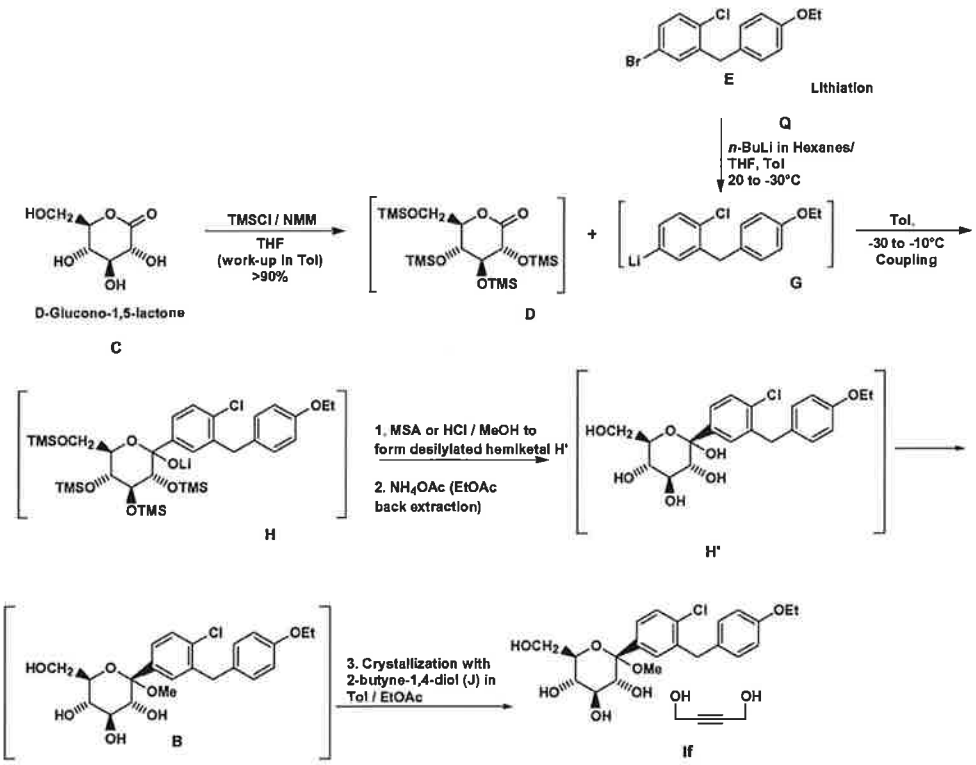
SCHEME IVA



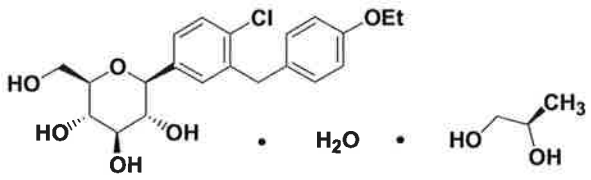
[0090] Referring now to Figure 22, a schematic process flow diagram (similar to that disclosed in U.S. Patent No. 7,164,015 ~~which is incorporated herein by reference~~), is shown. In this embodiment, the entire process for preparing compound If as shown in Scheme IVA is performed under non-cryogenic conditions. An aromatic reactant E having a group suitable for Li and halogen exchange is stored in a first vessel **1** at room temperature. A lithium reagent Q is fed into a second vessel **2**, also at room temperature. The aromatic reactant E and the lithium reagent Q are transferred from the vessels **1** and **2** via pumps **3** and **4**, respectively, to a first jacketed static mixer **5**. The temperature of a reaction to produce a lithiated anion species is regulated at from about -30°C to about 20°C, in the first mixer **5** by a chiller **6**.

[0091] The lithiated anion species G thus formed is fed directly from the first mixer **5** to a second static mixer **22** along a conventional transfer line **19**. A carbonyl substituted reactant D is fed into a third vessel **20** at room temperature and is

[00251] The anorectic agent which may be optionally employed in combination with the compound of the present invention include topiramate (Johnson & Johnson), dexamphetamine, phentermine, phenylpropanolamine or mazindol.

~~**[00252]** The aforementioned patents and patent applications are incorporated herein by reference.~~

[~~00253~~ 00252] The above other therapeutic agents, when employed in combination with the compound of the present invention may be used, for example, in those amounts indicated in the Physicians' Desk Reference, as in the patents set out above or as otherwise determined by one of ordinary skill in the art.



Ib .

~~3. The crystalline structure according to Claim 2 characterized by one or more of the following:~~

~~a) a powder x-ray diffraction pattern comprising 2Θ values (CuKα λ = 1.5418 Å) selected from the group consisting of 3.9 ± 0.1, 8.0 ± 0.1, 8.7 ± 0.1, 15.3 ± 0.1, 15.6 ± 0.1, 17.2 ± 0.1, 19.2 ± 0.1, 19.9 ± 0.1 and 20.3 ± 0.1, at room temperature;~~

~~b) a solid state ^{13}C NMR spectrum having substantially similar peak positions at 15.8, 17.6, 39.0, 60.9, 63.2, 67.4, 69.7, 77.3, 79.2, 79.8, 113.3, 123.6, 129.0, 130.4, 132.0, 135.6, 139.2 and 157.9 ppm, as determined on a 400MHz spectrometer relative to TMS at zero;~~

~~c) a differential scanning calorimetry thermogram having an endotherm in the range of about 43°C to 60°C; or~~

~~d) thermal gravimetric analysis curve with about 18.7% weight loss from about room temperature up to about 235°C.~~

~~4. The crystalline structure according to Claim 3 characterized by a powder x-ray diffraction pattern comprising 2Θ values (CuKα λ = 1.5418 Å) selected from the group consisting of 3.9 ± 0.1, 8.0 ± 0.1, 8.7 ± 0.1, 15.3 ± 0.1, 15.6 ± 0.1, 17.2 ± 0.1, 19.2 ± 0.1, 19.9 ± 0.1 and 20.3 ± 0.1, at room temperature.~~

~~5~~3. The crystalline structure according to Claim ~~3 or Claim 4~~2 characterized by a solid state ^{13}C NMR spectrum having ~~substantially similar~~ peak positions at 15.8, 17.6, 39.0, 60.9, 63.2, 67.4, 69.7, 77.3, 79.2, 79.8, 113.3, 123.6, 129.0, 130.4, 132.0, 135.6, 139.2 and 157.9 ppm, as determined on a 400MHz spectrometer relative to TMS at zero.

~~6~~4. The crystalline structure according to any of Claims ~~3-5~~2 characterized by a differential scanning calorimetry thermogram having an endotherm in the range of ~~about~~ 43°C to 60°C.

~~7~~5. The crystalline structure according to any of Claims ~~3-6~~2 characteraized by a thermal gravimetric analysis curve with ~~about~~ 18.7% weight loss from ~~about~~ room temperature up to ~~about~~ 235°C.

~~8~~6. The crystalline structure of any of Claims 2-~~7~~5 in ~~substantially~~ pure form.

97. A pharmaceutical composition comprising a therapeutically effective amount of the crystalline structure as defined in any of Claims 2-~~8~~ 6 and a pharmaceutically acceptable carrier or diluent.

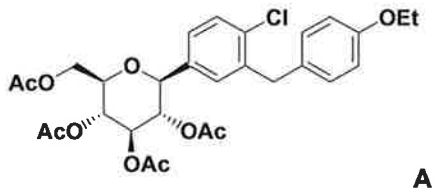
~~10~~8. A pharmaceutical composition comprising an effective amount of the crystal structure according to any of Claims 2-~~8~~ 6 in combination with one or more therapeutic agents selected from the group consisting of an antidiabetic agent, an anti-obesity agent, a anti-hypertensive agent, an anti-atherosclerotic agent and a lipid-lowering agent.

~~11~~9. Use of the crystalline structure according to any of Claims 2-~~8~~6 in the manufacture of a medicament for treating diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, dyslipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high density lipoprotein levels in a mammal.

~~12~~10. A process of preparing the crystalline structure as defined in any of Claims 2-~~8~~6

comprising:

reacting a compound of Formula A



A

in an organic solvent with base and (R)-propylene glycol, optionally adding seeds of the (R)-PG compound Ib, to yield the compound of Formula Ib.