FIG. 1

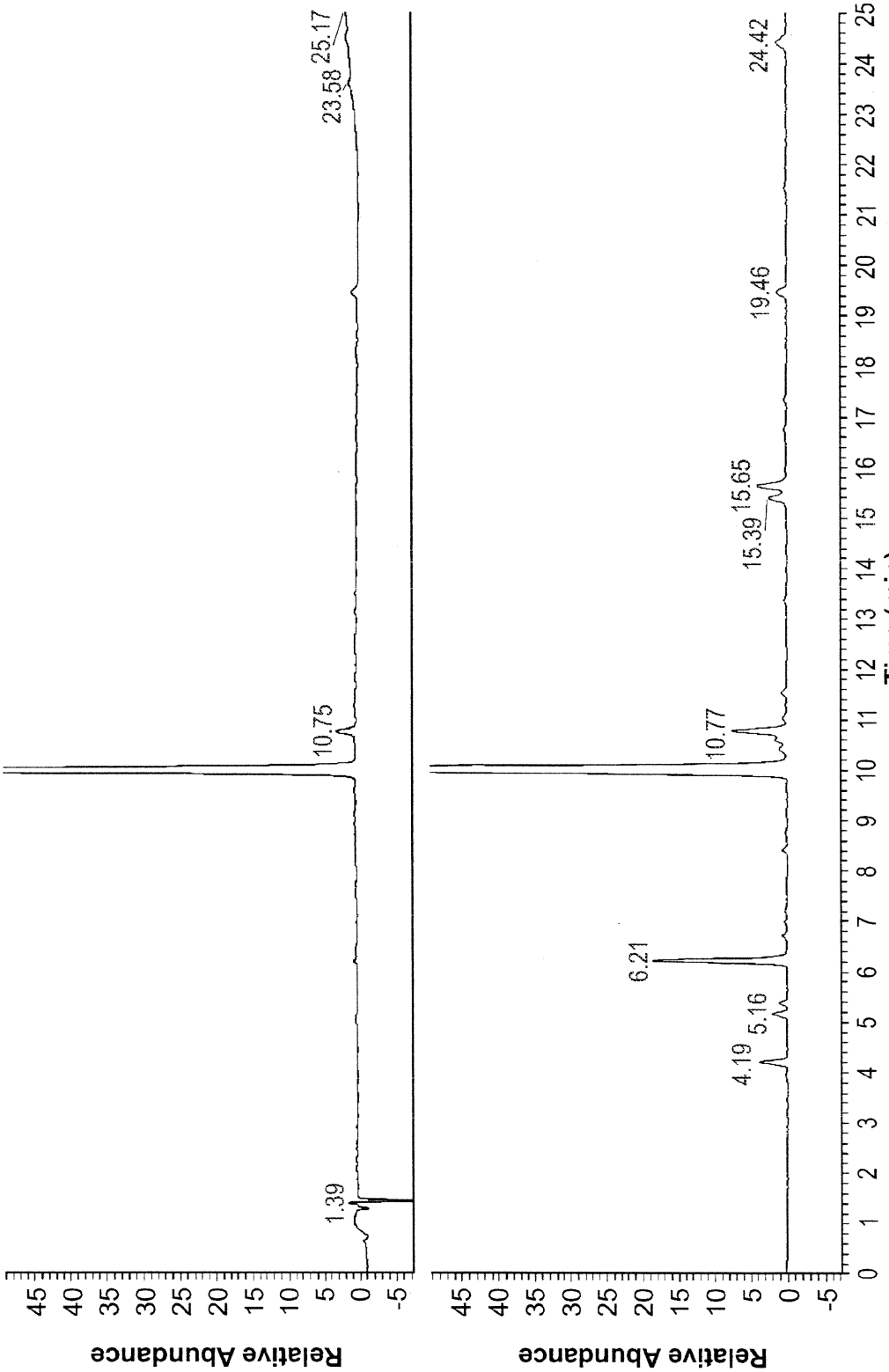

Relative Abundance
45
40
35
30
25
20
15
10
5
0
-5
1.39
10.75
23.58
25.17
Relative Abundance
45
40
35
30
25
20
15
10
5
0
-5
4.19
5.16
6.21
10.77
15.39
15.65
19.46
24.42
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Time (min)

FIG. 2

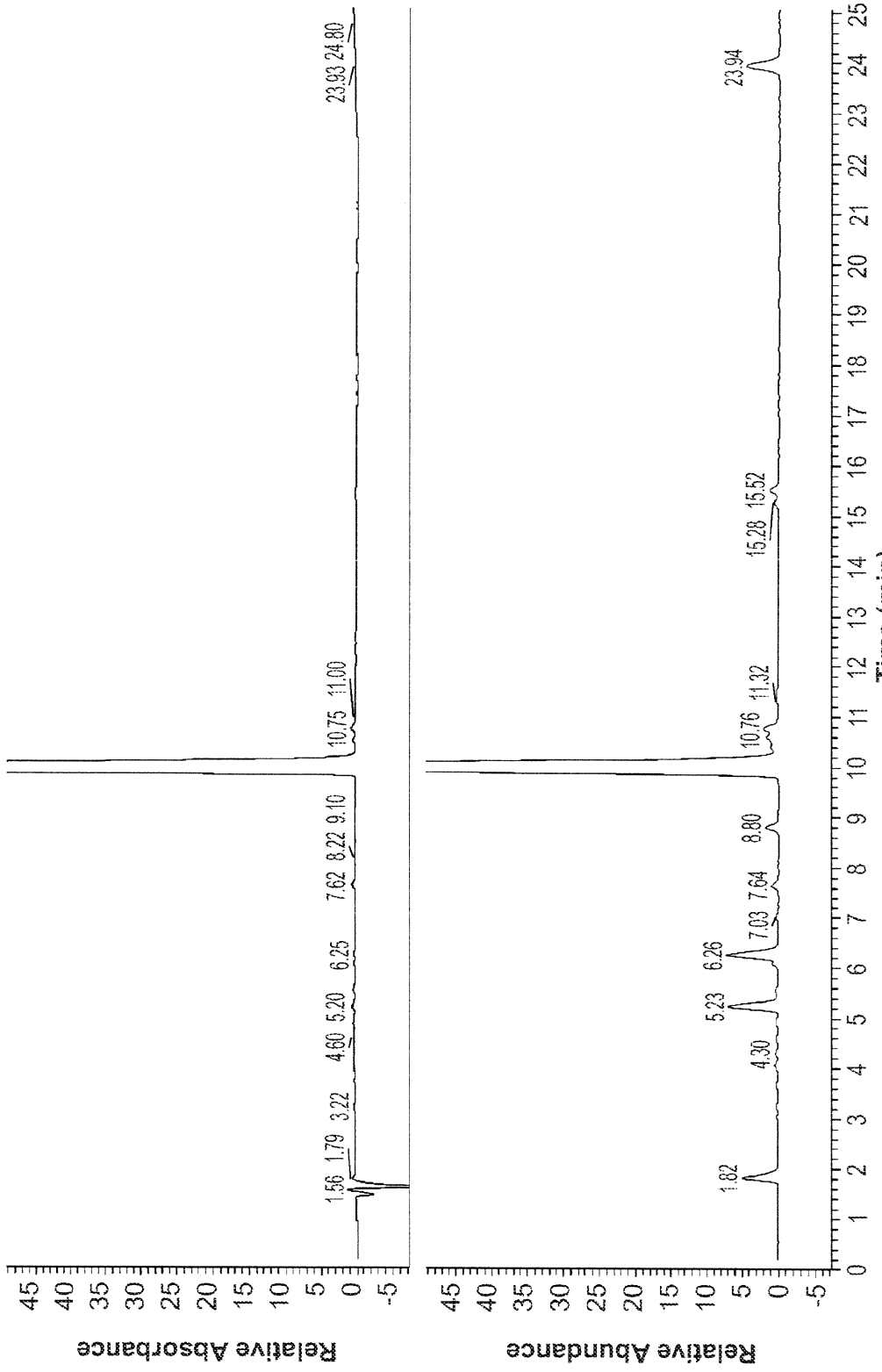

Relative Absorbance
45
40
35
30
25
20
15
10
5
0
-5
1.56
1.79
3.22
4.60
5.20
6.25
7.62
8.22
9.10
10.75
11.00
23.93
24.80
Relative Abundance
45
40
35
30
25
20
15
10
5
0
-5
1.82
4.30
5.23
6.26
7.03
7.64
8.80
10.76
11.32
15.28
15.52
23.94
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
Time (min)

FIG. 3

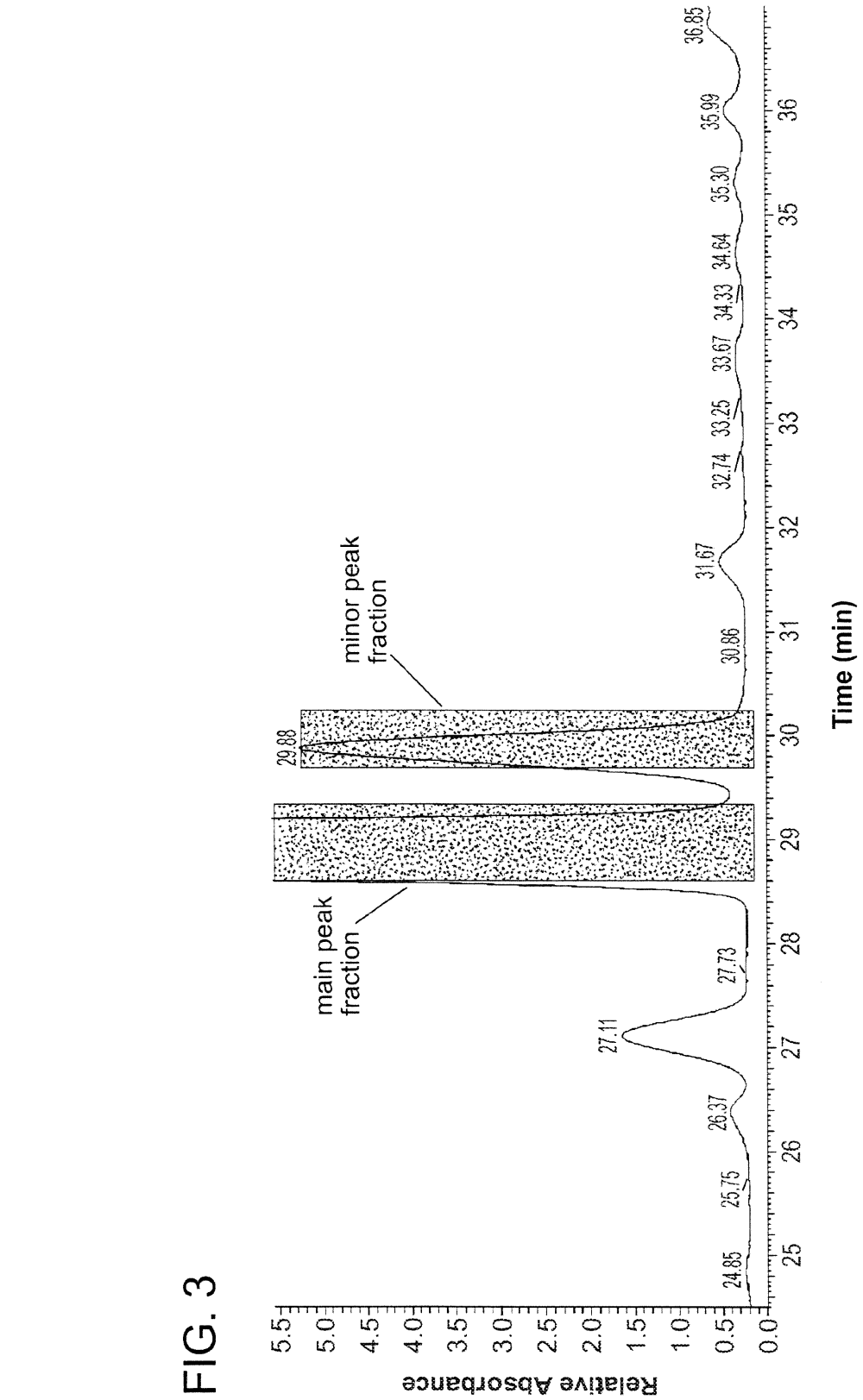

Relative Absorbance
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Time (min)
25
26
27
28
29
30
31
32
33
34
35
36
24.85
25.75
26.37
27.11
27.73
29.88
30.86
31.67
32.74
33.25
33.67
34.33
34.84
35.30
35.99
36.85
main peak fraction
minor peak fraction

FIG. 4A

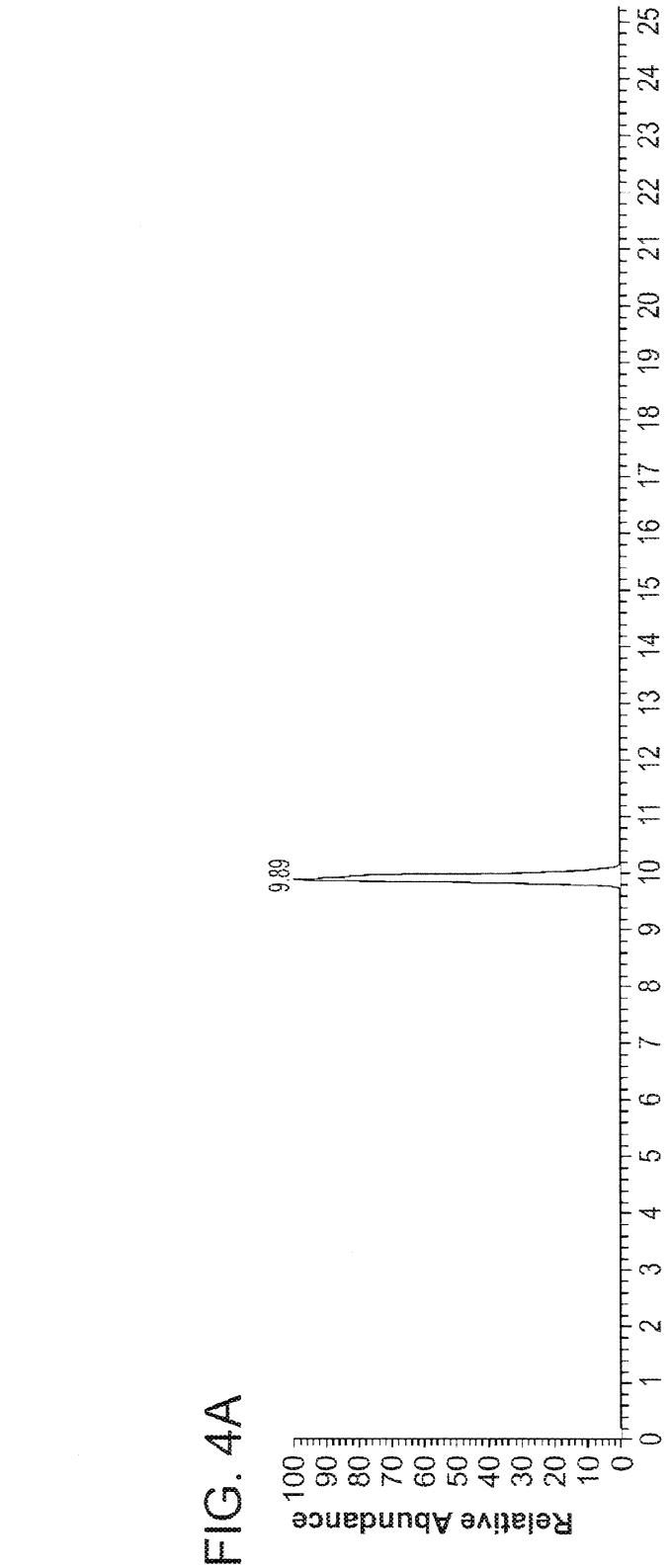

Relative Abundance
100
90
80
70
60
50
40
30
20
10
0
9.89
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Time (min)

FIG. 4B

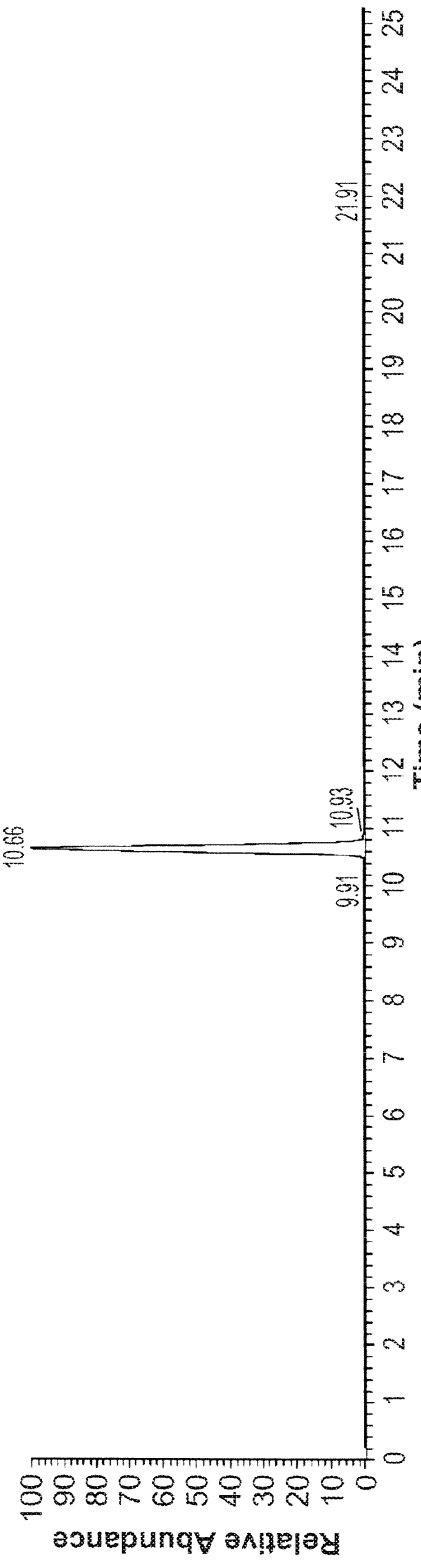

Relative Abundance
100
90
80
70
60
50
40
30
20
10
0
10.66
9.91
10.93
21.91
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Time (min)

FIG. 4C

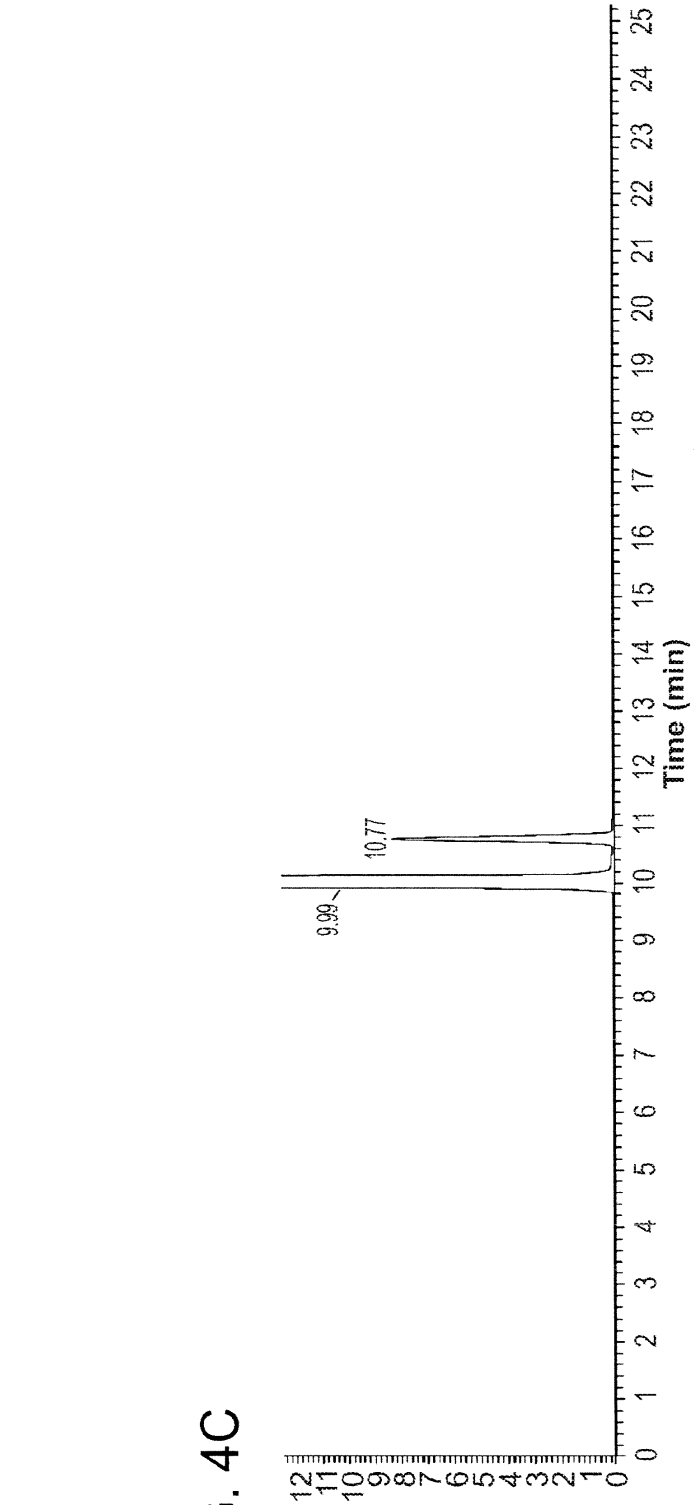

Relative Abundance
Time (min)
9.99
10.77

FIG. 4D

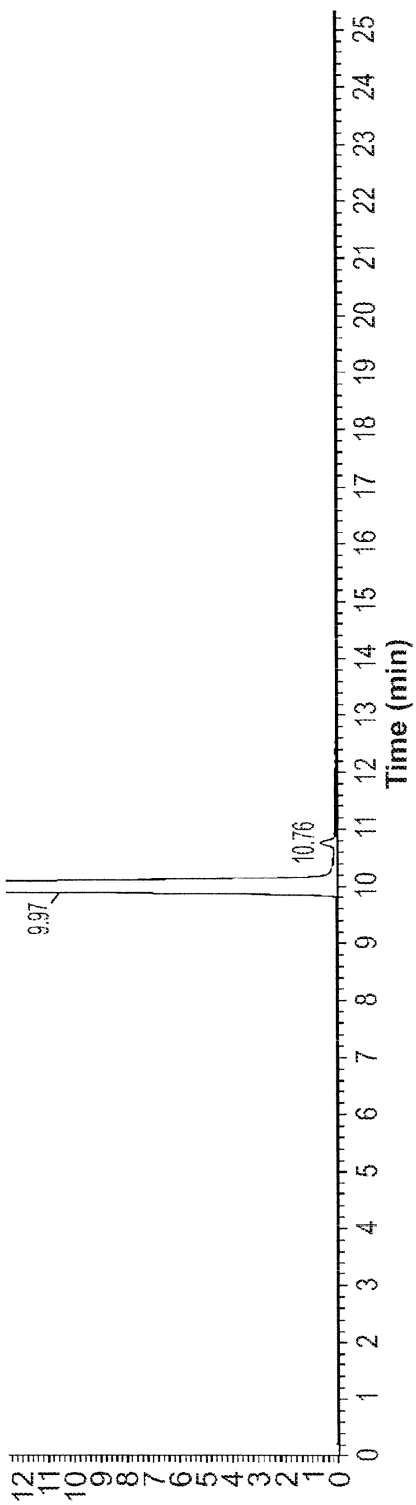

Relative Abundance
Time (min)
9.97
10.76

FIG. 5

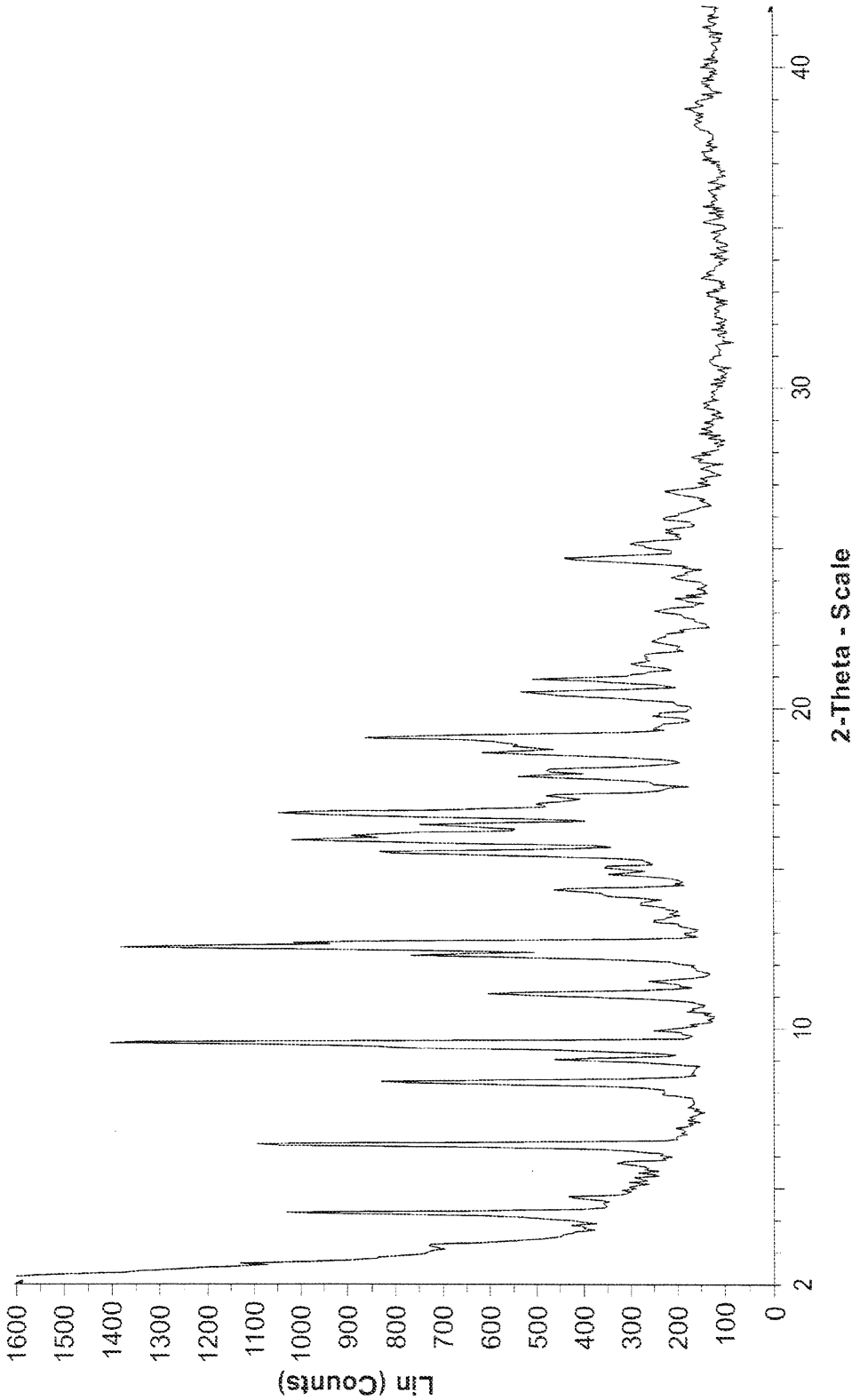

Lin (Counts)
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
2
10
20
30
40
2-Theta - Scale

FIG. 6

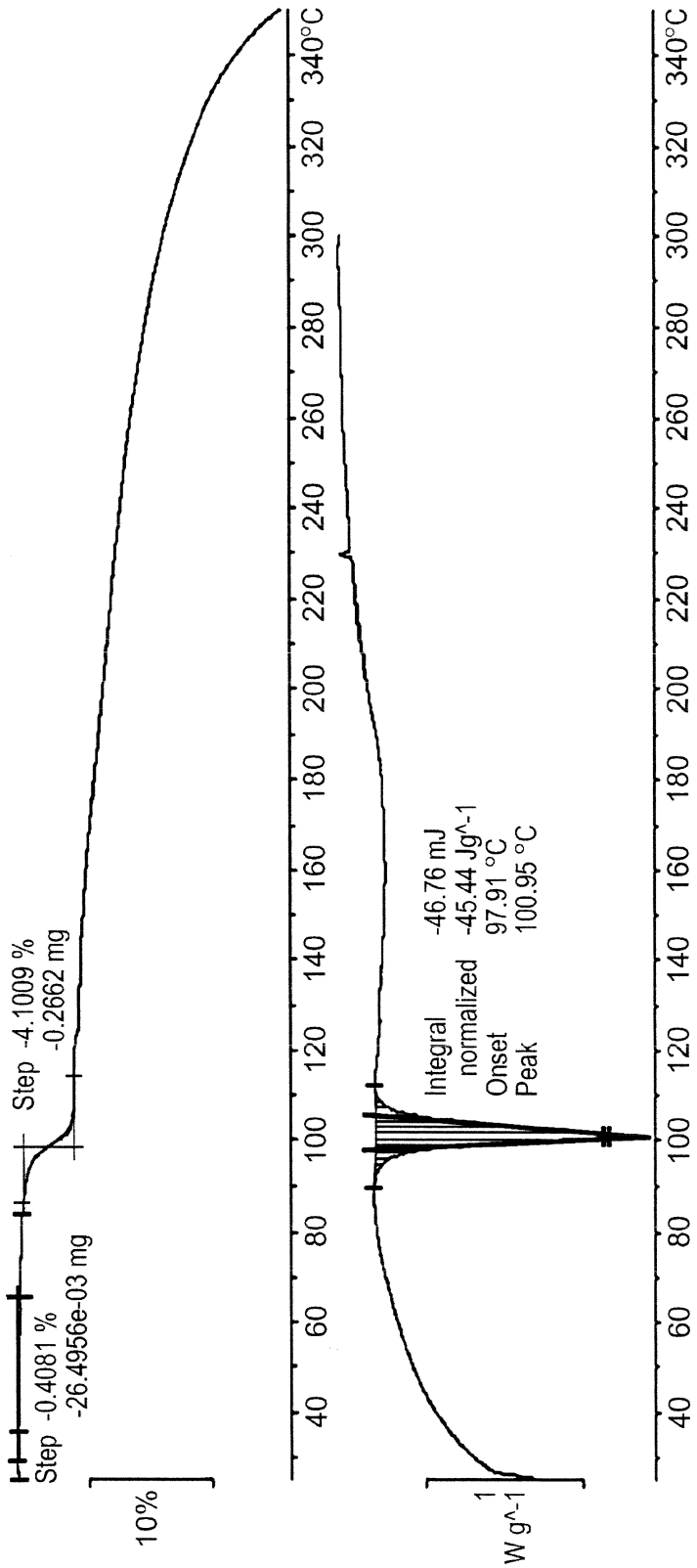

Step -4.1009 %
-0.2662 mg
Step -0.4081 %
-26.4956e-03 mg
10%
Integral -46.76 mJ
normalized -45.44 Jg^-1
Onset 97.91 °C
Peak 100.95 °C
1
W g^-1
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340°C

FIG. 7

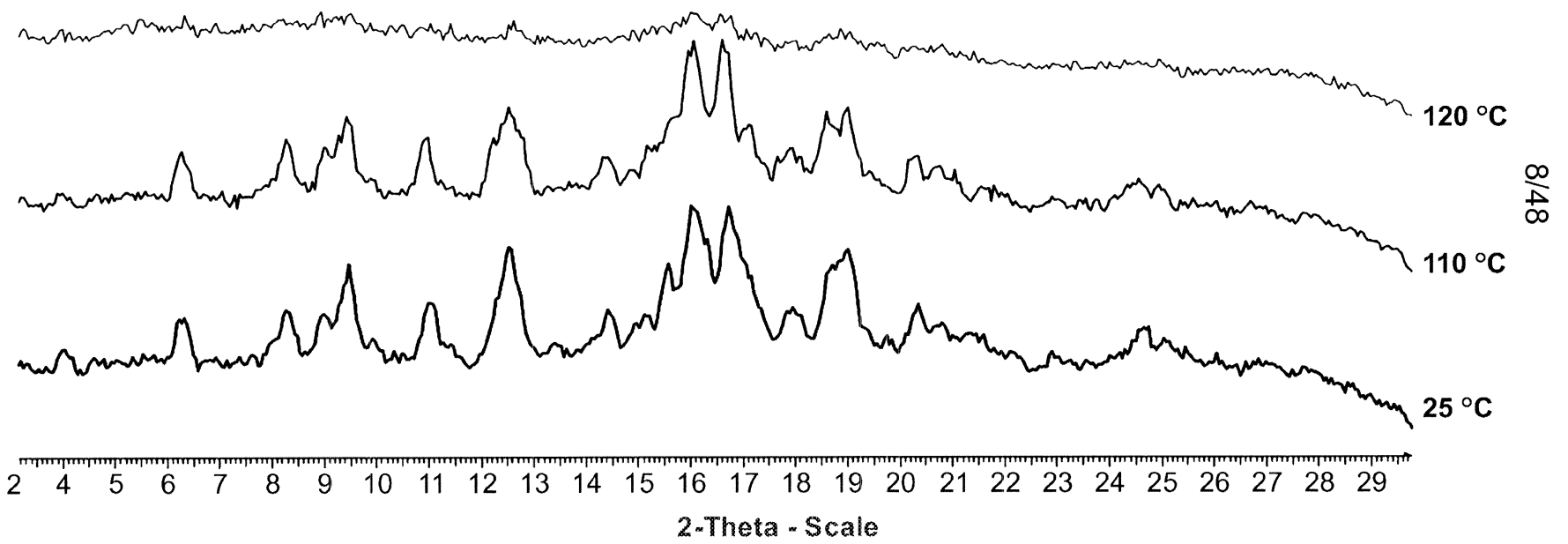

120 °C
110 °C
25 °C
2 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
2-Theta - Scale

FIG. 8A

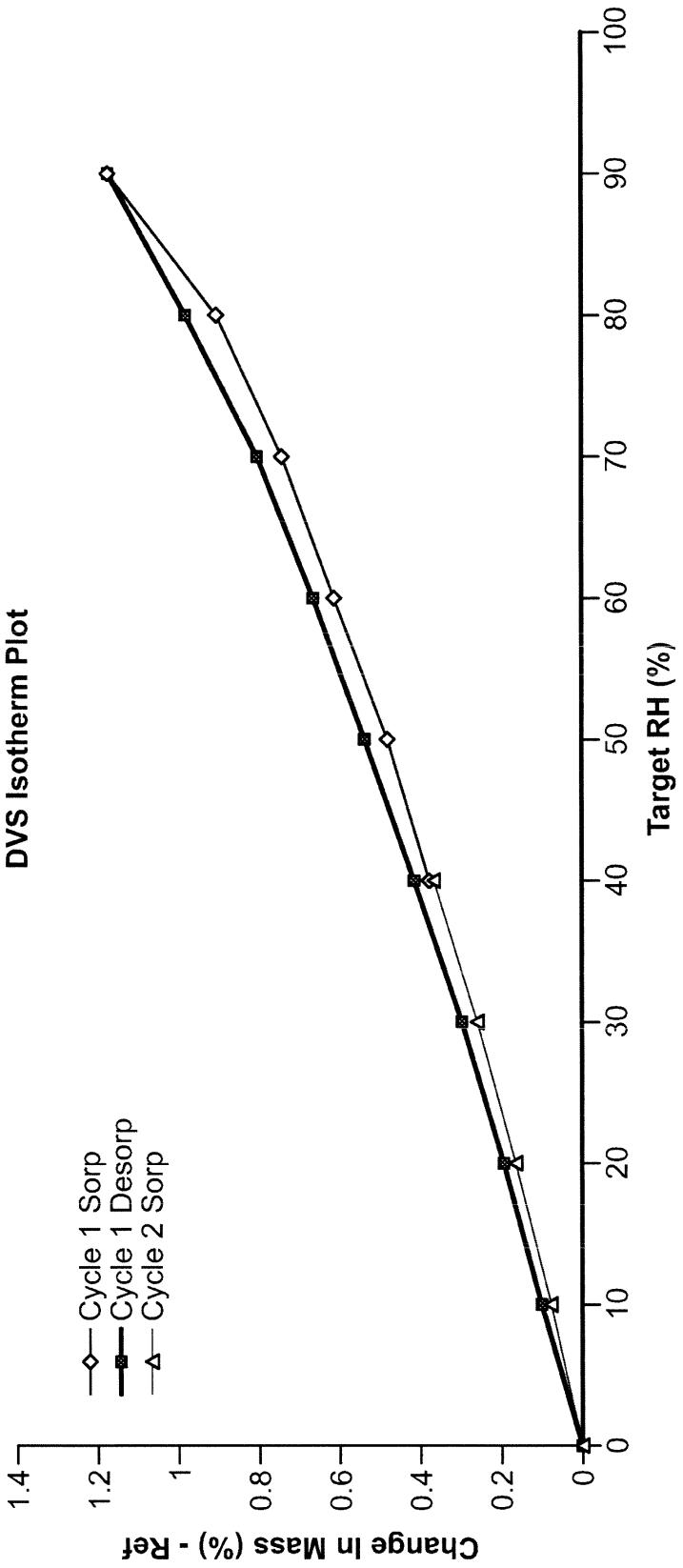

DVS Isotherm Plot
Cycle 1 Sorp
Cycle 1 Desorp
Cycle 2 Sorp
Change In Mass (%) - Ref
Target RH (%)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
10
20
30
40
50
60
70
80
90
100

FIG. 8B

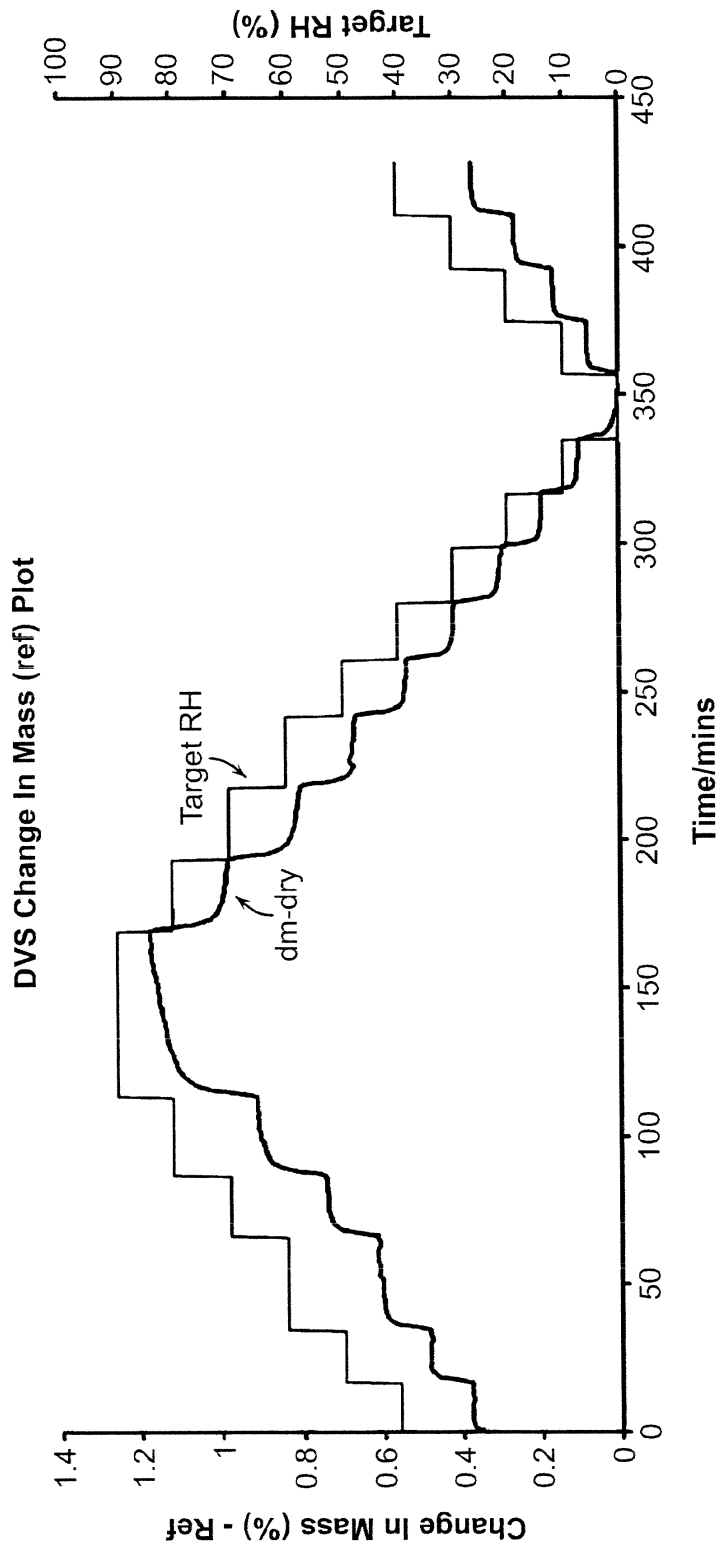

DVS Change In Mass (ref) Plot
Change In Mass (%) - Ref
Target RH (%)
Time/mins
Target RH
dm-dry
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0
10
20
30
40
50
60
70
80
90
100
0
50
100
150
200
250
300
350
400
450

FIG. 8C

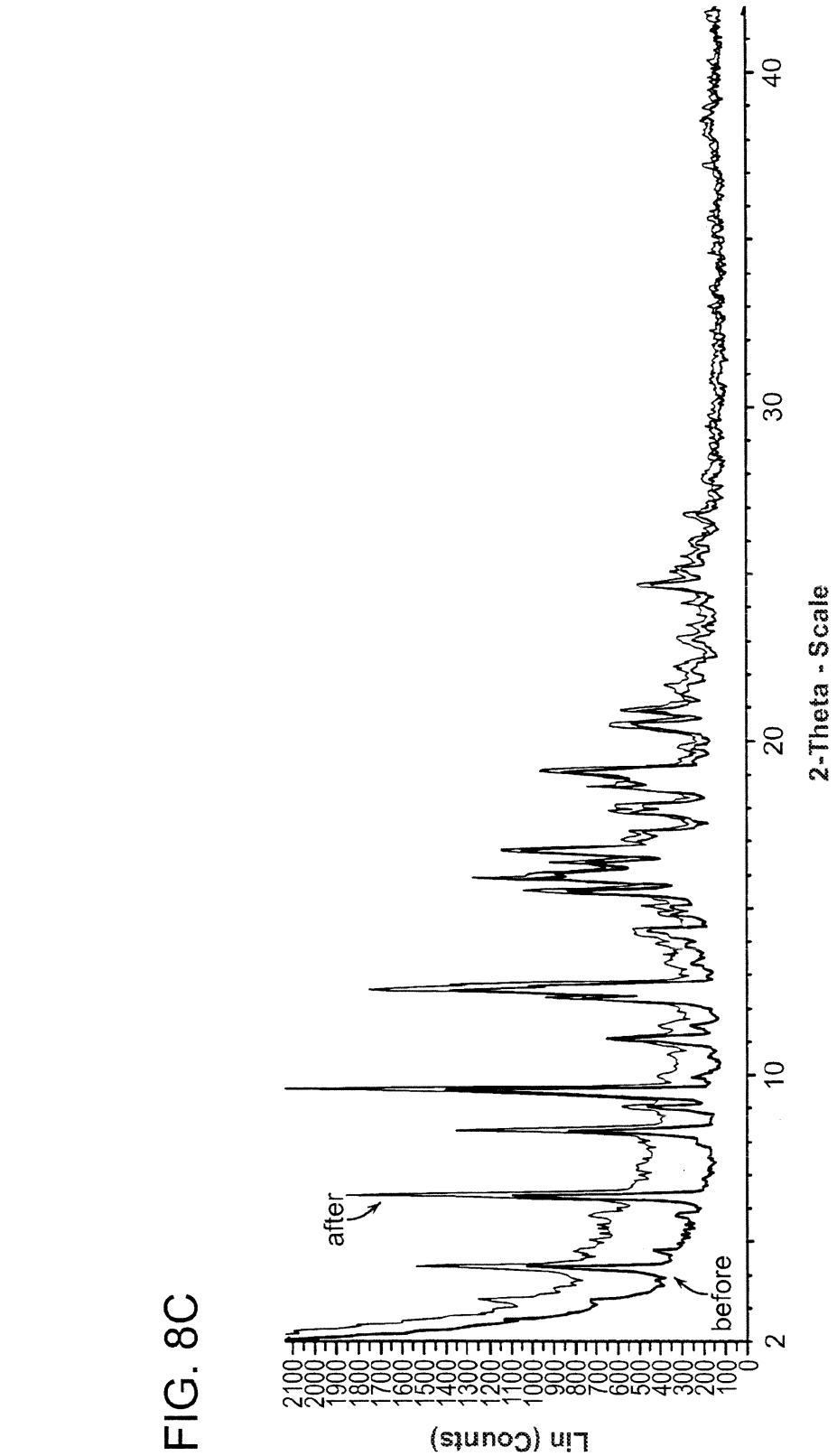

Lin (Counts)
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
2
10
20
30
40
2-Theta - Scale
after
before

FIG. 9

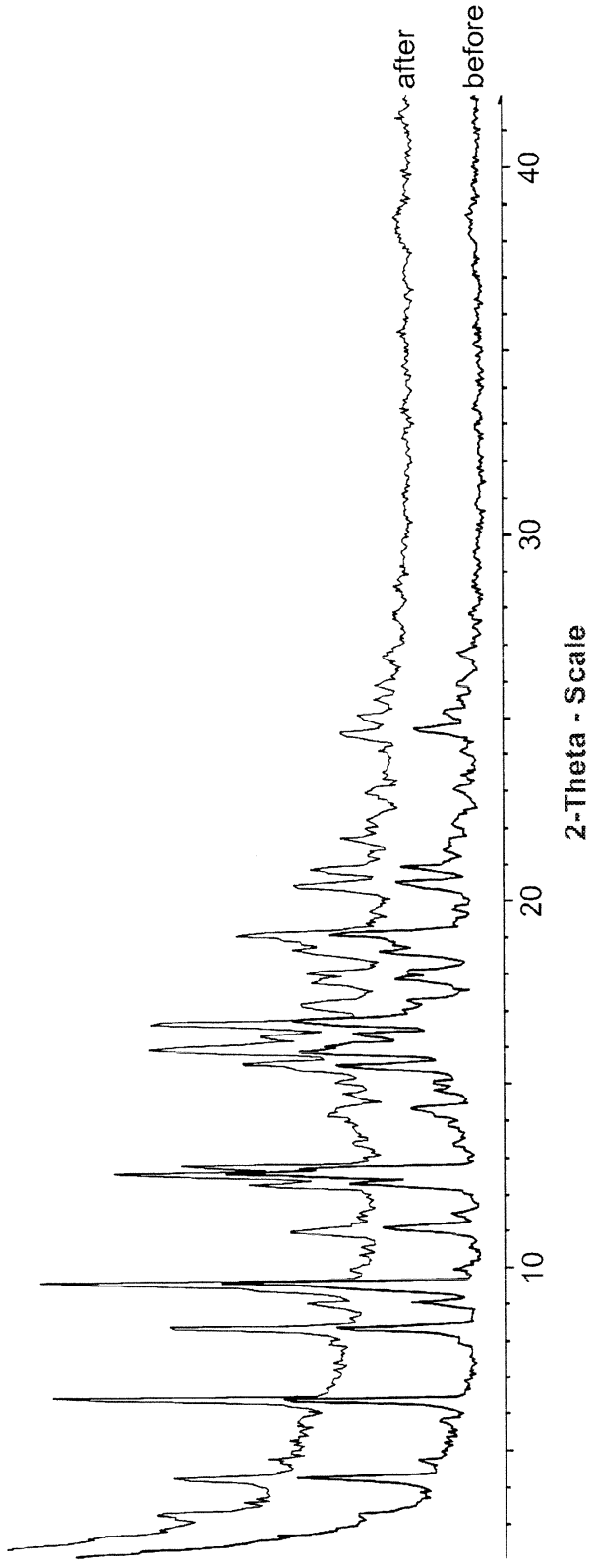


FIG. 10

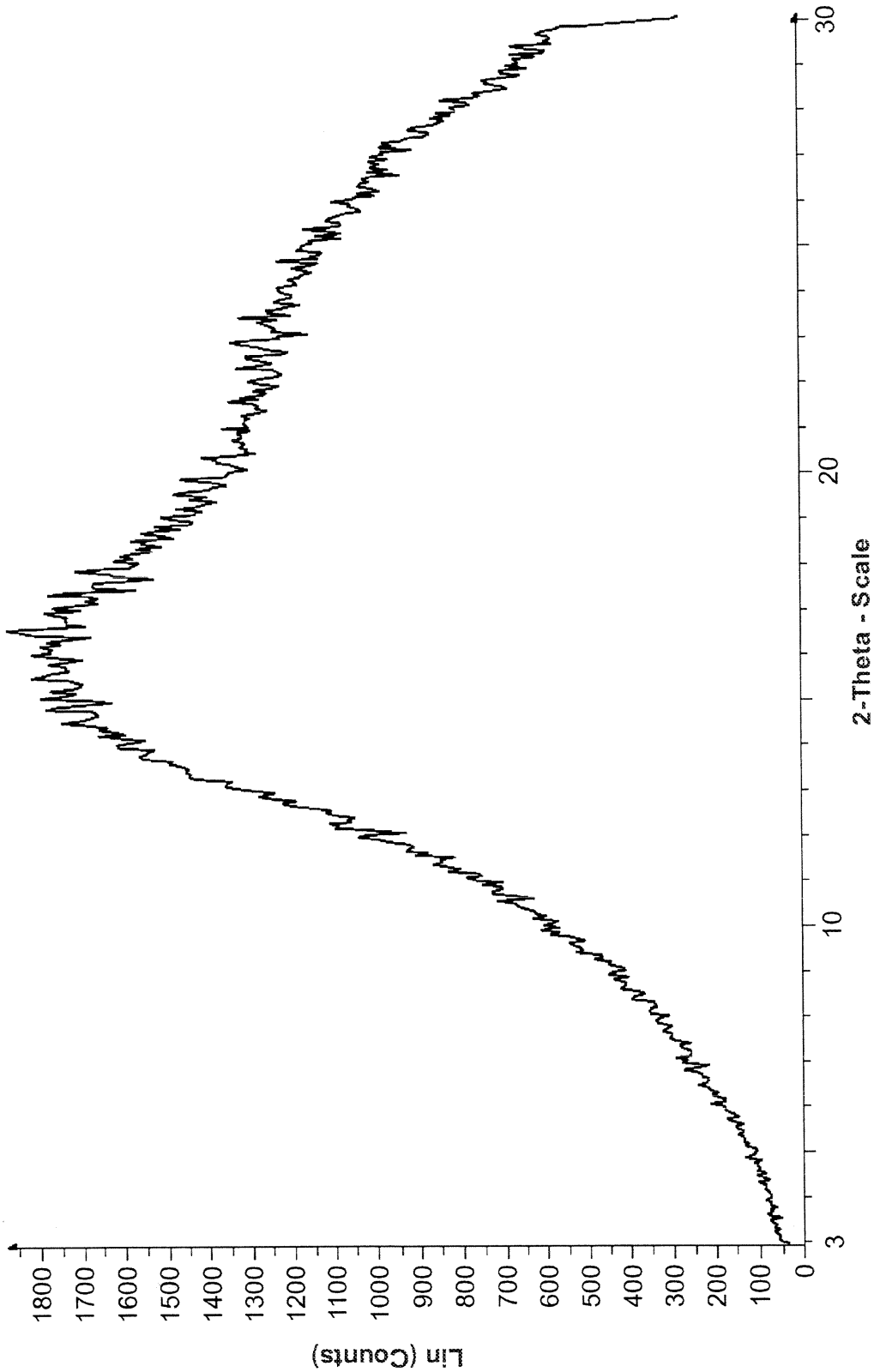

Lin (Counts)
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
3
10
20
30
2-Theta - Scale

FIG. 11

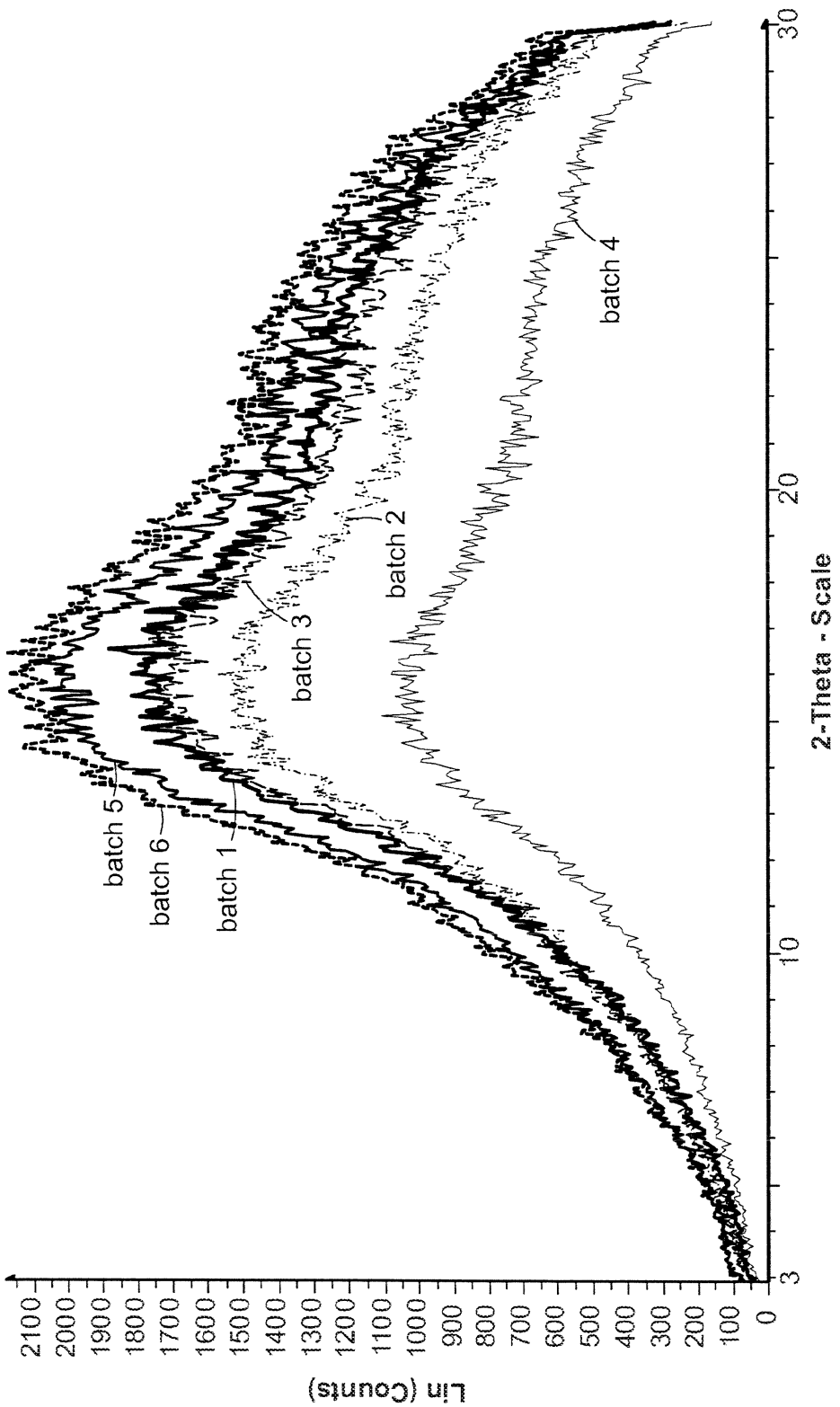

Lin (Counts)
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
3
10
20
30
2-Theta - Scale
batch 1
batch 2
batch 3
batch 4
batch 5
batch 6

FIG. 12

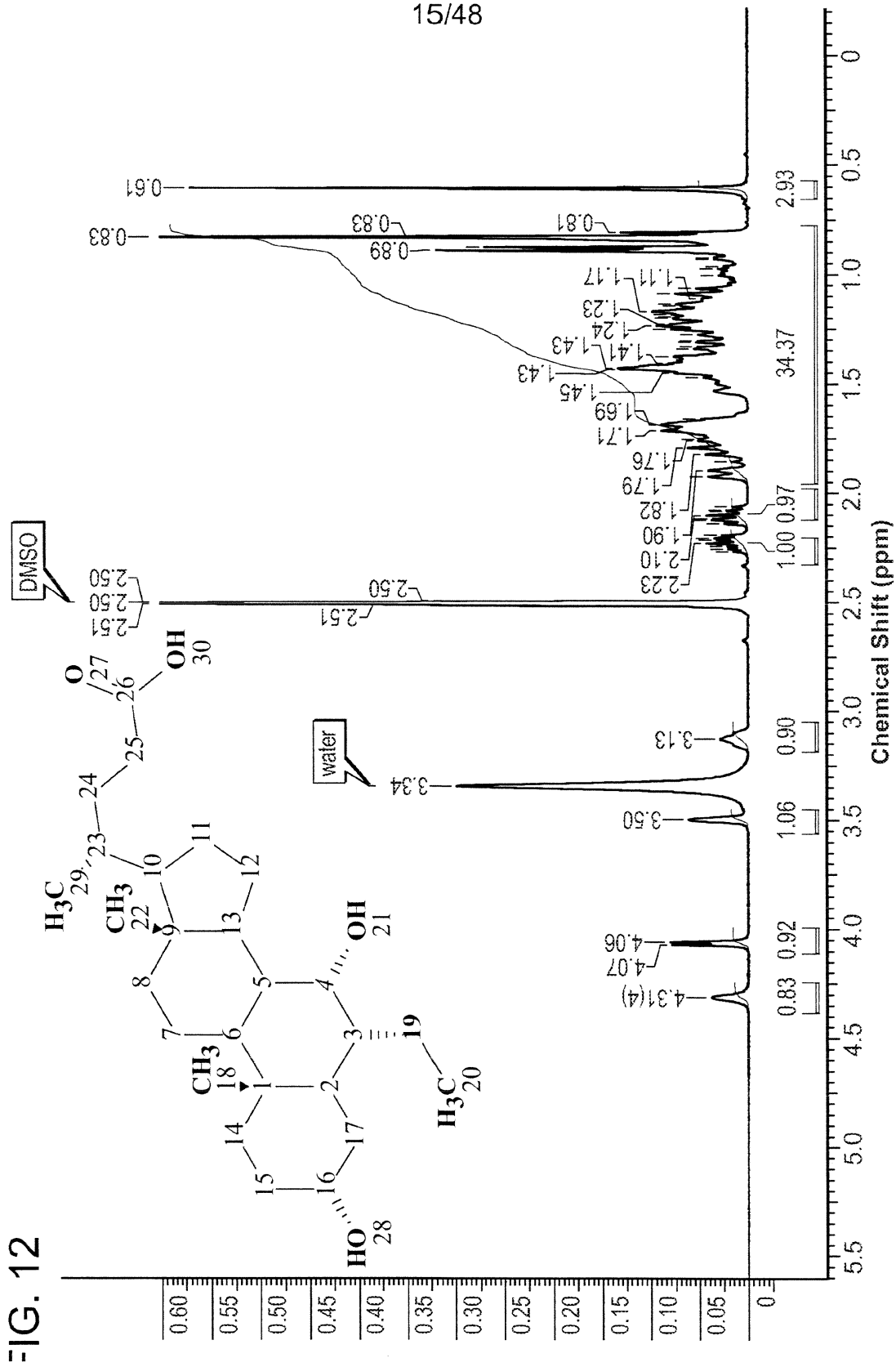
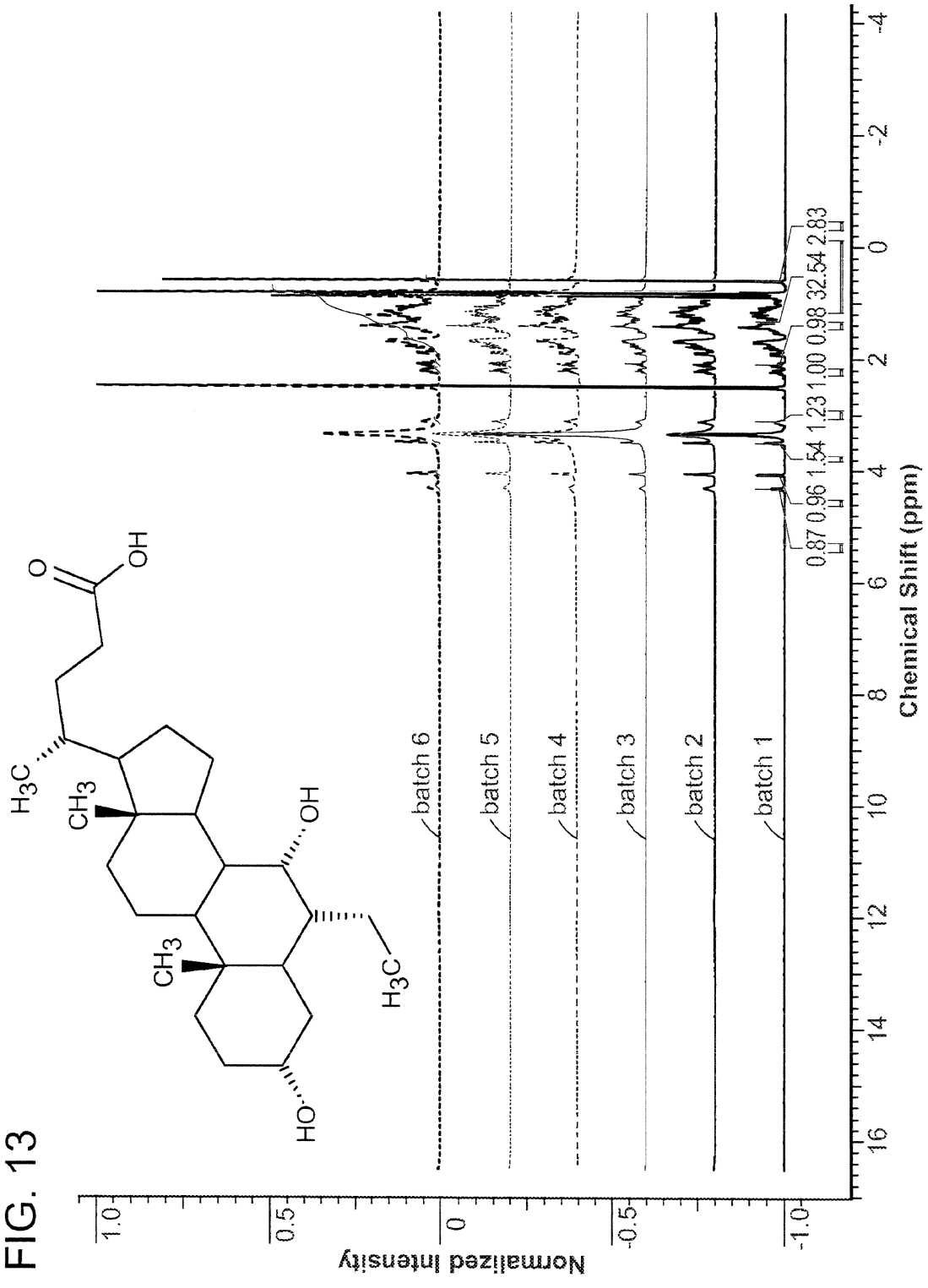


FIG. 13


H3C
CH3
CH3
OH
HO
H3C
O
OH
batch 6
batch 5
batch 4
batch 3
batch 2
batch 1
0.87 0.96 1.54 1.23 1.00 0.98 32.54 2.83
Chemical Shift (ppm)
Normalized Intensity
1.0
0.5
0
-0.5
-1.0
16
14
12
10
8
6
4
2
0
-2
-4

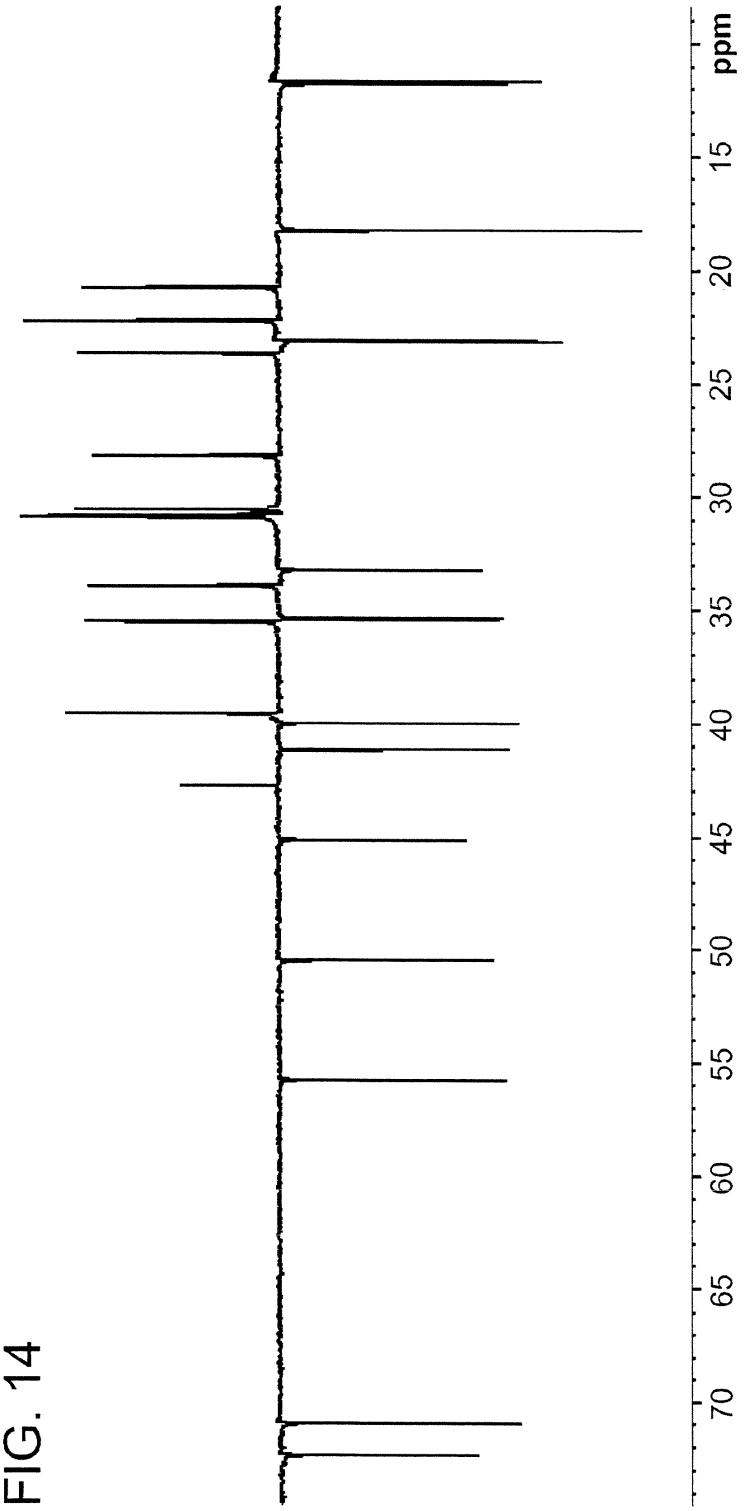


FIG. 14

FIG. 15

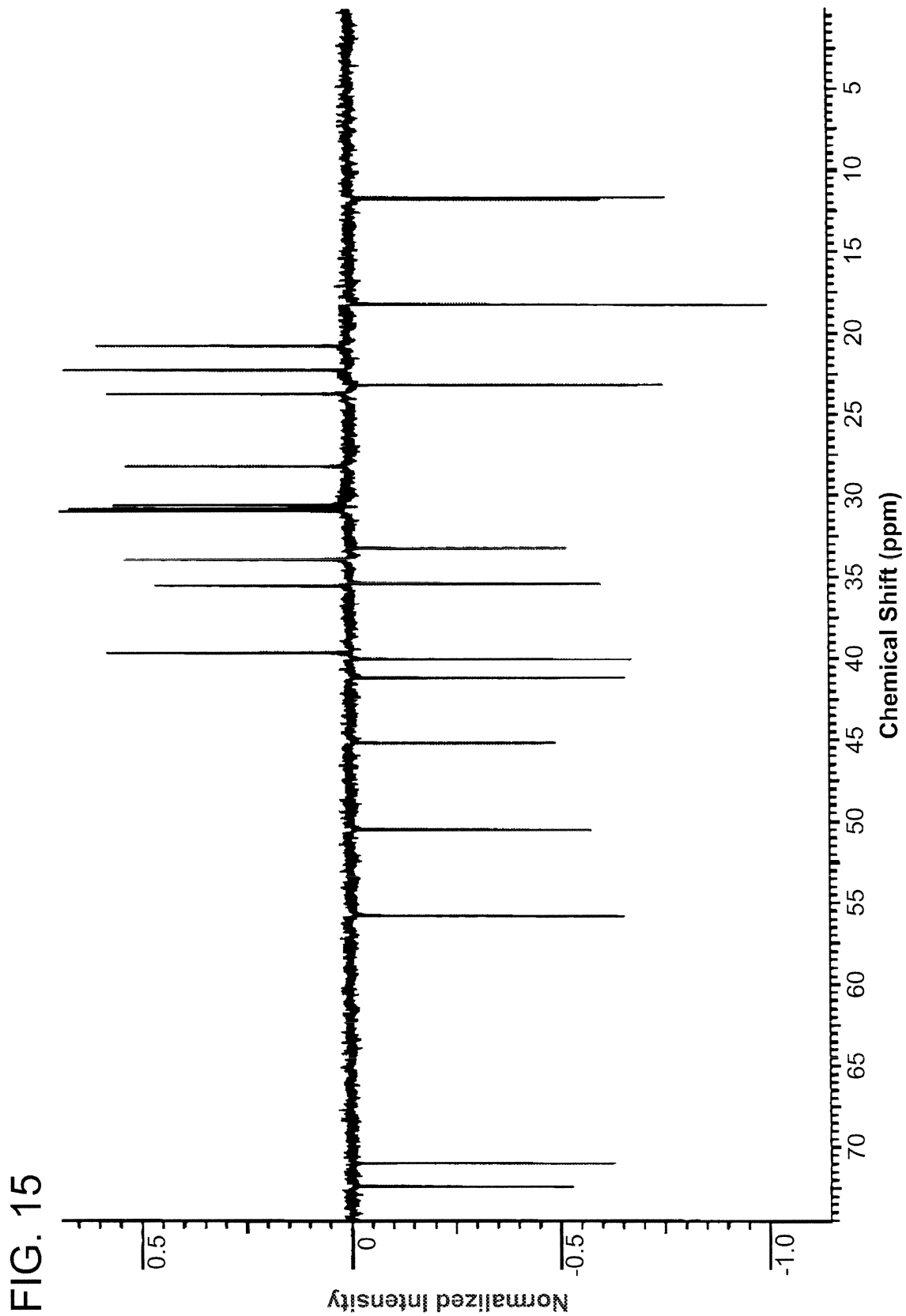

Normalized Intensity
0.5
0
-0.5
-1.0
70
65
60
55
50
45
40
35
30
25
20
15
10
5
Chemical Shift (ppm)

FIG. 16

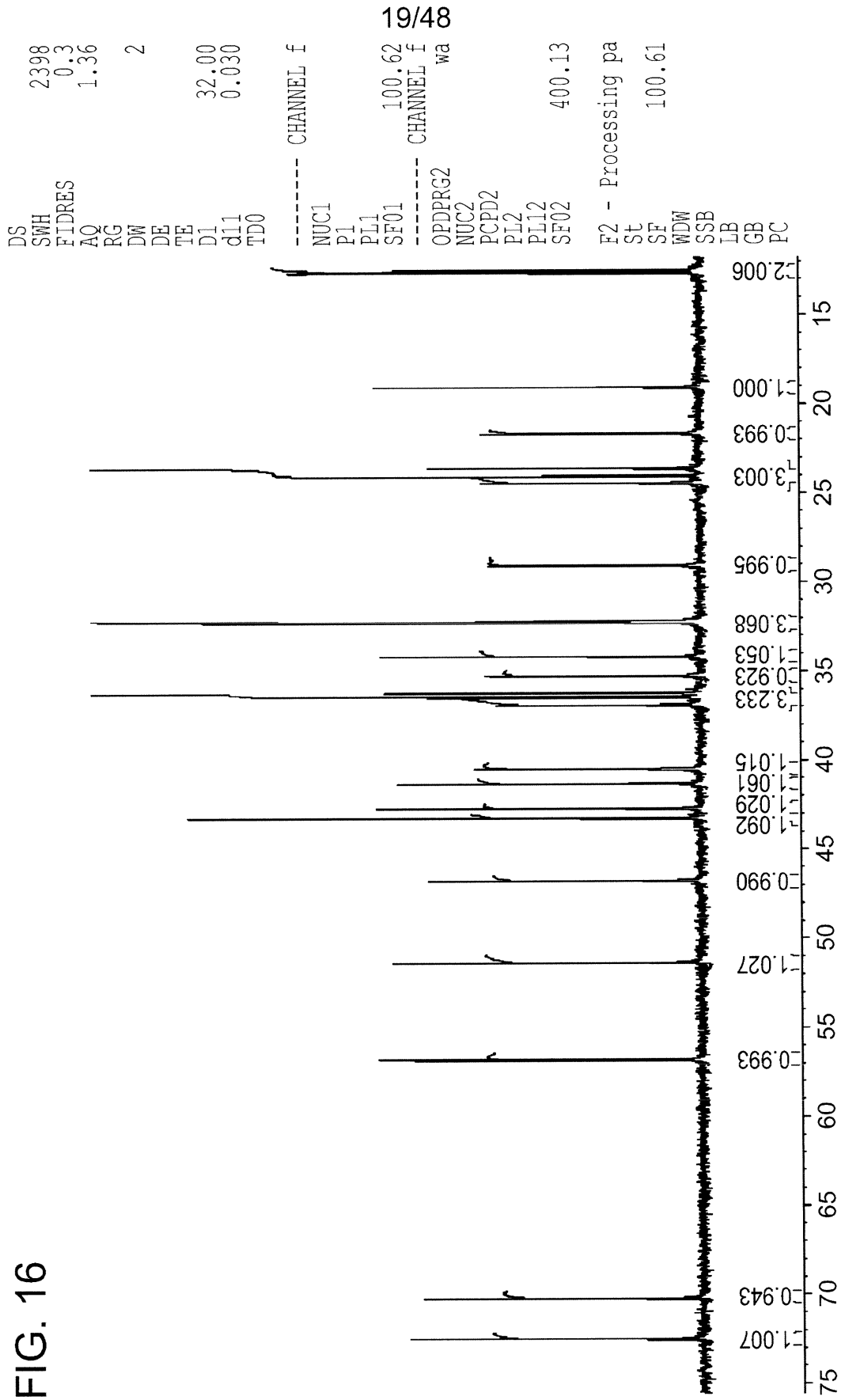

DS 16
SWH 2398
FIDRES 0.3
AQ 1.36
RG 2
DW
DE
TE
D1 32.00
d11 0.030
TD0
------ CHANNEL f
NUC1
P1
PL1 100.62
SF01
------ CHANNEL f
OPDPRG2 wa
NUC2
PCPD2
PL2
PL12
SF02 400.13
F2 - Processing pa
St
SF 100.61
WDW
SSB
LB
GB
PC
2.006
1.000
0.993
3.003
0.995
3.068
1.053
0.923
3.233
1.015
1.061
1.029
1.092
0.990
1.027
0.993
0.943
1.007
15
20
25
30
35
40
45
50
55
60
65
70
75

FIG. 17

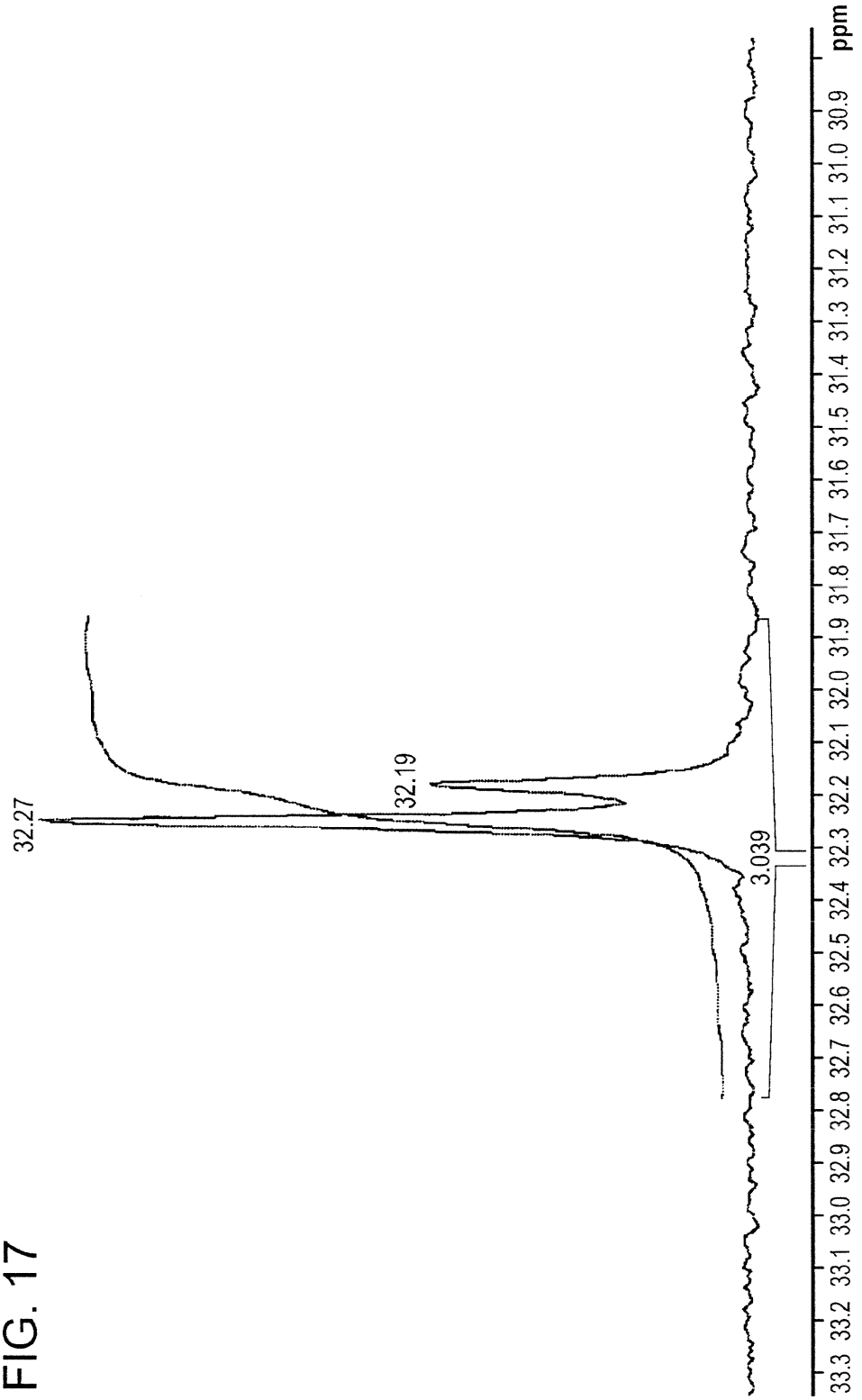

32.27
32.19
3.039
33.3 33.2 33.1 33.0 32.9 32.8 32.7 32.6 32.5 32.4 32.3 32.2 32.1 32.0 31.9 31.8 31.7 31.6 31.5 31.4 31.3 31.2 31.1 31.0 30.9
ppm

FIG. 18

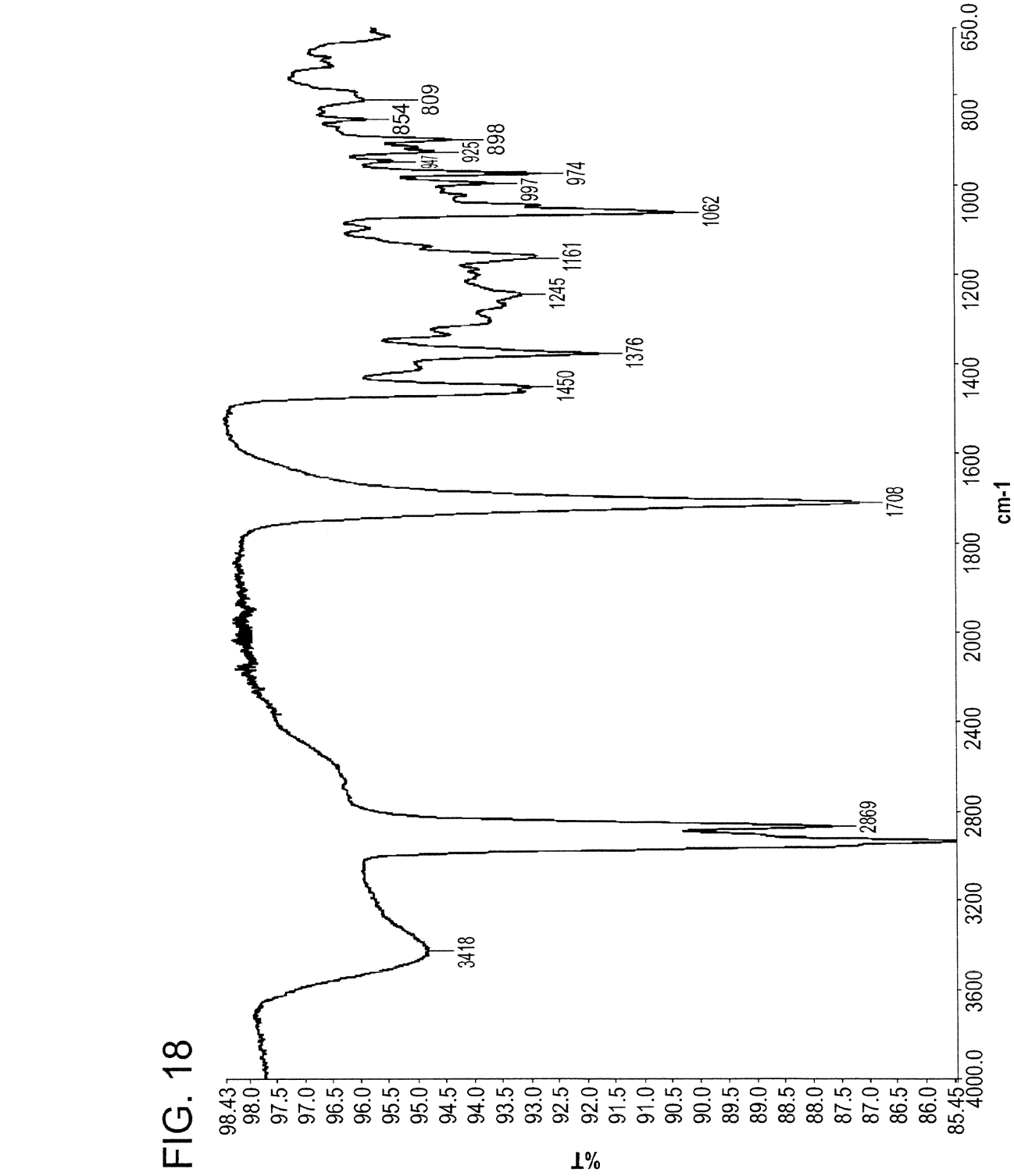

%T
cm-1
98.43
98.0
97.5
97.0
96.5
96.0
95.5
95.0
94.5
94.0
93.5
93.0
92.5
92.0
91.5
91.0
90.5
90.0
89.5
89.0
88.5
88.0
87.5
87.0
86.5
86.0
85.45
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
650.0
3418
2869
1708
1450
1376
1245
1161
1062
997
974
947
925
898
854
809

FIG. 19

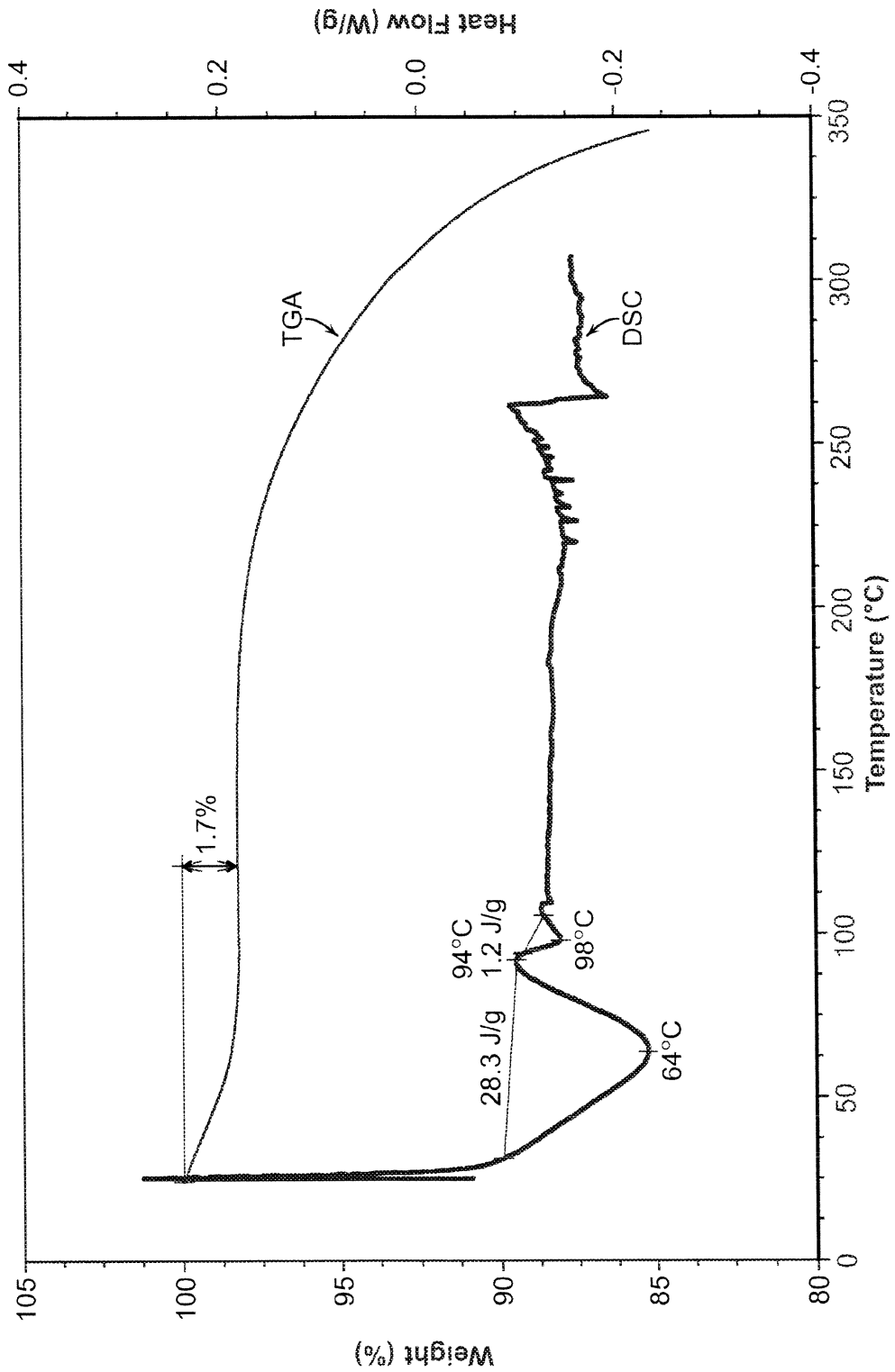

Weight (%)
105
100
95
90
85
80
Heat Flow (W/g)
0.4
0.2
0.0
-0.2
-0.4
0
50
100
150
200
250
300
350
Temperature (°C)
TGA
DSC
1.7%
94°C
1.2 J/g
98°C
28.3 J/g
64°C

FIG. 20

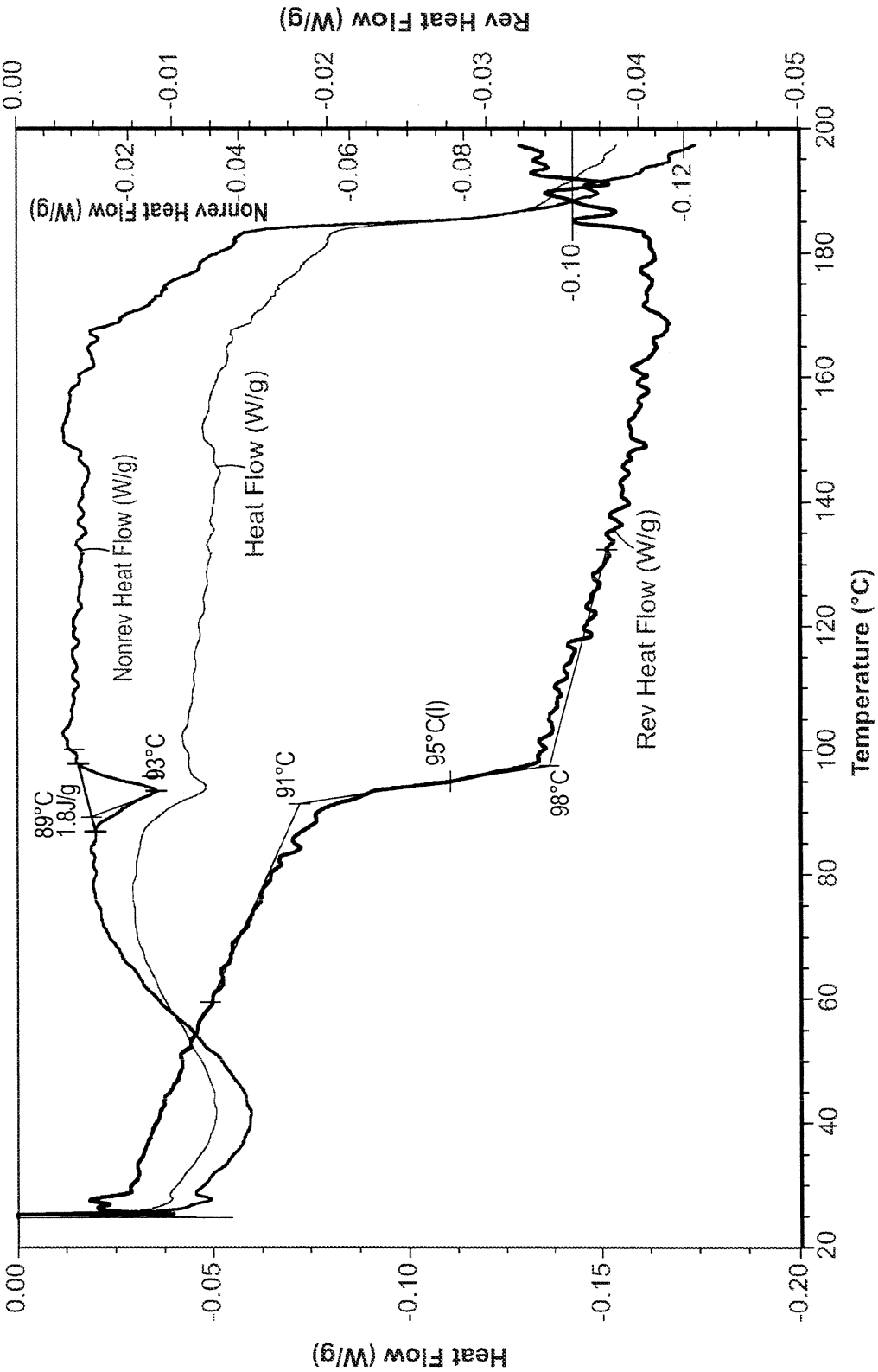

Rev Heat Flow (W/g)
Nonrev Heat Flow (W/g)
Heat Flow (W/g)
Rev Heat Flow (W/g)
Temperature (°C)
89°C
1.8J/g
93°C
91°C
95°C(l)
98°C
-0.10
-0.12

FIG. 21

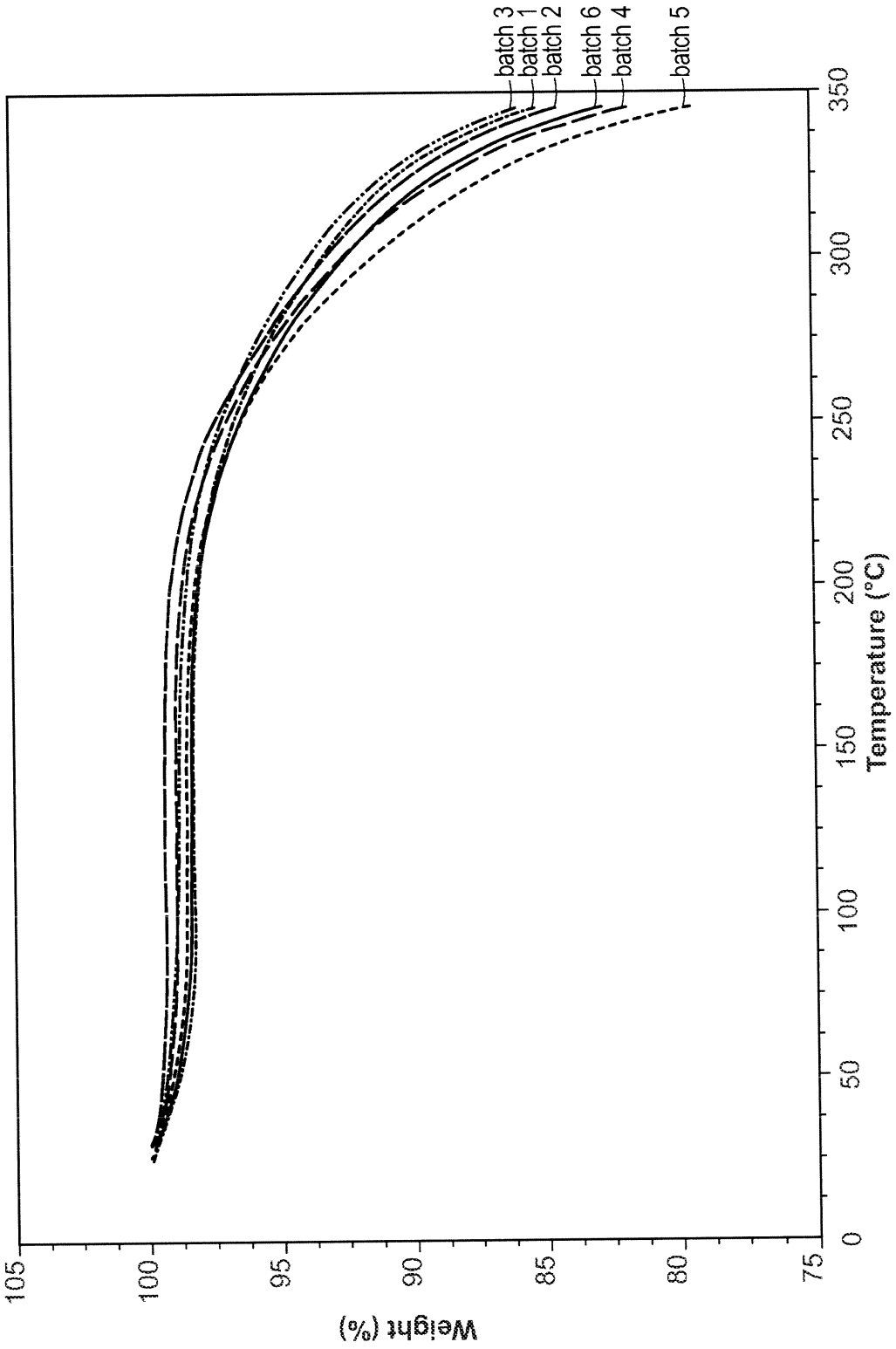
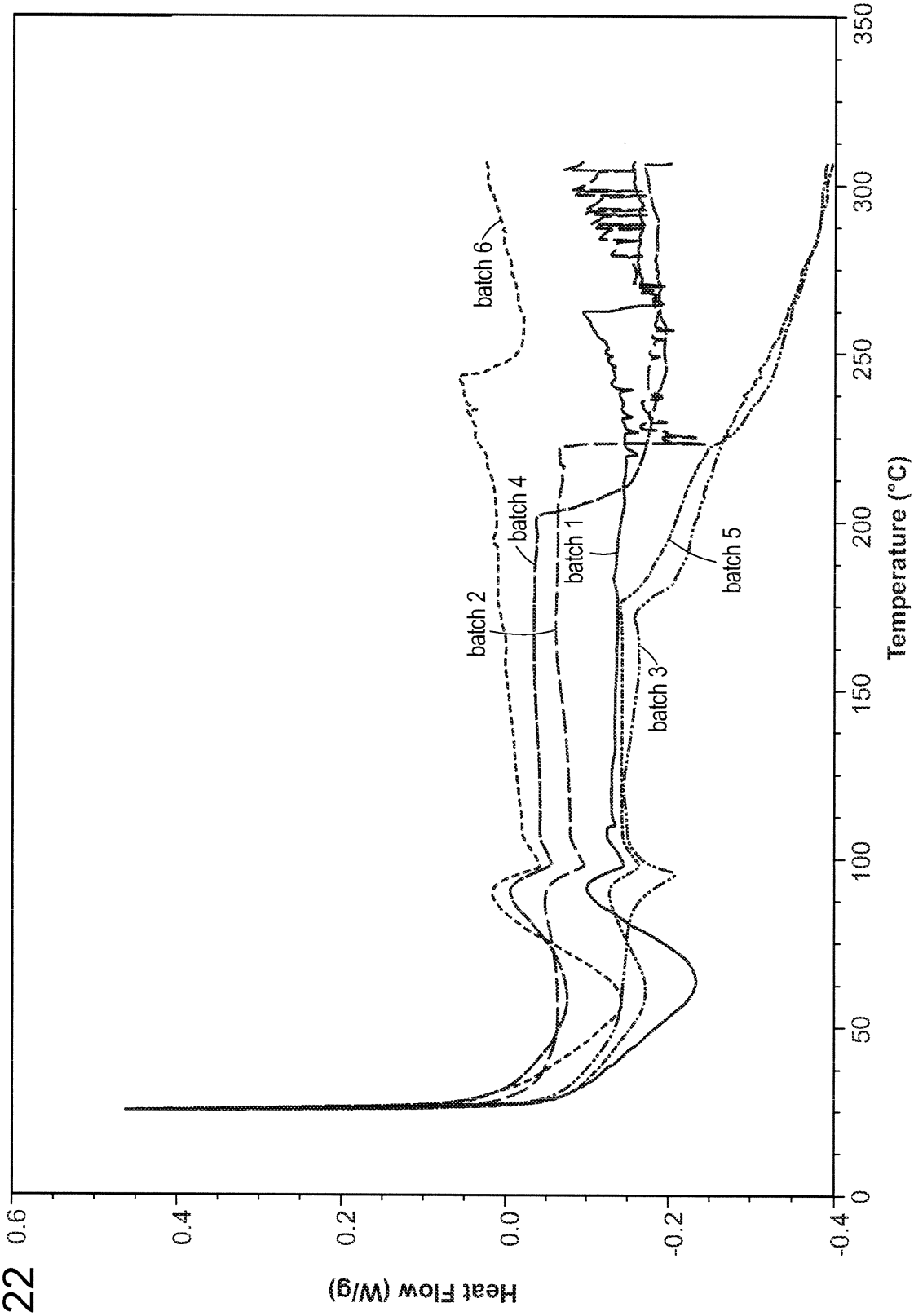

batch 3
batch 1
batch 2
batch 6
batch 4
batch 5
Weight (%)
Temperature (°C)
105
100
95
90
85
80
75
0
50
100
150
200
250
300
350

FIG. 22


Heat Flow (W/g)
0.6
0.4
0.2
0.0
-0.2
-0.4
0
50
100
150
200
250
300
350
Temperature (°C)
batch 6
batch 4
batch 1
batch 2
batch 5
batch 3

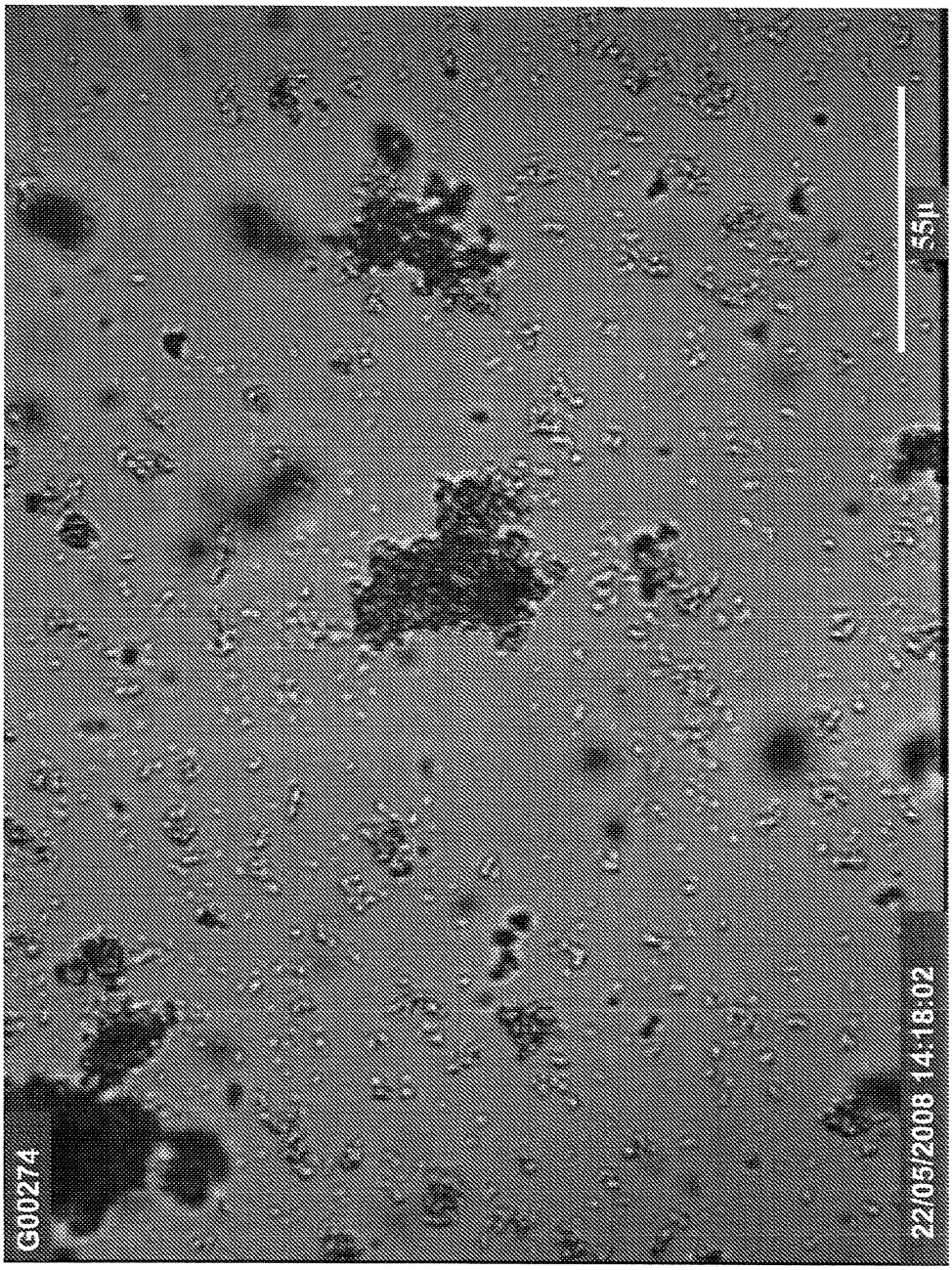


FIG. 23A

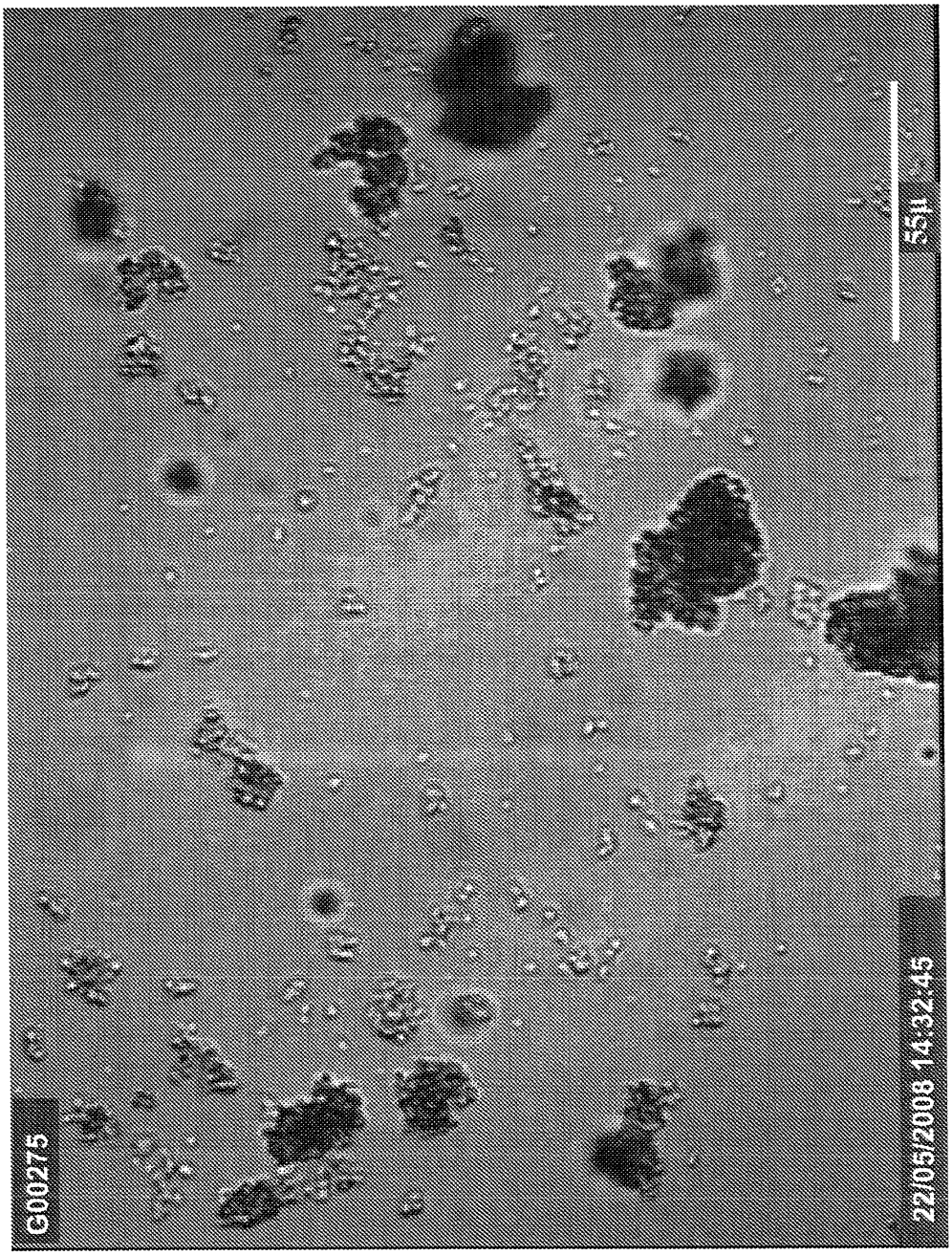


FIG. 23B

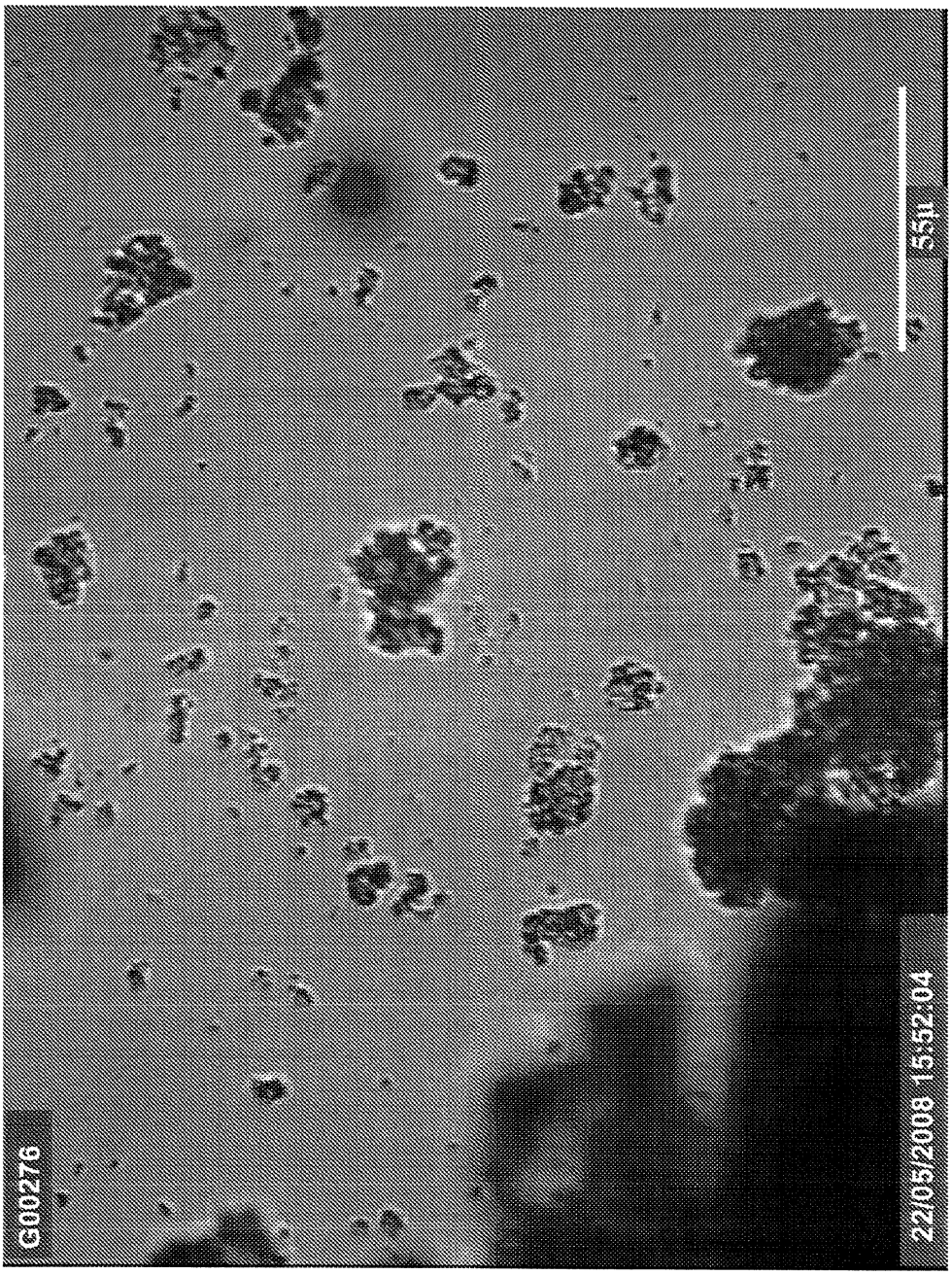


FIG. 23C

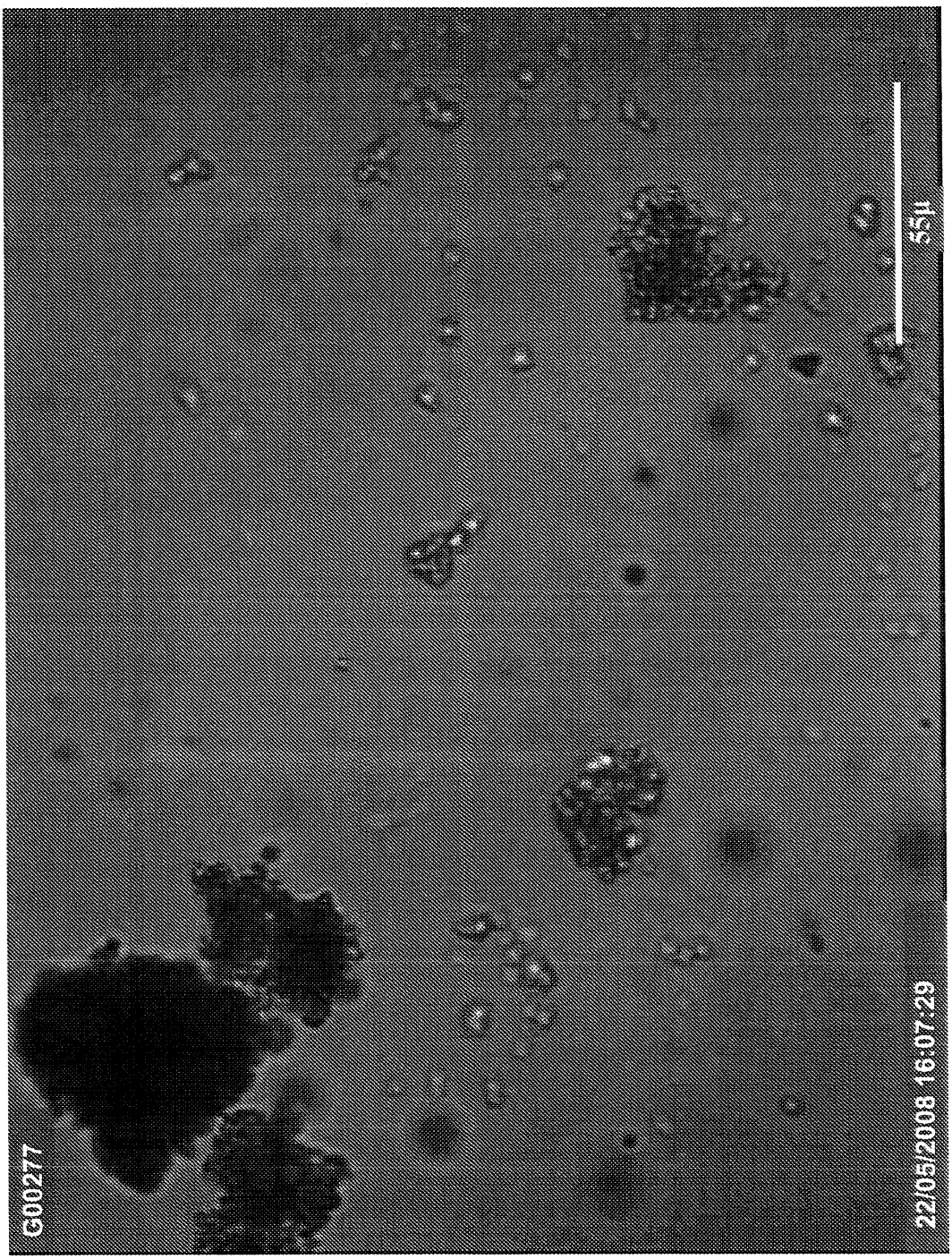


FIG. 23D

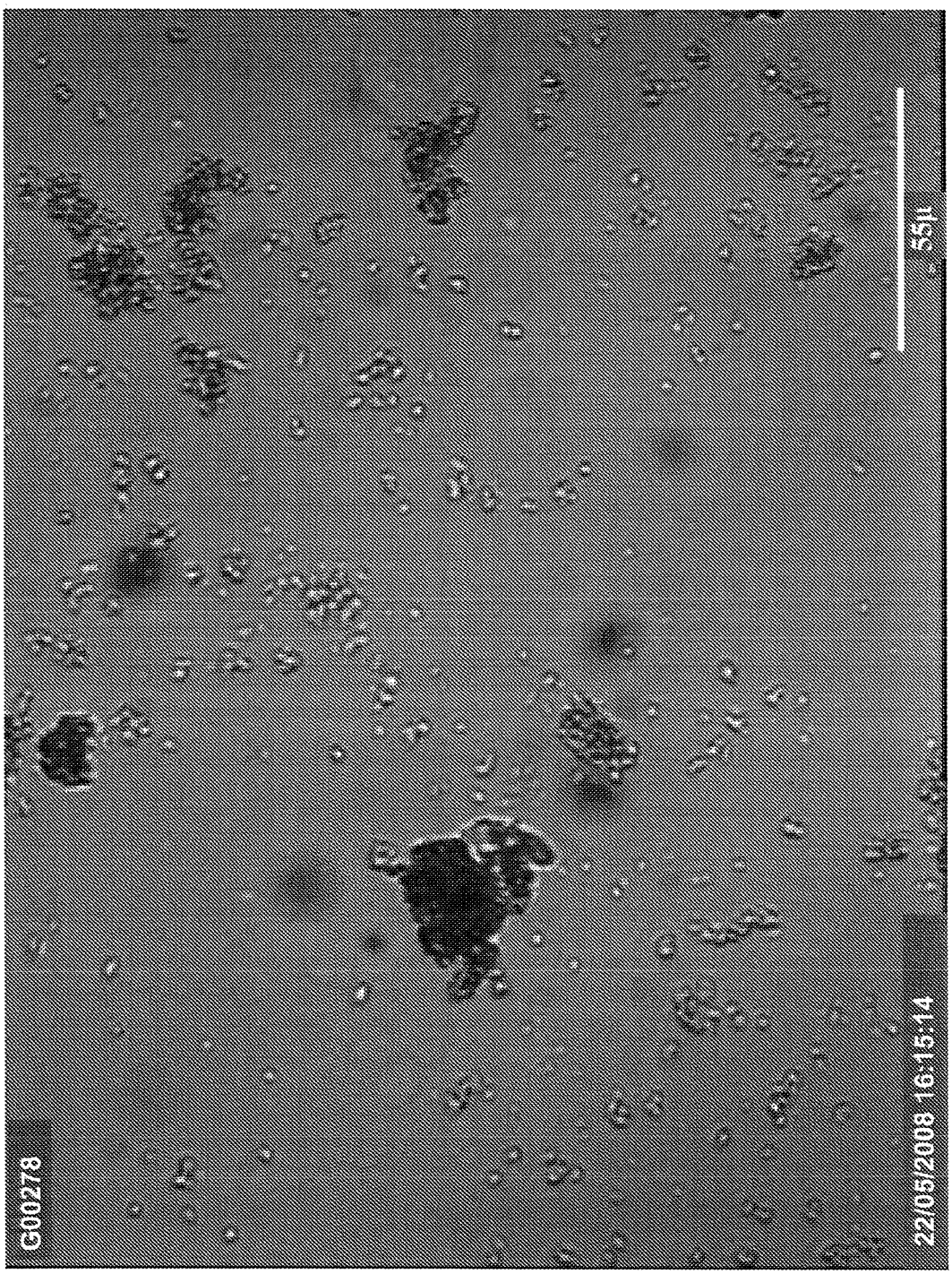


FIG. 23E

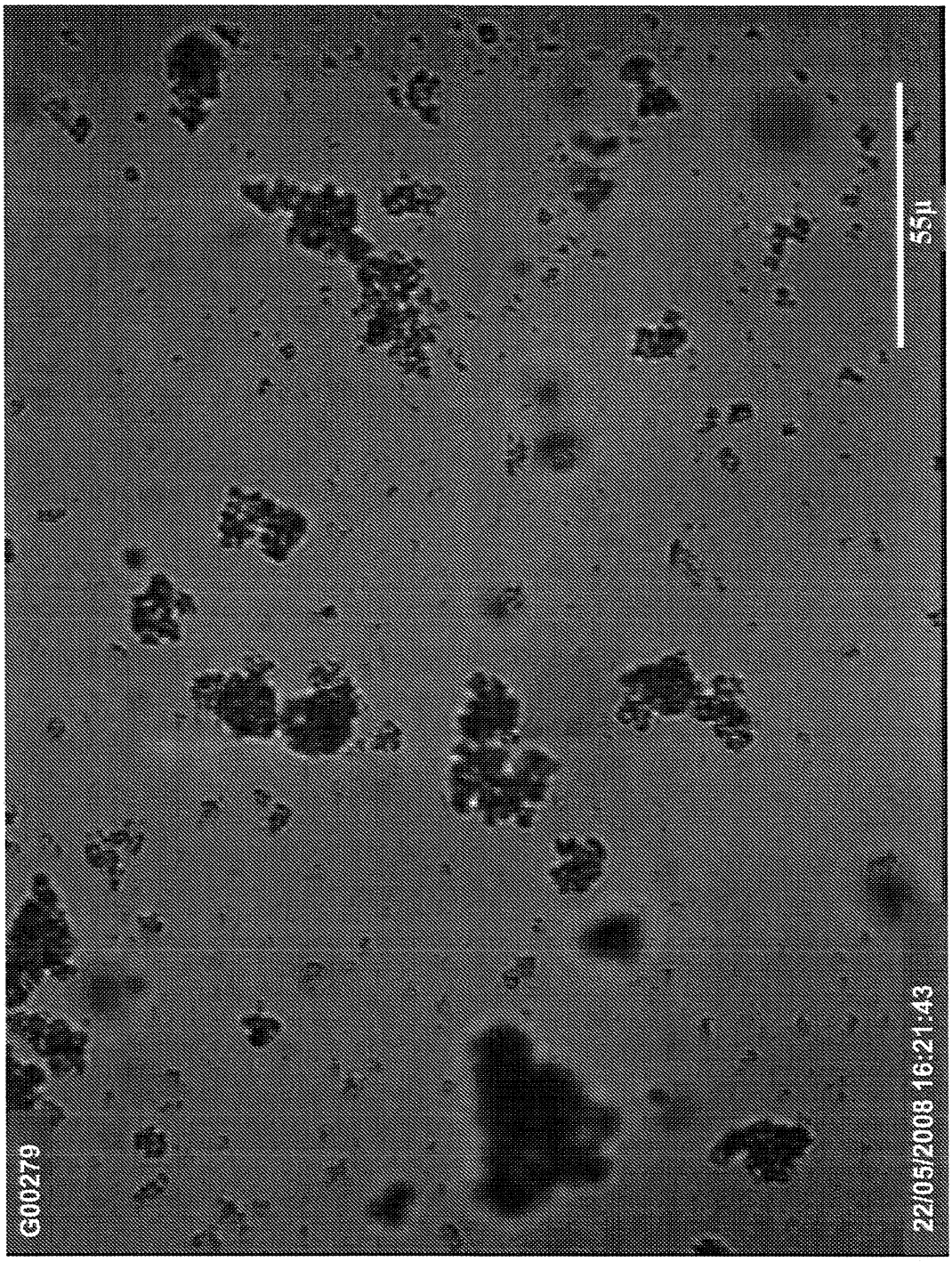


FIG. 23F

FIG. 24

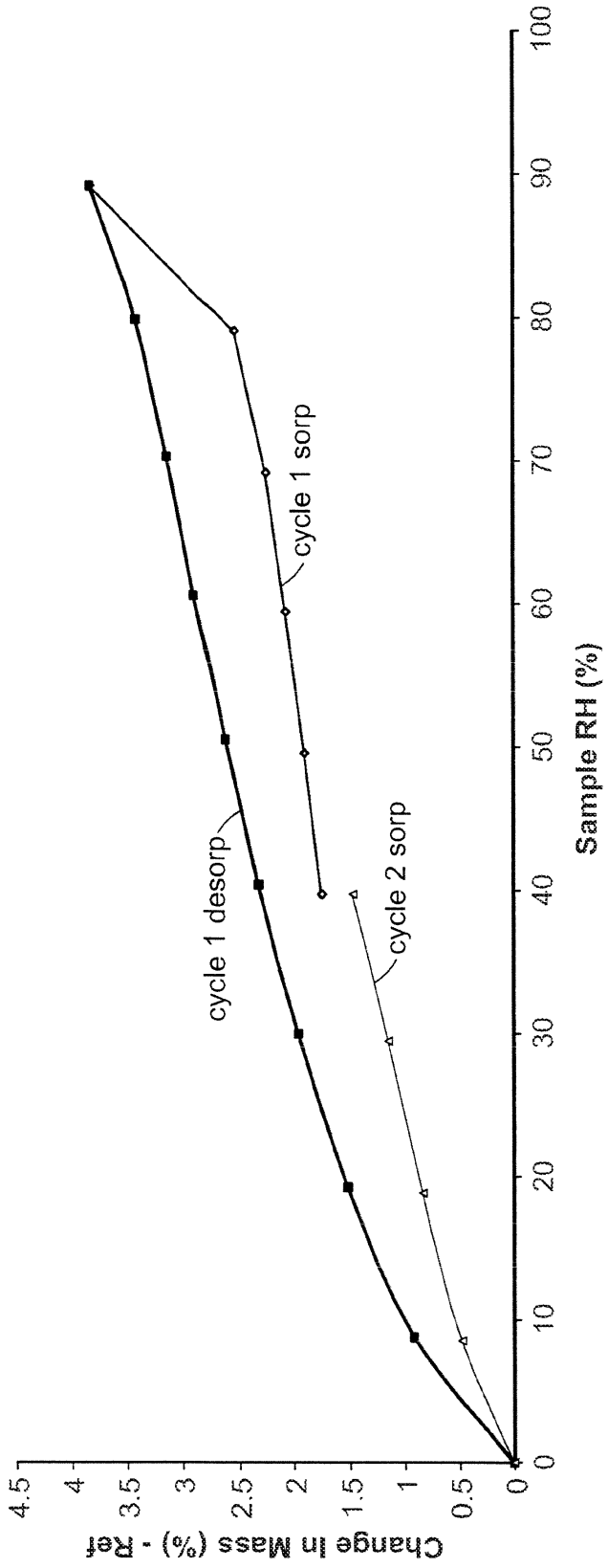

DVS Isotherm Plot
Change in Mass (%) - Ref
Sample RH (%)
cycle 1 desorp
cycle 1 sorp
cycle 2 sorp
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
0
10
20
30
40
50
60
70
80
90
100

FIG. 25

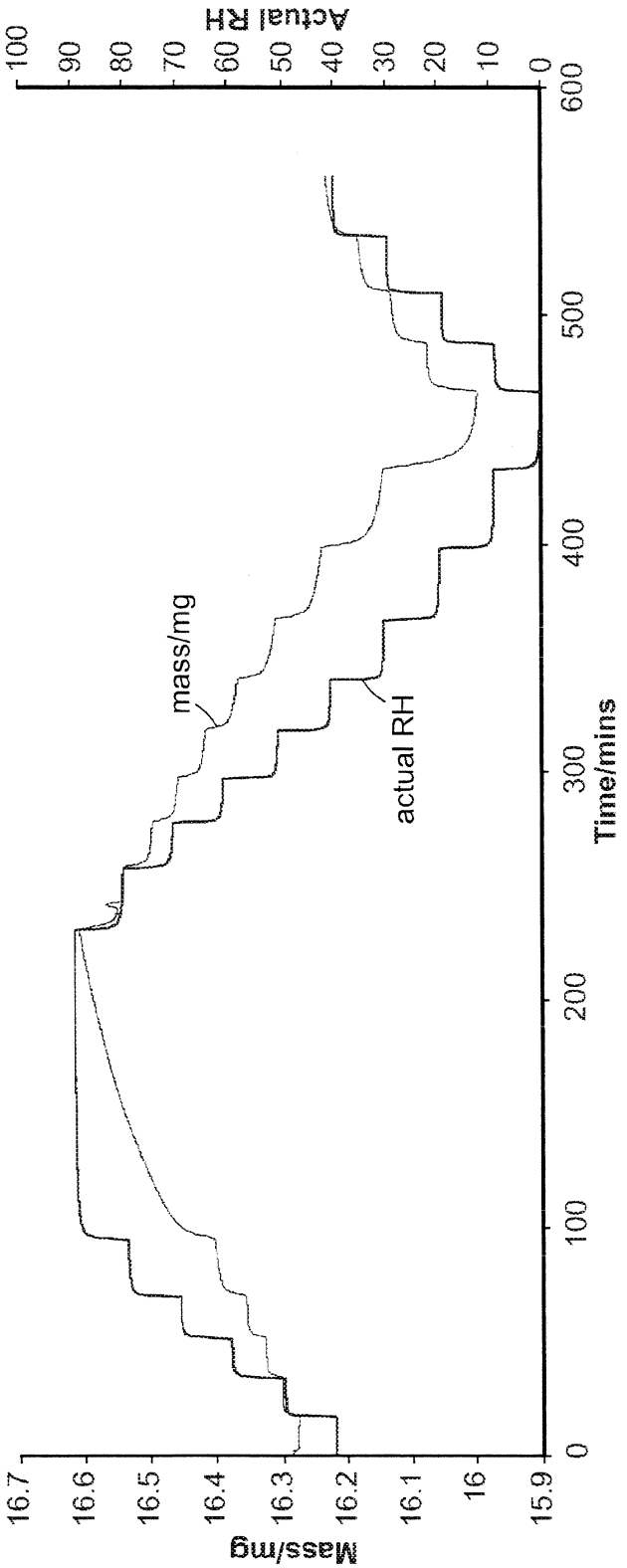

Mass/mg
16.7
16.6
16.5
16.4
16.3
16.2
16.1
16
15.9
Actual RH
100
90
80
70
60
50
40
30
20
10
0
0
100
200
300
400
500
600
Time/mins
mass/mg
actual RH

FIG. 26

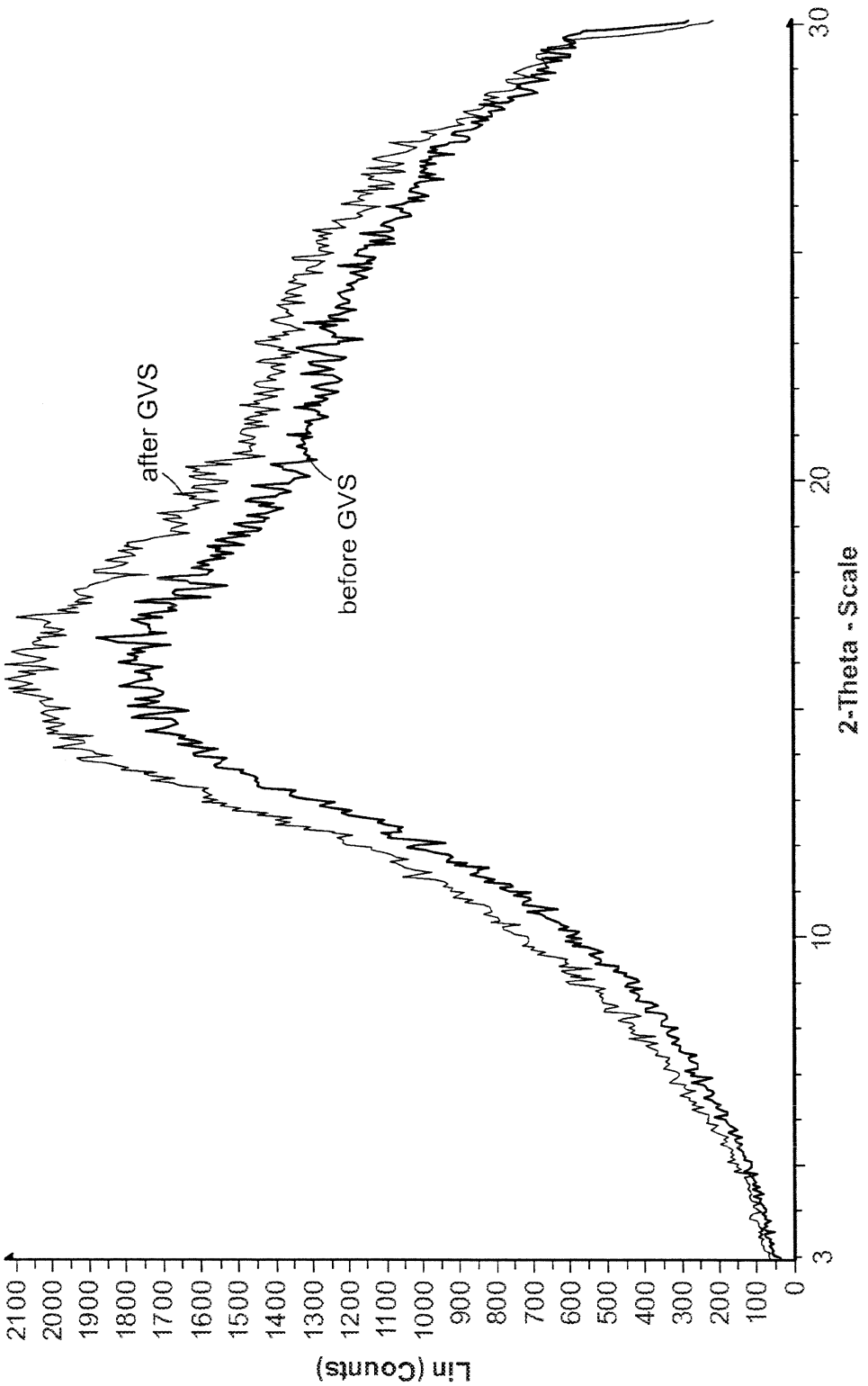

after GVS
before GVS
Lin (Counts)
2-Theta - Scale
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
3
10
20
30

FIG. 27

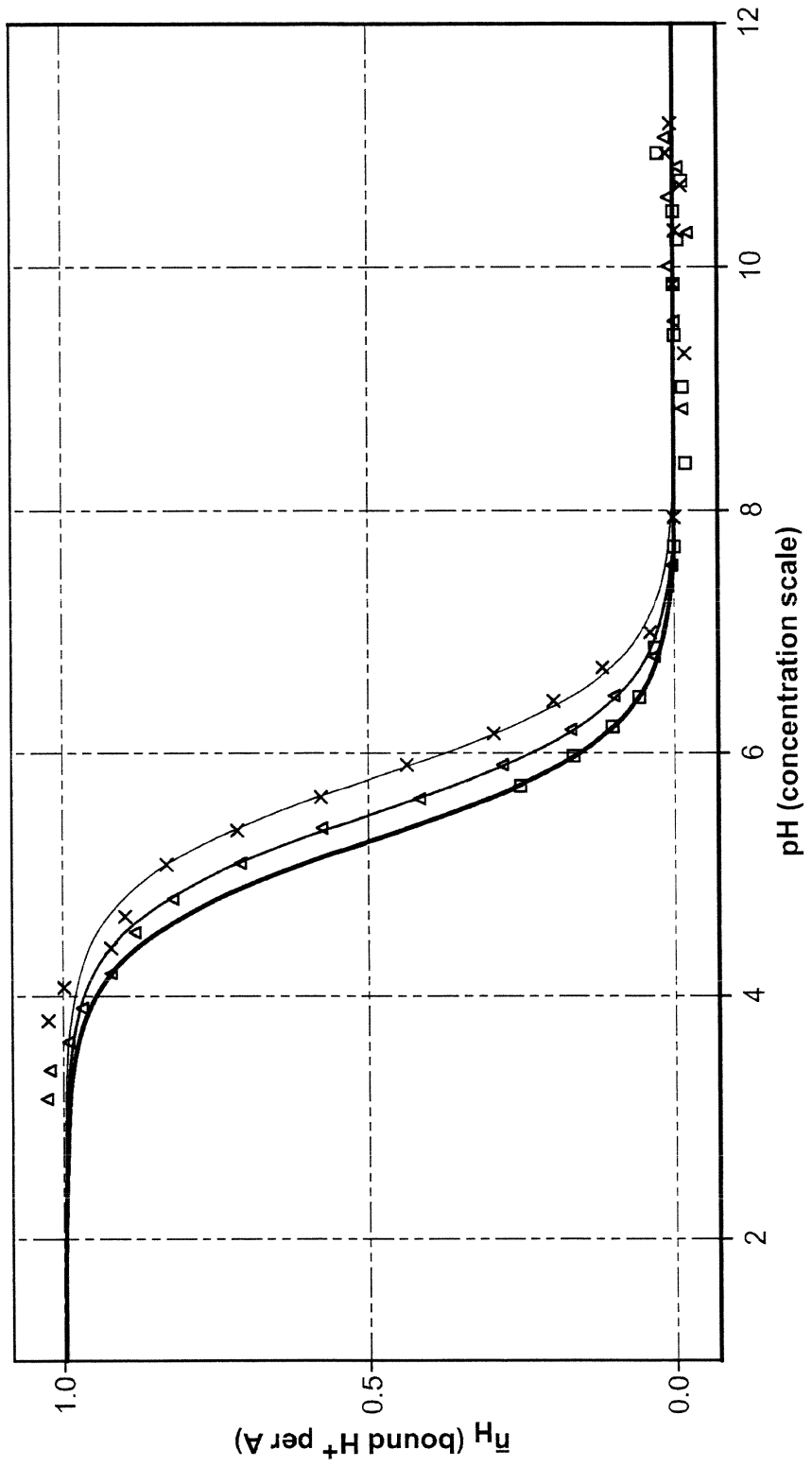
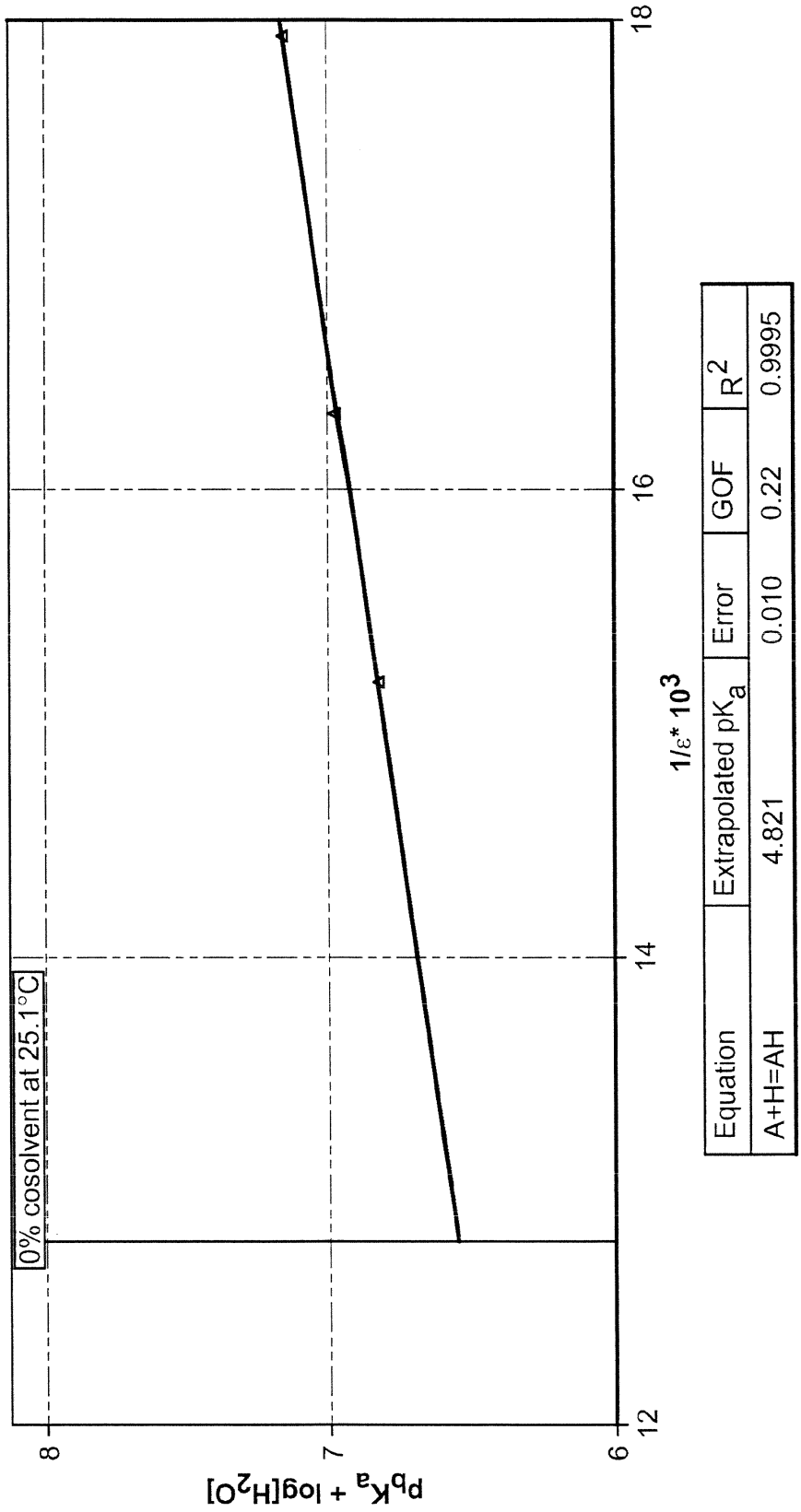


FIG. 28



Equation	Extrapolated pK_a	Error	GOF	R^2
A+H=AH	4.821	0.010	0.22	0.9995

FIG. 29

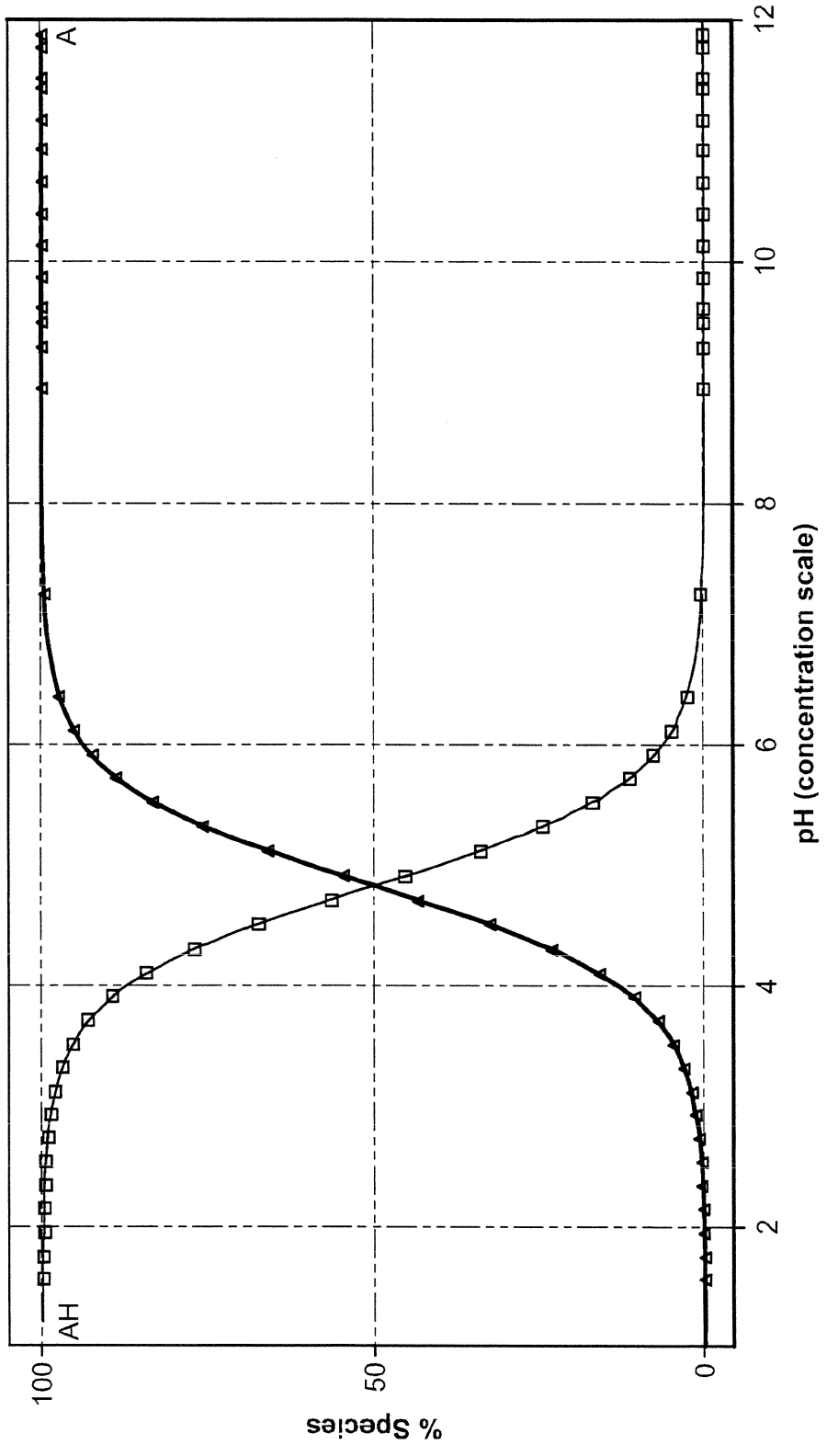


FIG. 30

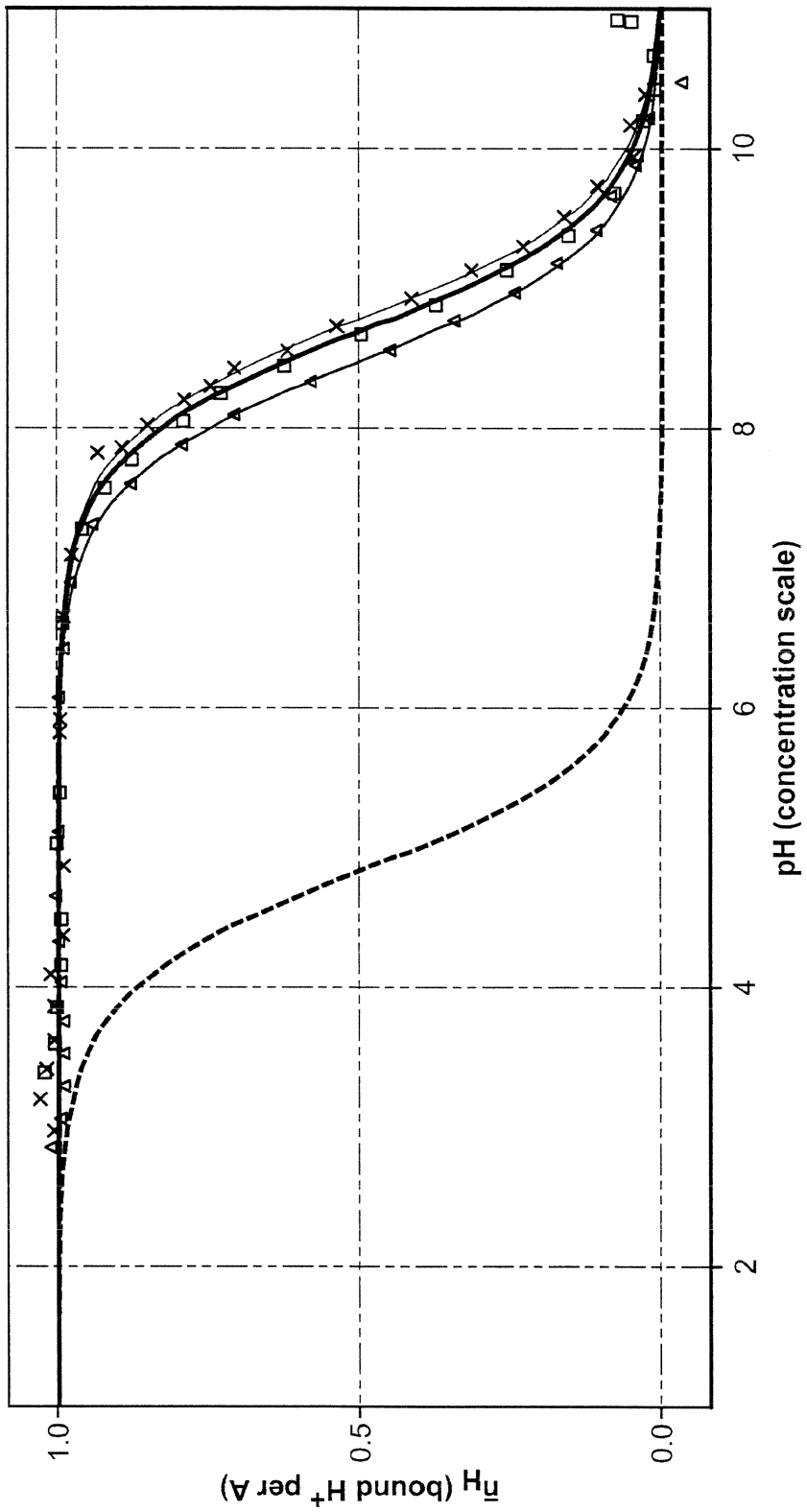


FIG. 31

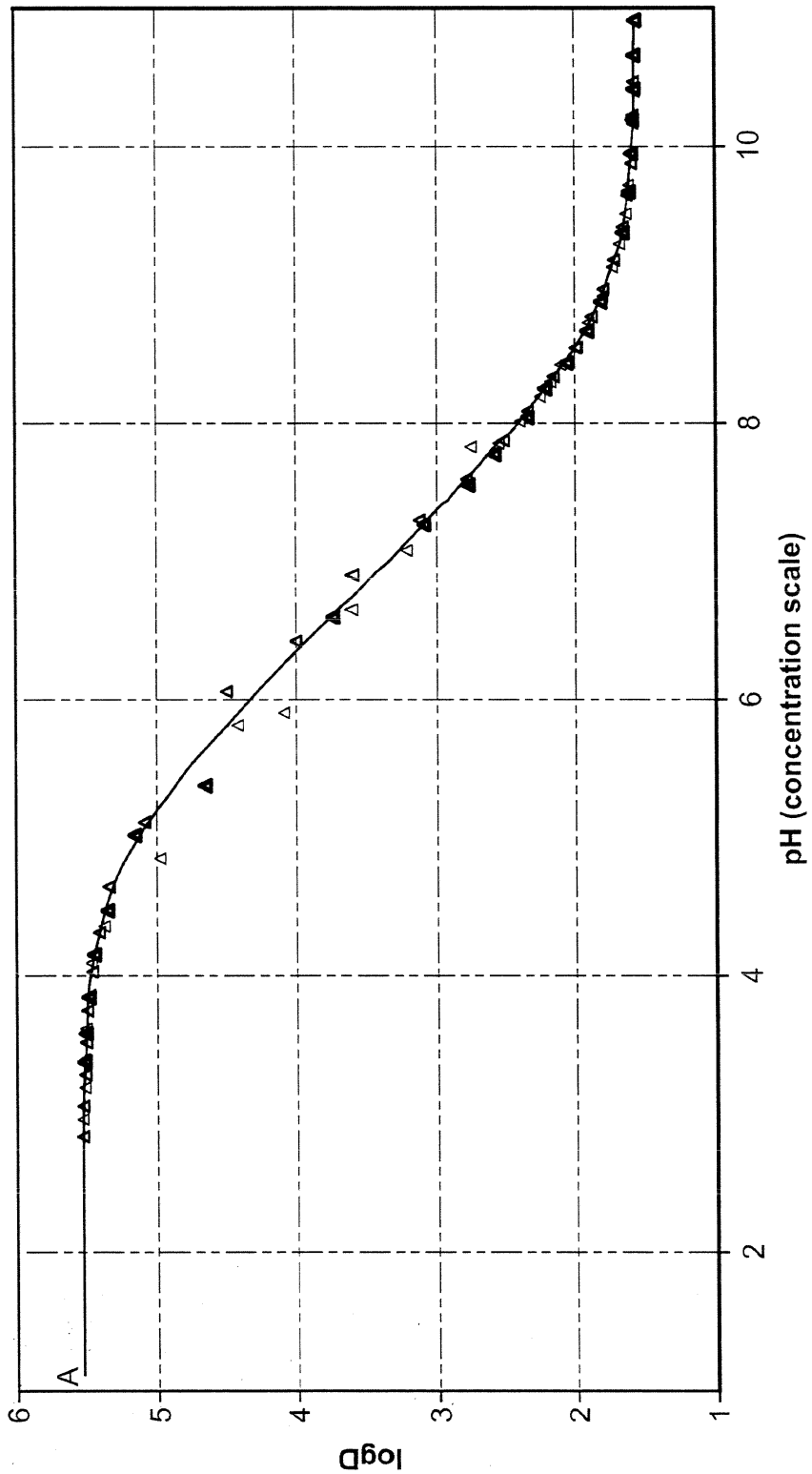


FIG. 32

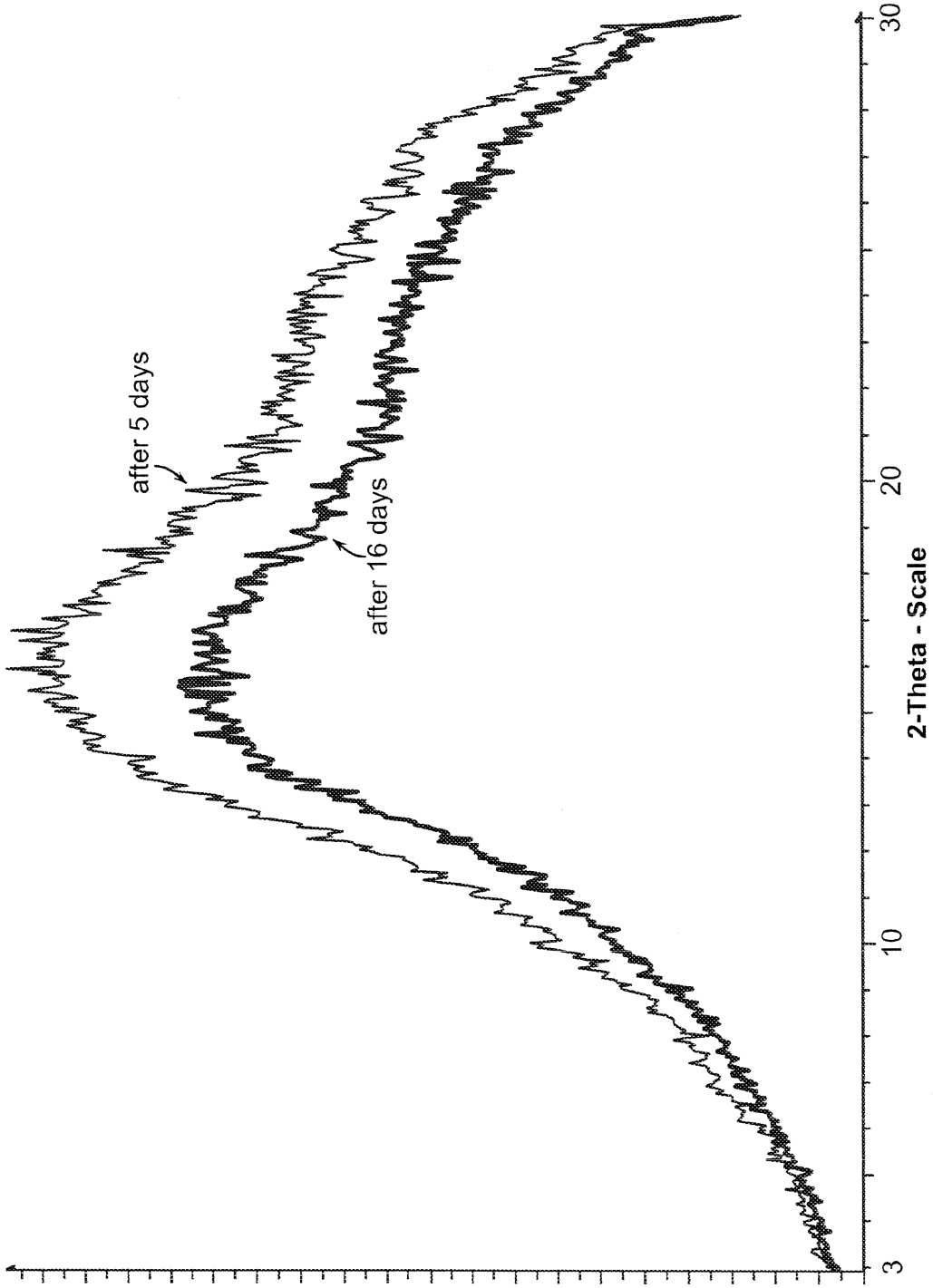
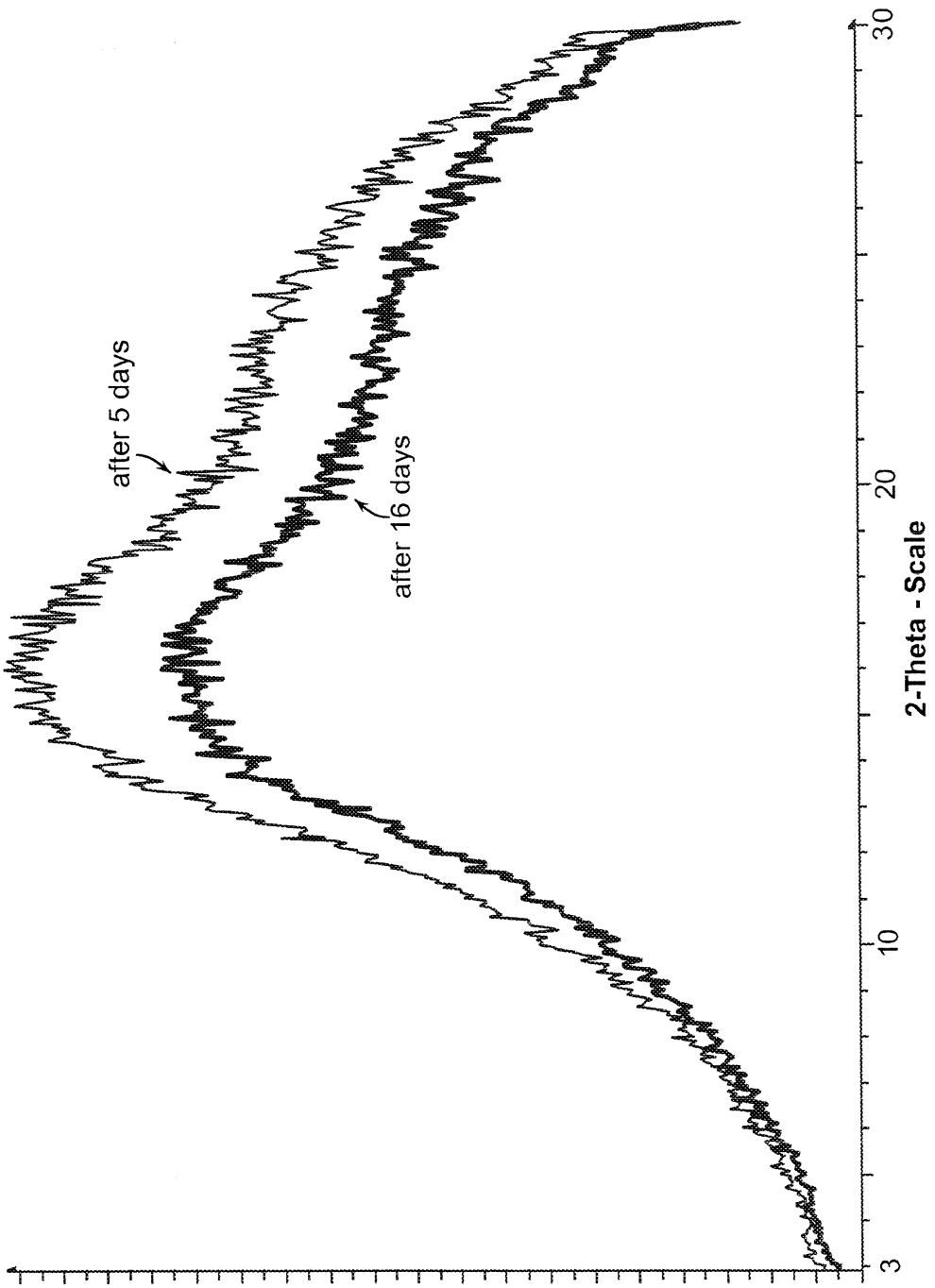

after 5 days
after 16 days
Lin (Counts)
2-Theta - Scale
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
3
10
20
30

FIG. 33


after 5 days
after 16 days
Lin (Counts)
2-Theta - Scale
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
3
10
20
30

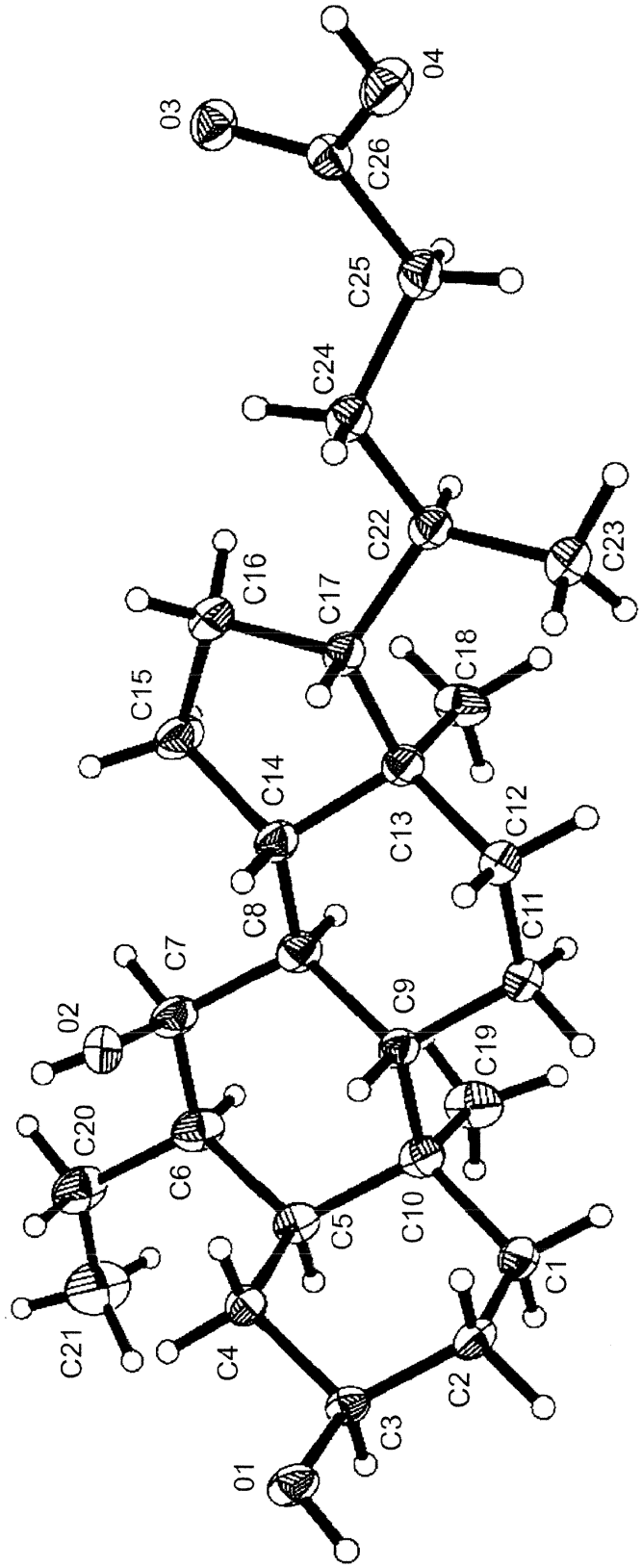

O3
O4
C26
C25
C24
C22
C23
C16
C17
C18
C15
C14
C13
C12
C8
C11
C7
O2
C9
C19
C20
C6
C5
C10
C1
C21
C4
C2
C3
O1

FIG. 34

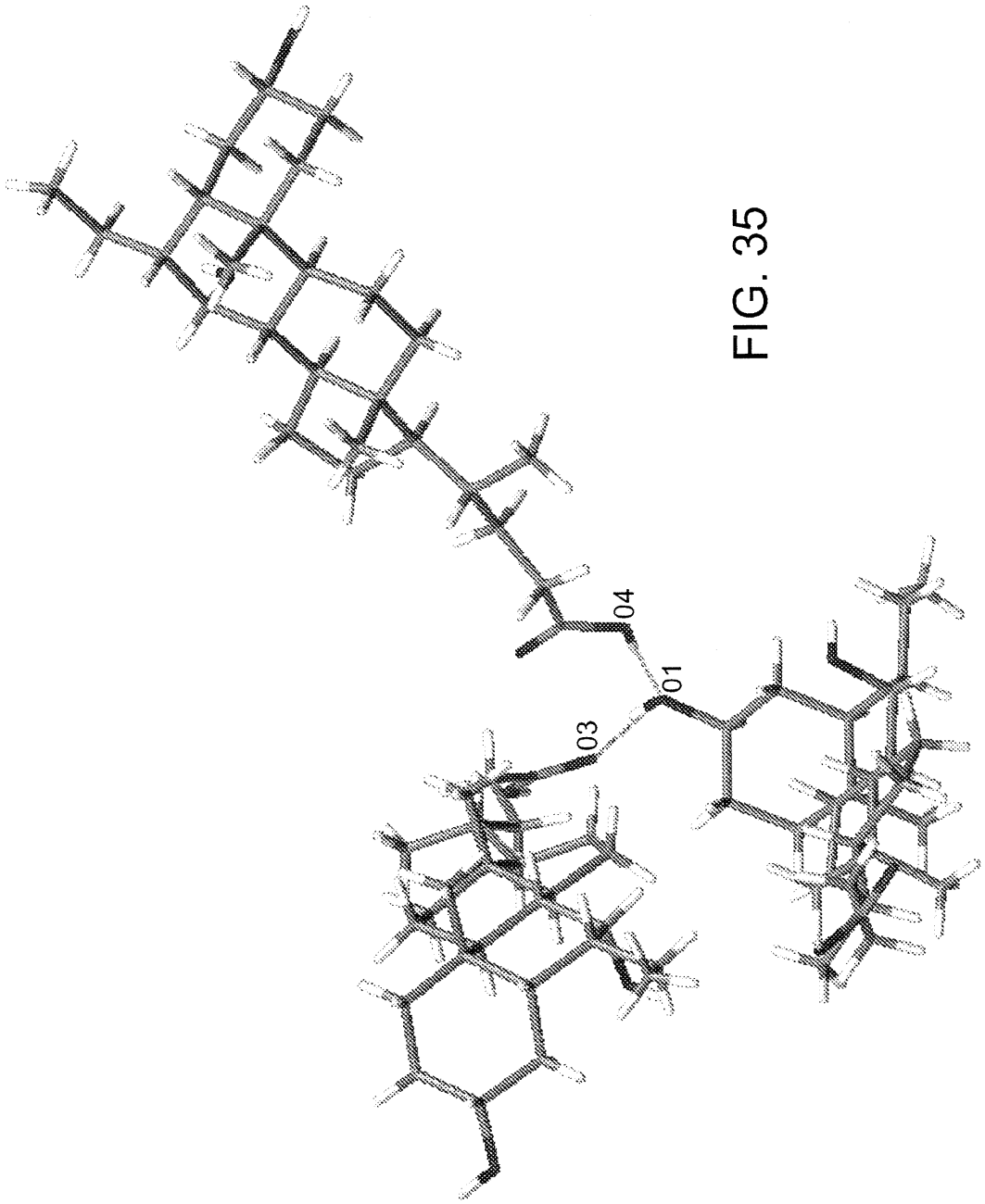


FIG. 35

FIG. 36

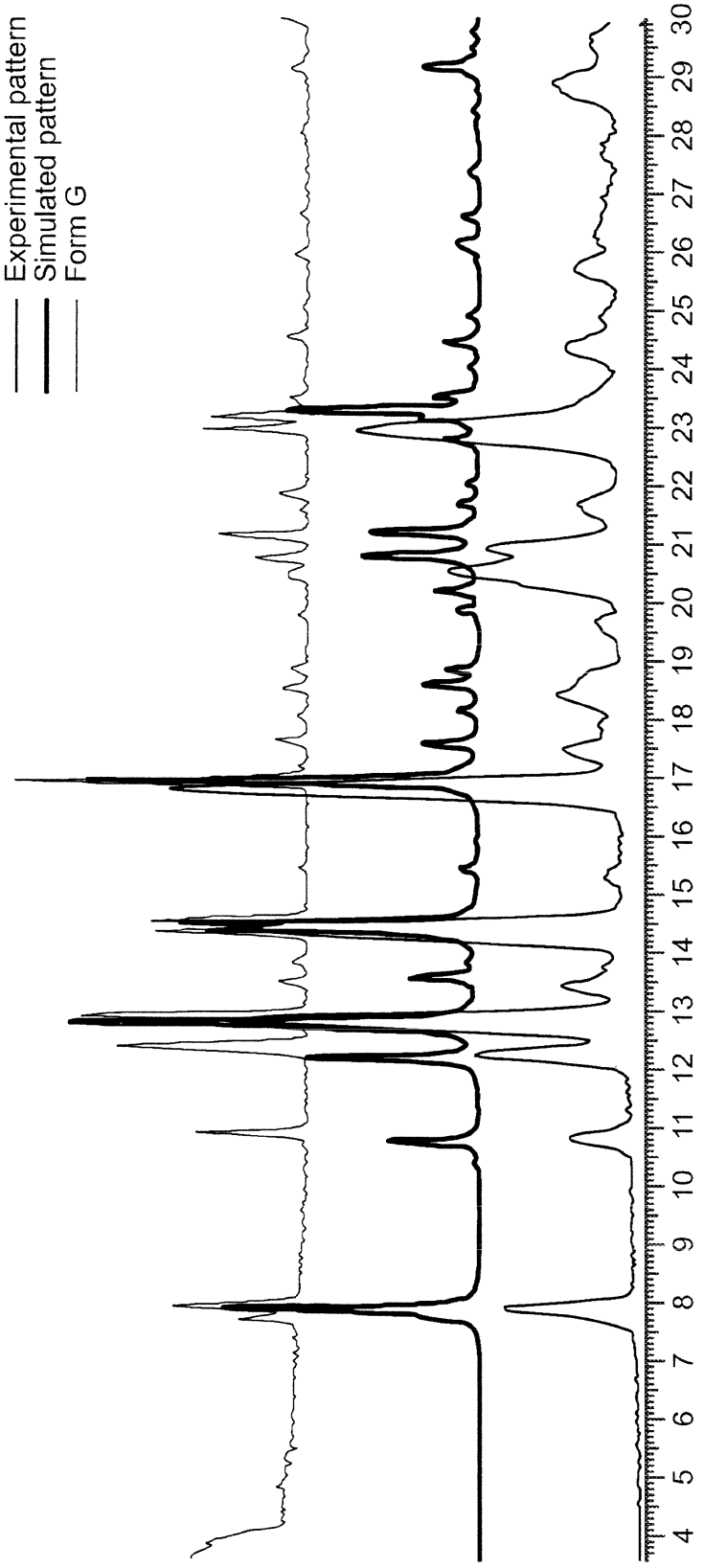

Experimental pattern
Simulated pattern
Form G
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
2-Theta - Scale

FIG. 37

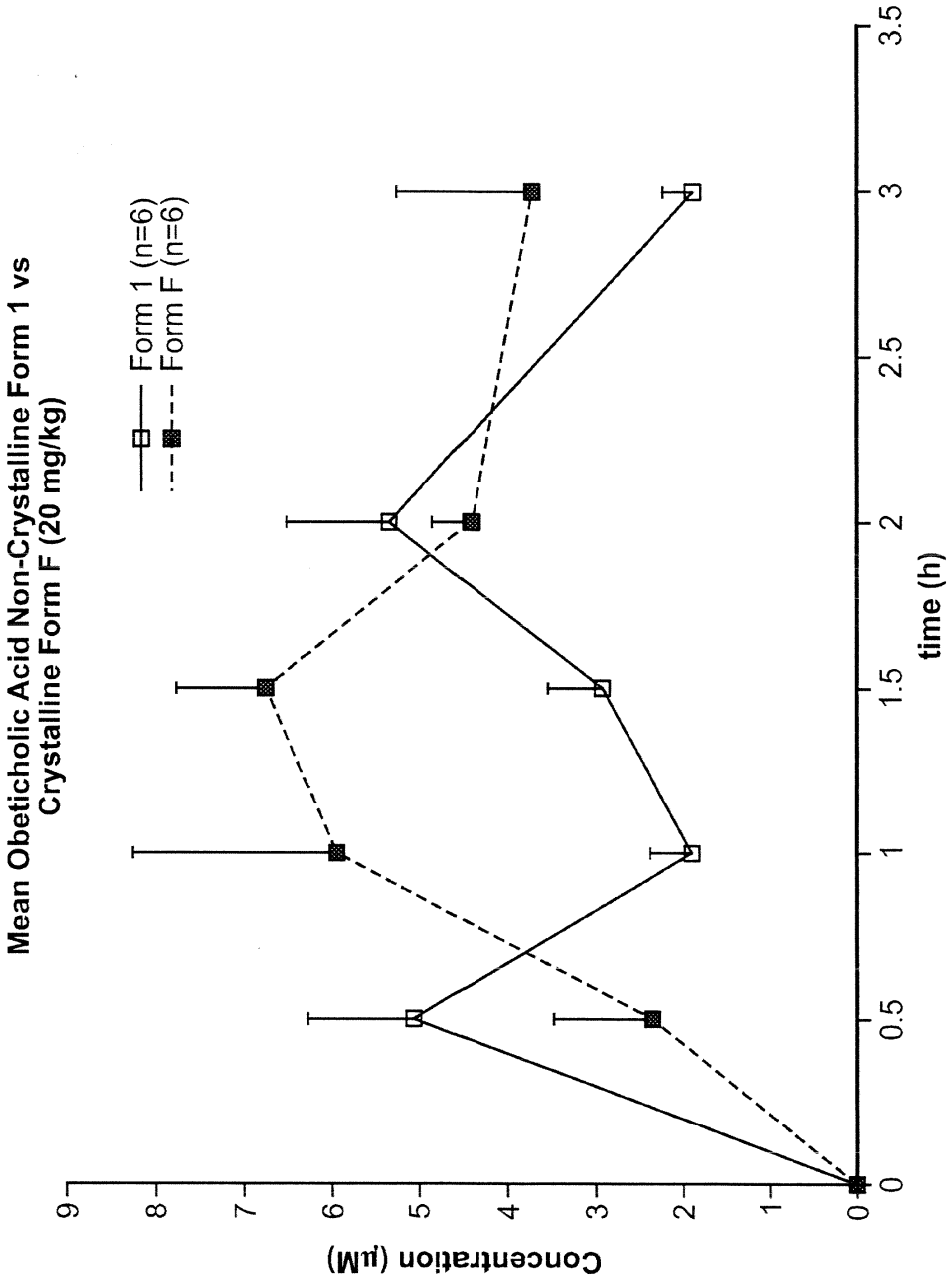

Mean Obeticholic Acid Non-Crystalline Form 1 vs
Crystalline Form F (20 mg/kg)
Form 1 (n=6)
Form F (n=6)
Concentration (μM)
time (h)
0
1
2
3
4
5
6
7
8
9
0
0.5
1
1.5
2
2.5
3
3.5

FIG. 38

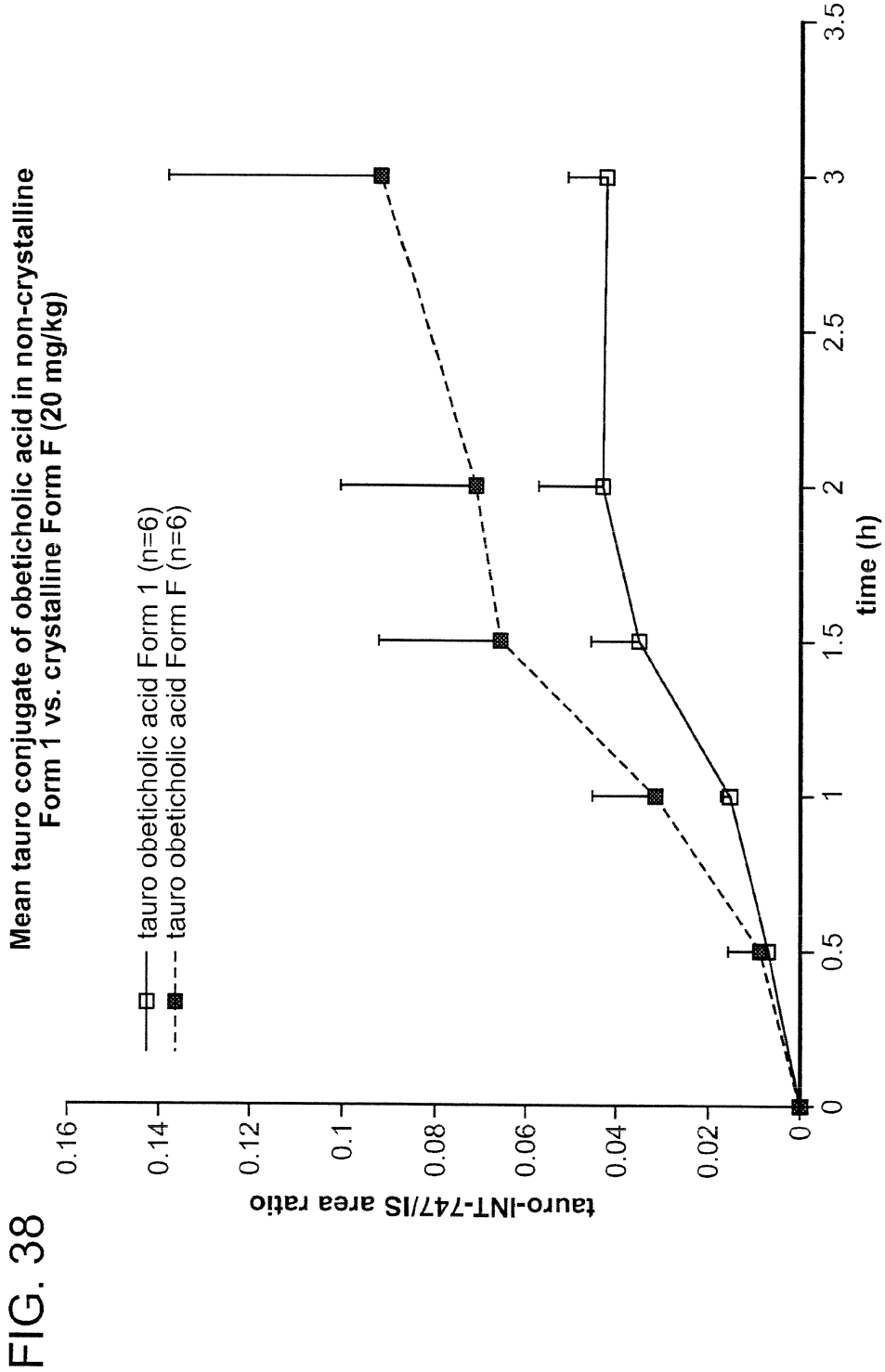

Mean tauro conjugate of obeticholic acid in non-crystalline Form 1 vs. crystalline Form F (20 mg/kg)
tauro obeticholic acid Form 1 (n=6)
tauro obeticholic acid Form F (n=6)
tauro-INT-747/IS area ratio
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.5
1
1.5
2
2.5
3
3.5
time (h)

FIG. 39

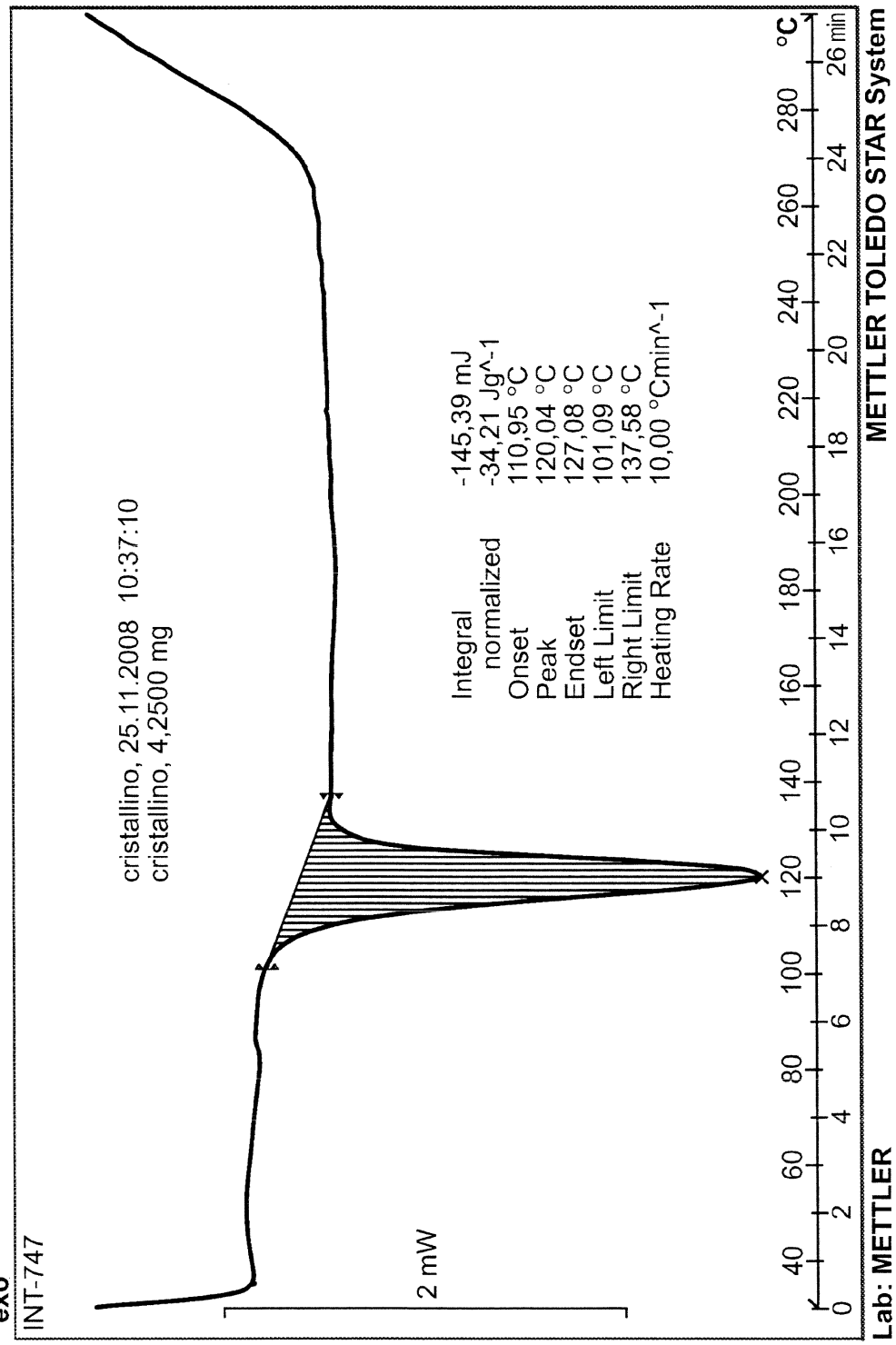
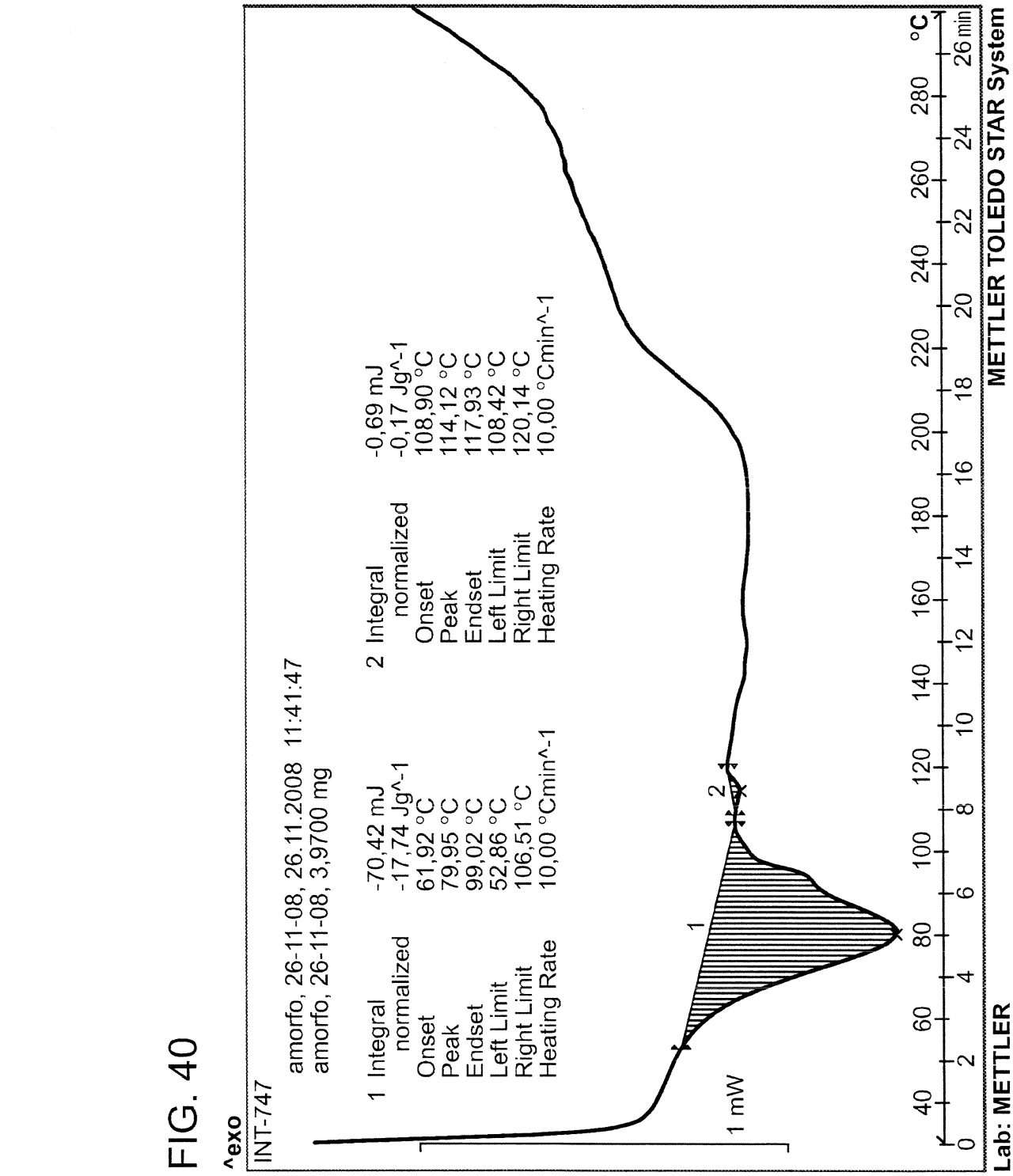

^exo
INT-747
cristallino, 25.11.2008 10:37:10
cristallino, 4,2500 mg
Integral -145,39 mJ
normalized -34,21 Jg^-1
Onset 110,95 °C
Peak 120,04 °C
Endset 127,08 °C
Left Limit 101,09 °C
Right Limit 137,58 °C
Heating Rate 10,00 °Cmin^-1
2 mW
°C
26 min
Lab: METTLER
METTLER TOLEDO STAR System

FIG. 40


^exo
INT-747
amorfo, 26-11-08, 26.11.2008 11:41:47
amorfo, 26-11-08, 3,9700 mg
1 Integral -70,42 mJ
normalized -17,74 Jg^-1
Onset 61,92 °C
Peak 79,95 °C
Endset 99,02 °C
Left Limit 52,86 °C
Right Limit 106,51 °C
Heating Rate 10,00 °Cmin^-1
2 Integral -0,69 mJ
normalized -0,17 Jg^-1
Onset 108,90 °C
Peak 114,12 °C
Endset 117,93 °C
Left Limit 108,42 °C
Right Limit 120,14 °C
Heating Rate 10,00 °Cmin^-1
1 mW
1
2
40 60 80 100 120 140 160 180 200 220 240 260 280 °C
0 2 4 6 8 10 12 14 16 18 20 22 24 26 min
Lab: METTLER
METTLER TOLEDO STAR System