(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 May 2010 (20.05.2010)

PCT

(10) International Publication Number
WO 2010/056059 A2

(51) International Patent Classification:
C07D 401/12 (2006.01)

(21) International Application Number:
PCT/KR2009/006678

(22) International Filing Date:
13 November 2009 (13.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10-2008-0113507
14 November 2008 (14.11.2008) KR

(71) Applicant *(for all designated States except US)*: **HANMI PHARM. CO., LTD.** [KR/KR]; #893-5 Hajeo-ri, Paltan-myeon, Hwaseong-si, Gyeonggi-do 445-910 (KR).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **JANG, Sun Young** [KR/KR]; 101-302 Daewoo Iaan Apt., Yuljeon-dong, Jangan-gu, Suwon-si, Gyeonggi-do 440-320 (KR). **KIM, Tai Won** [KR/KR]; 4004-504 Eoeunmokmaeul Halla Vivaldi Apt., Jung-dong, Giheung-gu, Yongin-si, Gyeonggi-do 446-750 (KR). **KIM, Sungbum** [KR/KR]; 313-701 Yanghyunmaeul Sinan Apt., Singal-dong, Giheung-gu, Yongin-si, Gyeonggi-do 446-589 (KR). **KIM, Byung-Ku** [KR/KR]; #13-1523 Gamcheon-2-dong, Saha-gu, Busan 604-801 (KR). **CHO, Soohwa** [KR/KR]; #523-47 Yeonhui-1-dong, Seodaemun-gu, Seoul 120-111 (KR). **HA, Tae Hee** [KR/KR]; 413-2101 Seohae Granble, Solbitmaeul, Bansong-dong, Hwaseong-si, Gyeonggi-do 445-758 (KR). **SUH, Kwee Hyun** [KR/KR]; 101-204 Greenvill Apt., #1258, Maetan-3-dong, Youngtong-gu, Suwon-si, Gyeonggi-do 443-792 (KR). **LEE, Gwan Sun** [KR/KR]; 3-404 Woochang Apt., Okeum-dong, Songpa-gu, Seoul 138-739 (KR).

(74) Agents: **JANG, Seongku** et al.; 19th Fl., Trust Tower, #275-7 Yangjae-dong, Seocho-ku, Seoul 137-130 (KR).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

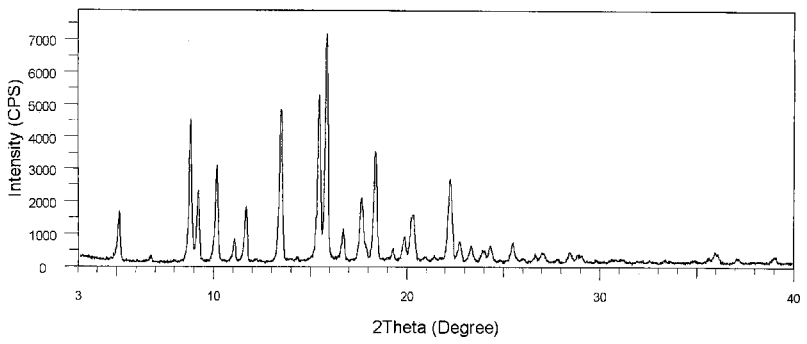
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: NOVEL CRYSTALLINE DEXLANSOPRAZOLE AND PHARMACEUTICAL COMPOSITION COMPRISING SAME

FIG. 2



(57) Abstract: A crystalline (+)-lansoprazole, whose X-ray diffraction spectrum comprises a major peak having a relative intensity of at least 20 % at an interplanar distance (d value) of 17.4 A, is homogeneous, non-hygroscopic, and stable, and a pharmaceutical composition comprising said crystal is effective for treating or preventing gastric acid-related diseases.

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NOVEL CRYSTALLINE DEXLANSOPRAZOLE AND PHARMACEUTICAL COMPOSITION COMPRISING SAME

FIELD OF THE INVENTION

The present invention relates to a novel crystalline (+)-lansoprazole and a pharmaceutical composition comprising same for treating or preventing gastric acid-related diseases.

BACKGROUND OF THE INVENTION

Lansoprazole, 2-[[3-methyl-4-(2,2,2,-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl-1*H*-benzimidazole disclosed in EP Patent No. 0 174 726 B1, is a proton pump inhibitor which suppresses gastric acid secretion to prevent ulcer. Lansoprozole molecule has a chiral center at the sulfur atom, and thus, two enantiomers thereof exist: dextrorotatory (+)-lansoprazole and levorotatory (-)-lansoprazole, as is disclosed in International Patent Publication No. WO 1992/08716. Further, WO 1996/02535 and WO 1997/02261 describe enantioselective synthesis methods thereof.

H. Katsuki *et al.* (H. Katsuki *et al.*, Pharm. Res. 13, 611-615 (1996)) have found that two enantiomers of lansoprazole are stereoselectively metabolized in human showing different pharmacokinetic profiles, and (+)-lansoprazole is more effective than the other due to its high bioavailability and less adverse effects it causes. Thus, there have been several approaches for preparing (+)-lansoprazole which is more useful in the preparation of pharmaceutical compositions for treating gastric acid-related diseases. However, unlike racemic lansoprazole, (+)-lansoprazole in the amorphous form is not sufficiently stable, and therefore, many studies have been conducted to develop a stable crystalline form of (+)-lansoprazole.

Several crystalline forms of anhydrous (+)-lansoprazole or hydrate have been reported. WO 2000/78745 discloses an anhydrous crystalline form (hereinafter referred to as "Crystalline Form I") having a melting point ranging about from 144 to 148 °C and a crystalline 1.5 hydrate (hereinafter referred to as "Crystalline Form II") having a melting point ranging about from 76 to 80 °C. Meanwhile, WO 2001/87874 discloses a crystalline hydrate having an unsteady number of crystal water molecules, and WO 2002/44167 discloses Crystalline Form I variants whose melt initiation temperatures are different, less than 131 °C or more than 131 °C.

A crystalline form of (+)-lansoprazole can be characterized by various methods, e.g., melting point measurement, X-ray diffraction (XRD) analysis, differential scanning calorimetry (DSC), solid state nuclear magnetic resonance (solid NMR) spectroscopy, infrared absorption (IR) spectroscopy, Raman spectroscopy, hydrate analysis, etc. In particular, a specific crystalline form can be identified by its XRD pattern in which 2 theta values (2θ) represent the interplanar angles, and d values, the interplanar distances.

The above-mentioned crystalline forms of (+)-lansoprazole have also been characterized by d values, but there exists problems that the reported variants of Crystalline Form I having same d values often show different melting points or melt initiation temperatures; and Crystalline Form II is often formed to exist in a crystalline hydrate whose number of crystal water molecules is not 1.5. The above facts suggest that the crystalline forms I and II are difficult to prepare in there pure homogeneous forms.

According to the guidelines and regulations which are promulgated by drug administrations in various countries, the homogeneity of a drug crystal is required for granting a permission to market the drug. In particular, it is strictly required that each drug component coincides with the specified homogeneity for every batch of the drug formulation. Accordingly, there has been a need for developing a crystalline (+)-lansoprazole which is homogeneous and stable.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a novel crystalline (+)-lansoprazole which is homogeneous and stable.

It is another object of the present invention to provide a pharmaceutical composition for treating or preventing gastric acid-related diseases, comprising the novel crystalline (+)-lansoprazole.

In accordance with one aspect of the present invention, there is provided a crystalline (+)-lansoprazole, whose X-ray diffraction spectrum comprises a peak having a 100 x I/I_o value of at least 20% (wherein I is the intensity of each peak, and I_o is the intensity of the highest peak) at an interplanar distance (d±0.3Å) of 17.4 Å.

In accordance with another aspect of the present invention, there is provided a pharmaceutical composition comprising the inventive crystalline (+)-lansoprazole as an active ingredient together with a pharmaceutically acceptable carrier, diluent, or excipient.

The inventive crystalline (+)-lansoprazole having a high melting temperature is homogeneous, non-hygroscopic, and stable, and it can be used in formulating a pharmaceutical composition for treating or preventing gastric acid-related diseases.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and other objects and features of the present invention will become apparent from the following description of the invention, when taken in conjunction with the accompanying drawings, which respectively show:

FIG. 1: an XRD scan of the crystalline (+)-lansoprazole obtained in Example 1;

FIGS. 2 to 5: XRD, DSC, DVS (dynamic vapor sorption), and IR spectra,

respectively, of the crystalline (+)-lansoprazole obtained in Example 3;

FIGS. 6 to 9: XRD, DSC, DVS, and IR spectra, respectively, of the crystalline (+)-lansoprazole obtained in Reference Example 1;

FIGS. 10 to 13: XRD, DSC, DVS, and IR spectra, respectively, of the crystalline (+)-lansoprazole obtained in Reference Example 2;

DETAILED DESCRIPTION OF THE INVENTION

The novel crystalline (+)-lansoprazole according to the present invention (hereinafter referred to as "Crystalline Form A") shows a characteristic peak having a relative intensity of at least 20% in its XRD spectrum obtained using Cu-K_α radiation at a interplanar distance (d value) of 17.4 Å. It also exhibits major peaks at d values of 17.4, 10.0, 9.6, 8.7, 7.6, 6.6, 5.7, 5.6, 5.0, 4.8, 4.4, and 4.0 Å. Herein, the relative intensity (%) is calculated using the equation of 100 x I/I_0 (wherein I is the intensity of each peak; I_0 is the intensity of the highest peak.)

Even when two crystals share a substantially equal form, their XRD spectra may show significantly different relative intensities (I/I_0,%) depending on the measuring conditions such as the quality of a crystal sample, particle size, the degree of sample grinding, grinding time, and other conditions. Moreover, a person skilled in the art would easily expect that d values may vary at a tolerance of ±0.3, or more likely ±0.1. Accordingly, it is obvious that Crystalline Form A according to the present invention exhibits d values that are unique characteristics thereof. The same with confirming a crystalline form based on 2 theta (2θ) which represents interplanar angle.

Crystalline Form A according to the present preferably has a characteristic melting point measured by visible observation in the range of 151 to 156 °C, preferably 152 to 155 °C, which is higher than those of the reported crystalline forms. Further, Crystalline Form A preferably shows a characteristic DSC melting endothermic transition peak which starts at about 151.7 °C and reaches its

maximum at about 155.3 °C. Generally, measurements of the melting point and the endothermic transition temperature provide values that are within a tolerance of ±2 °C, or ordinarily ±1 °C. Based on the above, Crystalline Form A of the present invention is a novel crystalline (+)-lansoprazole disclosed herein for the first time.

Crystalline Form A according to the present invention contains water in an amount of about 1 % or less, preferably 0.5 % or less. More preferably, Crystalline Form A may be an anhydrous crystal which contains no detectable water. In a DVS analysis under a relative humidity of 0 to 90 %, the water content of Crystalline Form A varied only within 1 %, which means that Crystalline Form A is an anhydrous crystal which is substantially non-hygroscopic.

Crystalline Form A of (+)-lansoprazole may be prepared by crystallization of an amorphous (+)-lansoprazole in a mixed solution of dichloromethane and diisopropyl ether. Preferably, a seed of Crystalline Form A of (+)-lansoprazole may be added to said mixed solution. A seed of Crystalline Form A of (+)-lansoprazole may be prepared using crystalline 1.5 H_2O hydrate of (+)-lansoprazole obtained according to the procedure disclosed in Example 3 of WO 2000/78745. For example, the crystalline 1.5 H_2O hydrate is dried for 3 to 24 h at 40 to 60 °C under a reduced pressure and then exposed to a condition of 80 to 110 °C for at least 1 min, followed by cooling to room temperature to obtain a seed of Crystalline Form A of (+)-lansoprazole.

Racemic or enantiomeric lansoprazole is known as an ATPase (a strong proton pump) inhibitor which suppresses gastric acid secretion in human. Particularly, Crystalline Form A of (+)-lansoprazole is very effective for suppressing gastric acid secretion. Accordingly, Crystalline Form A of (+)-lansoprazole is useful in treating or preventing gastric acid-related diseases. For example, Crystalline Form A of (+)-lansoprazole is useful in treating or preventing mammal diseases, preferably human diseases such as gastritis, duodenitis, reflux esophagitis, peptic ulcer, duodenal ulcer, NSAIDs(non-steroidal anti-inflammatory

drugs)-induced ulcer, stress ulcer, non-ulcer dyspepsia, gastrointestinal bleeding, hyperacidity, helicobacter pylori infection disease, and inflammatory disease.

Therefore, the present invention also provides a pharmaceutical composition comprising an effective amount of Crystalline Form A of (+)-lansoprazole as an active ingredient together with a pharmaceutically acceptable carrier, diluent, or excipient. The pharmaceutical composition according to the present invention may be administered to a patient in an effective amount via the various routes, e.g., the oral route or the non-oral route. Preferably, the inventive composition is prepared in the oral administration form such as a capsule, a tablet, a dispersion, and a suspension. The capsule or tablet may be of an enteric coated form or may contain a pellet of an enteric coated Crystalline Form A of (+)-lansoprazole.

Crystalline Form A of (+)-lansoprazole may be formulated with a pharmaceutically acceptable carrier, diluent or excipient, regardless of the administration form. Examples of suitable carriers, diluents and excipients are as follows: excipients such as starches, sugar, lactose, dextrin, mannitol, sorbitol, crystalline cellulose, low-substitited hydroxypropyl cellulose, sodium carboxymethyl cellulose, Arabic gum, amylopectin, light anhydrous silicic acid, and synthetic aluminum silicate; fillers or extending agents such as calcium phosphate and silica derivatives; binding agents such as starches, sugar, mannitol, trehalose, dextrin, amylopectin, sucrose, gluten, Arabic gum, methyl cellulose, carboxymethyl cellulose, sodium carboxymethyl cellulose, crystalline cellulose, cellulose derivatives including hydroxypropyl cellulose or hydroxypropyl methyl cellulose, gelatin, arginic acid salt, and polyvinyl pyrrolidone; lubricating agents such as talc, magnesium or calcium stearate, hydrogenated castor oil, talcum powder, and solid polyethylene glycol; disintegrants such as povidone, sodium croscarmellose, and crospovidone; and surfactants such as polysorbate, cetyl alcohol and glycerol monostearate.

Further, various pharmaceutical compositions comprising an effective amount of Crystalline Form A of (+)-lansoprazole together with or without

additives such as said carrier, diluent, and excipient, may be prepared in accordance with any of the conventional procedures (*see* Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA, 19th Edition, 1995.)

The inventive pharmaceutical composition may comprise Crystalline Form A of (+)-lansoprazole as an active ingredient in an amount of 0.1 to 95 wt%, preferably 1 to 70 wt%, based on the weight of the composition.

A typical daily dose of Crystalline Form A of (+)-lansoprazole for a mammal including human may range from about 5 to 250 mg/kg body weight, preferably 10 to 100 mg/kg body weight, and can be administered in a single dose or in divided doses per one day.

The following Examples are intended to further illustrate the present invention without limiting its scope.

The analysis data described in the following Examples and Reference Examples were measured under the following conditions.

1) The melting point was measured by a capillary type digital melting point apparatus (Barnstead Electrothermal, England.)
2) The specific rotation $[\alpha]_D$ was measured at 25 °C by polarimeter (DIP-1000, Jasco Corporation, Japan.)
3) The optical purity was determined from the Equation 1 using the data obtained by chiral HPLC (high performance liquid chromatography) under the conditions listed below:

<Condition>

- column: Chromtech™ AGP, diameter 4.6 mm x length 250 mm, particle size: 5 μm, detection wavelength: 285 mm;
- eluent: pH 7.0, phosphate buffer/acetonitrile=90/10; and
- flow rate: 0.8 mL/min.

Equation 1

Optical purity of enatiomer (% ee) = [A(+) - A(-)] / [A(+) + A(-)] x 100

wherein, A(+) is the peak area of (+)-lansoprazole, A(-) is the peak area of (-)-lansoprazole, and the unit "% ee" means enantiomeric excess.

4) The moisture content was measured by moisture tester (795 KFT, Metrohm AG, Switzerland.)

5) The IR spectrum was obtained by IR spectrometer (MB-100, Bomen Inc., Canada.)

6) The XRD spectrum was obtained by XRD spectrometer (D8 Advance, Bruker Corporation, Germany) using Cu-K_α radiation (wavelength λ=1.54056Å) according to the conventional method (*see* US Pharmacopoeia, USP31 NF26.)

7) The DSC curve was obtained by differential scanning calorimeter (STA S-1000, Scinco Co., Ltd., Korea) at a rate of +1 °C/min.

8) The DVS curve was obtained by DVS analyzer (Advantage I, SMS Ltd., England) under a relative humidity of 0 to 90 % in 2 cycles.

Example 1. Preparation of Crystalline Form A of (+)-lansoprazole

Crystalline 1.5 H_2O hydrate of (+)-lansoprazole was prepared according to the procedure disclosed in Example 3 of WO 2000/78745. 2.0 g of the crystalline 1.5 hydrate of (+)-lansoprazole was added to an uncapped glass vial, dried at 50 °C for 5 h under a reduced pressure of 2 torr or less and then exposed to a condition of 100 °C for 5 min, followed by cooling to room temperature to obtain 1.85 g of a crystal.

The XRD spectrum of the crystal thus obtained is shown in FIG. 1.

The analysis data of the crystal thus obtained are listed below:

m.p.: 151-153 °C;

specific rotation: $[\alpha]_D^{25}$ = +156.0° (c=1.0, chloroform);

optical purity: 99.9 % ee;

moisture content (Karl-Fisher titrator): 0.88 %; and

XRD (Cu-K_α radiation): the interplanar angles (2θ) and the interplanar distances (d value) of peaks having relative intensity (I/I_o x 100) values of at least 20% are summarized in Table 1.

Table 1

2θ (°)	d (Å)	I/I_o (%)	2θ (°)	d (Å)	I/I_o (%)
5.1	17.4	24.3	15.0	5.7	66.4
8.8	10.1	53.9	15.8	5.6	100.0
9.2	9.6	24.5	17.6	5.0	28.0
10.1	8.7	42.3	18.4	4.8	40.5
11.6	7.6	20.4	20.3	4.4	26.5
13.5	6.6	50.2	22.2	4.0	32.8

Example 2. Preparation of Crystalline Form A of (+)-lansoprazole

1.5 g of the Crystalline Form A of (+)-lansoprazole obtained in Example 1 was added to 15 mL of diisopropyl ether to obtain a suspension, which was stirred for 30 min. The precipitate formed was filtered, washed twice each with 2 mL of diisopropyl ether, and dried under a reduced pressure to obtain 1.44 g of a crystal (yield: 96%.)

The analysis data of the crystal are thus obtained listed below:

m.p.: 154.3-155.0 °C;

specific rotation: $[\alpha]_D^{25} = +156.3°$ (c=1.0, chloroform);

optical purity: 99.9 % ee;

purity: 99.9%;

moisture content (Karl-Fisher titrator): 0.3 %; and

XRD analysis results were the same as in Example 1.

Example 3. Preparation of Crystalline Form A of (+)-lansoprazole

30.0 g of amorphous (+)-lansoprazole was dissolved in 300 mL of methylene chloride, and 600 mL of diisopropyl ether was added thereto. The resulting mixture was seeded with 100 mg of the Crystalline Form A of (+)-lansoprazole obtained in Example 2, stirred for 10 min at room temperature, and then further stirred for 20 min at 0 to 5 °C. The precipitate formed was filtered, washed twice each with 100 mL of diisopropyl ether, and dried under a reduced pressure, to obtain 21.6 g of a crystal (yield: 72%.)

XRD, DSC, DVS, and IR spectra of the crystal thus obtained are shown in FIGS. 2, 3, 4, and 5, respectively.

The analysis data of the crystal thus obtained are listed below:

m.p.: 154.3 °C;

specific rotation: $[\alpha]_D^{25} = +158.3°$ (c=1.0, chloroform);

optical purity: 99.9 % ee;

moisture content (Karl-Fisher titrator): 0.5 %;

IR (KBr, cm^{-1}): 3287, 3070, 2967, 2891, 1577, 1474, 1442, 1409, 1311, 1261, 1178, 1109, 1035, 1005, 967, 834, 817, 802, 745;

DSC (1°/min): a melting endothermic peak which starts at 151.71 °C and reaches its maximum at 155.30 °C;

DVS (2 cycles): a moisture content of 1 % or less under a relative humidity of 0 to 90 %; and

XRD (Cu-K_α radiation): the diffraction angle (2θ) and distance between crystal faces (d) values of peaks having relative intensity (I/I_o x 100) values of at least 20% are summarized in Table 2.

Table 2

2θ (°)	d (Å)	I/I_0 (%)	2θ (°)	d (Å)	I/I_0 (%)
5.1	17.4	23.1	15.5	5.7	73.7
8.7	10.0	63.3	15.8	5.6	100.0
9.2	9.6	32.1	17.7	5.0	28.9
10.1	8.7	42.9	18.4	4.8	49.1
11.6	7.6	25.1	20.3	4.4	21.4
13.5	6.6	67.4	22.2	4.0	37.1

Reference Example 1 : Preparation of Crystalline Form I of (+)-lansoprazole (anhydrous crystal)

Anhydrous crystal of (+)-lansoprazole was prepared by the same manner as in Example 2 of WO 2000/78745.

XRD, DSC, DVS, and IR spectra of the crystal thus obtained are shown in FIGS. 6, 7, 8, and 9, respectively.

The analysis data of the crystal thus obtained are listed below:

m.p.: 147-148 °C;

specific rotation: $[\alpha]_D^{25}$ = +150.0° (c=1.0, chloroform);

optical purity: 99.9 % ee;

moisture content (Karl-Fisher titrator) : 0.4 %;

IR (KBr, cm^{-1}): 3082, 3036, 2984, 2890, 1585, 1479, 1441, 1356, 1306, 1266, 1225, 1161, 1111, 1084, 1044, 977, 957, 825, 800, 742;

DSC (1°/min): a melting endothermic peak which starts at 144.91 °C and reaches its maximum point at 147.79 °C;

DVS (2 cycles): a moisture content of more than 1% under a relative humidity of 0 to 90 %; and

XRD (Cu-K_α radiation): the diffraction angle (2θ) and distance between crystal faces (d) values of peaks having relative intensity (I/I_0 x 100) values of at least 20% are summarized in Table 3.

Table 3

2θ (°)	d (Å)	I/I_o (%)	2θ (°)	d (Å)	I/I_o (%)
7.5	11.8	97.0	21.5	4.1	46.6
13.0	6.8	100.0	22.5	3.9	26.0
13.5	6.5	22.1	22.8	3.9	18.9
15.1	5.8	33.5	24.1	3.7	44.9
15.4	5.7	97.8	26.1	3.4	33.5
20.0	4.4	29.6	28.7	3.1	24.3

Reference Example 2 : Preparation of Crystalline Form II of (+)-lansoprazole (crystalline 1.5 H_2O hydrate)

Crystalline 1.5 H_2O hydrate of (+)-lansoprazole was prepared according to the procedure disclosed in Example 3 of WO 2000/78745.

XRD, DSC, DVS, and IR spectra of the crystal thus obtained are shown in FIGS. 10, 11, 12, and 13, respectively.

The analysis data of the crystal thus obtained are listed below:

m.p.: 80-90 °C;

specific rotation: $[\alpha]_D^{25}$ = +154.7 (c=1.0, chloroform);

optical purity: 99.9 % ee;

moisture content (Karl-Fisher titrator): 6.8 %;

IR (KBr, cm^{-1}): 3631, 3363, 3072, 2976, 1645, 1583, 1475, 1443, 1315, 1262, 1249, 1200, 1110, 1079, 1033, 973, 917, 828, 743;

DSC (1°/min): a dehydration endothermic peak which starts at 69.51 °C and reaches its maximum at 84.57 °C, and a melting endothermic peak which starts at 146.50 °C and reaches its maximum at 151.73 °C;

DVS (2 cycles): a moisture content of more than 7 % under a relative humidity of 0 to 90 %; and

XRD (Cu-K_α radiation): the diffraction angle (2θ) and distance between crystal faces (d) values of peaks having relative intensity (I/I_o x 100) values of at least 20% are summarized in Table 4.

Table 4

2θ (°)	d (Å)	I/I_o (%)	2θ (°)	d (Å)	I/I_o (%)
6.7	13.2	21.3	14.9	5.9	19.2
9.2	9.6	30.4	15.7	5.6	66.3
10.0	8.9	100.0	17.7	5.0	93.4
11.0	8.0	46.0	25.8	3.4	19.1
13.4	6.6	35.9	30.0	3.0	10.8

As shown in the results above, the inventive crystalline (+)-lansoprazole prepared in Examples 1 to 3 are non-hygroscopic and stable, and their melting point are higher and almost same, in comparison with the conventional crystalline (+)-lansoprazole prepared in Reference Examples 1 and 2.

While the invention has been described with respect to the above specific embodiments, it should be recognized that various modifications and changes may be made to the invention by those skilled in the art which also fall within the scope of the invention as defined by the appended claims.

WHAT IS CLAIMED IS:

1. A crystalline (+)-lansoprazole, whose X-ray diffraction spectrum using Cu-K_α radiation comprises a peak having a 100 x I/I_0 value of at least 20% (wherein I is the intensity of each peak, and I_0 is the intensity of the highest peak) at an interplanar distance (d±0.3Å) of 17.4 Å.

2. The crystalline (+)-lansoprazole of claim 1, whose X-ray diffraction spectrum shows peaks having 100 x I/I_0 values of at least 20% (wherein I is the intensity of each peak, and I_0 is the intensity of the highest peak) at interplanar distances (d±0.3Å) of 17.4, 10.0, 9.6, 8.7, 7.6, 6.6, 5.7, 5.6, 5.0, 4.8, 4.4, and 4.0 Å.

3. The crystalline (+)-lansoprazole of claim 1, whose melting point is in the range of 151 to 156 °C.

4. The crystalline (+)-lansoprazole of claim 1, whose differential scanning calorimetry (DSC) scan shows an endothermic peak which starts at 151±2 °C and reaches its maximum at 155±2 °C.

5. The crystalline (+)-lansoprazole of claim 1, which contains water in an amount of 1 wt% or less based on the weight of the crystalline (+)-lansoprazole.

6. A pharmaceutical composition comprising the crystalline (+)-lansoprazole according to any one of claims 1 to 5 as an active ingredient together with a pharmaceutically acceptable carrier, diluent, or excipient.

7. The composition of claim 6, which is of the form of a capsule or a tablet for oral administration.

8. The composition of claim 7, which is of an enteric coated form.

9. The composition of claim 6, which comprises the crystalline (+)-lansoprazole in the form of an enteric coated pellet.

10. The composition of claim 6, which comprises the crystalline (+)-lansoprazole in an amount of 0.1 to 95 wt% based on the weight of the composition.

11. The composition of claim 6, which comprises the crystalline (+)-lansoprazole in an amount of 1 to 70 wt% based on the weight of the composition.

12. The composition of claim 6, which is for treating or preventing one or more diseases selected from the group consisting of gastritis, duodenitis, reflux esophagitis, peptic ulcer, duodenal ulcer, NSAIDs(non-steroidal anti-inflammatory drugs)-induced ulcer, stress ulcer, non-ulcer dyspepsia, gastrointestinal bleeding, hyperacidity, helicobacter pylori infection disease, and inflammatory disease.

13. The composition of claim 6, wherein the daily dose for a mammal including human of the crystalline (+)-lansoprazole is in the range of 5 to 250 mg/kg body weight.

14. The composition of claim 6, wherein the daily dose for a mammal including human of the crystalline (+)-lansoprazole is in the range from 10 to 100 mg/kg body weight.

FIG. 1

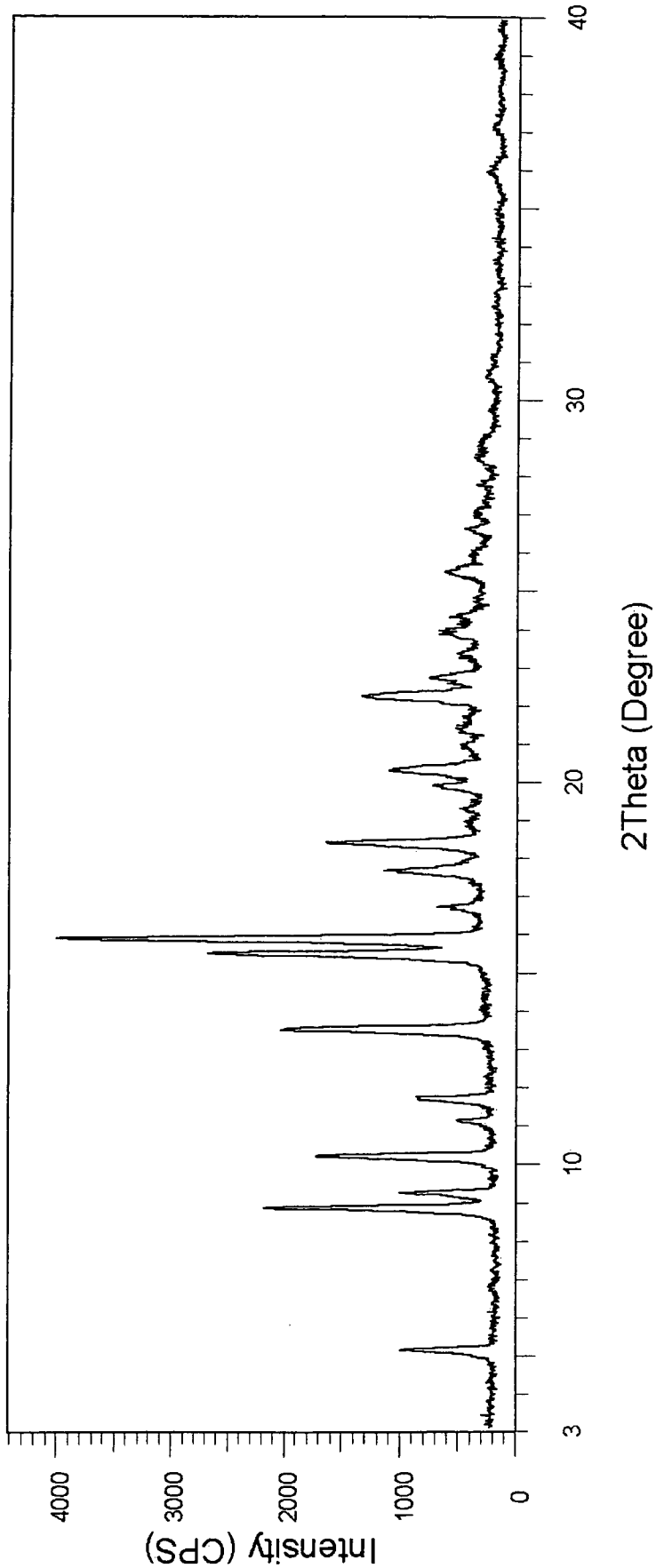

Intensity (CPS)
0
1000
2000
3000
4000
3
10
20
30
40
2Theta (Degree)

FIG. 2

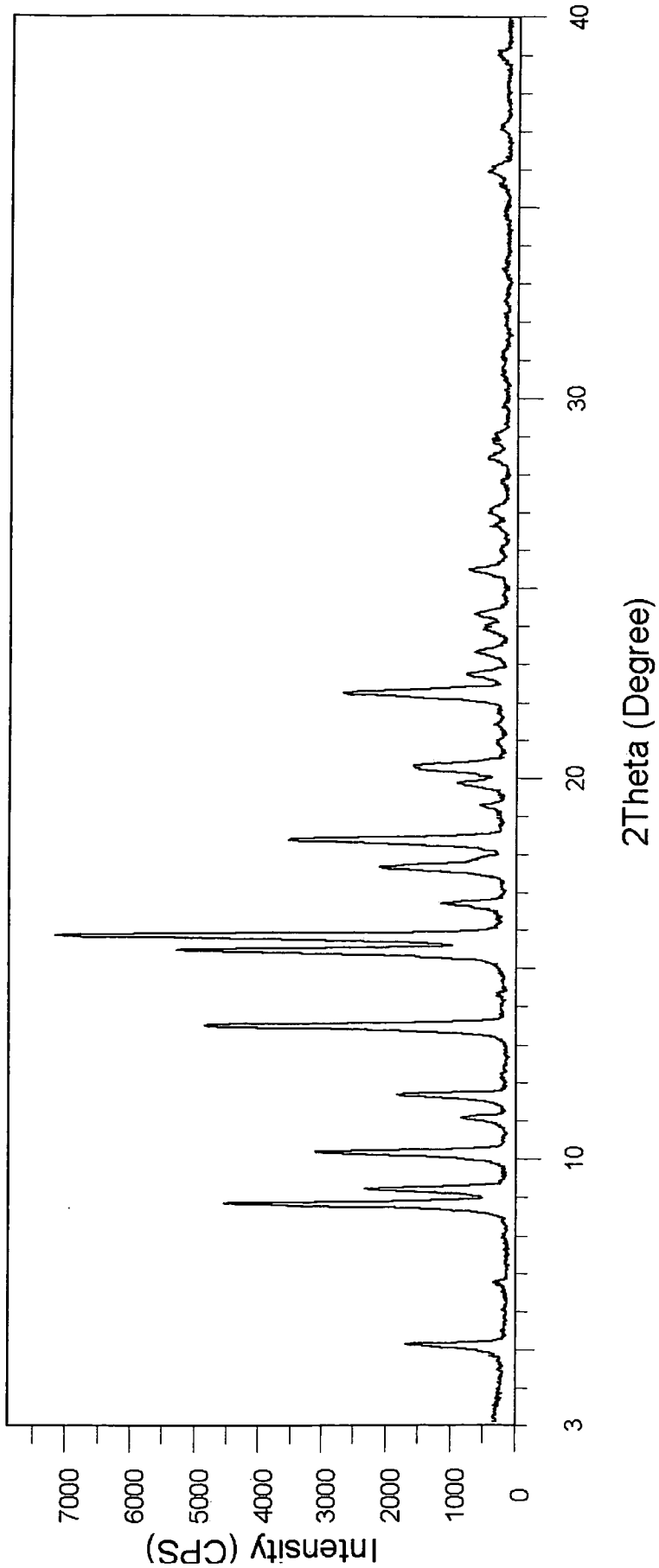

Intensity (CPS)
7000
6000
5000
4000
3000
2000
1000
0
3
10
20
30
40
2Theta (Degree)

FIG. 3

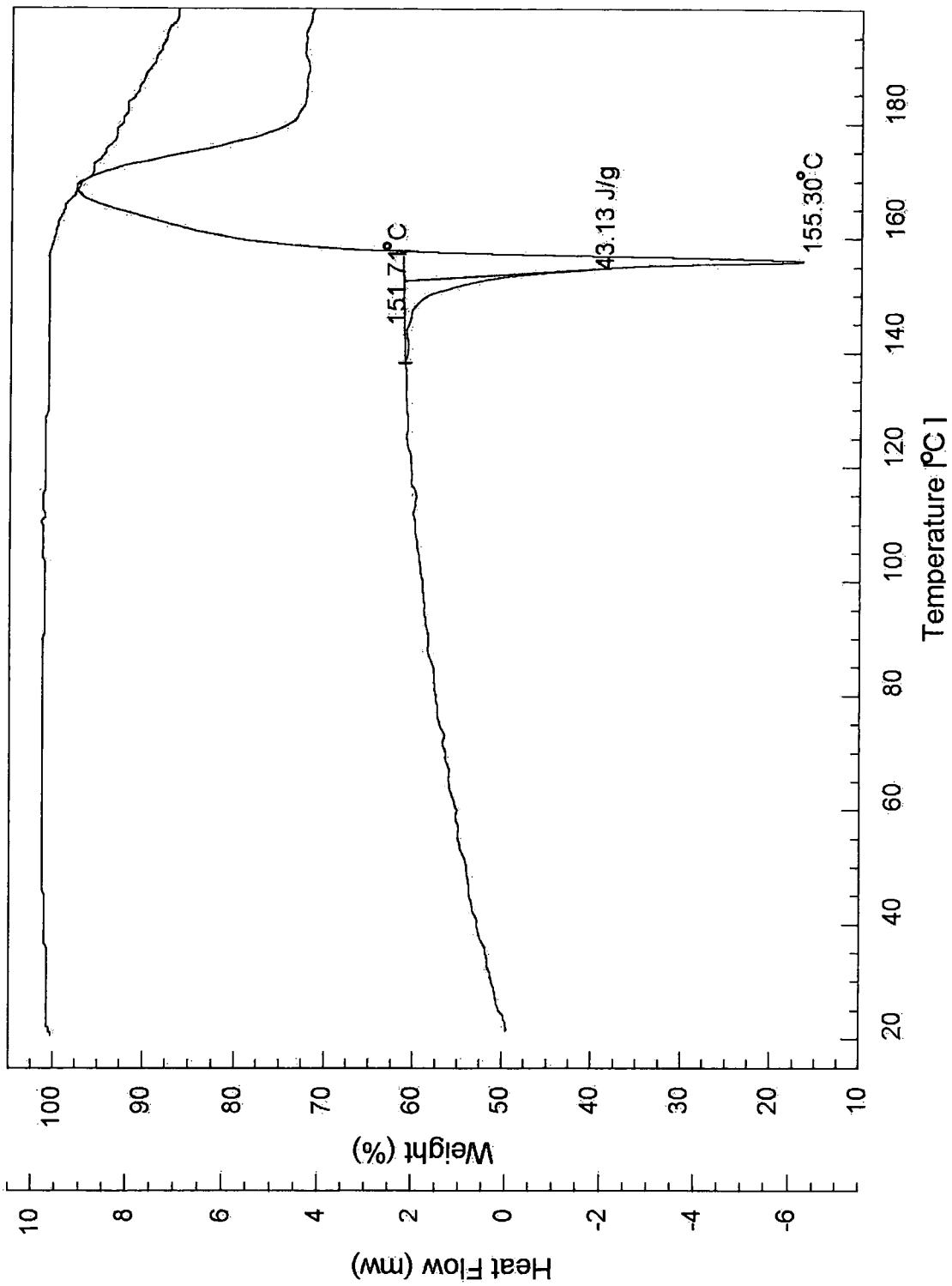


FIG. 4

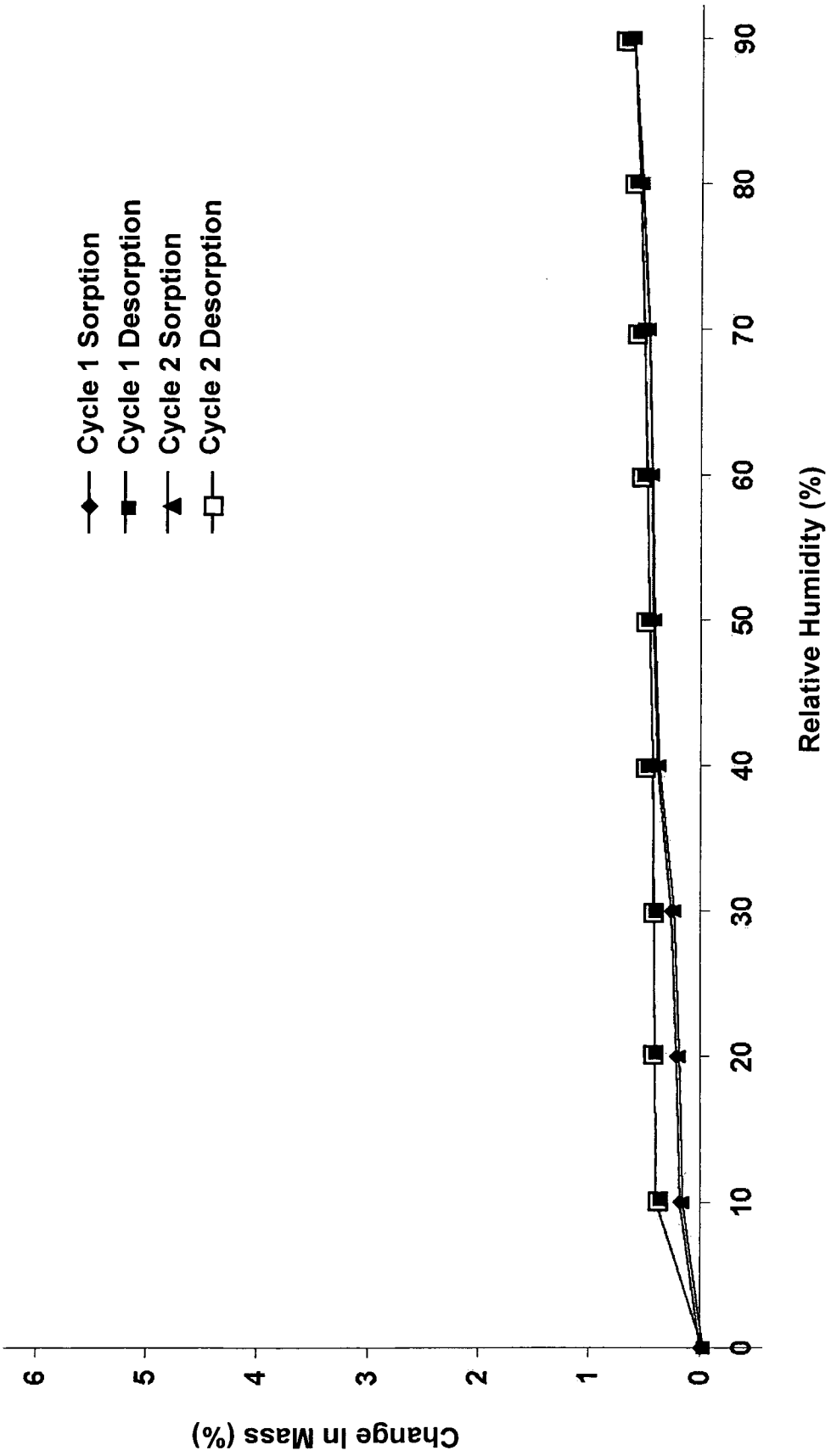

Cycle 1 Sorption
Cycle 1 Desorption
Cycle 2 Sorption
Cycle 2 Desorption
Change In Mass (%)
0
1
2
3
4
5
6
Relative Humidity (%)
0
10
20
30
40
50
60
70
80
90

FIG. 5

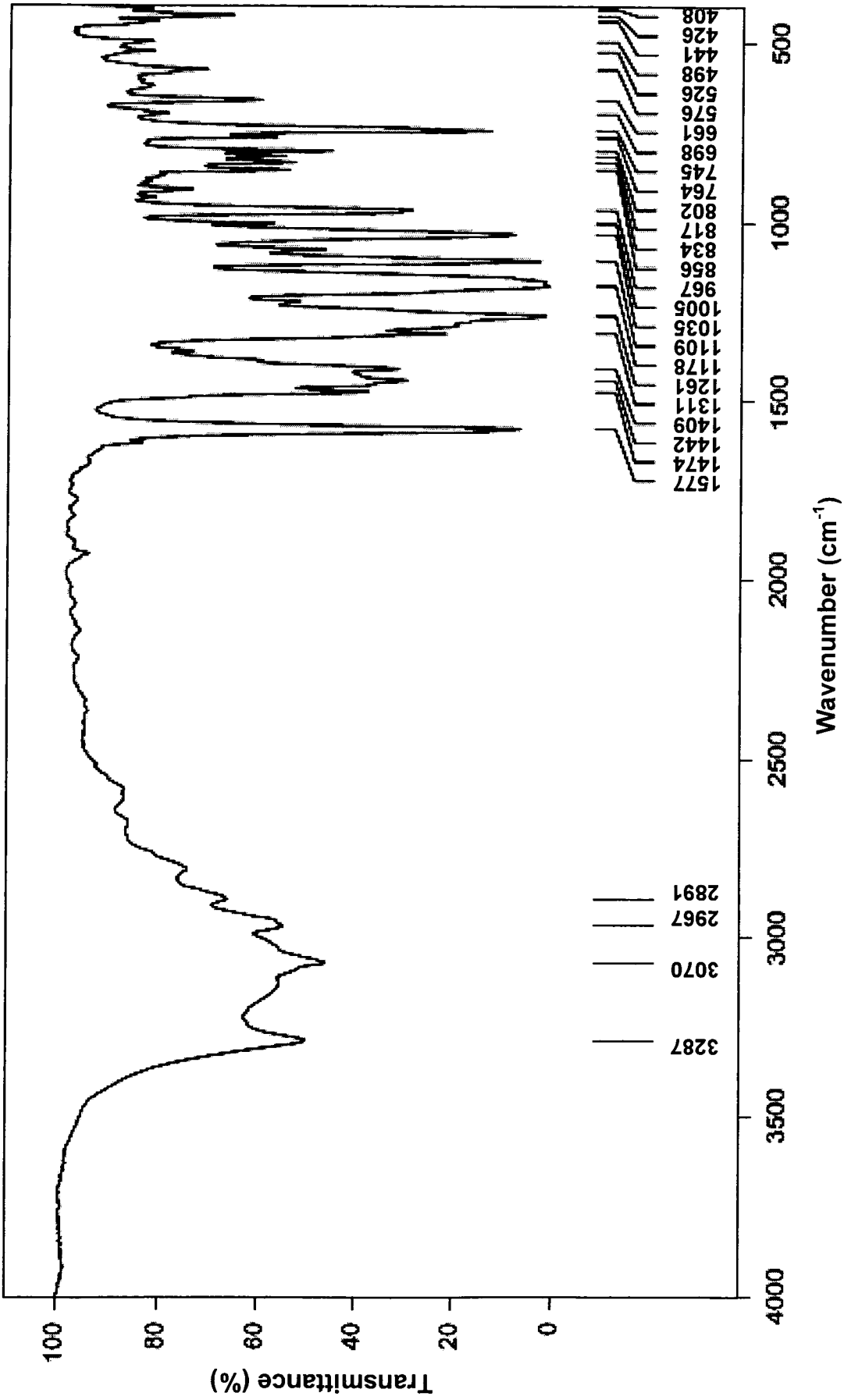

Transmittance (%)
100
80
60
40
20
0
4000
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm-1)
3287
3070
2967
2891
1577
1474
1442
1409
1311
1261
1178
1109
1035
1005
967
856
834
817
802
764
745
698
661
576
526
498
441
426
408

FIG. 6

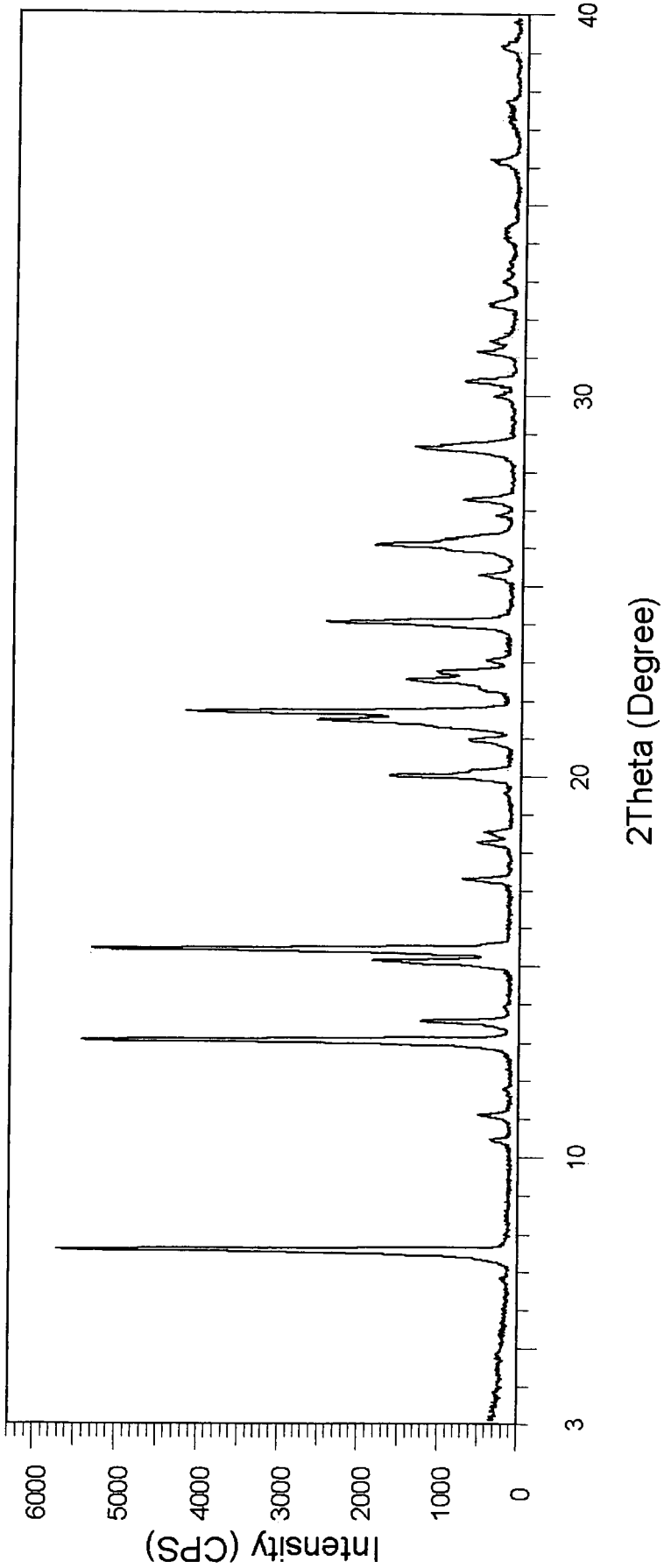

Intensity (CPS)
6000
5000
4000
3000
2000
1000
0
3
10
20
30
40
2Theta (Degree)

FIG. 7

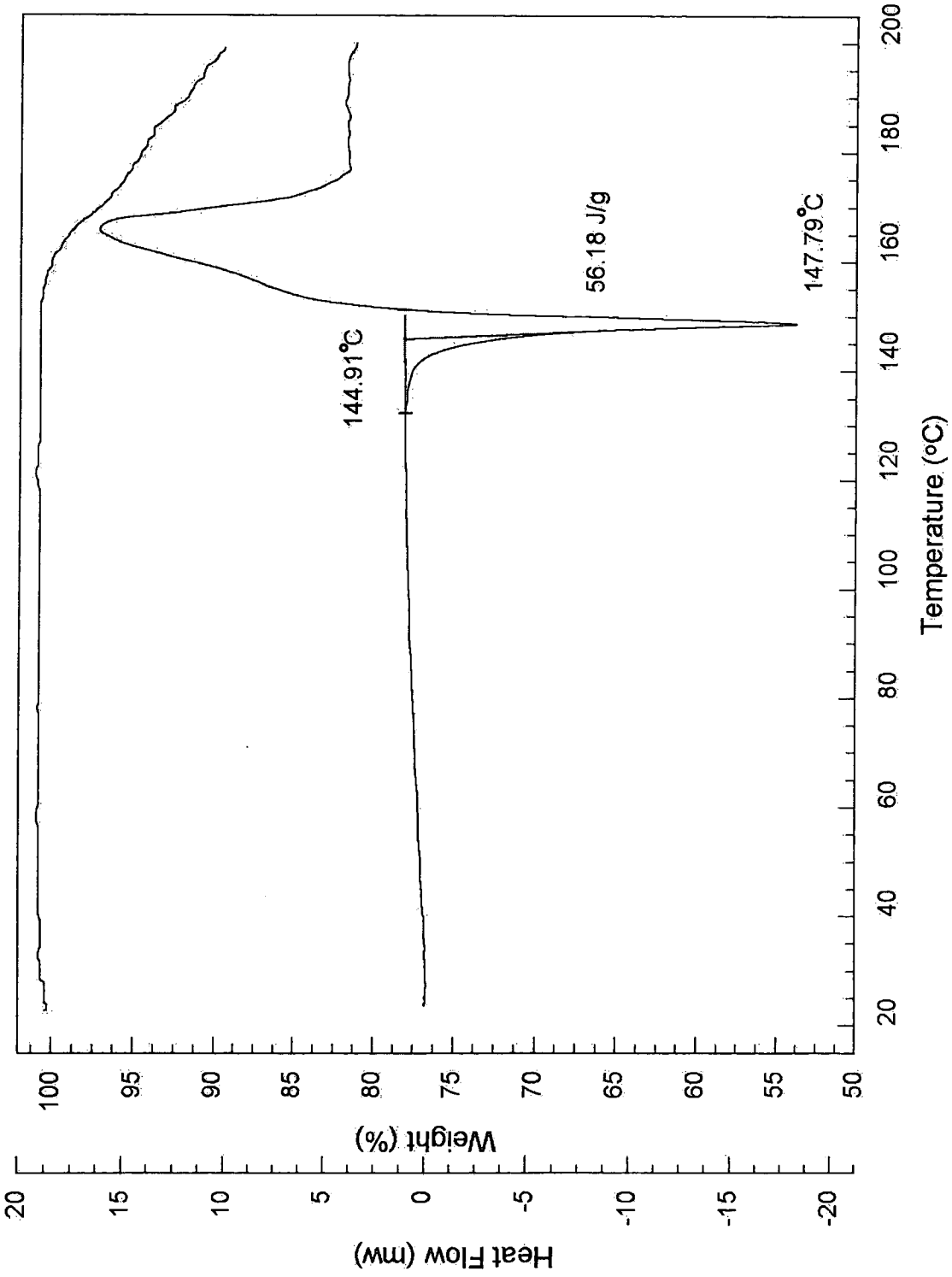


FIG. 8

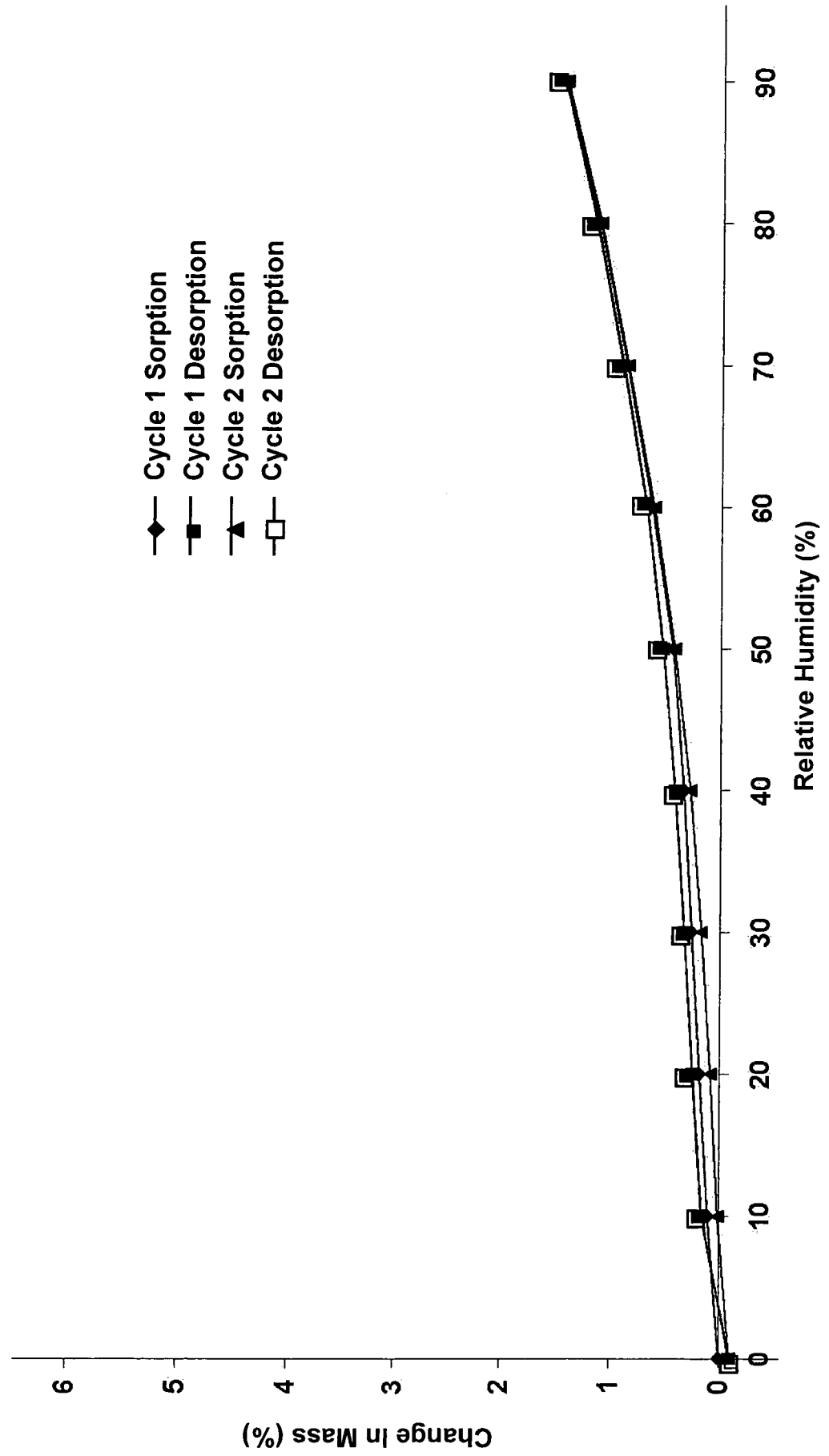

Cycle 1 Sorption
Cycle 1 Desorption
Cycle 2 Sorption
Cycle 2 Desorption
Change In Mass (%)
0
1
2
3
4
5
6
0
10
20
30
40
50
60
70
80
90
Relative Humidity (%)

FIG. 9

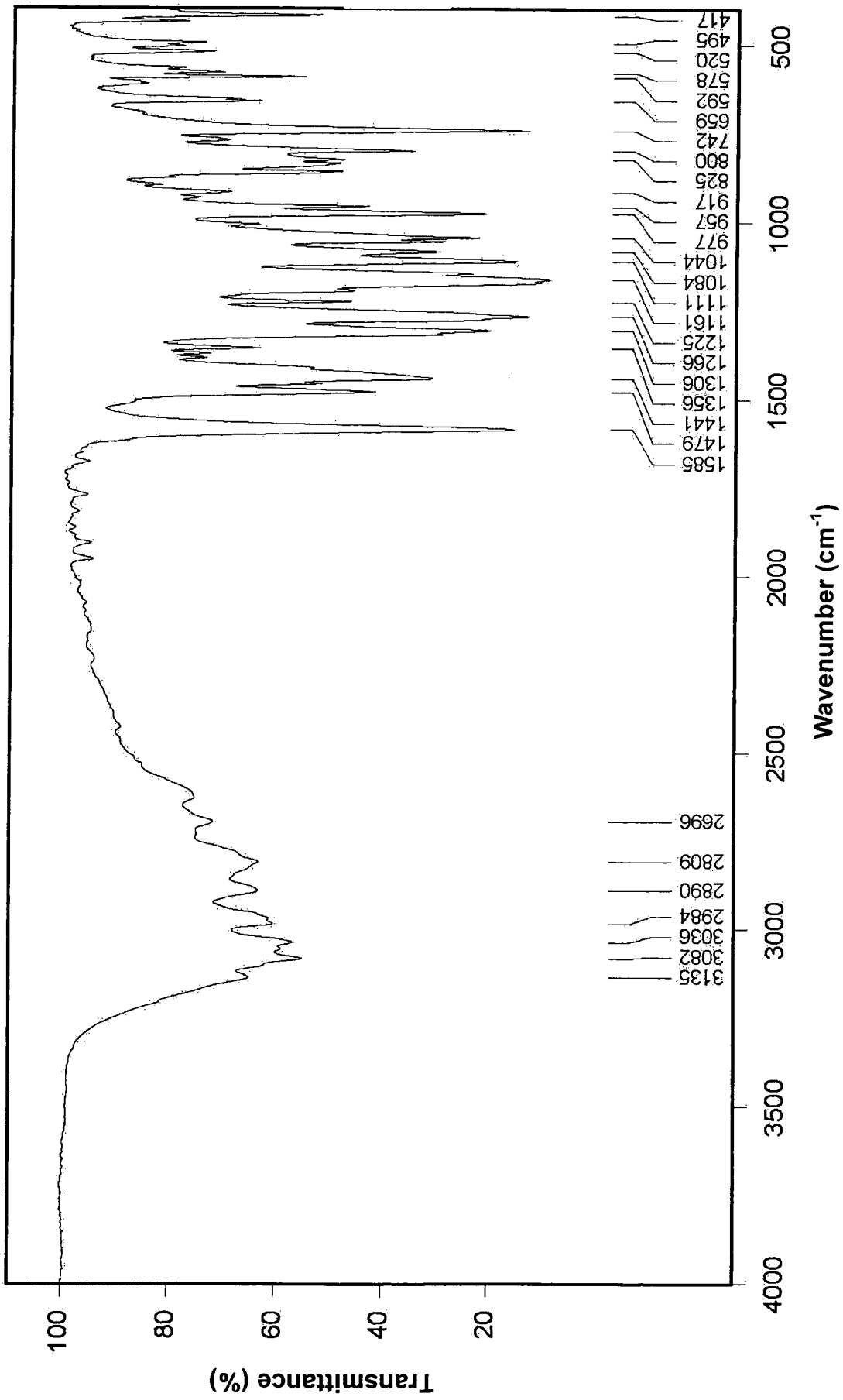

Transmittance (%)
100
80
60
40
20
Wavenumber (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
3135
3082
3036
2984
2890
2809
2696
1585
1479
1441
1356
1306
1266
1225
1161
1111
1084
1044
977
957
917
825
800
742
659
592
578
520
495
417

FIG. 10

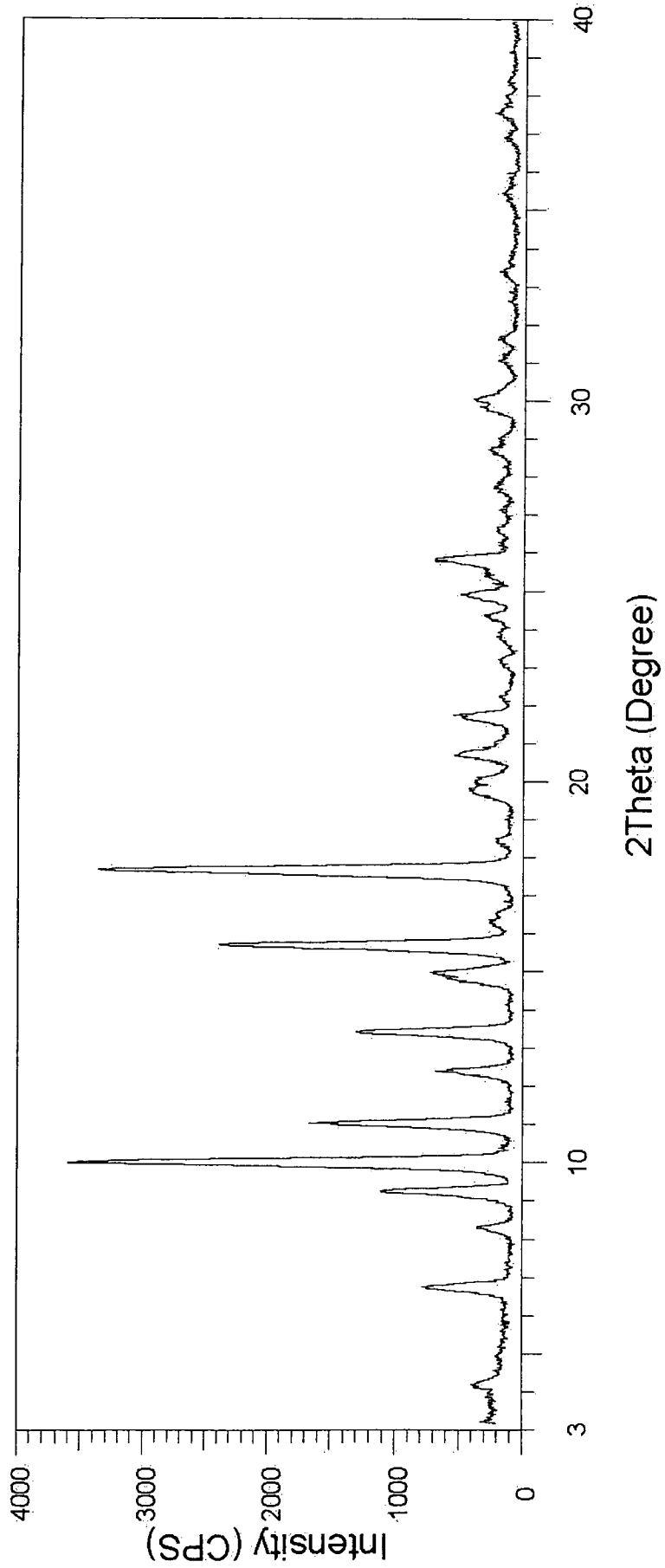

Intensity (CPS)
0
1000
2000
3000
4000
3
10
20
30
40
2Theta (Degree)

FIG. 11

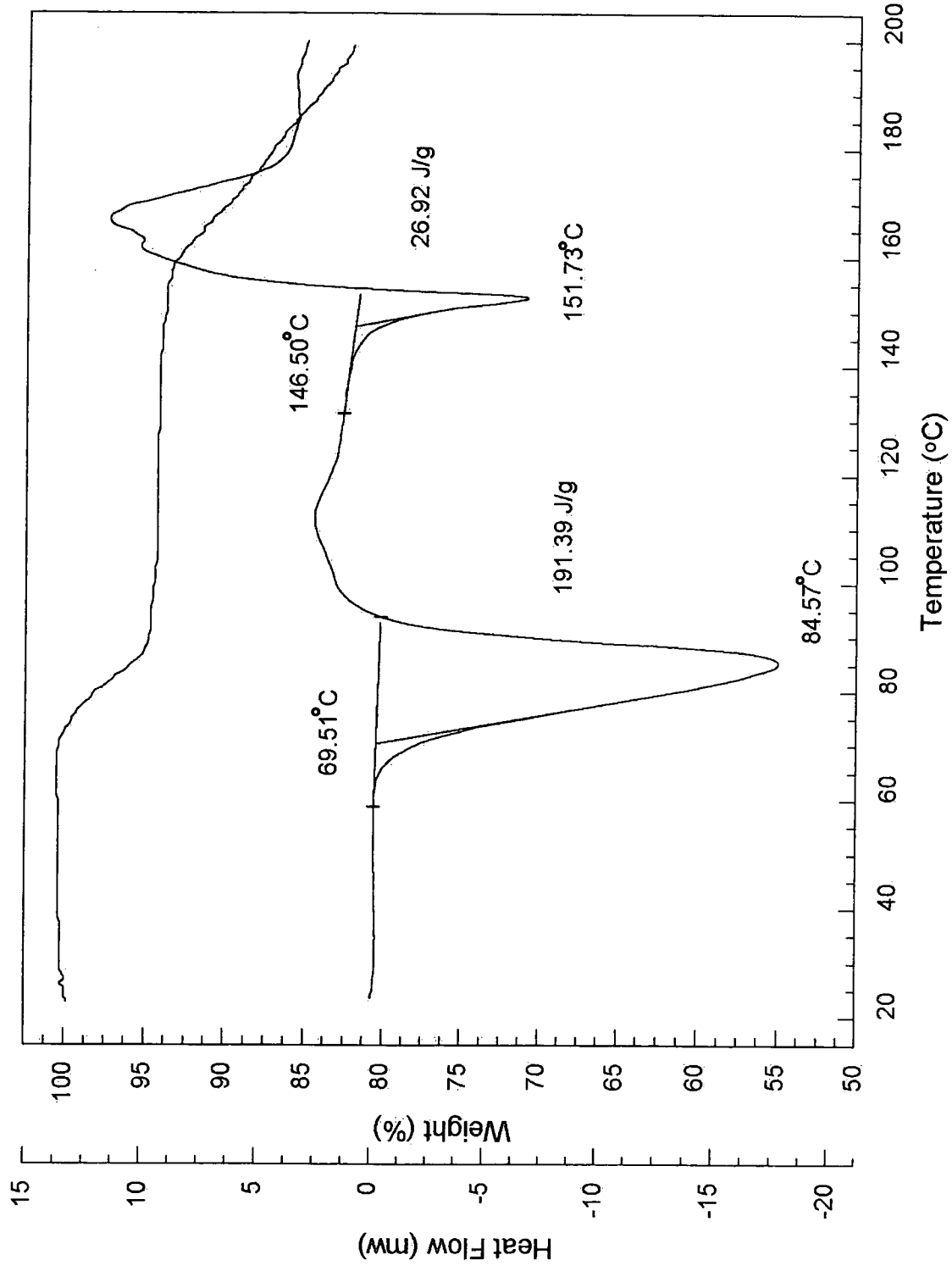

Heat Flow (mw)
Weight (%)
Temperature (°C)
26.92 J/g
151.73°C
146.50°C
191.39 J/g
84.57°C
69.51°C

FIG. 12

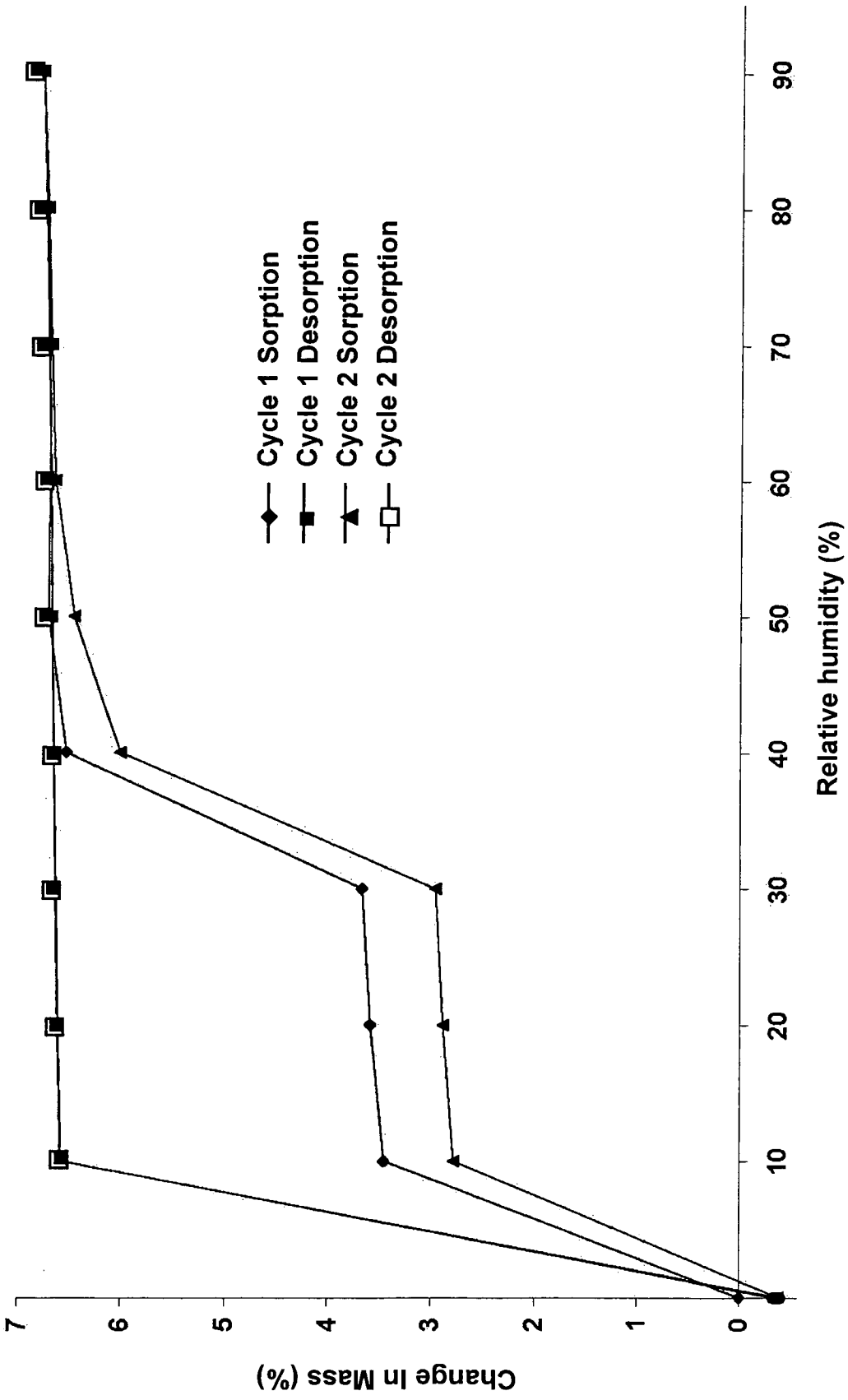
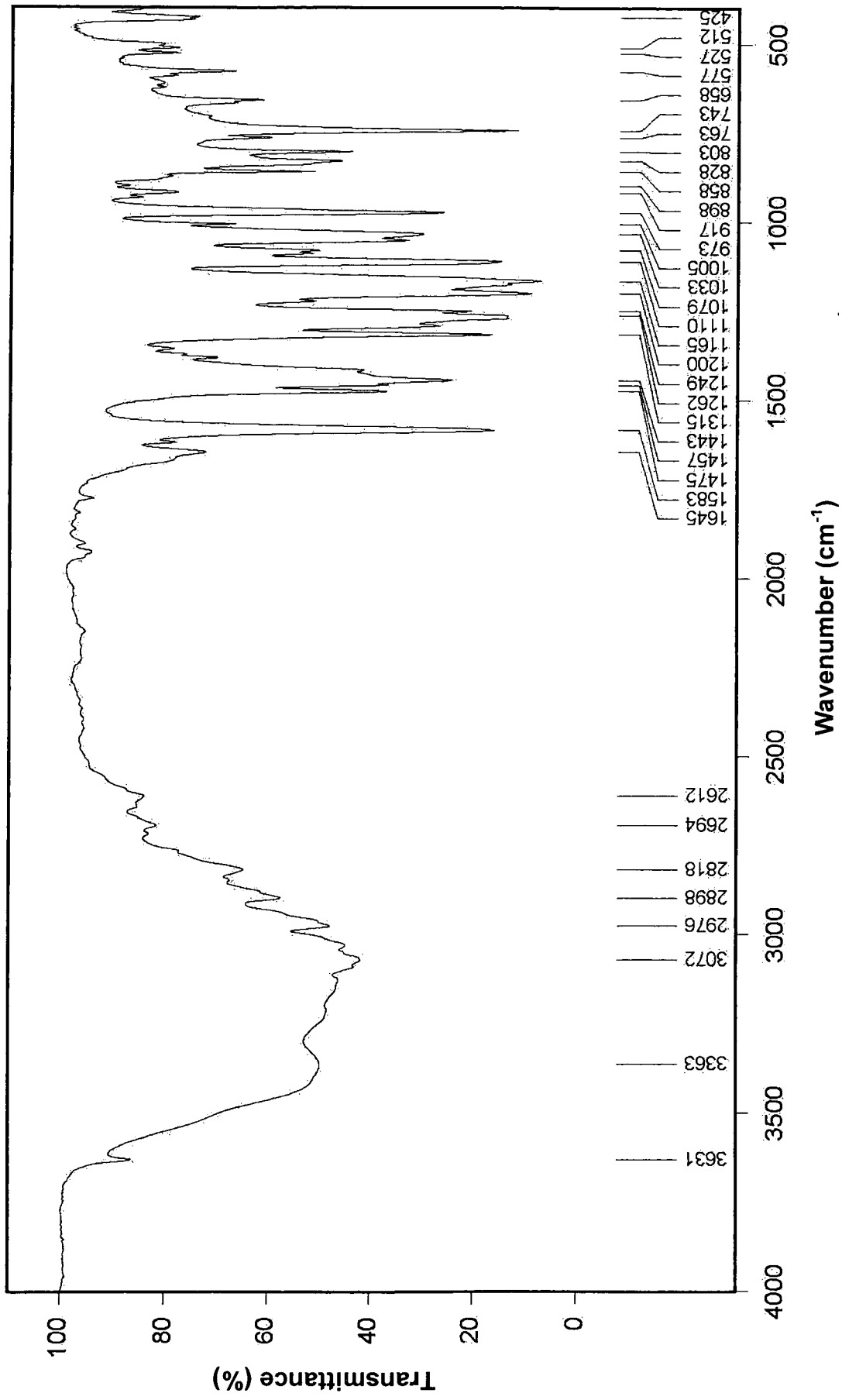

Change In Mass (%)
0
1
2
3
4
5
6
7
Relative humidity (%)
10
20
30
40
50
60
70
80
90
Cycle 1 Sorption
Cycle 1 Desorption
Cycle 2 Sorption
Cycle 2 Desorption

FIG. 13


Transmittance (%)
100
80
60
40
20
0
4000
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm-1)
3631
3363
3072
2976
2898
2818
2694
2612
1645
1583
1475
1457
1443
1315
1262
1249
1200
1165
1110
1079
1033
1005
973
917
898
858
828
803
763
743
658
577
527
512
425