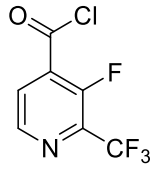
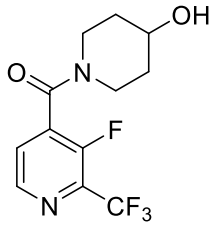
WHAT IS CLAIMED IS:

1. A process, comprising reacting a compound of Formula III:



III

or a salt thereof, with 4-hydroxypiperidine to form a compound of Formula IV:



IV

or a salt thereof.

2. The process of claim 1, wherein the reacting with 4-hydroxypiperidine is conducted in the presence of a base.

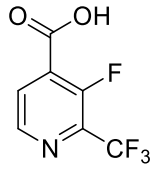
3. The process of claim 2, wherein the base is a tertiary amine.

4. The process of claim 3, wherein the tertiary amine is *N,N*-diisopropylethylamine.

5. The process of any one of claims 1-4, wherein the reacting with 4-hydroxypiperidine is conducted in a solvent component which comprises dichloromethane.

6. The process of any one of claims 1-5, wherein the reacting with 4-hydroxypiperidine is conducted at a temperature of from about 25 °C to about 35 °C.

7. The process of any one of claims 1-6, wherein the compound of Formula III is formed by a process comprising reacting a compound of Formula II:



II

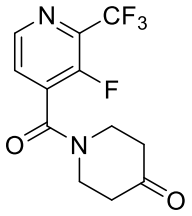
or a salt thereof, with oxalyl chloride to form the compound of Formula III, or a salt thereof.

8. The process of claim 7, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted in the presence of a catalytic amount of dimethyl formamide (DMF).

9. The process of claim 7 or claim 8, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted in a solvent component comprising dichloromethane.

10. The process of any one of claims 7-9, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted at a temperature of from about 15 °C to about 25 °C.

11. The process of any one of claims 1-10, further comprising reacting the compound of Formula IV, or a salt thereof, under oxidation conditions to form a compound of Formula V:



V

or a salt thereof.

12. The process of claim 11, wherein the oxidation conditions comprise a first oxidizing agent.

13. The process of claim 12, wherein the oxidation conditions comprise a second oxidizing agent.

14. The process of claim 12 or claim 13, wherein the first oxidizing agent is trichloroisocyanuric acid (TCIC).

15. The process of claim 14, wherein the TCIC is present at between about 0.5 and about 0.7 molar equivalents with respect to the compound of Formula IV.

16. The process of any one of claims 13-15, wherein the second oxidation agent is 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO).

17. The process of claim 16, wherein the TEMPO is present at between about 0.015 and about 0.025 molar equivalents with respect to the compound of Formula IV.

18. The process of any one of claims 11-17, wherein the reacting of the compound of Formula IV under oxidation conditions further comprises one or more of sodium bicarbonate, sodium carbonate, and sodium bromide.

19. The process of any one of claims 11-18, wherein the reacting of the compound of Formula IV under oxidation conditions further comprises a solvent component comprising dichloromethane.

20. The process of claim 19, wherein the solvent component further comprises water.

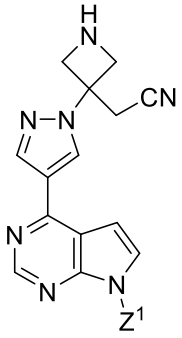
21. The process of claim 11, wherein the oxidation conditions comprise addition of trichloroisocyanuric acid to a solution comprising the compound of Formula IV and TEMPO at a temperature of from about 0 °C to about 5 °C.

22. The process of claim 21, wherein the addition of trichloroisocyanuric acid comprises adding the trichloroisocyanuric acid in at least two portions.

23. The process of claim 21 or claim 22, wherein the solution is stirred after said addition at a temperature of from about 0 °C to about 5 °C for about 30 min.

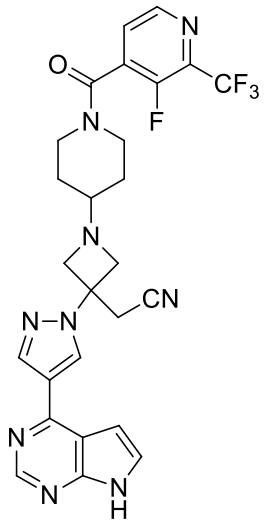
24. The process of claim 23, further comprising, after said stirring, warming said solution to a temperature of from about 20 °C to about 25 °C for a time of about one hour to about two hours.

25. The process of any one of claims 11-24, further comprising reacting the compound of Formula V with a compound of Formula VI:



VI

or a salt thereof, in the presence of a reducing agent, to form a compound of Formula I:



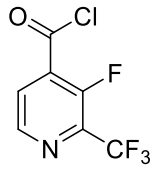
I

or a salt thereof;
wherein Z^1 is H or a protecting group.

26. The process of claim 25, wherein Z^1 is H.

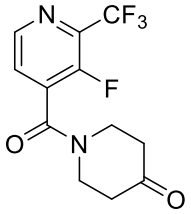
27. The process of claim 25 or claim 26, wherein the reducing agent is sodium cyanoborohydride or sodium triacetoxyborohydride.

28. A process, comprising reacting a compound of Formula III:



III

or a salt thereof, with 4-piperidone, or a salt thereof, to form a compound of Formula V:



V

or a salt thereof.

29. The process of claim 28, wherein the 4-piperidone, or a salt thereof, is 4-piperidone hydrochloride.

30. The process of claim 28, wherein the 4-piperidone, or a salt thereof, is 4-piperidone hydrochloride monohydrate.

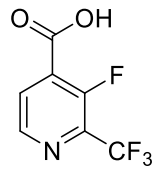
31. The process of any one of claims 28-30, wherein the reacting further comprises a base.

32. The process of claim 31, wherein the base is sodium carbonate.

33. The process of any one of claims 28-32, wherein the reacting of the compound of Formula III with the 4-piperidone is conducted in a solvent component comprising dichloromethane.

34. The process of any one of claims 28-33, wherein the reacting of the compound of Formula III with the 4-piperidone is conducted at a temperature of from about 0 °C to about 5 °C.

35. The process of any one of claims 28-34, wherein the compound of Formula III is formed by a process comprising reacting a compound of Formula II:



II

or a salt thereof, with oxalyl chloride to form the compound of Formula III, or a salt thereof.

36. The process of claim 35, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted in the presence of a catalytic amount of dimethyl formamide (DMF).

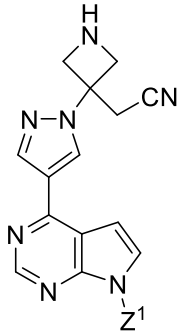
37. The process of claim 35 or claim 36, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted in a solvent component comprising dichloromethane.

38. The process of any one of claims 35-37, wherein the reacting of the compound of Formula II with oxalyl chloride is conducted at a temperature of from about 15 °C to about 25 °C.

39. The process of any one of claims 35-38, wherein the compound of Formula III is not isolated before reacting the compound of Formula III with 4-piperidone.

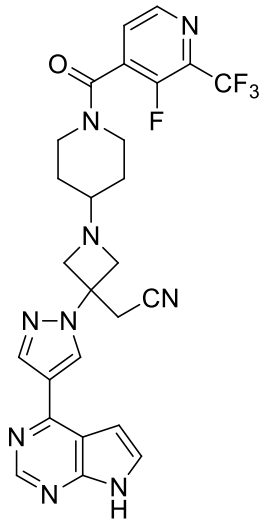
40. The process of any one of claims 35-39, wherein the reacting of the compound of Formula II with oxalyl chloride and the reacting of the compound of Formula III with 4-piperidone are conducted in a single reactor.

41. The process of any one of claims 28-40, further comprising reacting the compound of Formula V with a compound of Formula VI:



VI

or a salt thereof, in the presence of a reducing agent, to form a compound of Formula I:



I

or a salt thereof;

wherein Z^1 is H or a protecting group.

42. The process of claim 41, wherein Z^1 is H.

43. The process of claim 41 or claim 42, wherein the reducing agent is sodium cyanoborohydride or sodium triacetoxyborohydride.