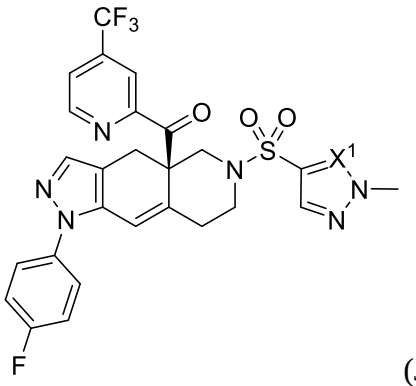
WHAT IS CLAIMED IS:

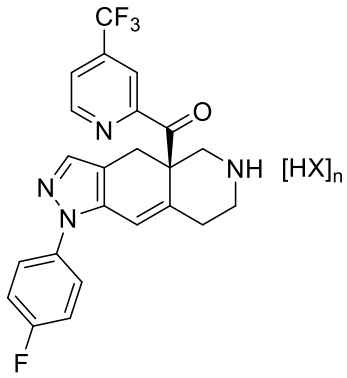
Claim 1. A method of preparing a compound of Formula J:



(J)

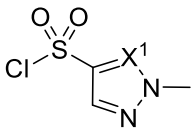
or a pharmaceutically acceptable salt thereof, comprising:

(a) forming a first reaction mixture comprising a compound of Formula IIb:



(IIb) , and

a sulfonyl chloride:



, to prepare the compound of Formula J in a yield of at least 60% and a purity of at least 98%,

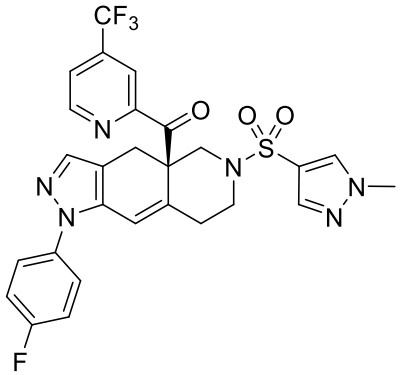
wherein

X^1 is –CH= or –N=;

HX is an acid solvate; and

subscript n is from 1 to 4.

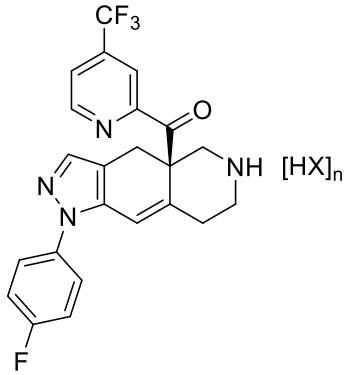
Claim 2. The method of claim 1, preparing the compound of Formula I:



(I)

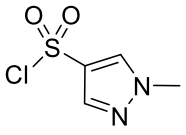
or a pharmaceutically acceptable salt thereof, comprising:

(a) forming the first reaction mixture comprising the compound of Formula IIb:



(IIb) , and

1-methyl-1H-pyrazole-4-sulfonyl chloride:



,

to prepare the compound of Formula I in a yield of at least 60% and a purity of at least 98%,

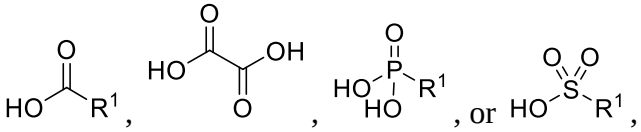
wherein

HX is the acid solvate; and

subscript n is from 1 to 4.

Claim 3. The method of claim 2, wherein

HX is HCl, HBr,

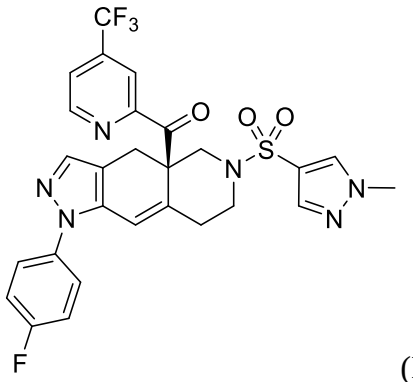


wherein

R^1 is C_{1-6} alkyl, C_{1-10} haloalkyl, phenyl, or 4-methylphenyl.

Claim 4. The method of any one of claims 1 to 3, wherein HX is HBr.

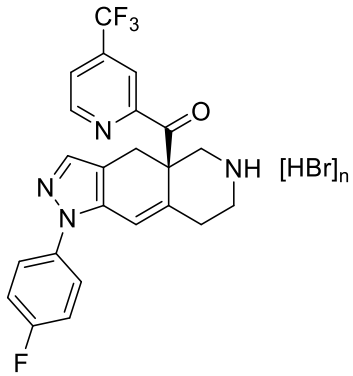
Claim 5. The method of claim 4, for preparing the compound of Formula I:



(I)

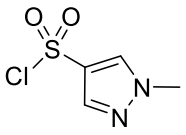
or a pharmaceutically acceptable salt thereof, comprising:

(a) forming the first reaction mixture comprising a compound of Formula IIb-1:



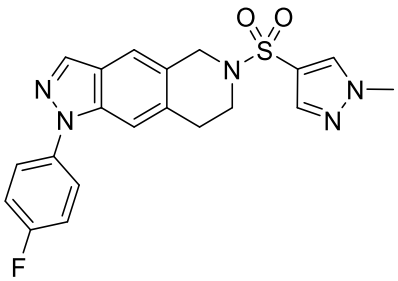
(IIb-1) , and

1-methyl-1H-pyrazole-4-sulfonyl chloride:



,

to prepare the compound of Formula I in a yield of at least 60% and a purity of at least 98%, wherein the compound of Formula I contains less than 1% (w/w) of a compound of Formula X-5:



(X-5) ,

and wherein subscript n is from 1 to 4.

Claim 6. The method of claim 5, wherein the first reaction mixture further comprises a non-nucleophilic amine base.

Claim 7. The method of claim 6, wherein the non-nucleophilic amine base comprises trimethyl amine, triethylamine, N,N-diisopropyl ethylamine (DIPEA), N,N-dimethyl isopropylamine (DIMPA), 1-ethylpiperidine, N-methylmorpholine, N-methylpyrrolidine, pyridine, N,N-dimethylaniline, N,N-diethylaniline, 2,6-lutidine, 2,4,6-collidine, 4-dimethyl aminopyridine (DMAP), quinuclidine, 4-pyrrolidinopyridine, 1,4-diazabicyclo[2.2.2]octane (DABCO), or mixtures thereof.

Claim 8. The method of any one of claims 5 to 7, wherein the sulfonyl chloride is present in a molar ratio of 1.2 to 2.3 to the compound of Formula IIb-1.

Claim 9. The method of any one of claims 5 to 8, further comprising after step (a):

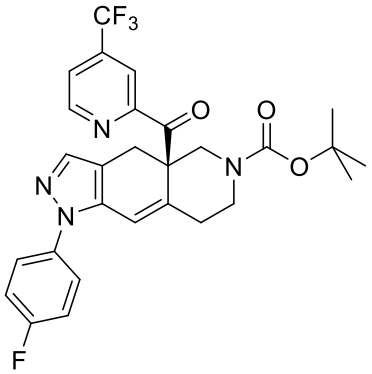
(a1) mixing the first reaction mixture with water having a pH of between 4 and 5 to form a first organic phase and a first aqueous phase;

(a2) mixing the first organic phase with water and sodium chloride wherein the water has a pH of between 5 and 6; and

(a3) mixing the first organic phase and silica gel.

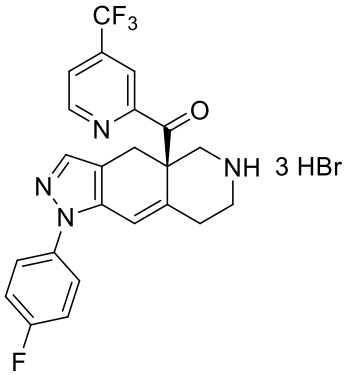
Claim 10. The method of any one of claims 5 to 9, wherein the compound of Formula IIb-1 is prepared by the step of:

(b) forming a second reaction mixture comprising a compound of Formula IIa:



(IIa) ,

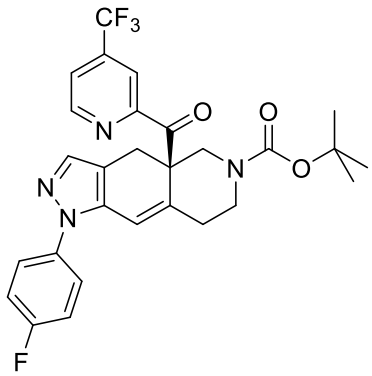
and gaseous HBr, to form the compound of Formula IIb-1 having the structure:



.

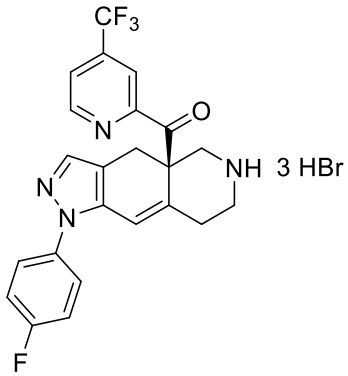
Claim 11. The method of any one of claims 5 to 10, wherein the compound of Formula I is prepared by the steps of:

(b) forming the second reaction mixture comprising a compound of Formula IIa:



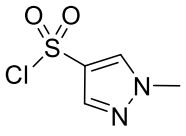
(IIa) ,

and gaseous HBr, to form the compound of Formula IIb-1 having the structure:



; and

(a) forming the first reaction mixture comprising the compound of Formula IIb-1: triethylamine, and 1-methyl-1H-pyrazole-4-sulfonyl chloride:



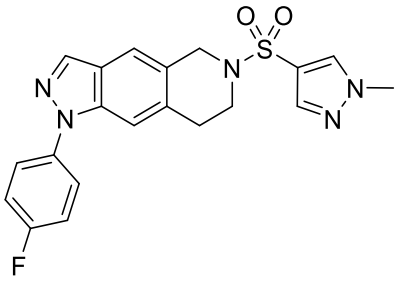
,

wherein the sulfonyl chloride is present in a molar ratio of about 1.2 to the compound of Formula IIb-1;

(a1) mixing the first reaction mixture with water having a pH of between 4 and 5 to form a first organic phase and a first aqueous phase;

(a2) mixing the first organic phase with water and sodium chloride wherein the water has a pH of between 5 and 6; and

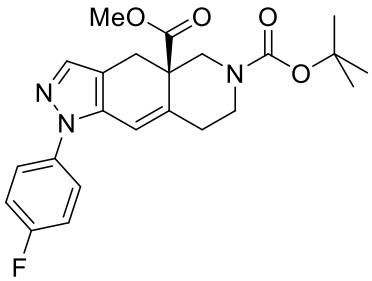
(a3) mixing the first organic phase and silica gel to prepare the compound of Formula I in a yield of at least 60% and a purity of at least 98%, wherein the compound of Formula I contains less than 1% (w/w) of the compound of Formula X-5:



(X-5) .

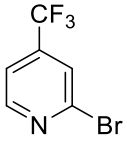
Claim 12. The method of claim 10 or 11, wherein the compound of Formula IIa is prepared by:

(c) forming a third reaction mixture comprising a Grignard reagent, a compound of Formula III:



(III) , and

2-bromo-4-(trifluoromethyl)pyridine:



,

wherein the pyridine is present in a molar ratio of 1.0 to 1.5 to the compound of Formula III, and wherein the Grignard reagent is present in a molar ratio of 1.5 to 1.7 to the compound of Formula III, to prepare the compound of Formula IIa.

Claim 13. The method of claim 12, wherein the Grignard reagent comprises iPrMgCl or iPrMgBr.

Claim 14. The method of any one of claims 12 to 13, wherein the third reaction mixture further comprises a third solvent comprising tetrahydrofuran, 2-methyltetrahydrofuran, toluene or xylene.

Claim 15. The method of claim 14, wherein the third solvent comprises 2-methyltetrahydrofuran and toluene.

Claim 16. The method of any one of claims 12 to 15, further comprising the steps of:

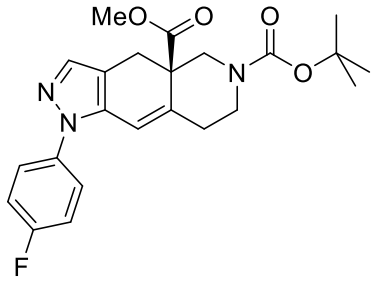
(c1) adding an acid and water to the third reaction mixture to form a workup mixture; and

(c2) distilling the workup mixture to form an intermediate mixture comprising the compound of Formula IIa, 2-methyltetrahydrofuran in an amount of less than 100 ppm, and water in an amount of less than 0.5% (w/w).

Claim 17. The method of claim 16, wherein the acid comprises formic acid, acetic acid, propanoic acid, butyric acid, hexanoic acid, octanoic acid, trifluoroacetic acid, or mixtures thereof.

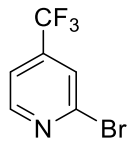
Claim 18. The method of claim 17, wherein the method of preparing the compound of Formula I comprises:

(c) forming the third reaction mixture comprising iPrMgBr, 2-methyltetrahydrofuran, toluene, the compound of Formula III:



(III) , and

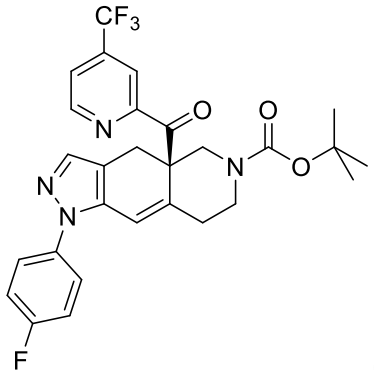
2-bromo-4-(trifluoromethyl)pyridine:



,

wherein the pyridine is present in the molar ratio of about 1.4 to the compound of Formula III, and wherein the Grignard reagent is present in the molar ratio

of about 1.65 to the compound of Formula III, to prepare the compound of Formula IIa:

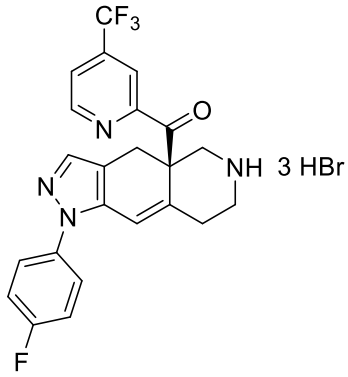


(IIa) ;

(c1) adding acetic acid and water to the third reaction mixture to form the workup mixture;

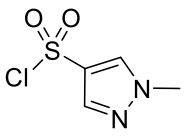
(c2) distilling the workup mixture to form an intermediate mixture comprising the compound of Formula IIa, 2-methyltetrahydrofuran in an amount of less than 100 ppm, and water in an amount of less than 0.5% (w/w);

(b) forming the second reaction mixture comprising the intermediate mixture and gaseous HBr, to form the compound of Formula IIb-1 having the structure:



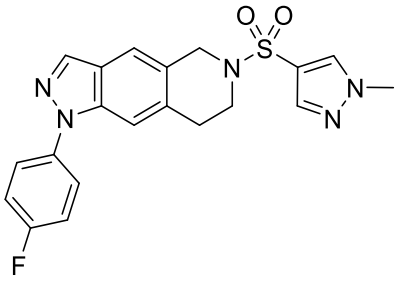
; and

(a) forming the first reaction mixture comprising the compound of Formula IIb-1, triethylamine, and 1-methyl-1H-pyrazole-4-sulfonyl chloride:



,

wherein the sulfonyl chloride is present in the molar ratio of about 1.2 to the compound of Formula IIb-1, to prepare the compound of Formula I in the yield of at least 60% and the purity of at least 98%, wherein the compound of Formula I contains less than 1% (w/w) of the compound of Formula X-5:



(X-5) .

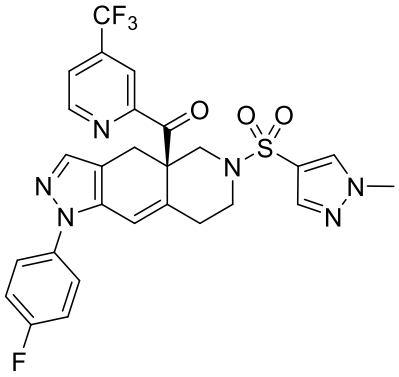
Claim 19. The method of claim 18, wherein the method further comprises following step (a):

(a1) mixing the first reaction mixture with water having the pH of between 4 and 5 to form the first organic phase and the first aqueous phase;

(a2) mixing the first organic phase with water and sodium chloride wherein the water has the pH of between 5 and 6; and

(a3) mixing the first organic phase and silica gel.

Claim 20. A method of purifying a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, comprising:

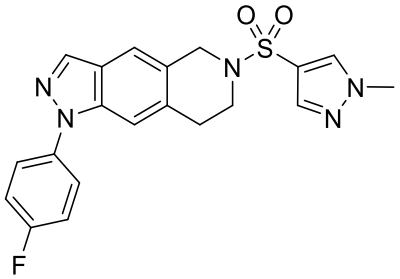
(a) eluting the compound of Formula I through a High Pressure Liquid Chromatography C18 column using

(i) a first mobile mixture comprising water in an amount of at least 95% (v/v), formic acid in an amount of 0.05 to 0.2% (v/v), and acetonitrile in an amount of 1 to 5% (v/v),

(ii) a second mobile mixture comprising water in an amount of 45 to 55% (v/v), formic acid in an amount of 0.01 to 0.1% (v/v), and acetonitrile in an amount of 45 to 55% (v/v), and

(iii) a third mobile phase comprising water in an amount of 5 to 15% (v/v), formic acid in an amount of 0.005 to 0.02% (v/v), and acetonitrile in an amount of at least 85% (v/v),

to form an eluted mixture comprising the compound of Formula I having a purity of at least 98% and the compound of Formula X-5 in an amount of less than 0.75% (w/w):



(X-5) ;

(a1) extracting the compound of Formula I from the eluted mixture into ethyl acetate to form an extracted mixture;

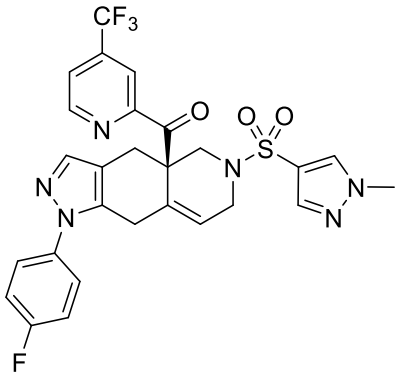
(a2) mixing the extracted mixture with methyl t-butyl ether (MTBE) under vacuum to form an MTBE mixture comprising less than 5% (v/v) ethyl acetate;

(d) filtering the MTBE mixture through a filter to form a filtered MTBE mixture comprising:

the compound of Formula I,

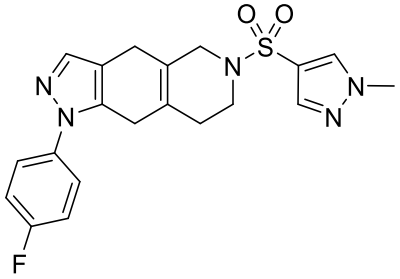
the compound of Formula X-5 in an amount of less than 0.5% (w/w),

a compound of Formula X-4 in an amount of less than 0.3% (w/w):



(X-4) , and

a compound of Formula X-6 in an amount of less than 0.25% (w/w):



(X-6) ;

(e) adding the filtered MTBE mixture to heptane to form a precipitated compound of Formula I, wherein the precipitated compound of Formula I comprises 1,4-dibromopentane in an amount of less than 20 ppm;

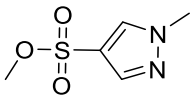
(f) dissolving the precipitated compound of Formula I in methanol to form a methanol mixture; and

(g) adding the methanol mixture to water to precipitate the purified compound of Formula I, wherein the purified compound of Formula I has a purity of at least 99%, and comprises

the compound of Formula X-5 in an amount of less than 0.5% (w/w),

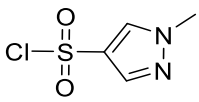
1,4-dibromopentane in an amount of less than 6 ppm,

methyl-1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 6 ppm:



, and

1-methyl-1H-pyrazole-4-sulfonyl chloride in an amount of less than 6 ppm:



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Claim 21. The method of claim 20, wherein the purified compound of Formula I has a purity of at least 99%, and comprises 1,4-dibromopentane in an amount of less than 8 ppm.

Claim 22. The method of claim 20, wherein the purified compound of Formula I has a purity of at least 99%, and further comprises

methyl bromide in an amount of less than 20 ppm, and

2-bromopropane in an amount of less than 20 ppm.

Claim 23. The method of claim 20, wherein the purified compound of Formula I has a purity of at least 99%, and comprises

the compound of Formula X-4 in an amount of less than 0.1% (w/w),

the compound of Formula X-5 in an amount of less than 0.2% (w/w),

the compound of Formula X-6 in an amount of less than 0.2% (w/w),

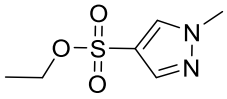
1,4-dibromopentane in an amount of less than 4 ppm,

1-methyl-1H-pyrazole-4-sulfonyl chloride in an amount of less than 4 ppm, and

methyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 4ppm.

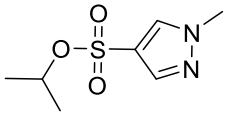
Claim 24. The method of any one of claims 20 to 23, wherein the purified compound of Formula I has a purity of at least 99%, and further comprises

ethyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 6 ppm:



, and

isopropyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 6 ppm:



.

Claim 25. The method of claim 20, wherein the purified compound of Formula I has a purity of at least 99%, and comprises

the compound of Formula X-4 in an amount of less than 0.1% (w/w),

the compound of Formula X-5 in an amount of less than 0.2% (w/w),

the compound of Formula X-6 in an amount of less than 0.2% (w/w),

methyl bromide in an amount of less than 4 ppm,

2-bromopropane in an amount of less than 4 ppm,

1,4-dibromopentane in an amount of less than 4 ppm,

1-methyl-1H-pyrazole-4-sulfonyl chloride in an amount of less than 4 ppm,

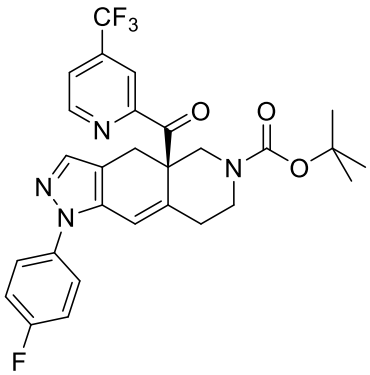
methyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 4ppm,

ethyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 4 ppm, and

isopropyl 1-methyl-1H-pyrazole-4-sulfonate in an amount of less than 4 ppm.

Claim 26. The method of any one of claims 20 to 25, wherein the compound of Formula I is prepared by the method of any one of claims 5 to 19.

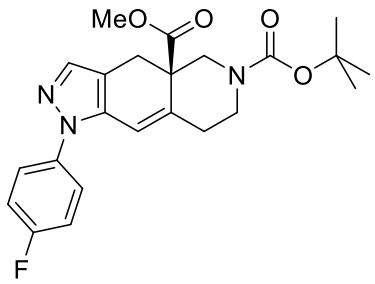
Claim 27. A method of preparing a compound of Formula IIa:



(IIa) ,

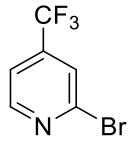
comprising the steps of:

(c) forming a third reaction mixture comprising a Grignard reagent, a compound of Formula III:



(III) , and

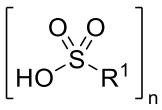
2-bromo-4-(trifluoromethyl)pyridine:



,

wherein the pyridine is present in a molar ratio of 1.0 to 1.5 to the compound of Formula III, and wherein the Grignard reagent is present in a molar ratio of 1.5 to 1.7 to the compound of Formula III, to prepare the compound of Formula IIa.

Claim 28. The method of any one of claims 1 to 3, wherein HX is



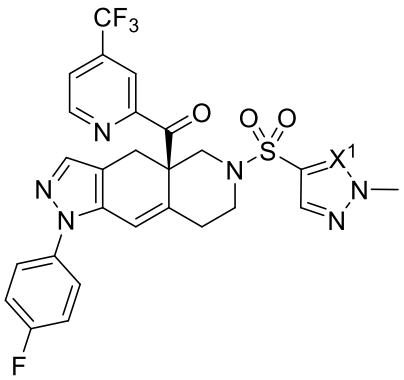
,

wherein

R^1 is C_{1-6} alkyl, C_{1-10} haloalkyl, phenyl, or 4-methylphenyl; and

subscript n is 1 to 4.

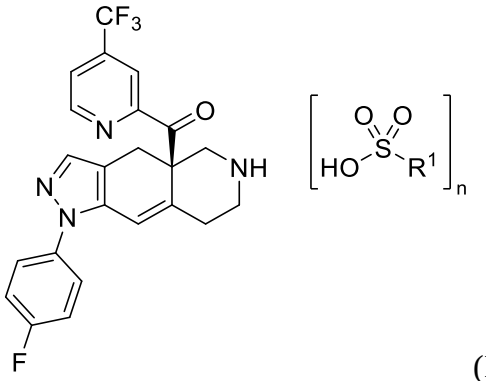
Claim 29. The method of claim 28, for preparing the compound of Formula J:



(J)

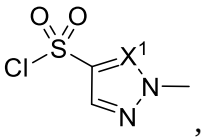
or a pharmaceutically acceptable salt thereof, comprises:

(a) forming a fourth reaction mixture comprising a compound of Formula IIb-2:



(IIb-2) ,

and the sulfonyl chloride:



,

to prepare the compound of Formula J in a yield of at least 75% and a purity of at least 98%,

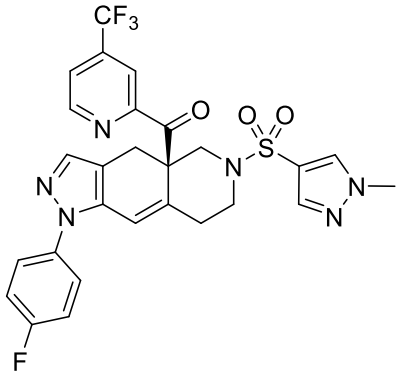
wherein

X^1 is –CH= or –N=;

R^1 is C_{1-6} alkyl, C_{1-10} haloalkyl, phenyl, or 4-methylphenyl; and

subscript n is 1 to 4.

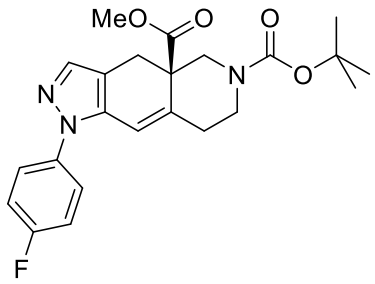
Claim 30. A method of preparing a compound of Formula I:



(I)

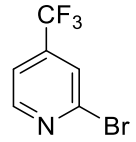
or a pharmaceutically acceptable salt thereof, comprising:

(c) forming a sixth reaction mixture comprising tetrahydrofuran, toluene, iPrMgCl, a compound of Formula III:



(III) , and

2-bromo-4-(trifluoromethyl)pyridine:

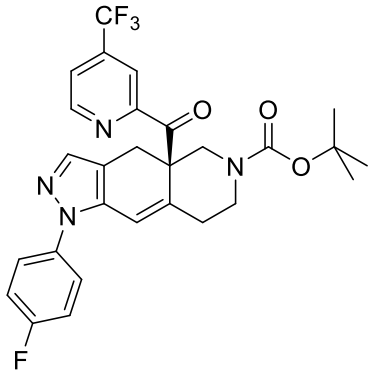


,

wherein the pyridine is present in a molar ratio of about 3.0 to the compound of Formula III, and wherein the Grignard reagent is present in a molar ratio of about 3.05 to the compound of Formula III;

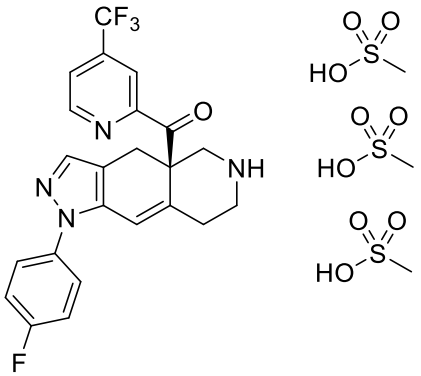
(c1) adding acetic acid and water to the sixth reaction mixture to form a workup mixture;

(c2) distilling the workup mixture to form an intermediate mixture comprising a compound of Formula IIa:



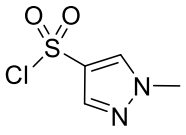
(IIa) ;

(b) forming a fifth reaction mixture comprising the intermediate mixture, acetonitrile, and methanesulfonic acid, to form a compound of Formula IIb-2:



(IIb-2) ;

(a) forming a fourth reaction mixture comprising the compound of Formula IIb-2, triethylamine, ethyl acetate, and 1-methyl-1H-pyrazole-4-sulfonyl chloride:



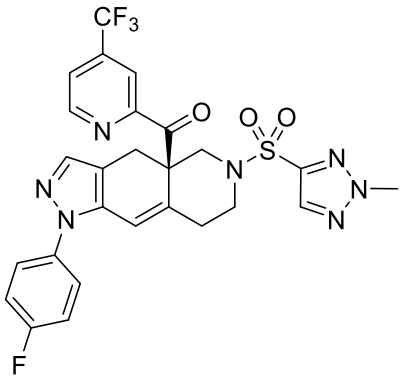
,

wherein the sulfonyl chloride is present in a ratio of about 1.0 to the compound of Formula IIb-2;

(a1) adding methanol to the fourth reaction mixture; and

(a2) adding water to the reaction mixture to precipitate the compound of Formula I in a yield of at least 75% and a purity of at least 98%.

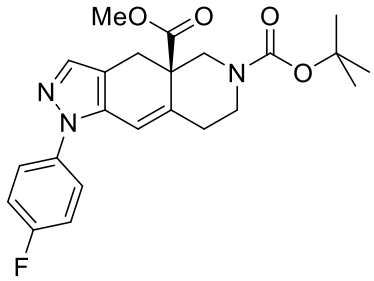
Claim 31. A method of preparing a compound of Formula Ia:



(Ia) ,

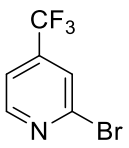
or a pharmaceutically acceptable salt thereof, comprising:

(c) forming a sixth reaction mixture comprising tetrahydrofuran, toluene, iPrMgCl, a compound of Formula III:



(III) , and

2-bromo-4-(trifluoromethyl)pyridine:

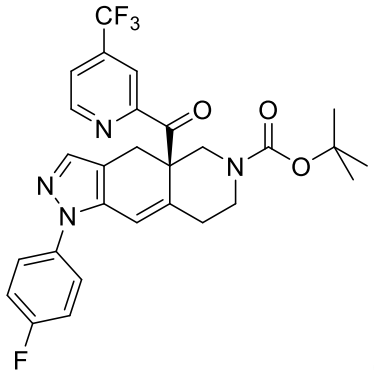


,

wherein the pyridine is present in a molar ratio of about 3.0 to the compound of Formula III, and wherein the Grignard reagent is present in a molar ratio of about 3.05 to the compound of Formula III;

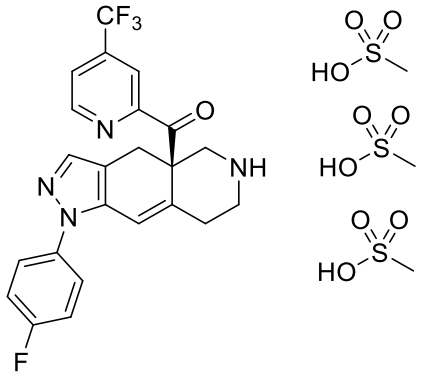
(c1) adding acetic acid and water to the sixth reaction mixture to form a workup mixture;

(c2) distilling the workup mixture to form an intermediate mixture comprising a compound of Formula IIa:



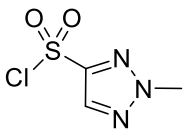
(IIa) ;

(b) forming a fifth reaction mixture comprising the intermediate mixture, acetonitrile, and methanesulfonic acid, to form a compound of Formula IIb-2:



(IIb-2) ;

(a) forming a fourth reaction mixture comprising the compound of Formula IIb-2, triethylamine, ethyl acetate, and 2-methyl-2H-1,2,3-triazole-4-sulfonyl chloride:



,

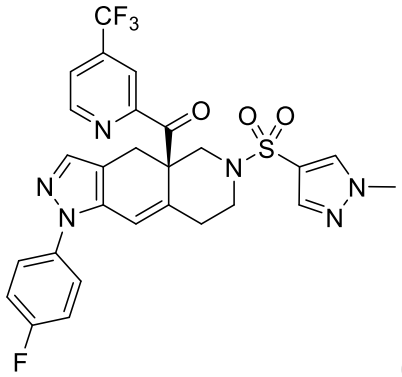
wherein the sulfonyl chloride is present in a ratio of about 1.0 to the compound of Formula IIb-2;

(a1) adding methanol to the fourth reaction mixture; and

(a2) adding water to the reaction mixture to precipitate the compound of Formula Ia in a yield of at least 75% and a purity of at least 98%.

32. A composition comprising:

a compound of Formula I in an amount of at least 99% (w/w):

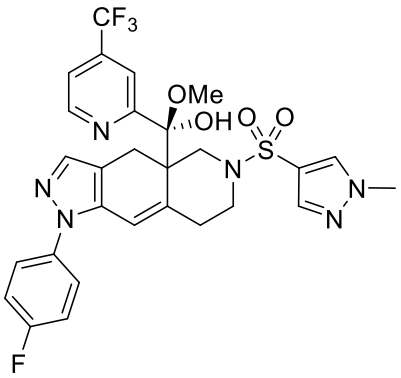


(I) ; and

one or more impurity in an amount of from 0.01 to 1% (w/w).

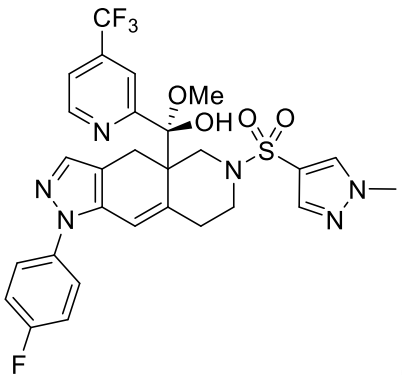
Claim 33. The composition of claim 32, wherein the impurity further comprises:

a compound of Formula X-D in an amount of less than 0.40% (w/w)



(X-D) ; and

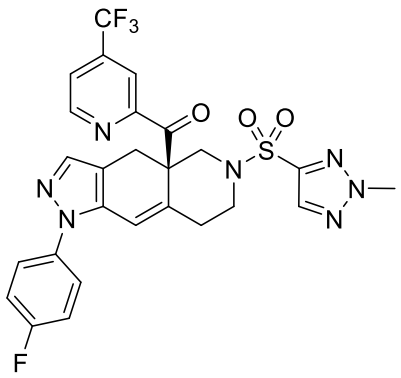
a compound of Formula X-E in an amount of less than 0.40% (w/w)



(X-E).

34. A composition comprising:

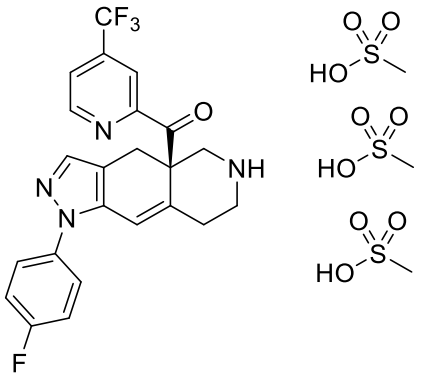
a compound of Formula Ia in an amount of at least 99% (w/w):



(Ia) ; and

one or more impurity in an amount of from 0.01 to 1% (w/w).

Claim 35. A crystalline form of (R)-(1-(4-fluorophenyl)-1,4,5,6,7,8-hexahydro-4aH-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone tris-methanesulfonic acid:



,

characterized by an X-ray powder diffraction (XRPD pattern having peaks at about 18.2°, 18.3°, and 19.7° 2-θ ± 0.2° 2-θ.

Claim 36. A pharmaceutical composition comprising a composition of any one of claims 32 to 33, and one or more pharmaceutically acceptable excipients.

Claim 37. Use of a composition of any one of claims 32 to 33, or a crystalline form according to claim 35 in the preparation of a medicament for treating a disorder or condition through modulating a glucocorticoid receptor.

Claim 38. Use of a composition of any one of claims 32 to 33, or a crystalline form according to claim 35 in the preparation of a medicament for treating a disorder or condition through antagonizing a glucocorticoid receptor.

Claim 39. Use of a composition of any one of claims 32 to 33, or a crystalline form according to claim 35 in the preparation of a medicament for treating fatty liver disease.

Claim 40. Use of a composition of any one of claims 32 to 33, or a crystalline form according to claim 35 in the preparation of a medicament for treating antipsychotic induced weight gain.