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(54) **Title**: COMPOUND OF CRYSTAL FORM OF ANDROSTA-3B,5A,6B-TRIOL AND METHOD FOR PREPARING SAME

(54) **发明名称** : 雄甾-3β,5α,6β-三醇的晶型化合物及其制备方法

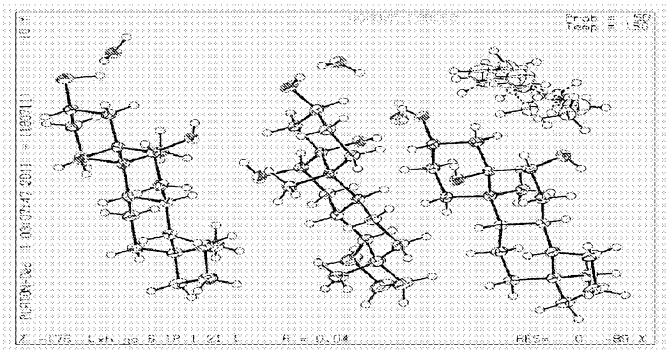

图 1 / Fig. 1

(57) **Abstract**: Disclosed are four compounds of crystal form of androsta-3β,5α,6β-triol (YC-6 for short) (YC-6 of A crystal form, YC-6 of B crystal form, YC-6 of C crystal form, YC-6 of D crystal form) and a method for preparing same. The four compounds of crystal form are characterized by remarkable differences in parameters such as lattice parameters, 2θ and intensity of X-ray powder diffraction, melting point, etc. Study on the polymorphism is significant for further researching the pharmaceutical effect, bioavailability and stability thereof.

(57) **摘要**: 一种雄甾-3β,5α,6β-三醇（简称 YC-6）的四种晶型化合物（A 晶型 YC-6、B 晶型 YC-6、C 晶型 YC-6、D 晶型 YC-6）及其制备方法。四种晶型化合物的特性在于它们的晶胞参数、X-射线粉末衍射的 2θ 和强度、熔点等参数存在显著差异，研究其多晶型现象对进一步研究其药效、生物利用度及稳定性具有重要意义。

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CRYSTALLINE FORMS OF 5α-ANDROSTANE-3β,5,6β-TRIOL AND PREPARATION METHODS THEREFOR

FIELD OF THE INVENTION

The present invention relates to crystalline forms of 5α-androstane-3β,5,6β-triol (also known as 5α-androst-3β,5,6β-triol). The present invention also relates to preparation methods for the crystalline forms of 5α-androstane-3β,5,6β-triol.

BACKGROUND OF THE INVENTION

Polymorphism is common in solid drugs, and drug compounds in different crystalline forms have different physical and chemical properties. Polymorphism is one of important factors that have influence on the effect and quality of solid drugs. Different crystalline forms may differ by several times in solubility, and also differ greatly in *in vivo* distribution and metabolism, causing differences in bioavailability. In addition, solid APIs (active pharmaceutical ingredients) in different crystalline forms and preparations thereof show different stabilities during preparation and storage process, which would cause crystalline transformation and thus influence the quality of the drugs. Therefore, the polymorphism would finally influence the quality, therapeutic effect and safety of solid drugs.

5α-androstane-3β,5,6β-triol is one of polyhydroxy steroids, and has significant neuroprotective effect. The study on its polymorphism is very important for further studying its efficacy, bioavailability and stability. X-ray single crystal diffractometer, X-ray powder diffractometer and differential thermal analyzer are main tools for quantitatively determining the specific type of polymorphism, which provides more qualitative and quantitative information for the study on crystalline form of solid drugs.

SUMMARY OF THE INVENTION

An object of the present invention is to provide four crystalline forms of 5α-androstane-3β,5,6β-triol (hereinafter abbreviated as YC-6).

Another object of the present invention is to provide methods for preparing the four crystalline forms of 5α-androstane-3β,5,6β-triol.

A first crystalline form of 5α-androstane-3β,5,6β-triol (hereinafter abbreviated as crystalline form A of YC-6) is provided by the present invention, wherein the crystalline form is a transparent block-shaped crystal, and belongs to the monoclinic crystal system and space group $P2_1$, and wherein the

crystalline form is characterized by lattice parameters of a = 17.8±0.2 Å, b = 7.3±0.2 Å, c = 22.1±0.2 Å, α = 90.0°, β = 103.3±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.4±0.2, 8.7±0.2, 9.3±0.2, 12.6±0.2, 13.0±0.2, 15.0±0.2, 15.6±0.2, 16.6±0.2, 17.3±0.2, 18.5±0.2, 19.6±0.2, 21.0±0.2, 21.8±0.2, 24.3±0.2, 27.9±0.2 degrees; and characterized by the endothermic transition temperature of 225±2 °C.

A method for preparing the crystalline form A of YC-6 is provided by the present invention, comprising: dissolving 5α-androstane-3β,5,6β-triol in a solvent at room temperature or at 50~80 °C, with a ratio of the 5α-androstane-3β,5,6β-triol to the solvent being 1g : 10~40 mL; adding another solvent to dilute; allowing to form a crystalline precipitate.

Preferably, in the above method, the solvent for dissolving is acetone, methanol, ethanol, isopropanol, dioxane or tetrahydrofuran, and the solvent for diluting is an original solvent or a poor solvent, wherein the original solvent is acetone, methanol, ethanol, isopropanol or dioxane (excluding tetrahydrofuran) with a dilution rate of 0~5 : 1, and the poor solvent is water with a dilution rate of 0~2 : 1.

A second crystalline form of 5α-androstane-3β,5,6β-triol (hereinafter abbreviated as crystalline form B of YC-6) is provided by the present invention, wherein the crystalline form is a transparent needle-shaped crystal, and belongs to the monoclinic crystal system and space group $P2_1$, and wherein the crystalline form is characterized by lattice parameters of a = 11.3±0.2 Å, b = 7.4 ±0.2 Å, c = 20.5±0.2 Å, α = 90.0°, β = 95.0±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.3±0.2, 8.6±0.2, 12.9±0.2, 17.2±0.2, 21.6±0.2 degrees; and characterized by the endothermic transition temperature of 223±2 °C.

A method for preparing the crystalline form B of YC-6 is provided by the present invention, comprising: dissolving 5α-androstane-3β,5,6β-triol in a solvent, with a ratio of the 5α-androstane-3β,5,6β-triol to the solvent being 1g : 10~120 mL; heating to 50~80 °C; adding another solvent to dilute; cooling; allowing to form a crystalline precipitate.

Preferably, in the above method, the solvent for dissolving is acetone, ethyl acetate or ethanol, and the solvent for diluting is an original solvent or a poor solvent, wherein the original solvent is acetone, ethyl acetate or ethanol, and the poor solvent is water, hexamethylene or petroleum ether.

More preferably, in the above method, the dilution rate is 2.5~5 : 1 when acetone or ethanol is used as the solvent for dissolving and water is used as the poor solvent for diluting; the dilution rate is 1~5 : 1 when acetone or

ethanol is used as the solvent for dissolving and hexamethylene or petroleum ether is used as the poor solvent for diluting; the dilution rate is 0~5 : 1 when ethyl acetate is used as the solvent for dissolving and ethyl acetate is used as the original solvent for diluting; and the dilution rate is 0~5 : 1 when ethyl acetate is used as the solvent for dissolving and hexamethylene or petroleum ether is used as the poor solvent for diluting.

A third crystalline form of 5α-androstane-3β,5,6β-triol (hereinafter abbreviated as crystalline form C of YC-6) is provided by the present invention, wherein the crystalline form is a transparent plate-shaped crystal, and belongs to the monoclinic crystal system and space group $P2_1$, and wherein the crystalline form is characterized by lattice parameters of a = 17.1±0.2 Å, b = 6.4±0.2 Å, c = 34.9±0.2 Å, α = 90.0°, β = 91.1±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.2±0.2, 8.5±0.2, 9.0±0.2, 12.5±0.2, 14.8±0.2, 15.4±0.2, 16.4±0.2, 16.8±0.2, 17.1±0.2, 18.3±0.2, 19.4±0.2, 20.8±0.2, 21.8±0.2, 24.1±0.2 degrees; and characterized by the endothermic transition temperature of 206±2 °C.

A method for preparing the crystalline form C of YC-6 is provided by the present invention, comprising: dissolving 5α-androstane-3β,5,6β-triol in ethanol at room temperature, with a ratio of the 5α-androstane-3β,5,6β-triol to the ethanol being 1g : 10~30 mL; adding ethanol in a ratio of 0~5 :1 to dilute; allowing to form a crystalline precipitate at 0~10 °C.

A fourth crystalline form of 5α-androstane-3β,5,6β-triol (hereinafter abbreviated as crystalline form D of YC-6) is provided by the present invention, wherein the crystalline form is a transparent column-shaped crystal, and belongs to the orthorhombic crystal system and space group $P2_12_12_1$, and wherein the crystalline form is characterized by lattice parameters of a = 6.3±0.2 Å, b = 12.6±0.2 Å, c = 26.7±0.2 Å, α = 90.0°, β = 90°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.0±0.2, 8.1±0.2, 8.5±0.2, 9.4±0.2, 12.5±0.2, 14.0±0.2, 14.9±0.2, 15.5±0.2, 16.4±0.2, 17.1±0.2, 18.3±0.2, 19.5±0.2, 20.5±0.2, 20.9±0.2, 21.5±0.2 degrees; and characterized by the endothermic transition temperature of 226±2 °C.

A method for preparing the crystalline form D of YC-6 is provided by the present invention, comprising: dissolving 5α-androstane-3β,5,6β-triol in tetrahydrofuran at room temperature, with a ratio of the 5α-androstane-3β,5,6β-triol to the tetrahydrofuran being 1g : 10~30 mL; adding tetrahydrofuran in a ratio of 0~5 :1 to dilute; allowing to form a crystalline precipitate.

The four crystalline forms of 5α-androstane-3β,5,6β-triol (i.e., crystalline forms A, B, C and D of YC-6) provided by the present invention have

significant differences in their lattice parameters, 2θ values and intensity in X-ray power diffraction, and melting points, etc. The study on its polymorphism is significant for further studying of itsefficacy, bioavailability and stability.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the X-ray single crystal diffraction diagrams of crystalline form A of YC-6.

Figure 2 shows the X-ray powder diffraction diagrams of crystalline form A of YC-6.

Figure 3 shows the differential thermal analysis diagrams of crystalline form A of YC-6.

Figure 4 shows the X-ray single crystal diffraction diagrams of crystalline form B of YC-6.

Figure 5 shows the X-ray powder diffraction diagrams of crystalline form B of YC-6.

Figure 6 shows the differential thermal analysis diagrams of crystalline form B of YC-6.

Figure 7 shows the X-ray single crystal diffraction diagrams of crystalline form C of YC-6.

Figure 8 shows the X-ray powder diffraction diagrams of crystalline form C of YC-6.

Figure 9 shows the differential thermal analysis diagrams of crystalline form C of YC-6.

Figure 10 shows the X-ray single crystal diffraction diagrams of crystalline form D of YC-6.

Figure 11 shows the X-ray powder diffraction diagrams of crystalline form D of YC-6.

Figure 12 shows the differential thermal analysis diagrams of crystalline form D of YC-6.

DETAILED DESCRIPTION OF THE INVENTION

Physical Characterization

X-ray single crystal diffraction diagrams for different crystalline forms of YC-6, which were obtained by the examples, were obtained using Xcalibur Nova biomacromolecule X-Ray single crystal diffractometer (Agilent Technologies (China) Co., Ltd), under the following settings: fixed target of copper; output power: 50W; two-dimensional surface detecting system: 165mmCCD; resolution: ≤0.005 degree; cooling nitrogen: -180~+25 °C; control accuracy: ≤0.5 °C; test temperature: 150 k.

X-ray powder diffraction diagrams for different crystalline forms of YC-6, which were obtained by the examples, were obtained using D/Max-IIIA X-ray powder diffractometer (Rigaku, Japan), under the following settings: fixed target of copper; power: 3 kW; detecting angle: 1~50 °; sensitivity: 3~5%; accuracy of the detecting angle: ±0.002.

Differential scanning for different crystalline forms of YC-6, which were obtained by the examples, were performed using STA409PC thermal analyzer (Netzsch, Germany), under the following settings: crucible: alumina crucible; carrier gas: N_2; temperature: 20~400 °C, 10.0 K/min, 400 °C maintained by 10 min.

Analysis Parameters of the single crystal diffraction, powder diffraction and DSC for the four crystalline forms of YC-6

(1) The crystal structure information of crystalline form A of YC-6 obtained by X-ray single crystal diffraction is: the crystalline form belongs to the monoclinic crystal system and space group $P2_1$, with lattice parameters of a = 17.76±0.08 Å, b = 7.30±0.08 Å, c = 22.05±0.08 Å, α = 90.0°, β = 103.23 ±0.5°, γ = 90.0°, V = 2775.36(5) $Å^3$.

The crystalline form A of YC-6 showed diffraction peaks at diffraction angle 2θ values of 4.4±0.1, 8.7±0.1, 9.3±0.1, 12.6±0.1, 13.0±0.1, 15.0±0.1, 15.6±0.1, 16.6±0.1, 17.3±0.1, 18.5±0.1, 19.6±0.1, 21.0±0.1, 21.8±0.1, 24.3±0.1, 27.9±0.1 degrees, with the X-ray powder diffraction diagrams showed in Figure 2.

The differential scanning calorimetry (DSC) diagrams of crystalline form A of YC-6 is showed in Figure 3, with the endothermic transition temperature of 225±2 °C.

(2) The crystal structure information of crystalline form B of YC-6 obtained by X-ray single crystal diffraction is: the crystalline form belongs to the

monoclinic crystal system and space group $P2_1$, with lattice parameters of a = 11.27±0.08 Å, b = 7.40±0.08 Å, c = 20.45±0.08 Å, α = 90.0°, β = 94.94±0.5°, γ = 90.0°, V = 1699.24(3) $Å^3$.

The crystalline form B of YC-6 showed diffraction peaks at diffraction angle 2θ values of 4.3±0.1, 8.6±0.1, 12.9±0.1, 17.2±0.1, 21.6±0.1 degrees, with the X-ray powder diffraction diagrams showed in Figure 5.

The differential scanning calorimetry (DSC) diagrams of crystalline form B of YC-6 is showed in Figure 6, with the endothermic transition temperature of 223±2 °C.

(3) The crystal structure information of crystalline form C of YC-6 obtained by X-ray single crystal diffraction is: the crystalline form belongs to the monoclinic crystal system and space group $P2_1$, with lattice parameters of a = 17.14±0.08 Å, b = 6.40±0.08 Å, c = 34.89±0.08 Å, α = 90.0°, β = 91.05 + 0.5°, γ = 90.0°, V = 3827.48(9) $Å^3$.

The crystalline form C of YC-6 showed diffraction peaks at diffraction angle 2θ values of 4.2±0.1, 8.5±0.1, 9.0±0.1, 12.5±0.1, 14.8±0.1, 15.4±0.1, 16.4±0.1, 16.8±0.2, 17.1±0.1, 18.3±0.1, 19.4±0.1, 20.8±0.1, 21.8±0.1, 24.1±0.1 degrees, with the X-ray powder diffraction diagrams showed in Figure 8.

The differential scanning calorimetry (DSC) diagrams of crystalline form C of YC-6 is showed in Figure 9, with the endothermic transition temperature of 206±2 °C.

(4) The crystal structure information of crystalline form D of YC-6 obtained by X-ray single crystal diffraction is: the crystalline form belongs to the orthorhombic crystal system and space group $P2_12_12_1$, with lattice parameters of a = 6.28±0.08 Å, b = 12.56±0.08 Å, c = 26.68±0.08 Å, α = 90.0°, β = 90.0°, γ = 90.0°, V = 2103.09(7) $Å^3$.

The crystalline form D of YC-6 showed diffraction peaks at diffraction angle 2θ values of 4.0±0.1, 8.1±0.1, 8.5±0.1, 9.4±0.1, 12.5±0.1, 14.0±0.1, 14.9±0.1, 15.5±0.1, 16.4±0.1, 17.1±0.1, 18.3±0.1, 19.5±0.1, 20.5±0.1, 20.9±0.1, 21.5±0.1 degrees, with the X-ray powder diffraction diagrams showed in Figure 11.

The differential scanning calorimetry (DSC) diagrams of crystalline form D of YC-6 is showed in Figure 12, with the endothermic transition temperature of 226±2 °C.

Example 1

Preparation of crystalline form A of YC-6: 0.5g of YC-6 was dissolved in 8 mL of acetone (50~60 °C), which was added by the same amount of acetone to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 60 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 2

Preparation of crystalline form A of YC-6: 0.5g of YC-6 was dissolved in 10 mL of acetone at room temperature, which was added by the same amount of acetone to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 60 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 3

Preparation of crystalline form A of YC-6: 0.5g of YC-6 was dissolved in 7 mL of ethanol at room temperature, which was added by the same amount of ethanol to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 60 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 4

Preparation of crystalline form A of YC-6: 0.5g of YC-6 was dissolved in 12 mL of acetone at room temperature, which was added by water (a half amount of that of the acetone) to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 60 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 5

Preparation of crystalline form A of YC-6: 0.5g of YC-6 was dissolved in 10 mL of ethanol at room temperature, which was added by water (a half amount

of that of the ethanol) to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 60 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

The tests showed that the crystals obtained in examples 1~5 share the same lattice parameters in X-ray single crystal diffraction, and that the crystals obtained thereby are all crystalline form A of YC-6.

Example 6

Preparation of crystalline form B of YC-6: 0.5g of YC-6 was dissolved in 30 mL of ethyl acetate, which was then heated to 70~80 °C. After that, the solution was added by 30 mL of ethyl acetate to dilute, and then cooled and allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 7

Preparation of crystalline form B of YC-6: 0.5g of YC-6 was dissolved in 30 mL of ethyl acetate, which was then heated to 70~80 °C. After that, the solution was added by 30 mL of hexamethylene to dilute, and then cooled and allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 8

Preparation of crystalline form B of YC-6: 0.5g of YC-6 was dissolved in 8 mL of acetone, which was then heated to 50~60 °C. After that, the solution was added by 24 mL of water to dilute, and then cooled and allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 9

Preparation of crystalline form B of YC-6: 0.5g of YC-6 was dissolved in 12 mL of acetone, which was then heated to 50~60 °C. After that, the solution

was added by 36 mL of hexamethylene to dilute, and then cooled and allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

The tests showed that the crystals obtained in examples 6~9 share the same lattice parameters in X-ray single crystal diffraction, and that the crystals obtained thereby are all crystalline form B of YC-6.

Example 10

Preparation of crystalline form C of YC-6: 0.5g of YC-6 was dissolved in 12 mL of ethanol at room temperature, which was added by the same amount of ethanol to dilute, and then allowed to form a crystalline precipitate at 10 °C. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 11

Preparation of crystalline form C of YC-6: 0.5g of YC-6 was dissolved in 15 mL of ethanol at room temperature, which was added by the same amount of ethanol to dilute, and then allowed to form a crystalline precipitate at 10 °C. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 12

Preparation of crystalline form C of YC-6: 0.5g of YC-6 was dissolved in 15 mL of ethanol at room temperature, which was added by twice amount of ethanol to dilute, and then allowed to form a crystalline precipitate at 10 °C. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

The tests showed that the crystals obtained in examples 10~12 share the same lattice parameters in X-ray single crystal diffraction, and that the crystals obtained thereby are all crystalline form C of YC-6.

Example 13

Preparation of crystalline form D of YC-6: 0.5g of YC-6 was dissolved in 10 mL of tetrahydrofuran at room temperature, which was added by the same amount of tetrahydrofuran to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 14

Preparation of crystalline form D of YC-6: 0.5g of YC-6 was dissolved in 10 mL of tetrahydrofuran at room temperature, which was added by twice amount of tetrahydrofuran to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

Example 15

Preparation of crystalline form D of YC-6: 0.5g of YC-6 was dissolved in 15 mL of tetrahydrofuran at room temperature, which was added by the same amount of tetrahydrofuran to dilute, and then allowed to form a crystalline precipitate. The single crystal obtained thereby was directly subjected to X-ray single crystal diffraction. Then the crystal was filtrated by suction and was air-dried at 70 °C to a constant weight, which was subjected to X-ray powder diffraction and differential scanning calorimetry.

The tests showed that the crystals obtained in examples 13~15 share the same lattice parameters in X-ray single crystal diffraction, and that the crystals obtained thereby are all crystalline form D of YC-6.

The above examples are merely provided for description of the present invention, and are not intended to limit the scope of the present invention. The objects of the present invention can be achieved by skilled persons in the art in accordance with the disclosure of the present invention and the parameter ranges involved.

CLAIMS

What is claimed is:

1. A crystalline form of 5α-androstane-3β,5,6β-triol, wherein the crystalline form is a transparent block-shaped crystal, and belongs to monoclinic crystal system and space group $P2_1$, and

wherein the crystalline form is characterized by lattice parameters of a = 17.8±0.2 Å, b = 7.3±0.2 Å, c = 22.1±0.2 Å, α = 90.0°, β = 103.3±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.4±0.2, 8.7±0.2, 9.3±0.2, 12.6±0.2, 13.0±0.2, 15.0±0.2, 15.6±0.2, 16.6±0.2, 17.3±0.2, 18.5±0.2, 19.6±0.2, 21.0±0.2, 21.8±0.2, 24.3±0.2, 27.9±0.2 degrees; and characterized by an endothermic transition temperature of 225±2 °C.

2. A method for preparing the crystalline form of claim 1, comprising:

dissolving 5α-androstane-3β,5,6β-triol in a solvent at room temperature or at 50~80 °C, with a ratio of the 5α-androstane-3β,5,6β-triol to the solvent being 1g : 10~40 mL;

adding another solvent to dilute; and

allowing to form a crystalline precipitate.

3. The method of claim 2, wherein the solvent for dissolving is acetone, methanol, ethanol, isopropanol, dioxane or tetrahydrofuran, and the solvent for diluting is an original solvent or a poor solvent, wherein the original solvent is acetone, methanol, ethanol, isopropanol or dioxane with a dilution rate of 0~5 : 1, and the poor solvent is water with a dilution rate of 0~2 : 1.

4. A crystalline form of 5α-androstane-3β,5,6β-triol, wherein the crystalline form is a transparent needle-shaped crystal, and belongs to monoclinic crystal system and space group $P2_1$, and

wherein the crystalline form is characterized by lattice parameters of a = 11.3±0.2 Å, b = 7.4 ±0.2 Å, c = 20.5±0.2 Å, α = 90.0°, β = 95.0±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.3±0.2, 8.6±0.2, 12.9±0.2, 17.2±0.2, 21.6±0.2 degrees; and characterized by an endothermic transition temperature of 223±2 °C.

5. A method for preparing the crystalline form of claim 4, comprising:

dissolving 5α-androstane-3β,5,6β-triol in a solvent, with a ratio of the 5α-androstane-3β,5,6β-triol to the solvent being 1g : 10~120 mL;

heating to 50~80 °C;

adding another solvent to dilute;

cooling; and

allowing to form a crystalline precipitate.

6. The method of claim 5, wherein the solvent for dissolving is acetone, ethyl acetate or ethanol, and the solvent for diluting is an original solvent or a poor solvent, wherein the original solvent is acetone, ethyl acetate or ethanol, and the poor solvent is water, hexamethylene or petroleum ether.

7. The method of claim 6, wherein

a dilution rate is 2.5~5 : 1 when acetone or ethanol is used as the solvent for dissolving and water is used as the poor solvent for diluting,

a dilution rate is 1~5 : 1 when acetone or ethanol is used as the solvent for dissolving and hexamethylene or petroleum ether is used as the poor solvent for diluting,

a dilution rate is 0~5 : 1 when ethyl acetate is used as the solvent for dissolving and ethyl acetate is used as the original solvent for diluting, and

a dilution rate is 0~5 : 1 when ethyl acetate is used as the solvent for dissolving and hexamethylene or petroleum ether is used as the poor solvent for diluting.

8. A crystalline form of 5α-androstane-3β,5,6β-triol, wherein the crystalline form is a transparent plate-shaped crystal, and belongs to monoclinic crystal system and space group $P2_1$, and

wherein the crystalline form is characterized by lattice parameters of a = 17.1±0.2 Å, b = 6.4±0.2 Å, c = 34.9±0.2 Å, α = 90.0°, β = 91.1±0.5°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.2±0.2, 8.5±0.2, 9.0±0.2, 12.5±0.2, 14.8±0.2, 15.4±0.2, 16.4±0.2, 16.8±0.2, 17.1±0.2, 18.3±0.2, 19.4±0.2, 20.8±0.2, 21.8±0.2, 24.1±0.2 degrees; and characterized by an endothermic transition temperature of 206±2 °C.

9. A method for preparing the crystalline form of claim 8, comprising:

dissolving 5α-androstane-3β,5,6β-triol in ethanol at room temperature, with a ratio of the 5α-androstane-3β,5,6β-triol to the ethanol being 1g : 10~30 mL;

adding ethanol in a ratio of 0~5 :1 to dilute; and

allowing to form a crystalline precipitate at 0~10 °C.

10. A crystalline form of 5α-androstane-3β,5,6β-triol, wherein the crystalline form is a transparent column-shaped crystal, and belongs to orthorhombic crystal system and space group $P2_12_12_1$, and

wherein the crystalline form is characterized by lattice parameters of a = 6.3±0.2 Å, b = 12.6±0.2 Å, c = 26.7±0.2 Å, α = 90.0°, β = 90°, γ = 90.0°; and characterized by diffraction peaks at diffraction angle 2θ values of 4.0±0.2, 8.1±0.2, 8.5±0.2, 9.4±0.2, 12.5±0.2, 14.0±0.2, 14.9±0.2, 15.5±0.2, 16.4±0.2, 17.1±0.2, 18.3±0.2, 19.5±0.2, 20.5±0.2, 20.9±0.2, 21.5±0.2 degrees; and characterized by an endothermic transition temperature of 226±2 °C.

11. A method for preparing the crystalline form of claim 10, comprising:

dissolving 5α-androstane-3β,5,6β-triol in tetrahydrofuran at room temperature, with a ratio of the 5α-androstane-3β,5,6β-triol to the tetrahydrofuran being 1g : 10~30 mL;

adding tetrahydrofuran in a ratio of 0~5 :1 to dilute; and

allowing to form a crystalline precipitate.

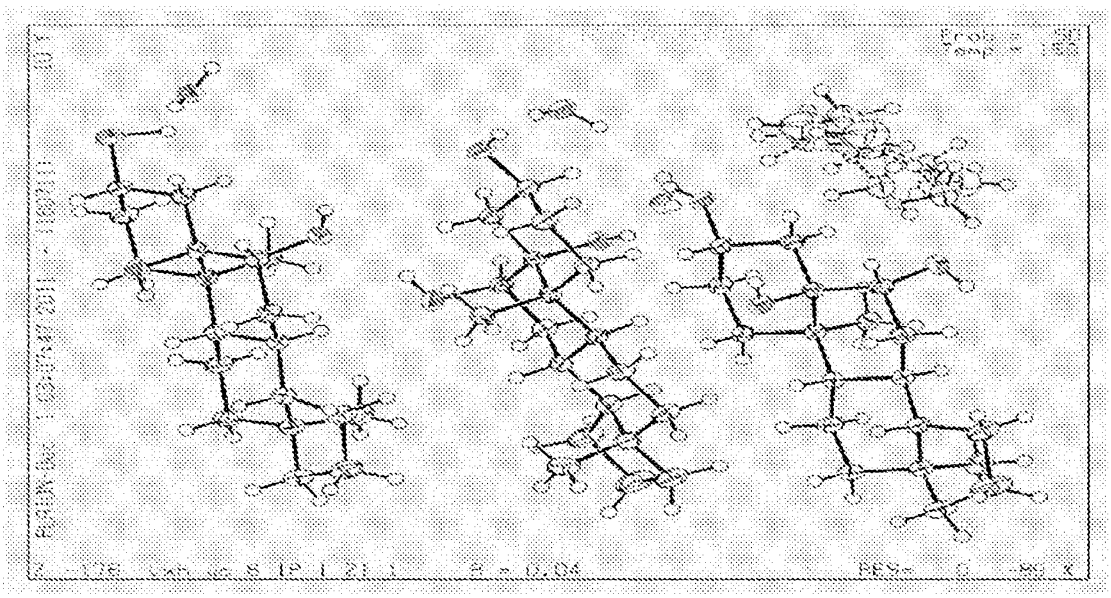

Figure 1

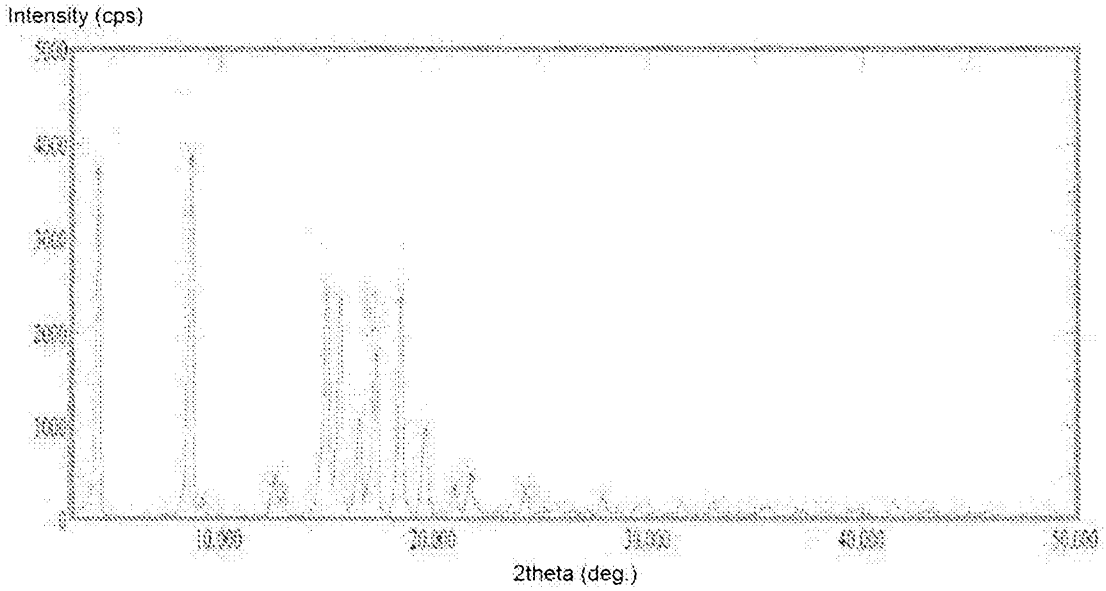

Figure 2

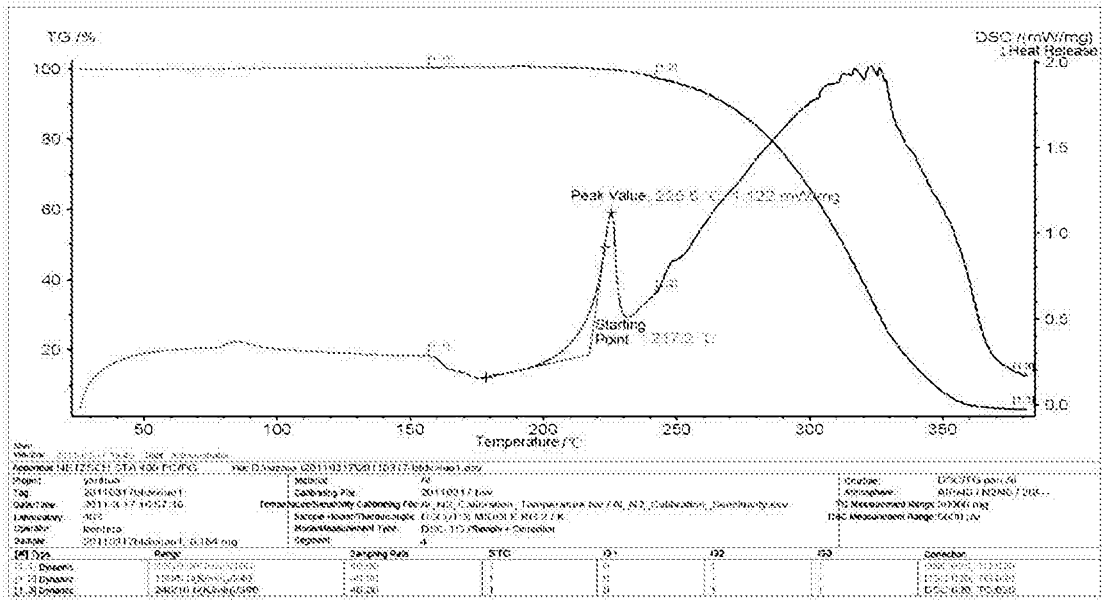

Figure 3

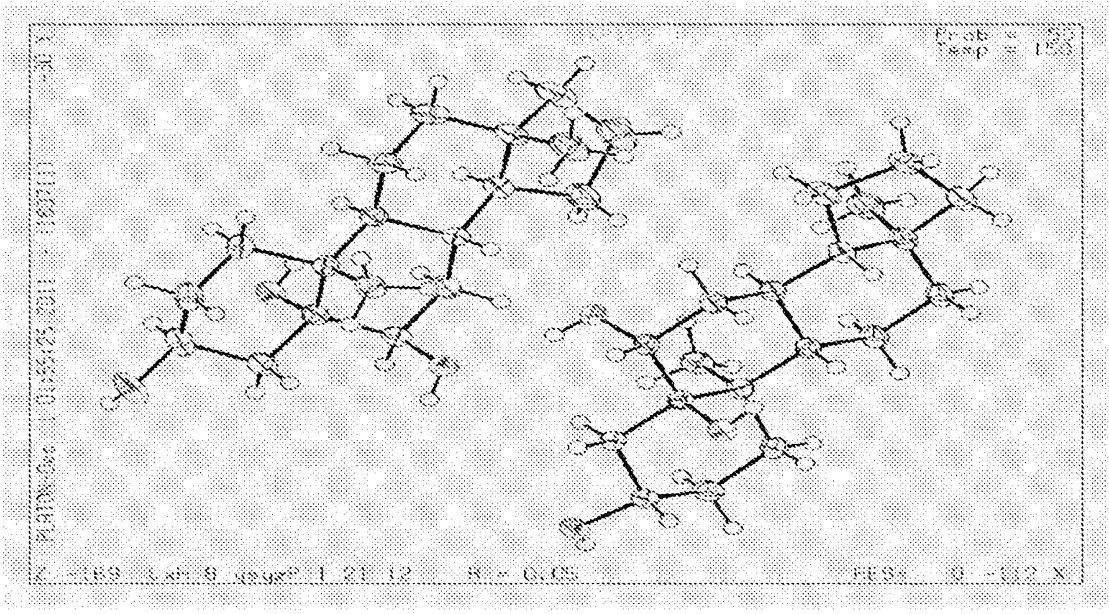

Figure 4

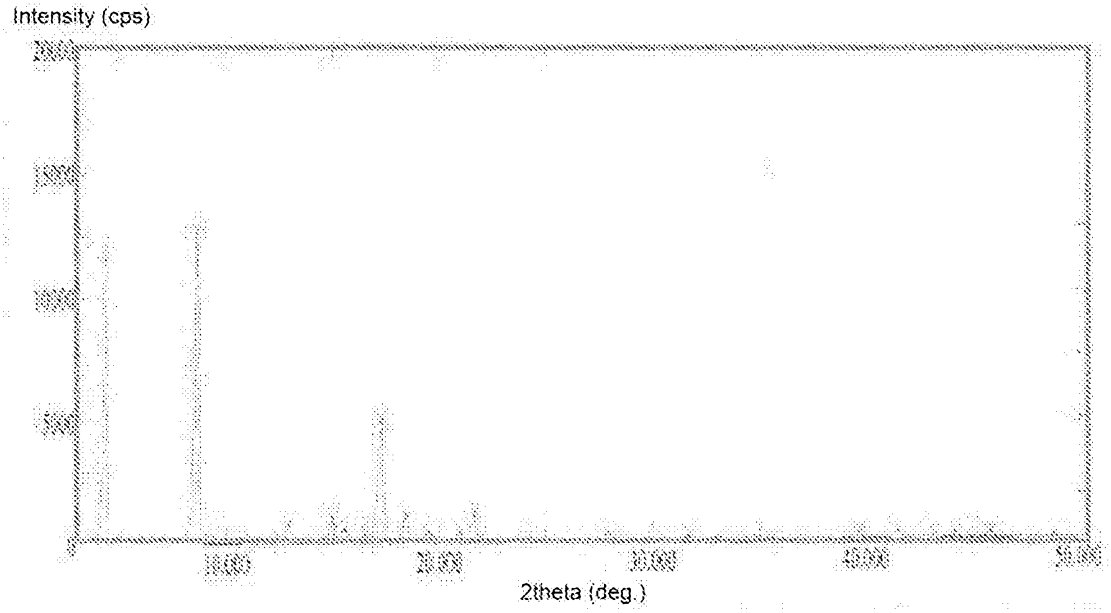

Figure 5

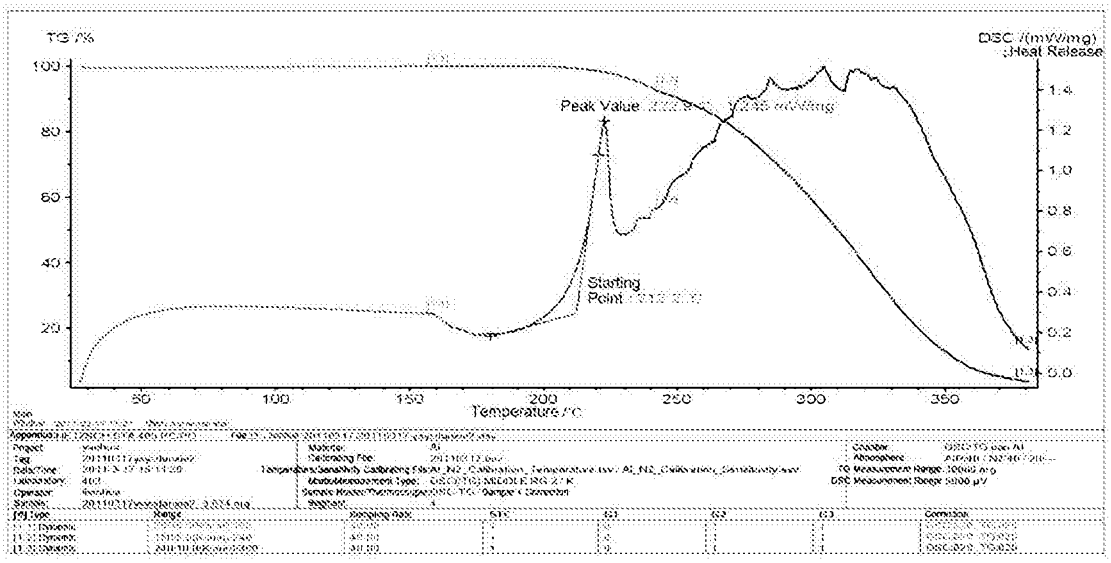

Figure 6

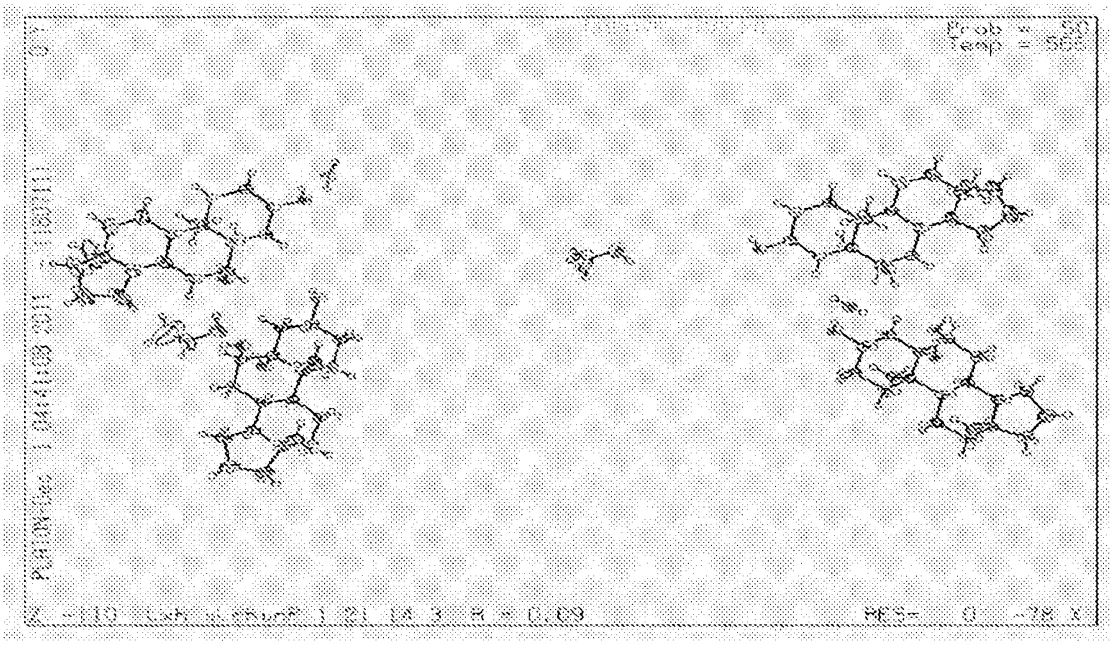

Figure 7

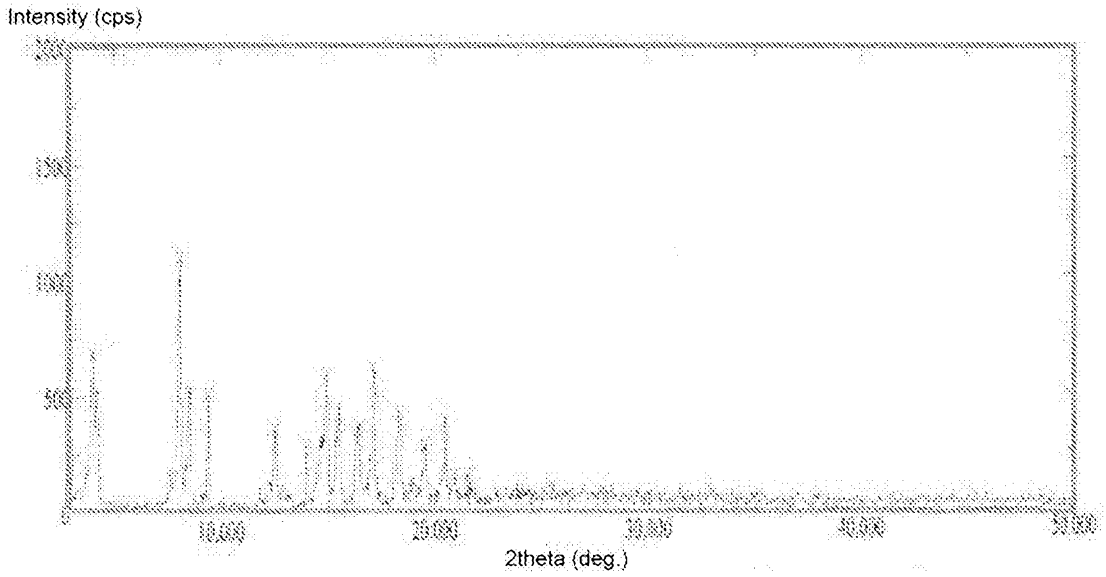

Figure 8

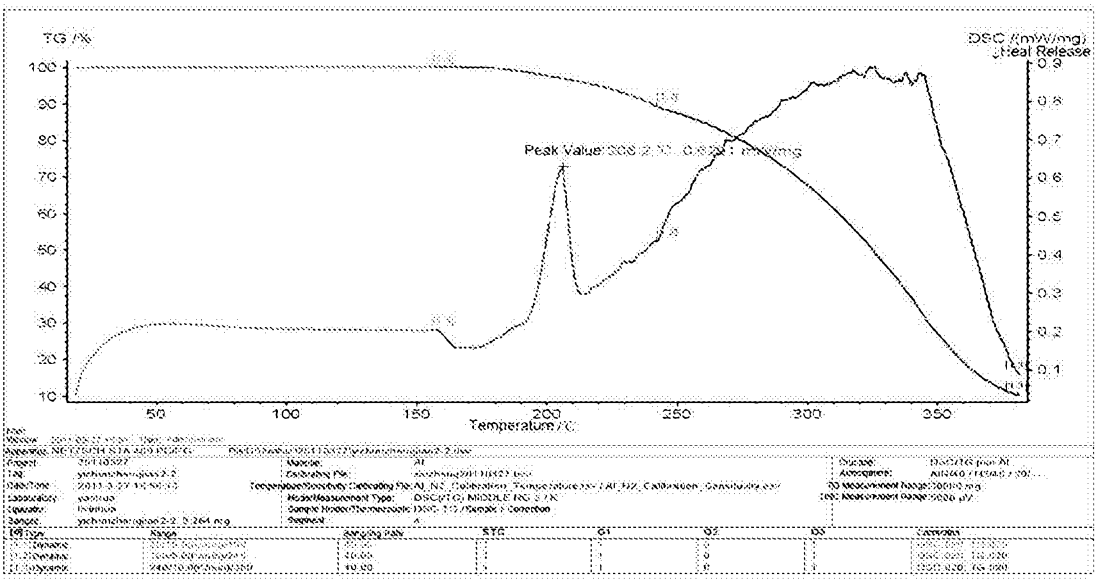

Figure 9

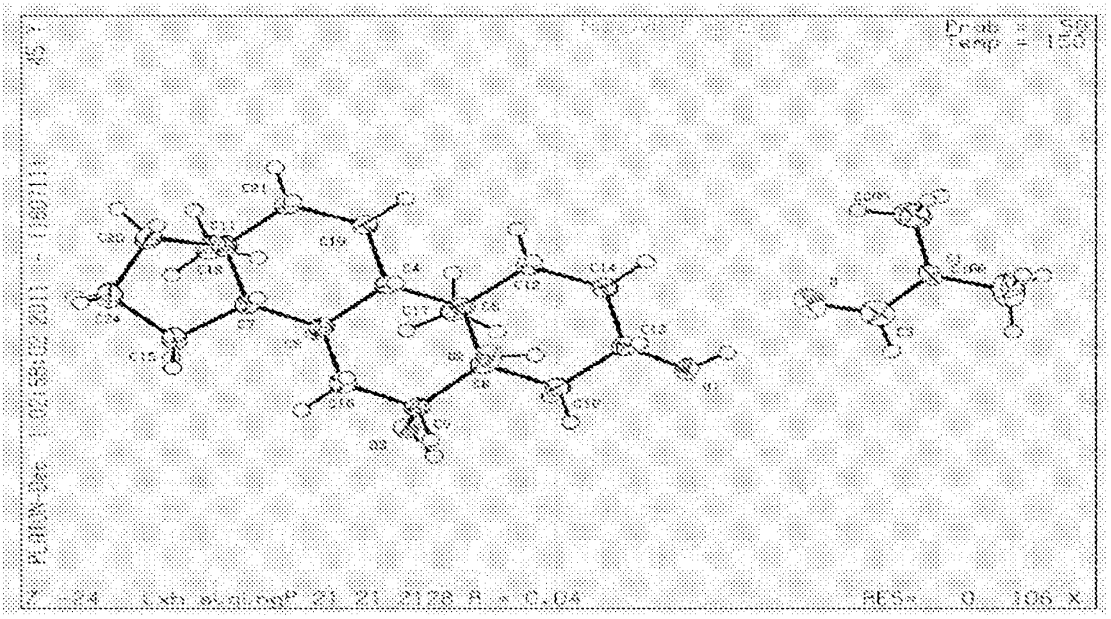

Figure 10

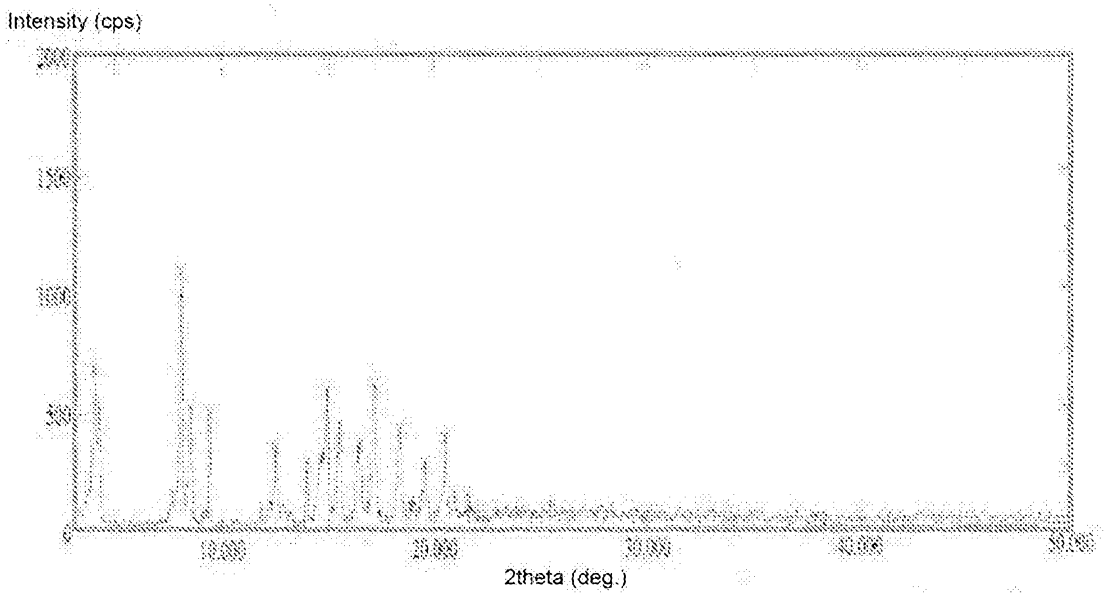

Figure 11

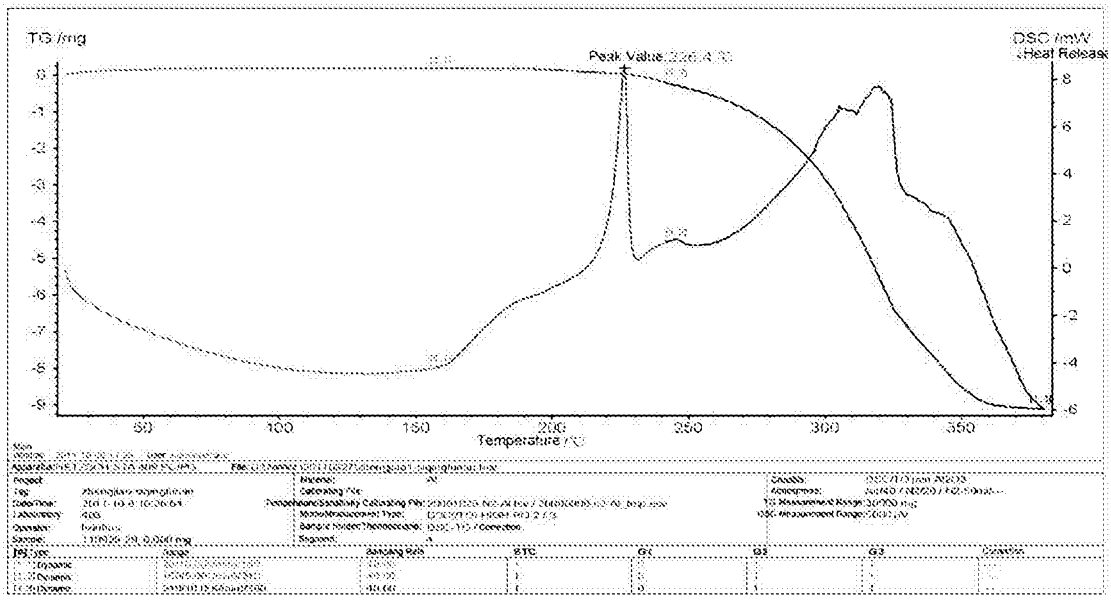

Figure 12