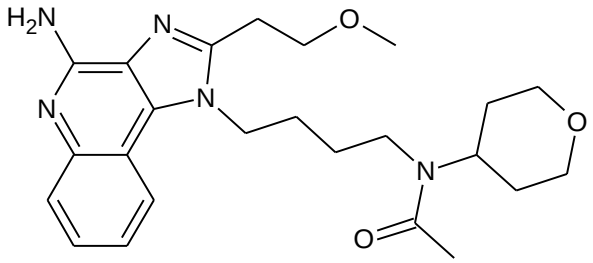
Claims

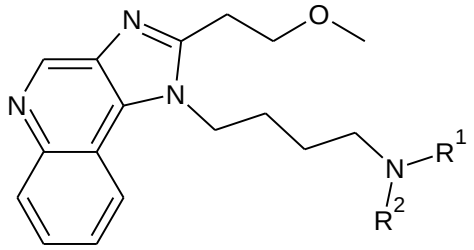
1. A process for synthesizing a compound having the formula (I):



(I)

or a solvate or salt thereof, the process comprising the following steps:

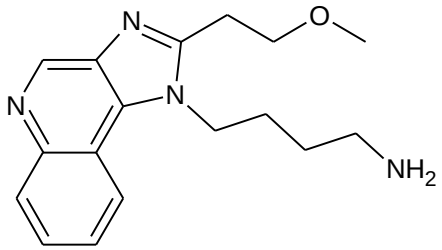
a) providing a compound of formula (3):



(3)

or a solvate or salt thereof, wherein each of R^1 and R^2 is independently selected from the group consisting of -H and an amino protecting group, and at least one of R^1 and R^2 is an amino protecting group;

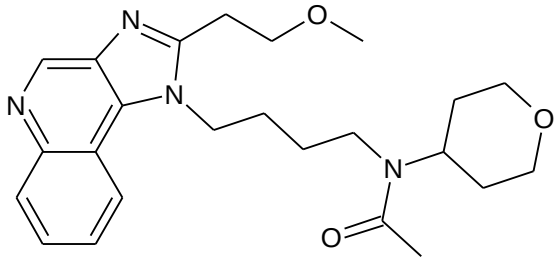
b) reacting the compound of formula (3) or a solvate or salt thereof with one or more reagents to remove the amino protecting group(s) at position R^1 and R^2 to give a compound of formula (4):



(4)

or a solvate or salt thereof;

c) reacting the compound of formula (4) or a solvate or salt thereof with one or more reagents for introducing (i) a tetrahydropyranyl group and (ii) an acetyl group to give a compound of formula (5):



(5)

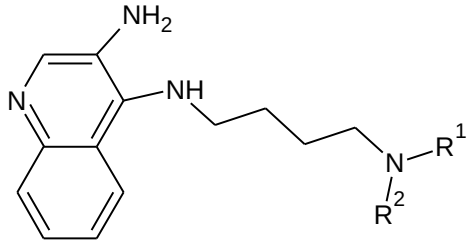
or a solvate or salt thereof; and

d) subjecting the compound of formula (5) or a solvate or salt thereof to an oxidative amination reaction to give the compound of formula (I) or a solvate or salt thereof.

2. The process of claim 1, further comprising the step of (i) precipitating the compound of formula (4) or a solvate or salt thereof before step c); (ii) precipitating the compound of formula (5) or a solvate or salt thereof before step d); and/or (iii) precipitating the compound of formula (I) or a solvate or salt thereof after step d).

3. The process of claim 1 or 2, wherein each of R^1 and R^2 is independently selected from the group consisting of -H, tert-butyloxycarbonyl (Boc), 9-fluorenylmethyloxy carbonyl (Fmoc), benzyloxycarbonyl (Cbz), tosylate (Ts), benzyl (Bn), allyloxycarbonyl (Alloc), trityl (Trt), dimethoxytrityl (DMT), and monomethoxytrityl (MMT).

4. The process of any one of claims 1 to 3, wherein step a) comprises reacting a compound of formula (1):



(1)

or a solvate or salt thereof with $HOOC(CH_2)_2OCH_3$ (formula (2)) or a derivative thereof to give a compound of formula (3) or a solvate or salt thereof.

5. The process of claim 4, wherein the derivative of formula (2) is (i) selected from the group consisting of carboxylic acid halides, orthoesters, and 1,1-dialkoxyalkyl alkanoates; and/or (ii) an orthoester, preferably an orthoester having the formula $(R^{10}O)_3C(CH_2)_2OCH_3$, wherein each R^{10} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, and heterocycloalkyl.

6. The process of claim 4 or 5, wherein the reaction of the compound of formula (1) with the compound of formula (2) is performed (i) in a solvent~~, such as an aromatic solvent~~; (ii) in the presence of an acid; (iii) at a suitable temperature~~, such as between 0°C and 120°C, e.g., at the reflux temperature of the solvent, if present~~; and/or (iv) for a sufficient amount of time~~, such as 30 min to 10 h~~.

7. The process of claim 6, wherein the solvent is an aromatic solvent; the suitable temperature is between 0°C and 120°C or at the reflux temperature of the solvent, if present; and/or the sufficient amount of time is from 30 min to 10 h.

~~7~~8. The process of any one of claims 1 to ~~6~~7, wherein step b) is performed (i) in a solvent~~, such as an aromatic solvent, e.g., the solvent used in step a)~~; (ii) at a suitable temperature~~, such as between 0°C and 40°C~~; and/or (iii) for a sufficient amount of time~~, such as 30 min to 5 h~~.

9. The process of claim 8, wherein the solvent is an aromatic solvent, or the solvent used in step a); the suitable temperature is between 0°C and 40°C; and/or the sufficient amount of time is from 30 min to 5 h.

~~8~~10. The process of any one of claims 1 to ~~7~~9, wherein each of R^1 and R^2 is independently selected from the group consisting of -H and tert-butyloxycarbonyl (Boc) and the one or more reagents to remove the amino protecting group(s) in step b) are selected from the group consisting of trifluoroacetic acid (TFA), HCl, CH_3SO_3H, and $(H_3C)_3SiCl$ (TMSCl), wherein preferably, after the reaction of the compound of formula (3) or a solvate or salt thereof with one or more reagents to remove the amino protecting group(s), step b) further comprises adding a base.

~~9~~11. The process of any one of claims 1 to ~~8~~10, wherein the one or more reagents for introducing a tetrahydropyranyl group in step c) are tetrahydropyranone and a reducing agent~~, such as tetrahydropyranone and a borohydride~~.

12. The process of claim 11, wherein the reducing agent is a borohydride.

~~10~~13. The process of any one of claims 1 to ~~9~~12, wherein in step c) the reaction of the compound of formula (4) or a solvate or salt thereof with one or more reagents for introducing a tetrahydropyranyl group is performed (i) in a solvent~~, such as a halogenated organic solvent~~; (ii) in the presence of an acid; (iii) at a suitable temperature~~, such as between -20°C and 40°C~~; and/or (iv) for a sufficient amount of time~~, such as 5 h to 24 h~~.

14. The process of claim 13, wherein the solvent is a halogenated organic solvent; the suitable temperature is between -20°C and 40°C; and/or the sufficient amount of time is from 5 h to 24 h.

~~11~~15. The process of any one of claims 1 to ~~10~~14, wherein the one or more reagents for introducing an acetyl group in step c) are selected from acetic anhydride and acetic halides.

~~12~~16. The process of any one of claims 1 to ~~11~~15, wherein in step c) the reaction of the compound of formula (4) or a solvate or salt thereof with one or more reagents for introducing an acetyl group is performed (i) in a solvent~~, such as a halogenated organic solvent~~; (ii) at a suitable temperature~~, such as between 0°C and 50°C~~; and/or (iii) for a sufficient amount of time~~, such as 6 h to 48 h~~.

17. The process of claim 16, wherein the solvent is a halogenated organic solvent; the suitable temperature is between 0°C and 50°C; and/or the sufficient amount of time is 6 h to 48 h.

~~13~~18. The process of any one of claims 1 to ~~12~~17, wherein step d) comprises reacting the compound of formula (5) or a solvate or salt thereof with first (i) an oxidation agent, and then with (ii) an acylating agent and an aminating agent.

~~14~~19. The process of claim ~~13~~18, wherein the oxidation agent is selected from oxidation agents capable of forming N-oxides, such as 3-chloroperoxybenzoic acid, and the oxidation reaction is preferably performed (i) in a solvent~~, such as a halogenated organic solvent~~; (ii) at a suitable temperature~~, such as between -10°C and 40°C~~; and/or (iii) for a sufficient amount of time~~, such as 30 min to 12 h~~.

~~15~~20. The process of claim ~~13~~ 18 or ~~14~~19, wherein the acylating agent is selected from the group consisting of alkysulfonyl halides and arylsulfonyl halides, such as methanesulfonyl chloride, benzenesulfonyl chloride, or p-toluenesulfonyl chloride, and the reaction with the acylating agent is preferably performed (i) in a solvent~~, such as a halogenated organic solvent~~; (ii) at a suitable temperature~~, such as between -10°C and 40°C~~; and/or (iii) for a sufficient amount of time~~, such as 30 min to 12 h~~.

~~16~~21. The process of any one of claims ~~13~~ 18 to ~~15~~20, wherein the aminating agent is selected from the group consisting of ammonia and its salts, such as aqueous NH_3, ammonium hydroxide, ammonium carbonate, ammonium bicarbonate, or ammonium phosphate, and the reaction with the aminating agent is preferably performed (i) in a solvent~~, such as a halogenated organic~~

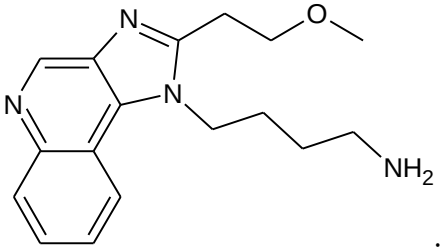
~~solvent~~; (ii) at a suitable temperature~~, such as between -10°C and 40°C~~; and/or (iii) for a sufficient amount of time~~, such as 30 min to 12 h~~.

22. The process of any one of claims 19 to 21, wherein the solvent is a halogenated organic solvent; the suitable temperature is between -10°C and 40°C; and/or the sufficient amount of time is from 30 min to 12 h.

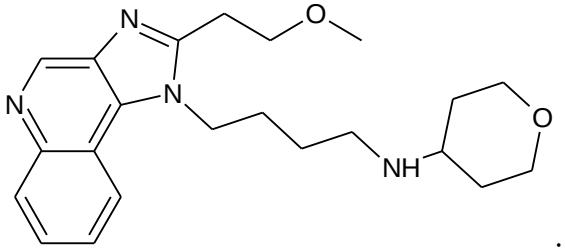
~~17~~23. The process of any one of claims 1 to ~~16~~22, wherein after step d) the process further comprises crystallizing the compound of formula (I) or a solvate or salt thereof, preferably from an alcoholic solvent.

~~18~~24. The process of any one of claims 1 to ~~17~~23, wherein one or more of steps a) to d) are performed in a chromatography-free manner.

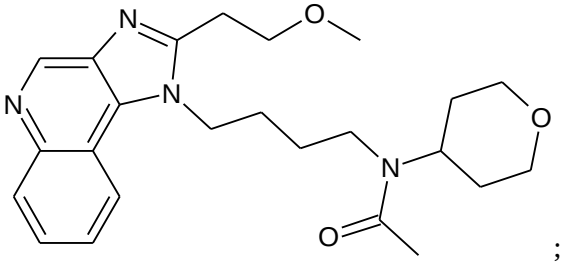
~~19~~25. A compound selected from the group consisting of:



;



;



;

and a solvate or salt thereof.

~~20~~26. Use of a compound of claim ~~19~~ 25 for synthesizing a compound of formula (I).