Electronic Supplementary Information

Molecularly Imprinted Artificial Esterases with Highly Specific Active Sites and Precisely Installed Catalytic Groups

Lan Hu and Yan Zhao*

Department of Chemistry, Iowa State University, Ames, Iowa 50011-3111, USA

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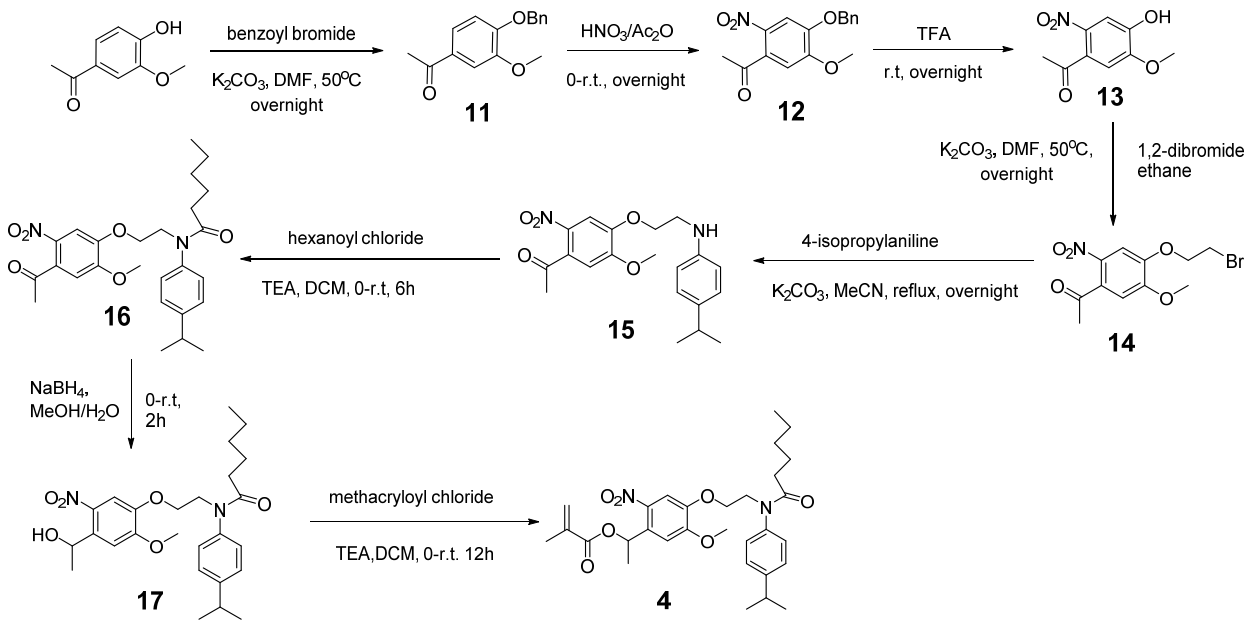
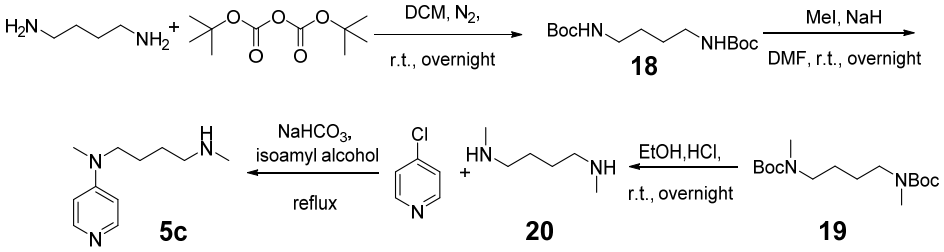
General Experimental Methods

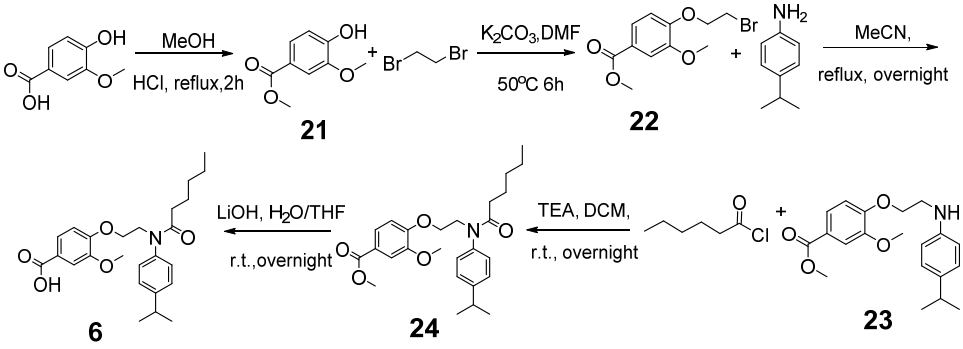
All reagents and solvents were of ACS-certified grade or higher and used as received from commercial suppliers. Millipore water was used to prepare buffers and nanoparticles. ^{1}H and ^{13}C NMR spectra were recorded on a VARIAN MR-400 or on a VARIAN VXR-400 spectrometer. Dynamic light scattering (DLS) was performed on a PD2000DLSPLUS dynamic light scattering detector. Mass spectrometry was performed on AGILENT 6540 QTOF mass spectrometer. UV-vis spectra were recorded on a Cary 100 Bio UV-visible spectrophotometer.



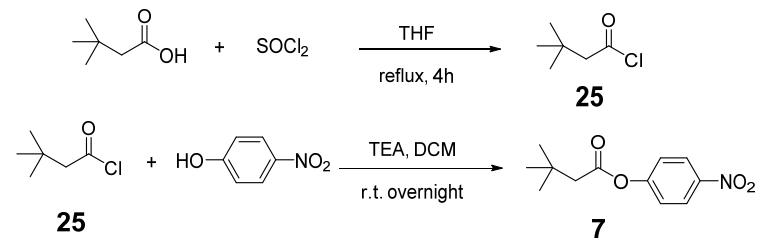
Scheme1S. Synthesis of compound **4**



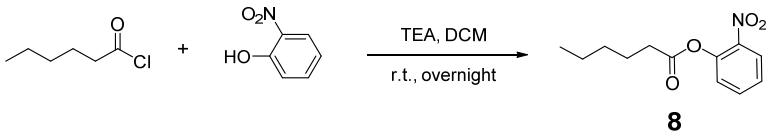
Scheme2S. Synthesis of compound **5c**



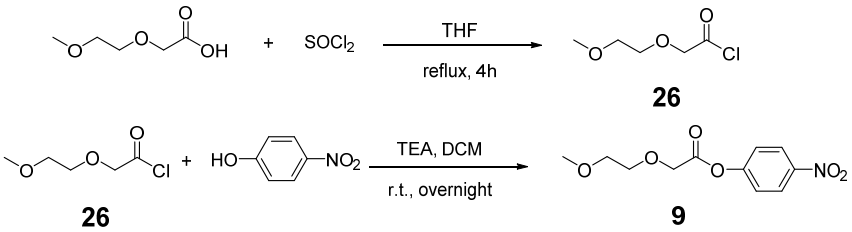
Scheme3S. Synthesis of compound **6**



Scheme4S. Synthesis of compound **7**



Scheme5S. Synthesis of compound **8**



Scheme6S. Synthesis of compound **9**

Syntheses

Syntheses of compounds **1**, **2**, **3**,[1] **5a**, **5b**,[2] **11**, **12**, **13**,[3] **18**,[4] **20**,[5] **21**,[6] **7**[7] were previously reported.

1-(4-(2-Bromoethoxy)-5-methoxy-2-nitrophenyl) ethan-1-one (14). K_2CO_3 (1.7 g, 12 mmol) was added to a solution of compound **13** (1.0 g, 4.7 mmol) in 10 mL DMF at room temperature. After the reaction mixture was stirred at 50 °C for 12 h, the solvent was removed by rotary evaporation. The residue was purified by column chromatography over silica gel using 1:1 hexane/ethyl acetate as the eluent to give a light yellow powder (0.63 g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.67 (s, 1H), 6.8 (s, 1H), 4.45 (t, *J* = 6.4 Hz, 2H), 4.00 (s, 3H), 3.73 (t, *J* = 6.4 Hz, 2H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.88, 154.53, 147.97, 138.06, 133.66, 109.10, 109.04, 77.37, 77.06, 76.74, 69.35, 56.74, 30.38, 28.14. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{11}H_{12}NO_5Br$, 317.9972; found, 317.9974.

1-(4-(2-((4-Isopropylphenyl) amino)ethoxy)-5-methoxy-2-nitrophenyl)ethan-1-one (15). K_2CO_3 (0.82 g, 6 mmol) was added to a solution of compound **14** (0.63 g, 2 mmol) in 10 mL of acetonitrile at room temperature. After the reaction mixture was stirred at 80 °C for 12 h, the solvent was removed by rotary evaporation. The residue was purified by column chromatography over silica gel using 1% methanol in dichloromethane as the eluent to give a light yellow oil (0.21 g, 28%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.66 (s, 1H), 7.14 (d, *J* = 4 Hz, 2H), 6.81-6.79 (m, 3H), 4.34 (t, *J* = 4.4 Hz, 2H), 4.00 (s, 3H), 3.67 (t, *J* = 4.4 Hz, 2H), 2.92-2.84

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(m, 1H), 2.53 (s, 1H), 1.24 (d, *J* = 5.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 200.1, 154.1, 149.2, 145.6, 138.6, 138.2, 134.4, 126.2, 113.3, 108.4, 108.1, 67.71, 55.96, 52.03, 43.38, 33.16, 24.23. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{20}H_{24}N_2O_5$, 373.1758; found, 373.1756.

N-(2-(4-Acetyl-2-methoxy-5-nitrophenoxy) ethyl)-N-(4-isopropylphenyl) hexanamide (16). Triethylamine (0.39 mL, 3.0 mmol) was added to a solution of compound **15** (0.21 g, 0.6 mmol) and hexanoyl chloride (0.42 mL, 3.0 mmol) in dry dichloromethane (5 mL) at 0 °C. After the reaction mixture was stirred at room temperature for 12 h, the solvent was removed by evaporation. The residue was purified by column chromatography over silica gel using 1:1 hexane/ethyl acetate as eluent to give a yellow oil (0.15 g, 55%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.58 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 12 Hz, 2H), 6.7 (s, 1H), 4.28 (t, *J* = 6.0 Hz, 2H), 4.08 (t, *J* = 6.0 Hz, 2H), 2.96-2.89 (m, 1H), 2.04 (t, *J*=7.6 Hz, 2H), 1.57-1.50 (m, 1H), 1.26 (d, *J* = 4.0 Hz, 6H), 1.20-1.11(m, 4H), 0.78 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 200.0, 173.9, 171.0, 154.2, 148.8, 148.7, 140.6, 138.3, 132.9, 128.1, 127.6, 108.8, 108.1, 66.50, 60.30, 56.52, 48.67, 34.22, 33.72, 31.52, 31.32, 30.29, 25.05, 23.89, 20.95, 14.16, 13.84. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{26}H_{34}N_2O_6$, 471.2490; found, 471.2481.

N-(2-(4-(1-Hydroxyethyl)-2-methoxy-5-nitrophenoxy) ethyl)-N-(4-isopropylphenyl) hexanamide (17). Sodium borohydride (0.035 g, 1.0 mmol) was added to a solution of compound **16** (0.15 g, 0.30 mmol) in 2:1 THF/MeOH (5 mL) at 0 °C. After the reaction mixture was stirred at room temperature for 2 h, 5 mL water was added. The mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic phase was concentrated by rotary evaporation to give a yellow oil (0.094 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.53 (s, 1H), 7.28-7.17 (m, 5H), 5.57-5.51 (m, 1H), 4.24 (t, *J* = 6.0 Hz, 2H), 4.07 (t, *J* = 6.0 Hz, 2H), 3.95 (s, 3H), 2.97-2.90 (m, 1H), 2.05 (t, *J* = 7.6 Hz, 2H), 1.53 (d, *J* = 8.0 Hz, 3H), 1.27 (d, *J* = 8.0 Hz, 6H), 1.22-1.13(m,

6H), 0.79 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 173.9, 155.0, 148.8, 145.7, 140.6, 138.3, 137.9, 128.1, 127.6, 108.8, 108.1, 66.50, 65.30, 60.10, 56.52, 48.67, 34.22, 33.72, 31.52, 31.32, 25.05, 24.46, 23.89, 14.16, 13.84. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{26}H_{36}N_2O_6$, 473.2646; found, 473.2650.

1-(4-(2-(N-(4-Isopropylphenyl) hexanamido) ethoxy)-5-methoxy-2-nitrophenyl) ethyl methacrylate (4). Triethylamine (0.14 ml, 1 mmol) was added to a solution of compound **17** (0.094 g, 0.30 mmol) in dry dichloromethane (5 mL) at 0 °C. After the reaction mixture was stirred at room temperature for 12 h, the solvent was removed by rotary evaporation. The residue was purified by column chromatography over silica gel using 1:1 hexane/ethyl acetate as eluent to a obtain a yellow oil (0.064 g, 41%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.55 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.00 (s, 1H), 6.7 (s, 1H), 6.52 (q, *J* = 6.4 Hz, 1H), 6.16 (s, 1H), 5.6 (s, 1H), 4.25 (t, *J* = 6.0 Hz, 2H), 4.08 (t, *J* = 6.0 Hz, 2H), 3.90 (s, 3H), 2.98-2.91 (m, 1H), 2.06 (t, *J* = 7.6 Hz, 2H), 1.65 (d, *J* = 8.0 Hz, 3H), 1.27 (d, *J* = 8.0 Hz, 6H), 1.21-1.14 (m, 6H), 0.80 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 173.9, 170.0, 165.9 155.0, 148.8, 147.0, 140.6, 139.7, 136.3, 135.4, 128.1, 127.6, 125.6, 109.0, 108.1, 68.67, 66.30, 60.10, 56.52, 48.67, 34.22, 33.72, 31.52, 31.32, 28.99, 25.05, 23.86, 22.59, 22.30, 21.93, 20.92, 18.21, 14.16, 13.84. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{30}H_{40}N_2O_7$, 541.2908; found, 541.2917.

Di-*tert*-butyl butane-1,4-diylbis(methylcarbamate) (19). Compound **18** (400 mg, 1.3 mmol) was added to a suspension of sodium hydride (101 mg, 4.2 mmol) in dry DMF (5 mL). The reaction mixture was stirred at room temperature for 2 h before the addition of methyl iodide (0.26 mL, 4.2 mmol). After 12 h, water (5 mL) was added. The mixture was extracted with dichloromethane (3 × 20 mL). The combined organic phase was concentrated by rotary evaporation and the residue was purified by column chromatography using 10% methanol in

dichloromethane as the eluent to give a yellow oily product (107 mg, 26%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.21 (s, 2H), 2.82 (s, 3H), 1.49-1.45 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 159.3, 47.88, 38.59, 32.69, 24.43, 22.80. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{16}H_{32}N_2O_4$, 317.2908; found, 317.2917.

N1, N4-Dimethyl-N1-(pyridin-4-yl)butane-1,4-diamine (5c). Compound **20** (200 mg, 1.7 mmol) was added to a mixture of 4-chloropyridine hydrochloride (129 mg, 0.86 mmol) and sodium bicarbonate (143 mg, 1.7 mmol) in 10 mL of isoamyl alcohol. The reaction mixture was heated at 100 °C for 24 h. Solvent was removed by rotary evaporation and the residue was purified by column chromatography using 10% methanol in dichloromethane as the eluent to give a yellow oily product (70 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.14 (d, *J* = 4.0 Hz, 2H), 6.43 (d, *J* = 4.0 Hz, 3H), 3.75 (s, 1H), 3.32 (d, *J* = 4.0 Hz, 2H), 2.9 (s, 3H), 2.6 (t, *J* = 8.0 Hz, 2H), 2.4 (s, 3H), 1.61-1.47 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 149.8, 149.6, 106.4, 51.28, 37.47, 35.87, 26.71, 24.49. ESI-HRMS (m/z): $[M + H]^+$ calcd for $C_{11}H_{19}N_3$, 194.1652; found, 194.1647.

Methyl 4-(2-bromoethoxy)-3-methoxybenzoate (22). Ethylene dibromide (0.75 mL, 5.0 mmol) was slowly added into a mixture of K_2CO_3 (690 mg, 5.0 mmol) and compound **18** (423 mg, 2.5 mmol) in DMF (5 mL). The mixture was stirred at 50 °C for overnight before water (5 mL) was added. The mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic phase was concentrated by rotary evaporation and the residue was purified by column chromatography using 3:1 hexane/ethyl acetate as eluent to give a white powder (230 mg, 32%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.66 (dd, *J* = 8.4; 2.0 Hz, 1H), 7.64 (d, *J* = 2.0 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.30 (t, *J* = 6.4 Hz, 2H), 3.92 (s, 3H), 3.90 (s, 3H), 3.68(t, *J* = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.12, 166.69, 151.35, 149.08, 123.71, 123.36, 112.81, 112.53, 77.31, 77.20,

77.00, 76.68, 68.70, 56.13, 52.06, 31.58, 28.29, 14.12. ESI-HRMS (m/z): [M + H]+ calcd for $C_{11}H_{13}BrO_4$, 290.1957; found, 290.1963.

Methyl 4-(2-((4-isopropylphenyl)amino)ethoxy)-3-methoxybenzoate (23). K_2CO_3 (377 mg, 2.25 mmol) was added to a mixture of compound **19** (650 mg, 2.25 mmol) and isobutyl aniline (0.36 mL, 5.6 mmol) in acetonitrile (10 mL). The reaction mixture was heated to reflux overnight. The solvent was removed by rotary evaporation. The residue was purified by column chromatography over silica gel using 20:1 dichloromethane/methanol as eluent to give a dark red oil (142 mg, 18%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H),7.06 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 2H), 4.26 (t, *J* = 5.6 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 3.58 (t, *J* = 5.6 Hz, 2H), 2.82-2.77 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 166.8, 152.1, 149.0, 145.6, 138.6, 127.2, 123.4, 123.1, 113.3, 112.4, 112.2, 67.71, 55.96, 52.03, 43.38, 33.16, 24.23. ESI-HRMS (m/z): [M + H]+ calcd for $C_{20}H_{25}NO_4$, 344.1856; found, 344.1863.

Methyl 4-(2-(N-(4-isopropylphenyl)hexanamido)ethoxy)-3-methoxybenzoate (24). Hexanoyl chloride (0.12 mL, 0.82 mmol) was slowly added to a solution of compound **23** (142 mg, 0.41 mmol) and triethylamine (0.12 mL, 0.82 mmol) in dry dichloromethane (5 mL) at 0 °C. The reaction was stirred overnight at room temperature. The solvent was removed by rotary evaporation and the residue was purified by column chromatography over silica gel using 20:1 dichloromethane/methanol as eluent to give an off-white powder (139 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 5.6 Hz, 1H), 7.58 (s, 1H),7.35 (s, 4H), 7.01 (d, *J* = 5.6 Hz, 1H), 4.27 (t, *J* = 3.6 Hz, 2H), 4.08 (t, *J* = 3.6 Hz, 2H), 3.90 (s, 6H), 2.99-2.96 (m, 1H), 2.11 (t, *J* = 5.0 Hz, 2H), 1.56-1.52 (m, 2H), 1.3 (d, *J* = 4.6 Hz, 6H). 1.22-1.15 (m, 4H), 0.81 (t, *J* = 4.52 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 173.9, 166.9, 152.1, 148.6, 140.9, 128.1, 127.5, 123.5, 112.3,

111.5, 65.66, 55.92, 51.98, 49.06, 34.28, 33.75, 31.37, 25.09, 23.95, 22.35, 22.29, 13.85. ESI-HRMS (m/z): [M + H]+ calcd for $C_{26}H_{35}NO_5$, 442.2588; found, 442.2596.

4-(2-(N-(4-Isopropylphenyl)hexanamido)ethoxy)-3-methoxybenzoic acid (6). LiOH (84 mg, 1.0 mmol) was added to a solution of compound **21** (230 mg, 0.52 mmol) in 1:4 H_2O/THF (5 mL). The reaction mixture was stirred at room temperature overnight. The solvent was removed by rotary evaporation and the residue was purified by column chromatography over silica gel using 10:1 dichloromethane/methanol as eluent to give a white powder (200 mg, 90%). ^{1}H NMR (400 MHz, CD_3OD, δ) 7.61 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.32 (s, 4H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.24 (t, *J* = 5.5 Hz, 2H), 4.05 (t, *J* = 5.5 Hz, 2H), 3.87 (s, 3H), 2.98 – 2.91 (m, 1H), 2.08 (t, *J* = 7.5 Hz, 2H), 1.50 (q, *J* = 7.3 Hz, 2H), 1.26 (d, *J* = 6.9 Hz, 6H), 1.14 (tdt, *J* = 10.7, 7.0, 4.4 Hz, 4H), 0.78 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD, δ) 174.7, 168.3, 152.2, 149.0, 148.9, 140.4, 128.06 , 127.22 , 123.46 , 112.43 , 111.59 , 65.28 , 55.01 , 48.70 , 47.58 , 47.36 , 47.15 , 46.94 , 33.79 , 33.66 , 30.93 , 24.89 , 22.96 , 21.88 , 12.74. ESI-HRMS (m/z): [M + H]+ calcd for $C_{25}H_{33}NO_5$, 428.2431; found, 428.2435.

2-Nitrophenyl hexanoate (8). Hexanoyl chloride (0.31 mL, 2.0 mmol) was added dropwise to a mixture *o*-nitrophenol (200 mg, 1.4 mmol) and triethylamine (0.22 mL, 1.4 mmol) in dry dichloromethane (10 mL). The reaction mixture was stirred at room temperature overnight. The solvent was removed by rotary evaporation and residue was purified by column chromatography using 20:1 dichloromethane/methanol as eluent to give a yellow oil (0.26 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.00 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.57 (ddd, *J* = 8.0, 2.0 Hz, 1H), 7.31 (ddd, *J* = 7.5, 1.3 Hz, 1H), 7.15 (dd, *J* = 8.0, 1.3 Hz, 1H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.73-1.66 (m, 2H), 1.38-1.25 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ) 171.33, 144.13, 141.81,

134.69, 126.49, 125.66, 125.22, 77.45, 77.13, 76.81, 33.92, 31.14, 24.11, 22.28, 13.86. ESI-HRMS (m/z): [M + H]+ calcd for $C_{12}H_{15}NO_4$, 238.2641; found, 238.2645.

4-Nitrophenyl 2-(2-methoxyethoxy)acetate (9). Thionyl chloride (0.1 ml, 1.3 mmol) was added to a solution of 2-(2-methoxyethoxy)acetic acid (0.1 ml, 0.8 mmol) in THF (20 ml). The reaction mixture was heated to reflux at 55 °C for 4 h and all volatile materials were removed by rotary evaporation. The residue was dissolved with triethylamine (0.2 mL, 1.3 mmol) in dry chloromethane (10 mL), followed by the addition of *p*-nitrophenol (183 mg, 1.3 mmol). The reaction was stirred at room temperature overnight. The solvent was removed by rotary evaporation and the residue was purified by column chromatography using 10:1 dichloromethane/methanol as eluent to give a white powder (144 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.28 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.45 (s, 2H), 3.83-3.81 (m, 2H), 3.64-3.62 (m, 2H), 3.4 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ) 169.56, 168.09, 154.81, 125.28, 122.24, 77.32, 77.01, 76.69, 72.01, 71.16, 68.59, 59.07. . ESI-HRMS (m/z): [M + H]+ calcd for $C_{12}H_{15}NO_4$, 238.4453; found, 238.4456.

MINP-COOH. A typical procedure is as follows.[8] DVB (2.8 μL, 0.02 mmol), AIBN in DMSO (10 μL of 8.2 mg mL^{-1}, 0.0005 mmol), **4** in DMSO (10 mL, 0.0004 mmol) were added to a 2.0 mL micellar solution of surfactant **1** (9.3 mg, 0.02 mmol) in H_2O. The mixture was ultrasonicated for 10 min. Compound **3** (4.13 mg, 0.024 mmol), $CuCl_2$ in H_2O (10 μL of 6.7 mg mL^{-1}, 0.0005 mmol), and sodium ascorbate in H_2O (10 μL of 99 mg mL^{-1}, 0.005 mmol) were then added and the reaction mixture was stirred slowly at room temperature (25 °C). After 12 h, compound **4** (15.9 mg, 0.06 mmol), $CuCl_2$ in H_2O (10 μL of 6.7 mg mL^{-1}, 0.0005 mmol), and sodium ascorbate in H_2O (10 μL of 99 mg mL^{-1}, 0.005 mmol) were added and the mixture was

[8] Awino, J. K.; Zhao, Y. *Chem.-Eur. J.* **2015**, *21*, 655-661.

stirred for another 6 h. The reaction vial was sealed with a rubber stopper and the reaction mixture was purged with nitrogen for 15 min before it was stirred at 75 °C for 16 h. The resultant solution (2.0 mL) was cooled to room temperature and poured into acetone (8.0 mL). The precipitate formed was washed five times with 1:4 water/acetone mixture and dried overnight in the dark to give an off-white powder. The power was dissolved in Millipore water (1 mL) and irradiated in a Rayonet reactor for 12 h. Water was removed under reduced pressure and the residual sample was washed five times with 1:4 water/acetone mixture in a centrifuge tube and dried to give the product as a white powder (15 mg, 75%).

MINP-DMAP. A typical procedure is as follows.[9] EDCI (10 μL of a 61 mg/mL solution in dry DMF, 0.004 mmol) was added to a stirred solution of MINP-COOH (20.0 mg, 0.0004 mmol) in dry DMF (1 mL) at 0 °C under nitrogen. After 2 h, compound **5a-c** (10 μL, 0.004 mmol) was added and the mixture was stirred for 24 h at room temperature. The mixture was concentrated in vacuo and poured into 2 mL of acetone. The precipitate formed was collected by centrifugation and rinsed five times with 2 mL of acetone to afford the product as an off-white powder (15 mg, 75%).

[9] Hu, L.; Zhao, Y. *Helv. Chim. Acta* **2017**, *100*, e1700147.

Kinetic measurements

Stock solutions (10 mM) of *p*-nitro phenyl hexanoate (PNPH) and other activated esters in methanol were prepared. The stock solutions were stored in a refrigerator and used within 3 d. Stock solutions of MINP-DMAP (60 μM) in 25 mM HEPES buffer were prepared. For the kinetic experiment, a typical procedure is as follows: An aliquot of 500 μL of the MINP-DMAP stock solution was combined with 1500 μL of the same HEPES buffer in a cuvette. The cuvette was placed in a UV-vis spectrometer and equilibrated to 40.0 °C. After 5 min, an aliquot of 10 μL of the PNPH stock solution was added. The concentration of the substrate (PNPH or other activated ester) in the reaction mixture was 50 μM and the concentration of the pyridyl group was 15 μM in all cases. The hydrolysis was monitored by the absorbance of *p*-nitrophenoxide anion at 400 nm. The experiments were generally performed in duplicates.

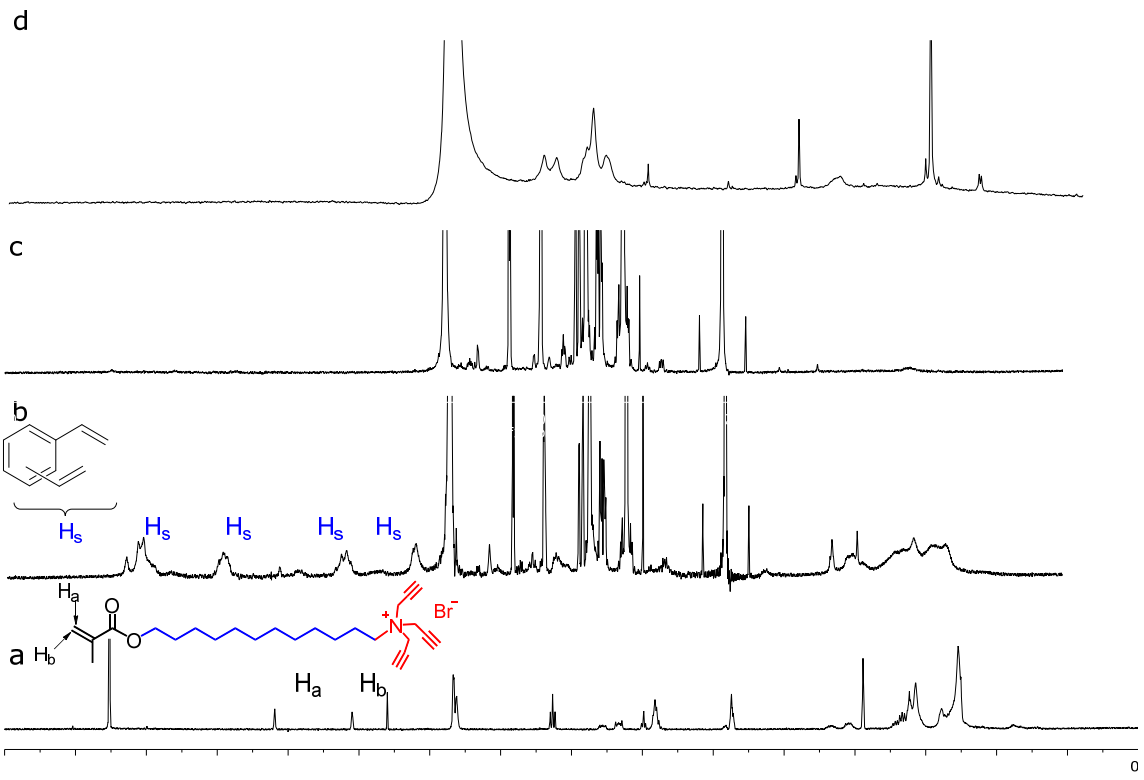


Figure S1. ^{1}H NMR spectra of (a) **1** in $CDCl_3$, (b) alkynyl-SCM in D_2O, (c) after core-crosslinking in D_2O, (d) purified MINP-COOH in D_2O.

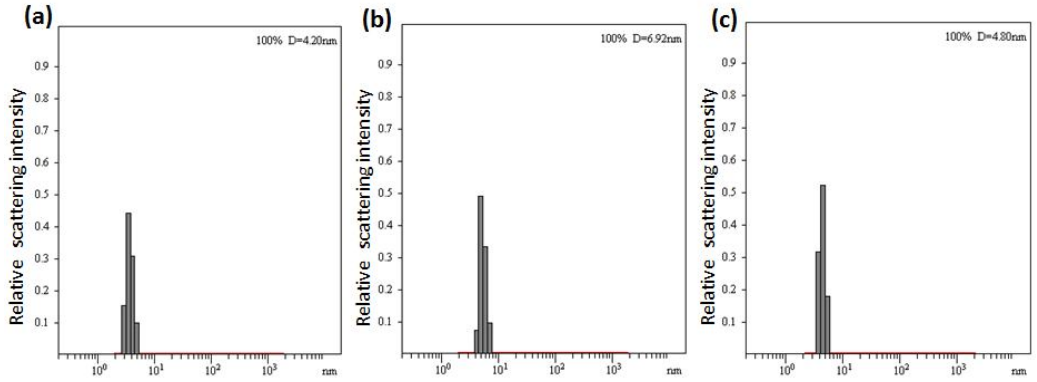


Figure S2. Distribution of the hydrodynamic diameters of the nanoparticles in water as determined by DLS for (a) alkynyl-SCM, (b) surface-functionalized SCM and (c) MINP-COOH after purification.

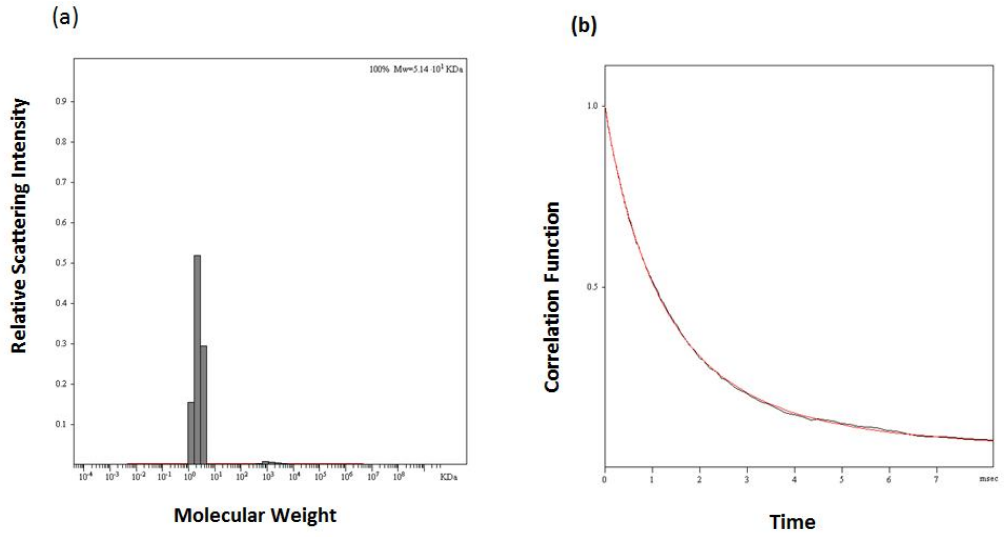


Figure S3. (a) Distribution of the molecular weights of the MINP-COOH. (b) The correlation curve for DLS. The molecular weight distribution was calculated by the PRECISION DECONVOLVE program assuming the intensity of scattering is proportional to the mass of the particle squared. If each unit of building block for the MINP-COOH is assumed to contain one molecule of compound **1** (MW = 465 g/mol), 1.2 molecules of compound **2** (MW = 172 g/mol), one molecule of DVB (MW = 130 g/mol), 0.8 molecules of compound **3** (MW = 264 g/mol), the molecular weight of MINP-COOH translates to 51 [=51400 / (465 + 1.2×172 + 130 + 0.8×264)] of such units.

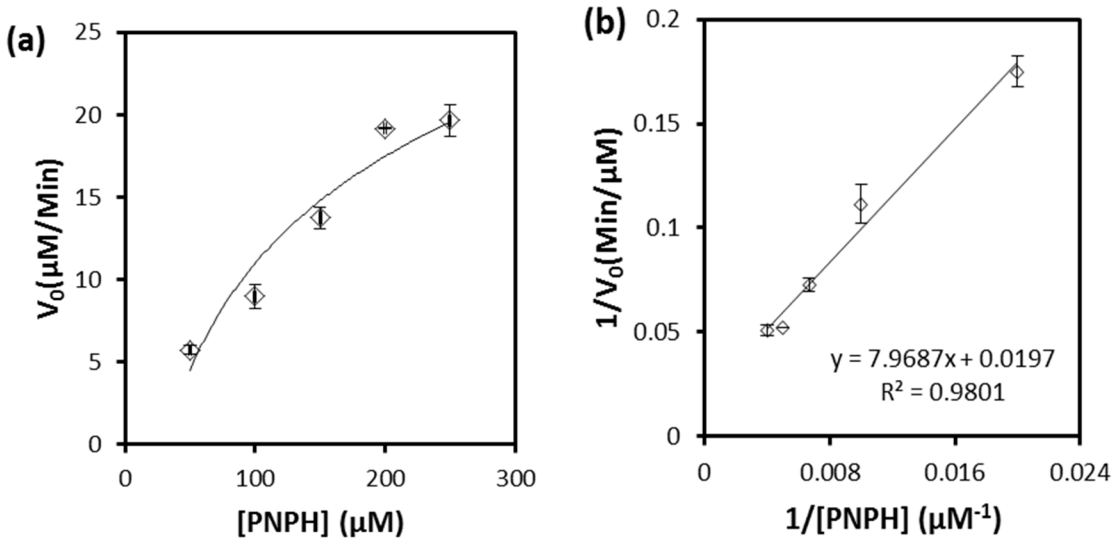


Figure S4. **(**a) Michaelis-Menten plot of MINP-DMAP(**5a**). (b) Double-reciprocal plot (Lineweaver-Burke) of MINP-DMAP(**5a**). The reaction rates were measured in 25 mM HEPEs buffer (pH 8.0) at 40 °C. [MINP-DMAP(**5a**)] = 5 μM.

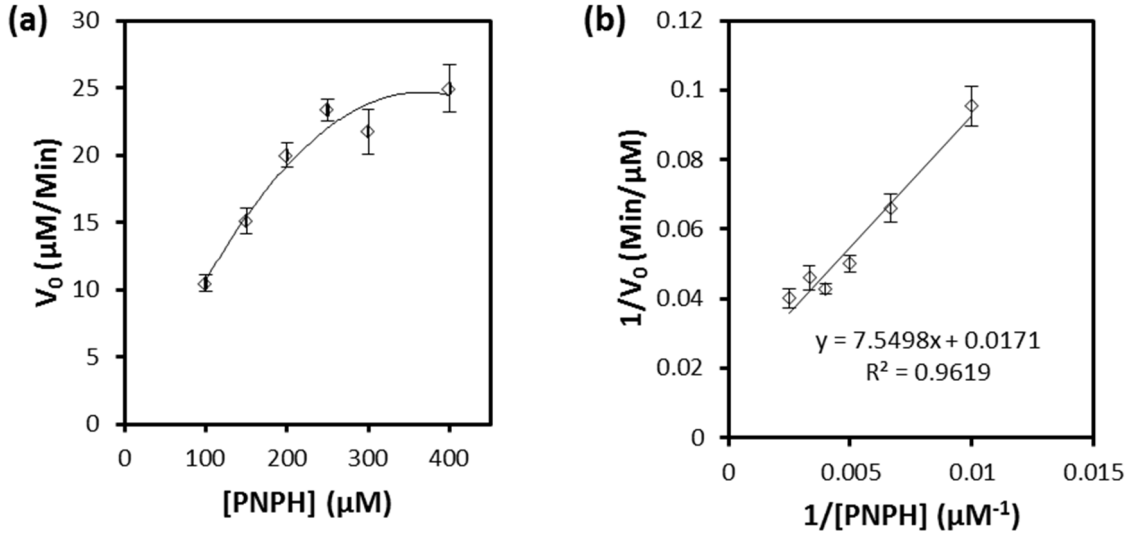


Figure S5. **(**a) Michaelis-Menten plot of MINP-DMAP(**5b**). (b) Double-reciprocal plot (Lineweaver-Burke) of MINP-DMAP(**5b**). The reaction rates were measured in 25 mM HEPEs buffer (pH 8.0) at 40 °C. [MINP-DMAP(**5b**)] = 5 μM.

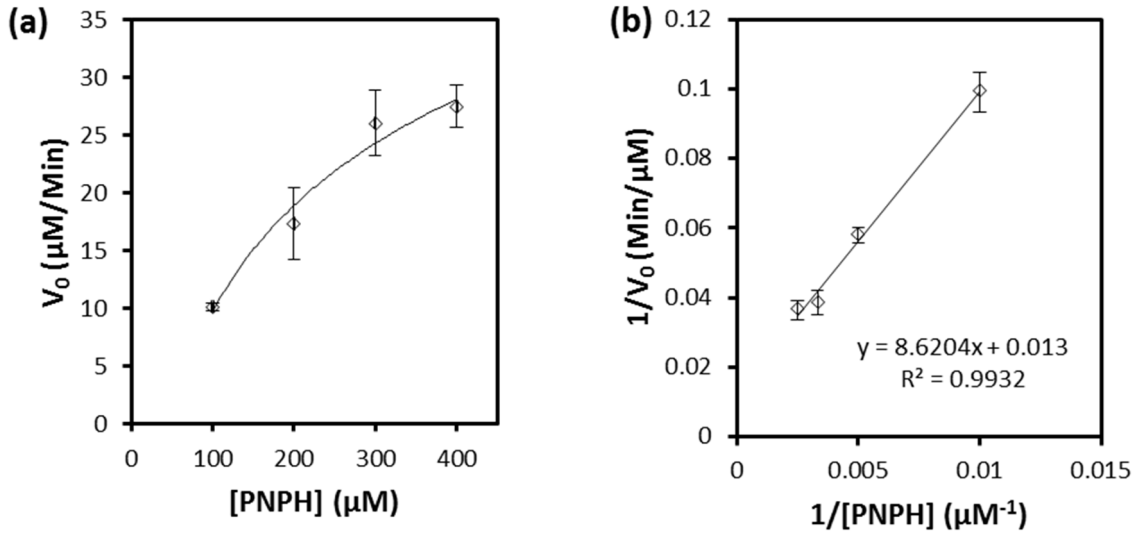
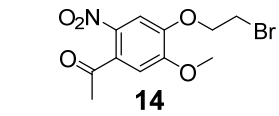


Figure S6. (a) Michaelis-Menten plot of MINP-DMAP(**5c**). (b) Double-reciprocal plot (Lineweaver-Burke) of MINP-DMAP(**5c**). The reaction rates were measured in 25 mM HEPEs buffer (pH 8.0) at 40 °C. [MINP-DMAP(**5c**)] = 5 μM.

[1]H and [13]C NMR spectra of key compounds



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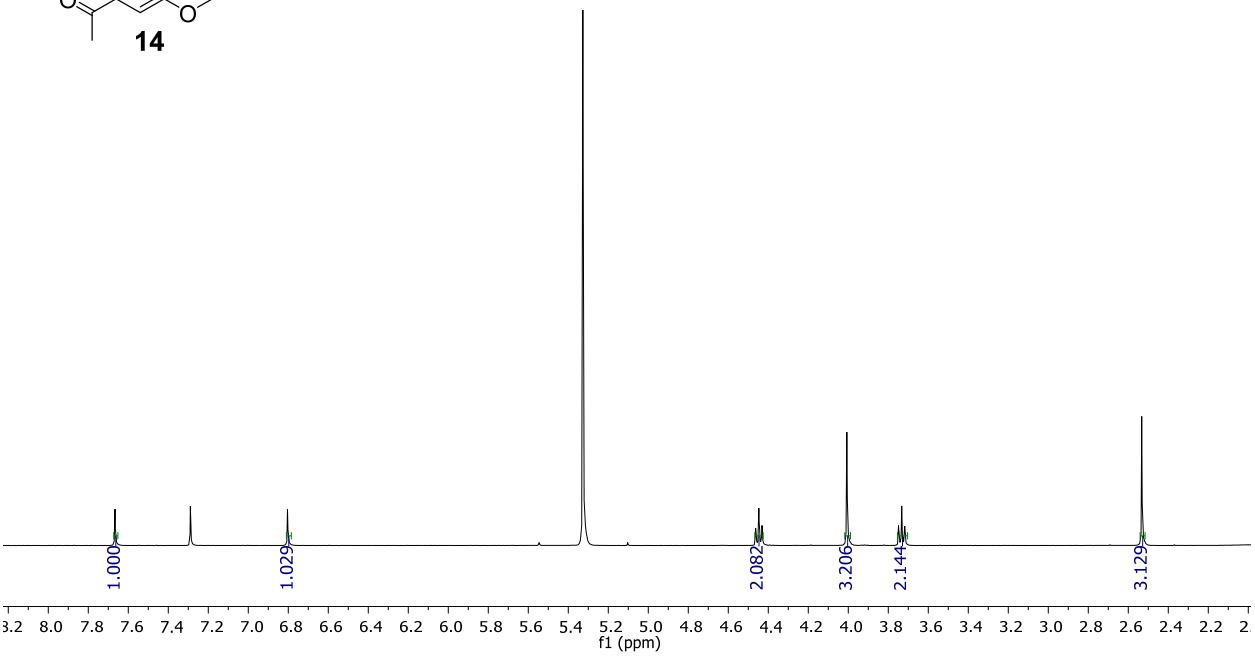

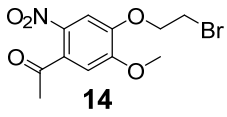

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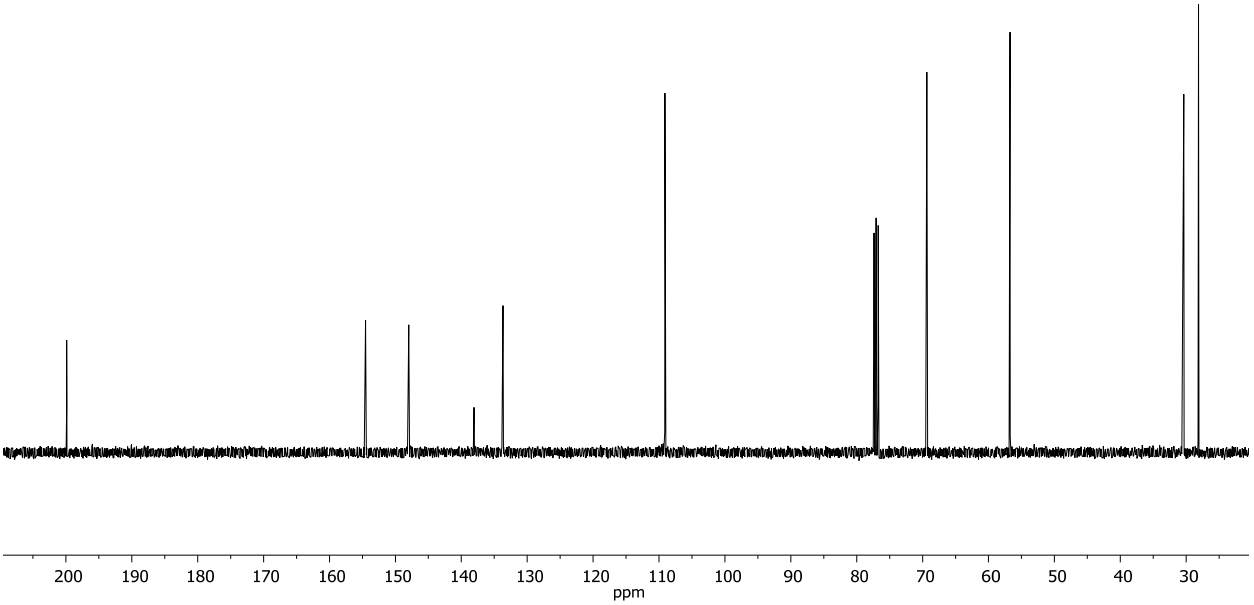

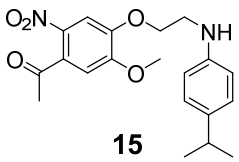
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O
O
NH
O

15

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3.160
5.506
7.5
7.0
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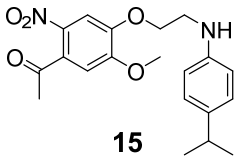
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O
O
NH
O

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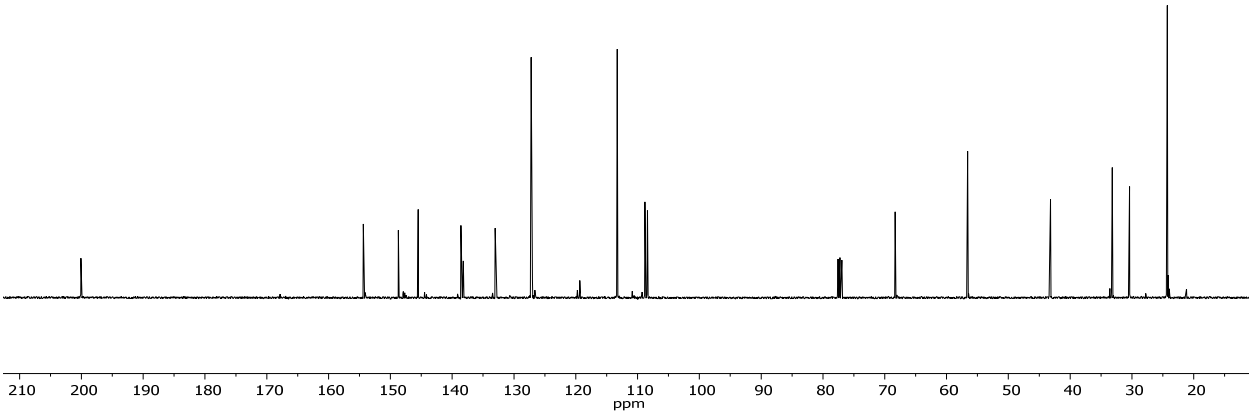
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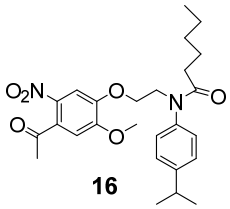
30
20
ppm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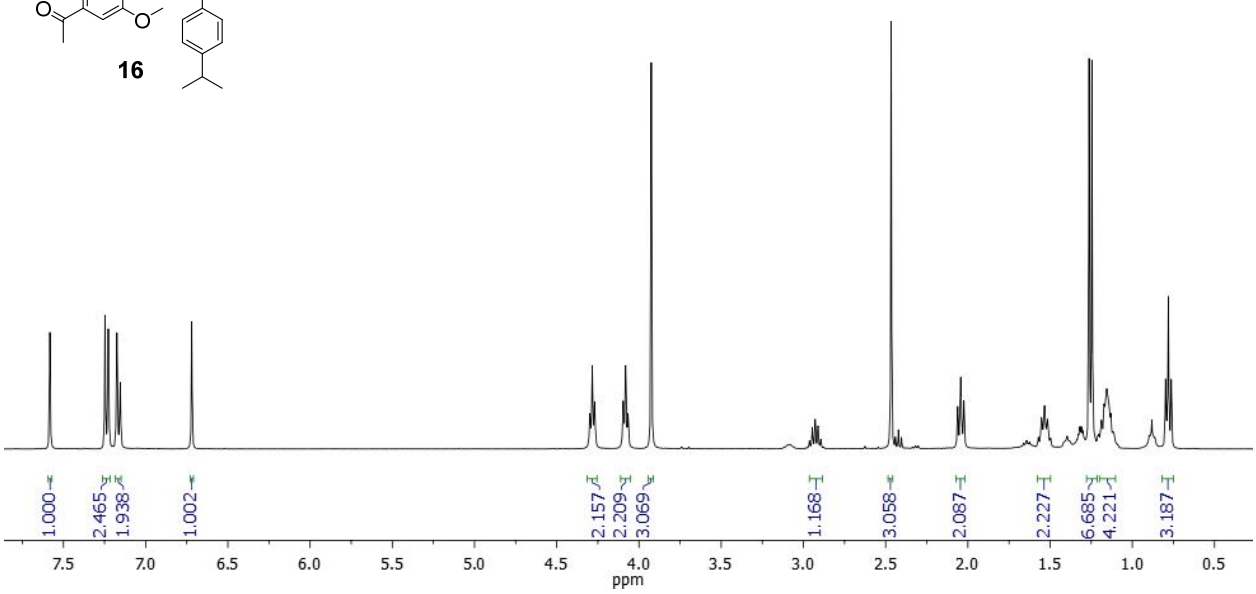
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6.5
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4.0
3.5
3.0
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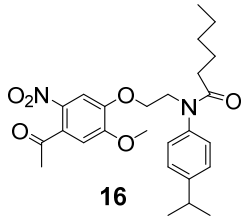
1.0
0.5
ppm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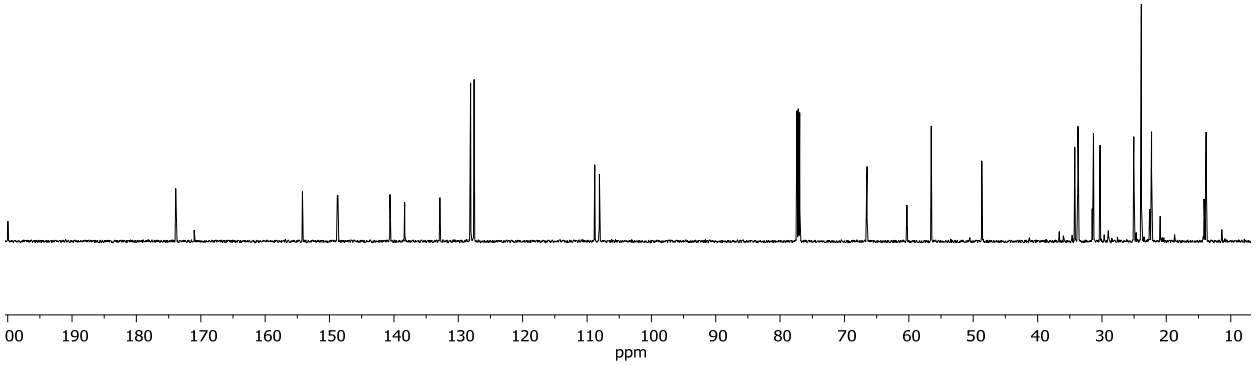
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180
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140
130
120
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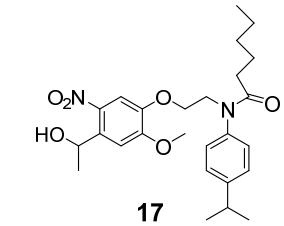
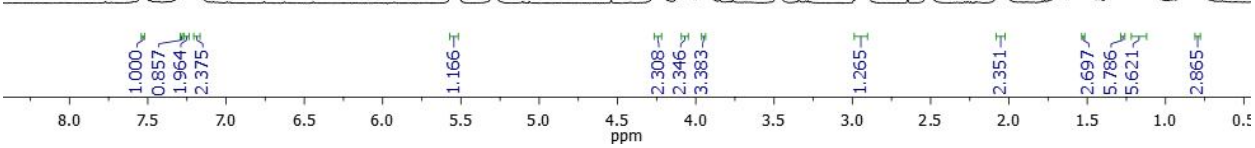
100
90
80
70
60
50
40
30
20
10
ppm


O2N
HO
O
N
O
O

17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3.383
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2.865
8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
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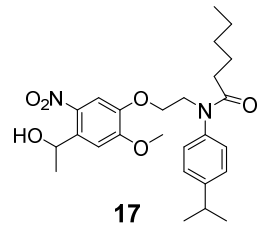
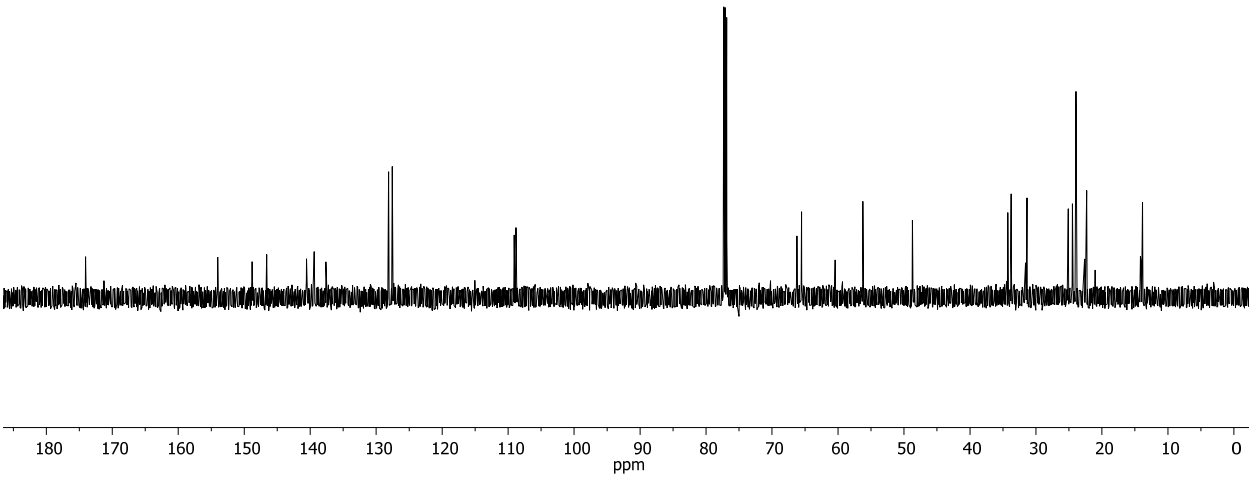
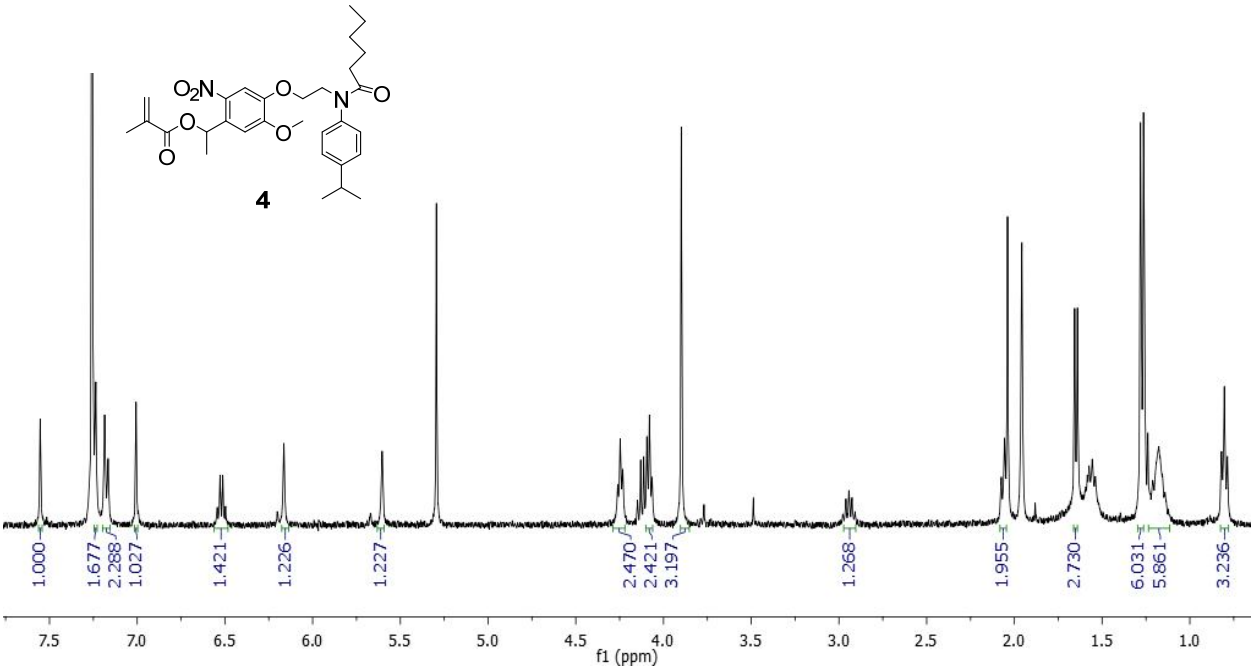
3.0
2.5
2.0
1.5
1.0
ppm


O2N
HO
O
N
O
O

17


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


4
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1.027
1.421
1.226
1.227
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2.421
3.197
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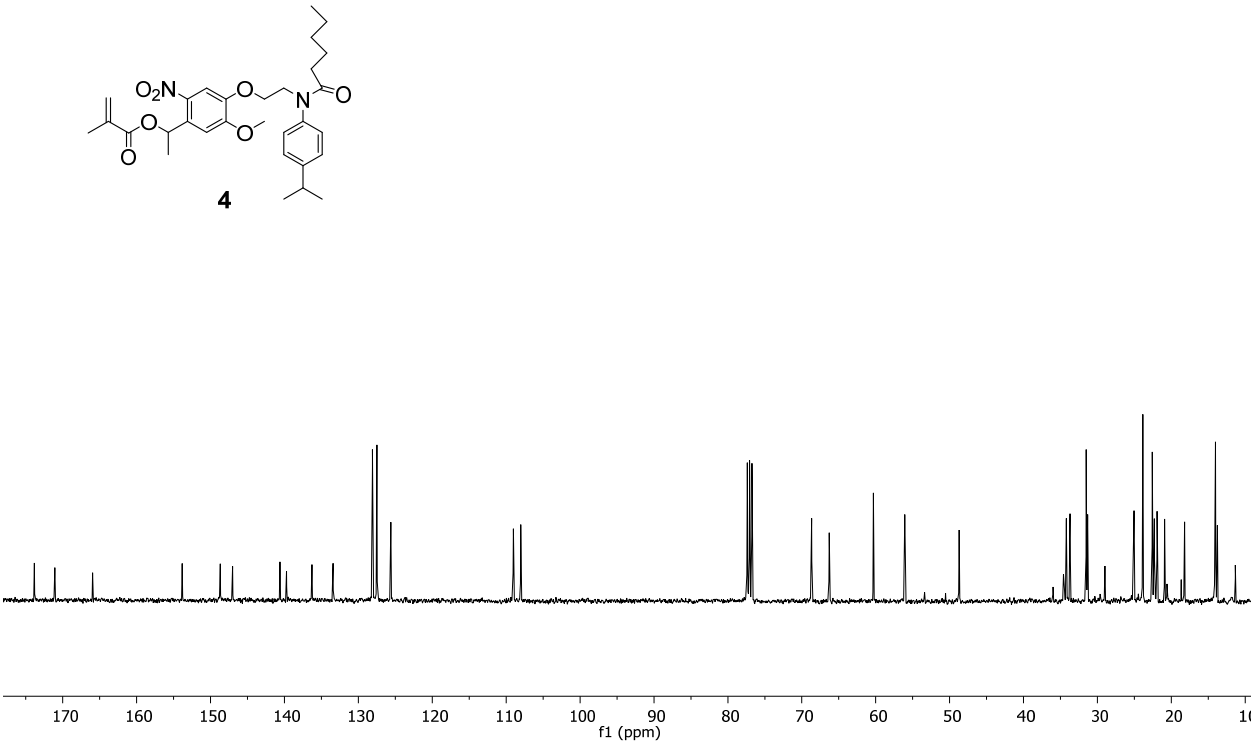
6.031
5.861
3.236
f1 (ppm)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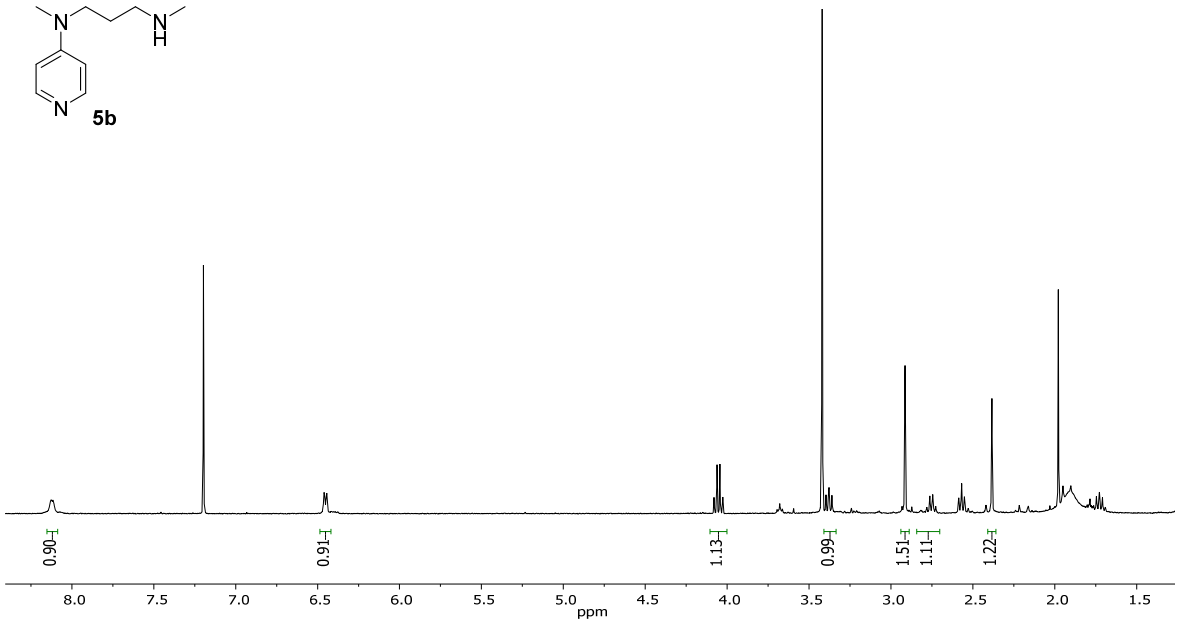
f1 (ppm)


N
N
H
N
5b
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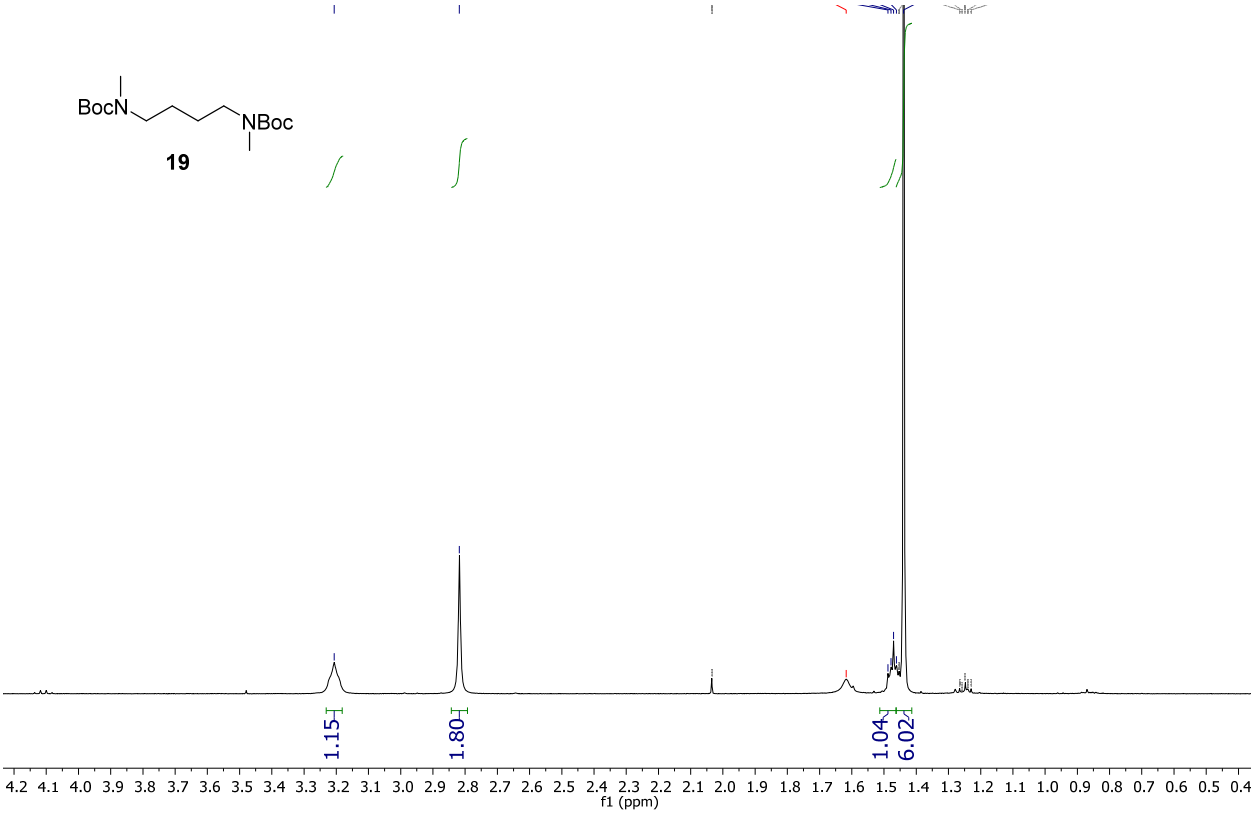
1.13
0.99
1.51
1.11
1.22
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm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NBoc
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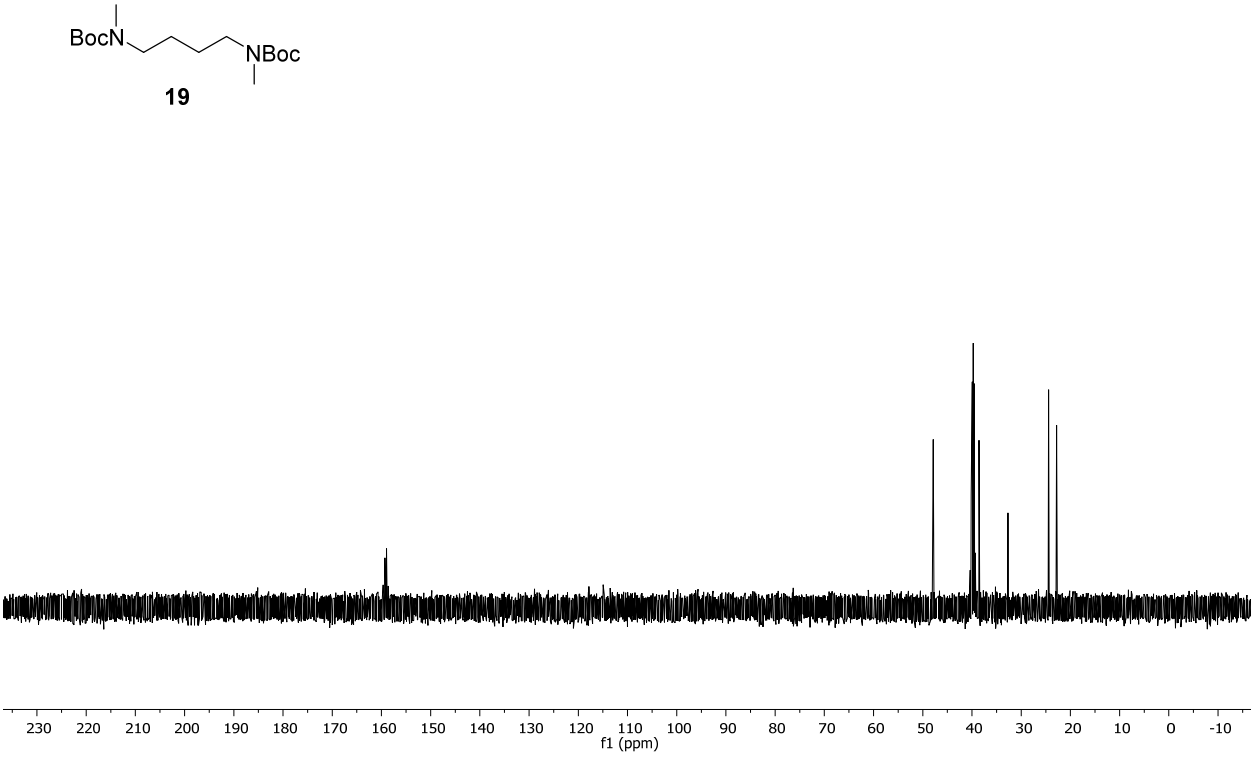
1.80
1.04
6.02
4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4
f1 (ppm)


BocN
NBoc
19
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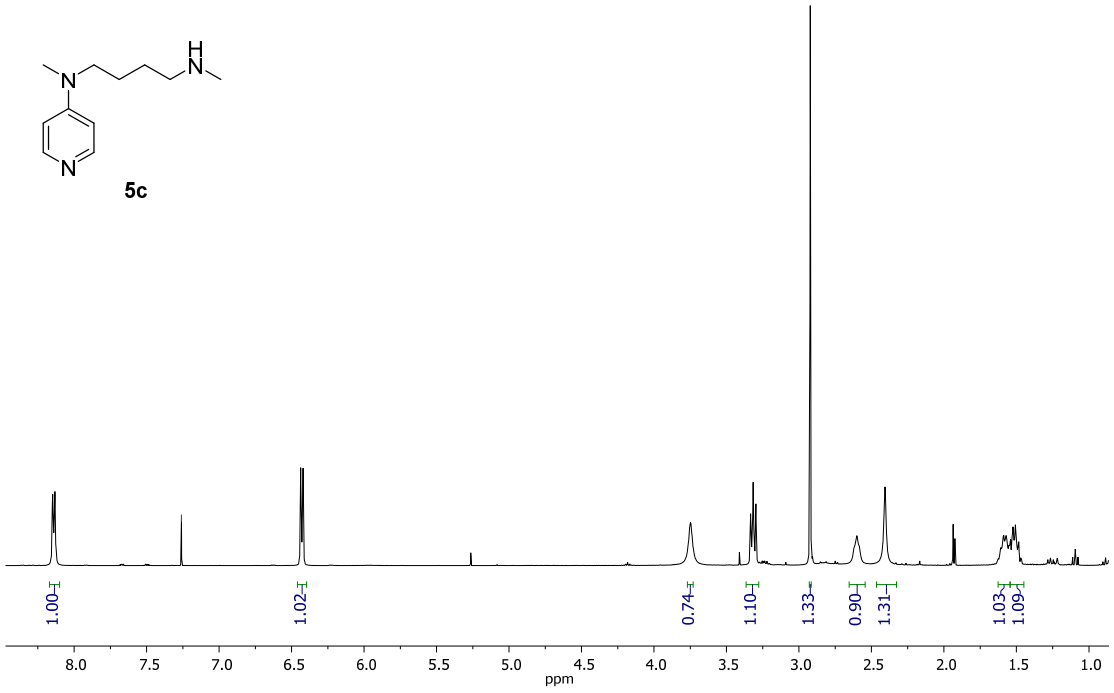
f1 (ppm)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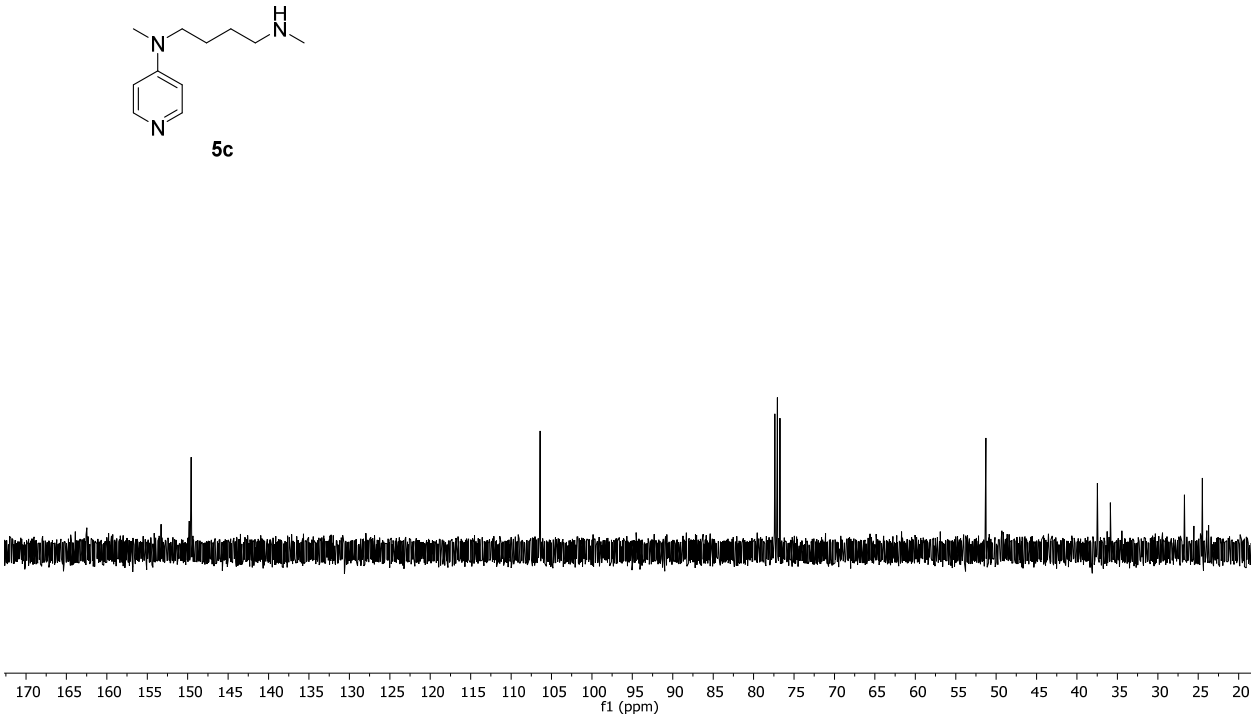
1.10
1.33
0.90
1.31
1.03
1.09
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm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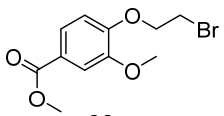
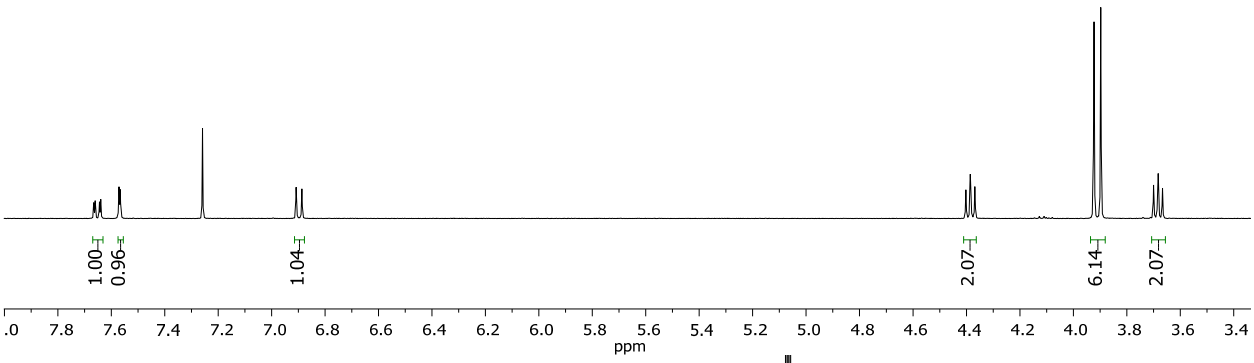
f1 (ppm)


O
Br
O
O
O

22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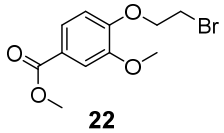
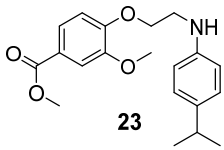
1.04
2.07
6.14
2.07
.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4
ppm


O
Br
O
O
O

22

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm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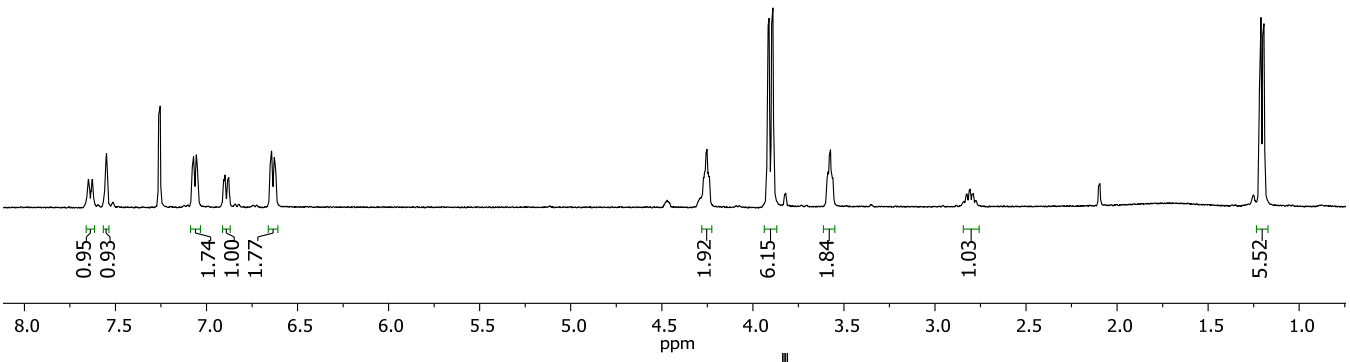
NH
O
O
O
23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7.0
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6.0
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5.0
4.5
4.0
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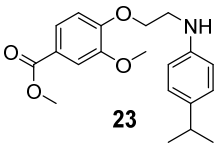
3.0
2.5
2.0
1.5
1.0
ppm


O
NH
O
O
O
23

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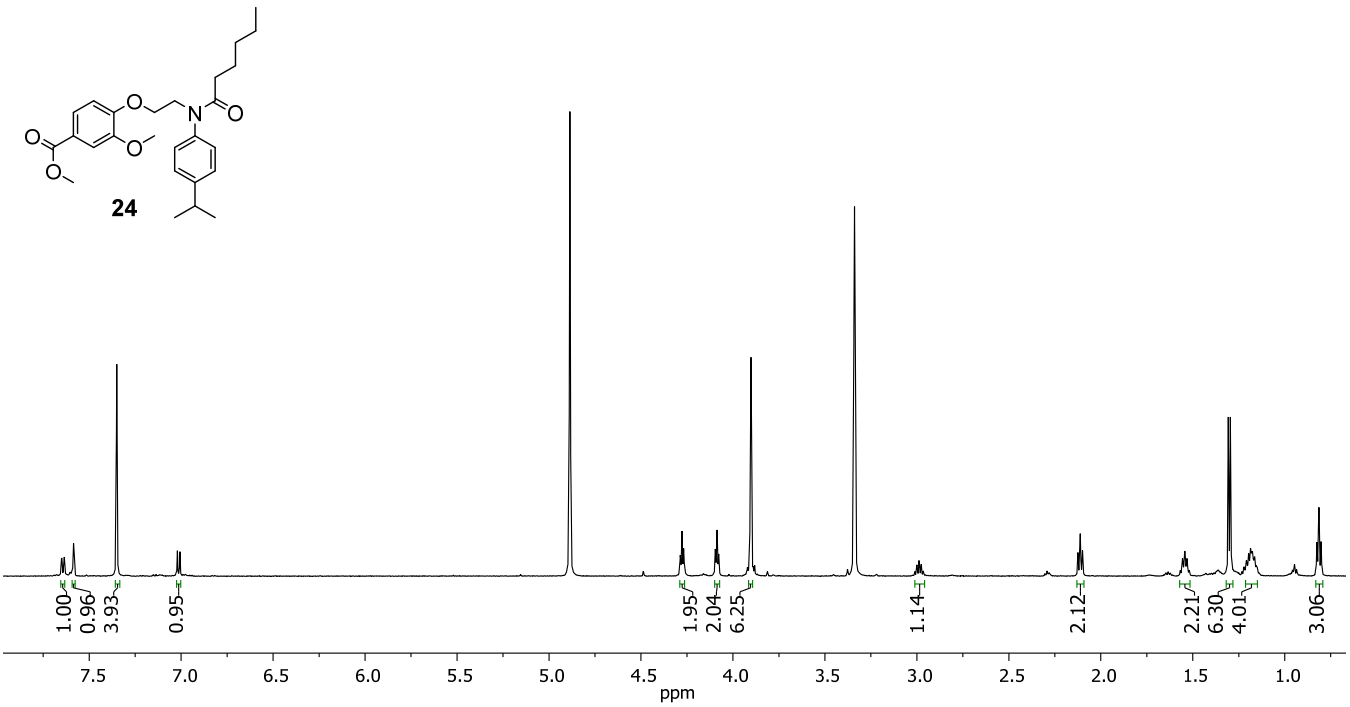
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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1.95
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6.25
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2.21
6.30
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3.06
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7.0
6.5
6.0
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4.5
4.0
3.5
3.0
2.5
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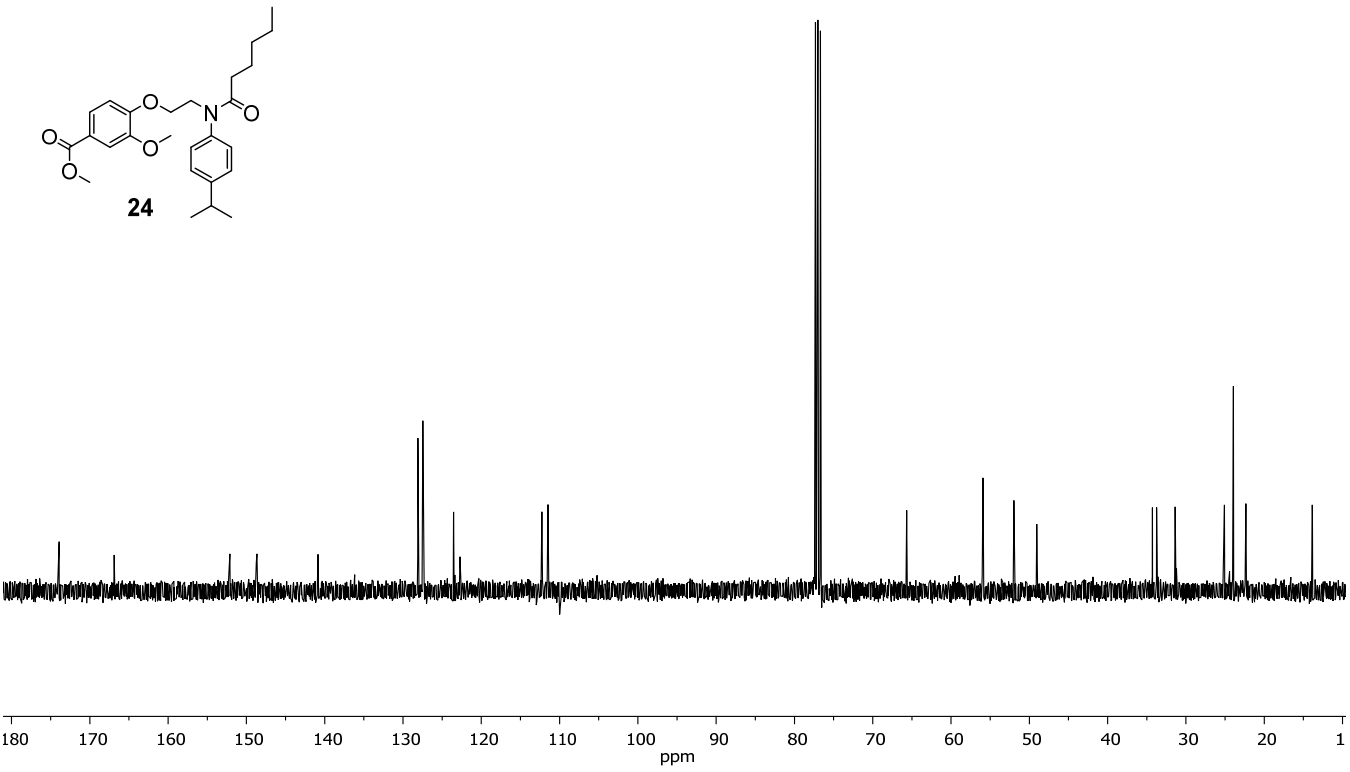
1.5
1.0
ppm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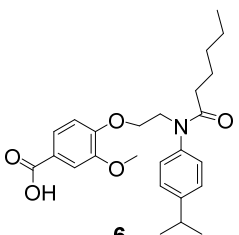
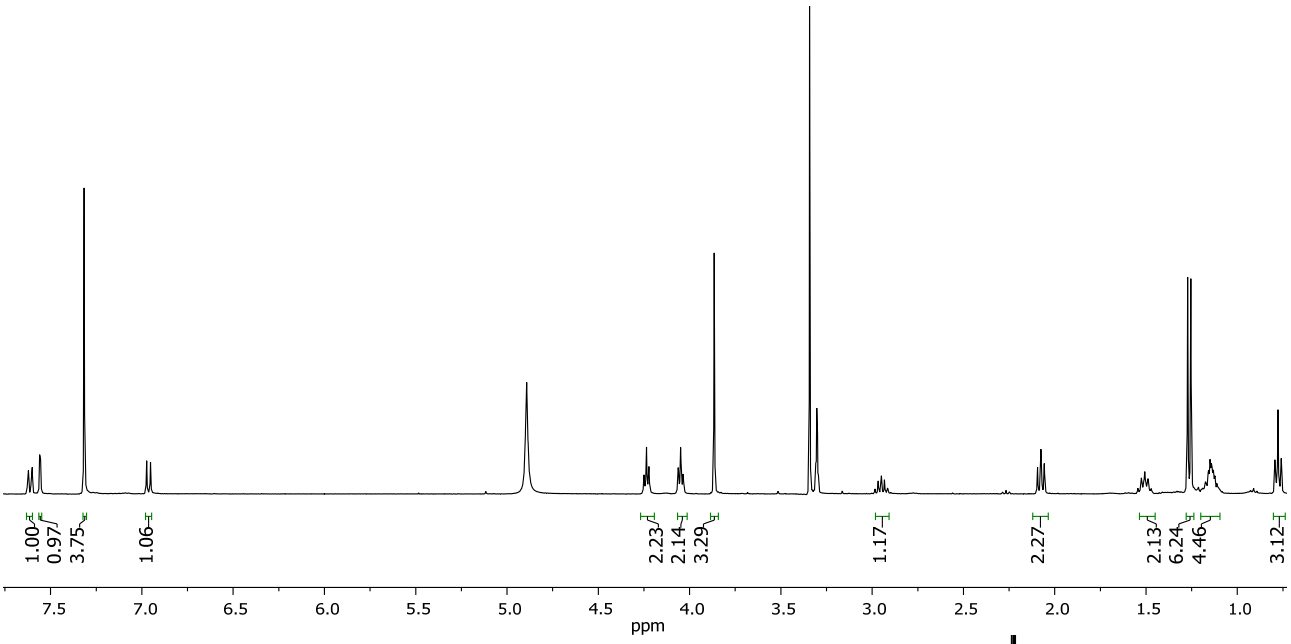
150
140
130
120
110
100
90
80
70
60
50
40
30
20
1
ppm


OH
6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7.0
6.5
6.0
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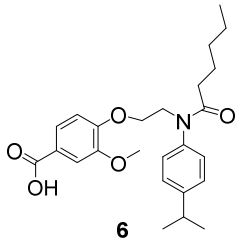
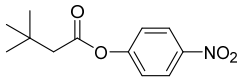
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

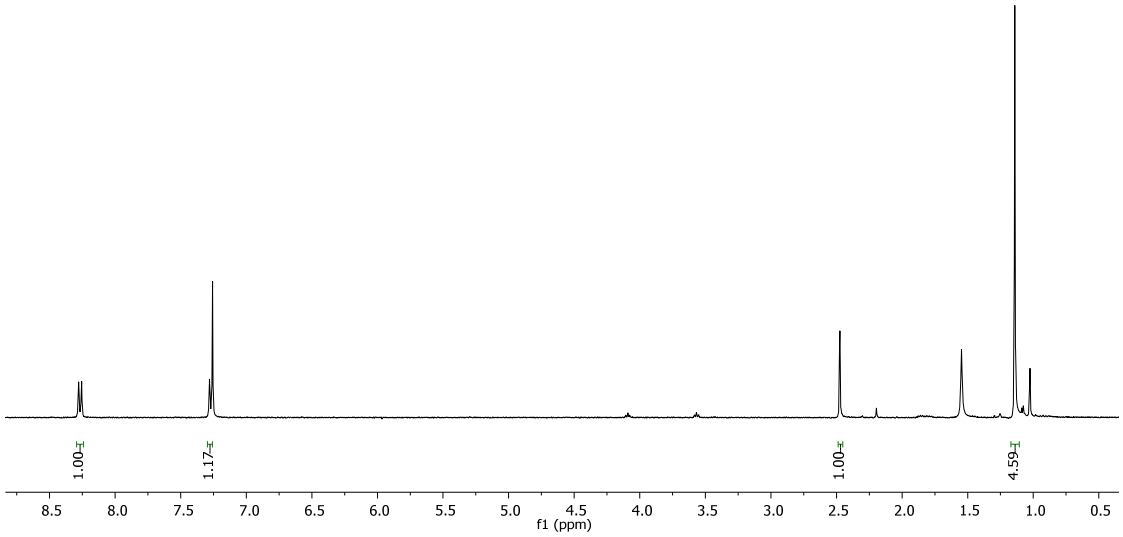

O
N
O
O
O
OH

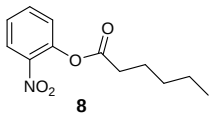
6

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
1
ppm

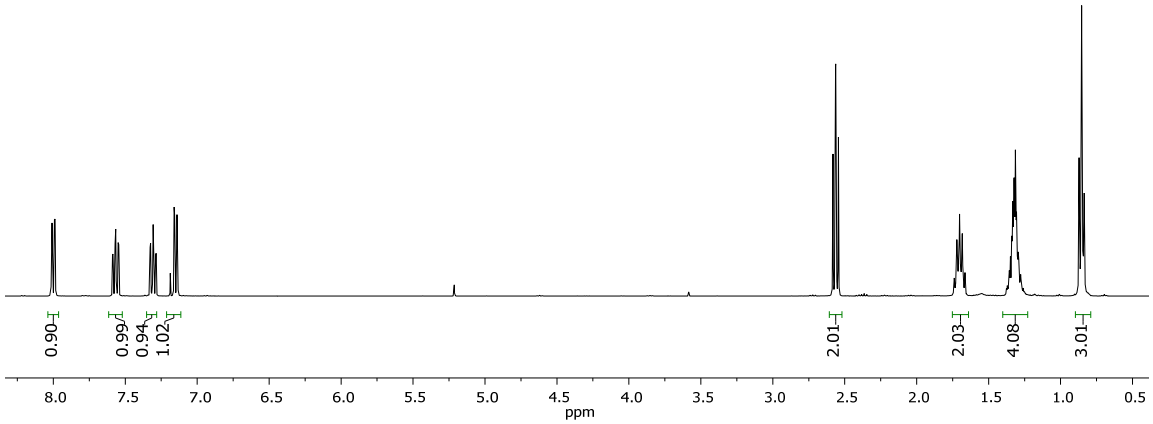

O
O
NO2

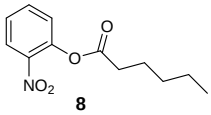
7


1.00
1.17
1.00
4.59
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
f1 (ppm)

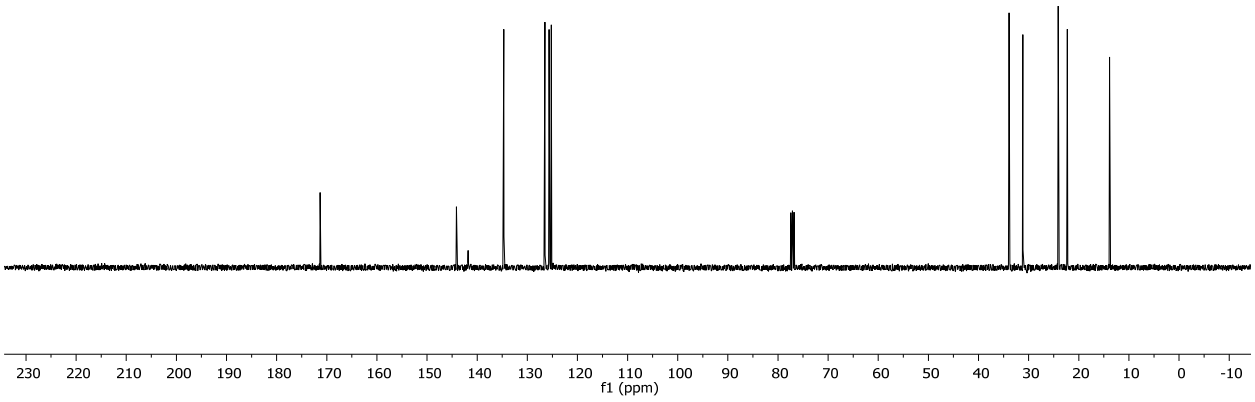

O
O
NO2

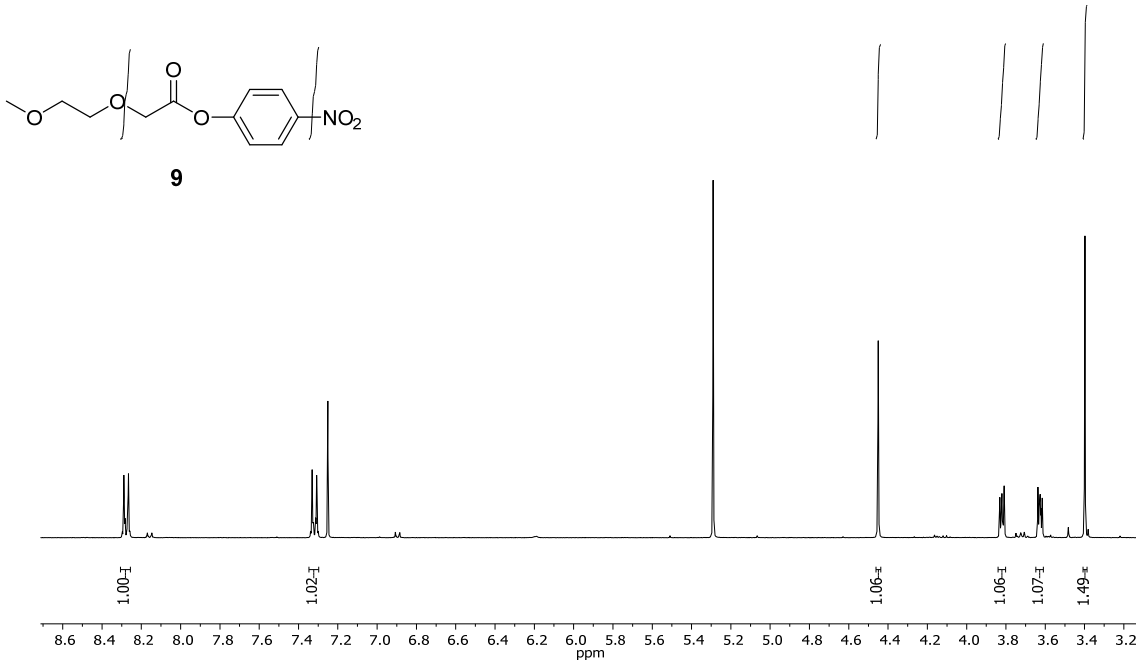
8

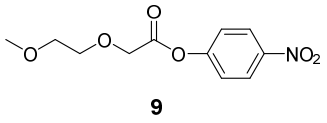

0.90
0.99
0.94
1.02
2.01
2.03
4.08
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

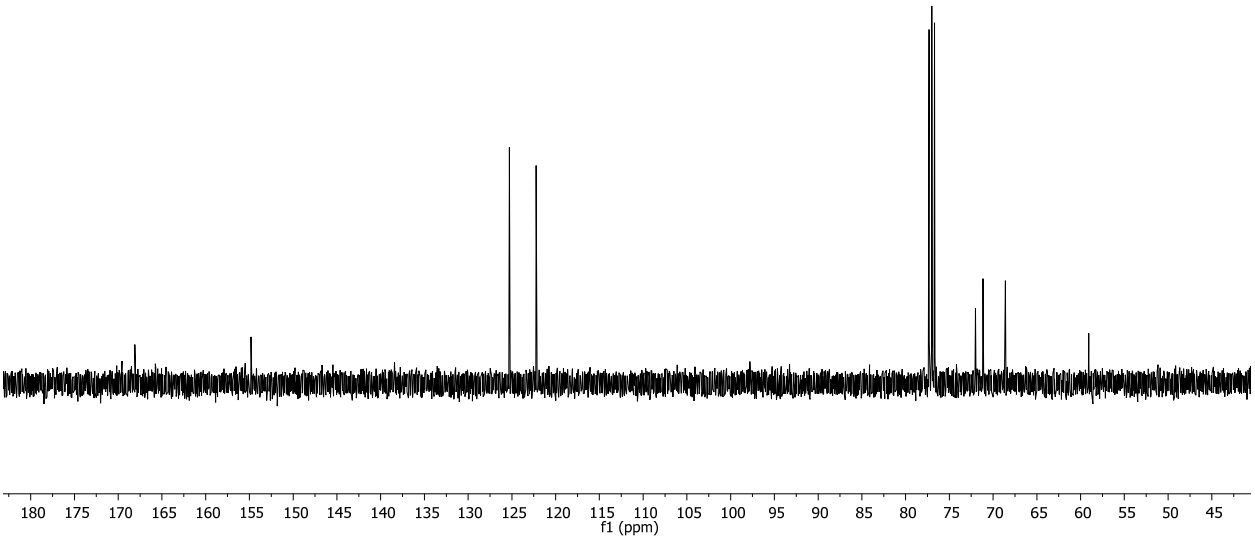

O
O
NO2

8


230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
O
O
O
NO2
9
1.00
1.02
1.06
1.06
1.07
1.49
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2
ppm


O
O
O
O
NO2
9


180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45
f1 (ppm)