Patent Claims

1. Process for manufacturing (S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxo-pyrrolidine-3-carboxylic acid 3,5-difluoro-benzylamide ("S-9"), characterized in that

a) 2-oxo-1-(1-(phenylsulfonyl)-1H-indol-5-yl)pyrrolidine-3-carboxylic acid ("5") is reacted with 3,5-difluorobenzyl amine to give 1-[1-(benzenesulfonyl)-1H-indol-5-yl]-N-[(3,5-difluorophenyl)methyl]-2-oxopyrrolidine-3-carboxamide ("12"),

b) "12" is then enantioselectively oxidized to give (3S)-1-[1-(benzenesulfonyl)-1H-indol-5-yl]-N-[(3,5-difluorophenyl)methyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide ("13"),

c) and subsequently the phenylsulfonyl group is cleaved off from "13" to give (S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxo-pyrrolidine-3-carboxylic acid 3,5-difluoro-benzylamide ("S-9").

2. Process according to claim 1,
wherein a) is carried out in presence of a base selected from triethylamine, DBU or di-isopropylethylamine.

3. Process according to claim 1 or 2,
wherein a) is carried out in dichloromethane.

4. Process according to claim 1, 2 or 3,
wherein a) is carried out in the presence of propanephosphonic acid anhydride.

5. Process according to claim 1,
wherein b) is carried out in presence of the oxidizing reagent (+)-(2R,4aS,7S,8aR)-4H-4a, 7-methanooxazirino[3, 2-i] [2, 1] benzisothiazole, 8,8-dichlorotetrahydro-9,9-dimethyl-3,3-dioxide.

6. Process according to claim 1 or 5,
wherein b) is carried out in presence of THF or diethylether.

7. Process according to claim 1, 5 or 6,
wherein b) is carried out in presence of NaHMDS.

8. Process according to claim 1,
wherein c) is carried out in presence of NaOH.