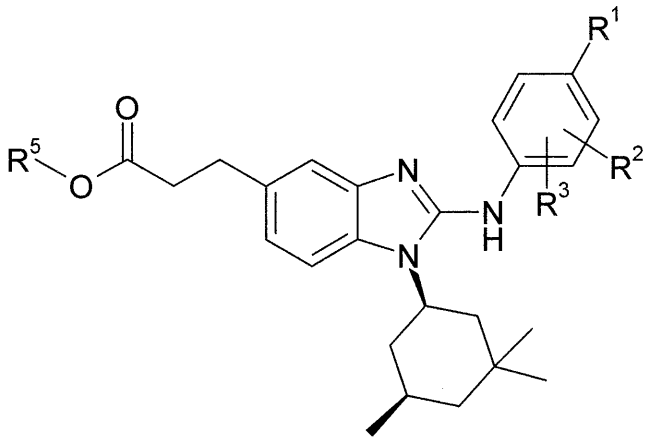
Claims

1. Method for preparing a compound of the general formula (Ia):



(Ia)

in which

R^1 represents a hydrogen atom or R^1 represents a group selected from the series of C_1-C_3-alkyl-, C_1-C_3-alkoxy-, C_1-C_3-haloalkyl- and C_1-C_3-haloalkoxy-,

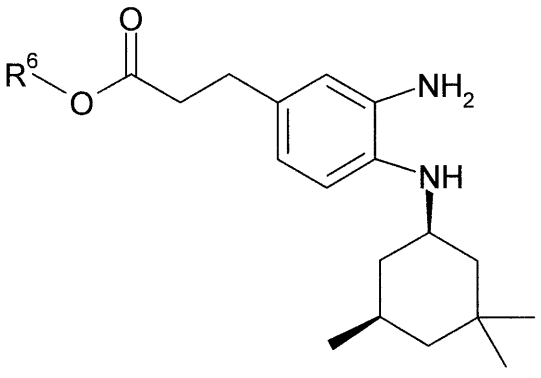
R^2 represents a hydrogen atom or a C_1-C_3-alkyl group,

R^3 represents a hydrogen atom or a C_1-C_3-alkyl group,

and

R^5 represents a C_1-C_3-alkyl group;

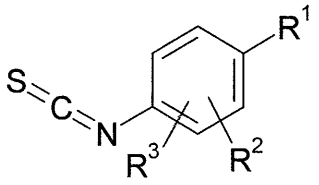
wherein the method comprises a step in which a compound of the general formula (IIa):



(IIa)

in which R^6 represents a C_1-C_6-alkyl group, or a salt or a solvate or a solvate of a salt of the compound of the general formula (IIa);

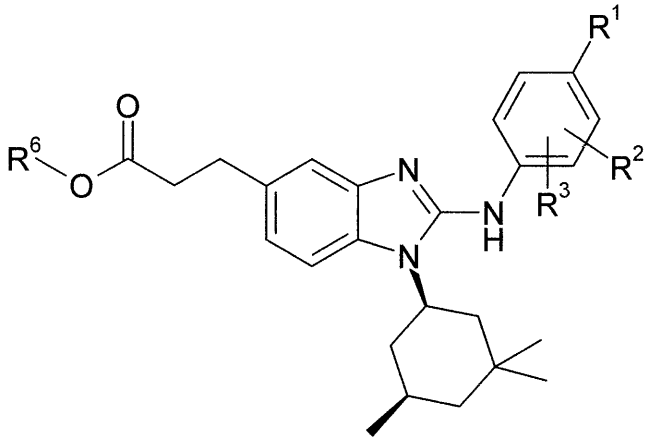
is reacted with a compound of the general formula (III):



(III)

in which R^1, R^2 and R^3 have the same definition as for the compound of the formula (Ia);

and in this reaction a compound of the general formula (IVa) is formed:



(IVa)

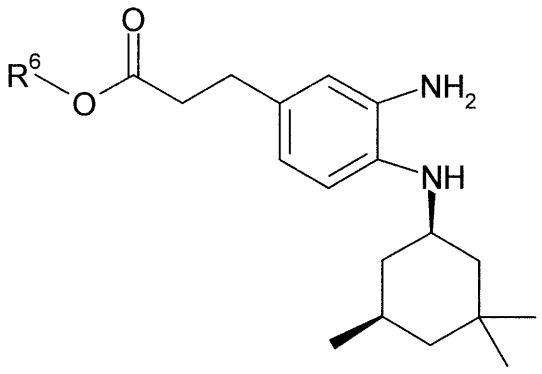
in which R^1, R^2 and R^3 have the same definition as for the compound of the formula (Ia) and R^6 has the same definition as for the compound of the formula (IIa).

2. Method according to Claim 1, wherein R^2 is a hydrogen atom, R^3 is a hydrogen atom and R^1 represents a group selected from the series of C_1-C_3-alkyl-, C_1-C_3-alkoxy-, C_1-C_3-haloalkyl- and C_1-C_3-haloalkoxy-.

3. Method according to Claim 1, wherein R^2 is a hydrogen atom, R^3 is a hydrogen atom and R^1 represents a group selected from the series of methyl-, methoxy-, trifluoromethyl- and trifluoromethoxy-.

4. Method according to any of Claims 1 to 3, wherein R^5 represents a methyl group.

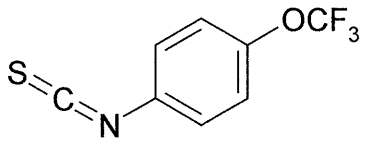
5. Method according to Claim 1 for preparing 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid, wherein the method comprises a step in which an alkyl ester of 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid of the formula (IIa):



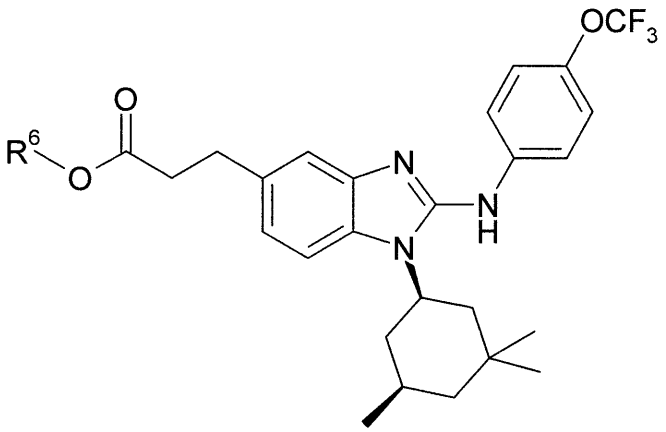
(IIa)

in which R^6 represents a C_1-C_6-alkyl group;
or a salt or a solvate or a solvate of a salt of the compound of the formula (IIa),

is reacted with 4-isothiocyanatophenyl trifluoromethyl ether,



and in this reaction an alkyl ester of 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid of the formula (IVa) is formed:

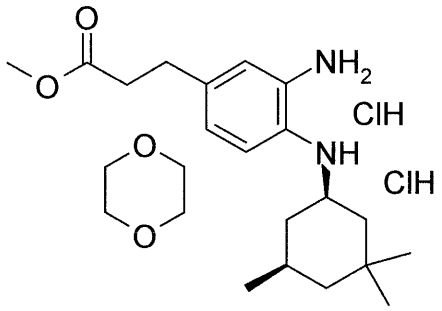


(IVa)

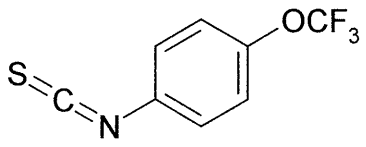
in which R^6 has the same definition as for the compound of the formula (IIa).

6. Method according to Claim 5 for preparing 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid, wherein the method comprises a step in which

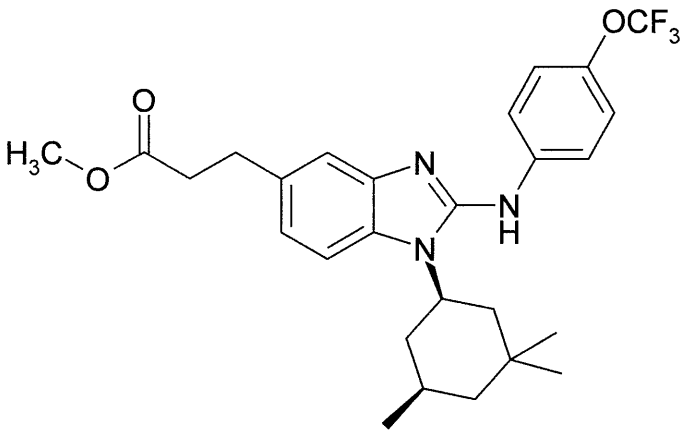
methyl 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoate - 1,4-dioxane hydrochloride (1:1:2)



is reacted with 4-isothiocyanatophenyl trifluoromethyl ether,



and in this reaction methyl 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoate is formed:



7. Method according to Claim 1 for preparing 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid comprising the following steps:

(a) reacting an alkyl ester of 3-(4-fluoro-3-nitrophenyl)propanoic acid with (1R,5R)-3,3,5-trimethylcyclohexanamine to give an alkyl ester of 3-(3-nitro-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid

(b) reducing the alkyl ester of 3-(3-nitro-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid from step (a) to give an alkyl ester of 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid

(c) reacting the alkyl ester of 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid from step (b) with 4-isothiocyanatophenyl trifluoromethyl ether to give an alkyl ester of 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid

(d) saponifying the alkyl ester of 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid to give 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid.

8. Method according to Claim 7, wherein the alkyl ester of 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-

yl)propanoic acid from step (a) is treated with a hydrochloric acid/dioxane mixture in order to obtain an alkyl ester of 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoic acid - 1,4-dioxane hydrochloride (1:1:2), which is then supplied to step (c).

9. Method according to Claim 7, wherein the saponification in step (d) is effected by means of an aqueous sodium hydroxide solution in THF and is subsequently neutralized with hydrochloric acid and the 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid is crystallized out by addition of *iso*propanol.

10. 3-(2-{[4-(Trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid in crystalline form which is obtained by treating 3-(2-{[4-(trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid dissolved in THF with *iso*propanol.

11. 3-(2-{[4-(Trifluoromethoxy)phenyl]amino}-1-[(1R,5R)-3,3,5-trimethylcyclohexyl]-1H-benzimidazol-5-yl)propanoic acid in crystalline form, which is characterized by maxima in the X-ray diffractogram at the following 2 theta angles: 6.5, 8.5, 11.2, 11.3, 11.9, 12.1, 13.4, 14.3, 14.8, 15.0, 15.1, 15.2, 15.3, 15.9, 16.4, 17.1, 17.4, 17.6, 18.0, 18.2, 19.1, 19.1, 19.6, 19.9, 20.1, 20.2, 20.8, 21.1, 21.6, 21.8, 22.4, 22.6, 22.9, 23.2, 23.4, 24.0, 24.3, 24.3, 24.7, 24.9.

12. Alkyl 3-(3-amino-4-{[(1R,5R)-3,3,5-trimethylcyclohexyl]amino}phenyl)propanoate - 1,4-dioxane hydrochloride (1:1:2).

13. Medicament comprising the compound according to either of Claims 10 or 11 in combination with an inert, nontoxic, pharmaceutically suitable excipient, and optionally one or more further active ingredients.

14. Medicament according to Claim 13 for use in the treatment and/or prophylaxis of tumours.