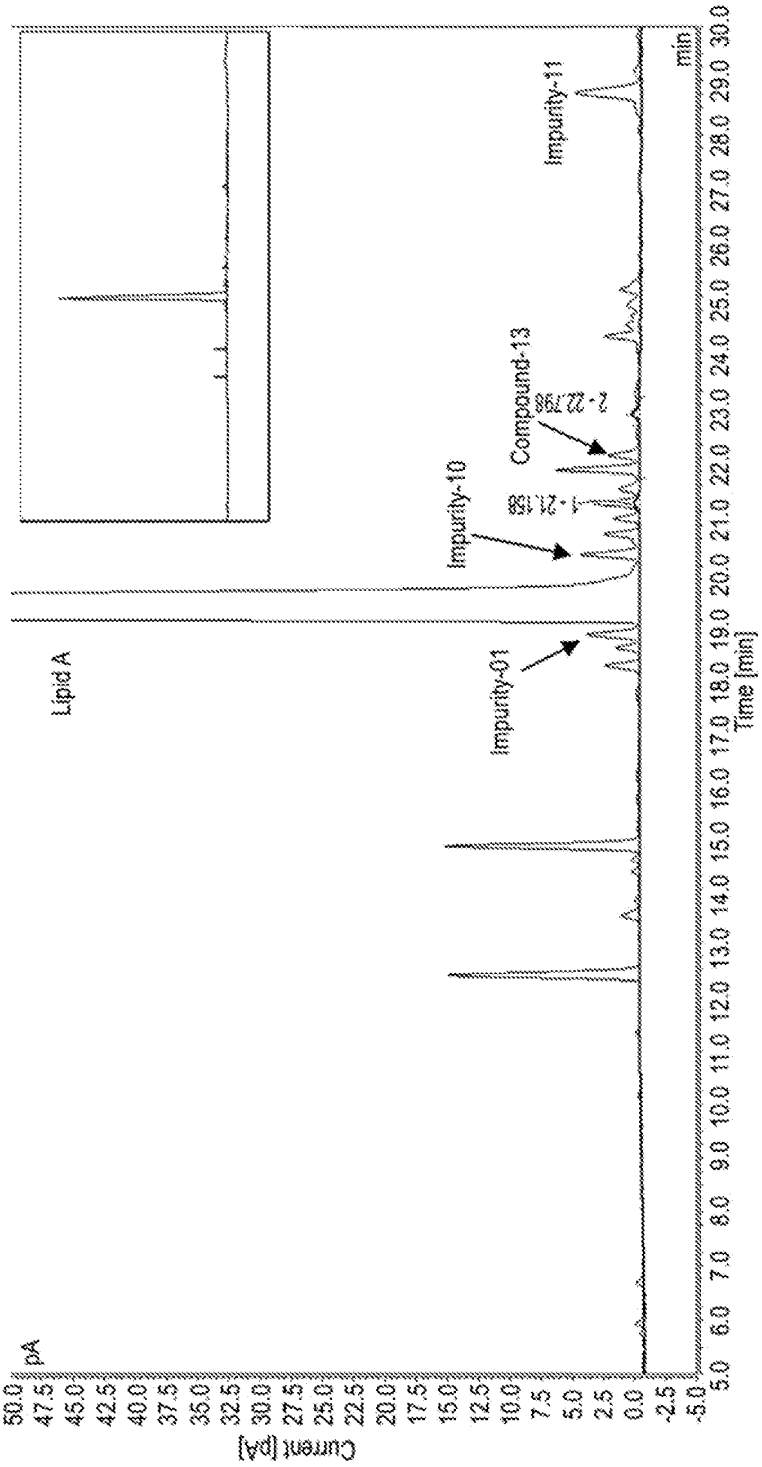

Lipid A
Impurity-01
Impurity-10
Compound-13
Impurity-11
Current [pA]
Time [min]
pA
min

FIG. 1

FIG. 2

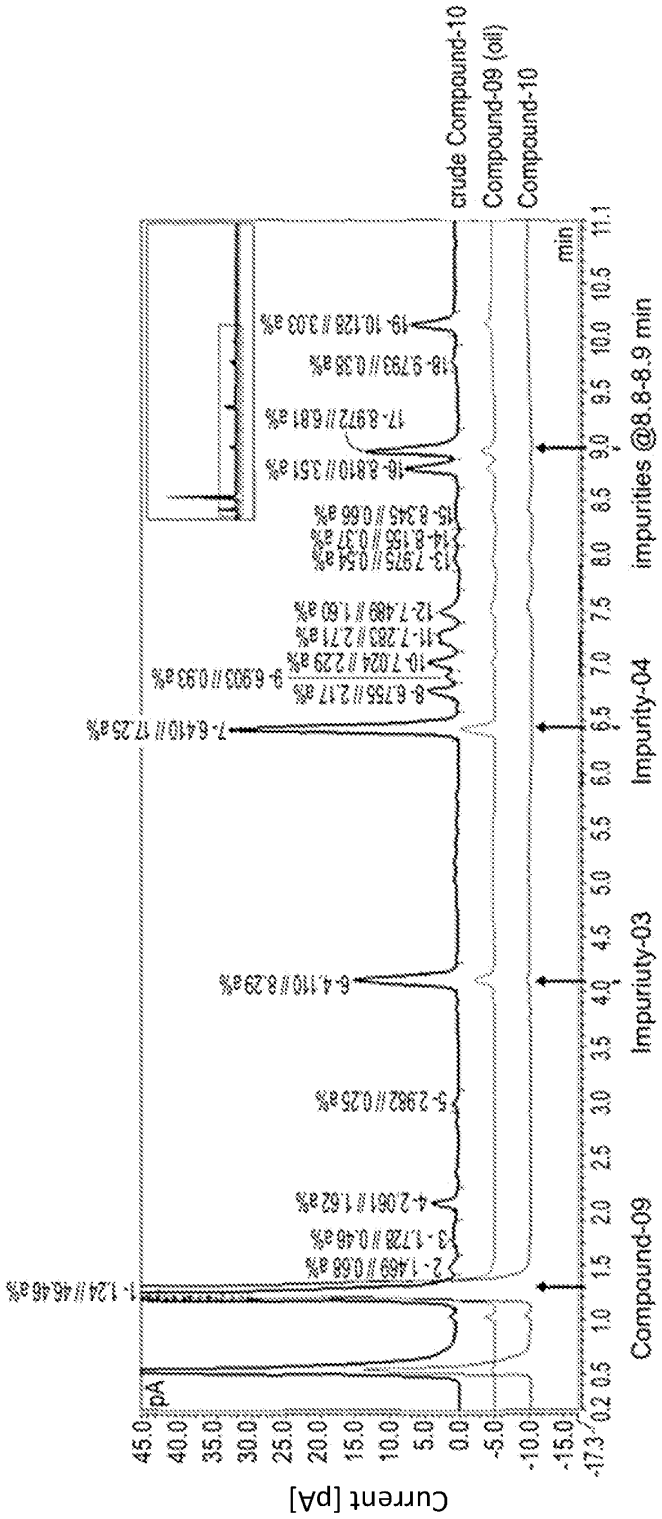

crude Compound-10
Compound-09 (oil)
Compound-10
min
Compound-09
Impurity-03
Impurity-04
impurities @8.8-8.9 min
Current [pA]
pA

FIG. 3

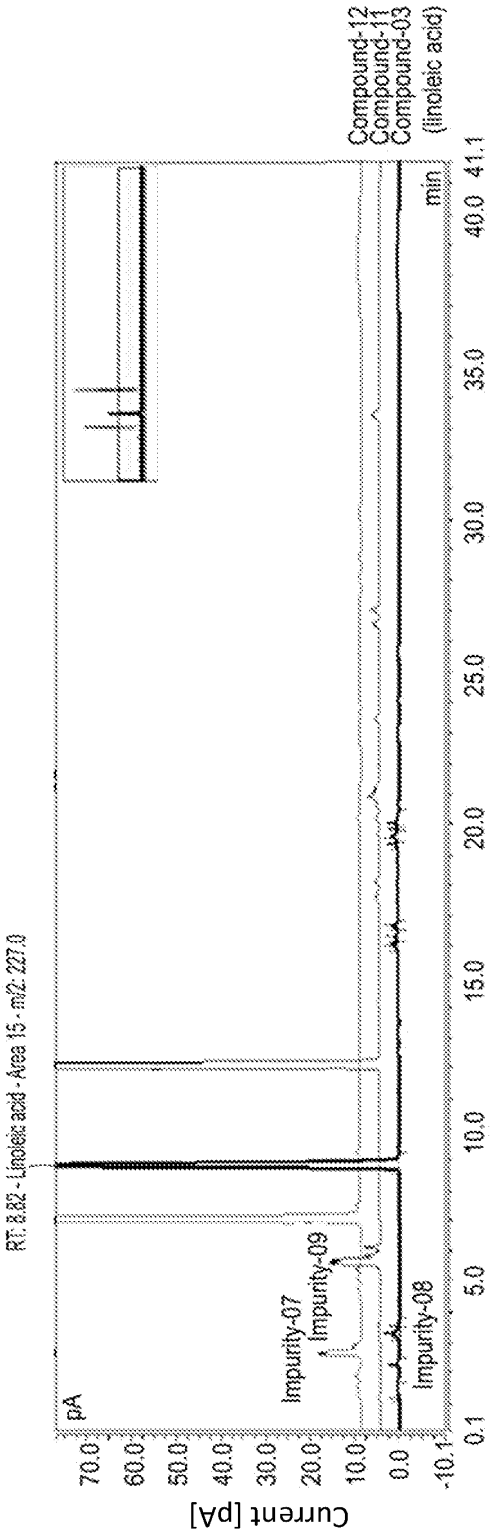

RT: 8.82 - Linoleic acid - Area 15 - m/z: 227.0
pA
Impurity-07
Impurity-09
Impurity-08
Compound-12
Compound-11
Compound-03
(linoleic acid)
min
Current [pA]
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.1
0.1
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
41.1

FIG. 4

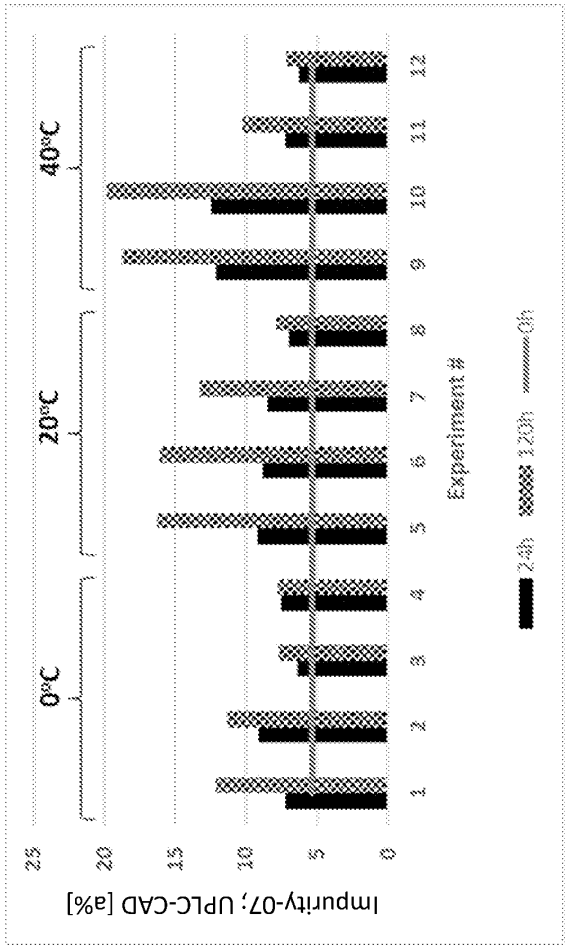
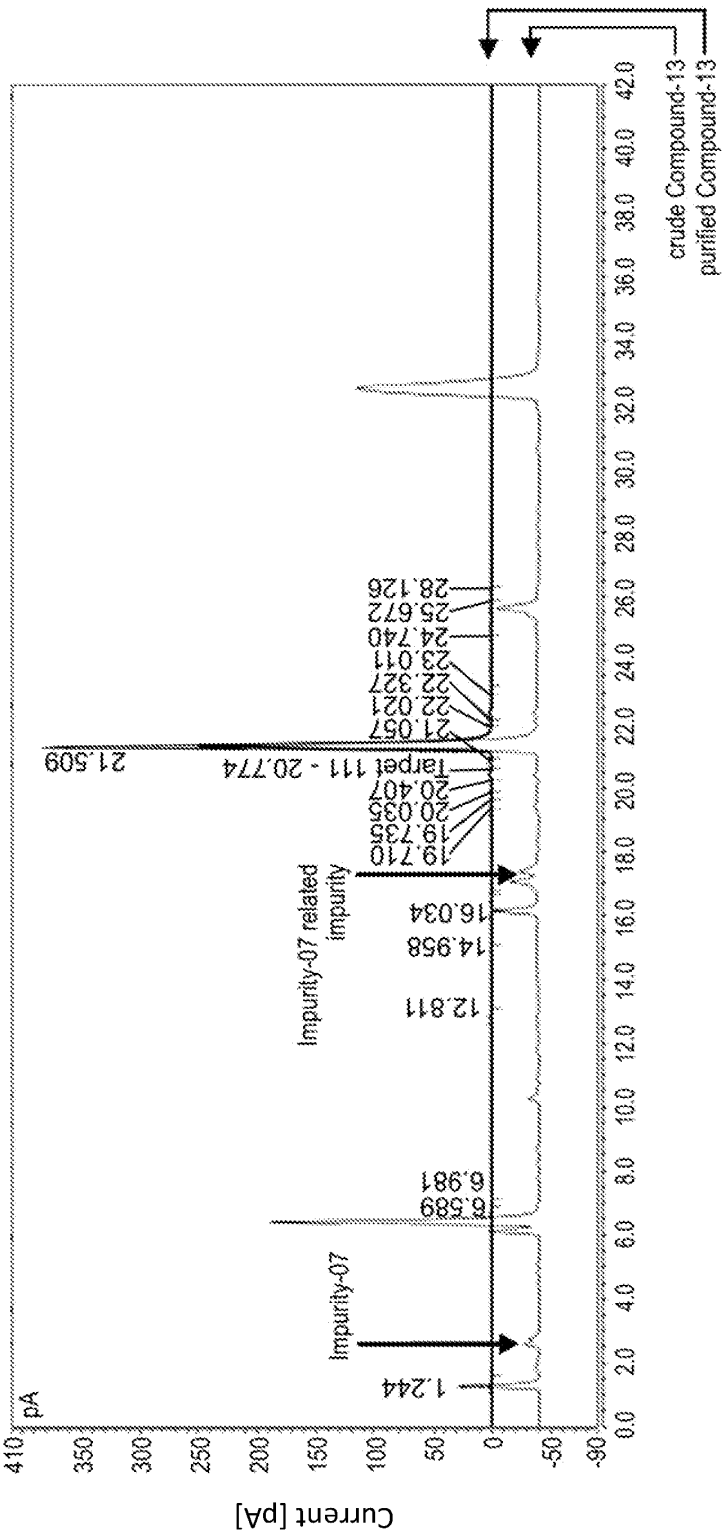

Impurity-07; UPLC-CAD [a%]
25
20
15
10
5
0
0°C
20°C
40°C
1
2
3
4
5
6
7
8
9
10
11
12
Experiment #
24h
120h
0h

FIG. 5


crude Compound-13
purified Compound-13
pA
Current [pA]
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

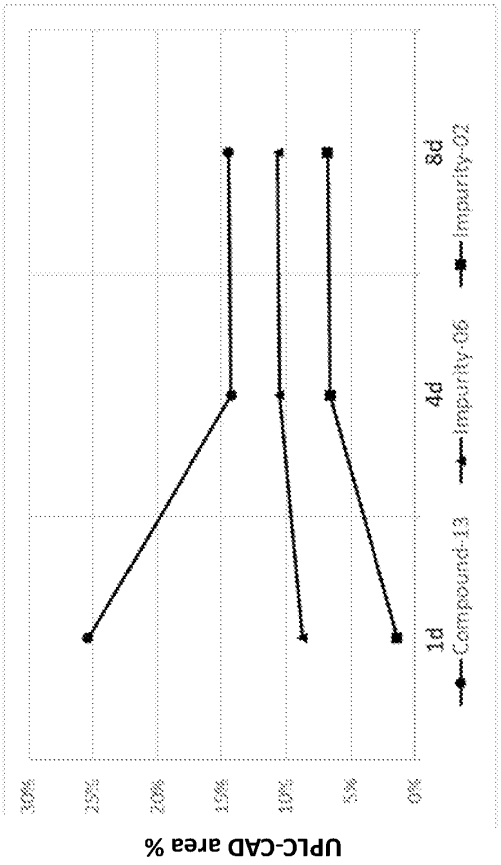

UPLC-CAD area %
30%
25%
20%
15%
10%
5%
0%
1d
4d
8d
Compound-13
Impurity-06
Impurity-02

FIG. 6

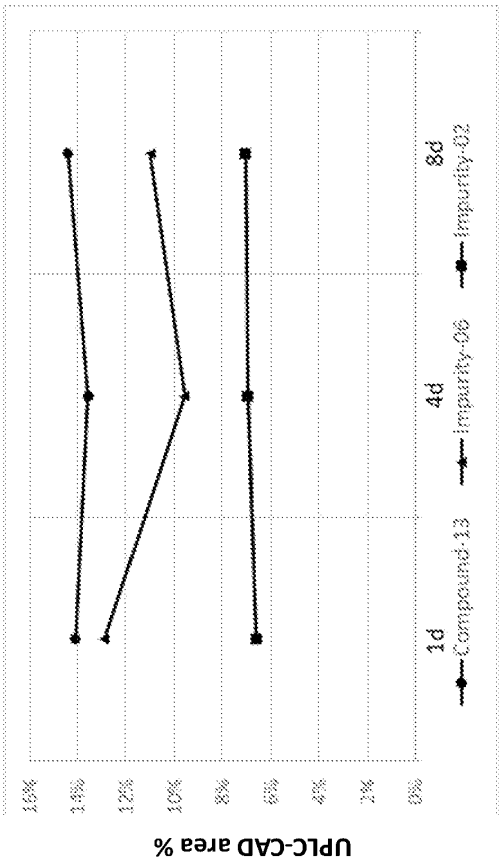

UPLC-CAD area %
16%
14%
12%
10%
8%
6%
4%
2%
0%
1d
4d
8d
Compound-13
Impurity-06
Impurity-02

FIG. 7

FIG. 8

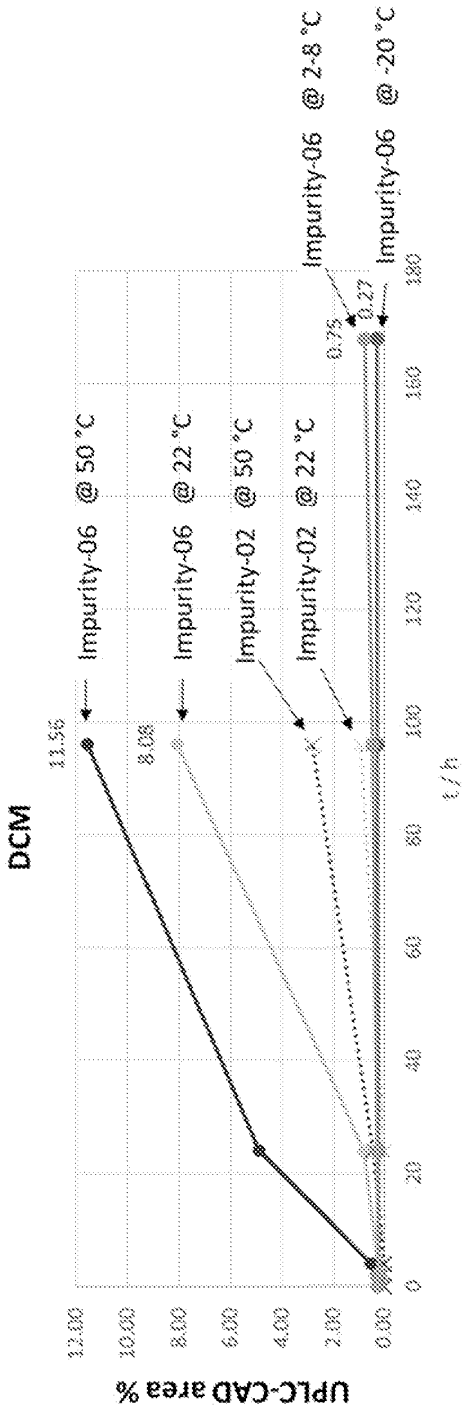

DCM
UPLC-CAD area %
t / h
Impurity-06 @ 50 °C
Impurity-06 @ 22 °C
Impurity-02 @ 50 °C
Impurity-02 @ 22 °C
Impurity-06 @ 2-8 °C
Impurity-06 @ -20 °C
11.56
8.08
0.75
0.27
12.00
10.00
8.00
6.00
4.00
2.00
0.00
0
20
40
60
80
100
120
140
160
180

FIG. 9

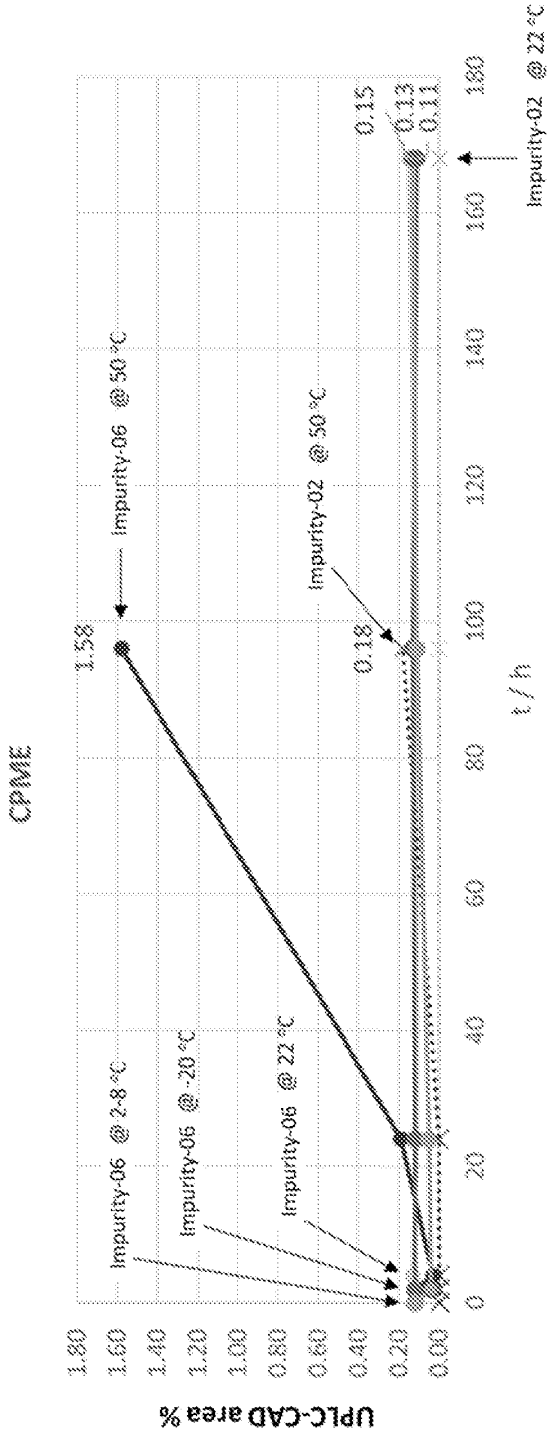

CPME
UPLC-CAD area %
t / h
1.58
0.18
0.15
0.13
0.11
Impurity-06 @ 50 °C
Impurity-02 @ 50 °C
Impurity-02 @ 22 °C
Impurity-06 @ 2-8 °C
Impurity-06 @ -20 °C
Impurity-06 @ 22 °C

FIG. 10

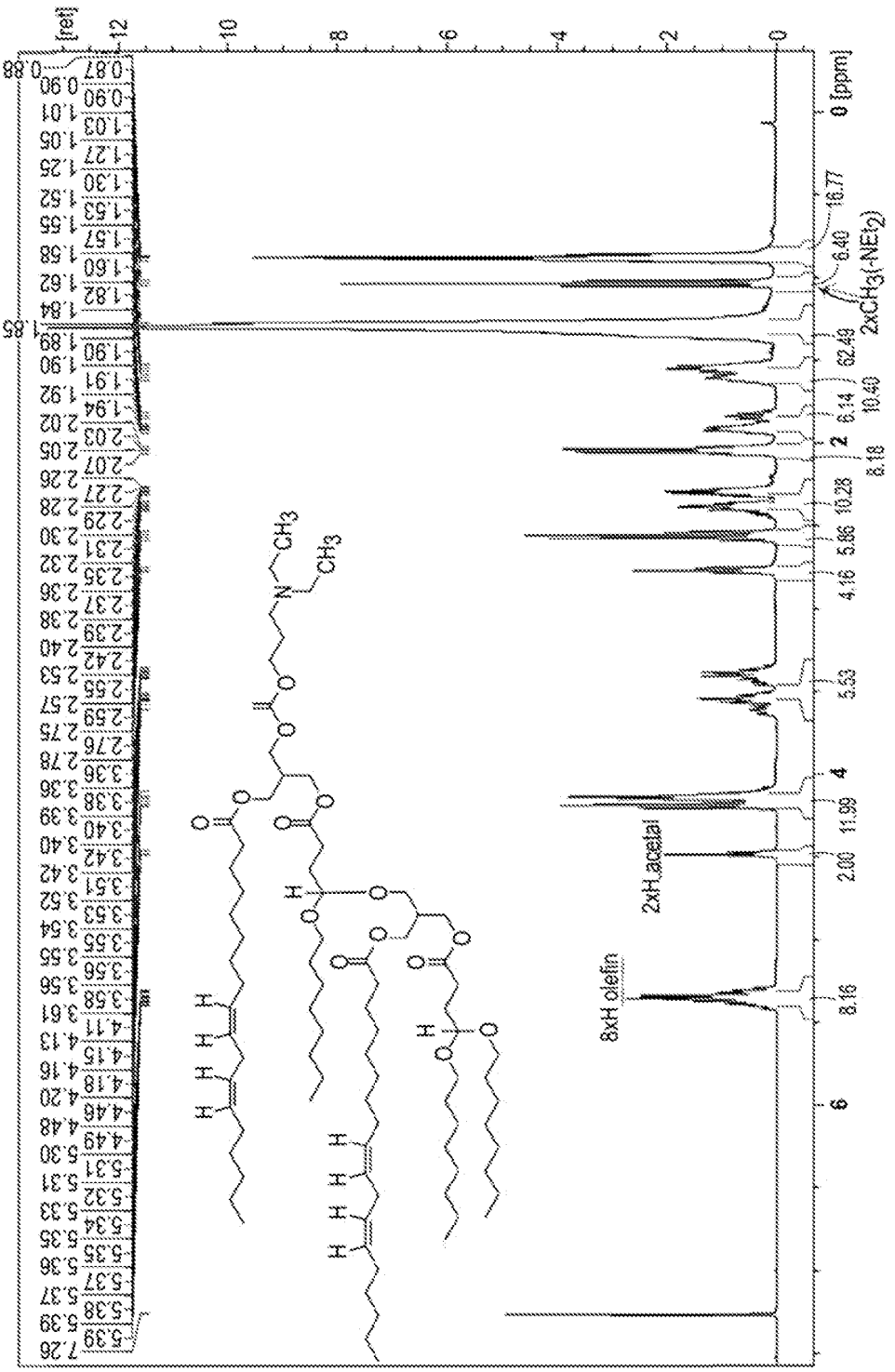


FIG. 11

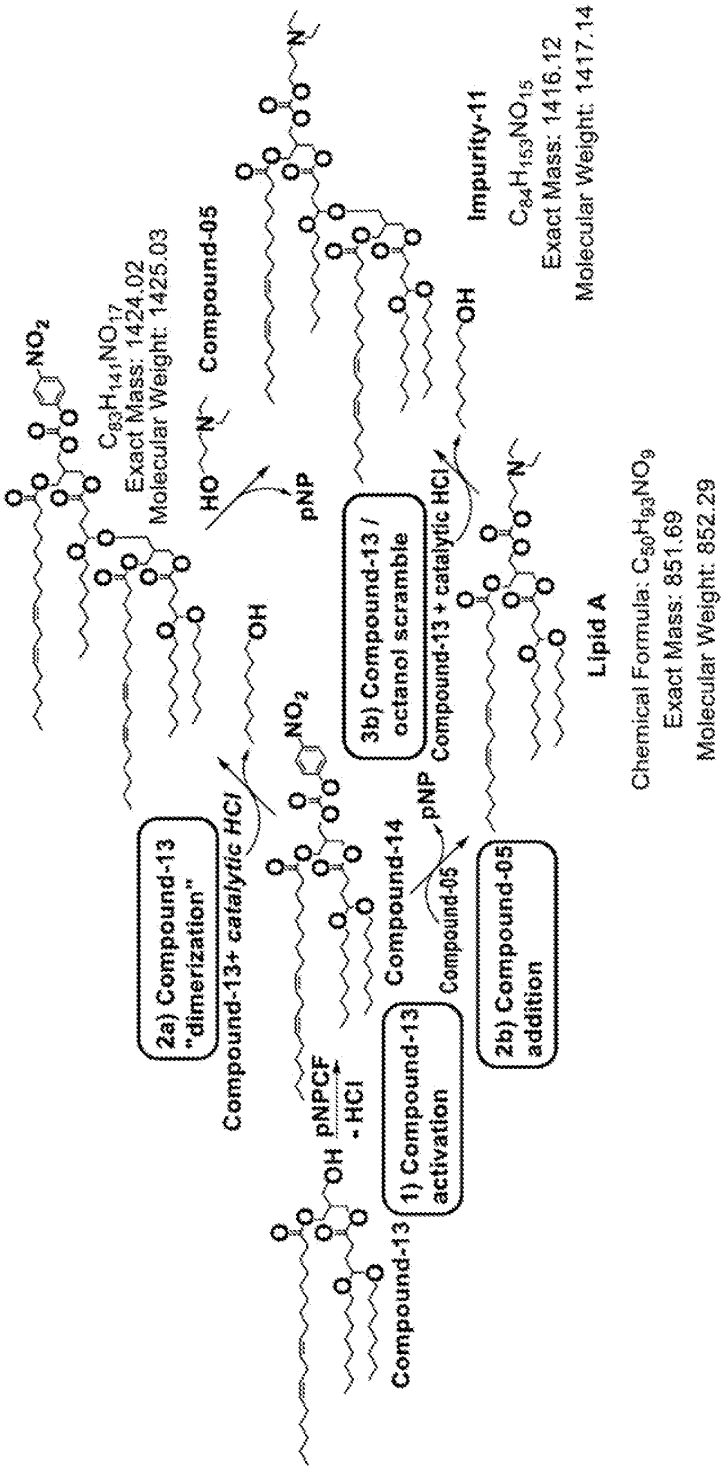

Compound-13
1) Compound-13 activation
pNPCF
. HCl
Compound-14
2a) Compound-13 "dimerization"
Compound-13+ catalytic HCl
Compound-05
pNP
2b) Compound-05 addition
Compound-05
pNP
3b) Compound-13 / octanol scramble
Compound-13 + catalytic HCl
Lipid A
Chemical Formula: $C_{80}H_{84}NO_9$
Exact Mass: 851.69
Molecular Weight: 852.29
Impurity-11
$C_{84}H_{153}NO_{15}$
Exact Mass: 1416.12
Molecular Weight: 1417.14
$C_{83}H_{141}NO_{17}$
Exact Mass: 1424.02
Molecular Weight: 1425.03

FIG. 12

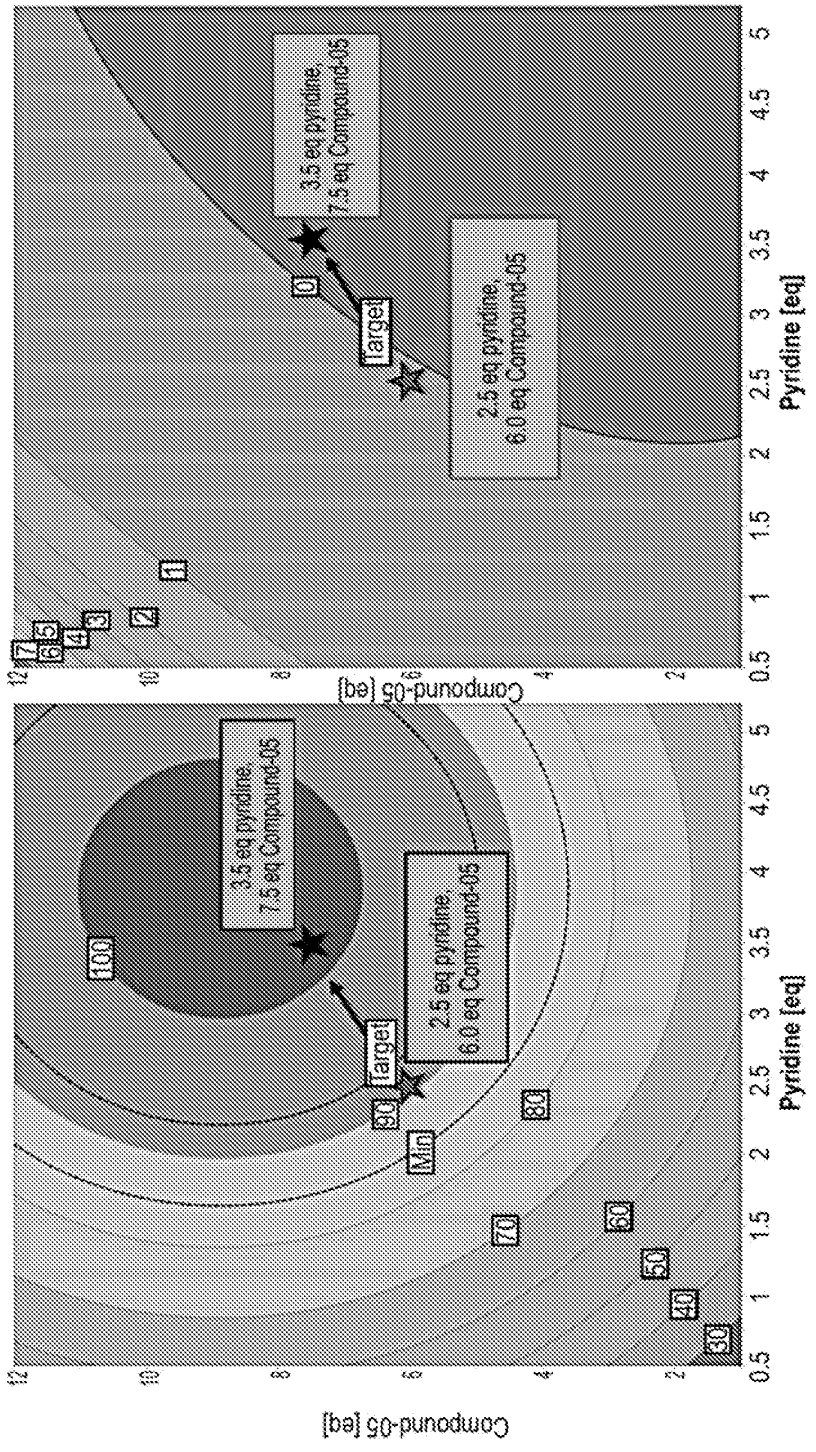

Lipid A [a%] Contour Lines
Impurity-11 [a%] Contour Lines
Compound-05 [eq]
Pyridine [eq]
3.5 eq pyridine,
7.5 eq Compound-05
2.5 eq pyridine,
6.0 eq Compound-05
Target
Min
100
90
80
70
60
50
40
30
0
1
2
3
4
5
6
7

FIG. 13

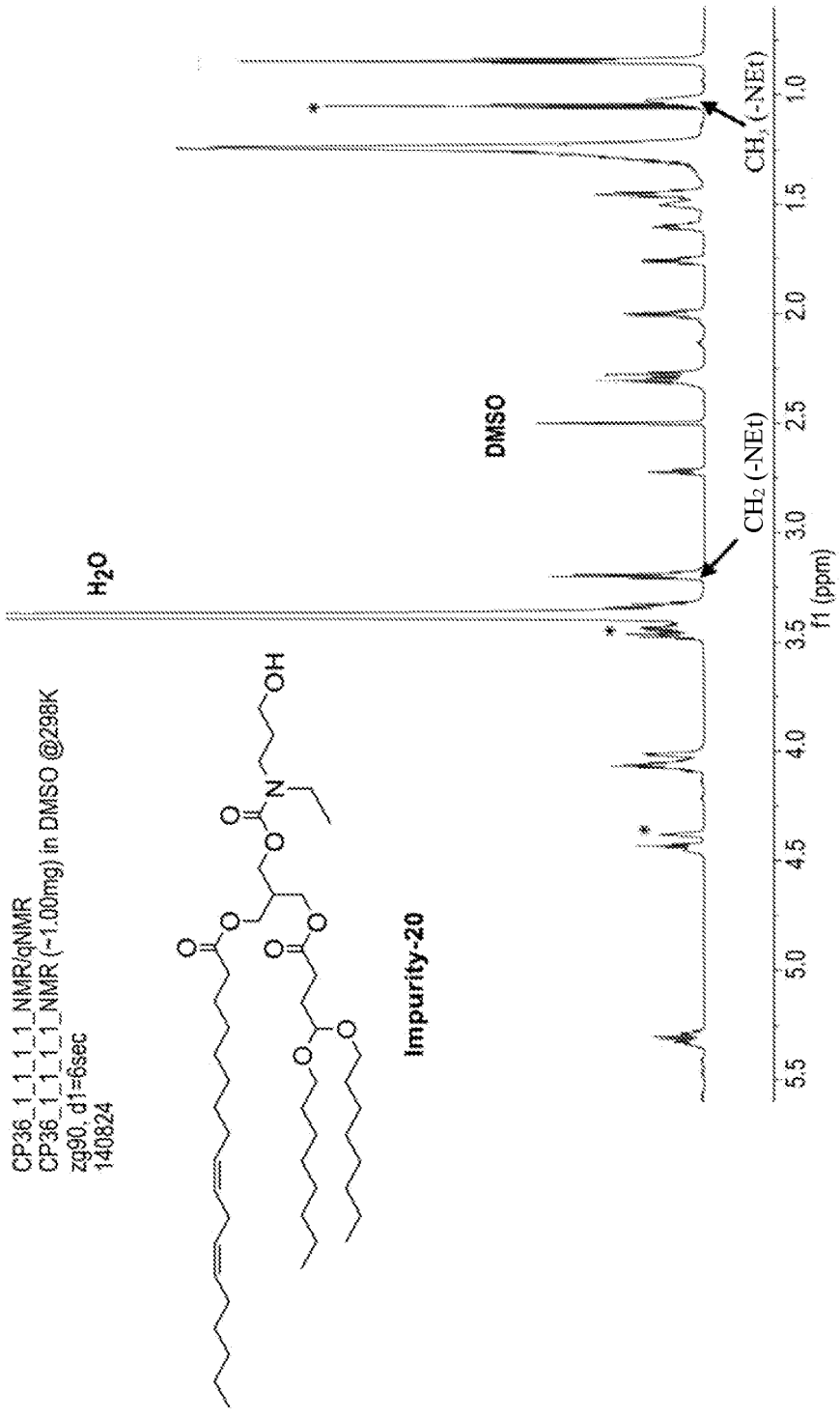
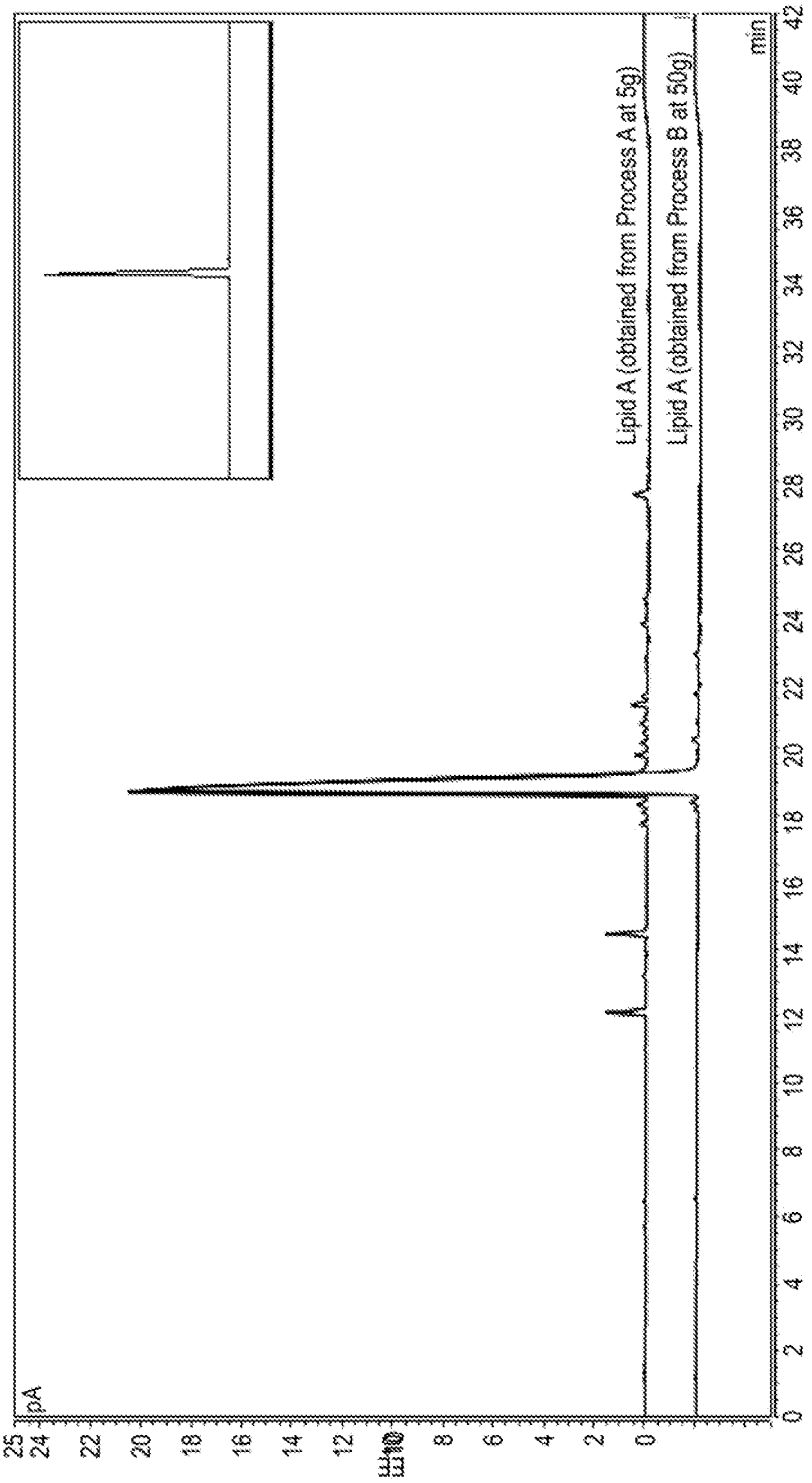

CP36_1_1_1_1_NMR/qNMR
CP36_1_1_1_1_NMR (~1.00mg) in DMSO @298K
zg90, d1=6sec
140824
H2O
DMSO
CH2 (-NEt)
CH3 (-NEt)
Impurity-20
f1 (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

FIG. 14


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