Inhibitors of *O*-acetylserine sulfhydrylase with a cyclopropane-carboxylic acid scaffold are effective colistin adjuvants in Gram negative bacteria.

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SUPPORTING INFORMATION

Analytical methods (HPLC-ESI-MS)

Samples were injected (10 µL) and chromatographically separated using a reversed-phase C18 XSelect® HSS T3 column 2.1 x 50 mm, 2.5 particle size (WATERS, Ireland). A gradient profile was applied using water (eluent A) and acetonitrile (eluent B), acidified with 0.2% and 0.1 % formic acid respectively, as a mobile phase. Mass spectrometry data were collected in positive electrospray mode over the range of m/z 100-600. Source settings were maintained using a capillary voltage of 2.5 kV (compounds **8a** and **9a**), 3.5 kV (compound **12h**), or 4.0 kV (compound **13h**); a cone of 25 V (compounds **8a** and **9a**) or 30 (compounds **12h** and **13h**), source temperature, 120°C; desolvation temperature, 350 °C, and desolvation gas flow, 700 L/h.

Method A: Initial conditions were set up at 5% of B, after 2.0 min of isocratic step, a linear change to 100% of B in 8.0 min. 100% B was achieved in 10 min and held for 5 min to allow for the column washing before returning to the initial conditions. Column recondition was achieved over 5 min, proving a total run time of 20 min. The column was maintained at 30°C and a flow rate of 0.200 mL/min was used.

Method B: The gradient started with 100% of A, after 2.0 min of isocratic step, a linear change to 90% of B in 8.0 min. 100% B was achieved in 10 min and held for 5 min to allow for the column washing before returning to the initial conditions. Column recondition was achieved over 1 min and held for 7 min, proving a total run time of 23 min. The column was maintained at 30°C and a flow rate of 0.200 mL/min was used.

Figure S1.

Ethyl 2-(3-(2-aminopyrimidin-5-yl)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylate (8a)

^{1}H NMR (400 MHz, DMSO-d_6)

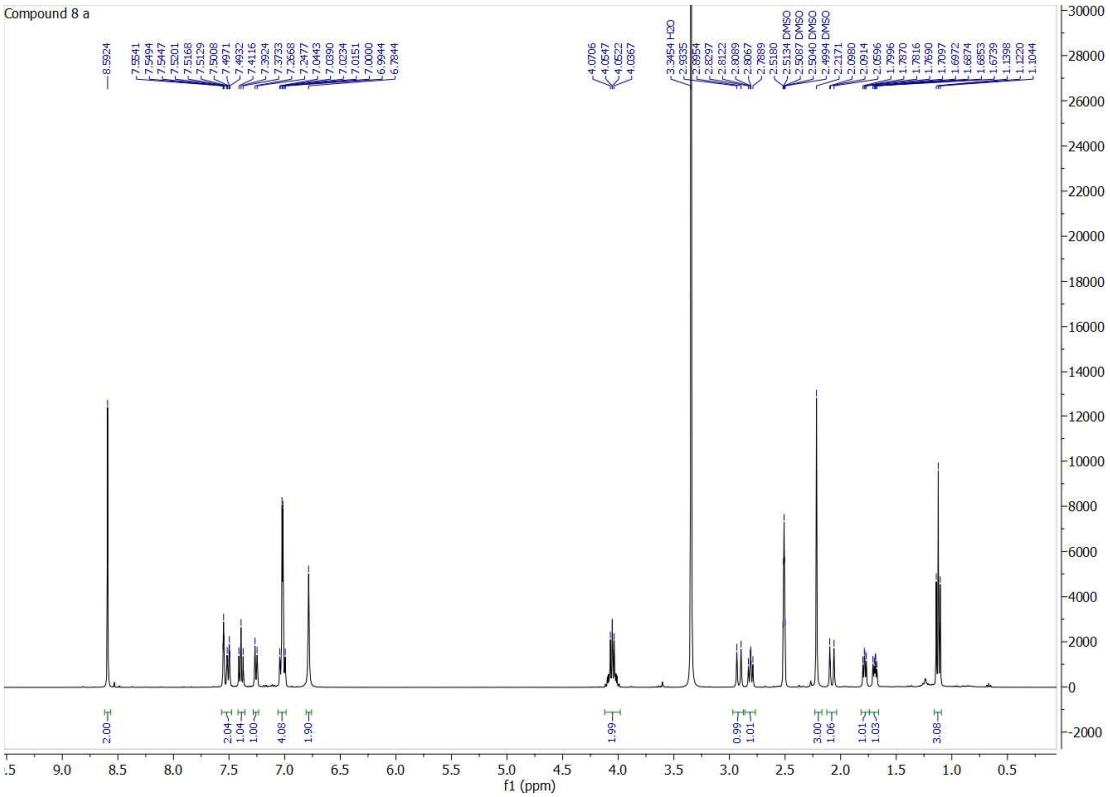


Figure S2.

Ethyl 2-(3-(2-aminopyrimidin-5-yl)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylate (8a)

^{13}C NMR (100.6 MHz, DMSO-d_6)

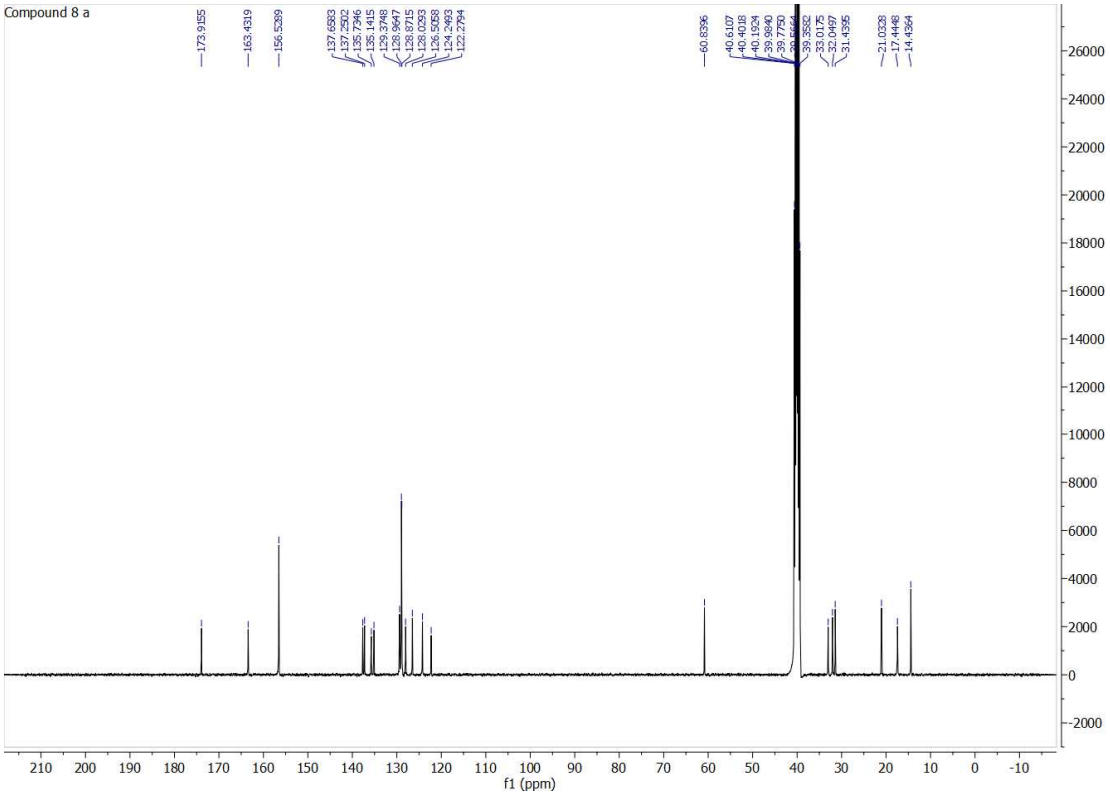
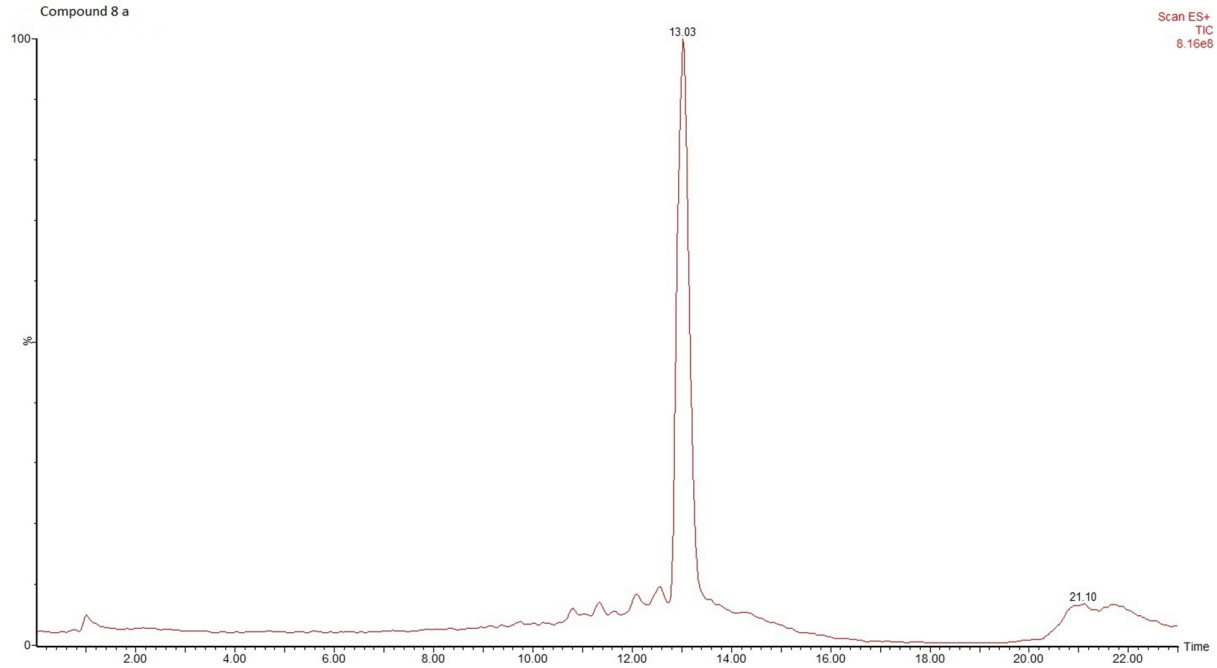


Figure S3.

HPLC/MS analysis (8a)

Method A


Compound 8 a
Scan ES+
TIC
8.16e8
100
%
0
13.03
21.10
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
22.00
Time

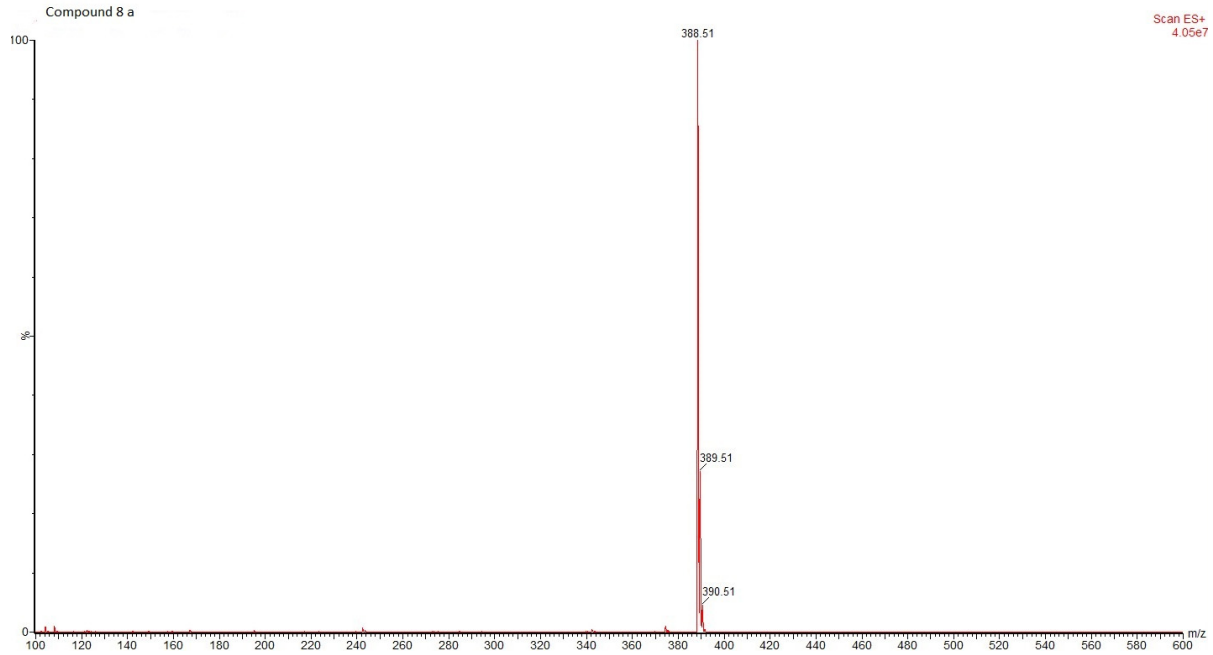

Compound 8 a
Scan ES+
4.05e7
100
%
0
388.51
389.51
390.51
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500
520
540
560
580
600
m/z

Figure S4.

2-(3-(2-aminopyrimidin-5-yl)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylic acid (9a)

^{1}H NMR (400 MHz, DMSO-d_6)

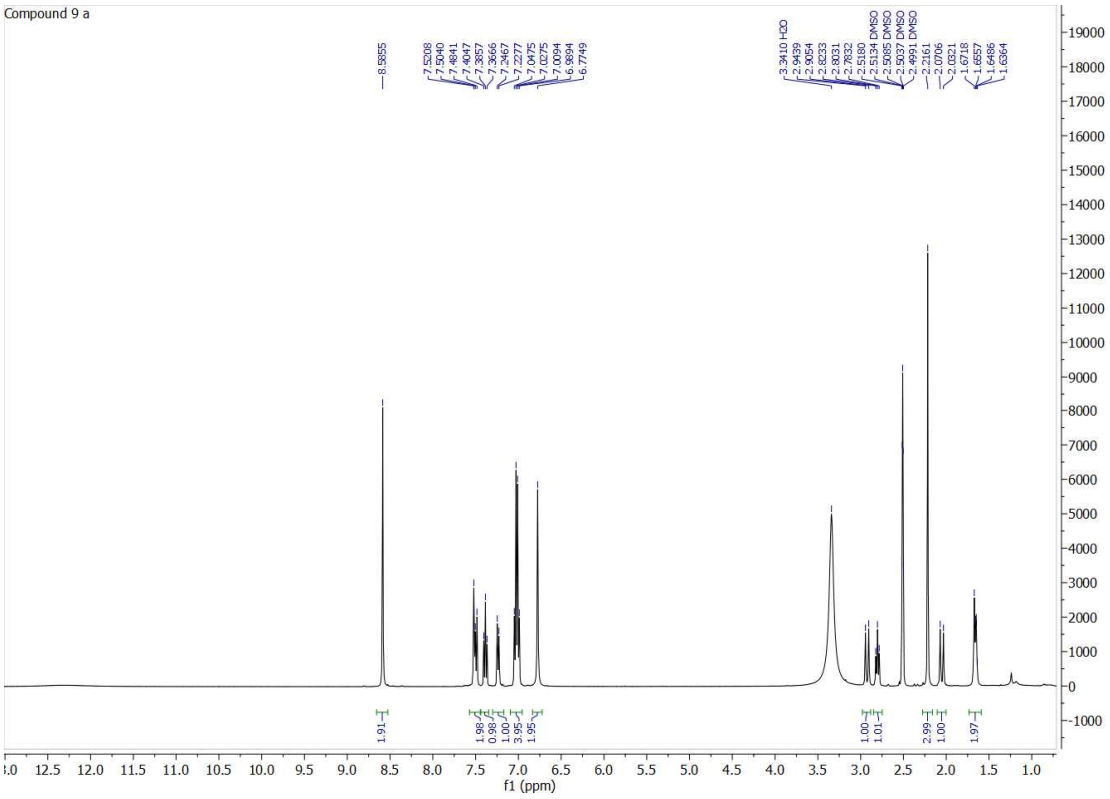


Figure S5.

2-(3-(2-aminopyrimidin-5-yl)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylic acid (9a)

^{13}C NMR (100.6 MHz, DMSO-d_6)

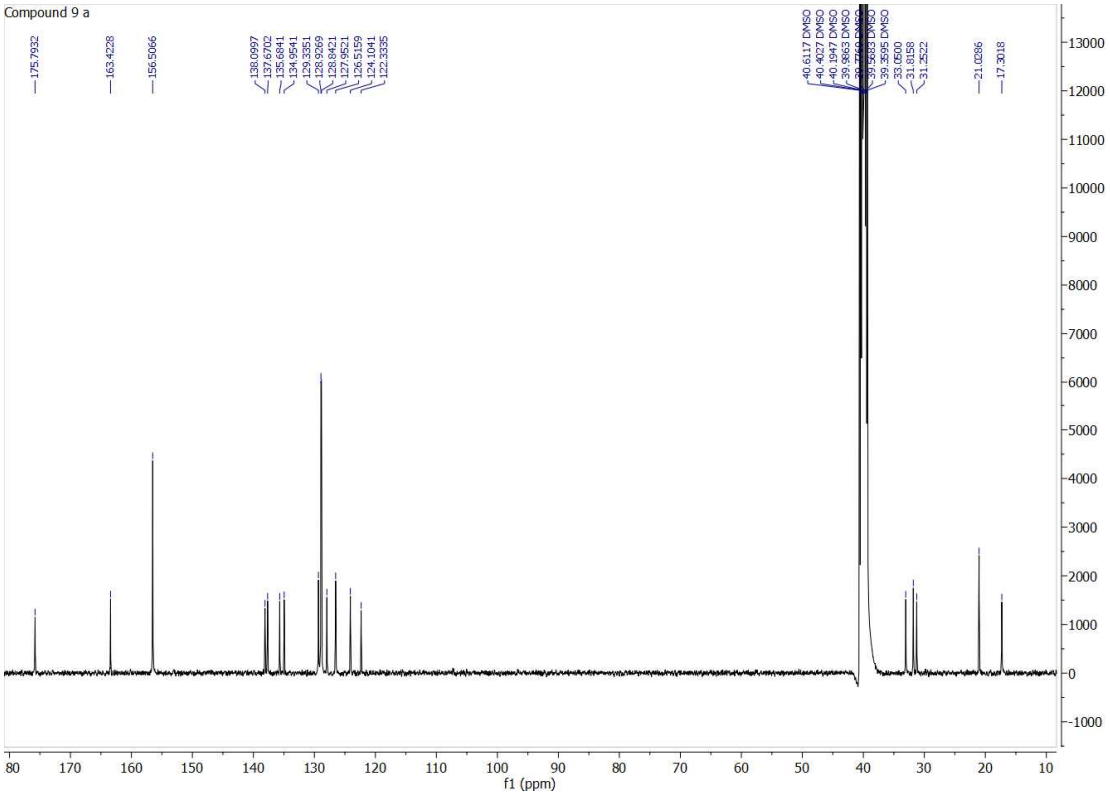
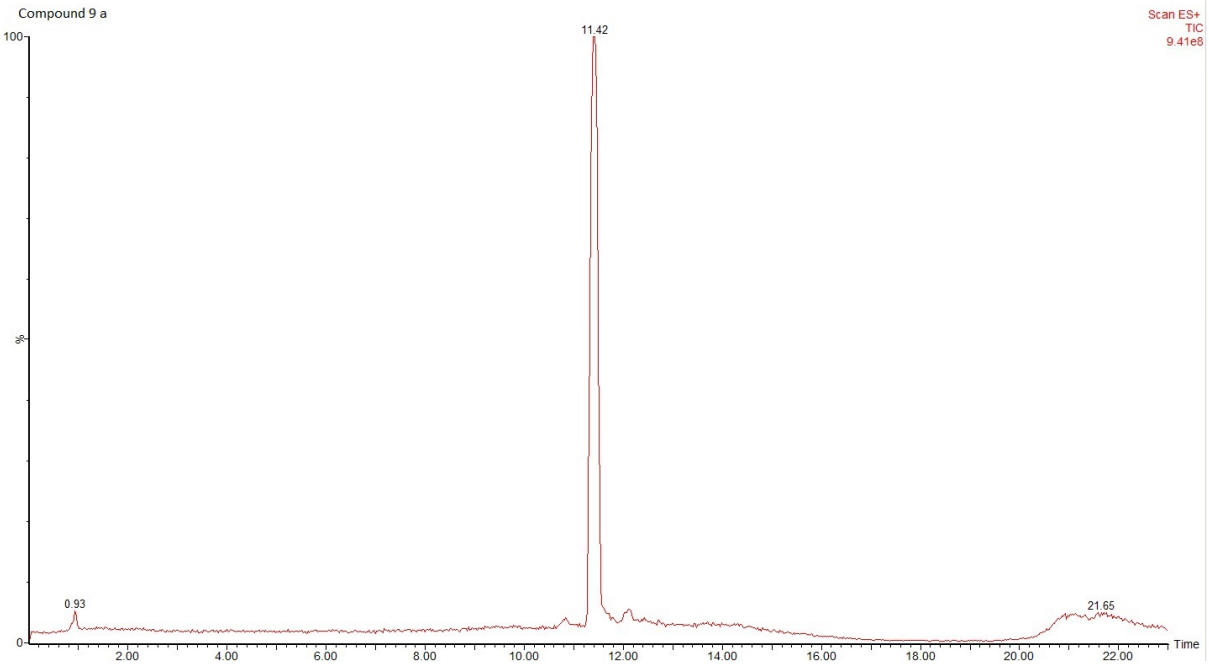


Figure S6.

HPLC/MS analysis (9a)

Method A



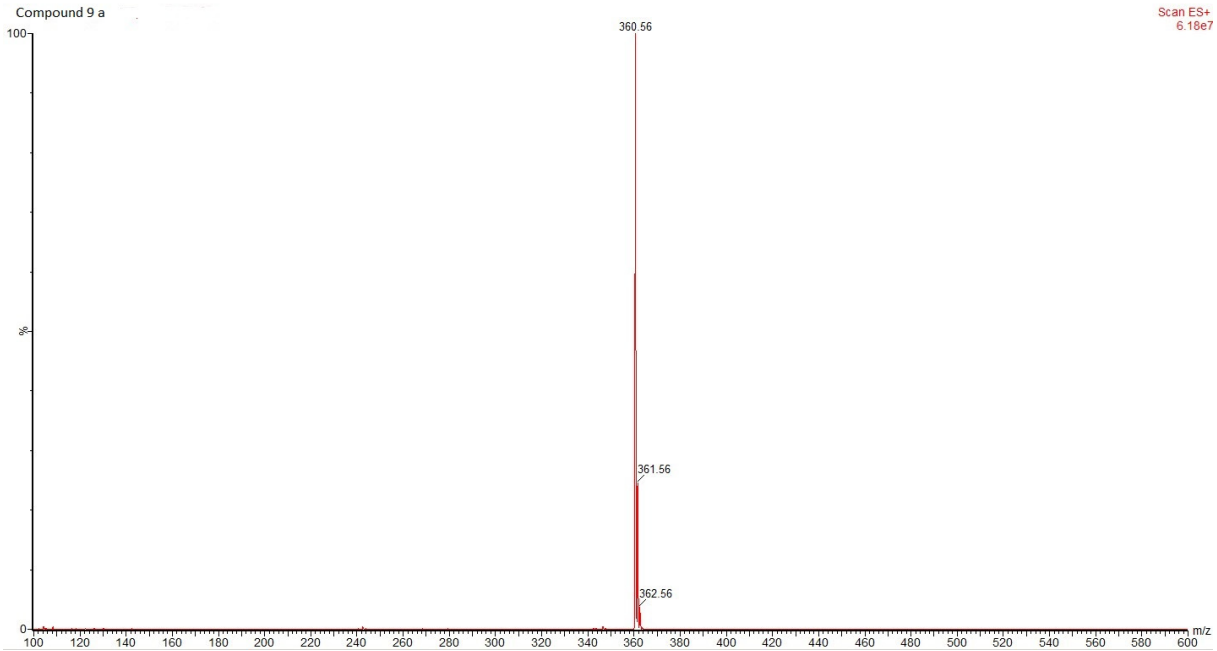


Figure S7.

Ethyl 2-(3-(2,6-dimethylmorpholino)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylate (12h)

^{1}H NMR (400 MHz, $CDCl_3$)

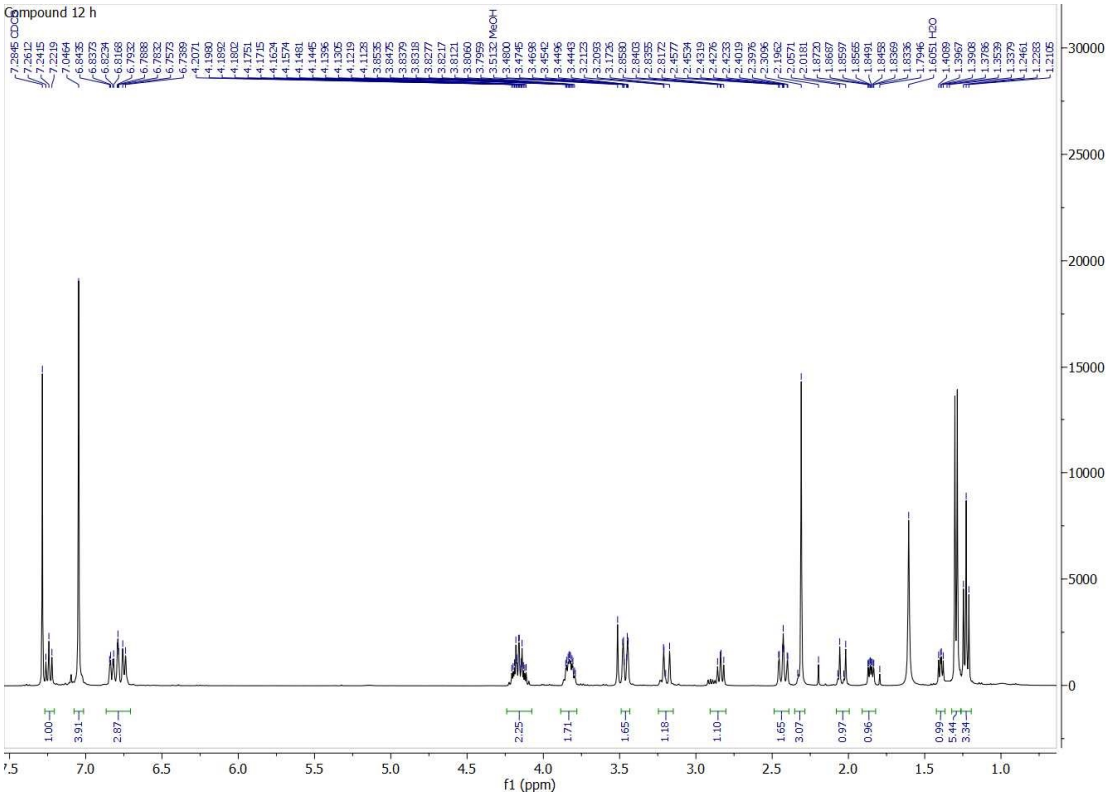


Figure S8.

Ethyl 2-(3-(2,6-dimethylmorpholino)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylate (12h)

^{13}C NMR (400 MHz, $CDCl_3$)

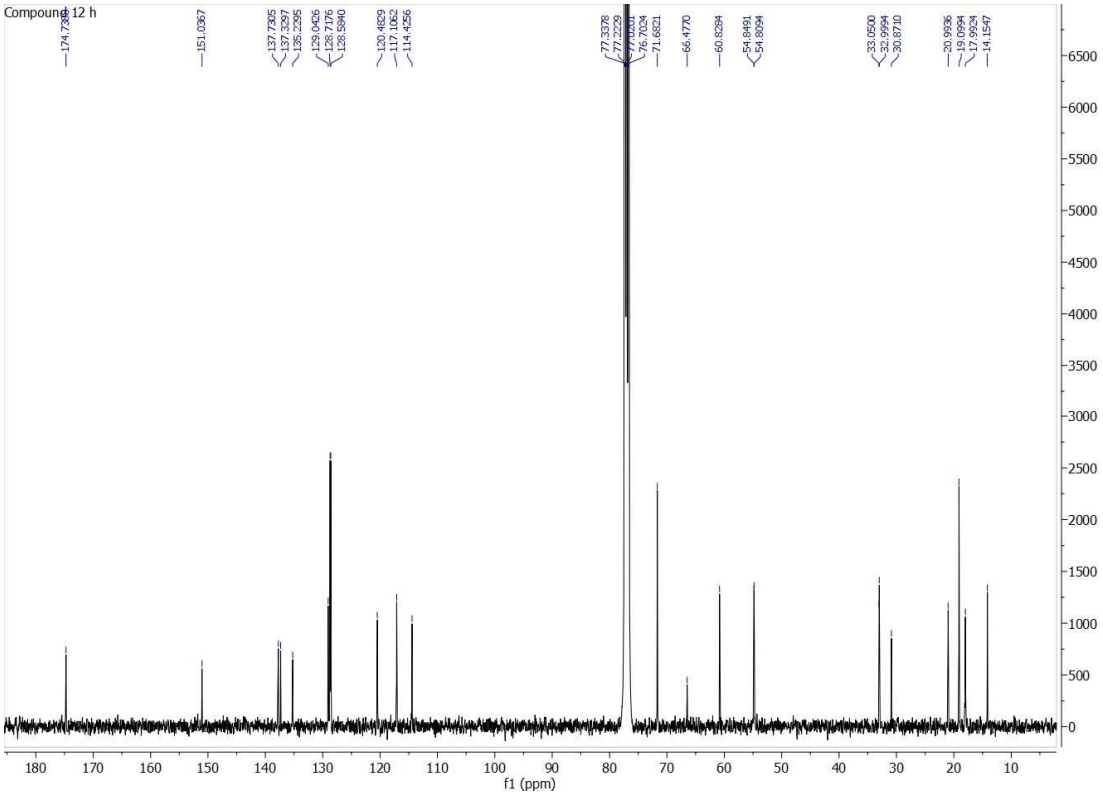
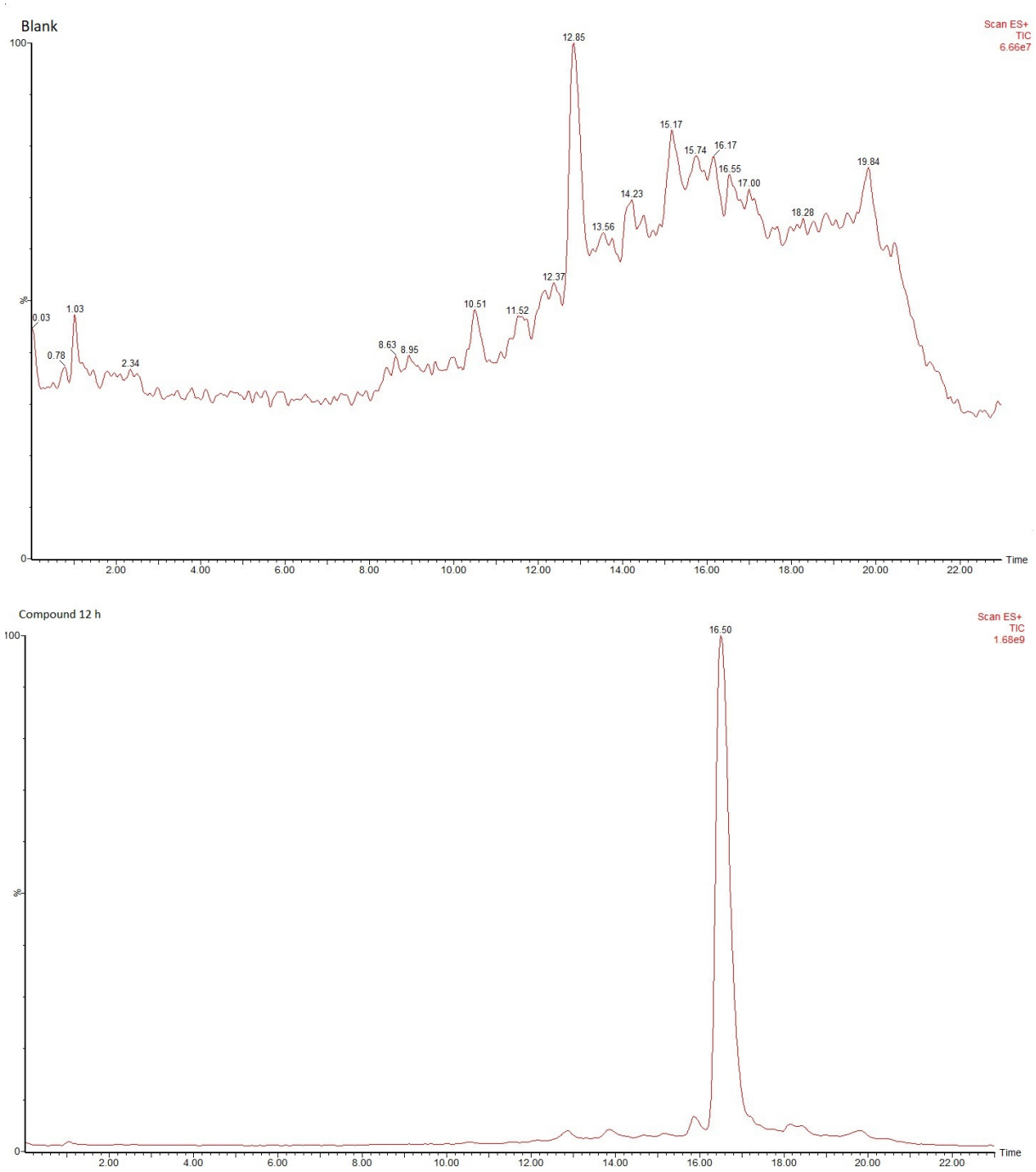


Figure S9.

HPLC/MS analysis (12h)

Method B



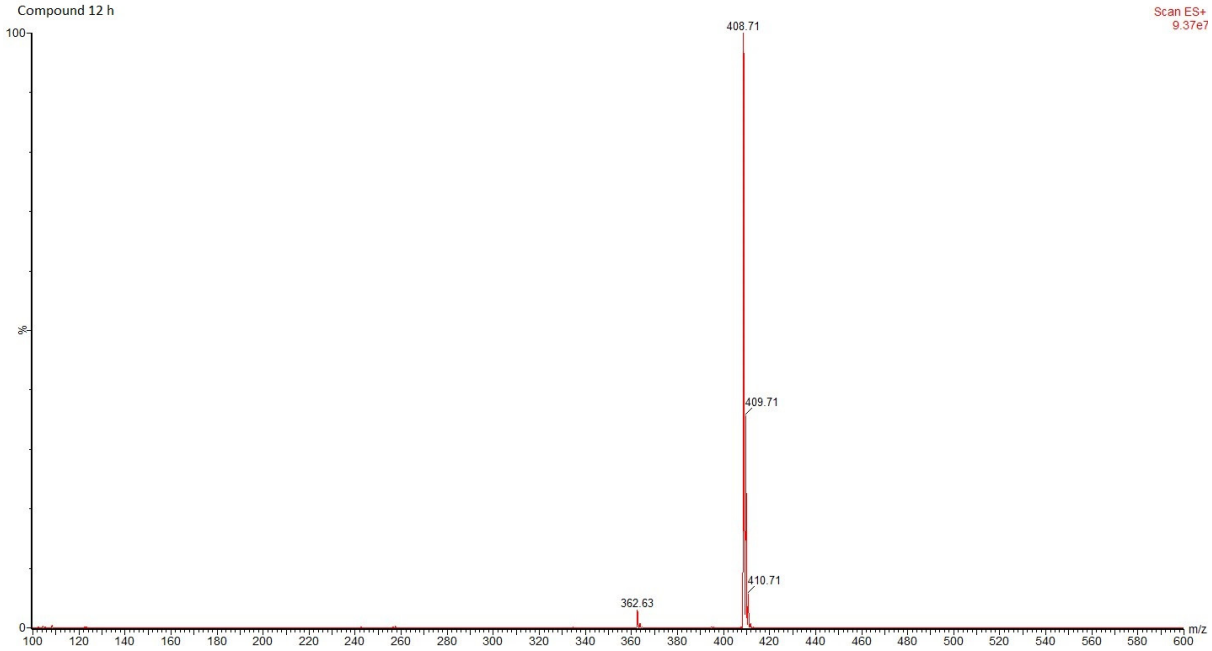

Compound 12 h
Scan ES+
9.37e7
100
%
0
408.71
409.71
410.71
362.63
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600
m/z

Figure S10.

2-(3-(2,6-dimethylmorpholino)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylic acid (13 h)

^{1}H NMR (400 MHz, DMSO-d_6)

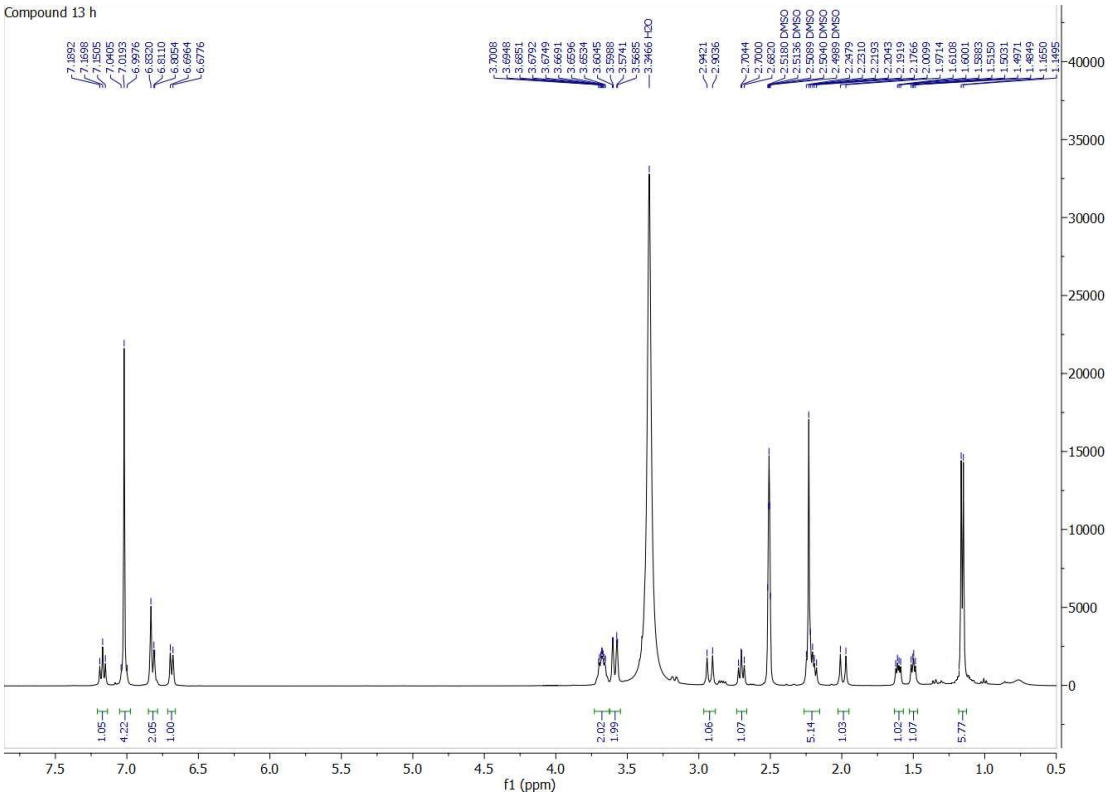


Figure S11.

2-(3-(2,6-dimethylmorpholino)phenyl)-1-(4-methylbenzyl)cyclopropane-1-carboxylic acid (13 h)

^{13}C NMR (100.6 MHz, DMSO-d_6)

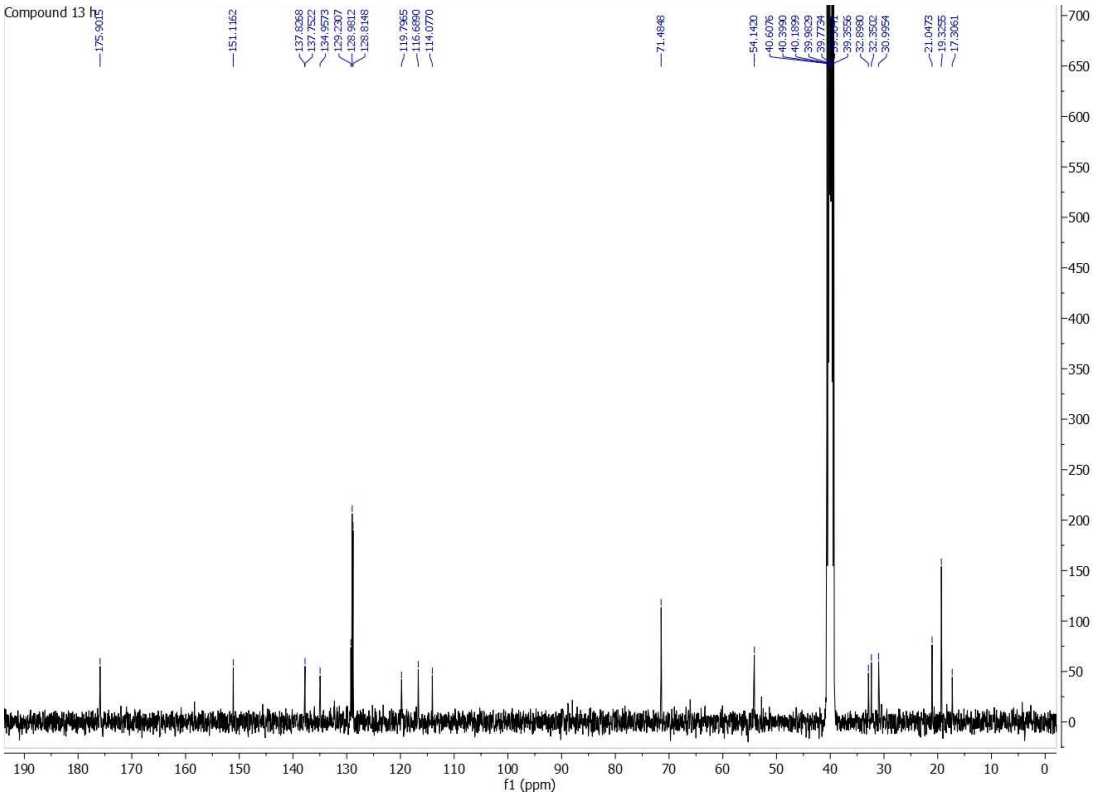
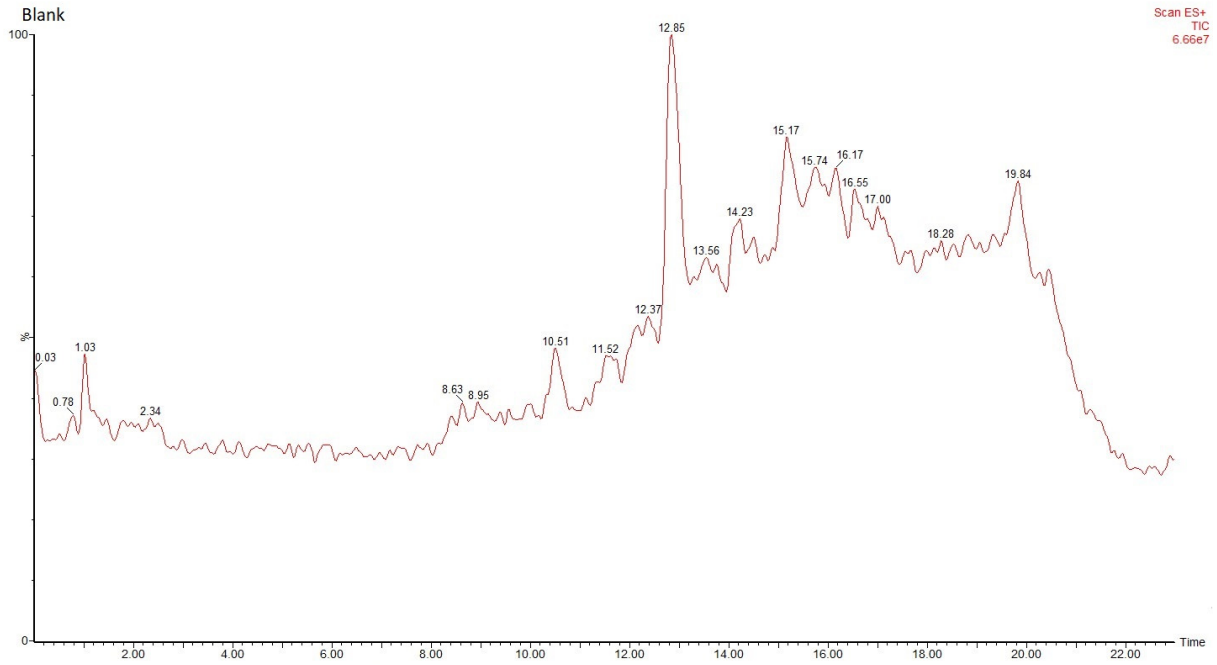
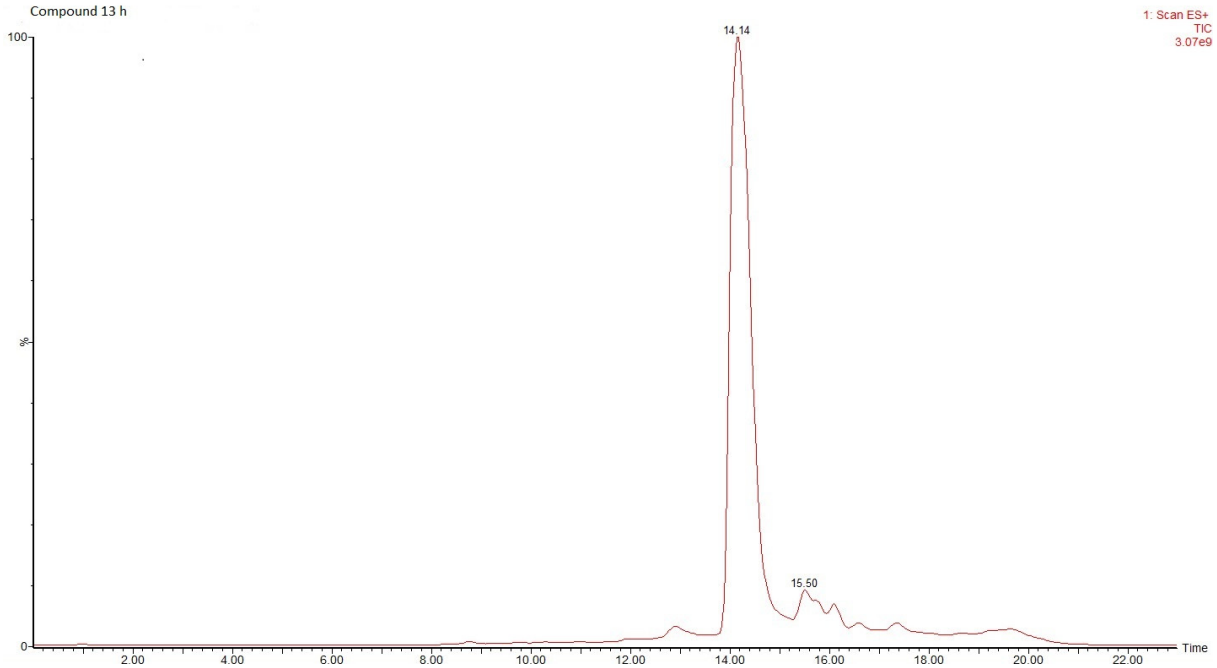


Figure S12.

HPLC/MS analysis (13h)

Method B






Compound 13 h
1: Scan ES+
1.65e7
100
%
0
380.61
381.61
382.56
108.25
m/z
100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400 410 420 430 440 450