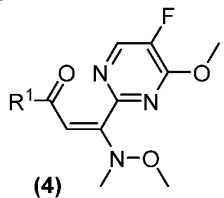


CLAIMS

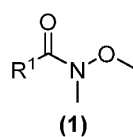
What is claimed is:

1. A process for preparing a compound of formula (4):

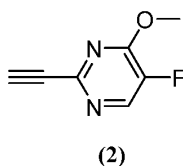


comprising the steps of:

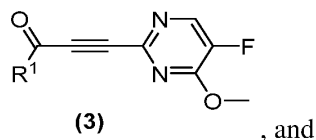
- i) coupling an amide of formula (1):



with a pyrimidine compound of formula (2):



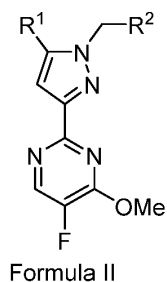
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3)



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4), wherein:

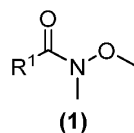
R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O.

2. A process for preparing a compound of Formula II:

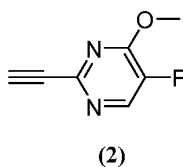


comprising the steps of:

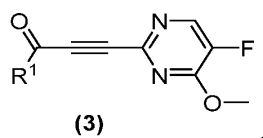
- i) coupling an amide of formula (1):



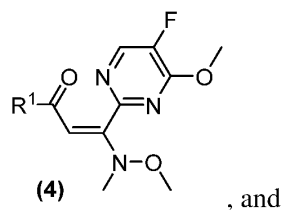
with a pyrimidine compound of formula (2):



in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3):



- ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4):



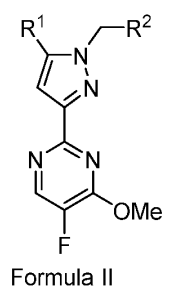
iii) condensing the compound of formula (4) with a hydrazine of formula $R^2\text{-CH}_2\text{-NH-NH}_2$ or a salt thereof, optionally in the presence of a base, to form the compound of Formula II, wherein:

R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O; and

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms; and

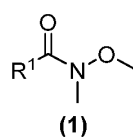
each R^5 is independently methyl, methoxy or halogen.

3. A process of preparing a compound of Formula II:

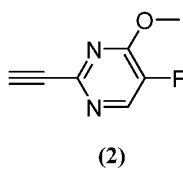


comprising the steps of:

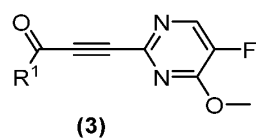
i) coupling an amide of formula (1):



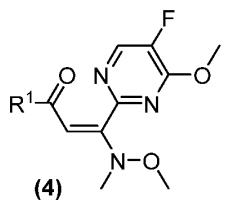
with a pyrimidine compound of formula (2):



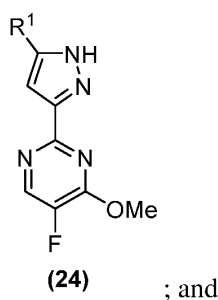
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3):



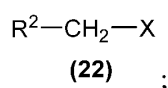
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula **(4)**:



iiia) condensing the compound of formula **(4)** with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula **(24)**:



iiib) alkylating intermediate of formula **(24)** with an alkylating agent of formula **(22)** to provide the compound of Formula II



wherein:

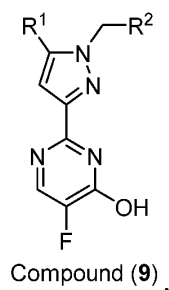
R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O; and

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms;

each R^5 is independently methyl, methoxy or halogen;

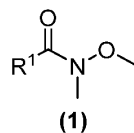
X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

4. A process of preparing Compound (9):

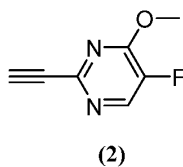


comprising the steps of:

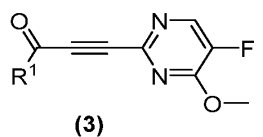
i) coupling an amide of formula (1):



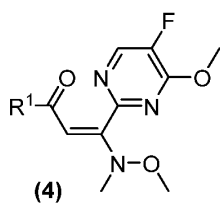
with a pyrimidine compound of formula (2):



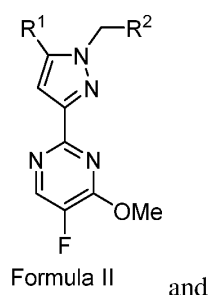
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3):



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (e.g. HCl salt) thereof, allowing the mixture to react to form the compound of formula (4):



iii) condensing the compound of formula (4) with a hydrazine of formula $R^2\text{-CH}_2\text{-NH-NH}_2$ or a salt (*e.g.* HCl salt) thereof, optionally in the presence of a base, to form the compound of Formula II;



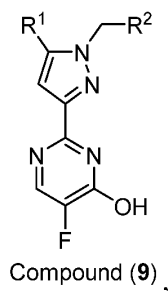
iv) de-methylating the compound of Formula II to form an alcohol Compound (9);
wherein

R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O; and

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms; and

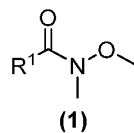
each R^5 is independently methyl, methoxy or halogen.

5. A process for preparing Compound (9):

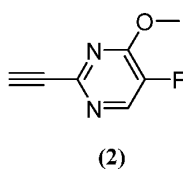


comprising the steps of:

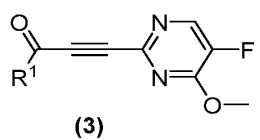
i) coupling an amide of formula (1):



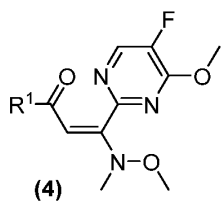
with a pyrimidine compound of formula (2):



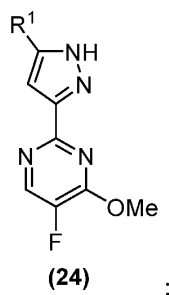
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3):



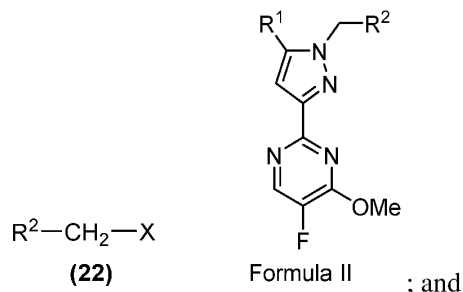
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4):



iiia) condensing the compound of formula (4) with hydrazine (*e.g.*, hydrazine hydrate) ,to form the compound of formula (24):



iiib) alkylating intermediate of formula (21) with an alkylating agent of formula (22) to provide the compound of Formula II:



iv) de-methylating the compound of Formula II to form an alcohol Compound (9);
wherein:

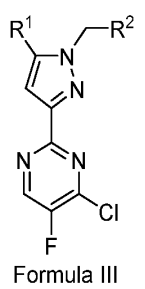
R¹ is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O; and

R² is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R⁵; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms;

each R⁵ is independently methyl, methoxy or halogen; and

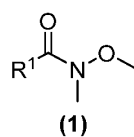
X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

6. A process of preparing a compound of formula III:

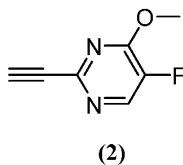


comprising the steps of:

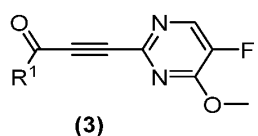
i) coupling an amide of formula (1):



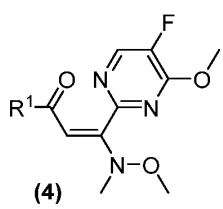
with a pyrimidine compound of formula **(2)**:



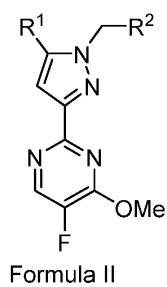
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula **(3)**:



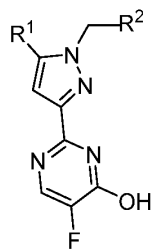
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula **(4)**:



iii) condensing the compound of formula **(4)** with a hydrazine of formula $R^2\text{-CH}_2\text{-NH-NH}_2$ or a salt thereof, optionally in the presence of a base, to form a compound of Formula II,



iv) de-methylating the compound of Formula II to form an alcohol compound of formula **(9)**:



(9) , and

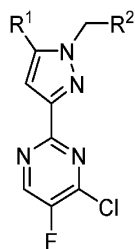
v) chlorinating the alcohol compound of formula (9) with phosphoryl chloride, to form the compound of Formula III, wherein:

R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O;

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms; and

each R^5 is independently methyl, methoxy or halogen.

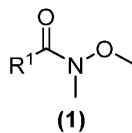
7. A process of preparing a compound of formula III:



Formula III ,

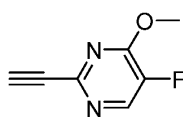
comprising the steps of:

i) coupling an amide of formula (1):



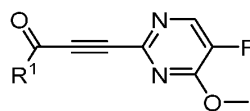
(1)

with a pyrimidine compound of formula (2):



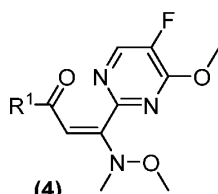
(2)

in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3):



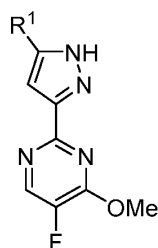
(3)

ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4):



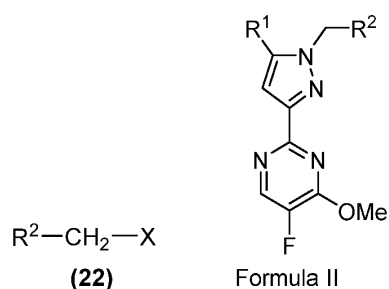
(4)

iiia) condensing the compound of formula (4) with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula (24):

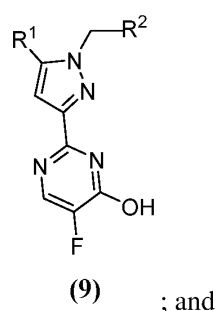


(24)

iiib) alkylating intermediate of formula (24) with an alkylating agent of formula (22) to provide the compound of Formula II:



iv) de-methylating the compound of Formula II to form an alcohol compound of formula **(9)**:



v) chlorinating the alcohol compound of formula **(9)** with phosphoryl chloride to form the compound of Formula III, wherein:

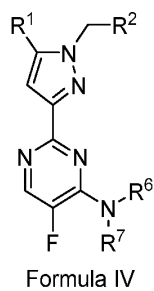
R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O; and

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms;

each R^5 is independently methyl, methoxy or halogen; and

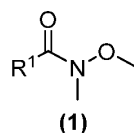
X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

8. A process of preparing a compound of Formula IV:

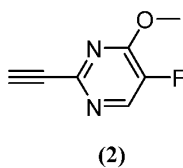


comprising the steps of:

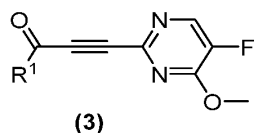
- i) coupling an amide of formula (1):



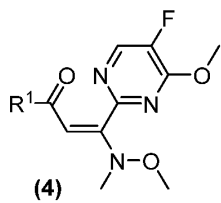
with a pyrimidine compound of formula (2):



in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3):

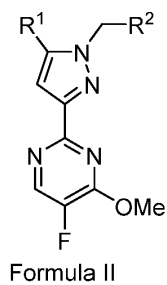


ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4):

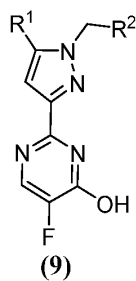


- iii) condensing the compound of formula (4) with a hydrazine of formula $R^2\text{-CH}_2\text{-NH-}$

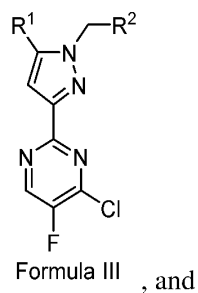
NH₂ or a salt thereof, optionally in the presence of a base, to form a compound of Formula II,



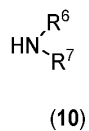
iv) de-methylating the compound of Formula II to form an alcohol compound of formula (9):



v) chlorinating the alcohol compound of formula (9) with phosphoryl chloride and, optionally, in the presence of a base, in an aprotic organic solvent to form a compound of Formula III:



vi) reacting with an amine compound of formula (10):



with the compound of Formula III, optionally in the presence of a base, to yield the compound of Formula IV, wherein:

R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O;

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms,

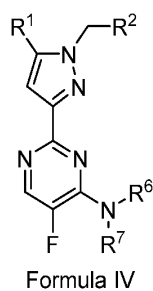
each R^5 is independently methyl, methoxy or halogen

R^6 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ;

R^7 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ; and

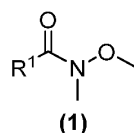
each R^8 is independently $-OH$, C_{1-3} haloalkyl, halogen or $-C(O)NH_2$.

9. A process of preparing a compound of Formula IV:

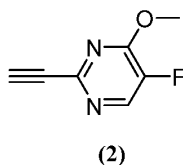


comprising the steps of:

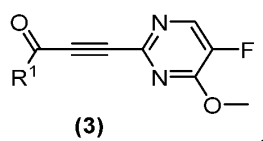
i) coupling an amide of formula (1):



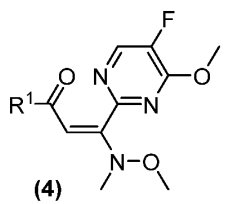
with a pyrimidine compound of formula (2):



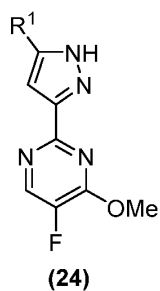
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3):



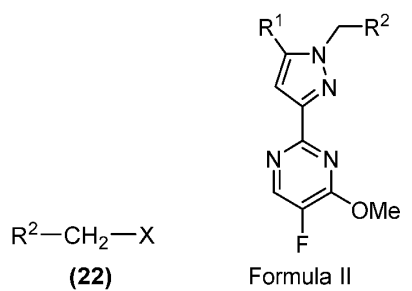
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula **(4)**:



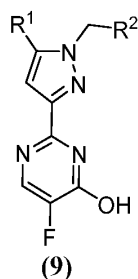
iiia) condensing the compound of formula **(4)** with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula **(24)**:



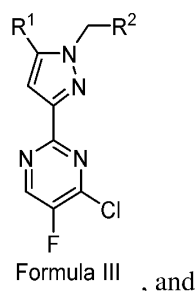
iiib) alkylating intermediate of formula **(24)** with an alkylating agent of formula **(22)** to provide the compound of Formula II:



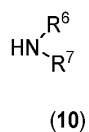
iv) de-methylating the compound of Formula II to form an alcohol compound of formula **(9)**:



v) chlorinating the alcohol compound of formula (9) with phosphoryl chloride to form a compound of Formula III:



vi) reacting an amine compound of formula (10):



with the compound of Formula III, optionally in the presence of a base, to yield the compound of Formula IV, wherein:

R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O;

R^2 is phenyl or a 6-membered heteroaryl, optionally substituted with up to three instances of R^5 ; wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms,

each R^5 is independently methyl, methoxy or halogen;

X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate);

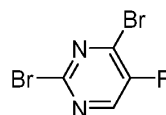
R^6 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ;

R^7 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ; and

each R^8 is independently $-OH$, C_{1-3} haloalkyl, halogen or $-C(O)NH_2$.

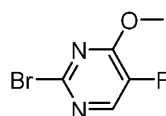
10. The process of any one of claims 1-9, wherein the compound of formula (2) is prepared by a process comprising the steps of:

a) reacting dibromopyrimidine compound of formula (5):



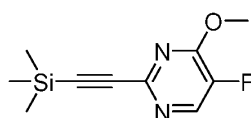
(5)

with a base in methanol or a methoxide salt in an aprotic solvent to form a bromopyrimidine compound of formula (6):



(6)

b) coupling the bromopyrimidine compound of formula (6) with ethynyltrimethylsilane, in an aprotic organic solvent in the presence of a base and a Pd catalyst, and optionally in the presence of a Cu(I) catalyst, to form a compound of formula (7):

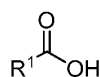


(7)

, and

c) de-silylating the compound of formula (7) to form the pyrimidine compound of formula (2).

11. The process of any one of claims 1-10, wherein the compound of formula (1) is prepared by reacting a carboxylic acid of formula (8)



(8)

with oxalyl chloride or an equivalent amide coupling reagent, followed by *N,O*-

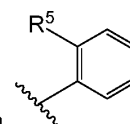
dimethylhydroxylamine or a salt thereof, in the presence of a base to form the amide of formula (1).

12. The process of any one of claims 1-11, wherein R^1 is a 5-membered heteroaryl ring.

13. The process of claim 12, wherein R^1 is an unsubstituted 5-membered heteroaryl ring containing up to 2 ring heteroatoms selected from the group consisting of N and O.

14. The process of any one of claims 2-13, wherein R^2 is phenyl optionally substituted with up to two instances of R^5 .

15. The process of any one of claims 2-13, wherein R^2 is phenyl optionally substituted with one instance of R^5 .



16. The process of any one of claims 2-13, wherein R^2 is represented by formula .

17. The process of any one of claims 2-13, wherein R^2 is a 6-membered heteroaryl, optionally substituted with up to two instances of R^5 ; and wherein said 6-membered heteroaryl ring contains up to 2 nitrogen ring atoms.

18. The process of any one of claims 2-17, wherein each R^5 is independently methyl or halogen.

19. The process of claim 18, wherein each R^5 is independently halogen.

20. The process of claim 18, wherein each R^5 is fluoro.

21. The process of any one of claims 8-20, wherein R^6 is hydrogen or C_{1-2} alkyl substituted with 0 to 3 instances of R^8 .

22. The process of claim 21, wherein R^6 is hydrogen.

23. The process of any one of claims 8-22, wherein R^7 is hydrogen or C_{1-2} alkyl substituted with 0 to 3 instances of R^8 .

24. The process of claim 23, wherein R^7 is C_{1-2} alkyl substituted with 3 instances of R^8 .

25. The process of any one of claims 8-24, wherein each R^8 is independently $-OH$, trifluoromethyl, or $-C(O)NH_2$.

26. The process of any one of claims 1-11, wherein:

R^1 is an unsubstituted 5-membered heteroaryl ring containing up to 2 ring heteroatoms selected from the group consisting of N and O;

R^2 is phenyl, optionally substituted with one or two instances of R^5 ;

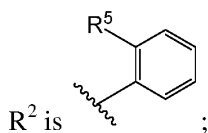
each R^5 is fluoro;

R^6 is hydrogen;

R^7 is C_{1-2} alkyl substituted with 3 instances of R^8 and each R^8 is independently $-OH$, trifluoromethyl, or $-C(O)NH_2$.

27. The process of any one of claims 1-11, wherein:

R^1 is an unsubstituted 5-membered heteroaryl ring containing up to 2 ring heteroatoms selected from the group consisting of N and O;



each R^5 is fluoro;

R^6 is hydrogen;

R^7 is C_{1-2} alkyl substituted with 3 instances of R^8 and each R^8 is independently $-OH$, trifluoromethyl, or $-C(O)NH_2$.

28. The process of any one of claims 1-27, wherein the base in step i) is n-butyllithium.

29. The process of any one of claims 1-28, wherein the process comprises contacting the reaction product of the amide of formula (1) and the pyrimidine compound of formula (2) with a solution comprising *N,O*-dimethylhydroxylamine or a salt thereof and an acid to form the compound of formula (4).

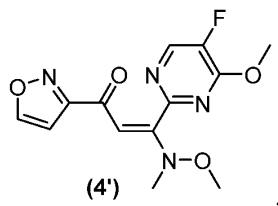
30. The process of claim 29, wherein the solution comprises *N,O*-dimethylhydroxylamine hydrochloride.

31. The process of claim 29 or 30, wherein the acid is an aqueous acid.

32. The process of claim 31, wherein the acid is hydrochloric acid.

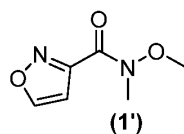
33. The process of claim 29 or 30, wherein the acid is glacial acetic acid.

34. A process of preparing a compound of formula (4'):

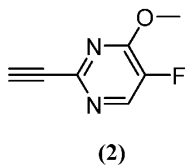


comprising the steps of:

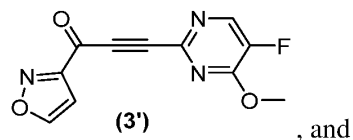
i) coupling an amide of formula (1'):



with a pyrimidine compound of formula (2):

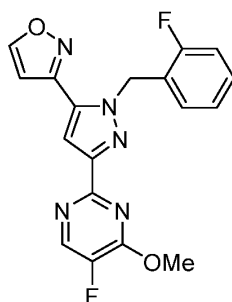


in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4').

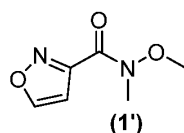
35. A process of preparing a compound of Formula V:



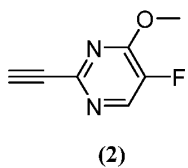
Formula V

comprising the steps of:

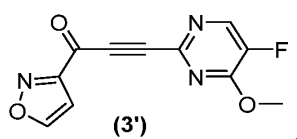
i) coupling an amide of formula (1'):



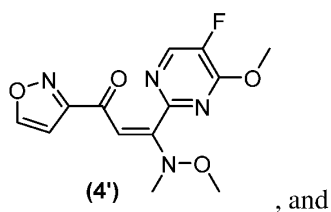
with a pyrimidine compound of formula (2):



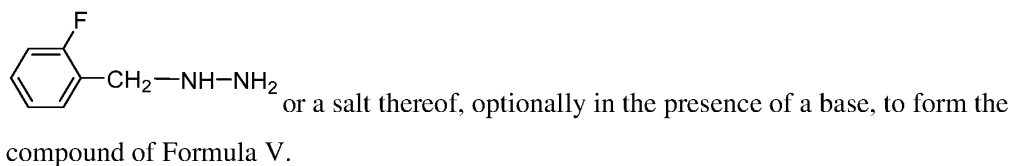
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



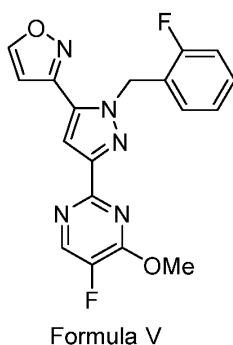
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



iii) condensing the compound of formula (4') with a hydrazine of formula

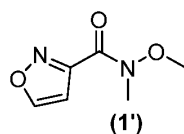


36. A process of preparing a compound of Formula V:

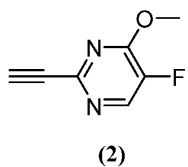


comprising the steps of:

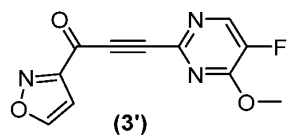
i) coupling an amide of formula (1'):



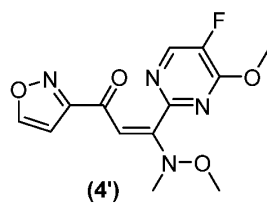
with a pyrimidine compound of formula (2):



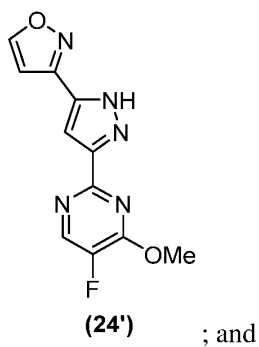
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



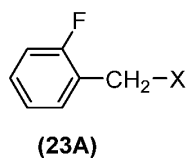
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



iiia) condensing the compound of formula **(4')** with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula **(24')**:

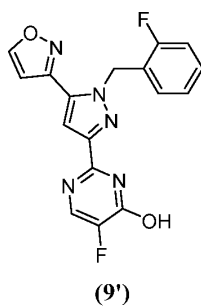


iiib) alkylating intermediate of formula **(24')** with an alkylating agent of formula **(23A)** to provide the compound of Formula V:



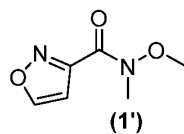
wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (*e.g.*, mesylate, tosylate or triflate).

37. A process for preparing Compound **(9')**:

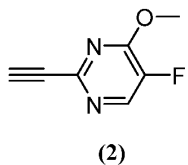


comprising the steps of:

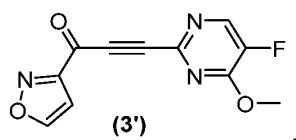
i) coupling an amide of formula **(1')**:



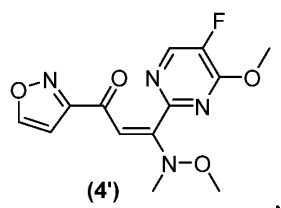
with a pyrimidine compound of formula (2):



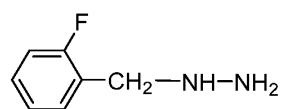
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



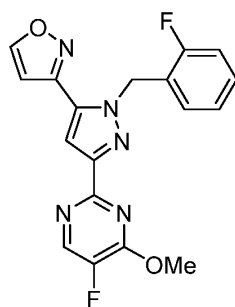
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



iii) condensing the compound of formula (4') with a hydrazine of formula



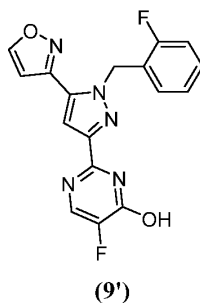
or a salt (*e.g.*, HCl salt) thereof, optionally in the presence of a base, to form the compound of Formula V:



Formula V, and

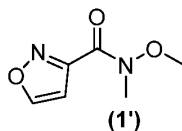
iv) de-methylating the compound of Formula V to form an alcohol Compound (**9'**).

38. A process for preparing Compound (**9'**):

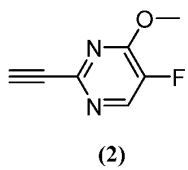


comprising the steps of:

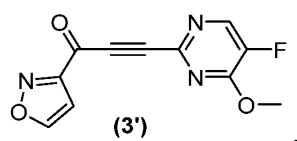
i) coupling an amide of formula (**1'**):



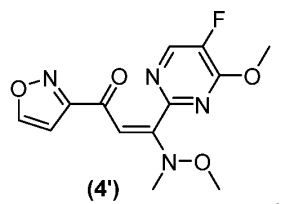
with a pyrimidine compound of formula (**2**):



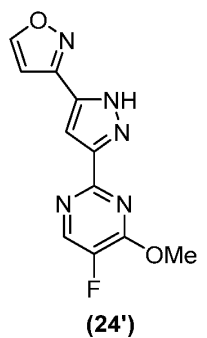
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (**3'**):



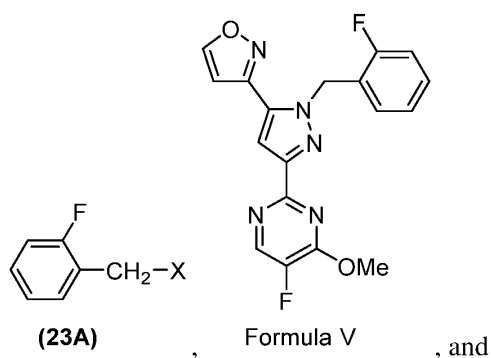
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula **(4')**:



iiia) condensing the compound of formula **(4')** with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula **(24')**:

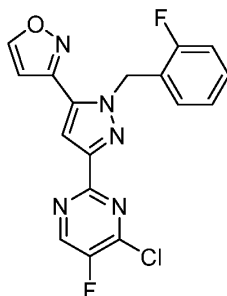


iiib) alkylating intermediate of formula **(24')** with an alkylating agent of formula **(23A)** to provide the compound of Formula V:



iv) de-methylating the compound of Formula V to form an alcohol Compound **(9')**; wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (*e.g.*, mesylate, tosylate or triflate).

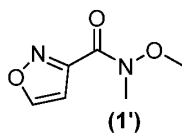
39. A process of preparing a compound of Formula VI:



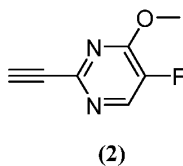
Formula VI

comprising the steps of:

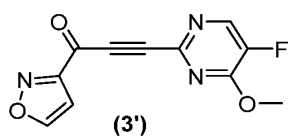
i) coupling an amide of formula (1'):



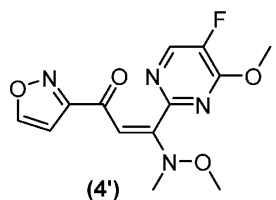
with a pyrimidine compound of formula (2):



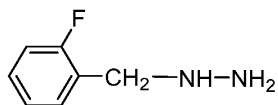
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



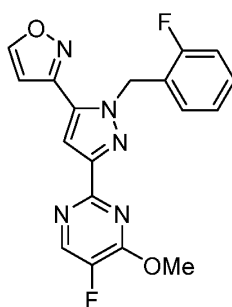
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



iii) condensing the compound of formula (4') with a hydrazine of formula

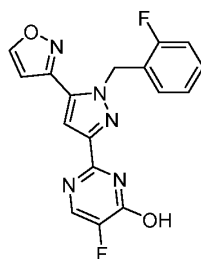


or a salt thereof, optionally in the presence of a base, to form a compound of Formula V:



Formula V

iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

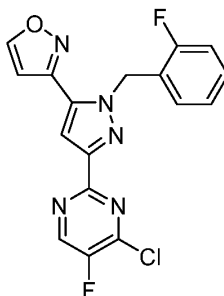


(9')

, and

v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form the compound of Formula VI.

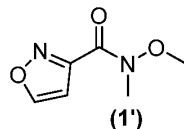
40. A process of preparing a compound of Formula VI:



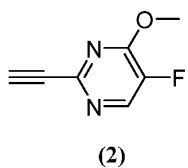
Formula VI

comprising the steps of:

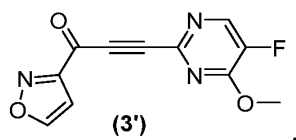
i) coupling an amide of formula (1'):



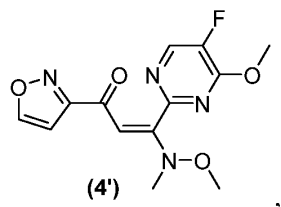
with a pyrimidine compound of formula (2):



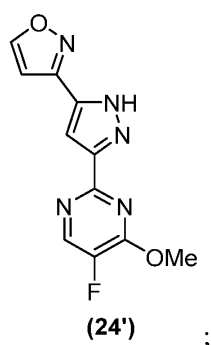
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



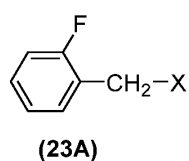
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



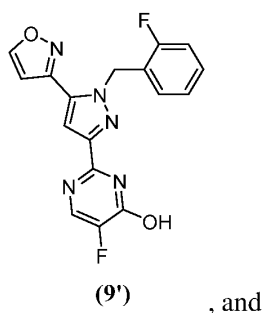
iiia) condensing the compound of formula (4') with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula (24'):



iiib) alkylating intermediate of formula **(24')** with an alkylating agent of formula **(23A)** to provide the compound of Formula V;

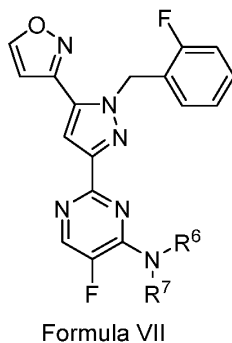


iv) de-methylating the compound of Formula V to form an alcohol compound of formula **(9')**:



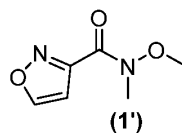
v) chlorinating the alcohol compound of formula **(9')** with phosphoryl chloride to form the compound of Formula VI, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

41. A process of preparing a compound formula VII:

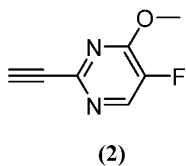


comprising the steps of:

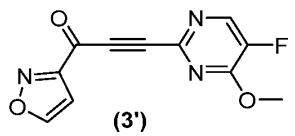
i) coupling an amide for formula (1'):



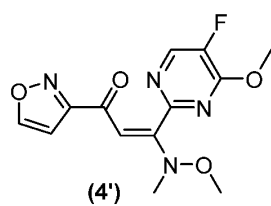
with a pyrimidine compound of formula (2):



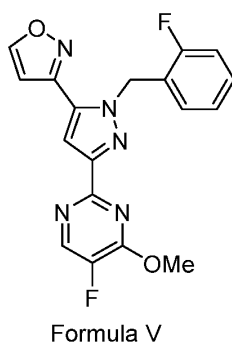
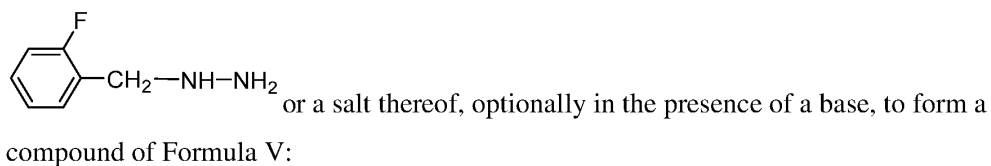
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



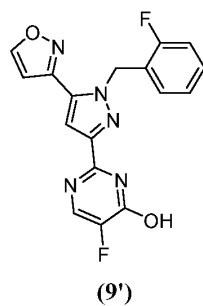
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



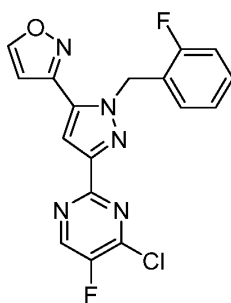
iii) condensing the compound of formula (4') with a hydrazine of formula



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



Formula VI ; and

vi) reacting an amine compound of formula (10):



(10)

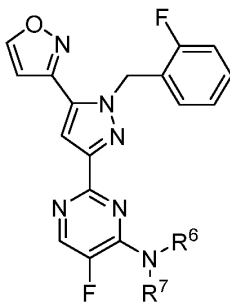
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula VII, wherein:

R^6 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ;

R^7 is hydrogen or C_{1-4} alkyl substituted with 0 to 3 instances of R^8 ; and

each R^8 is independently $-OH$, C_{1-3} haloalkyl, halogen or $-C(O)NH_2$.

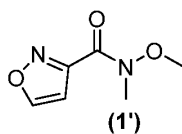
42. A process of preparing a compound of formula VII:



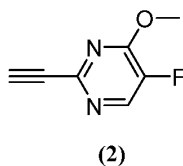
Formula VII ,

comprising the steps of:

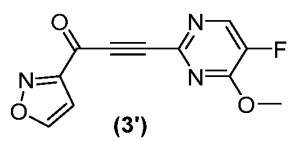
i) coupling an amide of formula (1'):



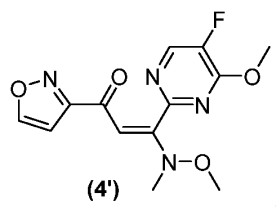
with a pyrimidine compound of formula (2):



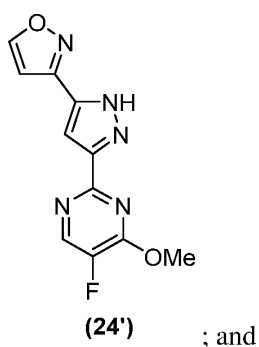
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):

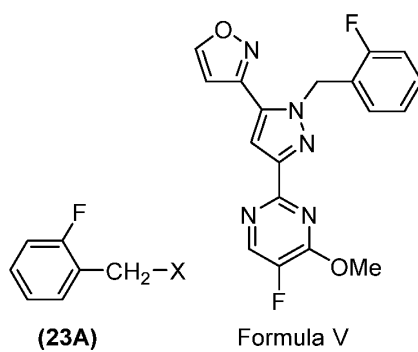


iiia) condensing the compound of formula (4') with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula (24'):

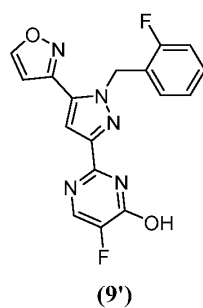


; and

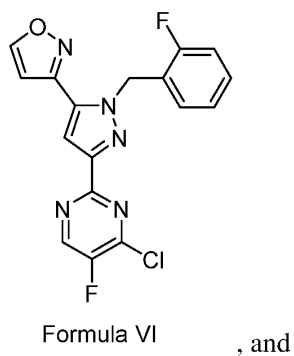
iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A) to provide the compound of Formula V:



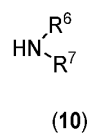
iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



vi) reacting an amine compound of formula (10):



with the compound of Formula VI, optionally in the presence of a base, to yield the compound

of Formula VII, wherein:

X is a leaving group selected from –Br, –I, –Cl, –F, and a sulfonate ester (e.g., mesylate, tosylate or triflate);

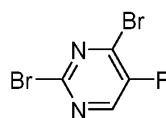
R⁶ is hydrogen or C₁₋₄ alkyl substituted with 0 to 3 instances of R⁸;

R⁷ is hydrogen or C₁₋₄ alkyl substituted with 0 to 3 instances of R⁸; and

each R⁸ is independently –OH, C₁₋₃ haloalkyl, halogen or –C(O)NH₂.

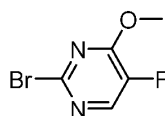
43. The process of any one of claims 34-42, wherein the compound of formula (2) is prepared by a process comprising the steps of:

a) reacting dibromopyrimidine compound of formula (5):



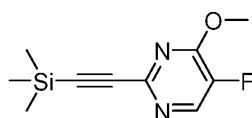
(5)

with a base in methanol or a methoxide salt in an aprotic solvent to form a bromopyrimidine compound of formula (6):



(6)

b) coupling the bromopyrimidine compound of formula (6) with ethynyltrimethylsilane, in an aprotic organic solvent in the presence of a base and a Pd catalyst, optionally in the presence of a Cu(I) catalyst, to a compound of formula (7):

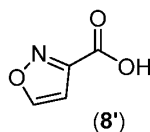


(7)

, and

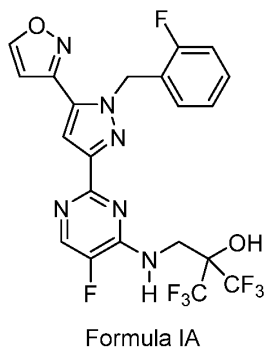
c) de-silylating the compound of formula (7) to form the pyrimidine compound of (2).

44. The process of any one of claims 34-43, wherein the compound of formula (1') is prepared by reacting a carboxylic acid of formula (8'):



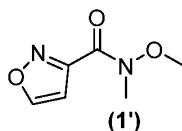
with oxalyl chloride or an equivalent amide coupling reagent, followed by *N,O*-dimethylhydroxylamine or a salt thereof, in the presence of a base to form the amide of formula (1').

45. The process of any one of claims 41-44, wherein R^6 is hydrogen or C_{1-2} alkyl substituted with 0 to 3 instances of R^8 .
46. The process of claim 45, wherein R^6 is hydrogen.
47. The process of any one of claims 41-46, wherein R^7 is hydrogen or C_{1-2} alkyl substituted with 0 to 3 instances of R^8 .
48. The process of claim 47, wherein R^7 is C_{1-2} alkyl substituted with 3 instances of R^8 .
49. The process of any one of claims 41-48, wherein each R^8 is independently $-OH$, trifluoromethyl, or $-C(O)NH_2$.
50. The process of claims 41-49, wherein R^6 is hydrogen; R^7 is C_{1-2} alkyl substituted with 3 instances of R^8 and each R^8 is independently $-OH$, trifluoromethyl, or $-C(O)NH_2$.
51. A process of preparing a compound of Formula IA:

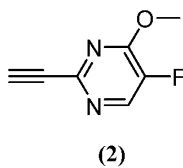


comprising the step of:

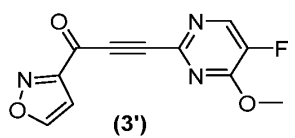
- i) coupling an amide of formula (1'):



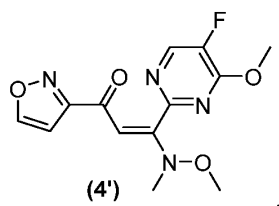
with a pyrimidine compound of formula (2):



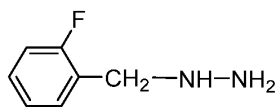
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



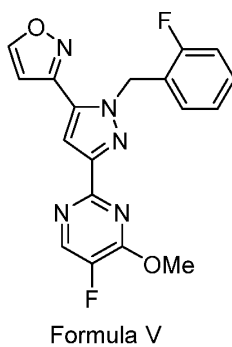
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



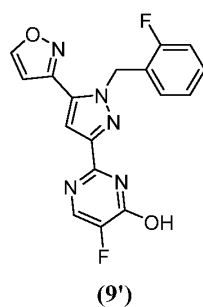
iii) condensing the compound of formula (4') with a hydrazine of formula



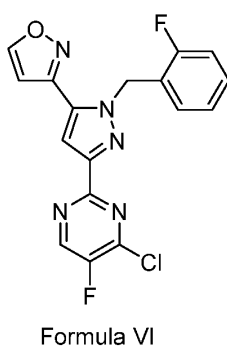
or a salt thereof, optionally in the presence of a base, to form a compound of Formula V:



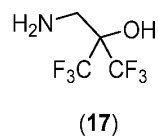
iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:

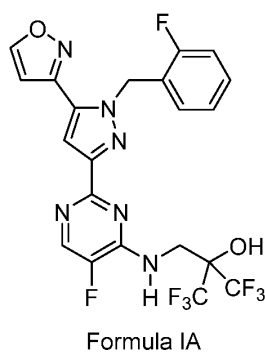


vi) reacting an amine of formula (17):



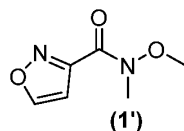
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IA.

52. A process of preparing a compound of Formula IA:

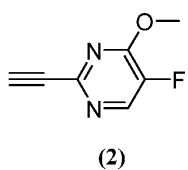


comprising the step of:

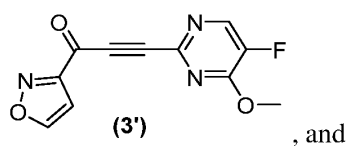
i) coupling an amide of formula (1'):



with a pyrimidine compound of formula (2):

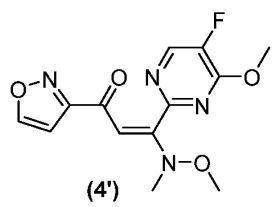


in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):



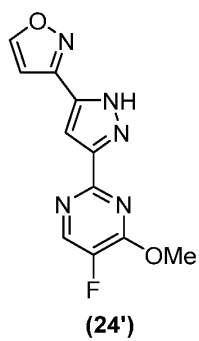
, and

ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):

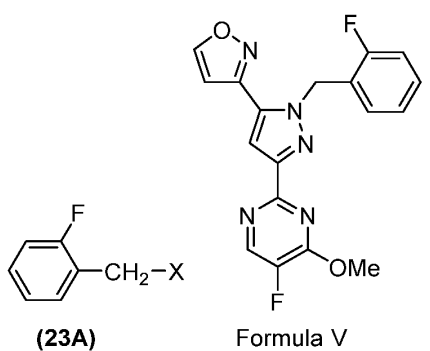


;

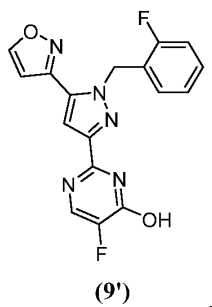
iiia) condensing the compound of formula (4') with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula (24'):



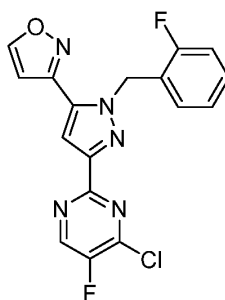
iiib) alkylating intermediate of formula **(24')** with an alkylating agent of formula **(23A)** to provide the compound of Formula V:



iv) de-methylating the compound of Formula V to form an alcohol compound of formula **(9')**:

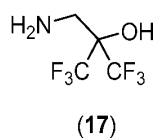


v) chlorinating the alcohol compound of formula **(9')** with phosphoryl chloride to form a compound of Formula VI:



Formula VI, and

vi) reacting an amine of formula (17):

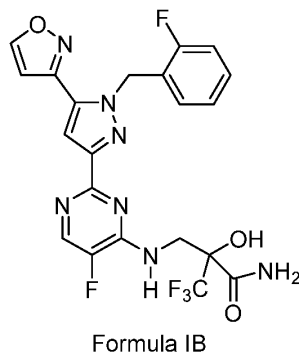


with the compound of Formula VIA, optionally in the presence of a base, to yield the compound of Formula IA, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

53. The process of claim 51 or 52, wherein the process further comprises re-crystallization of the compound of Formula IA in a mixture of methanol and water.

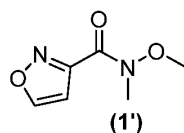
54. The process of claim 53, wherein the re-crystallization comprises the steps of: A') dissolving the compound of Formula IA in methanol at a temperature between 30 °C and 65 °C to obtain a methanol solution of the compound of Formula IA; B') filtering the methanol solution of the compound of Formula IA from step A') to form a filtered methanol solution of the compound of Formula IA; C') adding water to the filtered methanol solution of the compound of Formula IA at a temperature between 50 °C and 60 °C to yield a slurry; D') cooling the slurry of step 3) to yield a recrystallized compound of Formula IA; and E') filtering and drying the recrystallized compound of Formula IA.

55. A process of preparing a compound of Formula IB:

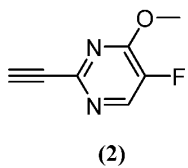


comprising the step of:

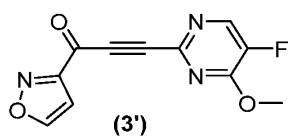
i) coupling an amide for formula (1'):



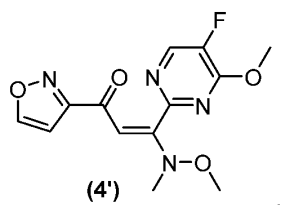
with a pyrimidine compound of formula (2):



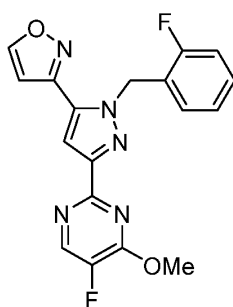
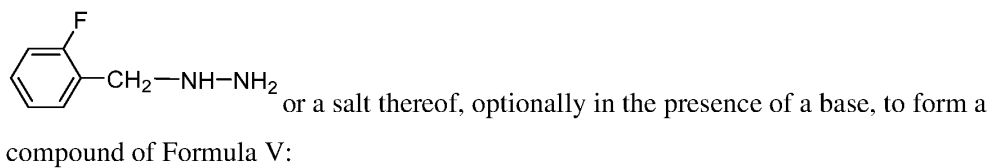
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):

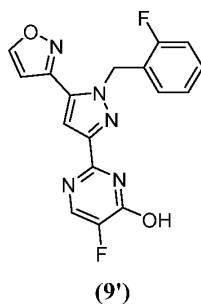


iii) condensing the compound of formula (4') with a hydrazine of formula

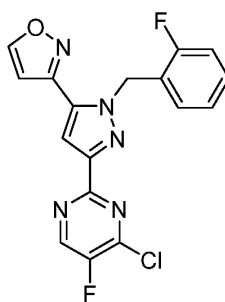


Formula V

iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



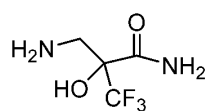
v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



Formula VI

, and

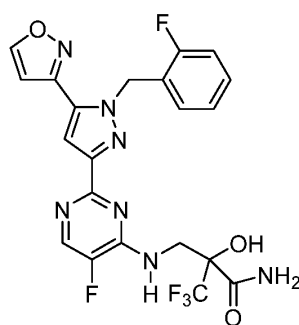
vi) reacting an amine of formula (13):



(13)

with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IB.

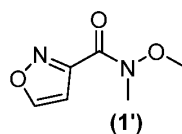
56. A process of preparing a compound of Formula IB:



Formula IB

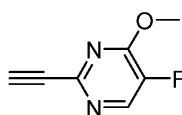
comprising the step of:

i) coupling an amide of formula (1'):



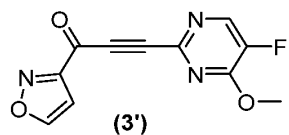
(1')

with a pyrimidine compound of formula (2):



(2)

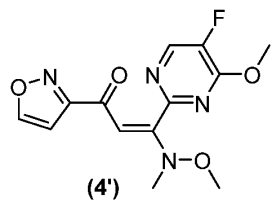
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):



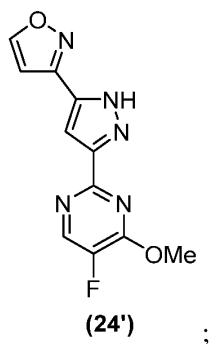
(3')

ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt

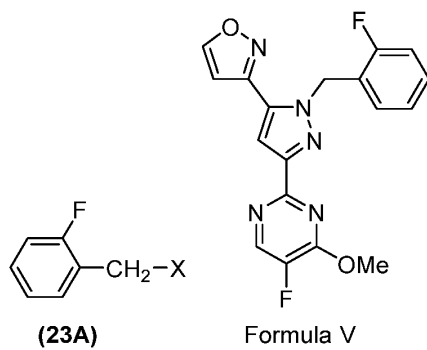
(e.g. HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



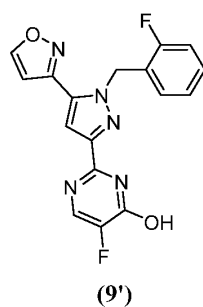
iiia) condensing the compound of formula (4') with hydrazine (e.g., hydrazine hydrate) to form the compound of formula (24'):



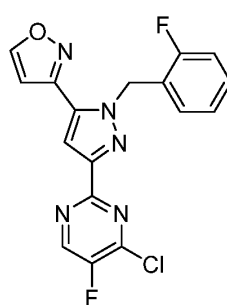
iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A) to provide the compound of Formula V:



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

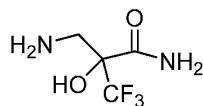


v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



Formula VI , and

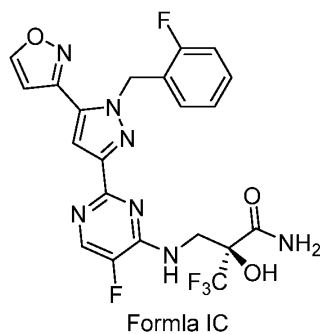
vi) reacting an amine of formula (13):



(13)

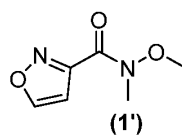
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IB, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

57. A process of preparing a compound of Formula IC:

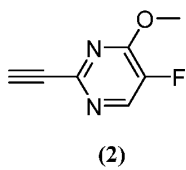


comprising the steps of:

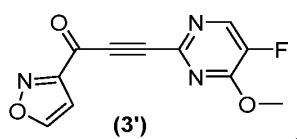
i) coupling an amide for formula (1'):



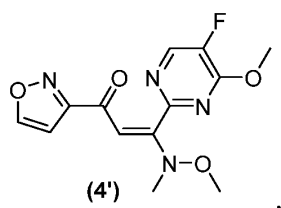
with a pyrimidine compound of formula (2):



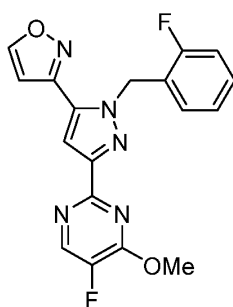
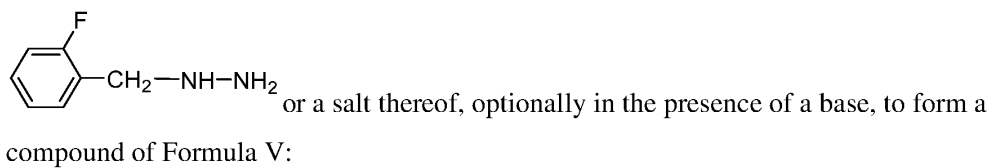
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):

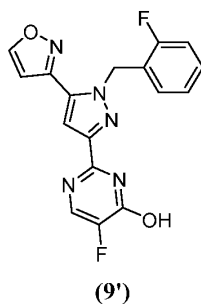


iii) condensing the compound of formula (4') with a hydrazine of formula

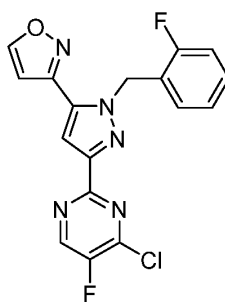


Formula V

iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



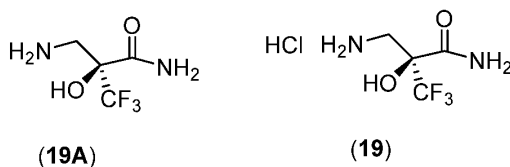
v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



Formula VI

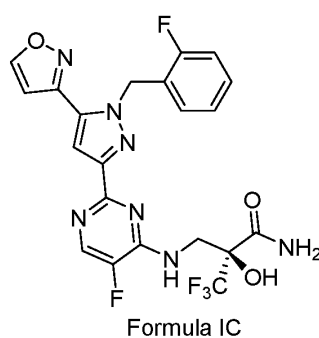
, and

vi) reacting an amine of formula (19A) or its HCl salt of formula (19):



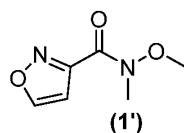
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IC.

58. A process of preparing a compound of Formula IC:

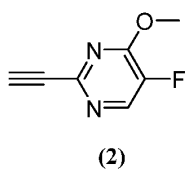


comprising the steps of:

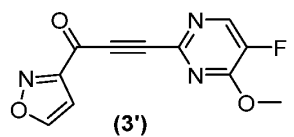
i) coupling an amide of formula (1'):



with a pyrimidine compound of formula (2):

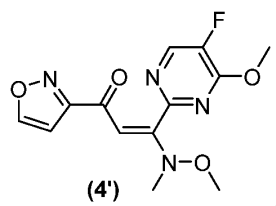


in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):

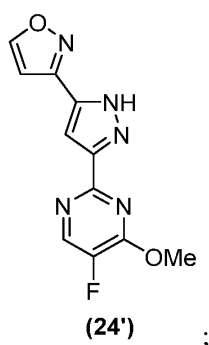


ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt

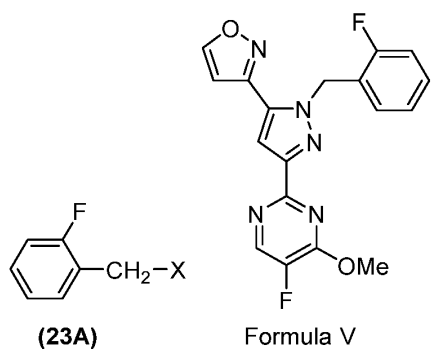
(e.g. HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



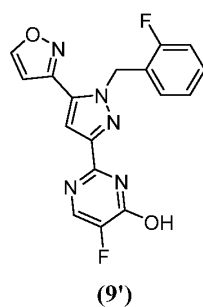
iii) condensing the compound of formula (4') with hydrazine (e.g., hydrazine hydrate) to form the compound of formula (24'):



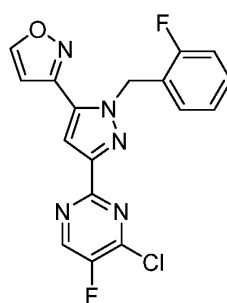
iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A) to provide the compound of Formula V:



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

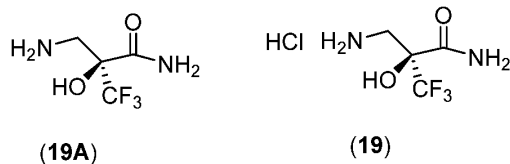


v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



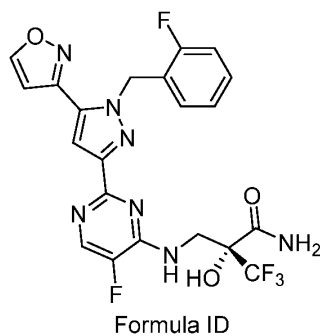
Formula VI , and

vi) reacting an amine of formula (19A) or its HCl salt of formula (19):



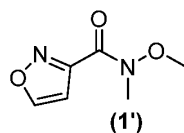
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IC, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

59. A process of preparing a compound of Formula ID:

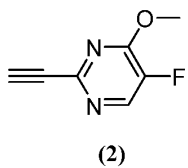


comprises the steps of:

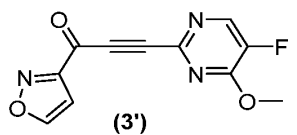
i) coupling an amide for formula (1'):



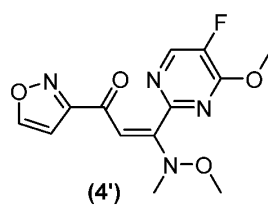
with a pyrimidine compound of formula (2):



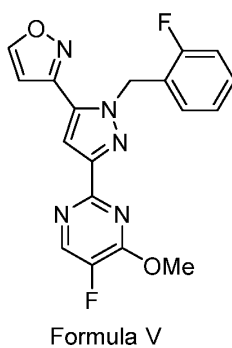
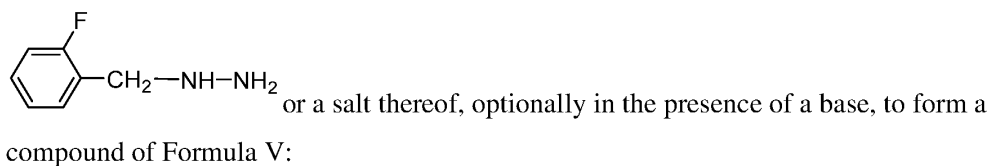
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



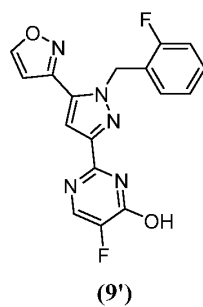
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



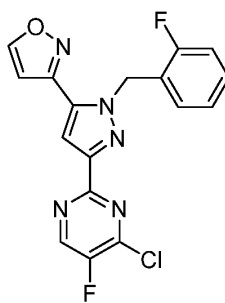
iii) condensing the compound of formula (4') with a hydrazine of formula



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

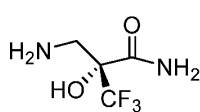
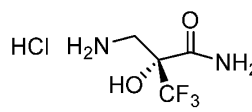


v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



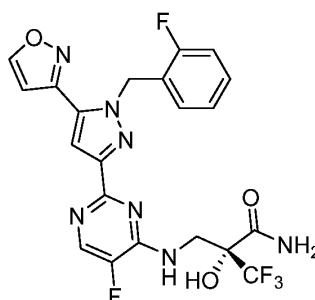
Formula VI, and

vi) reacting an amine of formula **(15A)** or its HCl salt of formula **(15)**:

**(15A)****(15)**

with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula ID.

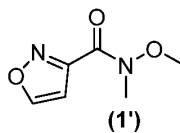
60. A process of preparing a compound of Formula ID:



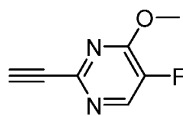
Formula ID,

comprising the steps of:

i) coupling an amide of formula **(1')**:

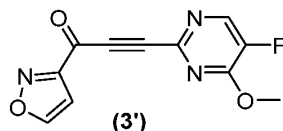
**(1')**

with a pyrimidine compound of formula **(2)**:



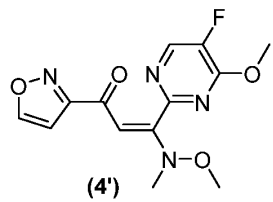
(2)

in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):



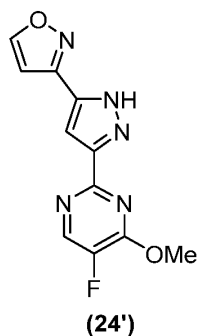
(3')

ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



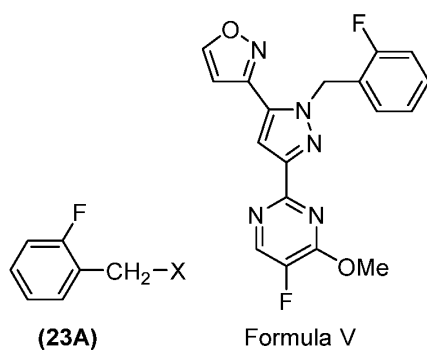
(4')

iiia) condensing the compound of formula (4') with hydrazine (*e.g.*, hydrazine hydrate) to form the compound of formula (24'):

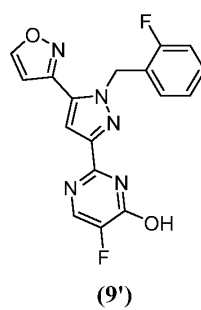


(24')

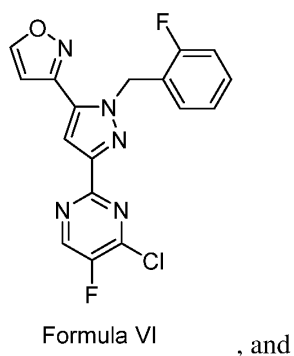
iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A) to provide the compound of Formula V:



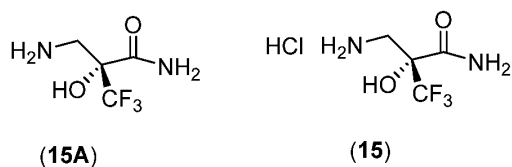
iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



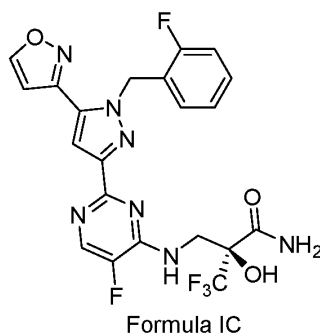
vi) reacting an amine of formula (15A) or its HCl salt of formula (15):



with the compound of Formula VI, optionally in the presence of a base, to yield the compound

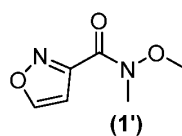
of Formula ID, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

61. A process of preparing a compound of Formula IC:

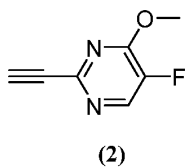


comprises the steps of:

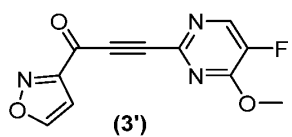
i) coupling an amide for formula (1'):



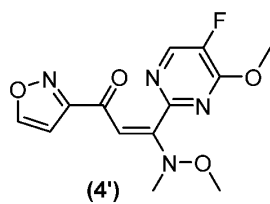
with a pyrimidine compound of formula (2):



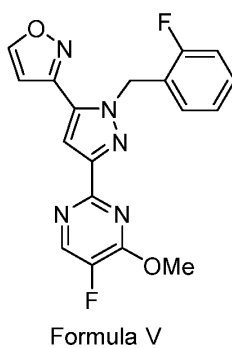
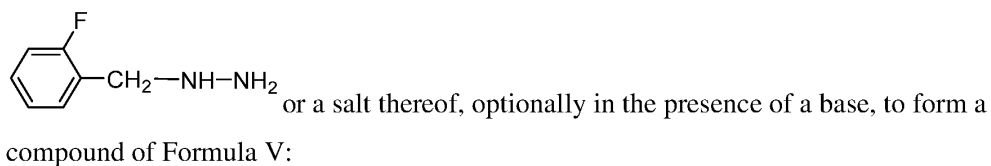
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



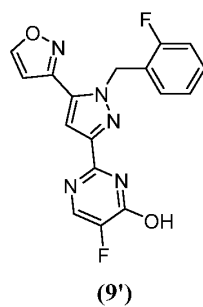
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



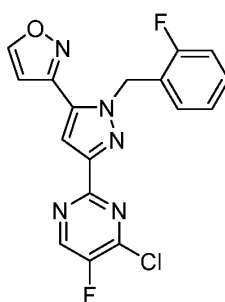
iii) condensing the compound of formula (4') with a hydrazine of formula



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

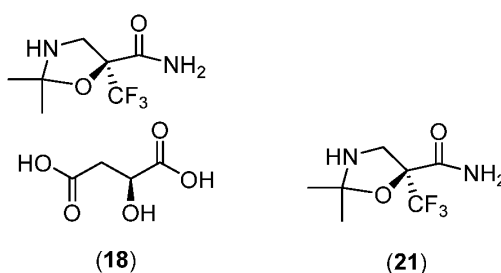


v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



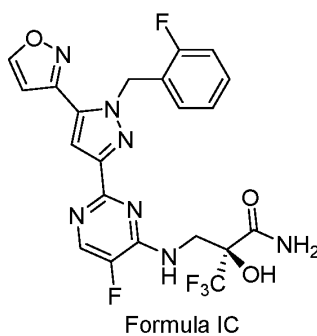
Formula VI ; and

vi) reacting an (*L*)-malic acid salt of an amine (**21**) represented by formula (**18**):



with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IC.

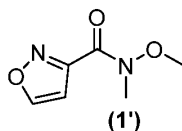
62. A process of preparing a compound of Formula IC:



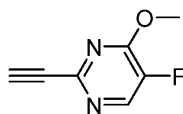
Formula IC ,

comprising the steps of:

i) coupling an amide of formula (**1'**):

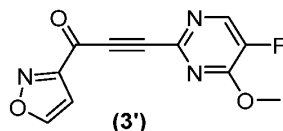


with a pyrimidine compound of formula (**2**):



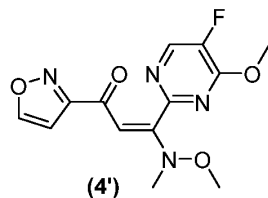
(2)

in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3'):



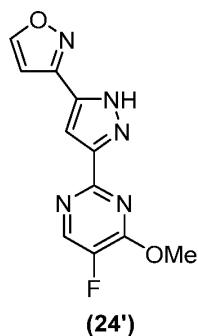
(3')

ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



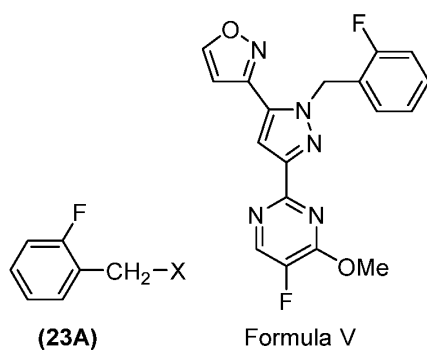
(4')

iiia) condensing the compound of formula (4') with a hydrazine (*e.g.*, hydrazine hydrate) to form a compound of formula (24'):

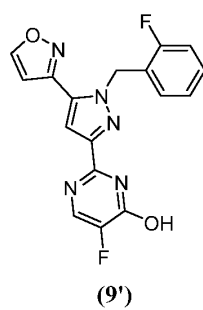


(24')

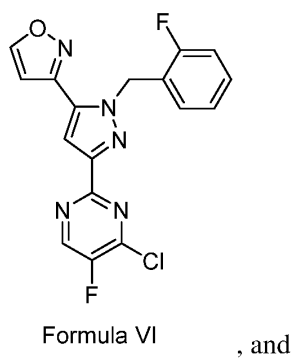
iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A) to provide the compound of Formula V:



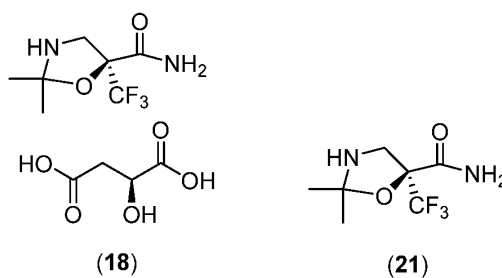
iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:

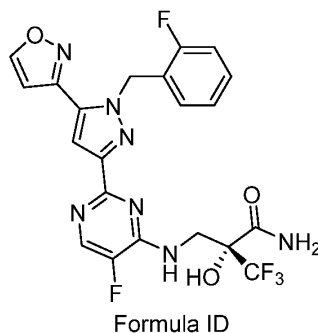


vi) reacting an (*L*)-malic acid salt of an amine (21) represented by formula (18):



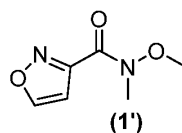
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula IC, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

63. A process of preparing a compound of Formula ID:

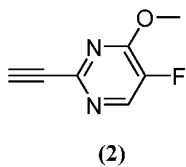


comprising the steps of:

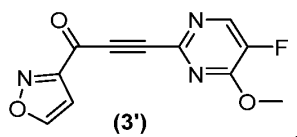
i) coupling an amide of formula (1'):



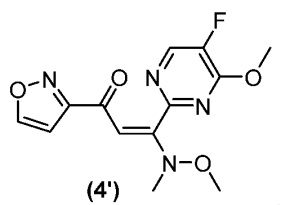
with a pyrimidine compound of formula (2):



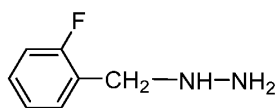
in an aprotic organic solvent in the presence of a base, to form, after quenching with an acid, an intermediate of formula (3')



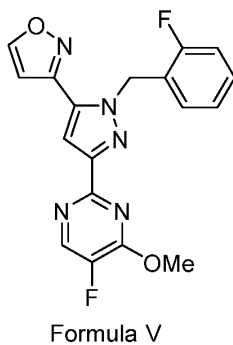
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt thereof, allowing the mixture to react to form the compound of formula (4'):



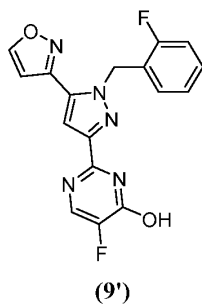
iii) condensing the compound of formula (4') with a hydrazine of formula



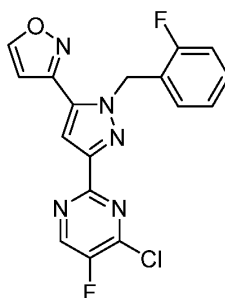
or a salt thereof, optionally in the presence of a base, to form a compound of Formula V:



iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):

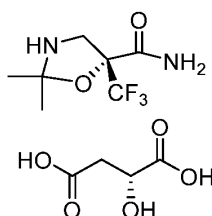


v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:

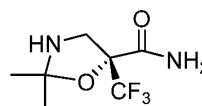


Formula VI , and

vi) reacting a (*D*)-malic acid salt of an amine (20) represented by formula (14):



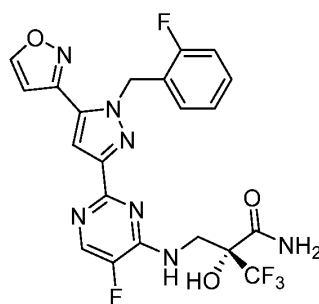
(14)



(20)

with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula ID.

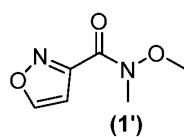
64. A process of preparing a compound of Formula ID:



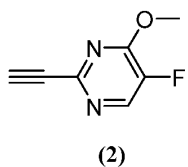
Formula ID ,

comprising the steps of:

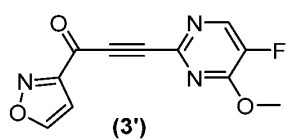
i) coupling an amide of formula (1'):



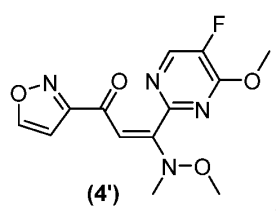
with a pyrimidine compound of formula (2):



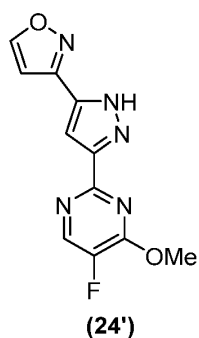
in an aprotic organic solvent in the presence of a base, to form, after quenching with acid, an intermediate of formula (3'):



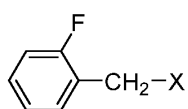
ii) at a pH >5, optionally in the presence of added *N,O*-dimethylhydroxylamine or a salt (*e.g.* HCl salt) thereof, allowing the mixture to react to form the compound of formula (4'):



iiia) condensing the compound of formula (4') with a hydrazine (*e.g.*, hydrazine hydrate) to form a compound of formula (24'):

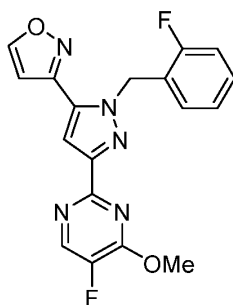


iiib) alkylating intermediate of formula (24') with an alkylating agent of formula (23A)



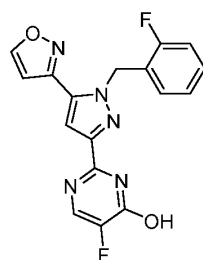
(23A)

to provide the compound of Formula V:



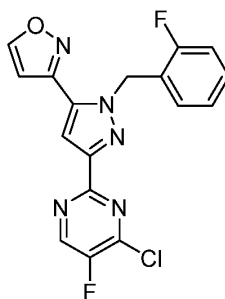
Formula V

iv) de-methylating the compound of Formula V to form an alcohol compound of formula (9'):



(9')

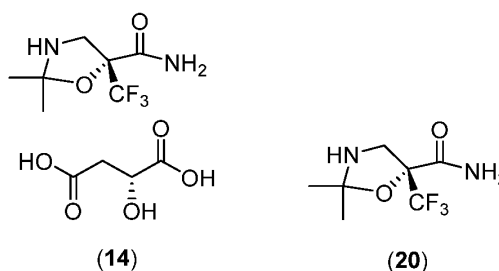
v) chlorinating the alcohol compound of formula (9') with phosphoryl chloride to form a compound of Formula VI:



Formula VI

, and

vi) reacting a (*D*)-malic acid salt of an amine (20) represented by formula (14):



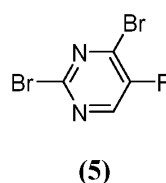
with the compound of Formula VI, optionally in the presence of a base, to yield the compound of Formula ID, wherein X is a leaving group selected from -Br, -I, -Cl, -F, and a sulfonate ester (e.g., mesylate, tosylate or triflate).

65. The process of claim 63 or 64, further comprising the step of crystallization of the compound of Formula ID to yield Form B of the compound.

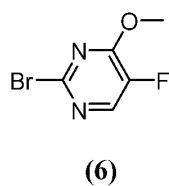
66. The process of claim 65, wherein the crystallization comprises the steps of: A) dissolving the compound of Formula ID in acetonitrile and water at between a temperature between 40 °C and 80 °C to form a solution of the compound; B) filtering the solution of step A) to form a filtered solution of the compound; C) heating the filtered solution at a temperature between 40 °C and 80 °C and adding water to yield a slurry; D) cooling the slurry of step C) to yield crystalline Form B of the compound of Formula ID; and E) filtering and drying the crystalline Form B of the compound of Formula ID.

67. The process of any one of claims 34-66, wherein the compound of formula (2) is prepared by a process comprising the steps of:

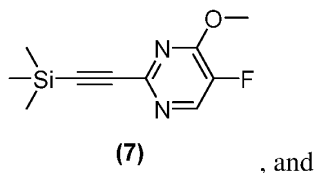
a) reacting dibromopyrimidine compound of formula (5):



with a base in methanol or a methoxide salt in an aprotic solvent to form a bromopyrimidine compound of formula (6):

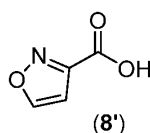


b) coupling the bromopyrimidine compound of formula (6) with ethynyltrimethylsilane, in an aprotic organic solvent in the presence of a base and a Pd catalyst, optionally in the presence of a Cu(I) catalyst, to form a compound of formula (7):



c) de-silylating the compound of formula (7) to form the pyrimidine compound of (2).

68. The process of any one of claims 34-67, wherein the compound of formula (1') is prepared by reacting a carboxylic acid of formula (8')



with oxalyl chloride or an equivalent amide coupling reagent, followed by *N,O*-dimethylhydroxylamine or a salt thereof, in the presence of a base to form the amide of formula (1').

69. The process of any one of claims 34-68, wherein the base in step i) is *n*-butyllithium.

70. The process of any one of claims 34-69, wherein the process comprises contacting the reaction product of the reaction between the amide of formula (1') and the pyrimidine compound of formula (2) with a solution comprising *N,O*-dimethylhydroxylamine or a salt thereof and an acid to form the compound of formula (4').

71. The process of claim 70, wherein the solution comprises *N,O*-dimethylhydroxylamine hydrochloride.

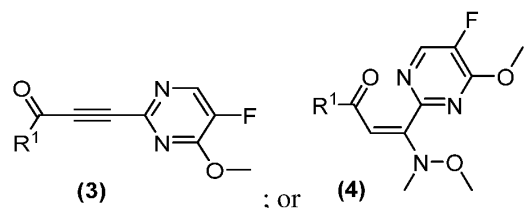
72. The process of claim 70 or 71, wherein the acid is an aqueous acid.

73. The process of claim 72, wherein the acid is hydrochloric acid.

74. The process of claim 70 or 71, wherein the acid is glacial acetic acid.

75. The process of any one of claims 3, 5, 7, 9, 11-33, 36, 40, 42-50, 52-54, 56, 58, 60, 62 and 64-74, wherein X is -Br.

76. A compound of formula (3) or (4):

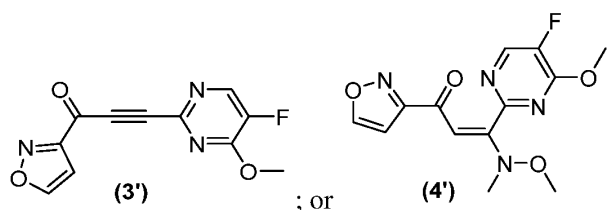


wherein R^1 is phenyl, or a 5 to 6-membered heteroaryl ring; optionally substituted with up to three instances independently selected from the group consisting of halogen or methyl; wherein said 5 or 6-membered heteroaryl ring contains up to 3 ring atoms selected from the group consisting of N, S or O.

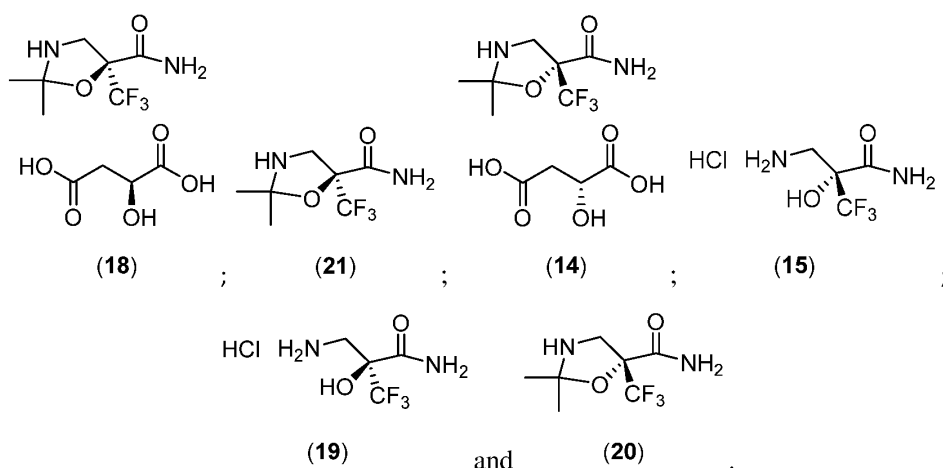
77. The compound of claim 76, wherein R^1 is a 5-membered heteroaryl ring.

78. The compound of claim 77, wherein R^1 is an unsubstituted 5-membered heteroaryl ring containing up to 2 ring heteroatoms selected from the group consisting of N and O.

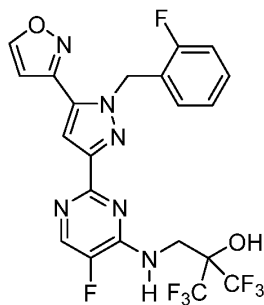
79. The compound of claim 78, wherein the compound is represented by formula (3') or (4'):



80. A compound represented by any one of the following formulae:



81. Crystalline Form A of the compound of Formula IA:



Formula IA

having at least one, two, three, four, five, six, seven or eight major peaks in an x-ray powder diffraction (XRPD) pattern selected from selected from 4.2, 9.1, 9.8, 17.2, 17.7, 18.2, 27.5, and 36.0 degree 2 θ angles.

82. The crystalline Form A of claim 81, having the XRPD pattern of FIG. 1.

83. The crystalline Form A of claim 81 or 82, having an endothermic onset at a temperature between 160 °C and 165 °C in a differential scanning calorimetry (DSC) profile.

84. The crystalline Form A of claim 83, wherein the endothermic onset is at 163.1 °C.

85. The crystalline Form A of any one of claims 81-84, wherein at least 70%, 80%, 90%, 95%, 98%, 99%, 99.5%, or 99.9% of the compound is the crystalline Form A of the compound.