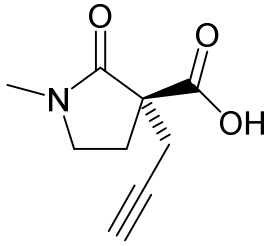
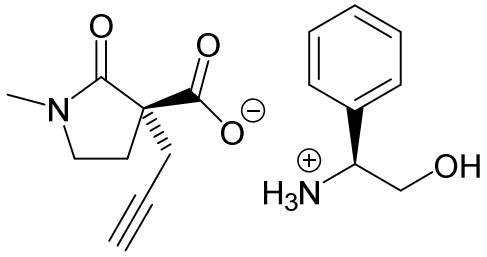
CLAIMS

1. A compound which is (S)-1-methyl-2-oxo-3-(prop-2-yn-1-yl)pyrrolidine-3-carboxylic acid (D6):



(D6).

2. A process of preparing the compound of D6 as defined in claim 1, from a compound which is (S)-1-methyl-2-oxo-3-(prop-2-yn-1-yl)pyrrolidine-3-carboxylic acid (S)-phenylglycinol salt (D5):



(D5)

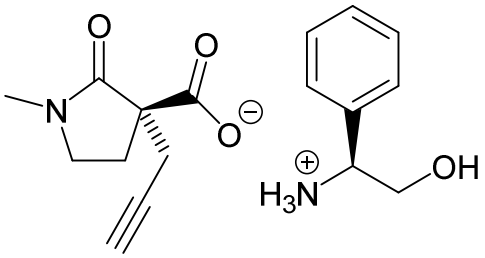
by eluting a solution comprising the compound of D5 through a resin.

3. The process of claim 2, wherein the solution comprises water or methanol.

4. The process of claim 2 or 3, wherein the resin is a cation-exchange resin.

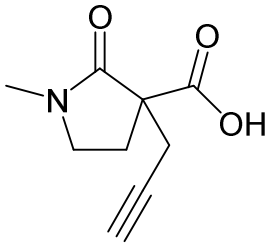
5. The process of claim 4, wherein the cation-exchange resin is Dowex (50WX4) resin.

6. The process of any one of claims 2-5, comprising preparing the compound of D5:



(D5)

from a compound of D4:



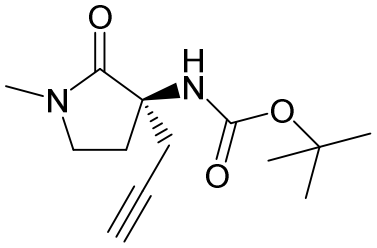
(D4)

by contacting the compound of D4 with S-(+)-2-phenylglycinol in a solution.

7. The process of claim 6, wherein the process further comprises a recrystallization step.

8. The process of claim 7, wherein the recrystallization step comprises seeding with crystalline (S)-1-methyl-2-oxo-3-(prop-2-yn-1-yl)pyrrolidine-3-carboxylic acid (S)-phenylglycinol salt.

9. The process of any one of claims 2-8, further comprising preparing a compound of D7:



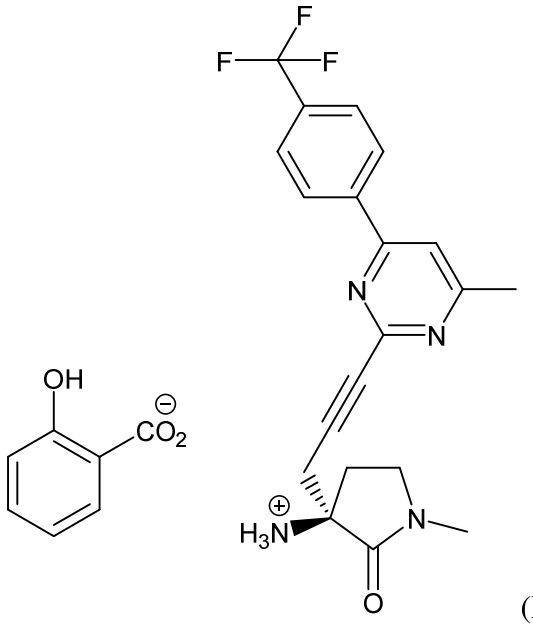
(D7)

from the compound of D6 by contacting the compound of D6 with a phosphoazide and a base.

10. The process of claim 9, wherein the phosphoazide is diphenylphosphorylazide.

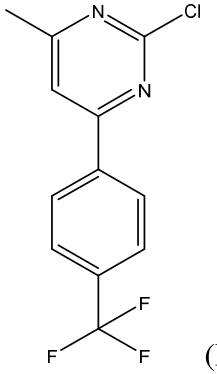
11. The process of claim 9 or 10, wherein the base is triethylamine.

12. The process of any one of claims 9-11, further comprising preparing a compound of D9:



(D9)

from the compound of D7 and a compound of D8:



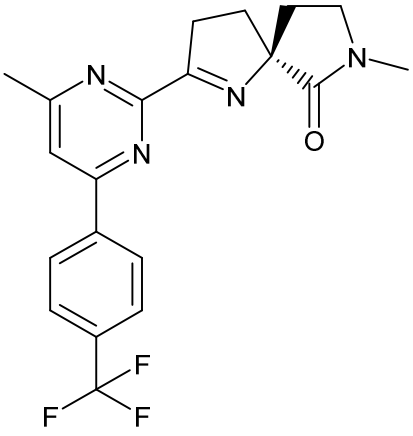
(D8)

by reacting the compound of D7 with the compound of D8 in the presence of a palladium catalyst, a copper salt, and a base.

13. The process of claim 12, wherein the palladium catalyst is dichloro{bis[2-(diphenylphosphino)phenyl]ether}palladium(II).

14. The process of claim 12 or 13, wherein the copper salt is copper(I) iodide.

15. The process of any one of claims 12-14, further comprising preparing a compound of D10:

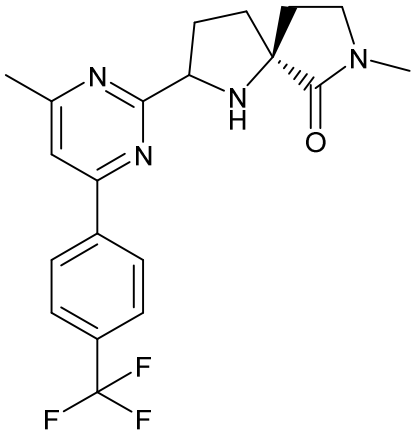


(D10)

from the compound of D9 by contacting the compound of D9 with a base.

16. The process of claim 15, wherein the base is potassium phosphate.

17. The process of claim 15 or 16, further comprising preparing a compound of formula (I):



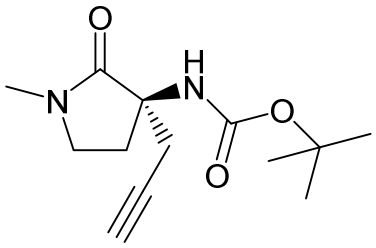
(I)

from the compound of D10 by contacting the compound of D10 with a reducing agent.

18. The process of claim 17, wherein the reducing agent is a borane.

19. The process of claim 18, wherein the borane is borane *tert*-butylamine complex.

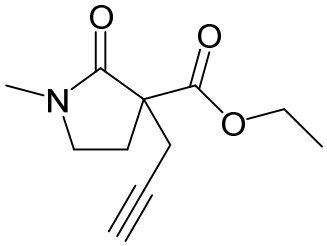
20. A process of preparing a compound which is (S) tert-Butyl (1-methyl-2-oxo-3-(prop-2-yn-1-yl)pyrrolidin-3-yl)carbamate (D7):



(D7)

which comprises:

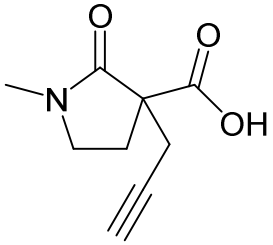
(i) preparing a compound of D1:



(D1)

from 1-methylpyrrolidin-2-one by contacting the 1-methylpyrrolidin-2-one with diethyl carbonate in the presence of a base followed by addition of 3-bromoprop-1-yne; followed by

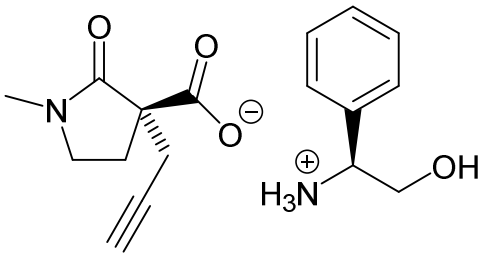
(ii) preparing a compound of D4:



(D4)

from a compound of D1 by reacting the compound of D1 with sodium hydroxide; followed by

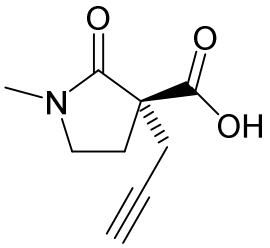
(iii) preparing a compound of D5:



(D5)

from a compound of D4 by contacting the compound of D4 with S-(+)-2-phenylglycinol in a solution; followed by

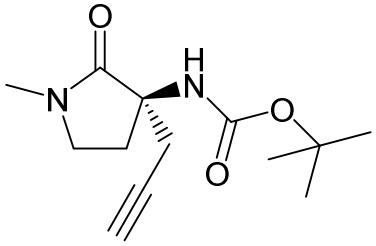
(iv) preparing a compound of D6:



(D6)

from a compound of D5 by eluting a solution comprising the compound of D5 through a resin; and followed by

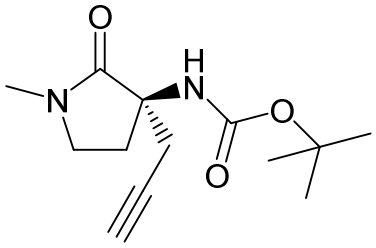
(v) preparing a compound of D7:



(D7)

from a compound of D6 by contacting the compound of D6 with a phosphoazide and a base.

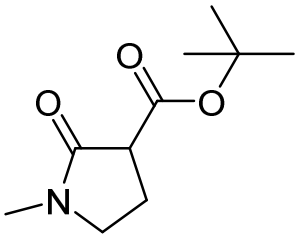
21. A process of preparing a compound which is (S) tert-Butyl (1-methyl-2-oxo-3-(prop-2-yn-1-yl)pyrrolidin-3-yl)carbamate (D7):



(D7)

which comprises:

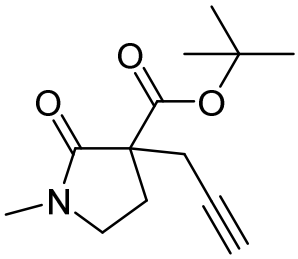
(a) preparing a compound of D2:



(D2)

from 1-methylpyrrolidin-2-one by contacting the 1-methylpyrrolidin-2-one with di-tert-butyl carbonate in the presence of a base; followed by

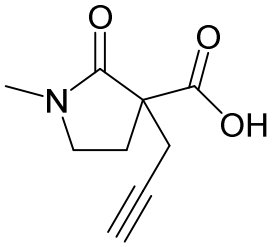
(b) preparing a compound of D3:



(D3)

from a compound of D2 by contacting the compound of D2 with 3-bromoprop-1-yne in the presence of a base; followed by

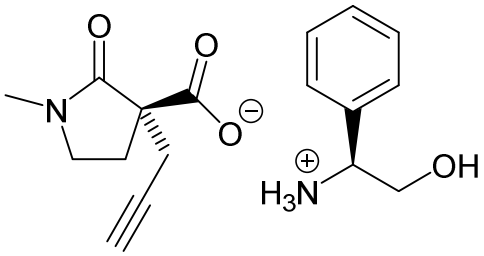
(c) preparing a compound of D4:



(D4)

from a compound of D3 by reacting the compound of D3 with trifluoroacetic acid; followed by

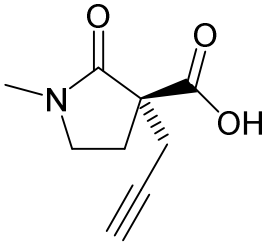
(iii) preparing a compound of D5:



(D5)

from a compound of D4 by contacting the compound of D4 with S-(+)-2-phenylglycinol in a solution; followed by

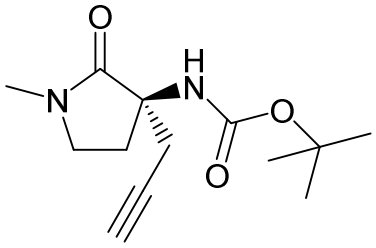
(iv) preparing a compound of D6:



(D6)

from a compound of D5 by eluting a solution comprising the compound of D5 through a resin; and followed by

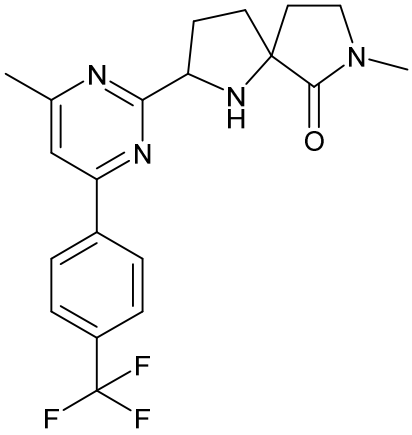
(v) preparing a compound of D7:



(D7)

from a compound of D6 by contacting the compound of D6 with a phosphoazide and a base.

22. A process of preparing a compound which is 7-methyl-2-[4-methyl-6-[4-(trifluoromethyl)-phenyl]pyrimidin-2-yl]-1,7-diazaspiro[4.4]nonan-6-one, i.e. a compound of formula (I):

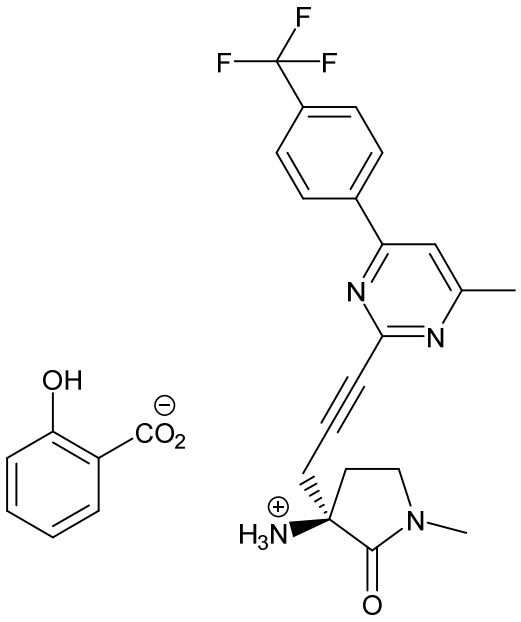


(I)

which comprises:

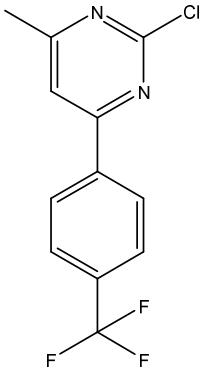
steps (i) to (v) as defined in claim 20; or steps (a) to (c) followed by steps (iii) to (v) as defined in claim 21; followed by:

(vi) preparing a compound of D9:



(D9)

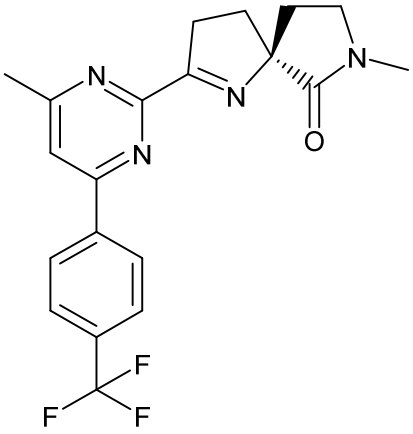
from a compound of D7 and a compound of D8:



(D8)

by contacting the compound of D7 with the compound of D8 in the presence of a palladium catalyst, a copper salt, and a base; followed by

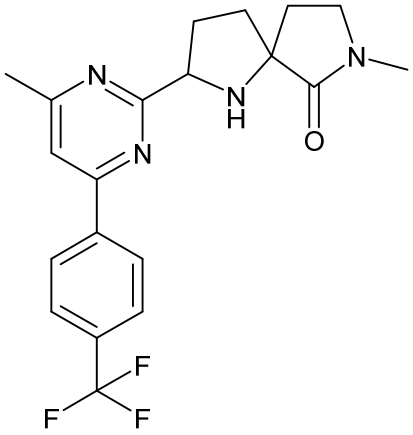
(vii) preparing a compound of D10:



(D10)

from a compound of D9 by contacting the compound of D9 with a base; followed by

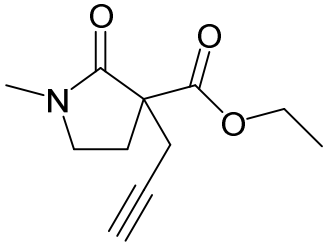
(viii) preparing a compound of formula (I):



(I)

from a compound of D10 by contacting the compound of D10 with a reducing agent.

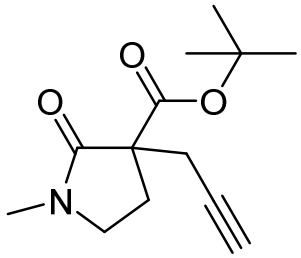
23. A process of preparing a compound which is D1:



(D1)

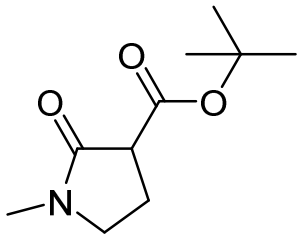
from 1-methylpyrrolidin-2-one comprising contacting the 1-methylpyrrolidin-2-one with diethyl carbonate in the presence of a base followed by addition of 3-bromoprop-1-yne.

24. A process of preparing a compound of D3:



(D3)

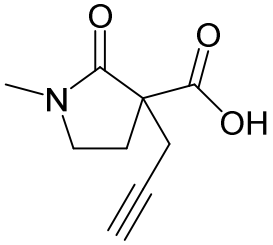
from a compound of D2:



(D2)

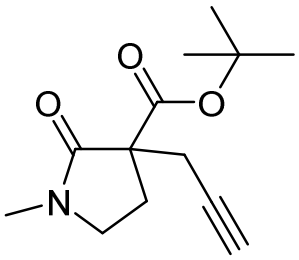
comprising contacting the compound of D2 with 3-bromoprop-1-yne in the presence of a base.

25. A process of preparing a compound of D4:



(D4)

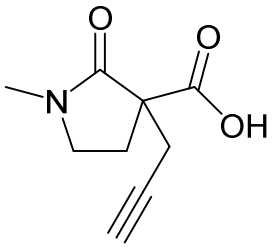
from a compound of D3:



(D3)

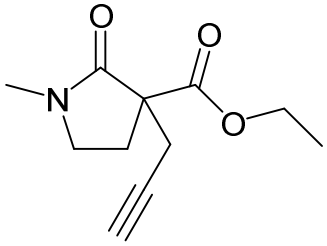
comprising contacting the compound of D3 with trifluoroacetic acid.

26. A process of preparing a compound of D4:



(D4)

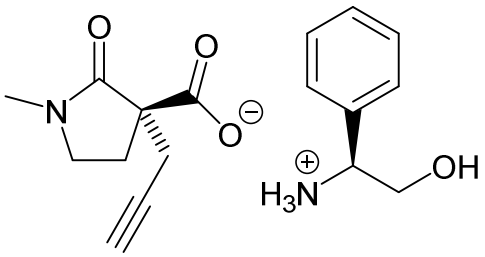
from a compound of D1:



(D1)

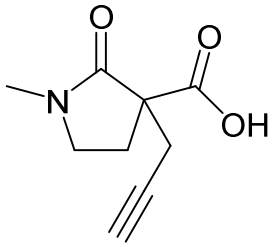
comprising contacting the compound of D1 with sodium hydroxide.

27. A process of preparing a compound of D5:



(D5)

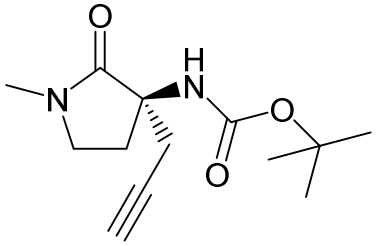
from a compound of D4:



(D4)

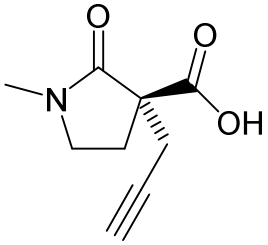
comprising contacting the compound of D4 with S-(+)-2-phenylglycinol in a solution.

28. A process of preparing a compound of D7:



(D7)

from a compound of D6:



(D6)

comprising contacting the compound of D6 with a phosphoazide and a base.