acetate at elevated temperature.

Scheme 10: Representative synthesis of M-P

Scheme 10 shows a general synthesis of an M-P molecule of the invention wherein, for illustrative purposes, PG is a protecting group. Imidazole 40 can be halogenated, for example, under the action of N-bromosuccinimide to provide bromoimidazole 40.1. Bromoimidazole 40.1 can be protected using standard conditions to give 40.2, such as SEM-Cl and sodium hydride when PG = SEM.

Scheme 11: Representative synthesis of P-M-A-A-M-P

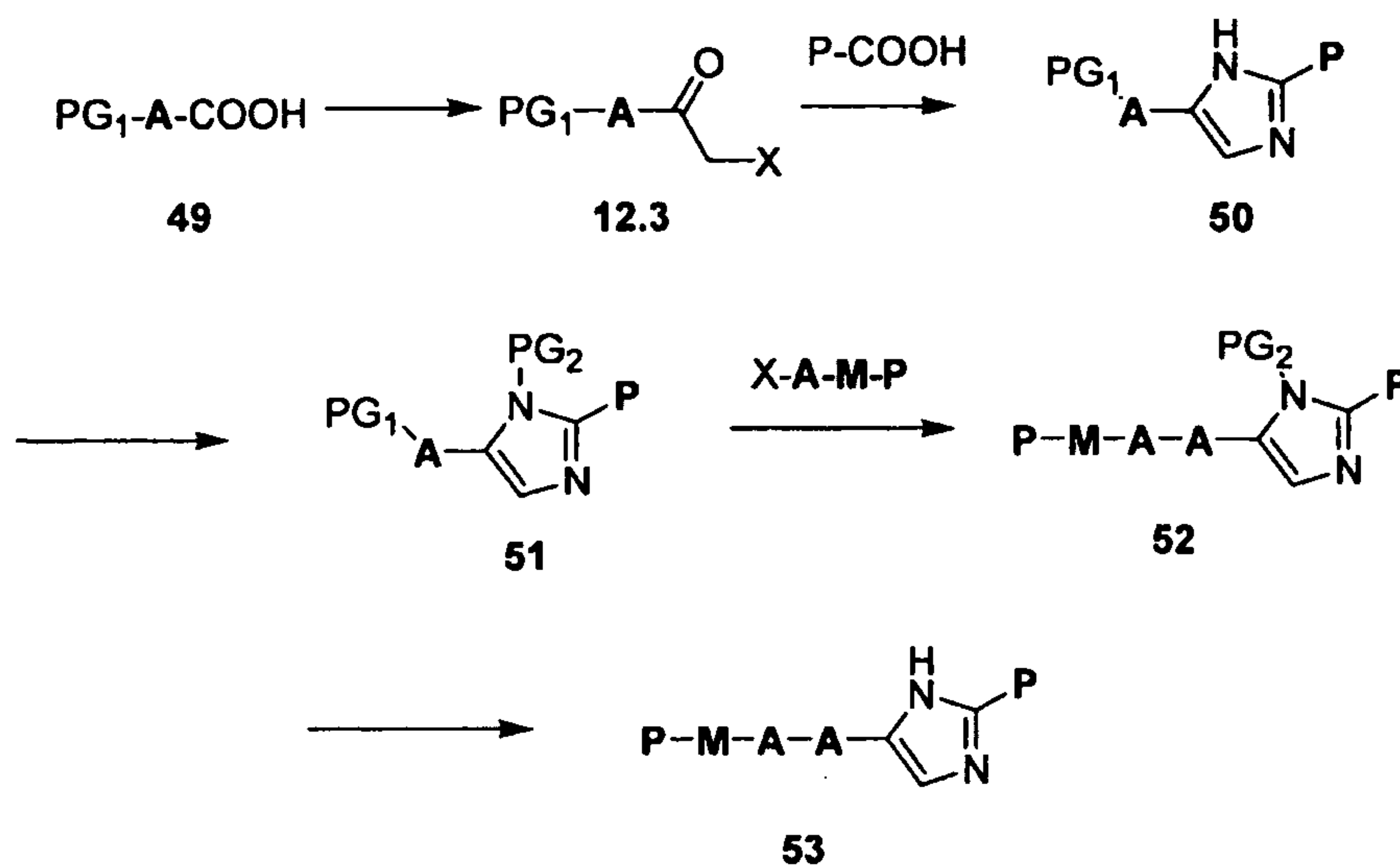
Scheme 11 shows a general synthesis of a P-M-A-A-M-P molecule of the invention wherein, for illustrative purposes, M = imidazole. Boronic ester 42, which can be prepared from bromide 41, is coupled with a suitably protected appropriate coupling partner (e.g. arylbromide 42.1, optionally protected with PG) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 43. Palladium mediated cross-coupling reactions that enable the A-A bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada and Stille reactions. If optionally protected, removal of the protecting group (PG) (for example, catalytic hydrogenation of a benzyl ether) provides the deprotected compound 43. Coupling of 43 with suitably protected imidazole 40.2 (for example, PG = SEM ether) using a metal catalyst (e.g. CuI) gives protected P-M-A-A-M-P (45). Deprotection (for example deprotection of a SEM ether using an acid such as TFA) provides the imidazole containing fragment P-M-A-A-M-P 45.

Scheme 12: Representative synthesis of P-M-W-M-P

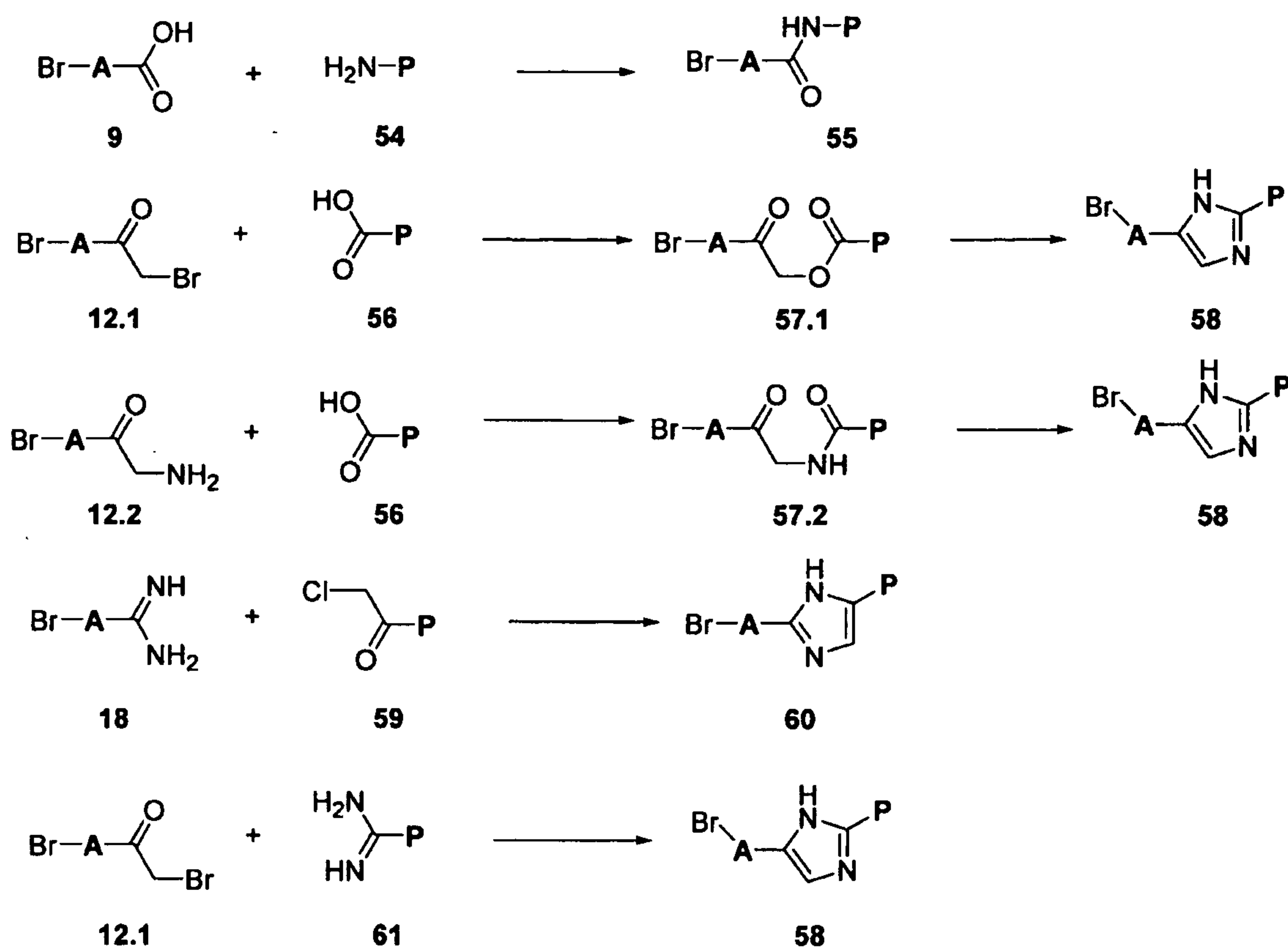
Scheme 12 shows a general synthesis of a P-M-W-M-P molecule of the invention wherein, for illustrative purposes, X = halogen or triflate, M = imidazole, and W is 46, PG = protecting group. Haloimidazole 40.3, such as a bromoimidazole, is subjected to a metal-halogen exchange reaction, such as BuLi in THF, and then treated with a CO₂ source, such as solid CO₂, to give

40.4. Coupling of 40.4 and 46 using peptide coupling conditions, such as HATU, gives 47. PG deprotection, such as TFA deprotection of a SEM group, gives the compound P-M-W-M-P 48.

Scheme 13: Representative synthesis of P-M-A-A-M-P

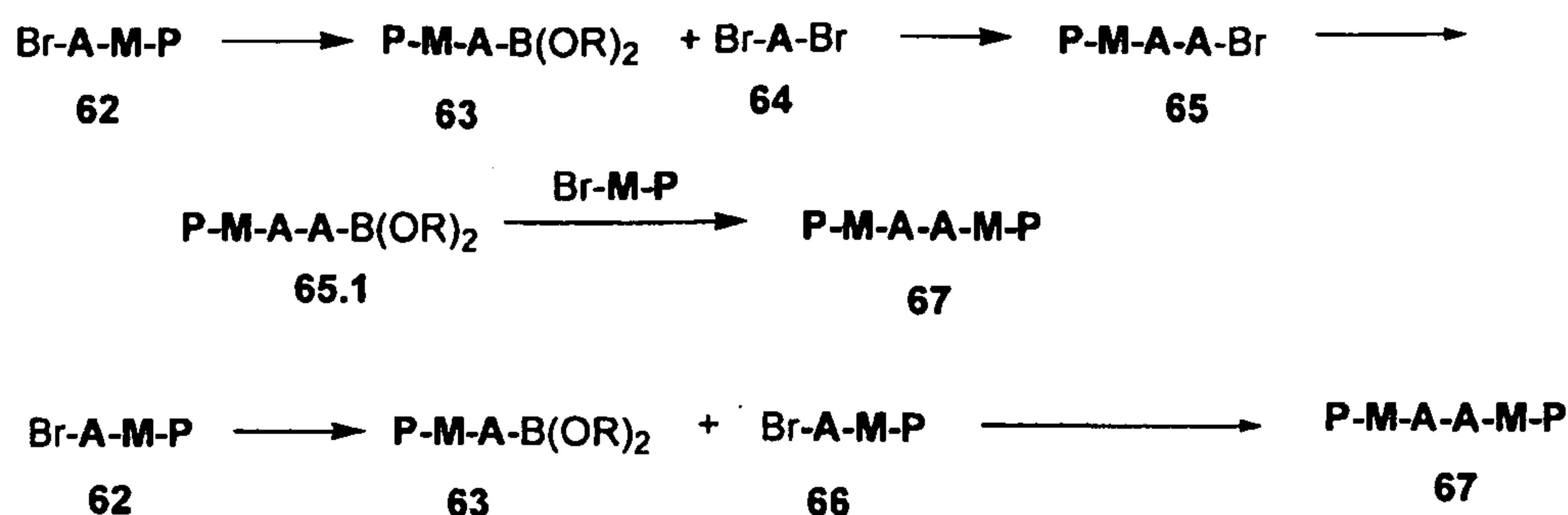


Scheme 13 shows a general synthesis of a P-M-A-A-M-P molecule of the invention wherein, for illustrative purposes, X = halogen, amine or triflate, M = imidazole, PG₁ and PG₂ = protecting groups. The protected acid 49 (PG₁ is a suitable protecting group, such as Cbz) is converted to α-halomethyl ketone 12.3., which is then transformed to PG₁-A-M-P 50 using the analogous conditions for converting 12.1 and 12.2 to 15. The imidazole is subjected to protection, with SEM for instance, to afford 51, which is deprotected, with H₂ and Pd to remove a Cbz for example, followed by coupling with fragment X-A-M-P, using standard Pd coupling conditions for example, to afford 52. PG deprotection, such as TFA deprotection of a SEM group, gives the compound P-M-A-A-M-P 53.

Scheme 14: Representative synthesis of A-M-P

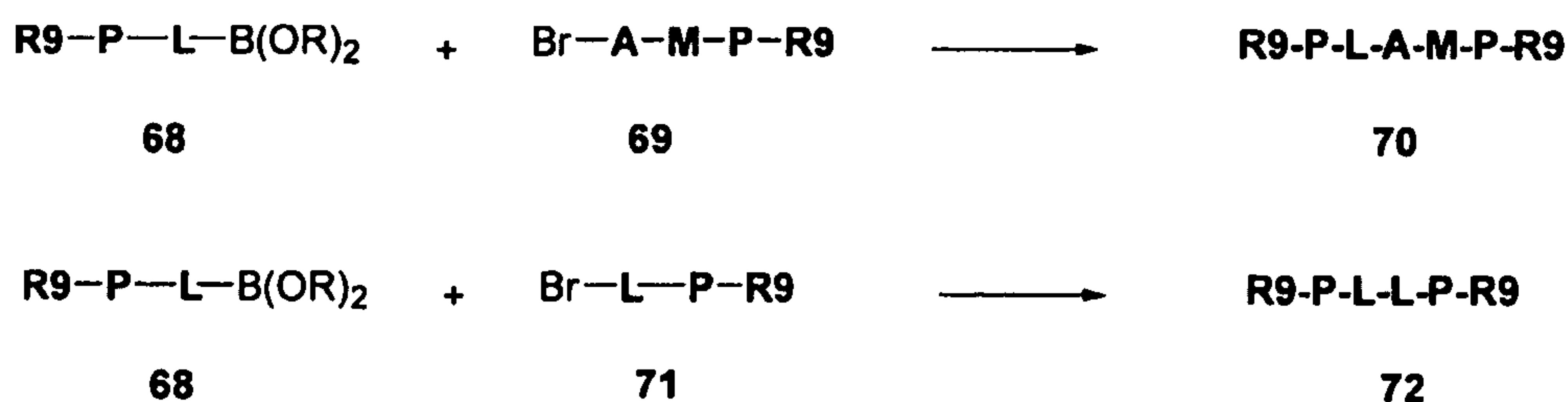
Scheme 14 shows a general synthesis of an **A-M-P** molecule of the invention wherein, for illustrative purposes, **M** is an amide bond, or an imidazole. Coupling of amine **54** with acid **9** is accomplished using a peptide coupling reagent (e.g. HATU) to afford amide containing **55**. The acid **56** is coupled with an α -haloketone, such as α -bromoketone **12.1**, under basic conditions (e.g. Et_3N) to afford **57.1**. Alternatively, the acid **56** is coupled with an α -aminoketone **12.2**, under amide formation conditions (e.g. EDC, Et_3N) to afford **57.2**. Reaction of **57.1** and **57.2** with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing molecule **A-M-P**.

The benzamidine **18** is coupled with an α -haloketone such as α -chloroketone **59** under basic conditions such as K_2CO_3 to afford the imidazole containing molecule **A-M-P 60**. **A-M-P 58** can be prepared analogously.

Scheme 15: Representative synthesis of P-M-A-A-M-P

Scheme 15 shows a general synthesis of a **P-M-A-A-M-P** molecule of the invention. Boronic acid or its ester **63**, can be prepared from bromide **62** using a palladium catalyst (e.g. Pd(PPh₃)₄) and a boron reagent (bis(pinacolato)diboron, for example), is coupled with an excess of appropriate coupling partner (e.g. a di-halo-aromatic or di-halo-heteroaromatic moiety **64**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford bromide **65**, which then is converted to boronic acid or ester **65.1**. Palladium mediated cross-coupling reactions that enable the A-A bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada and Stille reactions. Suzuki coupling of **65.1** with halo-imidazole such as bromo-imidazole using a palladium catalyst (such as Pd(PPh₃)₄) gives **P-M-A-A-M-P** fragment **67**.

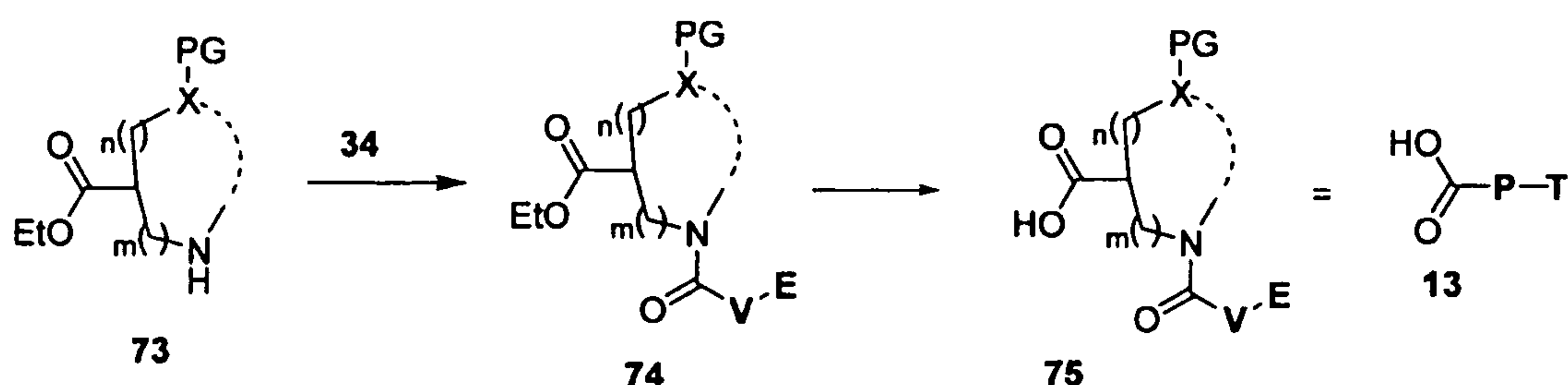
Alternatively, Suzuki coupling of **63** with halo-A-M-P fragment using a palladium catalyst (such as Pd(PPh₃)₄) gives **P-M-A-A-M-P** fragment **67**.

Scheme 16: Representative synthesis of R⁹-P-L-A-M-P-R⁹ and R⁹-P-L-L-P-R⁹

Scheme 16 shows a general synthesis of an **R⁹-P-L-A-M-P-R⁹** molecule and a **R⁹-P-L-L-P-R⁹** molecule of the invention wherein a transition metal-mediated cross-coupling reaction is utilized to construct the A-A bond. For illustrative purposes, the Suzuki reaction is employed to couple

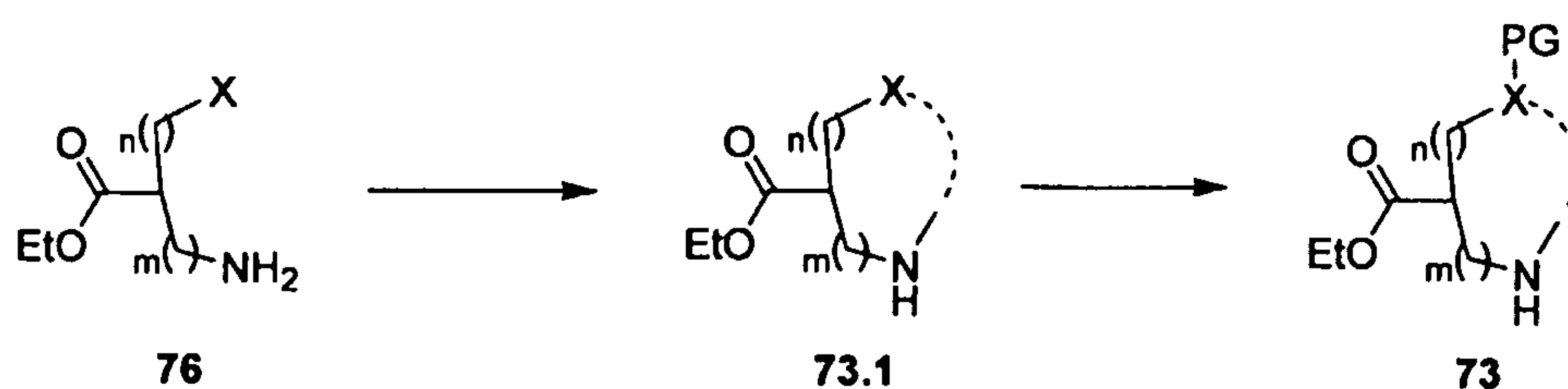
(RO)₂B-L-P-R₉ and Br-A-M-P-R₉. Boronic ester **68** is coupled with an appropriate coupling partner (e.g. arylbromide **69**) using a palladium catalyst (such as Pd(PPh₃)₄) to afford **70**. Similarly, R₉-P-L-L-P-R₉ **72** is prepared by coupling compounds **68** and **71**.

Scheme 17: Representative synthesis of P-T

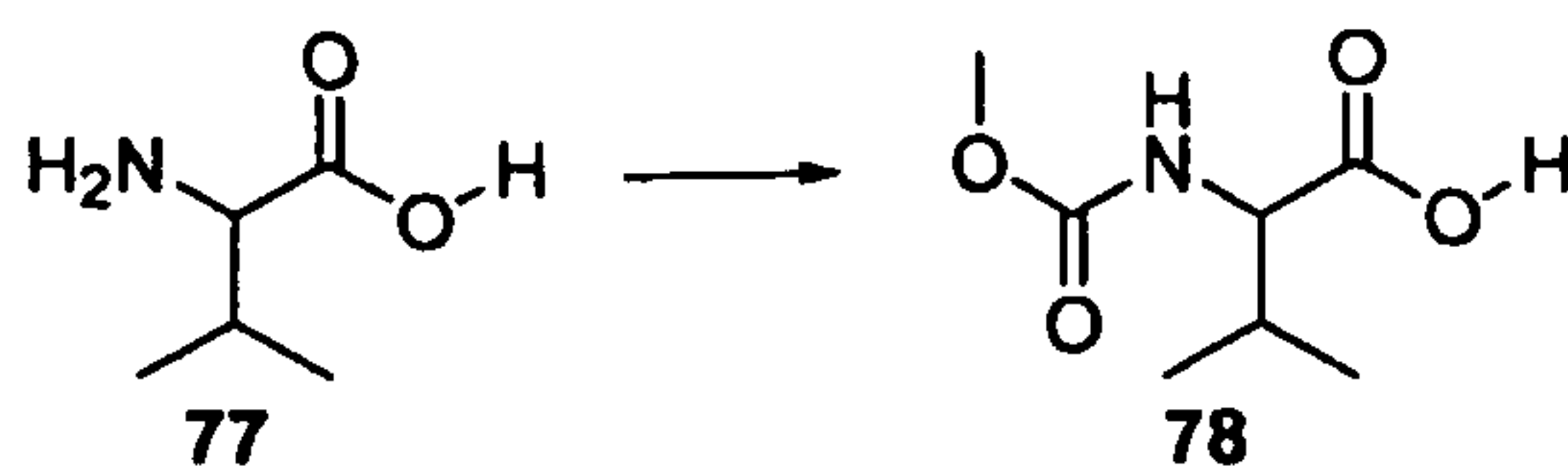


Scheme 17 shows a general synthesis of a P-T molecule of the invention wherein, for illustrative purposes, P = either an acyclic or cyclic amino ester (such as ethyl ester), optionally protected with PG if necessary, Z = carbonyl, X = carbon or heteroatom, and m and n = 0 - 5, independently. Coupling of amine **73** with acid **34** is accomplished using a peptide coupling reagent, such as HATU, to afford **75**, which after removal of ethyl group provides the P-T compound.

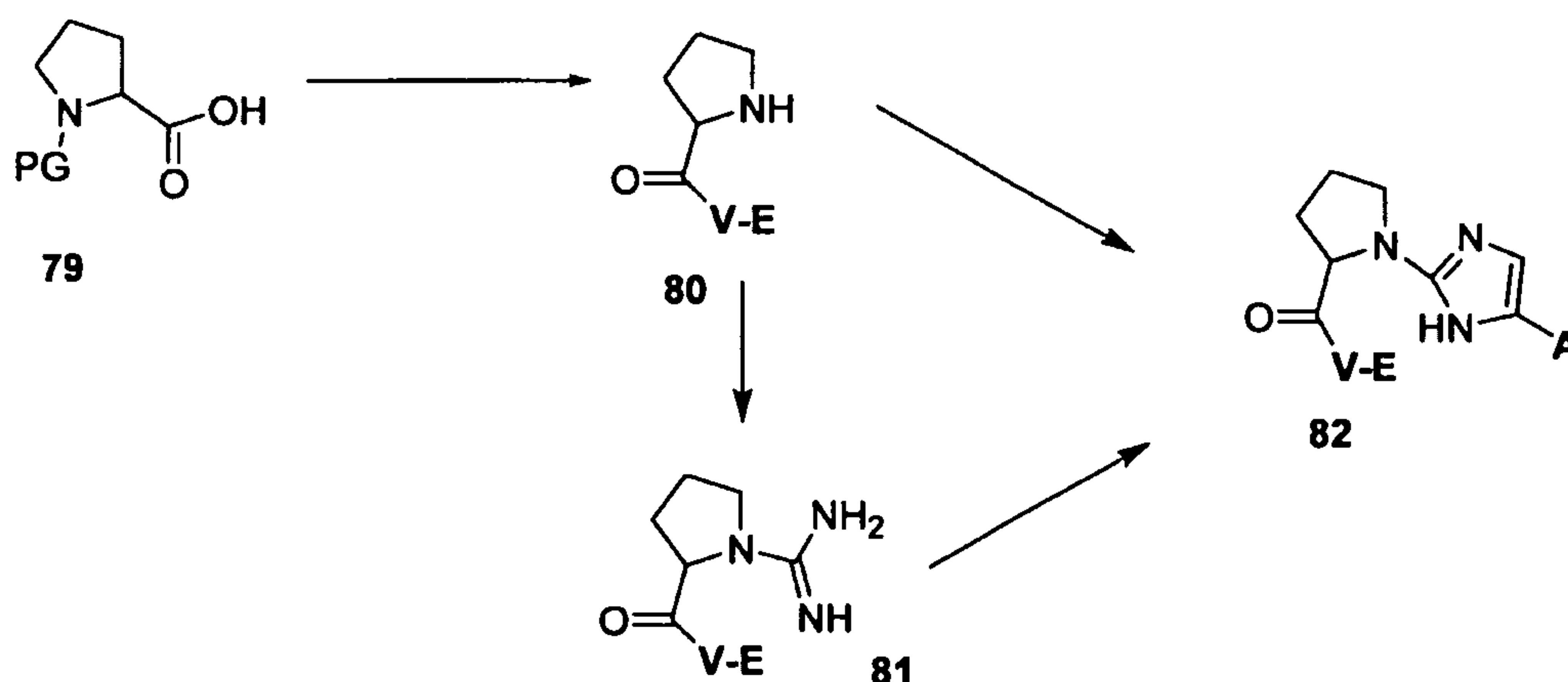
Scheme 18: Representative synthesis of P



Scheme 18 shows a general synthesis of a P molecule of the invention wherein X = carbon or heteroatom and m and n = 0 - 5, independently. For illustrative purposes, P is substituted with an ethoxycarbonyl group. Commercially available amino ester such as an ethyl ester is converted to substituted or cyclized amino ester **73.1**, through for example, reductive amination or Mitsunobu reaction. Compound **73.1** can be protected to provide compound **73** if necessary.

Scheme 19: Representative Synthesis of E-V

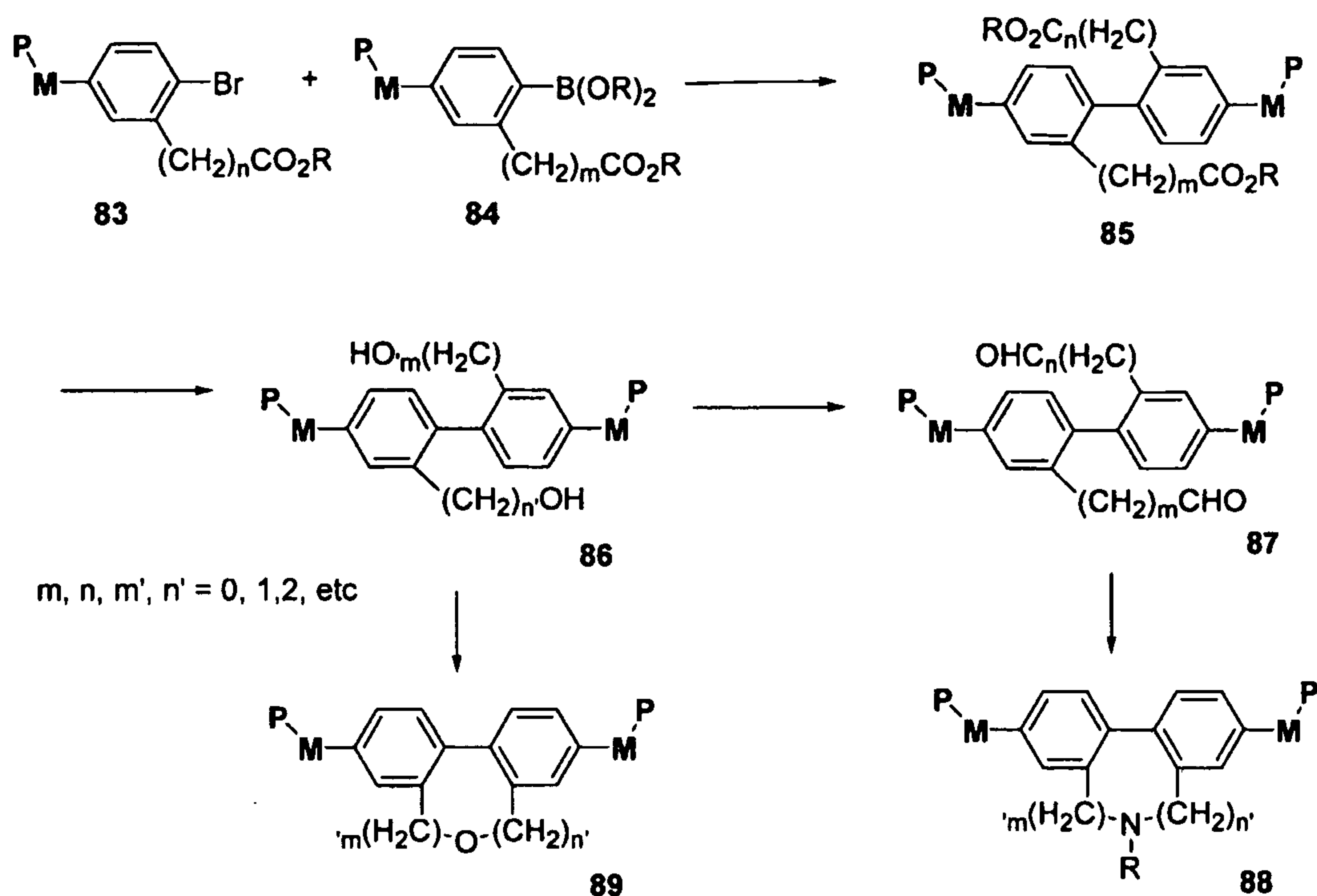
Scheme 19 shows a general synthesis of an E-V molecule of the invention wherein, for illustrative purposes, V is isobutyl and E is methoxycarbonylamino. Amino acid 77 can be converted to the corresponding carbamate 78, such as a methyl carbamate by reaction with methyl chloroformate under basic conditions (sodium bicarbonate).

Scheme 20: Synthesis of the E-V-Z-P-M-A

Scheme 20 shows the synthesis of a E-V-Z-P-M-A molecule of the invention wherein, for illustrative purposes, M is imidazole, P is pyrrolidine, and Z is carbonyl. An amino acid derivative can be reacted with an N-protected proline derivative via reaction conditions employing a coupling reagent, such as HATU, deprotection of the resulting coupling product, for example in the case of *tert*-butoxy carbonyl, the treatment with a proton source such as HCl yielded compound 80. The conversion of 80 to E-V-Z-P-M-A (82) can be obtained under reaction conditions of nucleophilic aromatic substitution, for example the displacement of methyl sulfonate under basic conditions and elevated temperatures.

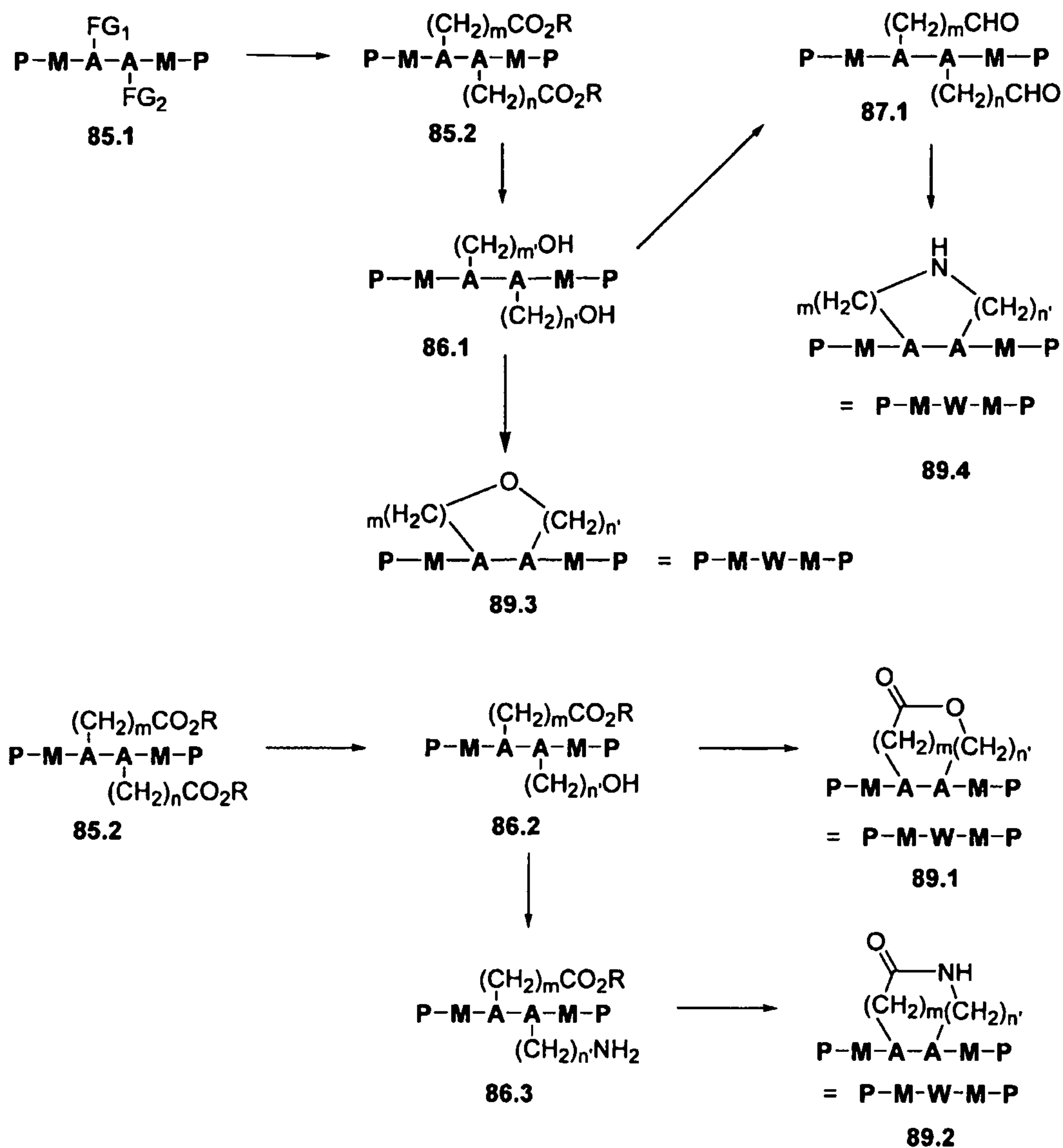
Alternatively, for illustrative purposes, the amino acid derivative 80 can be converted to a guanidinium containing compound 81, via a reaction with a guanidylation reagent. The E-V-Z-P-M-A compound 82 can be obtained via reaction with a 1,2 di-electrophile such as an α -halogenated carbonyl group under basic conditions.

Scheme 21: Representative synthesis of P-M-W-M-P



Scheme 21 shows a general synthesis of a P-M-W-M-P molecule of the invention wherein. Boronic ester **84** is coupled with an appropriate coupling partner (e.g. arylbromide **83**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford **85**. Carboxylate **85** is reduced with reagents such as DIBAL-H to afford diol **86**. The treatment of diol **86** with acids such as H₃PO₄ at elevated temperature generates P-M-W-M-P compound **89**. Alternatively, diol **86** can be oxidized with reagents such as pyridine-sulfur trioxide to form dialdehyde **87**, which react with amines in the presence of reducing reagents such as NaBH(OAc)₃ to provide P-M-W-M-P compound **88**.

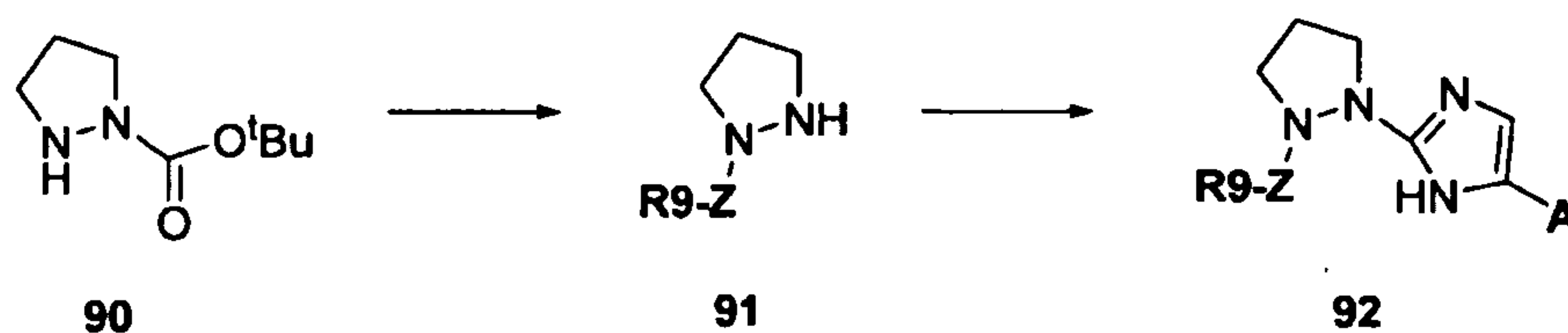
Scheme 21a: Representative synthesis of P-M-W-M-P



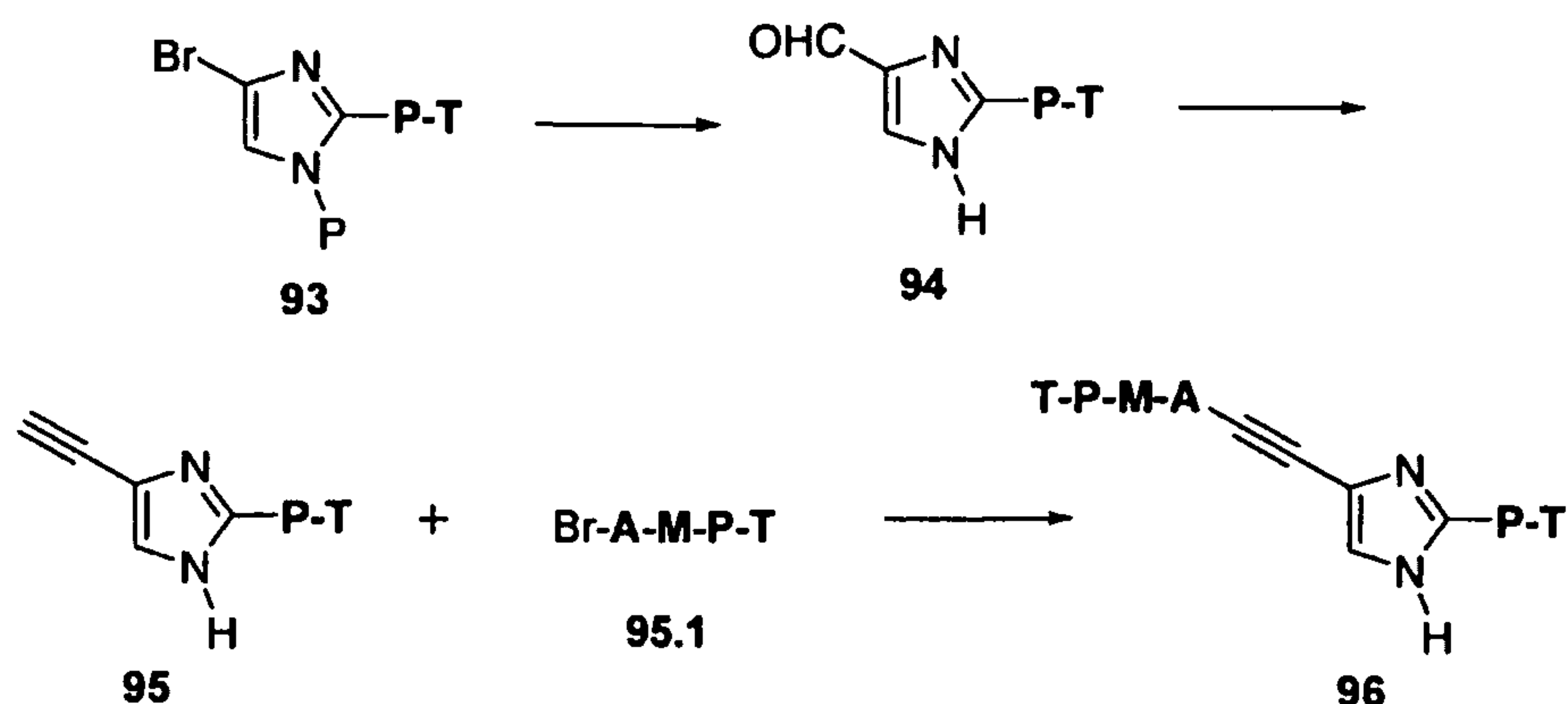
Scheme 21a shows a general synthesis of a P-M-W-M-P molecule of the invention. For illustrative purposes, FG₁ and FG₂ can be converted to esters attached to an A group. Carboxylate 85.2 is reduced with reagents, such as DIBAL-H, to afford diol 86.1. The treatment of diol 86.1 with acids, such as H₃PO₄, at elevated temperature generates P-M-W-M-P compound 89.3. Alternatively, diol 86.1 can be oxidized with reagents such as pyridine-sulfur trioxide to form dialdehyde 87.1, which reacts with amines in the presence of reducing reagents such as NaBH(OAc)₃ to provide P-M-W-M-P compound 89.4. The carboxylate 85.2 is selectively reduced to provide hydroxyl ester 86.2, which can be cyclized to form P-M-W-M-P compound 89.1. Compound 86.1 is converted to amine ester 86.3, for example through azide

formation and reduction with hydrogenation. Compound **86.3** can be cyclized to form **P-M-W-M-P** compound **89.2**.

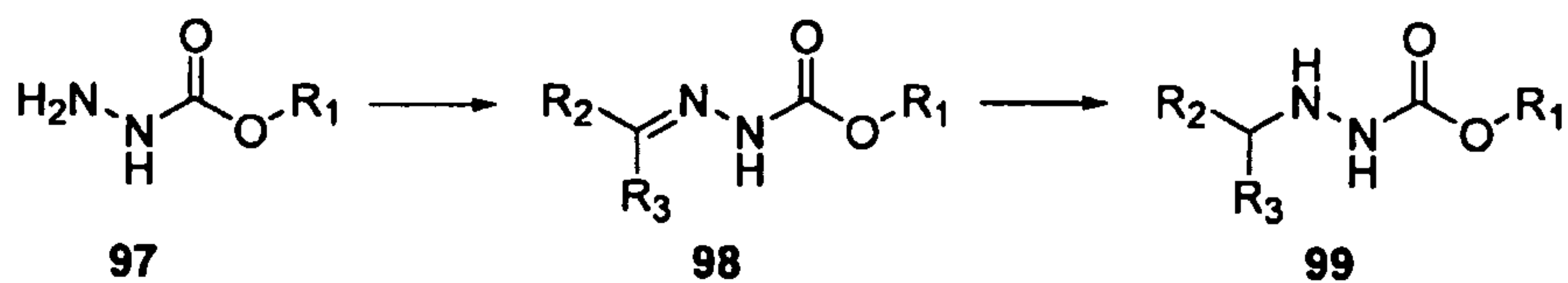
Scheme 22: Construction of a R⁹-Z-P-M-A



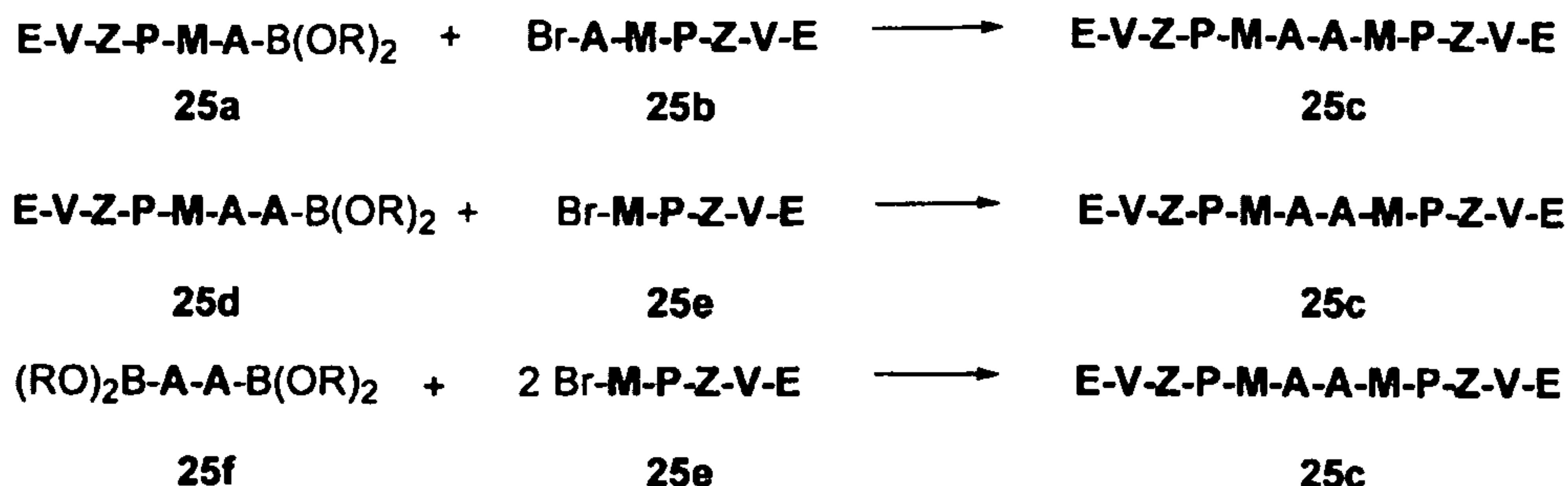
Scheme 22 shows the general synthesis of a **R⁹-Z-P-M-A** molecule, for illustrative purposes starting with *tert*-butoxy carbonyl derivative **90** (J. Am. Chem. Soc. 2003, 1221). Compound **90** can be acylated with substituent **T** wherein **Z** is carbonyl, via reaction conditions employing a coupling reagent such as HATU. Removal of the protecting group, for example in the case of *tert*-butoxycarbonyl by the treatment with a proton source such as HCl, yields compound **91**. A compound like **91** can be obtained under reaction conditions of nucleophilic aromatic substitution, for example the displacement of methyl sulfonate under basic conditions and elevated temperatures to provide the **R⁹-Z-P-M-A** compound **92**. Alternatively, **91** can be converted into a guanidinium derivative. When suitably substituted, cyclization provides the **R⁹-Z-P-M-A** compound **92**.

Scheme 23: Representative synthesis of T-P-M-A-A-M-P-T

Scheme 23 shows a general synthesis of a T-P-M-A-A-M-P-T molecule of the invention wherein, for illustrative purposes, M = imidazole and A = alkyne. Bromoimidazole 93 is alkynylated by lithiation and trapping with a formate equivalent (e.g. DMF). The aldehyde 94 is converted to alkyne 95 using a phosphorus-based reagent (e.g. Ohira-Bestmann reagent). Compound 95 is coupled with a Br-A-M-P-T under Sonogashira conditions to afford the alkyne-containing compound 96.

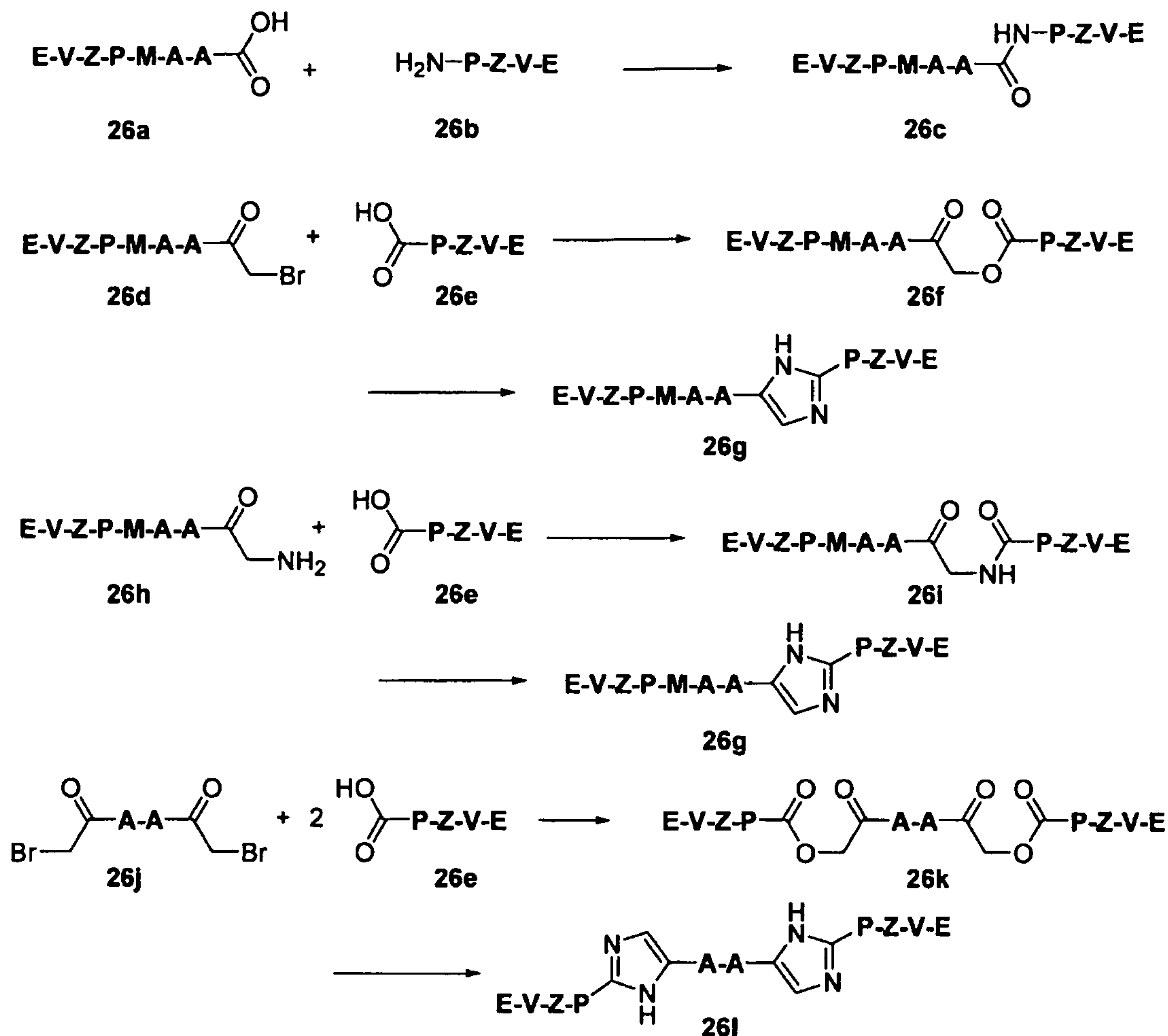
Scheme 24: Representative Synthesis of R9 Fragment

Scheme 24 shows a general synthesis of an R9 molecule of the invention. Reaction of hydrazine carboxylate 97 with a ketone or aldehyde, such as acetone, under acidic conditions (e.g. AcOH) affords the imine 98. Reaction of 98 under reducing conditions, such as PtO₂ and hydrogen gas, affords the substituted hydrazinecarboxylate 99.

Scheme 25: Representative synthesis of E-V-Z-P-M-A-A-M-P-Z-V-E

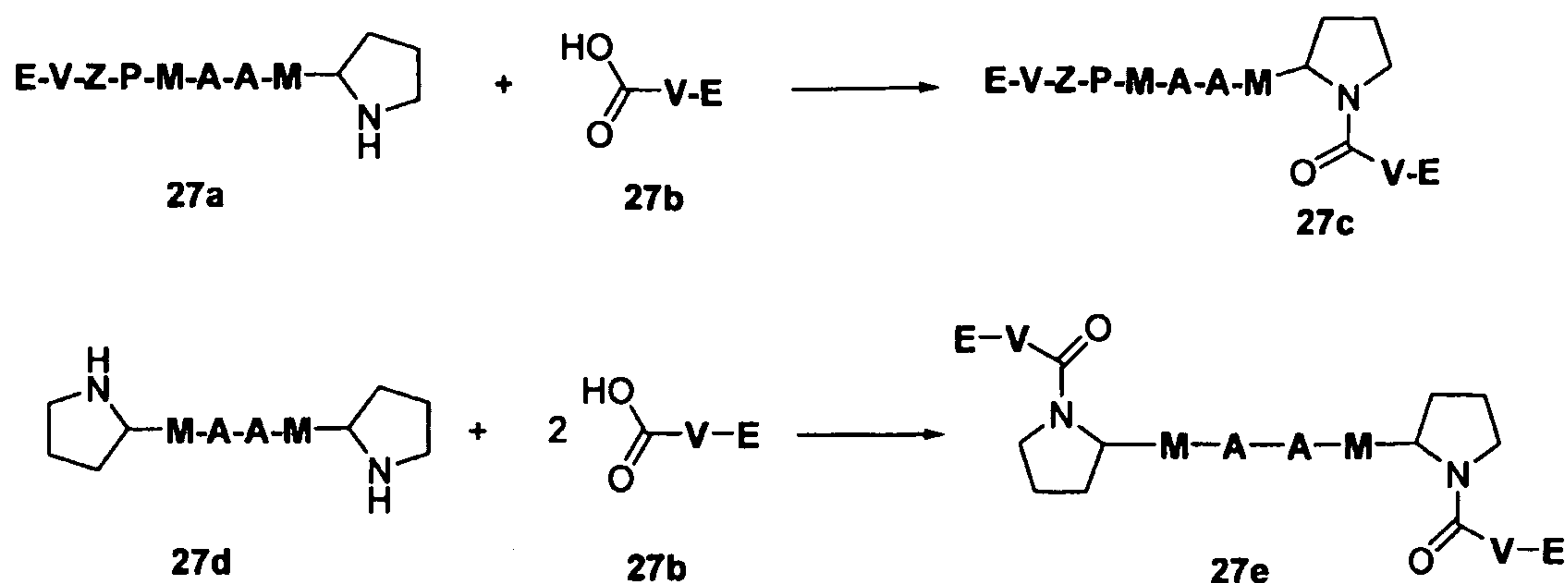
Scheme 25 shows a general synthesis of the E-V-Z-P-M-A-A-M-P-Z-V-E molecule of the invention, wherein a transition metal-mediated cross-coupling reaction is utilized to construct the A-A bond and/or A-M bond. For illustrative purposes, the Suzuki reaction is employed to couple Br-M-P-Z-V-E and (RO)₂B-A-A-M-P-Z-V-E or (RO)₂B-A-M-P-Z-V-E and Br-A-M-P-Z-V-E. Boronic ester 25a (or 25d) is coupled with an appropriate coupling partner (e.g. arylbromide 25b or 25e) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 25c. Formation of multiple A-M bonds can be conducted in a similar manner. For example, the Suzuki reaction can also be employed to couple (RO)₂B-A-A-B(OR)₂ (25f) and two equivalents of Br-M-P-Z-V-E. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the A-A and/or A-M bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

Scheme 26: Representative synthesis of E-V-Z-P-M-A-A-M-P-Z-V-E

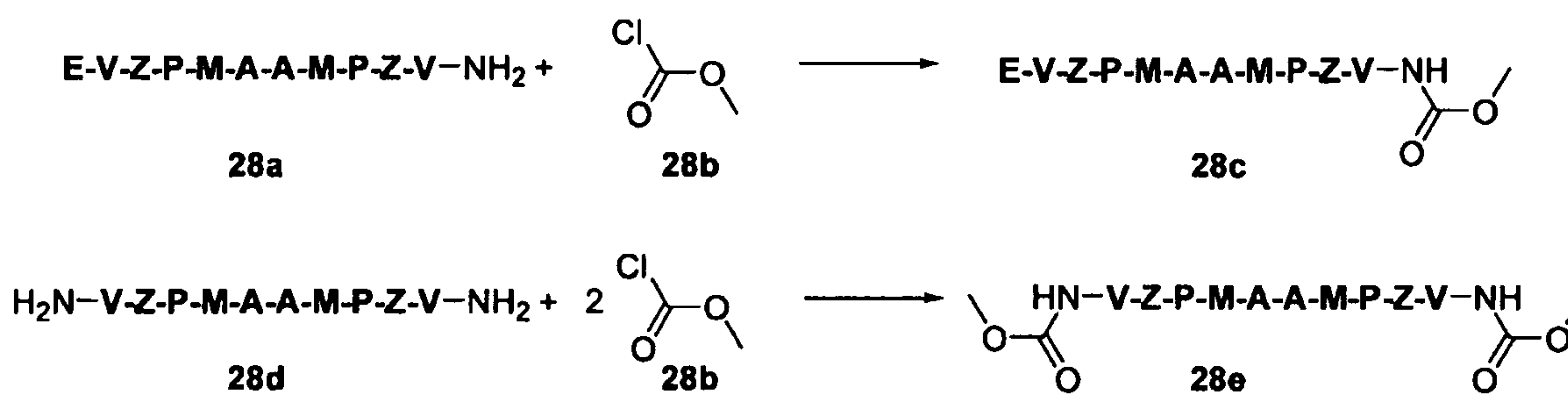


Scheme 26 shows a general synthesis of an E-V-Z-P-M-A-A-M-P-Z-V-E molecule of the invention wherein, for illustrative purposes, M is an amide, or an imidazole. Coupling of acid 26a with amine 26b is accomplished using a peptide coupling reagent (e.g. HATU) to afford the amide product 26c.

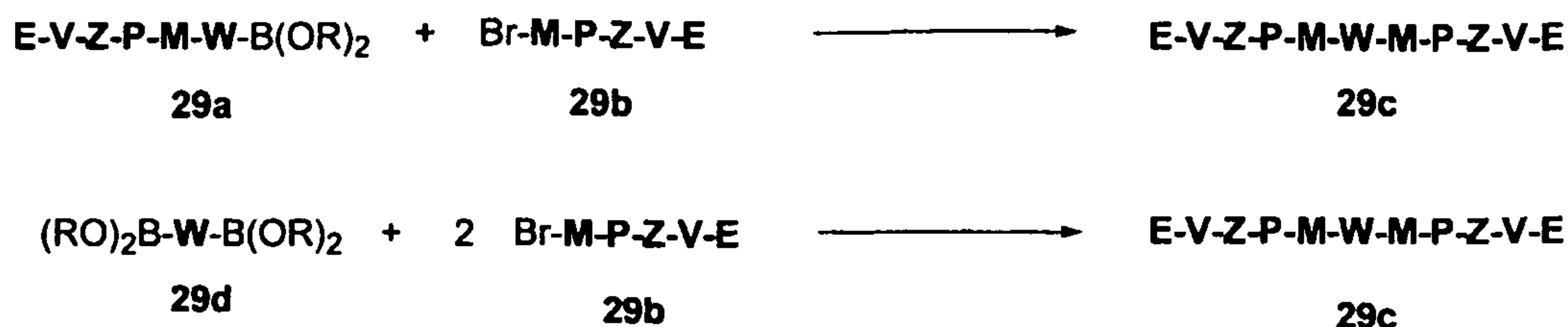
The formation of an imidazole is accomplished by coupling the acid 26d with an α -haloketone, such as α -bromoketone 26e, under basic conditions (e.g. Et_3N) to afford 26f. Alternatively, the acid 26d is coupled with an α -aminoketone 26h, under amide formation conditions (e.g. EDC, Et_3N) to afford 26i. Reaction of 26f or 26i with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing molecule 26g. The formation of multiple imidazoles is performed in the same manner, starting with a bis- α -haloketone such as α -bromoketone 26j, to provide molecule 26l.

Scheme 27: Representative synthesis of E-V-Z-P-M-A-A-M-P-Z-V-E

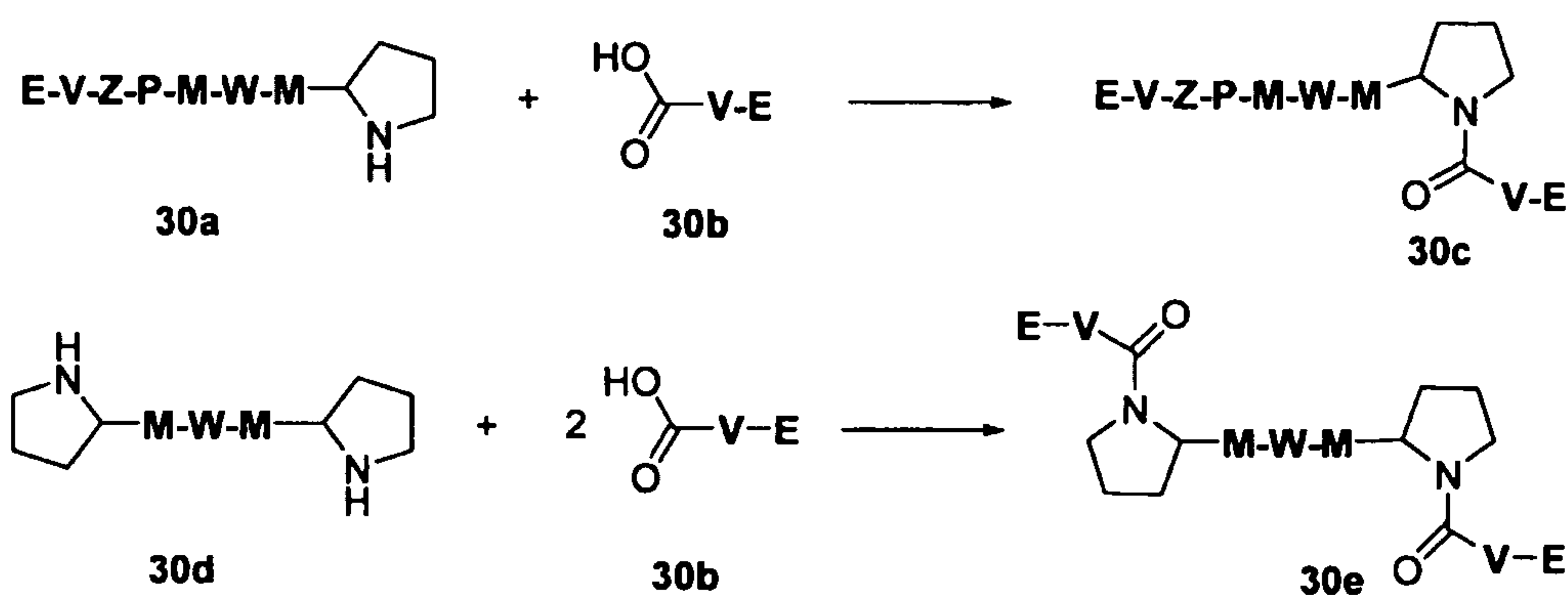
Scheme 27 shows a general synthesis of an E-V-Z-P-M-A-A-M-P-Z-V-E molecule of the invention wherein, for illustrative purposes, P is pyrrolidine and Z is a carbonyl. Coupling of amine 27a with acid 27b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 27c. Alternatively, amine 27d is coupled with two equivalents of 27b under similar conditions to provide 27e.

Scheme 28: Representative synthesis of E-V-Z-P-M-A-A-M-P-Z-V-E

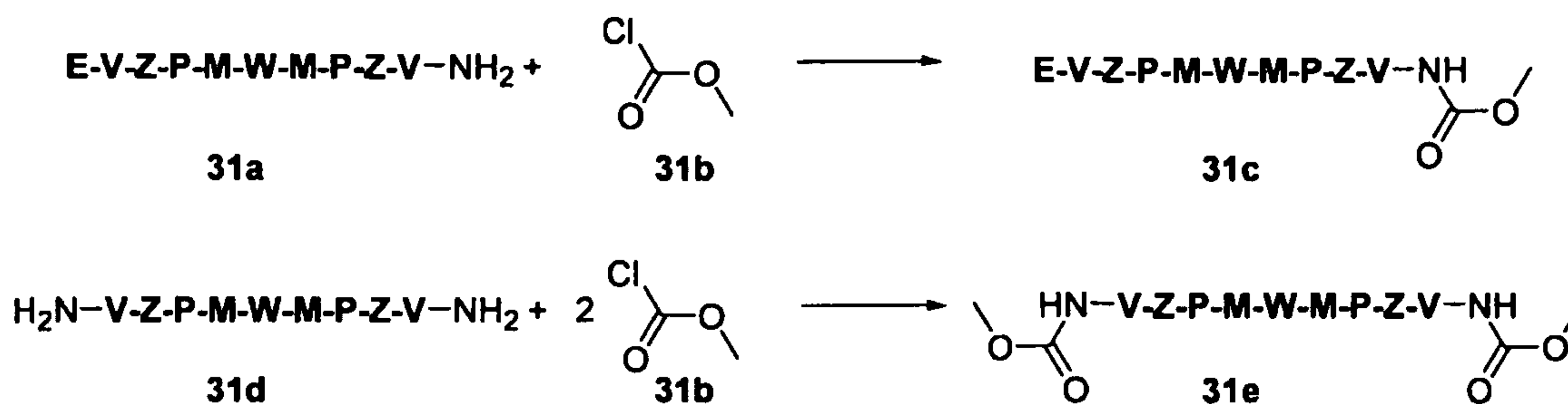
Scheme 28 shows a general synthesis of an E-V-Z-P-M-A-A-M-P-Z-V-E molecule of the invention wherein, for illustrative purposes, E is methoxycarbonylamino. The treatment of either 28a or 28d with one or two equivalents respectively of 28b under basic conditions (e.g. sodium bicarbonate) provides the molecule 28c or 28e.

Scheme 29: Representative synthesis of E-V-Z-P-M-W-M-P-Z-V-E

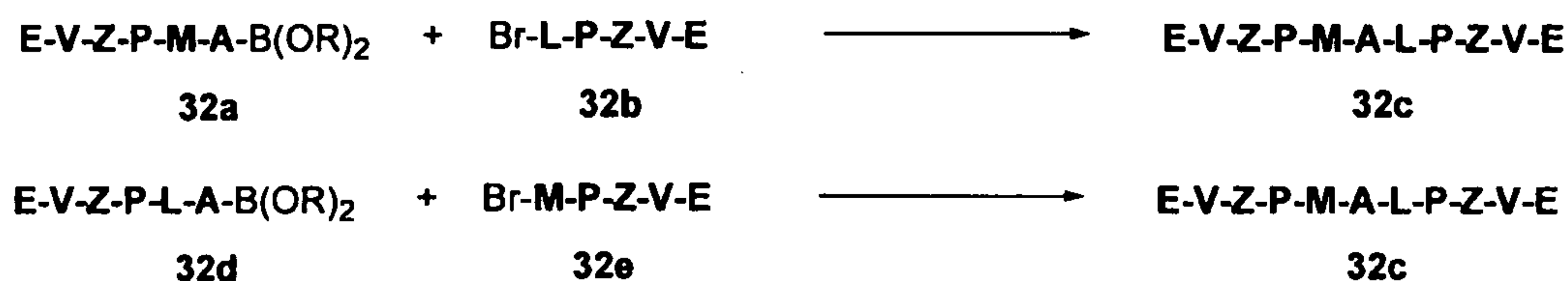
Scheme 29 shows a general synthesis of the E-V-Z-P-M-W-M-P-Z-V-E molecule of the invention, wherein transition metal-mediated cross-coupling reaction is utilized to construct the W-M bond. For illustrative purposes, the Suzuki reaction is employed to couple Br-M-P-Z-V-E to a (RO)₂B-W-M-P-Z-V-E or (RO)₂B-W-B(OR)₂ molecule. Boronic ester 29a (or 29d) is coupled with an appropriate coupling partner (e.g. arylbromide 29b) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 29c. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the M-W bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

Scheme 30: Representative synthesis of E-V-Z-P-M-W-M-P-Z-V-E

Scheme 30 shows a general synthesis of an E-V-Z-P-M-W-M-P-Z-V-E molecule of the invention wherein, for illustrative purposes, P is pyrrolidine and Z is a carbonyl. Coupling of amine 30a with acid 30b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 30c. Alternatively, amine 30d is coupled with two equivalents of 30b under similar conditions to provide 30e.

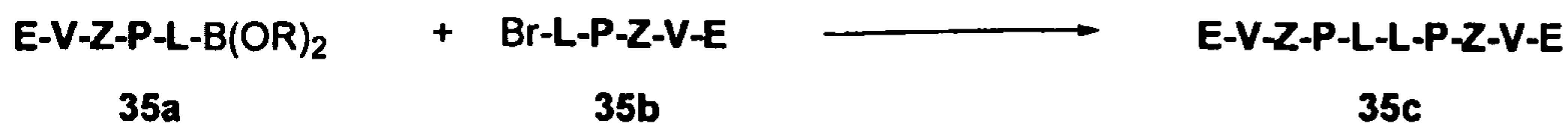
Scheme 31: Representative synthesis of E-V-Z-P-M-W-M-P-Z-V-E

Scheme 31 shows a general synthesis of an E-V-Z-P-M-W-M-P-Z-V-E molecule of the invention wherein, for illustrative purposes, E is methoxycarbonylamino. The treatment of either 31a or 31d with one or two equivalents respectively of 31b under basic conditions (e.g. sodium bicarbonate) provides the molecule 31c or 31e.

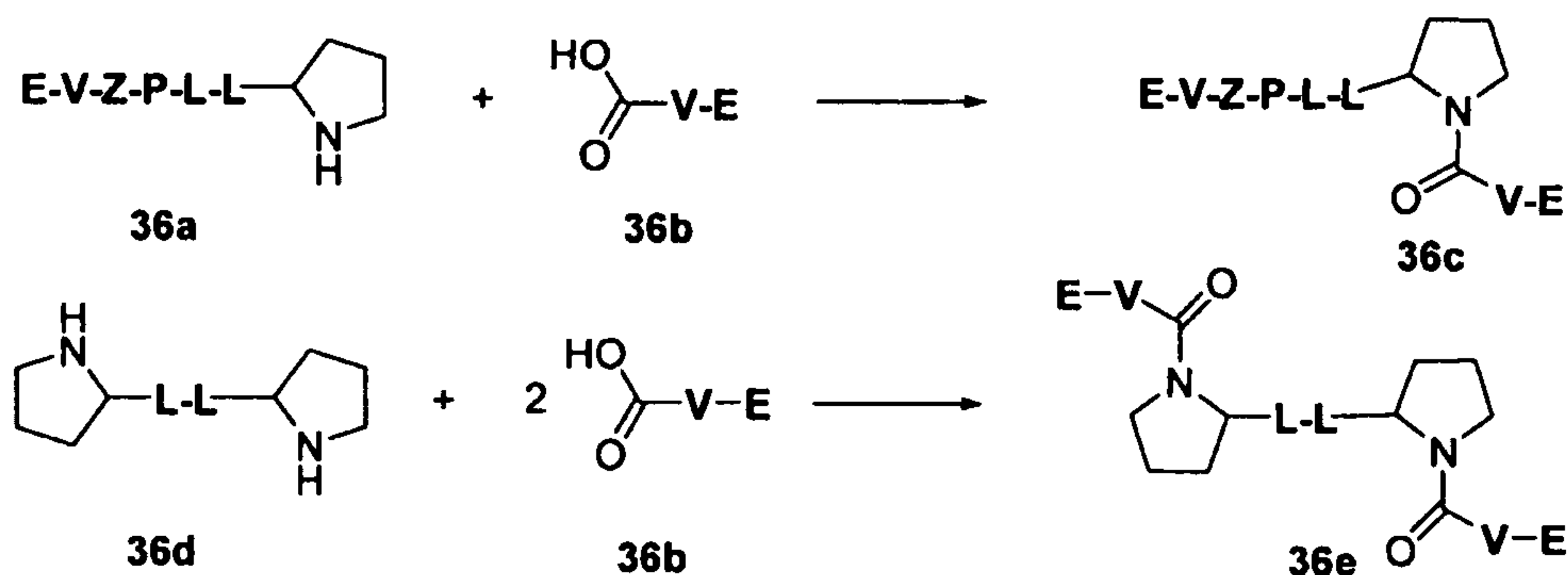
Scheme 32: Representative synthesis of E-V-Z-P-M-A-L-P-Z-V-E

Scheme 32 shows a general synthesis of the E-V-Z-P-M-A-L-P-Z-V-E molecule of the invention, wherein transition metal-mediated cross-coupling reaction is utilized to construct the M-A or A-L bond. For illustrative purposes, the Suzuki reaction is employed to couple a boronic ester to an arylbromide. Boronic ester 32a (or 32d) is coupled with an appropriate coupling partner (e.g. arylbromide 32b or 32e) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 32c. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable either the M-A or A-L bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

Scheme 33: Representative synthesis of E-V-Z-P-M-A-L-P-Z-V-E

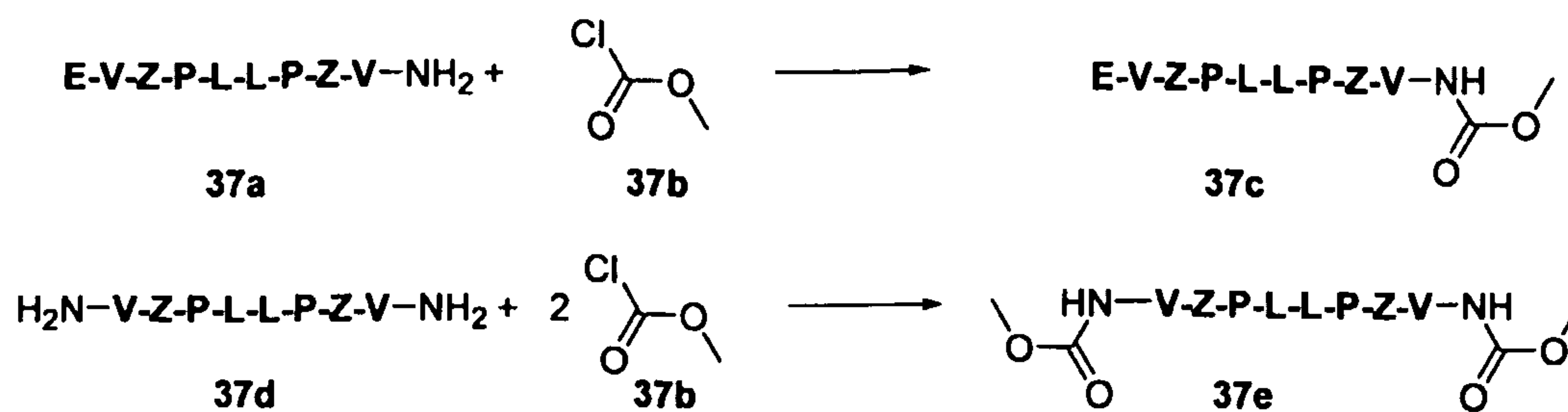
Scheme 35: Representative synthesis of E-V-Z-P-L-L-P-Z-V-E

Scheme 35 shows a general synthesis of the E-V-Z-P-L-L-P-Z-V-E molecule of the invention, wherein transition metal-mediated cross-coupling reaction is utilized to construct the L-L bond. For illustrative purposes, the Suzuki reaction is employed to couple a boronic ester to an arylbromide. Boronic ester 35a is coupled with an appropriate coupling partner (e.g. arylbromide 35b) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 35c. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable either the L-L bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

Scheme 36: Representative synthesis of E-V-Z-P-L-L-P-Z-V-E

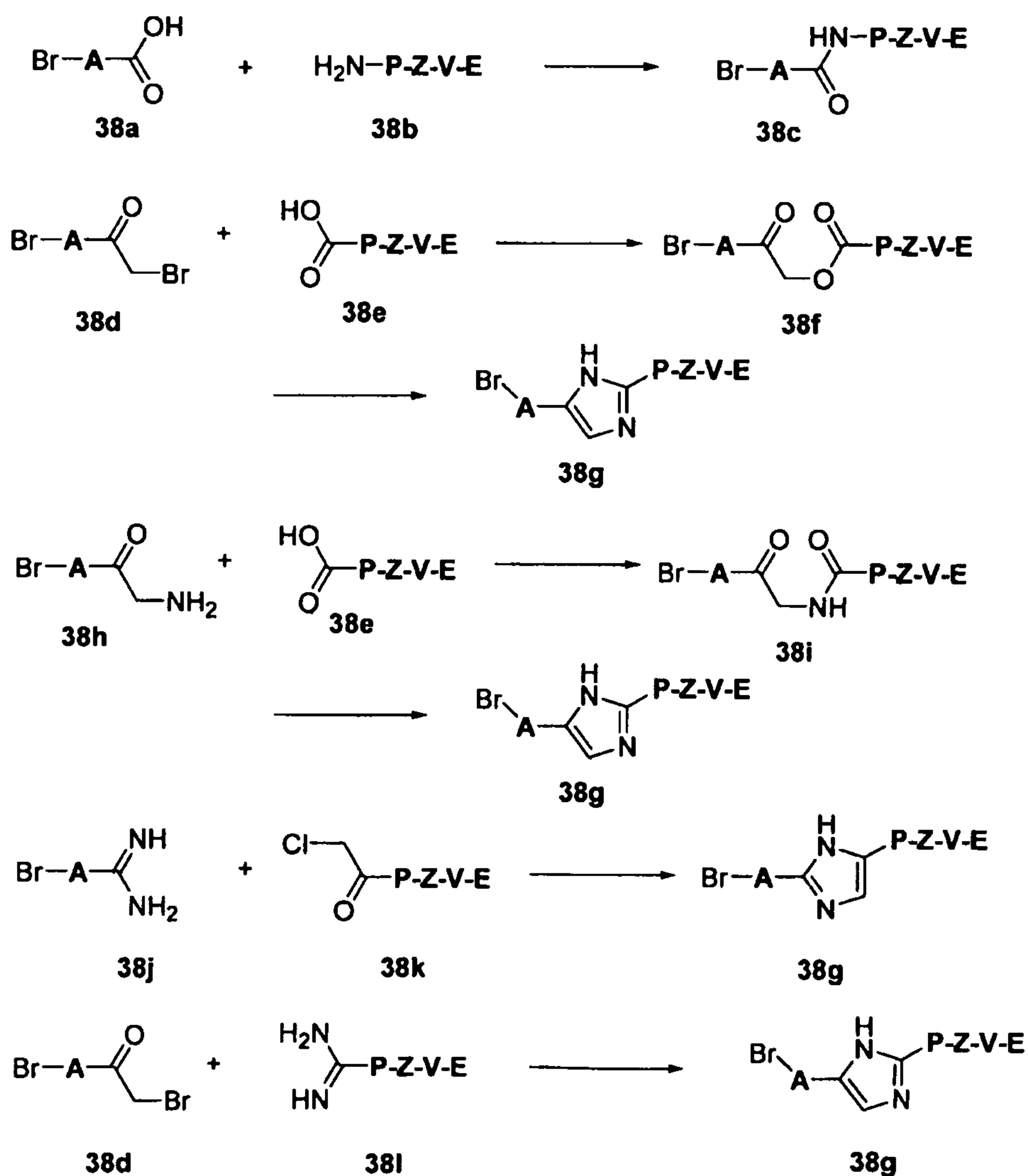
Scheme 36 shows a general synthesis of an E-V-Z-P-L-L-P-Z-V-E molecule of the invention wherein, for illustrative purposes, P is pyrrolidine and Z is a carbonyl. Coupling of amine 36a with acid 36b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 36c. Alternatively, amine 36d is coupled with two equivalents of 36b under similar conditions to provide 36e.

Scheme 37: Representative synthesis of E-V-Z-P-L-L-P-Z-V-E



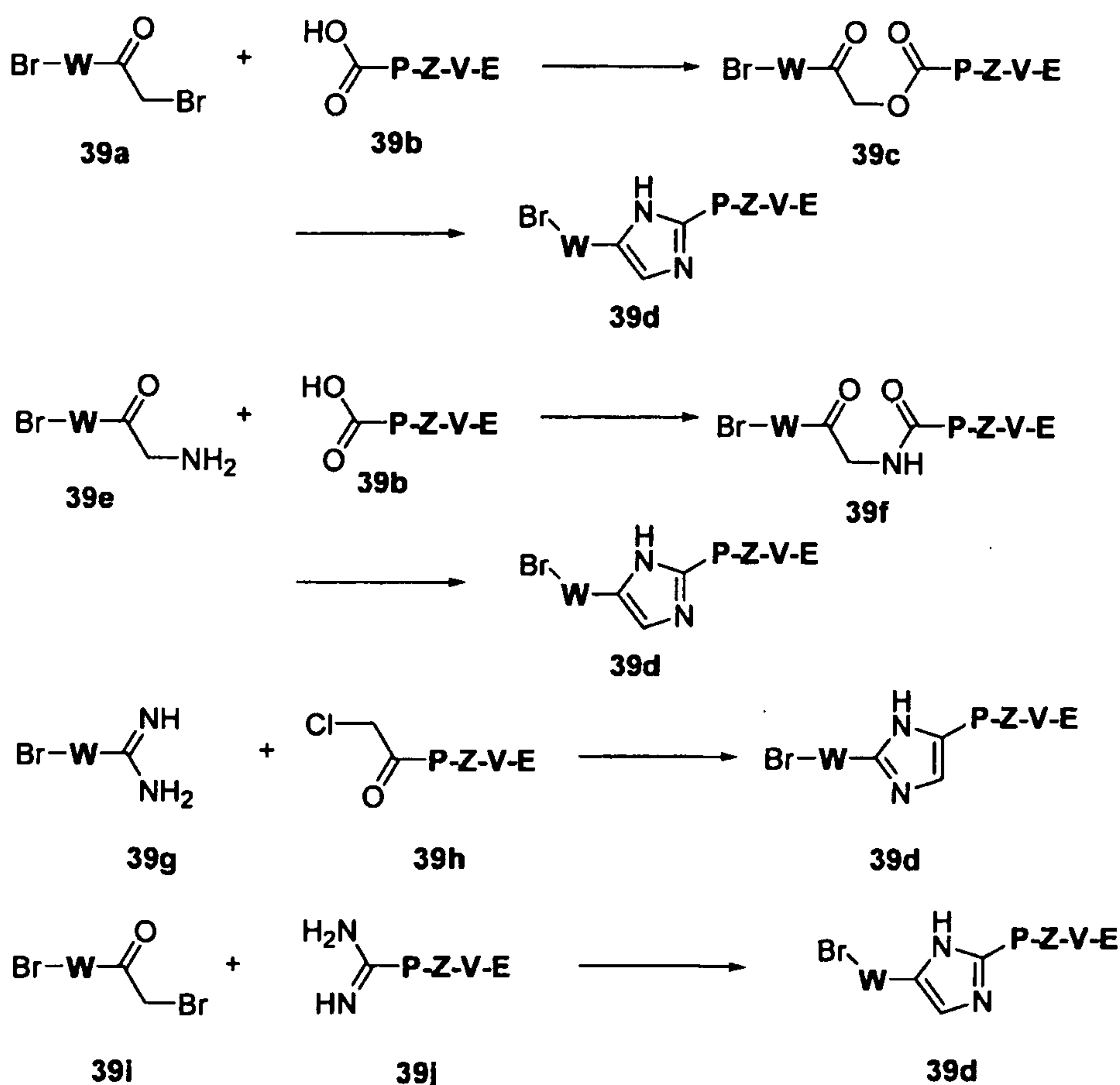
Scheme 37 shows a general synthesis of an E-V-Z-P-L-L-P-Z-V-E molecule of the invention wherein, for illustrative purposes, E is methoxycarbonylamino. The treatment of either 37a or 37d with 37b under basic conditions (e.g. sodium bicarbonate) provides the molecule 37c or 37e.

Scheme 38: Representative synthesis of R-A-M-P-R¹



Scheme 38 shows a general synthesis of an R-A-M-P-R¹ intermediate of the invention wherein, for illustrative purposes, M is an amide or an imidazole, R is a generic group that is depicted as Br, and R¹ is a generic group that is depicted as -Z-V-E. Coupling of amine 38b with acid 38a is accomplished using a peptide coupling reagent (e.g. HATU) to afford amide containing 38c. The acid 38e is coupled with an α -haloketone, such as α -bromoketone 38d, under basic conditions (e.g. Et₃N) to afford 38f. Alternatively, the acid 38e is coupled with an α -aminoketone 38h, under amide formation conditions (e.g. EDC, Et₃N) to afford 38i. Reaction of 38f or 38i with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing intermediate Br-A-M-P-Z-V-E (38g). The benzamidine 38j is coupled with an α -haloketone such as α -chloroketone 38k under basic conditions such as K₂CO₃ to afford 38g. The Br-A-M-P-Z-V-E intermediate can be prepared analogously from the coupling of 38d and 38l.

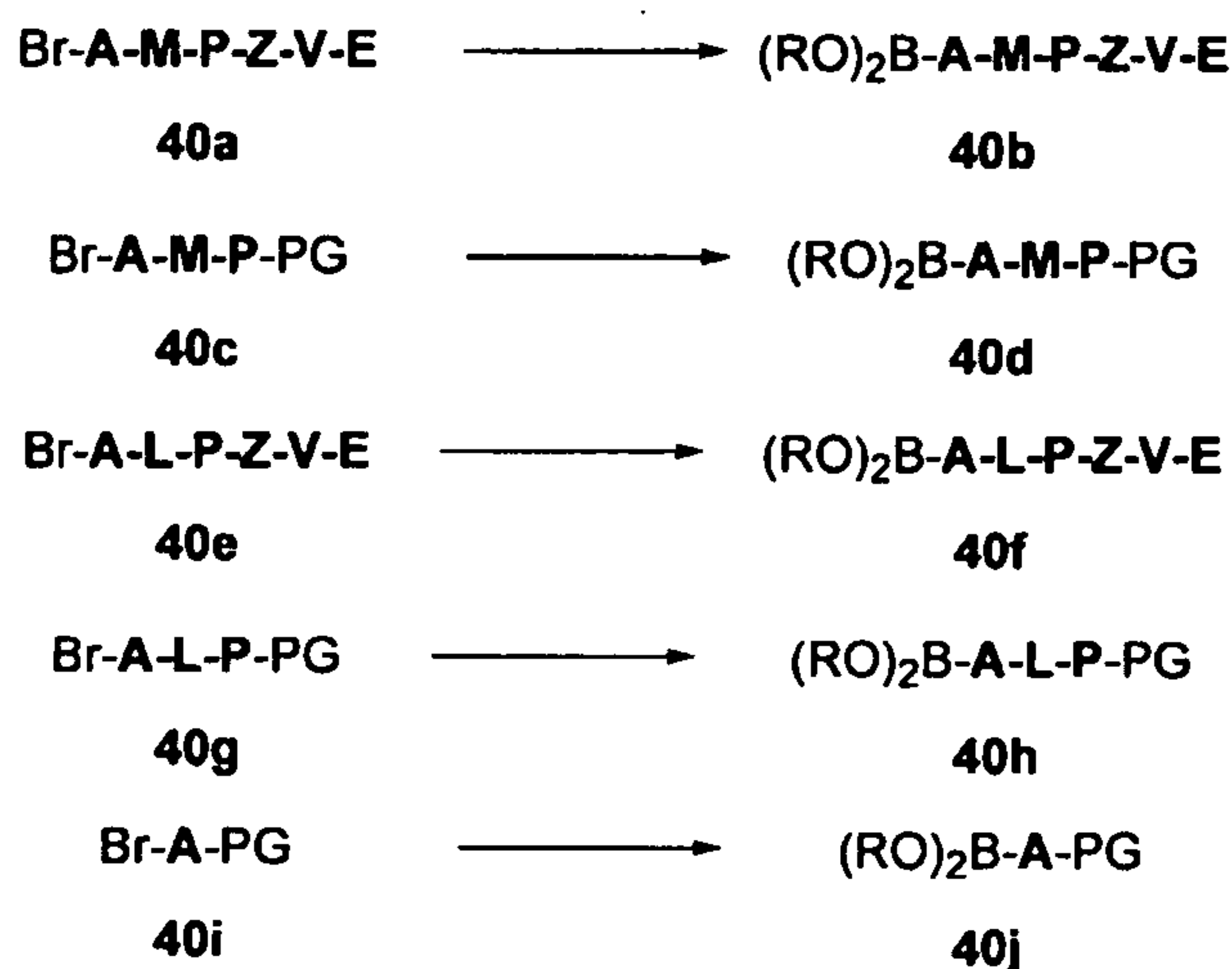
Scheme 39: Representative synthesis of R-W-M-P-R¹



Scheme 39 shows a general synthesis of an R-W-M-P-R¹ intermediate of the invention wherein, for illustrative purposes, M is an amide or an imidazole, R is a generic group that is depicted as Br, and R¹ is a generic group that is depicted as -Z-V-E. The acid 39b is coupled with an α -haloketone, such as α -bromoketone 39a, under basic conditions (e.g. Et₃N) to afford 39c. Alternatively, the acid 39b is coupled with an α -aminoketone 39e, under amide formation conditions (e.g. EDC, Et₃N) to afford 39f. Reaction of 39c or 39f with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing intermediate Br-A-M-P-Z-V-E (39d).

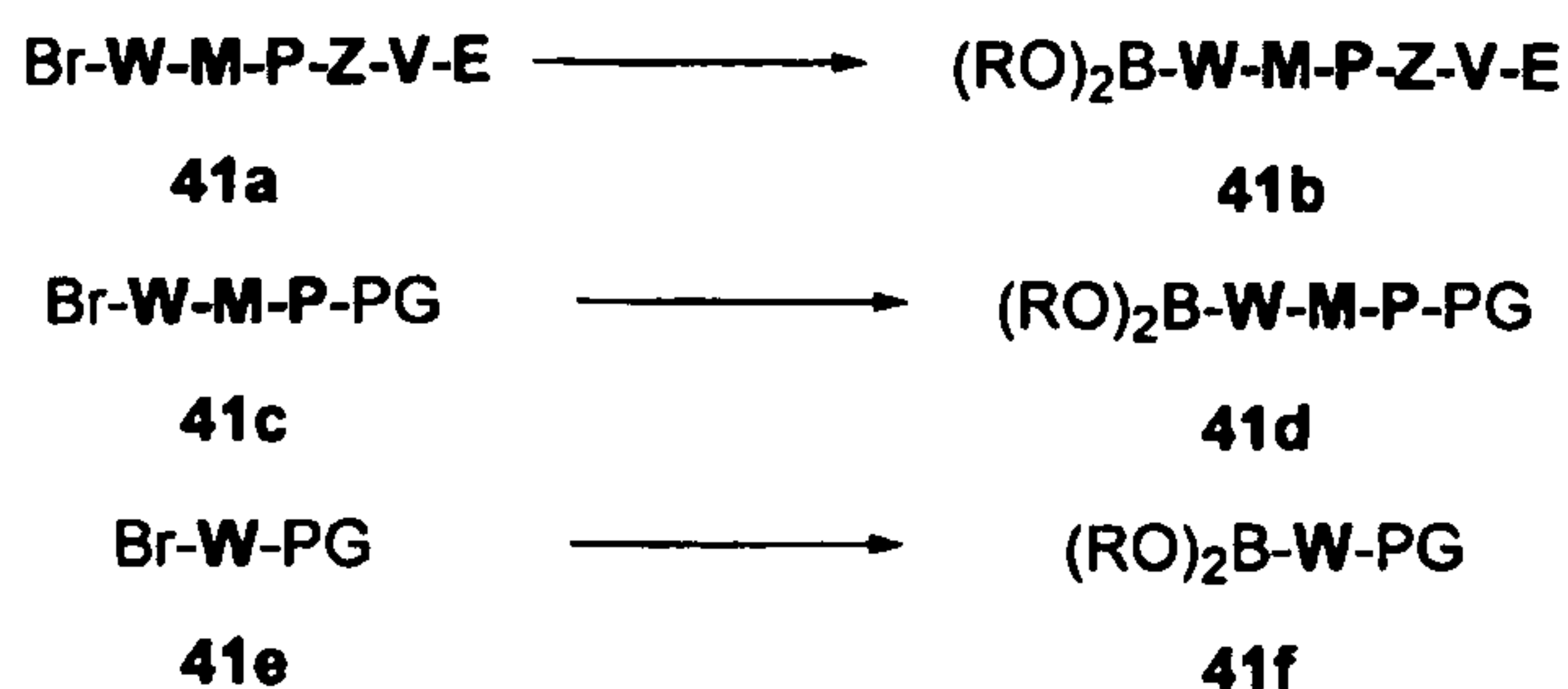
The benzamidine 39g is coupled with an α -haloketone such as α -chloroketone 39h under basic conditions such as K₂CO₃ to afford 39d. The Br-A-M-P-Z-V-E intermediate can be prepared analogously from the coupling of 39i and 39j.

Scheme 40: Representative synthesis of R-A-R¹



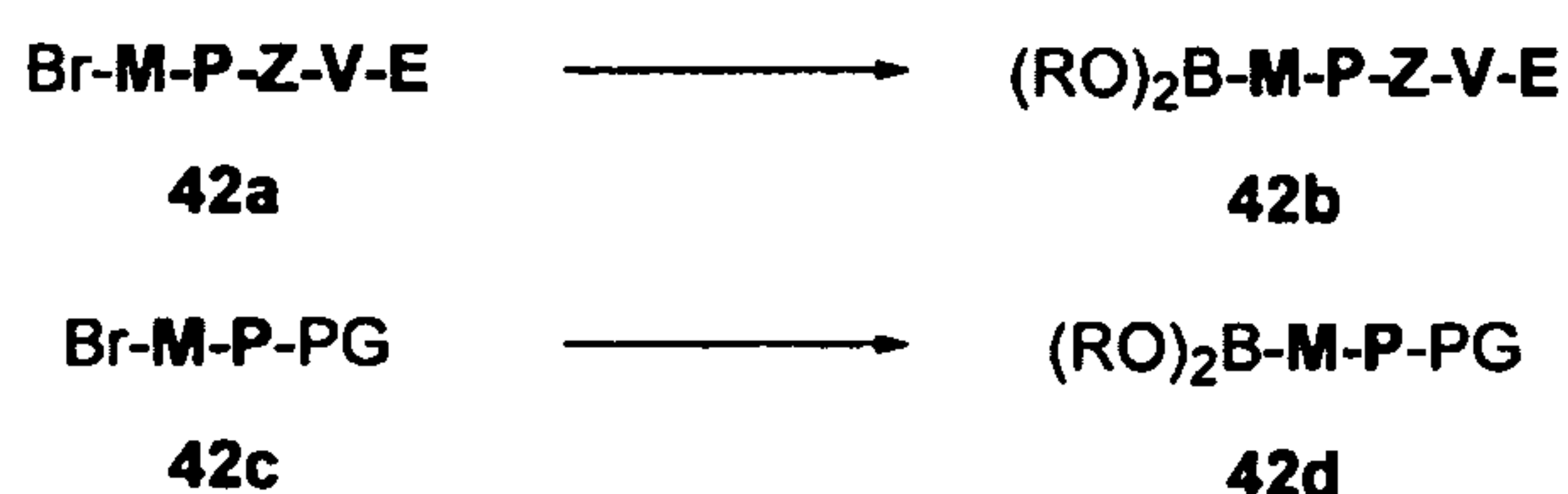
Scheme 40 shows a general synthesis of an R-A-R¹ intermediate of the invention wherein, for illustrative purposes, R is a generic group that is depicted as a boronic ester and R¹ is a generic group that is depicted as -M-P-Z-V-E, -M-P-PG, -L-P-Z-V-E, -L-P-PG, or a protecting group. A transition metal-mediated cross-coupling reaction is utilized to install the boronic ester on an A group. Treatment of the corresponding arylbromide with a palladium catalyst, such as PdCl₂(dppf), and a boron source such as bis(pinacolato)diborane provides the boronic ester 40b, 40d, 40f, 40h, or 40j.

Scheme 41: Representative synthesis of R-W-R¹



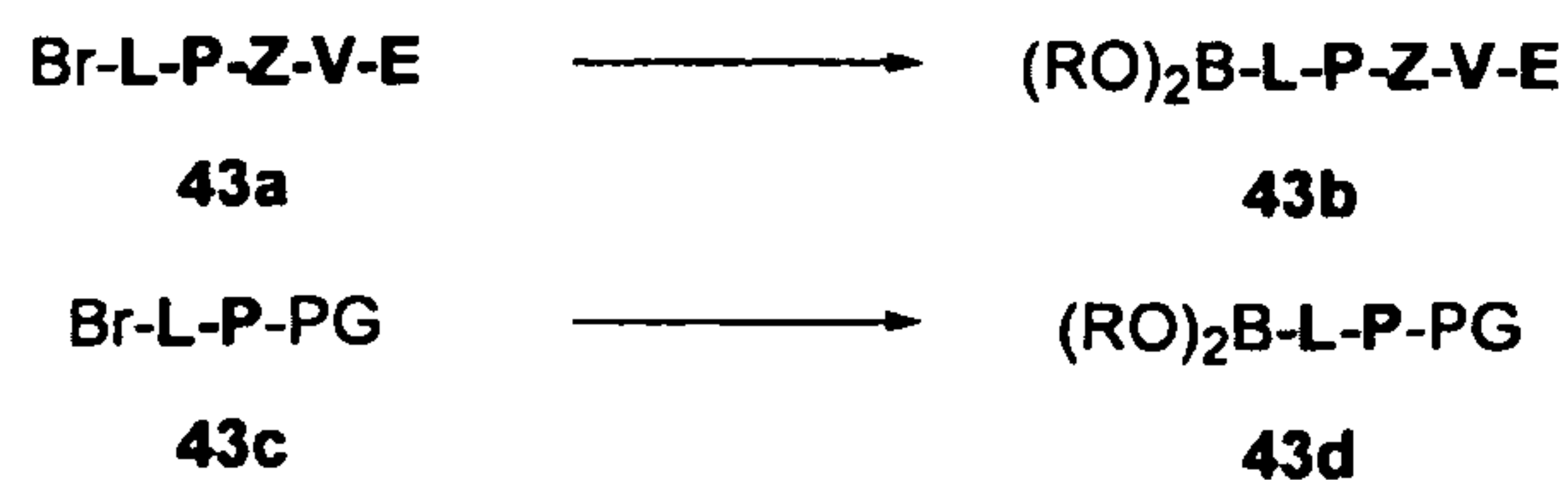
Scheme 41 shows a general synthesis of an R-W-R¹ intermediate of the invention wherein, for illustrative purposes, R is a generic group that is depicted as a boronic ester and R¹ is a generic group that is depicted as -M-P-Z-V-E, -M-P-PG, or a protecting group. A transition metal-mediated cross-coupling reaction is utilized to install the boronic ester on a W group. Treatment of the corresponding arylbromide with a palladium catalyst, such as PdCl₂(dppf), and a boron source such as bis(pinacolato)diborane provides the boronic ester **41b**, **41d**, or **41f**.

Scheme 42: Representative synthesis of R-M-R¹



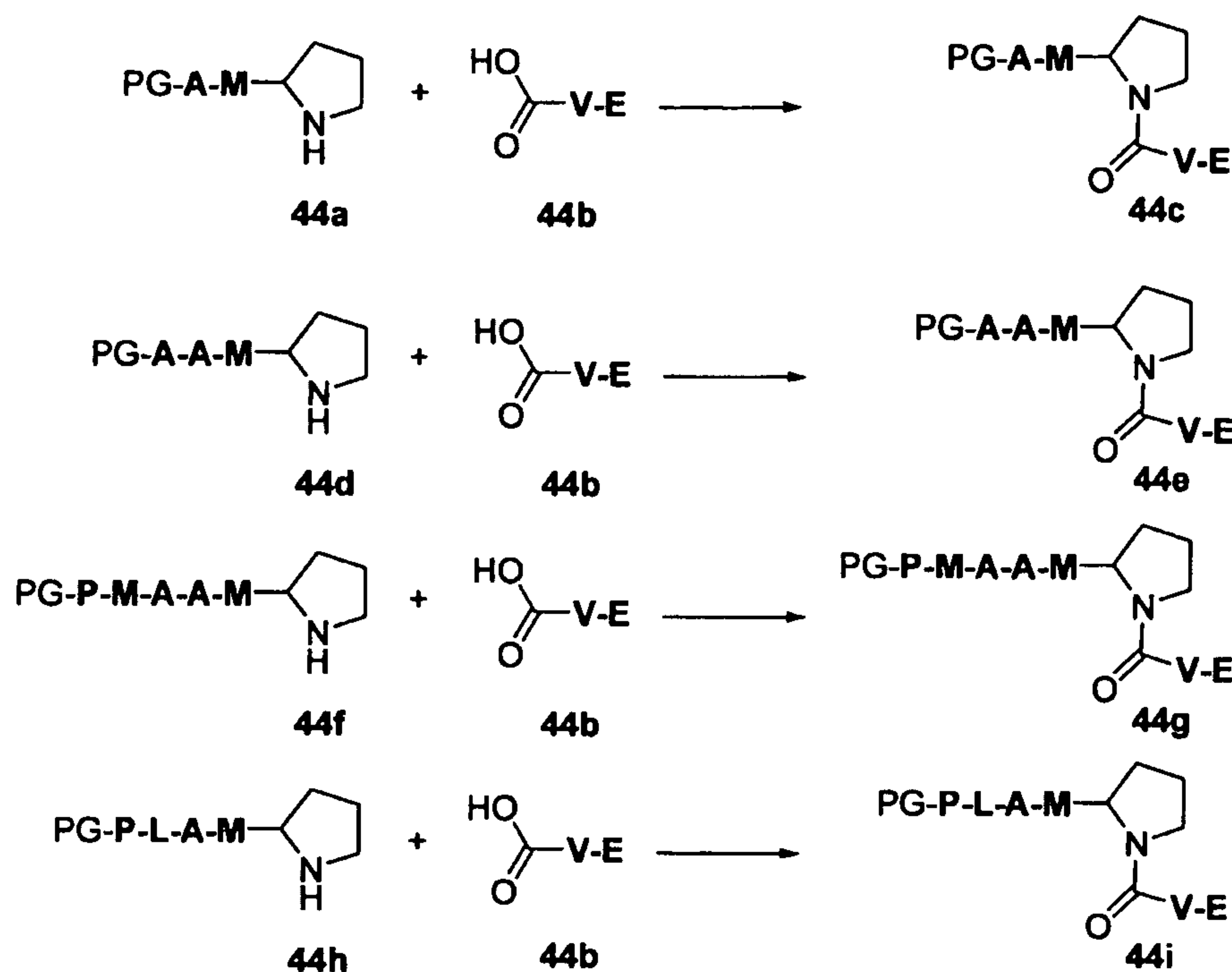
Scheme 42 shows a general synthesis of an R-M-R¹ intermediate of the invention wherein, for illustrative purposes, R is a generic group that is depicted as a boronic ester and R¹ is a generic group that is depicted as -P-Z-V-E or -P-PG. A transition metal-mediated cross-coupling reaction is utilized to install the boronic ester on an M group. Treatment of the corresponding arylbromide with a palladium catalyst, such as PdCl₂(dppf), and a boron source such as bis(pinacolato)diborane provides the boronic ester **42b** or **42d**.

Scheme 43: Representative synthesis of R-L-R¹

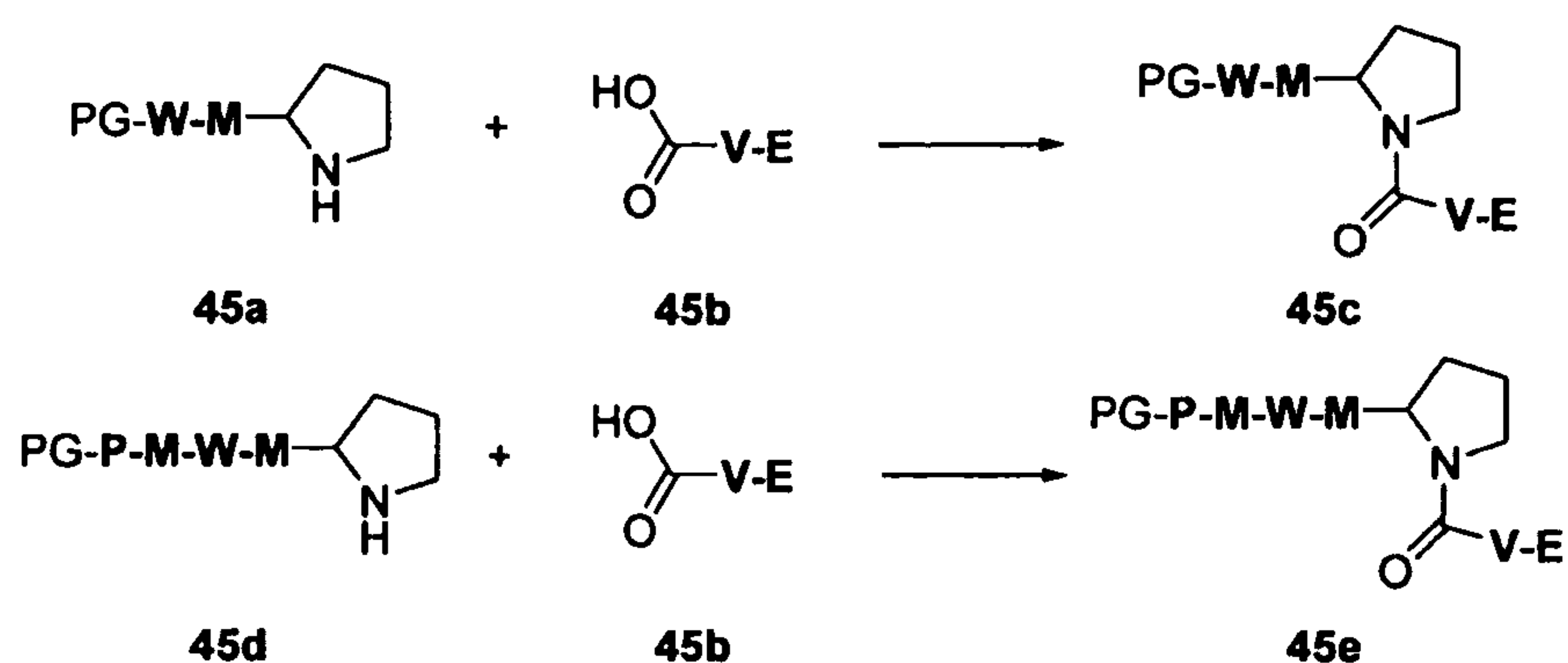


Scheme 43 shows a general synthesis of an R-L-R¹ intermediate of the invention wherein, for illustrative purposes, R is a generic group that is depicted as a boronic ester and R¹ is a generic group that is depicted as -P-Z-V-E or -P-PG. A transition metal-mediated cross-coupling reaction is utilized to install the boronic ester on an L group. Treatment of the corresponding arylbromide with a palladium catalyst, such as PdCl₂(dppf), and a boron source such as bis(pinacolato)diborane provides the boronic ester 43b or 43d.

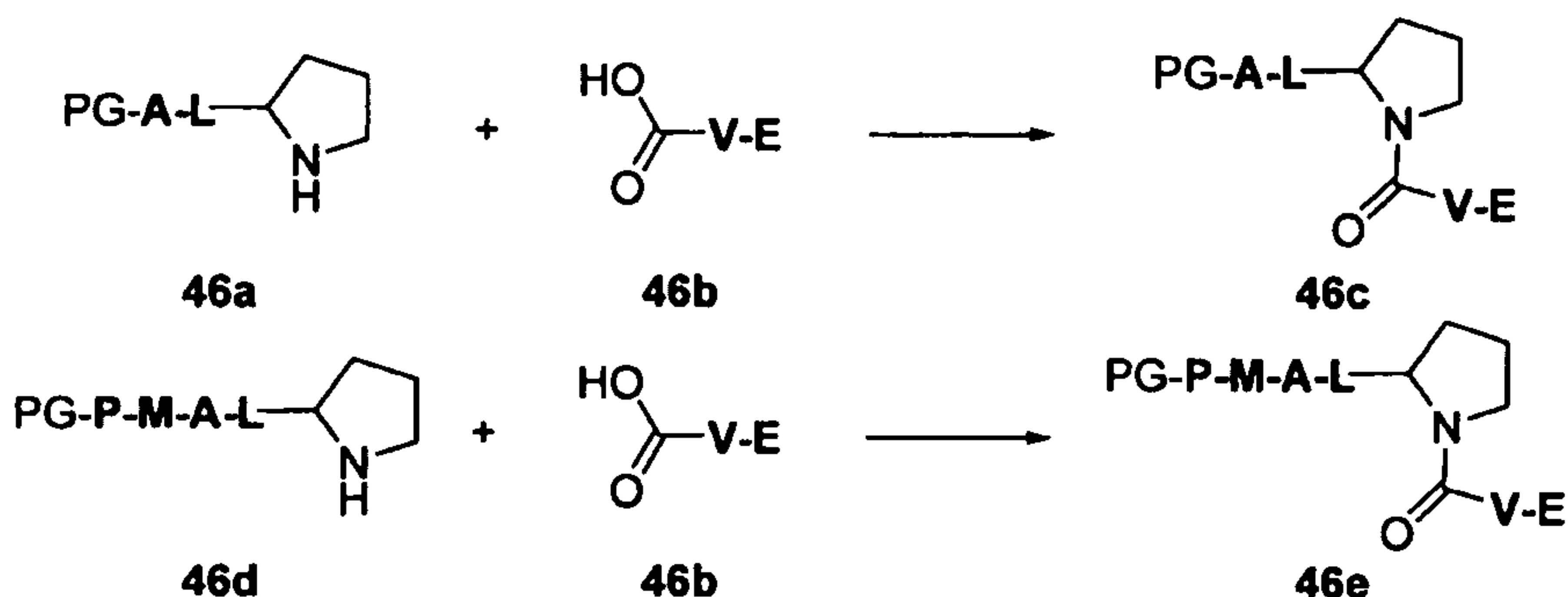
Scheme 44: Representative synthesis of R-A-M-P-Z-V-E



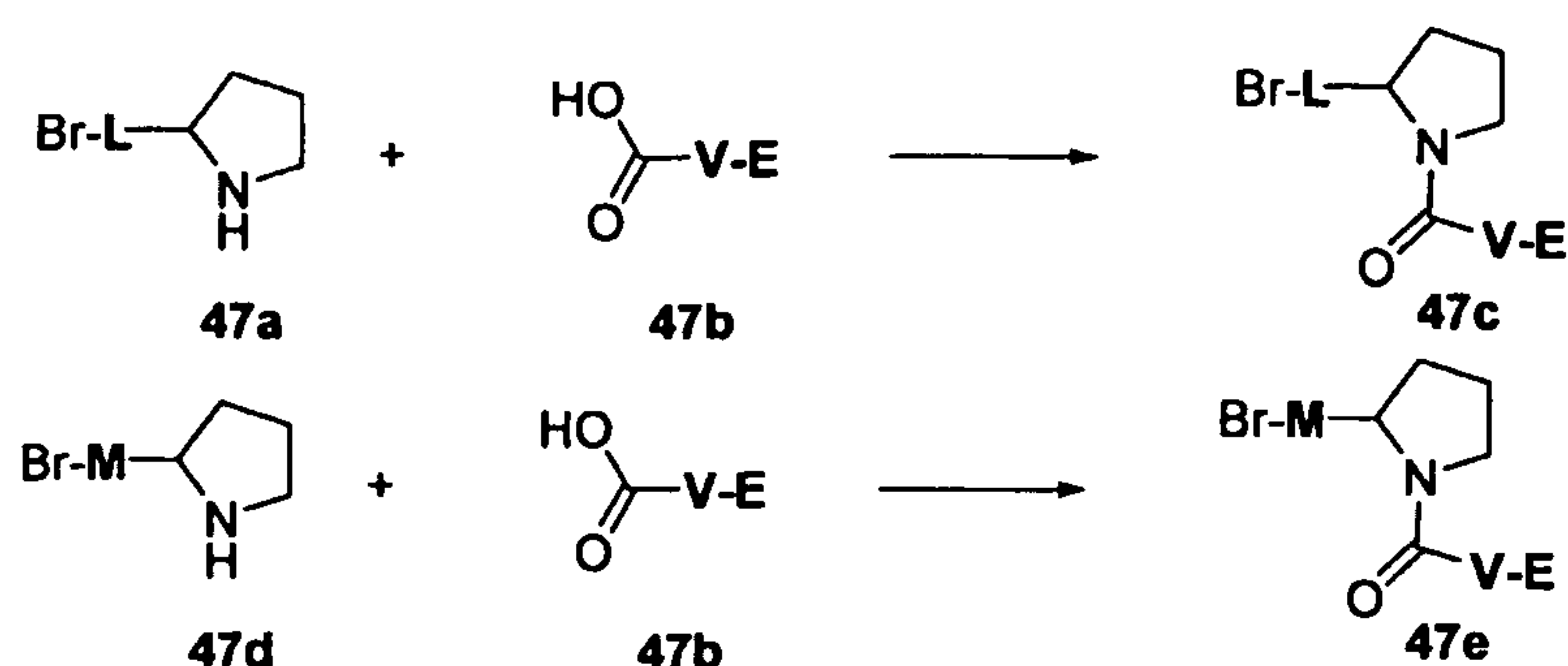
Scheme 44 shows a general synthesis of an R-A-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, P is pyrrolidine, Z is carbonyl, and R is a generic group that is depicted as either -A-PG, -A-M-P-PG, -L-P-PG, or a protecting group. Coupling of amine 44a, 44d, 44f, or 44h with acid 44b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 44c, 44e, 44g, or 44i, respectively.

Scheme 45: Representative synthesis of R-W-M-P-Z-V-E

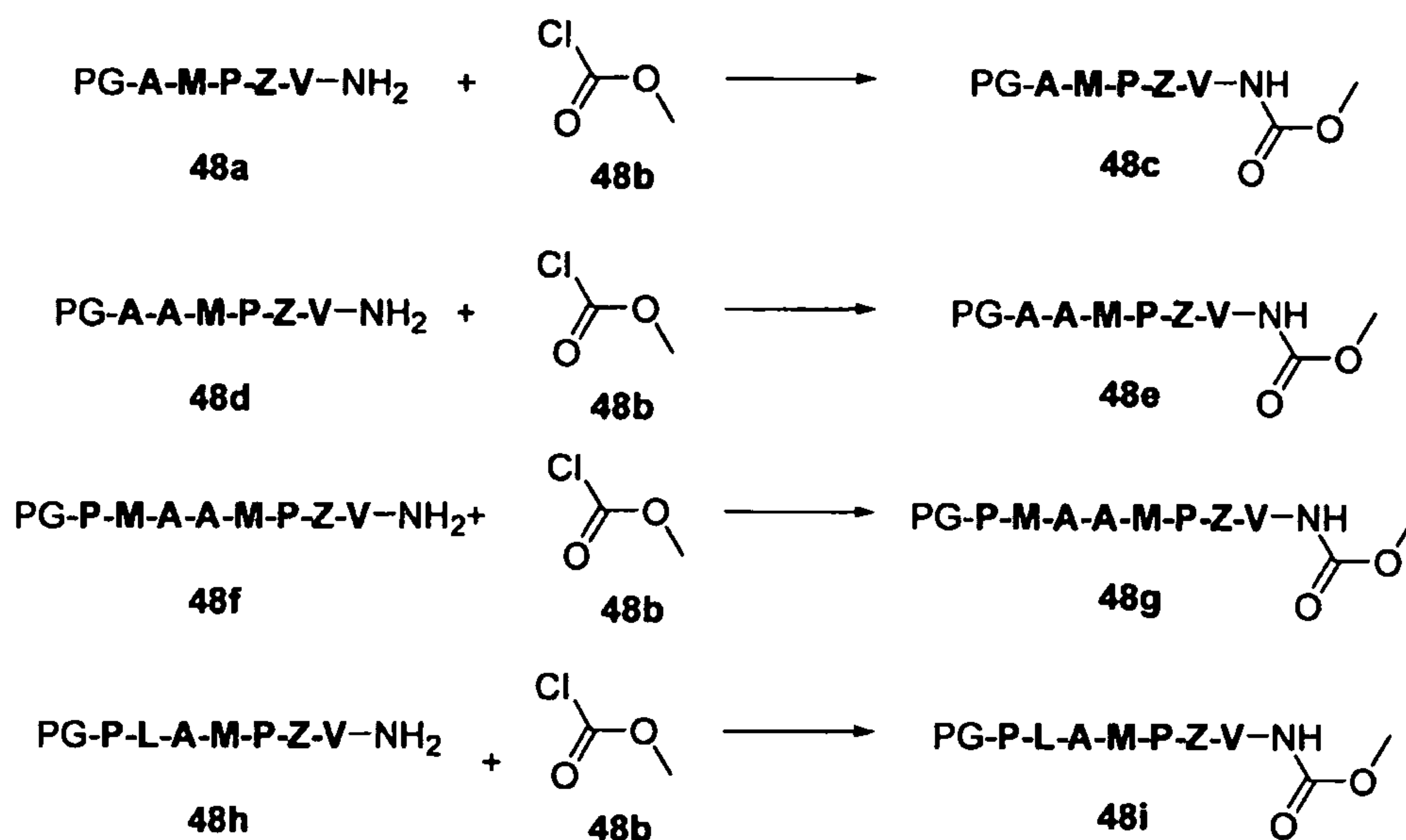
Scheme 45 shows a general synthesis of an R-W-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, P is pyrrolidine, Z is carbonyl, and R is a generic group that is depicted as either -M-P-PG or a protecting group. Coupling of amine 45a or 45d with acid 45b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 45c or 45e, respectively.

Scheme 46: Representative synthesis of R-A-L-P-Z-V-E

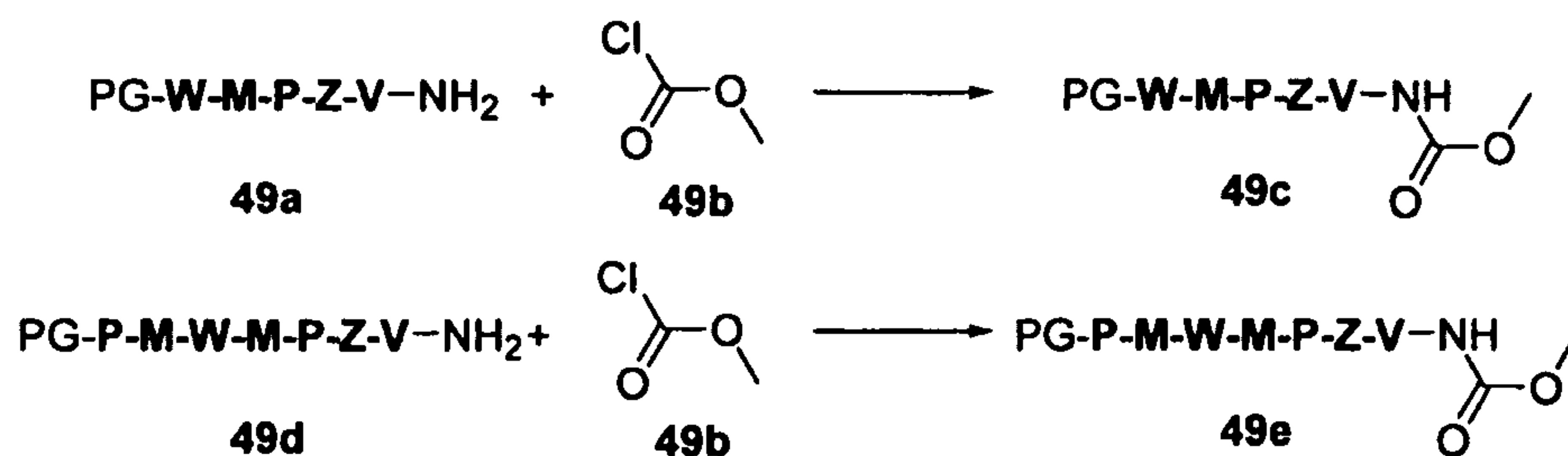
Scheme 46 shows a general synthesis of an R-A-L-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, P is pyrrolidine, Z is carbonyl, and R is a generic group that is depicted as either -M-P-PG or a protecting group. Coupling of amine 46a or 46d with acid 46b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 46c or 46e, respectively.

Scheme 47: Representative synthesis of R-L-P-Z-V-E and R-M-P-Z-V-E

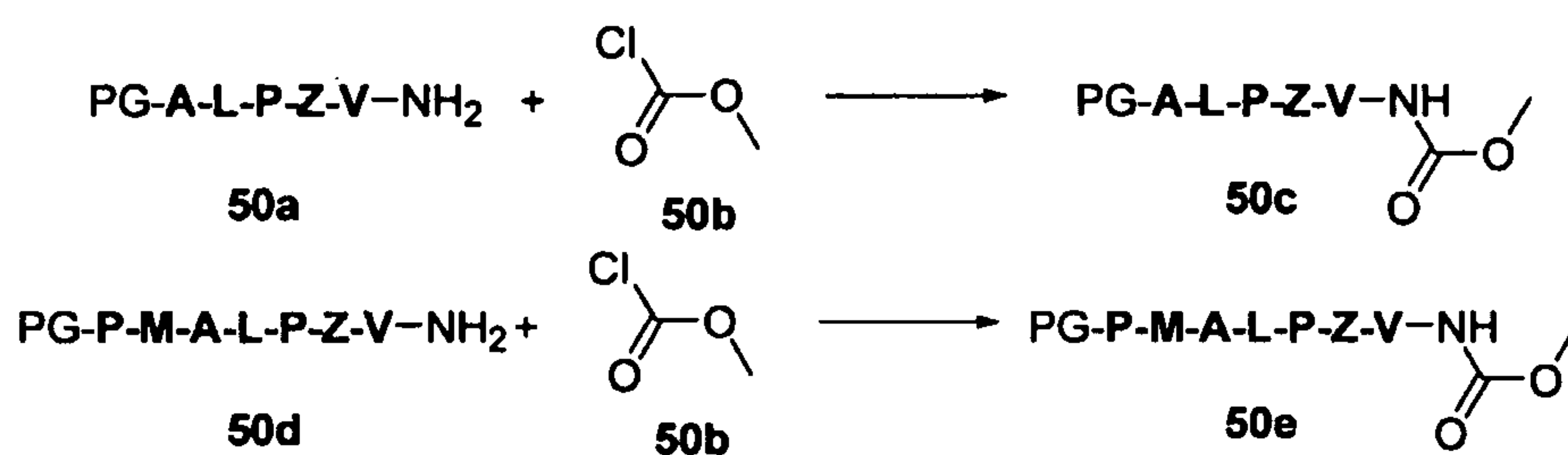
Scheme 47 shows a general synthesis of an R-L-P-Z-V-E or R-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, P is pyrrolidine, Z is carbonyl, and R is a generic group that is depicted as Br. Coupling of amine 47a or 47d with acid 47b is accomplished using a peptide coupling reagent (e.g. HATU) to afford 47c or 47e, respectively.

Scheme 48: Representative synthesis of R-A-M-P-Z-V-E

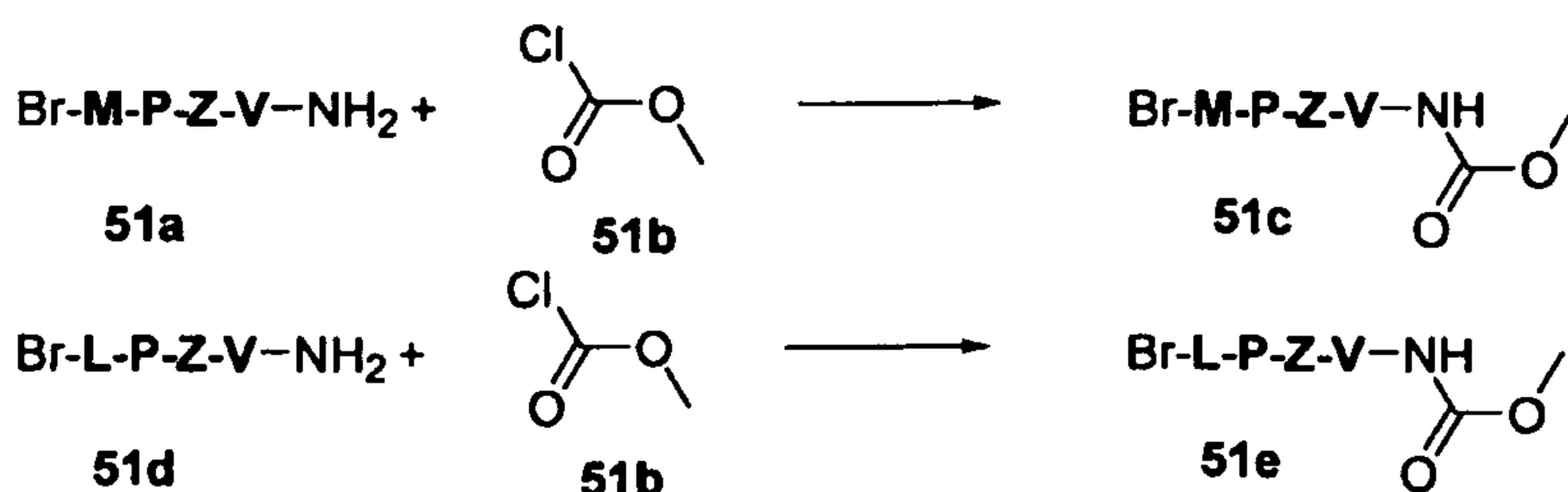
Scheme 48 shows a general synthesis of an R-A-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, E is methoxycarbonylamino and R is a generic group that is depicted as a either -A-PG, -A-M-P-PG, -L-P-PG, or a protecting group. Treatment of 48a, 48d, 48f, or 48h with 48b under basic conditions (e.g. sodium bicarbonate) provides the intermediate 48c, 48e, 48g, or 48i, respectively.

Scheme 49: Representative synthesis of R-W-M-P-Z-V-E

Scheme 49 shows a general synthesis of an R-W-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, E is methoxycarbonylamino and R is a generic group that is depicted as either -M-P-PG or a protecting group. Treatment of 49a or 49d with 49b under basic conditions (e.g. sodium bicarbonate) provides the intermediate 49c or 49e, respectively.

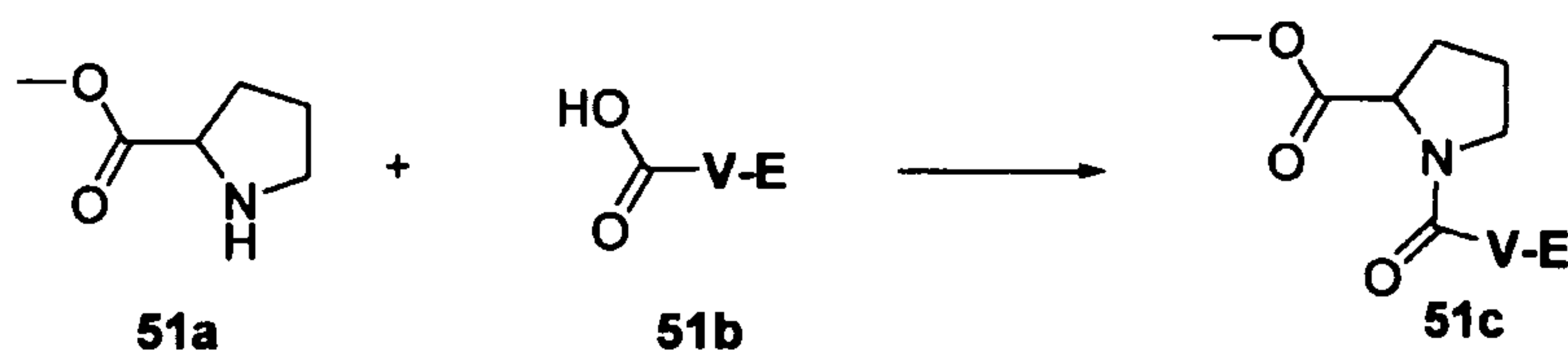
Scheme 50: Representative synthesis of R-A-L-P-Z-V-E

Scheme 50 shows a general synthesis of an R-A-L-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, E is methoxycarbonylamino and R is a generic group that is depicted as a either -M-P-PG or a protecting group. Treatment of 50a or 50d with 50b under basic conditions (e.g. sodium bicarbonate) provides the intermediate 50c or 50e, respectively.

Scheme 51: Representative synthesis of R-A-L-P-Z-V-E

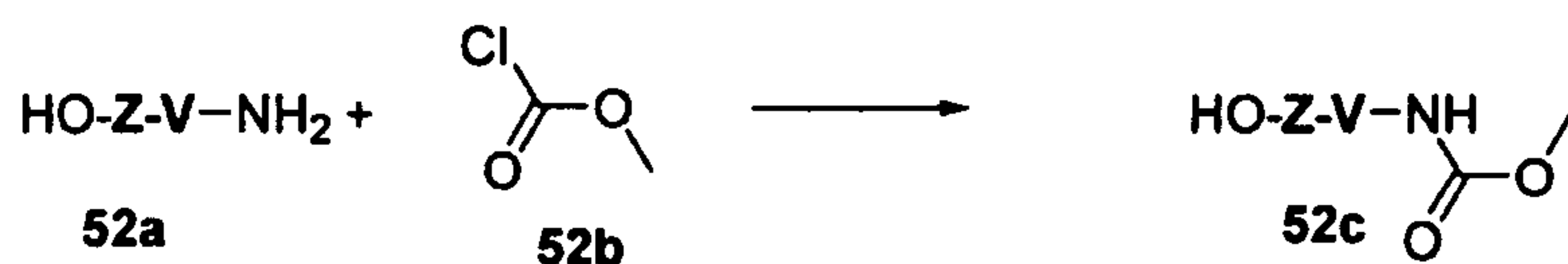
Scheme 51 shows a general synthesis of an R-L-P-Z-V-E or R-M-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, E is methoxycarbonylamino and R is a generic group that is depicted as a Br. Treatment of **51a** or **51d** with **51b** under basic conditions (e.g. sodium bicarbonate) provides the intermediate **51c** or **51e**, respectively.

Scheme 51a: Representative synthesis of R-P-Z-V-E

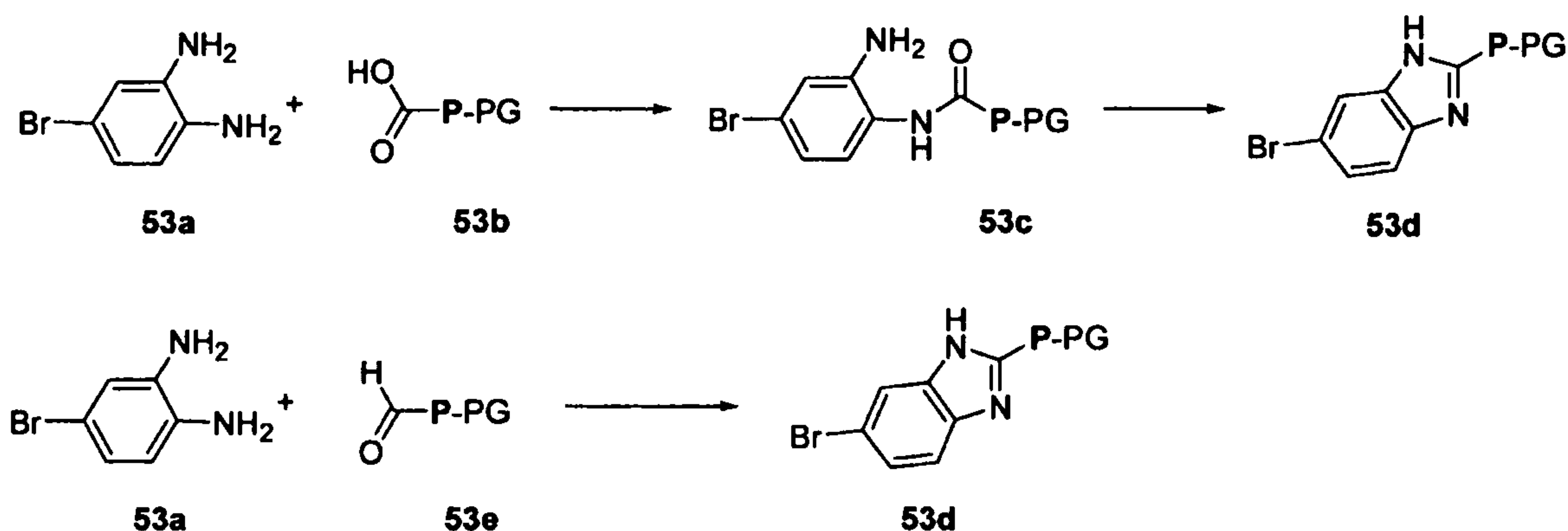


Scheme 51a shows a general synthesis of an R-P-Z-V-E intermediate of the invention wherein, for illustrative purposes, P is pyrrolidine, Z is carbonyl, and R is a generic group that is depicted as a methoxycarbonyl. Coupling of amine **51a** with acid **51b** is accomplished using a peptide coupling reagent (e.g. HATU) to afford **51c**.

Scheme 52: Representative synthesis of R-Z-V-E

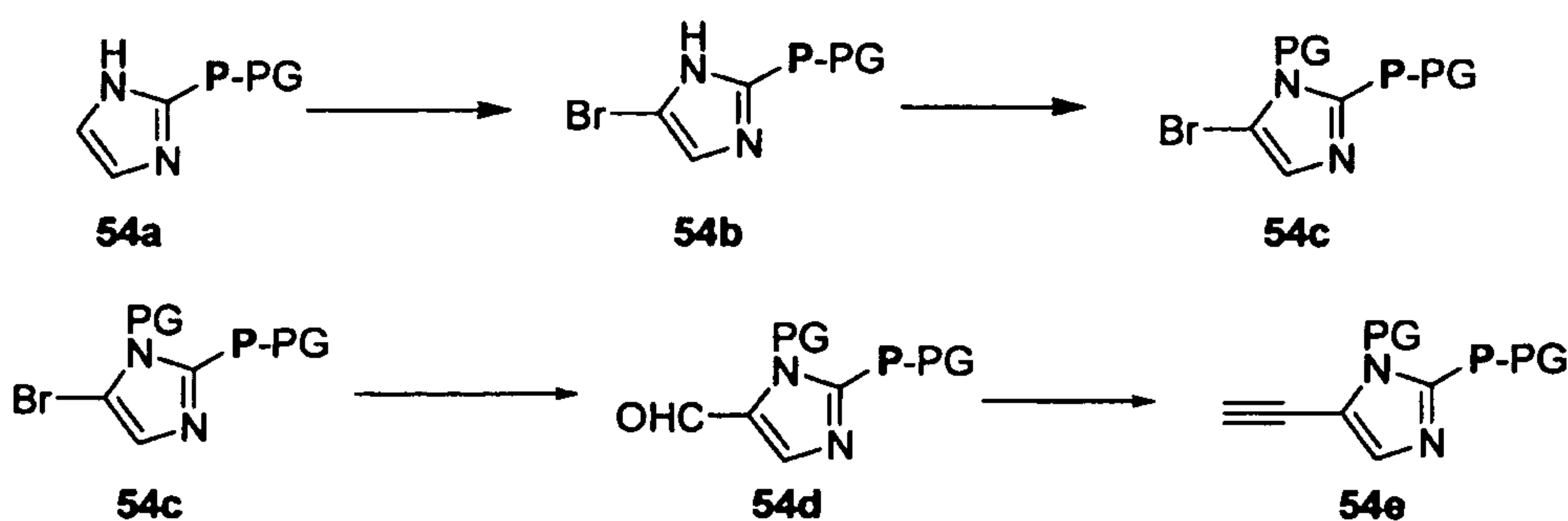


Scheme 52 shows a general synthesis of an R-Z-V-E intermediate of the invention wherein, for illustrative purposes, E is methoxycarbonylamino and R is a generic group that is depicted as a hydroxyl. Treatment of **52a** under basic conditions (e.g. sodium bicarbonate) with **52b** provides the intermediate **52c**.

Scheme 53: Representative synthesis of R-L-P-R¹

Scheme 53 shows a general synthesis of an R-L-P-R¹ intermediate of the invention wherein, for illustrative purposes, L is benzimidazole, R is a generic group that is depicted as a bromide, and R¹ is a protecting group. The acid 53b is coupled with 53a using a peptide coupling reagent such as HATU to afford 53c. Heating in solvent (such as refluxing ethanol) affords the R-L-P-R¹ intermediate 53d.

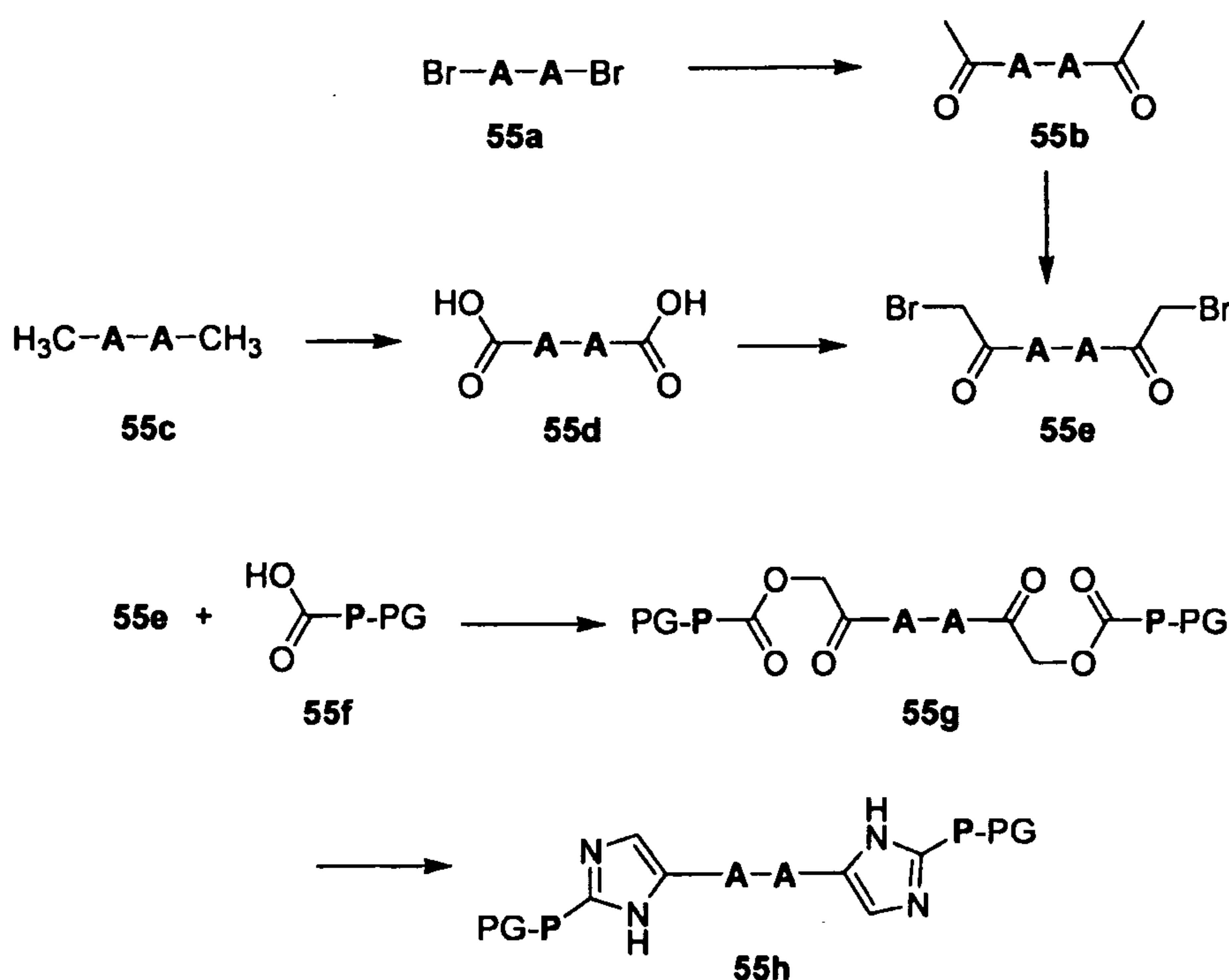
Alternatively, the R-L-P-R¹ intermediate 53d is obtained by reaction of a diamine (such as 53a) and carbonyl compound (such as aldehyde 53e) in a solvent under heating conditions (e.g. ethanol under microwave irradiation).

Scheme 54: Representative synthesis of R-M-P-R¹

Scheme 54 shows a general synthesis of an R-M-P-R¹ intermediate of the invention wherein, for illustrative purposes, M is imidazole, R is a generic group that is depicted as a bromide, aldehyde, or alkyne and R¹ is a protecting group. Imidazole 54a can be halogenated, for example, under the action of N-bromosuccinimide to provide bromoimidazole 54b.

Bromoimidazole **54b** can be protected using standard conditions to give **54c**, such as SEM-Cl and sodium hydride when PG = SEM. The bromoimidazole **54b** can be further elaborated, for example, to the corresponding aldehyde or alkyne. Lithiation of **54c** and condensation with a formate equivalent (e.g. DMF) provides the aldehyde **54d**. The aldehyde **54d** is converted to alkyne **54e** using a phosphorus-based reagent (e.g. Ohira-Bestmann reagent).

Scheme 55: Representative synthesis of R-P-M-A-A-M-P-R

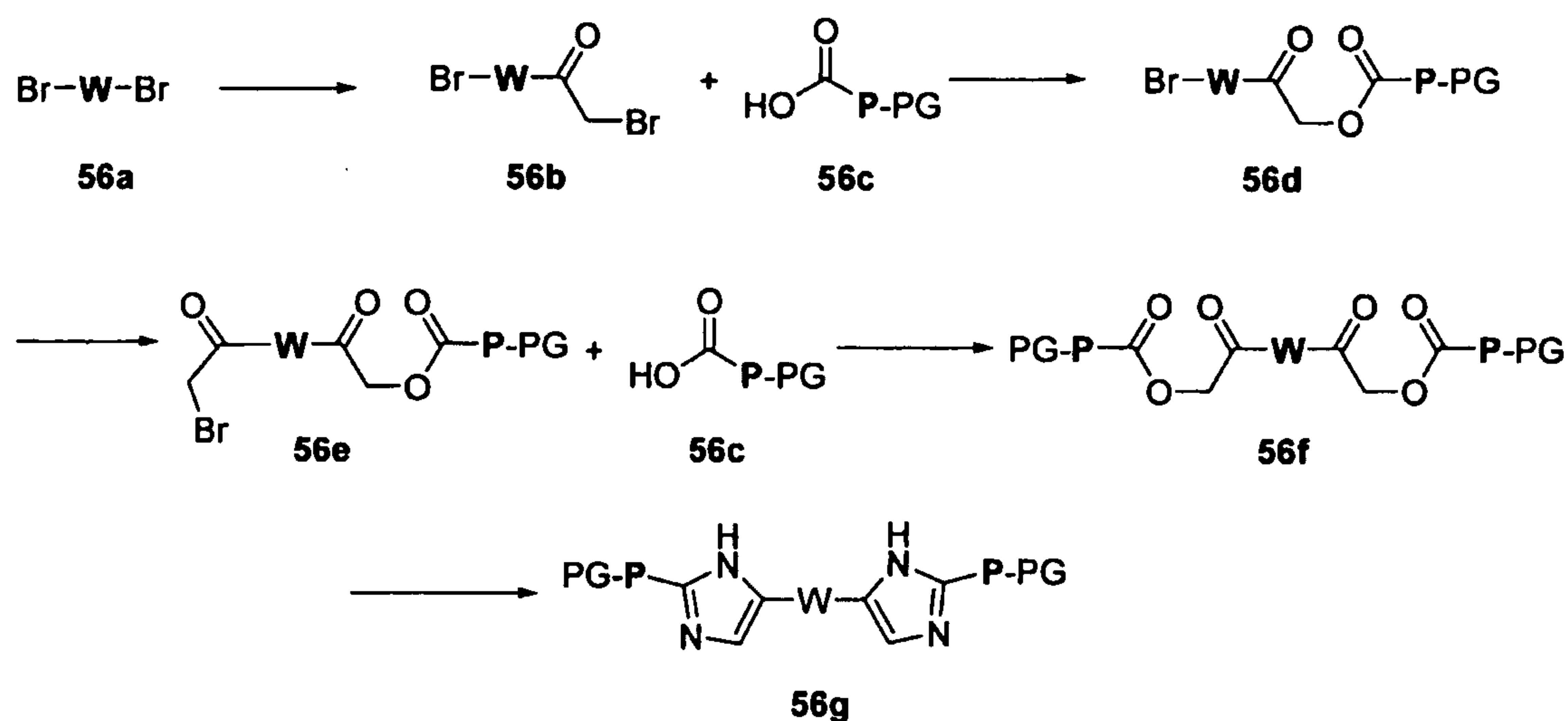


Scheme 55 shows a general synthesis of an R-P-M-A-A-M-P-R intermediate of the invention wherein, for illustrative purposes, **M** is imidazole and **R** is a generic group that is depicted as a protecting group. For example, the diketone **55b** is converted to **55e** using bromine. Compound **55b** can be commercially available or can be prepared from the corresponding dibromide **55a** through coupling with a vinyltin reagent such as tributyl(ethoxyvinyl)stannane in the presence of a palladium catalyst. Coupling of **55e** with acid **55f** under basic conditions such as diisopropylethylamine affords diester **55g**. Imidazole formation is accomplished by treatment of **55g** with ammonium acetate to provide the imidazole containing intermediate R-P-M-A-A-M-P-R (**55h**).

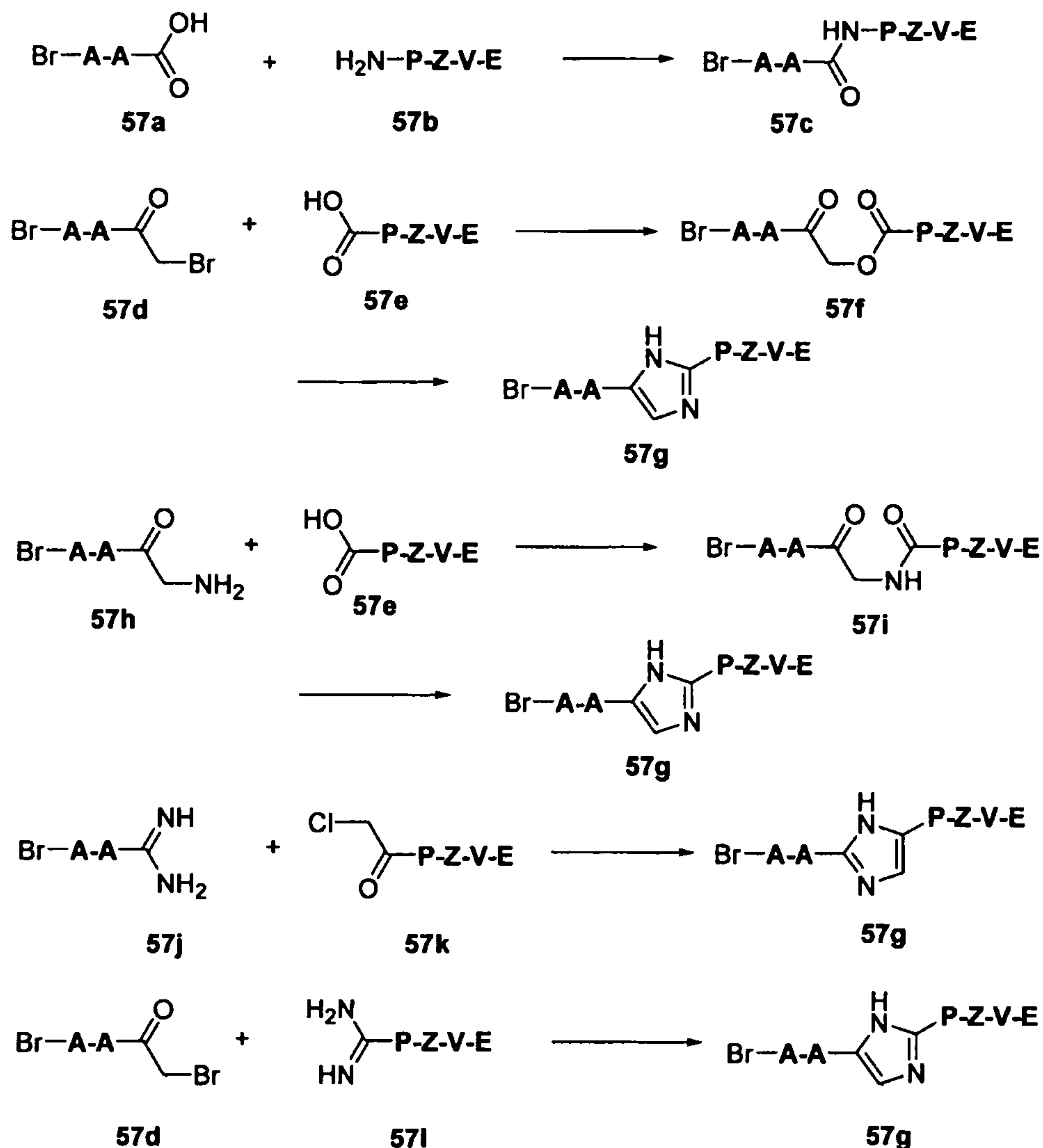
Alternatively, bromide **55e** can be synthesized from **55c**. The dimethyl compound **55c** can be converted to the corresponding diacid **55d** using potassium permanganate as oxidant.

Conversion of **55d** to **55e** can be accomplished by a multi-step homologation. For example, the treatment of **55d** with oxalyl chloride, followed by trimethylsilyl diazomethane and then hydrobromic acid can afford compound **55e**.

Scheme 56: Representative synthesis of R-P-M-W-M-P-R



Scheme **56** shows a general synthesis of an R-P-M-W-M-P-R intermediate of the invention wherein, for illustrative purposes, **M** is imidazole and **R** is a generic group that is depicted as a protecting group. The compound **56a** is coupled with vinyltin reagent such as tributyl(ethoxyvinyl)stannane in the presence of a palladium catalyst, followed by bromination and hydrolysis with NBS and water, to give the bromoketone **56b**. The reaction between bromide **56b** and a carboxylic acid under basic condition generates the ester **56d**. Following the same reaction sequence, compound **56d** can be elaborated to the diester **56f**. Conversion of **56f** to **56g** is accomplished with ammonia reagents such as ammonium acetate at elevated temperature.

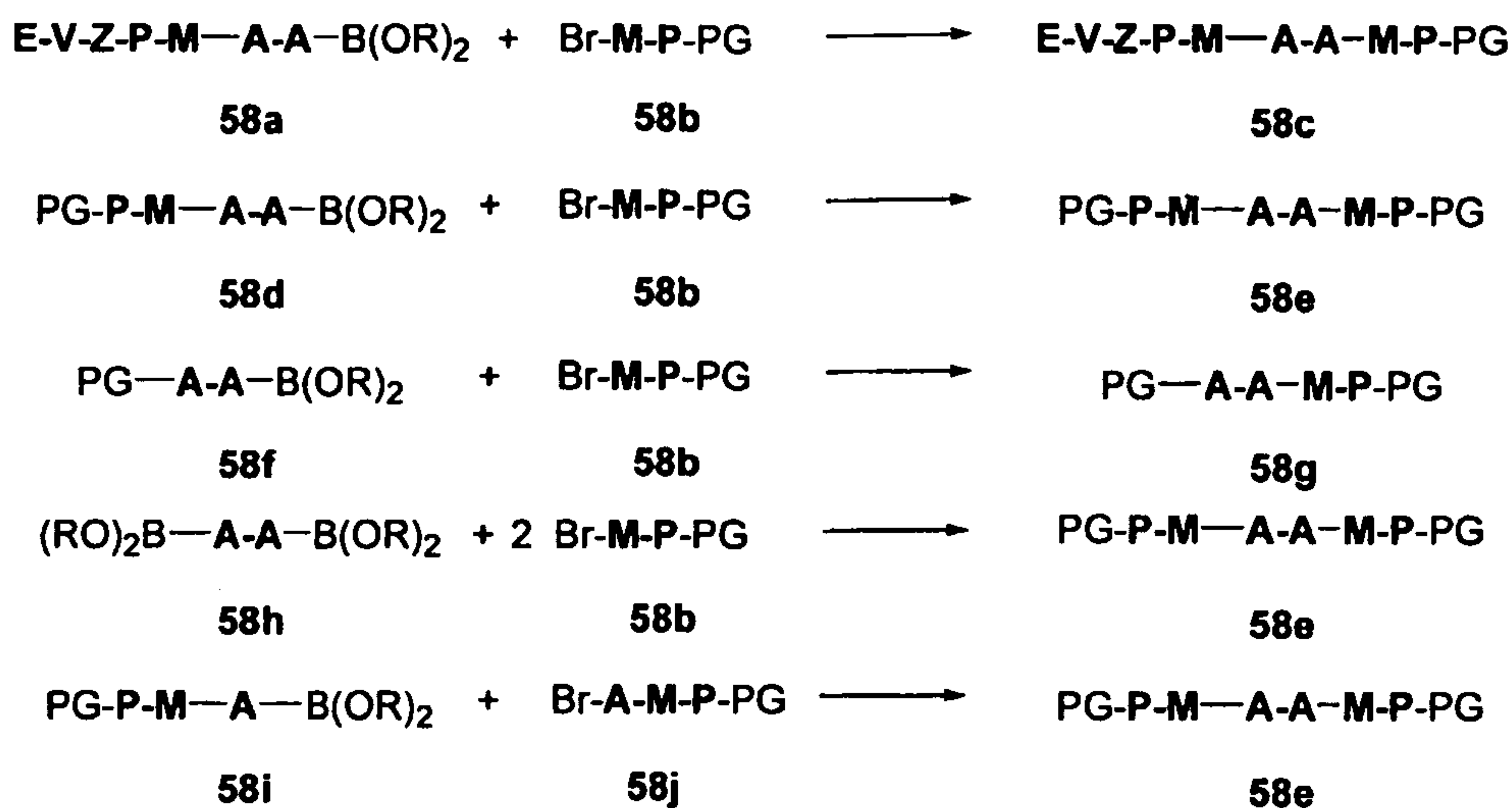
Scheme 57: Representative synthesis of R-A-A-M-P-R¹

Scheme 57 shows a general synthesis of an R-A-A-M-P-R¹ intermediate of the invention wherein, for illustrative purposes, M is an amide or an imidazole, R is a generic group that is depicted as Br, and R¹ is a generic group that is depicted as -Z-V-E. Coupling of amine 57b with acid 57a is accomplished using a peptide coupling reagent (e.g. HATU) to afford amide containing 57c.

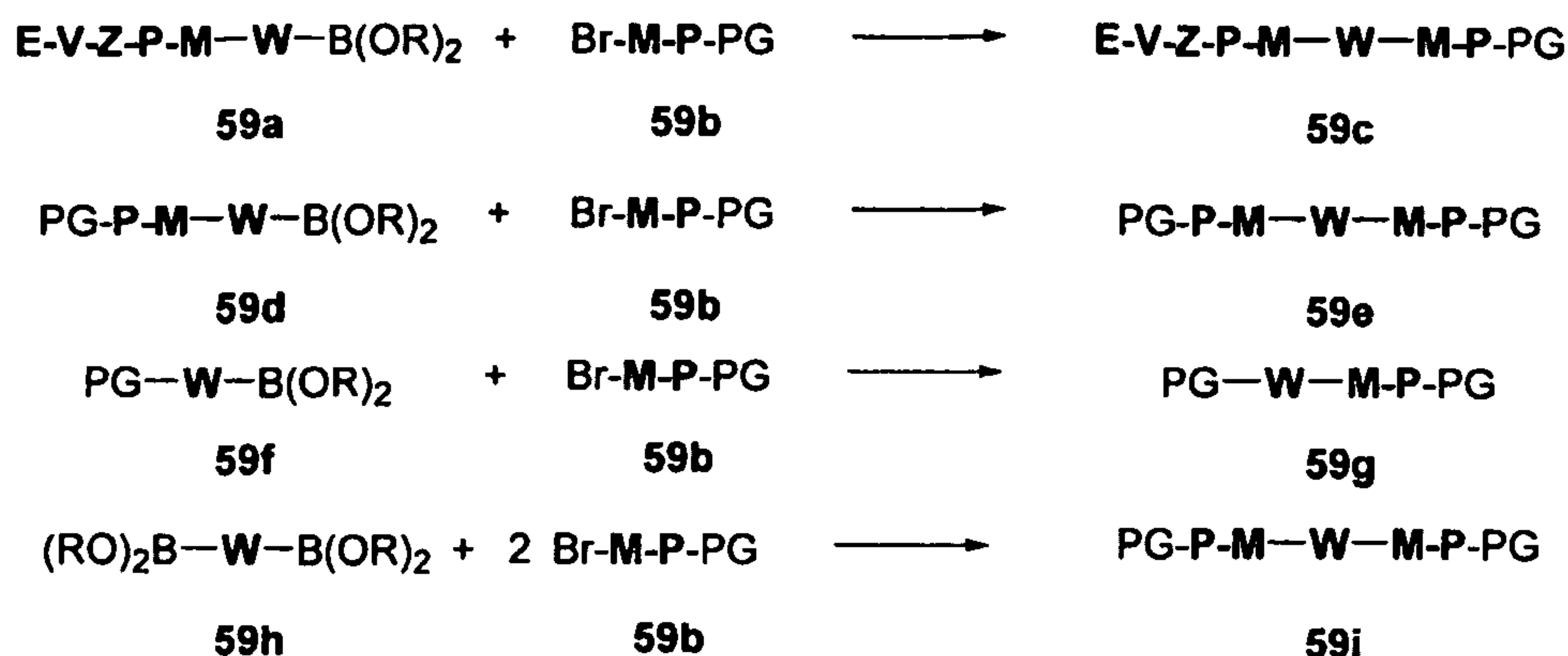
The acid 57e is coupled with an α -haloketone, such as α -bromoketone 57d, under basic conditions (e.g. Et₃N) to afford 57f. Alternatively, the acid 57e is coupled with an α -aminoketone 57h, under amide formation conditions (e.g. EDC, Et₃N) to afford 57i. Reaction of 57f or 57i with an amine or amine salt (e.g. ammonium acetate) affords the imidazole containing intermediate Br-A-M-P-Z-V-E (57g). Coupling of 57j and 57k and, in the

alternative, coupling of 57d and 57l under appropriate conditions can also be used in preparation of intermediate Br-A-M-P-Z-V-E (57g).

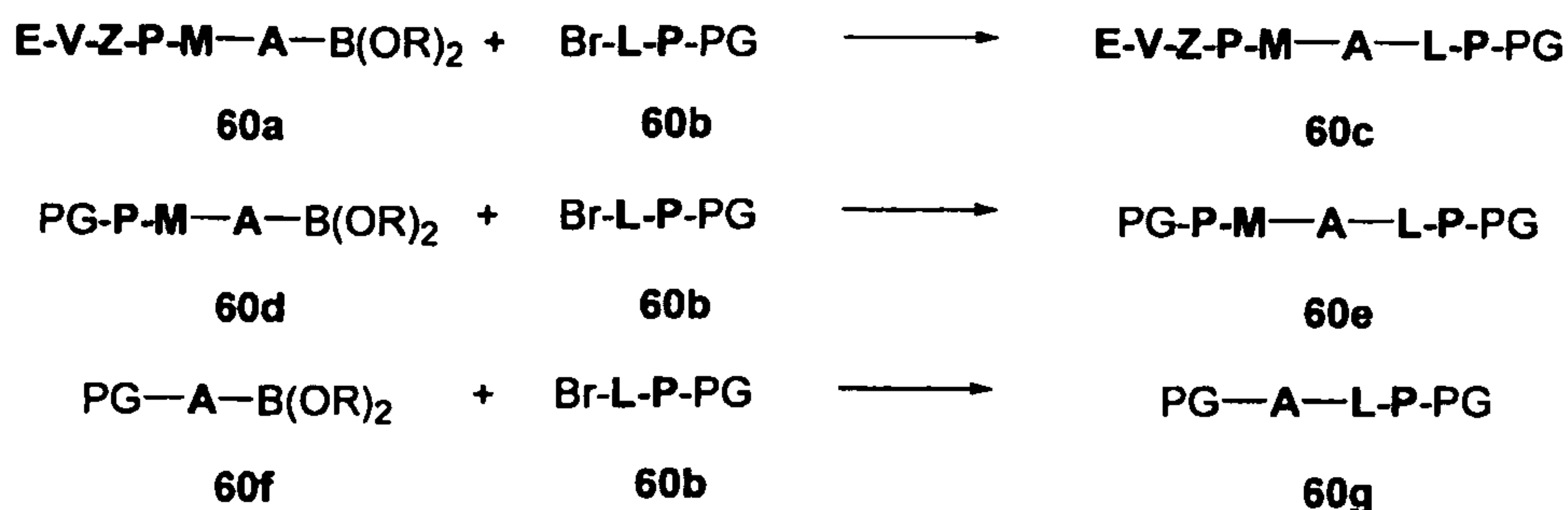
Scheme 58: Representative synthesis of R-A-A-M-P-R¹



Scheme 58 shows a general synthesis of the R-A-A-M-P-R¹ molecule of the invention, wherein a transition metal-mediated cross-coupling reaction is utilized to construct the A-A bond or A-M bond. For illustrative purposes, the Suzuki reaction is employed to couple two corresponding intermediates, R is a generic group that is depicted as -M-P-Z-V-E, -M-P-PG, or a protecting group, and R¹ is a generic group that is depicted as a protecting group. Boronic ester 58a, 58d, 58f or 58i is coupled with an appropriate coupling partner (e.g. arylbromide 58b or 58j) using a palladium catalyst, such as Pd(PPh₃)₄, to afford 58c, 58e, or 58g. Formation of multiple A-M bonds can be conducted in a similar manner. For example, the Suzuki reaction can also be employed to couple (RO)₂B-A-A-B(OR)₂ (58h) and two equivalents of Br-M-P-PG. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the A-A and/or A-M bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

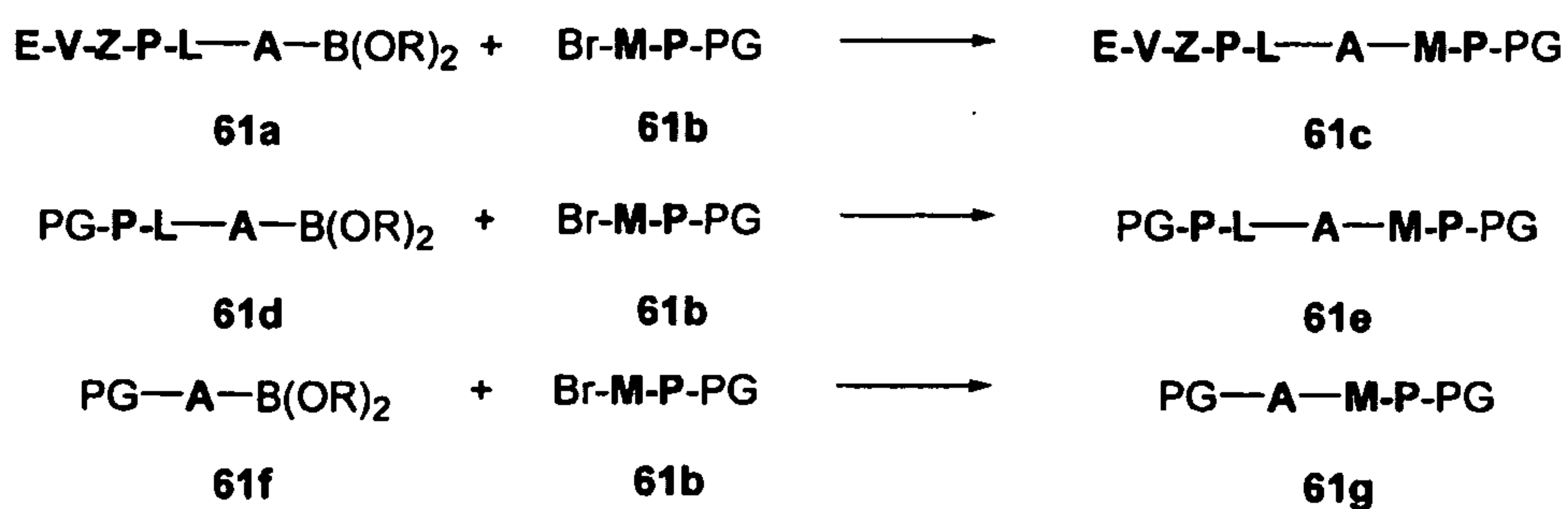
Scheme 59: Representative synthesis of R-W-M-P-R¹

Scheme 59 shows a general synthesis of the R-W-M-P-R¹ molecule of the invention, wherein a transition metal-mediated cross-coupling reaction is utilized to construct the W-M bond. For illustrative purposes, the Suzuki reaction is employed to couple two corresponding intermediates, R is a generic group that is depicted as -M-P-Z-V-E, -M-P-PG, or a protecting group, and R¹ is a generic group that is depicted as a protecting group. Boronic ester **59a**, **59d**, or **59f** is coupled with an appropriate coupling partner (e.g. arylbromide **59b**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford **59c**, **59e**, or **59g**. Formation of multiple W-M bonds can be conducted in a similar manner. For example, the Suzuki reaction can also be employed to couple (RO)₂B-W-B(OR)₂ (**59h**) and two equivalents of Br-M-P-PG. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the W-M bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

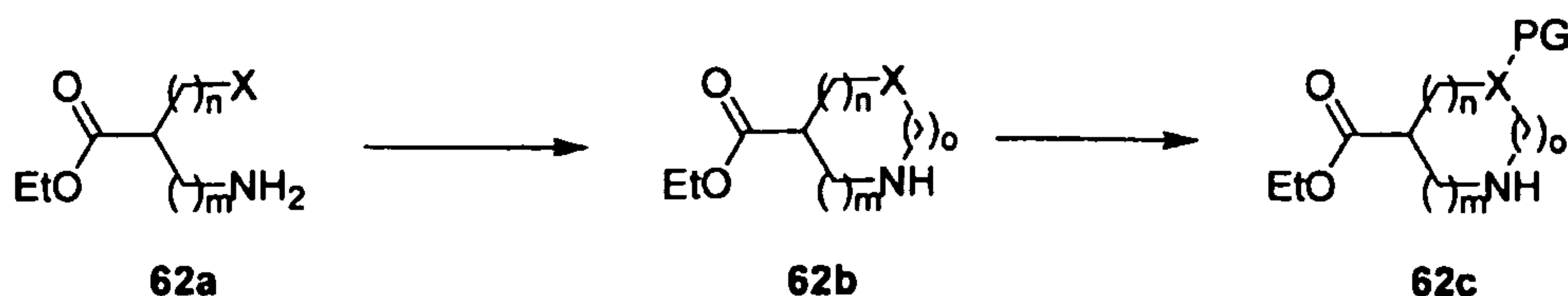
Scheme 60: Representative synthesis of R-A-L-P-R¹

Scheme 60 shows a general synthesis of the R-A-L-P-R¹ molecule of the invention, wherein a transition metal-mediated cross-coupling reaction is utilized to construct the A-L bond. For illustrative purposes, the Suzuki reaction is employed to couple two corresponding intermediates, R is a generic group that is depicted as -M-P-Z-V-E, -M-P-PG, or a protecting group, and R¹ is a generic group that is depicted as a protecting group. Boronic ester **60a**, **60d**, or **60f** is coupled with an appropriate coupling partner (e.g. arylbromide **60b**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford **60c**, **60e**, or **60g**. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the A-L bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

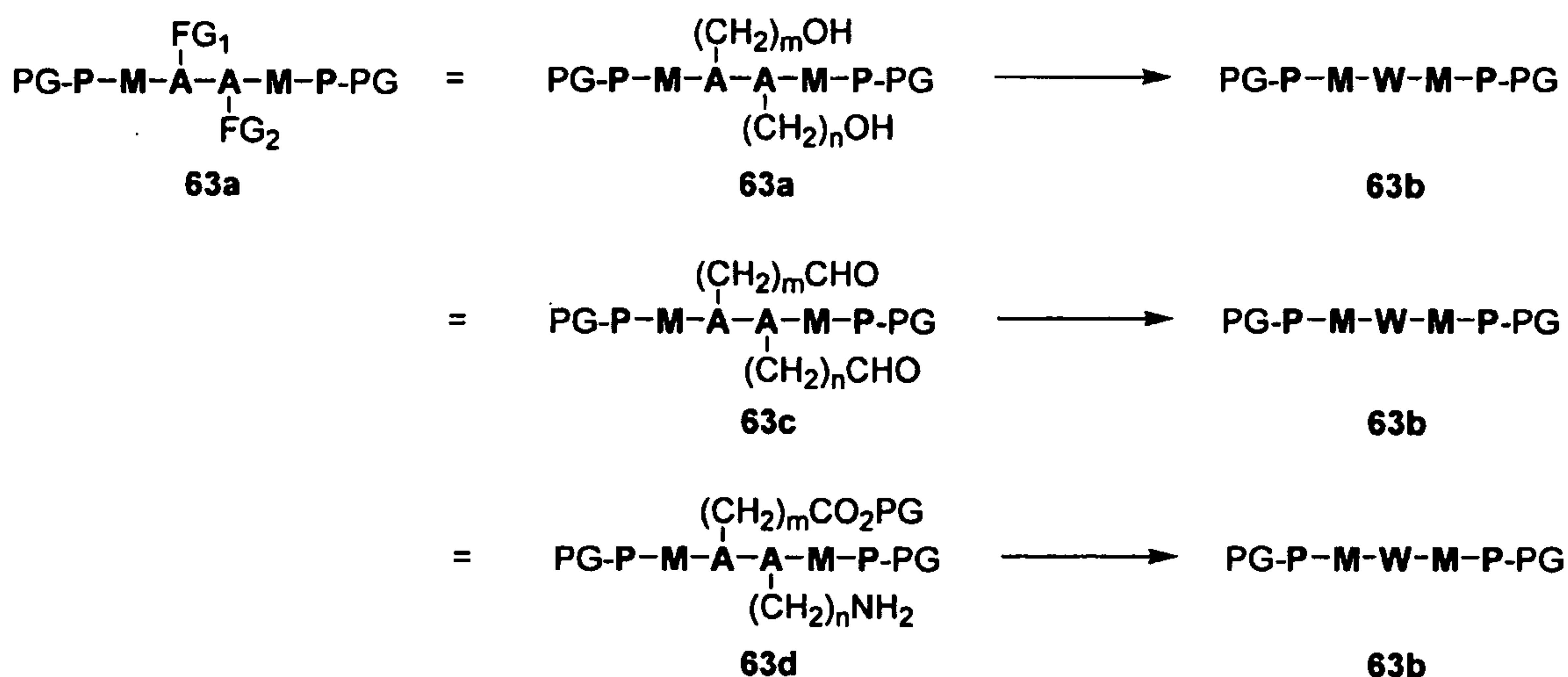
Scheme 61: Representative synthesis of R-A-M-P-R¹



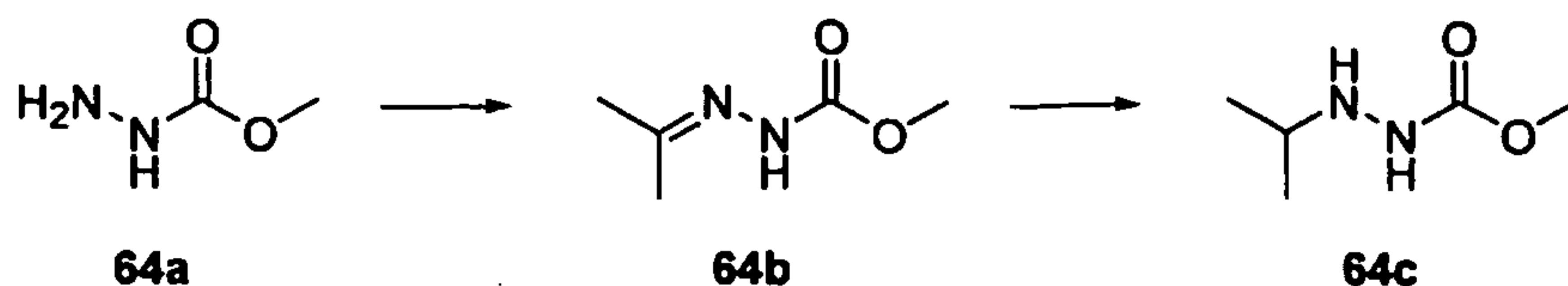
Scheme 61 shows a general synthesis of the R-A-M-P-R¹ molecule of the invention, wherein a transition metal-mediated cross-coupling reaction is utilized to construct the A-M bond. For illustrative purposes, the Suzuki reaction is employed to couple two corresponding intermediates, R is a generic group that is depicted as -L-P-Z-V-E, -L-P-PG, or a protecting group, and R¹ is a generic group that is depicted as a protecting group. Boronic ester **61a**, **61d**, or **61f** is coupled with an appropriate coupling partner (e.g. arylbromide **61b**) using a palladium catalyst, such as Pd(PPh₃)₄, to afford **61c**, **61e**, or **61g**. For each transition metal-mediated cross-coupling reaction the roles of the nucleophile and electrophile can be reversed to provide the same coupling product. Palladium mediated cross-coupling reactions that enable the A-M bond formation, but employ alternative coupling partners and reagents, include for example the Negishi, Kumada, Sonagashira and Stille reactions.

Scheme 62: Representative synthesis of R-P-H

Scheme 62 shows a general synthesis of a R-P-H molecule of the invention wherein, for illustrative purposes, R is a generic group that is depicted as ethoxycarbonyl and P is a carbocyclic or heterocyclic ring (e.g. X is carbon or heteroatom) and m, n, and o are 0 - 3, independently. The amino ester **62a** is converted to the substituted or cyclized amino ester **62b** through for example a reductive amination or Mitsunobu reaction. Compound **62b** can be protected to provide compound **62c** if necessary.

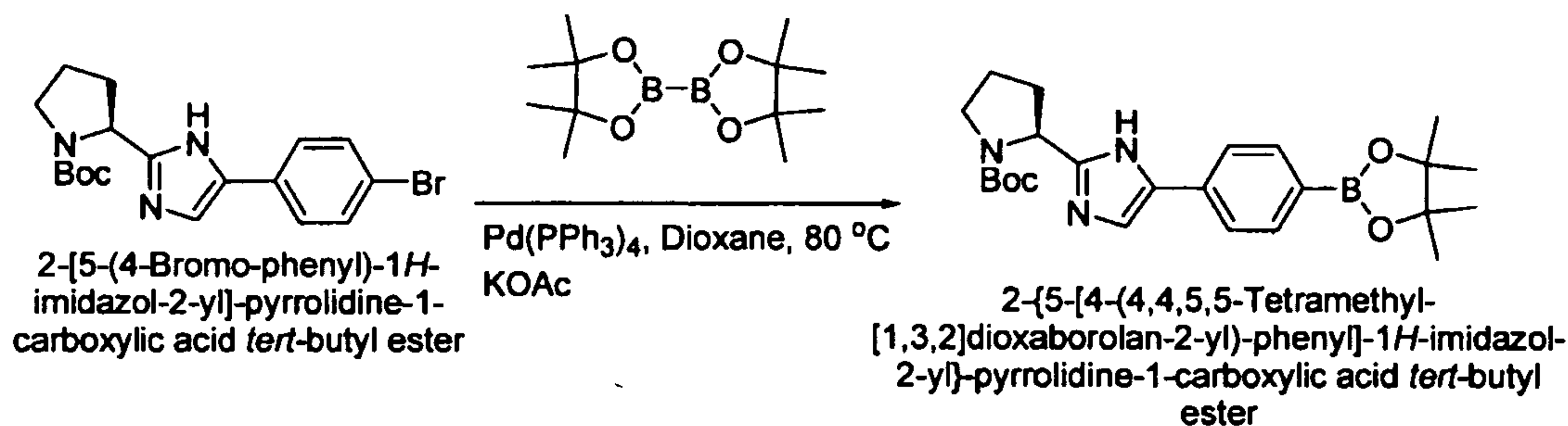
Scheme 63: Representative synthesis of R-P-M-W-M-P-R

Scheme 63 shows a general synthesis of a R-P-M-W-M-P-R intermediate of the invention wherein, for illustrative purposes, R is a generic group that is depicted as a protecting group and A is functionalized with a group depicted as either hydroxyalkyl, aminoalkyl, carbonylalkyl, or alkoxyalkyl. The cyclization of **63a**, **63c**, and **63d** can be performed through several functional group transformations which include, but are not limited to, Mitsunobu reaction, reductive amination, and lactamization.

Scheme 64: Representative Synthesis of H-V-E

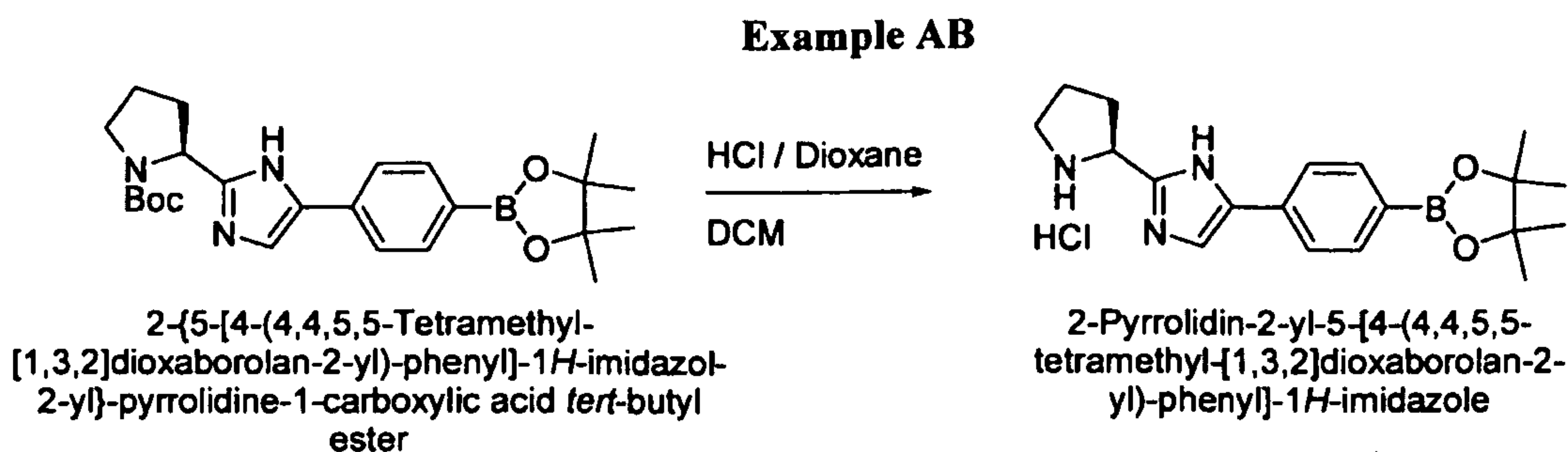
Scheme 64 shows a general synthesis of a H-V-E intermediate of the invention wherein, for illustrative purposes E is methoxycarbonylamino and V is isopropylamino. The reaction of hydrazine carboxylate **64a** with a ketone or aldehyde, such as acetone, under acidic conditions (e.g. AcOH) affords the imine **64b**. Reaction of **64b** under reducing conditions, such as PtO₂ and hydrogen gas, affords the substituted hydrazinecarboxylate **64c**.

The invention will now be illustrated by the following non-limiting Examples.

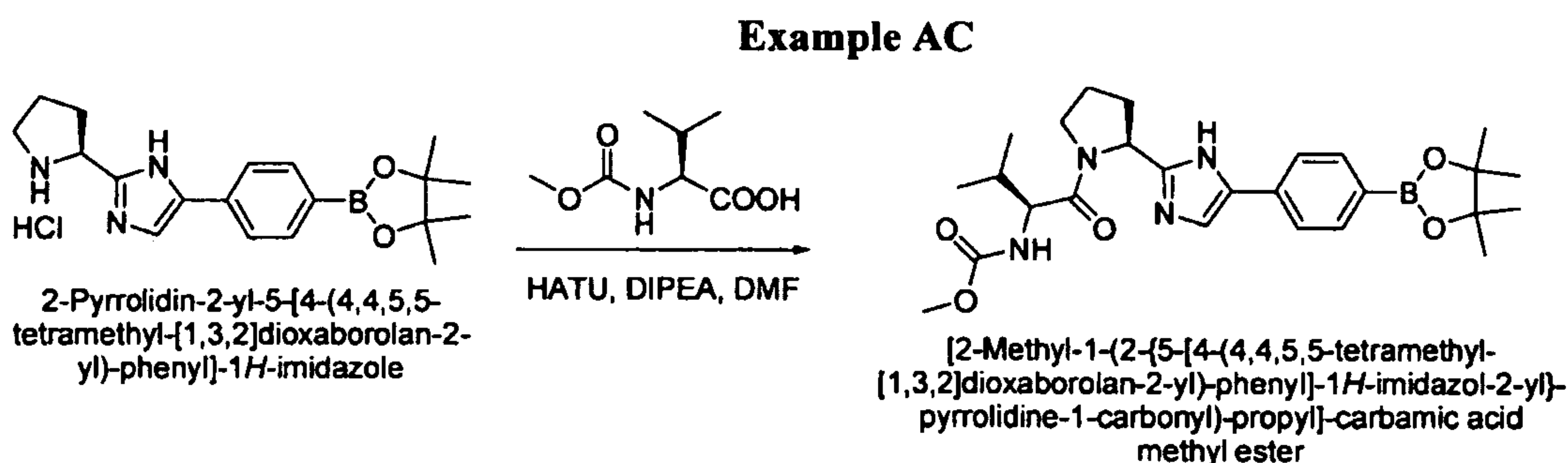
EXAMPLES**Example AA**

(S)-2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester: 1,4-Dioxane (300 mL) was added to a mixture of (S)-2-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (21.1 g, 53.7 mmol), bis(pinacolato)diboron (27.3g, 107.5 mmol), tetrakis(triphenylphosphine)palladium (0) (3.10 g, 2.68 mmol), and potassium acetate (15.02 g, 153.0 mmol), and heated at 80 °C for 16 hours. The mixture was cooled and the resulting solid was filtered. The majority of the 1,4-dioxane was removed from the filtrate under reduced pressure and resulting residue was taken up in ethyl acetate (300 mL). The organic phase was washed with saturated sodium bicarbonate (2x 150 mL), brine (100 mL) and dried over sodium sulfate. After filtration the solvent was removed from the filtrate under reduced pressure. The resulting oil was subjected to silica gel chromatography using a 330 g ISCO column and effluent of 20-100 % ethyl acetate and hexanes. The fractions containing product were combined and the solvent was removed under reduced pressure to provide (S)-2-{5-[4-(4,4,5,5-tetramethyl-

[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester (18 g, 76 %) and light yellow solid.

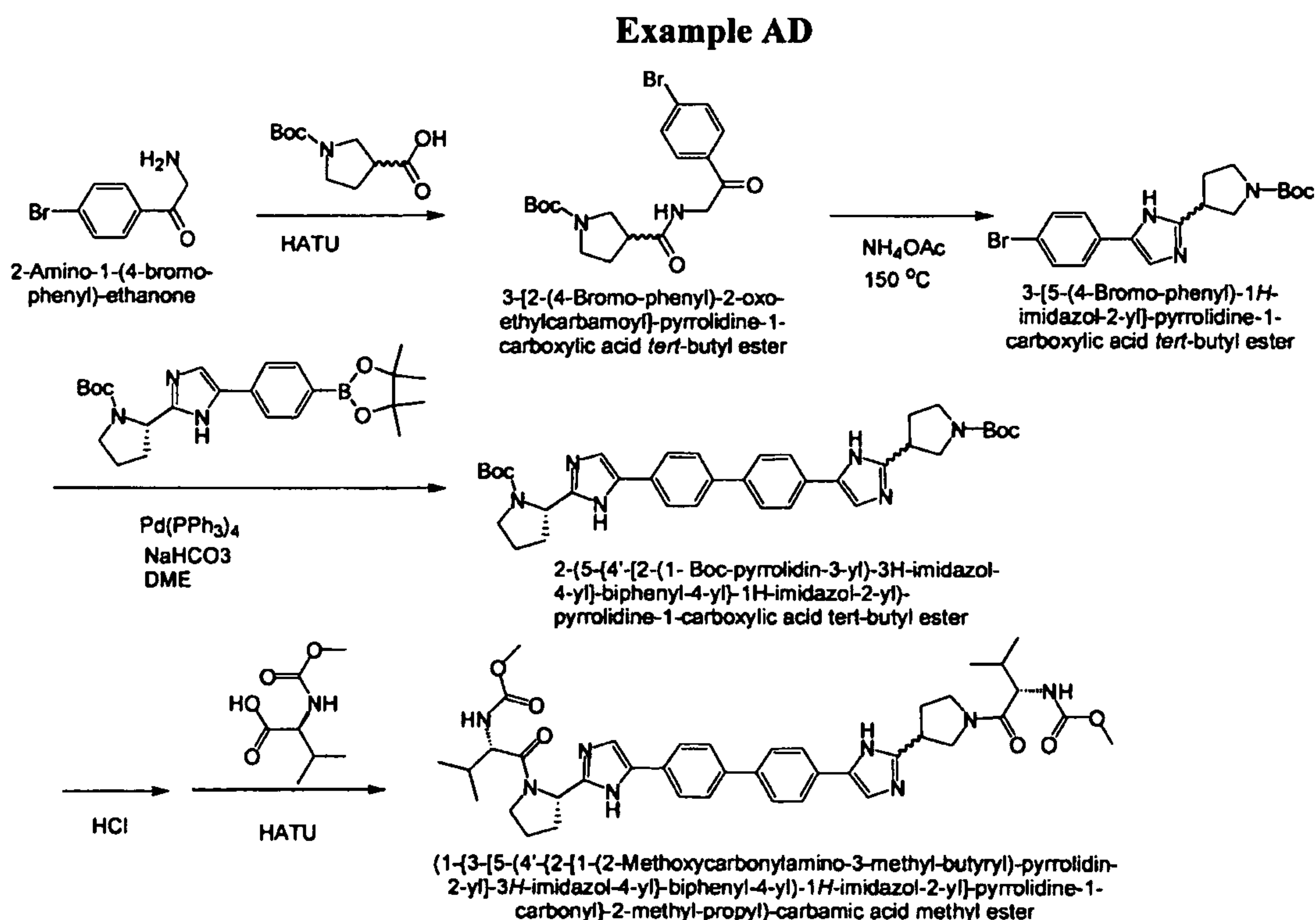


(S)-2-Pyrrolidin-2-yl-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazole hydrochloride: A solution of hydrogen chloride in 1,4-dioxane (4 N, 75 mL) was added to a solution of (S)-2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester (7.0 g, 15.9 mmol) in dichloromethane (50 mL). Gas evolution was observed. After 30 minutes, a solid formed. After 1.5 hours, the resulting solid was isolated by filtration with diethyl ether washing. Any residual solvent was removed under reduced pressure to provide (S)-2-pyrrolidin-2-yl-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazole hydrochloride (5.6 g, 95 %) as an off-white solid.



(S,S)-[2-Methyl-1-(2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carbonyl)-propyl]-carbamic acid methyl ester: Diisopropylethylamine (7.63 mL, 43.8 mmol) was added to a suspension of (S)-2-pyrrolidin-2-yl-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazole hydrochloride (7.33 g, 19.5 mmol), *O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (7.6 g, 19.9 mmol) and (S) 2-methoxycarbonylamino-3-methyl-butyric acid (3.59 g, 20.5 mmol) in dimethylformamide (75 mL). All solids dissolved. After 30 min the

reaction mixture was diluted with ethyl acetate (300 mL) and was washed with ½ saturated sodium chloride (1 x 300 mL), half saturated sodium bicarbonate (2 x 150 mL) and brine (1 x 100 mL). The organic phase was dried with sodium sulfate, filtered and the solvent was removed under reduced pressure. The resulting tan foam was subjected to silica gel chromatography with eluate of 20 -100 % ethyl acetate and hexanes, to provide (S,S)-[2-methyl-1-(2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carbonyl)-propyl]-carbamic acid methyl ester (6.6 g, 68 %) as a white foam: ¹H (DMSO-d₆): δ = 11.81 (br s, 1H), 7.72 (m, 2H), 7.61 (m, 2H), 7.51 (br s, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 5.05 (m, 1H), 4.04 (m, 2 H), 3.78 (m, 2H), 3.52 (s, 3H), 2.11 (m, 2H), 1.93 (m, 2H), 1.28 (s, 12H), 0.85 (dd, *J*₁ = 6.6 Hz, *J*₂ = 11.4 Hz, 6H).



3-[2-(4-Bromo-phenyl)-2-oxo-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: *N,N*-diisopropylethylamine (5.3 mL, 30.6 mmol) was added dropwise to a mixture of pyrrolidine-1,3-dicarboxylic acid 1-*tert*-butyl ester (2.2 g, 10.1 mmol), HATU (4.0 g, 10.5 mmol), the HCl salt of 2-amino-1-(4-bromophenyl)ethanone (2.4 g, 9.6 mmol), and DMF (40 mL), and stirred at ambient condition for 1 hour. Most of the volatile component was removed *in vacuo*, and the resulting residue was dissolved in ethyl acetate (150 mL), washed with water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was

purified by flash chromatography to provide the desired product as a white foam-like solid (3.5 g, 90%). m/z 432.9, 434.9 ($M + Na$)⁺.

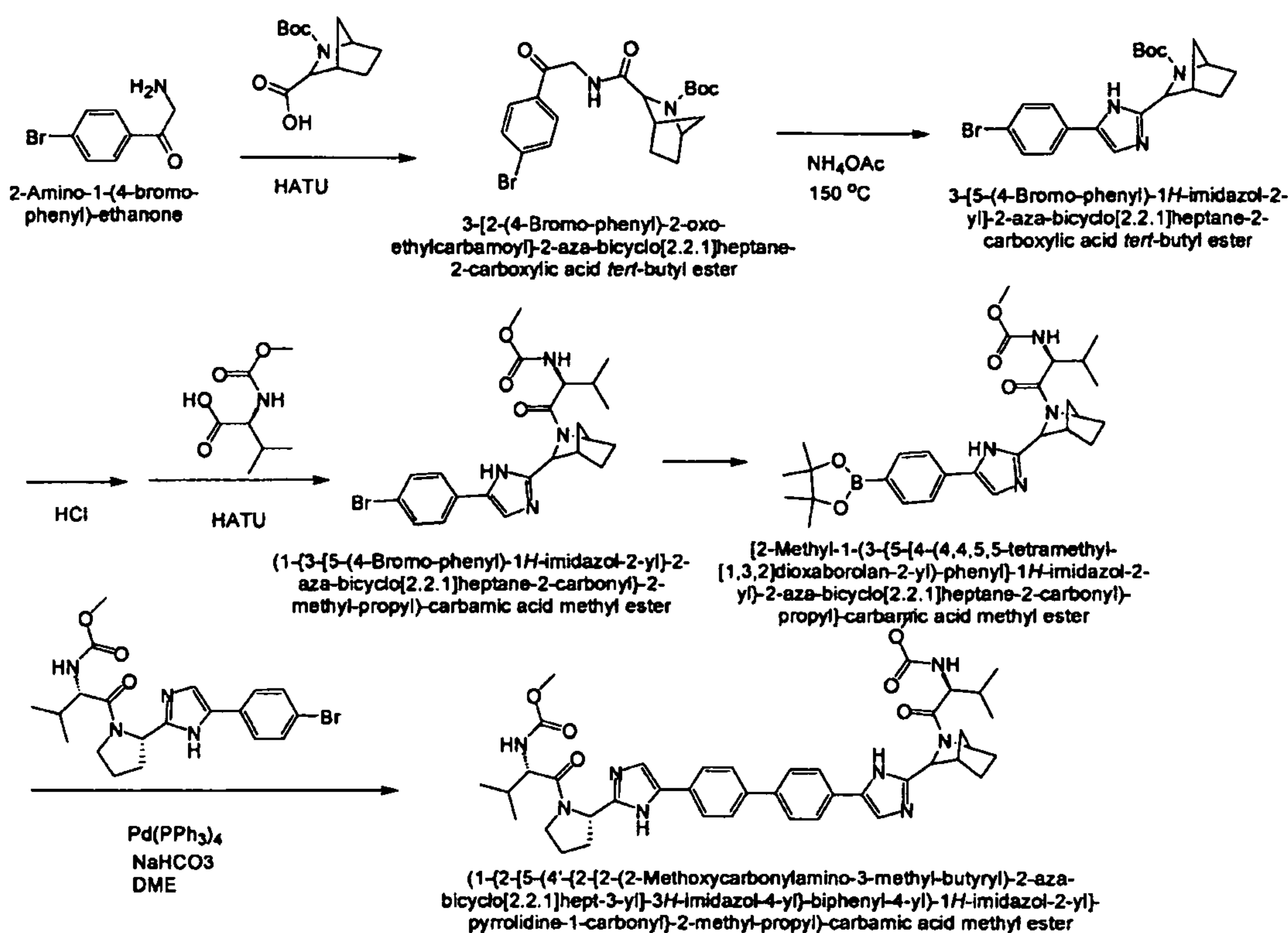
3-[5-(4-Bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: A mixture of 3-[2-(4-bromo-phenyl)-2-oxo-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (1.5 g, 3.6 mmol) and ammonium acetate (1.4 g, 18.2 mmol) in xylene (15 mL) was heated in a sealed tube at 140°C for 2 hours. The volatile component was removed *in vacuo*, and the residue was dissolved in ethyl acetate (150 mL), washed with NaHCO₃ solution, water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (795 mg, 56%). m/z 391.8, 393.8 ($M + H$)⁺.

2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Pd(Ph₃)₄ (54 mg, 0.046 mmol) was added to a mixture 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (378 mg, 0.97 mmol), 2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester (408 mg, 0.93 mmol), NaHCO₃ (273 mg, 3.26 mmol) in 1,2-dimethoxyethane (8 mL) and water (2 mL). The reaction mixture was flushed with nitrogen, heated at 80°C for 6 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with NaHCO₃ solution, water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (370 mg, 64%). m/z 625.1 ($M + H$)⁺.

(1-{3-[5-(4'-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: To a solution of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester (200 mg, 0.232 mmol) in methanol (5 mL) was added 4.0 M solution of HCl in dioxane (1 mL, excess). The mixture was stirred for 3 hours at 50°C and concentrated under reduced pressure. The residue was treated with ether to remove excess HCl. The obtained white solid was dissolved in DMF (5 mL). To the solution was added 2-methoxycarbonylamino-3-methyl-butyric acid (123 mg, 0.71 mmol), HATU (285 mg, 0.75 mmol) and *N,N*-diisopropylethylamine (0.14 mL, 0.77 mmol). The mixture was stirred at ambient for 2 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with 1 N

NaOH solution, water and brine, dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (100 mg, 42%). $^1\text{H-NMR}$ (300 MHz, CD_3OD) δ 8.00-7.80 (m, 10H), 5.26 (t, 1H), 4.40-3.42 (m, 15H), 2.65-2.00 (m, 8H), 1.50-0.93 (m, 12H); m/z 739.3 ($\text{M} + \text{H}$) $^+$.

Example AE



3-[2-(4-Bromo-phenyl)-2-oxo-ethylcarbamoyl]-2-aza-bicyclo[2.2.1]heptane-2-carboxylic acid *tert*-butyl ester: Following the procedure used to prepare compound 3-[2-(4-bromo-phenyl)-2-oxo-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that 2-aza-bicyclo[2.2.1]heptane-2,3-dicarboxylic acid 2-*tert*-butyl ester was used instead of pyrrolidine-1,3-dicarboxylic acid 1-*tert*-butyl ester.

3-[5-(4-Bromo-phenyl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carboxylic acid *tert*-butyl ester: Following the procedure used to prepare compound 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that 3-[2-(4-bromo-phenyl)-2-oxo-ethylcarbamoyl]-2-aza-bicyclo[2.2.1]heptane-2-carboxylic acid *tert*-butyl ester was used instead of 3-[2-(4-bromo-phenyl)-2-oxo-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester.

(1-{3-[5-(4-Bromo-phenyl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: To a solution of 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carboxylic acid *tert*-butyl ester (1.0 g, 2.4 mmol) in methanol (20 mL) was added 4.0 M solution of HCl in dioxane (4.0 mL, excess). The mixture was stirred for 3 hours at 50°C and concentrated under reduced pressure. The residue was treated with ether to remove excess HCl. The obtained white solid was dissolved in DMF (20 mL). To the solution was added 2-methoxycarbonylamino-3-methyl-butyric acid (0.46 g, 2.6 mmol), HATU (1.0 g, 2.6 mmol) and *N,N*-diisopropylethylamine (2.5 mL, 14.4 mmol). The mixture was stirred at ambient for 2 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (200 mL), washed with 1 N NaOH solution, water and brine, dried over MgSO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (1.0 g, 89%). *m/z* 475.1, 477.1 (M + H)⁺.

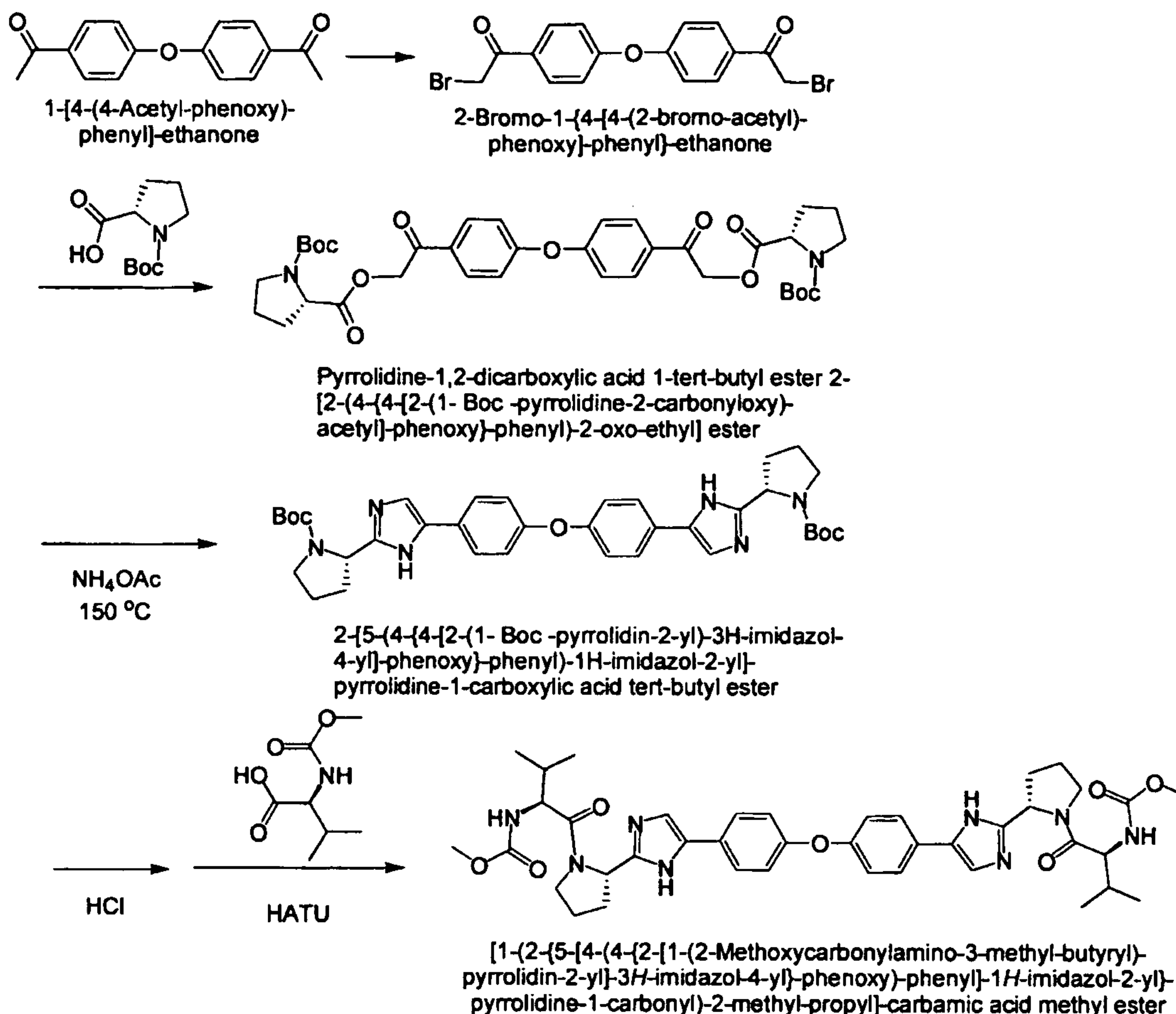
[2-Methyl-1-(3-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-2-aza-bicyclo[2.2.1]heptane-2-carbonyl)-propyl]-carbamic acid methyl ester: Pd(PPh₃)₄ (73 mg, 0.06 mmol) was added to a sealed tube containing a mixture of (1-{3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester (600 mg, 1.27 mmol), bis(pinacolato)diboron (675 mg, 2.66 mmol), potassium acetate (324 mg, 3.3 mmol) and 1,4-dioxane (15 mL). The reaction mixture was flushed with nitrogen, heated at 80°C for 16 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with NaHCO₃ solution, water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (440 mg, 66%). *m/z* 523.2 (M + H)⁺.

(1-{2-[5-(4'-{2-[2-(2-Methoxycarbonylamino-3-methyl-butyryl)-2-aza-bicyclo[2.2.1]hept-3-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Following the procedure used to prepare compound 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that [2-methyl-1-(3-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-2-aza-bicyclo[2.2.1]heptane-2-carbonyl)-propyl]-carbamic acid methyl ester and (1-{2-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester were used instead of

2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester and 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.90-7.70 (m, 10H), 7.20-7.10 (m, 1H), 5.24 (t, 1H), 4.63 (s, 1H), 4.40-3.80 (m, 4H), 3.68 (s, 3H), 3.66 (s, 3H), 2.60-1.60 (m, 13H), 1.05-0.90 (m, 12H); m/z 765.2 (M + H)⁺.

(1-{3-[5-(4'-{2-[2-(2-Methoxycarbonylamino-3-methyl-butyryl)-2-aza-bicyclo[2.2.1]hept-3-yl]-3H-imidazol-4-yl]-biphenyl-4-yl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Following the procedure used to prepare compound 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that [2-methyl-1-(3-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-2-aza-bicyclo[2.2.1]heptane-2-carbonyl)-propyl]-carbamic acid methyl ester and (1-{3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester were used instead of 2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester and 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.90-7.20 (m, 10H), 4.83-4.25 (m, 5H), 3.90-3.40 (m, 6H), 2.90-2.70 (m, 2H), 2.40-2.10 (m, 3H), 2.10-1.40 (m, 11H), 1.10-0.90 (m, 12H); m/z 791.3 (M + H)⁺.

Example AF



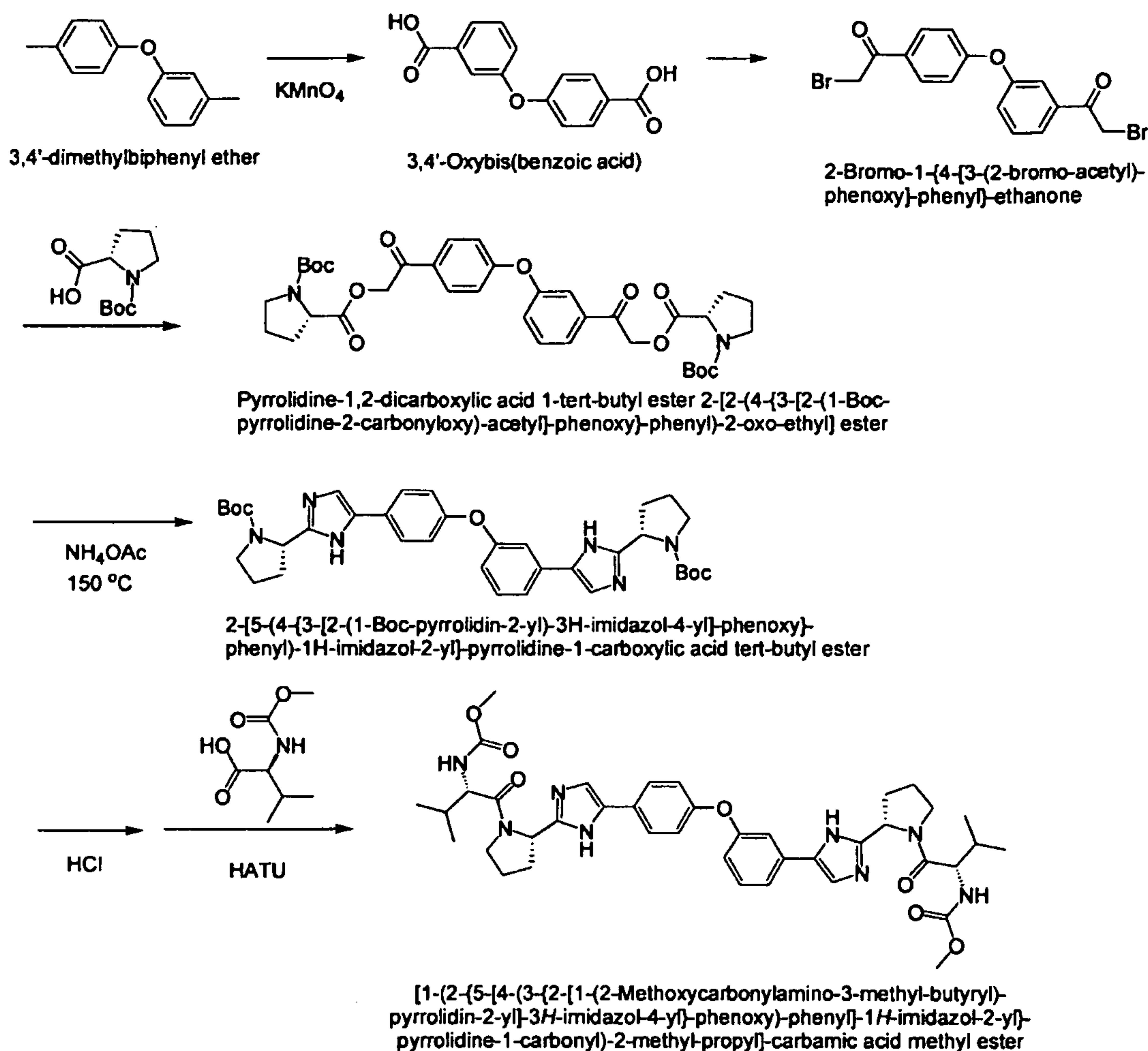
2-Bromo-1-[4-[4-(2-bromo-acetyl)-phenoxy]-phenyl]-ethanone: Bromine (2.02 mL, 39.3 mmol) in dichloromethane (25 mL) was added slowly to a stirred solution of 4-acetylphenyl ether (5.0 g, 19.7 mmol) in dichloromethane (65 mL) at 30°C. The mixture was stirred at ambient for 16 hours, and then the volatile component was removed *in vacuo*. The residue was recrystallized from ethanol (40 mL) to get a yellow crystal like product (2.3 g, 29%).

Pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-[2-(4-[4-(2-(1-Boc-pyrrolidine-2-carboxyloxy)-acetyl)-phenoxy]-phenyl)-2-oxo-ethyl] ester: To a stirred mixture of 2-bromo-1-[4-[4-(2-bromo-acetyl)-phenoxy]-phenyl]-ethanone (2.0 g, 4.9 mmol) and pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester (2.2 g, 10.2 mmol) in acetonitrile (20 mL) was added DIPEA (1.76 mL, 10.1 mmol). The slurry was stirred for 3 hours at ambient temperature. The mixture was diluted with ethyl acetate (150 mL), washed with water and brine, dried over MgSO_4 , filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (2.2 g, 65%). m/z 703.1 ($\text{M} + \text{Na}$)⁺.

2-[5-(4-{4-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: A mixture of pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-[2-(4-{4-[2-(1-Boc-pyrrolidine-2-carboxyloxy)-acetyl]-phenoxy}-phenyl)-2-oxo-ethyl] ester (250 mg, 0.37 mmol) and ammonium acetate (570 mg, 7.3 mmol) in xylene (8 mL) was heated in microwave machine at 140°C for 80 minutes. The volatile component was removed *in vacuo*, and the residue was dissolved in ethyl acetate (100 mL), washed with NaHCO₃ solution, water and brine, dried over MgSO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (62 mg, 26%). *m/z* 641.1 (M + H)⁺.

[1-(2-{5-[4-(4-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl)-2-methyl-propyl]-carbamic acid methyl ester: Following the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-[5-(4-{4-[2-(1- Boc -pyrrolidin-2-yl)-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1- Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.80-7.60 (m, 4H), 7.30-7.20 (m, 2H), 7.10-0.95 (m, 4H), 5.16 (t, 1H), 4.30-3.50 (m, 12H), 2.40-1.90 (m, 10H), 1.10-0.90 (m, 12H); *m/z* 755.2 (M + H)⁺.

Example AG



3,4'-Oxybis(benzoic acid): A mixture of 3,4'-dimethylbiphenyl ether (1.7 g, 8.6 mmol) and potassium permanganate (6.0 g, 38 mmol) in water (200 mL) was refluxed for 6 hours. The hot solution was filtered, cooled, and extracted with chloroform. The aqueous layer was acidified by 2 N HCl. The precipitate was filtered off and washed with water to give a white solid (0.55 g, 25%). m/z 257.1 (M - H)⁻.

2-Bromo-1-(4-{3-(2-bromo-acetyl)-phenoxy}-phenyl)-ethanone: A mixture of 3,4'-oxybis(benzoic acid) (0.55 g, 2.1 mmol) and oxalyl chloride (10.6 mL, 21.3 mmol) in dichloromethane (40 mL) containing DMF (4 drops) was stirred at ambient temperature for 4 hours, then concentrated and co-evaporated with toluene (3x) and dried under high vacuum. The resulting residue was suspended in dichloromethane (15 mL) at 0°C and treated with 2.0 M trimethylsilyldiazomethane in ether (3.2 mL, 6.4 mmol) over 15 minutes to give a brown mixture. Reaction mixture was warmed to ambient temperature overnight and then

concentrated. The resulting brown solid was suspended in ethyl acetate (15 mL) and cooled to 0°C. HBr in acetic acid (1.2 mL, 33%W, 6.4 mmol) was added over 5 minutes and reaction mixture was warmed to ambient temperature over 1 hour. Solid sodium bicarbonate (0.3 g) was added and stirred for 30 minutes. Water was added giving a biphasic mixture with a brown precipitate. The solid was removed by filtration and filtrate was extracted with dichloromethane, dried over MgSO₄ and concentrated. The residue was purified by flash column chromatography to give a brown solid (0.47 g).

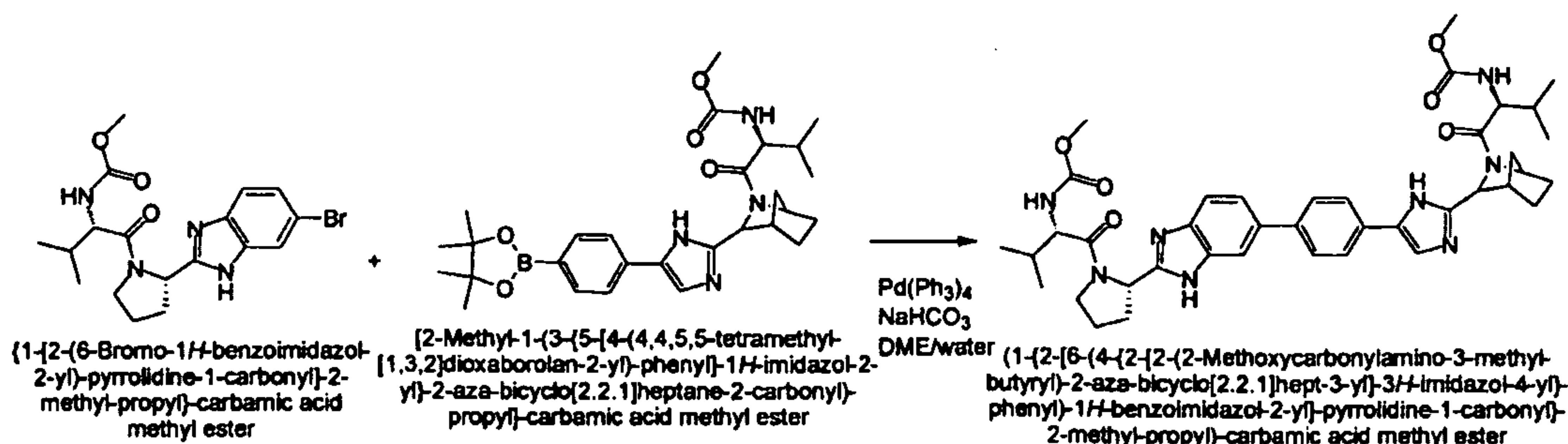
Pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-[2-(4-{3-[2-(1-Boc-pyrrolidine-2-carboxyloxy)-acetyl]-phenoxy}-phenyl)-2-oxo-ethyl] ester: Following the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-bromo-1-{4-[3-(2-bromo-acetyl)-phenoxy]-phenyl}-ethanone was used instead of 2-bromo-1-{4-[4-(2-bromo-acetyl)-phenoxy]-phenyl}-ethanone. *m/z* 703.1 (M + Na)⁺.

2-[5-(4-{3-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Following the procedure used to prepare compound 2-[5-(4-{4-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-[2-(4-{3-[2-(1-Boc-pyrrolidine-2-carboxyloxy)-acetyl]-phenoxy}-phenyl)-2-oxo-ethyl] ester was used instead of pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-[2-(4-{4-[2-(1-Boc-pyrrolidine-2-carboxyloxy)-acetyl]-phenoxy}-phenyl)-2-oxo-ethyl] ester. *m/z* 641.0 (M + H)⁺.

[1-(2-{5-[4-(3-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl)-2-methyl-propyl]-carbamic acid methyl ester: Following the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-[5-(4-{3-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-phenoxy}-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.80-7.10 (m,

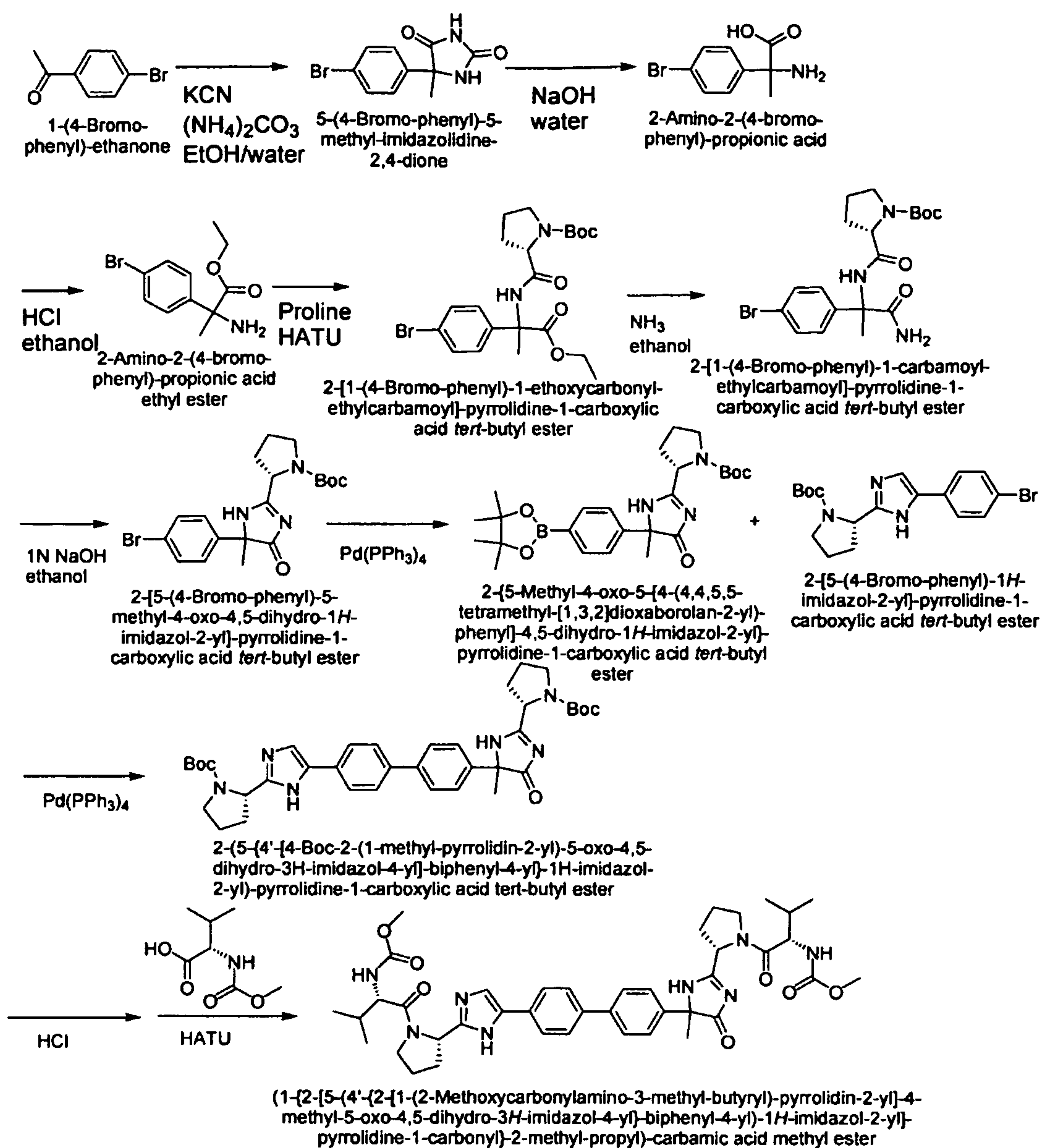
10H), 5.30-5.15 (m, 2H), 4.30-4.20 (m, 2H), 4.18-4.05 (m, 2H), 3.95-3.80 (m, 2H), 3.70-3.60 (m, 6H), 2.65-2.45 (m, 2H), 2.40-2.00 (m, 8H), 1.05-0.85 (m, 12H); m/z 755.3 (M + H)⁺.

Example AH



(1-[2-[6-(4-{2-[2-(2-Methoxycarbonylamino-3-methyl-butyl)-2-aza-bicyclo[2.2.1]hept-3-yl]-3H-imidazol-4-yl]-phenyl)-1H-benzimidazol-2-yl]-pyrrolidine-1-carbonyl]-2-methyl-propyl)-carbamic acid methyl ester: Following the procedure used to prepare compound 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that [2-methyl-1-(3-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-2-aza-bicyclo[2.2.1]heptane-2-carbonyl)-propyl]-carbamic acid methyl ester and {1-[2-(6-bromo-1H-benzimidazol-2-yl)-pyrrolidine-1-carbonyl]-propyl}-carbamic acid methyl ester were used instead of 2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester and 3-[5-(4-bromo-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 8.10-7.80 (m, 7H), 5.42-5.30 (m, 1H), 4.65 (s, 1H), 4.40-4.25 (m, 2H), 4.20-3.90 (m, 2H), 3.80-3.60 (m, 6H), 3.00-2.80 (m, 1H), 2.70-2.55 (m, 1H), 2.50-1.60 (m, 12H), 1.10-0.80 (m, 12H); m/z 739.3 (M + H)⁺.

Example A1



5-(4-Bromo-phenyl)-5-methyl-imidazolidine-2,4-dione: A mixture of 4-bromo acetophenone (8.0 g, 40.2 mmol), ammonium carbonate (40 g, 402 mmol) and potassium cyanide (3.4 g, 52.3 mmol) in a mixed solvent of ethanol (90 mL) and water (90 mL) was stirred at 55°C for 5 hours, then 12 hours at ambient. The solution was adjusted to pH = 6 with 6 N HCl carefully and subsequently stirred at room temperature for 2 hours. The precipitate was filtered off, washed with water. The collected white solid was dried under vacuum to give the product (9.2 g, 85%). m/z 267.1, 269.1 ($M - H$)⁻.

2-Amino-2-(4-bromo-phenyl)-propionic acid: A mixture of 5-(4-bromo-phenyl)-5-methyl-imidazolidine-2,4-dione (4.0 g, 14.9 mmol) and 3 N NaOH (50 mL) was heated in a sealed tube at 145°C for two days, then diluted with water (100 mL). The solution was adjusted to pH = 4 with 6 N HCl carefully and subsequently stirred at room temperature for 2 hours. The precipitate was filtered off, washed with water. The collected white solid was dried under vacuum to give the product (2.5 g, 65%). m/z 243.7, 245.7 (M + H)⁺.

2-Amino-2-(4-bromo-phenyl)-propionic acid ethyl ester: To a solution of 2-amino-2-(4-bromo-phenyl)-propionic acid (1.0 g, 4.1 mmol) in ethanol (20 mL) was bubbled through HCl gas for five minutes. The mixture was stirred at ambient for 24 hours, then refluxed for 18 hours. The volatile component was removed *in vacuo*, and the residue was dissolved in ethyl acetate (150 mL), washed with NaHCO₃ solution, water and brine, dried over MgSO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product (800 mg, 72%). m/z 271.7, 273.7 (M + H)⁺.

2-[1-(4-Bromo-phenyl)-1-ethoxycarbonyl-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: *N,N*-diisopropylethylamine (4.1 mL, 23.6 mmol) was added dropwise to a mixture of pyrrolidine-1,3-dicarboxylic acid 1-*tert*-butyl ester (0.7 g, 3.2 mmol), HATU (1.2 g, 3.2 mmol) and 2-amino-2-(4-bromo-phenyl)-propionic acid ethyl ester (0.8 g, 2.9 mmol) in DMF (20 mL), and stirred at ambient condition for 3 hours. Most of the volatile component was removed *in vacuo*, and the resulting residue was dissolved in ethyl acetate (150 mL), washed with water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a colorless oil (0.8 g, 58%). m/z 490.9, 492.9 (M + Na)⁺.

2-[1-(4-Bromo-phenyl)-1-carbamoyl-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: To a stirred solution of 2-[1-(4-bromo-phenyl)-1-ethoxycarbonyl-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (280 mg, 0.6 mmol) in ethanol (8 mL) was bubbled through NH₃ gas for 5 minutes at -78°C. The solution was stirred at ambient for 3 days in a sealed tube. Most of the volatile component was removed *in vacuo*, and the resulting residue was dissolved in ethyl acetate (150 mL), washed with water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a colorless oil (169 mg, 64%). m/z 439.8, 441.8 (M + H)⁺.

2-[5-(4-Bromo-phenyl)-5-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: To a stirred solution of 2-[1-(4-bromo-phenyl)-1-carbamoyl-ethylcarbamoyl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (160 mg, 0.36 mmol) in ethanol (10 mL) was added 1 N NaOH (5 mL), and stirred at ambient condition for 3 hours. Most of the volatile component was removed *in vacuo*, and the resulting residue was dissolved in ethyl acetate (100 mL), washed with water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (120 mg, 79%). *m/z* 421.8, 423.8 (M + H)⁺.

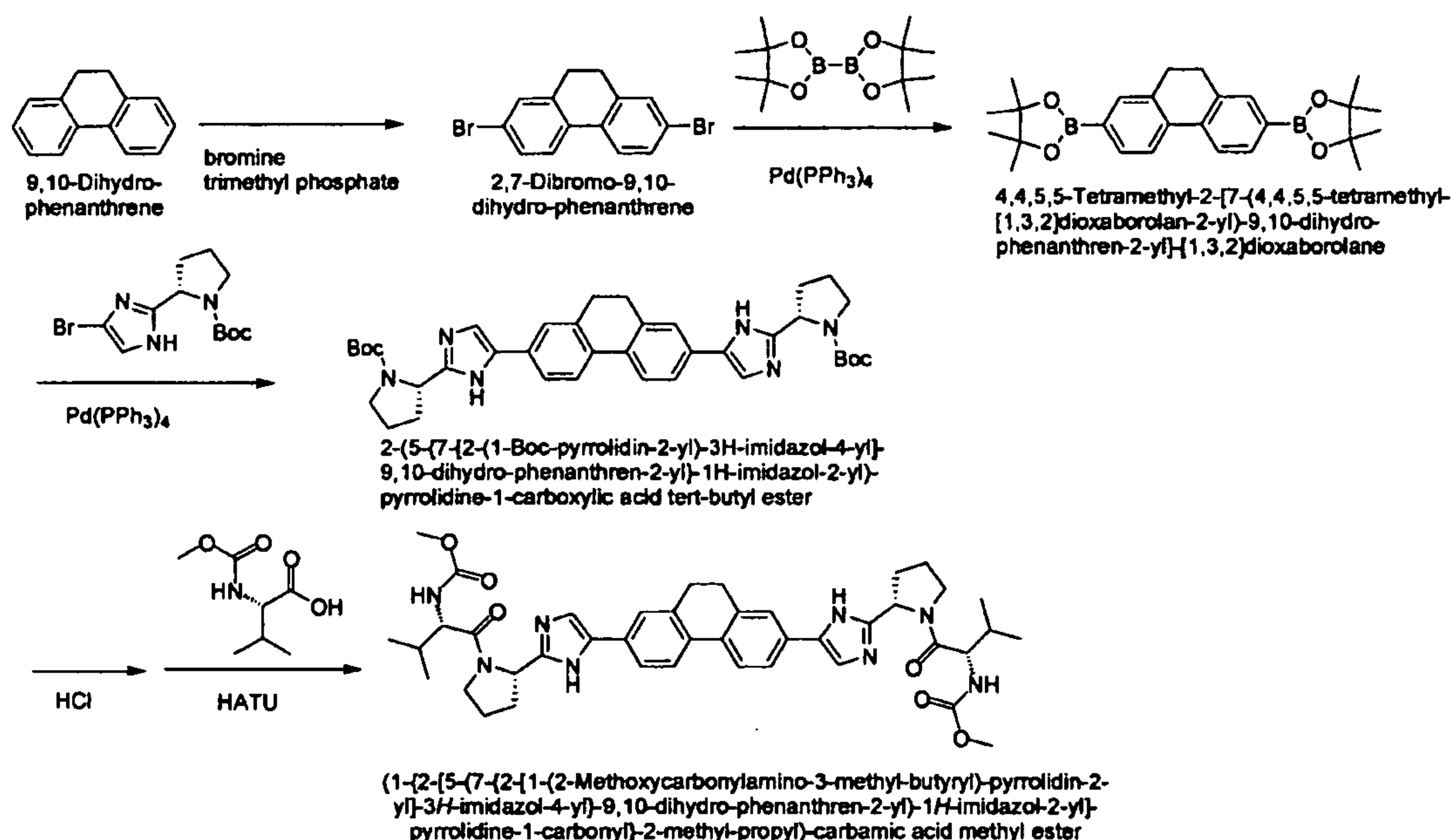
2-{5-Methyl-4-oxo-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-4,5-dihydro-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Pd(PPh₃)₄ (31 mg, 0.03 mmol) was added to a sealed tube containing a mixture of 2-[5-(4-bromo-phenyl)-5-methyl-4-oxo-4,5-dihydro-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (113 mg, 0.27 mmol), bis(pinacolato)diboron (144 mg, 0.57 mmol), potassium acetate (66 mg, 0.68 mmol) and 1,4-dioxane (3 mL). The reaction mixture was flushed with nitrogen, heated at 80°C for 16 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with NaHCO₃ solution, water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a colorless oil (100 mg, 79%). *m/z* 470.0 (M + H)⁺.

2-(5-{4'-[4-Boc-2-(1-methyl-pyrrolidin-2-yl)-5-oxo-4,5-dihydro-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Following the procedure used to prepare compound 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that 2-{5-methyl-4-oxo-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-4,5-dihydro-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-{5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester. *m/z* 655.1 (M + H)⁺.

(1-{2-[5-(4'-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-4-methyl-5-oxo-4,5-dihydro-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Following the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-(5-{4'-[4-Boc-2-(1-methyl-pyrrolidin-2-yl)-5-

oxo-4,5-dihydro-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.90-7.50 (m, 9H), 5.25 (t, 1H), 4.23 (d, 2H), 4.18-3.75 (m, 4H), 3.75-3.30 (m, 6H), 2.65-2.40 (m, 2H), 2.40-1.70 (m, 12H), 1.10-0.80 (m, 12H); m/z 769.2 (M + H)⁺.

Example AJ



2,7-Dibromo-9,10-dihydro-phenanthrene: To a stirred solution of 9,10-dihydrophenanthrene (10 g, 55.5 mmol) in trimethylphosphate (60 mL) was added a solution of bromine (6.13 mL, 119.3 mmol) in trimethylphosphate (40 mL) slowly. After addition, the mixture was stirred at ambient for 18 hours, the volatile component was removed *in vacuo*. The residue was recrystallized from chloroform to give a white crystal (9.45 g, 51%).

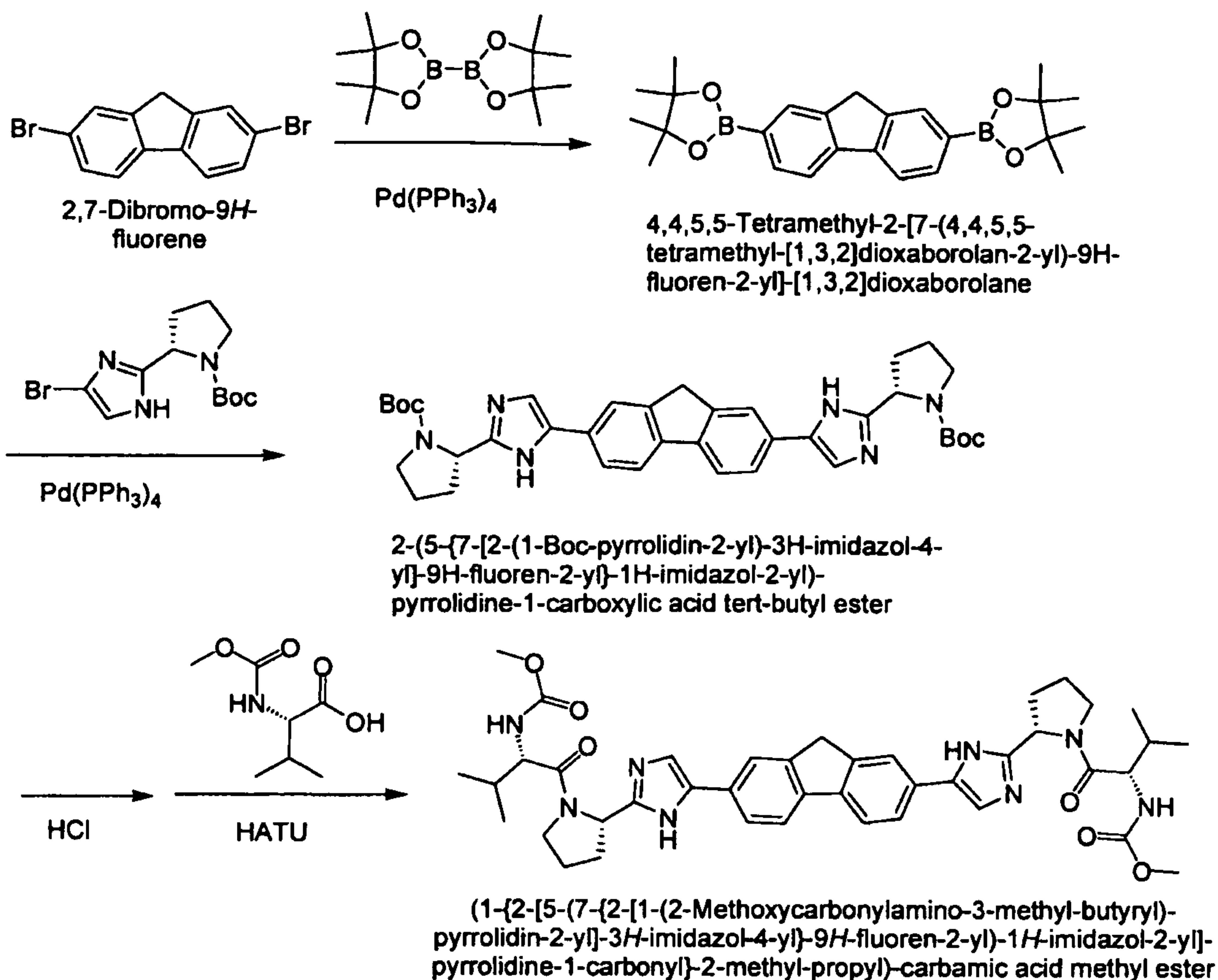
4,4,5,5-Tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydrophenanthren-2-yl]-[1,3,2]dioxaborolane: Pd(PPh₃)₄ (24 mg, 0.03 mmol) was added to a sealed tube containing a mixture of 2,7-dibromo-9,10-dihydro-phenanthrene (1.0 g, 3.0 mmol), bis(pinacolato)diboron (3.8 g, 14.9 mmol), potassium acetate (1.5 g, 14.9 mmol) and 1,4-dioxane (30 mL). The reaction mixture was flushed with nitrogen, heated at 80°C for 16 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (300 mL), washed with water and brine, dried over Na₂SO₄, filtered and concentrated *in*

vacuo. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (1.2 g, 93%). m/z 432.8 (M + H)⁺.

2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9,10-dihydro-phenanthren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Pd(PPh₃)₄ (31 mg, 0.03 mmol) was added to a mixture 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydro-phenanthren-2-yl]-[1,3,2]dioxaborolane (115 mg, 0.27 mmol), 2-(4-bromo-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester (173 mg, 0.55 mmol), NaHCO₃ (159 mg, 1.9 mmol) in 1,2-dimethoxyethane (5 mL) and water (1 mL). The reaction mixture was flushed with nitrogen, heated at 80°C for 6 hours, and then the volatile component was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with NaHCO₃ solution, water and brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The obtained residue was purified by flash chromatography to provide the desired product as a white solid (42 mg, 24%). m/z 651.0 (M + H)⁺.

(1-{2-[5-(7-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-9,10-dihydro-phenanthren-2-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Followed the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9,10-dihydro-phenanthren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 7.99 (d, 2H), 7.88 (s, 2H), 7.80-7.65 (m, 4H), 5.30-5.20 (m, 2H), 4.24 (d, 2H), 4.20-4.05 (m, 2H), 3.95-3.80 (m, 2H), 3.75-3.60 (m, 6H), 3.00 (s, H), 2.65-2.50 (m, 2H), 2.40-2.00 (m, 8H), 1.05-0.80 (m, 12H); m/z 765.3 (M + H)⁺.

Example AK

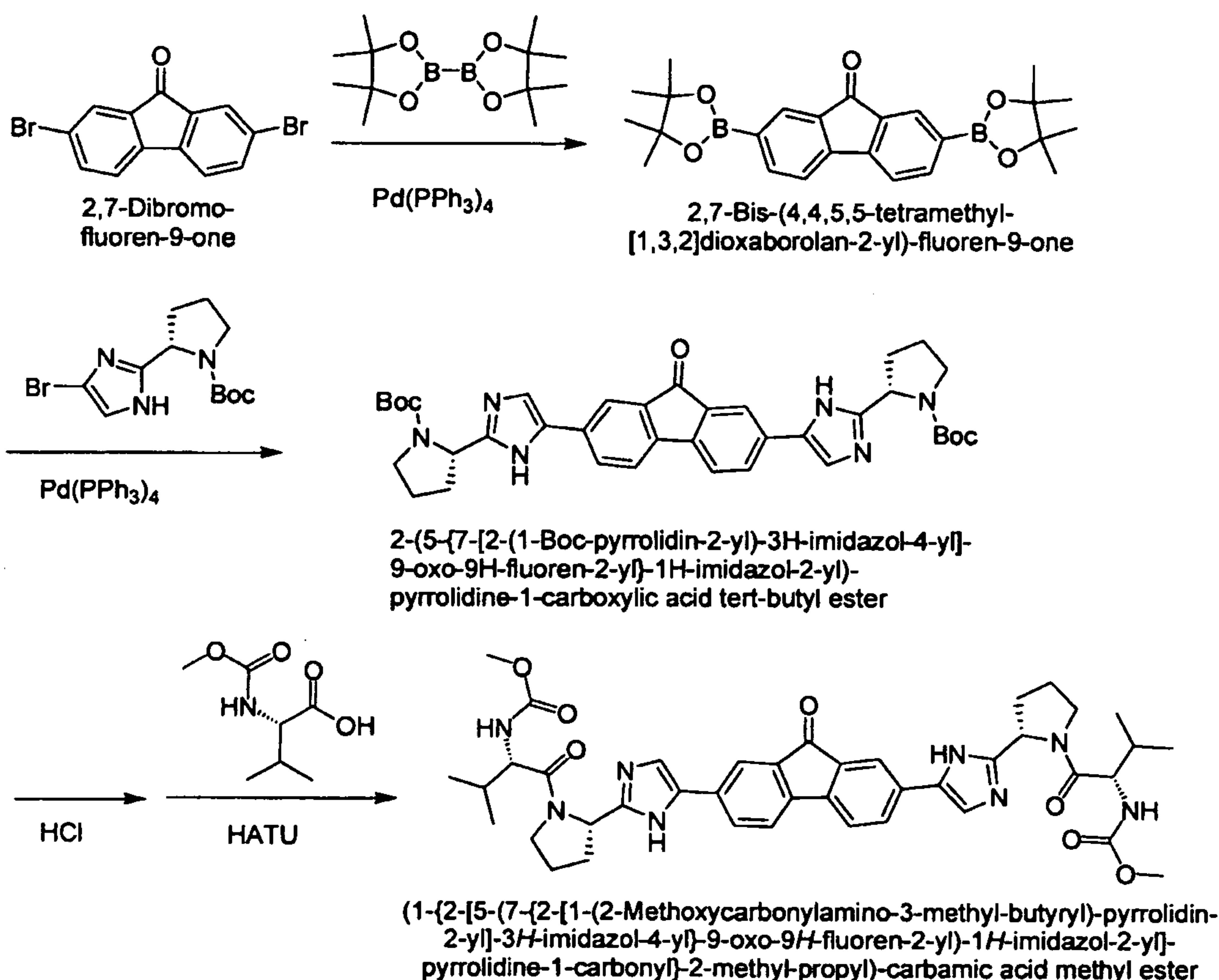


4,4,5,5-Tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9H-fluoren-2-yl]-[1,3,2]dioxaborolane: Followed the procedure used to prepare 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydro-phenanthren-2-yl]-[1,3,2]dioxaborolane, except that 2,7-dibromofluorene was used instead of 2,7-dibromo-9,10-dihydro-phenanthrene. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 8.01 (s, 2H), 7.84 (s, 4H), 3.90 (s, 2H), 1.38 (s, 24H).

2-(5-(7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9H-fluoren-2-yl)-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Followed the procedure used to prepare compound 2-(5-(7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9,10-dihydro-phenanthren-2-yl)-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9H-fluoren-2-yl]-[1,3,2]dioxaborolane was used instead of 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydro-phenanthren-2-yl]-[1,3,2]dioxaborolane. m/z 637.1 ($\text{M} + \text{H}$) $^+$.

(1-{2-[5-(7-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-9H-fluoren-2-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Followed the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9H-fluoren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 8.03 (d, 2H), 7.96 (s, 2H), 7.88 (s, 2H), 7.77 (d, 2H), 5.26 (t, 2H), 4.24 (d, 2H), 4.20-4.05 (m, 4H), 3.95-3.80 (m, 2H), 3.75-3.60 (m, 6H), 2.65-2.50 (m, 2H), 2.40-2.00 (m, 8H), 1.05-0.90 (m, 12H); m/z 751.3 (M + H)⁺.

Example AL

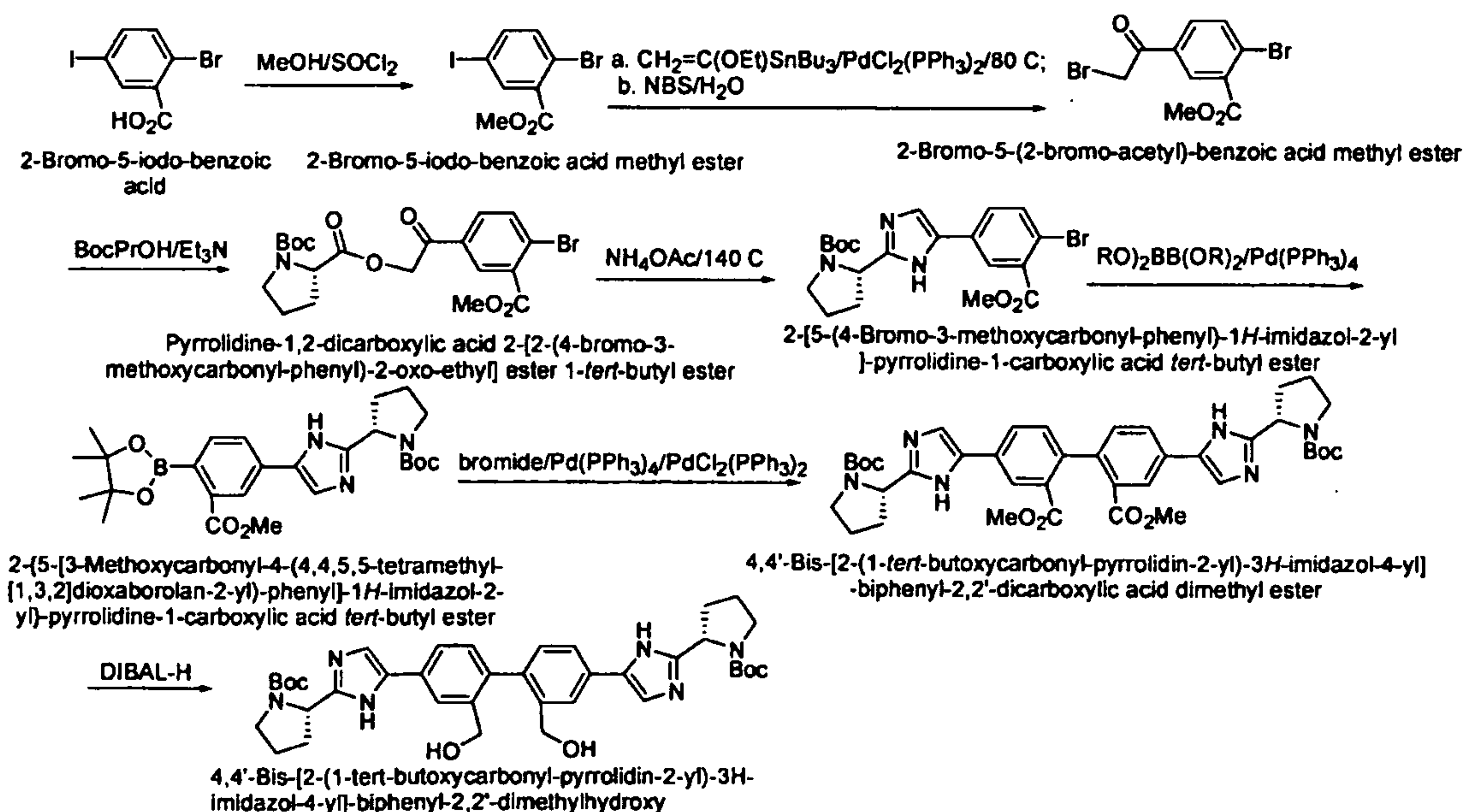


2,7-Bis-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-fluoren-9-one: Followed the procedure used to prepare 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydro-phenanthren-2-yl]-[1,3,2]dioxaborolane, except that 2,7-dibromo-9-fluorenone was used instead of 2,7-dibromo-9,10-dihydro-phenanthrene.

2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9-oxo-9H-fluoren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester: Followed the procedure used to prepare compound 2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9,10-dihydro-phenanthren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester, except that 2,7-bis-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-fluoren-9-one was used instead of 4,4,5,5-tetramethyl-2-[7-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-9,10-dihydro-phenanthren-2-yl]-[1,3,2]dioxaborolane. m/z 650.9 (M + H)⁺.

(1-{2-[5-(7-{2-[1-(2-Methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl]-9-oxo-9H-fluoren-2-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester: Followed the procedure used to prepare compound (1-{3-[5-(4'-{2-[1-(2-methoxycarbonylamino-3-methyl-butyryl)-pyrrolidin-2-yl]-3H-imidazol-4-yl}-biphenyl-4-yl)-1H-imidazol-2-yl]-pyrrolidine-1-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, except that 2-(5-{7-[2-(1-Boc-pyrrolidin-2-yl)-3H-imidazol-4-yl]-9-oxo-9H-fluoren-2-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester was used instead of 2-(5-{4'-[2-(1-Boc-pyrrolidin-3-yl)-3H-imidazol-4-yl]-biphenyl-4-yl}-1H-imidazol-2-yl)-pyrrolidine-1-carboxylic acid *tert*-butyl ester. ¹H-NMR (300 MHz, CD₃OD) δ 8.05-7.85 (m, 8H), 5.22 (t, 2H), 4.23 (d, 2H), 4.20-4.05 (m, 2H), 3.95-3.80 (m, 2H), 3.67 (s, 6H), 2.65-2.50 (m, 2H), 2.40-2.00 (m, 8H), 1.05-0.90 (m, 12H); m/z 765.3 (M + H)⁺.

Example AM



2-Bromo-5-iodo-benzoic acid methyl ester: To the solution of 2-bromo-5-iodo-benzoic acid (10 g, 31 mmol) in methanol (100 ml) was added thionyl chloride (5 ml, 68 mmol). The mixture

was heated at 55°C for 12 hours. The solvent and reagent were removed under reduced pressure and the mixture was diluted with EtOAc. The organic solution was washed with saturated sodium bicarbonate, water, and brine, and was dried with sodium sulfate. Concentration gave 2-bromo-5-iodo-benzoic acid methyl ester (10.5 g).

2-Bromo-5-(2-bromo-acetyl)-benzoic acid methyl ester: To the solution of 2-bromo-5-iodo-benzoic acid methyl ester (4.33 g, 12.7 mmol) and tributyl(ethoxyvinyl)stannane (4.79 g, 13.3 mmol) in dioxane (56 ml) was added PdCl₂(PPh₃)₂ (322 mg). The mixture was heated at 80°C for 17 hours and was cooled to 0°C. Water (19 ml) was added, followed by slow addition of NBS (2.33 g, 12.9 mmol) over 10 minutes period. The mixture was stirred at 0°C for additional 40 minutes, and the solvent was removed under reduced pressure. The mixture was diluted with EtOAc, and was washed with water and brine and dried with sodium sulfate. Concentration and purification by flash column chromatography (hexane/EtOAc = 2/1) gave 2-bromo-5-(2-bromo-acetyl)-benzoic acid methyl ester (3.48 g).

Pyrrolidine-1,2-dicarboxylic acid 2-[2-(4-bromo-3-methoxycarbonyl-phenyl)-2-oxo-ethyl] ester 1-*tert*-butyl ester: To the solution of (s)Boc-PrOH (2.5 g, 11.6 mmol) and triethylamine (1.55 ml, 11.1 mmol) in acetonitrile (34 ml) was added a solution of 2-bromo-5-(2-bromo-acetyl)-benzoic acid methyl ester (3.48 g, 10.4 mmol) in acetonitrile (17 ml). The mixture was stirred for 10 hours, and the solvent was evaporated. The mixture was diluted with EtOAc, and washed with water and brine, and was dried with sodium sulfate. Purification by flash column chromatography (hexane/EtOAc = 1/1.5) gave pyrrolidine-1,2-dicarboxylic acid 2-[2-(4-bromo-3-methoxycarbonyl-phenyl)-2-oxo-ethyl] ester 1-*tert*-butyl ester (3.9 g): *m/z*: 491.9 (M + Na)⁺.

2-[5-(4-Bromo-3-methoxycarbonyl-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester: The mixture of pyrrolidine-1,2-dicarboxylic acid 2-[2-(4-bromo-3-methoxycarbonyl-phenyl)-2-oxo-ethyl] ester 1-*tert*-butyl ester (460 mg, 1 mmol) and ammonium acetate (860 mg, 11 mmol) in xylenes (5 ml) was heated at 140°C for 80 minutes under microwave. The mixture was quenched with water, and extracted with EtOAc. The organic phase was washed with water and brine, and was dried with sodium sulfate. Concentration and purification by flash column chromatography (EtOAc) gave 2-[5-(4-bromo-3-methoxycarbonyl-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (320 mg). *m/z*: 449.8 (M + H)⁺, 448.1 (M - H)⁻.

2-{5-[3-Methoxycarbonyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester: To the solution of 2-[5-(4-bromo-3-methoxycarbonyl-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (200 mg, 0.44 mmol) and bis(pinacolato)diboron (225 mg, 0.89 mmol) in 1,4-dioxane (3.4 ml) and DMF (2 ml) was added potassium acetate (110 g, 1.1 mmol), followed by Pd(PPh₃)₄ (20 mg) and PdCl₂(dppf)CH₂Cl₂ (20 mg). The mixture was heated at 80°C for 12 hours. The mixture was diluted with EtOAc, and was washed with water and brine, and was dried with sodium sulfate. Concentration and purification by flash column chromatography (EtOAc) gave 2-{5-[3-Methoxycarbonyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester (168 mg). *m/z*: 498.0 (M + H)⁺.

4,4'-Bis-[2-(1-*tert*-butoxycarbonyl-pyrrolidin-2-yl)-3H-imidazol-4-yl]-biphenyl-2,2'-dicarboxylic acid dimethyl ester: To the solution of 2-[5-(4-bromo-3-methoxycarbonyl-phenyl)-1H-imidazol-2-yl]-pyrrolidine-1-carboxylic acid *tert*-butyl ester (158 mg, 0.35 mmol) and 2-{5-[3-Methoxycarbonyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-1H-imidazol-2-yl}-pyrrolidine-1-carboxylic acid *tert*-butyl ester (166 mg, 0.33 mmol) in 1,2-dimethoxyether (3 ml) and water (1 ml) was added sodium bicarbonate (91 mg, 1.1 mmol), followed by Pd(PPh₃)₄ (15 mg) and PdCl₂(dppf)CH₂Cl₂ (15 mg). The mixture was heated at 80°C for 7 hours. The mixture was diluted with EtOAc, and was washed with water and brine, and was dried with sodium sulfate. Concentration and purification by flash column chromatography (EtOAc) gave 4,4'-Bis-[2-(1-*tert*-butoxycarbonyl-pyrrolidin-2-yl)-3H-imidazol-4-yl]-biphenyl-2,2'-dicarboxylic acid dimethyl ester (85 mg). *m/z*: 741.0 (M + H)⁺, 370.9 (M + 2H)^{+/2}.

4,4'-Bis-[2-(1-*tert*-butoxycarbonyl-pyrrolidin-2-yl)-3H-imidazol-4-yl]-biphenyl-2,2'-dimethylhydroxy: To the solution of 4,4'-Bis-[2-(1-*tert*-butoxycarbonyl-pyrrolidin-2-yl)-3H-imidazol-4-yl]-biphenyl-2,2'-dicarboxylic acid dimethyl ester (85 mg, 0.11 mmol) in THF (2 ml) at -78°C was added DIBAL-H THF solution (1.4 ml, 1.4 mmol). The mixture was warmed to 25°C and stirred for 5 hours. The mixture was cooled to 0°C and quenched with 2.0 N NaOH solution until PH=11. The mixture was extracted with EtOAc. The organic phase was washed with water and brine, and was dried with sodium sulfate. Concentration and purification by flash column chromatography (DCM/MeOH) gave 4,4'-bis-[2-(1-*tert*-butoxycarbonyl-pyrrolidin-2-yl)-3H-imidazol-4-yl]-biphenyl-2,2'-dimethylhydroxy (54 mg). *m/z*: 685.1 (M + H)⁺, 343.0 (M + 2H)^{+/2}.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3
CONTENANT LES PAGES 1 À 435

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 3
CONTAINING PAGES 1 TO 435

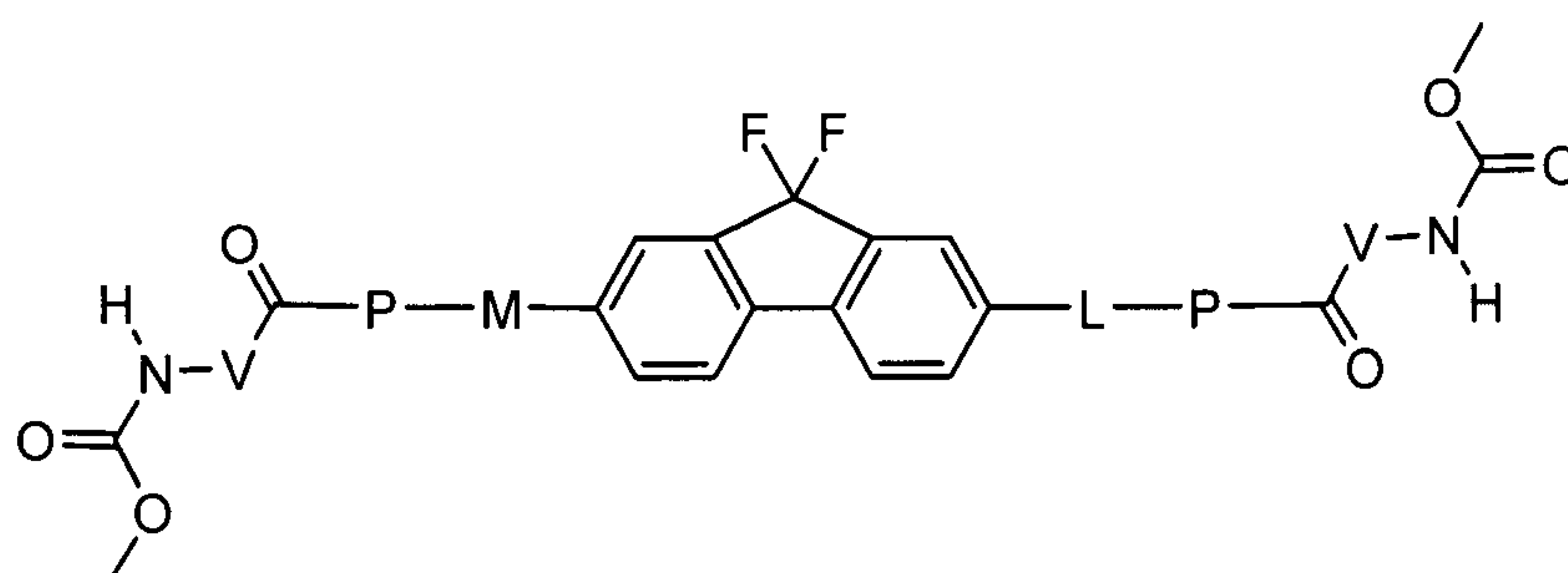
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CLAIMS

1. A compound of formula:



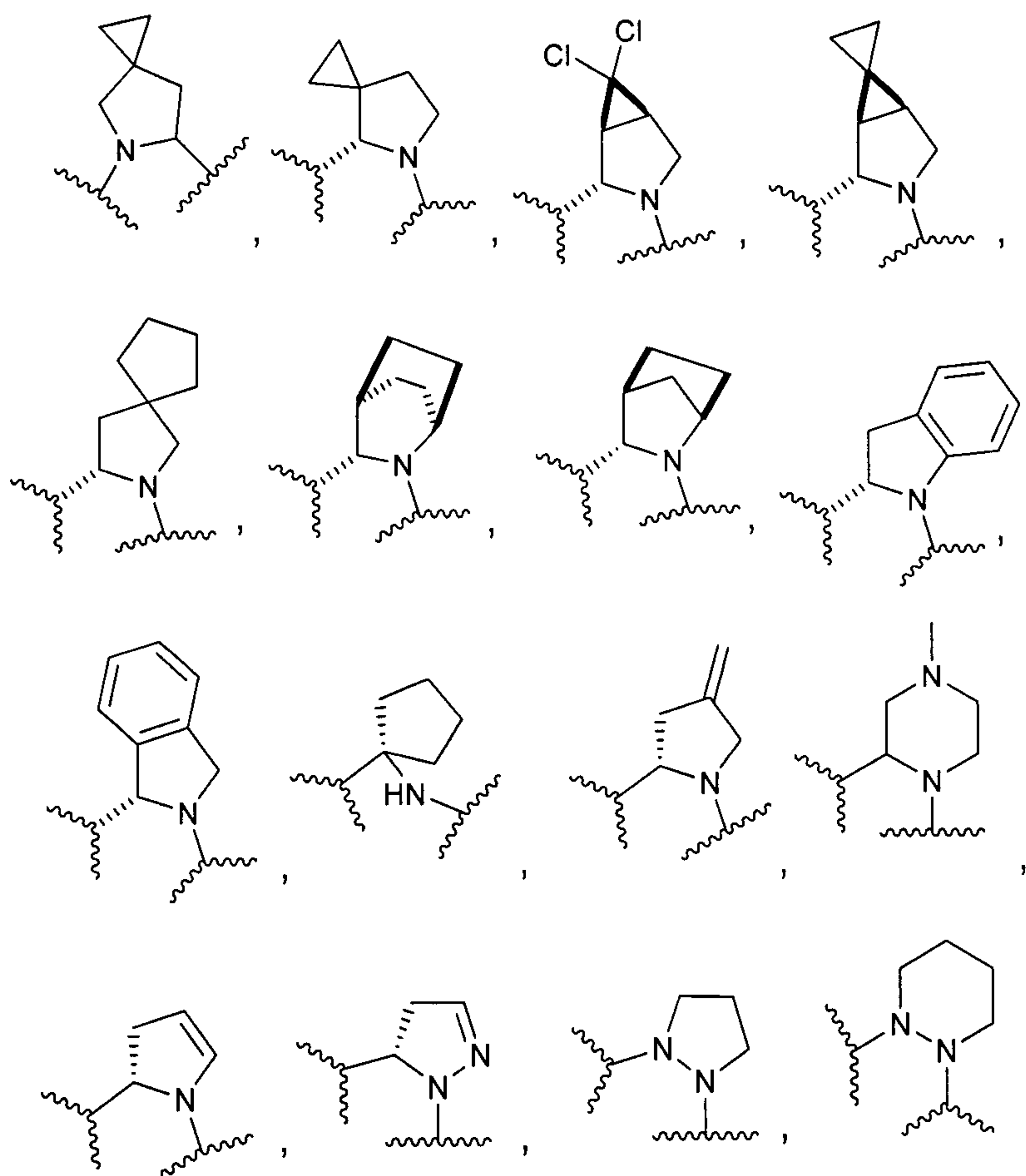
wherein:

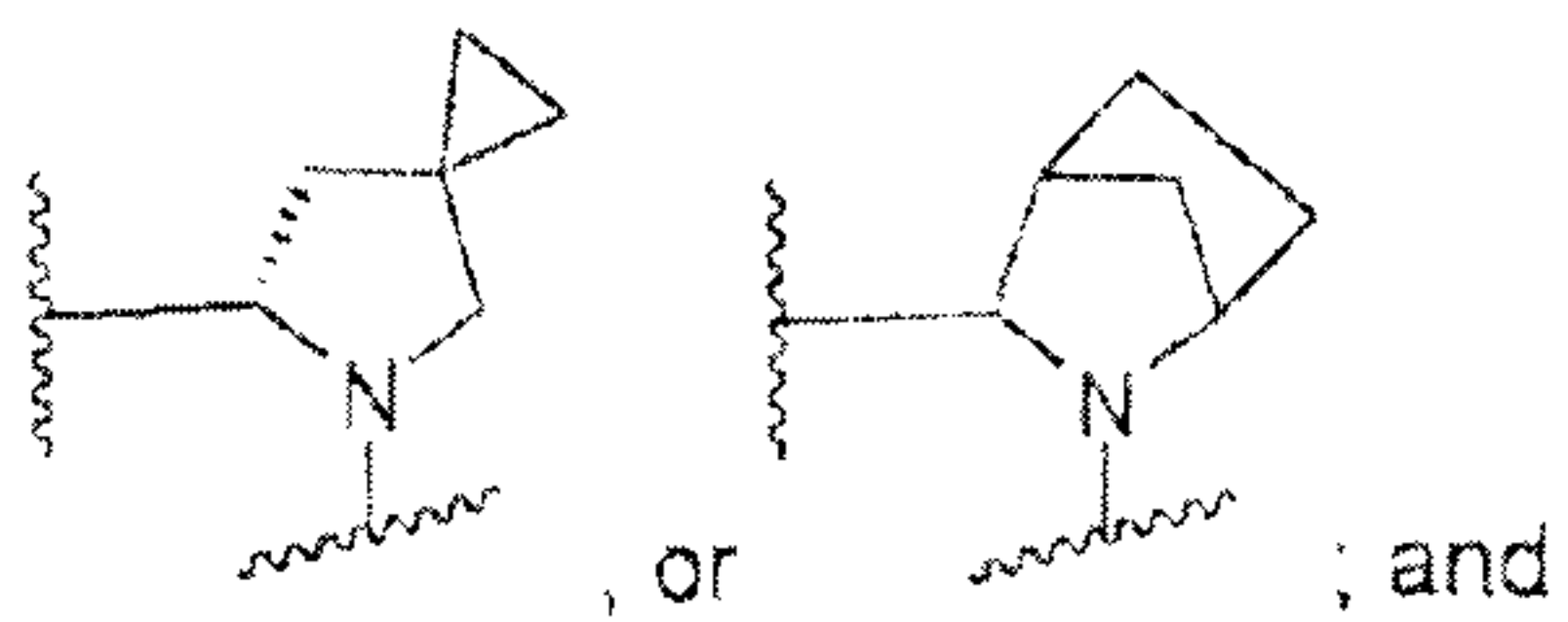
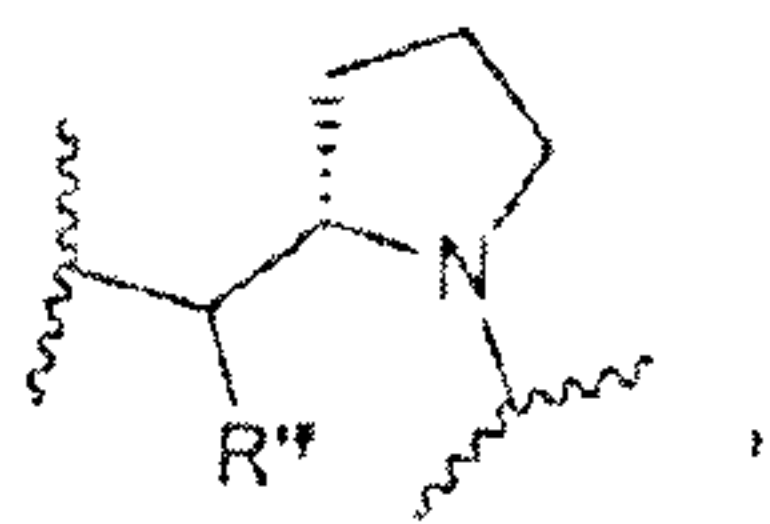
each V is independently alkyl;

L is benzimidazolyl;

M is a 5-membered heteroaryl ring;

each P is independently:

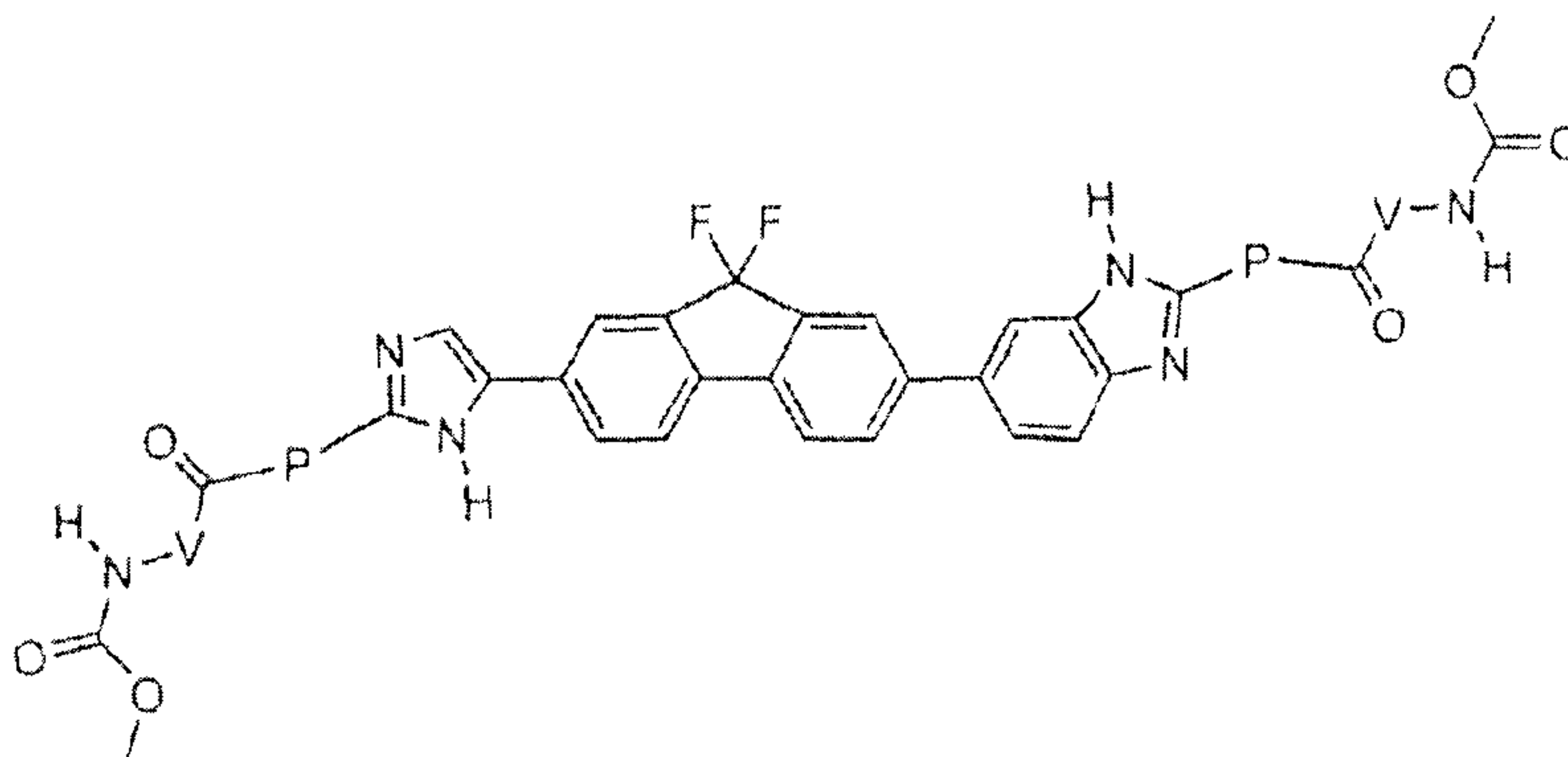




R'' is hydrogen or methyl;

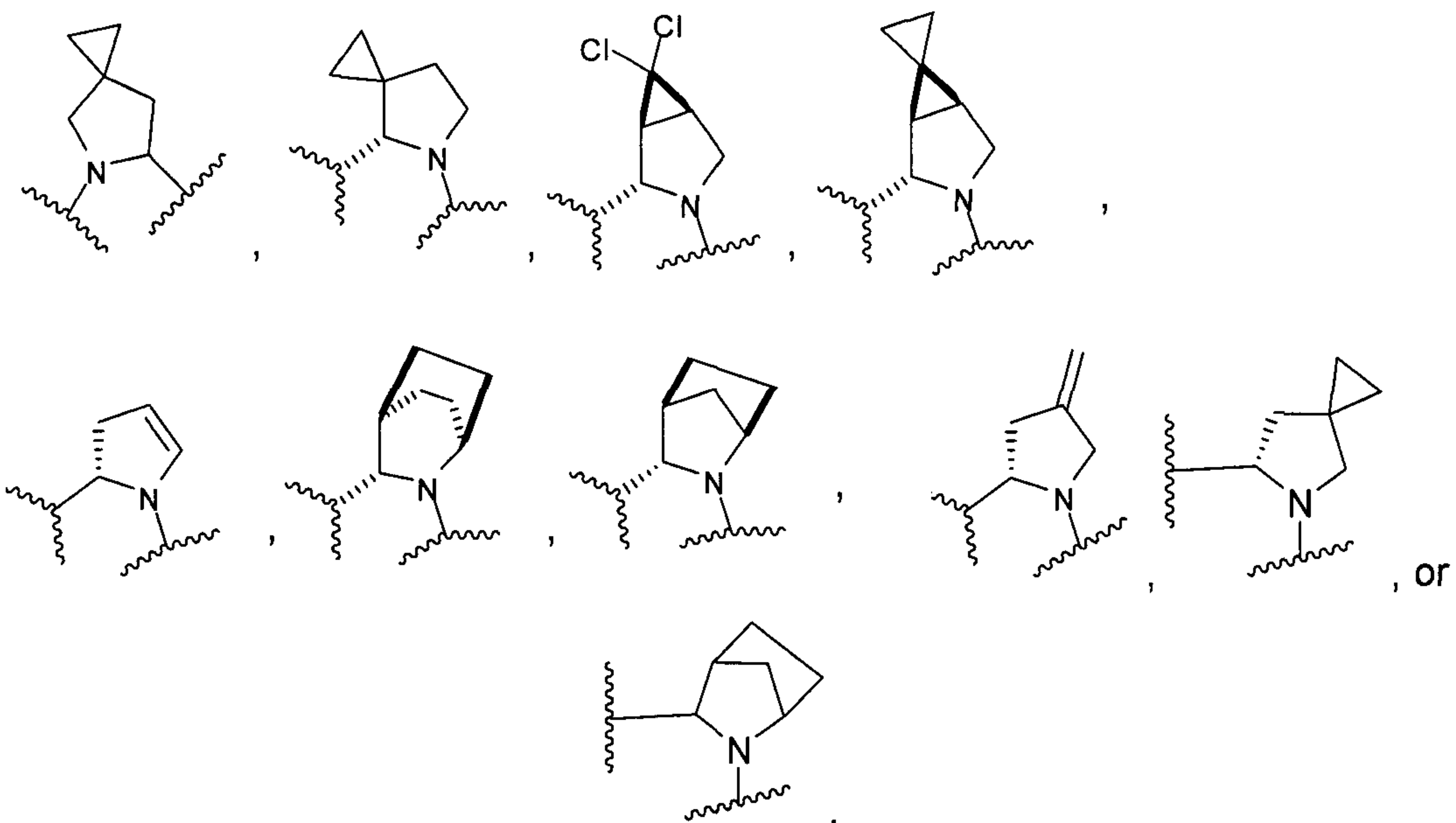
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 that is:

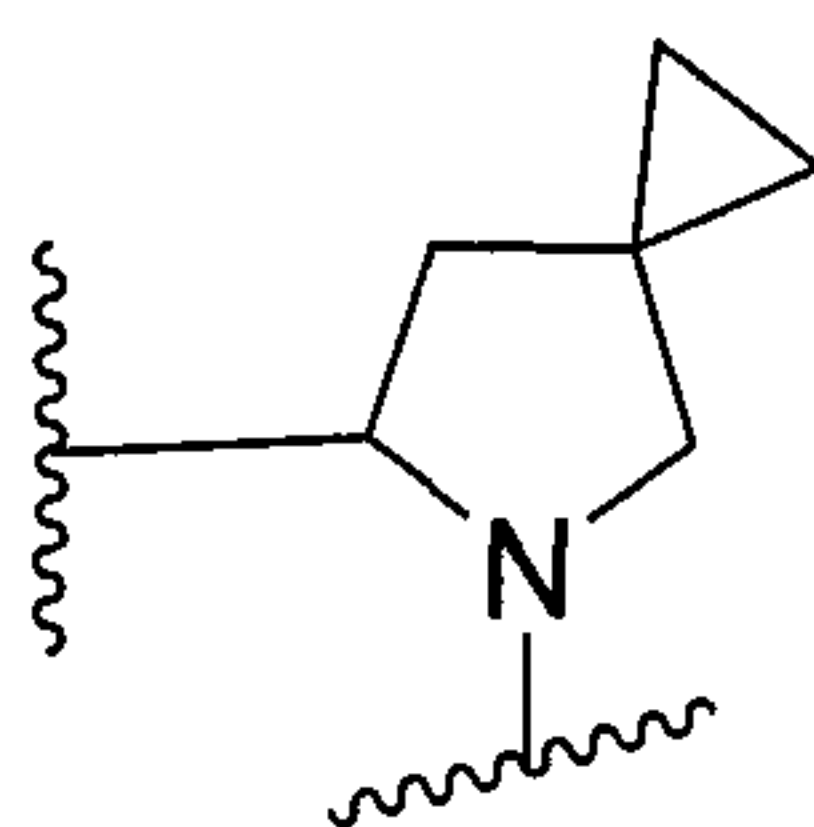


or a pharmaceutically acceptable salt thereof.

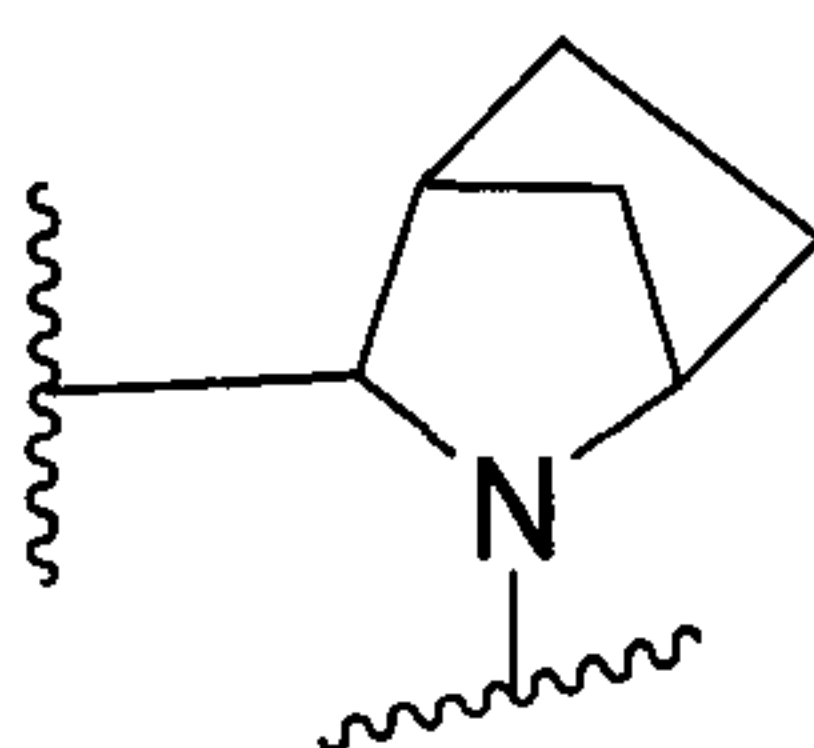
3. The compound of claim 1 or 2, wherein each P is independently:



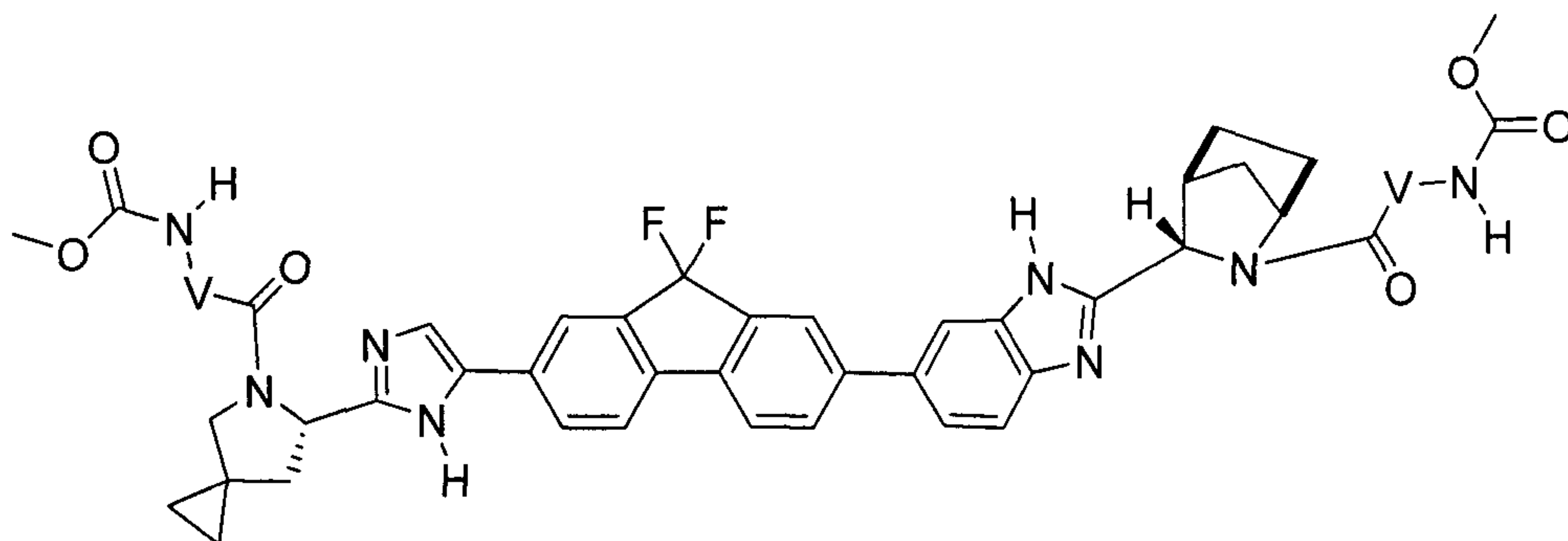
4. The compound of any one of claims 1-3, wherein at least one P is:



5. The compound of any one of claims 1-3, wherein one P is:

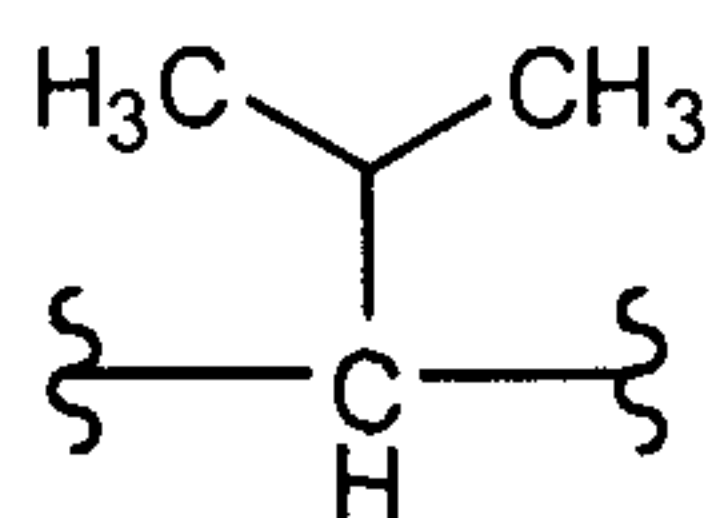


6. The compound of claim 1 that is:

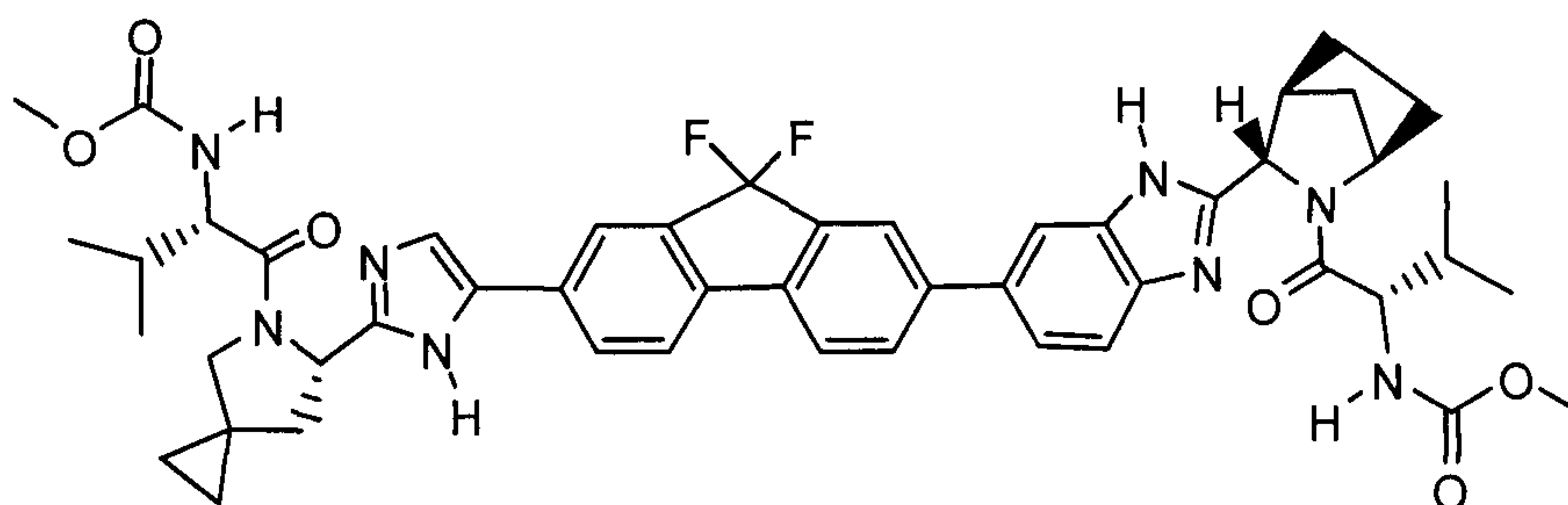


or a pharmaceutically acceptable salt thereof.

7. The compound of any one of claims 1-6, wherein each V is:



8. The compound of claim 1 which is:



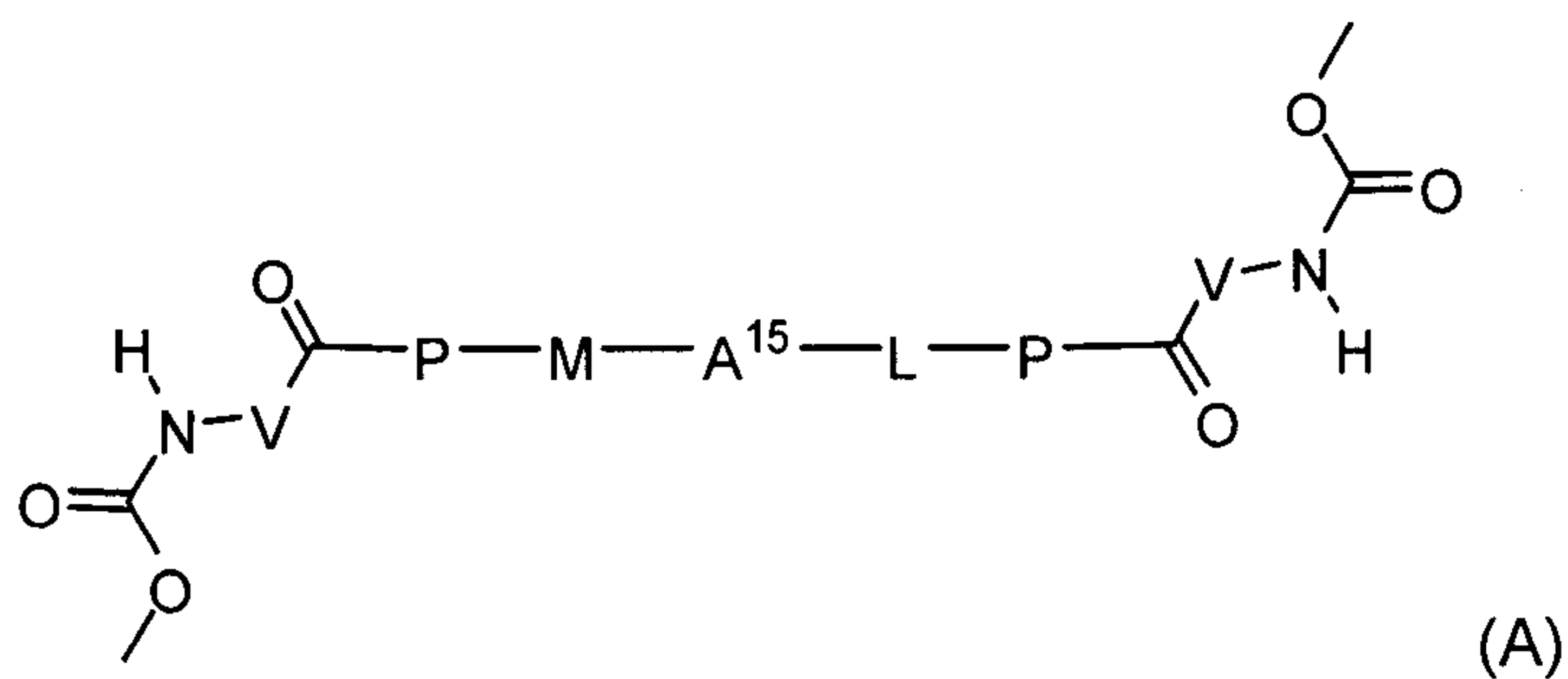
or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition comprising a compound as defined in any one of claims 1-8, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

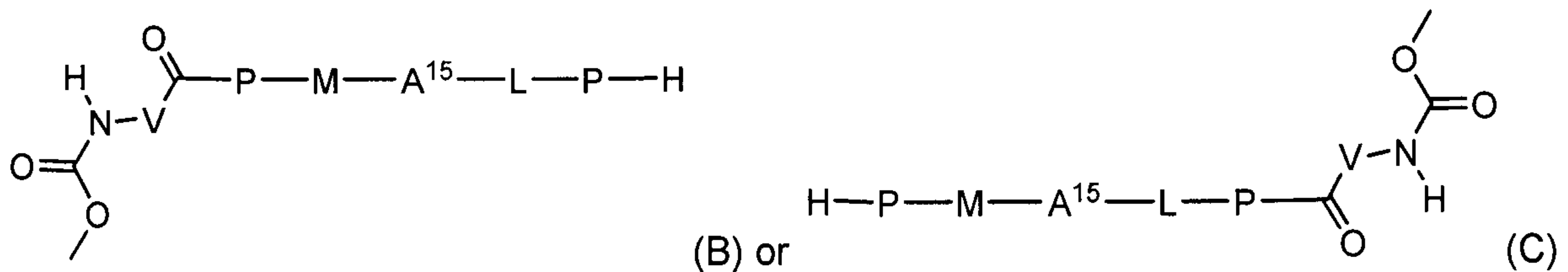
10. The pharmaceutical composition of claim 9, further comprising at least one additional therapeutic agent.

11. The pharmaceutical composition of claim 10, wherein said additional therapeutic agent is selected from the group consisting of ribavirin analog, NS3 protease inhibitor, NS5b polymerase inhibitor, alpha-glucosidase 1 inhibitor, hepatoprotectant, non-nucleoside inhibitor of HCV, and other drug for treating HCV.

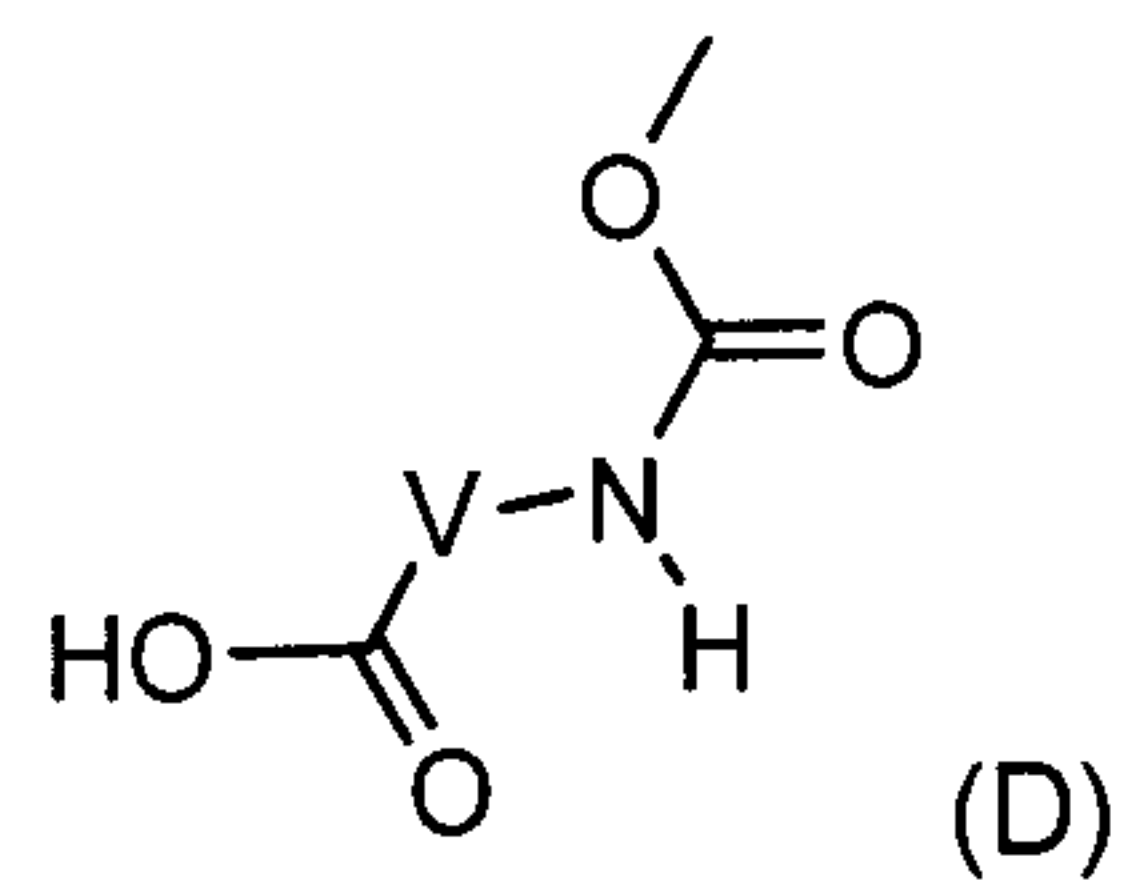
12. The pharmaceutical composition according to claim 10, further comprising a nucleoside analogue.
13. The pharmaceutical composition according to claim 12, wherein said nucleoside analogue is ribavirin, viramidine, levovirin, an L-nucleoside, or isatoribine.
14. A compound according to any one of claims 1-8 or a pharmaceutically acceptable salt thereof, for use in the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.
15. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 8 for the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.
16. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 8 in the preparation of a medicament for the prophylactic or therapeutic treatment of hepatitis C or a hepatitis C associated disorder.
17. A method for preparing a compound of formula (A):



comprising contacting a compound of formula (B) or (C):



with a compound of formula (D):



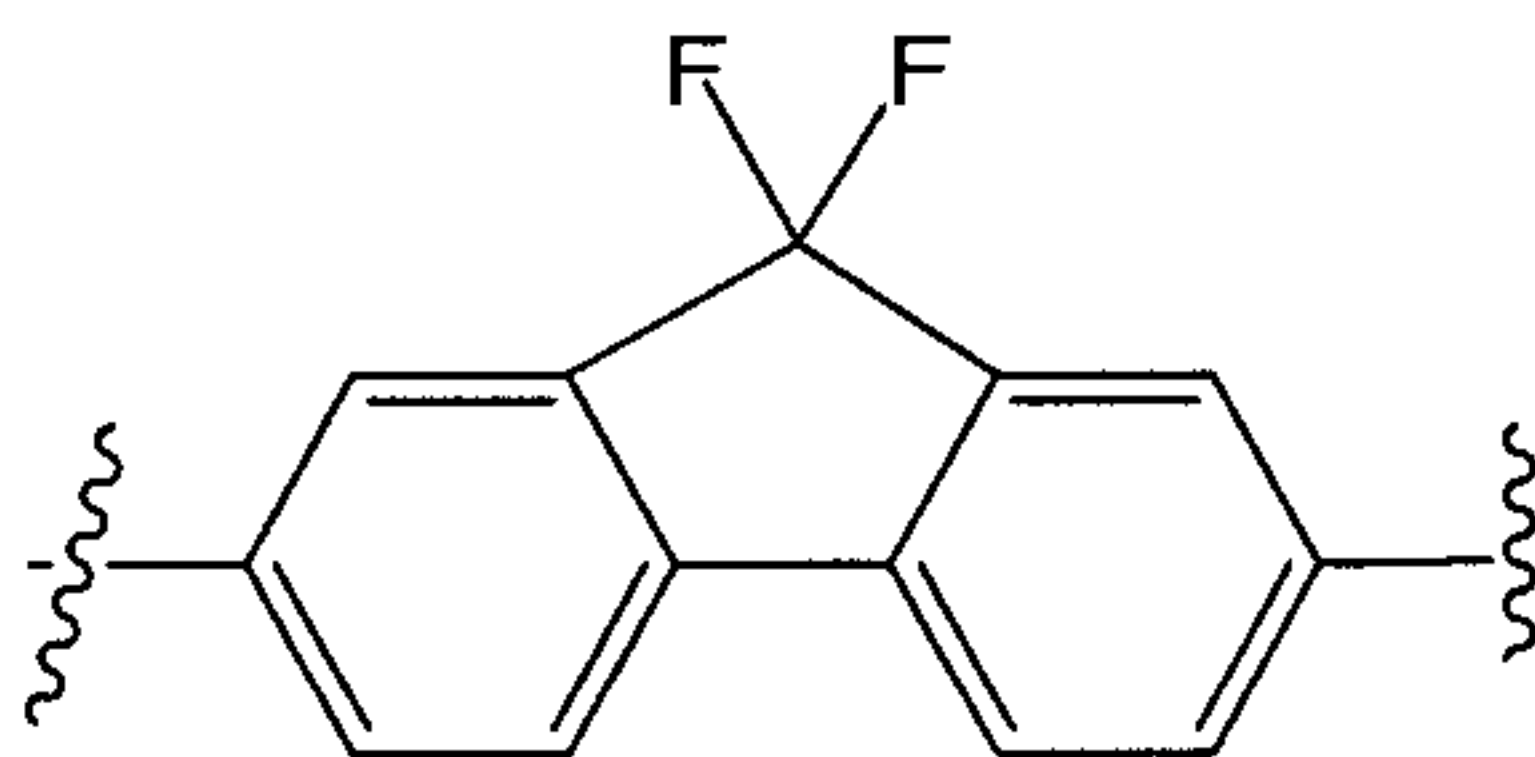
to yield a compound of formula (A), wherein:

V is alkyl;

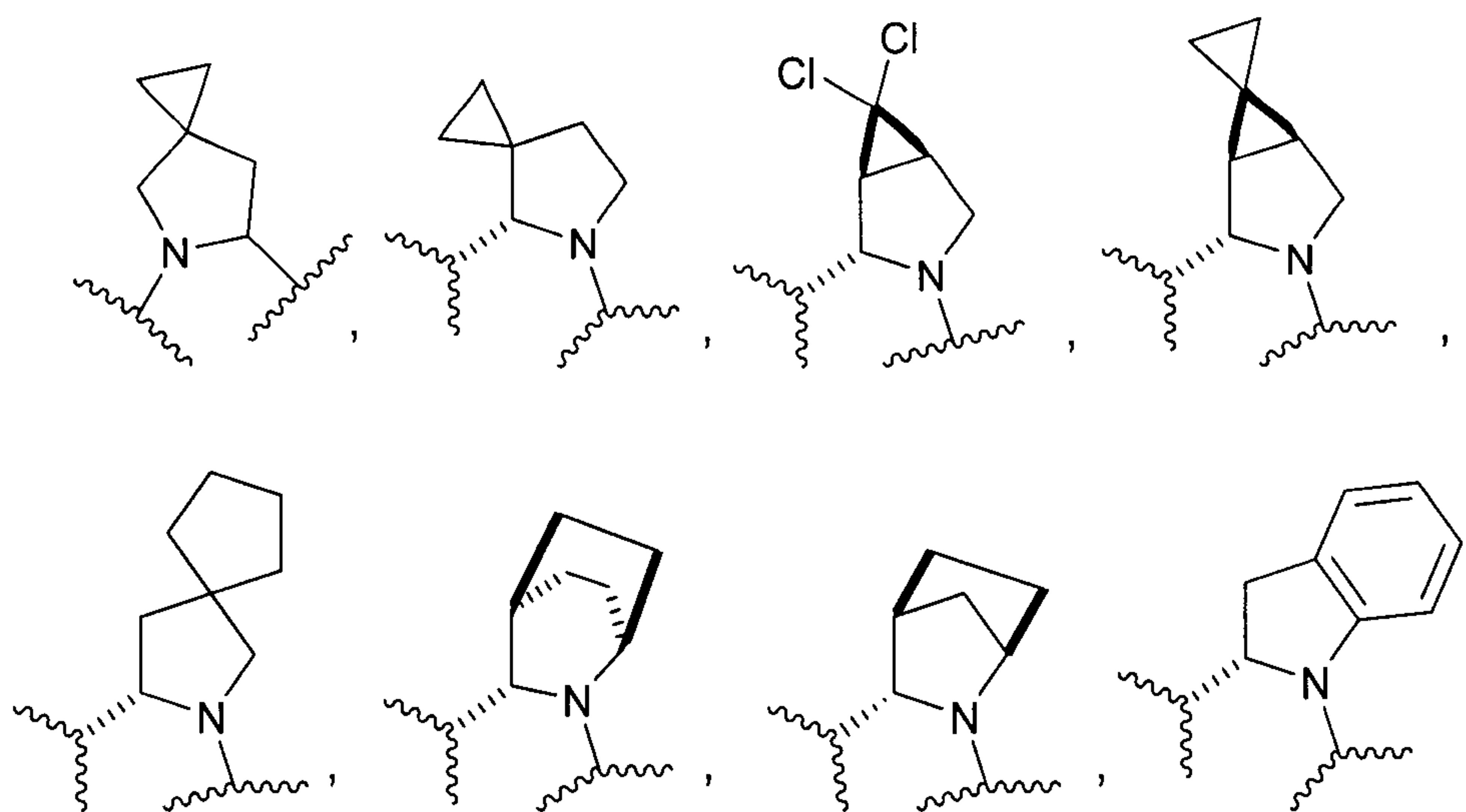
L is benzimidazolyl;

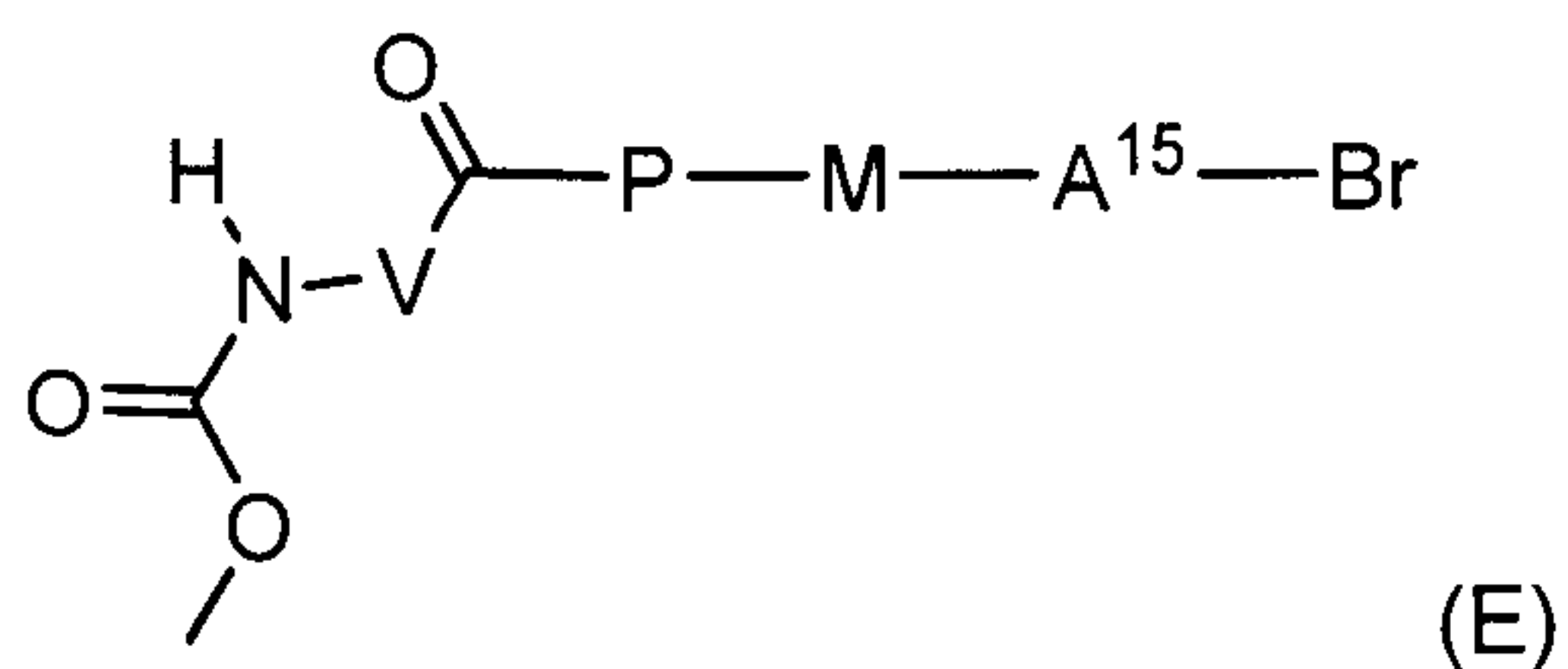
M is a 5-membered heteroaryl ring;

A¹⁵ is:

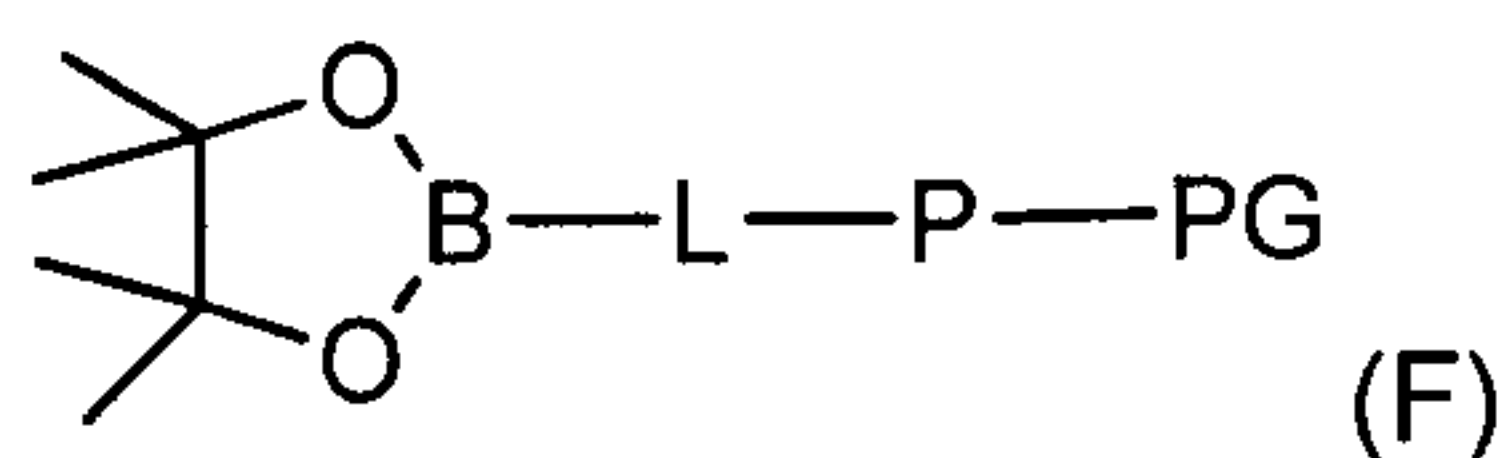


each P is independently:

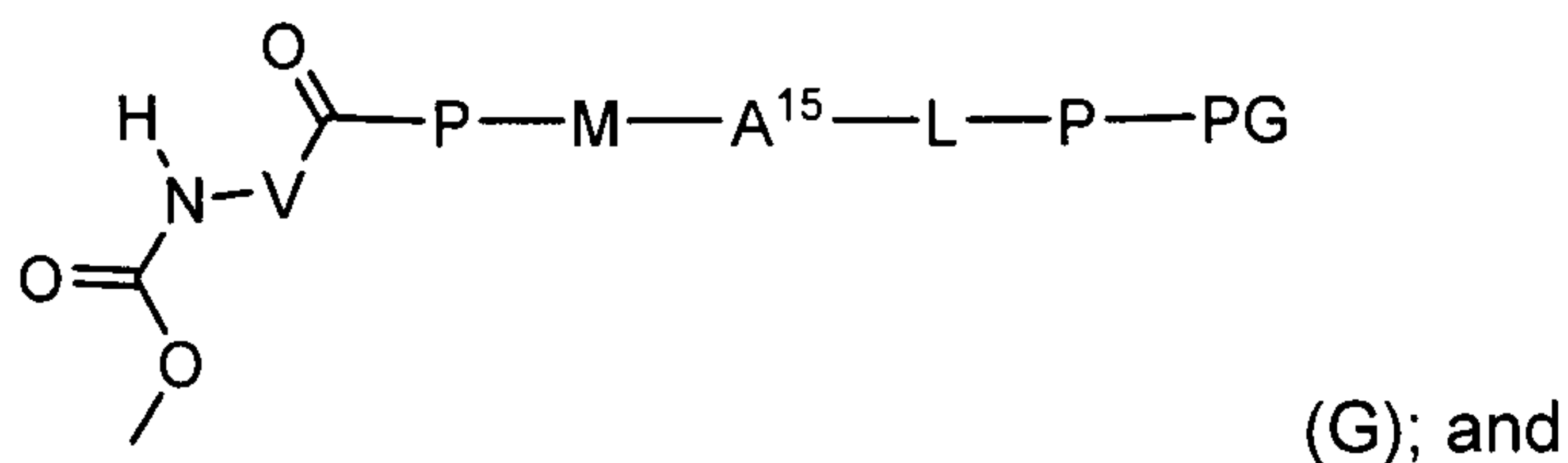




with a compound of formula (F):

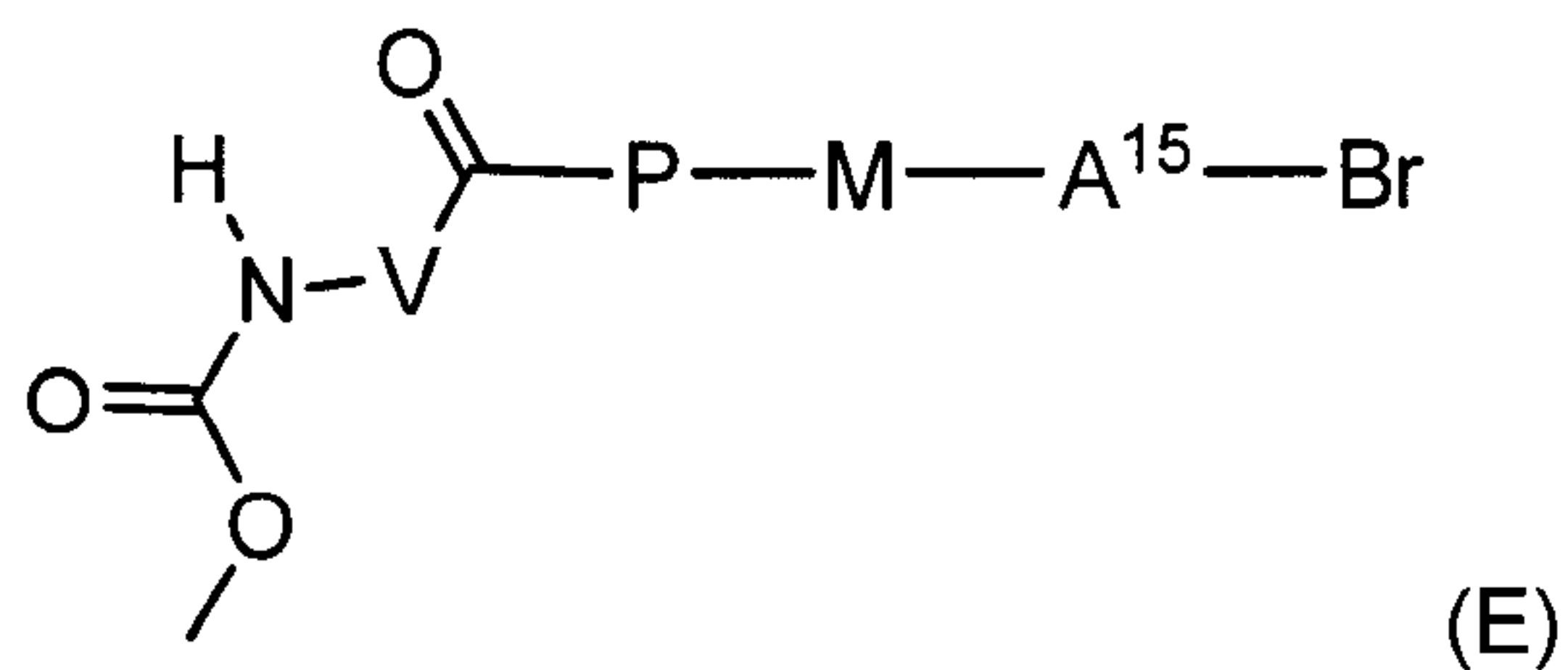


wherein PG is an amine protecting group, to yield a compound of formula (G):

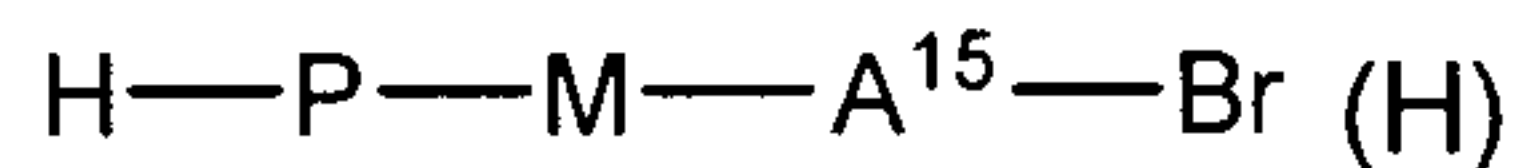


(b) deprotecting a compound of formula (G) under conditions sufficient to yield a compound of formula (B).

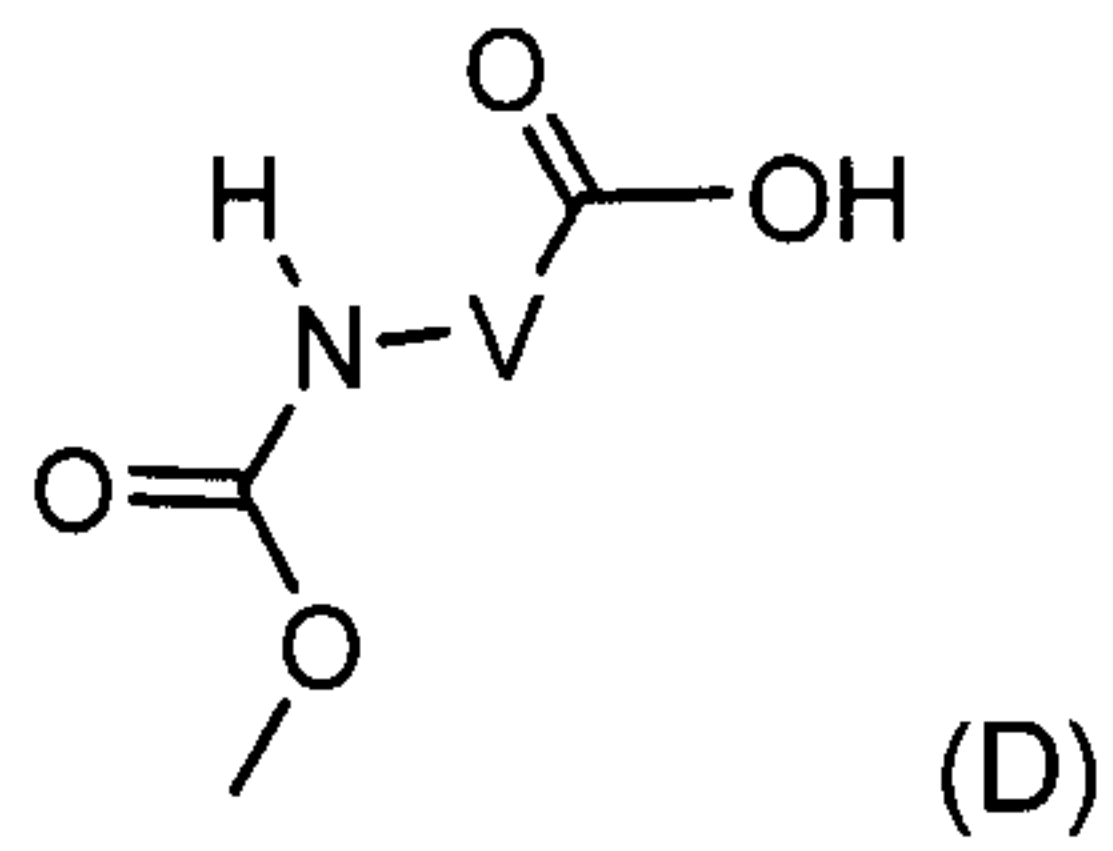
19. The method of claim 18, wherein the compound of formula (E):



is prepared by contacting a compound of formula (H):

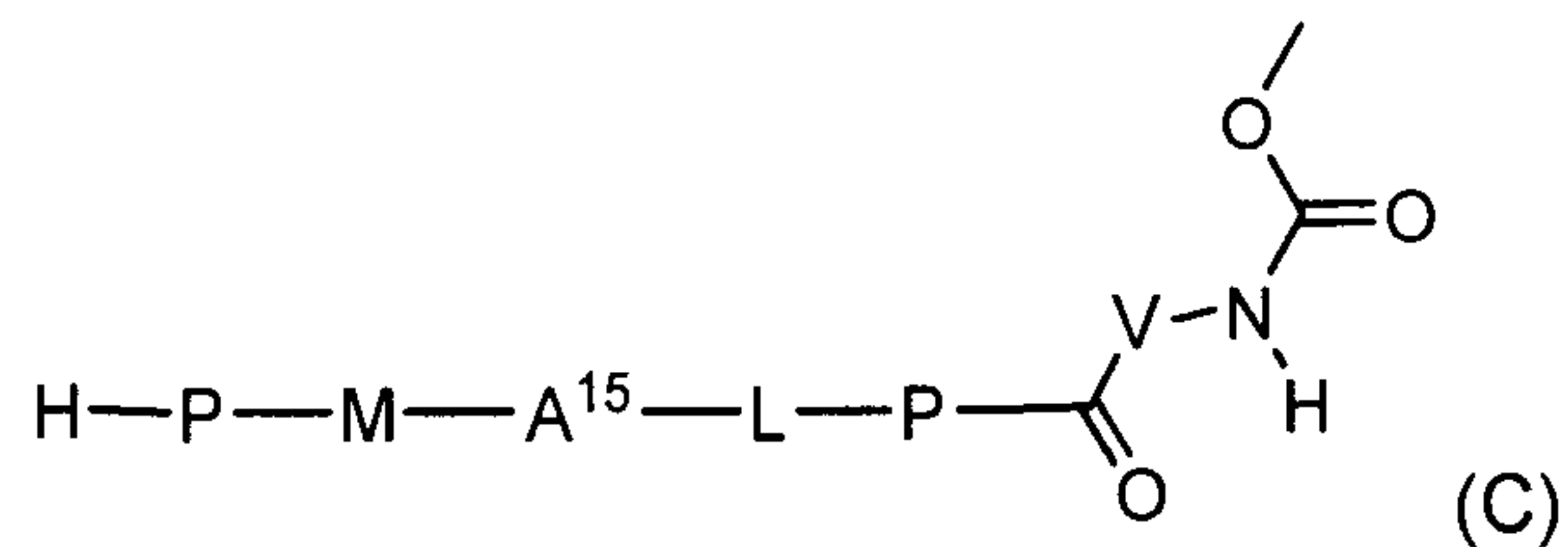


with a compound of formula (D):



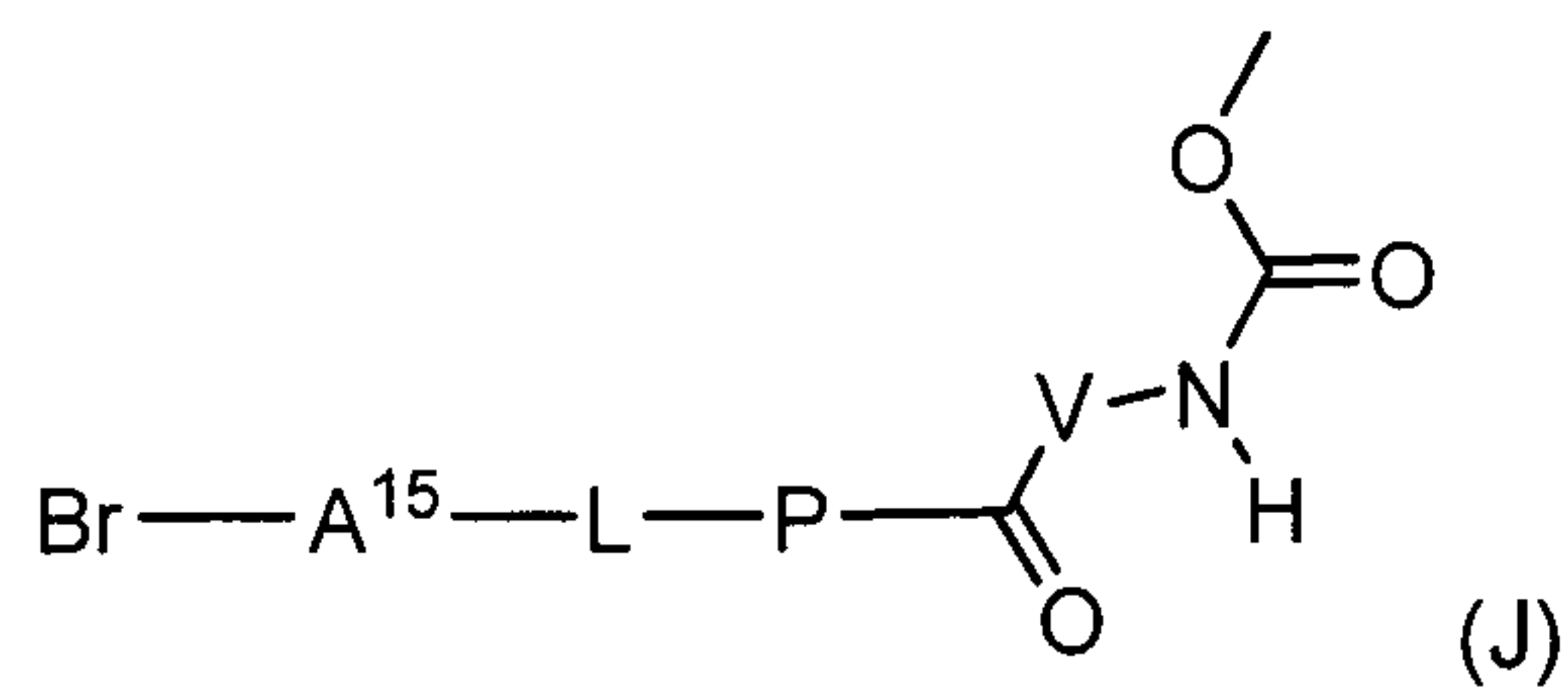
to yield a compound of formula (E).

20. The method of claim 17, wherein the compound of formula (C):

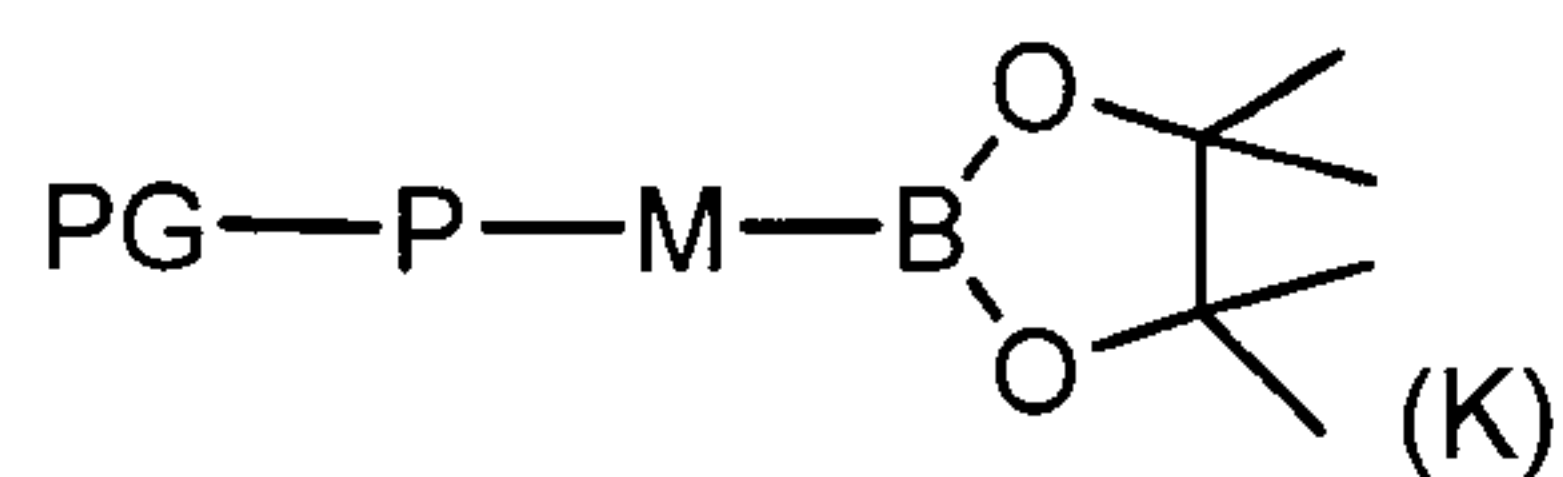


is prepared by:

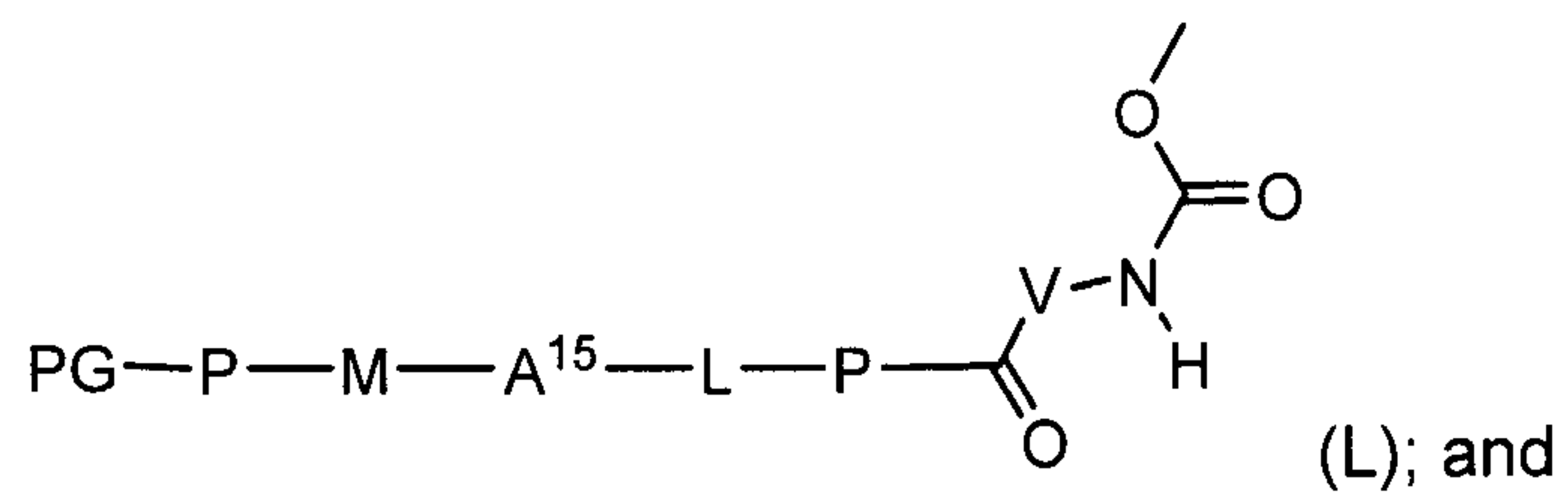
(a) contacting a compound of formula (J):



with a compound of formula (K):

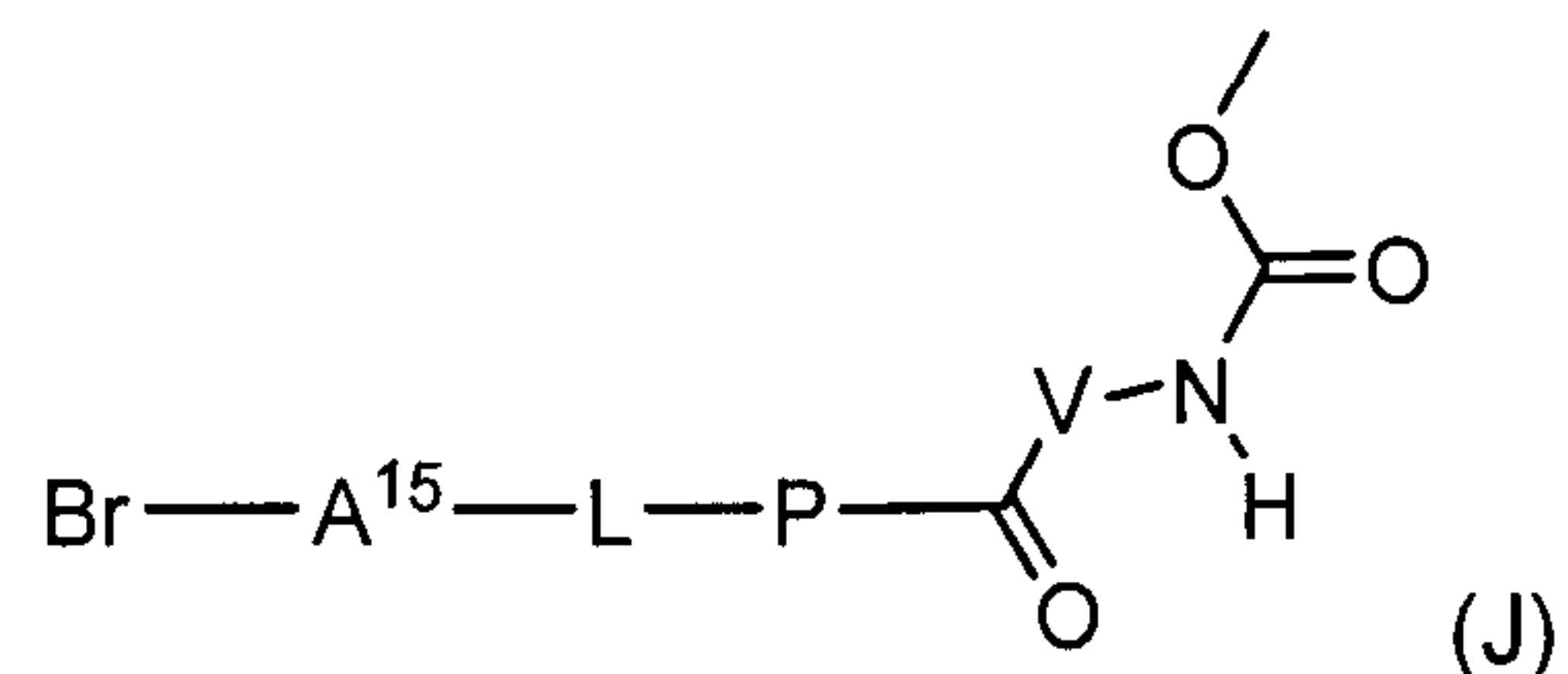


wherein PG is an amine protecting group, to yield a compound of formula (L):

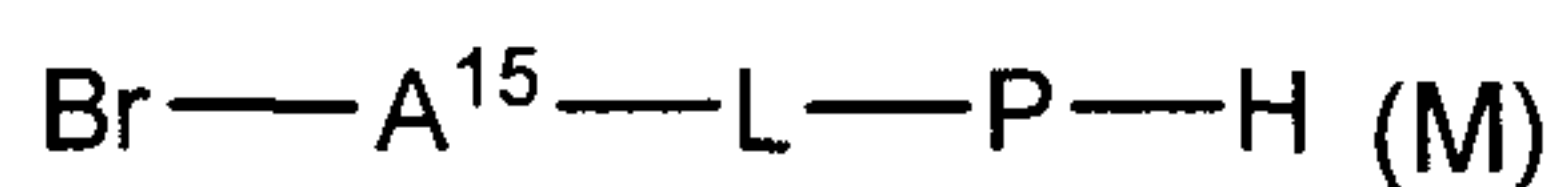


(b) deprotecting a compound of formula (L) under conditions sufficient to yield a compound of formula (C).

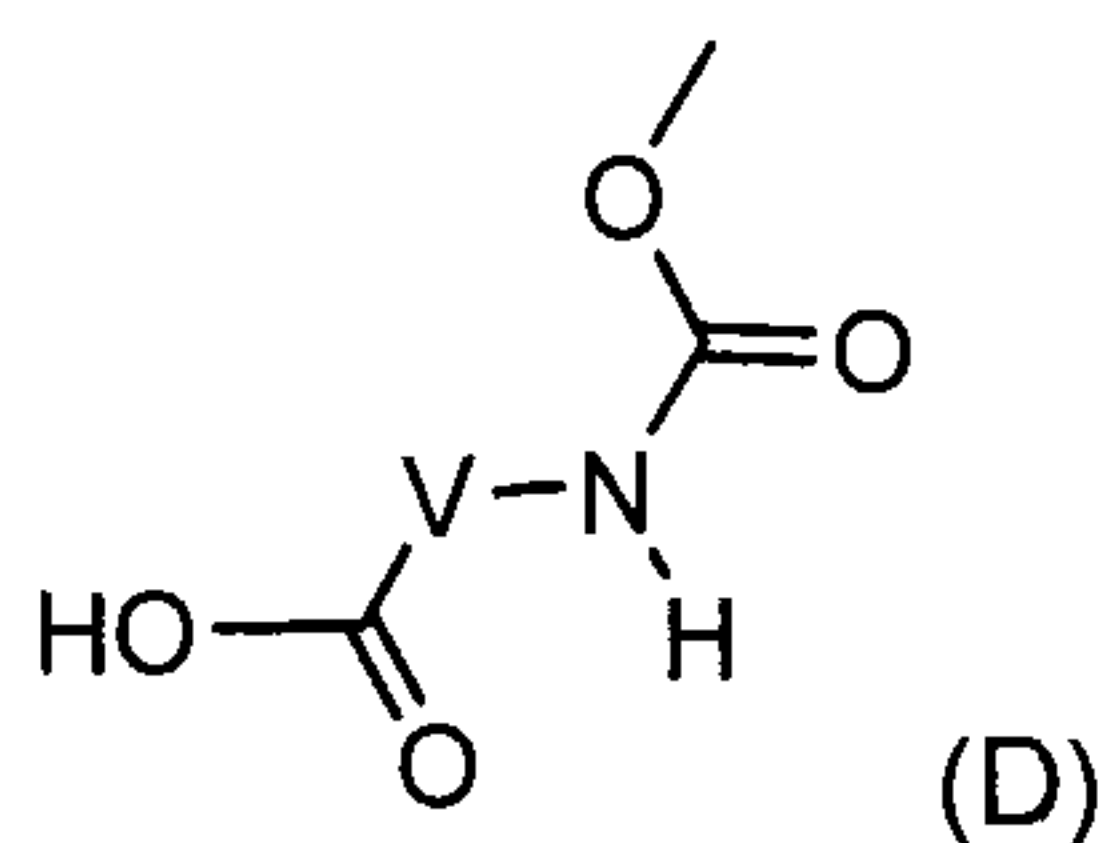
21. The method of claim 20, wherein the compound of formula (J):



is prepared by contacting a compound of formula (M):

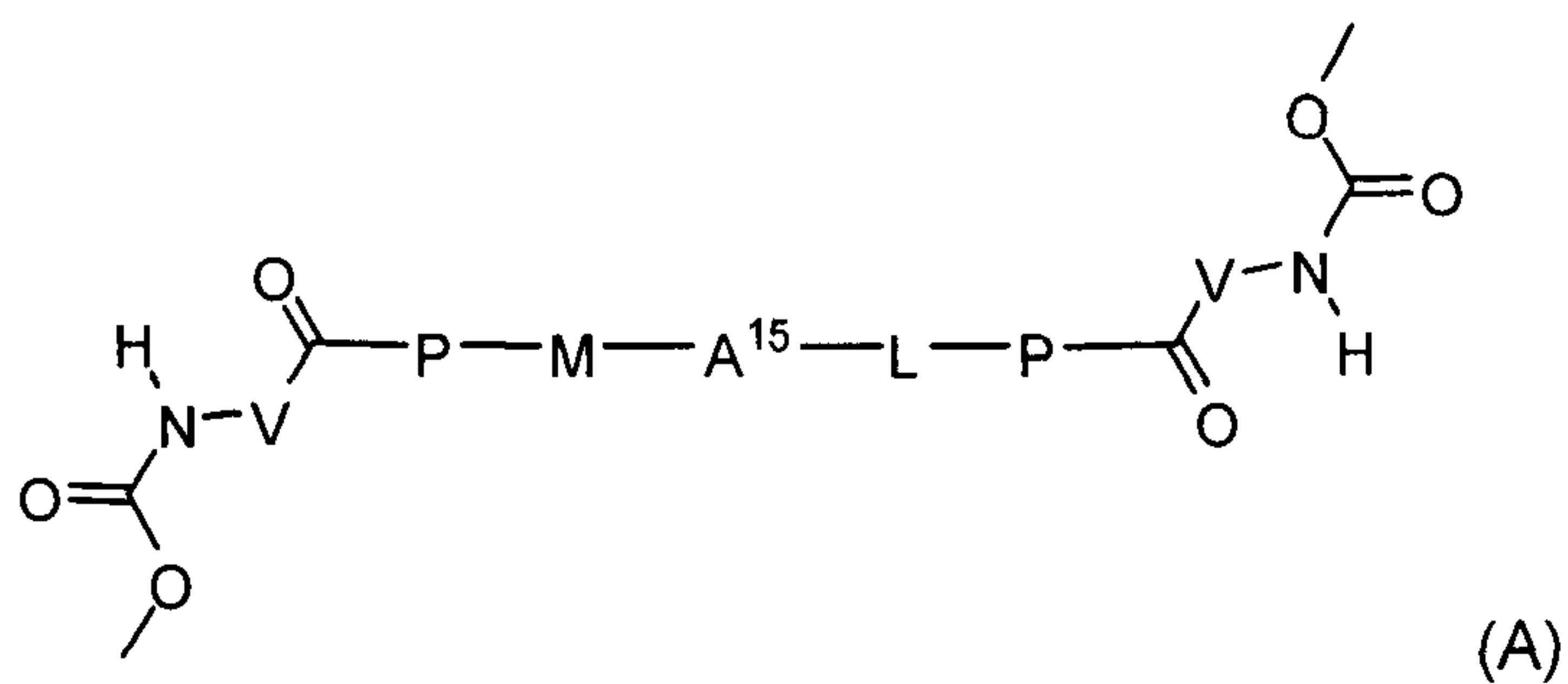


with a compound of formula (D):

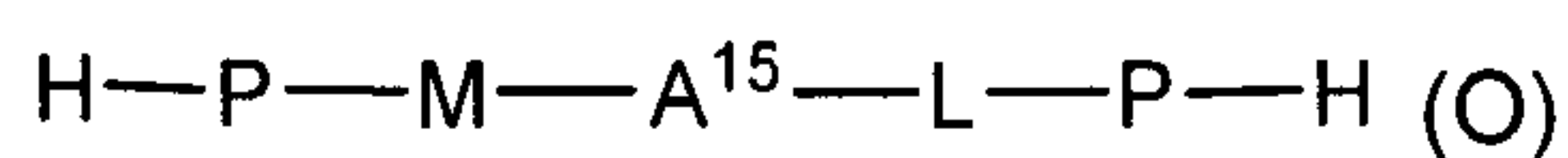


to yield a compound of formula (J).

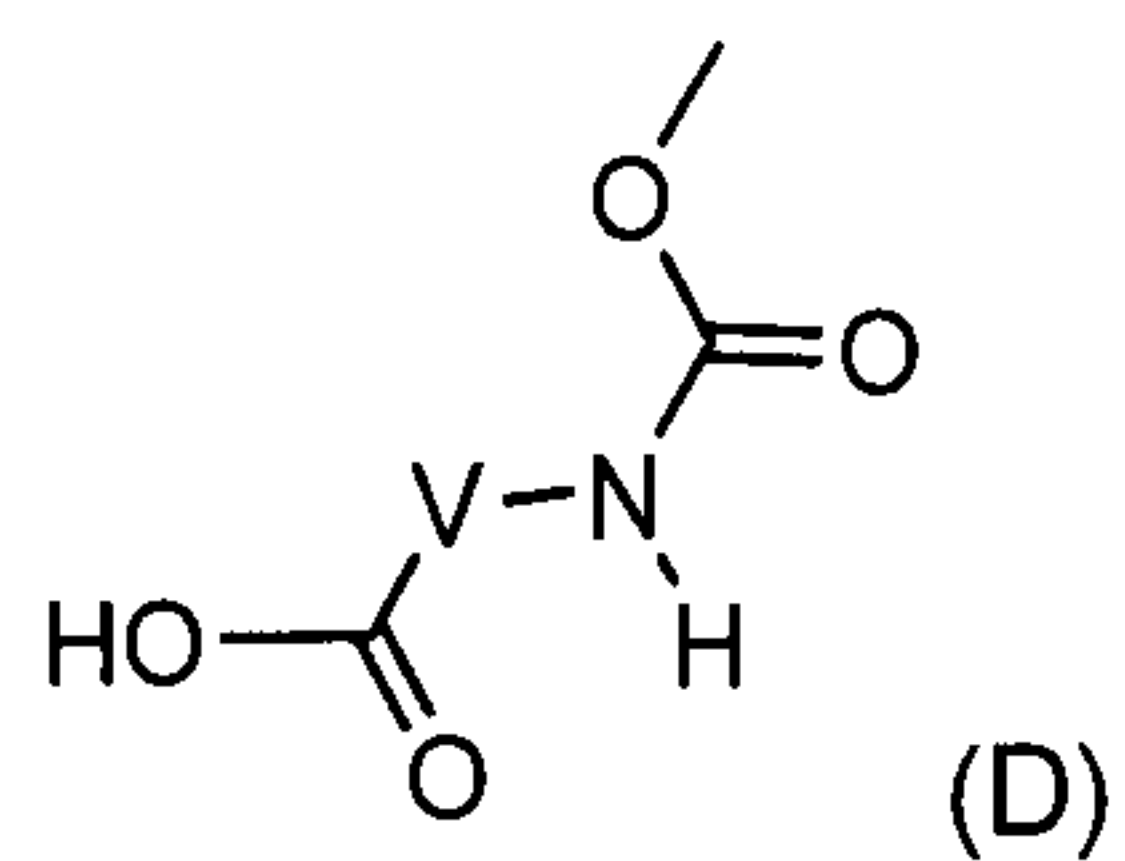
22. A method for preparing a compound of formula (A):



comprising contacting a compound of formula (O):



with at least two equivalents of a compound of formula (D):



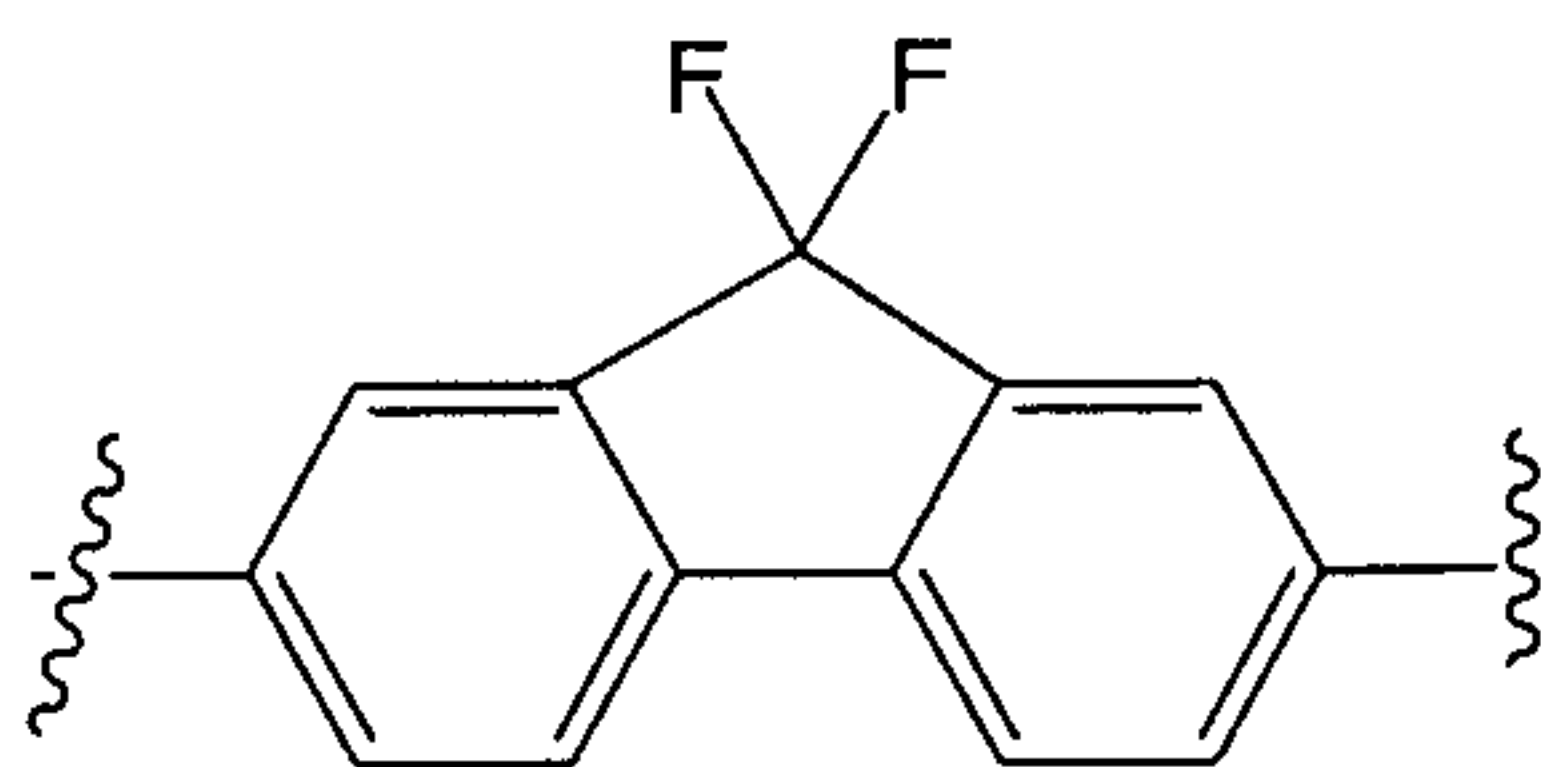
to yield a compound of formula (A), wherein:

V is alkyl;

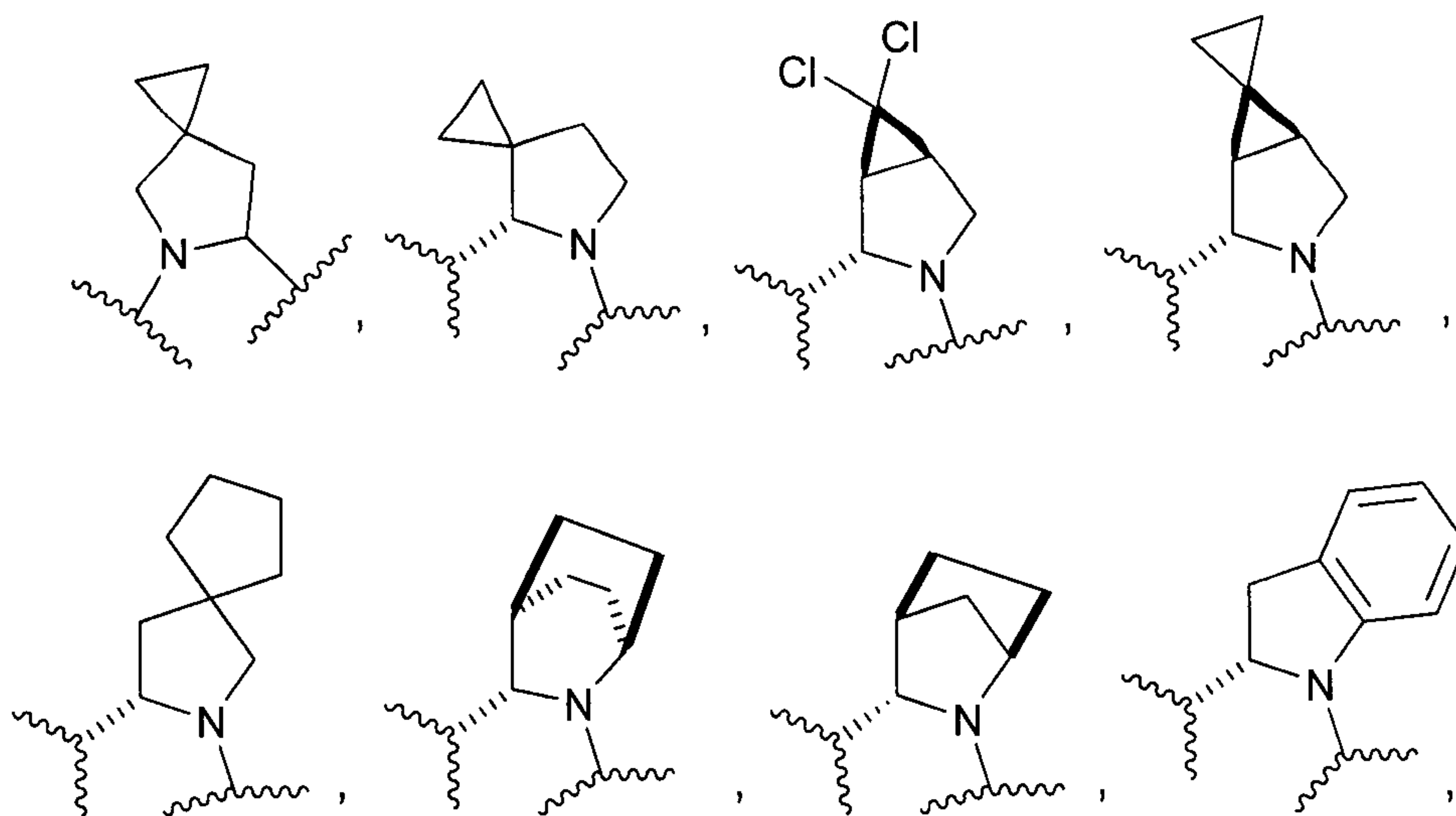
L is benzimidazolyl;

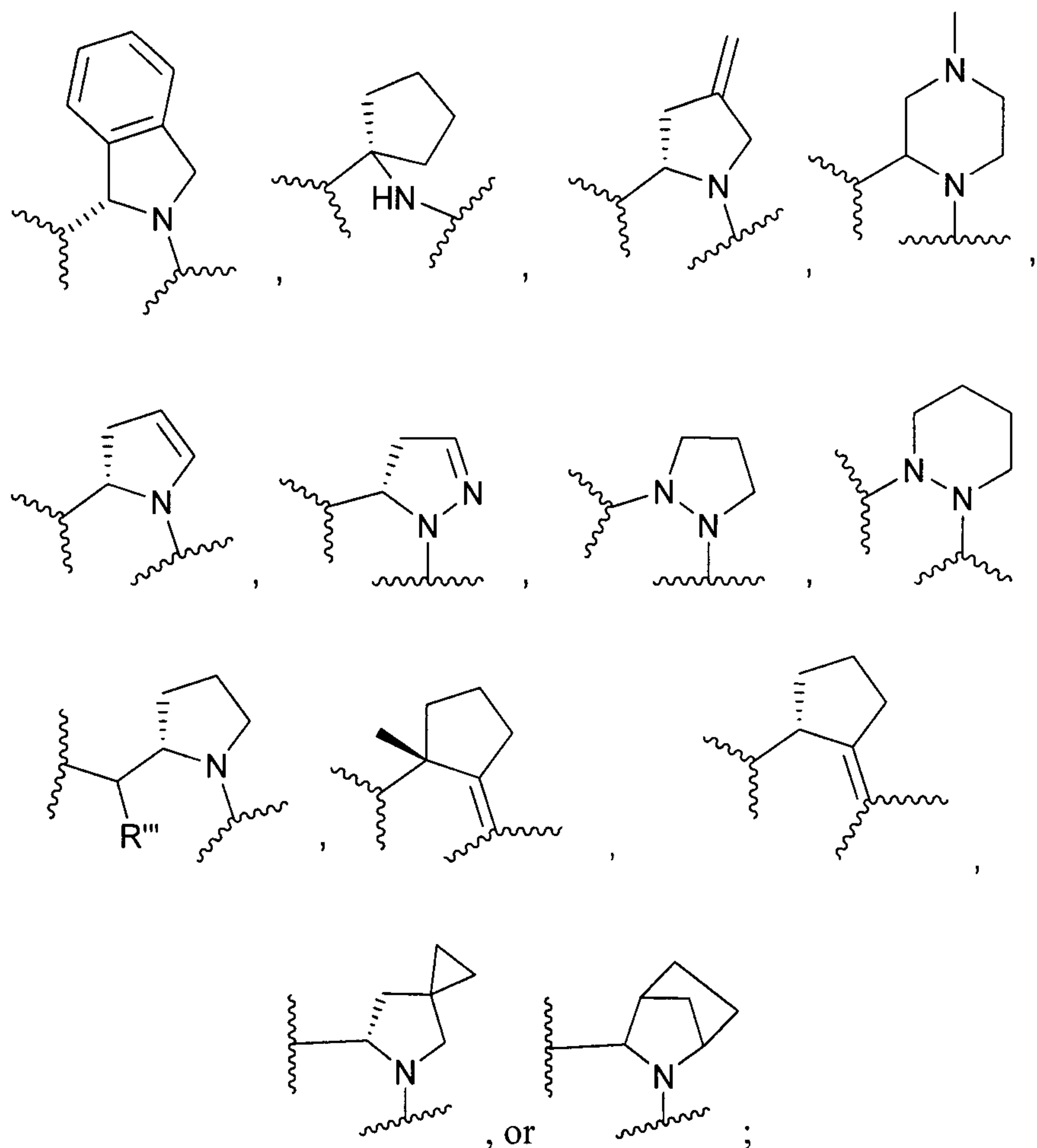
M is a 5-membered heteroaryl ring;

A¹⁵ is:



each P is independently:

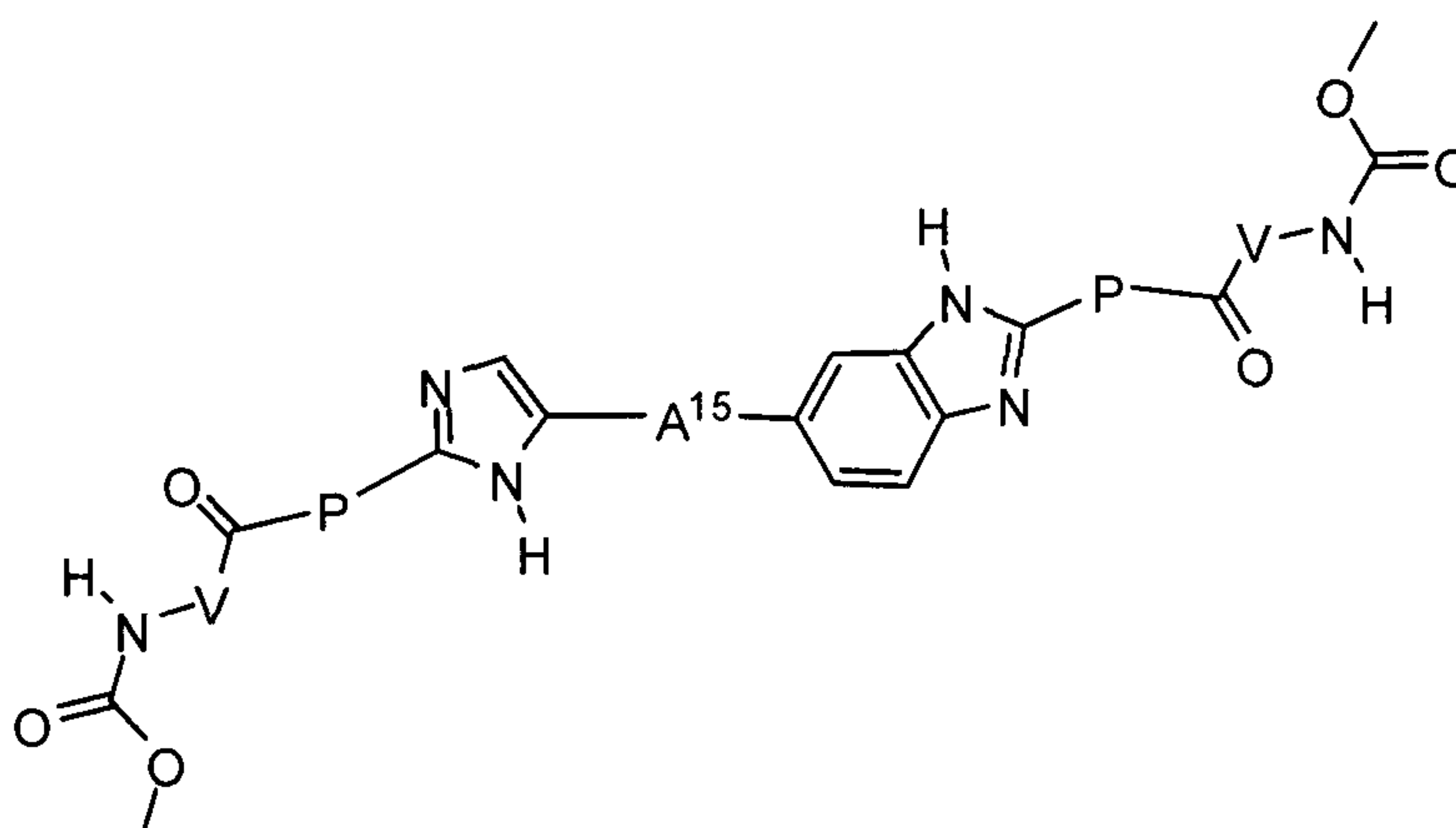




and R''' is hydrogen or alkyl.

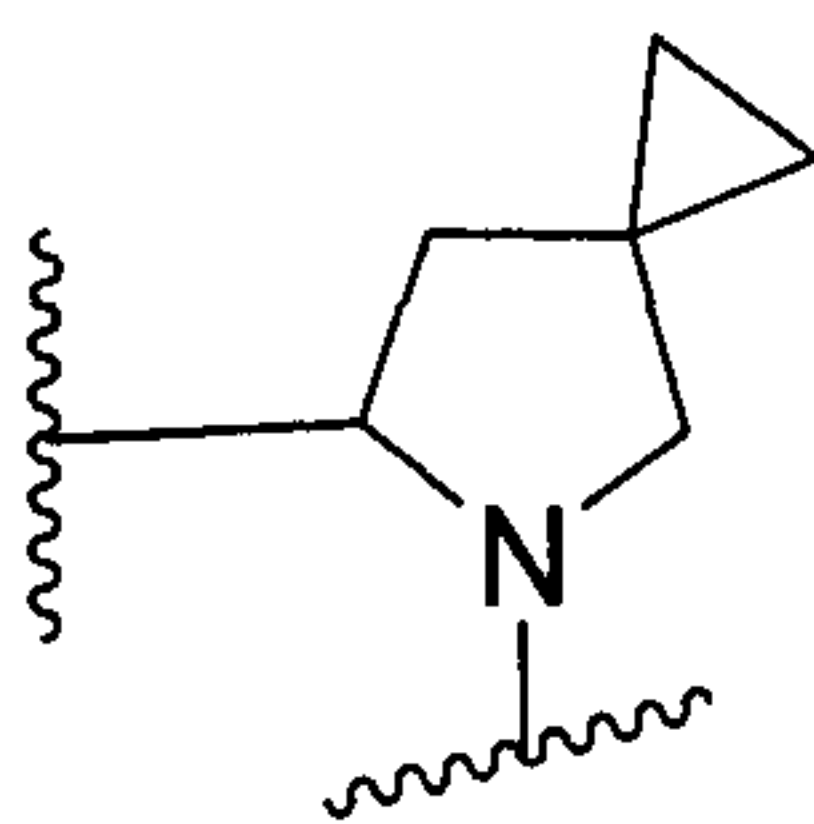
23. The method of claim 17, wherein the method further comprises a coupling agent that is 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate.
24. The method of claim 18, wherein PG is tert-butyloxycarbonyl.
25. The method of claim 18, wherein step (a) further comprises a transition metal catalyst that is tetrakis(triphenylphosphine)palladium(0).
26. The method of claim 18, wherein step (b) further comprises hydrochloric acid.
27. The method of claim 19, wherein the method further comprises a coupling agent that is 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate.

28. The method of claim 20, wherein PG is tert-butyloxycarbonyl.
29. The method of claim 20, wherein step (a) further comprises a transition metal catalyst that is tetrakis(triphenylphosphine)palladium(0).
30. The method of claim 20, wherein step (b) further comprises hydrochloric acid.
31. The method of claim 21, wherein the method further comprises a coupling agent that is 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate.
32. The method of claim 22, wherein the method further comprises a coupling agent that is 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate.
33. The method of claim 22, wherein the compound is a compound of formula:

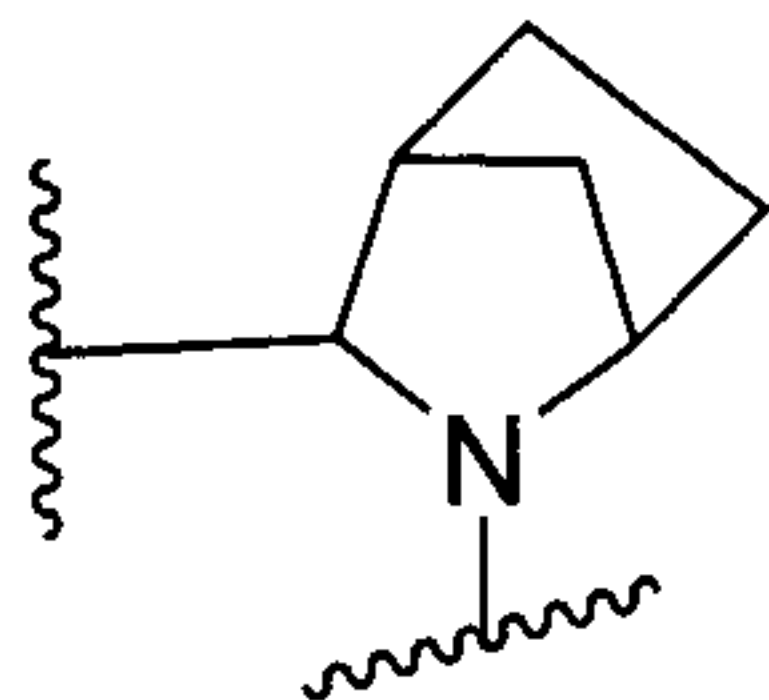


or a pharmaceutically acceptable salt thereof.

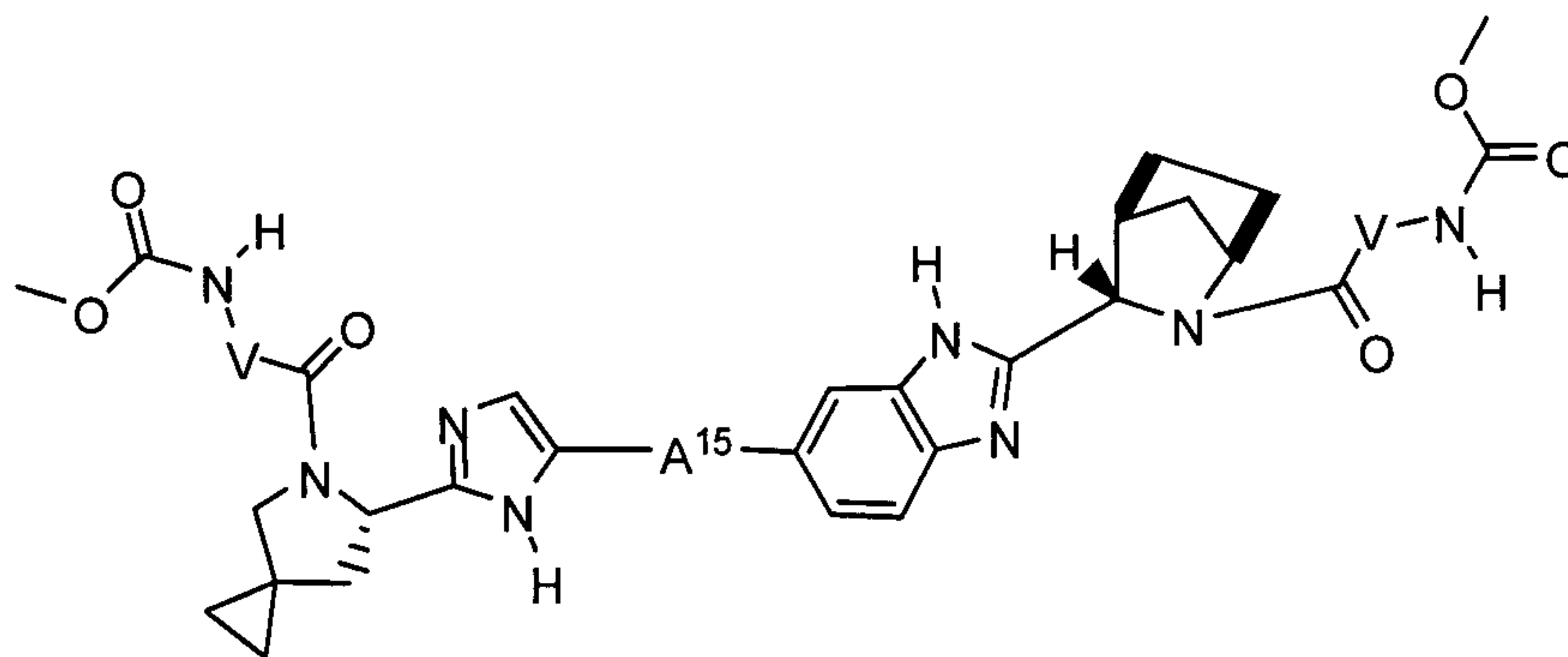
34. The method of claim 22, wherein at least one P is



35. The method of claim 22, wherein at least one P is

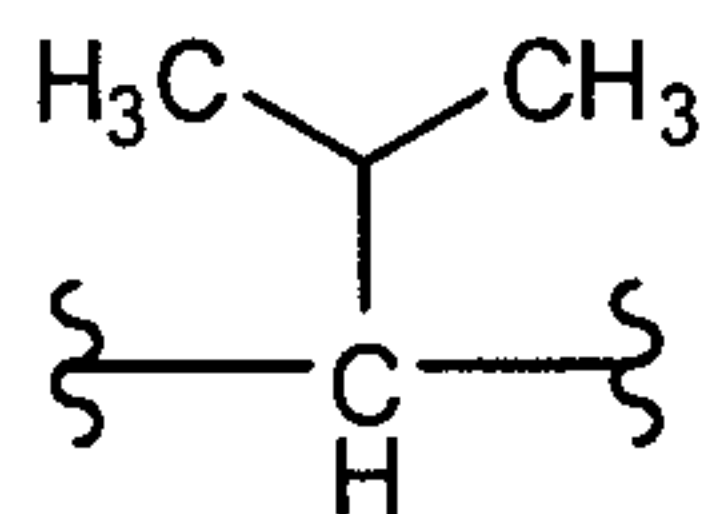


36. The method of claim 22, wherein the compound is a compound of formula:

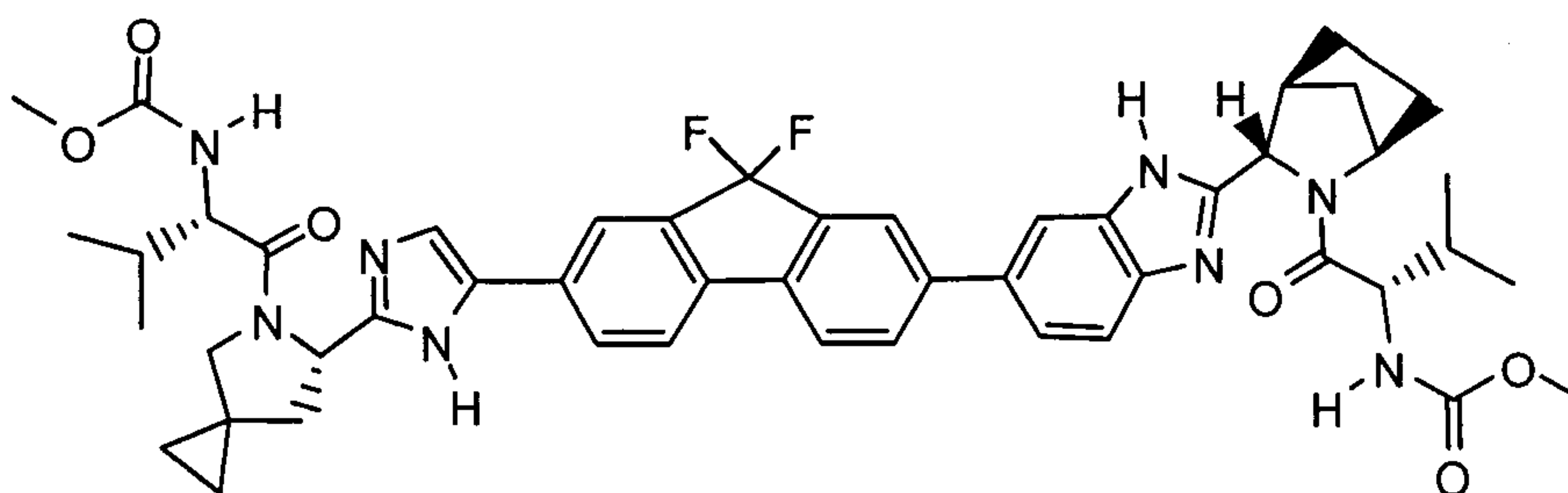


or a pharmaceutically acceptable salt thereof.

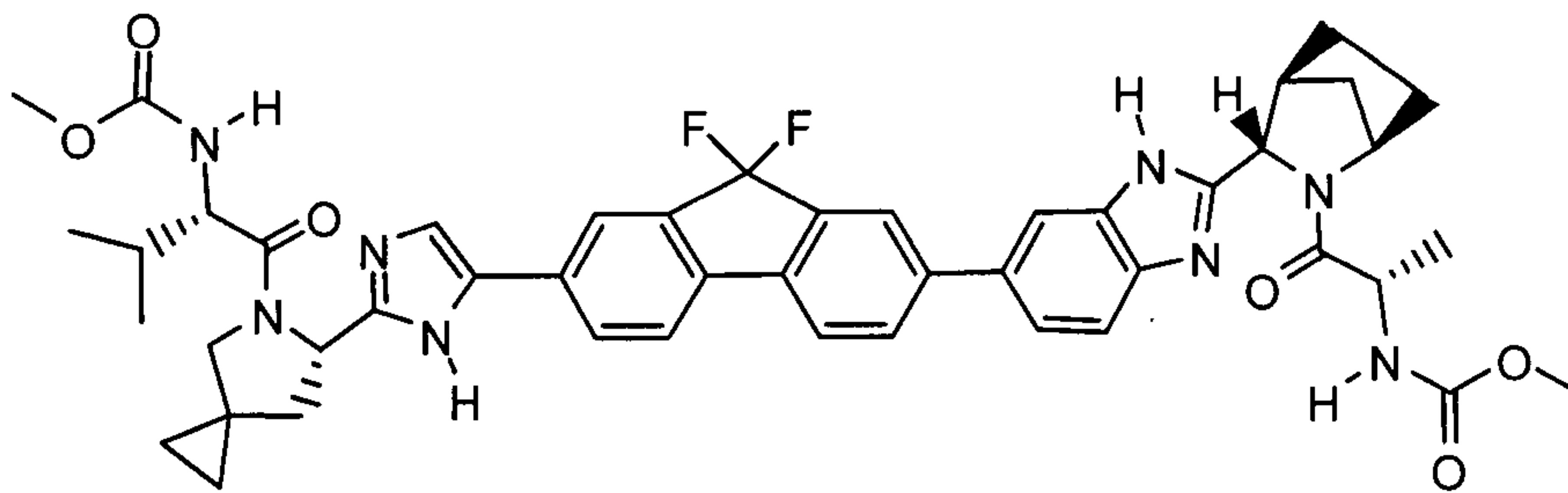
37. The method of claim 22, wherein each V is:



38. The method of claim 22, wherein the compound is a compound of formula:

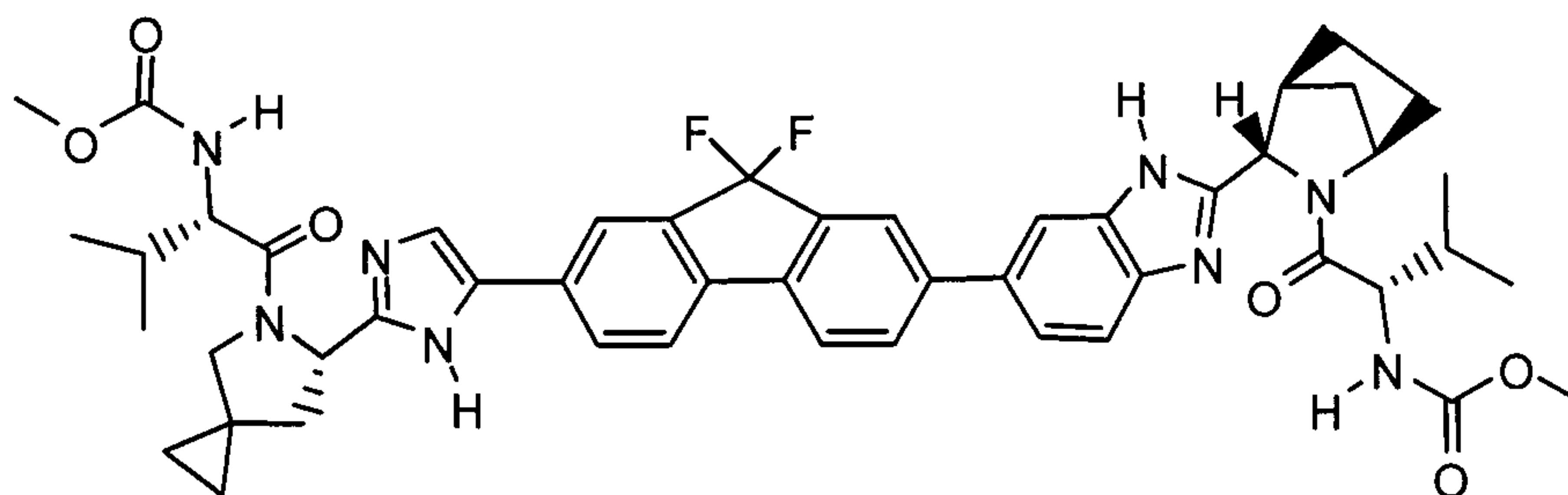


or



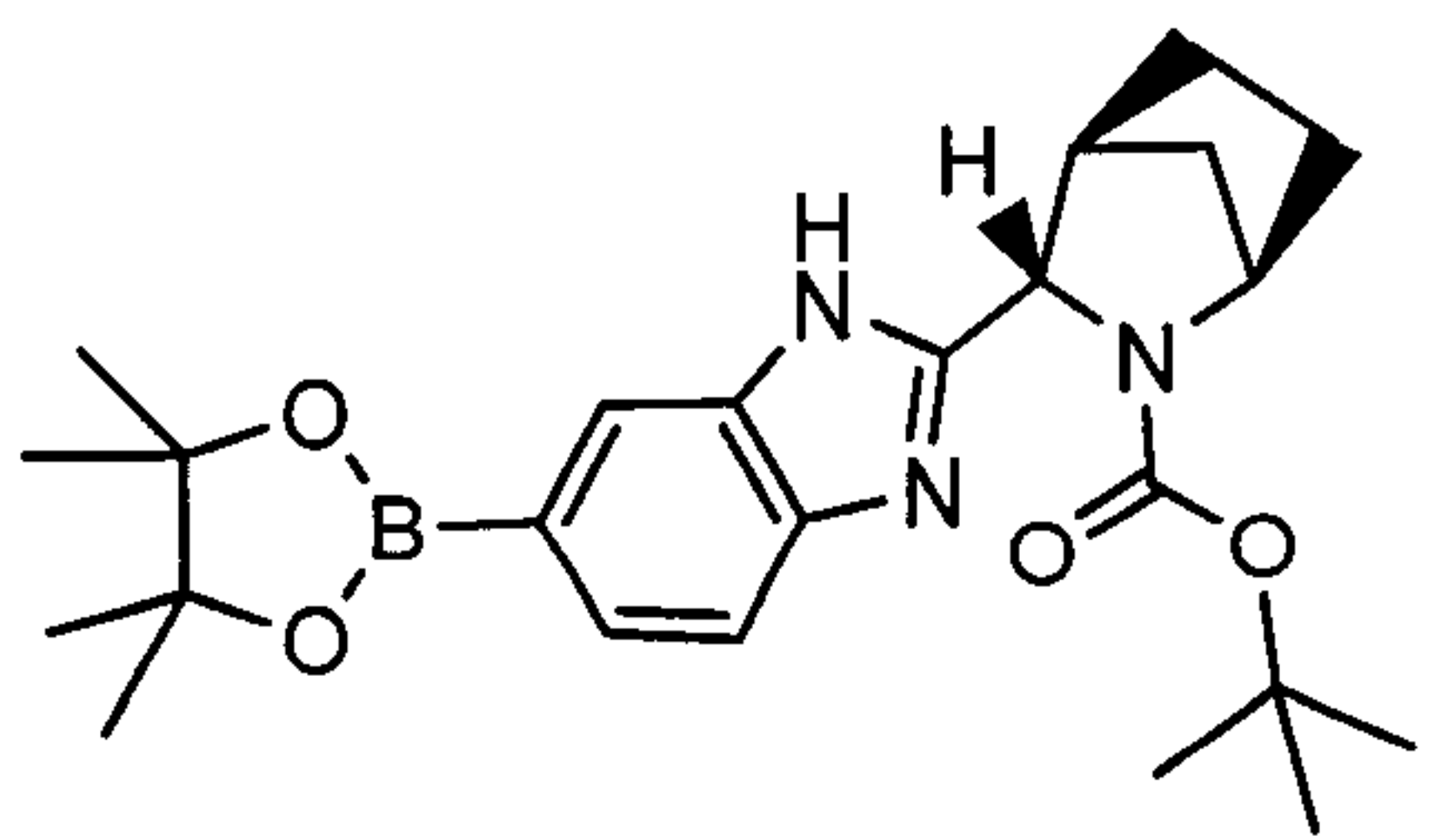
or a pharmaceutically acceptable salt thereof.

39. The method of claim 22, wherein the compound is a compound of formula:

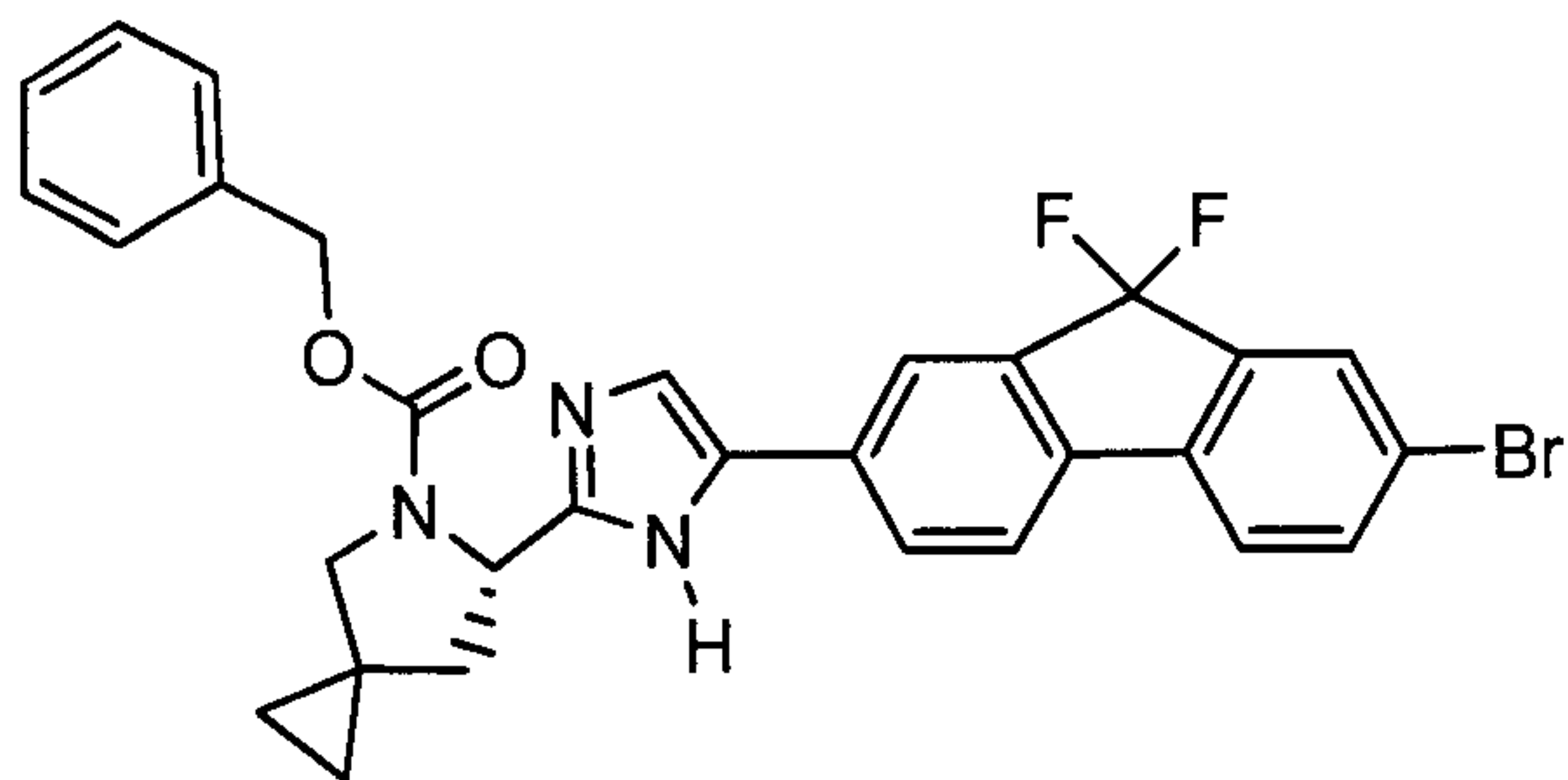


or a pharmaceutically acceptable salt thereof.

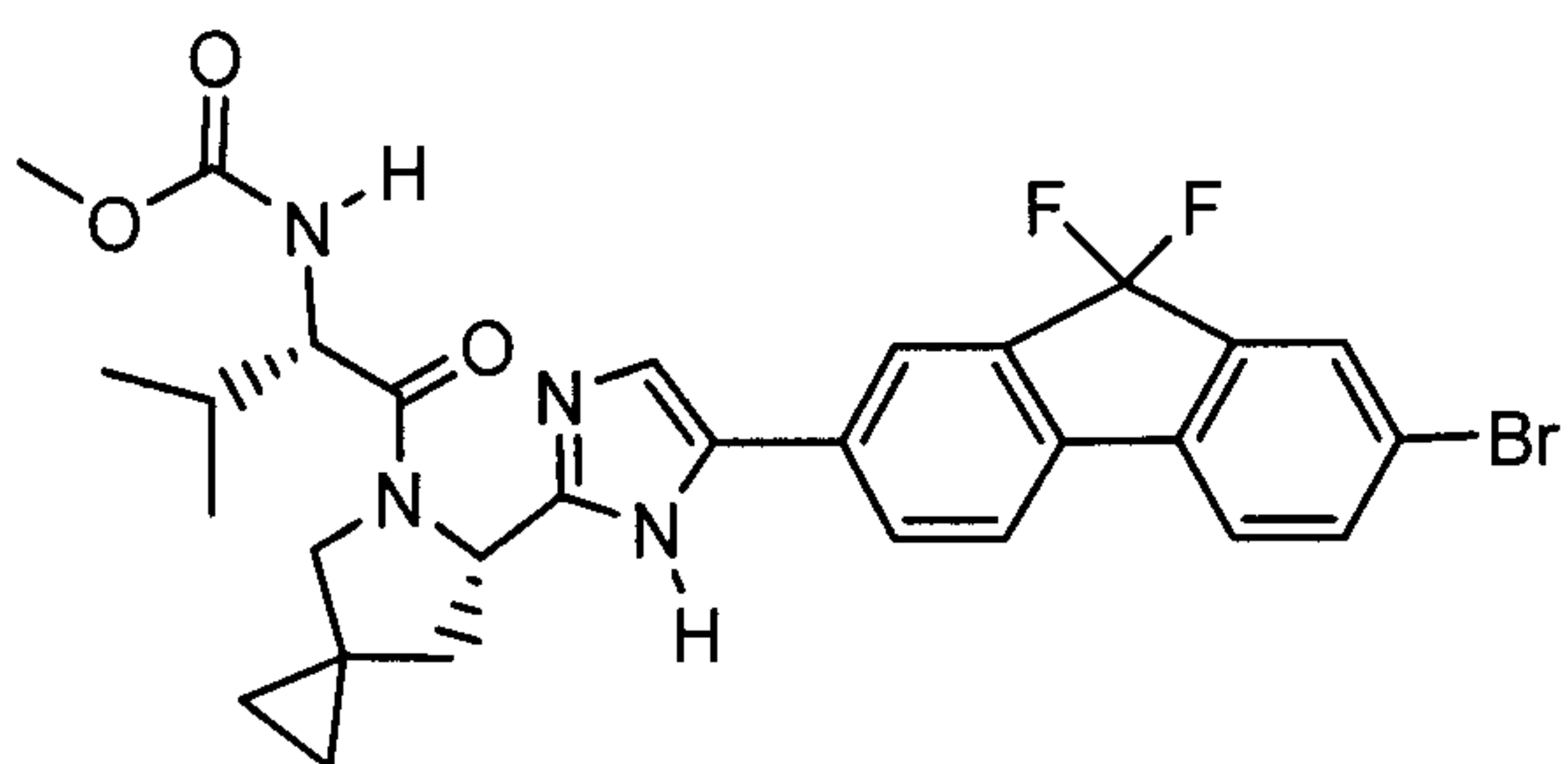
40. A compound of formula:



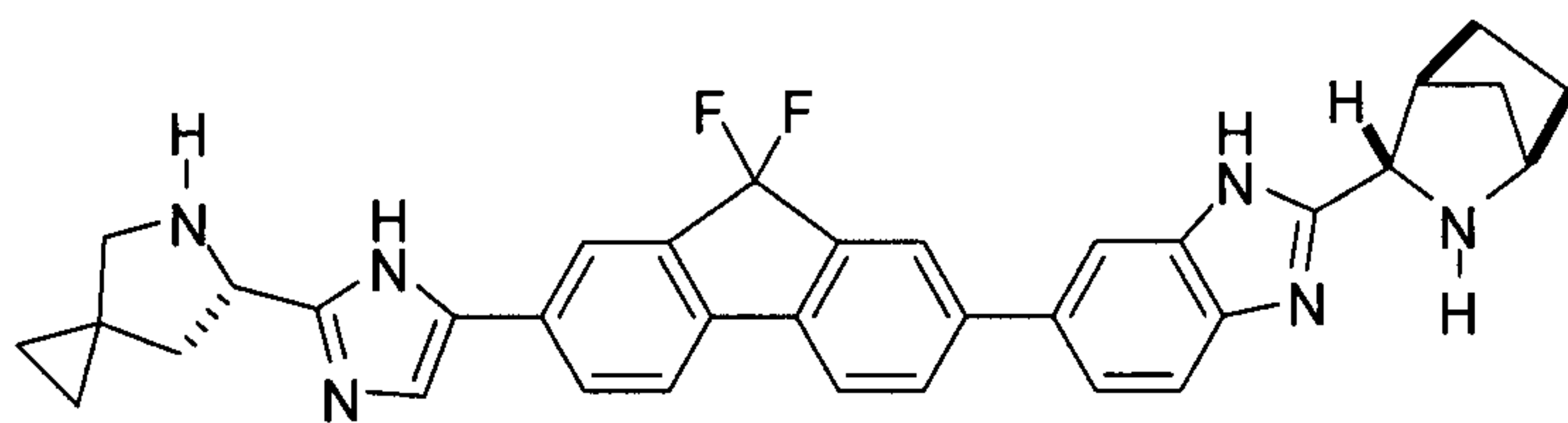
41. A compound of formula:



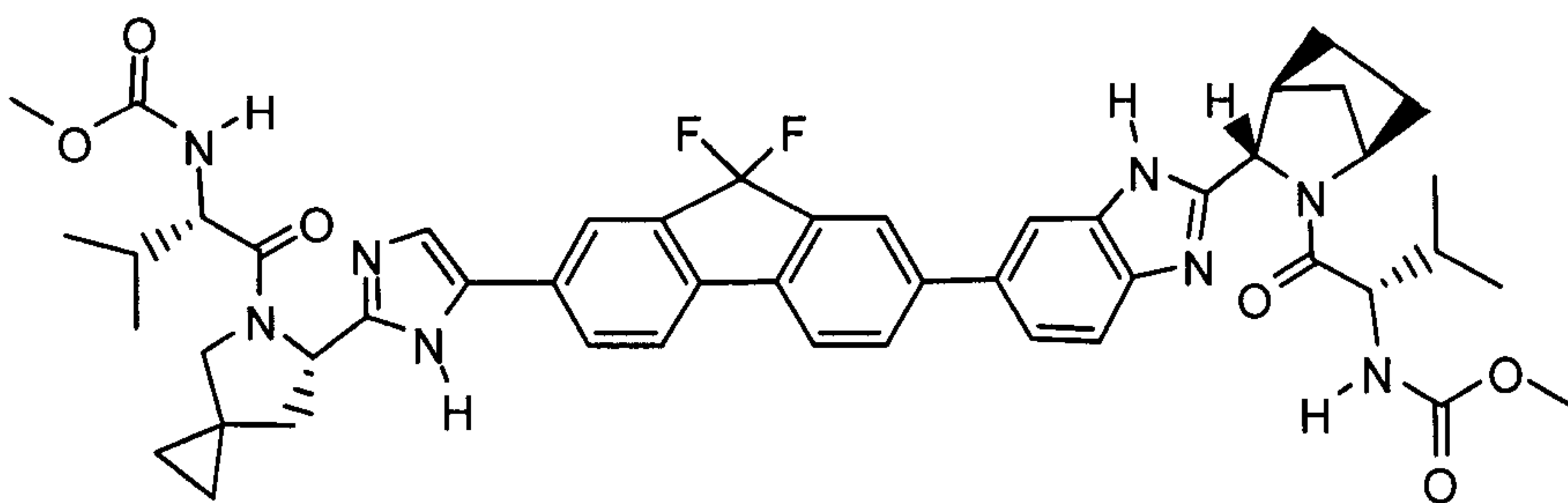
42. A compound of formula:



43. A compound of formula:

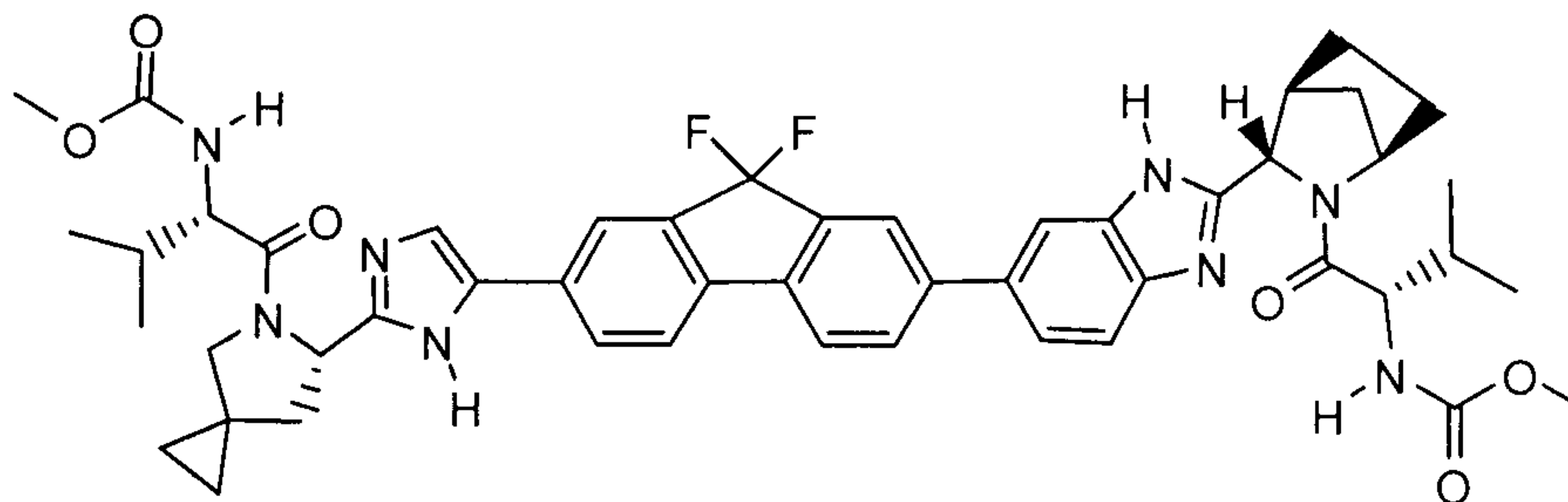


44. A compound of formula:



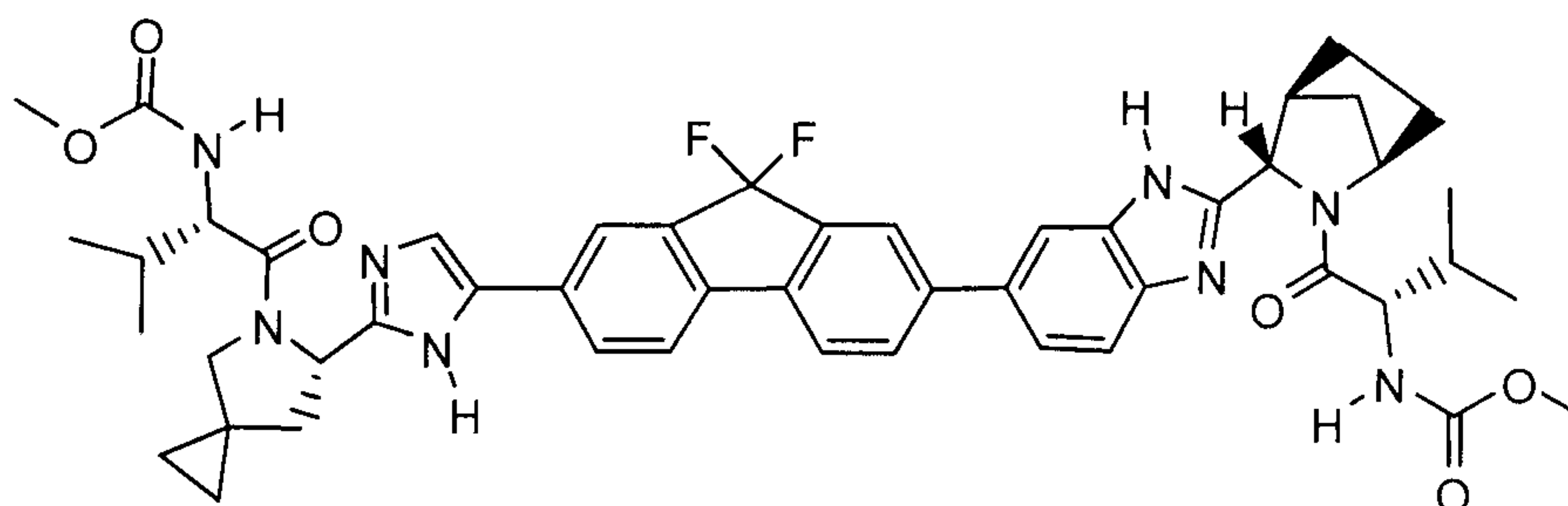
45. A pharmaceutical composition comprising the compound of claim 44 and at least one pharmaceutically acceptable carrier.
46. The pharmaceutical composition of claim 45, further comprising a NS5B polymerase inhibitor.
47. A compound of claim 44, for use in the prophylactic or therapeutic treatment of hepatitis C.
48. Use of a compound of claim 44 for the prophylactic or therapeutic treatment of hepatitis C.
49. Use of a composition of claim 45 or 46 for the prophylactic or therapeutic treatment of hepatitis C.
50. Use of a compound of claim 44, in the preparation of a medicament for the prophylactic or therapeutic treatment of hepatitis C.
51. A compound of claim 44, for use in the treatment of hepatitis C.
52. Use of a compound of claim 44 for treatment of hepatitis C.
53. Use of a composition of claim 45 or 46 for the treatment of hepatitis C.
54. Use of a compound of claim 44, in the preparation of a medicament for the treatment of hepatitis C.

54. A pharmaceutically acceptable salt of a compound of formula



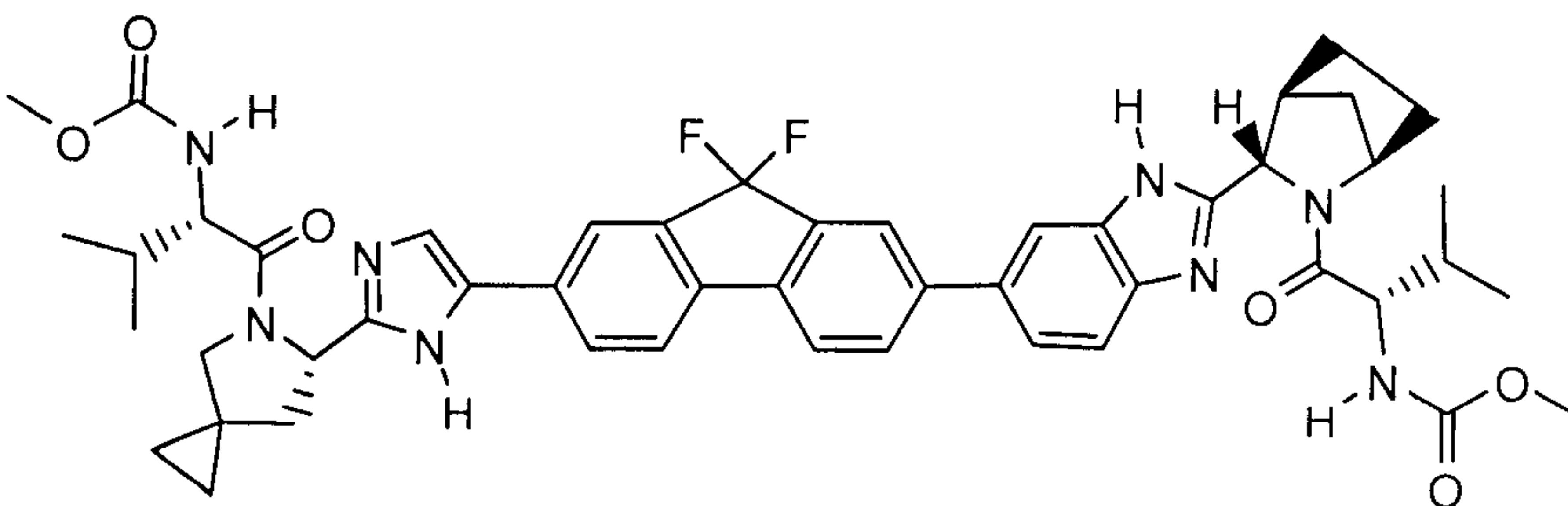
55. A pharmaceutical composition comprising the pharmaceutically acceptable salt of claim 54 and a pharmaceutically acceptable carrier.

56. A compound of formula



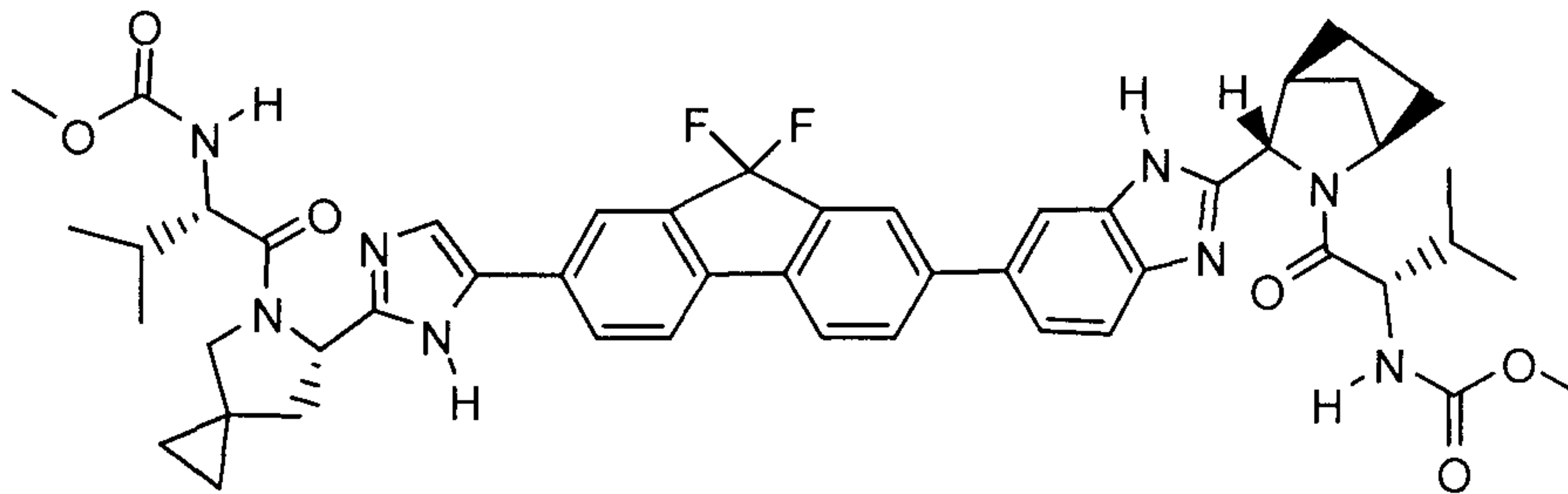
for the treatment of chronic hepatitis C.

57. Use of a compound of formula



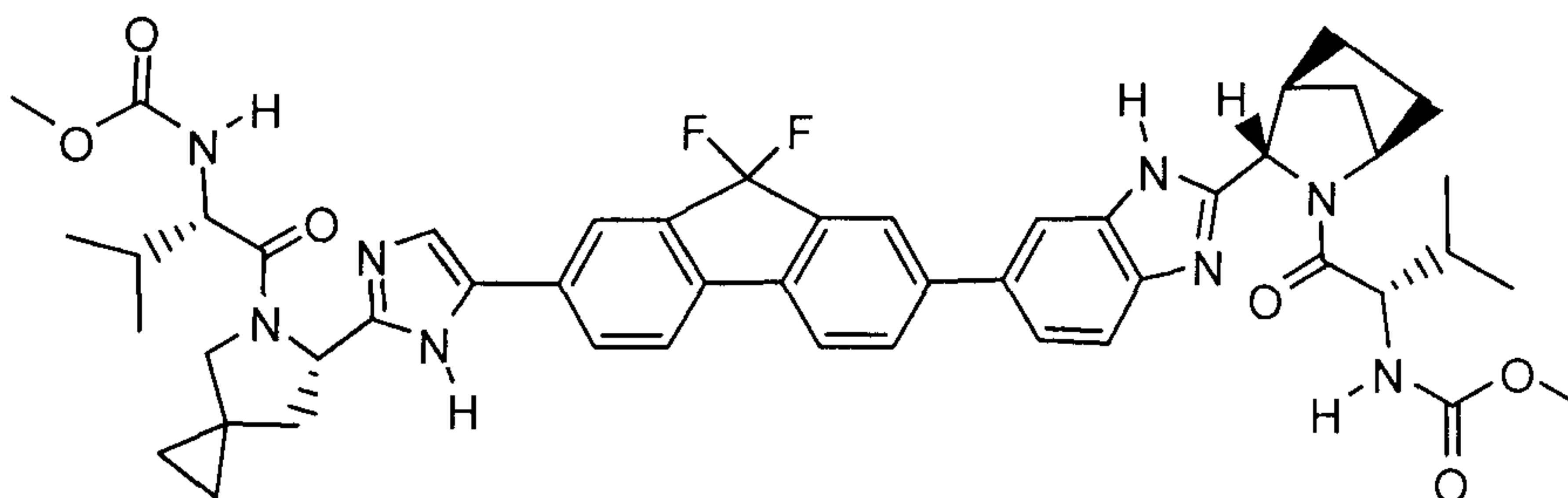
for the treatment of chronic hepatitis C.

58. Use of a compound of formula



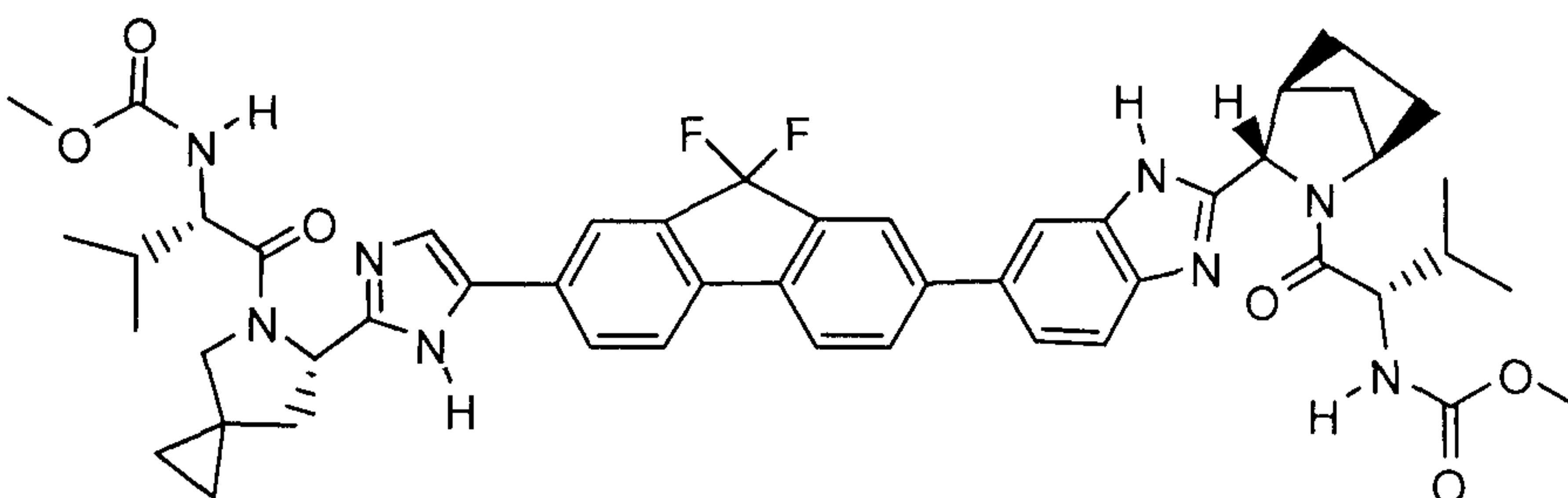
in the preparation of a medicament for the treatment of chronic hepatitis C.

59. A compound of formula



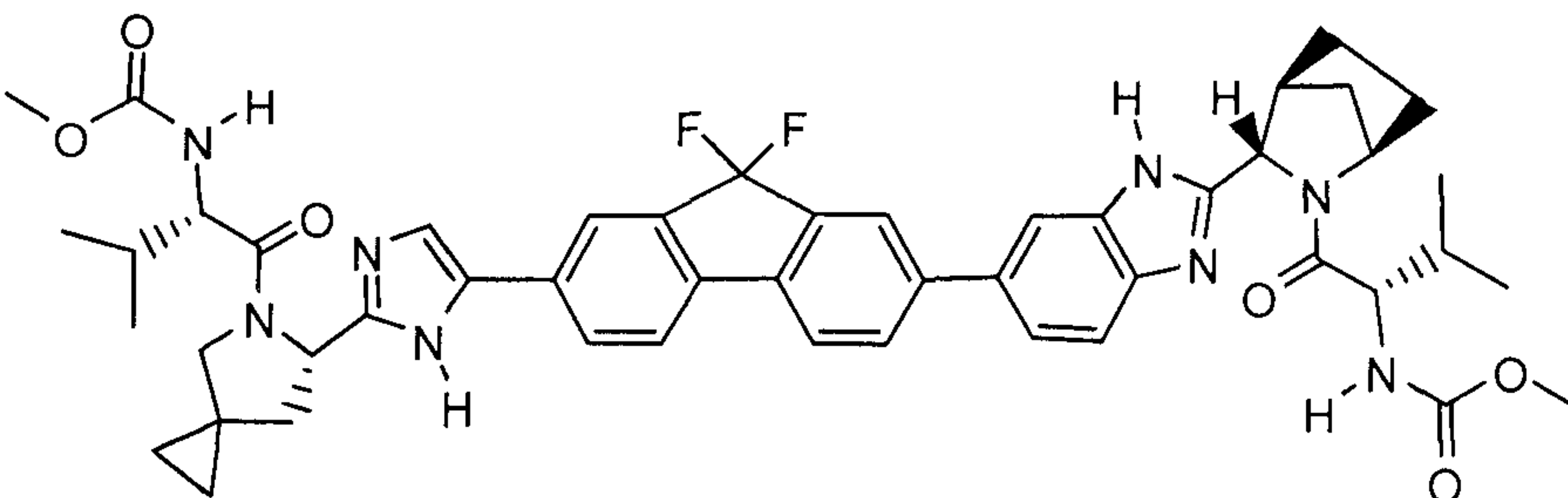
for the treatment of chronic genotype 1 hepatitis C.

60. Use of a compound of formula



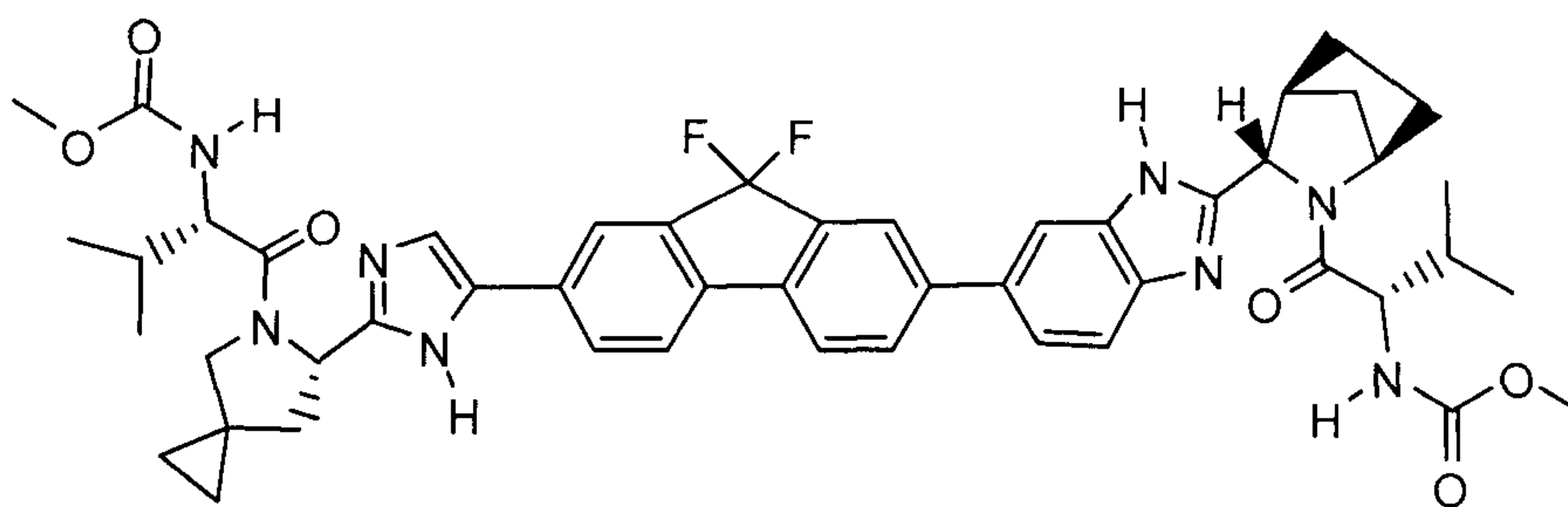
for the treatment of chronic genotype 1 hepatitis C.

61. Use of a compound of formula



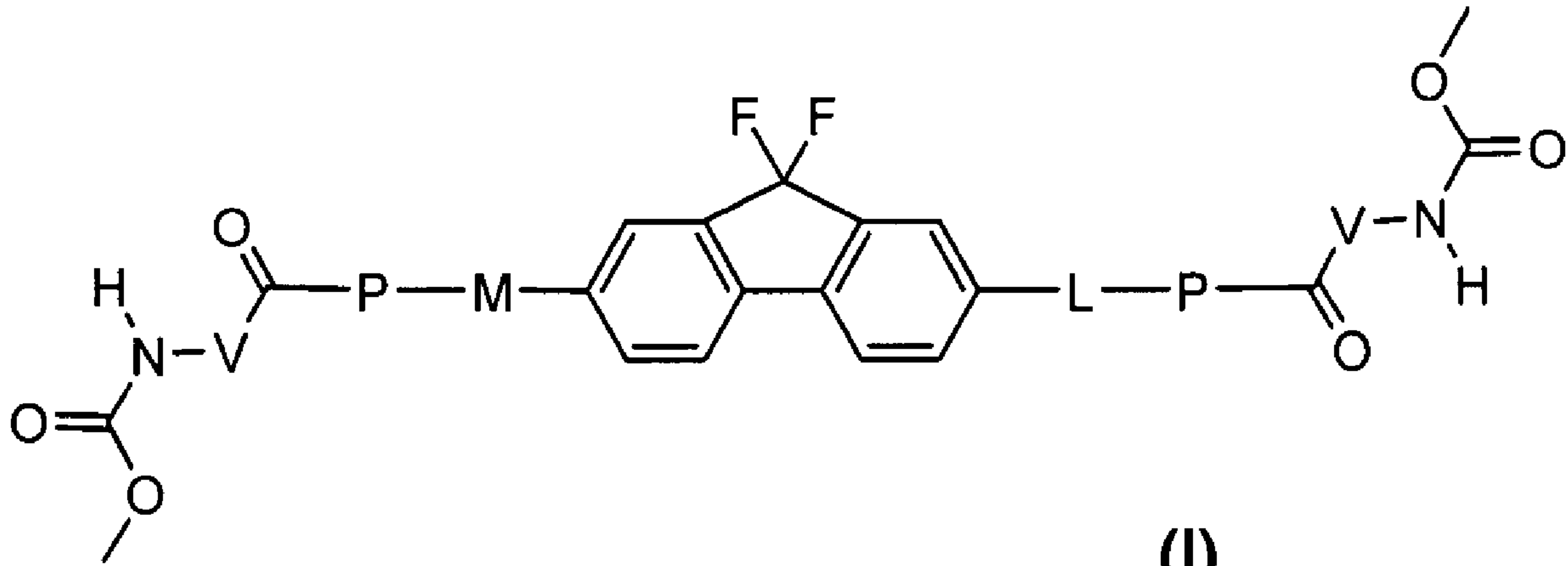
in the preparation of a medicament for the treatment of chronic genotype 1 hepatitis C.

62. A unit dosage form comprising a compound of formula:



and a pharmaceutically acceptable carrier.

63. The unit dosage form of claim 62 being a tablet.



(I)