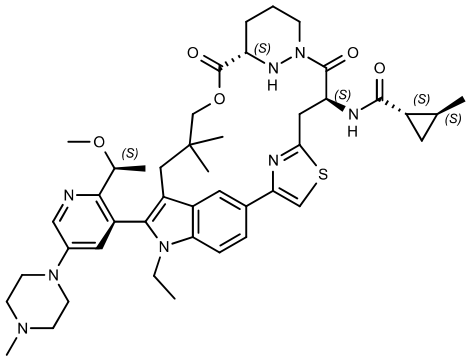
CLAIMS

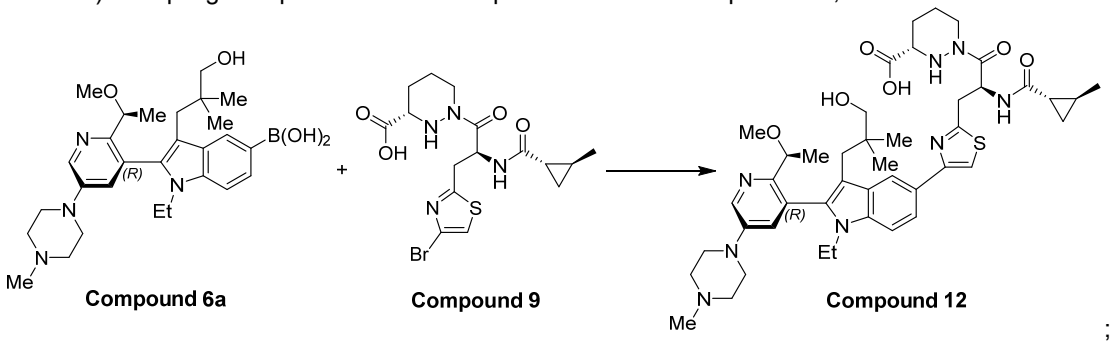
1. A method of preparing Compound A:



Compound A

the method comprising the steps of:

a) coupling Compound 6a and Compound 9 to form Compound 12, or a salt thereof:

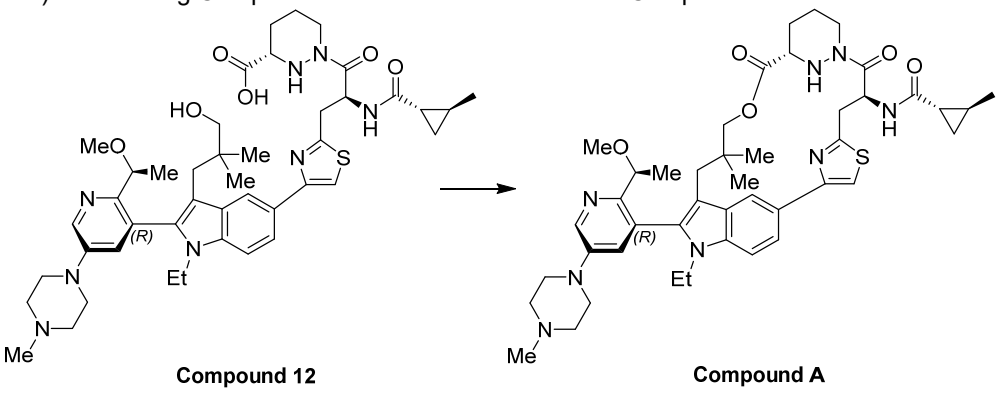


Compound 6a **Compound 9** **Compound 12**

;

and

b) lactonizing Compound 12 or a salt thereof to form Compound A:



Compound 12 **Compound A**

.

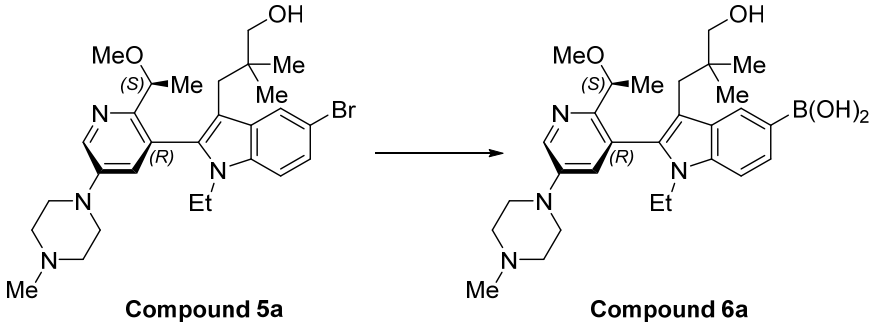
2. The method of claim 1, wherein the method further comprises the step of purifying Compound A, wherein the purifying comprises forming a salt of Compound A, isolating the salt, and converting the isolated salt of Compound A to a free base form of Compound A.

3. The method of claim 2, wherein the salt of Compound A is a hydrochloride salt of Compound A or a lactate salt of Compound A.

4. The method of any one of claims 1 to 3, wherein Compound 6a and Compound 9 are coupled in the presence of a palladium catalyst and a base.

5. The method of any one of claims 1 to 4, wherein lactonizing Compound 12 or a salt thereof occurs in the presence of EDCI, DMAP, HOBt, or DIPEA, or a combination thereof.

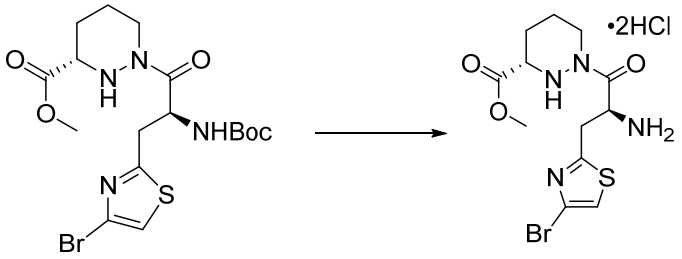
6. The method of any one of claims 1 to 5, wherein Compound 6a is prepared by borylating Compound 5a:



Compound 5a **Compound 6a** .

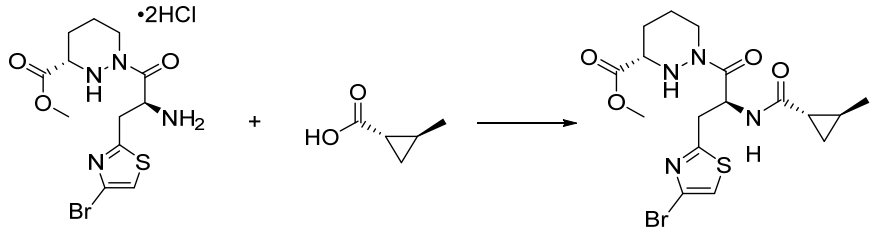
7. The method of any one of claims 1 to 6, wherein Compound 9 is prepared by:

a) deprotecting Compound 9e to form Compound 9f:



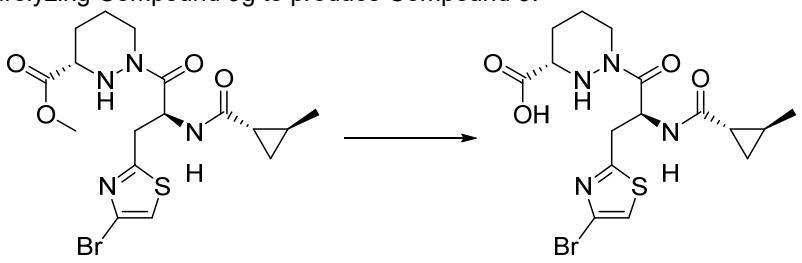
Compound 9e **Compound 9f** ;

b) coupling Compound 9f with Compound 3 to form Compound 9g:



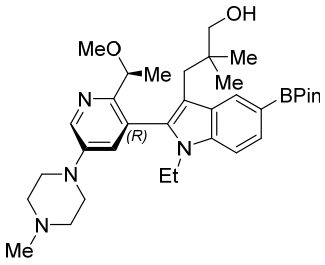
Compound 9f **Compound 3** **Compound 9g** ; and

c) hydrolyzing Compound 9g to produce Compound 9:



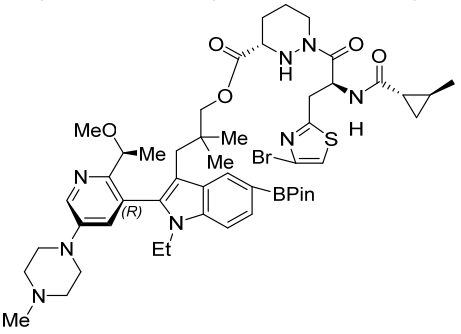
Compound 9g **Compound 9** .

8. A compound having the structure of Compound 10, Compound 11, or Compound 12:



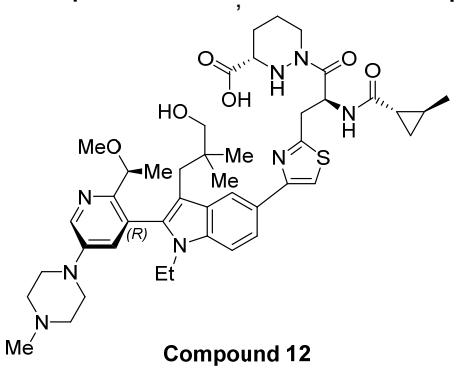
Compound 10

,



Compound 11

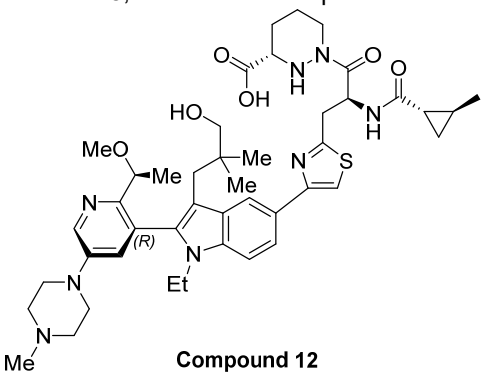
, or



Compound 12

, or a salt thereof.

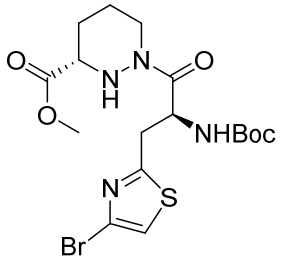
9. The compound of claim 8, wherein the compound has the structure of Compound 12:



Compound 12

, or a salt thereof.

10. A method of preparing Compound 9e :

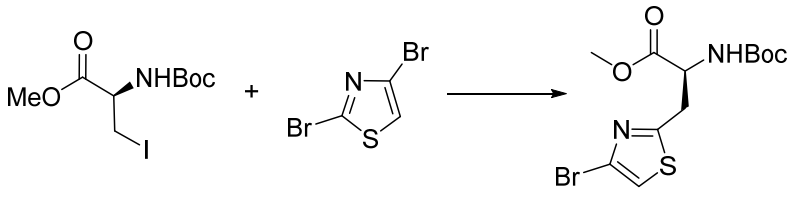


Compound 9e

,

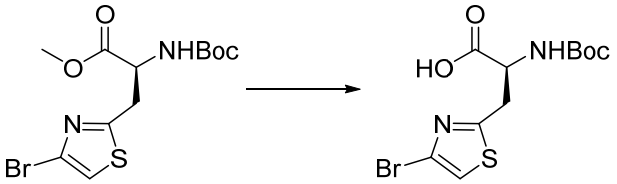
the method comprising:

a) coupling Compound 2a with Compound 9a to form Compound 9b:



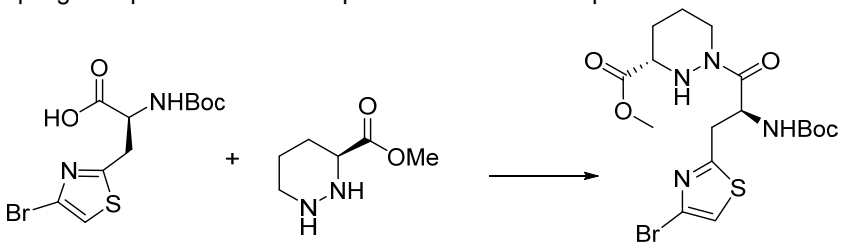
Compound 2a **Compound 9a** **Compound 9b** ;

b) hydrolyzing Compound 9b to form Compound 9c:



Compound 9b **Compound 9c** ; and

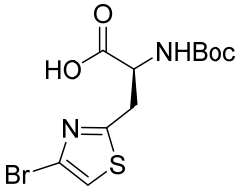
c) coupling Compound 9c and Compound 9d to form Compound 9e:



Compound 9c **Compound 9d** **Compound 9e** .

11. The method of claim 10, wherein:
Compound 2a and Compound 9a are coupled in the presence of a Zn catalyst;
Compound 9b is hydrolyzed in the presence of LiOH; and
Compound 9c and Compound 9d are coupled in the presence of EDCI.

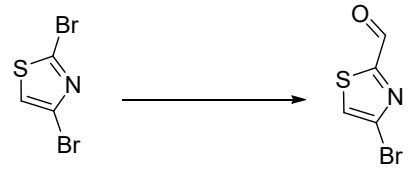
12. A method of preparing Compound 9c:



Compound 9c ,

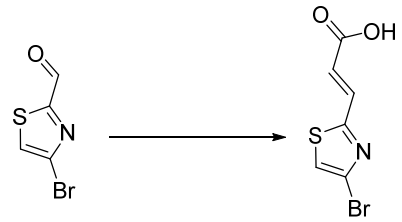
or a salt thereof, the method comprising:

a) formylating Compound 9c-1 to form Compound 9c-2:



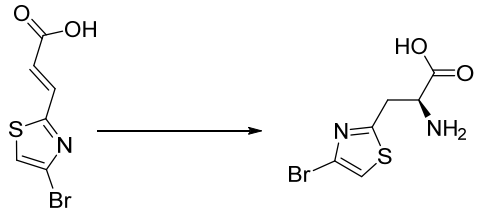
Compound 9c-1 **Compound 9c-2** ;

b) condensing Compound 9c with malonic acid to form Compound 9c-3:



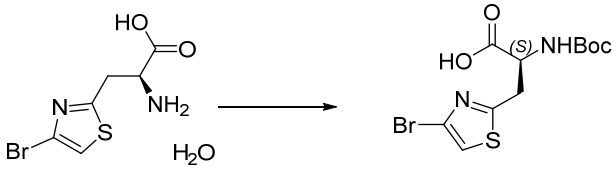
Compound 9c-2 **Compound 9c-3** ;

c) aminating Compound 9c-3 to form Compound 9c-4:



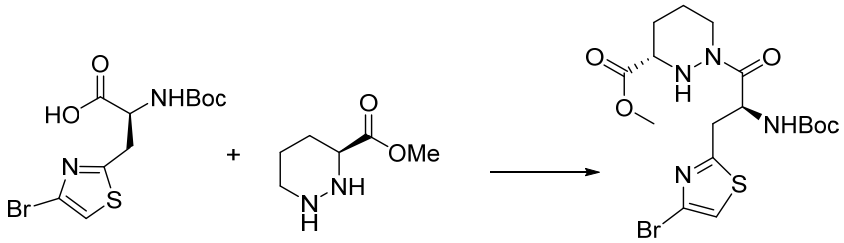
Compound 9c-3 **Compound 9c-4** ; and

d) protecting Compound 9c-4 to form Compound 9c:



Compound 9c-4 **Compound 9c** .

13. The method of claim 12, further comprising coupling Compound 9c and Compound 9d to form Compound 9e:



Compound 9c **Compound 9d** **Compound 9e** .

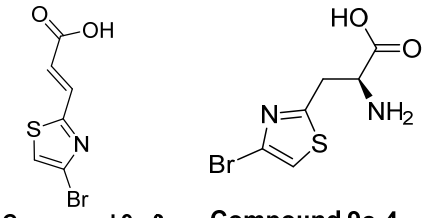
14. The method of claim 12 or 13, wherein formylating Compound 9c-1 comprises combining Compound 9c-1 with iPr-MgCl.

15. The method of any one of claims 12 to 14, wherein the aminating of Compound 9c-3 is catalyzed by an enzyme.

16. The method of claim 15, wherein the enzyme is phenylalanine ammonia lyase.

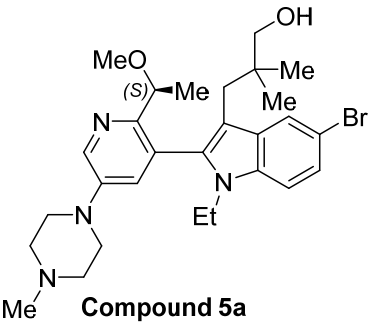
17. The method of any one of claims 12 to 16, wherein protecting Compound 9c-4 comprises combining Compound 9c-4 with Boc_2O and a base.

18. A compound, wherein the compound has the structure of Compound 9c-3 or Compound 9c-4:



Compound 9c-3 or **Compound 9c-4** .

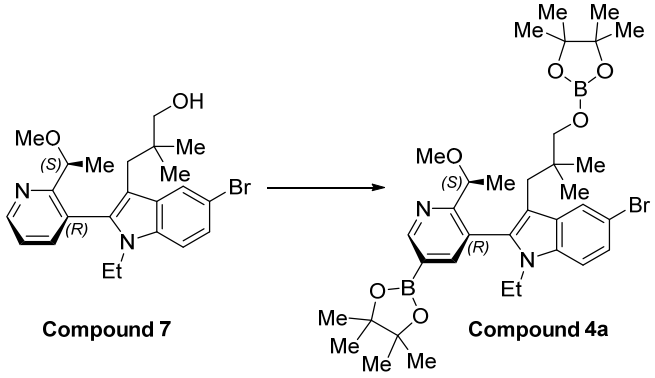
19. A method of preparing Compound 5a:



Compound 5a

the method comprising:

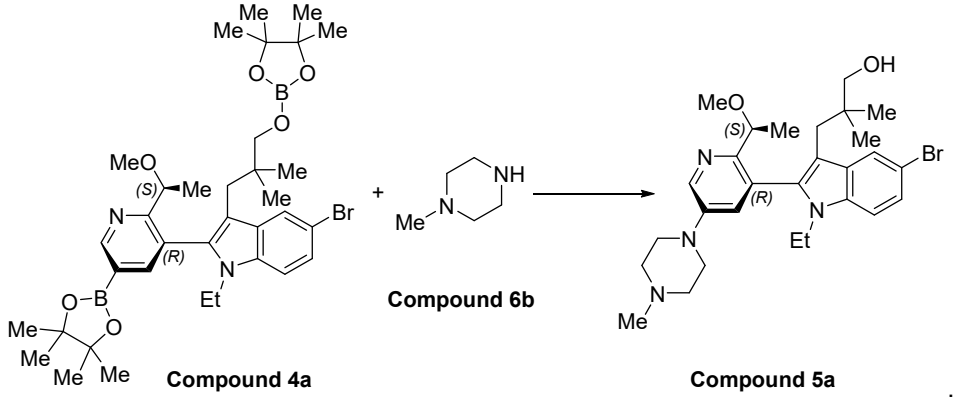
a) borylating Compound 7 to form Compound 4a:



Compound 7 **Compound 4a**

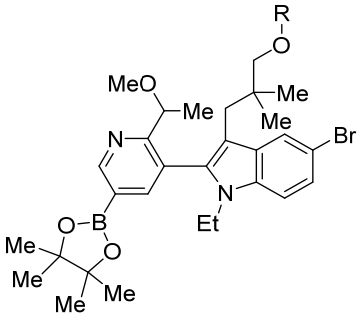
; and

b) coupling Compound 4a and Compound 6b to form Compound 5a:

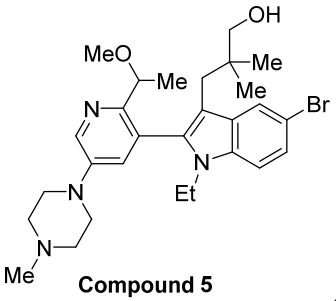


Compound 4a **Compound 6b** **Compound 5a** .

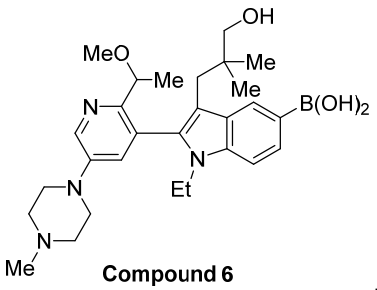
20. A compound having the structure of Formula III, Compound 5, or Compound 6:



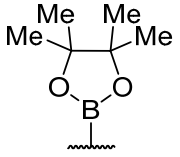
Formula III



Compound 5

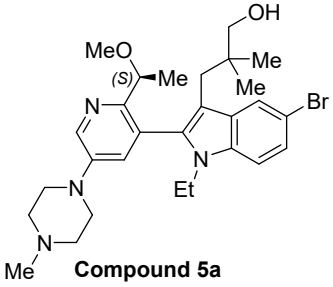


Compound 6



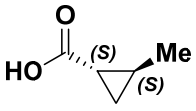
or a salt thereof, wherein R is H or .

21. The compound of claim 20, wherein the compound has the structure of Compound 5a:



Compound 5a

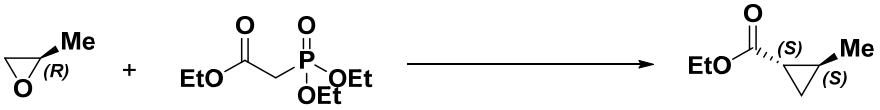
22. A method of preparing Compound 3:



Compound 3

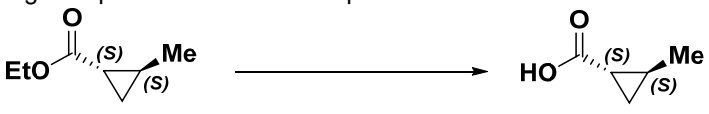
the method comprising:

a) contacting Compound 3a and Compound 3b in the presence of a base to form Compound 3c:



Compound 3a **Compound 3b** **Compound 3c** ; and

b) hydrolyzing Compound 3c to form Compound 3:

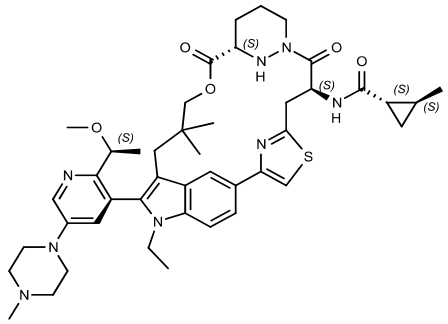


Compound 3c **Compound 3** .

23. The method of claim 22, wherein the base is n-BuLi.

24. The method of claim 22 or 23, wherein Compound 3 in step (b) is produced as a crude mixture comprising Compound 3, and the method further comprises contacting the crude mixture with a chiral phenylethylamine to isolate Compound 3.

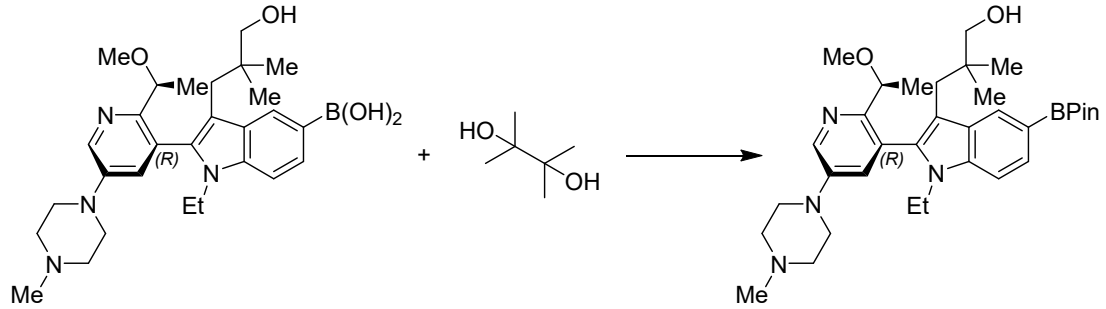
25. A method of preparing Compound A:



Compound A

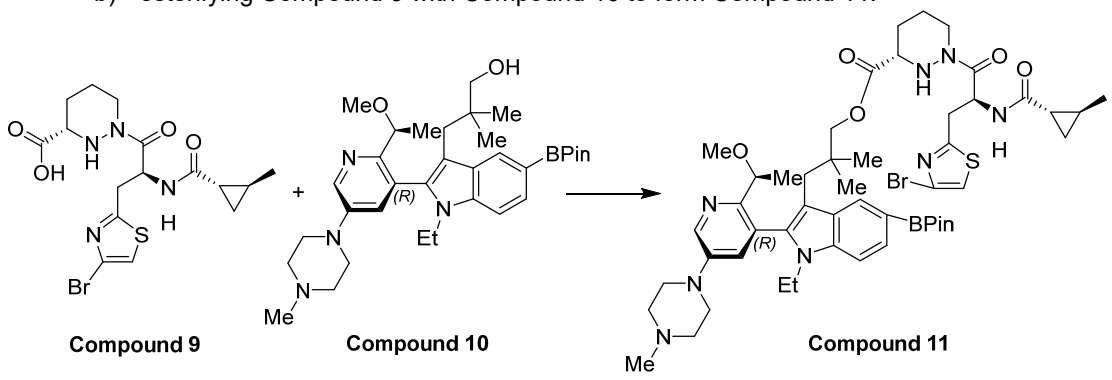
the method comprising:

a) contacting Compound 6a with pinacol to form Compound 10:



Compound 6a **Pinacol** **Compound 10** ;

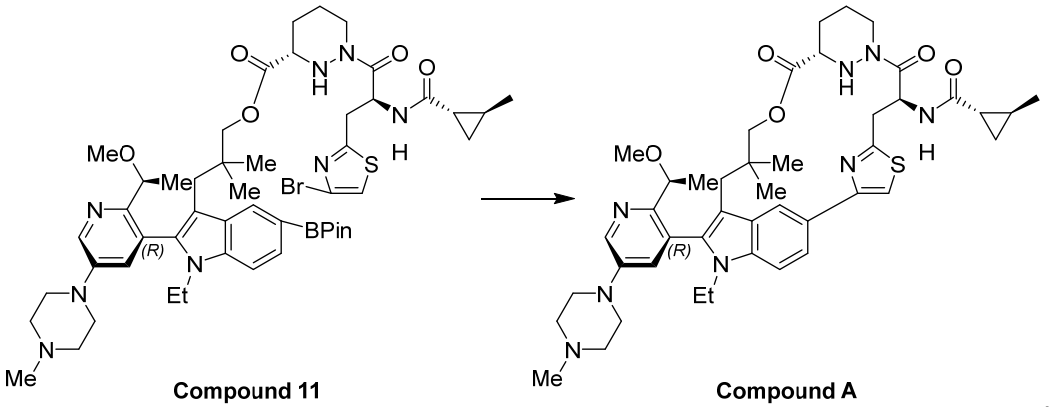
b) esterifying Compound 9 with Compound 10 to form Compound 11:



Compound 9 **Compound 10** **Compound 11** ;

and

c) cyclizing Compound 11 to form Compound A:



26. The method of claim 25, wherein the esterifying occurs in the presence of EDCI and a base; and the cyclizing takes place in the presence of a palladium catalyst.