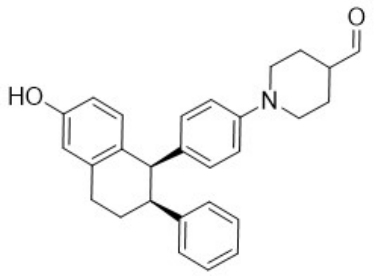
CLAIMS

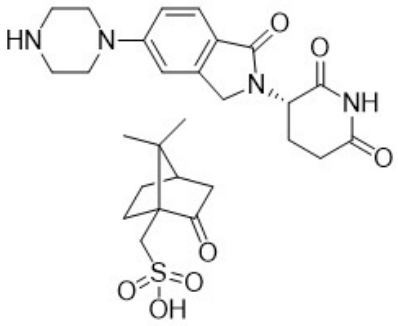
We claim:

Claim 1. A method comprising reductively aminating **Intermediate I-9**:



I-9

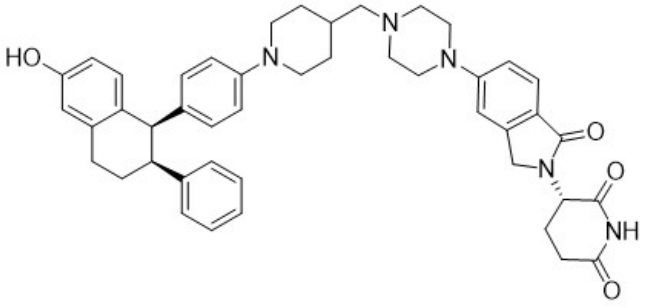
with salt **Intermediate I-8**:



I-8

,

a base, and a reducing agent in a solvent to provide **Compound 1**:



Compound 1

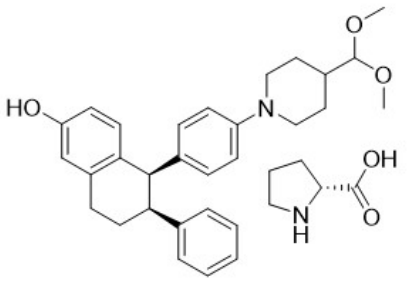
.

Claim 2. The method of claim 1, wherein the base is N-methyl-morpholine, trimethylamine, triethylamine, N,N-diisopropylethylamine, N,N-dimethylaniline, lithium carbonate, sodium carbonate, potassium carbonate, or magnesium carbonate.

Claim 3. The method of claim 1 or 2, wherein the reducing agent is sodium triacetoxyborohydride, sodium borohydride, sodium cyanoborohydride, or hydrogen in the presence of a catalyst.

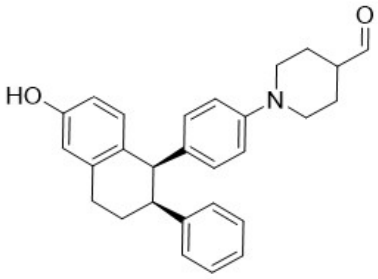
Claim 4. The method of any one of claims 1-3, wherein the solvent is dimethylacetamide, N-methyl-2-pyrrolidone, or 2-methyl tetrahydrofuran.

Claim 5. A method comprising reacting **Intermediate I-6:**



I-6

with an acid, and, optionally, an additive, in a solvent to provide **Intermediate I-9**:



I-9

.

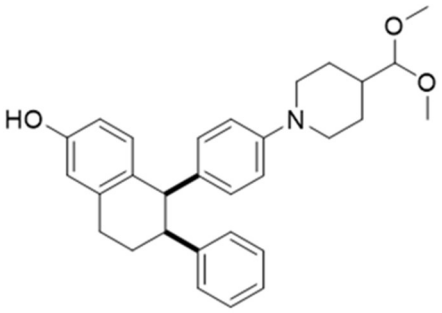
Claim 6. The method of claim 5, wherein the **Intermediate I-6** and the acid are reacted in a solvent that comprises water and an ethereal solvent, wherein the ethereal solvent is 2-methyltetrahydrofuran or tetrahydrofuran.

Claim 7. The method of claim 5 or 6, wherein the acid in the reaction is HCl.

Claim 8. The method of claim 5, wherein the additive is dibutylhydroxytoluene, ascorbic acid, alpha-tocopherol, or ethylenediaminetetraacetic acid.

Claim 9. A method, comprising

(a) combining racemic **Intermediate I-5**:



I-5

with an additive in a solvent to prepare a first reaction mixture;

(b) heating the first reaction mixture at reflux to prepare a fourth solution, followed by cooling the fourth solution to a temperature of about 50 °C to about 100 °C;

(c) combining (R)-proline and water to prepare a fifth solution, wherein the molar ratio of (R)-proline to the total amount of **Intermediate I-5** is about 0.40:1 to about 1.00:1;

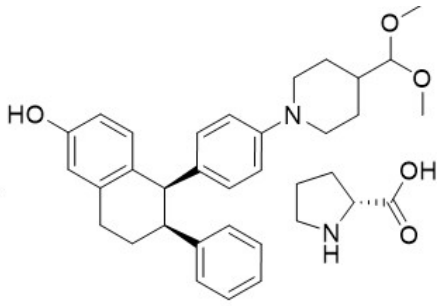
(d) adding about 1% to less than about 50% by volume of the fifth solution to the fourth solution to prepare a second reaction mixture;

(e) adding a first amount of an agent that induces nucleation to the second reaction mixture to prepare a third reaction mixture;

(f) adding about 1% to less than about 50% by volume of the second solution to the third reaction mixture to prepare a fourth reaction mixture;

(g) adding a second amount of the agent that induces nucleation to the fourth reaction mixture to prepare a fifth reaction mixture; and

(h) adding the remainder of the second solution to the fifth reaction mixture to prepare a sixth reaction mixture to provide **Intermediate I-6:**

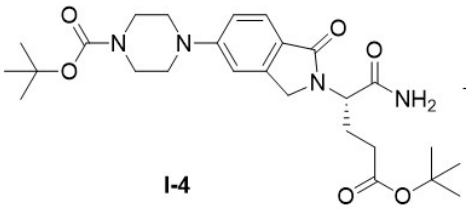


I-6

Claim 10. The method of claim 9, wherein the agent that induces nucleation is a crystallization promoter, wherein the crystallization promoter is a seed crystal comprising **Intermediate I-6**.

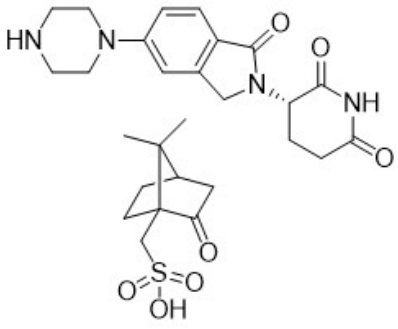
Claim 11. The method of claim 9 or 10, wherein the additive is an antioxidant, a radical scavenger, an oxygen scavenger, or a metal chelator or wherein the additive is dibutylhydroxytoluene, ascorbic acid, alpha-tocopherol, or ethylenediaminetetraacetic acid.

Claim 12. A method, comprising reacting **Intermediate I-4**:



I-4

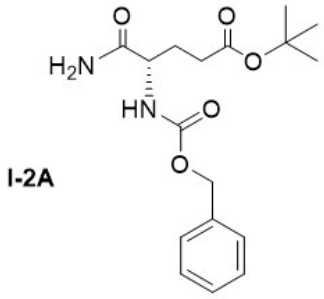
and camphorsulfonic acid in a solvent to provide salt **Intermediate I-8**:



I-8

and one or more byproducts.

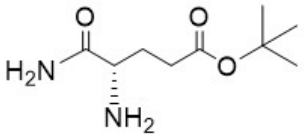
Claim 13. A method, comprising reacting **Intermediate I-2A**:



I-2A

,

a hydrogen source and $Pd(OH)_2$ in a solvent to provide **Intermediate I-3A**:

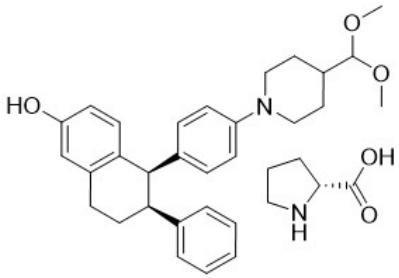


I-3A

.

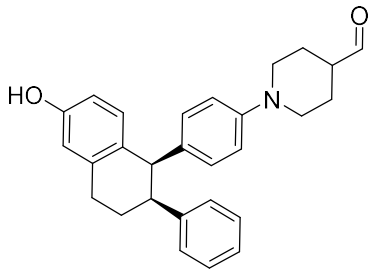
Claim 14. The method of claim 13, wherein the hydrogen source is hydrogen gas.

Claim 15. The method of claim 1, wherein **Intermediate I-9** is prepared by a method comprising mixing **Intermediate I-6**:



I-6

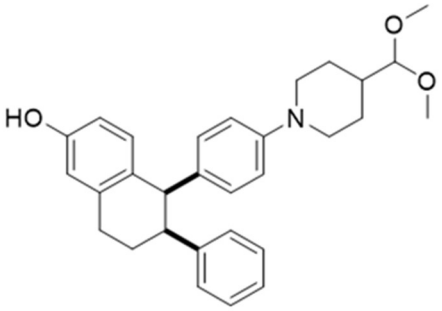
and an acid in a solvent to provide **Intermediate I-9**:



I-9

Claim 16. The method of claim 15, wherein **Intermediate I-6** is prepared by a method comprising

(a) combining racemic **Intermediate I-5**:



I-5

with an additive in a solvent to prepare a first reaction mixture;

(b) heating the first reaction mixture at reflux to prepare a first solution, followed by cooling the first solution to a temperature of about 50 °C to about 100 °C;

(c) combining (R)-proline and water to prepare a second solution, wherein the molar ratio of (R)-proline to the total amount of **Intermediate I-5** is about 0.40:1 to about 1.00:1;

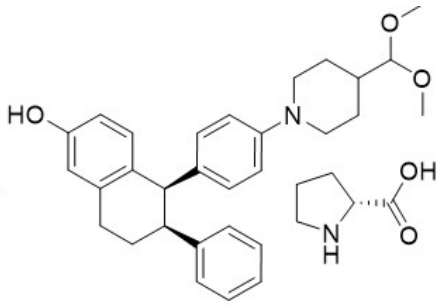
(d) adding about 1% to less than about 50% by volume of the second solution to the first solution to prepare a second reaction mixture;

(e) adding a first amount of an agent that induces nucleation to the second reaction mixture to prepare a third reaction mixture;

(f) adding about 1% to less than about 50% by volume of the second solution to the third reaction mixture to prepare a fourth reaction mixture;

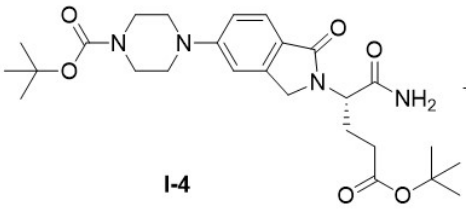
(g) adding a second amount of the agent that induces nucleation to the fourth reaction mixture to prepare a fifth reaction mixture; and

(h) adding the remainder of the second solution to the fifth reaction mixture to prepare a sixth reaction mixture to provide **Intermediate I-6:**



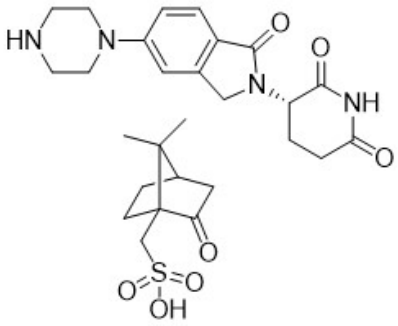
I-6

Claim 17. The method of claim 1, wherein **Intermediate I-8** is prepared by a method comprising reacting **Intermediate I-4**:



I-4

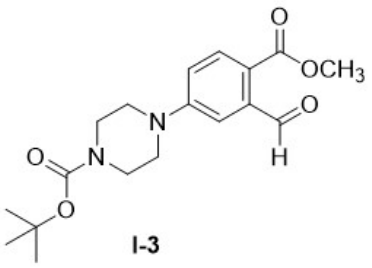
and camphorsulfonic acid in a solvent to provide **Intermediate I-8**:



I-8

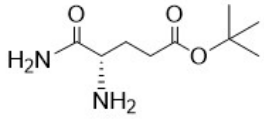
and one or more byproducts.

Claim 18. The method of claim 17, wherein **Intermediate I-4** is prepared by a method comprising reacting **Intermediate I-3**:



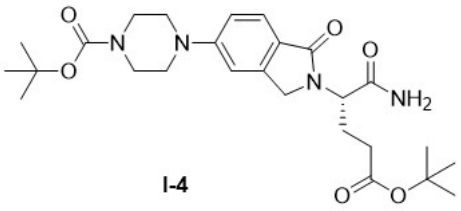
I-3

with **Intermediate I-3A**:



I-3A

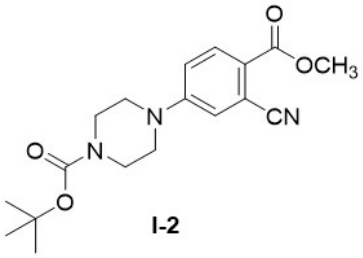
in a solvent in the presence of a reducing agent to provide **Intermediate I-4**:



I-4

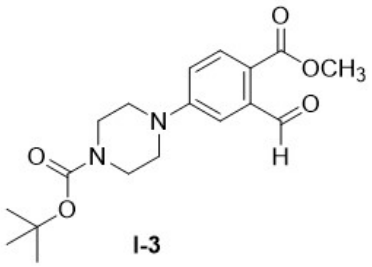
.

Claim 19. The method of claim 18, wherein **Intermediate I-3** is prepared by a method comprising reducing **Intermediate I-2**:



I-2

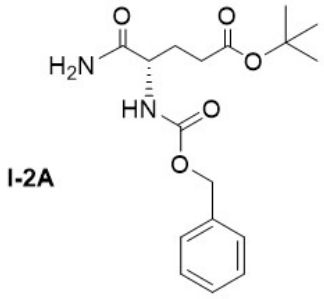
in a solvent in the presence of a reducing agent to provide **Intermediate I-3**:



I-3

.

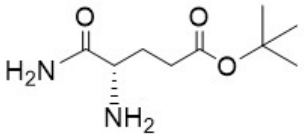
Claim 20. The method of claim 18, wherein the **Intermediate I-3A** is prepared by a method comprising reacting **Intermediate I-2A**:



I-2A

,

a hydrogen source, and, optionally, a catalyst, in a solvent to provide **Intermediate I-3A**:

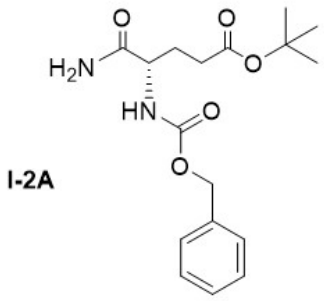


I-3A

.

Claim 21. A method, comprising:

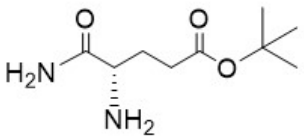
(a) reacting **Intermediate I-2A**:



I-2A

,

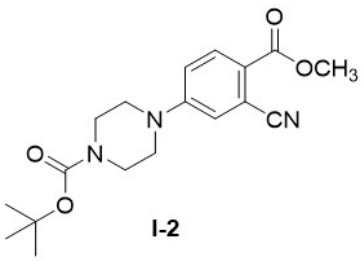
a hydrogen source, and, optionally, a catalyst, in a solvent to provide **Intermediate I-3A**:



I-3A

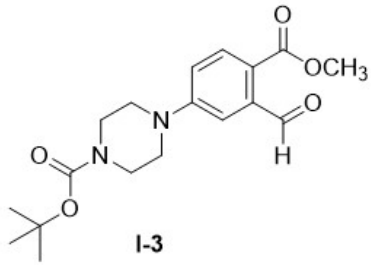
;

(b) reducing **Intermediate I-2**:



I-2

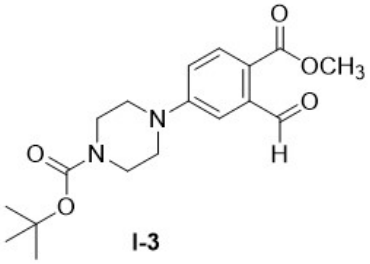
in a solvent in the presence of a reducing agent to provide **Intermediate I-3**:



I-3

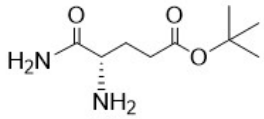
;

(c) reacting **Intermediate I-3**:



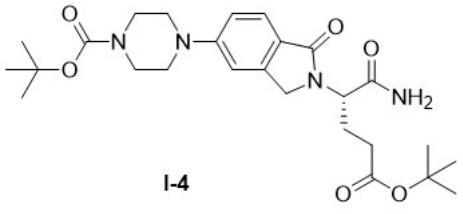
I-3

with **Intermediate I-3A**:



I-3A

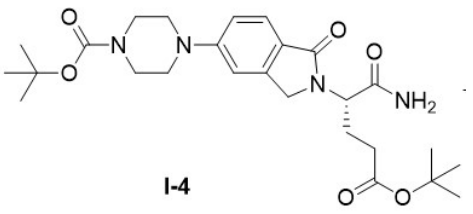
in a solvent in the presence of a reducing agent to provide **Intermediate I-4**:



I-4

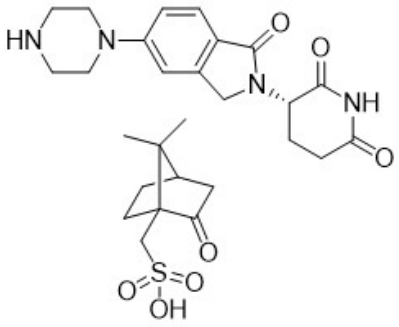
;

(d) reacting **Intermediate I-4:**



I-4

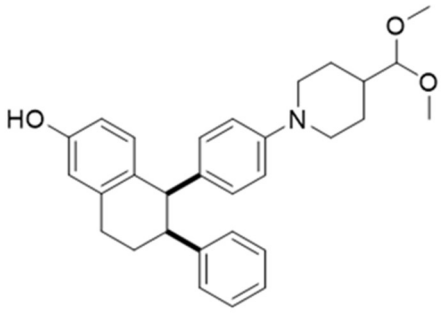
and camphorsulfonic acid in a solvent to provide salt **Intermediate I-8**:



I-8

and one or more byproducts;

(e1) combining racemic **Intermediate I-5:**



I-5

with an additive in a solvent to prepare a first reaction mixture;

(e2) heating the first reaction mixture at reflux to prepare a first solution, followed by cooling the first solution to a temperature of about 50 °C to about 100 °C;

(e3) combining (R)-proline and water to prepare a second solution, wherein the molar ratio of (R)-proline to the total amount of **Intermediate I-5** is about 0.40:1 to about 1.00:1;

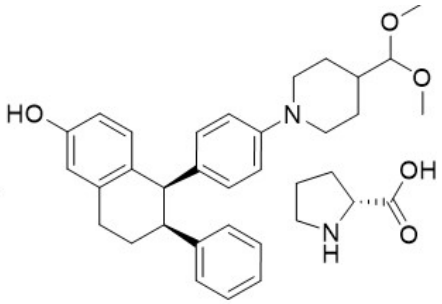
(e4) adding about 1% to less than about 50% by volume of the second solution to the first solution to prepare a second reaction mixture;

(e5) adding a first amount of an agent that induces nucleation to the second reaction mixture to prepare a third reaction mixture;

(e6) adding about 1% to less than about 50% by volume of the second solution to the third reaction mixture to prepare a fourth reaction mixture;

(e7) adding a second amount of the agent that induces nucleation to the fourth reaction mixture to prepare a fifth reaction mixture; and

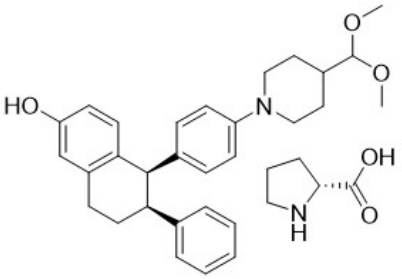
(e8) adding the remainder of the second solution to the fifth reaction mixture to prepare a sixth reaction mixture to provide **Intermediate I-6:**



I-6

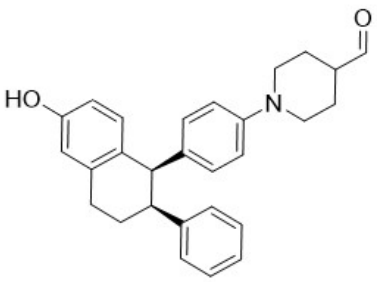
;

(h) reacting **Intermediate I-6:**



I-6

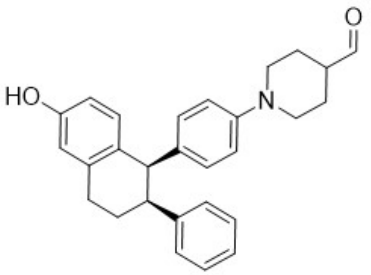
with an acid to provide **Intermediate I-9**:



I-9

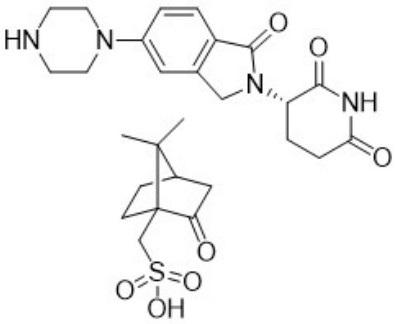
;

(i) reductively aminating **Intermediate I-9:**



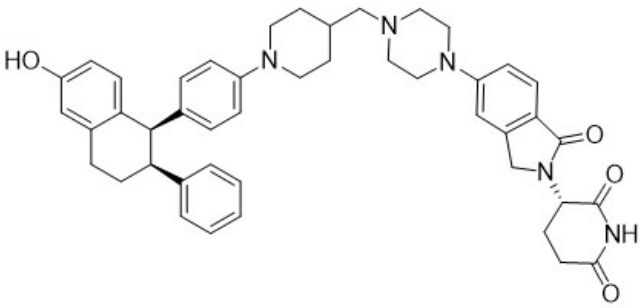
I-9

with salt **Intermediate I-8**:



I-8

in the presence of a base and a reducing agent to provide Compound 1:



Compound 1

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