654340 COMMONWEALTH OF AUSTRALIA

P/00/001
Section 29

The Patents Act 1990

PATENT REQUEST: CONVENTION PATENT

We, DR KARL THOMAE GMBH, being the person identified below as the Applicant, request the grant of a patent to the person identified below as the Nominated Person, for an invention described in the accompanying standard complete specification
Full application details follow:-

Applicant:	DR KARL THOMAE GMBH
Address:	D-7950 Biberach an der Riss, Germany
Nominated Person:	DR KARL THOMAE GMBH
Address:	D-7950 Biberach an der Riss, Germany
Invention Title:	UREA DERIVATIVES
Names of actual Inventors:	Frank HIMMELSBACH, Helmut PIEPER, Volkhard AUSTEL, Günter LINZ, Thomas MÜLLER Wolfgang EISERT, and Johannes WEISENBERGER
Address for service in Australia:	CALLINAN LAWRIE, 278 High Street, Kew 3101, Victoria, Australia
Attorney Code:	CL

Convention Details

Application Number	Country	Country Code	Date of Application
P 4107857.8	Germany	DE	12 March 1991

D A T E D this 11th day of March, 1992.

DR KARL THOMAE GMBH
By their Patent Attorneys:
CALLINAN LAWRIE

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NOTICE OF ENTITLEMENT

We, DR KARL THOMAE GmbH

of, D-7950 Biberach an der Riss, Germany

being the applicant and person nominated for grant of patent in respect of Application No.

state the following:-

(a) The person nominated for the grant of the patent has entitlement from the actual inventors by virtue of being a person who would, if a patent were to be granted upon an application made by the said actual inventors, be entitled to have the patent assigned to it; and

is the applicant of the basic application.

(b) The basic application listed on the request form is the first application made in a Convention country in respect of the invention.

..... Signature

12 March 1992
..... Date

Jeffrey A. Ryder
Patent Attorney for the Applicant

AU9212803

(12) PATENT ABRIDGMENT (11) Document No. AU-B-12803/92
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 654340

(54) Title
UREA DERIVATIVES

International Patent Classification(s)

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	C07D 213/74	C07D 213/75	C07D 213/85	C07D 233/32
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	C07D 239/10	C07D 239/28	C07D 239/42	C07D 241/24
	C07D 249/12	C07D 285/10	C07D 309/04	C07D 309/12
	C07D 401/04	C07D 401/10	C07D 401/12	C07D 403/04
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(74) Attorney or Agent
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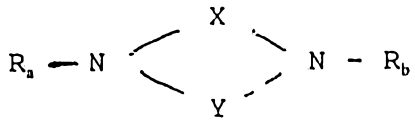
(57) Claim

1. Compounds of formula I



(I)

(wherein

X represents a carbimino group optionally substituted at the nitrogen atom by an alkyl, aralkyl, aryl, heteroaryl or cyano group, or X represents a carbonyl, thiocarbonyl, sulphinyl or sulphonyl group;

Y represents a straight-chained C_{2-4}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, wherein the above-mentioned alkylene or alkenylene groups may additionally be mono- or—

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disubstituted by a fluorine, chlorine or bromine atom or by an alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl groups, which substituents may be identical or different and wherein, in addition, one or two methylene groups may each be replaced by a carbonyl group, or

Y represents a 1,2-cycloalkylene group having 4 to 7 carbon atoms optionally substituted by R_c or R_d or by R_c and R_d, or

Y represents a 1,2-cycloalkenylene group having 4 to 7 carbon atoms or a 1,2-phenylene group, in which one or two methine groups may be substituted by a nitrogen atom and which may be substituted in the carbon skeleton by a fluorine, chlorine or bromine atom, by a C_{1-4}-alkyl group, by a trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, carboxy, nitro, $(R_1)_2N$-, $(R_1)_2NCO$- or $(R_1)_2NSO_2$- group, wherein the groups R_1 may be identical or different and may each represent a hydrogen atom or an alkyl, aralkyl, aryl or heteroaryl group, or by a R_1NH- group substituted by an alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, and wherein, additionally, one or two -CH=CH- groups may each be replaced by a $-CO-NR_1-$ group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-5}-aminoalkyl group, in which at one of the nitrogen atoms, one or two hydrogen

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atoms may be replaced by a C_{1-4}-alkyl group or one hydrogen atom may be replaced by a C_{2-5}-alkoxycarbonyl group or by an alkylcarbonyl, arylcarbonyl, aryloxycarbonyl or aralkoxycarbonyl group, or A may represent a cyano or cyano(C_{1-4}-alkyl) group or, if A is bound to a nitrogen atom of groups B or C which is not part of a lactam group, A may also represent a hydrogen atom or an alkyl group;

B represents a bond, or

an alkylene or alkenylene group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group, optionally alkyl-substituted in the carbon skeleton, and in which additionally one or two -CH=N- groups may be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group C, provided that the latter is not attached to group B by a heteroatom or a carbonyl group, or

a cyclopropylene group optionally substituted by an alkyl, aralkyl or aryl group, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and additionally a

methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to one another may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a biphenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms or by alkyl, trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl-NR_1- or alkylsulphonyl-NR_1- groups, and in which the substituents may be identical or different and R_1 is as hereinbefore defined;

C represents an alkylene or alkenylene group optionally substituted by a hydroxy, alkoxy or $(R_1)_2N$- group, or

an alkylenecarbonyl group connected to the group B via the carbonyl group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH-groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

an indanylene or 1,2,3,4-tetrahydronaphthylene group, wherein in each case the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

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a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be substituted in the carbon skeleton by an alkyl group, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group B, provided that the latter is not a bond or does not adjoin the group C with a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties located in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-5}-alkylene group or a C_{2-5}-alkenylene group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, carboxyalkoxy, alkoxycarbonylalkoxy, aralkoxycarbonyl-alkoxy, $(R_1)_2N-$, $(R_1)_2NCO-$, $(R_1)_2NSO_2-$ or nitro groups, or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl,

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arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group E, provided that the latter is not a bond or is not bound to the group D by means of a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to the nitrogen atom may each be replaced by a carbonyl group, or

a C_{2-6}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, $R_1N<$, (alkylcarbonyl)N<, (aralkylcarbonyl)N<, (arylcarbonyl)N<, (heteroarylcarbonyl)N<, (alkylsulphonyl)N<, (arylsulphonyl)N<, aminocarbonyl or carbonylamino group;

E represents a bond, or

a C_{1-5}-alkylene or C_{2-5}-alkenylene group optionally substituted by one or two alkyl groups, or by a hydroxy, alkoxy, amino, alkylamino, aralkylamino, dialkylamino,

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bis(aralkyl)amino, carboxyalkyl, alkoxycarbonylalkyl or aralkoxycarbonylalkyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group D, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may be replaced by a carbonyl group, or

an alkylenearylene group linked to the group D via the aryl moiety, or

an alkylene group linked to the group D via the group W, where W is as hereinbefore defined;

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F represents a carbonyl group substituted by a hydroxy or C_{1-6}-alkoxy group, whilst a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group, or

F may represent a sulpho, phosphono, O-alkylphosphono or tetrazol-5-yl group, whilst if A represents a cyano group or an amino or aminoalkyl group optionally benzoylated or benzyloxy-carbonylated at the nitrogen atom, the separation of the nitrogen atom of these groups and group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, perfluoroalkyl, aralkyl, aryl or heteroaryl group or, if the third of the groups R_a, R_b, R_c and R_d is connected to an unsaturated carbon atom of group Y, it may represent an alkoxy, alkylsulphenyl or $(R_1)_2N$- group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, aralkyl, aryl or heteroaryl group or R_a or R_b together with an adjacent group R_c or R_d may also represent a bond;

and, unless otherwise specified, any alkyl, alkylene, alkenylene or alkoxy moiety contains 1 to 3 carbon atoms,

any said aryl group, unless otherwise specified is a phenyl group which is optionally monosubstituted by a trifluoromethyl, carboxy, $(R_1)_2NCO$-, alkoxycarbonyl, alkylcarbonyl, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, nitro, $(R_1)_2N$-, alkylcarbonyl-NR_1-, aralkylcarbonyl-NR_1-, arylcarbonyl-NR_1-,

heteroarylcarbonyl-NR_1-, alkylsulphonyl-NR_1-, aralkylsulphonyl-NR_1-, arylsulphonyl-NR_1- or $(R_1)_2N$-sulphonyl group or may be mono-, di- or trisubstituted by fluorine, chlorine or bromine atoms or by hydroxy, C_{1-4}-alkoxy or C_{1-4}-alkyl groups, and
any said heteroaryl group, unless otherwise specified is a 5-membered heteroaromatic ring which contains an oxygen, sulphur or nitrogen atom, a nitrogen atom and an oxygen, sulphur or nitrogen atom or two nitrogen atoms and an oxygen, sulphur or nitrogen atom, or a 6-membered heteroaromatic ring which contains one, two or three nitrogen atoms and in which, additionally, one or two -CH=N- groups may be replaced by a -CO-NR_1- group, whilst the above-mentioned heteroaromatic rings may additionally be substituted by one or two alkyl groups or by a fluorine, chlorine or bromine atom or by a hydroxy or alkoxy group)

and the tautomers, the stereoisomers, and the addition salts thereof.

12. A method of treatment of the human or non-human animal body to combat conditions in which cell aggregations or cell-matrix interactions occur, said method comprising administering to said body a compound of formula I as claimed in any one of claims 1 to 7 or a physiologically acceptable addition salt thereof.

P/00/011
Regulation 3.2

654340

AUSTRALIA

PATENTS ACT 1990

COMPLETE SPECIFICATION

FOR A STANDARD PATENT

ORIGINAL

TO BE COMPLETED BY APPLICANT

Name of Applicant: DR KARL THOMAE GMBH

Actual Inventors: Frank HIMMELSBACH, Helmut PIEPER, Volkhard AUSTEL, Günter LINZ, Thomas MÜLLER Wolfgang EISERT, and Johannes WEISENBERGER

Address for Service: CALLINAN LAWRIE, 278 High Street, Kew, Victoria 3101, Australia

Invention Title: "UREA DERIVATIVES"

The following statement is a full description of this invention, including the best method of performing it known to us:-

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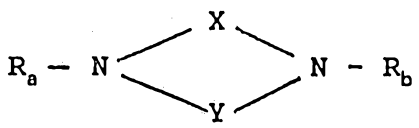
Urea derivatives

The invention relates to cyclic urea derivatives, processes for their preparation and pharmaceutical compositions containing them.

It has been found that certain novel urea derivatives possess valuable pharmacological properties, in particular aggregation inhibiting effects.

Thus viewed from one aspect the invention provides compounds of formula I



(I)

(wherein X represents a carbimino group optionally substituted at the nitrogen atom by an alkyl, aralkyl, aryl, heteroaryl or cyano group, or a carbonyl, thiocarbonyl, sulphinyl or sulphonyl group;

Y represents a straight-chained C_{2-4}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, wherein the above-mentioned alkylene or alkenylene groups may additionally be mono- or disubstituted by fluorine, chlorine or bromine atoms or by alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl groups, which substituents may be identical or different and wherein, in addition, one or two methylene groups may each be replaced by a carbonyl group, or

Y represents a 1,2-cycloalkylene group having 4 to 7 carbon atoms optionally substituted by R_c or R_d or by R_c and R_d, or

Y represents a 1,2-cycloalkenylene group having 4 to 7 carbon atoms or a 1,2-phenylene group in which one or two methine groups may be replaced by a nitrogen atom and which may be substituted in the carbon skeleton by a fluorine, chlorine or bromine atom, by a C_{1-4}-alkyl group, by a trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, carboxy, nitro, $(R_1)_2N$-, $(R_1)_2NCO$- or $(R_1)_2NSO_2$- group (wherein the groups R_1 may be identical or different and may each represent a hydrogen atom or an alkyl, aralkyl, aryl or heteroaryl group), or by a R_1NH- group substituted by an alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, and wherein, additionally, one or two -CH=CH- groups may each be replaced by a $-CO-NR_1-$ group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein

A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-5}-aminoalkyl group in which at one of the nitrogen atoms, one or two hydrogen atoms may be replaced by a C_{1-4}-alkyl group or one hydrogen atom may be replaced by a C_{2-5}-alkoxycarbonyl group or by an alkylcarbonyl, arylcarbonyl, aryloxycarbonyl or aralkoxycarbonyl group, or A may represent a cyano or cyano(C_{1-4}-alkyl) group or, if A is bound to a nitrogen atom of groups B or C which is not part of a lactam group, A may also represent a hydrogen atom or an alkyl

group;

B represents a bond, or

an alkylene or alkenylene group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group, optionally alkyl-substituted in the carbon skeleton and in which additionally one or two -CH=N- groups may be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group C, provided that the latter is not attached to group B by a heteroatom or a carbonyl group, or

a cyclopropylene group optionally substituted by an alkyl, aralkyl or aryl group, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and additionally a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to one another may

each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a biphenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms or by alkyl, trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl-NR_1- or alkylsulphonyl-NR_1- groups, and in which the substituents may be identical or different and R_1 is as hereinbefore defined;

C represents an alkylene or alkenylene group optionally substituted by a hydroxy, alkoxy or $(R_1)_2N$- group, or

an alkylenecarbonyl group connected to the group B via the carbonyl group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

an indanylene or 1,2,3,4-tetrahydronaphthylene group, wherein in each case the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be substituted in the carbon skeleton by an alkyl group,

whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group B, provided that the latter is not a bond or does not adjoin the group C with a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties located in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein
D represents a C_{1-5}-alkylene group or a C_{2-5}-alkenylene group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, carboxyalkoxy, alkoxycarbonylalkoxy, aralkoxycarbonyl-alkoxy, $(R_1)_2N-$, $(R_1)_2NCO-$, $(R_1)_2NSO_2-$ or nitro groups, or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl,

alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group E, provided that the latter is not a bond or is not bound to the group D by means of a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to the nitrogen atom may each be replaced by a carbonyl group, or

a C_{2-6}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, $R_1N<$, (alkylcarbonyl)$N<$, (aralkylcarbonyl)$N<$, (arylcarbonyl)$N<$, (heteroarylcarbonyl)$N<$, (alkylsulphonyl)$N<$, (arylsulphonyl)$N<$, aminocarbonyl or carbonylamino group;

E represents a bond, or

a C_{1-5}-alkylene or C_{2-5}-alkenylene group optionally

substituted by one or two alkyl groups, or by a hydroxy, alkoxy, amino, alkylamino, aralkylamino, dialkylamino, bis(aralkyl)amino, carboxyalkyl, alkoxycarbonylalkyl or aralkoxycarbonylalkyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group D, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

an alkylenearylene group linked to the group D via the aryl moiety, or

an alkylene group linked to the group D via the group W, where W is as hereinbefore defined;

F represents a carbonyl group substituted by a hydroxy or C_{1-6}-alkoxy group, whilst a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group, or

F may represent a sulpho, phosphono, O-alkylphosphono or tetrazol-5-yl group, whilst if A represents a cyano group or an amino or aminoalkyl group optionally benzoylated or benzyloxy-carbonylated at the nitrogen atom, the separation of the nitrogen atom of these groups and group F is at least 10 bonds;

Where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, perfluoroalkyl, aralkyl, aryl or heteroaryl group or, if the third of the groups R_a, R_b, R_c and R_d is connected to an unsaturated carbon atom of group Y, it may represent an alkoxy, alkylsulphenyl or $(R_1)_2N$- group; and

Where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, aralkyl, aryl or heteroaryl group, or

R_a or R_b together with an adjacent group R_c or R_d may also represent a bond;

and, unless otherwise specified any alkyl, alkylene, alkenylene or alkoxy moiety contains 1 to 3 carbon atoms,

any said aryl group, unless otherwise specified is a phenyl group which is optionally monosubstituted by a trifluoromethyl, carboxy, $(R_1)_2NCO-$, alkoxycarbonyl, alkylcarbonyl, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, nitro, $(R_1)_2N-$, alkylcarbonyl-NR_1-, aralkylcarbonyl-NR_1-, arylcarbonyl-NR_1-, heteroarylcarbonyl-NR_1-, alkylsulphonyl-NR_1-, aralkylsulphonyl-NR_1-, arylsulphonyl-NR_1- or $(R_1)_2N-$sulphonyl group, or mono-, di- or trisubstituted by fluorine, chlorine or bromine atoms or by hydroxy, C_{1-4}-alkoxy or C_{1-4}-alkyl groups, and

any said heteroaryl group, unless otherwise specified is a 5-membered heteroaromatic ring which contains an oxygen, sulphur or nitrogen atom, a nitrogen atom and an oxygen, sulphur or nitrogen atom or two nitrogen atoms and an oxygen, sulphur or nitrogen atom, or a 6-membered heteroaromatic ring which contains one, two or three nitrogen atoms and in which, additionally, one or two -CH=N- groups may each be replaced by a -CO-NR_1- group, whilst the above-mentioned heteroaromatic rings may additionally be substituted by one or two alkyl groups or by a fluorine, chlorine or bromine atom or by a hydroxy or alkoxy group).

and the tautomers, the stereoisomers thereof, including the mixtures thereof, and the addition salts thereof, particularly the physiologically acceptable addition salts with inorganic or organic acids or bases.

Preferred compounds according to the invention include those of formula I wherein

X represents a carbimino group optionally substituted at the nitrogen atom by an alkyl, aralkyl, aryl, heteroaryl or cyano group, or a carbonyl, thiocarbonyl, sulphinyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by fluorine, chlorine or bromine atoms or by alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl groups, whilst the substituents may be identical or different and, in addition, one or two methylene groups may each be replaced by a carbonyl group, or

Y represents a 1,2-cyclohexylene group optionally substituted by R_c or R_d or by R_c and R_d, or

Y represents a 1,2-cyclohexenylene group or a 1,2-phenylene group wherein one or two CH groups may each be replaced by a nitrogen atom and which may be substituted in the carbon skeleton by a fluorine, chlorine or bromine atom, by a C_{1-4}-alkyl group, by a trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, carboxy, nitro, $(R_1)_2N$-, $(R_1)_2NCO$- or $(R_1)_2NSO_2$- group (wherein the groups R_1 may be identical or different and may each represent a hydrogen atom, an alkyl, aralkyl, aryl or heteroaryl group), or by a R_1NH- group substituted by an alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, and wherein, additionally, one or two -CH=CH- groups may each be replaced by a $-CO-NR_1-$ group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein

A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-5}-aminoalkyl group in which at one of the nitrogen atoms, one or two hydrogen atoms may be replaced by a C_{1-4}-alkyl group or a hydrogen atom may be replaced by a C_{2-5}-alkoxycarbonyl group, by an alkylcarbonyl, arylcarbonyl, aryloxycarbonyl or aralkoxycarbonyl group, or A represents a cyano or cyano(C_{1-4}-alkyl) group or, if A is bound to a nitrogen atom of groups B or C which is not part of a lactam group, A may also represent a hydrogen atom or an alkyl group;

B represents a bond, or

an alkylene or alkenylene group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, in which the substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by an alkyl group, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$-group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group C, provided that the latter does not adjoin the group B with a heteroatom or a carbonyl group, or

a C_{3-5}-cycloalkylene group, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a biphenylene group;

C represents an alkylene or alkenylene group optionally substituted by a hydroxy group, or

an alkylenecarbonyl group connected to the group B via the carbonyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein, in each case, the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by an alkyl group, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group B, provided that the latter does not represent a bond or is not adjacent to the group C with a

heteroatom, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group and the nitrogen atoms may not be bound to a nitrogen atom of the cyclic urea;

a second of the groups R_a, R_b, R_c to R_d represents a group of formula

F - E - D -

wherein
D represents a C_{1-5}-alkylene group or a C_{2-5}-alkenylene group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, carboxyalkoxy, alkoxycarbonylalkoxy, aralkoxycarbonyl-alkoxy, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted by an alkyl group in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms instead of being bound to the group R_1 may also be bound to the group E, provided that the latter does not represent a bond or is

not bound by a heteroatom to the group D, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a C_{3-6}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, $R_1N<$, (alkylcarbonyl)$N<$, (aralkylcarbonyl)$N<$, (arylcarbonyl)$N<$, (heteroarylcarbonyl)$N<$, (alkylsulphonyl)$N<$ or (arylsulphonyl)$N<$ group and the alkylene group linked to a nitrogen atom of the cyclic urea contains 2 or 3 carbon atoms;

E represents a bond, or

a C_{1-5}-alkylene or C_{2-5}-alkenylene group optionally substituted by one or two alkyl groups or by a hydroxy, alkoxy, amino, alkylamino, aralkylamino, dialkylamino, bis(aralkyl)amino, carboxyalkyl, alkoxycarbonylalkyl or aralkoxycarbonylalkyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1-NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, in which the substituents may be identical or different,

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N-

groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group D, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

an alkylenearylene group linked to the group D via the aryl group, or

an alkylene group linked to the group D via the group W', wherein W' represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, $R_1N<$, (alkycarbonyl)$N<$, (aralkylcarbonyl)$N<$, (arylcarbonyl)$N<$, (heteroarylcarbonyl)$N<$, (alkylsulphonyl)$N<$, (arylsulphonyl)$N<$ or aminocarbonyl group wherein the nitrogen atom is bound to the alkylene group;

F represents a carbonyl group substituted by a hydroxy or C_{1-6}-alkoxy group, whilst a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group, or F may represent a sulpho, phosphono, O-alkylphosphono or tetrazol-5-yl group, whilst if A represents a cyano group or an amino or aminoalkyl group optionally benzoylated or benzyloxycarbonylated at the nitrogen atom, the separation of the nitrogen atom of these groups and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d is a hydrogen atom, an alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl group or, if the third of the groups R_a,

R_b, R_c and R_d is bound to an unsaturated carbon atom of group Y, it may represent an alkoxy, alkylsulphenyl or $(R_1)_2N$- group; and

where present the fourth of groups R_a, R_b, R_c and R_d represents a hydrogen atom or an alkyl, aralkyl, aryl or heteroaryl group;

and the tautomers, stereoisomers, and addition salts thereof.

Particularly preferred compounds according to the invention include those of formula I wherein

X represents a carbimino group optionally substituted at the nitrogen atom by a methyl, phenyl or pyridyl group, or X represents a carbonyl, thiocarbonyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, which may be substituted by a chlorine atom, by one or two methyl groups or by a trifluoromethyl, phenyl or acetyl group, whilst additionally a methylene group may be replaced by a carbonyl group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH-group, optionally substituted by R_c or R_d, or a 1,2-phenylene or 2,3-pyridinylene group;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein
A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-4}-aminoalkyl group in which at one

of the nitrogen atoms, one or two hydrogen atoms may each be replaced by a C_{1-4}-alkyl group or a hydrogen atom may be replaced by a (C_{1-4}-alkoxy)carbonyl or benzyloxycarbonyl group, or, if A is bound to a nitrogen atom of group C which is not part of a lactam group, A may also represent a hydrogen atom or a methyl group;

B represents a bond, or

a phenylene group optionally substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom, or by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group, or

a C_{3-6}-cycloalkylene group, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or biphenylene group;

C represents an ethylene group optionally substituted by a hydroxy group, or

a methylenecarbonyl group linked to the group B via the carbonyl group, or

a phenylene group optionally substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom, or by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group,

an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, cyclohexylene or piperidinylene group, wherein the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea;

a second of groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group,

a phenylene group which may be substituted by a fluorine, chlorine or bromine atom, or by a methyl, methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, carboxymethoxy, methoxycarbonylmethoxy, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group, or

a pyridinylene, cyclohexylene or piperidinylene group, whilst additionally in a pyridinylene group a -CH=N- group may be replaced by a -CO-NH- group, whilst the nitrogen atom, instead of being bound to the hydrogen atom, may also be bound to the group E, provided that the latter is not a bond or is not bound by a heteroatom to group D, or

a C_{3-5}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom or a sulphinyl, sulphonyl, imino, methylimino, acetylimino, benzoylimino or methanesulphonylimino group and the alkylene group linked to the cyclic urea contains 2 or 3 carbon atoms;

E represents a bond, or

a C_{1-3}-alkylene group optionally substituted by one or two methyl groups or by a hydroxy, methoxy, amino,

dimethylamino, dibenzylamino, carboxymethyl or methoxycarbonylmethyl group or a C_{2-3}-alkenylene group, or

a phenylene group, or

a C_{1-2}-alkylene group linked to group D by the group W', wherein W' represents an oxygen or sulphur atom or a sulphinyl, sulphonyl or aminocarbonyl group, the amino group being bound to the alkylene group;

F represents a carbonyl group which is substituted by a hydroxy group, by a C_{1-4}-alkoxy group or by a phenyl(C_{1-2}-alkoxy) group, or F represents a phosphono, O-methylphosphono or tetrazol-5-yl group, whilst if A represents an amino or aminoalkyl group optionally benzyloxycarbonylated at the nitrogen atom, the separation of the nitrogen atom of this group and group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, a methyl, ethyl, trifluoromethyl or phenyl group; and

where present the fourth of groups R_a, R_b, R_c to R_d represents a hydrogen atom or a methyl group;

and the tautomers, stereoisomers, including mixtures thereof, and addition salts thereof.

More particularly preferred compounds according to the invention include those of formula I wherein

X represents a carbonyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by

R_c and R_d, which may also be substituted by one or two methyl groups or by a trifluoromethyl or phenyl group, whilst additionally a methylene group may be replaced by a carbonyl group, or Y represents an -N=CH- or -CH=N- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein
A represents an amino, amidino or straight-chained or branched C_{1-4}-aminoalkyl group, in which at one of the nitrogen atoms, a hydrogen atom may be replaced by (C_{1-4}-alkoxy)carbonyl or benzyloxycarbonyl group;

B represents a bond, or

a phenylene group optionally substituted by a fluorine or chlorine atom, or

a cyclopropylene, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group;

C represents a phenylene group optionally substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom or by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, amino, acetylamino, benzoylamino or methanesulphonylamino group, or, if A represents an amino group and B represents a bond, C may represent an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

C represents a pyridinylene, pyrimidinylene,

pyrazinylene, pyridazinylene, cyclohexylene or piperidinylene group, whilst the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group, or

a phenylene group optionally substituted by a fluorine, chlorine or bromine atom or by a methyl, methoxy, methylsulphenyl, methylsulphinyl or methylsulphonyl group, or

a pyridinylene, cyclohexylene or piperidinylene group, whilst additionally in a pyridinylene group the -CH=N- group may be replaced by a -CO-NH- group and the nitrogen atom, instead of being bound to the hydrogen atom, may also be bound to the group E, provided that the latter is not a bond or is not bound to the group D by a heteroatom; or

a $-CH_2CH_2-N(COCH_3)-CH_2-$ group wherein the ethylene moiety is bound to the cyclic urea;

E represents a bond, or

an ethylene group optionally substituted by one or two methyl groups or by an amino or dibenzylamino group, or

an ethenylene or phenylene group, or

a methylene group linked to group D by the group W', wherein W' represents an oxygen or sulphur atom or a sulphinyl or sulphonyl group;

F represents a carbonyl group substituted by a hydroxy group or by a C_{1-4}-alkoxy group, or F may represent a phosphono, O-methylphosphono or tetrazol-5-yl group, whilst if A represents an amino or aminoalkyl group optionally benzyloxycarbonylated at the nitrogen atom, the separation of the nitrogen atom of this group and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl, ethyl or phenyl group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl group;

and the tautomers, the stereoisomers including the mixtures thereof and the addition salts thereof.

Most particularly preferred compounds according to the invention include those of formula I wherein

X represents a carbonyl or sulphonyl group;

Y represents an ethylene or ethenylene group optionally substituted by R_c or R_d and optionally substituted by a methyl or phenyl group, or Y represents a carbonylmethylene or methylenecarbonyl group optionally substituted by a methyl group, or Y represents a -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein
A represents an aminomethyl, aminoethyl or amidino group

optionally substituted by a (C_{1-4}-alkoxy)carbonyl group;

B represents a bond or a 1,4-phenylene group; and

C represents a 1,4-phenylene group optionally substituted by a methyl group, a 3,6-pyridazinylene or 1,4-piperidinylene group, whilst the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea, or, if A represents an amino group and B represents a bond, C may represent an indanylene group, wherein the saturated ring is attached to A and the aromatic ring to the cyclic urea ring;

a second of the groups R_a, R_b, R_c and R_d represents a group of the formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group, a 1,4-phenylene or 1,4-cyclohexylene group;

E represents a bond, or

an ethylene group optionally substituted by an amino or dibenzylamino group, or an ethenylene group, or

a 1,4-phenylene group, or

a methylene group linked by the group W' to the group D, wherein W' represents an oxygen or sulphur atom or a sulphinyl or sulphonyl group;

F represents a carbonyl group substituted by a hydroxy group or by a C_{1-4}-alkoxy group, whilst if A represents an aminomethyl group, the separation of the nitrogen atom of this group and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl, ethyl or phenyl group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl group;

particularly those compounds of formula I wherein there is a further ring member between the linking points of those of groups R_a, R_b, R_c and R_d which represent the A-B-C- and F-E-D- groups, on the cyclic urea;

the tautomers, the stereoisomers including mixtures thereof and the addition salts thereof.

Especially preferred compounds of formula I include

(a) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one;

(b) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-cyclohexyl]-imidazolidin-2-one;

(c) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2,4-dione;

(d) 2-(4-amidino-phenyl)-5-[4-(2-carboxy-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide;

(e) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-one;

(f) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one;

(g) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(h) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-ethyl-4H-1,2,4-triazol-3-one;

(i) 2-(4-amidino-phenyl)-4-[4-(2-carboxyethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(j) 4-(4-amidino-phenyl)-2-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(k) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one;

(l) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(m) 2-(4-amidino-phenyl)-5-ethyl-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(n) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(o) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(p) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

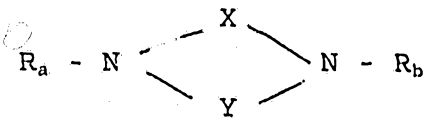
(q) 4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-2-(4-methoxycarbonylamidino-phenyl)-5-methyl-4H-1,2,4-triazol-3-one; or

(r) 2-(4-amidino-phenyl)-4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

and the tautomers, stereoisomers and addition salts thereof.

Viewed from a further aspect the invention also provides a process for the preparation of compounds of the invention, said processing comprising at least one of the following steps:

a) (to prepare compounds of formula I wherein F represents a carboxy group) converting a compound of formula II



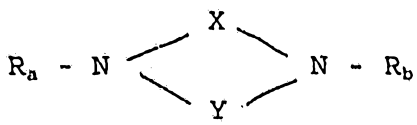
(II)

(wherein
R_a, R_b, X and Y are as hereinbefore defined with the proviso that one of the groups R_a, R_b, R_c and R_d must represent a group of formula

$$F' - E - D -$$

wherein E and D are as hereinbefore defined and F' represents a group which may be converted into a carboxyl group by hydrolysis, treatment with acids, thermolysis or hydrogenolysis) into a corresponding carboxy compound;

b) (to prepare compounds of formula I wherein A represents an R_4NH-C(=NH)- group optionally substituted by an alkyl group) reacting a compound of formula III



(III)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

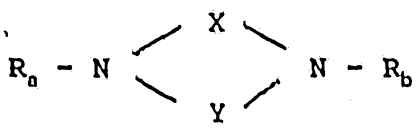
Z_1 - C(=NH) - B -

wherein B and C are as hereinbefore defined and Z_1 represents an alkoxy or aralkoxy group such as a methoxy, ethoxy, n-propoxy, isopropoxy or benzyloxy group or an alkylthio or aralkylthio group such as a methylthio, ethylthio, n-propylthio or benzylthio group or an amino group) which is optionally formed in the reaction mixture, with an amine of formula IV

$$R_4 - NH_2 \qquad (IV)$$

(wherein
R_4 represents a hydrogen atom or a C_{1-4}-alkyl group) or with an acid addition salt thereof;

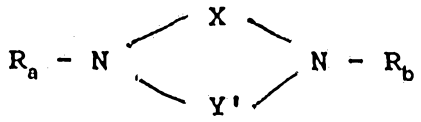
c) (to prepare compounds of formula I wherein at least one of the groups B, C, D and E contains a sulphinyl or sulphonyl group) oxidising a compound of formula V



(V)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that at least one of the groups Y, B, C, D or E contains a sulphenyl or sulphinyl group);

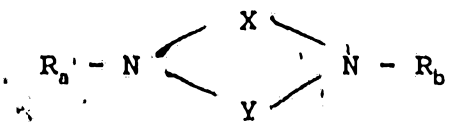
d) (to prepare compounds of formula I wherein Y represents a straight-chained C_{2-4}-alkylene group, optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl groups) hydrogenating a compound of formula VI



(VI)

(wherein
R_a, R_b and X are as hereinbefore defined and
Y' represents a straight-chained C_{2-4}-alkenylene group, optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl groups);

e) (to prepare compounds of formula I wherein A represents an aminoalkyl, amidino or guanidino group substituted by a (C_{1-4}-alkoxy)carbonyl group or by an aralkoxycarbonyl, aryloxycarbonyl, alkylcarbonyl or arylcarbonyl group) reacting a compound of formula VII



(VII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined with the proviso that one of the groups R_a, R_b, R_c to R_d represents a group of formula

A' - B - C -

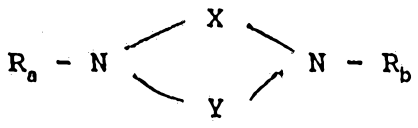
wherein
B and C are as hereinbefore defined and
A' represents an H_2N-C_{1-5}alkyl-, H_2N-C(=NH)- or H_2N-C(=NH)-NH- group) with a compound of formula VIII

$Z_2 - R_5$ (VIII)

(wherein

R_5 represents a (C_{1-4}-alkoxy)carbonyl group an aralkoxycarbonyl, aryloxycarbonyl, alkylcarbonyl or arylcarbonyl group and
Z_2 represents a nucleophilic leaving group such as a halogen atom, e.g. a chlorine or bromine atom, or an aryloxy, arylthio, alkoxycarbonyloxy, aralkoxycarbonyloxy or imidazolyl group);

f) (to prepare compounds of formula I wherein F represents a carbonyl group substituted by a C_{1-6}-alkoxy group, wherein a (C_{1-3}-alkoxy) group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group) reacting a compound of formula IX



(IX)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula

$$F'' - E - D -$$

wherein
E and D are as hereinbefore defined and
F'' represents a carboxy or alkoxycarbonyl group) with an alcohol of formula X

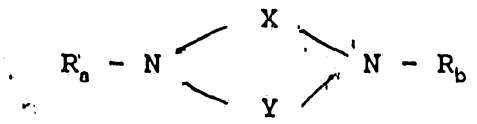
$$HO - R_6 \qquad (X)$$

(wherein
R_6 represents a C_{1-6}-alkyl group which may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl

group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group);

g) (to prepare compounds of formula I wherein A represents an NH_2-C(=NH)- group and B or, if B represents a bond, C represents a C_{4-5}-cycloalkylene group, optionally substituted by an alkyl, aralkyl or aryl group, wherein a CH moiety is replaced by a nitrogen atom, or a C_{6-7}-cycloalkylene group, optionally substituted by an alkyl, aralkyl or aryl group, wherein one or two CH moieties in the 1,4-position relative to each other are each replaced by a nitrogen atom, whilst B or, if B is a bond, C is linked to the group A via one of the above-mentioned nitrogen atoms) reacting a compound of formula

XI



(XI)

(wherein

R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula

H - B' - C - or H - C' -

wherein

C is as hereinbefore defined and

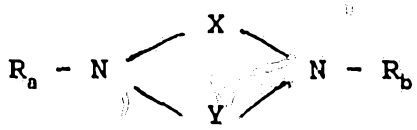
B' or C' represents a C_{4-5}-cycloalkylene group, optionally substituted by an alkyl, aralkyl or aryl group, wherein a CH moiety is replaced by a nitrogen atom, or a C_{6-7}-cycloalkylene group, optionally substituted by an alkyl, aralkyl or aryl group, wherein one or two CH moieties in the 1,4-position relative to

each other are each replaced by a nitrogen atom, the hydrogen atom being linked to a nitrogen atom of the group B' or C') with a compound of formula XII

$$Z_3\text{-}C(=NH)\text{-}NH_2 \qquad \text{(XII)}$$

(wherein
Z_3 represents a nucleophilic leaving group such as an alkoxy or alkylthio group, e.g. a methylthio or ethylthio group);

h) (to prepare compounds of formula I, wherein A represents an $H_2N\text{-}CH_2\text{-}V\text{-}$ group, wherein V represents a bond or a straight-chained or branched $C_{1\text{-}4}$-alkylene group) reducing a compound of general formula XIII



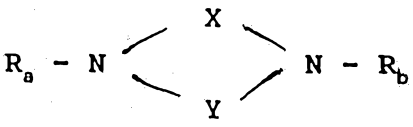
(XIII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$NC - V - B - C -$$

wherein
B and C are as hereinbefore defined and
V represents a bond or a straight-chained or branched $C_{1\text{-}4}$-alkylene group);

i) (to prepare compounds of formula I wherein C represents an alkylene group substituted by a hydroxy group) reducing a compound of formula XIV



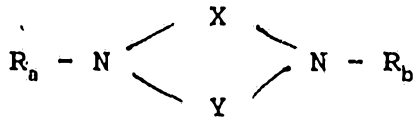
(XIV)

wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

A - B - C" -

wherein
A and B are as hereinbefore defined and
C" represents an alkylene group in which a methylene group is replaced by a carbonyl group);

j) (to prepare compounds of formula I wherein A represents an H_2N-C(=NH)-NH- group) reacting a compound of formula XV



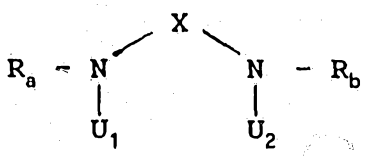
(XV)

(wherein
R_a, R_b, X and Y are as hereinbefore defined with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

H_2N - B - C -

wherein
B and C are as hereinbefore defined) with cyanamide or an acid addition salt thereof or with an S-alkyl-isothiourea, O-methylisothiourea or 1-amidino-3,5-dimethylpyrazole;

k) cyclising a compound of formula



(XVI)

(wherein

R_a, R_b and X are as hereinbefore defined,

one of the groups U_1 or U_2 represents a hydrogen atom and the other group U_1 or U_2 represents a group of the formula

$$- Y'' - Z_4$$

wherein

Y" represents a straight-chained C_{2-4}-alkylene or alkenylene group, optionally substituted by R_c or R_d or by R_c and R_d, wherein each carbon atom may be mono- or disubstituted by an alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl group, whilst the substituents may be identical or different, or Y" represents a 1,2-cycloalkylene group having 4 to 7 carbon atoms optionally substituted by R_c or R_d or by R_c and R_d, or Y" represents a 1,2-cycloalkenylene group having 4 to 7 carbon atoms, a -CH=N- group optionally substituted by the groups R_c or R_d, wherein the nitrogen atom is linked to one of the nitrogen atoms in formula XVI, or a $-CH_2-NH-$ group optionally substituted by R_c or R_d and Z_4 represents a nucleophilic leaving group such as a halogen atom, a hydroxy, alkoxy or sulphonic acid ester group, e.g. a chlorine, bromine or iodine atom, a methoxy, ethoxy, isopropyloxy, methanesulphonyloxy or p-toluenesulphonyloxy group, or, together with an adjacent methylene group of the group Y", Z_4 represents a carbonyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl or dialkoxymethyl group);

l) (to prepare compounds of formula I wherein R_a or R_c

represents an E-F-D- group) cyclising a compound of formula XVII

$$R_c - CO - CHR_d - NR_a - CO - NHR_b \qquad (XVII)$$

(wherein
R_a to R_d are as hereinbefore defined) which is optionally formed in the reaction mixture, optionally with subsequent hydrogenation.

m) (to prepare compounds of formula I wherein X represents a carbonyl group) reacting a compound of formula XVIII

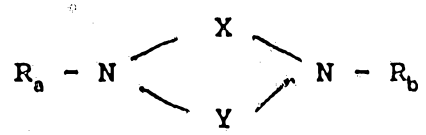
$$R_a - NH - Y - NH - R_b \qquad (XVIII)$$

(wherein
R_a, R_b and Y are as hereinbefore defined) with a compound of formula XIX

$$Z_5 - CO - Z_6 \qquad (XIX)$$

(wherein
Z_5 and Z_6, which may be identical or different, represent nucleophilic leaving groups such as halogen atoms, alkoxy or aryloxy groups, e.g. they each represent a chlorine atom or a methoxy, ethoxy or phenyloxy group);

n) (to prepare compounds of formula I wherein R_a to R_d are as hereinbefore defined, with the proviso that at least one of the groups R_a and R_b does not represent a hydrogen atom) reacting a compound of formula XX



(XX)

(wherein
X and Y are as hereinbefore defined,
one of the groups R_a or R_b represents a hydrogen atom and the other group R_a or R_b is as hereinbefore defined, with a compound of formula XXI

$$Z_7 - R' \qquad \text{(XXI)}$$

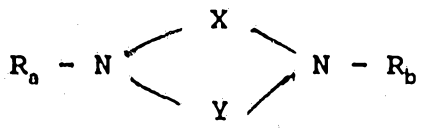
(wherein
R' has the meanings given hereinbefore for R_a or R_b, with the exception of a hydrogen atom, and
Z_7 represents a nucleophilic leaving group such as a halogen atom or a sulphonic acid ester group, e.g. a chlorine, bromine or iodine atom or a methanesulphonyloxy or p-toluenesulphonyloxy group)

or, if R_a or R_b represents a -D-COO-alkyl group, with the proviso that there are two carbon atoms between the nitrogen atom of the cyclic urea and the alkoxycarbonyl group, or reacting with a compound of formula XXII

$$D' - COO\text{-alkyl} \qquad \text{(XXII)}$$

(wherein
D' has the meanings given for D hereinbefore, with the proviso that the alkoxycarbonyl group immediately precedes a carbon-carbon double or triple bond);

o) (prepare compounds of formula I wherein F represents a carboxy, alkoxycarbonyl, aralkoxycarbonyl or aryloxycarbonyl group) oxidising a compound of formula XXIII



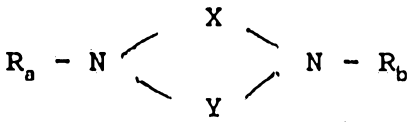
(XXIII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a to R_d represents a group of the formula

$$CH_2 = CH - E - D -$$

where E and D are as hereinbefore defined), with optional subsequent esterification.

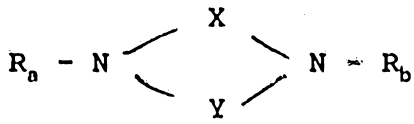
p) (to prepare compounds of formula I wherein F represents an O-alkyl-phosphono group) reacting a compound of formula XXIV



(XXIV)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that F represents a dialkoxyphosphoryl group, with an alkali metal iodide);

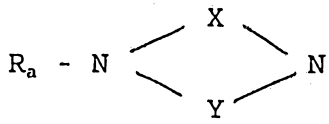
q) (to prepare compounds of formula I wherein F represents a phosphono group) reacting a compound of formula XXV



(XXV)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that F represents an O-alkylphosphono- or dialkoxyphosphoryl group) with an alkali metal iodide in the presence of a trialkylhalosilane;

r) (to prepare compounds of formula I wherein W represents an $R_1N<$ group) reacting a compound of formula XXVI



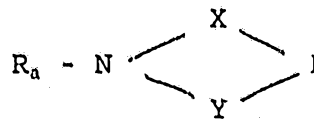
(XXVI)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a Z_8-D"- group, wherein D" represents a C_{1-3}-alkylene group and Z_8 represents a nucleophilic leaving group such as a halogen atom or a sulphonic acid ester group, e.g. a chlorine, bromine or iodine atom or a methane-sulphonyloxy or p-toluenesulphonyloxy group) with a compound of formula XXVIII

$$R_1NH - E' - F \qquad \text{(XXVII)}$$

(wherein
F and R_1 are as hereinbefore defined and
E' represents a C_{1-3}-alkylene group);

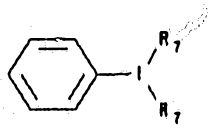
s) (to prepare compounds of formula I wherein A represents an amino or aminoalkyl group) reacting a compound of formula XXVII



(XXVIII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents an H_2N-CO-T-B-C- group, where B and C are as hereinbefore defined and T represents a bond or a C_{1-5}-

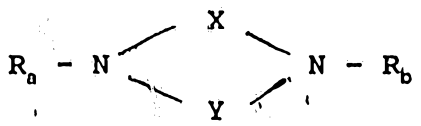
alkylene group, with a phenyl iodine(III) compound of formula XXIX



(XXIX)

(wherein
R_7 represents an acyl group or an organic carboxylic acid such as the acetoxy or trifluoroacetoxy group);

t) (to prepare compounds of formula I wherein A represents an amino or aminoalkyl group substituted by one or two alkyl groups at the nitrogen atom) reacting a compound of formula XXX



(XXX)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$A'' - B - C -$$

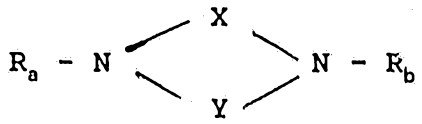
(wherein
B and C are as hereinbefore defined and
A" represents an amino, alkylamino, aminoalkyl or alkylaminoalkyl group, with a compound of formula XXXI

$$Z_9 - (R_8-C-R_9) - Z_{10} \qquad (XXXI)$$

(wherein
R_8 and R_9, which may be identical or different, represent

hydrogen atoms or alkyl groups,
one of the groups Z_9 or Z_{10} represents a nucleophilic leaving group such as a halogen atom, e.g. a chlorine, bromine or iodine atom, or a sulphonic acid ester group, e.g. a methanesulphonyloxy or p-toluenesulphonyloxy group, and
the other group Z_9 or Z_{10} represents a hydrogen atom or an alkyl group or
Z_9 and Z_{10} together represent an oxygen atom);

u) (to prepare compounds of formula I wherein A represents a cyano group) reacting a compound of formula XXXII



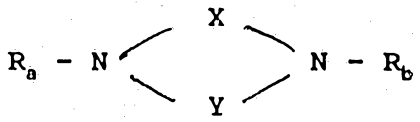
(XXXII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$A''' - B - C -$$

wherein
B and C are as hereinbefore defined and
A''' represents a halogen atom, e.g. a bromine or iodine atom) with copper(I)cyanide;

v) (to prepare compounds of formula I wherein A represents an aminoalkyl group where the amino group is not bound to a quaternary carbon atom, or an amino group which is bound to a CH- or CH_2 group of group B or C) reducing of a compound of formula XXXIII



(XXXIII)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

A"" - B - C -

wherein
B and C are as hereinbefore defined and
A"" contains an N-hydroxy-imino group);

(w) resolving a compound of formula I by isomer separation into cis-/trans-isomers, enantiomers and/or diastereomers thereof;

(x) converting a compound of formula I into an addition salt thereof, more particularly for pharmaceutical use into a physiologically acceptable salt thereof with an organic or inorganic acid or base, or converting a salt of a compound of formula I into the free compound; and

(y) performing a process as defined in any one of steps (a) to (x) above on a corresponding protected compound and subsequently removing the protecting group used.

In step (a) functional derivatives of the carboxyl group such as the optionally substituted amides, esters, thioesters, trimethylsilylesters, orthoesters, iminoesters, amidines or anhydrides, or the nitrile group may be converted by hydrolysis into a carboxyl group; esters with tertiary alcohols, e.g. the tert.-butylester group, may be converted into a carboxyl group by treatment with an acid or thermolysis; and esters

with aralkanols, e.g. the benzylester, may be converted into a carboxyl group by hydrogenolysis.

The hydrolysis of step (a) is expediently carried out either in the presence of an acid such as hydrochloric, sulphuric, phosphoric, trichloroacetic or trifluoroacetic acid, in the presence of a base such as lithium hydroxide, sodium hydroxide or potassium hydroxide in a suitable solvent such as water, water/methanol, water/ethanol, water/isopropanol, methanol, ethanol or water/dioxane at temperatures between -10°C and 120°C, preferably at temperatures between ambient temperature and the boiling temperature of the reaction mixture. In the case of treatment with an organic acid such as trichloroacetic or trifluoroacetic acid, any alcoholic hydroxy groups present may simultaneously be converted into a corresponding acyloxy group such as the trifluoroacetoxy group.

If F' in a compound of formula II represents a cyano or aminocarbonyl group, these groups may also be converted into the carboxyl group with a nitrite, e.g. sodium nitrite, in the presence of an acid such as sulphuric acid, which may expediently be used as solvent at the same time, at temperatures between 0 and 50°C.

If F' in a compound of formula II represents, for example, a tert.-butyloxycarbonyl group, the tert.-butyl group may also be cleaved by treatment with an acid such as trifluoroacetic, formic, p-toluenesulphonic, sulphuric, phosphoric or polyphosphoric acid, optionally in an inert solvent such as methylene chloride, chloroform, benzene, toluene, tetrahydrofuran or dioxane, preferably at temperatures between -10 and 120°C, more preferably at temperatures between 0 and 60°C, or thermally, optionally in an inert solvent such

as methylene chloride, chloroform, benzene, toluene, tetrahydrofuran or dioxane and preferably in the presence of a catalytic quantity of an acid such as p-toluenesulphonic, sulphuric, phosphoric or polyphosphoric acid, preferably at the boiling temperature of the solvent used, more preferably at temperatures between 40°C and 100°C.

If F' in a compound of formula II represents, for example, a benzyloxycarbonyl group, the benzyl group may also be cleaved hydrogenolytically in the presence of a hydrogenation catalyst such as palladium/charcoal in a suitable solvent such as methanol, ethanol, ethanol/water, glacial acetic acid, ethyl acetate, dioxane or dimethylformamide, preferably at temperatures between 0 and 50°C, e.g. at ambient temperature, under a hydrogen pressure of from 1 to 5 bar. During hydrogenolysis, other groups may be reduced at the same time, e.g. a nitro group to the amino group or a benzyloxy group to the hydroxy group.

The reaction of step (b) is expediently carried out in a solvent such as methanol, ethanol, n-propanol, water, methanol/water, tetrahydrofuran or dioxane at temperatures between 0 and 150°C, preferably at temperatures between 20 and 120°C, with a corresponding free amine or with a corresponding acid addition salt such as the corresponding ammonium carbonates, acetates or chlorides.

A compound of formula III is obtained for example by reacting a corresponding nitrile with a corresponding alcohol such as methanol, ethanol, n-propanol, isopropanol or benzyl alcohol in the presence of an acid such as hydrochloric acid or by reacting a corresponding amide with a trialkyloxonium salt such as

triethyloxonium-tetrafluoroborate in a solvent such as methylene chloride, tetrahydrofuran or dioxane at temperatures between 0 and 50°C, but preferably at 20°C, or a corresponding nitrile with hydrogen sulphide, conveniently in a solvent such as pyridine or dimethylformamide and in the presence of a base such as triethylamine and subsequent alkylation of the thioamide formed with a corresponding alkyl or aralkyl halide, or by reacting a corresponding nitrile with an alkoxide such as sodium methoxide in a solvent such as dioxane or tetrahydrofuran, but preferably in the alcohol in question.

The oxidation of step (c) is preferably carried out in a solvent or mixture of solvents, e.g. in water, water/pyridine, acetone, methylene chloride, glacial acetic acid, glacial acetic acid/acetic hydride, dilute sulphuric acid or trifluoroacetic acid, and depending on the oxidising agent used, at temperatures between -80 and 100°C.

In order to prepare a corresponding S-oxide compound of formula I the oxidation is conveniently carried out with one equivalent of the oxidizing agent used, eg. with hydrogen peroxide in glacial acetic acid, trifluoroacetic acid or formic acid at 0 to 20°C or in acetone at 0 to 60°C, with a peracid such as performic acid in glacial acetic acid or trifluoroacetic acid at 0 to 50°C or with m-chloro-perbenzoic acid in methylene chloride or chloroform at -20 to 60°C, with sodium metaperiodate in aqueous methanol or ethanol at -15 to 25°C, with bromine in glacial acetic acid or aqueous acetic acid optionally in the presence of a weak base such as sodium acetate, with N-bromo-succinimide in ethanol, with tert.butyl hypochlorite in methanol at -80 to -30°C, with iodobenzodichloride in aqueous pyridine at 0 to 50°C, with nitric acid in glacial acetic acid at

0 to 20°C, with chromic acid in glacial acetic acid or in acetone at 0 to 20°C and with sulphuryl chloride in methylene chloride at -70°C, with the thioether-chlorine complex so obtained conveniently being hydrolysed with aqueous ethanol.

In order to prepare an S,S-dioxide compound of formula I the oxidation is conveniently carried out, starting from a corresponding alkylsulphinyl compound, with one or more equivalents of the oxidising agent used, or starting from a corresponding alkylsulphenyl compound with two or more equivalents of the oxidising agent used, e.g. with hydrogen peroxide in glacial acetic acid/acetic anhydride, trifluoroacetic acid or in formic acid at 20 to 100°C or in acetone at 0 to 60°C, with a peracid such as performic acid or m-chloroperbenzoic acid in glacial acetic acid, trifluoroacetic acid, methylene chloride or chloroform at temperatures between 0 and 60°C, with nitric acid in glacial acetic acid at 0 to 20°C, with chromic acid or potassium permanganate in glacial acetic acid, water/sulphuric acid or in acetone at 0 to 20°C.

The hydrogenation of step (d) is conveniently carried out in a solvent such as methanol, ethanol, ethyl acetate or glacial acetic acid, optionally with the addition of an acid such as hydrochloric acid, with hydrogen in the presence of a catalyst such as palladium/charcoal or platinum, at temperatures between 0 and 100°C, but preferably between 20 and 50°C, and under a hydrogen pressure of 1 to 7 bar, but preferably from 3 to 5 bar.

The acylation of step (e) is conveniently carried out in a solvent such as tetrahydrofuran, methylene chloride, chloroform, dimethylformamide, water or mixtures of these solvents, optionally in the presence of a base

such as sodium carbonate, potassium carbonate or sodium hydroxide solution or in the presence of a tertiary organic base such as triethylamine, N-ethyl-diisopropylamine, N-methyl-morpholine or pyridine, which may simultaneously serve as solvents, at temperatures between -30 and 100°C, but preferably at temperatures between -10 and 80°C.

The reaction of step (f) is expediently carried out in a solvent or mixture of solvents such as methylene chloride, dimethylformamide, dimethylsulphoxide, benzene, toluene, chlorobenzene, tetrahydrofuran, benzene/tetrahydrofuran or dioxane, optionally in the presence of an acid such as hydrochloric acid or in the presence of a dehydrating agent, e.g. in the presence of isobutylchloroformate, thionylchloride, trimethylchlorosilane, hydrochloric acid, sulphuric acid, methanesulphonic acid, p-toluenesulphonic acid, phosphorus trichloride, phosphorus pentoxide, N,N'-dicyclohexylcarbodiimide, N,N'-dicyclohexylcarbodiimide/N-hydroxysuccinimide or 1-hydroxy-benzotriazole and optionally also in the presence of 4-dimethylaminopyridine, N,N'-carbonyldiimidazole or N,N'-thionyldiimidazole or triphenylphosphine/carbon tetrachloride, conveniently at temperatures between 0 and 150°C, preferably at temperatures between 0 and 50°C.

The reaction of a corresponding alkoxy compound with an alcohol of formula X is preferably carried out in a corresponding alcohol as solvent, optionally in the presence of an additional solvent such as methylene chloride or ether, preferably in the presence of an acid such as hydrochloric acid at temperatures between 0 and 100°C, preferably at temperatures between 20 and 80°C.

The reaction of step (g) is conveniently carried out in a solvent or mixture of solvents such as

dimethylformamide, dimethylsulphoxide, benzene, toluene, chlorobenzene, tetrahydrofuran, benzene/tetrahydrofuran or dioxane, preferably in the presence of an acid-binding agent, e.g. an alkoxide such as potassium tert.-butoxide, an alkali metal hydroxide such as sodium or potassium hydroxide, an alkali metal carbonate such as sodium carbonate or potassium carbonate or an alkali metal hydride such as sodium hydride, conveniently at temperatures between 50 and 150°C, preferably at temperatures between 75 and 125°C.

The reduction of step (h) is preferably carried out in a suitable solvent such as methanol, methanol/water, methanol/water/ammonia, ethanol, ether, tetrahydrofuran, dioxane or dimethylformamide, optionally with the addition of an acid such as hydrochloric acid, in the presence of catalytically activated hydrogen, e.g. hydrogen in the presence of Raney nickel, platinum or palladium/charcoal, or in the presence of a metal hydride such as sodium borohydride, lithium borohydride or lithium aluminium hydride, at temperatures between 0 and 100°C, preferably at temperatures between 20 and 80°C.

The reduction of step (i) is preferably carried out in a suitable solvent such as methanol, methanol/water, ethanol, ether, tetrahydrofuran, dioxane or glacial acetic acid, in the presence of catalytically activated hydrogen, e.g. hydrogen in the presence of platinum or palladium/charcoal, or in the presence of a metal hydride such as sodium borohydride, lithium borohydride or lithium aluminium hydride, at temperatures between -5 and 20°C, preferably at temperatures between 0 and 10°C.

The reaction of step (j) is conveniently carried out in a solvent such as dioxane, dioxane/water or tetrahydrofuran, preferably at temperatures between 60

and 120°C, most preferably at the boiling temperature of the reaction mixture.

The reaction of step (k) is preferably carried out in a solvent such as ethanol, isopropanol, methylene chloride, dioxane, toluene, dimethylformamide or dimethyl-sulphoxide, optionally in the presence of a base such as pyridine, an acid such as hydrochloric, sulphuric, polyphosphoric or trifluoroacetic acid, and a dehydrating agent such as N,N'-dicyclohexylcarbodiimide, at temperatures between 20 and 200°C. However, the reaction may also be carried out without a solvent.

If Z_4 represents a nucleophilic leaving group such as a halogen atom or a sulphonic ester group, the reaction is preferably carried out in the presence of a base such as potassium carbonate, sodium hydride or potassium tert.butoxide, at temperatures between 20 and 60°C; if the group Z_4 represents a hydroxy or alkoxy group or together with an adjacent methylene group of the group Y" represents a carbonyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl or dialkoxymethyl group, the reaction is preferably carried out in the presence of an acid such as hydrochloric or trifluoroacetic acid, which may simultaneously serve as solvent, at temperatures between 20 and 80°C, or in the melt at temperatures between 50 and 250°C, preferably at temperatures between 100 and 200°C.

The cyclisation of step (l) is preferably carried out in a solvent such as water, ethanol/water, ethanol, benzene, toluene or dioxane and conveniently in the presence of a base such as pyridine, which may also serve as solvent, at elevated temperatures, e.g. at the boiling temperature of the solvent used.

The optional subsequent hydrogenation is preferably

carried out using hydrogen in the presence of a catalyst such as palladium/charcoal or platinum, in a solvent such as methanol, ethanol, ethyl acetate or glacial acetic acid, optionally with the addition of an acid such as hydrochloric acid, at temperatures between 0 and 50°C, but preferably at ambient temperature, and under a hydrogen pressure of 1 to 7 bar, preferably 3 to 5 bar.

The reaction of step (m) is preferably carried out in a solvent such as methylene chloride, chloroform, toluene or dioxane, optionally in the presence of a base such as triethylamine or pyridine at temperatures between 0 and 50°C, preferably at ambient temperature.

The alkylation of step (n) is expediently carried out in a solvent or mixture of solvents such as methylene chloride, dimethylformamide, dimethylsulphoxide, benzene, toluene, chlorobenzene, tetrahydrofuran, benzene/tetrahydrofuran or dioxane, preferably in the presence of an acid binding agent, e.g. an alkoxide such as potassium tert.butoxide, an alkali metal hydroxide such as sodium or potassium hydroxide, an alkali metal carbonate such as potassium carbonate, an alkali metal amide such as sodium amide or an alkali metal hydride such as sodium hydride or a tertiary organic base such as ethyl-diisopropylamine, conveniently at temperatures between 0 and 150°C, preferably at temperatures between 0 and 50°C.

The arylation of step (n) is expediently carried out with an aryl compound of general formula XXI wherein Z_7 represents an iodine atom, preferably in a solvent such as toluene or xylene, and preferably in the presence of one or more reaction accelerators such as tris-[2-(2-methoxy-ethoxy)ethyl]amine, copper(I)chloride or copper(II)chloride, at elevated temperatures, e.g. at

temperatures between 100 and 200°C, but preferably at the boiling temperature of the reaction mixture. However, the reaction may also be carried out without a solvent.

The addition of an alkenyl compound of formula XXII is preferably carried out in a solvent such as dimethylformamide and in the presence of a base such as sodium hydride, at temperatures between 0 and 50°C, preferably at ambient temperature.

The oxidation of step (o) is conveniently carried out in a solvent such as methylene chloride, acetonitrile, acetonitrile/water, methylene chloride/acetonitrile/water or carbon tetrachloride/acetonitrile/water, in the presence of an oxidising agent such as potassium permanganate or ruthenium tetroxide, the ruthenium tetroxide preferably being formed in the reaction mixture by reacting a ruthenium salt such as ruthenium trichloride with an oxidising agent such as sodium periodate, at temperatures between -10 and 50°C, preferably at temperatures between 15 and 30°C.

The optional subsequent esterification of step (o) is expediently carried out in a suitable solvent, e.g. in a corresponding alcohol, pyridine, toluene, methylene chloride, tetrahydrofuran or dioxane, in the presence of an acid activating and/or dehydrating agent such as hydrogen chloride, concentrated sulphuric acid, thionyl chloride, ethylchloroformate, carbonyldiimidazole or N,N'-dicyclohexylcarbodiimide or the isourea esters thereof, optionally in the presence of a reaction accelerator such as copper chloride, or by transesterification, e.g. with a corresponding carbonic acid diester, at temperatures between 0 and 100°C, but preferably at temperatures between 20°C and the boiling temperature of the solvent in question.

The reaction of step (p) is preferably carried out in a solvent such methylethylketone, in the presence of an alkali metal iodide such as sodium iodide, at temperatures between 25 and 100°C, preferably at the boiling temperature of the reaction mixture.

The reaction of step (q) is preferably carried out in a solvent such as acetonitrile, in the presence of an alkali metal iodide such as sodium iodide, and a trialkylhalosilane such as trimethylchlorosilane, at temperatures between 25 and 80°C, but preferably at temperatures between 30 and 50°C.

The reaction of step (r) is expediently carried out in a solvent or mixture of solvents such as methylene chloride, dimethylformamide, dimethylsulphoxide, benzene, toluene, chlorobenzene, tetrahydrofuran, benzene/tetrahydrofuran or dioxane, preferably in the presence of an acid binding agent, e.g. an alkoxide such as potassium tert.butoxide, an alkali metal hydroxide such as sodium or potassium hydroxide, an alkali metal carbonate such as potassium carbonate, an alkali metal amide such as sodium amide or an alkali metal hydride such as sodium hydride or a tertiary organic base such as ethyl diisopropylamine, conveniently at temperatures between 0 and 150°C, preferably at temperatures between 0 and 50°C.

The reaction of step (s) is preferably carried out in an aqueous solvent such as water or water/acetonitrile. at temperatures between 0 and 50°C, but preferably at ambient temperature.

The alkylation of step (t) with a compound of formula XXXI wherein Z_9 or Z_{10} represents a nucleophilic leaving group is conveniently carried out in a solvent such as tetrahydrofuran, dioxane, dimethylsulphoxide or

dimethylformamide, optionally in the presence of a base such as sodium carbonate, potassium carbonate or sodium hydroxide solution or in the presence of a tertiary organic base such as N-ethyl-diisopropylamine or N-methyl-morpholine, which may be simultaneously serve as solvent, at temperatures between -30 and 100°C, but preferably at temperatures between -10 and 80°C.

The alkylation with a carbonyl compound of general formula XXXI is preferably carried out in the presence of a complex metal hydride such as sodium borohydride, lithium borohydride or sodium cyanoborohydride, conveniently at a pH of 6 to 7 and at ambient temperature or in the presence of a hydrogenation catalyst, e.g. with hydrogen in the presence of palladium/charcoal, at a hydrogen pressure of 5 bar.

The reaction of step (u) is preferably carried out in a solvent such as dimethylformamide, dimethylacetamide or N-methyl-pyrrolidone, at temperatures between 100 and 250°C, preferably between 150°C and the boiling temperature of the reaction mixture.

The reduction of step (v) is preferably carried out in a suitable solvent such as methanol, methanol/water, methanol/water/ammonia, ethanol, ether, tetrahydrofuran, dioxane or dimethylformamide, optionally with the addition of an acid such as hydrochloric acid, in the presence of catalytically activated hydrogen, e.g. hydrogen in the presence of Raney nickel, platinum or palladium/charcoal, at temperatures between 0 and 100°C, preferably at temperatures between 20 and 80°C.

If according to the invention a compound of formula I is obtained, this may be converted by bromination into a corresponding bromine compound of formula I, or

if a compound of formula I is obtained, this may be converted by nitrogenation into a corresponding nitro compound of formula I, or

if a compound of formula I is obtained which contains a nitro group, this may be converted by reduction into a corresponding amino compound or

if a compound of formula I is obtained which contains an R_1NH- group or wherein W represents an imino group, this may be converted by acylation or sulphonation into a corresponding compound of formula I which contains an R_1NH- group substituted by an alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, or

if a compound of formula I is obtained wherein X represents a carbonyl group, this may be converted by means of a sulphurising agent into a corresponding thiocarbonyl compound.

The subsequent bromination is preferably carried out in a solvent such as glacial acetic acid, with a brominating agent such as bromine, at temperatures between 0 and 40°C, preferably at ambient temperature.

The subsequently nitrogenation is carried out with a nitrogenating agent such as concentrated sulphuric acid/nitric acid or fuming nitric acid, which may conveniently serve as solvents, optionally in a solvent such as nitrobenzene, at temperatures between 0 and 50°C, preferably at ambient temperature.

The subsequent reduction of the nitro group is preferably carried out in a solvent such as water, water/ethanol, methanol, glacial acetic acid, ethyl

acetate or dimethylformamide, expediently with hydrogen in the presence of a hydrogenation catalyst such as Raney nickel, platinum or palladium/charcoal, with metals such as iron, tin or zinc in the presence of an acid such as zinc/acetic acid or zinc/calcium chloride, with salts such as iron(II)sulphate, tin(II)chloride, sodium sulphide, sodium hydrogen sulphite or sodium dithionite, or with hydrazine in the presence of Raney nickel, at temperatures between 0 and 100°C, but preferably at temperatures between 20 and 80°C.

The subsequent acylation or sulphonylation of an R_1-NH-group is expediently carried out in a solvent such as methylene chloride, chloroform, carbon tetrachloride, ether, tetrahydrofuran, dioxane, benzene, toluene, acetonitrile or dimethylformamide, optionally in the presence of an acid activating agent or a dehydrating agent, e.g. in the presence of ethyl chloroformate, thionylchloride, phosphorus trichloride, phosphorus pentoxide, N,N'-dicyclohexylcarbodiimide, N,N'-dicyclohexylcarbodiimide/N-hydroxysuccinimide, N,N'-carbonyldiimidazole or N,N'-thionyldiimidazole or triphenylphosphine/carbon tetrachloride, optionally in the presence of an inorganic base such as sodium carbonate or a tertiary organic base such as triethylamine, pyridine or 4-dimethylaminopyridine, which may simultaneously be used as solvent, at temperatures between -25 and 150°C, but preferably at temperatures between -10°C and the boiling temperature of the solvent used. However, the subsequent acylation or sulphonylation is preferably carried out with a corresponding acid halide or acid anhydride, as described hereinbefore, and this may also be carried out without a solvent.

The reaction is carried out with a sulphurising agent such as phosphorus pentasulphide or 2,4-bis-(4-

methoxyphenyl)-1,3-di-thia-2,4-diphosphetan-2,4-disulphide, expediently in a solvent such as pyridine, toluene or xylene, at temperatures between 50 and 150°C, e.g. at the boiling temperature of the reaction mixture.

In reaction steps a) to v) described above and in the subsequent reactions, any reactive groups present such as hydroxy, carboxy, amino, alkylamino or imino groups, may optionally be protected during the reaction by means of conventional protecting groups which are cleaved again after the reaction.

For example, suitable protective groups for a hydroxy group include a trimethylsilyl, acetyl, benzoyl, tert.-butyl, trityl, benzyl and tetrahydropyranyl groups, whilst protective groups for a carboxyl group include trimethylsilyl, methyl, ethyl, tert.-butyl, benzyl and tetrahydropyranyl groups, protecting groups for amino, alkylamino or imino groups include acetyl, benzoyl, ethoxycarbonyl, tert.-butoxycarbonyl, benzyloxycarbonyl, benzyl, methoxybenzyl and 2,4-dimethoxybenzyl group, and an additional example of a protecting group for an amino group is the phthalyl group.

The optional subsequent cleaving of a protecting group may be carried out, for example, hydrolytically in an aqueous solvent, e.g. in water, isopropanol/water, tetrahydrofuran/water or dioxane/water, in the presence of an acid such as trifluoroacetic acid, hydrochloric acid or sulphuric acid or in the presence of an alkali metal base such as sodium hydroxide or potassium hydroxide, or by ether cleavage, e.g. in the presence of iodotrimethylsilane, at temperatures between 0 and 100°C, preferably at temperatures between 10 and 50°C.

However, a benzyl, methoxybenzyl or benzyloxycarbonyl group is preferably cleaved, for example, by

hydrogenolysis, e.g. with hydrogen in the presence of a catalyst such as palladium/charcoal, in a solvent such as methanol, ethanol, ethyl acetate or glacial acetic acid, optionally with the addition of an acid such as hydrochloric acid, at temperatures between 0 and 50°C, but preferably at ambient temperature, under a hydrogen pressure of from 1 to 7 bar, but preferably from 3 to 5 bar.

The cleaving of a methoxybenzyl group may also be carried out in the presence of an oxidising agent such as Ce(IV)ammonium nitrate, in a solvent such as methylene chloride, acetonitrile or acetonitrile/water, at temperatures between 0 and 50°C, but preferably at ambient temperature.

Moreover, a 2,4-dimethoxybenzyl group is preferably cleaved in trifluoroacetic acid in the presence of anisole.

A tert.-butyl or tert.-butyloxycarbonyl group is preferably cleaved by treatment with an acid such as trifluoroacetic or hydrochloric acid, optionally using a solvent such as methylene chloride, dioxane or ether.

The cleaving of a phthalyl group is preferably carried out in the presence of hydrazine or a primary amine such as methylamine, ethylamine or n-butylamine in a solvent such as methanol, ethanol, isopropanol, toluene/water or dioxane, at temperatures between 20 and 50°C.

The compounds of formula I obtained may, as already mentioned hereinbefore, be resolved into the enantiomers and/or diastereomers thereof. Thus, for example, cis/trans mixtures may be resolved into their cis and trans isomers and compounds having at least one optically active carbon atom may be resolved into their

enantiomers.

Thus, for example, the cis/trans mixtures obtained may be separated by chromatography into their cis and trans isomers, the compounds of formula I obtained in the form of racemates may be separated by known methods (see Allinger N. L. and Eliel E. L. in "Topics in Stereochemistry", Vol. 6, Wiley Interscience, 1971) into their optical antipodes and compounds of formula I having at least 2 asymmetric carbon atoms can be separated on the basis of their physical-chemical differences into their diastereomers by methods known per se, e.g. by chromatography and/or fractional crystallisation, and if these diastereomers are obtained in racemic form they may subsequently be separated into the enantiomers as mentioned above.

Enantiomer separation is preferably achieved by column separation on chiral phases or by recrystallisation from an optically active solvent or by reacting with an optically active substance which forms salts or derivatives such as esters or amides with the racemic compound, more particularly acids and their activated derivatives or alcohols, and separating the diastereomeric salt mixture obtained in this way, e.g. on the basis of different solubilities, whilst the free antipodes may be liberated from the pure diastereomeric salts by the action of suitable agents. Particularly common optically active acids are, for example, the D and L forms of tartaric or dibenzoyltartaric acid, di-o-tolyl-tartaric acid, malic, mandelic and camphorsulphonic acid, glutamic acid, aspartic acid or quinic acid. An optically active alcohol might be, for example, (+)- or (-)-menthol and an optically active acyl group in amides might be (+) or (-)-menthyloxycarbonyl.

The compounds of formula I obtained may, if desired, be converted into the acid addition salts thereof, more particularly for pharmaceutical use the physiologically acceptable salts thereof with inorganic or organic acids. Examples of suitable acids include hydrochloric, hydrobromic, sulphuric, phosphoric, fumaric, succinic, lactic, citric, tartaric and maleic acid.

In addition, the new compounds of formula I thus obtained, should they contain a carboxyl group, may if desired subsequently be converted into the addition salts thereof with inorganic or organic bases, more particularly for pharmaceutical use into the physiologically acceptable addition salts thereof. Examples of suitable bases include sodium hydroxide, potassium hydroxide, cyclohexylamine, ethanolamine, diethanolamine and triethanolamine.

Some of the compounds used as starting materials are known from the literature. Otherwise these compounds may be obtained by methods known from the literature (see the Examples), e.g. by the methods described in published German patent applications DE-A-4035961 and DE-A-4102024.

For example, the cyclic urea derivatives may be obtained by cyclising a correspondingly substituted urea which in turn is obtained by known methods, or by reacting a correspondingly substituted diamine with phosgene and optionally subsequently introducing sulphur and oxidising the resulting thio compound.

As already mentioned hereinbefore, the new cyclic urea derivatives of formula I and the addition salts thereof, particularly the physiologically acceptable addition salts thereof with inorganic or organic acids or bases, have valuable properties. Thus, the compounds of

formula I wherein A contains an optionally substituted amino, amidino or guanidino group or a group which can optionally be converted in vivo into an optionally substituted amino, amidino or guanidino group, e.g. an amino, amidino or guanidino group substituted by an alkoxycarbonyl group, and -D-E-F contains carboxyl, sulpho, phosphono, O-alkyl-phosphono or 5-tetrazolyl groups or groups which can be converted in vivo into a carboxyl, sulpho, phosphono, O-alkyl-phosphono or tetrazolyl group, e.g. alkoxy-substituted carbonyl groups, have valuable pharmacological properties, not only an antiinflammatory effect which inhibits the breakdown of bone but in particular antithrombotic and antiaggregatory effects and inhibitory effects on tumours or metastases.

The compounds of formula I wherein A represents a cyano or cyanoalkyl group are valuable intermediate products for preparing the corresponding aminomethyl and amidino compounds of formula I.

By way of example, the compounds of formula I were tested for their biological effects in the following way:

1. Fibrinogen binding to human thrombocytes

Blood obtained by puncture of an antecubital vein is anticoagulated with trisodium citrate (final concentration: 13 mM) and centrifuged for 10 minutes at 170 *g. The supernatant platelet-rich plasma is placed on a Sepharose 2B column (Pharmacia) and eluted with a solution of 90 mM common salt, 14 mM trisodium citrate, 5 mM glucose and 50 mM tris(hydroxymethyl)aminomethane, adjusted to pH 7.4. The gel-filtered platelets (GFP) appearing in front of the plasma proteins are used for the binding tests.

50 µl of a 60 mM calcium chloride solution, 50 µl of a 0.6 mM adenosine diphosphate solution, 100 µl of substance solution or solvent and 50 µl of fibrinogen solution (containing 3 µg I^{125}-fibrinogen) are added to 750 µl of GFP and incubated for 20 minutes at ambient temperature. The non-specific binding is measured in the presence of 3 mg/ml of cold fibrinogen.

900 µl of the incubate are carefully pipetted onto 250 µl of silicon oil (AP 38: AR 20, 1:2 v/v, Wacker Chemie) in Eppendorf vessels and centrifuged for 2 minutes at 10,000 *g. The aqueous supernatant and some of the oil are removed, the tip of the vessel with the platelet pellet is cut off and the quantity of bound fibrinogen is measured in a gamma-counter. The concentration of substance which inhibits fibrinogen binding by 50% is calculated from a series of concentrations and given as the IC_{50}.

2. Antithrombotic effect

Method: The thrombocyte aggregation is measured in platelet-rich plasma from healthy test subjects using the Born and Cross method (J. Physiol. 170: 397 (1964)). In order to inhibit coaggulation the blood is mixed with 3.14% sodium citrate in a ratio by volume of 1:10.

Collagen-induced aggregation: The decrease in the optical density of the platelet suspension is measured photometrically and recorded after the addition of the aggregation-initiating substance. The speed of aggregation is concluded from the angle of inclination of the density curve. The point on the curve at which there is maximum transmittance is used to calculate the optical density.

The quantity of collagen used is as little as possible

but sufficient to give an irreversible reaction curve. Standard commercial collagen produced by Hormonchemie of Munich is used. Before the addition of collagen the plasma is incubated with the substance for 10 minutes at 37°C.

From the measurements obtained, an EC_{50} is determined graphically, relating to a 50% change in the optical density in terms of inhibiting aggregation.

The Table which follows contains the findings:

Substance (Example No.)	Fibrinogen Binding test IC_{50}[nM]	Inhibition of platelet aggregation EC_{50}[nM]
1	1 800	9 900
1(1)	45	1 500
1(2)	96	320
1(3)	190	1 700
1(4)	3 900	>100 000
1(5)	6 100	32 000
1(6)	17	70
1(7)	2 400	10 000
1(21)	31	620
1(24)	470	1 100
1(28)	52	390
1(36)	37	100
1(46)	11	40
1(48)	210	1 100
1(49)	26	140
1(50)	45	290
1(51)	3 600	13 000
1(55)	860	60 000
1(59)	150	350
1(62)	13	40

Substance (Example No.)	Fibrinogen Binding test IC_{50}[nM]	Inhibition of platelet aggregation EC_{50}[nM]
1(66)	9.1	50
1(67)	30	60
1(77)	4 900	8 000
1(82)	17 000	29 000
1(94)	310	400
1(117)	230	5 400
1(118)	170	460
1(119)	210	730
1(137)		280
1(138)	21	40
1(139)	6.8	30
1(140)	21	30
1(141)	310	630
1(143)	>10 000	22 000
1(144)		600
1(145)	7.7	50
1(146)	6.5	50
1(147)	27	160
1(148)	25	110
1(149)	470	1 300
1(150)	370	9 900
1(153)	150	380
1(154)	28	310
1(156)	3 600	4 100

Substance (Example No.)	Fibrinogen Binding test IC_{50}[nM]	Inhibition of platelet aggregation EC_{50}[nM]
2	6 000	12 000
2(2)	25 000	630
2(3)	18 000	3 100
2(4)	15 000	42 000
2(5)	5 600	25 000
2(6)	240	160
2(20)	5 700	690
2(27)	2 500	490
2(34)	7 400	350
2(43)	420	100
2(45)	370	280
2(47)	32 000	>100 000
2(48)	22 000	>100 000
2(53)	4 500	200
2(57)	640	320
2(58)	4 700	140
2(71)	13 000	14 000
2(75)	8 000	27 000
2(81)	19 000	1 500
2(104)	7 100	2 100
2(105)	28 000	1 100
2(106)	2 700	6 600
2(115)	530	80
2(116)	59 000	49 000
2(117)		630
2(118)	2 000	70
2(119)	280	40
2(122)		1 200
2(123)	3 100	70
2(124)	1 200	130
2(127)	5 600	18 000
4(9)	2 600	9 500

Substance (Example No.)	Fibrinogen Binding test IC_{50}[nM]	Inhibition of platelet aggregation EC_{50}[nM]
4(11)	45 000	2 300
4(13)	32	310
4(14)	41	200
4(15)	42	300
4(16)	1 500	1 900
4(18)	48	210
5	9 300	32 000
5(1)	>10 000	20 000
5(8)	8 000	31 000
5(11)	5 700	
5(12)	3 700	
5(13)	>10 000	24 000
5(18)	>10 000	8 060
8	750	600
8(1)	68 000	21 000
8(2)	450	370
8(3)	29 000	6 200
8(5)	3 000	5 900
11(11)		210
11(12)	43	30
18	1 900	240
18(5)	420	120
30	4 400	8 300
31	250	500
31(1)	170	370

Moreover, the compound of Example 5(18) for example inhibits the collagen-induced thrombocyte aggregation ex vivo in Rhesus monkeys after oral administration of 1 mg/kg for up to 8 hours.

The new compounds are well tolerated since the intravenous administration of 30 mg/kg of the compound of Example 1(138) in mice did not lead to the death of any of the three animals tested. Similar results are obtained with the compounds of Examples 1(66) and 1(139) at a dose of 30 mg/kg, although in both cases one animal was sedated.

In view of their inhibitory effect on cell-cell and cell-matrix interactions, the new cyclic urea derivatives of formula I and the physiologically acceptable addition salts thereof are suitable for combating or preventing diseases in which smaller or larger clumps of cells are produced or cell-matrix interactions are involved, e.g. in combating or preventing venous and arterial thrombosis, cerebrovascular diseases, pulmonary embolisms, cardiac infarct, arteriosclerosis, osteoporosis and tumour metastasis. They are also suitable as an accompanying therapy in thrombolysis with fibrinolytics or vascular interventions such as transluminal angioplasty or in the treatment of shock, diabetes and inflammation.

Thus viewed from a further aspect the invention provides a pharmaceutical composition comprising a compound of formula I or a physiologically acceptable addition salt thereof together with at least one pharmaceutical carrier or excipient.

Viewed from a still further aspect the present invention provides the use of a compound of formula I or a physiologically acceptable salt thereof for the manufacture of a therapeutic agent for use in combatting conditions in which cell aggregations or cell-matrix interactions occur.

Viewed from a yet still further aspect the present

invention provides a method of treatment of the human or non-human animal body to combat conditions in which cell aggregations or cell-matrix interactions occur, said method comprising administering to said body a compound of formula I or a physiologically acceptable addition salt thereof.

For combating or preventing the above-mentioned diseases, the dose is between 0.1 µg and 20 mg/kg of body weight, preferably 1 µg to 10 mg/kg of body weight, in up to 4 doses per day. For this purpose, the compounds of formula I prepared according to the invention may be formulated, optionally in conjunction with other active substances, together with one or more inert conventional carriers and/or diluents, e.g. with corn starch, lactose, glucose, microcrystalline cellulose, magnesium stearate, polyvinylpyrrolidone, citric acid, tartaric acid, water, water/ethanol, water/glycerol, water/sorbitol, water/polyethylene glycol, propylene glycol, stearyl alcohol, carboxymethylcellulose or fatty substances such as hard fat or suitable mixtures thereof, to produce conventional galenic preparations such as plain or coated tablets, capsules, powders, suspensions, solutions, sprays or suppositories.

The following non-limiting Examples are provided to illustrate the invention. All percentages and ratios given are by weight other than eluant or solvent ratios which are by volume.

Example I

1-(3-Buten-1-yl)-3-(4'-cyano-4-biphenylyl)-imidazolin-2-one

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9 g of 1-(4'-cyano-4-biphenylyl)-imidazolidin-2-one are dissolved at 50°C in 300 ml of dimethylformamide and 1.6 g of a 55% suspension of sodium hydride in oil are added in batches thereto. The mixture is stirred for a further 45 minutes, allowed to cool to ambient temperature and, within 10 minutes, a solution of 4.16 ml of 1-bromo-3-butene in 15 ml of dimethylformamide is added dropwise to the resulting suspension and stirred for 3 days at ambient temperature. The reaction mixture is poured onto 400 ml of water and, after washing with water, the precipitate obtained is purified by column chromatography on silica gel (eluant: methylene chloride/ethyl acetate = 9:1).
Yield: 3.6 g (33% of theory),
Melting point: 171-175°C
R_f value: 0.54 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compounds are obtained analogously:

(1) N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoroacetamide
Heating for 20 hours to 70-80°C
R_f value: 0.47 (silica gel; diisopropylether)

(2) N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[3-(2,3,5,6-tetrahydro-2-pyranyloxy)-propyl]-trifluoroacetamide
Heating for 40 hours to 60°C
R_f value: 0.49 (silica gel; diisopropylether)

(3) 1-methoxycarbonylmethyl-3H-benzimidazol-2-one
The base used is potassium tert.-butoxide and the solvent is methanol
R_f value: 0.89 (silica gel; methylene chloride/methanol = 85:15)

(4) 1-(3-buten-1-yl)-3-(4'-cyano-3'-fluoro-4-biphenylyl)-imidazolidin-2-one

(5) 1-(3-buten-1-yl)-3-(3'-chloro-4'-cyano-4-biphenylyl)-imidazolidin-2-one

(6) 1-(3-buten-1-yl)-3-(4'-cyano-3-methoxy-4-biphenylyl)-imidazolidin-2-one

(7) 1-(3-buten-1-yl)-3-(4'-cyano-3-methylthio-4-biphenylyl)-imidazolidin-2-one

(8) 1-(3-buten-1-yl)-3-(4'-cyano-2,3-dimethyl-4-biphenylyl)-imidazolidin-2-one

(9) 1-(3-buten-1-yl)-3-[4-(5-cyano-2-pyridyl)-phenyl]-imidazolidin-2-one

(10) 1-(3-buten-1-yl)-3-[4-(5-cyano-2-pyrazinyl)-phenyl]-imidazolidin-2-one

(11) 1-(3-buten-1-yl)-3-[4-(5-cyano-2-pyrimidinyl)-phenyl]-imidazolidin-2-one

(12) 1-(3-buten-1-yl)-3-[6-(4-cyano-phenyl)-3-pyridazinyl]-imidazolidin-2-one

(13) 1-(3-buten-1-yl)-3-[2-(4-cyano-phenyl)-5-pyrimidinyl]-imidazolidin-2-one

(14) N-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoroacetamide

(15) N-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoroacetamide

(16) N-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoroacetamide
The methyl 3-(4-amino-3-methoxy-phenyl)-propionate required for the trifluoroacetylation with trifluoroacetic anhydride is obtained from 3-(3-methoxy-phenyl)-propionic acid by nitrogenation, esterification and reduction with palladium/charcoal in methanol.

(17) N-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoro-acetamide
The 3-(4-amino-3-methyl-phenyl)-propionic acid is obtained from 3-(3-methyl-phenyl)-propionic acid analogously to Example I (16).

(18) N-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoroacetamide
The 3-(4-amino-3-methylthio-phenyl)-propionic acid is obtained from 3-(4-amino-phenyl)-propionic acid analogously to Example III (10).

(19) 1-[6-(4-cyano-phenyl)-3-pyridazinyl]-imidazolidin-2-one
Prepared from imidazolidin-2-one and 3-chloro-6-(4-cyano-phenyl)-pyridazine in dimethylsulphoxide
R_f value: 0.30 (silica gel; methylene chloride/methanol = 19:1)

(20) 1-(4-cyano-phenyl)-3-(ethoxycarbonylmethyl)-imidazolidin-2-one
Melting point: 112-115°C

Example II

1-(4'-Cyano-4-biphenylyl)-imidazolidin-2-one

A solution of 5.7 g of potassium tert.-butoxide in 15 ml of dimethylformamide is added dropwise at ambient temperature within 10 minutes to a solution of N-(2-chloroethyl)-N'-(4'-cyano-4-biphenylyl)-urea in 100 ml of dimethylformamide. The mixture is stirred for one hour at ambient temperature, poured onto 300 ml of water and the product precipitated is filtered off.
Yield: 13 g (98% of theory),
Melting point: above 200°C
R_f value: 0.12 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compounds are obtained analogously:

(1) 1-(4'-cyano-4-biphenylyl)-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Melting point: above 200°C
R_f value: 0.44 (silica gel; methylene chloride/methanol = 9:1)

(2) 1-(4'-cyano-3'-fluoro-4-biphenylyl)-imidazolidin-2-one

(3) 1-(3'-chloro-4'-cyano-4-biphenylyl)-imidazolidin-2-one

(4) 1-(4'-cyano-3-methoxy-4-biphenylyl)-imidazolidin-2-one

(5) 1-(4'-cyano-3-methylthio-4-biphenylyl)-imidazolidin-2-one

(6) 1-(4'-cyano-2,3-dimethyl-4-biphenylyl)-imidazolidin-2-one

(7) 1-[4-(5-cyano-2-pyridyl)-phenyl]-imidazolidin-2-one

(8) 1-[4-(5-cyano-2-pyrazinyl)-phenyl]-imidazolidin-2-one

(9) 1-[4-(5-cyano-2-pyrimidinyl)-phenyl]-imidazolidin-2-one

(10) 1-[2-(4-cyano-phenyl)-5-pyrimidinyl]-imidazolidin-2-one

(11) 1-[2-(4'-cyano-4-biphenylyl)-ethyl]-imidazolidin-2-one

(12) 1-(1-benzyl-4-piperidinyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(13) 1-(4-cyano-phenyl)-imidazolidin-2-one
Potassium carbonate is used as base, heating to 60°C for 6 hours.
Melting point: 172-175°C
R_f value: 0.23 (silica gel; cyclohexane/ethyl acetate = 1:3)

(14) 1-(4-cyano-phenyl)-3-[4-[2-(dimethoxy-phosphoryl)-ethyl]-phenyl]-imidazolidin-2-one
Prepared analogously to Example 14.

(15) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: 171-172°C

(16) 2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4-dihydro-2H,5H-thiadiazol-1,1-dioxide
Melting point: 110-112°C

(17) 1-(4-bromo-2-methyl-phenyl)-3-[4-(2-methoxy-carbonyl-ethyl)-phenyl]-imidazolidin-2-one
Prepared from N-(4-bromo-2-methyl-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea via the mesylate and iodide without purification of these products.
Melting point: 164-166°C

Example III

N-(2-Chloroethyl)-N'-(4'-cyano-4-biphenylyl)-urea

1.1 ml of 2-chloroethyl-isocyanate is added to a solution of 4-amino-4'-cyano-biphenyl in 15 ml of dimethylformamide and the mixture is stirred for 3 hours at ambient temperature. The reaction mixture is poured onto 50 ml of water, stirred for 3 hours and the product precipitated is filtered off.
Yield: 1.4 g (91% of theory),
R_f value: 0.40 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compounds are obtained analogously:

(1) N-(4'-cyano-4-biphenylyl)-N-(2,2-diethoxy-ethyl)-N'-(2-ethoxycarbonyl-ethyl)-urea
The work is done in dioxane as solvent in the presence of ethyl-diisopropylamine at 50°C. Purification is carried out by chromatography on silica gel (eluant: cyclohexane/ethyl acetate = 1:1).
The ethyl 3-isocyanato-propionate used is obtained from β-alanine-ethylester-hydrochloride and phosgene in toluene as the solvent.
Melting point: 85-88°C

R_f value: 0.28 (silica gel; cyclohexane/ethyl acetate = 1:1)

(2) N-(tert.butyloxycarbonylmethyl)-N-(4'-cyano-4-biphenylyl)-N'-(2-ethoxycarbonyl-ethyl)-urea
Prepared analogously to Example III (1).
Melting point: 118-120°C (from tert.butyl-methylether)
R_f value: 0.46 (silica gel; cyclohexane/ethyl acetate = 1:1)

(3) N-(4'-cyano-4-biphenyl)-N-[3-(2,3,5,6-tetrahydro-2-pyranyloxy)-propyl]-N'-(2-ethoxycarbonyl-ethyl)-urea
Prepared analogously to Example III (1).
R_f value: 0.49 (silica gel; cyclohexane/ethyl acetate = 1:3)

(4) N-(3-chloropropyl)-N'-(4'-cyano-4-biphenylyl)-urea
R_f value: 0.39 (silica gel; cyclohexane/ethyl acetate = 1:1)

(5) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
Solvent: dioxane
R_f value: 0.32 (silica gel; cyclohexane/ethyl acetate = 3:7)

(6) N-(4-cyano-phenyl)-N'-(3-hydroxy-propyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
Solvent: dioxane
Melting point: 86-89°C
R_f value: 0.27 (silica gel; cyclohexane/ethyl acetate = 3:7)

(7) N-(2-chloroethyl)-N'-(4'-cyano-3'-fluoro-4-biphenylyl)-urea
The 4-amino-4'-cyano-3'-fluoro-biphenyl used as starting material is obtained from 4-bromo-2-fluoro-benzonitrile

by reacting with phenyl boronic acid in the presence of palladium(II)acetate and tris-o-tolyl-phosphine with subsequent nitrogenation and reduction of the nitro group with 5% palladium charcoal in ethyl acetate.

(8) N-(3'-chloro-4'-cyano-4-biphenylyl)-N'-(2-chloroethyl)-urea
The 4-amino-3'-chloro-4'-cyano-biphenyl used as starting material is obtained analogously to Example III (7).

(9) N-(2-chloroethyl)-N'-(4'-cyano-3-methoxy-4-biphenylyl)-urea
The 4-amino-4'-cyano-3-methoxy-biphenyl used as starting material is obtained analogously to Example III (7).

(10) N-(2-chloroethyl)-N'-(4'-cyano-3-methylthio-4-biphenylyl)-urea
The starting material 4-amino-4'-cyano-3-methylthio-biphenyl is obtained from 4'-amino-4-biphenyl-carboxylic acid by reacting with ammonium rhodanide and bromine in acetic acid, saponifying the resulting 2-amino-benzothiazole derivative with dilute potassium hydroxide solution, methylating the mercapto group, protecting the amino group by means of the phthalyl derivative, converting the carboxyl group into a cyano group (via the acid chloride and the acid amide with subsequent dehydration with phosphorusoxychloride/pyridine) and cleaving the phthalyl group with aqueous methylamine solution.

(11) N-(2-chloroethyl)-N'-(4'-cyano-2,3-dimethyl-4-biphenylyl)-urea
The starting material 4-amino-4'-cyano-2,3-dimethyl-biphenyl is obtained analogously to Example III (7).

(12) N-(2-chloroethyl)-N'-[4-(5-cyano-2-pyridyl)-phenyl]-urea

The starting material 2-(4-amino-phenyl)-5-cyano-pyridine is obtained analogously to Example III (7), using 4-(2,2,5,5-tetramethyl-1-aza-2,5-disila-1-cyclopentanyl)-phenyl boronic acid (prepared from 4-(2,2,5,5-tetramethyl-1-aza-2,5-disila-1-cyclopentanyl)-phenyl-lithium and trimethoxyborane) and hydrolytically removing the silyl protecting group.

(13) N-(2-chloroethyl)-N'-[4-(5-cyano-2-pyrazinyl)-urea
The starting material 2-(4-amino-phenyl)-5-cyano-pyrazine is obtained from 4-nitro-phenylglyoxal by condensation with glycinamide, treating the product with phosphorusoxytribromide, bromine exchange with copper(I)cyanide and subsequent reduction of the nitro group analogously to Example III (7).

(14) N-(2-chloroethyl)-N'-[4-(5-cyano-2-pyrimidinyl)-phenyl]-urea
The starting material 2-(4-amino-phenyl)-5-cyano-pyrimidine is obtained from 4-nitro-benzamidine and 3-dimethylamino-2-formyl-acrylonitrile with subsequent reduction of the nitro group analogously to Example III (7).

(15) N-(2-chloroethyl)-N'-[2-(4-cyano-phenyl)-5-pyrimidinyl]-urea
The starting material 5-amino-2-(4-cyano-phenyl)-pyrimidine is obtained by first condensing ethyl 4-amidino-benzoate with diethylmalonate in the presence of sodium methoxide, nitrogenating the resulting pyrimidinedione and chlorinating with phosphorus oxychloride/phosphorus pentachloride and catalytically hydrogenating the product. The resulting 5-amino-2-(4-ethoxycarbonyl-phenyl)-pyrimidine is converted into the aminocarbonyl compound and dehydrated with phosphorus oxychloride/pyridine to obtain the nitrile.

(16) N-[4-(4-cyano-phenyl)-cyclohexyl]-N-(2,2-diethoxyethyl)-N'-(2-ethoxycarbonyl-ethyl)-urea
The starting material N-[4-(4-cyano-phenyl)-cyclohexyl]-N-(2,2-diethoxy-ethyl)-amine is obtained by reductive amination of 4-(4-cyano-phenyl)-cyclohexanone with 2,2-diethoxyethylamine in the presence of sodium cyanoborohydride.

(17) N-(2-chloroethyl)-N'-[2-(4'-cyano-4-biphenylyl)-ethyl]-urea
The starting material 2-(4'-cyano-4-biphenylyl)-ethylamine is obtained from 2-(4'-cyano-4-biphenylyl)-ethylbromide and potassium phthalimide and subsequently reacting with aqueous methylamine solution.

(18) N-(4-cyano-3-fluoro-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The 4-amino-2-fluoro-benzonitrile from which the isocyanate is obtained analogously to Example III (1) is obtained from 2-fluoro-4-nitro-benzoic acid by conversion into the acid amide, cleaving the water by heating with phosphorus oxychloride/pyridine and reduction with hydrogen in the presence of 5% palladium/charcoal in ethyl acetate.

(19) N-(3-chloro-4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
(The isocyanate is prepared analogously to Example III (1))

(20) N-(4-cyano-2-methylthio-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The 4-amino-3-methylthio-benzonitrile which is converted into the isocyanate analogously to Example III (1) is obtained from 4-amino-3-methylthio-benzoic acid analogously to Example III (10).

(21) N-(4-cyano-2-methyl-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
(The isocyanate is prepared analogously to Example III (1))

(22) N-(4-cyano-2-methoxy-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The starting material 4-amino-3-methoxy-benzonitrile, which is converted into the isocyanate analogously to Example III (1), is obtained from 3-methoxy-4-nitro-benzoic acid analogously to Example III (18)

(23) N-(4-cyano-phenyl)-N'-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N'-(2-hydroxy-ethyl)-urea

(24) N-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-(2-hydroxy-ethyl)-N'-(4-cyano-phenyl)-urea

(25) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(26) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-urea

(27) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-urea

(28) N-(4-cyano-phenyl)-N-(2-hydroxy-ethyl)-N'-[5-(2-methoxycarbonyl-ethyl)-2-pyridyl]-urea

(29) N-(4-cyano-phenyl)-N-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-urea

(30) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-(4-methoxycarbonylmethyloxy-phenyl)-urea

(31) N-(4-tert.butyloxy-carbonylmethylthio-phenyl)-N-(2-hydroxy-ethyl)-N'-(4-cyano-phenyl)-urea
Melting point: 111-114°C

(32) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(3-methoxycarbonyl-2-methyl-2-propyl)-phenyl]-urea
Melting point: 113-116°C

(33) N-(4-cyano-phenyl)-N'-[4-[2-(dimethoxy-phosphoryl)-ethyl]-phenyl]-N'-(2-hydroxy-ethyl)-urea

(34) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[2-(4-ethoxycarbonyl-phenyl)-ethyl]-urea

(35) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-urea

(36) N-(5-cyano-2-pyridyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(37) N-(1-benzyl-4-piperidinyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(38) N-(4-cyano-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(3-methoxycarbonyl-propyl)-phenyl]-urea

(39) N-(4-cyano-phenyl)-N'-(2,2-diethoxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
R_f value: 0.60 (silica gel; cyclohexane, ethyl acetate = 1:1)

(40) N-(2-chloroethyl)-N'-(4-cyano-phenyl)-urea
R_f value: 0.29 (silica gel; methylene chloride, methanol = 40:1, developed three times)

(41) N-(4-cyano-phenyl)-N'-(2,2-dimethoxy-ethyl)-N'-[2-(4-methoxycarbonyl-phenyl)-ethyl]-urea
Melting point: 109-110°C

(42) N-(4-cyano-phenyl)-N'-(2-hydroxy-propyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The work is done in dioxane without an auxiliary base.
R_f value: 0.40 (silica gel; ethyl acetate/cyclohexane = 2:1)

(43) N-acetylamino-N-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-N'-(4-cyano-phenyl)-urea
The work is done in dioxane without an auxiliary base.
Melting point: 126-128°C

(44) N-(4-cyano-phenyl)-N'-(2-hydroxy-propyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The work is done in dioxane without an auxiliary base.
R_f value: 0.25 (silica gel; cyclohexane/ethyl acetate = 1:1)

(45) N-(4-cyano-phenyl)-N'-formylamino-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The work is done in dioxane without an auxiliary base.
Melting point: 166-168°C

(46) N-(4-cyano-phenyl)-N-formylamino-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
Melting point: 180-183°C

(47) N-acetylamino-N-(4-cyano-phenyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
Melting point: 153-155°C

(48) N-(2-chloro-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
Melting point: 124-125°C

(49) N-[1-(4-cyano-phenyl)-4-piperidinyl]-N-(2,2-dimethoxyethyl)-N'-(2-ethoxycarbonyl-ethyl)-urea
Melting point: 90-92°C

(50) N-(4-cyano-phenyl)-N-(propionylamino)-N'-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-urea
Melting point: 149-153°C

(51) N-(4-cyano-phenyl)-N'-(2,2-diethoxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-urea
R_f value: 0.68 (silica gel; cyclohexane/ethyl acetate = 1:1)

(52) N-(4-cyano-phenyl)-N'-[4-(2-dibenzylamino-2-methoxycarbonyl-ethyl)-phenyl]-N'-(2,2-diethoxy-ethyl)-urea
R_f value: 0.52 (silica gel; cyclohexane/ethyl acetate = 2:1)

(53) N-[4-(2-tert.butyloxycarbonylamino-2-methoxycarbonyl-ethyl)-phenyl]-N'-(4-cyano-phenyl)-N'-(2,2-diethoxy-ethyl)-urea
R_f value: 0.15 (silica gel; cyclohexane/ethyl acetate = 2:1)

(54) N-(4-bromo-2-methyl-phenyl)-N'-(2-hydroxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
The work is done in dioxane without an auxiliary base.
Melting point: 101-104°C

Example IV

N-(4'-Cyano-4-biphenylyl)-N-(2,2-diethoxy-ethyl)-amine

A mixture of 10 g of 4-amino-4'-cyano-biphenyl, 8.3 ml of bromoacetaldehyde-diethylacetal, 13.9 ml of ethyl-diisopropylamine and 20 ml of dimethylformamide is stirred for 16 hours at a bath temperature of 160°C. It

is evaporated to dryness and the residue is purified by column chromatography over silica gel (eluant: cyclohexane/ethyl acetate = 2:1).
Yield: 3 g (19% of theory),
Melting point: 88-90°C
R_f value: 0.54 (silica gel; cyclohexane/ethyl acetate = 2:1)

The following compounds are obtained analogously:

(1) N-(tert.butyloxycarbonyl-methyl)-N-(4'-cyano-4-biphenylyl)-amine
The work is done at ambient temperature, recrystallising from cyclohexane/ethyl acetate = 20:2
Melting point: 151-153°C
R_f value: 0.76 (silica gel; cyclohexane/ethyl acetate = 1:1)

(2) N-(4'-cyano-4-biphenylyl)-N-[3-(2,3,5,6-tetrahydro-2-pyranyl)-propyl]-amine
The work is done at 110°C.
Melting point: 111-113°C
R_f value: 0.65 (silica gel; cyclohexane/ethyl acetate = 1:1)

(3) N-(2,2-diethoxy-ethyl)-N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-amine
R_f value: 0.35 (silica gel; cyclohexane/ethyl acetate = 8:2)

(4) N-(2,2-diethoxy-ethyl)-N-[2-(4-methoxycarbonyl-phenyl)-ethyl]-amine
The starting materials used are 2,2-dimethoxy-ethylamine and methyl 4-(2-chloro-ethyl)-benzoate.
Heating is carried out for 72 hours to 50°C.
R_f value: 0.46 (silica gel; ethyl acetate/methanol = 4:1)

(5) N-(4-cyano-phenyl)-glycine-tert.-butylester
Melting point: 110-112°C

(6) methyl 4-[(2,2-diethoxy-ethyl)-amino]-cinnamate
R_f value: 0.79 (silica gel; cyclohexane/ethyl acetate = 1:1)

(7) methyl 2-dibenzylamino-3-[4-[(2,2-diethoxy-ethyl)-amino]-phenyl]-propionate
R_f value: 0.59 (silica gel; cyclohexane/ethyl acetate = 2:1)

(8) methyl 2-dibenzylamino-3-(4-nitro-phenyl)-propionate
The work is done in methanol.
R_f value: 0.65 (silica gel; cyclohexane/ethyl acetate = 2:1)

(9) methyl 2-tert.butyloxycarbonylamino-3-[4-(2,2-diethoxy-ethylamino)-phenyl]-propionate
R_f value: 0.45 (silica gel; cyclohexane/ethyl acetate = 2:1)

Example V

N-(4'-Cyano-4-biphenylyl)-N-(3-methanesulphonyloxy-propyl)-N'-(2-ethoxycarbonyl-ethyl)-urea

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A mixture of 2 g of N-(4'-cyano-4-biphenylyl)-N-(3-hydroxypropyl)-N'-(2-ethoxycarbonyl-ethyl)-urea, 0.45 ml of methanesulphonyl chloride and 15 ml of methylene chloride is cooled to 0°C and within 15 minutes mixed with 0.8 ml of triethylamine. The mixture is stirred for one hour at 0°C and a further hour at ambient temperature, 25 ml of methylene chloride are added and the mixture is extracted with water. It is evaporated down and the residue is crystallised by triturating with tert.-butylmethylether.
Yield: 1.9 g (79% of theory),

R_f value: 0.47 (silica gel; ethyl acetate)

The following compounds are obtained analogously:

(1) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
R_f value: 0.39 (silica gel; cyclohexane/ethyl acetate = 3:7)

(2) N-(4-cyano-phenyl)-N'-(3-methanesulphonyloxy-propyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea
R_f value: 0.43 (silica gel; cyclohexane/ethyl acetate = 3:7)

(3) N-(4-cyano-3-fluoro-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(4) N-(3-chloro-4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(5) N-(3-cyano-2-methylthio-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(6) N-(4-cyano-2-methyl-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(7) N-(4-cyano-2-methoxy-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(8) N-(4-cyano-phenyl)-N'-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N'-(2-methanesulphonyloxy-ethyl)-urea

(9) N-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-(2-methanesulphonyloxy-ethyl)-N'-(4-cyano-phenyl)-urea

(10) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(11) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-urea

(12) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-urea

(13) N-(4-cyano-phenyl)-N-(2-methanesulphonyloxy-ethyl)-N'-[5-(2-methoxycarbonyl-ethyl)-2-pyridyl]-urea

(14) N-(4-cyano-phenyl)-N-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-urea

(15) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-(4-methoxycarbonylmethyloxy-phenyl)-urea

(16) N-(4-tert.butyloxycarbonylmethylthio-phenyl)-N-(2-methanesulphonyloxy-ethyl)-N'-(4-cyano-phenyl)-urea
R_f value: 0.35 (silica gel; methylene chloride/ethyl acetate = 95:5)

(17) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(3-methoxycarbonyl-2-methyl-2-propyl)-phenyl]-urea
R_f value: 0.57 (silica gel; cyclohexane/ethyl acetate = 3:7)

(18) N-(4-cyano-phenyl)-N'-[4-[2-(dimethoxy-phosphoryl)-ethyl]-phenyl]-N'-(2-methanesulphonyloxy-ethyl)-urea

(19) N-(4-cyano-phenyl)-N'-[2-(4-ethoxycarbonyl-phenyl)-ethyl]-N'-(2-methanesulphonyloxy-ethyl)-urea

(20) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-urea

(21) N-(5-cyano-2-pyridyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(22) N-(1-benzyl-4-piperidinyl)-N'-(2-methane-sulphonyloxy-ethyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea

(23) N-(4-cyano-phenyl)-N'-(2-methanesulphonyloxy-ethyl)-N'-[4-(3-methoxycarbonyl-propyl)-phenyl]-urea

(24) 1-(4-cyano-phenyl)-3-(2-methanesulphonyloxy-ethyl)-imidazolidin-2-one
Melting point: 98-100°C

(25) N'-(4-cyanomethyl-phenyl)-N'-(2-methane-sulphonyloxy-ethyl)-N'-(4-methoxycarbonylmethyl-phenyl)-urea
R_f value: 0.19 (silica gel; cyclohexane/ethyl acetate = 6:4)

Example VI

N-(4'-Cyano-4-biphenylyl)-N-(3-hydroxy-propyl)-N'-(2-ethoxycarbonyl-ethyl)-urea

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4.1 g of N-(4'-cyano-4-biphenylyl)-N-[3-(2,3,5,6-tetrahydro-2-pyranyloxy)-propyl]-N'-(2-ethoxycarbonyl-ethyl)-urea are dissolved in 15 ml of ethanol, 0.2 ml of ethereal hydrochloric acid are added and the mixture is stirred for 2 hours at ambient temperature. It is evaporated to dryness, taken up in 200 ml of methylene chloride, extracted with 10% sodium bicarbonate solution

and the organic phase is evaporated to dryness. The residue is purified by column chromatography on silica gel (eluant: ethyl acetate).
Yield: 2.1 g (64% of theory),
Melting point: 120-122°C
R_f value: 0.36 (silica gel; ethyl acetate)

The following compound is obtained analogously:

(1) 1-(4-cyano-phenyl)-piperidin-4-one
Prepared from the corresponding ethylene ketal with pyridinium toluenesulphonate in acetone/water at 100°C
Melting point: 102-104°C

Example VII

N-(2-Hydroxy-ethyl)-N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-amine

1.5 g of N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-N-[2-(2,3,5,6-tetrahydro-2-pyranyloxy)-ethyl]-trifluoro-acetamide are stirred for 2 hours in a mixture of 20 ml of methanol and 2.5 ml of 4N sodium hydroxide solution at ambient temperature. Then the mixture is neutralised with glacial acetic acid, evaporated down and all the water is eliminated by boiling with toluene using a water separator. The residue is concentrated by evaporation, taken up in 20 ml of methanol, 2 ml of methanolic hydrochloric acid are added and the resulting mixture is left to stand for 16 hours at ambient temperature. The precipitate is filtered off, the filtrate is evaporated down and stirred with 10 ml of methylene chloride and 5 ml of 0.1N sodium hydroxide solution. The organic phase is evaporated down and the remaining oil is used directly for further processing.
Yield: 0.65 g (78% of theory),
R_f value: 0.43 (silica gel; cyclohexane/ethyl acetate = 3:7)

The following compounds are obtained analogously:

(1) N-(3-hydroxy-propyl)-N-[4-(2-methoxycarbonyl-ethyl)-phenyl]-amine
R_f value: 0.44 (silica gel; cyclohexane/ethyl acetate = 3:7)

(2) N-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-(2-hydroxy-ethyl)-amine

(3) N-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-N-(2-hydroxy-ethyl)-amine

(4) N-(2-hydroxy-ethyl)-N-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-amine

(5) N-(2-hydroxy-ethyl)-N-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-amine

(6) N-(2-hydroxy-ethyl)-N-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-amine

Example VIII

3-(4-Cyano-phenyl)-3H-imidazo[4,5-b]pyridin-2-one

0.21 g of 3-amino-2-[(4-cyano-phenyl)-amino]-pyridine and 0.26 g of N-ethyl-diisopropylamine are dissolved in 4.5 ml of methylene chloride and, whilst cooling with ice, 0.5 ml of a 20% solution of phosgene in toluene is added in batches and resulting mixture is stirred for 1.5 hours at ambient temperature. A further 0.3 ml of the phosgene solution is added and stirring is continued for 20 minutes. The precipitate obtained is filtered off and washed with methylene chloride.
Yield: 0.17 g (72% of theory),
R_f value: 0.47 (silica gel; methylene chloride/methanol = 19:1)

The following compound is obtained analogously:

(1) 3-(4'-cyano-4-biphenylyl)-3H-imidazo[4,5-b]pyridin-2-one
R_f value: 0.44 (silica gel; methylene chloride/methanol = 9:1)

Example IX

1-[4-(2-Methoxycarbonyl-ethyl)-phenyl]-3-(4-piperidinyl)-imidazolidin-2-one

Prepared by treating 1-(1-benzyloxycarbonyl-4-piperidinyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one with hydrogen at 3 bars in the presence of 5% palladium/charcoal in methanol.

Example X

2-[(2-Ethoxycarbonyl-ethyl)-aminosulphonyloxy]-phenol

1.54 g of β-alanine ethylester-hydrochloride and 1.9 g of 1,2-sulphonyldioxybenzene are dissolved in 10 ml of dimethylformamide, 1.55 g of ethyl-diisopropylamine are added and the mixture is stirred for two hours at ambient temperature. The solvent is distilled off in vacuo and the residue is purified by column chromatography (silica gel; eluant: cyclohexane/ethyl acetate = 8:2)
Yield: 1.4 g (48% of theory)
R_f value: 0.31 (silica gel; cyclohexane/ethyl acetate = 7:3)

The following compound is obtained analogously:

(1) 4-cyano-4'-[(2-ethoxycarbonyl-ethyl)-aminosulphonylamino]-biphenyl
The work is done without an auxiliary base and by

heating for 15 hours to 80°C
Melting point: 103-105°C
R_f value: 0.21 (silica gel; cyclohexane/ethyl acetate = 7:3)

Example XI

Methyl 3-[4-[(2-hydroxy-propyl)-amino]-phenyl]-propionate

6 g of methyl 3-(4-amino-phenyl)-propionate hydrochloride are suspended in methylene chloride and 27.9 ml of 1N sodium hydroxide solution are added. The organic phase is separated off, the mixture is extracted twice more with methylene chloride and the combined organic phases are evaporated down. The residue is taken up in 50 ml of methanol and 1.9 ml of propylene oxide and 2 ml of water are added. It is stirred for 48 hours at ambient temperature, evaporated down and purified over silica gel (eluant: cyclohexane/ethyl acetate = 1:1).
Yield: 3.5 g (54% of theory),
R_f value: 0.40 (silica gel; cyclohexane/ethyl acetate = 1:1)

Example XII

4-[(2-Hydroxy-propyl)-amino]-benzonitrile

12.1 g of 4-fluoro-benzonitrile, 7.5 g of 2-hydroxy-propylamine and 17.4 ml of N-ethyl-diisopropylamine are heated together to 100°C for 2.5 hours. The mixture is poured onto 250 ml of water, extracted five times with 50 ml of ethyl acetate and the combined organic phases are evaporated down. The product remaining is purified by column chromatography (silica gel; eluant: ethyl acetate) and crystallised by triturating with a 1:1-mixture of tert.butyl-methylether and petroleum ether.

Yield: 2.2 g (13% of theory),
Melting point: 70-73°C

The following compound is obtained analogously:

(1) 1-(4-cyano-phenyl)-4,4-ethylenedioxy-piperidine
Melting point: 136-138°C

Example XIII

1-[4-(2-Methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one

---

2 g of 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one are hydrogenated in a mixture of 20 ml of methanol and 30 ml of glacial acetic acid in the presence of a platinum/rhodium catalyst with hydrogen at 5 bars at 50°C for 50 minutes. The catalyst is filtered off, the filtrate is evaporated down and the remaining product is used without further purification.
Yield: 2.03 g (100% of theory),
R_f value: 0.29 (silica gel; ethyl acetate/cyclohexane = 9:1)

Example XIV

Methyl 3-[4-[(2-chloro-ethyl)-aminosulphonylamino]-phenyl]-propionate

---

At -30°C, 6.7 g of N-(2-chloroethyl)-N-chlorosulphonyl-amine, dissolved in 10 ml of methylene chloride, are added dropwise to a solution of 8.6 g of methyl 3-(4-amino-phenyl)-propionate hydrochloride and 12.9 g of N-ethyl-diisopropylamine in 40 ml of methylene chloride. The mixture is stirred for a further 2 hours, whilst coming up to ambient temperature. The reaction mixture is washed with water, evaporated down and purified by column chromatography (silica gel; cyclohexane/ethyl

acetate = 7:3).
Yield: 8.3 g (65% of theory),
Melting point: 97-99°C

The following compound is obtained analogously:

(1) Tert.butylester of N-(4-cyano-phenyl)-N-methoxycarbonyl-glycine
Potassium carbonate and 4-dimethylamino-pyridine in chloroform are used.
R_f value: 0.42 (silica gel; cyclohexane/ethyl acetate = 7:3)

Example XV

1-(4-Cyano-phenyl)-4-[(2,2-dimethoxy-ethyl)-amino]-piperidine

---

11 g of 1-(4-cyano-phenyl)-piperidin-4-one are dissolved in 90 ml of acetonitrile, then mixed with 10 ml of water and 6.9 g of aminoacetaldehyde-dimethylacetal. 18.3 ml of 3N hydrochloric acid are added dropwise and 4.5 g of sodium cyanoborohydride are added. After 20 minutes' stirring at ambient temperature the acetonitrile is evaporated off in vacuo and the residue is extracted with ethyl acetate. The residue remaining after evaporation of the ethyl acetate phases is purified by chromatography on silica gel (eluant: methylene chloride/methanol = 100:3).
Yield: 10.8 g (74% of theory),
R_f value: 0.34 (silica gel; methylene chloride/methanol/concentrated ammonia = 95:5:0.1)

The following compounds are obtained analogously:

(1) Methyl 3-[4-[(2-hydroxy-ethyl)-amino]-phenyl]-3-methyl-butyrate
R_f value: 0.35 (silica gel; cyclohexane/ethyl acetate =

1:1)

(2) Methyl 4-[(2-hydroxy-ethyl)-amino]-phenylacetate
R_f value: 0.25 (silica gel; cyclohexane/ethyl acetate = 1:1)

Example XVI

N-(4-Cyano-phenyl)-N-methoxycarbonyl-glycine-[4-(2-methoxycarbonyl-ethyl)-anilide]

A mixture of 3.7 g of N-(4-cyano-phenyl)-N-methoxycarbonyl-glycine, 2.4 g of 1-hydroxy-benzotriazole, 150 ml of tetrahydrofuran, 2.81 g of methyl 3-(4-amino-phenyl)-propionate, 4.2 g of N,N'-dicyclohexylcarbodiimide and 1.62 g of triethylamine is stirred for 64 hours at ambient temperature. The precipitate formed is filtered off, the filtrate is evaporated down and the residue is purified by column chromatography over silica gel (eluant: cyclohexane/ethyl acetate = 1:1 to 2:3).
Yield: 5.5 g (88% of theory),
Melting point: 100-110°C

The following compound is obtained analogously:

(1) N-(4-cyano-phenyl)-N'-propionyl-hydrazine
Carbonyldiimidazole in tetrahydrofuran is used.
Melting point: 143-145°C

Example XVII

N-(4-Cyano-phenyl)-N-methoxycarbonyl-glycine

g of the tert.butylester of N-(4-cyano-phenyl)-N-methoxycarbonyl-glycine are dissolved in 70 ml of methylene chloride and a solution of 18 ml of trifluoroacetic acid in 18 ml of methylene chloride is

added dropwise thereto. The mixture is left to stand for 16 hours at ambient temperature, evaporated down, the residue is taken up in tert.butylmethylether, washed with water and the organic phase is evaporated down. The residue is briefly boiled with 50 ml of diethylether and, after cooling in the ice bath, filtered off. Another fraction can be obtained from the mother liquors.
Yield: 3.85 g (68% of theory),
Melting point: 134-137°C

Example XVIII

Methyl 3-(4-amino-phenyl)-2-dibenzylamino-propionate

5.35 g of methyl 2-dibenzylamino-3-(4-nitro-phenyl)-propionate, dissolved in 100 ml of methanol, are treated with hydrogen under a pressure of 5 bars in the presence of 1 g of Raney nickel at ambient temperature for 8 hours. The catalyst is filtered off, the filtrate is evaporated down and the crude product remaining is used without purification.
Yield: 4.9 g (92% of theory),
R_f value: 0.45 (silica gel; cyclohexane/ethyl acetate = 2:1)

The following compounds are obtained analogously:

(1) 3-amino-2-[(4-cyano-phenyl)-amino]-pyridine
The work is done in a 3:1 mixture of ethyl acetate and methanol with 10% palladium/charcoal
R_f value: 0.62 (silica gel; methylene chloride/methanol = 9:1)

(2) 3-amino-2-[(4'-cyano-4-biphenylyl)-amino]-pyridine
The work is done in a 3:1 mixture of ethyl acetate and methanol with 10% palladium/charcoal
R_f value: 0.66 (silica gel; methylene chloride/methanol =

19:1)

Example XIX

1-(4-Cyano-phenyl)-3-(2-hydroxy-ethyl)-imidazolidin-2-one

0.71 g of lithium borohydride are added in batches to a solution of 8.8 g of 1-(4-cyano-phenyl)-3-(ethoxycarbonylmethyl)-imidazolidin-2-one in 500 ml of tetrahydrofuran with stirring at ambient temperature. The mixture is stirred for 1 hour at ambient temperature and for 2 hours at 60°C, then after cooling in an ice bath 16.5 ml of 2N hydrochloric acid are added and the resulting mixture is evaporated down in vacuo. The residue is digested with 50 ml of methanol, the methanol phase is evaporated down and the residue is purified over silica gel (eluant: ethyl acetate/methanol = 9:1)
Yield: 5.0 g (67% of theory),
Melting point: 112-114°C

Example XX

N-(4-Cyanomethyl-phenyl)-N'-(2-hydroxy-ethyl)-N'-(4-methoxycarbonylmethyl-phenyl)-urea

---

1.46 g of carbonyldiimidazole and 1.04 g of imidazole are dissolved in 20 ml of tetrahydrofuran. The mixture is cooled to 0°C and 1.18 g of 4-amino-benzylcyanide are added. After about 3 minutes a solution of methyl 4-[(2-hydroxy-ethyl)-amino]-phenylacetate in 7 ml of tetrahydrofuran is rapidly added dropwise, the ice cooling is taken away and the mixture is stirred for 16 hours at ambient temperature (a precipitate formed initially is filtered off). The mixture is concentrated down, the residue is taken up in ethyl acetate, washed with 1N hydrochloric acid and water and the organic phase is evaporated down. The residue is purified by

chromatography on silica gel (eluant: ethyl acetate/methylene chloride = 1:1).
Yield: 1.4 g (42% of theory),
Melting point: 140-142°C

Example XXI

1-[4-(1-Hydroxyimino-ethyl)-phenyl]-3-[4-(2-methoxycarbonylethyl)-phenyl]-imidazolidin-2-one

---

1.1 g of 1-(4-acetyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one are suspended in a mixture of 10 ml of dioxane and 10 ml of methanol, mixed with a solution of 0.25 g of hydroxylamine-hydrochloride in 4 ml of water and refluxed for 2.5 hours. Then the mixture is evaporated down in vacuo and the residue is triturated with water, whereupon it crystallises.
Yield: 1.1 g (92% of theory),
Melting point: 241-243°C (sinters from 235°C)

The following compound is obtained analogously:

(1) 1-(1-hydroxyimino-5-indanyl)-3-[4-(2-methoxycarbonylethyl)-phenyl]-imidazolidin-2-one
R_f value: 0.13 (silica gel; methylene chloride/ethyl acetate = 9:1)

Example XXII

1-(4-Acetyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

---

Prepared analogously to Example 25 from 1-[4-(2-methoxycarbonylethyl)-phenyl]-imidazolidin-2-one and 4-bromo-acetophenone.
Melting point: 198-200°C
R_f value: 0.33 (silica gel; methylene chloride/ethyl acetate = 25:1)

The following compound is obtained analogously:

(1) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-(1-oxo-5-indanyl)-imidazolidin-2-one
Melting point: 204-206°C
R_f value: 0.39 (silica gel; methylene chloride/ethyl acetate = 9:1)

Example 1

1-(4'-Amidino-4-biphenylyl)-3-carboxymethyl-imidazolidin-2-one

0.35 g of 1-(4'-amidino-4-biphenylyl)-3-methoxycarbonylmethyl-imidazolin-2-one hydrochloride are suspended in 9 ml of methanol. 2.7 ml of 1N sodium hydroxide solution are added and the mixture is stirred for 16 hours at ambient temperature. The solvent is distilled off in vacuo and the residue is mixed with 10 ml of water. Ammonium chloride is added as a buffer. The product precipitated is filtered off.

Yield: 0.19 g (62% of theory),

Melting point: above 200°C

R_f value: 0.61 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

Calc. x H_2O:	C 60.65	H 5.67	N 15.72
Found:	61.20	5.57	15.98

The following compounds are obtained analogously:

(1) 1-(4'-amidino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

Melting point: above 200°C

R_f value: 0.58 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

Calc. x 0.5 H_2O:	C 63.14	H 5.87	N 15.51
Found:	63.37	5.80	15.13

(2) 1-(4'-amidino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2,4-dione

The starting material used is 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-imidazolidin-2,4-dione hydrochloride

Melting point: above 200°C

R_f value: 0.66 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

Calc. x 0.25 H_2O: C 61.52 H 5.01 N 15.11
Found: 61.89 4.97 14.97

(3) 1-(4'-amidino-4-biphenylyl)-3-(2-carboxy-ethyl)-3H-imidazol-2-one
The starting material used is 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride
Melting point: above 200°C
R_f value: 0.68 (Reversed Phase Plate RP8; 5% sodium chloride solution/methanol = 4:6)
Calc. x 0.25 H_2O: C 64.30 H 5.24 N 15.79
Found: 64.61 5.34 15.45

(4) 1-(4'-amidino-4-biphenylyl)-3-(2-carboxy-ethyl)-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
The starting material used is 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3,4,5,6-tetrahydro-1H-pyrimidin-2-one and the work is done in ethanol as solvent
Melting point: above 200°C
R_f value: 0.54 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)
Calc. x 0.25 H_2O: C 64.76 H 6.12 N 15.11
Found: 64.62 6.13 14.82

(5) 1-(4'-amidino-4-biphenylyl)-3-carboxymethyl-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Melting point: above 200°C
R_f value: 0.63 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)
Calc. x 0.75 H_2O: C 62.37 H 5.92 N 15.31
Found: 62.39 5.94 15.55

(6) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Lithium hydroxide is used and the solvent is a 5:4

mixture of tetrahydrofuran and water.
Melting point: above 270°C
R_f value: 0.68 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

(7) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Lithium hydroxide is used and, as the solvent, a 5:4 mixture of tetrahydrofuran and water is used.
Melting point: above 270°C
R_f value: 0.60 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

(8) 1-[2-(4'-amidino-4-biphenylyl)-ethyl]-3-carboxymethyl-3H-benzimidazol-2-one
R_f value: 0.55 (silica gel; methylene chloride, methanol = 6:4)

(9) 1-(4'-amidino-3'-fluoro-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(10) 1-(4'-amidino-3'-chloro-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(11) 1-(4'-amidino-3-methoxy-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(12) 1-(4'-amidino-3-bromo-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(13) 1-(4'-amidino-3-methylthio-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(14) 1-(4'-amidino-3-methylsulphonyl-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(15) 1-(4'-amidino-3-methylsulphinyl-4-biphenylyl)-3-(2-

carboxy-ethyl)-imidazolidin-2-one

(16) 1-(4'-amidino-2,3-dimethyl-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(17) 1-(4'-amidino-3-nitro-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(18) 1-(4'-amidino-3-amino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(19) 1-(3-acetamino-4'-amidino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(20) 1-(4'-amidino-3-benzoylamino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(21) 2-(4'-amidino-4-biphenylyl)-5-(2-carboxy-ethyl)-3,4-dihydro-2H,5H-1,2,5-thiadiazol-1,1-dioxide
Melting point: above 260°C
R_f value: 0.63 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

Calc.:	C 55.66	H 5.19	N 14.42	S 8.25
Found:	54.42	5.32	14.56	8.26

(22) 1-[4-(4-amidino-phenyl)-cyclohexyl]-3-(2-carboxy-ethyl)-3H-imidazol-2-one

(23) 1-[4-(4-amidino-phenyl)-cyclohexyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one

(24) 1-[1-(4-amidino-phenyl)-4-piperidinyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one
Melting point: above 275°C
R_f value: 0.66 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 0.5 H_2O: C 58.68 H 7.11 N 19.01

Found: 58.16 7.22 18.76

(25) 1-[4-(5-amidino-2-pyridyl)-phenyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one

(26) 1-[4-(5-amidino-2-pyrazinyl)-phenyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one

(27) 1-[4-(5-amidino-2-pyrimidinyl)-phenyl]-2-(2-carboxy-ethyl)-imidazolidin-2-one

(28) 1-[6-(4-amidino-phenyl)-3-pyridazinyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one
Melting point: from 300°C (decomp.)
R_f value: 0.47 (silica gel; butanol/glacial acetic acid/water = 4:1:1)

(29) 1-[2-(4-amidino-phenyl)-5-pyrimidinyl]-3-(2-carboxy-ethyl)-imidazolidin-2-one

(30) 1-[2-(4'-amidino-4-biphenyl)-ethyl]-3-carboxy-methyl-imidazolidin-2-one

(31) 1-(4-amidino-3-fluoro-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(32) 1-(4-amidino-3-chloro-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(33) 1-(4-amidino-2-methylthio-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(34) 1-(4-amidino-2-methylsulphinyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(35) 1-(4-amidino-2-methylsulphonyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(36) 1-(4-amidino-2-methyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 270°C
R_f value: 0.56 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc.: C 65.56 H 6.05 N 15.29
Found: 65.43 6.04 15.36

(37) 1-(4-amidino-2-methoxy-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(38) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-fluoro-phenyl]-imidazolidin-2-one

(39) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-chloro-phenyl]-imidazolidin-2-one

(40) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-methoxy-phenyl]-imidazolidin-2-one

(41) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-methyl-phenyl]-imidazolidin-2-one

(42) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-methylthio-phenyl]-imidazolidin-2-one

(43) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-methylsulphinyl-phenyl]-imidazolidin-2-one

(44) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-2-methylsulphonyl-phenyl]-imidazolidin-2-one

(45) 1-(4-amidino-phenyl)-3-[5-(2-carboxy-ethyl)-2-pyridyl]-imidazolidin-2-one

(46) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)cyclohexyl]-imidazolidin-2-one

Melting point: above 200°C
R_f value: 0.59 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc. x 0.4 H_2O: C 62.41 H 7.38 N 15.32
Found: 62.43 7.31 15.18

(47) 1-(4-amidino-phenyl)-3-(4-carboxymethyloxy-phenyl)-imidazolidin-2-one

(48) 1-(4-amidino-phenyl)-3-(4-carboxymethylthio-phenyl)-imidazolidin-2-one
Melting point: above 275°C
R_f value: 0.56 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 0.5 H_2O: C 56.98 H 5.05 N 14.76 S 8.45
Found: 56.94 5.15 14.98 8.42

(49) 1-(4-amidino-phenyl)-3-(4-carboxymethylsulphinyl-phenyl)-imidazolidin-2-one
Melting point: 252-254°C (decomp.)
R_f value: 0.79 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 1.5 H_2O: C 52.28 H 5.12 N 13.55 S 7.74
Found: 52.34 4.97 13.62 8.26

(50) 1-(4-amidino-phenyl)-3-(4-carboxymethylsulphonyl-phenyl)-imidazolidin-2-one
Melting point: above 260°C
R_f value: 0.82 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 0.5 H_2O: C 52.55 H 4.66 N 13.62 S 7.78
Found: 52.88 4.83 13.67 7.99

(51) 1-(4-amidino-phenyl)-3-[4-(3-carboxy-2-methyl-2-propyl)-phenyl]-imidazolidin-2-one
Lithium hydroxide is used
Melting point: above 260°C

R_f value: 0.76 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(52) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-2-methyl-propyl)-phenyl]-imidazolidin-2-one

(53) 1-(4-amino-cyclohexyl)-3-[4-[(2-carboxy-ethyl)-aminocarbonyl]-phenyl]-imidazolidin-2-one

(54) 4-(4'-amidino-4-biphenyl)-1-(2-carboxy-ethyl)-3-phenyl-imidazolidin-2-one

(55) 1-(4-amidino-phenyl)-3-[2-(4-carboxyphenyl)-ethyl]-imidazolidin-2-one
The work is done with lithium hydroxide and a 2:1 mixture of methanol and dioxane.
Melting point: 320-325°C (decomp.)
R_f value: 0.55 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(56) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethenyl)-phenyl]-imidazolidin-2-one

(57) 1-(5-amidino-2-pyridyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(58) 1-(1-amidino-4-piperidinyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(59) 1-(4-aminomethyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 260°C
R_f value: 0.61 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

Calc. x H_2O:	C 63.85	H 6.49	N 11.76
Found:	64.17	6.50	11.59

(60) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-thione

(61) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-2-imino-imidazolidine

(62) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2,4-dione
Lithium hydroxide is used
Melting point: above 260°C
R_f value: 0.83 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 0.5 H_2O: C 60.79 H 5.10 N 14.93
Found: 60.69 5.04 15.12

(63) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2,4-dione

(64) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4,4-dimethyl-imidazolidin-2,5-dione

(65) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4,4-dimethyl-imidazolidin-2,5-dione

(66) 2-(4-amidino-phenyl)-5-[4-(2-carboxy-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide
Melting point: above 275°C
R_f value: 0.53 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc.: C 55.66 H 5.19 N 14.42 S 8.25
Found: 55.84 5.24 14.23 8.01

(67) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-one
Lithium hydroxide is used.
Melting point: above 260°C
R_f value: 0.58 (Reversed Phase Plate RP8; 10% sodium

chloride solution/methanol = 4:6)

(68) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-2-methylimino-imidazolidine

(69) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-2-phenylimino-imidazolidine

(70) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-2-(3-pyridylimino)-imidazolidine

(71) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4-trifluoromethyl-3H-imidazol-2-one

(72) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-phenyl-3H-imidazol-2-one

(73) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-phenyl-imidazolidin-2-one

(74) 1-[(4-amidino-phenyl)-carbonylmethyl]-3-(3-carboxy-propyl)-imidazolidin-2-one

(75) 1-[2-(4-amidino-phenyl)-ethyl]-3-(3-carboxy-propyl)-imidazolidin-2-one

(76) 1-[2-(4-amidino-phenyl)-2-hydroxy-ethyl]-3-(3-carboxy-propyl)-imidazolidin-2-one

(77) 1-(4-amidino-phenyl)-3-(4-carboxy-butyl)-imidazolidin-2-one
R_f value: 0.50 (silica gel; n-butanol/glacial acetic acid/water = 4:1:1)

(78) 1-(4-amidino-phenyl)-3-(2-carboxymethylthio-ethyl)-imidazolidin-2-one

(79) 1-(4-amidino-phenyl)-3-(2-carboxymethylsulphinyl-ethyl)-imidazolidin-2-one

(80) 1-(4-amidino-phenyl)-3-(2-carboxymethylsulphonyl-ethyl)-imidazolidin-2-one

(81) 1-(4-amidino-phenyl)-3-(2-carboxymethyloxy-ethyl)-imidazolidin-2-one

(82) 1-(4-amidino-phenyl)-3-(2-carboxymethylamino-ethyl)-imidazolidin-2-one
Lithium hydroxide is used
Melting point: 298°C (decomp. sintering from 285°C)
R_f value: 0.14 (silica gel; methanol/2N ammonia = 5:1, developing three times)

(83) 1-[2-(N-acetyl-N-carboxymethyl-amino)-ethyl]-3-(4-amidino-phenyl)-imidazolidin-2-one

(84) 1-(4-amidino-phenyl)-3-[2-(N-benzoyl-N-carboxymethylamino)-ethyl]-imidazolidin-2-one

(85) 1-(4-amidino-phenyl)-3-[1-(2-carboxy-ethyl)-2-oxo-1H-4-pyridyl]-imidazolidin-2-one

(86) 1-[4-(2-carboxy-ethyl)-phenyl]-3-(4-ethoxycarbonyl-amidino-phenyl)-imidazolidin-2-one

(87) 1-(4-amidino-phenyl)-3-[4-(3-carboxy-propyl)-phenyl]-imidazolidin-2-one

(88) 1-(4'-amidino-3-methanesulphonylamino-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(89) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-5-one

(90) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-4H-1,2,4-triazol-5-one

(91) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-5-one

(92) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-4H-1,2,4-triazol-5-one

(93) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl-3H-imidazol-2-one

(94) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one hydrochloride
Lithium hydroxide is used
Melting point: 288-294°C (decomp.)

(95) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one

(96) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-thione

(97) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione

(98) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-thione

(99) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one

(100) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3,5-dimethyl-3H-imidazol-2-one

(101) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one

(102) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(103) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-imidazolidin-2-one

(104) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-imidazolidin-2-one

(105) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-one

(106) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-3H-imidazol-2-one

(107) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one

(108) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-thione

(109) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione

(110) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-thione

(111) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one

(112) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3,5-dimethyl-3H-imidazol-2-one

(113) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one

(114) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-

phenyl]-imidazolidin-2-one

(115) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-imidazolidin-2-one

(116) 1-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-3-phenyl-imidazolidin-2-one

(117) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3H-imidazol-2-one hydrochloride
Melting point: above 280°C

Calc. x H_2O:	C 56.35	H 5.48	N 13.84	Cl 8.76
Found:	56.56	5.31	13.82	8.96

(118) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-methyl-3H-imidazol-2-one hydrochloride
Melting point: above 280°C

Calc. x H_2O:	C 57.34	H 5.53	N 13.37	Cl 8.46
Found:	57.37	5.91	13.39	8.79

(119) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-phenyl-3H-imidazol-2-one hydrochloride
Melting point: above 280°C

Calc. x H_2O:	C 62.43	H 5.24	N 11.65	Cl 7.37
Found:	62.66	5.14	11.83	7.67

(120) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3H-imidazol-2-thione

(121) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-methyl-3H-imidazol-2-thione

(122) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-phenyl-3H-imidazol-2-thione

(123) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-5-methyl-3H-imidazol-2-one

(124) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3,5-dimethyl-3H-imidazol-2-one

(125) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-5-methyl-3-phenyl-3H-imidazol-2-one

(126) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-imidazolidin-2-one

(127) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-methyl-imidazolidin-2-one

(128) 1-[4-(2-carboxy-ethyl)-phenyl]-3-(3-guanidino-phenyl)-imidazolidin-2-one

(129) 1-(4-amidino-phenyl)-3-[1-(2-carboxy-ethyl)-4-piperidinyl]-imidazolidin-2-one

(130) 1-[4-(2-carboxy-ethyl)-phenyl]-3-(4-methylamidino-phenyl)-imidazolidin-2-one

(131) 1-(4-n-butylamidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(132) 2-(4-amidino-4'-biphenylyl)-4-(2-carboxy-ethyl)-4H-1,2,4-triazol-3-one

(133) 2-(4-amidino-4'-biphenylyl)-4-(2-carboxy-ethyl)-5-methyl-4H-1,2,4-triazol-3-one

(134) 4-(4-amidino-4'-biphenylyl)-2-(2-carboxy-ethyl)-4H-1,2,4-triazol-3-one

(135) 4-(4-amidino-4'-biphenylyl)-2-(2-carboxy-ethyl)-5-methyl-4H-1,2,4-triazol-3-one

(136) 3-(4-amidino-phenyl)-1-(4-carboxy-butyl)-3H-

imidazo[4,5-b]pyridin-2-one hydrochloride
R_f value: 0.23 (silica gel; methylene chloride/methanol = 19:1)

(137) 4-(4-amidino-phenyl)-2-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one
R_f value: 0.60 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(138) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one
R_f value: 0.54 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc. x 1.8 H_2O: C 60.54 H 5.99 N 14.12
Found: 60.95 5.88 14.15

(139) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one
Melting point: 303-305°C
R_f value: 0.63 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc.: C 62.45 H 5.24 N 19.17
Found: 62.28 5.28 18.70

(140) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-ethyl-4H-1,2,4-triazol-3-one
Melting point: above 250°C
R_f value: 0.53 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)
Calc. x 1.5 H_2O: C 59.10 H 5.95 N 17.23
Found: 58.71 6.10 17.03

(141) 1-(4-aminomethyl-phenyl)-3-(4-carboxymethyloxy-phenyl)-imidazolidin-2-one
Melting point: above 250°C
R_f value: 0.58 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

Calc. x 0.5 H_2O: C 61.70 H 5.75 N 11.99
Found: 61.48 5.81 12.22

(142) 1-(4-aminomethyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Melting point: 229-231°C
R_f value: 0.56 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(143) 3-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3H-imidazo[4,5-b]pyridin-2-one
R_f value: 0.28 (silica gel; methylene chloride/methanol = 8:2)

(144) 3-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one
R_f value: 0.54 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(145) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: 310-313°C
R_f value: 0.58 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc.: C 59.99 H 5.03 N 19.44
Found: 60.03 5.04 19.15

(146) 4-(4-amidino-phenyl)-2-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: 313-316°C
R_f value: 0.61 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc.: C 61.53 H 4.88 N 19.93
Found: 61.42 4.97 20.22

(147) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethenyl)-phenyl]-3H-imidazol-2-one

Melting point: above 350°C
R_f value: 0.45 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(148) 1-(4-amidino-phenyl)-3-[4-(2-amino-2-carboxy-ethyl)-phenyl]-3H-imidazol-2-one
Lithium hydroxide is used
R_f value: 0.06 (silica gel; methylene chloride/methanol/conc. ammonia = 8:4:1)

(149) 1-[4-(2-amino-2-carboxy-ethyl)-phenyl]-3-(4-aminomethyl-phenyl)-imidazolidin-2-one
Lithium hydroxide is used
R_f value: 0.15 (silica gel; methylene chloride/methanol/conc. ammonia = 16:4:1)

(150) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-2-dibenzylamino-ethyl)-phenyl]-3H-imidazol-2-one
Lithium hydroxide is used
R_f value: 0.50 (silica gel; methylene chloride/methanol = 4:1)

(151) 1-[4-(2-amino-ethyl)-phenyl]-3-(4-carboxymethyl-phenyl)-imidazolidin-2-one
Melting point: above 250°C
R_f value: 0.41 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(152) 1-[4-(2-amino-2-propyl)-phenyl]-3-[4-(2-carboxyethyl)-phenyl)-imidazolidin-2-one

(153) 1-[4-(1-amino-ethyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Melting point: 267-269°C (decomp.)
R_f value: 0.40 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(154) 1-(1-amino-5-indanyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Melting point: 234-236°C (decomp.)

(155) 1-(1-amino-1,2,3,4-tetrahydro-6-naphthyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(156) 1-(4-aminomethyl-2-methyl-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Melting point: 237-239°C (decomp.)
R_f value: 0.50 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc. x 0.8 H_2O: C 65.31 H 6.74 N 11.42
Found: 65.31 6.68 11.43

(157) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-2-dimethylamino-ethyl)-phenyl]-3H-imidazol-2-one

(158) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-1-carboxymethyl-ethyl)-phenyl]-imidazolidin-2-one

(159) 1-(4-amidino-phenyl)-3-[3,4-bis-carboxymethyloxy-phenyl]-imidazolidin-2-one

(160) 3-(4-aminomethyl-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one

(161) 1-(4-amino-cyclohexyl)-3-[4-(3-carboxy-propyl)-phenyl]-imidazolidin-2-one

(162) 1-(4-amino-cyclohexyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(163) 1-(4'-aminomethyl-4-biphenylyl)-3-(2-carboxy-ethyl)-imidazolidin-2-one

(164) 1-(4-aminomethyl-3-fluoro-phenyl)-3-[4-(2-carboxy-

ethyl)-phenyl]-imidazolidin-2-one

(165) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-imidazolidin-2-one

(166) 1-(4-aminomethyl-phenyl)-3-[3-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(167) 1-(4-aminomethyl-phenyl)-3-[4-(2-carboxy-1-carboxymethyl-ethyl)-phenyl]-imidazolidin-2-one

(168) 4-(4-aminomethyl-phenyl)-2-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-3-one

(169) 1-[4-(2-amino-ethyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Half concentrated hydrochloric acid was used at ambient temperature.
Melting point: above 250°C
R_f value: 0,57 (Reversed Phase Plate RP8, glacial acetic acid/water = 4:6)

(170) 1-[4-(1-amino-2-methyl-2-propyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(171) 1-[4-[(2-carboxy-ethyl)-aminocarbonyl]-phenyl]-3-(4-piperidinyl)-imidazolidin-2-one

(172) 1-[4-(2-carboxy-ethyl)-phenyl]-3-[4-(dimethylamino-methyl)-phenyl]-imidazolidin-2-one

(173) 1-[4-(2-carboxy-ethyl)-phenyl]-3-[4-(methylamino-methyl)-phenyl]-imidazolidin-2-one

(174) 1-[4-(2-carboxy-ethyl)-phenyl]-3-[4-(n-propylamino-methyl)-phenyl]-imidazolidin-2-one

(175) 2-(4-aminomethyl-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(176) 1-[4-(1-amino-cyclopropyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(177) 1-[4-(1-amino-cyclopentyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

(178) 1-(4-amidino-phenyl)-3-[4-(2-amino-2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
Lithium hydroxide is used
R_f value: 0.07 (silica gel; methylene chloride/methanol/conc. ammonia = 8:4:1)

(179) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-2-hydroxy-ethyl)-phenyl]-3H-imidazol-2-one

(180) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-2-methoxy-ethyl)-phenyl]-3H-imidazol-2-one

(181) 1-[4-(2-amino-ethyl)-phenyl]-3-(4-carboxymethyloxy-phenyl)-imidazolidin-2-one
the hydrochloride of the ethylester was refluxed in water
melting point: above 350°C
R_f value: 0.58 (Reversed Phase Plate RP8; glacial acetic acid/water = 4:6)

(182) 1-[3-(2-amino-ethyl)-phenyl]-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one
melting point: above 250°C
R_f value: 0.42 Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

Calc. x 0.3 H_2O:	C 66.95	H 6.63	N 11.71
Found:	66.64	6.65	11.82

(183) 1-[4-[(2-carboxy-ethyl)-aminocarbonyl]-phenyl]-3-(1-methyl-4-piperidinyl)-imidazolidin-2-one

(184) 1-(4-aminomethyl-cyclohexyl)-3-[4-(2-carboxyl-ethyl)-phenyl]-imidazolidin-2-one

(185) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-2-methyl-propyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(186) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-trifluoromethyl-4H-1,2,4-triazol-3-one

(187) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-phenyl-4H-1,2,4-triazol-3-one

Example 2

1-(4'-Amidino-4-biphenylyl)-3-methoxycarbonylmethyl-imidazolidin-2-one hydrochloride

85 ml of an ice-cooled saturated solution of hydrogen chloride in methanol are added to 3.1 g of 1-(4'-cyano-4-biphenylyl)-3-methoxycarbonylmethyl-imidazolidin-2-one. The resulting suspension is covered with petroleum ether and stirred for 3.5 hours at ambient temperature. The mixture is evaporated to dryness and dried for a further 15 minutes at 1 mbar. The residue is suspended in 80 ml of absolute methanol, 2.7 g of ammonium carbonate are added and the resulting mixture is stirred for 16 hours at ambient temperature. The precipitate is filtered off, the mother liquor is evaporated down and the residue is purified by column chromatography on silica gel (eluant: methylene chloride/methanol/conc. ammonia = 3:1:0.2).

Yield: 0.7 g (20% of theory),

Melting point: above 200°C

R_f value: 0.53 (silica gel; methylene chloride/methanol/conc. ammonia = 3:1:0.2)

The following compounds are obtained analogously:

(1) 1-(4'-amidino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride
A four-fold excess of ammonium chloride is used, refluxing for 6 hours.
Melting point: above 200°C
R_f value: 0.40 (silica gel; methylene chloride/methanol/conc. ammonia = 5:1:0.2)

(2) 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-imidazolidin-2,4-dione hydrochloride
Ethanolic hydrochloric acid is used in the first phase of the reaction. In the reaction with ammonium carbonate, the mixture is heated to 50°C for 4 hours. For purification the evaporation residue is stirred with water.
Melting point: above 200°C
R_f value: 0.50 (silica gel; methylene chloride/methanol = 4:1)

Calc.: x HCl x H_2O:	C 56.18	H 5.61	N 12.48	Cl 7.90
Found:	56.41	5.70	12.29	7.78

(3) 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride
In the first phase of the reaction ethanolic hydrochloric acid is used. In the reaction with ammonium carbonate ethanol is used as solvent.
Melting point: above 200°C
R_f value: 0.27 (silica gel; methylene chloride/methanol conc. ammonia = 3:1:0.2)

Calc. x 1.2 HCl x H_2O:	C 57.30	H 5.77	N 12.73	Cl 9.66
Found:	57.36	5.83	12.38	9.26

(4) 1-(4'-amidino-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3,4,5,6-tetrahydro-1H-pyrimidin-2-one hydrochloride

In the first phase of the reaction ethanolic hydrochloric acid is used. In the reaction with ammonium carbonate the mixture is heated to 50°C for 4 hours. For purification the evaporation residue is stirred with water.

Melting point: 212-215°C

R_f value: 0.47 (silica gel; methylene chloride/methanol conc. ammonia = 3:1:0.2)

Calc. x HCl:	C 61.32	H 6.32	N 13.00	Cl 8.23
Found:	60.71	6.40	12.85	8.04

(5) 1-(4'-amidino-4-biphenylyl)-3-methoxycarbonylmethyl-3,4,5,6-tetrahydro-1H-pyrimidin-2-one hydrochloride

Melting point: above 200°C

R_f value: 0.50 (silica gel; methylene chloride/methanol conc. ammonia = 3:1:0.2)

(6) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

Melting point: from 260°C (decomp.)

The product can also be obtained by reacting 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one with methanolic hydrochloric acid.

R_f value: 0.49 (Reversed Phase Plate RP8; 10% sodium chloride solution/methanol = 4:6)

(7) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4,5,6-tetrahydro-1H-pyrimidin-2-one hydrochloride

R_f value: 0.08 (silica gel; methylene chloride/methanol = 95:5)

(8) 1-[2-(4'-amidino-4-biphenylyl)-ethyl]-3-methoxycarbonylmethyl-3H-benzimidazol-2-one

R_f value: 0.18 (silica gel; methylene chloride/methanol = 8:2)

(9) 1-(4'-amidino-3'-fluoro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(10) 1-(4'-amidino-3'-chloro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(11) 1-(4'-amidino-3-methoxy-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(12) 1-(4'-amidino-3-bromo-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(13) 1-(4'-amidino-3-methylthio-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(14) 1-(4'-amidino-3-methylsulphonyl-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(15) 1-(4'-amidino-2,3-dimethyl-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(16) 1-(4'-amidino-3-nitro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(17) 1-(4'-amidino-3-amino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(18) 1-(3-acetamino-4'-amidino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(19) 1-(4'-amidino-3-benzoylamino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(20) 2-(4'-amidino-4-biphenylyl)-5-(2-methoxycarbonyl-ethyl)-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide hydrochloride
Melting point: 243-245°C

R_f value: 0.43 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(21) 1-[4-(4-amidino-phenyl)-cyclohexyl]-3-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride

(22) 1-[4-(4-amidino-phenyl)-cyclohexyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(23) 1-[1-(4-amidino-phenyl)-4-piperidinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(24) 1-[4-(5-amidino-2-pyridyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(25) 1-[4-(5-amidino-2-pyrazinyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(26) 1-[4-(5-amidino-2-pyrimidinyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(27) 1-[6-(4-amidino-phenyl)-3-pyridazinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride
Melting point: 303-305°C (decomp., sintering from 240°C)
R_f value: 0.42 (silica gel; methylene chloride/methanol/conc. ammonia = 8:2:0.1)

(28) 1-[2-(4-amidino-phenyl)-5-pyrimidinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(29) 1-[2-(4'-amidino-biphenylyl)-ethyl]-3-methoxycarbonylmethyl-imidazolidin-2-one hydrochloride

(30) 1-(4-amidino-3-fluoro-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(31) 1-(4-amidino-3-chloro-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(32) 1-(4-amidino-2-methylthio-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(33) 1-(4-amidino-2-methylsulphonyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(34) 1-(4-amidino-2-methyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride
Melting point: 143-146°C
R_f value: 0.37 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(35) 1-(4-amidino-2-methoxy-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(36) 1-(4-amidino-phenyl)-3-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(37) 1-(4-amidino-phenyl)-3-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(38) 1-(4-amidino-phenyl)-3-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(39) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-imidazolidin-2-one hydrochloride

(40) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-imidazolidin-2-one hydrochloride

(41) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methylsulphonyl-phenyl]-imidazolidin-2-one hydrochloride

(42) 1-(4-amidino-phenyl)-3-[5-(2-methoxycarbonyl-ethyl)-2-pyridyl]-imidazolidin-2-one hydrochloride

(43) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one hydrochloride
Melting point: above 200°C
R_f value: 0.44 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(44) 1-(4-amidino-phenyl)-3-(4-methoxycarbonyl-methyloxy-phenyl)-imidazolidin-2-one hydrochloride

(45) 1-(4-amidino-phenyl)-3-(4-methoxycarbonyl-methylthio-phenyl)-imidazolidin-2-one
Melting point: from 197°C (decomp.)
R_f value: 0.25 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(46) 1-(4-amidino-phenyl)-3-(4-methoxycarbonyl-methylsulphonyl-phenyl)-imidazolidin-2-one hydrochloride
Melting point: from 249°C (decomp.)
R_f value: 0.43 (Silica gel; methylene chloride/methanol = 8:2)

(47) 1-(4-amidino-phenyl)-3-[4-(3-methoxycarbonyl-2-methyl-2-propyl)-phenyl]-imidazolidin-2-one hydrochloride
Melting point: 228-236°C (decomp.)
R_f value: 0.19 (Silica gel; methylene chloride/methanol

= 9:1)

(48) 1-(4-amidino-phenyl)-3-[2-(4-methoxycarbonyl-phenyl)-ethyl]-imidazolidin-2-one
Melting point: 226-228°C (decomp.)
R_f value: 0.40 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(49) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-imidazolidin-2-one hydrochloride

(50) 1-(5-amidino-2-pridyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

(51) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-thione hydrochloride

(52) 1-(4-amidino-phenyl)-2-imino-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidine hydrochloride

(53) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,4-dione hydrochloride
Melting point: above 260°C
R_f value: 0.19 (silica gel; methylene chloride/methanol = 9:1)

Calc.:	C 57.62	H 5.08	N 13.44	Cl 8.50
Found:	56.94	5.03	13.33	8.99

(54) 3-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,4-dione hydrochloride

(55) 1-(4-amidino-phenyl)-4,4-dimethyl-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,5-dione hydrochloride

(56) 3-(4-amidino-phenyl)-4,4-dimethyl-1-[4-(2-

methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,5-dione hydrochloride

(57) 2-(4-amidino-phenyl)-5-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide hydrochloride
Melting point: 245-248°C (decomp.)
R_f value: 0.44 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(58) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride
Melting point: 240°C (decomp., sintering from 208°C)
R_f value: 0.33 (silica gel; methylene chloride/methanol = 5:1)

(59) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-2-methylimino-imidazolidine hydrochloride

(60) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-2-phenylimino-imidazolidine hydrochloride

(61) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-2-(3-pyridyl-imino)-imidazolidine hydrochloride

(62) 3-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-trifluoromethyl-3H-imidazol-2-one hydrochloride

(63) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-phenyl-3H-imidazol-2-one hydrochloride

(64) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-phenyl-3H-imidazolidin-2-one hydrochloride

(65) 1-[(4-amidino-phenyl)-carbonylmethyl]-3-(3-methoxycarbonyl-propyl)-imidazolidin-2-one hydrochloride

(66) 1-[2-(4-amidino-phenyl)-ethyl]-3-(3-methoxycarbonyl-propyl)-imidazolidin-2-one hydrochloride

(67) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-5-one hydrochloride

(68) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-4H-1,2,4-triazol-5-one hydrochloride

(69) 3-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-5-one hydrochloride

(70) 3-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-4H-1,2,4-triazol-5-one hydrochloride.

(71) 1-(4-amidino-phenyl)-3-(4-methoxycarbonyl-butyl)-imidazolidin-2-one hydrochloride
R_f value: 0.72 (silica gel; methylene chloride/methanol = 2:1)

(72) 1-(4-amidino-phenyl)-3-(2-methoxycarbonylthio-ethyl)-imidazolidin-2-one hydrochloride

(73) 1-(4-amidino-phenyl)-3-(2-methoxycarbonyl-methylsulphonyl-ethyl)-imidazolidin-2-one hydrochloride

(74) 1-(4-amidino-phenyl)-3-(2-methoxycarbonyloxy-ethyl)-imidazolidin-2-one hydrochloride

(75) 1-(4-amidino-phenyl)-3-(2-methoxycarbonyl-methylamino-ethyl)-imidazolidin-2-one hydrochloride-acetate

Melting point: 197°C (decomp., sintering from 172°C)
R_f value: 0.44 (silica gel; methylene chloride/methanol/conc. ammonia = 8:2:0.1, developing twice)

(76) 1-[2-(N-acetyl-N-methoxycarbonylmethyl-amino)-ethyl]-3-(4-amidino-phenyl)-imidazolidin-2-one hydrochloride

(77) 1-(4-amidino-phenyl)-3-[2-(N-benzoyl-N-methoxycarbonylmethyl-amino)-ethyl]-imidazolidin-2-one hydrochloride

(78) 1-(4-amidino-phenyl)-3-[1-(2-methoxycarbonyl-ethyl)-2-oxo-1H-4-pyridyl]-imidazolidin-2-one hydrochloride

(79) 1-(4'-amidino-3-methanesulphonylamino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride

(80) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride

(81) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-one hydrochloride
Melting point: 242-246°C (decomp.)
R_f value: 0.50 (silica gel; methylene chloride/methanol = 4:1)

(82) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one hydrochloride

(83) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-thione hydrochloride

(84) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-

ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione hydrochloride

(85) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-thione hydrochloride

(86) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one hydrochloride

(87) 4-(4-amidino-phenyl)-3,5-dimethyl-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride

(88) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one hydrochloride

(89) 4-(4'-amidino-4-biphenylyl)-3,5-dimethyl-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride

(90) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-5-methyl-3-phenyl-3H-imidazol-2-one hydrochloride

(91) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-5-methyl-3H-imidazol-2-one hydrochloride

(92) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride

(93) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-one hydrochloride

(94) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one hydrochloride

(95) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-

ethyl)-phenyl]-3H-imidazol-2-thione hydrochloride

(96) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione hydrochloride

(97) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-thione hydrochloride

(98) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one hydrochloride

(99) 1-(4-amidino-phenyl)-3,5-dimethyl-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride

(100) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one hydrochloride

(101) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-thione hydrochloride

(102) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-methyl-3H-imidazol-2-thione hydrochloride

(103) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-phenyl-3H-imidazol-2-thione hydrochloride

(104) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride
Melting point: 278-282°C (decomp.)
R_f value: 0.30 (silica gel; methylene chloride/methanol = 4:1)

(105) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-

ethyl)-3-methyl-3H-imidazol-2-one hydrochloride
Melting point: 258-260°C (decomp.)
R_f value: 0.56 (silica gel; methylene chloride/ethanol = 4:1)

(106) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-phenyl-3H-imidazol-2-one hydrochloride
Melting point: 250-253°C
R_f value: 0.55 (silica gel; methylene chloride/ethanol = 4:1)

(107) 1-(4-amidino-phenyl)-3-[4-(3-methoxycarbonyl-propyl)-phenyl]-imidazolidin-2-one hydrochloride

(108) 1-(4-amidino-phenyl)-3-[1-(2-methoxycarbonyl-ethyl)-4-piperidinyl]-imidazolidin-2-one hydrochloride

(109) 2-(4-amidino-4'-biphenylyl)-4-(2-methoxycarbonyl-ethyl)-4H-1,2,4-triazol-3-one hydrochloride

(110) 2-(4-amidino-4'-biphenylyl)-4-(2-methoxycarbonyl-ethyl)-5-methyl-4H-1,2,4-triazol-3-one hydrochloride

(111) 4-(4-amidino-4'-biphenylyl)-2-(2-methoxycarbonyl-ethyl)-4H-1,2,4-triazol-3-one hydrochloride

(112) 4-(4-amidino-4'-biphenylyl)-2-(2-methoxycarbonyl-ethyl)-5-methyl-4H-1,2,4-triazol-3-one hydrochloride

(113) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-(4-methyl-amidino-phenyl)-imidazolidin-2-one
The iminoester is taken up in absolute methanol and reacted with a 20-fold excess of a methanolic methylamine solution

(114) 1-(4-n-butylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

Prepared analogously to (113) with n-butylamine

(115) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one hydrochloride
Melting point: 248°C (decomp.)
R_f value: 0.40 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(116) 3-(4-amidino-phenyl)-1-(4-methoxycarbonyl-butyl)-3H-imidazo[4,5-b]pyridin-2-one dihydrochloride
R_f value: 0.34 (silica gel; methylene chloride/methanol = 19:1)

(117) 4-(4-amidino-phenyl)-2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one hydrochloride
Melting point: 273-275°C
R_f value: 0.55 (silica gel; methylene chloride/methanol = 4:1)

(118) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one hydrochloride
Melting point: 272-274°C
R_f value: 0.37 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(119) 2-(4-amidino-phenyl)-5-ethyl-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one hydrochloride
Melting point: above 250°C
R_f value: 0.36 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

Calc. x HCl:	C 58.67	H 5.63	N 16.29	Cl 8.25
Found:	58.01	5.65	16.26	9.14

(120) 3-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-

ethyl)-3H-imidazo[4,5-b]pyridin-2-one-hydrochloride
R_f value: 0.61 (silica gel; methylene chloride/methanol = 8:2)

(121) 1-(4-amidino-phenyl)-3-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride
Prepared from 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one, whilst the iminoester formed as an intermediate product is obtained by reacting with ethanolic hydrochloric acid.
R_f value: 0.54 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(122) 3-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one hydrochloride-hydrate
Melting point: 95-100°C
R_f value: 0.57 (silica gel; methylene chloride/methanol = 4:1)

(123) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one hydrochloride
Melting point: 275-277°C
R_f value: 0.55 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(124) 4-(amidino-phenyl)-2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one hydrochloride
Melting point: 289-291°C (decomp.)
R_f value: 0.49 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(125) 1-[1-(4-amidino-phenyl)-4-piperidinyl]-3-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one hydrochloride
Melting point: above 275°C
R_f value: 0.53 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(126) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-3H-imidazol-2-one hydrochloride
Melting point: 253-264°C
R_f value: 0.28 (Reversed Phase Plate RP8; methanol/10% sodium chloride solution = 6:4)

(127) 1-(4-amidino-phenyl)-3-[4-(2-dibenzylamino-2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride
R_f value: 0.37 (silica gel; methylene chloride/methanol/conc. ammonia = 4:1:0.25)

(128) 1-(4-amidino-phenyl)-3-[4-(2-amino-2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one dihydrochloride
R_f value: 0.18 (silica gel; methylene chloride/methanol/conc. ammonia = 16:4:1)

(129) 1-(4-amidino-phenyl)-3-[4-(2-dimethylamino-2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(130) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-1-methoxycarbonylmethyl-ethyl)-phenyl]-imidazolidin-2-one

(131) 1-(4-amidino-phenyl)-3-(3,4-bis-methoxycarbonyl-methyloxy-phenyl)-imidazolidin-2-one

(132) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl-phenyl]-4-methyl-imidazolidin-2-one

(133) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-2-methyl-propyl)-phenyl]-imidazolidin-2-one

(134) 1-(4-amidino-phenyl)-3-[4-(2-phosphono-ethyl)-phenyl]-imidazolidin-2-one

(135) 1-(4-amidino-phenyl)-3-[4-[2-(O-methyl-phosphono)-

ethyl]-phenyl]-imidazolidin-2-one

(136) 1-(4-amidino-phenyl)-3-[4-[2-(5-tetrazolyl)-ethyl]-phenyl]-imidazolidin-2-one

(137) 1-(4-amidino-phenyl)-3-[4-(2-hydroxy-2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(138) 1-(4-amidino-phenyl)-3-[4-(2-methoxy-2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(139) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-2-methylpropyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(140) 2-(4-amidino-phenyl)-4-[4-(2-phosphono-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(141) 2-(4-amidino-phenyl)-4-[4-[2-(O-methoxy-phosphono)-ethyl]-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(142) 2-(4-amidino-phenyl)-4-[4-[2-methoxycarbonyl-ethyl]-phenyl]-5-trifluoromethyl-4H-1,2,4-triazol-3-one

(143) 2-(4-amidino-phenyl)-4-[4-[2-methoxycarbonyl-ethyl]-phenyl]-5-phenyl-4H-1,2,4-triazol-3-one

(144) 2-(4-amidino-phenyl)-4-[4-[2-(5-tetrazolyl)-ethyl]-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

Example 3

1-(4'-Amidino-3-methylsulphinyl-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

---

Prepared from 1-(4'-amidino-3-methylthio-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one by oxidation with bromine in glacial acetic acid in the

presence of sodium acetate at ambient temperature.

The following compounds are obtained analogously:

(1) 1-(4-amidino-2-methylsulphinyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(2) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methylsulphinyl-phenyl]-imidazolidin-2-one

(3) 1-(4-amidino-phenyl)-3-(2-methoxycarbonylmethyl-sulphinyl-ethyl)-imidazolidin-2-one

Example 4

1-(4-Cyano-phenyl)-3-[2-(4-methoxycarbonyl-phenyl)-ethyl]-imidazolidin-2-one

---

8.1 g of 1-(4-cyano-phenyl)-3-[2-(4-methoxycarbonyl-phenyl)-ethyl]-3H-imidazol-2-one are dissolved in 750 ml of ethyl acetate and treated with hydrogen under 5 bar in the presence of 2 g of 10% palladium/charcoal for 2.5 hours at 50°C. The catalyst is filtered off, the filtrate is evaporated down to about 100 ml, 100 ml of tert.butylmethylether are added, the resulting mixture is cooled in an ice/acetone bath and the precipitate formed is filtered off then washed with tert.-butylmethylether.
Yield: 6.4 g (79% of theory),
Melting point: 194-197°C
R_f value: 0.63 (silica gel; methylene chloride/ethyl acetate/cyclohexane = 3:1:1)

The following compounds are obtained analogously:

(1) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(2) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-imidazolidin-2-one

(3) 4-(4-amidino-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-imidazolidin-2-one

(4) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]imidazolidin-2-one

(5) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-imidazolidin-2-one

(6) 1-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-imidazolidin-2-one

(7) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(8) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-methyl-imidazolidin-2-one

(9) 4-(4'-amidino-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-phenyl-imidazolidin-2-one hydrochloride
The hydrochloride of the free acid is used as starting material and is reduced in methanol at ambient temperature.
Melting point: 225-235°C (decomp.)

(10) 1-[4-(4-amidino-phenyl)-cyclohexyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(11) 1-[1-(4-amidino-phenyl)-4-piperidinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one hydrochloride
Dilute methanolic hydrochloric acid is used and the work is done at ambient temperature.
R_f value: 0.47 (Reversed Phase Plate; methanol/10% sodium chloride solution = 6:4)

(12) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride
Melting point: 160-162°C
R_f value: 0.59 (silica gel; cyclohexane/ethyl acetate = 3:7)

(13) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-phenyl-imidazolidin-2-one hydrochloride
The work is done in ethanol at ambient temperature.
Melting point: 236-240°C

(14) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-3-methyl-imidazolidin-2-one hydrochloride
The work is done in ethanol at ambient temperature.
R_f value: 0.55 (Reversed Phase Plate RP18; methanol/5% sodium chloride solution = 6:4)

(15) 4-(4'-amidino-4-biphenylyl)-1-(2-carboxy-ethyl)-imidazolidin-2-one hydrochloride
The work is done in ethanol at ambient temperature.
R_f value: 0.61 (Reversed Phase Plate RP18; methanol/5% sodium chloride solution = 6:4)

(16) 4-(4-amidino-phenyl)-1-[4-(2-carboxy-ethyl)-phenyl]-3-methyl-imidazolidin-2-one hydrochloride
The work is done in dioxane/water (= 1:1).
Melting point: 208-210°C

(17) 1-(4-amidino-phenyl)-3-[4-(2-amino-2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one dihydrochloride
The work is done in methanol at ambient temperature.
R_f value: 0.37 (silica gel; methylene chloride/methanol/conc. ammonia = 8:4:1)

(18) 1-(4-amidino-phenyl)-3-[4-(2-amino-2-carboxy-ethyl)-phenyl]-imidazolidin-2-one

Melting point: 295°C (decomp.)
R_f value: 0.07 (silica gel; methylene chloride/methanol/conc. ammonia = 8:4:1)

Example 5

1-(4-Ethoxycarbonylamidino-phenyl)-3-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

At ambient temperature, 10 ml of 0.2N sodium hydroxide solution are added dropwise, with vigorous stirring, to a mixture of 0.3 g of 1-(4-amidino-phenyl)-3-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one hydrochloride, 0.07 ml of ethyl chloroformate and 40 ml of methylene chloride. After stirring for 0.5 hours at ambient temperature the methylene chloride phase is separated off and evaporated to dryness.
Yield: 0.29 g (90% of theory),
R_f value: 0.48 (silica gel; methylene chloride/methanol = 15:1)

Calc.:	C 63.99	H 5.82	N 12.44
Found:	64.11	5.98	12.35

The following compounds are obtained analogously:

(1) 1-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 260°C
R_f value: 0.73 (silica gel; methylene chloride/methanol = 95:5)

(2) 1-(4-benzyloxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(3) 1-(4-isopropylcarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(4) 1-(4-isobutyloxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(5) 1-(4-ethoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(6) 4-(4-methoxycarbonylamidino-phenyl)-2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: 296-298°C
R_f value: 0.46 (silica gel; methylene chloride/methanol = 15:1)

(7) 4-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-2-(4-methoxycarbonylamidino-phenyl)-5-methyl-4H-1,2,4-triazol-3-one
Melting point: 175-188°C (decomp.)
R_f value: 0.28 (silica gel; methylene chloride/methanol = 95:5)

(8) 1-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one
Melting point: above 260°C
R_f value: 0.27 (silica gel; methylene chloride/methanol = 95:5)

Calc.:	C 62.55	H 5.25	N 13.26
Found:	62.24	5.33	13.45

(9) 1-(4-ethoxycarbonylamidino-phenyl)-3-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 335°C
R_f value: 0.49 (silica gel; methylene chloride/methanol = 15:1)

(10) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one
Melting point: 211-213°C (decomp.)

R_f value: 0.54 (silica gel; methylene chloride/methanol = 15:1)

(11) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: above 340°C
R_f value: 0.45 (silica gel; methylene chloride/methanol = 15:1)

(12) 1-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one
R_f value: 0.29 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(13) 1-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,4-dione
Melting point: 250°C (decomp., sintering from 198°C)
R_f value: 0.45 (silica gel; ethyl acetate)
Calc.: C 60.27 H 5.06 N 12.78
Found: 60.18 5.12 12.82

(14) 1-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one
Melting point: 212-213°C
R_f value: 0.58 (silica gel; methylene chloride/methanol = 9:1)

(15) 1-(4-ethoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one
Melting point: 198-199°C
R_f value: 0.58 (silica gel; methylene chloride/methanol = 9:1)

(16) 2-(4-methoxycarbonylamidino-phenyl)-5-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-

thiadiazole-1,1-dioxide
Melting point: above 275°C
R_f value: 0.23 (silica gel; methylene chloride/methanol = 100:3)

(17) 2-(4-ethoxycarbonylamidino-phenyl)-5-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide
Melting point: above 275°C
R_f value: 0.22 (silica gel; methylene chloride/methanol = 100:3)

(18) 4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-2-(4-methoxycarbonylamidino-phenyl)-5-methyl-4H-1,2,4-triazol-3-one
Melting point: 200-201°C
R_f value: 0.43 (silica gel; methylene chloride/methanol = 95:5)
Calc.: C 62.62 H 6.09 N 14.60
Found: 62.77 6.20 14.88

Example 6

1-(4-Amidino-phenyl)-3-[4-(2-butyloxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

---

Prepared from 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride by stirring with saturated butanolic hydrochloric acid for three days at ambient temperature.

The following compound is obtained analogously:

(1) 1-(4-amidino-phenyl)-3-[4-[2-(2-phenyl-ethyloxycarbonyl)-ethyl]-phenyl]-imidazolidin-2-one hydrochloride

Example 7

1-(1-Amidino-4-piperidinyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

Prepared from 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-(4-piperidinyl)-imidazolidin-2-one and S-ethylisothiourea-hydrobromide by heating to 100°C for four hours in dimethylformamide in the presence of sodium carbonate.

Example 8

1-(4-Aminomethyl-phenyl)-3-(4-methoxycarbonylmethyloxy-phenyl)-imidazolidin-2-one hydrochloride

2 g of 1-(4-cyano-phenyl)-3-(4-methoxycarbonylmethyloxy-phenyl)-imidazolidin-2-one are treated with 5 bars of hydrogen for 2.5 hours at ambient temperature in a mixture of 40 ml of methanol and 4 ml of methanolic hydrochloric acid in the presence of 0.5 g of 10% palladium/charcoal. 200 ml of methanol and 50 ml of water are added and the mixture is filtered while hot. The product crystallises out on cooling.
Yield: 1.38 g (62% of theory),
Melting point: above 250°C
R_f value: 0.40 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

Calc. x HCl:	C 58.24	H 5.66	N 10.72	Cl 9.05
Found:	58.04	5.65	10.92	9.57

The following compounds are obtained analogously:

(1) 1-(4-aminomethyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4,5,6-tetrahydro-1H-pyrimidin-2-one hydrochloride
Melting point: 272-274°C (decomp.)

R_f value: 0.30 (silica gel; toluene/dioxane/methanol/conc. ammonia = 2:5:2.1)

(2) 1-(4-aminomethyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride
Melting point: above 250°C
R_f value: 0.47 (silica gel; toluene/dioxane/methanol/conc. ammonia = 4:10:4:1)

Calc. x HCl:	C 61.61	H 6.20	N 10.78	Cl 9.09
Found:	61.30	6.29	10.88	9.12

(3) 1-[4-(2-amino-2-methoxycarbonyl-ethyl)-phenyl]-3-(4-aminomethyl-phenyl)-imidazolidin-2-one dihydrochloride
R_f value: 0.66 (silica gel; methylene chloride/methanol/conc. ammonia = 16:4:1)

(4) 1-[4-(2-amino-ethyl)-phenyl]-3-(4-methoxycarbonyl-methyl-phenyl)-imidazolidin-2-one
The work is done at 40°C
Melting point: above 250°C
R_f value: 0.31 (silica gel; toluene/dioxane/methanol/conc. ammonia = 4:10:4:1)

(5) 1-(4-aminomethyl-2-methyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 275°C
R_f value: 0.38 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(6) 3-(4-aminomethyl-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one

(7) 1-(4'-aminomethyl-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(8) 1-(4-aminomethyl-3-fluoro-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(9) 1-(4-aminomethyl-phenyl)-3-[3-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(10) 1-(4-aminomethyl-phenyl)-3-[4-(2-methoxycarbonyl-1-methoxycarbonylmethyl-ethyl)-phenyl]-imidazolidin-2-one

(11) 4-(4-aminomethyl-phenyl)-2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one

(12) 1-[4-(2-amino-ethyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: above 200°C
R_f value: 0.63 (Reversed Phase Plate RP8; glacial acetic acid/water = 1:1)

(13) 1-[4-(1-amino-2-methyl-2-propyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(14) 2-(4-aminomethyl-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

(15) 1-[4-(2-amino-ethyl)-phenyl]-3-(4-methoxycarbonyl-methyloxy-phenyl)-imidazolidin-2-one

(16) 1-[3-(2-amino-ethyl)-phenyl]-3-(4-methoxycarbonyl-ethyl)-phenyl)-imidazolidin-2-one-hydrochloride
The starting 1-(3-cyanomethyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one was reduced in a mixture of 50 ml of dioxane, 10 ml of methanol and 1 ml of methanolic hydrochloric acid
melting point: above 260°C
R_f value: 0.29 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(17) 1-(4-aminomethyl-cyclohexyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

Example 9

1-[2-(4-Amidino-phenyl)-2-hydroxy-ethyl]-3-(3-methoxycarbonyl-propyl)-imidazolidin-2-one

---

Prepared by reduction of 1-[(4-amidino-phenyl)-carbonylmethyl]-3-(3-methoxycarbonyl-propyl)-imidazolidin-2-one hydrochloride with sodium borohydride in methanol at 0-5°C.

Example 10

1-(3-Guanidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

---

Prepared from 1-(3-amino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride by refluxing for three hours with cyanamide in dioxane.

Example 11

1-(4'-Cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

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2 g of 1-(2-carboxy-ethyl)-3-(4'-cyano-4-biphenylyl)-imidazolidin-2-one are suspended in 150 ml of methanol, 6 ml of concentrated methanolic hydrochloric acid are added and the mixture is stirred for 16 hours at ambient temperature. The precipitate is filtered off and purified by column chromatography on silica gel (eluant: methylene chloride/ethyl acetate = 9:1).
Yield: 0.5 g (23% of theory),
Melting point: 150-155°C
R_f value: 0.50 (silica gel; methylene chloride/ethyl acetate = 9:1)

The following compounds are obtained analogously:

(1) 1-(4'-cyano-3'-fluoro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(2) 1-(3'-chloro-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(3) 1-(4'-cyano-3-methoxy-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(4) 1-(4'-cyano-3-methylthio-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(5) 1-(4'-cyano-2,3-dimethyl-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(6) 1-[4-(5-cyano-2-pyridyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(7) 1-[4-(5-cyano-2-pyrazinyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(8) 1-[4-(5-cyano-2-pyrimidinyl)-phenyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(9) 1-[6-(4-cyano-phenyl)-3-pyridazinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(10) 1-[2-(4-cyano-phenyl)-5-pyrimidinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(11) 2-(4-amidino-phenyl)-4-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one hydrochloride
Isopropanolic hydrochloric acid is used
Melting point: 255-257°C
R_f value: 0.33 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)

(12) 2-(4-amidino-phenyl)-4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one hydrochloride
Melting point: above 250°C
R_f value: 0.22 (Reversed Phase Plate RP8; methanol/5% sodium chloride solution = 6:4)
Calc. x HCl: C 60.32 H 6.16 N 15.29 Cl 7.74
Found: 60.19 H 6.28 N 15.37 Cl 7.78

(13) 2-(4-amidino-phenyl)-5-ethyl-4-[4-(2-isopropyloxy-carbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: above 250°C
R_f value: 0.27 (Reversed Phase Plate, RP8; methanol/5% sodium chloride solution = 6:4)

(14) 1-(4-amidino-phenyl)-3-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one
Melting point: 246-249°C
R_f value: 0.34 (Reversed Phase Plate, RP8; methanol/5% sodium chloride solution = 6:4)

(15) 4-(4-amidino-phenyl)-2-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one

(16) 1-(4-amidino-phenyl)-3-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(17) 1-(4-amidino-phenyl)-3-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one
Melting point: above 250°C
R_f value: 0.28 (Reversed Phase Plate, RP8; methanol/5% sodium chloride solution = 6:4)

(18) 1-(4-amidino-phenyl)-3-[4-(2-isopropyloxycarbonyl-ethyl)-phenyl]-imidazolidin-2,4-dione
Melting point: above 250°C
R_f value: 0.37 (Reversed Phase Plate, RP8; methanol/

5% sodium chloride solution = 6:4)

Example 12

1-(2-Carboxy-ethyl)-3-(4'-cyano-4-biphenylyl)-imidazolidin-2-one

---

3.4 g of 1-(3-buten-1-yl)-3-(4'-cyano-4-biphenylyl)-imidazolidin-2-one are dissolved in a mixture of 20 ml of methylene chloride and 20 ml of acetonitrile and 25 mg of ruthenium trichloride trihydrate are added. A mixture of 16 g of sodium metaperiodate and 65 ml of water is added and stirred for 2.5 hours. Then 100 ml of methylene chloride and 20 ml of water are added, the phases are separated and the aqueous phase is washed several times with methylene chloride. The combined organic phases are evaporated down and the powdery residue is used as it is without any further purification.

Yield: 2 g (56% of theory),

R_f value: 0.12 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compounds are obtained analogously:

(1) 1-(2-carboxy-ethyl)-3-(4'-cyano-3'-fluoro-4-biphenylyl)-imidazolidin-2-one

(2) 1-(2-carboxy-ethyl)-3-(3'-chloro-4'-cyano-4-biphenylyl)-imidazolidin-2-one

(3) 1-(2-carboxy-ethyl)-3-(4'-cyano-3-methoxy-4-biphenylyl)-imidazolidin-2-one

(4) 1-(2-carboxy-ethyl)-3-(4'-cyano-3-methylthio-4-biphenylyl)-imidazolidin-2-one

(5) 1-(2-carboxy-ethyl)-3-(4'-cyano-2,3-dimethyl-4-biphenylyl)-imidazolidin-2-one

(6) 1-(2-carboxy-ethyl)-3-[4-(5-cyano-2-pyridyl)-phenyl]-imidazolidin-2-one

(7) 1-(2-carboxy-ethyl)-3-[4-(5-cyano-2-pyrazinyl)-phenyl]-imidazolidin-2-one

(8) 1-(2-carboxy-ethyl)-3-[4-(5-cyano-2-pyrimidinyl)-phenyl]-imidazolidin-2-one

(9) 1-(2-carboxy-ethyl)-3-[6-(4-cyano-phenyl)-3-pyridazinyl]-imidazolidin-2-one

(10) 1-(2-carboxy-ethyl)-3-[2-(4-cyano-phenyl)-5-pyrimidinyl]-imidazolidin-2-one

Example 13

1-(4'-Cyano-4-biphenylyl)-3-methoxycarbonylmethyl-imidazolidin-2-one

4 g of 1-(4'-cyano-4-biphenylyl)-imidazolidin-2-one are dissolved at 50°C in 150 ml of dimethylformamide and 0.73 g of a 95% suspension of sodium hydride in oil is added in batches thereto. The mixture is allowed to cool to ambient temperature, then a solution of 1.7 ml of methyl bromoacetate in 15 ml of dimethylformamide is added dropwise thereto and the mixture is stirred for 64 hours at ambient temperature. The reaction mixture is poured onto 300 ml of water. The precipitate formed is purified by column chromatography (silica gel; methylene chloride/ethyl acetate = 9:1).
Yield: 3.2 g (63% of theory),
R_f value: 0.54 (silica gel; cyclohexane/ethyl acetate = 1:2)

The following compounds are obtained analogously:

(1) 1-(4'-cyano-4-biphenylyl)-3-methoxycarbonylmethyl-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Melting point: 145-150°C
R_f value: 0.28 (silica gel; cyclohexane/ethyl acetate = 1:2)

(2) 1-[2-(4'-cyano-4-biphenylyl)-ethyl]-3-methoxycarbonylmethyl-3H-benzimidazol-2-one
Potassium tert.butoxide is used as base. The 4-cyano-4'-(2-iodoethyl)-biphenyl used is obtained from 4-(2-bromoethyl)-4'-cyano-biphenyl by reacting with sodium iodide in acetone at ambient temperature.
R_f value: 0.89 (silica gel; methylene chloride/methanol = 95:5)

(3) 1-[2-(4'-cyano-4-biphenylyl)-ethyl]-3-methoxycarbonylmethyl-imidazolidin-2-one

(4) 2-(4'-cyano-4-biphenylyl)-5-(2-ethoxycarbonyl-ethyl)-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide
The work is done in dimethylformamide with potassium tert.butoxide and 1-bromo-2-chloro-ethane as alkylating agents
Melting point: 183-185°C

(5) 1-(4-cyano-phenyl)-3-(4-ethoxycarbonyl-butyl)-imidazolidin-2-one
R_f value: 0.62 (silica gel; cyclohexane/ethyl acetate = 1:3)

(6) 3-(4-cyano-phenyl)-1-(4-ethoxycarbonyl-butyl)-3H-imidazo[4,5-b]pyridin-2-one
R_f value: 0.78 (silica gel; methylene chloride/methanol = 9:1)

Example 14

1-(4'-Cyano-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3,4,5,6-tetrahydro-1H-pyrimidin-2-one

---

1.9 g of N-(4'-cyano-4-biphenylyl)-N-(3-methanesulphonyloxy-propyl)-N'-(2-ethoxycarbonyl-ethyl)-urea are dissolved in 2 ml of dimethylformamide, 0.18 g of a 55% suspension of sodium hydride in oil is added thereto at ambient temperature and the mixture is stirred at ambient temperature for 2 hours. 20 ml of water are added and the precipitate formed is purified by column chromatography (silica gel; ethyl acetate).
Yield: 1.0 g (64% of theory),
Melting point: 137-138°C
R_f value: 0.57 (silica gel; cyclohexane/ethyl acetate = 1:5)

The following compounds are obtained analogously:

(1) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one
Melting point: 160-162.5°C
R_f value: 0.59 (silica gel; cyclohexane/ethyl acetate = 3:7)

(2) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4,5,6-tetrahydro-1H-pyrimidin-2-one
Melting point: 149-152°C
R_f value: 0.25 (silica gel; cyclohexane/ethyl acetate = 1:1)

(3) 1-(4-cyano-3-fluoro-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(4) 1-(3-chloro-4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(5) 1-(4-cyano-2-methylthio-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(6) 1-(4-cyano-2-methyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(7) 1-(4-cyano-2-methoxy-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(8) 1-(4-cyano-phenyl)-3-[2-fluoro-4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(9) 1-[2-chloro-4-(2-methoxycarbonyl-ethyl)-phenyl]-3-(4-cyano-phenyl)-imidazolidin-2-one

(10) 1-(4-cyano-phenyl)-3-[2-methoxy-4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(11) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methyl-phenyl]-imidazolidin-2-one

(12) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methylthio-phenyl]-imidazolidin-2-one

(13) 1-(4-cyano-phenyl)-3-[5-(2-methoxycarbonyl-ethyl)-2-pyridyl]-imidazolidin-2-one

(14) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one

(15) 1-(4-cyano-phenyl)-3-(4-methoxycarbonylmethyloxy-phenyl)-imidazolidin-2-one

(16) 1-(4-tert.butyloxycarbonylmethylthio-phenyl)-3-(4-cyano-phenyl)-imidazolidin-2-one
Melting point: 169-171°C

(17) 1-(4-cyano-phenyl)-3-[4-(3-methoxycarbonyl-2-methyl-2-propyl)-phenyl]-imidazolidin-2-one
Sodium iodide is added and potassium tert.butoxide is used as base.
Melting point: 177-179°C

(18) 1-(4-cyano-phenyl)-3-[2-(4-ethoxycarbonyl-phenyl)-ethyl]-imidazolidin-2-one

(19) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-imidazolidin-2-one

(20) 1-(5-cyano-2-pyridyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(21) 1-(4-cyano-phenyl)-3-[4-(3-methoxycarbonyl-propyl)-phenyl]-imidazolidin-2-one

(22) 1-(4-cyanomethyl-phenyl)-3-(4-methoxycarbonyl-methyl)-phenyl]-imidazolidin-2-one
The iodide [R_f value: 0.66 (silica gel; cyclohexane/ethyl acetate = 3:7)] obtained from the corresponding mesylate is used.
Melting point: 157-160°C
R_f value: 0.30 (silica gel; cyclohexane/ethyl acetate = 4:6)

Example 15

1-(4'-Cyano-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-3H-imidazol-2-one

A mixture of 2.8 g of N-(4'-cyano-4-biphenylyl)-N-(2,2-diethoxy-ethyl)-N'-(2-ethoxycarbonyl-ethyl)-urea, 2.8 ml of 2N hydrochloric acid and 28 ml of ethanol is refluxed for 45 minutes. The reaction mixture is cooled to 0°C, the product precipitated is suction filtered and washed

with ethanol at 0°C.
Yield: 1.4 g (63% of theory),
Melting point: 140-142°C
R_f value: 0.40 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compounds are obtained analogously:

(1) 1-[4-(4-cyano-phenyl)-cyclohexyl]-3-(2-ethoxycarbonyl-ethyl)-3H-imidazol-2-one

(2) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one
The work is done with methanolic hydrochloric acid.
Melting point: 153-155°C

(3) 1-(4-cyano-phenyl)-3-[2-(4-methoxycarbonyl-phenyl)-ethyl]-3H-imidazol-2-one
Melting point: 181-183°C

(4) 1-[1-(4-cyano-phenyl)-4-piperidinyl]-3-(2-ethoxycarbonyl-ethyl)-3H-imidazol-2-one
Melting point: 153-155°C

(5) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethenyl)-phenyl]-3H-imidazol-2-one
Melting point: 210-212°C
R_f value: 0.76 (silica gel; methylene chloride/ethyl acetate = 9:1)

(6) 1-(4-cyano-phenyl)-3-[4-(2-dibenzylamino-2-methoxy-carbonyl-ethyl)-phenyl]-3H-imidazol-2-one
R_f value: 0.40 (silica gel; cyclohexane/ethyl acetate = 2:1)

(7) 1-[4-(2-amino-2-methoxycarbonyl-ethyl)-phenyl]-3-(4-cyano-phenyl)-3H-imidazol-2-one hydrochloride

R_f value: 0.82 (silica gel; methylene chloride/methanol/conc. ammonia = 16:4:1)

Example 16

1-(4'-Cyano-4-biphenylyl)-3-(2-ethoxycarbonyl-ethyl)-imidazolidin-2,4-dione

---

5 g of N-(tert.butyloxycarbonyl-methyl)-N-(4'-cyano-4-biphenylyl)-N'-(2-ethoxycarbonyl-ethyl)-urea are dissolved in 30 ml of methylene chloride, 30 ml of trifluoroacetic acid are added and the resulting mixture is stirred at ambient temperature for 16 hours. It is evaporated to dryness, digested with water and the precipitate is recrystallised from tert.butyl-methylether/ethyl acetate = 1:1.3.
Yield: 2.9 g (55% of theory),
Melting point: 177-178°C
R_f value: 0.57 (silica gel; methylene chloride/ethyl acetate = 7:1)

The following compound is obtained analogously:

(1) 1-(4-aminomethyl-phenyl)-3-[4-[2-(5-tetrazolyl)-ethyl]-phenyl]-imidazolidin-2-one

Example 17

1-(3-Bromo-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

---

Prepared by reacting 1-(4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one with bromine in glacial acetic acid at ambient temperature.

Example 18

1-(4-Amidino-phenyl)-3-(methoxycarbonylmethylsulphonyl-phenyl)-imidazolidin-2-one

---

2.1 g of 1-(4-amidino-phenyl)-3-(methoxycarbonylmethyl-thio-phenyl)-imidazolidin-2-one are suspended in 10 ml of formic acid, 1.3 ml of 30% hydrogen peroxide are added and the mixture is stirred at ambient temperature for 16 hours. The precipitate formed is filtered off (see Example (2)), excess peroxide is destroyed by the addition of sodium bisulphite solution and the remainder is evaporated down in vacuo. The residue is extracted by boiling with a mixture of 100 ml of methylene chloride and 60 ml of methanol. The solution obtained is evaporated down and the residue is purified by column chromatography (silica gel; methylene chloride/methanol = 9:1). In addition to 1 mol of water the product contains 0.5 mol of hydrochloric acid and 1 mol of formic acid.
Yield: 0.25 g (10% of theory)
R_f value: 0.43 (silica gel; methylene chloride/methanol = 8:2)

The following compounds are obtained analogously:

(1) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-2-methylsulphonyl-phenyl]-imidazolidin-2-one

(2) 1-(4-cyano-phenyl)-3-(4-methoxycarbonylmethyl-sulphonyl-phenyl)-imidazolidin-2-one
(Obtained as a by-product of Example 18)
Melting point: 246-249°C

(3) 1-(4-cyano-2-methylsulphonyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(4) 1-(4'-cyano-3-methylsulphonyl-4-biphenylyl)-3-(2-

methoxycarbonyl-ethyl)-imidazolidin-2-one

(5) 1-(4-amidino-phenyl)-3-(4-methoxycarbonylmethyl-sulphinyl-phenyl)-imidazolidin-2-one
The work is done in glacial acetic acid at 10°C with equimolar amounts of hydrogen peroxide
Melting point: from 215°C (decomp.)
R_f value: 0.48 (Reversed Phase Plate RP8, methanol/10% sodium chloride solution = 6:4)

Example 19

1-(4'-Cyano-3-nitro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

---

Prepared by reacting 1-(4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one with fuming nitric acid at 0°C.

Example 20

1-(3-Amino-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

---

Prepared by reduction of 1-(4'-cyano-3-nitro-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one with hydrogen at 5 bars in the presence of 5% palladium/charcoal in ethyl acetate at ambient temperature.

Example 21

1-(3-Acetamino-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

---

Prepared from 1-(3-amino-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one and acetylchloride in methylene chloride at ambient temperature using ethyl-diisopropylamine.

The following compounds are obtained analogously:

(1) 1-(3-benzoylamino-4'-cyano-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

(2) 1-(4'-cyano-3-methanesulphonylamino-4-biphenylyl)-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

Example 22

1-(4-Cyano-phenyl)-3-[4-(2-phosphono-ethyl)-phenyl]-imidazolidin-2-one

---

Prepared from a mixture of 1-(4-cyano-phenyl)-3-[4-[2-(dimethoxy-phosphoryl)-ethyl]-phenyl]-imidazolidin-2-one, sodium iodide and trimethylchlorosilane in acetonitrile by stirring at 40°C.

The following compound is obtained analogously:

(1) 1-(4-cyano-phenyl)-3-[4-[2-(O-methyl-phosphono)-ethyl]-phenyl]-imidazolidin-2-one
Sodium iodide is used on its own and the work is done by refluxing in methylethylketone.

Example 23

1-(4-Cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-thione

---

Prepared by heating 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one with 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetan-2,4-disulphide in xylene.

The following compounds are obtained analogously:

(1) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-thione

(2) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-thione

Example 24

4-(4'-Cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-methyl-3H-imidazol-2-one

---

A mixture of 8.4 g of 4-cyano-4'-[(2-methoxycarbonyl-ethyl)-aminomethyl-carbonyl]-biphenyl hydrochloride, 2.8 ml of methylisocyanate and 50 ml of pyridine is refluxed for 3 hours and then stirred into a mixture of ice and hydrochloric acid. It is extracted with ethyl acetate, the organic phase is concentrated by evaporation and the residue is triturated, until it crystallises, with a 1:1 mixture of ethyl acetate and ether.
Yield: 2.1 g (35% of theory),
Melting point: 128-130°C

The following compounds are obtained analogously:

(1) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one
Trimethylsilylisocyanate is used.

(2) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one

(3) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione
Methylisothiocyanate is used.

(4) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-thione
Phenylisothiocyanate is used.

(5) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one

(6) 4-(4-cyano-phenyl)-3,5-dimethyl-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(7) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one

(8) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(9) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-one

(10) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-phenyl-3H-imidazol-2-one

(11) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-thione

(12) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-

phenyl]-3-phenyl-3H-imidazol-2-thione

(13) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3-phenyl-3H-imidazol-2-one

(14) 1-(4-cyano-phenyl)-3,5-dimethyl-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3H-imidazol-2-one

(15) 1-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-3H-imidazol-2-one

(16) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one
Potassium isocyanate and water are used as solvents.
Melting point: 235-240°C

(17) 4-(4-cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-methyl-3H-imidazol-2-one
Prepared from the methyl 4-[(4-cyano-phenacyl)-amino]-cinnamate prepared in situ according to Example IV without the addition of auxiliary base
Melting point: 140-144°C

(18) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-phenyl-3H-imidazol-2-one
Melting point: 103-107°C

(19) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-thione

(20) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-methyl-3H-imidazol-2-thione

(21) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3-phenyl-3H-imidazol-2-thione

(22) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-

ethyl)-5-methyl-3H-imidazol-2-one

(23) 4-(4'-cyano-4-biphenylyl)-3,5-dimethyl-1-(2-methoxycarbonyl-ethyl)-3H-imidazol-2-one

(24) 4-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-5-methyl-3-phenyl-3H-imidazol-2-one

Example 25

1-(4-Cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one

---

A mixture of 2.25 g of 1-[4-(2-methoxycarbonyl-ethyl)-cyclohexyl]-imidazolidin-2-one, 2.25 g of 4-iodo-benzonitrile, 0.29 g of tris-[2-(2-methoxy-ethoxy)-ethyl]-amine, 2.46 g of potassium carbonate, 0.2 g of copper(I)chloride, 0.2 g of copper(I)iodide and 60 ml of xylene is heated under nitrogen for 4 hours using a water separator. The mixture is allowed to cool to 50°C, 150 ml of ethyl acetate are added, the precipitate is filtered off while hot and washed with hot ethyl acetate. The ethyl acetate phases are evaporated to dryness and the residue is purified by column chromatography over silica gel (eluant: cyclohexane/ethyl acetate = 1:1).
Yield: 1.7 g (54% of theory),
R_f value: 0.56 (silica gel; cyclohexane/ethyl acetate = 1:1)

The following compound is obtained analogously:

(1) 2-(4-cyano-phenyl)-5-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide
4-Fluoro-benzonitrile and sodium hydride in N-methyl-pyrrolidone are used without copper salts.
Melting point: 160-162°C

Example 26

3-(4-Cyano-phenyl)-1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one

---

3 g of N-(4-cyano-phenyl)-N'-(2-hydroxy-propyl)-N'-[4-(2-methoxycarbonyl-ethyl)-phenyl]-urea are dissolved in a mixture of 40 ml of methylene chloride and 20 ml of dimethylsulphoxide and 0.64 ml of pyridine, 0.61 ml of trifluoroacetic acid and 4.9 g of N,N'-dicyclohexyl-carbodiimide are added successively. The mixture is stirred for 4.5 hours at ambient temperature, a further 5 ml of trifluoroacetic acid are added and the mixture is heated for one hour to 50°C. It is left to stand for 16 hours at ambient temperature, diluted with 150 ml of methylene chloride and washed several times with water. The methylene chloride phase is evaporated down and the residue is purified by column chromatography over silica gel (eluant: methylene chloride/cyclohexane/ethyl acetate = 2:1:1).

Yield: 0.8 g (28% of theory),

R_f value: 0.55 (silica gel; methylene chloride/cyclohexane/ethyl acetate = 3:1:1)

The following compound is obtained analogously:

(1) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one

Melting point: 168-170°C

R_f value: 0.55 (silica gel; methylene chloride/cyclohexane/ethyl acetate = 2:1:1)

Example 27

4-(4-Cyano-phenyl)-2-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one

---

1.75 g of N-acetylamino-N-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-N'-(4-cyano-phenyl)-urea are heated to 180°C for 1.5 hours. The compound is triturated with 8 ml of ethanol and the resulting product is filtered off.
Yield: 0.66 g (40% of theory),
Melting point: 170-172°C
R_f value: 0.91 (silica gel; ethyl acetate/cyclohexane = 2:1)

The following compounds are obtained analogously:

(1) 4-(4-cyano-phenyl)-2-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
Melting point: 213-215°C
R_f value: 0.69 (silica gel; methylene chloride/ethyl acetate = 9:1)

(2) 2-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one
R_f value: 0.62 (silica gel; methylene chloride/ethyl acetate = 9:1)

(3) 2-(4-cyano-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one
Melting point: 163-164°C
R_f value: 0.65 (silica gel; methylene chloride/ethyl acetate = 9:1)

(4) 1-(4-cyano-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2,4-dione
Melting point: 188-190°C
R_f value: 0.57 (silica gel; cyclohexane/ethyl acetate = 4:6)

(5) 2-(4-cyano-phenyl)-4-[4-(2-ethoxycarbonyl-ethyl)-phenyl]-5-ethyl-4H-1,2,4-triazol-4-one
The starting compound is refluxed in xylene in the presence of toluenesulphonic acid
Melting point: 159-161°C
R_f value: 0.68 (silica gel; methylene chloride/ethyl acetate = 9:1)

Example 28

1-[6-(4-Cyano-phenyl)-3-pyridazinyl]-3-(2-methoxycarbonyl-ethyl)-imidazolidin-2-one

2.2 g of 1-[6-(4-cyano-phenyl)-3-pyridazinyl]-imidazolidin-2-one are stirred into 160 ml of dimethylformamide with 0.33 g of a 60% suspension of sodium hydride in oil for 3 hours at ambient temperature. 2 ml of methyl acrylate are added and the mixture is stirred for a further 16 hours at ambient temperature. The reaction mixture is poured onto a mixture of 300 ml of water and 8 ml of 1N hydrochloric acid, the product precipitated is filtered off, brought to the boil with methanol and, after cooling, filtered again.
Yield: 1.8 g (60% of theory),
R_f value: 0.46 (silica gel; methylene chloride/methanol = 15:1, developing twice)

The following compound is obtained analogously:

(1) 3-(4'-cyano-4-biphenylyl)-1-(2-methoxycarbonyl-ethyl)-3H-imidazo[4,5-b]pyridin-2-one
R_f value: 0.81 (silica gel; methylene chloride/methanol = 19:1)

Example 29

1-(2-tert.Butoxycarbonylmethylamino-ethyl)-3-(4-cyano-phenyl)-imidazolidin-2-one

A solution of 4.6 g of 1-(4-cyano-phenyl)-3-(2-methanesulphonyloxy-ethyl)-imidazolidin-2-one in 75 ml of dimethylformamide is mixed with 2.1 g of potassium carbonate at ambient temperature, with stirring, and then 2.1 ml of glycine-tert.butylester are added dropwise. The resulting mixture is stirred for 16 hours at ambient temperature and 30 hours at 60°C. The solvent is distilled off in vacuo and the residue is taken up in a mixture of 150 ml of ice water and 100 ml of methylene chloride. The methylene chloride phase is separated off and washed with water. The aqueous phases are then extracted once more with methylene chloride and finally the combined organic phases are evaporated down. The residue is purified over silica gel (eluant: ethyl acetate/methanol/conc. ammonia = 9.5:0.5:0.1).
Yield: 1.4 g (27% of theory),
Melting point: 104-106°C
R_f value: 0.32 (silica gel; ethyl acetate/methanol/conc. ammonia = 9:1:0.1)

Example 30

1-[2-(N-Acetyl-N-carboxymethyl-amino)-ethyl]-3-(4-amidino-phenyl)-imidazolidin-2-one

A mixture of 0.3 g of 1-(4-amidino-phenyl)-3-(2-carboxymethylamino-ethyl)-imidazolidin-2-one prepared under ice cooling, 20 ml of water and 2.35 ml of acetanhydride is allowed to return to ambient temperature with stirring and stirred for a further 30 minutes. It is then evaporated to dryness in vacuo and the residue is purified by chromatography on silica gel

(eluant: methanol/glacial acetic acid/water = 6:1:1)
Yield: 0.2 g (57% of theory),
Melting point: 302-304°C (decomp.)
R_f value: 0.54 (silica gel; methanol/2N aqueous ammonia = 4:1)

Example 31

1-[4-(1-Amino-ethyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

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0.5 g of 1-[4-(1-hydroxyimino-ethyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one are treated with hydrogen at 5 bars for 3.5 hours at ambient temperature in a mixture of 50 ml of methanol and 1 ml of methanolic hydrochloric acid in the presence of 100 mg of 10% palladium/charcoal. The mixture is evaporated down and the residue is taken up in a mixture of 20 ml of methylene chloride, 15 ml of methanol, 20 ml of water and 0.1 ml of 6N hydrochloric acid. The aqueous phase is separated off and evaporated down to about one third of its volume, whereupon the product crystallises out.
Yield: 0.28 g (53% of theory),
Melting point: 264-266°C
R_f value: 0.51 (Reversed Phase Plate RP8, methanol/5% sodium chloride solution = 6:4)

The following compounds are obtained analogously:

(1) 1-(1-amino-5-indanyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride
Melting point: 223-226°C (sintering from 208°C)

(2) 1-(1-amino-1,2,3,4-tetrahydro-6-naphthyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one hydrochloride

Example 32

1-(4-Amino-cyclohexyl)-3-[4-(3-methoxycarbonyl-propyl)-phenyl]-imidazolidin-2-one

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Prepared from 1-(4-aminocarbonyl-cyclohexyl)-3-[4-(3-methoxycarbonyl-propyl)-phenyl]-imidazolidin-2-one by treating with [bis-(trifluoroacetoxy)iodo]benzene in acetonitrile/water at ambient temperature.

The following compounds are obtained analogously:

(1) 1-(4-amino-cyclohexyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

(2) 1-[4-amino-2-propyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

Example 33

1-[4-[(2-Methoxycarbonyl-ethyl)-aminocarbonyl]-phenyl]-3-(4-piperidinyl)-imidazolidin-2-one

---

Prepared by treating 1-(1-benzyloxycarbonyl-4-piperidinyl)-3-[4-[(2-methoxycarbonyl-ethyl)-aminocarbonyl]-phenyl]-imidazolidin-2-one with hydrogen at 3 bars in the presence of 5% palladium/charcoal in methanol.

The following compounds are obtained analogously:

(1) 1-(4-amino-cyclohexyl)-3-[4-[(2-methoxycarbonyl-ethyl)-aminocarbonyl]-phenyl]-imidazolidin-2-one

(2) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-[4-

(methylaminomethyl)-phenyl]-imidazolidin-2-one

(3) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-[4-(n-propylamino-methyl)-phenyl]-imidazolidin-2-one

Example 34

1-[4-(1-Amino-cyclopropyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

---

Prepared from 1-[4-(1-tert.butyloxycarbonylamino-cyclopropyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one by stirring for two hours in a 1:1 mixture of methylene chloride and trifluoroacetic acid.

The following compound is obtained analogously:

(1) 1-[4-(1-amino-cyclopentyl)-phenyl]-3-[4-[(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

Example 35

1-[4-(2-Methoxycarbonyl-ethyl)-phenyl]-3-[4-(methylamino-methyl)-phenyl]-imidazolidin-2-one

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Prepared from 1-(4-aminomethyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one by alkylation with methyliodide in dimethylsulphoxide.

The following compounds are obtained analogously:

(1) 1-[4-(2-methoxycarbonyl-ethyl)-phenyl]-3-[4-(n-propylamino-methyl)-phenyl]-imidazolidin-2-one

(2) 1-[4-(2-methoxycarbonyl-ethyl)-aminocarbonyl]phenyl]-3-(1-methyl-4-piperidinyl)-

imidazolidin-2-one

Example 36

1-(4-Cyano-2-methyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

---

3.0 g of 1-(4-bromo-2-methyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one and 1.3 g of copper(I)cyanide are heated in 10 ml of dimethylformamide for 10 hours at a bath temperature of 175°C. The dimethylformamide is evaporated off in vacuo, the residue is digested with chloroform and filtered off. The chloroform solution is washed with water and saturated saline solution and concentrated by evaporation. The residue is purified by column chromatography (silica gel; methylene chloride/ethyl acetate = 100:2).
Yield: 1.4 g (54% of theory),
Melting point: 151-153°C

Example 37

1-[4-(Dimethylamino-methyl)-phenyl]-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one

---

Prepared from 1-(4-aminomethyl-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-imidazolidin-2-one by treating with formaldehyde and sodium cyanoborohydride.

Example 38

Dry ampoules containing 2.5 mg of active substance per 1 ml

Composition:

Active substance	2.5 mg
Mannitol	50.0 mg
Water for injections ad	1.0 ml

Preparation:

The active substance and mannitol are dissolved in water. After packaging, the ampoules are freeze-dried.

The solution ready for use is made up with water for injections.

Example 39

Dry ampoule containing 35 mg of active substance per 2 ml

Composition:

Active substance	35.0 mg
Mannitol	100.0 mg
Water for injections ad	2.0 ml

Preparation:

The active substance and mannitol are dissolved in water. After packaging, the ampoules are freeze-dried.

The solution ready for use is made up with water for injections.

Example 40

Tablet containing 50 mg of active substance

Composition:

(1)	Active substance	50.0 mg
(2)	Lactose	98.0 mg
(3)	Corn starch	50.0 mg
(4)	Polyvinylpyrrolidone	15.0 mg
(5)	Magnesium stearate	2.0 mg
		215.0 mg

Preparation:

Components (1), (2) and (3) are mixed together and granulated with an aqueous solution of component (4). Component (5) is added to the dried granules. From this mixture, compressed tablets are made, which are biplanar, facetted on both sides and notched on one side. Diameter of tablets: 9 mm.

Example 41

Tablet containing 350 mg of active substance

Composition:

(1)	Active substance	350.0 mg
(2)	Lactose	136.0 mg
(3)	Corn starch	80.0 mg
(4)	Polyvinylpyrrolidone	30.0 mg
(5)	Magnesium stearate	4.0 mg
		600.0 mg

Preparation:

Components (1), (2) and (3) are mixed together and granulated with an aqueous solution of component (4).

Component (5) is added to the dried granules. From this mixture, compressed tablets are made, which are biplanar, facetted on both sides and notched on one side. Diameter of tablets: 12 mm.

Example 42

Capsules containing 50 mg of active substance

Composition:

(1) Active substance	50.0 mg
(2) Dried corn starch	58.0 mg
(3) Powdered lactose	50.0 mg
(4) Magnesium stearate	2.0 mg
	160.0 mg

Preparation:

Component (1) is triturated with component (3). This triturate is added to the mixture of components (2) and (4) with thorough mixing.

The powdered mixture is packed into hard gelatin oblong capsules, size 3, in a capsule filling machine.

Example 43

Capsule containing 350 mg of active substance

Composition:

(1) Active substance	350.0 mg
(2) Dried corn starch	46.0 mg
(3) Powdered lactose	30.0 mg
(4) Magnesium stearate	4.0 mg
	430.0 mg

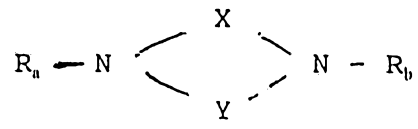
Preparation:

Component (1) is triturated with component (3). This triturate is added to the mixture of components (2) and (4) with thorough mixing.

The powdered mixture is packed into hard gelatin oblong capsules, size 0, in a capsule filling machine.

The claims defining the invention are as follows:

1. Compounds of formula I



(I)

(wherein

X represents a carbimino group optionally substituted at the nitrogen atom by an alkyl, aralkyl, aryl, heteroaryl or cyano group, or X represents a carbonyl, thiocarbonyl, sulphinyl or sulphonyl group;

Y represents a straight-chained C_{2-4}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, wherein the above-mentioned alkylene or alkenylene groups may additionally be mono- or disubstituted by a fluorine, chlorine or bromine atom or by an alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl groups, which substituents may be identical or different and wherein, in addition, one or two methylene groups may each be replaced by a carbonyl group, or

Y represents a 1,2-cycloalkylene group having 4 to 7 carbon atoms optionally substituted by R_c or R_d or by R_c and R_d, or

Y represents a 1,2-cycloalkenylene group having 4 to 7 carbon atoms or a 1,2-phenylene group, in which one or two methine groups may be substituted by a nitrogen atom and which may be substituted in the carbon skeleton by a fluorine, chlorine or bromine atom, by a C_{1-4}-alkyl group, by a trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl,

arylcarbonyl, alkoxycarbonyl, carboxy, nitro, $(R_1)_2N$-, $(R_1)_2NCO$- or $(R_1)_2NSO_2$- group, wherein the groups R_1 may be identical or different and may each represent a hydrogen atom or an alkyl, aralkyl, aryl or heteroaryl group, or by a R_1NH- group substituted by an alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, and wherein, additionally, one or two -CH=CH- groups may each be replaced by a $-CO-NR_1-$ group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-5}-aminoalkyl group, in which at one of the nitrogen atoms, one or two hydrogen atoms may be replaced by a C_{1-4}-alkyl group or one hydrogen atom may be replaced by a C_{2-5}-alkoxycarbonyl group or by an alkylcarbonyl, arylcarbonyl, aryloxycarbonyl or aralkoxycarbonyl group, or A may represent a cyano or cyano(C_{1-4}-alkyl) group or, if A is bound to a nitrogen atom of groups B or C which is not part of a lactam group, A may also represent a hydrogen atom or an alkyl group;

B represents a bond, or

an alkylene or alkenylene group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl,

alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group, optionally alkyl-substituted in the carbon skeleton, and in which additionally one or two -CH=N- groups may be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group C, provided that the latter is not attached to group B by a heteroatom or a carbonyl group, or

a cyclopropylene group optionally substituted by an alkyl, aralkyl or aryl group, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and additionally a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to one another may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a biphenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms or by alkyl, trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl-NR_1- or

alkylsulphonyl-NR_1- groups, and in which the substituents may be identical or different and R_1 is as hereinbefore defined;

C represents an alkylene or alkenylene group optionally substituted by a hydroxy, alkoxy or $(R_1)_2N$- group, or

an alkylenecarbonyl group connected to the group B via the carbonyl group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH-groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

an indanylene or 1,2,3,4-tetrahydronaphthylene group, wherein in each case the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be substituted in the carbon skeleton by an alkyl group, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group B, provided that the latter is not a bond or does not adjoin the group C with a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety

may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties located in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-5}-alkylene group or a C_{2-5}-alkenylene group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, carboxyalkoxy, alkoxycarbonylalkoxy, aralkoxycarbonyl-alkoxy, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups, or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group E,

provided that the latter is not a bond or is not bound to the group D by means of a heteroatom, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to the nitrogen atom may each be replaced by a carbonyl group, or

a C_{2-6}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, $R_1N<$, (alkylcarbonyl)N<, (aralkylcarbonyl)N<, (arylcarbonyl)N<, (heteroarylcarbonyl)N<, (alkylsulphonyl)N<, (arylsulphonyl)N<, aminocarbonyl or carbonylamino group;

E represents a bond, or

a C_{1-5}-alkylene or C_{2-5}-alkenylene group optionally substituted by one or two alkyl groups, or by a hydroxy, alkoxy, amino, alkylamino, aralkylamino, dialkylamino, bis(aralkyl)amino, carboxyalkyl, alkoxycarbonylalkyl or aralkoxycarbonylalkyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted

by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or triazinylene group which may be alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group D, or

a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which a CH moiety may be replaced by a nitrogen atom and in addition a methylene group adjacent to the nitrogen atom may be replaced by a carbonyl group, or

a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, and in which one or two CH moieties in the 1,4-position relative to each other may each be replaced by a nitrogen atom, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may be replaced by a carbonyl group, or

an alkylenearylene group linked to the group D via the aryl moiety, or

an alkylene group linked to the group D via the group W, where W is as hereinbefore defined;

F represents a carbonyl group substituted by a hydroxy or C_{1-6}-alkoxy group, whilst a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-

oxido-thiomorpholino group, or

F may represent a sulpho, phosphono, O-alkylphosphono or tetrazol-5-yl group, whilst if A represents a cyano group or an amino or aminoalkyl group optionally benzoylated or benzyloxy-carbonylated at the nitrogen atom, the separation of the nitrogen atom of these groups and group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, perfluoroalkyl, aralkyl, aryl or heteroaryl group or, if the third of the groups R_a, R_b, R_c and R_d is connected to an unsaturated carbon atom of group Y, it may represent an alkoxy, alkylsulphenyl or $(R_1)_2N$- group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, an alkyl, aralkyl, aryl or heteroaryl group or R_a or R_b together with an adjacent group R_c or R_d may also represent a bond;

and, unless otherwise specified, any alkyl, alkylene, alkenylene or alkoxy moiety contains 1 to 3 carbon atoms,

any said aryl group, unless otherwise specified is a phenyl group which is optionally monosubstituted by a trifluoromethyl, carboxy, $(R_1)_2NCO$-, alkoxycarbonyl, alkylcarbonyl, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, nitro, $(R_1)_2N$-, alkylcarbonyl-NR_1-, aralkylcarbonyl-NR_1-, arylcarbonyl-NR_1-, heteroarylcarbonyl-NR_1-, alkylsulphonyl-NR_1-, aralkylsulphonyl-NR_1-, arylsulphonyl-NR_1- or $(R_1)_2N$-sulphonyl group or may be mono-, di- or trisubstituted by fluorine, chlorine or bromine atoms or by hydroxy, C_{1-4}-alkoxy or C_{1-4}-alkyl groups, and

any said heteroaryl group, unless otherwise specified is a 5-membered heteroaromatic ring which contains an oxygen, sulphur or nitrogen atom, a nitrogen atom and an oxygen, sulphur or nitrogen atom or two nitrogen atoms and an oxygen, sulphur or nitrogen atom, or a 6-membered heteroaromatic ring which contains one, two or three nitrogen atoms and in which, additionally, one or two -CH=N- groups may be replaced by a $-CO-NR_1-$ group, whilst the above-mentioned heteroaromatic rings may additionally be substituted by one or two alkyl groups or by a fluorine, chlorine or bromine atom or by a hydroxy or alkoxy group)

and the tautomers, the stereoisomers, and the addition salts thereof.

2. Compounds of formula I as claimed in claim 1 wherein

X represents a carbimino group optionally substituted at the nitrogen atom by an alkyl, aralkyl, aryl, heteroaryl or cyano group, or X represents a carbonyl, thiocarbonyl, sulphinyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by a fluorine, chlorine or bromine atom or by an alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl group, whilst the substituents may be identical or different and, in addition, one or two methylene groups may be replaced by a carbonyl group, or

Y represents a 1,2-cyclohexylene group optionally substituted by R_c or R_d or by R_c and R_d, or

Y represents a 1,2-cyclohexenylene group or a 1,2-

phenylene group wherein one or two CH groups may each be replaced by a nitrogen atom and which may be substituted in the carbon skeleton by a fluorine, chlorine or bromine atom, by a C_{1-4}-alkyl group, by a trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, carboxy, nitro, $(R_1)_2N$-, $(R_1)_2NCO$- or $(R_1)_2NSO_2$- group, wherein the groups R_1 may be identical or different and may each represent a hydrogen atom, an alkyl, aralkyl, aryl or heteroaryl group, or by a R_1NH- group substituted by an alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl group, and wherein, additionally, one or two -CH=CH- groups may each be replaced by a $-CO-NR_1-$ group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group optionally substituted by R_c or R_d,

one of the groups R_a, R_b, R_c and R_d represents a group formula

A - B - C -

wherein A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-5}-aminoalkyl group in which, at one of the nitrogen atoms, one or two hydrogen atoms may be replaced by a C_{1-4}-alkyl group or a hydrogen atom may be replaced by a C_{2-5}-alkoxycarbonyl group, by an alkylcarbonyl, arylcarbonyl, aryloxycarbonyl or aralkoxycarbonyl group, or A represents a cyano or cyano(C_{1-4}-alkyl) group or, if A is bound to a nitrogen atom of groups B or C which is not part of a lactam group, A may also represent a hydrogen atom or an alkyl group;

B represents a bond, or

an alkylene or alkenylene group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by an alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, in which the substituents may be identical or different,

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by an alkyl group, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$-group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group C; provided that the latter does not adjoin the group B with a heteroatom or a carbonyl group, or

a C_{3-5}-cycloalkylene group, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may each be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a biphenylene group;

C represents an alkylene or alkenylene group optionally substituted by a hydroxy group, or

an alkylenecarbonyl group connected to the group B via the carbonyl group, or

a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different,

an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein, in each case, the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbonyl skeleton by an alkyl group, whilst additionally one or two =CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group B, provided that the latter does not represent a bond or is not adjacent to the group C with a heteroatom, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may each be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group and the nitrogen atoms may not be bound to a nitrogen atom of the cyclic urea;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

wherein D represents a C_{1-5}-alkylene group or a C_{2-5}-alkenylene group, or

a phenylene group which may be mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, carboxyalkoxy, alkoxycarbonylalkoxy, aralkoxycarbonyl-alkoxy, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups, or by R_1NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, which substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted by an alkyl group in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1$- group and one of the nitrogen atoms instead of being bound to the group R_1 may also be bound to the group E, provided that the latter does not represent a bond or is not bound by a heteroatom to the group D, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may each be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

a C_{3-6}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, R_1N-, (alkylcarbonyl)N-, (aralkylcarbonyl)N-, (arylcarbonyl)N-, (heteroarylcarbonyl)N-, (alkylsulphonyl)N- or (arylsulphonyl)N-group and the alkylene group linked to a nitrogen atom of the cyclic urea contains 2 or 3 carbon atoms;

E represents a bond, or

a C_{1-5}-alkylene or C_{2-5}-alkenylene group optionally substituted by one or two alkyl groups or by a hydroxy, alkoxy, amino, alkylamino, aralkylamino, dialkylamino, bis(aralkyl)amino, carboxyalkyl, alkoxycarbonylalkyl or aralkoxycarbonylalkyl group, or

E represents a phenylene group optionally mono- or disubstituted by fluorine, chlorine or bromine atoms, by C_{1-4}-alkyl groups, by trifluoromethyl, hydroxy, alkoxy, alkylsulphenyl, alkylsulphinyl, alkylsulphonyl, $(R_1)_2N$-, $(R_1)_2NCO$-, $(R_1)_2NSO_2$- or nitro groups or by R_1-NH- groups substituted by alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkylsulphonyl, aralkylsulphonyl or arylsulphonyl groups, in which the substituents may be identical or different, or

a pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally alkyl-substituted in the carbon skeleton, whilst additionally one or two -CH=N- groups may each be replaced by a $-CO-NR_1-$ group and one of the nitrogen atoms, instead of being bound to the group R_1, may also be bound to the group D, or

a cyclohexylene group wherein one or two CH moieties in the 1,4-position relative to each other may each be replaced by nitrogen atoms, whilst additionally one or two of the methylene groups adjacent to a nitrogen atom may each be replaced by a carbonyl group, or

an alkylenearylene group linked to the group D via the aryl group, or

an alkylene group linked to the group D via the group W', wherein W' represents an oxygen or sulphur atom, a sulphinyl, sulphonyl, R_1N-, (alkycarbonyl)N-,

(aralkylcarbonyl)N<, (arylcarbonyl)N<, (heteroaryl-carbonyl)N<, (alkylsulphonyl)N<, (arylsulphonyl)N< or aminocarbonyl group wherein the nitrogen atom is bound to the alkylene group;

F represents a carbonyl group substituted by a hydroxy or C_{1-6}-alkoxy group, whilst a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group, or F may represent a sulpho, phosphono, O-alkylphosphono or tetrazol-5-yl group, whilst if A represents a cyano group or an amino or aminoalkyl group optionally benzoylated or benzyloxy-carbonylated at the nitrogen atom, the separation of the nitrogen atom of these groups and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d is a hydrogen atom, an alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl group or, if the third of the groups R_a, R_b, R_c and R_d is bound to an unsaturated carbon atom of group Y, it may represent an alkoxy, alkylsulphenyl or $(R_1)_2N$- group; and

where present the fourth of groups R_a, R_b, R_c and R_d represents a hydrogen atom or an alkyl, aralkyl, aryl or heteroaryl group;

and the tautomers, stereoisomers, and addition salts thereof.

3. Compounds of formula I as claimed in claim 1, wherein

X represents a carbimino group optionally substituted at the nitrogen atom by a methyl, phenyl or pyridyl group,

or X represents a carbonyl, thiocarbonyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, and which may be substituted by a chlorine atom, by one or two methyl groups or by a trifluoromethyl, phenyl or acetyl group, whilst additionally a methylene group may be replaced by a carbonyl group, or

Y represents a -CO-NH-, -NH-CO-, -CH=N- or -N=CH- group, optionally substituted by R_c or R_d, or a 1,2-phenylene or 2,3-pyridinylene group,

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein A represents an amino, amidino, guanidino, or straight-chained or branched C_{1-4}-aminoalkyl group in which at one of the nitrogen atoms, one or two hydrogen atoms may each be replaced by a C_{1-4}-alkyl group or a hydrogen atom may be replaced by a (C_{1-4}-alkoxy)carbonyl or benzyloxycarbonyl group, or, if A is bound to a nitrogen atom of group C which is not part of a lactam group, A may also represent a hydrogen atom or a methyl group;

B represents a bond, or

a phenylene group which may be substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom, or by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group, or

a C_{3-6}-cycloalkylene group, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene or biphenylene group;

C represents an ethylene group optionally substituted by a hydroxy group, or

a methylenecarbonyl group linked to the group B via the carbonyl group,

a phenylene group optionally substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom, by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group, or

an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, cyclohexylene or piperidinylene group, wherein the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea;

a second of groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group, or

a phenylene group which may be substituted by a fluorine, chlorine or bromine atom, or by a methyl, methoxy, methylsulphenyl, methylsulphinyl,

methylsulphonyl, carboxymethoxy, methoxycarbonylmethoxy, nitro, amino, acetylamino, benzoylamino or methanesulphonylamino group, or

a pyridinylene, cyclohexylene or piperidinylene group, whilst additionally in a pyridinylene group a -CH=N- group may be replaced by a -CO-NH- group, whilst the nitrogen atom, instead of being bound to the hydrogen atom, may also be bound to the group E, provided that the latter is not a bond or is not bound by a heteroatom to group D, or

a C_{3-5}-alkylene group interrupted by the group W, wherein W represents an oxygen or sulphur atom, or a sulphinyl, sulphonyl, imino, methylimino, acetylimino, benzoylimino or methanesulphonylimino group and the alkylene group linked to the cyclic urea contains 2 or 3 carbon atoms;

E represents a bond, or

a C_{1-3}-alkylene group optionally substituted by one or two methyl groups or by a hydroxy, methoxy, amino, dimethylamino, dibenzylamino, carboxymethyl or methoxycarbonylmethyl group, or E represents a C_{2-3}-alkenylene group, or

a phenylene group, or

a C_{1-2}-alkylene group linked to group D by the group W', wherein W' represents an oxygen or sulphur atom, a sulphinyl, sulphonyl or aminocarbonyl group, the amino group being bound to the alkylene group;

F represents a carbonyl group which is substituted by a hydroxy group, by a C_{1-4}-alkoxy group or by a phenyl(C_{1-2}-alkoxy) group, or F represents a phosphono, O-methylphosphono or tetrazol-5-yl group, whilst if A

represents an amino or aminoalkyl group optionally benzyloxycarbonylated at the nitrogen atom, the separation of the nitrogen atom of this group and group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom, a methyl, ethyl, trifluoromethyl or phenyl group; and

where present the fourth of groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl group;

and the tautomers, stereoisomers, including mixtures thereof, and addition salts thereof.

4. Compounds of formula I as claimed in claim 1, wherein

X represents a carbonyl or sulphonyl group;

Y represents a straight-chained C_{2-3}-alkylene or alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, and which may also be substituted by one or two methyl groups or by a trifluoromethyl or phenyl group, whilst additionally a methylene group may be replaced by a carbonyl group, or Y represents an -N=CH- or -CH=N- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein A represents an amino, amidino, or straight-chained or branched C_{1-4}-aminoalkyl group in which at one of the nitrogen atoms, a hydrogen atom may be replaced by a (C_{1-4}-alkoxy)carbonyl group or benzyloxycarbonyl

group;

B represents a bond, or

a phenylene group optionally substituted by a fluorine or chlorine atom, or

a cyclopropylene, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group;

C represents a phenylene group optionally substituted by one or two methyl groups, by a fluorine, chlorine or bromine atom or by a methoxy, methylsulphenyl, methylsulphinyl, methylsulphonyl, amino, acetylamino, benzoylamino or methanesulphonylamino group, or, if A represents an amino group and B represents a bond, C may represent an indanylene or 1,2,3,4-tetrahydronaphthylene group wherein the saturated ring is bound to the group A and the aromatic ring is bound to the cyclic urea skeleton, or

C represents a pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, cyclohexylene or piperidinylene group, whilst the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group,

a phenylene group optionally substituted by a fluorine, chlorine or bromine atom or by a methyl, methoxy, methylsulphenyl, methylsulphinyl or methylsulphonyl group, or

a pyridinylene, cyclohexylene or piperidinylene group, whilst additionally in a pyridinylene group the -CH=N- group may be replaced by a -CO-NH- group and the nitrogen atom, instead of being bound to the hydrogen atom, may also be bound to the group E, provided that the latter is not a bond or is not bound to the group D by a heteroatom, or

a $-CH_2CH_2-N(COCH_3)-CH_2-$ group wherein the ethylene moiety is bound to the cyclic urea;

E represents a bond, or

an ethylene group optionally substituted by one or two methyl groups or by an amino or dibenzylamino group, or

an ethenylene or phenylene group, or

a methylene group linked to group D by the group W', wherein W' represents an oxygen or sulphur atom or a sulphinyl or sulphonyl group;

F represents a carbonyl group substituted by a hydroxy group or by a C_{1-4}-alkoxy group, or F may represent a phosphono, O-methylphosphono or tetrazol-5-yl group, whilst if A represents an amino or aminoalkyl group optionally benzyloxycarbonylated at the nitrogen atom, the separation of the nitrogen atom of this group and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl, ethyl or phenyl group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl group;

and the tautomers, the stereoisomers and the addition salts thereof.

5. Compounds of formula I as claimed in claim 1, wherein

X represents a carbonyl or sulphonyl group;

Y represents an ethylene or ethenylene group optionally substituted by R_c or R_d and optionally substituted by a methyl or phenyl group, or Y represents a carbonylmethylene or methylenecarbonyl group optionally substituted by a methyl group, or a -CH=N- or -N=CH- group optionally substituted by R_c or R_d;

one of the groups R_a, R_b, R_c and R_d represents a group of formula

A - B - C -

wherein A represents an aminomethyl, aminoethyl or amidino group optionally substituted by a (C_{1-4}-alkoxy)carbonyl group;

B represents a bond or a 1,4-phenylene group; and

C represents a 1,4-phenylene group optionally substituted by a methyl group, a 3,6-pyridazinylene or 1,4-piperidinylene group, whilst the nitrogen atom may not be bound to a nitrogen atom of the cyclic urea, or, if A represents an amino group and B represents a bond, C may represent an indanylene group, wherein the saturated ring is attached to A and the aromatic ring to the cyclic urea ring;

a second of the groups R_a, R_b, R_c and R_d represents a group of formula

F - E - D -

wherein D represents a C_{1-4}-alkylene group, a 1,4-phenylene or 1,4-cyclohexylene group;

E represents a bond, or

an ethylene group optionally substituted by an amino or dibenzylamino group, or an ethenylene group, or

a 1,4-phenylene group, or

a methylene group linked by the group W' to the group D, wherein W' represents an oxygen or sulphur atom or a sulphinyl or sulphonyl group;

F represents a carbonyl group substituted by a hydroxy group or by a C_{1-4}-alkoxy group, whilst if A represents an aminomethyl-group, the separation of the nitrogen atom of this group and the group F is at least 10 bonds;

where present a third of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl, ethyl or phenyl group; and

where present the fourth of the groups R_a, R_b, R_c and R_d represents a hydrogen atom or a methyl group;

and the tautomers, the stereoisomers and the addition salts thereof.

6. Compounds of formula I as claimed in claim 1, wherein

R_a, R_b, R_c and R_d, X and Y are as defined in claims 1 to 5, and wherein there is an additional ring member between the linking points of those groups R_a, R_b, R_c and

R_d which represent the A-B-C- and F-E-D- groups, on the cyclic urea,

the tautomers, the stereoisomers and the addition salts thereof.

7. A compound as claimed in claim 1 being:

(a) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2-one;

(b) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-cyclohexyl]-imidazolidin-2-one;

(c) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-imidazolidin-2,4-dione;

(d) 2-(4-amidino-phenyl)-5-[4-(2-carboxy-ethyl)-phenyl]-3,4-dihydro-2H,5H-1,2,5-thiadiazole-1,1-dioxide;

(e) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-3H-imidazol-2-one;

(f) 1-(4-amidino-phenyl)-3-[4-(2-carboxy-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one;

(g) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(h) 2-(4-amidino-phenyl)-4-[4-(2-carboxy-ethyl)-phenyl]-5-ethyl-4H-1,2,4-triazol-3-one;

(i) 2-(4-amidino-phenyl)-4-[4-(2-carboxyethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(j) 4-(4-amidino-phenyl)-2-[4-(2-carboxy-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(k) 1-(4-amidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4-methyl-3H-imidazol-2-one;

(l) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(m) 2-(4-amidino-phenyl)-5-ethyl-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(n) 2-(4-amidino-phenyl)-4-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(o) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

(p) 2-(4-methoxycarbonylamidino-phenyl)-3-[4-(2-methoxycarbonyl-ethyl)-phenyl]-4H-1,2,4-triazol-3-one;

(q) 4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-2-(4-methoxycarbonylamidino-phenyl)-5-methyl-4H-1,2,4-triazol-3-one; or

(r) 2-(4-amidino-phenyl)-4-[4-(2-isobutyloxycarbonyl-ethyl)-phenyl]-5-methyl-4H-1,2,4-triazol-3-one;

or a tautomer, stereoisomer or addition salt thereof.

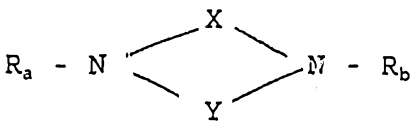
8. A compound as claimed in any one of claims 1 to 7 being a pysiologically acceptable addition salt of a compound of formula I as defined in any one of claims 1 to 7.

9. A pharmaceutical composition containing a compound of formula I as claimed in any one of claims 1 to 7 or a physiologically acceptable addition salt thereof together with at least one physiologically acceptable

carrier or excipient.

10. A process for the preparation of compounds as claimed in claim 1, said process comprising at least one of the following steps:

a) (to prepare compounds of formula I wherein F represents a carboxy group) converting a compound of formula II



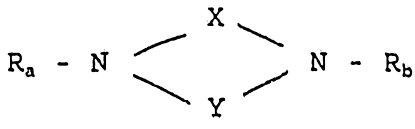
(II)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7 with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula

F' - E - D -

wherein E and D are as defined in claims 1 to 7 and F' represents a group which may be converted into a carboxyl group by hydrolysis, treatment with acids, thermolysis or hydrogenolysis) into a corresponding carboxy compound;

b) (to prepare compounds of formula I wherein A represents an R_4NH-C(=NH)- group optionally substituted by an alkyl group) reacting a compound of formula III



(III)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d

represents a group of the formula

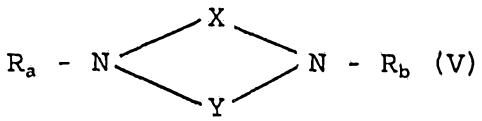
$$Z_1 - C(=NH) - B -$$

wherein B and C are as defined in claims 1 to 7 and Z_1 represents an alkoxy, aralkoxy, alkylthio, aralkylthio or amino group) which is optionally formed in the reaction mixture, with an amine of formula IV

$$R_4 - NH_2 \quad (IV)$$

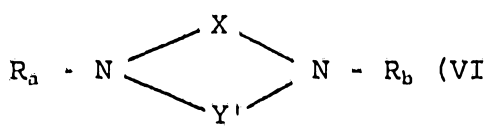
(wherein
R_4 represents a hydrogen atom or a C_{1-4}-alkyl group) or with an acid addition salt thereof;

c) (to prepare compounds of formula I wherein at least one of the groups B, C, D and E contains a sulphinyl or sulphonyl group) oxidising a compound of formula V



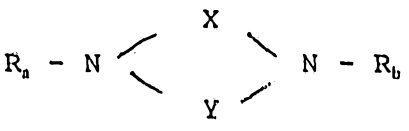
(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that at least one of the groups Y, B, C, D or E contains a sulphenyl or sulphinyl group);

d) (to prepare compounds of formula I wherein Y represents a straight-chained C_{2-4}-alkylene group optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl groups) hydrogenating a compound of formula VI



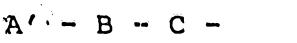
(wherein
R_a, R_b and X are as defined in claims 1 to 7 and
Y' represents a straight-chained C_{2-4}-alkenylene group optionally substituted by R_c or R_d or by R_c and R_d, which may be mono- or disubstituted by alkyl, trifluoromethyl, aralkyl, aryl or heteroaryl groups);

e) (to prepare compounds of formula I wherein A represents an aminoalkyl, amidino or guanidino group substituted by a (C_{1-4}-alkoxy)carbonyl group or by an aralkoxycarbonyl, aryloxycarbonyl, alkylcarbonyl or arylcarbonyl group) reacting a compound of formula VII

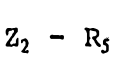


(VII)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7 with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula



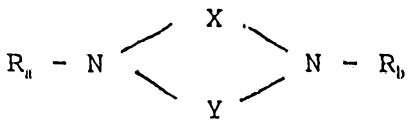
wherein B and C are as defined in claims 1 to 7 and
A' represents an H_2N-C_{1-5}alkyl-, H_2N-C(=NH)- or H_2N-C(=NH)-NH- group) with a compound of formula VIII



(VIII)

(wherein
R_5 represents a (C_{1-4}-alkoxy)carbonyl group, an aralkoxycarbonyl, aryloxycarbonyl, alkylcarbonyl or arylcarbonyl group and Z_2 represents a nucleophilic leaving group);

f) (to prepare compounds of formula I wherein F represents a carbonyl group substituted by a C_{1-6}-alkoxy group, wherein a C_{1-3}-alkoxy group may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group) reacting a compound of formula IX



(IX)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula

F" - E - D -

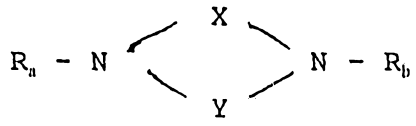
wherein E and D are as defined in claims 1 to 7 and F" represents a carboxy or alkoxycarbonyl group) with an alcohol of formula X

HO - R_6 (X)

(wherein
R_6 represents a C_{1-6}-alkyl group which may be substituted in the 1-, 2- or 3-position by an aryl or heteroaryl group or in the 2- or 3-position by a pyrrolidin-2-on-1-yl, morpholino, thiomorpholino or 1-oxido-thiomorpholino group);

g) (to prepare compounds of formula I wherein A represents an NH_2-C(=NH)- group and B or, if B represents a bond, C represents a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, wherein a CH moiety is replaced by a nitrogen atom, or a C_{6-7}-

cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, wherein one or two CH moieties in the 1,4-position relative to each other are each replaced by a nitrogen atom, whilst B or, if B is a bond, C is linked to the group A via one of the above-mentioned nitrogen atoms) reacting a compound of formula XI



(XI)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of formula

H - B′ - C - or H - C′ -

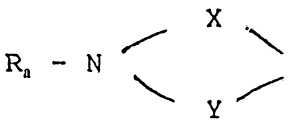
wherein C is as defined in claims 1 to 7 and
B′ or C′ represents a C_{4-5}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, wherein a CH moiety is replaced by a nitrogen atom, or a C_{6-7}-cycloalkylene group optionally substituted by an alkyl, aralkyl or aryl group, wherein one or two CH moieties in the 1,4-position relative to each other are each replaced by a nitrogen atom, the hydrogen atom being linked to a nitrogen atom of the group B′ or C′) with a compound of formula XII

$$Z_3\text{-}C(=NH)\text{-}NH_2 \qquad \text{(XII)}$$

(wherein
Z_3 represents a nucleophilic leaving group);

h) (to prepare compounds of formula I, wherein A represents an $H_2N\text{-}CH_2\text{-}V$- group, wherein V represents a

bond or a straight-chained or branched C_{1-4}-alkylene group) reducing a compound of formula XIII



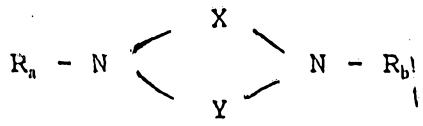
(XIII)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7 with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

NC - V - B - C -

wherein B and C are as defined in claims 1 to 7 and V represents a bond or a straight-chained or branched C_{1-4}-alkylene);

i) (to prepare compounds of formula I wherein C represents an alkylene group substituted by a hydroxy group) reducing a compound of formula XIV



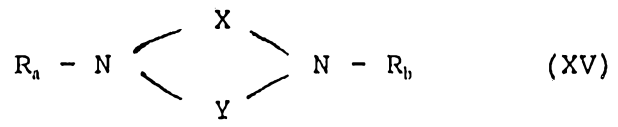
(XIV)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

A - B - C" -

wherein A and B are as hereinbefore defined and C" represents an alkylene group in which a methylene group is replaced by a carbonyl group);

j) (to prepare compounds of formula I wherein A represents an $H_2N-C(=NH)-NH-$ group) reacting a compound of formula XV



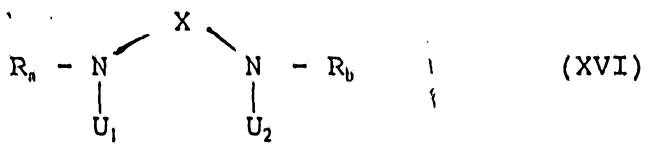
(XV)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7 with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$H_2N - B - C -$$

wherein B and C are as hereinbefore defined) with cyanamide or an acid addition salt thereof or with an S-alkyl-isothiourea, O-methylisothiourea or 1-amidino-3,5-dimethylpyrazole;

k) cyclising a compound of formula XVI



(XVI)

(wherein
R_a, R_b and X are as defined in claims 1 to 7,
one of the groups U_1 or U_2 represents a hydrogen atom and the other group U_1 or U_2 represents a group of the formula

$$- Y'' - Z_4$$

wherein Y'' represents a straight-chained C_{2-4}-alkylene or alkenylene group, optionally substituted by R_c or R_d or by R_c and R_d, wherein each carbon atom may be mono- or

disubstituted by an alkyl, trifluoromethyl, aralkyl, aryl, heteroaryl or alkylcarbonyl group, whilst the substituents may be identical or different, or a 1,2-cycloalkylene group having 4 to 7 carbon atoms optionally substituted by R_c or R_d or by R_c and R_d, or a 1,2-cycloalkenylene group having 4 to 7 carbon atoms, a -CH=N- group optionally substituted by the groups R_c or R_d, wherein the nitrogen atom is linked to one of the nitrogen atoms in formula XVI, or a $-CH_2-NH-$ group optionally substituted by R_c or R_d and
Z_4 represents a nucleophilic leaving group or together with an adjacent methylene group of the group Y", a carbonyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl or dialkoxymethyl group);

l) (to prepare compounds of formula I wherein R_a or R_c represents an E-F-D- group) cyclising a compound of formula XVII

$$R_c - CO - CHR_d - NR_a - CO - NHR_b \qquad (XVII)$$

(wherein
R_a, R_b, R_c and R_d are as defined in claims 1 to 7) which is optionally formed in the reaction mixture and optionally hydrogenating a compound thus obtained;

m) (to prepare compounds of formula I wherein X represents a carbonyl group) reacting a compound of formula XVIII

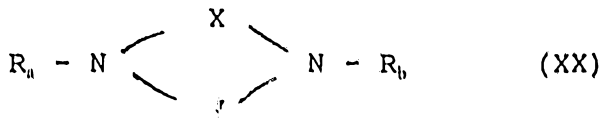
$$R_a - NH - Y - NH - R_b \qquad (XVIII)$$

(wherein
R_a, R_b and Y are as defined in claims 1 to 7) with a compound of formula XIX

$$Z_5 - CO - Z_6 \qquad (XIX)$$

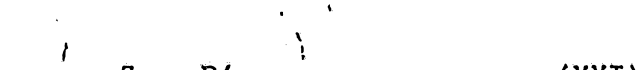
(wherein
Z_5 and Z_6, which may be identical or different, represent nucleophilic leaving groups);

n) (to prepare compounds of formula I wherein R_a, R_b, R_c and R_d are defined as in claims 1 to 7, with the proviso that at least one of the groups R_a and R_b does not represent a hydrogen atom) reacting a compound of formula XX



(XX)

(wherein
X and Y are as hereinbefore defined,
one of the groups R_a or R_b represents a hydrogen atom and the other group R_a or R_b is as defined in claims 1 to 7)
with a compound of formula XXI



(XXI)

(wherein
R′ has the meanings given hereinbefore for R_a or R_b, with the exception of a hydrogen atom, and
Z_7 represents a nucleophilic leaving group),

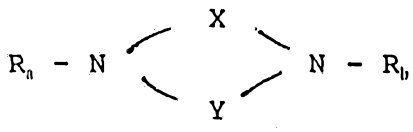
or if R_a or R_b represents a -D-COO-alkyl group with the proviso that there are two carbon atoms between the nitrogen atom of the cyclic urea and the alkoxycarbonyl group, reacting with a compound of formula XXII

(XXII)

(wherein
D′ has the meanings given for D in claims 1 to 7, with the proviso that the alkoxycarbonyl group is immediately

preceded by a carbon-carbon double or triple bond);

o) (to prepare compounds of formula I wherein F represents a carboxy, alkoxycarbonyl, aralkoxycarbonyl or aryloxycarbonyl group) oxidising a compound of formula XXIII



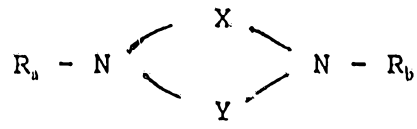
(XXIII)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$CH_2 = CH - E - D -$$

wherein E and D are defined as in claims 1 to 7) with optional subsequent esterification;

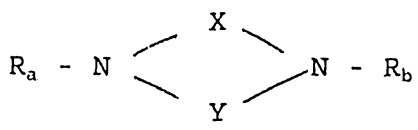
p) (to prepare compounds of formula I wherein F represents an O-alkyl-phosphono group) reacting a compound of formula XXIV



(XXIV)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that F represents a dialkoxyphosphoryl group) with an alkali metal iodide;

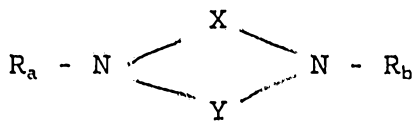
q) (to prepare compounds of formula I wherein F represents a phosphono group) reacting a compound of formula XXV



(XXV)

(wherein
R_a, R_b, X and Y are as hereinbefore defined, with the proviso that F represents an O-alkylphosphono- or dialkoxyphosphoryl group) with an alkali metal iodide in the presence of a trialkylhalosilane;

r) (to prepare compounds of formula I wherein W represents an $R_1N<$ group) reacting a compound of formula XXVI



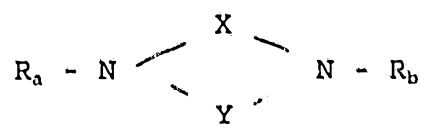
(XXVI)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a Z_8-D"- group, wherein D" represents a C_{1-3}-alkylene group and Z_8 represents a nucleophilic leaving group) with a compound of formula XXVII

$$R_1NH - E' - F \qquad \text{(XXVII)}$$

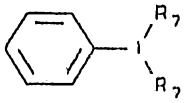
(wherein
F and R_1 are as hereinbefore defined and
E' represents a C_{1-3}-alkylene group);

s) (to prepare compounds of formula I wherein A represents an amino or aminoalkyl group) reacting a compound of formula XXVIII



(XXVIII)

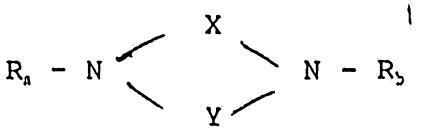
(wherein
R_a, R_b, X and Y are defined as in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents an H_2N-CO-T-B-C group, where B and C are as hereinbefore defined and T represents a bond or a C_{1-5}-alkylene group, with a phenyl iodine(III) compound of formula XXIX



(XXIX)

(wherein
R_7 in each case represents an acyl group or an organic carboxylic acid);

t) (to prepare compounds of formula I wherein A represents an amino or aminoalkyl group substituted by one or two alkyl groups at the nitrogen atom) reacting a compound of formula XXX



(XXX)

(wherein
R_a, R_b, X and Y are defined as in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

A" - B - C -

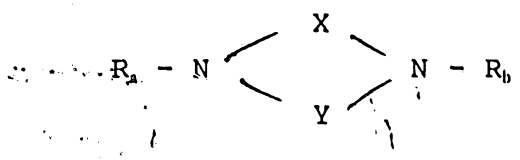
wherein B and C are as defined in claims 1 to 7 and A" represents an amino, alkylamino, aminoalkyl or

alkylaminoalkyl group) with a compound of formula XXXI

$$Z_9 - (R_8\text{-}C\text{-}R_9) - Z_{10} \qquad \text{(XXXI)}$$

(wherein
R_8 and R_9, which may be identical or different, represent hydrogen atoms or alkyl groups,
one of the groups Z_9 or Z_{10} represents a nucleophilic leaving group and
the other group Z_9 or Z_{10} represents a hydrogen atom or an alkyl group or
Z_9 and Z_{10} together represent an oxygen atom);

u) (to prepare compounds of formula I wherein A represents a cyano group) reacting a compound of formula XXXII



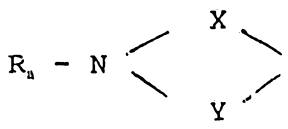
(XXXII)

(wherein
R_a, R_b, X and Y are as defined in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

$$A''' - B - C -$$

wherein B and C are as defined in claims 1 to 7 and
A''' represents a halogen atom) with copper(I)cyanide;

v) (to prepare compounds of formula I wherein A represents an aminoalkyl group where the amino group is not bound to a quaternary carbon atom, or an amino group which is bound to a CH or CH_2 group of group B or C) reducing a compound of formula XXXIII



(XXXIII)

(wherein
R_a, R_b, X and Y are defined as in claims 1 to 7, with the proviso that one of the groups R_a, R_b, R_c and R_d represents a group of the formula

A"" - B - C -

wherein B and C are as hereinbefore defined and A"" contains an N-hydroxy-imino group);

w) resolving a compound of formula I thus obtained into the cis-/trans-isomers, enantiomers and/or diastereomers thereof;

x) converting a compound of formula I into an addition salt thereof, more particularly for pharmaceutical use into a physiologically acceptable salt thereof with an inorganic or organic acid or base, or converting a salt of a compound of formula I into the free compound; and

y) performing a process as defined in any one of steps (a) to (x) above on a corresponding protected compound and subsequently removing the protecting group used.

11. Use of a compound of formula I as claimed in any one of claims 1 to 7 or a physiologically acceptable salt thereof for the manufacture of a therapeutic agent for use in combatting conditions in which cell aggregations or cell-matrix interactions occur.

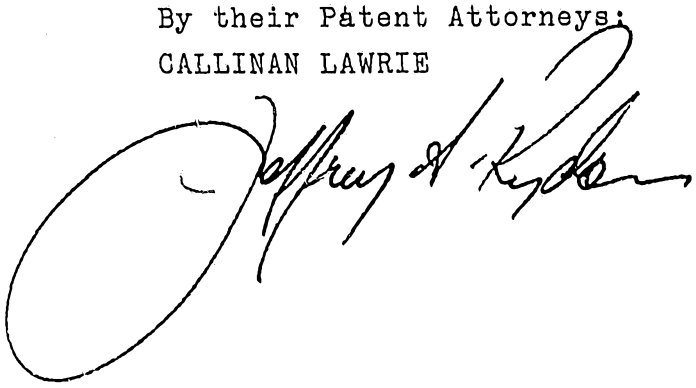
12. A method of treatment of the human or non-human animal body to combat conditions in which cell aggregations or cell-matrix interactions occur, said

method comprising administering to said body a compound of formula I as claimed in any one of claims 1 to 7 or a physiologically acceptable addition salt thereof.

13. A compound of formula I as claimed in claim 1 or a pharmaceutical composition thereof substantially as herein disclosed in any one of the Examples.

DATED THIS 27TH DAY OF JUNE 1994

DR KARL THOMAE GMBH
By their Patent Attorneys:
CALLINAN LAWRIE



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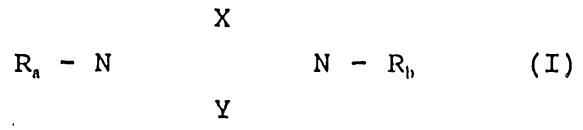
Abstract

Urea Derivatives

The invention relates to cyclic urea derivatives of formula I



(I)

(wherein R_a, R_b, X and Y are defined as in claim 1) and the stereoisomers and salts thereof, compounds which have valuable pharmacological properties, and in particular aggregation-inhibiting effects.