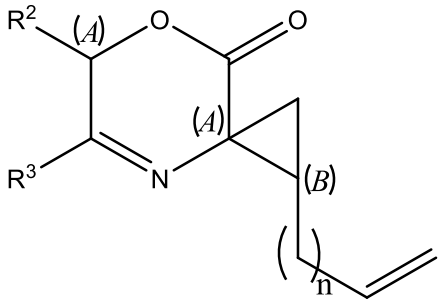
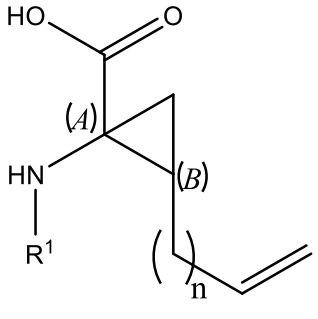


Id

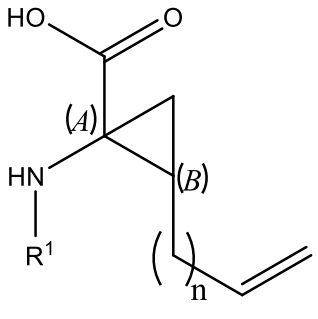
where R^2 is isopropyl, R^3 is phenyl, A is either *S* or *R*, B is *R* when A is *S* or B is *S* when A is *R* and n is 5, to aqueous NaOH in ethanol to hydrolyze the oxazine ring, and then expose this product to a halide salt of a protecting group in aqueous THF to protect the amine group, to produce a compound of Formula I



I

where R^1 is a protecting group, A is either *S* or *R*, B is *R* when A is *S* or B is *S* when A is *R* and n is 5.

[00024] There is provided a compound of Formula I



I

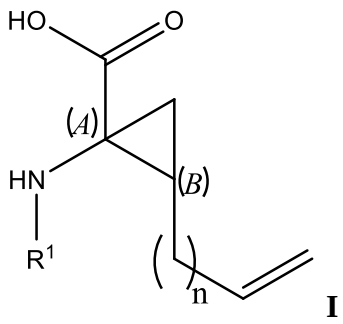
wherein:

R^1 is a protecting group;

n is an integer between 1 and 10, and;

A and B are chiral centers such that when A is *S*, B is *R* and when A is *R*, B is *S*.

[00024a] In a second aspect of the present disclosure there is provided a compound of Formula I



I

wherein:

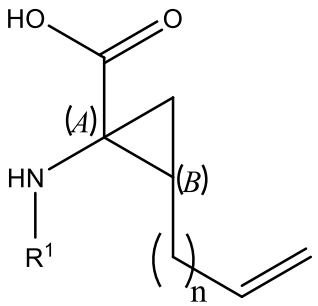
R^1 is a protecting group removable in a basic solution;

n is an integer between 1 and 10, and;

A and B are chiral centers such that when A is *S*, B is *R* and when A is *R*, B is *S*.

CLAIMS

1. A method for producing a compound of Formula I



I

wherein:

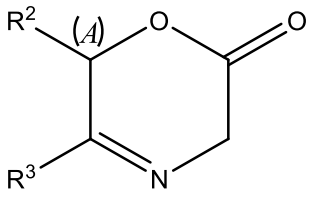
R^1 is a protecting group;

n is an integer between 1 and 10, and;

A and B are chiral centers such that when A is *S*, B is *R* and when A is *R*, B is *S*;

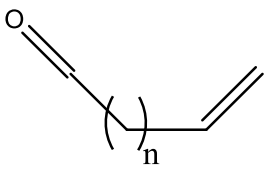
said method comprising the steps of:

a) condensing a chiral compound of Formula Ia



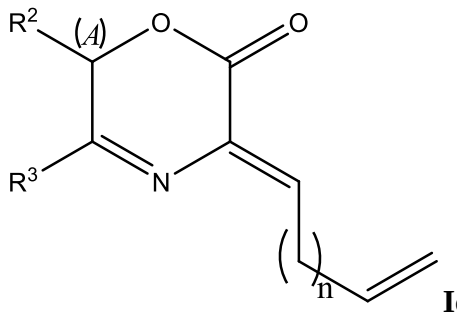
Ia

with a compound of Formula Ib



Ib

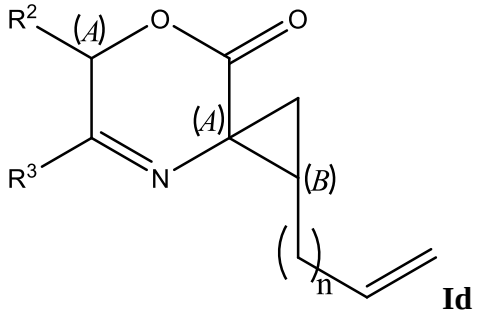
to produce a compound of Formula Ic



Ic

wherein A is a chiral center, R^2 is an aliphatic group with a tertiary or quaternary carbon atom covalently bonded to the chiral center A, and R^3 is aryl or heteroaryl;

b) reacting the non-terminal carbon-carbon double bond formed in step a) to produce a cyclopropyl group, so as to form a compound of Formula Id



Id

and;

c) hydrolyzing the compound of Formula Id and protecting a free amine produced by the hydrolysis with a reagent comprising R^1 to produce the compound of Formula I.

2. The method of claim 1 wherein:
   - R^1 is a protecting group which is removable in a basic solution; and/or
   - R^2 is a branched hydrocarbyl group; and/or
   - R^3 is aryl; and/or
   - n is an integer between 1 and 6; and/or
   - A is *S* and B is *R* or A is *R* and B is *S*.

3. The method of claim 1 or claim 2, wherein step a) is conducted in the presence of a catalyst and a base, wherein the catalyst is a quaternary ammonium salt and the base is a basic inorganic salt.

4. The method of claim 3 wherein the catalyst is a tetraalkylammonium salt.

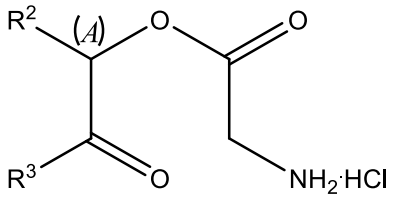
5. The method of claim 4, wherein the catalyst is tetra-n-butylammonium bromide.

6. The method of any one of claims 1 to 5, wherein step a) is conducted in a dipolar aprotic solvent and at a temperature between 0°C and 25°C, and step b) is conducted at a temperature between 20°C and 100°C.

7. The method of any one of claims 1 to 6, wherein step b) comprises the reaction of compound Ic with a trialkyl sulfoxonium halide, in the presence of a group I hydride and an organic solvent, wherein:
   - the trialkyl sulfoxonium halide species comprises three alkyl groups independently selected from methyl, ethyl, propyl, butyl and pentyl, wherein at least one alkyl group is methyl; and/or
   - the halide group of the trialkyl sulfoxonium halide species is selected from the group comprising fluoride, chloride, bromide and iodide, optionally wherein the trialkyl sulfoxonium halide species is trimethyl sulfoxonium chloride; and/or
   - wherein the group I hydride is LiH, NaH or KH; and/or
   - wherein the organic solvent is a polar aprotic solvent, optionally wherein the organic solvent is tetrahydrofuran.

8. The method of any one of claims 1 to 7, wherein step c) comprises exposing the compound of Formula Id to an aqueous strong base and a compound of general formula R^1X, wherein R^1 is as defined in claim 1 or claim 2, X is a halogen selected from fluorine, chlorine, bromine and iodine, and the strong base is LiOH, NaOH, KOH or NH_4OH, and wherein step c) is conducted at room temperature.

9. The method of any one of claims 1 to 8, further comprising the step of preparing the compound of Formula Ia by carrying out a dehydration reaction of a compound of Formula IIa



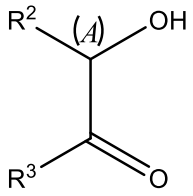
IIa.

to form an oxazine ring, wherein the dehydration reaction comprises exposing the compound of Formula Ia to a trialkylamine, wherein the trialkylamine comprises three alkyl groups, each independently selected from the group comprising methyl, ethyl, propyl and butyl, and

wherein the dehydration reaction is conducted at room temperature in an acidified organic solvent, wherein the acidified organic solvent is an acidified organic ester and comprises HF, HCl, HBr or HI.

10. The method of claim 9, wherein about one molar equivalent of the trialkylamine is used when compared to the amount of conjugate acid of Formula IIa that is present.

11. The method of claim 9 or 10, further comprising a step of preparing the compound of Formula IIa, said step comprising the addition of a protected glycine compound to a compound of Formula IIb



IIb

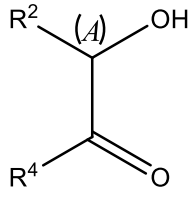
wherein the protected glycine compound comprises a covalently bound protecting group.

12. The method of claim 11, wherein the glycine is added by exposing a compound of Formula IIa to a nucleophilic catalyst, a coupling agent and the protected glycine compound, wherein:

- the nucleophilic catalyst is a basic nucleophilic catalyst; and/or
- the coupling agent is capable of converting carboxylic acids to activated esters; and/or
- the protecting group is an acid labile protecting group.

13. The method of claim 12, wherein the reaction is conducted at room temperature.

14. The method of claim 12 or 13, further comprising a step of preparing the compound of Formula IIb by conducting a reaction between a compound of Formula IIc



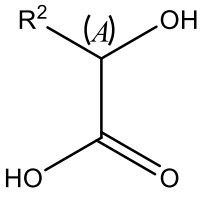
IIc

wherein R^4 is a dialkylamino group, and a Grignard reagent of general formula R^3MgBr in an organic ether solvent, optionally:

- wherein the dialkylamino group of R^4 comprises two alkyl groups, each independently selected from the group comprising methyl, ethyl, propyl and butyl; and/or
- the Grignard reagent is arylmagnesium bromide, optionally wherein the Grignard reagent is phenylmagnesium bromide.

15. The method of claim 14, wherein the reaction begins at a temperature of -78 °C and rises to room temperature during the reaction.

16. The method of claim 14 or 15, further comprising a step preparing the compound of Formula IIc by performing an amidation reaction on a compound of Formula IId



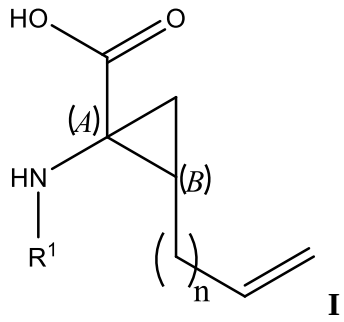
IId

wherein the amidation reaction is conducted by exposing a compound of Formula IId to a base, a catalyst, a coupling agent and a dialkyamine hydrohalide salt, wherein:

- the dialkyamine hydrohalide salt is of general formula $R^4H{\cdot}HX$, wherein R^4 is a dialkylamino group comprising two alkyl groups, and each alkyl group is independently selected from the group comprising methyl, ethyl, propyl and butyl, and X is a halogen; and/or

- the dehydrating agent is N,N'-dicyclohexylcarbodiimide or (2-(thiophen-2-yl)phenyl)boronic acid; and/or
- the catalyst is hydroxybenzotriazole; and/or
- the base is a sterically hindered base.

17. A compound of Formula I



I

wherein:

R^1 is a protecting group removable in a basic solution;

n is an integer between 1 and 10, and;

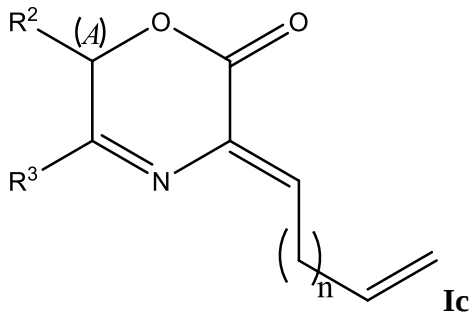
A and B are chiral centers such that when A is *S*, B is *R* and when A is *R*, B is *S*.

18. A compound according to claim 17, wherein A is *S* and B is *R*.

19. A compound according to claim 17, wherein A is *R* and B is *S*.

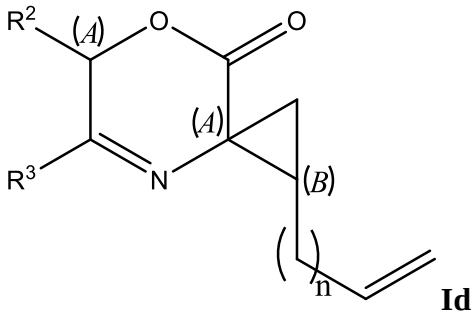
20. A compound of Formula I according to claim 17 being selected from the group consisting of: Fmoc-protected (1*S*,2*R*)-1-amino-2-(but-3-en-1-yl)cyclopropane-1-carboxylic acid; Fmoc-protected (1*R*,2*S*)-1-amino-2-(hept-6-en-1-yl)cyclopropane-1-carboxylic acid; Fmoc-protected (1*R*,2*S*)-1-amino-2-(but-3-en-1-yl)cyclopropane-1-carboxylic acid; and Fmoc-protected (1*S*,2*R*)-1-amino-2-(hept-6-en-1-yl)cyclopropane-1-carboxylic acid.

21. A compound of Formula Ic



Ic

or Formula Id



Id

wherein:

R^2 is an aliphatic group with a secondary or tertiary carbon atom covalently bonded to the chiral center A, optionally a branched hydrocarbyl group;

R^3 is aryl or heteroaryl;

n is an integer between 1 and 10, and;

A is a chiral center and B is a chiral center such that when A is *S*, B is *R* and when A is *R*, B is *S*.