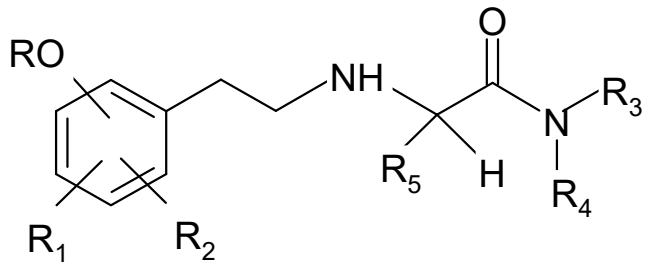
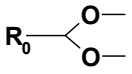
CLAIMS

1. A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein R is (C_3-C_{10})alkyl, or ω-trifluoro(C_3-C_{10})alkyl;

R_1 and R_2 are, independently, hydrogen, hydroxy, (C_1-C_8)alkoxy, (C_1-C_8) alkylthio, halo, trifluoromethyl or 2,2,2-trifluoroethyl; or one of R_1 and R_2 is at the ortho position to the R-O- group and, taken together with the same R-O-, represents a  group where R_0 is (C_2-C_9)alkyl;

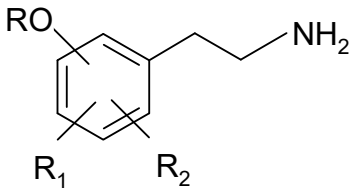
R_3 and R_4 are independently hydrogen or (C_1-C_6)alkyl; or taken together with the adjacent nitrogen atom form a 5-6 membered monocyclic saturated heterocycle, optionally containing one additional heteroatom chosen among -O-, -S- and -NR_7- where R_7 is hydrogen or (C_1-C_6) alkyl;

R_5 is hydrogen or (C_1-C_6)alkyl;

and wherein optionally one or more hydrogen atom in the groups R, R_1, R_2, R_3, R_4 and R_5, preferably in the R group, can be substituted by a deuterium atom;

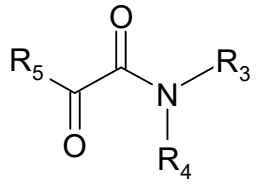
said process comprising the steps of:

i) reacting a compound of formula (II) or a salt thereof



(II)

wherein R, R_1, R_2, are as above defined, with a compound of formula (III):



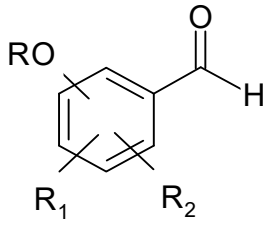
(III)

wherein R_3, R_4 and R_5 are as above defined, under reducing conditions, to obtain the compound of formula (I) as above defined, and

ii) optionally salifying the obtained compound of formula (I);

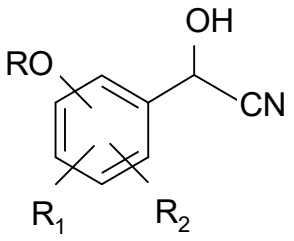
wherein the compound of formula (II) is obtained by a process comprising the following steps:

i') reacting a compound of formula (IV):



(IV)

wherein R, R_1, R_2, are as defined in claim 1, with MCN wherein M is an alkali metal chosen from Li, Na and K, to obtain a compound of formula (V):



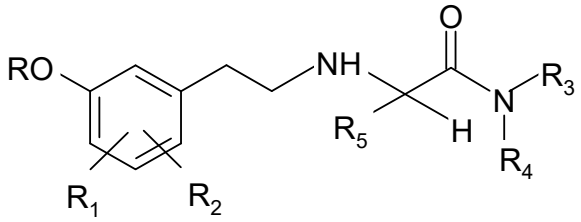
(V)

wherein R, R_1 and R_2 are as above defined, and

ii') reducing the obtained compound of formula (V) to obtain a compound of formula (II) as above defined and

iii') optionally salifying the obtained compound of formula (II).

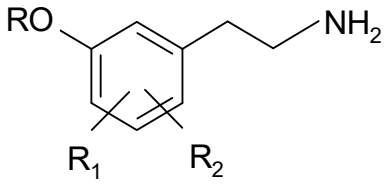
2. The process according to claim 1 for obtaining a compound of formula (I'):



(I')

wherein R, R_1, R_2, R_3, R_4 and R_5 are as defined above and

the compound of formula (II) has the following formula (II'):



(II').

3. The process according to ~~any one of the preceding claims~~claim 1 or 2 for obtaining a compound of formula (I) or (I') wherein R is n-butyl or CD_3-CD_2-CH_2-CH_2- and R_1, R_2, R_3, R_4 and R_5 are hydrogen.

4. The process according to any one of the preceding claims 1 to 3 for obtaining a compound of formula (I') wherein the compound of formula (I') is 2-[2-(3-butoxyphenyl)-ethylamino]-N,N-dimethylacetamide.

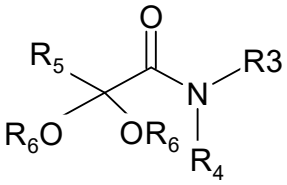
~~4~~5. The process according to any one of the preceding claims 1 to 4 wherein the compound of formula (II) is in the form of a salt with an acid selected from hydrochloric acid, benzenesulfonic acid, hydrobromic acid camphorsulfonic acid, methanesulfonic acid, ethanesulfonic acid, fumaric acid, lactic acid, maleic acid, mandelic acid, sulfuric acid, tartaric acid, succinic acid, paratoluenesulfonic acid and 2-naphtalenesulfonic acid.

~~5~~6. The process according to any one of the preceding claims 1 to 5 wherein step i) is carried out under conditions of catalytic hydrogenation.

~~6~~7. The process according to claim ~~5~~ 6 wherein the catalytic hydrogenation is carried out by using a catalyst comprising at least one metal selected from Pd, Pt, Ir, Ni and Ru on an inert support.

~~7~~8. The process according to claim ~~6~~ 7 wherein the catalytic hydrogenation is carried out wherein the catalyst is wet 5% Pt/C (50% H_2O) or wet 10% Pd/C (50% H_2O).

~~8~~9. The process according to any one of the preceding claims 1 to 8 wherein the compound of formula (III) is obtained in situ by hydrolysis of a compound of formula (VII):

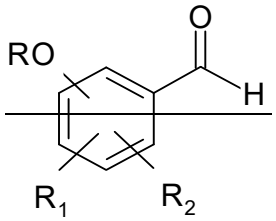


(VII)

wherein R_3, R_4 and R_5 are as defined above and R_6 is a (C_1-C_4)alkyl, preferably methyl, ethyl, iso-propyl.

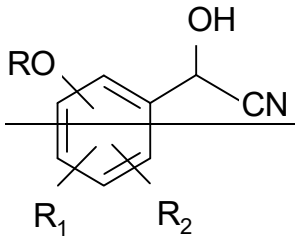
~~9. The process according to claim 1 wherein the compound of formula (II) as defined in claim 1, is obtained by a process comprising the following steps:~~

~~i') reacting a compound of formula (IV):~~



~~(IV)~~

~~wherein R, R_1, R_2, are as defined in claim 1, with MCN wherein M is an alkali metal chosen from Li, Na and K, to obtain a compound of formula (V):~~



~~(V)~~

~~wherein R, R_1 and R_2 are as above defined, and~~

~~ii') reducing the obtained compound of formula (V) to obtain a compound of formula (II) as above defined and~~

~~iii') optionally salifying the obtained compound of formula (II).~~

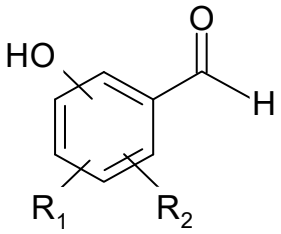
10. The process according to any one of claims 1 to 9 wherein the salt of the compound of formula (II) may be isolated by crystallization or directly used in the step i) defined in claim 1.

11. The process according to any one of claims ~~9 or~~1 to 10 wherein step i') is preferably carried out in a biphasic system consisting of water and an organic solvent in the presence of an acid at a temperature ranging from 0°C to 10°C, preferably from 0°C to 5°C.

12. The process according to any one of claims ~~9~~ 1 to 11 wherein the reducing step ii') is preferably a catalytic hydrogenation which is carried out by using a~~n~~ heterogeneous catalyst selected from the group consisting of nickel, rhodium, platinum and palladium catalysts on an inert support.

13. The process according to claim 12 wherein the heterogeneous catalyst is preferably wet 5% Pt/C (50% H_2O) or wet 10% Pd/C (50% H_2O).

14. The process according to any one of claims 1 to 9 wherein the compound of formula (IV) as defined in claim 9 is obtained by alkylating a compound of formula (VI):



(VI)

wherein R_1 and R_2 are as defined in claim1 with a compound of formula RX wherein R is as defined in claim 1 and X is Cl, Br, I or a leaving group selected from the group consisting of mesylates, tosylates and brosylates.