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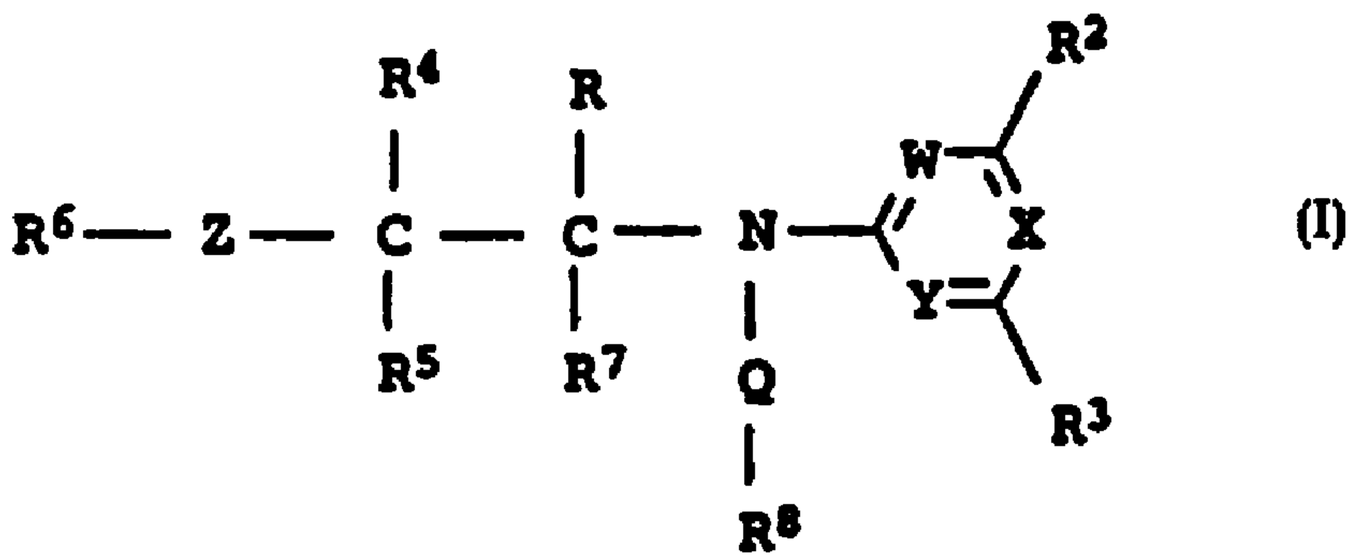
(54) **DERIVES D'ACIDES AMINES, LEUR PREPARATION ET LEUR UTILISATION**

(54) **NOVEL AMINO ACID DERIVATIVES, THEIR PREPARATION AND USE**



(I)

(57) L'invention concerne des dérivés d'acides aminés de formule (I) dans laquelle les restes ont la notation donnée dans la description, et leur utilisation comme inhibiteurs des récepteurs d'endothéline.

(57) The invention relates to amino acid derivatives of formula (I), in which the groups have the meaning given in the description. It also relates to the use thereof as inhibitors for endothelin receptors.

PCT

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Veröffentlicht
Mit internationalem Recherchenbericht.

(54) Title: AMINO ACID DERIVATIVES, THE PREPARATION AND USE THEREOF AS ENDOTHELIN ANTAGONISTS

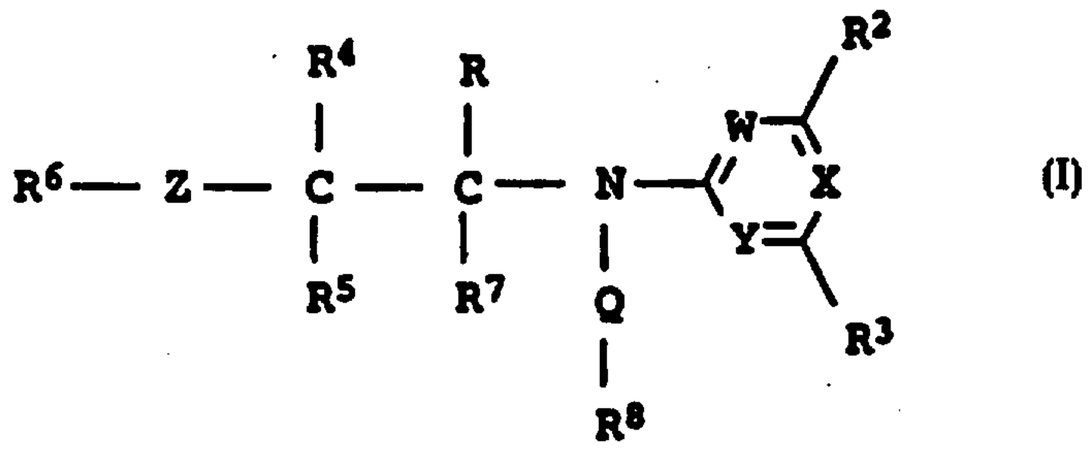
(54) Bezeichnung: AMINOSÄUREDERIVATE, IHRE HERSTELLUNG UND VERWENDUNG ALS ENDOTHELINANTAGONISTEN

(57) Abstract

The invention relates to amino acid derivatives of formula (I), in which the groups have the meaning given in the description. It also relates to the use thereof as inhibitors for endothelin receptors.

(57) Zusammenfassung

Die Erfindung betrifft Aminosäurederivate der Formel (I), in der die Reste die in der Beschreibung angegebene Bedeutung besitzen, sowie deren Verwendung als Hemmstoffe für Endothelinrezeptoren.



(I)

0050/46259

Novel amino acid derivatives, their preparation and use

The present invention relates to novel amino acid derivatives and to their preparation and use.

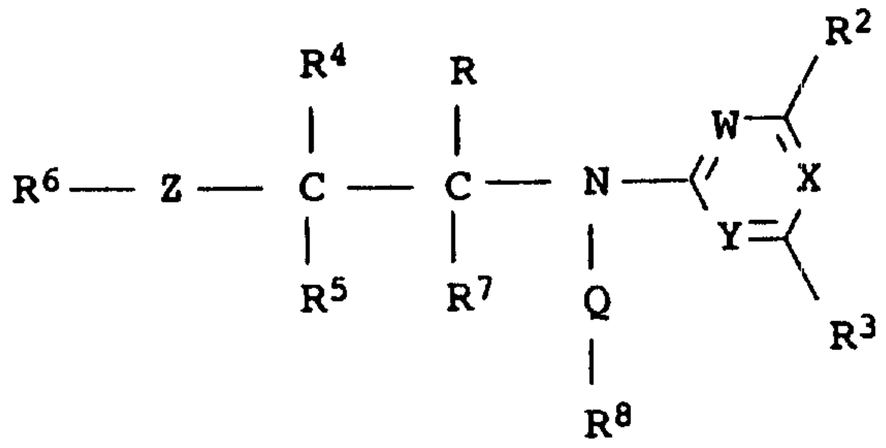
Endothelin is a peptide which is composed of 21 amino acids and which is synthesized and released by the vascular endothelium. Endothelin exists in three isoforms ET-1, ET-2 and ET-3. "Endothelin" or "ET" hereinafter means one or all endothelin isoforms. Endothelin is a potent vasoconstrictor and has a strong effect on vascular tone. It is known that this vasoconstriction is caused by binding of endothelin to its receptor (Nature 332 (1988) 411-415; FEBS Letters 231 (1988) 440-444, and Biochem. Biophys. Res. Commun. 154 (1988) 868-875).

Elevated or abnormal release of endothelin causes a persistent vasoconstriction in the peripheral, renal and cerebral blood vessels, which may lead to illnesses. As reported in the literature, elevated plasma endothelin levels are found in patients with hypertension, acute myocardial infarct, pulmonary hypertension, Raynaud's syndrome, atherosclerosis and in the airways of asthmatics (Japan J. Hypertension 12 (1989) 79, J. Vascular Med. Biology 2 (1990) 207, J. Am. Med. Association 264 (1990) 2868).

Accordingly, substances which specifically inhibit the binding of endothelin to the receptor ought also to antagonize the various abovementioned physiological effects of endothelin and therefore be valuable drugs.

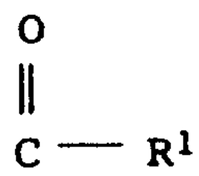
We have found that certain amino acid derivatives are good inhibitors of endothelin receptors.

The invention relates to amino acid derivatives of the formula I



I

where R is formyl, tetrazolyl, cyano, COOH or a radical which can be hydrolyzed to COOH, for example R is



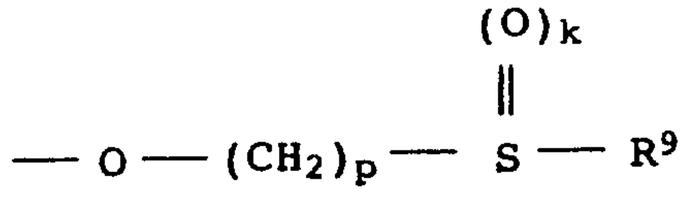
where R^1 has the following meanings:

a) hydrogen

b) succinylimidyl [sic]

c) a 5-membered heteroaromatic ring which is linked via a nitrogen atom, such as pyrrolyl, pyrazolyl, imidazolyl and triazolyl, which can carry one or two halogen atoms or one or two C_1-C_4-alkyl or one or two C_1-C_4-alkoxy groups;

d) R^1 is furthermore



where k can assume the values 0, 1 and 2, p can assume the values 1, 2, 3 and 4, and R^9 is
C_1-C_4-alkyl, C_3-C_7-cycloalkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl or unsubstituted or substituted phenyl which can be substituted by one or more, eg. from one to three, of the following radicals:
halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, mercapto, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino;

e) R^1 is furthermore OR^{10} where R^{10} is:

hydrogen, the cation of an alkali metal such as lithium, sodium, potassium or the cation of an alkaline earth metal such as calcium, magnesium and barium, and physiologically tolerated alkylammonium ion or the ammonium ion,

C_3-C_8-cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

C_1-C_8-alkyl, in particular C_1-C_4-alkyl such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl;

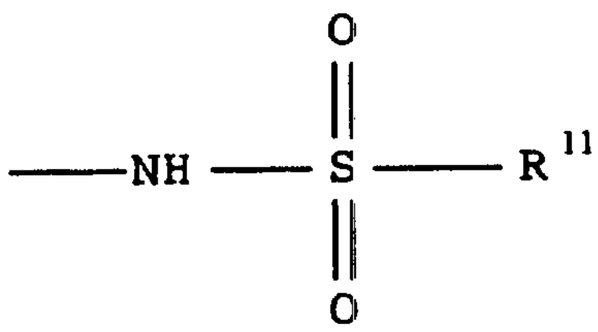
CH_2-phenyl which can be substituted by one or more of the following radicals: halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino,

C_3-C_6-alkenyl or C_3-C_6-alkynyl, it being possible for these groups in turn to carry from one to five halogen atoms;

R^{10} can furthermore be a phenyl radical which can carry from one to five halogen atoms and/or from one to three of the following radicals: nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino;

a 5-membered heteroaromatic ring which is linked via a nitrogen atom and contains from one to three nitrogen atoms and can carry one or two halogen atoms and/or one or two of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenyl, C_1-C_4-haloalkoxy and/or C_1-C_4-alkylthio, in particular 1-pyrazolyl, 3-methyl-1-pyrazolyl, 4-methyl-1-pyrazolyl, 3,5-dimethyl-1-pyrazolyl, 3-phenyl-1-pyrazolyl, 4-phenyl-1-pyrazolyl, 4-chloro-1-pyrazolyl, 4-bromo-1-pyrazolyl, 1-imidazolyl, 1-benzimidazolyl, 1,2,4-triazol-1-yl, 3-methyl-1,2,4-triazol-1-yl, 5-methyl-1,2,4-triazol-1-yl, 1-benzotriazolyl, 3,4-dichloro-1-imidazolyl;

f) R^1 is furthermore

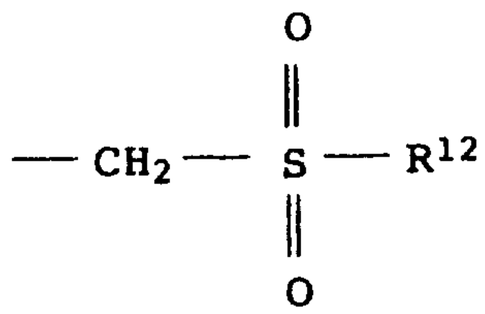


where R^{11} is:

C_1-C_4-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_3-C_8-cycloalkyl as mentioned above in particular, it being possible for these radicals to carry a C_1-C_4-alkoxy, C_1-C_4-alkylthio and/or a phenyl radical as mentioned above;

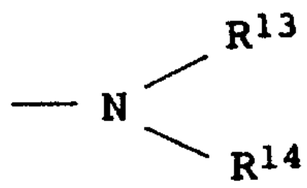
phenyl which is unsubstituted or substituted, in particular as mentioned above;

g) R^1 is



where R^{12} has the same meaning as R^{11};

h) R^1 can furthermore be



where R^{13} and R^{14} can be identical or different and have the following meanings:

hydrogen, C_1-C_7-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-alkenyl, C_3-C_7-alkynyl, benzyl, phenyl, unsubstituted or substituted, as described above,

or R^{13} and R^{14} together form a C_4–C_7-alkylene chain which is closed to form a ring and is unsubstituted or substituted, eg. by C_1–C_4-alkyl, and which may contain a hetero atom, eg. oxygen, nitrogen or sulfur, such as $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)_7-$, $-(CH_2)_2-O-(CH_2)_2-$, $-(CH_2)_2-S-(CH_2)_2-$, $-CH_2-NH-(CH_2)_2-$, $-(CH_2)_2-NH-(CH_2)_2-$;

a tetrazole [sic] or a nitrile [sic].

The other substituents have the following meanings:

W is nitrogen or $C-NO_2$, and W can furthermore be a CH group when one or more of the substituents R^2, R^3, R^{15} and/or R^{16} are nitro;

R^2 is hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, hydroxyl, mercapto, C_1-C_4-alkylthio, nitro, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino, cyano, phenyl, unsubstituted or mono- to trisubstituted by halogen, hydroxyl, amino, mono- or dialkyl-(C_1-C_3)-amino, C_1-C_3-alkyl, C_1-C_3-alkoxy, mercapto or C_1-C_3-alkylthio;
or
a five- or six-membered heteroaromatic ring which contains from one to three nitrogen atoms and/or one sulfur or oxygen

atom and which carries from one to three substituents as described above;

R^2 can furthermore form with the adjacent carbon atom and X a 5- or 6-membered alkylene or alkylidene ring in which, in each case, one or two carbon atoms can be replaced by a hetero atom such as nitrogen, sulfur or oxygen, and which can be mono- to trisubstituted by the following radicals: halogen, nitro, cyano, hydroxyl, mercapto, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy, C_1-C_3-alkylthio, amino, C_1-C_3-alkylamino, C_1-C_3-dialkylamino;

X is nitrogen or CR^{15} where R^{15} is hydrogen or C_1-C_5-alkyl, C_1-C_5-alkoxy, C_1-C_5-alkylthio, nitro, phenyl, hydroxyl, mercapto, halogen, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino or cyano,

or CR^{15} is linked to R^2 to form a 5- or 6-membered ring as described above, and furthermore CR^{15} can form together with R^3 and its adjacent carbon atom a 5- or 6-membered ring as described above;

R^3 can have the same meaning as R^2 and furthermore form together with the adjacent carbon atom and Y a 5- or 6-membered alkylene or alkylidene ring in which, in each case, one or two carbon atoms can be replaced by nitrogen, oxygen or sulfur; the 5- or 6-membered ring can be unsubstituted or mono- to trisubstituted by the following radicals;
halogen, nitro, cyano, hydroxyl, mercapto, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy, C_1-C_3-alkylthio, amino, C_1-C_3-alkylamino or C_1-C_3-dialkylamino;
nitrogen in the 5-membered ring can also be substituted by a formyl or acetyl group; R^2 and R^3 can be identical or different;

Y is nitrogen or CR^{16} where R^{16} is hydrogen, C_1-C_5-alkyl, C_1-C_5-alkoxy, C_1-C_5-alkylthio, nitro, phenyl, hydroxyl, halogen, cyano, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino or mercapto, or CR^{16} forms together with R^3 and its adjacent carbon atom a 5- or 6-membered ring as described above;

R^4 is hydrogen, C_1-C_7-alkyl, C_3-C_7-cycloalkyl; or phenyl or naphthyl which can be substituted by one or more of the following radicals;
halogen, nitro, cyano, hydroxyl, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, phenyl,

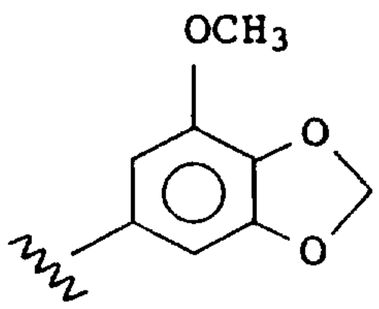
C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino,

R^4 can also be a five- or six-membered heteroaromatic ring which contains one nitrogen, sulfur or oxygen atom and which can carry one or two of the following radicals: halogen, cyano, nitro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenoxy, C_1-C_4-alkylthio, C_1-C_4-alkylamino or C_1-C_4-dialkylamino;

in addition, R^4 and R^5 can be phenyl groups which are connected to each other in the ortho positions by a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2, NH or N-alkyl group;

R^5 is C_1-C_7-alkyl, C_3-C_7-cycloalkyl or phenyl or naphthyl which can be substituted by from one to three of the following radicals; halogen, nitro, cyano, hydroxyl, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, phenyl, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino, where two radicals on adjacent carbon atoms can form together with the latter, connected via an alkylene or alkylidene group, a five- or six-membered ring in which one or more methylene or methylidene [sic] groups can be replaced by oxygen, for example: $-(CH_2)_3-$, $-(CH_2)_4-$, $-CH=CH-O-$, $-O-CH_2-O-$, $-O-(CH_2)_2-O-$, $-CH=CH-CH_2-$ or $-O-CH=CH-O-$;

R^5 can be, for example, the following radicals:



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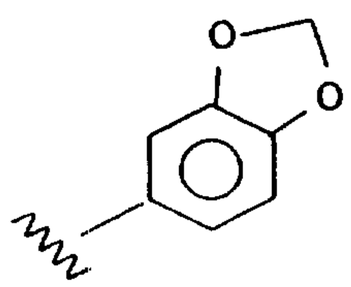

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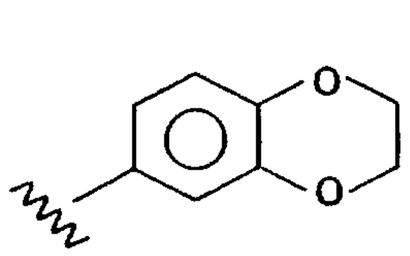

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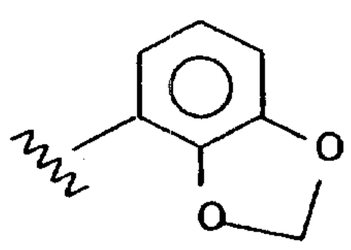

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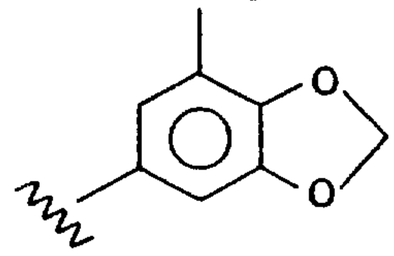

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Furthermore, R^5 can be a five- or six-membered heteroaromatic ring which contains one nitrogen, sulfur or oxygen atom and which can carry one or two of the following radicals: halogen, cyano, nitro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy,

phenoxy, C_1-C_4-alkylthio, C_1-C_4-alkylamino or C_1-C_4-dialkylamino;

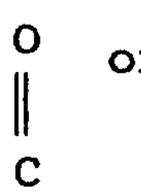
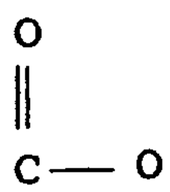
in addition, R^5 can form together with R^4 a tricyclic system as described above, and R^5 can additionally be an unsubstituted or substituted phenyl or heteroaromatic radical as described above which is linked in the ortho position to R^8 to form a 6-membered ring where Q must be a single bond and R^8 must be a CH-R^{17} group;

R^6 is hydrogen, C_1-C_4-alkyl or C_1-C_4-haloalkyl

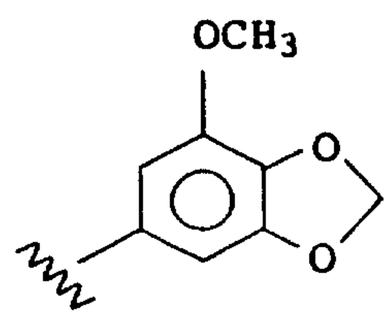
Z is a single bond, oxygen, sulfur, sulfoxide [sic] or sulfonyl;

R^7 is hydrogen or C_1-C_4-alkyl, C_2-C_4-alkylene [sic], C_2-C_4-alkynyl;

Q is a single bond,

a  or  group

R^8 is hydrogen, C_1-C_4-alkyl, C_2-C_4-alkylene [sic], phenyl or benzyl, and R^8 can furthermore be directly connected to R^5 as described above, in which case R^8 is a CH-R^{17} group where R^{17} is hydrogen, C_1-C_4-alkyl, phenyl or phenyl which is mono- to trisubstituted by methoxy, or is one of the following radicals



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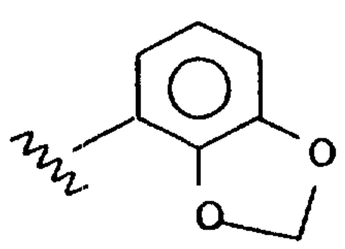

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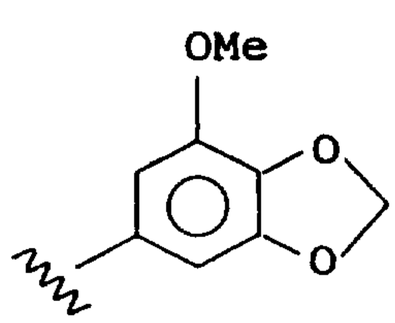

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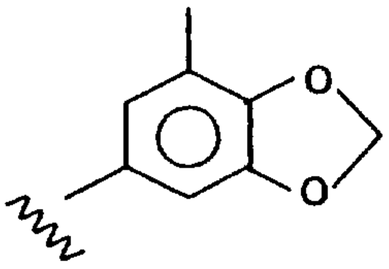

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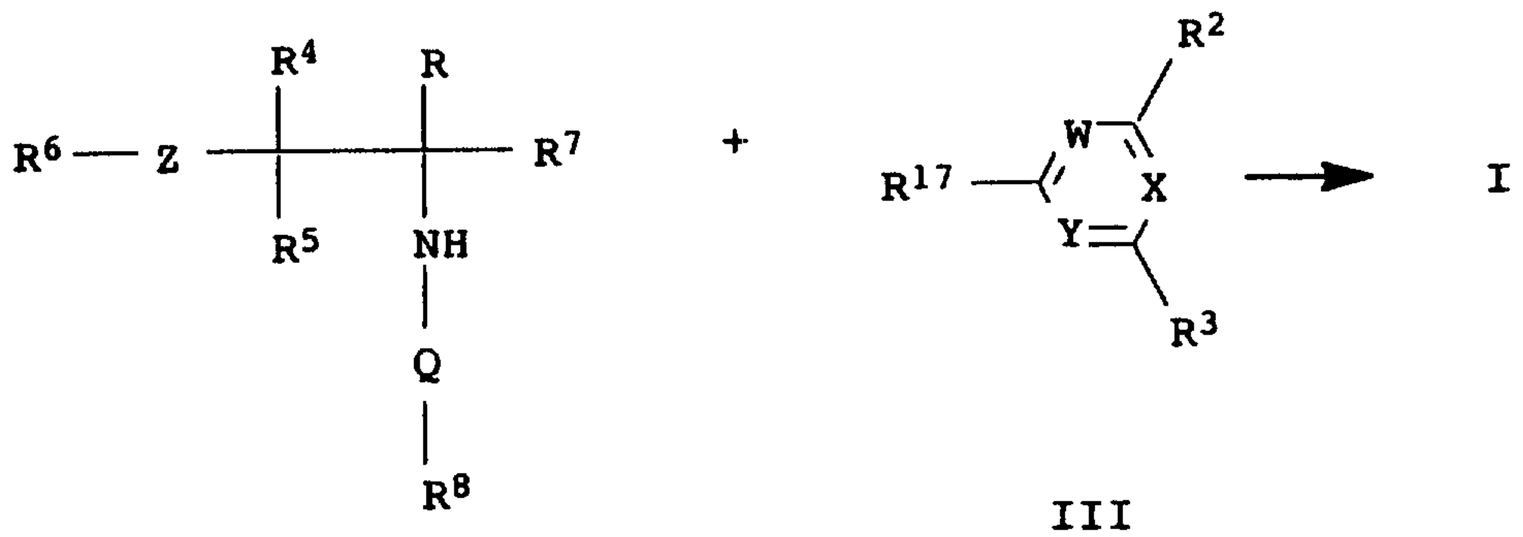
The compounds, as well as the intermediates II for preparing them, may have one or more asymmetrical substituted carbon atoms. Compounds of this type may exist as pure enantiomers or pure

diastereomers or as mixture thereof. The use of an enantiomerically pure compound as active ingredient is preferred.

The invention furthermore relates to the use of the abovementioned amino acid derivatives for producing drugs, in particular for producing inhibitors of endothelin receptors.

The compounds according to the invention are prepared by reacting an amino acid derivative II with a heterocyclic derivative III where R^{17} is halogen or R^{18}-SO_2, where R^{18} can be C_1–C_4-alkyl, C_1–C_4-haloalkyl or phenyl. In this, R is a carboxylic ester or a carboxylic acid. II with R=CO_2H is preferably used. If the preparation of II results in the amino acid ester, this is first hydrolyzed to the amino acid (R=CO_2H) by standard methods of amino acid chemistry.



II III

The reaction preferably takes place in an inert solvent with the addition of a base, as described in the literature, eg. in J. Am. Chem Soc. 98 (1976) 8472-8475 or J. Chem. Soc. Perkin Trans I (1988) 691-696.

Examples of such solvents or diluents are water, aliphatic, alicyclic and aromatic hydrocarbons, which may be chlorinated, such as hexane, cyclohexane, petroleum ether, naphtha, benzene, toluene, xylene, methylene chloride, chloroform, carbon tetrachloride, ethyl chloride and trichloroethylene, ethers such as diisopropyl ether, dibutyl ether, methyl tert-butyl ether, propylene oxide, dioxane and tetrahydrofuran, ketones such as acetone, methyl ethyl ketone, methyl isopropyl ketone and methyl isobutyl ketone, nitriles such as acetonitrile and propionitrile, alcohols such as methanol, ethanol, isopropanol, butanol and ethylene glycol, esters such as ethyl acetate and amyl acetate, amides such as dimethylformamide and dimethylacetamide, sulfoxides and sulfones such as dimethyl sulfoxide and sulfolane, bases such as pyridine, N-methylpyrrolidone, cyclic ureas such as

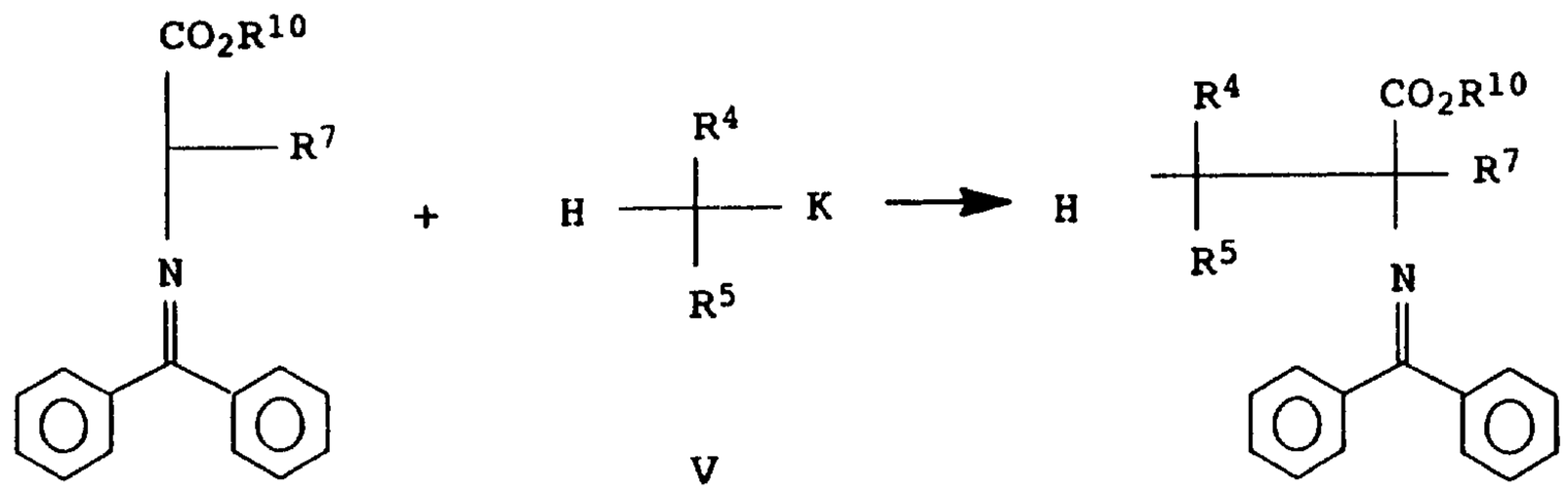
1,3-dimethyl-2-imidazolidinone and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone.

The reaction is moreover preferably carried out at a temperature in the range from 0°C to the boiling point of the solvent or mixture of solvents.

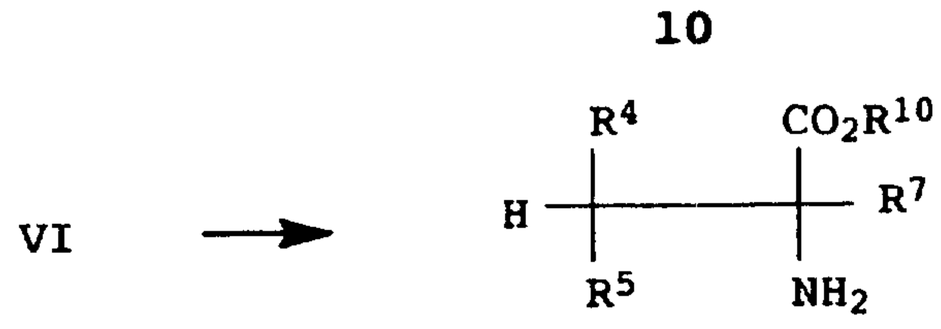
It is possible to use as base an alkali metal or alkaline earth metal hydride such as sodium hydride, potassium hydride or calcium hydride, a carbonate such as alkali metal carbonate, eg. sodium or potassium carbonate, an alkali metal or alkaline earth metal hydroxide such as sodium or potassium hydroxide, an organometallic compound such as butyllithium, or an alkali metal amide such as lithium diisopropylamide.

The invention also relates to those compounds of the formula II which have not been disclosed. They can be prepared in a known manner.

The compounds IIa according to the invention, where R^6=H and Z is a bond, can be prepared, for example, by a method described in Tetrahedron Lett. 30 (1978) 2651, by reacting a suitable imine IV with a compound V with the aid of a base in an inert solvent. This reaction is, where appropriate, carried out in a 2-phase mixture with a phase-transfer catalyst under phase-transfer conditions, for example in methylene chloride and 5-20% strength aqueous sodium hydroxide solution with a quaternary ammonium salt such as tetra-n-butylammonium bisulfate. In this, K means halogen or OR^{19} where R^{19} is methylsulfonyl, toluylsulfonyl or trifluoromethylsulfonyl. The imine VI is subsequently cleaved.



IV VI

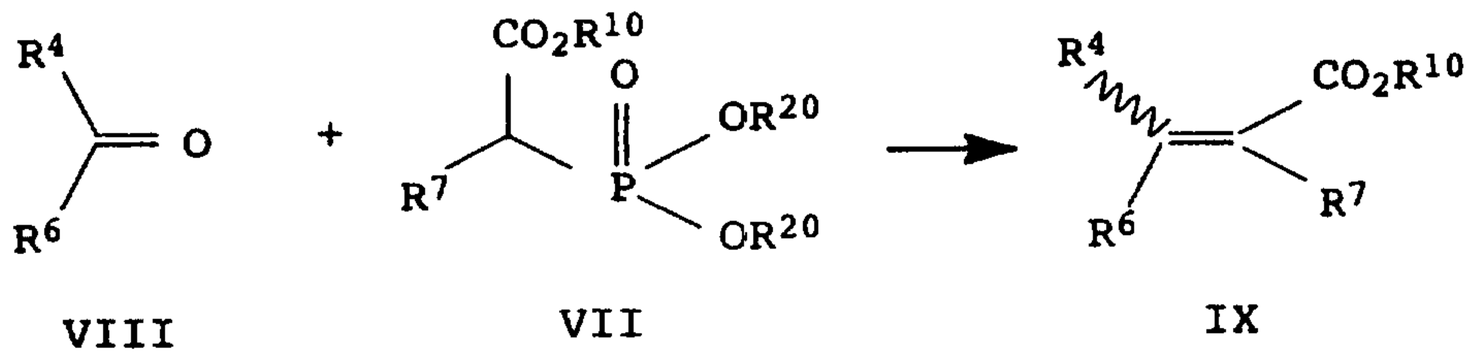


VI IIa

VI can be hydrolyzed to IIa in a suitable solvent using inorganic or organic strong acids such as hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid, perchloric acid, acetic acid, trifluoromethylsulfonic acid or trifluoroacetic acid in various concentrations. Solvents which can be used are water, C_1–C_4-alcohols, acetonitrile, diethyl ether, tetrahydrofuran, dioxane or toluene. As a rule, the hydrolysis takes place in two stages. In the first step, VI is hydrolyzed with dilute acid to the amino acid ester IIa where R^{10} + hydrogen. Thereafter the amino acid ester is hydrolyzed with more concentrated acid or with a strong acid to the amino acid IIa where R^{10}=H.

Reaction of compound IIa with III as described above results in compounds Ia according to the invention where R^6 is hydrogen, R^8 is hydrogen and Z and Q are each a single bond.

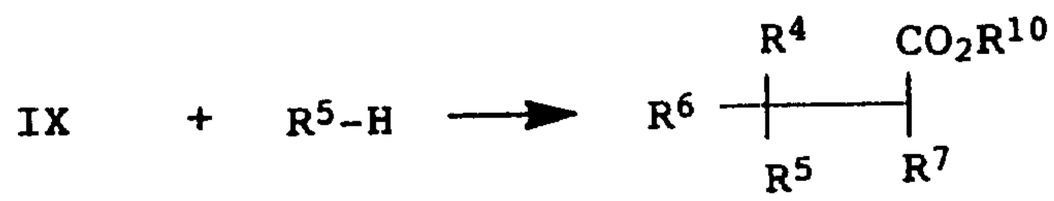
The compounds IIb according to the invention where Z is a bond, R^5 is an aromatic or heteroaromatic radical and R^6 is a C_1–C_4-alkyl group are prepared by reacting a suitable phosphonate compound VII with a carbonyl compound VIII in a Wittig-Horner reaction to give the α,β-unsaturated compound IX



VIII VII IX

where R^{20} is C_1-C_6-alkyl or benzyl.

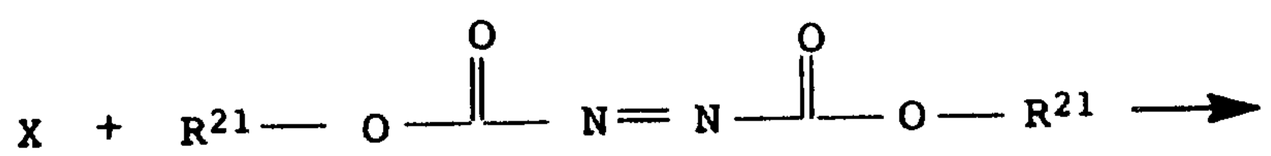
Compound IX can be converted into the carboxylic acid derivative X by a method from Chem. Ber. 64 (1931) 1493 et seq. using R^5–H with the aid of a Friedel-Crafts catalyst such as aluminum trichloride.



IX + R^5-H → R^6-CH(R^5)-C(R^4)(CO_2R^{10})-CH(R^7)

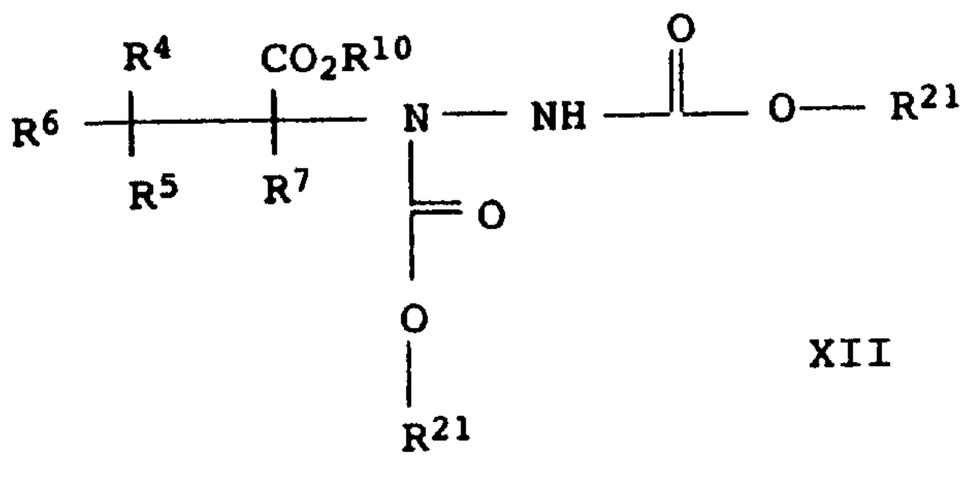
X

Compounds X can be converted by known methods into hydrazino acid derivatives XII as described, for example, in J. Am. Chem. Soc., 108 (1986) 6395-6397. The aminating reagent used is dialkyl azodicarboxylate XI where R^{21} is 2,2-dimethylethyl or benzyl.



X + R^{21}-O-C(=O)-N=N-C(=O)-O-R^{21} →

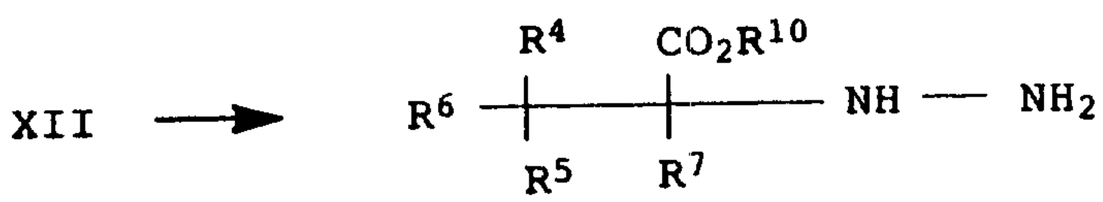
XI



R^6-CH(R^5)-C(R^4)(CO_2R^{10})-CH(R^7)-N(-C(=O)-O-R^{21})-NH-C(=O)-O-R^{21}

XII

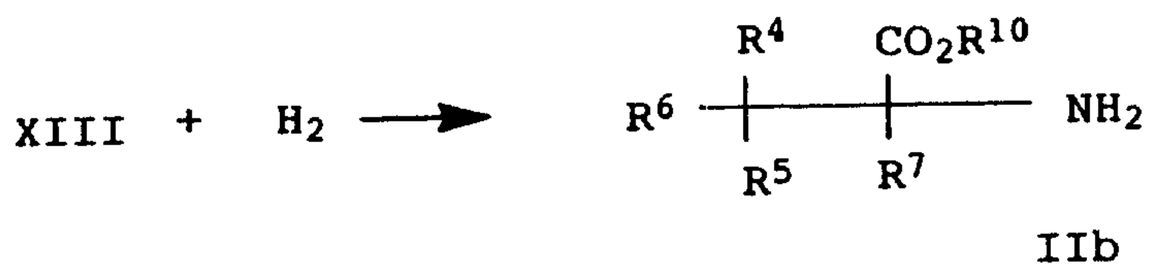
Hydrolysis of XII with a strong inorganic or organic acid in a suitable solvent as described above leads to the α-hydrazino carboxylic acid derivative XIII. If R^{21} is benzyl, the conversion of XII into XIII can also take place by hydrogenolysis with hydrogen and a suitable catalyst such as palladium on active carbon of various concentrations, for example 10% palladium on carbon.



XII → R^6-CH(R^5)-C(R^4)(CO_2R^{10})-CH(R^7)-NH-NH_2

XIII

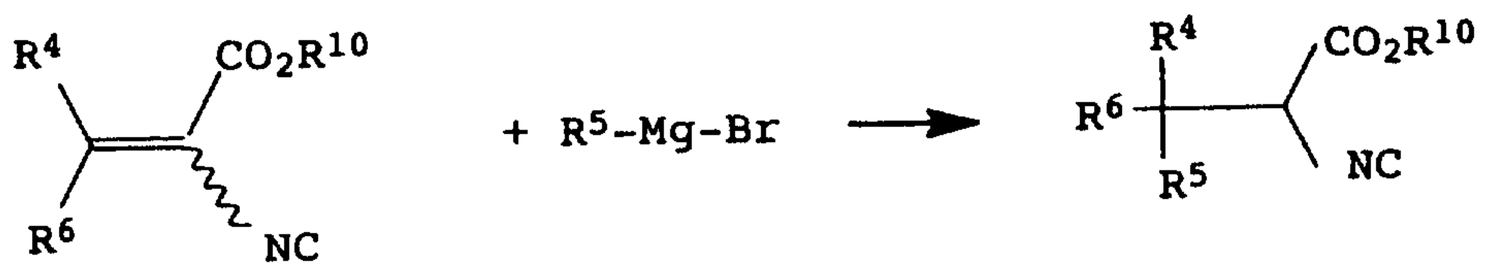
α-Hydrazino carboxylic acid derivatives XIII can be reduced with hydrogen under pressure, eg. 10-50 bar, with a suitable catalyst, eg. Raney nickel, to the α-amino acid derivatives IIb.



IIb

Compounds IIb can be reacted with III to give the compounds Ib according to the invention as described above.

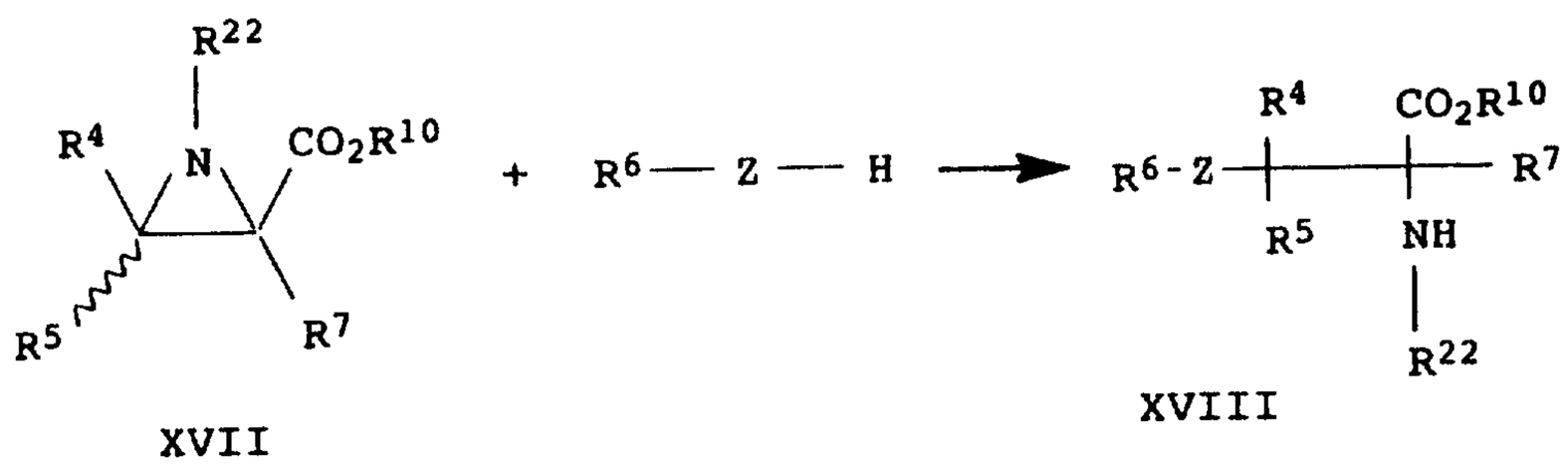
Compounds IIb can also be prepared by reacting a compound XIV with a Grignard compound XV, and hydrolyzing the product XVI with acid to IIb, similar to the description in Liebigs Ann. (1977) 1174-1182:



XIV XV XVI

IIb

The compounds IIc according to the invention where R^6 is C_1-C_4-alkyl, and Z is oxygen, sulfur, S=O or SO_2, can be prepared by opening a suitable aziridine XVII with an alcohol or thiol R^6-Z-H to give XVIII.

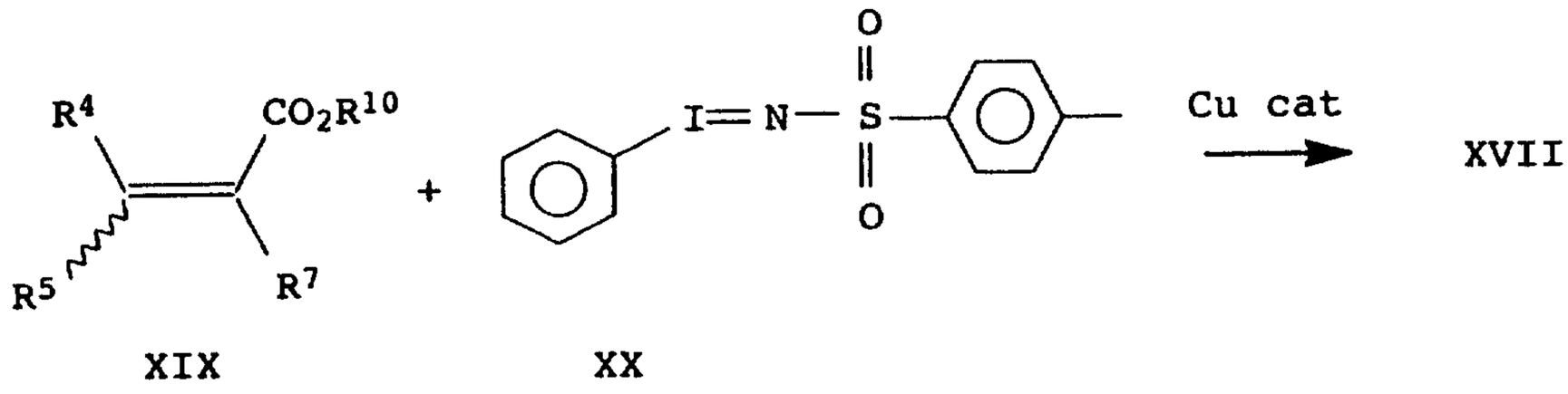


XVII XVIII

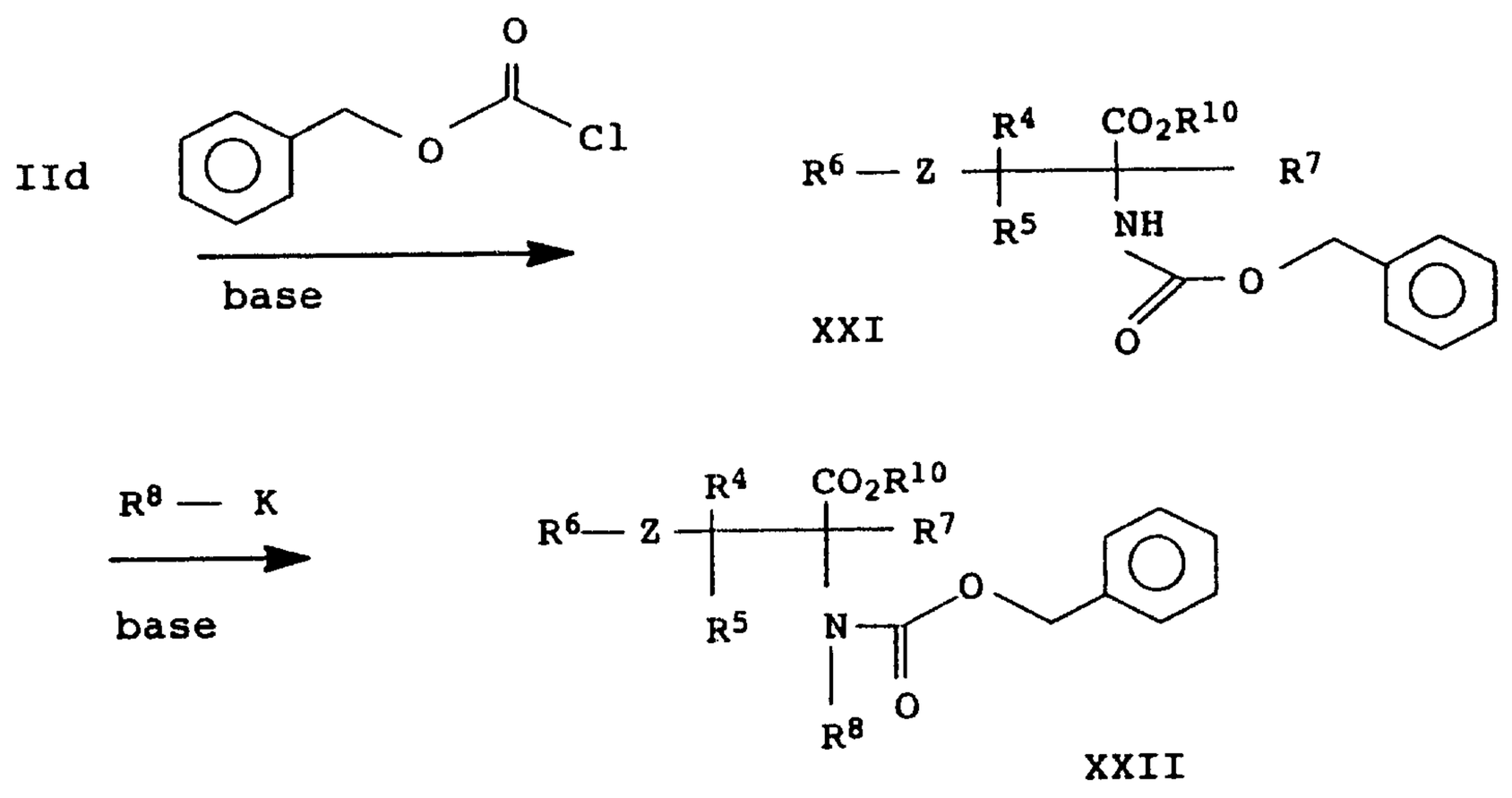
This method is described, for example, in J. Chem. Soc. Perkin Trans. II (1981) 121-126. Subsequent oxidation, eg. with meta-chloroperbenzoic acid in a suitable solvent, in the case where Z=sulfur provides the corresponding compounds XVIII with Z=SO or SO_2 depending on the molar ratio of the components. R^{22} is hydrogen or a suitable protective group such as benzyl, benzyloxycarbonyl, tert-butyloxycarbonyl. If R^{22} is hydrogen, then XVIII corresponds to IIc. When R^{22} ≠ hydrogen, the protective group

must be removed by known methods of hydrolysis, with addition of acid, or hydrogenolysis with a suitable catalyst to result in compound IIe in this way. The compounds IIc according to the invention can be reacted as described above with III to give Ic.

Compounds XVII, which are likewise according to the invention, can be prepared by reacting α,β-unsaturated carbonyl compounds XIX which are known or have been prepared by known methods with an aminating reagent XX and a suitable catalyst, for example as disclosed in J. Org. Chem. 56 (1991) 6744-6.

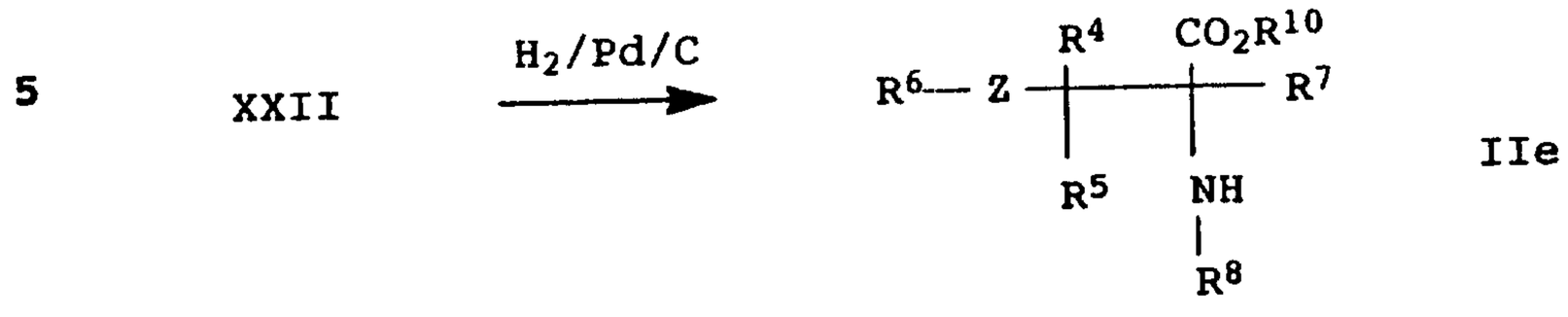


The compounds Id according to the invention where Q is a bond and R^8 is not hydrogen can be prepared by converting an amino acid derivative IId (Q is a bond and R^8 is hydrogen) by known methods for example into an N-benzyloxycarbonyl derivative XXI and reacting the latter



in an inert solvent, eg. tetrahydrofuran, with a strong base, eg. potassium tert-butoxide, and an alkylating agent R^8-K where K is normally halogen or sulfate. The derivative XXII resulting from this can be deprotected by known methods to give the amino compound IIe, for example by eliminating the benzyloxycarbonyl

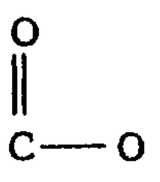
group with hydrogen with catalysis by palladium/active carbon in an inert solvent.

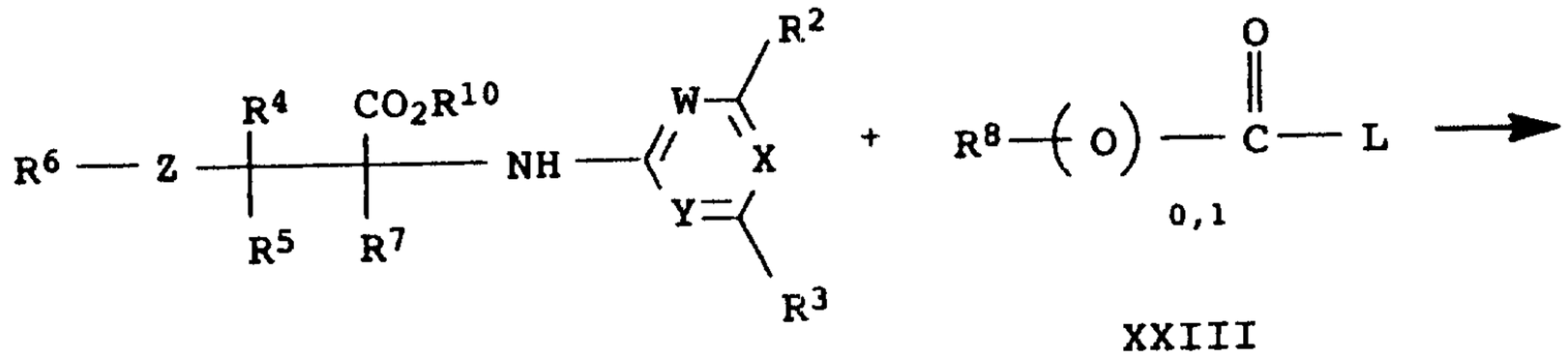


XXII IIe

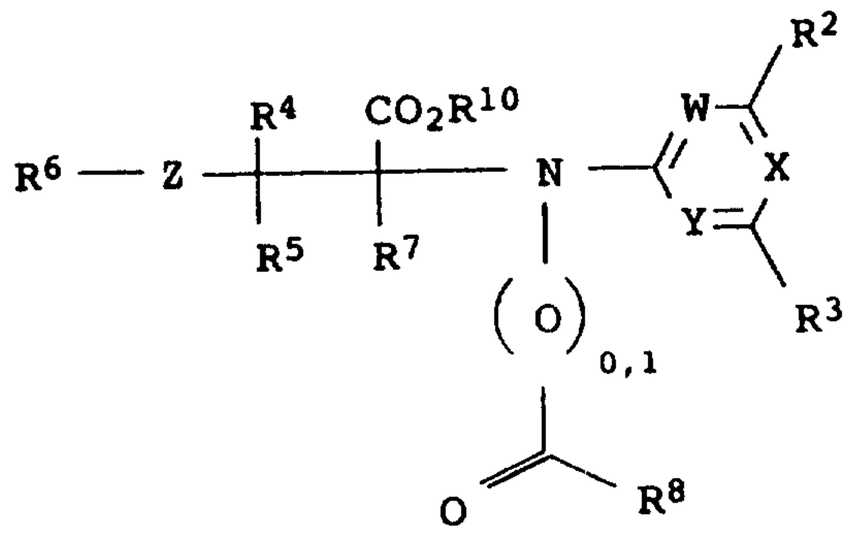
IIe is then reacted with III to give compounds Id as described above.

The compounds Ie according to the invention where Q is a  or

 group can be prepared, for example, by reacting compounds Ia–d with XXIII under basic conditions in an inert solvent to give Ie.



Ia-d XXIII

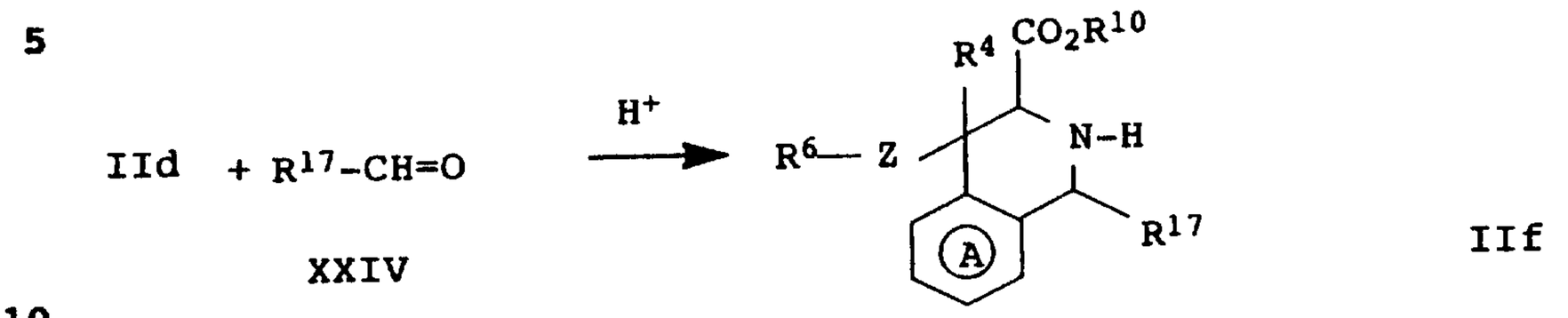


Ie

In this, L is halogen, OR^{23} where R^{23} is one of the following radicals:
C_1-C_4-alkyl, benzyl, succinimidyl or 2,4,5-trichlorophenyl;
L can also be azido, p-tolylsulfonyl, methylsulfonyl, trifluoromethylsulfonyl or an anhydride moiety.

The compounds If according to the invention where R^5 is linked to R^8 can be prepared from the tetrahydroisoquinoline derivatives IIf, which in turn can be prepared from the amino acid

derivatives IId by reacting with aldehydes of the structure XXIV in the presence of acid, eg. hydrochloric acid or sulfuric acid, similar to Synthesis (1990) 550-556.



IIf is then reacted with III to give compound If as described above.

Compounds of the formula I can be obtained in enantiomerically pure form by starting from enantiomerically pure compounds II which can be prepared in enantiomerically pure and, where appropriate, diastereomerically pure form by classical racemate resolution or by enantioselective syntheses (eg. Pure Appl. Chem. 55 (1983) 1799 et seq.; Helv. Chim. Acta 71 (1988) 224 et seq.; J. Am. Chem. Soc, 110 (1988) 1547-1557; Chem. Eng. News (1989) 25-27), and reacting these compounds II with III as described above. Another possibility for obtaining enantiomerically pure compounds of the formula I is classical racemate resolution of racemic or diastereomeric compounds I with suitable enantiomerically pure bases such as brucine, strychnine, quinine, quinidine, cinchonidine, cinchonine, yohimbine, morphine, dehydroabietylamine, ephedrine (-), (+), deoxyephedrine (+), (-), threo-2-amino-1-(p-nitrophenyl)-1,3-propanediol (+), (-), threo-2-(N,N-dimethylamino)-1-(p-nitrophenyl)-1,3-propanediol (+), (-) threo-2-amino-1-phenyl-1,3-propanediol (+), (-), α-methylbenzylamine (+), (-), α-(1-naphthyl)ethylamine (+), (-), α-(2-naphthyl)ethylamine (+), (-), aminomethylpinone, N,N-dimethyl-1-phenylethylamine, N-methyl-1-phenylethylamine, 4-nitrophenylethylamine, pseudoephedrine, norephedrine, norpseudoephedrine, amino acid derivatives and peptide derivatives.

Preferred compounds of the formula I, both as pure enantiomers and pure diastereomers or as mixture thereof, are those in which the substituents have the following meanings:

R is a carboxylic acid, a carboxylic acid salt or a group which can be hydrolyzed to a carboxylic acid, as described above.

R^2 is hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, nitro, C_1-C_4-alkoxy, C_1-C_5-alkylthio, cyano, amino, methylamino, hydroxyl or dimethylamino;

W is nitrogen, C-NO_2, also CH when at least one of the radicals R^2, R^3, R^{15} and R^{16} is a nitro group;

X is nitrogen or CR^{15} where R^{15} is hydrogen, C_1–C_4-alkyl, C_1–C_4-alkoxy, nitro, cyano, halogen or phenyl, or CR^{15} forms with R^3 and the adjacent carbon atom a 5- or 6-membered alkylene or alkylidene ring in which one or two carbon atoms can be replaced by a hetero atom such as nitrogen, oxygen or sulfur, and which can be mono- or disubstituted by a C_1–C_3-alkyl (or C_1–C_3-alkoxy group); nitrogen in a 5-membered ring may additionally be substituted by a CHO or $COCH_3$ group;

R^3 can have the same meaning as R^2 and additionally form with X and the adjacent carbon atom an unsubstituted or substituted 5- or 6-membered ring as described above; R^3 can furthermore form with the adjacent carbon atom and Y a 5- or 6-membered alkylene or alkylidene ring in which one or two carbon atoms can be replaced by nitrogen, oxygen or sulfur and which can be mono- or disubstituted by a C_1–C_3-alkyl or C_1–C_3-alkoxy group, and a nitrogen atom in a 5-membered ring can be substituted by a CHO or $COCH_3$ group;

R^4 has the meaning of hydrogen, C_1–C_6-alkyl, C_3–C_7-cycloalkyl or phenyl which can be substituted by one or more of the following radicals: halogen, C_1–C_4-alkyl, C_1–C_4-alkoxy, phenyl, furthermore R^4 and R^5 can be phenyl groups which are connected to each other in the ortho positions by a direct linkage, a CH_2 group, a CH_2–CH_2 group or an oxygen atom;

R^5 can have the same meaning as R^4 apart from hydrogen and C_1–C_6-alkyl, R^5 can additionally be phenyl which can be substituted exclusively or in addition to the abovementioned radicals by two radicals on adjacent carbon atoms, which together represent a 1,3-dioxomethylene or 1,4-dioxoethylene group and form with the adjacent carbon atoms a 5- or 6-membered ring;

R^6 is hydrogen or C_1–C_4-alkyl;

Z is a single bond, oxygen or sulfur;

R^7 is hydrogen or C_1–C_4-alkyl;

Q is single bond, a carbonyl group or an oxycarbonyl group;

R^8 is hydrogen or C_1–C_4-alkyl.

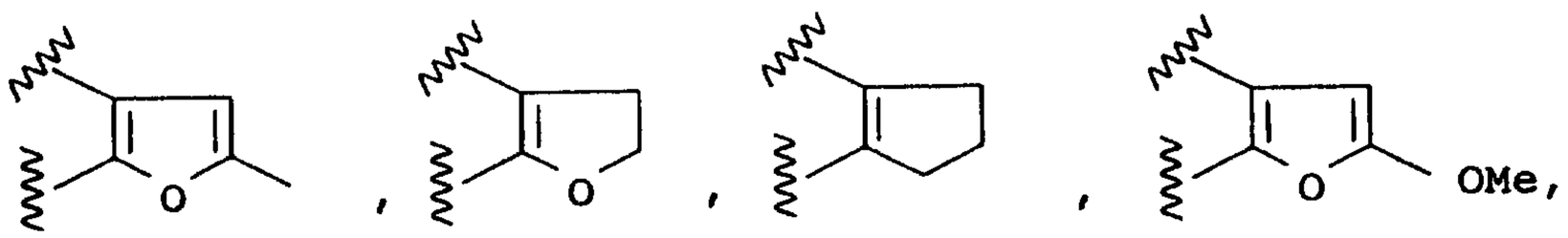
Particularly preferred compounds of the formula I, both as pure enantiomers or pure diastereomers or as mixture thereof, are those in which the substituents have the following meanings:

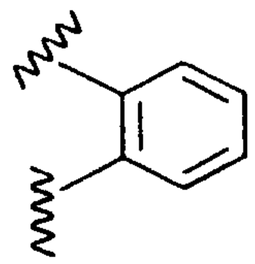
R is a carboxylic acid, a carboxylic acid salt or a group which can be hydrolyzed to a carboxylic acid, as described above;

R^2 is hydrogen, chlorine, methyl, ethyl, CF_3, nitro, methoxy, ethoxy, hydroxyl, methylthio, amino, N-methylamino or dimethylamino;

W is nitrogen;

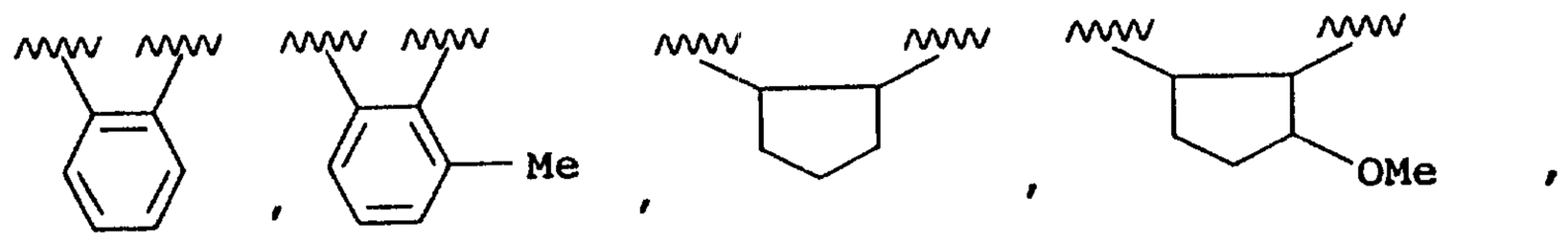
X is nitrogen or CR^{15} where R^{15} is hydrogen, methyl, nitro or cyano, or CR^{15} forms with R^3 and the adjacent carbon atom a 5- or 6-membered alkylene or alkylidene ring in which one carbon atom can be replaced by oxygen, and which can be substituted by a methyl or methoxy group; the 5- or 6-membered alkylene or alkylidene ring can have the following structures, for example:

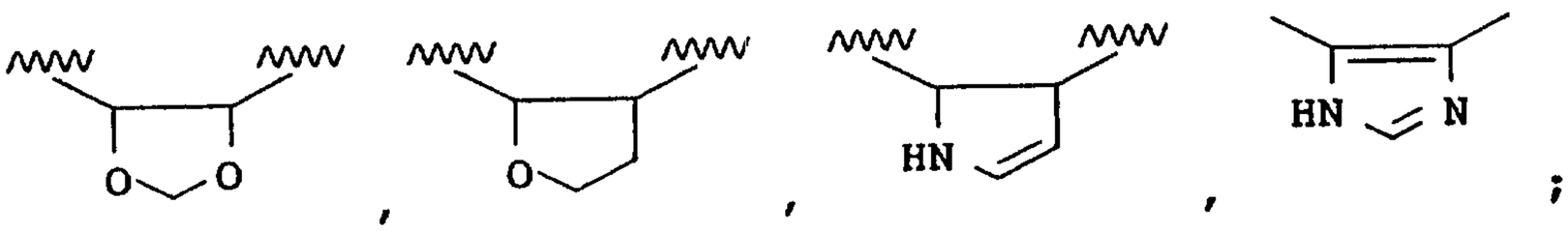



;

R^3 can have the same meaning as R^2 and additionally form with X and the adjacent carbon atom an unsubstituted or substituted 5- or 6-membered ring as described above; R^3 can furthermore form with the adjacent carbon atom a substituted or unsubstituted 5- or 6-membered alkylene or alkylidene ring in which one or two carbon atoms can be replaced by nitrogen or

oxygen and which can be substituted by a methyl or methoxy group; examples of such alkylene or alkylidene rings are:





R^4 has the meaning of hydrogen, methyl, ethyl, n-propyl, 1-methylethyl, cyclohexyl, or phenyl which can be substituted by one or two methoxy groups, furthermore R^4 and R^5 can be phenyl groups which are connected to each other in the ortho positions by a direct linkage, a CH_2 or CH_2–CH_2 group;

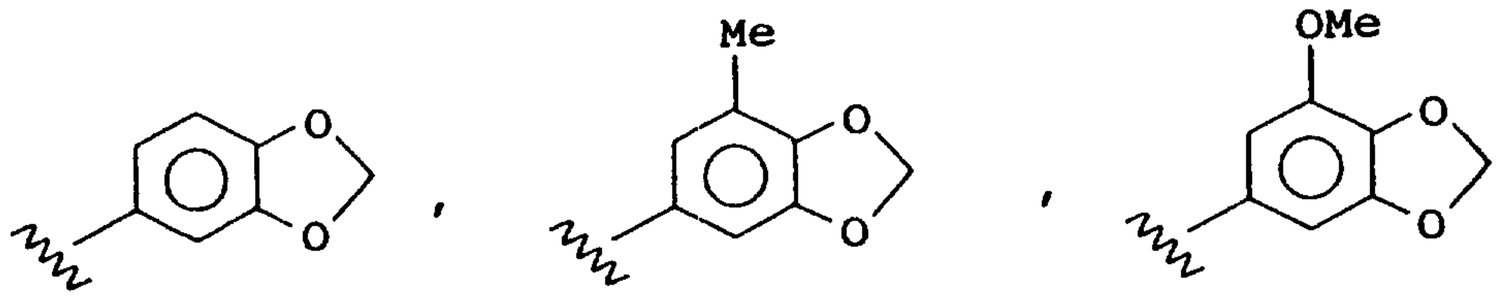
R^5 is cyclohexyl or phenyl which can be substituted by phenyl, one to three methoxy groups, or exclusively or in addition to a methoxy group by two radicals on adjacent carbon atoms which together represent a 1,3-dioxomethylene or 1,4-dioxoethylene group and form with the adjacent carbon atoms a 5- or 6-membered ring, R^5 can additionally be an unsubstituted or substituted phenyl ring which is linked in the ortho position to R^8 to form a 6-membered ring when Q is a single bond and R^8 is a CH–R^{17} group;

R^6 is hydrogen, methyl, ethyl, n-propyl or 1-methylethyl;

R^7 is hydrogen or methyl;

Q is a single bond, a carbonyl group or an oxycarbonyl group;

R^8 is hydrogen, methyl or 1,1-dimethylethyl, R^8 can additionally be directly connected to R^5 as described above when R^8 is a CH–R^{17} group in which R^{17} is hydrogen, methyl, ethyl, phenyl or phenyl which is mono- to trisubstituted by methoxy, or one of the following radicals:



The compounds of the present invention provide a novel therapeutic potential for the treatment of hypertension, pulmonary hypertension, myocardial infarct, angina pectoris, acute kidney failure, renal insufficiency, cerebral vasospasms, cerebral ischemia, subarachnoid hemorrhages, migraine, asthma, atherosclerosis, endotoxic shock, endotoxin-induced organ failure, intravascular coagulation, restenosis following angioplasty, benign prostate hyperplasia, ischemic kidney failure and that caused by intoxication, and hypertension.

The good effect of the compounds can be shown in the following tests:

Receptor binding studies

Cloned human ET_A receptor-expressing CHO cells and guinea-pig cerebellar membranes with > 60% ET_B by comparison with ET_A receptors were used for the binding studies.

Membrane preparation

The ET_A receptor-expressing CHO cells were grown in F_{12} medium containing 10% fetal calf serum, 1% glutamine, 100 U/ml penicillin and 0.2% streptomycin (Gibco BRL, Gaithersburg, MD, USA). After 48 h, the cells were washed with PBS and incubated with 0.05% trypsin-containing PBS for 5 min. The F_{12} medium was then neutralized, and the cells were collected by centrifugation at 300 x g. To lyse the cells, the pellet was briefly washed with lysis buffer (5 mM tris-HCl, pH 7.4 with 10% glycerol) and then incubated at a concentration of 10^7 cells/ml of lysis buffer at 4°C for 30 min. The membranes were centrifuged at 20,000 x g for 10 min, and the pellet was stored in liquid nitrogen.

Guinea-pig cerebella were homogenized in a Potter-Elvejhem homogenizer and obtained by differential centrifugation at 1,000 x g for 10 min and repeated centrifugation of the supernatant at 20,000 x g for 10 min.

Binding assays

For the ET_A and ET_B receptor binding assays, the membranes were suspended in incubation buffer (50 mM tris-HCl, pH 7.4 with 5 mM $MnCl_2$, 40 µg/ml bacitracine and 0.2% BSA) at a concentration of 50 µg of protein per assay mixture, and incubated with 25 pM ^{125}I-ET_1 (ET_A receptor assay) or 25 pM ^{125}I-RZ_3 (ET_B receptor assay) at 25°C in the presence and absence of test substance. The non-specific binding was determined using 10^{-7} M ET_1. After 30 min, the free and bound radioligand were separated by filtration through GF/B glass fiber filters (Whatman, England) on a Skatron cell collector (Skatron, Lier, Norway), and the filters were washed with ice-cold tris-HCl buffer, pH 7.4 with 0.2% BSA. The radioactivity collected on the filters was quantified using a Packard 2200 CA liquid scintillation counter.

Functional in vitro assay system for searching for endothelin receptor (subtype A) antagonists

This assay system is a functional, cell-based assay for endothelin receptors. When certain cells are stimulated with endothelin 1 (ET1) they show an increase in the intracellular calcium concentration. This increase can be measured in intact cells loaded with calcium-sensitive dyes.

Fibroblasts which had been isolated from rats and in which an endogenous endothelin receptor of subtype A had been detected were loaded with the fluorescent dye Fura 2-an as follows: After trypsinization, the cells were resuspended in buffer A (120 mM NaCl, 5 mM KCl, 1.5 mM $MgCl_2$, 1 mM $CaCl_2$, 25 mM HEPES, 10 mM glucose, pH 7.4) to a density of 2 x 10^6/ml and incubated with Fura 2-am (2 µM), Pluronic F-127 (0.04%) and DMSO (0.2%) at 37°C in the dark for 30 min. The cells were then washed twice with buffer A and resuspended at 2 x 10^6/ml.

The fluorescence signal from 2 x 10^5 cells per ml with Ex/Em 380/510 was recorded continuously at 30°C. To the cells were added the test substances and after an incubation time of 3 min ET1. The maximum change in fluorescence was determined over 30 minutes. The response of the cells to ET1 without previous addition of a test substance served as control and was set equal to 100%.

In vivo testing of ET antagonists

Male SD rats weighing 250 - 300 g were anesthetized with amobarbital, artifically ventilated, vagotomized and pithed. The carotid artery and jugular vein were cathetized.

Intravenous administration of 1 µg/kg ET1 to control animals leads to a marked rise in blood pressure which persists for a lengthy period.

The test compounds were injected i.v. (1 ml/kg) into the test animals 5 min before ET1 administration. To determine the ET-antagonistic properties, the rise in blood pressure in the test animals was compared with that in the control animals.

Sudden death of mice induced by endothelin-1

The principle of the test is the inhibition of the sudden heart death of mice caused by endothelin, probably owing to constriction of the coronary vessels, by pretreatment with endothelin receptor antagonists. Intravenous injection of 10 nmol/kg endothelin in a volume of 5 ml/kg of body weight is followed within a few minutes by the death of the animals.

The lethal dose of endothelin-1 is checked in each case on a small group of animals. Intravenous administration of the test substance is usually followed after 5 min by the injection of endothelin-1 which was lethal in the reference group. The times before administration increase with other modes of administration, possibly up to several hours.

The survival rate is recorded, and effective doses which protect 50% of the animals from endothelin-induced heart death for 24 h or longer (ED 50) are determined.

Functional test on vessels for endothelin receptor antagonists

First a contraction is induced by K^+ in segments of rabbit aorta after a previous tension of 2 g and a relaxation time of 1 h in Krebs-Henseleit solution at 37°C and pH 7.3 - 7.4. Washing out is followed by construction of an endothelin dose-effect plot up to the maximum.

Potential endothelin antagonists are administered to other preparations of the same vessel 15 min before starting the endothelin dose-effect plot. The effects of endothelin are calculated as a % of the K^+-induced contraction. Effective endothelin antagonists result in a shift in the endothelin dose-effect plot to the right.

The compounds according to the invention can be administered orally or parenterally (subcutaneously, intravenously, intramuscularly, intraperitoneally) in a conventional way. Administration

can also take place with vapors or sprays through the nasopharyngeal space.

The dosage depends on the age, condition and weight of the patient and on the mode of administration. As a rule, the daily dose of active ingredient is about 0.5 - 50 mg/kg of body weight on oral administration and about 0.1 - 10 mg/kg of body weight on parenteral administration.

The novel compounds can be used in conventional solid or liquid pharmaceutical forms, eg. as uncoated or (film-)coated tablets, capsules, powders, granules, suppositories, solutions, ointments, creams or sprays. These are produced in a conventional way. For this purpose the active ingredients can be processed with conventional pharmaceutical aids such as tablet binders, bulking agents, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, release-slowing agents, antioxidants and/or propellent gases (cf. H. Sucker et al.: Pharmazeutische Technologie, Thieme-Verlag, Stuttgart, 1991). The administration forms obtained in this way normally contain from 0.1 to 90% by weight of active ingredient.

Synthesis examples

Example 1

Di(3-methoxyphenyl)methyl bromide

22.53 g (92.9 mmol) of di(m-methoxyphenyl)methyl alcohol were dissolved in 200 ml of diethyl ether and, under a nitrogen atmosphere, 28.76 g (138.3 mmol) of thionyl bromide dissolved in 20 ml of diethyl ether were added dropwise. After 6 hours at room temperature, the mixture was poured into ice-water, and the organic phase was separated off, washed with water and saturated $NaHCO_3$ solution, then dried with $MgSO_4$ and concentrated. 27.73 g (97.8%) of crude product were obtained and were immediately reacted further.

Example 2

Methyl 2-N-(diphenylmethylene)amino-3,3-di(3-methoxyphenyl)-propionate [sic]

19.05 g (75.2 mmol) of N-diphenylmethylenylglycine [sic] methyl ester were dissolved in 200 ml of THF and, at -78°C under an argon atmosphere, 75 ml of a 1.5 molar solution of LDA in THF were slowly added dropwise. After 45 minutes, 27.73 g (90.3 mmol) of

di(3-methoxyphenyl)methyl bromide in 60 ml of THF were added dropwise. After 90 minutes, the mixture was allowed to reach room temperature and was then stirred for 22 hours. Then 20 ml of phosphate buffer were added, the THF was stripped off under reduced pressure, and the residue was extracted three times with ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. 43.3 g of crude product were obtained and were immediately reacted further.

Example 3

Methyl 2-amino-3,3-di(3-methoxyphenyl)propionate

43.3 g (75.2 mmol) of methyl 2-N-(diphenylmethylene)amino-3,3-di(3-methoxyphenyl)propionate [sic] (crude product) were dissolved in 1 l of THF and, after addition of 506 ml of 0.5 normal hydrochloric acid, stirred at room temperature for 90 minutes. After the THF had been stripped off under reduced pressure, the aqueous residue was extracted with ethyl acetate. The aqueous phase was then made alkaline (pH 9-10) with 25% strength ammonia solution.

The aqueous phase was then extracted four times with ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. 14.27 g (60.1%) of product were obtained.

Example 4

2-Amino-3,3-di(3-methoxyphenyl)propionic acid

6.0 g (19.0 mmol) of methyl 2-amino-3,3-di(3-methoxyphenyl)propionate were refluxed in 140 ml of 6 normal hydrochloric acid for 6 hours. The mixture was then cooled to 0°C, and the precipitate was filtered off, washed with water and dried. The solid was then dissolved in 50 ml of ethanol, 20 ml of propene oxide were added and the mixture was refluxed for 30 minutes. After cooling, the precipitate was filtered off, washed with ethanol and dried. 2.20 g (38.4%) of a white powder of melting piont 168-173°C were obtained.

Example 5

3,3-Di(3-methoxyphenyl)-2-(4,6-dimethoxy-2-pyrimidinylamino)-propionic acid

2.20 g (7.3 mmol) of 2-amino-3,3-di(3-methoxyphenyl)propionic acid, 0.66 g (3.04 mmol) of 4,6-dimethoxy-2-methylsulfonylpyrimidine [sic] and 0.39 g (3.65 mmol) of sodium carbonate were introduced into a mixture of 16 ml of DMF and 16 ml of water and stirred at 80°C for 10 hours. Water and ethyl acetate were then added to the reaction mixture. The aqueous phase was acidified with 6 normal hydrochloric acid and extracted three times with ethyl acetate. Drying with $MgSO_4$ and concentration resulted in the crude product, which was chromatographed on silica gel with dichloromethane/methanol (50:1). 0.455 g (34.1%) of a white powder of melting point 58-66°C was obtained.

Example 6

3,3-Diphenyl-2-(4,6-dimethyl-2-pyrimidinylamino)propionic acid

2.60 g (10.8 mmol) of 2-amino-3,3-diphenylpropionic acid and 0.64 g (4.5 mmol) of 2-chloro-4,6-dimethylpyrimidine were introduced into a mixture of 16 ml of DMF and 16 ml of water, 0.57 g (5.4 mmol) of sodium carbonate was added and the mixture was stirred at 80°C for 24 hours. Then 100 ml of ethyl acetate and a little water were added, and the phases were separated. The aqueous phase was acidified (pH 1-2) with 6 normal hydrochloric acid. The resulting precipitate was filtered off with suction and washed with ethyl acetate, then dried. 0.30 g (19.2%) of a white powder of melting point 172-174°C was obtained.

Example 7

2-(4,6-Dimethoxy-2-triazinylamino)-2-(9-fluorenyl)acetic acid

2.29 g (9.6 mmol) of 2-amino-2-(9-fluorenyl)acetic acid, 0.70 g (4.0 mmol) of 4,6-dimethoxy-2-chlorotriazine and 0.51 g (4.8 mmol) of sodium carbonate were introduced into a mixture of 16 ml of DMF and 16 ml of water and stirred at 80°C for 13 hours. Then ethyl acetate and water were added and the phases were separated. The aqueous phase was acidified with 6 normal HCl and extracted three times with ethyl acetate. The organic phases were dried with $MgSO_4$ and concentrated. The crude product was chromatographed on silica gel with ethyl acetate/n-heptane (1:1). 0.44 g (29.1%) of a white powder was obtained; R_F = 0.135, melting point 182-186°C.

Example 8

2-(3-Nitro-6-methoxy-2-pyridinylamino)-3,3-diphenylpropionic acid

2.50 g (10.4 mmol) of 2-amino-3,3-diphenylpropionic acid, 0.84 g (4.3 mmol) of 2-chloro-3-nitro-6-methoxypyridine and 0.55 g (5.2 mmol) of sodium carbonate were introduced into 18 ml of DMF and 18 ml of water, and the mixture was stirred at 80°C for 5 hours. Ethyl acetate and water were then added, and the phases were separated. The aqueous phase was acidified with 6 normal hydrochloric acid and extracted three times with ethyl acetate. After drying with $MgSO_4$ and concentration under reduced pressure, the crude product was recrystallized from isopropanol. 0.34 g (20.1%) of a yellow powder of melting point 172-180°C was obtained.

The examples listed in following Tables 1-5 can be prepared by the methods described at the outset.

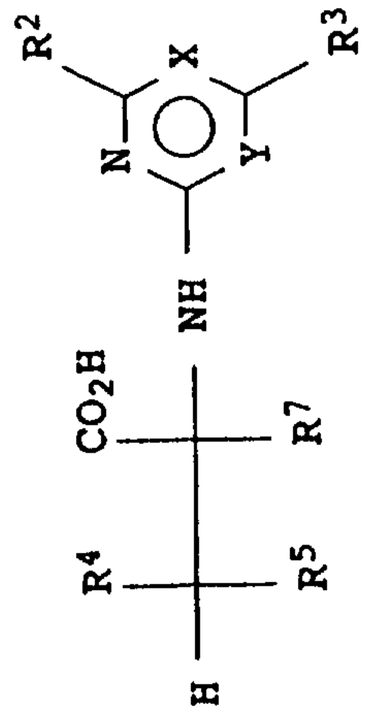


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Table 1

No.	R^4	R^5	R^7	X	R^2	R^3	Y	M.p. [°C]
I-1	H	Phenyl	H	CH	Me	Me	N	
I-2	H	Phenyl	H	CH	OMe	Me	N	
I-3	H	Phenyl	H	CH	Me	Me	N	
I-4	H	Phenyl	H	CH	Me	Et	N	
I-5	H	Phenyl	H	CH	Et	Et	N	
I-6	H	Phenyl	H	CH	CF_3	Me	N	
I-7	H	Phenyl	H	CH	CF_3	OMe	N	
I-8	H	Phenyl	H	C-$(CH_2)_3$	Me	-	N	
I-9	H	Phenyl	H	C-$(CH_2)_3$	OMe	-	N	
I-10	H	Phenyl	H	C-$(CH_2)_2$	OMe	O	N	
I-11	H	Phenyl	H	N	OMe	OMe	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-12	H	Phenyl	H	OMe	N	Me	N	
I-13	H	Phenyl	H	OMe	N	OMe	N	
I-14	H	Phenyl	Me	OMe	CH	OMe	CH	
I-15	H	Phenyl	Me	OMe	CH	Me	N	
I-16	H	Phenyl	Me	OMe	CH	N=C	N	
I-17	H	Phenyl	H	OMe	N	H	-NH-C	
I-18	H	Phenyl	H	OMe	N	H	$C-NO_2$	
I-19	H	Phenyl	H	OMe	C-Me	OMe	N	
I-20	H	Phenyl	H	OMe	CH	Me	N	188-193
I-21	H	Phenyl	H	H	N	NH_2	CH	
I-22	H	Phenyl	H	H	N	H	N	
I-23	H	Phenyl	H	H	CH	OMe	N	
I-24	Me	Phenyl	H	OMe	CH	OMe	N	
I-25	Me	Phenyl	H	OMe	CH	Me	N	
I-26	Me	Phenyl	H	Me	CH	Me	N	
I-27	Me	Phenyl	H	Me	CH	Et	N	
I-28	Me	Phenyl	H	Et	CH	Et	N	
I-29	Me	Phenyl	H	Me	CH	CF_3	N	
I-30	Me	Phenyl	H	OMe	CH	CF_3	N	
I-31	Me	Phenyl	H	Me	$C-(CH_2)_3-$		N	
I-32	Me	Phenyl	H	OMe	$C-(CH_2)_3-$		N	
I-33	Me	Phenyl	H	OMe	$C-(CH_2)_3-O$		N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-34	Me	Phenyl	H	Me	C-$(CH_2)_3$-O		N	
I-35	Me	Phenyl	H	OMe	N	OMe	N	
I-36	Me	Phenyl	H	OMe	CH	H	N	
I-37	Me	Phenyl	H	OMe	N	OMe	CH	
I-38	Me	Phenyl	H	Cl	N	Me	CH	
I-39	Me	Phenyl	H	Me	N	Me	CH	
I-40	Me	Phenyl	H	OMe	N	N=CH-NH-C		
I-41	Me	Phenyl	H	Cl	N	N=CH-NH-C		
I-42	Me	Phenyl	H	OMe	N	H	$C-NO_2$	
I-43	Me	Phenyl	H	OMe	C-Me	H	N	
I-44	Me	Phenyl	H	Me	C-Me	H	N	
I-45	Me	Phenyl	H	NH_2	N	NH_2	N	
I-46	Me	Phenyl	H	$NHCH_3$	N	$NHCH_3$	N	
I-47	Me	Phenyl	H	SMe	CH	H	N	
I-48	Me	Phenyl	Me	OMe	CH	OMe	N	
I-49	Me	Phenyl	Me	OMe	CH	Me	N	
I-50	Me	Phenyl	Me	Me	CH	Me	N	
I-51	Et	Phenyl	H	OMe	CH	OMe	N	
I-52	Et	Phenyl	H	OMe	CH	Me	N	
I-53	Et	Phenyl	H	Me	CH	Me	N	
I-54	Et	Phenyl	H	Me	CH	Et	N	
I-55	Et	Phenyl	H	Et	CH	Et	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-56	Et	Phenyl	H	Me	CH	CF_3	N	
I-57	Et	Phenyl	H	OMe	CH	CF_3	N	
I-58	Et	Phenyl	H	OMe	CH	H	N	
I-59	Et	Phenyl	H	SMe	CH	H	N	
I-60	Et	Phenyl	H	Et	CH	OMe	N	
I-61	Et	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-62	Et	Phenyl	H	OMe	C-$(CH_2)_3$-		N	
I-63	Et	Phenyl	H	Me	C-$(CH_2)_2$-O		N	
I-64	Et	Phenyl	H	OMe	C-$(CH_2)_2$-O		N	
I-65	Et	Phenyl	H	OMe	N	OMe	N	
I-66	Et	Phenyl	H	NH_2	N	NH_2	N	
I-67	Et	Phenyl	H	NHMe	N	NHMe	N	
I-68	Et	Phenyl	H	OMe	N	OMe	CH	
I-69	Et	Phenyl	H	Me	N	Me	CH	
I-70	Et	Phenyl	H	Cl	N	Me	CH	
I-71	Et	Phenyl	H	OMe	N	N=CH-NH-C		
I-72	Et	Phenyl	H	Cl	N	N=CH-NH-C		
I-73	Et	Phenyl	H	OMe	N	H	C-NO_2	
I-74	Et	Phenyl	H	OMe	C-Me	H	N	
I-75	Et	Phenyl	H	Me	C-Me	H	N	
I-76	Et	Phenyl	Me	OMe	CH	OMe	N	
I-77	Et	Phenyl	Me	OMe	CH	Me	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-78	Et	Phenyl	Me	Me	CH	Me	N	
I-79	H	4-Methoxyphenyl	H	OMe	CH	OMe	N	
I-80	H-	4-Methoxyphenyl	H	OMe	CH	Me	N	
I-81	H	4-Methoxyphenyl	H	Me	CH	Me	N	
I-82	H	4-Methoxyphenyl	H	Me	CH	Et	N	
I-83	H	4-Methoxyphenyl	H	Et	CH	Et	N	
I-84	H	4-Methoxyphenyl	H	Me	CH	CF_3	N	
I-85	H	4-Methoxyphenyl	H	OMe	CH	CF_3	N	
I-86	H	4-Methoxyphenyl	H	OMe	CH	H	N	
I-87	H	4-Methoxyphenyl	H	SMe	CH	H	N	
I-88	H	4-Methoxyphenyl	H	Et	CH	OMe	N	
I-89	H	4-Methoxyphenyl	H	Me	C-$(CH_2)_3$-		N	
I-90	H	4-Methoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-91	H	4-Methoxyphenyl	H	Me	C-$(CH_2)_2$-O		N	
I-92	H	4-Methoxyphenyl	H	OMe	C-$(CH_2)_2$-O		N	
I-93	H	4-Methoxyphenyl	H	OMe	N	OMe	N	
I-94	H	4-Methoxyphenyl	H	NH_2	N	NH_2	N	
I-95	H	4-Methoxyphenyl	H	NHMe	N	NHMe	N	
I-96	H	4-Methoxyphenyl	H	OMe	N	OMe	CH	
I-97	H	4-Methoxyphenyl	H	Cl	N	Me	CH	
I-98	H	4-Methoxyphenyl	H	OMe	N	N=CH-NH-C		
I-99	H	4-Methoxyphenyl	H	Cl	N	N=CH-NH-C		

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-100	H	4-Methoxyphenyl	H	Me	N	Me	CH	
I-101	H	4-Methoxyphenyl	H	OMe	N	Me	CH	
I-102	H	4-Methoxyphenyl	H	OMe	N	H	C-NO_2	
I-103	H	4-Methoxyphenyl	H	OMe	C-Me	H	N	
I-104	H	4-Methoxyphenyl	H	Me	C-Me	H	N	
I-105	H	4-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-106	H	4-Methoxyphenyl	Me	OMe	CH	Me	N	
I-107	H	4-Methoxyphenyl	Me	Me	CH	Me	N	
I-108	H	3-Methoxyphenyl	H	OMe	CH	OMe	N	
I-109	H	3-Methoxyphenyl	H	OMe	CH	Me	N	
I-110	H	3-Methoxyphenyl	H	Me	CH	Me	N	
I-111	H	3-Methoxyphenyl	H	Me	CH	Et	N	
I-112	H	3-Methoxyphenyl	H	Et	CH	Et	N	
I-113	H	3-Methoxyphenyl	H	Me	CH	CF_3	N	
I-114	H	3-Methoxyphenyl	H	OMe	CH	CF_3	N	
I-115	H	3-Methoxyphenyl	H	OMe	CH	H	N	
I-116	H	3-Methoxyphenyl	H	SMe	CH	H	N	
I-117	H	3-Methoxyphenyl	H	Et	CH	OMe	N	
I-118	H	3-Methoxyphenyl	H	Me	C-$(CH_2)_3$-		N	
I-119	H	3-Methoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-120	H	3-Methoxyphenyl	H	Me	C-$(CH_2)_2$-O		N	
I-121	H	3-Methoxyphenyl	H	OMe	C-$(CH_2)_2$-O		N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-122	H	3-Methoxyphenyl	H	OMe	N	OMe	N	
I-123	H	3-Methoxyphenyl	H	NH_2	N	NH_2	N	
I-124	H	3-Methoxyphenyl	H	NHMe	N	NHMe	N	
I-125	H	3-Methoxyphenyl	H	OMe	N	OMe	CH	
I-126	H	3-Methoxyphenyl	H	Cl	N	Me	CH	
I-127	H	3-Methoxyphenyl	H	OMe	N	N=CH-NH-C		
I-128	H	3-Methoxyphenyl	H	Cl	N	N=CH-NH-C		
I-129	H	3-Methoxyphenyl	H	Me	N	Me	CH	
I-130	H	3-Methoxyphenyl	H	OMe	N	Me	CH	
I-131	H	3-Methoxyphenyl	H	OMe	N	H	$C-NO_2$	
I-132	H	3-Methoxyphenyl	H	OMe	C-Me	H	N	
I-133	H	3-Methoxyphenyl	H	Me	C-Me	H	N	
I-134	H	3-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-135	H	3-Methoxyphenyl	Me	OMe	CH	Me	N	
I-136	H	3-Methoxyphenyl	Me	Me	CH	Me	N	
I-137	H	3,4-Dimethoxyphenyl	H	OMe	CH	OMe	N	
I-138	H	3,4-Dimethoxyphenyl	H	OMe	CH	Me	N	
I-139	H	3,4-Dimethoxyphenyl	H	Me	CH	Me	N	
I-140	H	3,4-Dimethoxyphenyl	H	Me	CH	Et	N	
I-141	H	3,4-Dimethoxyphenyl	H	Et	CH	Et	N	
I-142	H	3,4-Dimethoxyphenyl	H	Me	CH	CF_3	N	
I-143	H	3,4-Dimethoxyphenyl	H	OMe	CH	CF_3	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-144	H	3,4-Dimethoxyphenyl	H	OMe	CH	H	N	
I-145	H	3,4-Dimethoxyphenyl	H	SMe	CH	H	N	
I-146	H	3,4-Dimethoxyphenyl	H	Et	CH	OMe	N	
I-147	H	3,4-Dimethoxyphenyl	H	Me	C-$(CH_2)_3$-		N	
I-148	H	3,4-Dimethoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-149	H	3,4-Dimethoxyphenyl	H	Me	C-$(CH_2)_2$-O		N	
I-150	H	3,4-Dimethoxyphenyl	H	OMe	C-$(CH_2)_2$-O		N	
I-151	H	3,4-Dimethoxyphenyl	H	OMe	N	OMe	N	
I-152	H	3,4-Dimethoxyphenyl	H	NH_2	N	NH_2	N	
I-153	H	3,4-Dimethoxyphenyl	H	NHMe	N	NHMe	N	
I-154	H	3,4-Dimethoxyphenyl	H	OMe	N	OMe	CH	
I-155	H	3,4-Dimethoxyphenyl	H	Cl	N	Me	CH	
I-156	H	3,4-Dimethoxyphenyl	H	OMe	N	N=CH-NH-C		
I-157	H	3,4-Dimethoxyphenyl	H	Cl	N	N=CH-NH-C		
I-158	H	3,4-Dimethoxyphenyl	H	Me	N	Me	CH	
I-159	H	3,4-Dimethoxyphenyl	H	OMe	N	Me	CH	
I-160	H	3,4-Dimethoxyphenyl	H	OMe	N	H	C-NO_2	
I-161	H	3,4-Dimethoxyphenyl	H	OMe	C-Me	H	N	
I-162	H	3,4-Dimethoxyphenyl	H	Me	C-Me	H	N	
I-163	H	3,4-Dimethoxyphenyl	Me	OMe	CH	OMe	N	
I-164	H	3,4-Dimethoxyphenyl	Me	OMe	CH	Me	N	
I-165	H	3,4-Dimethoxyphenyl	Me	Me	CH	Me	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-166	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	OMe	N	228-235 (decomp.)
I-167	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	Me	N	
I-168	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	Me	N	
I-169	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	Et	N	
I-170	H	3,4(1,3-Dioxomethylene)phenyl	H	Et	CH	Et	N	
I-171	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	CF_3	N	
I-172	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	CF_3	N	
I-173	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	H	N	
I-174	H	3,4(1,3-Dioxomethylene)phenyl	H	SMe	CH	H	N	
I-175	H	3,4(1,3-Dioxomethylene)phenyl	H	Et	CH	OMe	N	
I-176	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	C_$(CH_2)_3$-		N	
I-177	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-$(CH_2)_3$-		N	
I-178	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-$(CH_2)_2$-C		N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-179	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-180	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	OMe	N	
I-181	H	3,4(1,3-Dioxomethylene)phenyl	H	NH_2	N	NH_2	N	
I-182	H	3,4(1,3-Dioxomethylene)phenyl	H	NHMe	N	NHMe	N	
I-183	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	OMe	CH	
I-184	H	3,4(1,3-Dioxomethylene)phenyl	H	Cl	N	Me	CH	
I-185	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	N=CH-NH-C		
I-186	H	3,4(1,3-Dioxomethylene)phenyl	H	Cl	N	N=CH-NH-C		
I-187	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	N	Me	CH	
I-188	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	Me	CH	
I-189	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	H	C-NO_2	
I-190	H	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-Me	H	N	
I-191	H	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-Me	H	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-192	H	3,4(1,3-Dioxomethylene)phenyl	Me	OMe	CH	OMe	N	
I-193	H	3,4(1,3-Dioxomethylene)phenyl	Me	OMe	CH	Me	N	
I-194	H	3,4(1,3-Dioxomethylene)phenyl	Me	Me	CH	Me	N	
I-195	Cyclohexyl	Cyclohexyl	H	OMe	CH	OMe	N	
I-196	Cyclohexyl	Cyclohexyl	H	OMe	CH	Me	N	
I-197	Cyclohexyl	Cyclohexyl	H	Me	CH	Me	N	
I-198	Cyclohexyl	Cyclohexyl	H	Me	CH	Et	N	
I-199	Cyclohexyl	Cyclohexyl	H	Et	CH	Et	N	
I-200	Cyclohexyl	Cyclohexyl	H	Me	CH	CF_3	N	
I-201	Cyclohexyl	Cyclohexyl	H	OMe	CH	CF_3	N	
I-202	Cyclohexyl	Cyclohexyl	H	OMe	CH	H	N	
I-203	Cyclohexyl	Cyclohexyl	H	SMe	CH	H	N	
I-204	Cyclohexyl	Cyclohexyl	H	Et	CH	OMe	N	
I-205	Cyclohexyl	Cyclohexyl	H	Me	C-$(CH_2)_3$-		N	
I-206	Cyclohexyl	Cyclohexyl	H	OMe	C-$(CH_2)_3$-		N	
I-207	Cyclohexyl	Cyclohexyl	H	Me	C-$(CH_2)_2$-C		N	
I-208	Cyclohexyl	Cyclohexyl	H	OMe	C-$(CH_2)_2$-C		N	
I-209	Cyclohexyl	Cyclohexyl	H	OMe	N	OMe	N	
I-210	Cyclohexyl	Cyclohexyl	H	NH_2	N	NH_2	N	
I-211	Cyclohexyl	Cyclohexyl	H	NHMe	N	NHMe	N	
I-212	Cyclohexyl	Cyclohexyl	H	OMe	N	OMe	CH	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-213	Cyclohexyl	Cyclohexyl	H	Cl	N	Me	CH	
I-214	Cyclohexyl	Cyclohexyl	H	OMe	N	N=CH-NH-C		
I-215	Cyclohexyl	Cyclohexyl	H	Cl	N	N=CH-NH-C		
I-216	Cyclohexyl	Cyclohexyl	H	Me	N	Me	CH	
I-217	Cyclohexyl	Cyclohexyl	H	OMe	N	Me	CH	
I-218	Cyclohexyl	Cyclohexyl	H	OMe	N	H	$C-NO_2$	
I-219	Cyclohexyl	Cyclohexyl	H	OMe	C-Me	H	N	
I-220	Cyclohexyl	Cyclohexyl	H	Me	C-Me	H	N	
I-221	Cyclohexyl	Cyclohexyl	Me	OMe	CH	OMe	N	
I-222	Cyclohexyl	Cyclohexyl	Me	OMe	CH	Me	N	
I-223	Cyclohexyl	Cyclohexyl	Me	Me	CH	Me	N	
I-224	H	p-Phenylphenyl	H	OMe	CH	OMe	N	
I-225	H	p-Phenylphenyl	H	OMe	CH	Me	N	
I-226	H	p-Phenylphenyl	H	Me	CH	Me	N	
I-227	H	p-Phenylphenyl	H	Me	CH	Et	N	
I-228	H	p-Phenylphenyl	H	Et	CH	Et	N	
I-229	H	p-Phenylphenyl	H	Me	CH	CF_3	N	
I-230	H	p-Phenylphenyl	H	OMe	CH	CF_3	N	
I-231	H	p-Phenylphenyl	H	OMe	CH	H	N	
I-232	H	p-Phenylphenyl	H	SMe	CH	H	N	
I-233	H	p-Phenylphenyl	H	Et	CH	OMe	N	
I-234	H	p-Phenylphenyl	H	Me	$C-(CH_2)_3-$		N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-235	H	p-Phenylphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-236	H	p-Phenylphenyl	H	Me	C-$(CH_2)_2$-C		N	
I-237	H	p-Phenylphenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-238	H	p-Phenylphenyl	H	OMe	N	OMe	N	
I-239	H	p-Phenylphenyl	H	NH_2	N	NH_2	N	
I-240	H	p-Phenylphenyl	H	NHMe	N	MHMe	N	
I-241	H	p-Phenylphenyl	H	OMe	N	OMe	CH	
I-242	H	p-Phenylphenyl	H	Cl	N	Me	CH	
I-243	H	p-Phenylphenyl	H	OMe	N	N=CH-NH-C		
I-244	H	p-Phenylphenyl	H	Cl	N	N=CH-NH-C		
I-245	H	p-Phenylphenyl	H	Me	N	Me	CH	
I-246	H	p-Phenylphenyl	H	OMe	N	Me	CH	
I-247	H	p-Phenylphenyl	H	OMe	N	H	C-NO_2	
I-248	H	p-Phenylphenyl	H	OMe	C-Me	H	N	
I-249	H	p-Phenylphenyl	H	Me	C-Me	H	N	
I-250	H	p-Phenylphenyl	Me	OMe	CH	OMe	N	
I-251	H	p-Phenylphenyl	Me	OMe	CH	Me	N	
I-252	H	p-Phenylphenyl	Me	Me	CH	Me	N	
I-253	Phenyl	Phenyl	H	OMe	CH	OMe	N	69
I-254	Phenyl	Phenyl	H	OMe	CH	Me	N	
I-255	Phenyl	Phenyl	H	Me	CH	Me	N	172-174
I-256	Phenyl	Phenyl	H	Me	CH	Et	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-257	Phenyl	Phenyl	H	Et	CH	Et	N	
I-258	Phenyl	Phenyl	H	Me	CH	CF_3	N	
I-259	Phenyl	Phenyl	H	OMe	CH	CF_3	N	
I-260	Phenyl	Phenyl	H	OMe	CH	H	N	
I-261	Phenyl	Phenyl	H	SMe	CH	H	N	
I-262	Phenyl	Phenyl	H	Et	CH	OMe	N	
I-263	Phenyl	Phenyl	H	CF_3	CH	H	N	203-208
I-264	Phenyl	Phenyl	H	Me	CH	H	N	
I-265	Phenyl	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-266	Phenyl	Phenyl	H	OMe	C-$(CH_2)_3$-		N	
I-267	Phenyl	Phenyl	H	Me	C-$(CH_2)_2$-C		N	
I-268	Phenyl	Phenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-269	Phenyl	Phenyl	H	OMe	N	OMe	N	172-175
I-270	Phenyl	Phenyl	H	NH_2	N	NH_2	N	
I-271	Phenyl	Phenyl	H	NHMe	N	NHMe	N	
I-272	Phenyl	Phenyl	H	Me	N	Me	N	
I-273	Phenyl	Phenyl	H	SMe	N	SMe	N	68-75
I-274	Phenyl	Phenyl	H	H	CH	H	N	
I-275	Phenyl	Phenyl	H	OMe	N	OMe	CH	
I-276	Phenyl	Phenyl	H	Cl	N	Me	CH	
I-277	Phenyl	Phenyl	H	OMe	N	N=CH-NH-C		
I-278	Phenyl	Phenyl	H	Cl	N	N=CH-NH-C		

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-279	Phenyl	Phenyl	H	H	N	N=CH-NH-C		
I-280	Phenyl	Phenyl	H	SMe	N	H	CH	
I-281	Phenyl	Phenyl	H	CMe_3	N	CF_3	CH	56-63
I-282	Phenyl	Phenyl	H	OMe	N	Me	CH	
I-283	Phenyl	Phenyl	H	OMe	N	H	$C-NO_2$	
I-284	Phenyl	Phenyl	H	OMe	C-Me	H	N	
I-285	Phenyl	Phenyl	H	Me	C-Me	H	N	
I-286	Phenyl	Phenyl	H	OMe	CH	H	$C-NO_2$	172-180
I-287	Phenyl	Phenyl	H	Me	CH	H	$C-NO_2$	
I-288	Phenyl	Phenyl	H	OMe	CH	H	$C-NH_2$	
I-289	Phenyl	Phenyl	H	OMe	$C-NO_2$	OMe	CH	
I-290	Phenyl	Phenyl	H	OMe	$C-NO_2$	H	CH	
I-291	Phenyl	Phenyl	H	Me	$C-NO_2$	Me	CH	
I-292	Phenyl	Phenyl	H	Me	$C-NH_2$	Me	CH	
I-293	Phenyl	Phenyl	H	Me	$C-NO_2$	OMe	CH	
I-294	Phenyl	Phenyl	H	Me	$C-NH_2$	OMe	CH	
I-295	Phenyl	Phenyl	Me	OMe	CH	OMe	N	
I-296	Phenyl	Phenyl	Me	OMe	CH	Me	N	
I-297	Phenyl	Phenyl	Me	Me	CH	Me	N	
I-298	Phenyl	Phenyl	Me	OMe	N	OMe	N	
I-299	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	CH	OMe	N	58-66
I-300	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	CH	Me	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-301	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	CH	Me	N	
I-302	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	CH	Et	N	
I-303	3-Methoxyphenyl	3-Methoxyphenyl	H	Et	CH	Et	N	
I-304	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	CH	CF_3	N	
I-305	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	CH	CF_3	N	
I-306	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	CH	H	N	
I-307	3-Methoxyphenyl	3-Methoxyphenyl	H	SMe	CH	H	N	
I-308	3-Methoxyphenyl	3-Methoxyphenyl	H	Et	CH	OMe	N	
I-309	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	C-$(CH_2)_3$-		N	
I-310	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-311	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	C-$(CH_2)_2$-C		N	
I-312	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-313	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	N	OMe	N	
I-314	3-Methoxyphenyl	3-Methoxyphenyl	H	NH_2	N	NH_2	N	
I-315	3-Methoxyphenyl	3-Methoxyphenyl	H	NHMe	N	NHMe	N	
I-316	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	N	OMe	CH	
I-317	3-Methoxyphenyl	3-Methoxyphenyl	H	Cl	N	Me	CH	
I-318	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	N	N=CH-NH-C		
I-319	3-Methoxyphenyl	3-Methoxyphenyl	H	Cl	N	N=CH-NH-C		
I-320	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	N	Me	CH	
I-321	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	N	Me	CH	
I-322	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	N	H	C-NO_2	

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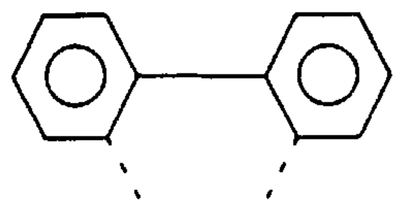
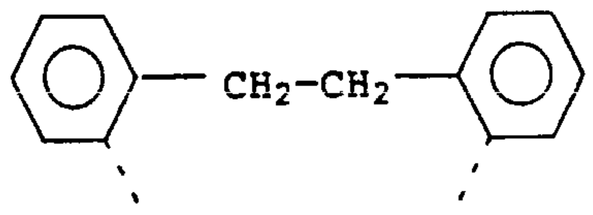
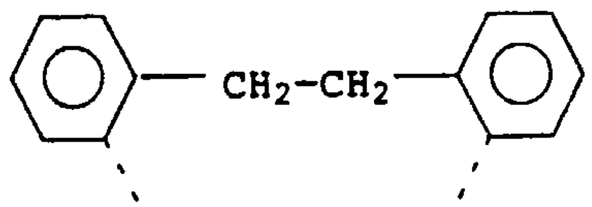
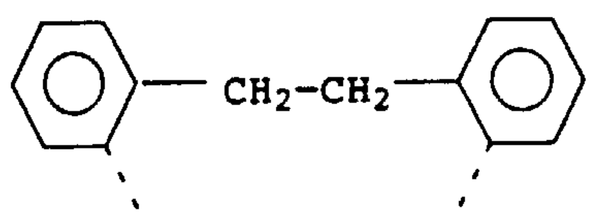
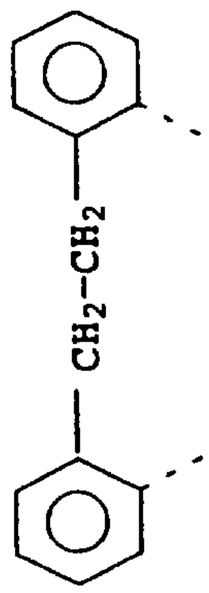
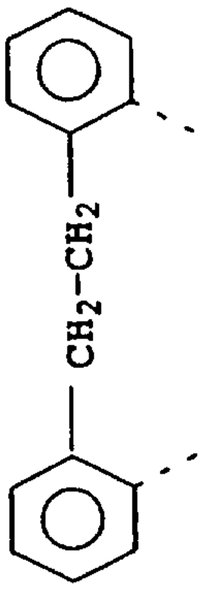
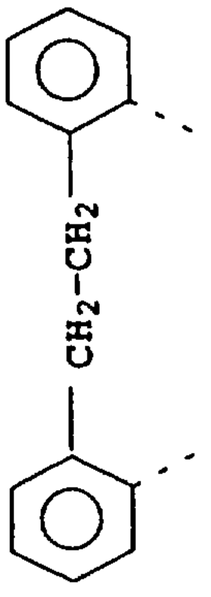
No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-323	3-Methoxyphenyl	3-Methoxyphenyl	H	OMe	C-Me	H	N	
I-324	3-Methoxyphenyl	3-Methoxyphenyl	H	Me	C-Me	H	N	
I-325	3-Methoxyphenyl	3-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-326	3-Methoxyphenyl	3-Methoxyphenyl	Me	OMe	CH	Me	N	
I-327	3-Methoxyphenyl	3-Methoxyphenyl	Me	Me	CH	Me	N	
I-328			H	OMe	N	OMe	N	182-186
I-329			H	OMe	CH	OMe	N	
I-330			H	Me	CH	Me	N	
I-331			H	Me	CH	OMe	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-332			H	OMe	C-Me	H	N	
I-333			H	OMe	CH	H	N	
I-334			H	OMe	N	OMe	CH	

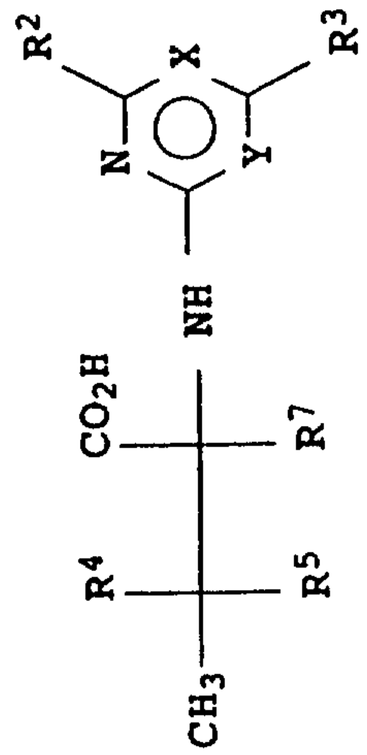


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Table 2

No.	R^4	R^5	R^7	X	R^2	R^3	Y	M.p. [°C]
I-335	Phenyl	Phenyl	H	CH	OMe	OMe	N	
I-336	Phenyl	Phenyl	H	CH	OMe	Me	N	
I-337	Phenyl	Phenyl	H	CH	Me	Me	N	
I-338	Phenyl	Phenyl	H	CH	Me	Et	N	
I-339	Phenyl	Phenyl	H	CH	Et	Et	N	
I-340	Phenyl	Phenyl	H	CH	Me	CF_3	N	
I-341	Phenyl	Phenyl	H	CH	OMe	CF_3	N	
I-342	Phenyl	Phenyl	H	CH	OMe	H	N	
I-343	Phenyl	Phenyl	H	CH	SMe	H	N	
I-344	Phenyl	Phenyl	H	CH	Et	OMe	N	
I-345	Phenyl	Phenyl	H	CH	CF_3	H	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-346	Phenyl	Phenyl	H	Me	CH	H	N	
I-347	Phenyl	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-348	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_3$-		CH	
I-349	Phenyl	Phenyl	Me	Me	C-$(CH_2)_2$-C		N	
I-350	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_2$-C		N	
I-351	Phenyl	Phenyl	H	OMe	N	OMe	N	
I-352	Phenyl	Phenyl	H	NH_2	N	NH_2	N	
I-353	Phenyl	Phenyl	H	NHMe	N	NHMe	N	
I-354	Phenyl	Phenyl	H	Me	N	Me	N	
I-355	Phenyl	Phenyl	H	SMe	N	SMe	N	
I-356	Phenyl	Phenyl	H	H	CH	H	N	
I-357	Phenyl	Phenyl	H	OMe	N	OMe	CH	
I-358	Phenyl	Phenyl	H	Cl	N	Me	CH	
I-359	Phenyl	Phenyl	H	OMe	N	N=CH-NH-C		
I-360	Phenyl	Phenyl	H	Cl	N	N=CH-NH-C		
I-361	Phenyl	Phenyl	H	H	N	N=CH-NH-C		
I-362	Phenyl	Phenyl	H	SMe	N	H	CH	
I-363	Phenyl	Phenyl	H	CMe_3	N	CF_3	CH	
I-364	Phenyl	Phenyl	H	OMe	N	Me	CH	
I-365	Phenyl	Phenyl	H	OMe	N	H	C-NO_2	
I-366	Phenyl	Phenyl	H	OMe	C-Me	H	N	
I-367	Phenyl	Phenyl	H	Me	C-Me	H	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-368	Phenyl	Phenyl	H	OMe	CH	H	$C-NO_2$	
I-369	Phenyl	Phenyl	H	Me	CH	H	$C-NO_2$	
I-370	Phenyl	Phenyl	H	OMe	CH	H	$C-NH_2$	
I-371	Phenyl	Phenyl	H	OMe	$C-NO_2$	OMe	CH	
I-372	Phenyl	Phenyl	H	OMe	$C-NO_2$	H	CH	
I-373	Phenyl	Phenyl	H	Me	$C-NO_2$	Me	CH	
I-374	Phenyl	Phenyl	H	Me	$C-NH_2$	Me	CH	
I-375	Phenyl	Phenyl	H	Me	$C-NO_2$	OMe	CH	
I-376	Phenyl	Phenyl	H	Me	$C-NH_2$	OMe	CH	
I-377	Phenyl	Phenyl	Me	OMe	CH	OMe	N	
I-378	Phenyl	Phenyl	Me	OMe	CH	Me	N	
I-379	Phenyl	Phenyl	Me	Me	CH	Me	N	
I-380	Phenyl	Phenyl	Me	OMe	N	OMe	N	
I-381	Me	Phenyl	H	OMe	CH	OMe	N	
I-382	Me	Phenyl	H	OMe	CH	Me	N	
I-383	Me	Phenyl	H	Me	CH	Me	N	
I-384	Me	Phenyl	H	Me	CH	Et	N	
I-385	Me	Phenyl	H	Et	CH	Et	N	
I-386	Me	Phenyl	H	Me	CH	CF_3	N	
I-387	Me	Phenyl	H	OMe	CH	CF_3	N	
I-388	Me	Phenyl	H	OMe	CH	H	N	
I-389	Me	Phenyl	H	SMe	CH	H	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-390	Me	Phenyl	H	Et	CH	OMe	N	
I-391	Me	Phenyl	H	CF_3	CH	H	N	
I-392	Me	Phenyl	H	Me	CH	H	N	
I-393	Me	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-394	Me	Phenyl	H	OMe	C-$(CH_2)_3$-		N	
I-395	Me	Phenyl	H	Me	C-$(CH_2)_2$-C		N	
I-396	Me	Phenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-397	Me	Phenyl	H	OMe	N	OMe	N	
I-398	Me	Phenyl	H	NH_2	N	NH_2	N	
I-399	Me	Phenyl	H	NHMe	N	NHMe	N	
I-400	Me	Phenyl	H	Me	N	Me	N	
I-401	Me	Phenyl	H	SMe	N	SMe	N	
I-402	Me	Phenyl	H	H	CH	H	N	
I-403	Me	Phenyl	H	OMe	N	OMe	CH	
I-404	Me	Phenyl	H	Cl	N	Me	CH	
I-405	Me	Phenyl	H	OMe	N	N=CH-NH-C		
I-406	Me	Phenyl	H	Cl	N	N=CH-NH-C		
I-407	Me	Phenyl	H	H	N	N=CH-NH-C		
I-408	Me	Phenyl	H	SMe	N	H	CH	
I-409	Me	Phenyl	H	CMe_3	N	CF_3	CH	
I-410	Me	Phenyl	H	OMe	N	Me	CH	
I-411	Me	Phenyl	H	OMe	N	H	C-NO_2	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-412	Me	Phenyl	H	OMe	C-Me	H	N	
I-413	Me	Phenyl	H	Me	C-Me	H	N	
I-414	Me	Phenyl	H	OMe	CH	H	$C-NO_2$	
I-415	Me	Phenyl	H	Me	CH	H	$C-NO_2$	
I-416	Me	Phenyl	H	OMe	CH	H	$C-NH_2$	
I-417	Me	Phenyl	H	OMe	$C-NO_2$	OMe	CH	
I-418	Me	Phenyl	H	OMe	$C-NO_2$	H	CH	
I-419	Me	Phenyl	H	Me	$C-NO_2$	Me	CH	
I-420	Me	Phenyl	H	Me	$C-NH_2$	Me	CH	
I-421	Me	Phenyl	H	Me	$C-NO_2$	OMe	CH	
I-422	Me	Phenyl	H	Me	$C-NH_2$	OMe	CH	
I-423	Me	Phenyl	Me	OMe	CH	OMe	N	
I-424	Me	Phenyl	Me	OMe	CH	Me	N	
I-425	Me	Phenyl	Me	Me	CH	Me	N	
I-426	Me	Phenyl	Me	OMe	N	OMe	N	
I-427	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	OMe	N	
I-428	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	Me	N	
I-429	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	Me	N	
I-430	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	Et	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-431	Me	3,4(1,3-Dioxomethylene)phenyl	H	Et	CH	Et	N	
I-432	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	CF_3	N	
I-433	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	CF_3	N	
I-434	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	H	N	
I-435	Me	3,4(1,3-Dioxomethylene)phenyl	H	SMe	CH	H	N	
I-436	Me	3,4(1,3-Dioxomethylene)phenyl	H	Et	CH	OMe	N	
I-437	Me	3,4(1,3-Dioxomethylene)phenyl	H	CF_3	CH	H	N	
I-438	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	Ch [sic]	H	N	
I-439	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	$C-(CH_2)_3-$		N	
I-440	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	$C-(CH_2)_3-$		N	
I-441	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	$C-(CH_2)_2-C$		N	
I-442	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	$C-(CH_2)_2-C$		N	
I-443	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	OMe	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-444	Me	3,4(1,3-Dioxomethylene)phenyl	H	NH_2	N	NH_2	N	
I-445	Me	3,4(1,3-Dioxomethylene)phenyl	H	NHMe	N	NHMe	N	
I-446	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	N	Me	N	
I-447	Me	3,4(1,3-Dioxomethylene)phenyl	H	SMe	N	SMe	N	
I-448	Me	3,4(1,3-Dioxomethylene)phenyl	H	H	CH	H	N	
I-449	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	OMe	CH	
I-450	Me	3,4(1,3-Dioxomethylene)phenyl	H	Cl	N	Me	CH	
I-451	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	N=CH-NH-C		
I-452	Me	3,4(1,3-Dioxomethylene)phenyl	H	Cl	N	N=CH-NH-C		
I-453	Me	3,4(1,3-Dioxomethylene)phenyl	H	H	N	N=CH-NH-C		
I-454	Me	3,4(1,3-Dioxomethylene)phenyl	H	SMe	N	H	CH	
I-455	Me	3,4(1,3-Dioxomethylene)phenyl	H	CMe_3	N	CF_3	CH	
I-456	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	Me	CH	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-457	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	N	H	C-NO_2	
I-458	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-Me	H	N	
I-459	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-Me	H	N	
I-460	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	H	C-NO_2	
I-461	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	CH	H	C-NO_2	
I-462	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	CH	H	C-NH_2	
I-463	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-NO_2	OMe	CH	
I-464	Me	3,4(1,3-Dioxomethylene)phenyl	H	OMe	C-NO_2	H	CH	
I-465	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-NO_2	Me	CH	
I-466	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-NH_2	Me	CH	
I-467	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-NO_2	OMe	CH	
I-468	Me	3,4(1,3-Dioxomethylene)phenyl	H	Me	C-NH_2	OMe	CH	
I-469	Me	3,4(1,3-Dioxomethylene)phenyl	Me	OMe	CH	OMe	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-470	Me	3,4(1,3-Dioxomethylene)phenyl	Me	OMe	CH	Me	N	
I-471	Me	3,4(1,3-Dioxomethylene)phenyl	Me	Me	CH	Me	N	
I-472	Me	3,4(1,3-Dioxomethylene)phenyl	Me	OMe	N	OMe	N	
I-473	Me	3,4-Dimethoxyphenyl	H	OMe	N	OMe	N	
I-474	Me	3,4-Dimethoxyphenyl	H	OMe	CH	OMe	N	
I-475	Me	3,4-Dimethoxyphenyl	H	Me	CH	OMe	N	
I-476	Me	3,4-Dimethoxyphenyl	H	Me	CH	Me	N	
I-477	Me	3,4-Dimethoxyphenyl	H	OMe	N	OMe	CH	
I-478	Me	3,4-Dimethoxyphenyl	Me	OMe	CH	OMe	N	
I-479	Me	3,4-Dimethoxyphenyl	Me	OMe	N	OMe	N	
I-480	Me	3,4-Dimethoxyphenyl	H	OMe	CH	H	N	
I-481	Me	3,4-Dimethoxyphenyl	H	OMe	C-Me	H	N	
I-482	Me	4-Methoxyphenyl	H	OMe	CH	OMe	N	
I-483	Me	4-Methoxyphenyl	H	Me	CH	OMe	N	
I-484	Me	4-Methoxyphenyl	H	Me	CH	Me	N	
I-485	Me	4-Methoxyphenyl	H	OMe	N	OMe	CH	
I-486	Me	4-Methoxyphenyl	H	OMe	CH	H	N	
I-487	Me	4-Methoxyphenyl	H	OMe	C-Me	H	N	
I-488	Me	4-Methoxyphenyl	H	OMe	N	OMe	N	
I-489	Me	4-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-490	Me	4-Methoxyphenyl	Me	OMe	N	OMe	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-491	Me	3-Methoxyphenyl	H	OMe	CH	OMe	N	
I-492	Me	3-Methoxyphenyl	H	Me	CH	OMe	N	
I-493	Me	3-Methoxyphenyl	H	Me	CH	Me	N	
I-494	Me	3-Methoxyphenyl	H	OMe	N	OMe	CH	
I-495	Me	3-Methoxyphenyl	H	OMe	CH	H	N	
I-496	Me	3-Methoxyphenyl	H	OMe	C-Me	H	N	
I-497	Me	3-Methoxyphenyl	H	OMe	N	OMe	N	
I-498	Me	3-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-499	Me	3-Methoxyphenyl	Me	OMe	N	OMe	N	
I-500	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	OMe	N	
I-501	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	Me	N	
I-502	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	Me	N	
I-503	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	Et	N	
I-504	4-Methoxyphenyl	4-Methoxyphenyl	H	Et	CH	Et	N	
I-505	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	CF_3	N	
I-506	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	CF_3	N	
I-507	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	N	
I-508	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	CH	H	N	
I-509	4-Methoxyphenyl	4-Methoxyphenyl	H	Et	CH	OMe	N	
I-510	4-Methoxyphenyl	4-Methoxyphenyl	H	CF_3	CH	H	N	
I-511	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	H	N	
I-512	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-$(CH_2)_3$-		N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-513	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-514	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-$(CH_2)_2$-C		N	
I-515	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-516	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	OMe	N	
I-517	4-Methoxyphenyl	4-Methoxyphenyl	H	NH_2	N	NH_2	N	
I-518	4-Methoxyphenyl	4-Methoxyphenyl	H	NHMe	N	NHMe	N	
I-519	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	N	Me	N	
I-520	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	N	SMe	N	
I-521	4-Methoxyphenyl	4-Methoxyphenyl	H	H	CH	H	N	
I-522	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	OMe	CH	
I-523	4-Methoxyphenyl	4-Methoxyphenyl	H	Cl	N	Me	CH	
I-524	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	N=CH-NH-C		
I-525	4-Methoxyphenyl	4-Methoxyphenyl	H	Cl	N	N=CH-NH-C		
I-526	4-Methoxyphenyl	4-Methoxyphenyl	H	H	N	N=CH-NH-C		
I-527	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	N	H	CH	
I-528	4-Methoxyphenyl	4-Methoxyphenyl	H	CMe_3	N	CF_3	CH	
I-529	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	Me	CH	
I-530	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	H	C-NO_2	
I-531	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-Me	H	N	
I-532	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-Me	H	N	
I-533	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	C-NO_2	
I-534	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	H	C-NO_2	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-535	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	$C-NH_2$	
I-536	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	$C-NO_2$	OMe	CH	
I-537	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	$C-NO_2$	H	CH	
I-538	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NO_2$	Me	CH	
I-539	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NH_2$	Me	CH	
I-540	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NO_2$	OMe	CH	
I-541	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NH_2$	OMe	CH	
I-542	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-543	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	CH	Me	N	
I-544	4-Methoxyphenyl	4-Methoxyphenyl	Me	Me	CH	Me	N	
I-545	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	N	OMe	N	

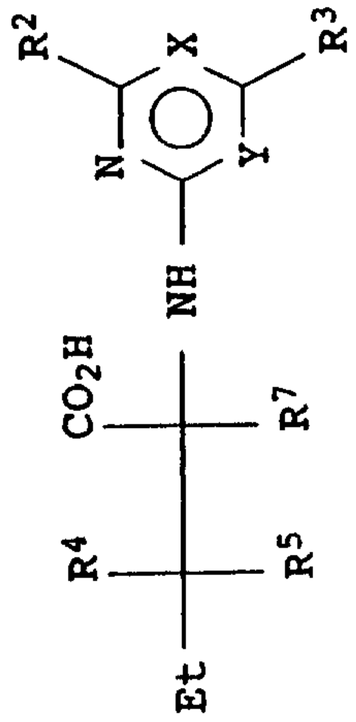

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Table 3

No.	R^4	R^5	R^7	R^3	X	R^2	Y	M.p. [°C]
I-546	Phenyl	Phenyl	H	OMe	CH	OMe	N	
I-547	Phenyl	Phenyl	H	Me	CH	OMe	N	
I-548	Phenyl	Phenyl	H3	Me	CH	Me	N	
I-549	Phenyl	Phenyl	H	Et	CH	Me	N	
I-550	Phenyl	Phenyl	H	Et	CH	Et	N	
I-551	Phenyl	Phenyl	H	CF_3	CH	Me	N	
I-552	Phenyl	Phenyl	H	CF_3	CH	OMe	N	
I-553	Phenyl	Phenyl	H	H	CH	OMe	N	
I-554	Phenyl	Phenyl	H	H	CH	SMe	N	
I-555	Phenyl	Phenyl	H	OMe	CH	Et	N	
I-556	Phenyl	Phenyl	H	H	CH	CF_3	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-557	Phenyl	Phenyl	H	Me	CH	H	N	
I-558	Phenyl	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-559	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_3$-		CH	
I-560	Phenyl	Phenyl	Me	Me	C-$(CH_2)_2$-C		N	
I-561	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_2$-C		N	
I-562	Phenyl	Phenyl	H	OMe	N	OMe	N	
I-563	Phenyl	Phenyl	H	NH_2	N	NH_2	N	
I-564	Phenyl	Phenyl	H	NHMe	N	NHMe	N	
I-565	Phenyl	Phenyl	H	Me	N	Me	N	
I-566	Phenyl	Phenyl	H	SMe	N	SMe	N	
I-567	Phenyl	Phenyl	H	H	CH	H	N	
I-568	Phenyl	Phenyl	H	OMe	N	OMe	CH	
I-569	Phenyl	Phenyl	H	Cl	N	Me	CH	
I-570	Phenyl	Phenyl	H	OMe	N	N=CH-NH-C		
I-571	Phenyl	Phenyl	H	Cl	N	N=CH-NH-C		
I-572	Phenyl	Phenyl	H	H	N	N=CH-NH-C		
I-573	Phenyl	Phenyl	H	SMe	N	H	CH	
I-574	Phenyl	Phenyl	H	CMe_3	N	CF_3	CH	
I-575	Phenyl	Phenyl	H	OMe	N	Me	CH	
I-576	Phenyl	Phenyl	H	OMe	N	H	C-NO_2	
I-577	Phenyl	Phenyl	H	OMe	C-Me	H	N	
I-578	Phenyl	Phenyl	H	Me	C-Me	H	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-579	Phenyl	Phenyl	H	OMe	CH	H	$C-NO_2$	
I-580	Phenyl	Phenyl	H	Me	CH	H	$C-NO_2$	
I-581	Phenyl	Phenyl	H	OMe	CH	H	$C-NH_2$	
I-582	Phenyl	Phenyl	H	OMe	$C-NO_2$	OMe	CH	
I-583	Phenyl	Phenyl	H	OMe	$C-NO_2$	H	CH	
I-584	Phenyl	Phenyl	H	Me	$C-NO_2$	Me	CH	
I-585	Phenyl	Phenyl	H	Me	$C-NH_2$	Me	CH	
I-586	Phenyl	Phenyl	H	Me	$C-NO_2$	OMe	CH	
I-587	Phenyl	Phenyl	H	Me	$C-NH_2$	OMe	CH	
I-588	Phenyl	Phenyl	Me	OMe	CH	OMe	N	
I-589	Phenyl	Phenyl	Me	OMe	CH	Me	N	
I-590	Phenyl	Phenyl	Me	Me	CH	Me	N	
I-591	Phenyl	Phenyl	Me	OMe	N	OMe	N	
I-592	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	OMe	N	
I-593	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	Me	N	
I-594	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	Me	N	
I-595	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	Et	N	
I-596	4-Methoxyphenyl	4-Methoxyphenyl	H	Et	CH	Et	N	
I-597	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	CF_3	N	
I-598	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	CF_3	N	
I-599	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	N	
I-600	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	CH	H	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-601	4-Methoxyphenyl	4-Methoxyphenyl	H	Et	CH	OMe	N	
I-602	4-Methoxyphenyl	4-Methoxyphenyl	H	CF_3	CH	H	N	
I-603	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	H	N	
I-604	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-$(CH_2)_3$-		N	
I-605	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-$(CH_2)_3$-		N	
I-606	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-$(CH_2)_2$-C		N	
I-607	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-$(CH_2)_2$-C		N	
I-608	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	OMe	N	
I-609	4-Methoxyphenyl	4-Methoxyphenyl	H	NH_2	N	NH_2	N	
I-610	4-Methoxyphenyl	4-Methoxyphenyl	H	NHMe	N	NHMe	N	
I-611	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	N	Me	N	
I-612	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	N	SMe	N	
I-613	4-Methoxyphenyl	4-Methoxyphenyl	H	H	CH	H	N	
I-614	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	OMe	CH	
I-615	4-Methoxyphenyl	4-Methoxyphenyl	H	Cl	N	Me	CH	
I-616	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	N=CH-NH-C		
I-617	4-Methoxyphenyl	4-Methoxyphenyl	H	Cl	N	N=CH-NH-C		
I-618	4-Methoxyphenyl	4-Methoxyphenyl	H	H	N	N=CH-NH-C		
I-619	4-Methoxyphenyl	4-Methoxyphenyl	H	SMe	N	H	CH	
I-620	4-Methoxyphenyl	4-Methoxyphenyl	H	CMe_3	N	CF_3	CH	
I-621	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	Me	CH	
I-622	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	N	H	C-NO_2	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-623	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	C-Me	H	N	
I-624	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	C-Me	H	N	
I-625	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	$C-NO_2$	
I-626	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	CH	H	$C-NO_2$	
I-627	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	CH	H	$C-NH_2$	
I-628	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	$C-NO_2$	OMe	CH	
I-629	4-Methoxyphenyl	4-Methoxyphenyl	H	OMe	$C-NO_2$	H	CH	
I-630	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NO_2$	Me	CH	
I-631	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NH_2$	Me	CH	
I-632	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NO_2$	OMe	CH	
I-633	4-Methoxyphenyl	4-Methoxyphenyl	H	Me	$C-NH_2$	OMe	CH	
I-634	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	CH	OMe	N	
I-635	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	CH	Me	N	
I-636	4-Methoxyphenyl	4-Methoxyphenyl	Me	Me	CH	Me	N	
I-637	4-Methoxyphenyl	4-Methoxyphenyl	Me	OMe	N	OMe	N	
I-638	Et	Phenyl	H	OMe	CH	OMe	N	
I-639	Et	Phenyl	H	Me	CH	OMe	N	
I-640	Et	Phenyl	H	Me	CH	Me	N	
I-641	Et	Phenyl	H	OMe	CH	OMe	CH	
I-642	Et	Phenyl	H	OMe	C-Me	H	N	
I-643	Et	Phenyl	H	OMe	N	H	N	
I-644	Et	Phenyl	H	OMe	CH	OMe	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-645	Et	Phenyl	Me	OMe	N	OMe	N	
I-646	Et	Phenyl	Me	Me	CH	OMe	N	
I-647	Et	Phenyl	Me	Me	CH	Me	N	

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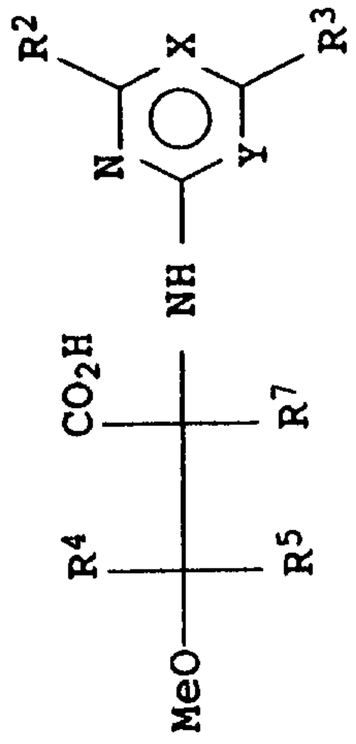

I

Table 4

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.P. [°C]
I-648	Phenyl	Phenyl	H	OMe	CH	OMe	N	
I-649	Phenyl	Phenyl	H	OMe	CH	Me	N	
I-650	Phenyl	Phenyl	H	Me	CH	Me	N	
I-651	Phenyl	Phenyl	H	Me	CH	Et	N	
I-652	Phenyl	Phenyl	H	Et	CH	Et	N	
I-653	Phenyl	Phenyl	H	Me	CH	CF_3	N	
I-654	Phenyl	Phenyl	H	OMe	CH	CF_3	N	
I-655	Phenyl	Phenyl	H	OMe	CH	H	N	
I-656	Phenyl	Phenyl	H	SMe	CH	H	N	
I-657	Phenyl	Phenyl	H	Et	CH	OMe	N	
I-658	Phenyl	Phenyl	H	CF_3	CH	H	N	

No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-659	Phenyl	Phenyl	H	Me	CH	H	N	
I-660	Phenyl	Phenyl	H	Me	C-$(CH_2)_3$-		N	
I-661	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_3$-		CH	
I-662	Phenyl	Phenyl	Me	Me	C-$(CH_2)_2$-C		N	
I-663	Phenyl	Phenyl	Me	OMe	C-$(CH_2)_2$-C		N	
I-664	Phenyl	Phenyl	H	OMe	N	OMe	N	
I-665	Phenyl	Phenyl	H	NH_2	N	NH_2	N	
I-666	Phenyl	Phenyl	H	NHMe	N	NHMe	N	
I-667	Phenyl	Phenyl	H	Me	N	Me	N	
I-668	Phenyl	Phenyl	H	SMe	N	SMe	N	
I-669	Phenyl	Phenyl	H	H	CH	H	N	
I-670	Phenyl	Phenyl	H	OMe	N	OMe	CH	
I-671	Phenyl	Phenyl	H	Cl	N	Me	CH	
I-672	Phenyl	Phenyl	H	OMe	N	N=CH-NH-C		
I-673	Phenyl	Phenyl	H	Cl	N	N=CH-NH-C		
I-674	Phenyl	Phenyl	H	H	N	N=CH-NH-C		
I-675	Phenyl	Phenyl	H	SMe	N	H	CH	
I-676	Phenyl	Phenyl	H	CMe_3	N	CF_3	CH	
I-677	Phenyl	Phenyl	H	OMe	N	Me	CH	
I-678	Phenyl	Phenyl	H	OMe	N	H	C-NO_2	
I-679	Phenyl	Phenyl	H	OMe	C-Me	H	N	
I-680	Phenyl	Phenyl	H	Me	C-Me	H	N	

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No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-681	Phenyl	Phenyl	H	OMe	CH	H	C-NO_2	
I-682	Phenyl	Phenyl	H	Me	CH	H	C-NO_2	
I-683	Phenyl	Phenyl	H	OMe	CH	H	C-NH_2	
I-684	Phenyl	Phenyl	H	OMe	C-NO_2	OMe	CH	
I-685	Phenyl	Phenyl	H	OMe	C-NO_2	H	CH	
I-686	Phenyl	Phenyl	H	Me	C-NO_2	Me	CH	
I-687	Phenyl	Phenyl	H	Me	C-NH_2	Me	CH	
I-688	Phenyl	Phenyl	H	Me	C-NO_2	OMe	CH	
I-689	Phenyl	Phenyl	H	Me	C-NH_2	OMe	CH	
I-690	Phenyl	Phenyl	Me	OMe	CH	OMe	N	
I-691	Phenyl	Phenyl	Me	OMe	CH	Me	N	
I-692	Phenyl	Phenyl	Me	Me	CH	Me	N	
I-693	Phenyl	Phenyl	Me	OMe	N	OMe	N	
I-694	Me	Phenyl	H	OMe	CH	OMe	N	
I-695	Me	Phenyl	H	OMe	CH	Me	N	
I-696	Me	Phenyl	H	Me	CH	Me	N	
I-697	Me	Phenyl	H	OMe	N	OMe	CH	
I-698	Me	Phenyl	H	OMe	CH	H	N	
I-699	Me	Phenyl	H	OMe	C-Me	H	N	
I-700	Me	Phenyl	H	OMe	N	OMe	N	
I-701	Me	Phenyl	Me	OMe	CH	OMe	N	
I-702	Me	Phenyl	Me	OMe	N	OMe	N	

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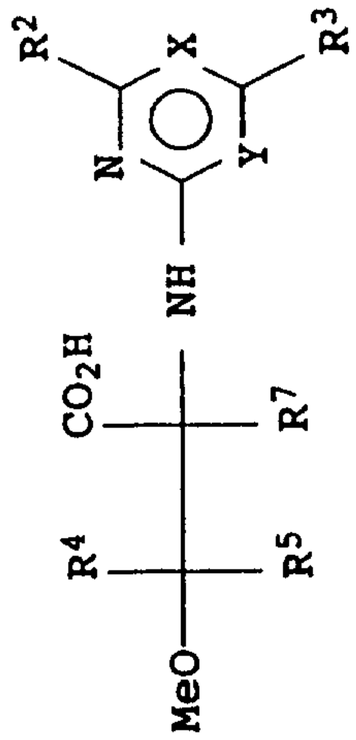
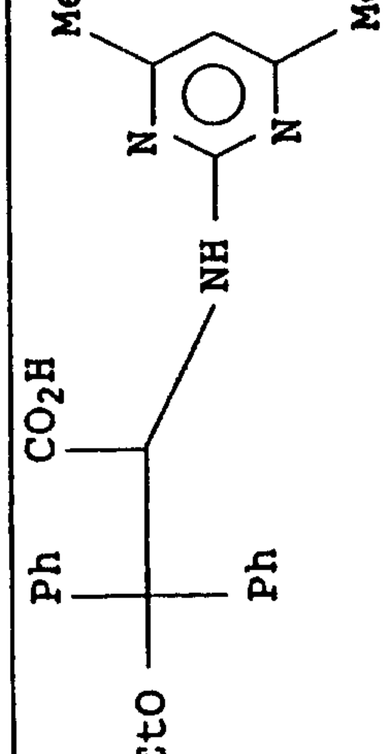
No.	R^4	R^5	R^7	R^2	X	R^3	Y	M.p. [°C]
I-703	Me	Phenyl	Me	Me	CH	Me	N	
I-704	H	Phenyl	H	OMe	CH	OMe	N	
I-705	H	Phenyl	H	OMe	CH	Me	N	
I-706	H	Phenyl	H	Me	CH	Me	N	
I-707	H	Phenyl	H	OMe	N	OMe	CH	
I-708	H	Phenyl	H	OMe	CH	H	N	
I-709	H	Phenyl	H	OMe	C-Me	H	N	
I-710	H	Phenyl	H	OMe	N	OMe	N	
I-711	H	Phenyl	Me	OMe	CH	OMe	N	
I-712	H	Phenyl	Me	OMe	N	OMe	N	
I-713	H	Phenyl	Me	Me	CH	Me	N	

Table 5

66

No.	Structure	M.P. [°C]
I-714		
I-715		

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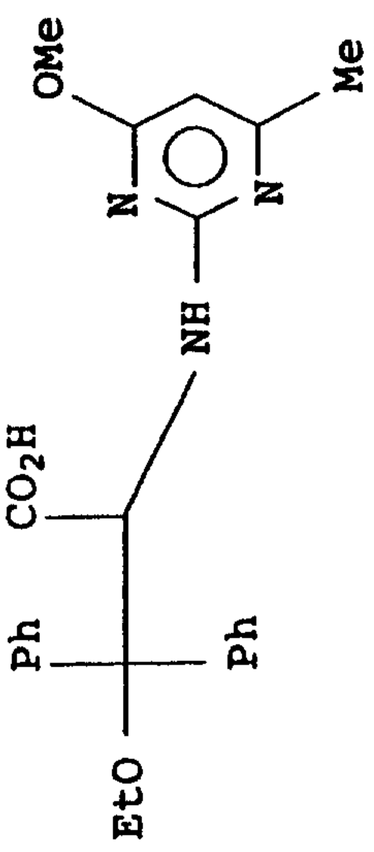
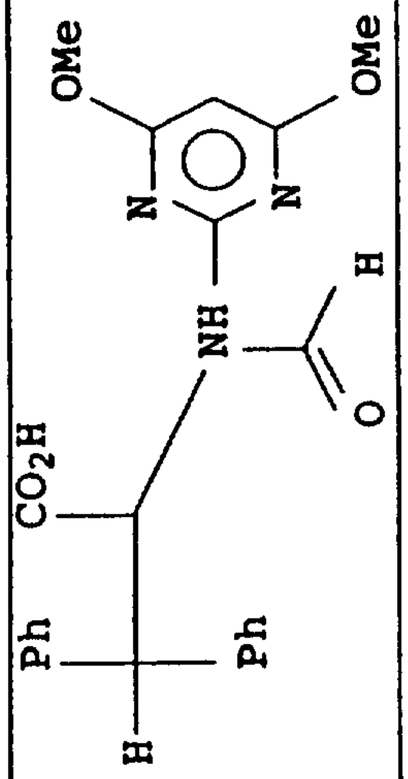
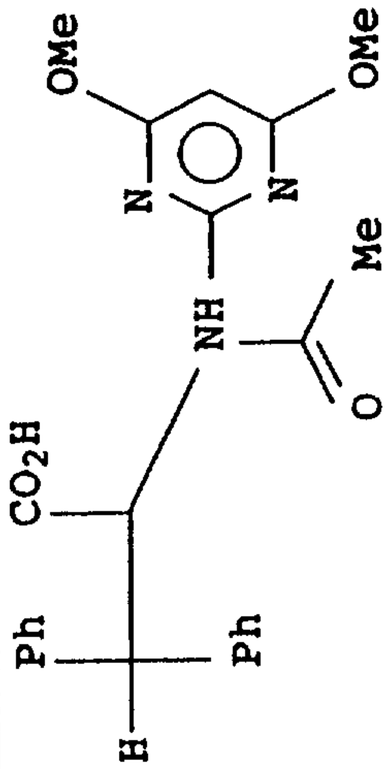
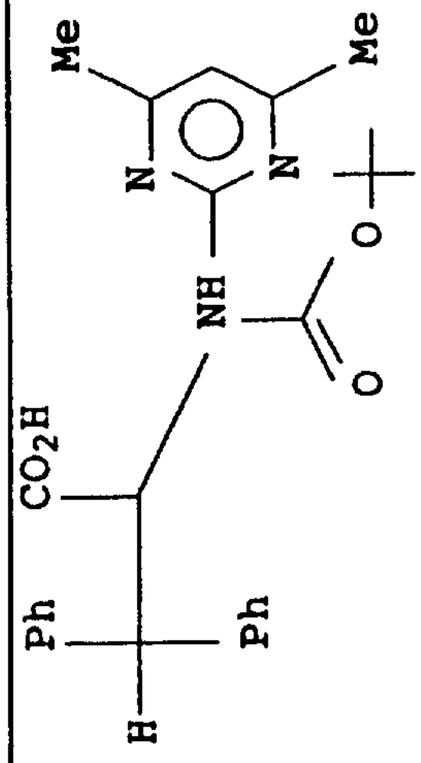
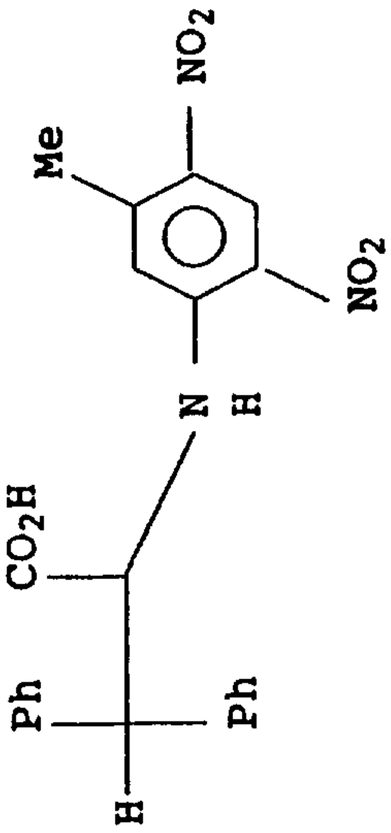
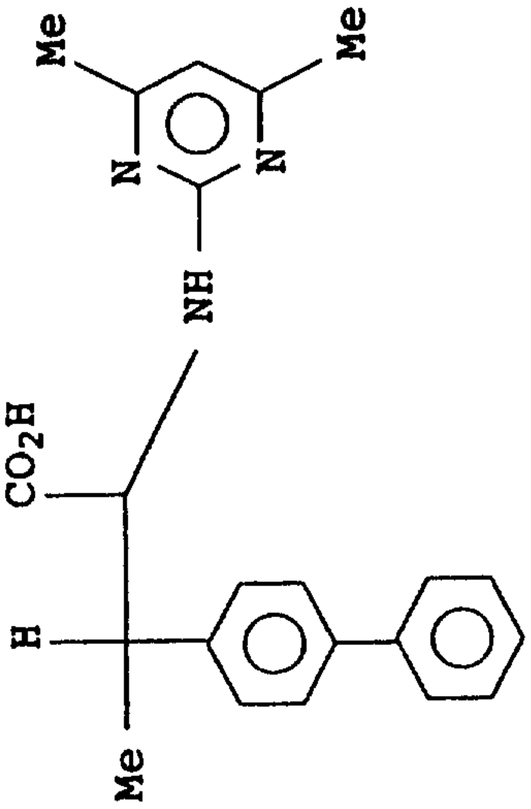
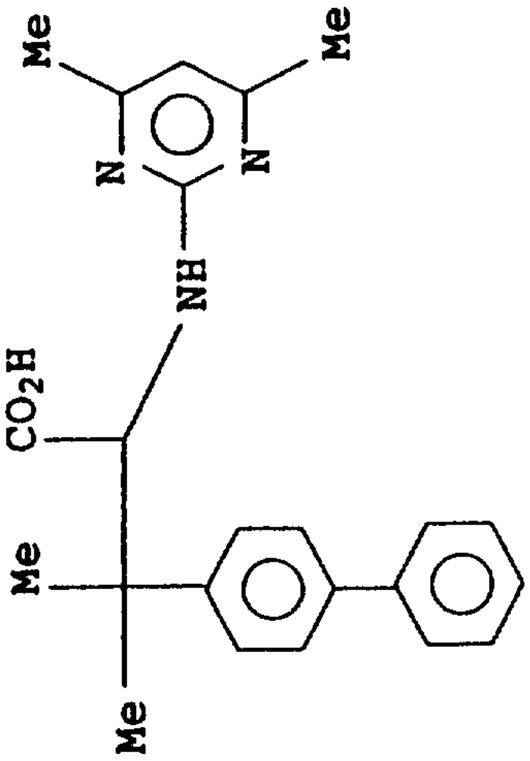
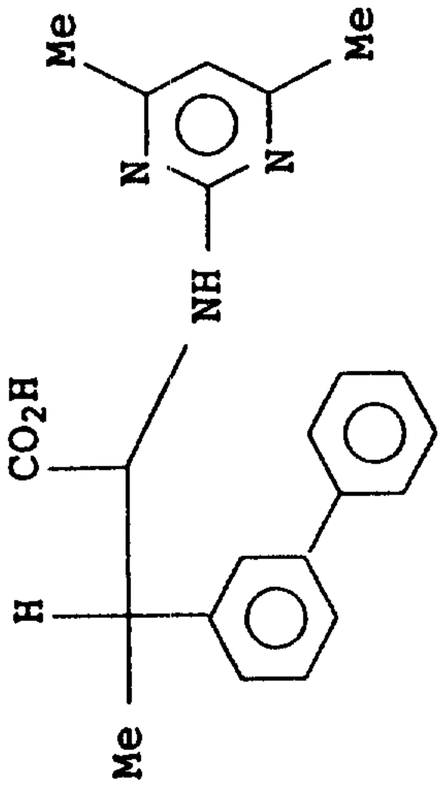
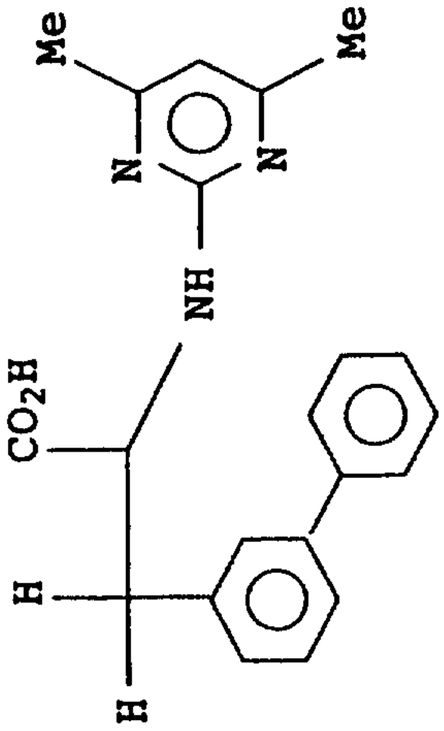
No.	Structure	M.p. [°C]
I-716		
I-717		
I-718		

No.	Structure	M.p. [°C]
I-719		
I-720		
I-721		

No.	Structure	M.p. [°C]
I-722		
I-723		
I-724		

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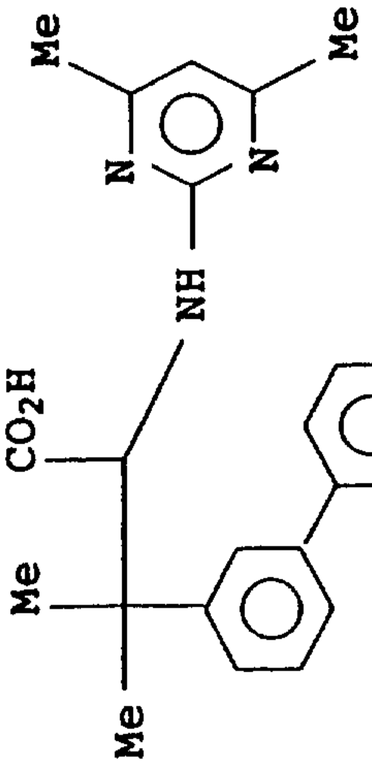
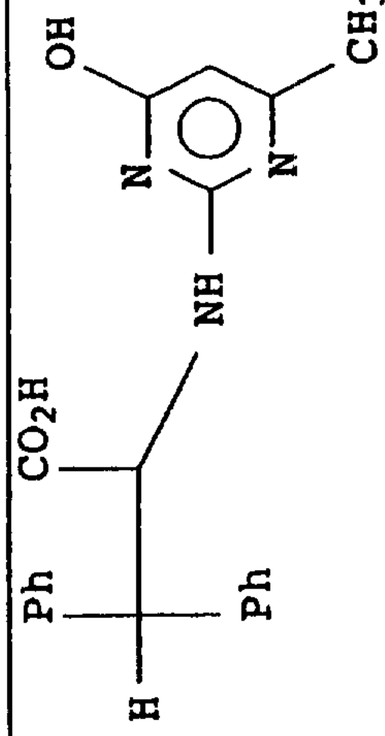
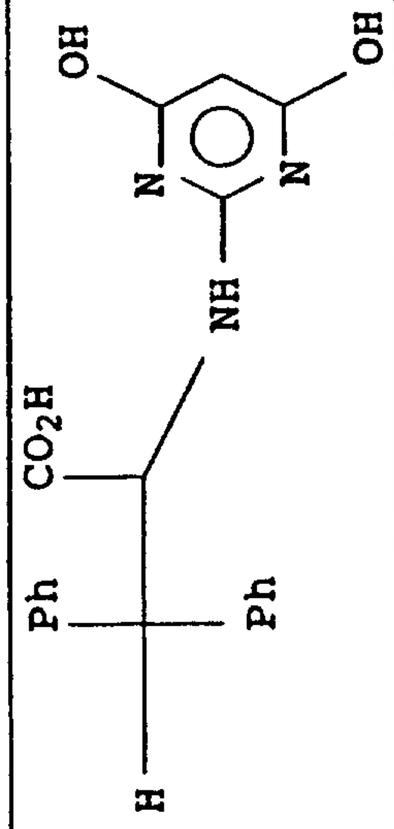
No.	Structure	M.p. [°C]
I-725		
I-726		
I-727		

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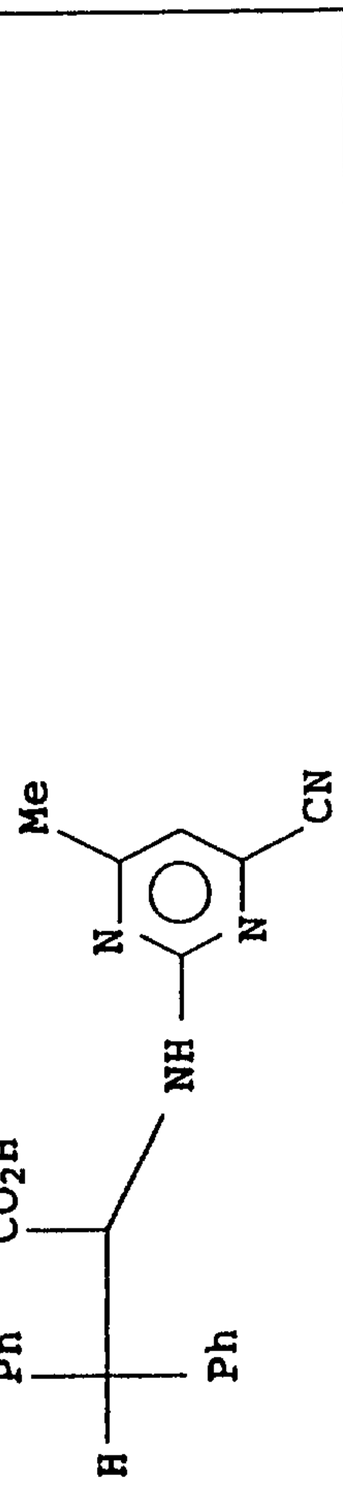
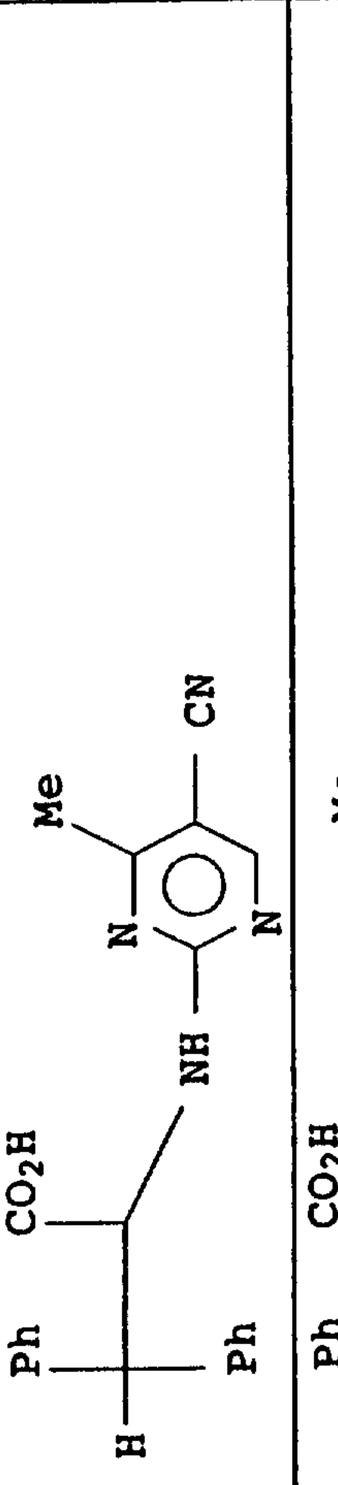
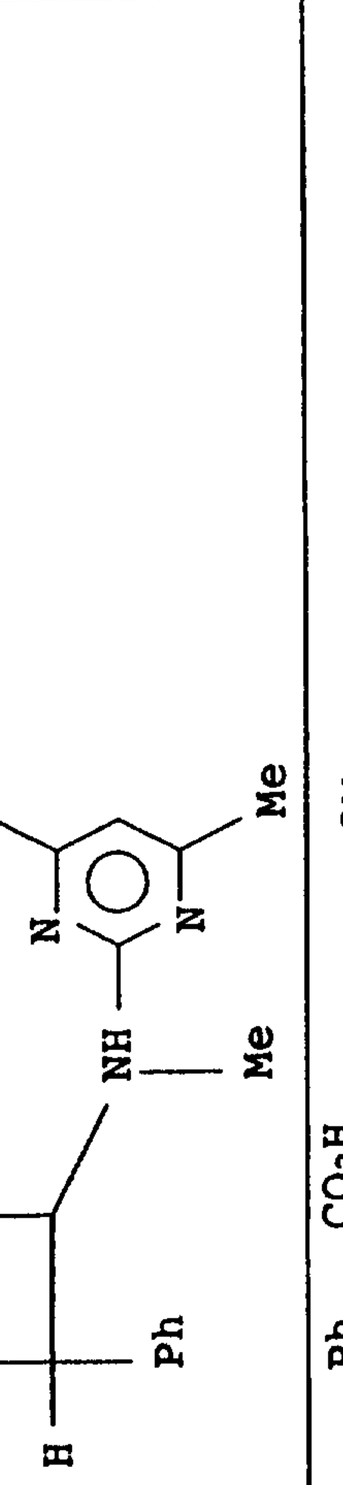
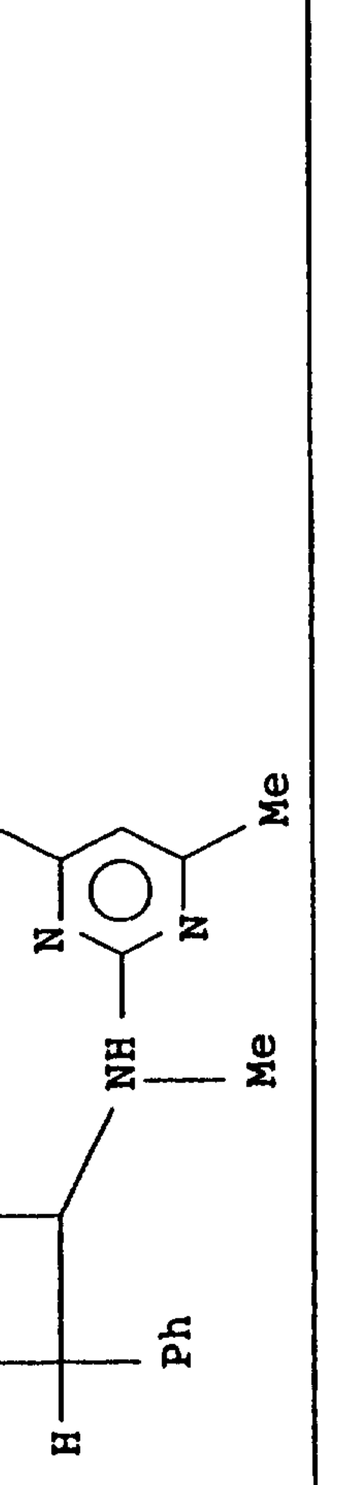
No.	Structure	M.p. [°C]
I-728		
I-729		
I-730		
I-731		

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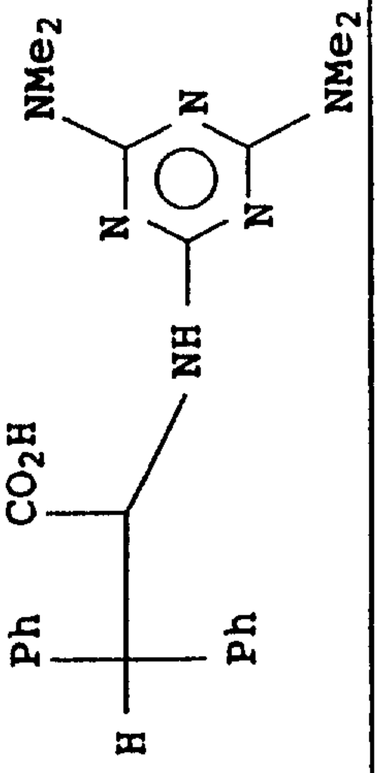
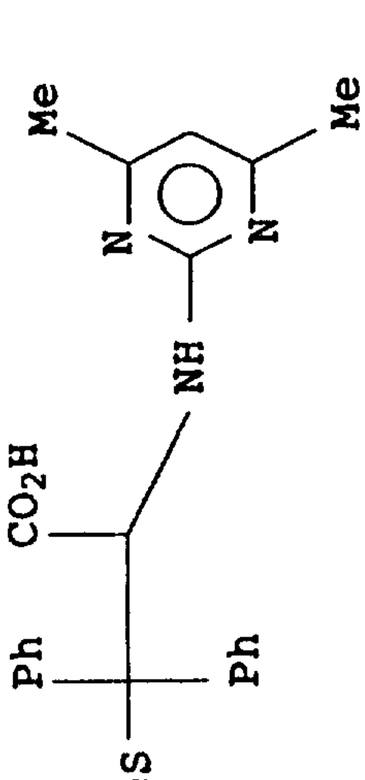
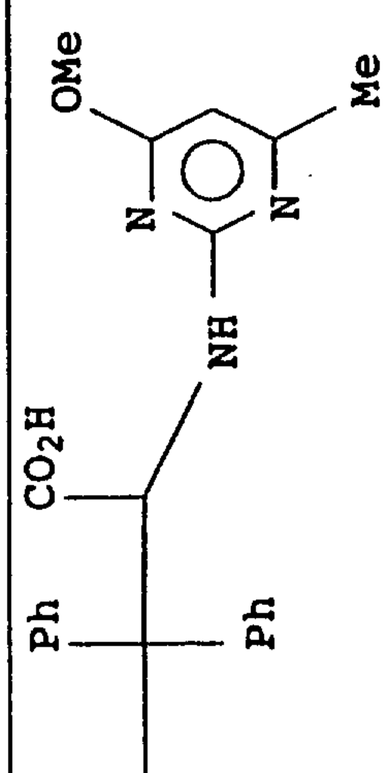
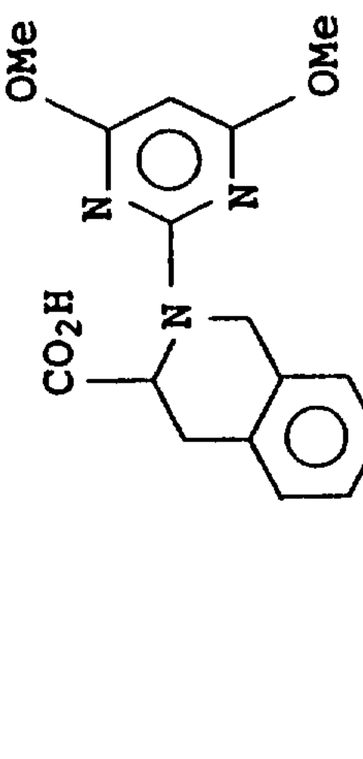
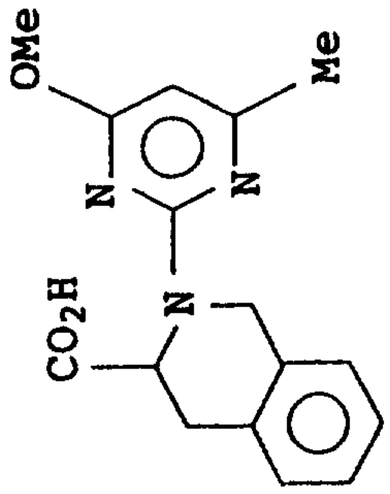
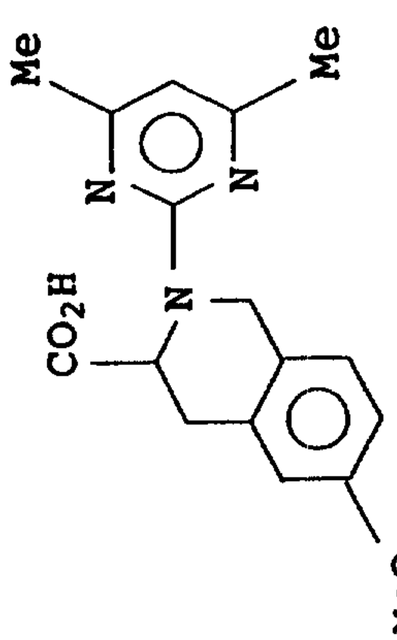
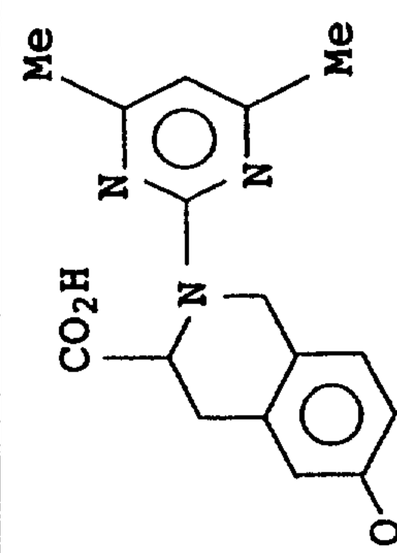
No.	Structure	M.p. [°C]
I-732		
I-733		
I-734		
I-735		

No.	Structure	M.p. [°C]
I-736		
I-737		
I-738		

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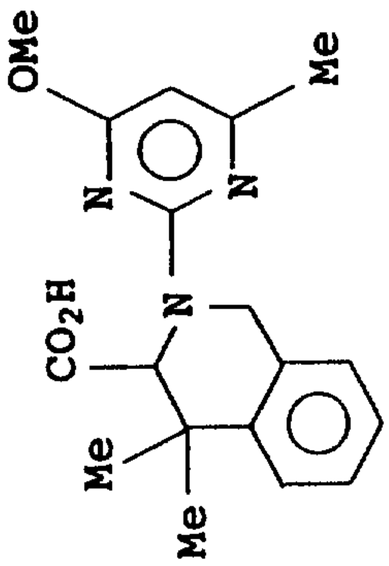
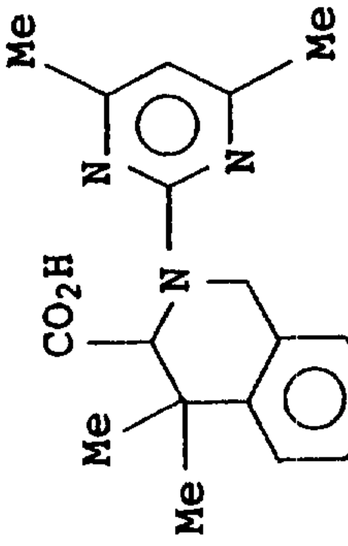
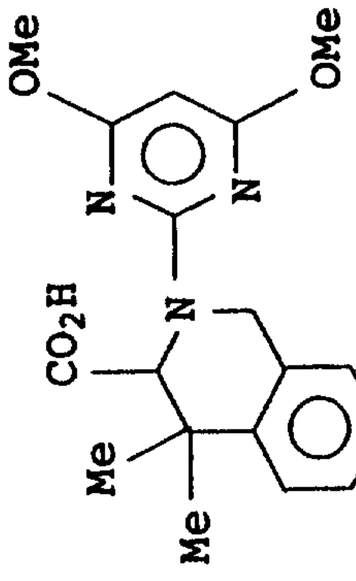
No.	Structure	M.p. [°C]
I-739		
I-740		
I-741		

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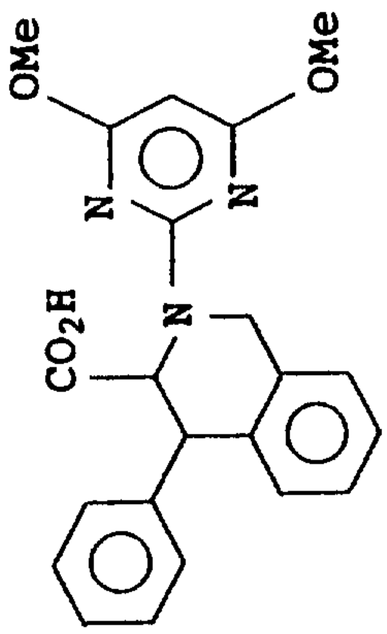
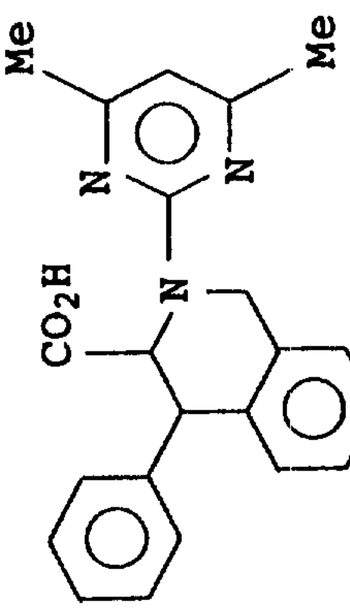
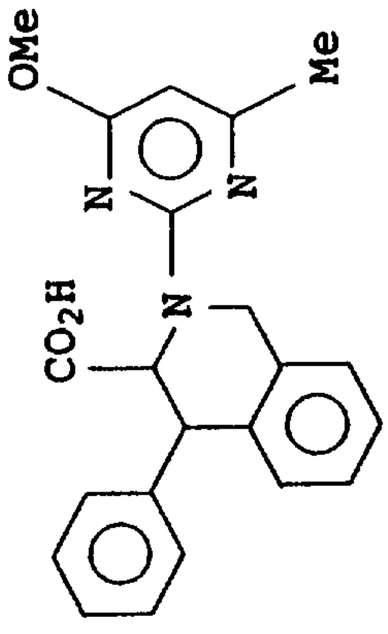
No.	Structure	M.p. [°C]
I-742		
I-743		
I-744		

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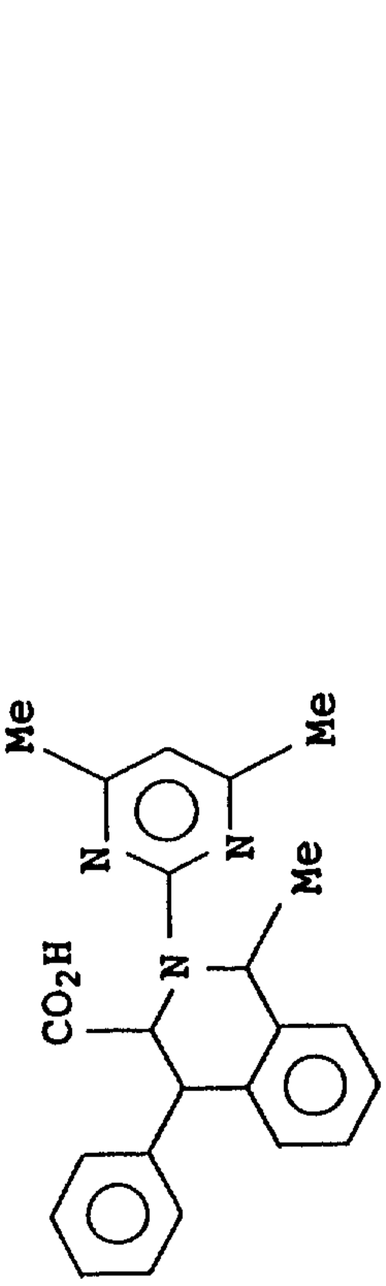
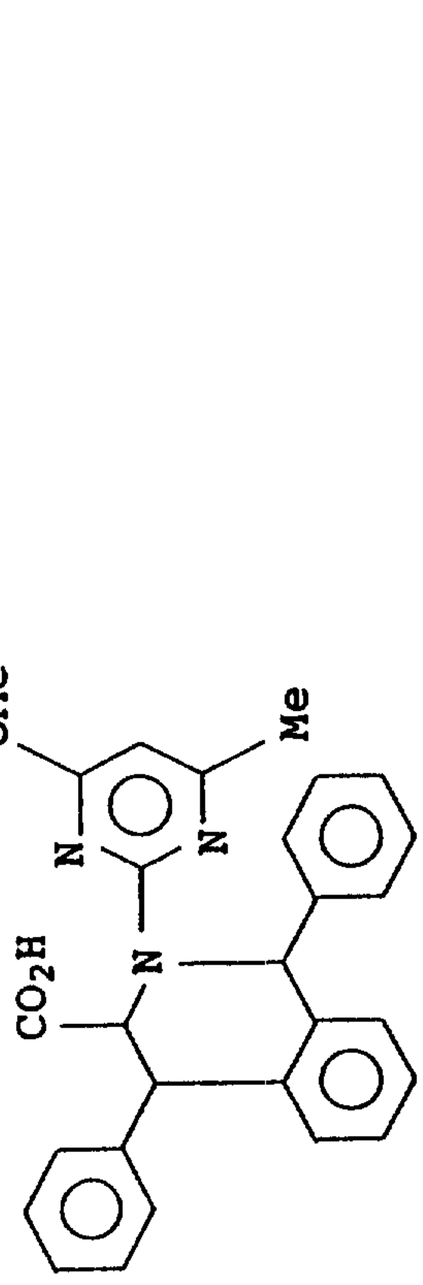
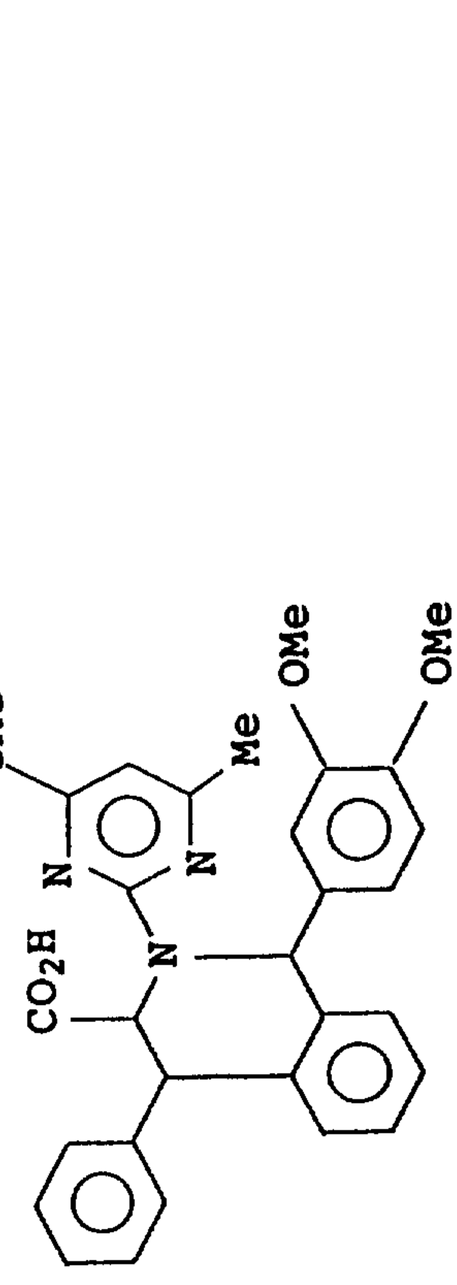
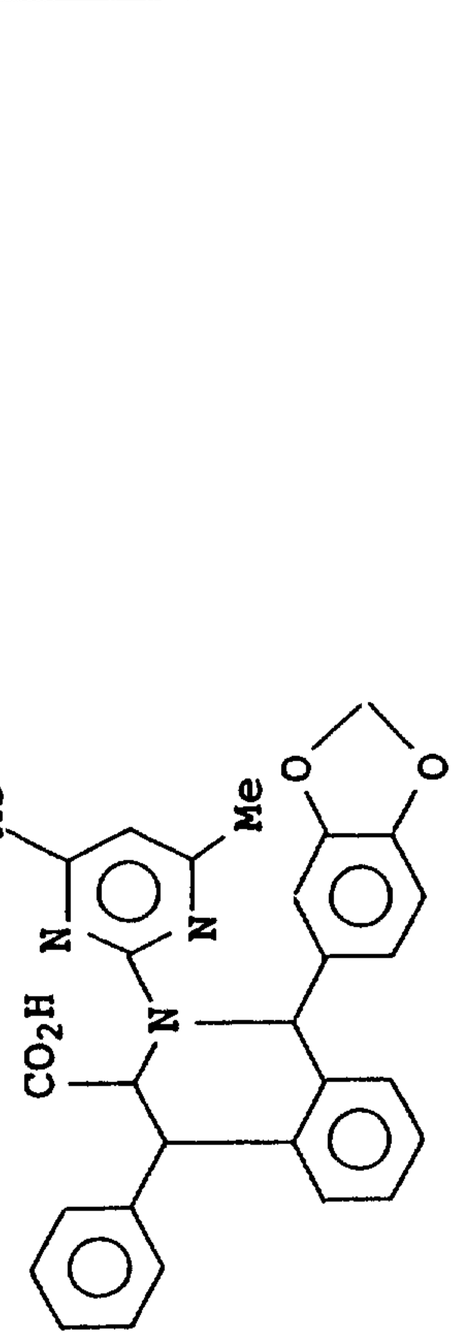
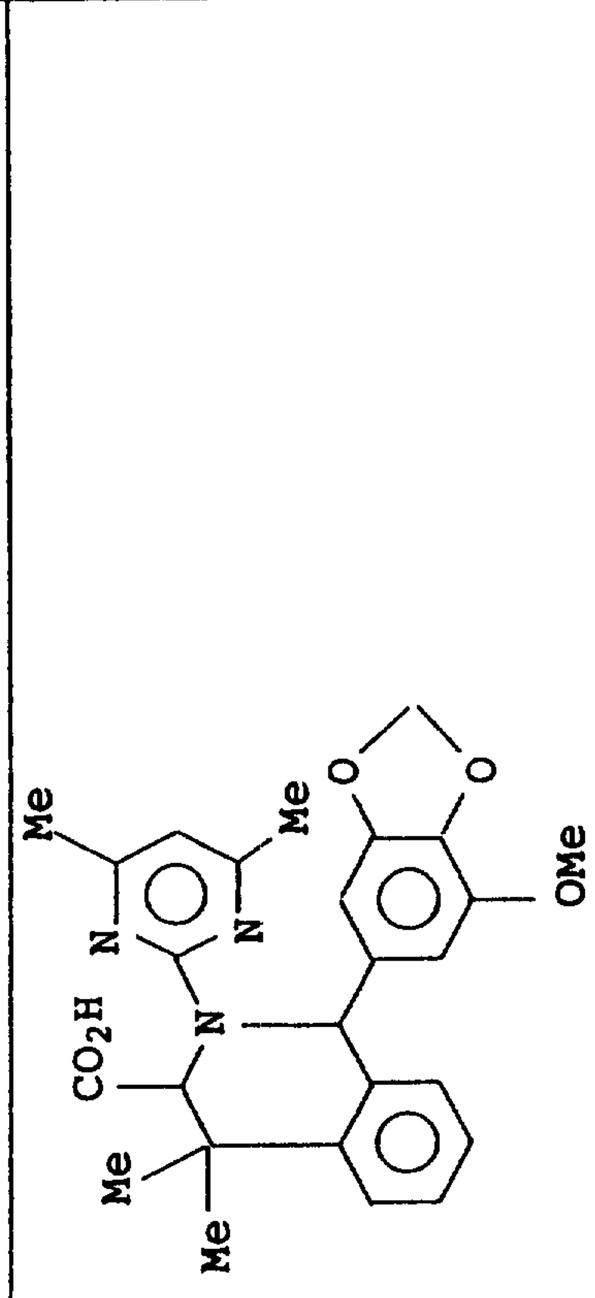
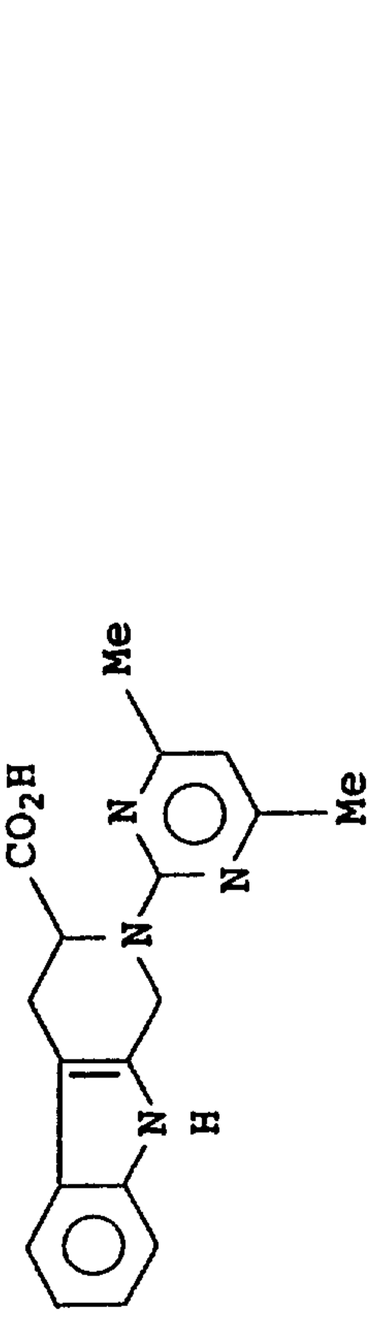
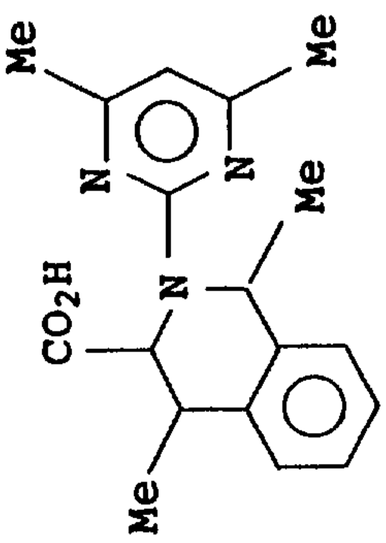
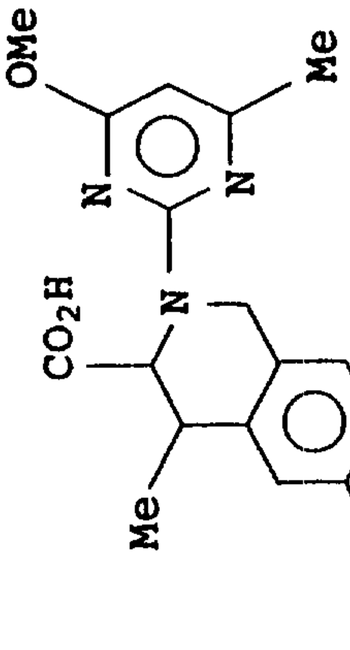
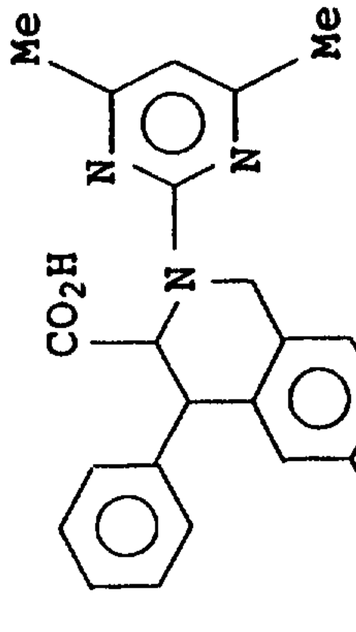
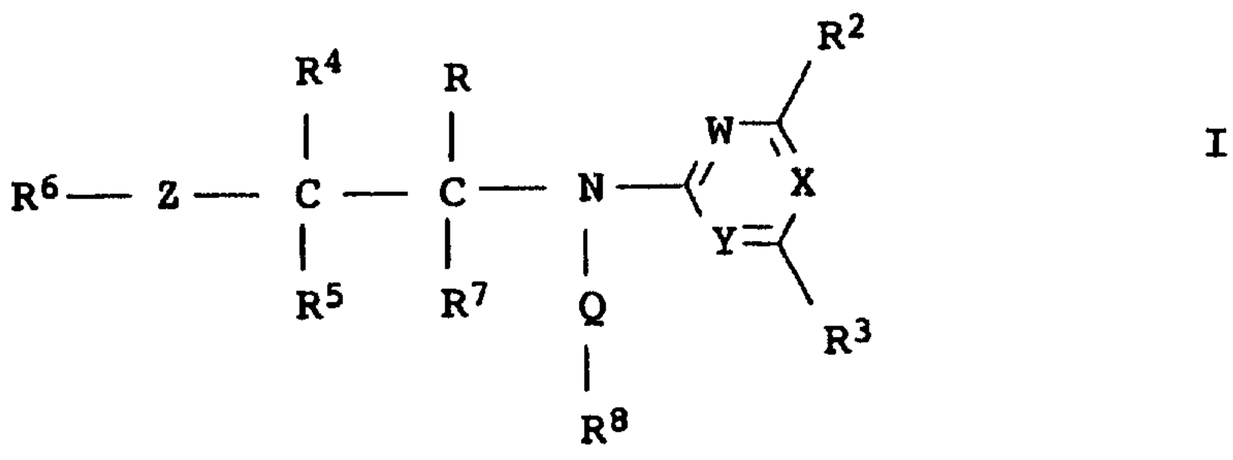
No.	Structure	M.p. [°C]
I-745		
I-746		
I-747		

No.	Structure	M.p. [°C]
I-748		
I-749		
I-750		

No.	Structure	M.p. [°C]
I-751		
I-752		
I-753		

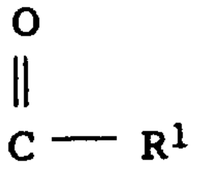
We claim:

1. An amino acid derivative of the formula I



I

where R is formyl, tetrazolyl, cyano, nitrile [sic], COOH or a radical which can be hydrolyzed to COOH, for example R is



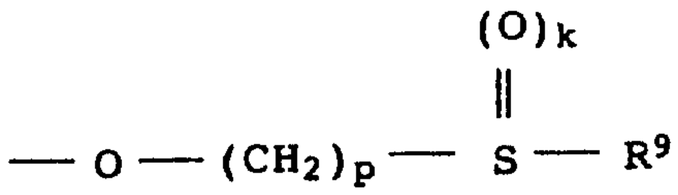
where R^1 has the following meanings:

a) hydrogen

b) succinylimidyl [sic]

c) a 5-membered heteroaromatic ring which is linked via a nitrogen atom, such as pyrrolyl, pyrazolyl, imidazolyl and triazolyl, which can carry one or two halogen atoms or one or two C_1-C_4-alkyl or one or two C_1-C_4-alkoxy groups;

d) R^1 is furthermore



where k can assume the values 0, 1 and 2, p can assume the values 1, 2, 3 and 4, and R^9 is C_1-C_4-alkyl, C_3-C_7-cycloalkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl or unsubstituted or substituted phenyl which can be substituted by one or more, eg. from one to three, of the following radicals: halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy,

C_1-C_4-alkylthio, mercapto, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino;

e) R^1 is furthermore OR^{10} where R^{10} is:

hydrogen, the cation of an alkali metal such as lithium, sodium, potassium or the cation of an alkaline earth metal such as calcium, magnesium and barium, and physiologically tolerated alkylammonium ion or the ammonium ion,

C_3-C_8-cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

C_1-C_8-alkyl, in particular C_1-C_4-alkyl such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl;

CH_2-phenyl which can be substituted by one or more of the following radicals: halogen, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino,

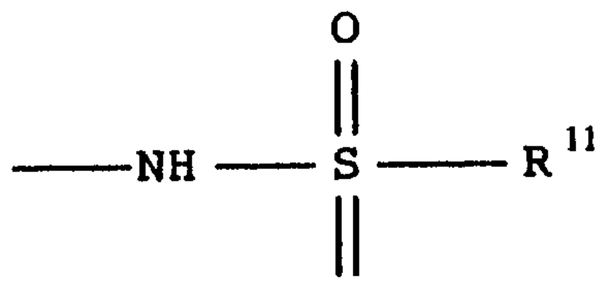
C_3-C_6-alkenyl or C_3-C_6-alkynyl, it being possible for these groups in turn to carry from one to five halogen atoms;

R^{10} can furthermore be a phenyl radical which can carry from one to five halogen atoms and/or from one to three of the following radicals: nitro, cyano, C_1-C_4-alkyl, C_1-C_4-haloalkyl, hydroxyl, C_1-C_4-alkoxy, mercapto, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino;

a 5-membered heteroaromatic ring which is linked via a nitrogen atom and contains from one to three nitrogen atoms and can carry one or two halogen atoms and/or one or two of the following radicals: C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenyl, C_1-C_4-haloalkoxy and/or C_1-C_4-alkylthio, in particular 1-pyrazolyl, 3-methyl-1-pyrazolyl, 4-methyl-1-pyrazolyl, 3,5-dimethyl-1-pyrazolyl, 3-phenyl-1-pyrazolyl, 4-phenyl-1-pyrazolyl, 4-chloro-1-pyrazolyl, 4-bromo-1-pyrazolyl, 1-imidazolyl, 1-benzimidazolyl, 1,2,4-triazol-1-yl, 3-methyl-1,2,4-triazol-1-yl,

5-methyl-1,2,4-triazol-1-yl, 1-benzotriazolyl, 3,4-dichloro-1-imidazolyl;

f) R^1 is furthermore

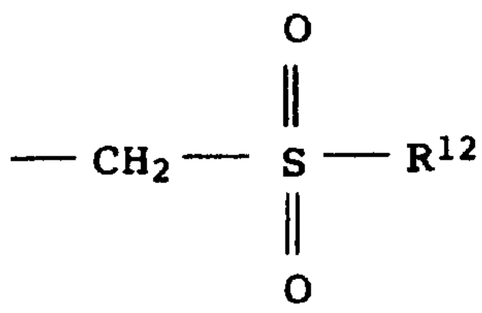


where R^{11} is:

C_1-C_4-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_3-C_8-cycloalkyl as mentioned above in particular, it being possible for these radicals to carry a C_1-C_4-alkoxy, C_1-C_4-alkylthio and/or a phenyl radical as mentioned above;

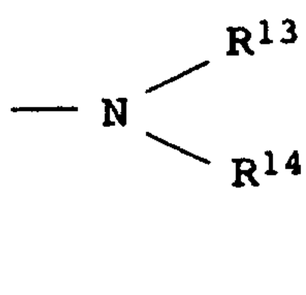
phenyl which is unsubstituted or substituted, in particular as mentioned above;

g) R^1 is



where R^{12} has the same meaning as R^{11};

h) R^1 can furthermore be



where R^{13} and R^{14} can be identical or different and have the following meanings:

hydrogen, C_1-C_7-alkyl, C_3-C_7-cycloalkyl, C_3-C_7-alkenyl, C_3-C_7-alkynyl, benzyl, phenyl, unsubstituted or substituted, as described above,

or R^{13} and R^{14} together form a C_4–C_7-alkylene chain which is closed to form a ring and is unsubstituted or substituted, eg. by C_1–C_4-alkyl, and which may contain a hetero atom, eg. oxygen, nitrogen or sulfur, such as $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)_7-$, $-(CH_2)_2-O-(CH_2)_2-$, $-(CH_2)_2-S-(CH_2)_2-$, $-CH_2-NH-(CH_2)_2-$, $-(CH_2)_2-NH-(CH_2)_2-$;

a tetrazole [sic] or a nitrile [sic].

The other substituents have the following meanings:

W is nitrogen or $C-NO_2$, and W can furthermore be a CH group when one or more of the substituents R^2, R^3, R^{15} and/or R^{16} are nitro;

R^2 is hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, hydroxyl, mercapto, C_1-C_4-alkylthio, nitro, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino, cyano, phenyl, unsubstituted or mono- to trisubstituted by halogen, hydroxyl, amino, mono- or dialkyl-(C_1-C_3)-amino, C_1-C_3-alkyl, C_1-C_3-alkoxy, mercapto or C_1-C_3-alkylthio;
or
a five- or six-membered heteroaromatic ring which contains from one to three nitrogen atoms and/or one sulfur or oxygen atom and which carries from one to three substituents as described above;

R^2 can furthermore form with the adjacent carbon atom and X a 5- or 6-membered alkylene or alkylidene ring in which, in each case, one or two carbon atoms can be replaced by a hetero atom such as nitrogen, sulfur or oxygen, and which can be mono- to trisubstituted by the following radicals: halogen, nitro, cyano, hydroxyl, mercapto, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy, C_1-C_3-alkylthio, amino, C_1-C_3-alkylamino, C_1-C_3-dialkylamino;

X is nitrogen or CR^{15} where R^{15} is hydrogen or C_1-C_5-alkyl, C_1-C_5-alkoxy, C_1-C_5-alkylthio, nitro, phenyl, hydroxyl, mercapto, halogen, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino or cyano,

or CR^{15} is linked to R^2 to form a 5- or 6-membered ring as described above, and furthermore CR^{15} can form together with R^3 and its adjacent carbon atom a 5- or 6-membered ring as described above;

R^3 can have the same meaning as R^2 and furthermore form together with the adjacent carbon atom and Y a 5- or 6-membered alkylene or alkylidene ring in which, in each case, one or two carbon atoms can be replaced by nitrogen, oxygen or sulfur; the 5- or 6-membered ring can be unsubstituted or mono- to trisubstituted by the following radicals;
halogen, nitro, cyano, hydroxyl, mercapto, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy, C_1-C_3-alkylthio, amino, C_1-C_3-alkylamino or C_1-C_3-dialkylamino;
nitrogen in the 5-membered ring can also be substituted by a formyl or acetyl group; R^2 and R^3 can be identical or different;

Y is nitrogen or CR^{16} where R^{16} is hydrogen, C_1-C_5-alkyl, C_1-C_5-alkoxy, C_1-C_5-alkylthio, nitro, phenyl, hydroxyl, halogen, cyano, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino or mercapto, or CR^{16} forms together with R^3 and its adjacent carbon atom a 5- or 6-membered ring as described above;

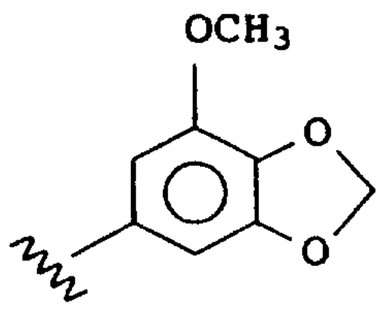
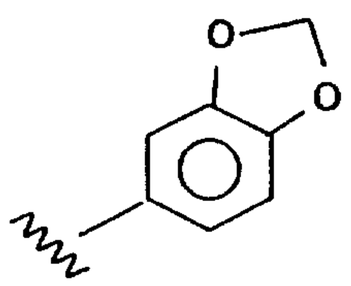
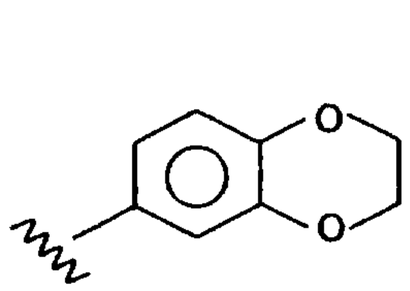
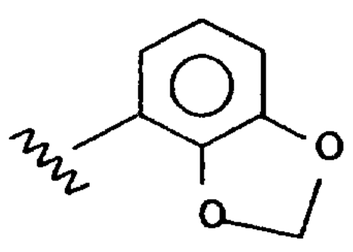
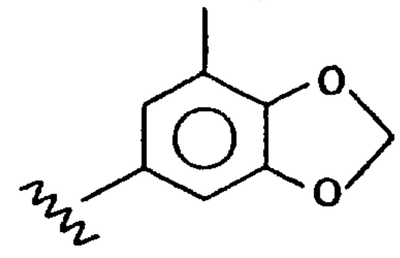
R^4 is hydrogen, C_1-C_7-alkyl, C_3-C_7-cycloalkyl; or phenyl or naphthyl which can be substituted by one or more of the following radicals;
halogen, nitro, cyano, hydroxyl, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, phenyl, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino,

R^4 can also be a five- or six-membered heteroaromatic ring which contains one nitrogen, sulfur or oxygen atom and which can carry one or two of the following radicals: halogen, cyano, nitro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenoxy, C_1-C_4-alkylthio, C_1-C_4-alkylamino or C_1-C_4-dialkylamino;

in addition, R^4 and R^5 can be phenyl groups which are connected to each other in the ortho positions by a direct linkage, a methylene, ethylene or ethenylene group, an oxygen or sulfur atom or an SO_2, NH or N-alkyl group;

R^5 is C_1-C_7-alkyl, C_3-C_7-cycloalkyl or phenyl or naphthyl which can be substituted by from one to three of the following radicals; halogen, nitro, cyano, hydroxyl, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, phenoxy, phenyl, C_1-C_4-alkylthio, amino, C_1-C_4-alkylamino or C_1-C_4-dialkylamino, where two radicals on adjacent carbon atoms can form together with the latter, connected via an alkylene or alkylidene group, a five- or six-membered ring in which one or more methylene or methylidene [sic] groups can be replaced by oxygen, for example: $-(CH_2)_3-$, $-(CH_2)_4-$, $-CH=CH-O-$, $-O-CH_2-O-$, $-O-(CH_2)_2-O-$, $-CH=CH-CH_2-$ or $-O-CH=CH-O-$;

R^5 can be, for example, the following radicals:

Furthermore, R^5 can be a five- or six-membered heteroaromatic ring which contains one nitrogen, sulfur or oxygen atom and which can carry one or two of the following radicals: halogen, cyano, nitro, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, phenoxy, C_1-C_4-alkylthio, C_1-C_4-alkylamino or C_1-C_4-dialkylamino;

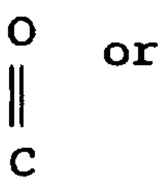
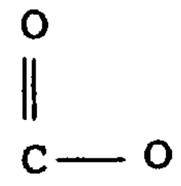
in addition, R^5 can form together with R^4 a tricyclic system as described above, and R^5 can additionally be an unsubstituted or substituted phenyl or heteroaromatic radical as described above which is linked in the ortho position to R^8 to form a 6-membered ring where Q must be a single bond and R^8 must be a $CH-R^{17}$ group;

R^6 is hydrogen, C_1-C_4-alkyl or C_1-C_4-haloalkyl

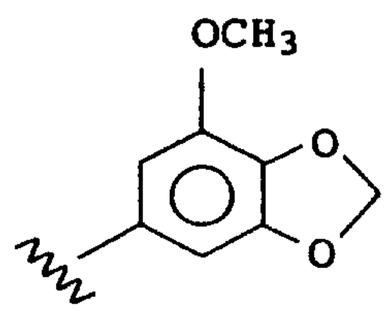
Z is a single bond, oxygen, sulfur, sulfinyl or sulfonyl;

R^7 is hydrogen or C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl;

Q is a single bond,

a  or  group

R^8 is hydrogen, C_1-C_4-alkyl, C_2-C_4-alkenyl, phenyl or benzyl, and R^8 can furthermore be directly connected to R^5 as described above, in which case R^8 is a CH-R^{17} group where R^{17} is hydrogen, C_1-C_4-alkyl, phenyl or phenyl which is mono- to trisubstituted by methoxy, or is one of the following radicals



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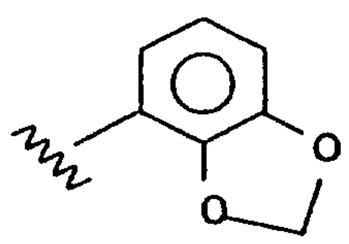

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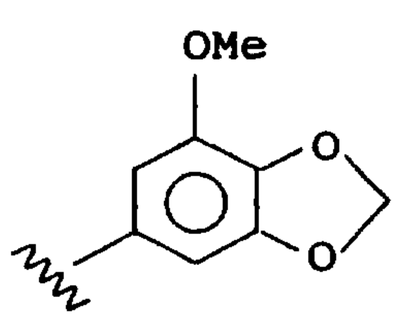

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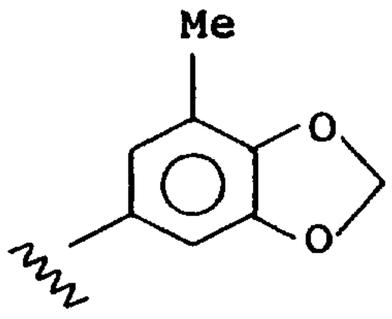

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2. The use of a compound as claimed in claim 1 for the treatment of diseases.

3. The use as claimed in claim 2, wherein it is employed as endothelin antagonist.

4. A drug containing a compound as claimed in claim 1 as active ingredient.