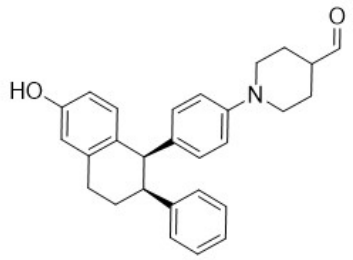
CLAIMS

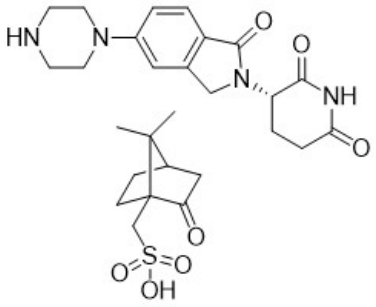
We claim:

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



I-9

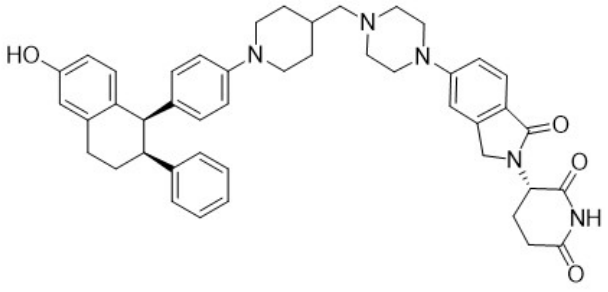
with **Intermediate I-8**:



I-8

,

In the presence of 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. The method of any one of claims 1–4, wherein the base is N-methyl-morpholine; the reducing agent is sodium triacetoxyborohydride; and the solvent is dimethylacetamide.

Claim 6. The method of any one of claims 1-5, wherein the molar ratio of N-methyl-morpholine to **Intermediate I-8** is 1.00:1, 1.05:1, 1.10:1, 1.15:1, 1.20:1, 1.25:1, 1.30:1, 1.35:1, 1.40:1, 1.45:1, 1.50:1, 1.55:1, 1.60:1, 1.65:1, 1.70:1, 1.75:1, 1.80:1, 1.85:1, 1.90:1, 1.95:1, 2.00:1, 2.05:1, 2.10:1, 2.15:1, 2.20:1, 2.25:1, 2.30:1, 2.35:1, 2.40:1, or 2.45:1.

Claim 7. The method of any one of claims 1-6, wherein the molar ratio of sodium triacetoxyborohydride to **Intermediate I-8** is 1.00:1, 1.05:1, 1.10:1, 1.15:1, 1.20:1, 1.25:1, 1.30:1, 1.35:1, 1.40:1, 1.45:1, 1.50:1, 1.55:1, 1.60:1, 1.65:1, 1.70:1, 1.75:1, 1.80:1, 1.85:1, 1.90:1, 1.95:1, 2.00:1, 2.05:1, or 2.10:1.

Claim 8. The method of any one of claims 1-7, wherein the method is conducted at a temperature of -30°C to 30°C.

Claim 9. The method of any one of claims 1–8, wherein the method is conducted at a temperature of 0°C, 5°C, 10°C, 15°C, or 20°C.

Claim 10. The method of any one of claims 1-9, further comprising quenching with water, an alcohol, or a combination thereof, to form a first solution.

Claim 11. The method of claim 10, further comprising forming a precipitate comprising **Compound 1**, wherein the first solution is added to a second solution of an alcohol and water to form the precipitate comprising **Compound 1**.

Claim 12. The method of claim 11, wherein the alcohol is ethanol.

Claim 13. The method of claim 11, wherein the first solution is added to the second solution of alcohol and water at a temperature of 50°C to 90°C.

Claim 14. The method of claim 11, wherein the ratio of alcohol:water in the second solution is 1:1 (v/v).

Claim 15. The method of claim 11, further comprising adding an agent that induces nucleation to a mixture of the first solution and the second solution.

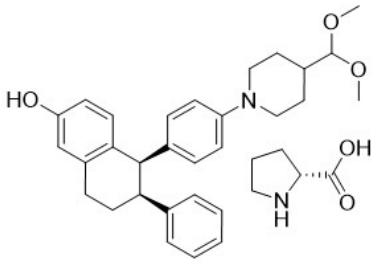
Claim 16. The method of claim 15, wherein the agent that induces nucleation is a crystallization promoter.

Claim 17. The method of claim 16, wherein the crystallization promoter is a seed crystal of **Compound 1**.

Claim 18. The method of claim 11, further comprising cooling and filtering the precipitate to provide a filtrate that is washed with water and an alcohol.

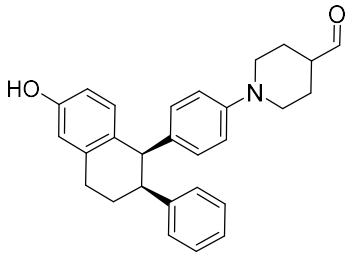
Claim 19. The method of claim 18, wherein the filtrate is washed with water and ethanol.

Claim 20. 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**:

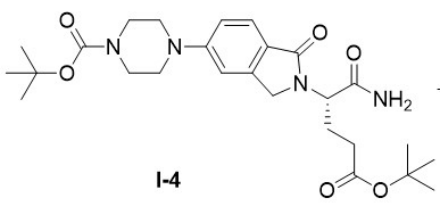


I-9

Claim 21. The method of claim 20, wherein **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.

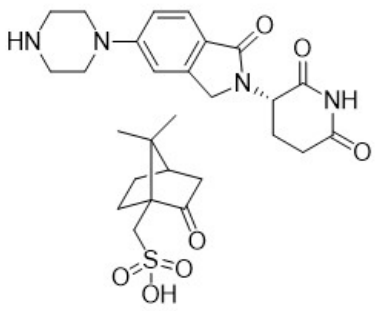
Claim 22. The method of claim 20, wherein the additive is dibutylhydroxytoluene, ascorbic acid, alpha-tocopherol, or ethylenediaminetetraacetic acid.

Claim 23. The method of claim 1, wherein **Intermediate I-8** is prepared by a method comprising reacting **Intermediate I-4**:



I-4

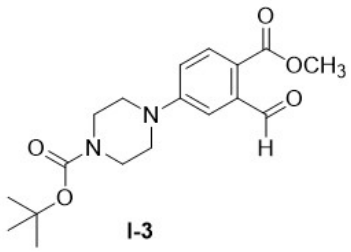
and camphorsulfonic acid in a solvent to provide **Intermediate I-8**:



I-8

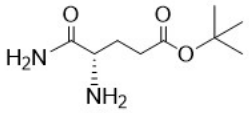
and one or more byproducts.

Claim 24. The method of claim 23, wherein **Intermediate I-4** is prepared by a method comprising reacting **Intermediate I-3**:



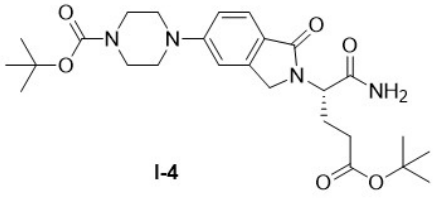
I-3

with **Intermediate I-3A**:



I-3A

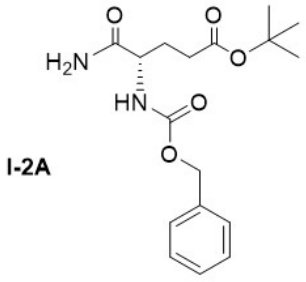
in a solvent in the presence of a reducing agent to provide **Intermediate I-4**:



I-4

.

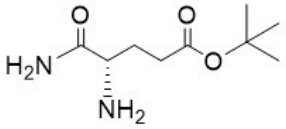
Claim 25. The method of claim 24, wherein the **Intermediate I-3A** is prepared by a method comprising reacting **Intermediate I-2A**:



I-2A

,

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



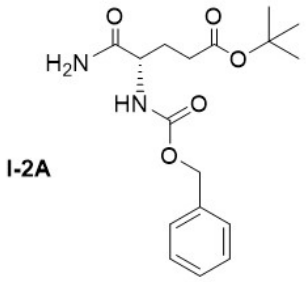
I-3A

.

Claim 26. The method of claim 24, wherein the reducing agent is sodium cyanoborohydride.

Claim 27. A method for preparing **Compound 1**, comprising:

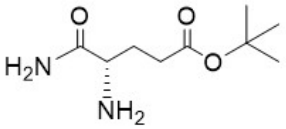
(a) reacting **Intermediate I-2A**:



I-2A

,

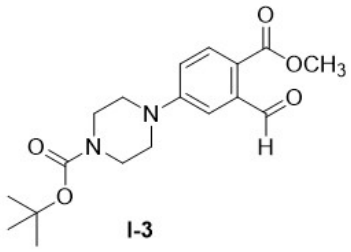
a hydrogen source, and, optionally, a catalyst, in a solvent to provide **Intermediate I-3A**:



I-3A

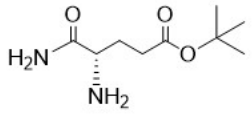
;

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



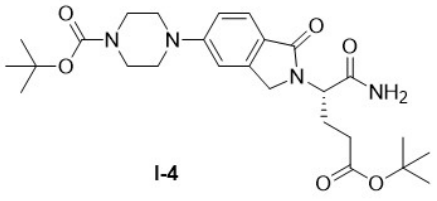
I-3

with **Intermediate I-3A**:



I-3A

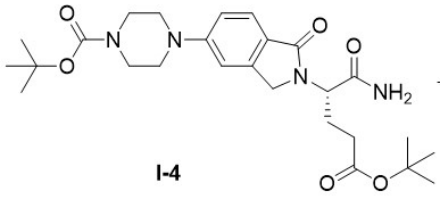
in a solvent in the presence of a reducing agent to provide **Intermediate I-4**:



I-4

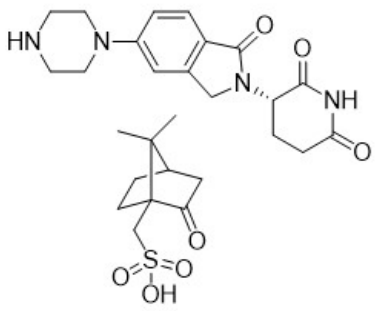
;

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



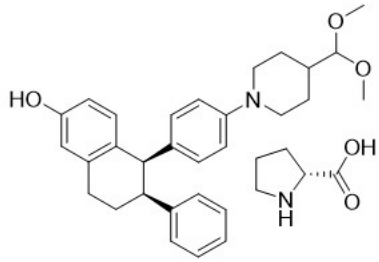
I-4

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



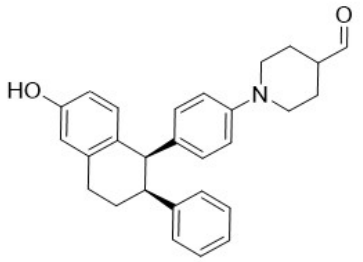
I-8

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



I-6

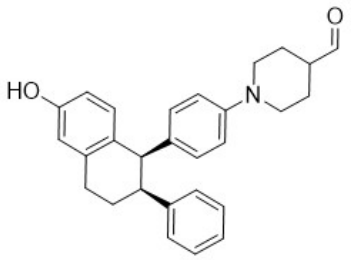
with an acid to provide **Intermediate I-9**:



I-9

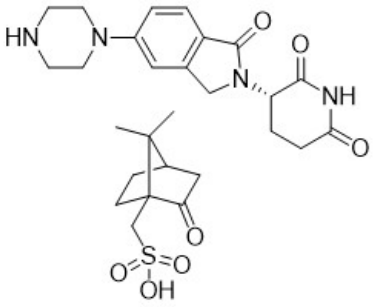
;

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



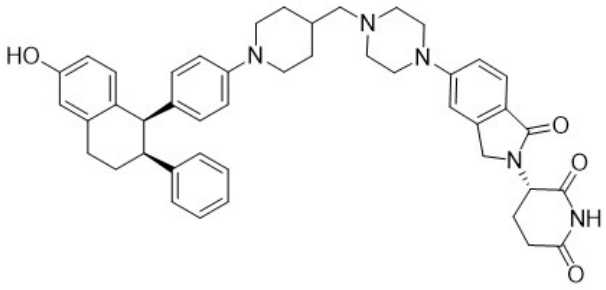
I-9

with **Intermediate I-8**:



I-8

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

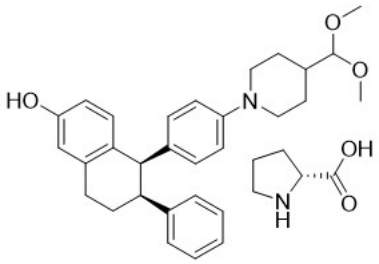


Compound 1

.

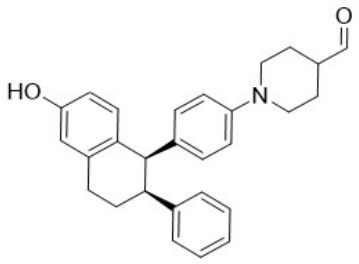
Claim 28. A method for preparing **Compound 1**, comprising:

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



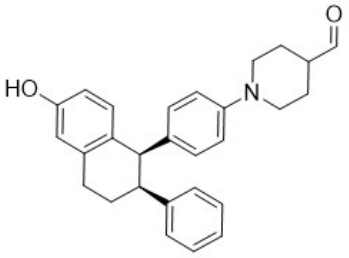
I-6

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



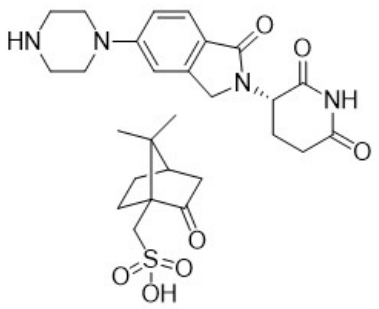
I-9

(b) contacting **Intermediate I-9:**



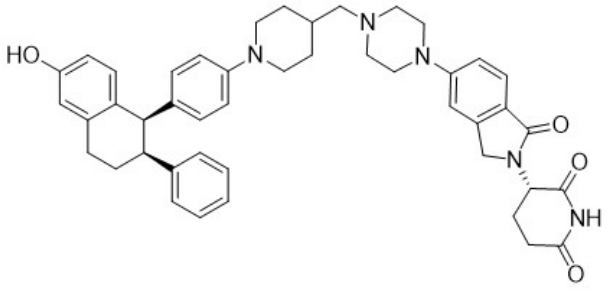
I-9

with **Intermediate I-8**:



I-8

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

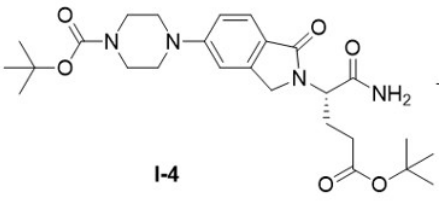


Compound 1

.

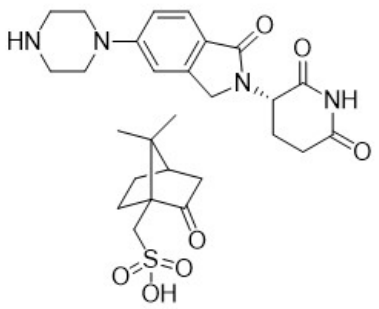
Claim 29. A method for preparing **Compound 1**, comprising:

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



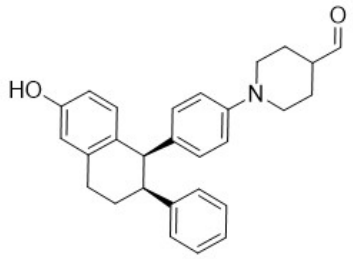
I-4

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



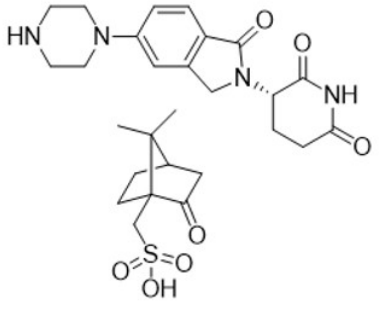
I-8

(b) contacting **Intermediate I-9:**



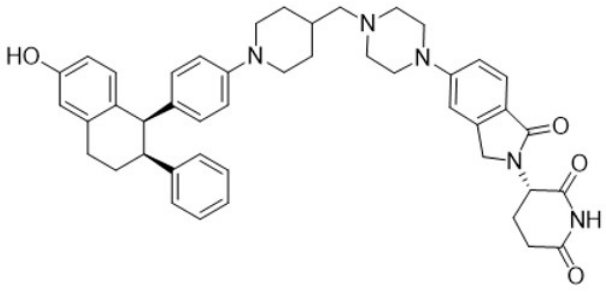
I-9

with **Intermediate I-8**:



I-8

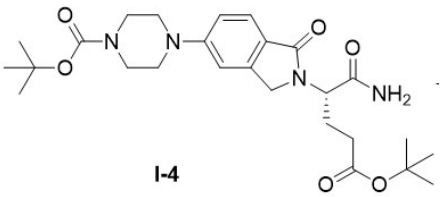
in the presence of a base and a reducing agent to provide Compound 1:



Compound 1

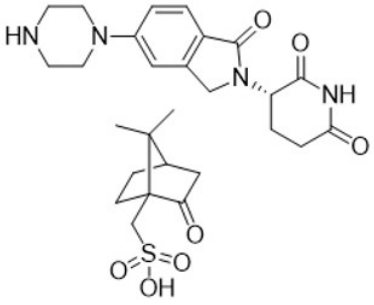
Claim 30. A method for preparing **Compound 1**, comprising:

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



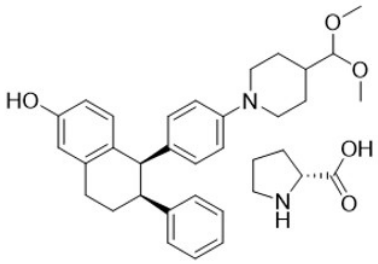
I-4

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



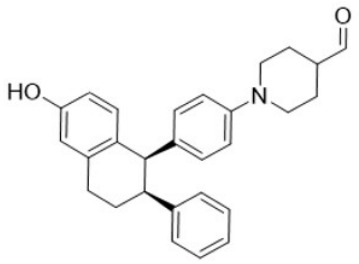
I-8

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



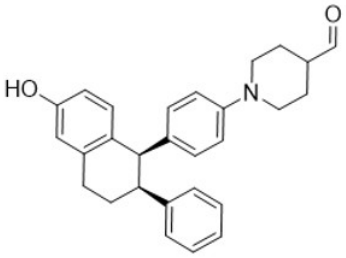
I-6

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



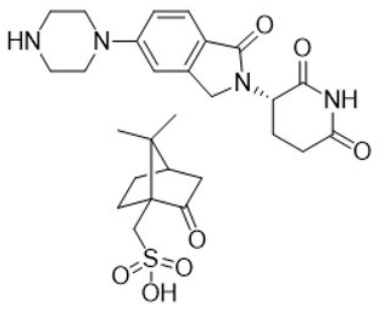
I-9

(c) contacting **Intermediate I-9:**



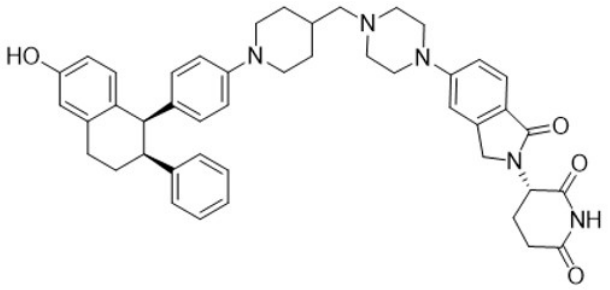
I-9

with **Intermediate I-8**:



I-8

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



Compound 1

.