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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 March 2009 (19.03.2009)

PCT

(10) International Publication Number
WO 2009/035535 A2

(51) International Patent Classification:
C07C 213/00 (2006.01)

(21) International Application Number:
PCT/US2008/010414

(22) International Filing Date:
5 September 2008 (05.09.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/967,934 7 September 2007 (07.09.2007) US

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(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, 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, 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, MT, NL, NO, PL, PT, RO, SE, SI, SK, 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*

WO 2009/035535 A2

(54) Title: METHOD OF CRYSTALLIZING CARVEDILOL PHOSPHATE AND THE PRODUCT THEREOF

(57) Abstract: The present invention provides for a crystalline polymorph of Carvedilol phosphate salt and a process for making the same.

METHOD OF CRYSTALLIZING CARVEDILOL PHOSPHATE AND THE PRODUCT THEREOF

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present application claims priority to Provisional Patent Application 60/967,934, filed September 7, 2007. The contents of this provisional patent application is hereby incorporated by reference.

SUMMARY OF THE INVENTION

[0002] The present invention provides a method of crystallizing Carvedilol-phosphate salt, and a novel crystalline polymorph of Carvedilol-phosphate salt.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings:

[0003] Figure 1 shows the X-ray powder diffraction pattern of the crystalline polymorph of Carvedilol-phosphate salt of the present invention in intensity versus degrees in two theta.

[0004] Figure 2 is the diffuse reflectance spectrum of the crystalline polymorph of Carvedilol-phosphate salt of the present invention.

[0005] Figure 3 provides the peak positions within the diffuse reflectance spectrum of Figure 2, as well as an expansion of a certain region of that spectrum.

[0006] Figure 4 shows the X-ray powder diffraction pattern of the crystalline polymorph of Carvedilol-phosphate salt of the present invention in intensity versus d-spacing.

[0007] Figure 5 lists the peak positions and their intensities of the X-ray powder diffraction pattern of

the crystalline polymorph of Carvedilol-phosphate salt of the present invention.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

[0008] The present invention provides a method of crystallizing Carvedilol-phosphate salt by the following procedure:

Carvedilol phosphate salt formation

[0009] To a solution of Carvedilol (5 g; 0.0123 mol.) in acetone(90 mL) is added 85% H_3PO_4 (0.85 g; 0.0074 mol.) slowly. The resulting mixture is agitated at 20 - 30°C. The mixture is filtered and then washed with 20 mL acetone. The solids are dried under vacuum at<50°C to give 4.76 g Carvedilol-phosphate salt (hemihydrate).

[0010] Representative infrared spectrum and X-ray powder diffraction pattern for the Carvedilol-phosphate salt is provided herein.

CLAIMS

We claim:

1. A crystalline polymorph of Carvedilol-phosphate salt exhibiting an X-ray powder diffraction pattern comprising a peak in degrees 2θ ±.0.2° 2θ at 25.1.

2. A crystalline polymorph of Carvedilol-phosphate salt according to claim 1 further comprising peaks in degrees 2θ ±.0.2° 2θ at 24.1 and 23.6.

3. The crystalline polymorph of Carvedilol-phosphate salt according to claim 1 further comprising peaks in degrees 2θ ±.0.2° 2θ at 12.0 and 20.9.

4. The crystalline polymorph of Carvedilol-phosphate salt according to claim 1 exhibiting an X-ray powder diffraction pattern substantially as shown in Figure 1.

5. The crystalline polymorph of Carvedilol-phosphate salt according to claim 1 exhibiting an IR diffuse reflectance spectrum substantially as shown in Figure 2.

6. A method of preparing a crystalline polymorph of Carvedilol-phosphate salt comprising the steps of: (a) dissolving Carvedilol in acetone to form a solution; and (b) adding a solution comprising H_3PO_4 to produce the crystalline polymorph of Carvedilol-phosphate salt.

XRD pattern of Carvedilol Phosphate:

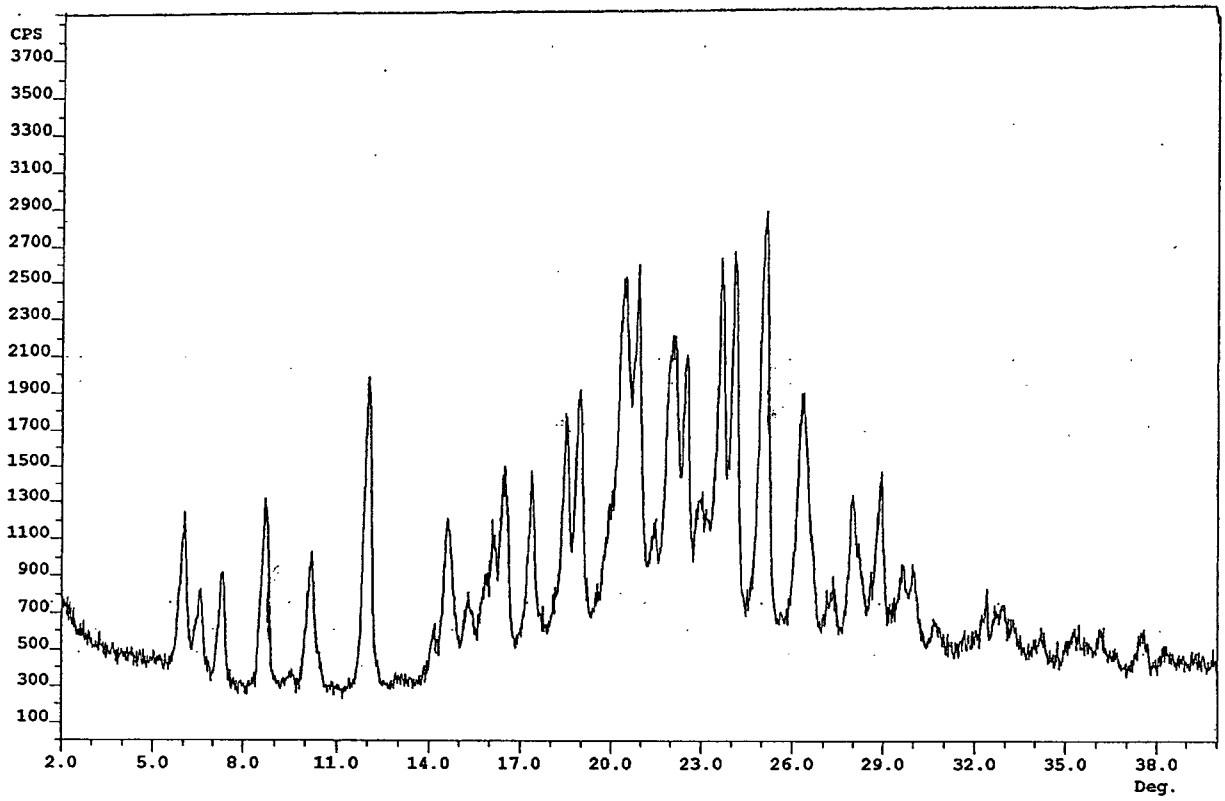


FIGURE 1

IR pattern of Carvedilol Phosphate:

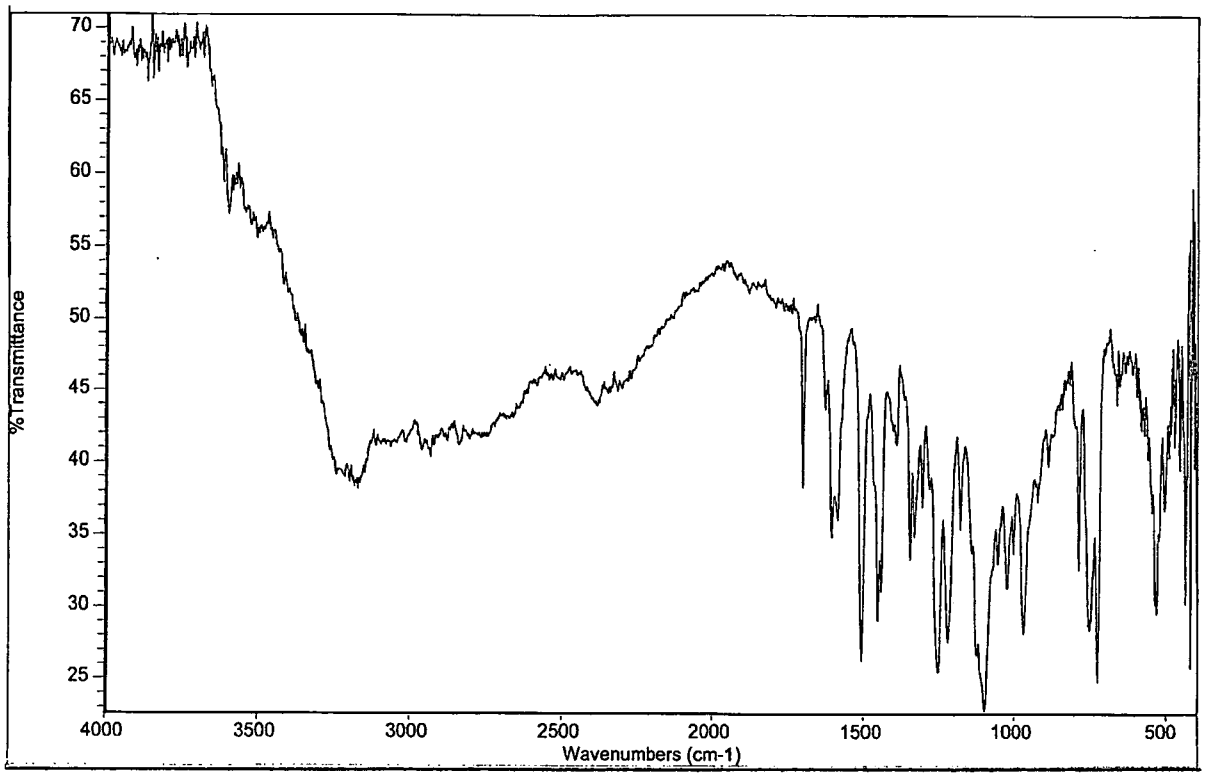
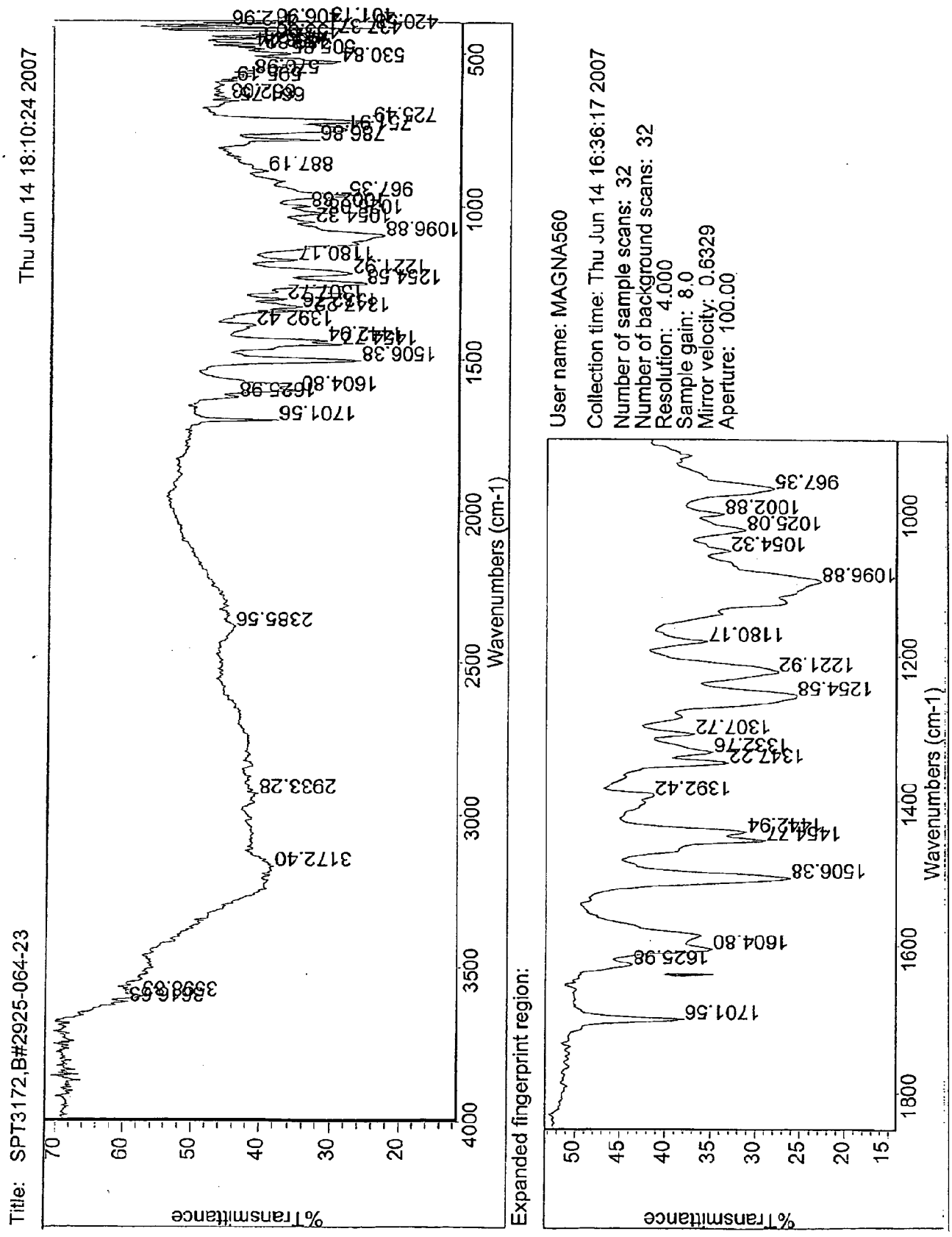


FIGURE 2

FIGURE 3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Thu Jun 14 18:10:24 2007
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1625.98
1604.80
1506.38
1442.94
1392.42
1254.58
1180.17
1096.88
887.19
530.84
Expanded fingerprint region:
User name: MAGNA560
Collection time: Thu Jun 14 16:36:17 2007
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Number of background scans: 32
Resolution: 4.000
Sample gain: 8.0
Mirror velocity: 0.6329
Aperture: 100.00
%Transmittance
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1625.98
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1506.38
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1347.22
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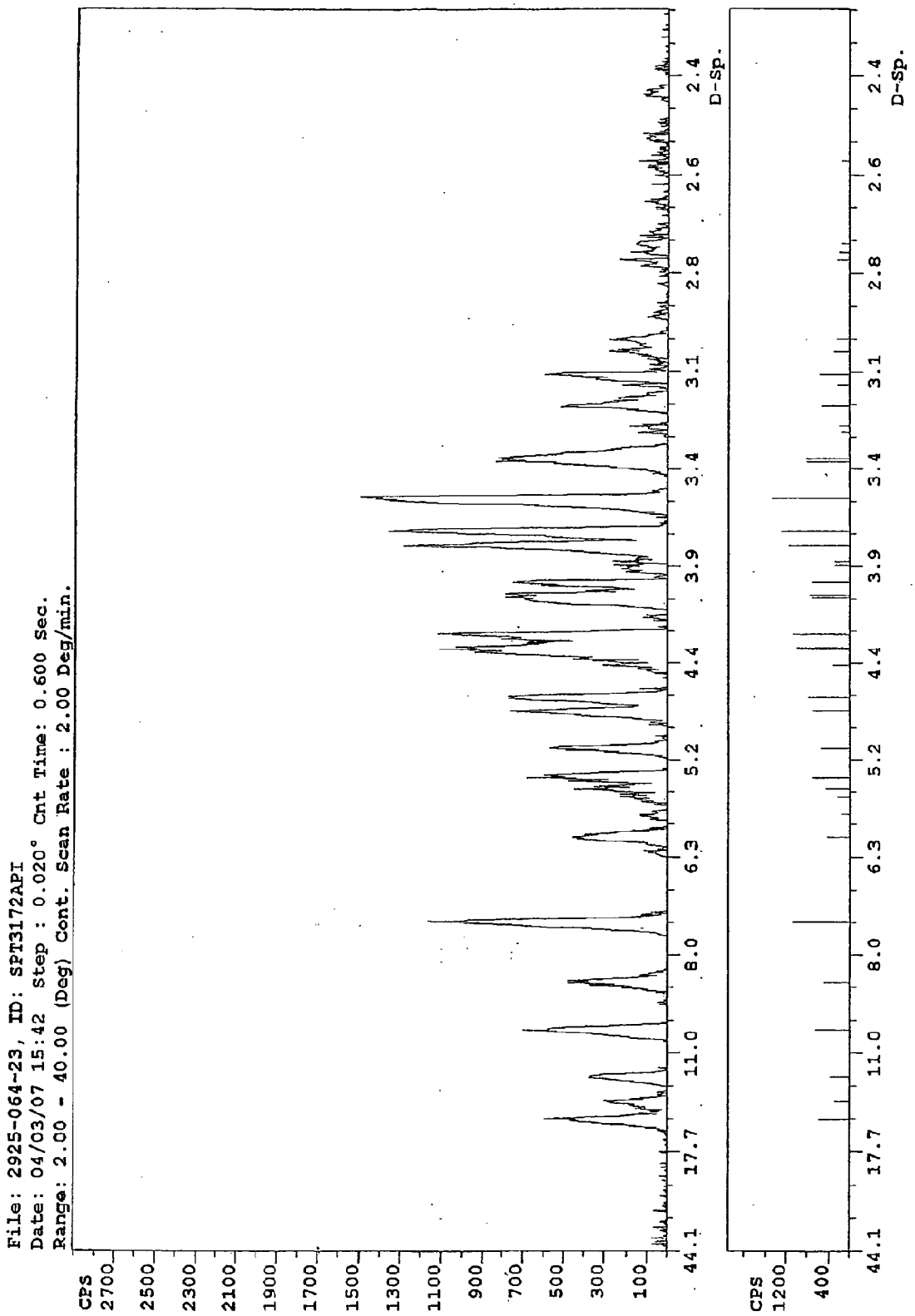
1025.08
1002.88
967.35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Date: 04/03/07 15:42 Step : 0.020° Cnt Time: 0.600 Sec.
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CPS
2700
2500
2300
2100
1900
1700
1500
1300
1100
900
700
500
300
100
44.1
17.7
11.0
8.0
6.3
5.2
4.4
3.9
3.4
3.1
2.8
2.6
2.4
D-Sp.
CPS
1200
400
44.1
17.7
11.0
8.0
6.3
5.2
4.4
3.9
3.4
3.1
2.8
2.6
2.4
D-Sp.

FIGURE 4

File: Untitled4

ID: SPT3172API B#2925-064-23

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Stop Angle: 40 deg.
Num Points: 1901
Step Size: 0.02 deg.
Datafile Res: 1600
Scan Rate: 2.000000
Scan Mode: Continuous
Wavelength: 1.540562

Peaks:

Position (Deg.)	Position (DSp.)	ESD (Deg.)	Corr.Fact	Intensity (cps)	Rel. Int. (%)	FWHM (L)	ESD (Deg.)	Area	Source	Curve	Strain	CSize	CSize Source
6.0000	14.7180	0.0000	0.0000	591.67	40.10	0.1600	0.0000	82.8	PFind	None	0.00	0.00	None
6.5406	13.5026	0.0000	0.0000	271.75	18.42	0.1400	0.0000	32.6	PFind	None	0.00	0.00	None
7.2894	12.1173	0.0000	0.0000	365.73	24.79	0.1600	0.0000	58.5	PFind	None	0.00	0.00	None
8.7037	10.1511	0.0000	0.0000	630.52	42.74	0.0600	0.0000	100.9	PFind	None	0.00	0.00	None
10.1400	8.7163	0.0000	0.0000	478.33	32.42	0.1600	0.0000	76.5	PFind	None	0.00	0.00	None
12.0087	7.3638	0.0000	0.0000	1089.12	73.82	0.1600	0.0000	174.3	PFind	None	0.00	0.00	None
14.6200	6.0539	0.0000	0.0000	426.13	28.88	0.0400	0.0000	68.2	PFind	None	0.00	0.00	None
15.3000	5.7863	0.0000	0.0000	131.67	8.92	0.0200	0.0000	2.6	PFind	None	0.00	0.00	None
15.8400	5.5902	0.0000	0.0000	230.00	15.59	0.0400	0.0000	9.2	PFind	None	0.00	0.00	None
16.1006	5.5003	0.0000	0.0000	451.67	30.61	0.1000	0.0000	54.2	PFind	None	0.00	0.00	None
16.4400	5.3875	0.0000	0.0000	683.33	46.32	0.1600	0.0000	82.0	PFind	None	0.00	0.00	None
17.3612	5.1037	0.0000	0.0000	538.57	36.50	0.1600	0.0000	86.2	PFind	None	0.00	0.00	None
18.4994	4.7922	0.0000	0.0000	676.07	45.96	0.1400	0.0000	108.5	PFind	None	0.00	0.00	None
18.9294	4.6843	0.0000	0.0000	779.95	52.86	0.0400	0.0000	109.2	PFind	None	0.00	0.00	None
19.9419	4.4487	0.0000	0.0000	292.42	19.82	0.1600	0.0000	17.5	PFind	None	0.00	0.00	None
20.4619	4.3368	0.0000	0.0000	1001.58	67.89	0.1600	0.0000	160.3	PFind	None	0.00	0.00	None
20.8762	4.2516	0.0000	0.0000	1064.30	72.14	0.1600	0.0000	127.7	PFind	None	0.00	0.00	None
22.0400	4.0297	0.0000	0.0000	710.92	48.19	0.1200	0.0000	113.7	PFind	None	0.00	0.00	None
22.1069	4.0176	0.0000	0.0000	753.18	51.05	0.1200	0.0000	90.4	PFind	None	0.00	0.00	None
22.5063	3.9472	0.0000	0.0000	696.07	47.18	0.1600	0.0000	111.4	PFind	None	0.00	0.00	None
23.0200	3.8603	0.0000	0.0000	261.67	17.74	0.0200	0.0000	26.2	PFind	None	0.00	0.00	None
23.1400	3.8406	0.0000	0.0000	263.33	17.85	0.1600	0.0000	10.5	PFind	None	0.00	0.00	None
23.6406	3.7603	0.0000	0.0000	1166.87	79.09	0.1600	0.0000	186.7	PFind	None	0.00	0.00	None
24.0812	3.6925	0.0000	0.0000	1297.98	87.97	0.1200	0.0000	207.7	PFind	None	0.00	0.00	None
25.0938	3.5458	0.0000	0.0000	1475.38	100.00	0.1400	0.0000	206.6	PFind	None	0.00	0.00	None
26.2200	3.3960	0.0000	0.0000	805.30	54.58	0.0200	0.0000	112.7	PFind	None	0.00	0.00	None
26.3175	3.3836	0.0000	0.0000	810.85	54.96	0.1600	0.0000	129.7	PFind	None	0.00	0.00	None
27.1200	3.2853	0.0000	0.0000	148.33	10.05	0.0200	0.0000	3.0	PFind	None	0.00	0.00	None
27.3200	3.2617	0.0000	0.0000	180.00	12.20	0.1400	0.0000	3.6	PFind	None	0.00	0.00	None
27.9469	3.1899	0.0000	0.0000	515.62	34.95	0.1200	0.0000	51.6	PFind	None	0.00	0.00	None
28.5800	3.1207	0.0000	0.0000	220.00	14.91	0.1200	0.0000	8.8	PFind	None	0.00	0.00	None
28.9019	3.0867	0.0000	0.0000	572.15	38.78	0.1200	0.0000	68.7	PFind	None	0.00	0.00	None
29.6000	3.0154	0.0000	0.0000	285.00	19.32	0.1400	0.0000	17.1	PFind	None	0.00	0.00	None
29.9750	2.9786	0.0000	0.0000	235.77	15.98	0.1000	0.0000	33.0	PFind	None	0.00	0.00	None
32.4000	2.7610	0.0000	0.0000	238.33	16.15	0.0200	0.0000	4.8	PFind	None	0.00	0.00	None
32.6400	2.7412	0.0000	0.0000	181.67	12.31	0.0600	0.0000	0.0	PFind	None	0.00	0.00	None
32.9069	2.7196	0.0000	0.0000	147.83	10.02	0.0000	0.0000	20.7	PFind	None	0.00	0.00	None
35.4200	2.5322	0.0000	0.0000	143.33	9.71	0.1400	0.0000	2.9	PFind	None	0.00	0.00	None

FIGURE 5