FIG. 1

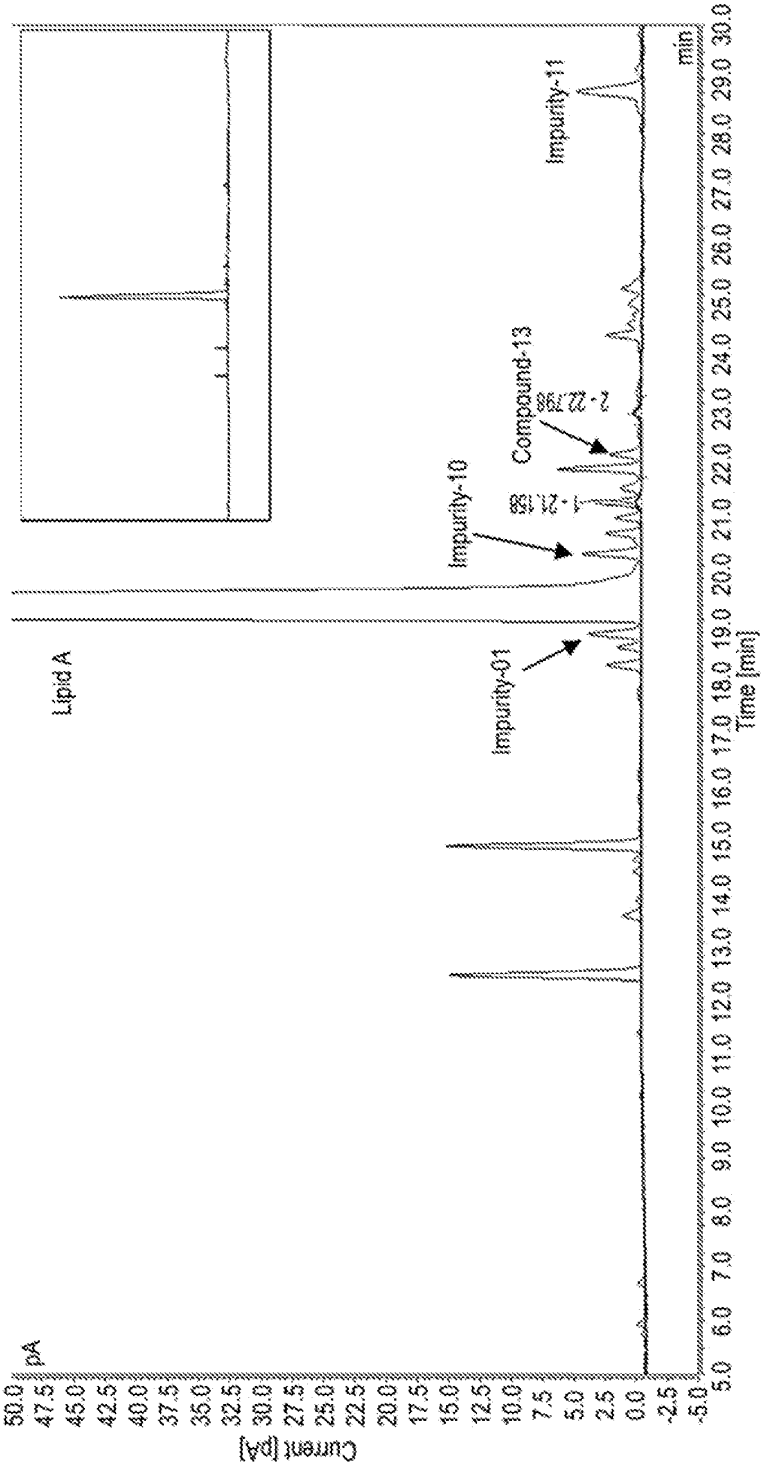

pA
Current [pA]
Time [min]
min
Lipid A
Impurity-01
Impurity-10
Compound-13
Impurity-11

FIG.2

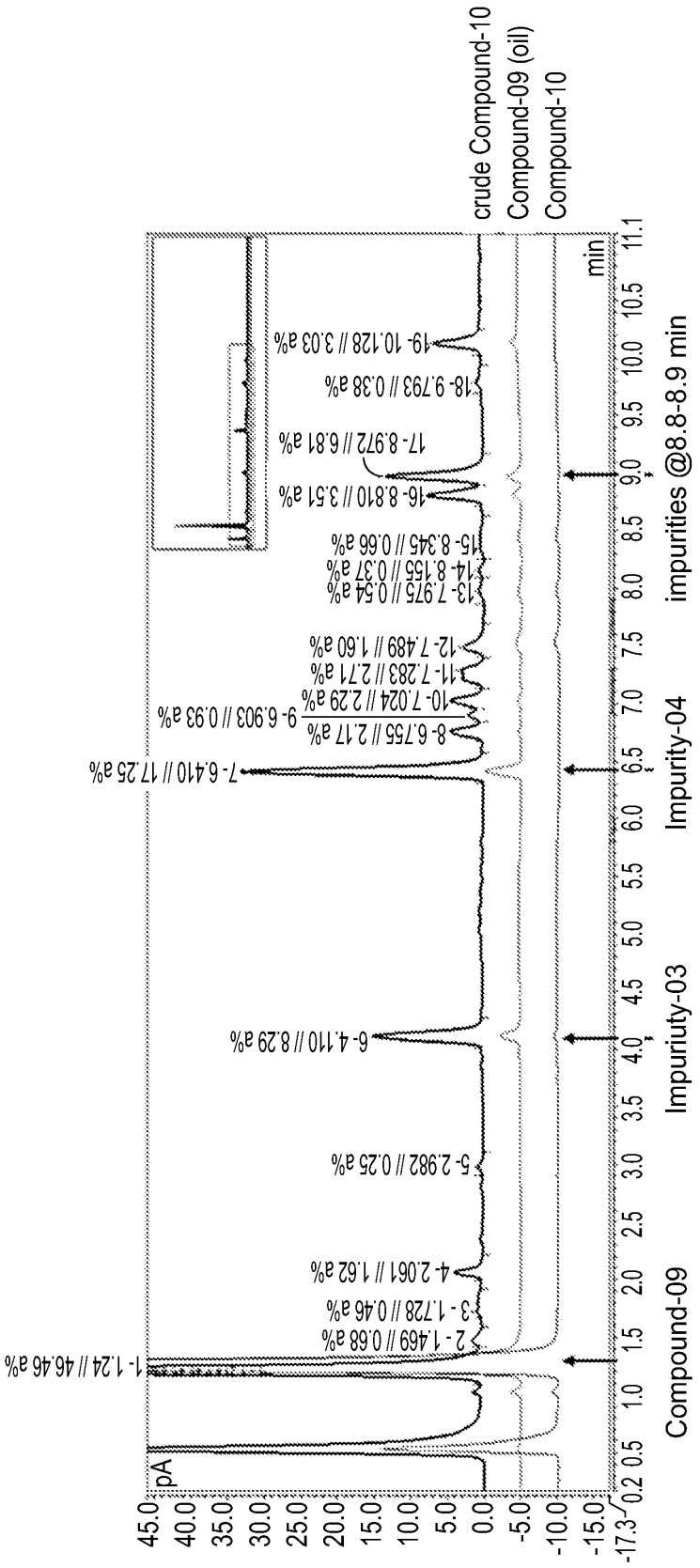
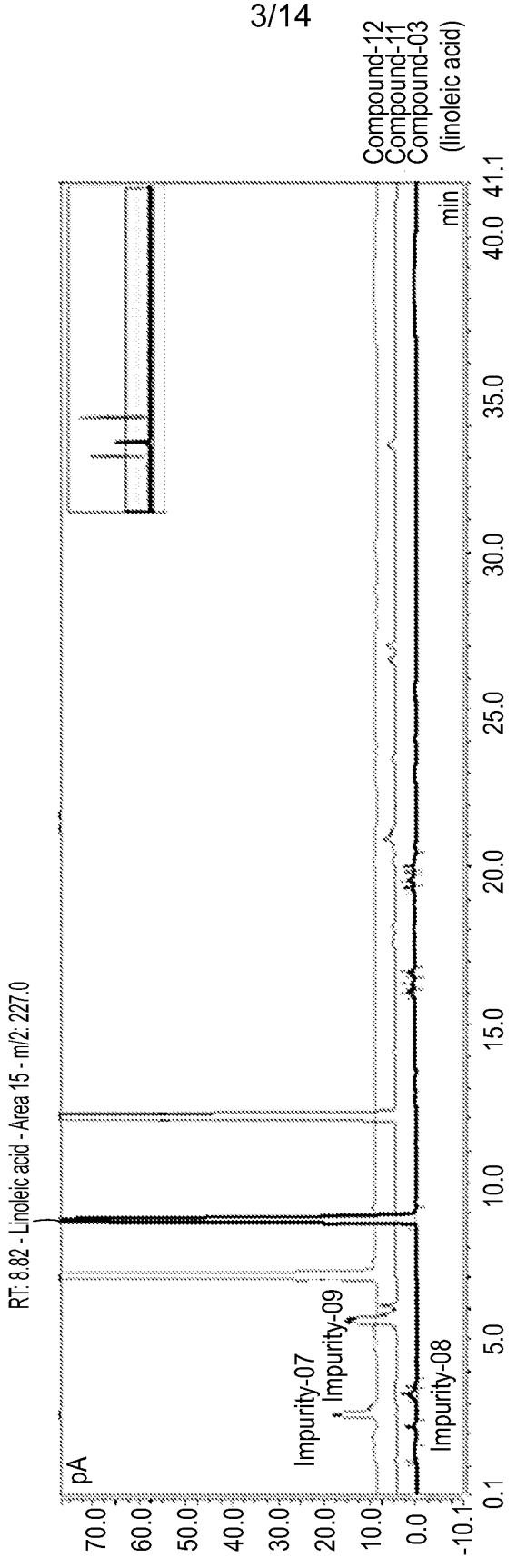

crude Compound-10
Compound-09 (oil)
Compound-10
min
pA
1- 1.24 // 46.46 a%
2- 1.469 // 0.68 a%
3- 1.728 // 0.46 a%
4- 2.061 // 1.62 a%
5- 2.982 // 0.25 a%
6- 4.110 // 8.29 a%
7- 6.410 // 17.25 a%
8- 6.755 // 2.17 a%
9- 6.903 // 0.93 a%
10- 7.024 // 2.29 a%
11- 7.283 // 2.71 a%
12- 7.489 // 1.60 a%
13- 7.975 // 0.54 a%
14- 8.155 // 0.37 a%
15- 8.345 // 0.66 a%
16- 8.810 // 3.51 a%
17- 8.972 // 6.81 a%
18- 9.793 // 0.38 a%
19- 10.128 // 3.03 a%
Compound-09
Impuriuty-03
Impurity-04
impurities @8.8-8.9 min

FIG.3


RT: 8.82 - Linoleic acid - Area 15 - m/2: 227.0
pA
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.1
0.1
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
41.1
min
Impurity-07
Impurity-09
Impurity-08
Compound-12
Compound-11
Compound-03
(linoleic acid)

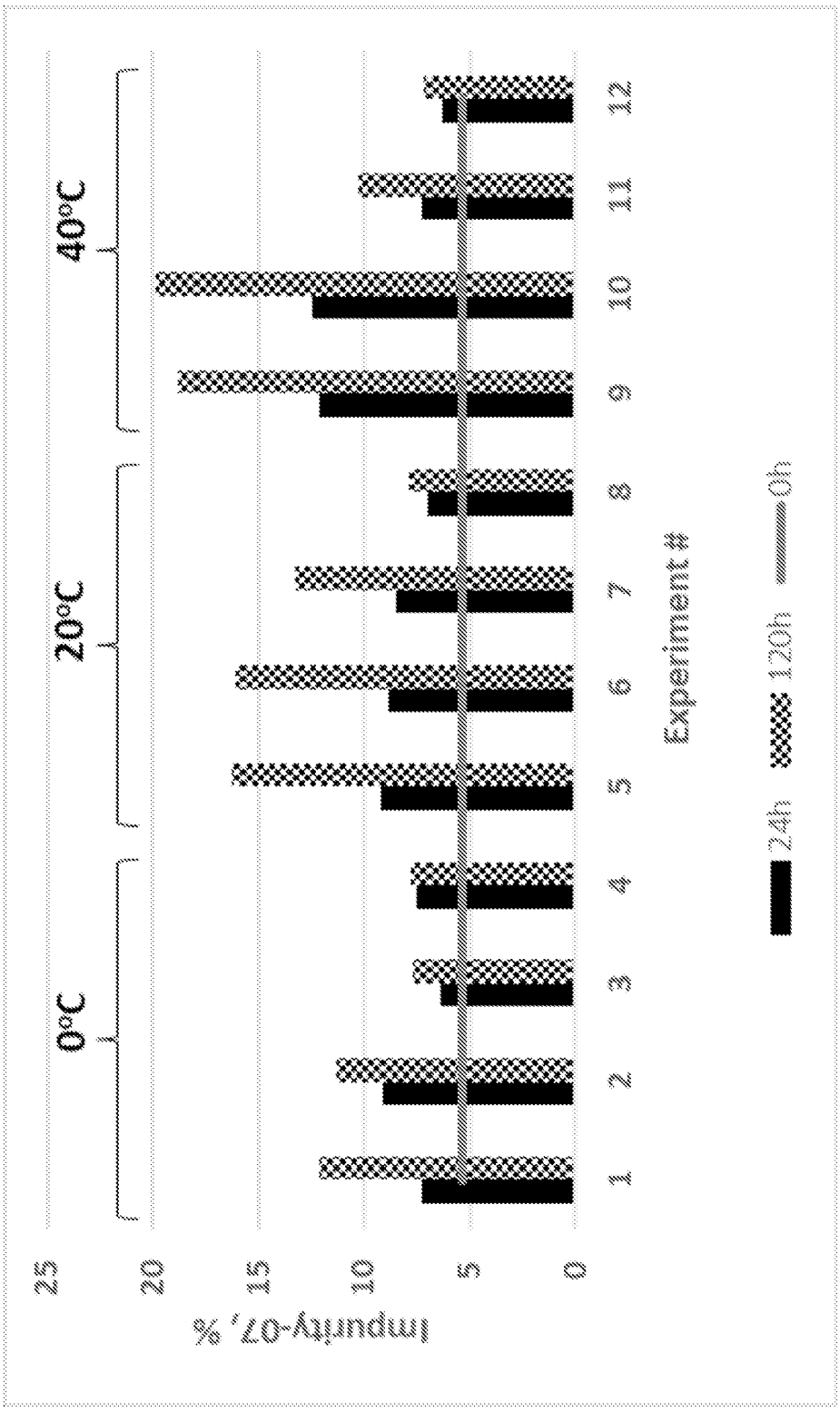

Impurity-07, %
25
20
15
10
5
0
0°C
20°C
40°C
1
2
3
4
5
6
7
8
9
10
11
12
Experiment #
24h
120h
0h

FIG. 4

FIG. 5

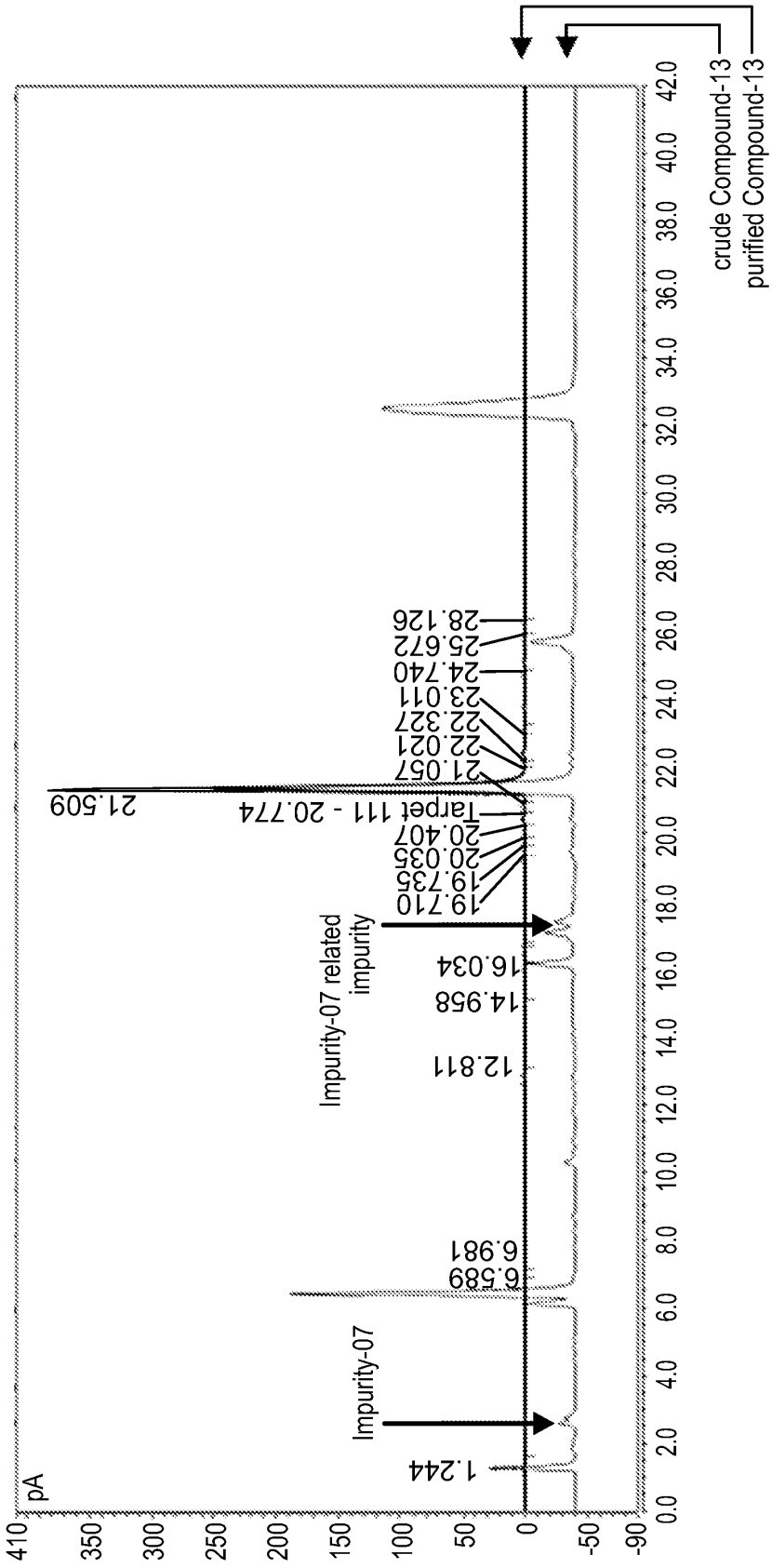

crude Compound-13
purified Compound-13
pA
410
350
300
250
200
150
100
50
0
-50
-90
0.0
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
22.0
24.0
26.0
28.0
30.0
32.0
34.0
36.0
38.0
40.0
42.0
1.244
Impurity-07
6.589
6.981
12.811
14.958
16.034
Impurity-07 related impurity
19.710
19.735
20.035
20.407
Target 111 - 20.774
21.509
21.057
22.021
22.327
23.011
24.740
25.672
28.126

FIG. 6

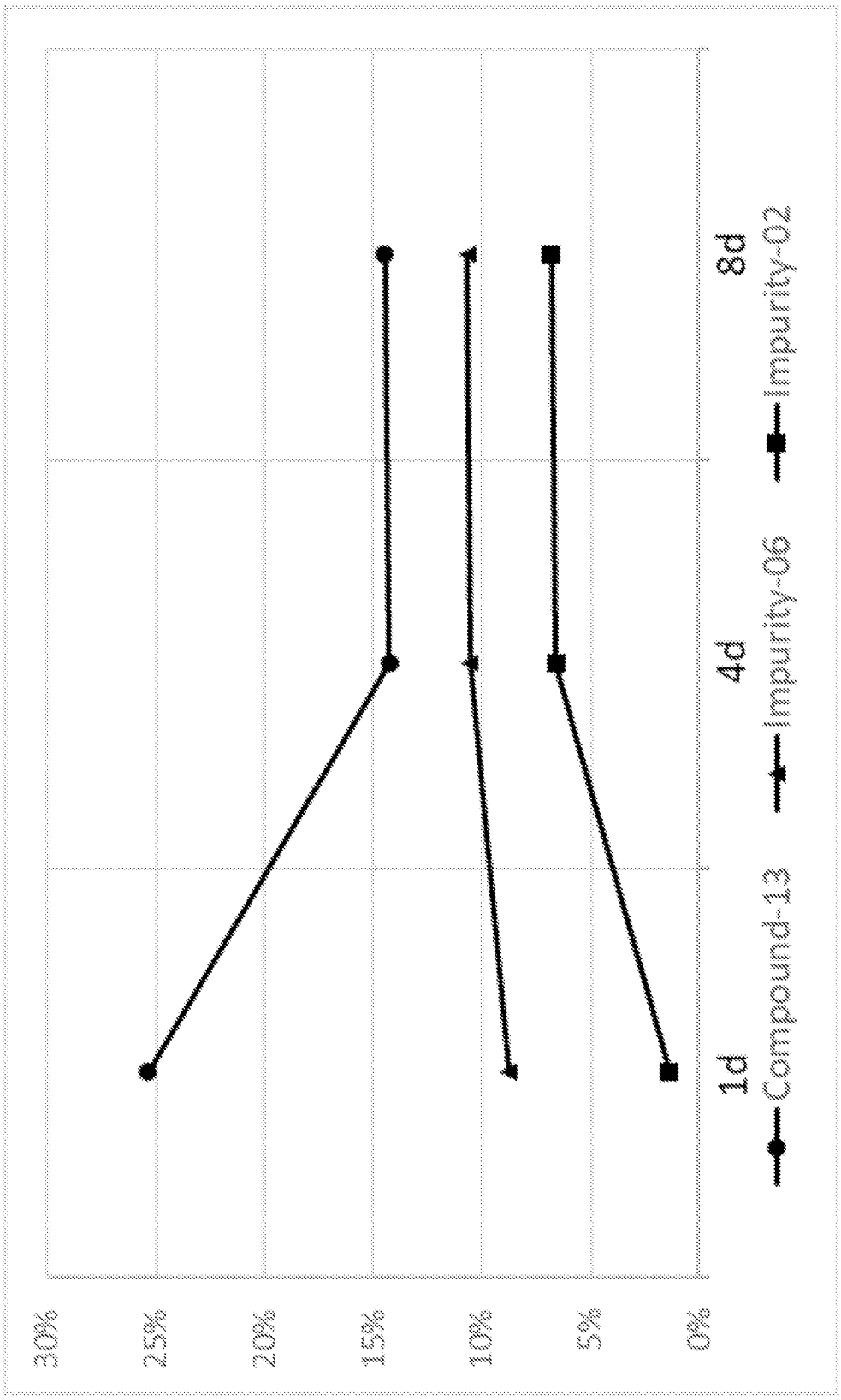
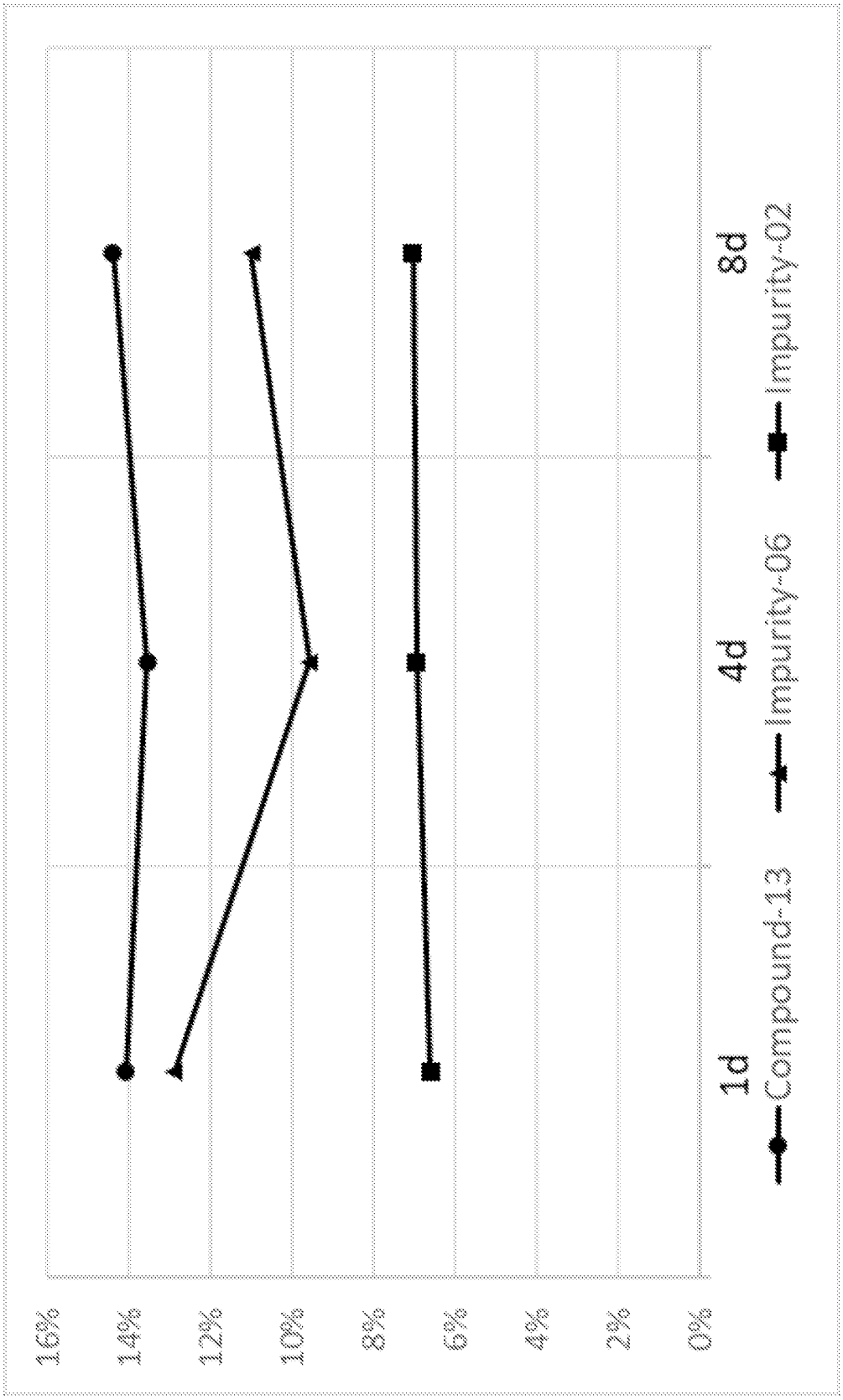


FIG. 7



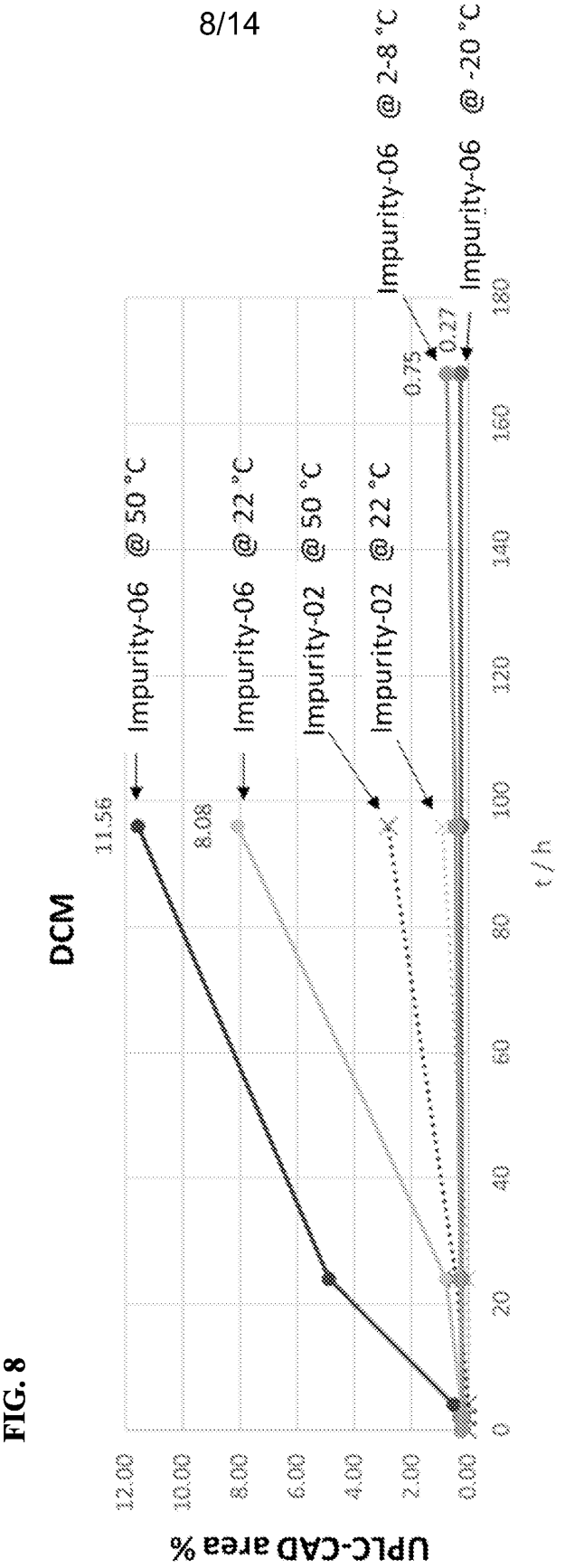

DCM
Impurity-06 @ 50 °C
Impurity-06 @ 22 °C
Impurity-02 @ 50 °C
Impurity-02 @ 22 °C
Impurity-06 @ 2-8 °C
Impurity-06 @ -20 °C
11.56
8.08
0.75
0.27
UPLC-CAD area %
t / h
0.00
2.00
4.00
6.00
8.00
10.00
12.00
0
20
40
60
80
100
120
140
160
180

FIG. 8

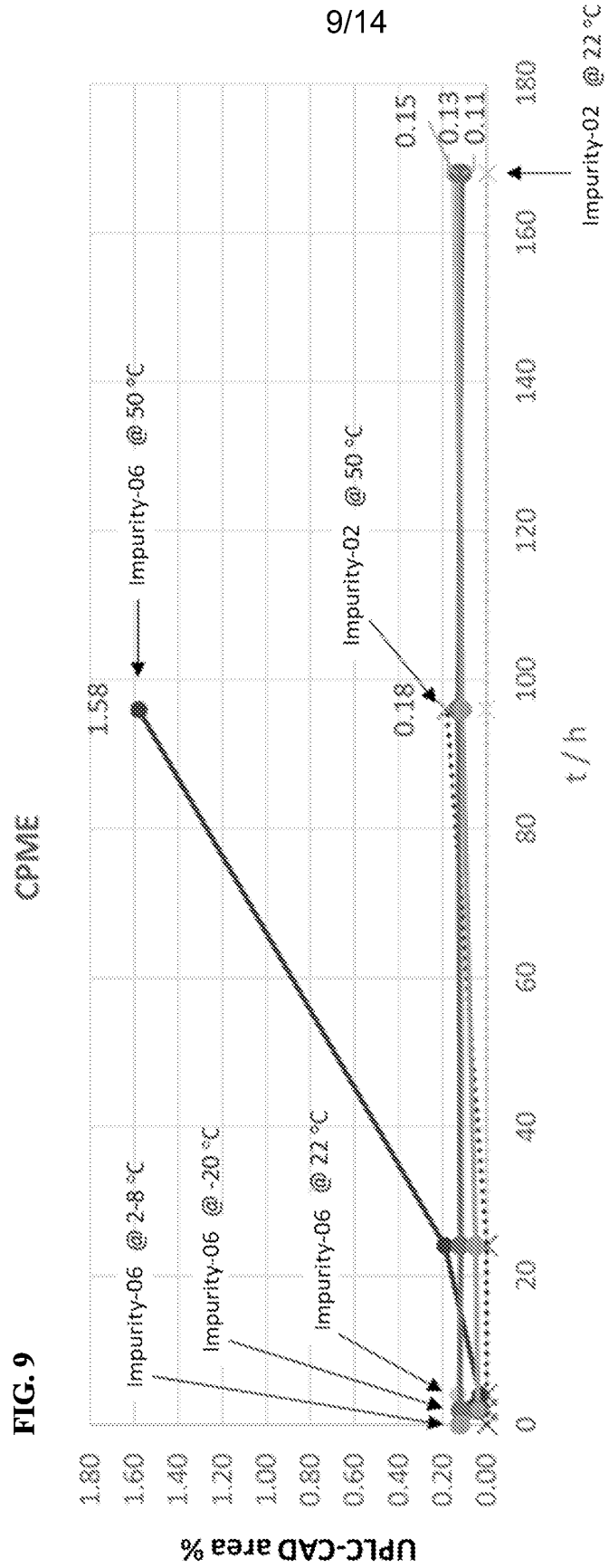

CPME
UPLC-CAD area %
t / h
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0
20
40
60
80
100
120
140
160
180
1.58
0.18
0.15
0.13
0.11
Impurity-06 @ 50 °C
Impurity-02 @ 50 °C
Impurity-02 @ 22 °C
Impurity-06 @ 2-8 °C
Impurity-06 @ -20 °C
Impurity-06 @ 22 °C

FIG. 9

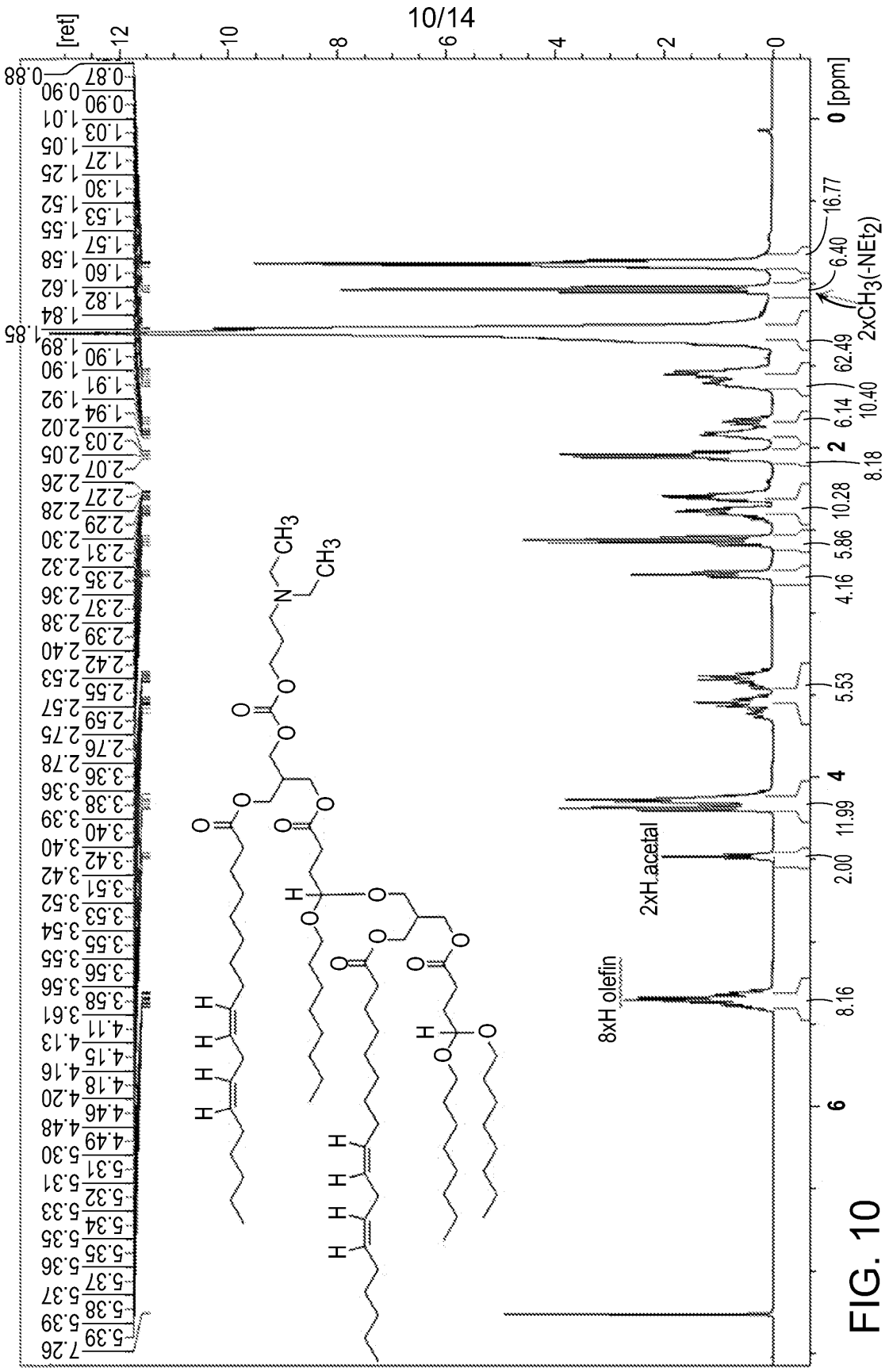

[ret]
12
10
8
6
4
2
0
0 [ppm]
16.77
6.40
2xCH3(-NEt2)
62.49
6.14
10.40
2
8.18
10.28
5.86
4.16
5.53
4
11.99
2.00
2xH_acetal
8xH_olefin
8.16
6
CH3
CH3
N

FIG. 10

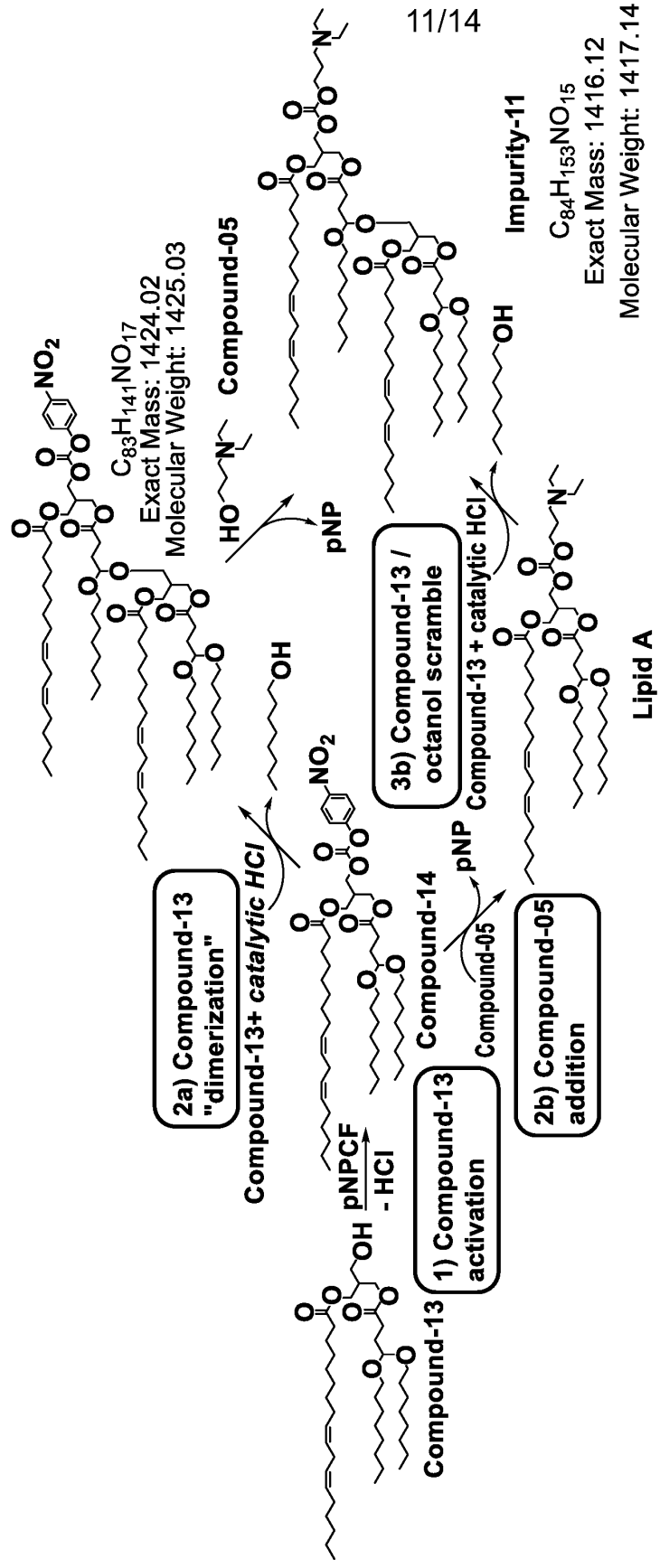

Compound-13
1) Compound-13 activation
pNPCF
- HCl
Compound-14
2a) Compound-13 "dimerization"
Compound-13+ catalytic HCl
Compound-05
2b) Compound-05 addition
pNP
Compound-13 + catalytic HCl
3b) Compound-13 / octanol scramble
Lipid A
Chemical Formula: C50H93NO9
Exact Mass: 851.69
Molecular Weight: 852.29
Impurity-11
C84H153NO15
Exact Mass: 1416.12
Molecular Weight: 1417.14
C83H141NO17
Exact Mass: 1424.02
Molecular Weight: 1425.03
Compound-05
pNP

FIG. 11

FIG. 12

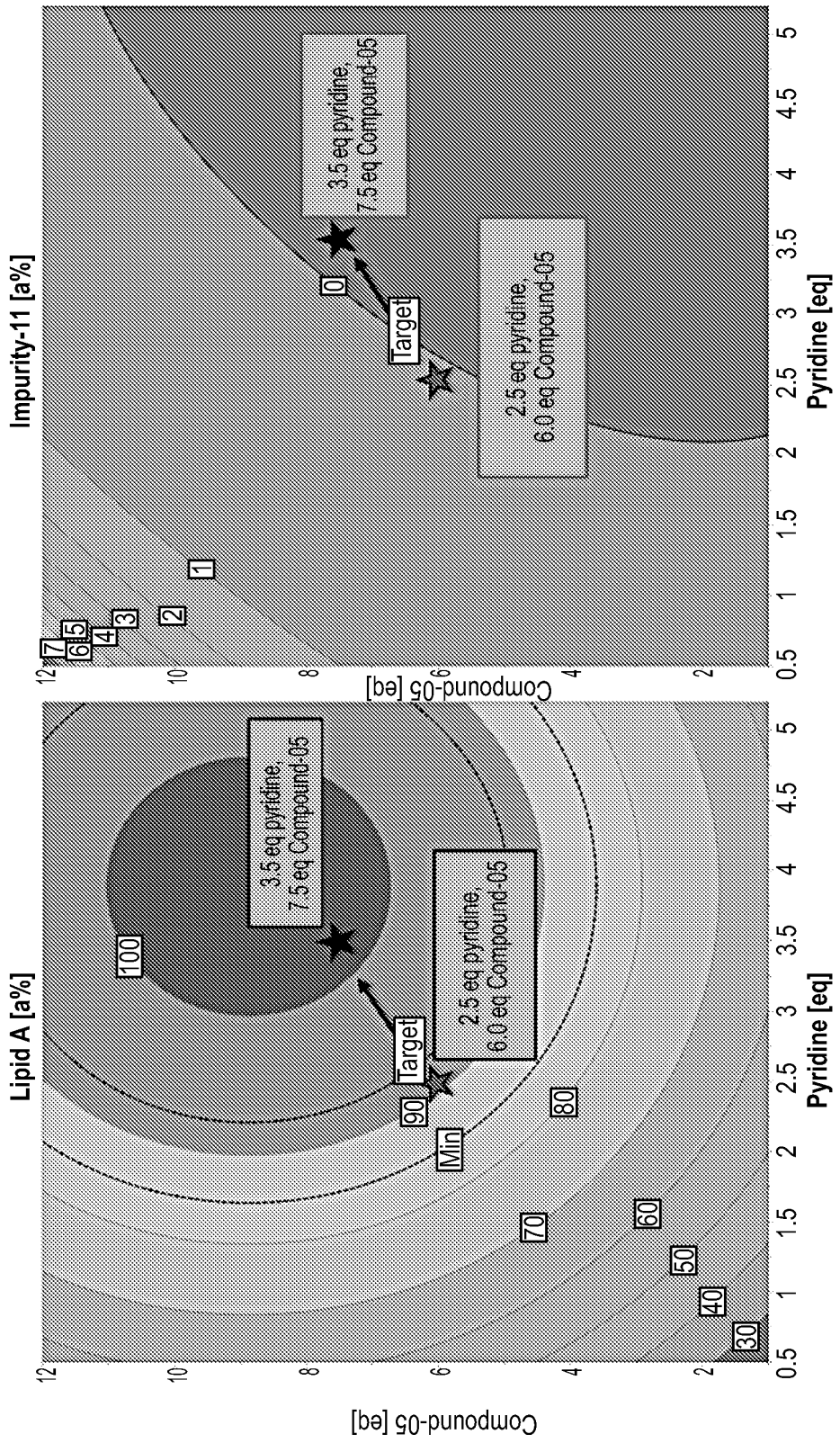

Impurity-11 [a%]
Compound-05 [eq]
Pyridine [eq]
3.5 eq pyridine,
7.5 eq Compound-05
2.5 eq pyridine,
6.0 eq Compound-05
Target
0
1
2
3
4
5
6
7
Lipid A [a%]
Compound-05 [eq]
Pyridine [eq]
3.5 eq pyridine,
7.5 eq Compound-05
2.5 eq pyridine,
6.0 eq Compound-05
Target
Min
100
90
80
70
60
50
40
30

FIG. 13

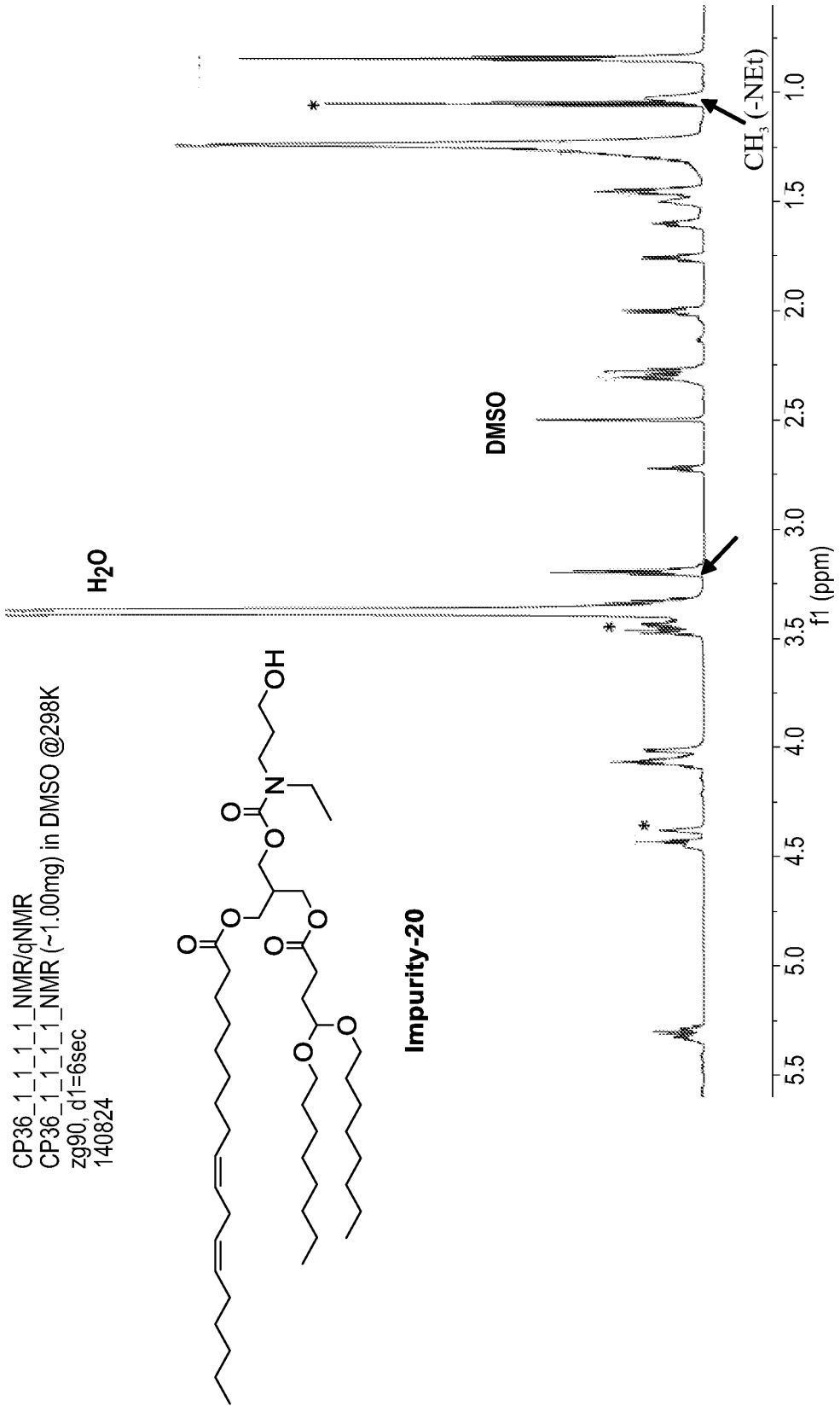
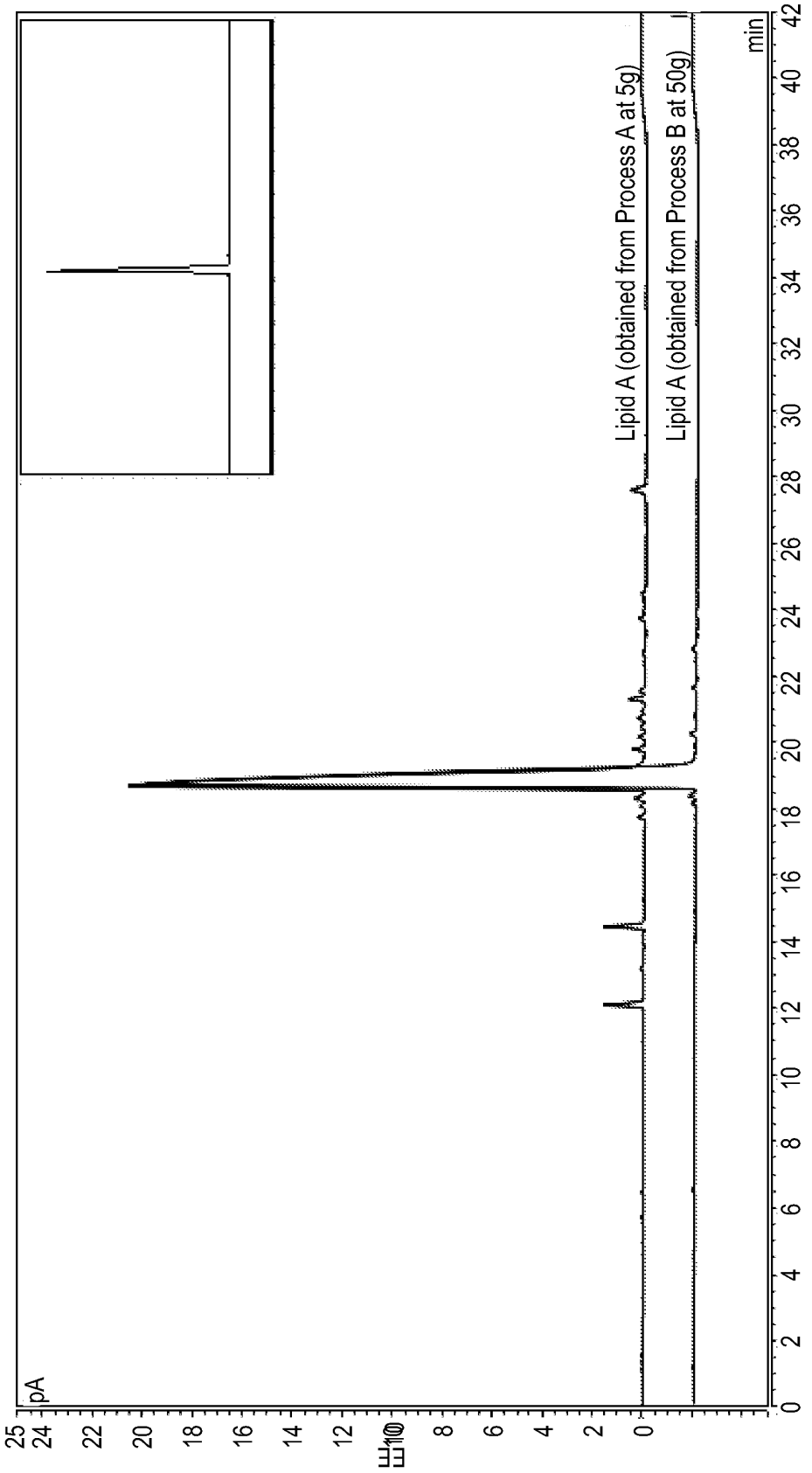

CP36_1_1_1_1_NMR/qNMR
CP36_1_1_1_1_NMR (~1.00mg) in DMSO @298K
zg90, d1=6sec
140824
H2O
DMSO
CH3 (-NEt)
Impurity-20
OH
N
O
f1 (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

FIG. 14


pA
min
Lipid A (obtained from Process A at 5g)
Lipid A (obtained from Process B at 50g)