

P247519 JGS:GS 3137T/8

614343

PATENT APPLICATION FORM
COMMONWEALTH OF AUSTRALIA
Patents Act 1952

Regulation 9

We, BAYER AKTIENGESELLSCHAFT

of D-5090 Leverkusen, Bayerwerk, Germany

hereby apply for the grant of a Standard Patent for an invention
entitled ~~NEW COMPOUNDS~~ 1,3,4,5-Tetrahydrobenz (c,d) indoles
which is described in the accompanying complete specification.

For a Convention application - details of basic application-

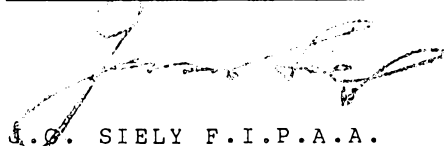
<u>Number</u>	<u>Country</u>	<u>Date of Application</u>
P 38 09 155.0	Germany	18 March 1988

Our address for service is ARTHUR S. CAVE & CO., Patent and Trade
Mark Attorneys, Level 10, 10 Barrack Street, Sydney, New South
Wales, Australia 2000.

Dated this 17th day of March, 1989.

BAYER AKTIENGESELLSCHAFT
By Its Patent Attorneys,
ARTHUR S. CAVE & CO.

5006273 20/03/89


J.G. SIELY F.I.P.A.A.

To:
Commissioner of Patents

ARTHUR S. CAVE & CO.
PATENT AND TRADE MARK ATTORNEYS
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ASC 1

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PATENT DECLARATION FORM (CONVENTION)
COMMONWEALTH OF AUSTRALIA
Patents Act 1952

Regulation
12 (2)

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION
FOR A PATENT

To be signed by the applicant(s) or in the case of a body corporate to be signed by a person authorised by the body corporate.

In support of the Convention application made for a patent for an invention entitled

(a) Insert title of invention.

(a) 1,3,4,5-Tetrahydrobenz[c,d]indoles

(b) Insert full name(s) of declarant(s).

I/We (b) Joachim Gremm and Rudi Mayer

(c) Insert address(es) of declarant(s).

of (c) Bayer Aktiengesellschaft, Leverkusen, Germany

do solemnly and sincerely declare as follows:—

1. I am/We are the applicant(s) for the patent

(OR, IN THE CASE OF AN APPLICATION BY A BODY CORPORATE.)

1. I am/We are authorised by Bayer Aktiengesellschaft

the applicant for the patent to make this declaration on its behalf.

2. The basic application(s) as defined by Section 141 of the Act was/were made in the following country or countries on the following date(s) namely:—

(d) Insert country in which basic application(s) was/were filed.
(e) Insert date of basic application(s).
(f) Insert full names of basic applicant(s).

in (d) Germany on (e) March 18, 1988

by (f) Bayer Aktiengesellschaft

in (d) on (e)

by (f)

in (d) on (e)

by (f)

3. I am/We are the actual inventor(s) of the invention referred to in the basic application.

(OR, WHERE A PERSON OTHER THAN THE INVENTOR IS THE APPLICANT)

(g) Insert full name(s) of actual inventor(s)

3. (g) 1) Bodo Junge 2) Bernd Richter 3) Thomas Glaser
4) Jörg Traber

(h) Insert address(es) of actual inventor(s).

of (h) 1) Spiekern 23, D 5600 Wuppertal 23, Germany
2) Am Katterbach 13, D 5060 Bergisch-Gladbach 2, Germany
3) Meslinerstrasse 21a, D 5064 Roesrath, Germany
4) Loewenburgstrasse 12, D 5204 Lohmar, Germany

is/are the actual inventor(s) of the invention and the facts upon which the applicant(s) is/are entitled to make the application are as follows:

(i) Set out how applicant(s) derive(s) title from actual inventor(s) i.e., assignee of the invention from the actual inventor(s).

(i) The company is the Assignee of the said invention from the said inventors

Attestation or legalization not required.

4. The basic application(s) referred to in paragraph 2 of this Declaration was/were the first application(s) made in a Convention country in respect of the invention the subject of the application.

Declared at Leverkusen this 3rd day of February 1989

To:

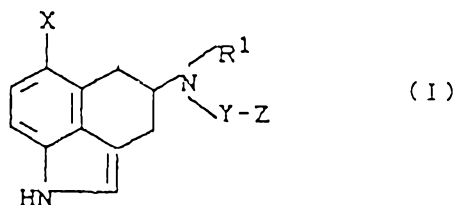
Joachim Gremm
Rudi Mayer

The Commissioner of Patents

(12) PATENT ABRIDGMENT (11) Document No. AU-B-31526/89
 (19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 614343

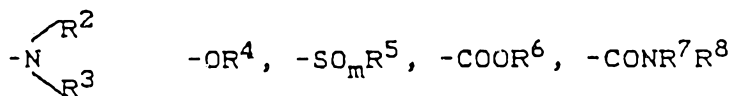
- (54) Title
 1,3,4,5-TETRAHYDROBENZ(C,D) INDOLES
- International Patent Classification(s)
 (51)⁴ C07D 209/90 A61K 031/40 A61K 031/54 C07D 401/12
 C07D 403/12 C07D 417/12 A61K 031/425 A61K 031/445
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- (21) Application No. : 31526/89 (22) Application Date : 20.03.89
- (30) Priority Data
- (31) Number (32) Date (33) Country
 3809155 18.03.88 DE FEDERAL REPUBLIC OF GERMANY
- (43) Publication Date : 28.09.89
- (44) Publication Date of Accepted Application : 29.08.91
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- (72) Inventor(s)
 BODO JUNGE; BERND RICHTER; THOMAS GLASER; JORG TRABER
- (74) Attorney or Agent
 ARTHUR S CAVE & CO , GPO Box 3876, SYDNEY NSW 2001
- (57) Claim

1. 1,3,4,5-Tetrahydrobenz[c,d]indoles of the formula



in which

- R^1 - stands for H, alkyl, aralkyl or heteroarylalkyl,
 X - stands for H, OCH₃, OH, SCH₃, halogen, CN or CONH₂,
 Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms
 and
 Z - stands for cyano or for a group of the formula



where

- R^4 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl,

- alkoxycarbonyl, aryloxycarbonyl or aralkoxycarbonyl
- R^5 - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different halogen, cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy, or for a group of the formula $-NR^7R^8$,
- R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,
- R^7 and R^8 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,
- m - stands for a number 0, 1 or 2,
- R^2 and R^3 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or - for a group of the formula $-COR^9$ or $-SO_2R^{10}$,
wherein
- R^9 - denotes hydrogen, or
- a group NHR^{11} , or
- denotes alkyl or alkoxy, or
- denotes aryl, aralkyl, aralkoxy or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

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(10) 614343

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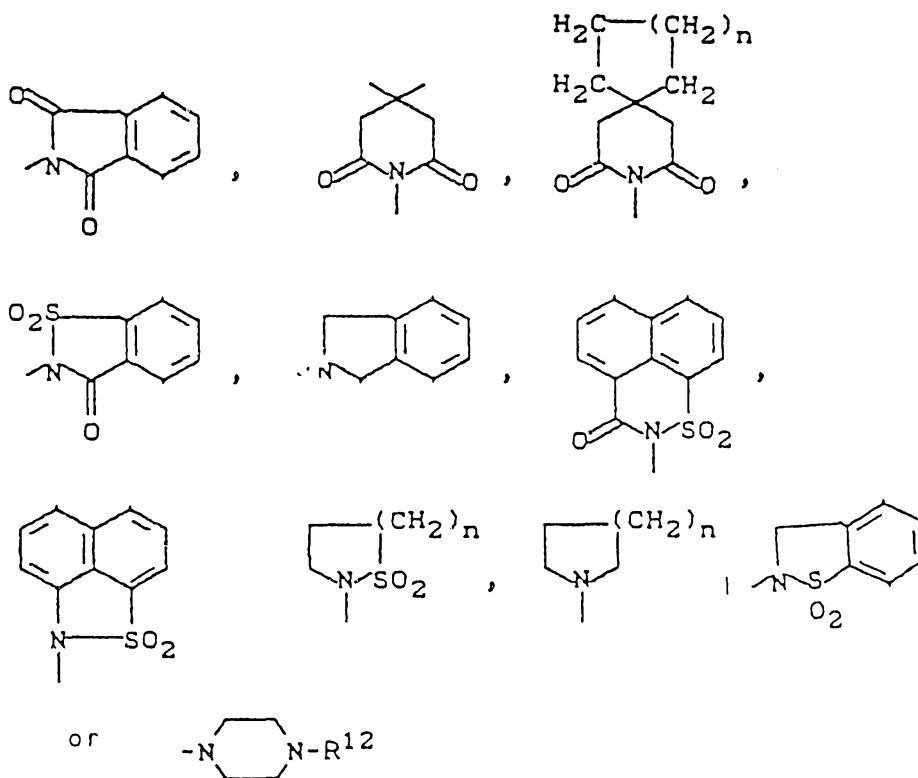
- R^{10} - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoromethoxy or alkoxycarbonyl, or
- denotes aryl, aralkyl or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino, or
 - denotes a group NR^7R^8 ,
where
 R^7 and R^8 have the abovementioned meaning
and
- R^{11} - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or trifluoromethoxy, or
- denotes aryl, aralkyl or heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where

R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising

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wherein

n - denotes a number 1 or 2,

and

R¹² - stands for acyl, alkoxycarbonyl, alkylsulphonyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbomoyl or sulphamoyl

and their salts.

9. A method for the treatment of disorders of the central nervous system which comprises administering, to a subject suffering from or subject to such disorders, a compound according to any one of claims 1 to 3 or a medicament according to claims 7 or 8.

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AUSTRALIA

PATENTS ACT 1952

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority:
Related Art:

TO BE COMPLETED BY APPLICANT

Name of Applicant: BAYER AKTIENGESELLSCHAFT
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AUSTRALIA

Complete Specification for the invention entitled ~~NEW COMPOUNDS.~~
1,3,4,5-Tetrahydrobenz (c,d)indoles
The following statement is a full description of this invention
including the best method of performing it known to me:-

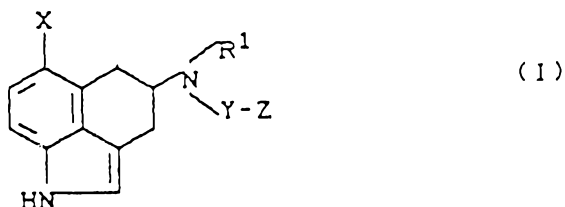


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The invention relates to substituted 1,3,4,5-tetrahydrobenz[*c,d*]indoles, processes for their preparation and their use in medicaments.

From DE 3,346,573, EP 153,083 and EP 162,695 it is already known that 6-substituted 1,3,4,5-tetrahydrobenz[*c,d*]indole-4-amines possess a high affinity for serotonin receptors of the 5-HT₁ type and can be used for the treatment of diseases.

New 6-substituted 4-amino-1,3,4,5-tetrahydrobenz[*c,d*]indoles of the general formula (I),



in which

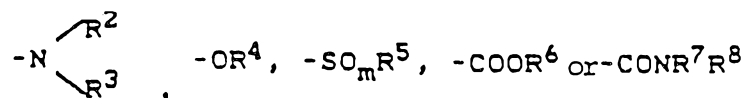
R¹ - stands for H, alkyl, aralkyl or heteroarylalkyl,

X - stands for H, OCH₃, OH, SCH₃, halogen, CN or CONH₂,

Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms

and

Z - stands for cyano or for a group of the formula



where

R⁴ - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy-carbonyl, aryloxy-carbonyl or aralkoxy-carbonyl

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R^5 - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different halogen, cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy, or for a group of the formula $-NR^7R^8$,

R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

R^7 and R^8 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

m - stands for a number 0, 1 or 2,

R^2 and R^3 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or

- for a group of the formula $-COR^9$ or $-SO_2R^{10}$,

wherein

R^9 - denotes hydrogen, or

- a group NHR^{11} , or

- denotes alkyl or alkoxy, or

- denotes aryl, aralkyl, aralkoxy or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

R¹⁰ - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoromethoxy or alkoxy-carbonyl, or
5 - denotes aryl, aralkyl or hetero-aryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino, or
10 - denotes a group NR⁷R⁸,
where
R⁷ and R⁸ have the abovementioned meaning

and

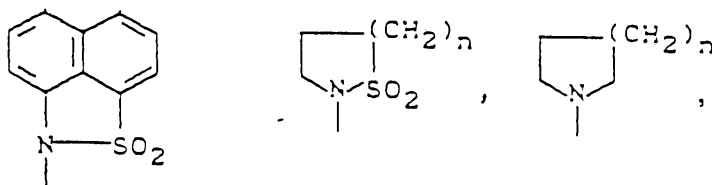
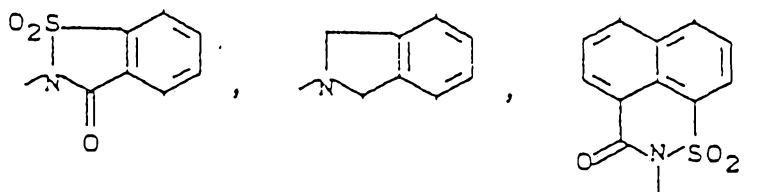
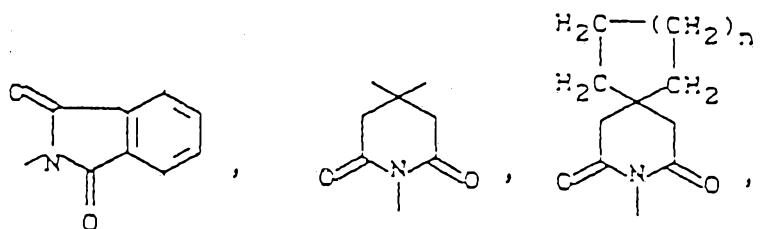
R¹¹ - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or trifluoromethoxy, or
- denotes aryl, aralkyl or heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where

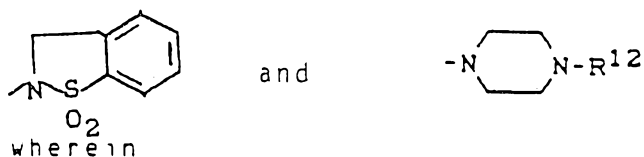
R² and R³, together with the nitrogen atom, form

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a heterocyclic ring from the series comprising



5



wherein

n - denotes a number 1 or 2,

and

R¹² - stands for acyl, alkoxycarbonyl, alkylsulphonyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbamoyl or sulphamoyl

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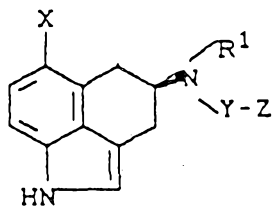
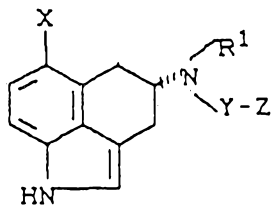
and their salts,
have now been found.

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The substances according to the invention have several asymmetric carbon atoms and can therefore exist in different stereochemical forms. Moreover, compounds having a sulfoxide group can likewise exist in different stereochemical forms. The invention relates to both the individual isomers and their mixtures. For example, the following isomeric forms of the 1,3,4,5-tetrahydrobenz-[c,d]indoles substituted with bases may be made:

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The 1,3,4,5-tetrahydrobenz[c,d]indoles substituted with bases according to the invention can also exist in the form of their salts. In general, salts with inorganic or organic acids may be mentioned here.

In the context of the present invention, physiologically acceptable salts are preferred. Physiologically acceptable salts of the 1,3,4,5-tetrahydrobenz[c,d]indoles substituted with bases can be salts of the substances according to the invention with mineral acids, carboxylic acids or sulphonic acids. For example, salts with hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, ethanesulphonic acid, toluenesulphonic acid, benzenesulphonic acid, naphthalenedisulphonic acid, acetic acid, propionic acid, lactic acid, oxalic acid, malonic acid, succinic acid, maleic acid, fumaric acid, malic acid, tartaric acid, citric acid or benzoic acid are particularly preferred.

The substances according to the invention surprisingly show an advantageous action on the central nervous system and can be used for therapeutic treatment of humans and animals. Compared to the already known structurally related compounds, they are distinguished, above all, by a better tolerability.

Alkyl in general stands for a straight-chain or branched hydrocarbon radical having 1 to 12 carbon atoms. Lower

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alkyl having 1 to about 6 carbon atoms is preferred. Examples which may be mentioned are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, isopentyl, hexyl, isohexyl, heptyl, isoheptyl, octyl and isooctyl.

5 Alkenyl in general stands for a straight-chain or branched hydrocarbon radical having 2 to 12 carbon atoms and one or more, preferably having one or two, double bonds. The lower alkyl radical having 2 to about 6 carbon atoms and one double bond is preferred. An alkenyl radical having
10 2 to 4 carbon atoms and one double bond is particularly preferred. Examples which may be mentioned are allyl, propenyl, isopropenyl, butenyl, isobutenyl, pentenyl, isopentenyl, hexenyl, isohexenyl, heptenyl, isoheptenyl, octenyl and isooctenyl.

15 Cycloalkyl in general stands for a cyclic hydrocarbon radical having 5 to 8 carbon atoms. The cyclopentane and cyclohexane ring are preferred. Examples which may be mentioned are cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

20 Aryl in general stands for an aromatic radical having 6 to about 12 carbon atoms. Preferred aryl radicals are phenyl, naphthyl and biphenyl.

Aralkyl in general stands for an aryl radical having 7 to 14 carbon atoms which is bonded via an alkylene chain.
25 Aralkyl radicals having 1 to 6 carbon atoms in the aliphatic moiety and 6 to 12 carbon atoms in the aromatic moiety are preferred. Examples which may be mentioned are the following aralkyl radicals: benzyl, naphthylmethyl, phenethyl and phenylpropyl.

30 Alkoxy in general stands for a straight-chain or branched hydrocarbon radical having 1 to 12 carbon atoms which is bonded via an oxygen atom. Lower alkoxy having 1 to about 6 carbon atoms is preferred. An alkoxy radical having 1 to 4 carbon atoms is particularly preferred.

35 Examples which may be mentioned are methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, pentoxy,

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isopentoxy, hexoxy, isohexoxy, heptoxy, isoheptoxy, octoxy or isoctoxy.

5 Aryloxy in general stands for an aromatic radical having 6 to about 12 carbon atoms which is bonded via an oxygen atom. Preferred aryloxy radicals are phenoxy or naphthyloxy.

10 Aralkoxy in general stands for an aralkyl radical having 7 to 14 carbon atoms, the alkylene chain being bonded via an oxygen atom. Aralkoxy radicals having 1 to 6 carbon atoms in the aliphatic moiety and 6 to 12 carbon atoms in the aromatic moiety are preferred. Examples which may be mentioned are the following aralkoxy radicals: benzyloxy, naphthylmethoxy, phenethoxy and phenylpropoxy.

15 Acyl stands for phenyl or straight-chain or branched lower alkyl having 1 to about 6 carbon atoms which are bonded via a carbonyl group. Phenyl and alkyl radicals having up to 4 carbon atoms are preferred. Examples which may be mentioned are: benzoyl, acetyl, 20 ethylcarbonyl, propylcarbonyl, isopropylcarbonyl, butylcarbonyl and isobutylcarbonyl.

Alkoxy carbonyl can be represented, for example, by the formula



In this connection, alkyl stands for a straight-chain or branched hydrocarbon radical having 1 to 12 carbon atoms. Lower alkoxy carbonyl having 1 to about 6 carbon atoms in the alkyl moiety is preferred. An alkoxy carbonyl having 30 1 to 4 carbon atoms in the alkyl moiety is particularly preferred. Examples which may be mentioned are the following alkoxy carbonyl radicals: methoxy carbonyl, ethoxy carbonyl, propoxy carbonyl, isopropoxy carbonyl, butoxy carbonyl or isobutoxy carbonyl.

Aryloxy carbonyl can be represented, for example, by the Le A 25 851



formula -COO-aryl. In this connection, aryl in general stands for an aromatic radical having 6 to 12 carbon atoms. Examples which may be mentioned are: phenoxycarbonyl and naphthyloxycarbonyl.

5 Aralkoxycarbonyl can be represented, for example, by the formula -COO-aralkyl. In this connection, aralkyl in general stands for an aryl radical having 7 to 14 carbon atoms which is bonded via an alkylene chain, aralkyl radicals having 1 to 6 carbon atoms in the aliphatic moiety
10 and 6 to 12 carbon atoms in the aromatic moiety being preferred. For example, aralkoxycarbonyl radicals which may be mentioned are: benzyloxycarbonyl and naphthylmethyloxycarbonyl.

Heteroaryl in the scope of the abovementioned definition
15 stands for a 5- to 6-membered aromatic ring which can contain oxygen, sulphur and/or nitrogen as hetero atoms and onto which can be fused a further aromatic ring. 5- and 6-membered aromatic rings which contain one oxygen, one sulphur and/or up to 2 nitrogen
20 atoms and which are optionally fused to benzene are preferred. Heteroaryl radicals which may be mentioned as particularly preferred are: thienyl, furyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, thiazolyl, benzothiazolyl, iso-
25 thiazolyl, oxazolyl, benzoxazolyl, isoxazolyl, imidazolyl, benzimidazolyl, pyrazolyl and indolyl.

Halogen in general stands for fluorine, chlorine, bromine or iodine, preferably for fluorine, chlorine or bromine. Particularly preferably, halogen stands for fluorine or
30 chlorine.

Preferred compounds of the general formula (I) are those in which

35 R^1 - stands for H, C_1 - C_4 -alkyl or benzyl,
X - stands for H, OCH_3 , OH, SCH_3 , F, Cl, Br, CN or $CONH_2$,

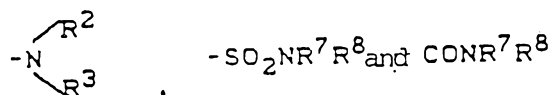
Patent A 25 851



Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms

and

5 z - stands for cyano or for a group of the formula



wherein

R⁷ and R⁸ are identical or different, and

10 - stand for hydrogen, lower alkyl, phenyl, benzyl or phenethyl,

R² and R³ are identical or different and

15 - stand for hydrogen, lower alkyl, phenyl or benzyl, where the phenyl radicals can be substituted by fluorine, chlorine, bromine, lower alkyl, lower alkoxy or trifluoromethyl, or - stand for a group of the formula -COR⁹ or -SO₂R¹⁰,

wherein

20 R⁹ - denotes hydrogen or a group NHR¹¹, or

- denotes lower alkyl or lower alkoxy, or

25 - denotes phenyl, benzyl, benzyloxy, thienyl, furyl, pyridyl, pyrimidyl, quinolyl, isoquinolyl, benzothiazolyl, benzoxazolyl, thiazolyl, oxazolyl, isoxazolyl or isothiazolyl, each of which is optionally substituted by lower alkyl, lower alkoxy, fluorine, chlorine, bromine, trifluoromethyl, dimethylamino or diethylamino,

30 R¹⁰ - denotes lower alkyl which is optionally substituted by cyano, fluorine, chlorine, bromine, trifluoromethyl or lower alkoxy-carbonyl, or

- denotes phenyl, naphthyl, benzyl, thienyl, furyl,

pyrimidyl, pyridyl, quinolyl, isoquinolyl,
 benzothiazolyl, benzoxazolyl, thiazolyl,
 oxazolyl, isoxazolyl or isothiazolyl, each
 of which is optionally substituted by lower
 alkyl, lower alkoxy, fluorine, chlorine,
 bromine, trifluoromethyl, dimethylamino or
 diethylamino, or

- denotes a group NR^7R^8 ,

where

R^7 and R^8 have the abovementioned meaning,

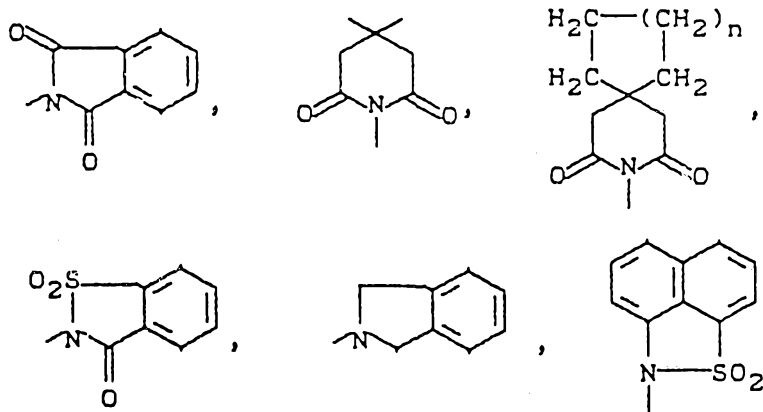
and

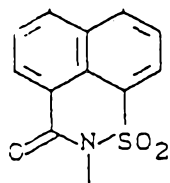
R^{11} - denotes lower alkyl which is optionally
 substituted by cyano, fluorine, chlorine
 or bromine, or

- denotes phenyl, benzyl, thienyl, furyl,
 pyridyl, pyrimidyl, quinolyl, isoquinolyl,
 benzothiazolyl, benzoxazolyl, thiazolyl,
 oxazolyl, isoxazolyl or isothiazolyl, each
 of which is optionally substituted by lower
 alkyl, lower alkoxy, fluorine, chlorine,
 bromine, trifluoromethyl, dimethylamino or
 diethylamino,

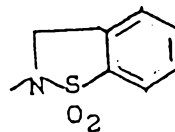
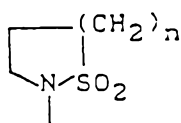
or

R^2 and R^3 , together with the nitrogen atom, form
 a heterocyclic ring from the series comprising





or



wherein

n - denotes a number 1 or 2

and their salts.

5 Particularly preferred compounds of the formula

(I) are those in which

R¹ - stands for H, CH₃, ethyl, n-propyl or benzyl,

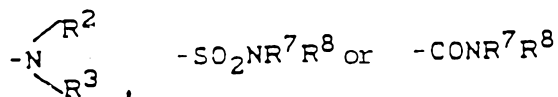
X - stands for H, OCH₃, OH, SCH₃, F, Cl, CN or CONH₂,

Y - stands for a straight-chain alkylene chain having

10 2 to 4 carbon atoms

and

Z - stands for cyano or for a group of the formula



where

15 R⁷ and R⁸ are identical or different and

- stand for hydrogen, methyl, ethyl, propyl, isopropyl, butyl, isobutyl or tert.butyl,

R² and R³ are identical or different, and

20 - stand for hydrogen, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert.butyl or

- stand for phenyl which is optionally substituted by fluorine, chlorine, methyl or methoxy, or

- for a group -COR⁹ or -SO₂R¹⁰,

wherein

25 R⁹ - denotes hydrogen or a group NHR¹¹, or

- denotes methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, propoxy, isopropoxy, or

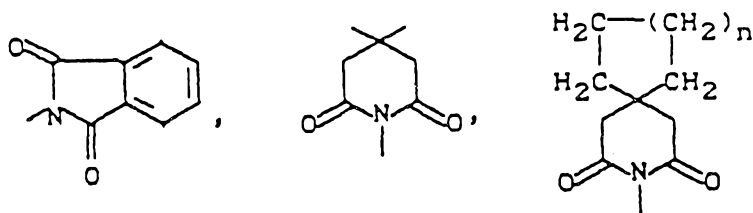
- phenyl, benzyl, benzyloxy, thienyl, furyl, pyridyl, pyrimidyl, quinolyl or isoquinolyl,

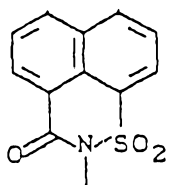
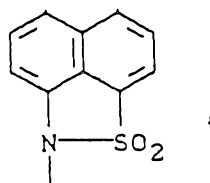
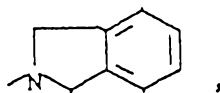
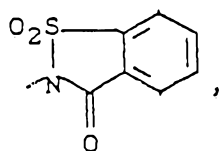
each of which is optionally substituted by methyl, methoxy, fluorine or chlorine,
 R^{10} - denotes methyl, ethyl, propyl, isopropyl, butyl or isobutyl, each of which is optionally substituted by fluorine, chlorine, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl or isobutoxycarbonyl, or
 - denotes phenyl, naphthyl, benzyl, thienyl, furyl, pyridyl, pyrimidyl, quinolyl or isoquinolyl, each of which is optionally substituted by methyl, ethyl, propyl, isopropyl, methoxy, fluorine or chlorine, or
 - denotes a group NR^7R^8 ,
 where
 R^7 and R^8 have the abovementioned meaning,

and

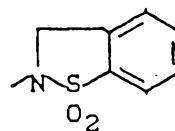
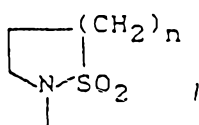
R^{11} - denotes methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, isopentyl, hexyl or isohexyl, each of which is optionally substituted by fluorine or chlorine, or
 - denotes phenyl or benzyl, each of which can be substituted by fluorine, chlorine, methyl or methoxy,

or
 R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising





and



wherein

n - denotes a number 1 or 2

5 and their salts.

Compounds according to the invention which may be mentioned by way of example are:

6-methoxy-4-[4-(N-1,2-benzisothiazol-3(2H)-one-1,1-dioxide-yl)]-butylamino-1,3,4,5-tetrahydrobenz[c,d]indole

10 hydrochloride,

4-[4-(N-1,2-benzisothiazol-3(2H)-one-1,1-dioxide-yl)]-butylamino-1,3,4,5-tetrahydrobenz[c,d]indole,

6-methoxy-4-[N-propyl-N-(ethoxycarbonylaminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole,

15 6-methoxy-4-[N-propyl-N-(methylsulphonylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole,

6-methoxy-4-[N-propyl-N-(butylsulphonylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole,

20 6-methoxy-4-[N-propyl-N-(tosylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride,

6-methoxy-4-[N-propyl-N-(2-naphthylsulphonylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride,

6-methoxy-4-[N-propyl-N-(1-phenylureidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole,

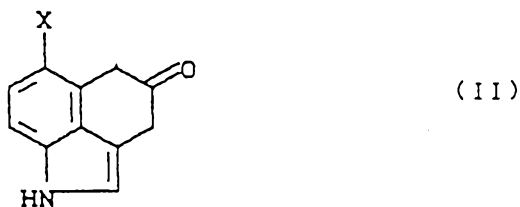
25 6-methoxy-4-(dimethylsulphamoyl)ethyl-amino-1,3,4,5-tetrahydrobenz[c,d]indole,

6-methoxy-4-[N-propyl-N-(dimethylsulphamoyl)ethyl]-amino-

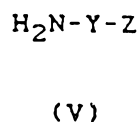
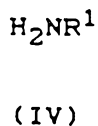
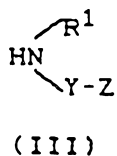
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1,3,4,5-tetrahydrobenz[c,d]indole,
 6-methoxy-4-(methylsulphonylamidopropyl)-amino-1,3,4,5-
 tetrahydrobenz[c,d]indole hydrochloride,
 6-methoxy-4-[N-benzyl-N-(methylsulphonylamidopropyl)]-
 5 amino-1,3,4,5-tetrahydrobenz[c,d]indole,
 6-methoxy-4-(4-fluorophenylsulphonylamidopropyl)-amino-
 1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride,
 6-methoxy-4-[N-benzyl-N-(4-fluorophenylsulphonylamido-
 propyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole.

10 It has furthermore been found that compounds of
 the formula (I) are obtained by
 reductive amination [A] of ketones of the formula (II)



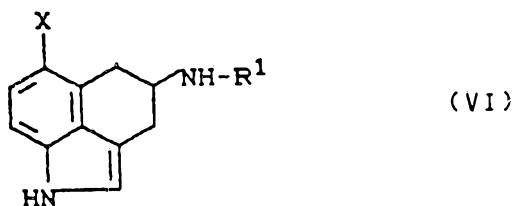
15 in which X has the abovementioned meaning,
 with amines of the formula (III), (IV) or (V)



in which R¹, Y and Z have the abovementioned meanings.

In addition, compounds of the general formula (I)
 are obtained

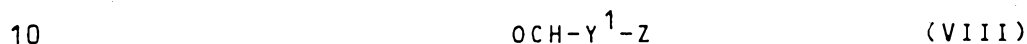
20 when
 compounds of the general formula (VI)



in which R¹ and X have the abovementioned meanings,
are reacted [B] with alkylating agents of the formula
(VII)



5 in which Y and Z have the abovementioned meanings, and L
denotes a leaving group customary in alkylating agents,
such as Cl, Br, I, OTs, OMs or OSO₂CF₃,
or reductively alkylated [C] with aldehydes of the formula
(VIII)



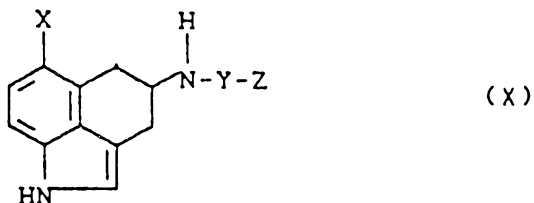
in which Z has the abovementioned meaning and Y¹ is an
alkylene chain Y shortened by one methylene group,
or reacted with reactive acid derivatives of the general
formula (IX)



in which Y¹ and Z have the abovementioned meanings and
M denotes a leaving group customary in acylating agents,
such as chlorine, bromine, alkoxy, aryloxy, imidazolyl,
thiazolyl, methanesulphonyloxy or alkoxycarbonyloxy, and
20 the acid amides obtained are reduced [D] catalytically
with hydrogen or with complex metal hydrides to give com-
pounds of the formula (I).

Compounds of the formula (I) are also obtained
when

25 compounds of the formula (X)



in which X, Y and Z have the abovementioned meanings,
are alkylated [E] with alkylating agents of the formula
(XI)



in which R¹ and L have the abovementioned meanings,
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or reductively alkylated [F] with aldehydes of the formula (XII)



in which R^{13} is a radical R^1 shortened by one methylene group,

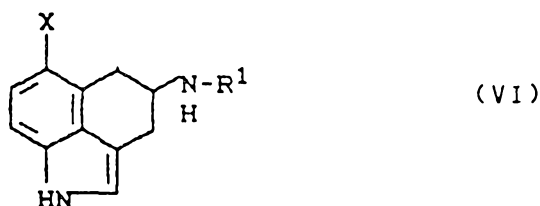
or reacted with reactive acid derivatives of the general formula (XIII)



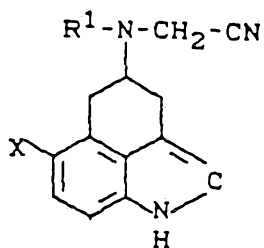
in which R^{13} and M have the abovementioned meanings, and the acid amides obtained are reduced [G] catalytically with hydrogen or with complex metal hydrides to give compounds of the formula (I).

In addition, compounds of the formula (I) are obtained from compounds of the formula (VI) by first reacting the latter stepwise by alkylation or reductive alkylation to give intermediates having suitable functional groups and then converting [H] these intermediates into compounds of the formula (I) by modification of the functional groups by oxidation, reduction, hydrolysis or reaction with electrophilic reagents.

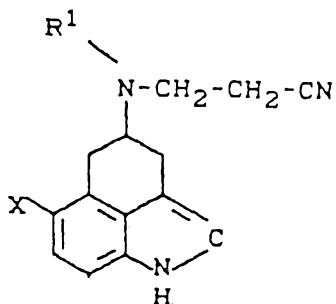
For example, the compounds of the formula (VI)



in which X and R^1 have the abovementioned meanings, are alkylated with chloroacetonitrile or acrylonitrile to give compounds of the formulae (XIV) and (XV)

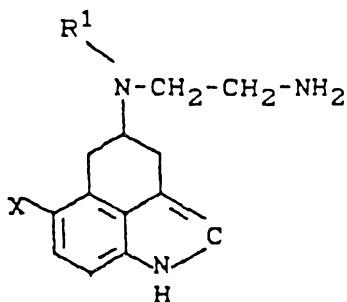


(XIV)

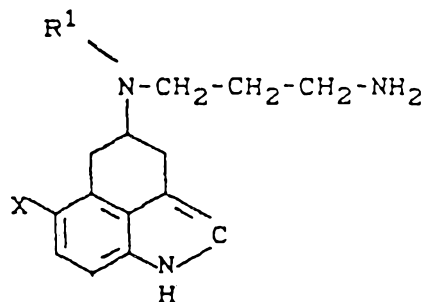


(XV)

the nitriles obtained are hydrogenated to give the amines (XVI) and (XVII)



(XVI)

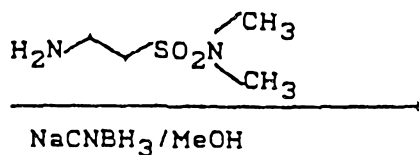
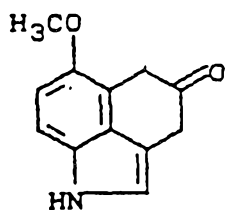


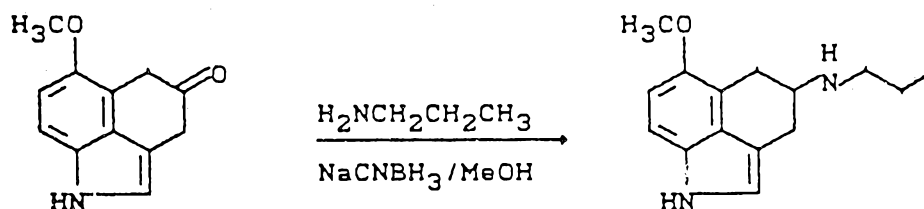
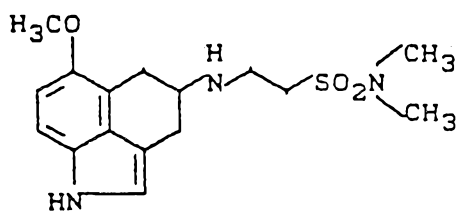
(XVII)

5 and these are converted into compounds of the formula (I) according to the invention in a manner known per se by alkylation, reductive alkylation, acylation, reaction with isocyanates or sulphonylation.

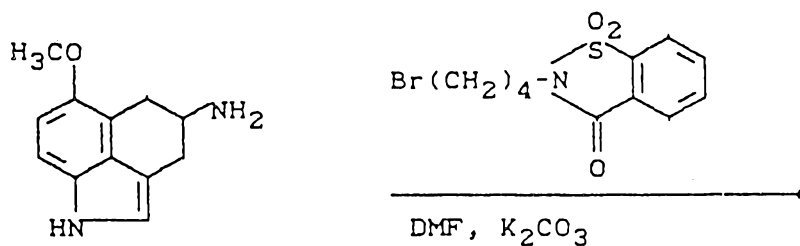
10 The following reaction schemes serve to illustrate by way of example the process for the preparation of compounds of the formula (I).

Process A

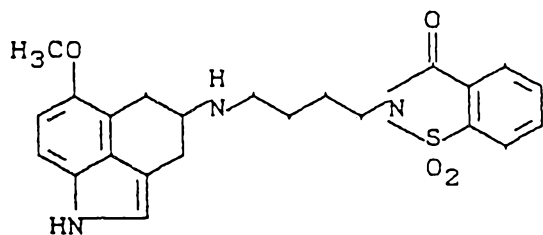




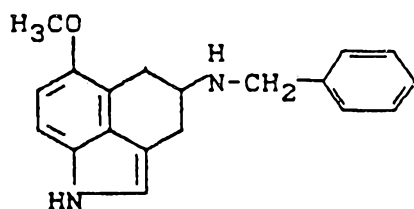
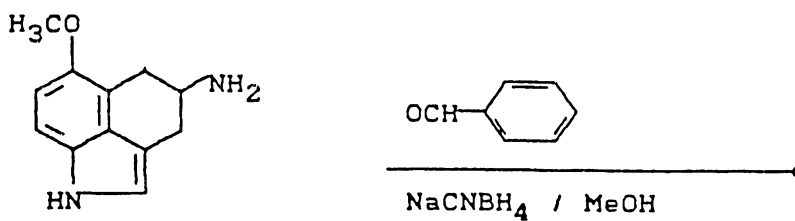
Process B



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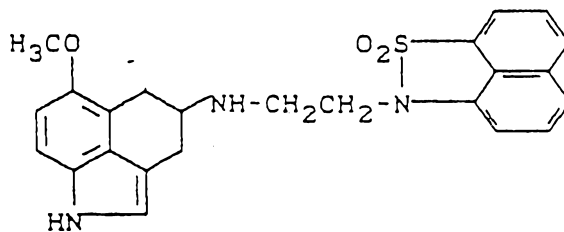
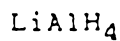
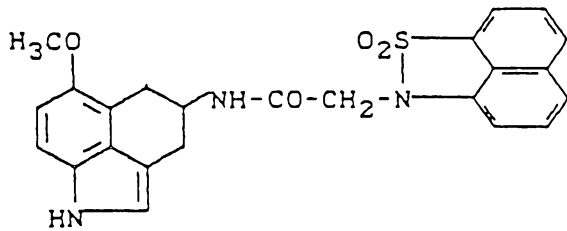
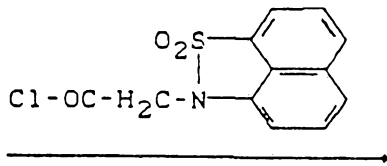
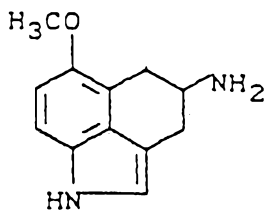


Process C

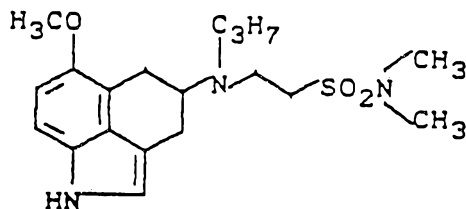
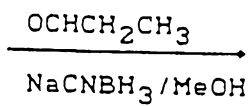
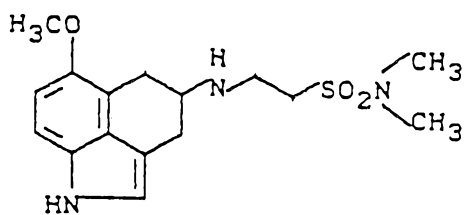


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Process D



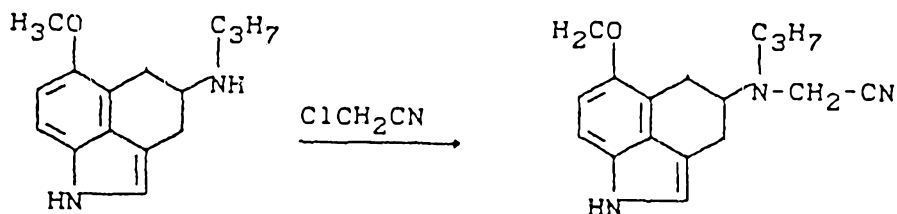
5 Process F



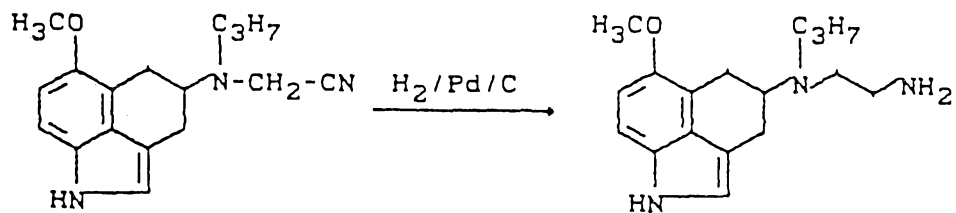
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Process H

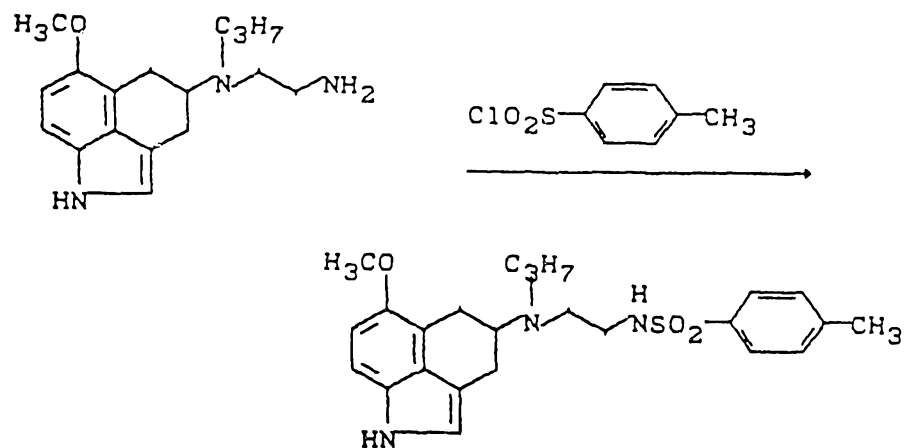
(1)



(2)



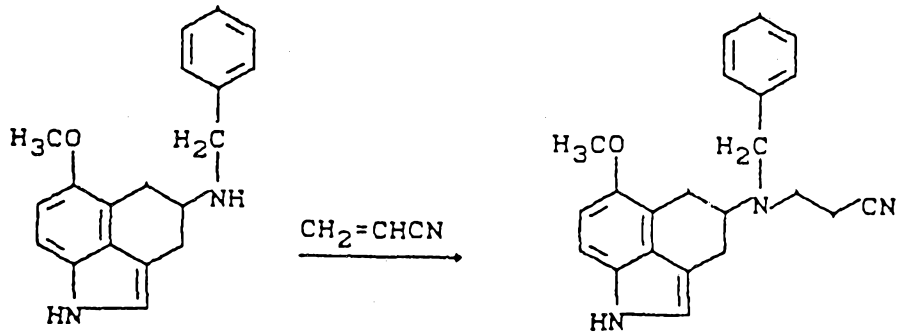
(3)



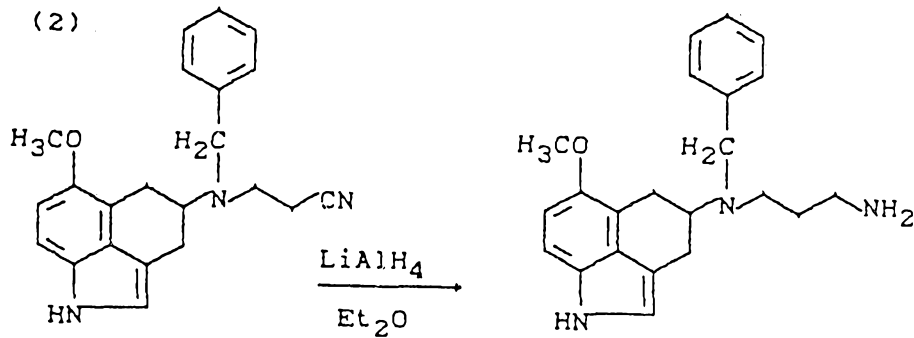
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Process H

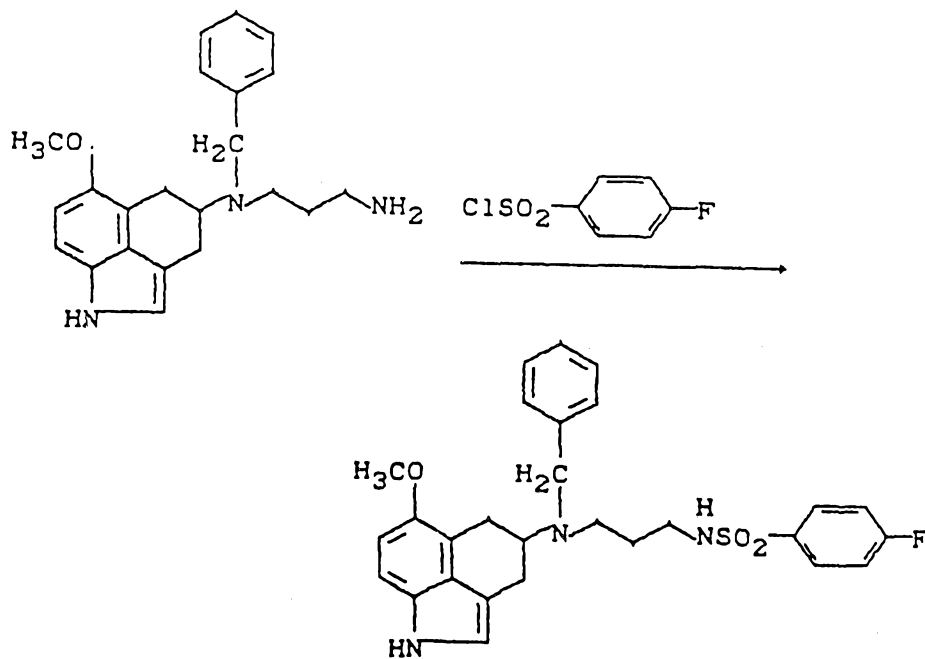
(1)



(2)



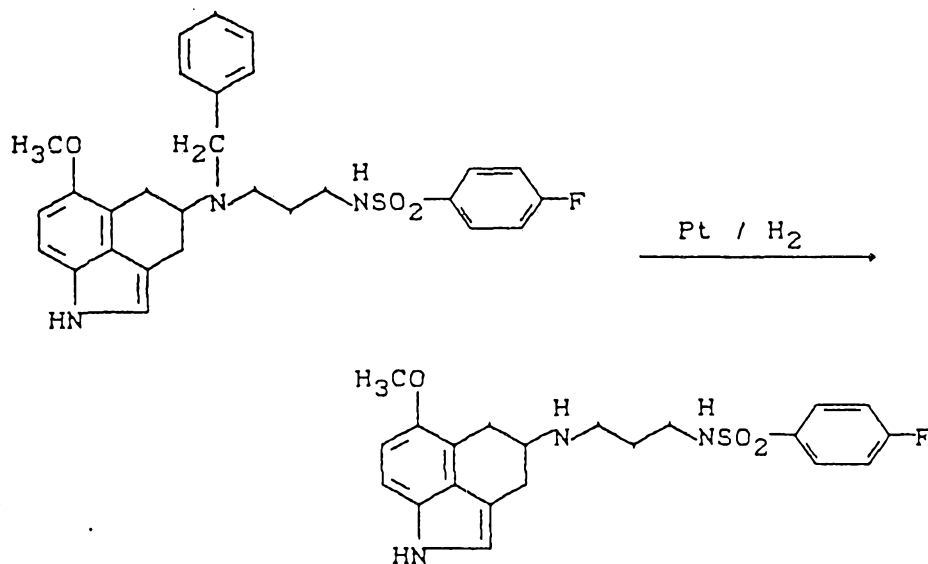
(3)



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(4)



The ketones of the general formula (II) used as starting materials are known or can be prepared by known methods [EP 0,162,695 and EP 0,153,083].

The amines of the general formula (III), (IV) and (V) used as starting materials are known or can be prepared by known methods [Houben-Weyl's "Methoden der organischen Chemie" ("Methods of Organic Chemistry") volume XI/1 and XI/2].

The preparation of the Schiff's bases or enamines by reaction of the tetralones (II) with amines (III) takes place in inert organic solvents, if appropriate in the presence of a catalyst and if appropriate in the presence of a water-binding agent.

The process according to the invention can be carried out in two steps, i.e. with isolation of the enamines. It is similarly possible to carry out the process according to the invention as a one-pot process.

Inert solvents which are suitable in this case are the customary organic solvents which do not change under the reaction conditions. These preferably include alcohols such as methanol, ethanol, propanol or

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isopropanol, or ethers such as diethyl ether, butyl methyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or diethylene glycol dimethyl ether, or halogenated hydrocarbons such as, for example, methylene chloride, chloroform or carbon tetrachloride, or hydrocarbons such as benzene, toluene, xylene, or mineral oil fractions, or amides such as dimethylformamide or hexamethylphosphoric triamide, or acetic acid. In addition, it is possible to use mixtures of the solvents mentioned.

In general, acids are used as catalysts. These preferably include inorganic acids such as, for example, hydrochloric acid or sulphuric acid, or organic sulphonic or carboxylic acids such as, for example, methanesulphonic acid, ethanesulphonic acid, benzenesulphonic acid, toluenesulphonic acid, acetic acid or propionic acid.

The water formed in the reaction can be removed, if desired, mixed with the solvent used during or after the reaction, for example by distillation or by addition of water-binding agents, such as, for example, phosphorus pentoxide or preferably by molecular sieve.

The reaction may be carried out in a temperature range from 0°C to +150°C, more preferably from +20°C to +100°C.

The reaction can be carried out at atmospheric, elevated and at reduced pressure (for example 0.5-5 bar). In general, the reaction is carried out at atmospheric pressure.

When carrying out the reaction, the starting substances may be employed in a molar ratio of tetralone (II) to amine (III) of 0.5:2 to 1:1. Molar amounts of the reactants are, more preferably used.

The reduction of the enamines either takes place by means of hydrogen in water or inert organic solvents such as alcohols, ethers or halogenated hydrocarbons, or their mixtures, using catalysts such as Raney nickel, palladium, palladium on animal charcoal or platinum, or else

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using hydrides in inert solvents, if appropriate in the presence of a catalyst.

Preferably, the reaction is carried out using hydrides, such as complex borohydrides or aluminium hydrides. Sodium borohydride, lithium aluminium hydride or sodium cyanoborohydride are particularly preferably employed in this case.

Suitable solvents in this case are all inert organic solvents which do not change under the reaction conditions. These preferably include alcohols such as methanol, ethanol, propanol or isopropanol, or ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or diethylene glycol dimethyl ether, or amides such as hexamethylphosphoric triamide, or dimethylformamide or acetic acid. It is likewise possible to use mixtures of the solvents mentioned.

Acids are in general used as catalysts in the reduction with sodium cyanoborohydride. These preferably include inorganic acids such as, for example, hydrochloric acid or sulphuric acid or organic carboxylic acids or sulphonic acids, such as, for example, acetic acid, trifluoroacetic acid, trichloroacetic acid, methanesulphonic acid, ethanesulphonic acid, benzenesulphonic acid or toluenesulphonic acid.

When carrying out the process according to the invention, it has proved favourable to carry out the reaction of the tetralones (II) with the amines (III) as a one-pot process in an inert solvent, preferably in ethyl acetate or in alcohols such as, for example, methanol, ethanol, propanol or isopropanol, or their mixtures in the presence of reducing agent, preferably complex hydrides such as, for example, sodium borohydride or sodium cyanoborohydride, if appropriate in the presence of a dehydrating agent, preferably molecular sieve.

Preferably, the reaction is carried out at atmospheric pressure in a temperature range from 0°C to

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+150°C, specifically from 0°C to +100°C. It is likewise possible to carry out the reaction at underpressure or at overpressure (for example in a bomb tube).

5 If the process according to the invention is carried out as a one-pot reaction, it has proved favourable to employ the amine in an excess of up to 10-fold, preferably in an excess of up to 5-fold, over the tetralone.

10 The amines of the formula (VI) and (X) are known (EP 0,162,695 and EP 0,153,083) or can be prepared by known processes from the ketones of the formula (II) or amines of the formula (VI) ($R^1 = H$) by reductive amination, or by alkylation or reductive alkylation.

15 The customary organic solvents, which do not change under the reaction conditions, can be used here as solvents for the reaction of the amines (VI) and (X) with the alkylating agents (VII) and (XI). These preferably include alcohols such as methanol, ethanol, propanol or isopropanol, or ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or butyl methyl
20 ether, or ketones such as acetone or butanone, or amides such as dimethylformamide or hexamethylphosphoric triamide, or dimethyl sulphoxide, acetonitrile, ethyl acetate, or halogenated hydrocarbons such as methylene chloride, chloroform or carbon tetrachloride, or pyridine, picoline
25 or N-methylpiperidine. Mixtures of the solvents mentioned can likewise be used.

Suitable bases are the customary inorganic or organic bases. These preferably include alkali metal hydroxides such as, for example, sodium hydroxide or
30 potassium hydroxide, or alkali metal carbonates such as sodium carbonate or potassium carbonate, or alkali metal alkoxides such as, for example, sodium methoxide or potassium methoxide, or sodium ethoxide or potassium ethoxide, or organic amines such as triethylamine, picoline or
35 N-methylpiperidine, or amides such as sodium amide or lithium diisopropylamide, or organometallic compounds such

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as butyllithium or phenyllithium.

The reaction may be carried out in a temperature range from 0°C to +150°C, more preferably from room temperature to +80°C.

5 The reaction is in general carried out at atmospheric pressure. However, it is likewise possible to carry out the reaction at elevated or reduced pressure.

Alkali metal iodides, preferably sodium iodide or potassium iodide, are in general employed as reaction
10 accelerators.

The base in this connection may be employed in an amount from 1 to 5, more preferably from 1 to 2, moles relative to 1 mole of the halogen compound. The halogen compound is preferably employed in an excess of up to 10-fold, preferably in an excess of up to 5-fold, over the alkyl-
15 substituted 2-aminotetralin (Ib).

The reductive alkylation of the amines (VI) and (X) with the aldehydes (VIII) and (XII) in general takes place in one step. If the amine (VI) is a primary amine,
20 the reaction can also be carried out as two steps, a Schiff's base or an enamine being obtained first.

The preparation of the Schiff's bases or enamines in the first step takes place in inert organic solvents, if appropriate in the presence of a catalyst and if appropriate in the presence of a water-binding agent. The
25 process according to the invention can be carried out in 2 steps, i.e. with isolation of the intermediates. It is likewise possible to carry out the reduction as a one-pot process.

30 The customary organic solvents which do not change under the reaction conditions are suitable as inert solvents in this connection. These preferably include alcohols such as methanol, ethanol, propanol or isopropanol, or ethers such as diethyl ether, butyl methyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or diethyl-
35 ene glycol diethyl ether, or halogenated hydrocarbons

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such as, for example, methylene chloride, chloroform or carbon tetrachloride, or hydrocarbons such as benzene, toluene, xylene, or mineral oil fractions, or amides such as dimethylformamide or hexamethylphosphoric triamide or
5 acetic acid. In addition, it is possible to use mixtures of the solvents mentioned.

Protonic acids are in general used as catalysts. These preferably include inorganic acids such as, for example, hydrochloric acid or sulphuric acid, or organic
10 carboxylic acids having 1-6 C-atoms, if appropriate substituted by fluorine, chlorine and/or bromine, such as, for example, acetic acid, trifluoroacetic acid, trichloroacetic acid or propionic acid, or sulphonic acids having
15 C₁-C₄-alkyl radicals or having aryl radicals such as, for example, methanesulphonic acid, ethanesulphonic acid, benzenesulphonic acid or toluenesulphonic acid.

The water formed in the reaction can be removed, if desired, mixed with the solvent used during or after the reaction, for example by distillation or by addition
20 of water-binding agents, such as, for example, phosphorus pentoxide or, preferably by molecular sieve.

The reaction may be carried out in a temperature range from 0°C to 150°C, more preferably from +20°C to +100°C.

25 The reaction can be carried out at atmospheric, elevated and at reduced pressure (for example 0.5-5 bar). In general, the reaction is carried out at atmospheric pressure.

30 When carrying out the reaction, the compound (V) is preferably employed in an amount of 0.1-10, more preferably of 0.5-5, moles relative to 1 mole of monosubstituted basic 2-aminotetralin (Ic).

The reduction of the Schiff's bases or enamines in the second step either takes place by means of hydrogen
35 in water or in inert organic solvents such as alcohols, ethers or halogenated hydrocarbons, or their mixtures, with
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catalysts such as Raney nickel, palladium, palladium on animal carbon or platinum, or with hydrides in inert solvents, if appropriate in the presence of a catalyst.

5 Preferably, the reaction is carried out using hydrides, such as complex borohydrides or aluminium hydrides. Sodium borohydride, lithium aluminium hydride or sodium cyanoborohydride are particularly preferably employed in this connection.

10 All inert organic solvents which do not change under the reaction conditions are suitable as solvents in this connection. These preferably include alcohols such as methanol, ethanol, propanol or isopropanol, or ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether, or diethylene glycol dimethyl ether or
15 amides such as hexamethylphosphoric triamide or dimethylformamide, or acetic acid. It is likewise possible to use mixtures of the solvents mentioned.

20 Protonic acids are in general used as catalysts in the reduction using sodium cyanoborohydride. These preferably include inorganic acids such as, for example, hydrochloric acid or sulphuric acid, or organic carboxylic acids having 1-6 C-atoms, if appropriate substituted by fluorine, chlorine and/or bromine, such as, for example, acetic acid, trifluoroacetic acid, trichloroacetic acid
25 or propionic acid, or sulphonic acids having C₁-C₄-alkyl radicals or having aryl radicals such as, for example, methanesulphonic acid, ethanesulphonic acid, benzenesulphonic acid or toluenesulphonic acid.

30 When carrying out the process according to the invention, it has proved favourable to carry out the reaction of the aldehydes (VIII) and (XII) with the amines (VI) and (X) as a one-pot process in an inert solvent, preferably in acetic acid or alcohols such as, for example, methanol, ethanol, propanol or isopropanol or their
35 mixtures, in the presence of inorganic or organic acids such as, for example, hydrochloric acid or acetic acid,

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and in the presence of a reductant, preferably of complex hydrides such as, for example, sodium borohydride or sodium cyanoborohydride, if appropriate in the presence of a dehydrating agent, preferably molecular sieve.

5 In this case, the reaction may be carried out at atmospheric pressure in a temperature range from 0°C to +150°C, more preferably from 0°C to +100°C. It is likewise possible to carry out the reaction at underpressure or at overpressure (for example in a bomb tube).

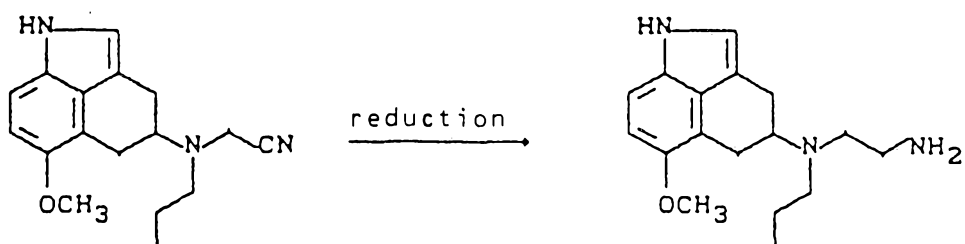
10 The conversion of functional groups into other functional groups in the abovementioned preparation processes takes place, depending on the type of the functional groups, by oxidation, reduction, hydrolysis or by reaction with electrophilic reagents and is illustrated in the following.

15 1. The reduction of the nitrile group to the amino group in general takes place using metal hydrides, preferably using lithium aluminium hydride, aluminium hydride (prepared, for example, by reaction of lithium aluminium hydride with 100% strength sulphuric acid or with aluminium chloride) or their mixtures in inert solvents such as ethers or chlorinated hydrocarbons, preferably in ethers such as, for example, tetrahydrofuran, diethyl ether or dioxane in a temperature range from -20°C to +100°C, preferably from 0°C to +50°C at atmospheric pressure.

20 The reduction is additionally possible by hydrogenating the nitriles in inert solvents such as alcohols, for example methanol, ethanol, propanol or isopropanol in the presence of a noble metal catalyst such as platinum, palladium, palladium on animal carbon or Raney nickel, in a temperature range from 0°C to +150°C, preferably from room temperature to +100°C at atmospheric pressure or at overpressure.

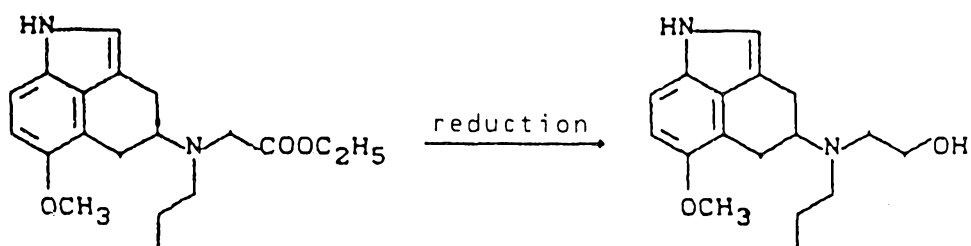
30 The reaction can be illustrated by the following equation:

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2. The reduction of alkoxy-carbonyl groups to alcohol groups in general takes place using hydrides, preferably using lithium aluminium hydride in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons or their mixtures, preferably in ethers such as, for example, diethyl ether, tetrahydrofuran or dioxane in a temperature range from 0°C to +150°C, preferably from +20°C to +100°C at atmospheric pressure.

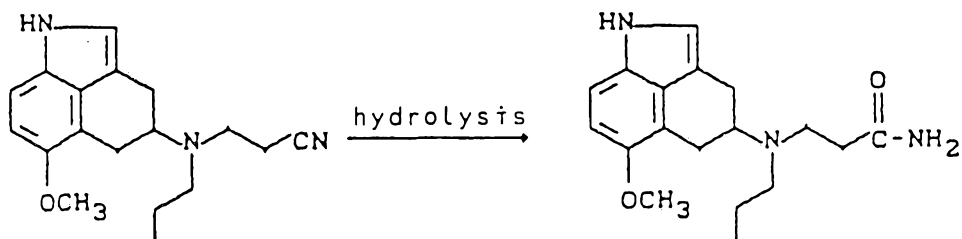
The reaction can be illustrated by the following equation:



3. The hydrolysis of the nitrile group to the carboxamide group in general takes place with the aid of strong mineral acids, preferably using hydrogen chloride in inert solvents such as water and/or alcohols such as, for example, methanol, ethanol, propanol or isopropanol in a temperature range from 0°C to +150°C, preferably from +20°C to +100°C at atmospheric pressure.

The reaction can be illustrated by the following equation:

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4. By the reaction of NH- or OH-acidic compounds (Z in formula (I) is equivalent to OH or NR^2R^3 , where R^2 is H and R^3 is H, alkyl, aryl or aralkyl) with electrophilic reagents, a large number of additional compounds according to the invention are obtained:

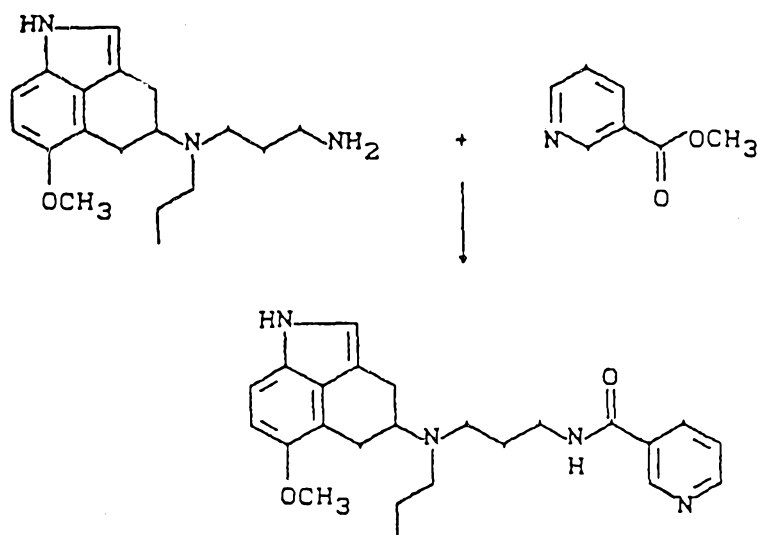
a) The conversion of amines into carboxamides in general takes place by reaction with carboxylic acid esters in inert solvents such as ethers or their mixtures or hydrocarbons, preferably in ethers such as, for example, diethyl ether, tetrahydrofuran or dioxane, if appropriate in the presence of bases such as alkali metals, alkali metal hydrides, alkali metal alkoxides or organolithium compounds, preferably in the presence of alkali metals such as, for example, sodium or alkali metal hydrides such as sodium hydride or potassium hydride in a temperature range from $+20^{\circ}\text{C}$ to $+150^{\circ}\text{C}$, preferably at the boiling point of the solvent used at atmospheric pressure.

Moreover, it is possible to prepare the amides using carboxylic acid halides or anhydrides, preferably using carboxylic acid chlorides in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons or their mixtures, preferably in ethers such as, for example, diethyl ether, tetrahydrofuran, or halogenated hydrocarbons such as methylene chloride or chloroform, if appropriate in the presence of bases such as alkali metal carbonates, for example sodium carbonate or potassium carbonate, or organic amines such as, for example, triethylamine

or pyridine, in a temperature range from -20°C to $+100^{\circ}\text{C}$, preferably from 0°C to $+60^{\circ}\text{C}$ at atmospheric pressure.

The reaction can be illustrated by the following equation:

5



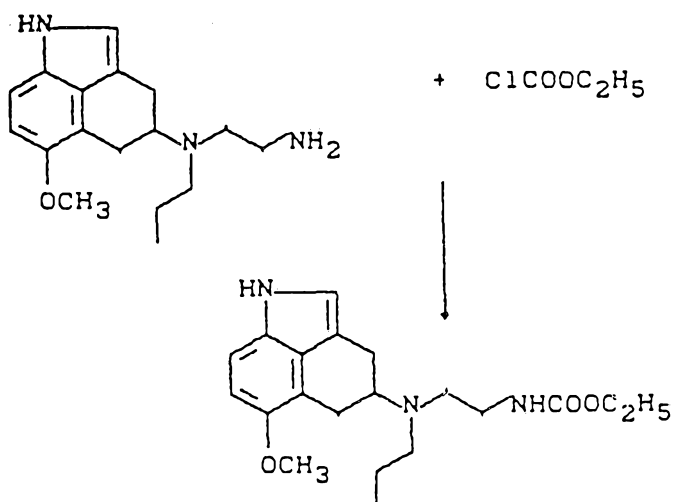
b) The conversion of amines into carbamates in general takes place using carbonic acid esters, preferably using carbonic acid esters which carry a phenyl ester radical or using chlorocarbonic acid esters, in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons or their mixtures, preferably in ethers such as, for example, diethyl ether, tetrahydrofuran or dioxane, in a temperature range from $+20^{\circ}\text{C}$ to $+150^{\circ}\text{C}$, preferably from $+20^{\circ}\text{C}$ to $+100^{\circ}\text{C}$ at atmospheric pressure. The reaction can also be carried out in a two-phase system, where the aqueous phase contains an auxiliary base such as sodium carbonate or potassium carbonate or sodium hydrogen carbonate or potassium hydrogen carbonate.

10

15

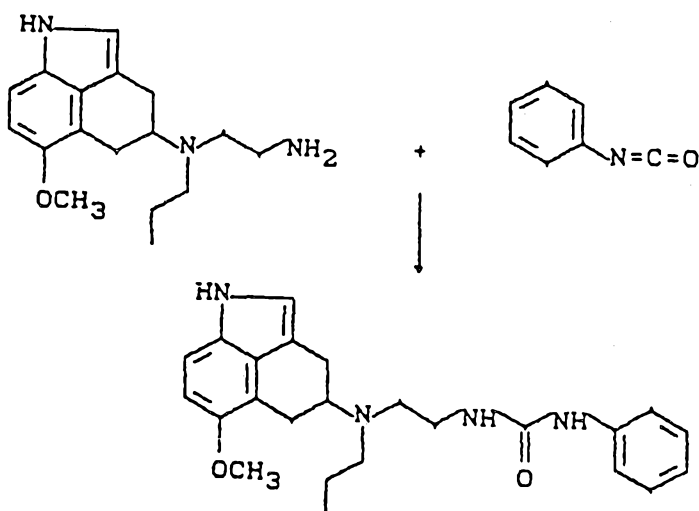
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The reaction can be illustrated by the following equation:



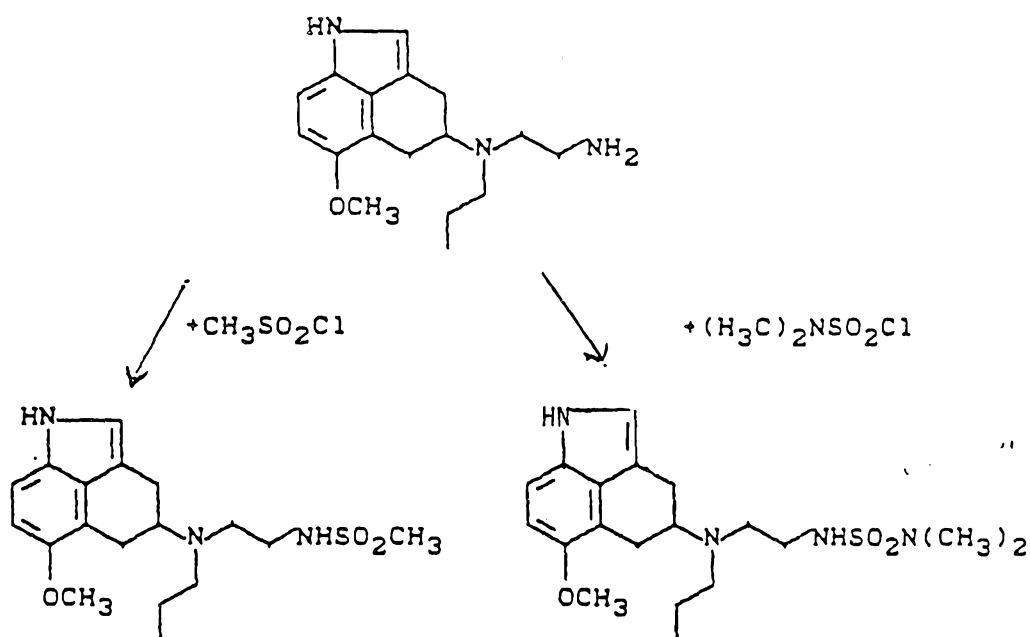
c) The conversion of amines into ureas in general takes place by reaction with isocyanates in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons or their mixtures, preferably in ethers such as, for example, diethyl ether or tetrahydrofuran, or in halogenated hydrocarbons such as, for example, methylene chloride or chloroform, in a temperature range from -20°C to $+150^{\circ}\text{C}$, preferably from 0°C to $+100^{\circ}\text{C}$ at atmospheric pressure.

The reaction can be illustrated by the following equation:



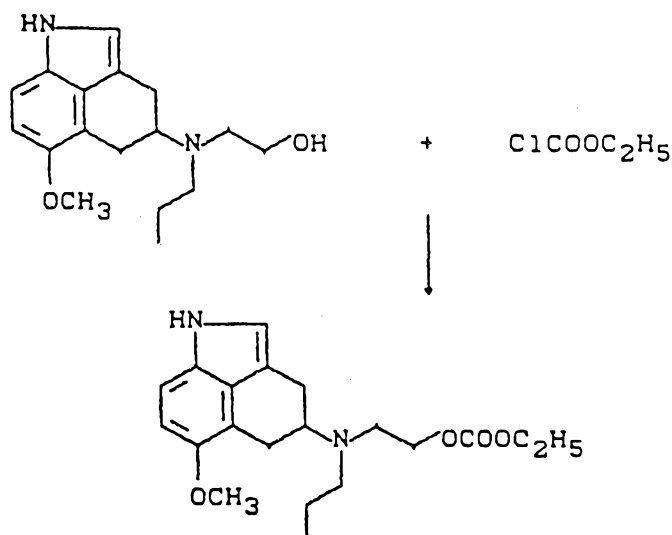
d) The conversion of amines into sulphonamides or aminosulphamoyl derivatives in general takes place using sulphonyl halides or using amidosulphonyl halides, preferably using the corresponding chlorides in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons or their mixtures, preferably in halogenated hydrocarbons such as, for example, methylene chloride or chloroform, if appropriate in the presence of bases such as alkali metal hydroxides, alkali metal carbonates, alkali metal alkoxides or organic amines, preferably using alkali metal hydroxides such as sodium hydroxide or potassium hydroxide, alkali metal carbonates such as, for example, sodium carbonate or potassium carbonate, or organic amines such as triethylamine or pyridine, in a temperature range from -20°C to $+100^{\circ}\text{C}$, preferably from 0°C to $+50^{\circ}\text{C}$ at atmospheric pressure.

The reaction can be illustrated by the following equation:



e) The conversion of the hydroxyl group to carbonic acid esters in general takes place by reacting with halogenoformic acid esters, preferably with chloroformic acid esters in inert solvents such as ethers, hydrocarbons or halogenated hydrocarbons, preferably in halogenated hydrocarbons such as methylene chloride or chloroform, or in ethers such as diethyl ether or tetrahydrofuran, if appropriate in the presence of bases such as alkali metal hydroxides, alkali metal carbonates or organic amines, preferably in the presence of organic amines such as triethylamine, pyridine, picoline or dimethylaminopyridine in a temperature range from -20°C to $+100^{\circ}\text{C}$, preferably from 0°C to room temperature at atmospheric pressure.

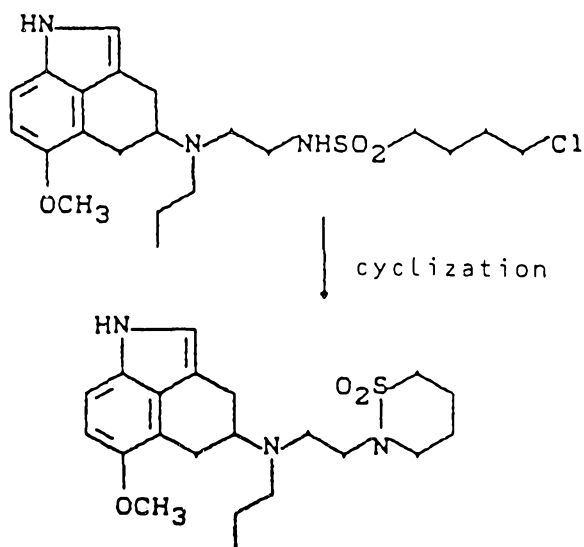
The reaction can be illustrated by the following equation:



f) Cyclic sulphonamides are in general prepared by reaction of intramolecular electrophiles in inert dipolar aprotic solvents, preferably in dimethylformamide, hexamethylphosphoric triamide or dimethyl sulphoxide, if appropriate in the presence of bases such

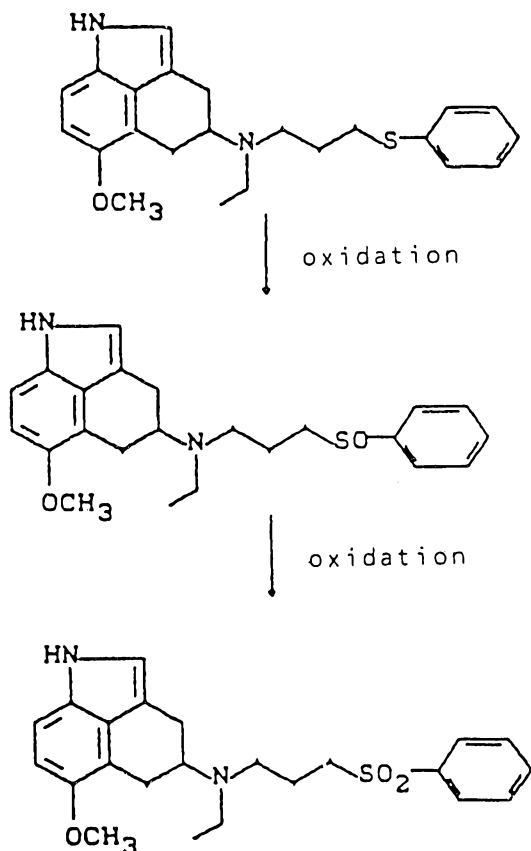
as alkali metals, alkali metal hydrides, alkali metal amides, alkali metal alkoxides or organolithium compounds, preferably in the presence of alkali metal hydrides such as sodium hydride or potassium hydride, or alkali metal amides such as sodium amide or lithium diisopropylamide, if appropriate in the presence of catalytic amounts of an alkali metal iodide, for example sodium iodide or potassium iodide, in a temperature range from -20°C to $+100^{\circ}\text{C}$, preferably from 0°C to $+50^{\circ}\text{C}$ at atmospheric pressure.

The reaction can be illustrated by the following equation:



5. The oxidation of the thioether groups to sulphoxides or sulphones in general takes place using oxidants such as peroxy compounds or hydrogen peroxide itself, preferably using hydrogen peroxide, in inert solvents such as carboxylic acids and carboxylic acid anhydrides, preferably in acetic acid, in a temperature range from -20°C to $+100^{\circ}\text{C}$, preferably from 0°C to $+50^{\circ}\text{C}$.

The reaction can be illustrated by the following equation:



The amines of the general formula (III), (IV) and (V) employed as starting materials are known or can be prepared by known methods [Houben-Weyl's "Methoden der organischen Chemie" ("Methods of Organic Chemistry"), Vol. XI/1 and XI/2].

Amines which can be used, for example, according to the invention are:

- 10 ammonia, methylamine, ethylamine, propylamine, isopropylamine, butylamine, 4-dimethylaminobutylamine, 4-diethylaminobutylamine, 3-dimethylaminopropylamine, 3-diethylaminopropylamine, 2-dimethylaminoethylamine, 2-diethylaminoethylamine, 2-amino-1-ethoxycarbonylamido-ethane,
- 15 3-amino-1-ethoxycarbonylamido-propane, 4-amino-1-ethoxycarbonylamido-butane, 3-aminoquinuclidine,

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2-[(phenylaminocarbonyl)amino]ethylamine, 2-[(phenylamino-
carbonyl)amino]propylamine, 4-aminomethyl-piperidine,
4-(ethoxycarbonyl)amino-ethyl-piperidine, N-methylpiper-
zine, 4-amino-1-carboxyethyl-piperidine, N,N-dimethylpro-
5 pylidene-diamine, N,N-dimethylpropylidene-diamine, N,N-
diethylethylidene-diamine, N,N-dimethylethylene-diamine,
N-(2-aminoethyl)ethyl carbamate and N-(2-aminoethyl)pro-
pyl carbamate.

The halogen compounds of the general formulae
10 (VII) and (XI) are known or can be prepared by known
methods [Beilstein's Handbuch der organischen Chemie
(Beilstein's Handbook of Organic Chemistry) 2, 197, 201,
250, 278; 3, 9, 10; 21, 461, 462, 463].

Halogen compounds which can be used, for example,
15 according to the invention are:
chloroacetonitrile, 2-chloropropionitrile, 3-chlorobuty-
ronitrile, 3-bromopropylphthalimide, 3-chloropropylphtha-
limide, 2-bromoethylphthalimide, 2-bromoethylphthalimide,
4-bromobutylphthalimide, 4-chlorobutylphthalimide, chloro-
20 acetyldiethylamide, chloroacetyldimethylamide, methyl
chloroacetate, ethyl chloroacetate, ethyl bromoacetate,
methyl bromoacetate, 2- δ -bromobutyl-1,2-benzothiazol-
3(2H)-one-1,1-dioxide and 2- γ -bromopropyl-1,2-benzoisothiazol-
3(2H)-one-1,1-dioxide.

25 The carbonyl compounds of the general formulae
(VIII) and (XII) employed as starting substances are known
or can be prepared by known methods [Beilstein's Handbuch
der organischen Chemie (Beilstein's Handbook of Organic
Chemistry) 1, 594, 629, 662].

30 Aldehydes which can be used, for example, accord-
ing to the invention are:
acetaldehyde, propionaldehyde, butyraldehyde and
benzaldehyde.

35 The compounds according to the invention can be
used as active compounds in medicaments. The substances
according to the invention have a particularly high

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affinity for cerebral 5-hydroxy-tryptamine receptors of the 5-HT₁ type. These are connected with agonistic, partial agonistic or antagonistic actions on the serotonin receptor. In comparison to the structurally related known compounds, they surprisingly exhibit a larger therapeutic range.

The high-affinity ligands for the serotonin-1 receptor described in the present invention thus represent active compounds for combating diseases which are characterized by disturbances of the serotonergic system, in particular with the involvement of receptors which possess high affinity for 5-hydroxytryptamine (5-HT₁ type). They are therefore suitable for the treatment of disorders of the central nervous system such as anxiety, tension and depression states, sexual dysfunctions caused by the central nervous system, sleep disturbances, and for the treatment of cognitive deficits for the improvement of learning and memory capacities and for the treatment of Alzheimer's disease. Furthermore, these active compounds are also suitable for the modulation of the cardiovascular system. They also intervene in the regulation of the cerebral circulation and thus represent effective agents for combating migraine. They are also suitable for the prophylaxis and combating of the consequences of cerebral infarct events (Apoplexia cerebri) such as stroke or cerebral ischaemia. The compounds according to the invention can likewise be employed for combating pain conditions. They are also suitable for combating disorders of the intestinal tract which are characterized by disturbances of the serotonergic system and also by disturbances of the carbohydrate metabolism.

The new active compounds can be converted in a known manner into the customary formulations, such as tablets, coated tablets, pills, granules, aerosols, syrups, emulsions, suspensions and solutions, using inert, non-toxic, pharmaceutically suitable excipients or

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solvents. In this connection, the therapeutically active compound is in each case present in a concentration from about 0.5 to 90% by weight of the total mixture, i.e. in amounts which are sufficient to achieve the dosage range indicated.

The formulations are prepared, for example, by extending the active compounds with solvents and/or excipients, if appropriate using emulsifiers and/or dispersants, where, for example, in the case of the use of water as a diluent, organic solvents can be used, if desired, as auxiliary solvents.

Auxiliaries which may be mentioned, for example, are:

water, non-toxic organic solvents, such as paraffins (for example mineral oil fractions), vegetable oils (for example groundnut/sesame oil), alcohols (for example: ethyl alcohol, glycerol), excipients, such as, for example, ground natural minerals (for example kaolins, argillaceous earths, talc, chalk), ground synthetic minerals (for example highly disperse silica, silicates), sugars (for example sucrose, lactose and dextrose), emulsifiers (for example polyoxyethylene fatty acid esters), polyoxyethylene fatty alcohol ethers (for example lignin, sulphite waste liquors, methylcellulose, starch and polyvinylpyrrolidone) and lubricants (for example magnesium stearate, talc, stearic acid and sodium sulphate).

Administration takes place in a customary manner, preferably orally or parenterally, in particular perlingually or intravenously. In the case of oral administration, tablets can, of course, also contain additives, such as sodium citrate, calcium carbonate and dicalcium phosphate together with various additives, such as starch, preferably potato starch, gelatin and the like in addition to the excipients mentioned. Furthermore, lubricants, such as magnesium stearate, sodium lauryl sulphate and talc can additionally be used for tableting. In the case

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of aqueous suspensions, various flavour improvers or colourants can be added to the active compounds in addition to the abovementioned auxiliaries.

5 In the case of parenteral administration, solutions of the active compounds using suitable liquid excipients can be employed.

10 In general, it has proved advantageous on intravenous administration to administer amounts from about 0.001 to 1 mg/kg, preferably about 0.01 to 0.5 mg/kg of body weight to attain effective results, and on oral administration the dosage is about 0.01 to 20 mg/kg, preferably 0.1 to 10 mg/kg of body weight.

15 In spite of this, it can sometimes be necessary to deviate from the amounts mentioned, depending on the body weight or the type of application route, on the individual behaviour towards the medicament, the manner of its formulation and the point in time or interval at which administration takes place. Thus, in some cases it may be sufficient to manage with less than the previously mentioned minimum amount, whereas in other cases the upper limit mentioned must be exceeded. In the case of the administration of larger amounts, it may be advisable to divide these into a number of individual doses over the day.

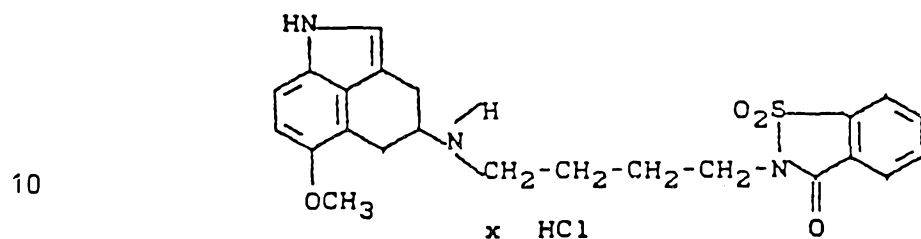
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Preparation examples

Example 1

6-Methoxy-4-[4-(N-1,2-benzisothiazol-3(2H)-one-1,1-dioxide-yl)]-butylamino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride



2.5 g of 6-methoxy-4-amino-1,3,4,5-tetrahydrobenz[c,d]-indole and 1.3 g of triethylamine are initially introduced in 50 ml of dimethylformamide. A solution of 2-(4-bromobutyl)-1,2-benzisothiazol-3(2H)-one-1,1-dioxide in 20 ml of dimethylformamide is added dropwise and the mixture is stirred for 4 hours at 50°C. It is then poured into water and extracted using methylene chloride. The crude product is chromatographed twice over silica gel 60 (40-63 μm) using ethyl acetate:ethanol 9:1. After the second chromatography, the clean fractions are combined, ethereal HCl is added and the solvent is stripped off at room temperature. The title compound is obtained as a hydrochloride in the form of a powder.

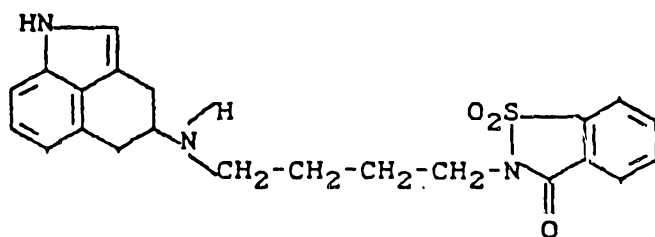
TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

R_f: 0.458

Yield: 2.5 g (40.5% of theory).

Example 2

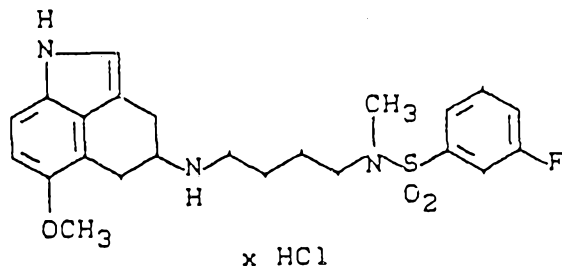
4-[4-(N-1,2-Benzisothiazol-3(2H)-one-1,1-dioxide-yl)]-butylamino-1,3,4,5-tetrahydrobenz[c,d]indole



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Example 4

6-Methoxy-4-/[4]- (N-4-fluorobenzenesulfonyl-N-methyl)-amidobutyl]-amino-1,3,4,5-tetrahydrobenz/[c,d]indole hydrochloride



This compound was prepared in analogy to the procedure given in example 1 with 6-methoxy-4-amino-1,3,4,5-tetrahydrobenz/[c,d]indole and N-methyl-N-(4-bromomethyl)-4-fluorobenzenesulfonamide as starting material.

M.p.: 168-170°C

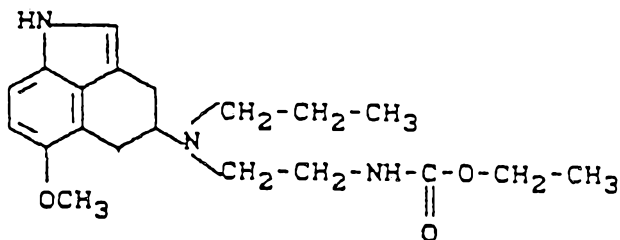
TCC : (silica gel 60) toluene/methanol 7:3

R_f : 0.32

Yield: 36 % of theory

Example 5

6-Methoxy-4-[N-propyl-N-(ethyloxycarbonylaminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



660 mg of 6-methoxy-4-[N-propyl-N-(aminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially introduced in 25 ml of methylene chloride. 5 ml of a 50% strength aqueous potassium carbonate solution are added. A solution of 236 µl of ethyl chloroformate and 5 ml of methylene chloride are added dropwise at 0°C with vigorous stirring. The mixture is stirred for 1 hour at 0°C. It is diluted with water and the phases are separated. The aqueous phase is extracted once more using methylene chloride. The organic phases are combined, dried over sodium sulphate and filtered. 1.5 g of

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activated carbon are added to the solution and the mixture is stirred for 2 hours at room temperature. It is then filtered and the filtrate is evaporated. The substance is obtained as a viscous resin.

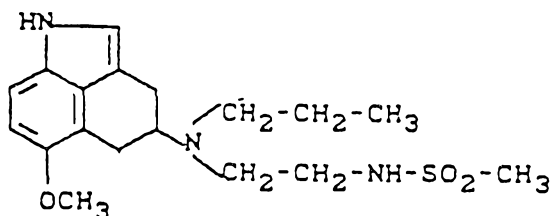
5 TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

R_f: 0.606

Yield: 540 mg (64% of theory)

Example 6

6-Methoxy-4-[N-propyl-N-(methylsulphonylamidoethyl)]-
10 amino-1,3,4,5-tetrahydrobenz[c,d]indole



20 1.14 g of 6-methoxy-4-[N-propyl-N-(aminoethyl)]-
amino-1,3,4,5-tetrahydrobenz[c,d]indole and 553 mg of
potassium carbonate are initially introduced in 40 ml
of methylene chloride. A solution of 550 mg of methane-
25 sulphonyl chloride and 5 ml of methylene chloride is added
dropwise at room temperature and the mixture is stirred
for 4 hours at room temperature. It is then diluted with
water, and the organic phase is separated off and evapora-
ted. The residue is chromatographed over silica gel 60
30 (40-63 μm) using cyclohexane:ethyl acetate 1:1. The oil
obtained is crystallized using petroleum ether/diisopro-
pyl ether. Colorless crystals are obtained.

m.p.: 118°C

TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

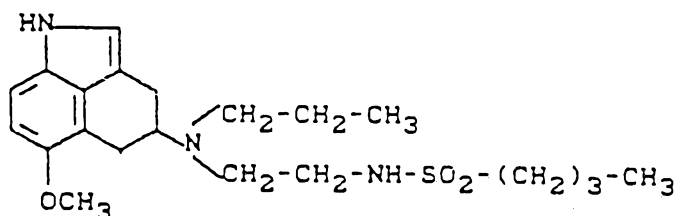
35 R_f: 0.617

Yield: 930 mg (63.7% of theory)

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Example 7

6-Methoxy-4-[N-propyl-N-(butylsulphonylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



1.15 g of 6-methoxy-4-[N-propyl-N-(aminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole and 553 mg of potassium carbonate are initially introduced in 40 ml of methylene chloride. 752 mg of butanesulphonyl chloride are added dropwise at room temperature and the mixture is stirred for 4 h at room temperature. It is then diluted with water, and the organic phase is separated off and evaporated. The residue is chromatographed over silica gel 60 (40-63 μ m) using cyclohexane:ethyl acetate 1:1.

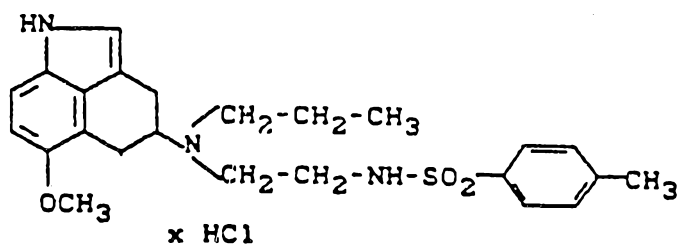
15 The compound is obtained as a viscous resin.
TLC: (silica gel 60) cyclohexane:ethyl acetate 1:1

20 R_f : 0.767

Yield: 1.24 g (76.1% of theory).

Example 8

25 6-Methoxy-4-[N-propyl-N-(tosylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride



2.32 g of 6-methoxy-4-[4-propyl-N-(aminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially introduced in 45 ml of methylene chloride with 4.5 ml of
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50% strength potassium carbonate solution. A solution of 1.7 g of tosyl chloride and 15 ml of methylene chloride is added dropwise at room temperature with vigorous stirring. The mixture is stirred for 3 hours at room temperature. It is then diluted using water and methylene chloride, the phases are separated and the organic phase is evaporated. The residue is chromatographed over silica gel 60 (40-63 μ m) using diisopropyl ether:ethanol 3:2.

The oil obtained is dissolved in diethyl ether and ethereal hydrochloric acid is added. The solvent is stripped off and the hydrochloride in the form of a powder is dried in a high vacuum at 50°C.

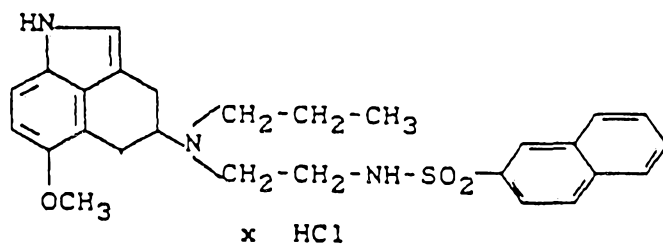
TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

R_f: 0.708

Yield: 2 g (52% of theory).

Example 9

6-Methoxy-4-[N-propyl-N-(2-naphthylsulphonylamidoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride



862 g of 6-methoxy-4-[N-propyl-N-(aminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially introduced in 15 ml of methylene chloride with 1.5 ml of 50% potassium carbonate solution. A solution of 748 mg of 2-naphthalenesulphonyl chloride and 5 ml of methylene chloride is added dropwise at room temperature. The mixture is stirred overnight at room temperature, then diluted using water and methylene chloride and the organic phase is separated off. The crude product is chromatographed over silica gel 60 (40-63 μ m) using cyclohexane: ethyl acetate 1:1. The product is dissolved in ethyl

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acetate. The salt is then precipitated using ethereal hydrochloric acid. The mixture is diluted using ether and filtered with suction. The compound is obtained as the hydrochloride in the form of a powder.

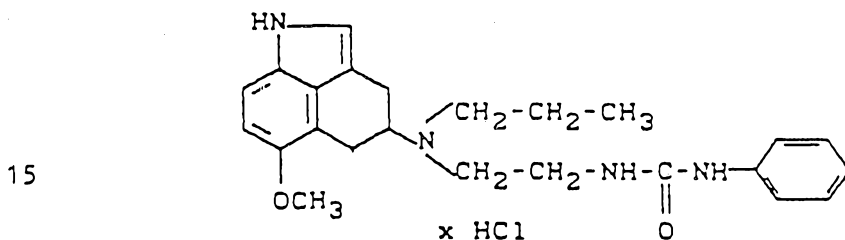
5 TLC: cyclohexane:ethyl acetate 1:1

R_f: 0.307

Yield: 910 mg (59.1% of theory).

Example 10

6-Methoxy-4-[N-propyl-N-(phenylureidoethyl)]-amino-1,3,4,5-
10 tetrahydrobenz[c,d]indole



1.18 g of 6-methoxy-4-[N-propyl-N-(aminoethyl)]-
amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially
20 introduced in 20 ml of methylene chloride. A few drops
of triethylamine are added and 420 mg of phenyl isocyanate
are then added dropwise at room temperature. The mixture
is stirred overnight at room temperature and evaporated.
The residue is chromatographed over silica gel 60
25 (40-63 μm) using ethyl acetate:ethanol 9:1. The residue
is dissolved in diethyl ether and the salt is precipitated
using ethereal hydrochloric acid.

The substance is obtained as the hydrochloride in
the form of a powder.

30 TLC: (silica gel 60) ethyl acetate:ethanol 9:1

R_f: 0.176

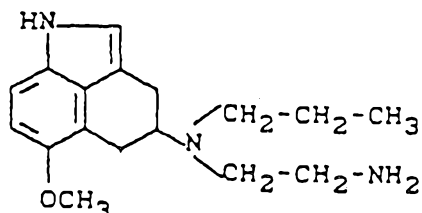
Yield: 760 mg (42% of theory).

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Example 11

6-Methoxy-4-[N-propyl-N-(aminoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



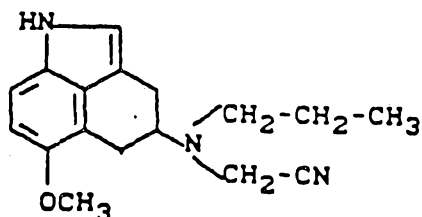
10 3.44 g of lithium aluminum hydride are initially introduced in 50 ml of absolute diethyl ether and the mixture is heated to reflux. A solution of 6.4 g of 6-methoxy-4-[N-propyl-N-(cyanomethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole in 75 ml of absolute diethyl ether is
15 added dropwise and the mixture is stirred for 4 hours under reflux. It is then cautiously decomposed using water and filtered with suction. The residue is boiled twice with ethyl acetate. The organic phases are combined and evaporated. The product can be crystallized from the
20 oily residue using petroleum ether:diisopropyl ether. A colourless powder is obtained.

m.p.: 146-147°C

Yield: 4.6 g (70.8% of theory).

Example 12

25 6-Methoxy-4-[N-propyl-N-(cyanomethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



35 7.2 g of 6-methoxy-4-propylamino-1,3,4,5-tetrahydrobenz[c,d]indole are brought to reaction in 150 ml of methyl ethyl ketone at 70°C with 11.5 g of chloroaceto-
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nitrile in the presence of 20.7 g of potassium carbonate and 1 g of potassium iodide. The reaction is complete after 3.5-4 hours. The mixture is filtered and evaporated. The crude product is chromatographed over silica gel 60 (63-200 μm) using cyclohexane:ethyl acetate 1:1. The substance is obtained as a viscous oil.

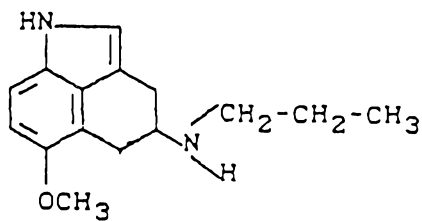
TLC: (silica gel 60) cyclohexane:ethyl acetate 1:1

R_f : 0.447

Yield: 8 g (94% of theory)

Example 13

6-Methoxy-4-propylamino-1,3,4,5-tetrahydrobenz[c,d]indole



1.25 g of 6-methoxy-4-amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially introduced in 40 ml of methanol. 265 μl of glacial acetic acid and 492 mg of sodium cyanoborohydride are added and the mixture is heated to 60 $^{\circ}\text{C}$. 440 μl of propionaldehyde are added dropwise at this temperature during the course of 30 min. The mixture is stirred for 1 h at 60 $^{\circ}\text{C}$ and then evaporated. The residue is taken up in methylene chloride and washed once with water. The organic phase is evaporated, and the residue is taken up in ethyl acetate and stirred for 10 min with 5 molar sodium hydroxide solution. The organic phase is separated off, extracted once more using ethyl acetate and evaporated. The residue is chromatographed over silica gel 60 (40-63 μm) using diisopropyl ether:ethanol 3:2. The product is a viscous oil.

TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

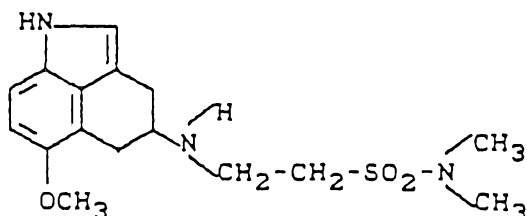
R_f : 0.204

Yield: 800 mg (53% of theory)

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Example 14

6-Methoxy-4-(dimethylsulphamoylethyl)-amino-1,3,4,5-tetrahydrobenz[c,d]indole



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1 g of 6-methoxy-4-oxo-1,3,4,5-tetrahydrobenz-
[c,d]indole are initially introduced in 30 ml of methanol
with 5 g of molecular sieve (4 Å). 2.3 g of acetic acid
are added and the mixture is cooled to 0°C. 1.14 g of
2-dimethylsulphamoylethylamine are added and the mixture
is stirred for 30 minutes at 0°C. It is allowed to come to
room temperature and 1.3 g of sodium cyanoborohydride are
added and the mixture is stirred for 4 hours at room tem-
perature. It is then filtered and evaporated. The resi-
due is taken up in ethyl acetate, 20% strength sodium
hydroxide solution is added and the mixture is stirred
for 15 min. The phases are separated, and the aqueous
phase is washed with ethyl acetate and the combined orga-
nic phases are evaporated. The residue is chromatographed

over silica gel 60 (40-63 μm) using diisopropylamine:
ethanol 4:1 as eluent. The substance is obtained as a
viscous oil.

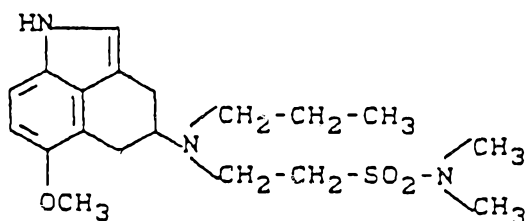
TLC: (silica gel 60) ethyl acetate:ethanol 9:1

R_f: 0.189

Yield: 400 mg (24% of theory)

Example 15

6-Methoxy-4-[N-propyl-N-(dimethylsulphamoyl)ethyl]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



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362 mg of 6-methoxy-4-(dimethylsulphamoyl)ethyl-amino-1,3,4,5-tetrahydrobenz[c,d]indole are initially introduced in 7.5 ml of methanol. 480 mg of glacial acetic acid and 93 mg of propionaldehyde are added. 270 mg of sodium cyanoborohydride are then added and the mixture is stirred for 2 h at room temperature. After evaporating, the residue is taken up in ethyl acetate, 20% strength sodium hydroxide solution is added and the mixture is stirred for 10 minutes. The ethyl acetate phase is separated off and extracted using 3N hydrochloric acid. The hydrochloric acid phase is rendered alkaline and extracted a number of times using ethyl acetate. The organic phase is evaporated and chromatographed over silica gel 60 (63-200 μ m) using ethyl acetate. The product obtained is again chromatographed over silica gel 60 (63-200 μ m) using a cyclohexane/ethyl acetate gradient with the addition of a little triethylamine. The product obtained is dissolved in ether and the hydrochloride is precipitated using ethereal hydrochloric acid. A colorless hygroscopic solid is obtained.

TLC: (silica gel 60) ethyl acetate

R_f: 0.466

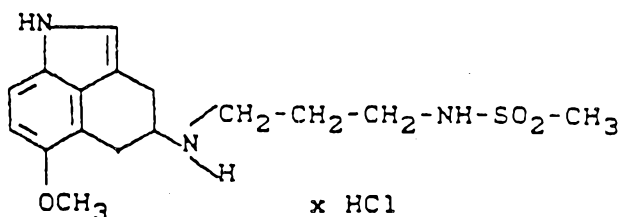
Yield: 125 mg (28.1% of theory).

Example 16

35 6-Methoxy-4-(methylsulphonylamidopropyl)-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride

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500 mg of palladium-carbon (10% strength) are prehydrogenated in 20 ml of methanol and 5 ml of methanol/hydrochloric acid (1 mol x 1⁻¹). A solution of 1.2 g of 6-methoxy-4-[N-benzyl-N-(methylsulphonylamidopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole in 40 ml of methanol is added and the mixture is hydrogenated until hydrogen uptake is complete. The solution is filtered from the catalyst, neutralized and evaporated. The residue is chromatographed over silica gel 60 (40-63 μm) using ethyl acetate:ethanol 9:1. The clean fractions are combined, ethereal hydrochloric acid is added and the solvent is stripped off at room temperature. The compound is obtained as the hydrochloride in the form of a powder.

TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

R_f: 0.274

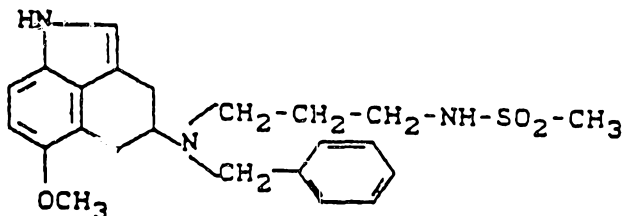
Yield: 557 mg (55.3% of theory)

Example 17

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6-Methoxy-4-[N-benzyl-N-(methylsulphonylamidopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole

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35

1.7 g of 6-methoxy-4-[N-benzyl-N-(aminopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole and 672 mg of potassium carbonate are initially introduced in 50 ml of methylene chloride. A solution of 613 mg of methanesulphonyl chloride and 10 ml of methylene chloride is added

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dropwise at room temperature and the mixture is stirred overnight at room temperature. The precipitate is then filtered off and the solution is concentrated on a rotary evaporator. The residue is chromatographed over silica gel 60 (840-63 μm) using cyclohexane:ethyl acetate 1:1. Crystals of m.p.: 132-133 $^{\circ}\text{C}$ are obtained.

TLC: (silica gel 60) cyclohexane:ethyl acetate 1:1

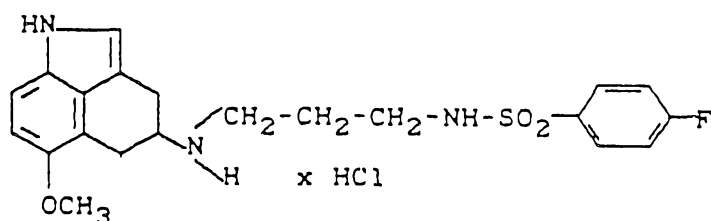
R_f: 0.182

Yield: 1.2 g (57.7% of theory)

10 Example 18

6-Methoxy-4-(4-fluorophenylsulphonylamidopropyl)-amino-1,3,4,5-tetrahydrobenz[c,d]indole hydrochloride

15



20

800 mg of palladium-carbon (10% strength) are prehydrogenated in 25 ml of methanol and 6.5 ml of methanol/hydrochloric acid (1 mol x 1⁻¹). A solution of 1.6 g of 6-methoxy-4-[N-benzyl-N-(4-fluorophenylsulphonylamidopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole in 25 ml of methanol is added and the mixture is hydrogenated until hydrogen uptake is complete. The solution is filtered off from the catalyst, neutralized and evaporated. The residue is chromatographed over silica gel 60 (40-63 μm) using ethyl acetate:ethanol 9:1. The product is taken up in ether and the salt is precipitated using ethereal hydrochloric acid.

25

30

TLC: (silica gel 60) diisopropyl ether:ethanol 3:2

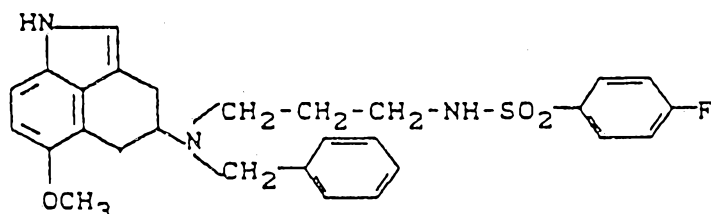
R_f: 0.481

Yield: 840 mg (58.7% of theory)

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Example 19

6-Methoxy-4-[N-benzyl-N-(4-fluorophenylsulphonylamidopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



10 12.5 g of 6-methoxy-4-[N-benzyl-N-(aminopropyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole and 470 mg of potassium carbonate are initially introduced in 30 ml of methylene chloride. A solution of 730 mg of 4-fluorobenzenesulphonyl chloride in 5 ml of methylene chloride is
15 added dropwise at room temperature and the mixture is stirred overnight at room temperature. It is then diluted using water and methylene chloride, and the organic phase is separated off and evaporated. The crude product is chromatographed over silica gel 60 (40-63 μ m) using cyclohexane:ethyl acetate 7:3. The substance is obtained as a
20 viscous resin.

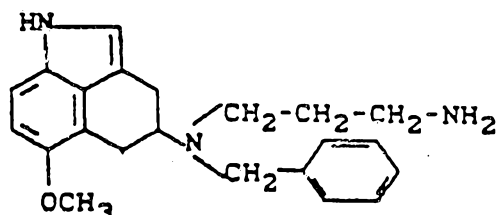
TLC: (silica gel 60) cyclohexane:ethyl acetate 7:3

R_f: 0.172

Yield: 12.5 g (72.5% of theory)

25 Example 20

6-Methoxy-4-(N-benzyl-N-aminopropyl)-amino-1,3,4,5-tetrahydrobenz[c,d]indole



35 882 mg of lithium aluminum hydride are initially introduced in 15 ml of absolute diethyl ether under argon. A suspension of 2 g of 6-methoxy-4-[N-benzyl-N-(2-cyano-

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ethyl)-amino-1,3,4,5-tetrahydrobenz[c,d]indole in 50 ml of absolute diethyl ether is added dropwise under reflux. The mixture is stirred for 4 hours under reflux and then cooled to room temperature. It is decomposed using 8 ml of ethyl acetate, 1 ml of water and 2 ml of 15% strength potassium hydroxide solution. The mixture is filtered with suction and the residue is washed three times with ethyl acetate. The mother liquor is evaporated and the residue obtained is chromatographed over silica gel 60 (40-63 μ m) using methanol:triethylamine 95:5. The substance is obtained as a viscous oil.

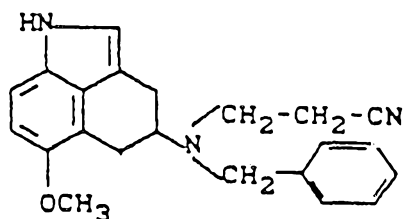
TLC: (silica gel 60) methanol:triethylamine 95:5

R_f: 0.186

Yield: 1.35 g (66.5% of theory).

Example 21

6-Methoxy-4-[N-benzyl-N-(2-cyanoethyl)]-amino-1,3,4,5-tetrahydrobenz[c,d]indole



2.05 g of 6-methoxy-4-benzylamino-1,3,4,5-tetrahydrobenz[c,d]indole and 1.86 g of acrylonitrile and 25 mg of copper(II) acetate are stirred under reflux for 12 hours. The reaction mixture is chromatographed over silica gel 60 (63-200 μ m) using cyclohexane:ethyl acetate 7:3. A colourless powder of melting point 126°C is obtained.

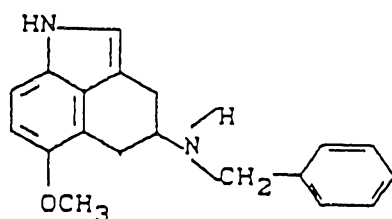
TLC: (silica gel 60) cyclohexane:ethyl acetate 1:1

R_f: 0.445

Yield: 2.05 g (84.7% of theory)

Example 22

6-Methoxy-4-benzylamino-1,3,4,5-tetrahydrobenz[c,d]indole



10 2 g of 6-methoxy-4-amino-1,3,4,5-tetrahydrobenz-
[c,d]indole are initially introduced in 75 ml of metha-
nol. 450 μ l of acetic acid and 800 mg of sodium cyano-
borohydride are added, the mixture is heated to 60°C and
1.12 g of benzaldehyde are added dropwise during the
15 course of 30 minutes. The mixture is stirred for 1 hour
at 60°C and then evaporated. The residue is taken up in
ethyl acetate and stirred for 10 minutes with 20% strength
sodium hydroxide solution. The organic phase is separated
off and evaporated. The residue is dissolved in methylene
20 chloride, activated carbon is added and the mixture is
stirred for 1 hour at room temperature. The solution is
filtered and evaporated. The brown crystals obtained are
chromatographed over silica gel 60 (40-63 μ m) using ethyl
acetate:ethanol 9:1.

25 A crystalline powder of m.p.: 143-144°C is
obtained.

TLC: ethyl acetate:ethanol 9:1

R_f: 0.359

Yield: 2.05 g (70.2% of theory).

Use Example

30 Example 23

Affinity for the 5-HT₁ receptor

The high affinity of the compounds according to
the invention for 5-hydroxytryptamine receptors of the
subtype 1 is represented by way of example in Table 1.

35 The values indicated are data which have been determined
from receptor binding studies with calf hippocampus mem-

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membrane preparations. ³H-Serotonin was used for this as a radioactively labelled ligand.

Table 1

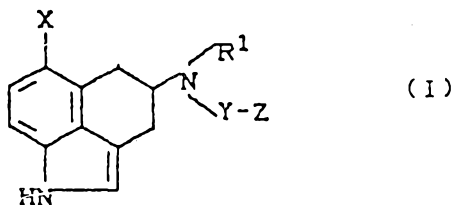
Compound of

5	<u>Example No.</u>	<u>Ki (nmol/L)</u>
	1	2
	2	2
	5	1
	6	6
10	8	1
	9	2
	15	8
	18	0.7

Furthermore, the antidepressive action properties
15 of the compounds were investigated. For this, the influence of the compounds on the so-called "behavioral despair" behavior was investigated according to Porsolt et al. Arch. Int. Pharmacodyn. Ther. 229, 327 (1977). By way of example, the compounds according to Examples 3, 4,
20 7 and 13 show positive action.

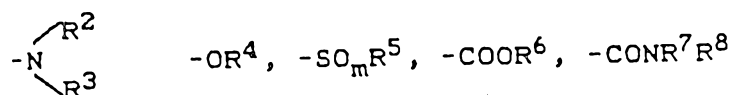
The claims defining the invention are as follows:

1. 1,3,4,5-Tetrahydrobenz[c,d]indoles of the formula



in which

- R^1 - stands for H, alkyl, aralkyl or heteroarylalkyl,
 X - stands for H, OCH₃, OH, SCH₃, halogen, CN or CONH₂,
 Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms
 and
 Z - stands for cyano or for a group of the formula



where

- R^4 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy-carbonyl, aryloxy-carbonyl or aralkoxy-carbonyl
 R^5 - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different halogen, cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy, or for a group of the formula $-NR^7 R^8$,
 R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

- R^7 and R^8 are identical or different and
 - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,
- m - stands for a number 0, 1 or 2,
- R^2 and R^3 are identical or different and
 - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or
 - for a group of the formula $-COR^9$ or $-SO_2R^{10}$,
 wherein
- R^9 - denotes hydrogen, or
 - a group NHR^{11} , or
 - denotes alkyl or alkoxy, or
 - denotes aryl, aralkyl, aralkoxy or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,
- R^{10} - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoromethoxy or alkoxycarbonyl, or
 - denotes aryl, aralkyl or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen,

cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino, or

- denotes a group NR^7R^8 ,

where

R^7 and R^8 have the abovementioned meaning

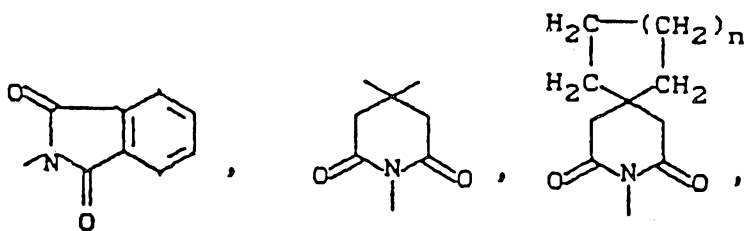
and

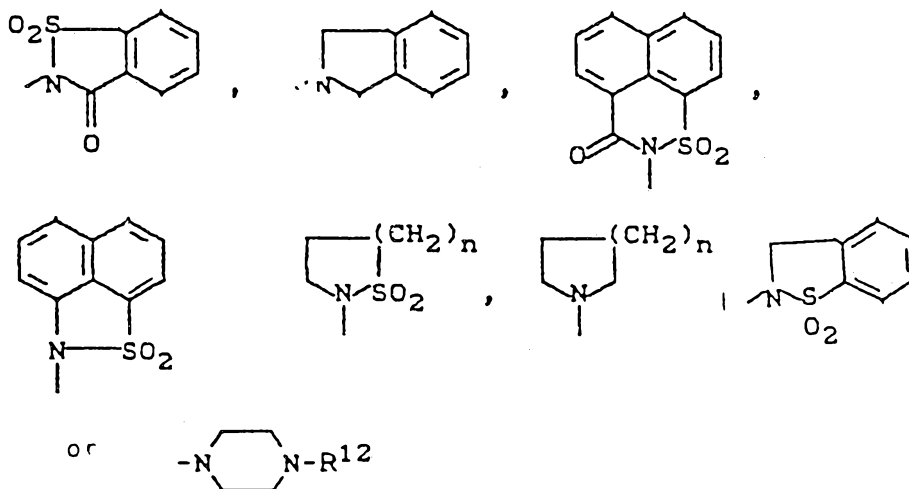
R^{11} - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or trifluoromethoxy, or

- denotes aryl, aralkyl or heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where

R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising





wherein

n - denotes a number 1 or 2,

and

R^{12} - stands for acyl, alkoxycarbonyl, alkylsulphenyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbomoyl or sulphamoyl

and their salts.

2. 1,3,4,5-Tetrahydrobenz[c,d]indoles according to Claim 1, wherein

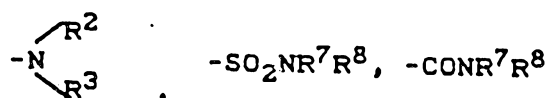
R^1 - stands for H, C_1 - C_4 -alkyl or benzyl

X - stands for H, OCH_3 , OH, SCH_3 , F, Cl, Br, CN or CONH_2 ,

Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms

and

Z - stands for cyano or for a group of the formula



wherein

R^7 and R^8 are identical or different, and

- stand for hydrogen, lower alkyl, phenyl,

benzyl or phenethyl,
 R^2 and R^3 are identical or different and
- stand for hydrogen, lower alkyl, phenyl or
benzyl, where the phenyl radicals can be substi-
tuted by fluorine, chlorine, bromine, lower
alkyl, lower alkoxy or trifluoromethyl, or
- stand for a group of the formula $-COR^9$ or
 $-SO_2R^{10}$,

wherein

- R^9 - denotes hydrogen or a group NHR^{11} , or
- denotes lower alkyl or lower alkoxy, or
- denotes phenyl, benzyl, benzyloxy, thienyl,
furyl, pyridyl, pyrimidyl, quinolyl, iso-
quinolyl, benzothiazolyl, benzoxazolyl,
thiazolyl, oxazolyl, isoxazolyl or iso-
thiazolyl, each of which is optionally
substituted by lower alkyl, lower alkoxy,
fluorine, chlorine, bromine, trifluoro-
methyl, dimethylamino or diethylamino,
 R^{10} - denotes lower alkyl which is optionally
substituted by cyano, fluorine, chlorine,
bromine, trifluoromethyl or lower alkoxy-
carbonyl, or
- denotes phenyl, naphthyl, benzyl, thienyl, furyl,
pyrimidyl, pyridyl, quinolyl, isoquinolyl,
benzothiazolyl, benzoxazolyl, thiazolyl,
oxazolyl, isoxazolyl or isothiazolyl, each
of which is optionally substituted by lower
alkyl, lower alkoxy, fluorine, chlorine,
bromine, trifluoromethyl, dimethylamino or
diethylamino, or
- denotes a group NR^7R^8 ,

where

R^7 and R^8 have the abovementioned meaning,

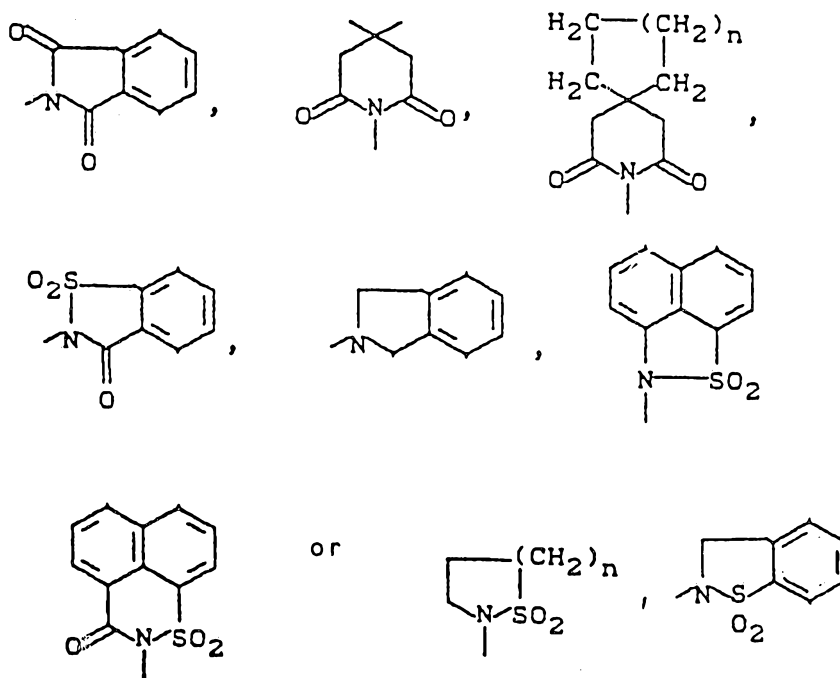
and

R^{11} - denotes lower alkyl which is optionally

substituted by cyano, fluorine, chlorine or bromine, or

- denotes phenyl, benzyl, thienyl, furyl, pyridyl, pyrimidyl, quinolyl, isoquinolyl, benzothiazolyl, benzoxazolyl, thiazolyl, oxazolyl, isoxazolyl or isothiazolyl, each of which is optionally substituted by lower alkyl, lower alkoxy, fluorine, chlorine, bromine, trifluoromethyl, dimethylamino or diethylamino,

or
 R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising



wherein

n - denotes a number 1 or 2

and their salts.

3. 1,3,4,5-Tetrahydrobenz[c,d]indoles according to Claims 1 and 2,

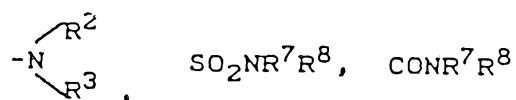
wherein

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R¹ - stands for hydrogen, methyl, ethyl, n-propyl or benzyl,
 X - stands for H, OCH₃, OH, SCH₃, F, Cl, CN or CONH₂,
 Y - stands for a straight-chain alkylene chain having
 2 to 4 carbon atoms

and

Z - stands for cyano or for a group of the formula



where

R⁷ and R⁸ are identical or different and

- stand for hydrogen, methyl, ethyl, propyl,
 isopropyl, butyl, isobutyl or tert.butyl,

R² and R³ are identical or different, and

- stand for hydrogen, methyl, ethyl, propyl, iso-
 propyl, butyl, isobutyl, tert.butyl or
 - stand for phenyl which is optionally substituted
 by fluorine, chlorine, methyl or methoxy, or
 - for a group -COR⁹ or -SO₂R¹⁰,

wherein

R⁹ - denotes hydrogen or a group NHR¹¹, or

- denotes methyl, ethyl, propyl, isopropyl,
 methoxy, ethoxy, propoxy, isopropoxy, or
 - phenyl, benzyl, benzyloxy, thienyl, furyl,
 pyridyl, pyrimidyl, quinolyl or isoquinolyl,
 each of which is optionally substituted by
 methyl, methoxy, fluorine or chlorine,

R¹⁰ - denotes methyl, ethyl, propyl, isopropyl,
 butyl or isobutyl, each of which is optionally
 substituted by fluorine, chlorine, methoxycar-
 bonyl, ethoxycarbonyl, propoxycarbonyl, isopro-
 poxycarbonyl, butoxycarbonyl or isobutoxycar-
 bonyl, or

- denotes phenyl, naphthyl, benzyl, thienyl, furyl, pyri-
 dyl, pyrimidyl, quinolyl or isoquinolyl, each

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of which is optionally substituted by methyl, ethyl, propyl, isopropyl, methoxy, fluorine or chlorine, or

- denotes a group NR^7R^8 ,

where

R^7 and R^8 have the abovementioned meaning,

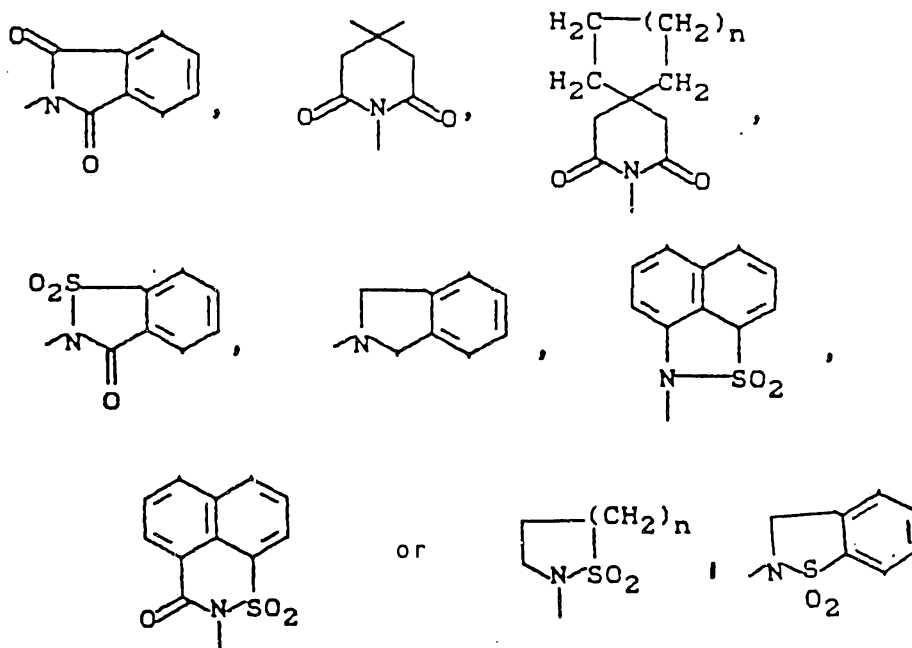
and

R^{11} - denotes methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, isopentyl, hexyl or isohexyl, each of which is optionally substituted by fluorine or chlorine, or

- denotes phenyl or benzyl, each of which can be substituted by fluorine, chlorine, methyl or methoxy,

or

R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising

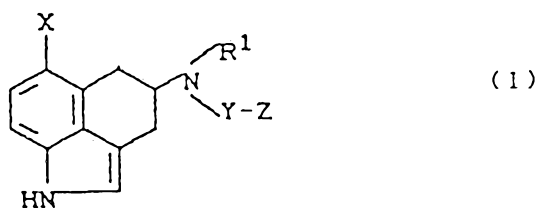


wherein

n - denotes a number 1 or 2

and their salts.

4. Process for the preparation of 1,3,4,5-tetrahydrobenz[c,d]indoles of the formula



in which

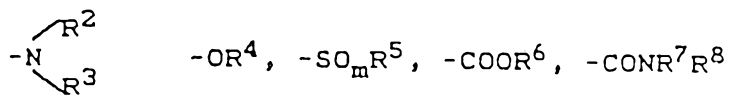
R¹ - stands for H, alkyl, aralkyl or heteroarylalkyl,

X - stands for H, OCH₃, OH, SCH₃, halogen, CN or CONH₂,

Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms

and

Z - stands for cyano or for a group of the formula



where

R⁴ - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy carbonyl, aryloxy carbonyl or aralkoxy carbonyl

R⁵ - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different halogen,

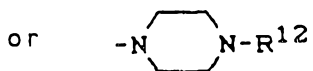
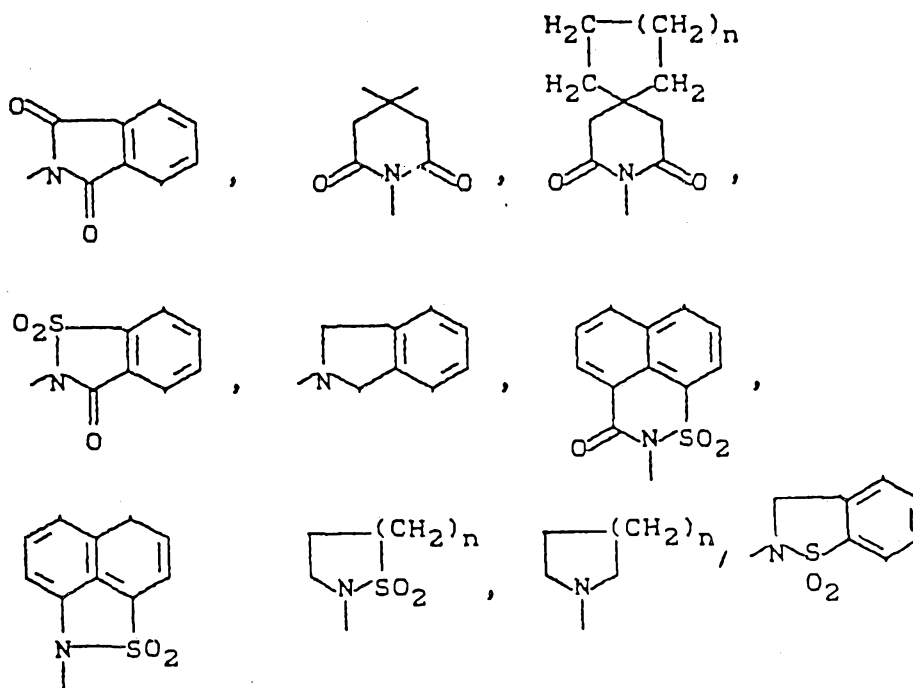


- cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy, or for a group of the formula $-NR^7R^8$,
- R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,
- R^7 and R^8 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,
- m - stands for a number 0, 1 or 2,
- R^2 and R^3 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or
- for a group of the formula $-COR^9$ or $-SO_2R^{10}$,
- wherein
- R^9 - denotes hydrogen, or
- a group NHR^{11} , or
 - denotes alkyl or alkoxy, or
 - denotes aryl, aralkyl, aralkoxy or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,
- R^{10} - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoromethoxy or alkoxycarbonyl, or
- denotes aryl, aralkyl or hetero-

aryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino, or
- denotes a group NR^7R^8 ,
where
 R^7 and R^8 have the abovementioned meaning

and
 R^{11} - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or trifluoromethoxy, or
- denotes aryl, aralkyl or heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where
 R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising



wherein

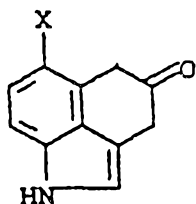
n - denotes a number 1 or 2,

and

R¹² - stands for acyl, alkoxycarbonyl, alkylsulphonyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbamoyl or sulphamoyl

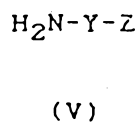
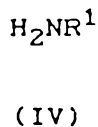
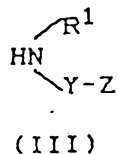
and their salts,

characterized in that ketones of the formula (II)



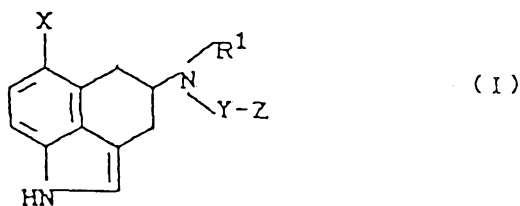
(II)

in which X has the abovementioned meaning, are reductively aminated [A] with amines of the formula (III), (IV) or (V)



in which R^1 , Y and Z have the abovementioned meanings.

5. Process for the preparation of 1,3,4,5-tetrahydrobenz[c,d]indoles of the formula



in which

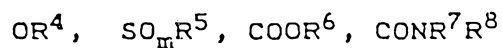
R^1 - stands for H, alkyl, aralkyl or heteroarylalkyl,

X - stands for H, OCH_3 , OH, SCH_3 , halogen, CN or CONH_2 ,

Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms

and

Z - stands for cyano or for a group of the formula



where

R^4 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy-carbonyl, aryloxy-carbonyl or aralkoxy-carbonyl

R^5 - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted,



disubstituted or trisubstituted by identical or different halogen, cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy, or for a group of the formula $-NR^7R^8$,

R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

R^7 and R^8 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

m - stands for a number 0, 1 or 2,

R^2 and R^3 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or

- for a group of the formula $-COR^9$ or $-SO_2R^{10}$,

wherein

R^9 - denotes hydrogen, or

- a group NHR^{11} , or
- denotes alkyl or alkoxy, or
- denotes aryl, aralkyl, aralkoxy or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

R^{10} - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoro-

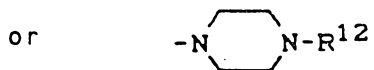
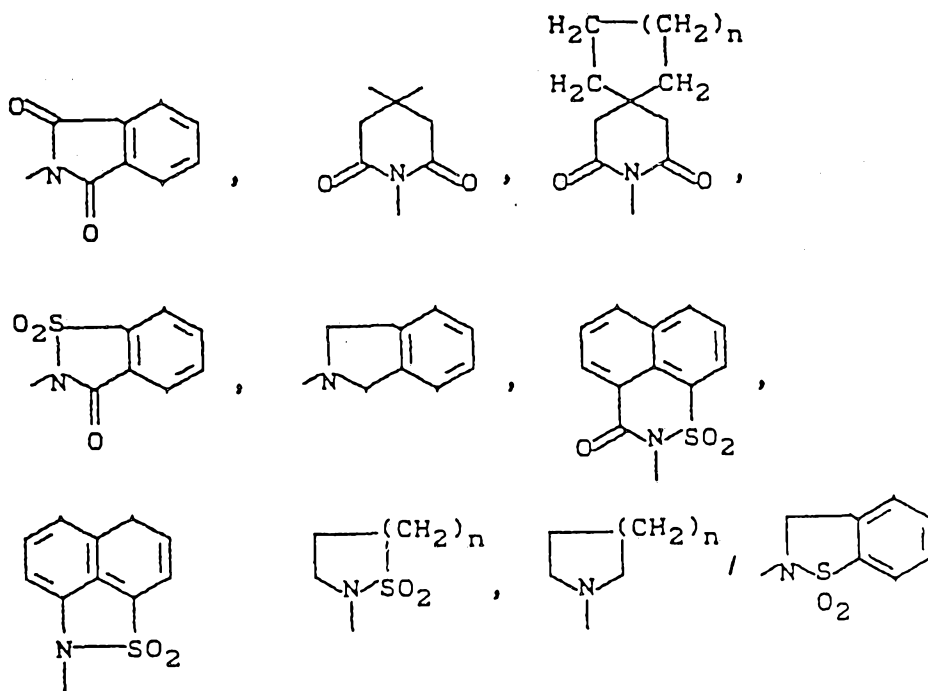
- methoxy or alkoxycarbonyl, or
- denotes aryl, aralkyl or heteroaryl, where the radicals mentioned can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino, or
 - denotes a group NR^7R^8 ,
where
 R^7 and R^8 have the abovementioned meaning

and

- R^{11} - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or trifluoromethoxy, or
- denotes aryl, aralkyl or heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where

R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising



wherein

n - denotes a number 1 or 2,

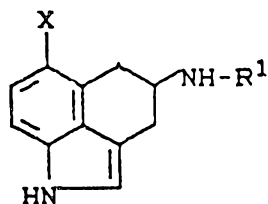
and

R¹² - stands for acyl, alkoxycarbonyl, alkylsulphonyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbamoyl or sulphamoyl

and their salts,

characterized in that compounds of the general formula

(VI)



(VI)

in which R¹ and X have the abovementioned meanings, are reacted [B] with alkylating agents of the formula (VII)

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in which Y and Z have the abovementioned meanings, and L denotes a leaving group customary in alkylating agents, or reductively alkylated [C] with aldehydes of the formula (VIII)

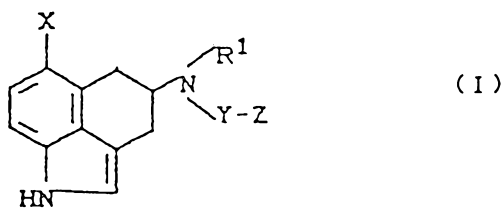


in which Z has the abovementioned meaning and Y^1 is an alkylene chain Y shortened by one methylene group, or reacted with reactive acid derivatives of the general formula (IX)



in which Y^1 and Z have the abovementioned meanings and M denotes a leaving group customary in acylating agents, such as chlorine, bromine, alkoxy, aryloxy, imidazolyl, thiazolyl, methanesulphonyloxy or alkoxycarbonyloxy, and the acid amides obtained are reduced [D] catalytically with hydrogen or with complex metal hydrides to give compounds of the formula (I).

6. Process for the preparation of 1,3,4,5-tetrahydro-benz[c,d]indoles of the formula



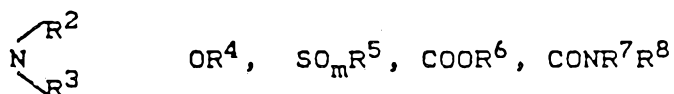
in which

- R^1 - stands for H, alkyl, aralkyl or heteroarylalkyl,
 - X - stands for H, OCH_3 , OH, SCH_3 , halogen, CN or $CONH_2$,
 - Y - stands for a straight-chain or branched, saturated or unsaturated alkylene chain having up to 6 carbon atoms
- and

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Z - stands for cyano or for a group of the formula



where

R^4 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy-carbonyl, aryloxy-carbonyl or aralkoxy-carbonyl

R^5 - stands for alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different halogen, cyano, alkyl, alkoxy, trifluoromethyl or trifluoromethoxy,

R^6 - stands for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

R^7 and R^8 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl,

m - stands for a number 0, 1 or 2, or - for a group of the formula $NR^7 R^8$,

R^2 and R^3 are identical or different and - stand for hydrogen, alkyl, alkenyl, cycloalkyl, aryl or aralkyl, where the aryl radicals can be substituted by halogen, cyano, alkyl, alkoxy or trifluoromethyl, or

- for a group of the formula $-COR^9$ or $-SO_2R^{10}$,

wherein

- R^9 - denotes hydrogen or
- denotes a group NHR^{11}
- denotes alkyl or alkoxy or
- denotes aryl, aralkyl, aralkoxy

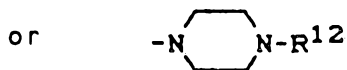
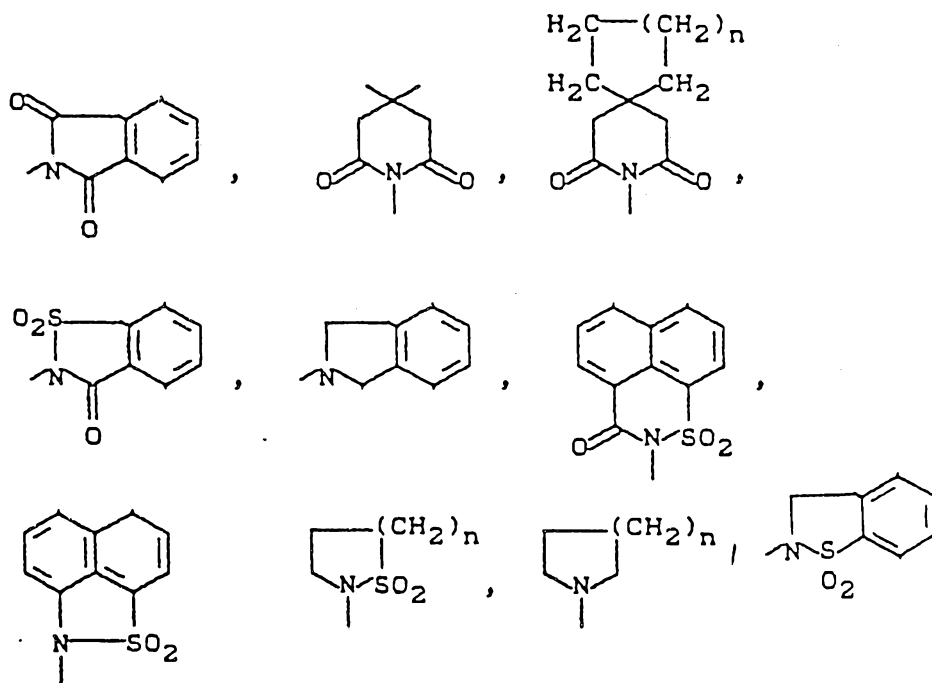
or heteroaryl,
it being possible for the aforementioned radicals to be substituted by up to 3 identical or different substituents from amongst alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

- R^{10} - denotes alkyl which can be substituted by cyano, halogen, trifluoromethyl, trifluoromethoxy or alkoxy carbonyl or
- denotes aryl, aralkyl or heteroaryl, it being possible for the aforementioned radicals to be substituted by up to 3 identical or different substituents from amongst alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino or
 - denotes a group NR^7R^8 ,
wherein
 R^7 and R^8 have the abovementioned meaning

and
 R^{11} - denotes alkyl which is optionally substituted by cyano, halogen, trifluoromethyl or

heteroaryl, where the aryl radicals can be monosubstituted, disubstituted or trisubstituted by identical or different alkyl, alkoxy, alkylthio, halogen, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, amino, alkylamino or dialkylamino,

or where R^2 and R^3 , together with the nitrogen atom, form a heterocyclic ring from the series comprising



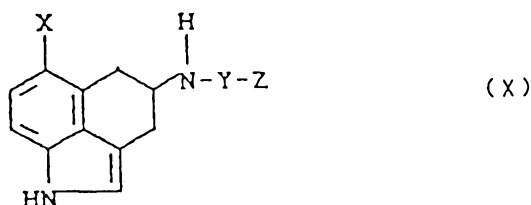
wherein

n - denotes a number 1 or 2,

and

R^{12} - stands for acyl, alkoxycarbonyl,

alkylsulphonyl, phenylsulphonyl, tolylsulphonyl, benzylsulphonyl, carbamoyl or sulphamoyl and their salts, characterized in that compounds of the formula (X)



in which X, Y and Z have the abovementioned meanings, are alkylated with alkylating agents of the formula (XI)

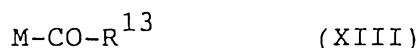


in which R^1 has the abovementioned meaning and L is as defined in claim 5, or reductively alkylated using aldehydes of the formula (XII)



in which R^{13} is a radical R^1 shortened by one methylene group,

or reacted with reactive acid derivatives of the general formula (XIII)



in which R^{13} has the abovementioned meaning and M is as defined in claim 5, and the acid amides obtained are reduced catalytically with hydrogen or with complex metal hydrides to give compounds of the formula (I).

7. Medicament, containing 1,3,4,5-tetrahydrobenz-[c,d]indoles according to claim 1, in association with an inert non-toxic pharmaceutically suitable excipient or solvent.

8. Medicament according to claim 7, characterized in that it contains 0.5 to 90% by weight of 1,3,4,5-tetrahydrobenz-[c,d]indoles, based on the total mixture.

9. A method for the treatment of disorders of the central nervous system which comprises administering, to a subject



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suffering from or subject to such disorders, a compound according to any one of claims 1 to 3 or a medicament according to claims 7 or 8.

DATED this 28th day of May, 1991.

BAYER AKTIENGESELLSCHAFT
By Its Patent Attorneys
ARTHUR S. CAVE & CO.

