

effect dissolution. The solution was cooled to 45 °C, and water (28mL) was added over 15 minutes, maintaining the temperature between 40 and 45 °C. The slurry was cooled to 20 to 25 °C over an hour, then further cooled to 0 to 5 °C and held at that temperature for 30 minutes before being filtered. The filter cake was washed with 20% v/v IPA in water and the product dried under suction overnight, then in vacuo (40°C).

Example 3. Preparation of Selinexor~~SelinexorSelinexor~~ Lot No. PC-14-005 (Form A).

[00280] The acetonitrile solvate of selinexor (Form D) was prepared in accordance with the procedure described in Example 6.

[00281] The acetonitrile solvate of selinexor (1.07Kg) was suspended in a mixture of IPA (2.52Kg) and water (3.2Kg) and the mixture heated to 70 to 75 °C to dissolve. The temperature was then adjusted to 40 to 45 °C and held at that temperature for 30 minutes. Water (10.7Kg) was added while maintaining the temperature at 40 to 45 °C, then the batch was cooled to 20 to 25 °C and agitated at that temperature for 4 hours before being further cooled to 0 to 5 °C. After a further hour of agitation, the slurry was filtered and the filter cake washed with a cold mixture of IPA (0.84Kg) and water (4.28Kg) before being dried.

Example 4. Preparation of Selinexor~~SelinexorSelinexor~~ Lot No. PC-14-009 (Form A).

[00282] The acetonitrile solvate of selinexor (Form D) was prepared in accordance with the procedure described in Example 6.

[00283] The acetonitrile solvate of selinexor (1.5Kg) was suspended in IPA (3.6Kg) and water (4.5Kg) and warmed to 37 to 42 °C with gentle agitation. The suspension was agitated at that temperature for 4 hours, and was then cooled to 15 to 20 °C over 1 hour. Water (15.1Kg) was added, maintaining the temperature, then the agitation was continued for 1 hour and the batch was filtered. The filter cake was washed with a mixture of IPA (1.2Kg) and water (6Kg), then dried under a flow of nitrogen.

Example 5. Preparation of Selinexor Lot Nos. 1339-BS-142-1, 1339-BS-142-2 and PC-14-008 (Form A).

[00284] A reactor, under nitrogen, was charged with **KG1** (1Kg, 1.0 Eq), **KJ8** (0.439 Kg, 1.4 Eq) and MeTHF (7L, 7 parts with respect to **KG1**). Diisopropylethylamine (0.902Kg, 2.45 Eq with respect to **KG1**) was added to the reaction mixture at -20 °C to -25 °C with a MeTHF rinse. To the reaction mixture, 50% T3P® in ethyl acetate (2.174Kg, 1.2 Eq with respect to **KG1**) was then charged, maintaining the temperature at -20 °C to -25 °C with a MeTHF rinse. After the completion of the addition, the reaction mixture was stirred briefly

solution in EtAOc, 34.4Kg) was added maintaining the temperature at -20 °C. The mixture stirred to complete the reaction first at -20 °C, then at ambient temperature.

[00288] Upon completion of the reaction, water (79Kg) was added over about 1 hour. The layers were separated and the organic layer was washed with a mixture of water (55Kg) and brine (18Kg), The mixture was filtered, and the methyl-THF/ethyl acetate in the mixture distillatively replaced with acetonitrile (volume of approximately 220L). The mixture was warmed to dissolve the solids, then slowly cooled to 0 to 5 °C before being filtered. The filter cake was washed with acetonitrile to provide the acetonitrile solvate of selinexor~~SelinexorSelinexor~~ (Form D).

[00289] The acetonitrile solvate of selinexor~~SelinexorSelinexor~~ was dried, then mixed with isopropanol (23Kg) and water (55Kg). The slurry was warmed to about 38 °C and held at that temperature for approximately 4 hours before being cooled to 15 to 20 °C. Water (182Kg) was added. After a further 5 hours of agitation, the mixture was filtered and the filter cake washed with a mixture of isopropanol (14Kg) and water (73Kg), before being dried under vacuum (45 °C). The dried product was packaged to provide selinexor~~SelinexorSelinexor~~ Lot No. 1405463 (Form A).

Example 7. Polymorphism Studies of Selinexor.

[00290] A comprehensive polymorphism assessment of selinexor was performed in a range of different solvents, solvent mixtures and under a number of experimental conditions based on the solubility of selinexor. Three anhydrous polymorphs of selinexor~~SelinexorSelinexor~~ were observed by XRPD investigation, designated Form A, Form B and Form C. Form A is a highly crystalline, high-melting form, having a melting point of 177 °C, and was observed to be stable from a physico-chemical point of view when exposed for 4 weeks to 25 °C/97% relative humidity (RH) and to 40 °C/75% RH. A solvated form of selinexor was also observed in acetonitrile, designated Form D. A competitive slurry experiment confirmed Form A as the stable anhydrous form under the conditions investigated, except in acetonitrile, in which solvate formation was observed. It was further found that in acetonitrile, below 50 °C, only Form D is observed, at 50 °C both Form A and Form D are observed, and at 55 °C, Form A is observed .

General Instrument and Methodology Details

X-ray Powder Diffraction (XRPD)

[00297] Mettler DSC 823e. DSC data were collected on a Mettler DSC 823E equipped with a 34 position auto-sampler. The instrument was calibrated for energy and temperature using certified indium. Typically, 0.5-3 mg of each sample, in a pin-holed aluminum pan, was heated at 10 °C/minute from 25 °C to 300 °C. A nitrogen purge at 50 ml/min was maintained over the sample. The instrument control and data analysis software was STARe v9.20.

Thermogravimetric Analysis (TGA)

[00298] Mettler TGA/SDTA 851e. TGA data were collected on a Mettler TGA/SDTA 851e equipped with a 34 position auto-sampler. The instrument was temperature calibrated using certified indium. 5-30 mg of each sample was loaded onto a pre-weighed aluminum crucible and was heated at 10 °C/min from ambient temperature to 350 °C. A nitrogen purge at 50 ml/min was maintained over the sample. The instrument control and data analysis software was STARe v9.20.

Chemical Purity Determination by High Performance Liquid Chromatography (HPLC)

[00299] Purity analysis was performed on an Agilent HP1100 series system equipped with a diode array detector using ChemStation software vB.02.01-SR1 (or SR2) as follows:

Sample Preparation	~0.4mg/mL in 1:1 ACN/MeOH
Column	Zorbax SB-Phenyl, 4.6 mm X 150 mm, 5µm
Column Temperature (°C)	40
Injection (µl)	10
Detection: Wavelength, Bandwidth (nm)	245 nm
Flow Rate (ml/min)	1.0
Phase A	20mM Ammonium Acetate in Water (no pH specified)
Phase B	70% ACN, 30% MeOH (v/v)

Solubility Assessment

[00300] The polymorphism assessment of selinexor~~SelinexorSelinexor~~ included a solubility assessment, performed on Form A. About 20 mg of selinexor~~SelinexorSelinexor~~ prepared in accordance with the process described in Example 1 were weighed into vials and the solubility was visually assessed at 50 °C in thirty solvents and solvent mixtures. After each solvent addition, samples were kept under agitation for 10 minutes at 50 °C before each

corresponding to particles approximately 80-90 μm and a minor tertiary mode approximately 400 μm .

Example 9. Process for Preparation of Selinexor~~SelinexorSelinexor~~.

[00325] A new process for the preparation of the compound of Formula I was developed. The new process uses a T3P®-mediated coupling of **KG1** with the hydrazinyl pyrazine (**KJ8**) to prepare selinexor such as described in International Publication No. WO 2013/019548, but incorporates changes to the reaction design. In particular, the process described herein wherein the unstable active T3P® ester is generated *in situ* can result in one or more of the following advantages over the process for the preparation of the compound of Formula I described in International Publication No. WO 2013/019548:

- A reduction of the isomerization of the double bond in **KH8**;
- A reduction in the production of side products such as 3-(3,5-Bis-trifluoromethyl-phenyl)-1H-[1,2,4]triazole (**KF9**);
- An increase in purity; and
- An increase in yield.

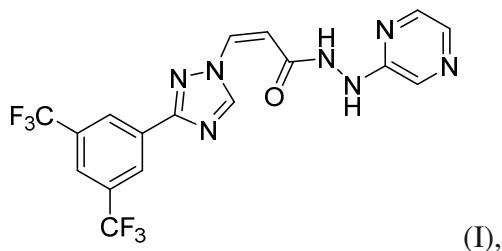
The process described herein has been implemented into multi-kilogram processes, see for example the 1Kg scale process (see Example 5), providing the desired final product in about 80% yield overall. Details of the improved process for preparing selinexor are described in Examples 5 and 6.

Chemistry Development

[00326] A series of experiments aimed at generating the activated ester transiently were carried out. These experiments are summarized in Table 5. Initially, the addition mode of the raw materials into T3P® was maintained, but subsequently the order of addition of the raw materials was reversed when it was observed that the kinetics of the reaction of **KJ8** with T3P® were overshadowed by the rate of formation (and presumably quench) of the T3P® ester of **KG1**. In addition to the improvements in the characteristics of the product of the coupling between **KG1** and **KJ8** discussed above, the addition of T3P® to a mixture of **KG1**, **KJ8** and DIPEA provided a greatly simplified reactor flow and the need to very carefully handle the T3P® activated ester of **KG1** once formed. Adding the T3P® last also allowed for much better control over the addition rates, avoiding the need to transfer the activated ester as rapidly as possible (a task that is much more difficult and potentially dangerous at larger

CLAIMS

1. A composition, comprising particles of a single crystalline form of a compound represented by Structural Formula I:

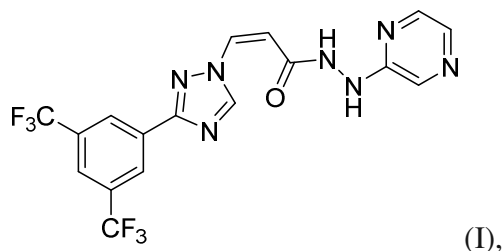


- wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° ; and
- the particles have a unimodal particle size distribution characterized by a $d(0.9)$ of 100 microns or less.
2. The composition of claim 1, where the a unimodal particle size distribution characterized by a $d(0.9)$ of 70 microns or less.
 3. The composition of claim 1 or 2, wherein the crystalline form is characterized by X-ray powder diffraction peaks at 2θ angles of 4.4° , 19.9° , 21.3° and 22.0° .
 4. The composition of claim 3, wherein the crystalline form is characterized by X-ray powder diffraction peaks at 2θ angles of 4.4° , 19.9° , 20.3° , 21.3° , 22.0° , 23.5° and 25.0° .
 5. The composition of claim 4, wherein the crystalline form is characterized by X-ray powder diffraction peaks at 2θ angles of 4.4° , 13.1° , 15.8° , 18.2° , 19.9° , 20.3° , 21.3° , 22.0° , 23.5° , 23.7° , 25.0° , 27.0° , 28.3° and 28.5° .
 6. The composition of claim 1 or 2, wherein the crystalline form is characterized by an X-ray powder diffraction pattern substantially in accordance with that depicted in FIG. 1A.

7. The composition of any one of claims 1-6, wherein the crystalline form is further characterized by a differential scanning calorimetry thermogram comprising an endothermic peak at 179 °C.
8. The compositions of any one of claims 1-7, wherein the particles have a particle size distribution characterized by a d(0.9) of from 10 microns to 100 microns.
9. The compositions of claims 1-7, wherein the particles have a particle size distribution characterized by a d(0.9) of from 10 microns to 70 microns.
10. The composition of any one of claims 1-9, wherein the particles have a particle size distribution characterized by a d(0.5) of from 10 microns to 35 microns.
11. The composition of any one of claims 1-10, wherein the particles have a particle size distribution characterized by a d(0.1) of from 5 microns to 15 microns.
12. The composition of any one of claims 1-11, wherein the particles have a particle size distribution characterized by a d(0.9):d(0.1) ratio of from 2 to 10.
13. The composition of any one of claims 1-12, wherein the particles have a particle size distribution characterized by a d(0.9):d(0.5) ratio of from 1.5 to 4.5.
14. A pharmaceutical composition, comprising ~~a~~the composition of any one of claims 1-13, and a pharmaceutically acceptable carrier.
15. The composition of ~~Claim~~claim 1 for use in the treatment of a disorder associated with CRM1 activity, the method comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 14.
16. The composition for use according to claim 15, wherein the disorder is a proliferative disorder, cancer, an inflammatory disorder, an autoimmune disorder, a viral infection, an ophthalmological disorder, a neurodegenerative disorder, a disorder of abnormal tissue growth, a disorder related to food intake, an allergic disorder, or a respiratory disorder.
17. The composition for use according to claim 16, wherein the disorder is cancer.

18. The composition for use according to ~~Claim~~claim 1 for use in promoting wound healing in a subject in need thereof, comprising administering to the subject in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 14.

19. A single crystalline form of a compound represented by Structural Formula I:



wherein the single crystalline form is Form D and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 3.7° , 7.3° , 10.9° , 18.3° and 21.9° .

20. The single crystalline form of claim 19, characterized by X-ray powder diffraction peaks at 2θ angles of 3.7° , 7.3° , 10.9° , 18.3° and 21.9° .

21. The single crystalline form of claim 20, characterized by X-ray powder diffraction peaks at 2θ angles of 3.7° , 7.3° , 9.7° , 10.9° , 18.3° , 19.2° and 21.9° .

22. The single crystalline form of claim 21, characterized by X-ray powder diffraction peaks at 2θ angles of 3.7° , 7.3° , 9.7° , 10.9° , 11.1° , 18.3° , 19.2° , 19.5° , 20.6° and 21.9° .

23. The single crystalline form of claim 19, characterized by an X-ray powder diffraction pattern substantially in accordance with that depicted in FIG. 2A.

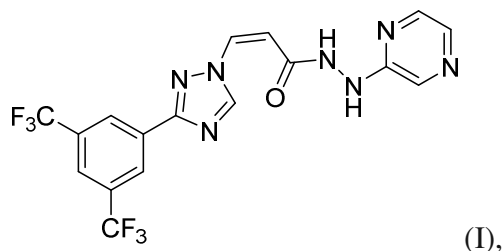
24. The single crystalline form of any one of claims 19-23, wherein the compound of Structural Formula I is in the form of ~~a~~an acetonitrile solvate.

~~25. The single crystalline form of claim 24, wherein the solvate is an acetonitrile solvate.~~

~~26~~25. The single crystalline form of claim 24 ~~or 25~~, wherein the solvate comprises from about 0.5 to about 1.5 molar equivalents of solute per molar equivalent of the compound of Structural Formula I.

~~27~~26. The single crystalline form of claim ~~26~~25, wherein the solvate comprises about one molar equivalent of solute per molar equivalent of the compound of Structural Formula I.

~~28~~27. A method of preparing a single crystalline form of a compound represented by Structural Formula I:

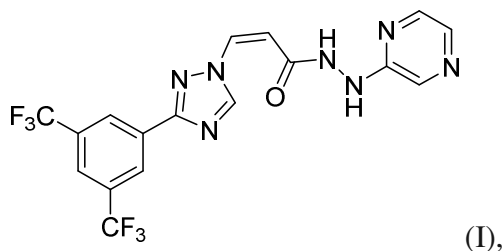


wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° , the method comprising:

- (a) suspending single crystalline Form ~~B, C or D~~ of the compound of Structural Formula I, ~~or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I, in isopropanol or a mixture of isopropanol and water to form a slurry, wherein single crystalline Form D is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 3.7° , 7.3° , 10.9° , 18.3° and 21.9° ; single crystalline Form B is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 9.4° , 11.1° , 16.5° , 18.3° and 18.8° and single crystalline Form C is characterized by at least three X-ray diffraction peaks at 2θ angles selected from 3.7° , 11.2° , 12.1° and 18.6° ;~~
- (b) heating the slurry to a temperature less than or equal to about 70°C to form a second slurry or a solution;
- (c) cooling the second slurry or the solution and adding water to the second slurry or the solution, thereby forming solid particles of crystalline Form A of the compound of Structural Formula I; and
- (d) isolating the solid particles of crystalline Form A,

thereby preparing a composition comprising particles of single crystalline Form A of the compound of Structural Formula I.

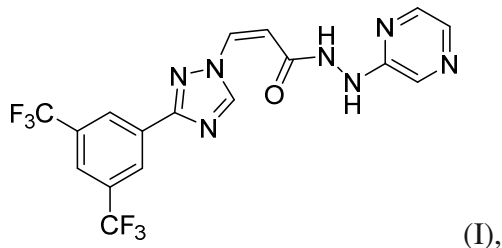
2928. A method of preparing a single crystalline form of a compound represented by Structural Formula I:



wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° , the method comprising:

- (a) suspending single crystalline Form B, C or D of the compound of Structural Formula I, or a mixture comprising two or more of single crystalline B, C or D of the compound of Structural Formula I, in isopropanol or a mixture of isopropanol and water to form a slurry, wherein single crystalline Form D is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 3.7° , 7.3° , 10.9° , 18.3° and 21.9° , single crystalline Form B is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 9.4° , 11.1° , 16.5° , 18.3° and 18.8° and single crystalline Form C is characterized by at least three X-ray diffraction peaks at 2θ angles selected from 3.7° , 11.2° , 12.1° and 18.6° ;
 - (b) heating the slurry to a temperature less than or equal to about 70°C to form a second slurry or a solution;
 - (c) adding water to the second slurry or the solution and cooling the second slurry or the solution, thereby forming solid particles of crystalline Form A of the compound of Structural Formula I; and
 - (d) isolating the solid particles of crystalline Form A,
- thereby preparing a composition comprising particles of single crystalline Form A of the compound of Structural Formula I.

- ~~3029.~~ The method of claim ~~2827~~ or ~~2928~~ wherein the solid particles have a unimodal particle size distribution characterized by a d(0.9) of 100 microns or less.
- ~~3130.~~ The method of any one of claims ~~2827-3029~~, wherein the ratio of isopropanol to water by volume in the mixture of isopropanol and water is from about 0.1 to about 4.
- ~~3231.~~ The method of any one of claims ~~2827-3130~~, wherein single crystalline Form ~~B, C or D~~ of the compound of Structural Formula I ~~or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I~~, is suspended in an amount of isopropanol or mixture of isopropanol and water of from about 5 to about 10 parts by weight with respect to single crystalline Form ~~B, C or D~~ of the compound of Structural Formula I ~~or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I~~.
- ~~3332.~~ The method of any one of claims ~~2827-3231~~, wherein the slurry is heated to a temperature of from about 35 °C to about 70 °C.
- ~~3433.~~ The method of any one of claims ~~2827-3332~~, wherein the second slurry or the solution is cooled to from about 0 °C to about 55 °C.
- ~~3534.~~ The method of any one of claims ~~2827-3433~~, wherein water is added to the second slurry or the solution in an amount of from about 5 parts by weight to about 15 parts by weight with respect to single crystalline Form ~~B, C or D~~ of the compound of Structural Formula I ~~or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I~~.
- ~~3635.~~ A method of preparing a single crystalline form of a compound represented by Structural Formula I:



wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° ,
the method comprising:

heating single crystalline Form B, C or D of the compound of Structural Formula I or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I and inducing formation of solid particles of crystalline Form A; or

maturing single crystalline Form B, C or D or of the compound of Structural Formula I, or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I in a solvent system and inducing formation of solid particles of crystalline Form A; or

drying single crystalline Form B, C or D of the compound of Structural Formula I, or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I, thereby forming solid particles of crystalline Form A; or

any combination of the foregoing; and

isolating the solid particles of crystalline Form A,

thereby preparing single crystalline Form A of the compound of Structural Formula I.

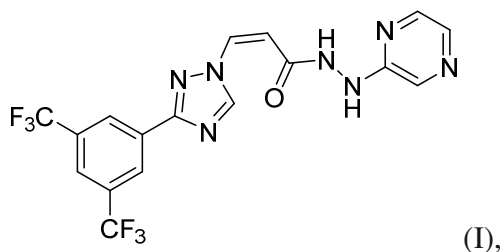
37. — The method of claim 36, comprising:

heating a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I and inducing formation of solid particles of crystalline Form A; or

maturing a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I in a solvent system and inducing formation of solid particles of crystalline Form A; or

drying a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I, thereby forming solid particles of crystalline Form A; or
any combination of the foregoing.

3836. A method of preparing a single crystalline form of a compound represented by Structural Formula I:



wherein the single crystalline form is Form D and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 3.7° , 7.3° , 10.9° , 18.3° and 21.9° , the method comprising:

dissolving the compound of Structural Formula I in a solvent system comprising greater than 20% by volume acetonitrile;

inducing formation of solid particles of crystalline Form D of the compound of Structural Formula I, wherein the temperature of the solvent system is below 50°C ; and

isolating the solid particles of crystalline Form D, thereby preparing single crystalline Form D of the compound of Structural Formula I.

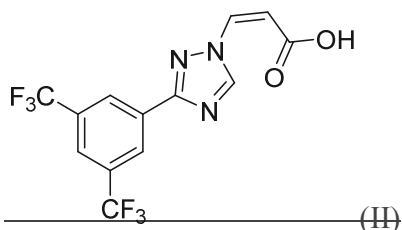
3937. The method of claim 3836, wherein single crystalline Form D is in the form of a solvate.

4038. The method of claim 3937, wherein the solvate is an acetonitrile solvate.

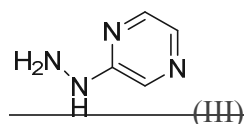
~~41. The method of any one of claims 38-39, wherein the solvent system comprises greater than 20% by volume acetonitrile.~~

4239. The method of any one of claims 3836-4138, wherein inducing formation of solid particles of crystalline Form D comprises cooling the solution formed by dissolving the compound of Structural Formula I in a solvent system comprising acetonitrile.

~~43. A method of preparing a compound of Structural Formula I, comprising:
combining a trialkylamine, 2-methyltetrahydrofuran, a compound of Structural Formula H;~~



and a compound of Structural Formula III:



to form a reaction mixture;

cooling the reaction mixture to from about -80°C to about 0°C ;

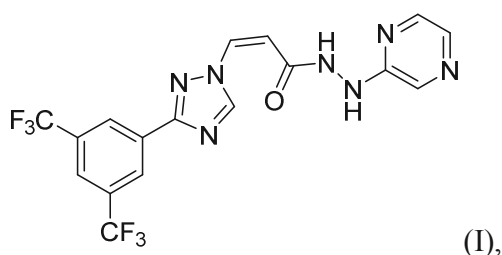
treating the reaction mixture with propylphosphonic anhydride to provide a mixture comprising the compound of Structural Formula I; and

isolating the compound of Structural Formula I from the mixture.

44. The method of claim 43, wherein the trialkylamine is diisopropylethylamine.

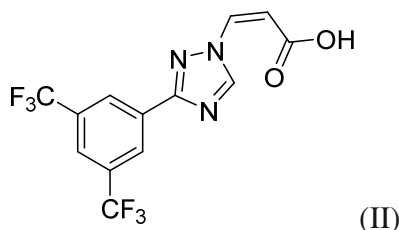
45. The method of claim 43 or 44, comprising cooling the reaction mixture to from about -50°C to about -15°C .

4640. A method of preparing a single crystalline form of a compound represented by Structural Formula I:

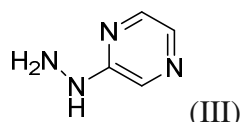


wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° , the method comprising:

- (a) combining a trialkylamine, 2-methyltetrahydrofuran, a compound of Structural Formula II:



and a compound of Structural Formula III:



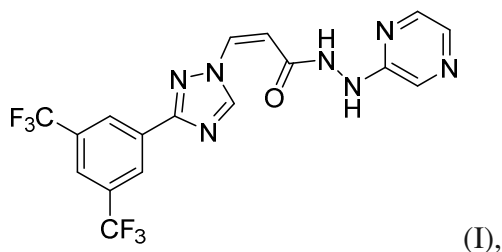
to form a reaction mixture;

- (b) cooling the reaction mixture to from about -80 °C to about 0 °C;
- (c) treating the reaction mixture with propylphosphonic anhydride to provide a mixture comprising the compound of Structural Formula I;
- (d) isolating the compound of Structural Formula I from the mixture;
- (e) dissolving the isolated compound of Structural Formula I in a solvent system comprising acetonitrile;
- (f) inducing formation of solid particles of crystalline Form D of the compound of Structural Formula I and isolating the solid particles of crystalline Form D to obtain single crystalline Form D of the compound of Structural Formula I, ~~or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I, wherein single crystalline Form D is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 3.7°, 7.3°, 10.9°, 18.3° and 21.9°;~~
- (g) heating single crystalline Form D, ~~or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I, and inducing formation of solid particles of crystalline Form A; or maturing single crystalline Form D, or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I, in a solvent system and inducing formation of~~

solid particles of crystalline Form A; or drying single crystalline Form D, ~~or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I~~, thereby forming solid particles of crystalline Form A; or any combination of the foregoing; and

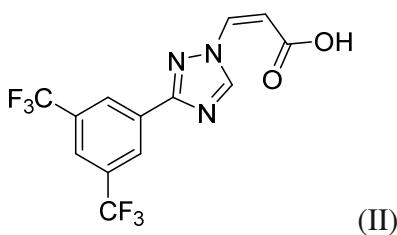
- (h) isolating the particles of crystalline Form A, thereby preparing single crystalline Form A of the compound of Structural Formula I.

4741. A method of preparing a single crystalline form of a compound represented by Structural Formula I:

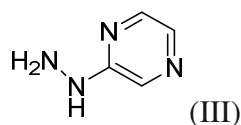


wherein the single crystalline form is Form A and is characterized by at least three X-ray powder diffraction peaks at 2θ angles selected from 4.4° , 19.9° , 21.3° and 22.0° , the method comprising:

- (a) combining a trialkylamine, 2-methyltetrahydrofuran, a compound of Structural Formula II:



and a compound of Structural Formula III:



to form a reaction mixture;

- (b) cooling the reaction mixture to from about -80°C to about 0°C ;

- (c) treating the reaction mixture with propylphosphonic anhydride to provide a mixture comprising the compound of Structural Formula I;
- (d) isolating the compound of Structural Formula I from the mixture;
- (e) dissolving the isolated compound of Structural Formula I in a solvent system comprising acetonitrile;
- (f) inducing formation of solid particles of crystalline Form D of the compound of Structural Formula I and isolating the solid particles of crystalline Form D, ~~or solid particles of single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I, to obtain single crystalline Form D of the compound of Structural Formula I, or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of crystalline Form B, C or D of the compound of Structural Formula I, wherein~~ single crystalline Form D is characterized by at least three X-ray powder diffraction peaks at 2 θ angles selected from 3.7°, 7.3°, 10.9°, 18.3° and 21.9°;
- (g) ~~suspending single crystalline Form D, or single crystalline Form B or C of the compound of Structural Formula I or a mixture comprising two or more of single crystalline Form B, C or D of the compound of Structural Formula I in~~ isopropanol or a mixture of isopropanol and water to form a slurry;
- (h) heating the slurry to a temperature less than or equal to about 70 °C to form a second slurry or a solution;
- (i) cooling the second slurry or the solution and adding water to the second slurry or the solution, thereby forming solid particles of crystalline Form A of the compound of Structural Formula I; and
- (j) isolating the solid particles of crystalline Form A, thereby preparing single crystalline Form A of the compound of Structural Formula I.