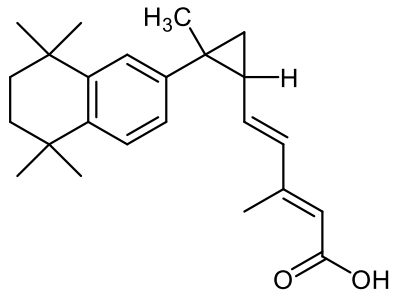
CLAIMS

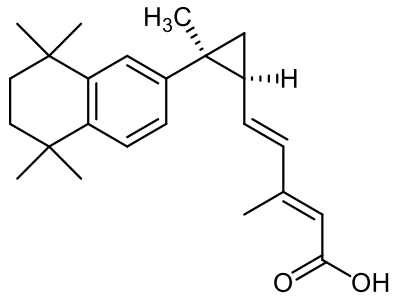
1. A method of making Compound 38,



Compound 38,

or a pharmaceutically acceptable salt thereof, wherein:

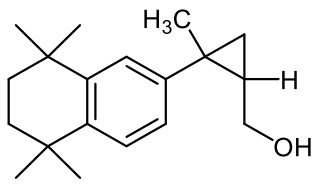
Compound 38 has an enantiomeric excess of Compound A,



Compound A,

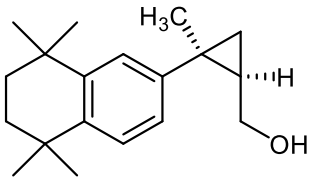
of least about 98.0 %;

comprising a synthetic process of preparing an intermediate compound, wherein the intermediate compound is Formula (XIa),



(XIa),

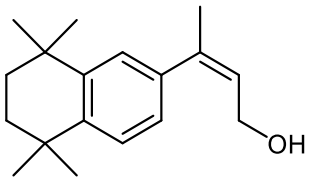
or a hydrate or a solvate thereof, wherein the intermediate compound has an enantiomeric excess of a compound of Formula (XI),



(XI),

or a hydrate or a solvate thereof,

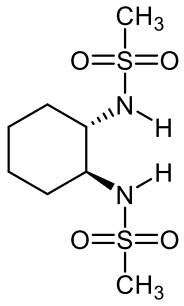
of at least about 80.0 %; wherein the process of preparing the intermediate compound, comprises contacting a compound of Formula (XII),



(XII),

or a solvate thereof, with:

a) CH_2I_2, Et_2Zn, ZnI_2, and an enantioselectivity inducer of Formula (XV) or its enantiomer,

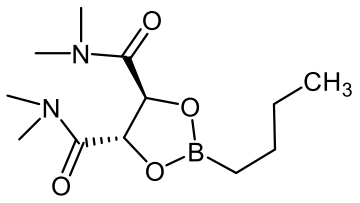


(XV),

or a solvate thereof,

such that the intermediate compound is prepared; or

b) (i) an enantioselectivity inducer of Formula (XIII),



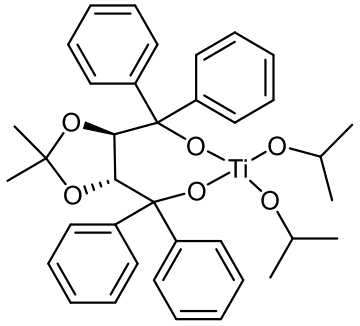
(XIII),

or a solvate thereof,

in a solution in the presence of CH_2I_2 and Et_2Zn to form a reaction product of the compound of Formula (XII), or a solvate thereof; and

(ii) subsequently, contacting the solution of step (i) with H_2O_2, such that the compound of Formula (XI) or a solvate thereof is prepared; or

c) an enantioselectivity inducer of Formula (XIV) or its enantiomer,



(XIV),

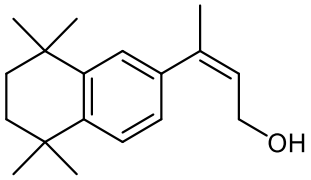
or a solvate thereof,

in the presence of CH_2I_2 and dialkylzinc such that the intermediate compound is prepared,

wherein the entire method of making Compound 38 comprises only a single synthetic step to produce the compound of Formula (XI).

2. The method of claim 1, wherein the process of preparing the intermediate compound, comprises:

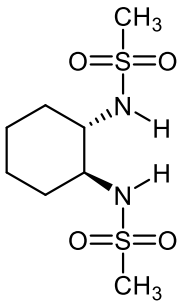
contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

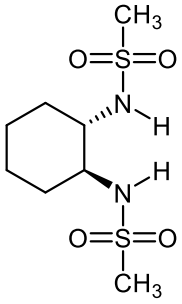
with CH_2I_2, Et_2Zn, ZnI_2, and the enantioselectivity inducer of Formula (XV) or its enantiomer,



(XV),

or a solvate thereof, such that the intermediate compound is prepared.

3. The method of claim 2, wherein the enantioselectivity inducer or a solvate thereof, is

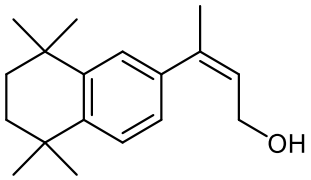


(XV),

or a solvate thereof.

4. The method of claim 1, wherein the process of preparing the intermediate compound, comprises:

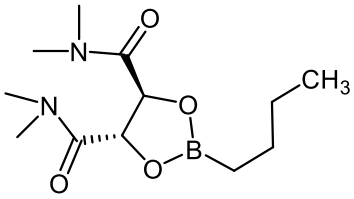
(i) contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

with the enantioselectivity inducer of Formula (XIII),



(XIII),

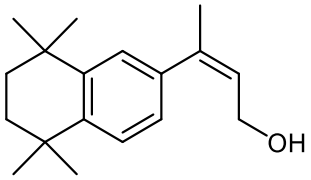
or a solvate thereof,

in a solution in the presence of CH_2I_2 and Et_2Zn to form a reaction product of the compound of Formula (XII), or a solvate thereof; and

(ii) subsequently, contacting the solution of step (i) with H_2O_2, such that the compound of Formula (XI) or a solvate thereof is prepared.

5. The method of claim 1, wherein the process of preparing the intermediate compound, comprises:

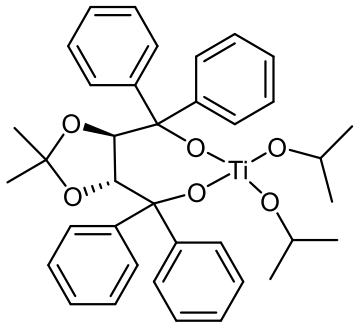
contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

with the enantioselectivity inducer of Formula (XIV) or its enantiomer,



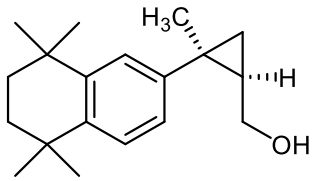
(XIV),

or a solvate thereof,

in the presence of CH_2I_2 and dialkylzinc such that the intermediate compound is prepared.

6. The method of claim 2, wherein the ZnI_2 is formed by reacting Et_2Zn with I_2.

7. A method of synthesizing and working-up a compound of Formula (XI),

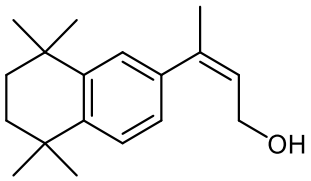


(XI),

or a hydrate or a solvate thereof,

having an enantiomeric excess of at least about 85 % over its enantiomer; wherein the of Formula (XI) compound is prepared by a process comprising:

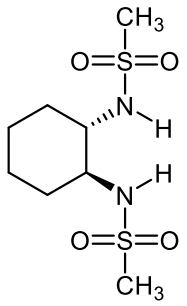
contacting a compound of Formula (XII),



(XII),

or a solvate thereof, with

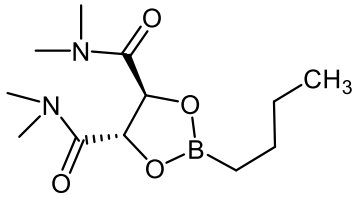
a) CH_2I_2, Et_2Zn, ZnI_2, and an enantioselectivity inducer of Formula (XV) or its enantiomer,



(XV),

or a solvate thereof,
such that the compound of Formula (XI) is prepared; or

b) (i) an enantioselectivity inducer of Formula (XIII),

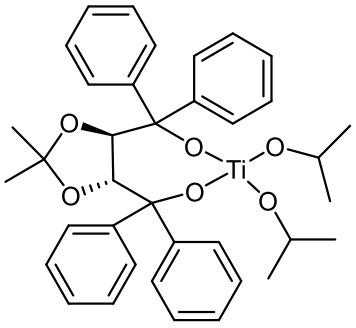


(XIII),

or a solvate thereof,
in a solution in the presence of CH_2I_2 and Et_2Zn to form a reaction product of the compound of Formula (XII), or a solvate thereof; and

(ii) subsequently, contacting the solution of step (i) with H_2O_2, such that the compound of Formula (XI) or a solvate thereof is prepared; or

c) an enantioselectivity inducer of Formula (XIV) or its enantiomer,



(XIV),

or a solvate thereof,

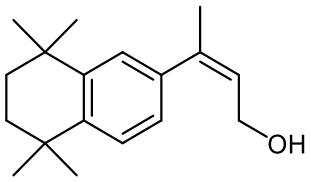
in the presence of CH_2I_2 and dialkylzinc such that the compound of Formula (XI) is prepared,

wherein the synthesis and work-up comprise a single synthetic step.

8. The method of claim 7, wherein the compound is present in an enantiomeric excess is at least about 98.0 % over its enantiomer.

9. The method of claim 7, wherein the compound is synthesized and worked-up by a process comprising:

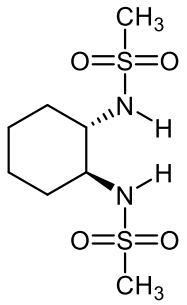
contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

with CH_2I_2, Et_2Zn, ZnI_2, and the enantioselectivity inducer of Formula (XV) or its enantiomer,

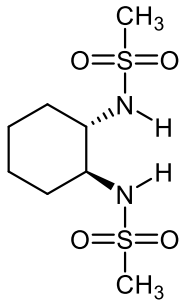


(XV),

or a solvate thereof,

such that the compound is prepared.

10. The method of claim 9, wherein the enantioselectivity inducer is

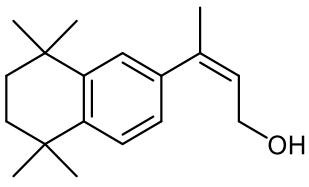


(XV),

or a solvate thereof.

11. The method of claim 7, wherein the compound is synthesized and worked-up by a process comprising:

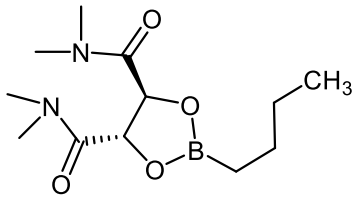
(i) contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

with the enantioselectivity inducer of Formula (XIII),



(XIII),

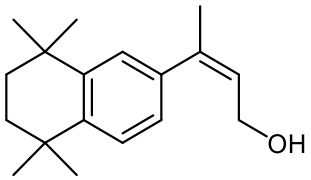
or a solvate thereof,

in a solution in the presence of CH_2I_2 and Et_2Zn to form a reaction product of the compound of Formula (XII), or a solvate thereof; and

(ii) subsequently, contacting the solution of step (i) with H_2O_2, such that the compound of Formula (XI) or a solvate thereof is prepared.

12. The method of claim 7, wherein the compound is synthesized and worked-up by a process comprising:

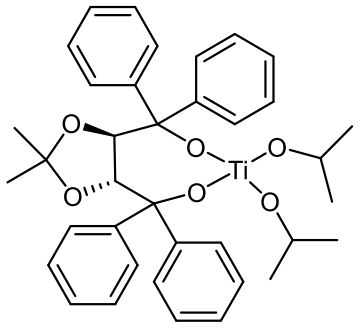
contacting a compound of Formula (XII),



(XII),

or a solvate thereof,

with the enantioselectivity inducer of Formula (XIV) or its enantiomer,



(XIV),

or a solvate thereof,

in the presence of CH_2I_2 and dialkylzinc such that the compound of claim 23 is prepared.

13. The method of claim 9, wherein the ZnI_2 is formed by reacting Et_2Zn with I_2.

~~14. The method of claim 1, further comprising purification of the compound of Formula (XI), wherein said purification comprises recrystallization.~~

~~15. The method of claim 4, further comprising purification of the compound of Formula (XI), wherein said purification consists of solvent stripping, filtration, extraction, distillation, evaporation, recrystallization, or combinations thereof.~~

~~16. The method of claim 7, wherein said working-up comprises purification of the compound of Formula (XI), wherein said purification comprises recrystallization.~~

~~17. The method of claim 11, wherein said working-up comprises purification of the compound of Formula (XI), wherein said purification consists of solvent stripping, filtration, extraction, distillation, evaporation, recrystallization, or combinations thereof.~~