Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Supporting Information for

Hydantoin Derivative Dimers as Broad-spectrum Antimicrobial Agents against ESKAPE Pathogens with Enhanced Killing Rate and Stability

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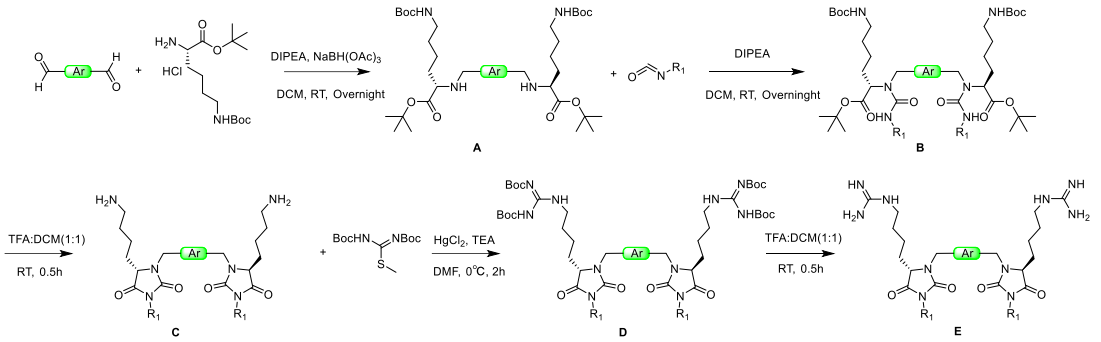
1. Synthesis of Compound 1−20.

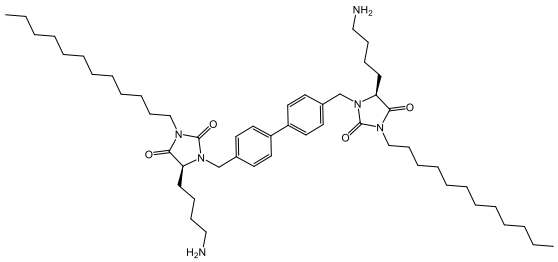


Scheme S1. General synthetic procedure of compound **1**−**20**.

Firstly, Ne-Boc-*L*-Lysine tert-butyl ester hydrochloride (2.2 equiv) was dissolved in DCM and DIPEA (2.2 equiv) was added dropwise at room temperature. Aromatic aldehydes (1.0 equiv) were added to the reaction mixture and stirred for 3 hours, then STAB (sodium triacetoxyborohydride, 6.0 equiv) was added into the solution. After being stirred at room temperature for 6 hours, the reaction mixture was quenched with Na_2CO_3 (aq) and extracted with DCM. The organic extract was washed with brine, dried with anhydrous Na_2SO_4 and purified by flash column chromatography (1:1 hexanes/EtOAc) to obtain **A**. Next, R_1NCO (2.5 equiv) was added to react with **A** (1.0 equiv) and DIPEA (2.5 equiv) at room temperature for 12 hours. After being quenched with HCl (1.0 M) and extracted with DCM, the organic extract was washed with brine and dried with anhydrous Na_2SO_4. Flash column chromatography (1:1 hexanes/EtOAc) was used to obtain purified **B**. **B** was then deprotected in the presence of TFA/DCM (1:1), which cyclized spontaneously in situ to yield **C**, which were final products of compound **1-17**.

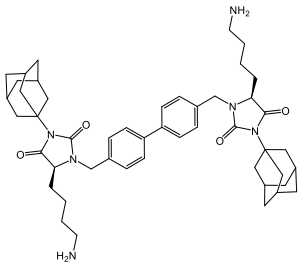
For the synthesis of compound **18-20**, **C** (1.0 equiv), TEA (6.0 equiv) and 1,3-bis(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea (2.0 equiv) were added into a 25 mL flask with 7 mL DMF at 0 ℃. After stirring for 10 minutes, $HgCl_2$ (2.0 equiv) was added into the mixture and stirred for 2 hours. Then the reaction mixture was diluted using EA and washed with water and brine. After being dried over Na_2SO_4 the EA extract was purified by flash column chromatography (1:1 hexanes/EtOAc) to obtain **D**. Finally, **D** was deprotected in the presence of TFA/DCM (1:1) to yield the final product **E** (compound **18-20**).

Compound 1



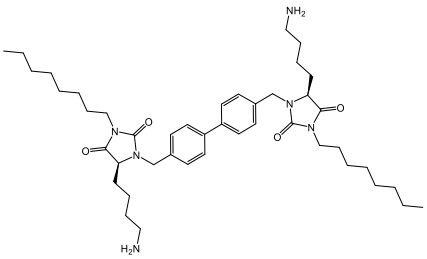
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-dodecylimidazolidine-2,4-dione) (1). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.68 (s, 4H), 7.64 (d, *J* = 8.4 Hz, 4H), 7.39 (d, *J* = 8.4 Hz, 4H), 4.72 (d, *J* = 15.8 Hz, 2H), 4.39 (d, *J* = 15.8 Hz, 2H), 4.00 (t, *J* = 4.5 Hz, 2H), 3.39 (m, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 1.74 (m, 4H), 1.50 (m, 8H), 1.22 m, 38H), 1.04 (m, 2H), 0.83 (t, *J* = 7.0 Hz, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.3, 59.1, 44.1, 38.7, 38.6, 31.7, 29.5, 29.4, 29.4, 29.1, 28.9, 27.8, 27.0, 26.5, 22.5, 20.2, 14.4. **HRMS** (ESI) $C_{52}H_{85}N_6O_4^+$ $[M + H]^+$ calcd = 857.6629; found = 857.6635.

Compound 2



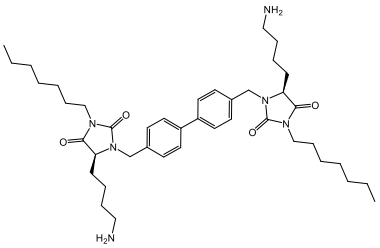
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(3-((3R,5R,7R)-adamantan-1-yl)-5-(4-aminobutyl)imidazolidine-2,4-dione) (2). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.74 (s, 4H), 7.66 (d, *J* = 8.2 Hz, 4H), 7.37 (d, *J* = 8.2 Hz, 4H), 4.64 (d, *J* = 15.6 Hz, 2H), 4.33 (d, *J* = 15.6 Hz, 2H), 3.86 – 3.80 (m, 2H), 2.63 (t, *J* = 7.6 Hz, 4H), 2.36 (m, 12H), 2.06 (s, 6H), 1.65 (m, 14H), 1.47 (m, 4H), 1.35 (s, 1H), 1.22 (s, 1H), 1.15 (m, 2H), 1.04 (m, 2H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.8, 157.3, 139.4, 136.6, 128.9, 127.4, 59.5, 58.2, 44.2, 38.8, 36.2, 29.5, 28.3, 27.1, 19.8. **HRMS** (ESI) $C_{48}H_{65}N_6O_4^+$ $[M + H]^+$ calcd = 789.5064; found = 789.5068.

Compound 3



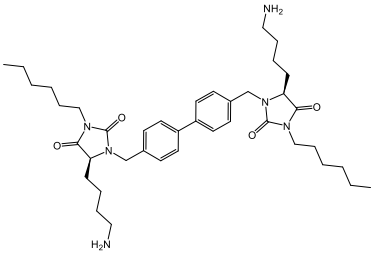
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-octylimidazolidine-2,4-dione) (3). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.78 (s, 4H), 7.64 (d, J = 8.2 Hz, 4H), 7.39 (d, J = 8.4 Hz, 4H), 4.72 (d, J = 15.7 Hz, 2H), 4.39 (d, J = 15.7 Hz, 2H), 4.01 (t, J = 4.5 Hz, 2H), 3.38 (m, 4H), 2.63 (t, J = 7.7 Hz, 4H), 1.74 (m, 4H), 1.50 (m, 8H), 1.22 (m, 22H), 1.03 (m, 2H), 0.83 (t, J = 7.0 Hz, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.3, 59.1, 44.2, 38.8, 38.6, 31.6, 29.0, 28.9, 27.8, 27.1, 26.5, 22.5, 20.2, 14.4. **HRMS** (ESI) $C_{44}H_{69}N_6O_4^+$ $[M + H]^+$ calcd = 745.5377; found = 745.5382.

Compound 4



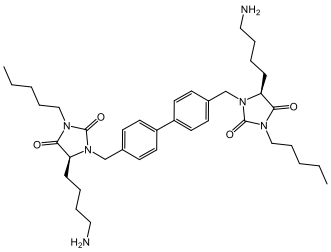
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-heptylimidazolidine-2,4-dione) (4). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.11 (s, 4H), 7.65 (d, *J* = 8.1 Hz, 4H), 7.39 (d, *J* = 8.1 Hz, 4H), 4.72 (d, *J* = 15.7 Hz, 2H), 4.39 (d, *J* = 15.7 Hz, 2H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.38 (m, 4H), 2.62 (t, *J* = 7.7 Hz, 4H), 1.74 (m, 4H), 1.52 (m, 8H), 1.22 (m, 18H), 1.03 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 6H).**^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.3, 59.1, 44.2, 38.8, 38.6, 31.6, 28.6, 27.8, 27.2, 26.5, 22.4, 20.2, 14.4. **HRMS** (ESI) $C_{42}H_{65}N_6O_4^+$ $[M + H]^+$ calcd = 717.5064; found = 717.5069.

Compound 5



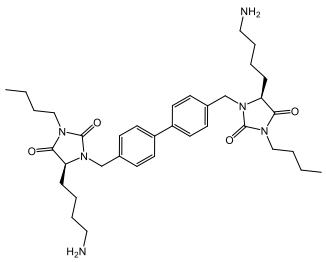
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (5). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.85 (s, 4H), 7.65 (d, *J* = 8.3 Hz, 4H), 7.39 (d, *J* = 8.4 Hz, 4H), 4.72 (d, *J* = 15.8 Hz, 2H), 4.39 (d, *J* = 15.8 Hz, 2H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.38 (m, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 1.74 (m, 4H), 1.50 (m, 8H), 1.24 (m, 14H), 1.03 (m, 2H), 0.87 – 0.81 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.3, 59.2, 44.2, 38.9, 38.6, 31.1, 27.9, 27.8, 27.3, 26.2, 22.4, 20.2, 14.3.**HRMS** (ESI) $C_{40}H_{61}N_6O_4^+$ $[M + H]^+$ calcd = 689.4751; found = 689.4760.

Compound 6



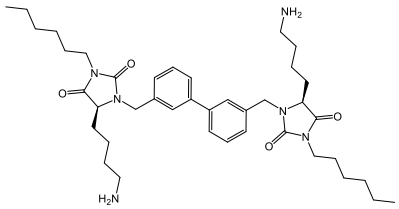
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-pentylimidazolidine-2,4-dione) (6). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.65 (d, *J* = 8.4 Hz, 4H), 7.62 (s, 4H), 7.39 (d, *J* = 8.2 Hz, 4H), 4.72 (d, *J* = 15.8 Hz, 2H), 4.39 (d, *J* = 15.7 Hz, 2H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.39 (m, 4H), 2.62 (t, *J* = 7.7 Hz, 4H), 1.74 (m, 4H), 1.50 (m, 8H), 1.25 (m, 10H), 1.02 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.4, 59.1, 44.2, 38.8, 38.6, 28.7, 27.8, 27.5, 27.2, 22.1, 20.2, 14.3. **HRMS** (ESI) $C_{38}H_{57}N_6O_4^+$ $[M + H]^+$ calcd = 661.4438; found = 661.4438.

Compound 7



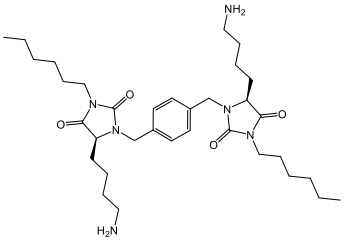
(5S,5'S)-1,1'-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(5-(4-aminobutyl)-3-butylimidazolidine-2,4-dione) (7). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.98 (s, 4H), 7.66 (d, *J* = 8.2 Hz, 4H), 7.39 (d, *J* = 8.4 Hz, 4H), 4.71 (d, *J* = 15.8 Hz, 2H), 4.40 (d, *J* = 15.7 Hz, 2H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.40 – 3.37 (m, 4H), 2.62 (t, *J* = 7.7 Hz, 4H), 1.77 – 1.71 (m, 4H), 1.49 (m, 8H), 1.27 – 1.23 (m, 4H), 1.19 (m, 2H), 1.02 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 6H).**^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.4, 136.5, 128.9, 127.3, 59.2, 44.2, 39.1, 38.3, 30.0, 27.9, 20.2, 19.8, 13.9. **HRMS** (ESI) $C_{36}H_{53}N_6O_4^+$ $[M + H]^+$ calcd = 633.4125; found = 633.4131.

Compound 8



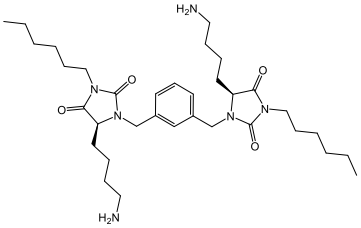
(5S,5'S)-1,1'-([1,1'-biphenyl]-3,3'-diylbis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (8). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.70 (s, 4H), 7.59 (s, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 4.75 (d, *J* = 15.7 Hz, 2H), 4.45 (d, *J* = 15.7 Hz, 2H), 4.09 – 4.00 (m, 2H), 3.39 (m, 4H), 2.60 (t, *J* = 7.7 Hz, 4H), 1.74 (m, 4H), 1.49 (m, 8H), 1.22 (m, 14H), 1.01 (m, 2H), 0.81 (t, *J* = 7.0 Hz, 6H).**^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 140.8, 138.1, 129.7, 127.4, 126.8, 126.5, 59.2, 44.5, 39.0, 38.6, 31.1, 27.8, 27.5, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{40}H_{61}N_6O_4^+$ $[M + H]^+$ calcd = 689.4751; found = 689.4758.

Compound 9



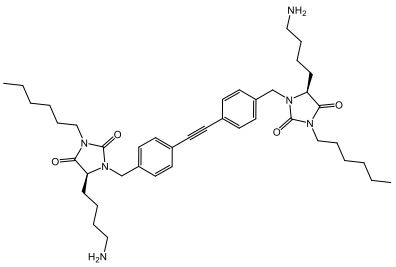
(5S,5'S)-1,1'-(1,4-phenylenebis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (9). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.17 (s, 4H), 7.28 (s, 4H), 4.67 (d, *J* = 15.6 Hz, 2H), 4.35 (d, *J* = 15.6 Hz, 2H), 3.97 (t, *J* = 4.5 Hz, 2H), 3.38 (m, 4H), 2.62 (t, *J* = 7.8 Hz, 4H), 1.71 (m, 4H), 1.50 (m, 4H), 1.45 (m, 4H), 1.24 (m, 12H), 1.17 (m, 2H), 1.00 (m, 2H), 0.87 – 0.81 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.8, 136.5, 128.5, 59.1, 44.1, 38.8, 38.6, 31.1, 27.8, 27.0, 26.2, 22.4, 20.1, 14.3. **HRMS** (ESI) $C_{34}H_{57}N_6O_4^+$ $[M + H]^+$ calcd = 613.4438; found = 613.4446.

Compound 10



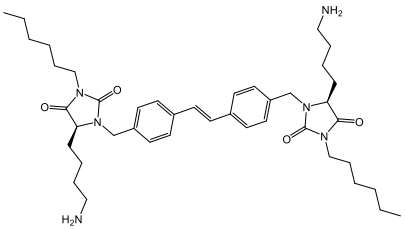
(5S,5'S)-1,1'-(1,3-phenylenebis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (10). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.05 (s, 4H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 6.5 Hz, 3H), 4.66 (d, *J* = 15.8 Hz, 2H), 4.36 (d, *J* = 15.7 Hz, 2H), 3.98 (t, *J* = 4.5 Hz, 2H), 3.39 (m, 4H), 2.63 (t, *J* = 8.0 Hz, 4H), 1.70 (m, 4H), 1.51 (m, 4H), 1.44 (m, 4H), 1.25 (m, 12H), 1.15 (m, 2H), 1.00 (m, 2H), 0.87 – 0.83 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.8, 137.7, 129.4, 127.4, 59.1, 44.4, 38.8, 38.6, 31.1, 27.8, 27.1, 26.2, 22.4, 20.1, 14.3. **HRMS** (ESI) $C_{34}H_{57}N_6O_4^+$ $[M + H]^+$ calcd = 613.4438; found = 613.4442.

Compound 11



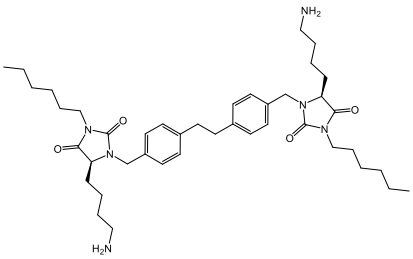
(5S,5'S)-1,1'-((ethyne-1,2-diylbis(4,1-phenylene))bis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (11). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.76 (s, 4H), 7.53 (d, *J* = 8.2 Hz, 4H), 7.36 (d, *J* = 8.2 Hz, 4H), 4.69 (d, *J* = 16.0 Hz, 2H), 4.41 (d, *J* = 16.1 Hz, 2H), 4.02 (t, *J* = 4.5 Hz, 2H), 3.40 (m, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 1.72 (m, 4H), 1.49 (m, 8H), 1.23 (m, 14H), 1.02 (m, 2H), 0.84 (t, *J* = 6.9 Hz, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 138.2, 132.1, 128.6, 121.8, 89.7, 59.3, 44.3, 38.8, 38.6, 31.1, 27.9, 27.8, 27.1, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{42}H_{61}N_6O_4^+$ $[M + H]^+$ calcd = 713.4751; found = 713.4758.

Compound 12



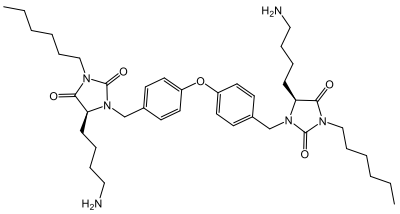
(5S,5'S)-1,1'-((((E)-ethene-1,2-diyl)bis(4,1-phenylene))bis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (12). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.74 (s, 4H), 7.59 (d, *J* = 8.4 Hz, 4H), 7.31 (d, *J* = 8.4 Hz, 4H), 7.25 (s, 2H), 4.67 (d, *J* = 15.8 Hz, 2H), 4.36 (d, *J* = 15.8 Hz, 2H), 3.99 (t, *J* = 4.5 Hz, 2H), 3.42 – 3.38 (m, 4H), 2.62 (t, *J* = 7.7 Hz, 4H), 1.72 (m, 4H), 1.49 (m, 8H), 1.23 (m, 14H), 1.02 (m, 2H), 0.87 – 0.82 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 136.8, 136.6, 128.7, 128.6, 127.2, 59.1, 44.3, 38.8, 38.6, 31.1, 27.9, 27.8, 27.0, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{42}H_{63}N_6O_4^+$ $[M + H]^+$ calcd = 715.4908; found = 715.4910.

Compound 13



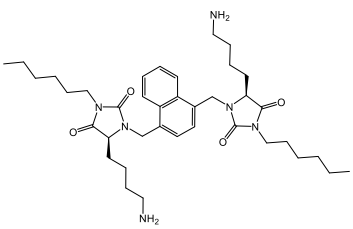
(5S,5'S)-1,1'-((ethane-1,2-diylbis(4,1-phenylene))bis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (13). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ7.89 (s, 4H), 7.20 (s, 8H), 4.62 (d, *J* = 15.6 Hz, 2H), 4.32 (d, *J* = 15.6 Hz, 2H), 3.93 (t, *J* = 4.5 Hz, 2H), 3.37 (m, 4H), 2.83 (s, 4H), 2.59 (t, *J* = 7.8 Hz, 4H), 1.69 (m 4H), 1.47 (m, 8H), 1.24 (m, 12H), 1.14 (m, 2H), 0.98 (m, 2H), 0.86 – 0.81 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ173.0, 156.8, 141.3, 134.7, 129.1, 128.3, 59.0, 44.3, 38.7, 38.6, 37.1, 31.1, 27.8, 27.8, 27.0, 26.2, 22.4, 20.1, 14.3. **HRMS** (ESI) $C_{42}H_{65}N_6O_4^+$ [M + H]$^+$ calcd = 717.5064; found = 717.5070.

Compound 14



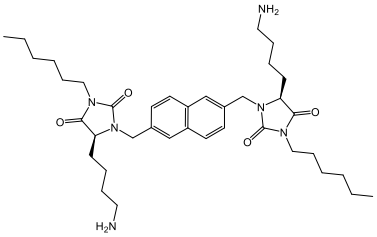
(5S,5'S)-1,1'-((oxybis(4,1-phenylene))bis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (14). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.07 (s, 4H), 7.33 (d, *J* = 8.5 Hz, 4H), 6.97 (d, *J* = 8.7 Hz, 4H), 4.66 (d, *J* = 15.4 Hz, 2H), 4.33 (d, *J* = 15.6 Hz, 2H), 3.99 (t, *J* = 4.5 Hz, 2H), 3.37 (s, 4H), 2.63 (t, *J* = 7.7 Hz, 4H), 1.73 (s, 4H), 1.50 (d, *J* = 7.3 Hz, 8H), 1.23 (d, *J* = 8.1 Hz, 14H), 1.01 (s, 2H), 0.83 (t, *J* = 7.0 Hz, 6H).**^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.8, 156.4, 132.3, 130.2, 119.2, 59.0, 43.9, 38.8, 38.6, 31.1, 27.8, 27.2, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{40}H_{61}N_6O_5^+$ [M + H]$^+$ calcd = 705.4700; found = 705.4708.

Compound 15



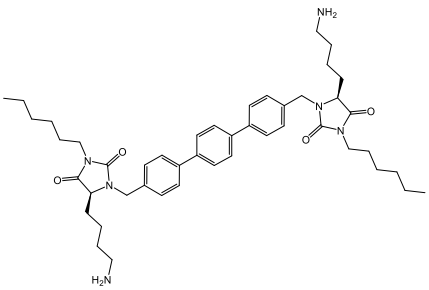
(5S,5'S)-1,1'-(naphthalene-1,4-diylbis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (15). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.21 (m, 2H), 7.60 (m, 2H), 7.48 (s, 2H), 7.27 (s, 4H), 5.14 (d, *J* = 15.8 Hz, 2H), 4.90 (d, *J* = 15.7 Hz, 2H), 3.95 – 3.90 (m, 2H), 3.41 (m, 4H), 2.46 (t, *J* = 7.6 Hz, 4H), 1.61 (m, 4H), 1.52 (m, 4H), 1.35 (m, 2H), 1.24 (m, 14H), 1.05 (m, 2H), 0.92 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.8, 132.9, 131.6, 126.9, 126.5, 124.6, 59.3, 43.0, 38.9, 38.6, 31.1, 28.1, 27.8, 27.5, 26.1, 22.4, 20.0, 14.3. **HRMS** (ESI) $C_{38}H_{59}N_6O_4^+$ $[M + H]^+$ calcd = 663.4595; found = 663.4589.

Compound 16



(5S,5'S)-1,1'-(naphthalene-2,6-diylbis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (16). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.83 (s, 2H), 7.65 (s, 4H), 7.43 (d, *J* = 8.5 Hz, 2H), 4.88 (d, *J* = 15.8 Hz, 2H), 4.48 (d, *J* = 15.8 Hz, 2H), 4.05 – 3.99 (m, 2H), 3.40 (m, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 1.74 (m, 4H), 1.53 (m, 4H), 1.46 (m, 4H), 1.24 (m, 14H), 1.03 (m, 2H), 0.86 – 0.79 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 134.9, 132.6, 128.7, 126.7, 59.0, 44.5, 38.7, 38.6, 31.1, 27.8, 27.0, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{38}H_{59}N_6O_4^+$ $[M + H]^+$ calcd = 663.4595; found = 663.4598.

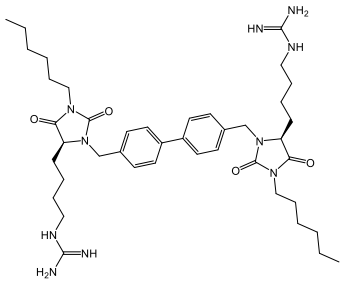
Compound 17



(5S,5'S)-1,1'-([1,1':4',1''-terphenyl]-4,4''-diylbis(methylene))bis(5-(4-aminobutyl)-3-hexylimidazolidine-2,4-dione) (17). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.76 (s, 4H), 7.70 (d, *J* = 8.2 Hz, 8H), 7.42 (d, *J* = 8.4 Hz, 4H), 4.73 (d, *J* = 15.8 Hz, 2H), 4.41 (d, *J* = 15.7 Hz, 2H), 4.04 (t,

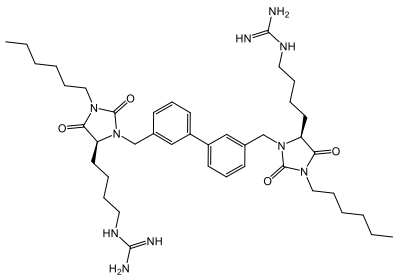
J = 4.5 Hz, 2H), 3.39 (s, 4H), 2.63 (t, *J* = 7.6 Hz, 4H), 1.75 (m, 4H), 1.51 (m, 8H), 1.25 (m, 14H), 1.04 (m, 2H), 0.88 – 0.82 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 156.9, 139.2, 136.6, 129.0, 127.6, 127.2, 59.2, 44.2, 38.8, 38.6, 31.1, 27.8, 27.1, 26.2, 22.4, 20.2, 14.3. **HRMS** (ESI) $C_{46}H_{65}N_6O_4^+$ $[M + H]^+$ calcd = 765.5064; found = 765.5073.

Compound 18



1,1'-(((4S,4'S)-([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(1-hexyl-2,5-dioxoimidazolidine-3,4-diyl))bis(butane-4,1-diyl))diguanidine (18). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 7.99 (s, 2H), 7.63 (d, *J* = 8.2 Hz, 4H), 7.46 (s, 4H), 7.39 (d, *J* = 8.4 Hz, 4H), 7.16 (s, 2H), 4.74 (d, *J* = 15.8 Hz, 2H), 4.39 (d, *J* = 15.8 Hz, 2H), 4.00 (t, *J* = 4.5 Hz, 2H), 3.40 (m, 4H), 3.02 (q, *J* = 7.1 Hz, 4H), 1.77 – 1.71 (m, 4H), 1.51 (m, 4H), 1.38 (m, 2H), 1.31 (m, 2H), 1.24 (m, 14H), 1.04 (m, 2H), 0.87 – 0.81 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 157.6, 156.9, 139.4, 136.4, 128.9, 127.3, 59.0, 44.1, 40.8, 38.6, 31.1, 28.6, 27.8, 26.2, 22.4, 20.1, 14.3. **HRMS** (ESI) $C_{42}H_{65}N_{10}O_4^+$ $[M + H]^+$ calcd = 773.5187; found = 773.5193.

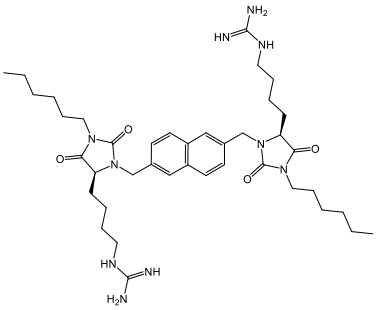
Compound 19



1,1'-(((4S,4'S)-([1,1'-biphenyl]-3,3'-diylbis(methylene))bis(1-hexyl-2,5-dioxoimidazolidine-3,4-diyl))bis(butane-4,1-diyl))diguanidine (19). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.02 (t, *J* = 5.7 Hz, 2H), 7.60 (s, 2H), 7.56 (d, *J* = 7.9 Hz, 2H), 7.52 (s, 2H), 7.44 (t, *J* = 7.7 Hz, 4H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.20 (s, 2H), 4.76 (d, *J* = 15.7 Hz, 2H), 4.44 (d, *J* = 15.7 Hz, 2H), 4.04 (t, *J* = 4.3 Hz, 2H), 3.39 (m, 4H), 2.99 (m, 4H), 1.75 (m, 4H), 1.50 (m, 4H), 1.35 (m, 2H), 1.28 (m, 2H), 1.21 (m, 12H),

1.14 (m, 2H), 1.01 (m, 2H), 0.82 (m, 6H). **^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 157.6, 156.9, 140.8, 138.0, 129.7, 127.5, 126.9, 126.5, 59.1, 44.4, 40.8, 38.5, 31.1, 28.7, 27.8, 27.7, 26.2, 22.4, 20.0, 14.3. **HRMS** (ESI) $C_{42}H_{65}N_{10}O_4^+$ $[M + H]^+$ calcd = 773.5187; found = 773.5192.

Compound 20



1,1'-(((4S,4'S)-(naphthalene-2,6-diylbis(methylene))bis(1-hexyl-2,5-dioxoimidazolidine-3,4-diyl))bis(butane-4,1-diyl))diguanidine (20). **^{1}H NMR (600 MHz, DMSO-d$_6$)** δ 8.00 (t, *J* = 5.8 Hz, 2H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.84 (s, 2H), 7.53 (s, 2H), 7.45 – 7.42 (m, 4H), 7.36 (s, 2H), 4.87 (d, *J* = 15.8 Hz, 2H), 4.49 (d, *J* = 15.8 Hz, 2H), 4.01 (t, *J* = 4.4 Hz, 2H), 3.43 – 3.38 (m, 4H), 3.03 – 2.94 (m, 4H), 1.72 (m, 4H), 1.52 (m, 4H), 1.34 (m, 2H), 1.24 (m, 16H), 1.01 (m, 2H), 0.87 – 0.79 (m, 6H).**^{13}C {1H} NMR (151 MHz, DMSO-d$_6$)** δ 173.0, 157.6, 156.9, 134.8, 132.6, 128.7, 126.7, 126.7, 59.0, 44.5, 40.8, 38.6, 31.1, 28.6, 27.8, 27.7, 26.2, 22.4, 20.1, 14.3. **HRMS** (ESI) $C_{40}H_{63}N_{10}O_4^+$ $[M + H]^+$ calcd = 747.5031; found = 747.5036.

2. Minimum Inhibitory Concentrations (MICs) Assay

All compounds were tested against following bacteria strains: *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Bacillus subtilis* (ATCC 6633), methicillin-resistant *S. aureus* (ATCC 43300), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (CMCC 10104), *Acinetobacter baumannii* (ATCC 19606) and *Klebsiella pneumoniae* (ATCC 10031). One colony of each bacteria was inoculated in 4 mL TSB buffer at 37 °C overnight, which was then diluted 100 times, and the bacteria were allowed to grow to the mid-logarithmic phase. 50 μL compounds in 2-fold serial dilution of TSB were added in the 96-well plate, then 50 μL diluted bacterial in TSB medium (1×10^6 CFU/mL) was added to each well. After 16 h of incubation at 37 °C, the absorption at 600 nm wavelength on a Tecan SPARK microplate reader was recorded.

Minimum inhibitory concentrations were determined as the lowest concentrations that inhibited bacteria growth completely.

3. Hemolytic Assay

Fresh red blood cells (RBCs) of mice were washed with 1× PBS buffer and centrifuged 10 minutes at 3500 rpm for 3 times until the supernatant was clear, then RBCs were diluted into 5% v/v suspension in 1× PBS. 50 μL compounds in PBS were 2-fold serially diluted in a 96-well plate, and incubated with 50 μL RBCs suspension for 1 hour at 37 °C. The mixture was then centrifuged for 10 minutes at 3500 rpm. Subsequently, 30 μL of the supernatant was added to 100 μL PBS, then the absorbance of mixture was read on a Tecan SPARK microplate reader at 540 nm. The hemolytic activity was calculated by the formula % hemolysis = $(Abs_{sample}-Abs_{PBS}) / (Abs_{Triton}-Abs_{PBS}) \times 100\%$. 1% Triton X-100 were used as the positive control and 1× PBS buffer was used as the negative control.

4. Stability Assay

Thermal stability was evaluated as following procedures: compound **18** were preincubated for 1 hour at various temperatures (40–120 °C), and MIC assays were used to detect the residual antibacterial activity.

Salt and serum stability was evaluated as following procedures: the *S. aureus* and *E. coli* in the exponential growth phase were incubated with compound **18** supplemented with 10 mM NaCl, 10 mM KCl, 10 mM $MgCl_2$, 10% Dulbecco's modified Eagle medium (DMEM), and 10% fetal bovine serum (FBS) for 16–18 hours. The stability of compound was evaluated by the change of its antibacterial activity under different conditions.

5. Time kill Assay

Bacteria *S. aureus* (ATCC 29213) and *E. coli* (ATCC 25922) suspensions were allowed to grow at 37 °C to the mid-logarithmic phase, and diluted to 1×10^6 CFU/mL, then incubated with the compound **18** at the concentration of 1× MIC, 2 × MIC and 4 × MIC at 15min, 30 min, 60 min, 120 min, respectively. The resulted mixture was then diluted by 10^2 to 10^4 fold, from which 100 μL was spread on the TSB agar plate. The number of bacteria colonies was counted after 20 h of incubation

at 37 °C.

6. Membrane Depolarization Assay

The *S. aureus* (ATCC 29213) and *E. coli* (ATCC 25922) bacterial cells were collected at the mid-log phase, then washed with 5 mM HEPES and 5 mM glucose. The bacteria were re-suspended in a 1 : 1 : 1 ratio (10^6 CFU mL^{-1}) of 5 mM glucose, 5 mM HEPES, and 100 mM KCl solution. 192 μL of bacterial suspension and 8 μL of 10 μM DiSC3(5) were added into a 96-well plate at 37 °C. After that, the fluorescence of the suspension was monitored for a half-hour at 37 °C at the excitation wavelength of 622 nm and the emission wavelength of 670 nm. Compound **18** was added to the wells immediately when the minimum value of fluorescence was reached. An increase in fluorescence was recorded.

7. Inner and Outer Membrane Permeabilization Assay

S. aureus (ATCC 29213) and *E. coli* (ATCC 25922) were cultured overnight at 37°C, and the bacteria were resuspended in PBS. The suspension was diluted to OD_{600} = 0.1, following by the addition of propidium iodide (PI) to a final concentration of 5 μM for 30 minutes, then treated with compound **18** at different concentrations for 1 hour in the dark. The fluorescence was measured at the excitation wavelength of 535 nm and emission wavelength of 615 nm using the Tecan SPARK microplate reader.

E. coli (ATCC 25922) cells were cultured overnight at 37°C, and the bacteria were resuspended in PBS. The suspension was diluted to OD_{600} = 0.1, following by the addition of 1-*N*-phenylnaphthylamine (NPN) to a final concentration of 10 μM for 30 minutes, then treated with compound **18** at different concentrations for 1 hour in the dark. The fluorescence was measured at the excitation wavelength 350 nm and emission wavelength of 420 nm using the Tecan SPARK microplate reader.

8. ROS Assay

S. aureus (ATCC 29213) and *E. coli* (ATCC 25922) were cultured overnight at 37°C, and the bacteria were washed three times and resuspended in PBS. The suspension was diluted to OD_{600} = 0.1, mixed with DCFH-DA (5 μM), and used as the working solution. Bacteria were placed

into a 96-well plate and treated with compound **18** at different concentrations for 30 minutes at 37°C in the dark. An increase in fluorescence was recorded. (Ex = 488 nm, Em = 530 nm).

9. Scanning Electron Microscopy (SEM)

S. aureus (ATCC 29213) and *E. coli* (ATCC 25922) bacteria cells grew in the mid log phase and were incubated with compound **18** at 37 °C for 6 h. Then, the mixture was centrifuged at 3000 rpm for 15 min and the bacterial pellets were collected at the bottom of the centrifuge tube and washed with PBS four times. The samples with no treatment were used as the control samples. To the bacterial precipitate, glutaraldehyde (2.5%) was added and dried by gradient concentration of ethanol, then plated with gold at the critical point. Finally, the bacterial morphology was photographed using a Hitachi S-4700 electron microscope.

10. Fluorescence Microscopy

Both propidium iodide (PI) and Hoechst 33342 fluorescent dyes were used in the studies to determine the ability of the compound **18** to compromise the membranes of *S. aureus* (ATCC 29213) and *E. coli* (ATCC 25922), respectively. In brief, bacterial suspensions were incubated at 37 °C to the mid-logarithmic phase and then diluted by 100 fold, followed by incubation with compound **18** for 2 h at 37 °C. After centrifugation for 15 min at 5000 rpm, cell pellets were washed with 1× PBS buffer, and incubated with Hoechst 33342 (10 μg/mL) for 10 min in the dark at 37 °C, then washed 2 times with PBS. Then the cell pellets were incubated with PI (5 μg/mL) for 15 min on ice in the dark. The pellets were then diluted in 100 μL PBS, and 10~20 μL of the suspension was applied on chamber slides and observed under ABI A1R HD25 confocal microscope using 40 × objective.

11. LPS Competitive Experiment

The impact of exogenous LPS on the activity of compound **18** were assessed by the checkerboard microdilution assay. Brieflfly, lipopolysaccharide (LPS) (0–250 μg/mL) and compound **18** were co-incubation with bacterial suspensions in 96-well plate. After 16–18 hours incubation, the antibacterial activity of compound **18** in the presence of LPS were recorded.

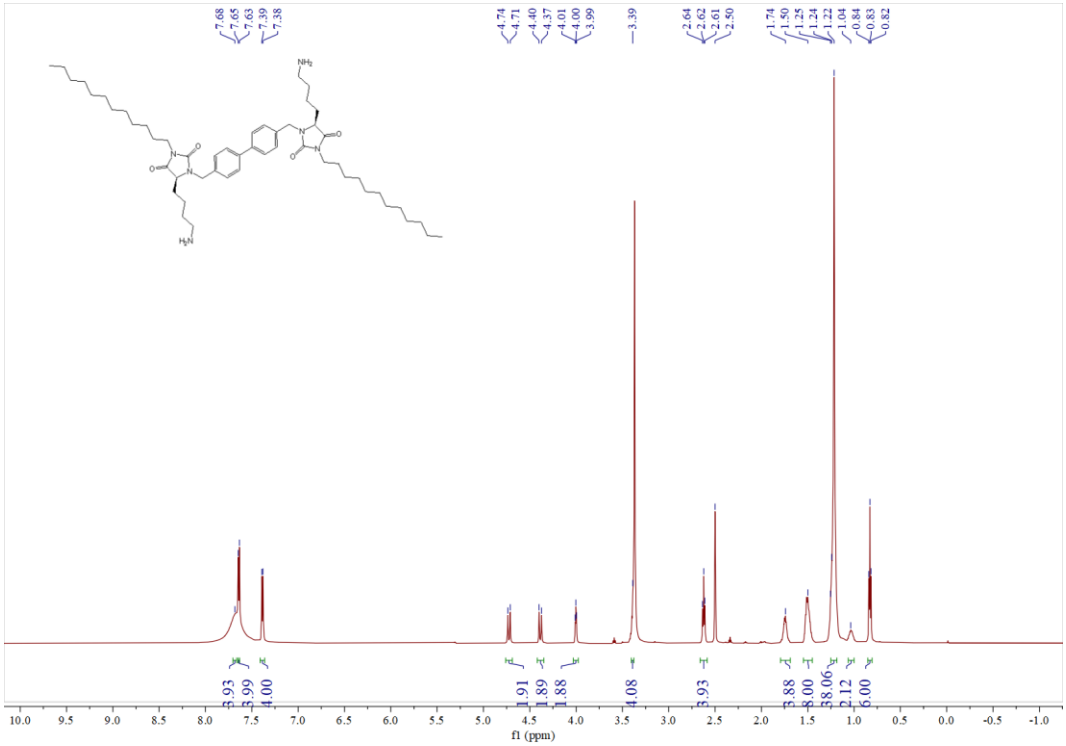
12. Drug Resistance Assay

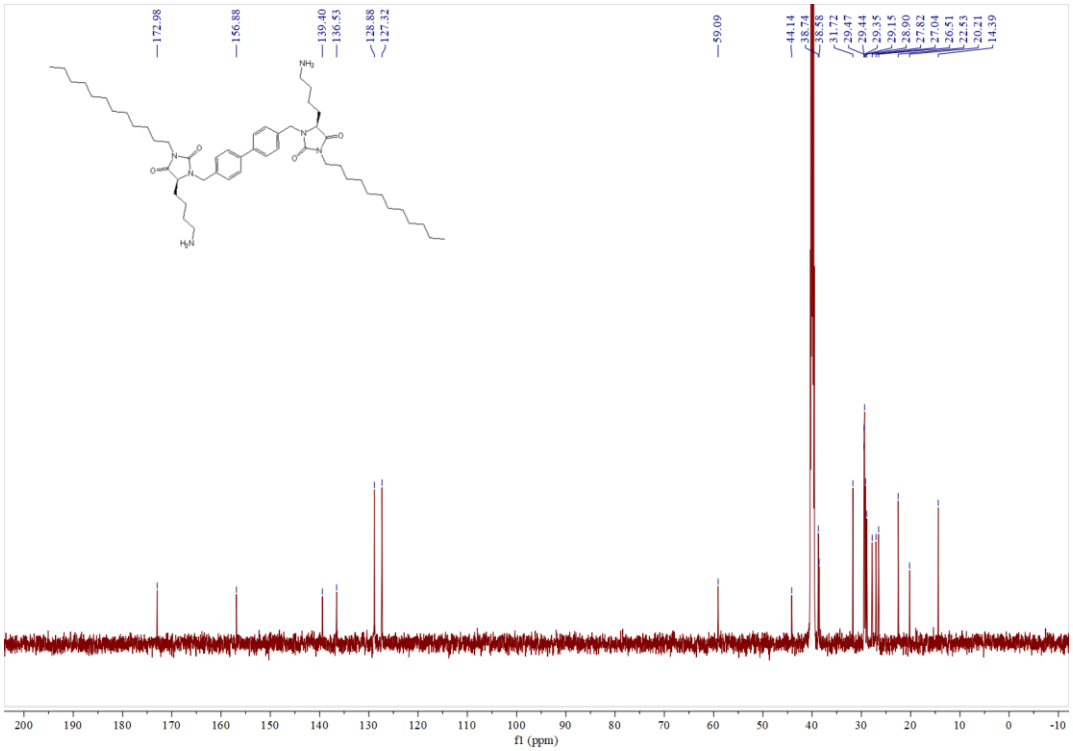
The lead compound **18** was chosen for drug resistance studies. Briefly, after its MIC was

determined, the bacteria solution from the well of the 1/2 MIC was withdrawn and diluted to 1 × 10^6 CFU/mL for the next MIC measurement. The measurement was repeated for 25 passages.

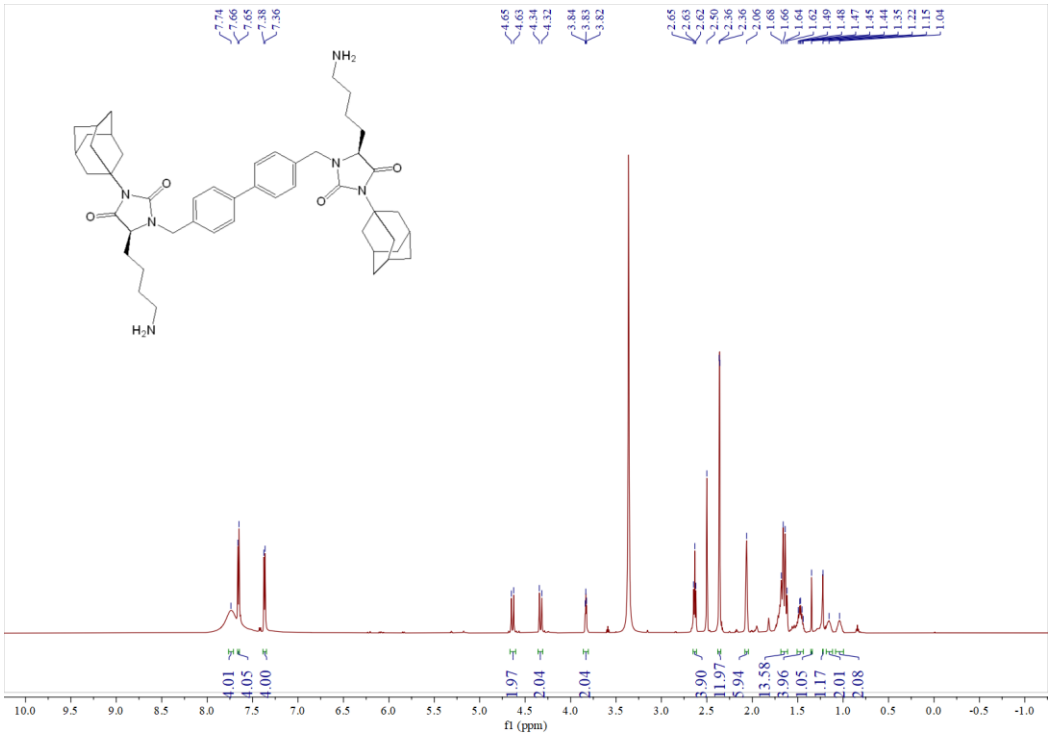
13. ^{1}HNMR and ^{13}CNMR spectra of compounds 1–20.

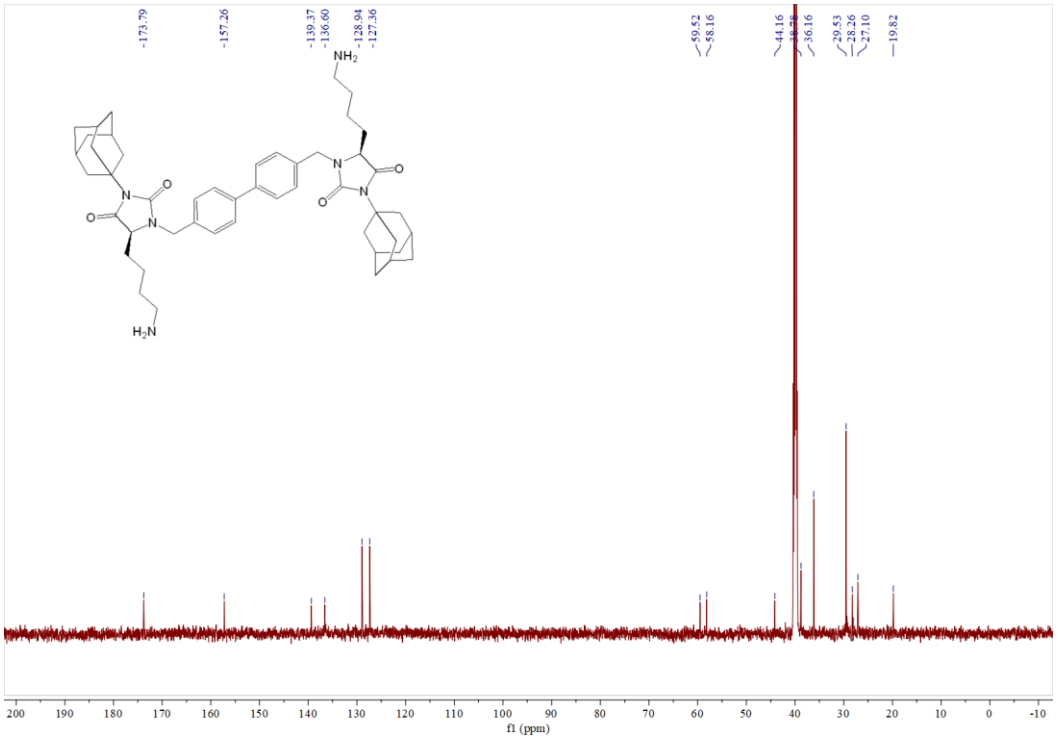
Compound 1



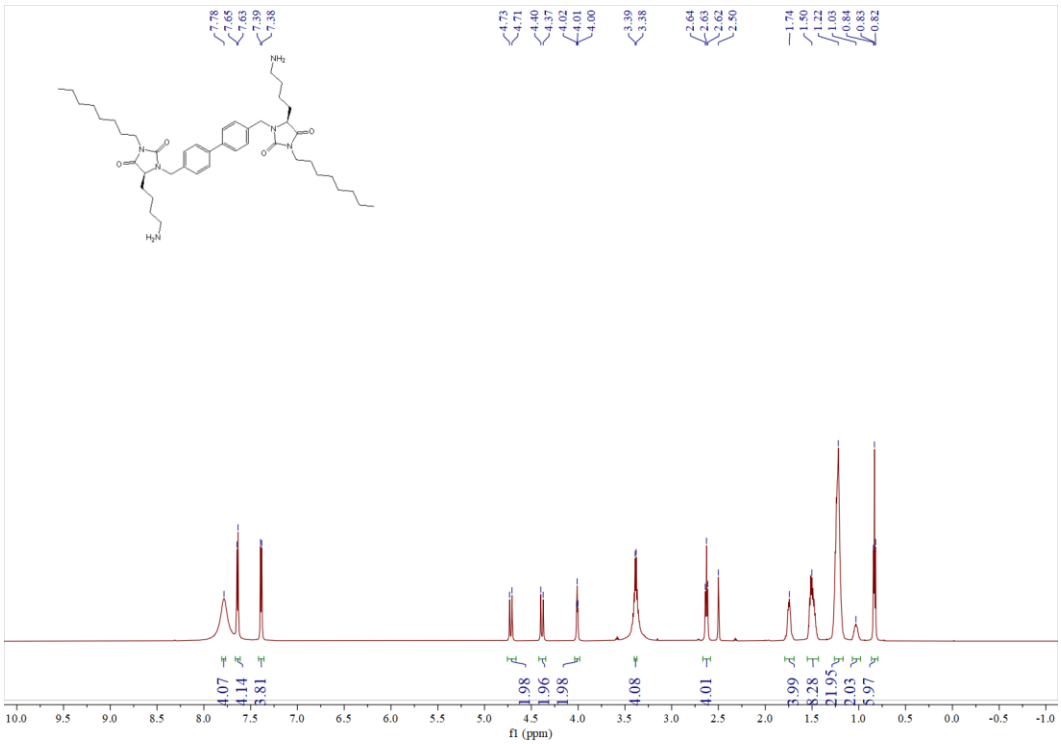


Compound 2





Compound 3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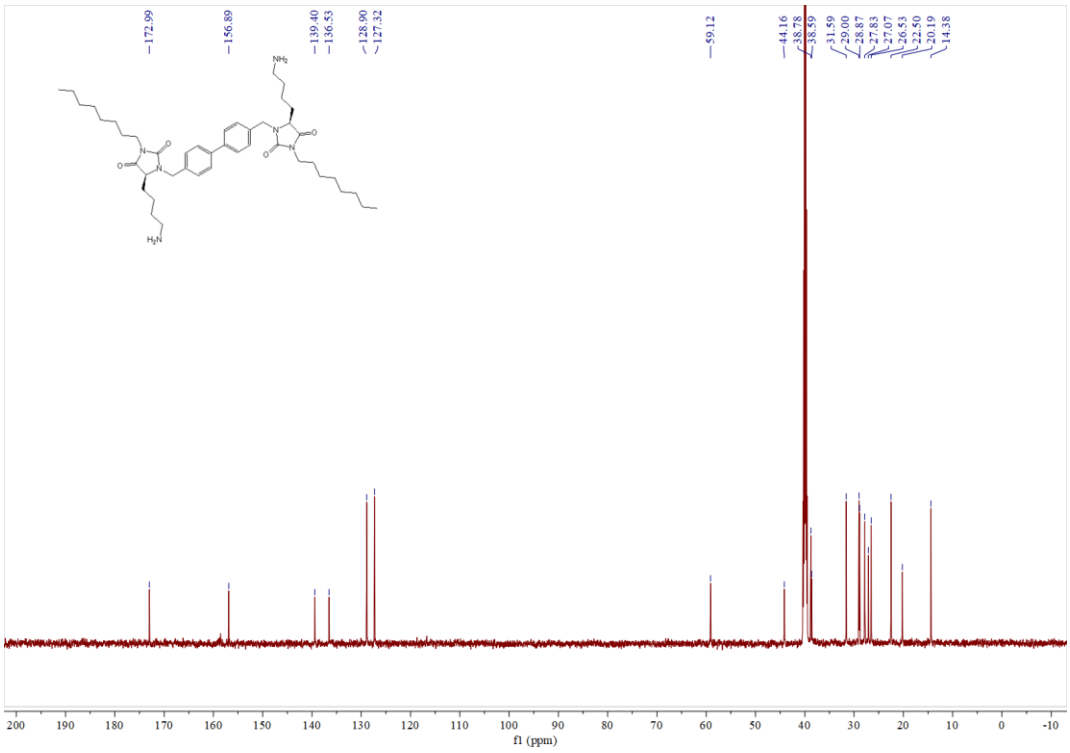
7.65
7.63
7.39
7.38
4.73
4.71
4.40
4.37
4.02
4.01
4.00
3.39
3.38
2.64
2.63
2.62
2.50
1.74
1.50
1.22
1.03
0.84
0.83
0.82
4.07
4.14
3.81
1.98
1.96
1.98
4.08
4.01
3.99
8.28
21.95
2.03
5.97
f1 (ppm)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128.90
127.32
59.12
44.16
38.78
38.59
31.59
29.00
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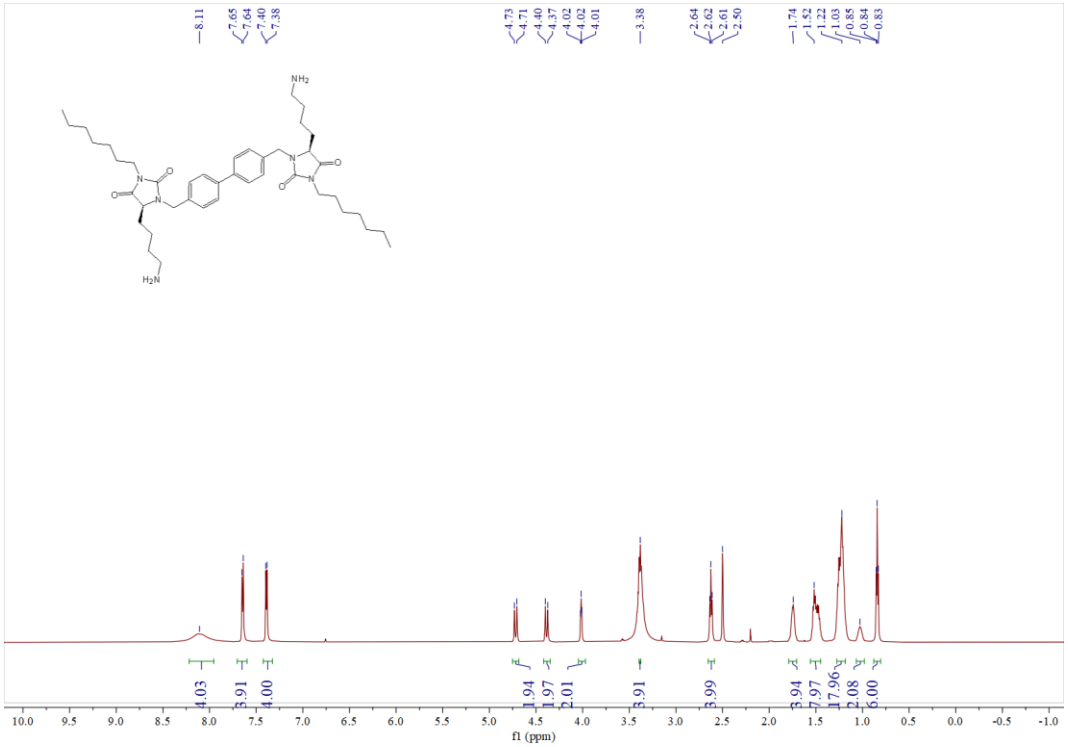
22.50
20.19
14.38
f1 (ppm)

Compound 4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7.38
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4.02
4.01
3.38
2.64
2.62
2.61
2.50
1.74
1.52
1.22
1.03
0.85
0.84
0.83
NH2
H2N
4.03
3.91
4.00
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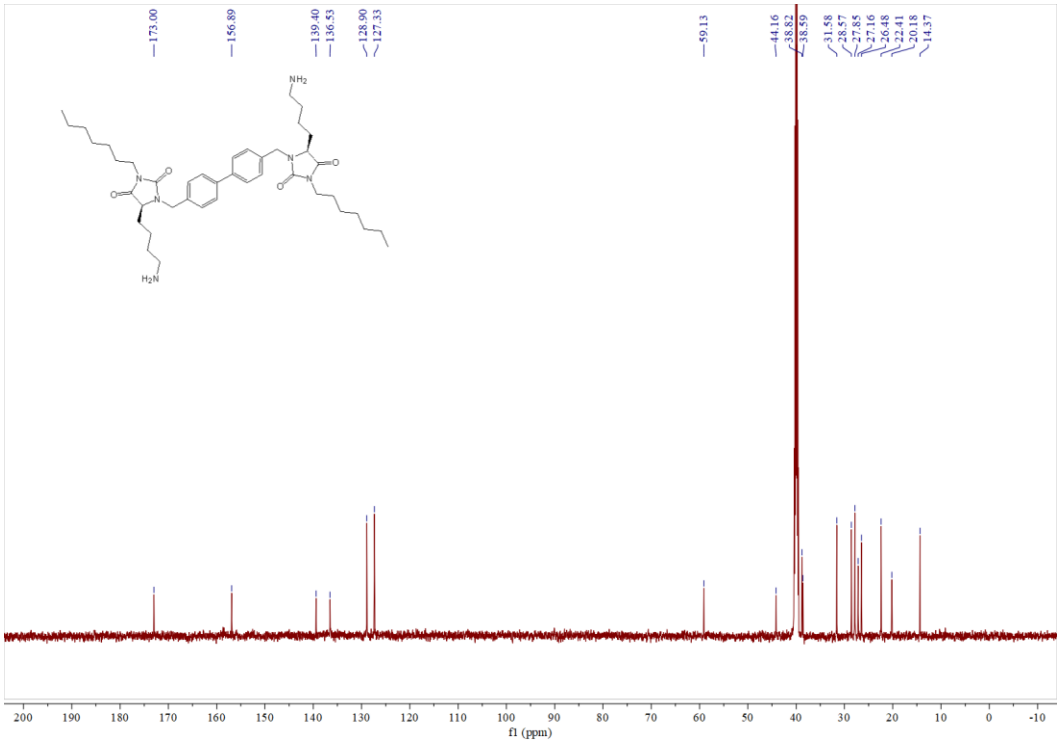
1.97
2.01
3.91
3.99
3.94
7.97
17.96
2.08
6.00
f1 (ppm)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31.58
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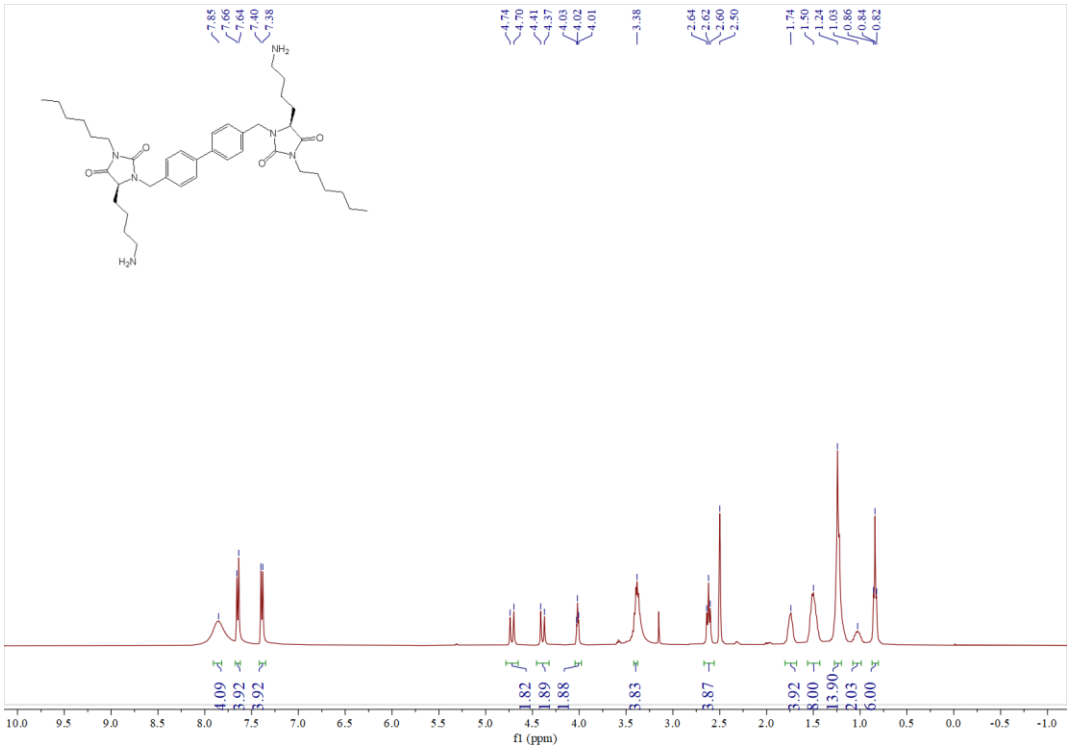
14.37
NH2
H2N
f1 (ppm)

Compound 5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7.66
7.64
7.40
7.38
4.74
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4.41
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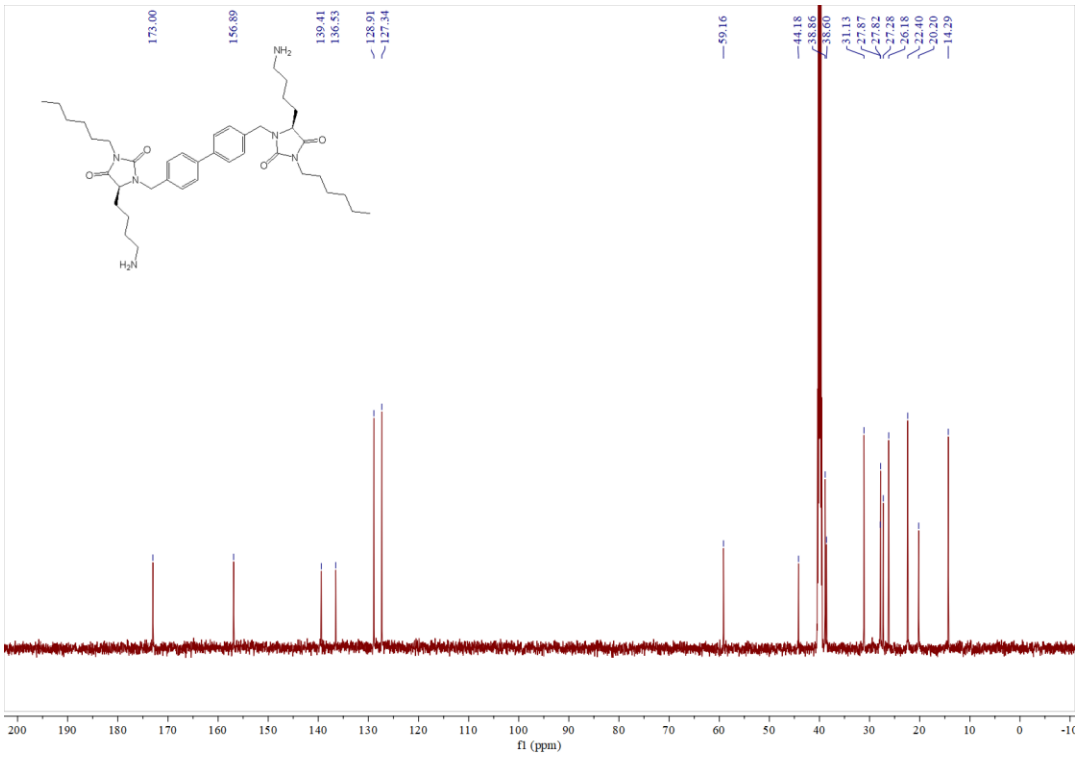
4.03
4.02
4.01
3.38
2.64
2.62
2.60
2.50
1.74
1.50
1.24
1.03
0.86
0.84
0.82
4.09
3.92
3.92
1.82
1.89
1.88
3.83
3.87
3.92
8.00
13.90
2.03
6.00
f1 (ppm)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136.53
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127.34
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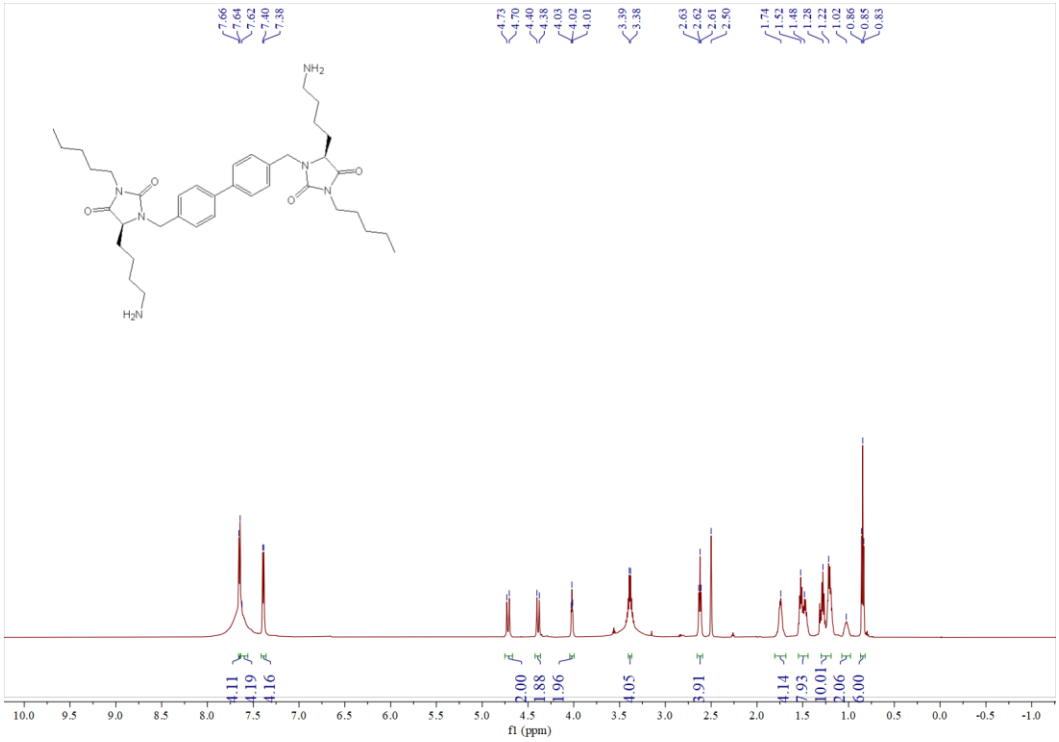
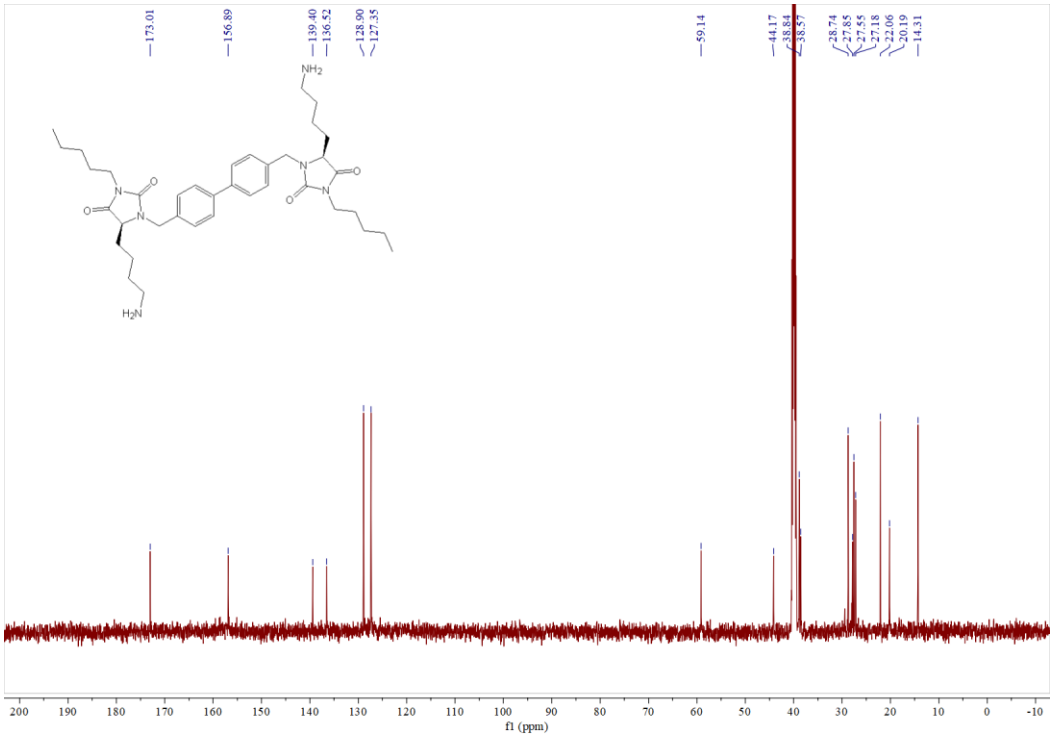
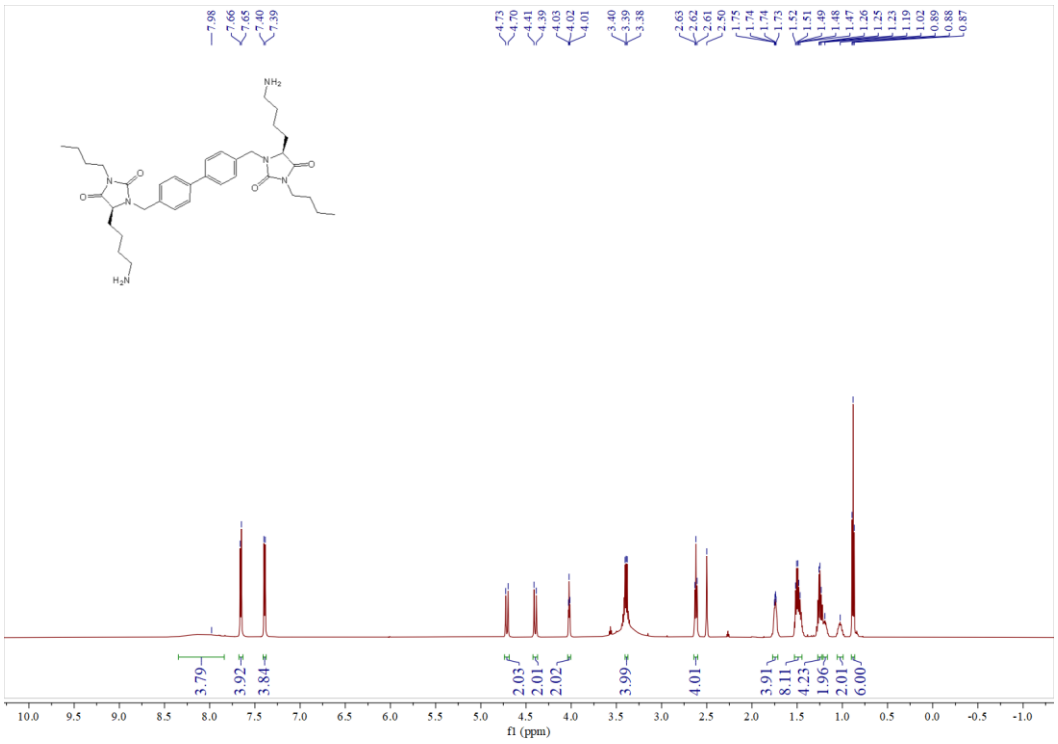
44.18
38.86
38.60
31.13
27.87
27.82
27.28
26.18
22.40
20.20
14.29
f1 (ppm)

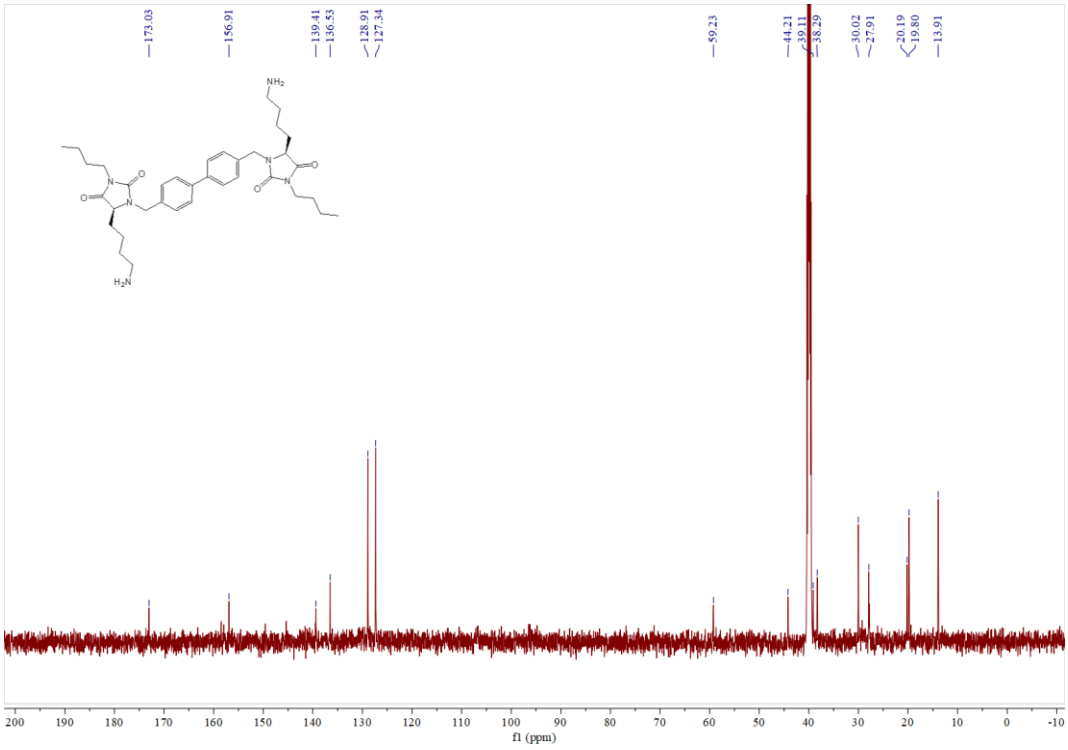
Compound 6


7.66
7.64
7.62
7.40
7.38
4.73
4.70
4.40
4.38
4.03
4.02
4.01
3.39
3.38
2.63
2.62
2.61
2.50
1.74
1.52
1.48
1.28
1.22
1.02
0.86
0.85
0.83
NH2
H2N
4.11
4.19
4.16
2.00
1.88
1.96
4.05
5.91
4.14
7.93
10.01
2.06
6.00
f1 (ppm)

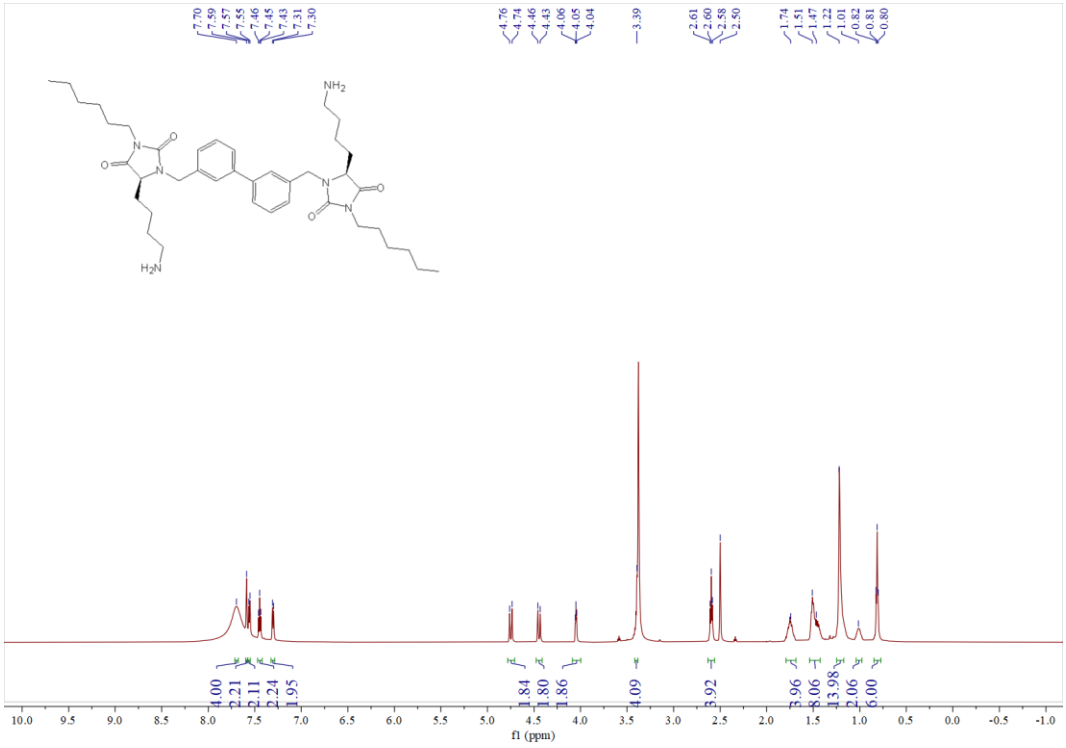

173.01
156.89
139.40
136.52
128.90
127.35
59.14
44.17
38.84
38.57
28.74
27.85
27.55
27.18
22.06
20.19
14.31
NH2
H2N
f1 (ppm)

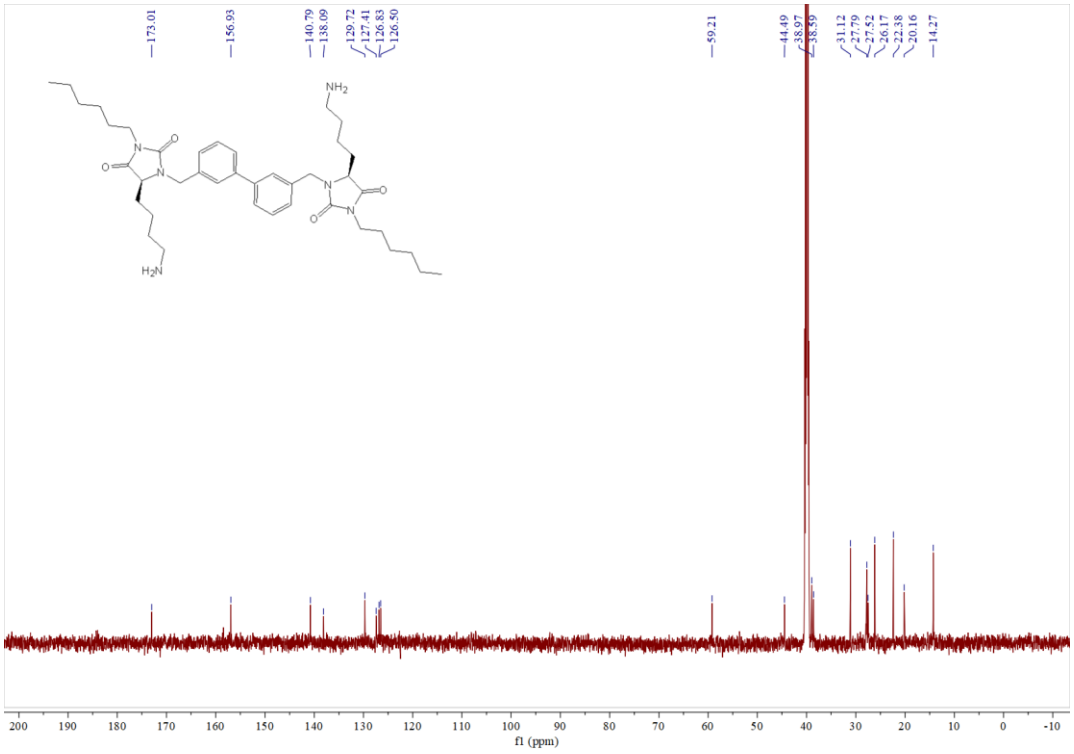
Compound 7


7.98
7.66
7.65
7.40
7.39
4.73
4.70
4.41
4.39
4.03
4.02
4.01
3.40
3.39
3.38
2.63
2.62
2.61
2.50
1.75
1.74
1.74
1.73
1.52
1.51
1.49
1.48
1.47
1.26
1.25
1.23
1.19
1.02
0.89
0.88
0.87
NH2
H2N
3.79
3.92
3.84
2.03
2.01
2.02
3.99
4.01
3.91
8.11
4.23
1.96
2.01
6.00
f1 (ppm)

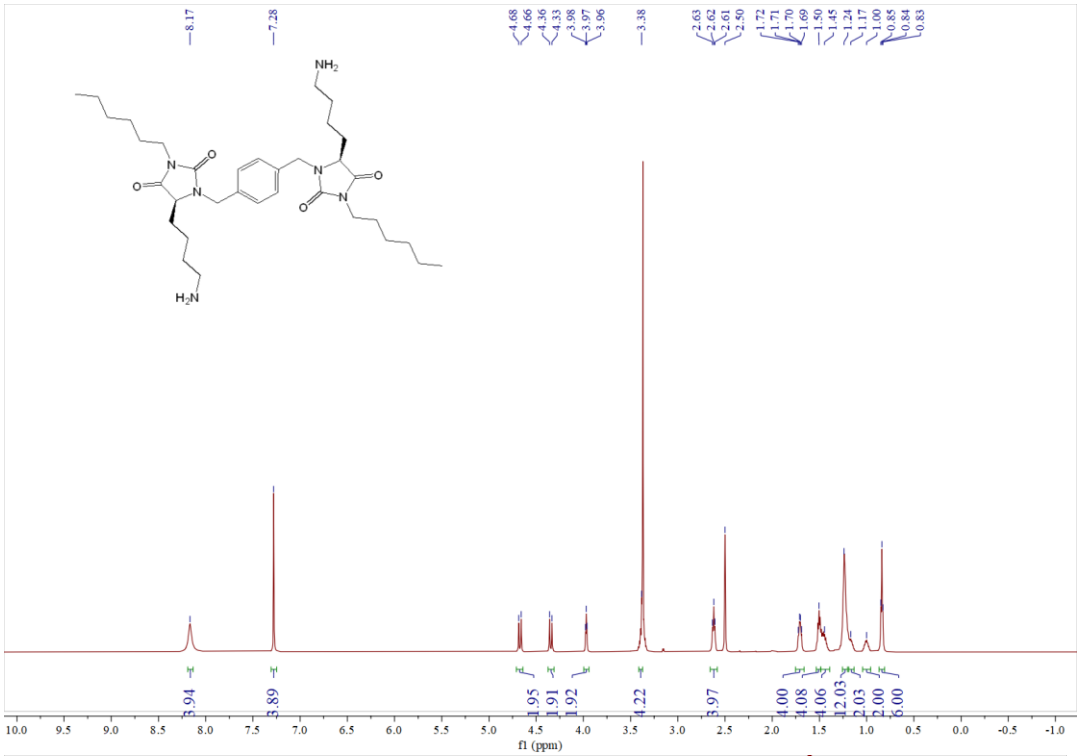

173.03
156.91
139.41
136.53
128.91
127.34
59.23
44.21
39.11
38.29
30.02
27.91
20.19
19.80
13.91
NH2
H2N
f1 (ppm)

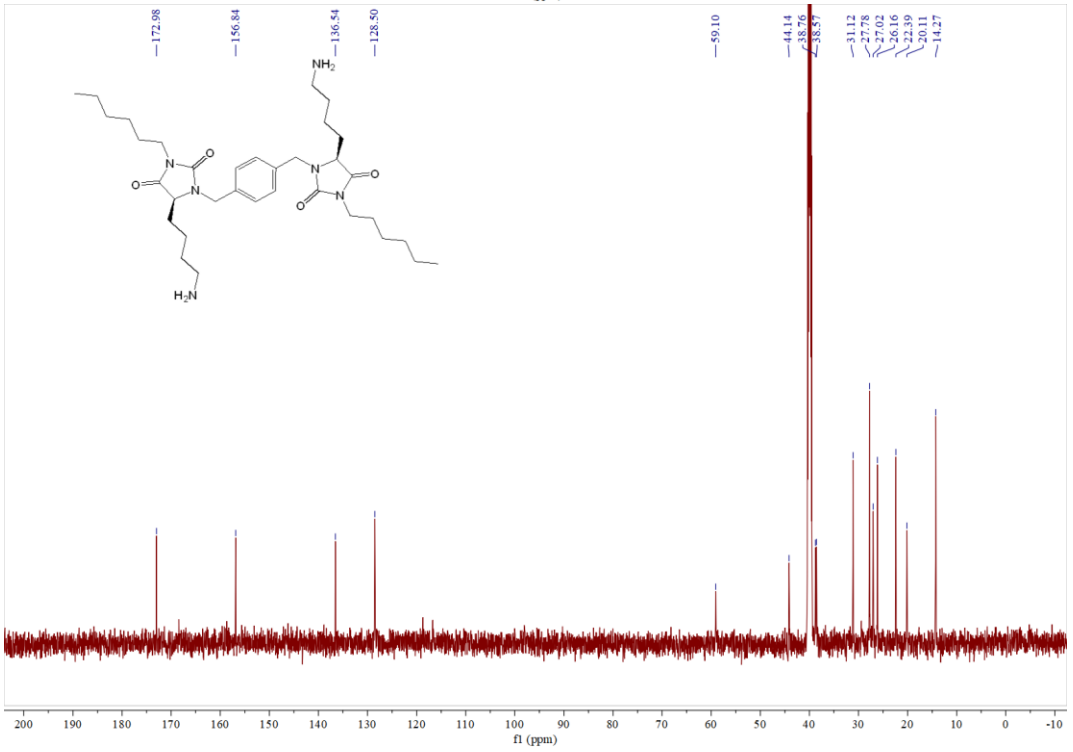
Compound 8


7.70
7.59
7.57
7.55
7.46
7.45
7.43
7.31
7.30
4.76
4.74
4.46
4.43
4.06
4.05
4.04
3.39
2.61
2.60
2.58
2.50
1.74
1.51
1.47
1.22
1.01
0.82
0.81
0.80
NH2
H2N
4.00
2.21
2.11
2.24
1.95
1.84
1.80
1.86
4.09
3.92
3.96
8.06
13.98
2.06
6.00
f1 (ppm)

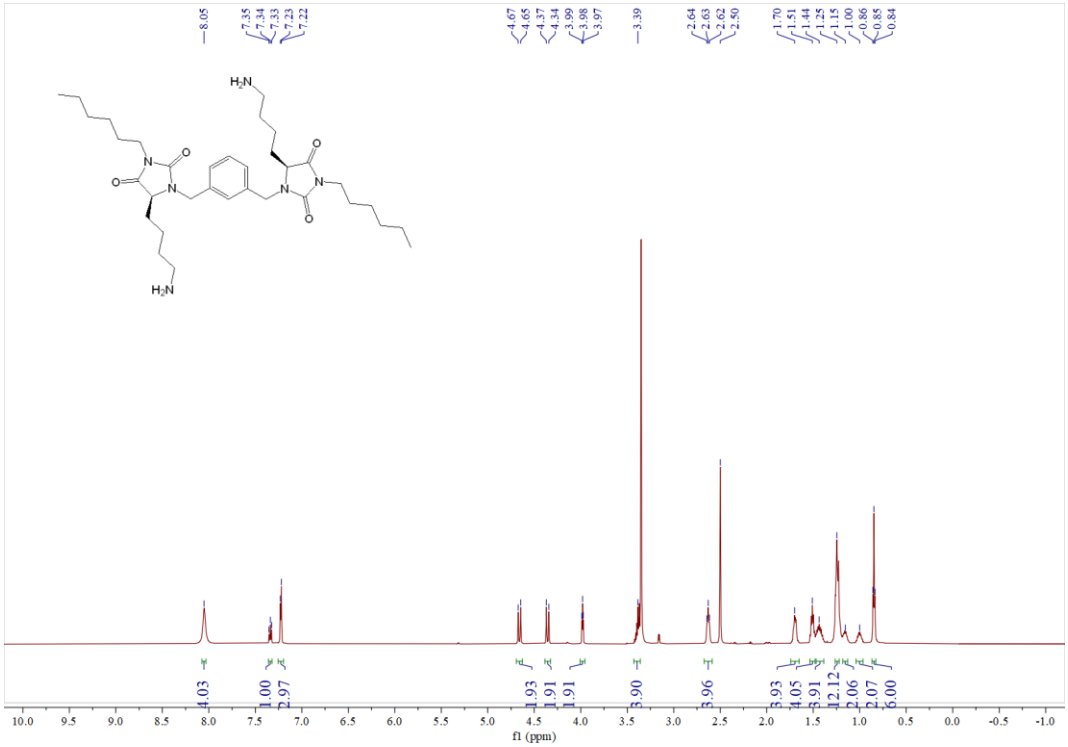

173.01
156.93
140.79
138.09
129.72
127.41
126.83
126.50
59.21
44.49
38.97
38.59
31.12
27.79
27.52
26.17
22.38
20.16
14.27
NH2
H2N
f1 (ppm)

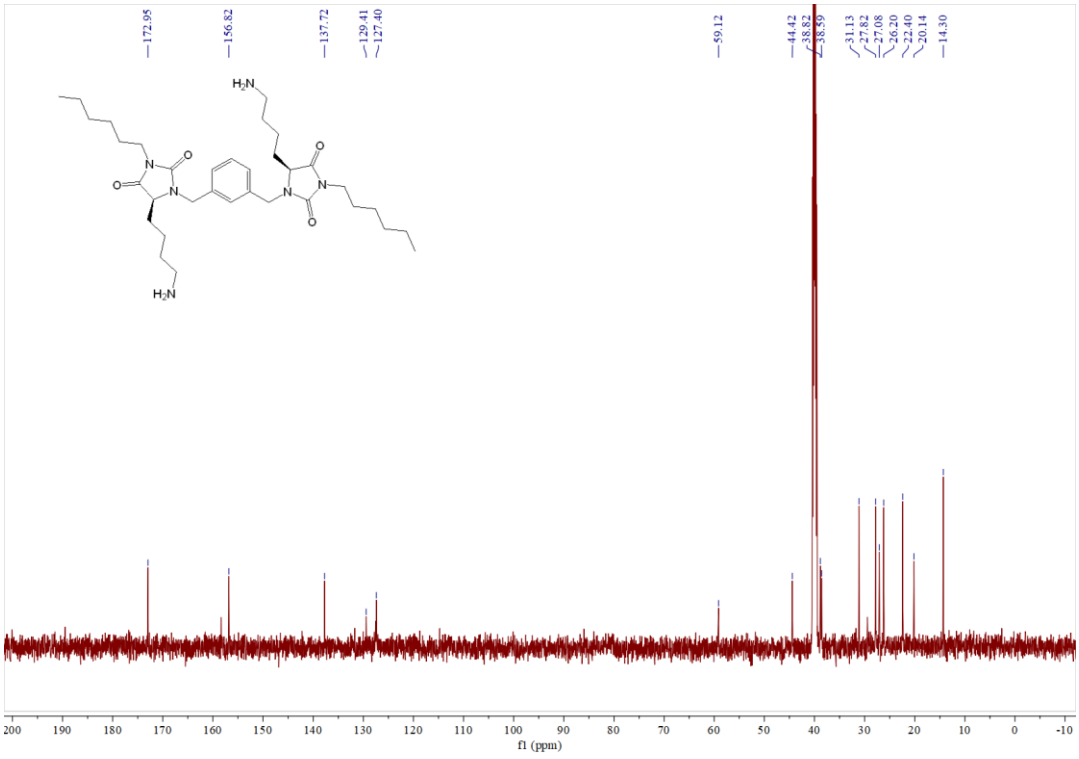
Compound 9


8.17
7.28
4.68
4.66
4.36
4.33
3.98
3.97
3.96
3.38
2.63
2.62
2.61
2.50
1.72
1.71
1.70
1.69
1.50
1.45
1.24
1.17
1.00
0.85
0.84
0.83
NH2
H2N
3.94
3.89
1.95
1.91
1.92
4.22
3.97
4.00
4.08
4.06
12.03
2.03
2.00
6.00
f1 (ppm)

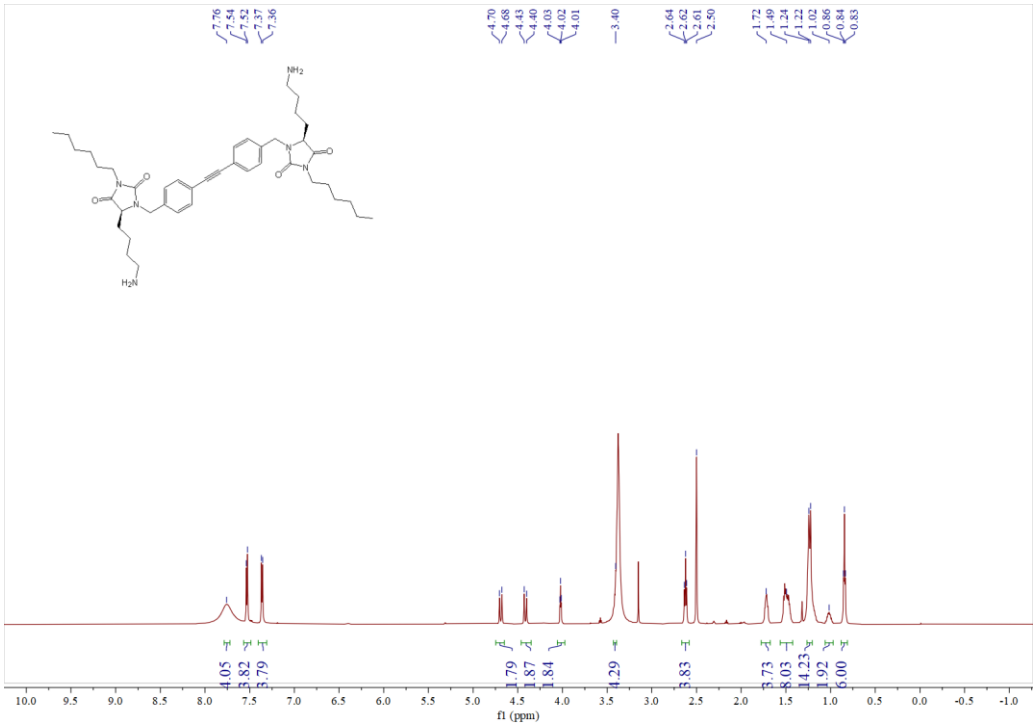

172.98
156.84
136.54
128.50
59.10
44.14
38.76
38.57
31.12
27.78
27.02
26.16
22.39
20.11
14.27
NH2
H2N
f1 (ppm)

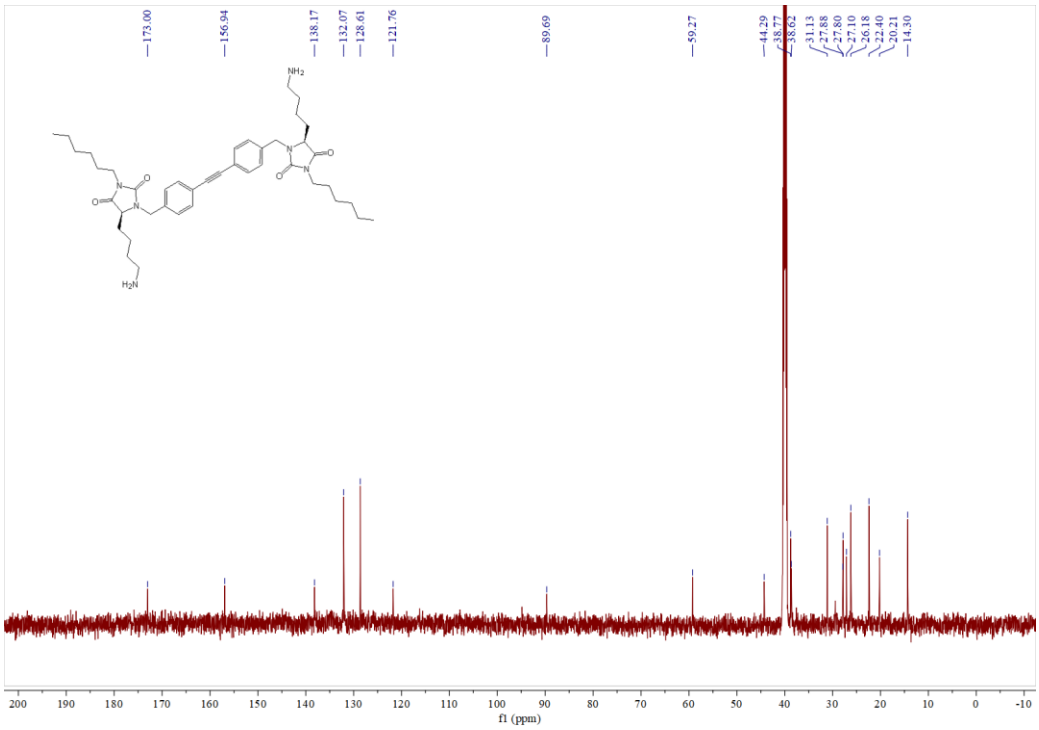
Compound 10


8.05
7.35
7.34
7.33
7.23
7.22
4.67
4.65
4.37
4.34
3.99
3.98
3.97
3.39
2.64
2.63
2.62
2.50
1.70
1.51
1.44
1.25
1.15
1.00
0.86
0.85
0.84
4.03
1.00
2.97
1.93
1.91
1.91
3.90
3.96
3.93
4.05
3.91
12.12
2.06
2.07
6.00
f1 (ppm)

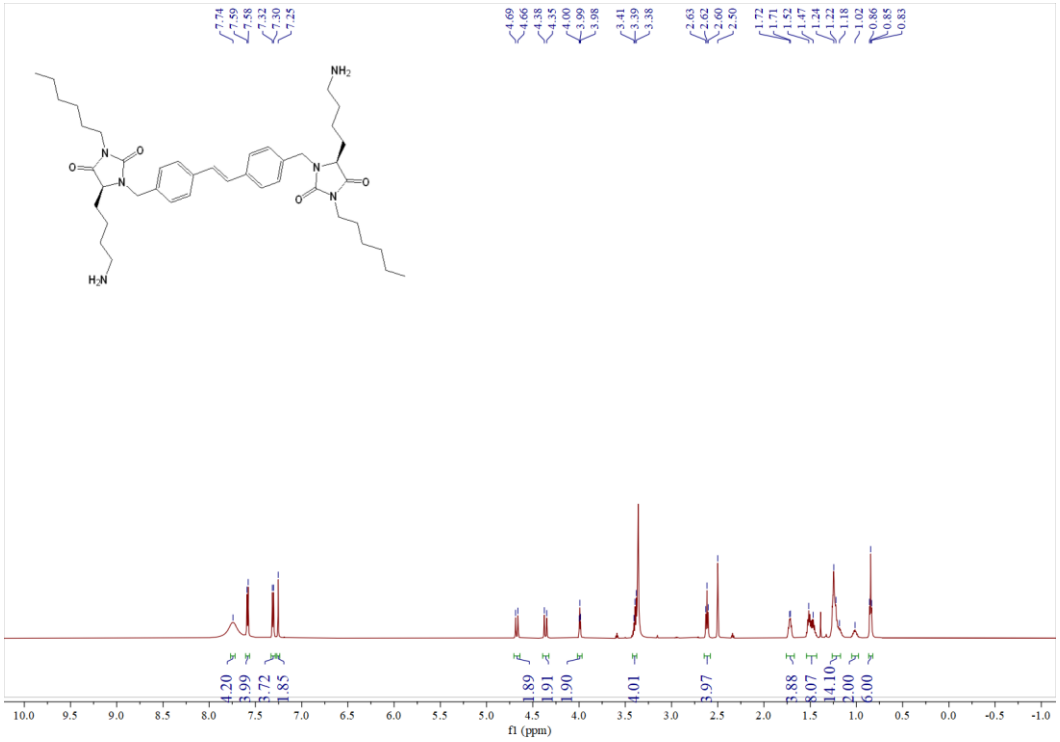

172.95
156.82
137.72
129.41
127.40
59.12
44.42
38.82
38.59
31.13
27.82
27.08
26.20
22.40
20.14
14.30
f1 (ppm)

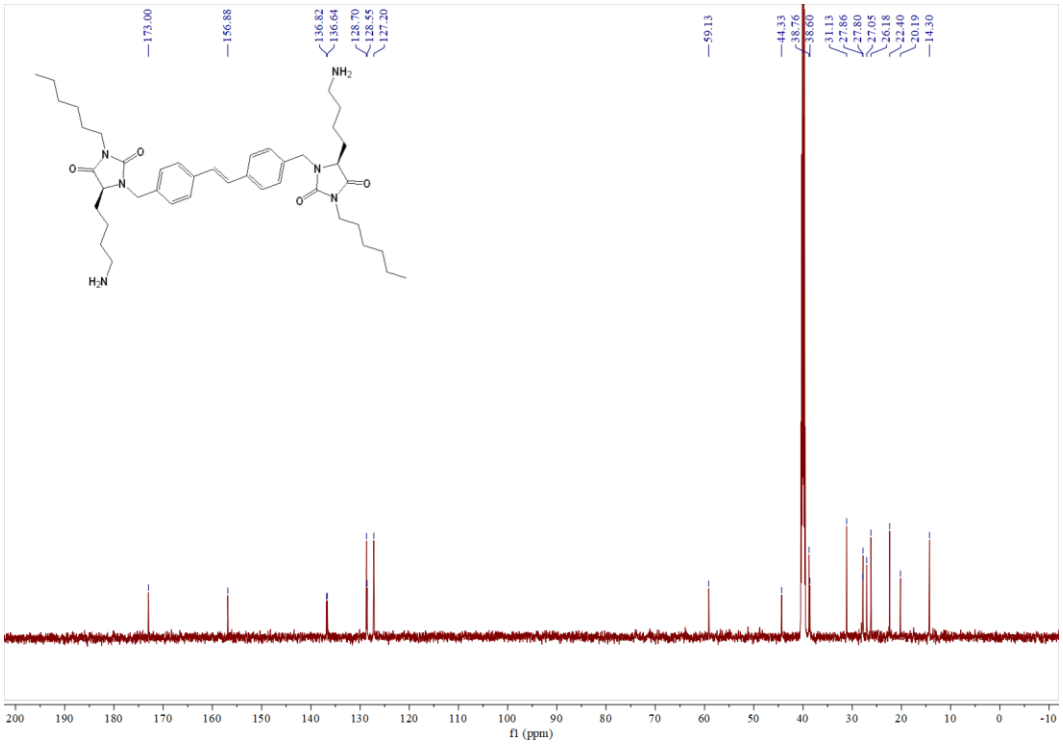
Compound 11


7.76
7.54
7.52
7.37
7.36
4.70
4.68
4.43
4.40
4.03
4.02
4.01
3.40
2.64
2.62
2.61
2.50
1.72
1.49
1.24
1.22
1.02
0.86
0.84
0.83
NH2
H2N
4.05
3.82
3.79
1.79
1.87
1.84
4.29
3.83
3.73
8.03
14.23
1.92
6.00
f1 (ppm)

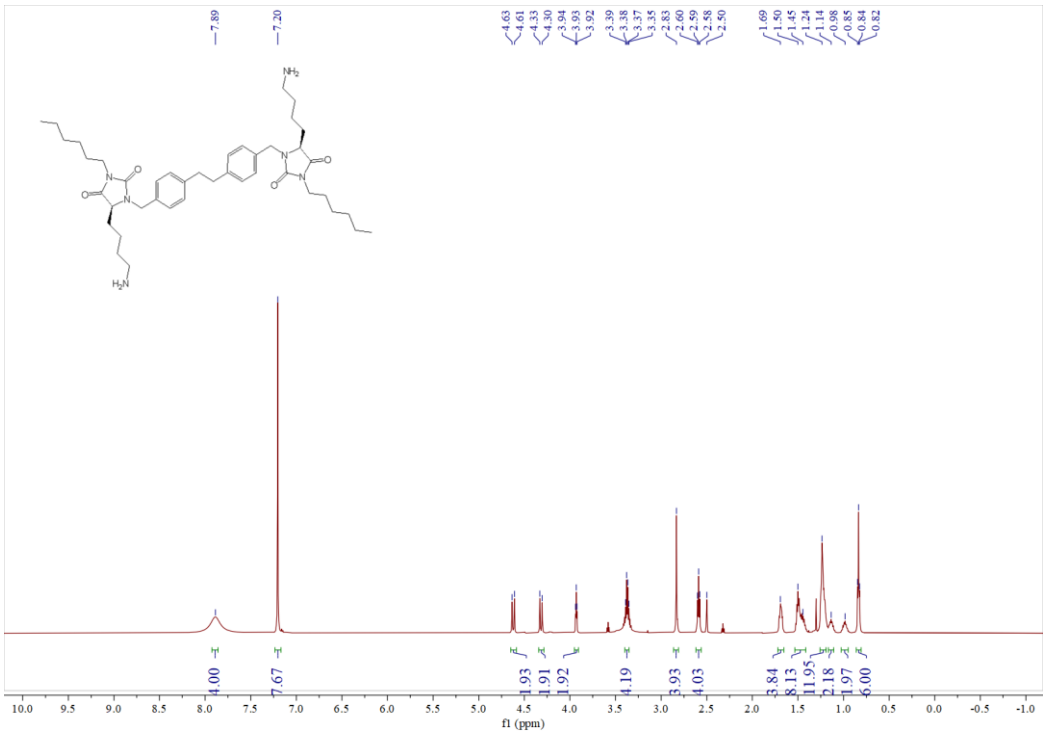

173.00
156.94
138.17
132.07
128.61
121.76
89.69
59.27
44.29
38.77
38.62
31.13
27.88
27.80
27.10
26.18
22.40
20.21
14.30
NH2
H2N
f1 (ppm)

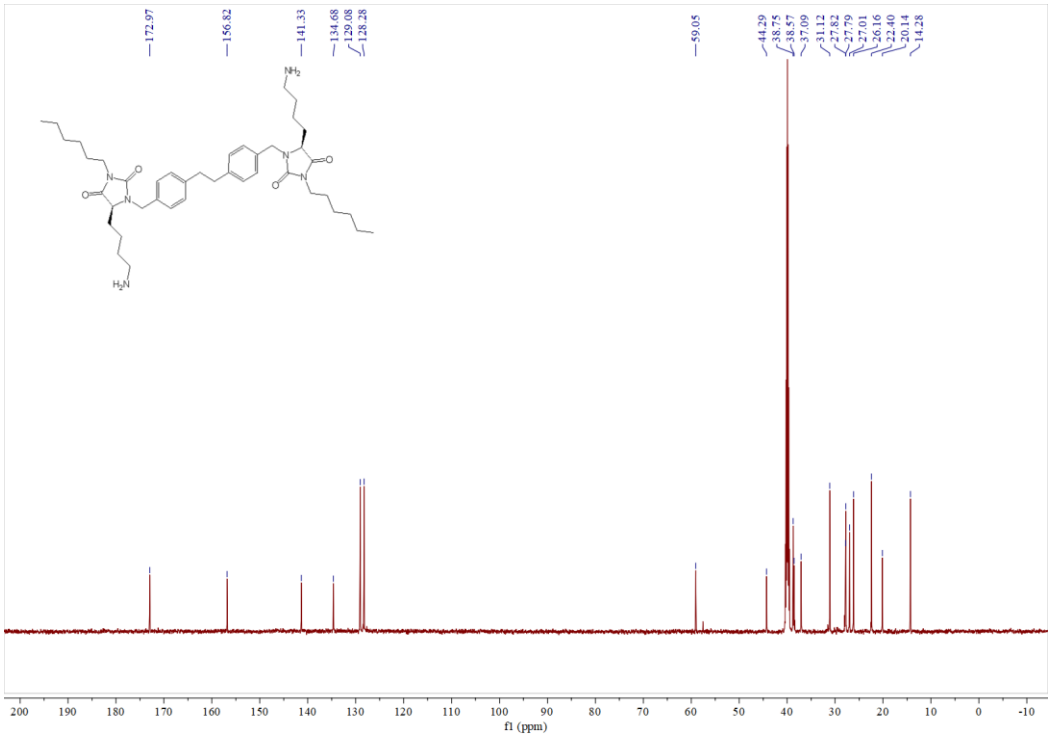
Compound 12


7.74
7.59
7.58
7.32
7.30
7.25
4.69
4.66
4.38
4.35
4.00
3.99
3.98
3.41
3.39
3.38
2.63
2.62
2.60
2.50
1.72
1.71
1.52
1.47
1.24
1.22
1.18
1.02
0.86
0.85
0.83
NH2
H2N
4.20
5.99
3.72
1.85
1.89
1.91
1.90
4.01
5.97
3.88
8.07
14.10
2.00
6.00
f1 (ppm)

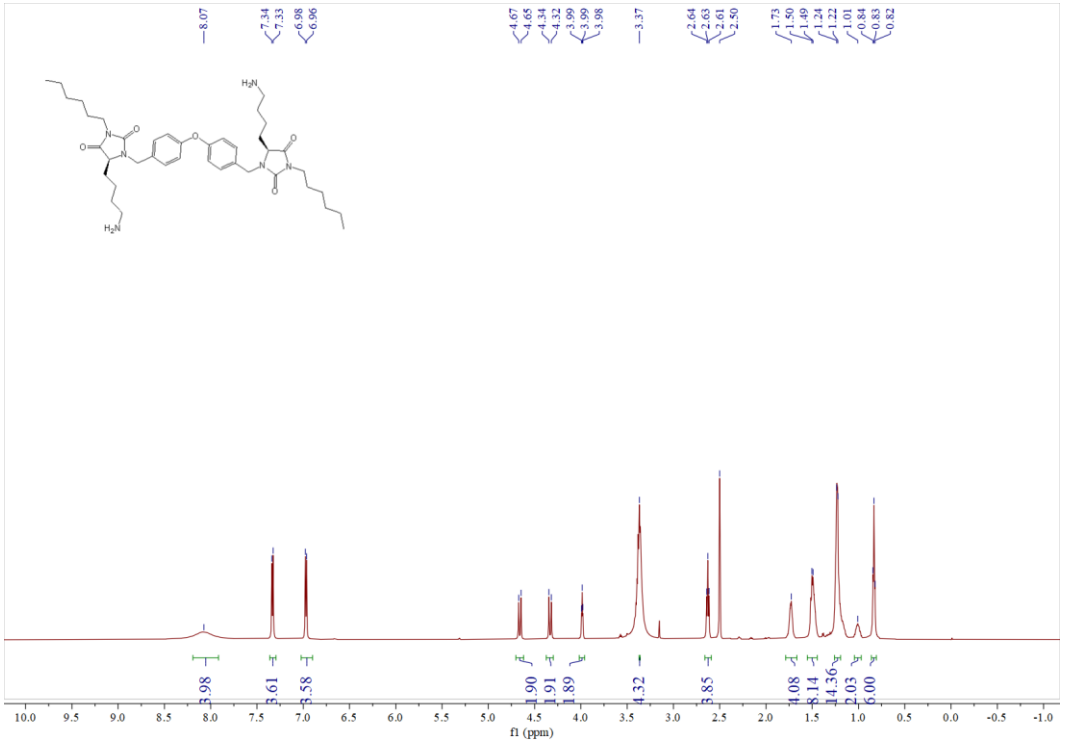

173.00
156.88
136.82
136.64
128.70
128.55
127.20
59.13
44.33
38.76
38.60
31.13
27.86
27.80
27.05
26.18
22.40
20.19
14.30
NH2
H2N
f1 (ppm)

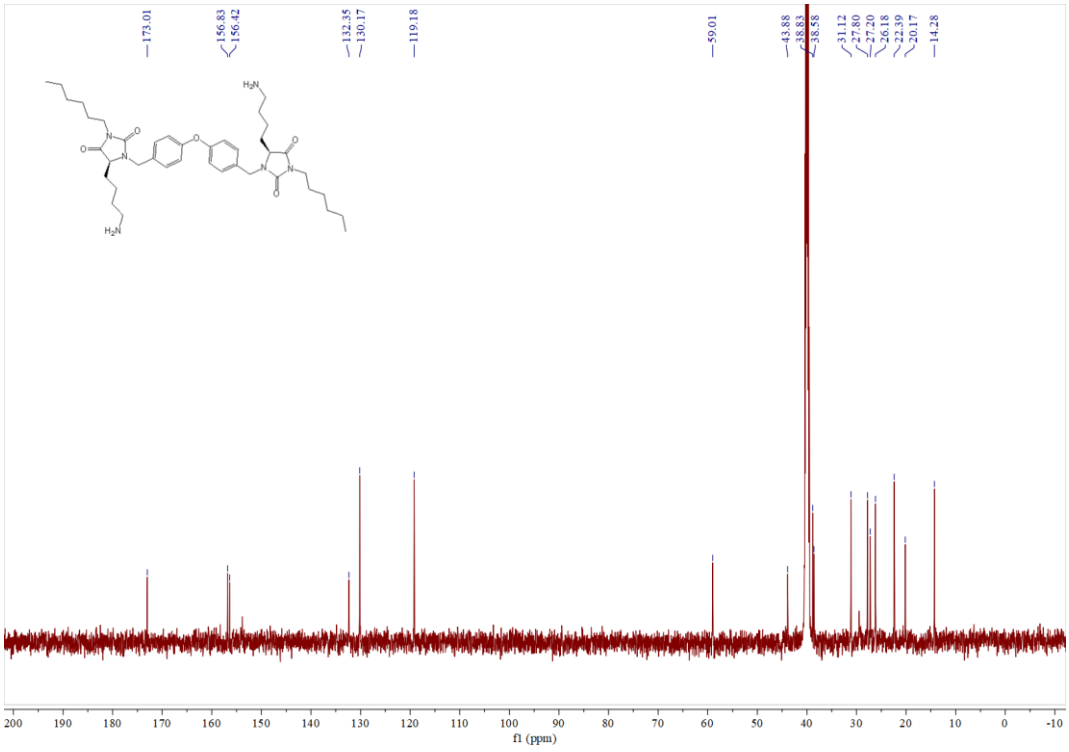
Compound 13


7.89
7.20
4.63
4.61
4.33
4.30
3.94
3.93
3.92
3.39
3.38
3.37
3.35
2.83
2.60
2.59
2.58
2.50
1.69
1.50
1.45
1.24
1.14
0.98
0.85
0.84
0.82
NH2
H2N
4.00
7.67
1.93
1.91
1.92
4.19
3.93
4.03
3.84
8.13
11.95
2.18
1.97
6.00
f1 (ppm)

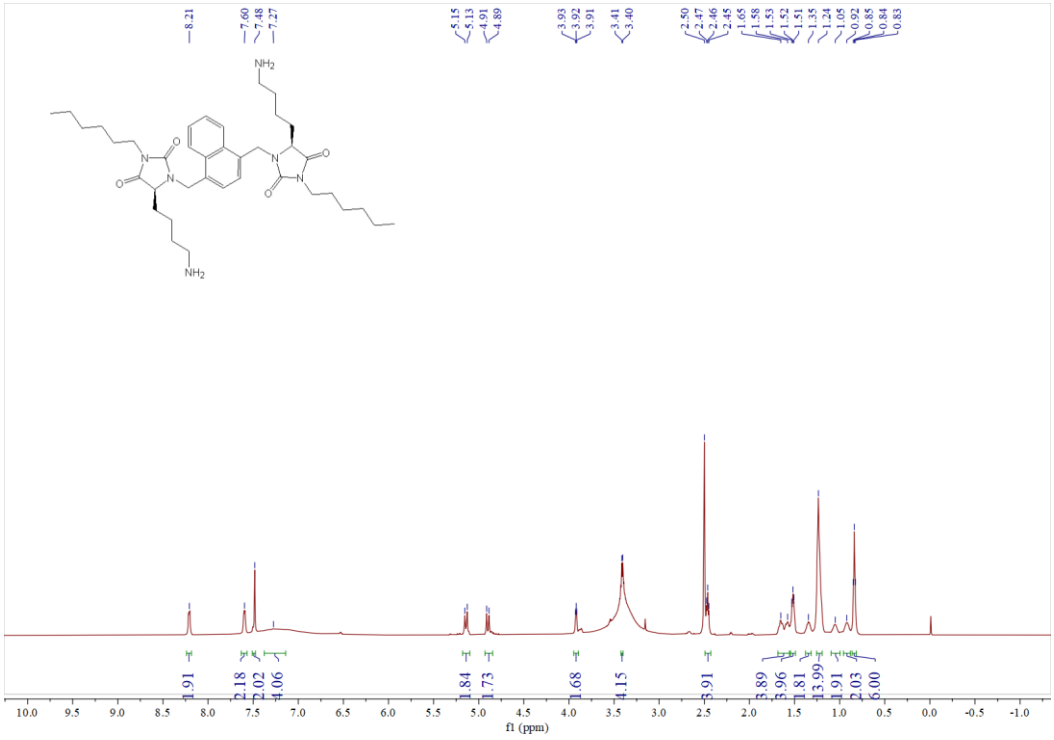

172.97
156.82
141.33
134.68
129.08
128.28
59.05
44.29
38.75
38.57
37.09
31.12
27.82
27.79
27.01
26.16
22.40
20.14
14.28
NH2
H2N
f1 (ppm)

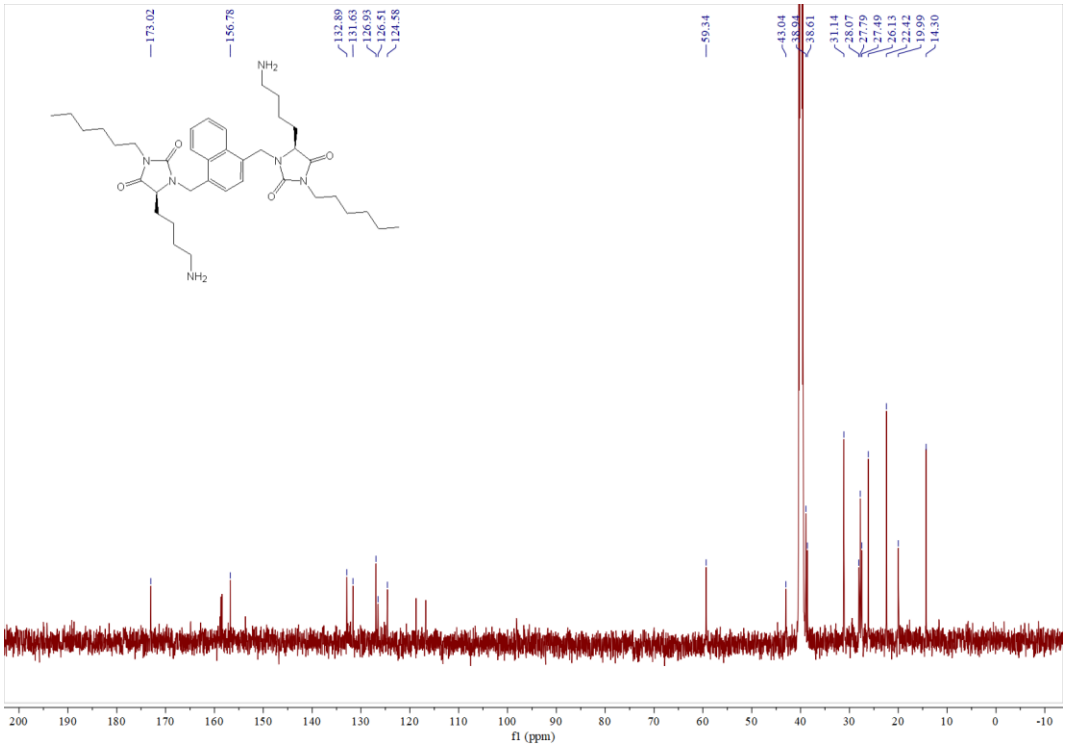
Compound 14


8.07
7.34
7.33
6.98
6.96
4.67
4.65
4.34
4.32
3.99
3.99
3.98
3.37
2.64
2.63
2.61
2.50
1.73
1.50
1.49
1.24
1.22
1.01
0.84
0.83
0.82
5.98
3.61
3.58
1.90
1.91
1.89
4.32
5.85
4.08
8.14
14.36
2.03
6.00
f1 (ppm)

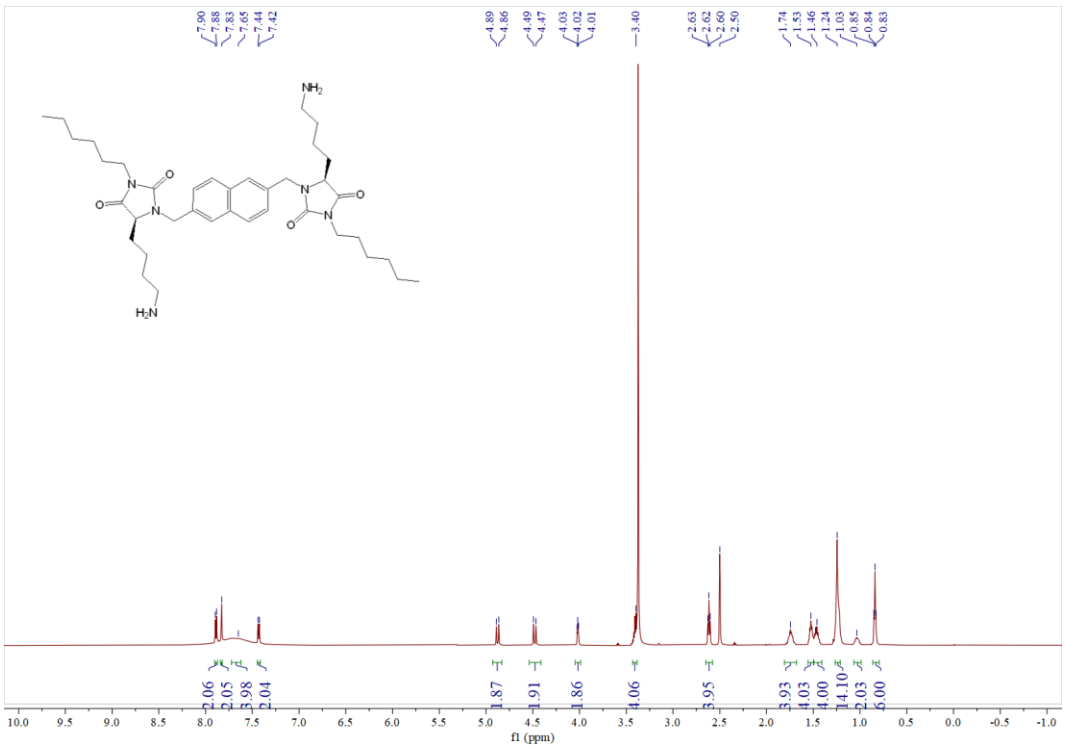

173.01
156.83
156.42
132.35
130.17
119.18
59.01
43.88
38.83
38.56
31.12
27.80
27.20
26.18
22.39
20.17
14.28
f1 (ppm)

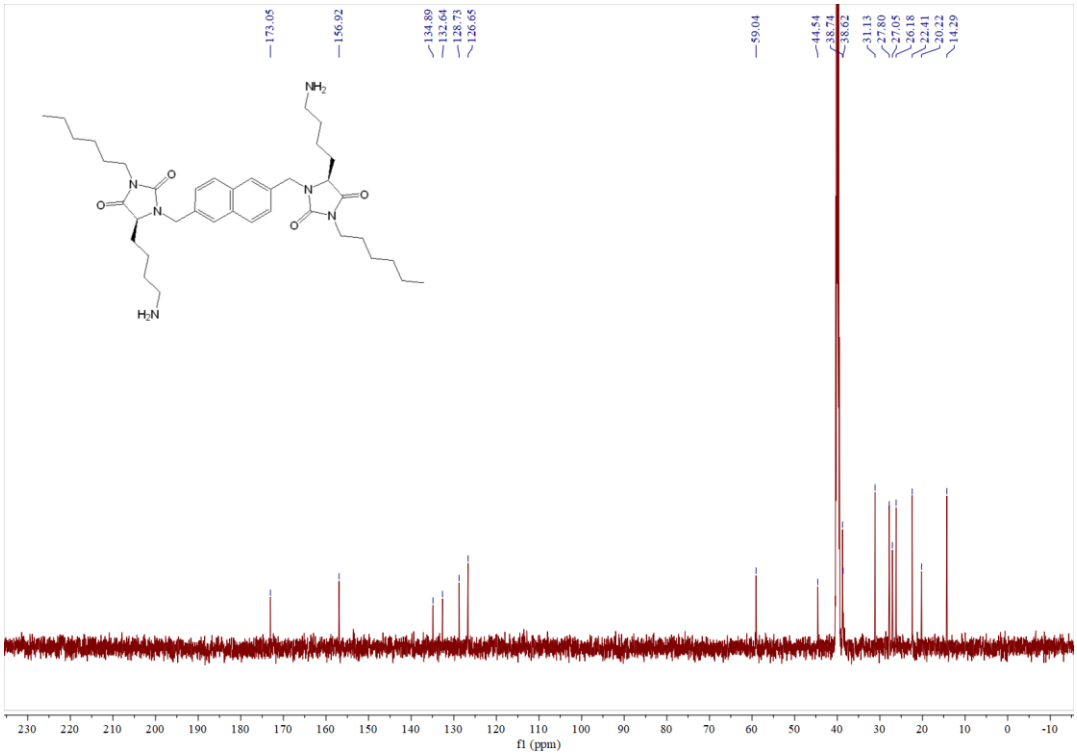
Compound 15


8.21
7.60
7.48
7.27
5.15
5.13
4.91
4.89
3.93
3.92
3.91
3.41
3.40
2.50
2.47
2.46
2.45
1.65
1.58
1.53
1.52
1.51
1.35
1.24
1.05
0.92
0.85
0.84
0.83
NH2
NH2
1.91
2.18
2.02
4.06
1.84
1.73
1.68
4.15
5.91
3.89
5.96
1.81
13.99
1.91
2.03
5.00
f1 (ppm)

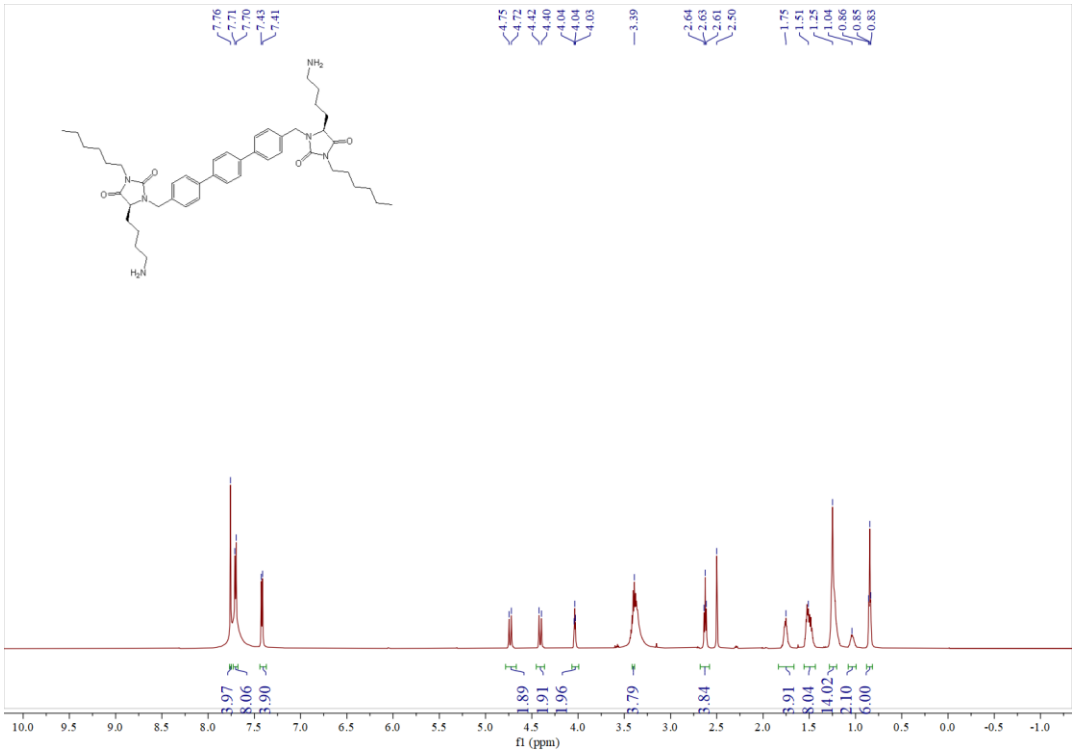

173.02
156.78
132.89
131.65
126.93
126.51
124.58
59.34
43.04
38.94
38.61
31.14
28.07
27.79
27.49
26.13
22.42
19.99
14.30
NH2
NH2
f1 (ppm)

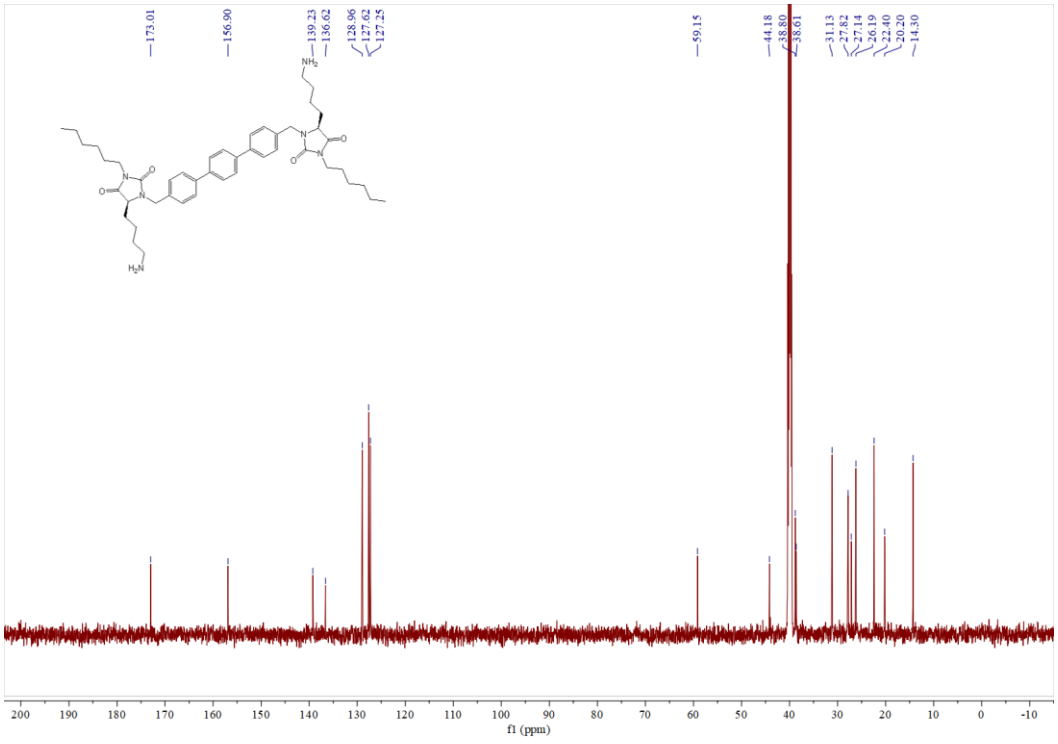
Compound 16


7.90
7.88
7.83
7.65
7.44
7.42
4.89
4.86
4.49
4.47
4.03
4.02
4.01
3.40
2.63
2.62
2.60
2.50
1.74
1.53
1.46
1.24
1.03
0.85
0.84
0.83
NH2
H2N
2.06
2.05
3.98
2.04
1.87
1.91
1.86
4.06
3.95
3.93
4.03
4.00
14.10
2.03
6.00
f1 (ppm)

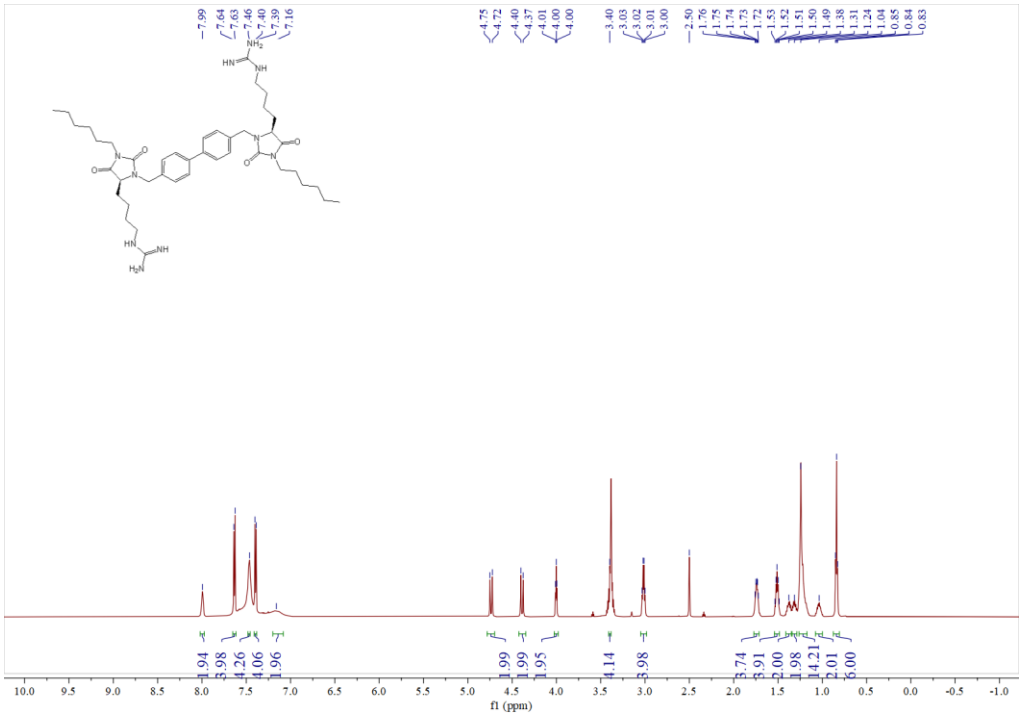

173.05
156.92
134.89
132.64
128.73
126.65
59.04
44.54
38.74
38.62
31.13
27.80
27.05
26.18
22.41
20.22
14.29
NH2
H2N
f1 (ppm)

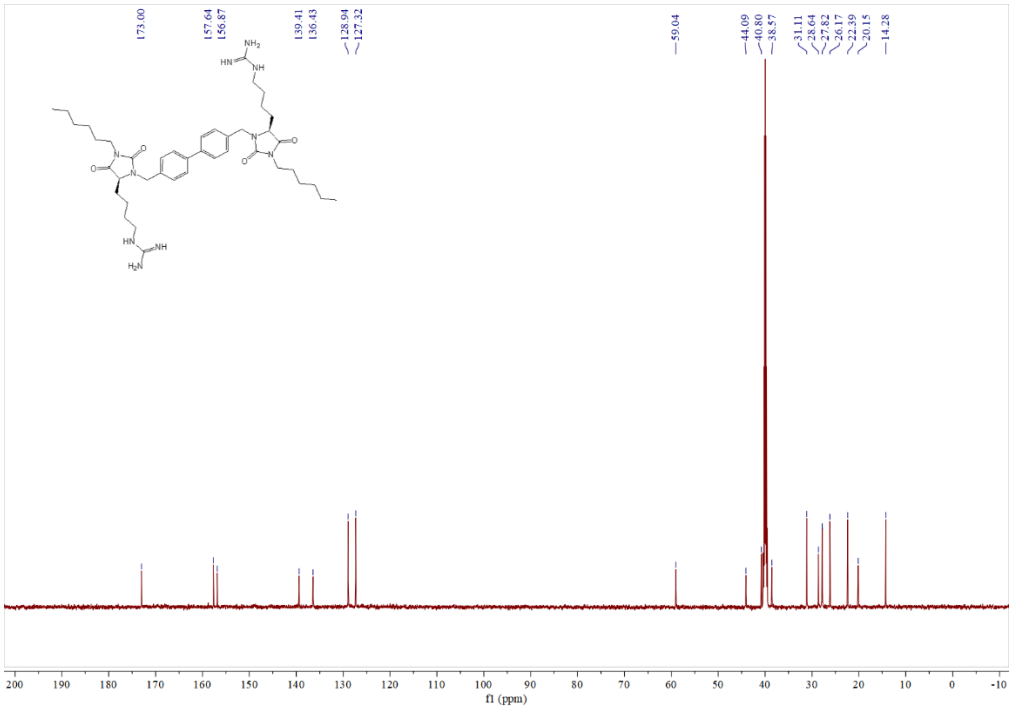
Compound 17


7.76
7.71
7.70
7.43
7.41
4.75
4.72
4.42
4.40
4.04
4.04
4.03
3.39
2.64
2.63
2.61
2.50
1.75
1.51
1.25
1.04
0.86
0.85
0.83
3.97
8.06
3.90
1.89
1.91
1.96
3.79
3.84
3.91
8.04
14.02
2.10
6.00
f1 (ppm)

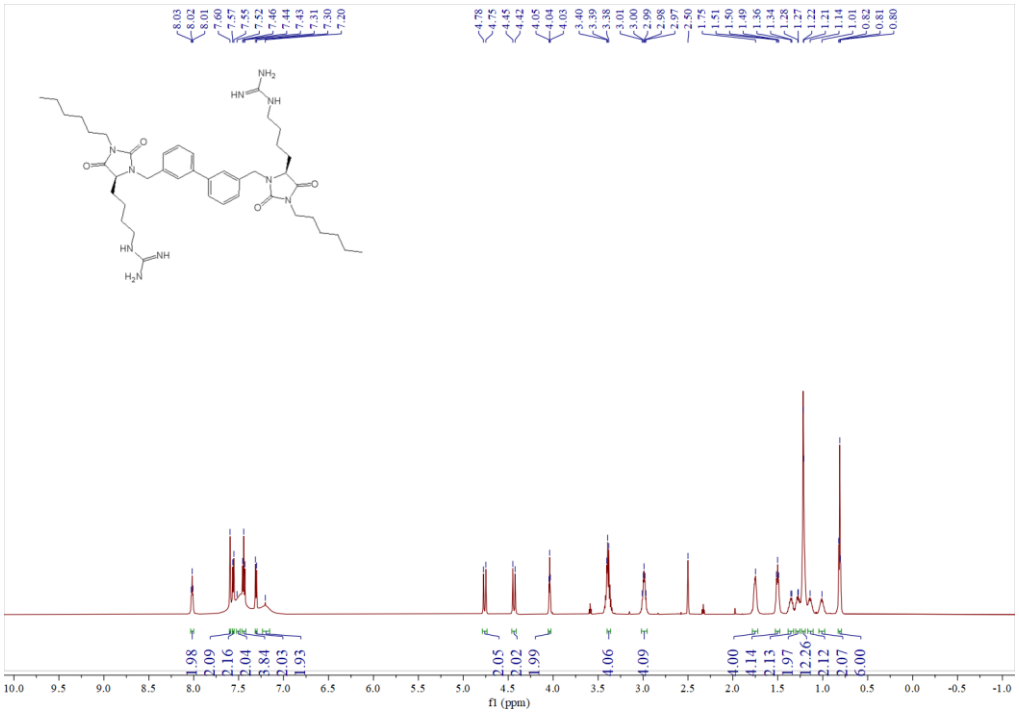

173.01
156.90
139.23
136.62
128.96
127.62
127.25
59.15
44.18
38.80
38.61
31.13
27.82
27.14
26.19
22.40
20.20
14.30
f1 (ppm)

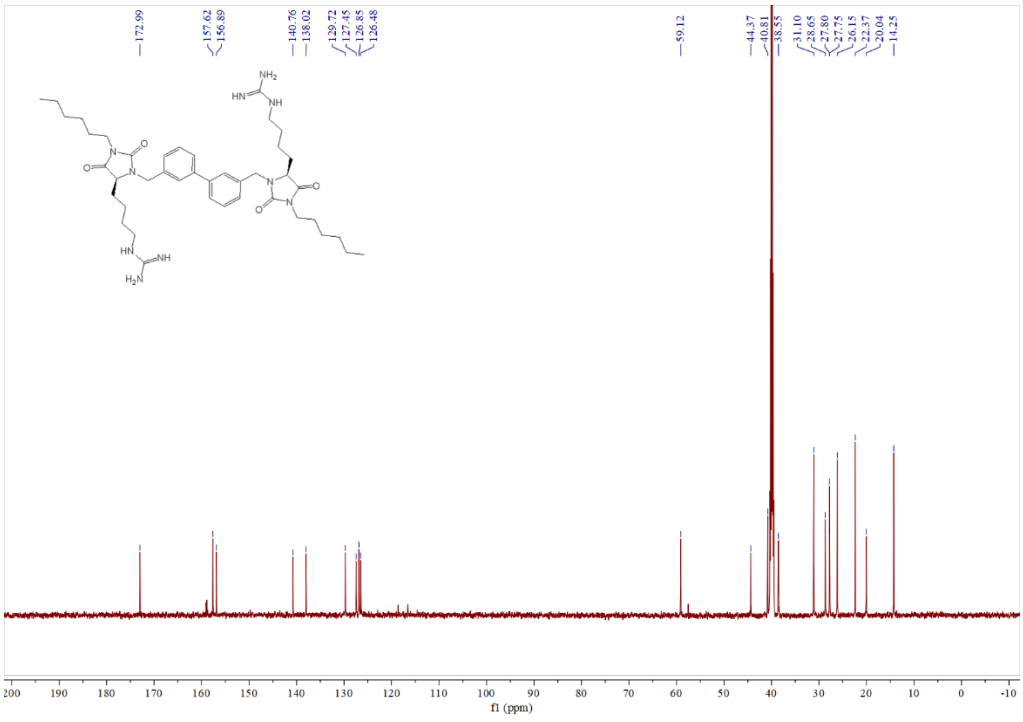
Compound 18


7.99
7.64
7.63
7.46
7.40
7.39
7.16
4.75
4.72
4.40
4.37
4.01
4.00
4.00
3.40
3.03
3.02
3.01
3.00
2.50
1.76
1.75
1.74
1.73
1.72
1.55
1.52
1.51
1.50
1.49
1.38
1.31
1.24
1.04
0.85
0.84
0.83
1.94
3.98
4.26
4.06
1.96
1.99
1.99
1.95
4.14
3.98
3.74
3.91
2.00
1.98
14.21
2.01
6.00
f1 (ppm)

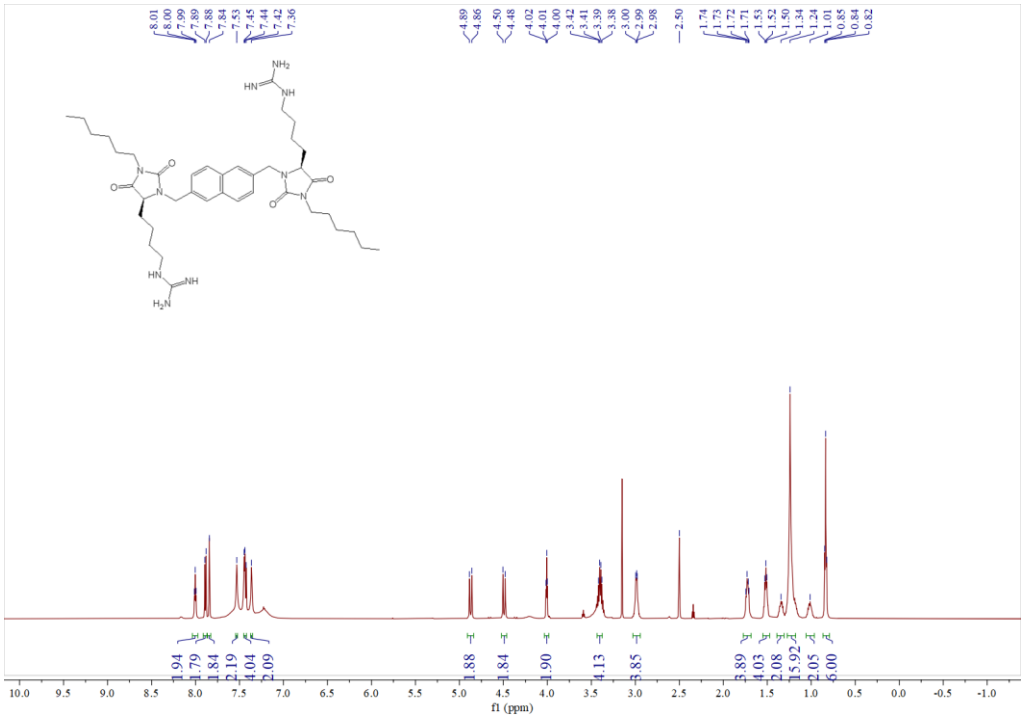

173.00
157.64
156.87
139.41
136.43
128.94
127.32
59.04
44.69
40.80
38.57
31.11
28.64
27.82
26.17
22.39
20.15
14.28
f1 (ppm)

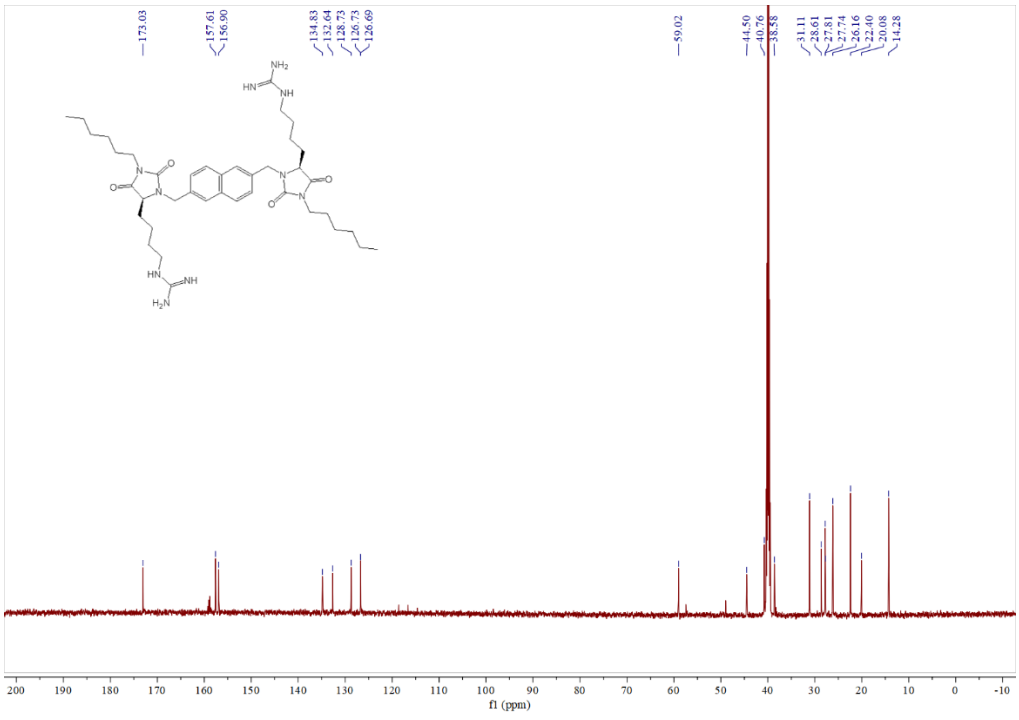
Compound 19


8.03
8.02
8.01
7.60
7.57
7.55
7.52
7.46
7.44
7.43
7.31
7.30
7.20
4.78
4.75
4.45
4.42
4.05
4.04
4.03
3.40
3.39
3.38
3.01
3.00
2.99
2.98
2.97
2.50
1.75
1.51
1.50
1.49
1.36
1.34
1.28
1.27
1.22
1.21
1.14
1.01
0.82
0.81
0.80
1.98
2.09
2.16
2.04
5.84
2.03
1.93
2.05
2.02
1.99
4.06
4.09
4.00
4.14
2.13
1.97
12.26
2.12
2.07
6.00
f1 (ppm)


172.99
157.62
156.89
140.76
138.02
129.72
127.45
126.85
126.48
59.12
44.37
40.81
38.55
31.10
28.65
27.80
27.75
26.15
22.37
20.04
14.25
f1 (ppm)

Compound 20





14. HPLC analysis of compounds 1–20.

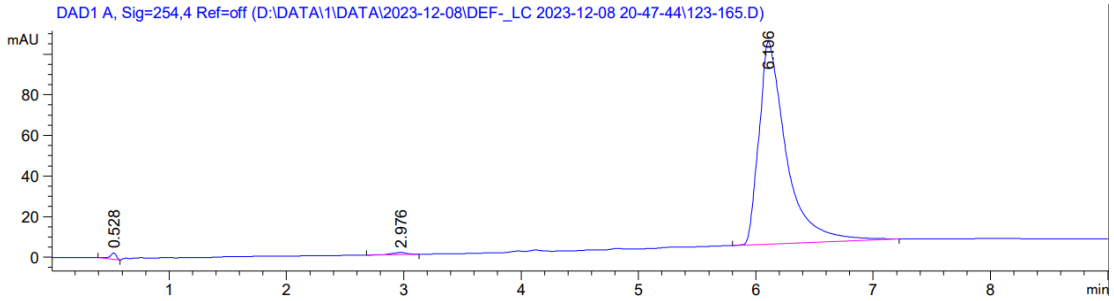
Table S1. Purity of compounds **1**–**20** (under 254 nm).

Compound	Purity (%)	Compound	Purity (%)
1	99.7	**11**	99.5

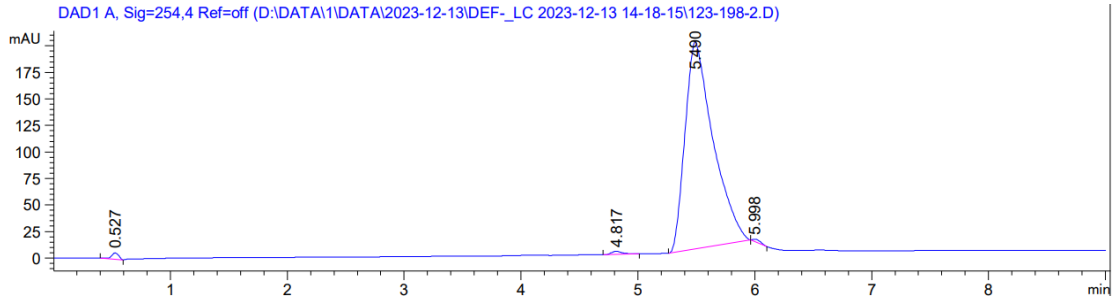
2	98.3	**12**	95.2
3	99.6	**13**	98.0
4	99.7	**14**	95.8
5	99.6	**15**	95.9
6	99.5	**16**	96.7
7	98.6	**17**	99.4
8	99.4	**18**	99.6
9	97.1	**19**	99.2
10	96.0	**20**	98.6

HPLC spectra of compounds 1–20

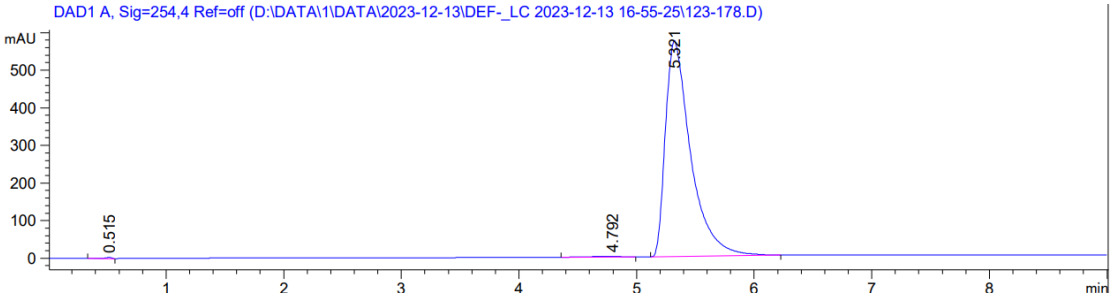
Compound 1



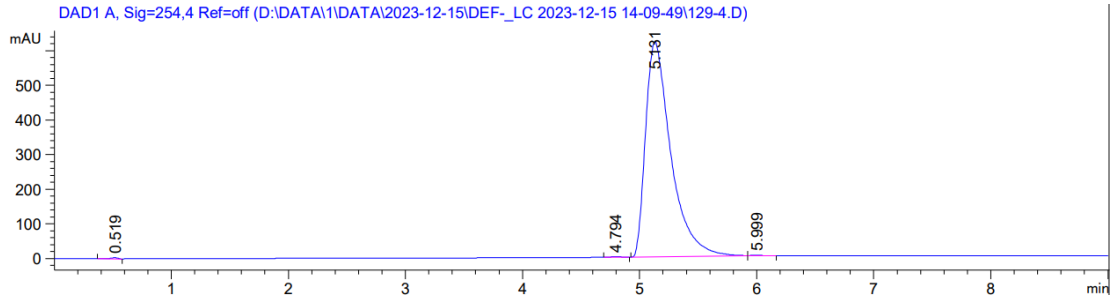
Compound 2



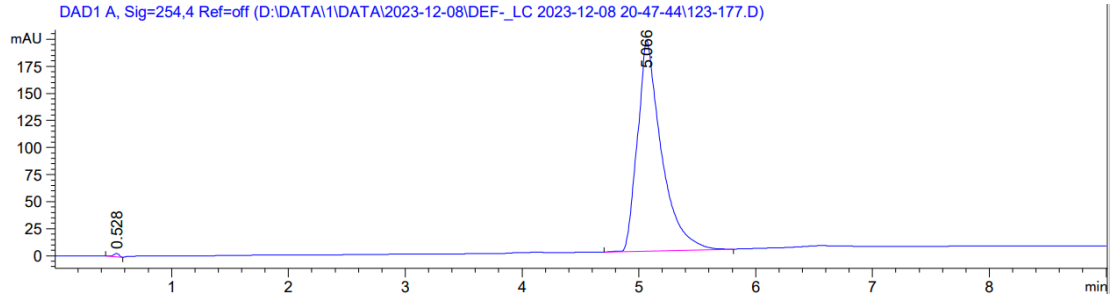
Compound 3



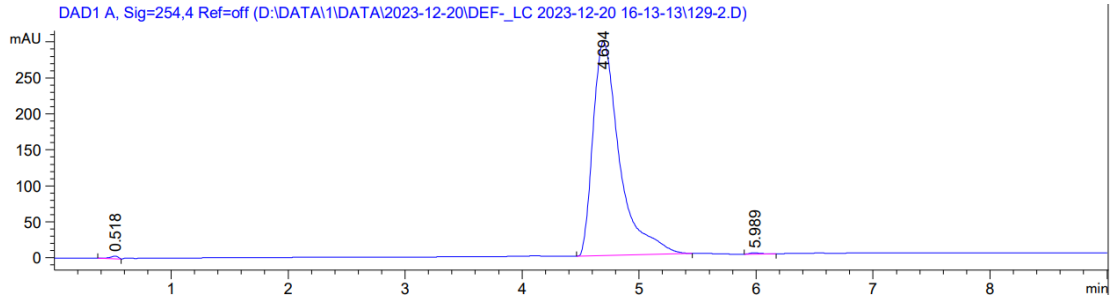
Compound 4



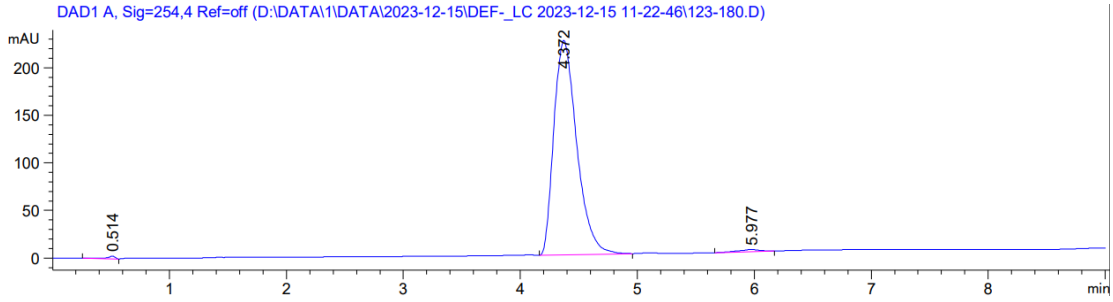
Compound 5



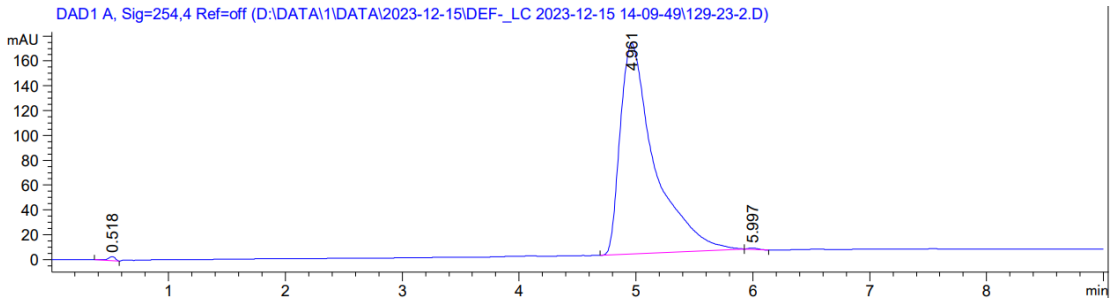
Compound 6



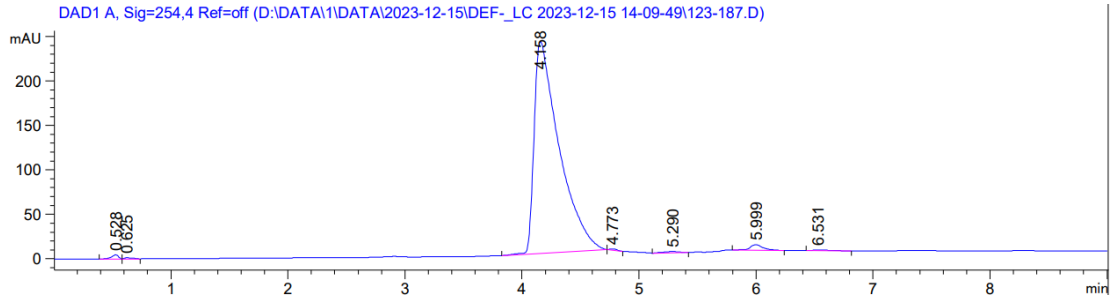
Compound 7



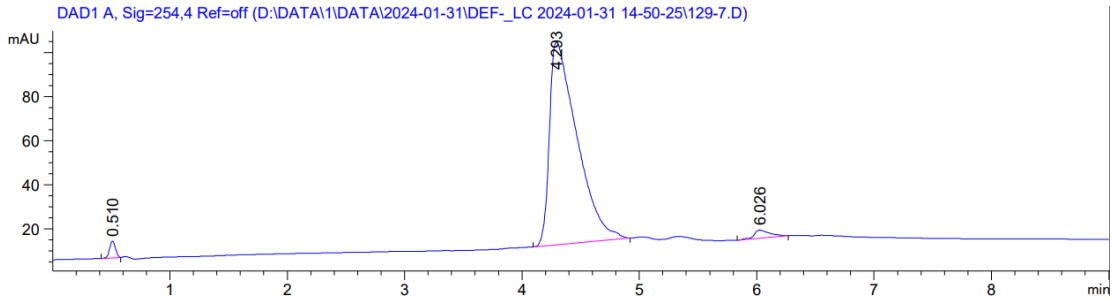
Compound 8



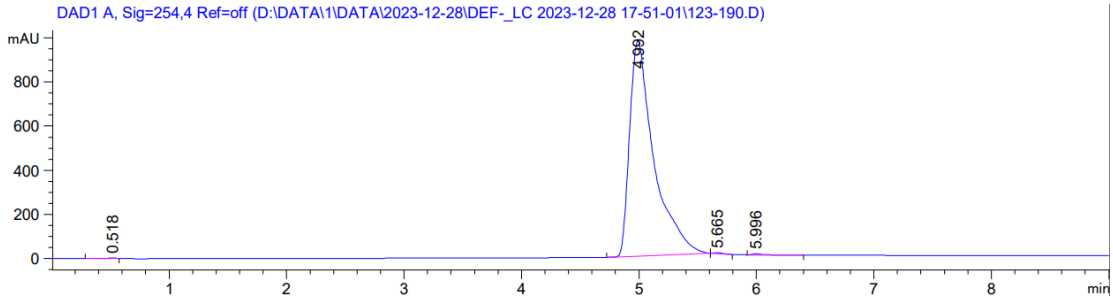
Compound 9



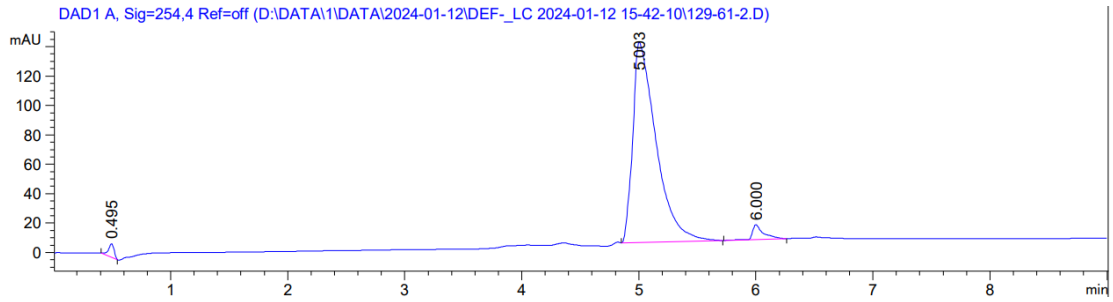
Compound 10



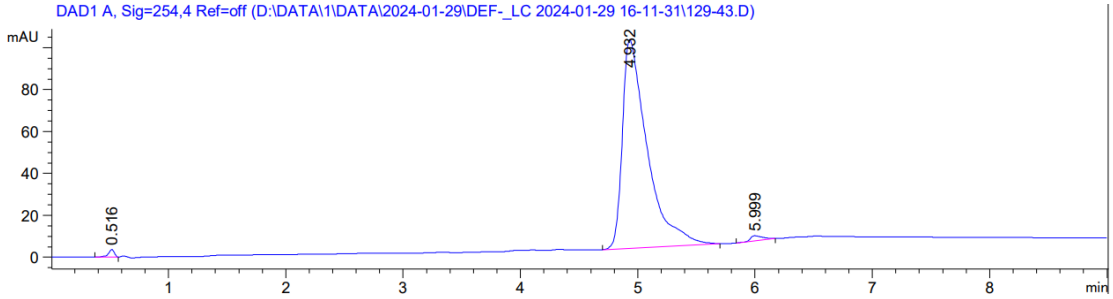
Compound 11



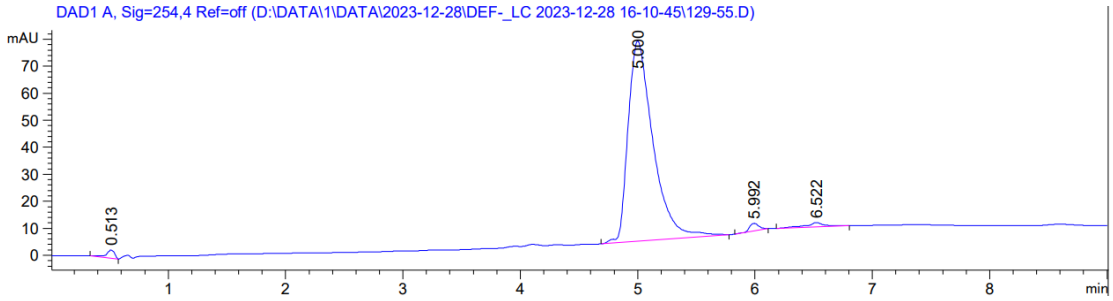
Compound 12



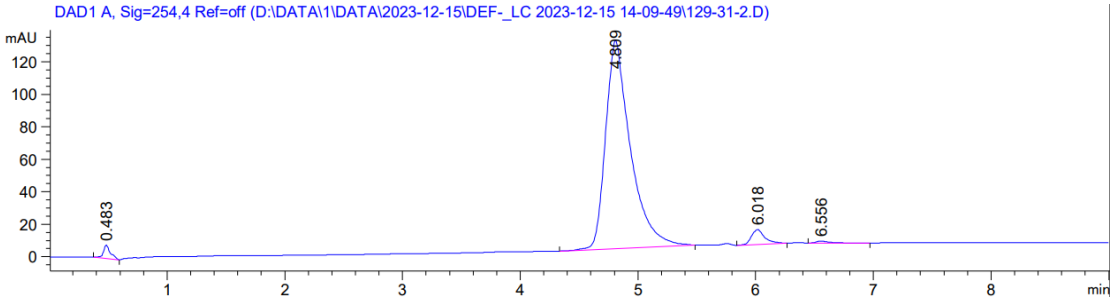
Compound 13



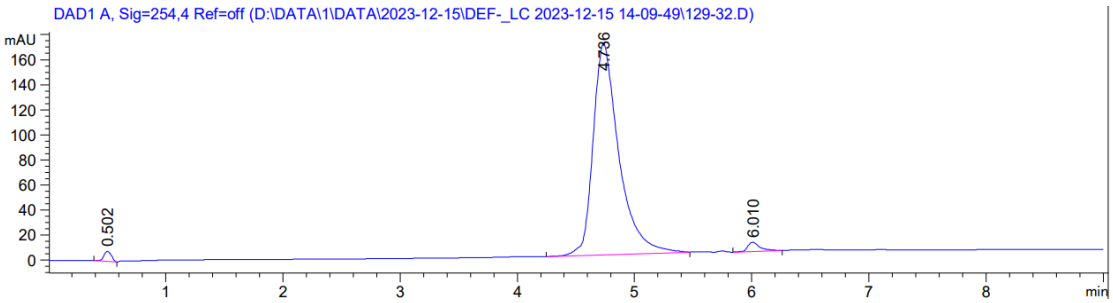
Compound 14



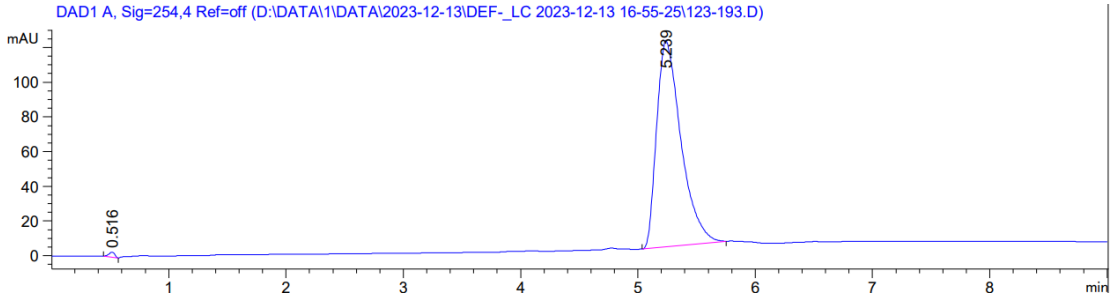
Compound 15



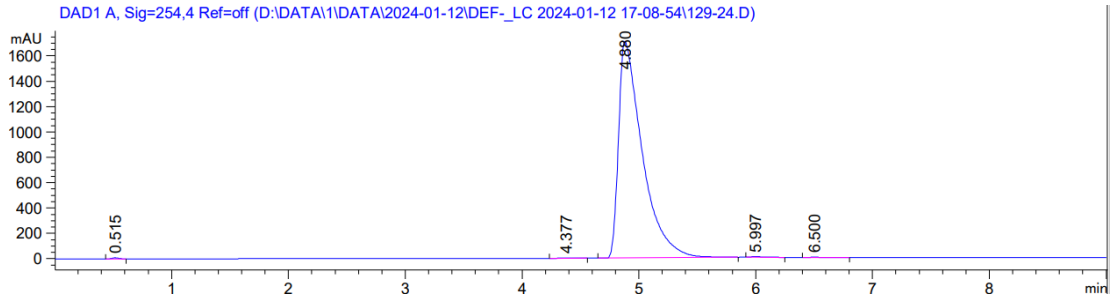
Compound 16



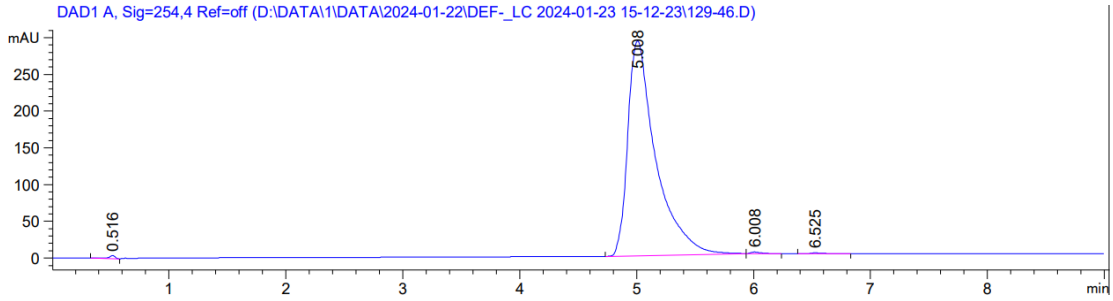
Compound 17



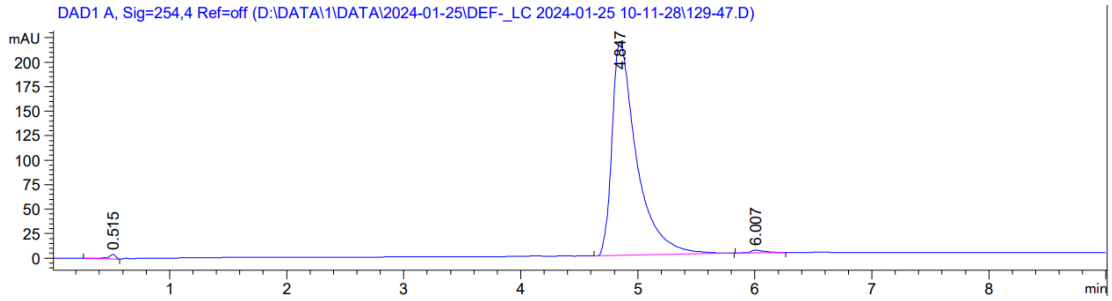
Compound 18



Compound 19



Compound 20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6
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8
min