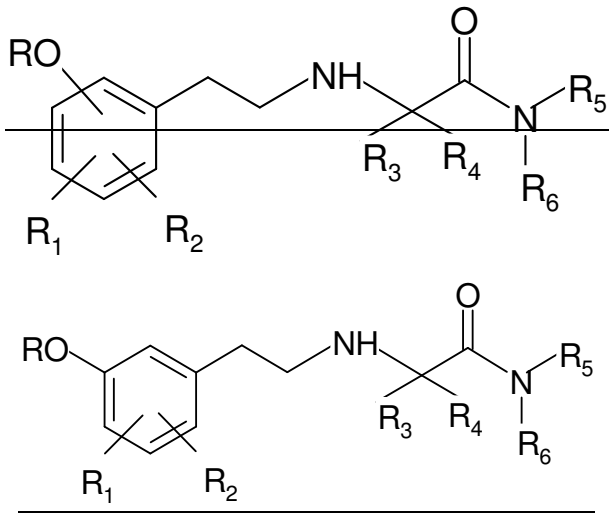
CLAIMS

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

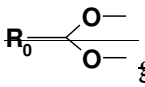


(I')

wherein

R is (~~C3~~C4-~~C10~~C6)alkyl, or CD3-CD2-~~ω-trifluoro~~(~~C3~~C2-~~C10~~C4)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 in 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~~;

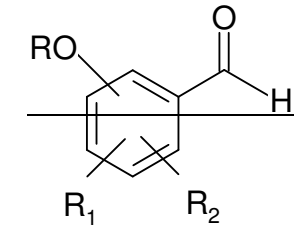
R_3 and R_4 are both~~, independently,~~ hydrogen~~, (C_1-C_4)alkyl; or R_4 is hydrogen and R_5 is a group selected from -CH_2-OH, -CH_2-O-(C_1-C_6)alkyl, -$CH(CH_3)$-OH, -$(CH_2)_2$-S-CH_3, benzyl and 4-hydroxybenzyl; or R_4 and R_5, taken together with the adjacent carbon atom, form a (C_3-C_6)cycloalkyl residue~~; and

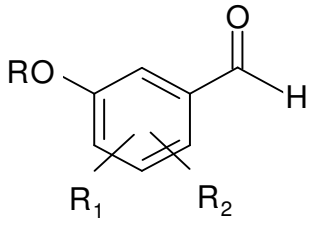
R_5 and R_6 are, independently, hydrogen or (C_1-~~C_6~~C_3)alkyl;~~ or taken together with the adjacent nitrogen atom form a 5-6 membered monocyclic saturated heterocycle, optionally containing one additional heteroatom chosen among -O-, -S- and -NR_7- where R_7 is hydrogen or (C_1-C_6) alkyl;~~

~~and wherein optionally one or more hydrogen atom in the groups R, R_1, R_2, R_3, R_4, R_5 and R_6, preferably in the R group, can be substituted by a deuterium atom;~~

said process comprising the steps of:

a) reacting a compound of formula (II'):





(II')

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

$$[(R_9)_3\,P\,CH_2OR_8]^+X^-$$

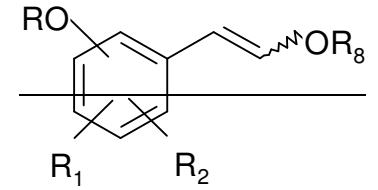
(III)

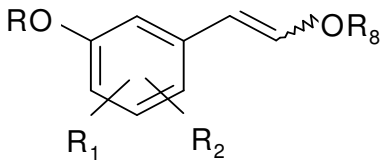
wherein

R_9 is aryl, preferably phenyl, tolyl, or a (C1-C6) alkyl, preferably methyl, ethyl or n-propyl;

X is Cl, Br or I, preferably Cl and Br;

R_8 is (C_1-C_6) alkyl, preferably methyl, ethyl or n-propyl or aryl, preferably phenyl or tolyl; in the presence of a strong base to obtain a compound of formula (IV'):

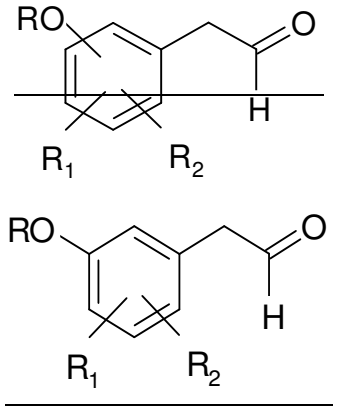




(IV')

wherein R, R_1, R_2 and R_8 are as above defined and

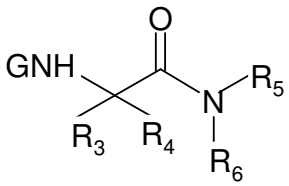
b) hydrolyzing the obtained compound of formula (IV') in a polar solvent under anhydrous or aqueous acidic conditions to obtain a compound of formula (V'):



(V')

wherein R, R_1 and R_2 are as above defined and

c) reacting the obtained compound of formula (V') with a compound of formula (VI) or a salt thereof:



(VI)

wherein R_3, R_4, R_5 and R_6 are as above defined and G is hydrogen or a protecting group of the amino group, to obtain a condensation compound;

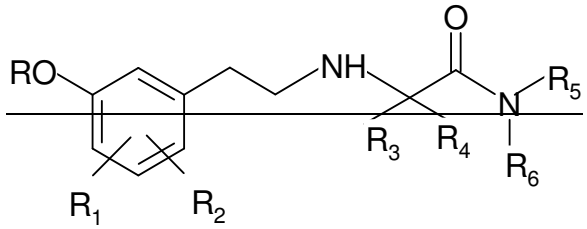
d) reducing the obtained condensation compound to obtain the compound of formula (I')

or alternatively

c') directly reacting the compound of formula (IV') as above defined with the compound of formula (VI) as above defined and reducing the obtained condensation compound to obtain the compound of formula (I'); and

e) optionally converting the obtained compound of formula (I') into a pharmaceutically acceptable salt thereof.

~~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, R_5 and R_6 are as defined in claim 1.~~

~~3. The process according anyone of the preceding claims for obtaining a compound of formula (I) as defined in claim 1 or (I') as defined in claim 2 wherein:~~

~~R is (C_4-C_6)alkyl or CD_3-CD_2-(C_2-C_4)alkyl;~~

~~R_1 and R_2 are, independently, hydrogen or halo, preferably fluoro;~~

~~R_3 and R_4 are both hydrogen; and~~

~~R_5 and R_6 are, independently, hydrogen or (C_1-C_3)alkyl.~~

~~4~~2. The process according to claim 1 ~~anyone of the preceding claims~~ for obtaining a compound of formula ~~(I) as defined in claim 1 or~~ (I') as defined in claim ~~2~~ 1 wherein R is n-butyl or CD_3-CD_2-CH_2-CH_2- and R_1, R_2, R_3, R_4, R_5 and R_6 are hydrogen.

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

~~5~~4. The process according to any one of the preceding claims 1 to 3 wherein the strong base of step a) is selected in the group consisting of alkyl lithium, lithium hexamethyldisilazide, lithium isopropylamide, potassium tert-butoxide.

~~6~~5. The process according to claim ~~5~~ 4 wherein the strong base is lithium hexamethyldisilazide.

~~7~~6. The process according to any one of the preceding claims 1 to 5 wherein the side product $(R_9)_3$ P formed in step a), wherein R_9 is as defined in claim 1, is oxidized to $(R_9)_3$ PO and removed.

~~8~~7. The process according to claim ~~7~~ 6 wherein $(R_9)_3$~~(R9)3~~ PO is removed by filtration.

~~9~~8. The process according to claim ~~7~~ 6 or ~~8~~ 7 wherein the obtained product (IV') is purified by chromatography.

9. The process according to any one of the preceding claims 1 to 9 wherein the hydrolysis of step b) is carried out in the polar solvent selected from acetonitrile, tetrahydrofuran or 2-methyltetrahydrofuran, ethanol, methanol, 1-butanol, methyl tetrabutyl ether (MTBE) or ethyl acetate or a mixture thereof.

10. The process according to any one of the preceding claims 1 to 9 wherein the hydrolysis of step b) is carried out in aqueous acidic conditions.

11. The process according to claim 10 wherein the hydrolysis of step b) is carried out in acetonitrile and aqueous hydrochloric acid.

12. The process according to any one of the preceding claims 1 to 11 wherein G in the compound of formula (VI) is hydrogen.

13. The process according to any one of claims 1 to 11 wherein G in the compound of formula (VI) is a protecting group of the amino group selected from the group consisting of a carbamate N-carboxy alkyl group, N- t-butyl carbamate (BOC), N-benzyl carbamate (Cbz), bromobenzyl carbamate, p-chlorobenzylcarbamate and 9-fluorenylmethyl carbamate (Fmoc).

14. The process according to any one of the preceding claims 1 to 13 wherein the reducing agent used in step d) is selected from the group consisting of sodium

borohydride, sodium triacetoxyborohydride (STAB-H), Pd/H_2, and $NaBH_3CN$~~NaBH3CN~~.

15. The process according to any one of the preceding claims 1 to 14 wherein the reducing agent used in step d) is sodium triacetoxyborohydride (STAB-H).

16. The process according to any one of the preceding claims 1 to 15 wherein step b), step c) and step d) are carried out without isolating the intermediate products.

17. The process according to claim 16 wherein step b), step c) and step d) are carried out in acetonitrile and aqueous hydrochloric acid.

18. The process according to any one of the preceding claims 1 to 17 wherein the pharmaceutically acceptable acid of step e) is selected from the group consisting of HCl, HBr, CH_3SO_3H, paratoluenesulfonic acid and phosphoric acid.

19. The process according to any one of the preceding claims 1 to 18 wherein the compound of formula (II') wherein R, R_1 and R_2 are as defined in claim 1 is prepared by alkylation of a compound of formula (II') wherein R is hydrogen by reaction with a compound of formula RY wherein R is as defined in claim 1 and Y is a leaving group.

20. The process according to claim 19 wherein Y is selected from the group consisting of chloride, bromide, mesylate, para-toluenesulphonate, brosylate, nosylate and phosphate.