



**EUROPEAN PATENT SPECIFICATION**

- (45) Date of publication of patent specification: 19.08.92 / (51) Int. Cl.<sup>5</sup>: **A61K 31/135, A61K 31/16, A61K 31/275, A61K 31/27, C07C 233/00, C07C 235/00, C07C 237/00**
- (21) Application number: **87301246.2**
- (22) Date of filing: **13.02.87**

(54) **Use of aromatic diamines for the treatment of angina pectoris, and diamines therefor.**

- (30) Priority: **15.02.86 GB 8603765**
- (43) Date of publication of application: **26.08.87 Bulletin 87/35**
- (45) Publication of the grant of the patent: **19.08.92 Bulletin 92/34**
- (64) Designated Contracting States:  
**BE CH DE ES FR GB GR IT LI LU NL SE**
- (56) References cited:  
**EP-A- 0 247 345            BE-A- 647 534**  
**DE-A- 3 242 344            DE-B- 1 118 212**  
**DE-B- 1 170 961            FR-M- 965**  
**GB-A- 862 467            GB-A- 1 050 132**  
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**CHEMICAL ABSTRACTS, vol. 77, no. 7, 14th August 1972, page 505, abstract no. 61967g, Columbus, Ohio, US; F. GATTA et al.: "Synthesis of 7,8 - dimethoxy - 1,4 - benzodiazepines", & ANN. IST. SUPER. SANITA 1971, 7(P.T.4), 533-9 & 9TH COLLECTIVE INDEX, P- 15074CS**

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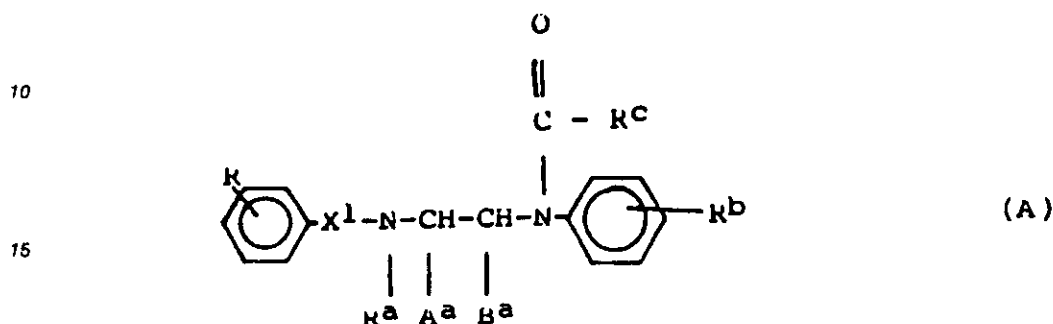
CHEMICAL ABSTRACTS, vol. 87, no. 19, 7th  
November 1977, page 14, abstract no.  
145548r, Columbus, Ohio, US; F.G. VAN DEN  
BRINK et al.: "pD<sub>2</sub>-, pA<sub>2</sub>- and pD'<sub>2</sub>'values of  
a series of compounds in a histaminic and a  
cholinergic system", & EUR. J. PHARMACOL.  
1977, 44(3), 251-70 & 10TH COLLECTIVE IN-  
DEX, P.  
20307CS,20308CS,20328CS,20329CS,20331CS

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Description

The present invention relates to a method of treatment or prophylaxis of angina pectoris in mammals, and to novel compounds useful in such a method.

5 British Patent 862467 discloses a class of compounds of formula (A):



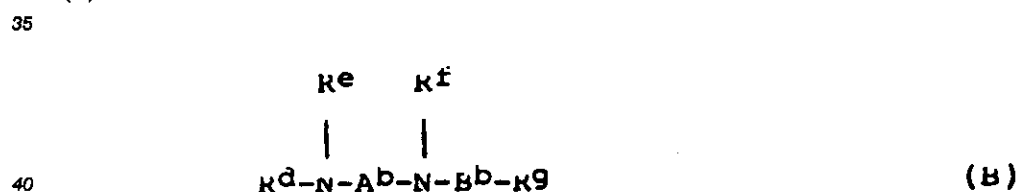
20 in which R is hydrogen or halogen or a lower alkoxy, hydroxy, lower alkanoyloxy, lower alkyl, nitro, amino or lower alkanoylamino radical,

R<sup>b</sup> is hydrogen or halogen or a lower alkyl, lower alkoxy, hydroxy or lower alkanoyloxy radical,

R<sup>a</sup> and R<sup>c</sup> are lower alkyl radicals, X<sup>1</sup> is a divalent hydrocarbon radical of 1-4 carbon atoms, and wherein said lower radicals contain not more than six carbon atoms, and where A<sup>a</sup> and B<sup>a</sup> can each be a hydrogen  
25 atom, a methyl group or ethyl group with the proviso that together they may not contain more than two carbon atoms, and acid addition salts thereof. The compounds are described as active as analgesics. Compounds specifically disclosed in the patent include those where [R, X<sup>1</sup>, R<sup>a</sup>, A<sup>a</sup>, B<sup>a</sup>, R<sup>c</sup>, R<sup>b</sup>] take the

30 following combinations of values:  
[H, CH<sub>2</sub>, CH<sub>3</sub>, H, H, nC<sub>3</sub>H<sub>7</sub>, H], [H, CH<sub>2</sub>, CH<sub>3</sub>, H, H, iC<sub>3</sub>H<sub>7</sub>, H], [H, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, H, CH<sub>3</sub>, nC<sub>3</sub>H<sub>7</sub>, H], [H, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>3</sub>, H, nC<sub>3</sub>H<sub>7</sub>, H], [H, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>3</sub>, H, iC<sub>3</sub>H<sub>7</sub>, H] and [H, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>3</sub>, H, nC<sub>4</sub>H<sub>9</sub>, H].

In European Journal of Pharmacology, 44(1977) 251-270, Frans G. Van den Brink and Erik J. Lien, a group of compounds are studied in a histaminic and a cholinergic system. The compounds are of formula (B):

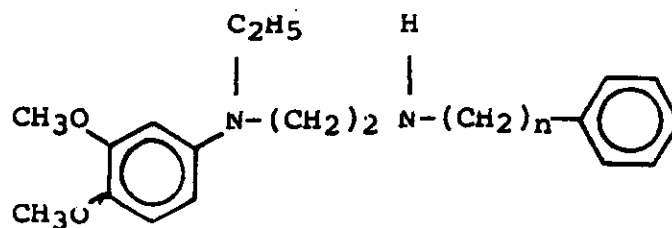


where the variables [R<sup>d</sup>, R<sup>e</sup>, A<sup>b</sup>, R<sup>f</sup>, B<sup>b</sup>, R<sup>g</sup>] take the following values:

- 45 [phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phenyl]  
[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phenyl]  
[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]  
[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>3</sub>, phenyl]  
[4-chlorophenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phenyl]  
[4-chlorophenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]  
50 [phenyl, 4-chlorobenzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]  
[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-chlorophenyl]

In Ann. 1st. Super. Sanita 1971, 7 (Pt. 4), 533-9, the compounds

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10 where n is 1 or 2, are described as chemical intermediates in the preparation of certain benzodiazepines.

GB 1,050,132 describes N,N'-substituted diaminoethane compounds which are described as possessing physiological activity on the heart and the blood circulation.

It has been discovered that compounds of formula (1) and pharmaceutical salts thereof:



wherein

R<sub>1</sub> and R<sub>4</sub> are independently phenyl optionally substituted by one, two or three of halogen, trifluoromethyl, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl, cyano, hydroxy, nitro, NR<sub>5</sub>R<sub>6</sub> or O<sub>2</sub>SNR<sub>5</sub>R<sub>6</sub> wherein R<sub>5</sub> and R<sub>6</sub> are independently hydrogen or C<sub>1-6</sub> alkyl or together are C<sub>3-6</sub> polymethylene, or disubstituted at adjacent carbon atoms by C<sub>1-2</sub> alkylendioxy and optionally further substituted by one of the above groups;

R<sub>2</sub> is selected from (CH<sub>2</sub>)<sub>z</sub> CN where z is O or an integer from 1 to 4, C<sub>1-12</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl C<sub>1-4</sub> alkyl, phenyl C<sub>1-4</sub> alkyl, pyridyl, pyridyl C<sub>1-4</sub> alkyl, COR<sub>7</sub>, COCH<sub>2</sub>COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> and CSNHR<sub>7</sub>, where R<sub>7</sub> is selected from C<sub>3-12</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl C<sub>1-4</sub> alkyl, phenyl and phenyl C<sub>1-4</sub> alkyl, any alkyl moiety in R<sub>7</sub> optionally substituted by hydroxy or C<sub>1-4</sub> alkanoyloxy, any pyridyl or phenyl moiety in R<sub>2</sub> optionally substituted as defined for R<sub>1</sub> and R<sub>4</sub> and any cycloalkyl moiety in R<sub>2</sub> optionally substituted by one or two C<sub>1-4</sub> alkyl groups;

R<sub>3</sub> is hydrogen or C<sub>1-4</sub> alkyl;

A represents C<sub>2-5</sub> alkylene; and

B represents C<sub>1-4</sub> alkylene, have been found to possess cardiovascular activity, in particular calcium antagonistic activity which indicates that they are of potential use in the treatment of angina pectoris.

An amount effective to treat the disorder hereinbefore described depends on the relative efficacies of the compounds of the formula (1), the nature and severity of the disorders being treated and the weight of the mammal. However, a unit dose will normally contain 0.1 to 500 mg for example 2 to 50 mg, of the compound of the invention. Unit doses will normally be administered once or more than once a day, for example 2,3,4,5 or 6 times a day, more usually 2 to 4 times a day, such that the total daily dose is normally in the range, for a 70 kg adult of 0.1 to 2500 mg, more usually 50 to 2000 mg, for example 10 to 75mg, that is in the range of approximately 0.002 to 35 mg/kg/day, more usually 1 to 30 mg/kg/day, for example 0.15 to 1 mg/kg/day.

At the above described dosage range, no toxicological effects are indicated for the compounds of the invention.

In such treatment, the compound may be administered by any suitable route, e.g. by the oral, parenteral or topical routes. For such use, the compound will normally be employed in the form of a pharmaceutical composition in association with a human or veterinary pharmaceutical carrier, diluent and/or excipient, although the exact form of the composition will naturally depend on the mode of administration.

Compositions are prepared by admixture and are suitably adapted for oral, parenteral or topical administration, and as such may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, pastilles, reconstitutable powders, injectable and infusible solutions or suspensions, suppositories and transdermal devices. Orally administrable compositions are preferred, in particular shaped oral compositions, since they are more convenient for general use.

Tablets and capsules for oral administration are usually presented in a unit dose, and contain conventional excipients such as binding agents, fillers, diluents, tableting agents, lubricants, disintegrants, colourants, flavourings, and wetting agents. The tablets may be coated according to well known methods in

the art.

Suitable fillers for use include cellulose, mannitol, or lactose. Suitable disintegrants include starch, polyvinylpyrrolidone and starch derivatives such as sodium starch glycolate. Suitable lubricants include, for example, magnesium stearate. Suitable pharmaceutically acceptable wetting agents include sodium lauryl sulphate.

These solid oral compositions may be prepared by conventional methods of blending, filling or tableting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are, of course, conventional in the art.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethyl cellulose, aluminium stearate gel or hydrogenated edible fats, emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example, almond oil, fractionated coconut oil, oily esters such as esters of glycerine, propylene glycol, or ethyl alcohol, preservatives, for example methyl or propyl *p*-hydroxybenzoate or sorbic acid, and if desired conventional flavouring or colouring agents.

For parenteral administration, fluid unit dose forms are prepared containing a compound of the present invention and a sterile vehicle. The compound, depending on the vehicle and the concentration, can be either suspended or dissolved. Parenteral solutions are normally prepared by dissolving the compound in a vehicle and filter sterilising before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are also dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum.

Parenteral suspensions are prepared in substantially the same manner except that the compound is suspended in the vehicle instead of being dissolved and sterilized by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the active compound.

For topical administration, the composition may be in the form of a transdermal ointment or patch for systemic delivery of the compound and may be prepared in a conventional manner, for example, as described in the standard textbooks such as 'Dermatological Formulations' - B.W. Barry (Drugs and the Pharmaceutical Sciences - Dekker) or Harrys Cosmeticology (Leonard Hill Books).

In addition such compositions may contain further active agents such as anti-hypertensive agents and diuretics.

As is common practice, the compositions will usually be accompanied by written or printed directions for use in the medical treatment concerned.

The invention also provides the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing, for the preparation of a medicament for the treatment or prophylaxis of angina pectoris in mammals.

The invention further provides a pharmaceutical composition for use in the treatment or prophylaxis of angina pectoris in mammals, which comprises a compound of formula (I) or a pharmaceutically acceptable salt thereof, or a solvate or any of the foregoing, and a pharmaceutically acceptable carrier.

Such compositions may be prepared in the manner hereinbefore described.

In formula (I), it is understood that alkyl and alkylene includes straight- and branched-chain alkyl and alkylene.

Suitable values for  $R_1$  and  $R_4$  include phenyl, phenyl di-substituted by methylenedioxy and optionally further substituted by chloro, or phenyl substituted by one, two or three of fluoro, chloro, bromo, trifluoromethyl, methoxy, ethoxy, *n*- or *iso*-propoxy, methyl, ethyl, *n*- or *iso*-propyl, cyano, hydroxy or amino optionally substituted by one or two methyl groups.  $R_1$  and  $R_4$  are preferably the same group, most preferably 3,4-dimethoxyphenyl.

Suitable values for phenyl moieties in  $R_2$  include phenyl, 2-, 3- and 4-nitrophenyl, 3,5-dinitrophenyl, 3-methoxyphenyl, 3-methoxy-6-methylphenyl, 2-trifluoromethylphenyl, 2,4,6-trimethylphenyl, 2,6-dichlorophenyl, 2-chloro-3,4-methylenedioxyphenyl, 4-cyanophenyl, 4-chlorophenyl and 4-methylphenyl.

Suitable values for cycloalkyl moieties in  $R_2$  include cyclopentyl, cyclohexyl and menthyl.

Suitable values for alkylene moieties in  $R_2$  include  $-CH_2-$ ,  $-CH(CH_3)-$ ,  $-CH_2CH_2CH_2-$  and  $-CH_2CH_2-$ . Suitable values for  $R_2$  when alkyl include *n*-pentyl. Alkyl  $R_7$  in  $R_2$  may be  $C_4-12$ , more preferably  $C_5-12$  alkyl groups which are preferably straight-chain. Suitable values for alkyl  $R_7$  in  $R_2$  includes *n*- and *iso*- $C_3H_7$ , *n*- $C_4H_9$ , *n*- $C_5H_{11}$ , *n*- $C_6H_{13}$ , *n*- $C_7H_{15}$ , *n*- $C_8H_{17}$  and *n*- $C_{11}H_{23}$ .

Suitable values for pyridyl moieties in  $R_2$  include 2-pyridyl optionally 3,5-dinitro-substituted.

Suitable values for optional substituents on alkyl moieties in  $R_7$  include acetoxy.

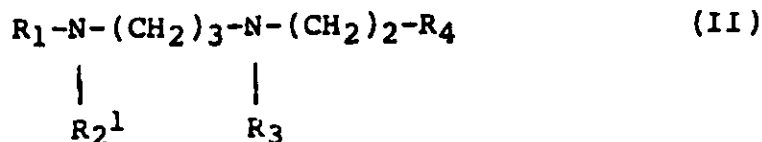
Suitable values for  $z$  in  $R_2$  include 0 or 1.

Suitable values for  $C_{1-4}$  alkyl groups in  $R_2$  include methyl and ethyl.

Suitable values for  $R_3$  include hydrogen, methyl, ethyl, n- and iso-propyl, and n, iso-, sec- and t-butyl. Preferably  $R_3$  is methyl.

Suitable values for A and B include  $-(CH_2)_2-$  and  $-(CH_2)_3-$ .

There is a sub-group of compounds within formula (I) of formula (II):



wherein:

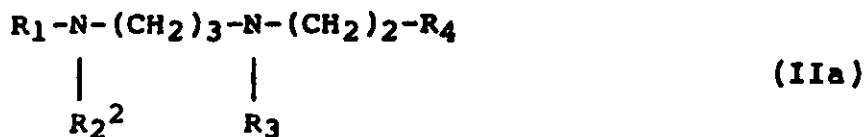
$R_1$ ,  $R_3$  and  $R_4$  are as defined in formula (I); and

$R_2^1$  is  $(CH_2)_zCN$ ,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl or phenyl  $C_{1-4}$  alkyl wherein  $z$  is as defined in formula (I) and any phenyl, alkyl, or cycloalkyl moieties in  $R_2^1$  are optionally substituted as defined for corresponding variables  $R_2$  in formula (I).

Suitable and preferred values for  $R_2^1$ ,  $R_1$ ,  $R_3$  and  $R_4$  are as described for the corresponding variables under formula (I).

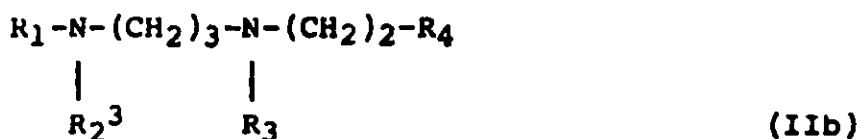
A preferred value for  $R_1$  and  $R_4$  is 3,4-dimethoxyphenyl.

There is another group of compounds within formula (I) of formula (IIa):



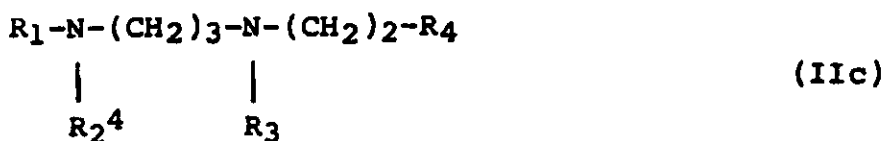
wherein  $R_2^2$  is  $COR_7$  where  $R_7$  is as defined in formula (I), and the remaining variables are as defined in formula (I).

There is further group of compounds within formula (I) of formula (IIb):



wherein  $R_2^3$  is  $CO_2R_7$  or  $SO_2R_7$  where  $R_7$  is as defined in formula (I), and the remaining variables are as defined in formula (I).

There is another group of compounds within formula (I) of formula (IIc):



wherein  $R_2^4$  is  $CONHR_7$  or  $CSNHR_7$  where  $R_7$  is as defined in formula (I), and the remaining variables are as defined in formula (I).

Suitable and preferred values for the variables of formulae (IIa), (IIb) and (IIc) are as described for the

corresponding variables under formula (II).

It will of course be realized that the compounds of formula (I) possess two chiral centres and therefore exist in more than one stereoisomeric form. The invention extends to any of the stereoisomeric forms, including enantiomers of the compounds of formula (I) and to mixtures thereof, including racemates. The different stereoisomeric forms may be separated or resolved one from the other by the usual methods or any given isomer may be obtained by stereospecific or asymmetric syntheses.

The pharmaceutically acceptable salts of the compounds of formula (I) include acid addition salts with conventional acids such as hydrochloric, hydrobromic, boric, phosphoric, sulphuric and pharmaceutically acceptable organic acids such as acetic, tartaric, maleic, citric, succinic, benzoic, ascorbic, methanesulphonic,  $\alpha$ -keto-glutaric,  $\alpha$ -glycerophosphoric, and glucose-1-phosphoric acids. Preferably the acid addition salt is a hydrochloride.

Pharmaceutically acceptable salts also include quaternary salts. Examples of quaternary salts include such compounds quaternised by compounds such as  $R_8$ -T wherein  $R_8$  is  $C_{1-6}$  alkyl, phenyl- $C_{1-6}$  alkyl or  $C_{5-7}$  cycloalkyl, and T is a radical corresponding to an anion of an acid. Suitable examples of  $R_8$  include methyl, ethyl and *n*- and *iso*-propyl; and benzyl and phenethyl. Suitable T include halide such as chloride, bromide and iodide.

Pharmaceutically acceptable salts also include pharmaceutically acceptable N-oxides.

The compounds of the formula (I) and their pharmaceutically acceptable salts may also form solvates with pharmaceutically acceptable solvates.

It will also be realised that salts of the compounds of the formula (I) which are not pharmaceutically acceptable may be useful as intermediates in the preparation of pharmaceutically acceptable salts of compounds of the formula (I) or the compounds of the formula (I) themselves.

The invention further provides a compound of formula (I) or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing, with the proviso that the variables [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] do not take the following combinations of values:

- [phenyl,  $CO_nC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]
- [phenyl,  $COiC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]
- [phenyl,  $CONC_3H_7$ ,  $CH(CH_3)CH_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl,  $CONC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl,  $COiC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl,  $CONC_4H_9$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl, benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]
- [phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]
- [phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_3$ , phenyl]
- [4-chlorophenyl, benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]
- [4-chlorophenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl, 4-chlorobenzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]
- [phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , 4-chlorophenyl]

for use as an active therapeutic substance, and particularly for the treatment or prophylaxis of angina pectoris.

The class of compounds as just defined will be referred to hereinafter as compounds of formula (IA).

The invention also provides a pharmaceutical composition comprising a compound of formula (IA) and a pharmaceutically acceptable carrier.

In another aspect the invention provides a compound of formula (IA) with the proviso that the variables [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] do not take the following combinations of values:

- [3,4-dimethoxyphenyl,  $C_2H_5$ ,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]
- [3,4-dimethoxyphenyl,  $C_2H_5$ ,  $(CH_2)_2$ , H,  $CH_2$ , phenyl]

The class of compounds as just defined will be referred to hereinafter as compounds of formula (IB).

Suitable and preferred values for variables in formula (IB) are as defined for the corresponding variables in formula (I).

In one sub-group of the formula (IB),  $R_1$  and  $R_4$  are independently phenyl substituted as defined in formula (I).

In another sub-group of the formula (IB),  $R_2$  is  $COR_7$  where  $R_7$  is phenyl or phenyl  $C_{1-4}$  alkyl, the phenyl moiety optionally substituted as defined for  $R_1$  and  $R_4$ .

In a further subgroup of formula (IB),  $R_2$  is  $C_{3-12}$  alkyl.

In another subgroup of formula (IB),  $R_1$  and  $R_4$  are independently phenyl substituted by one, two or three of halogen, trifluoromethyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl, cyano, hydroxy, nitro,  $NR_5R_6$  or  $O_2SNR_5R_6$

wherein  $R_5$  and  $R_6$  are independently hydrogen or  $C_{1-6}$  alkyl or together are  $C_{3-6}$  polymethylene, or disubstituted at adjacent carbon atoms by  $C_{1-2}$  alkylendioxy;

$R_2$  is selected from  $(CH_2)_z CN$  where  $z$  is O or an integer from 1 to 4,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl  $C_{1-4}$  alkyl,  $COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  and  $CSNHR_7$ , where  $R_7$  is selected from  $C_{3-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl and phenyl  $C_{1-4}$  alkyl, any phenyl moiety in  $R_2$  optionally substituted as defined for  $R_1$  and  $R_4$ ;

$R_3$  is hydrogen or  $C_{1-4}$  alkyl;

A represents  $C_{2-5}$  alkylene; and

B represents  $C_{1-4}$  alkylene.

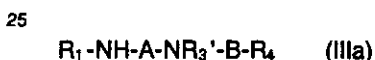
10 A process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof comprises reacting together  $R_{10}X$  and  $YR_{11}$  wherein one of X and Y is a leaving group or aldehyde or ketone function and the other is a nitrogen nucleophile, the nitrogen nucleophile,  $R_{10}$  and  $R_{11}$ , and the aldehyde or ketone function when present, being such that a compound of formula (III) is formed:



in which  $R_2'$ , A',  $R_3'$  and B' are  $R_2$ , A,  $R_3$  and B respectively or groups convertible thereto, and thereafter, optionally or as necessary, converting  $R_2'$ , A',  $R_3'$ , and/or B' to  $R_2$ , A,  $R_3$  and/or B, interconverting  $R_2$  and/or  $R_3$  and/or forming a pharmaceutically acceptable salt.

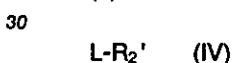
20 Suitable examples of  $R_2'$  convertible to  $R_2$  include hydrogen and  $C_{1-3}$  alkanoyl.  $R_2'$   $C_{1-3}$  alkanoyl may be converted to  $R_2$   $C_{1-3}$  alkyl by reduction under conventional conditions, for example with  $LiAlH_4$  as the reducing agent in an inert solvent such as tetrahydrofuran.  $R_2'$  hydrogen may be converted to  $R_2$  by conventional amine alkylation or acylation.

In a preferred embodiment the process comprises reacting a compound of formula (IIIa):



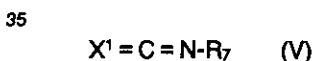
wherein the variables are as defined in formula (III),

(a) with a compound of formula (IV):



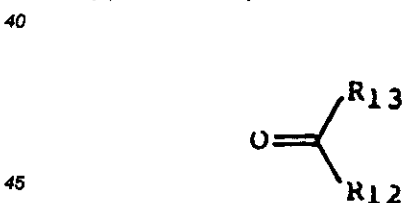
wherein  $R_2'$  is  $R_2$  as defined in formula (I) or a group convertible thereto, and L is a leaving group;

(b) with a compound of formula (V):



wherein  $X'$  is O or S and  $R_7$  is as defined in formula (I); or

(c) with a compound of formula (VI):



(VI)

wherein  $R_{12}$  and  $R_{13}$  are such that



55 is  $R_2$  as defined in formula (I) and thereafter, optionally or as necessary, converting  $R_3'$  when a protecting group to  $R_3$  and/or converting  $R_3$  when hydrogen to another  $R_3$  and/or converting  $R_2'$  to  $R_2$  and/or converting  $R_2$  to other  $R_2$  and/or forming a pharmaceutically acceptable salt.

In the compound of formula (IV), the leaving group L is a group readily displaceable by a nucleophile. Suitable examples of L are hydroxy, halogen such as chloro, bromo and iodo and acyloxy such as mesyloxy, tosyloxy, triflate, C<sub>1-4</sub> alkanoyloxy, C<sub>1-4</sub> alkoxy-carbonyloxy and activated hydrocarbyloxy such as pentachlorophenoxy.

5 If the leaving group is hydroxy, then the reaction is preferably carried out in an inert non-hydroxylic solvent, such as benzene, toluene or diethyl ether in the presence of a dehydrating catalyst, such as a carbodiimide, for example dicyclohexylcarbodiimide. The reaction may be carried out at a non-extreme temperature such as -10 to 100°C, for example 0 to 80°C.

10 If the leaving group is a halide, then the reaction is preferably carried out at a non-extreme temperature in an inert non-hydroxylic solvent, such as trichloromethane, xylene, benzene, toluene or diethyl ether. It is also preferably carried out in the presence of an acid acceptor, such as an organic base, in particular a tertiary amine, such as triethylamine, trimethylamine, pyridine or picoline, some of which can also function as a solvent. Alternatively, the acid acceptor can be inorganic, such as calcium carbonate, sodium carbonate or potassium carbonate.

15 If the leaving group is acyloxy, then the reaction is preferably carried in substantially the same manner as if the leaving group were hydroxy. Suitable examples of acyloxy leaving groups include C<sub>1-4</sub> alkanoyloxy, mesyloxy, tosyloxy and triflate.

If the leaving group is C<sub>1-4</sub> alkoxy-carbonyloxy, then the reaction is preferably carried out in an inert solvent, such as methylenechloride, at a non-extreme temperature in the presence of an acid acceptor, such as triethylamine.

20 If the leaving group is activated hydrocarbyloxy then the reaction is preferably carried out in an inert polar solvent, such as dimethylformamide. It is also preferred that the activated hydrocarbyloxy group is a pentachlorophenyl ester and that the reaction is carried out at ambient temperature.

When R<sub>2</sub> is an alkyl-type moiety, the leaving group is preferably halide or tosyloxy. When R<sub>2</sub> is an acyl-type moiety, the leaving group is preferably halide or hydroxy, more preferably halide.

25 The reaction between the compounds or formulae (IIIa) and (V) may be carried out under conditions suitable for the preparation of a urea, for example in an inert solvent such as chloroform at moderate temperature, suitably the boiling point of the solvent, for example 40° - 80°C.

30 The reaction between the compounds or formulae (IIIa) and (VI) may be carried out under conditions suitable for a reductive alkylation, in the presence of a suitable reducing agent such as NaCNBH<sub>3</sub> in an inert solvent such as methanol.

35 Examples of N-protecting groups for R<sub>3</sub>' include C<sub>1-6</sub> alkanoyl, for example acetyl, propionyl, *n*- and *iso*-butyryl and 2,2-dimethylpropanoyl, benzoyl or benzyl optionally substituted in the phenyl ring by one or two substituents selected from C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, trifluoromethyl, halogen or nitro; and C<sub>1-4</sub> alkoxy-carbonyl, for example *tert*-butoxycarbonyl.

Conversion of protected amino to amino may be effected conventionally.

When the protecting group is C<sub>1-6</sub> alkanoyl or optionally substituted benzoyl as defined, conversion to amino is conveniently effected by conventional base hydrolysis.

40 When the protecting group is C<sub>1-4</sub> alkoxy-carbonyl or optionally substituted benzyl as defined, conversion to amino may be carried out conventionally, for example by hydrogenolysis. Suitable reactions are conventionally transition-metal catalysed hydrogenation, using for example palladium- or platinum-charcoal, at atmospheric pressure or a light excess thereover. A dry, inert, polar solvent such as dry ethanol and ambient temperatures are apt.

45 Subsequent conversion of R<sub>3</sub> when hydrogen to other R<sub>3</sub> may be carried out by conventional amine alkylation, for example with the appropriate aldehyde or ketone in a solvent such as acetonitrile or methanol, in the presence of a reducing agent such as an alkaline porohydride e.g. sodium cyanoborohydride.

Alternatively, conversion of an R<sub>3</sub>' C<sub>1-4</sub> alkanoyl protecting group to the corresponding R<sub>3</sub> C<sub>1-4</sub> alkyl group may be carried out directly by reduction under conventional conditions, for example with LiAlH<sub>4</sub> as the reducing agent in an inert solvent such as tetrahydrofuran.

50 Examples of group A' and B' convertible to A and B include alkylene chains containing a carbonyl group which may be reduced under conventional conditions with a suitable reducing agent such as LiAlH<sub>4</sub> in an inert solvent such as tetrahydrofuran.

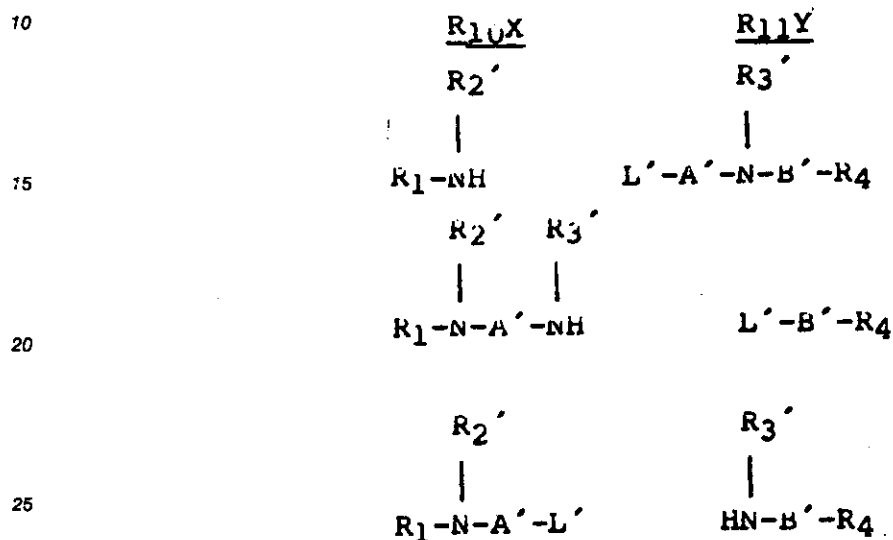
Interconversion of groups R<sub>2</sub> may be carried out conventionally. Thus, for example, a group R<sub>2</sub> of the formula COR<sub>7</sub> may be reduced to the corresponding alkyl group CH<sub>2</sub>R<sub>7</sub> under the conditions just described for the reduction of R<sub>3</sub>' to R<sub>3</sub>.

55 It will be appreciated that the selective removal or reduction of an R<sub>3</sub>' protecting group will generally only be carried out in the presence of alkyl-type R<sub>2</sub> groups. Where R<sub>2</sub>' and R<sub>3</sub>' are both alkanoyl groups, simultaneous reduction of both moieties may be performed to give the corresponding R<sub>2</sub> and R<sub>3</sub> alkyl

groups.

In the reaction between the compounds  $R_{10}X$  and  $R_{11}Y$ , the leaving group may be any suitable group as defined above for L, such as halo, particulary chloro or bromo, tosyloxy or mesyloxy and the nucleophilic substitution reaction carried out as described above for the reaction of compounds of formulae (IIIa) and (IV), preferably in an inert solvent such as xylene, toluene or trichloromethane at elevated temperature in the presence of a base such as triethylamine.

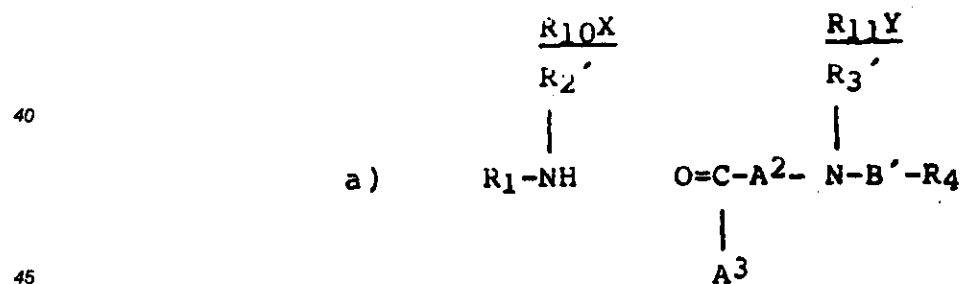
Suitable pairs of  $R_{10}X$  and  $R_{11}Y$  include:



wherein L' is a leaving group and the remaining variables are as previously defined. The leaving group L' is a group readily displaceable by a nucleophile. Suitable examples for L' are as described above for L.

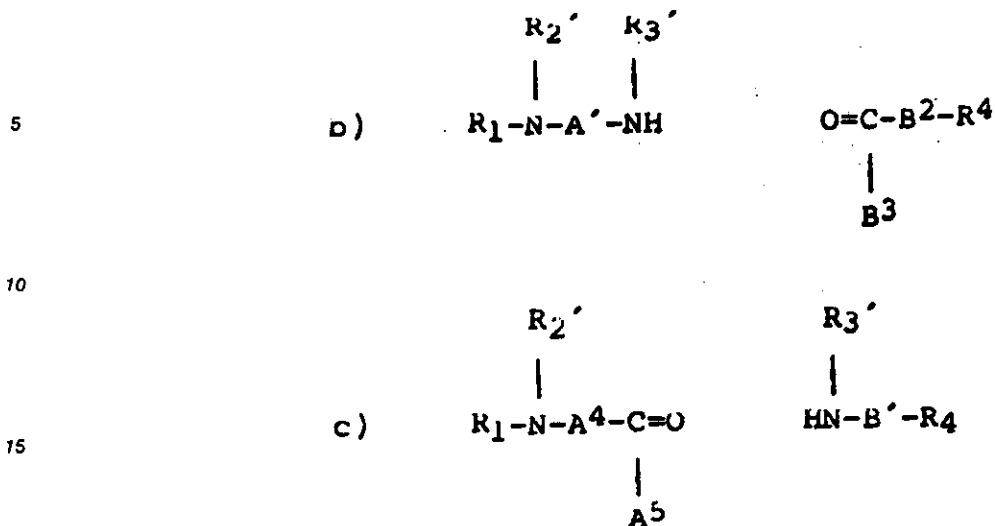
Where X or Y is an aldehyde or ketone function, the reaction is a reductive alkylation which may be carried out conventionally, for example in a solvent such as toluene or methanol with a reducing agent such as  $NaBH_4$  or  $NaCNBH_3$ .

Suitable pairs of  $R_{10}X$  and  $R_{11}Y$  include:



50

55



20 in which A', B', R<sub>1</sub>, R<sub>2</sub>', R<sub>3</sub>' and R<sub>4</sub> are as previously defined,

a) provides a compound of formula (I) in which the alkylene moiety -A- is of the form



30 b) provides a moiety -B- of the form



and

c) provides a moiety -A- of the form



45 Pharmaceutically acceptable salts including N-oxides of the compounds of formula (I) may be formed conventionally. The salts may be formed for example by reaction of the base compound of formula (I) with a pharmaceutically acceptable organic or inorganic acid.

50 N-oxides are produced by reaction of a compound of formula (I) with an organic peracid, such as m-chloroperbenzoic acid in, for example, a chlorinated hydrocarbon solvent at below ambient temperature.

Quaternary ammonium salts may be prepared by reaction of a compound of formula (I) with the appropriate alkyl, aryl or aralkyl, chloride, bromide or iodide. This reaction may be carried out in a solvent, such as acetone, methanol, ethanol or dimethylformamide, at ambient or elevated temperature with or without pressure.

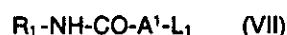
55 Racemates of compounds of the formula (I) may be resolved conventionally, e.g., by salification with a chiral acid if appropriate and separation of the resultant salts.

Alternatively, either may be synthesised from corresponding chiral preceding intermediates.

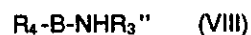
The invention also provides novel intermediates of the formula (IIa).

Compounds of formula (IIIa) may be prepared by any suitable conventional procedures, in particular nucleophilic substitution and/or reductive alkylation by analogy with the reaction of compounds  $R_{10}X$  and  $R_{11}Y$  described above.

Thus, for example, compounds of formula (IIIa) may be prepared by reacting the compound of formula (VII):



in which  $L_1$  is a leaving group,  $A^1$  is a group such that  $CH_2A^1$  represents A, and  $R_1$  is as above defined, with a compound of formula (VIII)



in which  $R_3''$  is  $R_3'$  or a group convertible thereto, and  $R_4$  and B are as above defined, to give a compound of formula (IX):



and thereafter reducing the compound of formula (IX) and, optionally or as necessary, converting  $R_3''$  to  $R_3'$ .

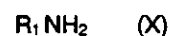
The leaving group  $L_1$  is a group readily displaceable by a nucleophile. Suitable and preferred values for  $L_1$  are described for L as hereinbefore defined. The reaction is carried out in an analogous manner to that between compounds of formulae (IIIa) and (IV), suitably in trichloromethane in the presence of triethylamine as the acid acceptor.

Where  $R_3'$  in the compound of formula (III) is an alkanoyl function, suitable groups  $R_3''$  convertible thereto include hydrogen, which may be converted to alkanoyl by reaction with the appropriate acid halide under conditions mentioned above for the reaction of the compounds of formulae (IIIa) and (IV) where L is halide, suitably in trichloromethane in the presence of triethylamine. Alternatively, when  $R_3$  in formula (I) is an alkyl moiety,  $R_3''$  may be the same alkyl moiety. The reduction of the compound of formula (IX) may be carried out under conventional amide reduction conditions as described above for the reduction of  $R_3'$  to  $R_3$ , suitably with  $LiAlH_4$  in tetrahydrofuran.

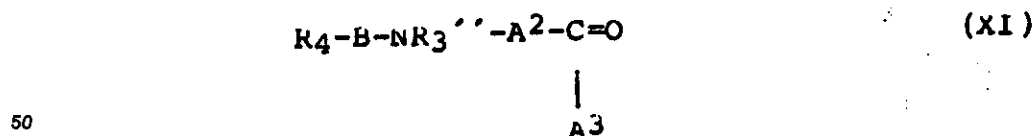
Compounds of the formula (IIIa) in which the alkylene moiety -A- is of the form



may be prepared by the reductive alkylation of compound of formula (X):



in which  $R_1$  is as above defined, with a compound of formula (XI):



where the variables are as above defined, followed by the optional conversion of  $R_3''$  to  $R_3'$  as described above.

The reductive alkylation may be carried out conventionally for example in a solvent such as toluene with a reducing agent such as  $NaBH_4$ .

Compounds of formula (IIIa) may alternatively be prepared by reacting a compound of formula (XII):



wherein the variables are as above defined, with a compound of formula (XIII):



wherein  $L_3$  is a leaving group and the remaining variables are as above defined, as described above for the nucleophilic substitution reaction of compounds  $R_{10}X$  and  $R_{11}Y$ .

Examples of the leaving group  $L_3$  include those described below for  $L_2$ .

10 Compounds  $R_{10}X$  and  $R_{11}Y$  are known compounds or may be prepared by processes analogous to those for preparing known compounds. Thus, for example, compound  $R_{11}Y$  such as compounds of formula (XI) may be prepared by the reaction of a compound of formula (XIV):



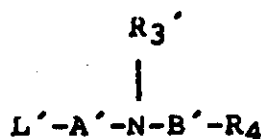
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in which  $L_2$  is a leaving group and  $A^2$  and  $A^3$  are as above defined, with a compound of formula (VIII) above, followed by deprotection of the protected carbonyl moiety under acid conditions. The reaction between the compounds of formulae (XIV) and (VIII) is preferably carried out in an inert solvent such as  $CHCl_3$ , with heating in the presence of a base such as triethylamine. Examples of the leaving group  $L_2$  include halogen, tosylate, or other leaving groups described above for  $L$ .

25

Compounds  $R_{11}Y$  of the form.

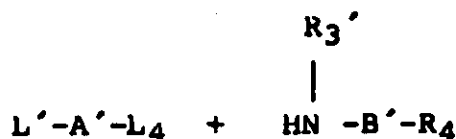
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35

may be prepared as follows:

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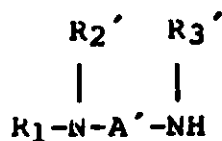


45

where  $L_4$  is a leaving group such as described above for  $L_3$  and the remaining variables are as previously described, under mildly basic conditions such as  $K_2CO_3$  in an inert solvent such as dimethylformamide. Suitable examples of the groups  $L'$  and  $L_4$  are chloro and bromo respectively.

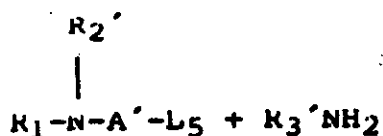
Compounds  $R_{10}X$  of the form:

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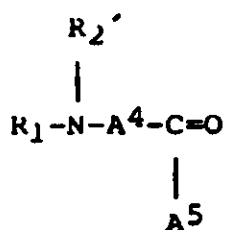
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may be prepared as follows:

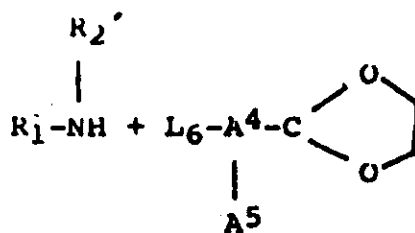


where  $L_5$  is a leaving group such as described for  $L_4$  and the remaining variables are as previously described, in an inert solvent such as described above for the reaction of  $R_{10}X$  and  $R_{11}Y$ .

Compounds  $R_{10}X$  of the form:

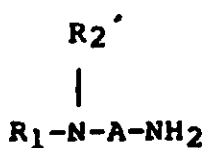


may be prepared as follows:



where  $L_6$  is a leaving group such as described above for  $L_2$  and the remaining variables are as defined, in an inert solvent such as described above for the reaction for the reaction of  $R_{10}X$  and  $R_{11}Y$ , in the presence of a base such as triethylamine at elevated temperature, followed by deprotection with acid.

Compounds  $R_{10}X$  of the form:



such as compounds of formula (XII) may be prepared by the reaction of a compound of formula (XV)



wherein each of  $A^6$ ,  $A^7$  and  $A^8$  is hydrogen or alkyl such that



10 is A as above defined, with a compound of formula (XVI):



followed by reduction of the resulting nitrile.

20 The reaction of the compounds of formulae (XV) and (XVI) is base catalysed, and the reduction step may be carried out using  $\text{LiAlH}_4$ .

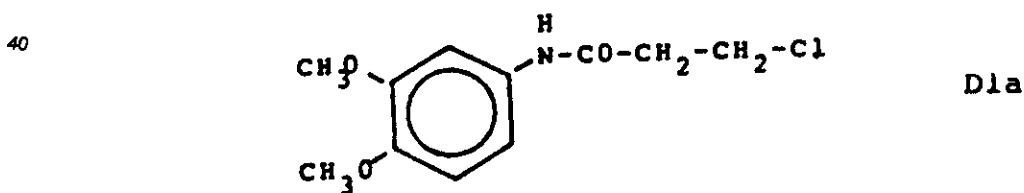
The compounds of formulae (IV) to (VIII), (X) and (XIII) to (XVI), and analogous compounds  $\text{R}_{10}\text{X}$  and  $\text{R}_{11}\text{Y}$  are known compounds or may be prepared by processes analogous to those for preparing known compounds. Thus, compounds of formula (VII) may be prepared by reaction of the appropriately substituted  
 25 aniline with a compound  $\text{L}_1\text{A}'\text{COCl}$  under the conditions mentioned above for the reaction of the compounds of formulae (IIIa) and (IV). Compounds of formula (VIII) may be prepared by the conventional amine alkylation or acylation of a compound  $\text{R}_4\text{BNH}_2$  under similar conditions.

The invention therefore provides a process for the preparation of a compound of formula (IB) which process comprises reacting together  $\text{R}_{10}\text{X}$  and  $\text{YR}_{11}$  as hereinbefore defined, to give a compound of  
 30 formula (III) as defined, and thereafter, optionally or as necessary, converting  $\text{R}_2'$ ,  $\text{A}'$ ,  $\text{R}_3'$  and /or  $\text{B}'$  to  $\text{R}_2$ ,  $\text{A}$ ,  $\text{R}_3$  and/or  $\text{B}$ , interconverting  $\text{R}_2$  and/or  $\text{R}_3$  and/or forming a pharmaceutically acceptable salt.

The following examples illustrate the invention and the following descriptions illustrate intermediates thereto.

35 Description 1

a) 3-(3,4-Dimethoxyphenyl)-1-chloro-propionamide (D1a)



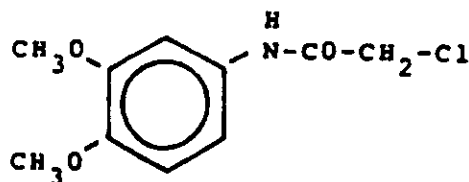
To a stirred dry solution of 85 g 3-chloropropionylchloride in 500 ml chloroform, a solution of 75 g 3,4-dimethoxyaniline and 54 g triethylamine in 200 ml chloroform was added dropwise with cooling at about 8 -  
 50  $10^\circ\text{C}$ . The solution was then kept overnight at room temperature.

Thereafter, the solution was extracted with 1M NaOH and 0.5 icewater. The organic phase was neutralised, separated and dried over  $\text{Na}_2\text{SO}_4$ . The solvent was concentrated so that a white product was precipitated which was washed three times with ether.

The yield of the white crystalline product D1a was 60% and TLC-pure.

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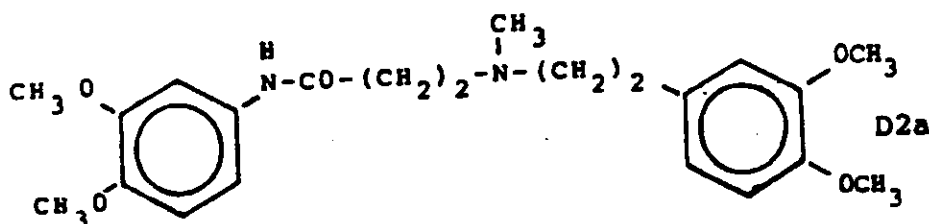
b) 2-(3,4-Dimethoxyphenyl)-1-chloro-acetamide (D1b)



10 Compound D1b was prepared by the procedure of a) above, but using 2-chloroacetylchloride as the acylating agent.

### Description 2

15 a) 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-3-propion-(3,4-dimethoxy)-anilide.(D2a)



(i) N-Methoxycarbonyl-2-(3,4-dimethoxyphenyl)-ethylamine

30 Equimolar amounts of 2-(3,4-dimethoxyphenyl)-ethylamine, triethylamine and methyl chloroformate in dry tetrahydrofuran were mixed together carefully at around 20°C. After reaction overnight at room temperature, the solid was sucked off, the solvent evaporated and the residue extracted with small amounts of water in dichloromethane. After drying, the solvent was removed. The thus obtained product N-methoxycarbonyl-2-(3,4-dimethoxyphenyl)-ethylamine in nearly quantitative yield is sufficiently pure for  
35 further reaction.

(ii) N-Methyl-2-(3,4-dimethoxyphenyl)-ethylamine

40 The product of (i) was reduced in dry tetrahydrofuran or diethylether in conventional manner by the addition of 3 equivalents of LiAlH<sub>4</sub> and subsequent refluxing of the mixture for 0.5-1hr. After cooling and filtration, the solvent was evaporated and the product obtained by first extraction of the ethereal phase at pH 4, then at pH 10 with methylene chloride. Drying and evaporation of the solvent yielded 50-60% nearly pure oily product.

45 (iii) 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-3-propion-(3,4-dimethoxy)-anilide (title compound)

To a solution of 51g 3-(3,4-Dimethoxyphenyl)-1-chloropropionamide (D1a) in 900 ml acetonitrile, 40 g N-methyl-2-(3,4-dimethoxyphenyl)-ethylamine from (ii) and 24 g triethylamine were added and the mixture refluxed for 7h under moisture protection.

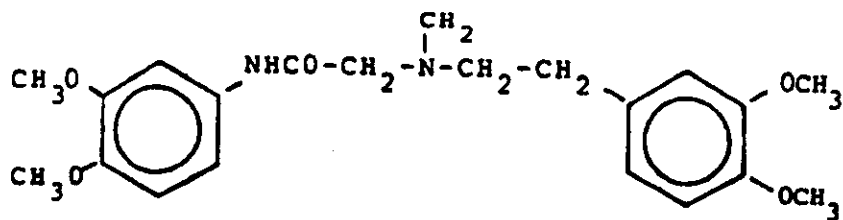
50 The solvent was removed in vacuo and the residue was extracted several times with ether at pH 6-7. Then the inorganic phase at PH 10 was extracted with methylenechloride, washed with water, dried over Na<sub>2</sub>SO<sub>4</sub> and the organic solvent removed in vacuo.

Yield; 70 g yellow oil = 65%.

The compound was sufficiently pure for further reaction.

55

b) 1-[N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-2-acet-(3,4-dimethoxy)anilide. (D2b)

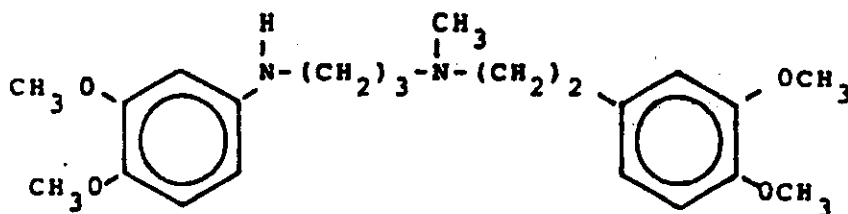


D2b

15 Compound D2b was prepared by the procedure of a) above but using intermediate D1b.

16 Description 3

17 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-(3,4-dimethoxy)-aniline (D3)



D3

30 To a suspension of 6 g  $\text{LiAlH}_4$  in 270 ml absolute tetrahydrofuran, a solution of 42 D2a in 240 ml THF was added dropwise under stirring, while the solvent was gently boiling.

35 The mixture was refluxed for 2h, then stirred at room temperature for 1h. Then excess  $\text{LiAlH}_4$  and the complex formed was hydrolysed in the usual way by dropwise successive addition of 4.5 ml  $\text{H}_2\text{O}$ , 4.5 ml 15%  $\text{NaOH}$  and 14 ml water.

40 After stirring for 1 h, the white precipitate was sucked off, washed carefully with THF and the filtrate evaporated to dryness in vacuo.

The resulting dark green oil was extracted at pH 7 - 7.5 with excess ether. Then the aqueous phase at pH 12-13 was extracted with ether several times, and the extract washed with a small amount of water, dried over  $\text{Na}_2\text{SO}_4$  and evaporated to dryness in vacuo.

32 g = 80% of a dark green oil was obtained, sufficiently pure for further reaction.

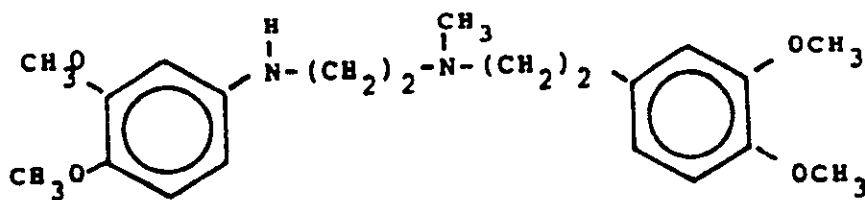
45 The oil formed a crystalline grey-white hydrochloride when treated with ethanolic hydrochloride in refluxing absolute tetrahydrofuran. M.pt.  $153^\circ\text{C}$ .

Description 4

1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-ethyl-2-(3,4-dimethoxy)-aniline (D4)

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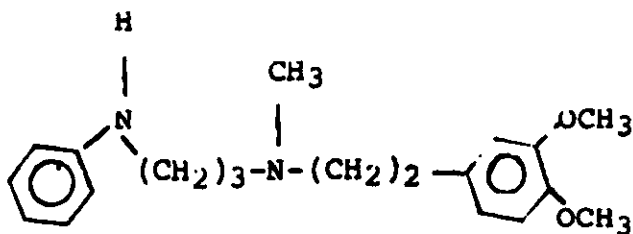


D4

Compound D4 was prepared by the procedure of Description 3 but using intermediate D2b.  
The following compounds of Descriptions 5 to 8 were prepared analogously to compound D3.

15 Description 5

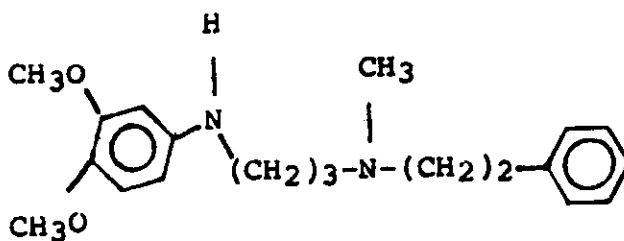
1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)ethylamino]propyl-3-aniline (D5)



D5

30 Description 6

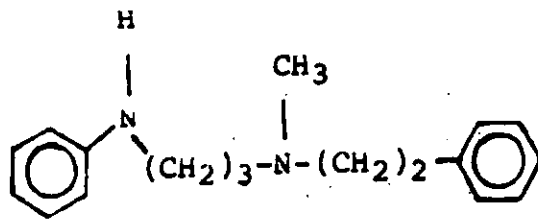
1-[N-Methyl-N-2-phenylethylamino]propyl-3-(3,4-dimethoxy)-aniline (D6)



D6

50 Description 7

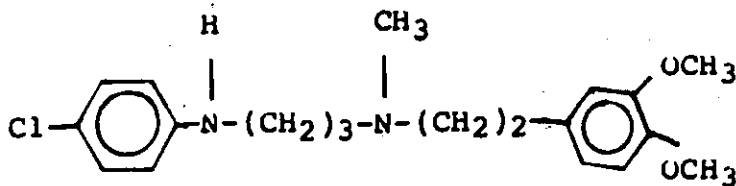
1-[N-Methyl-N-2-phenylethylamino]propyl-3-aniline (D7)



D7

15 Description 8

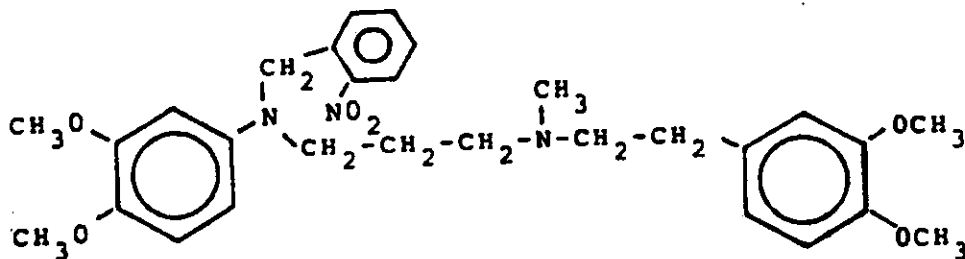
1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)ethylamino]-propyl-3-(4-chloro)-aniline (D8)



D8

30 Example 1

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-nitro)-benzylamine (E1)



E1

50 10 g 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)ethylamino]-propyl-3-(3,4-dimethoxy)-aniline (D3), 3 g triethylamine and 5 g 2-nitrobenzyl-chloride in 100 ml chloroform were refluxed under protection from moisture for 8h.

To complete the reaction, 0.7 g 2-nitrobenzylchloride and 0.5 g triethylamine were added and refluxed for another 2h. Then the solvent was removed in *vacuo* and the residue extracted with ether several times at pH 6 and then extracted with dichloromethane twice at pH9.

After drying over Na<sub>2</sub>SO<sub>4</sub>, the CH<sub>2</sub>Cl<sub>2</sub>-phase was concentrated and the product purified by column-chromatography on Al<sub>2</sub>O<sub>3</sub>, using methylene chloride with 1-2% methanol as eluent.

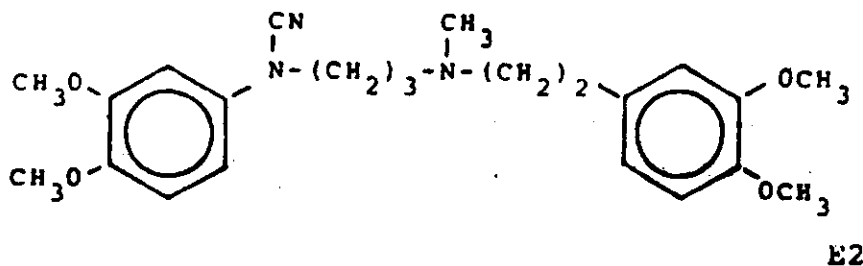
Yield was 4 g of nearly pure material (red oil) ≈ 31%.

In another bath, the raw material was purified using preparative TLC on silicagel with chloroform/methanol (9/1) as eluent. Yield was 22% of pure, red oily product.

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.29(s,3H); 2.35-2.8(m,6H); 3.39(t(J = 7.3Hz),2H); 3.75(s,3H); 3.78(s,3H), 3.82(s,3H); 3.85(s,3H); 4.83(s,2H); 6.05-6.35 (m,2H); 6.6-6.85(m,4H); 7.3-7.6(m,3H); 8.0-8.2(m,1H)

### Example 2

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanamide (E2)



Compound E2 was prepared by reaction of 1 g amine D3 in 10 ml chloroform and 1 g K<sub>2</sub>CO<sub>3</sub> with 0.32 g bromocyan (BrCN) at 0°C. Reaction was completed by stirring the mixture at room temperature for 1 h. After removing the solid by filtration and evaporation of the solvent in vacuo, the residue was purified by TLC-chromatography as described in Example 1.

Yield: 0.3 g = 30% of an red oily product.

Elementary Analysis:	C	H	N
calc.	66.80	7.55	10.16
found	66.74	7.49	10.14

### Example 3

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanomethylamine (E3)

Compound E3 was prepared from intermediate D3 and cyanomethylbromide by the procedure of Example 1.

Elementary Analysis:	C	H	N
calc.	67.42	7.78	9.83
found	67.35	7.66	9.78

The compounds of the following Examples 4 to 7 were prepared from intermediate D3 and the appropriately substituted benzylchloride by the procedure of Example 1:

### Example 4

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzylamine (E4)

Elementary Analysis:	C	H	N
calc.	72.77	8.00	5.85
found	72.69	8.04	5.78

5

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.27(s,3H); 2.3-2.8(m,6H); 3.36(t(J = 7.3Hz),2H); 3.74(s,3H); 3.78(s,3H); 3.84(s,6H); 4.44(s,2H); 6.1-6.45(m,2H), 6.6-6.9(m,4H); 7.1-7.4(m,5H).

10

Example 5

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-nitro)-benzylamine (E5)

15

Nmr (CDCl<sub>3</sub>): 1.55-2.05(m,2H); 2.28(s,3H); 2.3-2.8(m,6H); 3.38(t(J = 7.4Hz),2H); 3.77(s,3H); 3.79(s,3H); 3.83-3.84(2xs, 6H); 4.49(s,2H); 6.1-6.4(m,2H); 6.6-6.9(m,4H); 7.3-7.7(m,2H); 7.95-8.2(m,2H).

20

Example 6

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitro)-benzylamine (E6)

25

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.28(s,3H); 2.3-2.8(m,6H), 3.37(t(J = 7.5Hz),2H), 3.76(s,3H); 3.78(s,3H), 3.83(s,3H), 3.84(s,3H), 4.5(s,2H), 6.1-6.4(m,2H), 6.55-6.9(m,4H); 7.38(d(J = 8.7Hz),2H); 8.1(d(J = 8.7Hz),2H).

30

Example 7

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-benzylamine (E7)

Nmr (CDCl<sub>3</sub>): 1.5-2.0(m,2H); 2.28(s,3H); 2.31(s,3H); 2.35-2.8 (m,6H); 3.35(t(J = 7.5Hz),2H); 3.76(s,3H); 3.78(s,3H); 3.84(s,6H); 4.41(s,2H); 6.15-6.45 (m,2H), 6.55-6.85(m,4H); 6.9-7.2(m,4H).

35

The compounds of the following Examples 8 and 9 were prepared from intermediate D4 and the appropriately substituted benzylchloride by the procedure of Example 1:

Example 8

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamine (E8)

Nmr (CDCl<sub>3</sub>): 2.34(s,3H); 2.5-2.8(m,6H); 3.49(t(J = 7.7Hz),2H), 3.74(s,3H); 3.79(s,3H); 3.84(s,6H); 4.47(s,2H); 6.1-6.45(m,2H); 6.6-6.9(m,4H); 7.1-7.4(m,5H).

45

Example 9

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-nitro)-benzylamine (E9)

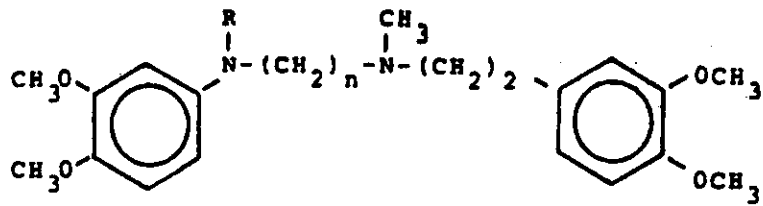
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Nmr (CDCl<sub>3</sub>): 2.33(s,3H); 2.45-2.8(m,6H); 3.48(t(J = 7.2Hz),2H); 3.76(s,3H); 3.79(s,3H); 3.84(s,6H); 4.51(s,2H); 6.1-6.4(m,2H), 6.55-6.9(m,4H); 7.3-7.7(m,2H); 8.0-8.2(m,2H).

The structure of the compounds of Examples 3 to 9 are illustrated in the following Table 1:

55

TABLE 1



15

20

25


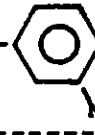



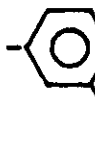
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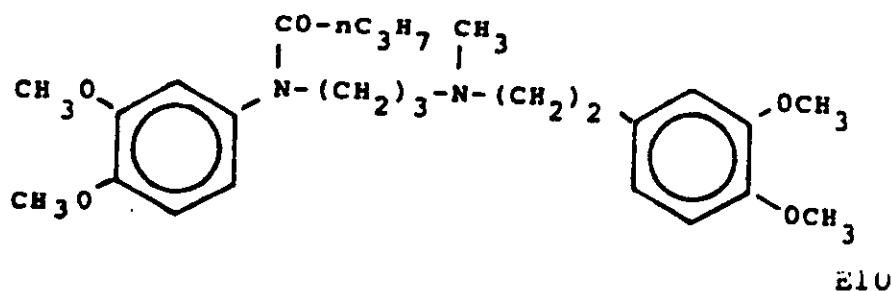
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Example No.	R	n
3	-CH <sub>2</sub> CN	3
4	-CH <sub>2</sub> - 	3
5	CH <sub>2</sub> - 	3
6	CH <sub>2</sub> - 	3
7	CH <sub>2</sub> - 	3
8	CH <sub>2</sub> - 	2
9	CH <sub>2</sub> - 	2

55 Example 10

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butanoic acid amide (E10)



15 1 g Amine D3, 0.3 g triethylamine and 0.32 g butyric acidchloride in 40 ml dry chloroform was refluxed for 3h. Isolation of the pure red oily product was achieved according to the procedure described in Example 1.

Yield 0.74 g = 65%

Nmr (CDCl<sub>3</sub>): 0.83(t(J = 6.8Hz),3H); 1.35-2.2(m,6H); 2.25(s,3H), 2.3-2.8(m,6H); 3.6-4.0(m + 2s,14H); 6.6-7.0(m,6H).

20 The compounds of the following Examples 11 to 19 were prepared from intermediate D3 and the appropriate acid chloride by the procedure of Example 10:

#### Example 11

25 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-methyl)-propanoic acid amide (E11)

30

Elementary Analysis:	C	H	N
calc.	68.10	8.35	6.11
found	68.12	8.42	5.91

35 Nmr (CDCl<sub>3</sub>): 1.02(d(J = 6.7Hz),6H); 1.5-1.95(m,2H); 2.26(s,3H), 2.3-2.8(m,7H), 3.5-4.0(m + 2s,14H); 6.55-7.0 (m,6H).

#### Example 12

40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-pentanoic acid amide (E12)

Nmr (CDCl<sub>3</sub>): 0.82(t(J = 6.2Hz),3H); 1.0-2.2(m,8H); 2.25(s,3H), 2.3-2.8(m,6H); 3.55-4.0(m + s,14H); 6.6-7.0(m,6H).

#### 45 Example 13

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzamide (E13)

50

Elementary Analysis:	C	H	N
calc.	70.71	7.36	5.68
found	70.60	7.38	5.64

55

#### Example 14

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-phenyl)-ethanoic acid amide (E14)

Elementary Analysis:	C	H	N
calc.	71.12	7.56	5.53
found	71.19	7.55	5.47

Example 15

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-phenyl)-propanoic acid amide (E15)

Nmr (CDCl<sub>3</sub>): 1.4-1.95(m,2H); 2.24(s,3H); 2.3-3.05(m,10H); 3.5-3.95(m + 2s,14H); 6.4-6.9(m,6H); 7.0-7.4(m,5H).

Example 16

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-phenyl sulphonamide (E16)

Elementary Analysis	C	H	N
calc.	64.18	7.05	5.16
found	64.09	7.02	5.15

Example 17

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-dodecanoic acid amide (E17)

Nmr (CDCl<sub>3</sub>): 0.87(t(J = 5.2Hz),3H), 1.0-2.2(m,22H); 2.26(s,3H); 2.3-2.8(m,6H); 3.6-4.0(m + 2s,14H); 6.6-7.0(m,6H).

Example 18

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-octanoic acid amide (E18)

Nmr (CDCl<sub>3</sub>): 0.84(t(J = 7Hz),3H); 1.0-2.2(m,14H); 2.25(s,3H), 2.3-2.8(m,6H); 3.5-4.0(m + 2s,14H); 6.55-7.0(m,6H).

Example 19

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexanoic acid amide (E19)

Nmr (CDCl<sub>3</sub>): 0.84(t(J = 5.3Hz),3H), 1.0-2.2(m,10H), 2.27(s,3H), 2.3-2.8(m,6H); 3.5-4.0(m + 2s,14H); 6.6-7.0(m,6H).

The compounds of the following Examples 20 to 23 were prepared from intermediate D4 and the appropriate acid chloride by the procedure of Example 10:

Example 20

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-dodecanoic acid amide (E20)

5 Nmr (CDCl<sub>3</sub>): 0.87(t(J = 6Hz),3H); 1.0-1.8(m,18H); 1.8-2.15(m,2H), 2.3(s,3H); 2.35-2.8(m,6H); 3.355-3.95 (m + 3s,14H); 6.55-6.95(m,6H).

Example 21

10 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-pentanoic acid amide (E21)

Nmr (CDCl<sub>3</sub>): 0.82(t(J = 6.2Hz),3H); 0.95-1.8(m,4H); 1.9-2.2 (m,2H); 2.30(s,3H); 2.4-2.8(m,6H); 3.6-3.95 (m + 3s,14H); 6.5-6.95(m,6H).

15 Example 22

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(2-methyl)-propanoic acid amide (E22)

20 Nmr (CDCl<sub>3</sub>): 1.02(d(J = 6.7Hz),6H); 2.30(s,3H); 2.35-2.8(m,7H), 3.6-3.95(m + s, 14H), 6.65-6.95(m,6H).

Example 23

25 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-phenyl)-propanoic acid amide (E23)

Nmr (CDCl<sub>3</sub>): 2.29(s,3H); 2.A-3.05(m,10H); 3.6-3.95(m + 3s,14H); 6.4-6.9(m,6H); 7.0-7.35(m,5H).

The structures of the compounds of Example 11 to 23 are illustrated in Table 1:

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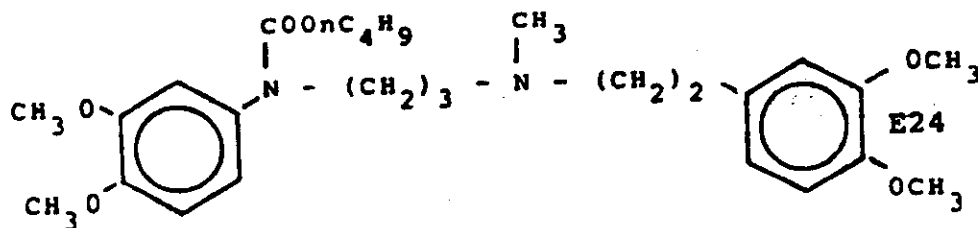
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TABLE 1 (Contd.)

Example No.	R	n
11	$\text{COi-C}_3\text{H}_7$	3
12	$\text{CO}_n\text{-C}_4\text{H}_9$	3
13	$\text{CO-C}_6\text{H}_5$	3
14	$\text{COCH}_2\text{-C}_6\text{H}_5$	3
15	$\text{CO}(\text{CH}_2)_2\text{-C}_6\text{H}_5$	3
16	$\text{SO}_2\text{-}$  $\text{-CH}_3$	3
17	$\text{CO}_n\text{C}_{11}\text{H}_{23}$	3
18	$\text{CO}_n\text{C}_7\text{H}_{15}$	3
19	$\text{CO}_n\text{C}_5\text{H}_{11}$	3
20	$\text{COC}_{11}\text{H}_{23}$	2
21	$\text{CO}_n\text{C}_4\text{H}_9$	2
22	$\text{COiC}_3\text{H}_7$	2
23	$\text{CO}(\text{CH}_2)_2\text{-}$ 	2

55 Example 24

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3, 4-dimethoxyphenyl)-ethyl-N'methylamino]-propyl)-n-butyl-urethane (E24)



1. 1 g Amine D3, 0.3 g triethylamine and 0.37 g n-butylchloro-formate in 20 ml chloroform were refluxed for 4h. Isolation of the pure red oily product was achieved according to the procedure described in Example

15 1. Yield: 0.9 g  $\approx$  74%

20

Elementary Analysis:	C	H	N
calc.	66.37	8.25	5.73
found	66.47	8.25	5.76

25 Example 25

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-phenyl-urethane (E25)

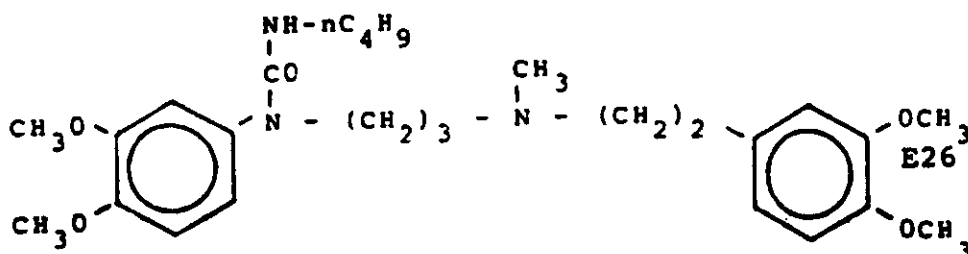
30 Compound E25 was prepared from intermediate D3 and phenyl chloroformate by the procedure of Example 24.

35

Elementary Analysis:	C	H	N
calc.	68.48	7.13	5.50
found	68.58	7.22	5.39

40 Example 26

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-butyl-urea(E26)



1 g Amine D3 and 0.28 g n-butylisocyanate in 25 ml chloroform were refluxed for 2h. After removing the solvent in vacuo, the pure product was isolated by TLC-chromatography as

described in Example 1..

Yield : 0.9 g  $\approx$  75% of an red, oily product

Nmr (CDCl<sub>3</sub>): 0.87(t(J = 6.0Hz),3H); 1.1-1.55(m,4H), 1.55-1.95(m,2H); 2.26(s,3H); 2.3-2.8(m,6H), 3.0-3.35(m,2H); 3.5-3.95(m + 2s(3.85, 3.89),14H); 4.3A(t exch.D<sub>2</sub>O,1H); 6.55-7.0(m,6H).

5 The compounds of the following Examples 27 to 31 were prepared from intermediate D3 and the appropriate isocyanate by the procedure of Example 26:

Example 27

10 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-propyl-urea (E27)

Elementary Analysis:	C	H	N
calc.	65.93	8.30	8.87
found	65.87	8.29	8.51

20 Example 28

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-i-propyl-urea (E28)

Elementary Analysis:	C	H	N
calc.	65.93	8.30	8.87
found	65.98	8.23	8.82

Example 29

35 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-t-butyl-urea(E29)

Elementary Analysis:	C	H	N
calc.	66.50	8.47	8.61
found	66.38	8.46	8.71

45 Example 30

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-benzylurea (E30)

50 Nmr (CDCl<sub>3</sub>): 1.5-1.95(m,2H); 2.25(s,3H); 2.3-2.85(m,6H); 3.6-3.95(m + 3s,14H); 4.41(d(J = 5.8Hz)-,exch.D<sub>2</sub>O s,2H); 4.82(t(J = 5.8Hz)exch.D<sub>2</sub>O,1H); 6.6-6.95 (m,6H); 7.1-7.45(m,5H).

Example 31

55 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-phenylurea (E31)

Elementary Analysis:	C	H	N
calc.	68.61	7.34	8.27
found	68.28	7.28	7.94

5

The compounds of the following Examples 32 and 33 were prepared from intermediate D4 and the appropriate isocyanate by the procedure of Example 26:

10

Example 32

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-(1-phenyl)-ethyl-urea (E32)

15

Nmr (CDCl<sub>3</sub>): 1.35(d(J = 6.7Hz),3H); 2.29(s,3H); 2.4-2.75 (m,6H); 3.6-3.95(m + 3s,14H); 4.76(t(J = 8Hz), 1H exch.D<sub>2</sub>O); 4.96(q(J = 6.8Hz),1H), 6.65-6.9(m,6H); 7.1-7.4(m,5H).

Example 33

20

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-n-propyl-urea (E33)

25

Nmr (CDCl<sub>3</sub>): 0.82(t(J = 6.8Hz),3H); 1.1-1.6(m,2H), 2.32(s,3H), 2.45-2.8(m,6H); 2.9-3.3(m,exch.D<sub>2</sub>O to 3.15, t(J = 5.84),2H); 3.65-3.95(m + 2s,14H), 4.36(t(J = 5Hz) exch.D<sub>2</sub>O,1H); 6.55-6.95 (m,6H).

The structures of the compounds of Examples 25 and 27 to 33 are illustrated in Table 1:

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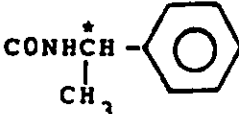
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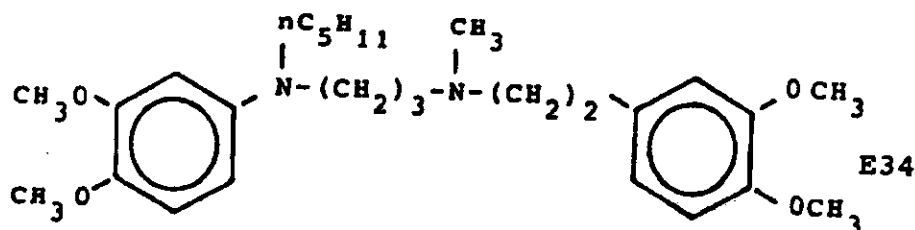
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TABLE 1 (Cont.)

Example No.	R	n
25	COO - 	3
27	CONHnC <sub>3</sub> H <sub>7</sub>	3
28	CONHnC <sub>3</sub> H <sub>7</sub>	3
29	CONH t-C <sub>4</sub> H <sub>9</sub>	3
30	CONHCH <sub>2</sub> - 	3
31	CONH - 	3
32	 R- (+)	2
33	CONHnC <sub>3</sub> H <sub>7</sub>	2

55 Example 34

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-pentylamine (E34)



A mixture of 1.7 g E12 and 0.13 g LiAlH<sub>4</sub> in 16 ml dry tetrahydrofuran was refluxed under protection from moisture for 2h. Thereafter, the product was worked up according to the procedure described for compound D3. Pure product was obtained by TLC as described for Example 1.

15 Yield: 0.24 g = 15% of a oily red product

Nmr (CDCl<sub>3</sub>): 0.9(t(J=5.2Hz),3H); 1.1-2.0(m,8H); 2.30(s,3H), 2.34-2.8(m,6H); 3.0-3.4(m,4H); 3.8(s,3H); 3.84(s,9H), 6.1-6.45(m,2H), 6.6-6.95(m,4H).

Hydrochloride salt m.pt. 191°C (prepared by treatment of the free base in ethyl acetate with ethanolic HCl. The salt crystallised on cooling and was washed with ether).

20 Example 35

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]ethyl)-n-pentylamine (E35).

25 The title compound was prepared from compound E21 by the procedure of Example 34.

Nmr (CDCl<sub>3</sub>): 0.91(t(J=6Hz),3H), 1.1-1.8(m,6H); 2.38(s,3H); 2.4-2.85(m,6H), 3.05-3.5(m,4H), 3.81, 3.85, 3.86(s,s,s,12H); 6.1-6.4(m,2H); 6.55-6.9(m,4H).

The compounds of Examples 34 and 35 have also been prepared from compounds D3 and D4 respectively by the procedure of Example 1 but using n-pentyl iodide in place of 2-nitrobenzyl chloride. Yield 20-35%.

30 The compound of Example 34 has also been prepared from compound D3 and valeraldehyde by the procedure of Example 61 at pH3. Yield 50-60%.

The compounds of the following Examples 36 to 46 were prepared from intermediate D3 (Examples 36 to 44) or D2 (Examples 45 and 46) by the procedure of Example 1. Example 37 utilized 3-(3-methoxyphenyl)-1-bromopropane. Example 44 utilized 2-chloro-3,5-dinitropyridine. The remaining examples utilized the appropriate alkyl chloride.

Example 36

40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzylamine

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.29(s,3H); 2.3-2.9(m,6H), 3.2-3.55(m,2H), 3.78, 3.80, 3.83(3s,12H); 4.53(s,2H); 6.1-6.5(m,2H); 6.6-6.9(m,4H); 8.35-8.5 (m,2H); 8.8-8.95(m,1H).

45 Example 37

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3-(3-methoxyphenyl)-propylamine

50 Nmr (CDCl<sub>3</sub>): 1.5-2.1(m,4H); 2.29(s,3H); 2.3-3.0(m,8H); 3.1-3.4(m,4H); 3.77, 3.79, 3.84, 3.85(4s,15H), 6.1-6.4(m,2H); 6.6-6.95(m,7H); 7.0-7.3(m,1H).

55 Example 38

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-2,5-dimethylbenzylamine

Nmr (CDCl<sub>3</sub>): 1.5-2.0(m,2H); 2.25, 2.28 (2s,9H); 2.3-2.9(m,6H); 3.2-3.55(m,2H), 3.76, 3.79,3.84, 3.85-4.34(s,12H); 4.34(s,2H); 6.1-6.4(m,2H); 6.6-7.2(m,7H)

Example 39

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-trifluoromethyl-benzylamine

10 Nmr (CDCl<sub>3</sub>): 1.5-2.1(m,2H), 2.29(s,3H); 2.3-2.8(m,6H), 3.25-3.6(m,2H), 3.7, 3.77, 3.82, 3.84(4s,12H); 4.67(s,2H); 6.05-6.3(m,2H); 6.6-6.9(m,4H), 7.25-7.5(m,3H); 7.5-7.75(m,1H).

Example 40

15 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-trifluoromethyl-benzylamine

Nmr (CDCl<sub>3</sub>): 1.5-2.0(m,2H); 2.27(s,3H); 2.3-2.9(m,6H); 3.2-3.5(m,2H); 3.75, 3.79, 3.83, 3.84(4s,12H), 4.46(s,2H), 6.1-6.4(m,2H); 6.55-6.9(m,4H); 7.3-7.65(m,4H).

20 Example 41

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,4,6-trimethyl-benzylamine

25 Nmr (CDCl<sub>3</sub>): 1.4-1.85(m,2H); 2.1-2.4(m + 2s (2.19, 2.27), 14H); 2.4-3.2(m,6H); 3.76, 3.82, 3.84(3s, 12H);4.17(s,2H); 6.35-6.9(m,8H).

Example 42

30 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,6-dichlorobenzyl-amine

Nmr (CDCl<sub>3</sub>): 1.4-1.9(m,2H), 2.21(s,3H), 2.25-2.28(m,6H), 3.0-3.3(m,2H), 3.81,3.84(2s,12H); 4.5(s,2H), 6.4-6.9(m,6H); 6.95-7.4(m,3H).

35 Example 43

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-chloro-3,4-methylenedioxybenzylamine

40 Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.3(s,3H); 2.35-2.9(m,6H), 3.2-3.55(m,2H); 3.77, 3.78, 3.83, 3.85-4.34(s,12H); 4.41(s,2H); 5.90(s,2H), 6.05-6.35(m,2H); 6.6-6.9(m,6H).

Example 44

45 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3,5-dinitro-2-amino-pyridine

50 Nmr (CDCl<sub>3</sub>): 1.5-2.1(m,2H); 2.26(s,3H); 2.3-2.8(m,6H), 3.82, 3.84, 3.86(3s,12H); 4.0-4.3(m,2H), 6.5-6.9(m,6H); 8.61(d(J = 2.5Hz),1H), 9.17(d(J = 2.5Hz),1H).

Example 45

55 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl)-4-nitro-benzyl-amine

Nmr (CDCl<sub>3</sub>): 2.33(s,3H), 2.5-2.8(m,6H); 3.3-3.6(m,2H), 3.75, 3.79, 3.84(3s,12H); 4.52(s,2H); 6.05-6.4(m,2H), 6.55-6.9(m,4H), 7.3-7.5(m,2H), 8.05-8.25(m,2H).

Example 46(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl) benzylamine

5 Nmr (CDCl<sub>3</sub>): 2.34(s,3H), 2.5-2.9(m,6H); 3.35-3.65(m,2H); 3.74, 3.79, 3.84(3s,12H); 4.47(s,2H); 6.1-6.45(m,2H); 6.6-6.95(m,4H); 7.1-7.4(m,5H).

Example 47

10 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl) phenylacetamide

Nmr (CDCl<sub>3</sub>): 2.29(s,3H); 2.4-2.75(m,6H); 3.44(s,2H); 3.55-4.0(m + 3s (3.69, 3.84, 3.90),14H), 6.5-7.5(m,11H).

15 The compounds of the following Examples 47 to 56 were prepared from amine D2 (Example 47) or D3 (Example 48 to 56) and the appropriate acid chloride by the procedure of Example 10.

Example 56 utilized the acid chloride 3-phenyl-2-acetoxy-propanoic acid chloride prepared from L(-) phenyl lactic acid by conversion to the acetate by reaction with acetyl chloride in chloroform in the presence of triethylamine, followed by conversion to the acid chloride by treatment with thionyl chloride in chloroform.

20

Example 48

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-(4'-nitrophenyl)-butyramide

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Nmr (CDCl<sub>3</sub>): 1.5-2.2(m,6H); 2.25(s,3H); 2.3-3.0(m,8H), 3.55-3.8(m,2H), 3.84,3.85, 3.89(3s,12H); 6.5-6.95(m,6H), 7.25(d(J = 8.8Hz),2H), 8.09(d(J = 8.8Hz),2H).

Example 49

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitrophenyl)-acetamide

35 Nmr (CDCl<sub>3</sub>): 1.5-1.95(m,2H); 2.25(s,3H); 2.3-2.95(m,6H); 3.53(s,2H), 3.6-3.75(m,2H); 3.79, 3.85, 3.92-(3s,12H); 6.45-7.0(m,6H), 7.25(d(J = 8.7Hz),2H); 8.09(d(J = 8.7Hz),2H).

Example 50

40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N'-4-nitrobenzamide

Nmr (CDCl<sub>3</sub>): 1.6-2.05(m,2H); 2.27(s,3H); 2.3-2.9(m,6H); 3.6-4.1(m + 4s(3.73,3.81,3.85,3.86),14H); 6.4-6.9(m,6H); 7.44(d(J = 8.9Hz),2H); 8.03(d(J = 8.9Hz),2H).

As the hydrochloride salt:

45 m.pt. 84°C

elementary analysis:	C	H	N	O	Cl
calc.	60.67	6.32	7.32	19.51	6.18
found:	60.27	6.30	7.30	19.85	5.93

50

Example 51

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-heptanamide

Nmr (CDCl<sub>3</sub>): 0.7-1.0(A(m),3H); 1.0-2.2(m,12H); 2.27(s,3H); 2.3-2.9(m,6H); 3.5-3.8(m,2H); 3.84, 3.86, 3.90(3s,12H); 6.6-7.0(m,6H).

Example 52(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-cyanobenzamide hydrochloride

5

m.pt. 86°C

Nmr (CDCl<sub>3</sub>): 2.1-2.6(m,2H); 2.81(d(J = 4Hz), after D<sub>2</sub>O exch.s, 3H); 2.95-3.5(m,6H); 3.8, 3.85, 3.99 (s,s,t(J = 6Hz),14H); 6.4-7.0(m,6H); 7.3-7.8(m,4H); 12.7(exch.D<sub>2</sub>O,1H).10 Example 53(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-trifluoromethylbenzamide hydrochloride

15 m.pt. 67°C

Nmr (CDCl<sub>3</sub>): 2.1-2.6(m,2H); 2.83(s,3H); 2.9-3.5(m,6H); 3.78, 3.81, 3.86, 4.01 (s,s,s,t(J = 6.6Hz),14H); 6.4-7.0(m,6H); 7.3-7.65(m,4H); 12.5 (D<sub>2</sub>O exch., 1H).20 Example 54(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzamide hydrochloride

m.pt. 128°C

25 Nmr (CDCl<sub>3</sub>): 2.0-2.6(m,2H); 2.84(d(J = 4.7Hz) after D<sub>2</sub>O exch. s,3H); 2.9-3.5(m,6H); 3.8, 3.87, 4.04 (s,s,t(J = 6.5Hz),14H); 6.6-7.0(m,6H); 8.53(d(J = 1.7Hz),2H); 8.89(d(J = 1.7Hz),1H); 12.7-(exch. D<sub>2</sub>O,1H).30 Example 55(N-[3,4-Dimethoxyphenyl]-N-3-(N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-chlorobenzamide hydrochloride

m.pt. solid foam

35 Nmr (CDCl<sub>3</sub>): 2.1-2.6(m,2H); 2.8(s,3H); 2.9-3.4(m,6H); 3.79, 3.82, 3.85, 3.86 (4s + t(J = 6.6Hz),14H); 6.4-6.9(m,6H); 7.0-7.4(m,4H); 12.5(exch.D<sub>2</sub>O, 1H).Example 5640 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-(3-phenyl-2-acetoxy)-propanoic acid amide hydrochloride

m.pt. 167°C

45 Nmr (CDCl<sub>3</sub>): 2.0-2.6(m + s(2.25),5H); 2.82(d(J = 4.3Hz) after D<sub>2</sub>O exch. s,3H); 3.0-3.6(m,6H); 3.6-4.3-(m + 4s(3.75, 3.81, 3.84, 3.86),17H); 6.5-7.35(m,11H); 12.5(exch. D<sub>2</sub>O,1H).Example 5750 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N-4-nitrophenylurea

The title compound was prepared from amine D3 and p-nitrophenylisocyanate by the procedure of Example 26.

55 Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.32(s,3H); 2.35-2.9(m,6H); 3.6-4.0(m + 3s (3.84, 3.88, 3.92),14H); 6.5-7.0(m,6H); 7.45(d(J = 9.2Hz),2H); 7.55(m,1H, exch. with D<sub>2</sub>O); 8.11(d(J = 9.2Hz),2H).

The compounds of the following Examples 58 to 60 were prepared from intermediate D3 and the appropriate alkylchloroformate by the procedure of Example 24.

Example 58(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-hexyl-urethane

5 Nmr (CDCl<sub>3</sub>): 0.86(A,3H); 1.0-2.0(m,10H), 2.25(s,3H), 2.3-2.9(m,6H); 3.66(A(J = 7Hz),2H); 3.84, 3.85, 3.87 (3s,12H); 4.07(A(J = 6.3Hz),2H); 6.5-6.95(m,6H).

Example 59(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-octyl-urethane

10 Nmr (CDCl<sub>3</sub>): 0.87(m(A),3H), 1.1-2.0(m,14H); 2.25(s,3H), 2.3-2.9(m,6H); 3.5-3.8(m(A),2H), 3.84, 3.85, 3.87 (3s,12H); 3.95-4.2(m(A),2H); 6.5-6.95(m,6H).

Example 60(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-5-(-)-menthyl-urethane

15 Nmr (CDCl<sub>3</sub>): 0.75-2.1(m,20H); 2.25(s,3H); 2.3-2.9(m,6H), 3.5-3.8(m,2H); 3.84, 3.85, 3.87 (3s,12H); 4.4-4.8(m,1H); 6.5-6.95(m,6H).

Example 61(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-cyclohexyl-amine

1g Amine (D3) was dissolved in 30ml absolute methanol and ethanolic-HCl was added to pH 7. Then 0.3g cyclohexanone, 0.5g NaCNBH<sub>3</sub> and 3 A molecular sieve was added and the mixture stirred for three days at room temperature.

30 For working up, the solid was filtered off, the filtrate evaporated to dryness and the residue at pH 12 extracted with methylene chloride. The extract was washed with water, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The pure, oily product was isolated by TLC as described in Example 1.

Yield: 0.09g ≈ 7%

35 Nmr (CDCl<sub>3</sub>): 1.0-2.1(m,12H); 2.28(s,3H), 2.3-2.9(m,7H), 2.95-3.3(m,2H); 3.81, 3.84 (2s,12H), 6.2-6.5(m,2H); 6.6-6.95(m,4H).

The compounds or the following Examples 62 to 64 were prepared from amine D3 and the appropriate aldehyde or ketone by the procedure of Example 61.

Example 62(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-isopropylamine.

40 Nmr (CDCl<sub>3</sub>): 1.12(d(J = 6.6 Hz), 6H); 1.5-1.9(m,2H); 2.28(s,3H); 2.3-3.25(m,8H); 3.6-3.9(m + 3s- (3.81,3.84,3.85),13H); 6.2-6.5(m,2H); 6.6-6.85(m,4H).

Example 63(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexylamine

50 Nmr (CDCl<sub>3</sub>): 0.89(A,3H); 1.1-2.0(m,10H); 2.3(s,3H); 2.35-2.9(m,6H); 3.0-3.4(m,4H); 3.80, 3.84, 3.85 (3s,12H); 6.1-6.45(m,2H); 6.6-7.0(m,4H).

Example 64(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butylamine

55 Nmr (CDCl<sub>3</sub>): 0.94(A(J = 6Hz),3H); 1.1-2.0(m,6H), 2.3(s,3H), 2.35-3.0(m,6H); 3.0-3.4(m,4H); 3.80(s,3H); 3.85(s,9H); 6.1-6.45(m,2H); 6.6-7.0(m,4H).

Example 65(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino-propyl]-1-(3-oxo)-butyramide

5 The title compound was prepared by the reaction of amine D3 with 1.1 equivalents of diketene in methylene chloride at room temperature for 4 hours.

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.10(s,3H), 2.26(s,3H); 2.3-3.0(m,6H); 3.28(s,2H); 3.55-3.95(m + 4s-  
10 (3.84,3.86,3.89,3.90),14H); 6.55-7.0(m,6H).

The structured of the compounds of Examples 36 to 65 are illustrated in the following Table 1:

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Table 1 (contd)

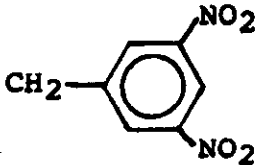
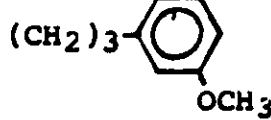
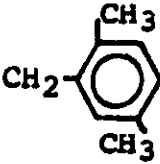
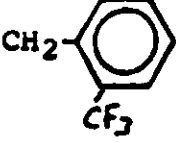
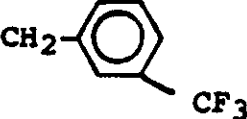
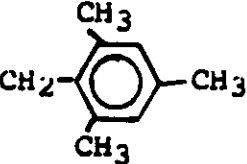
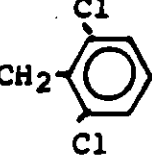
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39		3
40		3
41		3
42		3

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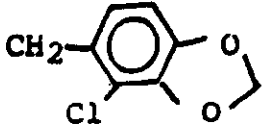
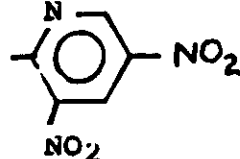

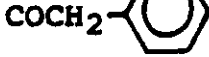





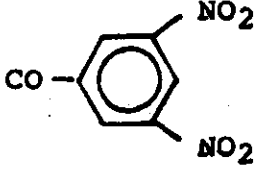

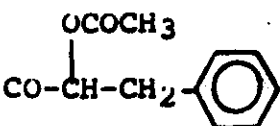

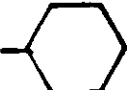
Example No.	R	n
43		3
44		3
45		2
46		2
47		2
48		3
49		3
50		3
51	$\text{CO}_n\text{C}_6\text{H}_{13}$	3
52		3
53		3

Table 1 (contd)

Example No.	R	n
54		3
55		3
56		3
57		3
58	COO <sub>n</sub> C <sub>6</sub> H <sub>13</sub>	3
59	COO <sub>n</sub> C <sub>8</sub> H <sub>17</sub>	3
60	COO(-)-menthyl	3
61		3
62	iC <sub>3</sub> H <sub>7</sub>	3
63	nC <sub>6</sub> H <sub>13</sub>	3
64	nC <sub>4</sub> H <sub>9</sub>	3
65	COCH <sub>2</sub> COCH <sub>3</sub>	3

The compounds of Examples 66 to 68 were prepared from the amine D5 and the corresponding alkyl chloride by the procedure of Example 1.

#### Example 66

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitro-benzylamine.

Nmr (CDCl<sub>3</sub>): 1.55-2.05(m,2H); 2.29(s,3H); 2.3-2.9(m,6H); 3.46(A(J = 7.2Hz),2H); 3.82(s,3H); 3.84-(s,3H), 4.59(s,2H); 6.5-6.95(m,6H); 7.0-7.5(m,4H); 8.15(d(J = 8.7Hz),2H).

Example 67

5

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-nitro-benzylamine.

Nmr (CDCl<sub>3</sub>): 1.55-2.05(m,2H), 2.29(s,3H); 2.30-2.9(m,6H); 3.48(A(J = 7.2Hz),2H); 3.82(s,3H); 3.84-(s,3H); 4.59(s,2H); 6.5-6.9(m,6H); 7.05-7.6(m,4H); 7.95-8.2(m,2H).

10

Example 68

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-nitro-benzylamine.

15 Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.30(s,3H); 2.35-2.9(m,6H); 3.45(A(J = 7.2Hz),2H); 3.82(s,3H); 3.84-(s,3H); 4.93(s,2H); 6.4-6.9(m,6H); 7.0-7.6(m,5H); 8.0-8.3(m,1H).

Example 69

20 (N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-valeramide

Nmr (CDCl<sub>3</sub>): 0.8(A(J = 6.2Hz),3H); 0.95-2.2(m,8H); 2.24(s,3H); 2.3-2.9(m,6H); 3.55-3.8(m,2H); 3.84-(s,3H); 3.85(s,3H); 6.55-6.95(m,3H); 7.0-7.6(m,5H).

The title compound was prepared from amine D5 and pentanoic acid chloride by the procedure of Example 10.

25

The structures of the compounds of Examples 66 to 69 are illustrated in the following Table 2,

30

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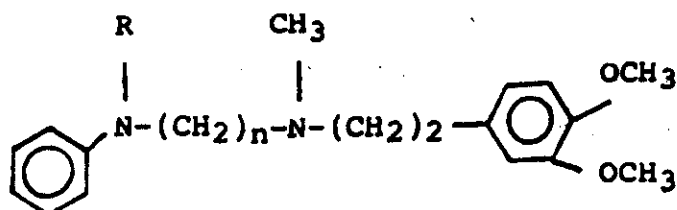
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Table 2



15

Example No.	R	n
66		3
67		3
68		3
69	CO <sub>n</sub> C <sub>4</sub> H <sub>9</sub>	3

20

25

30

35 The following compounds of Examples 70 to 73 were prepared from the amine D6 and the corresponding alkyl chloride by the procedure of Example 1.

40 Example 70

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-benzylamine.

Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.28(s,3H); 2.3-2.9(m,6H); 3.35(A(J=7Hz),2H); 3.74(s,3H); 3.78(s,3H); 4.44(s,2H); 6.1-6.45(m,2H); 7.74(d(J=8.5Hz), 1H); 7.0-7.5(m,10H).

45 Example 71

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-2-nitrobenzylamine

50 Nmr (CDCl<sub>3</sub>): 1.55-2.05(m,2H); 2.30(s,3H); 2.35-2.9(m,6H); 3.34(A(J=7.2Hz),2H); 3.74(s,3H); 3.78(s,3H); 4.80(s,2H); 6.05-6.4(m,2H); 6.72(d(J=8.6Hz), 1H); 7.05-7.7(m,8H); 7.95-8.15(m,1H).

55 Example 72

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamine

Nmr (CDCl<sub>3</sub>): 1.6-2.0(m,2H); 2.28(s,3H); 2.3-2.95(m,6H); 3.35(A(J=7.4Hz),2H); 3.76(s,3H); 3.78(s,3H);

4.48(s,2H); 6.1-6.4(m,2H); 6.72(d(J = 8.6Hz), 1H), 7.0-7.65(m,7H); 7.9-8.2(m,1H).

Example 73

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamine

Nmr (CDCl<sub>3</sub>): 1.5-2.0(m 2H); 2.29(s,3H); 2.3-2.95(m,6H); 3.2-3.5(m,2H); 3.75(s,3H); 3.78(s,3H); 4.50-  
(s,2H); 6.05-6.4(m,2H); 6.73(d(J = 8.8Hz),1H); 7.0-7.5(m,7H); 8.14(d(J = 8.6Hz),2H).

10 Example 74

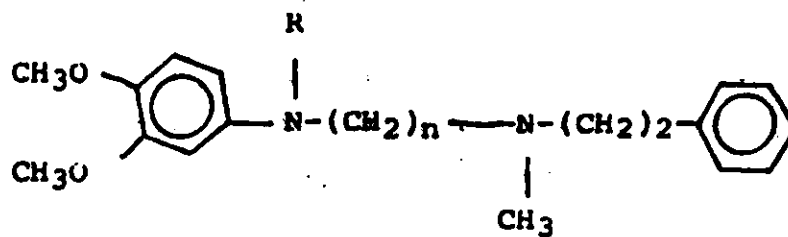
(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramide

The title compound was prepared from amine D6 and pentanoic acid chloride by the procedure of  
15 Example 10.

Nmr (CDCl<sub>3</sub>): 0.82(A(J = 6.2Hz),3H); 0.95-2.2(m,8H); 2.28(s,3H); 2.3-2.95(m,6H); 3.69(A(J = 7.3Hz),2H);  
3.86(s,3H); 3.90(s,3H); 6.55-6.95(m,3H); 7.0-7.5(m,5H).

The structures of the compounds of Examples 70 to 74 are illustrated in the following Table 3:

20 Table 3



35

Example No.	R	n
70		3
71		3
72		3
73		3
74	CO <sub>n</sub> C <sub>4</sub> H <sub>9</sub>	3

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The following compounds of Examples 75 to 77 were prepared from amine D7 and the corresponding alkyl chloride by the procedure of Example 1.

Example 75(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-3-nitrobenzylamine

5 Nmr (CDCl<sub>3</sub>): 0.55-2.0(m,2H); 2.29(s,3H); 2.3-2.9(m,6H), 3.3-3.6(m,2H); 4.56(s,2H); 6.5-6.9(m,3H), 7.0-7.35(m,7H); 7.4-7.65(m,2H); 7.9-8.3(m,2H).

Example 76(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamine

10 Nmr (CDCl<sub>3</sub>): 1.55-2.0(m,2H); 2.29(s,3H); 2.3-3.0(m,6H), 3.3-3.6(m,2H); 4.57(s,2H); 6.5-6.9(m,3H); 7.0-7.5(m,9H), 8.14(d(J = 8.6Hz),2H).

Example 77(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-2-nitrobenzylamine

20 Nmr (CDCl<sub>3</sub>): 1.55-2.05(m,2H); 2.30(s,3H); 2.35-3.0(m,6H), 3.3-3.6(m,2H), 4.90(s,2H); 6.4-6.8(m,3H); 7.0-7.6(m,10H); 8.0-8.3(m,1H).

Example 78(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramide

25

The title compound was prepared from amine D7 and pentanoic acid chloride by the procedure of Example 10.

Nmr (CDCl<sub>3</sub>): 0.80(A(J = 6.2Hz),3H); 0.95-2.2(m,8H); 2.24(s,3H); 2.3-2.9(m,6H), 3.72(A(J = 7.3Hz),2H), 7.0-7.6(m,10H).

30

The structures of the compounds of Examples 75 to 76 are illustrated in the following Table 4:

35

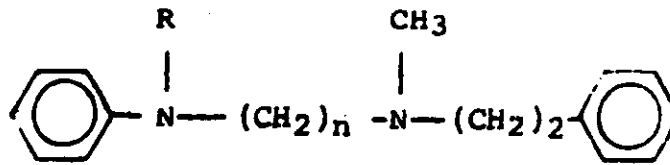
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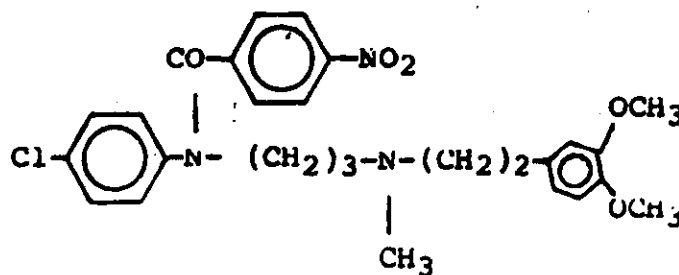
Table 4



Example No.	R	n
75		3
76		3
77		3
78	$\text{CO}_n\text{C}_4\text{H}_9$	3

## Example 79

(N-(4-Chloro)phenyl-N-3-[N'-2-(3,4-dimethoxy-phenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitrobenzamide hydrochloride



The title compound was prepared from amine D8 and 4-nitrobenzoyl chloride by the procedure of Example 10.

m.pt. 115°C

Nmr (CDCl<sub>3</sub>): 2.1-2.6(m,2H); 2.83(d(J=4.5Hz) exch.D<sub>2</sub>O s,3H); 2.95-3.5(m,6H); 3.85, 3.87, 4.02 (2s + t (J=6.5Hz),8H); 6.6-6.9(m,3H); 6.95-7.6(m,6H); 7.9-8.2(m,2H); 12.6 exch.D<sub>2</sub>O s,1H).

The compounds of Examples 1 to 51 and 57 to 78 are all oils in their free base form.

## PHARMACOLOGICAL DATA

1. Coronary Vasodilating activity

a) Vasopressin test in anaesthetized rats

5 Vasopressin (Lysopressin: 1 I.U./kg) was administered intravenously in order to provoke coronary spasm (ST-segment elevation in the ECG). Compound E1 was active against coronary spasm at a dose of 0.6g/kg i.d.

The ability of test compounds to reduce coronary spasm is taken as a measure of their anti-anginal potential in spasm-induced angina pectoris. (Ref. Drug.Res. 33(11), 8,1117-1121 (1983)).

10

b) Pig isolated coronary artery

15 Coronary artery spirals were prepared and in lengths from 1.5 to 2 cm were incubated at 32.5° in Ca<sup>++</sup>-free Krebs-Henseleit solution containing tris buffer and 60 mM KCl. Ca<sup>++</sup> in concentrations ranging from 0.1 mM - 7 mM was given every 10 min to produce a control dose-response curve. Following a wash out circle using EDTA, either placebo or drug was administered, and an equilibration time of 30 minutes allowed before the second dose-response curve was made. Dose-ratios were calculated at ED<sub>50</sub>-levels, from these the log K<sub>B</sub> was calculated. Compound E4 showed a log K<sub>B</sub> of 5.85, which indicates moderate to medium Ca<sup>++</sup>-antagonistic activity in coronary artery in vitro.

20

2. Haemodynamic profile in anaesthetized rats.

25 The effect of compounds of the invention on heart rate, systolic left ventricular pressure, left ventricular dp/dt max and mean arterial blood pressure was investigated so as to obtain information on the anti-anginal potential of these compounds, by reducing the oxygen demand of the ischaemic heart. Results are shown in Table 5.

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TABLE 5

Compound number	haemodynamic effects (rat)			i.v. duration of action on heart rate (rat) (min)	
	D <sub>hr20</sub> *	%effect of D <sub>hr20</sub> on			
		LVP**	BP***		dp/dt <sub>max</sub>
E1	1.6	-2	0	-3	10
E4	3.2	-3	-6	-12	10
E6	0.4	+5	+1	-5	60
E12	1.6	-6	-11	-6	10
E15	1.6	-7	-8	-7	10
E24	3.2	-13	-15	-8	10
E25	0.8	-10	-14	-2	10
E27	6.4	-2	-4	-1	5 - 10
E30	1.6	-10	-15	-20	10
E32	3.2	-7	-13	-3	10
E34	1.6	-9	-9	-10	5 - 10
E44	3.2	-6	-10	-8	10
E50	1.6	-1	-1	-5	10
a (E50)	16	-	-6	-	>90)

\*D<sub>hr20</sub> = i.v. dose which reduces heart rate by ca. 20%

\*\*LVP = systolic left ventricular pressure

\*\*\*BP = mean arterial blood pressure

a = i.d. administration

### Results

The above results demonstrate that the compounds of the invention have therapeutic potential in both stable and variant angina pectoris. Of special interest is the bradycardic activity without marked hypotension of the test compounds.

### Toxicity

No toxic effects were observed in the above of the tests.

### Claims

Claims for the following Contracting States : BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

5

1. The use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing:

10



15

wherein

20

$R_1$  and  $R_4$  are independently phenyl optionally substituted by one, two or three of halogen, trifluoromethyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl, cyano, hydroxy, nitro,  $NR_5R_6$  or  $O_2SNR_5R_6$  wherein  $R_5$  and  $R_6$  are independently hydrogen or  $C_{1-6}$  alkyl or together are  $C_{3-6}$  polymethylene, or disubstituted at adjacent carbon atoms by  $C_{1-2}$  alkylenedioxy and optionally further substituted by one of the above groups;

25

$R_2$  is selected from  $(CH_2)_zCN$  where  $z$  is 0 or an integer from 1 to 4,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl  $C_{1-4}$  alkyl, pyridyl, pyridyl  $C_{1-4}$  alkyl,  $COR_7$ ,  $COCH_2COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  and  $CSNHR_7$ , where  $R_7$  is selected from  $C_{3-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl and phenyl  $C_{1-4}$  alkyl, any alkyl moiety in  $R_7$  optionally substituted by hydroxy or  $C_{1-4}$  alkanoyloxy, any pyridyl or phenyl moiety in  $R_2$  optionally substituted as defined for  $R_1$  and  $R_4$  and any cycloalkyl moiety in  $R_2$  optionally substituted by one or two  $C_{1-4}$  alkyl groups;

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$R_3$  is hydrogen or  $C_{1-4}$  alkyl;

A represents  $C_{2-5}$  alkylene; and

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B represents  $C_{1-4}$  alkylene,

for the preparation of a medicament for the treatment or prophylaxis of angina pectoris in mammals.

40

2. A compound of formula (IA) which comprises a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing, with the proviso that the variables [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] do not take the following combinations of values:

[phenyl,  $CO_nC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

45

[phenyl,  $COiC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

[phenyl,  $CO_nC_3H_7$ ,  $CH(CH_3)CH_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl,  $CO_nC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

50

[phenyl,  $COiC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl,  $CO_nC_4H_9$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

55

[phenyl, benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]

[phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>3</sub>, phenyl]

5 [4-chlorophenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

[4-chlorophenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

[phenyl, 4-chlorobenzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

10

[phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-chlorophenyl]

for use as an active therapeutic substance.

- 15 3. A compound of formula (IA) as defined in claim 2 for the treatment or prophylaxis of angina pectoris.
4. A pharmaceutical composition comprising a compound of formula (IA) as defined in claim 2 and a pharmaceutically acceptable carrier.
- 20 5. A compound of formula (IB) which comprises a compound of formula (IA) as defined in claim 2 with the proviso that the variables [R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B, R<sub>4</sub>] do not take the following combinations of values:

[3,4-dimethoxyphenyl, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

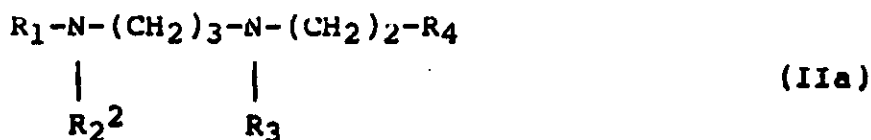
25 [3,4-dimethoxyphenyl C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, CH<sub>2</sub>, phenyl]

6. A compound according to claim 5, wherein R<sub>1</sub> and R<sub>4</sub> are independently phenyl substituted as defined in claim 1.

30 7. A compound according to claim 5, wherein R<sub>2</sub> is COR<sub>7</sub> where R<sub>7</sub> is phenyl or phenyl C<sub>1-4</sub> alkyl, the phenyl moiety optionally substituted as defined for R<sub>1</sub> and R<sub>4</sub>.

8. A compound according to claim 5 of formula (IIa):

35

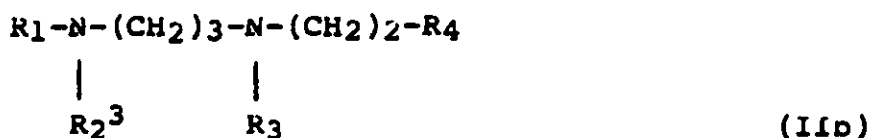


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wherein R<sub>2</sub><sup>2</sup> is COR<sub>7</sub> where R<sub>7</sub> is as defined in claim 5, and the remaining variables are as defined in claim 5.

9. A compound according to claim 5 of formula (IIb):

45

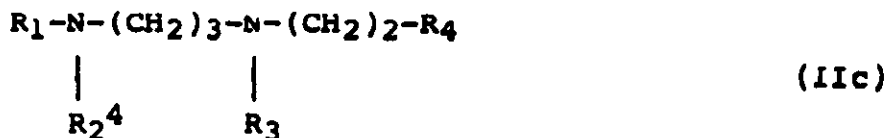


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wherein R<sub>2</sub><sup>3</sup> is CO<sub>2</sub>R<sub>7</sub> or SO<sub>2</sub>R<sub>7</sub> where R<sub>7</sub> is as defined in claim 5, and the remaining variables are as defined in claim 5.

55

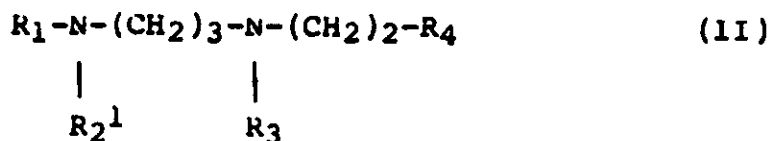
10. A compound according to claim 5 of formula (IIc):



wherein  $R_2^4$  is  $CONHR_7$  or  $CSNHR_7$  where  $R_7$  is as defined in claim 5, and the remaining variables are as defined in claim 5.

11. A compound according to claim 5, wherein  $R_2$  is  $C_{3-12}$  alkyl.

12. A compound according to claim 5 of formula (II):



wherein:

$R_1$ ,  $R_3$  and  $R_4$  are as defined in claim 7; and

$R_2^1$  is  $(CH_2)_zCN$ ,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl or phenyl  $C_{1-4}$  alkyl wherein  $z$  is as defined in claim 5 and any phenyl, alkyl, or cycloalkyl moieties in  $R_2^1$  are optionally substituted as defined for corresponding variables  $R_2$  in claim 5.

13. A compound according to claim 5, wherein  $R_1$  and  $R_4$  are independently phenyl substituted by one, two or three of halogen, trifluoromethyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl, cyano, hydroxy, nitro,  $NR_5R_6$  or  $O_2SNR_5R_6$  wherein  $R_5$  and  $R_6$  are independently hydrogen or  $C_{1-6}$  alkyl or together are  $C_{3-6}$  polymethylene, or disubstituted at adjacent carbon atoms by  $C_{1-2}$  alkylendioxy;

$R_2$  is selected from  $(CH_2)_zCN$  where  $z$  is 0 or an integer from 1 to 4,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl  $C_{1-4}$  alkyl,  $COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  and  $CSNHR_7$ , where  $R_7$  is selected from  $C_{3-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl and phenyl  $C_{1-4}$  alkyl, any phenyl moiety in  $R_2$  optionally substituted as defined for  $R_1$  and  $R_4$ ;

$R_3$  is hydrogen or  $C_{1-4}$  alkyl;

A represents  $C_{2-5}$  alkylene; and

B represents  $C_{1-4}$  alkylene.

14. A compound according to any of claims 5 to 13 in which  $R_1$  and  $R_4$  are 3,4-dimethoxyphenyl.

15. (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanomethylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitro)-benzylamine,

5 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamine,

10 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butanoic acid amide,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-methyl)-propanoic acid amide,

20 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-pentanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzamide,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-phenyl)-ethanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-phenyl)-propanoic acid amide,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-phenylsulphonamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-dodecanoic acid amide,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-octanoic acid amide,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-dodecanoic acid amide,

45 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-pentanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(2-methyl)-propanoic acid amide,

50 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-phenyl)-propanoic acid amide,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-butylurethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-phenyl-urethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-butyl-urea,

5 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-propylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-i-propylurea,

10 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-t-butyl-urea,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-benzylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-phenylurea,

20 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-(1-phenyl)-ethyl-urea,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-n-propyl-urea,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-pentylamine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-n-pentylamine,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzylamine,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3-(3-methoxyphenyl)-propylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-2,5-dimethylbenzylamine,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-trifluoromethyl-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-trifluoromethyl-benzylamine,

45 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,4,6-trimethyl-benzylamine,

50 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,6-dichlorobenzyl-amine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-chloro-3,4-methylenedioxybenzylamine,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3,5-dinitro-2-amino-pyridine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl) -4-nitro-benzyl-

amine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl) benzylamine.

5 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl) phenylacetamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-(4'-nitrophenyl)-butyramide,

10 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitrophenyl)-acetamide,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N'-4-nitrobenzamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-heptanamide,

20 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-cyanobenzamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-trifluoromethylbenzamide,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzamide,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-chlorobenzamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-(3-phenyl-2-acetoxy)-propanoic acid amide,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N-4-nitrophenylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-hexyl-urethane,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-octyl-urethane,

45 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-5-(-)-menthyl-urethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-cyclohexyl-amine,

50 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-isopropylamine,

N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexylamine,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino-propyl]-1-(3-oxo)-butyramide,

(N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitro-benzylamine,

(N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-nitro-benzylamine,

5

(N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-nitro-benzylamine,

(N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-valeramide,

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(N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-2-nitrobenzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamine,

15

(N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methyl-amino]-propyl)-valeramide,

20

(N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamine,

(N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-4-nitrobenzylamine,

(N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-2-nitrobenzylamine,

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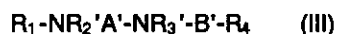
(N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-valeramide,

(N-(4-chloro)phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitrobenzamide,  
or a pharmaceutically acceptable salt of any of the foregoing.

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16. A process for the preparation of a compound according to claim 5, which process comprises reacting together  $R_{10}X$  and  $YR_{11}$  wherein one of X and Y is a leaving group or aldehyde or ketone function and the other is a nitrogen nucleophile, the nitrogen nucleophile,  $R_{10}$  and  $R_{11}$ , and the aldehyde or ketone function when present, being such that a compound of formula (III) is formed:

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in which  $R_2'$ ,  $A'$ ,  $R_3'$  and  $B'$  are  $R_2$ ,  $A$ ,  $R_3$  and  $B$  respectively or groups convertible thereto, and  $R_1$ ,  $R_2$ ,  $A$ ,  $R_3$ ,  $B$  and  $R_4$  are as defined in claim 5, and thereafter, optionally or as necessary, converting  $R_2'$ ,  $A'$ ,  $R_3'$ , and/or  $B'$  to  $R_2$ ,  $A$ ,  $R_3$  and/or  $B$ , interconverting  $R_2$  and/or  $R_3$  and/or forming a pharmaceutically acceptable salt.

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17. 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-(3,4-dimethoxy)-aniline,

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1-[N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-ethyl-2-(3,4-dimethoxy)-aniline,

1-[N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-aniline,

1-[N-methyl-N-2-phenylethylamino]propyl-3-(3,4-dimethoxy)-aniline or

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1-[N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-(4-chloro)-aniline.

#### Claims for the following Contracting State : ES

- 55 1. The use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing:



wherein

$R_1$  and  $R_4$  are independently phenyl optionally substituted by one, two or three of halogen, trifluoromethyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl, cyano, hydroxy, nitro,  $NR_5R_6$  or  $O_2SNR_5R_6$  wherein  $R_5$  and  $R_6$  are independently hydrogen or  $C_{1-6}$  alkyl or together are  $C_{3-6}$  polymethylene, or disubstituted at adjacent carbon atoms by  $C_{1-2}$  alkylenedioxy and optionally further substituted by one of the above groups;

$R_2$  is selected from  $(CH_2)_z$  CN where  $z$  is 0 or an integer from 1 to 4,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl  $C_{1-4}$  alkyl, pyridyl, pyridyl  $C_{1-4}$  alkyl,  $COR_7$ ,  $COCH_2COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  and  $CSNHR_7$ , where  $R_7$  is selected from  $C_{3-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl and phenyl  $C_{1-4}$  alkyl, any alkyl moiety in  $R_7$  optionally substituted by hydroxy or  $C_{1-4}$  alkanoyloxy, any pyridyl or phenyl moiety in  $R_2$  optionally substituted as defined for  $R_1$  and  $R_4$  and any cycloalkyl moiety in  $R_2$  optionally substituted by one or two  $C_{1-4}$  alkyl groups;

$R_3$  is hydrogen or  $C_{1-4}$  alkyl;

A represents  $C_{2-5}$  alkylene; and

B represents  $C_{1-4}$  alkylene,

for the preparation of a medicament for the treatment or prophylaxis of angina pectoris in mammals.

2. A process for the preparation of a compound of formula (IB) which comprises a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof, or a solvate of any of the foregoing, with the proviso that the variables [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] do not take the following combinations of values:

[phenyl,  $CO_nC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

[phenyl,  $COiC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

[phenyl,  $CO_nC_3H_7$ ,  $CH(CH_3)CH_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl,  $CO_nC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl,  $COiC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl,  $CO_nC_4H_9$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl, benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]

[phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , phenyl]

[phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , phenyl]

[phenyl, benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_3$ , phenyl]

[4-chlorophenyl, benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , phenyl]

[4-chlorophenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

[phenyl, 4-chlorobenzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

5 [phenyl, benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-chlorophenyl]

[3,4-dimethoxyphenyl, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phenyl]

[3,4-dimethoxyphenyl, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, CH<sub>2</sub>, phenyl],

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which process comprises reacting together R<sub>10</sub>X and YR<sub>11</sub> wherein one of X and Y is a leaving group or aldehyde or ketone function and the other is a nitrogen nucleophile, the nitrogen nucleophile, R<sub>10</sub> and R<sub>11</sub>, and the aldehyde or ketone function when present, being such that a compound of formula (III) is formed:

15



in which R<sub>2</sub>' A', R<sub>3</sub>' and B' are R<sub>2</sub>, A, R<sub>3</sub> and B respectively or groups convertible thereto, and R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B and R<sub>4</sub> are as defined in claim 1, and thereafter, optionally or as necessary, converting R<sub>2</sub>', A', R<sub>3</sub>', and/or B' to R<sub>2</sub>, A, R<sub>3</sub> and/or B, interconverting R<sub>2</sub> and/or R<sub>3</sub> and/or forming a pharmaceutically acceptable salt.

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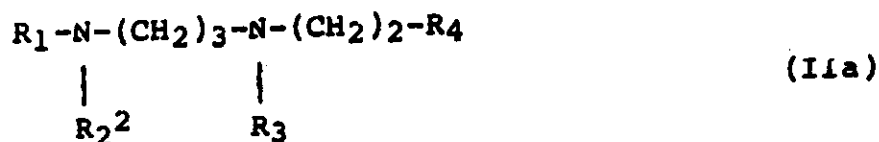
3. A process according to claim 2, wherein R<sub>1</sub> and R<sub>4</sub> are independently phenyl substituted as defined in claim 1.

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4. A process according to claim 2, wherein R<sub>2</sub> is COR<sub>7</sub> where R<sub>7</sub> is phenyl or phenyl C<sub>1-4</sub> alkyl, the phenyl moiety optionally substituted as defined for R<sub>1</sub> and R<sub>4</sub>.

5. A process according to claim 2 for preparing a compound of formula (IIa):

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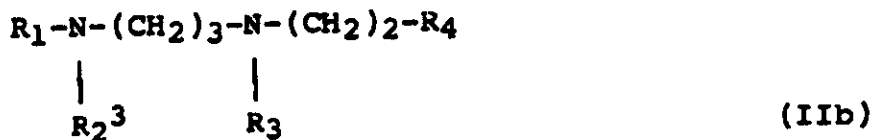


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wherein R<sub>2</sub><sup>2</sup> is COR<sub>7</sub> where R<sub>7</sub> is as defined in claim 2, and the remaining variables are as defined in claim 2.

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6. A process according to claim 2 for preparing a compound of formula (IIb):



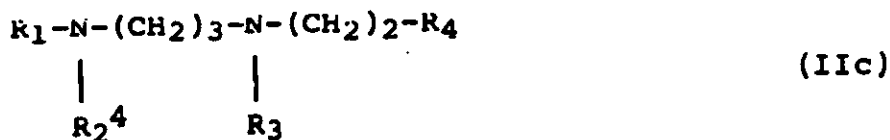
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wherein R<sub>2</sub><sup>3</sup> is CO<sub>2</sub>R<sub>7</sub> or SO<sub>2</sub>R<sub>7</sub> where R<sub>7</sub> is as defined in claim 2, and the remaining variables are as defined in claim 2.

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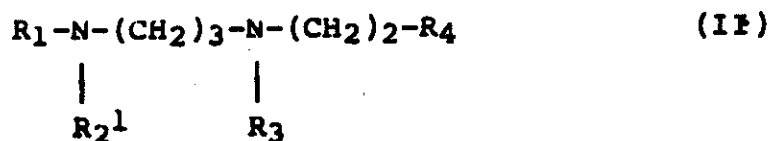
7. A process according to claim 2 for preparing a compound of formula (IIc):

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wherein  $R_2^4$  is  $CONHR_7$  or  $CSNHR_7$  where  $R_7$  is as defined in claim 2, and the remaining variables are as defined in claim 2.

8. A process according to claim 2, wherein  $R_2$  is  $C_{3-12}$  alkyl.
9. A process according to claim 2 for preparing a compound of formula (II):



wherein:

$R_1$ ,  $R_3$  and  $R_4$  are as defined in claim 4; and

$R_2^1$  is  $(CN)_zCN$ ,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl or phenyl  $C_{1-4}$  alkyl wherein  $z$  is as defined in claim 2 and any phenyl, alkyl, or cycloalkyl moieties in  $R_2^1$  are optionally substituted as defined for corresponding variables  $R_2$  in claim 2.

10. A process according to claim 2, wherein  $R_1$  and  $R_4$  are independently phenyl substituted by one, two or three of halogen, trifluoromethyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl, cyano, hydroxy, nitro,  $NR_5R_6$  or  $O_2SNR_5R_6$  wherein  $R_5$  and  $R_6$  are independently hydrogen or  $C_{1-6}$  alkyl or together are  $C_{3-6}$  polymethylene, or disubstituted at adjacent carbon atoms by  $C_{1-2}$  alkylendioxy;

$R_2$  is selected from  $(CH_2)_zCN$  where  $z$  is O or an integer from 1 to 4,  $C_{1-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl  $C_{1-4}$  alkyl,  $COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  and  $CSNHR_7$ , where  $R_7$  is selected from  $C_{3-12}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl  $C_{1-4}$  alkyl, phenyl and phenyl  $C_{1-4}$  alkyl, any phenyl moiety in  $R_2$  optionally substituted as defined for  $R_1$  and  $R_4$ ;

$R_3$  is hydrogen or  $C_{1-4}$  alkyl;

A represents  $C_{2-5}$  alkylene; and

B represents  $C_{1-4}$  alkylene.

11. A process according to any of claims 2 to 10 in which  $R_1$  and  $R_4$  are 3,4-dimethoxyphenyl.
12. A process according to claim 2 for preparing (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanomethylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3'-4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitro)-benzylamine,

5 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamine,

10 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-nitro)-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butanoic acid amide,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-methyl)-propanoic acid amide,

20 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-pentanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzamide,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-phenyl)-ethanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-phenyl)-propanoic acid amide,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-phenylsulphonamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-dodecanoic acid amide,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-octanoic acid amide,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexanoic acid amide,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-dodecanoic acid amide,

45 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-pentanoic acid amide,

(M-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(2-methyl)-propanoic acid amide,

50 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-phenyl)-propanoic acid amide,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-butylurethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-phenyl-urethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-butyl-urea,

5 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-propylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-i-propylurea,

10 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-t-butyl-urea,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-benzylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-phenylurea,

20 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-(1-phenyl)-ethyl-urea,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-n-propyl-urea,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-pentylamine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]ethyl)-n-pentylamine,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzylamine,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3-(3-methoxyphenyl)-propylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-2,5-dimethylbenzylamine,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-trifluoromethyl-benzylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-trifluoromethyl-benzylamine,

45 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,4,6-trimethyl-benzylamine,

50 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,6-dichlorobenzyl-amine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-chloro-3,4-methylenedioxobenzylamine,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3,5-dinitro-2-amino-pyridine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl) -4-nitro-benzyl-

amine,

(N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl) benzylamine.

5 (N-[3,4-dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl) phenylacetamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-(4'-nitrophenyl)-butyramide,

10 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitrophenyl)-acetamide,

15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N'-4-nitrobenzamide,

(M-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-heptanamide,

20 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-cyanobenzamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-trifluoromethylbenzamide,

25 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzamide,

30 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-chlorobenzamide,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-(3-phenyl-2-acetoxy)-propanoic acid amide,

35 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N-4-nitrophenylurea,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-hexyl-urethane,

40 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-octyl-urethane,

45 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-5-(-)-menthyl-urethane,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-cyclohexyl-amine,

50 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-isopropylamine,

N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexylamine,

55 (N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butylamine,

(N-[3,4-dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino-propyl]-1-(3-oxo)-butyramide,

(N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitro-benzylamine,  
 (N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-nitro-benzylamine,  
 5 (N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-nitro-benzylamine,  
 (N-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-valeramide,  
 10 (N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-benzylamine,  
 (N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-2-nitrobenzylamine,  
 (N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamine,  
 15 (N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamine,  
 (N-[3,4-dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methyl-amino]-propyl)-valeramide,  
 20 (N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamine,  
 (N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-4-nitrobenzylamine,  
 (N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-2-nitrobenzylamine,  
 25 (N-phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-valeramide,  
 (N-(4-chloro)phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitrobenzamide,  
 or a pharmaceutically acceptable salt of any of the foregoing.

**Patentansprüche**

**Patentansprüche für folgende Vertragsstaaten : BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE**

1. Verwendung einer Verbindung der Formel (I) oder eines pharmazeutisch verträglichen Salzes davon,  
 oder eines Solvates eines der genannten Stoffe:



in der

R<sub>1</sub> und R<sub>4</sub> unabhängig Phenylgruppen bedeuten, die gegebenenfalls mit einem, zwei oder drei Resten, nämlich Halogenatomen, Trifluormethyl-, C<sub>1-4</sub>-Alkoxy-, C<sub>1-4</sub>-Alkyl-, Cyano-, Hydroxy- oder Nitrogruppen, oder Resten der Formeln NR<sub>5</sub>R<sub>6</sub> oder O<sub>2</sub>SNR<sub>5</sub>R<sub>6</sub> substituiert sind, wobei R<sub>5</sub> und R<sub>6</sub> unabhängig voneinander Wasserstoffatome oder C<sub>1-6</sub>-Alkylreste bedeuten oder zusammen eine C<sub>3-6</sub>-Polymethylengruppe sind, oder an benachbarten Kohlenstoffatomen durch C<sub>1-2</sub>-Alkylendioxyreste disubstituiert und gegebenenfalls zusätzlich durch einen oder zwei der genannten Reste substituiert sind;

R<sub>2</sub> ausgewählt ist aus (CH<sub>2</sub>)<sub>z</sub>CN, wobei z 0 oder eine ganze Zahl von 1 bis 4 ist, C<sub>1-12</sub>-Alkyl-, C<sub>3-7</sub>-Cycloalkyl-, C<sub>3-7</sub>-Cycloalkyl-C<sub>1-4</sub>-alkyl-, Phenyl-C<sub>1-4</sub>-alkyl-, Pyridyl- oder Pyridyl-C<sub>1-4</sub>-alkylresten oder Resten der Formeln COR<sub>7</sub>, COCH<sub>2</sub>COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> und CSNHR<sub>7</sub>, wobei R<sub>7</sub> ausgewählt ist aus C<sub>3-12</sub>-Alkyl-, C<sub>3-7</sub>-Cycloalkyl-, C<sub>3-7</sub>-Cycloalkyl-C<sub>1-4</sub>-alkyl-, Phenyl- und Phenyl-C<sub>1-4</sub>-alkylresten, wobei alle Alkylreste in R<sub>7</sub> gegebenenfalls durch Hydroxyl- oder C<sub>1-4</sub>-Alkanoyloxyre-

ste substituiert sind, alle Pyridyl- oder Phenylgruppen in  $R_2$  gegebenenfalls wie für die Reste  $R_1$  und  $R_4$  definiert substituiert sein können und alle Cycloalkylreste in  $R_2$  gegebenenfalls durch einen oder zwei  $C_{1-4}$ -Alkylreste substituiert sein können;

5  $R_3$  ein Wasserstoffatom oder einen  $C_{1-4}$ -Alkylrest bedeutet;

A einen  $C_{2-5}$ -Alkylrest bedeutet; und

B einen  $C_{1-4}$ -Alkylrest darstellt,

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für die Herstellung eines Arzneimittels zur Behandlung oder Vorbeugung von Angina pectoris in Säugern.

2. Verbindung der Formel (IA) umfassend eine Verbindung der Formel (I) gemäß Anspruch 1 oder ein pharmazeutisch verträgliches Salz davon, oder ein Solvat eines der vorstehend genannten Stoffe, mit der Maßgabe, daß die Variablen [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] nicht die folgenden Kombinationen von Bedeutungen annehmen:

- 20 [Phenyl,  $COnc_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , Phenyl]  
 [Phenyl,  $COiC_3H_7$ ,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , Phenyl]  
 [Phenyl,  $COnc_3H_7$ ,  $CH(CH_3)CH_2$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 [Phenyl,  $COnc_3H_7$ ,  $CH_2CN(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 [Phenyl,  $COiC_3H_7$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 [Phenyl,  $COnc_4H_9$ ,  $CH_2CH(CH_3)$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 25 [Phenyl, Benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , Phenyl]  
 [Phenyl, Benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $CH_2$ , Phenyl]  
 [Phenyl, Benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl],  
 [Phenyl, Benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_3$ , Phenyl]  
 [4-Chlorphenyl, Benzyl,  $(CH_2)_2$ , H,  $(CH_2)_2$ , Phenyl]  
 30 [4-Chlorphenyl, Benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 [Phenyl, 4-Chlorbenzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , Phenyl]  
 [Phenyl, Benzyl,  $(CH_2)_2$ ,  $CH_3$ ,  $(CH_2)_2$ , 4-Chlorphenyl]

zur Verwendung als therapeutischer Wirkstoff.

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3. Verbindung der Formel (IA) gemäß Anspruch 2 zur Behandlung oder Prophylaxe von Angina pectoris.

4. Arzneimittel, umfassend eine Verbindung der Formel (IA) nach Anspruch 2 und einen pharmazeutisch verträglichen Träger.

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5. Verbindung der Formel (IB), umfassend eine Verbindung der Formel (IA) gemäß Anspruch 2, mit der Maßgabe, daß die Variablen [ $R_1$ ,  $R_2$ , A,  $R_3$ , B,  $R_4$ ] nicht die folgenden Kombinationen von Bedeutungen annehmen:

45

- [3,4-Dimethoxyphenyl,  $C_2H_5$ ,  $(CH_2)_2$ , H,  $(CH_2)_2$ , Phenyl]  
 [3,4-Dimethoxyphenyl,  $C_2H_5$ ,  $(CH_2)_2$ , H,  $CH_2$ , Phenyl].

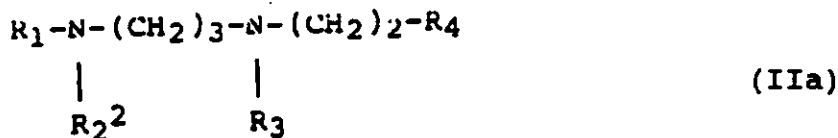
6. Verbindung nach Anspruch 5, wobei  $R_1$  und  $R_4$  unabhängig gemäß der Definition in Anspruch 1 substituierte Phenylgruppen bedeuten.

50

7. Verbindung nach Anspruch 5, in der  $R_2$  einen Rest  $COR_7$  bedeutet, wobei  $R_7$  einen Phenyl- oder Phenyl- $C_{1-4}$ -Alkylrest bedeutet, wobei die Phenylgruppe gegebenenfalls wie für  $R_1$  und  $R_4$  definiert substituiert ist.

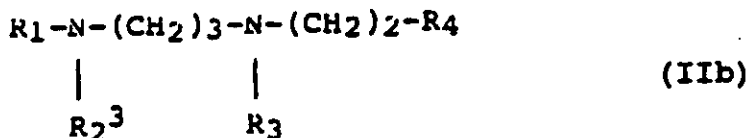
55

8. Verbindung nach Anspruch 5 der Formel (IIa):



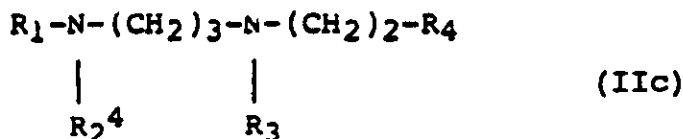
in der  $R_2^2$  einen Rest  $COR_7$  bedeutet, in dem  $R_7$  wie in Anspruch 5 definiert ist, und die übrigen Variablen wie in Anspruch 5 definiert sind.

9. Verbindung nach Anspruch 5 der Formel (IIb):



in der  $R_2^3$  einen Rest  $CO_2R_7$  oder  $SO_2R_7$  bedeutet, wobei  $R_7$  wie in Anspruch 5 definiert ist und die übrigen Variablen wie in Anspruch 5 definiert sind.

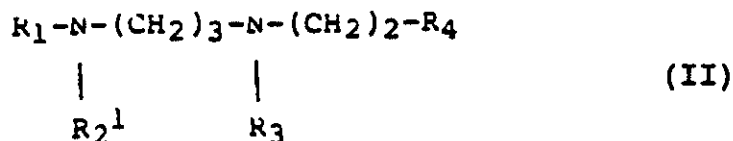
10. Verbindung nach Anspruch 5 der Formel (IIc):



in der  $R_2^4$  einen Rest  $CONHR_7$  oder  $CSNHR_7$  bedeutet, wobei  $R_7$  wie in Anspruch 5 definiert ist, und die übrigen Variablen wie in Anspruch 5 definiert sind.

11. Verbindung nach Anspruch 5, in der  $R_2$  einen  $C_3-12$ -Alkylrest bedeutet.

12. Verbindung nach Anspruch 5 der Formel (II):



in der

$R_1$ ,  $R_3$  und  $R_4$  wie in Anspruch 7 definiert sind; und

$R_2^1$  einen Rest  $(CH_2)_zCN$ , einen  $C_1-12$ -Alkyl-,  $C_3-7$ -Cycloalkyl-,  $C_3-7$ -Cycloalkyl- $C_1-4$ -alkyl-, oder Phenyl- $C_1-4$ -alkylrest bedeutet, wobei  $z$  wie in Anspruch 5 definiert ist, und alle Phenyl-, Alkyl- oder Cycloalkylreste in  $R_2^1$  gegebenenfalls wie für die entsprechenden Variablen  $R_2$  in Anspruch 5 definiert substituiert sind.

13. Verbindung nach Anspruch 5, in der  $R_1$  und  $R_4$  unabhängig Phenylgruppen bedeuten, die durch ein, zwei oder drei Halogenatome, Trifluormethyl-,  $C_1-4$ -Alkoxy-,  $C_1-4$ -Alkyl-, Cyano-, Hydroxy- oder Nitrogruppen, oder Reste  $NR_5R_6$  oder  $O_2SNR_5R_6$  substituiert sind, wobei  $R_5$  und  $R_6$  unabhängig Wasserstoffatome oder  $C_1-6$ -Alkylreste bedeuten oder zusammen einen  $C_3-6$ -Polymethylenrest darstellen, oder an benachbarten Kohlenstoffatomen durch  $C_1-2$ -Alkylendioxygruppen disubstituiert sind;

R<sub>2</sub> ausgewählt ist aus (CH<sub>2</sub>)<sub>z</sub>CN, wobei z 0 oder eine ganze Zahl von 1 bis 4 ist, C<sub>1-12</sub>-Alkyl-, C<sub>3-7</sub>-Cycloalkyl-, C<sub>3-7</sub>-Cycloalkyl-C<sub>1-4</sub>-alkyl oder Phenyl-C<sub>1-4</sub>-alkylresten, oder Resten COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> und CSNHR<sub>7</sub>, wobei R<sub>7</sub> ausgewählt ist aus C<sub>3-12</sub>-Alkyl-, C<sub>3-7</sub>-Cycloalkyl-, C<sub>3-7</sub>-Cycloalkyl-C<sub>1-4</sub>-alkyl-, Phenyl- und Phenyl-C<sub>1-4</sub>-Alkylresten, wobei alle Phenylgruppen in R<sub>2</sub> gegebenenfalls wie für R<sub>1</sub> und R<sub>4</sub> definiert substituiert sein können;

R<sub>3</sub> ein Wasserstoffatom oder einen C<sub>1-4</sub>-Alkylrest bedeutet;

A einen C<sub>2-5</sub>-Alkylenrest darstellt; und

B einen C<sub>1-4</sub>-Alkylenrest bedeutet.

14. Verbindung nach einem der Ansprüche 5 bis 13, in der R<sub>1</sub> und R<sub>4</sub> eine 3,4-Dimethoxyphenylgruppe bedeuten.

15. (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanomethylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-buttersäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-methyl)-propionsäureamid

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-pentansäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-phenyl)-essigsäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-phenyl)-propionsäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-phenylsulfonamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-  
dodecansäure-amid,

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-octansäure-  
amid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexansäure-  
amid,

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(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-dodecansäure-  
amid,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-pentansäure-  
amid,

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(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(2-methyl)-  
propionsäure-amid,

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(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-phenyl)-  
propionsäure-amid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-  
butylurethan,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-phenyl-  
urethan,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-butyl-  
harnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-propyl-  
harnstoff,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-i-propyl-  
harnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-t-butyl-  
harnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-  
benzylharnstoff,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-  
phenylharnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-(1-phenyl)-  
ethylharnstoff,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl-N''-n-propyl-  
harnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-pentylamin,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-n-pentylamin,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-  
dinitrobenzylamin,

- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3-(3-methoxyphenyl)-propylamin,
- 5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-2,5-dimethylbenzylamin,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-trifluormethylbenzylamin,
- 10 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-trifluormethylbenzylamin,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,4,6-trimethyl-benzylamin,
- 15 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,6-dichlorbenzylamin,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-chlor-3,4-methylenedioxybenzylamin,
- 20 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3,5-dinitro-2-aminopyridin,
- 25 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl)-4-nitro-benzylamin,
- (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamin,
- 30 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl)-phenylacetamid,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-(4'-nitrophenyl)-butyramid,
- 35 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitrophenyl)-acetamid,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N'-4-nitrobenzamid,
- 40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-heptanamid,
- 45 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-cyanobenzamid,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-trifluoromethylbenzamid,
- 50 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzamid,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-chlorbenzamid,
- 55 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-(3-phenyl-2-

acetoxy)-propionsäure-amid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N-4-nitrophenylharnstoff,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-hexylurethan,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-octylurethan,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-5-(-)-menthylurethan,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-cyclohexylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-isopropylamin,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butylamin,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino-propyl]-1-(3-oxo)-butyramid,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitro-benzylamin,

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(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-nitro-benzylamin,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-nitro-benzylamin,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-valeramid,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-2-nitrobenzylamin,

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(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramid,

45

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-3-nitrobenzylamin,

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamin,

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(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-2-nitrobenzylamin,

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramid,

(N-(4-Chlor)-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitrobenzamid,

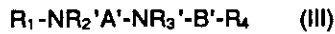
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oder ein pharmazeutisch verträgliches Salz einer der vorstehenden Verbindungen.

16. Verfahren zur Herstellung einer Verbindung nach Anspruch 5, umfassend die Umsetzung von Verbin-

dungen der Formeln  $R_{10}X$  und  $YR_{11}$ , wobei einer der Reste X und Y eine austretende Gruppe oder eine Aldehyd- oder Ketonfunktion ist und der andere einen nukleophilen Stickstoff bedeutet, wobei der nukleophile Stickstoff,  $R_{10}$  und  $R_{11}$ , und die Aldehyd- oder Ketonfunktion, sofern vorhanden, dergestalt sind, daß eine Verbindung der Formel (III) erzeugt wird:

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in der  $R_2'$ ,  $A'$ ,  $R_3'$  und  $B'$  die Reste  $R_2$ ,  $A$ ,  $R_3$  bzw.  $B$  sind oder in diese umwandelbare Reste darstellen, und  $R_1$ ,  $R_2$ ,  $A$ ,  $R_3$ ,  $B$  und  $R_4$  wie in Anspruch 5 definiert sind, und danach, gegebenenfalls oder wenn notwendig, Umwandlung von  $R_2'$ ,  $A'$ ,  $R_3'$  und/oder  $B'$  in  $R_2$ ,  $A$ ,  $R_3$  und/oder  $B$ , Austausch von  $R_2$  und/oder  $R_3$  und/oder Erzeugung eines pharmazeutisch verträglichen Salzes.

17. 1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-(3,4-dimethoxy)-anilin,

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1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-ethyl-2-(3,4-dimethoxy)-anilin,

1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-anilin,

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1-[N-Methyl-N-2-phenylethylamino]-propyl-3-(3,4-dimethoxy)-anilin oder

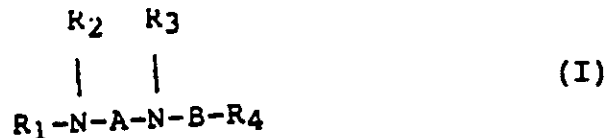
1-[N-Methyl-N-2-(3,4-dimethoxyphenyl)-ethylamino]-propyl-3-(4-chlor)-anilin.

#### Patentansprüche für folgenden Vertragsstaat : ES

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1. Verwendung einer Verbindung der Formel (I) oder eines pharmazeutisch verträglichen Salzes davon, oder eines Solvates eines der genannten Stoffe:

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in der

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$R_1$  und  $R_4$  unabhängig Phenylgruppen bedeuten, die gegebenenfalls mit einem, zwei oder drei Resten, nämlich Halogenatomen, Trifluormethyl-,  $C_{1-4}$ -Alkoxy-,  $C_{1-4}$ -Alkyl-, Cyano-, Hydroxy- oder Nitrogruppen, oder Resten der Formeln  $NR_5R_6$  oder  $O_2SNR_5R_6$  substituiert sind, wobei  $R_5$  und  $R_6$  unabhängig voneinander Wasserstoffatome oder  $C_{1-6}$ -Alkylreste bedeuten oder zusammen eine  $C_{3-6}$ -Polymethylengruppe sind, oder an benachbarten Kohlenstoffatomen durch  $C_{1-2}$ -Alkylendioxyreste disubstituiert und gegebenenfalls zusätzlich durch einen oder zwei der genannten Reste substituiert sind;

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$R_2$  ausgewählt ist aus  $(CH_2)_zCN$ , wobei  $z$  0 oder eine ganze Zahl von 1 bis 4 ist,  $C_{1-12}$ -Alkyl-,  $C_{3-7}$ -Cycloalkyl-,  $C_{3-7}$ -Cycloalkyl- $C_{1-4}$ -alkyl-, Phenyl- $C_{1-4}$ -alkyl-, Pyridyl- oder Pyridyl- $C_{1-4}$ -alkylresten oder Resten der Formeln  $COR_7$ ,  $COCH_2COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  und  $CSNHR_7$ , wobei  $R_7$  ausgewählt ist aus  $C_{3-12}$ -Alkyl-,  $C_{3-7}$ -Cycloalkyl-,  $C_{3-7}$ -Cycloalkyl- $C_{1-4}$ -alkyl-, Phenyl- und Phenyl- $C_{1-4}$ -alkylresten, wobei alle Alkylreste in  $R_7$  gegebenenfalls durch Hydroxyl- oder  $C_{1-4}$ -Alkanoyloxyreste substituiert sind, alle Pyridyl- oder Phenylgruppen in  $R_2$  gegebenenfalls wie für die Reste  $R_1$  und  $R_4$  definiert substituiert sein können und alle Cycloalkylreste in  $R_2$  gegebenenfalls durch einen oder zwei  $C_{1-4}$ -Alkylreste substituiert sein können;

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$R_3$  ein Wasserstoffatom oder einen  $C_{1-4}$ -Alkylrest bedeutet;

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$A$  einen  $C_{2-5}$ -Alkylrest bedeutet; und

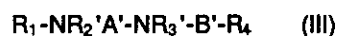
$B$  einen  $C_{1-4}$ -Alkylrest darstellt,

für die Herstellung eines Arzneimittels zur Behandlung oder Vorbeugung von Angina pectoris in Säugern.

2. Verfahren zur Herstellung einer Verbindung der Formel (IB), welche eine Verbindung der Formel (I) gemäß Anspruch 1 umfaßt, oder eines pharmazeutisch verträglichen Salzes davon, oder eines Solvats eines der vorstehend genannten Stoffe, mit der Maßgabe, daß die Variablen [R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B, R<sub>4</sub>] nicht die folgenden Kombinationen von Bedeutungen annehmen:

[Phenyl, COnC<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, Phenyl]  
 [Phenyl, COiC<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, Phenyl]  
 [Phenyl, COnC<sub>3</sub>H<sub>7</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, COnC<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, COiC<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, COnC<sub>4</sub>H<sub>9</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, Phenyl]  
 [Phenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl],  
 [Phenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>3</sub>, Phenyl]  
 [4-Chlorphenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [4-Chlorphenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, 4-Chlorbenzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [Phenyl, Benzyl, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-Chlorphenyl]  
 [3,4-Dimethoxyphenyl, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, Phenyl]  
 [3,4-Dimethoxyphenyl, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, CH<sub>2</sub>, Phenyl],

umfassend die Umsetzung von Verbindungen der Formeln R<sub>10</sub>X und YR<sub>11</sub>, wobei einer der Reste X und Y eine austretende Gruppe oder eine Aldehyd- oder Ketonfunktion ist und der andere einen nukleophilen Stickstoff bedeutet, wobei der nukleophile Stickstoff, R<sub>10</sub> und R<sub>11</sub>, und die Aldehyd- oder Ketonfunktion, sofern vorhanden, dergestalt sind, daß eine Verbindung der Formel (III) erzeugt wird:

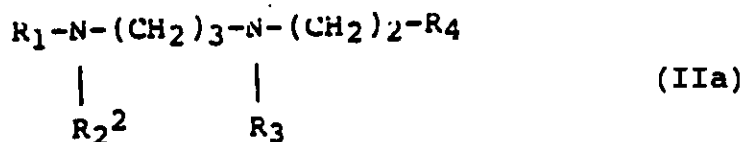


in der R<sub>2</sub>', A', R<sub>3</sub>' und B' die Reste R<sub>2</sub>, A, R<sub>3</sub> bzw. B sind oder in diese umwandelbare Reste darstellen, und R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B und R<sub>4</sub> wie in Anspruch 1 definiert sind, und danach, gegebenenfalls oder wenn notwendig, Umwandlung von R<sub>2</sub>', A', R<sub>3</sub>' und/oder B' in R<sub>2</sub>, A, R<sub>3</sub> und/oder B, Austausch von R<sub>2</sub> und/oder R<sub>3</sub> und/oder Erzeugung eines pharmazeutisch verträglichen Salzes.

3. Verfahren nach Anspruch 2, wobei R<sub>1</sub> und R<sub>4</sub> unabhängig gemäß der Definition in Anspruch 1 substituierte Phenylgruppen bedeuten.

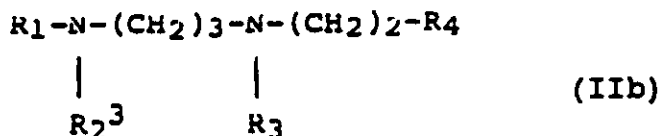
4. Verfahren nach Anspruch 2, in der R<sub>2</sub> einen Rest COR<sub>7</sub> bedeutet, wobei R<sub>7</sub> einen Phenyl- oder Phenyl-C<sub>1-4</sub>-Alkylrest bedeutet, wobei die Phenylgruppe gegebenenfalls wie für R<sub>1</sub> und R<sub>4</sub> definiert substituiert ist.

5. Verfahren nach Anspruch 2 zur Herstellung einer Verbindung der Formel (IIa):



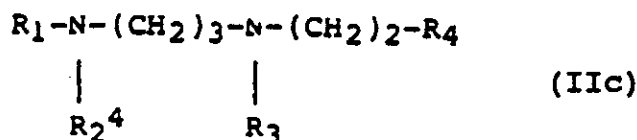
in der R<sub>2</sub><sup>2</sup> einen Rest COR<sub>7</sub> bedeutet, in dem R<sub>7</sub> wie in Anspruch 2 definiert ist, und die übrigen Variablen wie in Anspruch 2 definiert sind.

6. Verfahren nach Anspruch 2 zur Herstellung einer Verbindung der Formel (IIb):



in der  $R_2^3$  einen Rest  $CO_2R_7$  oder  $SO_2R_7$  bedeutet, wobei  $R_7$  wie in Anspruch 2 definiert ist und die übrigen Variablen wie in Anspruch 2 definiert sind.

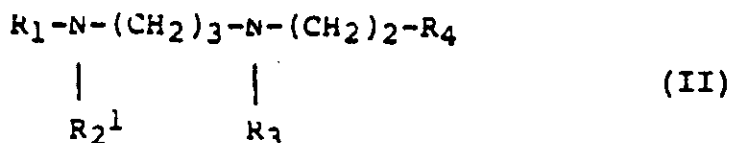
7. Verfahren nach Anspruch 2 zur Herstellung einer Verbindung der Formel (IIc):



in der  $R_2^4$  einen Rest  $CONHR_7$  oder  $CSNHR_7$  bedeutet, wobei  $R_7$  wie in Anspruch 2 definiert ist, und die übrigen Variablen wie in Anspruch 2 definiert sind.

8. Verfahren nach Anspruch 2, in der  $R_2$  einen  $C_3-12$ -Alkylrest bedeutet.

9. Verfahren nach Anspruch 2 zur Herstellung einer Verbindung der Formel (II):



in der

$R_1$ ,  $R_3$  und  $R_4$  wie in Anspruch 4 definiert sind; und

$R_2^1$  einen Rest  $(CH_2)_zCN$ , einen  $C_1-12$ -Alkyl-,  $C_3-7$ -Cycloalkyl-,  $C_3-7$ -Cycloalkyl- $C_1-4$ -alkyl-, oder Phenyl- $C_1-4$ -alkylrest bedeutet, wobei  $z$  wie in Anspruch 2 definiert ist, und alle Phenyl-, Alkyl- oder Cycloalkylreste in  $R_2^1$  gegebenenfalls wie für die entsprechenden Variablen  $R_2$  in Anspruch 2 definiert substituiert sind.

10. Verfahren nach Anspruch 2, in der  $R_1$  und  $R_4$  unabhängig Phenylgruppen bedeuten, die durch ein, zwei oder drei Halogenatome, Trifluormethyl-,  $C_1-4$ -Alkoxy-,  $C_1-4$ -Alkyl-, Cyano-, Hydroxy- oder Nitrogruppen, oder Reste  $NR_5R_6$  oder  $O_2SNR_5R_6$  substituiert sind, wobei  $R_5$  und  $R_6$  unabhängig Wasserstoffatome oder  $C_1-6$ -Alkylreste bedeuten oder zusammen einen  $C_3-6$ -Polymethylenrest darstellen, oder an benachbarten Kohlenstoffatomen durch  $C_1-2$ -Alkylendioxygruppen disubstituiert sind;

$R_2$  ausgewählt ist aus  $(CH_2)_zCN$ , wobei  $z$  0 oder eine ganze Zahl von 1 bis 4 ist,  $C_1-12$ -Alkyl-,  $C_3-7$ -Cycloalkyl-,  $C_3-7$ -Cycloalkyl- $C_1-4$ -alkyl- oder Phenyl- $C_1-4$ -alkylresten, oder Resten  $COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  und  $CSNHR_7$ , wobei  $R_7$  ausgewählt ist aus  $C_3-12$ -Alkyl-,  $C_3-7$ -Cycloalkyl-,  $C_3-7$ -Cycloalkyl- $C_1-4$ -alkyl-, Phenyl- und Phenyl- $C_1-4$ -Alkylresten, wobei alle Phenylgruppen in  $R_2$  gegebenenfalls wie für  $R_1$  und  $R_4$  definiert substituiert sein können;

$R_3$  ein Wasserstoffatom oder einen  $C_1-4$ -Alkylrest bedeutet;

A einen  $C_2-5$ -Alkylenrest darstellt; und

B einen  $C_1-4$ -Alkylenrest bedeutet.

11. Verfahren nach einem der Ansprüche 2 bis 10, in dem R<sub>1</sub> und R<sub>4</sub> eine 3,4-Dimethoxyphenylgruppe bedeutet.

12. Verfahren nach Anspruch 2 zur Herstellung von

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanamid,

10 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-cyanomethylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzylamin,

15 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-nitro)-benzylamin,

20 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitro)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-benzylamin,

25 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-nitro)-benzylamin,

30 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-buttersäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-methyl)-propionsäureamid

35 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-pentansäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-benzamid,

40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(2-phenyl)-essigsäureamid,

45 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(3-phenyl)-propionsäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-methyl)-phenylsulfonamid,

50 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-dodecansäureamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-octansäureamid,

55 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexansäureamid,

- (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-dodecansäureamid,
- 5 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-pentansäureamid,
- (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(2-methyl)-propionsäureamid,
- 10 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-(3-phenyl)-propionsäureamid,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-butylurethan,
- 15 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-phenylurethan,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-butylharnstoff,
- 20 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-n-propylharnstoff,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-i-propylharnstoff,
- 25 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-t-butylharnstoff,
- 30 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-benzylharnstoff,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-N''-phenylharnstoff,
- 35 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-N''-(1-phenyl)-ethylharnstoff,
- 40 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-N''-n-propylharnstoff,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-n-pentylamin,
- 45 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-n-pentylamin,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzylamin,
- 50 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3-(3-methoxyphenyl)-propylamin,
- (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-2,5-dimethylbenzylamin,
- 55 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-trifluormethylbenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-trifluormethylbenzylamin,

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,4,6-trimethyl-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2,6-dichlorbenzylamin,

10 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-chlor-3,4-methylendioxybenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3,5-dinitro-2-aminopyridin,

15 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl)-4-nitro-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-ethyl)-benzylamin,

20 (N-[3,4-Dimethoxyphenyl]-N-2-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-ethyl)-phenylacetamid,

25 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-(4'-nitrophenyl)-butyramid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-(4-nitrophenyl)-acetamid,

30 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N'-4-nitrobenzamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-heptanamid,

35 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-cyanobenzamid,

40 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-trifluormethylbenzamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-3,5-dinitrobenzamid,

45 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-4-chlorbenzamid,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-(3-phenyl-2-acetoxy)-propionsäure-amid,

50 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-N-4-nitrophenylharnstoff,

55 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-hexylurethan,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-n-octylurethan,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-5-(-)-menthylurethan,

5 (N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-cyclohexyl-amin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-isopropylamin,

10

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-hexylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino]-propyl)-butylamin,

15

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methylamino-propyl]-1-(3-oxo)-butyramid,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitro-benzylamin,

20

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-3-nitro-benzylamin,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-2-nitro-benzylamin,

(N-Phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-valeramid,

25

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-benzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenylethyl)-N'-methylamino]-propyl)-2-nitrobenzylamin,

30

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methylamino]-propyl)-3-nitrobenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamin,

(N-[3,4-Dimethoxyphenyl]-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramid,

35

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-3-nitrobenzylamin,

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-4-nitrobenzylamin,

40

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-2-nitrobenzylamin,

(N-Phenyl-N-3-[N'-(2-phenyl-ethyl)-N'-methyl-amino]-propyl)-valeramid,

(N-(4-Chlor)-phenyl-N-3-[N'-2-(3,4-dimethoxyphenyl)-ethyl-N'-methyl-amino]-propyl)-4-nitrobenzamid,

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oder eines pharmazeutisch verträglichen Salzes einer der vorstehenden Verbindungen.

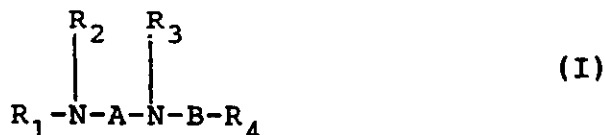
#### Revendications

Revendications pour les Etats contractants suivants : BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE

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1. Utilisation d'un composé de formule (I) ou d'un sel de celui-ci acceptable du point de vue pharmaceutique ou d'un solvate de l'un quelconque des précédents :

55



dans laquelle

R<sub>1</sub> et R<sub>4</sub> sont indépendamment un groupe phényle éventuellement substitué par un, deux ou trois atomes d'halogène, groupe trifluorométhyle, alcoxy en C<sub>1-4</sub>, alkyle en C<sub>1-4</sub>, cyano, hydroxy, nitro, NR<sub>5</sub>R<sub>6</sub> ou O<sub>2</sub>SNR<sub>5</sub>R<sub>6</sub> où R<sub>5</sub> et R<sub>6</sub> sont indépendamment un atome d'hydrogène ou un groupe alkyle en C<sub>1-6</sub> ou forment ensemble un radical polyméthylène en C<sub>3-6</sub>, ou disubstitués sur des atomes de carbone adjacents par un groupe alkylènedioxy en C<sub>1-2</sub> et substitué éventuellement de plus par l'un des groupes ci-dessus ;

R<sub>2</sub> est choisi parmi les groupes (CH<sub>2</sub>)<sub>z</sub>CN dans lequel z est 0 ou un entier de 1 à 4, alkyle en C<sub>1-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phénylalkyle en C<sub>1-4</sub>, pyridyle, pyridyl-alkyle en C<sub>1-4</sub>, COR<sub>7</sub>, COCH<sub>2</sub>COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> et CSNHR<sub>7</sub>, où R<sub>7</sub> est choisi parmi un groupe alkyle en C<sub>3-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phényle et phényl-alkyle en C<sub>1-4</sub>, une quelconque partie alkyle dans R<sub>7</sub> étant éventuellement substituée par un groupe hydroxy ou alcanoyloxy en C<sub>1-4</sub>, une quelconque partie pyridyle ou phényle dans R<sub>2</sub> étant éventuellement substituée de la façon définie pour R<sub>1</sub> et R<sub>4</sub> et une quelconque partie cycloalkyle dans R<sub>2</sub> étant éventuellement substituée par un ou deux groupes alkyle en C<sub>1-4</sub> ;

R<sub>3</sub> est un atome d'hydrogène ou un groupe alkyle en C<sub>1-4</sub> ;

A représente un groupe alkylène en C<sub>2-5</sub> ; et

B représente un groupe alkylène en C<sub>1-4</sub>,

pour la préparation d'un médicament pour le traitement ou la prophylaxie de l'angine de poitrine chez les mammifères.

2. Composé de formule (IA) qui comprend un composé de formule (I) suivant la revendication 1 ou un sel de celui-ci acceptable du point de vue pharmaceutique, ou un solvate de l'un quelconque des précédents, à la condition que les variables (R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B, R<sub>4</sub>) ne prennent pas les combinaisons de valeurs suivantes :

[phényle, CO<sub>n</sub>C<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]  
 [phényle, COiC<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]  
 [phényle, CO<sub>n</sub>C<sub>3</sub>H<sub>7</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, CO<sub>n</sub>C<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, COiC<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, CO<sub>n</sub>C<sub>4</sub>H<sub>9</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]  
 [phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>3</sub>, phényle]  
 [4-chlorophényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [4-chlorophényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, 4-chlorobenzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]  
 [phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-chlorophényle]  
 utile en tant que substance thérapeutique active.

3. Composé de formule (IA) suivant la revendication 2 pour le traitement ou la prophylaxie de l'angine de poitrine.

4. Composition pharmaceutique comprenant un composé de formule (IA) suivant la revendication 2 et un support acceptable du point de vue pharmaceutique.

5. Composé de formule (IB) qui comprend un composé de formule (IA) suivant la revendication 2 à la condition que les variables (R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B, R<sub>4</sub>) ne prennent pas les combinaisons de valeurs suivantes :

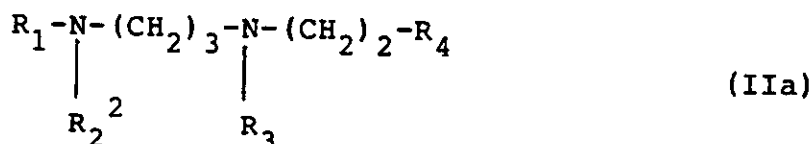
[3,4-diméthoxyphényle, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[3,4-diméthoxyphényle, C<sub>2</sub>H<sub>5</sub>, (CH<sub>2</sub>)<sub>2</sub>, H, CH<sub>2</sub>, phényle]

6. Composé suivant la revendication 5, dans lequel R<sub>1</sub> et R<sub>4</sub> sont indépendamment un groupe phényle substitué tel que défini dans la revendication 1.

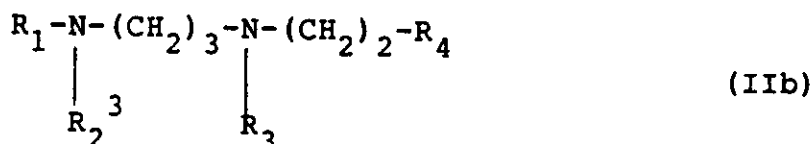
7. Composé suivant la revendication 5, dans lequel R<sub>2</sub> est un groupe COR<sub>7</sub> dans lequel R<sub>7</sub> est un groupe phényle ou phényl-alkyle en C<sub>1-4</sub>, la partie phényle étant éventuellement substituée de la façon définie pour R<sub>1</sub> et R<sub>4</sub>.

8. Composé suivant la revendication 5 de formule (IIa) :



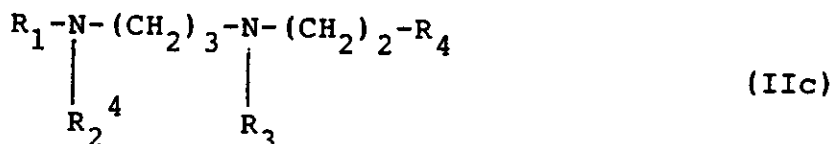
dans laquelle R<sub>2</sub><sup>2</sup> est COR<sub>7</sub> dans lequel R<sub>7</sub> est tel que défini dans la revendication 5, et les variables restantes sont telles que définies dans la revendication 5.

9. Composé suivant la revendication 5 de formule (IIb) :



dans laquelle R<sub>2</sub><sup>3</sup> est CO<sub>2</sub>R<sub>7</sub> ou SO<sub>2</sub>R<sub>7</sub> dans lesquels R<sub>7</sub> est tel que défini dans la revendication 5, et les variables restantes sont telles que définies dans la revendication 5.

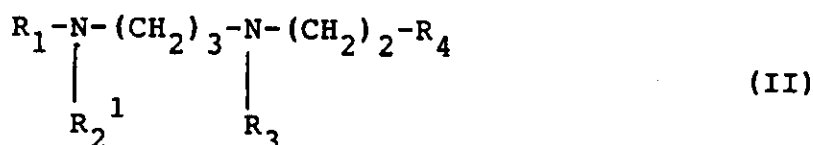
10. Composé suivant la revendication 5 de formule (IIc) :



dans laquelle R<sub>2</sub><sup>4</sup> est CONHR<sub>7</sub> ou CSNHR<sub>7</sub> dans lesquels R<sub>7</sub> est tel que défini dans la revendication 5 et les variables restantes sont telles que définies dans la revendication 5.

11. Composé suivant la revendication dans lequel R<sub>2</sub> est un groupe alkyle en C<sub>3-12</sub>.

12. Composé suivant la revendication 5 de formule (II) :



dans laquelle :

R<sub>1</sub>, R<sub>3</sub> et R<sub>4</sub> sont tels que définis dans la revendication 7 ; et

R<sub>2</sub><sup>1</sup> est un groupe (CH<sub>2</sub>)<sub>z</sub>CN, alkyle en C<sub>1-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub> ou phénylalkyle en C<sub>1-4</sub> où z est tel quel défini dans la revendication 5 et de quelconques parties phényle, alkyle ou cycloalkyle dans R<sub>2</sub><sup>1</sup> sont éventuellement substituées de la façon définie pour les variables correspondantes R<sub>2</sub> dans la revendication 5.

5

13. Composé suivant la revendication 5, dans lequel R<sub>1</sub> et R<sub>4</sub> sont indépendamment un groupe phényle substitué par un, deux ou trois atomes d'halogène, groupe trifluorométhyle, alcoxy en C<sub>1-4</sub>, alkyle en C<sub>1-4</sub>, cyano, hydroxy, nitro, NR<sub>5</sub>R<sub>6</sub> ou O<sub>2</sub>SNR<sub>5</sub>R<sub>6</sub> dans lesquels R<sub>5</sub> et R<sub>6</sub> sont indépendamment un atome d'hydrogène ou un groupe alkyle en C<sub>1-4</sub> ou forment ensemble un radical polyméthylène en C<sub>3-6</sub>, ou disubstitués sur des atomes de carbone adjacents par un radical alkylènedioxy en C<sub>1-2</sub>; R<sub>2</sub> est choisi parmi le groupe (CH<sub>2</sub>)<sub>z</sub>CN dans lequel z est 0 ou un entier de 1 à 4, alkyle en C<sub>1-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phényl-alkyle en C<sub>1-4</sub>, COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> et CSNHR<sub>7</sub>, où R<sub>7</sub> est choisi parmi les groupes alkyle en C<sub>3-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phényle et phénylalkyle en C<sub>1-4</sub>, un quelconque groupe phényle dans R<sub>2</sub> étant éventuellement substitué de la façon définie pour R<sub>1</sub> et R<sub>4</sub>; R<sub>3</sub> est un atome d'hydrogène ou un groupe alkyle en C<sub>1-4</sub>; A représente un groupe alkylène en C<sub>2-5</sub>; et B représente un groupe alkylène en C<sub>1-4</sub>.

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14. Composé suivant l'une quelconque des revendications 5 à 13, dans lequel R<sub>1</sub> et R<sub>4</sub> sont un groupe 3,4-diméthoxyphényle.

15. Composé comprenant les suivants :

25

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-nitro)-benzylamine,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-cyanamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-cyanométhylamine,

30

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-benzylamine,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-nitro)-benzylamine,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-nitro)-benzylamine,

35

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-méthyl)-benzylamine,

(N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(3-nitro)-benzylamine,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)butyramide,

40

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-méthyl)-propionamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-valéramide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-benzamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-phényl)-éthanamide,

45

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-phényl)-propionamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-méthyl)-phénylsulfonamide,

50

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-dodécaneamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-octaneamide,

(N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-hexaneamide,

(N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-dodécaneamide,

55

(N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-pentaneamide,

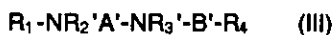
(N-[3,4-diméthoxyphényl]-N-2-[N'-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(2-méthyl)-propionamide,

(N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(3-phényl)-

propionamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-butyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-phényluréthane,  
 5 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-n-butylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]propyl)-N''-n-propylurée,  
 10 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-i-propylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-t-butylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-benzylurée,  
 15 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-phénylurée,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl-N''-(1-phényl)-éthylurée,  
 20 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl-N''-n-propylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-pentylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-n-pentylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-dinitrobenzylamine,  
 25 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-(3-méthoxyphényl)-propylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,5-diméthylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-trifluorométhylbenzylamine,  
 30 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-trifluorométhylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,4,6-triméthylbenzylamine,  
 35 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,6-dichlorobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-chloro-3,4-méthylènedioxobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-dinitro-2-aminopyridine,  
 40 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-4-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,5-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-phénylacétamide,  
 45 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-(4'-nitrophényl)-butyramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-nitrophényl)-acétamide,  
 50 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N'-4-nitrobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-heptanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-cyanobenzamide,  
 55 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-trifluorométhylbenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-

dinitrobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl-4-chlorobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-phényl-2-acétoxy)-propionamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl-N-4-nitrophénylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)n-hexyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-octyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-5-(  
 )méthyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-cyclohexylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propylisopropylamine,  
 N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-hexylamine,  
 N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propylbulylamino(  
 propyl)-butylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylaminopropyl]-1-(3-oxo)-butyramide,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-valéramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-2-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-3-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-4-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2)phényléthyl)-N'-méthylamino]-propyl-valéramide,  
 (N-phényl-N-3-[(N'-(2-phényléthyl)-N'-méthylamino)-propyl]-3-nitrobenzylamine,  
 (N-phényl-N-3-[(N'-(2-phényléthyl)-N'-méthylamino)-propyl]-4-nitrobenzylamine,  
 (N-phényl-N-3-[(N'-(2-phényléthyl)-N'-méthylamino)-propyl]-2-nitrobenzylamine,  
 (N-phényl-N-3-[(N'-(2-phényléthyl)-N'-méthylamino)-propyl]-valéramide,  
 (N-(4-chloro)phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-nitrobenzamide,  
 ou un sel acceptable du point de vue pharmaceutique de l'un quelconque des précédents.

16. Procédé pour la préparation d'un composé suivant la revendication 5, qui comprend la réaction de  $R_{10}X$  et  $YR_{11}$  dans lesquels l'un des X et Y est un groupe mobile ou une fonction aldéhyde ou cétone et l'autre est un nucléophile comprenant de l'azote, le nucléophile comprenant de l'azote,  $R_{10}$  et  $R_{11}$  et la fonction aldéhyde ou cétone lorsqu'elle est présente, étant telle qu'il se forme un composé de formule (III) :



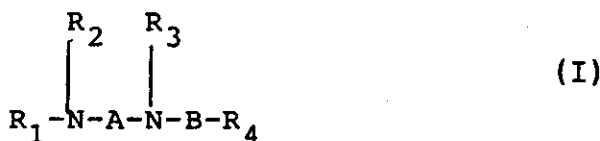
dans laquelle  $R_2'$ ,  $A'$ ,  $R_3'$  et  $B'$  sont  $R_2$ ,  $A$ ,  $R_3$  et  $B$  respectivement ou des groupes pouvant être convertis en ceux-ci, et  $R_1$ ,  $R_2$ ,  $A$ ,  $R_3$ ,  $B$  et  $R_4$  sont tels que définis dans la revendication 5, et ensuite, éventuellement ou si cela est nécessaire, la conversion de  $R_2'$ ,  $A'$ ,  $R_3'$  et/ou  $B'$  en  $R_2$ ,  $A$ ,  $R_3$  et/ou  $B$ , l'interconversion de  $R_2$  et/ou  $R_3$  et/ou la formation d'un sel acceptable du point de vue pharmaceutique.

17. Composé comprenant les suivants :

1-[N-méthyl-N-2-(3,4-diméthoxyphényl)-éthylamino]-propyl-3-(3,4-diméthoxy)-aniline,  
 1-[N-méthyl-N-2-(3,4-diméthoxyphényl)-éthylamino]-éthyl-2-(3,4-diméthoxy)-aniline,  
 1-[N-méthyl-N-2-(3,4-diméthoxyphényl)-éthylamino]-propyl-3-aniline,  
 1-[N-méthyl-N-2-phényléthylamino]-propyl-3-(3,4-diméthoxy)-aniline ou  
 1-[N-méthyl-N-2-(3,4-diméthoxyphényl)-éthylamino]-propyl-3-(4-chloro)-aniline.

## Revendications pour l'Etat contractant suivant : ES

1. Utilisation d'un composé de formule (I) ou d'un sel de celui-ci acceptable du point de vue pharmaceutique ou d'un solvate de l'un quelconque des précédents :



dans laquelle

R<sub>1</sub> et R<sub>4</sub> sont indépendamment un groupe phényle éventuellement substitué par un, deux ou trois atomes d'halogène, groupe trifluorométhyle, alcoxy en C<sub>1-4</sub>, alkyle en C<sub>1-4</sub>, cyano, hydroxy, nitro, NR<sub>5</sub>R<sub>6</sub> ou O<sub>2</sub>SNR<sub>5</sub>R<sub>6</sub> où R<sub>5</sub> et R<sub>6</sub> sont indépendamment un atome d'hydrogène ou un groupe alkyle en C<sub>1-6</sub> ou forment ensemble un radical polyméthylène en C<sub>3-6</sub>, ou disubstitués sur des atomes de carbone adjacents par un groupe alkylènedioxy en C<sub>1-2</sub> et substitué éventuellement de plus par l'un des groupes ci-dessus ;

R<sub>2</sub> est choisi parmi les groupes (CH<sub>2</sub>)<sub>z</sub>CN dans lequel z est 0 ou un entier de 1 à 4, alkyle en C<sub>1-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phénylalkyle en C<sub>1-4</sub>, pyridyle, pyridyl-alkyle en C<sub>1-4</sub>, COR<sub>7</sub>, COCH<sub>2</sub>COR<sub>7</sub>, SO<sub>2</sub>R<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub>, CONHR<sub>7</sub> et CSNHR<sub>7</sub>, où R<sub>7</sub> est choisi parmi un groupe alkyle en C<sub>3-12</sub>, cycloalkyle en C<sub>3-7</sub>, cycloalkyle en C<sub>3-7</sub>-alkyle en C<sub>1-4</sub>, phényle et phényl-alkyle en C<sub>1-4</sub>, une quelconque partie alkyle dans R<sub>7</sub> étant éventuellement substituée par un groupe hydroxy ou alcanoyloxy en C<sub>1-4</sub>, une quelconque partie pyridyle ou phényle dans R<sub>2</sub> étant éventuellement substituée de la façon définie pour R<sub>1</sub> et R<sub>4</sub> et une quelconque partie cycloalkyle dans R<sub>2</sub> étant éventuellement substituée par un ou deux groupes alkyle en C<sub>1-4</sub> ;

R<sub>3</sub> est un atome d'hydrogène ou un groupe alkyle en C<sub>1-4</sub> ;

A représente un groupe alkylène en C<sub>2-5</sub> ; et

B représente un groupe alkylène en C<sub>1-4</sub>,

pour la préparation d'un médicament pour le traitement ou la prophylaxie de l'angine de poitrine chez les mammifères.

2. Procédé pour la préparation d'un composé de formule (IB) qui comprend un composé de formule (I) suivant la revendication 1 ou un sel de celui-ci acceptable du point de vue pharmaceutique, ou un solvant de l'un quelconque des précédents, à la conditions que les variables (R<sub>1</sub>, R<sub>2</sub>, A, R<sub>3</sub>, B, R<sub>4</sub>) ne prennent pas les combinaisons de valeurs suivantes :

[phényle, CO<sub>n</sub>C<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]

[phényle, COIC<sub>3</sub>H<sub>7</sub>, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]

[phényle, CONC<sub>3</sub>H<sub>7</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, CONC<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, COIC<sub>3</sub>H<sub>7</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, CONC<sub>4</sub>H<sub>9</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>), CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>, phényle]

[phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>3</sub>, phényle]

[4-chlorophényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, H, (CH<sub>2</sub>)<sub>2</sub>, phényle]

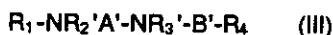
[4-chlorophényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, 4-chlorobenzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, phényle]

[phényle, benzyle, (CH<sub>2</sub>)<sub>2</sub>, CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>, 4-chlorophényle]

utile en tant que substance thérapeutique active.

lequel procédé comprend la réaction de R<sub>10</sub> avec YR<sub>11</sub> dans lesquels l'un des X et Y est un groupe mobile ou une fonction aldéhyde ou cétone et l'autre est un nucléophile contenant de l'azote, le nucléophile contenant de l'azote, R<sub>10</sub> et R<sub>11</sub> et la fonction aldéhyde ou cétone lorsqu'elle est présente, étant telle qu'il se forme un composé de formule (III) :

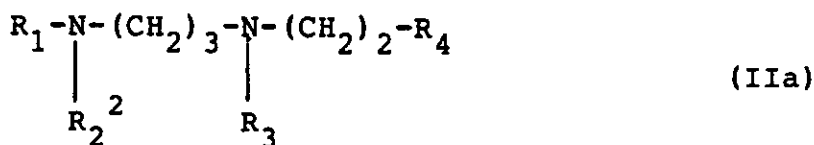


dans laquelle  $R_2'$ ,  $A'$ ,  $R_3'$  et  $B'$  sont  $R_2$ ,  $A$ ,  $R_3$  et  $B$  respectivement ou des groupes pouvant être convertis en ceux-ci, et  $R_1$ ,  $R_2$ ,  $A$ ,  $R_3$ ,  $B$  et  $R_4$  sont tels que définis dans la revendication 1, et ensuite, éventuellement et si cela est nécessaire la conversion de  $R_2'$ ,  $A'$ ,  $R_3'$ , et/ou  $B'$  en  $R_2$ ,  $A$ ,  $R_3$  et/ou  $B$ , l'interconversion de  $R_2$  et/ou  $R_3$  et/ou la formation d'un sel acceptable du point de vue pharmaceutique.

3. Procédé suivant la revendication 2, dans lequel  $R_1$  et  $R_4$  sont indépendamment un groupe phényle substitué de la façon définie dans la revendication 1.

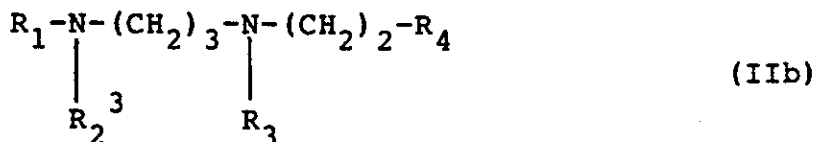
4. Procédé suivant la revendication 2, dans lequel  $R_2$  est  $COR_7$  dans lequel  $R_7$  est un groupe phényle ou phényl-alkyle en  $C_{1-4}$ , la partie phényle étant éventuellement substituée de la façon définie pour  $R_1$  et  $R_4$ .

5. Procédé suivant la revendication 2, pour préparer un composé de formule (IIa) :



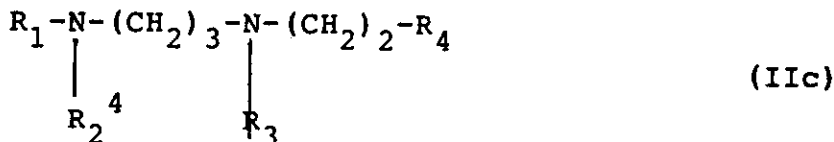
dans laquelle  $R_2^2$  est  $COR_7$  où  $R_7$  est tel que défini dans la revendication 2, et les variables restantes sont telles que définies dans la revendication 2.

6. Procédé suivant la revendication 2, pour préparer un composé de formule (IIb) :



dans laquelle  $R_2^3$  est  $CO_2R_7$  ou  $SO_2R_7$  où  $R_7$  est tel que défini dans la revendication 2, et les variables restantes sont telles que définies dans la revendication 2.

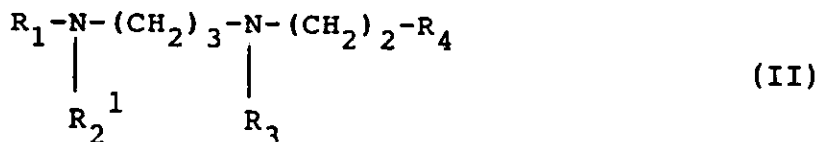
7. Procédé suivant la revendication 2, pour préparer un composé de formule (IIc) :



dans laquelle  $R_2^4$  est  $CONHR_7$  ou  $CSNHR_7$  où  $R_7$  est tel que défini dans la revendication 2, et les variables restantes sont telles que définies dans la revendication 2.

8. Procédé suivant la revendication 2, dans lequel  $R_2$  est un groupe alkyle en  $C_{3-12}$ .

9. Procédé suivant la revendication 2, pour préparer un composé de formule (II) :



dans laquelle :

$R_1$ ,  $R_3$  et  $R_4$  sont tels que définis dans la revendication 4, et  $R_2^1$  est un groupe  $(CH_2)_zCN$ , alkyle en  $C_{1-12}$ , cycloalkyle en  $C_{3-7}$ , cycloalkyle en  $C_{3-7}$ -alkyle en  $C_{1-4}$  ou phényl-alkyle en  $C_{1-4}$  dans lequel  $z$  est tel que défini dans la revendication 2, et de quelconques groupes phényle, alkyle ou cycloalkyle dans  $R_2^1$  sont éventuellement substitués de la façon définie pour les variables correspondantes  $R_2$  dans la revendication 2.

10. Procédé suivant la revendication 2, dans lequel  $R_1$  et  $R_4$  sont indépendamment un groupe phényle substitué par un, deux ou trois atomes d'halogène, groupe trifluorométhyle, alcoxy en  $C_{1-4}$ , alkyle en  $C_{1-4}$ , cyano, hydroxy, nitro,  $NR_5R_6$  ou  $O_2SNR_5R_6$  dans lesquels  $R_5$  et  $R_6$  sont indépendamment un atome d'hydrogène ou un groupe alkyle en  $C_{1-6}$  ou forment ensemble un radical polyméthylène en  $C_{3-6}$ , ou disubstitués sur des atomes de carbone adjacents par un radical alkylènedioxy en  $C_{1-2}$  ;  
 $R_2$  est choisi parmi un groupe  $(CH_2)_zCN$  dans lequel  $z$  est 0 ou un entier de 1 à 4, alkyle en  $C_{1-12}$ , cycloalkyle en  $C_{3-7}$ , cycloalkyle en  $C_{3-7}$ -alkyle en  $C_{1-4}$ , phényl-alkyle en  $C_{1-4}$ ,  $COR_7$ ,  $SO_2R_7$ ,  $CO_2R_7$ ,  $CONHR_7$  et  $CSNHR_7$  où  $R_7$  est choisi parmi les groupes alkyle en  $C_{3-12}$ , cycloalkyle en  $C_{3-7}$ , cycloalkyle en  $C_{3-7}$ -alkyle en  $C_{1-4}$ , phényle et phényl-alkyle en  $C_{1-4}$ , de quelconques groupes phényle dans  $R_2$  étant éventuellement substitués de la façon définie pour  $R_1$  et  $R_4$  ;  
 $R_3$  est un atome d'hydrogène ou un groupe alkyle en  $C_{1-4}$  ;  
 A représente un groupe alkylène en  $C_{2-5}$  ; et  
 B représente un groupe alkylène en  $C_{1-4}$  .
11. Procédé suivant l'une quelconque des revendications 2 à 10, dans lequel  $R_1$  et  $R_4$  sont des groupes 3,4-diméthoxyphényl.
12. Procédé suivant la revendication 2, pour préparer les composés suivants :  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-nitro)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-cyanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-cyanométhylamine,  
 (N-[3,4-diméthoxyphényl]-N-3[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-nitro)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-nitro)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-méthyl)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(3-nitro)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)butyramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-méthyl)-propionamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-valéramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-benzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(2-phényl)-éthanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-phényl)-propionamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-méthyl)-phénylsulfonamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-

- dodécanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-octanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-hexanamide,  
 (N-[3,4-diméthoxyphényl]-N-2-[3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-dodécanamide,  
 5 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-pentanamide,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(2-méthyl)-  
 propionamide,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-(3-phényl)-  
 propionamide,  
 10 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-  
 butyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-  
 phényluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-n-  
 15 butylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]propyl)-N''-n-  
 propylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-([N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-i-propylu-  
 20 rée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-t-  
 butylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-  
 benzylurée  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N''-  
 25 phénylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl-N''-(1-phényl)-  
 éthylurée,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl-N''-n-propylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-pentylamine,  
 30 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-n-pentylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-  
 dinitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-(3-  
 méthoxyphényl)-propylamine,  
 35 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,5-  
 diméthylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-  
 trifluorométhylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-  
 40 trifluorométhylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,4,6-  
 triméthylbenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2,6-  
 dichlorobenzylamine,  
 45 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-chloro-3,4-  
 méthylènedioxobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-dinitro-2-  
 aminopyridine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-4-  
 50 nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-benzylamine,  
 (N-[3,4-diméthoxyphényl]-N-2-[N'-2-(3,5-diméthoxyphényl)-éthyl-N'-méthylamino]-éthyl)-  
 phénylacétamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-(4'-  
 55 nitrophényl)-butyramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(4-  
 nitrophényl)-acétamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N'-4-

nitrobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-  
 heptanamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-  
 5 cyanobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-  
 trifluorométhylbenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3,5-  
 10 dinitrobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-  
 chlorobenzamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-(3-phényl-2-  
 acétoxy)-propionamide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-N-4-  
 15 nitrophénylurée,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-  
 hexyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-n-  
 20 octyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-5-(-  
 )méthyluréthane,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-  
 cyclohexylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)isopropylamine,  
 25 N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-hexylamine,  
 N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)butylamino(-  
 propyl)-butylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylaminopropyl]-1-(3-oxo)-  
 butyramide,  
 30 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-3-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-2-nitrobenzylamine,  
 (N-phényl-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-valéramide,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-benzylamine,  
 35 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-2-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-3-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-4-nitrobenzylamine,  
 (N-[3,4-diméthoxyphényl]-N-3-[N'-(2)phényléthyl)-N'-méthylamino]-propyl)-valéramide,  
 (N-phényl-N-3-([N'-(2-phényléthyl)-N'-méthylamino]-propyl)-3-nitrobenzylamine,  
 40 (N-phényl-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-4-nitrobenzylamine,  
 (N-phényl-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-2-nitrobenzylamine,  
 (N-phényl-N-3-[N'-(2-phényléthyl)-N'-méthylamino]-propyl)-valéramide,  
 (N-(4-chloro)phényl)-N-3-[N'-2-(3,4-diméthoxyphényl)-éthyl-N'-méthylamino]-propyl)-4-nitrobenzamide,  
 ou un sel acceptable du point de vue pharmaceutique de l'un quelconque des précédents.

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REGISTER ENTRY FOR EP0233762/

European Application No EP87301246.2 filing date 13.02.1987

Priority claimed:

15.02.1986 in United Kingdom - doc: 8603765

Designated States BE CH DE ES FR GB GR IT LI LU NL SE

Title USE OF AROMATIC DIAMINES FOR THE TREATMENT OF ANGINA, AND DIAMINES  
THEREFOR

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Classified to

A5B C2C U1S

A61K C07C

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Publication No EP0233762 dated 26.08.1987

Publication in English

Examination requested 13.02.1987

Patent Granted with effect from 19.08.1992/(Section 25(1)) with title USE OF  
AROMATIC DIAMINES FOR THE TREATMENT OF ANGINA PECTORIS, AND DIAMINES  
THEREFOR/

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12.04.1989 EPO: Search report published on 10.05.1989

Entry Type 25.11 Staff ID.

Auth ID. EPT

20.07.1992 Notification from EPO of change of Applicant/Proprietor details  
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Entry Type 25.14 Staff ID. RD06 Auth ID. EPT

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Gronau (Leine), Federal Republic of Germany [ADP No. 60023553001]  
Entry Type 25.14 Staff ID. RD06 Auth ID. EPT
- 24.08.1995 Notification of change of Address For Service name and address of  
JILL BARBARA VALENTINE, Beecham Pharmaceuticals Patents & Trade  
Marks Dept. Great Burgh Yew Tree Bottom Road, Epsom Surrey KT18  
5XQ, United Kingdom [ADP No. 50508373001]  
to  
SMITHKLINE BEECHAM P.L.C., SB House, Great West Road, BRENTFORD,  
Middlesex, TW8 9BD, United Kingdom [ADP No. 05791553001]  
dated 10.05.1995. Official evidence filed on GB2262447  
Entry Type 7.1 Staff ID. SA2 Auth ID. AA

\*\*\*\* END OF REGISTER ENTRY \*\*\*\*

OA80-01  
EP

OPTICS - PATENTS

18/06/96 08:01:18  
PAGE: 1

RENEWAL DETAILS

PUBLICATION NUMBER EP0233762 /

PROPRIETOR(S)

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DATE FILED 13.02.1987 /

DATE GRANTED 19.08.1992 /

DATE NEXT RENEWAL DUE 13.02.1997

DATE NOT IN FORCE

DATE OF LAST RENEWAL 11.01.1996

YEAR OF LAST RENEWAL 10

STATUS PATENT IN FORCE /

\*\*\*\* END OF REPORT \*\*\*\*