

# Supporting information

## Synthesis of Novel Lipophilic Polyamines via Ugi Reaction and Evaluation of Their Anticancer Activity

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1,8-diamino-*N*<sup>8</sup>-acetyl-*N*<sup>1</sup>-*tert*-butyl-1,7-dioxo-*N*<sup>3</sup>,*N*<sup>6</sup>-dibenzyl-3,6-diazaoctane  
(**11a**)

Yield: 11%, colorless oil. Eluent: CHCl<sub>3</sub>-MeOH (10:1). <sup>1</sup>H NMR (600 MHz, acetone-d<sub>6</sub>, main rotamer) δ 1.31 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>), 1.93 (s, 3H, COCH<sub>3</sub>), 2.62 (br. s, 2H, CH<sub>2</sub>NCH<sub>2</sub>), 3.05 (s, 2H, COCH<sub>2</sub>N), 3.50 (s, 2H, CH<sub>2</sub>NCO), 3.60 (s, 2H, COCH<sub>2</sub>NH), 4.05 (d, 2H, *J* = 4.8 Hz, PhCH<sub>2</sub>), 4.37 (s, 2H, PhCH<sub>2</sub>NCO), 7.07 – 7.46 (m, 12H, 2 Ph, 2 NH). <sup>13</sup>C NMR (150 MHz, acetone-d<sub>6</sub>, main rotamer) δ 22.71, 28.96, 42.04, 44.42, 50.41, 52.11, 59.47, 59.95, 127.58, 128.34, 128.72, 129.35, 129.40, 129.67, 137.71, 138.67, 169.62, 170.21, 170.36. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>37</sub>N<sub>4</sub>O<sub>3</sub> 453.2860, found: 453.2860.

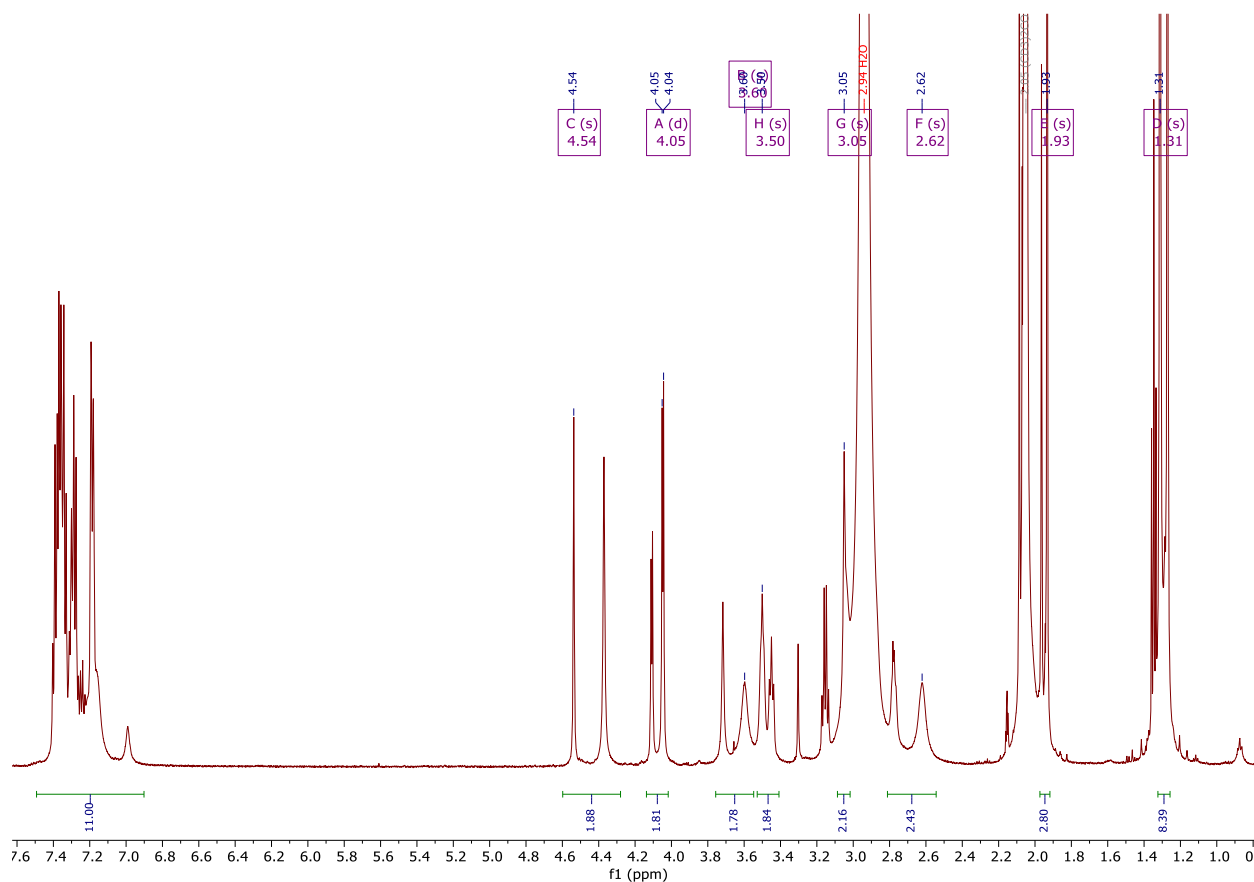


Figure S1. <sup>1</sup>H NMR spectrum of compound **11a**.

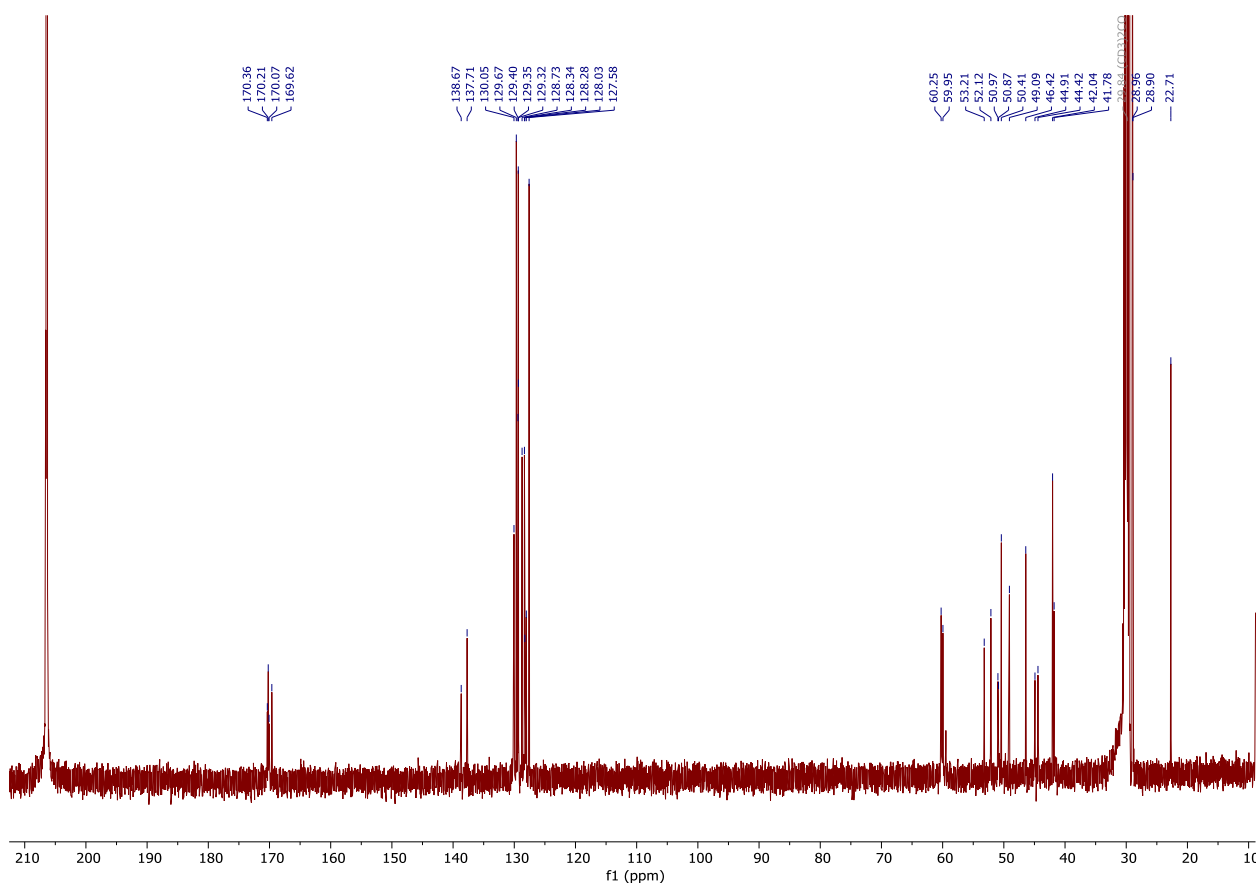


Figure S2.  $^{13}\text{C}$  NMR spectrum of compound **11a**.

Compound\_02\_C26H36N4O3\_fms #64 RT: 1.19 AV: 1 NL: 1.30E8  
T: FTMS + p ESI Full ms [300.0000-1000.0000]

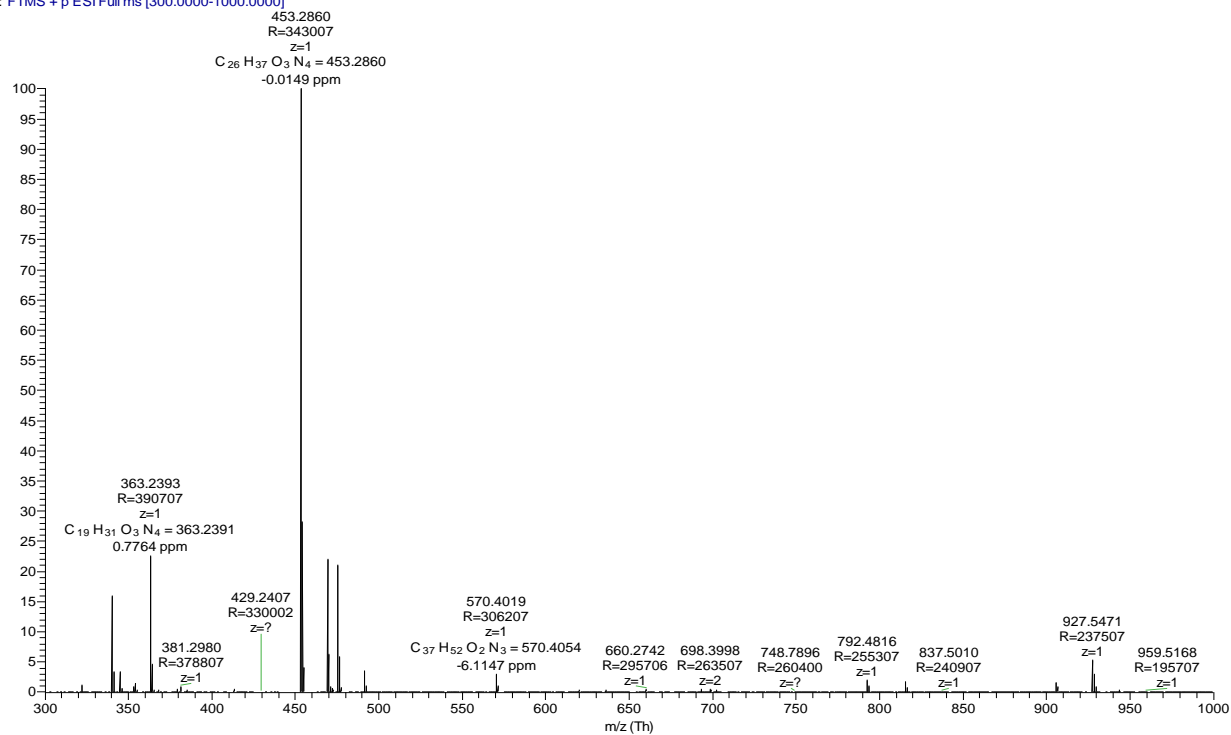


Figure S3. HRMS spectrum of compound **11a**.

1,8-diamino-*N*<sup>8</sup>-acetyl-*N*<sup>1</sup>-octadecyl-1,7-dioxo-*N*<sup>3</sup>,*N*<sup>6</sup>-dibenzyl-3,6-diazaoctane  
(**11b**)

Yield: 10%, colorless oil. Eluent: CHCl<sub>3</sub>-MeOH (10:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, main rotamer) δ 0.88 (t, 3H, *J* = 7.0 Hz, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.25 (br. s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.39 – 1.57 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 2.05 (s, 3H, COCH<sub>3</sub>), 2.59 (t, 2H, *J* = 6.5 Hz, COCH<sub>2</sub>NCH<sub>2</sub>), 3.16 (s, 2H, COCH<sub>2</sub>N), 3.20 – 3.35 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 3.47 (t, 2H, *J* = 6.5 Hz, CONCH<sub>2</sub>), 3.57 (s, 2H, COCH<sub>2</sub>NH), 4.04 (s, 2H, PhCH<sub>2</sub>), 4.14 (s, 2H, PhCH<sub>2</sub>NCO), 6.51 (s, 1H, NHCOCH<sub>2</sub>), 6.97 – 7.50 (m, 11H, 2 Ph, CH<sub>3</sub>CONH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, main rotamer) δ 14.09, 22.67, 29.34, 29.37, 29.61, 29.65, 29.69, 29.78, 31.91, 39.14, 41.60, 43.90, 49.61, 51.18, 59.04, 59.76, 125.29, 126.32, 128.21, 128.60, 129.02, 129.13, 134.96, 138.05, 168.83, 169.88, 170.64. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>40</sub>H<sub>65</sub>N<sub>4</sub>O<sub>3</sub> 649.5051, found: 649.5051.

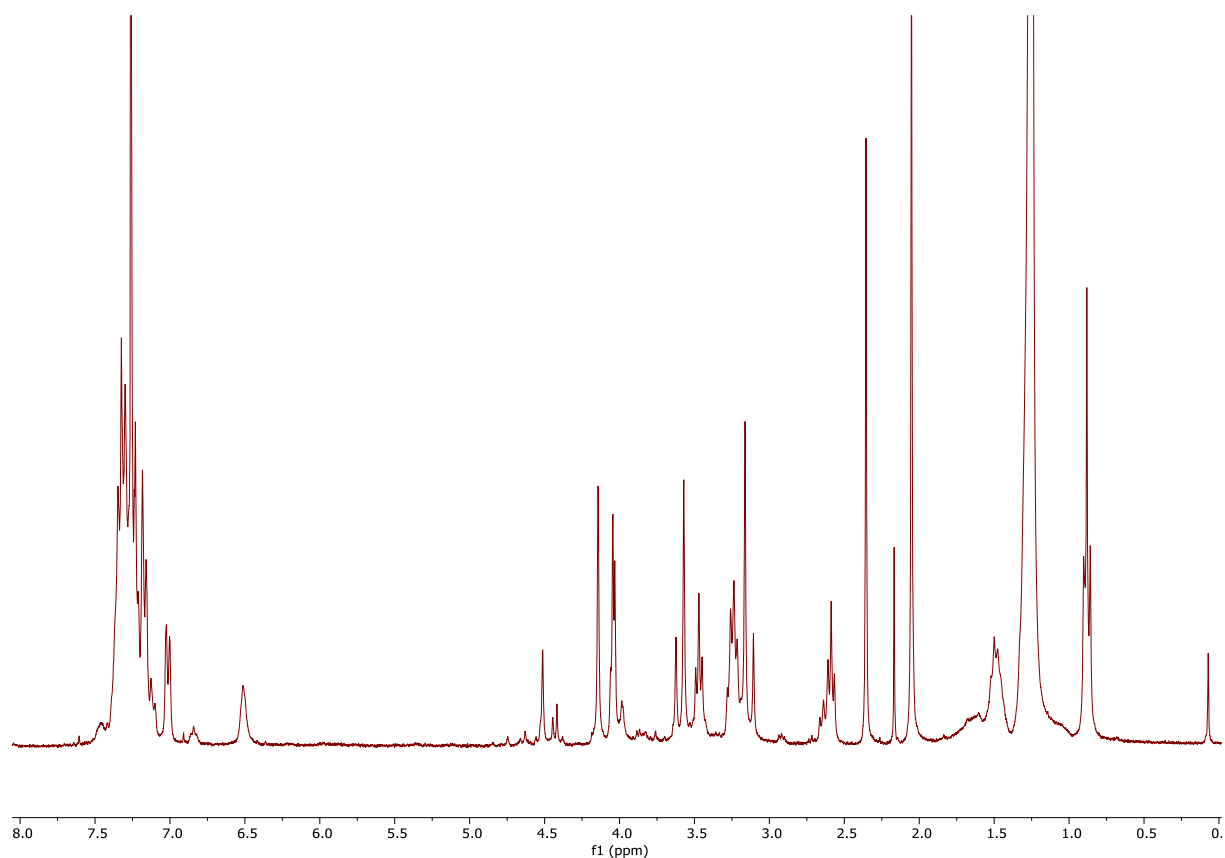


Figure S4. <sup>1</sup>H NMR spectrum of compound **11b**.



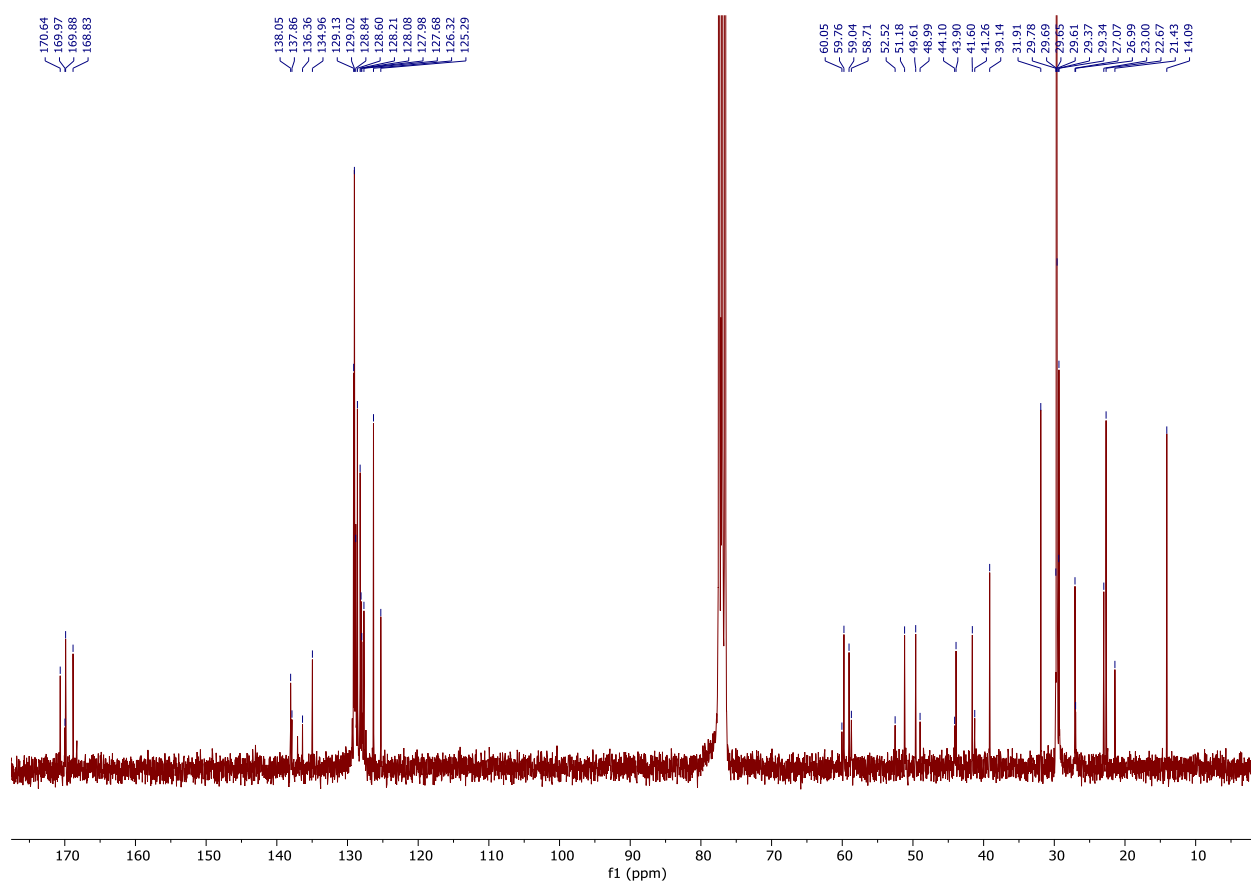
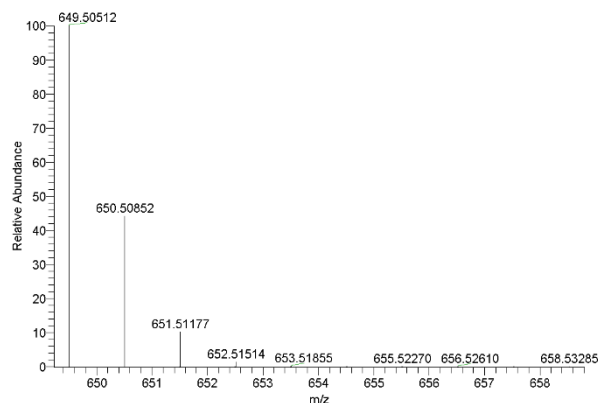


Figure S5.  $^{13}\text{C}$  NMR spectrum of compound **11b**.

Compound\_01\_C40H64N4O3\_fms

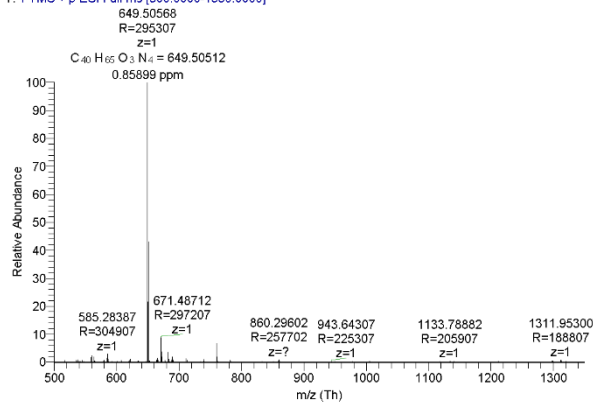
C40H64N4O3 +H: C40 H65 N4 O3 c(gss, sfp:40)(Val) Chr...



Compound\_01\_C40H64N4O3\_fms#40 RT: 0.73  
T: FTMS + p ESI Full ms [500.0000-1350.0000]  
m/z= 558.81-1180.56

m/z	Intensity	Relative	Resolution	Charge	Delta (ppm)	Composition
559.45837	2729123.0	2.36	317807.00	1.00		
563.30194	2127826.5	1.84	309707.00	1.00		
585.28387	3295314.8	2.85	304907.00	1.00		
586.28741	1294085.1	1.12	322102.00	1.00		
621.47430	1315818.8	1.14	305407.00	1.00		
649.50214	7066528.5	6.12	390300.00	0.00	-4.59	C <sub>40</sub> H <sub>65</sub> O <sub>3</sub> N <sub>4</sub>
649.50568	115511120.0	100.00	295307.00	1.00	0.86	C <sub>40</sub> H <sub>65</sub> O <sub>3</sub> N <sub>4</sub>
650.50531	48814544.0	42.26	289202.00	1.00		
651.50555	10407006.0	9.01	296102.00	1.00		
665.50031	1750305.8	1.52	290807.00	1.00		
671.48712	10419124.0	9.02	297207.00	1.00		
672.49060	4413619.0	3.82	301502.00	1.00		
681.42004	4199438.0	3.64	280907.00	1.00		
682.42365	1882626.8	1.63	288502.00	1.00		
683.41748	1267754.4	1.10	293002.00	1.00		
689.53687	2300143.3	1.99	282307.00	1.00		
711.57507	1524660.4	1.32	283607.00	1.00		
739.60651	1290939.3	1.12	277707.00	1.00		
760.30188	7722131.0	6.69	274607.00	1.00		
761.30560	2329272.0	2.02	272102.00	1.00		

Compound\_01\_C40H64N4O3\_fms#40 RT: 0.73 AV: 1 NL: 1.13E8  
T: FTMS + p ESI Full ms [500.0000-1350.0000]



Compound\_01\_C40H64N4O3\_fms RT: 0.02 - 1.73 Mass: 500.00 - 1350.00 NL: 1.48E8

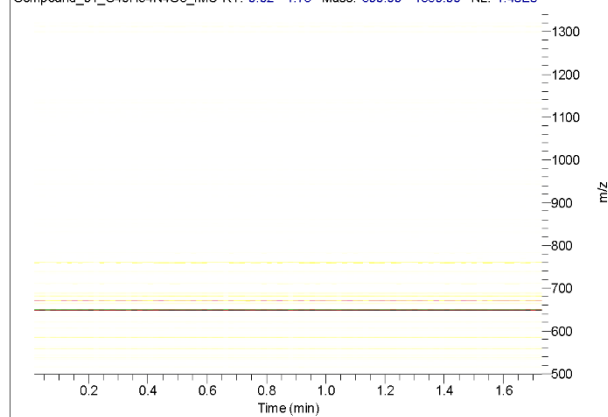


Figure S6. HRMS spectrum of compound **11b**.

1,9-diamino-*N*<sup>9</sup>-acetyl-*N*<sup>1</sup>-octadecyl-1,8-dioxo-*N*<sup>3</sup>,*N*<sup>7</sup>-dibenzyl-3,7-diazanonane  
(**11c**)

Yield: 48%, colorless oil. Eluent: EA-MeOH (9:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, COSY, HSQC, HMBC) δ 0.87 (t, 3H, *J* = 6.9 Hz, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.25 (br. s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.38 – 1.52 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 1.64 – 1.80 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N), 2.04 (s, 3H, COCH<sub>3</sub>), 2.36 – 2.58 (m, 2H, PhCH<sub>2</sub>NCH<sub>2</sub>), 3.06 (s, 2H, COCH<sub>2</sub>N), 3.09 – 3.31 (m, 3H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>, PhCH<sub>2</sub>N(CO)CH<sub>2</sub>), 3.39 (t, 1H, *J* = 7.3 Hz, PhCH<sub>2</sub>N(CO)CH<sub>2</sub>), 3.57 (s, 2H, COCH<sub>2</sub>NH), 4.05 (d, 2H, *J* = 3.9 Hz, PhCH<sub>2</sub>), 4.41 (s, 2H, PhCH<sub>2</sub>NCO), 6.57 (s, 1H, NHCOCH<sub>2</sub>), 6.84 – 7.54 (m, 11H, 2 Ph, CH<sub>3</sub>CONH). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 14.09, 22.67, 22.99, 26.97, 29.31, 29.34, 29.58, 29.61, 29.64, 29.66, 29.69, 31.91, 39.04, 41.51, 44.21, 48.78, 50.08, 51.98, 57.97, 59.91, 126.30, 127.87, 128.06, 128.71, 128.80, 129.13, 135.27, 136.60, 168.06, 170.00, 170.10. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>41</sub>H<sub>67</sub>N<sub>4</sub>O<sub>3</sub> 663.5208, found: 663.5196. HRMS ESI *m/z*: [M+Na]<sup>+</sup> calcd for C<sub>41</sub>H<sub>66</sub>NaN<sub>4</sub>O<sub>3</sub> 685.5033, found: 685.5001.

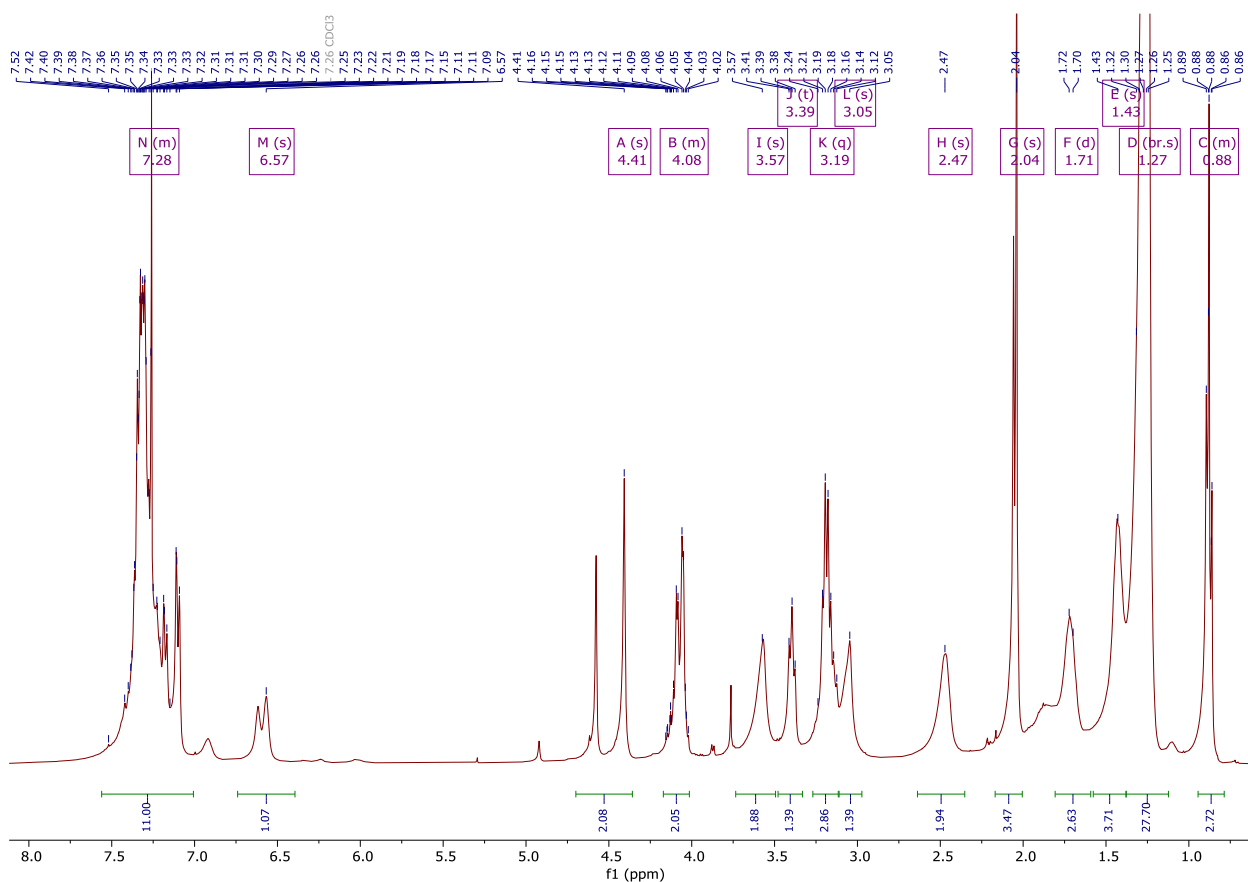


Figure S7. <sup>1</sup>H NMR spectrum of compound **11c**.

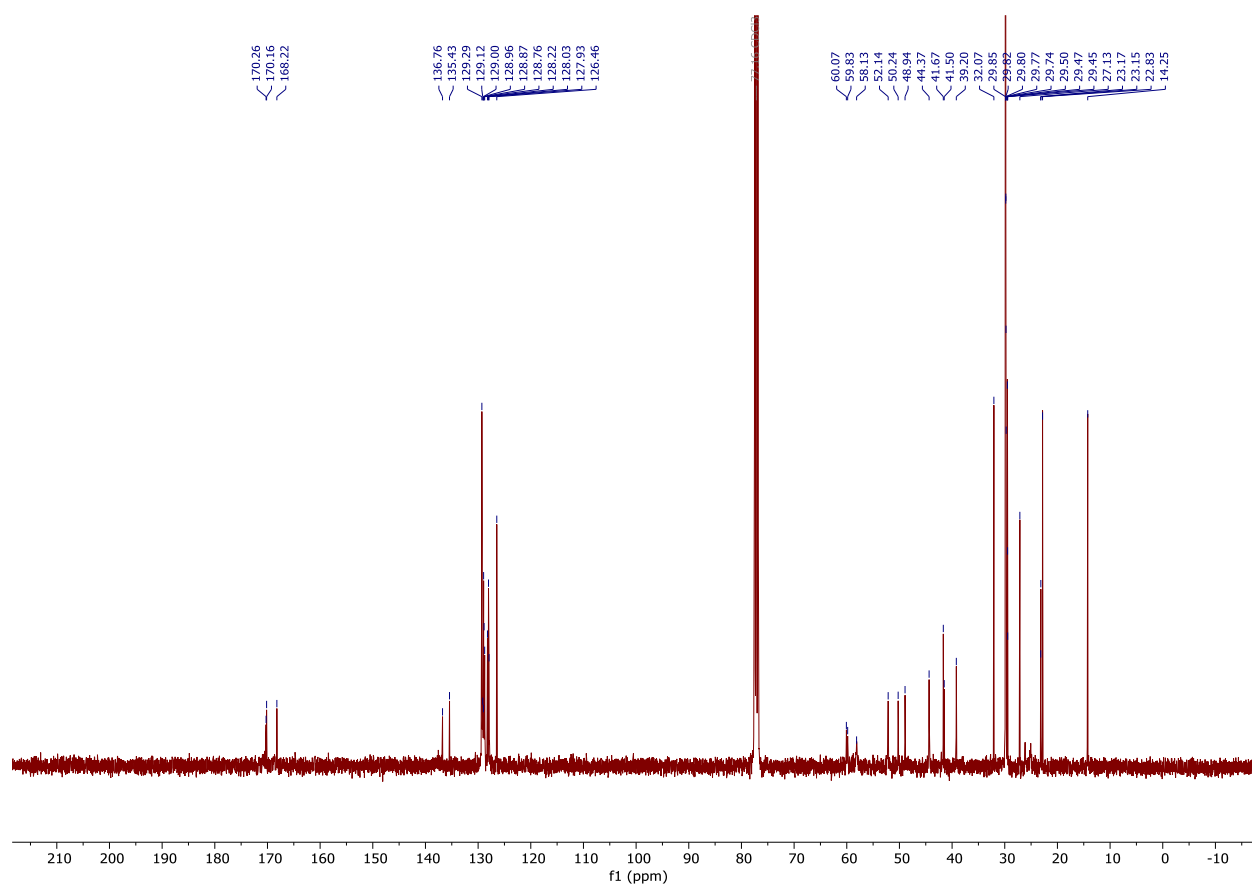
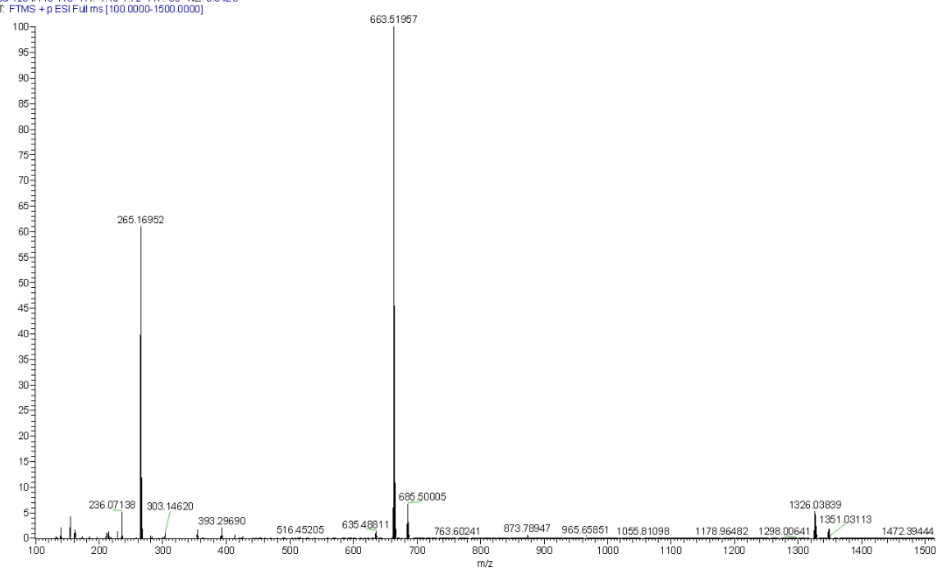


Figure S8. <sup>13</sup>C NMR spectrum of compound **11c**.

**3a-128**

3a-128 #113-173 RT: 1.15-1.72 AV: 30 NL: 6.64E8  
T: FTMS +p ESI Full ms [100.0000-1500.0000]



3a-128 #113-173 RT: 1.15-1.72 AV: 30 NL: 6.64E8  
T: FTMS +p ESI Full ms [100.0000-1500.0000]

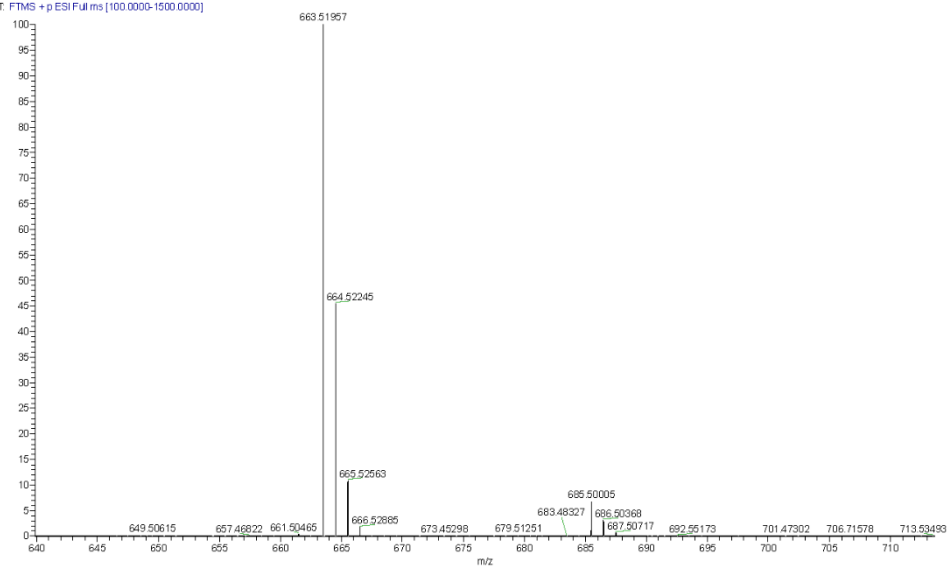


Figure S9. HRMS spectrum of compound **11c**.

1,6-diamino-*N*<sup>1</sup>-acetyl-*N*<sup>6</sup>-octadecyl-6-oxo-*N*<sup>1</sup>,*N*<sup>3</sup>-dibenzyl-4-azahexane (**11d**)

Yield: 35%, colorless oil. Eluent: PE-EA (4:6). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.80 (t, 3H, *J* = 6.6 Hz, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.18 (br. s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.29 – 1.41 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 1.55 – 1.70 (m, 2H, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N), 2.01 (s, 3H, COCH<sub>3</sub>), 2.31 – 2.43 (m, 2H, PhCH<sub>2</sub>NCH<sub>2</sub>), 2.96 (s, 2H, COCH<sub>2</sub>N), 3.05 – 3.17 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 3.29 (t, 2H, *J* = 7.5 Hz, PhCH<sub>2</sub>N(CO)CH<sub>2</sub>), 3.48 (s, 2H, PhCH<sub>2</sub>), 4.37 (s, 2H, PhCH<sub>2</sub>NCO), 6.76 – 7.38 (m, 11H, 2 Ph, NH). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 13.99, 21.29, 21.65, 22.56, 25.09, 26.09, 26.85, 29.16, 29.19, 29.23, 29.47, 29.50, 29.54, 29.58, 31.80, 38.83, 38.86, 43.58, 45.96, 48.18, 51.85, 52.14, 52.27, 57.94, 59.61, 126.11, 127.30, 127.32, 127.46, 127.57, 127.59, 127.86, 128.23, 128.38, 128.48, 128.50, 128.55, 128.64, 128.69, 128.73, 128.84, 128.95, 129. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>39</sub>H<sub>63</sub>N<sub>3</sub>O<sub>2</sub> 606.4993, found: 606.4991.

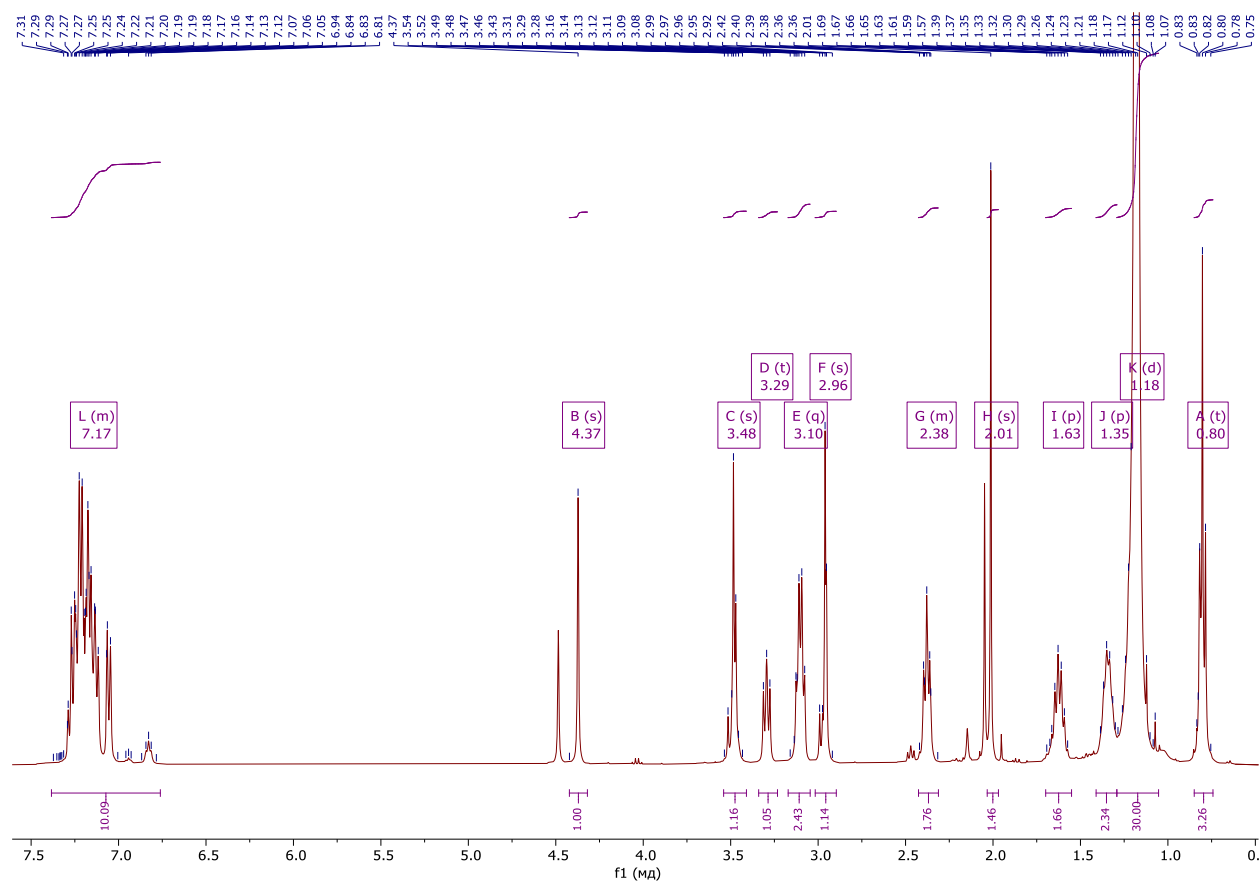


Figure S10. <sup>1</sup>H NMR spectrum of compound **11d**.

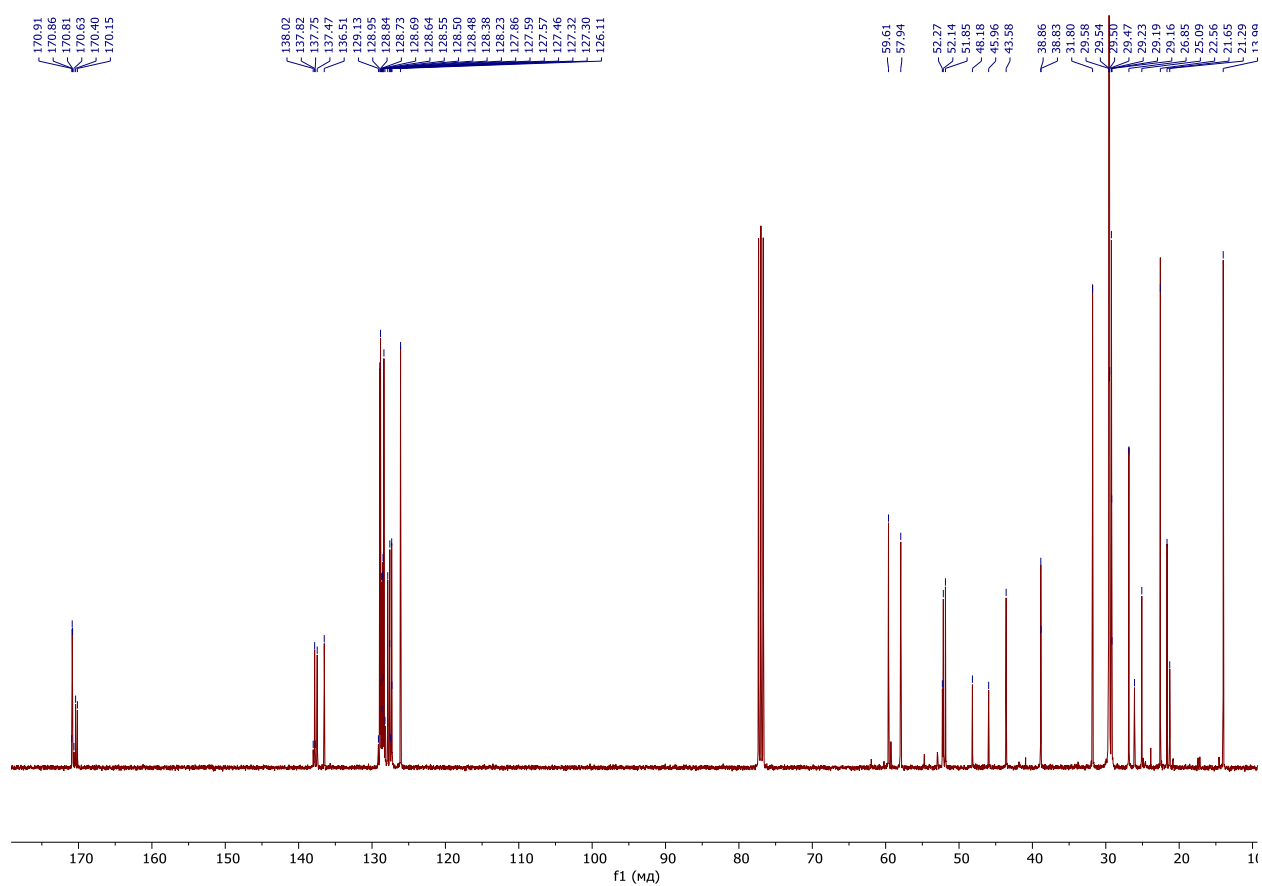
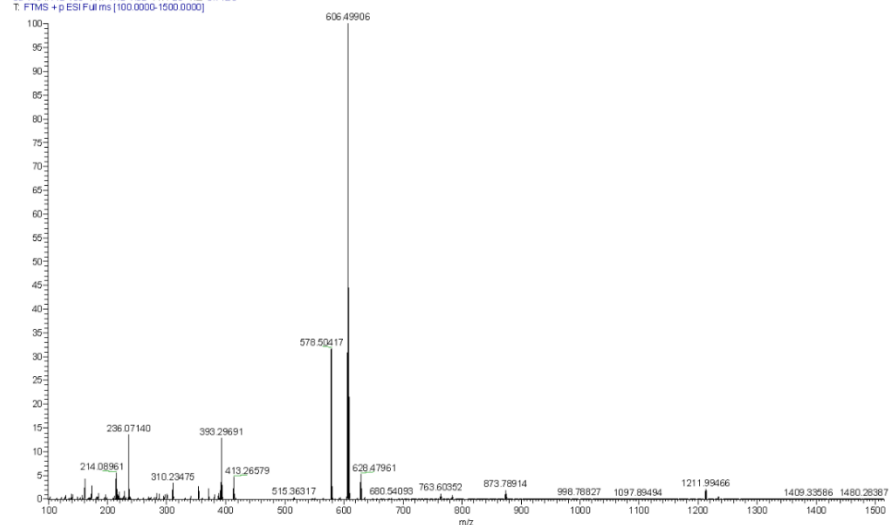


Figure S11. <sup>13</sup>C NMR spectrum of compound **11d**.

**3a-118**

3a-118 #112-163 RT: 1.12-1.62 AV: 26 NL: 3.71E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



3a-118 #112-163 RT: 1.12-1.62 AV: 26 NL: 3.71E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

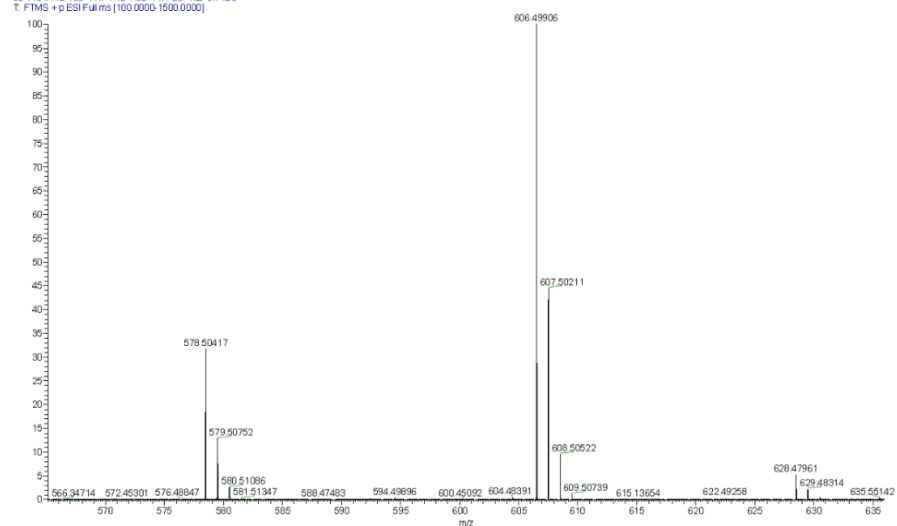


Figure S12. HRMS spectrum of compound **11d**.

1,7-diamino-*N*<sup>1</sup>-acetyl-*N*<sup>7</sup>-octadecyl-7-oxo-*N*<sup>1</sup>,*N*<sup>4</sup>-dibenzyl-5-azaheptane (**11e**)

Yield: 30%, colorless oil. Eluent: EA. <sup>1</sup>H NMR (300 MHz, main rotamer, CDCl<sub>3</sub>) δ 0.71 (t, 3H, *J* = 6.7 Hz, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.12 (br.s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.19 – 1.41 (m, 6H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>, NCH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>N), 1.93 (s, 3H, COCH<sub>3</sub>), 2.21 – 2.36 (m, 2H PhCH<sub>2</sub>NCH<sub>2</sub>), 2.88 (s, 2H, NCH<sub>2</sub>CO), 2.94 – 3.22 (m, 4H, COCH<sub>2</sub>N, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 3.40 (s, 2H, PhCH<sub>2</sub>), 4.32 (s, 2H, PhCH<sub>2</sub>NCO), 6.78 – 7.31 (m, 2 Ph, NH, 11H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.22, 21.56, 21.88, 22.78, 24.67, 25.32, 26.37, 27.06, 29.44, 29.79, 32.01, 39.01, 46.01, 47.88, 48.26, 52.18, 54.80, 58.14, 59.65, 59.92, 126.25, 127.48, 127.70, 128.01, 128.64, 128.83, 128.93, 129.03, 136.90, 137.74, 138.08, 138.24, 170.94, 171.15. HRMS FTICR *m/z*: [M+H]<sup>+</sup> calcd for C<sub>40</sub>H<sub>66</sub>N<sub>3</sub>O<sub>2</sub> 620.5150, found: 620.5136.

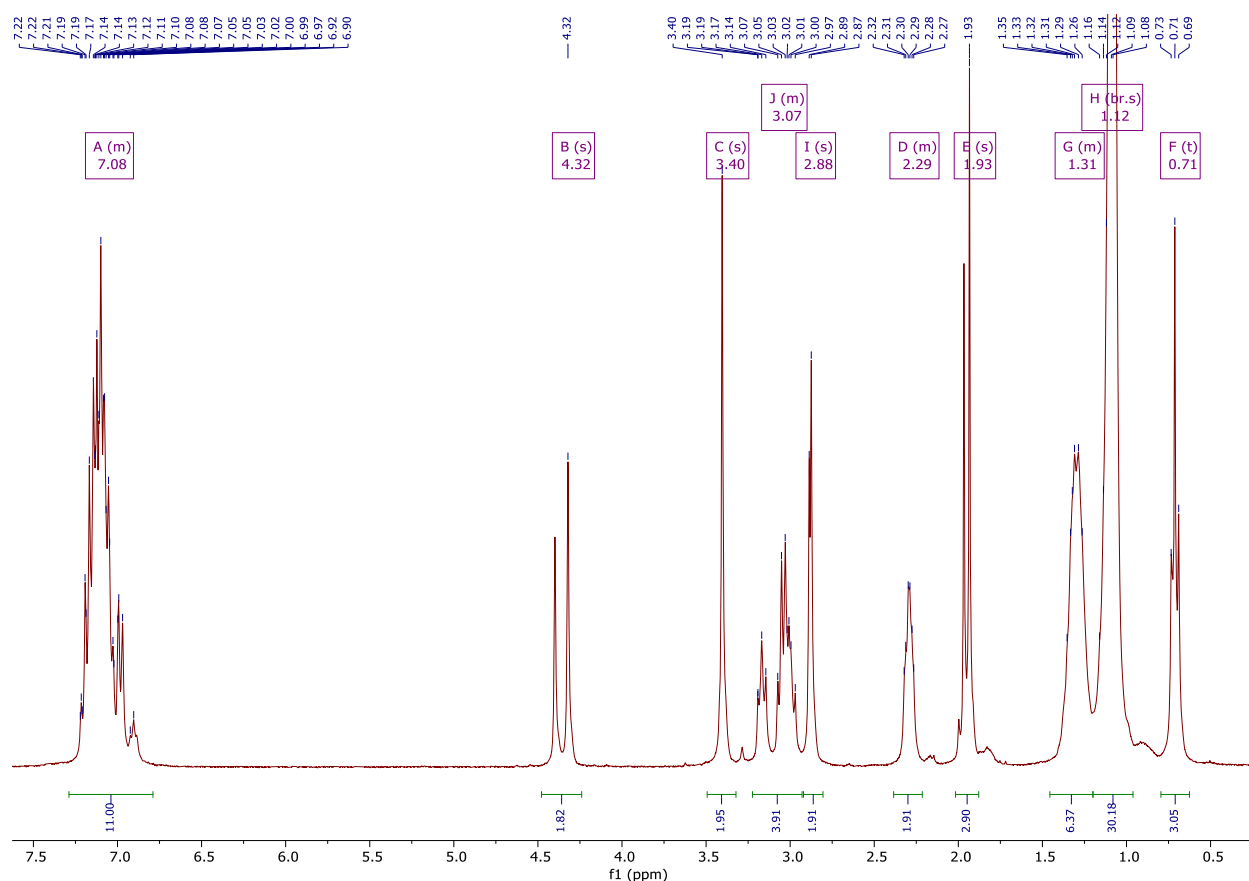


Figure S13. <sup>1</sup>H NMR spectrum of compound **11e**.



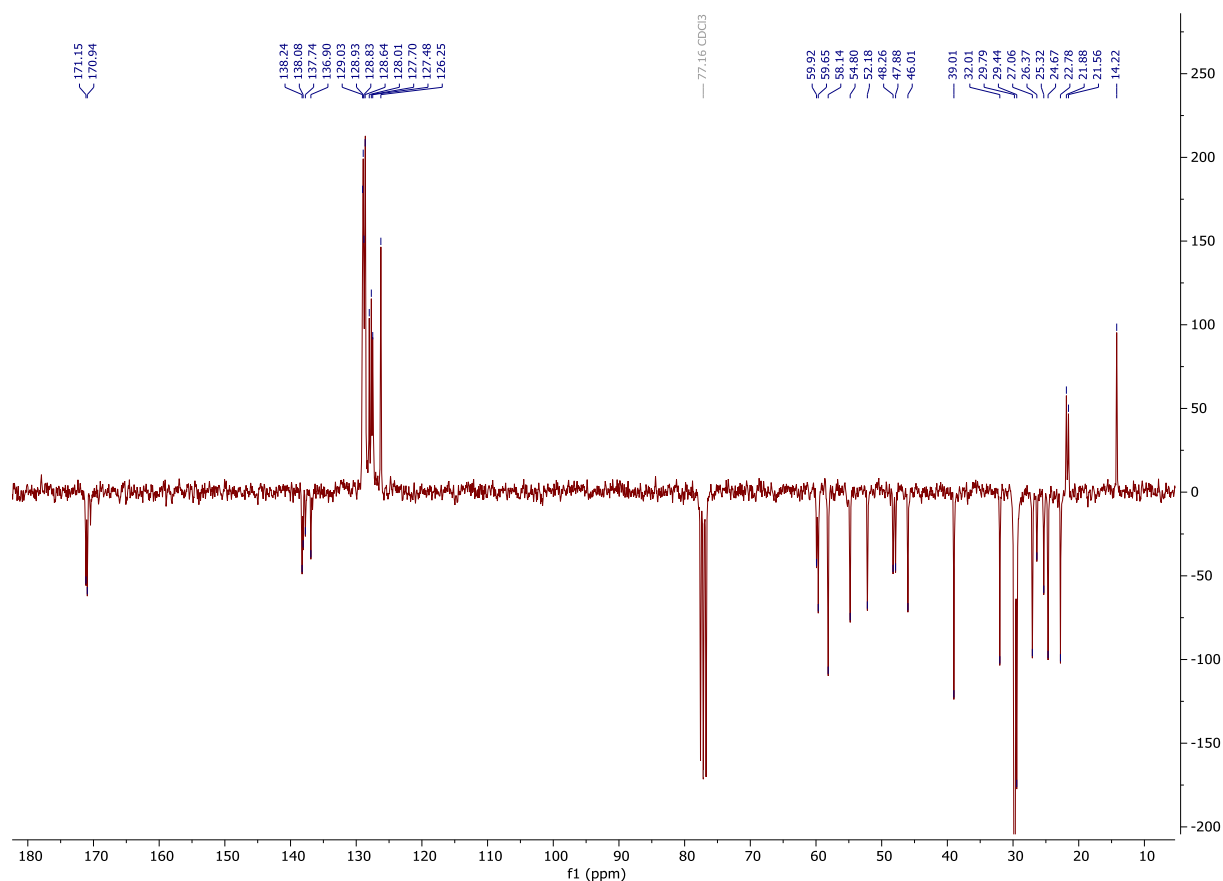


Figure S14. <sup>13</sup>C (APT) NMR spectrum of compound **11e**.

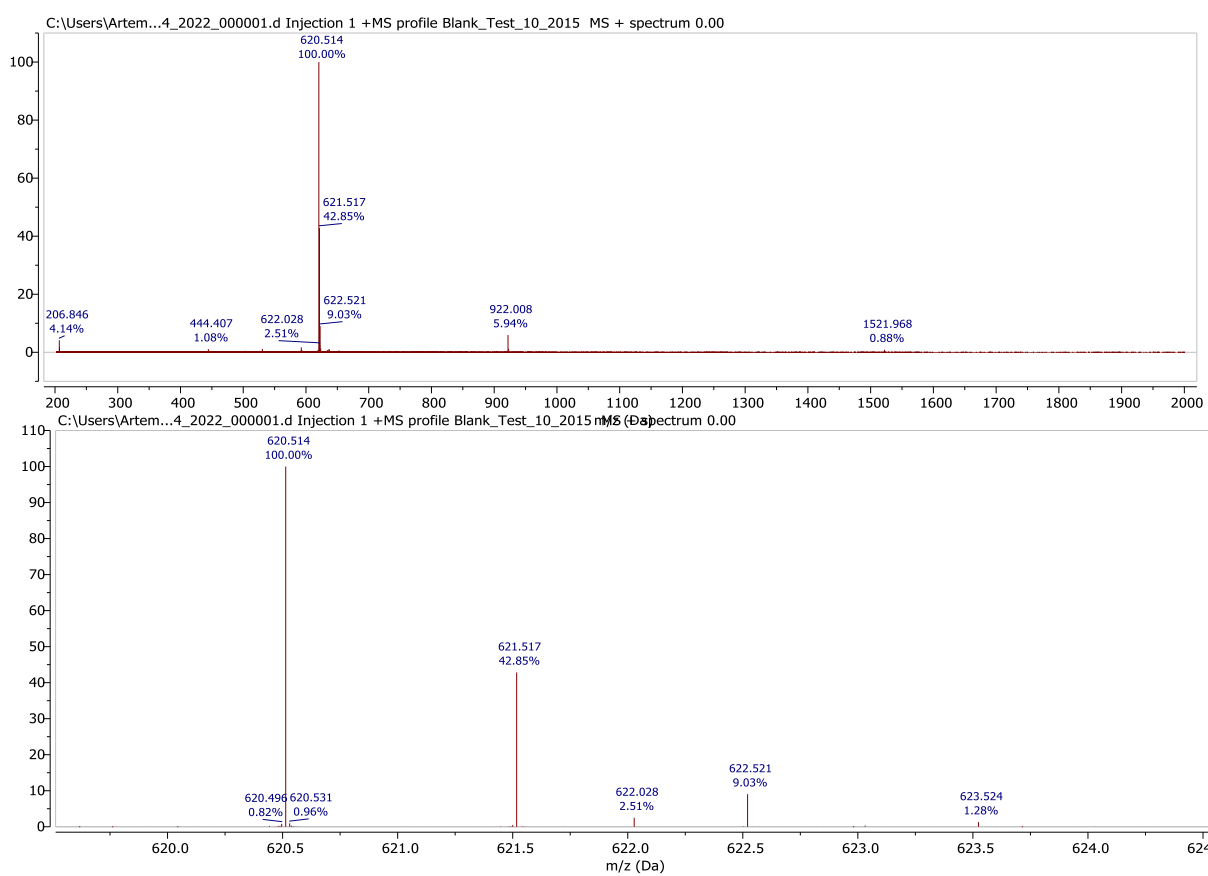


Figure S15. HRMS spectrum of compound **11e**.

*N*<sup>1</sup>-(*N*-acetylglycyl)-*N*<sup>4</sup>-[(*N*-octadecyl)aminocarbonyl]methylpiperazin (**12a**)

Yield: 60%, colorless oil. Eluent: DCM-MeOH (20:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, <sup>1</sup>H-<sup>1</sup>H COSY) δ 0.84 (d, 3H, *J* = 6.9 Hz (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.22 (br. s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.41 – 1.54 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 2.01 (s, 3H, COCH<sub>3</sub>), 2.47 – 2.55 (m, 4H, 2 COCH<sub>2</sub>NCH<sub>2</sub> Pip), 3.00 (s, 2H, COCH<sub>2</sub>N), 3.19 – 3.29 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 3.38 – 3.46 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 3.60 – 3.66 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 4.02 (d, 2H, *J* = 4.1 Hz, COCH<sub>2</sub>NH), 6.61 (t, 1H, *J* = 4.1 Hz, NHCOCH<sub>3</sub>), 6.92 (t, 1H, *J* = 5.5 Hz, CH<sub>2</sub>CONH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.06, 22.64, 22.93, 26.95, 29.24, 29.31, 29.53, 29.56, 29.61, 29.65, 29.67, 31.88, 39.00, 41.23, 41.98, 44.35, 52.97, 53.19, 61.49, 166.55, 169.00, 170.08. HRMS FTICR *m/z*: [M+H]<sup>+</sup> calcd for C<sub>28</sub>H<sub>55</sub>N<sub>4</sub>O<sub>3</sub> 495.4269, found: 495.4269.

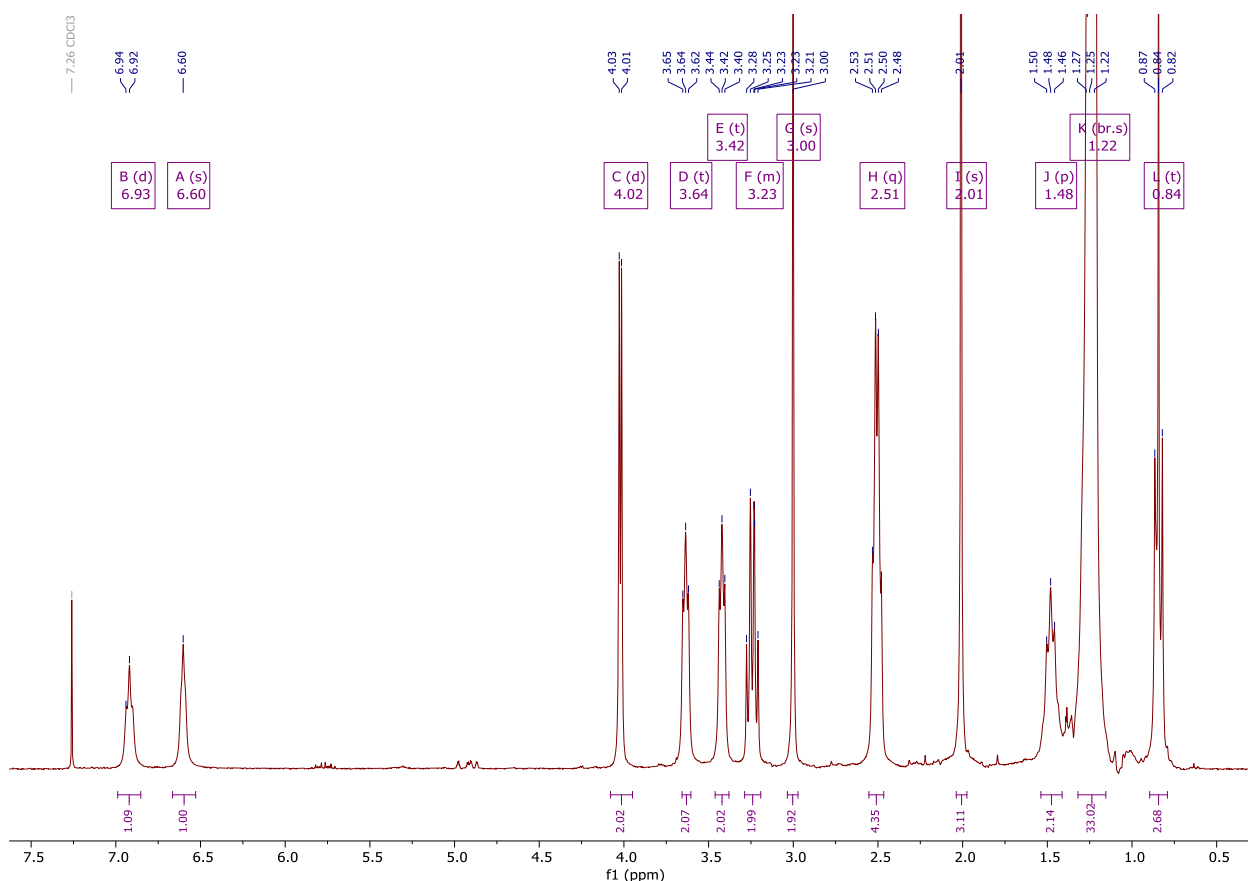


Figure S16. <sup>1</sup>H NMR spectrum of compound **12a**.

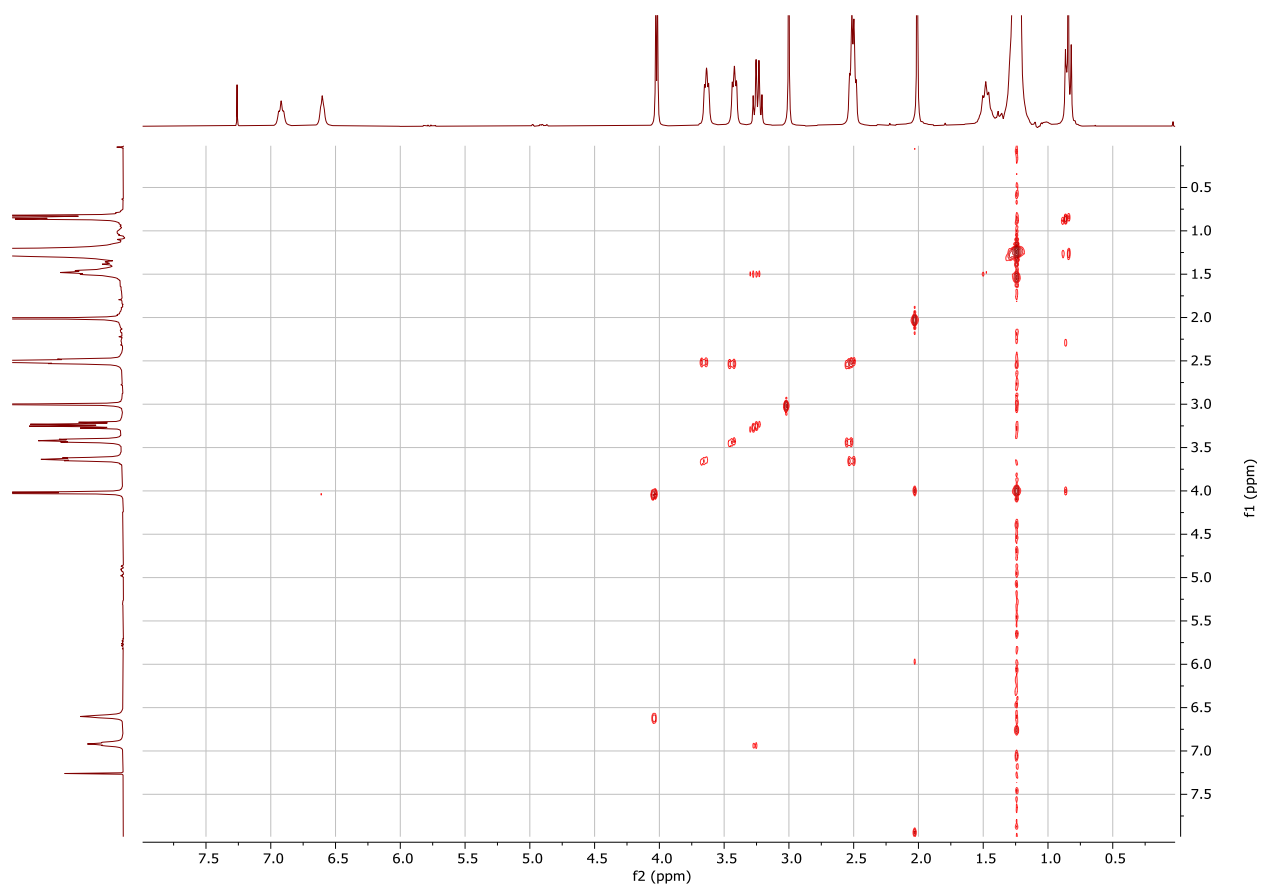


Figure S17.  $\{^1\text{H}-^1\text{H}\}$  COSY NMR spectrum of compound **12a**.

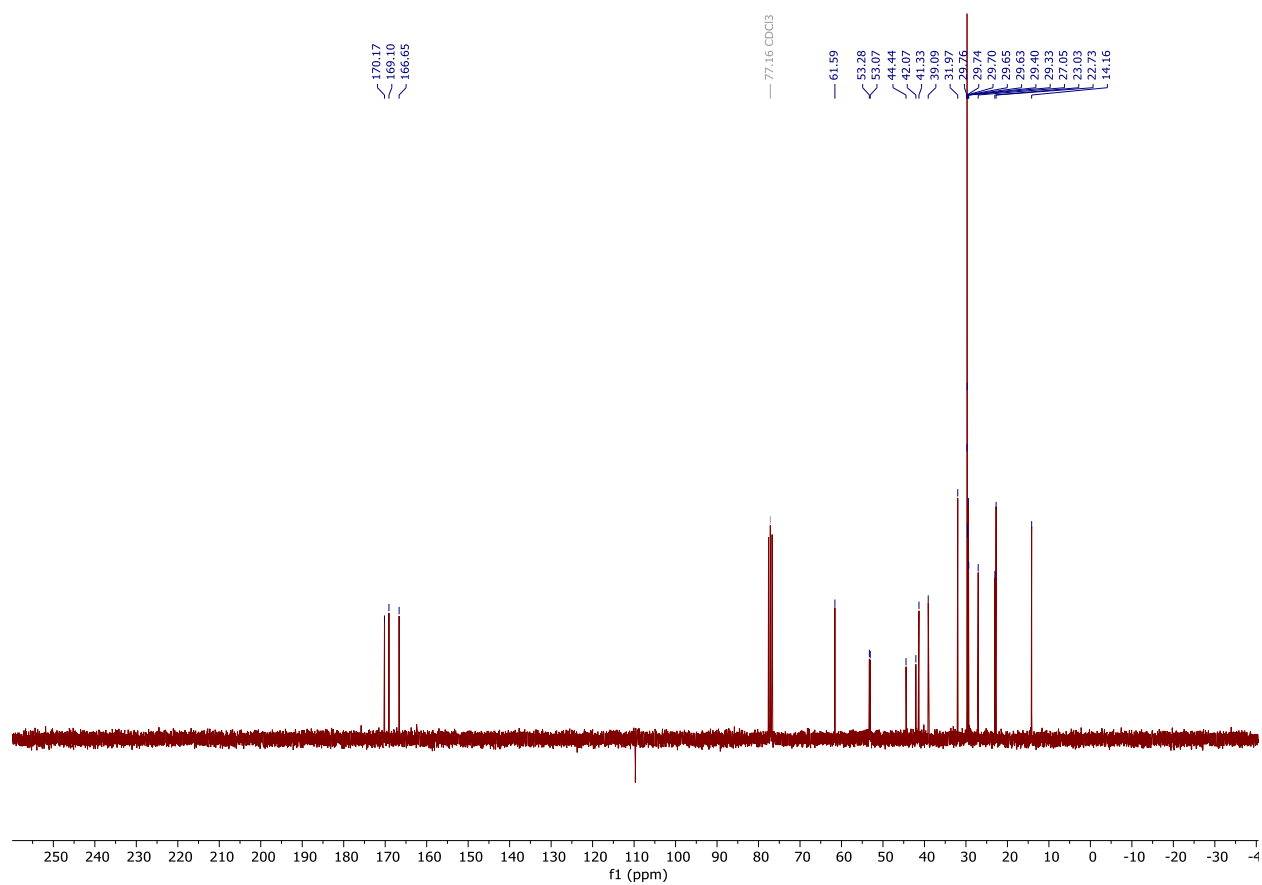


Figure S18.  $^{13}\text{C}$  NMR spectrum of compound **12a**.

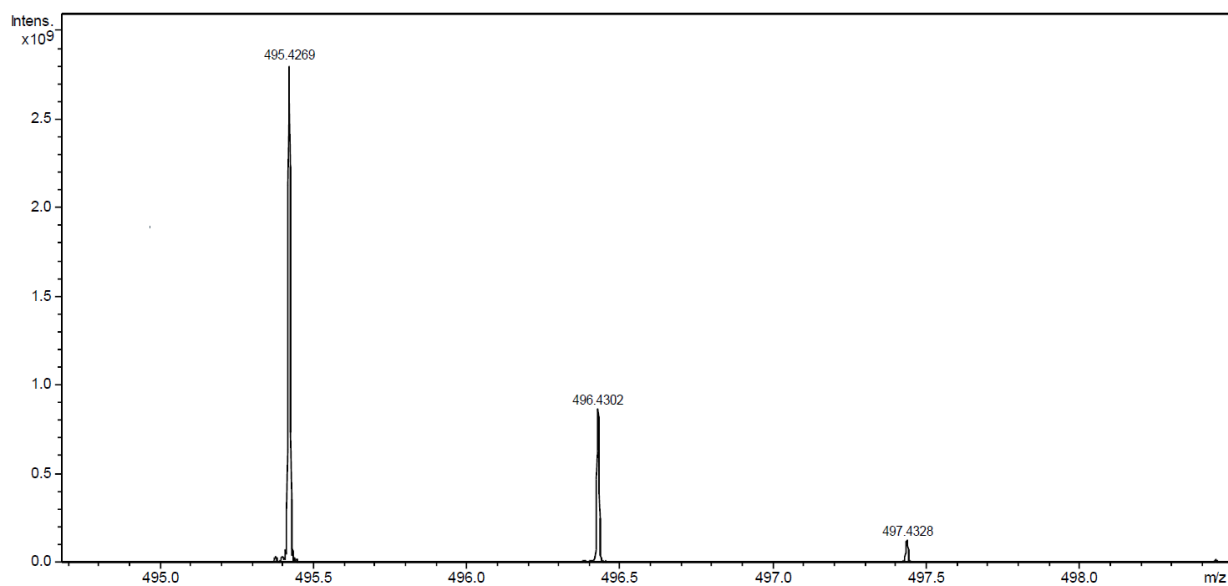


Figure S19. HRMS spectrum of compound **12a**.

*N*<sup>1</sup>-acetyl-*N*<sup>4</sup>-[(*N*-octadecyl)aminocarbonyl]methylpiperazin (**12b**)

Yield: 80%, colorless oil. Eluent: DCM-MeOH (30:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, <sup>1</sup>H-<sup>1</sup>H COSY) δ 0.90 (t, 3H, *J* = 7.0 Hz, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.26 (br. s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.48 – 1.61 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 2.11 (s, 3H, COCH<sub>3</sub>), 2.49 – 2.59 (m, 4H, 2 COCH<sub>2</sub>NCH<sub>2</sub> Pip), 3.05 (s, 2H, COCH<sub>2</sub>N), 3.20 – 3.37 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 3.46 – 3.54 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 3.63 – 3.69 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 7.06 (br. s, 1H, NH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.09, 21.28, 22.66, 26.94, 29.24, 29.32, 29.54, 29.57, 29.62, 29.66, 31.89, 38.98, 41.32, 46.15, 53.12, 53.45, 61.47, 168.95, 169.13. HRMS FTICR *m/z*: [M+H]<sup>+</sup> calcd for C<sub>28</sub>H<sub>55</sub>N<sub>4</sub>O<sub>3</sub> 438.4054, found: 438.4054.

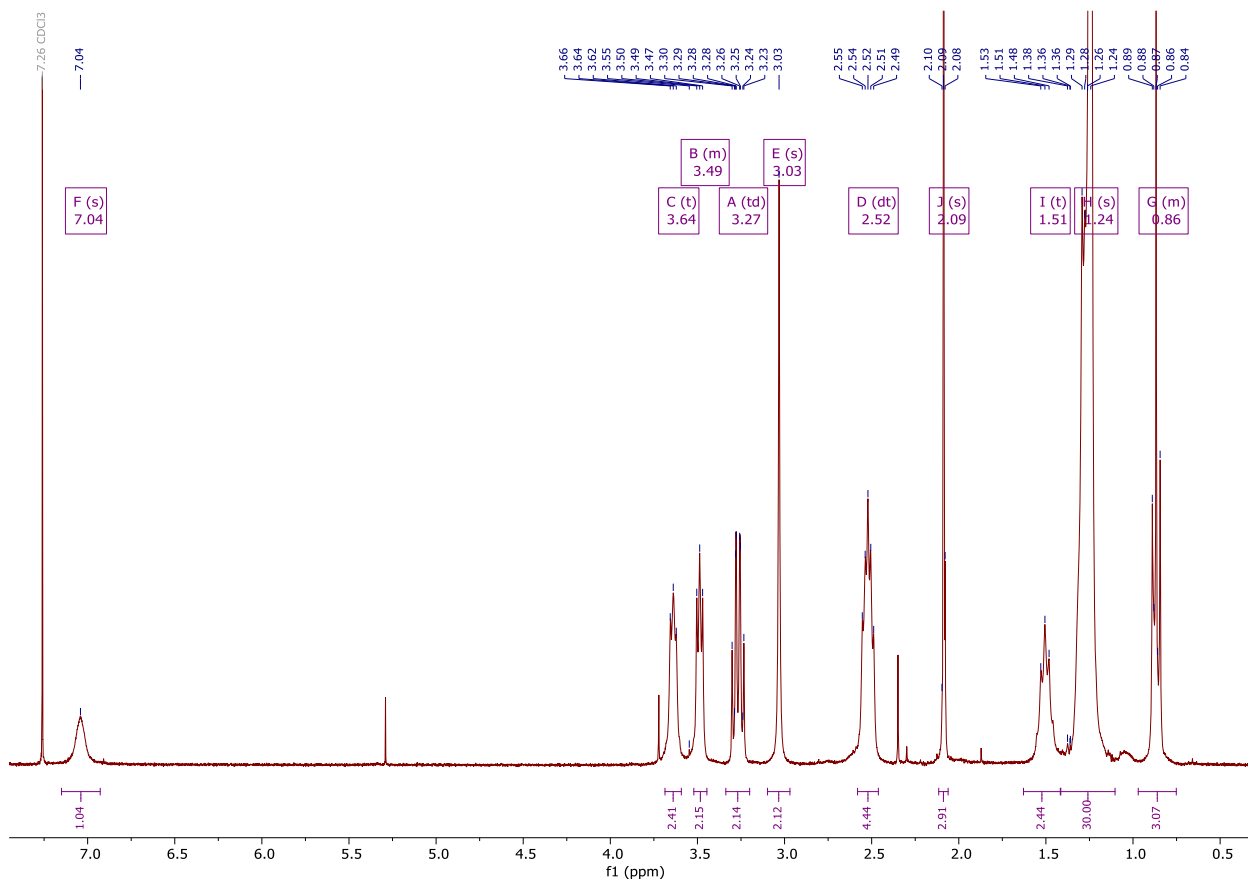


Figure S20. <sup>1</sup>H NMR spectrum of compound **12b**.

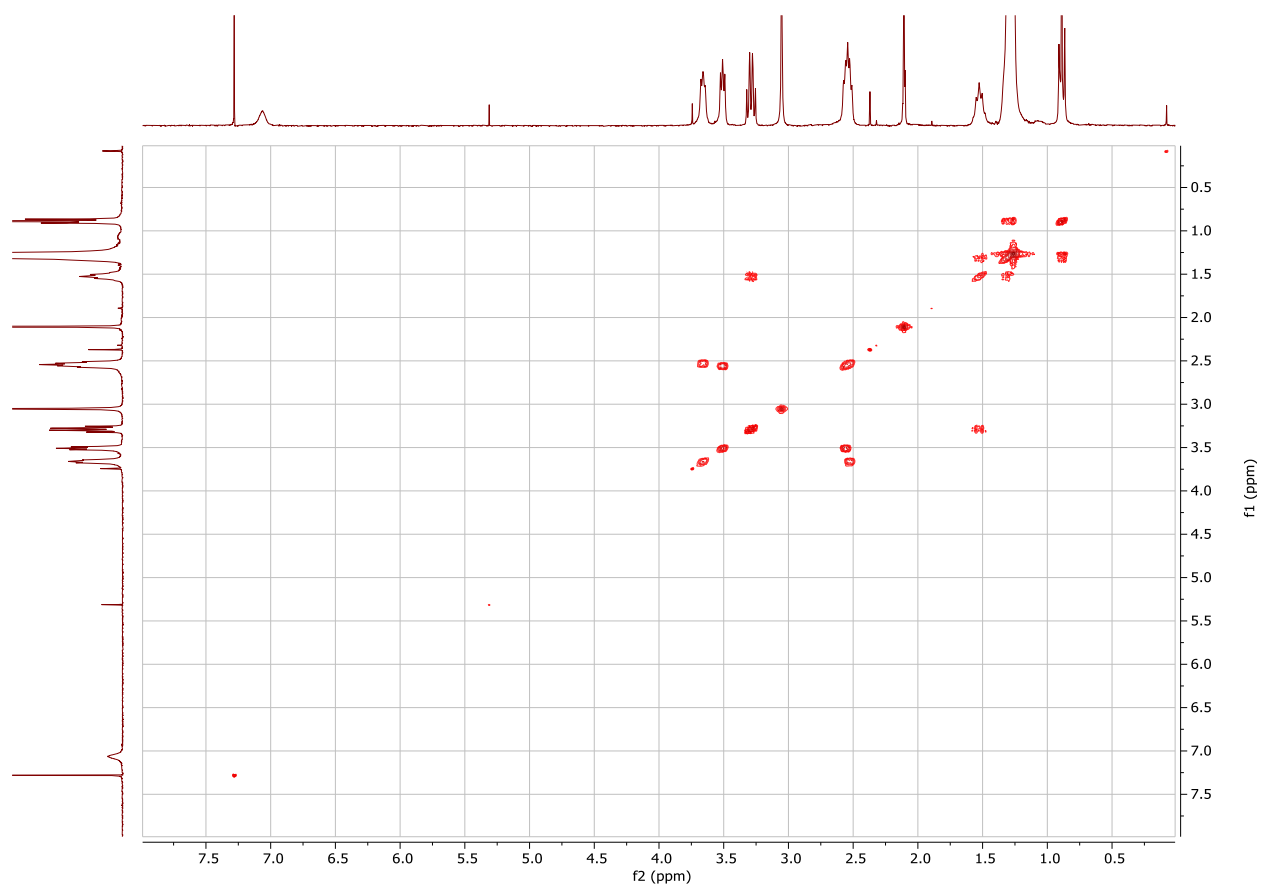


Figure S21.  $\{^1\text{H}-^1\text{H}\}$  COSY NMR spectrum of compound **12b**.

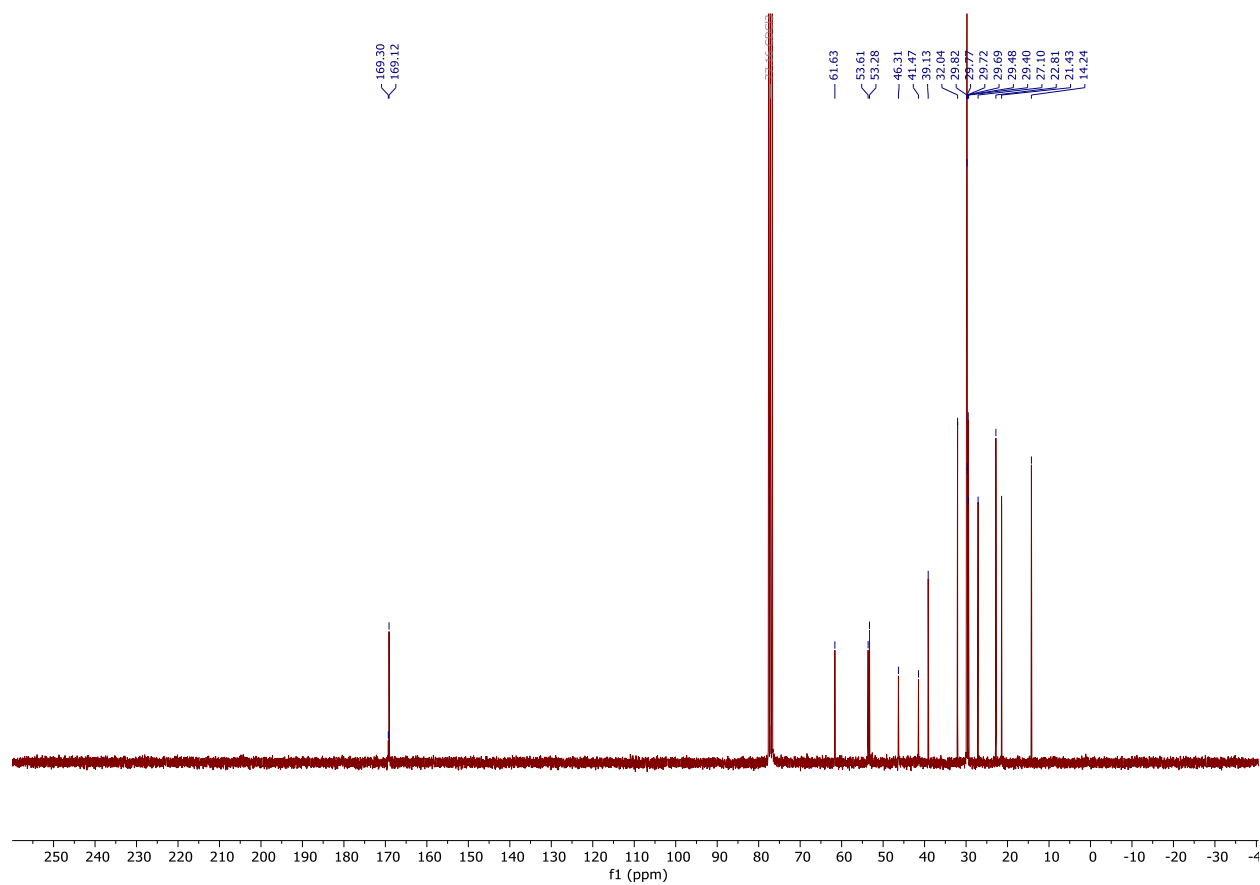


Figure S22.  $^{13}\text{C}$  NMR spectrum of compound **12b**.

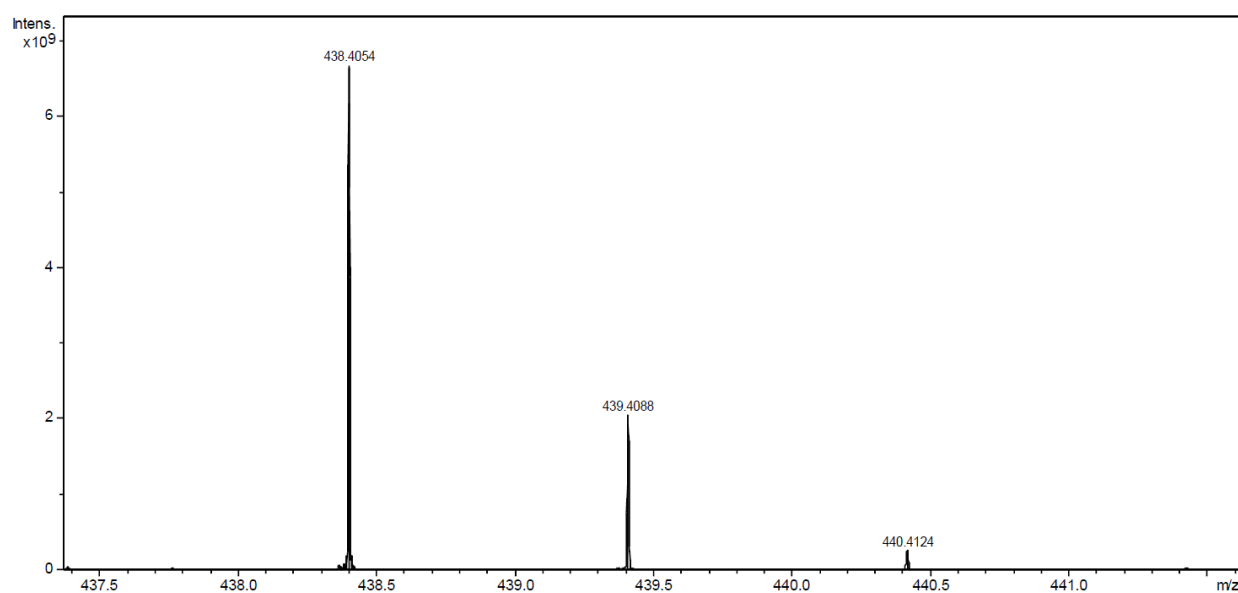


Figure S23. HRMS spectrum of compound **12b**.

Yield: 47%, colorless oil. Eluent: DCM-MeOH (15:1). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>, COSY, HSQC, HMBC) δ 0.85 (t, 3H, *J* = 6.9 Hz, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.09 (t, 3H, *J* = 7.0 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.24 (br. s, 14H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.43 – 1.51 (m, 2H, OCH<sub>2</sub>CH<sub>2</sub>), 1.86 (s, 3H, COCH<sub>3</sub>), 2.34 – 2.42 (m, 2H, 2 COCH<sub>2</sub>NCH<sub>2</sub>H<sub>a</sub> Pip), 2.42 – 2.48 (m, 2H, 2 COCH<sub>2</sub>NCH<sub>2</sub>H<sub>a</sub> Pip), 2.93 (d, *J* = 15.5 Hz, 1H, COCH<sub>2</sub>H<sub>b</sub>N), 2.96 (d, *J* = 15.5 Hz, 1H, COCH<sub>2</sub>H<sub>b</sub>N), 3.07 – 3.13 (m, 1H, CONHCH<sub>2</sub>H<sub>b</sub>), 3.25 – 3.32 (m, 1H, NHCH<sub>2</sub>H<sub>b</sub>CH), 3.33 – 3.40 (m, 4H, CH<sub>2</sub>OCH<sub>2</sub>), 3.40 – 3.52 (m, 6H, CHOCH<sub>2</sub>H<sub>b</sub>CH<sub>3</sub>, 2 CONCH<sub>2</sub> Pip), 3.52 – 3.59 (m, 1H, OCH<sub>2</sub>H<sub>b</sub>CH<sub>3</sub>), 3.92 (d, 2H, *J* = 5.5 Hz, COCH<sub>2</sub>NH), 7.63 -7.70 (m, 1H, CHCH<sub>2</sub>NH), 7.91 (t, 1H, *J* = 5.5 Hz, COCH<sub>2</sub>NH). <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 13.86, 15.50, 22.04, 22.35, 25.57, 28.66, 28.79, 28.95, 28.97, 28.99, 29.00, 29.11, 31.25, 39.59, 40.32, 41.27, 44.00, 52.38, 52.74, 60.87, 64.39, 70.59, 71.05, 76.33, 166.95, 168.84, 169.19. HRMS FTICR *m/z*: [M+H]<sup>+</sup> calcd for C<sub>27</sub>H<sub>53</sub>N<sub>4</sub>O<sub>5</sub> 513.4010, found: 513.4010.

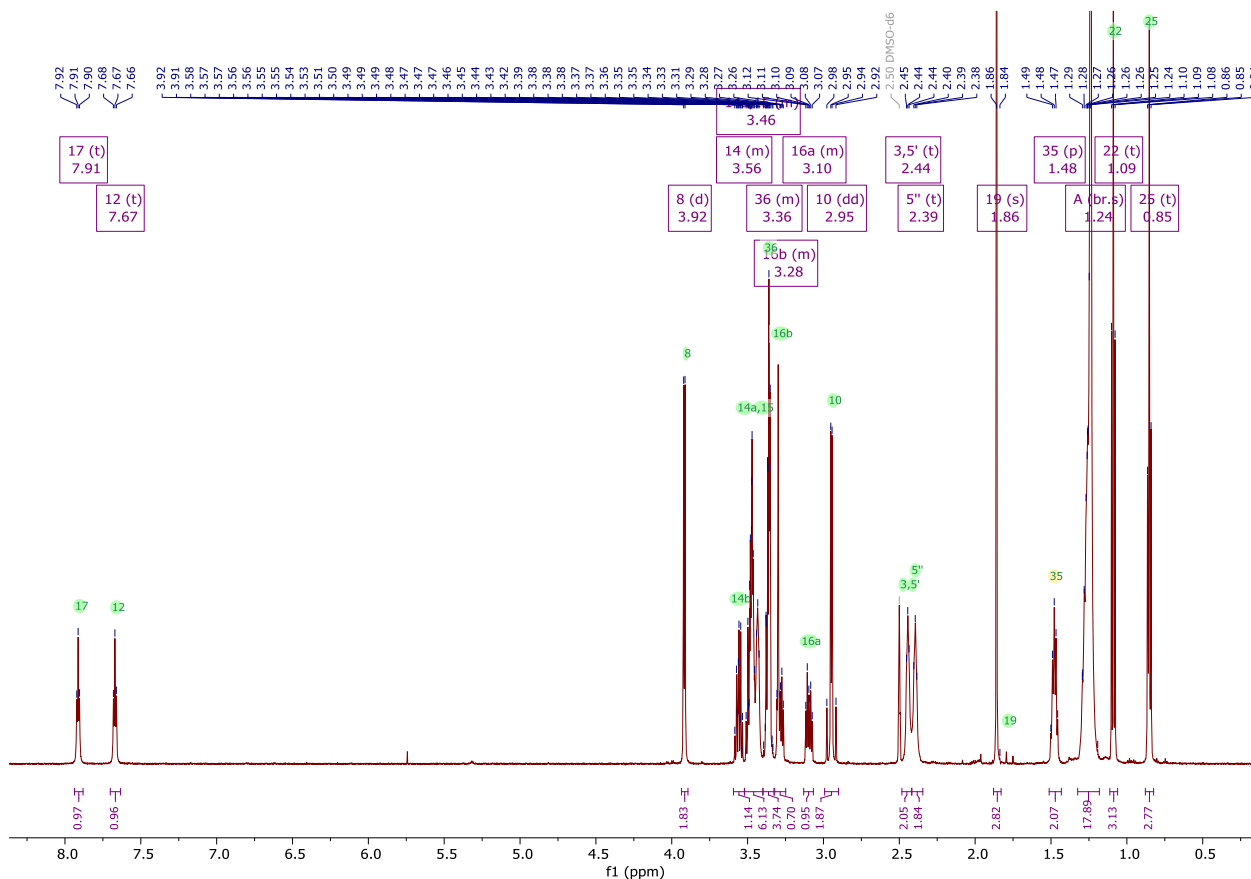


Figure S24. <sup>1</sup>H NMR spectrum of compound **12c**.



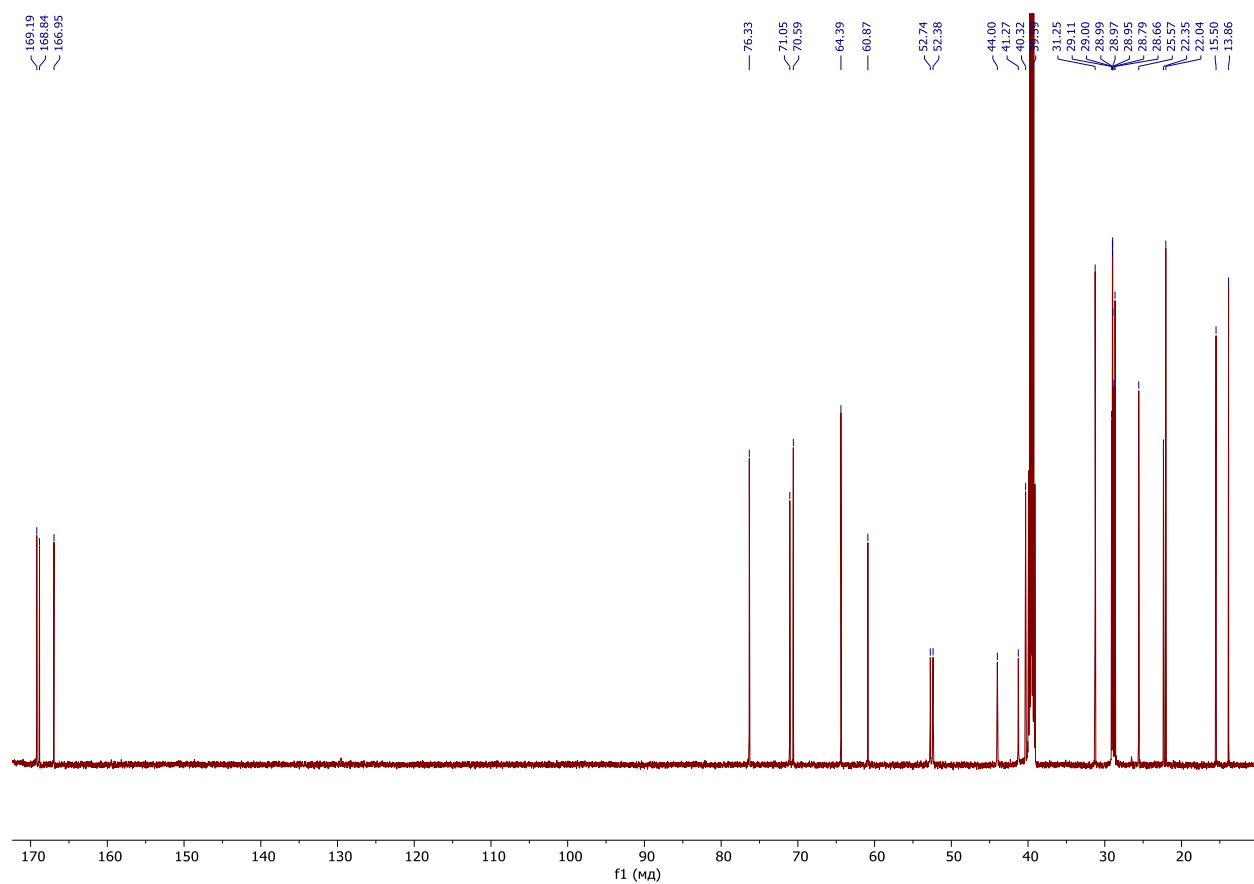


Figure S25.  $^{13}\text{C}$  NMR spectrum of compound **12c**.

DEPT-135

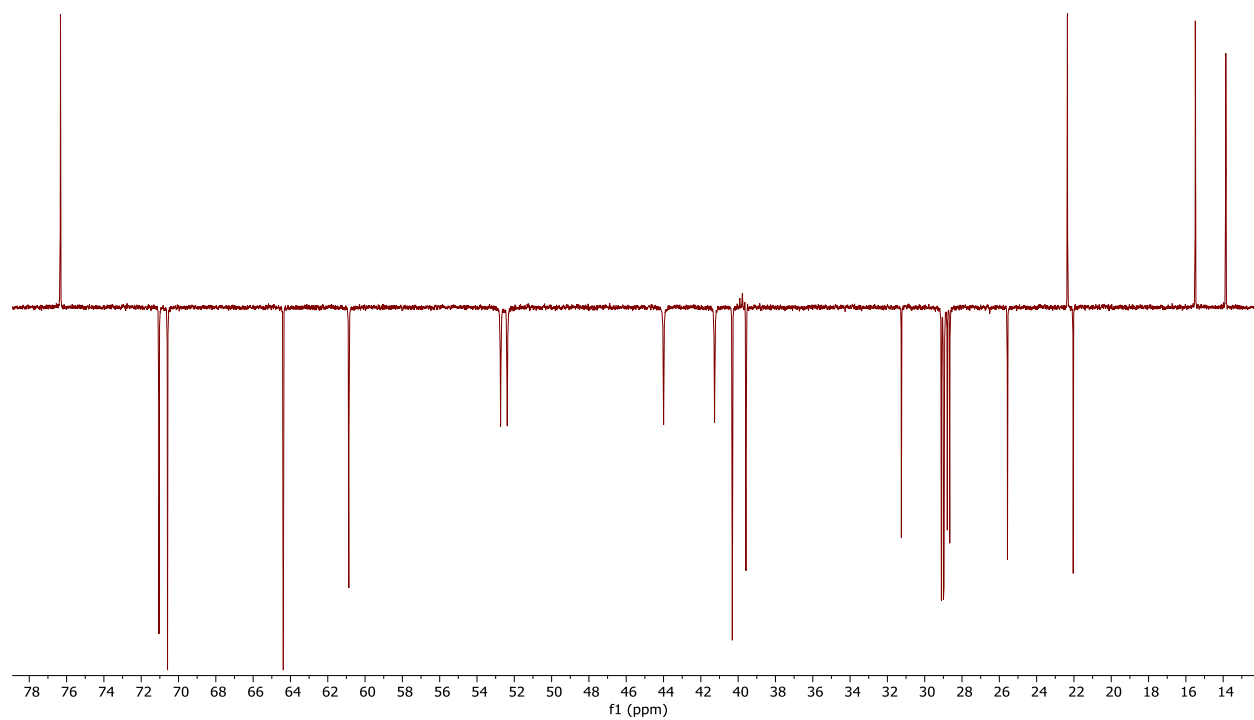


Figure S26. DEPT-135 NMR spectrum of compound **12c**.

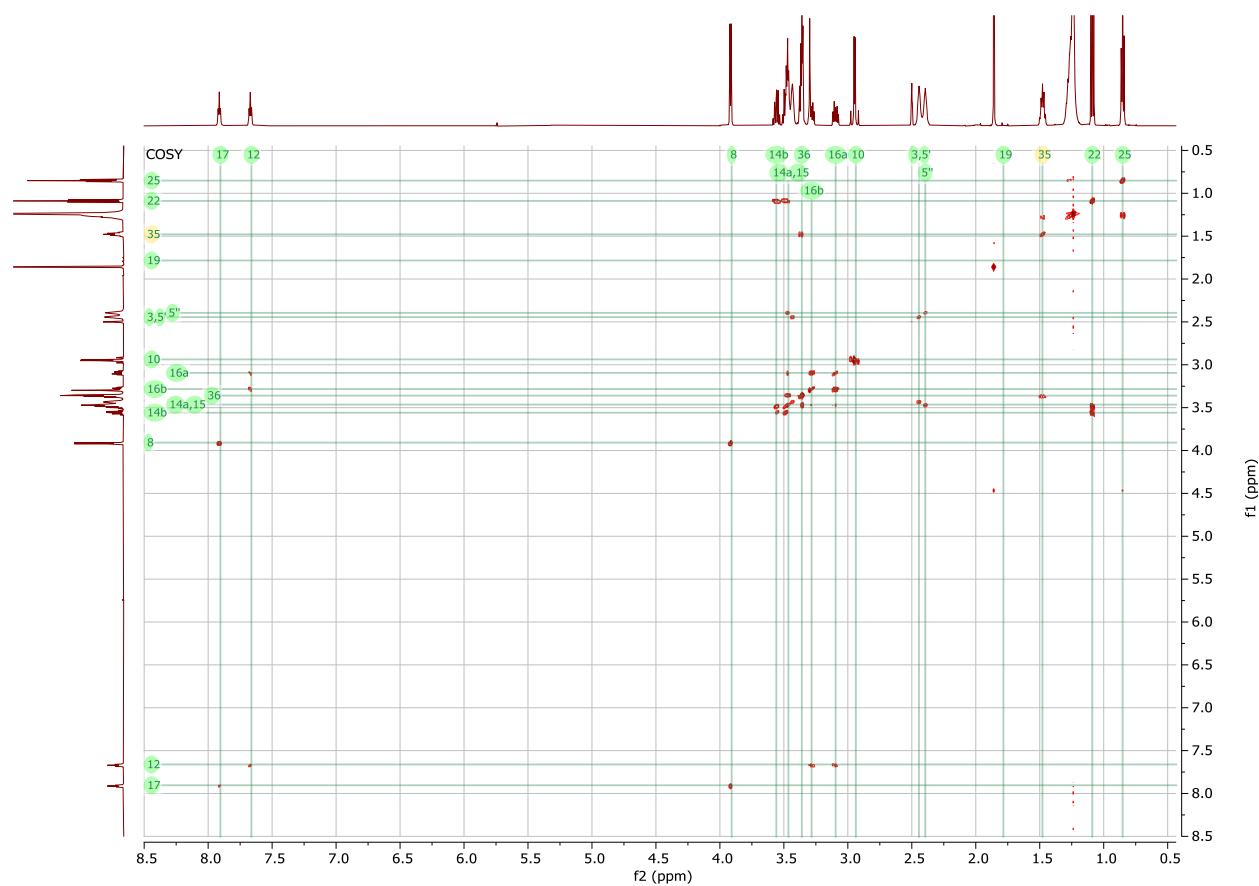


Figure S27.  $\{^1\text{H}-^1\text{H}\}$  COSY NMR spectrum of compound **12c**.

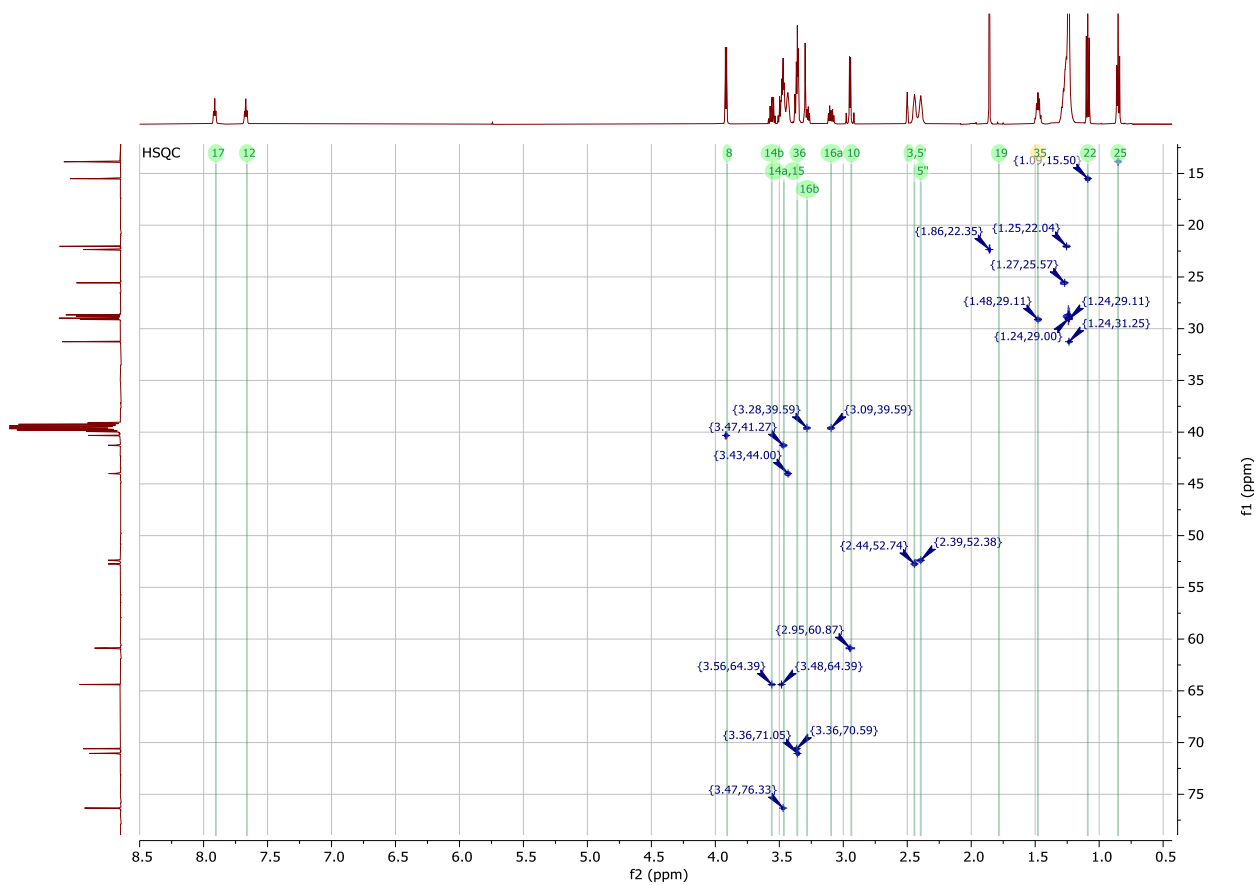


Figure S28.  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **12c**.



Figure S29.  $\{^1\text{H}-^{13}\text{C}\}$  HMBC NMR spectrum of compound **12c**.

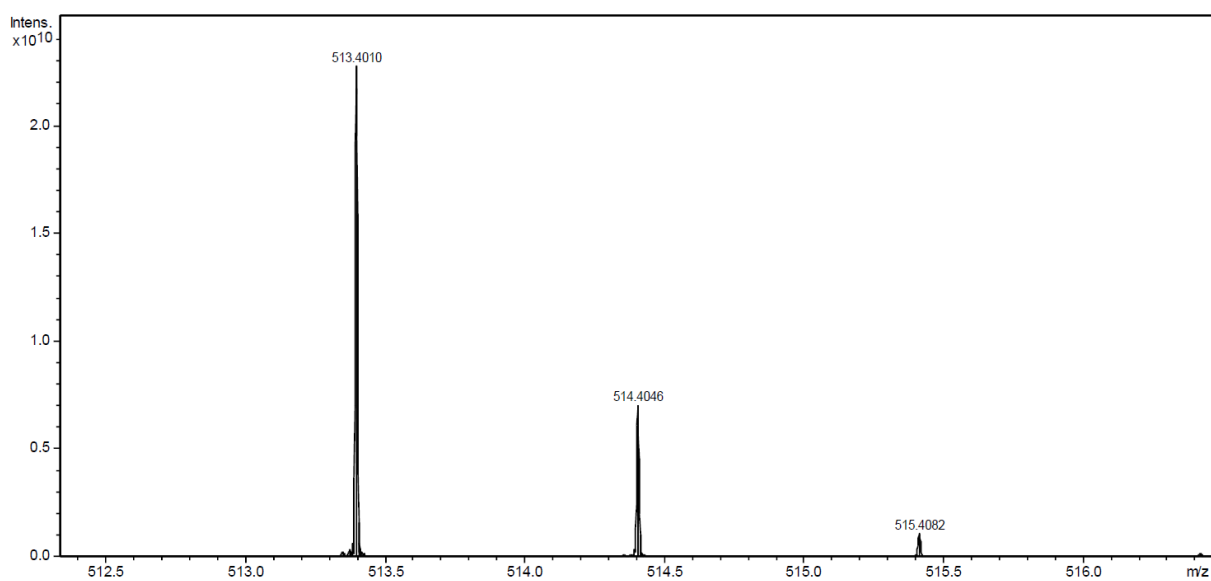


Figure S30. HRMS spectrum of compound **12c**.

*N*<sup>1</sup>-acetyl-*N*<sup>4</sup>-[*N*-(*rac*-1-decyloxy-2-ethyloxyprop-3-yl)aminocarbonyl]methylpiperazin (**12d**)

Yield: 54%, colorless oil. Eluent: DCM-MeOH (30:1). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>, HSQC, HMBC) δ 0.85 (t, 3H, *J* = 7.0 Hz, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.09 (t, 3H, *J* = 7.0 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.24 (br. s, 14H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.44 – 1.51 (m, 2H, OCH<sub>2</sub>CH<sub>2</sub>), 1.98 (s, 3H, COCH<sub>3</sub>), 2.35 – 2.39 (m, 2H, 2 COCH<sub>2</sub>NCH<sub>e</sub>H<sub>a</sub> Pip), 2.43 – 2.45 (m, 2H, 2 COCH<sub>2</sub>NCH<sub>e</sub>H<sub>a</sub> Pip), 2.93 (d, 1H, *J* = 15.5 Hz, COCH<sub>a</sub>H<sub>b</sub>N), 2.96 (d, 1H, *J* = 15.5 Hz, COCH<sub>a</sub>H<sub>b</sub>N), 3.05 – 3.13 (m, 1H, CONHCH<sub>a</sub>H<sub>b</sub>), 3.29 (ddd, 1H, *J* = 13.4, 6.3, 5.1 Hz, CONHCH<sub>a</sub>H<sub>b</sub>), 3.32 – 3.39 (m, 4H, CH<sub>2</sub>OCH<sub>2</sub>), 3.40 – 3.52 (m, 6H, CH<sub>2</sub>OCH<sub>a</sub>H<sub>b</sub>CH<sub>3</sub>, 2 CONCH<sub>2</sub> Pip), 3.52 – 3.59 (m, 1H, CH<sub>2</sub>OCH<sub>a</sub>H<sub>b</sub>CH<sub>3</sub>), 7.63 – 7.68 (m, 1H, NH). <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>, DEPT-135) δ 13.84, 15.48, 22.04, 25.56, 28.66, 28.79, 28.95, 28.97, 28.99, 29.00, 29.10, 31.25, 39.56, 40.72, 45.57, 52.43, 52.90, 60.89, 64.36, 64.42, 70.59, 71.06, 76.30, 168.04, 168.82. HRMS FTICR *m/z*: [M+H]<sup>+</sup> calcd for C<sub>28</sub>H<sub>55</sub>N<sub>4</sub>O<sub>3</sub> 456.3796, found: 456.3796.

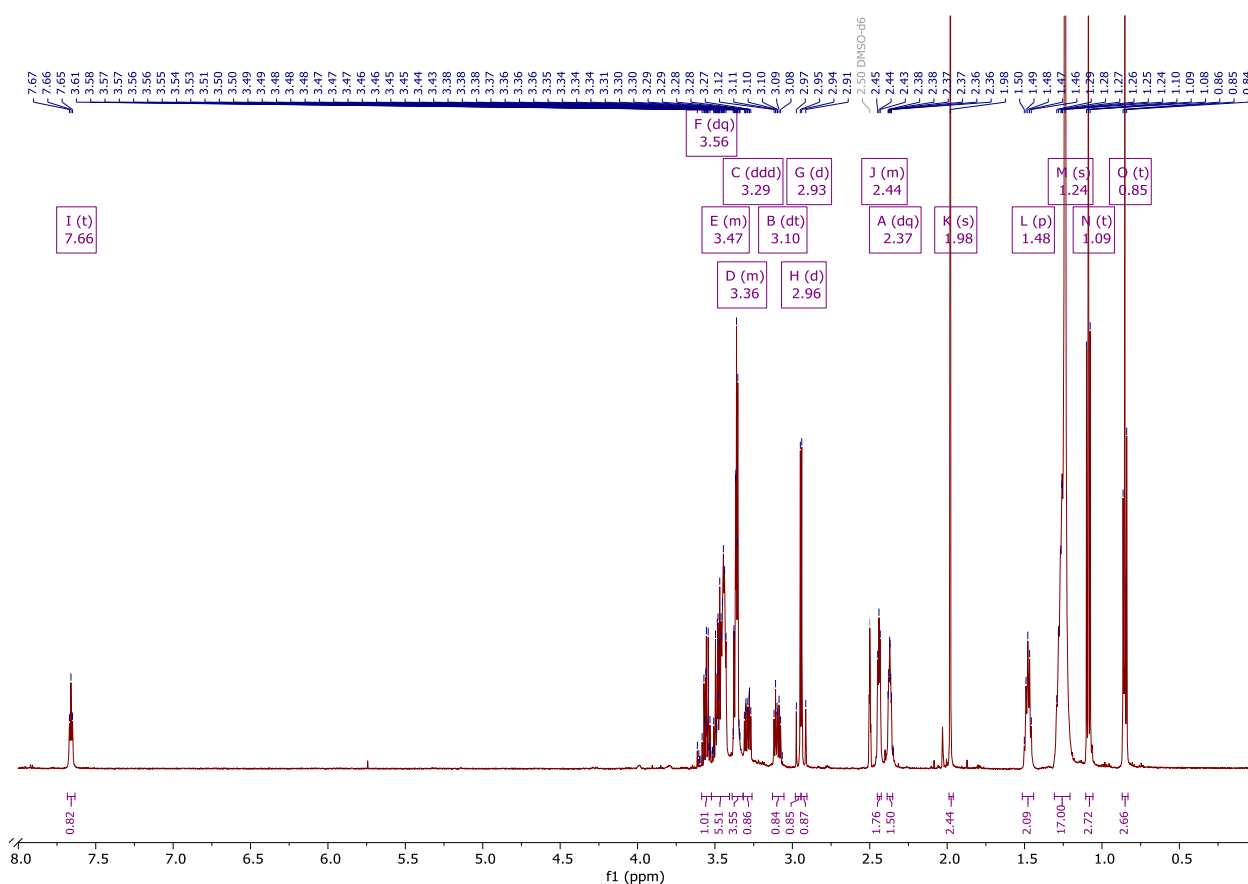


Figure S31. <sup>1</sup>H NMR spectrum of compound **12d**.

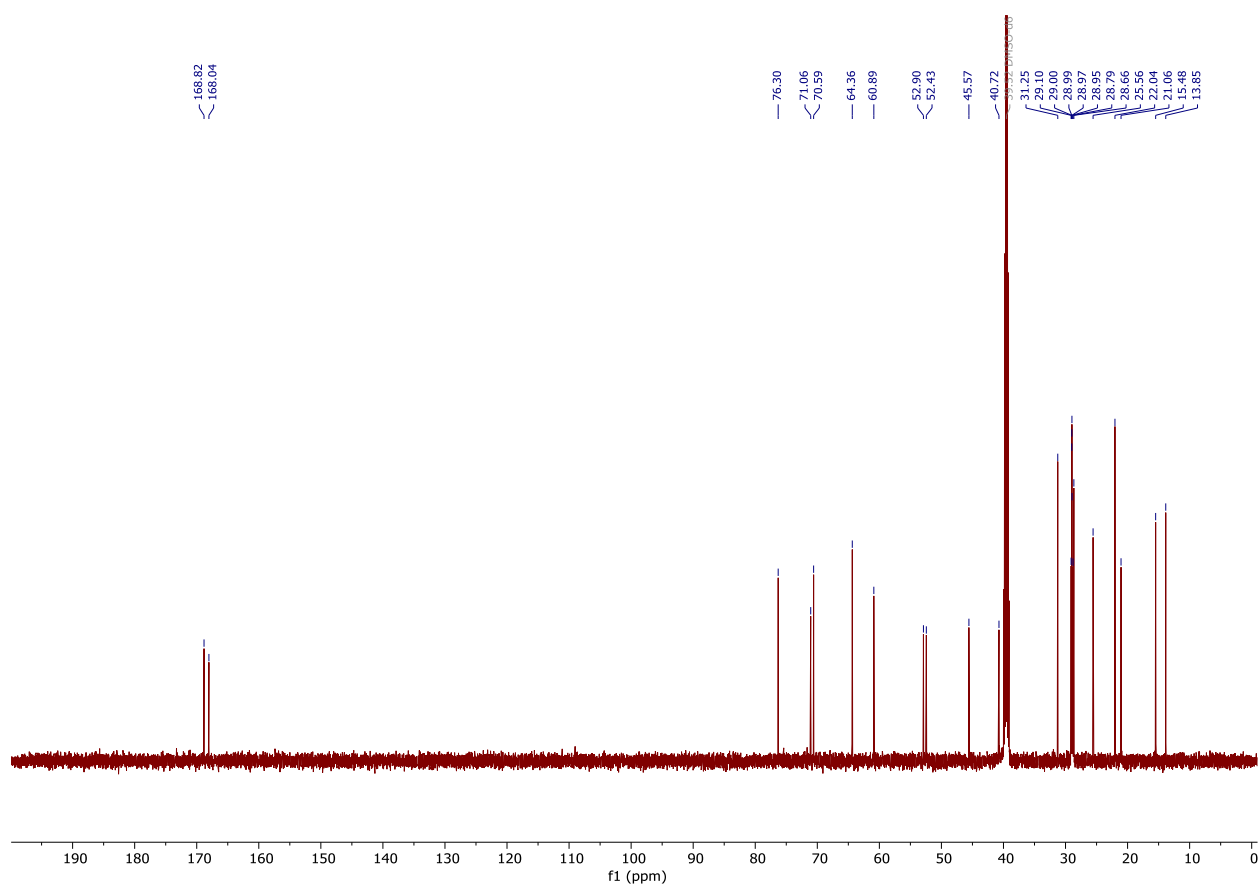


Figure S32.  $^{13}\text{C}$  NMR spectrum of compound **12d**.

DEPT-135

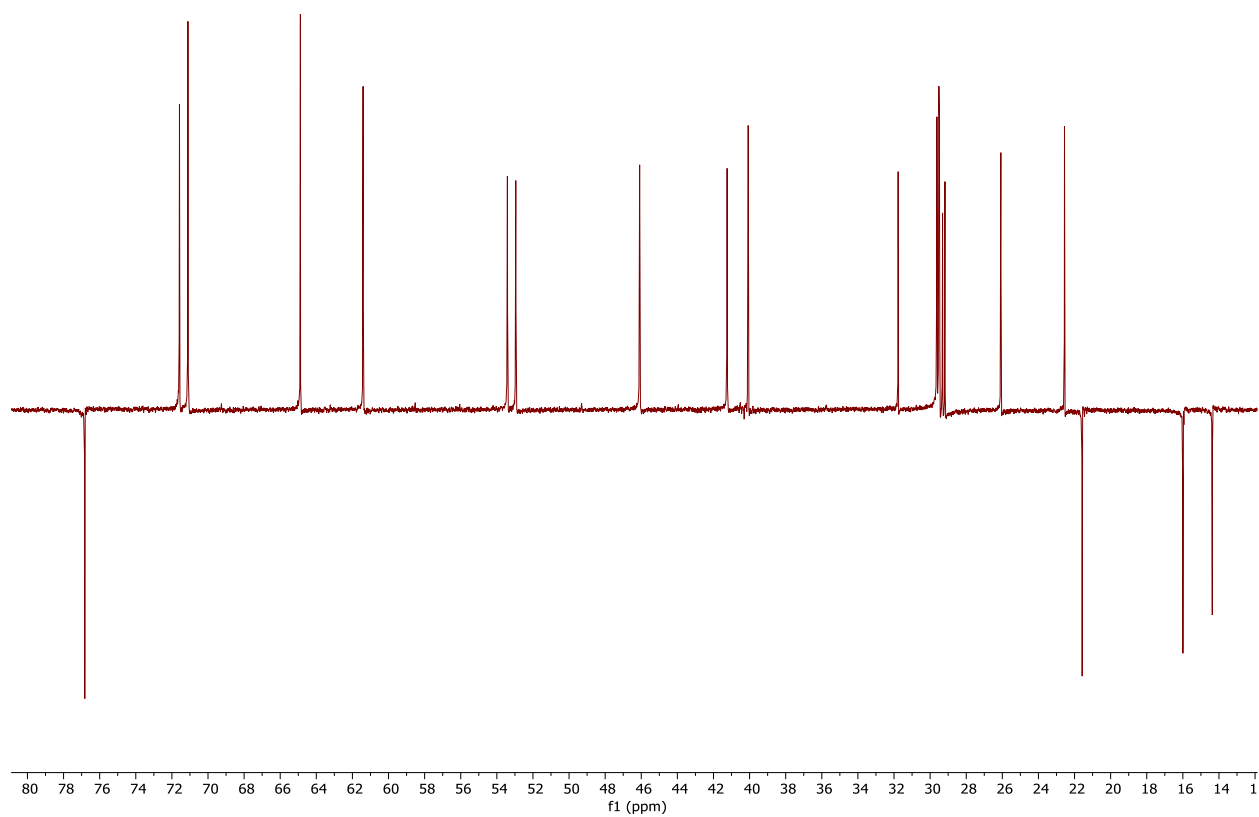


Figure S33. DEPT-135 NMR spectrum of compound **12d**.

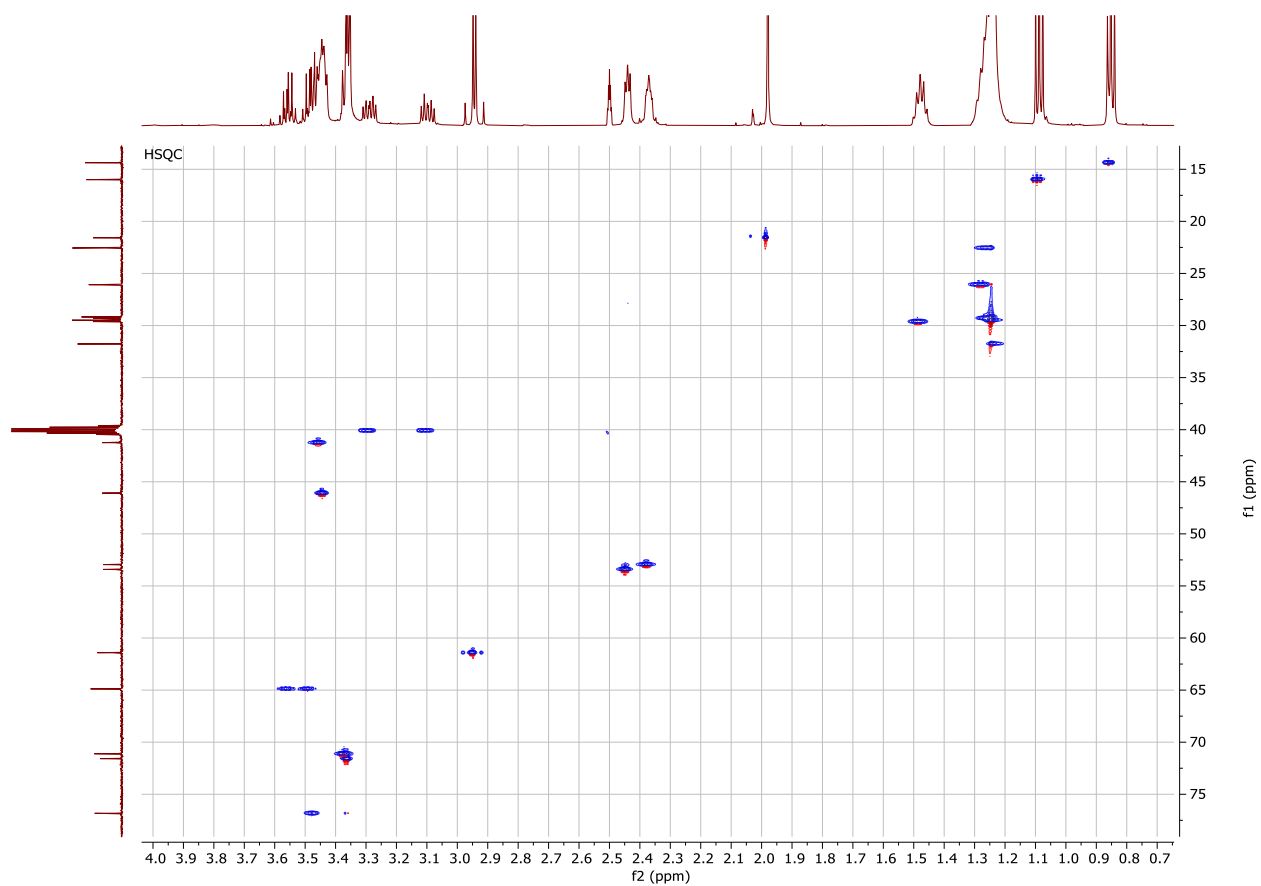


Figure S34.  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **12d**.

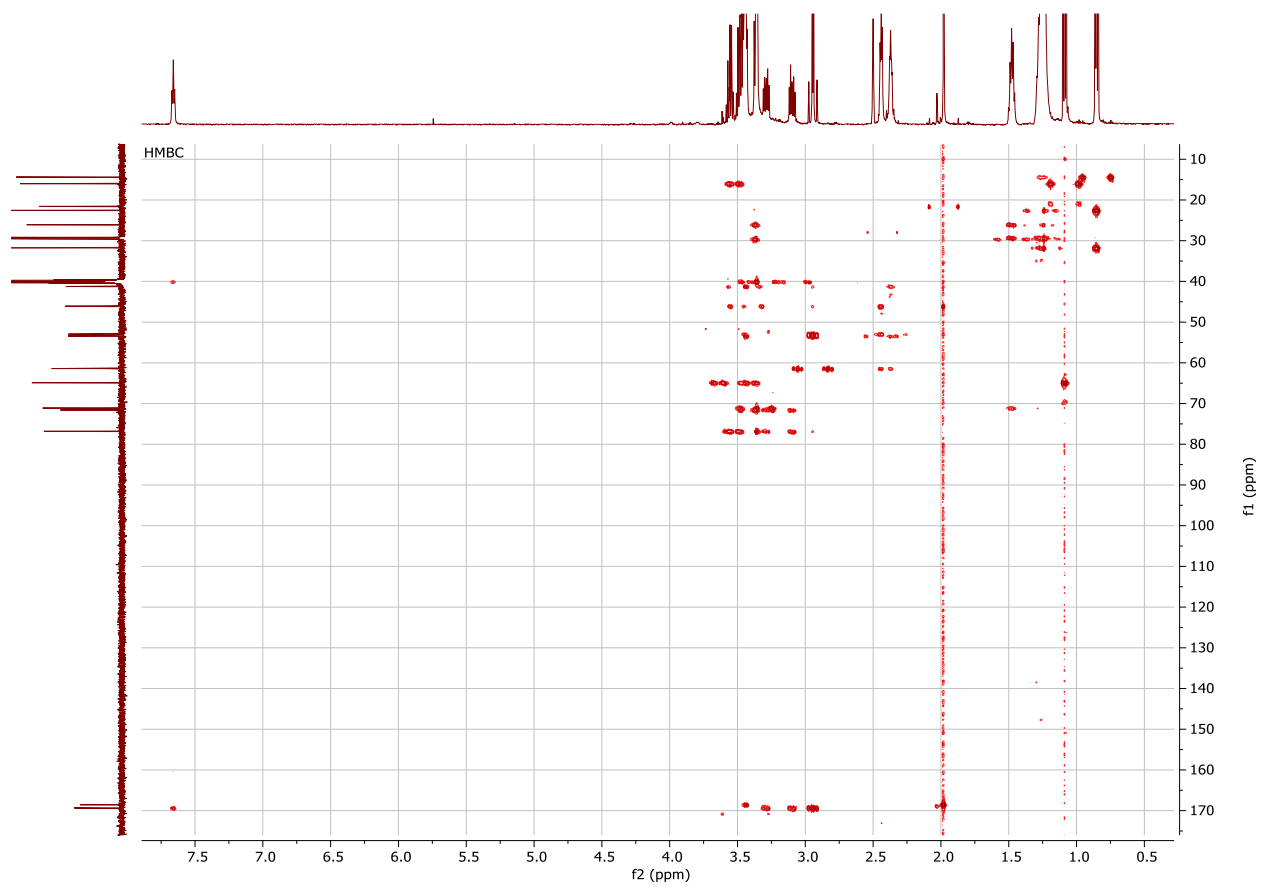


Figure S35.  $\{^1\text{H}-^{13}\text{C}\}$  HMBC NMR spectrum of compound **12d**.

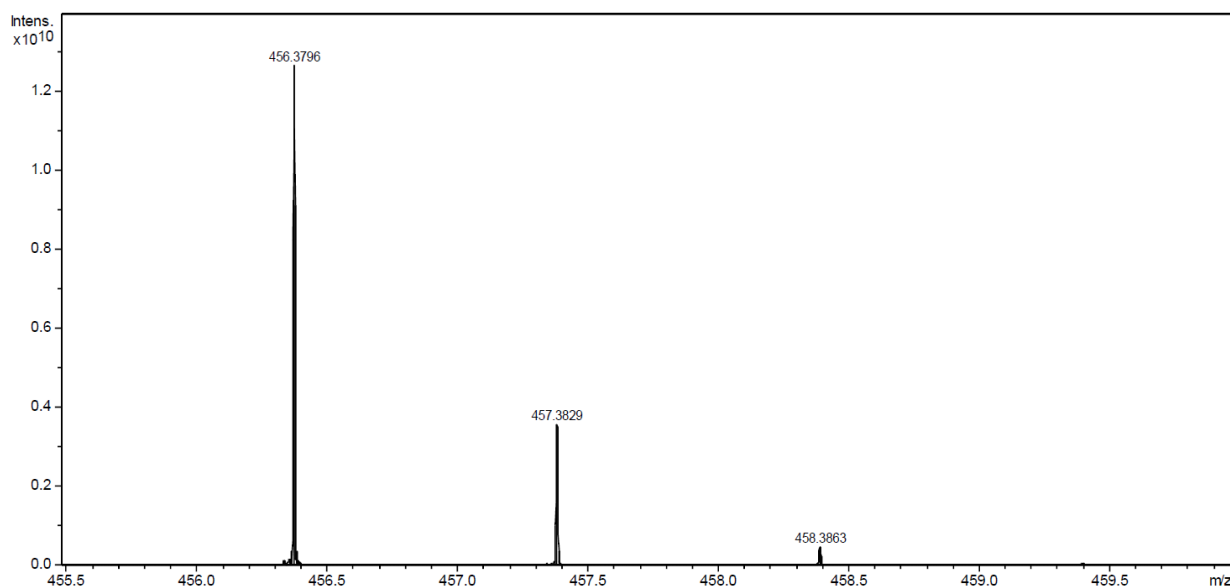


Figure S36. HRMS spectrum of compound **12d**.

*N*<sup>1</sup>-acetyl-*N*<sup>4</sup>-[*N*-(cyclohexyl)aminocarbonyl]methylpiperazin (**12e**)

Yield: 75%, colorless oil. Eluent: EA-MeOH (4:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.04 – 1.25 (m, 3H, 2 CHCH<sub>2</sub>H<sub>e</sub>H<sub>a</sub>, CHCH<sub>2</sub>CH<sub>2</sub>H<sub>e</sub>H<sub>a</sub>), 1.25 – 1.45 (m, 2H, 2 CHCH<sub>2</sub>CH<sub>e</sub>H<sub>a</sub>), 1.61 (m, 3H, 2 NHCHCH<sub>e</sub>H<sub>a</sub>, CHCH<sub>2</sub>CH<sub>2</sub>CH<sub>e</sub>H<sub>a</sub>), 1.77 – 1.90 (m, 2H, 2 NHCHCH<sub>e</sub>H<sub>a</sub>), 2.04 (s, 3H, COCH<sub>3</sub>), 2.35 – 2.57 (m, 4H, 2 COCH<sub>2</sub>NCH<sub>2</sub> Pip), 2.96 (s, 2H, COCH<sub>2</sub>N), 3.39 – 3.50 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 3.54 – 3.64 (m, 2H, 2 CONCH<sub>e</sub>H<sub>a</sub> Pip), 3.65 – 3.86 (m, 1H, CONHCH), 6.88 (d, 1H, *J* = 8.2 Hz, NH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 21.31, 24.73, 25.54, 33.12, 41.44, 46.28, 47.46, 53.12, 53.46, 61.60, 168.39, 169.03. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub> 268.20195, found: 268.20195.

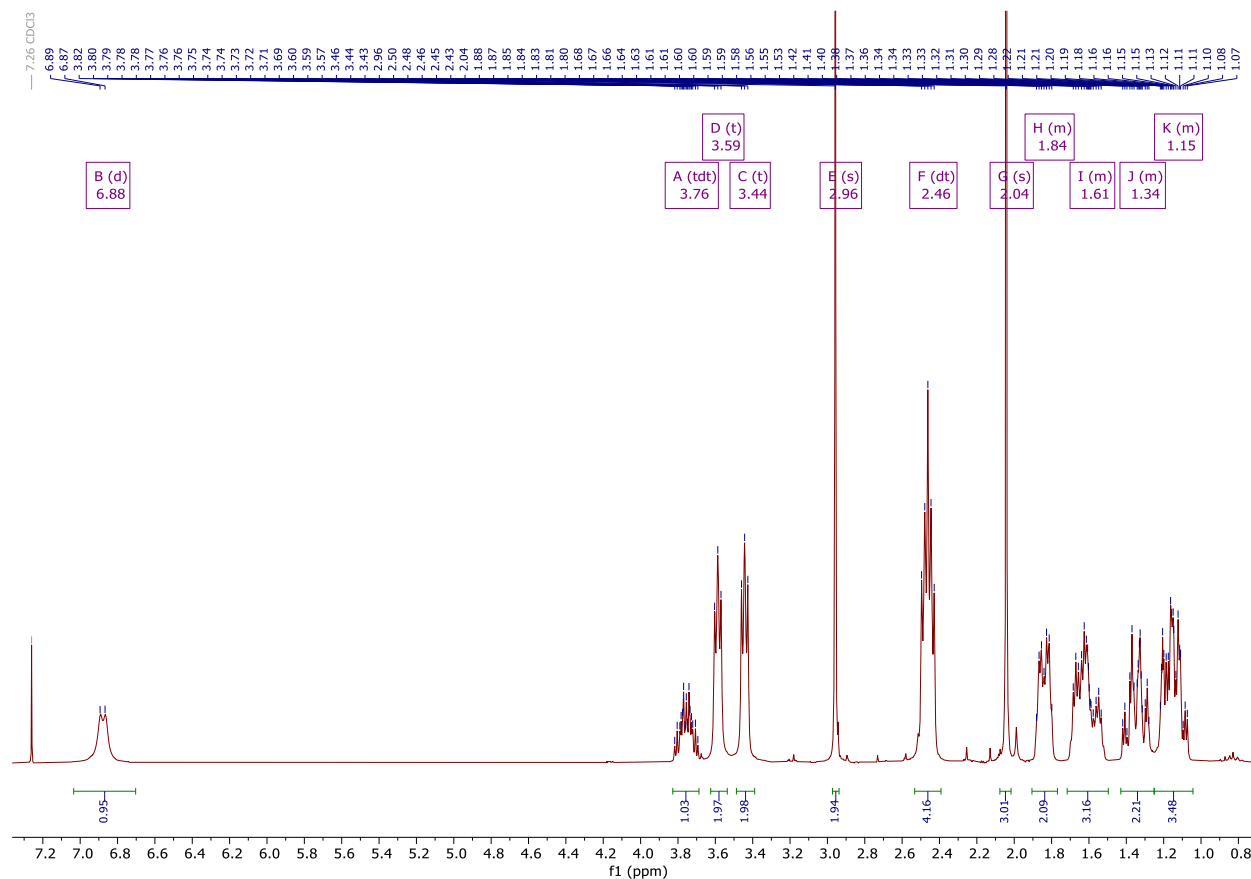


Figure S37. <sup>1</sup>H NMR spectrum of compound **12e**.



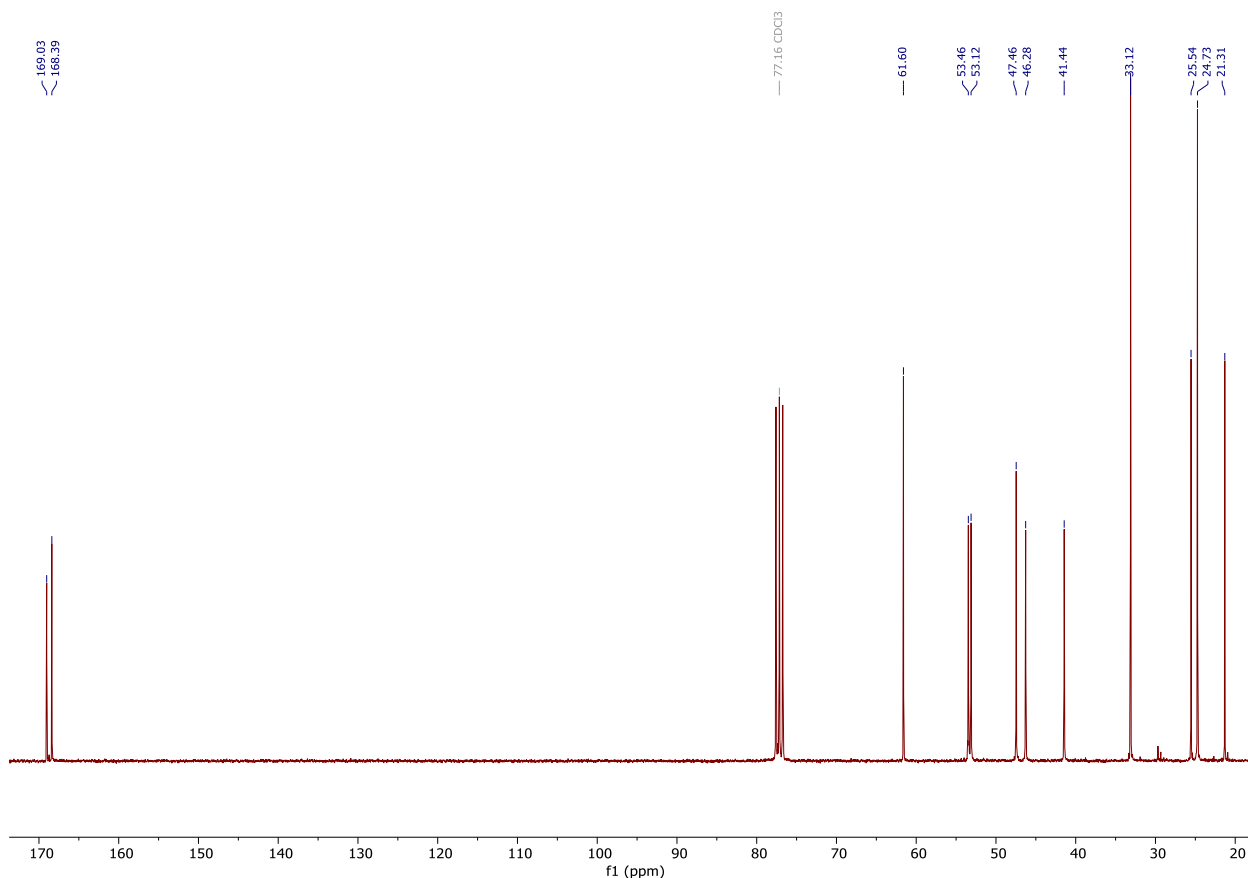
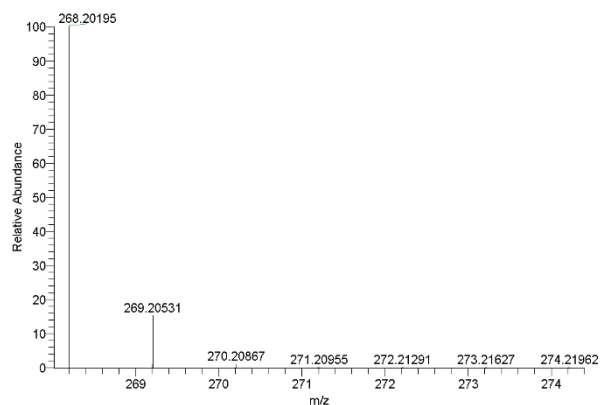


Figure S38. <sup>13</sup>C NMR spectrum of compound **12e**.

Compound\_03\_C14H25N3O2\_fMS

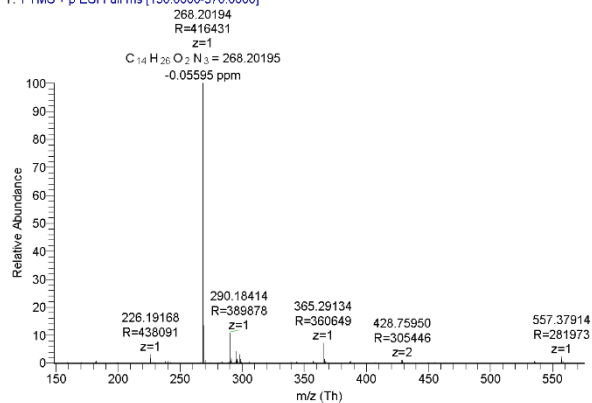
C14H25N3O2 +H: C14 H26 N3 O2 c(gss, s/p.40)(Val) Chr...



Compound\_03\_C14H25N3O2\_fMS#1 RT: 0.02  
T: FTMS + p ESI Full ms [150.0000-570.0000]  
m/z= 192.15-555.33

m/z	Intensity	Relative	Resolution	Charge	Delta (ppm)	Composition
226.19	9018243.0	2.55	525907.00	1.00		
268.20	353148640.0	100.00	474507.00	1.00	-0.53	C <sub>14</sub> H <sub>26</sub> O <sub>2</sub> N <sub>3</sub>
269.20	54435588.0	15.41	452502.00	1.00		
290.18	16823700.0	4.76	451107.00	1.00		
295.16	14283968.0	4.04	441107.00	2.00		
295.66	4684177.5	1.33	427102.00	2.00		
298.21	9374585.0	2.65	436502.00	0.00		
298.31	8541824.0	2.42	450302.00	0.00		
365.29	20945494.0	5.93	390407.00	1.00	0.35	C <sub>19</sub> H <sub>40</sub> O <sub>2</sub> N
366.29	4428046.5	1.25	386302.00	1.00		

Compound\_03\_C14H25N3O2\_fMS #23-30 RT: 0.42-0.54 AV: 8 NL: 2.54E8  
T: FTMS + p ESI Full ms [150.0000-570.0000]



Compound\_03\_C14H25N3O2\_fMS RT: 0.02 - 1.16 Mass: 150.00 - 570.00 NL: 3.72E8

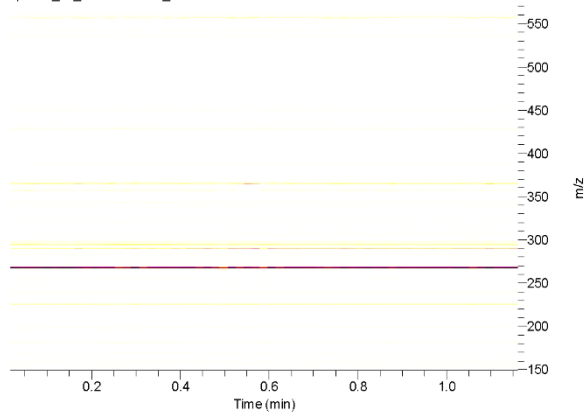


Figure S39. HRMS spectrum of compound **12e**.

$N^1$ -[*N*-(*rac*-1-decyloxy-2-ethoxyprop-3-yl)aminocarbonyl]methylpiperazin (**13a**)

Yield: 50%, colorless oil. Eluent: EA-MeOH-NH<sub>3</sub>·H<sub>2</sub>O (7:3:0.1) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.87 (t, *J* = 6.3 Hz, 3H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.21 (t, 3H, *J* = 7.0 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.26 (br.s, 14H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.48 – 1.63 (m, 2H, OCH<sub>2</sub>CH<sub>2</sub>), 2.43 – 2.63 (m, 5H, CH<sub>2</sub>NHCH<sub>2</sub> Pip), 2.87 – 2.96 (m, 4H, 2 NCH<sub>2</sub> Pip), 2.99 (s, 2H, COCH<sub>2</sub>N), 3.17 – 3.75 (m, 9H, CH<sub>2</sub>OCH<sub>2</sub>, CHOCH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHCO), 7.50 (br.s, 1H, CONH). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.26, 15.80, 22.82, 26.23, 29.46, 29.61, 29.72, 29.75, 40.23, 46.13, 54.71, 62.33, 65.53, 71.51, 72.01, 76.90, 170.30. HRMS ESI [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>44</sub>N<sub>3</sub>O<sub>3</sub> 386.3377, found 386.3371.

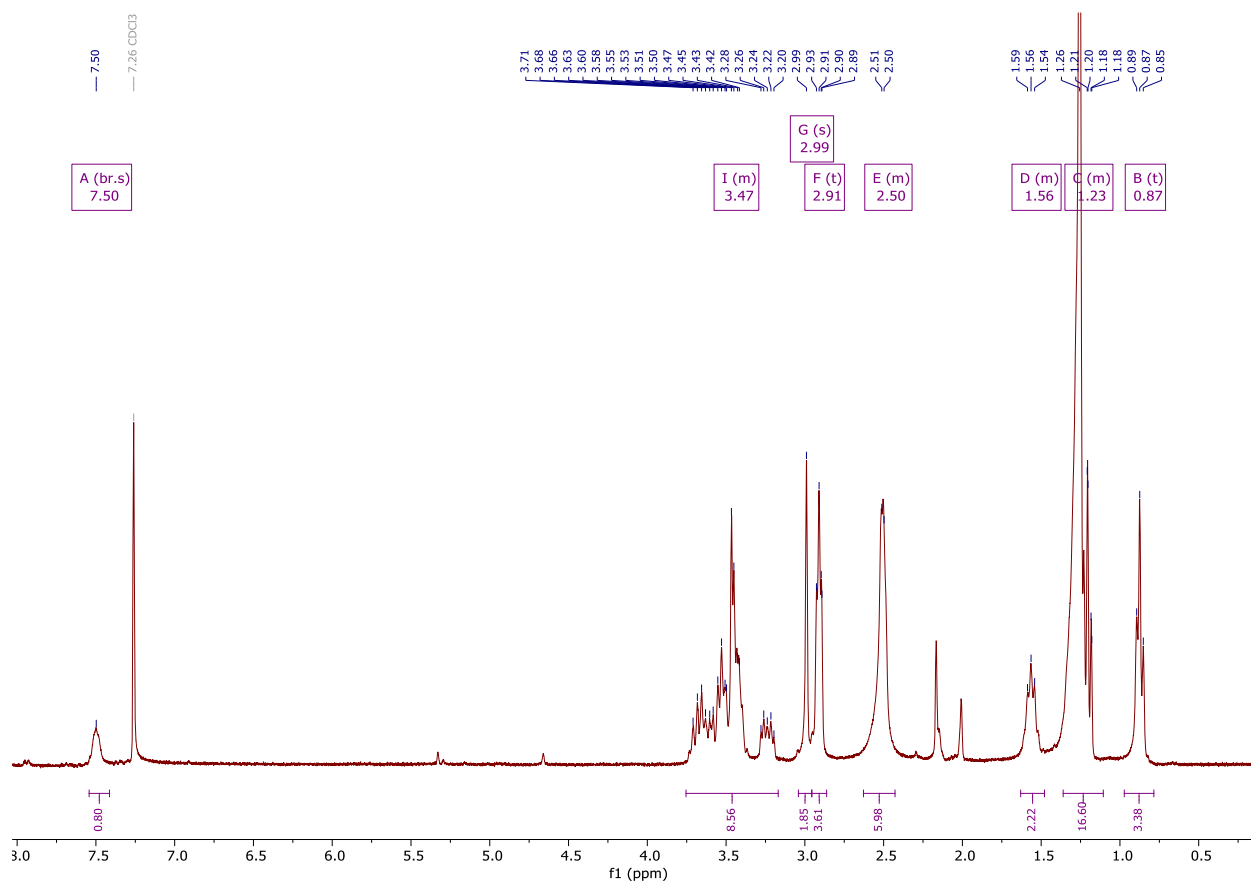


Figure S40. <sup>1</sup>H NMR spectrum of compound **13a**.

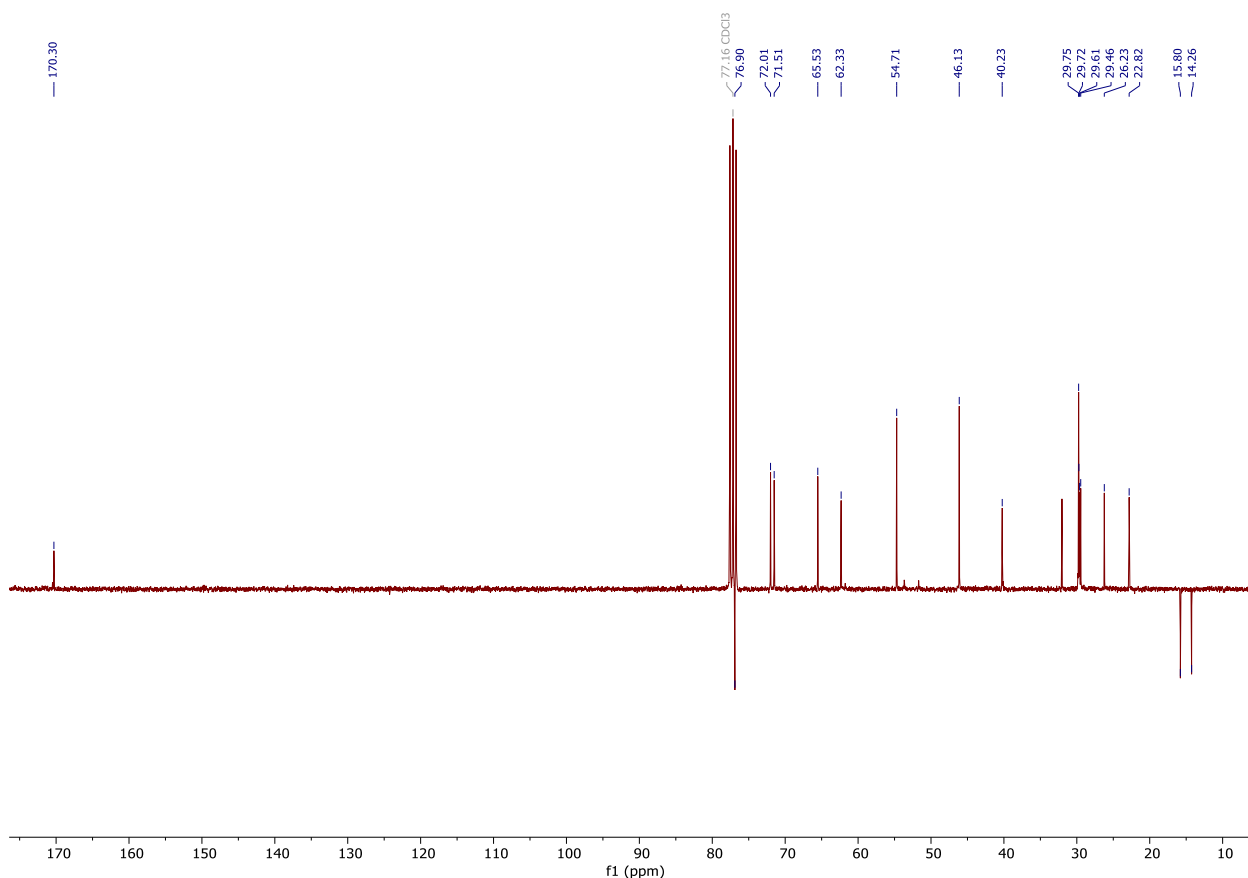


Figure S41.  $^{13}\text{C}$  (APT)C NMR spectrum of compound **13a**.

5a-2di #547-577 RT: 3.77-3.96 AV: 16 SB: 23 3.89-4.02, 4.12-4.28 NL: 5.90E9  
T: FTMS + p ESI Full ms [95.0000-1000.0000]

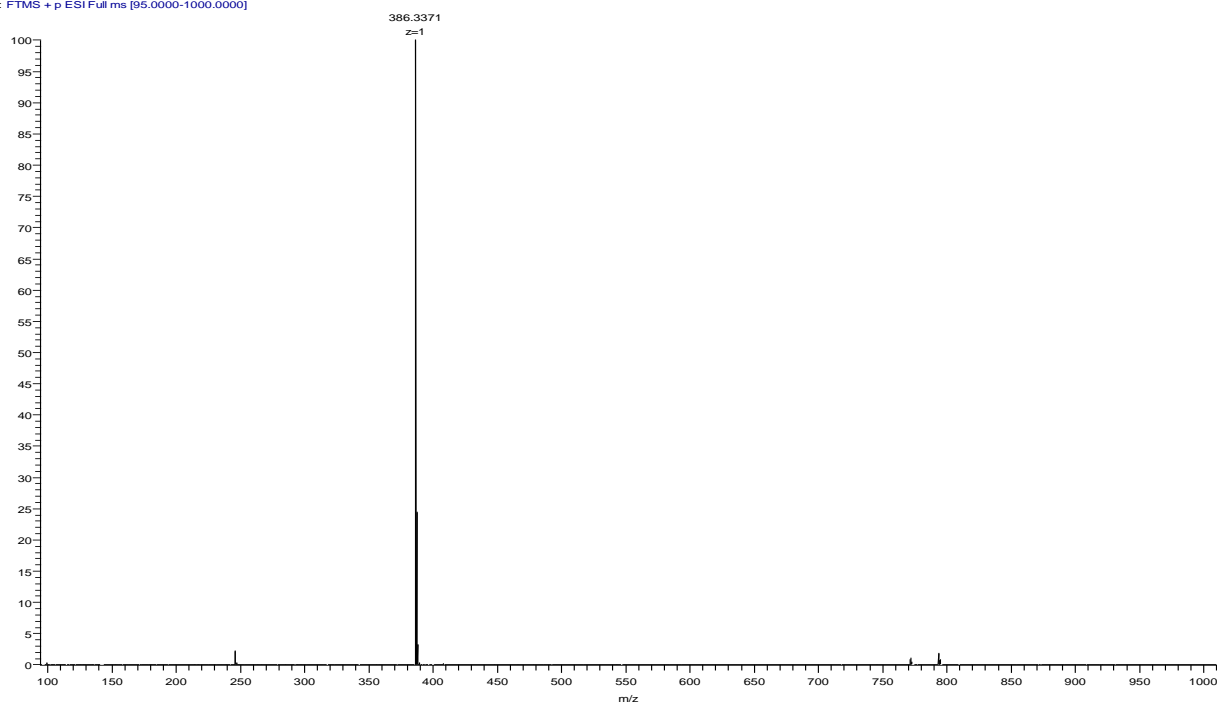


Figure S42.  $\{^1\text{H}-^{13}\text{C}\}$  HMBC NMR spectrum of compound **13a**.

$N^1,N^4$ -bis[ $N$ -(*rac*-1-decyloxy-2-ethyloxyprop-3-yl)aminocarbonyl]methylpiperazin (**13b**)

Yield: 22%, colorless oil. Eluent: EA-MeOH (95:5).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t, 6H,  $J = 6.5$  Hz,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.19 (t, 6H,  $J = 7.0$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.27 (br.s, 28H,

(CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.50 – 1.63 (m, 4H, OCH<sub>2</sub>CH<sub>2</sub>), 2.56 (br.s, 8H Pip), 3.01 (s, 4H, COCH<sub>2</sub>N), 3.16 – 3.31 (m, 2H, 2 CH<sub>a</sub>H<sub>b</sub>NHCO), 3.34 – 3.48 (m, 8H, 2 CHOCH<sub>2</sub>CH<sub>3</sub>, 2 CH<sub>a</sub>H<sub>b</sub>NHCO), 3.48 – 3.56 (m, 4H, 2 CH<sub>2</sub>OCH<sub>2</sub>), 3.56 – 3.74 (m, 4H, 2 CH<sub>2</sub>OCH<sub>2</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.26, 15.83, 22.82, 26.23, 29.46, 29.62, 29.71, 29.75, 29.77, 32.04, 40.26, 53.75, 61.67, 65.49, 71.51, 72.01, 76.81, 170.05. HRMS ESI [M+H]<sup>+</sup>calcd for C<sub>38</sub>H<sub>77</sub>N<sub>4</sub>O<sub>6</sub> 685.5838, found 685.5828. HRMS ESI [M+2H]<sup>2+</sup>calcd for C<sub>38</sub>H<sub>78</sub>N<sub>4</sub>O<sub>6</sub> 343.2955, found 343.2954.

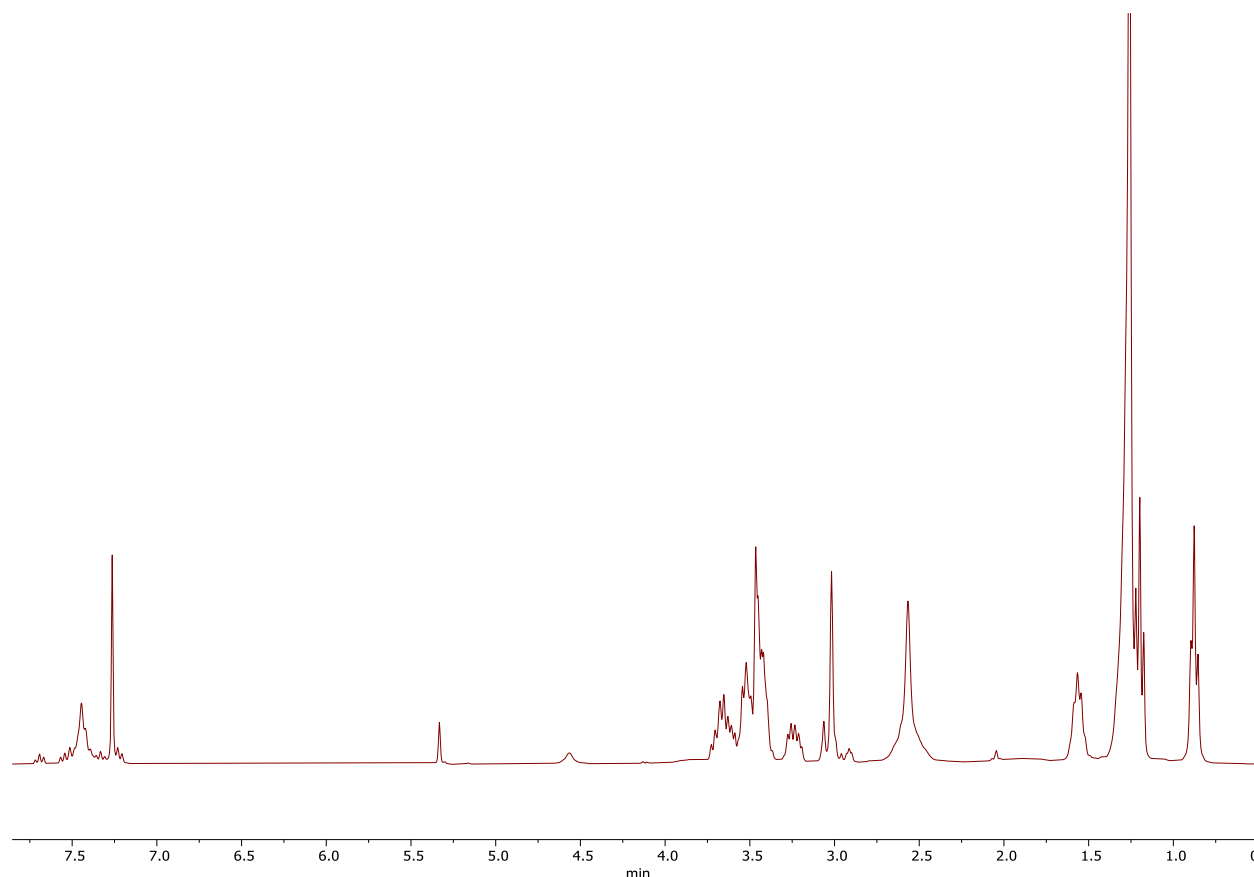


Figure S43. <sup>1</sup>H NMR spectrum of compound **13b**.

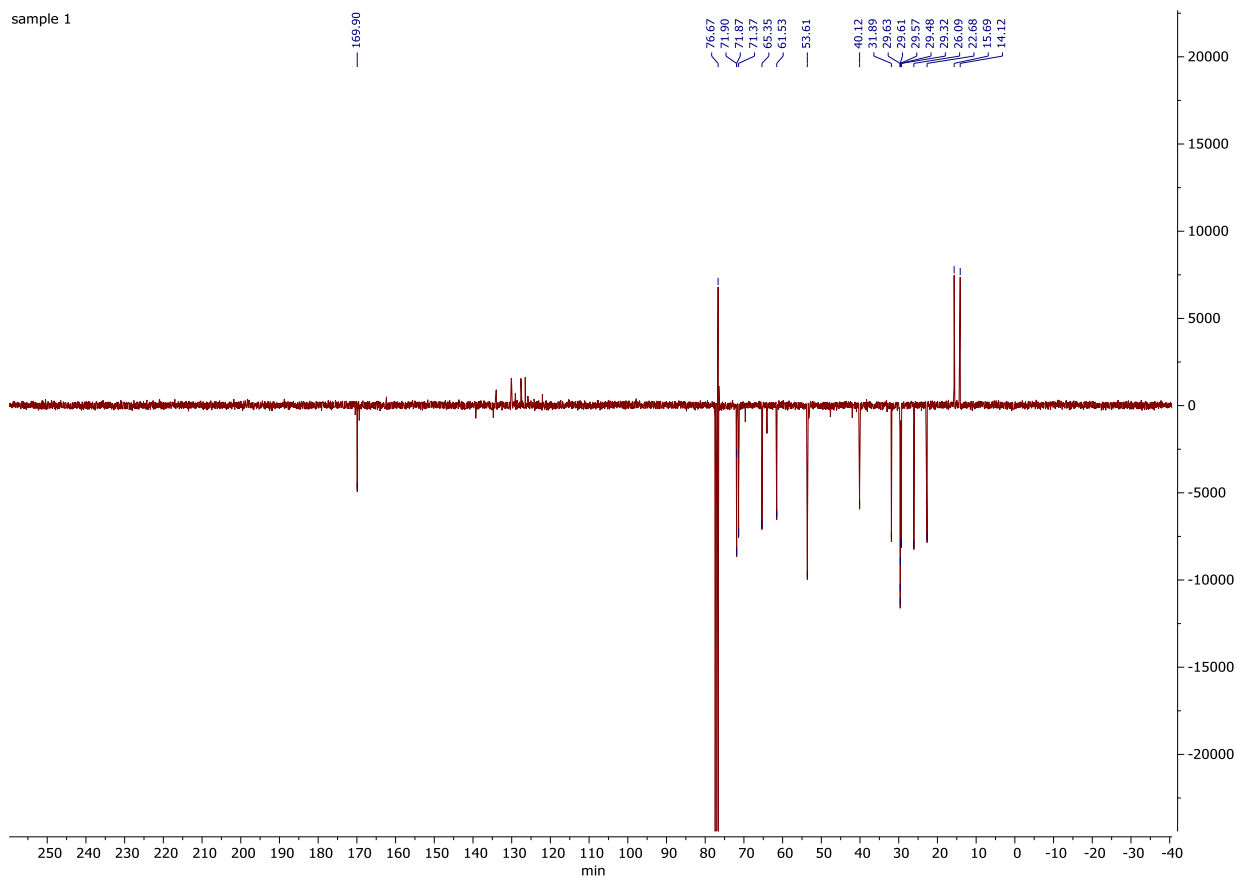


Figure S44.  $^{13}\text{C}$  (APT) NMR spectrum of compound **13b**.

5a-2di #734-765 RT: 4.99-5.18 AV: 16 SB: 23 3.89-4.02, 4.12-4.28 NL: 7.36E9  
T: FTMS + p ESI Full ms [95.0000-1000.0000]

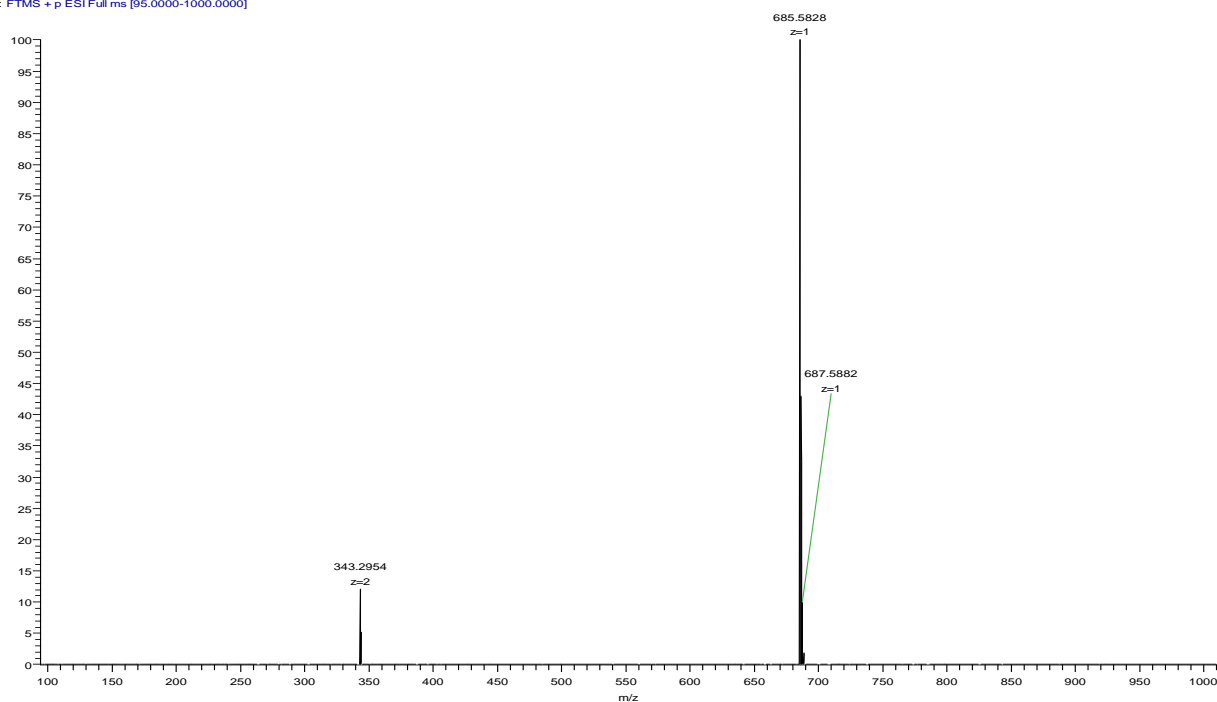


Figure S45. HMRS spectrum of compound **13b**.

$N^1$ -[*N*-(isopropyl)aminocarbonyl]methyl- $N^4$ -[*N*-(*rac*-1-decyloxy-2-ethoxyprop-3-yl)aminocarbonyl]methylpiperazin (**15a**)

Yield: 80%, colorless oil. Eluent: EA-MeOH (85:15).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7.0$  Hz, 3H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.16 (d,  $J = 6.6$  Hz, 6H,  $\text{CH}(\text{CH}_3)_2$ ), 1.20 (t,  $J = 7.0$  Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.27 (br.s, 14H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.50 – 1.62 (m, 2H,  $\text{OCH}_2\text{CH}_2$ ), 2.56 (br.s, 8H Pip protons), 2.97 (s, 2H,  $\text{CHNHC}(\text{O})\text{CH}_2$ ), 3.03 (d,  $J = 1.6$  Hz, 2H,  $\text{COCH}_2\text{N}$ ), 3.23 (ddd,  $J = 4.8, 6.4, 13.7$  Hz, 1H,  $\text{CHCH}_a\text{H}_b\text{NH}$ ), 3.34 – 3.75 (m, 8H,  $\text{CHCH}_a\text{H}_b\text{NH}$ ,  $\text{CHOCH}_2\text{CH}_3$ ,  $\text{CH}_2\text{OCH}_2$ ), 4.01 – 4.16 (m, 1H,  $\text{CH}(\text{CH}_3)_2$ ), 6.86 (br.d,  $J = 8.4$  Hz, 1H,  $\text{NHCH}$ ), 7.44 (br.t,  $J = 5.6$  Hz, 1H,  $\text{NHCH}_2$ ).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  14.26, 15.83, 22.83, 22.96, 26.25, 29.47, 29.63, 29.72, 29.76, 29.78, 32.04, 40.27, 40.87, 53.69, 53.74, 61.65, 61.72, 65.49, 71.54, 72.03, 76.82, 168.98, 170.03. HRMS ESI  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{26}\text{H}_{53}\text{N}_4\text{O}_4$  485.4061, found 485.4062.

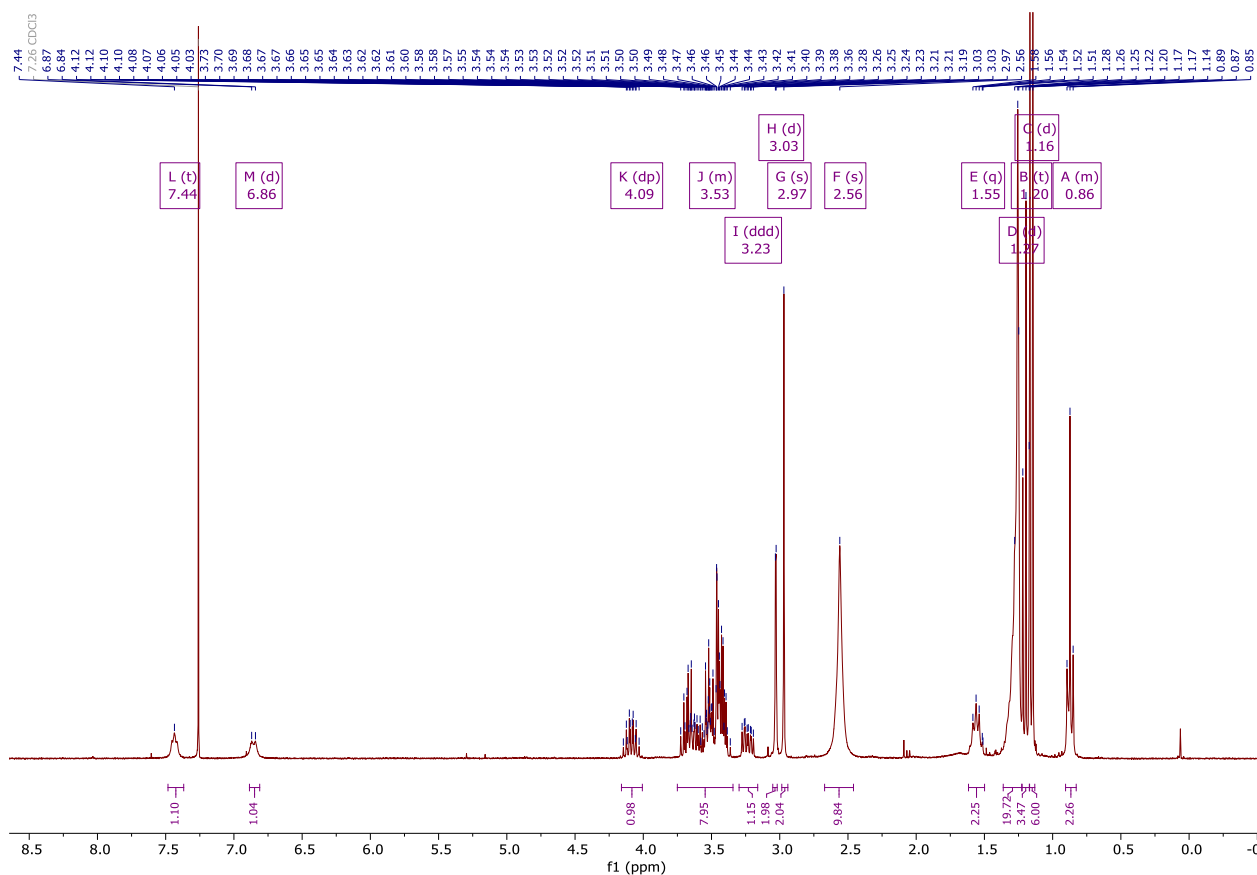


Figure S46.  $^1\text{H}$  NMR spectrum of compound **15a**.

5A-4.135.fid

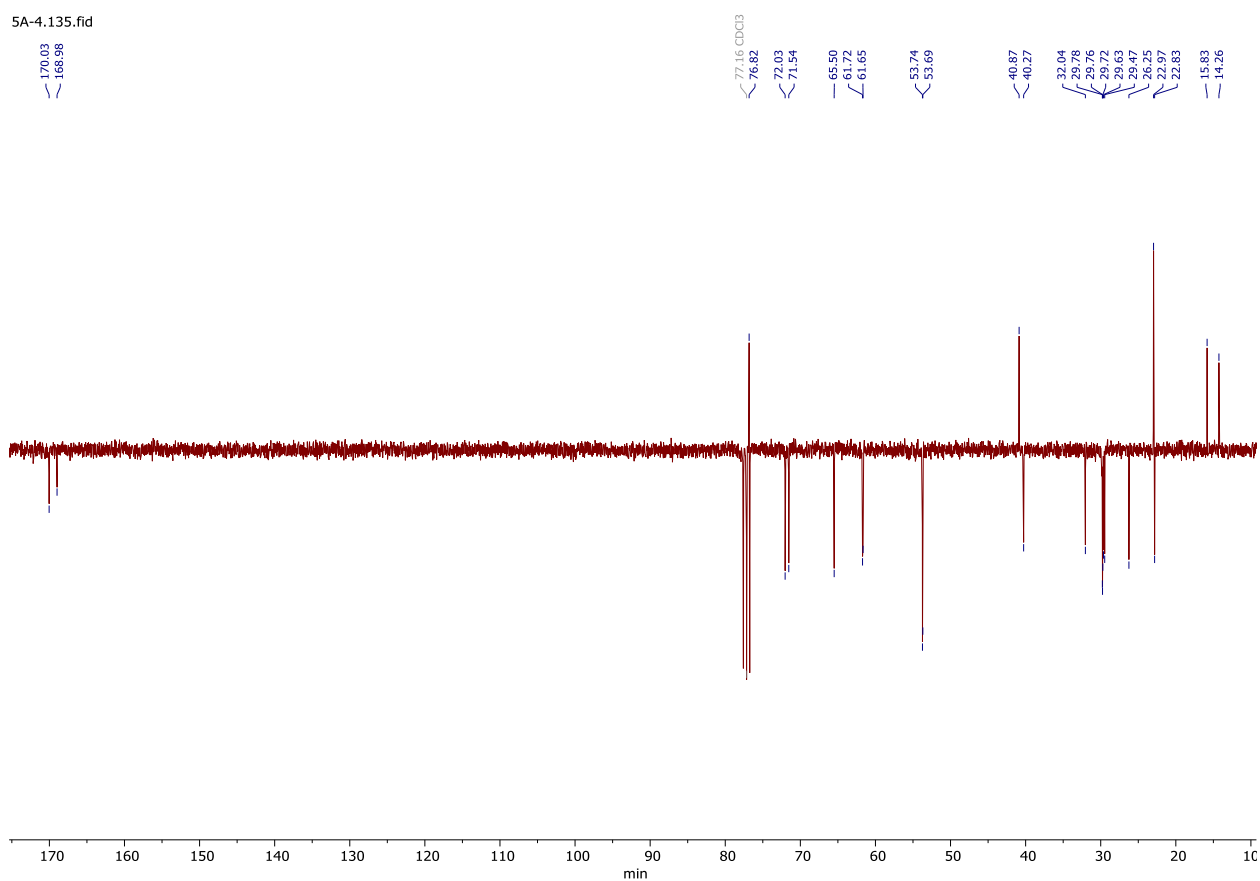


Figure S47. <sup>13</sup>C NMR spectrum of compound **15a**.

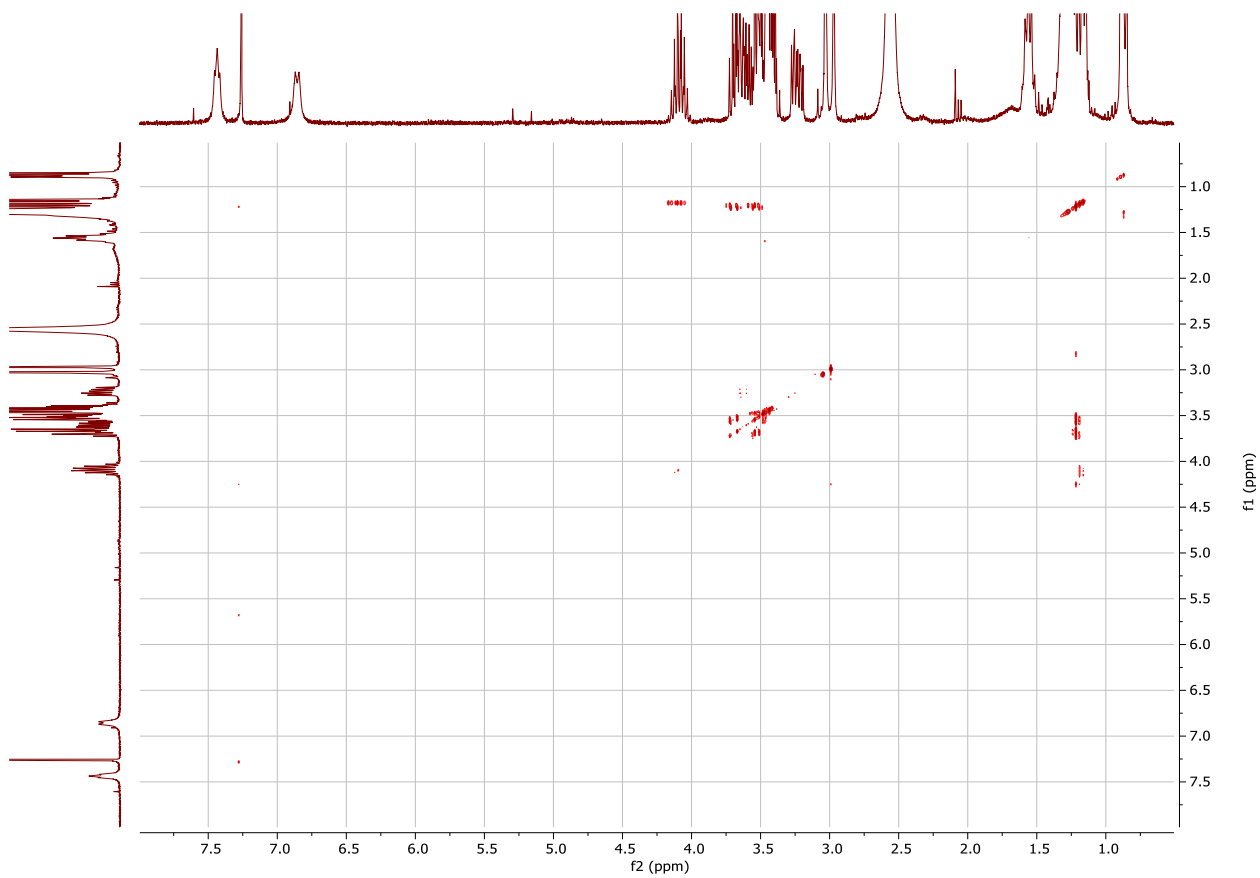


Figure S48. <sup>1</sup>H-<sup>1</sup>H COSY NMR spectrum of compound **15a**.

5a-4 #553-594 RT: 3.81-4.06 AV: 21 SB: 23 3.89-4.02 , 4.12-4.29 NL: 6.28E9  
T: FTMS + p ESI Full ms [95.0000-1000.0000]

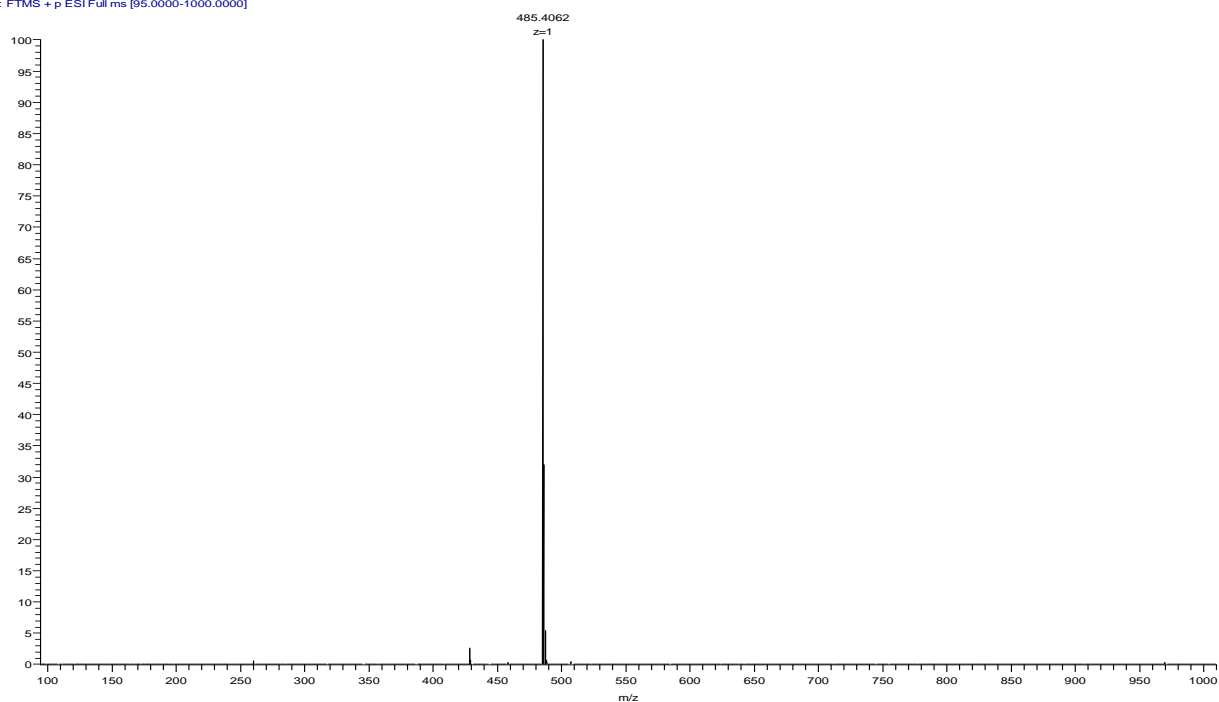


Figure S49. HRMS spectrum of compound **15a**.



$N^1$ -[*N*-(pentyl)aminocarbonyl]methyl- $N^4$ -[*N*-(*rac*-(1-decyloxy-2-ethyloxyprop-3-yl)aminocarbonyl]methylpiperazin (**15b**)

Yield: 75%, colorless oil. Eluent: EA-MeOH (9:1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , COSY, HSQC, HMBC)  $\delta$  0.83 – 0.94 (m, 6H,  $(\text{CH}_2)_7\text{CH}_3$ ,  $(\text{CH}_2)_4\text{CH}_3$ ), 1.20 (t, 3H,  $J = 7.0$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.23 – 1.39 (br. s, 18H,  $(\text{CH}_2)_7\text{CH}_3$ ,  $\text{NHCH}_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 1.46 – 1.63 (m, 4H,  $\text{NHCH}_2\text{CH}_2$ ,  $\text{OCH}_2\text{CH}_2$ ), 2.42 – 2.70 (br.s, 8H, Pip protons), 2.96 – 3.07 (m, 4H, 2  $\text{COCH}_2\text{N}$ ), 3.18 – 3.32 (m, 3H,  $\text{CHOCH}_a\text{H}_b\text{N}$ ,  $\text{NHCH}_2\text{CH}_2$ ), 3.37 – 3.59 (m, 6H, 2  $\text{CH}_2\text{OCH}_2$ ,  $\text{OCH}_a\text{H}_b\text{CH}_3$ ,  $\text{CHO}$ ), 3.59 – 3.76 (m, 2H,  $\text{OCH}_a\text{H}_b\text{CH}_3$ ,  $\text{CHOCH}_a\text{H}_b\text{N}$ ), 7.09 (br. s, 1H, NH), 7.45 (bras, 1H, NH).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  14.12, 14.22, 15.79, 22.43, 22.78, 26.20, 29.22, 29.43, 29.45, 29.58, 29.68, 29.720, 29.74, 32.00, 39.01, 40.23, 53.63, 53.72, 61.59, 61.61, 65.44, 71.48, 71.98, 76.75, 169.74, 169.96. MS ESI  $m/z$ :  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{28}\text{H}_{57}\text{N}_4\text{O}_4$  513.44, found: 513.50.

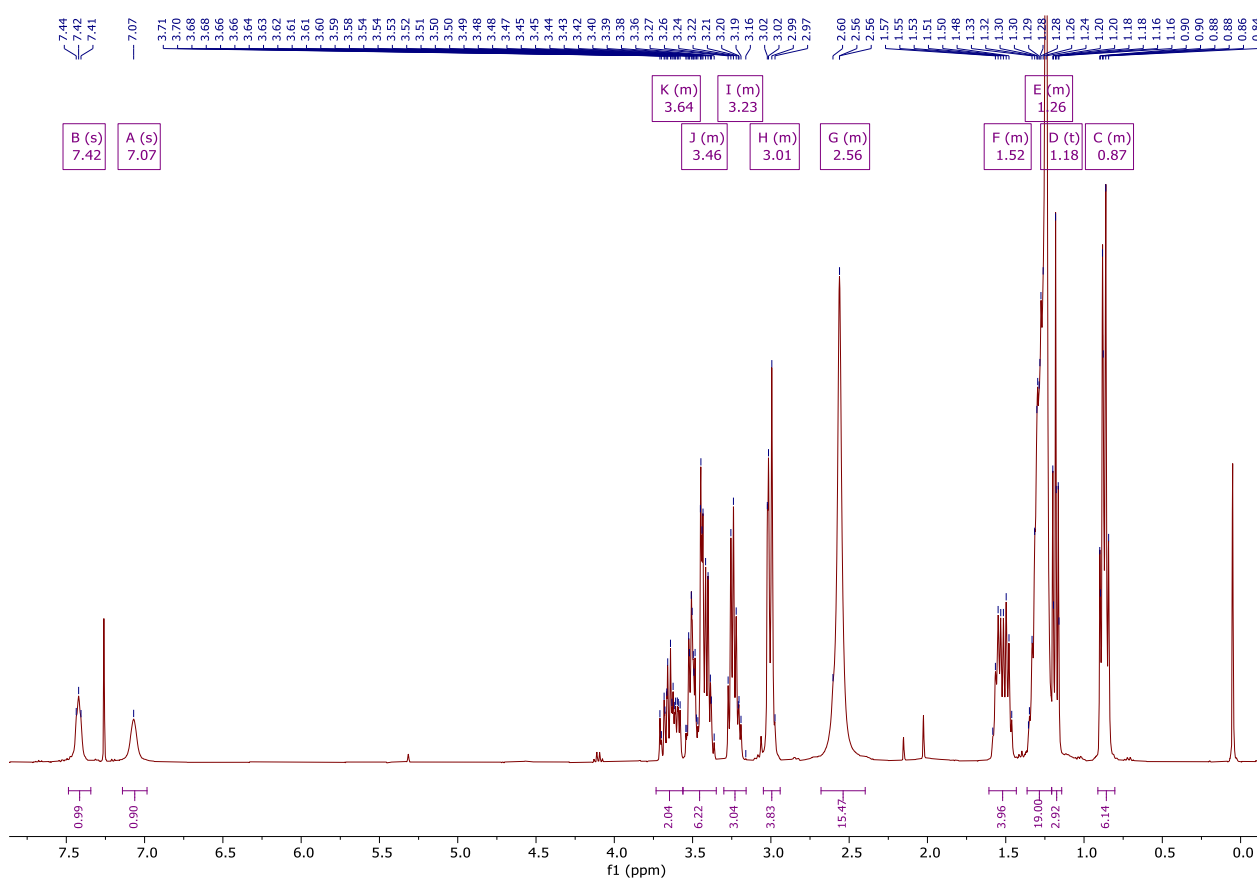


Figure S50.  $^1\text{H}$  NMR spectrum of compound **15b**.

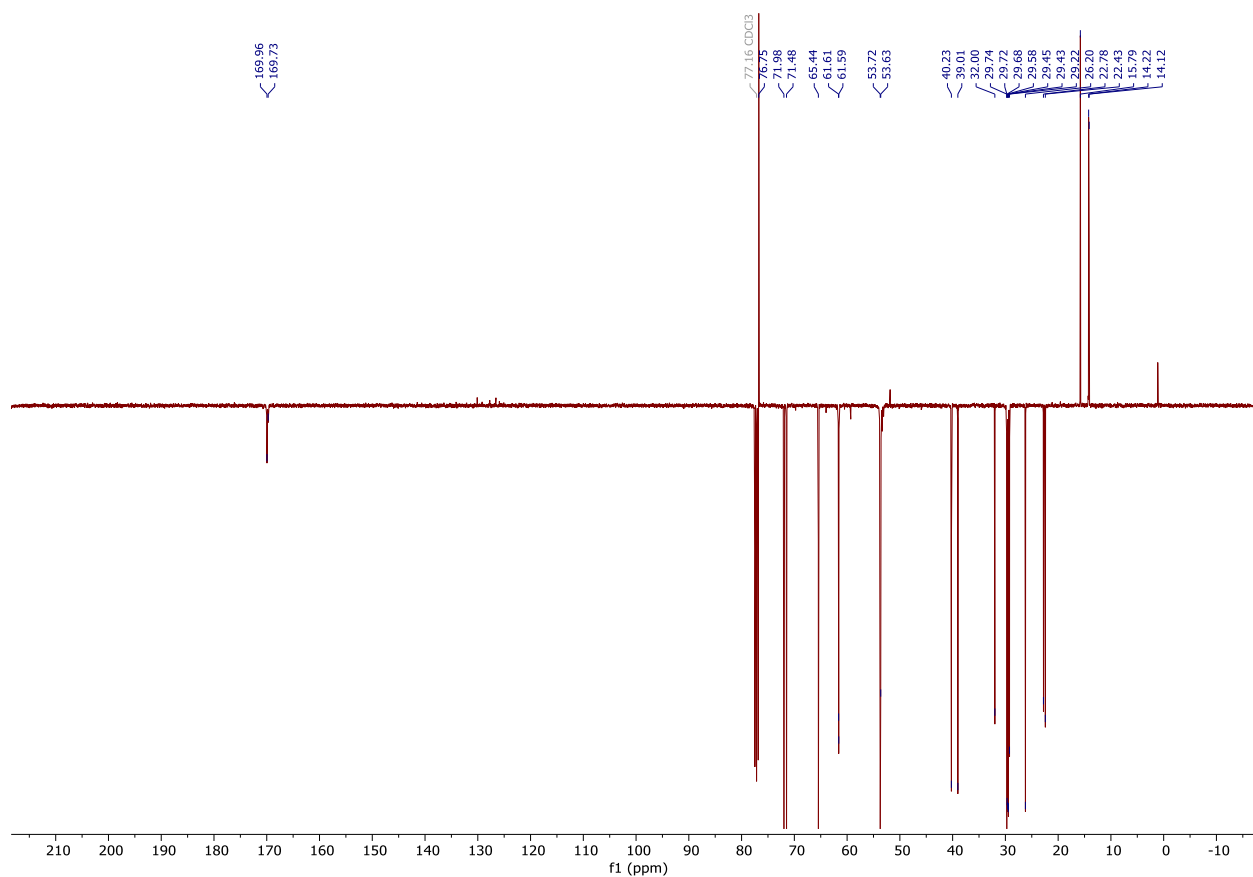


Figure S51. <sup>13</sup>C (APT) NMR spectrum of compound **15b**.

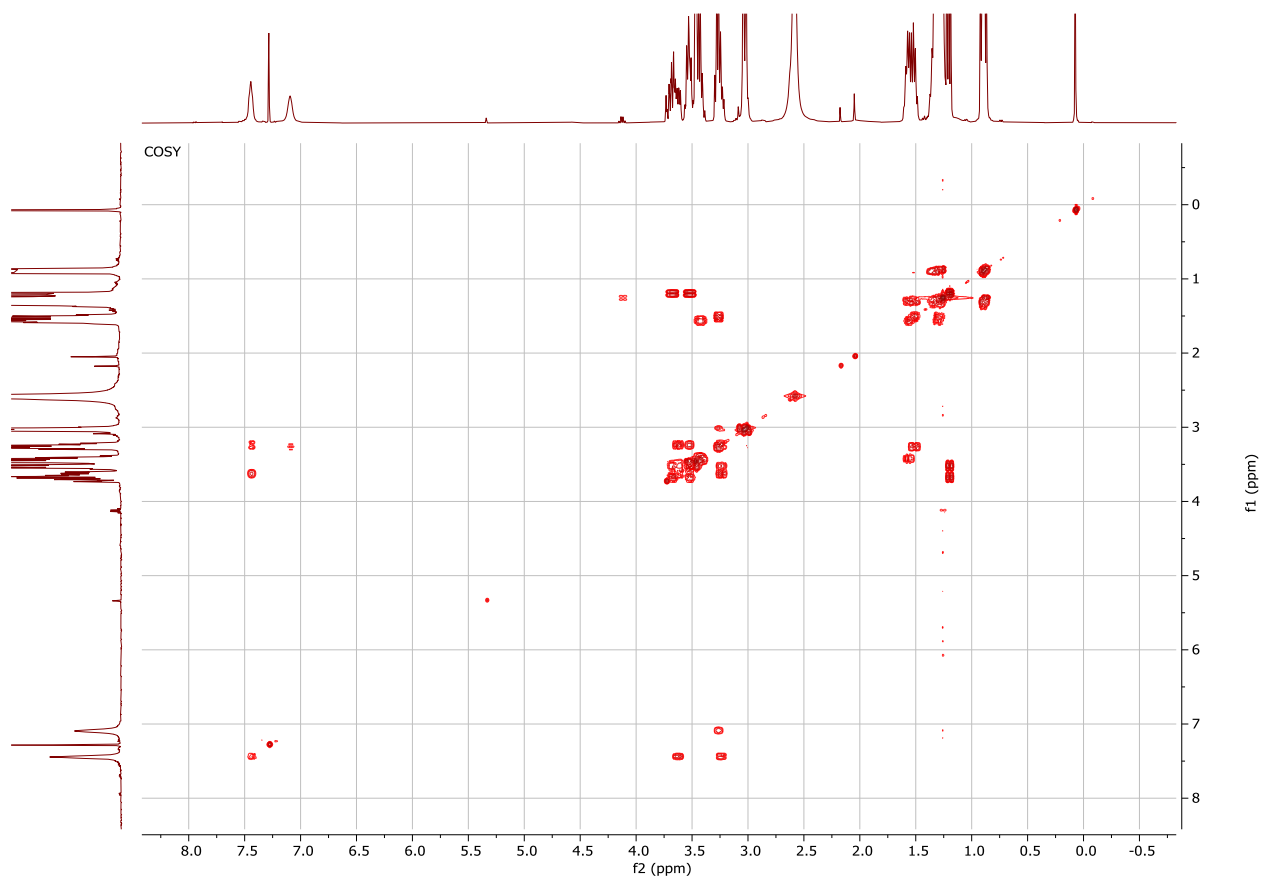


Figure S52. {<sup>1</sup>H-<sup>1</sup>H} COSY NMR spectrum of compound **15b**.

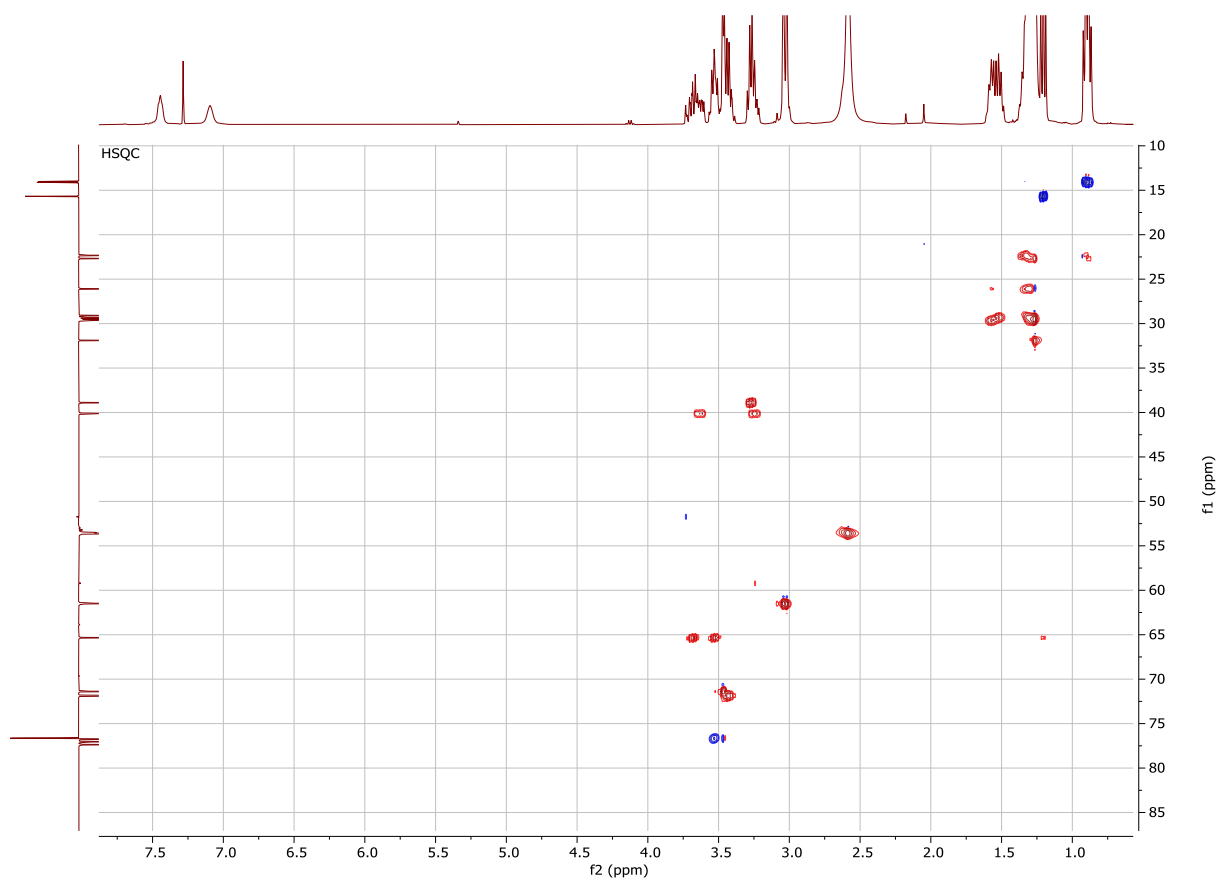


Figure S53.  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **15b**.

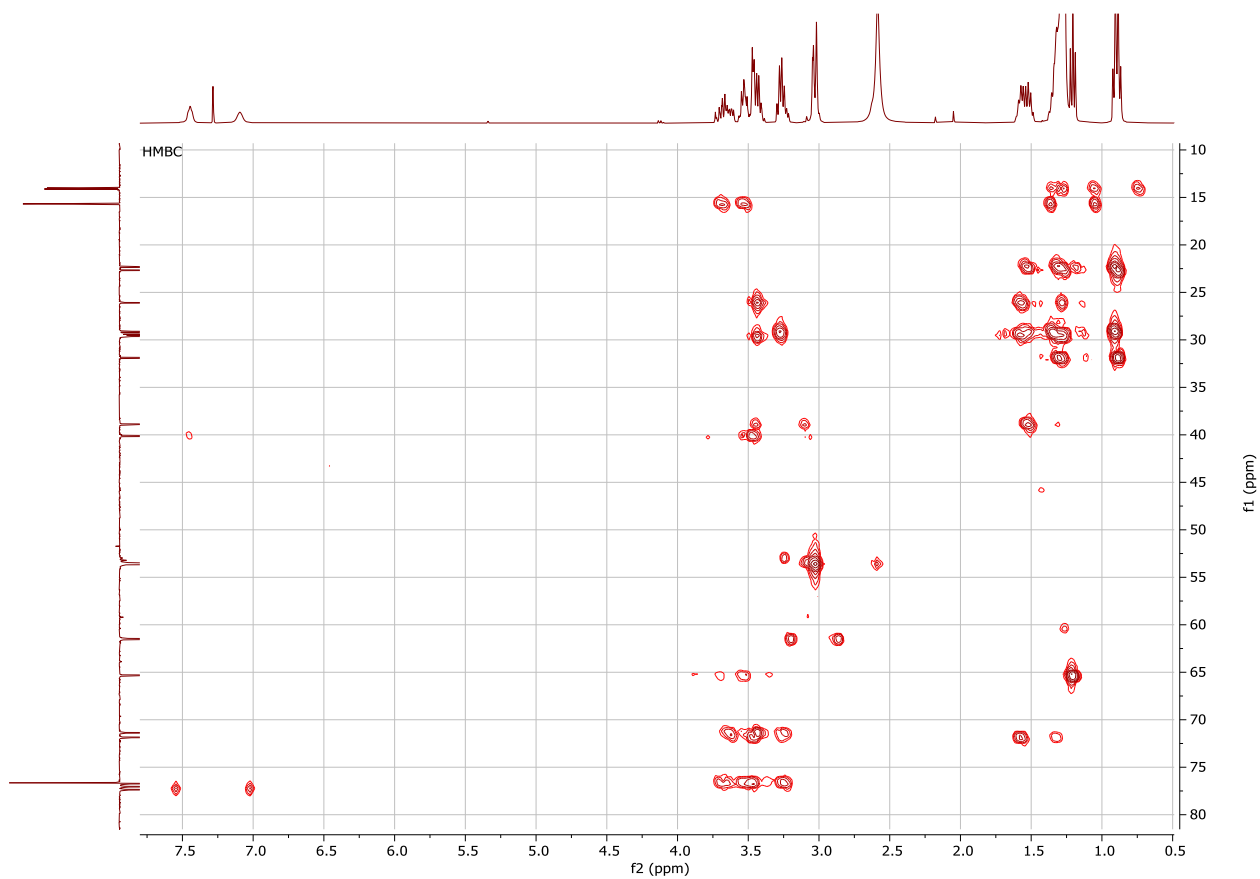
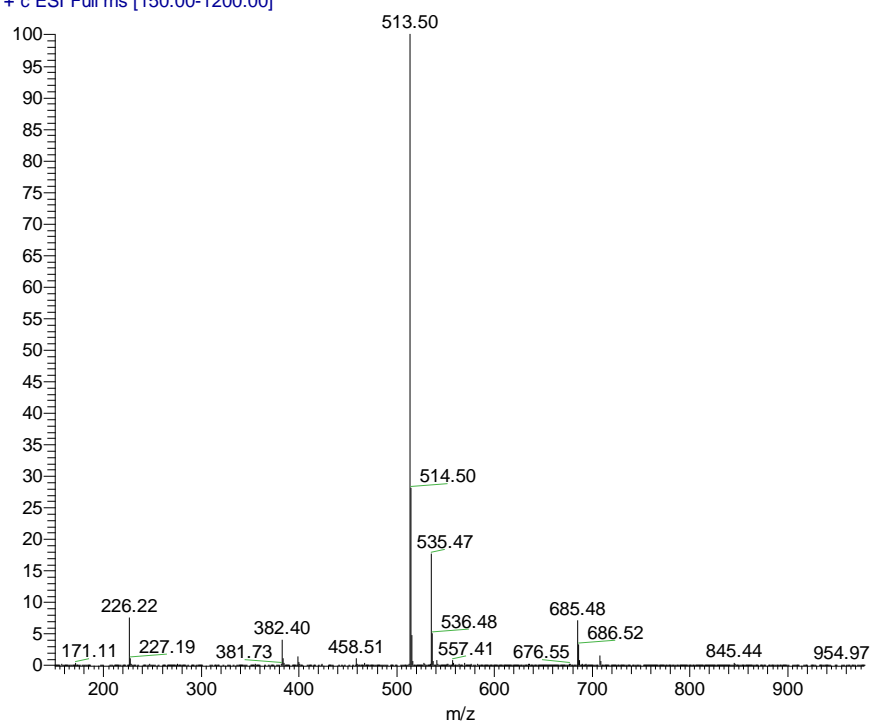


Figure S54.  $\{^1\text{H}-^{13}\text{C}\}$  HMBC NMR spectrum of compound **15b**.

4A-10 #2-5 RT: 0.02-0.07 AV: 4 NL: 9.35E8  
T: + c ESI Full ms [150.00-1200.00]



1

Figure S55. HRMS spectrum of compound **15b**.

$N^1$ -[ $N$ -(2,3,4,6-tetra- $O$ -acetyl- $\beta$ -D-glucopyranosyl)aminocarbonyl]methyl- $N^4$ -[ $N$ -(*rac*-1-decyloxy-2-ethyloxyprop-3-yl)aminocarbonyl]methylpiperazin (**15c**)

Yield: 30%, colorless oil. Eluent: EA-MeOH (95:5)  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85 (t,  $J$  = 7.0 Hz, 3H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.16 (t, 7.0 Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.21 – 1.31 (m, 14H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.49 – 1.57 (m, 2H,  $\text{OCH}_2\text{CH}_2$ ), 1.96, 1.98, 2.0, 2.05 (s, 3H, 4  $\text{COCH}_3$ ), 2.46 (m, 4H,  $\text{CH}_2\text{NCH}_2$  Pip), 2.58 (br.s, 4H,  $\text{CH}_2\text{NCH}_2$  Pip), 2.92 (dd,  $J$  = 2.3, 16.7 Hz, 1H,  $\text{CHNHC}(\text{O})\text{CH}_a\text{H}_b$ ), 3.02 (d,  $J$  = 16.4 Hz, 1H,  $\text{CH}_2\text{NHC}(\text{O})\text{CH}_a\text{H}_b$ ), 3.05 (d,  $J$  = 16.4 Hz, 1H,  $\text{CH}_2\text{NHC}(\text{O})\text{CH}_a\text{H}_b$ ), 3.09 (dd,  $J$  = 3.5, 16.7 Hz, 1H,  $\text{CHNHC}(\text{O})\text{CH}_a\text{H}_b$ ), 3.21 (dddd,  $J$  = 4.8, 6.8, 8.0, 13.8 Hz, 1H,  $\text{CH}_a\text{H}_b\text{NH}$ ), 3.34 – 3.54 (m, 6H,  $\text{CH}_2\text{OCH}_a\text{H}_b$ ,  $\text{CHOCH}_2\text{CH}_3$ ), 3.56 – 3.69 (m, 2H,  $\text{CH}_a\text{H}_b\text{NH}$ ,  $\text{CHCH}_a\text{H}_b$ ), 3.80 (ddd,  $J$  = 2.2, 4.4, 10.1 Hz, 1H, H-5), 4.05 (dd,  $J$  = 2.2, 12.5 Hz, 1H, H-6), 4.29 (dd, 1H,  $J$  = 4.4, 12.5 Hz, H-6), 4.98 (dd,  $J$  = 9.5, 9.6 Hz, H-2), 5.05 (dd,  $J$  = 9.4, 10.1 Hz, 1H, H-4), 5.22 (dd,  $J$  = 9.5, 9.8 Hz, 1H, H-1), 5.28 (dd,  $J$  = 9.4, 9.6 Hz, 1H, H-3), 7.81 (d,  $J$  = 9.8 Hz, 1H,  $\text{CH}_2\text{NH}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  14.16, 15.74, 20.55, 20.56, 20.62, 20.78, 22.72, 26.15, 29.36, 29.53, 29.62, 29.66, 29.69, 31.94, 40.20, 40.23, 53.24, 53.70, 61.38, 68.25, 70.46, 71.46, 71.47, 72.95, 73.79, 76.70, 76.74, 76.93, 77.15, 77.36, 77.82, 169.55, 169.94, 170.18, 170.21, 170.61, 171.13. HRMS ESI  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{37}\text{H}_{65}\text{N}_4\text{O}_{13}$  773.4543, found 773.4535.

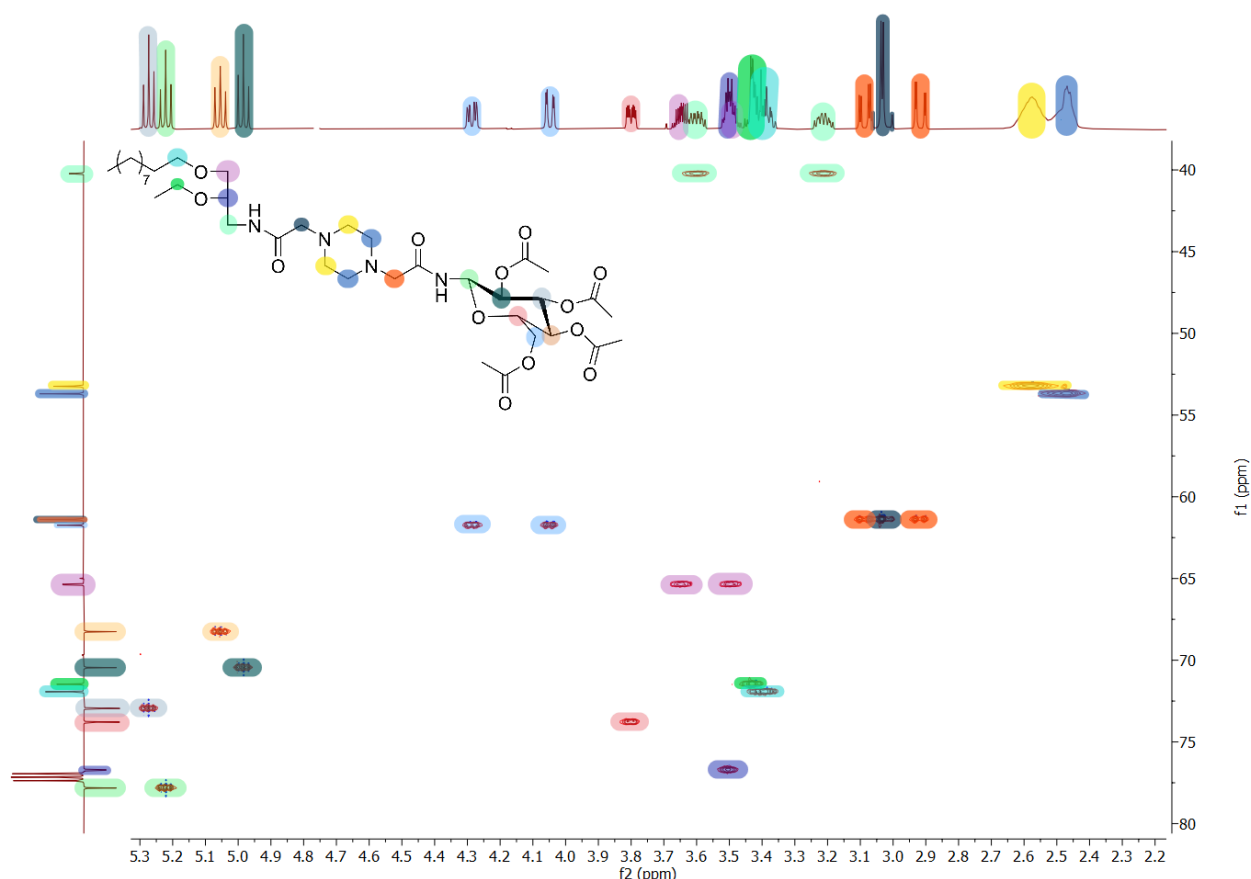


Figure S56. Fragment of  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **15c**.

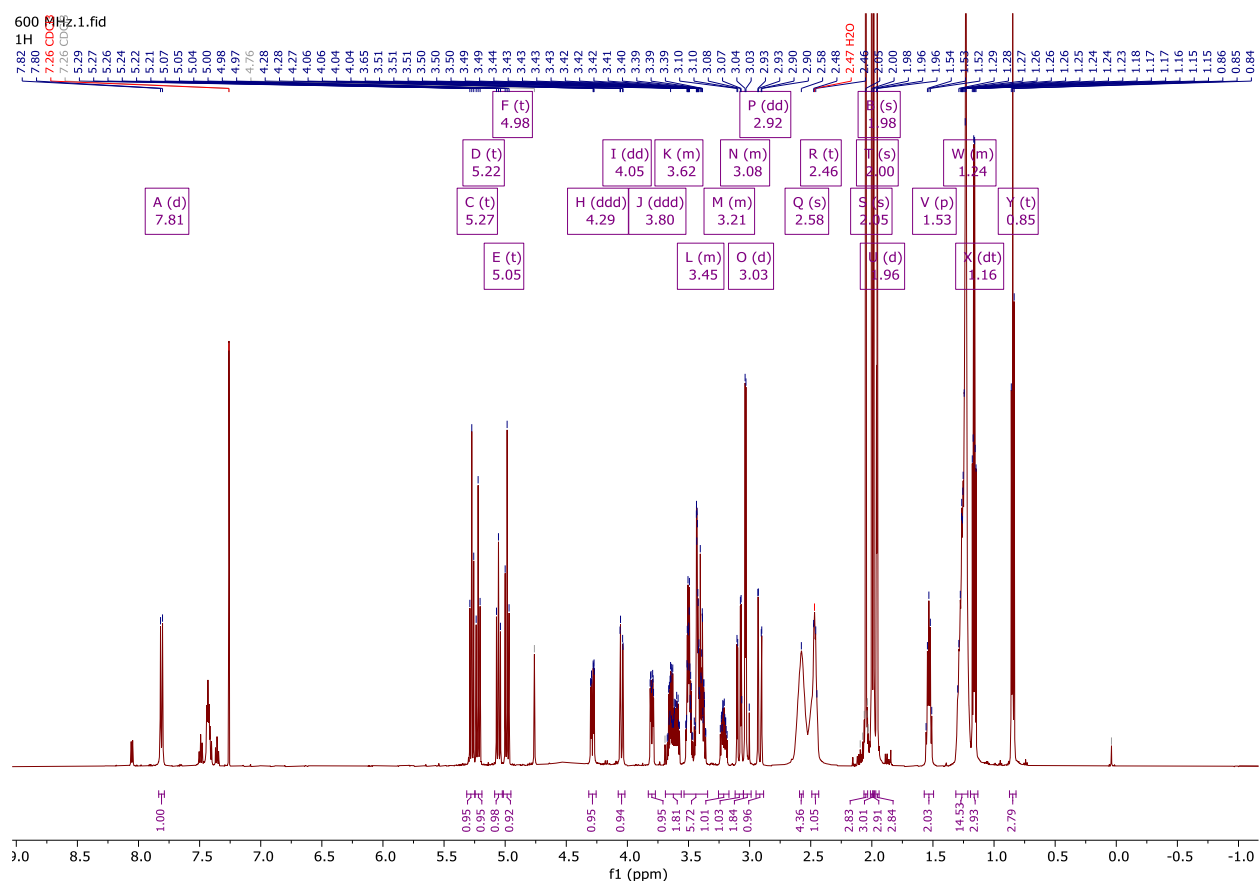


Figure S57.  $^1\text{H}$  NMR spectrum of compound **15c**.

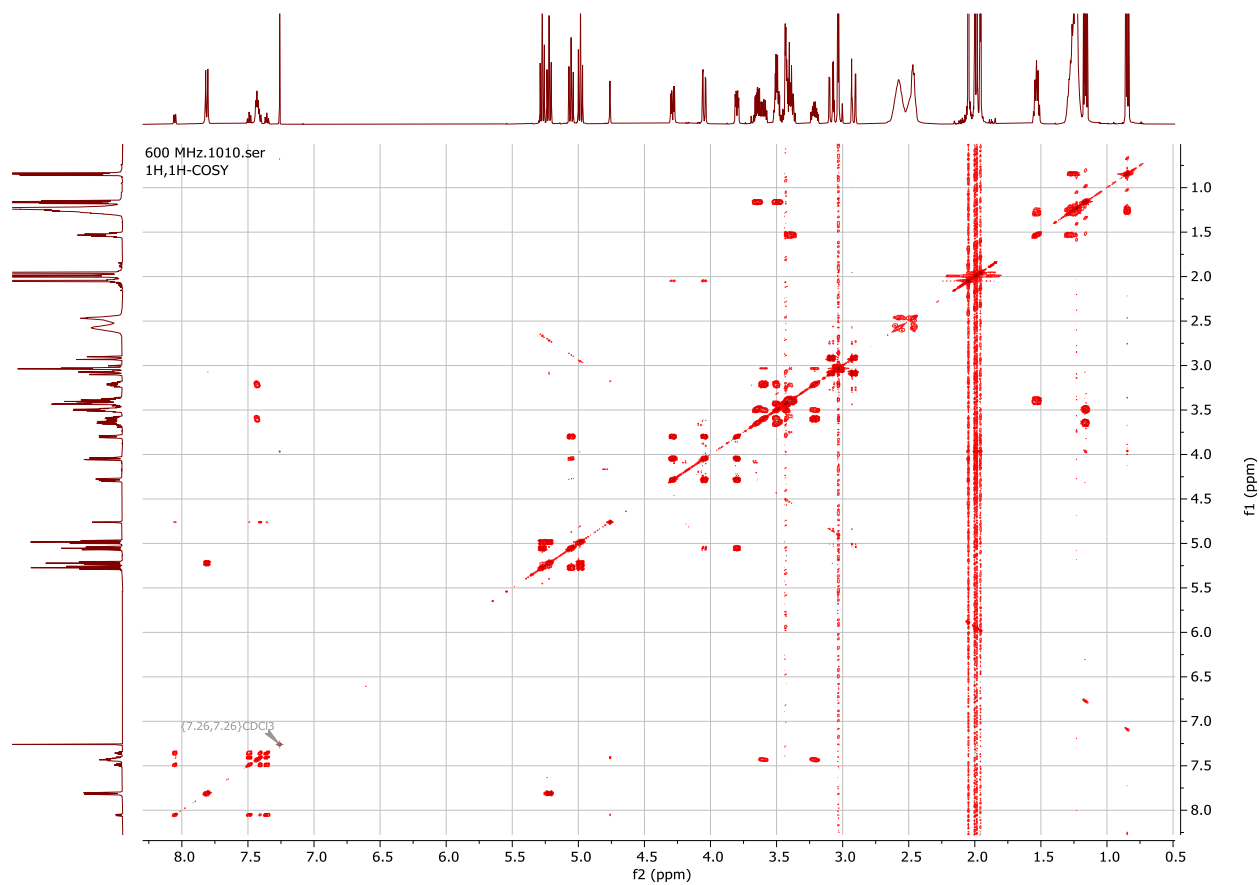


Figure S58.  $\{^1\text{H}-^1\text{H}\}$  COSY NMR spectrum of compound **15c**.

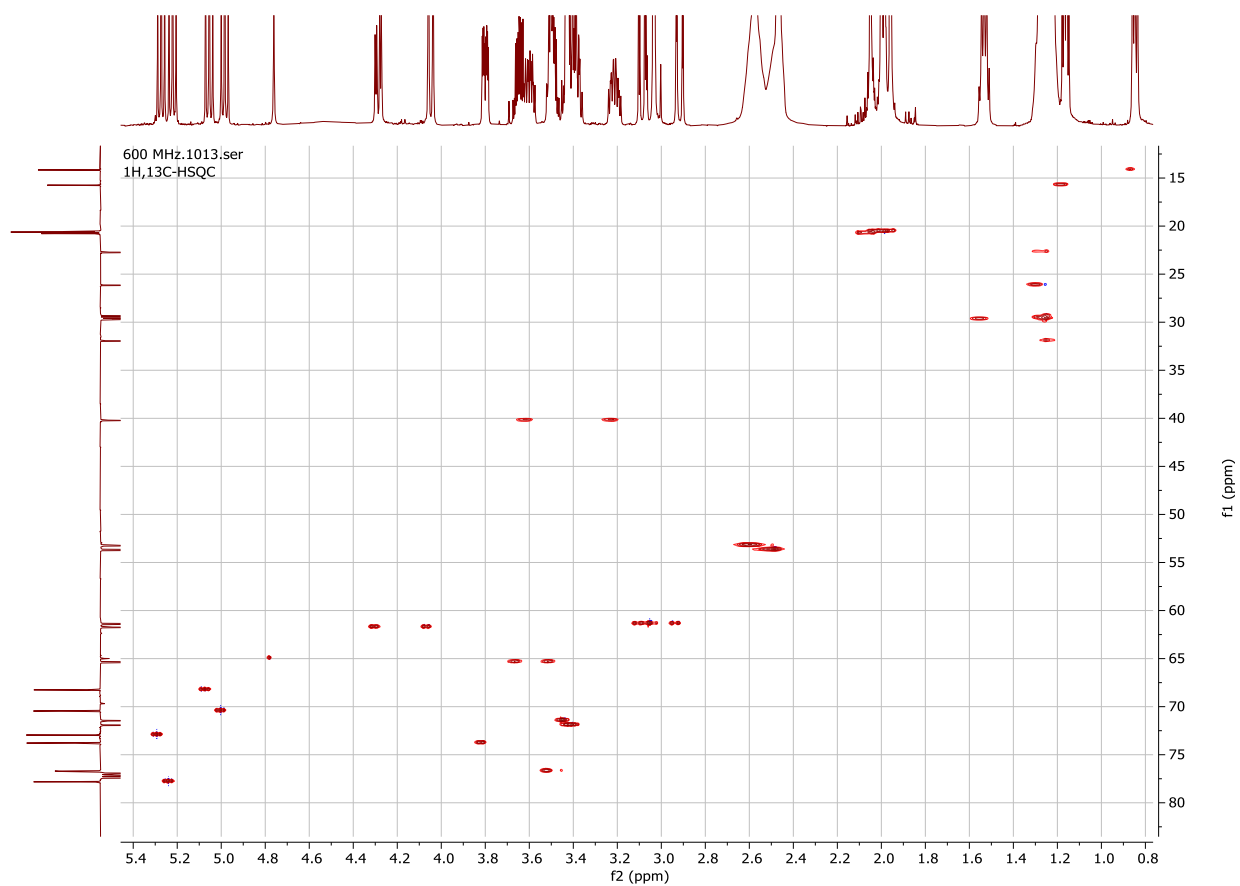


Figure S59.  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **15c**.

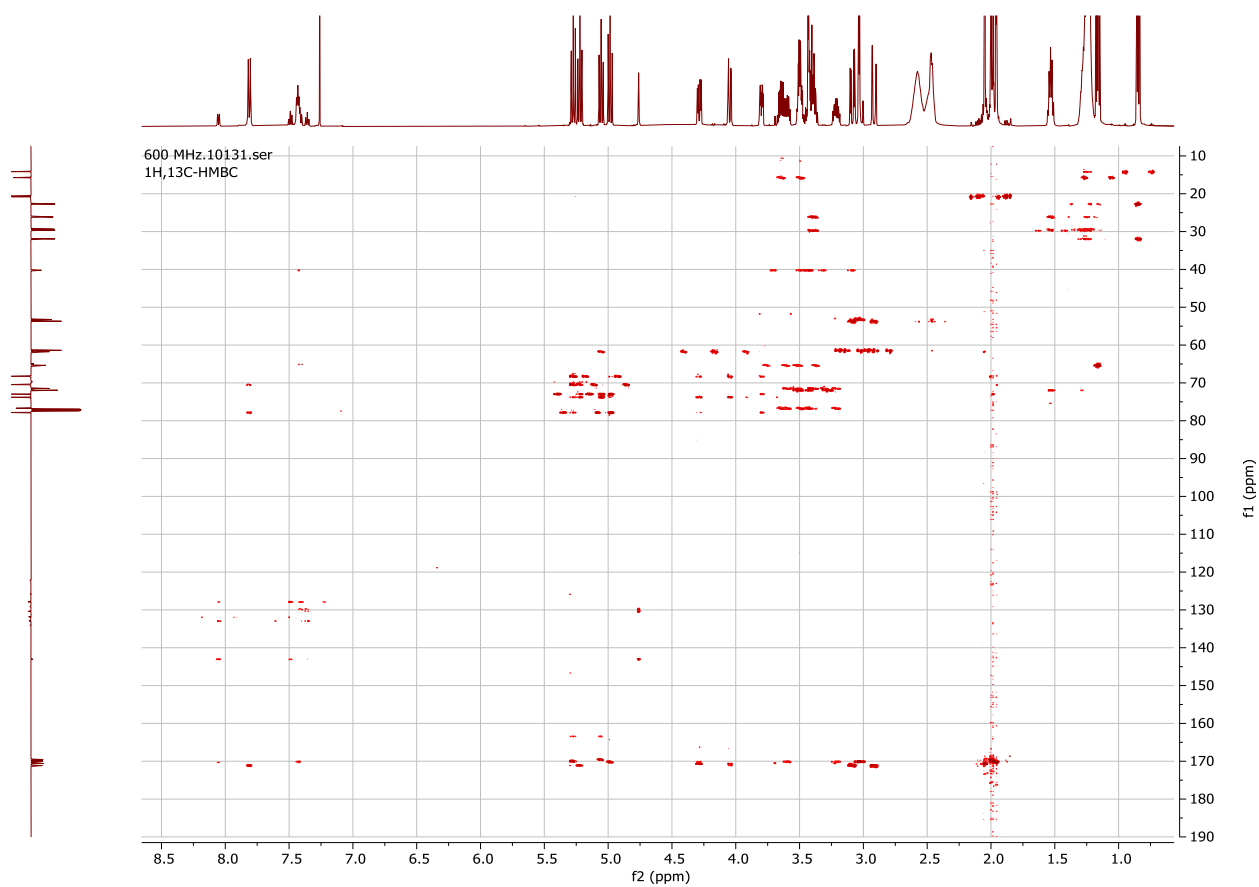


Figure S60.  $\{^1\text{H}-^{13}\text{C}\}$  HMBC NMR spectrum of compound **15c**.

5a-6 #599-618 RT: 4.08-4.19 AV: 10 SB: 23 3.89-4.02 , 4.12-4.29 NL: 3.60E9  
T: FTMS + p ESI Full ms [95.0000-1000.0000]

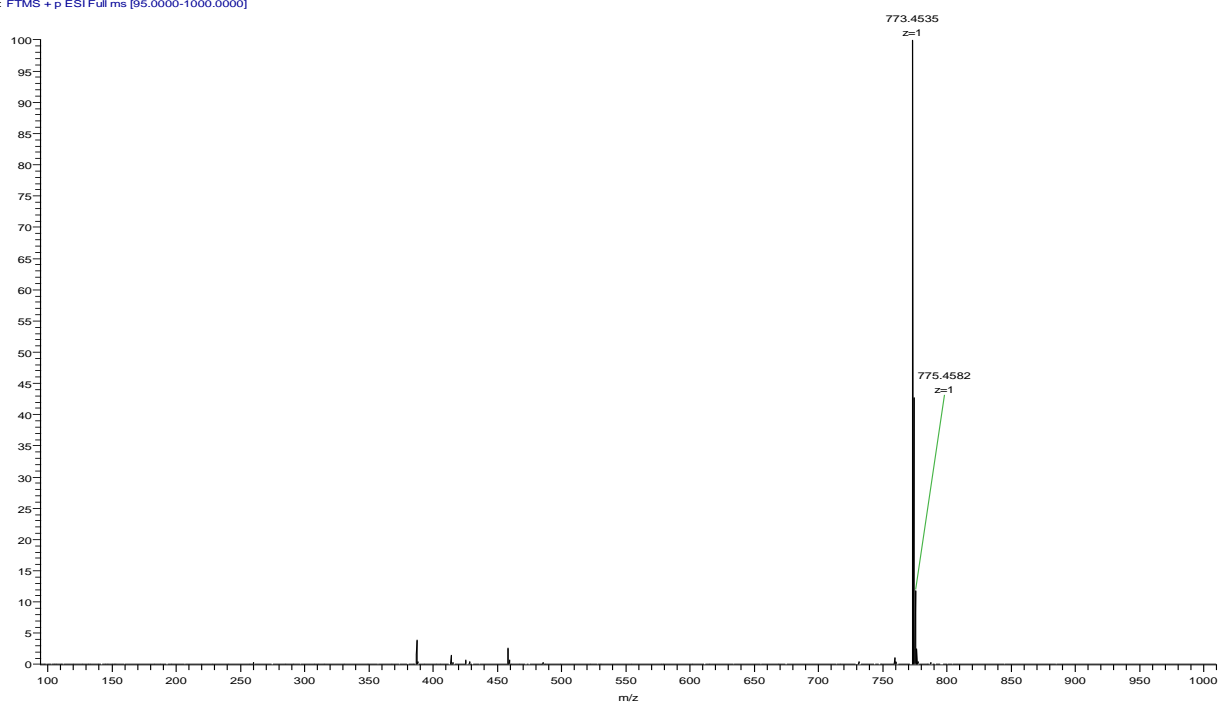


Figure S61. HRMS spectrum of compound **15c**.



1,9-diamino-*N*<sup>9</sup>-ethyl-*N*<sup>1</sup>-octadecyl-*N*<sup>3</sup>,*N*<sup>7</sup>-dibenzyl-3,7-diazanonane (**16a**)

Yield 410 mg (66%), colorless oil. Eluent: ACN-NH<sub>3</sub>·H<sub>2</sub>O (9:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.91 (t, *J* = 7.0 Hz, 3H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.07 (t, *J* = 7.1 Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>), 1.29 (s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.44 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 1.61 – 1.79 (m, 2H, PhCH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.34 – 2.75 (m, 16H, 4 NHCH<sub>2</sub>, 4 NCH<sub>2</sub>), 3.55 (s, 4H, 2 PhCH<sub>2</sub>), 7.16 – 7.43 (m, 10H, 2 Ph). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 14.17, 15.14, 22.73, 24.77, 29.40, 29.65, 29.70, 29.75, 43.94, 47.19, 47.44, 49.94, 52.63, 52.65, 53.66, 59.01, 59.03, 126.85, 126.94, 128.22, 128.39, 128.78, 128.84, 134.17, 139.81, 139.84. MS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>41</sub>H<sub>73</sub>N<sub>4</sub> 621.58, found: 621.52.

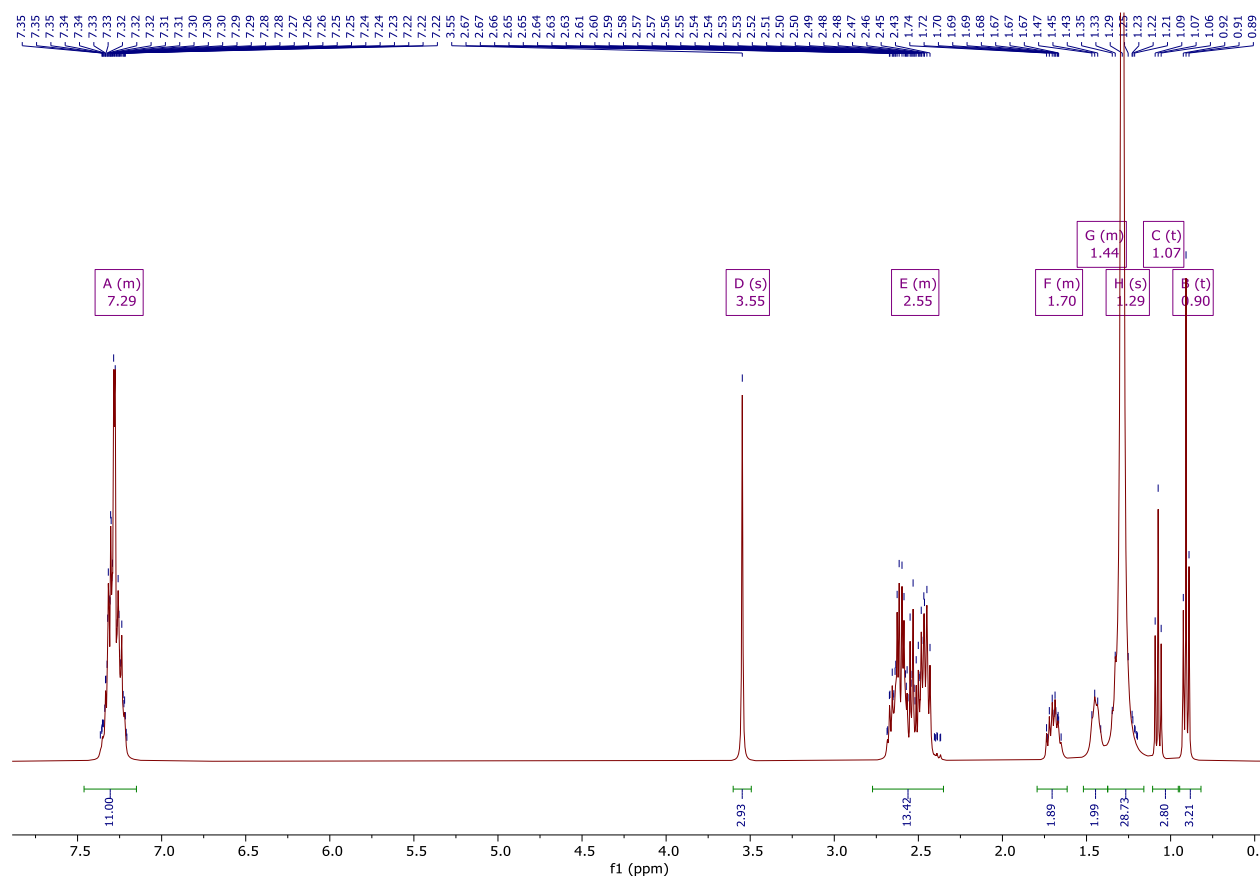


Figure S62.  $^1\text{H}$  NMR spectrum of compound **16a**.

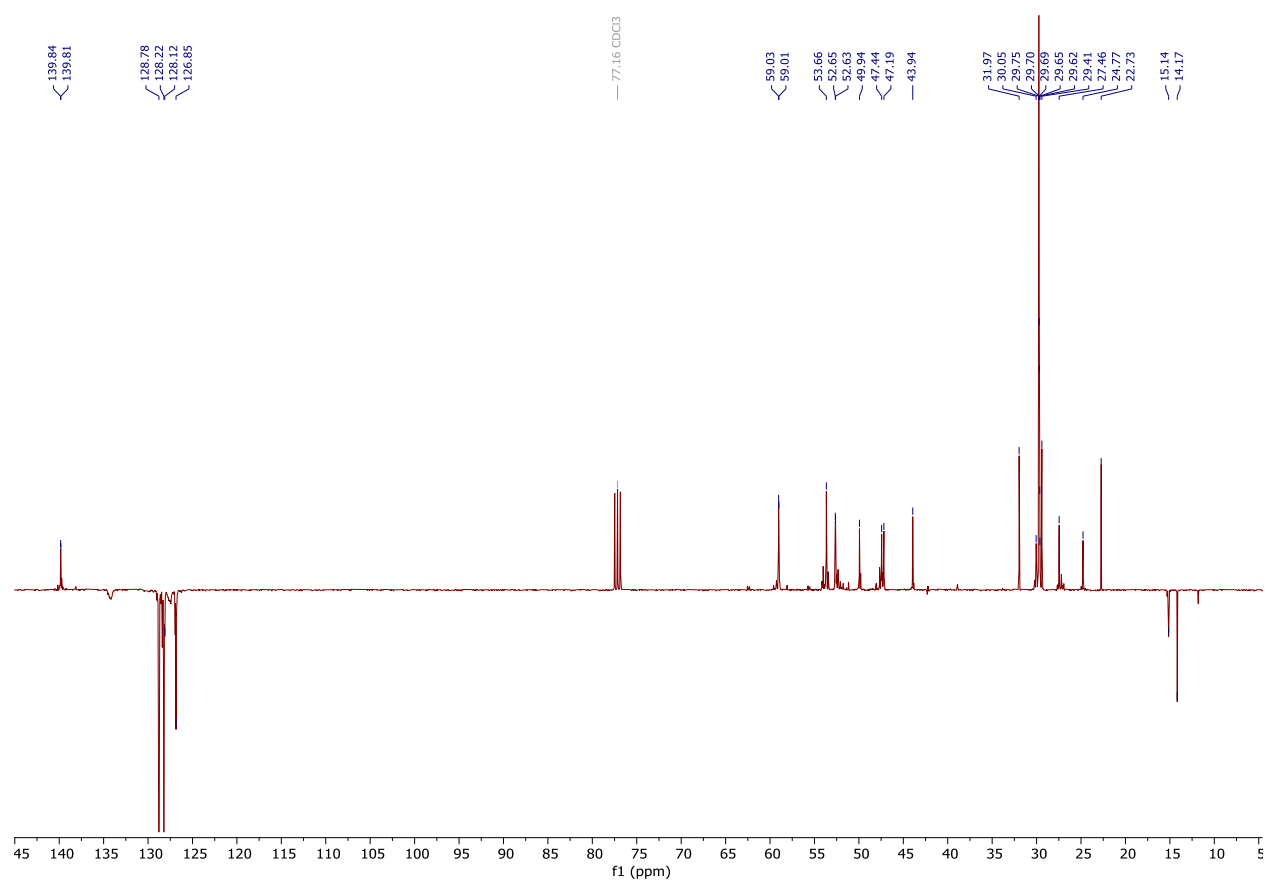


Figure S63. <sup>1</sup>H (APT) NMR spectrum of compound **16a**.

4A-8 #2-5 RT: 0.02-0.06 AV: 4 NL: 2.41E8  
T: + c ESI Full ms [150.00-1200.00]

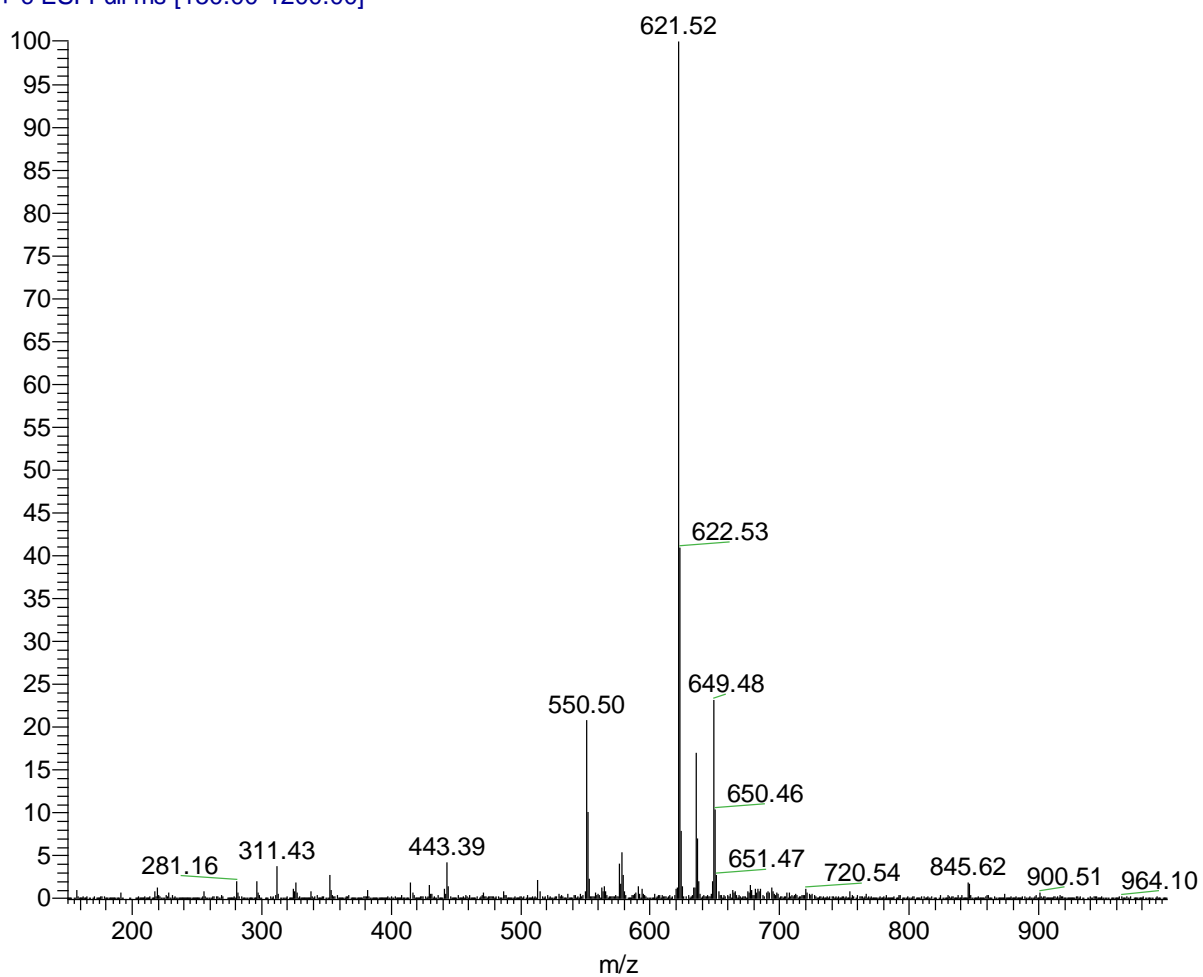


Figure S64. HRMS spectrum of compound **16a**.

*N*<sup>1</sup>-ethyl-*N*<sup>4</sup>-[(*N*-octadecyl)aminoethyl]piperazin (**16b**)

Yield: 31%, colorless oil. Eluent: ACN-NH<sub>3</sub>·H<sub>2</sub>O (95:5). <sup>1</sup>H NMR (300 MHz, MeOD) δ 0.90 (t, *J* = 6.5 Hz, 3H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.10 (td, *J* = 3.2, 7.2 Hz, 3H, NCH<sub>2</sub>CH<sub>3</sub>), 1.31 (br.s, 30H, (CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>), 1.55 – 1.75 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 2.14 (td, *J* = 2.8, 12.5 Hz, 1H, NHCH<sub>2</sub>CH<sub>2</sub>N), 2.39 – 3.11 (m, 13H, Pip protons, NHCH<sub>2</sub>CH<sub>2</sub>N, NCH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, MeOD) δ 11.80, 14.49, 23.77, 27.11, 28.01, 30.47, 30.51, 30.71, 30.82, 33.10, 52.34, 52.48, 52.70, 53.17, 53.28, 53.69, 54.65, 56.54. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>56</sub>N<sub>3</sub> 410.4469, found: 410.4468.

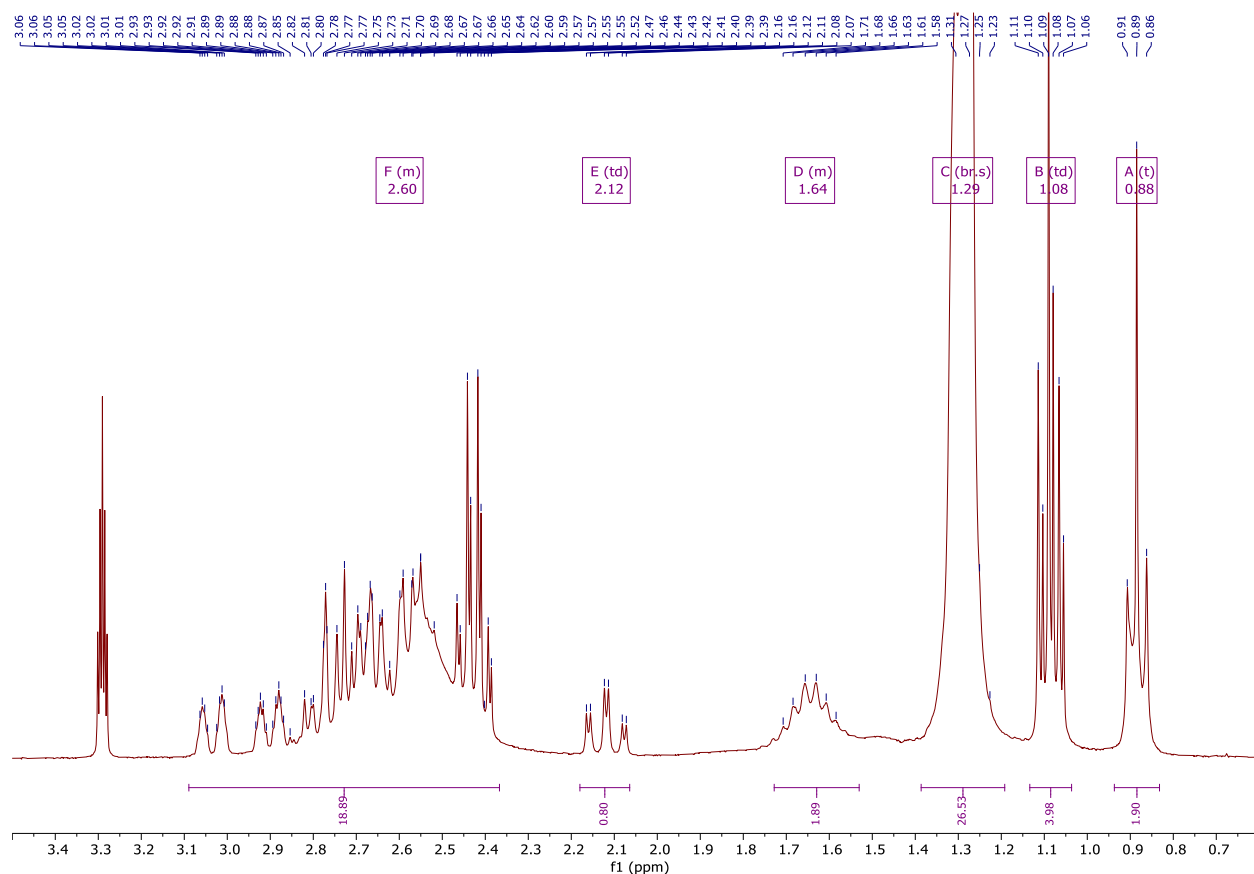


Figure S65. <sup>1</sup>H NMR spectrum of compound **16b**.

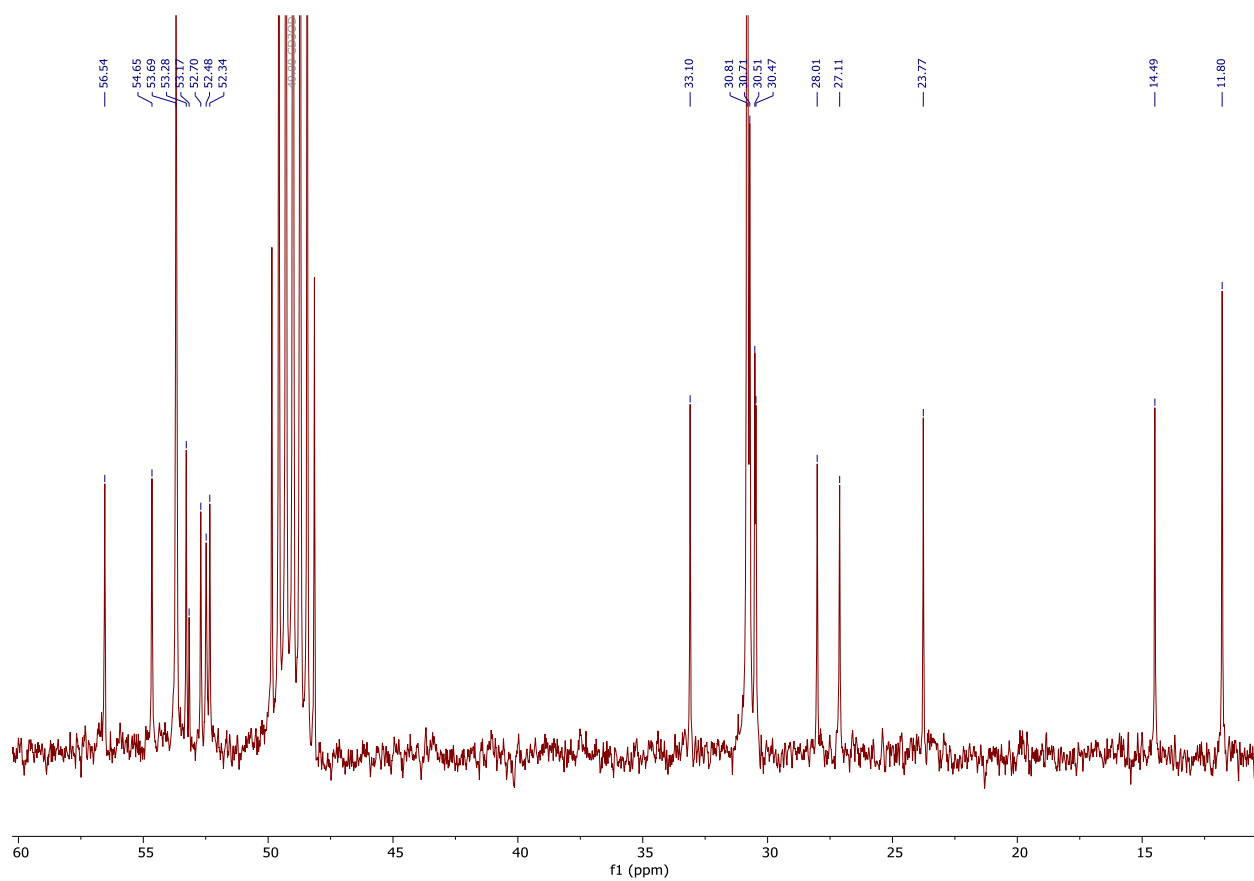


Figure S66.  $^{13}\text{C}$  NMR spectrum of compound **16b**.

## Display Report

### Analysis Info

Analysis Name D:\Data\Kolotyrkina\2021\Maksimenko\0415003.d  
Method tune\_50-1600.m  
Sample Name /MAKS 5A-42  
Comment C26H55N3 mH 410.4468 calibrant added CH3CN

Acquisition Date 15.04.2021 9:28:17

Operator BDAL@DE  
Instrument / Ser# microTOF 10248

### Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste

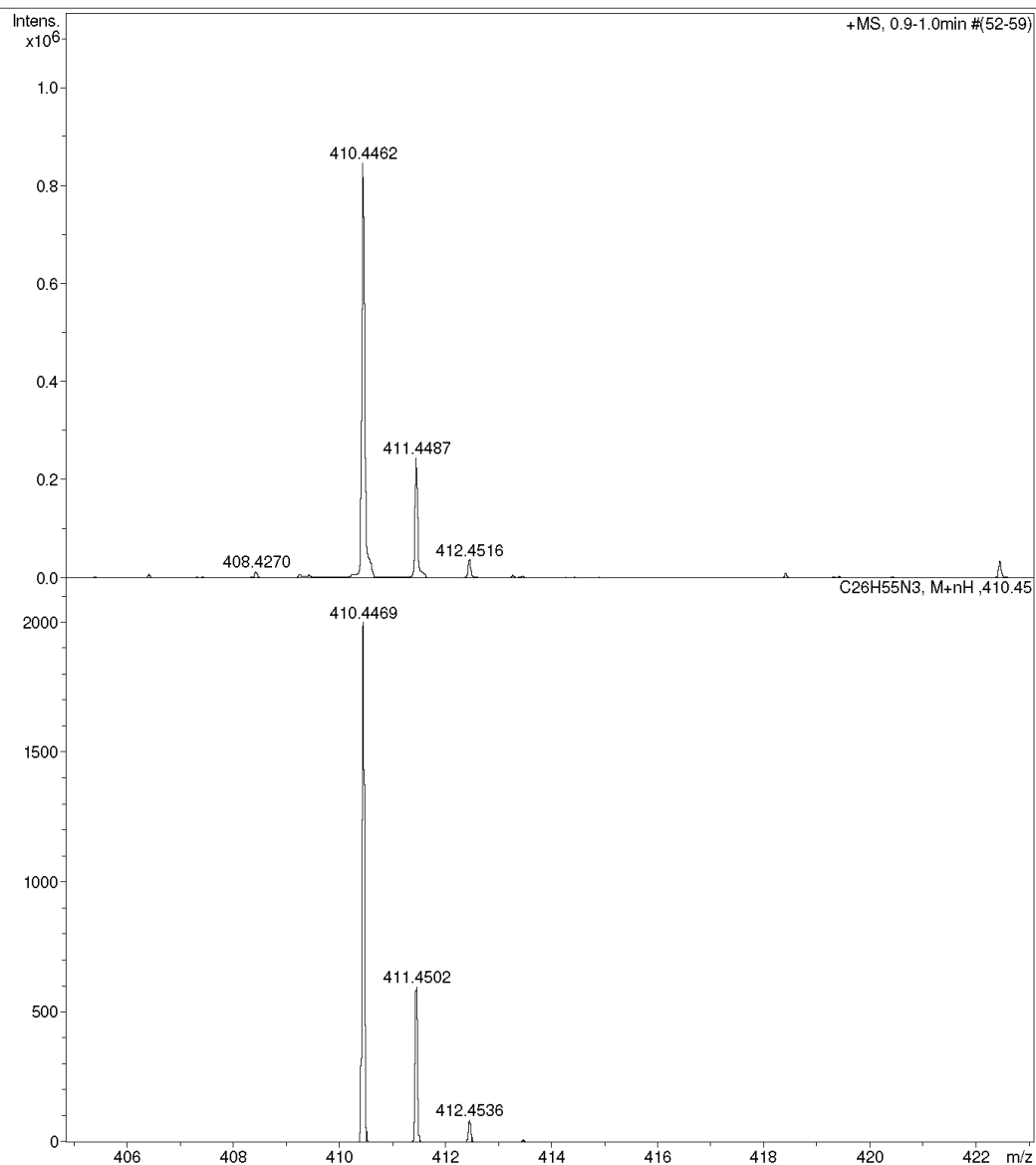


Figure S67. HRMS spectrum of compound **16b**.

$N^1$ -[2-(ethylamino)ethyl]- $N^4$ -[ $N$ -(*rac*-1-decyloxy-2-ethoxyprop-3-yl)amino]ethylpiperazin (**16c**)

Yield: 23%, colorless oil. Eluent: ACN- $\text{NH}_3 \cdot \text{H}_2\text{O}$  (9:1).  $^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  0.88 (t,  $J$  = 7.0 Hz, 3H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.03 (t,  $J$  = 7.2 Hz, 3H,  $\text{NCH}_2\text{CH}_3$ ), 1.16 (t,  $J$  = 7.0 Hz,  $\text{OCH}_2\text{CH}_3$ , 3H), 1.29 (br.s,  $(\text{CH}_2)_7\text{CH}_3$ , 14H), 1.51 – 1.57 (m, 3H,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_7$ ), 2.35 (q,  $J$  = 7.2 Hz, 2H,  $\text{NHCH}_2\text{CH}_3$ ), 2.37-2.58 (m, 14H,  $3\text{CH}_2\text{NH}$ , Pip protons), 2.58 – 2.71 (m, 4H,  $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2$ ), 3.38 – 3.46 (m, 4H,  $\text{CH}_2\text{OCH}_2$ ), 3.48 – 3.54 (m, 2H,  $\text{CHOCH}_a\text{H}_b\text{CH}_3$ ), 3.65 (dq,  $J$  = 7.0, 9.3 Hz, 1H,  $\text{OCH}_a\text{H}_b\text{CH}_3$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  12.35, 14.30, 16.00, 23.12, 26.60, 29.77, 29.93, 30.03, 30.08, 30.18, 32.35, 47.14, 51.64, 52.64, 53.40, 53.81, 58.33, 65.62, 71.95, 72.28, 78.26.

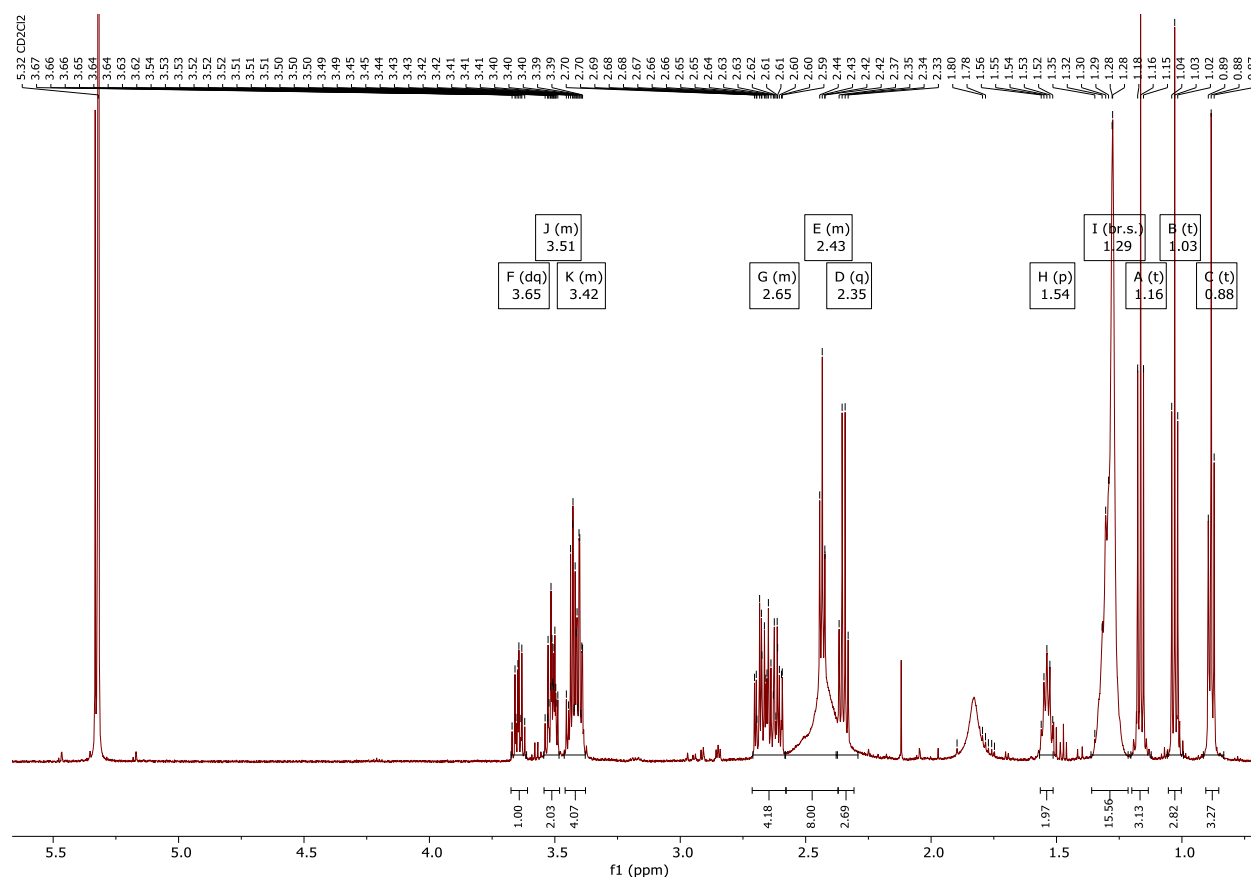


Figure S68.  $^1\text{H}$  NMR spectrum of compound **16c**.

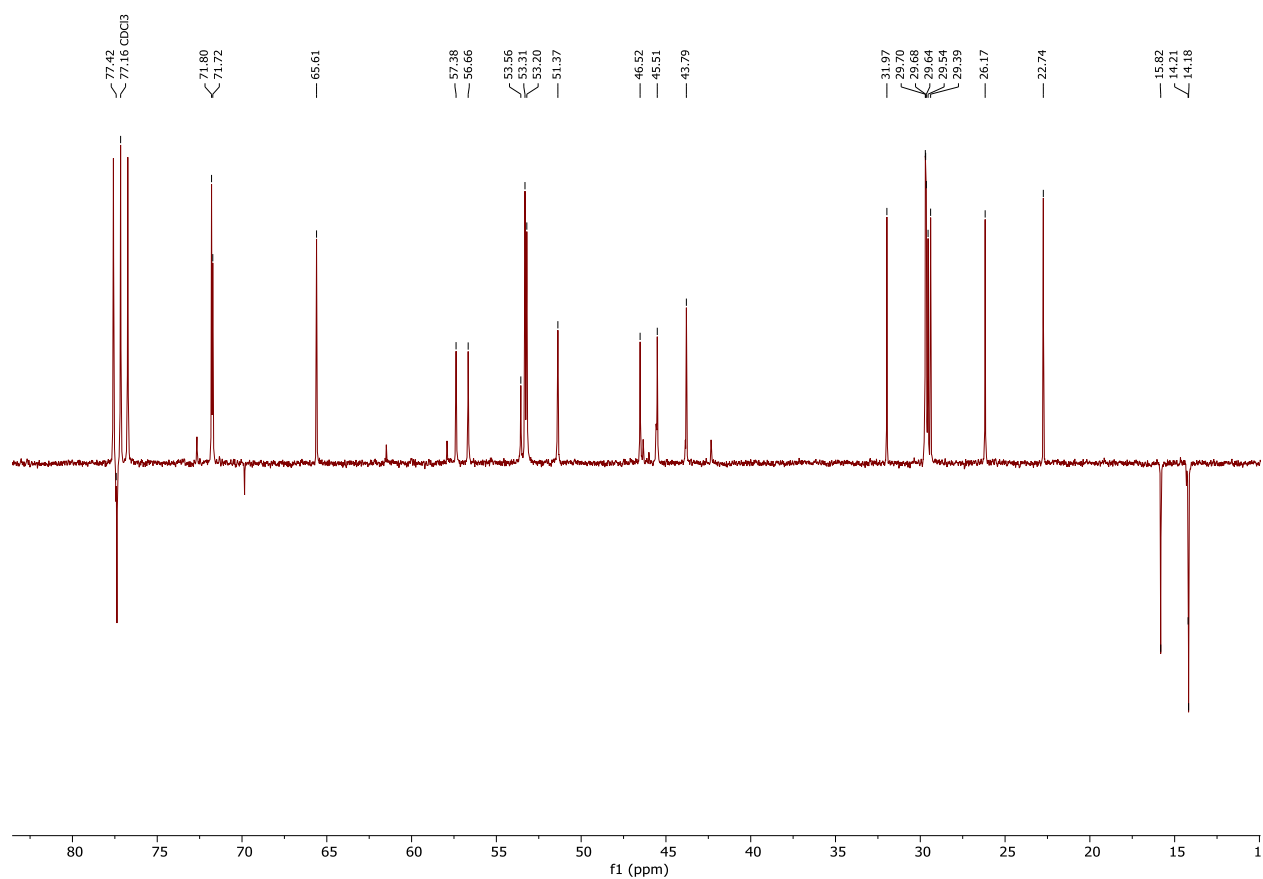


Figure S69.  $^{13}\text{C}$  (APT) NMR spectrum of compound **16c**.



*N*<sup>1</sup>-ethyl-*N*<sup>4</sup>-[*N*-(*rac*-1-decyloxy-2-ethoxyprop-3-yl)amino]ethylpiperazin (**16d**)

Yield 184 mg (38%), colorless oil. Eluent: EA-MeOH-NH<sub>3</sub>·H<sub>2</sub>O (7:3:0.2). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.77 – 0.94 (t, 3H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.09 – 1.34 (m, 20H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, NCH<sub>2</sub>CH<sub>3</sub>), 1.45 – 1.59 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>15</sub>), 2.31 – 2.82 (m, 16H, 2 NHCH<sub>2</sub>, Pip protons), 3.30 – 3.75 (m, 7H, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.18, 14.21, 15.82, 22.74, 26.17, 29.39, 29.54, 29.64, 29.68, 29.70, 31.97, 43.79, 45.51, 46.52, 51.37, 53.20, 53.31, 53.56, 56.66, 57.38, 65.61, 71.72, 71.80, 77.42. HRMS ESI m/z: [M+2Na]<sup>2+</sup> calcd for C<sub>23</sub>H<sub>49</sub>N<sub>3</sub>O<sub>2</sub>Na<sub>2</sub> 222.6805, found: 222.2215.

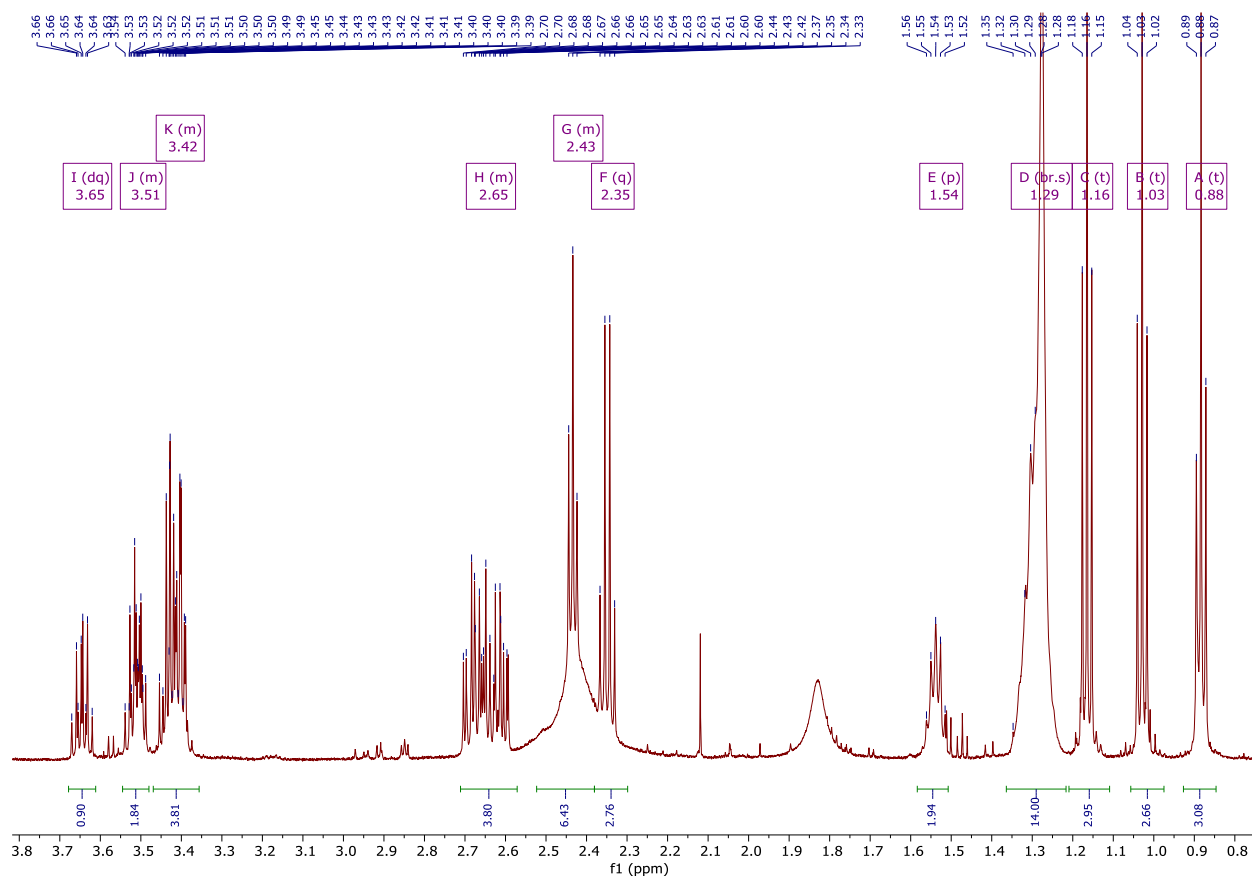


Figure S70. <sup>1</sup>H NMR spectrum of compound **16d**.

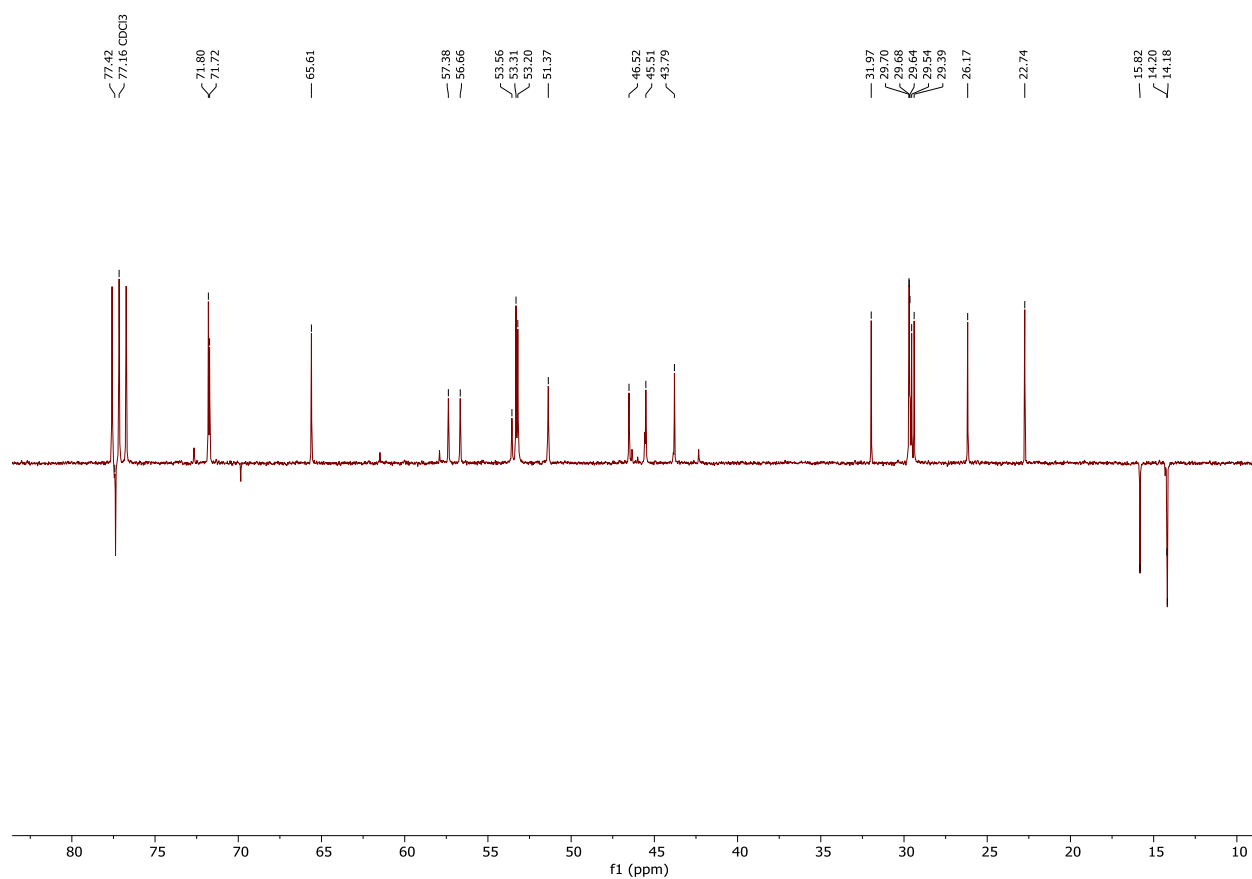


Figure S71. <sup>13</sup>C (APT) NMR spectrum of compound **16d**.

## Display Report

### Analysis Info

Analysis Name D:\Data\Kolotyrkina\2021\Maksimenko\0413019.d  
Method tune\_50-1600.m  
Sample Name /MAKS 5A-56  
Comment C23H49N3O2 mH 400.3897 calibrant added CH3OH

Acquisition Date 13.04.2021 12:29:16

Operator BDAL@DE  
Instrument / Ser# microTOF 10248

### Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste

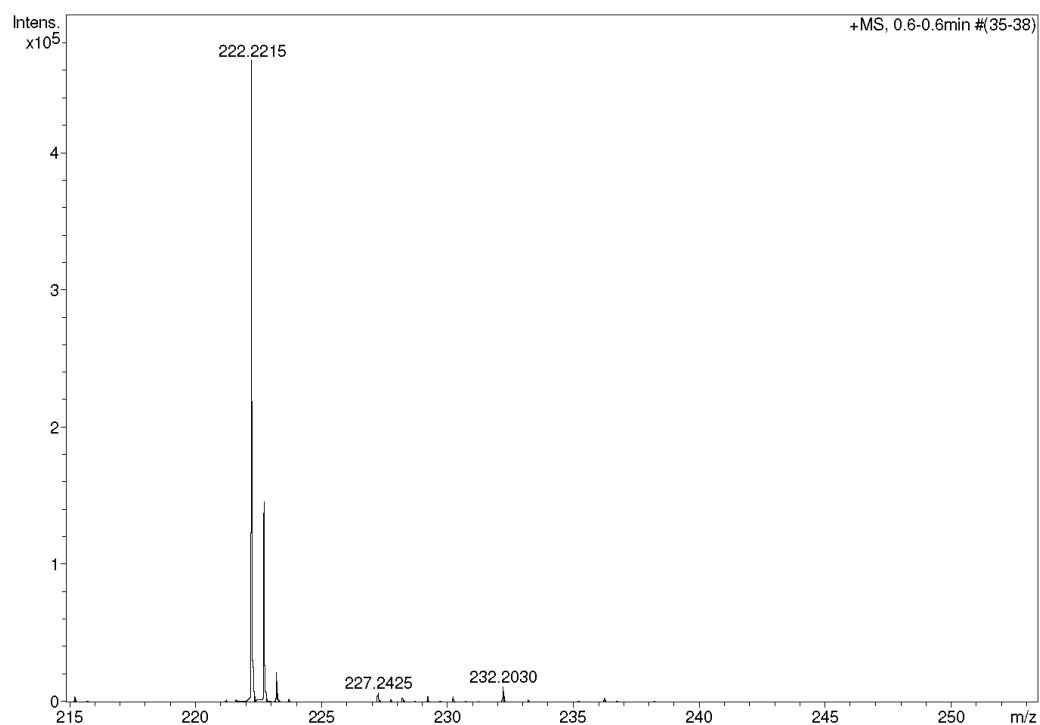
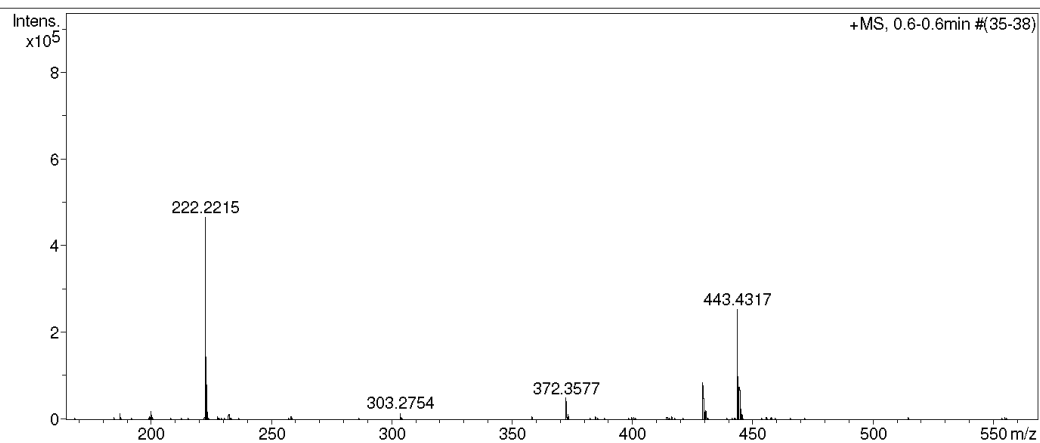


Figure S72. HRMS spectrum of compound **16d**.

$N^1$ -[2-[*N*-(isopropylamino)ethyl]- $N^4$ -[*N*-(*rac*-1-decyloxy-2-ethyloxyprop-3-yl)amino]ethylpiperazin (**16e**)

Yield: 25%, colorless oil. Eluent: EA-MeOH-NH<sub>3</sub>·H<sub>2</sub>O (7:3:0.3). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.86 (t, *J* = 7.0 Hz, 3H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.08 (d, *J* = 6.3 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.18 (t, *J* = 7.0 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.25 (d, *J* = 5.6 Hz, 14H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>), 1.47 – 1.60 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>7</sub>), 2.34 – 2.58 (m, 12H, 2 CH<sub>2</sub>N and Pip protons), 2.60 – 2.79 (m, 6H, 3 NHCH<sub>2</sub>), 2.82 (sept, *J* = 6.3 Hz, 1H, CH(CH<sub>3</sub>)<sub>2</sub>), 3.36 – 3.63 (m, 6H, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>CHOCH<sub>2</sub>H<sub>b</sub>), 3.69 (dq, *J* = 7.0, 9.3 Hz, 1H, CHOCH<sub>2</sub>H<sub>b</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.21, 15.86, 22.69, 22.79, 26.23, 29.44, 29.59, 29.69, 29.73, 29.77, 32.02, 43.83, 46.74, 49.15, 51.57, 53.38, 57.59, 57.74, 65.66, 71.83, 71.92, 77.66. HRMS ESI *m/z*: [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>57</sub>N<sub>4</sub>O<sub>2</sub> 457.4476, found: 457.4483. HRMS ESI *m/z*: [M+2H]<sup>2+</sup> calcd for C<sub>26</sub>H<sub>58</sub>N<sub>4</sub>O<sub>2</sub> 229.2275, found: 229.2276.

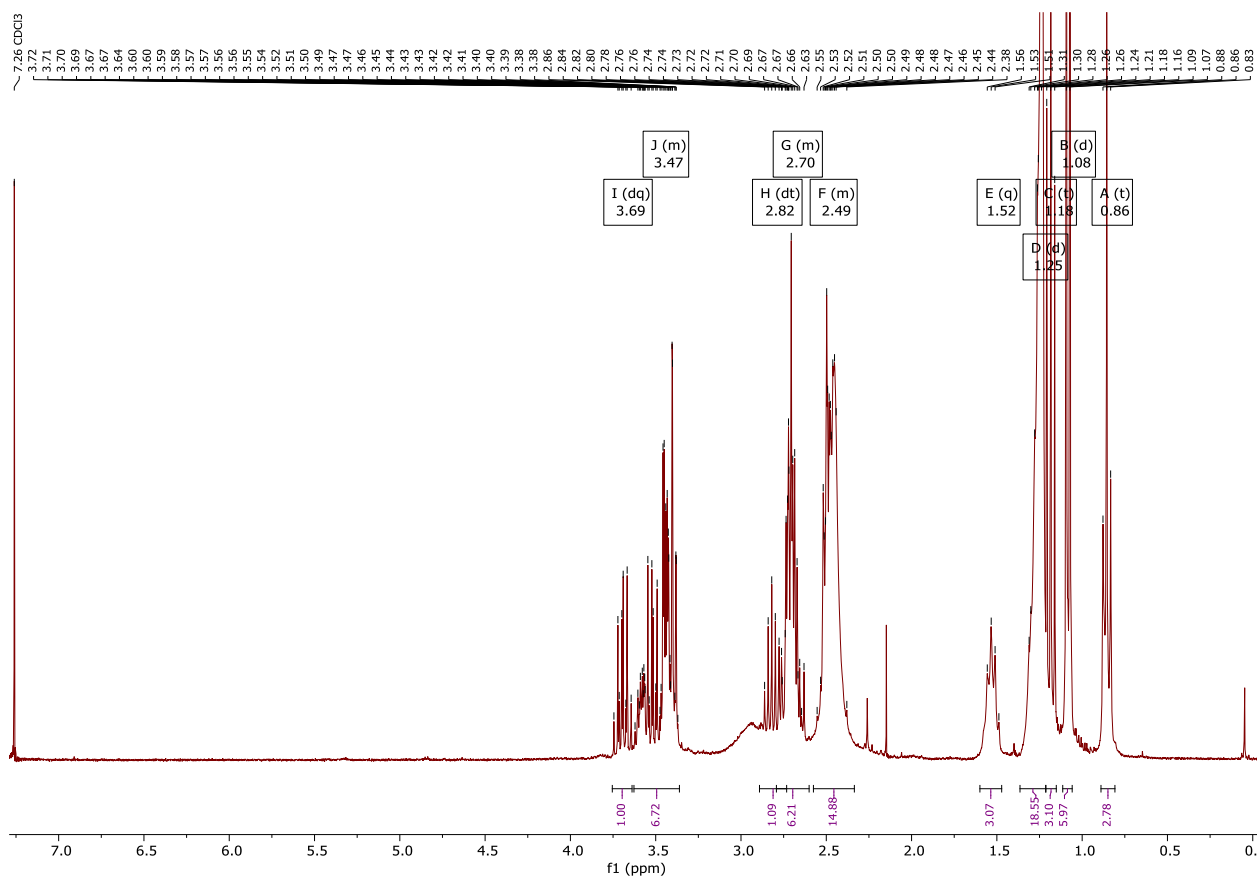


Figure S73. <sup>1</sup>H NMR spectrum of compound **16e**.

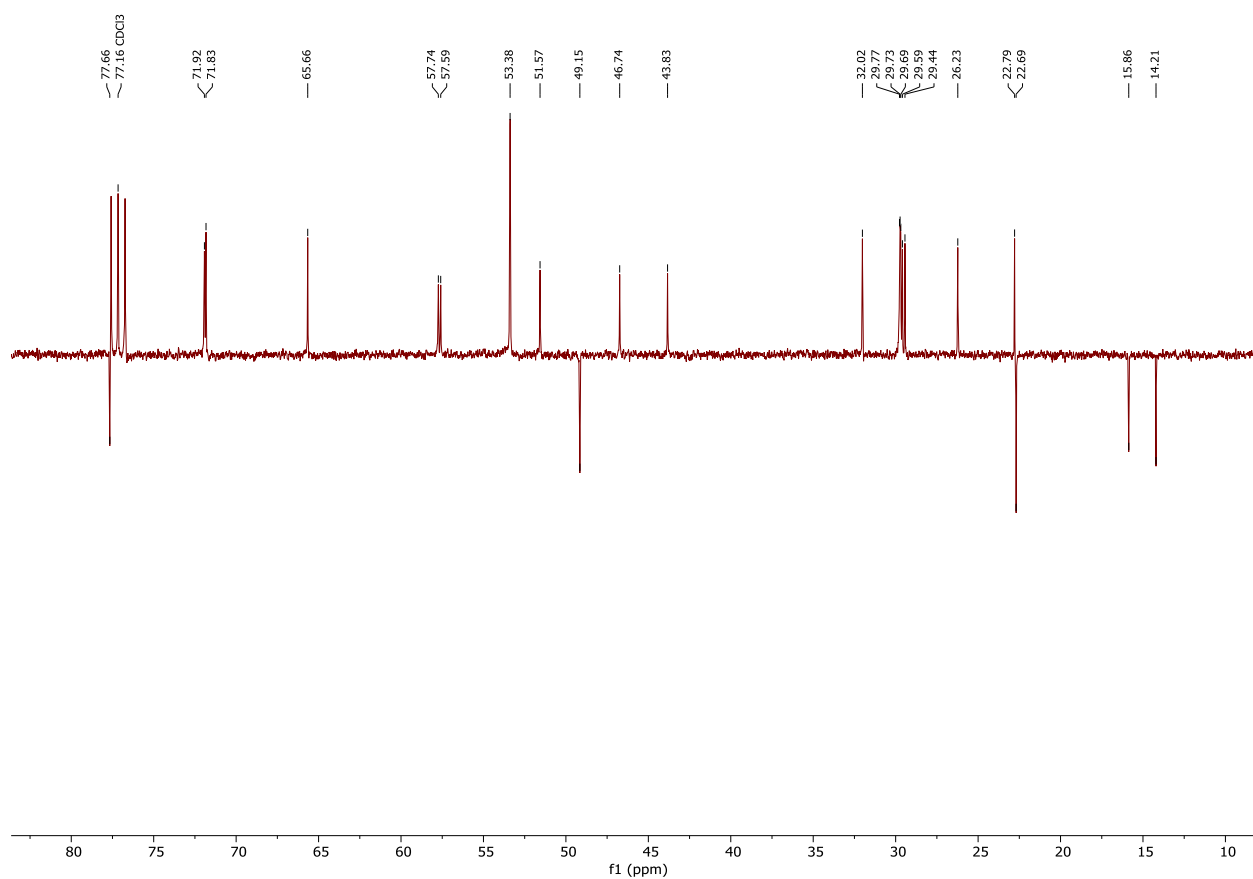


Figure S74. <sup>13</sup>C (APT) NMR spectrum of compound **16e**.

5a-10 #435-482 RT: 3.00-3.30 AV: 24 SB: 22 3.89-4.02 , 4.12-4.28 NL: 1.86E10  
T: FTMS + p ESI Full ms [95.0000-1000.0000]

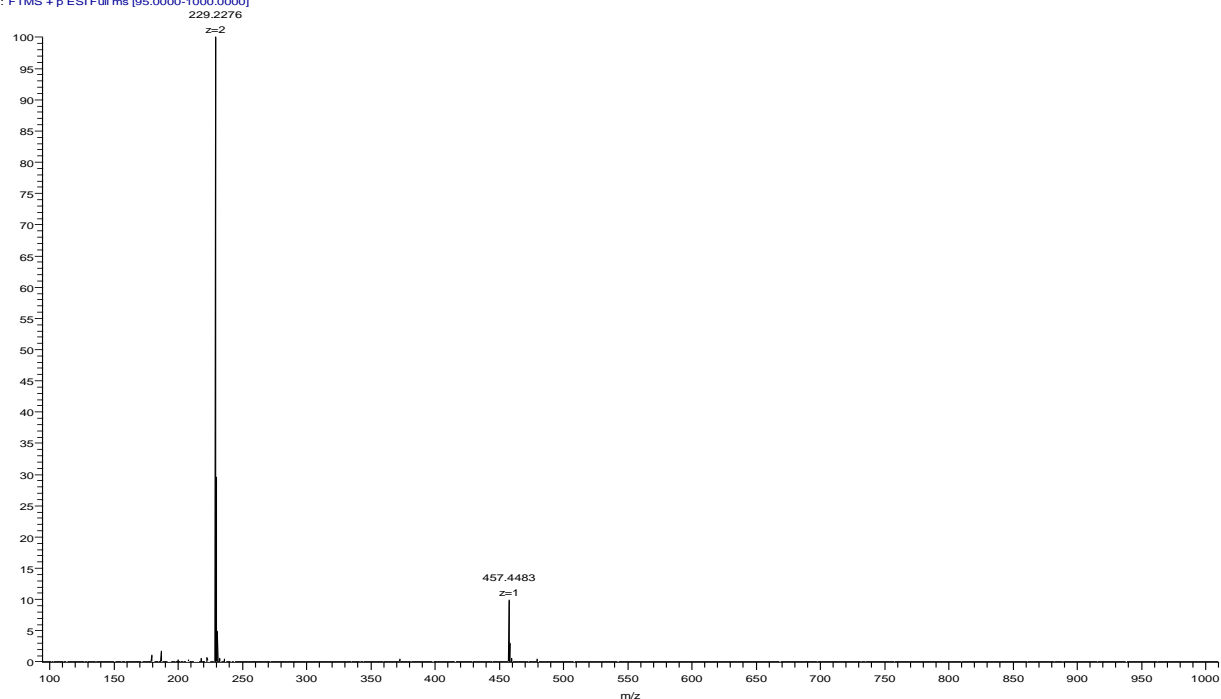


Figure S75. HRMS spectrum of compound **16e**.

$N^1$ -[2-(*N*-pentylamino)ethyl]- $N^4$ -[*N*-(*rac*-1-decyloxy-2-ethoxyprop-3-yl)amino]ethylpiperazin (**16f**)

Yield: 43%, colorless oil. Eluent: ACN-NH<sub>3</sub>-H<sub>2</sub>O (9:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.79 – 0.91 (m, 6H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 1.17 (t, *J* = 7.0 Hz, 3H, OCH<sub>2</sub>CH<sub>3</sub>), 1.25 (br.s, 18H, (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 1.41 – 1.58 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>7</sub>, NCH<sub>2</sub>CH<sub>2</sub>), 2.13 – 2.76 (m, 20H, 2 NCH<sub>2</sub>, 4 NHCH<sub>2</sub>, Pip protons), 3.32 – 3.60 (m, 1H, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>H<sub>b</sub>), 3.68 (dq, *J* = 7.1, 9.4 Hz, 1H, OCH<sub>2</sub>H<sub>b</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 14.16, 14.21, 22.68, 22.77, 26.21, 29.42, 29.57, 29.64, 29.67, 29.71, 29.74, 29.78, 31.99, 46.55, 46.77, 50.14, 51.64, 53.39, 53.43, 57.95, 65.65, 71.77, 71.99, 77.82. HRMS ESI *m/z*: [M+2Na]<sup>+</sup> calcd for C<sub>23</sub>H<sub>49</sub>N<sub>3</sub>O<sub>2</sub>Na<sub>2</sub> 222.6805, found: 222.2215.

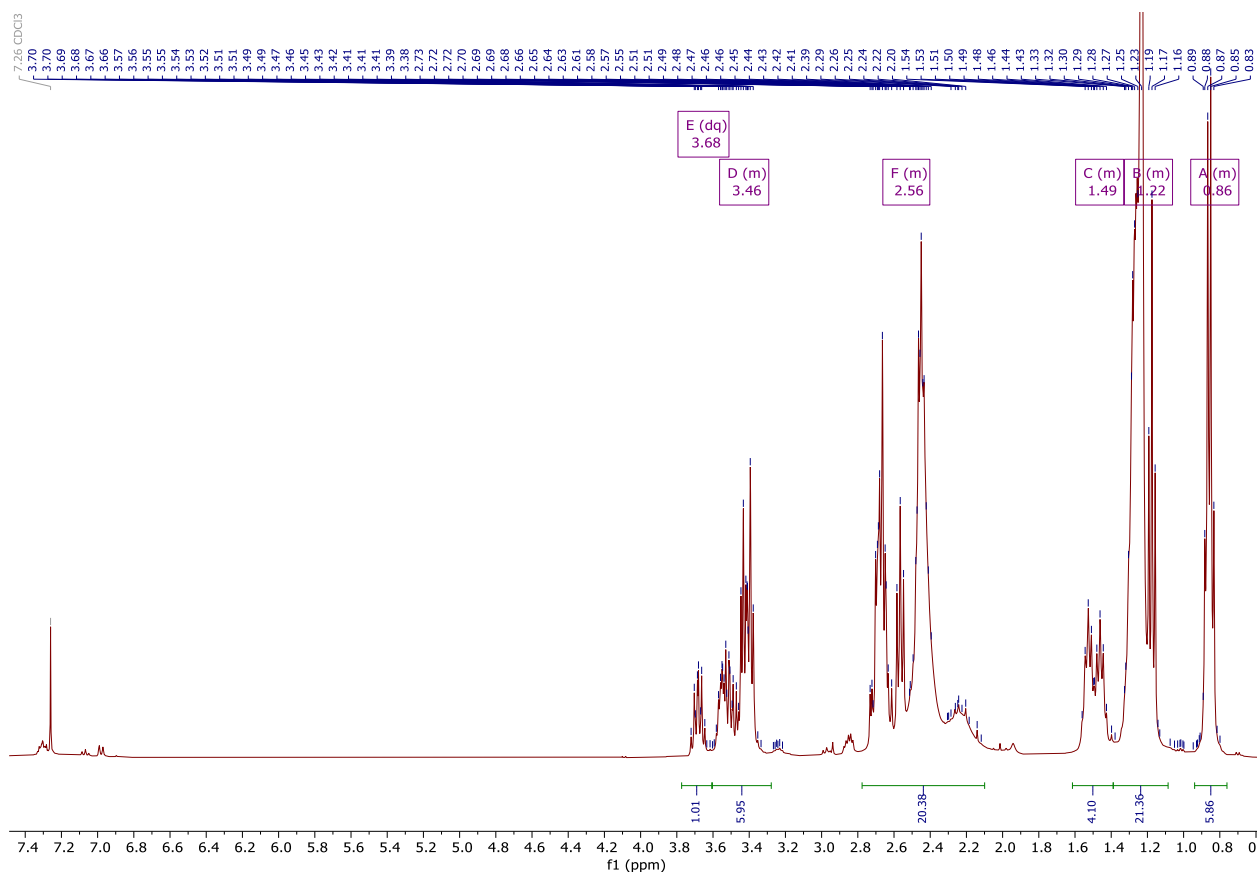


Figure S76. HRMS spectrum of compound **16f**.

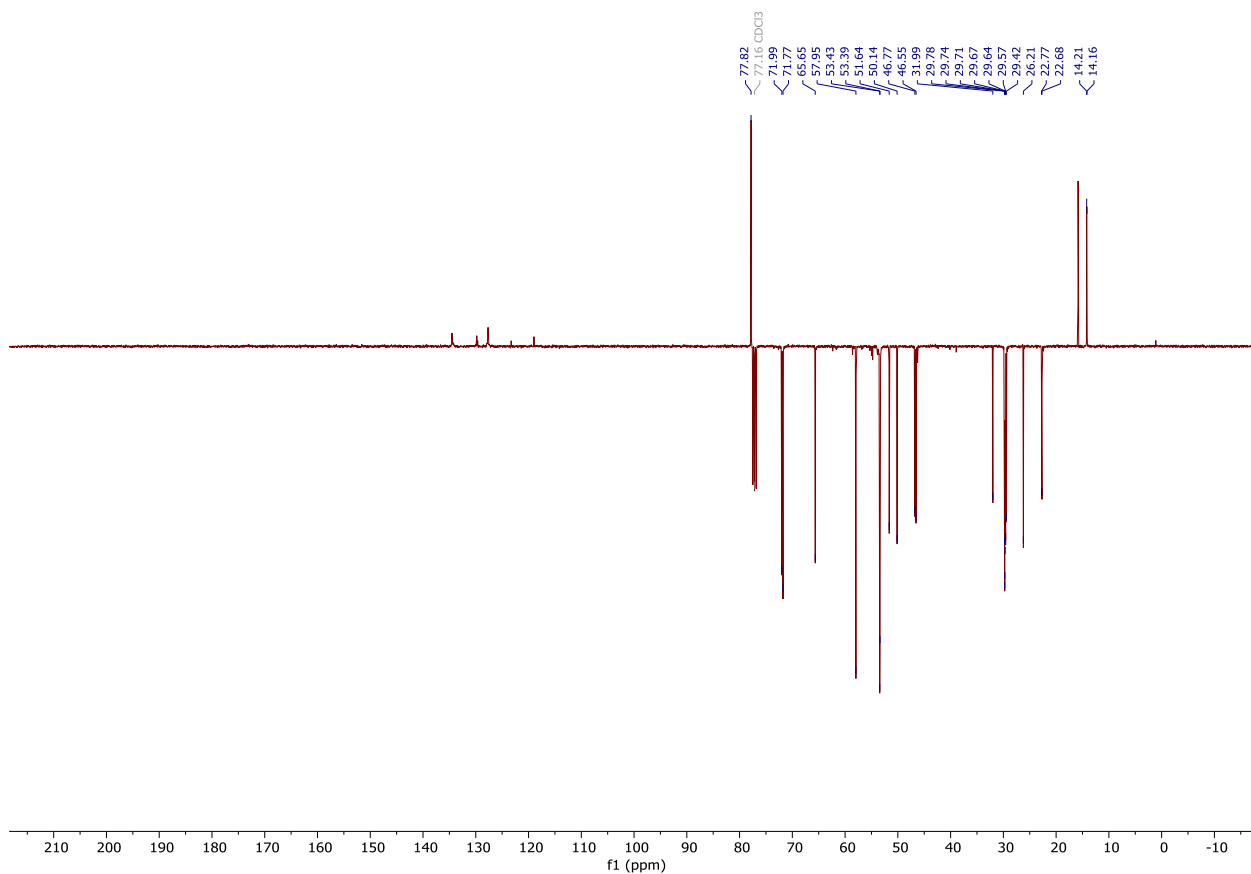


Figure S77. <sup>13</sup>C (APT) spectrum of compound **16f**.

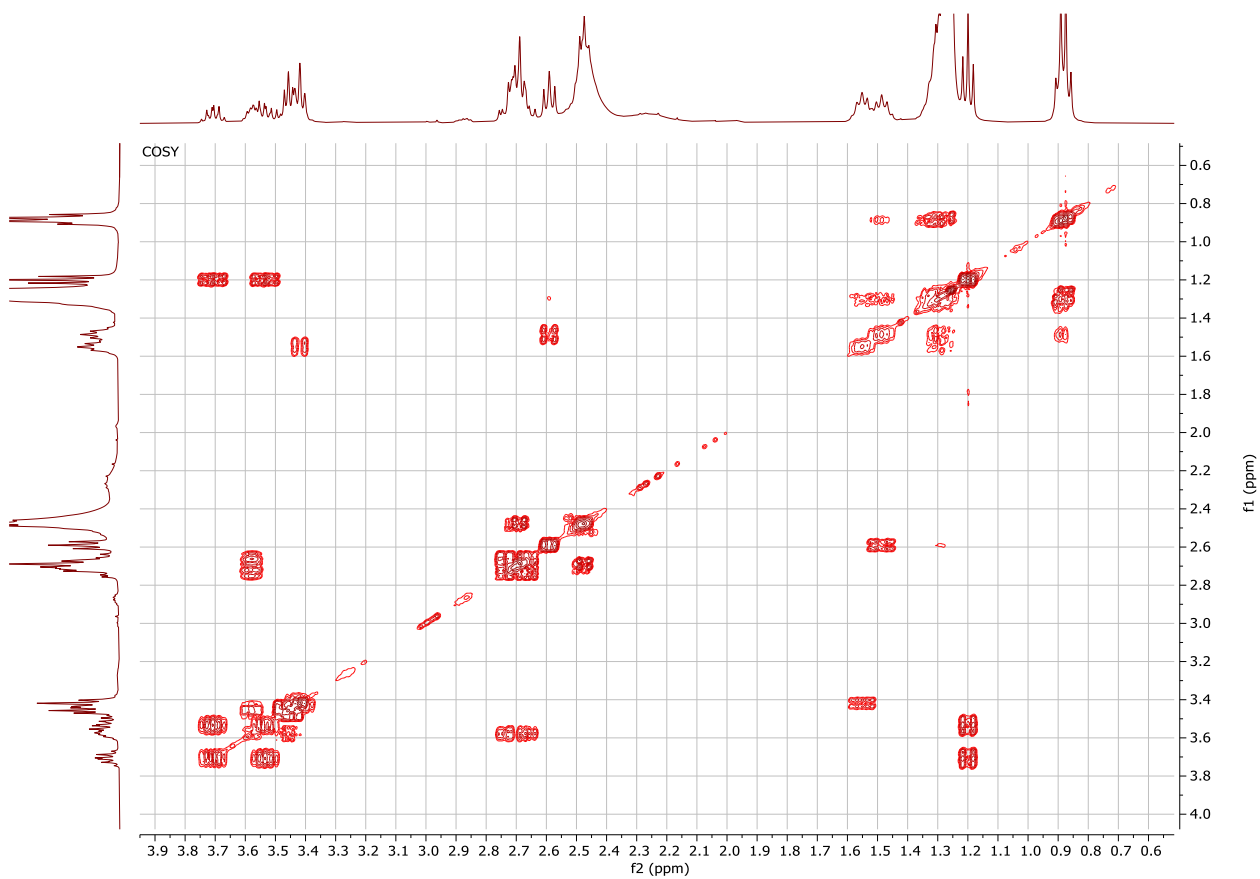


Figure S78. {<sup>1</sup>H-<sup>1</sup>H} COSY NMR spectrum of compound **16f**.

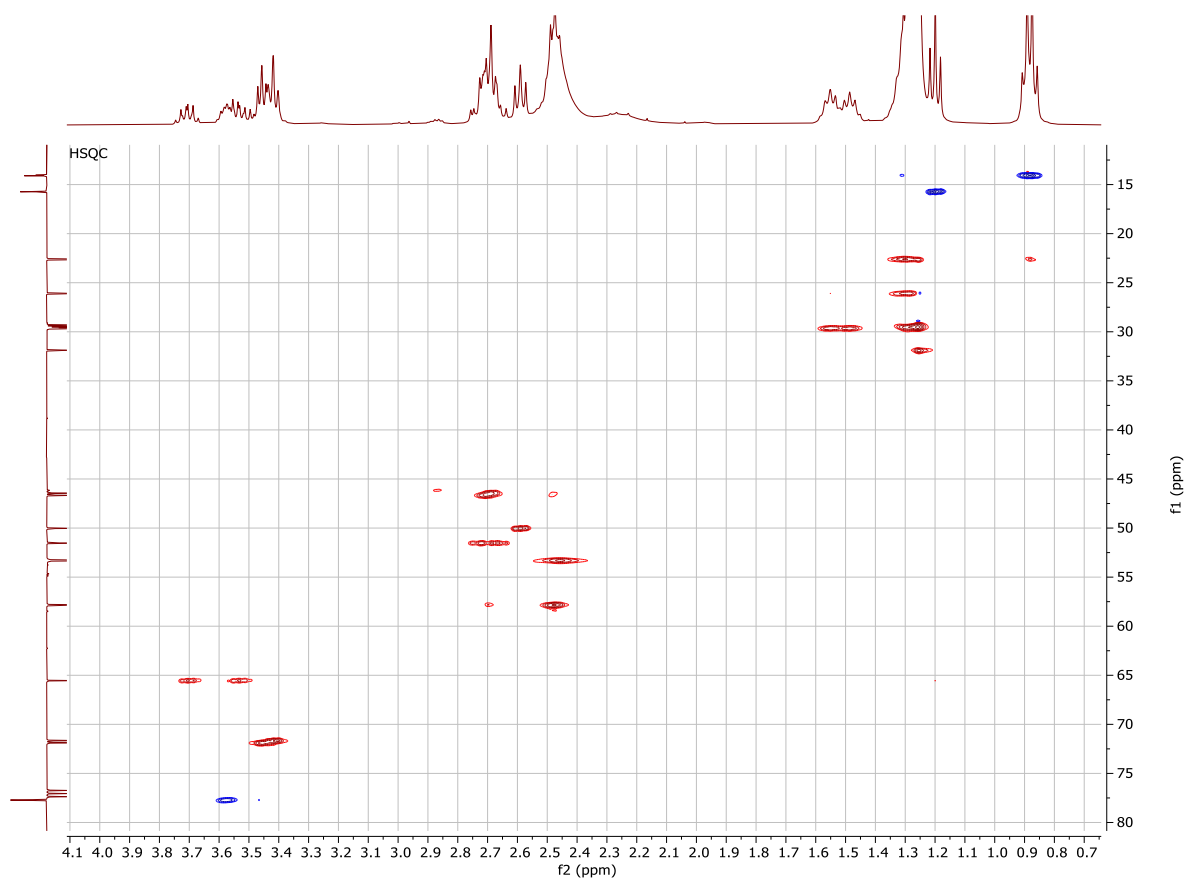


Figure S79.  $\{^1\text{H}-^{13}\text{C}\}$  HSQC NMR spectrum of compound **16f**.



$N^1$ -[( $\beta$ -D-glucopyranosyl)aminocarbonyl]methyl- $N^4$ -[( $N$ -(*rac*-1-decyloxy-2-ethyloxyprop-3-yl)aminocarbonyl)methyl]piperazin (**17**)

Yield: 89%, colorless oil. Eluent: EA-MeOH (8:2).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7.0$  Hz, 3H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.18 (t,  $J = 7.0$  Hz, 3H,  $\text{OCH}_2\text{CH}_3$ ), 1.20 – 1.33 (m, 14H,  $(\text{CH}_2)_7\text{CH}_3$ ), 1.50 – 1.58 (m, 2H,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_7$ ), 2.57 (br.s, 8H, Pip protons), 2.96 – 3.14 (m, 2H, 2  $\text{NCH}_2\text{CO}$ ), 3.14 – 3.23 (m, 1H, H-6), 3.35 – 3.63 (m, 11H, H-1, H-2, H-3, H-4, H-6,  $\text{CHOCH}_a\text{H}_b\text{CH}_3$ ,  $\text{CH}_2\text{OCH}_2$ ), 3.63 – 3.70 (m, 1H,  $\text{OCH}_a\text{H}_b\text{CH}_3$ ), 3.74 – 3.87 (m, 2H,  $\text{CH}_2$ ), 7.43 (br. t,  $J = 5.9$  Hz, 1H,  $\text{CH}_2\text{NH}$ ), 7.99 (d,  $J = 8.3$  Hz, 1H,  $\text{CHNH}$ ).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  14.23, 15.86, 22.79, 26.20, 29.44, 29.60, 29.69, 29.73, 29.75, 32.01, 40.41, 40.45, 53.30, 53.59, 61.56, 65.50, 65.53, 71.37, 71.39, 72.00, 76.80, 76.85, 77.96, 79.77, 170.44, 171.92.

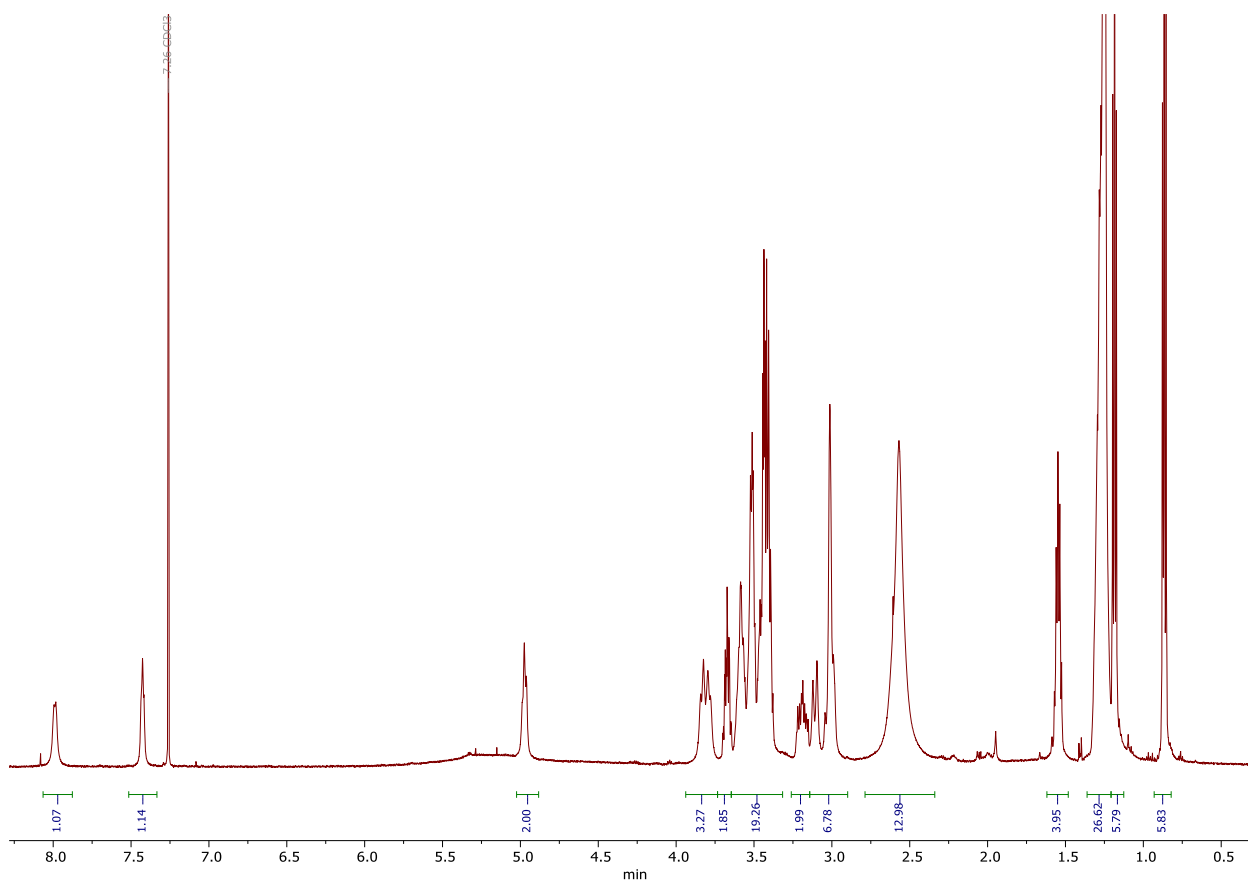


Figure S69.  $^1\text{H}$  NMR spectrum of compound **17**.

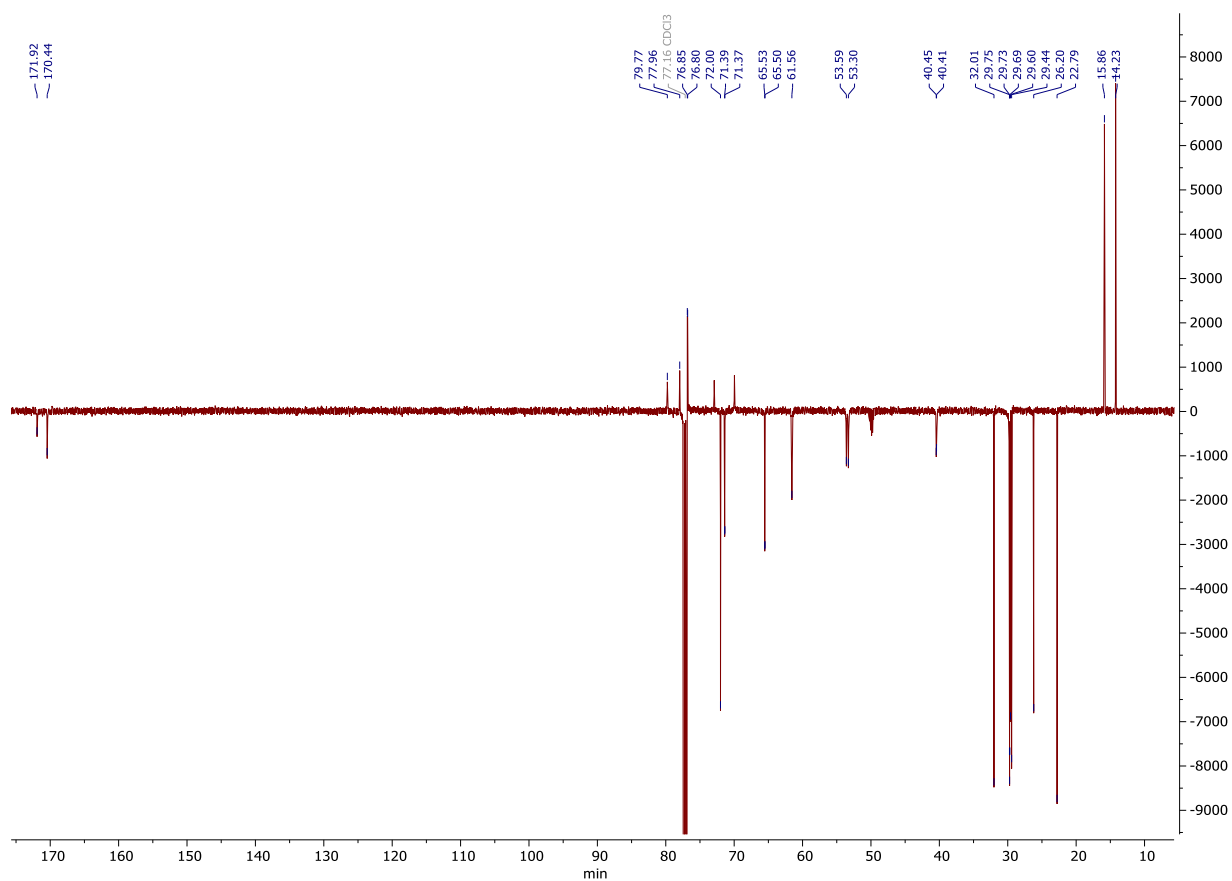


Figure S80.  $^{13}\text{C}$  (APT) NMR spectrum of compound 17.

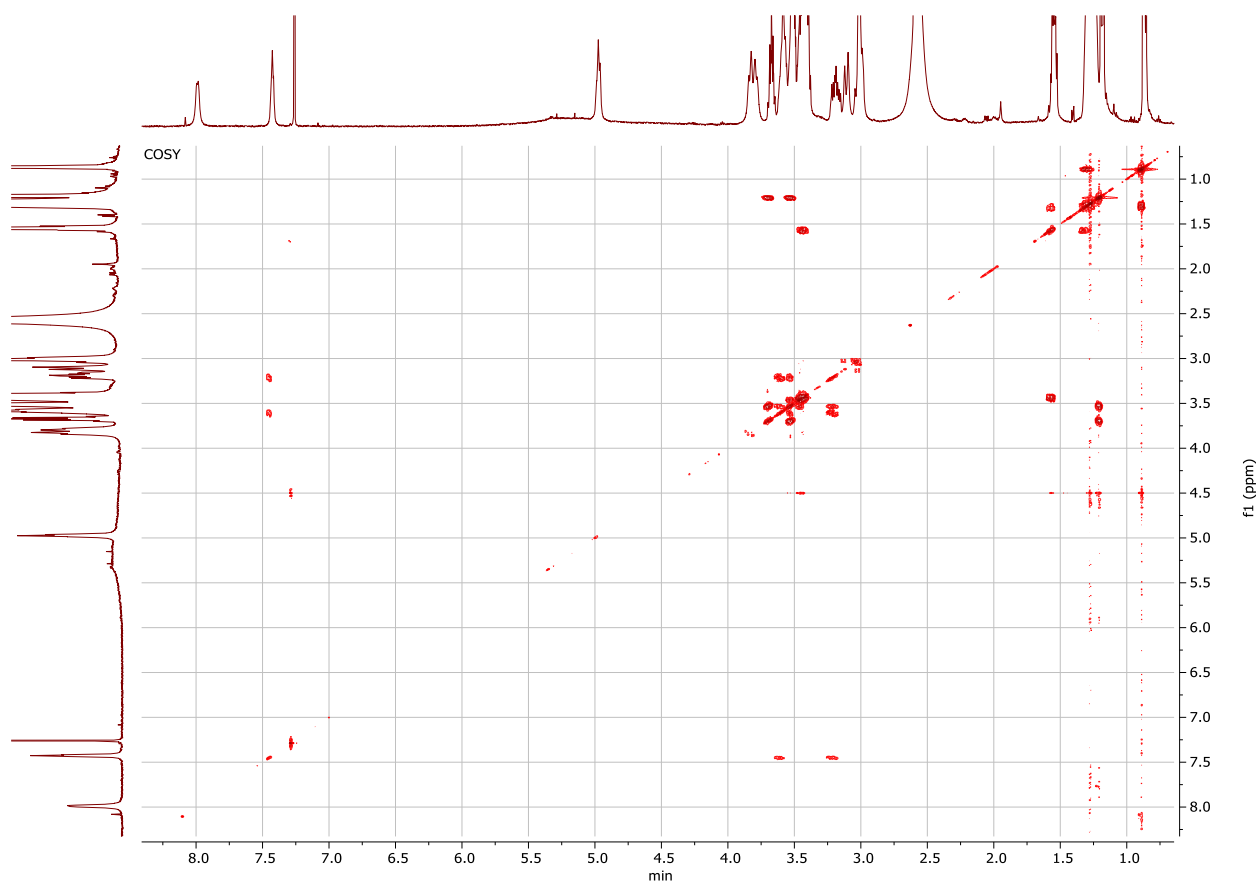


Figure S81.  $\{^1\text{H}\text{-}^1\text{H}\}$  COSY NMR spectrum of compound 17.

## Cell viability

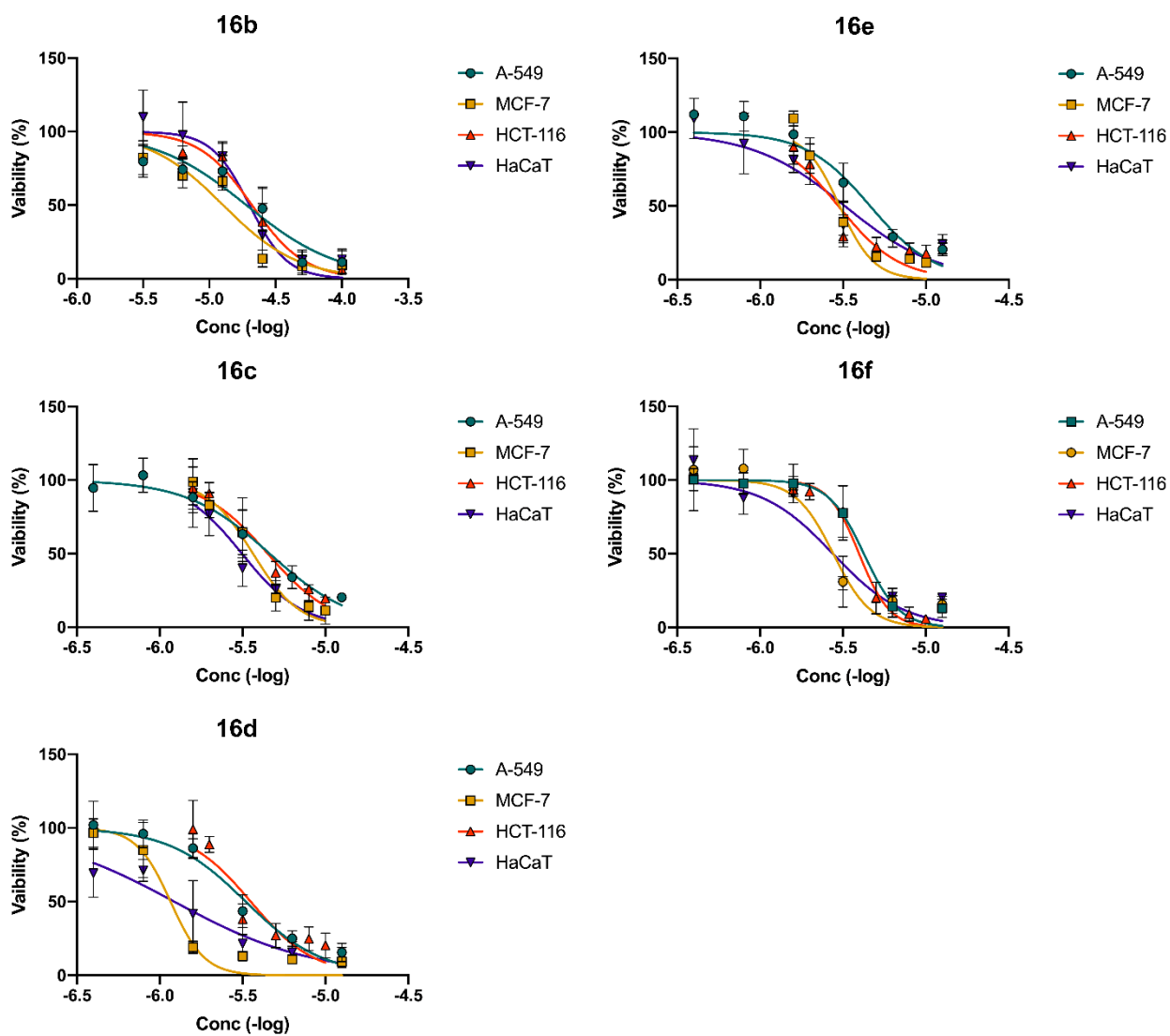


Figure S82. Cell viability of obtained compounds.