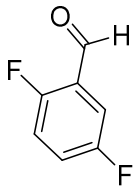


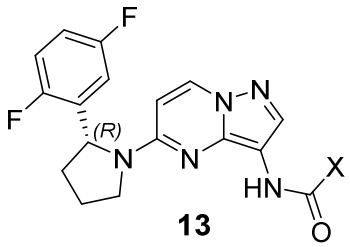
16

with (R)-2-methylpropane-2-sulfinamide,

to form a compound of formula **17**.

In one example, provided herein is a process for preparing a pharmaceutical composition, comprising mixing (i) a compound of **Formula I** or salt thereof prepared according to any of the processes described herein, and (ii) a pharmaceutically acceptable carrier, to form the composition.

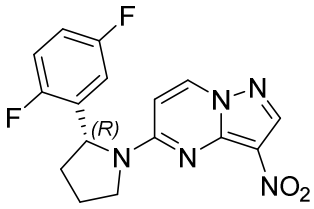
In one example, provided herein is a process for preparing a compound of formula **13**



13

or a salt thereof by a process comprising

a) treating a compound of formula **11**



11

or a salt thereof with a nitro reduction system to form a first mixture;

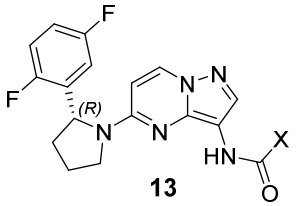
and

b) treating the first mixture with XC(O)Z to form a compound of formula **13** or a salt thereof,

wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula **13,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl; and wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl;

provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.

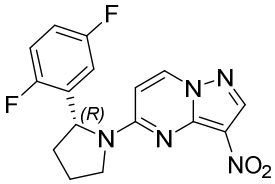
In one aspect, provided herein is a process for preparing a compound of formula **13** in isolated form



13

or a salt thereof by a process comprising

a) treating a compound of formula **11**



11

or a salt thereof with a nitro reduction system to form a first mixture~~;~~ and

b) treating the first mixture with XC(O)Z to form a compound of formula **13** or a salt thereof, and

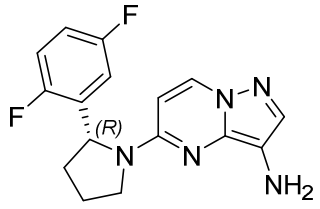
c) isolating the compound of formula **13** or salt thereof,

wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula 13**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl, and wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl;

provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.

In some examples, provided herein is a process for preparing a compound of formula **13** or a salt thereof comprising

a) isolating a compound of formula **12**



12

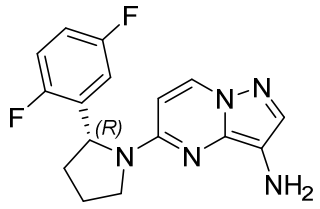
or a salt thereof;

b) treating a compound of formula **12** with XC(O)Z to form a compound of formula **13** or a salt thereof; and

c) optionally isolating the compound of formula **13**.

In one aspect, provided herein is a process for preparing a compound of formula **13** in isolated form or a salt thereof comprising

a) isolating a compound of formula **12**



12;

b) treating a compound of formula **12** with XC(O)Z to form a compound of formula **13** or a salt thereof; and

c) isolating the compound of formula **13**,

wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula 13**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl, and

wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl;

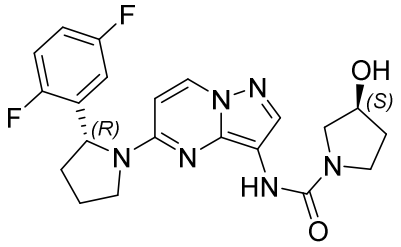
provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.

In one example, provided herein is a process for preparing a compound of formula **12** or a salt thereof comprising

a) treating a compound of formula **11**

WE CLAIM:

1. A process for preparing a compound of Formula I

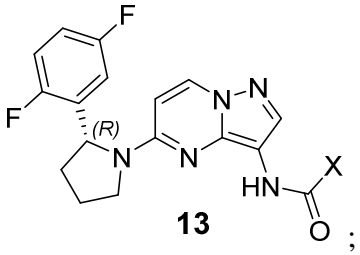


Formula I

or a salt thereof,

comprising:

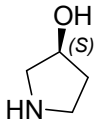
(a) providing an isolated compound of formula **13**



13 ;

(b) optionally forming a salt of formula **13**;

(c) treating the compound of formula **13** or a salt thereof with a compound of formula **14**



14

or a salt thereof to form a compound of Formula I;

and

(d) optionally forming a salt of the compound of Formula I;

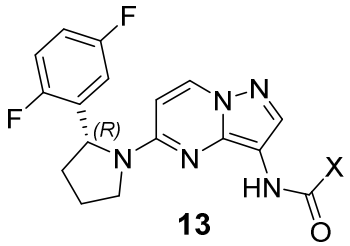
wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula **13,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH,

C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl.

2. The process of claim 1, wherein X is C_6-C_{10} aryloxy.

3. The process of claim 2, wherein X is phenoxy.

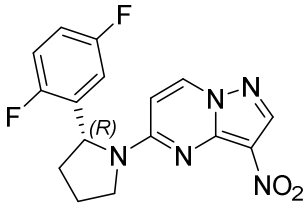
4. The process of any one of the preceding claims, further comprising preparing the compound of formula **13**



13

or a salt thereof by a process comprising

(a) treating a compound of formula **11**



11

or a salt thereof with a nitro reduction system to form a first mixture~~;~~

and

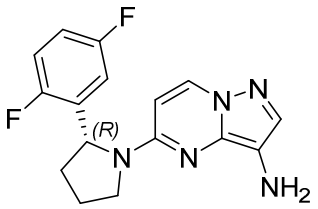
(b) treating the first mixture with XC(O)Z to form a compound of formula **13** or a salt thereof,

wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group

consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl; provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.

5. The process of claim 4, wherein the process comprises:
   forming the compound of formula **13** in a second mixture; and
   isolating the compound of formula **13** from the second mixture.

6. The process of claim 4 or 5, wherein the first mixture comprises a compound of formula **12**



12

or a salt thereof, and the processes comprises isolating the compound of formula **12** or a salt thereof from the first mixture prior to treating with XC(O)Z.

7. The process of claim 6, wherein the salt of the compound of formula **12** is the fumarate salt.

8. The process of claim 6 or 7, wherein Z is halogen or is a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z.

9. The process of claim 6 or 7, wherein Z is chlorine, bromine, or imidazolyl.

10. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises a metal, a metal salt, or an oxide of a metal.

11. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises palladium, platinum, rhodium, ruthenium, nickel, copper, iron, tin, or zinc.

12. The process of any one of claims 4 to 11, wherein the nitro reduction system comprises an acid.

13. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises a metal hydride or a mixed metal hydride.

14. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises $LiAlH_4$, $NaBH_4$, or diisobutylaluminium hydride (*DIBAL*).

15. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises H_2.

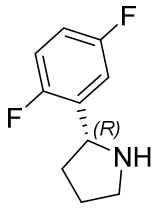
16. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises an organic compound capable of providing hydrogen.

17. The process of claim 16, wherein the nitro reduction system comprises cyclohexene.

18. The process of any one of claims 4 to 9, wherein the nitro reduction system comprises Pd, Pd/C, Raney nickel, Pt/C, PtO_2, Fe/acid, or Zn/acid.

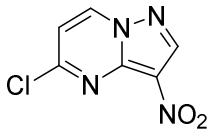
19. The process of claim 32, wherein the nitro reduction system comprises Pt/C.

20. The process of any one of claims 4-19, further comprising preparing the compound of formula **11** or a salt thereof by a process comprising treating a compound of formula **10**



10

or a salt thereof, with a compound of formula **5**



5

or a salt thereof, to form the compound of formula **11** or salt thereof.

21. The process of claim 20, wherein the salt of the compound of formula **10** is a malate salt.

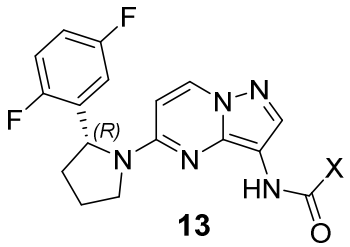
22. The process of claim 20 or 21, wherein the salt of the compound of formula **10** is the D-malate salt.

23. The process of any of claims 5-22, wherein X is phenoxy, Z is chlorine, and XC(O)Z is phenyl chloroformate.

24. The process of any of claims 1-23, further comprising the step of mixing (i) a compound of **Formula I** or salt thereof and (ii) a pharmaceutically acceptable carrier, to form the pharmaceutical composition.

25. The process of any one of the preceding claims, wherein the salt of the compound of **Formula I** is the hydrogen sulfate salt.

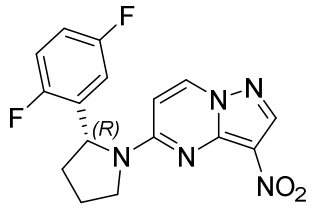
26. A process for preparing a compound of formula **13** in isolated form



13

or a salt thereof by a process comprising

a) treating a compound of formula **11**



11

or a salt thereof with a nitro reduction system to form a first mixture~~;~~

and

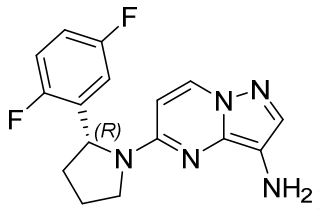
b) treating the first mixture with XC(O)Z to form a compound of formula **13** or a salt thereof, and

c) isolating the compound of formula **13** or salt thereof,

wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula 13**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl, and wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl; provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.

27. A process for preparing a compound of formula **13** in isolated form or a salt thereof comprising

a) isolating a compound of formula **12**



12;

b) treating a compound of formula **12** with XC(O)Z to form a compound of formula **13** or a salt thereof; and

c) isolating the compound of formula **13**,

wherein X is halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy or a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of the compound of formula 13**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^1R^2, where R^1 and R^2 are each independently selected from hydrogen and C_1-C_6 alkyl, and wherein Z is a leaving group selected from halogen, C_1-C_6 alkoxy, C_6-C_{10} aryloxy and a 5-membered heteroaryl containing at least one nitrogen directly bonded to the C=O of XC(O)Z**,** each optionally substituted with one or more substituents independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, OH, C_1-C_6 alkoxy, and NR^5R^6, where R^5 and R^6 are each independently selected from hydrogen and C_1-C_6 alkyl; provided that if Z is optionally substituted C_1-C_6 alkoxy, optionally substituted C_6-C_{10} aryloxy, or optionally substituted 5-membered heteroaryl, then Z and X are the same.