Electronic Supplementary Information (ESI)

Reduction-responsive liposomal nanocarriar with self-reporting ability for efficient gene delivery

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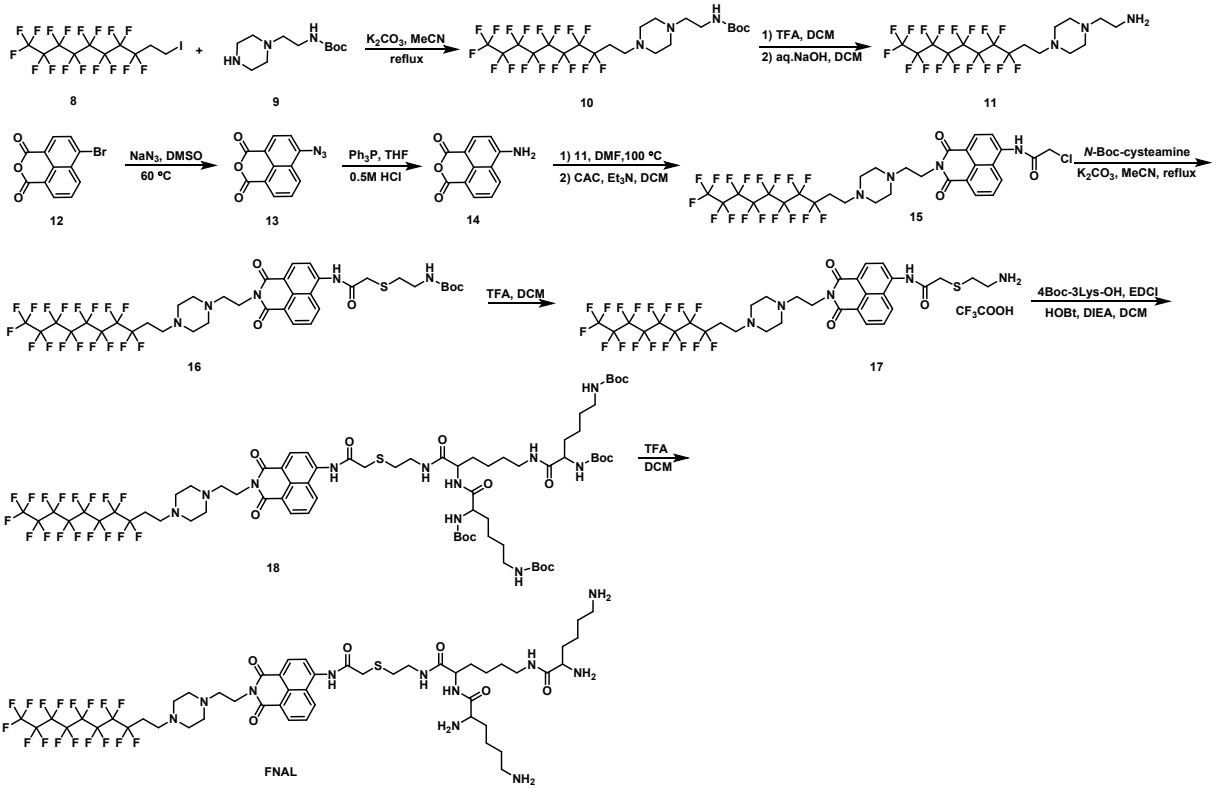
1. Synthesis of FNAL



Scheme 1S. Synthetic routes of target lipid FNAL.

*Preparation of compound **10***

The synthetic procedure is similar to compound **5**. To the solution of compound **9** (0.50 g, 2.18 mmol), K_2CO_3 (0.45 g, 3.27 mmol), and MeCN (50 mL) was added 1H,1H,2H,2H-Heptadecafluoro-1-iododecane (1.50 g, 2.62 mmol). The heterogeneous mixture was refluxed for 12 h. After filtration, the solvent was evaporated off, and residues were purified by column chromatography on silica gel (EA/DCM = 1/2 to 2/1) to yield pure compound **10** (0.72 g, 49%) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.45 (s, 9H, -Boc), 2.20-2.37 (m, 2H, -$CF_2CH_2CH_2$-), 2.38-2.60 (m, 10H, -$CH_2N(CH_2CH_2)_2NCH_2CH_2$-), 2.63-2.72 (m, 2H, -$N(CH_2CH_2)_2NCH_2CH_2$-), 3.14-3.28 (m, 2H, -$N(CH_2CH_2)_2NCH_2CH_2$-).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 28.4, 28.8, 37.1, 49.3, 52.7, 52.8, 52.9, 57.0, 79.2, 155.9.

HR-MS (ESI): Calcd for $C_{21}H_{26}F_{17}N_3O_2$ $[M+H]^+$ 676.1826, found 676.1821.

*Preparation of compound **11***

Firstly, compound **10** was deprotected the Boc group following the procedure used in preparation of compound **6**. Then, the obtained white solid (trifluoroacetate) was alkalized by aq. NaOH to free the trifluoroacetic acid. Briefly, the solid was suspended in 50 mL DCM, and then aqueous NaOH (5 equiv., NaOH/H_2O=1/2, w/w) was added. The mixture was stirred for 5 minutes and then the organic layer was separated and dried with Na_2SO_4. After filtration, the solvent was evaporated off, and the product was used directly.

*Preparation of compound **15***

To a solution of compound **14** (0.17 g, 0.78 mmol) in DMF (50 ml) was added compound **11** (0.45 g, 0.78 mmol). After the reaction mixture was reacted at 100 ºC overnight, the residue was cooled to room temperature, concentrated to afford an orange solid, which was further purified by column chromatography on silica gel (EA/DCM = 1/1, then EA/DCM/THF=1/1/0.3) to yield orange solid products (0.47 g, 78%). The obtained solid was used immediately to the next reaction. 30 mL anhydrous DCM was added to the round bottom flask with the obtained orange solid (0.24 g, 0.31 mmol), then Et_3N (86 μL, 0.62 mmol) and chloroacetyl chloride (50 μL, 0.62 mmol) was added. After the stirring at room temperature overnight, the mixture was then washed with H_2O (50 mL), saturated aqueous $NaHCO_3$ solution (50 mL) and saturated brine (50 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated to afford an orange solid, which was further purified by column chromatography on silica gel (DCM/MeOH=100/1 to 50/1) to yield compound **15** as orange solid (0.17 g, 84%).

^{1}H NMR ($CDCl_3$ and three drop CD_3OD, 400 MHz, δ): 2.21-2.34 (m, 2H, -$CF_2CH_2CH_2$-), 2.39-2.74 (m, 12H, -$CH_2N(CH_2CH_2)_2NCH_2$-), 4.30 (t, 2H, *J*= 6.8 Hz, -$N(CH_2CH_2)_2NCH_2CH_2$-), 4.35 (s, 2H, -CH_2Cl), 7.79 (t, 1H, *J*=8.4 Hz, Ar-H), 8.20-8.38 (m, 2H, Ar-H), 8.53-8.61 (m, 2H, Ar-H).

HR-MS (ESI): Calcd for $C_{30}H_{24}ClF_{17}N_4O_3$ $[M+H]^+$ 847.1338, found 847.1340.

*Preparation of compound **16***

To the solution of compound **15** (0.16 g, 0.19 mmol), K_2CO_3 (0.05 g, 0.38 mmol), and MeCN (20 mL) was added *N*-Boc-cysteamine (0.07 g, 0.38 mmol). The heterogeneous mixture was refluxed for 12 h. After filtration, the solvent was evaporated off, and residues were purified by column chromatography on silica gel (EA/DCM = 1/4 to 1/1) to yield pure compound **16** (0.16 g, 85%) as orange solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.37 (s, 9H, -Boc), 2.18-2.37 (m, 2H, -$CF_2CH_2CH_2$-), 2.39-2.74 (m, 12H, -$CH_2N(CH_2CH_2)_2NCH_2$-), 2.85 (t, 2H, -SCH_2CH_2NH-), 3.37-3.47 (m, 2H, -SCH_2CH_2NH-), 4.35 (s, 2H, -CH_2S-), 4.33 (t, 2H, *J*= 6.8 Hz, -$N(CH_2CH_2)_2NCH_2CH_2$-), 7.81 (t, 1H, *J*=8.0 Hz, Ar-H), 8.20-8.48 (m, 2H, Ar-H), 8.58-8.64 (m, 2H, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 23.4, 23.6, 24.0, 28.6, 32.2, 34.8, 44.4, 44.5, 48.3, 48.4, 50.7, 75.3, 114.1, 118.5, 119.2, 121.8, 122.1, 124.1, 126.5, 127.5, 133.5, 158.8, 159.3, 162.6.

HR-MS (ESI): Calcd for $C_{37}H_{38}F_{17}N_5O_5S$ $[M+H]^+$ 988.2395, found 988.2401.

*Preparation of compound **17***

Compound **16** was deprotected the Boc group following the procedure used in preparation of compound **6**, and the obtained compound **17** was used directly.

*Preparation of compound **18***

Compound **17** (0.20 g, 0.16 mmol) was added to the anhydrous DCM solution (50mL) of 4Boc-3Lys-OH (0.19 g, 0.24 mmol), EDCI (0.05 g, 0.24 mmol), HOBt (0.04 g, 0.24 mmol) and DIEA (0.08 g, 0.64 mmol) after activation in ice-salt-bath for 1 h and then the reaction mixture was stirred at room temperature overnight. The mixture was then washed with saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and saturated brine (50 mL).The organic phase was dried over Na_2SO_4, filtered, and concentrated to afford an oil solid, which was further purified by column chromatography on silica gel (DCM/MeOH=100/1 to 20/1) to yield compound **18** as yellowish solid (0.18 g, 45%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.17-1.53 (m, 42H, -Boc, -$NHCH_2CH_2CH_2CH_2CH$-), 1.54-2.04 (m, 12H, -$NHCH_2CH_2CH_2CH$-), 2.20-2.38 (m, 2H, -$CF_2CH_2CH_2$-), 2.51 (s, 4H, -$N(CH_2CH_2)_2NCH_2CH_2$-), 2.59-2.79 (m, 8H, -SCH_2CH_2NH-, -$CH_2N(CH_2CH_2)_2NCH_2CH_2$-), 2.82-2.90 (m, 2H, -$CH_2N(CH_2CH_2)_2NCH_2CH_2$-) 2.95-3.17 (m, 6H, -$NHCH_2CH_2CH_2CH_2CH$-), 3.41-3.71 (m, 4H, -$CH_2S$-, -$SCH_2CH_2NH$-), 3.95-4.37 (m, 5H, -$N(CH_2CH_2)_2NCH_2CH_2N$-, -*CH*(NH)CO-), 7.73-7.81 (m, 1H, Ar-H), 8.36-8.63 (m, 4H, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 22.6, 28.3, 28.4, 28.8, 29.0, 29.7, 37.3, 49.2, 52.9, 53.0, 55.5, 79.3, 80.0, 118.7, 123.0, 126.6, 128.9, 131.2, 132.2, 156.3, 163.6, 164.2.

^{19}F NMR ($CDCl_3$, 376 Hz, δ): -80.7 (t, 3F, CF_3-), -114.0 (m, 2F, -CF_2-), -121.8 (m, 6F, -$(CF_2)_3$-), -122.7 (m, 2F, -CF_2-), -123.4 (m, 2F, -CF_2-), 126.1(m, 2F, -CF_2-).

HR-MS (ESI): Calcd for $C_{70}H_{96}F_{17}N_{11}O_{14}S$ $[M+H+Na]^{2+}$ 847.8354, found 847.8355.

Preparation of target lipid FNAL

The final lipid FNAL were synthesized by Boc deprotection procedure described in preparation of compound **6** with yield of 95%.

^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.31-1.94 (m, 18H, -NHCH$_2$C*H*$_2$C*H*$_2$C*H*$_2$CH-), 2.40-2.55 (m, 2H, -CF$_2$C*H*$_2$CH$_2$-), 2.78-3.02 (m, 10H, -SC*H*$_2$CH$_2$NH-, -N(C*H*$_2$C*H*$_2$)$_2$N-), 3.12-3.30 (m, 2H, -CH$_2$C*H*$_2$N(CH$_2$CH$_2$)$_2$N-), 3.33-3.53 (m, 6H, -SCH$_2$C*H*$_2$NH-, -N(CH$_2$CH$_2$)$_2$NC*H*$_2$CH$_2$-, NHC*H*$_2$CH$_2$CH$_2$CH$_2$CH-), 3.60 (s, 2H, -C*H*$_2$S-), 3.77-3.95 (m, 4H, 2(NH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$CH-)$_2$), 4.03-4.11 (-*CH*(NH)CO-), 4.20-4.30 (m, 2H, -*CH*(NH$_2$)CO-), 4.50 (t, 2H, *J*=5.6 Hz, -N(CH$_2$CH$_2$)$_2$NCH$_2$C*H*$_2$N-), 7.84 (t, 1H, *J*=7.6 Hz, Ar-H), 8.19-8.37 (m, 1H, Ar-H), 8.51-8.63 (m, 3H, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 21.5, 26.5, 26.7, 28.5, 30.5, 30.7, 34.8, 38.8, 49.6, 51.8, 52.8, 54.8, 114.9, 117.8, 118.6, 120.6, 120.7, 122.4, 126.5, 128.8, 128.9, 131.3, 131.6, 139.9, 168.5, 170.5, 172.6.

^{19}F NMR ($CDCl_3$, 376 Hz, δ): -82.3 (t, 3F, C*F*$_3$-), -114.8 (m, 2F, -C*F*$_2$-), -121.8 (m, 6F, -(C*F*$_2$)$_3$-), -123.7 (m, 2F, -C*F*$_2$-), -124.3 (m, 2F, -C*F*$_2$-), 127.2(m, 2F, -C*F*$_2$-).

HR-MS (ESI): Calcd for $C_{50}H_{68}F_{17}N_{11}O_7S$ $[M+2H]^{2+}$ 636.7396, found 636.7395.

2. Supplementary figures

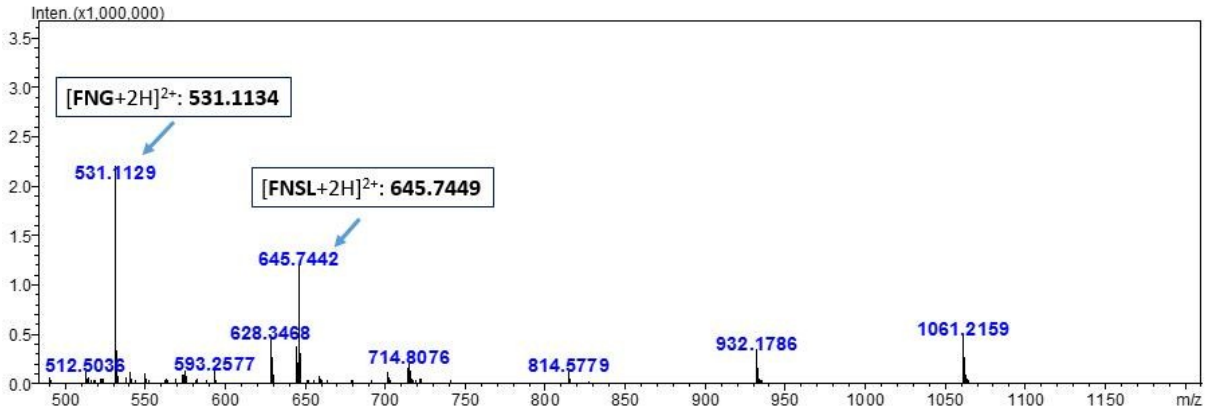


Fig. S1 ESI Mass spectrometry of FNSL incubated with GSH (10 mM) after 12 h.

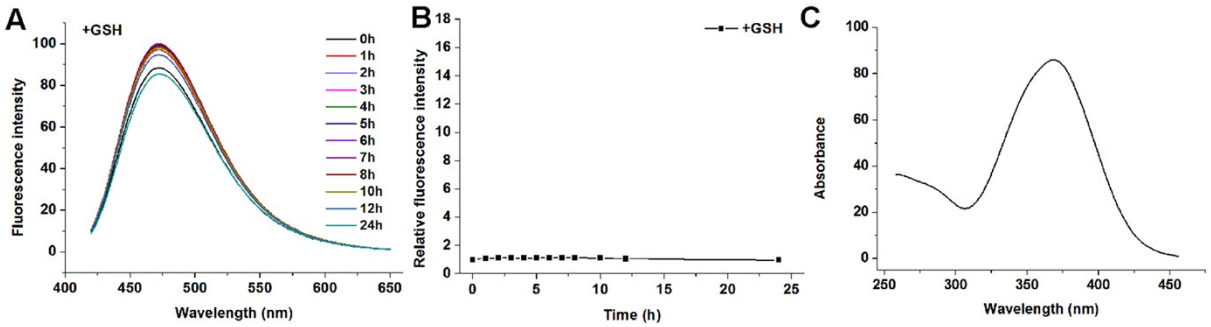


Fig. S2 Time-dependent fluorescent spectra of FNAL liposome (20 μM) with 5 mM GSH (A); The relative fluorescence intensity of FNAL liposome at 470 nm with GSH (λ_{ex} = 370 nm) (B); The absorption spectra of FNAL (20 μM) in the presence of 5 mM GSH at 12 h (C).

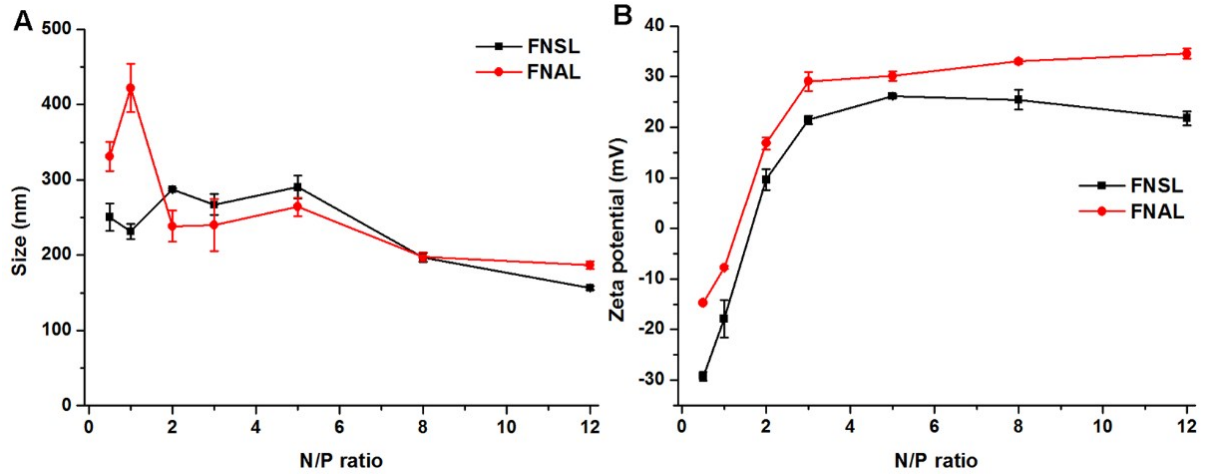


Fig. S3 Particle sizes (A) and zeta-potentials (B) of lipoplexes obtained at various N/P ratios in 10 mM of Hepes solution (pH = 7.4) by dynamic light scattering (DLS). Data represent mean ± SD (n = 3).

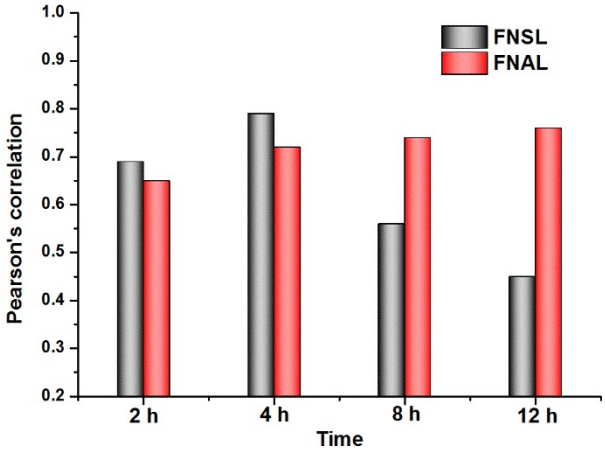


Fig. S4 The colocalization analysis for Fig. 6.

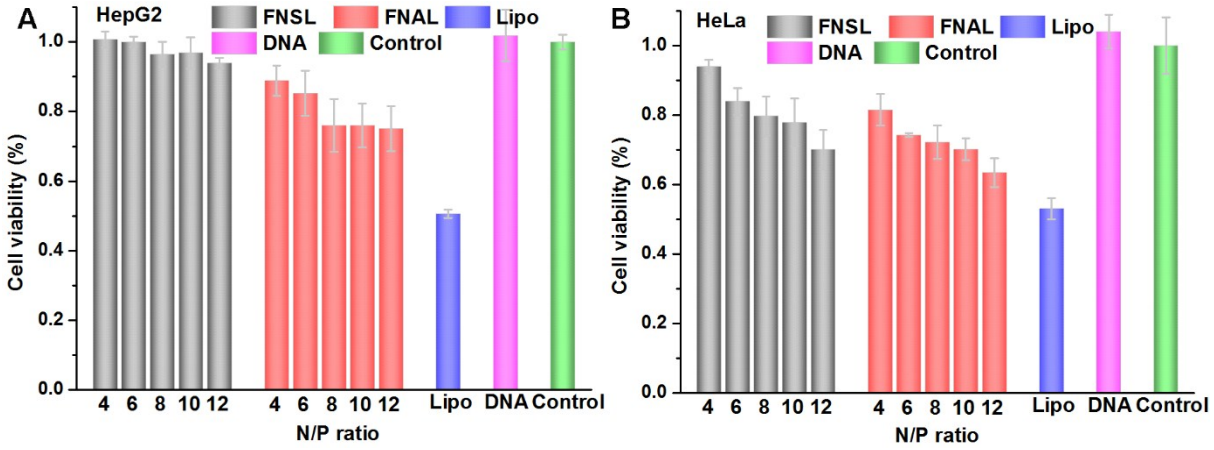


Fig. S5 Cytotoxicity of lipoplexes at various N/P ratios against HepG2 (A) and HeLa cells (B). The percentage of cell viability was expressed relative to blank control cells. Lipo and naked DNA were used as controls.

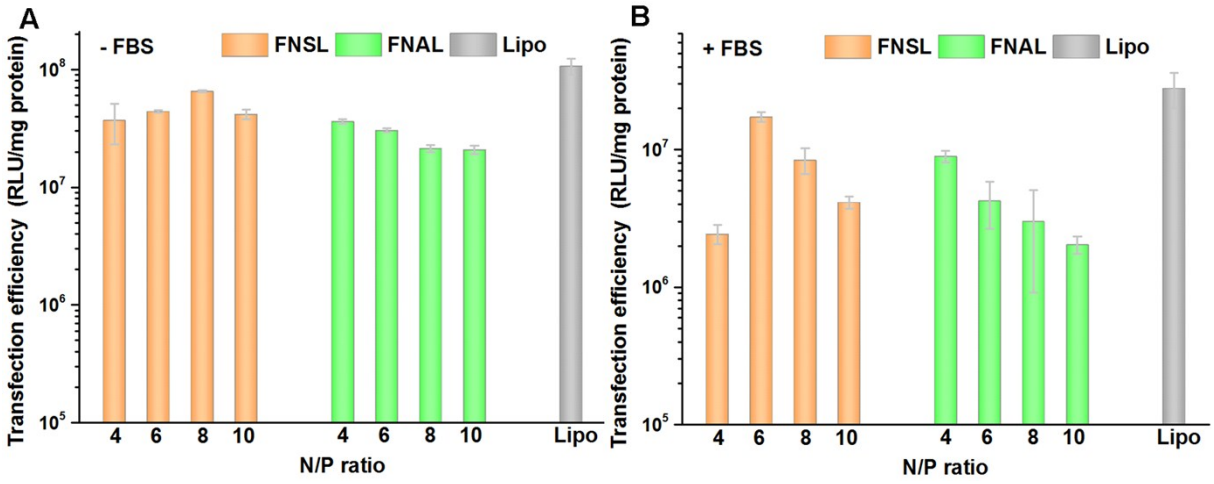


Fig. S6 Luciferase expression induced by lipoplexes at various N/P ratios in HeLa cells without (A) or with (B) 10% serum. Lipo 2000 was used as control.

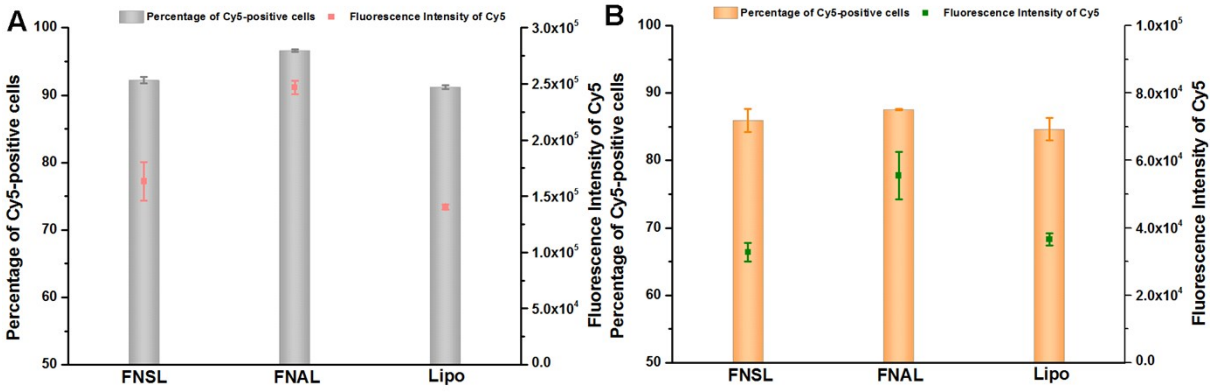


Fig. S7 Cellular uptake of lipoplexes (N/P = 8) in HepG2 (A) and HeLa cells (B) quantified by flow cytometry. Data represent mean ± SD (n = 3).

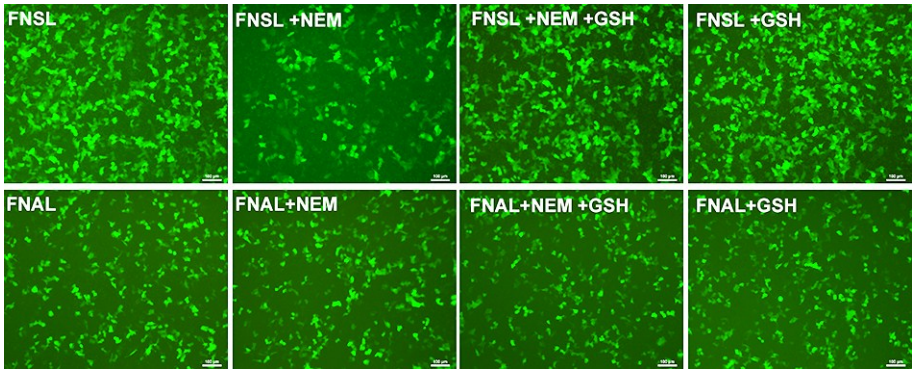


Fig. S8 Fluorescence microscopy images of eGFP expression HepG2 cells (N/P = 10) in the treatment of exogenous NEM (1 mM) or GSH (5 mM) without serum.

3. Analysis data of intermediate compounds

3: ^{1}H NMR (DMSO-d6, 400 MHz, δ): 1.17-1.40 (m, 13H, -Boc, -$SO_2NHCH_2CH_2CH_2CH_2$-), 2.65-2.92 (m, 4H, -$SO_2NHCH_2CH_2CH_2CH_2$-), 6.70-6.73 (t, 1H, *J*=5.2 Hz, Ar-H), 8.06-8.10 (t, 1H, *J*=8.4 Hz, Ar-H), 8.37-8.42 (m, 2H, Ar-H), 8.60-8.63 (m, 2H, Ar-H, -SO_2NH-), 9.09-9.11 (d, 1H, *J*=8.4 Hz, Ar-H).

^{13}C NMR (DMSO-d6, 100 MHz, δ): 27.0, 28.7, 42.7, 77.8, 120.6, 123.8, 126.7, 128.9, 129.3, 131.1, 131.4, 132.2, 133.0, 142.4, 155.9, 160.3, 160.7.

HR-MS (ESI): Calcd for $C_{21}H_{24}N_2O_7S$ $[M+Na]^+$471.1196, found 471.1206.

4: ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.41-1.51 (m, 13H, -$SO_2NHCH_2CH_2CH_2CH_2$-, -Boc), 2.57 (s, 4H, $HN(CH_2CH_2)_2CH_2CH_2$-), 2.69 (t, 2H, *J*=6.8 Hz, $HN(CH_2CH_2)_2NCH_2CH_2$-), 2.87 (s, 4H, $HN(CH_2CH_2)_2NCH_2CH_2$-), 2.96-3.10 (m, 4H, -$SO_2NHCH_2CH_2CH_2CH_2$-), 4.33 (t, 2H,

J=6.8 Hz, HN(CH_2CH_2)$_2$NCH_2CH_2-), 7.87-7.91 (t, 1H, *J*=8.0 Hz, Ar-H), 8.40-8.42 (d, 1H, *J*=7.6 Hz, Ar-H), 8.61-8.67 (m, 2H, Ar-H), 9.06-9.08 (d, 1H, *J*=8.8 Hz, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 26.2, 27.5, 28.4, 37.5, 39.5, 43.0, 45.9, 54.4, 56.1, 79.6, 123.1, 126.5, 126.9, 128.7, 128.8, 129.0, 129.5, 131.0, 131.7, 140.9, 156.4, 163.0, 163.5.

HR-MS (ESI): Calcd for $C_{27}H_{37}N_5O_6S$ $[M+H]^+$560.2537, found 560.2544

5: ^{1}H NMR ($CDCl_3$, 400 MHz, δ) 1.42-1.51 (m, 13H, -$SO_2NHCH_2CH_2CH_2CH_2$-, -Boc), 2.20-2.37 (m, 2H, -$CF_2CH_2CH_2$-), 2.49 (s, 4H, -N(CH_2CH_2)$_2$NCH_2CH_2-), 2.58-2.75 (m, 8H, -CH_2N(CH_2CH_2)$_2$NCH_2CH_2-), 2.98-3.10 (m, 4H, -$SO_2NHCH_2CH_2CH_2CH_2$-), 4.34 (t, 2H, *J*=6.8 Hz, -N(CH_2CH_2)$_2$NCH_2CH_2N-), 7.88-7.92 (m, 1H, Ar-H), 8.42-8.44 (d, 1H, *J*=8.0 Hz, Ar-H), 8.62-8.69 (m, 2H, Ar-H), 9.06-9.08 (d, 1H, *J*=8.4 Hz, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ): 26.1, 27.6, 28.3, 28.6, 28.8, 29.0, 37.3, 39.5, 43.1, 49.3, 53.0, 53.1, 55.4, 79.6, 123.2, 126.6, 126.9, 128.8, 128.9, 129.1, 129.5, 131.0, 131.7, 140.8, 156.4, 163.0, 163.5.

HR-MS (ESI): Calcd for $C_{37}H_{40}F_{17}N_5O_6S$ $[M+H]^+$1006.2501, found 1006.2506.

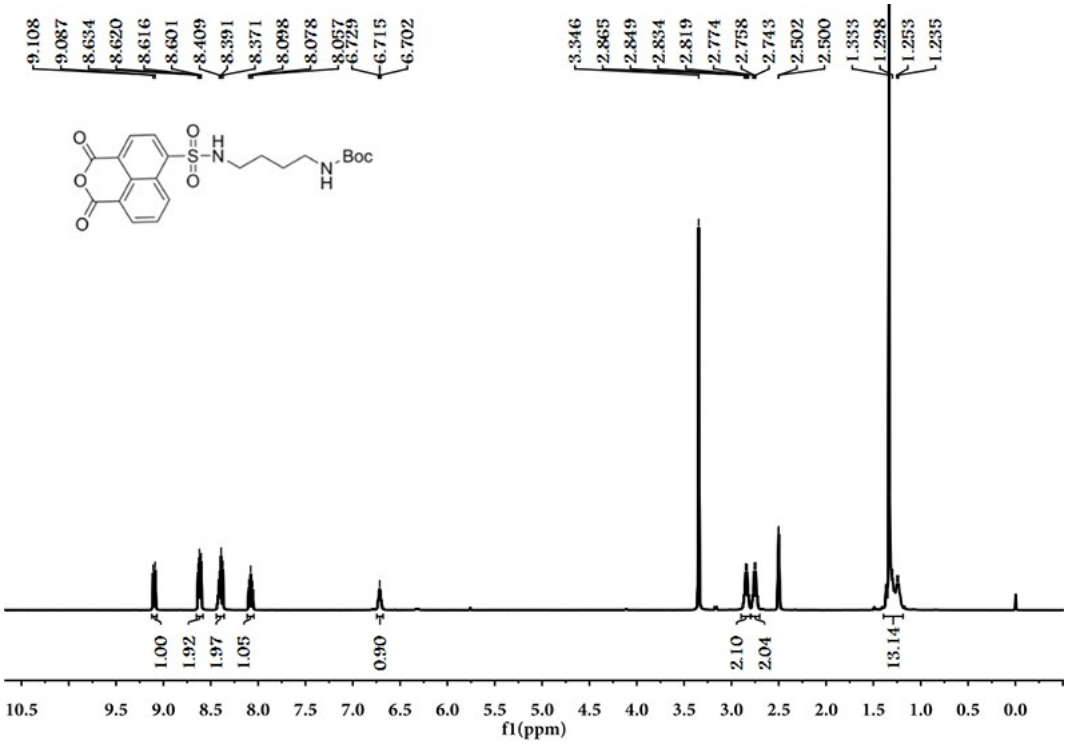
7: ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.25-1.60 (m, 46H, -$SO_2NHCH_2CH_2CH_2CH_2$-, -Boc, -$NHCH_2CH_2CH_2CH_2CH$-), 1.62-1.95 (m, 12H, -$NHCH_2CH_2CH_2CH_2CH$-), 2.19-2.33 (m, 2H, -$CF_2CH_2CH_2$-), 2.49 (s, 4H, -N(CH_2CH_2)$_2$NCH_2CH_2-), 2.57-2.84 (m, 6H, -CH_2N(CH_2CH_2)$_2$NCH_2CH_2-), 2.87-3.36 (m, 10H, -$SO_2NHCH_2CH_2CH_2CH_2$-, -$NHCH_2CH_2CH_2CH_2CH$-), 3.99-4.36 (m, 5H, -N(CH_2CH_2)$_2$NCH_2CH_2N-, -*CH*(NH)CO-), 7.83-7.90 (m, 1H, Ar-H), 8.38-8.44 (m, 1H, Ar-H), 8.60-8.69 (m, 2H, Ar-H), 9.15 (d, 2H, *J*=8.4 Hz, Ar-H).

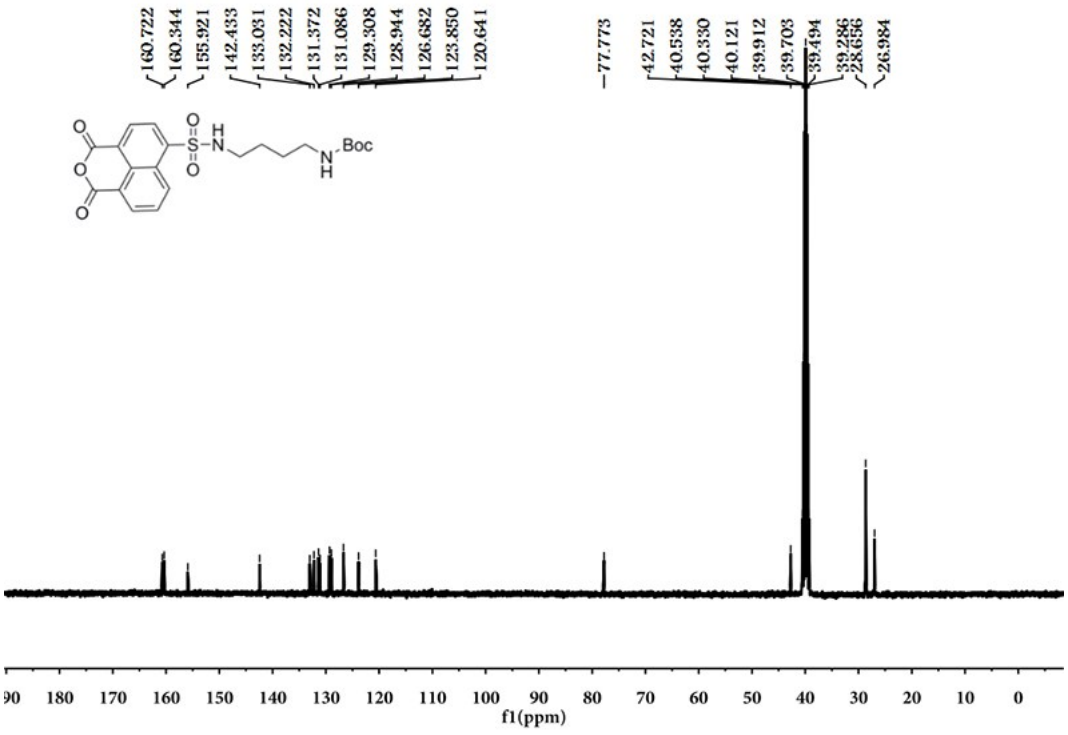
^{13}C NMR ($CDCl_3$, 100 MHz, δ): 22.6, 28.3, 28.4, 28.8, 37.6, 38.4, 39.7, 39.9, 42.9, 49.2, 53.0, 53.1, 55.4, 77.2, 79.2, 123.0, 123.1, 126.3, 127.0, 127.1, 128.6, 128.7, 129.0, 129.6, 131.7, 141.1, 141.3, 156.2, 163.1, 163.6, 163.7.

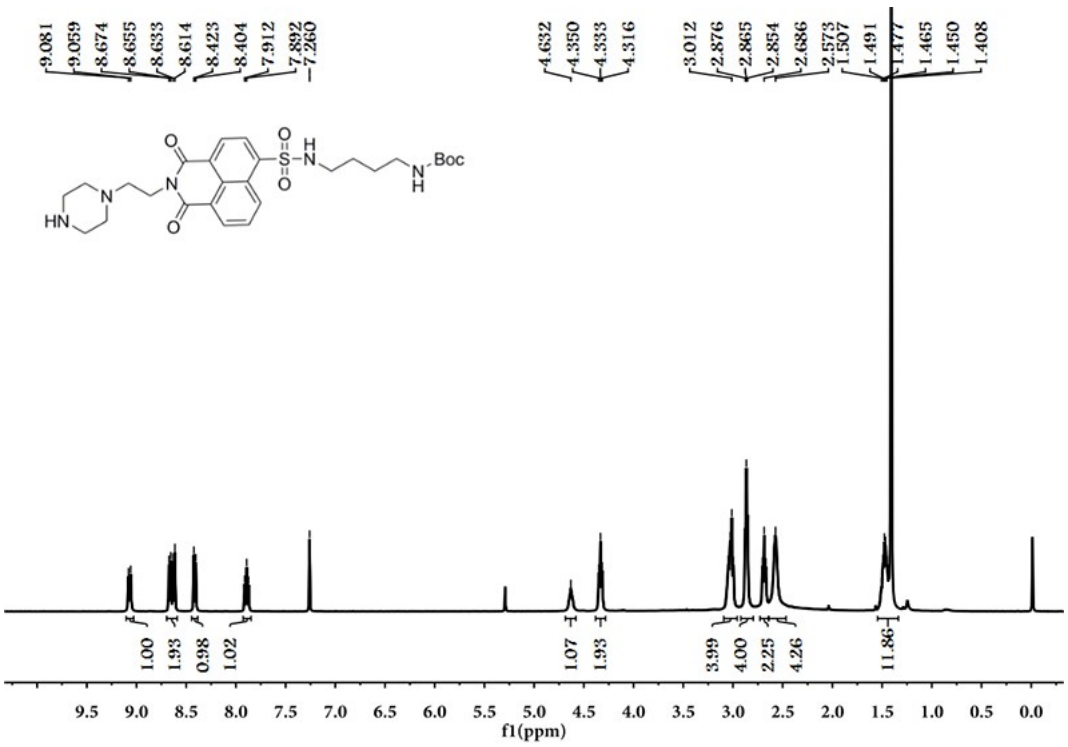
^{19}F NMR ($CDCl_3$, 376 Hz, δ): -80.8 (t, 3F, CF_3-), -114.0 (m, 2F, -CF_2-), -121.8 (m, 6F, -(CF_2)$_3$-), -122.7 (m, 2F, -CF_2-), -123.5 (m, 2F, -CF_2-), 126.1(m, 2F, -CF_2-).

HR-MS (ESI): Calcd for $C_{70}H_{100}F_{17}N_{11}O_{15}S$ $[M+H+Na]^{2+}$ 856.8407, found 856.8412.

4. NMR spectra



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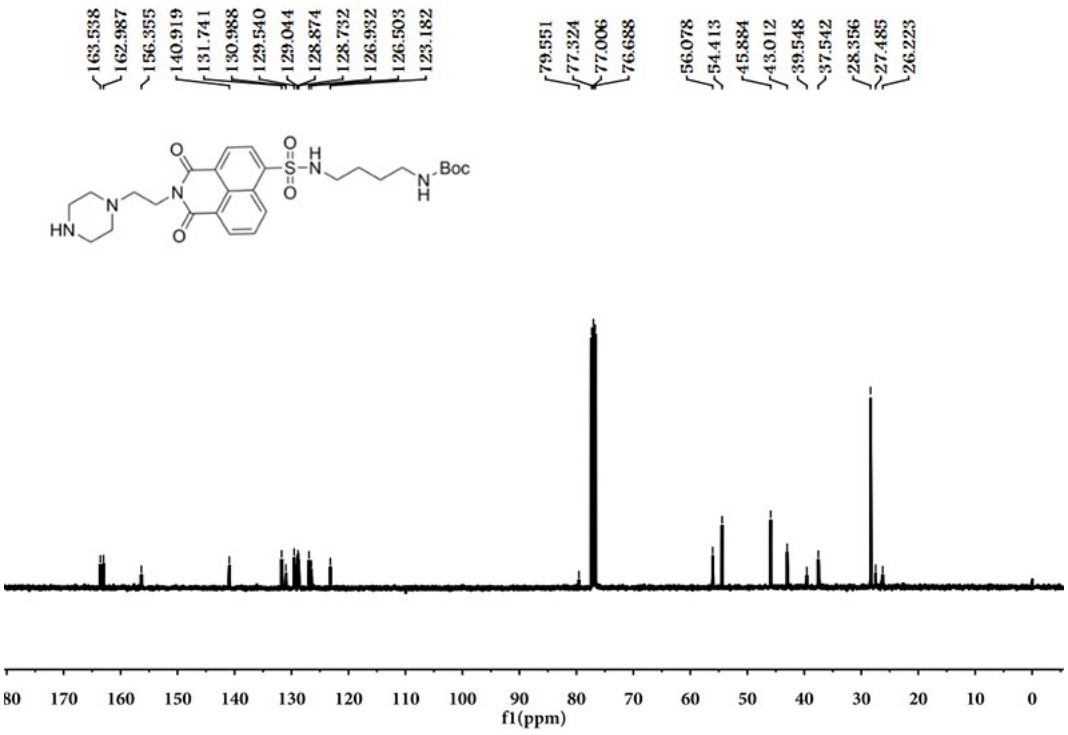
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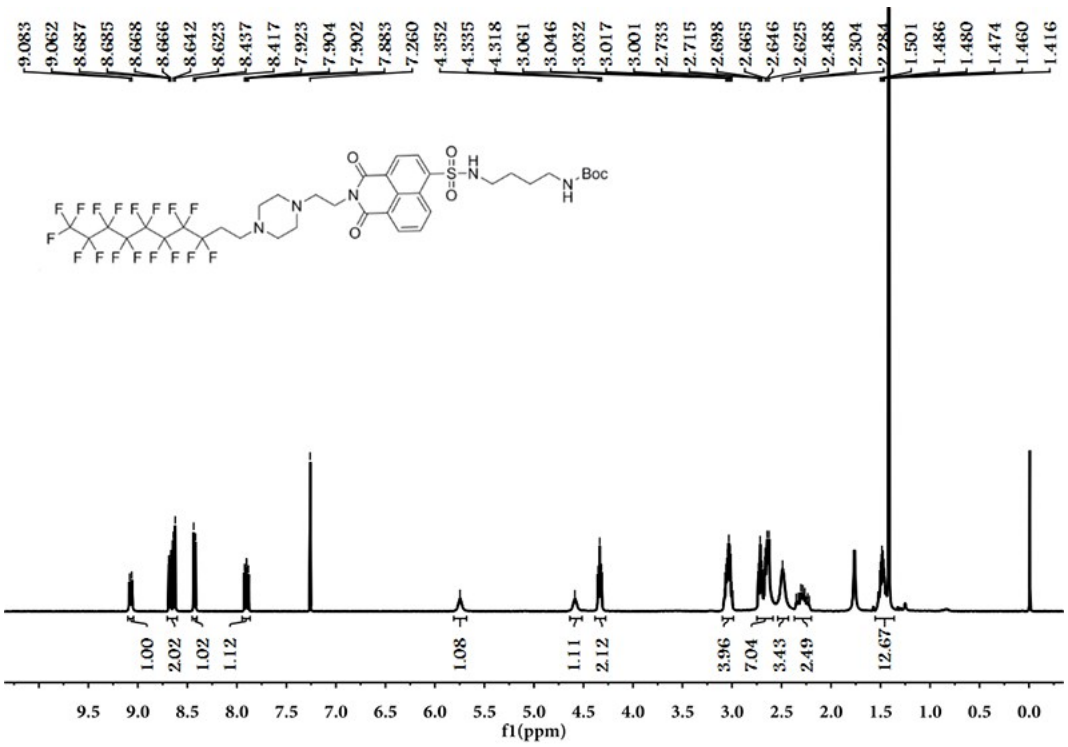
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8.623
8.437
8.417
7.923
7.904
7.902
7.883
7.260
4.352
4.335
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3.046
3.032
3.017
3.001
2.733
2.715
2.698
2.665
2.646
2.625
2.488
2.304
2.284
1.501
1.486
1.480
1.474
1.460
1.416
Boc
1.00
2.02
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1.08
1.11
2.12
3.96
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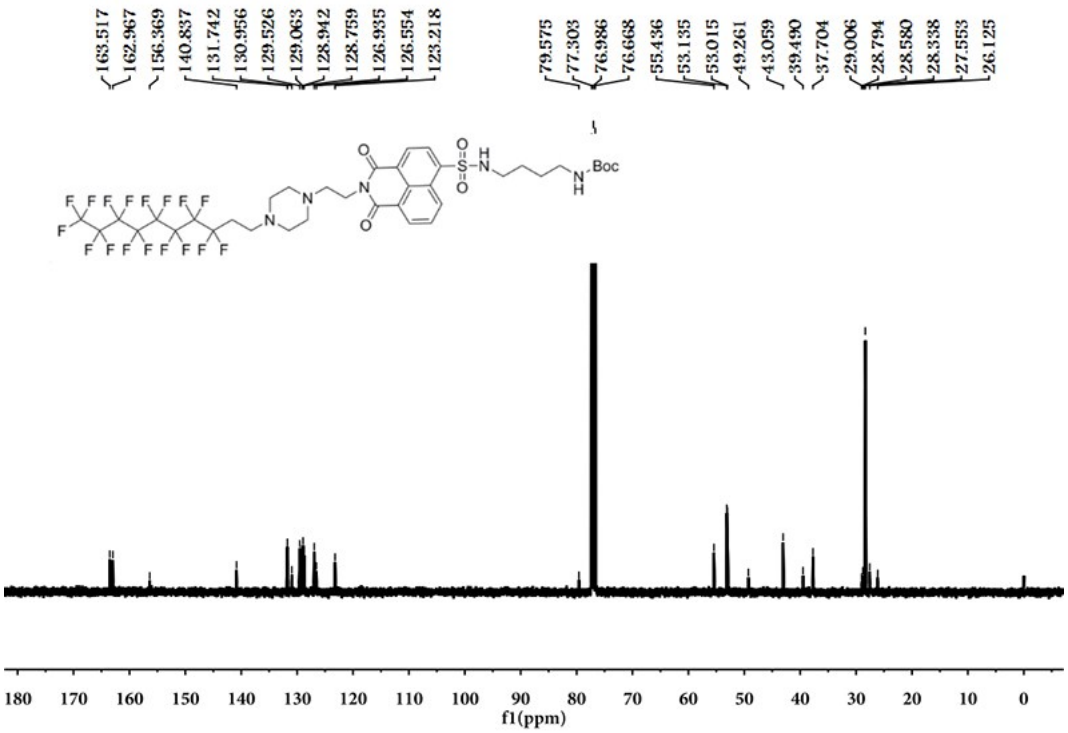
3.43
2.49
12.67
f1(ppm)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123.218
79.575
77.303
76.986
76.668
55.436
53.135
53.015
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28.794
28.580
28.338
27.553
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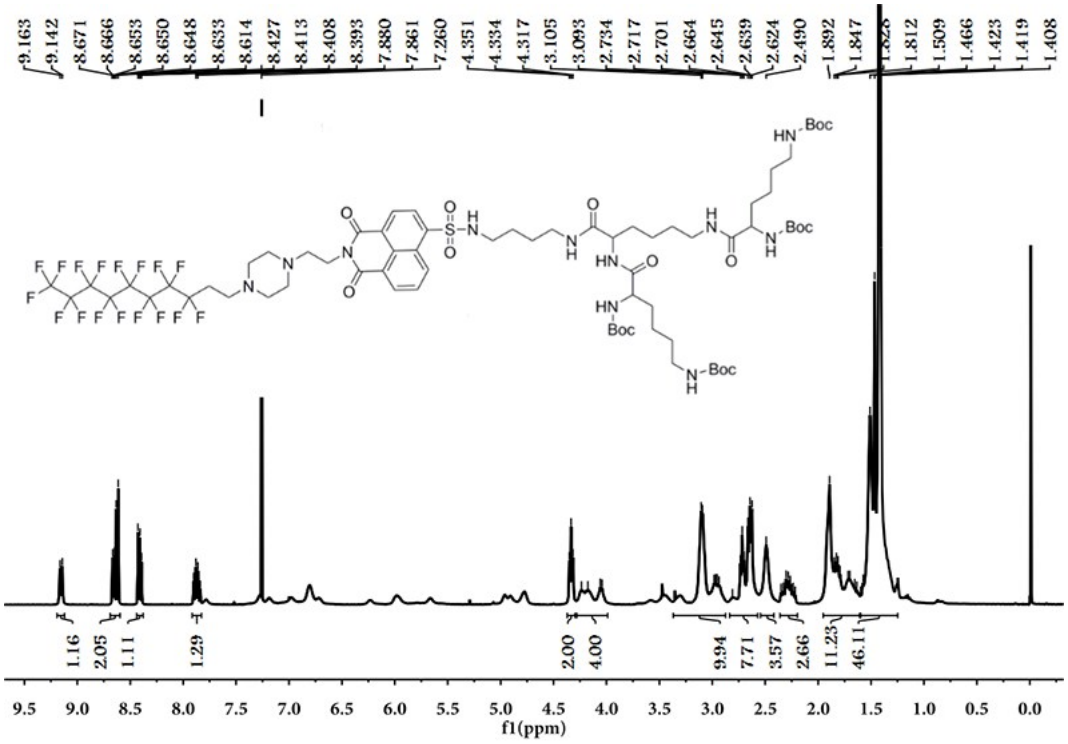
Boc
f1(ppm)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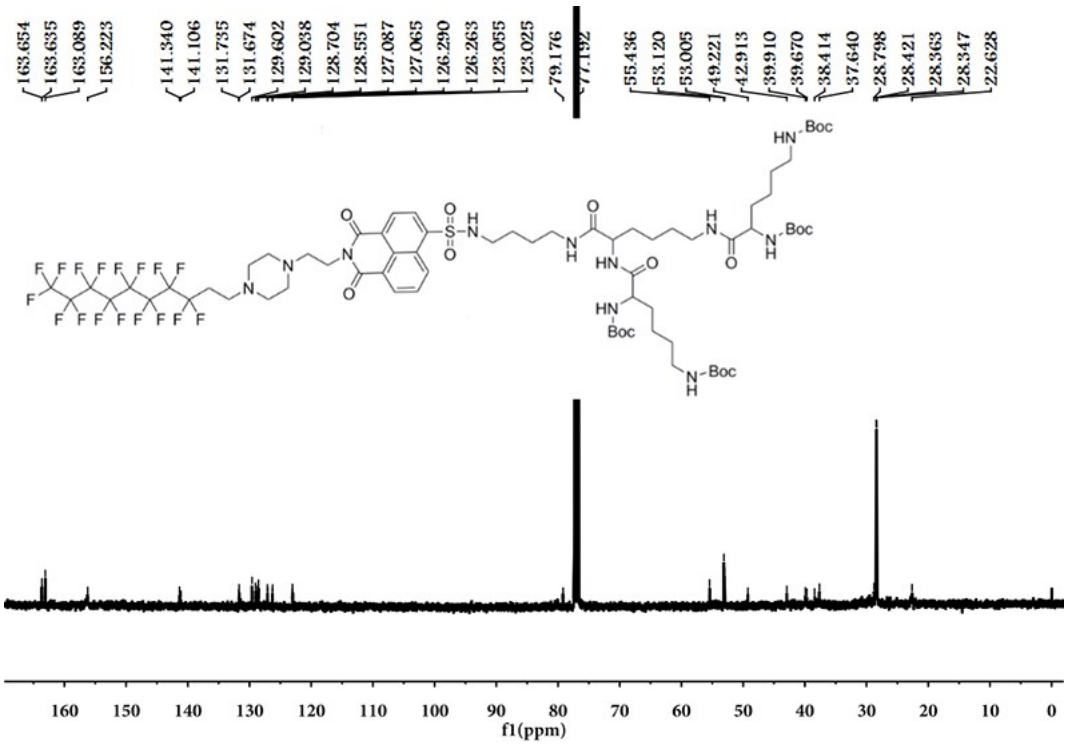
7.880
7.861
7.260
4.351
4.334
4.317
3.105
3.093
2.734
2.717
2.701
2.664
2.645
2.639
2.624
2.490
1.892
1.847
1.812
1.509
1.466
1.423
1.419
1.408
1.16
2.05
1.11
1.29
2.00
4.00
9.94
7.71
3.57
2.66
11.23
46.11
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1(ppm)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131.674
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128.704
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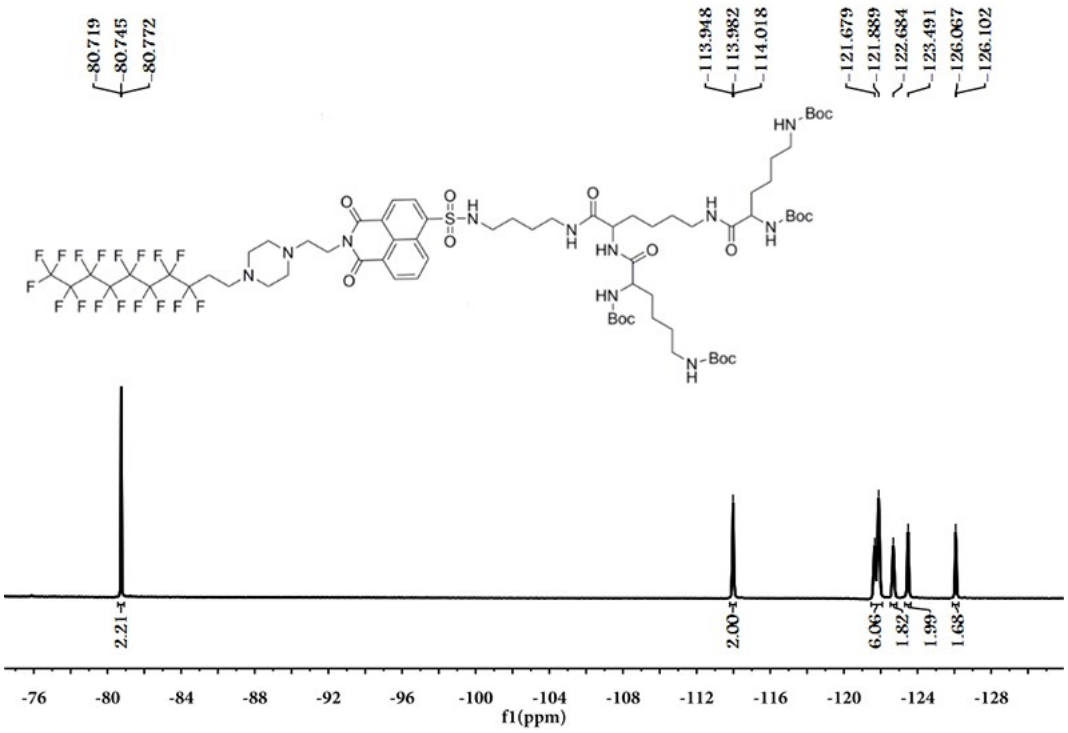
127.065
126.290
126.263
123.055
123.025
79.176
55.436
53.120
53.005
49.221
42.913
39.910
39.670
38.414
37.640
28.798
28.421
28.363
28.347
22.628
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1(ppm)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-123.491
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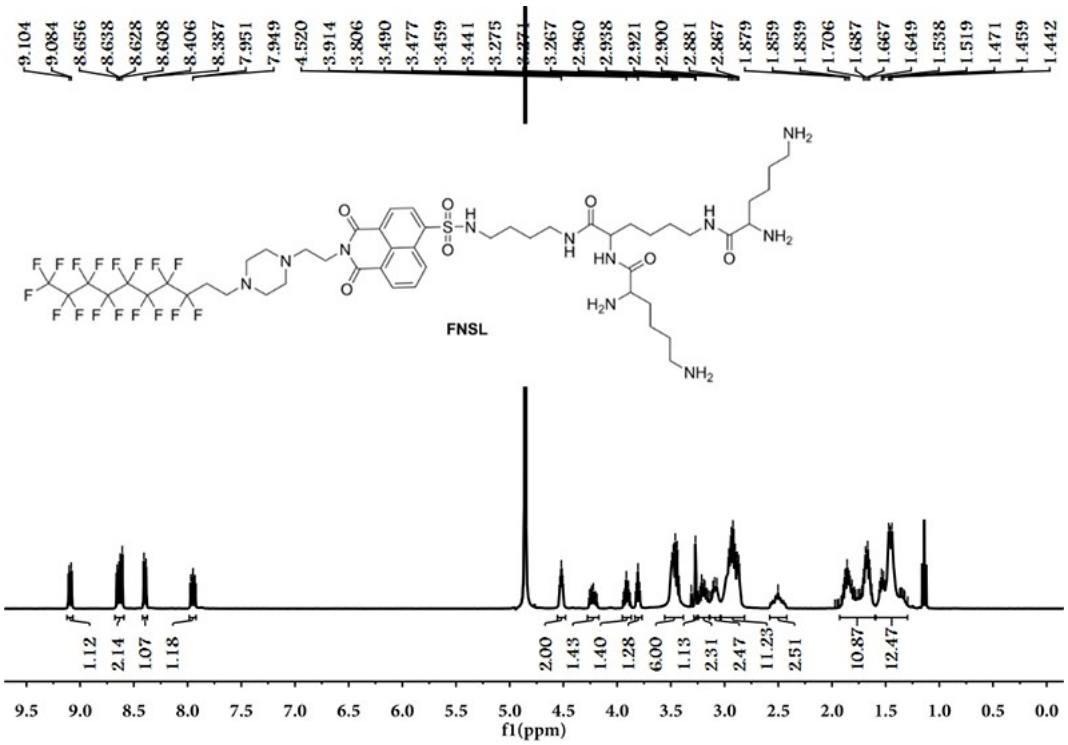
-126.102
HN-Boc
N-Boc
HN-Boc
N-Boc
HN-Boc
2.21
2.00
6.06
1.82
1.99
1.68
-76 -80 -84 -88 -92 -96 -100 -104 -108 -112 -116 -120 -124 -128
f1(ppm)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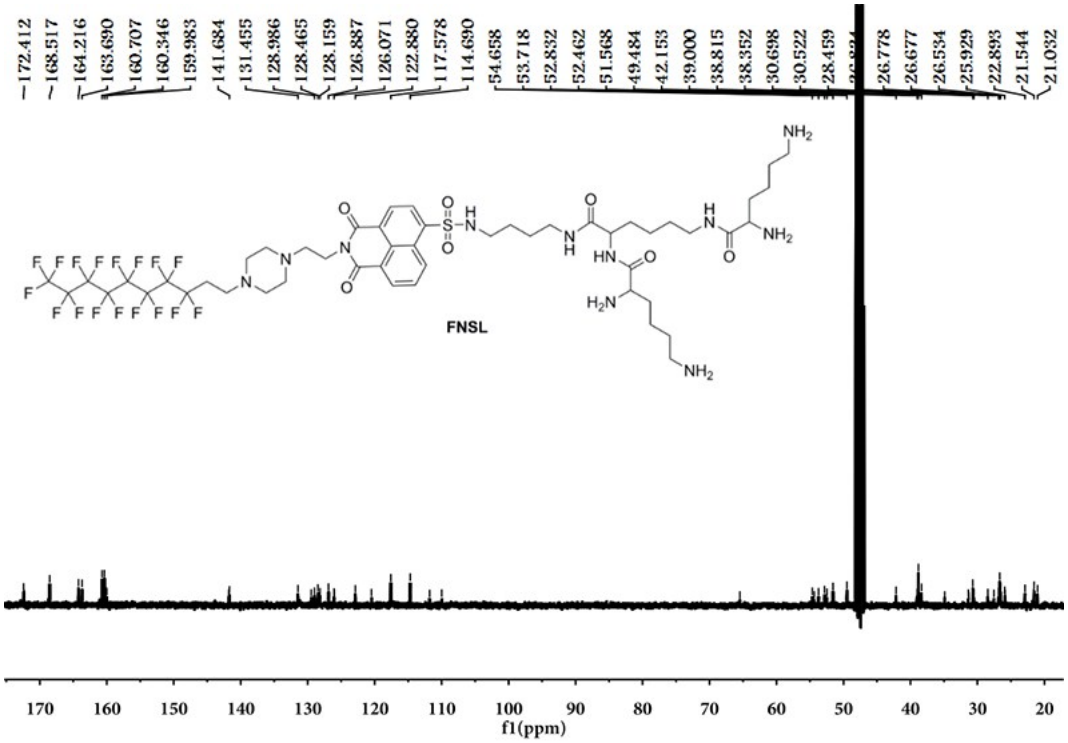
3.490
3.477
3.459
3.441
3.275
3.267
2.960
2.938
2.921
2.900
2.881
2.867
1.879
1.859
1.839
1.706
1.687
1.667
1.649
1.538
1.519
1.471
1.459
1.442
NH2
NH2
NH2
FNSL
1.12
2.14
1.07
1.18
2.00
1.43
1.40
1.28
6.00
1.13
2.31
2.47
11.23
2.51
10.87
12.47
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1(ppm)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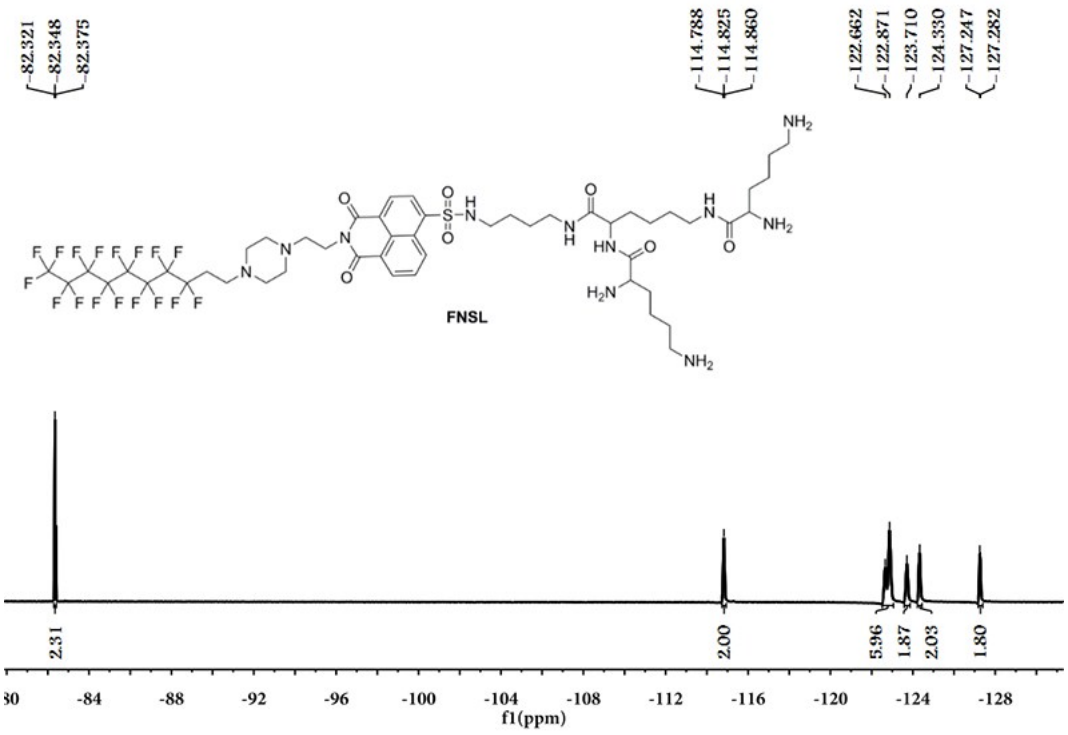
126.071
122.880
117.578
114.690
54.658
53.718
52.832
52.462
51.568
49.484
42.153
39.000
38.815
38.352
30.698
30.522
28.459
26.778
26.677
26.534
25.929
22.893
21.544
21.032
FNSL
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1(ppm)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122.871
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124.330
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127.282
FNSL
2.31
2.00
5.96
1.87
2.03
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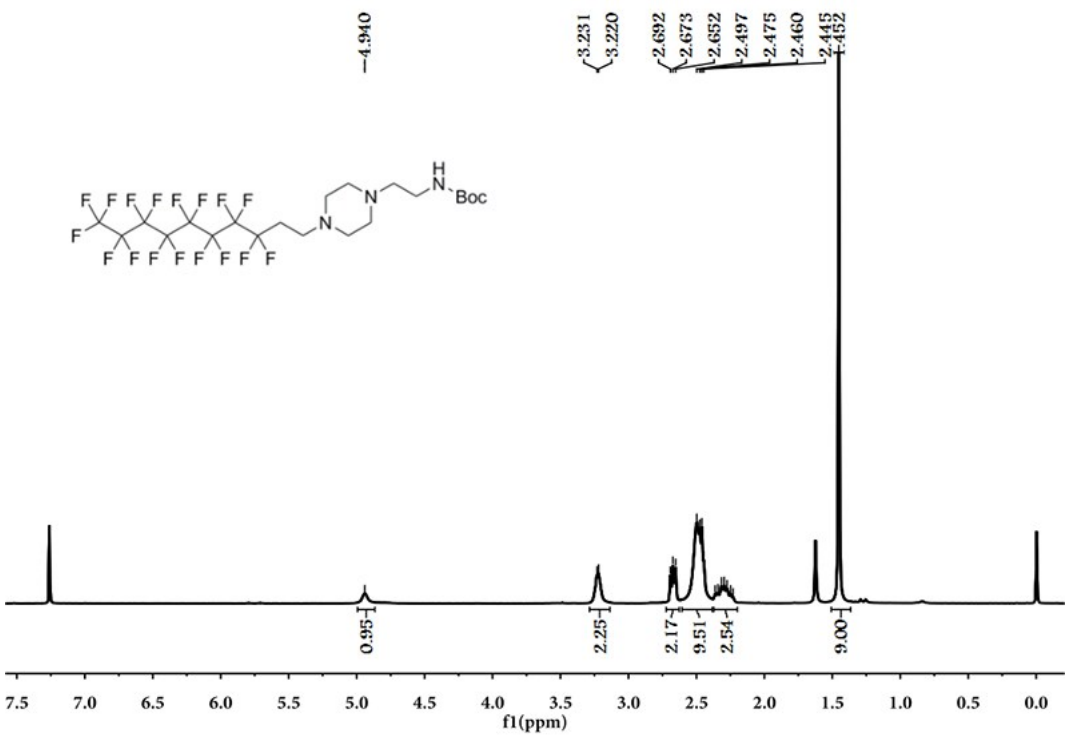
-84
-88
-92
-96
-100
-104
-108
-112
-116
-120
-124
-128
f1(ppm)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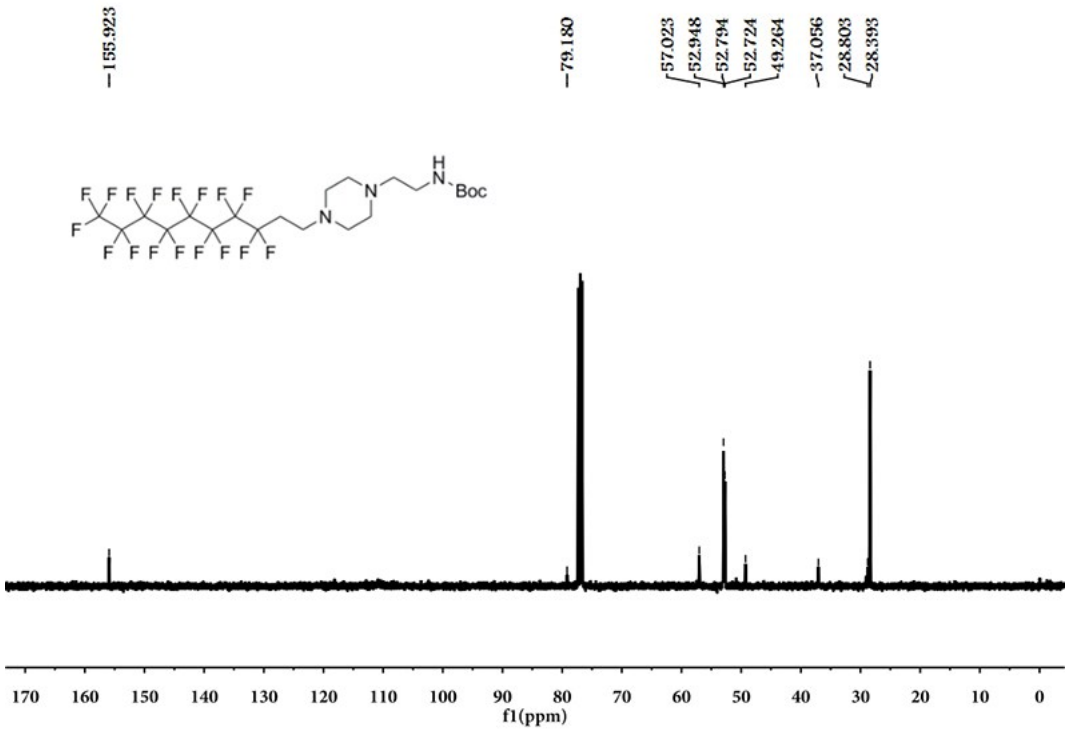
2.652
2.497
2.475
2.460
2.445
1.452
Boc
0.95
2.25
2.17
9.51
2.54
9.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1(ppm)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37.056
28.803
28.393
Boc
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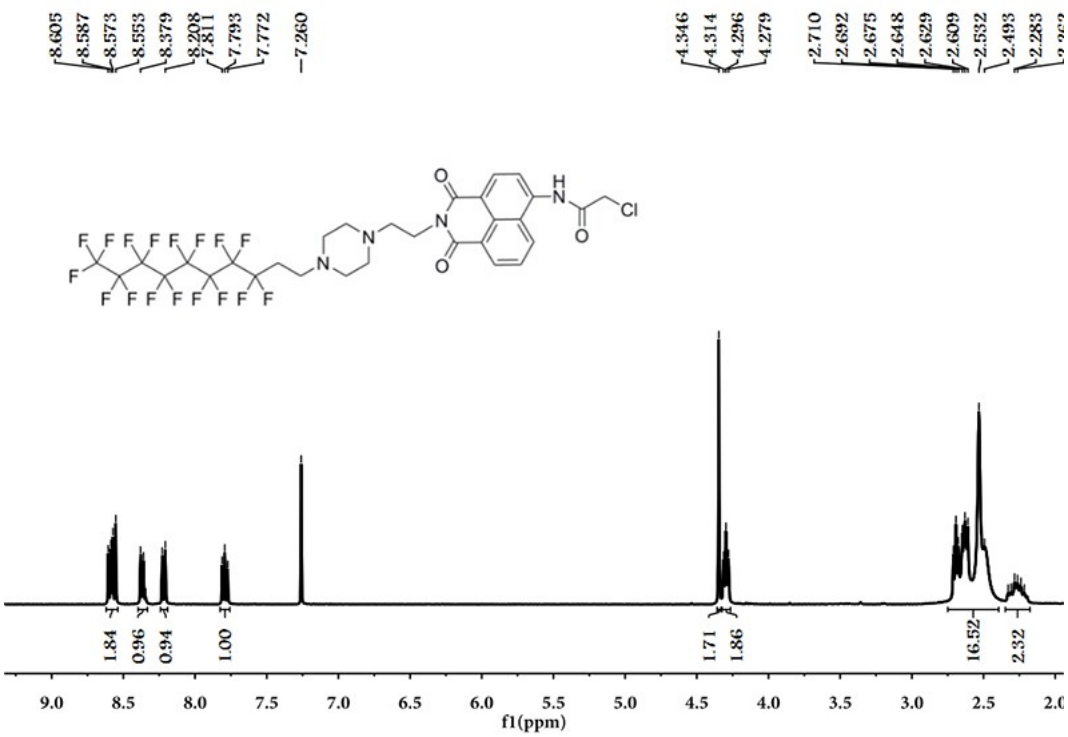
f1(ppm)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7.793
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4.296
4.279
2.710
2.692
2.675
2.648
2.629
2.609
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1.84
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1.86
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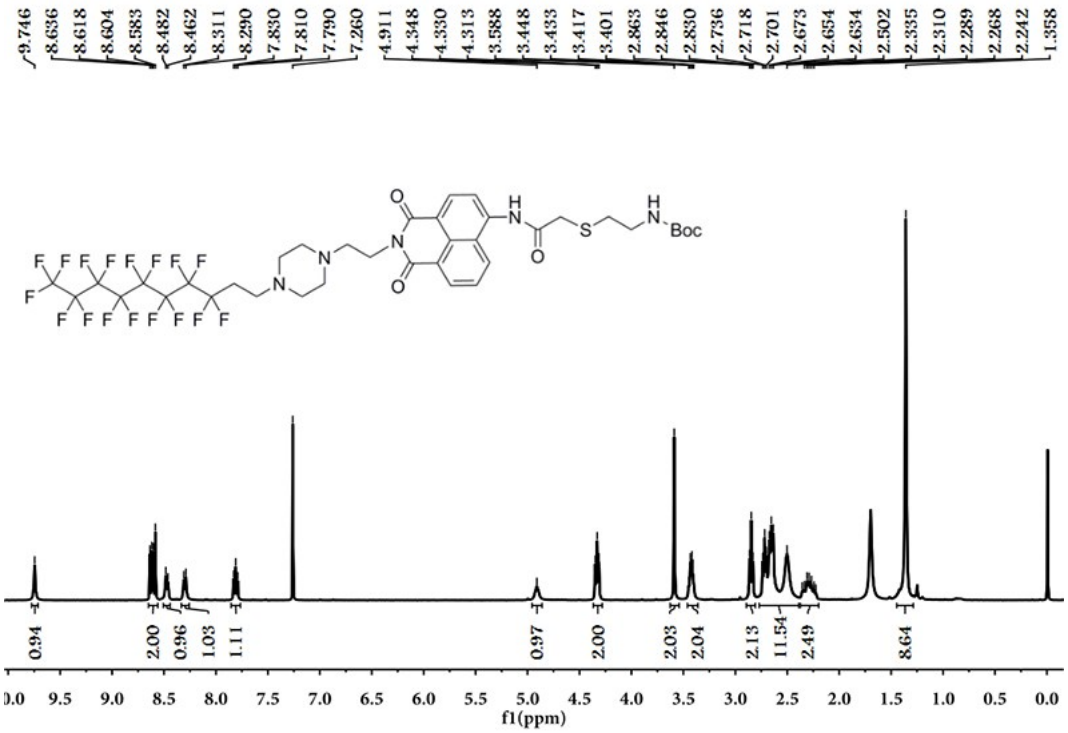
f1(ppm)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8.311
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7.810
7.790
7.260
4.911
4.348
4.330
4.313
3.588
3.448
3.433
3.417
3.401
2.863
2.846
2.830
2.736
2.718
2.701
2.673
2.654
2.634
2.502
2.335
2.310
2.289
2.268
2.242
1.358
Boc
0.94
2.00
0.96
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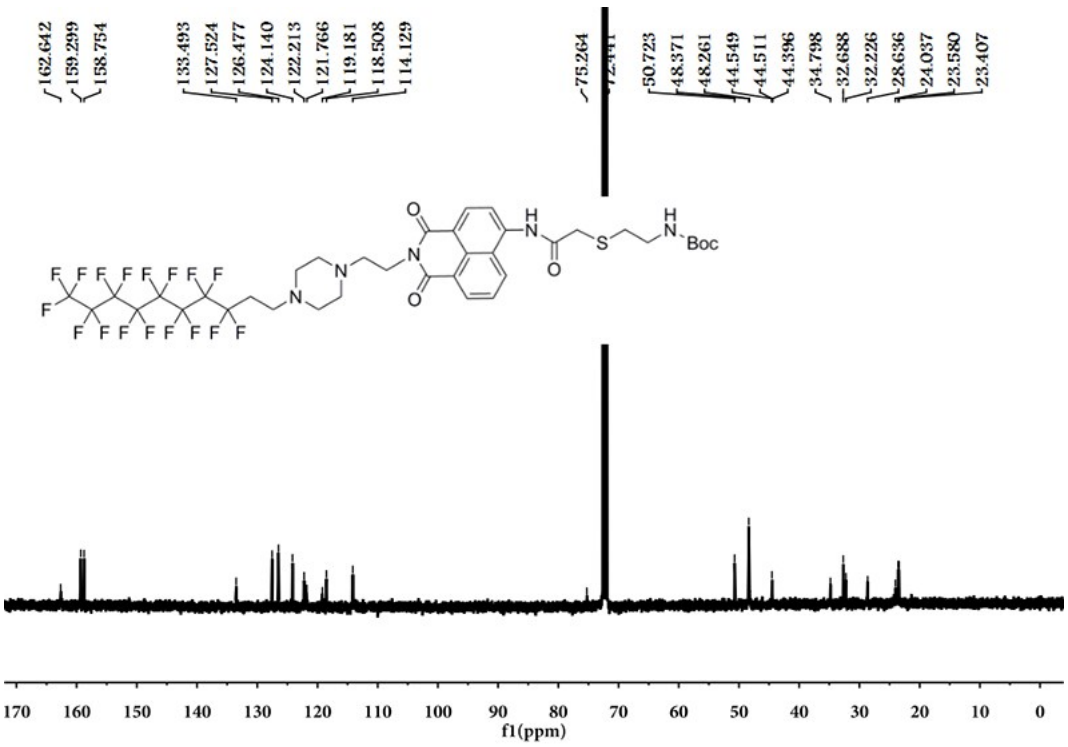
0.97
2.00
2.03
2.04
2.13
11.54
2.49
8.64
f1(ppm)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50.723
48.371
48.261
44.549
44.511
44.396
34.798
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24.037
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23.407
Boc
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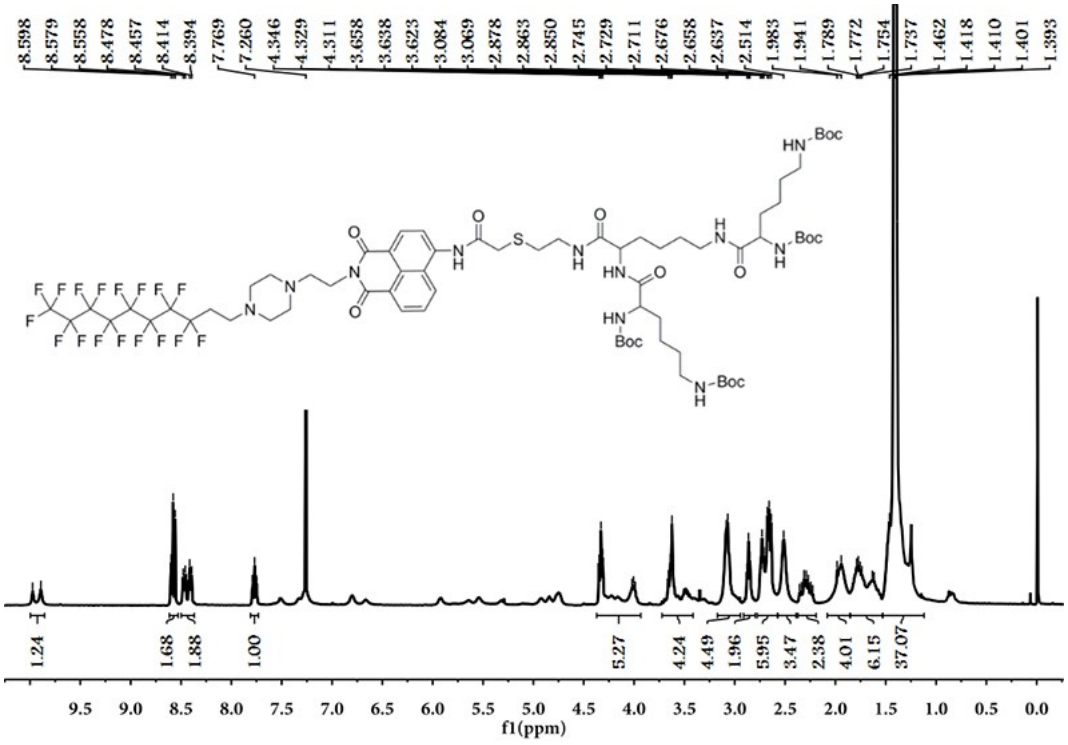
f1(ppm)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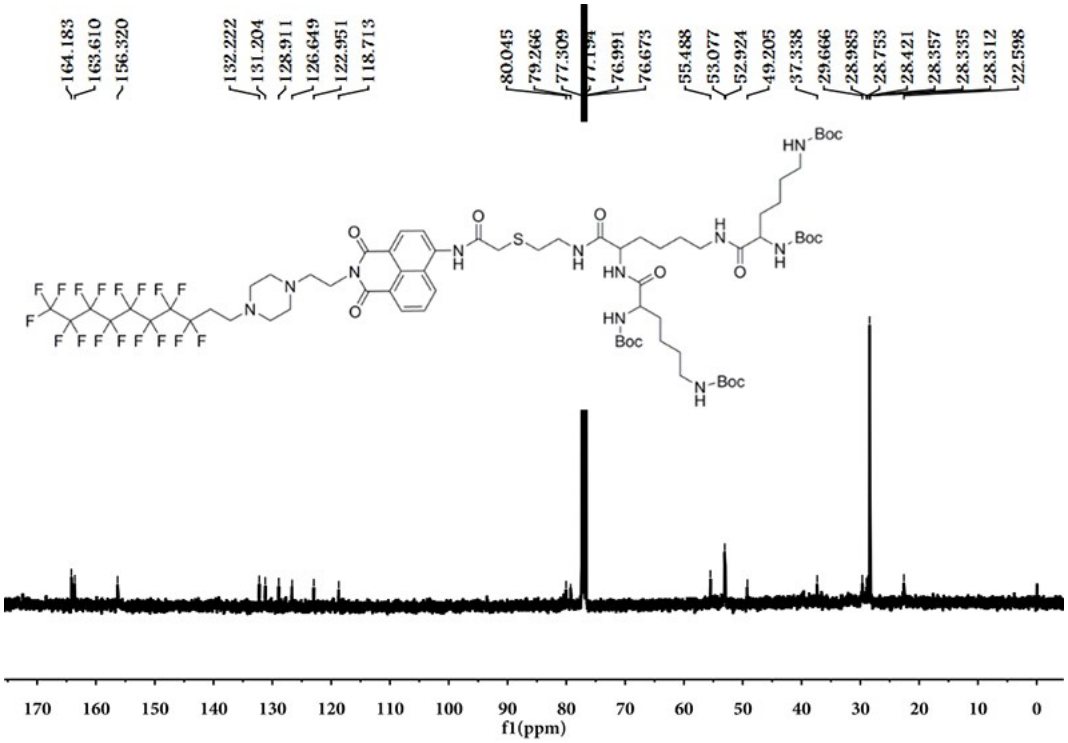
3.658
3.638
3.623
3.084
3.069
2.878
2.863
2.850
2.745
2.729
2.711
2.676
2.658
2.637
2.514
1.983
1.941
1.789
1.772
1.754
1.737
1.462
1.418
1.410
1.401
1.393
Boc
1.24
1.68
1.88
1.00
5.27
4.24
4.49
1.96
5.95
3.47
2.38
4.01
6.15
37.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1(ppm)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122.951
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80.045
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77.309
76.991
76.673
55.488
53.077
52.924
49.205
37.338
29.666
28.985
28.753
28.421
28.357
28.335
28.312
22.598
HN-Boc
N-Boc
HN-Boc
N-Boc
HN-Boc
N-Boc
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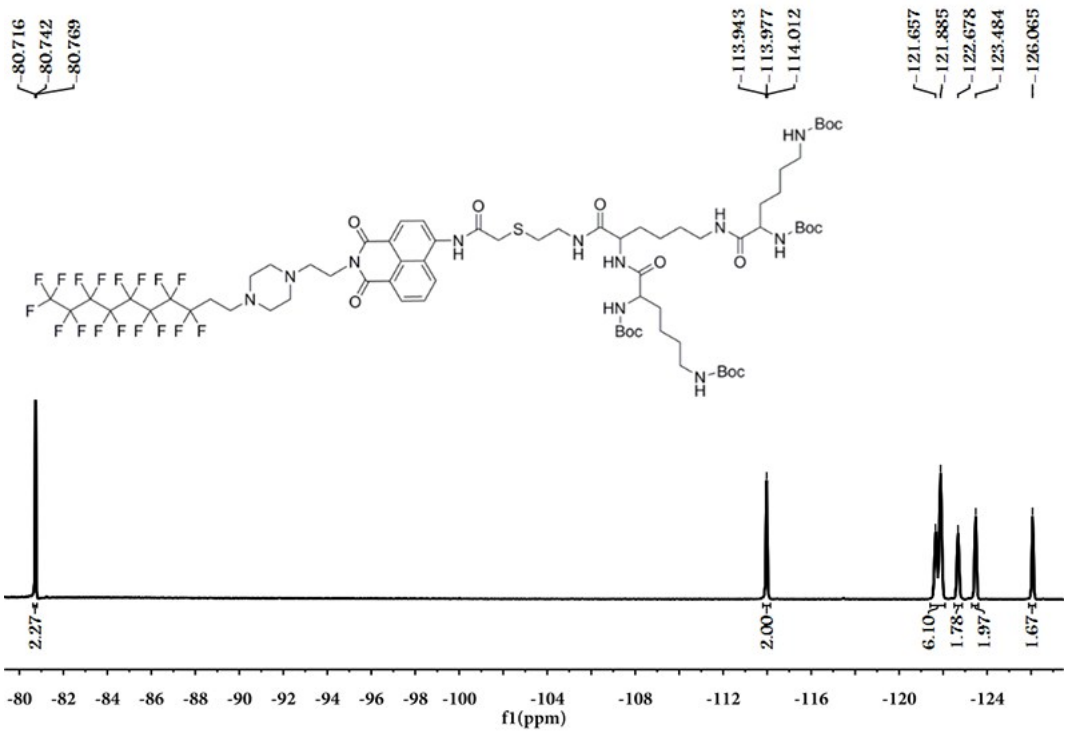
f1(ppm)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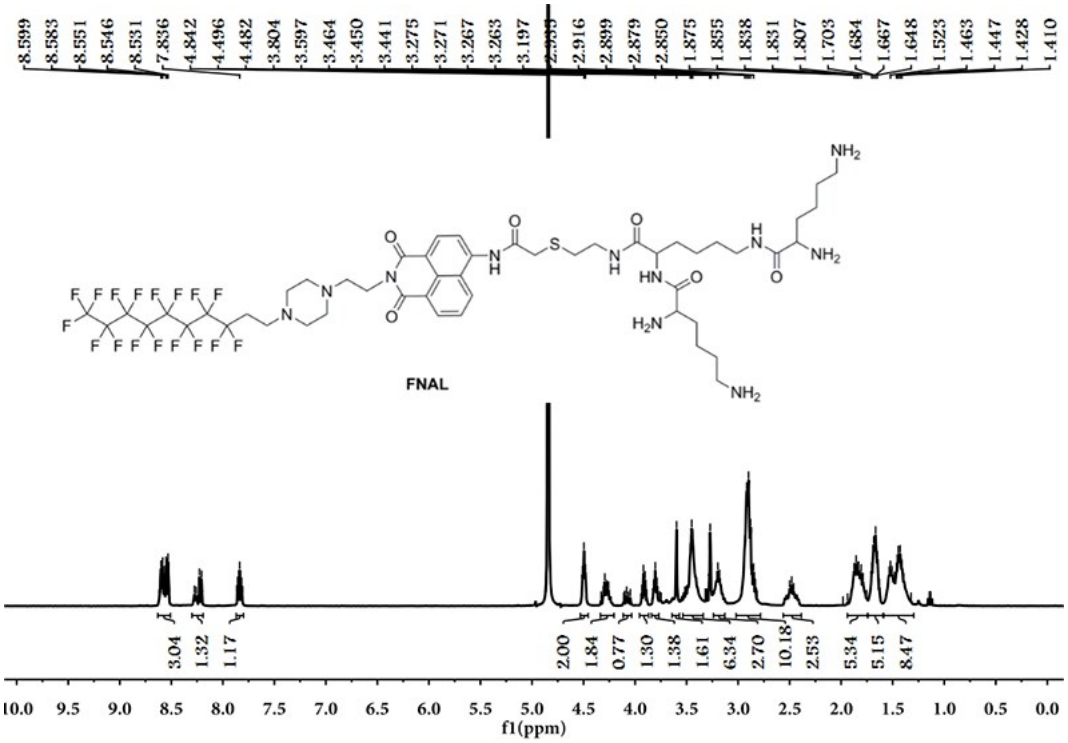
123.484
126.065
HN-Boc
N-Boc
HN-Boc
N-Boc
HN-Boc
N-Boc
2.27
2.00
6.10
1.78
1.97
1.67
-80 -82 -84 -86 -88 -90 -92 -94 -96 -98 -100 -104 -108 -112 -116 -120 -124
f1(ppm)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3.450
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3.263
3.197
2.916
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2.850
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1.855
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1.831
1.807
1.703
1.684
1.667
1.648
1.523
1.463
1.447
1.428
1.410
FNAL
3.04
1.32
1.17
2.00
1.84
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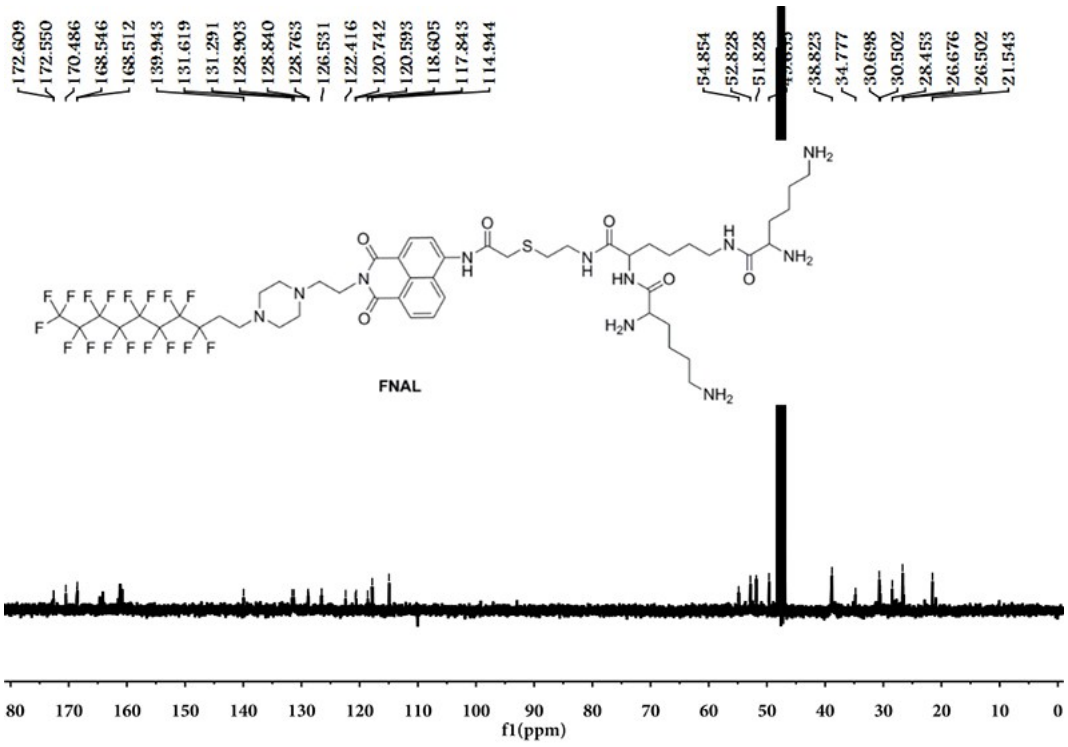
5.34
5.15
8.47
f1(ppm)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122.416
120.742
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114.944
54.854
52.828
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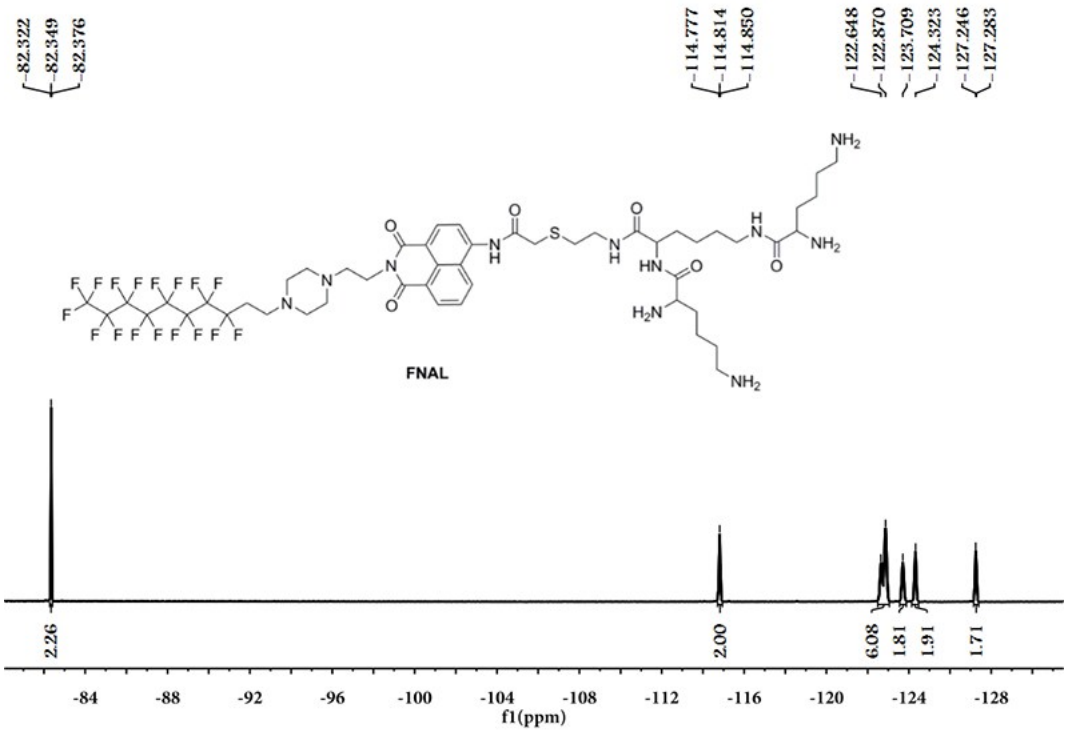
34.777
30.698
30.502
28.453
26.676
26.502
21.543
FNAL
f1(ppm)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-124.323
-127.246
-127.283
FNAL
2.26
2.00
6.08
1.81
1.91
1.71
-84
-88
-92
-96
-100
-104
-108
-112
-116
-120
-124
-128
f1(ppm)