

SULPHONAMIDE DERIVATIVES, THEIR PREPARATION AND THEIR
THERAPEUTIC APPLICATION

The present invention relates to sulfonamide
5 derivatives, to the process for preparing them and to
their therapeutic use.

Orexins A and B (or hypocretins 1 and 2) are
hypothalamus neuropeptides of 33 and 28 amino acids,
respectively, recently identified as endogenous ligands
10 of two seven-domain transmembrane receptors, known as
orexin 1 and orexin 2 receptors (Sakurai T., Cell, Vol.
92, 573-585, 1998; De Lecea L., Proc. Natl. Acad. Sci.,
Vol. 95, 322-327, 1998).

The orexin 2 receptor has the property of
15 recognizing the two forms of orexin A and B
equivalently. In contrast, the orexin 1 receptor, which
shows 64% homology with the orexin 2 receptor, is more
selective and binds orexin A ten times better than
orexin B (Sakurai T., Cell, Vol. 92, 573-585, 1998).

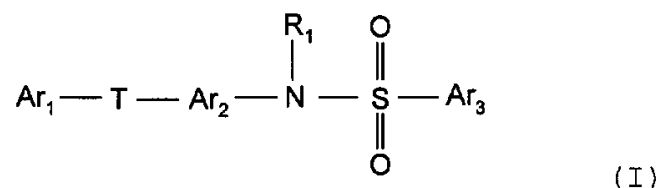
20 Via these receptors, the orexins control
various central and peripheral functions, especially
taking of food and drink, certain cardiovascular
endocrine functions and the awake/sleep cycle
(Sakurai T., Regulatory Peptides, Vol. 85, 25-30,
25 1999).

It has now been found that certain
sulfonamide derivatives show strong affinity for the

orexin 2 receptors and are powerful antagonists of these receptors.

Thus, one subject of the present invention is compounds corresponding to the general formula (I)

5



in which

• **Ar₁** represents

- an aryl group such as a phenyl group optionally

10 substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a cyano group, a group -CO-NR_aR_b, a group -NR_aR_b,

15 with R_a and R_b being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,

- a heterocyclyl group chosen from pyridyl,

pyrimidinyl, thiazolyl and thienyl, the said

heterocyclyl groups being optionally substituted with a

20 halogen atom, a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group,

- a (C₃-C₆) cycloalkyl group;

• **T** represents

- a group -(CH₂)_n- with n = 0, 1 or 2,

25 - a group >CH-R_2 with R₂ being a hydroxyl group or a

(C₁-C₄) alkyl group,

- a group >N-R_3 with R₃ being a (C₁-C₄) alkyl group,

- a group >C(OH)-R_4 with R₄ being a (C₁-C₄) alkyl group;

5 • **Ar₂** represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a

10 fluoro(C₁-C₄)alkyl group, a fluoro(C₁-C₄)alkoxy group, or with a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,

- a heterocyclyl group such as pyridyl optionally substituted with a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group;

• **Ar₃** represents

- an aryl group chosen from phenyl and naphthyl, the said aryl groups being optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a fluoro(C₁-C₄)alkoxy group, a nitro group, a hydroxyl group,

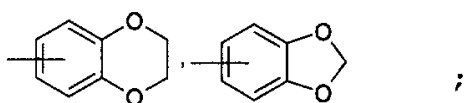
25 or with a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,

- a heterocyclyl group such as pyridyl optionally substituted with a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group,

or with a group -NR_xR_y with R_x and R_y being,

5 independently of each other, a hydrogen atom, a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group,

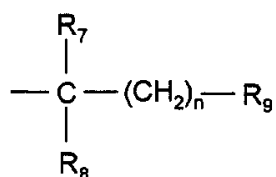
- a group chosen from



10 • R₁ represents

- a -C(O)-CF₃ group,

- a group of formula



15 in which

n = 0, 1, 2 or 3

. R₇ represents

- a hydrogen atom, a (C₁-C₄) alkyl group, a fluorine atom or a (C₁-C₄) alkoxy group,

20 - a group -(CH₂)_m-aryl, with m = 1 or 2 and the aryl group being a phenyl group optionally substituted with a halogen atom, a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group,

. R₈ represents

25 - a hydrogen atom, a fluorine atom or a (C₁-C₄)

alkyl group,

. R₉ represents

- a hydrogen atom, a (C₁-C₄) alkyl group, a
(C₃-C₆) cycloalkyl group, a hydroxyl group, a
5 (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group,
a -C≡CH group, a -C≡N group, a phenoxy group or
a (C₁-C₄) alkenyl group,

- a group -NR₁₀R₁₁ with R₁₀ and R₁₁ being,
independently of each other, a hydrogen atom, a
10 (C₁-C₄) alkyl group, a (C₁-C₄) alkylcarbonyl
group, a (C₁-C₄) alkylsulfonyl group, a benzyl
group or a -(CH₂)₂-N(CH₃)₂ group,

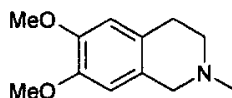
or alternatively R₁₀ and R₁₁ form, together with
the nitrogen atom that bears them, a
15 pyrrolidine, a pyrrolidinone, a morpholine or a
piperidine,

- a group -CO-NR₁₂R₁₃ with R₁₂ and R₁₃ being,
independently of each other,

. a hydrogen atom,

20 . a (C₁-C₄) alkyl group optionally
substituted with a -C≡N group, an aryl
group such as phenyl or a heterocyclyl
group such as pyridyl, the said aryl and
heterocyclyl groups being optionally
25 substituted with a (C₁-C₄) alkyl group or
a hydroxyl group,
or alternatively R₁₂ and R₁₃ form,

together with the nitrogen atom that bears them, a group



- 5 - a group $-\text{COOR}_{14}$ with R_{14} being a $(\text{C}_1\text{-C}_4)$ alkyl group,
- a group $-\text{NH-CO-NR}_{15}\text{R}_{16}$ with R_{15} and R_{16} being, independently of each other, a hydrogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group, a phenyl group or a benzyl group, the said phenyl and benzyl groups being
10 optionally substituted with one or more substituents chosen from a halogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group and a $(\text{C}_1\text{-C}_4)$ alkoxy group,
- a group $-\text{SO}_2\text{-NR}_{17}\text{R}_{18}$ with R_{17} and R_{18} being, independently of each other, a hydrogen atom or
15 a $(\text{C}_1\text{-C}_4)$ alkyl group,
- a group $-\text{SO}_2\text{-R}_{19}$ with R_{19} being a $(\text{C}_1\text{-C}_4)$ alkyl group or an aryl group such as phenyl,
- a heterocyclyl group chosen from 1,3-dioxolanyl, imidazolyl, tetrazolyl, triazolyl
20 optionally substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group, thiazolyl, pyrimidyl, oxadiazolyl or pyridyl, the imidazolyl being optionally substituted on the nitrogen atom with a $(\text{C}_1\text{-C}_4)$ alkyl group or a benzyl, the tetrazolyl being
25 optionally substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group or a benzyl, and the oxadiazolyl being

optionally substituted with a (C₁-C₄) alkyl,
- a group -NH-CO-OR₁₅, R₁₅ corresponding to the
above definition,
in the form of base, of acid-addition salt, of hydrate
5 or of solvate, in the form of enantiomers,
diastereoisomers, rotamers or atropoisomers, or
mixtures thereof.

Among the compounds that are the subject of the
invention, mention may be made of a first group of
10 compounds of general formula (I) in which

• **Ar₁** represents

- an aryl group such as a phenyl group optionally
substituted with one or more groups chosen,
independently of each other, from the following groups:
15 a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy
group, a fluoro(C₁-C₄)alkyl group,
- a heterocyclyl group chosen from pyridyl, thiazolyl
and thienyl, the thienyl being optionally substituted
with a (C₁-C₄) alkyl group,
20 - a (C₃-C₆) cycloalkyl group;

• **T** represents

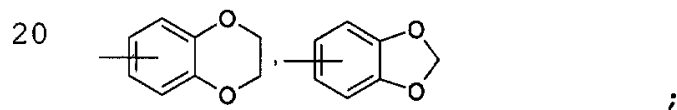
- a group -(CH₂)_n- with n = 1
- a group $\begin{array}{c} > \\ \text{CH} \end{array} \text{---} \text{R}_2$ with R₂ being a hydroxyl group or a
(C₁-C₄) alkyl group,
25 - a group $\begin{array}{c} > \\ \text{N} \end{array} \text{---} \text{R}_3$ with R₃ being a (C₁-C₄) alkyl group,
- a group $\begin{array}{c} > \\ \text{C}(\text{OH}) \end{array} \text{---} \text{R}_4$ with R₄ being a (C₁-C₄) alkyl
group;

• **Ar₂** represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a
5 (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkoxy group, a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

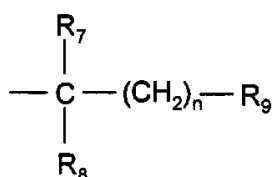
• **Ar₃** represents

- 10 - an aryl group chosen from phenyl and naphthyl, the phenyl group being optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl
15 group, a fluoro(C₁-C₄)alkoxy group, a nitro group, or a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,
- a group chosen from



• **R₁** represents

- a -C(O)-CF₃ group,
- a group of formula



in which

$n = 0, 1$ or 2 ,

. R_7 represents

5 - a hydrogen atom or a $(\text{C}_1\text{-C}_4)$ alkyl group

. R_8 represents

 - a hydrogen atom,

. R_9 represents

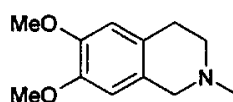
10 - a hydrogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group, a
 hydroxyl group, a $(\text{C}_1\text{-C}_4)$ alkoxy group, a
 fluoro $(\text{C}_1\text{-C}_4)$ alkyl group, a $-\text{C}\equiv\text{CH}$ group or a $-\text{C}\equiv\text{N}$
 group,

15 - a group $-\text{NR}_{10}\text{R}_{11}$ with R_{10} and R_{11} being,
 independently of each other, a hydrogen atom, a
 $(\text{C}_1\text{-C}_4)$ alkyl group, a $(\text{C}_1\text{-C}_4)$ alkylcarbonyl group
 or a benzyl,

 or alternatively R_{10} and R_{11} form, together with
 the nitrogen atom that bears them, a
 pyrrolidine, a piperidine or a pyrrolidinone,

20 - a group $-\text{CO}-\text{NR}_{12}\text{R}_{13}$ with R_{12} and R_{13} being,
 independently of each other, a hydrogen atom or
 a $(\text{C}_1\text{-C}_4)$ alkyl group,
 or alternatively R_{12} and R_{13} form, together with
 the nitrogen atom that bears them, a group

25



- or a group -COOR_{14} with R_{14} being a $(\text{C}_1\text{-C}_4)$ alkyl group,
 - a group $\text{-NH-CO-NR}_{15}\text{R}_{16}$ with R_{15} and R_{16} being,
5 independently of each other, a hydrogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group, a phenyl or a benzyl,
 - a heterocyclyl group chosen from imidazolyl optionally substituted on the nitrogen atom with a $(\text{C}_1\text{-C}_4)$ alkyl group, tetrazolyl optionally
10 substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group, and triazolyl,
- in the form of base, of acid-addition salt, of hydrate or of solvate, in the form of enantiomers, diastereoisomers, rotamers or atropoisomers, or
15 mixtures thereof.

Among the compounds that are the subject of the invention, mention may be made of a second group of compounds of general formula (I) in which

• **Ar₁** represents

- 20 - an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group, a $(\text{C}_1\text{-C}_4)$ alkoxy group, a fluoro $(\text{C}_1\text{-C}_4)$ alkyl group,
- 25 - a heterocyclyl group chosen from pyridyl, thiazolyl and thienyl, the thienyl being optionally substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group;

• **T** represents

- a group $-(CH_2)_n-$ with $n = 1$

- a group $\begin{array}{c} >CH-R_2 \end{array}$ with R_2 being a hydroxyl group;

• **Ar₂** represents

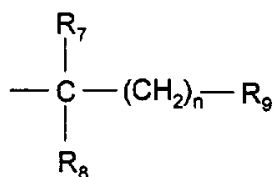
5 - an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group; a group -NR_cR_d with R_c and R_d being, independently of each other,
10 a hydrogen atom or a (C₁-C₄) alkyl group;

• **Ar₃** represents

- an aryl group such as phenyl, the phenyl group being optionally substituted with one or more groups chosen, independently of each other, from the following groups:
15 a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group,
or alternatively a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

20 • **R₁** represents

- a group of formula



in which

25 $n = 0, 1 \text{ or } 2,$

- . R₇ represents
 - a hydrogen atom or a (C₁-C₄) alkyl group,
 - . R₈ represents
 - a hydrogen atom,
 - 5 . R₉ represents
 - a hydrogen atom, a -C≡CH group or a -C≡N group,
 - a group -CO-NR₁₂R₁₃ with R₁₂ and R₁₃ being, independently of each other, a hydrogen atom or
 - 10 a (C₁-C₄) alkyl group,
 - a heterocyclyl chosen from imidazolyl optionally substituted on the nitrogen atom with a (C₁-C₄) alkyl group, tetrazolyl optionally substituted with a (C₁-C₄) alkyl group, and
 - 15 triazolyl,
- in the form of base, of acid-addition salt, of hydrate or of solvate, in the form of enantiomers, diastereoisomers, rotamers or atropoisomers, or mixtures thereof.
- 20 Among the compounds that are the subject of the invention, mention may be made of a third group of compounds of general formula (I) in which
- **Ar₁** represents
 - an aryl group such as phenyl optionally substituted
 - 25 with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group,

- a heterocyclyl group such as thienyl, optionally substituted with a (C₁-C₄) alkyl group,

• **T** represents

- a group -(CH₂)_n- with n = 1

5 • **Ar₂** represents

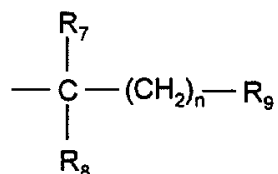
- a phenyl group optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a group -NR_cR_d with R_c and
10 R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

• **Ar₃** represents

- a phenyl group optionally substituted with one or more groups chosen, independently of each other, from
15 the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group,
or alternatively a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

20 • **R₁** represents

- a group of formula



in which

25 n = 0, 1 or 2,

- . R₇ represents
 - a hydrogen atom or a (C₁-C₄) alkyl group;
- . R₈ represents
 - a hydrogen atom;
- 5 . R₉ represents
 - a group -CO-NR₁₂R₁₃ with R₁₂ and R₁₃ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,
 - a heterocycle chosen from imidazolyl
 - 10 substituted on the nitrogen atom with a (C₁-C₄) alkyl group, tetrazolyl substituted with a (C₁-C₄) alkyl group, and triazolyl,
 - in the form of base, of acid-addition salt, of hydrate or of solvate, in the form of enantiomers,
 - 15 diastereoisomers, rotamers or atropoisomers, or mixtures thereof.

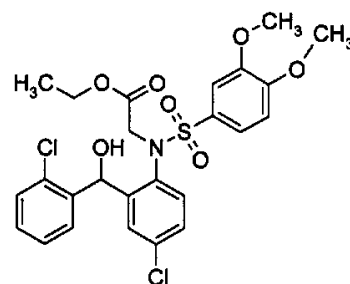
When Ar₂ is an optionally substituted phenyl group, the bonds T-Ar₂, on the one hand, and Ar₂-N, on the other hand, are in an ortho position. In other
20 words, the nitrogen atom and the substituent T are on two adjacent carbon atoms.

Examples of compounds according to the invention that may be mentioned include the following compounds:

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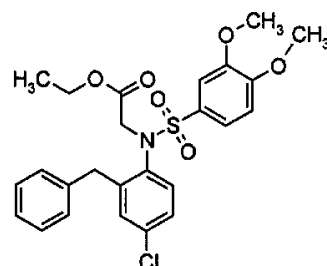
Compound 1:

Ethyl N-(4-chloro-2-[(2-chlorophenyl)(hydroxymethyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



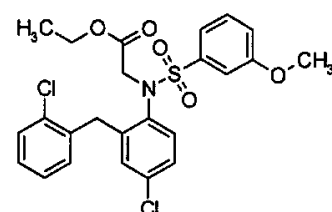
Compound 2:

Ethyl N-(2-benzyl-4-chlorophenyl)-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



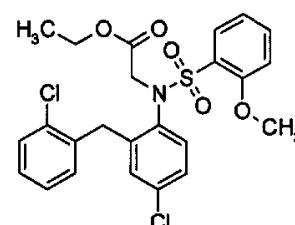
Compound 3:

Ethyl N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(3-methoxyphenyl)sulfonyl]glycinate



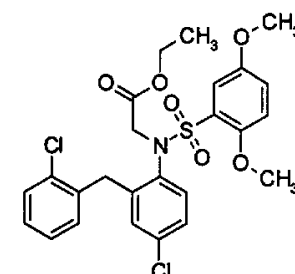
Compound 4:

Ethyl N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(2-methoxyphenyl)sulfonyl]glycinate



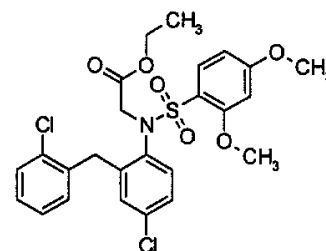
Compound 5:

Ethyl N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(2,5-dimethoxyphenyl)sulfonyl]glycinate



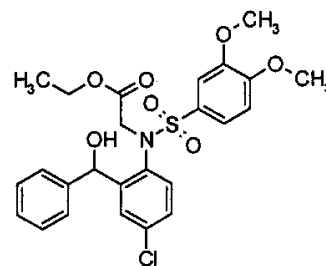
Compound 6:

Ethyl N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(2,4-dimethoxyphenyl)sulfonyl]glycinate



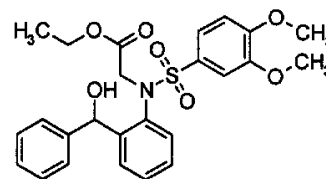
Compound 7:

Ethyl N-{4-chloro-2-[hydroxy(phenyl)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



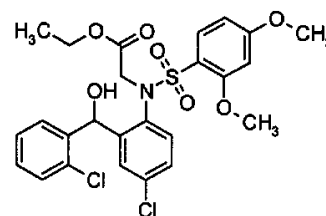
Compound 8:

Ethyl N-[(3,4-dimethoxyphenyl)sulfonyl]-N-{2-[hydroxy(phenyl)methyl]phenyl}glycinate



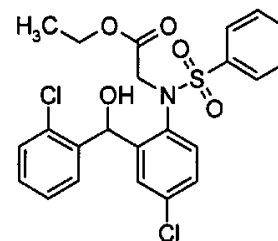
Compound 9:

Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(2,4-dimethoxyphenyl)sulfonyl]glycinate



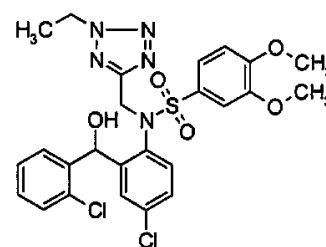
Compound 10:

Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-(phenylsulfonyl)glycinate



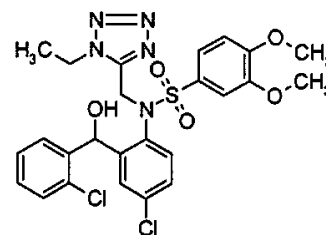
Compound 11:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



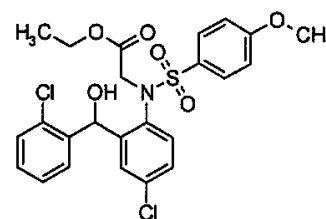
Compound 12:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



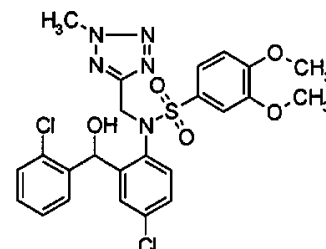
Compound 13:

Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(4-methoxyphenyl)sulfonyl]glycinate



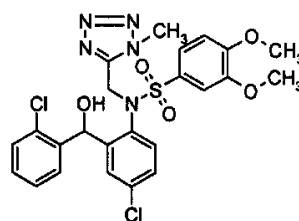
Compound 14:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide



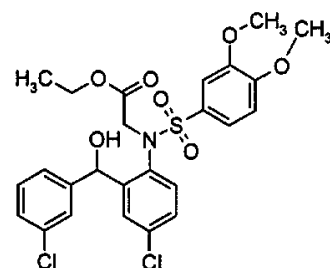
Compound 15:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide



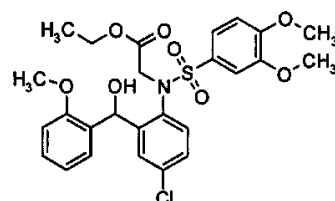
Compound 16:

Ethyl N-{4-chloro-2-[(3-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



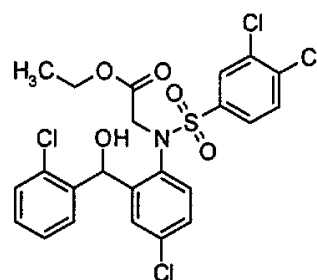
Compound 17:

Ethyl N-{4-chloro-2-[hydroxy(2-methoxyphenyl)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



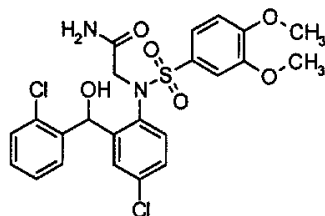
Compound 18:

Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(3,4-dichlorophenyl)sulfonyl]glycinate



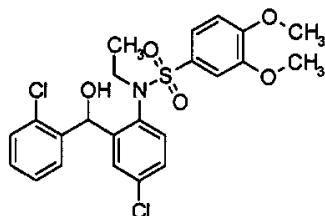
Compound 19:

N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N₂~[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



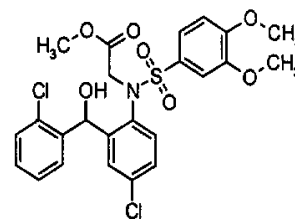
Compound 20:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-ethyl-3,4-dimethoxybenzenesulfonamide



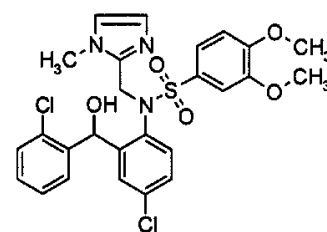
Compound 21:

Methyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



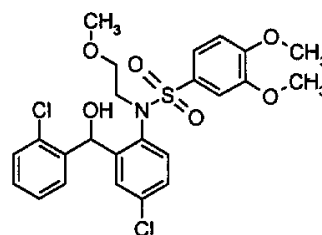
Compound 22:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(1-methyl-1H-imidazol-2-yl)methyl]benzenesulfonamide



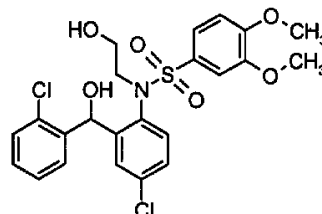
Compound 23:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-(2-methoxyethyl)benzenesulfonamide



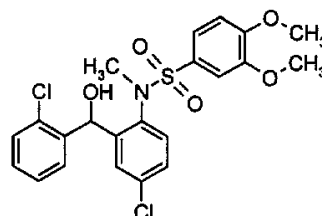
Compound 24:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-(2-hydroxyethyl)-3,4-dimethoxybenzenesulfonamide



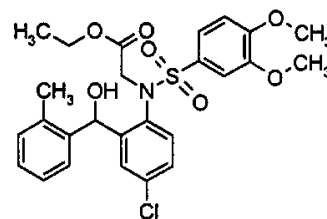
Compound 25:

N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-methylbenzenesulfonamide



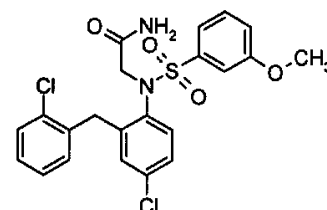
Compound 26:

Ethyl N-{4-chloro-2-[hydroxy(2-methylphenyl)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate



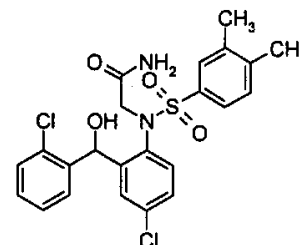
Compound 27:

N²-[4-chloro-2-(2-chlorobenzyl)phenyl]-N²-[(3-methoxyphenyl)sulfonyl]glycinamide



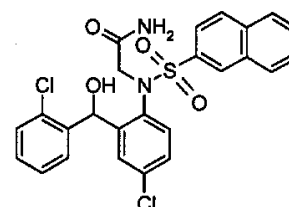
Compound 28:

N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N²-[(3,4-dimethylphenyl)sulfonyl]glycinamide



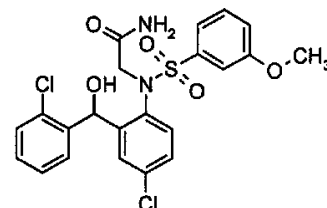
Compound 29:

N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N²-(2-naphthylsulfonyl)glycinamide



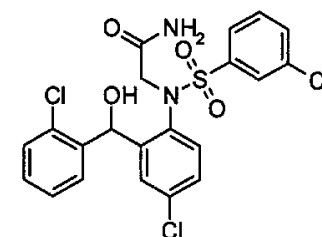
Compound 30:

N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N²-[(3-methoxyphenyl)sulfonyl]glycinamide



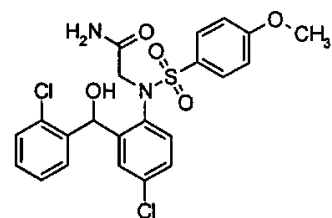
Compound 31:

N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N²-[(3-chlorophenyl)sulfonyl]glycinamide



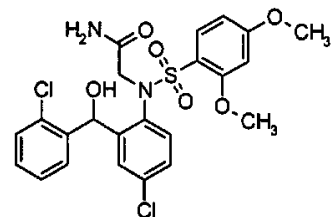
Compound 32:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(4-methoxyphenyl)sulfonyl]glycinamide



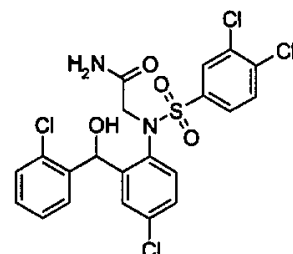
Compound 33:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(2,4-dimethoxyphenyl)sulfonyl]glycinamide



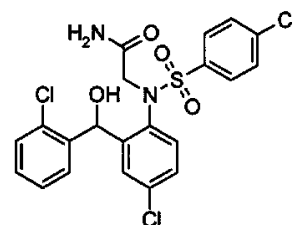
Compound 34:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(3,4-dichlorophenyl)sulfonyl]glycinamide



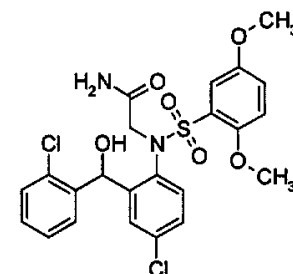
Compound 35:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N -[(4-chlorophenyl)sulfonyl]glycinamide



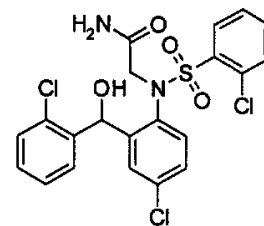
Compound 36:

N^2 {4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(2,5-dimethoxyphenyl)sulfonyl]glycinamide



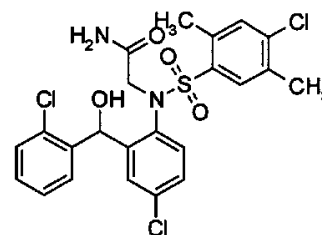
Compound 37:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(2-chlorophenyl)sulfonyl]glycinamide



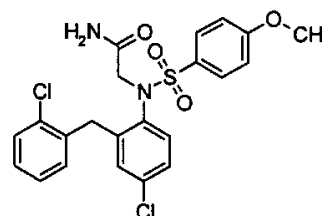
Compound 38:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide



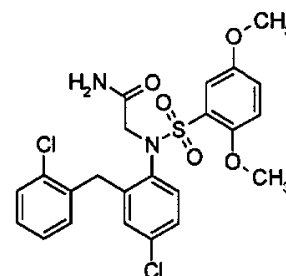
Compound 39:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(4-methoxyphenyl)sulfonyl]glycinamide



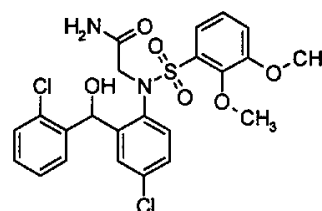
Compound 40:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,5-dimethoxyphenyl)sulfonyl]glycinamide



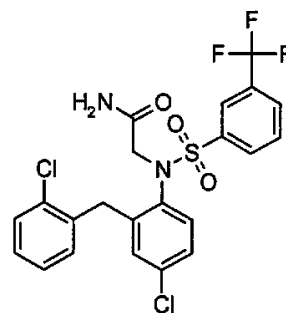
Compound 41:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(2,3-dimethoxyphenyl)sulfonyl]glycinamide



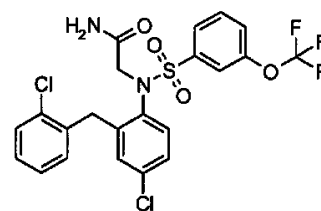
Compound 42:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -{[3-(trifluoromethyl)phenyl]sulfonyl}-
 glycinamide



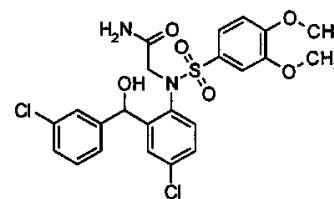
Compound 43:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -{[3-(trifluoromethoxy)phenyl]sulfonyl}-
 glycinamide



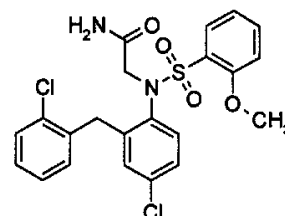
Compound 44:

N^2 -{4-chloro-2-[(3-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



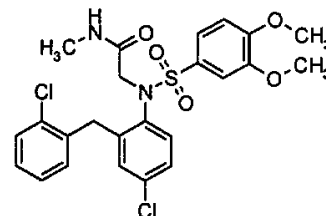
Compound 45:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2-methoxyphenyl)sulfonyl]glycinamide



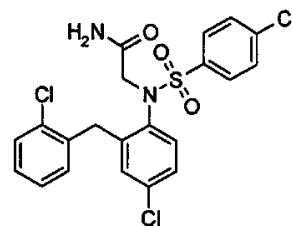
Compound 46:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -
 methylglycinamide



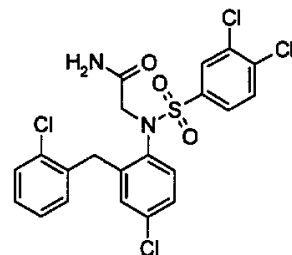
Compound 47:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(4-chlorophenyl)sulfonyl]glycinamide



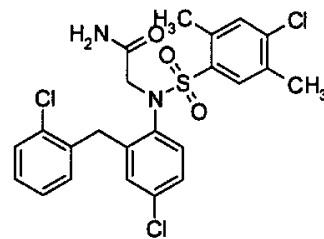
Compound 48:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,4-dichlorophenyl)sulfonyl]glycinamide



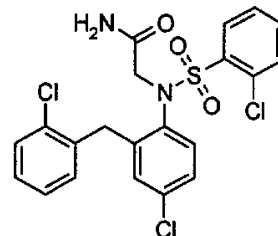
Compound 49:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide



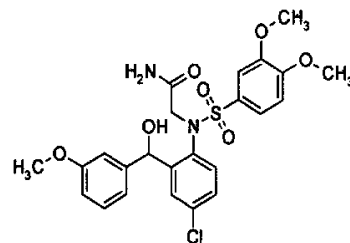
Compound 50:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2-chlorophenyl)sulfonyl]glycinamide



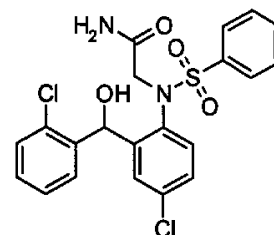
Compound 51:

N^2 -{4-chloro-2-[hydroxy(3-methoxyphenyl)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



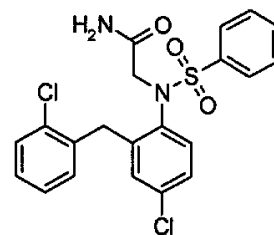
Compound 52:

N^2 -[4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl]-
 N^2 -(phenylsulfonyl)glycinamide



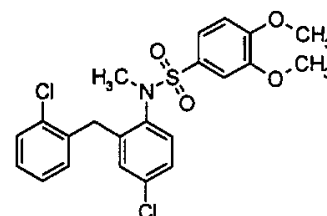
Compound 53:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -(phenylsulfonyl)glycinamide



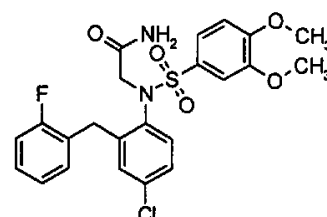
Compound 54:

N -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 3,4-dimethoxy- N -
 methylbenzenesulfonamide



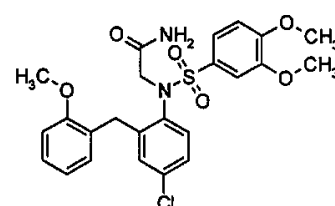
Compound 55:

N^2 -[4-chloro-2-(2-fluorobenzyl)phenyl]-
 N^2 -[(3,4-
 dimethoxyphenyl)sulfonyl]glycinamide



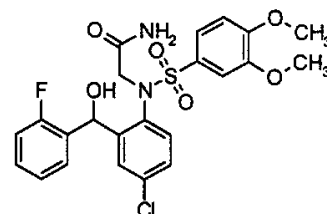
Compound 56:

N^2 -[4-chloro-2-(2-methoxybenzyl)phenyl]-
 N^2 -[(3,4-
 dimethoxyphenyl)sulfonyl]glycinamide



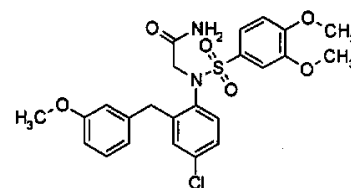
Compound 57:

N^2 -[4-chloro-2-[(2-fluorophenyl)(hydroxy)methyl]phenyl]-
 N^2 -[(3,4-
 dimethoxyphenyl)sulfonyl]glycinamide



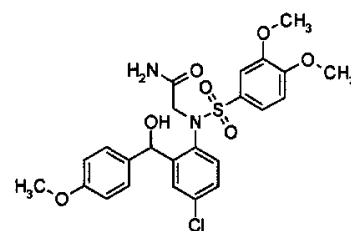
Compound 58:

N^2 -[4-chloro-2-(3-methoxybenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



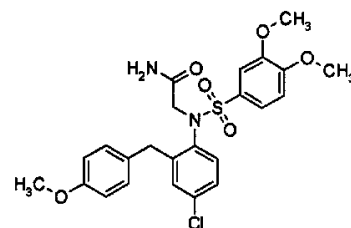
Compound 59:

N^2 -{4-chloro-2-[hydroxy(4-methoxyphenyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



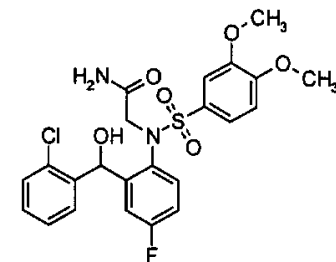
Compound 60:

N^2 -[4-chloro-2-(4-methoxybenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



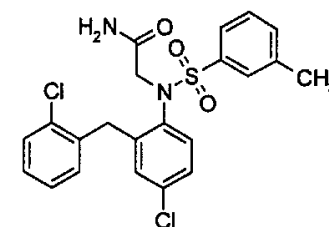
Compound 61:

N^2 -{2-[(2-chlorophenyl)(hydroxy)methyl]-4-fluorophenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



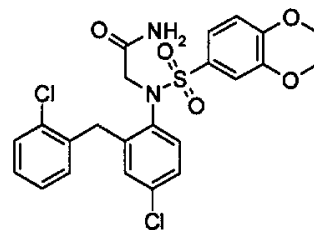
Compound 62:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]- N^2 -[(3-methylphenyl)sulfonyl]glycinamide



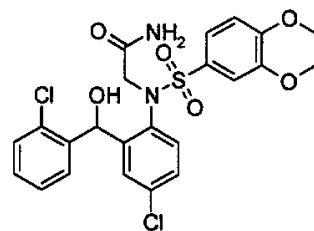
Compound 63:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -(2,3-dihydro-1,4-benzodioxin-6-
 ylsulfonyl)glycinamide



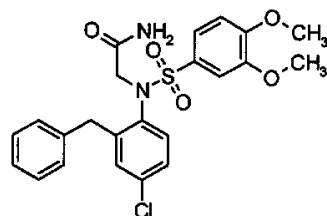
Compound 64:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -(2,3-dihydro-1,4-benzodioxin-6-
 ylsulfonyl)glycinamide



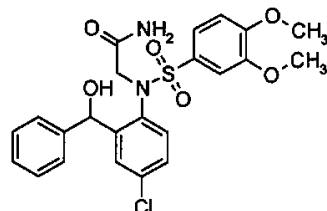
Compound 65:

N^2 -(2-benzyl-4-chlorophenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



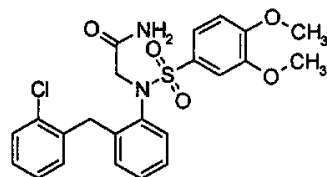
Compound 66:

N^2 -{4-chloro-2-[(hydroxy(phenyl)methyl)phenyl]}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



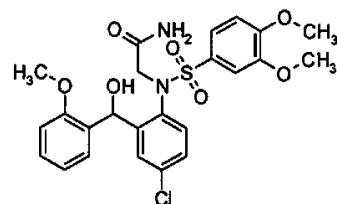
Compound 67:

N^2 -[2-(2-chlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



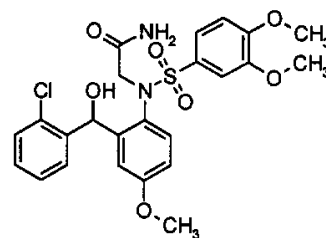
Compound 68:

N^2 -{4-chloro-2-[hydroxy(2-methoxyphenyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



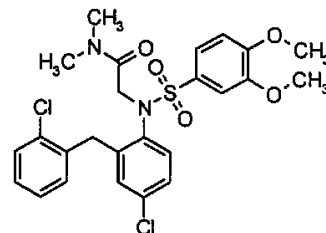
Compound 69:

N^2 -{2-[(2-chlorophenyl) (hydroxy)methyl]-
4-methoxyphenyl}- N^2 -[(3,4-
dimethoxyphenyl) sulfonyl]glycinamide



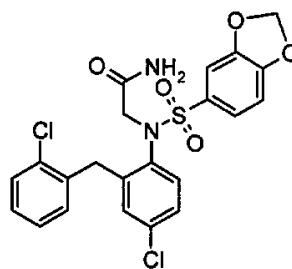
Compound 70:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl) sulfonyl]-
 N^1, N^1 -dimethylglycinamide



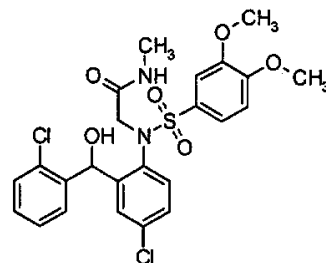
Compound 71:

N^2 -(1,3-benzodioxol-5-ylsulfonyl)- N^2 -[4-
chloro-2-(2-
chlorobenzyl)phenyl]glycinamide



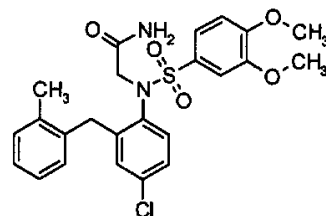
Compound 72:

N^2 -{4-chloro-2-[(2-
chlorophenyl) (hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl) sulfonyl]- N^1 -
methylglycinamide



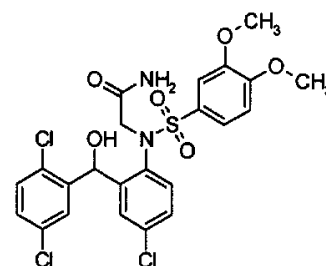
Compound 73:

N^2 -[4-chloro-2-(2-methylbenzyl)phenyl]-
 N^2 -[(3,4-
dimethoxyphenyl) sulfonyl]glycinamide



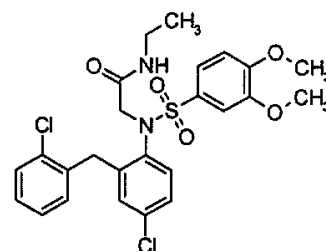
Compound 74:

N^2 -{4-chloro-2-[(2,5-dichlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



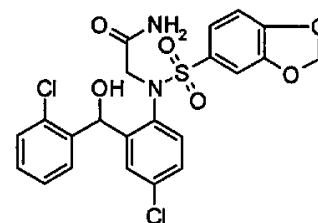
Compound 75:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -ethylglycinamide



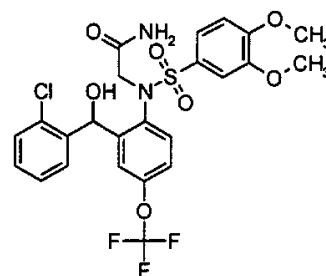
Compound 76:

N^2 -(1,3-benzodioxol-5-ylsulfonyl)- N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-glycinamide



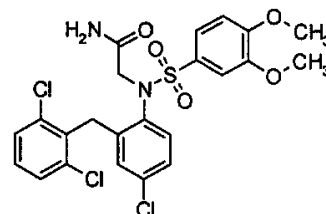
Compound 77:

N^2 -[2-[(2-chlorophenyl)(hydroxy)methyl]-4-(trifluoromethoxy)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



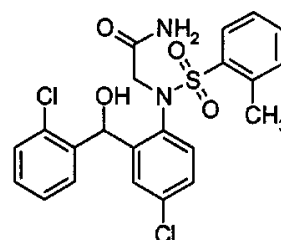
Compound 78:

N^2 -[4-chloro-2-(2,6-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



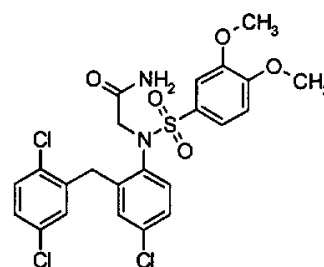
Compound 79:

N^2 -[4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl]- N^2 -[(2-methylphenyl)sulfonyl]glycinamide



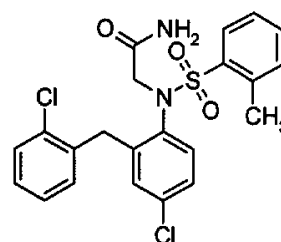
Compound 80:

N^2 -[4-chloro-2-(2,5-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



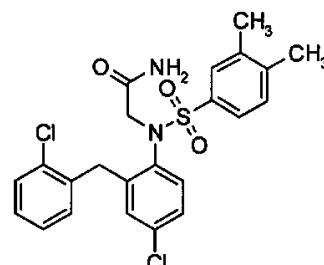
Compound 81:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]- N^2 -[(2-methylphenyl)sulfonyl]glycinamide



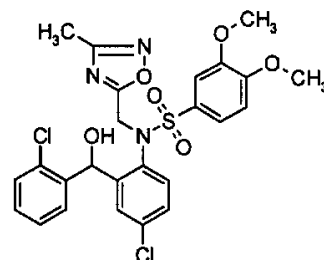
Compound 82:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]- N^2 -[(3,4-dimethylphenyl)sulfonyl]glycinamide



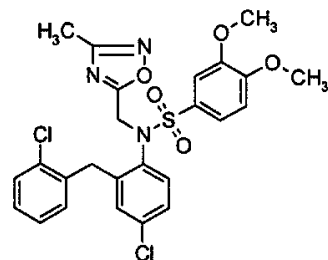
Compound 83:

N -[4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl]-3,4-dimethoxy- N -[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]benzenesulfonamide



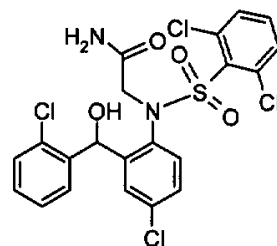
Compound 84:

N-[4-chloro-2-(2-chlorobenzyl)phenyl]-
3,4-dimethoxy-N-[(3-methyl-1,2,4-
oxadiazol-5-
yl)methyl]benzenesulfonamide



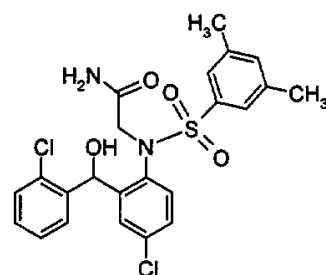
Compound 85:

N²-(4-chloro-2-[(2-
chlorophenyl)(hydroxy)methyl]phenyl)-
N²-(2,6-
dichlorophenyl)sulfonyl]glycinamide



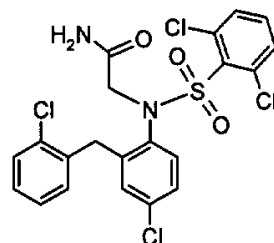
Compound 86:

N²-(4-chloro-2-[(2-
chlorophenyl)(hydroxy)methyl]phenyl)-
N²-(3,5-
dimethylphenyl)sulfonyl]glycinamide



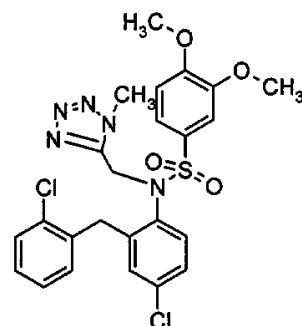
Compound 87:

N²-(4-chloro-2-(2-chlorobenzyl)phenyl)-
N²-(2,6-
dichlorophenyl)sulfonyl]glycinamide



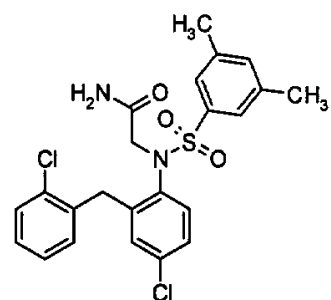
Compound 88:

N-[4-chloro-2-(2-chlorobenzyl)phenyl]-
3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-
5-yl)methyl]benzenesulfonamide



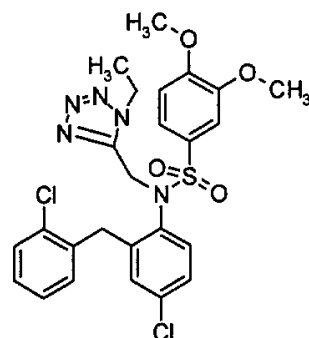
Compound 89:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,5-dimethylphenyl)sulfonyl]glycinamide



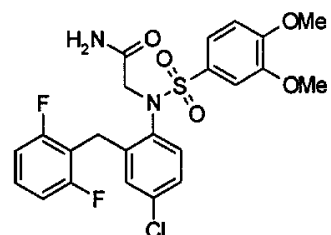
Compound 90:

N -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N -[(1-ethyl-1H-tetrazol-5-yl)methyl]-
 3,4-dimethoxybenzenesulfonamide



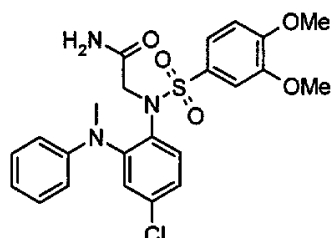
Compound 91:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



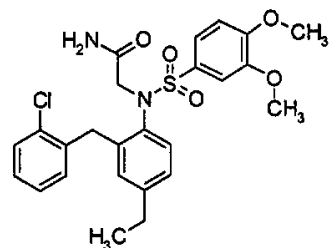
Compound 92:

N^2 -[4-chloro-2-[methyl(phenyl)amino]phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



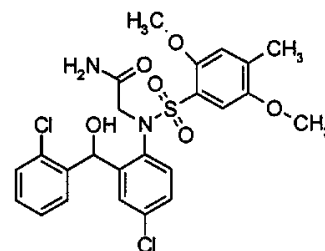
Compound 93:

N^2 -[2-(2-chlorobenzyl)-4-ethylphenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



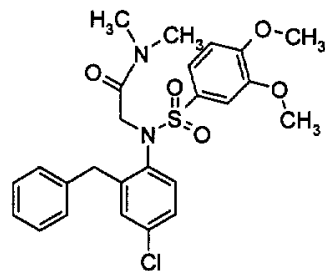
Compound 94:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(2,5-dimethoxy-4-methylphenyl)sulfonyl]glycinamide



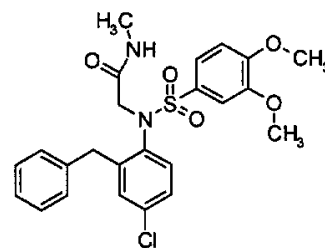
Compound 95:

N^2 -(2-benzyl-4-chlorophenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1, N^1 -dimethylglycinamide



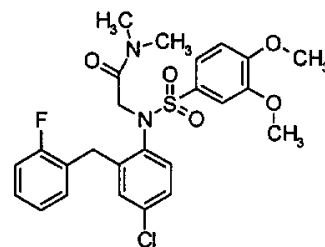
Compound 96:

N^2 -(2-benzyl-4-chlorophenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



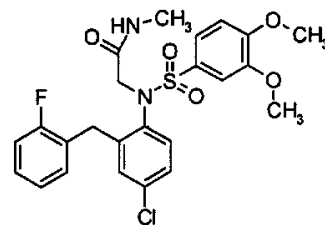
Compound 97:

N^2 -[4-chloro-2-(2-fluorobenzyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]-
 N^1, N^1 -dimethylglycinamide



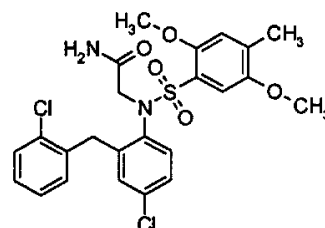
Compound 98:

N^2 -[4-chloro-2-(2-fluorobenzyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



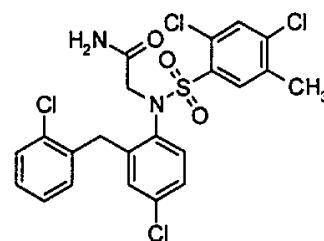
Compound 99:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,5-dimethoxy-4-methylphenyl)sulfonyl]glycinamide



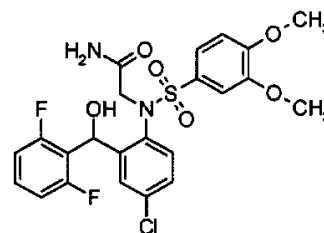
Compound 100:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,4-dichloro-5-methylphenyl)sulfonyl]glycinamide



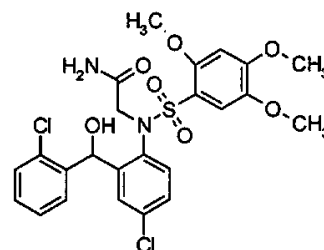
Compound 101:

N^2 -[4-chloro-2-[(2,6-difluorophenyl)(hydroxy)methyl]phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



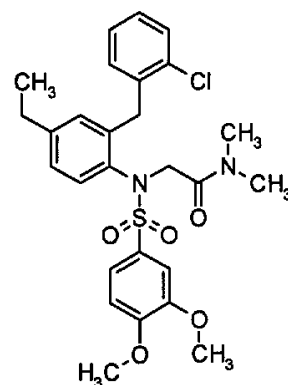
Compound 102:

N^2 -[4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl]-
 N^2 -[(2,4,5-trimethoxyphenyl)sulfonyl]glycinamide



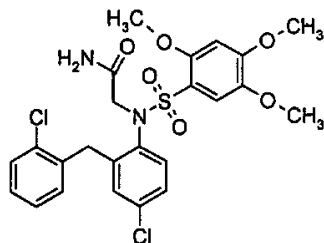
Compound 103:

N^2 -[2-(2-chlorobenzyl)-4-ethylphenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]-
 N^1, N^1 -dimethylglycinamide



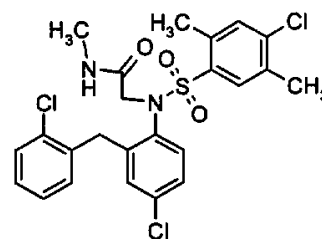
Compound 104:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,4,5-trimethoxyphenyl)sulfonyl]glycinamide



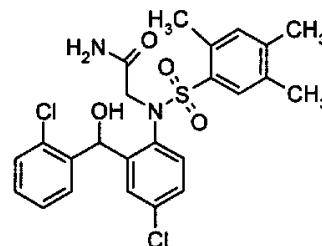
Compound 105:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(4-chloro-2,5-
 dimethylphenyl)sulfonyl]- N^1 -
 methylglycinamide



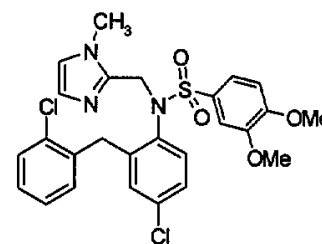
Compound 106:

N^2 -{4-chloro-2-[(2-
 chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(2,4,5-
 trimethylphenyl)sulfonyl]glycinamide



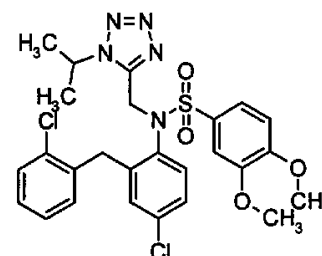
Compound 107:

N -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 3,4-dimethoxy- N -[(1-methyl-1H-imidazol-
 2-yl)methyl]benzenesulfonamide



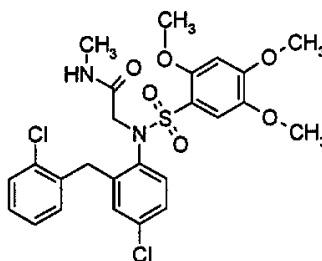
Compound 108:

N -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N -[(1-isopropyl-1H-tetrazol-5-
 yl)methyl]-3,4-
 dimethoxybenzenesulfonamide



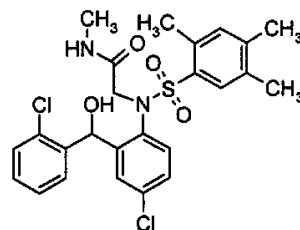
Compound 109:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^1 -methyl- N^2 -[(2,4,5-
 trimethoxyphenyl)sulfonyl]glycinamide



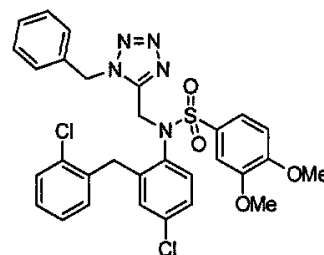
Compound 110:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^1 -methyl- N^2 -[(2,4,5-trimethylphenyl)sulfonyl]glycinamide



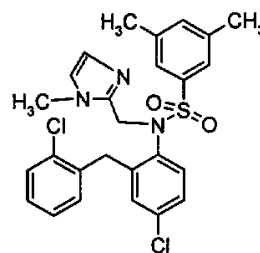
Compound 111:

N -[(1-benzyl-1H-tetrazol-5-yl)methyl]- N -[4-chloro-2-(2-chlorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



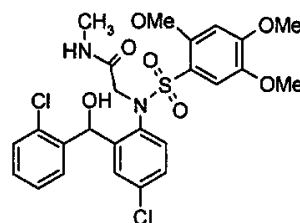
Compound 112:

N -[4-chloro-2-(2-chlorobenzyl)phenyl]-3,5-dimethyl- N -[(1-methyl-1H-imidazol-2-yl)methyl]benzenesulfonamide



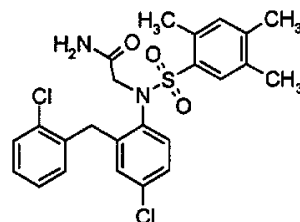
Compound 113:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^1 -methyl- N^2 -[(2,4,5-trimethoxyphenyl)sulfonyl]glycinamide



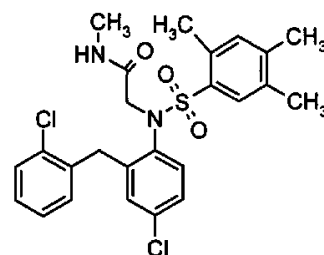
Compound 114:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]- N^2 -[(2,4,5-trimethylphenyl)sulfonyl]glycinamide



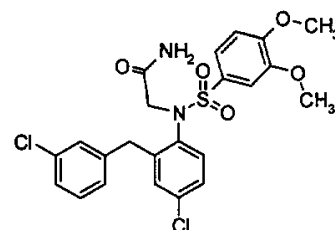
Compound 115:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^1 -methyl- N^2 -[(2,4,5-
 trimethylphenyl)sulfonyl]glycinamide



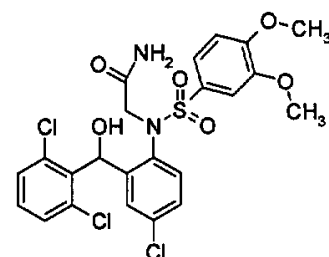
Compound 116:

N^2 -[4-chloro-2-(3-chlorobenzyl)phenyl]-
 N^2 -[(3,4-
 dimethoxyphenyl)sulfonyl]glycinamide



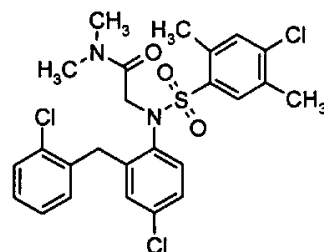
Compound 117:

N^2 -[4-chloro-2-[(2,6-
 dichlorophenyl)(hydroxy)methyl]phenyl]-
 N^2 -[(3,4-
 dimethoxyphenyl)sulfonyl]glycinamide



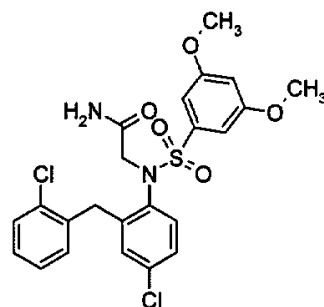
Compound 118:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(4-chloro-2,5-
 dimethylphenyl)sulfonyl]- N^1, N^1 -
 dimethylglycinamide



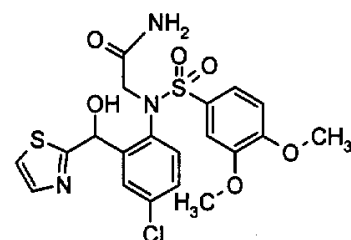
Compound 119:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,5-
 dimethoxyphenyl)sulfonyl]glycinamide



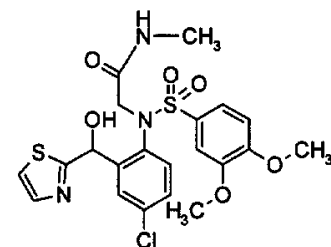
Compound 120:

N^2 -{4-chloro-2-[hydroxy(1,3-thiazol-2-yl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



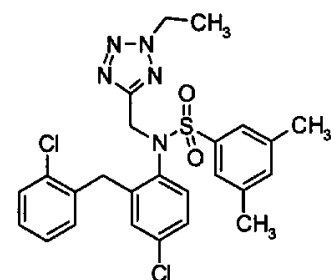
Compound 121:

N^2 -{4-chloro-2-[hydroxy(1,3-thiazol-2-yl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



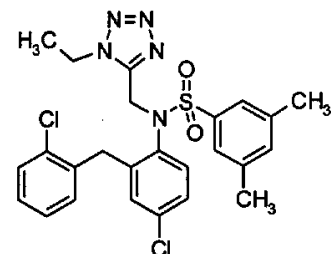
Compound 122:

N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,5-dimethylbenzenesulfonamide



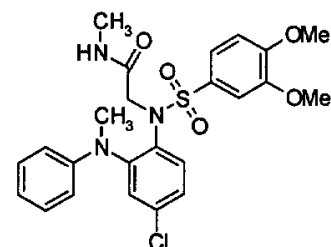
Compound 123:

N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,5-dimethylbenzenesulfonamide



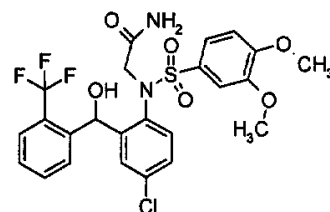
Compound 124:

N^2 -{4-chloro-2-[methyl(phenyl)amino]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



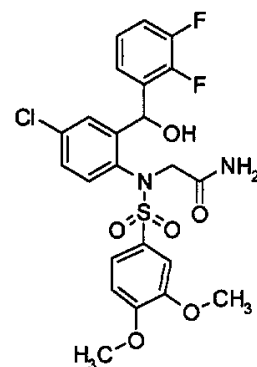
Compound 125:

N^2 -(4-chloro-2-(hydroxy[2-(trifluoromethyl)phenyl]methyl)phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



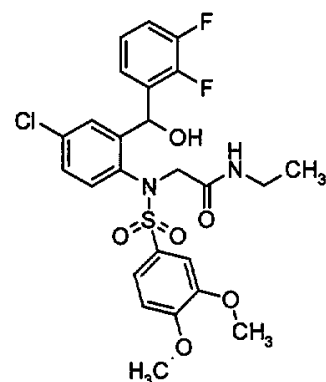
Compound 126:

N^2 -(4-chloro-2-[(2,3-difluorophenyl)(hydroxy)methyl]phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



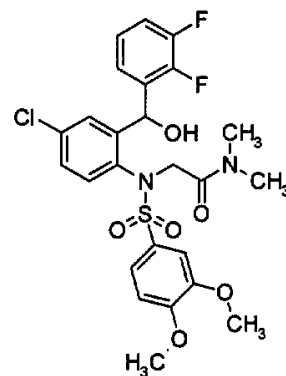
Compound 127:

N^2 -(4-chloro-2-[(2,3-difluorophenyl)(hydroxy)methyl]phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -ethylglycinamide



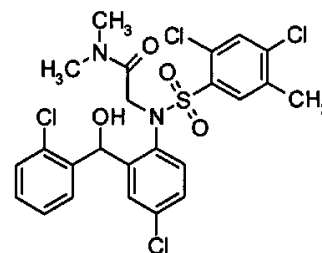
Compound 128:

N^2 -(4-chloro-2-[(2,3-difluorophenyl)(hydroxy)methyl]phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1, N^1 -dimethylglycinamide



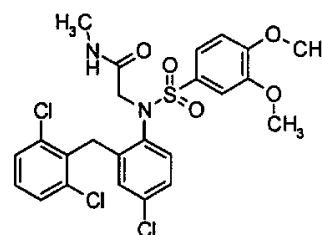
Compound 129:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(2,4-dichloro-5-methylphenyl)sulfonyl]- N^1, N^1 -
 dimethylglycinamide



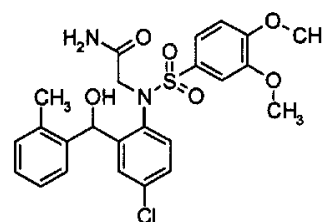
Compound 130:

N^2 -[4-chloro-2-(2,6-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -
 methylglycinamide



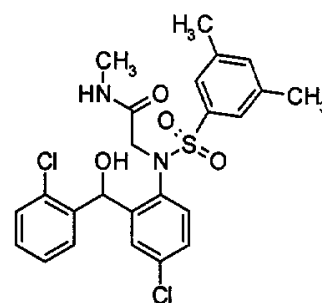
Compound 131:

N^2 -{4-chloro-2-[hydroxy(2-methylphenyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



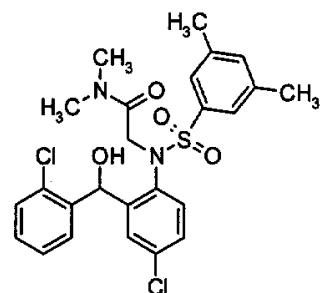
Compound 132:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,5-dimethylphenyl)sulfonyl]- N^1 -
 methylglycinamide



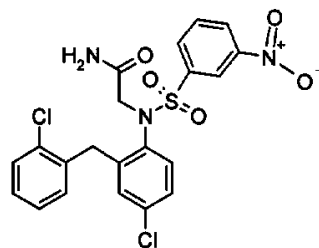
Compound 133:

N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,5-dimethylphenyl)sulfonyl]- N^1, N^1 -
 dimethylglycinamide



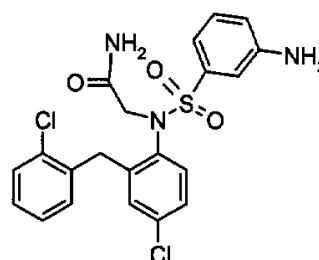
Compound 134:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3-nitrophenyl)sulfonyl]glycinamide



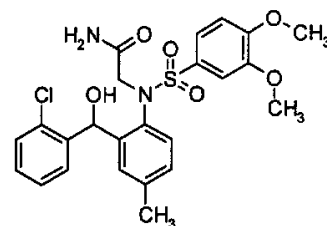
Compound 135:

N^2 -[(3-aminophenyl)sulfonyl]- N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]glycinamide



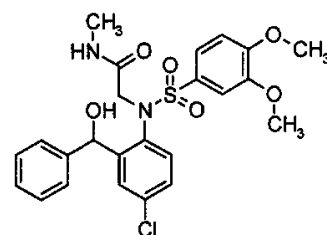
Compound 136:

N^2 -{2-[(2-chlorophenyl)(hydroxy)methyl]-4-methylphenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



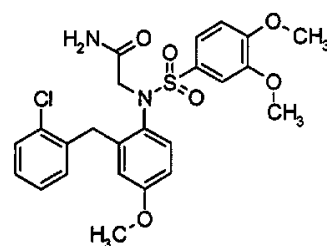
Compound 137:

N^2 -{4-chloro-2-[hydroxy(phenyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



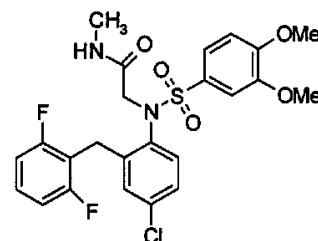
Compound 138:

N^2 -[2-(2-chlorobenzyl)-4-methoxyphenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



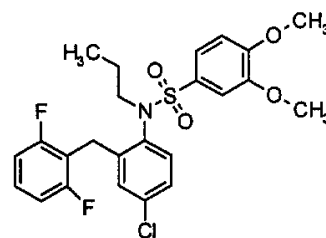
Compound 139:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



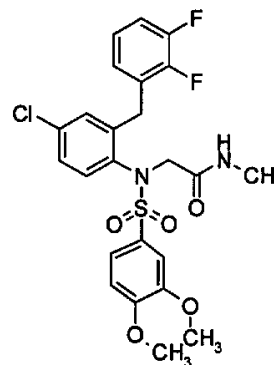
Compound 140:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-propylbenzenesulfonamide



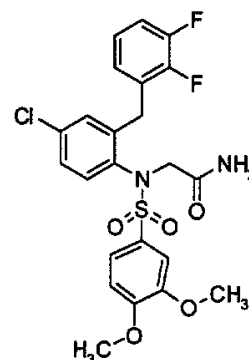
Compound 141:

N^2 -[4-chloro-2-(2,3-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



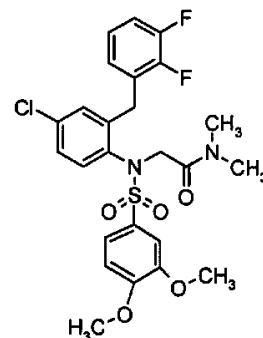
Compound 142:

N^2 -[4-chloro-2-(2,3-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



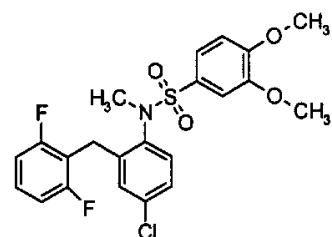
Compound 143:

N^2 -[4-chloro-2-(2,3-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1, N^1 -dimethylglycinamide



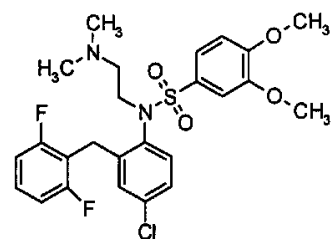
Compound 144:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-methylbenzenesulfonamide



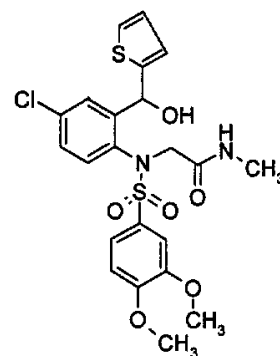
Compound 145:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-(dimethylamino)ethyl]-3,4-dimethoxybenzenesulfonamide



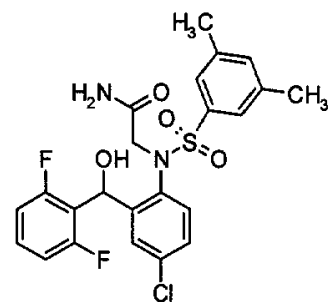
Compound 146:

N^2 -{4-chloro-2-[hydroxy(2-thienyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



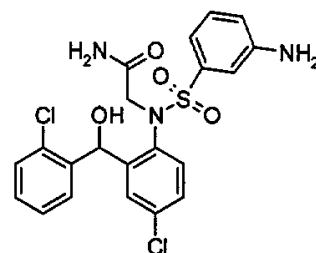
Compound 147:

N^2 -{4-chloro-2-[(2,6-difluorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(3,5-dimethylphenyl)sulfonyl]glycinamide



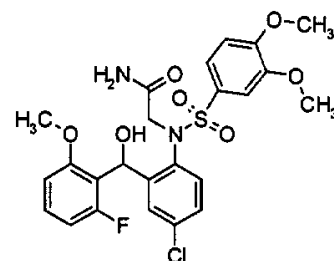
Compound 148:

N^2 -[(3-aminophenyl)sulfonyl]- N^2 -(4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl)-glycinamide



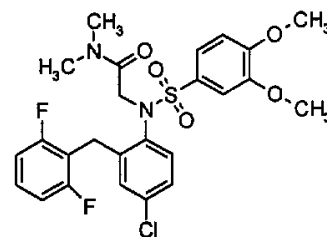
Compound 149:

N^2 -(4-chloro-2-[(2-fluoro-6-methoxyphenyl)(hydroxy)methyl]phenyl)- N^2 -(3,4-dimethoxyphenyl)sulfonyl]glycinamide



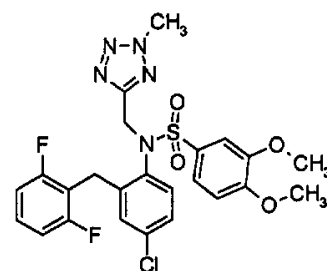
Compound 150:

N^2 -(4-chloro-2-(2,6-difluorobenzyl)phenyl)- N^2 -(3,4-dimethoxyphenyl)sulfonyl]- N^1, N^1 -dimethylglycinamide



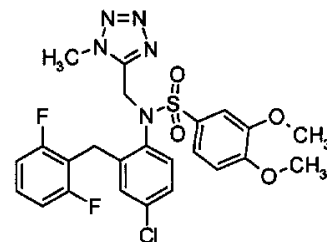
Compound 151:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide



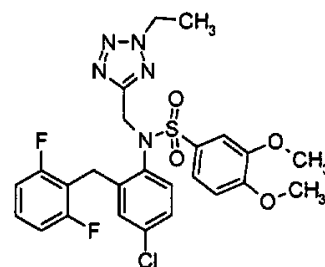
Compound 152:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide



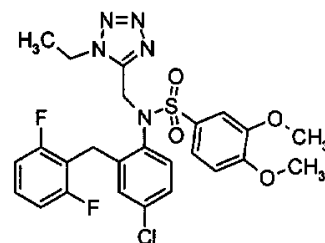
Compound 153:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



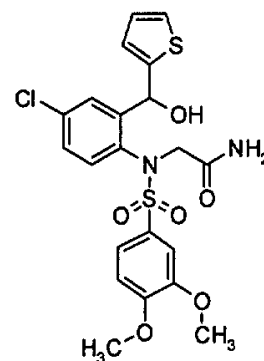
Compound 154:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



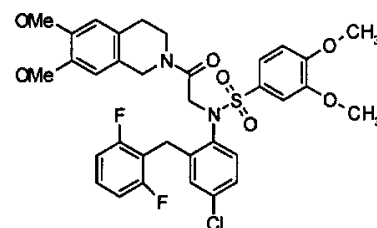
Compound 155:

N²-{4-chloro-2-[hydroxy(2-thienyl)methyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



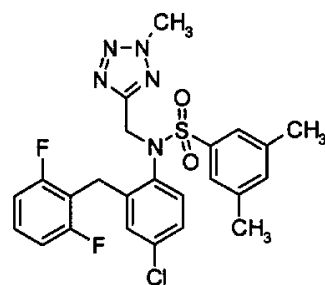
Compounds 156:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl]-3,4-dimethoxybenzenesulfonamide



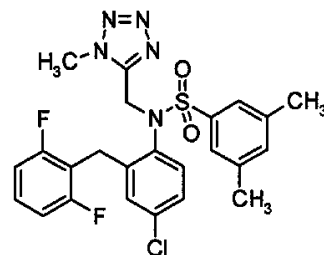
Compound 157:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,5-dimethyl-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide



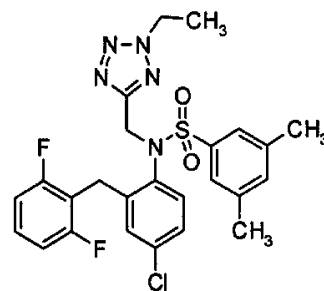
Compound 158:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,5-dimethyl-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide



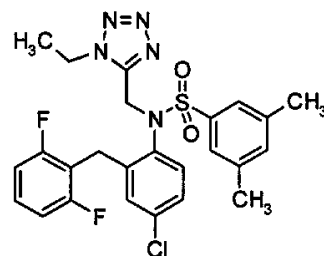
Compound 159:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,5-dimethylbenzenesulfonamide



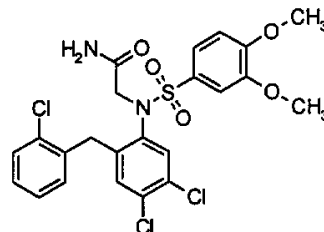
Compound 160:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,5-dimethylbenzenesulfonamide



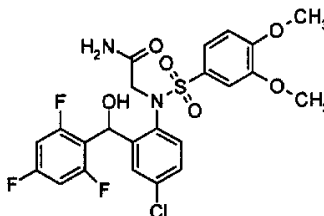
Compound 161:

N²-[4,5-dichloro-2-(2-chlorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



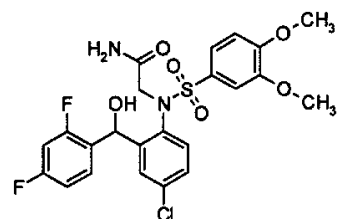
Compound 162:

N²-{4-chloro-2-[hydroxy(2,4,6-trifluorophenyl)methyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



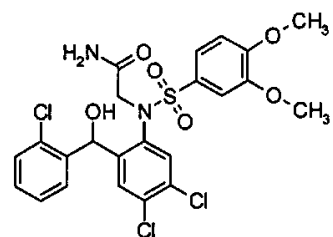
Compound 163:

N^2 -{4-chloro-2-[(2,4-difluorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



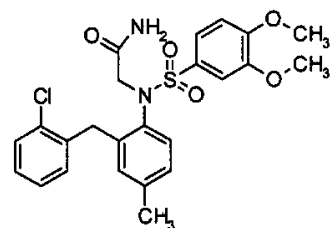
Compound 164:

N^2 -{4,5-dichloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



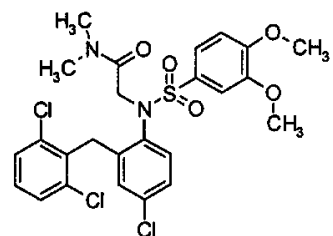
Compound 165:

N^2 -[2-(2-chlorobenzyl)-4-methylphenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



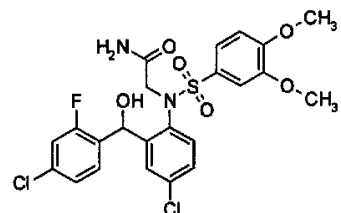
Compound 166:

N^2 -[4-chloro-2-(2,6-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 , N^1 -dimethylglycinamide



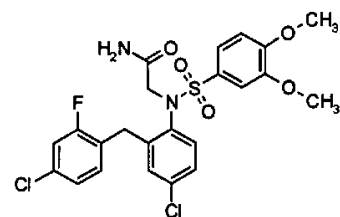
Compound 167:

N^2 -{4-chloro-2-[(4-chloro-2-fluorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



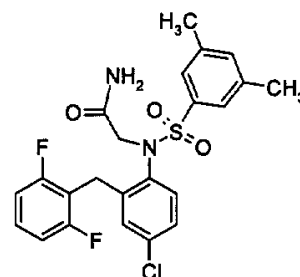
Compound 168:

N^2 -[4-chloro-2-(4-chloro-2-fluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



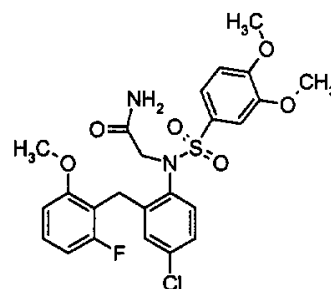
Compound 169:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,5-dimethylphenyl)sulfonyl]glycinamide



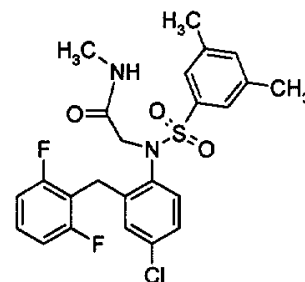
Compound 170:

N^2 -[4-chloro-2-(2-fluoro-6-methoxybenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



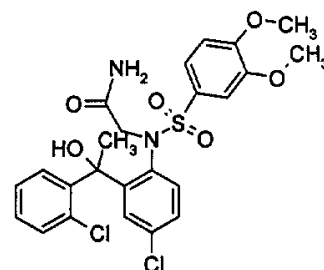
Compound 171:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,5-dimethylphenyl)sulfonyl]- N^1 -methylglycinamide



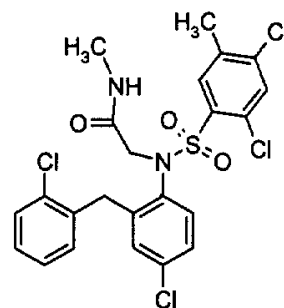
Compound 172:

N^2 -[4-chloro-2-[1-(2-chlorophenyl)-1-hydroxyethyl]phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



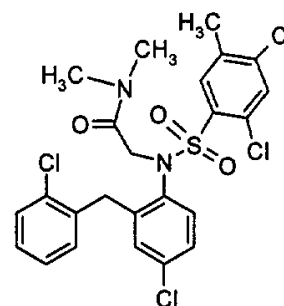
Compound 173:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,4-dichloro-5-methylphenyl)sulfonyl]- N^1 -
 methylglycinamide



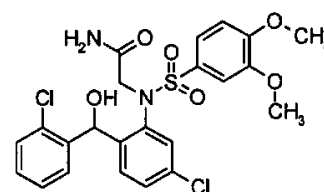
Compound 174:

N^2 -[4-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(2,4-dichloro-5-methylphenyl)sulfonyl]- N^1,N^1 --
 dimethylglycinamide



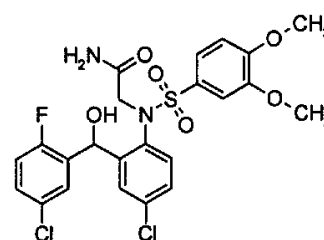
Compound 175:

N^2 -{5-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



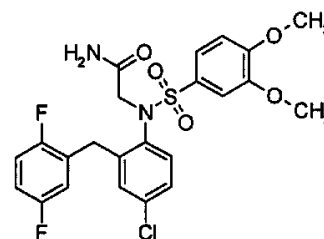
Compound 176:

N^2 -{4-chloro-2-[(5-chloro-2-fluorophenyl)(hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



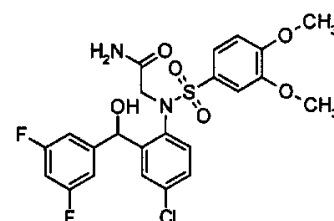
Compound 177:

N^2 -[4-chloro-2-(2,5-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



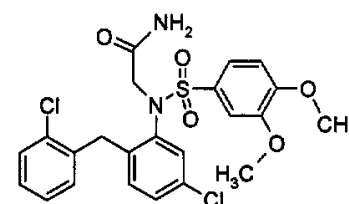
Compound 178:

N^2 -[4-chloro-2-[(3,5-difluorophenyl)(hydroxymethyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



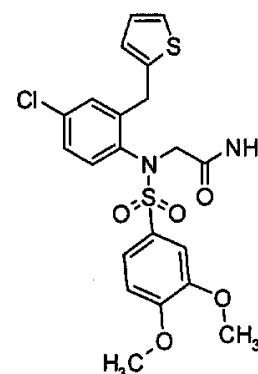
Compound 179:

N^2 -[5-chloro-2-(2-chlorobenzyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



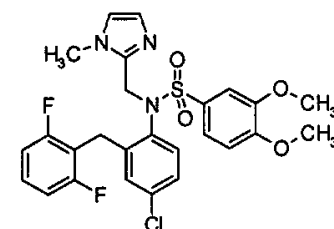
Compound 180:

N^2 -[4-chloro-2-(2-thienylmethyl)phenyl]-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



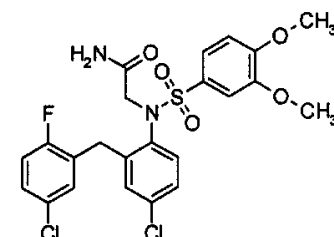
Compound 181:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-
 [(1-methyl-1H-imidazol-2-yl)methyl]benzenesulfonamide



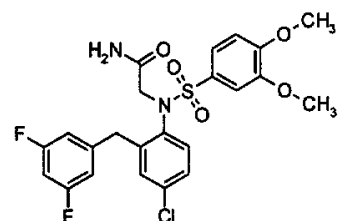
Compound 182:

N^2 -[4-chloro-2-(5-chloro-2-fluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



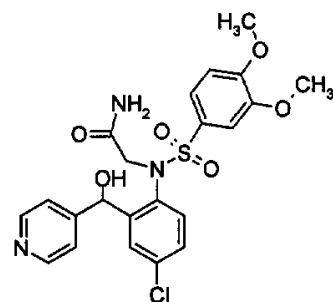
Compound 183:

N^2 -[4-chloro-2-(3,5-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



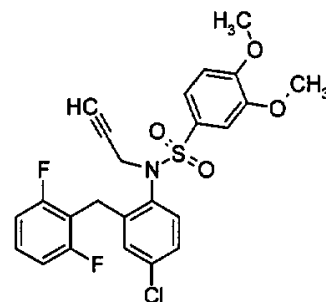
Compound 184:

N^2 -{4-chloro-2-[hydroxy(pyridin-4-yl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



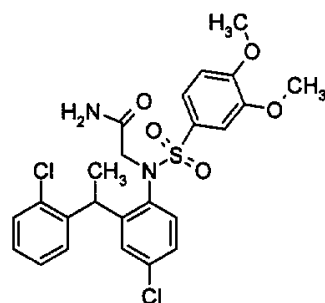
Compound 185:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-prop-2-yn-1-ylbenzenesulfonamide



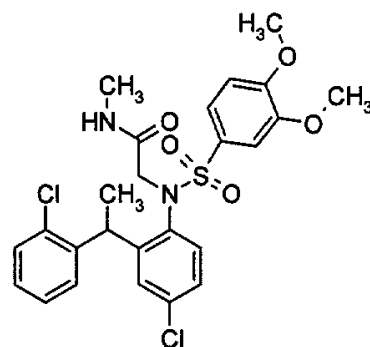
Compound 186:

N^2 -{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



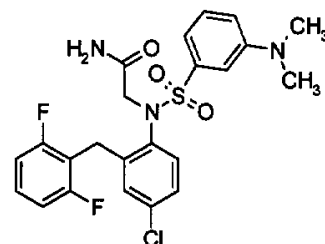
Compound 187:

N^2 -{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide



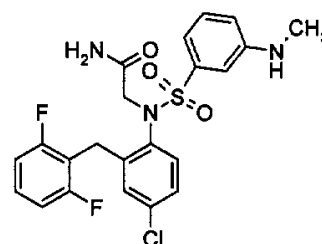
Compound 188:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -{[3-(dimethylamino)phenyl]sulfonyl}-glycinamide



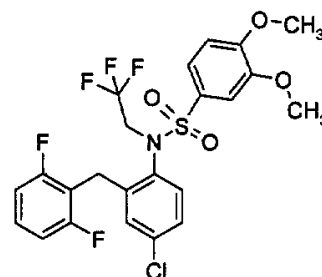
Compound 189:

N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -{[3-(methylamino)phenyl]sulfonyl}-glycinamide



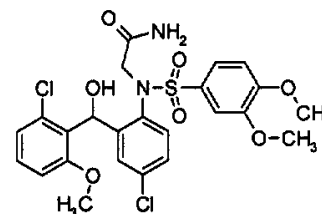
Compound 190:

N -[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy- N -(2,2,2-trifluoroethyl)benzenesulfonamide



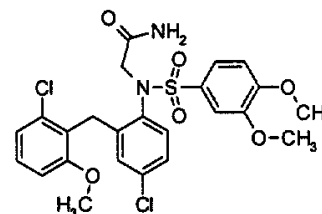
Compound 191:

N^2 -{4-chloro-2-[(2-chloro-6-methoxyphenyl)(hydroxymethyl)phenyl]}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



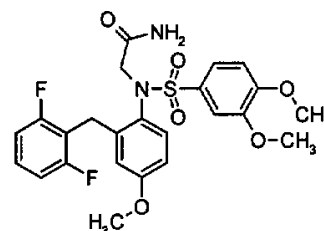
Compound 192:

N^2 -[4-chloro-2-(2-chloro-6-methoxybenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



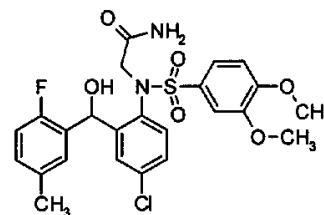
Compound 193:

N^2 -[2-(2,6-difluorobenzyl)-4-methoxyphenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



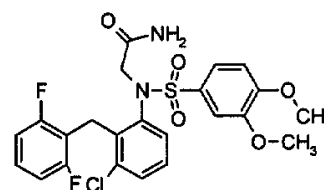
Compound 194:

N^2 -(4-chloro-2-[(2-fluoro-5-methylphenyl)(hydroxy)methyl]phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



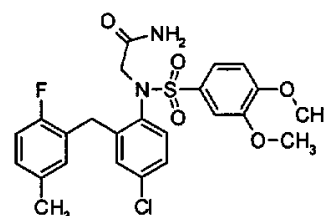
Compound 195:

N^2 -[3-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



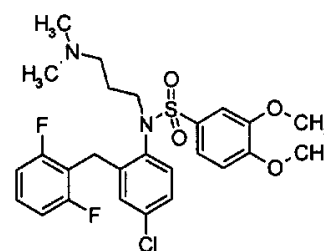
Compound 196:

N^2 -[4-chloro-2-(2-fluoro-5-methylbenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



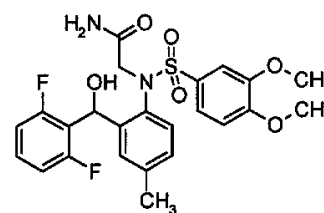
Compound 197:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[3-(dimethylamino)propyl]-3,4-dimethoxybenzenesulfonamide



Compound 198:

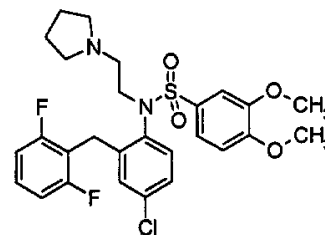
N^2 -(2-[(2,6-difluorophenyl)(hydroxy)methyl]-4-methylphenyl)- N^2 -[(3,4-



dimethoxyphenyl) sulfonyl]glycinamide

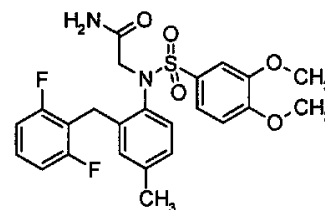
Compound 199:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-pyrrolidin-1-ylethyl)benzenesulfonamide



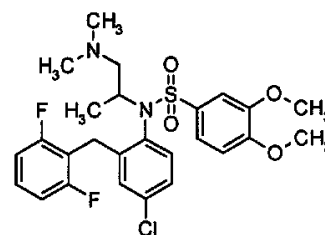
Compound 200:

N²-[2-(2,6-difluorobenzyl)-4-methylphenyl]-N²-[(3,4-dimethoxyphenyl) sulfonyl]glycinamide



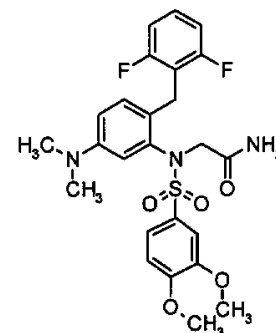
Compound 201:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-(dimethylamino)-1-methylethyl]-3,4-dimethoxybenzenesulfonamide



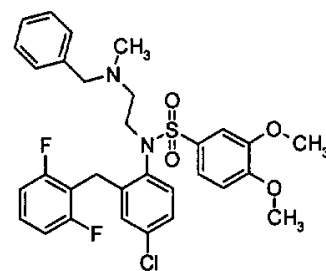
Compound 202:

N²-[2-(2,6-difluorobenzyl)-5-(dimethylamino)phenyl]-N²-[(3,4-dimethoxyphenyl) sulfonyl]glycinamide



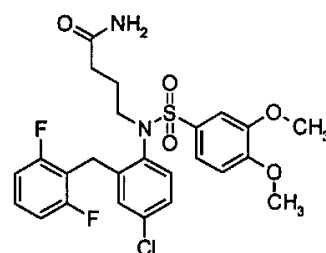
Compound 203:

N-{2-[benzyl(methyl)amino]ethyl}-N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



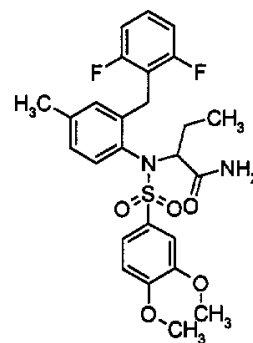
Compound 204:

4-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



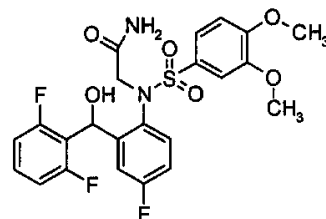
Compound 205:

2-{[2-(2,6-difluorobenzyl)-4-methylphenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



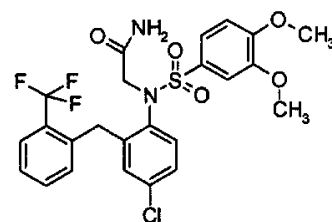
Compound 206:

N²-{2-[(2,6-difluorophenyl)(hydroxymethyl)-4-fluorophenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



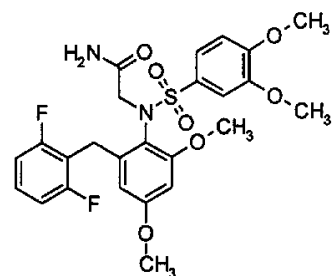
Compound 207:

N²-{4-chloro-2-[2-(trifluoromethyl)benzyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



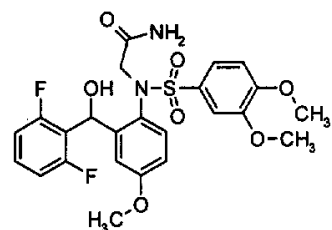
Compound 208:

N^2 -[2-(2,6-difluorobenzyl)-4,6-dimethoxyphenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



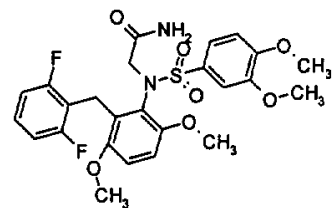
Compound 209:

N^2 -{2-[(2,6-difluorophenyl)(hydroxy)methyl]-4-methoxyphenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



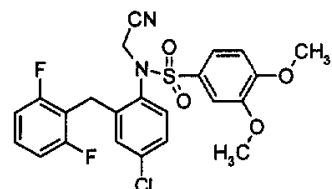
Compound 210:

N^2 -[2-(2,6-difluorobenzyl)-3,6-dimethoxyphenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



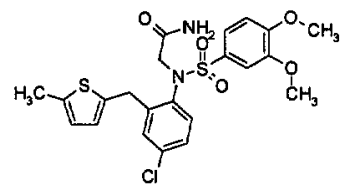
Compound 211:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(cyanomethyl)-3,4-dimethoxybenzenesulfonamide



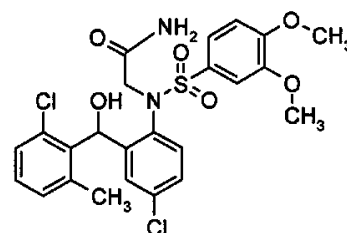
Compound 212:

N^2 -{4-chloro-2-[(5-methyl-2-thienyl)methyl]phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



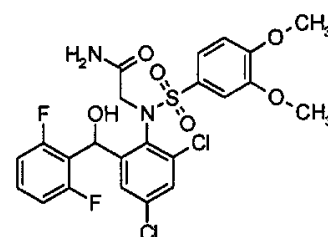
Compound 213:

N^2 -{4-chloro-2-[(2-chloro-6-methylphenyl) (hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



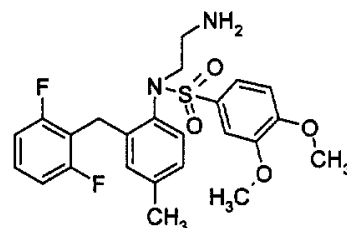
Compound 214:

N^2 -{2,4-dichloro-6-[(2,6-difluorophenyl) (hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



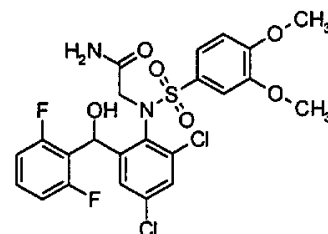
Compound 215:

N-(2-aminoethyl)-N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide



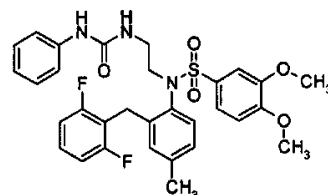
Compound 216:

N^2 -{2,4-dichloro-6-[(2,6-difluorophenyl) (hydroxy)methyl]phenyl}-
 N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



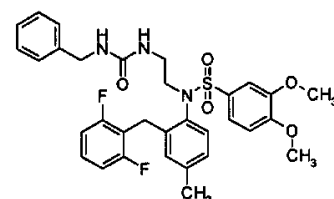
Compound 217:

N-{2-[(anilinocarbonyl)amino]ethyl}-N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide



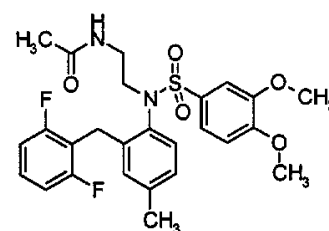
Compound 218:

N-(2-
{ [(benzylamino) carbonyl] amino} ethyl) -N-
[2-(2,6-difluorobenzyl)-4-
methylphenyl]-3,4-
dimethoxybenzenesulfonamide



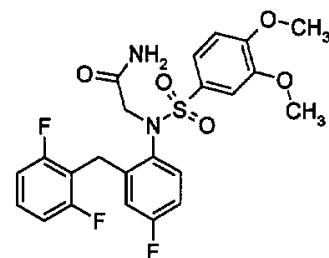
Compound 219:

N-(2-{ [2-(2,6-difluorobenzyl)-4-
methylphenyl] [(3,4-
dimethoxyphenyl) sulfonyl] amino} ethyl) -
acetamide



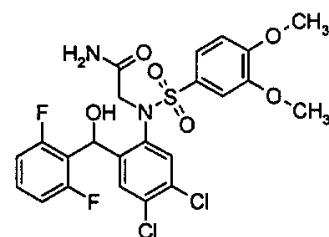
Compound 220:

N²-[2-(2,6-difluorobenzyl)-4-
fluorophenyl]-N²-[(3,4-
dimethoxyphenyl) sulfonyl]glycinamide



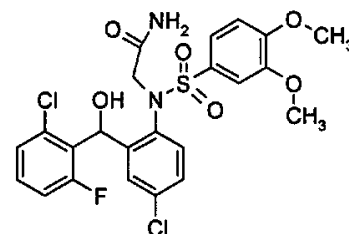
Compound 221:

N²-{4,5-dichloro-2-[(2,6-
difluorophenyl) (hydroxy) methyl] phenyl}-
N²-[(3,4-
dimethoxyphenyl) sulfonyl]glycinamide



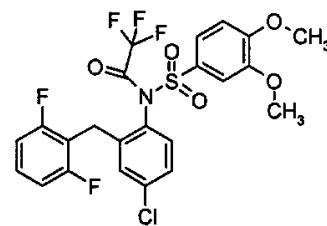
Compound 222:

N²-{4-chloro-2-[(2-chloro-6-
fluorophenyl) (hydroxy) methyl] phenyl}-
N²-[(3,4-
dimethoxyphenyl) sulfonyl]glycinamide



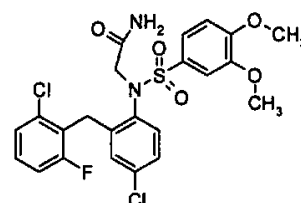
Compound 223:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-2,2,2-trifluoroacetamide



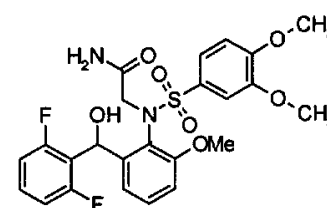
Compound 224:

N²-[4-chloro-2-(2-chloro-6-fluorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



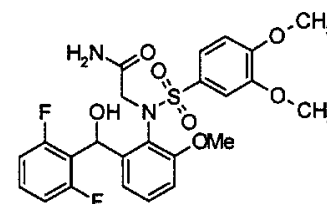
Compound 225:

N²-{2-[(2,6-difluorophenyl)(hydroxy)methyl]-6-methoxyphenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



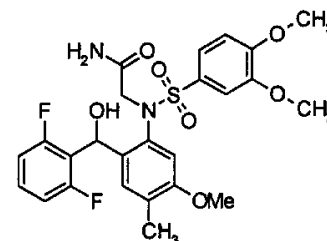
Compound 226:

N²-{2-[(2,6-difluorophenyl)(hydroxy)methyl]-6-methoxyphenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



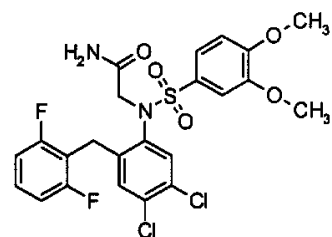
Compound 227:

N²-{2-[(2,6-difluorophenyl)(hydroxy)methyl]-5-methoxy-4-methylphenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



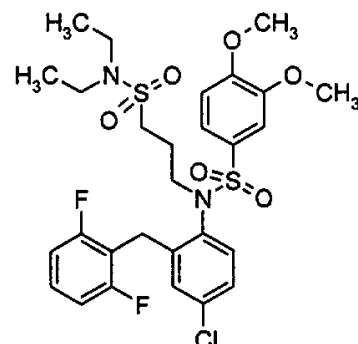
Compound 228:

N^2 -[4,5-dichloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



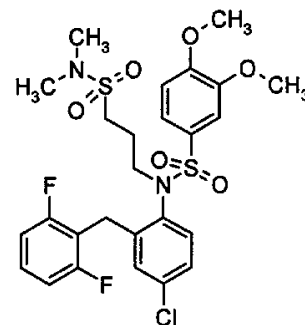
Compound 229:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-{3-[(diethylamino)sulfonyl]propyl}-3,4-dimethoxybenzenesulfonamide



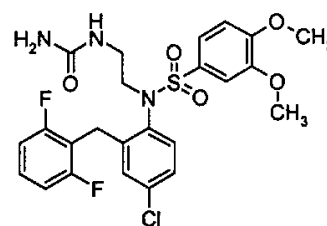
Compound 230:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-{3-[(dimethylamino)sulfonyl]propyl}-3,4-dimethoxybenzenesulfonamide



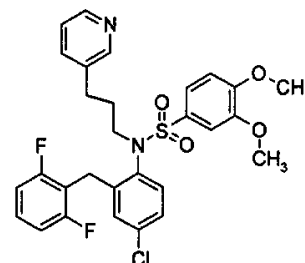
Compound 231:

N-{2-[(aminocarbonyl)amino]ethyl}-N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



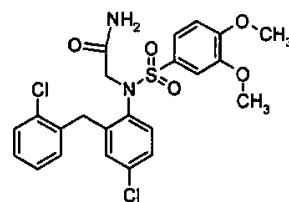
Compound 232:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(3-pyridin-3-ylpropyl)benzenesulfonamide



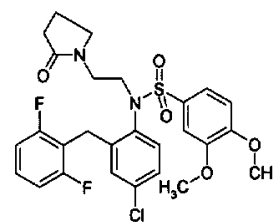
Compound 233:

*N*²-[4-chloro-2-(2-chlorobenzyl)phenyl]-
*N*²-[(3,4-
dimethoxyphenyl)sulfonyl]glycinamide



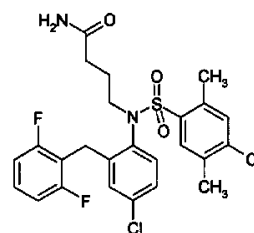
Compound 234:

N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-3,4-dimethoxy-*N*-
[2-(2-oxopyrrolidin-1-
yl)ethyl]benzenesulfonamide



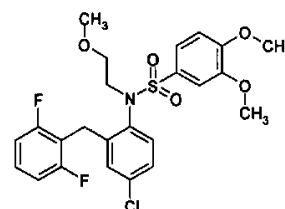
Compound 235:

4-{[4-chloro-2-(2,6-
difluorobenzyl)phenyl][(4-chloro-2,5-
dimethylphenyl)sulfonyl]amino}-
butanamide



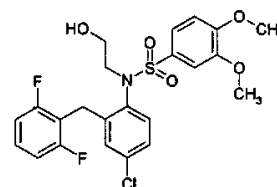
Compound 236:

N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-3,4-dimethoxy-*N*-
(2-methoxyethyl)benzenesulfonamide



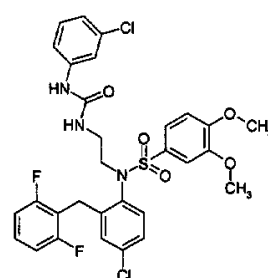
Compound 237:

N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-*N*-(2-
hydroxyethyl)-3,4-
dimethoxybenzenesulfonamide



Compound 238:

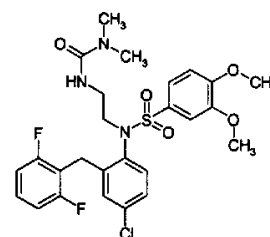
N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-*N*-[2-({[(3-
chlorophenyl)amino]carbonyl}amino)-



ethyl]-3,4-dimethoxybenzenesulfonamide

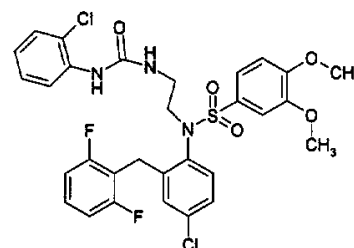
Compound 239:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(2-
{[(dimethylamino)carbonyl]amino}ethyl)-
3,4-dimethoxybenzenesulfonamide



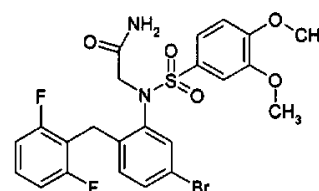
Compound 240:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-({[(2-chlorophenyl)amino]carbonyl}amino)-
ethyl]-3,4-dimethoxybenzenesulfonamide



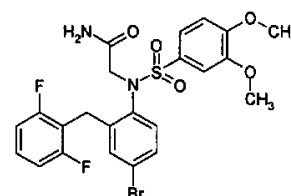
Compound 241:

N~2~- [5-bromo-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



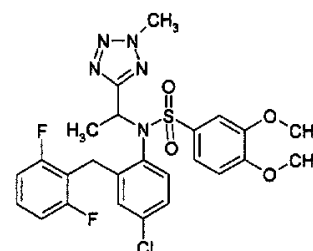
Compound 242:

N~2~- [4-bromo-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



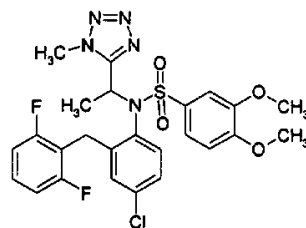
Compound 243:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-
[1-(2-methyl-2H-tetrazol-5-yl)ethyl]benzenesulfonamide

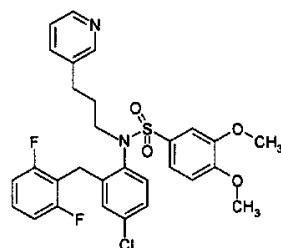


Compound 244:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[1-(1-methyl-1H-tetrazol-5-yl)ethyl]benzenesulfonamide

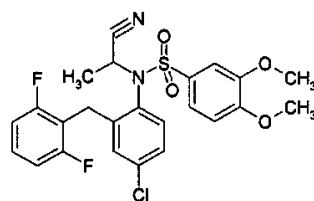


Compound 245: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(3-pyridin-3-ylpropyl)benzenesulfonamide



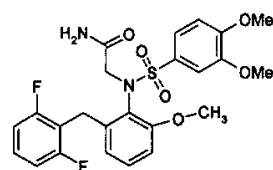
Compound 246:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(1-cyanoethyl)-3,4-dimethoxybenzenesulfonamide



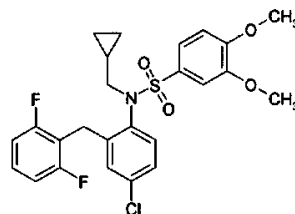
Compound 247:

N~2~- [2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



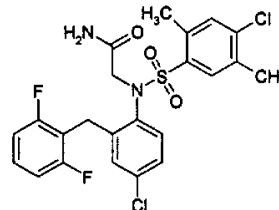
Compound 248:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(cyclopropylmethyl)-3,4-dimethoxybenzenesulfonamide



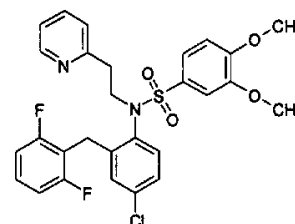
Compound 249:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide



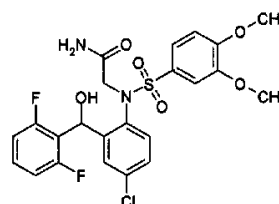
Compound 250:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-pyridin-2-ylethyl)benzenesulfonamide



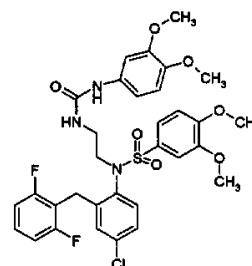
Compound 251:

N-[4-chloro-2-[(2,6-difluorophenyl)(hydroxymethyl)phenyl]-N-[3,4-dimethoxyphenyl)sulfonyl]glycinamide



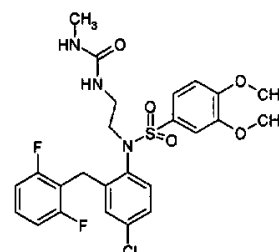
Compound 252:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-([(3,4-dimethoxyphenyl)amino]carbonyl)amino]ethyl]-3,4-dimethoxybenzenesulfonamide



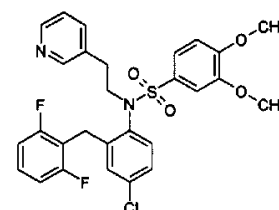
Compound 253:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-([(methylamino)carbonyl]amino)ethyl)-benzenesulfonamide



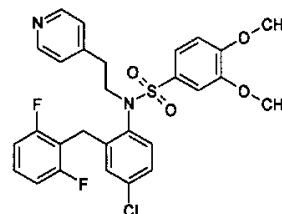
Compound 254:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-pyridin-3-ylethyl)benzenesulfonamide



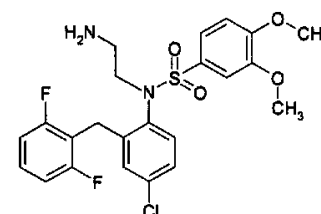
Compound 255:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-pyridin-4-ylethyl)benzenesulfonamide



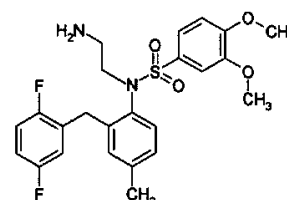
Compound 256:

N-(2-aminoethyl)-N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



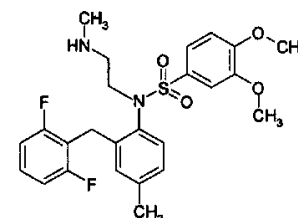
Compound 257:

N-(2-aminoethyl)-N-[2-(2,5-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide



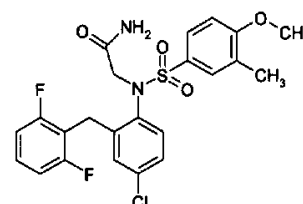
Compound 258:

N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxy-N-[2-(methylamino)ethyl]benzenesulfonamide



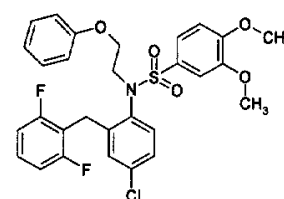
Compound 259:

N~2~-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~-[(4-methoxy-3-methylphenyl)sulfonyl]glycinamide



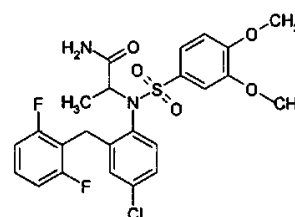
Compound 260:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-phenoxyethyl)benzenesulfonamide



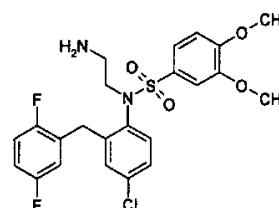
Compound 261:

N~2~- [4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]alaninamide



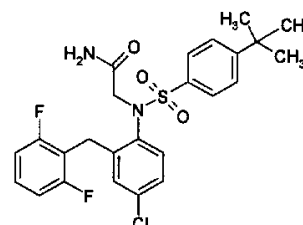
Compound 262:

N-(2-aminoethyl)-N-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



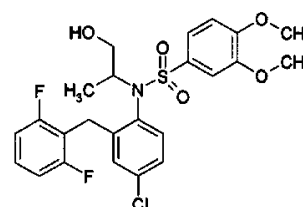
Compound 263:

N~2~- [(4-tert-butylphenyl)sulfonyl]-N~2~- [4-chloro-2-(2,6-difluorobenzyl)phenyl]glycinamide



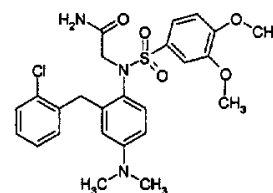
Compound 264:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(2-hydroxy-1-methylethyl)-3,4-dimethoxybenzenesulfonamide



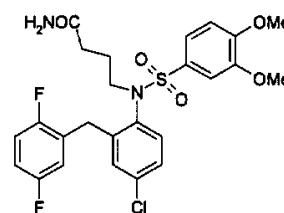
Compound 265:

N~2~- [2-(2-chlorobenzyl)-4-(dimethylamino)phenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



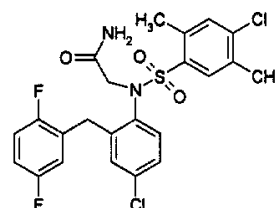
Compound 266:

4-{[4-chloro-2-(2,5-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



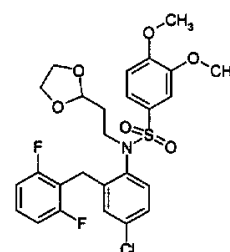
Compound 267:

N-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-N-[4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide



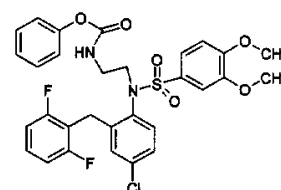
Compound 268:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-(1,3-dioxolan-2-yl)ethyl]-3,4-dimethoxybenzenesulfonamide



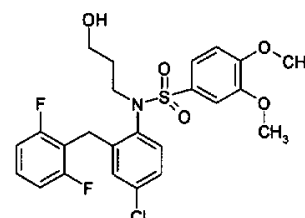
Compound 269:

phenyl (2-([4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino)ethyl)-carbamate



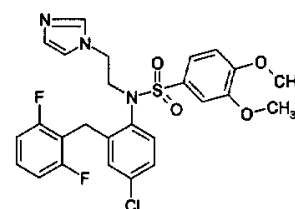
Compound 270:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(3-hydroxypropyl)-3,4-dimethoxybenzenesulfonamide



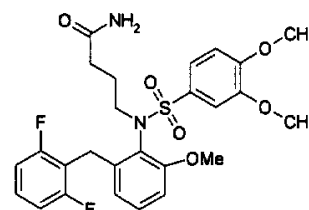
Compound 271:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[2-(1H-imidazol-1-yl)ethyl]-3,4-dimethoxybenzenesulfonamide



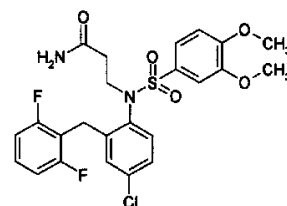
Compound 272:

4-{[2-(2,6-difluorobenzyl)-6-methoxyphenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



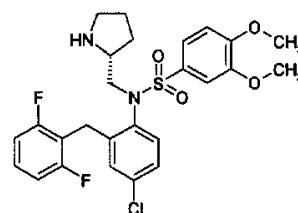
Compound 273:

N~3~-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~3~-[(3,4-dimethoxyphenyl)sulfonyl]-beta-alaninamide



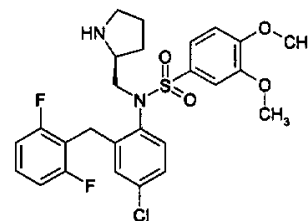
Compound 274:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(2R)-pyrrolidin-2-ylmethyl]benzenesulfonamide



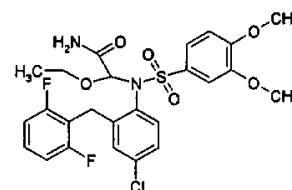
Compound 275:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(2S)-pyrrolidin-2-ylmethyl]benzenesulfonamide



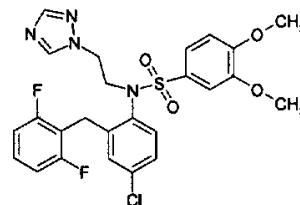
Compound 276:

2-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-2-ethoxyacetamide



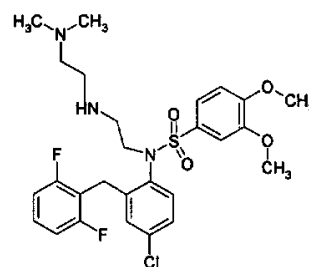
Compound 277:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[2-(1H-1,2,4-triazol-1-yl)ethyl]benzenesulfonamide



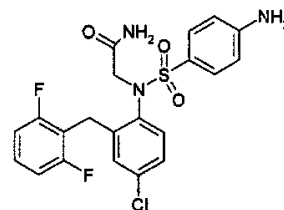
Compound 278:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(2-{[2-(dimethylamino)ethyl]amino}ethyl)-3,4-dimethoxybenzenesulfonamide



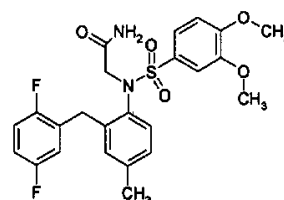
Compound 279:

N~2~-[(4-aminophenyl)sulfonyl]-N~2~-[4-chloro-2-(2,6-difluorobenzyl)phenyl]glycinamide



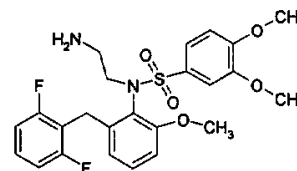
Compound 280:

N~2~-[2-(2,5-difluorobenzyl)-4-methylphenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



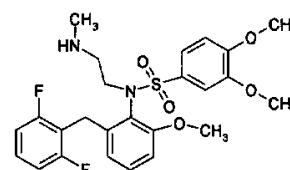
Compound 281:

N-(2-aminoethyl)-N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxybenzenesulfonamide



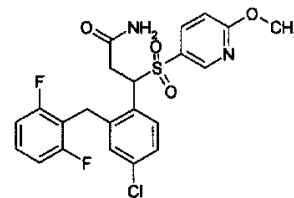
Compound 282:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxy-N-[2-(methylamino)ethyl]benzenesulfonamide



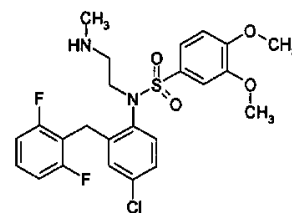
Compound 283:

N~2~- [4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(6-methoxypyridin-3-yl)sulfonyl]glycinamide



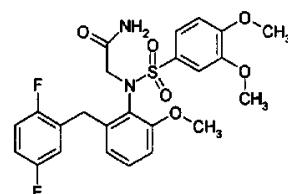
Compound 284:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[2-(methylamino)ethyl]benzenesulfonamide



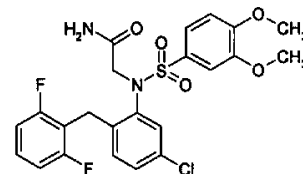
Compound 285:

N~2~- [2-(2,5-difluorobenzyl)-6-methoxyphenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



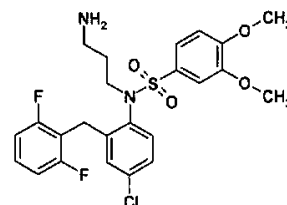
Compound 286:

N~2~- [5-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



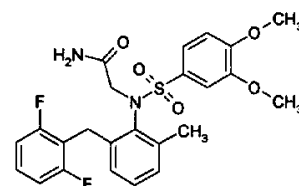
Compound 287:

N-(3-aminopropyl)-N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide



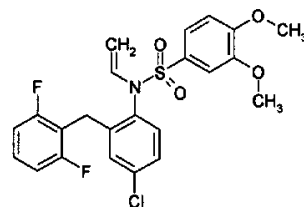
Compound 288:

N~2~- [2-(2,6-difluorobenzyl)-6-methylphenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]glycinamide



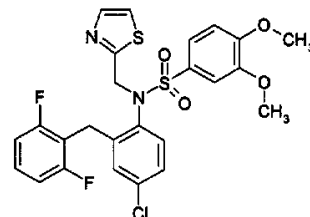
Compound 289:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-vinylbenzenesulfonamide



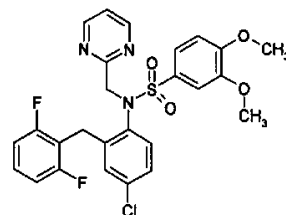
Compound 290:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(1,3-thiazol-2-ylmethyl)benzenesulfonamide



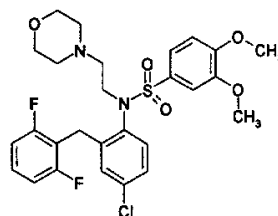
Compound 291:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(pyrimidin-2-ylmethyl)benzenesulfonamide



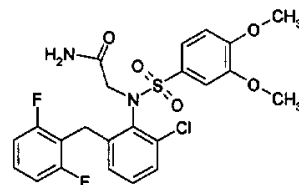
Compound 292:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(2-morpholin-4-ylethyl)benzenesulfonamide



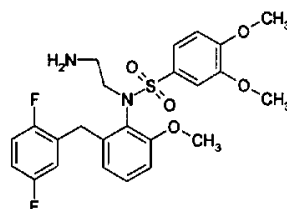
Compound 293:

N~2~-[2-chloro-6-(2,6-difluorobenzyl)phenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



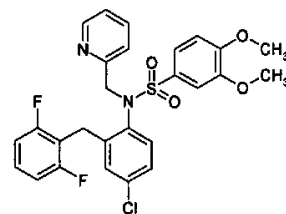
Compound 294:

N-(2-aminoethyl)-N-[2-(2,5-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxybenzenesulfonamide



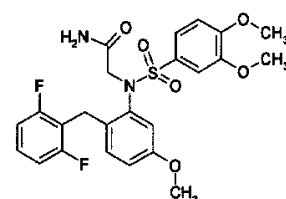
Compound 295:

N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(pyridin-2-ylmethyl)benzenesulfonamide



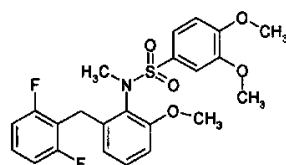
Compound 296:

N~2~-[2-(2,6-difluorobenzyl)-5-methoxyphenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



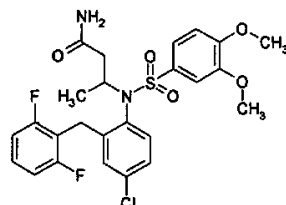
Compound 297:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxy-N-methylbenzenesulfonamide



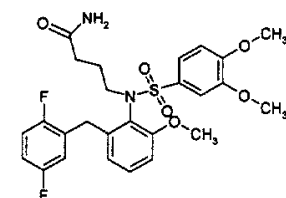
Compound 298:

3-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



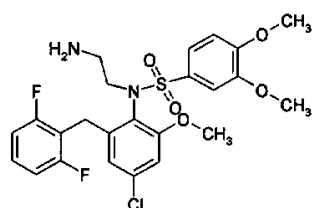
Compound 299:

4-{[2-(2,5-difluorobenzyl)-6-methoxyphenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-butanamide



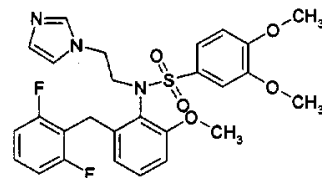
Compound 300:

N-(2-aminoethyl)-N-[4-chloro-2-(2,6-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxybenzenesulfonamide



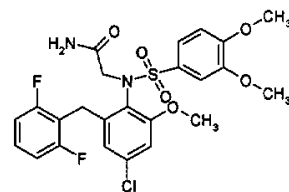
Compound 301:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[2-(1H-imidazol-1-yl)ethyl]-3,4-dimethoxybenzenesulfonamide



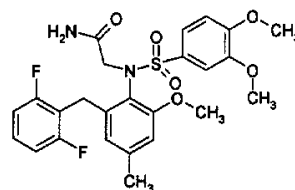
Compound 302:

N~2~-[4-chloro-2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



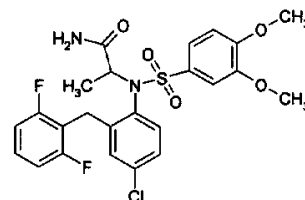
Compound 303:

N~2~-[2-(2,6-difluorobenzyl)-6-methoxy-4-methylphenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



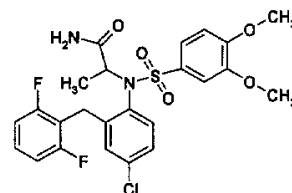
Compound 304:

(+)-N~2~-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]alaninamide



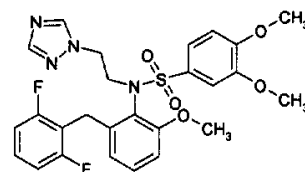
Compound 305:

(-)-N~2~-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~-[(3,4-dimethoxyphenyl)sulfonyl]alaninamide



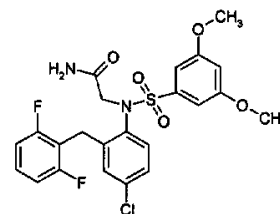
Compound 306:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-3,4-dimethoxy-N-[2-(1H-1,2,4-triazol-1-yl)ethyl]benzenesulfonamide



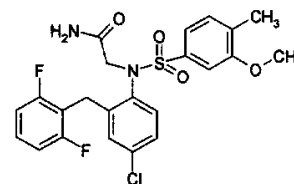
Compound 307:

N~2~- [4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3,5-dimethoxyphenyl)sulfonyl]glycinamide



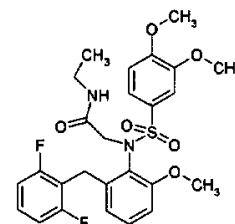
Compound 308:

N~2~- [4-chloro-2-(2,6-difluorobenzyl)phenyl]-N~2~- [(3-methoxy-4-methylphenyl)sulfonyl]glycinamide



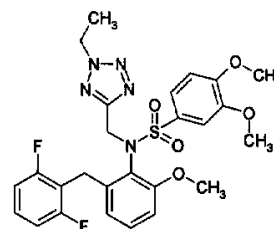
Compound 309:

N~2~- [2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N~2~- [(3,4-dimethoxyphenyl)sulfonyl]-N-ethylglycinamide



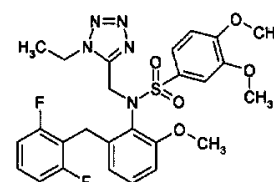
Compound 310:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



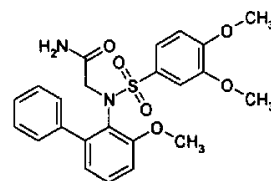
Compound 311:

N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide



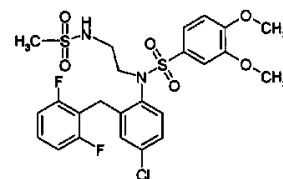
Compound 312:

N~2~-[(3,4-dimethoxyphenyl)sulfonyl]-
N~2~-[(3-methoxybiphenyl-2-
yl)glycinamide



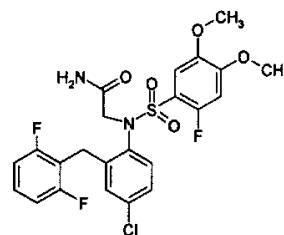
Compound 313:

N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-3,4-dimethoxy-N-
{2-[(methylsulfonyl)amino]ethyl}-
benzenesulfonamide



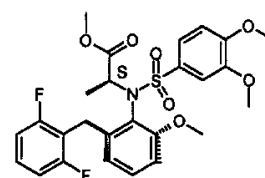
Compound 314:

N~2~-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-N~2~-[(2-fluoro-
4,5-
dimethoxyphenyl)sulfonyl]glycinamide



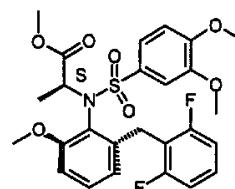
Compound 315:

methyl N-[2-(2,6-difluorobenzyl)-6-
methoxyphenyl]-N-[(3,4-
dimethoxyphenyl)sulfonyl]-L-alaninate



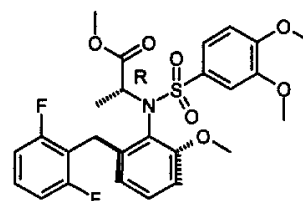
Compound 316:

methyl N-[2-(2,6-difluorobenzyl)-6-
methoxyphenyl]-N-[(3,4-
dimethoxyphenyl)sulfonyl]-L-alaninate



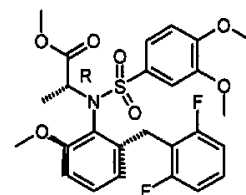
Compound 317:

methyl N-[2-(2,6-difluorobenzyl)-6-
methoxyphenyl]-N-[(3,4-
dimethoxyphenyl)sulfonyl]-D-alaninate



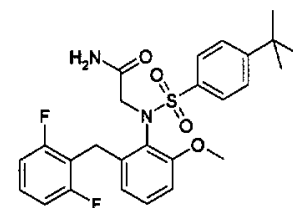
Compound 318:

methyl N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-D-alaninate



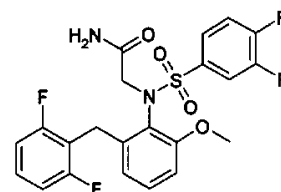
Compound 319:

N~2~-[(4-tert-butylphenyl)sulfonyl]-N~2~-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]glycinamide



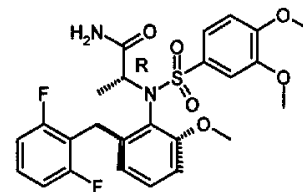
Compound 320:

N~2~-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N~2~-[(3,4-difluorophenyl)sulfonyl]glycinamide



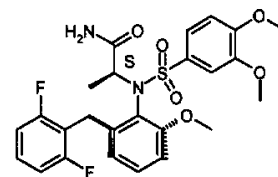
Compound 321:

N²-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]-R-alaninamide



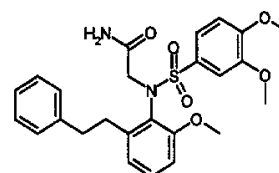
Compound 322:

N²-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]-S-alaninamide



Compound 323:

N²-[2-methoxy-6-(2-phenylethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide



In the context of the invention, the following meanings apply:

- a (C₁-C₄) alkyl group: a saturated, linear or branched
5 aliphatic group containing from 1 to 4 carbon atoms, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl or tert-butyl;
- an optionally substituted (C₁-C₄) alkyl group: an alkyl group as defined above in which one or more
10 hydrogen atoms have been substituted with a substituent;
- a (C₃-C₆) cycloalkyl group: a saturated cyclic alkyl group containing from 3 to 6 carbon atoms, for example cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl. The
15 cycloalkyl group may optionally be substituted with a (C₁-C₄) alkyl group, for example methylcyclopropyl, dimethylcyclopropyl, methylcyclobutyl, methylcyclopentyl, methylcyclohexyl or dimethylcyclohexyl;
- 20 - a (C₁-C₄) alkoxy group: a (C₁-C₄) alkyl-O-radical in which the (C₁-C₄) alkyl group is as defined above, for example methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy or tert-butoxy;
- a (C₁-C₄) alkylcarbonyl group: a (C₁-C₄) alkyl-C(O)-
25 group in which the (C₁-C₄) alkyl group is as defined above;
- a fluoro(C₁-C₄)alkyl group: a (C₁-C₄) alkyl group as defined above, one or more hydrogen atoms of which have

been substituted with one or more fluorine atoms.

Examples that may be mentioned include the $-\text{CF}_3$ and

$-\text{CH}_2-\text{CF}_3$ groups;

- a (C_1-C_4) alkenyl group: a linear or branched

5 monounsaturated or polyunsaturated aliphatic group containing from 1 to 4 carbon atoms, for example having one or two ethylenic unsaturations;

- a fluoro (C_1-C_4) alkoxy group: a (C_1-C_4) alkoxy group as defined above, one or more hydrogen atoms of which have

10 been substituted with one or more fluorine atoms.

Examples that may be mentioned include the $-\text{O}-\text{CF}_3$ and

$-\text{O}-\text{CH}_2-\text{CF}_3$ groups;

- a halogen atom; a fluorine atom, a chlorine atom, a bromine atom or an iodine atom;

15 - an aryl group: a monocyclic or bicyclic aromatic group containing between 6 and 10 carbon atoms, for example phenyl or naphthyl. The aryl group may optionally be substituted with 1, 2, 3 or 4 substituents. Examples of substituents that may be

20 mentioned include a halogen atom, a (C_1-C_4) alkyl group, a (C_1-C_4) alkoxy group, a fluoro (C_1-C_4) alkyl group, a fluoro (C_1-C_4) alkoxy group, a hydroxyl group, a $-\text{CN}$ group, a nitro group and a group $-\text{CO}-\text{NR}_a\text{R}_b$ with R_a and R_b being, independently of each other, a hydrogen atom or

25 a (C_1-C_4) alkyl group;

- a heterocyclyl group: a saturated, unsaturated or aromatic monocyclic or bicyclic group containing

between 5 and 10 atoms and comprising from 1 to 4 hetero atoms chosen from nitrogen, oxygen and sulfur. Examples that may be mentioned include 1,3-dioxolanyl, imidazolyl, tetrazolyl, oxadiazolyl, pyridyl, 5 thiazolyl, thienyl, pyrimidinyl and triazolyl. The heterocyclyl group may optionally be substituted with 1, 2, 3, 4 or 5 substituents. Examples of substituents that may be mentioned include a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a hydroxyl group 10 and a -CN group.

As already indicated, the compounds of general formula (I) may comprise one or more asymmetric carbons. They may therefore exist in the form of enantiomers or diastereoisomers. These enantiomers and 15 diastereoisomers, and also mixtures thereof, including racemic mixtures, form part of the invention.

By virtue of their structure, the compounds of general formula (I) may also exist in the form of rotamers. In the context of the invention, the term 20 "rotamers" means compounds that have identical structural formulae but different set spatial conformations. These differences in the set spatial conformations of these compounds can give them different physicochemical properties and even, in 25 certain cases, different biological activities.

The compounds of general formula (I) may also exist in the form of atropoisomers. Atropoisomers are

compounds of identical structural formulae, but which have a particular spatial configuration, resulting from a restricted rotation about a single bond, due to large steric hindrance on either side of this single bond.

- 5 Atropoisomerism is independent of the presence of stereogenic components, such as an asymmetric carbon.

The compounds of formula (I) may exist in the form of bases or of acid-addition salts. Such addition salts form part of the invention.

- 10 These salts are advantageously prepared with pharmaceutically acceptable acids, but the salts of other acids that are useful, for example, for purifying or separating the compounds of general formula (I) also form part of the invention.

- 15 The compounds of general formula (I) may also be in the form of hydrates or solvates, i.e. in the form of associations or combinations with one or more water molecules or with a solvent. Such hydrates and solvates also form part of the invention.

- 20 In the text hereinbelow, the term "leaving group" means a group that may be readily cleaved from a molecule, with loss of an electron pair, by breaking a heterolytic bond. This group may thus be readily replaced with another group, for example during a
25 substitution reaction. Such leaving groups are, for example, halogens, or an activated hydroxyl group such as a mesylate, tosylate, triflate, acetyl, etc.

Examples of leaving groups and references for preparing them are given in "Advanced Organic Chemistry", J. March, 3rd Edition, Wiley Interscience, pp. 310-316.

A subject of the present invention is also
5 the process for preparing the compounds of general formula (I).

Thus, the compounds of general formula (I) may be prepared via the processes illustrated in scheme 1. According to this scheme, the compounds of formula
10 (I) may be obtained:

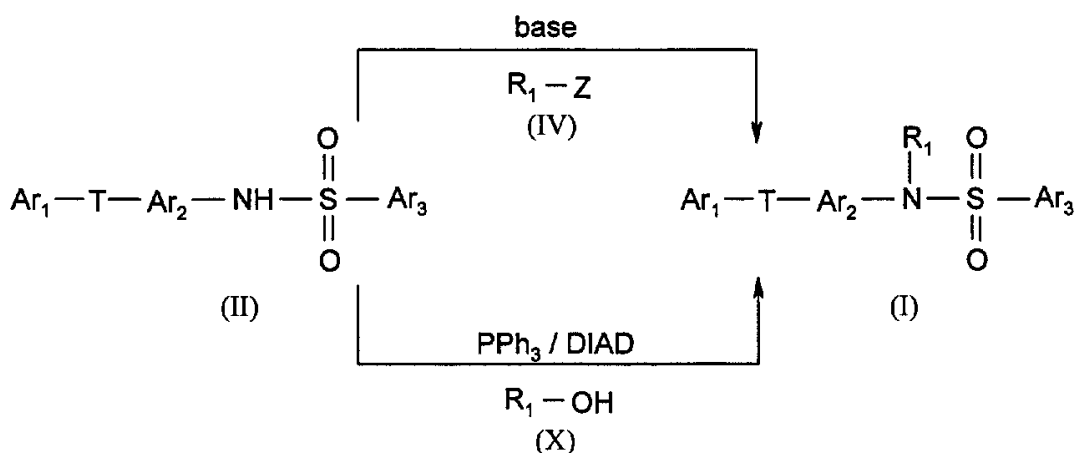
- either via alkylation of the compounds of general formula (II) with compounds of general formula (IV), in the presence of a base, according to an adaptation of the process described by Levin et al., Bioorg. Med.
15 Chem., 2001, EN 11; 22; 2975-2978;
- or via a Mitsunobu reaction between the alcohols of formula (X) and the compounds of general formula (II).

In the compounds of general formulae (II), (IV) and (X), Ar₁, Ar₂, Ar₃, T and R₁ are as defined in
20 formula (I) and Z is a leaving group such as a halogen atom chosen from bromine, chlorine and iodine; or alternatively a mesylate, a tosylate or a triflate.

The base may be an organic base, for instance potassium *tert*-butoxide, or a mineral base, for
25 instance potassium carbonate, or alternatively a phase-transfer agent, for instance tetrabutylammonium bromide.

In the Mitsunobu reaction, diisopropyl azodicarboxylate (DIAD) may be replaced with analogues thereof, for instance diethyl azodicarboxylate and di-tert-butyl azodicarboxylate, and the triphenylphosphine may be grafted onto a resin (R.G. Gentles et al., J. Comb. Chem. 2002, 4, 442-456).

Scheme 1



The compounds of structure (I) for which R_1 is a sequence of the type $-\text{CR}_7\text{R}_8-(\text{CH}_2)_n-\text{R}_9$, with $R_9 = -\text{CONR}_{12}\text{R}_{13}$, may be obtained from the corresponding esters of formula $-\text{CR}_7\text{R}_8-(\text{CH}_2)_n\text{COOR}_{14}$, according to the following reaction sequence: saponification of the carboxylate function $-\text{COOR}_{14}$; activation of the carboxylic acid function generated, for example with chloroformates to form mixed anhydrides; amidation reaction with amines of the type $\text{NHR}_{12}\text{R}_{13}$ with n , R_7 , R_8 , R_{12} , R_{13} and R_{14} as defined above.

The compounds of structure (I) for which R_1 is a sequence of the type $-\text{CR}_7\text{R}_8-(\text{CH}_2)_n-\text{R}_9$ with $R_9 =$

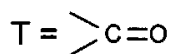
-NH-CO-NR₁₅R₁₆ may be obtained from compounds (I) for which R₉ = NH₂ via the action of isocyanates of the type R₁₅NCO or R₁₆NCO with n, R₇, R₈, R₁₅ and R₁₆ as defined above.

5 The compounds of structure (I) for which R₁ is a sequence of the type -CR₇R₈-(CH₂)_n-R₉, R₉ = -NR₁₀R₁₁ in which R₁₀ and R₁₁, independently of each other, represent a hydrogen atom and a (C₁-C₄) alkylcarbonyl group, may be obtained from compounds (I) for which R₉ = NH₂ via
10 the action of carboxylic acids of formula (C₁-C₄)alkyl-COOH or the acid chlorides thereof of formula (C₁-C₄)alkyl-COCl with n, R₇, R₈, R₁₀ and R₁₁ as defined above.

 The compounds (I) for which R₉ is a
15 heterocyclyl group such as substituted tetrazolyl are obtained via standard chemical reactions known to those skilled in the art, from compounds (I) for which R₉ is a cyano group.

 The compounds of structure (I) for which T =
20 -(CH₂)_n with n = 1 may be obtained, in certain cases, from compounds of structure (I) for which T = -CHOH, via the action of hydride, for example triethylsilane, in the presence of boron trifluoride etherate.

 The compounds of structure (I) for which T =
25 >CH-R_2 with R₂ being a hydroxyl group may be obtained, in certain cases, from the corresponding compounds for which



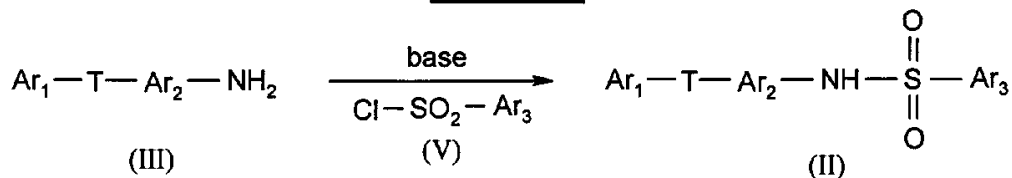
via the action of hydride, for example sodium borohydride.

The compounds of structure (II) are obtained
5 beforehand according to scheme 2, via sulfonylation of
the compound of formula (III) with sulfonyl chlorides
of formula (V) in the presence of a base chosen from
tertiary amines such as pyridine, according to the
process described by Stauffer et al., Bioorg. Med.
10 Chem., 2000, EN 8, 6, 1293-1316. Tertiary amines that
may also be used include triethylamine and
diisopropylethylamine.

In certain cases, it may even be envisaged to
use a mixture of tertiary amines.

15 The compounds of formula (V) are commercial
or may be obtained by adaptation of the processes
described, for example, by A.J. Prinsen et al., Recl.
Trav. Chim. Netherlands 1965, EN 84, 24.

In the compounds of formulae (III) and (V),
20 Ar₁, Ar₂, Ar₃ and T are as defined in formula (I).

Scheme 2

(IIIa): T= -CH₂-

5 (IIIb): T= >CH(OH)

(IIIc): T= >CH(OH)-(C₁-C₄)alkyl

(IIId): T= >CH-(C₁-C₄)alkyl

(IIIe): T= >N-(C₁-C₄)alkyl

(IIIf): T= >CH=O

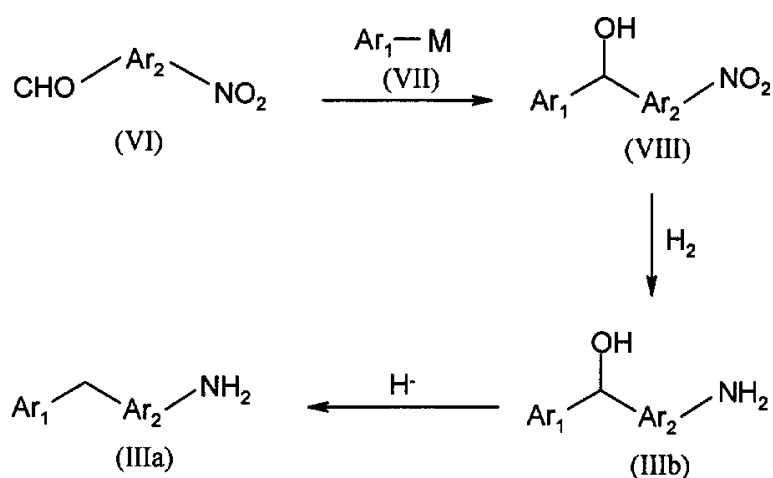
10 (IIIg): T= -CH₂CH₂-

The compounds of formulae (IIIa), (IIIb) and (IIIf) are prepared according to schemes 3 to 5. The 2-nitroaldehyde derivatives of formula (VI) react with
 15 organometallic compounds of formula (VII) in which M represents an MgBr, MgI, ZnI or Li group to give the compounds of structure (VIII). The organometallic compounds of formula (VII) are commercial or are formed according to the standard processes described in the
 20 literature. The nitro alcohols of formula (VIII) are reduced via hydrogenation, for example under the action of tin metal and concentrated hydrochloric acid in ethanol, to give the compounds of structure (IIIb). The derivatives of formula (IIIb) are reduced via the
 25 action of hydrides, for example with a mixture of triethylsilane and trifluoroacetic acid in dichloromethane to give the derivatives of formula

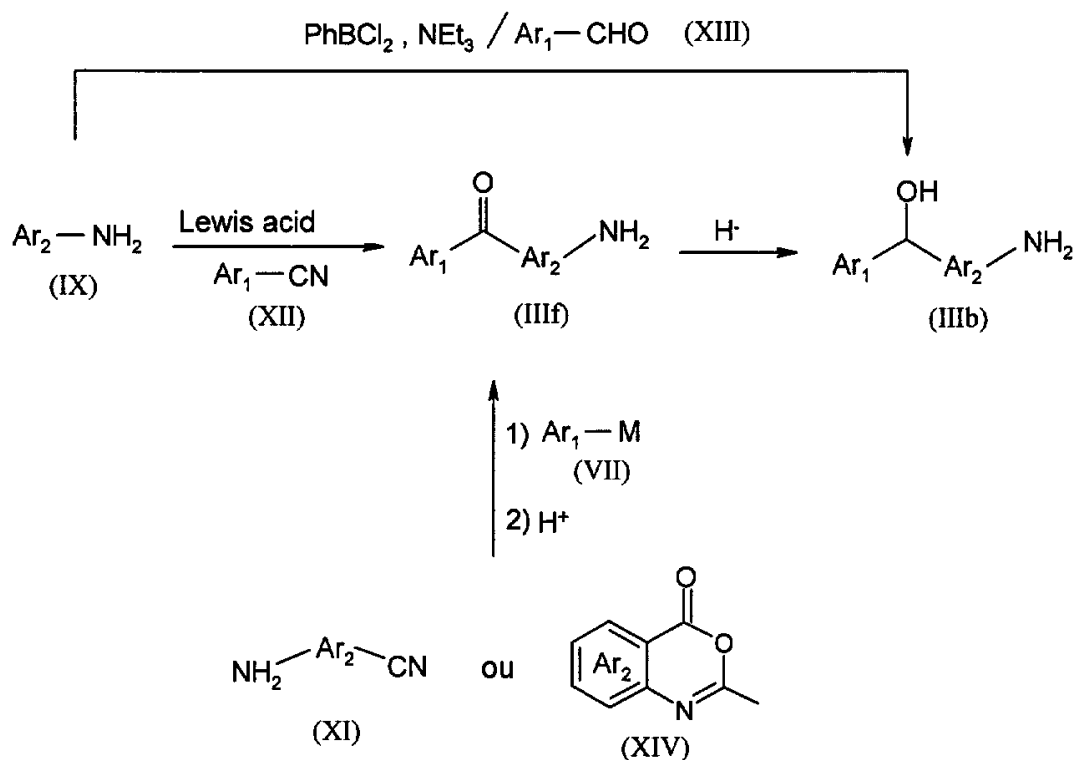
(IIIa).

The nitroaldehydes of formula (VI) are commercial or may be prepared, for example, according to an adaptation of the process described by J. Kenneth
5 Horner et al., J. Med. Chem., 1968, 11; 5; 946.

Scheme 3



Other possibilities for synthesizing the
10 compounds of general formula (IIIb) and (IIIf) are presented in scheme 4.

Scheme 4

- 5 The anilines of formula (IX) are condensed with nitriles of formula (XII), in the presence of a Lewis acid, for instance boron trichloride with aluminium trichloride or with gallium trichloride, to give the compounds of formula (IIIc), according to the
- 10 process described by T. Sugawara et al., J.A.C.S. 1978; 100; 4842. The compounds of formula (IIIc) may be obtained via condensation of aminonitriles (XI) with the organometallic derivatives (VII), according to the process described by R. Fryer et al., J. Heterocycl.
- 15 Chem., 1991, EN 28; 7, 1661. The compounds of formula (IIIc) may also be obtained from the intermediate (XIV) according to an adaptation of the process described by

D. Lednicer, J. Heterocyclic. Chem., 1971; 903.

The carbonyl function of the compounds (IIIIf) is reduced via the action of a hydride, for example sodium borohydride in ethanol, to give the compounds of structure (IIIb).

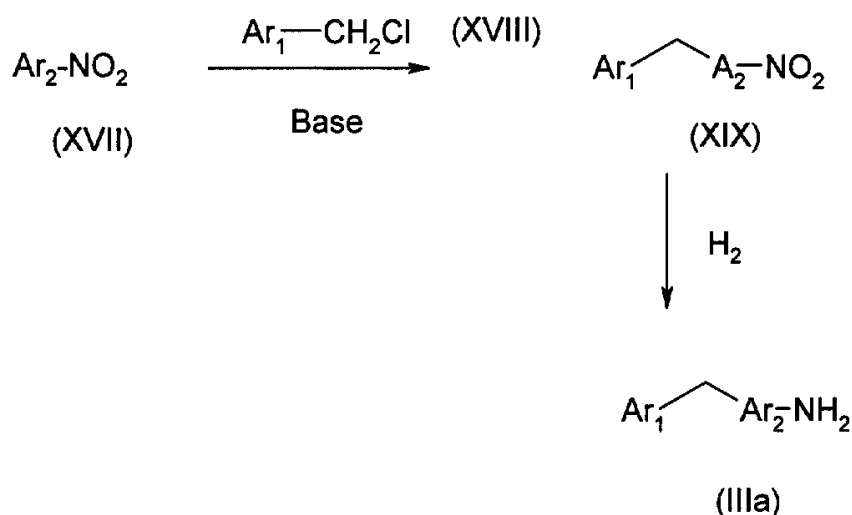
Another method for preparing the compounds of formula (IIIb) consists in condensing the anilines of formula (IX) with benzaldehyde derivatives of formula (XIII) in the presence of phenyldichloroborane and triethylamine, according to the process described by T. Toyoda et al., Tet. Lett., 1980, 21, 173.

It should be noted that the compounds of formula (IIIIf), under the action of triethylsilane and trifluoroacetic acid, for example, may give the compounds of formula (IIIa).

Another possibility for synthesizing the compounds of general formula (IIIa), in which Ar₁ represents a heteroaryl, is presented in scheme 5.

Scheme 5

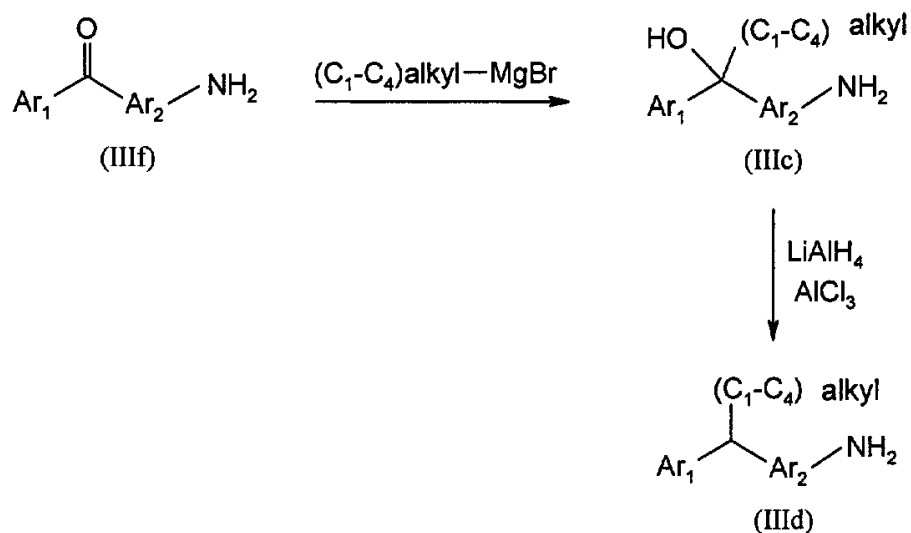
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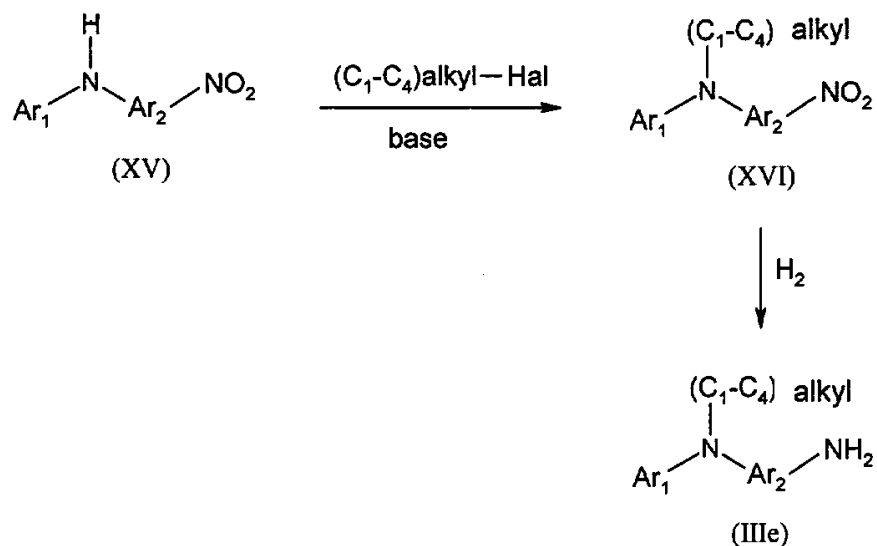
The nitrophenyls of formula (XVII) are condensed onto chloromethyl heteroaryls of formula (XVIII) in the presence of a base, for example potassium *tert*-butoxide, to give the derivatives (XIX) according to the process described by Florio S. et al., Eur. J. Org. Chem., 2004, 2118, which are reduced, for example, via the action of tin metal in the presence of 12M hydrochloric acid, to give the derivatives of formula (IIIa).

10 The compounds of formulae (IIIc) and (IIId) are prepared according to scheme 6.

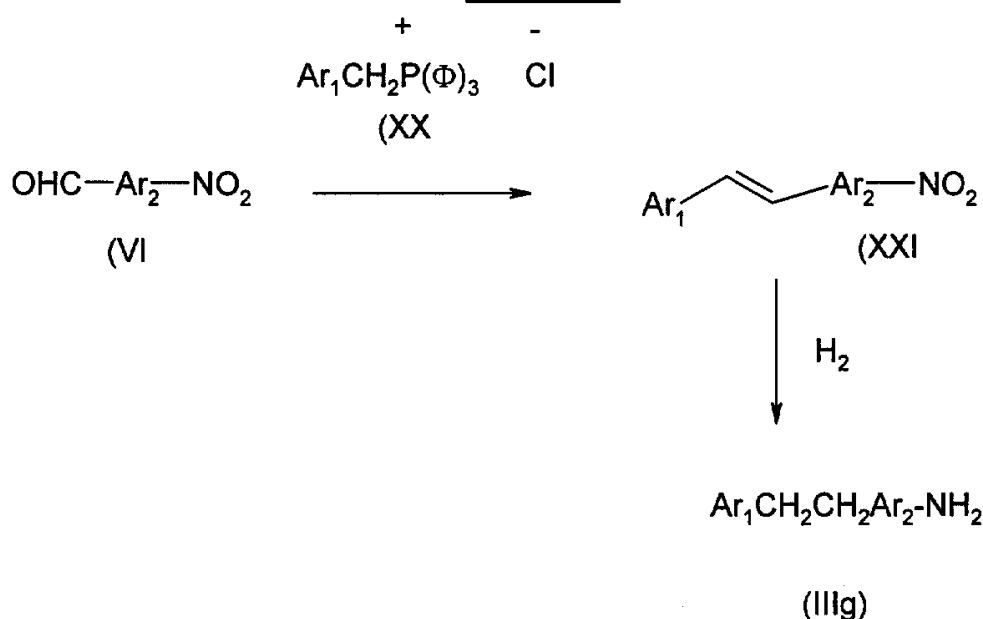
 The compounds of formula (IIIe), under the action of a (C₁-C₄) alkylmagnesium reagent, give the derivatives of formula (IIIc). These compounds are 15 dehydroxylated under the action of aluminium trichloride and lithium aluminium hydride to give the compounds (IIId).

Scheme 6

The compounds of formula (IIIe) are prepared according to scheme 7. The derivatives (XV), under the action of a base, for example caesium carbonate and a $\text{C}_1\text{-C}_4$ alkyl halide, give the derivatives (XVI). The nitro group of these derivatives may be reduced, for example, in the presence of tin metal and hydrochloric acid in ethanol to give the compounds of formula (IIIe).

Scheme 7

The compounds of formula (IIIg) are prepared according to scheme 8. The nitroaldehydes (VI), via condensation with the derivatives (XX) according to a Wittig reaction, give the compounds (XXI). These derivatives are reduced, for example by catalytic hydrogenation with palladium, to give the compounds of formula (IIIg).

Scheme 8

In all the schemes and for all the compounds
 5 of formulae (II) to (XXI), the meanings of Ar₁, T, Ar₂,
 Ar₃ and R₁ are as defined for the compounds of general
 formula (I).

In schemes 1 to 8, the starting compounds and
 the reagents, when their mode of preparation is not
 10 described, are commercially available or described in
 the literature, or alternatively may be prepared via
 methods described therein or known to those skilled in
 the art.

When a compound comprises a reactive
 15 function, for example a hydroxyl group, it may
 necessitate prior protection before reaction. A person
 skilled in the art can determine the need for prior
 protection.

The compounds of formulae (II) to (XXI) are

useful as synthetic intermediates for the preparation of the compounds of general formula (I) and form an integral part of the present invention.

The examples that follow describe the
5 preparation of the compounds in accordance with the invention. These examples are not limiting and serve merely to illustrate the invention.

The numbers of the compounds given as examples refer to those given in the above table. The
10 elemental microanalyses, the mass spectra and the NMR spectra confirm the structures of the compounds obtained.

The analysis conditions by liquid chromatography coupled to mass spectrometry LC/MS are
15 the following:

- for the liquid chromatography part: C18 symmetry column (2.1×50 mm) 3-5 µm. Eluent A = H₂O +0.005% TFA, pH=3.14; eluent B=CH₃CN +0.005% TFA, with a gradient of from 100% A to 90% B over 10 minutes,
20 then 5 minutes at 90% B
- for the mass spectrometry part: positive electrospray ionization mode.

When the ¹H NMR spectrum reveals rotamers,
25 only the interpretation corresponding to the major rotamer is described.

In the following tables:

- m.p. (°C) represents the melting point of the compound in degrees Celsius
- MH⁺ represents the mass peak of the ionized product
- 5 - the retention time is expressed in minutes
- n.d. means "not determined".

Example 1: Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate (compound 1)

10

- Example 1.1: N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxybenzene sulfonamide

To 5.3 g of (2-amino-5-chlorophenyl)(2-chlorophenyl)methanone dissolved in 50 ml of pyridine
15 are added 5.29 g of 3,4-dimethoxybenzenesulfonyl chloride, and the mixture is left for 3 hours at room temperature. The reaction medium is concentrated, the residue is taken up in diisopropyl ether and the
20 precipitate formed is filtered off to give, after drying, 5.2 g of the expected product.

¹H NMR δ in ppm (DMSO d6): 3.75 (s, 3H); 3.83 (s, 3H); 7.06-7.69 (unresolved complex, 11H).

- 25 • Example 1.2: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide

16 g of N-[4-chloro-2-(2-chlorobenzoyl)-

phenyl]-3,4-dimethoxybenzenesulfonamide dissolved in 900 ml of ethanol are added portionwise 3.93 g of sodium borohydride, and the mixture is left for 18 hours at room temperature. The reaction medium is concentrated and the residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is solidified with diisopropyl ether; after filtering off and drying the precipitate, 14.66 g of the expected product are obtained.

^1H NMR δ in ppm (DMSO d_6): 3.77 (s, 3H); 3.84 (s, 3H); 6.27 (s, 1H); 6.96-7.44 (unresolved complex, 10H).

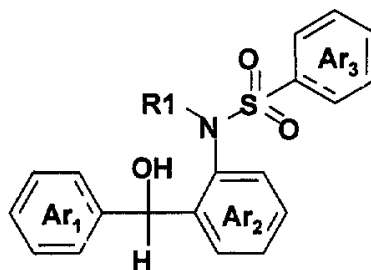
• Example 1.3: Ethyl N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(3,4-dimethoxyphenyl)sulfonyl]glycinate

To 6 g of N-{4-chloro-2-[(2-chlorophenyl)-(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide dissolved in 50 ml of DMF at 0°C is added portionwise 0.674 g of sodium hydride. After 1 hour at 0°C, 1.4 ml of ethyl 2-bromoacetate are introduced and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane to give 1.3 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.03 (t, 3H); 2.90 (d, 1H); 3.77 (s, 3H); 3.87 (t, 3H); 4.11 (d, 1H); 4.73 (q, 2H); 5.94 (d, 1H); 6.47 (s, 1H); 7.10-7.77 (unresolved complex, 10H).

5 m.p.=86°C.

Table I illustrates the chemical structures and physical properties of a number of compounds of the invention obtained according to this example.



10

Table I

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
8	H	H	CH ₂ CO ₂ Et	3,4-diOMe	58.8	486/8.15
7	H	4-Cl	CH ₂ CO ₂ Et	3,4-diOMe	152	521/8.78
9	2-Cl	4-Cl	CH ₂ CO ₂ Et	2,4-diOMe	155	555/9.34
10	2-Cl	4-Cl	CH ₂ CO ₂ Et	H	109.8	495/9.40
13	2-Cl	4-Cl	CH ₂ CO ₂ Et	4-OMe	98.2	524/9.47
18	2-Cl	4-Cl	CH ₂ CO ₂ Et	3,4-diCl	140	562/10.46
19	2-Cl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	154.7	526/7.52
28	2-Cl	4-Cl	CH ₂ CONH ₂	3,4-diMe	205	n.d.
31	2-Cl	4-Cl	CH ₂ CONH ₂	3-Cl	187	499/8.32
32	2-Cl	4-Cl	CH ₂ CONH ₂	4-OMe	207	495/7.86

Example 2: N-{4-chloro-2-[(2-chlorophenyl)-(hydroxy)methyl]phenyl}-N-ethyl-3,4-dimethoxybenzenesulfonamide (compound 20)

5

To 1 g of N-{4-chloro-2-[(2-chlorophenyl)-(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide, obtained in Example 1.2, dissolved in 43 ml of acetonitrile are successively added 1.2 ml of

10 triethylamine and 0.68 ml of iodoethane, and the mixture is refluxed for 8 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a

15 column of silica gel, eluting with a 4/6 (v/v) cyclohexane/ethyl acetate solvent mixture to obtain, after crystallization from cyclohexane, 0.418 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 0.12 (t, 3H); 2.94 (m, 1H);

20 3.21 (m, 1H); 3.75 (s, 3H); 3.88 (s, 3H); 6.02 (d, 1H); 6.51 (d, 1H); 6.80 (d, 1H); 6.96-7.49 (unresolved complex, 8H); 7.91 (d, 1H).

m.p.=153.9°C

Table II illustrates the chemical structures

25 and the physical properties of a number of compounds of the invention obtained according to this example.

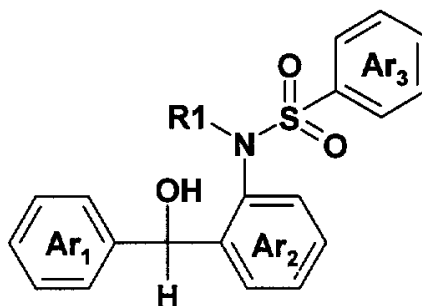


Table II

Compound No.	Nature and position of the substituents					MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃	m.p. (°C)	
21	2-Cl	4-Cl	CH ₂ COCH ₃	3,4-diOMe	158.5	540/8.72
23	2-Cl	4-Cl	(CH ₂) OMe	3,4-diOMe	112.2	526/8.77
29	2-Cl	4-Cl	CH ₂ CONH ₂	naphthyl	218	515/8.52
30	2-Cl	4-Cl	CH ₂ CONH ₂	3-OMe	114.8	495/7.87

5

Example 3: N²-{4-chloro-2-[(2-chlorophenyl)(hydroxy)-methyl]phenyl}-N²-[(2,4-dimethoxyphenyl)sulfonyl]-glycinamide (compound 33)

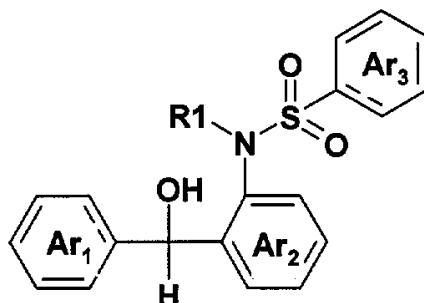
To 1.5 g of N-{4-chloro-2-[(chlorophenyl)-(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide, obtained in Example 1.2, dissolved in 15 ml of DMF are added at room temperature 1.25 g of caesium carbonate and 0.68 g of 2-bromoacetamide, and the mixture is maintained at 100°C for 2 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with

a dichloromethane/methanol solvent gradient to give 0.601 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.85 (s, 6H); 4.40 (d, 1H); 4.66 (d, 1H); 6.45-7.62 (unresolved complex, 14H).

5 m.p.=158 °C

Table III illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this example.



10

Table III

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
36	2-Cl	4-Cl	CH ₂ CONH ₂	2,5-diOMe	109	525/7.57
38	2-Cl	4-Cl	CH ₂ CONH ₂	2,5-diMe, 4-Cl	126.3	527/9.16

Example 4: N^2 -{4-chloro-2-[(2-chlorophenyl)-(hydroxy)methyl]phenyl}- N^2 -[(3,4-dichlorophenyl)-

15 sulfonyl]glycinamide (compound 34)

- Example 4.1: (2-amino-5-chlorophenyl)(2-chlorophenyl)methanol

To 20 g of (2-amino-5-chlorophenyl)(2-chlorophenyl)methanone dissolved in 80 ml of ethanol

are introduced portionwise 8.6 g of sodium borohydride, and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is
5 dried over anhydrous sodium sulfate and concentrated to give 21.63 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 5.16 (s, 2H); 5.70 (d, 1H); 5.98 (d, 1H); 6.63 (d, 1H); 6.85-7.29 (unresolved complex, 6H).

- 10 • Example 4.2: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dichlorobenzenesulfonamide

To 0.9 g of (2-amino-5-chlorophenyl)(2-chlorophenyl)methanol dissolved in 4 ml of pyridine is
15 added 0.822 g of 3,4-dichlorobenzenesulfonyl chloride, and the mixture is left for 30 minutes at room temperature. The reaction medium is taken up in ethyl acetate and washed with water, and then with 1M hydrochloric acid solution. The organic phase is dried
20 over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane, to give 0.601 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 6.07 (s, 1H); 6.25 (s, 1H);
25 7.06-7.69 (unresolved complex, 11H).

- Example 4.3: N^2 -{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}- N^2 -[(3,4-dichlorophenyl)sulfonyl]glycinamide

To 1.315 g of N-{4-chloro-2-[(2-chloro-phenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzene-sulfonamide, obtained in Example 1.2, dissolved in 10 ml of tetrahydrofuran are added, at room temperature, 0.37 g of potassium tert-butoxide and 0.46 g of 2-bromoacetamide, and the mixture is refluxed for 3 hours. After 18 hours at room temperature, the reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a dichloromethane/methanol solvent gradient to give 1.06 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 4.41 (q, 2H); 6.42 (d, 1H); 6.67 (s, 2H); 7.02 (m, 1H); 7.18-7.92 (unresolved complex, 10H).

20 m.p.=135°C

Table IV illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this process.

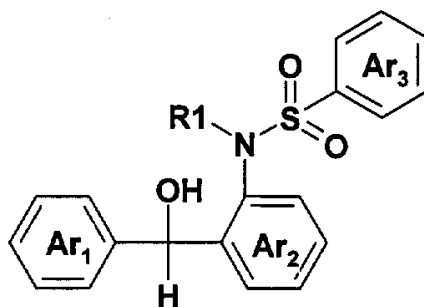


Table IV

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
35	2-Cl	4-Cl	CH ₂ CONH ₂	4-Cl	130	499/8.41
37	2-Cl	4-Cl	CH ₂ CONH ₂	2-Cl	137	499/7.75
41	2-Cl	4-Cl	CH ₂ CONH ₂	2,3-diOMe	222	526/8.76
64	2-Cl	4-Cl	CH ₂ CONH ₂	3,4- ethylenedioxy	102.1	523/7.64
79	2-Cl	4-Cl	CH ₂ CONH ₂	2-Me	134	479/8.24
106	2-Cl	4-Cl	CH ₂ CONH ₂	2,4,5-triMe	150.2	507/8.95
110	2-Cl	4-Cl	CH ₂ CONHMe	2,4,5-triMe	171.7	521/9.25
113	2-Cl	4-Cl	CH ₂ CONHMe	2,4,5-triOMe	119.6	569/7.67
129	2-Cl	4-Cl	CH ₂ CON(Me) ₂	2,4-diCl-5-Me	204.8	557/10.35
132	2-Cl	4-Cl	CH ₂ CONHMe	3,5-diMe	109	489*/9.48
133	2-Cl	4-Cl	CH ₂ CON(Me) ₂	3,5-diMe	142	520/9.85
52	2-Cl	4-Cl	CH ₂ CONH ₂	H	170.6	465/7.75
85	2-Cl	4-Cl	CH ₂ CONH ₂	2,6-diCl	149	533/8.01
72	2-Cl	4-Cl	CH ₂ CONHMe	3,4-diOMe	88	539/7.89
86	2-Cl	4-Cl	CH ₂ CONH ₂	3,5-diMe	137	493/8.60
94	2-Cl	4-Cl	CH ₂ CONH ₂	2,5-diOMe,4- Me	180.8	539/8.25
102	2-Cl	4-Cl	CH ₂ CONH ₂	2,4,5-triOMe	123.5	555/7.36
83	2-Cl	4-Cl	(3-methyl- 1,2,4- oxadiazol- 5-yl) methyl	3,4-diOMe	90	564/9.15

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
22	2-Cl	4-Cl	(1-methyl- 1H- imidazol- 2-yl) methyl	3,4-diOMe	199	562/5.30
148	2-Cl	4-Cl	CH ₂ CONH ₂	3-NH ₂	189.6	462*/7.86

*: the ion observed is the M-H₂O + H⁺

Compound 83 is obtained by alkylation with
the derivative 5-bromomethyl-3-methyl[1,2,4]oxadiazole,
5 which is synthesized as follows:

- Synthesis of (1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)acetyl chloride

To 10.25 g of (1,3-dioxo-1,3-dihydro-2H-
10 isoindol-2-yl)acetic acid dissolved in 50 ml of
dichloromethane are added, at room temperature, 4.6 ml
of oxalyl chloride and 2 drops of DMF, and the mixture
is left for 18 hours at room temperature. The resulting
mixture is evaporated to dryness to give 11 g of the
15 expected product.

- Synthesis of 2-(3-methyl[1,2,4]oxadiazol-5-yl)isoindol-1,3-dione

To 4.4 g of (1,3-dioxo-1,3-dihydro-2H-
20 isoindol-2-yl)acetyl chloride in 20 ml of pyridine are
added 1.48 g of acetamidoxime, and the mixture is

refluxed for 1 hour. The reaction medium is concentrated and taken up in ethyl acetate and water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is

5 chromatographed on a column of silica gel, eluting with a 7/3 (v/v) toluene/ethyl acetate mixture to give 1.2 g of expected product.

^1H NMR δ in ppm (DMSO d_6): 2.26 (s, 2H); 2.34 (s, 3H); 3.92 (s, 2H).

10

- Synthesis of 1-(3-methyl[1,2,4]oxadiazol-5-yl)methanamine

To 5 g of 2-(3-methyl[1,2,4]oxadiazol-5-yl)isoindol-1,3-dione dissolved in 100 ml of ethanol
15 are added 2 ml of hydrazine hydrate, and the mixture is refluxed for 2 hours. The insoluble material is filtered off and the filtrate is concentrated. The residue is taken up in diethyl ether, the insoluble material is filtered off and the filtrate is
20 concentrated to give 2 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 2.39 (s, 3H); 4.88 (s, 2H).

- Synthesis of 5-bromomethyl-3-methyl[1,2,4]oxadiazole

25 To 2.26 g of 1-(3-methyl[1,2,4]oxadiazol-5-yl)methanamine dissolved in 10 ml of water and 20 ml of 6M hydrobromic acid are added dropwise, at 70°C, 2.76 g

of sodium nitrite dissolved in 10 ml of water. After
1 hour at 80°C, the medium is cooled to room
temperature, taken up in ethyl acetate and washed with
water. The organic phase is dried over anhydrous sodium
5 sulfate and concentrated to give 2.6 g of the expected
product.

^1H NMR δ in ppm (DMSO d_6): 2.39 (s, 3H); 4.88 (s, 2H).

Compound 22 is obtained by alkylation with
the derivative 2-chloromethyl-1-methylimidazole, which
10 is synthesized as follows:

- Synthesis of 1-methyl-2-imidazolemethanol

To 10 g of 1-methyl-2-imidazolecarboxaldehyde
dissolved in 200 ml of methanol are added 5.2 g of
15 sodium borohydride, and the mixture is left for
48 hours at room temperature. The solvents are
evaporated off and the residue is taken up in ethyl
acetate and washed with water. The organic phase is
dried over anhydrous sodium sulfate and concentrated to
20 give 6.5 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.67 (s, 3H); 4.49 (d, 2H);
5.36 (t, 1H); 6.78 (d, 1H); 7.08 (d, 1H).

m.p.=108.2°C

25 • Synthesis of 2-chloromethyl-1-methylimidazole

To 1.12 g of 1-methyl-2-imidazolemethanol are
added dropwise 1.8 ml of thionyl chloride at 0°C. After

18 hours at 20°C, the mixture is heated at 70°C for 2 hours. The reaction medium is concentrated to give the expected product quantitatively.

¹H NMR δ in ppm (DMSO d₆): 3.90 (s, 3H); 5.22 (s, 2H);
5 5.36 (t, 1H); 7.77 (d, 1H); 7.80 (d, 1H).

Compound 148 is obtained from the corresponding nitro derivative via a reduction reaction with nascent hydrogen.

Example 5: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-methylbenzenesulfonamide (compound 25)

• Example 5.1: N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxy-N-methylbenzenesulfonamide
15

To 1 g of N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxybenzenesulfonamide, obtained in Example 1.1, dissolved in 20 ml of dimethylformamide is added, at 0°C, 0.094 g of sodium
20 hydride; after one hour at this temperature, 0.16 ml of iodomethane is introduced and the mixture is left at room temperature for 18 hours. The precipitate is filtered off, taken up in ethyl acetate, dried over anhydrous sodium sulfate and concentrated. The residue
25 is washed with diethyl ether and filtered to give, after drying, 0.735 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 2.75 (s, 3H); 3.69 (s, 3H); 3.86 (s, 3H); 6.76-7.15 (unresolved complex, 4H); 7.51-7.75 (unresolved complex, 6H).

m.p.=136.6°C

5

- Example 5.2: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-methylbenzenesulfonamide

To 0.152 g of the compound obtained in
10 Example 5.1 dissolved in 5 ml of ethanol is added
0.036 g of sodium borohydride and the mixture is left
for 18 hours at room temperature. The reaction medium
is taken up in ethyl acetate and washed with water. The
organic phase is dried over anhydrous sodium sulfate
15 and concentrated. The residue is taken up in a minimum
amount of ethyl acetate and the precipitate formed is
filtered off and dried to give 0.067 g of the expected
product.

^1H NMR δ in ppm (DMSO d_6): 2.33 (s, 3H); 3.75 (s, 3H);
20 3.88 (s, 3H); 6.06 (d, 1H); 6.45 (d, 1H); 6.68 (m, 1H);
6.96-7.81 (unresolved complex, 9H).

m.p. = 173.2°C

Table V illustrates the chemical structures
and the physical properties of a number of compounds of
25 the invention obtained according to this process.

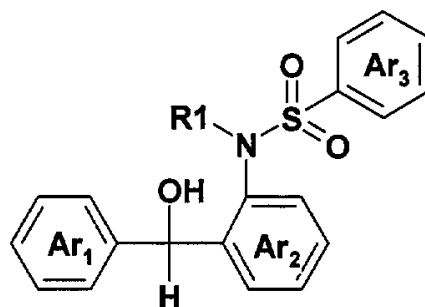


Table V

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
66	H	4-Cl	CH ₂ CONH ₂	3,4-diOMe	201.6	491/7.39
137	H	4-Cl	CH ₂ CONHMe	3,4-diOMe	111.5	487*/8.58
57	2-F	4-Cl	CH ₂ CONH ₂	3,4-diOMe	192.1	509/7.10

5 *: the ion observed is the M-H₂O + H⁺

Example 6: Synthesis of N²-(4-chloro-2-[hydroxy(3-methoxyphenyl)methyl]phenyl)-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 51)

10

- Example 6.1: (2-amino-5-chlorophenyl)(3-methoxyphenyl)methanone

To 5 g of 2-amino-5-chlorobenzonitrile dissolved in 100 ml of diethyl ether are added dropwise, at -5°C, 100 ml of a molar solution in tetrahydrofuran of 3-bromobenzenemagnesium, and the mixture is left for 18 hours at room temperature. The reaction medium is hydrolysed with ice containing 6M hydrochloric acid. The resulting mixture is extracted with ethyl acetate. The organic phase is dried over

15

20

anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a gradient of from 100 cyclohexane to 60/40 cyclohexane/dichloromethane (v/v) to give 7.26 g of the
5 expected product.

^1H NMR δ in ppm (DMSO d_6): 3.83 (s, 3H); 6.92 (d, 1H); 7.10-7.50 (unresolved complex, 8H).

- Example 6.2: (2-amino-5-chlorophenyl)(3-methoxyphenyl)methanol

10 To 3.66 g of (2-amino-5-chlorophenyl)(3-methoxyphenyl)methanone dissolved in 15 ml of ethanol are added, at 20°C, 1.59 g of sodium borohydride. After 24 hours at 20°C, the reaction medium is concentrated, taken up in ethyl acetate and washed twice with water.
15 The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is solidified with dichloromethane to give 2.37 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.74 (s, 3H); 5.14 (s, 2H);
20 5.70 (d, 1H); 5.94 (d, 1H); 6.61 (d, 1H); 6.81-7.27 (unresolved complex, 6H).

- Example 6.3: N-{4-chloro-2-[(3-methoxyphenyl)(hydroxymethyl)phenyl]-3,4-dimethoxybenzenesulfonamide

25 To 1 g of (2-amino-5-chlorophenyl)(3-methoxyphenyl)methanol dissolved in 6 ml of pyridine

are added, at room temperature, 1.08 g of 3,4-dimethoxybenzenesulfonyl chloride. After 18 hours, the reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane to give 1.65 g of the expected product. ¹H NMR δ in ppm (DMSO d6): 3.74 (s, 3H); 3.75 (s, 3H); 3.85 (s, 3H); 6.07 (s, 1H); 6.25 (s, 1H); 6.76-7.33 (unresolved complex, 10H); 9.43 (s, 1H).

- Example 6.4: *N*²-{4-chloro-2-[hydroxy(3-methoxyphenyl)methyl]phenyl}-*N*²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

To 0.7 g of *N*-{4-chloro-2-[(3-methoxyphenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide dissolved in 5 ml of THF are added, at room temperature, 0.2 g of potassium *tert*-butoxide and 0.25 g of 2-bromoacetamide. After 48 hours at 20°C, the reaction medium is concentrated, taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane to give 0.4 g of the expected product. ¹H NMR δ in ppm (DMSO d6): 3.76 (s, 3H); 3.78 (s, 3H); 3.90 (s, 3H); 4.12-4.53 (unresolved complex, 2H); 6.16

(d, 1H); 6.47 (d, 1H); 6.81-7.42 (unresolved complex, 11H); 7.76 (s, 1H).

m.p.=100 °C

Table VI illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this process.

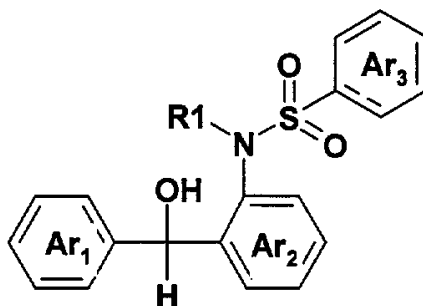


Table VI

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
16	3-Cl	4-Cl	CH ₂ CO ₂ Et	3,4-diOMe	149	554/9.48
17	2-OMe	4-Cl	CH ₂ CO ₂ Et	3,4-diOMe	119.6	550/8.98
26	2-Me	4-Cl	CH ₂ CO ₂ Et	3,4-diOMe	85.4	534/9.04
44	3-Cl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	120.1	525/8.95
59	4-OMe	4-Cl	CH ₂ CONH ₂	3,4-diOMe	181	521/7.30
68	2-OMe	4-Cl	CH ₂ CONH ₂	3,4-diOMe	104.6	521/7.26
131	2-Me	4-Cl	CH ₂ CONH ₂	3,4-diOMe	144.6	487/8.42
76	3-Cl	4-Cl	CH ₂ CONH ₂	3,4-methylenedioxy	229	509/7.73

10

Example 7: N²-{4-chloro-2-{hydroxy[2-(trifluoromethyl)phenyl]methyl}phenyl)-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 125)

- Example 7.1: 6-chloro-2-methyl-benzo[d][1,3]oxazin-4-one

To 15 g of 2-amino-5-chlorobenzoic acid are added 80 ml of acetic anhydride, and the mixture is refluxed for 2 hours. The reaction medium is concentrated and the residue is recrystallized from ethanol. After filtering off and rinsing the precipitate, 10.25 g of the expected product are obtained.

10 ^1H NMR δ in ppm (DMSO d_6): 2.40 (s, 3H); 7.58 (d, 1H); 7.97 (m, 2H).

- Example 7.2: (2-amino-5-chlorophenyl)-(2-trifluoromethylphenyl)methanone

15 To 1.1 g of magnesium in 22 ml of diethyl ether are added dropwise 6.05 ml of 2-trifluoromethylbromobenzene. To the magnesium reagent formed are added over 15 minutes 8 g of 6-chloro-2-methylbenzo[d][1,3]oxazin-4-one dissolved in 60 ml of
20 dichloromethane, and the mixture is left for 18 hours at room temperature. The reaction medium is hydrolysed with saturated ammonium chloride solution and extracted with diethyl ether. After concentrating the organic phase, 7 ml of ethanol and 7 ml of 3M sodium hydroxide
25 solution are added to the residue and the mixture is refluxed for 1 hour 30 minutes. At room temperature, the medium is extracted with diethyl ether and the

ether phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed to give 3.3 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 6.98 (d, 1H); 7.08-7.58
5 (unresolved complex, 8H).

- Example 7.3: N-[4-chloro-2-(2-trifluoromethylbenzoyl)phenyl]-3,4-dimethoxybenzenesulfonamide

10 Starting with 3.295 g of (2-amino-5-chlorophenyl)(2-trifluoromethylphenyl)methanone according to the process described in Example 1.1, 1.22 g of the expected product are obtained.

- 15 • Example 7.4: N-{4-chloro-2-[(2-trifluoromethylphenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide

Starting with 3 g of N-[4-chloro-2-(2-trifluoromethylbenzoyl)phenyl]-3,4-dimethoxybenzenesulfonamide according to the process
20 described in Example 1.2, 1.566 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 3.76 (s, 3H); 3.84 (s, 3H); 6.27 (s, 1H); 6.96-7.44 (unresolved complex, 12H).

- Example 7.5: N^2 -{4-chloro-2-{hydroxy[2-(trifluoromethyl)phenyl]methyl}phenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 0.7 g of N-{4-chloro-2-[(2-trifluoromethylphenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide according to the process described in Example 1.3, 0.265 g of expected product is obtained.

^1H NMR δ in ppm (DMSO d_6): 3.77 (s, 3H); 3.94 (s, 3H); 4.14-4.41 (unresolved complex, 2H); 6.50 (s, 1H); 6.80 (d, 1H); 6.80-7.88 (unresolved complex, 12H).

m.p.=128.8°C

Example 8: N^2 -{2-[(2-chlorophenyl)(hydroxy)methyl]-4-fluorophenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 61)

- Example 8.1: (2-nitro-5-fluorophenyl)(2-chlorophenyl)methanone

To 2.6 g of chromium trichloride suspended in 50 ml of THF are successively added 30 ml of a 0.5M solution in THF of 2-chlorophenyliodozinc, 2.54 g of 2-nitro-5-fluorobenzaldehyde and 5.7 ml of trimethylsilyl chloride. The mixture is heated at 65°C for 1 hour and then left at room temperature for 18 hours. 1M hydrochloric acid solution is added to the reaction medium, the precipitate formed is filtered off

and the filtrate is concentrated. The residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with cyclohexane, to give 1 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 6.95 (d, 1H); 7.05-7.57 (unresolved complex, 8H)

10 • Example 8.2: (2-amino-5-fluorophenyl)-(2-chlorophenyl)methanol

To 0.5 g of (2-nitro-5-fluorophenyl)(2-chlorophenyl)methanone dissolved in 10 ml of ethanol are added 0.44 g of tin and 1.5 ml of 12M hydrochloric acid, and the mixture is left for 3 hours at room temperature. The reaction medium is concentrated and the residue is taken up in ethyl acetate and washed with 2M sodium hydroxide solution and then with saturated ammonium chloride solution. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 0.453 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 5.16 (s, 2H); 5.77 (d, 1H); 5.98 (d, 1H); 6.83-7.34 (unresolved complex, 7H).

25 • Example 8.3: N-{4-fluoro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide

Starting with 0.45 g of (2-amino-5-fluorophenyl)(2-chlorophenyl)methanol according to the process described in Example 1.1, 0.56 g of the expected product is obtained.

5 ^1H NMR δ in ppm (DMSO d_6): n.d.

- Example 8.4: N^2 -{2-[(2-chlorophenyl)(hydroxy)methyl]-4-fluorophenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

10 Starting with 0.56 g of N-{4-fluoro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide, according to the process described in Example 4.3, 0.3 g of the expected product is obtained.

15 ^1H NMR δ in ppm (DMSO d_6): 3.76 (s, 3H); 3.86 (s, 3H); 4.05-4.46 (unresolved complex, 2H); 6.31 (d, 1H); 6.63 (m, 1H); 6.95-7.80 (unresolved complex, 12H).
m.p.=232°C

Table VII illustrates the chemical structures
20 and the physical properties of a number of compounds of the invention obtained according to Example 8 (activation of the reaction by addition of trimethylsilane and chromium trichloride described in Example 8.1 was not used for compounds 69, 136 and
25 175).

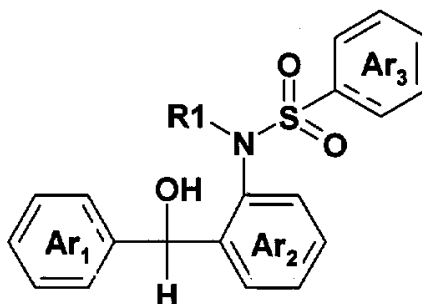


Table VII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
69	2-Cl	4-OMe	CH ₂ CONH ₂	3,4-diOMe	235.3	521/6.88
136	2-Cl	4-Me	CH ₂ CONH ₂	3,4-diOMe	189.2	487/7.90
175	2-Cl	5-Cl	CH ₂ CONH ₂	3,4-diOMe	197.1	507*/8.15

5 *: the ion observed is the M-H₂O + H⁺

Example 9: N²-{4-chloro-2-[(2,6-dichlorophenyl)(hydroxy)methyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 117)

10

- Example 9.1: (2-nitro-5-chlorophenyl)(2,6-dichlorophenyl)methanol

To 16.75 g of 1,3-dichlorobenzene dissolved in 250 ml of THF are added dropwise, at -70°C, 68 ml of a 1.6M solution in hexane of n-butyllithium. After one hour at -70°C, 10 g of 5-chloro-2-nitrobenzaldehyde dissolved in THF are introduced and the mixture is left for 3 hours at this temperature. The resulting mixture is hydrolysed by addition of 5 ml of acetic acid and is allowed to warm to room temperature. The resulting

15

20

mixture is concentrated and the residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v) cyclohexane/ethyl acetate mixture to give 7.975 g of the expected product.

5 ^1H NMR δ in ppm (DMSO d_6): 6.82 (s, 2H); 7.32-7.46 (unresolved complex, 3H); 7.65 (d, 1H); 7.90 (m, 1H).

• Example 9.2: (2-amino-5-chlorophenyl)(2,6-dichlorophenyl)methanol

10 To 3.9 g of (2-nitro-5-chlorophenyl)(2,6-dichlorophenyl)methanol dissolved in 37 ml of methanol are added 5.25 g of ammonium formate and 0.374 g of platinum oxide. The mixture is left for 5 hours at room temperature and then heated at 50°C for 18 hours. The
15 resulting mixture is filtered through Celite and the filtrate is concentrated. The residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a
20 column of silica gel, eluting with a 90/10 (v/v) cyclohexane/ethyl acetate mixture to give 1.378 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 5.16 (s, 2H); 6.17 (d, 1H); 6.35 (d, 1H); 6.64 (d, 1H); 6.72 (s, 1H); 7.01 (m, 1H);
25 7.38-7.55 (unresolved complex, 3H).

- Example 9.3: N-{4-chloro-2-[(2,6-dichlorophenyl)(hydroxymethyl)phenyl]-3,4-dimethoxybenzenesulfonamide

Starting with 1.9 g of (2-amino-5-chlorophenyl)(2,6-dichlorophenyl)methanol according to the process described in Example 4.2, 1.47 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 3.76 (s, 3H); 3.84 (s, 3H); 6.53 (s, 1H); 6.83-7.48 (unresolved complex, 10H); 9.29 (s, 1H).

- Example 9.4: N²-{4-chloro-2-[(2,6-dichlorophenyl)(hydroxymethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

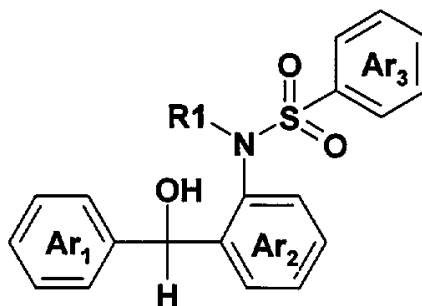
Starting with 0.7 g of N-{4-chloro-2-[(2,6-dichlorophenyl)(hydroxymethyl)phenyl]-3,4-dimethoxybenzenesulfonamide according to the process described in Example 4.3, 0.23 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 3.76 (s, 3H); 3.86 (s, 3H); 4.27 (q, 2H); 6.42 (s, 1H); 6.91-7.89 (unresolved complex, 9H); 8.02 (s, 1H).

m.p.=128.3°C

Table VIII illustrates the chemical structures and physical properties of a number of compounds of the invention obtained according to Example 9 (for all the compounds, the reduction

described in Example 9.2 is performed using tin metal and 12M hydrochloric acid instead of ammonium formate and platinum oxide).



5

Table VIII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
147	2,6-diF	4-Cl	CH ₂ CONH ₂	3,5-diMe	108.7	477/8.59
198	2,6-diF	4-Me	CH ₂ CONH ₂	3,4-diOMe	175.7	489*/7.40
206	2,6-diF	4-F	CH ₂ CONH ₂	3,4-diOMe	178.8	511/6.65
209	2,6-diF	4-OMe	CH ₂ CONH ₂	3,4-diOMe	114.2	523/7.14
221	2,6-diF	4,5-diCl	CH ₂ CONH ₂	3,4-diOMe	149.9	543/8.15
222	2-Cl, 6-F	4-Cl	CH ₂ CONH ₂	3,4-diOMe	147	565**/8.20
225 [#]	2,6-diF	6-OMe	CH ₂ CONH ₂	3,4-diOMe	228.7	523*/6.81
226 [#]	2,6-diF	6-OMe	CH ₂ CONH ₂	3,4-diOMe	210.1	523*/7.25
101	2,6-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	134.1	527/7.02

• *: the ion observed is the M-H₂O + H⁺,

• **: the ion observed is the MNa⁺,

• #: rotamers

		Enantiomers of compound 101	
		Levorotatory enantiomer	Dextrorotatory enantiomer compound 251
Optical [α] _D *	rotation	-64.4	+62.4

- C = 0.5 g/100 ml in methanol, at 25°C and at 589 nm.

Example 10: N^2 -(4-chloro-2-[(2,5-

5 dichlorophenyl)(hydroxy)methyl]phenyl)- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 74)

- Example 10.1: (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methanone

10 To 28 ml of a 1M solution of trichloroborane at -5°C are added 5.6 g of 4-chloroaniline dissolved in 30 ml of 1,2-dichloroethane. After 45 minutes at +15°C, 3.8 g of 2,5-dichlorobenzonitrile and 5 g of gallium trichloride are introduced and the mixture is refluxed
15 for 3 hours. At room temperature, the resulting mixture is hydrolysed with 2M hydrochloric acid solution and maintained at 80°C for 2 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate
20 and concentrated. The residue is chromatographed on a column of silica gel, eluting with a cyclohexane/dichloromethane gradient to give 6.38 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 6.90-6.96 (m, 2H); 7.37 (d, 25 1H); 7.60-7.72 (unresolved complex, 5H).

- Example 10.2: (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methanol

To 6.38 g of (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methanone dissolved in 50 ml of ethanol are added 2.4 g of sodium borohydride, and the mixture is left for 18 hours at room temperature. The resulting
5 mixture is concentrated and the residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 2.016 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 5.27 (s, 2H); 5.89 (d, 1H);
10 6.15 (d, 1H); 6.51 (d, 1H); 6.73 (d, 1H); 7.03 (d, 1H);
7.42-7.51 (m, 2H); 7.66 (s, 1H).

• Example 10.3: N-{4-chloro-2-[(2,5-dichlorophenyl)(hydroxy)methyl]phenyl}-3,4-
15 dimethoxybenzenesulfonamide

Starting with 2 g of (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methanol according to the process described in Example 4.2, 1.389 g of the expected product are obtained.

20 ¹H NMR δ in ppm (DMSO d₆): 3.77 (s, 3H); 3.84 (s, 3H);
6.29 (s, 2H); 6.91 (d, 1H); 7.06-7.50 (unresolved complex, 8H); 9.25 (s, 1H).

• Example 10.4: N²-{4-chloro-2-[(2,5-dichlorophenyl)(hydroxy)methyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide
25

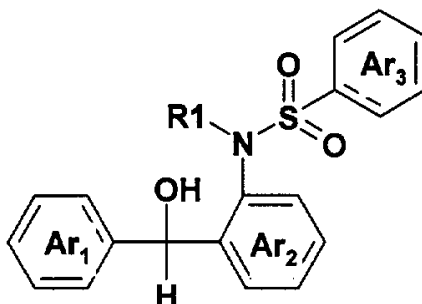
Starting with 2.42 g of N-{4-chloro-2-[(2,5-

dichlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide, according to the process described in Example 4.3, 1.5 g of the expected product are obtained.

- 5 ^1H NMR δ in ppm (DMSO d_6): 3.77 (s, 3H); 3.88 (s, 3H); 4.30 (q, 2H); 6.57-6.63 (m, 2H); 6.94-7.78 (unresolved complex, 11H).

m.p.=132°C

Table IX illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 10 (for all these compounds in Example 10.1, the gallium trichloride is replaced with aluminium trichloride).



15

Table IX

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
77	2-Cl	4-OCF ₃	CH ₂ CONH ₂	3,4-diOMe	116	n.d.
120	2-thiazolyl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	93	497/6.42
121	2-thiazolyl	4-Cl	CH ₂ CONHMe	3,4-diOMe	225	511/6.72
126	2,3-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	184.9	531**/8.16

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
127	2,3-diF	4-Cl	CH ₂ CONHEt	3,4- diOMe	93.4	555/8.86
128	2,3-diF	4-Cl	CH ₂ CON(Me) ₂	3,4- diOMe	100.5	537**/8.88
149	2-F, 6-OMe	4-Cl	CH ₂ CONH ₂	3,4- diOMe	197.3	521*/7.66
146	2-thienyl	4-Cl	CH ₂ CONHMe	3,4- diOMe	121.2	493**/8.20
155	2-thienyl	4-Cl	CH ₂ CONH ₂	3,4- diOMe	119	479**/7.87
162	2,4,6-triF	4-Cl	CH ₂ CONH ₂	3,4- diOMe	118.8	527*/7.96
163	2,4-diF	4-Cl	CH ₂ CONH ₂	3,4- diOMe	161.9	509*/8.28
164	2-Cl	4,5- diCl	CH ₂ CONH ₂	3,4- diOMe	146.7	541*/8.79
167	2-F, 4-Cl	4-Cl	CH ₂ CONH ₂	3,4- diOMe	205.1	525*/8.79
176	2-F, 5-Cl	4-Cl	CH ₂ CONH ₂	3,4- diOMe	195.2	525*/8.71
178	3,5-diF	4-Cl	CH ₂ CONH ₂	3,4- diOMe	205.7	509*/8.93
184	4-pyridyl	4-Cl	CH ₂ CONH ₂	3,4- diOMe	122	492/5.14
191	2-Cl, 6-OMe	4-Cl	CH ₂ CONH ₂	3,4- diOMe	143.6	537*/8.10
194	2-F, 5-Me	4-Cl	CH ₂ CONH ₂	3,4- diOMe	120.5	505*/8.40

• *: the ion observed is the M-H₂O + H⁺,

• **: the ion observed is the MNa⁺

Example 11: N^2 -{2-[(2,6-difluorophenyl)(hydroxy)methyl]-5-methoxy-4-methylphenyl}- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 227)

- 5 • Example 11.1: (2-amino-4-methoxy-5-methylphenyl)(2,6-difluorophenyl)methanol

To 6.05 g of dichlorophenylborane dissolved in 40 ml of dichloromethane, at -20°C , are successively added 5.226 g of 3-methoxy-4-methylaniline dissolved in 10 50 ml of dichloromethane, and 13.4 ml of triethylamine dissolved in 25 ml of dichloromethane. After 30 minutes at -20°C , 5.412 g of 2,6-difluorobenzaldehyde dissolved in 60 ml of dichloromethane are introduced. After 24 hours at room temperature, the mixture is hydrolysed 15 with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. To the oil obtained, dissolved in 80 ml of diethyl ether, are added 80 ml of 2M sodium hydroxide solution and the mixture is left stirring for 18 hours. The phases are separated by 20 settling and the organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is solidified with n-pentane to give 5.069 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.98 (s, 3H); 3.69 (s, 3H); 25 4.74 (s, 2H); 5.79 (d, 1H); 5.98 (d, 1H); 6.30 (s, 1H); 6.75 (s, 1H); 7.06 (m, 2H); 7.41 (m, 1H).

- Example 11.2: N-{2-[(2,6-difluorophenyl)(hydroxymethyl)-5-methoxy-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide

Starting with 5.06 g of (2-amino-4-methoxy-5-methylphenyl)(2,6-difluorophenyl)methanol according to the process described in Example 4.2, 8.5 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 2.03 (s, 3H); 3.38 (s, 3H); 3.78 (s, 3H); 3.84 (s, 3H); 5.99 (s, 1H); 6.17 (s, 1H); 6.42 (s, 1H); 6.98-7.40 (unresolved complex, 7H); 8.98 (s, 1H).

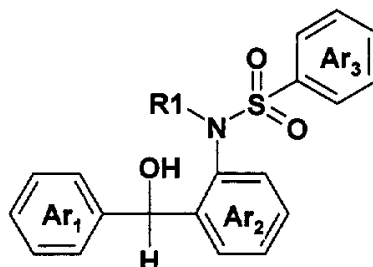
- Example 11.3: N²-{2-[(2,6-difluorophenyl)(hydroxymethyl)-5-methoxy-4-methylphenyl]-N²-(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 4.5 g of N-{2-[(2,6-difluorophenyl)(hydroxymethyl)-5-methoxy-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide, according to the process described in Example 4.3, 3.8 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 2.18 (s, 3H); 3.43 (s, 3H); 3.79 (s, 3H); 3.87 (s, 3H); 4.09-4.37 (unresolved complex, 2H); 6.60 (d, 1H); 6.77-7.75 (unresolved complex, 11H).

m.p.=203.8°C

Table X illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 11.



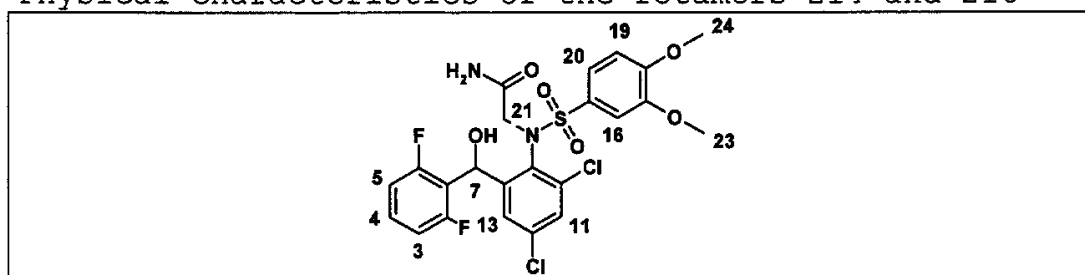
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Table X

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
213	2-Cl, 6-Me	4-Cl	CH ₂ CONH ₂	3,4-diOMe	130	521/8.67
214 [#]	2,6-diF	2,4-diCl	CH ₂ CONH ₂	3,4-diOMe	160.6	583**/7.80
216 [#]	2,6-diF	2,4-diCl	CH ₂ CONH ₂	3,4-diOMe	235.1	583**/8.24

** : the ion observed is the MNa⁺ , [#] : rotamers

Physical characteristics of the rotamers 214 and 216



Compound 214	$t_R=7.80$ min 543 a.m.u. (M- H ₂ O) ⁺ 583 a.m.u. (MNa ⁺)	$\delta=3.78$, s, 3H, OCH ₃ 23; $\delta=3.85$, s, 3H, OCH ₃ 24; $\delta=3.82$, q, 2H, CH ₂ 21; $\delta=6.21$, d, 1H, $J_{H7OH}=5.2$, OH; $\delta=6.57$, d, 1H, $J_{H7OH}=5.2$, H7; $\delta=6.62$, s, 1H, NH ₂ ; $\delta=6.90$, t, 2H, $J_{H3H4}=J_{H5H4}=J_{H3F}=J_{H5F}=8.4$ Hz, H3 and H5; $\delta=7.11$, s, 1H, NH ₂ ; $\delta=7.13$, d, 1H, $J_{H19H20}=8.4$, H19; $\delta=7.29$, m, 3H, H4, H16 and H20; $\delta=7.51$, s, 1H, $J_{H11H13}=2.8$, H11; δ $=7.88$, s, 1H, H13
Compound 216	$t_R=8.24$ min 543 a.m.u. (M- H ₂ O) ⁺ 583 a.m.u. (MNa ⁺)	$\delta=3.76$, s, 3H, OCH ₃ 23; $\delta=3.86$, s, 3H, OCH ₃ 24; $\delta=4.04$ and 4.53 , d, 2H, CH ₂ 21; $\delta=7.04$, d, 1H, $J_{H7OH}=5.6$, H7; $\delta=7.07$, s, 1H, H13; $\delta=7.13$, m, 4H, H3, H5, H16, H19; $\delta=7.30$, dd, 1H, $J_{H20H19}=8.8$, $J_{H20H16}=1.6$, H20; $\delta=7.47$, m, 1H, H4; $\delta=7.58$, s, 1H, NH ₂ ; $\delta=7.63$, d, 1H, $J_{H11H13}=2.4$, H11; $\delta=7.70$, d, 1H, $J_{OH7H}=5.6$, OH; $\delta=8.05$, s, 1H, NH ₂ .
¹ H NMR spectra acquired in DMSO, at a frequency of 400 Mz, the chemical shifts δ are expressed in ppm, the coupling constants J in hertz.		

Sample as a solution at 1 mg/ml of MeOH, 2 μ L injected.

Mass spectrometry: positive electrospray, sweep from 120 to 1500 a.m.u.,

Example 12: Ethyl N-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(3-methoxyphenyl)sulfonyl]glycinate (compound 3)

- 5 • Example 12.1: [4-chloro-2-(2-chlorobenzyl)phenyl]amine

To 10 g of (2-amino-5-chlorophenyl) (2-chlorophenyl)methanone dissolved in 100 ml of dichloromethane are added at room temperature 18.7 ml
10 of triethylsilane and 14.4 ml of trifluoroborane etherate, and the mixture is refluxed for 18 hours and then maintained at room temperature for 72 hours. The resulting mixture is hydrolysed with 2M sodium
15 hydroxide solution, and the phases are separated by settling. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a cyclohexane/ethyl acetate solvent mixture to give
4.46 g of the expected product.

20 ^1H NMR δ in ppm (DMSO d_6): 3.86 (s, 2H); 5.17 (s, 2H); 6.50 (d, 1H); 6.70 (d, 1H); 7.00-7.53 (unresolved complex, 5H).

- Example 12.2: N-[4-chloro-2-(2-chlorobenzyl)phenyl]-3-methoxybenzenesulfonamide

Starting with 0.71 g of [4-chloro-2-(2-chlorobenzyl)phenyl]amine dissolved in 5 ml of THF are
5 added 0.4 ml of pyridine and 0.8 g of 3-methoxybenzenesulfonyl chloride, and the mixture is left at room temperature for 18 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium
10 sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v) cyclohexane/ethyl acetate solvent mixture to give 0.666 g of expected product.

¹H NMR δ in ppm (DMSO d6): 3.78 (s, 3H); 3.97 (s, 2H);
15 6.71 (d, 1H); 6.96 (m, 2H); 7.23-7.34 (unresolved complex, 6H); 7.46-7.54 (unresolved complex, 2H); 9.89 (s, 1H).

- Example 12.3: ethylN-[4-chloro-2-(2-chlorobenzyl)phenyl]-N-[(3-methoxyphenyl)sulfonyl]glycinate

To 0.525 g of N-[4-chloro-2-(2-chlorobenzyl)phenyl]-2-methoxybenzenesulfonamide dissolved in 6 ml of DMF is added, at 0°C, 0.065 g of
25 sodium hydride, after 40 minutes at this temperature 0.14 ml of ethyl 2-bromoacetate is introduced, and the mixture is left at room temperature for 18 hours. The

reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with
5 a 90/10 (v/v) cyclohexane/ethyl acetate solvent mixture to give 0.272 g of the expected product, in the form of an oil.

^1H NMR δ in ppm (DMSO d_6): 1.18 (t, 3H); 3.82 (s, 3H); 3.98-4.12 (unresolved complex, 3H); 4.36 (s, 1H); 4.40
10 (q, 2H); 6.73 (d, 1H); 7.10-7.55 (unresolved complex, 10H).

Table XI illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 12.

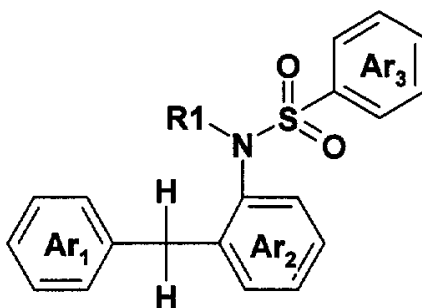


Table XI

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
2	H	4-Cl	CH ₂ CO ₂ Et	3,4-diOMe	139	504/9.06
4	2-Cl	4-Cl	CH ₂ CO ₂ Et	2-OMe	oil	508/10.03
5	2-Cl	4-Cl	CH ₂ CO ₂ Et	2,5-diOMe	80	538/9.91
6	2-Cl	4-Cl	CH ₂ CO ₂ Et	2,4-diOMe	80	538/9.98

Example 13: N²-[4-chloro-2-(2-chlorobenzyl)phenyl]-N²-[(3-methoxyphenyl)sulfonyl] glycineamide (compound 27)

5 To 1 g of N-[4-chloro-2-(2-chlorobenzyl)-phenyl]-3-methoxybenzenesulfonamide, obtained in Example 12.2, dissolved in 40 ml of acetonitrile are added at room temperature 1.34 ml of triethylamine, followed by 0.89 g of 2-bromoacetamide, and the mixture
10 is refluxed for 18 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v)
15 cyclohexane/ethyl acetate solvent mixture to give 0.58 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 3.82 (s, 3H); 4.08-4.58 (unresolved complex, 4H); 6.65 (s, 1H); 6.91 (d, 1H); 7.08-7.57 (unresolved complex, 11H).

20 m.p.=65.7°C

Example 14: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide
5 (compound 14) and N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide (compound 15)

- 10 • Example 14.1: N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-N-(cyanomethyl)-3,4-dimethoxybenzenesulfonamide

To 5.4 g of N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxybenzenesulfonamide,
15 obtained in Example 1.1, dissolved in 60 ml of DMF is added, at 0°C, 0.57 g of sodium hydride; after 40 minutes at this temperature, 0.9 ml of 2-bromoacetonitrile is introduced and the mixture is left at room temperature for 18 hours. The reaction
20 medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 5.3 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 3.76 (s, 3H); 3.85 (s, 3H);
25 4.71 (m, 2H); 7.08-7.63 (unresolved complex, 9H); 7.81 (m, 1H).

m.p.=164°C

- Example 14.2: N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxy-N-(1H-tetrazol-5-ylmethyl)benzenesulfonamide

To 1 g of N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-N-(cyanomethyl)-3,4-dimethoxybenzenesulfonamide dissolved in 20 ml of THF are successively added 0.3 g of dibutyltin oxide and 2.6 ml of azidotrimethylsilane, and the mixture is refluxed for 18 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is purified by filtration on silica H, eluting with dichloromethane, to give 0.95 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 3.87 (s, 3H); 5.00 (s, 2H); 6.88-7.76 (unresolved complex, 10H).

- Example 14.3: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-(1H-tetrazol-5-ylmethyl)benzenesulfonamide

To 0.95 g of N-[4-chloro-2-(2-chlorobenzoyl)phenyl]-3,4-dimethoxy-N-(1H-tetrazol-5-ylmethyl)benzenesulfonamide dissolved in 40 ml of ethanol is added 0.38 g of sodium borohydride, and the mixture is refluxed for 18 hours. The solvents are evaporated off and the residue is taken up in ethyl acetate and washed with water. The organic phase is

dried over anhydrous sodium sulfate and concentrated to give 0.93 g of the expected product.

- Example 14.4: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide (compound 14) and N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide (compound 15)

To 0.93 g of N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[(1H-tetrazol-5-yl)methyl]benzenesulfonamide dissolved in 25 ml of DMF are successively added 0.2 ml of iodomethane and 0.32 g of potassium carbonate, and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 99/1 (v/v) dichloromethane/methanol solvent mixture to give 0.34 g of compound 14.

¹H NMR δ in ppm (DMSO d₆): 3.77 (s, 3H); 3.87 (s, 3H); 4.15 (s, 3H); 4.70 (d, 1H); 5.15 (d, 1H); 6.01 (d, 1H); 6.60-7.83 (unresolved complex, 11H).

m.p.=94.8°C

0.19 g of compound 15 is obtained, the characteristics of which are as follows:

¹H NMR δ in ppm (DMSO d6): 3.60 (s, 3H); 3.79 (s, 3H);
5 3.88 (s, 3H); 4.25 (d, 1H); 4.77 (d, 1H); 5.96 (d, 1H);
6.36 (d, 1H); 6.65-7.79 (unresolved complex, 10H).

m.p.=118.3°C

The following compounds were synthesized according to this process:

- 10 • Compound 11: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(2-ethyl-2H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide.

m.p.= 113°C

- 15 • Compound 12: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-[(1-ethyl-1H-tetrazol-5-yl)methyl]-3,4-dimethoxybenzenesulfonamide.

m.p.=75°C

- Example 15: N²-[4-chloro-2-(2-chlorobenzyl)phenyl]-N²-
20 [(4-methoxyphenyl)sulfonyl]glycinamide (compound 39)

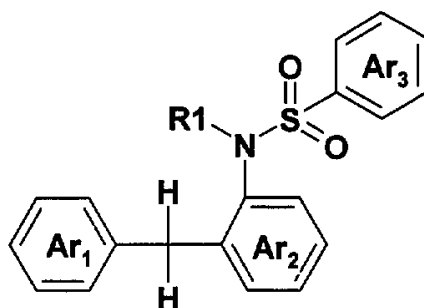
To 0.766 g of N-[4-chloro-2-(2-chlorobenzyl)phenyl]-4-methoxybenzenesulfonamide, obtained according to Example 12.2, dissolved in 5 ml
25 of THF are successively added 0.214 g of potassium tert-butoxide and 0.263 g of 2-bromoacetamide, and the mixture is left for 18 hours at room temperature. The

reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a dichloromethane/methanol gradient to give 0.50 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.89 (s, 3H); 4.02-4.29 (m, 3H); 4.58 (d, 1H); 6.66 (d, 1H); 6.89 (d, 1H); 7.14-7.65 (unresolved complex, 11H).

10 m.p.=150°C

Table XII illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to an adaptation of Example 15.



15

Table XII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
40	2-Cl	4- Cl	CH ₂ CONH ₂	2,5-diOMe	125	509/8.93
42	2-Cl	4- Cl	CH ₂ CONH ₂	3-CF ₃	119	517/9.25
43	2-Cl	4- Cl	CH ₂ CONH ₂	3-OCF ₃	129	533/9.38
45	2-Cl	4- Cl	CH ₂ CONH ₂	2-OMe	114	479/8.18
46	2-Cl	4- Cl	CH ₂ CONHMe	3,4-diOMe	146	523/8.42
47	2-Cl	4- Cl	CH ₂ CONH ₂	4-Cl	205	483/9.06
48	2-Cl	4- Cl	CH ₂ CONH ₂	3,4-diCl	166	517/9.64
49	2-Cl	4- Cl	CH ₂ CONH ₂	2,5-diMe, 4-Cl	214.5	511/9.76
50	2-Cl	4- Cl	CH ₂ CONH ₂	2-Cl	97	483/8.44
53	2-Cl	4- Cl	CH ₂ CONH ₂	H	150	449/8.40
55	2-F	4- Cl	CH ₂ CONH ₂	3,4-diOMe	183.3	493/7.80
62	2-Cl	4- Cl	CH ₂ CONH ₂	3-Me	95	463/8.66
63	2-Cl	4- Cl	CH ₂ CONH ₂	3,4-ethyl- enedioxy	111.6	507/8.19
71	2-Cl	4- Cl	CH ₂ CONH ₂	3,4-methyl- enedioxy	89	493/8.29
75	2-Cl	4- Cl	CH ₂ CONHEt	3,4-diOMe	101	537/8.79

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
81	2-Cl	4- Cl	CH ₂ CONH ₂	2-Me	160	463/9.32
82	2-Cl	4- Cl	CH ₂ CONH ₂	3,4-diMe	166	477/9.64
89	2-Cl	4- Cl	CH ₂ CONH ₂	3,5-diMe	84	477/9.24
105	2-Cl	4- Cl	CH ₂ CONHMe	2,5-diMe, 4-Cl	172.6	525/10.24
109	2-Cl	4- Cl	CH ₂ CONHMe	2,4,5- triOMe	160.4	553/8.17
104	2-Cl	4- Cl	CH ₂ CONH ₂	2,4,5- triOMe	221.2	539/7.80
119	2-Cl	4- Cl	CH ₂ CONH ₂	3,5-diOMe	110	509/8.71
118	2-Cl	4- Cl	CH ₂ CON(Me) ₂	2,5-diMe, 4-Cl	166.4	539/10.71
134	2-Cl	4- Cl	CH ₂ CONH ₂	3-NO ₂	91	494/8.72
173	2-Cl	4- Cl	CH ₂ CONHMe	2,4-diCl, 5-Me	108	545/10.74
174	2-Cl	4- Cl	CH ₂ CON(Me) ₂	2,4-diCl, 5-Me	204	559/11.27
54	2-Cl	4- Cl	Me	3,4-diOMe	106.6	466/9.73
65	H	4- Cl	CH ₂ CONH ₂	3,4-diOMe	184	475/7.75
70	2-Cl	4- Cl	CH ₂ CON(Me) ₂	3,4-diOMe	157.6	537/8.88
87	2-Cl	4- Cl	CH ₂ CONH ₂	2,6-diCl	163	517/8.70

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
95	H	4- Cl	CH ₂ CON (Me) ₂	3,4-diOMe	144.2	503/8.67
96	H	4- Cl	CH ₂ CONHMe	3,4-diOMe	89.6	489/8.25
97	2-F	4- Cl	CH ₂ CON (Me) ₂	3,4-diOMe	oil	521/8.63
98	2-F	4- Cl	CH ₂ CONHMe	3,4-diOMe	107.5	507/8.23
99	2-Cl	4- Cl	CH ₂ CONH ₂	2,5-diOMe, 4-Me	172.5	523/8.70
114	2-Cl	4- Cl	CH ₂ CONH ₂	2,4,5-triMe	184.9	491/9.48
115	2-Cl	4- Cl	CH ₂ CONHMe	2,4,5-triMe	188.5	505/9.82
84	2-Cl	4- Cl	(3-methyl- 1,2,4- oxadiazol- 5-yl) methyl	3,4-diOMe	111.4	548/10.20
107	2-Cl	4- Cl	(1-methyl- 1H- imidazol- 2- yl)methyl	3,4-diOMe	105	546/6.32
112	2-Cl	4- Cl	(1-methyl- 1H- imidazol- 2- yl)methyl	3,5-diMe	112	514/6.98
135	2-Cl	4- Cl	CH ₂ CONH ₂	3-NH ₂	103	464/8.44

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
188	2,6-diF	4-Cl	CH ₂ CONH ₂	3-NMe ₂	190	494/9.17
189	2,6-diF	4-Cl	CH ₂ CONH ₂	3-NHMe	195	480/8.65
249	2,6-diF	4-Cl	CH ₂ CONH ₂	2,5-diMe, 4-Cl	196.8	513/9.50
263	2,6-diF	4-Cl	CH ₂ CONH ₂	4-tBut	161.4	507/10.74
279	2,6-diF	4-Cl	CH ₂ CONH ₂	4-NH ₂	111	n.d.
307	2,6-diF	4-Cl	CH ₂ CONH ₂	3,5-diOMe	170.2	511/9.48
319	2,6-diF	6-OMe	CH ₂ CONH ₂	4-tBut	173	503/10.1
320	2,6-diF	6-OMe	CH ₂ CONH ₂	3,4-diF	259	483/9.13

Compound 84 is obtained by alkylation with the derivative 5-bromomethyl-3-methyl-[1,2,4]oxadiazole (synthesis described according to Example 4.3).

5 Compound 135 is obtained from 1.25 g of compound 134 by reduction of the nitro function as described in Example 8.2.

Compounds 188 and 189 are obtained by alkylation reaction with iodomethane in the presence of
10 caesium carbonate in THF of N²-[3-aminophenyl)sulfonyl]-N²-[4-chloro-2-(2,6-difluorobenzyl)phenyl]glycinamide.

For compounds 54, 65, 95, 96, 97 and 98, the potassium *tert*-butoxide is replaced with sodium hydride.

Compound 312 is obtained according to this
5 process, starting with 3-methoxybiphenyl-2-amine.
MH⁺=457; the retention time is 8.04 minutes
m.p. = 86.8°C

Example 16: N²-[4-chloro-2-(2-methoxybenzyl)phenyl]-N²-
10 [(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
56)

- Example 16.1: (2-amino-5-chlorophenyl)(2-methoxyphenyl)methane

15 To 1.438 g of (2-amino-5-chlorophenyl)(2-methoxyphenyl)methanone, obtained according to the process described in Example 10.1, dissolved in 16 ml of dichloromethane are successively added 2.61 ml of triethylsilane and 4 ml of boron trifluoride etherate,
20 and the mixture is refluxed for 18 hours. The cooled reaction medium is poured onto ice containing 2M sodium hydroxide solution, and, after separation of the phases by settling, the organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is
25 chromatographed on a column of silica gel to give 0.571 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.70 (s, 2H); 3.80 (s, 3H); 5.05 (s, 2H); 6.65 (m, 2H); 6.88-7.29 (unresolved complex, 5H).

- 5 • Example 16.2: N-[4-chloro-2-(2-methoxybenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide

To 0.57 g of (2-amino-5-chlorophenyl)(2-methoxyphenyl)methane dissolved in 5 ml of THF are
10 successively added 0.2 ml of pyridine and 0.547 g of 3,4-dimethoxybenzenesulfonyl chloride, and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium
15 sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane, to give 0.832 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.70 (s, 2H); 3.76 (s, 3H);
20 3.85 (s, 3H); 6.77-7.28 (unresolved complex, 10H) 9.52 (s, 1H).

- Example 16.3: N^2 -[4-chloro-2-(2-methoxybenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide
25

To 0.83 g of N-[4-chloro-2-(2-methoxybenzyl)phenyl]-3,4-methoxybenzenesulfonamide

dissolved in 10 ml of DMF is added, at 0°C, 0.081 g of sodium hydride. After 40 minutes at this temperature, 0.28 g of 2-bromoacetamide is introduced and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane, to give 0.77 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.80 (s, 6H); 3.88 (s, 3H); 3.91 (d, 1H); 4.18 (s, 2H); 4.30 (d, 1H); 6.75 (d, 1H); 6.91-7.28 (s, 11H).

Table XIII illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 16.

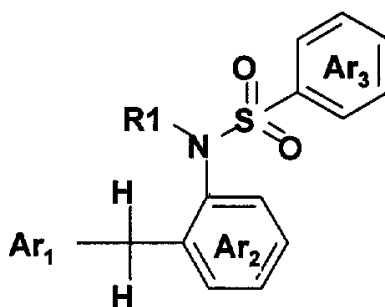


Table XIII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
58	3-OMe phenyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	109	505/7.79
60	4-OMe phenyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	214	505/7.73
73	2-Me phenyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	88	489/8.12
116	3-Cl phenyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	181.8	509/8.39
212	2-Me thienyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	100.1	495/8.86

Example 17: N²-[4-chloro-2-(2,6-dichlorobenzyl)phenyl]-
N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
5 78)

- Example 17.1: (2-amino-5-chlorophenyl)(2,6-dichlorophenyl)methane

To 4.85 g of (2-nitro-5-chlorophenyl)(2,6-dichlorophenyl)methanol, obtained in Example 9.1,
10 dissolved in 58 ml of ethanol are added 5.042 g of tin
and 19 ml of 12M hydrochloric acid, and the mixture is
refluxed overnight. The reaction medium is concentrated
and the residue is taken up in ethyl acetate and washed
15 with water containing 2M sodium hydroxide solution. The
organic phase is dried over anhydrous sodium sulfate

and concentrated to give 3.71 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.99 (s, 2H); 6.00 (d, 1H); 6.73 (d, 1H); 6.98 (d, 1H); 7.39-7.61 (unresolved complex, 3H).

- Example 17.2: N-[4-chloro-2-(2,6-dichlorobenzyl)phenyl]-3,4-methoxybenzenesulfonamide

10 Starting with 2 g of (2-amino-5-chlorophenyl) (2,6-dichlorophenyl)methane according to the process described in Example 12.2, 0.389 g of the expected product is obtained.

- 15
- Example 17.3: N^2 -[4-chloro-2-(2,6-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

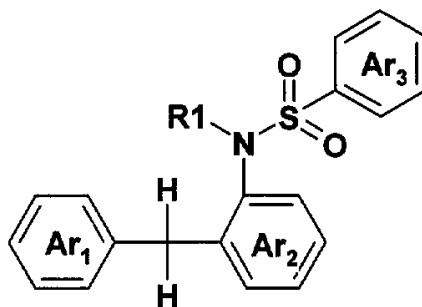
To 0.38 g of N-[4-chloro-2-(2,6-dichlorobenzyl)phenyl]-3,4-methoxybenzenesulfonamide
20 dissolved in 4 ml of DMF is added, at 0°C, 0.035 g of sodium hydride; after 40 minutes at this temperature, 0.121 g of 2-bromoacetamide is added and the mixture is left for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with
25 water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with

a 98/2 (v/v) dichloromethane/methanol mixture to give 0.225 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.80 (s, 3H); 3.88 (s, 3H); 4.10-4.70 (unresolved complex, 4H); 6.30 (d, 1H); 7.03-7.61 (unresolved complex, 10H).

m.p.=195.3°C

Table XIV illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 17.



10

Table XIV

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
130	2,6-diCl	4-Cl	CH ₂ CONHMe	3,4-diOMe	149.3	557/9.13
166	2,6-diCl	4-Cl	CH ₂ CON(Me) ₂	3,4-diOMe	102.7	571/9.63
67	2-Cl	H	CH ₂ CONH ₂	3,4-diOMe	240.2	475/7.45
91	2,6-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	231.6	511/8.48
242	2,6-diF	4-Br	CH ₂ CONH ₂	3,4-diOMe	209.7	555/8.31
280	2,6-diF	4-Me	CH ₂ CONH ₂	3,4-diOMe	180.4	490/8.80

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
286	2,6-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	165.3	511/8.89
297	2,6-diF	6-OMe	CH ₃	3,4-diOMe	116	464/9.92
308	2,6-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	169	495/9.84
314	2,6-diF	4-Cl	CH ₂ CONH ₂	2-F; 4,5-diOMe	212.3	525/8.96

Example 18: *N*²-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-*N*²-[(3,4-dimethoxyphenyl)sulfonyl]-*N*¹-methylglycinamide

5 (compound 139)

- Example 18.1: (2-amino-5-chlorophenyl)(2,6-fluorophenyl)methane

To 1 g of (2-amino-5-chlorophenyl)(2,6-fluorophenyl)methanol, obtained according to Example 9.2, dissolved in 10 ml of dichloromethane are added 1.8 ml of triethylsilane and 0.86 ml of trifluoroacetic acid, and the mixture is maintained at 50°C for 6 hours. The reaction medium is added to ice and taken up in dichloromethane and 100 ml of 2M sodium hydroxide solution. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a dichloromethane/cyclohexane mixture to give 0.997 g

of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.77 (s, 2H); 5.26 (s, 2H); 6.36 (s, 1H); 6.70 (d, 1H); 6.99 (m, 1H); 7.18 (t, 2H); 7.48 (m, 1H).

5

- Example 18.2: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide

Starting with 0.97 g of (2-amino-5-chlorophenyl) (2,6-fluorophenyl)methane according to an adaptation of the process described in Example 12.2, 1.58 g of the expected product are obtained.

^1H NMR δ in ppm (DMSO d_6): 3.76 (s, 3H); 3.85 (s, 3H); 3.96 (s, 2H); 6.64 (s, 1H); 6.90 (d, 1H); 7.10-7.50 (unresolved complex, 7H); 9.69 (s, 1H).

15

m.p.=144 °C

- Example 18.3: N^2 -[4-chloro-2-(2,6-difluorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]- N^1 -methylglycinamide

20

Starting with 0.7 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide according to an adaptation of process 15 (presence of co-solvent such as DMF and of sodium iodide), 0.669 g of the expected product is obtained.

25

^1H NMR δ in ppm (DMSO d_6): 2.53 (s, 3H); 3.81 (s, 3H); 3.89 (s, 3H); 4.02-4.61 (unresolved complex, 4H); 6.62

(s, 1H); 6.86 (d, 1H); 7.15-7.31 (unresolved complex, 6H); 7.47 (m, 1H); 7.90 (m, 1H).

m.p.=92.9°C

Table XV illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 18.

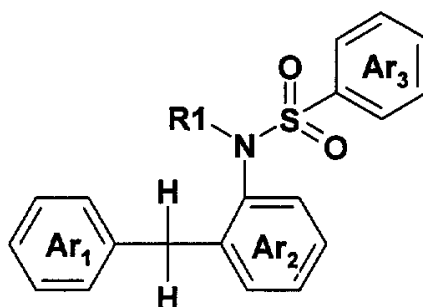


Table XV

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
140	2,6-diF	4-Cl	propyl	3,4-diOMe	135.1	496/10.82
150	2,6-diF	4-Cl	CH ₂ CON (Me) ₂	3,4-diOMe	130.2	539/9.2
145	2,6-diF	4-Cl	(CH ₂) ₂ N (Me) ₂	3,4-diOMe	121.2	525/6.47
144	2,6-diF	4-Cl	Me	3,4-diOMe	191.8	468/10.05
156	2,6-diF	4-Cl		3,4-diOMe	128.2	687/9.78
169	2,6-diF	4-Cl	CH ₂ CONH ₂	3,5-diMe	146	479/9.49
171	2,6-diF	4-Cl	CH ₂ CONHMe	3,5-diMe	196	493/9.80

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
185	2,6-diF	4-Cl	prop-2-yn-1-yl	3,4-diOMe	172	492/10.13
193	2,6-diF	4-OMe	CH ₂ CONH ₂	3,4-diOMe	189.7	507/7.93
195	2,6-diF	3-Cl	CH ₂ CONH ₂	3,4-diOMe	193.5	511/8.33
285	2,5-diF	6-OMe	CH ₂ CONH ₂	3,4-diOMe	193	507/8.58
200	2,6-diF	4-Me	CH ₂ CONH ₂	3,4-diOMe	196	491/8.20
202	2,6-diF	5-N(Me) ₂	CH ₂ CONH ₂	3,4-diOMe	141	520/7.84
205	2,6-diF	4-Me	CH(Et)CONH ₂	3,4-diOMe	197.6	519/8.84
211	2,6-diF	4-Cl	CH ₂ CN	3,4-diOMe	61.7	493/9.84
220	2,6-diF	4-F	CH ₂ CONH ₂	3,4-diOMe	184.7	495/8.16
224	2-Cl, 6-F	4-Cl	CH ₂ CONH ₂	3,4-diOMe	230	527/8.77
181	2,6-diF	4-Cl	(1-methyl-1H-imidazol-2-yl)methyl	3,4-diOMe	87	547/6.65
210	2,6-diF	3,6-diOMe	CH ₂ CONH ₂	3,4-diOMe	242.9	537/7.88
246	2,6-diF	4-Cl	CH(CH ₃)CN	3,4-diOMe	143.4	507/10.82
288	2,6-diF	6-Me	CH ₂ CONH ₂	3,4-diOMe	225.6	491/8.61
293	2,6-diF	6-Cl	CH ₂ CONH ₂	3,4-diOMe	227.4	511/8.63

For compounds 193, 195 and 220, the potassium *tert*-butoxide is replaced with sodium hydride.

5 Example 19: N^2 -[4-chloro-2-(2,5-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 80)

- Example 19.1: (2-amino-5-chlorophenyl)(2,5-
10 dichlorophenyl)methane

Starting with 1.72 g of (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methanol, obtained in Example 10.2 according to the process described in Example 18.1, 1.41 g of the expected product are
15 obtained.

- Example 19.2: N -[4-chloro-2-(2,5-chlorobenzyl)phenyl]-3,4-methoxybenzenesulfonamide

20 Starting with 1.41 g of (2-amino-5-chlorophenyl)(2,5-dichlorophenyl)methane according to an adaptation of the process described in Example 12.2, 2.3 g of the expected product are obtained.

- 25 • Example 19.3: N^2 -[4-chloro-2-(2,5-dichlorobenzyl)phenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 2.3 g of N-[4-chloro-2-(2,5-chlororobenzyl)phenyl]-3,4-methoxybenzenesulfonamide according to an adaptation of the process described in Example 15, 1 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 3.80 (s, 3H); 3.89 (s, 3H); 4.01-4.69 (unresolved complex, 4H); 6.72 (s, 1H); 6.89 (d, 1H); 7.15-7.61 (unresolved complex, 9H).

m.p.=200 °C

Table XVI illustrates the chemical structures and physical properties of a number of compounds of the invention obtained according to Example 19.

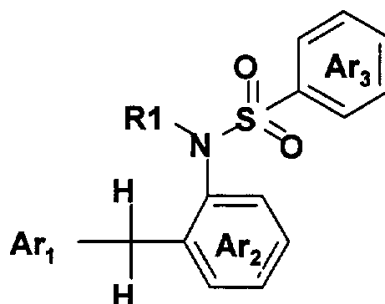


Table XVI

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
142	2,3-diFphenyl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	172.2	511/8.70
143	2,3-diFphenyl	4-Cl	CH ₂ CON(Me) ₂	3,4-diOMe	88.2	539/9.43
141	2,3-diFphenyl	4-Cl	CH ₂ CONHMe	3,4-diOMe	150.9	525/9.01
170	2-F, 6-OMe phenyl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	160	523/8.56

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
180	2-thienyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	183.9	481/8.41
192	2-Cl, 6- OMe phenyl	4- Cl	CH ₂ CONH ₂	3,4- diOMe	180.6	539/8.82

Example 20: N²-[4,5-dichloro-2-(2-chlorobenzyl)phenyl]-
N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
161)

- 5 To 0.9 g of (N²-{4,5-dichloro-2-[(2-
chlorophenyl)(hydroxy)methyl]phenyl}-
N²[(phenyl)sulfonyl]glycinamide, obtained according to
Example 10.4, dissolved in 10 ml of dichloromethane are
added 0.77 ml of triethylsilane and 1.2 ml of
10 trifluoroborane etherate, and the mixture is maintained
at 40°C for 3 hours. The reaction medium is taken up in
dichloromethane and 100 ml of 2M sodium hydroxide
solution. After separation of the phases by settling,
the organic phase is dried over anhydrous sodium
15 sulfate and concentrated. The residue is
chromatographed on a column of silica gel, eluting with
a dichloromethane/ethyl acetate mixture to give 0.622 g
of the expected product.
- ¹H NMR δ in ppm (DMSO d₆): 3.81 (s, 3H); 3.90 (s, 3H);
20 4.07-4.19 (unresolved complex, 3H); 4.51 (d, 1H); 6.87
(s, 1H); 7.14-7.57 (unresolved complex, 10H).

m.p.=163 °C

Table XVII illustrates the chemical structures and physical properties of a number of compounds of the invention obtained according to

5 Example 20.

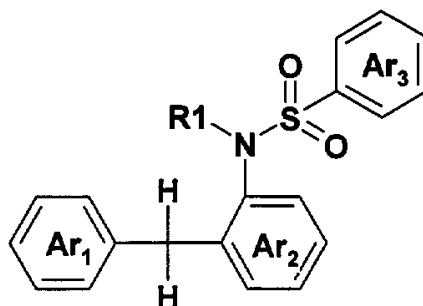


Table XVII

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
177	2,5-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	216.5	511/8.75
182	2-F, 5-Cl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	210.3	527/9.09
183	3,5-diF	4-Cl	CH ₂ CONH ₂	3,4-diOMe	184	511/8.96
196	2-F, 5-Me	4-Cl	CH ₂ CONH ₂	3,4-diOMe	231.6	507/8.98
100	2-Cl	4-Cl	CH ₂ CONH ₂	2,4-diCl, 5-Me	228.3	531/9.72
168	2-F, 4-Cl	4-Cl	CH ₂ CONH ₂	3,4-diOMe	195.2	527/9.32
208	2,6-diF	4,6-diOMe	CH ₂ CONH ₂	3,4-diOMe	191	537/7.98
228	2,6-diF	4,5-diCl	CH ₂ CONH ₂	3,4-diOMe	181.1	545/8.98

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
103	2-Cl	4-Et	CH ₂ CONMe ₂	3,4- diOMe	142.7	531/8.99
93	2-Cl	4-Et	CH ₂ CONH ₂	3,4- diOMe	86	503/8.21

Compound 247 is prepared from (N²-{2-[(2,6-difluorophenyl)(hydroxy)methyl]-6-methoxyphenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide obtained
 5 according to Example 9.4.
 m.p.=244.9; MH⁺=507; the retention time is 8.37 minutes.

Example 21: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
 3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-
 10 yl)methyl]benzenesulfonamide (compound 152) and N-[4-
 chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-
 [(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide
 (compound 151)

- 15 • Example 21.1: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(1H-tetrazol-5-yl)methyl]benzenesulfonamide

To 8.7 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(cyanomethyl)-3,4-
 20 dimethoxybenzenesulfonamide (compound 211), obtained in
 Example 18, dissolved in 100 ml of THF are added, at
 room temperature, 10 g of azidotrimethylsilane and

2.29 g of dibutyltin oxide, and the mixture is refluxed for 8 hours. The reaction medium is concentrated and the residue is chromatographed on a column of silica gel, eluting with a 99/1 (v/v) dichloromethane/methanol mixture to give 7 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.82 (s, 3H); 3.90 (s, 3H); 4.05 (q, 2H); 4.88 (d, 1H); 5.29 (d, 1H); 6.60 (s, 1H); 6.85 (d, 1H); 7.12-7.49 (unresolved complex, 7H).

- 10 • Example 21.2: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide

To 2.7 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(1H-tetrazol-5-yl)methyl]benzenesulfonamide dissolved in 50 ml of DMF are added, at room temperature, 1.07 g of iodomethane and 1.04 g of potassium carbonate. After 48 hours at room temperature, the medium is poured into water and then extracted with ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v) toluene/ethyl acetate mixture to give 1 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-[(1-methyl-1H-tetrazol-5-yl)methyl]benzenesulfonamide (compound 152)

25 ^1H NMR δ in ppm (DMSO d_6): 3.81 (s, 3H); 3.90 (s, 3H); 3.93 (q, 1H); 4.05 (m, 4H); 4.93 (d, 1H); 5.42 (d, 1H);

6.58 (s, 1H); 7.00 (d, 1H); 7.10-7.46 (unresolved complex, 7H).

m.p.=180.8°C

and 0.71g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-

5 3,4-dimethoxy-N-[(2-methyl-2H-tetrazol-5-yl)methyl]benzenesulfonamide (compound 151)

¹H NMR δ in ppm (DMSO d₆): 3.81 (s, 3H); 3.89 (s, 3H);
4.13 (s, 2H); 4.26 (s, 3H); 4.77 (d, 1H); 5.25 (d, 1H);
6.57 (s, 1H); 6.86 (d, 1H); 7.11-7.47 (unresolved

10 complex, 7H).

m.p.=136.3°C

Table XVIII illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to

15 Example 21.

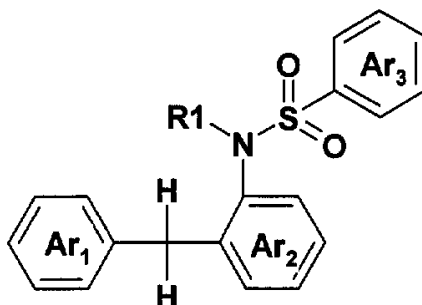


Table XVIII

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
153	2,6-diF	4-Cl	(2-ethyl-2H-tetrazol-5-yl)methyl	3,4-diOMe	139.7	564/9.81
154	2,6-diF	4-Cl	(1-ethyl-1H-tetrazol-5-yl)methyl	3,4-diOMe	150.9	564/9.48
159	2,6-diF	4-Cl	(2-ethyl-2H-tetrazol-5-yl)methyl	3,5-diMe	105.5	532/10.84
160	2,6-diF	4-Cl	(1-ethyl-1H-tetrazol-5-yl)methyl	3,5-diMe	134	532/10.46
157	2,6-diF	4-Cl	(2-methyl-2H-tetrazol-5-yl)methyl	3,5-diMe	159	518/10.53
158	2,6-diF	4-Cl	(1-methyl-1H-tetrazol-5-yl)methyl	3,5-diMe	240	518/10.20
122	2-Cl	4-Cl	(2-ethyl-2H-tetrazol-5-yl)methyl	3,5-diMe	oil	530/10.65
123	2-Cl	4-Cl	(1-ethyl-1H-tetrazol-5-yl)methyl	3,5-diMe	158	530/10.27
108	2-Cl	4-Cl	(1-isopropyl-1H-tetrazol-5-yl)methyl	3,4-diOMe	79	576/9.52
111	2-Cl	4-Cl	(1-benzyl-1H-tetrazol-5-yl)methyl	3,4-diOMe	98	624/9.89

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
90	2-Cl	4- Cl	(1-ethyl-1H- tetrazol -5-yl)methyl	3,4- diOMe	168.3	562/9.25
88	2-Cl	4- Cl	(1-methyl- 1H-tetrazol- 5-yl)methyl	3,4- diOMe	200.6	548/8.96
243	2,6- diF	4- Cl	1-(2-methyl- 2H-tetrazol- 5-yl)ethyl	3,4- diOMe	259.3	564/9.85
244	2,6- diF	4- Cl	1-(1-methyl- 1H-tetrazol- 5-yl)ethyl	3,4- diOMe	178.1	564/10.44
310	2,6- diF	6- OMe	(2-ethyl-2H- tetrazol-5- yl)methyl	3,4- diOMe	136.3	560/9.61
311	2,6- diF	6- OMe	(1-ethyl-1H- tetrazol-5- yl)methyl	3,4- diOMe	161.4	560/9.30

Example 22: N²-[2-(2-chlorobenzyl)-4-methylphenyl]-N²-
[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
165)

5

- Example 22.1: N-[4-methyl-2-(2-
chlorobenzyl)phenyl]-3,4-
dimethoxybenzenesulfonamide

Starting with 1 g of N-[4-methyl-2-[(2-
10 chlorophenyl)(hydroxy)methyl]phenyl]-3,4-
dimethoxybenzenesulfonamide, obtained according to

Example 8, according to an adaptation of the process described in Example 18.1, 0.47 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d6): 2.14 (s, 3H); 3.73 (s, 3H);
5 3.84 (s, 3H); 4.04 (s, 2H); 6.60 (s, 1H); 6.81-7.47
(unresolved complex, 9H); 9.43 (s, 1H).

- Example 22.2: N²-[2-(2-chlorobenzyl)-4-methylphenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

To 0.47 g of N-{4-methyl-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide dissolved in 5.7 ml of DMF is added, at 0°C, 0.048 g of sodium hydride. After
15 1 hour at this temperature, 0.166 g of 2-bromoacetamide is introduced and the mixture is left for 18 hours at room temperature. The medium is poured into water and then extracted with ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated.
20 The residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v) cyclohexane/ethyl acetate mixture to give 0.4 g of the expected product.
¹H NMR δ in ppm (DMSO d6): 2.16 (s, 3H); 3.79 (s, 3H);
3.88 (s, 3H); 4.05-4.25 (unresolved complex, 3H); 4.52
25 (d, 1H); 6.54 (s, 1H); 6.76 (d, 1H); 6.94-7.53
(unresolved complex, 10H).

m.p.=140.6 °C

N^2 -[5-Chloro-2-(2-chlorobenzyl)phenyl]- N^2 -
[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
179) is synthesized according to this process starting
with N-[5-chloro-2-[(2-

5 chlorophenyl)(hydroxy)methyl]phenyl]-3,4-
dimethoxybenzenesulfonamide obtained according to
Example 9.3, m.p.=86.4°C

N^2 -[2-(2-Chlorobenzyl)-4-methoxyphenyl]- N^2 -
[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound
10 138) is synthesized according to this process.
m.p.=184.6°C

Example 23: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
N-[3-(dimethylamino)propyl]-3,4-
15 dimethoxybenzenesulfonamide (compound 197)

To 0.45 g of [4-chloro-2-(2,6-
difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide
(prepared according to Example 18.2) are successively
20 added 0.207 g of potassium carbonate, 0.1 g of
tetrabutylammonium bromide, 20 ml of toluene and
0.237 g of 3-dimethylamino-1-bromopropane, and the
mixture is refluxed for 24 hours. 0.168 g of potassium
tert-butoxide and 0.237 g of 3-dimethylamino-1-
25 bromopropane are added and the mixture is refluxed for
4 hours. The reaction medium is poured into water and
extracted with ethyl acetate. The organic phase is

dried over anhydrous sodium sulfate and concentrated.
The residue is chromatographed on a column of silica
gel, eluting with a 99/1 (v/v) dichloromethane/methanol
mixture. The oil obtained is dissolved in methanol and
5 poured into a 0.5M sodium hydroxide solution, and the
precipitate formed is filtered off and dried under
vacuum to give 0.504 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.34-1.48 (unresolved
complex, 2H); 2.01 (s, 6H); 2.14 (t, 2H); 3.13 (m, 1H);
10 3.75 (s, 3H); 3.78 (m, 1H); 3.85 (s, 3H); 4.13 (d, 1H);
4.31 (d, 1H); 6.72-7.51 (unresolved complex, 9H).

m.p.=134°C

Table XIX illustrates the chemical structures
and the physical properties of a number of compounds of
15 the invention obtained according to Example 23.

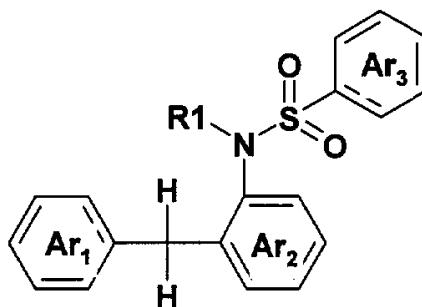


Table XIX

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
199	2,6-diF	4-Cl	2-pyrrolidin-1-ylethyl	3,4-diOMe	131.4	551/6.61
201	2,6-diF	4-Cl	2-(dimethylamino)-1-methylethyl	3,4-diOMe	128.6	539/6.44
203	2,6-diF	4-Cl	2-[benzyl(methyl)-amino]ethyl	3,4-diOMe	104.8	601/7.18
231	2,6-diF	4-Cl	(CH ₂) ₂ NHCONH ₂	3,4-diOMe	124.5	539/8.27
229	2,6-diF	4-Cl	(CH ₂) ₃ SO ₂ NEt ₂	3,4-diOMe	71.2	630/10.27
230	2,6-diF	4-Cl	(CH ₂) ₃ SO ₂ NMe ₂	3,4-diOMe	76.8	602/9.71
234	2,6-diF	4-Cl	2-(2-oxopyrrolidin-1-yl)ethyl	3,4-diOMe	138.6	565/8.80
236	2,6-diF	4-Cl	2-methoxyethyl	3,4-diOMe	83.8	512/9.38
241	2,6-diF	5-Br	CH ₃ CONH ₂	3,4-diOMe	93.5	555/8.99
248	2,6-diF	4-Cl	cyclopropylmethyl	3,4-diOMe	163.4	508/11.42
259	2,6-diF	4-Cl	CH ₃ CONH ₂	3-Me, 4-OMe	156.6	495/9.07
268	2,6-diF	4-Cl	2-(1,3-dioxolan-2-yl)ethyl	3,4-diOMe	288.8	554/10.50
283	2,6-diF	4-Cl	CH ₃ CONH ₂	6-OMe pyrid-3-yl	164	482/9.27

Example 24: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-(2-hydroxyethyl)-3,4-dimethoxybenzenesulfonamide (compound 24)

5

- Example 24.1: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-[2-(tetrahydro-2H-pyran-2-yloxy)ethyl]benzenesulfonamide

10 To 1 g of N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide, obtained in Example 1.2, dissolved in 40 ml of acetonitrile are successively added 1.2 ml of triethylamine and 1.29 ml of 2-(2-bromoethoxytetrahydro-2H-pyran, and the mixture is
15 refluxed for 18 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a
20 column of silica gel, eluting with a cyclohexane/ethyl acetate solvent mixture to give 0.479 g of the expected product.

- Example 24.2: N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-N-(2-hydroxyethyl)-3,4-dimethoxybenzenesulfonamide

25

To 0.479 g of N-{4-chloro-2-[(2-chlorophenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxy-N-

[2-(tetrahydro-2H-pyran-2-yloxy)ethyl]benzenesulfonamide dissolved in 4.7 ml of THF are added 9.15 ml of acetic acid and 2.25 ml of water, and the mixture is maintained at 40°C for 48 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a cyclohexane/ethyl acetate solvent mixture to give 0.209 g of the expected product.

¹H NMR δ in ppm (DMSO d6): 3.02 (m, 2H); 3.40 (m, 2H); 3.75 (s, 3H); 3.88 (s, 3H); 4.40 (t, 1H); 6.01 (d, 1H); 6.70-7.51 (unresolved complex, 10H); 7.86 (s, 1H).

m.p.=86.2°C

In the same manner, compound 237 is prepared, the physical properties of which are as follows:

MH⁺=498, the retention time is 8.99 minutes

m.p.=165.3°C

Example 25: N²-{4-chloro-2-[1-(2-chlorophenyl)-1-hydroxyethyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 172)

- Example 25.1: 1-(2-amino-5-chlorophenyl)-1-(2-chlorophenyl)ethanol

To 5 g of 2-amino-2',5-dichlorobenzophenone dissolved in 100 ml of diethyl ether, at -30°C, are

added 12.5 ml of 3M methylmagnesium bromide solution, and the mixture is maintained at room temperature for 18 hours. 6 ml of 3M methylmagnesium bromide solution are added and the mixture is left at room temperature
5 for 1 hour. The resulting mixture is hydrolysed with 2M hydrochloric acid solution and washed with water. The organic phase is dried over anhydrous sodium sulfate to give 4.3 g of the expected product.

¹H NMR δ in ppm (DMSO d6): 1.99 (s, 3H); 4.91 (s, 2H);
10 6.11 (s, 1H); 6.53 (d, 1H); 6.97-7.42 (unresolved complex, 5H); 7.97 (d, 1H).

- Example 25.2: N-{4-chloro-2-[1-(2-chlorophenyl)-1-hydroxyethyl]phenyl}-3,4-
15 dimethoxybenzenesulfonamide

To 1.5 g of 1-(2-amino-5-chlorophenyl)-1-(2-chlorophenyl)ethanol according to an adaptation of the process described in Example 1.1, 2.9 g of the expected product are obtained.

20 ¹H NMR δ in ppm (DMSO d6): 1.78 (s, 3H); 3.75 (s, 3H); 3.83 (s, 3H); 4.05 (q, 1H); 6.87 (s, 1H); 7.04-7.54 (unresolved complex, 5H); 7.82 (m, 2H); 8.60 (d, 2H); 10.00 (s, 1H).

- 25 • Example 25.3: N-{4-chloro-2-[1-(2-chlorophenyl)-1-hydroxyethyl]phenyl}N-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

To 1.3 g of N-{4-chloro-2-[1-(2-chlorophenyl)-1-hydroxyethyl]phenyl}-3,4-dimethoxybenzenesulfonamide dissolved in diethyl ether are successively added, at -5°C, 1.3 ml of a 2M
5 solution of lithium diisopropylamine in hexane, and 0.45 g of 2-bromoacetamide. After 18 hours at room temperature, 0.5 g of 2-bromoacetamide and 1.4 g of sodium iodide are successively added and the mixture is refluxed for 4 hours. The reaction medium is taken up
10 in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 95/5 (v/v) dichloromethane/methanol mixture to give 0.51 g of the
15 expected product.

¹H NMR δ in ppm (DMSO d₆): 2.11 (s, 3H); 3.74-3.98 (unresolved complex, 8H); 6.25 (s, 1H); 6.96-7.97 (unresolved complex, 12H).

20 Example 26: N²-{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 186)

• Example 26.1: 4-chloro-2-[1-(2-chlorophenyl)ethyl]phenylamine
25

To 54 ml of a 1M solution of lithium aluminium hydride in THF are added portionwise 7.1 g of

aluminium trichloride. To this solution are added 4 g of 1-(2-amino-5-chlorophenyl)-1-(2-chlorophenyl)ethanol, obtained in Example 25.1, dissolved in diethyl ether, and the mixture is stirred for 18 hours at room temperature and then refluxed for 4 hours. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 40/60 (v/v) dichloromethane/cyclohexane mixture to give 0.9 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.45 (d, 3H); 4.43 (q, 1H); 4.96 (s, 2H); 6.65 (m, 2H); 6.94 (d, 1H); 7.30-7.47 (unresolved complex, 4H).

- Example 26.2: N-{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}-3,4-dimethoxybenzenesulfonamide

Starting with 0.9 g of 4-chloro-2-[1-(2-chlorophenyl)ethyl]phenylamine according to the process described in Example 1.1, 1.7 g of the expected product are obtained.

- Example 26.3: N^2 -{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}- N^2 -{(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 0.9 g of N-{4-chloro-2-[1-(2-chlorophenyl)ethyl]phenyl}-3,4-dimethoxybenzenesulfonamide according to the process described in Example 12.3, 0.9 g of the expected

5 product are obtained.

^1H NMR δ in ppm (DMSO d_6): 1.35 (d, 3H); 2.75 (d, 1H); 3.79 (s, 3H); 3.86 (s, 3H); 4.25 (d, 1H); 4.74 (q, 1H); 6.92-7.64 (unresolved complex, 12H).

m.p.=150°C

10 Compound 187 is obtained according to this process. m.p.=151°C

Example 27: N-(2-aminoethyl)N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide

15 (compound 215)

To 1 g of N-[4-methyl-2-(2,6-difluorobenzyl)phenyl]-N-[2-(phthalimido)ethyl]-3,4-dimethoxybenzenesulfonamide, obtained according to an adaptation of the process described in Example 18,
20 dissolved in 15 ml of ethanol is added 0.4 g of hydrazine hydrate, and the mixture is refluxed for 3 hours. At room temperature, the insoluble material is filtered off and the filtrate is concentrated. The residue is chromatographed on a column of silica gel,
25 eluting with a 99/1 (v/v) dichloromethane/methanol mixture to give 0.26 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.62 (s, 2H); 2.17 (s, 3H); 2.40-2.67 (unresolved complex, 2H); 3.12 (m, 1H); 3.69 (m, 1H); 3.75 (s, 3H); 3.88 (s, 3H); 4.09 (d, 1H); 4.26 (d, 1H); 6.56 (m, 2H); 6.97-7.43 (unresolved complex, 5 7H).

m.p.=251.8°C

Table XX illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 28.

10

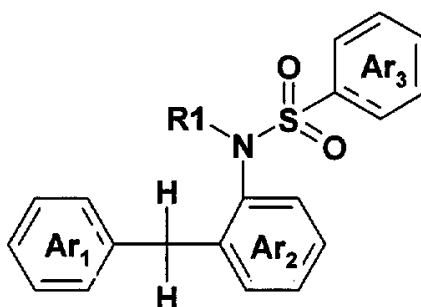


Table XX

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
256	2,6-diF	4-Cl	2-aminoethyl	3,4-diOMe	163.4	497/6.82
257	2,5-diF	4-Me	2-aminoethyl	3,4-diOMe	61.1	477/6.69
262	2,5-diF	4-Cl	2-aminoethyl	3,4-diOMe	141.1	497/6.88
281	2,6-diF	6-OMe	2-aminoethyl	3,4-diOMe	137.8	493/6.47
287	2,6-diF	4-Cl	3-aminopropyl	3,4-diOMe	149.1	511/6.91

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
294	2,5- diF	6- OMe	2-aminoethyl	3,4- diOMe	114.8	493/6.47
300	2,6- diF	4- Cl, 6- OMe	2-aminoethyl	3,4- diOMe	185.4	527/6.82

Example 28: N-(2-([(benzylamino)carbonyl]amino)ethyl)-
N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-
5 dimethoxybenzenesulfonamide (compound 218)

To 1 g of N-(2-aminoethyl)-N-[2-(2,6-
difluorobenzyl)-4-methylphenyl]-3,4-
dimethoxybenzenesulfonamide (compound 215) dissolved in
10 20 ml of THF is added 0.266 g of benzyl isocyanate,
and, after refluxing for 3 hours, the medium is
evaporated to dryness. The residue is chromatographed
on a column of silica gel, eluting with an 8/2 (v/v)
toluene/ethyl acetate mixture to give 0.65 g of the
15 expected product.

¹H NMR δ in ppm (DMSO d6): 2.17 (s, 3H); 3.05 (m, 2H);
3.24 (m, 1H); 3.74 (s, 3H); 3.78 (m, 1H); 3.87 (s, 3H);
4.07-4.25 (unresolved complex, 4H); 5.99 (t, 1H); 6.50
(t, 1H); 6.58 (d, 2H); 6.98-7.43 (unresolved complex,
20 12H).

m.p.=100.4°C

Table XXI illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to Example 28.

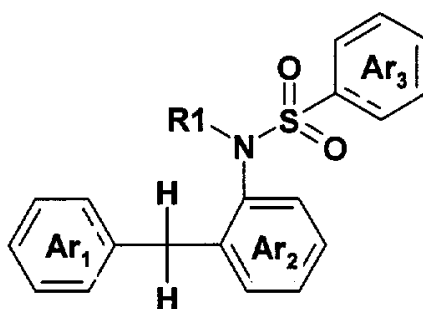


Table XXI

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
217	2,6-diF	4-Me	2-[(anilino-carbonyl)amino]-ethyl	3,4-diOMe	163.4	n.d
238	2,6-diF	4-Cl	2-([(3-chlorophenyl)amino]-carbonyl)amino)-ethyl	3,4-diOMe	149.3	650/10.87
240	2,6-diF	4-Cl	2-([(2-chlorophenyl)amino]-carbonyl)amino)-ethyl	3,4-diOMe	136.3	650/10.77
252	2,6-diF	4-Cl	2-([(3,4-dimethoxyphenyl)-amino]carbonyl)-amino)ethyl	3,4-diOMe	169.7	676/9.80

Example 29: N-(2-([2-(2,6-difluorobenzyl)-4-methylphenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}ethyl)acetamide
5 (compound 219)

To 1 g of N-(2-aminoethyl)N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide (compound 215) dissolved in
10 25 ml of THF are added 0.167 ml of pyridine and 0.22 g of acetic anhydride. After 48 hours at room temperature, the reaction medium is concentrated. The residue is chromatographed on a column of silica gel, eluting with a 99/1 (v/v) dichloromethane/methanol
15 mixture to give 0.505 g of the expected product.
¹H NMR δ in ppm (DMSO d6): 1.74 (s, 3H); 2.17 (s, 3H); 3.05-3.28 (m, 3H); 3.72 (m, 1H); 3.76 (s, 3H); 3.87 (s, 3H); 4.05 (d, 1H); 4.22 (d, 1H); 6.60 (d, 2H); 6.99-7.46 (unresolved complex, 7H); 7.85 (t, 1H).
20 m.p.=79.7°C

Example 30: N²-{4-chloro-2-[methyl(phenyl)amino]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]-N¹-methylglycinamide
(compound 124)

25

- Example 30.1: 5-chloro-2-nitro-N-diphenyl-N-methylamine

To 10 g of 5-chloro-2-nitrodiphenylamine dissolved in 20 ml of DMF are successively added 2.8 ml of iodomethane and 14.71 g of caesium carbonate, and the mixture is stirred for 18 hours at room temperature. The reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with 97/3 (v/v) cyclohexane/ethyl acetate mixture to give 10.51 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.32 (s, 3H); 6.78-6.93 (unresolved complex, 3H); 7.19-7.26 (m, 2H); 7.40 (d, 1H); 7.65 (d, 1H); 7.93 (d, 1H).

15 • Example 30.2: 2-amino-5-chloro-N-diphenyl-N-methylamine

To 10.49 g of 5-chloro-2-nitro-N-diphenyl-N-methylamine dissolved in 100 ml of ethanol are successively added 14.22 g of tin metal and 50 ml of 12M hydrochloric acid solution, and the mixture is refluxed for 1 hour. After evaporating off the ethanol, the reaction medium is taken up in ethyl acetate, basified and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 9.37 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.11 (s, 3H); 5.07 (s, 2H); 6.57-7.21 (unresolved complex, 8H).

- Example 30.3: N-{4-chloro-2-[methyl(phenyl)amino]phenyl}-3,4-dimethoxybenzenesulfonamide

5 Starting with 1.5 g of 2-amino-5-chloro-N-diphenyl-N-methylamine, the process is performed according to Example 1.1 to give 1.122 g of the expected product.

¹H NMR δ in ppm (DMSO d6): 2.93 (s, 3H); 3.67 (s, 3H);
10 3.84 (s, 3H); 6.37 (d, 2H); 6.74 (t, 1H); 7.05-7.37 (unresolved complex, 7H); 7.54 (d, 1H); 9.46 (s, 1H).

- Example 30.4: N²-(4-chloro-2-[methyl(phenyl)amino]phenyl)-N²-[(3,4-dimethoxyphenyl)sulfonyl]-N¹-methylglycinamide

15 Starting with 0.8 g of N-{4-chloro-2-[methyl(phenyl)amino]phenyl}-3,4-dimethoxybenzenesulfonamide according to the process described in Example 4.3, 0.766 g of the expected
20 product is obtained.

¹H NMR δ in ppm (DMSO d6): 2.41 (d, 3H); 3.16 (s, 3H);
3.77 (s, 3H); 3.88 (s, 3H); 4.12 (s, 2H); 6.66-6.84 (unresolved complex, 3H); 7.10-7.43 (unresolved complex, 8H); 7.72 (t, 1H).

25 m.p.=148.6°C

Compound 92 is obtained by this process:

m.p.=192.5°C

Example 31: 4-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]-amino}butanamide (compound 204)

5

- Example 31.1: 4-{[4-chloro-2-{[2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}butanoic acid

To 2.6 g of ethyl 4-{[4-chloro-2-{[2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}butanoate, obtained according to Example 18, dissolved in 50 ml of ethanol are added 22.8 ml of sodium hydroxide, and the mixture is left for 18 hours at room temperature. The solvent is evaporated off and the residue is taken up in 40 ml of 1M hydrochloric acid solution and extracted with ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is solidified with diisopropyl ether to give 1.7 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.54 (m, 2H); 2.27 (t, 2H); 3.27 (m, 1H); 3.76 (s, 3H); 3.85 (s, 3H); 4.23 (m, 2H); 6.75-7.51 (unresolved complex, 10H); 12.09 (s, 1H).

- 25
- Example 31.2: {[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}butanamide

To 1.7 g of 4-{{[4-chloro-2-{{[2-(2,6-difluorobenzyl)phenyl]]((3,4-dimethoxyphenyl)sulfonyl]amino}butanoic acid dissolved in 30 ml of THF, at 0°C, are added 0.42 ml of

5 N-ethylmorpholine and 0.42 ml of ethyl chloroformate; after 30 minutes at this temperature, a solution of ammonia in THF is introduced dropwise and the mixture is left for 1 hour at 20°C. The resulting mixture is poured into saturated sodium hydrogencarbonate solution

10 and taken up in ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated, and the residue is solidified with diethyl ether to give, after drying, 1.41 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 1.51 (m, 2H); 2.07 (t, 2H);

15 3.21 (m, 1H); 3.74 (m, 1H); 3.78 (s, 3H); 3.89 (s, 3H); 4.23 (q, 2H); 6.75 (m, 3H); 7.04-7.51 (unresolved complex, 8H).

m.p.=197°C

Table XXII illustrates the chemical

20 structures and the physical properties of a number of compounds of the invention obtained according to this example.

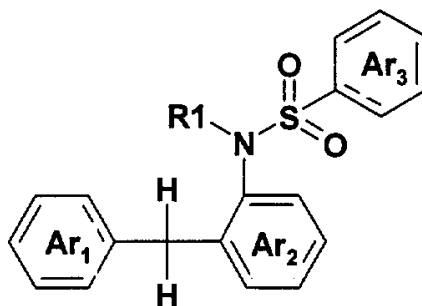


Table XXII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
235	2,6-diF	4-Cl	CH ₂ CH ₂ CH ₂ CONH ₂	2,5-diMe, 4-Cl	n.d	541/10.03
266	2,5-diF	4-Cl	CH ₂ CH ₂ CH ₂ CONH ₂	3,4-diOMe	150	539/9.15
272	2,6-diF	6-OMe	CH ₂ CH ₂ CH ₂ CONH ₂	3,4-diOMe	207.8	535/8.42
299	2,5-diF	6-OMe	CH ₂ CH ₂ CH ₂ CONH ₂	3,4-diOMe	189.3	535/8.54

5 Example 32: *N*²-(4-chloro-2-[2-(trifluoromethyl)benzyl]phenyl)-*N*²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 207)

- Example 32.1: (2-amino-5-chlorophenyl)(2-trifluoromethylphenyl)methanol

To 1.9 g of (2-amino-5-chlorophenyl)(2-trifluoromethylphenyl)methanone, obtained in Example 7.2, dissolved in 87 ml of ethanol is added 0.775 g of sodium borohydride, and the mixture is left at 20°C for

18 hours. The solvent is evaporated off and the residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 1.96 g of the expected

5 product.

^1H NMR δ in ppm (DMSO d_6): 5.15 (s, 2H); 5.97 (d, 1H); 6.11 (d, 1H); 6.35 (d, 1H); 6.72 (d, 1H); 6.99 (d, 1H); 7.53-7.81 (unresolved complex, 4H).

- 10 • Example 32.2: N-{4-chloro-2-[(2-trifluoromethylphenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide

Starting with 1.28 g of (2-amino-5-chlorophenyl)(2-trifluoromethylphenyl)methanol

- 15 according to the process described in Example 1.1, 2.06 g of the expected product are obtained.

^1H NMR δ in ppm (DMSO d_6): 3.76 (s, 3H); 3.85 (s, 3H); 6.34 (s, 2H); 6.89 (d, 1H); 6.98 (s, 1H); 7.08 (d, 1H); 7.23-7.33 (unresolved complex, 4H); 7.53-7.77

- 20 (unresolved complex, 3H); 9.25 (s, 1H).

- Example 32.3: N-[4-chloro-2-(2-trifluoromethylbenzyl)phenyl]-3-methoxybenzenesulfonamide

- 25 Starting with 2.06 g of N-{4-chloro-2-[(2-trifluoromethylphenyl)(hydroxy)methyl]phenyl}-3,4-dimethoxybenzenesulfonamide according to the method

described in Example 22.1, 0.94 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d6): 3.73 (s, 3H); 3.85 (s, 3H); 4.06 (s, 2H); 6.64 (s, 1H); 6.89-7.28 (unresolved complex, 6H); 7.48-7.60 (m, 2H); 7.75 (d, 1H); 9.72 (s, 1H).

- Example 32.4: N²-{4-chloro-2-[2-(trifluoromethyl)benzyl]phenyl}-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 0.94 g of N-[4-chloro-2-(2-trifluoromethylbenzyl)phenyl]-3-methoxybenzenesulfonamide according to Example 16.3, 0.723 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d6): 3.80 (s, 3H); 3.89 (s, 3H); 4.03 (d, 1H); 4.27 (q, 2H); 4.74 (d, 1H); 6.55 (s, 1H); 6.88 (d, 1H); 7.12-7.63 (unresolved complex, 9H); 7.82 (d, 1H).

m.p.=133°C

Example 33: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-2,2,2-trifluoroacetamide (compound 223)

To 2.2 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide, obtained in Example 18.2, dissolved in 40 ml of dichloromethane are added 0.8 ml of triethylamine and

1.46 g of trifluoroacetyl triflate, and, after
10 minutes, the medium is hydrolysed and concentrated.
The residue is chromatographed on a column of silica
gel, eluting with a dichloromethane/cyclohexane mixture
5 to give 1.1 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.86 (s, 3H); 3.93 (s, 3H);
4.19 (s, 2H); 6.92 (s, 1H); 7.17-7.54 (unresolved
complex, 7H); 7.71 (d, 1H).

m.p.=79.7°C

10

Example 34: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
3,4-dimethoxy-N-(2,2,2-
trifluoroethyl)benzenesulfonamide (compound 190)

To 1.48 g of N-[4-chloro-2-(2,6-
15 difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide,
obtained in Example 18.2, dissolved in 40 ml of xylene
are added 2.3 g of 2,2,2-trifluoroethyl
trichloromethanesulfonate, 0.44 g of potassium *tert*-
butoxide and 20 ml of N-methylpyrrolidone, and the
20 mixture is maintained at 150°C for 8 hours. The
reaction medium is taken up in ethyl acetate and washed
with water. The organic phase is dried over anhydrous
sodium sulfate and concentrated. The residue is
chromatographed on a column of silica gel, eluting with
25 dichloromethane, to give 0.455 g of the expected
product.

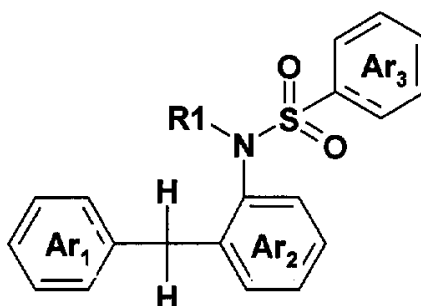
¹H NMR δ in ppm (DMSO d6): 3.82 (s, 3H); 3.90 (s, 3H); 4.14-4.35 (unresolved complex, 3H); 4.82 (m, 1H); 6.63 (s, 1H); 6.80 (d, 1H); 7.17-7.54 (unresolved complex, 7H).

5 m.p.=70°C

Example 35: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxy-N-(3-pyrid-3-ylpropyl)benzenesulfonamide (compound 232)

10 To 1.5 g of triphenylphosphine dissolved in 25 ml of THF is added 0.909 g of diisopropyl azodicarboxylate. After 15 minutes at room temperature, 0.61 g of 3-pyrid-3-ylpropan-1-ol is introduced and the mixture is left at 20°C for 15 minutes. 1.36 g of N-[4-
15 chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide are introduced and the mixture is left at room temperature for 18 hours. The medium is concentrated and the residue is chromatographed on a column of silica gel, eluting with
20 a toluene/ethyl acetate mixture passing from a ratio of 9/1 to 5/5 (v/v). 5 ml of 2M hydrochloric acid are added to the product obtained, dissolved in diethyl ether, and the solvents are then evaporated off. The residue is taken up in diisopropyl ether to give, after
25 filtration, 0.55 g of the expected product.
m.p.=102.8°C.

Table XXIII illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this example.

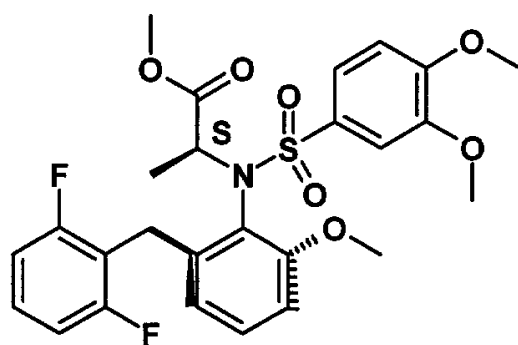


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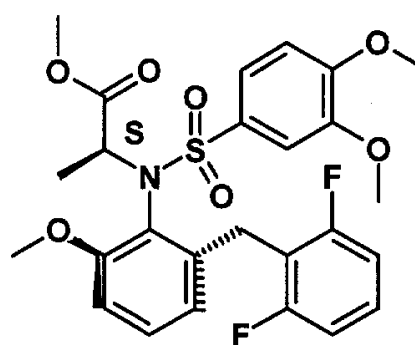
Table XXIII

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
245	2,6-diF	4-Cl	3-pyrid-3-ylpropyl	3,4-diOMe	102.8	573/8.10
250	2,6-diF	4-Cl	2-pyrid-2-ylethyl	3,4-diOMe	75.1	559/8.24
254	2,6-diF	4-Cl	2-pyrid-3-ylethyl	3,4-diOMe	90.3	559/7.14
255	2,6-diF	4-Cl	2-pyrid-4-ylethyl	3,4-diOMe	164.3	559/8.29
260	2,6-diF	4-Cl	2-phenoxyethyl	3,4-diOMe	64.3	574/10.88
274	2,6-diF	4-Cl	(2R)-pyrrolidin-2-ylmethyl	3,4-diOMe	204.8	537/7.07
275	2,6-diF	4-Cl	(2S)-pyrrolidin-2-ylmethyl	3,4-diOMe	214.1	537/7.07
278	2,6-diF	4-Cl	{ [2-(dimethylamino)-ethyl]-amino } ethyl	3,4-diOMe	103	568/6.29
290	2,6-diF	4-Cl	1,3-thiazol-2-ylmethyl	3,4-diOMe	184	551/10.26

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
291	2,6-diF	4-Cl	pyrimid-2-ylmethyl	3,4-diOMe	104	546/9.89
292	2,6-diF	4-Cl	2-morpholino-4-ylethyl	3,4-diOMe	185.3	567/7.35
295	2,6-diF	4-Cl	pyrid-2-ylmethyl	3,4-diOMe	200.8	545/16.9
315	2,6-diF	6-OMe	CH(CH ₃)COOEt	3,4-diOMe	94.3	536/9.98
316	2,6-diF	6-OMe	CH(CH ₃)COOEt	3,4-diOMe	130.2	536/9.89
317	2,6-diF	6-OMe	CH(CH ₃)COOEt	3,4-diOMe	73.3	536/9.98
318	2,6-diF	6-OMe	CH(CH ₃)COOEt	3,4-diOMe	130.8	536/9.89

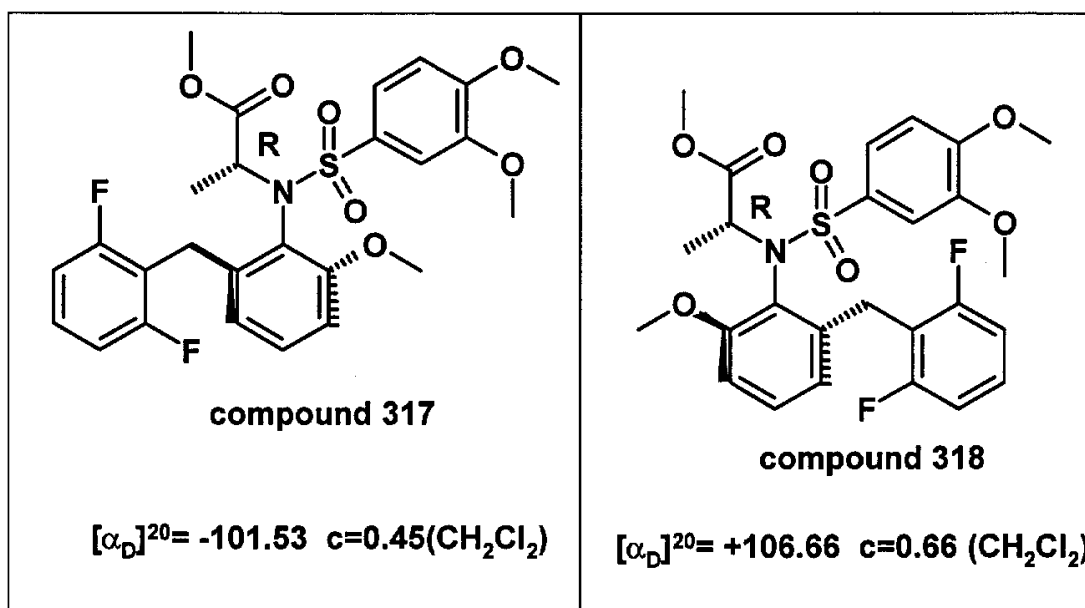


compound 315

[α_D]²⁰ = +97.59 c=0.66 (CH₂Cl₂)

compound 316

[α_D]²⁰ = -106.25 c=0.66 (CH₂Cl₂)



Compounds 315/316 and 317/318 are pairs of atropoisomers. Each atropoisomer is characterized by its optical rotation (α_D). The centre of atropoisomerism is generated by the steric hindrance around the N-aromatic bond.

Example 36: ethyl N-[(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxy-N-[2-

(methylamino)ethyl]benzenesulfonamide (compound 258)

- Example 36.1: ethyl N-(2-bromoethyl)-N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide

To 1 g of N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide dissolved in 1.1 ml of dimethylformamide are successively added 0.38 g of potassium carbonate and 0.48 ml of 1,2-

dibromoethane, and the mixture is maintained at 100°C for 4 hours. After cooling to room temperature, the reaction medium is hydrolysed and extracted with ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated to give 1.24 g of expected product.

¹H NMR δ in ppm (DMSO d6): 2.17 (s, 3H); 3.42 (m, 2H); 3.73 (m, 1H); 3.76 (s, 3H); 3.88 (s, 3H); 4.03-4.15 (unresolved complex, 2H); 4.45 (d, 1H); 6.63 (d, 1H); 6.98-7.48 (unresolved complex, 8H).

- Example 36.2: ethyl N-[(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxy-N-[2-(methylamino)ethyl]benzenesulfonamide hydrobromide

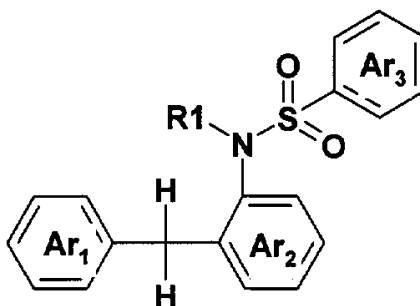
To 1.24 g of N-(2-bromoethyl)-N-[2-(2,6-difluorobenzyl)-4-methylphenyl]-3,4-dimethoxybenzenesulfonamide are added 10.7 ml of 2M solution of methylamine in methanol and the mixture is maintained at 105°C for 4 hours. The reaction is completed by addition of 10 ml of 2M solution of methylamine in methanol with refluxing for 8 hours. After cooling to room temperature, the medium is concentrated and the residue is chromatographed to give 0.849 g of the expected product.

m.p.=208.5°C

¹H NMR δ in ppm (DMSO d6): 2.20 (s, 3H); 2.58 (s, 3H); 2.85 (m, 1H); 3.06 (m, 1H); 3.52 (m, 1H); 3.77 (s, 3H);

3.90 (s, 3H); 3.99-4.07 (unresolved complex, 2H); 4.27 (d, 1H); 6.58-6.64 (unresolved complex, 2H); 7.01-7.49 (unresolved complex, 2H); 8.48 (s, 2H).

Table XXIV illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this example.



10

Table XXIV

Compound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ /retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
277	2,6-diF	4-Cl	2-(1H-1,2,4-triazol-1-yl)ethyl	3,4-diOMe	129.1	n.d.
282	2,6-diF	6-OMe	methylaminoethyl	3,4-diOMe	262.9	507/6.54
284	2,6-diF	4-Cl	methylaminoethyl	3,4-diOMe	54	511/6.94
306	2,6-diF	6-OMe	2-(1H-1,2,4-triazol-1-yl)ethyl	3,4-diOMe	132.1	545/8.76

Example 37: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
N-(3-hydroxypropyl)-3,4-dimethoxybenzenesulfonamide
(compound 270)

- 5 • Example 37.1: N-(3-([tert-
butyl(dimethyl)silyloxy]propyl)-N-[4-chloro-2-
(2,6-difluorobenzyl)phenyl]-3,4-
dimethoxybenzenesulfonamide

To 4.3 g of triphenylphosphine in 20 ml of
10 tetrahydrofuran are added, at room temperature, 3.25 ml
of diisopropyl azodicarboxylate. After 30 minutes,
3.5 ml of 3-[tert-butyl(dimethyl)silyloxy]propanol
dissolved in 30 ml of tetrahydrofuran are introduced.
The mixture is left at room temperature for 30 minutes,
15 and 5 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
3,4-dimethoxybenzenesulfonamide are then introduced.
After 48 hours at room temperature, the reaction medium
is concentrated and then chromatographed on a column of
silica gel to give 8.09 g of the expected product.
20 ¹H NMR δ in ppm (DMSO d₆): -0.04 (s, 3H); -0.02 (s, 3H);
0.82 (s, 9H); 1.40-1.56 (unresolved complex, 2H); 3.18
(m, 1H); 3.54 (m, 2H); 3.76 (s, 3H); 3.82 (m, 1H); 3.90
(s, 3H); 4.13 (d, 1H); 4.26 (d, 1H); 6.72-7.23
(unresolved complex, 9H).

- Example 37.2: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(3-hydroxypropyl)-3,4-dimethoxybenzenesulfonamide

To 8 g of N-(3-([tert-butyl(dimethyl)silyl]oxy)propyl)-N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide in 80 ml of tetrahydrofuran at 0°C are added 2.98 g of tetrabutylammonium fluoride trihydrate. After 40 minutes at 25°C, the reaction medium is concentrated and then chromatographed on a column of silica gel, eluting with dichloromethane, to give 3.28 g of the expected product.

m.p.=138.3°C

¹H NMR δ in ppm (DMSO d₆): 1.35-1.55 (unresolved complex, 2H); 3.18 (m, 1H); 3.41 (m, 1H); 3.77 (s, 3H); 3.85 (m, 2H); 3.88 (s, 3H); 4.13 (d, 1H); 4.29 (d, 1H); 4.48 (t, 1H); 6.71-7.50 (unresolved complex, 9H)

Example 38: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-(2-hydroxy-1-methylethyl)-3,4-dimethoxybenzenesulfonamide (compound 264)

To 1.1 g of methyl N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]alaninate in 15 ml of tetrahydrofuran are added, at room temperature, 158 mg of lithium aluminium hydride. After refluxing for 5 hours, the mixture is cooled to room temperature and

hydrolysed with 15% sodium hydroxide solution. The medium is taken up in ethyl acetate and washed with water, the phases are separated by settling and the organic phase is dried over anhydrous sodium sulfate.

- 5 The organic phase is concentrated and the residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v) toluene/ethyl acetate mixture to give 0.215 g of the expected product.

m.p.=169.2°C

- 10 ¹H NMR δ in ppm (DMSO d6): 1.18 (d, 3H); 3.47 (m, 2H); 3.77 (s, 3H); 3.88 (s, 3H); 4.07-4.52 (unresolved complex, 3H); 4.98 (t, 1H); 6.61-7.49 (unresolved complex, 9H)

- 15 Example 39: 2-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-2-ethoxyacetamide (compound 276)

- 20 • Example 39.1: ethyl {[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino(fluoro)acetate
To 2 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide
25 in 15 ml of tetrahydrofuran are successively added, at room temperature, 0.742 g of potassium *tert*-butoxide and 0.78 ml of ethyl bromo(fluoro) acetate, and the

mixture is left at room temperature for 18 hours. To complete the reaction, 0.742 g of potassium *tert*-butoxide and 0.6 ml of ethyl bromo(fluoro) acetate are added. After 24 hours at room temperature, the reaction
5 medium is concentrated and the residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a toluene/ethyl
10 acetate mixture (100% toluene to 80% toluene/20% ethyl acetate) to give 0.825 g of product (HPLC purity 77%).
¹H NMR δ in ppm (DMSO d₆): 0.92 (t, 3H); 3.78 (s, 3H); 3.87 (s, 3H); 4.12-4.38 (unresolved complex, 5H); 6.73-7.33 (unresolved complex, 9H).

15

- Example 39.2: 5-chloro-3-(2,6-difluorophenyl)-1-[(3,4-dimethoxyphenyl)sulfonyl]indoline-2-carboxylic acid

To 0.825 g of ethyl {[4-chloro-2-(2,6-
20 difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino(fluoro)acetate in 10 ml of ethanol and 10 ml of 1,4-dioxane is added, at room temperature, 0.062 g of lithium hydroxide hydrate, and the mixture is left at room temperature for 6 hours.
25 The reaction medium is concentrated and the residue is taken up in ethyl acetate and washed with 1M hydrochloric acid solution. The organic phase is dried

over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a dichloromethane/methanol mixture (100% dichloromethane to 90% dichloromethane/10% methanol) to give 0.345 g of product (50% HPLC purity).

¹H NMR δ in ppm (DMSO d₆): 3.74 (s, 3H); 3.84 (s, 3H); 4.17 (d, 1H); 4.40 (d, 1H); 5.57 (s, 1H); 6.49 (s, 1H); 6.78-7.47 (unresolved complex, 8H).

- 10 • Example 39.3: 2-{[4-chloro-2-(2,6-difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)sulfonyl]amino}-2-ethoxyacetamide

To 0.34 g of 5-chloro-3-(2,6-difluorophenyl)-1-[(3,4-dimethoxyphenyl)sulfonyl]indoline-2-carboxylic acid in 10 ml of tetrahydrofuran are successively added, at 0°C, 90 μ l of N-ethylmorpholine and 68 μ l of ethyl chloroformate, the mixture is left at this temperature for 30 minutes, and 0.5 ml of 6M aqueous ammonia solution is introduced. The reaction medium is concentrated and the residue is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a dichloromethane/methanol mixture (100% dichloromethane to 98% dichloromethane/2% methanol) to give 0.256 g of product (99.6% HPLC purity).

m.p.=153.6°C

¹H NMR δ in ppm (DMSO d6): 1.25 (t, 3H); 3.57 (m, 2H);
3.84 (s, 3H); 3.87 (s, 3H); 4.31 (q, 2H); 6.53 (s, 1H);
6.52-7.55 (unresolved complex, 11H)

5

Example 40: phenyl (2-([4-chloro-2-(2,6-
difluorobenzyl)phenyl][(3,4-dimethoxyphenyl)
sulfonyl]amino)ethylcarbamate (compound 269)

To 1.4 g of ethyl N-[2,6-difluorobenzyl)-4-
10 chlorophenyl]-3,4-dimethoxy-N-[2-
(methylamino)ethyl]benzenesulfonamide in 6 ml of
tetrahydrofuran are successively added, at 0°C, 0.29 ml
of pyridine and 0.37 ml of phenyl chloroformate, and
the mixture is left at room temperature for 18 hours.
15 The reaction medium is taken up in ethyl acetate and
washed successively with 1M hydrochloric acid solution,
sodium hydrogen carbonate solution, and water. The
organic phase is dried over anhydrous sodium sulfate
and concentrated. The residue is chromatographed on a
20 column of silica gel to give 1.07 g of the expected
product.

m.p.=137.5°C

¹H NMR δ in ppm (DMSO d6): 3.05-3.24 (unresolved
complex, 4H); 3.76 (s, 3H); 3.87 (s, 3H); 4.09 (d, 1H);
25 4.30 (d, 1H); 6.78-7.46 (unresolved complex, 14H); 7.77
(t, 1H).

Example 41: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
3,4-dimethoxy-N-(2-
{[(methylamino)carbonyl]amino}ethyl)benzenesulfonamide
(compound 253)

5 To 0.42 g of phenyl(2-{[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-(3,4-
dimethoxyphenyl)sulfonyl]amino}ethyl)carbamate in 1.2 ml
of dimethyl sulfoxide is added, at room temperature,
0.053 ml of an aqueous solution of methylamine, and the
10 mixture is left at room temperature for 18 hours. The
reaction medium is taken up in ethyl acetate and washed
with water. The organic phase is dried over anhydrous
sodium sulfate and concentrated. The residue is
chromatographed on a column of silica gel to give
15 0.326 g of the expected product.

m.p.=105.7°C

¹H NMR δ in ppm (DMSO d6): 2.48 (s, 3H); 3.18 (q, 2H);
3.24 (m, 1H); 3.68 (m, 1H); 3.76 (s, 3H); 3.88 (s, 3H);
4.20 (q, 2H); 5.75-5.94 (unresolved complex, 2H); 6.73-
20 7.51 (unresolved complex, 9H).

In the same manner, compound 239 is prepared,
the physical properties of which are as follows:

MH+=568; the retention time is 9.44 minutes

m.p.=99.5°C

Example 42: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
N-[2-(1*H*-imidazol-1-yl)ethyl]-3,4-
dimethoxybenzenesulfonamide (compound 271)

To 2 ml of dimethylformamide are added, at
5 room temperature, 51 mg of sodium hydride at 50% in
oil, followed by 72 mg of imidazole. After 30 minutes
at this temperature, 0.4 g of ethyl N-(2-bromoethyl)-N-
[2-(2,6-difluorobenzyl)-4-chlorophenyl]-3,4-
dimethoxybenzenesulfonamide dissolved in 5 ml of
10 dimethylformamide is introduced. The reaction medium is
left for 18 hours at room temperature and then taken up
in ethyl acetate and washed with water. The organic
phase is dried over anhydrous sodium sulfate and
concentrated. The residue is chromatographed on a
15 column of silica gel, eluting with a 97/3 (v/v)
toluene/ethyl acetate mixture to give 0.082 g of the
expected product.

m.p.=159.5°C

¹H NMR δ in ppm (DMSO d₆): 3.66 (m, 1H); 3.76 (s, 3H);
20 3.89 (s, 3H); 3.99-4.15 (unresolved complex, 5H); 6.72-
7.56 (unresolved complex, 12H).

In the same manner, compound 301 is prepared,
the physical properties of which are as follows:

MH⁺=544; the retention time is 6.62 minutes

25 m.p.=153.6°C

Example 43: N³-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
N³-[(3,4-dimethoxyphenyl)sulfonyl]-β-alaninamide
(compound 273)

- 5 • Example 43.1: N-[4-chloro-2-(2,6-
 difluorobenzyl)phenyl]-N-[(3,4-
 dimethoxyphenyl)sulfonyl]-β-alanine

To 2.63 g of N-[4-chloro-2-(2,6-
difluorobenzyl)phenyl]-N-(3-hydroxypropyl)-3,4-
10 dimethoxybenzenesulfonamide (Example 37) dissolved in
35 ml of acetonitrile are added, at room temperature,
0.069 g of ruthenium trichloride, 1.65 g of sodium
periodate and 2.7 ml of water. The mixture is left for
10 hours at room temperature. The reaction medium is
15 filtered through talc and then concentrated. The
residue is taken up in dichloromethane and washed with
1M hydrochloric acid solution. The organic phase is
dried over anhydrous sodium sulfate and concentrated to
give 3.13 g of the expected product.

20 ¹H NMR δ in ppm (DMSO d6): 2.3 (m, 2H); 3.45 (m, 1H);
3.71 (s, 3H); 3.86 (m, 1H); 3.90 (s, 3H); 4.1-4.35
(unresolved complex, 2H); 6.74-7.47 (unresolved
complex, 9H); 12.3 (s, 1H).

- 25 • Example 43.2: N³-[4-chloro-2-(2,6-
 difluorobenzyl)phenyl]-N³-[(3,4-
 dimethoxyphenyl)sulfonyl]-β-alaninamide

To 0.8 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]- β -alanine dissolved in 16 ml of tetrahydrofuran are added, at 0°C, 0.21 ml of
5 N-ethylmorpholine and 0.16 ml of ethyl chloroformate. The mixture is left at room temperature for 1 hour, and 1.36 ml of ammonia (20%) in water are then introduced. After 48 hours at room temperature, the reaction medium is taken up in ethyl acetate and washed with water. The
10 organic phase is dried over anhydrous sodium sulfate and concentrated, and the residue is chromatographed on a column of silica gel, eluting with a 98/2 (v/v) dichloromethane/methanol mixture to give 0.295 g of the expected product.

15 m.p.=189.4°C

^1H NMR δ in ppm (DMSO d_6): 2.08-2.25 (unresolved complex, 2H); 3.42 (m, 1H); 3.76 (s, 3H); 3.88 (s, 3H) 3.92 (m, 1H); 4.13 (d, 1H); 4.27 (d, 1H); 6.75-7.51 (unresolved complex, 11H)

20 In the same manner, compound 298 is prepared, the physical properties of which are as follows:
MH+=539; the retention time is 9.15 minutes
m.p.=189.3°C

25 Example 44: N²-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]- β -alaninamide (compound 261)

- Example 44.1: methyl N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]alaninate

5 By reaction of 2 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-3,4-dimethoxybenzenesulfonamide with methyl lactate according to process 35, 1.393 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d6): 1.12 (t, 3H); 1.25 (d, 3H);
10 3.75 (s, 3H); 3.86 (s, 3H); 3.98 (d, 1H); 4.19 (q, 2H);
4.65 (d, 1H); 4.87 (q, 1H); 6.55 (s, 1H) 7.04-7.48
(unresolved complex, 8H).

- Example 44.2: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]alanine

15 To 1.373 g of methyl N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]alaninate dissolved in 20 ml
20 of ethanol is added 0.52 g of lithium hydroxide monohydrate, and the mixture is left at room temperature for 18 hours. The medium is concentrated and the residue is taken up in ethyl acetate and washed with 5% potassium hydrogen sulfate solution. The
25 organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 90/10 (v/v)

dichloromethane/methanol mixture to give 0.494 g of the expected product.

¹H NMR δ in ppm (DMSO d₆): 1.17 (d, 3H); 3.76 (s, 3H);
3.87 (s, 3H); 3.92 (d, 1H); 4.19 (d, 1H); 4.75 (q, 1H);
5 6.53-7.52 (unresolved complex, 9H); 12.9 (s, 1H).

- Example 44.3: N²-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]- β -alaninamide

10 To 0.47 g of N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]alanine dissolved in 20 ml of tetrahydrofuran are added, at 0°C, 0.13 ml of N-ethylmorpholine and 0.094 ml of ethyl chloroformate.
15 The mixture is left at room temperature for 1 hour, and 0.75 ml of ammonia (20%) in water is then introduced. After 24 hours at room temperature, the reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate
20 and concentrated, and the residue is chromatographed on a column of silica gel, eluting with a 95/5 (v/v) dichloromethane/methanol mixture to give 0.295 g of the expected product.

m.p.=108°C

25 ¹H NMR δ in ppm (DMSO d₆): 1.04 (d, 3H); 3.77 (s, 3H); 3.84 (s, 3H); 3.93 (d, 1H); 4.19 (d, 1H); 4.85 (q, 1H); 4.89 (d, 1H); 6.53-7.52 (unresolved complex, 9H).

The enantiomers of compound 261 are separated by chiral chromatography.

Laevorotatory enantiomer, compound 305

$[\alpha]_D$ (C=0.5 g/100 ml in methanol)=-28.2

5 Dextrorotatory enantiomer, compound 304

$[\alpha]_D$ (C=0.5 g/100 ml in methanol)=+25.4

Table XXV illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this example.

10

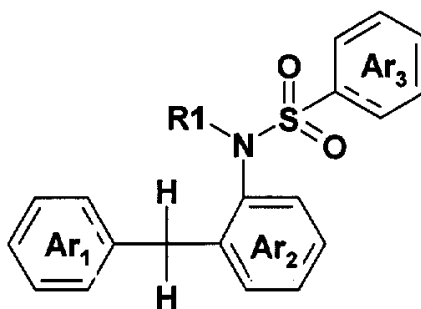


Table XXV

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
304	2,6-diF	4-Cl	CH(CH ₃)CONH ₂	3,4-diOMe	105.3	525/9.29
305	2,6-diF	4-Cl	CH(CH ₃)CONH ₂	3,4-diOMe	94.1	525/9.29

Example 45: N²-[2-(2-chlorobenzyl)-4-

(dimethylamino)phenyl]-N²-[(3,4-

5 dimethoxyphenyl)sulfonyl]glycinamide (compound 265)

- Example 45.1: N²-[4-amino-2-(2-chlorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

10 To 2 g of N²-[2-(2-chlorobenzyl)-4-nitrophenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide, obtained according to Example 15, dissolved in 150 ml of ethanol are successively added, at room temperature, 0.91 g of

15 tin and 3.2 ml of 12M hydrochloric acid. After 18 hours, the medium is concentrated, taken up in ethyl acetate and washed with sodium hydroxide solution (pH 14). The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is

20 chromatographed on a column of silica gel, eluting with a 95/5 (v/v) dichloromethane/methanol mixture to give 0.287 g of the expected product.

¹H NMR δ in ppm (DMSO d6): 3.79 (s, 3H); 3.88 (s, 3H); 3.94-4.40 (unresolved complex, 4H); 5.15 (s, 2H); 5.94 (d, 1H); 6.22 (d, 1H); 6.50 (d, 1H); 7.04-7.49 (unresolved complex, 9H).

5

- Example 45.2: N²-[2-(2-chlorobenzyl)-4-(dimethylamino)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

To 0.6 g of N²-[4-amino-2-(2-chlorobenzyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide dissolved in N-methylpyrrolidine are added 0.42 g of caesium carbonate and 0.9 ml of iodomethane, and the mixture is left at room temperature for 18 hours. The medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with a 100% to 90%/10% dichloromethane/acetone gradient to give the expected product.

20

m.p.=130.4°C

¹H NMR δ in ppm (DMSO d6): 2.73 (s, 6H); 3.78 (s, 3H); 3.84 (s, 3H); 3.98-4.08 (unresolved complex, 3H); 4.40 (d, 1H); 6.04 (d, 1H); 6.43 (d, 1H); 6.70 (d, 1H); 7.02-7.51 (unresolved complex, 9H).

25

Example 46: ethyl N-[4-chloro-2-(2-chlorophenyl)]-3,4-dimethoxy-N-vinylbenzenesulfonamide (compound 289)

To 0.18 g of 1-methyl-2-imidazolidone dissolved in N-methylpyrrolidone is added 0.086 g of sodium hydride at 50% in oil, the mixture is left at room temperature for 15 minutes, and 1 g of ethyl N-(2-bromoethyl)-N-[2-(2,6-difluorobenzyl)-4-chlorophenyl]-3,4-dimethoxybenzenesulfonamide is introduced. After 18 hours, the reaction medium is taken up in ethyl acetate and washed with water. The organic phase is dried over anhydrous sodium sulfate and concentrated, and the residue is chromatographed on a column of silica gel, eluting with dichloromethane, to give 0.67 g of the expected product.

m.p.=153°C

¹H NMR δ in ppm (DMSO d6): 3.54 (d, 1H); 3.79 (s, 3H); 3.89 (s, 3H); 3.94-4.20 (unresolved complex, 2H); 4.22 (d, 1H); 6.50 (d, 1H); 7.06-7.45 (unresolved complex, 9H).

20

Example 47: N²-[2-(2,6-difluorobenzyl)-5-methoxyphenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 296)

25 • Example 47.1: (2-amino-4-methoxyphenyl)(2,6-difluorophenyl)methane

To 6.22 g of (2-amino-4-methoxyphenyl)(2,6-

difluorophenyl)methanol, obtained according to Example 11.1, dissolved in 95 ml of dichloromethane are successively added, at room temperature, 11.7 ml of triethylsilane and 10.7 ml of trifluoroacetic acid.

- 5 After refluxing for 4 hours, the medium is hydrolysed with 6M sodium hydroxide solution. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is chromatographed on a column of silica gel, eluting with dichloromethane to give 1.505 g of
10 the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.69 (s, 3H); 4.93 (s, 2H); 6.04 (d, 1H); 6.21 (s, 1H); 6.48 (d, 1H); 7.01-7.35 (unresolved complex, 3H).

- 15 • Example 47.2: N-[2-(2,6-difluorobenzyl)-5-methoxyphenyl]-3,4-dimethoxybenzenesulfonamide

Starting with 1.5 g of (2-amino-4-methoxyphenyl)(2,6-difluorophenyl)methane according to Example 12.2, 0.32 g of the expected product is
20 obtained.

^1H NMR δ in ppm (DMSO d_6): 3.55 (s, 3H); 3.74 (s, 3H); 3.82 (s, 3H); 3.85 (d, 2H); 6.42 (d, 1H); 6.56-7.42 (unresolved complex, 8H); 9.54 (s, 1H).

- Example 47.3: N²-[2-(2,6-difluorobenzyl)-5-methoxyphenyl]-N²-[(3,4-dimethoxyphenyl)-sulfonyl]glycinamide

Starting with 0.312 g of N-[2-(2,6-difluorobenzyl)-5-methoxyphenyl]-3,4-dimethoxybenzenesulfonamide according to Example 12.3, 0.219 g of the expected product is obtained.

m.p.=188.2°C

¹H NMR δ in ppm (DMSO d6): 3.55 (s, 3H); 3.78 (s, 3H); 3.88 (s, 3H); 4.10-4.24 (unresolved complex, 3H); 4.43 (d, 1H); 6.41 (d, 1H); 6.57 (d, 1H); 6.83 (d, 1H); 7.05-7.48 (unresolved complex, 8H).

Table XXVI illustrates the chemical structures and the physical properties of a number of compounds of the invention obtained according to this example.

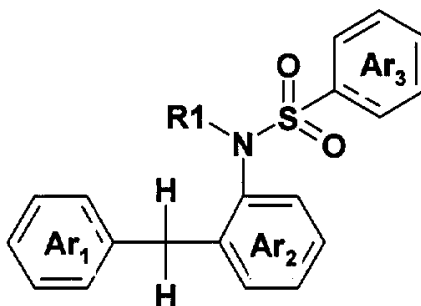


Table XXVI

Com- pound No.	Nature and position of the substituents				m.p. (°C)	MH ⁺ / retention time
	Ar ₁	Ar ₂	R ₁	Ar ₃		
302	2,6- diF	4-Cl,6- OMe	CH ₂ CONH ₂	3,4- diOMe	238.5	541/8.89
303	2,6- diF	4-Cl,6- Me	CH ₂ CONH ₂	3,4- diOMe	217	521/8.61

Example 48: N-[4-chloro-2-(2,6-difluorobenzyl)phenyl]-
3,4-dimethoxy-N-{2-[(methylsulfonyl)amino]ethyl}-

5 benzenesulfonamide (compound 313)

To 0.543 g of compound 256 dissolved in 10 ml
of tetrahydrofuran are added 106 µl of pyridine and
102 µl of methanesulfonyl chloride, and the mixture is
left at room temperature for 18 hours. The reaction
10 medium is concentrated and the residue is
chromatographed on a column of silica gel, eluting with
a dichloromethane/methanol mixture to give 0.425 g of
the expected product.

m.p.=133.2°C

15 ¹H NMR δ in ppm (DMSO d₆): 2.85 (s, 3H); 2.90 (m, 1H);
3.12 (m, 1H); 3.35 (m, 1H); 3.78 (s, 3H); 3.83 (m, 1H);
3.86 (s, 3H); 4.09 (d, 1H); 4.31 (d, 1H); 6.78-7.51
(unresolved complex, 10H).

20 Example 49: N²-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-
N²-[(3,4-dimethoxyphenyl)sulfonyl]-N-ethylglycinamide
(compound 309)

- Example 49.1: N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]glycine

5 To 1.8 g of ethyl N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-glycinate dissolved in 50 ml of ethanol are added 10 ml of 2M sodium hydroxide solution. After 18 hours at room temperature, the medium is extracted with diethyl ether
10 and the aqueous phase is acidified and extracted with dichloromethane. The organic phase is dried over anhydrous sodium sulfate and then concentrated to give 1.8 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.18 (s, 3H); 3.72 (s, 3H);
15 3.82 (d, 1H); 3.90 (s, 3H); 4.29 (d, 1H); 4.53 (d, 1H); 5.01 (d, 1H); 6.26 (d, 1H); 6.78 (d, 1H); 7.01-7.47 (unresolved complex, 7H); 12.75 (s, 1H).

- Example 49.2: N²-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]-N-ethylglycinamide

20 To 1.8 g of N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]glycine dissolved in 30 ml of tetrahydrofuran at 0°C are
25 introduced 0.5 ml of N-ethylmorpholine and 0.38 ml of ethyl chloroformate. After 15 minutes at 10°C, 0.8 g of ethylamine dissolved in tetrahydrofuran is added and

the mixture is left at room temperature for 30 minutes.
The medium is taken up in ethyl acetate and washed with
water, and the organic phase is dried over anhydrous
sodium sulfate and concentrated to give 1.4 g of the
5 expected product.

m.p.=180°C

¹H NMR δ in ppm (DMSO d6): 0.98 (t, 3H); 3.07 (m, 2H);
3.26 (s, 3H); 3.76 (s, 3H); 3.79 (m, 1H); 3.87 (s, 3H);
4.26 (d, 1H); 4.43 (d, 1H); 4.94 (d, 1H); 6.20 (d, 1H);
10 6.81 (d, 1H); 7.09-7.45 (unresolved complex, 7H); 7.88
(t, 1H).

Example 50: N²-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-
N²-[(4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide
15 (compound 267)

- Example 50.1: (2-nitro-5-chlorophenyl)(2,5-
difluorophenyl)methanol

To 15 g of 2,5-difluorobenzene dissolved in
20 150 ml of tetrahydrofuran are added, at -70°C, 50 ml of
1.6M butyllithium solution. After 2 hours at -70°C,
9.616 g of 2-nitro-5-chlorobenzaldehyde are introduced
and the mixture is left at this temperature for 3 hours
and then at room temperature for 18 hours. The medium
25 is hydrolysed with ammonium chloride solution and
extracted with ethyl acetate. The organic phase is
dried over anhydrous sodium sulfate and concentrated.

The residue is filtered through silica, eluting with dichloromethane, to give 8.89 g of the expected product.

- Example 50.2: (2-amino-5-chlorophenyl)(2,5-difluorophenyl)methanol

Starting with 8.55 g of (2-nitro-5-chlorophenyl)(2,5-difluorophenyl)methanol according to process 8.2, 2.7 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 5.18 (s, 2H); 5.89 (d, 1H); 6.15 (d, 1H); 6.68-7.36 (unresolved complex, 6H)

- Example 50.3: (2-amino-5-chlorophenyl)(2,5-difluorophenyl)methane

Starting with 2.7 g of (2-amino-5-chlorophenyl)(2,5-difluorophenyl)methanol according to process 18.1, 1.947 g of the expected product are obtained.

¹H NMR δ in ppm (DMSO d₆): 3.80 (s, 2H); 5.18 (s, 2H); 6.60 (unresolved complex, 6H)

- Example 50.4: N-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-2,5-dimethyl-4-chlorobenzenesulfonamide

Starting with 0.484 g of (2-amino-5-chlorophenyl)(2,5-difluorophenyl)methane according to

the process described in Example 12.2, 0.837 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 2.28 (s, 3H); 2.45 (s, 3H);
3.98 (s, 2H); 6.60 (m, 1H); 6.94-7.61 (unresolved
5 complex, 8H), 9.93 (s, 1H)

- Example 50.5: N²-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-N²-[(4-chloro-2,5-dimethylphenyl)sulfonyl]glycinamide

10 Starting with 0.83 g of N-[4-chloro-2-(2,5-difluorobenzyl)phenyl]-2,5-dimethyl-4-chlorobenzenesulfonamide according to Example 15, 0.424 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆):
15 2.16 (s, 3H); 2.36 (s, 3H); 3.92 (d, 1H); 4.23 (d, 1H);
4.40 (d, 1H); 6.87 (s, 1H) 6.96-7.75 (unresolved
complex, 8H)
m.p.=169.7°C

20 Example 51: N²-[4-chloro-2-(pyrid-2-ylmethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

- Example 51.1: 2-(5-chloro-2-nitrobenzyl)pyridine

To 22.44 g of potassium tert-butoxide in
25 500 ml of dimethyl sulfoxide are slowly added 8.66 g of
4-chloronitrobenzene and 8.2 g of

2-chloromethylpyridine dissolved in 100 ml of dimethyl sulfoxide. After 18 hours at room temperature, the mixture is hydrolysed with saturated ammonium chloride solution and extracted three times with

5 dichloromethane. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is filtered through silica H, eluting with dichloromethane, to give 10.695 g of the expected product.

10 ^1H NMR δ in ppm (DMSO d_6): 4.49 (s, 2H); 7.20-7.31 (unresolved complex, 2H); 7.60-7.78 (unresolved complex, 3H); 8.03 (d, 1H); 8.41 (d, 1H)
m.p.=69°C

15 • Example 51.2: 4-chloro-2-(pyrid-2-ylmethyl)aniline

Starting with 5g of 2-(5-chloro-2-nitrobenzyl)pyridine according to Example 8.2, 3.86 g of the expected product are obtained.

^1H NMR δ in ppm (DMSO d_6): 3.93 (s, 2H); 5.33 (s, 2H);
20 6.66 (d, 1H); 6.93-7.06 (unresolved complex, 2H); 7.21-7.38 (unresolved complex, 2H); 7.76 (m, 1H); 8.47 (d, 1H)

• Example 51.3: N-[4-chloro-2-(pyrid-2-ylmethyl)phenyl]-3,4-dimethoxybenzenesulfonamide
25

Starting with 1.86 g of 4-chloro-2-(pyrid-2-

ylmethyl)aniline according to Example 12.2, 2.12 g of the expected product are obtained.

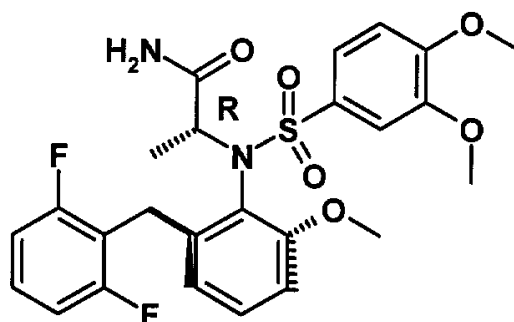
¹H NMR δ in ppm (DMSO d₆): 3.71 (s, 3H); 3.83 (s, 3H); 3.94 (s, 2H); 7.07-7.32 (unresolved complex, 8H); 7.74
5 (m, 1H); 8.54 (d, 1H)

- Example 51.4: N²-[4-chloro-2-(pyrid-2-ylmethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

10 Starting with 0.5 g of N-[4-chloro-2-(pyrid-2-ylmethyl)phenyl]-3,4-dimethoxybenzenesulfonamide according to Example 12.3, 0.257 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 3.79 (s, 3H); 3.88 (s, 3H);
15 4.03-4.48 (unresolved complex, 4H)); 6.93-7.37 (unresolved complex, 10H); 7.74 (t, 1H); 8.54 (d, 1H)
m.p.=88°C

Example 52: N²-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-
20 N²-[(3,4-dimethoxyphenyl)sulfonyl]-(R)-alaninamide
(compound 321)



compound 321

$$[\alpha_D]^{20} = +14.7 \quad c=0.19(\text{CH}_2\text{Cl}_2)$$

- Example 52.1: N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-(R)-alanine

5 To 0.164 g of methyl N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-(R)-alaninate dissolved in 8 ml of a 1,4-dioxane/water mixture (4/1) is added, at room temperature, 0.015 g of lithium hydroxide

10 monohydrate. The mixture is left at room temperature for 48 hours. The reaction medium is washed with 1M hydrochloric acid solution and extracted with ethyl acetate. The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is

15 chromatographed on a column of silica gel, eluting with a dichloromethane/ethanol mixture to give 0.08 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 1.64 (d, 3H); 3.22 (s, 3H); 3.70 (s, 3H); 3.85 (s, 3H); 4.11 (d, 1H); 4.22 (q, 1H); 4.77 (d, 1H); 6.31 (d, 1H); 6.78 (d, 1H); 7.02-7.44 (unresolved complex, 7H), 12.5 (s, 1H).

5

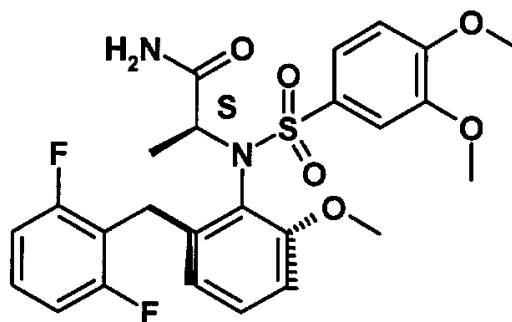
- Example 52.2: N^2 -[2-(2,6-difluorobenzyl)-6-methoxyphenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]-(R)-alaninamide

Starting with 0.098 g of N-[2-(2,6-difluorobenzyl)-6-methoxyphenyl]-N-[(3,4-dimethoxyphenyl)sulfonyl]-(R)-alanine according to Example 43.2, 0.08 g of the expected product is obtained.

^1H NMR δ in ppm (DMSO d_6): 1.34 (d, 3H); 3.32 (s, 3H); 3.74 (s, 3H); 3.85 (s, 3H); 4.22 (d, 2H); 4.41 (q, 1H); 6.27 (d, 1H); 6.88 (d, 1H); 7.07-7.44 (unresolved complex, 9H).

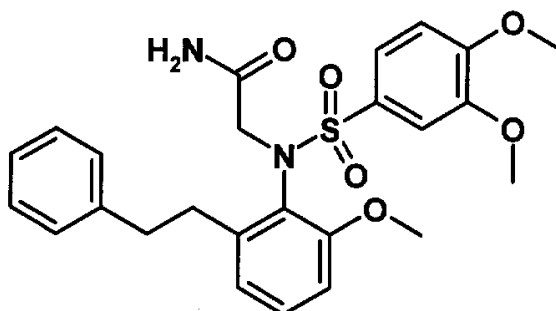
According to this process, N^2 -[2-(2,6-difluorobenzyl)-6-methoxyphenyl]- N^2 -[(3,4-dimethoxyphenyl)sulfonyl]-(S)-alaninamide (compound 322) is synthesized.

^1H NMR δ in ppm (DMSO d_6): 1.34 (d, 3H); 3.32 (s, 3H); 3.74 (s, 3H); 3.85 (s, 3H); 4.22 (d, 2H); 4.41 (q, 1H); 6.27 (d, 1H); 6.88 (d, 1H); 7.07-7.44 (unresolved complex, 9H).

**compound 322**

$$[\alpha_D]^{20} = -14.6 \text{ } c=0.15(\text{CH}_2\text{Cl}_2)$$

Example 53: N²-[2-methoxy-6-(2-phenylethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide (compound 323)

**compound 323**

5

Example 53.1: 1-methoxy-2-nitro-3-[(E)-2-phenylvinyl]benzene

To 10 ml of ethanol is added, at room temperature, 0.31 g of sodium. The mixture is left at room temperature for 15 minutes, and 4.05 g of benzyltriphenylphosphonium chloride and 2 g of 2-nitro-3-methoxybenzaldehyde are successively introduced.

After 18 hours at room temperature, the reaction medium is taken up in dichloromethane and washed with water.

The organic phase is dried over anhydrous sodium sulfate and concentrated. The residue is

5 chromatographed on a column of silica gel to give 2.254 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 3.92 (s, 3H); 6.55-7.56 (unresolved complex, 10H).

10 • Example 53.2: 2-methoxy-6-(2-phenylethyl)aniline

2.25 g of 1-methoxy-2-nitro-3-[(E)-2-phenylvinyl]benzene are added to 0.18 g of palladium-on-charcoal (10%) suspended in 90 ml of methanol, and placed under 4 bar of hydrogen. After 18 hours, the
15 reaction medium is filtered through talc and the filtrate is concentrated to give 2.115 g of the expected product.

^1H NMR δ in ppm (DMSO d_6): 2.74-2.88 (unresolved complex, 4H); 3.78 (s, 3H); 4.55 (s, 2H); 6.55-7.31
20 (unresolved complex, 8H).

• Example 53.3: N-[2-methoxy-6-(2-phenylethyl)-phenyl] (3,4-dimethoxyphenyl)sulfonamide

Starting with 2.11 g of 2-methoxy-6-(2-phenylethyl)aniline according to Example 12.2, 0.5 g of
25 the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 2.83 (m, 2H); 3.01 (m, 2H); 3.22 (s, 3H); 3.73 (s, 3H); 3.84 (s, 3H); 6.71-7.33 (unresolved complex, 11H); 8.99 (s, 1H).

- 5 • Example 53.4: N²-[2-methoxy-6-(2-phenylethyl)phenyl]-N²-[(3,4-dimethoxyphenyl)sulfonyl]glycinamide

Starting with 0.5 g of N-[2-methoxy-6-(2-phenylethyl)phenyl](3,4-dimethoxyphenyl)sulfonamide
10 according to Example 12.3, 0.187 g of the expected product is obtained.

¹H NMR δ in ppm (DMSO d₆): 2.83 (m, 3H); 3.26 (s, 3H); 3.40 (m, 1H); 3.73 (s, 3H); 3.84 (s, 3H); 6.76 (d, 1H); 7.03-7.36 (unresolved complex, 12H).

15 m.p.=243.9°C

The compounds of the invention underwent pharmacological trials that demonstrated their advantage as therapeutically active substances.

They were in particular tested as regards
20 their effects. More particularly, the affinity of the compounds of the invention for the orexin 2 receptors was determined in a test of *in vitro* binding according to the technique described below. This method consists in studying the displacement of radio-iodinated orexin
25 A bound to human orexin 2 receptors expressed in CHO cells. The test is performed on membranes in a Hepes

50 mM, MgCl₂ 1 mM, CaCl₂ 25 mM, NaN₃ 0.025%, bovine serum albumin (BSA) 1% incubation buffer and 100 pM of ligand, for 30 minutes at 25°C. The reaction is quenched by filtration and washing on a Whatman GF/C
5 filter. The non-specific binding is measured in the presence of 10⁻⁶M of human orexin B. The IC₅₀ values (concentration that inhibits 50% of the binding of the radio-iodinated orexin A to its receptors) are low, less than 300 nM, in particular less than 100 nM and
10 more particularly less than 30 nM.

The affinity of the compounds according to the invention for the orexin 1 receptors was also studied in a test of *in vitro* binding according to the same technique using radio-iodinated orexin A as ligand
15 in a membrane preparation of CHO cells expressing the human orexin 1 receptors. The compounds according to the invention show little or no affinity for the orexin 1 receptors.

The agonist or antagonist nature of the
20 compounds is determined *in vitro* in a test of measurement of intracellular calcium (FLIPR) on a cell preparation expressing the orexin 2 receptors, according to the general technique described in Sullivan et al., Methods Mol. Biol., 1999, vol. 114,
25 125-133, using 1 µM of Fluo-4 AM as fluorescent calcium indicator. For the antagonist test, the compounds are

preincubated for 30 minutes before addition of 0.25 nM or orexin B. The IC₅₀ values for the orexin 2 receptors measured in these studies are low and more particularly less than 100 nM.

5 The table below illustrates the affinity of a number of compounds according to the invention for the orexin receptors in a test of *in vitro* binding according to the technique described above, and also their antagonist nature determined *in vitro* in a test
10 of measurement of intracellular calcium (FLIPR) according to the general technique mentioned above.

Compound No.	IC ₅₀ OX 2 (nM)	IC ₅₀ OX 1 (nM)	Measurement of [Ca ²⁺] _i IC ₅₀ OX 2 (nM) - FLIPR
1	13	446	5
28	62	1500	19
30	82	966	26
44	85	> 10 µM	54
107	20	899	11
124	50	> 10 µM	65
137	19	> 10 µM	10
138	8	4760	11
202	9	1870	7

The biological results show that the compounds according to the invention are quite clearly
15 specific antagonists of the orexin 2 receptors.

Thus, the compounds according to the present invention, as orexin 2 receptor antagonists, may be

used in the prophylaxis and treatment of all diseases involving dysfunction associated with these receptors.

The compounds of the invention may be used for the preparation of a medicament for the prophylaxis
5 or treatment of all diseases involving dysfunction associated with the orexin 2 receptor, and more particularly in the prophylaxis or treatment of pathologies in which an orexin 2 receptor antagonist affords therapeutic benefit. Such pathologies are, for
10 example, obesity, appetite or taste disorders including cachexia, anorexia and bulimia (Smart et al., Eur. J. Pharmacol., 2002, 440, 2-3, 199-212), diabetes (Ouedraogo et al., Diabetes, 2002, 52, 111-117), metabolic syndromes (Sakurai, Curr. Opin. Nutr. Metab.
15 Care, 2003, 6, 353-360), vomiting and nausea (US 6,506,774), depression and anxiety (Salomon et al., Biol. Psychiatry, 2003, 54, 96-104; Jaszberenyi et al., J. Neuroendocrinol., 2000, 12, 1174-1178), addictions (Georgescu et al., J. Neurosci., 2003, 23, 8, 3106-
20 3111; Kane et al., Endocrinology, 2000, 141, 10, 3623-3629), mood and behaviour disorders, schizophrenia (Nishino et al., Psychiatry Res., 2002, 110, 1-7), sleep disorders (Sakurai, Neuroreport, 2002, 13, 8, 987-995), restless legs syndrome (Allen et al.,
25 Neurology, 2002, 59, 4, 639-641), memory learning disorders (van den Pol et al., 2002, J. Physiol.,

541(1), 169-185; Jaeger et al., *Peptides*, 2003, 23, 1683-1688; Telegdy et Adamik, *Regul. Pept.*, 2002, 104, 105-110), sexual and psychosexual dysfunctions (Gulia et al., *Neuroscience*, 2003, 116, 921-923), pain, visceral or neuropathic pain, hyperalgesia, allodynia (US 6,506,774; Suyama et al., *In vivo*, 2004, 18, 2, 119-123), digestive disorders (Takakashi et al., *Biochem. Biophys. Res. Comm.*, 1999, 254, 623-627; Matsuo et al., *Eur. J. Pharmacol.*, 2002, 105-109), irritable bowel syndrome (US 6,506,774), neuronal degenerescence (van den Pol, *Neuron*, 2000, 27, 415-418), ischaemic or haemorrhagic attacks (Irving et al., *Neurosci. Lett.*, 2002, 324, 53-56), Cushing's disease, Guillain-Barré syndrome (Kanbayashi et al., *Psychiatry Clin. Neurosci.*, 2002, 56, 3, 273-274), myotonic dystrophy (Martinez-Rodriguez et al., *Sleep*, 2003, 26, 3, 287-290), urinary incontinence (Blackstone et al., AGS Annual Meeting, poster P491,2002), hyperthyroidism (Malendowicz et al., *Biomed. Res.*, 2001, 22, 5, 229-233), pituitary function disorders (Voisin et al., *Cell. Mol. Life Sci.*, 2003, 60, 72-78) and hypertension or hypotension (Samson et al., *Brain Res.*, 1999, 831, 1-2, 248-253).

The use of the compounds according to the invention for the preparation of a medicament for

preventing or treating the pathologies mentioned above forms an integral part of the invention.

A subject of the invention is also medicaments comprising a compound of formula (I). These
5 medicaments find their therapeutic use especially in the prophylaxis or treatment of the pathologies mentioned above.

According to another of its aspects, the present invention relates to pharmaceutical
10 compositions containing, as active principle, at least one compound according to the invention. These pharmaceutical compositions contain an effective dose of a compound according to the invention and optionally one or more pharmaceutically acceptable excipients.

15 The said excipients are chosen, according to the pharmaceutical form and the desired mode of administration, from the usual excipients known to those skilled in the art.

In the pharmaceutical compositions of the
20 present invention for oral, sublingual, subcutaneous, intramuscular, intravenous, topical, local, intratracheal, intranasal, transdermal or rectal administration, the active principle of formula (I) above, or the possible salt, solvate or hydrate
25 thereof, may be administered in a unit administration form, as a mixture with standard pharmaceutical

excipients, to man and animals for the prophylaxis or treatment of the above disorders or diseases.

The appropriate unit forms of administration include oral forms such as tablets, soft or hard gel capsules, powders, granules, chewing gums and oral solutions or suspensions, sublingual, buccal, intratracheal, intraocular or intranasal administration forms, forms for administration by inhalation, subcutaneous, intramuscular or intravenous administration forms, and rectal or vaginal administration forms. For topical application, the compounds according to the invention may be used in creams, ointments or lotions.

For example, when a solid composition in the form of tablets is prepared, the main active ingredient is mixed with a pharmaceutical excipient, such as gelatin, starch, lactose, magnesium stearate, talc, gum arabic or the like. The tablets may be coated with sucrose, a cellulose derivative or other materials. The tablets may be made via various techniques, direct compression, dry granulation, wet granulation or hot-melting.

In order to obtain the desired prophylactic or therapeutic effect, the dose of active principle may range between 0.1 mg and 200 mg per kg of body weight and per day. Although these dosages are examples of an

average situation, there may be particular cases in which higher or lower dosages are appropriate, and such dosages also form part of the invention. According to the usual practice, the dosage that is appropriate to
5 each patient is determined by the doctor according to the mode of administration, the weight and the response of the said patient.

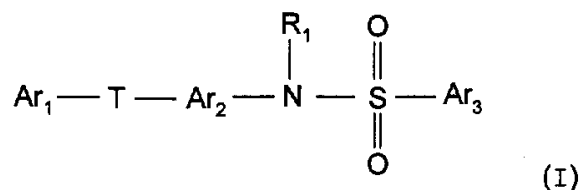
Each unit dose may contain from 0.1 to 1000 mg and preferably from 0.1 to 500 mg of active
10 principle in combination with one or more pharmaceutical excipients. This unit dose may be administered 1 to 5 times a day so as to administer a daily dosage of from 0.5 to 5000 mg and preferably from 0.5 to 2500 mg.

15 According to another of its aspects, the present invention also relates to a method for preventing or treating the pathologies indicated above, which comprises the administration of a compound according to the invention, a pharmaceutically
20 acceptable salt, a solvate or a hydrate of the said compound.

Claims

1. Compound corresponding to the general formula (I)

5



in which

• **Ar₁** represents

- an aryl group such as a phenyl group optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a cyano group, a group -CO-NR_aR_b, a group -NR_aR_b,
10 with R_a and R_b being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,
 - a heterocyclyl group chosen from pyridyl, pyrimidinyl, thiazolyl and thienyl, the said heterocyclyl groups being optionally substituted with a
15 halogen atom, a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group,
 - a (C₃-C₆) cycloalkyl group;
- **T** represents
- a group -(CH₂)_n- with n = 0, 1 or 2,
- 20

- a group >CH-R_2 with R_2 being a hydroxyl group or a (C₁-C₄) alkyl group,
- a group >N-R_3 with R_3 being a (C₁-C₄) alkyl group,
- a group >C(OH)-R_4 with R_4 being a (C₁-C₄) alkyl

5 group;

• **Ar₂** represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a
10 (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a fluoro(C₁-C₄)alkoxy group, or with a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,
- 15 - a heterocyclyl group such as pyridyl optionally substituted with a (C₁-C₄) alkyl group or a (C₁-C₄) alkoxy group;

• **Ar₃** represents

- an aryl group chosen from phenyl and naphthyl, the
20 said aryl groups being optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a fluoro(C₁-C₄)alkoxy group, a nitro group, a
25 hydroxyl group, or with a group -NR₅R₆ with R₅ and R₆ being,

independently of each other, a hydrogen atom or a
(C₁-C₄) alkyl group,

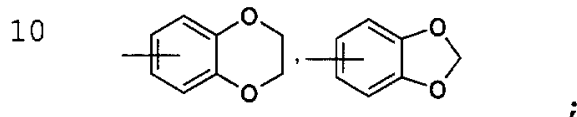
- a heterocyclyl group such as pyridyl optionally
substituted with a (C₁-C₄) alkyl group or a (C₁-C₄)

5 alkoxy group,

or with a group -NR_xR_y with R_x and R_y being,

independently of each other, a hydrogen atom, a (C₁-C₄)
alkyl group or a (C₁-C₄) alkoxy group,

- a group chosen from

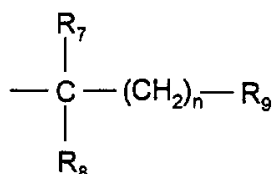


• R₁ represents

- a -C(O)-CF₃ group,

- a group of formula

15



in which

n = 0, 1, 2 or 3

. R₇ represents

20 - a hydrogen atom, a (C₁-C₄) alkyl group, a
fluorine atom or a (C₁-C₄) alkoxy group,

- a group -(CH₂)_m-aryl, with m = 1 or 2 and the
aryl group being a phenyl group optionally
substituted with a halogen atom, a (C₁-C₄) alkyl

group or a (C₁-C₄) alkoxy group,

. R₈ represents

- a hydrogen atom, a fluorine atom or a (C₁-C₄) alkyl group,

5 . R₉ represents

- a hydrogen atom, a (C₁-C₄) alkyl group, a hydroxyl group, a (C₃-C₆) cycloalkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a -C≡CH group, a -C≡N group, a phenoxy group or
10 a (C₁-C₄) alkenyl group,

- a group -NR₁₀R₁₁ with R₁₀ and R₁₁ being, independently of each other, a hydrogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkylcarbonyl group, a (C₁-C₄) alkylsulfonyl group, a benzyl
15 group or a -(CH₂)₂-N(CH₃)₂ group,
or alternatively R₁₀ and R₁₁ form, together with the nitrogen atom that bears them, a pyrrolidine, a pyrrolidinone, a morpholine or a piperidine,

20 - a group -CO-NR₁₂R₁₃ with R₁₂ and R₁₃ being, independently of each other,

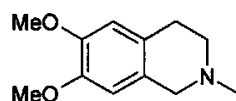
. a hydrogen atom,

. a (C₁-C₄) alkyl group optionally substituted with a -C≡N group, an aryl
25 group such as phenyl or a heterocyclyl group such as pyridyl, the said aryl and

heterocyclyl groups being optionally substituted with a (C₁-C₄) alkyl group or a hydroxyl group,

or alternatively R₁₂ and R₁₃ form,

5 together with the nitrogen atom that bears them, a group



- a group -COOR₁₄ with R₁₄ being a (C₁-C₄) alkyl group,

10 - a group -NH-CO-NR₁₅R₁₆ with R₁₅ and R₁₆ being, independently of each other, a hydrogen atom, a (C₁-C₄) alkyl group, a phenyl group or a benzyl group, the said phenyl and benzyl groups being optionally substituted with one or more

15 substituents chosen from a halogen atom, a (C₁-C₄) alkyl group and a (C₁-C₄) alkoxy group,

- a group -SO₂-NR₁₇R₁₈ with R₁₇ and R₁₈ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,

20 - a group -SO₂-R₁₉ with R₁₉ being a (C₁-C₄) alkyl group or an aryl group such as phenyl,

- a heterocyclyl group chosen from 1,3-dioxolanyl, imidazolyl, tetrazolyl, triazolyl optionally substituted with a (C₁-C₄) alkyl

25 group, thiazolyl, pyrimidyl, oxadiazolyl or

pyridyl, the imidazolyl being optionally substituted on the nitrogen atom with a (C₁-C₄) alkyl group or a benzyl, the tetrazolyl being optionally substituted with a (C₁-C₄) alkyl group
5 or a benzyl, and the oxadiazolyl being optionally substituted with a (C₁-C₄) alkyl,
- a group -NH-CO-OR₁₅, R₁₅ corresponding to the above definition,

in the form of base, of acid-addition salt, of hydrate
10 or of solvate, in the form of enantiomers, diastereoisomers, rotamers or atropoisomers, or mixtures thereof.

2. Compound of general formula (I) according to Claim 1, in which

15 • **Ar₁** represents

- an aryl group such as a phenyl group optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy
20 group, a fluoro(C₁-C₄)alkyl group,
- a heterocyclyl group chosen from pyridyl, thiazolyl and thienyl, the thienyl being optionally substituted with a (C₁-C₄) alkyl group,
- a (C₃-C₆) cycloalkyl group;

25 • **T** represents

- a group -(CH₂)_n- with n = 1,

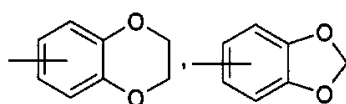
- a group >CH-R_2 with R_2 being a hydroxyl group or a (C₁-C₄) alkyl group,
- a group >N-R_3 with R_3 being a (C₁-C₄) alkyl group,
- a group >C(OH)-R_4 with R_4 being a (C₁-C₄) alkyl group;

5 • **Ar₂** represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a
- 10 fluoro(C₁-C₄)alkoxy group, a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

• **Ar₃** represents

- an aryl group chosen from phenyl and naphthyl, the
- 15 phenyl group being optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a fluoro(C₁-C₄)alkyl group, a fluoro(C₁-C₄)alkoxy group, a nitro group,
- 20 or a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group,
 - a group chosen from

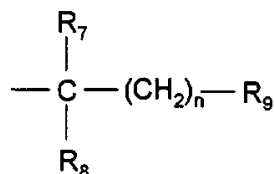


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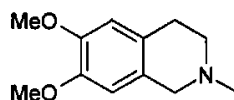
• **R₁** represents

- a $-C(O)-CF_3$ group,
- a group of formula



- 5 in which
- $n = 0, 1$ or 2 ,
- . R_7 represents
- a hydrogen atom or a (C_1-C_4) alkyl group
- . R_8 represents
- 10 - a hydrogen atom,
- . R_9 represents
- a hydrogen atom, a (C_1-C_4) alkyl group, a
- hydroxyl group, a (C_1-C_4) alkoxy group, a
- fluoro (C_1-C_4) alkyl group, a $-C\equiv CH$ group or a $-C\equiv N$
- 15 group,
- a group $-NR_{10}R_{11}$ with R_{10} and R_{11} being,
- independently of each other, a hydrogen atom, a
- (C_1-C_4) alkyl group, a (C_1-C_4) alkylcarbonyl group
- or a benzyl,
- 20 or alternatively R_{10} and R_{11} form, together with
- the nitrogen atom that bears them, a
- pyrrolidine, a piperidine or a pyrrolidinone,
- a group $-CO-NR_{12}R_{13}$ with R_{12} and R_{13} being,
- independently of each other, a hydrogen atom or
- 25 a (C_1-C_4) alkyl group,

or alternatively R_{12} and R_{13} form, together with the nitrogen atom that bears them, a group



- 5 - or a group $-\text{COOR}_{14}$ with R_{14} being a $(\text{C}_1\text{-C}_4)$ alkyl group,
- a group $-\text{NH-CO-NR}_{15}\text{R}_{16}$ with R_{15} and R_{16} being, independently of each other, a hydrogen atom, a $(\text{C}_1\text{-C}_4)$ alkyl group, a phenyl or a benzyl,
- 10 - a heterocyclyl group chosen from imidazolyl optionally substituted on the nitrogen atom with a $(\text{C}_1\text{-C}_4)$ alkyl group, tetrazolyl optionally substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group, and triazolyl,
- 15 in the form of base, of acid-addition salt, of hydrate or of solvate, in the form of enantiomers, diastereoisomers, rotamers or atropoisomers, or mixtures thereof.

3. Compound of general formula (I)

20 according to either of Claims 1 and 2, in which

• **Ar₁** represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a
- 25 $(\text{C}_1\text{-C}_4)$ alkyl group, a $(\text{C}_1\text{-C}_4)$ alkoxy group, a

fluoro(C₁-C₄)alkyl group,

- a heterocyclyl group chosen from pyridyl, thiazolyl and thienyl, the thienyl being optionally substituted with a (C₁-C₄) alkyl group;

5 • **T** represents

- a group $-(CH_2)_n-$ with $n = 1$,

- a group $\begin{array}{c} >CH-R_2 \end{array}$ with R₂ being a hydroxyl group;

• **Ar₂** represents

- an aryl group such as phenyl optionally substituted
10 with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group; a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

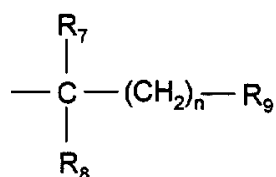
15 • **Ar₃** represents

- an aryl group such as phenyl, the phenyl group being optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy
20 group,

or alternatively a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;

• **R₁** represents

25 - a group of formula



in which

$n = 0, 1$ or 2 ,

. R_7 represents

5 - a hydrogen atom or a $(\text{C}_1\text{-C}_4)$ alkyl group,

. R_8 represents

 - a hydrogen atom,

. R_9 represents

10 - a hydrogen atom, a $-\text{C}\equiv\text{CH}$ group or a $-\text{C}\equiv\text{N}$
 group,

 - a group $-\text{CO}-\text{NR}_{12}\text{R}_{13}$ with R_{12} and R_{13} being,
independently of each other, a hydrogen atom or
a $(\text{C}_1\text{-C}_4)$ alkyl group,

15 - a heterocyclyl chosen from imidazolyl
 optionally substituted on the nitrogen atom with
 a $(\text{C}_1\text{-C}_4)$ alkyl group, tetrazolyl optionally
 substituted with a $(\text{C}_1\text{-C}_4)$ alkyl group, and
 triazolyl,

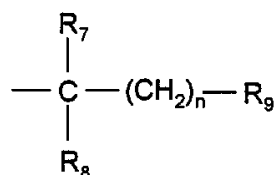
in the form of base, of acid-addition salt, of hydrate
20 or of solvate, in the form of enantiomers,
diastereoisomers, rotamers or atropoisomers, or
mixtures thereof.

4. Compound of general formula (I)

according to any one of Claims 1 to 3, in which

25 • Ar_1 represents

- an aryl group such as phenyl optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group,
- 5 - a heterocyclyl group such as thienyl, optionally substituted with a (C₁-C₄) alkyl group,
 - **T** represents
 - a group -(CH₂)_n- with n = 1,
 - **Ar₂** represents
 - 10 - a phenyl group optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl group, a (C₁-C₄) alkoxy group, a group -NR_cR_d with R_c and R_d being, independently of each other, a hydrogen atom
 - 15 or a (C₁-C₄) alkyl group;
 - **Ar₃** represents
 - a phenyl group optionally substituted with one or more groups chosen, independently of each other, from the following groups: a halogen atom, a (C₁-C₄) alkyl
 - 20 group, a (C₁-C₄) alkoxy group,
 - or alternatively a group -NR₅R₆ with R₅ and R₆ being, independently of each other, a hydrogen atom or a (C₁-C₄) alkyl group;
 - **R₁** represents
 - 25 - a group of formula



in which

$n = 0, 1$ or 2 ,

. R_7 represents

5 - a hydrogen atom or a $(\text{C}_1\text{-C}_4)$ alkyl group;

. R_8 represents

- a hydrogen atom;

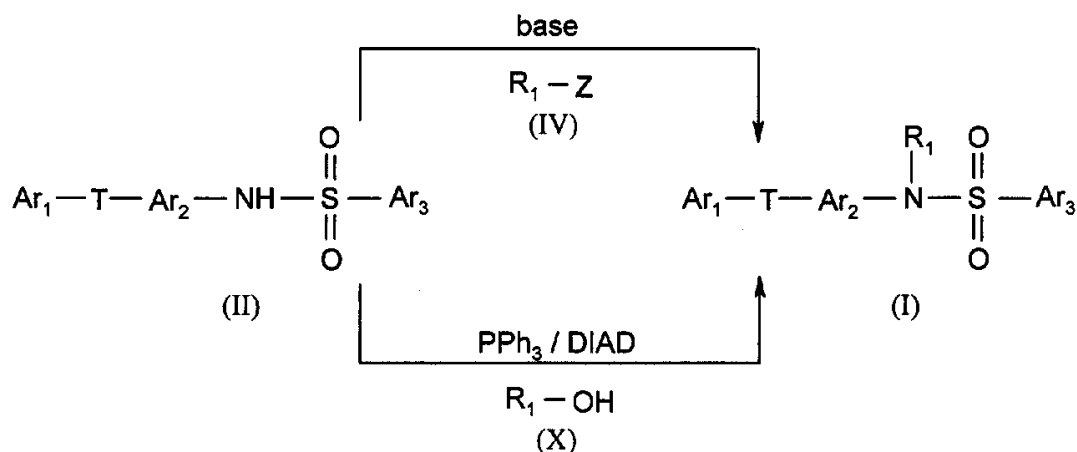
. R_9 represents

10 - a group $\text{-CO-NR}_{12}\text{R}_{13}$ with R_{12} and R_{13} being,
independently of each other, a hydrogen atom or
a $(\text{C}_1\text{-C}_4)$ alkyl group,
- a heterocycle chosen from imidazolyl
substituted on the nitrogen atom with a $(\text{C}_1\text{-C}_4)$
alkyl group, tetrazolyl substituted with a
15 $(\text{C}_1\text{-C}_4)$ alkyl group, and triazolyl,

in the form of base, of acid-addition salt, of hydrate
or of solvate, in the form of enantiomers,
diastereoisomers, rotamers or atropoisomers, or
mixtures thereof.

20 5. Process for preparing a compound of
formula (I) according to any one of Claims 1 to 4,
characterized in that
- either the compound of general formula (II) is
alkylated with the compound of general formula (IV), in
25 the presence of a base;

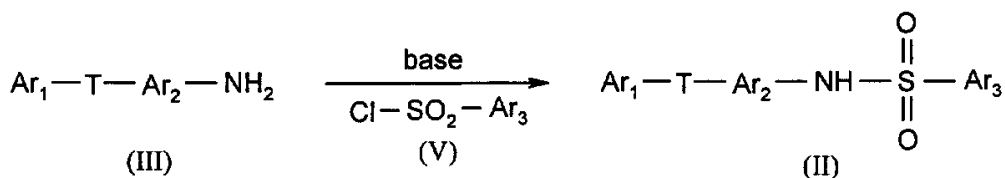
- or a Mitsunobu reaction is performed between an alcohol of formula (X) and a compound of general formula (II):



5

in the compounds of formulae (II), (IV) and (X), Ar₁, Ar₂, Ar₃, T and R₁ are as defined in formula (I) and Z is a leaving group.

6. Preparation process according to Claim 5, characterized in that the compound of formula (II) is obtained by sulfonylation of a compound of formula (III) with sulfonyl chlorides of formula (V), in the presence of a base:



15

in the compounds of formulae (III) and (V), Ar₁, Ar₂, Ar₃ and T are as defined in formula (I) of Claim 1 and Z is a leaving group.

7. Use of a compound of formula (I) according to any one of Claims 1 to 4, for the preparation of a medicament for the prophylaxis or treatment of any disease involving a dysfunction
5 associated with the orexin 2 receptor.

8. Use of a compound of formula (I) according to any one of Claims 1 to 4 for the preparation of a medicament for the prophylaxis or treatment of pathologies such as obesity, appetite or
10 taste disorders including cachexia, anorexia and bulimia, diabetes, metabolic syndromes, vomiting and nausea, depression and anxiety, addictions, mood and behaviour disorders, schizophrenia, sleep disorders, restless legs syndrome, memory learning disorders,
15 sexual and psychosexual dysfunctions, pain, visceral or neuropathic pain, hyperalgesia, allodynia, digestive disorders, irritable bowel syndrome, neuronal degenerescence, ischaemic or haemorrhagic attacks, Cushing's disease, Guillain-Barré syndrome, myotonic
20 dystrophy, urinary incontinence, hyperthyroidism, pituitary function disorders, hypertension or hypotension.

9. Medicament, characterized in that it comprises a compound of formula (I) according to any
25 one of Claims 1 to 4.

10. Pharmaceutical composition containing at least one compound of formula (I) according to any one of Claims 1 to 4 and optionally one or more pharmaceutically acceptable excipients.