(12) STANDARD PATENT (11) Application No. **AU 2002317910 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Cyclic nucleotide phosphodiesterase inhibitors, preparation and uses thereof

(51) International Patent Classification(s)

C07D 243/10 (2006.01)	***C07D 243/24*** (2006.01)
A61K 31/551 (2006.01)	***C07D 401/04*** (2006.01)
A61K 31/5513 (2006.01)	***C07D 401/10*** (2006.01)
A61K 31/695 (2006.01)	***C07D 403/04*** (2006.01)
A61P 3/04 (2006.01)	***C07D 403/06*** (2006.01)
A61P 25/00 (2006.01)	***C07D 405/04*** (2006.01)
A61P 25/24 (2006.01)	***C07D 405/10*** (2006.01)
A61P 29/00 (2006.01)	***C07D 409/04*** (2006.01)
A61P 43/00 (2006.01)	***C07D 409/10*** (2006.01)
C07D 243/02 (2006.01)	***C07D 491/056*** (2006.01)
C07D 243/14 (2006.01)	***C07F 7/08*** (2006.01)

(21) Application No: **2002317910** (22) Date of Filing: **2002.06.07**

(87) WIPO No: **WO02/098865**

(30) Priority Data

(31) Number	(32) Date	(33) Country
01/07458	**2001.06.07**	**FR**

(43) Publication Date: **2002.12.16**
(43) Publication Journal Date: **2003.05.08**
(44) Accepted Journal Date: **2008.06.19**

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(12) DEMANDE INTERNATIONALE PUBLIÉE EN VERTU DU TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS (PCT)

(19) Organisation Mondiale de la Propriété Intellectuelle
Bureau international

(43) Date de la publication internationale
12 décembre 2002 (12.12.2002)

PCT

(10) Numéro de publication internationale
WO 02/098865 A3

(51) Classification internationale des brevets[7] : C07D 243/02, 409/04, 405/10, 401/04, 243/24, 243/14, 409/10, 405/04, 403/04, A61K 31/551, 31/5513, A61P 25/24, 25/00

(21) Numéro de la demande internationale : PCT/FR02/01952

(22) Date de dépôt international : 7 juin 2002 (07.06.2002)

(25) Langue de dépôt : français

(26) Langue de publication : français

(30) Données relatives à la priorité :
01/07458 7 juin 2001 (07.06.2001) FR

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(81) États désignés *(national)* : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) États désignés *(régional)* : brevet ARIPO (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), brevet eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), brevet européen (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), brevet OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Déclaration en vertu de la règle 4.17 :
— *relative à la qualité d'inventeur (règle 4.17.iv)) pour US seulement*

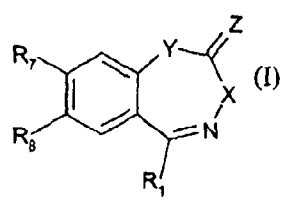
Publiée :
— *avec rapport de recherche internationale*

(88) Date de publication du rapport de recherche internationale: 27 février 2003

En ce qui concerne les codes à deux lettres et autres abréviations, se référer aux "Notes explicatives relatives aux codes et abréviations" figurant au début de chaque numéro ordinaire de la Gazette du PCT.

(54) Title: CYCLIC NUCLEOTIDE PHOSPHODIESTERASE INHIBITORS, PREPARATION AND USES THEREOF

(54) Titre : INHIBITEURS DES PHOSPHODIESTERASES DES NUCLEOTIDES CYCLIQUES, PREPARATION ET UTILISATIONS DE CES INHIBITEURS



(I)

(57) Abstract: The invention concerns novel benzodiazepinone derivatives and their uses in therapy particularly for treating pathologies involving the activity of a phosphodiesterase of cyclic nucleotides. The invention also concerns methods for preparing them and novel synthesis intermediates. The inventive compounds more particularly correspond to general formula (I).

(57) Abrégé : L'invention concerne de nouveaux dérivés de type benzodiazépinones et leurs applications dans le domaine thérapeutique tout particulièrement pour le traitement de pathologies impliquant l'activité d'une phosphodiestérase de nucléotides cycliques. Elle concerne également des procédés pour leur préparation et de nouveaux intermédiaires de synthèse. Les composés de l'invention répondent plus particulièrement à la formule générale (I) :

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Cyclic nucleotide phosphodiesterase inhibitors, preparation and uses thereof

The invention concerns novel benzodiazepine derivatives and their uses in the field of therapeutics particularly for treating pathologies involving the activity of a cyclic nucleotide phosphodiesterase. It also concerns methods for preparing them and novel synthesis intermediates.

The compounds whose synthesis is described in the present invention are novel and possess very interesting pharmacological properties : they are inhibitors of cyclic nucleotide phosphodiesterases and more particularly of cAMP-phosphodiesterase type 4 (PDE4) and, as such, they have very interesting therapeutic applications.

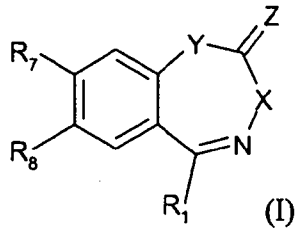
The functions of most tissues are modulated by endogenous substances such as hormones, transmitters, etc. or by exogenous substances. The biological effect of some of these substances is transmitted inside the cell by enzymatic effectors, such as adenylate cyclase or guanylate cyclase. Stimulation of such enzymes results in an elevation of intracellular levels of cyclic AMP (cAMP) or cyclic GMP (cGMP), second messengers involved in regulating many cellular activities. These cyclic nucleotides are degraded by a family of enzymes – the phosphodiesterases (PDE) – comprising at least seven groups. One of them, PDE4, is present in many different tissues (heart, brain, vascular or tracheobronchial smooth muscle, etc.) and specifically hydrolyzes cyclic AMP.

By slowing down the degradation of cyclic AMP, the PDE4 inhibitors increase or maintain cAMP levels in cells, and find use particularly in the treatment of inflammatory disorders or pathologies of tracheobronchial smooth muscle, by combining both an anti-inflammatory effect and smooth muscle relaxation.

The applicant has now demonstrated that certain benzodiazepines or benzodiazepinones have inhibitory effects on cyclic nucleotide phosphodiesterases, particularly inhibition of PDE4. The invention also describes novel compounds which show potent inhibitory activity towards PDE4, and preferentially display an excellent selectivity profile with respect to other PDE isoforms, in particular a weak action on PDE3. Moreover, the preferred compounds according to the invention possess anti-inflammatory properties that may be used in this respect to treat central or peripheral

nervous system disorders, and advantageously are devoid of hypotensive or emetic effects.

In one or more aspects the present invention may advantageously relate to compounds represented by general formula (I)



(I)

wherein :

. either X represents an NR_4 group and Y represents a CR_6R_6' group, R_4, R_6 and R_6' being defined hereinafter,

. or X represents a CR_4R_4' group and Y represents an NR_6 group, R_4, R_4' and R_6 being defined hereinafter,

. Z represents an oxygen or sulfur atom.

. R_1 is a (C_1-C_{12}) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group, (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, or an OR_2, SR_2 or NR_2R_3 group in which (i) R_2 and R_3, independently of each other, are selected in the group consisting of a hydrogen atom, a (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms or, (ii) R_2 and R_3 together form a linear or branched hydrocarbon having from 2 to 6 carbon atoms, possibly containing one or more double bonds and/or possibly interrupted by an oxygen, sulfur or nitrogen atom;

. R_4 and R_4', which are the same or different, represent a (C_3-C_6) cycloalkyl, unsubstituted (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group or a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, and, when X is the group CR_4R_4', R_4 and R_4', which are the same or different, are selected in the group

consisting of the hydrogen atom and a (C_1-C_{12}) alkyl, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, NO_2, CF_3, CN, NR'R'', SR', OR', COOR', CONR'R'' and NHCOR'R''group, R' and R'', independently of each other, being selected in the group consisting of the hydrogen atom, a (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms;

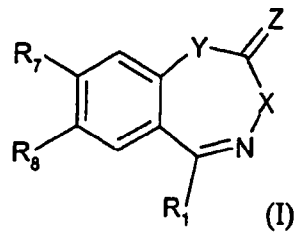
. R_6 and R_6', which are the same or different, are selected in the group consisting of the hydrogen atom, (C_1-C_6) alkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl, preferably a phenyl, benzyl group and a (C_1-C_6)alkylphenyl group;

. R_7 and R_8, independently of each other, are selected in the group consisting of the hydrogen atom, a (C_1-C_{12}) alkyl group and an OR_2 group, R_2 being defined hereinabove, with the condition that R_7 and R_8 do not both represent a hydrogen atom, or R_7 and R_8 together form a linear or branched hydrocarbon chain having from 2 to 6 carbon atoms, possibly containing one or more double bonds and/or possibly interrupted by an oxygen, sulfur or nitrogen atom;

the alkyl, alkenyl, alkynyl, alkylaryl, aralkyl, cycloalkyl, aryl, phenyl, heterocycle groups and the hydrocarbon chain defined hereinabove possibly being substituted by one or more substituents, which are the same or different, preferably selected in the group consisting of a halogen atom, a (C_1-C_{12}) alkyl, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, heterocycle, OH, =O, NO_2, NR'R'', CN, CF_3, COR', COOR', (C_1-C_6)alkoxy, (di)(C_1-C_6)alkylamino, NHCOR' and CONR'R'' group, in which R' and R'' are defined as hereinabove,

and the salts thereof.

In one aspect the present invention provides compounds represented by general formula (I)



(I)

wherein:

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X represents a CR_4R_4' group and Y represents an NR_6 group, R_4, R_4' and R_6 being defined hereinafter;

Z represents an oxygen atom;

R_1 is a (C_1-C_{12}) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-$_{12}$)alkyl(C_6-C_{18})aryl group, a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, or an OR_2, SR_2 or NR_2R_3 group in which (i) R_2 and R_3, independently of each other, are selected from the group consisting of a hydrogen atom, a (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms or, (ii) R_2 and R_3 together form a linear or branched hydrocarbon having from 2 to 6 carbon atoms, possibly containing one or more double bonds and/or possibly interrupted by an oxygen, sulfur or nitrogen atom;

R_4 and R_4', which are the same or different, represent are selected from the group consisting of the hydrogen atom and a (C_1-C_{12}) alkyl, a (C_3-C_6) cycloalkyl, unsubstituted (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group or a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, NO_2, CF_3, CN, NR'R", SR', OR', COOR', CONR'R" and NHCOR'R" group, R' and R", independently of each other, being selected from the group consisting of the hydrogen atom, a (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms;

R_6 is selected from the group consisting of the hydrogen atom, (C_1-C_6) alkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6C_{18})aryl, preferably a phenyl, benzyl group and a (C_1-C_6)alkylphenyl group;

R_7 and R_8, both represent an ethoxy group;

the alkyl, alkenyl, alkynyl, alkylaryl, aralkyl, cycloalkyl, aryl, phenyl, heterocycle groups and the hydrocarbon chain defined hereinabove possibly being substituted by one or more

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substituents, which are the same or different, selected from the group consisting of a halogen atom, a (C_1-C_{12}) alkyl, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, heterocycle, OH, =O, NO_2, NR'R", CN, CF_3, COR', COOR', (C_1-C_6)alkoxy, (di)(C_1-C_6)alkylamino, NHCOR' and CONR'R" group, in which R' and R" are defined as hereinabove,

and the salts thereof.

The invention also concerns pharmaceutical compositions comprising one or more compounds represented by general formula (I) such as defined hereinabove, and a pharmaceutically acceptable vehicle or excipient.

The invention further relates to the use of compounds represented by general formula (I) such as defined hereinabove for preparing a pharmaceutical composition designed to inhibit a cyclic nucleotide phosphodiesterase, particularly phosphodiesterase 4 (PDE4). More particularly, the invention concerns the use of the hereinabove

compounds for treating pathologies involving a deregulation of intracellular cyclic AMP levels.

In the context of the invention, the term "alkyl" designates a linear or branched hydrocarbon group advantageously containing from 1 to 12 carbon atoms, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, pentyl, neopentyl, n-hexyl, n-decyl, n-dodecyl, etc. C_1-C_4 groups are preferred. The alkyl groups may be substituted by an aryl group such as defined hereinafter, in which case it is called an arylalkyl group. Benzyl and phenethyl are specific examples of arylalkyl groups.

The term "cycloalkyl" denotes a cyclic hydrocarbon system, which may advantageously contain from 3 to 6 carbon atoms and be mono- or poly-cyclic. Examples include cyclopropyl and cyclohexyl groups in particular.

"Aryl" groups are mono-, bi- or tri-cyclic aromatic hydrocarbon systems, preferably monocyclic or bicyclic aromatic hydrocarbons containing from 6 to 18 carbon atoms, even more preferably 6 carbon atoms. Examples include phenyl, naphthyl and biphenyl groups.

"Heterocycle" groups denote hydrocarbon systems, aromatic or not, containing one or more cyclic heteroatoms. Preferably they are cyclic hydrocarbon systems containing from 5 to 18 carbon atoms and one or more cyclic heteroatoms, particularly from 1 to 3 or 4 cyclic heteroatoms chosen from among N, O and S. Preferred aromatic heterocyclic groups (heteroaryls) include in particular thienyl, benzothienyl, benzofuryl, naphthyl, pyridyl, pyrimidinyl, pyridazinyl, isoquinolinyl, morpholino, thiazolyl, furyl, pyranyl, pyrrolyl, 2*H*-pyrrolyl, imidazolyl, benzymidazolyl, pyrazolyl, isothiazolyl, isoxazolyl and indolyl groups. Among the preferred non-aromatic heterocyclic groups, piperidinyl and pyrrolidinyl groups are particular examples.

The aryl and heterocycle groups may be substituted by an OH function, an alkyl, alkenyl or alkynyl group. An aryl or a heterocycle substituted by an alkyl group is called an alkylaryl or alkylheterocycle group. Examples of alkylaryl groups include in particular tolyl, mesythyl and xylyl. An aryl or a heterocycle substituted by an alkenyl group is referred to as an alkenylaryl or alkenylheterocycle group. Examples of alkenylaryl groups include in particular the cinnamyl group. An aryl or a heterocycle substituted by an alkynyl group is called an alkynylaryl or alkynylheterocycle group.

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The aryl and heterocycle groups may also be substituted by a group independently chosen from among aryl or heterocycle groups, themselves possibly substituted by one or more substituents chosen preferably from among a halogen atom and an NO_2, CN, CF_3, OR', COR', COOR', alkoxy, NHCOR' or CONR'R'' group, R' and R'' being defined as hereinabove.

Specific examples of aryl and heterocycle groups substituted by an aryl or heterocycle group are the benzothienyl, benzofuryl, furylphenyl, benzyloxynaphthyl, pyridylphenyl, phenylphenyl and thienylphenyl groups. As noted, the hereinabove groups may be substituted. In this respect one example is the phenyl groups substituted by a phenyl group itself substituted by a halogen atom, an NO_2, CF_3, methoxy or methyl group.

"Alkenyl" groups are linear or branched hydrocarbon functions containing one or more double bonds, such as for instance the allyl group. They advantageously contain from 2 to 6 carbon atoms and, preferably, 1 or 2 double bonds. Alkenyl groups may be substituted by an aryl group such as defined hereinabove, in which case it is called an arylalkenyl group.

"Alkynyl" groups are linear or branched hydrocarbon functions containing one or more triple bonds, such as for instance the 3-(benzyloxy)prop-1-ynyl, phenylethynyl, prop-2-ynyl and tert-butyl-prop-2-ynylcarbamate groups. They advantageously contain from 2 to 6 carbon atoms and, preferably, 1 or 2 double bonds. Alkynyl groups may be substituted by an aryl group such as defined hereinabove, in which case it is called an. arylalkynyl group.

"Alkoxy" groups correspond to the alkyl and cycloalkyl groups defined hereinabove linked to the nucleus by means of an –O- (ether) bond. Methoxy and ethoxy groups are especially preferred.

"Halogen" designates a fluorine, chlorine, bromine or iodine atom.

"Heteroatom" is an atom chosen from among O, N and S.

In one or more aspects the present invention may advantageously provide compounds represented by general formula (I) hereinabove wherein X is a CR_4R_4' group and Y is an NR_6 group. Such compounds are represented by formula (II) below:

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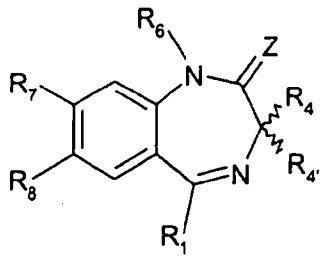
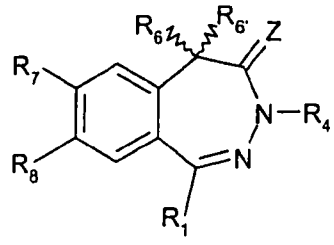


(II)

wherein R_1, R_4, $R_{4'}$, R_6, R_7 and R_8 are defined as hereinabove. Such compounds possess inhibitory properties that are especially marked and preferential for phosphodiesterase 4.

A further specific aspect of the invention relates to compounds having general formula (I) hereinabove wherein X is the NR_4 group and Y is the $CR_6R_{6'}$ group. Such compounds are represented by formula (III) below :



(III)

wherein R_1, R_4, R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove. Such compounds display especially marked and preferential inhibition of phosphodiesterase 4.

Particular compounds according to the invention are those in which :

- Z is the oxygen atom and/or
- R_7 and R_8, independently of each other, represent an OR_2 group wherein R_2 is a $(C_1$-$C_6)$alkyl group, preferably an ethyl or methyl group, and/or
- R_7 represents a hydrogen atom and R_8 represents a halogen atom or vice versa, and/or
- R_7 and R_8 each represent an ethoxy or methoxy group, and/or
- R_6 and R_6', which are the same or different, represent the hydrogen atom or a $(C_1$-$C_6)$ alkyl group, and/or
- R_6 represents the hydrogen atom or a $(C_1$-$C_6)$ alkyl group and R_6' is the hydrogen atom, and/or
- X is the CR_4R_4' group wherein R_4 and R_4', which are the same or different, represent a $(C_1$-$C_{12})$ alkyl or $(C_6$-$C_{18})$aryl$(C_1$-$C_4)$alkyl group, possibly

substituted by one or more substituents, which are the same or different, chosen from among a halogen atom and an OH, =O, NO_2, NH_2, CN, CF_3, COR', COOR', $(C_1$-$C_6)$alkoxy, (di)$(C_1$-$C_6)$alkylamino, NHCOR' or CONR'R'' group, in which R' and R'' are defined as hereinabove, and/or

- R_4' is the hydrogen atom, and/or
- X is the CR_4R_4' group in which R_4 represents a $(C_1$-$C_{12})$ alkyl or $(C_6$-$C_{18})$aryl$(C_1$-$C_4)$alkyl group, more particularly benzyl, possibly substituted by one or more substituents, which are the same or different, selected in the group consisting of a halogen atom and an OH, =O, NO_2, NH_2, CN, CF_3, COR', COOR', $(C_1$-$C_6)$alkoxy, (di)$(C_1$-$C_6)$alkylamino, NHCOR' and CONR'R'' group, in which R' and R'' are defined as hereinabove, and R_4' is the hydrogen atom, and/or
- X is the CR_4R_4· group in which R_4 and R_4' are a hydrogen atom, and/or
- R_1 is a $(C_6$-$C_{18})$ aryl group, more particularly phenyl, $(C_6$-$C_{18})$aryl$(C_1$-$C_4)$alkyl, more particularly benzyl, $(C_1$-$C_{12})$alkyl$(C_6$-$C_{18})$aryl or a $(C_5$-$C_{18})$ heterocycle, aromatic or not, containing 1 to 3 heteroatoms, possibly substituted.

A specific family of compounds is represented by compounds having general formula (II) such as defined hereinabove wherein R_4 and R_4' represent the hydrogen atom.

A specific family of compounds is represented by compounds having the general formula (II) such as defined hereinabove wherein R_7 and R_8 together form a hydrocarbon chain, such as for example the chain $-O-CH_2-CH_2-O-$.

Another family comprises compounds represented by general formula (I) wherein X is the CR_4R_4' group, Y is the NR_6 group, Z is the oxygen atom, R_7 and R_8 represent, independently of each other, an OR_2 group in which R_2 is a $(C_1$-$C_6)$ alkyl group, R_6 represents the hydrogen atom or a $(C_1$-$C_6)$ alkyl group and R_4 and R_4' represent the hydrogen atom.

Another family comprises compounds represented by general formula (I) wherein X is the CR_4R_4' group, Y is the NR_6 group, Z is the oxygen atom, R_7 represents a hydrogen atom and R_8 represents a halogen atom or vice versa.

Another family comprises compounds represented by general formula (I) wherein X is the NR_4 group, Y is the CR_6R_6' group, Z is the oxygen atom, R_7 and R_8 represent, independently of each other, an OR_2 group in which R_2 is a (C_1-C_6) alkyl group, R_6 and R'$_6$, which are the same or different, represent the hydrogen atom or a (C_1-C_6) alkyl group and R_4 represents a (C_1-C_{12}) alkyl or (C_6-C_{18})aryl(C_1-C_4)alkyl group, possibly substituted by one or more substituents, which are the same or different, chosen from among a halogen atom and an OH, =O, NO_2, NH_2, CN, CF_3, COR', COOR', (C_1-C_6)alkoxy, (di)(C_1-C_6)alkylamino, NHCOR' or CONR'R''group, in which R' and R'' are defined as hereinabove.

Another family comprises compounds having general formula (I) wherein X is the CR_4R_4' group, Y is the NR_6 group, Z is the oxygen atom, R_7 represents a hydrogen atom and R_8 represents an OR_2 function in which R_2 is a (C_1-C_6) alkyl group.

In a preferred manner, in the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove, the groups R_7 and R_8 represent, independently of each other, a methoxy or ethoxy group, more preferably they both represent a methoxy or ethoxy group.

In a preferred manner, in the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove, the R_6 and R_6' groups, which are the same or different, represent a hydrogen atom or a methyl, ethyl or n-propyl group. In an especially advantageous variant, in the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove the R_6 group represents a hydrogen atom or a methyl, ethyl or n-propyl group and the R_6' group is a hydrogen atom. In another particularly advantageous variant, in the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove, the R_6 and R_6' groups, which are the same or different, represent a methyl or ethyl group.

In the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove, preferred examples are those wherein R_4' is the hydrogen atom and, when R_4 is not the hydrogen atom, R_4 more preferably represents a methyl, ethyl, n-propyl, n-dodecyl or benzyl group.

As noted, in the compounds represented by general formula (I), (II) and (III) according to the invention and in the specific families described hereinabove, R_1 advantageously represents a (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group or a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, said group or heterocycle possibly being substituted.

According to a first variant of the invention, R_1 is a phenyl group, particularly a substituted phenyl, preferably a phenyl group substituted by :

(a) one or more halogen atoms, particularly chlorine, bromine or iodine, preferably chlorine, or

(b) one or more OR' groups, particularly methoxy or ethoxy, or

(c) a COR' group, particularly acetyl, or

(d) a trifluoromethyl group, or

(e) an alkyl or alkynyl group, for example heptinyl, or

(f) an aryl group or heterocycle, particularly a phenyl, furyl, pyridyl or thienyl group, said aryl group or heterocycle itself possibly being substituted by one or more groups chosen preferably from among groups (a)-(e).

According to another specific variant of the invention, R_1 is an aromatic heterocycle, particularly naphthyl, thienyl, furyl, indolyl or pyridyl, possibly substituted by one or more groups chosen preferably from among the groups (a)-(f) hereinabove. In a specific variant, R_1 is a naphthyl group possibly substituted by one or more groups chosen from among the groups (a)-(f) hereinabove.

According to a further specific variant of the invention, R_1 is a non-aromatic heterocycle, particularly piperidinyl or isoquinolinyl, possibly substituted by one or more groups chosen preferably from among the groups (a)-(f) hereinabove.

Specific examples of R_1 groups that are particularly advantageous for carrying out the invention are the 4-chlorophenyl, 3,4-dichlorophenyl, 2-naphthyl, 2-benzo[b]thienyl, 4-(2-furyl)phenyl, 3-pyridyl and 3-trifluoromethylphenyl groups.

The following compounds are especially preferred :

7,8-dimethoxy-1-(2-naphthyl)-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(4-chlorophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(2-benzo[b]thienyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin -4-one.
1-[4-(2-furyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(2-benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(4-chlorophenyl)-7,8-diethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
5-(4-chlorophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

Other particular compounds in the context of the invention are the following compounds :

7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(2-benzo[b]thienyl)-7,8-diethoxy-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
7,8-dimethoxy-3-methyl-1-(1-naphthyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
3-benzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin -4-one.
3-dodecyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
7,8-dimethoxy-3-(12-methoxy-12-oxododecyl)-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
3-ethyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
7,8-dimethoxy-1-phenyl-3-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-(4-iodophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
7,8-dimethoxy-1-[4-(2-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
7,8-dimethoxy-1-[4-(3-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.
1-[4-(3-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1[4-(3-pyridyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-[4-(4-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-[4-(3-acetamidophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-(4-bromophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-1-[4-(4-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-[4-[3-(trifluoromethyl)phenyl]phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1-[4-(2-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1-[4-(3-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1-[4-(4-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-[4-(4-chlorophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1-[4-(2-thienyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-{4-[3,5-bis-(trifluoromethyl)phenyl]phenyl}-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-[4-(heptyn-1-yl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-3-methyl-1-[4-(3-nitrophenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

3,5-dibenzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-1-phenyl-3-(3-hydroxypropyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one.

7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(3,4-dimethoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(2-benzo[b]thienyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(2-benzo[b]furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(2-furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(4-acetylphenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(2-thienyl)-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(3-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(2-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(5-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(6-benzyloxy-2-naphthyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(6-methoxy-2-naphthyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(2-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(piperidin-1-yl)-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(2-methylphenyl)-1,3-dihydro-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(4-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one.

5-(1,1'-biphenyl-3-yl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(4-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

8-bromo-5-(4-bromophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7-iodo-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7-methoxy-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-phenyl-1-propyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-diethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

ethyl (7,8-diethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-1-yl)acetate.

10-phenyl-2,3,6,8-tetrahydro-7H-[1,4] dioxino [2,3-h][1,4]benzodiazepin-7-one.

1-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-diethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dihydroxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(3-bromophenyl)-7,8-dimethoxy-1-methyl,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(3-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(3-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-{4-[3-(benzyloxy)prop-1-ynyl]phenyl}-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

tert-butyl 3-[4-(1-ethyl-7,8-dimethoxy-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-5-yl)phenyl]prop-2-ynyl carbamate.

5-(1,1'-biphenyl-4-yl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-5-[4-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-allyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-5-phenyl-3-prop-2-ynyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-5-[4-(2-phenylethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

ethyl (1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetate.

1-ethyl-7,8-dimethoxy-5-[3-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-(2-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetonitrile.

3-(2-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(4-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-[(3-bromophenyl)(hydroxy)methyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(3-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(1,1'-biphenyl-4-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(1-benzyl-4-hydroxypiperidin-4-yl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile.

3-benzyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-3-(2-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide.

3-[3-(aminomethyl)benzyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(1,1'-biphenyl-3-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-benzyl-7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

2-(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetamide.

3-(2-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-3-(2-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

8-ethoxy-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-5-phenyl-3-[3-(trifluoromethyl)benzyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-3-(3-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

1-ethyl-7,8-dimethoxy-3-(4-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-[1,2-bis(4-bromophenyl)ethyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile.

2-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile.

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide.

8-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

8-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(4-fluorophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(4-pyridyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(3, 5 bis trifluoromethylphenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-5-(4-N,N-dimethylaminophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-[(E)-2-phenylethenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(2-phenylethynyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(N-tetrahydro-1,2,3,4-isoquinolyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-isobutyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-(1H-imidazol-4-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-(1H-indol-3-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-(2-methylthioethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

(S) 3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

(S)-3-benzyl-7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-methyl-5-(2-phenylethyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

(7,8-dimethoxy-5-phenyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl(S)-butylcarbamate.

(S)-3-(4-aminobutyl)-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

(S)-N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]acetamide.

N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]guanidinium(S)-bis trifluoroacetate.

7,8-dimethoxy-1-ethyl-3-(2-nitrobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(3,5-dibromobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-3-(diphenylhydroxymethyl)-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-ethyl-3-(E-3-phenylpropen-2yl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-ethyl-3-(2-aminobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

7,8-dimethoxy-1-(2-hydroxyethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(2-cyanobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]acetamide.

3-(2-aminomethylbenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

[(7,8-dimethoxy-1-ethyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benz-2-yl]carboxamide.

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]methylacetamide.

7,8-dimethoxy-3,5-diphenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(2,4-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-(2,5-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3,5-diphenyl-8-ethoxy-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-benzyl-8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3-benzyl-8-ethoxy-1-ethyl-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

3,5-diphenyl-8-ethoxy-1-ethyl-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

5-phenyl-7-ethoxy-8-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one.

The compounds according to the invention may be in the form of salts, particularly acid or base salts, preferably compatible with pharmaceutical use. Among the pharmaceutically acceptable acids, non-limiting examples include hydrochloric, hydrobromic, sulfuric, phosphoric, acetic, trifluoroacetic, lactic, pyruvic, malonic, succinic, glutaric, fumaric, tartric, maleic, citric, ascorbic, methane or ethane sulfonic, camphoric acids, etc. Among the pharmaceutically acceptable bases, non-limiting examples include sodium hydroxide, potassium hydroxide, triethylamine, *tert*-butylamine, etc.

In one or more aspects the present invention may advantageously provide a composition comprising a compound such as defined hereinabove and a pharmaceutically acceptable vehicle or excipient.

The compounds or compositions of the invention may be administered in different ways and in different forms. For instance, they may be administered systemically, by the oral route, by inhalation or by injection, such as for example by the intravenous, intramuscular, subcutaneous, transdermal, intra-arterial route, etc., the

intravenous, intramuscular, subcutaneous, oral and inhalation routes being preferred. For injections, the compounds are generally prepared in the form of liquid suspensions, which may be injected through syringes or by infusion, for instance. In this respect, the compounds are generally dissolved in pharmaceutically compatible saline, physiologic, isotonic, buffered solutions, and the like, known to those skilled in the art. For instance, the compositions may contain one or more agents or vehicles chosen from among dispersives, solubilizers, stabilizers, preservatives, and the like. Agents or vehicles that may be used in the liquid and/or injectable formulations comprise in particular methylcellulose, hydroxymethylcellulose, carboxymethylcellulose, polysorbate 80, mannitol, gelatin, lactose, vegetable oils, acacia, and the like.

The compounds may also be administered in the form of gels, oils, tablets, suppositories, powders, capsules, gelules, aerosols, and the like, possibly by means of pharmaceutical forms or devices allowing extended and/or delayed release. For this type of formulation, an agent such as cellulose, carbonates or starches is advantageously used.

It is understood that the injection rate and/or injected dose may be adapted by those skilled in the art according to the patient, the pathology, the mode of administration, etc. Typically, the compounds are administered at doses ranging from 0.1 μg to 100 mg/kg of body weight, more generally from 0.01 to 10 mg/kg, typically between 0.1 and 10 mg/kg. Furthermore, repeated injections may be given, as the case may be. In addition, in the case of chronic treatments delayed or sustained release systems may be advantageous.

The compounds according to the invention may act on different cyclic nucleotide phosphodiesterases, particularly PDE4, and may also be active on certain PDE subtypes. For instance, four subtypes of PDE4 have been identified, named PDE4A-D. The compounds according to the invention may display specific biological properties according to the PDE4 subtype affected. Thus, the inventive compounds may be (selective) inhibitors of PDE-4A, PDE-4B, PDE-4C and/or PDE-4D. The compounds of the invention which inhibit PDE-4B are especially interesting for treating the inflammatory component of depression, psychiatric disorders or obesity, for example.

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The PDE4 inhibitor compounds according to the invention are of particular interest for treating pathologies involving bronchial inflammation and relaxation, and more particularly asthma and chronic obstructive pulmonary disease, but also other pathologies such as rhinitis, acute respiratory distress syndrome, allergy, skin disorders, such as dermatitis, psoriasis, rheumatoid arthritis, autoimmune diseases, different forms of sclerosis (particularly multiple sclerosis), dyskinesias, glomerulonephritis, osteoarthritis, cancer, septic shock, AIDS or obesity.

The compounds of the invention are also of particular interest for treating inflammatory disorders of the central nervous system, such as, more specifically, for treating an inflammatory disorder chosen from among depression, schizophrenia, bipolar disorder, attention deficit disorder, fibromyalgia, epilepsy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, and Lewy body dementia.

The invention also finds use for treating inflammatory disorders such as Crohn's disease.

In one or more aspects the present invention may advantageously provide the use of the compounds such as described hereinabove for preparing a medicament for treating inflammatory disorders of the nervous system, particularly central, which are chronic or acute.

In other aspects the present invention relates to the use of the compounds such as described hereinabove for preparing a medicament for treating inflammatory disorders of the central nervous system (e.g., neuroinflammation).

In the context of the invention, the term treatment denotes either a preventive or a curative treatment, which may be used alone or in combination with other agents or treatments. Moreover, it may be a treatment of chronic or acute disorders.

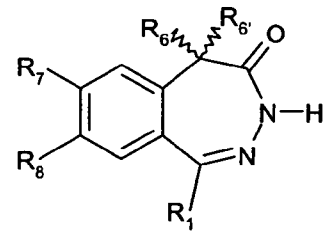
In other aspects the present invention relates to the use of the described compounds as anti-inflammatory agents, for instance for treating osteoporosis or rheumatoid arthritis.

The preferred compounds of the invention advantageously display potent inhibitory activity towards one or more PDE4 subtypes. The preferred compounds of the invention further display an advantageous selectivity profile, particularly weak activity with respect to PDE3.

The compounds of the invention may be prepared from commercially available products, by using a combination of chemical reactions known to those skilled in the art.

Figures 1 and 2 depict the synthetic reaction routes of compounds represented by formula (I).

In this respect, according to a first method, the compounds represented by general formula (III) according to the invention wherein Z is an oxygen atom may be obtained from a compound represented by formula (VI)

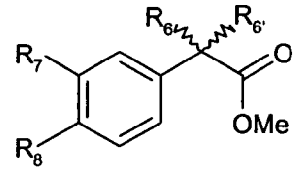


(VI)

wherein R_1 R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove, by reaction with an alkyl halogenide in the presence of potassium carbonate at room temperature. Preferably, the reaction is carried out in a polar aprotic solvent, DMF for example.

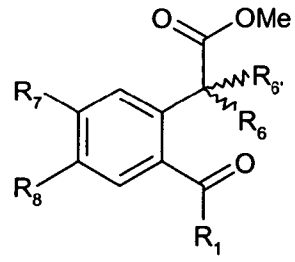
The compounds represented by general formula (VI) may be prepared by a method comprising the following steps :

a) reacting a compound represented by general formula (IV)



(IV)

wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove, with a compound containing an acyl group having the formula R_1CO so as to obtain a compound represented by formula (V)



(V)

wherein R_1, R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove;

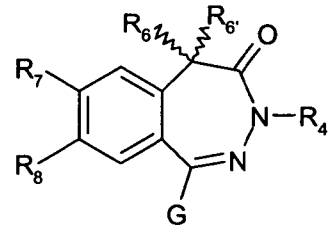
b) reacting a compound represented by formula (V) with hydrazine so as to obtain a compound represented by formula (VI) wherien R_1, R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove.

The acylating agent in step a) is preferably an acyl halogenide, particularly an acyl chloride. The reaction is advantageously carried out in the presence of a Lewis acid such as $SnCl_4$, in an inert solvent at room temperature. Solvents may be exemplified by hydrocarbons and their halogenated derivatives, for instance $CHCl_3$. When the reaction is complete, the resulting product is taken up in alcohol, methanol for example, and the reaction is continued at room temperature.

Step b) is advantageously carried out in the presence of hydrazine hydrate, for example in an alcohol, at a temperature comprised between 100 and 150°C, preferably at around 150°C, in a sealed tube for a time period ranging from 3 to 10 hours, preferably approximately 3 hours, and continued in the presence of an acid, for example acetic acid under ethanol reflux for 20 to 60 minutes.

The compounds represented by general formula (III) according to the invention may also be obtained directly from a compound represented by general formula (V) such as defined hereinabove, by reaction in the presence of a substituted hydrazine, for example methylhydrazine. Such reaction is advantageously carried out in an alcohol, ethanol for example, at a temperature comprised between 100 and 150°C, preferably at around 150°C, in a sealed tube for a time period ranging from 3 to 10 hours, preferably approximately 3 hours, and continued in the presence of an acid, for example acetic acid under ethanol reflux for 20 to 60 minutes.

In another embodiment, the compounds represented by general formula (III) according to the invention in which Z is an oxygen atom may be prepared from a compound represented by general formula (XIV)



(XIV)

wherein R_4 R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove and G is an activator group such as a halogen (Cl or Br for example) or an O-triflate group, by a palladium coupling reaction in the presence of boronic, alcyn-1-yl acid or ester or organometallic acid or ester such as organozincics or organostannans. When G is a halogen atom, compound (III) may also be prepared by a substitution reaction in the presence of a nucleophilic agent, such as an amine for example, in ethanol.

The compounds represented by general formula (XIV) may be obtained by a method comprising :

. reacting a compound represented by general formula (VII) as illustrated in Figure 1 wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove in the presence of paraformaldehyde, preferably by heating in acidic medium, to give a compound represented by general formula (VIII) such as illustrated in Figure 1;

. reacting a compound represented by general formula (VIII) in the presence of $KMnO_4$, followed by heating in an alcohol, to give a compound represented by general formula (IX) such as illustrated in Figure 1 wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove;

. heating under reflux the compound represented by general formula (IX) in acetyl chloride to give a compound represented by general formula (X) such as illustrated in Figure 1 wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove;

. reacting a compound represented by general formula (X) in the presence of hydrazine hydrate, preferably in ethanol, to give a compound represented by general formula (XI) such as illustrated in Figure 1 wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove;

. reacting a compound represented by general formula (XI) in the presence of AcOH at a temperature comprised between 50 and 150°C to give a compound represented by general formula (XII) such as illustrated in Figure 1 wherein R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove;

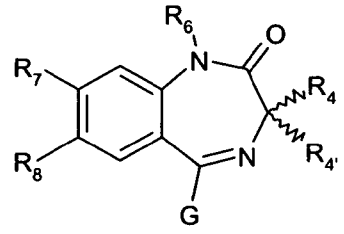
. reacting a compound represented by general formula (XII) in the presence of potassium carbonate and methyl iodide, preferably at room temperature in a solvent of the DMF type, to give a compound represented by general formula (XIII) such as illustrated in Figure 1 wherein R_4, R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove; and

. reacting a compound represented by general formula (XIII) in the presence of dimethylaniline and phosphorus oxyhalogenide (for example $POCl_3$ or $POBr_3$), at a temperature comprised between 80 and 150°C, preferably in anhydrous $CHCl_3$ medium, to give a compound represented by general formula (XIV) such as illustrated in Figure 1 wherein R_4, R_6, $R_{6'}$, R_7, R_8 and G are defined as hereinabove; or

. reacting a compound represented by general formula (XIII) with triflic anhydride in the presence of a base, for example n-BuLi in an anhydrous aprotic organic solvent, to give a compound represented by general formula (XIV) such as illustrated in Figure 1 wherein R_4, R_6, $R_{6'}$, R_7 and R_8 are defined as hereinabove and G is a triflate group.

The compounds represented by formula (III) in which Z is a sulfur atom are obtained from compounds having formula (III) in which Z is an oxygen atom by reaction with Lawesson reagent in toluene under reflux.

The compounds represented by general formula (II) according to the invention in which Z is an oxygen atom may be prepared from a compound represented by general formula (XVIII) :

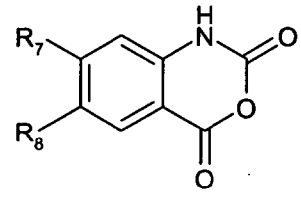


(XVIII)

wherein R_4, $R_{4'}$, R_6, R_7, R_8 and G are defined as hereinabove, by reacting with an acid compound of group R_1 in the presence of a palladium catalyst, such as illustrated in Figure 2. The reaction is advantageously carried out in a solvent of the type DMF at a temperature comprised between 80 and 150°C.

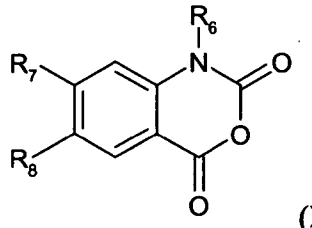
The compounds represented by general formula (XVIII) may be obtained by a method such as illustrated in Figure 2 and comprising :

. reacting a compound represented by general formula (XV) wherein R_7 and R_8 are defined as hereinabove :



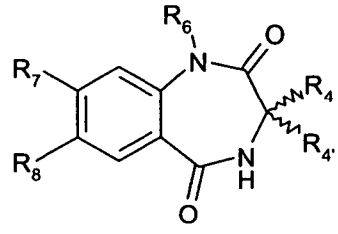
(XV)

in the presence of an alkyl halogenide, preferably in a solvent of the DMF type in the presence of NaH, to form a compound represented by general formula (XVI) wherein R_6 R_7 and R_8 are defined as hereinabove,



(XVI)

. heating under reflux the compound represented by general formula (XVI) in the presence of α-aminoacid ester hydrochloride and pyridine, followed by cycle formation in acidic medium, for example in the presence of acetic acid, at a temperature comprised between 100 and 150°C, to form a compound represented by general formula (XVII) wherein R_4, $R_{4'}$, R_6, R_7 and R_8 are defined as hereinabove,

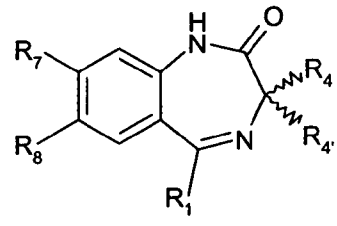


(XVII)

. reacting the compound represented by general formula (XVII) in the presence of dimethylaniline (or dimethylaminopyridine) and phosphorus oxyhalogenide (preferably $POCl_3$ or $POBr_3$), preferably at a temperature comprised between 80 and 150°C in anhydrous $CHCl_3$ medium and in a sealed tube, to form a compound represented by general formula (XVIII) wherein R_4, $R_{4'}$, R_6, R_7 and R_8 are defined as hereinabove and G is Cl or Br.

The compounds represented by formula (II) in which Z is a sulfur atom may be obtained from compounds represented by formula (II) in which Z is an oxygen atom by reaction with Lawesson reagent in toluene under reflux.

The compounds represented by general formula (II) according to the invention in which Z is an oxygen atom may also be prepared from a compound represented by general formula (XXII) :

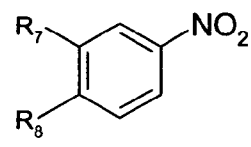


(XXII)

wherein R_1, $R_{4'}$, R_7, R_8, are defined as hereinabove, by reaction with an alkyl halogenide, preferably in a solvent of the type DMF or THF in the presence of a base, of the type NaH or K_2CO_3, preferably at room temperature (18-25°C).

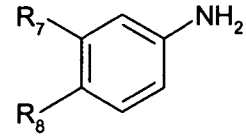
The compounds represented by general formula (XXII) may be obtained by a method comprising :

. reacting a compound represented by general formula (XIX) in which R_7 and R_8 are defined as hereinabove:



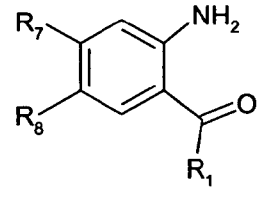
(XIX)

in the presence of hydrogen and a palladium catalyst in methanol to form a compound represented by general formula (XX) wherein R_7 and R_8 are defined as hereinabove,



(XX)

heating under reflux the compound represented by general formula (XX) in the presence of Lewis acids, of the type BCl_3, $AlCl_3$, and a nitrile having general formula R_1-CN, in a halogenated solvent ($C_2H_4Cl_2$, $CHCl_3$), to form a compound represented by general formula (XXI) wherein R_1, $R_{7'}$, R_8, are defined as hereinabove,



(XXI)

. heating under reflux the compound represented by general formula (XXI), in the presence of a amino–acid ester hydrochloride substituted or not on the a carbon and which may be a racemic mixture or a pure enantiomer, and pyridine at a temperature comprised between 100 and 150°C to form a compound represented by general formula (XXII) wherein R_1, $R_{4'}$, R_7, R_8 are defined as hereinabove (the molecules XXI and XXII were obtained by the method described in the reference : Yves Pascal, Charles R. Andrianjara, Eric Auclair, Nadine Avenel, Bernadette Bertin, Alain Calvet, Frederic Feru, Sophie Lardon, Indres Moodley, Malika Ouagued, Adrian Payne, Marie Pierre Pruniaux, and Corinne Szilagyi, *Bioorganic and Medicinal Chemistry Letters*, 2000, 10, 35-38).

The invention is illustrated by the following examples, which are given for purposes of illustration and not by way of limitation. Figures 1 and 2 depict the synthetic routes of the inventive compounds.

EXAMPLE 1 : SYNTHESIS OF COMPOUNDS REPRESENTED BY FORMULA III ACCORDING TO THE INVENTION BY A FIRST ROUTE

1.1. Synthesis of intermediates represented by formula V

The following compounds were synthesized :

4,5-dimethoxy-2-(1-naphthoyl)phenyl methyl acetate, **Vaa**.
2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl methyl acetate, **Vab**.
2-benzoyl-4,5-dimethoxyphenyl methyl acetate, **Vac**.
2-(4-iodobenzoyl)-4,5-dimethoxyphenyl methyl acetate, **Vad**.
2-(4-bromobenzoyl)-4,5-dimethoxyphenyl methyl aceetate, **Vae**.
2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl ethyl acetate, **Vaf**.
2-[2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl]ethyl valerate, **Vag**.
2-[2-(2-benzo[b]thienyl)carbonyl]-4,5-diethoxypeenyl]ethyl butyrate, **Vah**.
2-[2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl]-2,2-dimethyl methyl acetate, **Vai**.

4,5-dimethoxy-2-(1-naphthoyl)phenyl methyl acetate, Vaa.

To a solution of 315 mg (1.5 mmol) of 3,4-dimethoxyphenyl methyl acetate in 5 ml of anhydrous $CHCl_3$, add at 0°C and under an inert atmosphere 452 µl (3 mmol) of 1-naphthoyl chloride. Add dropwise 351 µl of $SnCl_4$. Allow to return to room temperature. After 6 hours at room temperature, evaporate to dryness. Add 10 ml of MeOH. Stir at room temperature for 30 minutes. Evaporate to dryness. Add 7 ml of iced H_2O. Allow to crystallize at 0°C for 1 hour. Filter. Wash twice with 1 ml of H_2O. Yield : 37 %. The product is used as is for the subsequent reactions.

2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl methyl acetate, Vab.

By replacing 1-naphthoyl chloride in example **Vaa** by 2-benzo[b]thiophene carbonyl chloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 58 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.63 (s, 3H, OCH_3), 3.88 (s, 2H, CH_2), 3.91 (s,

3H, OCH_3), 4.02 (s, 3H, OCH_3), 6.92 (s, 1**H Ar**), 7.26 (s, 1**H Ar**), 7.41-7.54 (m, 2**H Ar**), 7.81 (s, 1**H Ar**), 7.88-7.98 (m, 2**H Ar**).

2-benzoyl-4,5-dimethoxyphenyl methyl acetate, Vac.

By replacing 1-naphthoyl chloride in example **Vaa** by benzoyl chloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 85 %.

2-(4-iodobenzoyl)-4,5-dimethoxyphenyl methyl aceetate, Vad.

By replacing 1-naphthoyl chloride in example **Vaa** by 4-iodobenzoyl chloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 67 %.

2-(4-bromobenzoyl)-4,5-dimethoxyphenyl methyl acetate, Vae.

By replacing 1-naphthoyl chloride in example **Vaa** by 4-bromobenzoyl chloride and proceeding in the same manner, the abovenamed product is obtained. Yield: 10 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ 3.62 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 3.85 (s, 2H, CH_2), 3.97 (s, 3H, CH_3), 6.85 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.60-7.69 (m, 4**H Ar**).

2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl ethyl acetate, Vaf.

By replacing 3,4-dimethoxyphenyl methyl acetate in example **Vab** by 3,4-diethoxyphenyl ethyl acetate and proceeding in the same manner, the abovenamed product is obtained. Yield : 71 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.12 (t, J = 7,1, 3H, CH_3), 1.41-1.55 (m, 6H, 2 x CH_3), 3.60 (s, 2H, CH_2CO), 4.00-4.26 (m, 6H, 3 x CH_2), 6.89 (s, 1**H Ar**), 7.24 (s, 1**H Ar**), 7.41-7.53 (m, 2**H Ar**), 7.77 (s, 1**H Ar**), 7.85-7.94 (m, 2**H Ar**).

2-[2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl]ethyl valerate, Vag.

By replacing 3,4-dimethoxyphenyl methyl acetate in example **Vab** by 2-(3,4-diethoxyphenyl) ethyl valerate and proceeding in the same manner, the abovenamed product is obtained. Yield : 61 %.

2-[2-(2-benzo[b]thienyl)carbonyl]-4,5-diethoxyphenyl] ethyl butyrate, Vah.

By replacing 3,4-dimethoxyphenyl methyl acetate in example **Vab** by 2-(3,4-diethoxyphenyl)ethyl butyrate and proceeding in the same manner, the abovenamed product is obtained. Yield : 46 %.

2-[2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl]-2,2-dimethyl methyl acetate, Vai.

By replacing 3,4-dimethoxyphenyl methyl acetate in example **Vab** by 2-(3,4-dimethoxyphenyl)-2,2-dimethyl methyl acetate and proceeding in the same manner, the abovenamed product is obtained. Yield : 43 %.

1.2. Synthesis of compounds represented by formula VI

The following compounds were synthesized :

7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **VIaa**.
1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **VIab**.
1-(2-benzo[b]thienyl)-7,8-diethoxy-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **VIac**.
1-(benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **VIad**.
1-(2-benzo[b]thienyl)-7,8-dimethoxy-5,5-dimethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **VIae**.

7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, VIaa.

Heat 500 mg (1.59 mmol) of 2-benzoyl-4,5-dimethoxyphenyl methyl acetate **Vac**, 2 ml of hydrazine hydrate and 12 ml of EtOH in a sealed tube at 150°C for 3 hours. Cool to room temperature. Add 10 ml of AcOH. Heat under reflux for 25 minutes. Evaporate to dryness. Add 60 ml of iced H_2O. Allow to crystallize at 0°C for 5 minutes. Filter and wash twice with 5 ml of H_2O, twice with 3 ml of EtOH and twice with 5 ml of pentane. Recrystallize in EtOH/Et_2O. Yield : 82 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 3.51 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.67 (s, 1**H Ar**), 6.86 (s, 1**H Ar**), 7.43-7.48 (m, 3**H Ar**), 7.62-7.65 (m, 2**H Ar**), 8.66 (broad s, 1H exchangeable, N**H**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, VIab.

By replacing 2-benzoyl-4,5-dimethoxyphenyl methyl acetate **Vac** in example **VIaa** by 2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl ethyl acetate **Vaf** and proceeding in the same manner, the abovenamed product is obtained. Yield : 47 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.46 (t, J = 7.1, 3H, CH_3), 1.56 (t, J = 7.1, 3H, CH_3), 3.53 (s, 2H, CH_2CO), 4.07 (q, J = 6.92, 2H, CH_2), 4.23 (q, J = 6.92, 2H, CH_2), 6.89 (s, 1**H Ar**), 7.17 (s, 1**H Ar**), 7.39-7.48 (m, 3**H Ar**), 7.75-7.92 (m, 2**H Ar**), 8.40 (s, 1 exchangeable, N**H**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, VIac.

By replacing 2-benzoyl-4,5-dimethoxyphenyl methyl acetate **Vac** in example **VIaa** by 2-[2-(2-benzo[b]thienylcarbonyl)-4,5-diethoxyphenyl]ethyl valerate **Vag** and proceeding in the same manner, the abovenamed product is obtained. 0.84-1.58 (m, 11H, 3 x CH_3 and CH_2), 1.84-2.40 (m, 2H, $CHCH_2$), 3.09-3.16 (m, 1H, C**H**), 4.03-4.25 (m, 4H, 2 x CH_2), 6.77-6.84 (m, 1**H Ar**), 7.14 (s, 1**H Ar**), 7.34-7.46 (m, 3**H Ar**), 7.72-7.90 (m, 2**H Ar**), 8.46-8.54 (m, 1H exchangeable, N**H**).

1-(benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, VIad.

By replacing 2-benzoyl-4,5-dimethoxyphenyl methyl acetate **Vac** in example **VIaa** by 2-[2-(2-benzo[b]thienyl)carbonyl]-4,5-diethoxyphenyl] ethyl butyrate **Vah** and proceeding in the same manner, the abovenamed product is obtained. Yield : 23 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ 1.11 (t, J = 6.21, 3H, CH_3), 1.40-1.46 (m, 3H, CH_3), 1.53 (t, J = 7.92, 3H, CH_3), 1.96-2.43 (m, 2H, CH_2), 3.02-3.07 (t, J = 6.01, 1H, **5-H**), 4.04-4.24 (m, 4H, 2 x CH_2), 6.83 (s, 1**H Ar**), 7.15 (s, 1**H Ar**), 7.35-7.90 (m, 5**H Ar**), 8.39 (s, 1H exchangeable, N**H**).

1-(2-benzo[b]thienyl)-7,8-dimethoxy-5,5-dimethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, VIae.

By replacing 2-benzoyl-4,5-dimethoxyphenyl methyl acetate **Vac** in example **VIaa** by 2-[2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl]-2,2-dimethyl methyl acetate **Vai** and proceeding in the same manner, the abovenamed product is obtained. Yield : 7 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ 1.36 (s, 3H, 5-CH_3), 1.79 (s, 3H, 5-CH_3), 3.83 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.03 (s, 1**H Ar**), 7.17 (s, 1**H Ar**), 7.35-7.44 (m, 3**H Ar**), 7.73-7.89 (m, 2**H Ar**), 8.39 (s, 1H exchangeable, N**H**).

1.3. Synthesis of compounds represented by formula III

The following compounds were synthesized :

7,8-dimethoxy-3-methyl-1-(1-naphthyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaa**.

1-(2-benzo[b]thienyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIab**.

3-benzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIac**.

3-dodecyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIad**.

7,8-dimethoxy-3-(12-methoxy-12-oxododecyl)-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIae**.

7,8-dimethoxy-1-phenyl-3-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaf**.

3-ethyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIag**.

1-(4-iodophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIah**.

7,8-dimethoxy-1-[4-(2-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIai**.

7,8-dimethoxy-1-[4-(3-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaj**.

1-[4-(3-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIak**.

1-[4-(4-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIal**.

1-[4-(3-acetamidophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIam**.

1-(4-bromophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIan**.

7,8-dimethoxy-1-[4-(4-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIao**.

1-[4-[3-(trifluoromethyl)phenyl]phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIap**.

7,8-dimethoxy-3-methyl-1-[4-(2-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaq**.

7,8-dimethoxy-3-methyl-1-[4-(3-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIar**.

7,8-dimethoxy-3-methyl-1-[4-(4-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIas**.

1-[4-(4-chlorophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIat**.

7,8-dimethoxy-3-methyl-1-[4-(2-thienyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIau**.

1-[4-(2-furyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIav**.

1-{4-[3,5-bis-(trifluoromethyl)phenyl]phenyl}-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaw**.

1-[4-(heptyn-1-yl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIax**.

7,8-dimethoxy-3-methyl-1-[4-(3-nitrophenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIay**.

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIaz**.

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIba**.

1-(2-benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIbb**.

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIbc**.

3,5-dibenzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIbd**.

7,8-dimethoxy-1-phenyl-3-(3-hydroxypropyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, **IIIbe**.

7,8-dimethoxy-3-methyl-1-(1-naphthyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaa.

Heat 150 mg (0.41 mmol) of 4,5-dimethoxy-2-(1-naphthoyl)phenyl methyl acetate **Vaa**, 200 µl of methylhydrazine and 12 ml of EtOH in a sealed tube at 150°C for 3 hours. Allow to cool to room temperature. Add 1 ml of AcOH. Heat under reflux for 25 minutes. Evaporate to dryness. Add 5 ml of iced H_2O. Allow to crystallize at 0°C for 5 minutes. Filter and wash twice with 1 ml of H_2O, twice with 0.5 ml of EtOH and twice with 3 ml of pentane. Recrystallize in EtOH/Et_2O. Yield : 31 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.53 (s, 3H, CH_3), 3.57 (s, 3H, CH_3), 3.72 (s, 2H, CH_2), 4.00 (s, 3H, CH_3), 6.41 (s, 1H **Ar**), 6.95 (s, 1H **Ar**), 7.40-7.65 (m, 4H **Ar**), 7.78-7.82 (m, 1H **Ar**), 7.92-8.03 (m, 2H **Ar**).

1-(2-benzo[b]thienyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIab.

By replacing 4,5-dimethoxy-2-(1-naphthoyl)phenyl methyl acetate **Vaa** in example **IIIaa** by 2-(2-benzo[b]thienylcarbonyl)-4,5-dimethoxyphenyl methyl acetate **Vab** and proceeding in the same manner, the abovenamed product is obtained. Yield : 69 %. M : 112-115°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.44 (s, 3H, CH_3), 3.52 (s, 2H, CH_2), 3.86 (s, 3H, CH_3), 3.99 (s, 3H, CH_3), 6.89 (s, 1H **Ar**), 7.13 (s, 1H **Ar**), 7.37-7.44 (m, 3H **Ar**), 7.74-7.89 (m, 2H **Ar**).

3-benzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIac.

To a solution of 7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIaa** (100 mg, 0.34 mmol) in DMF (5 ml), under an inert atmosphere, add NaH in oil (12 mg, 0.30 mmol). Then add dropwise benzyl bromide (40 µl, 0.34 mmol). After 2 hours at room temperature, evaporate the DMF. Take up the residue in CH_2Cl_2, wash twice with water. Dry the organic phases on Na_2SO_4. Purify by silica gel column chromatography (AcOEt/hexane, 4:1). Yield : 71 %. M : 114-116°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.53-3.64 (m, 2H, CH_2), 3.73 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.93-5.32 (d, 2H, NCH_2Ph), 6.63 (s, 1H, **Ar**), 6.92 (s, 1H, **Ar**), 7.20-7.59 (m, 10H, **Ar**).

3-*n*-dodecyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIad.

By replacing benzyl bromide in example **IIIac** by *n*-dodecyl bromide and proceeding in the same manner, the abovenamed product is obtained in the form of a colorless oil. Yield : 46 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 0.88 (t, J = 4.5, 3H, CH_3), 1.25 (m, 18H, 9 x CH_2), 1.65 (m, 2H, NCH_2CH_2), 3.43 (m, 2H, NCH_2), 3.73 (s, 3H, OCH_3), 3.80 (broad s, 2H, CH_2), 3.97 (s, 3H, OCH_3), 6.67 (s, 1H, **Ar**), 6.88 (s, 1H, **Ar**), 7.44 (m, 3H, **Ar**), 7.66 (m, 2H, **Ar**).

7,8-dimethoxy-3-(12-methoxy-12-oxododecyl)-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIae.

By replacing benzyl bromide in example **IIIac** by methyl 12-bromododecanoate and proceeding in the same manner, the abovenamed product is obtained as a colorless oil.

Yield : 99 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 1.20 (m, 14H, 7 x CH_2), 1.56-1.64 (m, 4H, 2 x CH_2), 2.27 (t, J = 7.1, CH_2COO), 3.47 (broad m, 2H, NCH_2), 3.64 (s, 3H, $COOCH_3$), 3.70 (s, 3H, OCH_3), 3.75 (broad s, 2H, CH_2), 3.94 (s, 3H, OCH_3), 6.65 (s, 1H, **Ar**), 6.86 (s, 1H, **Ar**), 7.42 (m, 3H, **Ar**), 7.64 (m, 2H, **Ar**).

7,8-dimethoxy-1-phenyl-3-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaf.

Add dropwise under an inert atmosphere 400 µl of iodopropane to a solution of 200 mg (0.675 mmol) of 7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIaa** and 121 mg (0.878 mmol) of K_2CO_3 in solution in 5 ml of DMF. After 72 hours at room temperature, add 30 ml of H_2O and extract three times with 30 ml of Et_2O. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt 1/hexane 1). Yield : 72 %. M : 48-52°C. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 0.83 (t, J = 7.34, 3H, CH_3), 1.65-1.72 (m, 2H, CH_2CH_3), 2.85-3.62 (m, 4H, $CH_2CH_2CH_3$ + 5-CH_2), 3.74 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 6.67 (s, 1H **Ar**), 6.89 (s, 1H **Ar**), 7.43-7.47 (m, 3H **Ar**), 7.65-7.68 (m, 2H **Ar**).

3-ethyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIag.

By replacing iodopropane in example **IIIaf** by iodoethane and proceeding in the same manner, the abovenamed product is obtained. Yield : 84 %. M : 123-126°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.29 (t, J = 7.08, 3H, CH_3), 3.25-3.70 (m, 5H, 5-CH_2 + OCH_3), 2.90-4.00 (m, 5H, CH_2CH_3 + OCH_3), 6.71 (s, 1H **Ar**), 6.91 (s, 1H **Ar**), 7.46-7.51 (m, 3H **Ar**), 7.68-7.71 (m, 2H **Ar**).

1-(4-iodophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIah.

By replacing 4,5-dimethoxy-2-(1-naphthoyl)phenyl methyl acetate **Vaa** in example **IIIaa** by 2-(4-iodobenzoyl)-4,5-dimethoxyphenyl methyl acetate **Vad** and proceeding in the same manner, the abovenamed product is obtained. Yield : 32 %. M : 158-160°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.40-3.48 (s, 5H, CH_3 + CH_2), 3.75 (s, 3H, CH_3), 3.97

(s, 3H, CH_3), 6.64 (s, 1**H Ar**), 6.87 (s, 1**H Ar**), 7.59 (AB system, ? d = 0.38, J_{AB} = 8.80, 4**H Ar**).

7,8-dimethoxy-1-[4-(2-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIai.

Heat at 90°C for 12 hours under an inert atmosphere a mixture of 100 mg (0.229 mmol) of 1-(4-iodophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **IIIah**, 38 mg (0.25 mmol) of 2-methoxybenzene boronic acid, 215 µl of 2M Na_2CO_3, 25 mg (0.020 mmol) of *tetrakis* (triphenylphosphine) Pd (0) and 250 µl of EtOH in 5 ml of degassed toluene. Allow to cool to room temperature. Add 80 ml of H_2O and extract three times with 50 ml of Et_2O. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt). Recrystallize in Et_2O/pentane. The reaction yields 70 mg of the abovenamed product in the form of colorless crystals. Yield : 73 %. M : 185-186°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.78 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.80 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.04-7.73 (m, 8**H Ar**).

7,8-dimethoxy-1-[4-(3-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaj.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3-methoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 68 %. M : 92-99°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.41-3.50 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 4.12 (s, 3H, CH_3), 6.75 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 6.94-7.75 (m, 8**H Ar**).

1-[4-(3-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIak.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3-acetylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 76 %. M : 147-149°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.69 (s, 3H, CH_3CO),

3.43-3.53 (m, 5H, CH_2 + CH_3), 3.77 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.73 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.59-8.27 (m, 8**H Ar**).

1-[4-(4-acetylphenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIal.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 4-acetylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 68 %. M : 199-201°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.67 (s, 3H, CH_3CO), 3.43-3.54 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.73 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.70-7.80 (m, 6**H Ar**), 8.06-8.09 (m, 2**H Ar**).

1-[4-(3-acetamidophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4H-2,3-benzodiazepin-4-one, IIIam.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 4-acetamidobenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 61 %. MF : 244-246°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.23 (s, 3H, CH_3CO), 3.43-3.53 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.73 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.40-7.74 (m, 8**H Ar**), 7.90 (broad s, 1H exchangeable, N**H**).

1-(4-bromophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIan.

By replacing 2-(4-iodobenzoyl)-4,5-dimethoxyphenyl methyl acetate **Vad** in example **IIIah** by 2-(4-bromobenzoyl)-4,5-dimethoxyphenyl methyl acetate **Vae** and proceeding in the same manner, the abovenamed product is obtained. Yield : 37 %. M : 145-147 °C. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 3.40-3.49 (s, 5H, CH_3 + CH_2), 3.75 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.64 (s, 1**H Ar**), 6.87 (s, 1**H Ar**), 7.56 (AB system, ? d = 0.16, J_{AB} = 8.30, 4**H Ar**).

7,8-dimethoxy-1-[4-(4-methoxyphenyl)phenyl]-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIao.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 4-methoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 81 %. M : 222-224°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.41-3.50 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.88 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.75 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.37 (AB system, ? d = 0.67, J_{AB} = 8.7, 4**H Ar**), 7.59-7.65 (m, 4**H Ar**).

1-[4-[3-(trifluoromethyl)phenyl]phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIap.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3-trifluoromethylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 72 %. M : 100-103°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.43-3.53 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.73 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.52-7.89 (m, 8**H Ar**).

7,8-dimethoxy-3-methyl-1-[4-(2-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaq.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 2-methylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 84 %. M : 184-186°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.31 (s, 3H, PhCH_3), 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.78 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.78 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.28-7.73 (m, 8**H Ar**).

7,8-dimethoxy-3-methyl-1-[4-(3-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIar.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3-methylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 81 %. M : 154-156°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.45 (s, 3H, PhCH_3), 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.75 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.20-7.75 (m, 8**H Ar**).

7,8-dimethoxy-3-methyl-1-[4-(4-methylphenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIas.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 4-methylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 84 %. M : 191-192°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.42 (s, 3H, $PhCH_3$), 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, CH_3), 3.98 (s, 3H, CH_3), 6.75 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.28-7.74 (m, 8**H Ar**).

1-[4-(4-chlorophenyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIat.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 4-chlorobenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 44 %. M : 191-193°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : δ 3.41-3.52 (m, 5H, CH_2 + CH_3), 3.75 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 6.73 (s, 1**H Ar**), 6.89 (s, 1**H Ar**), 7.24-7.72 (m, 8**H Ar**).

7,8-dimethoxy-3-methyl-1-[4-(2-thienyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIau.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 2-thiophene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 41 %. M : 147-149°C.

1-[4-(2-furyl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIav.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 2-furanboronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 89 %. M : 178-179°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.74 (s,

3H, CH_3), 3.97 (s, 3H, CH_3), 6.51-6.53 (m, 1**H Ar**), 6.70 (s, 1**H Ar**), 6.76-6.78 (m, 1**H Ar**), 6.88 (s, 1**H Ar**), 7.52-7.75 (m, 5**H Ar**).

1-{4-[3,5-bis-(trifluoromethyl)phenyl]phenyl}-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaw.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3,5-bis(trifluoromethyl)benzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 32 %. M : 192-194°C. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ 3.40-3.51 (m, 5H, CH_2 + CH_3), 3.76 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 6.70 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.67-8.06 (m, 7**H Ar**).

1-[4-(heptyn-1-yl)phenyl]-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIax.

Stir for 3 hours at room temperature under an inert atmosphere a mixture of 1-(4-iodophenyl)-7,8-dimethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **IIIah**, 12 mg of CuI, 7 mg of $PdCl_2$, 23 mg of PPh_3, 2 ml of TEA, 4 ml of heptyne, in 12 ml of CH_3CN. Evaporate to dryness and purify by silica chromatography (AcOEt 1/hexane 1). Recrystallize in EtOH/pentane. Yield : 16 %. M : 110-112°C. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ 0.94 (t, J = 7.2, 3H, CH_3), 1.36-1.64 (m, 8H, 4 x CH_2), 2.44 (t, J = 7.2, 2H, $C{\equiv}CCH_2$), 3.43 (s, 3H, NCH_3), 3.72 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.64 (s, 1**H Ar**), 6.86 (s, 1**H Ar**), 7.43-7.60 (m, 4**H Ar**).

7,8-dimethoxy-3-methyl-1-[4-(3-nitrophenyl)phenyl]-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIay.

By replacing 2-methoxybenzene boronic acid in example **IIIai** by 3-nitrophenyl boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 89 %. M : 211-213°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.50-3.56 (m, 5H, CH_2 + CH_3), 3.80 (s, 3H, CH_3), 4.02 (s, 3H, CH_3), 6.75 (s, 1**H Ar**), 6.93 (s, 1**H Ar**), 7.65-8.56 (m, 8**H Ar**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIaz.

By replacing 7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIaa** in example **IIIag** by 1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIab** and proceeding in the same manner, the abovenamed product is obtained. Yield : 72 %. M : 100-103°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.26 (t, J = 7.1, 3H, CH_3), 1.44 (t, J = 7.0, 3H, CH_3), 1.52 (t, J = 7.1, 3H, CH_3), 3.29-3.56 (m, 2H, 5-CH_2), 3.85-4.25 (m, 6H, 3 x CH_2CH_3), 6.87 (s, 1H **Ar**), 7.15 (s, 1H **Ar**), 7.32-7.44 (m, 3H **Ar**), 7.71-7.89 (m, 2H **Ar**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIba.

By replacing ethyl iodide in example **IIIaz** by methyl iodide and proceeding in the same manner, the abovenamed product is obtained. Yield : 65 %. M : 157-160°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.43 (t, J = 7.0, 3H, CH_3), 1.52 (t, J = 7.2, 3H, CH_3), 3.38-3.58 (m, 5H, CH_3 + 5-CH_2), 4.05 (q, J = 7.2, 2H, CH_2CH_3), 4.19 (q, J = 7.0, 2H, CH_2CH_3), 6.87 (s, 1H **Ar**), 7.13 (s, 1H **Ar**), 7.35-7.44 (m, 3H **Ar**), 7.71-7.89 (m, 2H **Ar**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3-methyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIbb.

By replacing 1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIab** in example **IIIba** by 1-(benzo[b]thienyl)-7,8-diethoxy-5-ethyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIad** and proceeding in the same manner, the abovenamed product is obtained. Yield : 70 %. M : 79-81°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.07 (t, J = 7.2, 3H, CH_3), 1.42 (t, J = 7.0, 3H, CH_3), 1.52 (t, J = 7.0, 3H, CH_3), 1.92-2.47 (m, 2H, 5-CH_2CH_3), 2.96-3.04 (m, 1H, 5-**H**), 3.45 (s, 3H, 3-CH_3), 3.99-4.25 (m, 4H, 3 x OCH_2CH_3), 6.83 (s, 1H **Ar**), 7.13 (s, 1H **Ar**), 7.35-7.44 (m, 3H **Ar**), 7.72-7.90 (m, 2H **Ar**).

1-(2-benzo[b]thienyl)-7,8-diethoxy-3-methyl-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIbc.

By replacing 1-(2-benzo[b]thienyl)-7,8-diethoxy-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIab** in example **IIIba** by 1-(2-benzo[b]thienyl)-7,8-diethoxy-5-*n*-propyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIac** and proceeding in the same manner, the abovenamed product is obtained. Yield : 34 %. M : 61-63°C. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.01 (t, J = 7.34, 3H, $(CH_2)_2CH_3$), 1.39-4.55 (m, 8H, $CH_2CH_2CH_3$ + 2 x OCH_2CH_3), 1.75-2.42 (m, 2H, $CH_2CH_2CH_3$), 3.04-3.11 (m, 1H, 5-**H**), 3.45 (s, 3H, 3-CH_3), 3.99-4.23 (m, 4H, 2 x OCH_2CH_3), 6.83 (s, 1H **Ar**), 7.12 (s, 1H **Ar**), 7.35-7.44 (m, 3H **Ar**), 7.72-7.89 (m, 2H **Ar**).

3,5-dibenzyl-7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIbd.

To a solution of 7,8-dimethoxy-1-phenyl-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one **VIaa** (200 mg, 0.67 mmol) in DMF (10 ml), under an inert atmosphee, add NaH in oil (50 mg, 1.25 mmol). Then add dropwise benzyl bromide (150 µl, 1.26 mmol). After 2 hours at room temperature, evaporate the DMF. Take up the residue in CH_2Cl_2, wash twice with water. Dry the organic phases on Na_2SO_4. Purify by silica gel column chromatography (AcOEt/hexane, 4:1). Yield : 79 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 3.35-3.56 (m, 2H, CH_2Ph), 3.70 (s, 3H, OCH_3), 3.80 (m, 1H, **CH**), 3.97 (s, 3H, OCH_3), 4.87 (d, J = 10.2, 1H, NC**H**Ph), 5.30 (d, J = 10.2, 1H, NC**H**Ph), 6.61 (s, 1H, **Ar**), 6.93 (s, 1H, **Ar**), 7.06-7.42 (m, 13H, **Ar**), 7.59 (d, J = 4.8, 2H, **Ar**). SM : 477 (M + H), 500 (M + H +Na).

7,8-dimethoxy-1-phenyl-3-(3-hydroxypropyl)-3,5-dihydro-4*H*-2,3-benzodiazepin-4-one, IIIbe.

By replacing benzyl bromide in example **IIIac** by propan-1-ol bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 44 %. ^{1}H-NMR (200 MHz, $CDCl_3$) : d 1.88 (broad m, 2H, CH_2), 3.21 (broad s, 1H, **OH**), 3.44 (broad m, 4H, NCH_2 and CH_2O), 3.72 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 4.06 (m, 2H, CH_2), 6.66 (s, 1H, **Ar**), 6.88 (s, 1H, **Ar**), 7.44 (m, 3H, **Ar**), 7.64 (m, 2H, **Ar**).

EXAMPLE 2: SYNTHESIS OF COMPOUNDS REPRESENTED BY FORMULA III ACCORDING TO THE INVENTION BY A SECOND ROUTE

2.1. Synthesis of 6,7-dimethoxyisochroman-3-one, VIII.

Heat at 120°C for 1 hour a mixture of 19.6 g (100 mmol) of 3,4-dimethoxyphenyl acetic acid **(VII)**, 7.4 g (246 mmol) of paraformaldehyde and 20 ml of concentrated HCl in 100 ml of AcOH. Evaporate to dryness. Add 100 ml of H_2O, and extract three times with 200 ml of CH_2Cl_2. Wash the organic phases with 50 ml of 0.5 N $NaHCO_3$ and dry on Na_2SO_4. Evaporate to dryness. Allow to crystallize for 2 hours in 50 ml of Et_2O. Filter and wash twice with 10 ml of Et_2O and twice with 20 ml of pentane. Yield : 83 %. M : 106-108°C. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 3.64 (s, 2H, CH_2), 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 5.26 (s, 2H, CH_2), 6.71 (s, 1H **Ar**), 6.75 (s, 1H **Ar**).

2.2. Synthesis of 4,5-dimethoxyhomophthalic acid, IX.

Add dropwise 800 ml of a 10 % solution of $KMnO_4$ to a solution of 10.4 g (50 mmol) of 6,7-dimethoxy-3-isochromanone **VIII** in 55 ml of 10 % KOH. Stir at room temperature for 10 hours. Add 20 ml of EtOH and heat at 70 °C for 20 minutes. Concentrate the reaction medium to two-thirds. Acidify to pH 2-3 (check with pH paper) using concentrated HCl. Allow to crystallize at 0°C for 1 hour. Filter and wash twice with 10 ml of H_2O. Yield : 78 %. ^{1}H-NMR (300 MHz, $CDCl_3$) : d 3.93 (s, 2H, CH_3), 3.96 (s, 3H, OCH_3), 4.01 (s, 2H, CH_2), 6.74 (s, 1H **Ar**), 7.66 (s, 1H **Ar**).

2.3. Synthesis of 6,7-dimethoxyisochroman-1,3-diones, X.

Heat under reflux 3.6 g (15 mmol) of 4,5-dimethoxyhomophthalic acid **IX**, in 30 ml of acetyl chloride. Add 40 ml of Et_2O. Filter and wash twice with 3 ml of Et_2O then twice with 10 ml of pentane. Yield : 82 %. The product is used as is for the subsequent reactions.

2.4. Synthesis of 2-(2-hydrazino-2-oxoethyl)-4,5-dimethoxy benzoic acid, XI.

To a solution of 810 µl of hydrazine hydrate in 15 ml of EtOH, add 3 g (13.5 mmol) of 6,7-dimethoxyisochroman-1,3-diones **X**. Stir for 15 minutes at room temperature. Filter the precipitate. Wash twice with 5 ml of EtOH and twice with 10 ml of Et_2O. Yield : 96 %. ^{1}H-NMR (300 MHz, DMSO-D_6) : d 3.69 (s, 2H, CH_2), 3.73 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 6.55 (broad s, 2 H exchangeable, N**H**), 6.76 (s, 1H **Ar**), 7.34 (s, 1H **Ar**).

2.5. Synthesis of 7,8-dimethoxy-1,2,3,4-tetrahydro-5*H*-2,3-benzodiazepine-1,4-dione, XII.

To 15 ml of AcOH at 100 °C, add 1.5 g (5.9 mmol) of 2-(2-hydrazino-2-oxoethyl)-4,5-dimethoxy benzoic acid **XI**. After 5 minutes at 100°C, cool in an ice bath. Filter and wash twice with 1 ml of AcOH, twice with 2 ml of H_2O, twice with 10 ml of Et_2O. Yield : 78 %. ^{1}H-NMR (300 MHz, DMSO-D_6) : d 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.88 (s, 2H, CH_2), 6.97 (s, 1H **Ar**), 7.40 (s, 1H **Ar**), 9.85 (s, 1H exchangeable, 2-N**H**), 12.4 (s, 1H exchangeable, 3-N**H**).

2.6. Synthesis of 7,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-5*H*-2,3-benzodiazepine-1,4-diones, XIII.

Stir at room temperature a mixture of 200 mg (0.85 mmol) of 7,8-dimethoxy-1,2,3,4-tetrahydro-5*H*-2,3-benzodiazepine-1,4-dione **XII**, 130 mg (0.93 mmol) of K_2CO_3 and 58 µl (0.93 mmol) of methyl iodide in 3 ml of anhydrous DMF. After 24 hours add 40 ml of H_2O. Filter the precipitate and wash once with 1 ml of H_2O, twice with 3 ml of MeOH and twice with 5 ml of Et_2O. Yield : 87 %. ^{1}H-NMR (300 MHz, DMSO-D_6) : d 3.77 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.84 (s, 2H, CH_2), 7.00 (s, 1H **Ar**), 7.38 (s, 1H **Ar**), 9.87 (s, 1H exchangeable, N**H**).

2.7. Synthesis of 1-chloro-7,8-dimethoxy-3-methyl-3,5-dihydro-5*H*-2,3-benzodiazepin-4-one, XIVaa.

Heat at 115°C in a sealed tube for 1 hour a solution of 100 mg (0.40 mmol) of 7,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-5*H*-2,3-benzodiazepine-1,4-diones **XIII**, 250 µl

of dimethylaniline, 600 µl of $POCl_3$, in 10 ml of anhydrous $CHCl_3$. Allow to cool to room temperature. At –20°C add 3 g of silica, 15 ml of CH_2Cl_2 and 3 ml of triethylamine. Evaporate to dryness. Purify by chromatography (AcOEt). Triturate in 1 ml of Et_2O. Filter and wash twice with 2 ml of pentane. Yield : 88 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.68 (s, 3H, 3-CH_3), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.47 (s, 2H, CH_2), 7.03 (s, 1H **Ar**), 7.44 (s, 1H **Ar**).

2.8. Synthesis of 1-bromo-7,8-dimethoxy-3-methyl-3,5-dihydro-5*H*-2,3-benzodiazepin-4-one, XIVab.

By replacing $POCl_3$ in example **XIVaa** by $POBr_3$ and proceeding in the same manner, the abovenamed product is obtained. Yield : 48 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.84 (s, 3H, 3-CH_3), 3.91 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 4.61 (s, 2H, CH_2), 6.80 (s, 1H **Ar**), 7.58 (s, 1H **Ar**).

EXAMPLE 3 : SYNTHESIS OF COMPOUNDS REPRESENTED BY GENERAL FORMULA II ACCORDING TO THE INVENTION BY A FIRST ROUTE

3.1. Synthesis of intermediates represented by formula XVIII.

6,7-dimethoxy-1-methyl-1,2-dihydro-4*H*-3,1-benzoxazine-2,4-dione, XVI.

To a solution of 500 mg (3.06 mmol) of 6,7-dimethoxy-1,2-dihydro-4*H*-3,1-benzoxazine-2,4-dione **(XV)**, in 6 ml of anhydrous DMF, add under an inert atmosphere 134 mg (3.37 mmol) of 60 % NaH in oil. After 10 minutes at room temperature, add dropwise 219 µl (3.52 mmol) of MeI. Allow to stand at room temperature for 3 hours. Add 40 ml of a water-ice mixture. Filter the precipitate and wash twice with 1 ml of EtOH and 3 ml of Et_2O. One obtains 320 mg of the abovenamed product in the form of a white powder. Yield : 59 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.31 (s, 3H, 1-CH_3), 3.82 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.85 (s, 1**H Ar**), 7.32 (s, 1**H Ar**).

7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione, XVIIaa.

Heat under reflux for 6 hours a mixture of 320 mg (1.35 mmol) of 6,7-dimethoxy-1-methyl-1,2-dihydro-4*H*-3,1-benzoxazine-2,4-dione **(XVI)**, 452 mg (3.24 mmol) of methyl glycinate hydrochloride in 4 ml of pyridine. Add 3 ml of AcOH and heat at 130°C for 12 hours. Evaporate to dryness. Add 10 ml of a water-ice mixture. Allow to crystallize at 0°C for 30 minutes. Filter and wash twice with 2 ml of H_2O, twice with 1 ml of EtOH and twice with 5 ml of Et_2O. Recrystallize in EtOH. One obtains 240 mg of the abovenamed product in the form of colorless crystals. Yield : 71%. M : 260-263°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.42 (s, 3H, NCH_3), 3.75-3.92 (m, 2H, CH_2), 3.98 (s, 6H, 2 x OCH_3), 6.39 (sl, 1H exchangeable, NH), 6.69 (s, 1**H Ar**), 7.37 (s, 1**H Ar**).

7,8-dimethoxy-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione, XVIIab.

By replacing 6,7-dimethoxy-1-methyl-1,2-dihydro-4*H*-3,1-benzoxazine-2,4-dione **(XVI)** in example **XVIIaa** by 6,7-dimethoxy-1,2-dihydro-4*H*-3,1-benzoxazine-2,4-dione **(XV)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 54 %. ^{1}H-NMR (DMSO, 300 MHz) : d 3.55 (d, J = 5.3, 2H, CH_2), 3.77 (s, 6H, 2xOCH_3), 6.16 (s, 1**H Ar**), 6.67 (s, 1**H Ar**), 8.34 (t, J= 5.3, 1H, NH), 10.07 (s, 1H, NH).

7,8-dimethoxy-1-*n*-propyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione, XVIIac.

To a solution of 723 mg (3.06 mmol) of 7,8-dimethoxy-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIab)**, in 6 ml of anhydrous DMF, add under an inert atmosphere 134 mg (3.37 mmol) of 60 % NaH in oil. After 10 minutes at room temperature, add dropwise 328 µl (3.37 mmol) of *n*-PrI. Allow to stand at room temperature for 3 hours. Add 40 ml of a water-ice mixture. Filter the precipitate and wash twice with 1 ml of EtOH and 3 ml of Et_2O. One obtains 320 mg of the abovenamed product in the form of a white powder. Yield : 65 %. ^{1}H-NMR (DMSO, 200 MHz) : d 0.66-0.73 (m, 3H, CH_2CH_3), 1.27-1.39 (m, 2H, CH_2CH_3), 3.30-4.22 (m, 10H, CH_2+CH_2+2 x OCH_3), 6.97 (s, 1**H Ar**), 7.13 (s, 1**H Ar**), 8.56 (s, 1H, NH).

1-benzyl-7,8-dimethoxy-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione, XVIIad.

By replacing *n*-Pr-I in example **XVIIac** by Bn-Br and proceeding in the same manner, the abovenamed product is obtained. Yield : 45 %. ^{1}H-NMR (DMSO, 200 MHz) : d 3.53-3.77 (m, 8H, CH_2+2 x OCH_3), 4.90-5.36 (m, 2H, CH_2), 6.98-7.29 (m, 7**H Ar**), 8.61 (t, J=5.6, 1H, N**H**).

7,8-dimethoxy-1,3-dimethyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione, XVIIae.

By replacing methyl glycinate hydrochloride in example **XVIIaa** by methyl alaninate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 45 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.47 (d, J = 6.6, 3H, 3-CH_3), 3.40 (s, 3H, 1-CH_3), 3.92-3.97 (m, 7H, 3-C**H** + 2 x OCH_3), 6.13 (d, J = 4.9, 1H exchangeable, N**H**), 6.66 (s, 1**H Ar**), 7.33 (s, 1**H Ar**).

5-chloro-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, XVIIIaa.

Heat at 125°C in a sealed tube for ¾ hour a solution of 100 mg (0.40 mmol) of 7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIaa)**, 280 µl of dimethylaniline, 800 µl of $POCl_3$, in 10 ml of anhydrous $CHCl_3$. Allow to cool to room temperature. Add 3 g of silica and 5 ml of CH_2Cl_2. Add at 0°C, 1 ml of triethylamine. Evaporate to dryness. Purify by chromatography (AcOEt 1/hexane 1, then AcOEt). Triturate in 1 ml of Et_2O. Filter and wash twice with 2 ml of pentane. One obtains 93 mg of the abovenamed product as a white powder. Yield : 87 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.42 (s, 3H, NCH_3), 3.77 (broad s, 1H of CH_2), 3.99 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.65 (broad s, 1H of CH_2), 6.71 (s, 1**H Ar**), 7.22 (s, 1**H Ar**).

5-chloro-7,8-dimethoxy-1,3-dimethyl-1,3-dihydro-1,4-benzodiazepin-2-one, XVIIIab.

By replacing 7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIaa)** in example **XVIIIaa** by 7,8-dimethoxy-1,3-dimethyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIae)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 78 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.67

(d, J = 6.6, 3H, 3-CH_3), 3.44 (s, 3H, 1-CH_3), 3.68 (q, J = 6.6, 1H, 3-**CH**), 3.98 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.70 (s, 1**H Ar**), 7.21 (s, 1**H Ar**).

1-benzyl-5-chloro-7,8-dimethoxy-1,3-dihydro-1,4-benzodiazepine-2-one, XVIIIac.

By replacing 7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIaa)** in example **XVIIIaa** by 1-benzyl-7,8-dimethoxy-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIad)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 53 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.70-3.96 (m, 7H, **CH** + 2 x OCH_3), 4.65-4.78 (m, 1H **CH**), 5.09-5.12 (m, 2H, CH_2), 6.70 (s, 1**H Ar**), 7.15-7.39 (m, 6**H Ar**).

5-chloro-7,8-dimethoxy-1-*n*-propyl-1,3-dihydro-1,4-benzodiazepin-2-one, XVIIIad.

By replacing 7,8-dimethoxy-1-methyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIaa)** in example **XVIIIaa** by 7,8-dimethoxy-1-*n*-propyl-3,4-dihydro-1*H*-1,4-benzodiazepine-2,5-dione **(XVIIac)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 34 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 0.81-0.89 (m, 3H, CH_2CH_3), 1.46-1.61 (m, 2H, CH_2CH_3), 3.50-3.74 (m, 2H, 2 x **CH**), 3.98 (s, 6H, 2 x OCH_3), 4.22-4.66 (m, 2H, 2 x **CH**), 6.77 (s, 1**H Ar**), 7.30 (s, 1**H Ar**).

3.2. Synthesis of compounds represented by formula (II)

The following compounds were synthesized :

7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIaa**.

7,8-dimethoxy-5-(3,4-dimethoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIab**.

5-(2-benzo[b]thienyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIac**.

7,8-dimethoxy-5-(4-fluorophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIad**.

7,8-dimethoxy-1-methyl-5-(4-pyridyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIae**.

7,8-dimethoxy-1-methyl-5-(3, 5 bis trifluoromethylphenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIaf**.

5-(2-benzo[b]furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIag**.

5-(2-furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIah**.

5-(4-acetylphenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIai**.

7,8-dimethoxy-5-(4-N,N-dimethylaminophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIaj**.

7,8-dimethoxy-1-methyl-5-(2-thienyl)-1,3-dihydro-1,4-benzodiazepin-2-one, **IIak**.

7,8-dimethoxy-5-(3-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIal**.

7,8-dimethoxy-5-(2-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIam**.

5-(5-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIan**.

5-(6-benzyloxy-2-naphthyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIao**.

7,8-dimethoxy-5-(6-methoxy-2-naphthyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIap**.

5-(2-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIaq**.

7,8-dimethoxy-1-methyl-5-(piperidin-1-yl)-1,3-dihydro-1,4-benzodiazepin-2-one, **IIar**.

7,8-dimethoxy-1-methyl-5-[(E)-2-phenylethenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIas**.

7,8-dimethoxy-5-(3-hydroxymethylphenyl)-1-methyl-3-propyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIat**.

7,8-dimethoxy-1-methyl-5-(2-methylphenyl)-1,3-dihydro-1,4-benzodiazepin-2-one, **IIau**.

7,8-dimethoxy-1-methyl-5-(N-tetrahydro-1,2,3,4-isoquinolyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIav**.

7,8-dimethoxy-5-(4-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, **IIaw**.

5-(3-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIax**.

5-(1,1'-biphenyl-3-yl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIay**.

7,8-dimethoxy-1-methyl-5-(2-phenylethyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIaz**.

7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIaa.

Heat at 115°C for 12 hours under an inert atmosphere a mixture of 200 mg (0.74 mmol) of 5-chloro-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one **XVIIIaa**, 109 mg (0.89 mmol) of benzene boronic acid, 182 mg (0.86 mmol) of K_3PO_4, 23 mg (0.020 mmol) of tetrakis(triphenylphosphine) Pd (0) in 5 ml of DMF. Allow to cool to room temperature. Add 80 ml of H_2O and extract three times with 50 ml of Et_2O. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt). Recrystallize in EtOH. One obtains 122 mg of the abovenamed product in the form of colorless crystals. Yield : 53 %. M : 109-112°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.40 (s, 3H, NC**H$_3$**), 3.75 (s, 3H, OC**H$_3$**), 3.98 (s, 3H, OC**H$_3$**), 4.30 (AB system, ? d = 1.00, J_{AB} = 10.2, 2H, C**H$_2$**), 6.71 (s, 1**H Ar**), 6.78 (s, 1**H Ar**), 7.35-7.47 (m, 3**H Ar**), 7.64-7.68 (m, 2**H Ar**).

7,8-dimethoxy-5-(3,4-dimethoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIab.

By replacing benzene boronic acid in example **IIaa** by 3,4-dimethoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 82 %. M : 130-133°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.40 (s, 3H, NC**H$_3$**), 3.43 (s, 3H, OC**H$_3$**), 3.94 (s, 6H, 2 x OC**H$_3$**), 3.98 (s, 3H, OC**H$_3$**), 4.27 (AB system, ? d = 0.98, J_{AB} = 10.8, 2H, C**H$_2$**), 6.78-6.85 (m, 3**H Ar**), 7.04-7.09 (m, 1**H Ar**), 7.42-7.43 (m, 1**H Ar**).

5-(2-benzo[b]thienyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIac.

By replacing benzene boronic acid in example **IIaa** by benzo[b]thiophene-2-boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 83 %. M : 136-138°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.40 (s, 3H, NC**H$_3$**), 3.88 (s, 3H,

OCH_3), 4.00 (s, 3H, OCH_3), 4.32 (AB system, ? d = 0.93, J_{AB} = 10.7, 2H, CH_2), 6.80 (s, 1**H Ar**), 7.15 (s, 1**H Ar**), 7.31-7.42 (m, 3**H Ar**), 7.69-7.89 (m, 2**H Ar**).

7,8-dimethoxy-5-(4-fluorophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIad.

By replacing benzene boronic acid in example **IIaa** by 4-fluorobenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 20 %. M : 201-202°C. ^{1}H-NMR (DMSO, 300 MHz) : d 3.30 (s, 3H, NCH_3), 3.63 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.11 (AB system, ? d = 0.79, J_{AB} = 10.6, 2H, CH_2), 6.67 (s, 1**H Ar**), 7.08 (s, 1**H Ar**), 7.08-7.66 (m, 4**H Ar**).

7,8-dimethoxy-1-methyl-5-(4-pyridyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIae.

By replacing benzene boronic acid in example **IIaa** by (pyrid-4-yl))-4,4,5,5-tetramethyl-1,3-dioxolaborolane acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 25 %. M : 170-172°C. ^{1}H-NMR (DMSO, 200 MHz) : d 3.34 (s, 3H, NCH_3), 3.68 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.25 (AB system, ? d = 0.81, J_{AB} = 10.5, 2H, CH_2), 6.73 (s, 1**H Ar**), 7.58 (d, 2**H Ar**, J = 6.1), 8.72 (d, 2**H Ar**, J = 5.9).

7,8-dimethoxy-1-methyl-5-(3, 5 bis trifluoromethylphenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIaf.

By replacing benzene boronic acid in example **IIaa** by 3, 5 bis trifluoromethylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 20 %. M : 180-182°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.44 (s, 3H, NCH_3), 3.76-3.88 (m, 4H, 1HCH_2 + OCH_3), 4.02 (s, 3H, OCH_3), 4.89 (m, 1HCH_2), 6.61 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.98 (s, 1**H Ar**), 8.19 (s, 2**H Ar**).

5-(2-benzo[b]furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIag.

By replacing benzene boronic acid in example **IIaa** by 2-benzo[b]furanboronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 70 %. M : 139-141°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.40 (s, 3H, NCH_3), 3.89 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.41 (AB system, ? d = 1.03, J_{AB} = 10.3, 2H, CH_2), 6.80 (s, 1**H Ar**), 7.08 (s, 1**H Ar**), 7.14-7.65 (m, 5**H Ar**).

5-(2-furyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIah.

By replacing benzene boronic acid in example **IIaa** by 2-furanboronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 43 %. M : 172-173°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.38 (s, 3H, NCH_3), 3.88 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 4,28 (AB system, ? d = 0.98, J_{AB} = 10., 2H, CH_2), 6.50-6.54 (m, 1**H Ar**), 6.74-6.77 (m, 2**H Ar**), 7.07 (s, 1**H Ar**), 7.59-7.61 (m, 1**H Ar**).

5-(4-acetylphenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIai.

By replacing benzene boronic acid in example **IIaa** by 4-acetylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 49 %. M : 175-176°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 2.63 (s, 3H, CH_3CO), 3.42 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.30 (AB system, ? d = 1.03, J_{AB} = 10.3, 2H, CH_2), 6.64 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.86 (AB system, ? d = 0.23, J_{AB} = 8.08, 4**H Ar**).

7,8-dimethoxy-5-(4-N,N-dimethylaminophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIaj.

By replacing benzene boronic acid in example **IIaa** by 4-N,N-dimethylaminobenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 10 %. M : >290°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.02 (s, 6H, NCH_3), 3.38 (s, 3H, NCH_3), 3.74-3.78 (m, 4H, $1HCH_2$ + OCH_3), 3.97 (s, 3H, OCH_3), 4.67-4.71 (m, $1HCH_2$), 6.66-6.81 (m, 4**H Ar**), 7.54-7.64 (m, 2**H Ar**). Mass : $(M+H)^+$ = 354.23.

7,8-dimethoxy-1-methyl-5-(2-thienyl)-1,3-dihydro-1,4-benzodiazepin-2-one, IIak.

By replacing benzene boronic acid in example **IIaa** by 2-thiophene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 66 %. M : 180-182°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.38 (s, 3H, NCH_3), 3.87 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.24 (AB system, ? d = 0.91, J_{AB} = 10.8, 2H, CH_2), 6.77 (s, 1**H Ar**), 7.05-7.49 (m, 4**H Ar**).

7,8-dimethoxy-5-(3-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIal.

By replacing benzene boronic acid in example **IIaa** by 3-methoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 38 %. M : 99-102°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.40 (s, 3H, NCH_3), 3.77 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.1 (AB system, ? d = 0.98, J_{AB} = 10.7, 2H, CH_2), 6.73 (s, 1**H Ar**), 6.78 (s, 1**H Ar**), 6.99-7.35 (m, 4**H Ar**).

7,8-dimethoxy-5-(2-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIam.

By replacing benzene boronic acid in example **IIaa** by 2-methoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 54 %. M : 153-154°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.43 (s, 3H, NCH_3), 3.57 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 4.31 (AB system, ? d = 0.99, J_{AB} = 10.7, 2H, CH_2), 6.53 (s, 1**H Ar**), 6.75 (s, 1**H Ar**), 6.86-7.51 (m, 4**H Ar**).

5-(5-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIan.

By replacing benzene boronic acid in example **IIaa** by (1-*tert*-butyloxycarbonylindole)-5-boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 21 %. M : 148-151°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.40 (s, 3H, NCH_3), 3.92 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.32 (AB system, ? d = 0.85, J_{AB} = 10.9, 2H, CH_2),

6.75 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.10-7.76 (m, 5**H Ar**), 9.50 (broad s, 1H exchangeable, N**H**).

5-(6-benzyloxy-2-naphthyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIao.

By replacing benzene boronic acid in example **IIaa** by (6-benzyloxynaphthalene-2-boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 18 %. M : 143-146°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.43 (s, 3H, NCH_3), 3.72 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.34 (AB system, ? d = 0.98, J_{AB} = 10.6, 2H, CH_2), 5.21 (s, 2H, CH_2), 6.78 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.33-8.02 (m, 11**H Ar**).

7,8-dimethoxy-5-(6-methoxy-2-naphthyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIap.

By replacing benzene boronic acid in example **IIaa** by (6-methoxynaphthalene-2-boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 40 %. M : 193-194°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.43 (s, 3H, NCH_3), 3.72 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.34 (AB system, ? d = 0.98, J_{AB} = 10.6, 2H, CH_2), 6.79 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.16-8.00 (m, 6**H Ar**).

5-(2-indolyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIaq.

By replacing benzene boronic acid in example **IIaa** by (1-*tert*-butyloxycarbonylindole)-2-boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 21%. M : 146-148°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.39 (s, 3H, NCH_3), 3.89 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.31 (AB system, ? d = 0.87, J_{AB} = 10.8, 2H, CH_2), 6.75 (s, 1**H Ar**), 6.79 (s, 1**H Ar**), 7.12-7.65 (m, 5**H Ar**).

7,8-dimethoxy-1-methyl-5-(piperidin-1-yl)-1,3-dihydro-1,4-benzodiazepin-2-one, IIar.

Heat at 110°C in a sealed tube a mixture of 100 mg (0.37 mmol) of 5-chloro-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one **XVIIIaa** and 300 µl (3 mmol) of piperidine in 10 ml of EtOH for 48 hours. Evaporate to dryness and purify by silica chromatography (CH_2Cl_2 50/ AcOEt 40/ EtOH 10). Triturate in hexane, filter, dry. One obtains 70 mg of a beige powder. Yield : 60 %. M = 125-127°C. ^{1}H-NMR (200 MHz, DMSO) : δ 1.63-1.70 (m, 6H, 3 x CH_2), 3.20-3.23 (m, 4H, 2 x CH_2), 3.37 (s, 3H, NCH_3), 3.91 (AB system, Δδ= 0.71, J_{AB} = 11.5, 2H, 3-CH_2), 3.94 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.73 (s, 1**H Ar**), 6.99 (s, 1**H Ar**).

7,8-dimethoxy-1-methyl-5-[(E)-2-phenylethenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIas.

By replacing benzene boronic acid in example **IIaa** by (E)-2-phenylethenyl boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 20 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.38 (s, 3H, NCH_3), 3.76 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 4,26 (AB system, ? d = 0.93, J_{AB} = 10.6, 2H, CH_2), 6.77 (s, 1**H Ar**), 7.00 (s, 1H, =C**H**Ph), 7.12 (s, 2H, =C**H** + 1**H Ar**) 7.34-751 (m, 5**H Ar**). Mass : $(M+H)^+$ = 337.21.

7,8-dimethoxy-1-methyl-5-(2-phenylethynyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIat.

To a solution of 240 mg (0.89 mmol) of 5-chloro-7,8-dimethoxy-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one **XVIIIaa** in 7 ml of CH_3CN, add under an inert atmosphere 17 mg (0.1 mmol) of $PdCl_2$, 30 mg (0.16 mmol) of CuI. Stir for 5 minutes, then add 68 mg (0.23 mmol) of PPh_3, 185 µl of Net_3 and 150 µl of phenylacetylene. Heat the mixture at 55°C for 3 hours. Evaporate to dryness and purify by silica chromatography (AcOEt 1/ hexane 1, then AcOEt). Recrystallize in EtOH. Yield : 45 %. ^{1}H-NMR (DMSO, 200 MHz) : d 3.33 (s, 3H, NCH_3), 3.70-3.91 (m, 7H, 1HCH_2 + 2OCH_3), 4.50-5.60 (m, 1HCH_2), 7.06 (s, 1**H Ar**), 7.32 (s, 1**H Ar**), 7.48-7.68 (m, 5**H Ar**). Mass : $(M+H)^+$ = 335.16.

7,8-dimethoxy-1-methyl-5-(2-methylphenyl)-1,3-dihydro-1,4-benzodiazepin-2-one, IIau.

By replacing benzene boronic acid in example **IIaa** by 2-methylbenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 30 %. M : 139-141°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.99 (s, 3H, CH_3), 3.44 (s, 3H, NCH_3), 3.66 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 4.31 (system AB, ? d = 0.99, J_{AB} = 10.3, 2H, CH_2), 6.46 (s, 1**H Ar**), 6.77 (s, 1**H Ar**), 7.15-7.41 (m, 4**H Ar**).

7,8-dimethoxy-1-methyl-5-(N-tetrahydro-1,2,3,4-isoquinolyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIav.

By replacing piperidine in example **IIar** by tetrahydro-1,2,3,4-isoquinoline and proceeding in the same manner, the abovenamed product is obtained. Yield : 35 %. M : 154-157°C. ^{1}H-NMR (DMSO, 300 MHz) : d 2.70-3.10 (m, 2H, CH_2), 3.23 (s, 3H, NCH_3), 3.41-3.54 (m, 3H, $1CH_2$ + $1HCH_2$), 3.78 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.98 – 4.01 (m, $1HCH_2$), 4.33 – 4.44 (m, 2H, CH_2), 6.97 (s, 1**H Ar**), 7.02 (s, 1**H Ar**), 7.15 (s, 4**H Ar**). Mass : $(M + H)^+$ = 366.19.

7,8-dimethoxy-5-(4-methoxyphenyl)-1-methyl-1,3-dihydro-1,4-benzodiazepin-2-one, IIaw.

By replacing benzene boronic acid in example **IIaa** by 4-methoxybenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 30 %. M : 163-165°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.39 (s, 3H, NCH_3), 3.76 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 4.25 (AB system, ? d = 0.98, J_{AB} = 10.5, 2H, CH_2), 6.74-6.93 (m, 4**H Ar**), 7.59 (s, 1**H Ar**), 7.63 (s, 1**H Ar**).

5-(3-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIax.

By replacing benzene boronic acid in example **IIaa** by 3-bromobenzene boronic acid and proceeding in the same manner, the abovenamed product is obtained. Yield : 38 %. ^{1}H-NMR (DMSO, 200 MHz) : d 3.33 (s, 3H, NCH_3), 3.66 (s, 3H, OCH_3), 3.92 (s, 3H,

OCH_3), 4,23 (AB system, ? d = 0.98, J_{AB} = 10, 2H, CH_2), 6.72 (s, 1**H Ar**), 7.12 (s, 1**H Ar**), 7.37-7.80 (m, 4**H Ar**).

5-(1,1'-biphenyl-3-yl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIay.

Heat at 115°C for 12 hours under an inert atmosphere a mixture of 100 mg (0.26 mmol) of 5-(3-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **IIax,** 38 mg (0.31 mmol) of benzene boronic acid, 63 mg (0.30 mmol) of K_3PO_4, 9 mg (0.020 mmol) of tetrakis(triphenylphosphine) Pd (0) in 1 ml of DMF. Allow to cool to room temperature. Add 80 ml of H_2O and extract three times with 50 ml of Et_2O. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt 1/hexane 1). Recrystallize in EtOH. One obtains 13 mg of the abovenamed powder as colorless crystals. Yield : 13 %. M : 127°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.42 (s, 3H, NCH_3), 3.77 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.34 (AB system, ? d = 1.00, J_{AB} = 10.5, 2H, CH_2), 6.78 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.39-7.90 (m, 9**H Ar**).

7,8-dimethoxy-1-methyl-5-(2-phenylethyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIaz.

Stir a mixture of 80 mg (0.24 mmol) of 7,8-dimethoxy-1-methyl-5-(2-phenylethynyl)-1,3-dihydro-1,4-benzodiazepin-2-one 132 ,15 mg of 10 % Pd/C by weight in 5 ml of MeOH and 5 ml of CH_2Cl_2 under 70 psi of H_2 for 48 hours. Filter the suspension on celite, rinse three times with 10 ml of MeOH. Evaporate to dryness and purify by silica chromatography (AcOEt 1/ hexane 1, then AcOEt). Yield : 5 %. M : 112-115°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 2.95-3.07 (m, 4H, CH_2CH_2), 3.28 (s, 3H, NCH_3), 3.87 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.10 (AB system, ? d = 0.96, J_{AB} = 10.2, 2H, CH_2), 6.67 (s, 1H Ar), 6.78 (s, 1H Ar), 7.15-7.25 (m, 5H Ar). Mass : (M + H)+ = 339.15

EXAMPLE 4 : SYNTHESIS OF COMPOUNDS REPRESENTED BY GENERAL FORMULA II ACCORDING TO THE INVENTION BY A SECOND ROUTE

4.1. Synthesis of Intermediates.

2-ethoxy-1-methoxy-4-nitrobenzene, XIXaa.

Under an inert atmosphere at 0°C, add a solution of 10 g (59 mmol) of 2-ethoxy-5-nitrophenol dissolved in 125 ml of DMF, on a solution of 2.6 g (65 mmol) of 60 % NaH in oil dissolved in 125 ml of DMF. After 30 minutes at room temperature, add dropwise 5.2 ml (65 mmol) of EtI at 0°C. Allow to stand at room temperature for 12 hours. Add 1.5 l of a water-ice mixture. Filter the precipitate and wash three times with 100 ml of water then once with 100 ml of pentane. One obtains 9.8 g of the abovenamed product in the form of a white powder. Yield : 93 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.52 (t, 3H, -CH_3), 3.98 (s, 3H, OCH_3), 4.20 (q, 2H, OCH_2), 6.91 (d, 1**H Ar**), 7.75 (d, 1**H Ar**), 7.91 (dd, 1**H Ar**).

1,2-diethoxy-4-nitrobenzene, XIXab.

Under an inert atmosphere at 0°C, add a solution of 20 g (0.13 mol) of 4-nitrobenzene-1,2-diol dissolved in 150 ml of DMF, on a solution of 11.35 g (0.28 mol) of 60 % NaH dissolved in 150 ml of DMF. After 30 minutes at room temperature, add dropwise 5.2 ml (65 mmol) of EtI at 0°C. Allow to stand at room temperature for 12 hours. Add 2 l of a water-ice mixture. Filter the precipitate and wash three times with 100 ml of water then once with 100 ml of pentane. One obtains 20.4 g of the abovenamed product in the form of a white powder. Yield : 76 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.47-1.53 (m, 6H, 2 x -CH_3), 4.14-4.20 (m, 4H, 2 x OCH_2), 6.88 (d, 1**H Ar**), 7.74 (d, 1**H Ar**), 7.89 (dd, 1**H Ar**).

3-ethoxy-4-methoxyaniline, XXaa.

Leave under hydrogen pressure (Patm) for 12 hours, 5 g of 2-ethoxy-1-methoxy-4-nitrobenzene **(XIXaa)**, 500 mg of 10 % palladium on charcoal (10 % by weight of

product to reduce), in 200 ml of methanol. Filter on celite, rinse several times with methanol. Evaporate to dryness. Take up in ether and evaporate. One obtains 3.28 g of the abovenamed product as a pinkish white powder. Yield : 79 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.46 (t, 3H, -CH_3), 3.33 (s, 2H exchangeable, -NH_2), 3.81 (s, 3H, OCH_3), 4.05 (q, 2H, OCH_2), 6.22(d, 1**H Ar**), 6.28 (dd, 1**H Ar**), 6.71 (d, 1**H Ar**).

3,4-diethoxyaniline, XXab.

By replacing 2-ethoxy-1-methoxy-4-nitrobenzene (**XIXaa**) in example **XXaa** by 1,2-diethoxy-4-nitrobenzene (**XIXab**) and proceeding in the same manner, the abovenamed product is obtained. Yield : 80 %.^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.36-1.46 (m, 6H, 2 times -CH_3), 3.44 (s, 2H exchangeable, -NH_2), 3.97-4.07 (m, 4H, 2 x OCH_2), 6.19 (dd, 1**H Ar**), 6.23 (d, 1**H Ar**), 6.73 (d, 1**H Ar**).

(2-amino-4,5-dimethoxyphenyl)(phenyl)methanone, XXIaa.

Under an inert atmosphere at 0°C, add to a solution of 35 ml of boron tribromide (1M/CH_2Cl_2, 35.8 mmol), 5 g of 3,4-dimethoxyaniline (32.6 mmol) dissolved in 30 ml of dichloroethane, 6.7 ml of benzonitrile (65.2 mmol), and 4.79 g of $AlCl_3$ (35.8 mmol). Stir at room temperature for 30 minutes. Evaporate the dichloromethane. Heat under reflux for 12 hours. Allow to cool. Add 35 ml of 1 M HCl at 0°C, stir at 75°C for 1 hour. Add 150 ml of water and extract three times with 200 ml of CH_2Cl_2. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt 1/hexane 2). One obtains 6.1 g of the abovenamed product as a yellow powder. Yield : 73 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.66 (s, 3H, -OCH_3), 3.92 (s, 3H, -OCH_3), 6.22 (s, 2H exchangeable + 1H, 1**H Ar** + -NH_2), 6.95 (s, 1**H Ar**), 7.46-7.51 (m, 3**H Ar**), 7.61-7.64 (m, 2**H Ar**).

(2-amino-4-bromophenyl)(4-bromophenyl)methanone, XXIab.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 3-bromoaniline, and benzonitrile by 4-bromobenzonitrile, and proceeding in the same manner, the abovenamed product is obtained. Yield : 17 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : 6.18 (s,

2H exchangeable , -NH_2), 6.76 (dd, 1**H Ar**), 6.97 (d, 1**H Ar**), 7.30 (t, 1**H Ar**), 7.61 (AB system, ? d = 0.13, J_{AB} = 8.3, 4**H Ar**).

(2-amino-5-iodophenyl)[3-(trifluoromethyl)phenyl]methanone, XXIac.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 4-iodoaniline, and benzonitrile by 3-trifluoromethyl-benzonitrile, and proceeding in the same manner, the abovenamed product is obtained. Yield: 10 %. ^{1}H-NMR (DMSO, 300 MHz) : d 6.41 (d, 2**H Ar**), 6.74 (m, 1**H Ar**), 7.06 (d, 1**H Ar**), 7.26-7.38 (m, 2**H Ar**), 7.55-7.58 (m, 1**H Ar**).

2-amino-3-bromo-4,5-dimethoxybenzophenone, XXIad

To a solution of 900 mg (3.5 mmol) of (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**) in 60 ml of DMSO, add dropwise at 0°C 15 g of HBr 40 % by weight in water. Heat at 60°C for 24 hours. Add 400 ml of H_2O and extract four times with 200 ml of AcOEt; dry on $MgSO_4$, evaporate the AcOEt and purify by silica chromatography (AcOEt 1 / hexane 4). Yield : 65 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.67 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.59 (s, 2H, NH_2), 7.06 (s, 1**H Ar**), 7.47-7.65 (m, 5**H Ar**). Mass : $(M + H)^+$ = 335.98 + 337.98.

(2-amino-5-methoxyphenyl)[3-(trifluoromethyl)phenyl]methanone, XXIae.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 4-methoxyaniline, and benzonitrile by 3-trifluoromethyl-benzonitrile, and proceeding in the same manner, the abovenamed product is obtained. Yield: 23 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.70 (s, 3H, OCH_3), 6.18-6.24 (m, 2**H Ar**), 6.35 (s, 2H exchangeable, -NH_2), 7.35-7.81 (m, 6**H Ar**).

(2-amino-4,5-dimethoxyphenyl)(4-bromophenyl)methanone, XXIaf.

By replacing benzonitrile in example **XXIaa** by 4-bromobenzonitrile and proceeding in the same manner, the abovenamed product is obtained. Yield: 82 %. ^{1}H-NMR ($CDCl_3$,

300 MHz) : d 3.67 (s, 3H, -OCH_3), 3.91 (s, 3H, -OCH_3), 6.20 (s, 2H exchangeable + 1H, 1**H Ar** + -NH_2), 6.86 (s, 1**H Ar**), 7.55 (AB system, ? d = 0.10, J_{AB} = 8.7, 4**H Ar**).

(2-amino-4,5-diethoxyphenyl)(phenyl)methanone, XXIag.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 3,4-diethoxyaniline (**XXab**). By purifying by chromatography (AcOEt 1 / hexane 4), and proceeding in the same manner, the abovenamed product is obtained. Yield : 35 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.32 (t, 3H, -CH_3), 1.48 (t, 3H, -CH_3), 3.85 (q, 2H, OCH_2), 4.10 (q, 2H, OCH_2), 6.19 (s, 1**H Ar**), 6.23 (s, 2H exchangeable, -NH_2), 6.99 (s, 1**H Ar**), 7.42-7.62 (m, 5**H Ar**).

(7-amino-2,3-dihydro-1,4-benzodioxin-6-yl)(phenyl)methanone, XXIah.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 2,3-dihydro-1,4-benzodioxin-6-amine and proceeding in the same manner, the abovenamed product is obtained. Yield : 49 %. The product is used as is.

(2-amino-4,5-dimethoxyphenyl)(3-bromophenyl)methanone, XXIai.

By replacing benzonitrile in example **XXIaa** by 3-bromobenzonitrile and proceeding in the same manner, the abovenamed product is obtained. Yield : 32 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.70 (s, 3H, -OCH_3), 3.95 (s, 3H, -OCH_3), 6.23 (s, 1**H Ar**), 6.28 (s, 2H exchangeable, -NH_2), 6.88 (s, 1**H Ar**), 7.32 (s, 1**H Ar**), 7.40 (s, 1**H Ar**), 7.53-7.59 (m, 1**H Ar**), 7.63-7.69 (m, 1**H Ar**), 7.78-7.80 (m, 1**H Ar**).

(2-amino-4,5-dimethoxyphenyl)(2-bromophenyl)methanone, XXIaj.

By replacing benzonitrile in example **XXIaa** by 2-bromobenzonitrile and proceeding in the same manner, the abovenamed product is obtained. Yield : 30 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.60 (s, 3H, -OCH_3), 3.92 (s, 3H, -OCH_3), 6.20 (s, 1**H Ar**), 6.51 (s, 2H exchangeable, -NH_2), 6.57 (s, 1**H Ar**), 7.29-7.42 (m, 3**H Ar**), 6.64-7.69 (m, 1**H Ar**).

(2-amino-4-ethoxy-5-methoxyphenyl)(phenyl)methanone, XXIak.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 3-ethoxy-4-methoxyaniline (**XXaa**). By purifying by chromatography (AcOEt 1 / hexane 4) and proceeding in the same manner, the abovenamed product is obtained. Yield : 53 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.52 (t, 3H, -CH_3), 3.66 (s, 3H, OCH_3), 4.13 (q, 2H, OCH_2), 6.19 (s, 2H exchangeable, -NH_2), 6.20 (s, 1**H Ar**) 6.95 (s, 1**H Ar**), 7.43-7.64 (m, 5**H Ar**).

(2-amino-4-methoxyphenyl)(phenyl)methanone, XXIal.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 3-methoxyaniline. By purifying by chromatography (AcOEt 1 / hexane 4) and proceeding in the same manner, the abovenamed product is obtained. Yield : 68 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.82 (s, 3H, OCH_3), 6.15-6.20 (m, **2H Ar**), 6.37 (s, 2H exchangeable, -NH_2), 7.38-7.65 (m, 6**H Ar**).

(2-amino-5-methoxyphenyl)(phenyl)methanone, XXIam.

By replacing 3,4-dimethoxyaniline in example **XXIaa** by 4-methoxyaniline. By purifying by chromatography (AcOEt 1 / hexane 4) and proceeding in the same manner, the abovenamed product is obtained. Yield : 43 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.66 (s, 3H, OCH_3), 5.72 (s, 2H exchangeable, -NH_2), 6.73 (d, 1**H Ar**), 6.96-7.02 (m, 2**H Ar**), 7.44-7.54 (m, 3**H Ar**), 7.67-7.70 (m, 2**H Ar**).

(2-amino-5- hydroxy-4-methoxyphenyl)(phenyl)methanone, XXIan.

To 400 mg (1.55 mmol) of (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**), add dropwise 2.1 ml of HBr 40% by weight in water. Heat at 95°C for 12 hours. At 0°C add ammonia to pH = 8.9. Add 100 ml H_2O and extract three times with 100 ml of CH_2Cl_2. Dry on $MgSO_4$, evaporate the CH_2Cl_2 and purify by silica chromatography (AcOEt 1/hexane 4 then 1/1). Yield : 45 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.92 (s, 3H, OCH_3), 6.20 (s, 1**H Ar**), 7.00 (s, 1**H Ar**), 7.42-7.61 (m, 5**H Ar**).

(2-amino-5-ethoxy-4-methoxyphenyl)(phenyl)methanone, XXIao.

At 0°C under an inert atmosphere, add 50 mg (1.25 mmol) of 60 % NaH in oil to a solution of 300 mg (1.23 mmol) of (2-amino-5-hydroxy-4-methoxyphenyl)(phenyl)methanone (**XXIan**) in 5 ml of DMF. Stir at room temperature for 1 hour. Add dropwise at 0°C 210 mg (1.35 mmol) of ethyl iodide. Stir at room temperature overnight. Add 50 ml of H_2O and extract three times with 50 ml of AcOEt; dry on $MgSO_4$, evaporate the AcOEt and purify by silica chromatography (AcOEt 1/hexane 1). Yield : 85 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.26–1.36 (m, 3H, OCH_2CH_3), 3.81-3.87 (m, 2H, OCH_2CH_3), 3.90 (s, 3H, OCH_3), 6.20 (s, 1**H Ar**), 6.96 (s, 1**H Ar**), 7.42-7.61 (m, 4**H Ar**).

4.2. Synthesis of compounds represented by formula XXII

The following compounds were synthesized :

7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaa**.
8-bromo-5-(4-bromophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIab**.
7-iodo-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIac**.
7,8-dimethoxy-3-isobutyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIad**.
7-methoxy-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIae**.
5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaf**.
7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIag**.
10-phenyl-2,3,6,8-tetrahydro-7H-[1,4] dioxino [2,3-h][1,4]benzodiazepin-7-one, **XXIIah**.
7,8-diethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIai**.
3-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaj**.
5-(3-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIak**.
5-(2-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIal**.
8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIam**.

8-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIan**.

7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIao**.

3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIap**.

7,8-dimethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaq**.

7,8-dimethoxy-3-(1H-imidazol-4-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIar**.

7,8-dimethoxy-3-(1H-indol-3-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIas**.

7,8-dimethoxy-3-(2-methylthioethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIat**.

(S) 3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIau**.

(7,8-dimethoxy-5-phenyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl (S)-butylcarbamate, **XXIIav**.

(S)-3-(4-aminobutyl)-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaw**.

(S)-N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]acetamide, **XXIIax**.

N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]guanidinium (S)-bis trifluoroacetate, **XXIIay**.

7,8-dimethoxy-3,5-diphenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIaz**.

3,5-diphenyl-8-ethoxy-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIba**.

3-benzyl-8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIbb**.

5-phenyl-7-ethoxy -8-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **XXIIbc**.

7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaa.

Heat under reflux for 36 hours under an inert atmosphere a mixture of 4.5 g (17.6 mmol) of (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**), 5 g (36 mmol) of ethyl glycinate hydrochloride, and 30 ml of anhydrous pyridine. Add four 2.5 g (18 mmol) fractions of ethyl glycinate hydrochloride, every 6 hours. Allow to equilibrate to room temperature. Evaporate to dryness. Add 200 ml of water. Extract three times with 300

ml of dichloromethane. Dry the organic fractions on Na_2SO_4 Purify by chromatography (AcOEt 3/hexane 1/ 3% triethylamine). Recrystallize in EtOH/EtO_2. One obtains 2.2 g of the abovenamed product in the form of colorless crystals. Yield : 43 %. M :248-250°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 3.71 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.31 (s, 2H, CH_2), 6.64 (s, 1**H Ar**), 6.70 (s, 1**H** Ar), 7.27-7.59 (m, 5**H Ar**), 9.40 (s, 1H exchangeable, -N**H**).

8-bromo-5-(4-bromophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIab.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4-bromophenyl)(4-bromophenyl) methanone **(XXIab)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 3 %. M : 299°C. ^{1}H-NMR (DMSO, 200 MHz) : d 4.18 (s, 2H, CH_2), 7.21 (d, 1**H Ar**), 7.35-7.46 (m, 5**H Ar**), 7.63-7.68 (m, 2**H Ar**), 10.65 (s, 1H exchangeable, -N**H**).

7-iodo-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIac.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-5-iodophenyl)[3-(trifluoromethyl)phenyl] methanone **(XXIac)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 5 %. M : 209°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 4.36 (s, 2H, CH_2), 6.92 (d, 1**H Ar**), 7.51-7.59 (m, 2**H** Ar), 7.76-7.89 (m, 4**H** Ar), 8.30 (s, 1H exchangeable, -N**H**).

7,8-dimethoxy-3-isobutyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIad.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl leucinate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 30 %. M : 198-201°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 0.85-0.87 (m, 3H, CH_3), 1.03-1.05 (m, 3H, CH_3), 1.94-2.05 (m, 2H, CH_2), 2.3-2.4 (m, 1HCH_2), 3.62-3.68 (m,

1HCH_2), 3.74 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.63 (s, 1**H Ar**), 6.73 (s, 1**H Ar**), 7.37-7.58 (m, 5**H Ar**), 9.04 (s, 1H, N**H**).

7-methoxy-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIae.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-5-methoxyphenyl)[3-(trifluoromethyl) phenyl]methanone **(XXIae)** and proceeding in the same manner, the abovenamed product is obtained. Yield: 75 %. M : 197-199°C. ^{1}H-NMR (DMSO, 300 MHz): d 3.68 (s, 3H, OCH_3), 4.16 (s, 2H, CH_2), 6.74 (s, 1**H Ar**), 7,23 (s, 1**H** Ar), 7.68-7.90 (m, 4**H Ar**), 10.41 (s, 1H exchangeable, -N**H**).

5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaf.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-dimethoxyphenyl)(4-bromophenyl) methanone **(XXIaf)** and proceeding in the same manner, the abovenamed product is obtained. Yield: 43 %. Yield : 73 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.74 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 4.30 (s, 2H, CH_2), 6.78 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.50 (AB system, ? d = 0.08, J_{AB} = 8.3, 4**H Ar**), 8.75 (s, 1H exchangeable, -N**H**).

7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIag.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-diethoxyphenyl)(phenyl)methanone **(XXIag)** and proceeding in the same manner, the abovenamed product is obtained. Yield: 60 %. M : 233-236°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 1.39 (t, 3H, CH_3), 1.54 (t, 3H, CH_3), 3.94 (q, 2H, OCH_2), 4.18 (q, 2H, OCH_2), 4.35 (s, 2H, CH_2), 6.66 (s, 1**H Ar**), 6.74 (s, 1**H** Ar), 7.36-7.63 (m, 5**H Ar**), 9,51 (s, 1H exchangeable, -N**H**).

10-phenyl-2,3,6,8-tetrahydro-7H-[1,4] dioxino [2,3-h][1,4]benzodiazepin-7-one, XXIIah.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (7-amino-2,3-dihydro-1,4-benzodioxin-6-yl)(phenyl) methanone **(XXIah)** and proceeding in the same manner, the abovenamed product is obtained. Yield: 15 %. M : 263-265°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 4.21-4.49 (m, 6H, -OCH_2CH_2O- + CH_2), 6.64 (s, 1**H Ar**), 6.80 (s, 1**H** Ar), 7.32-7.58 (m, 5**H Ar**), 8,37 (s, 1H exchangeable, -N**H**).

7,8-diethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIai.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-diethoxyphenyl)(phenyl)methanone **(XXIag),** and ethyl glycinate hydrochloride by methyl analilate hydrochloride, and proceeding in the same manner, the abovenamed product is obtained. Yield: 13 %. M :195-198°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 1.39 (t, 3H, CH_3), 1.54 (t, 3H, CH_3), 1.77 (d, 3H, CH_3), 3.80 (q, 1H, CH), 3.94 (q, 2H, OCH_2), 4.18 (q, 2H, OCH_2), 6.64 (s, 1**H Ar**), 6.75 (s, 1**H** Ar), 7.36-7.63 (m, 5**H Ar**), 9.10 (s, 1H exchangeable, -N**H**).

3-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaj.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-diethoxyphenyl)(phenyl)methanone **(XXIag),** and ethyl glycinate hydrochloride by methyl phenylanalilate hydrochloride, and proceeding in the same manner, the abovenamed product is obtained. Yield: 19 %. M : 110-112°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 1.38 (t, 3H, CH_3), 1.55 (t, 3H, CH_3), 3.61-3.66 (m, 2H, CH_2), 3.82-3.98 (m, 3H, C**H** + OCH_2), 4.18 (q, 2H, OCH_2), 6.64 (s, 1**H Ar**), 6,75 (s, 1**H** Ar), 7.25-7.57 (m, 10**H Ar**), 8.65 (s, 1H exchangeable, -N**H**).

5-(3-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIak.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-dimethoxyphenyl)(3-bromophenyl) methanone **(XXIai)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 72 %. M : 256-258°C. ^{1}H-NMR (DMSO, 300 MHz) : d 3.61 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.10 (s, 2H, CH_2), 6.69 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.37-7.45 (m, 2**H Ar**), 7.67-7.73 (m, 2**H Ar**), 10.34 (s, 1H exchangeable, -N**H**).

5-(2-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIal.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4,5-dimethoxyphenyl)(2-bromophenyl) methanone **(XXIaj)** and proceeding in the same manner, the abovenamed product is obtained. Yield: 27 %. M : 280-281°C. ^{1}H-NMR (DMSO, 300 MHz) : d 3.49 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.12 (s, 2H, CH_2), 6.33 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.36-7.42 (m, 1**H Ar**), 7.49-7.51 (m, 2**H Ar**), 7.63-7.65 (m, 1**H Ar**), 10.43 (s, 1H exchangeable, -N**H**).

8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIam.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4-ethoxy-5-methoxyphenyl)(phenyl) methanone **(XXIak)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 60 %. ^{1}H-NMR ($CDCl_3$, 300 MHz): d 1.54 (t, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.17 (q, 2H, OCH_2), 4.33 (s, 2H, CH_2), 6.58 (s, 1**H Ar**), 6.73 (s, 1**H** Ar), 7.40-7.47 (m, 3**H Ar**), 7.58-7.61 (m, 3**H Ar**), 8.47 (s, 1H exchangeable, -N**H**).

8-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIan.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-4-methoxyphenyl)(phenyl)methanone **(XXIal)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 48 %. M : 174-176°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 3.87 (s, 3H, OCH_3), 4.32 (s, 2H, CH_2), 6.63-6.72 (m, 2**H Ar**), 7.20-7.56 (m, 6**H Ar**), 9.33 (s, 1H exchangeable, -N**H**).

7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIao.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl) methanone **(XXIaa)** in example **XXIIaa** by (2-amino-5-methoxyphenyl)(phenyl)methanone **(XXIam)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 32 %. M : 220-222°C. ^{1}H-NMR ($CDCl_3$, 200 MHz): d 3.72 (s, 3H, OCH_3), 4.32 (s, 2H, CH_2), 6.78 (m, **1H Ar**), 7.01 (m, **2H Ar**), 7.33-7.48 (m, 3**H Ar**), 7.56-7.60 (m, 2**H Ar**), 8.86 (s, 1H exchangeable, -N**H**).

3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIap.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl phenylalalinate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 216-218°C. ^{1}H-NMR (DMSO, 200 MHz) : d 3.37-3.49 (m, 2H, CH_2), 3.58-3.71 (m, 4H, 1C**H** + OCH_3), 3.84 (s, 3H, OCH_3), 6.65 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.22-7.48 (m, 10**H Ar**), 10.40 (s, 1H, N**H**).

7,8-dimethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaq.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl alalinate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 50 %. M : 247-248°C. ^{1}H-NMR (DMSO, 200 MHz) : d 1.52-1.55 (m, 3H, CH_3), 3.62-3.65 (m, 4H, 1C**H** + OCH_3), 3.85 (s, 3H, OCH_3), 6.70 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.43-7.56 (m, 10**H Ar**), 10.30 (s, 1H, N**H**). Mass : $(M + H)^+ = 311.12$.

7,8-dimethoxy-3-(1H-imidazol-4-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIar.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl histidinate dihydrochloride and proceeding in the same manner, the abovenamed product is

obtained. Yield: 5 %. M : 195°C, degradation. ^{1}H-NMR (DMSO, 200 MHz) : d 3.30-3.35 (m, 2H, CH_2), 3.62 (s, 3H, OCH_3), 3.70-3.76 (m, 1H, **CH**), 3.85 (s, 3H, OCH_3), 6.70 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 6.90 (s, 1**H Imidazole**), 7.47-7.53 (m, 5**H Ar**), 7.70 (s, 1**H Imidazole**), 10.37 (s, 1H, N**H**), 12.40 (broad s, 1H, N**H**). Mass : $(M + H)^+ = 377.15$.

7,8-dimethoxy-3-(1H-indol-3-ylmethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIas.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl tryptophanate dihydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 10 %. M : 180-185°C. ^{1}H-NMR (DMSO, 200 MHz) : d 3.44-3.57 (m, 5H, 1CH_2 + OCH_3), 3.83 (s, 3H, OCH_3), 4.35-4.41 (m, 1H, **CH**), 6.64 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 6.97-7.07 (m, 2**H Ar**), 7.21-7.63 (m, 7**H Ar**), 10.37 (s, 1H, N**H**), 10.83 (s, 1H, N**H Indole**). Mass : $(M + H)^+ = 426.19$.

7,8-dimethoxy-3-(2-methylthioethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIat.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl methionate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 15 %. M : 126-128°C. ^{1}H-NMR (DMSO, 300 MHz) : d 2.04 (s, 3H, SCH_3), 2.49-2.51 (m, 2H, SCH_2), 2.59-2.72 (m, 2H, CH_2), 3.57-3.62 (m, 4H, 1**CH** + OCH_3), 3.83 (s, 3H, OCH_3), 6.68 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.42-7.54 (m, 5**H Ar**), 10.37 (s, 1H, N**H**). Mass : $(M + H)^+ = 371.12$.

(S)-3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIau.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl L-phenylalalinate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 50 %. ^{1}H-NMR (DMSO, 200 MHz) : d 3.28-3.45 (m, 2H, CH_2), 3.55-3.68 (m, 4H, 1**CH** + OCH_3), 3.80 (s, 3H, OCH_3), 6.61 (s, 1**H Ar**), 6.78 (s, 1**H Ar**), 7.15-7.43 (m, 10**H Ar**), 10.34 (s, 1H, N**H**). Mass : $(M + H)^+ = 387.14$.

(7,8-dimethoxy-5-phenyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl (S)-butylcarbamate, XXIIav.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by 377 lysine Z hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield: 20 %. M : 95-98°C. ^{1}H-NMR (DMSO, 300 MHz) : d 1.26-1.44 (m, 4H, 2C**H**$_2$), 1.95-1.97 (m, 2H, C**H**$_2$), 2.95-3.03 (m, 2H, C**H**$_2$), 3.31-3.35 (m, H, C**H**), 3.55 (s, 3H, OC**H**$_3$), 3.81 (s, 3H, OC**H**$_3$), 4.95 (s, 2H, C**H**$_2$), 6.62 (s, 1**H Ar**), 6.77 (s, 1**H Ar**), 7.20-7.29 (m, 6H, 1N**H** + 5**H Ar**), 7.39-7.47 (m, 5**H Ar**), 10.29 (s, 1H, N**H**). Mass : $(M + H)^+$ = 502.25.

(S)-3-(4-aminobutyl)-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaw.

Stir a mixture of 60 mg (0.12 mmol) of (7,8-dimethoxy-5-phenyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl (S)-butylcarbamate (**XXIIav**), 6 mg of Pd/C 10% by weight in 10 ml of MeOH under an H_2 atmosphere at room temperature and pressure for 24 hours. Filter the suspension on celite, rinse three times with 10 ml of MeOH. Evaporate to dryness and purify by silica chromatography (AcOEt then AcOEt 5/ CH_2Cl_2 4/ EtOH 1). Yield : 68 %. ^{1}H-NMR (DMSO, 200 MHz) : d 1.55-1.63 (m, 4H, 2C**H**$_2$), 1.98-2.09 (m, 2H, C**H**$_2$), 2.75-2.81 (m, 2H, C**H**$_2$), 3.60 (s, 3H, OC**H**$_3$), 3.69-3.74 (m, H, C**H**), 3.84 (s, 3H, OC**H**$_3$), 6.67 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.41-7.53 (m, 5**H Ar**), 8.26 (broad s, 2H, N**H**$_2$), 10.37 (s, 1H, N**H**). Mass : $(M + H)^+$ = 368.21.

(S)-N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]acetamide, XXIIax.

To a solution of 20 mg (0.054 mmol) of (S)-3-(4-aminobutyl)-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaw**), add dropwise 11 mg (0.135 mmol) of pyridine in 2 ml of CH_2Cl_2, 6.5 mg (0.065 mmol) of acetic anhydride. Stir for 24 hours. Evaporate to dryness and purify by silica chromatography (AcOEt then AcOEt 5/ CH_2Cl_2 4/ EtOH 1). Yield : 98 %. M : 82-84°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.45-

1.66 (m, 4H, $2CH_2$), 1.97 (s, 3H, $COCH_3$), 2.22-2.27 (m, 2H, CH_2), 3.25-3.35 (m, 2H, CH_2), 3.53-3.57 (m, H, **CH**), 3.75 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 5.76 (broad s, 1H, AcN**H**), 6.57 (s, 1**H Ar**), 6.74 (s, 1**H Ar**), 7.39-7.58 (m, 5**H Ar**),), 8.07 (s, 1H, N**H**). Mass : $(M + H)^+ = 410.21$.

N-[4-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)butyl]guanidinium (S)-bis trifluoroacetate, XXIIay.

To a solution of 14 mg (0.04 mmol) of 1H-pyrazole-1-[N, N'-bis(*ter*-butoxycarbonyl)carboxamide] in 1 ml of anhydrous CH_3CN, add 20 mg (0.054 mmol) of (S)-3-(4-aminobutyl)-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaw**). Stir for 12 hours. Evaporate to dryness and purify by silica chromatography (AcOEt 1/ hexane 4). Add 2 ml of TFA at 0°C and stir at room temperature for 3 hours. Evaporate the TFA, take up in AcOEt, remove the supernatant, triturate in Et_2O, dry. Yield : 30 %. Mass : $(M + H)^+ = 410.15$.

7,8-dimethoxy-3,5-diphenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIaz.

By replacing ethyl glycinate hydrochloride in example **XXIIaa** by ethyl phenylglycinate hydrochloride and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 202-204°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.62-3.78 (m, 4H, C**H** + OCH_3), 3.93 (s, 3H, OCH_3), 6.61 (s, 1**H Ar**), 6.66 (s, 1**H Ar**), 7.24-7.50 (m, 10**H Ar**), 9.14 (s, 1H, N**H**).

3,5-diphenyl-8-ethoxy-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIba.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**) in example **XXIIaa** by (2-amino-4-ethoxy-5-methoxyphenyl)(phenyl)methanone **XXIak,** and ethyl glycinate hydrochloride by ethyl phenylglycinate hydrochloride, and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 168-169°C. ^{1}H-NMR (DMSO, 200 MHz) : d 1.38-1.42 (m, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.98-4.18 (m,

2H, CH_2), 4.76 (s, 1H, CH), 6.78 (s, 1H Ar), 6.88 (s, 1H Ar), 7.38-7.58 (m, 10H Ar), 10.49 (s, 1H, NH).

3-benzyl-8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIbb.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**) in example **XXIIaa** by (2-amino-4-ethoxy-5-methoxyphenyl)(phenyl)methanone **(XXIak),** and ethyl glycinate hydrochloride by ethyl phenylalalinate hydrochloride, and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 190-193°C. ^{1}H-NMR (DMSO, 200 MHz) : d 1.33-1.39 (m, 3H, CH_3), 3.36-3.64 (m, 3H, CH + CH_2Bn), 3.73 (s, 3H, OCH_3), 3.95-4.10 (m, 2H, CH_2), 6.59 (s, 1H Ar), 6.77 (s, 1H Ar), 7.21-7.44 (m, 10H Ar), 10.36 (s, 1H, NH).

5-phenyl-7-ethoxy -8-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, XXIIbc.

By replacing (2-amino-4,5-dimethoxyphenyl)(phenyl)methanone (**XXIaa**) in example **XXIIaa** by (2-amino-5-ethoxy-4-methoxyphenyl)(phenyl)methanone **(XXIao)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 45 %. M : °C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.36-1.44 (m, 3H, CH_3), 3.88-4.00 (m, 5H, OCH_2 + OCH_3), 4.30-4.42 (m, 2H, CH_2), 6.62 (s, 1H Ar), 6.73 (s, 1H Ar), 7.44-7.58 (m, 10H Ar), 8.88 (s, 1H, NH).

4.3. Synthesis of compounds represented by formula II

The following compounds were synthesized :

5-(4-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIba**.

3-benzyl-8-ethoxy-1-ethyl-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbb**.

1-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbc**.

1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbd**.

7,8-dimethoxy-5-phenyl-1-propyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbe**.

7,8-diethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbf**.

7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbg**.

7,8-dimethoxy-1-ethyl-3-(2-nitrobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbh**.

ethyl (7,8-diethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-1-yl)acetate, **IIbi**.

1-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbj**.

1-ethyl-7,8-dihydroxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbk**.

5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbl**.

5-(3-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbm**.

5-{4-[3-(benzyloxy)prop-1-ynyl]phenyl}-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbn**.

tert-butyl 3-[4-(1-ethyl-7,8-dimethoxy-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-5-yl)phenyl]prop-2-ynylcarbamate, **IIbo**.

5-(1,1'-biphenyl-4-yl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbp**.

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbq**.

1-ethyl-7,8-dimethoxy-5-[4-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbr**.

3-allyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbs**.

1-ethyl-7,8-dimethoxy-5-phenyl-3-prop-2-ynyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbt**.

1-ethyl-7,8-dimethoxy-5-[4-(2-phenylethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbu**.

ethyl (1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetate, **IIbv**.

1-ethyl-7,8-dimethoxy-5-[3-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbw**.

3-(3,5-dibromobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbx**.

7,8-dimethoxy-3-(diphenylhydroxymethyl)-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIby**.

7,8-dimethoxy-1-ethyl-3-(E-3-phenylpropen-2yl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIbz**.

7,8-dimethoxy-1-ethyl-3-(2-aminobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIca**.

(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetonitrile, **IIcb**.

3-(2-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcc**.

3-(4-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcd**.

3-(2-cyanobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIce**.

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]acetamide, **IIcf**.

3-(2-aminomethylbenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcg**.

3-[(3-bromophenyl)(hydroxy)methyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIch**.

[(7,8-dimethoxy-1-ethyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benz-2-yl]carboxamide, **IIci**.

3-(3-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcj**.

3-(1,1'-biphenyl-4-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIck**.

3-(1-benzyl-4-hydroxypiperidin-4-yl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcl**.

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]methylacetamide, **IIcm**.

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcn**.

3-(2,4-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIco**.

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, **IIcp**.

3-benzyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcq**.

1-ethyl-7,8-dimethoxy-3-(2-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcr**.

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide, **IIcs**.

3-[3-(aminomethyl)benzyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIct**.

3-(1,1'-biphenyl-3-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcu**.

3-benzyl-7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcv**.

2-(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetamide, **IIcw**.

7,8-dimethoxy-1-(2-hydroxyethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcx**.

3-(2-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcy**.

1-ethyl-7,8-dimethoxy-3-(2-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIcz**.

8-ethoxy-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIda**.

1-ethyl-7,8-dimethoxy-5-phenyl-3-[3-(trifluoromethyl)benzyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdb**.

1-ethyl-7,8-dimethoxy-3-(3-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdc**.

1-ethyl-7,8-dimethoxy-3-(4-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdd**.

3-[1,2-bis(4-bromophenyl)ethyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIde**.

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, **IIdf**.

2-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, **IIdg**.

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide, **IIdh**.

3-(2,5-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdi**.

(S)-3-benzyl-7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdj**.

3,5-diphenyl-8-ethoxy-1-ethyl-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdk**.

7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdl**.

8-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, **IIdm**.

5-(4-bromophenyl)-7,8-dimethoxy-1-methyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIba.

To a solution of 100 mg (0.267 mmol) of 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIaf)** in 2 ml of anhydrous DMF, add under an inert atmosphere 48 mg (0.35 mmol) of K_2CO_3. After 30 minutes at room temperature, add dropwise 25 µl (0.4 mmol) of MeI. Allow to stand at room temperature for 12 hours. Add 30 ml of water. Extract three times with 30 ml of EtO_2. Dry the organic fractions on Na_2SO_4. Purify by chromatography (AcOEt 1/hexane 1). Recrystallize in EtO_2. One obtains 78 mg of the abovenamed product as a white powder. Yield : 73 %. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.40 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 4.29 (AB system, ? d = 1.014, J_{AB} = 10.7, 2H, CH_2), 6.65 (s, 1**H Ar**), 6.78 (s, 1**H Ar**), 7.54 (s, 4**H Ar**).

3-benzyl-8-ethoxy-1-ethyl-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbb.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 3-benzyl-8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIbb**), and methyl iodide by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield: 65 %. F : 228-230°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.03-1.08 (m, 3H, NCH_2CH_3), 1.50-1.54 (m, 3H, OCH_2CH_3), 3.59-3.65 (m, 3H, 1HNCH_2 + CH_2Bn), 3.70 (s, 3H, OCH_3), 3.77-3.83 (m, 1H, 1C**H**), 4.12-4.18 (m, 2H, OCH_2), 4.30-4.41 (m, 1H, 1HNCH_2), 6.62 (s, 1**H Ar**), 6.79 (s, 1**H Ar**), 7.22-7.59 (m, 10**H Ar**).

1-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbc.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaa**), and MeI by benzyl bromide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 64 %. M : 148-149°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 3.67 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.38 (AB system, ? d = 0.96, J_{AB} = 10.0 2H, CH_2), 5.15 (AB system, ? d = 0.70, J_{AB} = 15.4, 2H, -NCH_2), 6.56 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.07-7.46 (m, 10**H Ar**).

1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbd.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaa**), and MeI by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 62 %. M : 86-88°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.15 (t, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.03 (AB system, ? d = 0.61, J_{AB} = 13.9, 2H, -NCH_2), 4.30 (AB system, ? d = 1.00, J_{AB} = 9.98, 2H, CH_2), 6.71 (s, 1**H Ar**), 6.88 (s, 1**H Ar**), 7.40-7.69 (m, 5**H Ar**).

7,8-dimethoxy-5-phenyl-1-propyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbe.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaa**), and MeI by (n)-propyl bromide, and proceeding in the same manner, the abovenamed product is obtained. Yield: 33 %. M : 136-138°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 0.75 (t, 3H, CH_3), 1.48 (m, 2H, CH_2), 3.75 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 3.94 (AB system, ? d = 0.87 J_{AB} = 13.4, 2H, -NCH_2), 4.28 (AB system, ? d = 0.97, J_{AB} = 10.26, 2H, CH_2), 6.68 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.40-7.66 (m, 5**H Ar**).

7,8-diethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbf.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIag**) and proceeding in the same manner, the abovenamed product is obtained. Yield: 28 %. M : 116-118°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.40 (t, 3H, CH_3), 1.56 (t, 3H, CH_3), 3.42 (s, 3H, NCH_3), 3.97 (q, 2H, OCH_2), 4.21 (q, 2H, OCH_2), 4.33 (AB system, ? d = 0.98 J_{AB} = 10.5, 2H, CH_2), 6.74 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.42-7.70 (m, 5**H Ar**).

7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbg.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIag**), and MeI by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 59 %. M : 99-102°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.11 (t, 3H, CH_3), 1.36 (t, 3H, CH_3), 1.53 (t, 3H, CH_3), 3.93 (q, 2H, OCH_2), 3.97 (AB system, ? d = 0.67, J_{AB} = 14.0, 2H, -NCH_2), 4.17 (q, 2H, OCH_2), 4.28 (AB system, ? d = 0.96 J_{AB} = 10.0, 2H, CH_2), 6.68 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.38-7.64 (m, 5**H Ar**).

7,8-dimethoxy-1-ethyl-3-(2-nitrobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbh.

To a solution of 920 µl (1.84 mmol) of 2M LDA / THF in 5 ml of anhydrous THF, add dropwise at -78°C under an inert atmosphere a solution of 300 mg (0.92 mmol) of 1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbd)** in 2 ml of THF. Allow to equilibrate to room temperature for 30 minutes. Add dropwise at -30°C a solution of 220 mg (1.01 mmol) of 2-nitrobenzyl bromide in 2 ml of THF. Stir at room temperature for 12 hours. Add 1 ml ofH_2O. Evaporate the THF. Purify by silica chromatography (AcOEt 1/ hexane 4, 1 / 1, then AcOEt). Recrystallize in EtOH /cHexane. Yield : 35 %. M : 158-160°C. ^{1}H-NMR (DMSO, 300 MHz) : d 0.87-0.91 (m, 3H, CH_3), 3.61-3.99 (m, 10H, NC**H** + $CHCH_2$ + $2OCH_3$), 4.35-4.40 (m, 1H, NC**H**), 6.60 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.37-7.90 (m, 9**H Ar**). Mass : $(M + H)^+ = 460.88$.

ethyl (7,8-diethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-1-yl)acetate, IIbi.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIaf)** in example **IIba** by 7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIag)**, and MeI by ethyl bromoacetate, and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 160-162°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.21 (t, 3H, CH_3), 1.36 (t, 3H, CH_3), 1.50 (t, 3H, CH_3), 3.88-4.26 (m, 7H, 3 x OCH_2 + 1H CH_2) 4.49 (AB system, ? d = 0.17, J_{AB} = 17.4, 2H, -NCH_2), 4.80 (m, 1H CH_2), 6.71 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.27-7.69 (m, 5**H Ar**).

1-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbj.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIaf)** in example **IIba** by 7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIag)**, and MeI by benzyl bromide, and proceeding in the same manner, the abovenamed product is obtained. Yield: 32 %. M : 158-160°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.33 (t, 3H, CH_3), 1.40 (t, 3H, CH_3), 3.84-3.95 (m, 3H, OCH_2 + 1H CH_2) 4.04 (q, 2H OCH_2), 4.87 (m, 1H CH_2), 5.15 (AB system, ? d = 0.74, J_{AB} = 15.4, 2H, -NCH_2), 6.58 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.07-7.46 (m, 10**H Ar**).

1-ethyl-7,8-dihydroxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbk.

Add dropwise at 0°C under an inert atmosphere, 0.68 ml of a 1 M solution of BBr_3 (0.68 mmol) in CH_2Cl_2 on 200 mg (0.62 mmol) of 7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbg)** in 5 ml of dichloromethane. Stir at room temperature for 12 hours. Quench at 0°C with methanol. Evaporate to dryness. Triturate again and evaporate. Purify by chromatography (AcOEt). Recrystallize in EtO_2/pentane. One obtains 30 mg of the abovenamed product as a yellow powder. Yield : 16 %. M : 230-231°C. ^{1}H-NMR (DMSO, 200 MHz) : d 0.96 (t, 3H, CH_3), 3.80 (AB system, ? d = 0.54, J_{AB} = 13.7, 2H, -NCH_2), 4.05 (AB system, ? d = 0.72, J_{AB} = 10.0, 2H, CH_2), 6.52 (s, 1**H Ar**), 6.91 (s, 1**H Ar**), 7.42-7.55 (m, 5**H Ar**), 9-10.5 (hump, 2H, 2 x –**OH**).

5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbl.

By replacing MeI in example **IIba** by iodoethane and proceeding in the same manner, the abovenamed product is obtained. Yield: 76 %. M : 93-95°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 3.98 (AB system, ? d = 0.54, J_{AB} = 14.2, 2H, -NCH_2), 4.25 (AB system, ? d = 0.98, J_{AB} = 10.3, 2H, CH_2), 6.63 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.53 (s, 4**H Ar**).

5-(3-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbm.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIaf)** in example **IIba** by 5-(3-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(XXIIak)**, and MeI by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 17 %. M : 122-126°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.14 (s, 3H, CH_3), 3.79-3.85 (m, 4H, 1H CH_2 + OCH_3), 3.99 (AB system, ? d = 0.62, J_{AB} = 13.9, 2H, -NCH_2), 4.04 (s, 3H, OCH_3), 4.78 (m, 1H, CH_2), 6.65 (s, 1**H Ar**), 6.86 (s, 1**H Ar**), 7.26-7.31 (m, 2**H Ar**), 7.52-7.62 (m, 2**H Ar**), 7.86 (s, 1**H Ar**).

5-{4-[3-(benzyloxy)prop-1-ynyl]phenyl}-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbn.

Stir for 12 hours under an inert atmosphere at 50°C, a mixture of 100 mg (0.27 mmol) of 5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbl)**, 194 mg (1.3 mmol) of [(prop-2-ynyloxy)methyl]benzene, 9.0 mg of CuI, 5.2 mg of $PdCl_2$, 18.0 mg of PPh_3, 0.5 ml of TEA, 2 ml of CH_3CN. Evaporate to dryness and purify by silica chromatography (AcOEt 1/hexane 1). Recrystallize in EtO_2/pentane. Yield : 37 %. M : 64-66°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.12 (s, 3H, CH_3), 3.72-3.83 (m, 4H, 1H CH_2 + OCH_3), 4.00 (AB system, ? d = 0.63, J_{AB} = 13.5, 2H, -NCH_2), 4.03 (s, 3H, OCH_3), 4.43 (s, 2H, OCH_2), 4.69 (m, 2H, =C-CH_2), 4.77 (m, 1H, OCH_2), 6.65 (s, 1H **Ar**), 6.86 (s, 1H **Ar**), 7.27-7.63 (m, 9H **Ar**).

tert-butyl 3-[4-(1-ethyl-7,8-dimethoxy-2-oxo-2,3-dihydro-1H-1,4-benzo diazepin-5-yl)phenyl]prop-2-ynylcarbamate, IIbo.

By replacing [(prop-2-ynyloxy)methyl]benzene in example **IIbn** by tert-butyl-prop-2-ynylcarbamate and proceeding in the same manner, the abovenamed product is obtained. Yield: 47 %. M : 95-97°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.10 (s, 3H, CH_3), 1.47 (m, 9H, CH_3), 3.72-3.78 (m, 4H, 1H CH_2 + OCH_3), 3.96 (s, 3H, OCH_3), 3.7 (AB system, ? d = 0.64, J_{AB} = 13.5, 2H, -NCH_2), 4.16 (m, 2H, =C-CH_2), 4.81 (m, 1H, OCH_2), 4.88 (s, 1H, -NH), 6.62 (s, 1H **Ar**), 6.84 (s, 1H **Ar**), 7.42-7.59 (m, 4H **Ar**).

5-(1,1'-biphenyl-4-yl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbp.

Heat at 90°C for 12 hours under an inert atmosphere a mixture of 100 mg (0.27 mmol) of 5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbl)**, 35 mg (0.30 mmol) of benzene boronic acid, 215 µl of 2M Na_2CO_3, 25 mg (0.020 mmol) of *tetrakis*(triphenylphosphine) Pd (0) and 250 µl of EtOH in 5 ml of degassed toluene. Allow to cool to room temperature. Evaporate to dryness. Purify by chromatography (AcOEt). Recrystallize in Et_2O. One obtains 62 mg of the abovenamed product in the form of colorless crystals. Yield : 52 %. M : 149-150°C. ^{1}H-NMR

($CDCl_3$, 200 MHz) : d 1.13 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.95 (AB system, ? d = 0.57, J_{AB} = 13.7, 2H, -NCH_2), 3.98 (s, 3H, OCH_3), 4.29 (AB system, ? d = 0.99 J_{AB} = 10.0, 2H, CH_2), 6.75 (s, 1**H Ar**), 6.86 (s, 1**H Ar**), 7.37-7.75 (m, 9**H Ar**).

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbq.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 4-chlorobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 22 %. M : 78-81°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.07 (s, 3H, CH_3), 3.54 (s, 1H, C**H**), 3.56 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.99 (AB system, ? d = 0.75, J_{AB} = 13.7, 2H, -NCH_2), 6.64 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.23-7.32 (m, 4**H Ar**), 7.39-7.45 (m, 3**H Ar**), 7.55-7.58 (m, 2**H Ar**).

1-ethyl-7,8-dimethoxy-5-[4-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbr.

By replacing [(prop-2-ynyloxy)methyl]benzene in example **IIbn** by phenylacetylene and proceeding in the same manner, the abovenamed product is obtained. Yield: 80 %. M : 166-168°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.16 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.02 (AB system, ? d = 0.65, J_{AB} = 13.9, 2H, -NCH_2), 4.32 (AB system, ? d = 0.98, J_{AB} = 10.5, 2H, CH_2), 6.70 (s, 1**H Ar**), 6.88 (s, 1**H Ar**), 7.37-7.70 (m, 9**H Ar**).

3-allyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbs.

By replacing 2-nitrobenzyl bromide in example **IIbh** by allyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 46 %. M : 176-179°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.11 (s, 3H, CH_3), 3.02-3.09 (m, 2H =CH_2), 3.60-3.73 (m, 2H, C**H** + 1H -NCH_2), 3.79 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.32-4.50 (m, 1H, -NCH_2), 5.08-5.25 (m, 2H, =C-CH_2), 5.94-6.14 (m, 1H, =C**H**), 6.73 (s, 1**H Ar**), 6.87 (s, 1**H Ar**), 7.42-7.49 (m, 3**H Ar**), 7.64-7.69 (m, 2**H Ar**).

1-ethyl-7,8-dimethoxy-5-phenyl-3-prop-2-ynyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbt.

By replacing 2-nitrobenzyl bromide in example **IIbh** by propargyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield: 22 %. M : 161-163°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.07 (s, 3H, CH_3), 3.11-3.18 (m, 2H, -CH_2C=), 3.59-3.86 (m, 6H, OCH_3 + =CH + 1H NCH_2 + CH), 3.97 (s, 3H, OCH_3), 4.35-4.42 (m, 1H, NCH_2), 6.71 (s, 1**H Ar**), 6.85 (s, 1**H Ar**), 7.39-7.42 (m, 3**H Ar**), 7.62-7.66 (m, 2**H Ar**).

1-ethyl-7,8-dimethoxy-5-[4-(2-phenylethyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbu.

Leave the following under hydrogen pressure (Patm) for 48 hours : 80 mg of 5-(1,1'-biphenyl-4-yl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIbp**), 16 mg of 10 % palladium on charcoal (20% by weight of product to reduce), in 30 ml of methanol and 1 ml of CH_2Cl_2. Filter on celite, rinse several times with methanol. Evaporate to dryness. Purify by silica chromatography (AcOEt 1/hexane 1). Recrystallize in ether. One obtains 28 mg of the abovenamed product in the form of a white powder. Yield : 35%. M : 148-150°C ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.27 (t, 3H, -CH_3), 3.00 (s, 4H, 2 x –CH_2). 3,37-3,40 (m, 2H, CH_2), 3.45- 3.65 (m, 4H, -OCH_3 + 1H NCH_2), 3.92 (s, 3H, OCH_3), 4.21-4.48 (m, 1H, NCH_2), 6.22 (d, 1**H Ar**), 6.77 (d, 1**H Ar**), 7.19-7.39 (m, 9**H Ar**).

ethyl (1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzo diazepin -3-yl)acetate, IIbv.

By replacing 2-nitrobenzyl bromide in example **IIbh** by ethyl acetate bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 11 %. M : 116-118°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 3.13-3.25 (m, 1H, -OCH_2), 3.43-3.56 (m, 1H, -OCH_2), 3.63-3.78 (m, 4H, OCH_3 + 1H NCH_2),

4.00 (s, 3H, OCH_3), 4.16-4.44 (m, 4H, CH + CH_2 + 1H NCH_2), 6.71 (s, 1**H Ar**), 6.90 (s, 1**H Ar**), 7.30-7.65 (m, 5**H Ar**).

1-ethyl-7,8-dimethoxy-5-[3-(phenylethynyl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbw.

By replacing 5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIbl**) in example **IIbn** by 5-(3-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIbm**), and [(prop-2-ynyloxy)methyl]benzene by phenylacetylene, and proceeding in the same manner, the abovenamed product is obtained. Yield : 33 %. M : 100-102°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.13 (s, 3H, CH_3), 3.51-3.82 (m , 5H, 1H NCH_2 + 1H CH_2 + OCH_3), 3.97 (s, 3H, OCH_3), 4.24-4.34 (m, 1H, NCH_2), 4.74-4.80 (m, 1H, CH_2), 6.66 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.26-7.83 (m, 9**H Ar**).

3-(3,5-dibromobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbx.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3,5-dibromobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 30 %. M : 178-179°C. ^{1}H-NMR (DMSO, 300 MHz) : d 0.85-0.89 (m, 3H, CH_3), 3.28-3.36 (m, 2H, $CHCH_2$), 3.59 (s, 3H, OCH_3), 3.69-3.75 (m, 2H, NCH + $CHCH_2$), 4.20-4.27 (m, 1H, NCH), 6.60 (s, 1**H Ar**), 7.13 (s, 1**H Ar**), 7.43-7.72 (m, 8**H Ar**). Mass : $(M + H)^+$ = 573.05.

7,8-dimethoxy-3-(diphenylhydroxymethyl)-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIby.

By replacing 2-nitrobenzyl bromide in example **IIbh** by benzophenone and proceeding in the same manner, the abovenamed product is obtained. Yield : 36 %. M : 228-230°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 0.98-1.03 (m, 3H, CH_3), 3.74 (s, 3H, OCH_3), 4.00 (AB system, ? d = 0.71, J_{AB} = 13.7, 2H, NCH_2), 4.03 (s, 3H, OCH_3), 4.57 (s, 1H, CHCOH),

6.41 (s, 1H, CHCO**H**), 6.66 (s, 1**H Ar**), 6.94 (s, 1**H Ar**), 7.27-7.51 (m, 15**H Ar**). Mass : $(M + H)^+ = 507.3$.

7,8-dimethoxy-1-ethyl-3-(E-3-phenylpropen-2yl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIbz.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-bromo-1-phenylprop-1-ene and proceeding in the same manner, the abovenamed product is obtained. Yield : 37 %. M : 162-164°C. ^{1}H-NMR (DMSO, 300 MHz) : d 0.86-0.91 (m, 3H, C**H$_3$**), 2.92-3.01 (m, 2H, C**H$_2$**CH=), 3.62 (s, 3H, OC**H$_3$**), 3.88 (s, 3H, OC**H$_3$**) 3.98 (AB system, ? d = 0.55, J_{AB} = 13.6, 2H, NC**H$_2$**), 6.32-6.40 (m, 1H, CH$_2$C**H**=), 6.50-6.56 (m, 1H, PhC**H**=), 6.66 (s, 1**H Ar**), 7.15 (s, 1**H Ar**), 7.16-7.60 (m, 10**H Ar**). Mass : $(M + H)^+ = 441.24$.

7,8-dimethoxy-1-ethyl-3-(2-aminobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIca.

Stir a mixture of 80 mg (0.17 mmol) of 7,8-dimethoxy-1-ethyl-3-(2-nitrobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **IIbh**, 10 mg of Pd/C 10 % by weight in 15 ml of MeOH under 65 psi of H_2 at room temperature for 2 hours. Filter the suspension on celite, rinse three times with 10 ml of MeOH. Evaporate to dryness and purify by silica chromatography (AcOEt 1 /hexane 4, 1 / 2). Recrystallize in EtOH. Yield : 70 %. M : degradation at 280°C ^{1}H-NMR (DMSO, 300 MHz) : d 0.86-0.90 (m, 3H, C**H$_3$**), 3.21-3.31 (m, 2H, CHC**H$_2$**), 3.59 (s, 3H, OC**H$_3$**), 3.69-3.76(m, 2H, NC**H** + C**H**CH$_2$), 3.88 (s, 3H, OC**H$_3$**), 4.22-4.30 (m, 1H, NC**H**), 6.46-6.51 (m, 1**H Ar**), 6.59-6.61 (m, 2**H Ar**), 6.85-6.88 (m, 1**H Ar**), 7.01-7.03 (m, 1**H Ar**), 7.41-7.53 (m, 5**H Ar**). Mass : $(M + H)^+ = 430.22$.

(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetonitrile, IIcb.

By replacing 2-nitrobenzyl bromide in example **IIbh** by acetonitrile chloride and proceeding in the same manner, the abovenamed product is obtained but the reaction is very slow. Yield : 3 %. M : 97-100°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.13 (s, 3H,

CH_3), 3.12-3.46 (m, 2H, -CH_2-CN), 3.80 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.05 (AB system, ? d = 0.68, J_{AB} = 13.9, 2H, -NCH_2), 6.75 (s, 1**H Ar**), 6.88 (s, 1**H Ar**), 7.45-7.50 (m, 3**H Ar**), 7.68-7.72 (m, 3**H Ar**).

3-(2-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcc.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2-bromobenzyle bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 27 %. M : 102-104°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.06 (s, 3H, CH_3), 3.52-3.82 (m, 6H, OCH_3 + 1H NCH_2 + CH + 1H -CH_2Ph), 3.92-4.05 (m, 4H, + 1H -CH_2Ph + OCH_3), 4.35-4.47 (m, 1H NCH_2), 6.63 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.05-7.11 (m, 1**H Ar**), 7.30-7.50 (m, 8**H Ar**).

3-(4-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcd.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 4-bromobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 61 %. M : 97-99°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.05 (s, 3H, CH_3), 3.50-3.54 (m, 2H, CH +1H -CH_2Ph), 3.56-3.77 (m, 5H, OCH_3 + 1H NCH_2 + 1H -CH_2Ph), 3.93 (s, 3H, OCH_3), 4.28-4.45 (m, 1H NCH_2), 6.62 (s, 1**H Ar**), 6.80 (s, 1**H Ar**), 7.12-7.25 (m, 2**H Ar**), 7.35-7.37 (m, 5**H Ar**), 7.53-7.58 (m, 2**H Ar**).

3-(2-cyanobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIce.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2-cyanobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 45 %. M : 154-156°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.05-1.10 (m, 3H, CH_3), 3.59-3.97 (m, 10H, $CHCH_2$ + 2OCH_3 + 1HNCH_2), 4.34-4.41 (m, 1H, 1HNCH_2), 6.61 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.29-7.77 (m, 9**H Ar**). Mass : $(M + H)^+$ = 440.23.

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]acetamide, IIcf.

To a solution of 40 mg (0.09 mmol) of 7,8-dimethoxy-1-ethyl-3-(2-aminobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **IIca**, add 18.4 mg (0.23 mmol) of pyridine in 4 ml of CH_2Cl_2, 11.5 mg (0.11 mmol) of acetic anhydride dropwise. Stir for 24 hours. Evaporate to dryness and purify by silica chromatography (AcOEt then AcOEt 5/ CH_2Cl_2 4/ EtOH 1). Yield : 70 %. M : 144-145°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 0.89-0.96 (m, 3H, CH_3), 2.01 (s, 1H, $COCH_3$), 3.36-3.45 (m, 2H, $CHCH_2$), 3.61 (s, 3H, OCH_3), 3.73-3.84 (m, 2H, $CHCH_2$ + 1HNCH_2), 3.91 (s, 3H, OCH_3), 6.60 (s, 1**H Ar**), 7.07-7.61 (m, 10**H Ar**). Mass : $(M + H)^+ = 472.23$.

3-(2-aminomethylbenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcg.

Stir a mixture of 100 mg (0.23 mmol) of 3-(2-cyanobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **IIce**, 10 mg of Raney nickel in 5 ml of MeOH under an H_2 atmosphere at room temperature and pressure for 12 hours. Filter the suspension on celite, rinse three times with 10 ml of MeOH. Evaporate to dryness and purify by silica chromatography (AcOEt 5 / CH_2Cl_2 4 / EtOH 1, CH_2Cl_2 4 / MeOH 1). Recrystallize in EtOH. Yield : 70 %. M : 280°C with degradation. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 0.98-1.02 (m, 3H, CH_3), 3.33-3.37 (m, 1H, 1H $CHCH_2$), 3.54-3.59 (m, 5H, OCH_3 + 1H NCH_2CH_3 + 1H $CHCH_2$), 3.79-3.84 m, 1H, $CHCH_2$), 3.89 (s, 3H, OCH_3), 4.25-4.32 (m, 3H, CH_2NH_2 + 1H NCH_2CH_3), 6.40 (s, 1**H Ar**), 6.78 (s, 1**H Ar**), 7.02-7.63 (m, 10**H Ar**). Mass : $(M + H)^+ = 444.22$

3-[(3-bromophenyl)(hydroxy)methyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIch.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-bromobenzaldehyde bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 41 %. M : 85-86°C. ^{1}H-NMR (DMSO, 200 MHz) : d 0.90 (s, 3H, CH_3), 3.34-3.65 (d, 1H, CH), 3.60 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.03 (AB system, ? d = 0.58, J_{AB} = 14.4, 2H, -

NCH_2), 5.54 (dd, 1H, -CH-Ph), 5.73 (d, 1H, -OH), 6.57 (s, 1**H Ar**), 7.22 (s, 1**H Ar**), 7.28-7.49 (m, 8**H Ar**), 7.66 (s, 1**H Ar**).

[(7,8-dimethoxy-1-ethyl-2-oxo-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benz-2-yl]carboxamide, IIci.

To a solution of 100 mg (0.23 mmol) of 3-(2-cyanobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **IIce** in 2 ml of EtOH, add 80 µl of 10 % (m/m) H_2O_{2aq} and dropwise 90 µl of 0.5 M $NaOH_{aq}$. Add 50 ml of H_2O and extract three times with ml of AcOEt; dry on $MgSO_4$, evaporate the AcOEt and purify by silica chromatography (AcOEt 1 /hexane 1 then AcOEt). Recrystallize in AcOEt. Yield : 65 %. M : 193-195°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.10-1.15 (m, 3H, CH_3), 3.25-3.31 (m, 1H, 1H $CHCH_2$), 3.66-3.73 (m, 4H, OCH_3 + 1H NCH_2CH_3), 3.95-4.00 (s, 4H, OCH_3 + 1H $CHCH_2$), 4.19-4.28 (m, 1H, $CHCH_2$), 4.38-4.45 (m, 1H, 1H NCH_2CH_3), 4.74 (broad s, 2H, $CONH_2$), 6.54 (s, 1**H Ar**), 6.88 (s, 1**H Ar**), 7.09-7.85 (m, 10**H Ar**). Mass : $(M+H)^+ = 458.23$.

3-(3-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcj.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-bromobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 56 %. M : 140-142°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.07 (s, 3H, CH_3), 3.52-3.77 (m, 7H, CH + $-CH_2Ph$ + OCH_3 + 1H NCH_2), 3.96 (s, 3H, OCH_3), 4.32-4.43 (m, 1H NCH_2), 6.63 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.15-7.19 (m, 1**H Ar**), 7.26-7.45 (m, 5**H Ar**), 7.55-7.60 (m, 3**H Ar**).

3-(1,1'-biphenyl-4-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIck.

By replacing 5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIbl**) in example **IIbp** by 3-(4-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIcd**) and proceeding in

the same manner, the abovenamed product is obtained. Yield : 48 %. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.08 (s, 3H, CH_3), 3.61-3.87 (m, 7H, OCH_3 + CH + 1H NCH_2 + -CH_2Ph), 4.01 (s, 3H, OCH_3), 4.38-4.45 (m, 1H NCH_2), 6.66 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.33-7.63 (m, 14**H Ar**).

3-(1-benzyl-4-hydroxypiperidin-4-yl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcl.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 1-benzyl-piperidin-4-one and proceeding in the same manner, the abovenamed product is obtained. Yield : 61 %. M : 197-199°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.07 (s, 3H, CH_3), 1.65-1.92 (m, 4H, 2 x CH_2), 2.28-2.32 (m, 1H, CH), 2.54-2.68 (m, 4H, 2 x CH_2), 3.35 (s, 1H CH_2-Ph), 3.57-3.72 (m, 2H, 1H CH_2-Ph + 1H -NCH_2), 3.77 (s, 3H, OCH_3), 3.99 (s, 3H, + OCH_3), 4.31-4.38 (m, 1H -NCH_2), 4.53 (s, 1H, -OH), 6.72 (s, 1**H Ar**), 7.86 (s, 1**H Ar**), 7.30-7.46 (m, 8**H Ar**), 7.66-7.68 (s, 1**H Ar**).

N-[2-(7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)benzyl]methylacetamide, IIcm.

By replacing 7,8-dimethoxy-1-ethyl-3-(2-aminobenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIca)** in example **IIcf** by 7,8-dimethoxy-1-ethyl-3-(2-aminomethylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIcg)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 122-124°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.07-1.14 (m, 3H, CH_3), 1.49 (s, 1H, $COCH_3$), 3.41-3.80 (m, 6H, $CHCH_2$ + 1HNCH_2 + OCH_3), 3.89-3.98 (m, 4H, $CHCH_2$ + OCH_3), 4.34-4.45 (m, 1HNCH_2), 6.60 (s, 1**H Ar**), 4.55-4.57 (m, 2H, CH_2NHAc), 6.52 (s, , 6.85 (s, 1**H Ar**), 7.18-8.45 (m, 9**H Ar**), 8.45 (m, 1H, NHAc).

3-(4-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcn.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 4-chlorobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 52 %. M :

109-111°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.07 (s, 3H, CH_3), 3.54 (d, 1H -CH_2Ph), 3.72-3.77 (m, 5H, 1H -CH_2Ph + CH + OCH_3), 3.95 (s, 3H, OCH_3), 4.00 (AB system, ? d = 0.73, J_{AB} = 13.4, 2H, -NCH_2), 6.63 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.26-7.42 (m, 7**H Ar**), 7.55-7.58 (m, 2**H Ar**).

3-(2,4-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIco.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2,4-dichlorobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 20 %. M : 92-94°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.02-1.09 (m, 3H, CH_3), 3.60-3.72 (m, 6H, + OCH_3, 1HNCH_2), 3.82-3.89 (m, 1H, $CHCH_2$), 3.96 (s, 3H, OCH_3), 4.33-4.44 (m, 1H, 1HNCH_2), 6.62 (s, 1**H Ar**), 6.82 (s, 1**H Ar**), 7.26-7.59 (m, 9**H Ar**).

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, IIcp.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-bromomethyl benzonitrile and proceeding in the same manner, the abovenamed product is obtained. Yield : 33 %. M : 95-97°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 3.63 (d, 1H -CH_2Ph), 3.68-3.85 (m, 5H, 1H -CH_2Ph + CH + OCH_3), 3.99 (s, 3H, OCH_3), 4.01 (AB system, ? d = 0.69, J_{AB} = 14.2, 2H, -NCH_2), 6.67 (s, 1**H Ar**), 6.86 (s, 1**H Ar**), 7.42-7.70 (m, 9**H Ar**).

3-benzyl-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcq.

By replacing 2-nitrobenzyl bromide in example **IIbh** by benzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 38 %. M : 157-159°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 3.61-3.86 (m, 7H, -CH_2Ph + 1H -NCH_2 + CH + OCH_3), 3.99 (s, 3H, OCH_3), 4.37-4.47 (m, 1H -NCH_2), 6.67 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.30-7.44 (m, 8**H Ar**), 7.60-7.64(m, 2**H Ar**).

1-ethyl-7,8-dimethoxy-3-(2-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcr.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2-methoxybenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 24 %. M : 100-102°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.09 (s, 3H, CH_3), 3.50-3.92 (m, 10H, -CH_2Ph + 1H -NCH_2 + C**H** + 2 x OCH_3), 3.99 (s, 3H, OCH_3), 4.39-4.49 (m, 1H -NCH_2), 6.66 (s, 1**H Ar**), 6.81-6.85 (m, 2**H Ar**), 6.95-7.02 (m, 1**H Ar**), 7.19-7.30 (m, 1**H Ar**), 7.39-7.59 (m, 6**H Ar**).

3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide, IIcs.

To a solution of 40 mg (0.91 mmol) of 3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile **(IIcp)** in 1 ml of ethanol, add under an inert atmosphere 27 µl (0.27 mmol) of 30 % (m/m) H_2O_2 in water, 36 µl (0.018 mmol) of 0.5 M NaOH in water. Stir under reflux for 12 hours. Evaporate to dryness. Take up in a 25 ml of a water-ice mixture. Filter the solid, wash twice with 20 ml of water and once with 5 ml of ether. One obtains 24 mg of the abovenamed product as a white powder. Yield : 59 %. M : 111-113°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 3.50-3.75 (m, 6H, 1H -CH_2Ph + 1H -NCH_2 + C**H** + OCH_3), 3.98-4.11 (m, 4H, 1H -CH_2Ph + OCH_3), 4.38-4.49 (m, 1H -NCH_2), 5.91 (m, 1H exchangeable CO-NH_2), 6.26 (m, 1H exchangeable CO-NH_2), 6.66 (s, 1**H Ar**), 6.85 (s, 1**H Ar**), 7.30-7.86 (m, 9**H Ar**).

3-[3-(aminomethyl)benzyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIct.

Leave under hydrogen pressure (Patm) for 12 hours, 40 mg of 3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl] benzonitrile **(IIcp)**, 0.4 ml of 30 % ammonia, 4 ml of methanol, 1 spatula tip of Raney nickel. Filter on celite, rinse several times with methanol. Evaporate to dryness. Take up in 50 ml of dichloromethane, wash three times with 50 ml of 0.5 M NH_3 and twice with water. Dry

the organic phase on Na_2SO_4. Evaporate to dryness. Recrystallize in ether. Filter. One obtains 40 mg of the abovenamed product in the form of a white powder. Yield : 55 %. M : 122-125°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (s, 3H, CH_3), 1.30 (m, 2H exchangeable -NH_2), 3.50-3.89 (m, 8H, 1H -CH_2Ph + 1H -NCH_2 + CH + CH_2-NH_2 + OCH_3), 3.98-4.11 (m, 4H, 1H -CH_2Ph + OCH_3), 4.37-4.47 (m, 1H -NCH_2), 6.67 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.20-7.64 (m, 9**H Ar**).

3-(1,1'-biphenyl-3-ylmethyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcu.

By replacing 5-(4-bromophenyl)-1-ethyl-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIbl**) in example **IIbp** by 3-(3-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIcj**) and proceeding in the same manner, the abovenamed product is obtained. Yield : 33 % M : 139-141°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.12 (s, 3H, CH_3), 3.50-3.89 (m, 7H, OCH_3 + CH + 1H NCH_2 + -CH_2Ph), 3.99 (s, 3H, OCH_3), 4.38-4.48 (m, 1H NCH_2), 6.67 (s, 1**H Ar**), 6.85 (s, 1**H Ar**), 7.43-7.68 (m, 14**H Ar**).

3-benzyl-7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcv.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 3-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaj**), and MeI by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 36 %. M : 128-130°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.10 (t, 3H, CH_3), 1.40 (t, 3H, CH_3), 1.55 (t, 3H, CH_3), 3.66 (m, 3H, CH_2Ph +CH), 3.94 (q, 2H, -OCH_2), 4.15 (AB system, ? d = 0.52, J_{AB} = 13.2, 2H, -NCH_2), 4.19 (q, 2H, -OCH_2), 6.67 (s, 1**H Ar**), 6.85 (s, 1**H Ar**), 7.33-7.63 (m, 10 **H Ar**).

2-(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetamide, IIcw.

Stir at 0°C under an inert atmosphere for 48 hours, 70 mg (0.17 mmol) of ethyl (1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)acetate **(IIbv)** and 1.5 ml of methanol at 35 % molar saturation with NH_3. Evaporate to dryness. Purify by silica chromatography (dichloromethane 9/ methanol 1). Recrystallize in ether. One obtains 12 mg of the abovenamed product as a white powder. Yield : 17 %. M : 105-107°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.10 (t, 3H, C**H$_3$**), 3.02-3.09 (m, 1H –C**H$_2$**), 3.22-3.29 (m, 1H –C**H$_2$**), 3.75 (s, 1H, OC**H$_3$**), 3.98 (s, 1H, OC**H$_3$**), 4.01 (AB system, ? d = 0.67, J_{AB} = 13.9, 2H, -NC**H$_2$**), 4.13 (t, 1H, C**H**), 5.52 (s, 1H exchangeable N**H$_2$**), 6.43 (s, 1H exchangeable N**H$_2$**), 6.67 (s, 1**H Ar**), 6.85 (s, 1**H Ar**), 7.38-7.47 (m, 3**H Ar**), 7.59-7.62 (m, 2**H Ar**).

7,8-dimethoxy-1-(2-hydroxyethyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcx.

To a solution of 150 mg (0.50 mmol) of 7,8-dimethoxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one **XXIIaa** in 5 ml of DMF, add at 0°C under an inert atmosphere 21 mg (0.52 mmol) of 60 % NaH in oil. Stir at room temperature for 1 hour. Add at 0°C, 53 mg (0.60 mmol) of ethylene carbonate. Stir at room temperature overnight. Add 50 ml of H_2O and extract three times with 50 ml ofAcOEt; dry on $MgSO_4$, evaporate the AcOEt and purify by silica chromatography (AcOEt 3 /hexane 1, then AcOEt). Recrystallize in $CHCl_3$ /cHexane. Yield : 40 %. M : 128-130°C. ^{1}H-NMR (DMSO, 300 MHz) : d 3.36-3.52 (m, 2H, HOC**H$_2$**), 3.60 (s, 3H, OC**H$_3$**), 3.70-3.86 (m, 5H, NC**H$_2$**+ OC**H$_3$**), 4.11 (AB system, ? d = 0.77, J_{AB} = 9.96, 2H, C**H$_2$**), 4.77 (m, 1H, O**H**), 6.60 (s, 1**H Ar**), 7.39 (s, 1**H Ar**), 7.42-7.58 (m, 4**H Ar**). Mass : $(M + H)^+$ = 341.16.

3-(2-chlorobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcy.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2-chlorobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 60 %. M : 78-81°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.09 (s, 3H, C**H$_3$**), 3.50-3.96 (m, 6H, 1H -C**H$_2$**Ph + 1H -NC**H$_2$** + C**H** + OC**H$_3$**), 3.90-3.98 (m, 3H, 1H -C**H$_2$**Ph + OC**H$_3$**), 4.38-4.44 (m, 1H -NC**H$_2$**), 6.63 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.16-7.65 (m, 9**H Ar**).

1-ethyl-7,8-dimethoxy-3-(2-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIcz.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2-methylbenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 73-75°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.08 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.62-3.73 (m, 6H, 1H -CH_2Ph + 1H -NCH_2 + CH + OCH_3), 3.83-3.86 (m, 1H -CH_2Ph), 3.97 (s, 3H, CH_3), 4.38-4.45 (m, 1H -NCH_2), 6.64 (s, 1**H Ar**), 6.84 (s, 1**H Ar**), 7.14 (m, 3**H Ar**), 7.34-7.44 (m, 4**H Ar**),7.56-7.58 (m, 2**H Ar**).

8-ethoxy-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIda.

By replacing in the example 7,8-dimethoxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one (**XXIIaa**) by 8-ethoxy-7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIam**), and ethylene carbonate by iodomethane, and proceeding in the same manner, the abovenamed product is obtained. Yield : 69 %. M : 138-140°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.54 (t, 3H, CH_3), 3.38 (s, 3H, NCH_3), 3.74 (s, 3H, OCH_3), 4.18 (q, 2H, -OCH_2), 4.29 (AB system, ? d = 0.98, J_{AB} = 10.5, 2H, -CH_2), 6.70 (s, 1**H Ar**), 6.77 (s, 1**H Ar**), 7.39-7.43 (m, 3**H Ar**), 7.63-7.68 (m, 3**H Ar**).

1-ethyl-7,8-dimethoxy-5-phenyl-3-[3-(trifluoromethyl)benzyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdb.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-trifluoromethylbenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 49 %. M : 151-153°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.09 (s, 3H, CH_3), 3.55-3.77 (m, 7H, -CH_2Ph + 1H -NCH_2 + CH + OCH_3), 3.96 (s, 3H, OCH_3), 4.32-4.44 (m, 1H -NCH_2), 6.63 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.37-7.48 (m, 5**H Ar**),7.55-7.58 (m, 3**H Ar**), 7.70 (s, 1**H Ar**).

1-ethyl-7,8-dimethoxy-3-(3-methoxybenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdc.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 3-methoxybenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 45 %. M : 155-157°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.08 (s, 3H, CH_3), 3.56-3.60 (m, 2H, 1H -CH_2Ph + CH), 3.72 (s, 3H, NCH_3), 3.77-3.80 (m, 1H CH_2Ph), 3.95 (s, 3H, OCH_3), 4.00 (AB system, ? d = 0.75, J_{AB} = 14.0, 2H, -NCH_2), 6.64 (s, 1**H Ar**), 6.74-6.77 (m, 1**H Ar**), 6.82 (s, 1**H Ar**), 6.95-6.98 (m, 2**H Ar**), 7.20 (t, 1**H Ar**), 7.37-7.45 (m, 3**H Ar**), 7.59-7.62 (m, 2**H Ar**).

1-ethyl-7,8-dimethoxy-3-(4-methylbenzyl)-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdd.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 4-methylbenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 24 %. M : 107-108°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.07 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.54-3.58 (m, 2H, 1H -CH_2Ph + CH), 3.72 (s, 3H, OCH_3), 3.75-3.80 (m, 1H CH_2Ph), 3.95 (s, 3H, OCH_3), 3.96 (AB system, ? d = 0.68, J_{AB} = 14.3, 2H, -NCH_2), 6.64 (s, 1**H Ar**), 6.81 (s, 1**H Ar**), 7.20 (AB system, ? d = 0.17, J_{AB} = 7.8, 2H, -NCH_2), 7.37-7.45 (m, 3**H Ar**), 7.59-7.62 (m, 2**H Ar**).

3-[1,2-bis(4-bromophenyl)ethyl]-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIde.

This product is obtained at the same time as 3-(4-bromobenzyl)-1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**IIcd**). Isolate by chromatography. Yield : 20 %. M : 195-198°C. ^{1}H-NMR (DMSO, 300 MHz) : d 0.89 (s, 3H, CH_3), 2.82 (m, 1H, C**H**-Ph), 3.16 (m, 1H, C**H**), 3.61 (s, 3H, OCH_3), 3.91 (AB system, ? d = 0.15, J_{AB} = 10.2, 2H, -CH_2Ph), 3.93 (s, 3H, OCH_3), 3.96 (AB system, ? d = 0.68, J_{AB} = 13.5, 2H, -NCH_2), 6.61 (s, 1**H Ar**), 7.05 (AB system, ? d = 0.16, J_{AB} = 7.9, 4**H Ar**), 7.23-7.39 (m, 8**H Ar**), 7.57 (s, 3**H Ar**).

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, IIdf.

By replacing 1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbd)** in example **IIbh** by 8-ethoxy-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIda)**, and 2-nitrobenzyl bromide by 3-bromomethyl-benzonitrile, and proceeding in the same manner, the abovenamed product is obtained. Yield : 35 %. M : 148-150°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.53 (s, 3H, CH_3), 3.40 (s, 3H, NCH_3), 3.58-3.62 (m, 2H, 1H -CH_2Ph + CH), 3.72 (s, 3H, OCH_3), 3.75-3.80 (m, 1H CH_2Ph), 4.17 (q, 2H, CH_2), 6.66 (s, 1**H Ar**), 6.76 (s, 1**H Ar**), 7.35-7.67 (m, 9**H Ar**).

2-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile, IIdg.

By replacing 1-ethyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIbd)** in example **IIbh** by 8-ethoxy-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one **(IIda)**, and 2-nitrobenzyl bromide by 2-bromomethyl-benzonitrile, and proceeding in the same manner, the abovenamed product is obtained. Yield : 58 %. M : 238-240°C. ^{1}H-NMR ($CDCl_3$, 200 MHz) : d 1.53 (s, 3H, CH_3), 3.40 (s, 3H, NCH_3), 3.71 (s, 3H, OCH_3), 3.78-3.90 (m, 3H, -CH_2Ph + CH), 4.17 (q, 2H, CH_2), 6.64 (s, 1**H Ar**), 6.76 (s, 1**H Ar**), 7.31-7.78 (m, 9**H Ar**).

3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzamide, IIdh.

By replacing 3-[(1-ethyl-7,8-dimethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile **(IIcp)** in example **IIcs** by 3-[(8-ethoxy-7-methoxy-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)methyl]benzonitrile **(IIdf)** and proceeding in the same manner, the abovenamed product is obtained. Yield : 86 %. M : 199-201°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.52 (s, 3H, CH_3), 3.39 (s, 3H, NCH_3), 3.66-3.79 (m, 3H, -CH_2Ph + CH + OCH_3), 4.17 (q, 2H, CH_2), 5.84 (m, 1H exchangeable –NH_2), 6.24 (m, 1H exchangeable –NH_2), 6.64 (s, 1**H Ar**), 6.74 (s, 1**H Ar**), 7.26-7.83 (m, 9**H Ar**).

3-(2,5-dichlorobenzyl)-7,8-dimethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdi.

By replacing 2-nitrobenzyl bromide in example **IIbh** by 2,5-dichlorobenzyl bromide and proceeding in the same manner, the abovenamed product is obtained. Yield : 22 %. M : 94-95°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.03-1.10 (m, 3H, CH_3), 3.64-3.82 (m, 7H, $CHCH_2$, OCH_3, $1HNCH_2$), 3.96 (s, 3H, OCH_3), 4.35-4.45 (m, 1H, $1HNCH_2$), 6.62 (s, 1**H Ar**), 6.83 (s, 1**H Ar**), 7.16-7.64 (m, 9**H Ar**).

(S)-3-benzyl-7,8-dimethoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdj.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by (S) 3-benzyl-7,8-dimethoxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one (**XXIIau**) and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 104-106°C. ^{1}H-NMR (DMSO, 200 MHz) : d 3.45 (s, 3H, NCH_3), 3.61-3.65 (m, 2H, CH_2), 3.75-3.84 (m, 4H, 1**CH** + OCH_3), 4.00 (s, 3H, OCH_3), 6.70 (s, 1**H Ar**), 6.79 (s, 1**H Ar**), 7.23-7.62 (m, 10**H Ar**). Mass : $(M + H)^+$ = 401.15

3,5-diphenyl-8-ethoxy-1-ethyl-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdk.

By replacing 5-(4-bromophenyl)-7,8-dimethoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIaf**) in example **IIba** by 3,5-diphenyl-8-ethoxy-7-methoxy-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIba**), and methyl iodide by ethyl iodide, and proceeding in the same manner, the abovenamed product is obtained. Yield : 65 %. M : 178-180°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 1.06-1.11 (m, 3H, NCH_2CH_3), 1.55-1.59 (m, 3H, OCH_2CH_3), 3.77 (s, 3H, OCH_3), 4.19-4.26 (m, 2H, OCH_2), 4.01 (AB system, ? d = 0.70, J_{AB} = 13.7, 2H, NCH_2), 6.77 (s, 1**H Ar**), 6.92 (s, 1**H Ar**), 7.35-7.74 (m, 10**H Ar**).

7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdl.

By replacing 7,8-dimethoxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one (**XXIIaa**) in the example by 7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIao**), and ethylene carbonate by iodomethane, and proceeding in the same manner, the abovenamed product is obtained. Yield : 55 %. M : 110-112°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.38 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 4.30 (AB system, ? d = 1.00, J_{AB} = 10.6, 2H, $-CH_2$), 6.77-6.78 (m, 1**H Ar**), 7.09-7.14 (m, 1**H Ar**), 7.31 (s, 1**H Ar**), 7.38-7.46 (m, 3**H Ar**), 7.44-7.67 (m, 2**H Ar**).

8-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one, IIdm.

By replacing 7,8-dimethoxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one (**XXIIaa**) in the example by 7-methoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (**XXIIan**), and ethylene carbonate by iodomethane, and proceeding in the same manner, the abovenamed product is obtained. Yield : 76 %. M : 114-116°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) : d 3.41 (s, 3H, NCH_3), 3.90 (s, 3H, OCH_3), 4.29 (AB system, ? d = 0.99, J_{AB} = 10.6, 2H, $-CH_2$), 6.71-6.75 (m, 1**H Ar**), 6.81-6.82 (m, 1**H Ar**), 7.22-7.25 (m, 1**H Ar**), 7.36-7.42 (m, 3**H Ar**), 7.50-7.62 (m, 2**H Ar**).

EXAMPLE 5 : PHARMACOLOGICAL ACTIVITY : INHIBITION OF PHOSPHODIESTERASES.

5.1. Isolation of phosphodiesterases from smooth muscle

A 3 g segment of bovine aortic media cut into pieces with scissors was homogenized with an ultra-turrax then a potter glass/glass homogenizer in 7 volumes by weight of buffer A containing a protease inhibitor cocktail (20 mM Tris-HCl, 0.25 M saccharose, 2 mM magnesium acetate, 1 mM dithiothreitol, 5 mM EGTA, 2000 U/ml aprotinin, 10 mg/l leupeptin and 10 mg/l soya trypsic inhibitor). The homogenizate was centrifuged at 105,000 g for 1 hour. The supernatant was loaded on a DEAE-Sephacel column (15 x 1.6 cm) pre-equilibrated with buffer B (buffer A without the saccharose, EGTA and

protease inhibitors). The column was washed until there was no detectable absorption at 280 nm, then eluted with a linear gradient of NaCl (0-0.5 M) in buffer B. 3-ml fractions were collected and enzyme activity was determined under the conditions described hereinafter to localize the different enzymes PDE1, PDE3, PDE4 and PDE5, which were aliquoted and frozen at –80°C (Lugnier et al., *Biochem. Phamacol.*, 35 (1986) 1746-1751). PDE2 was prepared from bovine endothelial cells by the same methods (Lugnier and Schini, *Biochem. Pharmacol.* 1990, 39 ; 75-84).

5.2. Protocol for measuring phosphodiesterase activity

Cyclic nucleotide phosphodiesterase activity was determined by a radioenzymatic method using tritium-labelled cyclic GMP or AMP (1 µM) as substrate (Lugnier et al., 1986). ^{3}H-labelled adenosine or guanosine monophosphate formed by hydrolysis of the radiolabelled cyclic nucleotide was then converted to ^{3}H-labelled adenosine or guanosine in a second reaction with one nucleotidase in excess. The nucleoside formed was separated from the nucleotides by anion exchange chromatography. Nucleoside radioactivity was determined by liquid scintillation counting. Enzymatic incubations were carried out under conditions allowing no more than 15 % hydrolysis of the substrate; each point was performed in duplicate.

5.2.1. Determination of inhibition of PDE4

The concentration of substance which inhibits enzymatic activity by 50 % (IC_{50}) at 1 µM cyclic AMP was calculated by nonlinear regression (Prism, GraphPad).

5.2.2. Selectivity

The activity of the compounds was evaluated on other phosphodiesterase isoforms, particularly basal state or calmodulin-activated PDE1 from vascular smooth muscle, basal state or cyclic GMP-activated PDE2 from vascular endothelial cells, PDE3 and PDE5 from vascular smooth muscle.

The results obtained are presented in Table 4 hereinafter and are expressed as the percentage inhibition of enzymatic activity produced by 10 μmol of the tested compound.

Table 1

Compounds represented by formula (III)

Compound	**PDE4 IC_{50} (μM) or percentage inhibition at 10 μM**
IIIaa	9.3
IIIab	0.30
IIIac	33 %
IIIad	3.9 %
IIIae	19 %
IIIaf	30 %
IIIag	36 %
IIIah	3.1
IIIai	1.8
IIIaj	2.7
IIIak	1.8
IIIal	2.4
IIIam	1.7
IIIan	1.8
IIIao	1.7
IIIap	1.9
IIIaq	1.9
IIIar	2.9
IIIas	2.9
IIIat	2.3
IIIau	3.8
IIIav	0.9
IIIaw	16
IIIax	7.8
IIIba	6.9
IIIbb	0.087
IIIzc	0.72

Table 2

Compounds represented by formula (XXII)

Compound	PDE4 IC_{50} (μM) or percentage inhibition at 10 μM
XXIIaa	25.8 %
XXIIab	10 %
XXIIac	35 %
XXIIad	14.9 %
XXIIae	21 %
XXIIaf	15
XXIIag	0.95
XXIIah	21.2 %
XXIIai	1.7
XXIIaj	4.4
XXIIak	13
XXIIal	23.9 %
XXIIam	0.7
XXIIan	12.1 %
XXIIao	11.5 %
XXIIap	36.10 %
XXIIaq	26.2 %
XXIIar	49.3 %
XXIIas	41.3 %
XXIIat	29 %
XXIIau	42.6 %
XXIIav	23 %
XXIIaw	4 %
XXIIax	6 %
XXIIay	19.6 %
XXIIaz	9.5
XXIIba	6.7
XXIIbb	15
XXIIbc	10 %

Table 3

Compounds represented by formula (II)

Compound	PDE4 IC_{50} (μM) or percentage inhibition at 10 μM	Compound	PDE4 IC_{50} (μM) or percentage inhibition at 10 μM
IIab	38 %	IIbu	12.4/18.7
IIac	2.3	IIbv	44.4 %
IIad	23 %	IIbw	46.1 %
IIae	3.4 %	IIbx	18 %
IIaf	11.7 %	IIby	8.2
IIag	4.8	IIbz	42.3 %
IIah	36 %	IIca	2.5
IIai	39 %	IIcb	28.5 %
IIaj	7.9 %	IIcc	4.97
IIak	16	IIcd	20.1 %
IIal	10	IIce	0.88/1.4
IIam	20 %	IIcf	21 %
IIan	3.6	IIcg	6.7
IIao	1.6	IIch	9.6
IIap	18 %	IIci	1.45
IIaq	7.9	IIcj	3.76
IIar	0 %	IIck	32.2 %
IIas	8.4	IIcl	4.3 %
IIat	3.9 %	IIcm	1.9
IIau	18.5 %	IIcn	45 %
IIav	15 %	IIco	34.3 %
IIaw	10	IIcp	9.2
IIax	8,2	IIcq	7.4
IIay	6.6	IIcr	2.7
IIaz	6.9 %	IIcs	1.25
IIba	17	IIct	18 %
IIbb	3.13	IIcu	4.8
IIbc	27.2 %	IIcv	3.1
IIbd	34.3 %	IIcw	9.4 %
IIbe	34.7 %	IIcx	9.9 %
IIbf	0.86	IIcy	2.8
IIbg	0.9/1.6	IIcz	4.4
IIbh	2.4	IIda	0.55 and 0.43
IIbi	23.1 %	IIdb	23
IIbj	6.5	IIdc	5.1
IIbk	14.2 %	IIdd	31.5 %

Table 3 continued

Compound	PDE4 IC_{50} (μM) or percentage inhibition at 10 μM	Compound	PDE4 IC_{50} (μM) or percentage inhibition at 10 μM
IIbl	15	IIde	0 %
IIbm	7.3	IIdf	1.5
IIbn	2.95	IIdg	1.1
IIbo	2.92	IIdh	0.52
IIbp	5.74	IIdi	8.15
IIbq	33.8 %	IIdj	48.3 %
IIbr	6.6/3.8	IIdk	1.1
IIbs	38.8 %	IIdl	34.6 %
IIbt	38.4 %	IIdm	16 %

Table 4

Selectivity

Compound	IC_{50} (μM) or percentage inhibition at 10 μM				
	PDE1	PDE2	PDE3	PDE4	PDE5
IIIab	3.81	16	5.8	0.30	4.3
IIIav	49 %	19	92 %	0.9	40
IIIbb	14	25 %	2.7	0.087	5.7
IIIzc	32 %	24 %	36 %	0.72	38 %
XXIIag	46 %	17 %	22 %	0.95	35 %
IIbg	47 %	20 %	40 %	0.9	-
XXIIai	55 %	6 %	55 %	1.7	-
XXIIam	29 %	36 %	36 %	0.7	35 %
IIda	26 %	7 %	47 %	0.5	14 %

All the compounds tested showed potent inhibition of PDE4. The preferred compounds according to the invention have an excellent potency and selectivity profile towards phosphodiesterase 4, in so far as these compounds are weaker inhibitors of the other PDEs, particularly PDE3.

EXAMPLE 6 : ANTI-INFLAMMATORY PROPERTIES OF THE INVENTIVE COMPOUNDS

Compounds according to the invention were assessed for anti-inflammatory properties on mononuclear cells from venous blood of healthy donors (n=4), by a protocol approved by the Alsace No. 1 Ethics Committee. More specifically, the cells were incubated for 24 hours in 24-well plates in the presence of the test compound, after activation by *Salmonella Abortis Equi* lipopolysaccharide (LPS) (5 µg/ml) (cf. De Groote et al., *Cytokine* 4, 1992, 239). After incubation, TNFα concentrations were determined in the culture supernatant by an ELISA method (Antibody Solutions, Half Moon Bay, CA, USA).

The results obtained revealed that the test compounds produced a marked, dose-related inhibition of TNFα, and only TNFα, production (relative to IL1β, IL6 and IL8 which were not significantly decreased). As an example, compounds **IIIab** and **IIda** at a concentration of 1 µM, inhibited TNFα production by 100 %, whereas at this same concentration, IL1β, IL6 and IL8 secretion levels were not at all altered.

Other compounds found to be potent inhibitors of PDE4, such as for example compounds **IIdh**, **XXIIag,** also have potent anti-TNFα activity, with IC_{50} values comprised between 1 and 0.1 µM. Some such compounds, for instance compound **XXIIag,** are capable of inhibiting the secretion of TNFα, but also of IL1β, and display a pharmacological profile distinct from the selective anti-TNFα compounds.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

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The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

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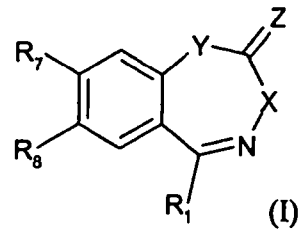
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS;

1. Compounds represented by general formula (I)



(I)

wherein:

X represents a CR_4R_4' group and Y represents an NR_6 group, R_4, R_4' and R_6 being defined hereinafter;

Z represents an oxygen atom;

R_1 is a (C_1-C_{12}) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-$_{12}$)alkyl(C_6-C_{18})aryl group, a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, or an OR_2, SR_2 or NR_2R_3 group in which (i) R_2 and R_3, independently of each other, are selected from the group consisting of a hydrogen atom, a (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms or, (ii) R_2 and R_3 together form a linear or branched hydrocarbon having from 2 to 6 carbon atoms, possibly containing one or more double bonds and/or possibly interrupted by an oxygen, sulfur or nitrogen atom;

R_4 and R_4', which are the same or different, are selected from the group consisting of the hydrogen atom and a (C_1-C_{12}) alkyl, a (C_3-C_6) cycloalkyl, unsubstituted (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group or a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, NO_2, CF_3, CN, NR'R", SR', OR', COOR', CONR'R" and NHCOR'R" group, R' and R", independently of each other, being selected from the

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group consisting of the hydrogen atom, a (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_6) cycloalkyl, (C_6-C_{12}) aryl group, and a (C_5-C_{12}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms;

R_6 is selected from the group consisting of the hydrogen atom, (C_1-C_6) alkyl, (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6C_{18})aryl, preferably a phenyl, benzyl group and a (C_1-C_6)alkylphenyl group;

R_7 and R_8, both represent an ethoxy group;

the alkyl, alkenyl, alkynyl, alkylaryl, aralkyl, cycloalkyl, aryl, phenyl, heterocycle groups and the hydrocarbon chain defined hereinabove possibly being substituted by one or more substituents, which are the same or different, selected from the group consisting of a halogen atom, a (C_1-C_{12}) alkyl, (C_6-C_{18}) aryl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, heterocycle, OH, =O, NO_2, NR'R", CN, CF_3, COR', COOR', (C_1-C_6)alkoxy, (di)(C_1-C_6)alkylamino, NHCOR' and CONR'R" group, in which R' and R" are defined as hereinabove,
and the salts thereof.

2. Compounds represented by general formula (I) according to claim 1 wherein R_6 represents the hydrogen atom or a (C_1-C_6) alkyl group.

3. Compounds according to claim 1 or claim 2 wherein R_4', represents a hydrogen atom.

4. Compounds represented by general formula (I) according to any one of the previous claims wherein R_4 represents a (C_1-C_{12}) alkyl or (C_6-C_{18})aryl(C_1-C_4)alkyl group, possibly substituted by one or more substituents, which are the same or different, chosen from among a halogen atom and an OH, =O, NO_2, NH_2, CN, CF_3, COR',

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COOR', (C_1-C_6)alkoxy, (di)(C_1-C_6)alkylamino, NHCOR' and CONR'R" group, in which R' and R" are defined as in claim 1.

5. Compounds represented by general formula (I) according to any one of claims 1 to 3 wherein R_4 and $R_{4'}$ represent the hydrogen atom.

6. Compounds represented by general formula (I) according to any one of claims 1 to 5 wherein R_1 is a (C_6-C_{18}) aryl, (C_6-C_{18})aryl(C_1-C_4)alkyl, (C_1-C_{12})alkyl(C_6-C_{18})aryl group or a (C_5-C_{18}) heterocycle, aromatic or not, containing 1 to 3 heteroatoms, said group or heterocycle possibly being substituted.

7. Compounds according to claim 6, wherein R_1 is a phenyl group, particularly a substituted phenyl, preferably a phenyl group substituted by:

(a) one or more halogen atoms, particularly chlorine, bromine or iodine, preferably chlorine, or

(b) one or more OR' groups, particularly methoxy or ethoxy, or

(c) a COR' group, particularly acetyl, or

(d) a trifluoromethyl group, or

(e) an alkyl or alkynyl group, for example heptinyl, or

(f) an aryl group or heterocycle, particularly a phenyl, furyl, pyridyl or thienyl group, said aryl group or heterocycle itself possibly being substituted by one or more groups preferably chosen from among the groups (a)-(e).

8. Compounds according to claim 7, wherein R_1 is a 4-chlorophenyl, 3,4-dichlorophenyl, 2-naphthyl, 2-benzo[b]thienyl, 4-(2-furyl)phenyl, 3-pyridyl or 3-trifluoromethylphenyl group.

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9. Compounds according to any one of claims 1 to 8 chosen from the following compounds:
7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
7,8-diethoxy-l-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
ethyl (7,8-diethoxy-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodi azepin-1-yl) acetate
1-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
7,8-diethoxy-3-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
3-benzyl-7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
3-benzyl-7,8-diethoxy-1-ethyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
and the salts thereof.

10. Compound according to any one of claims 1 to 9 which is 7,8-diethoxy-5-phenyl-1,3-dihydro-2H-1,4-diazepin-2-one and salts thereof.

11. Composition comprising a compound according to any one of claims 1 to 10 and a pharmaceutically acceptable vehicle or excipient.

12. Use of a compound according to any one of claims 1 to 10 for preparing a medicament designed to inhibit a cyclic nucleotide phosphodiesterase.

13. Use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating an inflammatory pathology of the central nervous system.

14. Use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating neuroinflammation.

15. Use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating asthma, chronic obstructive pulmonary disease, rhinitis, acute respiratory distress syndrome, allergy, skin disorders, such as dermatitis, psoriasis, rheumatoid arthritis, autoimmune diseases, different forms of sclerosis (particularly

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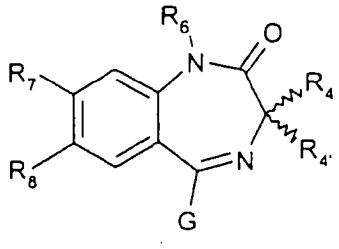
multiple sclerosis), dyskinesias, glomerulonephritis, osteoarthritis, cancer, septic shock, AIDS or obesity.

16. A use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating depression, schizophrenia, bipolar disorder, attention deficit disorder, fibromyalgia, epilepsy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, Lewy body dementia or Crohn's disease.

17. Use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating the inflammatory component of depression.

18. Use of a compound according to any one of claims 1 to 10 for preparing a medicament for treating the inflammatory component of obesity.

19. Method for preparing a compound according to any one of claims 1 to 10 by reacting a compound represented by general formula (XVIII):



(XVIII)

wherein R_4, R_4', R_6, R_7 and R_8 are defined as in claim 1 and G is an activator group such as a halogen, with an acid compound of group R_1 in the presence of a palladium catalyst.

20. Method for preparing a compound according to any one of claims 1 to 10 by reacting a compound represented by general formula (XXII):

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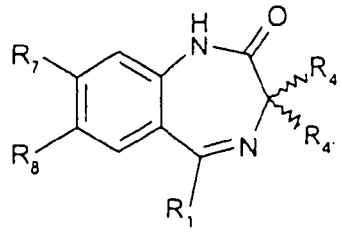

(XXII)

wherein R_1, R_4, $R_{4'}$, R_7 and R_8 are defined as in claim 1, with an alkyl halogenide, preferably in a solvent, in the presence of a base and preferably at room temperature.

21. Method of inhibiting a cyclic nucleotide phosphodiesterase comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

22. Method of treating an inflammatory pathology of the central nervous system comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

23. Method of treating neuroinflammation comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

24. Method of treating asthma, chronic obstructive pulmonary disease, rhinitis, acute respiratory distress syndrome, allergy, skin disorders, such as dermatitis, psoriasis, rheumatoid arthritis, autoimmune diseases, different forms of sclerosis (particularly multiple sclerosis), dyskinesias, glomerulonephritis, osteoarthritis, cancer, septic shock, AIDS or obesity comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

25. Method of treating the inflammatory component of depression, schizophrenia, bipolar disorder, attention deficit disorder, fibromyalgia, epilepsy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, Lewy body

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dementia or Crohn's disease comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

26. Method of treating the inflammatory component of depression comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

27. Method of treating the inflammatory component of obesity comprising administering a compound according to any one of claims 1 to 10 to a subject in need thereof.

28. Compounds according to claim 1, substantially as hereinbefore described with reference to any one of the examples and/or figures.

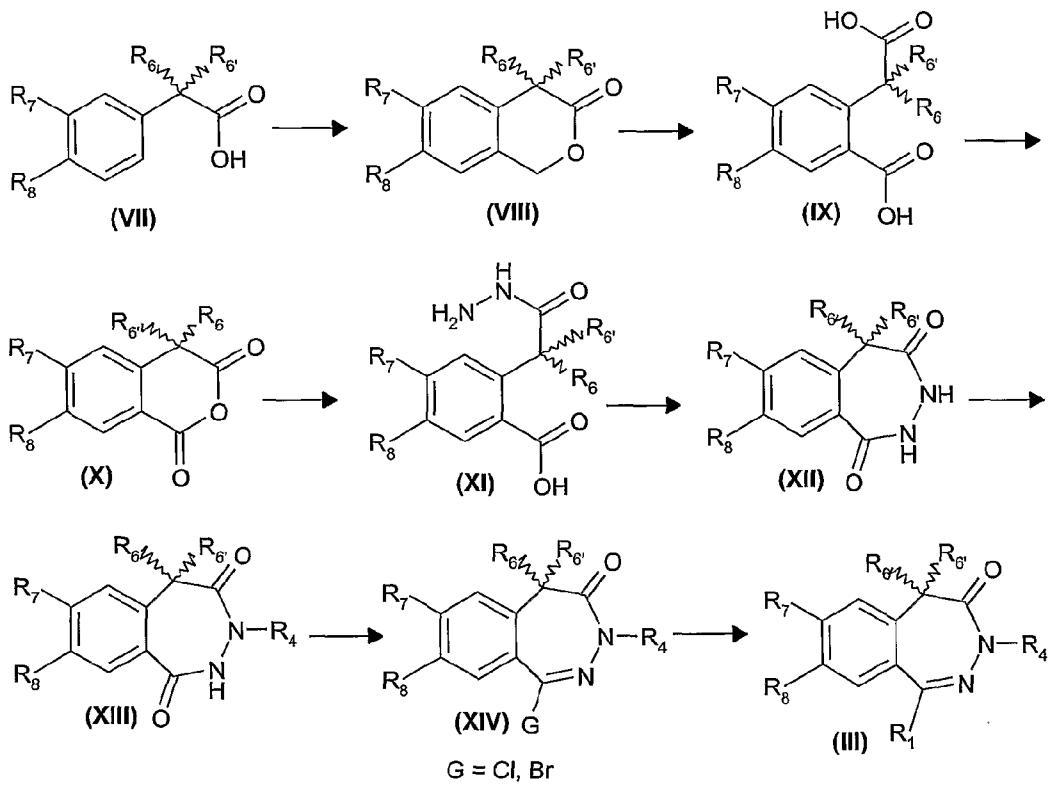

Figure 1

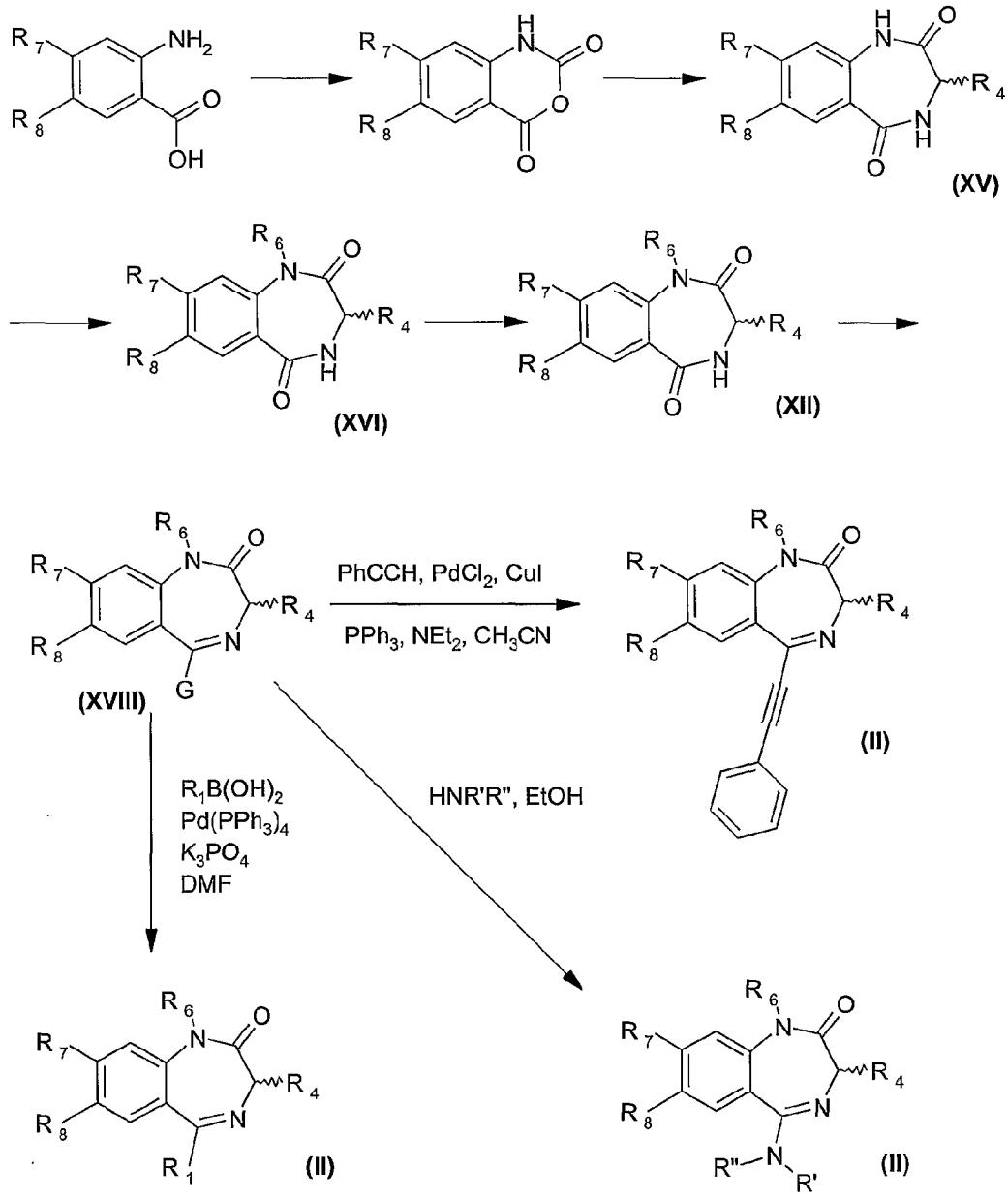
(XV)
(XVI)
(XII)
(XVIII)
PhCCH, PdCl2, CuI
PPh3, NEt2, CH3CN
(II)
R1B(OH)2
Pd(PPh3)4
K3PO4
DMF
HNR'R", EtOH
(II)
(II)

Figure 2