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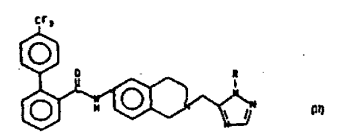
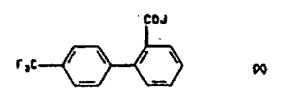
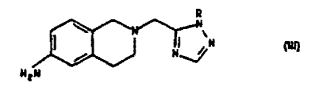
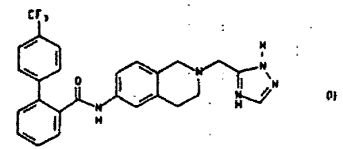
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 401/04	A1	(11) International Publication Number: WO 97/41111
		(43) International Publication Date: 6 November 1997 (06.11.97)
(21) International Application Number: PCT/IB97/00254	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 13 March 1997 (13.03.97)	Published With international search report.	
(30) Priority Data: 60/016,495 30 April 1996 (30.04.96) US		
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(54) Title: PROCESSES AND INTERMEDIATES FOR PREPARING 4'-TRIFLUOROMETHYLBIPHENYL-2-CARBOXYLIC ACID [2-(2H-[1,2,4]TRIAZOL-3-YLMETHYL)-1,2,3,4-TETRAHYDRO-ISOQUINOLIN-6-YL]-AMIDE

(57) Abstract

A process for preparing the compound of formula (I) which comprises treating the compound of formula (III) wherein R is H or R² and R² is selected from the group comprising allyl or a substituted methyl group wherein the substituents comprise one to three (C₆-C₁₀)aryl groups wherein the aryl groups are further optionally substituted with one or more substituents selected from nitro and (C₁-C₆)alkoxy; a) with a compound of formula (X) wherein J is a leaving group such as a halogen atom, an azido group, a (C₁-C₆)acyloxy group or a (C₆-C₁₀)aryloxy group, preferably a chlorine or bromine atom; and b) when R is R² further treating the product of step a) with an acid. A compound of formula (II) wherein R is R² and R² is as defined above and is, preferably, CH₃OC₆H₄CH₂.

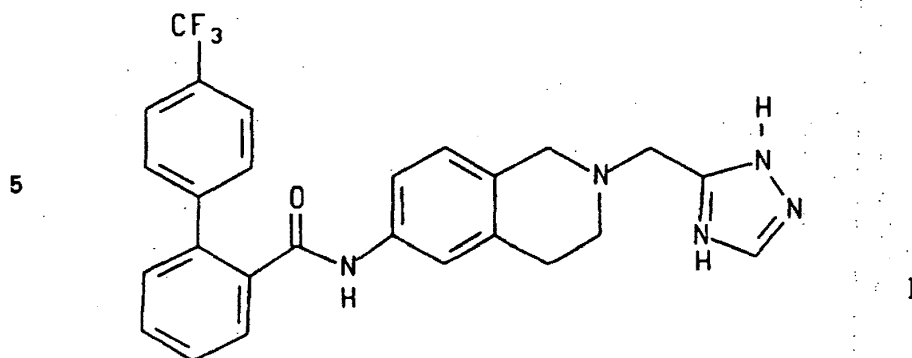


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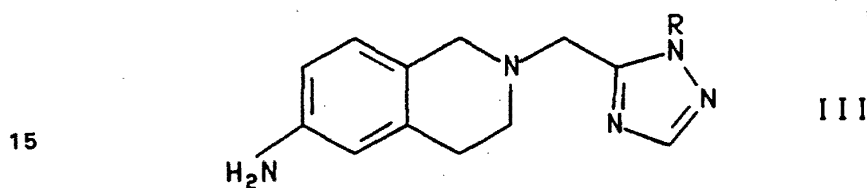
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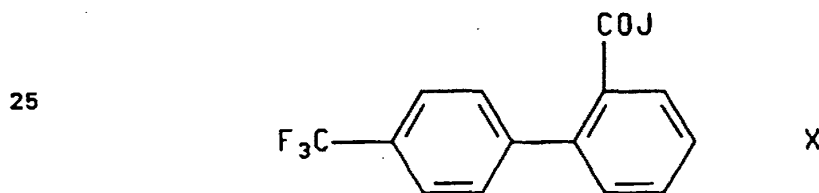
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which comprises treating the compound of the formula



wherein R is H or R² and R² is selected from allyl and a substituted methyl group wherein the substituents comprise one to three (C₆-C₁₀)aryl groups wherein the aryl groups are optionally substituted with one or more substituents selected from nitro and (C₁-C₆)alkoxy;

20 a) with a compound of the formula



wherein J is a leaving group such as a halogen atom, an azido group, a (C₁-C₆)acyloxy group or a (C₆-C₁₀)aroyloxy group, preferably a chlorine or bromine atom; and

30 b) when R is R² further treating the product of step a) with an acid such as trifluoroacetic acid (TFA), p-toluenesulfonic acid (PTSA), methane- or

trifluoromethanesulfonic acid and HBr in acetic acid, preferably trifluoroacetic acid.

Reference to a moiety as "heterocyclic" means any single ring or fused ring system containing at least one ring heteroatom independently selected from O, N, and S. Thus a polycyclic fused ring system containing one or more carbocyclic fused saturated, partially unsaturated, or aromatic rings (usually benzene rings) is within the definition of heterocyclyl so long as the system also contains at least one fused ring which contains at least one of the aforementioned heteroatoms. As a substituent, such heterocyclic rings may be attached to the remainder of the molecule from either a carbocyclic (e.g., benzene) ring or from a heterocyclic ring.

Reference to a moiety containing "one or more rings" is intended to mean that said moiety contains a single or fused cyclic moiety or moieties. The rings may be carbocyclic or heterocyclic, saturated or partially unsaturated, and aromatic or non-aromatic.

Reference to a fused polycyclic ring system or radical means that all rings in the system are fused.

Reference to "halo" in this specification is inclusive of fluoro, chloro, bromo, and iodo unless noted otherwise.

Reference to an "aryl" substituent (e.g. (C₆-C₁₀)aryl) means the ring or substituent is carbocyclic. Aromatic moieties which contain one or more heteroatoms are included as a subset of the term "heterocyclic", as discussed above.

Reference to an "acyl" substituent refers to an aliphatic or cyclic hydrocarbon moiety attached to a carbonyl group through which the substituent bonds.

Reference to "alkyl" and "alkoxy" include both straight and, when the moiety contains more than two carbon atoms, branched or cyclic chain radicals, but it is to be understood that references to individual radicals such as "propyl" or "propoxy" embrace only the straight chain ("normal") radical, branched chain isomers such as "isopropyl" or "isopropoxy" being referred to specifically.

Certain intermediates of the formula

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