Figure 35 shows a DSC thermogram (lower trace) of the L-malate salt Form R of compound (I) as obtained by Example 18, using Mettler DSC823e at a heating rate of 10°C.min^{-1} (peak max observed at 114°C). The upper trace shows TGA analysis for the same salt using a Mettler TGA/SDTA 851e at a heating rate of 10°C.min^{-1}.

Figure 36 shows a DSC thermogram (lower trace) of the HCl salt Form H of compound (I) as obtained by Example 8, using Mettler DSC823e at a heating rate of 10°C.min^{-1} (peak max observed at 68, 87, 104 and 148°C). The upper trace shows TGA analysis for the same salt using a Mettler TGA/SDTA 851e at a heating rate of 10°C.min^{-1}.

Figure 37 shows a DSC thermogram (lower trace) of the HCl salt Form I of compound (I) as obtained by Example 9, using Mettler DSC823e at a heating rate of 10°C.min^{-1} (peak max observed at 120 and 139°C). The upper trace shows TGA analysis for the same salt using a Mettler TGA/SDTA 851e at a heating rate of 10°C.min^{-1}.

Figure 38 shows a DSC thermogram (lower trace) of the HBr salt Form J of compound (I) as obtained by Example 10, using Mettler DSC823e at a heating rate of 10°C.min^{-1} (peak max observed at 142°C). The upper trace shows TGA analysis for the same salt using a Mettler TGA/SDTA 851e at a heating rate of 10°C.min^{-1}.

The present invention is further described with reference to the following ~~non-limiting~~ Examples.

EXAMPLES

Instrument and Methodology Details

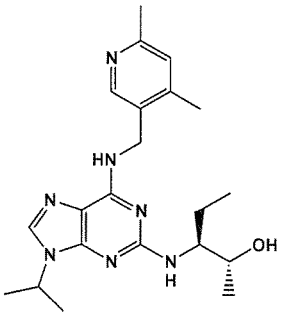
X-Ray Powder Diffraction (XRPD)

All XRPD patterns referred to herein are obtained using copper K-alpha radiation. As used herein, XRPD values as described in the accompanying specification, figures or tables refer to approximate values. Where the reference is to XRPD values listed in the tables, this refers to the 2-theta values, independent of any other parameters listed in the tables, such as peak intensity or the like.

XRPD on the phosphate (Forms B, C), citrate (Form F), benzenesulfonic acid (Form G) and L-tartrate (Form D) salts were carried out using a Bruker AXS C2 GADDS diffractometer as described below.

CLAIMS

1. A crystalline form of compound (I),



(I)

wherein said compound is in the form of an L-tartrate salt ~~the free base or a pharmaceutically acceptable salt thereof~~ or a pharmaceutically acceptable solvate ~~of the free base or salt form~~ thereof,

~~2. The crystalline form of claim 1 which is an L-tartrate salt~~ and ~~which~~ is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.67 ± 0.2, 8.237± 0.2, 9.777 ± 0.2, 11.96 ± 0.2, 12.38 ± 0.2, 13.06 ± 0.2, 13.38 ± 0.2, 13.94 ± 0.2, 14.90 ± 0.2, 15.40 ± 0.2, 15.95 ± 0.2, 16.27 ± 0.2, 16.54 ± 0.2, 17.36 ± 0.2, 17.57 ± 0.2, 17.86 ± 0.2, 19.64 ± 0.2, 19.86 ± 0.2, 20.12 ± 0.2, 20.73 ± 0.2, 21.14 ± 0.2, 21.58 ± 0.2, 22.57 ± 0.2, 22.95 ± 0.2, 23.29 ± 0.2, 23.57 ± 0.2, 24.07 ± 0.2, 24.63 ± 0.2, 25.30 ± 0.2, 26.38 ± 0.2, 27.09 ± 0.2, 27.67 ± 0.2, 27.97 ± 0.2, 28.91 ± 0.2, 29.28 ± 0.2, 30.08 ± 0.2, 30.41 ± 0.2, 31.90 ± 0.2 and 34.49 ± 0.2 (Form E) when using Cu Kα radiation and a scan speed of 0.146°/s, more preferably having two or more diffraction peaks at 2[theta] values selected from 6.67 ± 0.2, 13.06 ± 0.2, 13.38 ± 0.2, 14.90 ± 0.2, 17.36 ± 0.2, 17.57 ± 0.2, 19.64 ± 0.2, 20.73 ± 0.2, 23.57 ± 0.2 and 25.30 ± 0.2 (Form E); or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 20°C per minute which shows a maximum endothermic peak at a temperature between ~~about~~ 176°C and ~~about~~ 185°C.

~~3~~2. The crystalline form of claim 1 ~~which is an L-tartrate salt~~ which is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 3.82 ± 0.2, 7.57 ± 0.2, 8.12 ± 0.2, 10.53 ± 0.2, 11.39 ± 0.2, 12.00 ± 0.2, 13.54 ± 0.2, 15.15 ± 0.2, 16.35 ± 0.2, 16.88 ± 0.2, 17.37 ± 0.2, 18.51 ± 0.2, 18.98 ± 0.2, 19.77± 0.2, 21.06 ± 0.2, 22.70 ± 0.2, 23.47 ± 0.2, 24.66 ± 0.2 and 28.73 ± 0.2 [Form D] when using Cu Kα radiation and a scan speed of 0.146°/s, more preferably having two or more diffraction peaks at 2[theta] values selected from 3.82 ± 0.2, 7.57 ± 0.2, 15.15 ± 0.2, 16.88 ± 0.2, 19.77± 0.2, 22.70 ± 0.2, 23.47 ± 0.2, 24.66 ± 0.2 and 28.73 ± 0.2 [Form D]; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows a maximum endothermic peak at a temperature between ~~about~~ 145°C and ~~about~~ 154°C.

~~4. The crystalline form of claim 1, wherein compound (I) is in free base form and is characterized by:~~

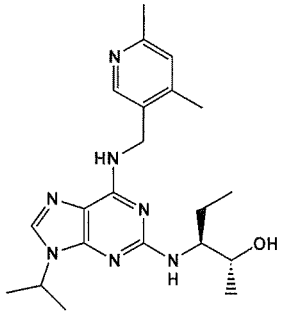
~~(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 9.60 ± 0.2, 10.22 ± 0.2, 11.29 ± 0.2, 11.66 ± 0.2, 12.26 ± 0.2, 12.62 ± 0.2, 13.17 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2, 15.15 ± 0.2, 15.57 ± 0.2, 16.99 ± 0.2, 17.68 ± 0.2, 18.30 ± 0.2, 18.39 ± 0.2, 18.63 ± 0.2, 18.97 ± 0.2, 19.32 ± 0.2 and 20.20 ± 0.2 [Form A], more preferably having two or more diffraction peaks at 2[theta] values selected from 7.53 ± 0.2, 12.26 ± 0.2, 14.06 ± 0.2, 14.85 ± 0.2 and 15.57 ± 0.2; or~~

~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 20°C per minute which shows a maximum endothermic peak at a temperature between about 130°C and about 140°C.~~

~~5. The crystalline form of claim 4, which is monoclinic P21/c space group with unit~~

~~cell dimensions of a = 15.19 ± 2 Å, b = 18.34 ± 2 Å, c = 8.65 ± 2 Å and [beta] = 95.53 ± 2°.~~

~~63~~. A crystalline form of compound (I),



(I)

wherein said compound is in the form of a citrate salt or a pharmaceutically acceptable solvate thereof, ~~The crystalline form of claim 1 which is a citrate salt which~~and is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 5.14 ± 0.2, 7.73 ± 0.2, 10.24 ± 0.2, 12.70 ± 0.2, 13.06 ± 0.2, 14.42 ± 0.2, 15.30 ± 0.2, 15.98 ± 0.2, 16.74 ± 0.2, 17.24 ± 0.2, 18.05 ± 0.2, 19.04 ± 0.2, 20.23 ± 0.2, 21.04 ± 0.2, 22.45 ± 0.2, 22.75 ± 0.2, 24.01 ± 0.2, 25.43 ± 0.2, 26.51 ± 0.2, 27.48 ± 0.2, 28.77 ± 0.2 and 29.71 ± 0.2 [Form F] when using Cu Kα radiation and a scan speed of 0.146°/s, more preferably having two or more diffraction peaks at 2[theta] values selected from 17.24 ± 0.2, 18.05 ± 0.2, 19.04 ± 0.2, 22.45 ± 0.2, 22.75 ± 0.2, 24.01 ± 0.2 and 25.43 ± 0.2 [Form F]; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows maximum endothermic peaks at a temperature between ~~about~~ 145°C and ~~about~~ 155°C and between ~~about~~ 165 °C and ~~about~~ 200°C.

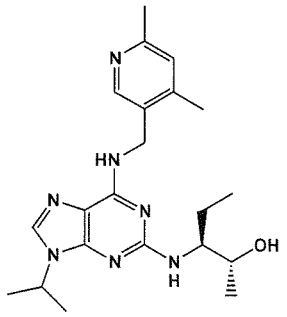
~~7. The crystalline form of claim 1, wherein the crystalline form is a benzenesulfonate salt which is characterized by:~~

~~(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 5.72 ± 0.2, 11.45 ± 0.2, 11.79 ± 0.2, 15.56 ± 0.2, 16.57 ± 0.2, 18.04 ± 0.2, 19.14 ± 0.2, 20.02 ± 0.2, 21.05 ± 0.2, 22.80 ± 0.2, 23.16 ± 0.2, 24.44 ± 0.2, 25.40 ± 0.2 and 28.74 ± 0.2 [Form G], more preferably having two or more diffraction~~

~~peaks at 2[theta] values selected from 15.56 ± 0.2, 16.57 ± 0.2, 18.04 ± 0.2, 20.02 ± 0.2, 21.05 ± 0.2, 22.80 ± 0.2, 23.16 ± 0.2 and 24.44 ± 0.2 [Form G]; or~~

~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows a maximum endothermic peak at a temperature between about 145°C and about 155°C.~~

~~84~~. A crystalline form of compound (I),



(I)

wherein said compound is in the form of a phosphate salt or a pharmaceutically acceptable solvate thereof~~The crystalline form of claim 1~~, and ~~wherein the crystalline form is a phosphate salt, which~~ is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.46 ± 0.2, 8.88 ± 0.2, 9.67 ± 0.2, 10.47 ± 0.2, 12.78 ± 0.2, 15.33 ± 0.2, 16.12 ± 0.2, 16.82 ± 0.2, 18.13 ± 0.2, 19.38 ± 0.2, 19.95 ± 0.2, 20.97 ± 0.2, 24.11 ± 0.2, 24.83 ± 0.2, 26.54 ± 0.2 and 28.11 ± 0.2 [Form B] when using Cu Kα radiation and a scan speed of 0.146°/s, more preferably having two or more diffraction peaks at 2[theta] values selected from 6.46 ± 0.2, 16.12 ± 0.2, 18.13 ± 0.2, 19.38 ± 0.2, 19.95 ± 0.2, 20.97 ± 0.2, 24.11 ± 0.2 and 24.83 ± 0.2 [Form B]; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows maximum endothermic peaks at a temperature between ~~about~~ 65°C and ~~about~~ 90°C and between ~~about~~ 114°C and ~~about~~ 130°C; or

(iii) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.49 ± 0.2, 8.91 ± 0.2, 9.75 ± 0.2, 10.52 ± 0.2, 13.03 ± 0.2, 15.44 ± 0.2, 16.27 ± 0.2, 17.85 ± 0.2, 18.29 ± 0.2, 19.52 ± 0.2,

20.02 ± 0.2, 21.11 ± 0.2, 22.80 ± 0.2, 24.92 ± 0.2, 28.33 ± 0.2 and 29.41 ± 0.2 [Form C] when using Cu Kα radiation and a scan speed of 0.146°/s, more preferably having two or more diffraction peaks at 2[theta] values selected from 6.49 ± 0.2, 16.27 ± 0.2, 18.29 ± 0.2, 19.52 ± 0.2, 20.02 ± 0.2, 21.11 ± 0.2, 22.80 ± 0.2, 24.92 ± 0.2 and 29.41 ± 0.2 [Form C]; or

(iv) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows maximum endothermic peaks at a temperature between ~~about~~ 66°C and ~~about~~ 90°C and between ~~about~~ 120°C and ~~about~~ 135°C.

~~9. The crystalline form of claim 1 which is a hydrochloride salt which is characterized by:~~

~~(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 5.6 ± 0.2, 8.6 ± 0.2, 9.5 ± 0.2, 10.9 ± 0.2, 11.2 ± 0.2, 12.7 ± 0.2, 13.0 ± 0.2, 14.3 ± 0.2, 16.0 ± 0.2, 17.3 ± 0.2, 17.7 ± 0.2, 18.8 ± 0.2, 19.1 ± 0.2, 20.3 ± 0.2, 20.7 ± 0.2, 22.9 ± 0.2, 23.6 ± 0.2, 24.5 ± 0.2, 25.0 ± 0.2, 25.5 ± 0.2, 25.8 ± 0.2, 26.4 ± 0.2 and 29.1 ± 0.2 [Form H]; or~~

~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows onset of endothermic peaks at temperatures of about 51°C, about 84°C, about 97°C and about 144°C, or a differential scanning calorimetry trace substantially in accordance with Figure 36; or~~

~~(iii) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 4.9 ± 0.2, 6.4 ± 0.2, 7.5 ± 0.2, 12.1 ± 0.2, 14.4 ± 0.2, 19.8 ± 0.2, 21.5 ± 0.2, 23.4 ± 0.2 and 25.7 ± 0.2 [Form I]; or~~

~~(iv) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows onset of endothermic peaks at temperatures of about 98°C and about 130°C, or a differential scanning calorimetry trace substantially in accordance with Figure 37.~~

~~10. The crystalline form of claim 1 which is a hydrobromide salt which is characterized by:~~

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.4 ± 0.2, 7.2 ± 0.2, 12.0 ± 0.2, 14.4 ± 0.2, 17.1 ± 0.2, 19.6 ± 0.2, 21.4 ± 0.2 and 25.5 ± 0.2 [Form J]; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10ºC per minute which shows a onset endothermic peak at a temperature of about 138 ºC, or a differential scanning calorimetry trace substantially in accordance with Figure 38; or

(iii) a differential scanning calorimetry trace recorded at a heating rate of 10ºC per minute which shows onset endothermic peak at temperatures of about 51ºC and 90ºC, or a differential scanning calorimetry trace substantially in accordance with Figure 29; or

(iv) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 5.7 ± 0.2, 16.4 ± 0.2, 17.7 ± 0.2, 18.4 ± 0.2, 19.6 ± 0.2, 20.5 ± 0.2, 24.1 ± 0.2, 25.3 ± 0.2, 26.0 ± 0.2 and 28.1 ± 0.2 [Form K].

11. The crystalline form of claim 1 which is a mesylate salt which is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.3 ± 0.2, 7.9 ± 0.2, 12.5 ± 0.2, 13.4 ± 0.2, 14.6 ± 0.2, 15.9 ± 0.2, 16.5 ± 0.2, 17.5 ± 0.2, 18.1 ± 0.2, 18.7 ± 0.2, 19.3 ± 0.2, 20.0 ± 0.2, 20.6 ± 0.2, 20.9 ± 0.2, 21.7 ± 0.2, 22.6 ± 0.2, 23.8 ± 0.2, 24.5 ± 0.2, 25.1 ± 0.2, 25.5 ± 0.2, 26.1 ± 0.2, 27.5 ± 0.2, 29.1 ± 0.2, 29.7 ± 0.2 and 30.3 ± 0.2 [Form L]; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10ºC per minute which shows a onset endothermic peak at a temperature of about 126ºC, or a differential scanning calorimetry trace substantially in accordance with Figure 30.

12. The crystalline form of claim 1 which is a maleate salt which is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 3.8 ± 0.2, 7.6 ± 0.2, 8.5 ± 0.2, 10.8 ± 0.2, 11.4 ± 0.2, 12.2 ± 0.2, 15.2 ± 0.2, 15.8 ± 0.2, 17.0 ± 0.2, 18.0 ± 0.2, 18.8 ± 0.2, 19.4 ± 0.2, 20.3 ± 0.2, 21.6 ± 0.2, 22.6 ± 0.2, 23.6 ± 0.2, 24.3 ± 0.2, 24.8 ± 0.2, 26.0 ± 0.2, 27.2 ± 0.2, 27.9 ± 0.2,

~~28.2 ± 0.2, 28.8 ± 0.2, 29.9 ± 0.2, 30.2 ± 0.2, 31.7 ± 0.2, 32.7 ± 0.2 and 33.2 ± 0.2 [Form M]; or~~

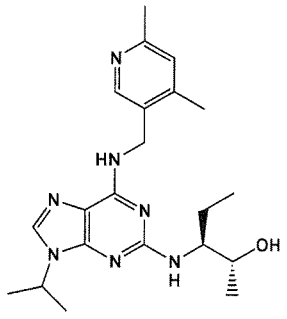
~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 10ºC per minute which shows an onset endothermic peak at a temperature of about 116ºC, or a differential scanning calorimetry trace substantially in accordance with Figure 31.~~

~~13. The crystalline form of claim 1 which is a gentisate salt which is characterized by:~~

~~(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.32 ± 0.2, 12.16 ± 0.2, 12.45 ± 0.2, 13.13 ± 0.2, 14.41 ± 0.2, 14.83 ± 0.2, 16.37 ± 0.2, 17.12 ± 0.2, 18.79 ± 0.2, 19.49 ± 0.2, 20.42 ± 0.2, 23.37 ± 0.2 and 23.77 ± 0.2 [Form O]; or~~

~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 10ºC per minute which shows an onset endothermic peak at a temperature of about 92ºC, or a differential scanning calorimetry trace substantially in accordance with Figure 32.~~

~~14~~5. A crystalline form of compound (I),



(I)

wherein said compound is in the form of a fumarate salt or a pharmaceutically acceptable solvate thereof, and ~~The crystalline form of claim 1 which is a fumarate salt which~~ is characterized by:

(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 3.8 ± 0.2, 7.7 ± 0.2, 8.1 ± 0.2, 8.8 ± 0.2, 10.2 ± 0.2, 11.3 ± 0.2, 13.1 ± 0.2, 15.2 ± 0.2, 15.5 ± 0.2, 16.5 ± 0.2, 17.7 ± 0.2, 19.1 ± 0.2, 19.6 ± 0.2, 20.0 ± 0.2, 20.9 ± 0.2, 21.5 ± 0.2, 21.9 ± 0.2, 22.7 ± 0.2, 23.2 ± 0.2, 23.8 ± 0.2, 24.1 ± 0.2, 25.0 ± 0.2, 25.3 ± 0.2, 26.7 ± 0.2, 27.9 ± 0.2

and 28.9 ± 0.2 [Form P] when using Cu Kα radiation and a scan speed of 0.146°/s; or

(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows a maximum endothermic peak at a temperature of about 140°C, or a differential scanning calorimetry trace substantially in accordance with Figure 33.

~~15. The crystalline form of claim 1 which is a malate salt more preferably the L-malate (L-malic acid), which is characterized by:~~

~~(i) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.7 ± 0.2, 8.6 ± 0.2, 9.3 ± 0.2, 11.0 ± 0.2, 12.7 ± 0.2, 13.6 ± 0.2, 14.1 ± 0.2, 15.1 ± 0.2, 15.8 ± 0.2, 16.5 ± 0.2, 17.8 ± 0.2, 18.7 ± 0.2, 19.5 ± 0.2, 19.8 ± 0.2, 21.1 ± 0.2, 22.5 ± 0.2, 23.5 ± 0.2, 24.9 ± 0.2 and 25.7 ± 0.2 [Form Q]; or~~

~~(ii) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows a maximum endothermic peak at a temperature of about 81°C, or a differential scanning calorimetry trace substantially in accordance with Figure 34; or~~

~~(iii) an x-ray powder diffraction pattern having two or more diffraction peaks at 2[theta] values selected from 6.77 ± 0.2, 9.85 ± 0.2, 12.19 ± 0.2, 13.36 ± 0.2, 13.59 ± 0.2, 14.15 ± 0.2, 15.88 ± 0.2, 16.44 ± 0.2, 17.33 ± 0.2, 17.75 ± 0.2, 19.73 ± 0.2, 20.11 ± 0.2, 20.50 ± 0.2, 20.84 ± 0.2, 21.30 ± 0.2, 22.23 ± 0.2, 23.27 ± 0.2, 23.83 ± 0.2, 24.19 ± 0.2, 24.61 ± 0.2, 25.18 ± 0.2, 25.67 ± 0.2, 26.03 ± 0.2, 26.31 ± 0.2, 26.91 ± 0.2, 27.78 ± 0.2, 28.76 ± 0.2, 31.12 ± 0.2, 32.35 ± 0.2 and 33.24 ± 0.2 [Form R]; or~~

~~(iv) a differential scanning calorimetry trace recorded at a heating rate of 10°C per minute which shows a maximum endothermic peak at a temperature of about 104°C, or a differential scanning calorimetry trace substantially in accordance with Figure 35.~~

~~16~~. A pharmaceutical composition comprising the crystalline form of any one of claims 1 to ~~15~~ and a pharmaceutically acceptable carrier, diluent or excipient.

~~17~~. A crystalline form according to any one of claims 1 to ~~15~~ for use in medicine.

~~18~~. A crystalline form according to any one of claims 1 to ~~15~~ for use in the prevention or treatment of proliferative disorders, immune-mediated and inflammatory disorders, autoimmune and autoimmune-mediated disorders, kidney disorders, cardiovascular disorders, ophthalmic disorders, neurodegenerative disorders, psychiatric disorders, viral disorders, metabolic disorders and/or respiratory disorders.

~~19. A process for preparing crystalline free base (Form A) of compound (I) according to claim 4, said method comprising the steps of crystallising compound (I) in free base Form A from methyl t-butyl ether (MTBE).~~

~~20~~9. A process for preparing a crystalline L-tartrate salt (Form D) of compound (I) according to claim ~~3~~ 2 which comprises the steps of:

(i) preparing a reaction mixture comprising compound (I) in free base form, L-tartaric acid and ethyl acetate; and

(ii) isolating the crystalline L-tartrate salt (Form D) from the reaction mixture.

~~21~~10. A process for preparing a crystalline L-tartrate salt (Form E) of compound (I) according to claim ~~2~~ 1 which comprises the steps of:

(A) (i) preparing a reaction mixture comprising compound (I) in free base form, L-tartaric acid, ethanol and water; and

(ii) isolating the crystalline L-tartrate salt (Form E) from the reaction mixture; or

(B) (i) preparing a reaction mixture comprising compound (I) in free base form, L-tartaric acid and ethyl acetate; and

(ii) isolating the crystalline L-tartrate salt (Form D) from the reaction mixture; and

(iii) recrystallizing the crystalline L-tartrate salt (Form D) obtained in step (B)(ii) from a mixture of ethanol and acetonitrile; and

(iv) isolating the crystalline L-tartrate salt (Form E) from the reaction mixture; or

(C) (i) preparing crystalline L-tartrate salt (Form D) by the process of claim 20;

(ii) preparing crystalline L-tartrate salt (Form E) by the process of steps (A)(i)-(ii) or B(i)-(iv) above;

(iii) forming a slurry of L-tartrate salt (Form D) and L-tartrate salt (Form E) in a solvent selected from ethyl acetate, propan-2-ol, IMS and acetonitrile; and

(iv) isolating the crystalline L-tartrate salt (Form E) from the slurry; or

(D) (i) preparing crystalline L-tartrate salt (Form D) by the process of claim 20;

(ii) preparing crystalline L-tartrate salt (Form E) by the process of steps (A)(i)-(ii) or B(i)-(iv) above;

(iii) dissolving the crystalline L-tartrate salt (Form D) obtained in step (D)(i) in a mixture of ethanol and acetonitrile and seeding with crystalline L-tartrate salt (Form E); and

(iv) isolating the crystalline L-tartrate salt (Form E) from the reaction mixture; or

(E) (i) preparing a reaction mixture comprising free base compound (I) in ethanol;

(ii) adding solution of tartaric acid in water/ethanol to the reaction mixture obtained in step (E)(i);

(iii) filtering the reaction mixture formed in step (E)(ii);

(iv) seeding the filtrate with crystalline L-tartrate salt (Form E) prepared in accordance with steps (A)(i)-(ii), (B)(i)-(iv) or (C)(i)-(iv) above; and

(iv) isolating crystalline L-tartrate salt (Form E) from the reaction mixture.