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Direct Synthesis of Macrodiolides via Hafnium(IV) Catalysis

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SUPPORTING INFORMATION

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General:

All reactions that were carried out under anhydrous conditions were performed under an inert argon or nitrogen atmosphere in glassware that had previously been dried overnight at 120 °C or had been flame dried and cooled under a stream of argon or nitrogen.[1] All chemical products were obtained from Sigma-Aldrich Chemical Company or Strem Chemicals and were reagent quality. Technical solvents were obtained from VWR International Co. Methyl 3-iodobenzoate[2] and methyl 4-iodobenzoate[2] were prepared according to literature procedure. Anhydrous solvents (CH_2Cl_2, Et_2O, THF, DMF, toluene, and *n*-hexane) were dried and deoxygenated using a GlassContour system (Irvine, CA). Isolated yields reflect the mass obtained following flash column silica gel chromatography. Organic compounds were purified using the method reported by W. C. Still[3] and using silica gel obtained from Silicycle Chemical division (40-63 nm; 230-240 mesh). Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel 60 coated with a fluorescence indicator (Silicycle Chemical division, 0.25 mm, F_{254}.). Visualization of TLC plate was performed by UV (254 nm), $KMnO_4$ or *p*-anisaldehyde stains. All mixed solvent eluents are reported as v/v solutions. Concentration refers to removal of volatiles at low pressure on a rotary evaporator. All reported compounds were homogeneous by thin layer chromatography (TLC) and by ^{1}H NMR. NMR spectra were taken in deuterated $CDCl_3$ using Bruker AV-300 and AV-400 instruments unless otherwise noted. Signals due to the solvent served as the internal standard ($CHCl_3$: δ 7.27 for ^{1}H, δ 77.0 for ^{13}C). The acquisition parameters are shown on all spectra. The ^{1}H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); the list of couplings constants (*J*) corresponds to the order of the multiplicity assignment. High resolution mass spectroscopy (HRMS) was done by the Centre régional de spectrométrie de masse at the Département de Chimie, Université de Montréal from an Agilent LC-MSD TOF system using ESI mode of ionization unless otherwise noted.

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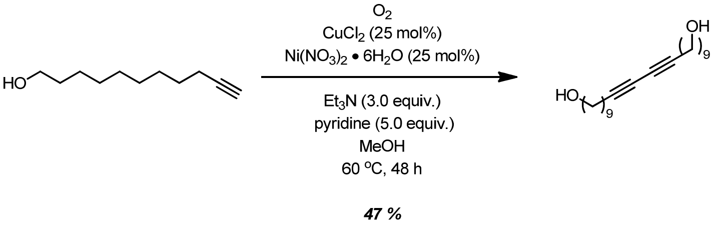
[1] Shriver, D. F.; Drezdon, M. A. in *The Manipulation of Air-Sensitive Compounds*; Wiley-VCH: New York, 1986.

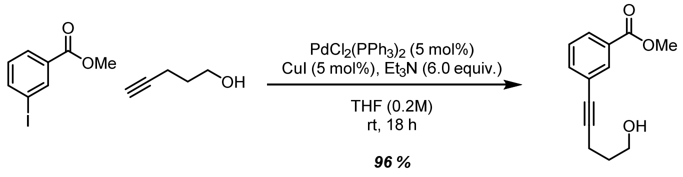
[2] Leatherbarrow, R. J.; Mo, B.; Offermann, D. A.; Sejberg, J. J. P.; Spivey, A. C.; McKendrick, J. E.; Beavil, A. J.; Holdom, M. D.; Sutton, B. J.; Helm, B. A. *J. Org. Chem.* **2012** , *77*, 3197-3214

[3] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

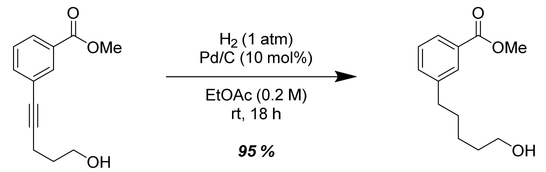
SYNTHETIS OF MACROCYCLE PRECURSORS



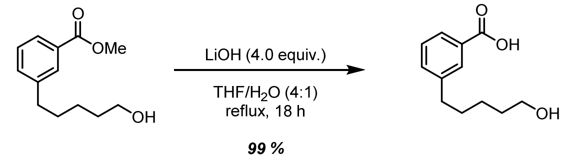
Docosa-10,12-diyne-1,22-diol (S1) $CuCl_2$ (55 mg, 0.413 mmol, 0.25 equiv.) and $Ni(NO_3)_2 \cdot 6H_2O$ (120 mg, 0.413 mmol, 0.25 equiv.) were dissolved in MeOH (15 mL). Then Et_3N (0.69 mL, 4.95 mmol, 3.0 equiv.) and pyridine (0.67 mL, 8.25 mmol, 5.0 equiv.) were added to the solution followed by 9-undecyn-1-ol (277 mg, 1.65 mmol, 1.0 equiv.). The reaction mixture was purged with O_2 and was stirred at 60 °C for 48 h (The reaction mixture was purged O_2 every 12 hours). The mixture was then cooled down to room temperature and silica gel was added. The slurry was concentrated under reduced pressure and flash chromatography (30 % EtOAc in hexanes) was performed to afford the desired product (130 mg, 47 %) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, *J*= 6.8 Hz, 4H), 2.25 (t, *J*= 6.8 Hz, 4H), 1.60-1.50 (m, 8H), 1.45-1.26 (m, 22H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.2, 65.3, 63.1, 32.8, 29.4, 29.0, 28.8, 28.3, 25.73, 25.70, 19.2 ppm; HRMS (ESI+) for $C_{22}H_{39}O_2$ $[M + H]^+$ calculated 335.2945 found: 335.2945.



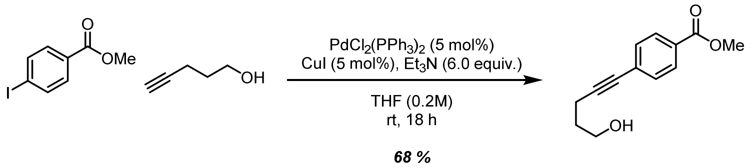
Methyl 3-(5-hydroxypent-1-yn-1-yl)benzoate (S2) Methyl 3-iodobenzoate (1.00 g, 3.82 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (20 mL, 0.2 M). Then $Pd(PPh_3)_2Cl_2$ (134 mg, 0.191 mmol, 0.05 equiv.) and CuI (36 mg, 0.191 mmol, 0.05 equiv.) were added to the solution and the reaction mixture was purged under N_2 for 5 minutes. Triethylamine (3.19 mL, 22.9 mmol, 6.0 equiv.) and the alkyne (0.35 mL, 3.82 mmol, 1.0 equiv.) were added and the reaction mixture was stirred at room temperature for 18 h. Silica gel (~ 5 mL) was added and the slurry was concentrated under reduce pressure and flash chromatography (20-40 % EtOAc in hexanes) was performed to afford the desired product as a colorless oil (796 mg, 96 %). ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.94 (d, *J*= 7.9 Hz, 1H), 7.56 (d, *J*= 7.7 Hz, 1H), 7.36 (dd, *J*= 7.8, 7.7 Hz, 1H), 3.92 (s, 3H), 3.83 (t, *J*= 6.2 Hz, 2H), 2.56 (t, *J*= 7.0 Hz, 2H), 1.91-1.84 (m, 2H), 1.59 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 135.7, 132.7, 130.3, 128.6, 128.3, 124.2, 90.4, 80.1, 61.7, 52.2, 31.3, 15.9 ppm; HRMS (ESI+) for $C_{13}H_{15}O_3$ $[M + H]^+$ calculated: 219.1016 found: 219.1018.



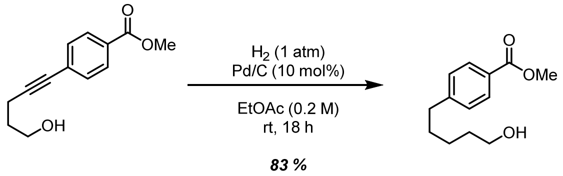
Methyl 3-(5-hydroxypent-1-yl)benzoate (S3) The alkyne (218 mg, 1.00 mmol) was dissolved in ethyl acetate (5 mL) under N_2. Then Pd/C (212 mg, 5% w/w, 0.100 mmol, 0.1 equiv.) was added and the reaction mixture was purged with H_2 for 10 minutes. A balloon, filled with H_2 and equipped with a syringe, was pierced into the septum and the reaction mixture was stirred at room temperature for 18 hours. The reaction mixture was passed through a short pad of Celite® after being purged by bubbling with N_2 for 10 minutes and concentrated under reduced pressure. Purification by flash chromatography (30% EtOAc in hexanes) was performed to afford the desired product as a colorless oil (212 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.88 (m, 2H), 7.39-7.37 (m, 2H), 3.94 (s, 3H), 3.67 (t, *J*= 6.5 Hz, 2H), 2.70 (t, *J*= 8.6 Hz, 2H), 1.74-1.60 (m, 4H), 1.46-1.41 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 142.8, 133.0, 130.1, 129.5, 128.3, 127.0, 62.8, 52.0, 35.6, 32.6, 31.1, 25.3 ppm; HRMS (ESI+) for $C_{13}H_{18}O_3Na$ [M + Na]$^+$ calculated: 245.1148 found: 245.1146.



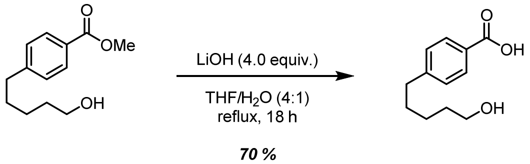
3-(5-Hydroxypent-1-yl)benzoic acid (S4) Methyl 3-(5-hydroxypent-1-yl)benzoate (200 mg, 0.901 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (8 mL). Then LiOH (87 mg, 3.60 mmol, 4.0 equiv.) was added as an aqueous solution (2 mL). The reaction mixture was stirred at 65 °C for 18 h. The reaction mixture was cooled to room temperature and HCl (1 M) was added until the pH was neutralized (pH = 7). Extraction with EtOAc (3 X 5 mL) was performed and the combined organic phases were washed with brine (15 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to afford the desired product as a white solid (187 mg, 99 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.94 (m, 2H), 7.44-7.36 (m, 2H), 3.67 (t, *J*= 6.6 Hz, 2H), 2.71 (t, *J*= 7.5 Hz, 2 H), 1.73-1.59 (m, 4H), 1.46-1.38 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 142.9, 133.7, 129.9, 129.5, 128.4, 127.6, 62.7, 35.6, 32.3, 31.0, 25.3 ppm; HRMS (ESI+) for $C_{12}H_{16}O_3Na$ [M + Na]$^+$ calculated: 231.0992 found: 231.0986.



Methyl 4-(5-hydroxypent-1-yn-1-yl)benzoate (S5) Methyl 3-iodobenzoate (1.00 g, 3.82 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (20 mL, 0.2 M). Then $Pd(PPh_3)_2Cl_2$ (134 mg, 0.191 mmol, 0.05 equiv.) and CuI (36 mg, 0.191 mmol, 0.05 equiv.) were added to the solution and the reaction mixture was purged under N_2 for 5 minutes. Triethylamine (3.19 mL, 22.9 mmol, 6.0 equiv.) and the alkyne (0.35 mL, 3.82 mmol, 1.0 equiv.) were added and the reaction mixture was stirred at room temperature for 18 h. Silica gel (~ 5 mL) was added and the slurry was concentrated under reduced pressure and flash chromatography (20-40 % EtOAc in hexanes) was performed to afford the desired product as a white solid (563 mg, 68 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J*= 8.6 Hz, 2H), 7.45 (d, *J*= 8.4 Hz, 2H), 3.92 (s, 3H), 3.84 (m, 2H), 2.58 (t, *J*= 7.0 Hz, 2H), 1.91-1.87 (m, 2H), 1.50 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 131.5, 129.4, 129.0, 128.6, 92.8, 80.6, 61.7, 52.2, 31.2, 16.1 ppm; HRMS (ESI+) for $C_{13}H_{15}O_3$ $[M + H]^+$ calculated: 219.1016 found: 219.1018.

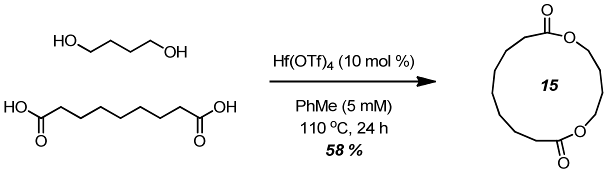


Methyl 4-(5-hydroxypent-1-yl)benzoate (S6) The alkyne (250 mg, 1.15 mmol, 1.00 equiv.) was dissolved in ethyl acetate (6 mL) under N_2. Then Pd/C (243 mg, 5% w/w, 0.115 mmol, 0.1 equiv.) was added and the reaction mixture was purged with H_2 for 10 minutes. A balloon filled with H_2 and equipped with a syringe was pierced into the septum and the reaction mixture was stirred at room temperature for 18 hours. The reaction mixture was passed through a short pad of Celite® after being purged by bubbling with N_2 for 10 minutes and concentrated under reduced pressure. Purification by flash chromatography (30% EtOAc in hexanes) was performed to afford the desired product as a white solid (212 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J*= 8.2 Hz, 2H), 7.24 (d, *J*= 8.0 Hz, 2H), 3.90 (s, 3H), 3.64 (t, *J*= 6.6 Hz, 2H), 2.68 (t, *J*= 7.7 Hz, 2H), 1.72-1.57 (m, 4H), 1.45-1.37 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 148.1, 129.6, 128.4, 127.7, 62.8, 51.9, 35.9, 32.5, 30.9, 25.4 ppm; HRMS (ESI+) for $C_{13}H_{19}O_3$ $[M + H]^+$ calculated: 223.1329 found: 223.1321.

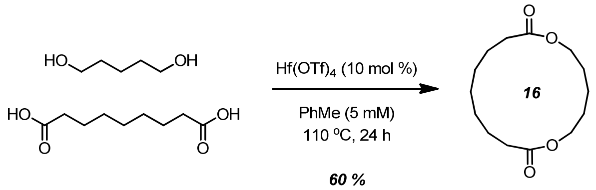


4-(5-Hydroxypent-1-yl)benzoic acid (S7) Methyl 4-(5-hydroxypent-1-yl)benzoate (200 mg, 0.900 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (7.2 mL). Then LiOH (86 mg, 3.60 mmol, 4.0 equiv.) was added as an aqueous solution (1.8 mL). The reaction mixture was stirred at 65 °C for 18 h. The reaction mixture was cooled to room temperature and HCl (1 M) was added until the pH of the mixture was neutralized (pH = 7). Extraction with EtOAc (3 X 5 mL) was performed and the combined organic phases were washed with brine (15 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to afford the desired product as a white solid (130 mg, 70 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J*= 8.1 Hz, 2H), 7.29 (d, *J*= 8.2 Hz, 2H), 3.67 (t, *J*= 6.6 Hz, 2H), 2.71 (t, *J*= 7.5 Hz, 2H), 1.72-1.60 (m, 4H), 1.47-1.40 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 149.1, 130.3, 128.6, 126.8, 62.8, 36.0, 32.5, 30.9, 25.4 ppm; HRMS (ESI+) for $C_{12}H_{16}O_3Na$ $[M + Na]^+$ calculated: 231.0992 found: 231.0988.

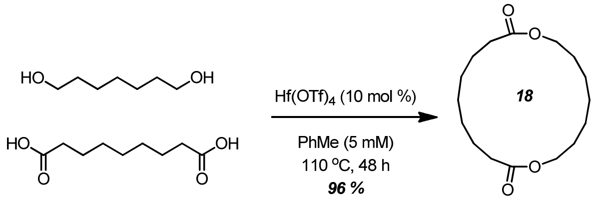
SYNTHESIS OF MACROCYCLES



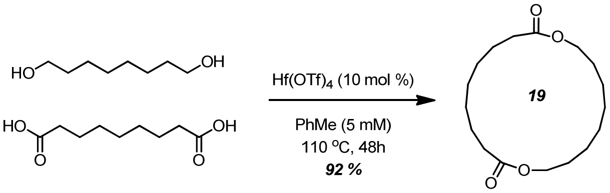
1,6-Dioxapentadecane-7,15-dione (4): 1,4-Butanediol (0.017 mL, 0.2 mmol, 1.0 equiv.) and 1,9-nonanedioic acid (38 mg, 0.2 mmol, 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (15.5 mg, 0.02 mmol, 0.1equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 1 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to afford the desired product as a white solid (28 mg, 58 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21 (m, 4H), 2.34 (m, 4H), 1.77 (m, 4H), 1.64 (m, 4H), 1.37-1.34 (m 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 63.6, 34.6, 27.8, 27.5, 26.5, 24.6 ppm; HRMS (ESI+) for $C_{13}H_{23}O_4$ $[M + H]^+$ calculated: 243.1591 found: 243.1599.



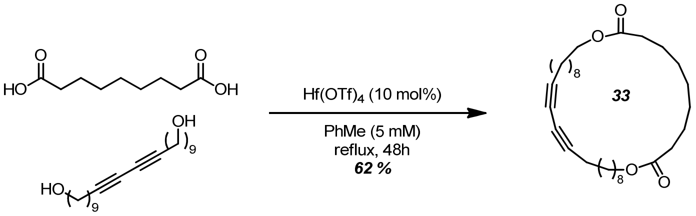
1,7-Dioxahexadecane-8,16-dione (5): 1,4-Pentanediol (0.021 mL, 0.2 mmol, 1.0 equiv.) and 1,9-nonanedioic acid (38 mg, 0.2 mmol, 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (15.5 mg, 0.02 mmol, 0.1equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 1 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to afford the desired product as a white solid (30 mg, 60 %). ^1H NMR (400MHz, $CDCl_3$) δ 4.14 (t, *J*= 5.4 Hz, 4H), 2.36 (t, *J*= 6.5 Hz, 4H), 1.71-1.62 (m, 8H), 1.57-1.48 (m, 2H), 1.37-1.30 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 64.1, 34.3, 28.7, 28.3, 27.7, 24.9, 23.9 ppm; HRMS (ESI+) for $C_{14}H_{25}O_4$ $[M + H]^+$ calculated: 257.1756 found: 257.1747.



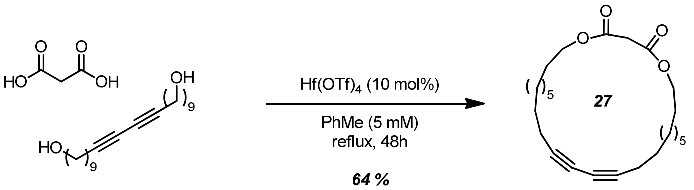
1,9-Dioxaoctadecane-10,18-dione (6): 1,7-Heptanediol (0.030 mL, 0.2 mmol, 1.0 equiv.) and 1,9-nonanedioic acid (38 mg, 0.2 mmol, 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (15.5 mg, 0.02 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 1 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to afford the desired product as a white solid (55 mg, 96 %). ^1H NMR (400 MHz, $CDCl_3$) δ 4.13 (t, *J*= 5.6 Hz, 4H), 2.32 (t, *J*= 6.4 Hz, 4H), 1.65-1.59 (m, 8H), 1.41-1.30 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 63.7, 34.9, 29.2, 28.8, 28.4, 28.0, 25.6, 25.5 ppm; HRMS (ESI+) for $C_{16}H_{29}O_4$ $[M + H]^+$ calculated: 285.2060 found: 285.2051.



1,10-Dioxanonadecane-11,19-dione (3): 1,8-Octanediol (29, 0.2 mmol, 1.0 equiv.) and 1,9-nonanedioic acid (38 mg, 0.2 mmol 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then Hf(OTf)$_4$ (7.8 mg, 0.01 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 1 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to the desired product as a white solid (55 mg, 92 %). ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.12 (t, *J*= 6.0 Hz, 4H), 2.32 (t, *J*= 6.8 Hz, 4H), 1.65-1.60 (m, 8H), 1.40-1.30 (m, 14H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 174.0, 64.3, 34.8, 29.3, 29.1, 28.9, 28.7, 26., 25.3 ppm; HRMS (ESI+) for $C_{17}H_{31}O_4$ [M + H]$^+$ calculated: 299.2217 found: 299.2226.

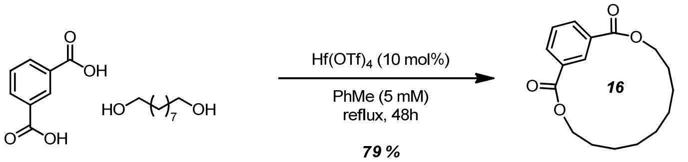


1,11-Dioxacyclotritriaconta-21,23-diyne-2,10-dione (7) The diol **S1** (33 mg, 0.1 mmol, 1.0 eq) and the diacid (19 mg, 0.1 mmol 1.0 eq) were dissolved in toluene (20 mL, 5 mM). Then Hf(OTf)$_4$ (7.8 mg, 0.01 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to afford the desired product as a yellow solid (30 mg, 62 %). ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.08 (t, *J*= 6.0 Hz, 4H), 2.30 (t, *J*=7.4 Hz, 4H), 2.26 (t, *J*=6.5 Hz, 4H), 1.65-1.60 (m, 8H), 1.55-1.48 (m, 4H), 1.40-1.30 (m, 26H) ppm ^{13}C NMR (100 MHz, CDCl$_3$) δ 173.9, 77.4, 65.4, 64.3, 34.4, 29.1, 29.0, 28.9, 28.7, 28.6, 28.5, 28.0, 25.9, 24.9, 19.1 ppm; HRMS (ESI+) for $C_{31}H_{50}O_4Na$ [M + Na]$^+$ calculated 509.3601 found: 509.3596.

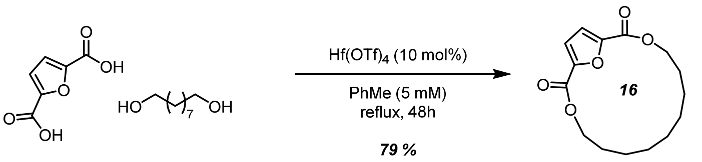


1,5-Dioxacycloheptacosa-15,17-diyne-2,4-dione (8) The diol **S1** (33 mg, 0.1 mmol, 1.0 equiv.) and the diacid (11 mg, 0.1 mmol 1.0 equiv.) were dissolved in toluene (20 mL, 5 mM). Then Hf(OTf)$_4$ (7.8 mg, 0.01 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5 % EtOAc in hexanes) to afford the desired product as a white solid (26 mg, 64 %). ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.15 (t, *J*= 6.8 Hz, 4H), 3.38 (s, 2H), 2.28 (t, *J*=6.0 Hz, 4H), 2.26 (t,

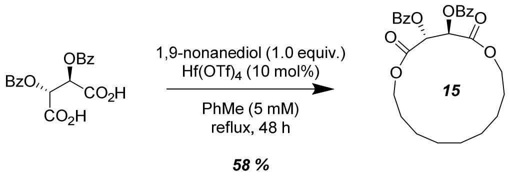
J=6.5 Hz, 4H), 1.70-1.60 (m, 4H), 1.53-1.30 (m, 24H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 77.4, 65.6, 41.8, 29.2, 28.8, 28.7, 27.8, 25.8, 19.1 ppm; HRMS (ESI+) for $C_{25}H_{38}O_4Na$ $[M + Na]^+$ calculated 425.2662 found: 425.2672.



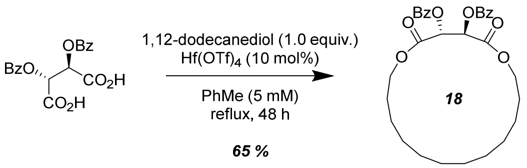
3,13-Dioxa-1(1,13)-benzenacyclotetradecaphane-2,14-dione (9) 1,9-Nonanediol (16 mg, 0.1 mmol, 1.0 equiv.) and isophthalic acid (17 mg, 0.1 mmol 1.0 equiv.) were dissolved in toluene (20 mL, 5 mM). Then $Hf(OTf)_4$ (7.8 mg, 0.01 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (23 mg, 79 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.26-8.23 (m, 2H), 7.57 (t, J= 7.8 Hz, 1H), 4.39 (t, J= 5.2 Hz, 4H), 1.82-1.20 (m, 14H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 133.7, 130.91, 130.89, 128.8, 65.3, 28.9, 28.4, 28.1, 26.2 ppm; HRMS (ESI+) for $C_{17}H_{23}O_4$ $[M + H]^+$ calculated 291.1591 found: 291.1592.



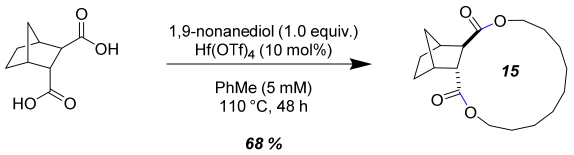
3,13-Dioxa-1(2,5)-furanacyclotetradecaphane-2,14-dione (10) 1,9-Nonanediol (16 mg, 0.1 mmol, 1.0 equiv.) and 2,5-furandicarboxylic acid (15 mg, 0.1 mmol 1.0 equiv.) were dissolved in toluene (20 mL, 5 mM). Then $Hf(OTf)_4$ (7.8 mg, 0.01 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (22 mg, 79 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 2H), 4.37 (t, J= 5.5 Hz, 4H), 1.80-1.75 (m, 4H), 1.63-1.35 (m, 10H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 146.5, 118.0, 65.8, 29.1, 28.4, 27.7, 26.2 ppm; HRMS (ESI+) for $C_{15}H_{20}O_5Na$ $[M + Na]^+$ calculated 303.1203 found: 303.1205.



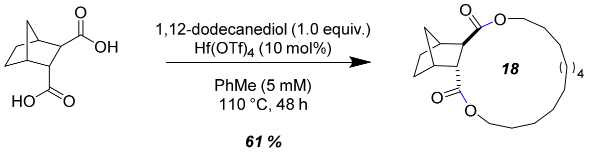
(3R, 4R)-2,5-Dioxo-1,6-dioxacyclopentadecane-3,4-diyl dibenzoate (11) 1,9-Nonanediol (32 mg, 0.2 mmol, 1.0 equiv.) and dibenzoyl-L-tartaric acid (71 mg, 0.2 mmol 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then Hf(OTf)$_4$ (15.5 mg, 0.02 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10-20 % EtOAc in hexanes) to afford the desired product as a colorless oil (56 mg, 58 %). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.06 (d, *J*= 7.9 Hz, 4H), 7.57 (t, *J*= 7.2 Hz, 2H), 7.43 (t, *J*= 7.6 Hz, 4H), 5.88 (s, 2H), 4.36-4.32 (m, 4H), 1.75-1.65 (m, 4H), 1.43-1.38 (m, 10H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.6, 165.1, 133.7, 130.1, 128.6, 128.5, 70.6, 65.6, 27.8, 26.4, 25.6, 23.5 ppm; HRMS (ESI+) for $C_{30}H_{36}O_8Na$ [M + Na]$^+$ calculated 547.2302 found: 547.2322.



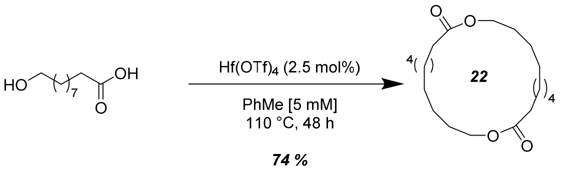
(3R, 4R)-2,5-Dioxo-1,6-dioxacyclooctadecane-3,4-diyl dibenzoate (12) 1,12-Dodecanediol (40 mg, 0.2 mmol, 1.0 equiv.) and dibenzoyl-L-tartaric acid (71 mg, 0.2 mmol 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then Hf(OTf)$_4$ (15.5 mg, 0.02 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10-20 % EtOAc in hexanes) to afford the desired product as a colorless oil (68 mg, 65 %). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.15 (d, *J*= 7.8 Hz, 4H), 7.62 (t, *J*= 7.4 Hz, 2H), 7.49 (t, *J*= 7.7 Hz, 4H), 5.95 (s, 2H), 4.40-4.35 (m, 2H), 4.16-4.10 (m, 4H), 1.73-1.64 (m, 2H), 1.52-1.43 (m, 8H), 1.43-1.38 (m, 10H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.5, 165.3, 133.7, 130.2, 128.7, 128.5, 71.4, 66.9, 28.5, 27.9, 27.8, 27.4, 25.9 ppm; HRMS (ESI+) for $C_{27}H_{30}O_8Na$ [M + Na]$^+$ calculated 505.1833 found: 3505.1848.



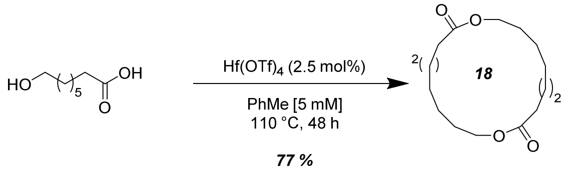
Nonane-1,9-diyl norbornene-2-*endo*,3-*exo*-dicarboxylate (13) 1,9-Nonanediol (32 mg, 0.2 mmol, 1.0 equiv.) and norbornane-2-*endo*,3-*exo*-dicarboxylic acid (37 mg, 0.2 mmol 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (15.5 mg, 0.02 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5% Et_2O in hexanes) to afford the desired product as a colorless oil (42 mg, 68 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (ddd, *J*= 12, 9.1, 3.0 Hz, 1H), 4.33 (ddd, *J*= 12, 8.4, 3.0 Hz, 1H), 3.98-3.89 (m, 2H), 3.05-3.01 (m, 1H), 2.75 (dd, *J*= 6.1, 1.4 Hz, 1H), 2.63-2.60 (m, 2H), 1.78-1.52 (m, 6H), 1.50-1.28 (m, 14H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 173.2, 63.8, 63.7, 51.1, 49.2, 40.5, 39.8, 38.7, 29.0, 28.0, 27.8, 26.7, 25.9, 25.6, 23.9, 23.7, 23.6 ppm; HRMS (ESI+) for $C_{18}H_{29}O_4$ $[M + H]^+$ calculated 309.2060 found: 309.2064.



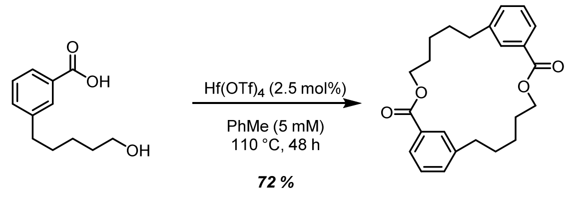
Dodecane-1,12-diyl norbornene-2-*endo*,3-*exo*-dicarboxylate (14) 1,12-Dodecanediol (40 mg, 0.2 mmol, 1.0 equiv.) and norbornane-2-*endo*,3-*exo*-dicarboxylic acid (37 mg, 0.2 mmol 1.0 equiv.) were dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (15.5 mg, 0.02 mmol, 0.1 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling down to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (5% Et_2O in hexanes) to afford the desired product as a colorless oil (42 mg, 68 %).^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (ddd, *J*= 18, 8.2, 4.2 Hz, 1H), 4.27 (ddd, *J*= 18, 8.2, 4.2 Hz, 1H), 3.98-3.93 (m, 2H), 3.15-3.12 (m, 1H), 2.83 (d, *J*= 5.3 Hz, 1H), 2.64-2.60 (m, 2H), 1.70-1.57 (m, 6H), 1.48-1.27 (m, 20H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 173.4, 64.7, 64.5, 50.1, 48.9, 41.4, 40.4, 38.3, 28.7, 28.5, 28.4, 28.1, 27.9, 27.6, 27.2, 27.0, 26.9, 25.5, 25.3, 24.2 ppm; HRMS (ESI+) for $C_{21}H_{34}O_4Na$ $[M + Na]^+$ calculated 373.2349 found: 373.2353.



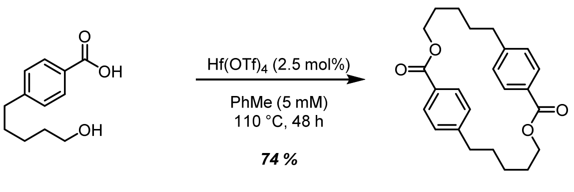
1,12-Dioxacyclodocosane-2,13-dione (16) 10-Hydroxydecanoic acid (38.8 mg, 0.20 mmol 1.0 equiv.) was dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (3.9 mg, 0.005 mmol, 0.025 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (26 mg, 74 %).^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (t, *J*= 5.9 Hz, 4H), 2.32 (t, *J*= 7.0 Hz, 4H), 1.65-1.60 (m, 4H), 1.40-1.28 (m, 20H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 64.0, 34.8, 29.4, 29.1, 29.0, 28.9, 28.6, 26.0, 25.4 ppm; HRMS (ESI+) for$C_{20}H_{37}O_4$ $[M + H]^+$ calculated: 341.2686 found: 341.2700.



1,10-Dioxacyclooctadecane-2,11-dione (17) 8-Hydroxydecanoic acid (32.0 mg, 0.20 mmol 1.0 equiv.) was dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (3.9 mg, 0.005 mmol, 0.025 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (22 mg, 77 %).^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (t, J= 5.9 Hz, 4H), 2.32 (t, J= 6.9 Hz, 4H), 1.67-1.57 (m, 8 H), 1.45-1.30 (m, 12 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 63.8, 34.9, 28.7, 28.60, 28.56, 25.7, 25.2 ppm; HRMS (ESI+) for $C_{16}H_{29}O_4$ $[M + H]^+$ calculated: 285.2060 found: 285.2069.



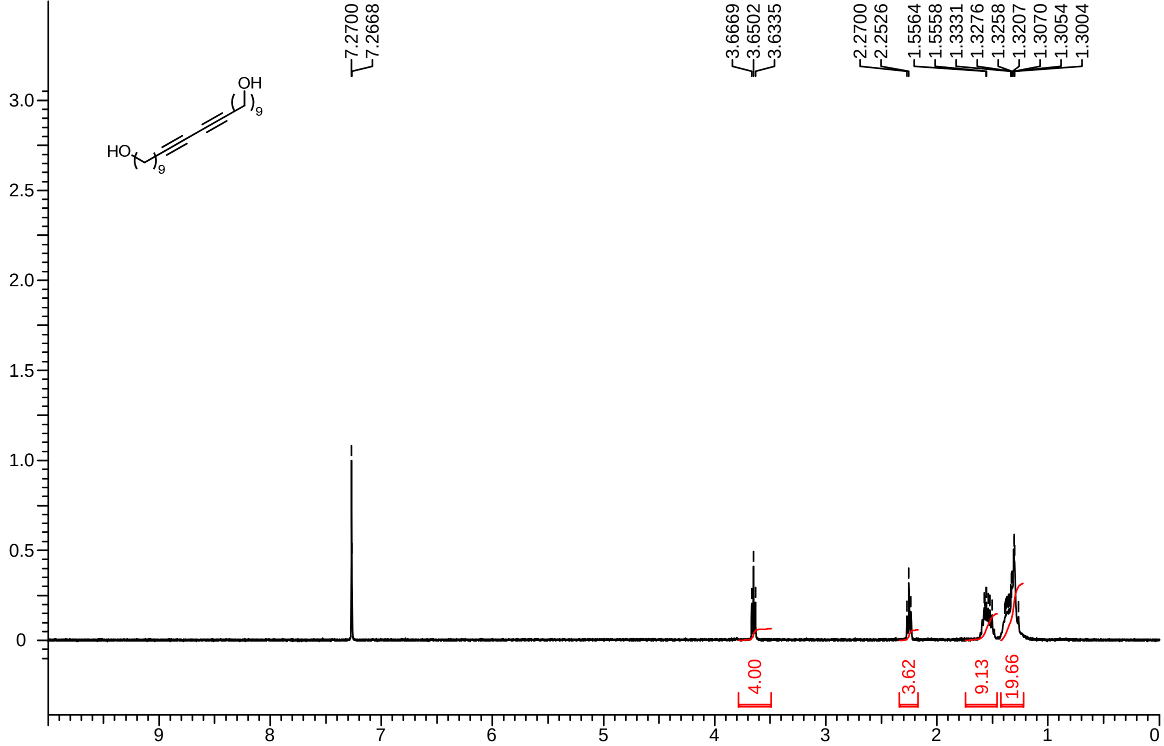
3,11-Dioxa-1,9(1,3)-dibenzenacyclohexadecaphane-2,10-dione (18) The hydroxyacid (67 mg, 0.322 mmol 1.0 equiv.) was dissolved in toluene (60 mL, 5 mM). Then $Hf(OTf)_4$ (6.2 mg, 0.008 mmol, 0.025 equiv.) was added to the solution and the reaction mixture heated to 110 ^{o}C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (44 mg, 72 %).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*= 7.0 Hz, 2H), 7.70 (s, 2 H), 7.35-7.30 (m, 4H), 4.32 (t, *J*= 5.3 Hz, 4H), 2.69 (t, *J*= 6.7 Hz, 4H), 1.77-1.68 (m, 8H), 1.43-1.40 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 142.3, 133.1, 130.2, 129.4, 128.3, 127.2, 64.7, 35.8, 30.4, 28.4, 25.5 ppm; HRMS (ESI+) for $C_{24}H_{28}O_4$ $[M + H]^+$ calculated: 381.2060 found: 381.2049.

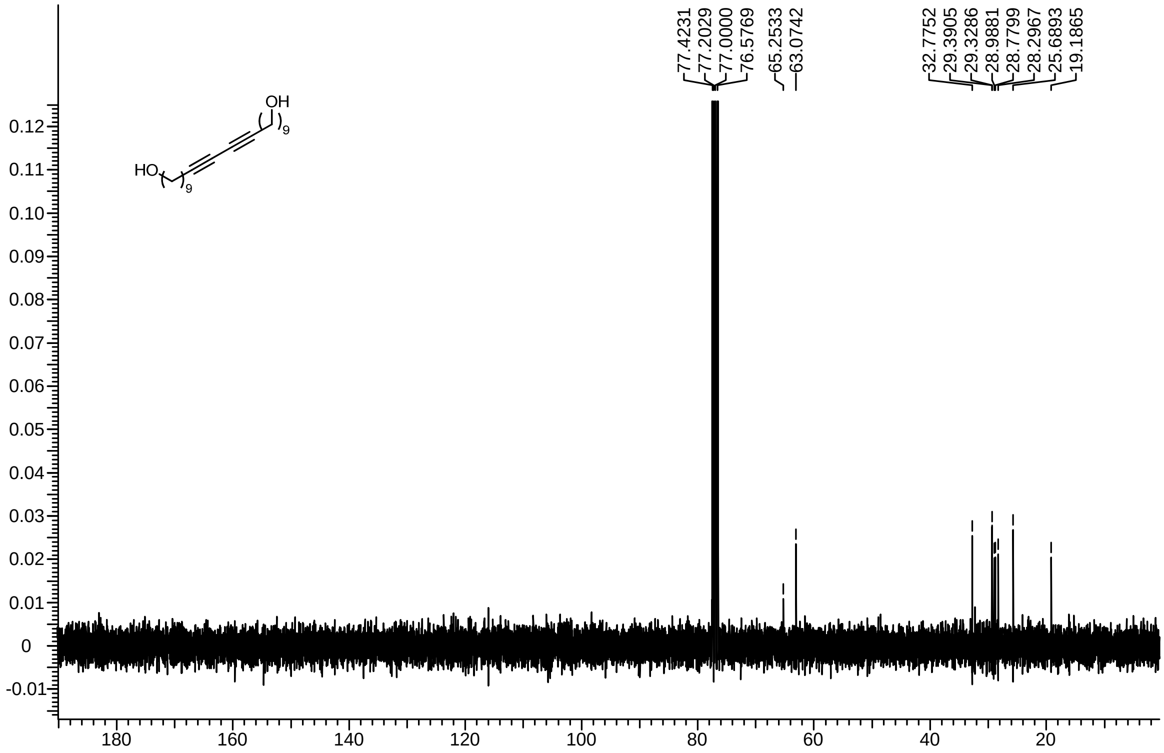


3,11-Dioxa-1,9(1,4)-dibenzenacyclohexadecaphane-2,10-dione (19) The hydroxyacid (42 mg, 0.200 mmol 1.0 equiv.) was dissolved in toluene (40 mL, 5 mM). Then $Hf(OTf)_4$ (3.9 mg, 0.005 mmol, 0.025 equiv.) was added to the solution and the reaction mixture heated to 110 °C. The reaction mixture was stirred at this temperature for 48 h. After cooling to room temperature, silica gel (~ 2 mL) was added and the slurry was concentrated under reduced pressure and purified by flash chromatography (10 % EtOAc in hexanes) to afford the desired product as a white solid (28 mg, 74 %).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J*= 8.3 Hz, 4H), 7.15 (d, *J*= 8.2 Hz, 4H), 4.35 (t, *J*= 5.3 Hz, 4H), 2.74 (t, *J*= 6.0 Hz, 4H), 1.80-1.70 (m, 8 H), 1.37-1.32 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 147.0, 129.4, 128.7, 127.8, 63.5, 34.1, 28.4, 27.7, 22.9 ppm; HRMS (ESI+) for $C_{24}H_{28}O_4$ $[M + H]^+$ calculated: 381.2060 found: 381.2061.

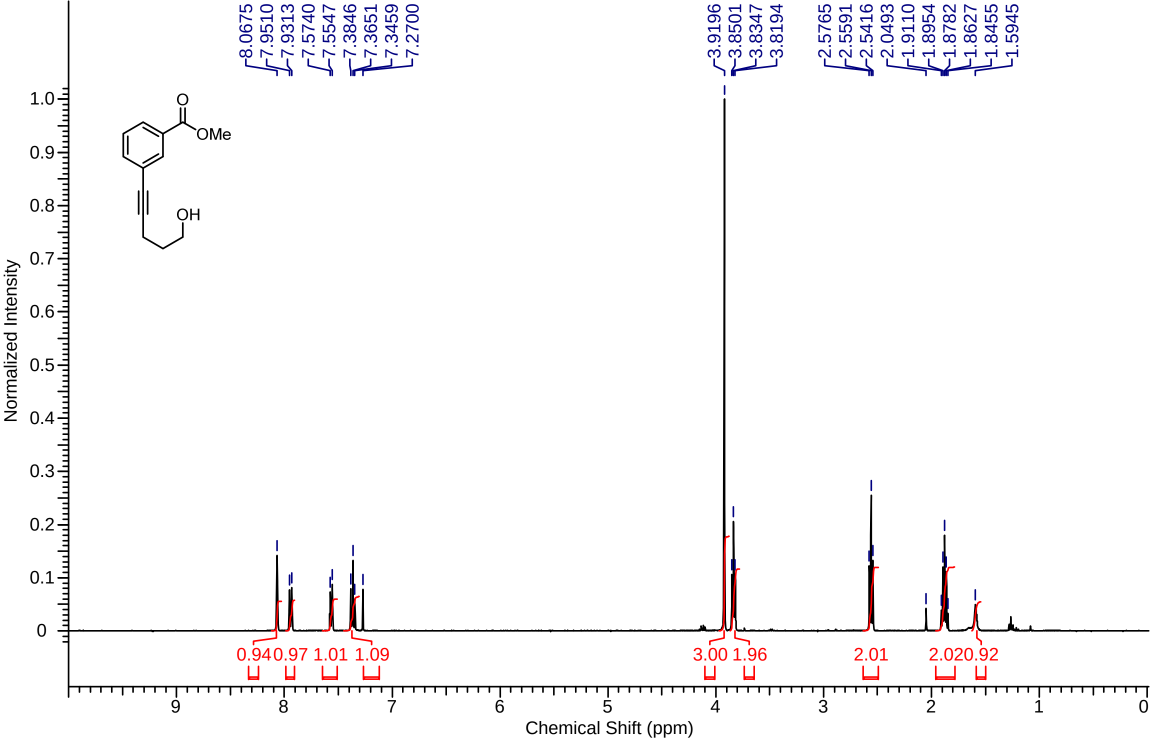
SPECTRAL DATA

Compound S1





Compound S2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1.9110
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O
OMe
OH
Normalized Intensity
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0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.94
0.97
1.01
1.09
3.00
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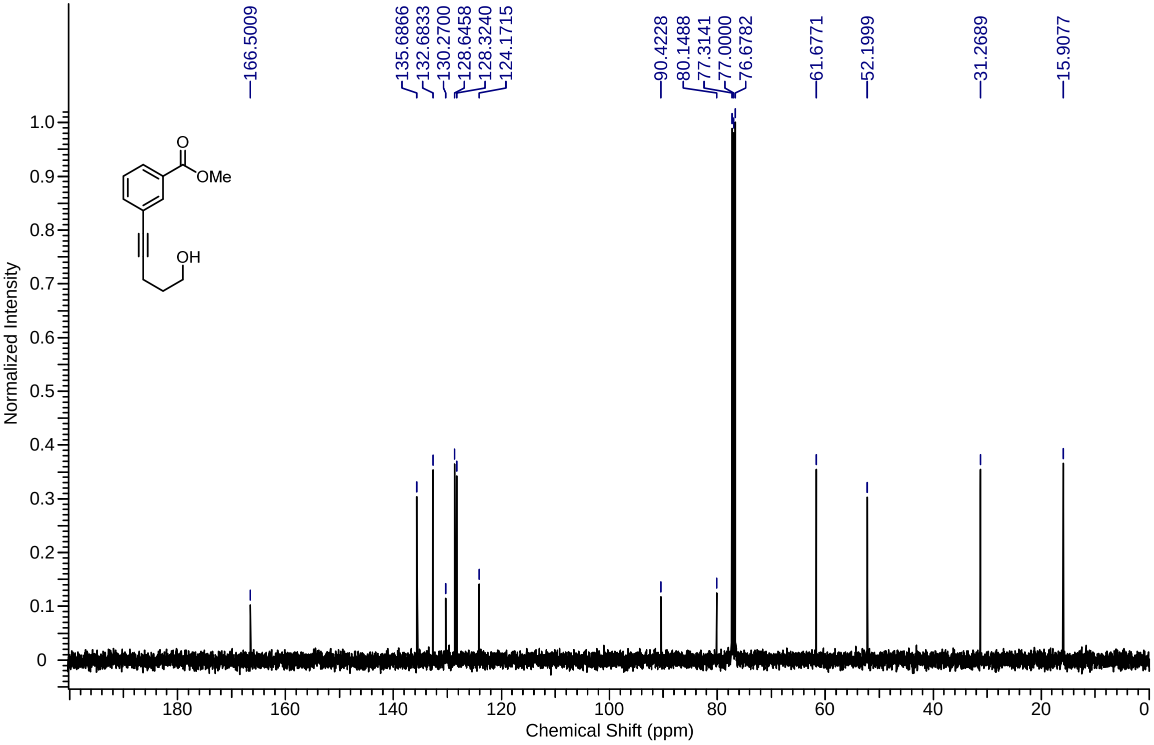
2.02
0.92
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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77.0000
76.6782
61.6771
52.1999
31.2689
15.9077
O
OMe
OH
Normalized Intensity
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0.9
0.8
0.7
0.6
0.5
0.4
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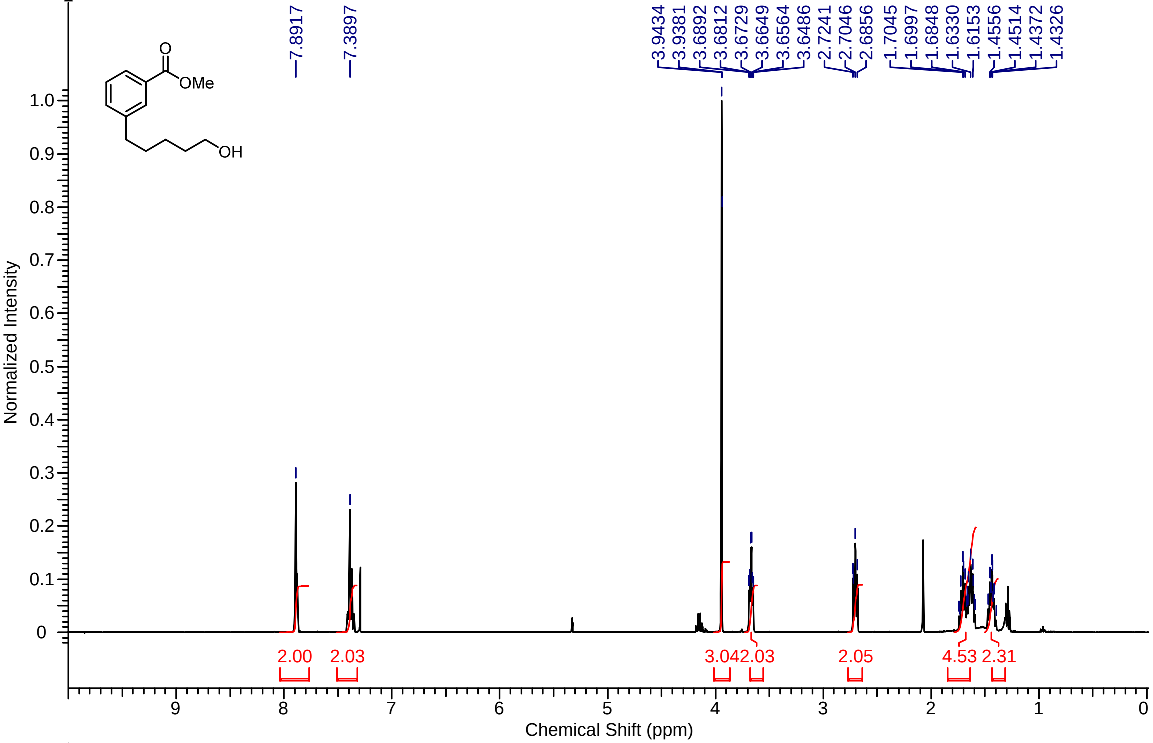
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

Compound S3



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2.7241
2.7046
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1.7045
1.6997
1.6848
1.6330
1.6153
1.4556
1.4514
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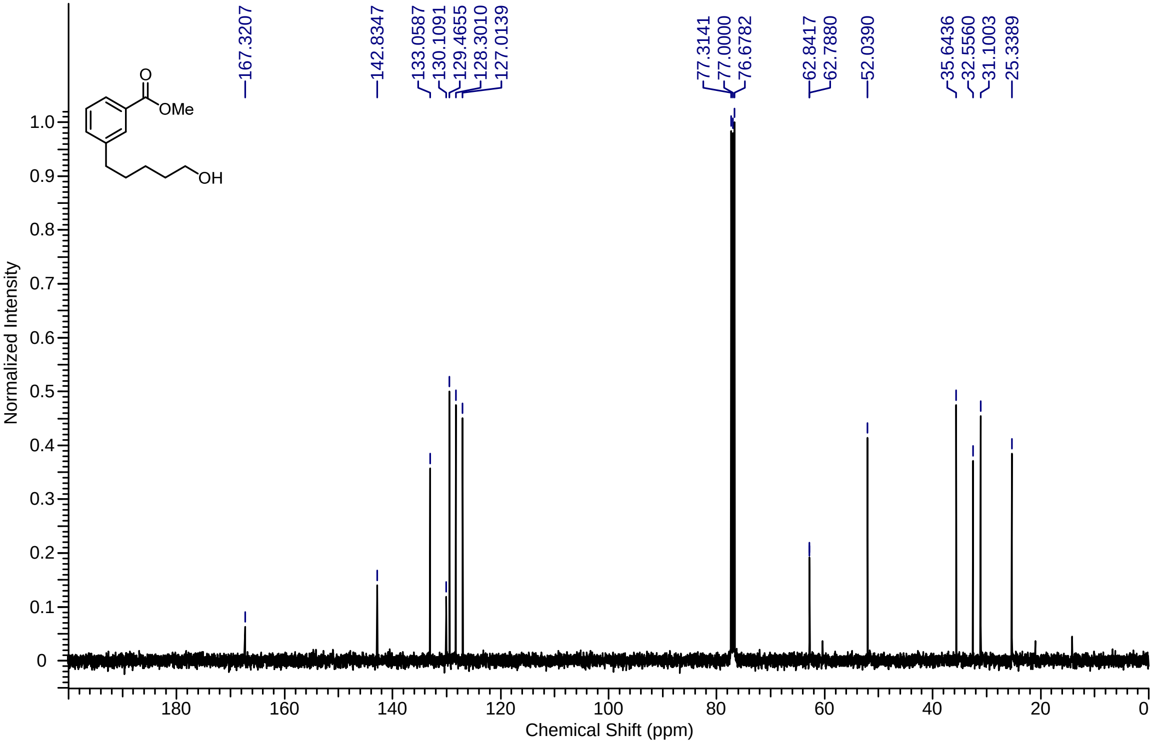
2.03
3.04
2.03
2.05
4.53
2.31
Normalized Intensity
Chemical Shift (ppm)



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76.6782
62.8417
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35.6436
32.5560
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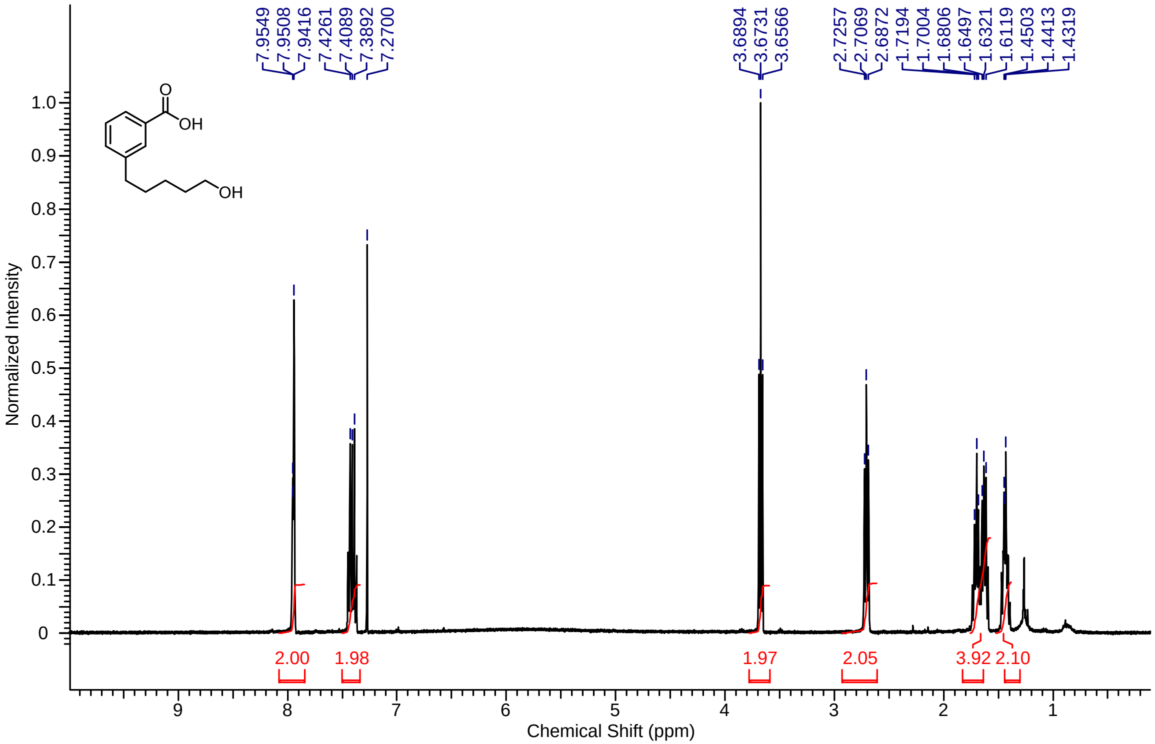
25.3389
Normalized Intensity
Chemical Shift (ppm)

Compound S4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1.4503
1.4413
1.4319
O
OH
OH
Normalized Intensity
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0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2.00
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1.97
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3.92
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9
8
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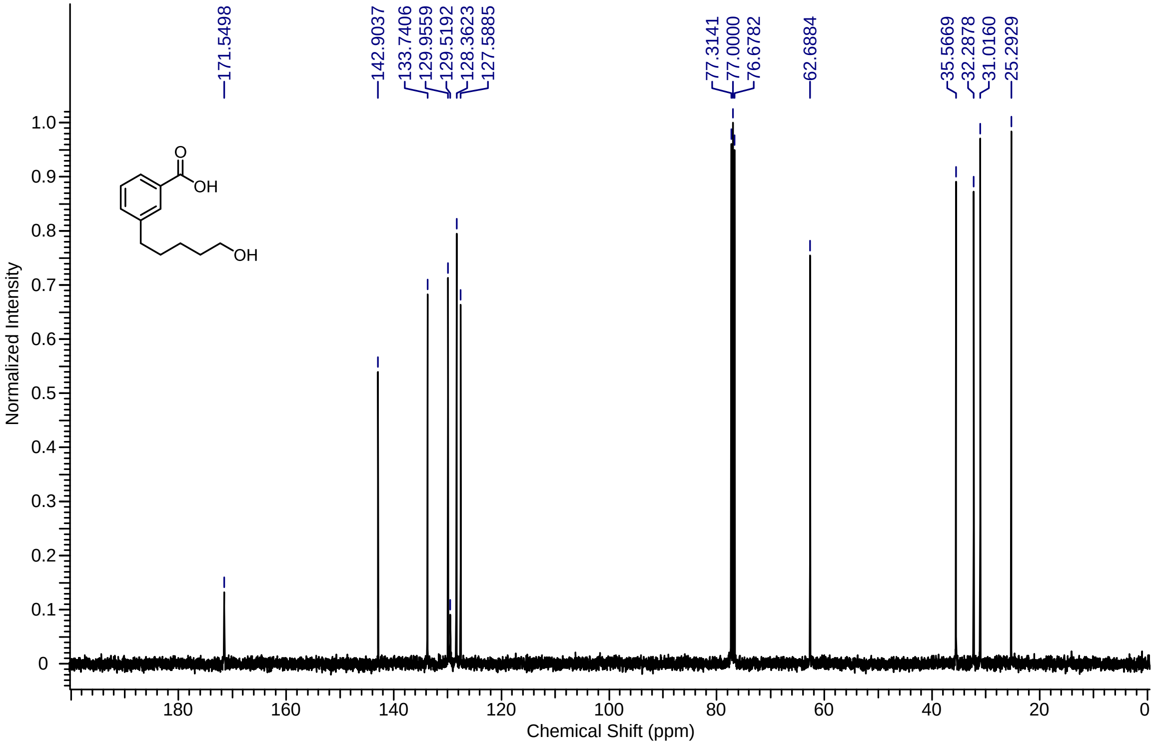
6
5
4
3
2
1
Chemical Shift (ppm)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35.5669
32.2878
31.0160
25.2929
O
OH
OH
Normalized Intensity
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0.9
0.8
0.7
0.6
0.5
0.4
0.3
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0
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140
120
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80
60
40
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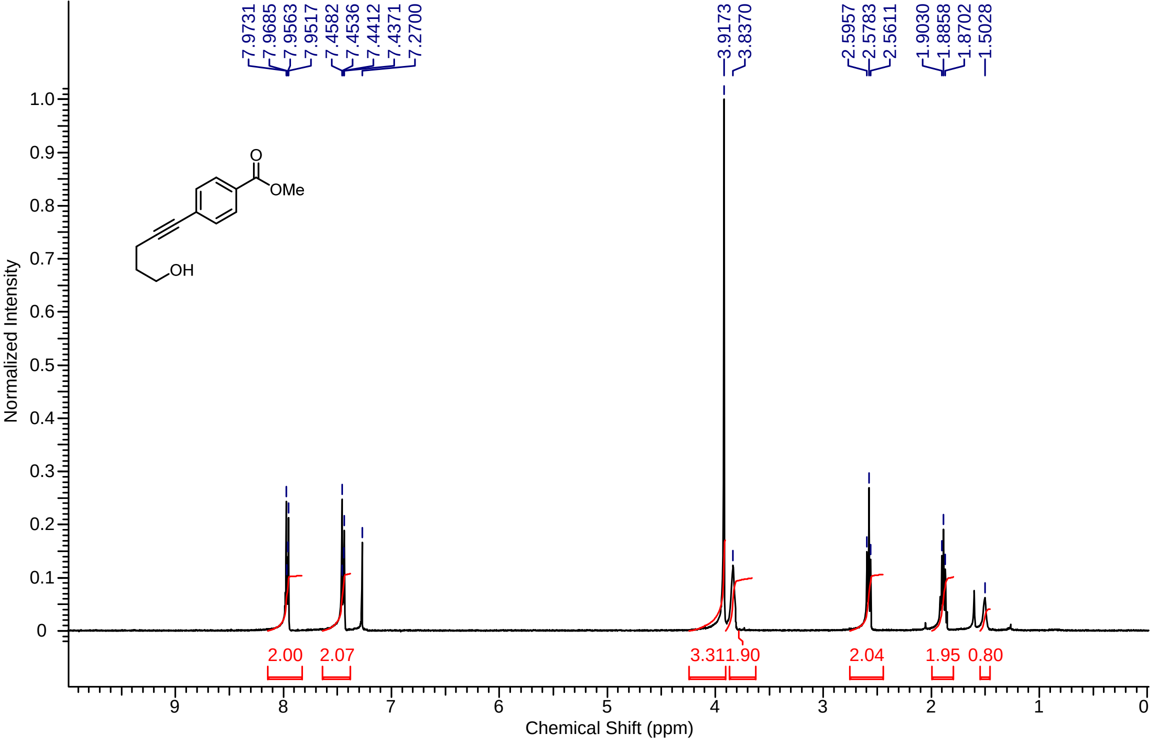
0
Chemical Shift (ppm)

Compound S5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2.5783
2.5611
1.9030
1.8858
1.8702
1.5028
O
OMe
OH
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2.00
2.07
3.31
1.90
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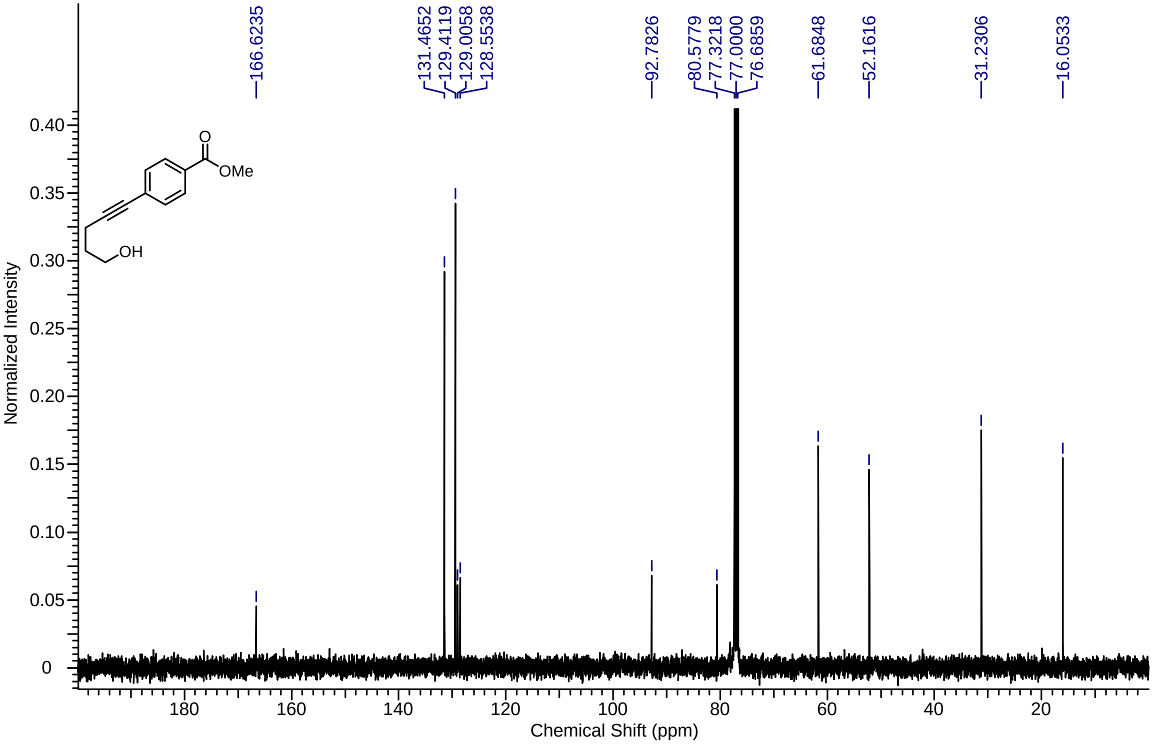
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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O
OMe
OH
Normalized Intensity
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0.35
0.30
0.25
0.20
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0
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60
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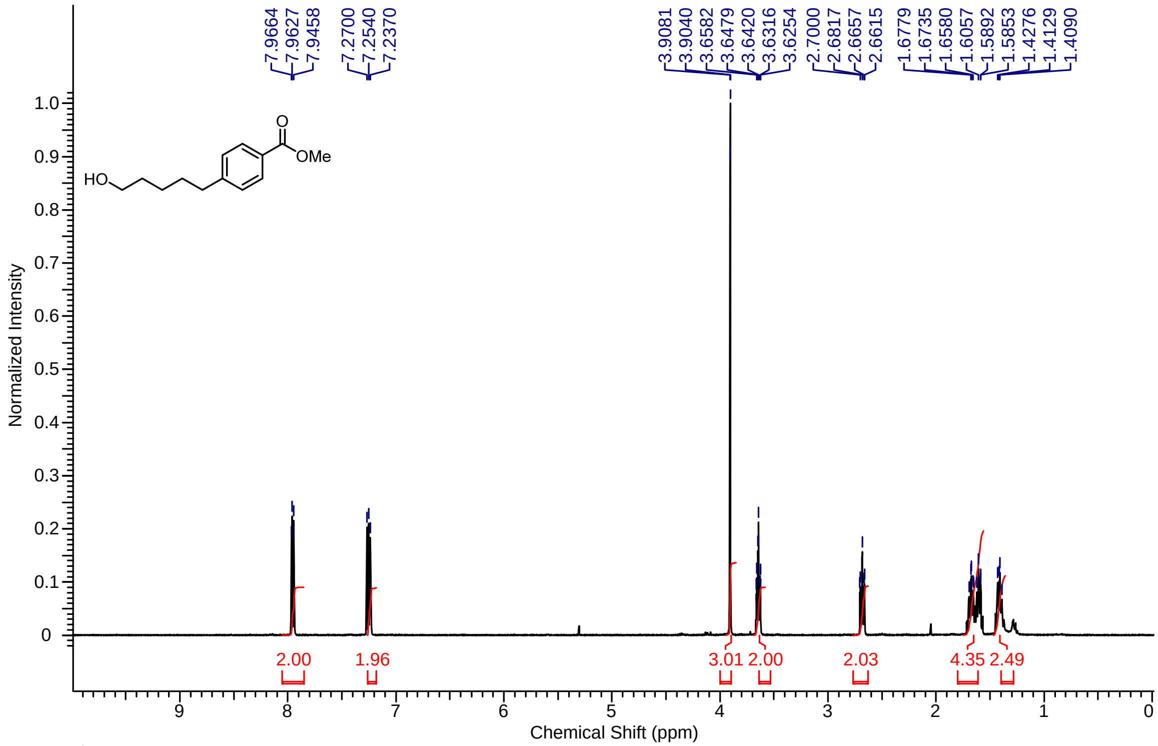
20
Chemical Shift (ppm)

Compound S6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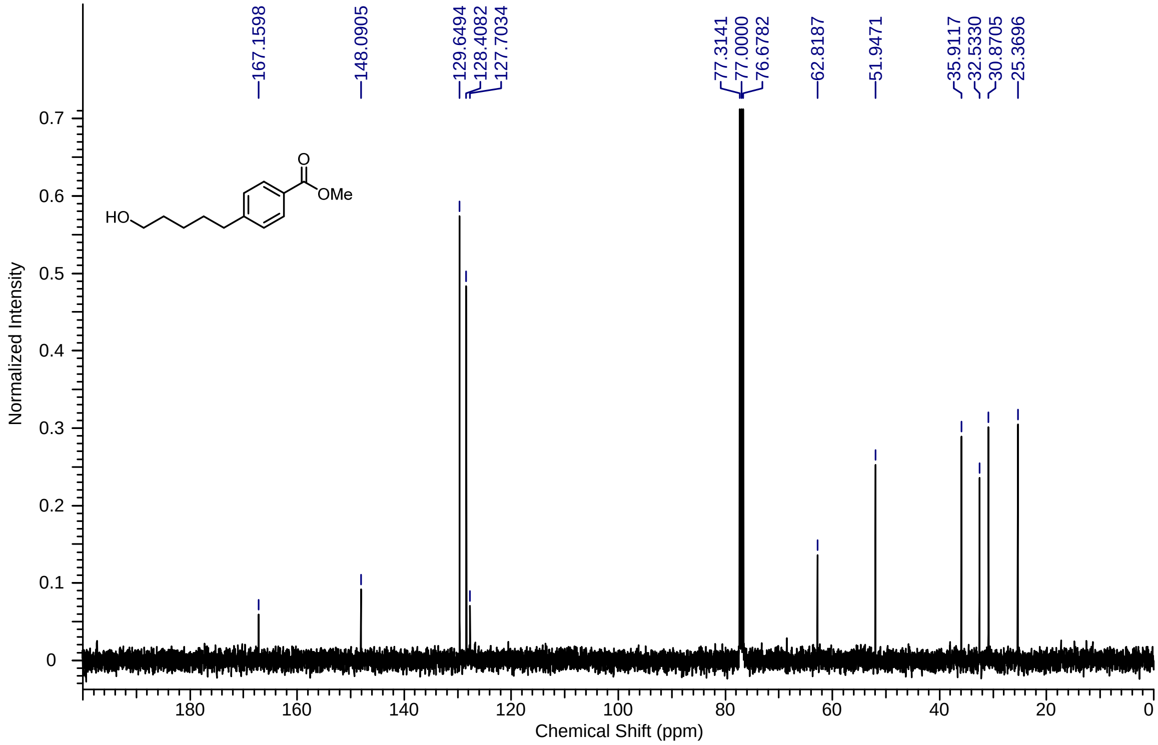
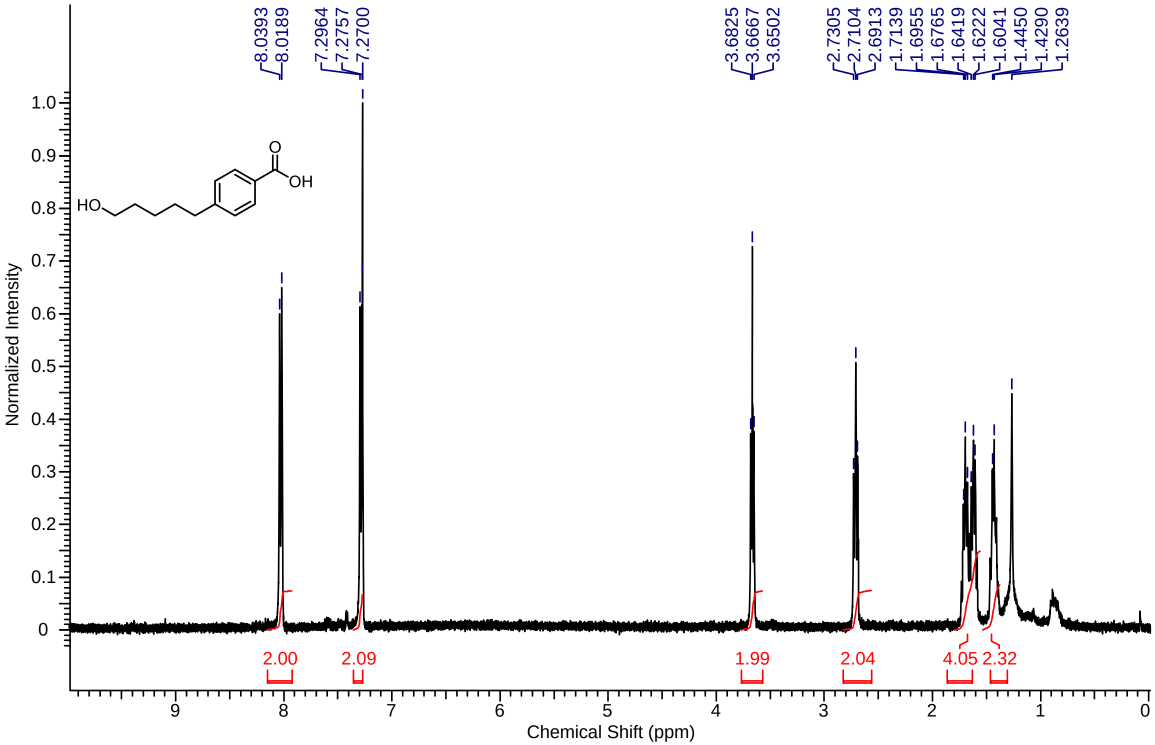
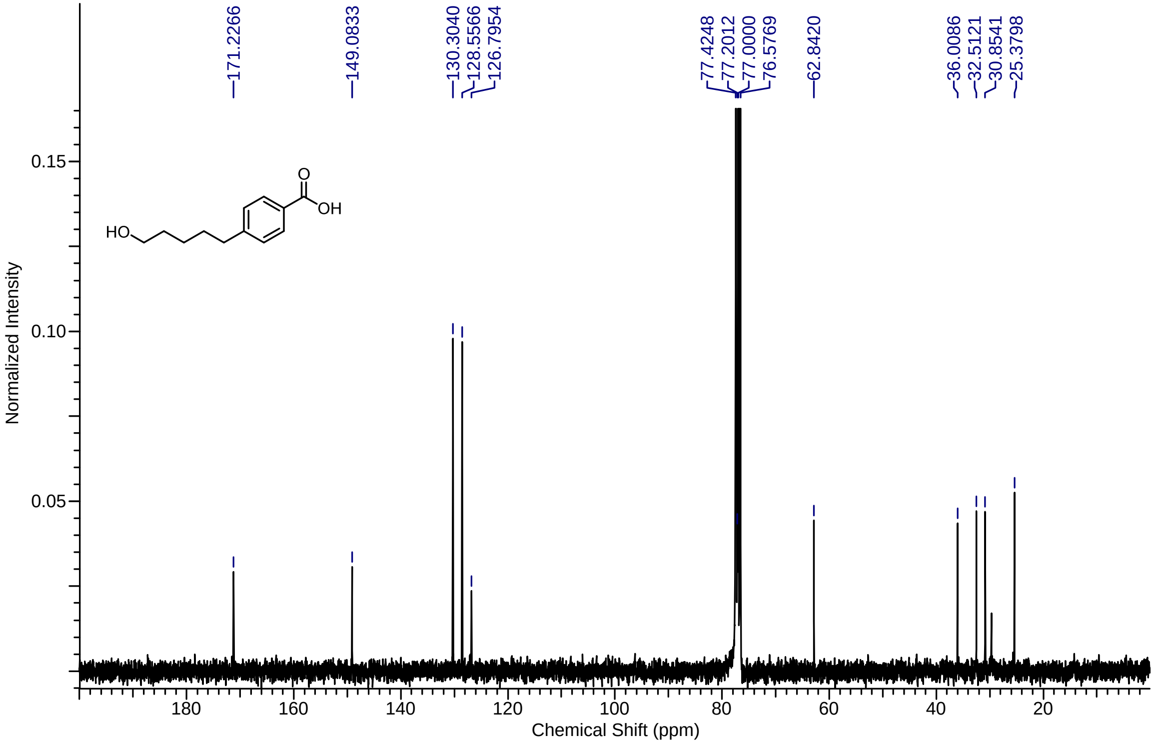
1.4090
O
OMe
HO
2.00
1.96
3.01
2.00
2.03
4.35
2.49
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

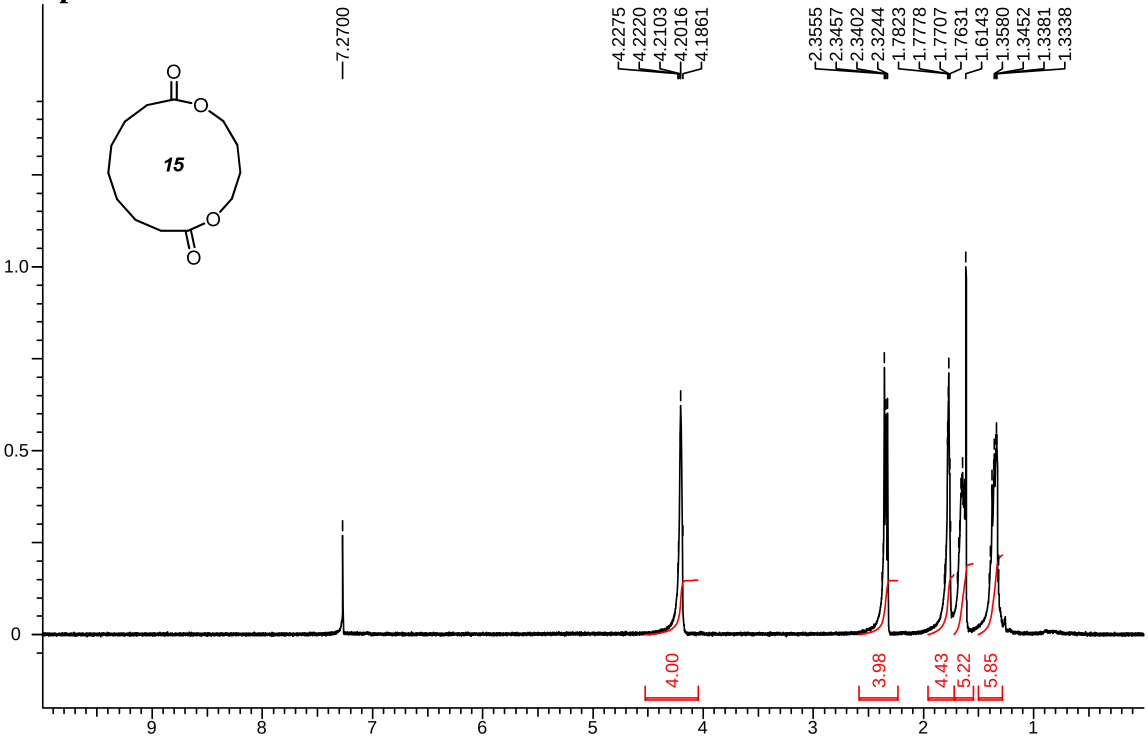

167.1598
148.0905
129.6494
128.4082
127.7034
77.3141
77.0000
76.6782
62.8187
51.9471
35.9117
32.5330
30.8705
25.3696
O
OMe
HO
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

Compound S7

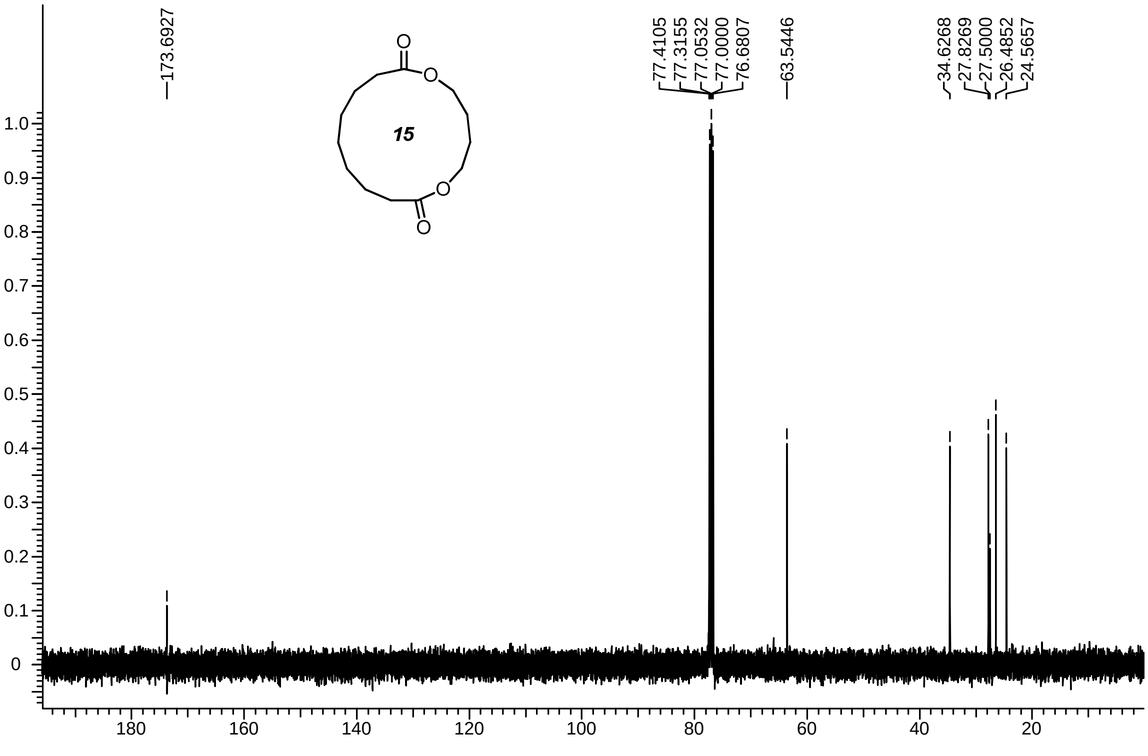

8.0393
8.0189
7.2964
7.2757
7.2700
3.6825
3.6667
3.6502
2.7305
2.7104
2.6913
1.7139
1.6955
1.6765
1.6419
1.6222
1.6041
1.4450
1.4290
1.2639
HO
O
OH
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2.00
2.09
1.99
2.04
4.05
2.32
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


171.2266
149.0833
130.3040
128.5566
126.7954
77.4248
77.2012
77.0000
76.5769
62.8420
36.0086
32.5121
30.8541
25.3798
HO
O
OH
Normalized Intensity
0.15
0.10
0.05
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)

Compound 4

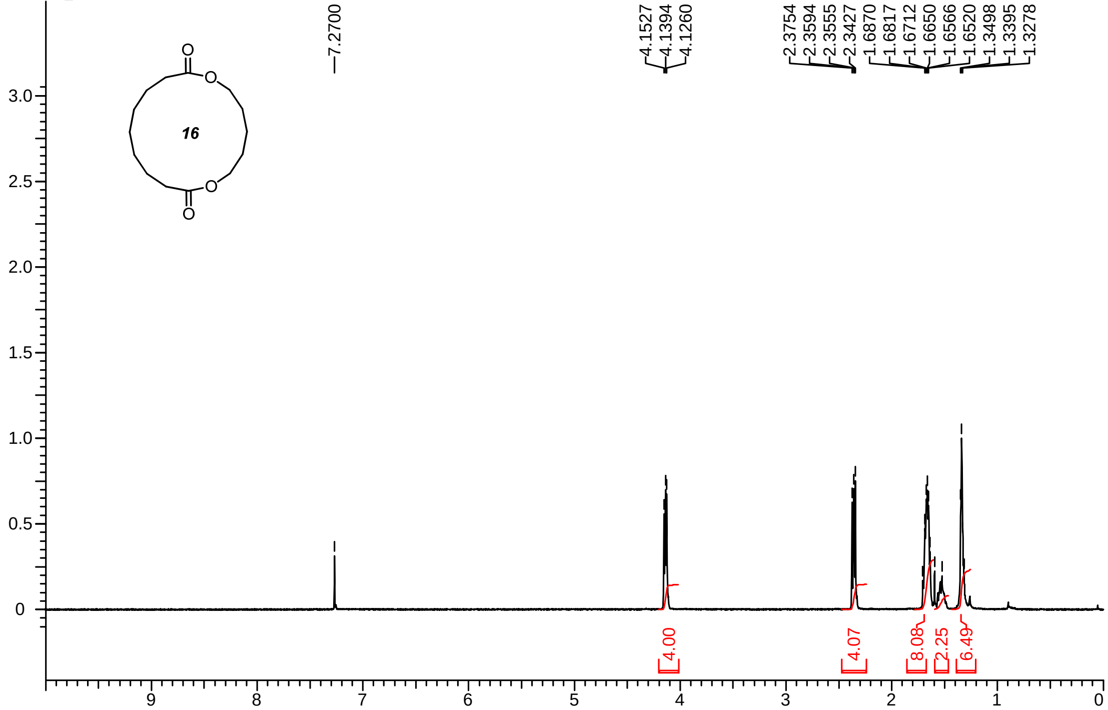


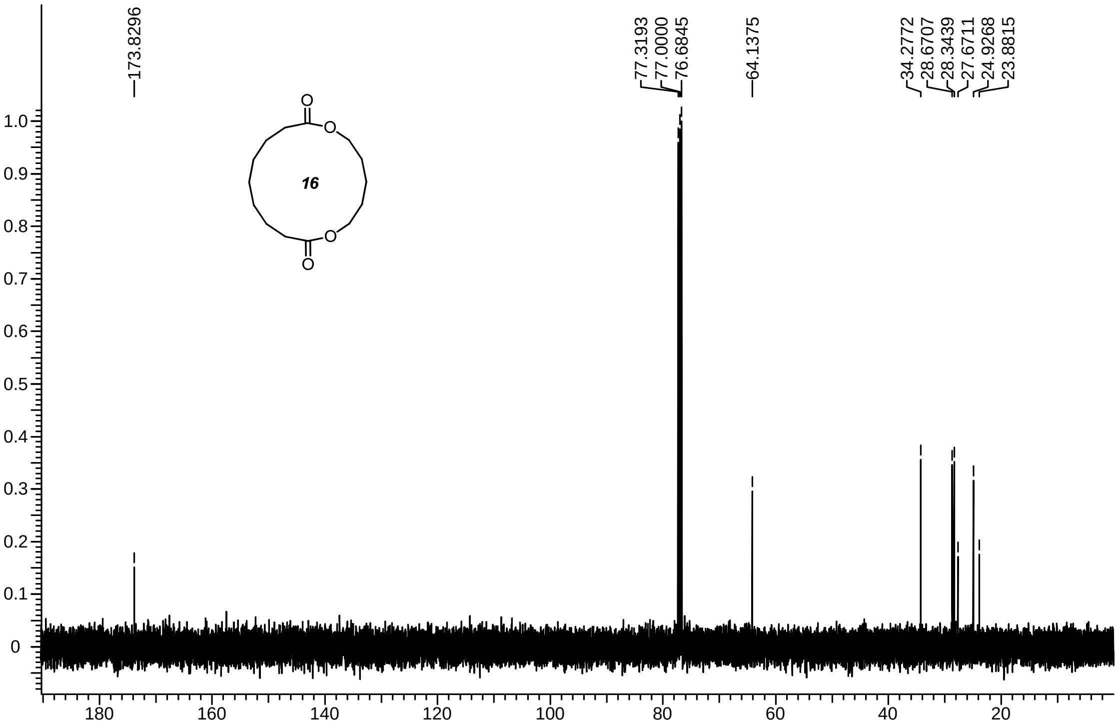
7.2700
4.2275
4.2220
4.2103
4.2016
4.1861
2.3555
2.3457
2.3402
2.3244
1.7823
1.7778
1.7707
1.7631
1.6143
1.3580
1.3452
1.3381
1.3338
15
O
O
O
O
1.0
0.5
0
4.00
3.98
4.43
5.22
5.85
9
8
7
6
5
4
3
2
1



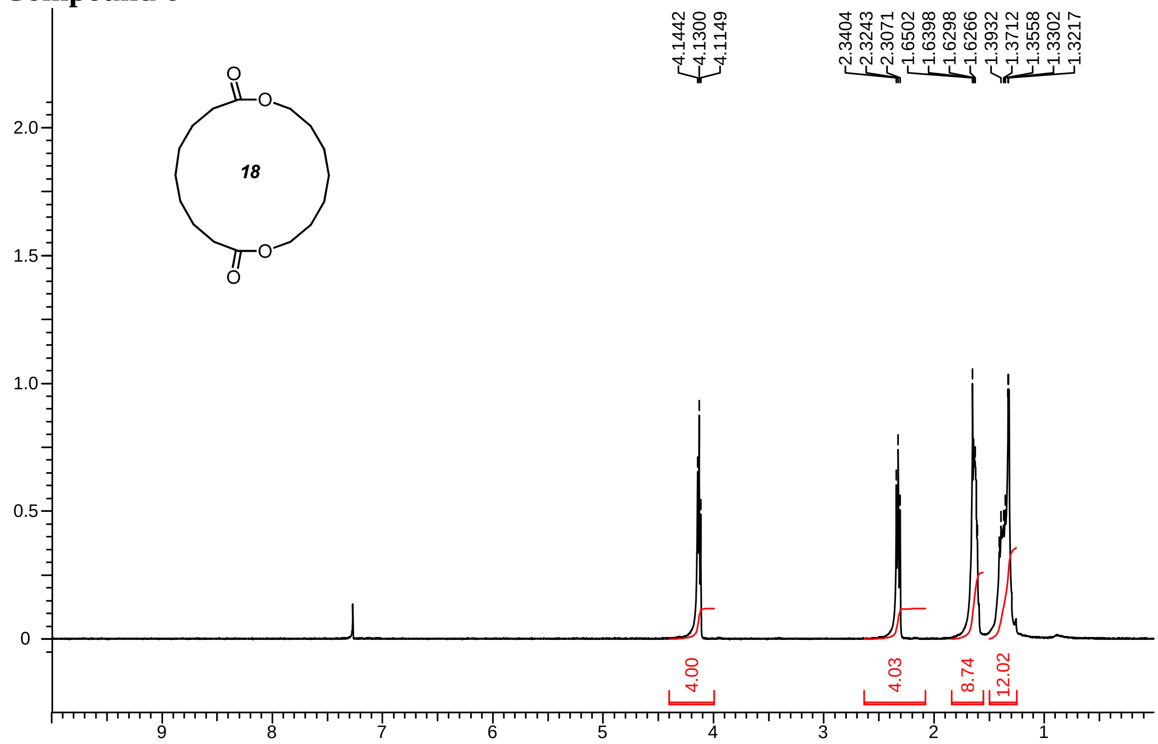
173.6927
77.4105
77.3155
77.0532
77.0000
76.6807
63.5446
34.6268
27.8269
27.5000
26.4852
24.5657
15
O
O
O
O
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20

Compound 5

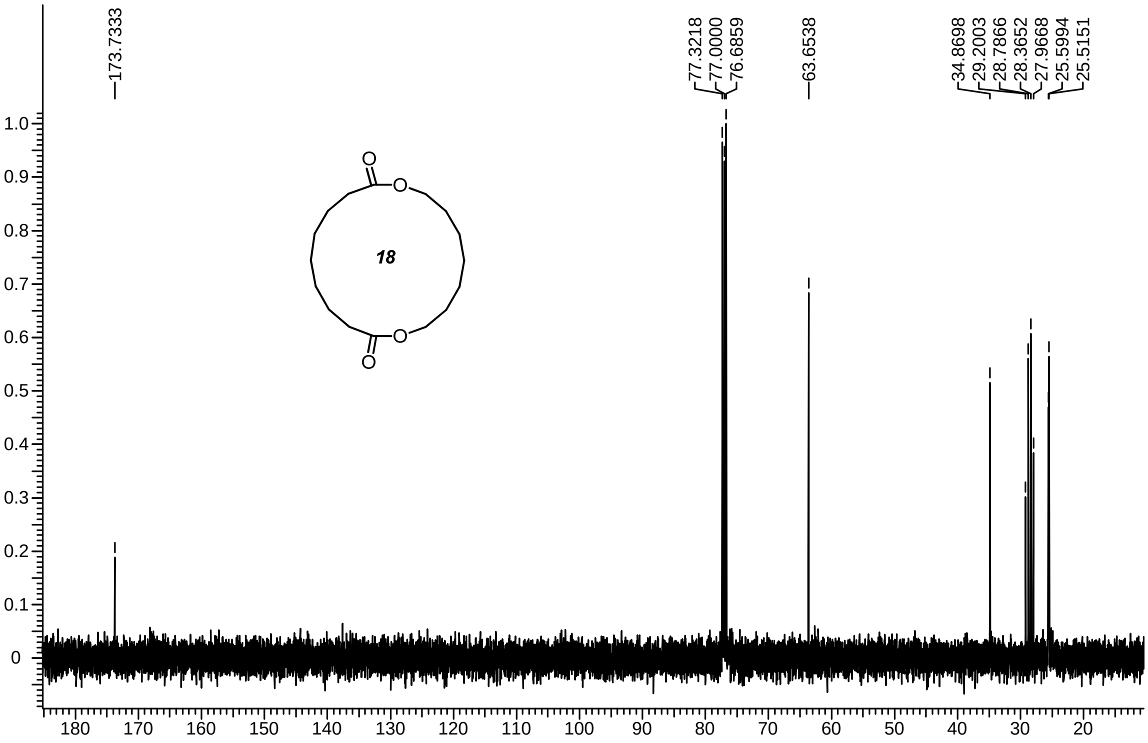

16
O
O
O
O
7.2700
4.1527
4.1394
4.1260
2.3754
2.3594
2.3555
2.3427
1.6870
1.6817
1.6712
1.6650
1.6566
1.6520
1.3498
1.3395
1.3278
3.0
2.5
2.0
1.5
1.0
0.5
0
4.00
4.07
8.08
2.25
6.49
9
8
7
6
5
4
3
2
1
0


16
O
O
O
O
173.8296
77.3193
77.0000
76.6845
64.1375
34.2772
28.6707
28.3439
27.6711
24.9268
23.8815
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20

Compound 6

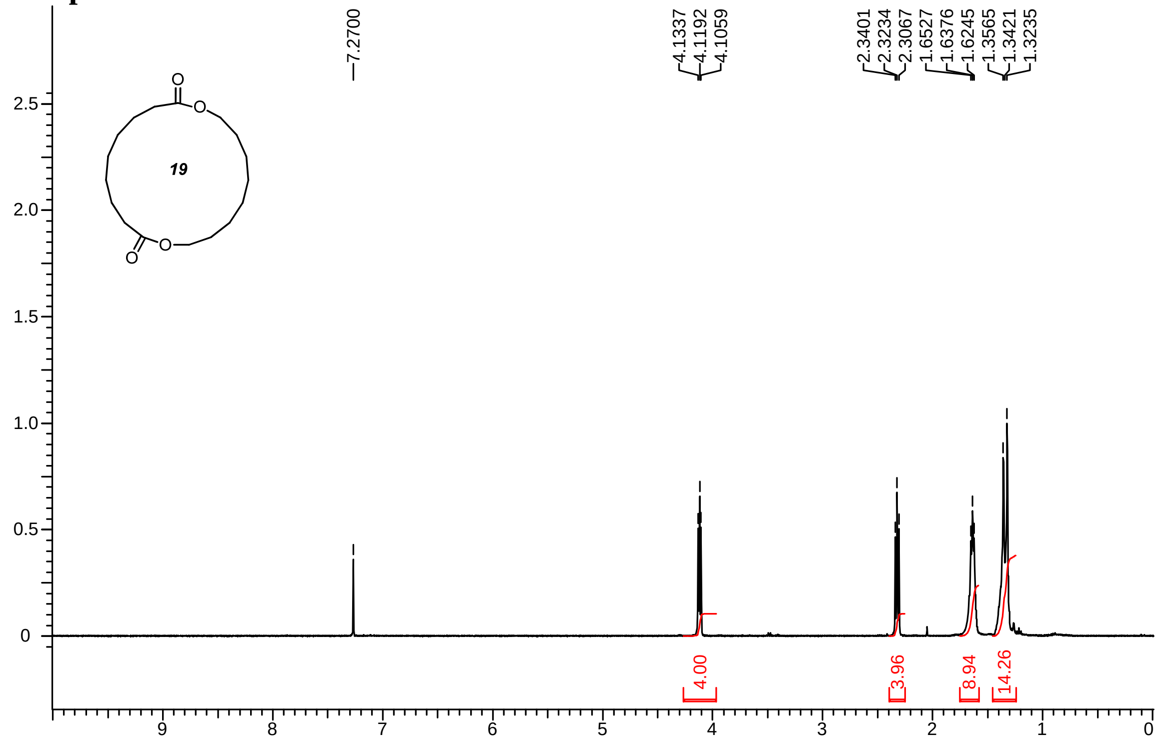


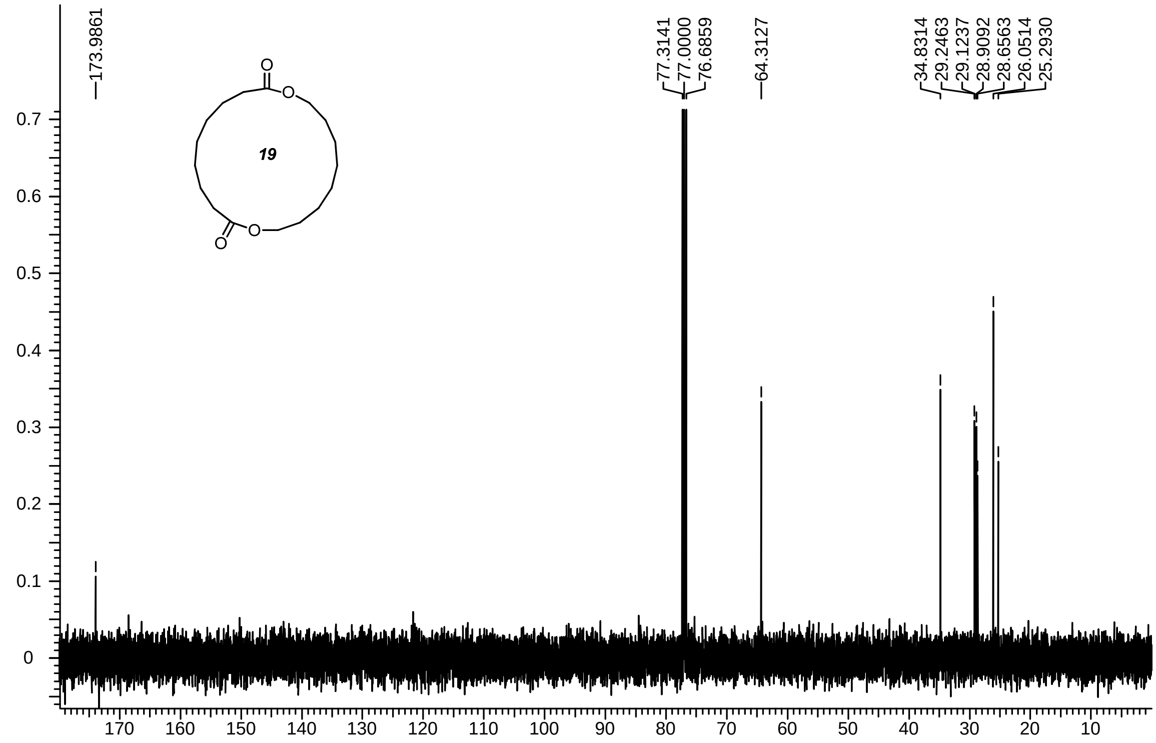
4.1442
4.1300
4.1149
2.3404
2.3243
2.3071
1.6502
1.6398
1.6298
1.6266
1.3932
1.3712
1.3558
1.3302
1.3217
18
O
O
O
O
2.0
1.5
1.0
0.5
0
4.00
4.03
8.74
12.02
9
8
7
6
5
4
3
2
1



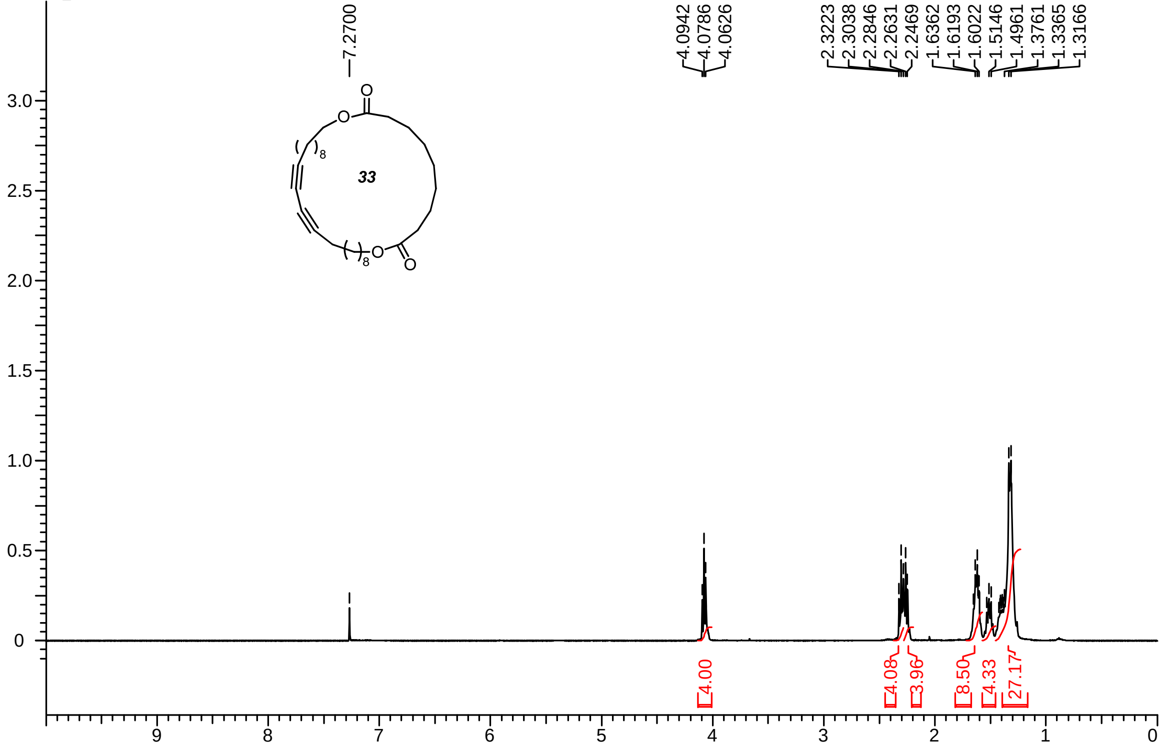
173.7333
77.3218
77.0000
76.6859
63.6538
34.8698
29.2003
28.7866
28.3652
27.9668
25.5994
25.5151
18
O
O
O
O
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

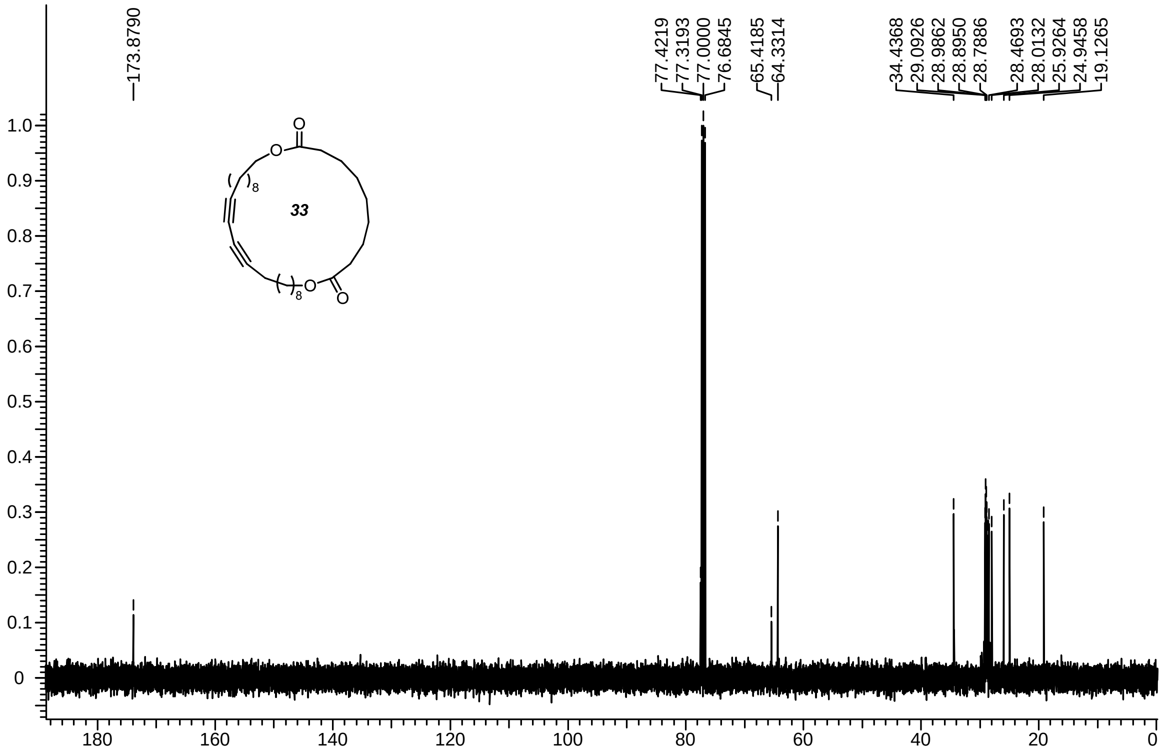
Compound 3


7.2700
4.1337
4.1192
4.1059
2.3401
2.3234
2.3067
1.6527
1.6376
1.6245
1.3565
1.3421
1.3235
19
O
O
O
O
2.5
2.0
1.5
1.0
0.5
0
4.00
3.96
8.94
14.26
9
8
7
6
5
4
3
2
1
0

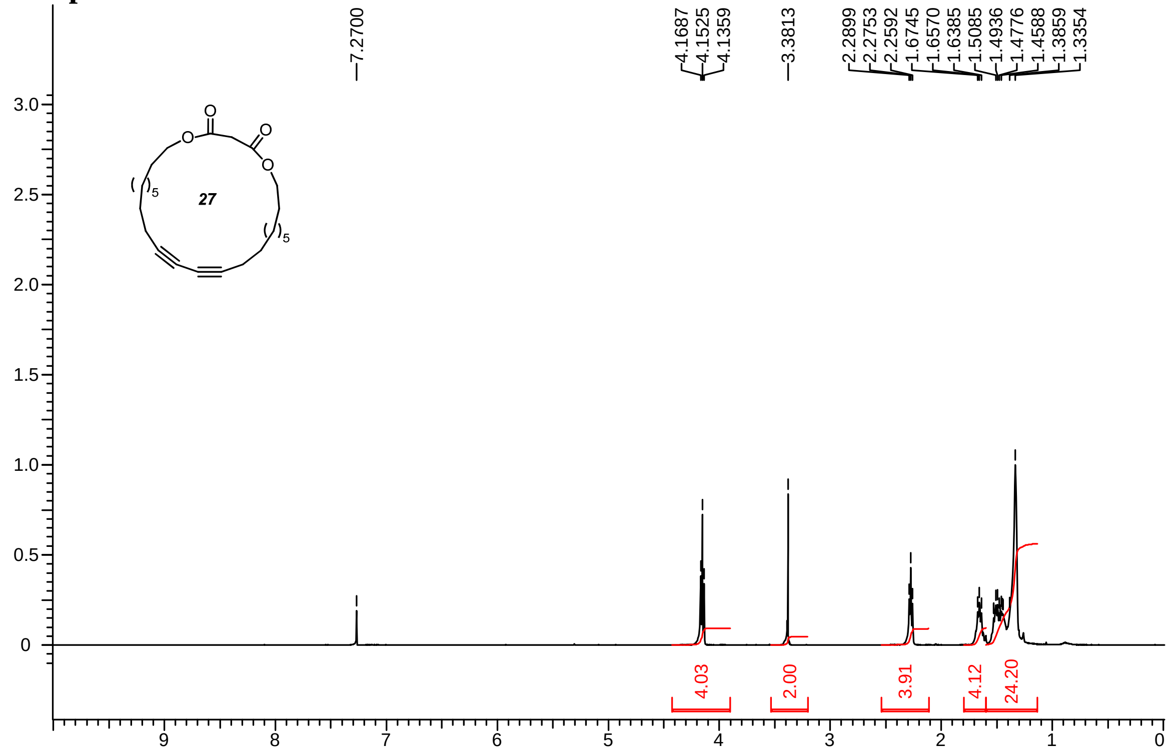

173.9861
77.3141
77.0000
76.6859
64.3127
34.8314
29.2463
29.1237
28.9092
28.6563
26.0514
25.2930
19
O
O
O
O
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

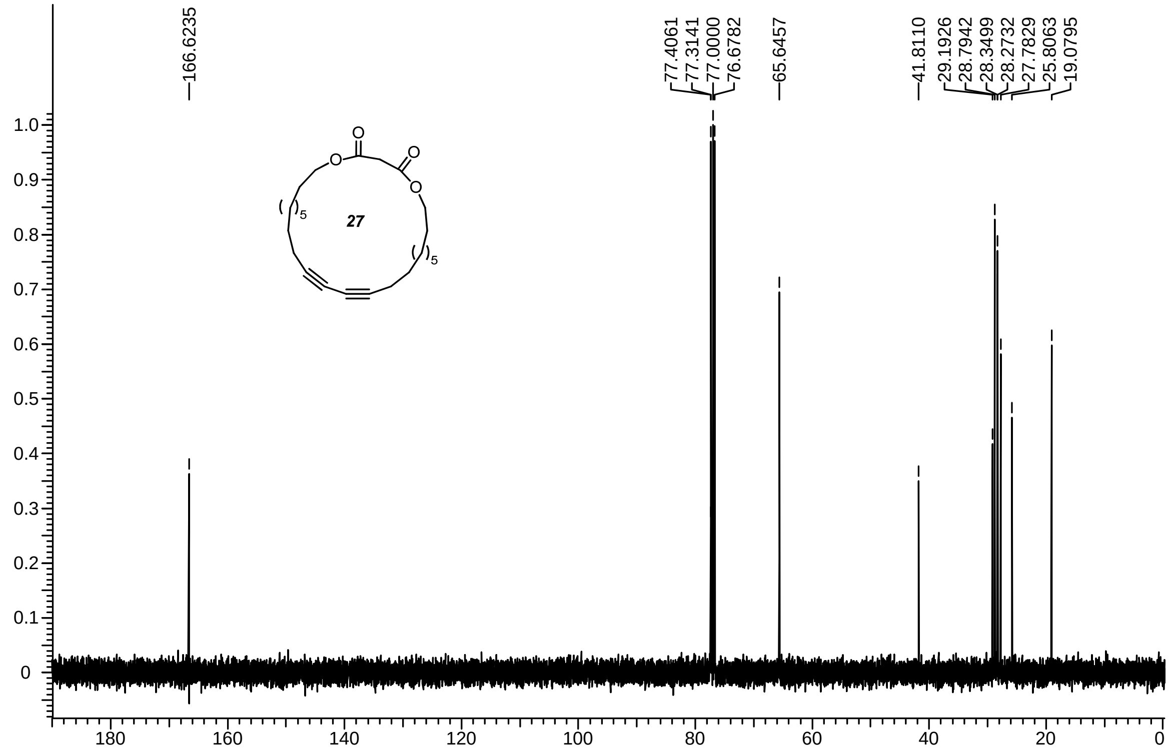
Compound 7


7.2700
4.0942
4.0786
4.0626
2.3223
2.3038
2.2846
2.2631
2.2469
1.6362
1.6193
1.6022
1.5146
1.4961
1.3761
1.3365
1.3166
O
O
( )8
33
( )8
O
O
3.0
2.5
2.0
1.5
1.0
0.5
0
4.00
4.08
3.96
8.50
4.33
27.17
9
8
7
6
5
4
3
2
1
0

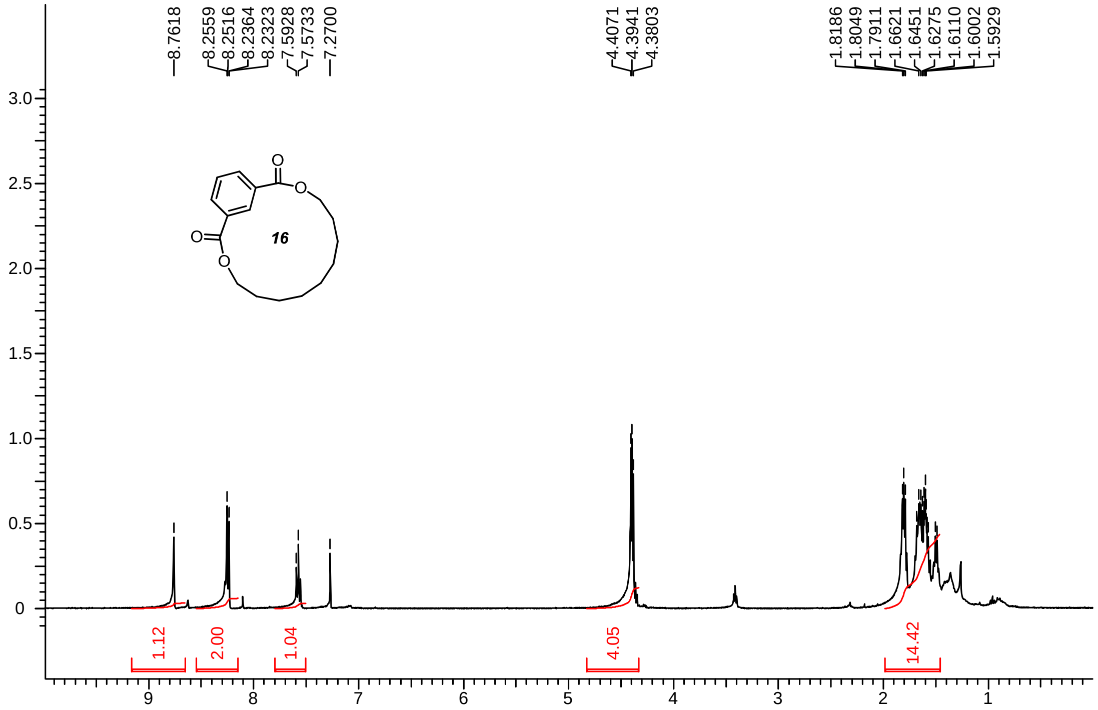

173.8790
77.4219
77.3193
77.0000
76.6845
65.4185
64.3314
34.4368
29.0926
28.9862
28.8950
28.7886
28.4693
28.0132
25.9264
24.9458
19.1265
O
O
( )8
33
( )8
O
O
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0

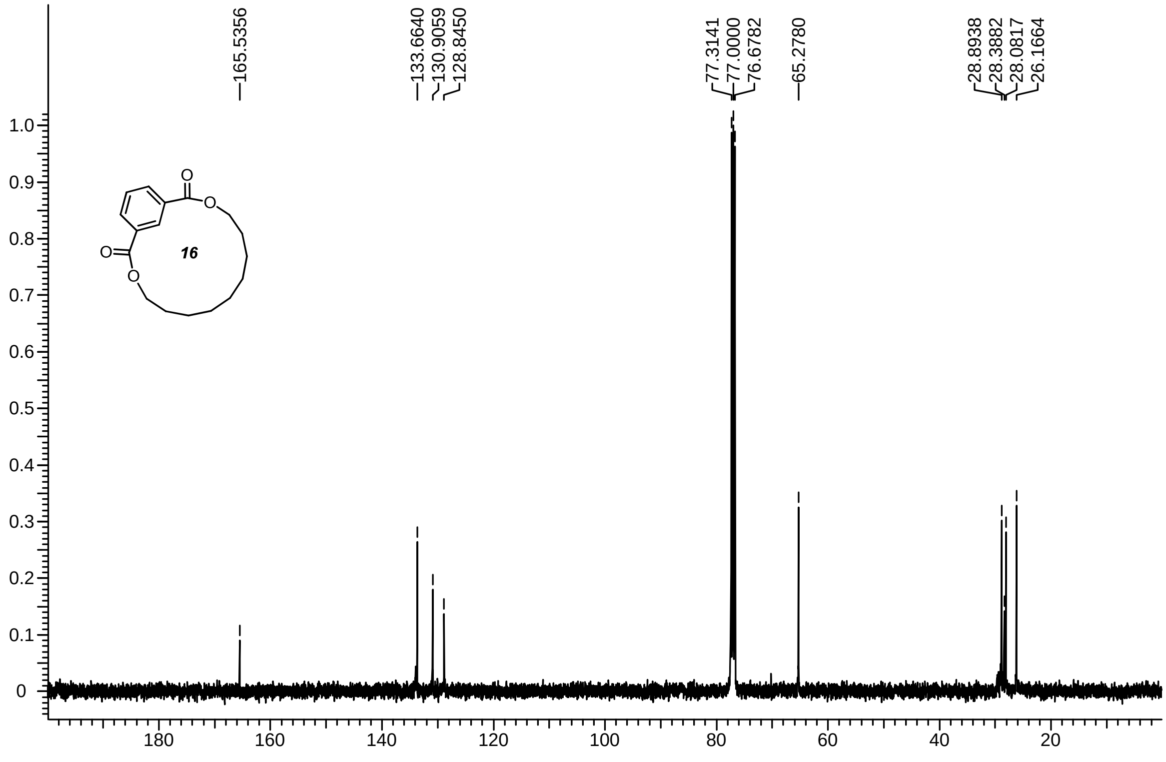
Compound 8


7.2700
4.1687
4.1525
4.1359
3.3813
2.2899
2.2753
2.2592
1.6745
1.6570
1.6385
1.5085
1.4936
1.4776
1.4588
1.3859
1.3354
27
( )5
( )5
O
O
O
O
4.03
2.00
3.91
4.12
24.20
3.0
2.5
2.0
1.5
1.0
0.5
0
9
8
7
6
5
4
3
2
1
0

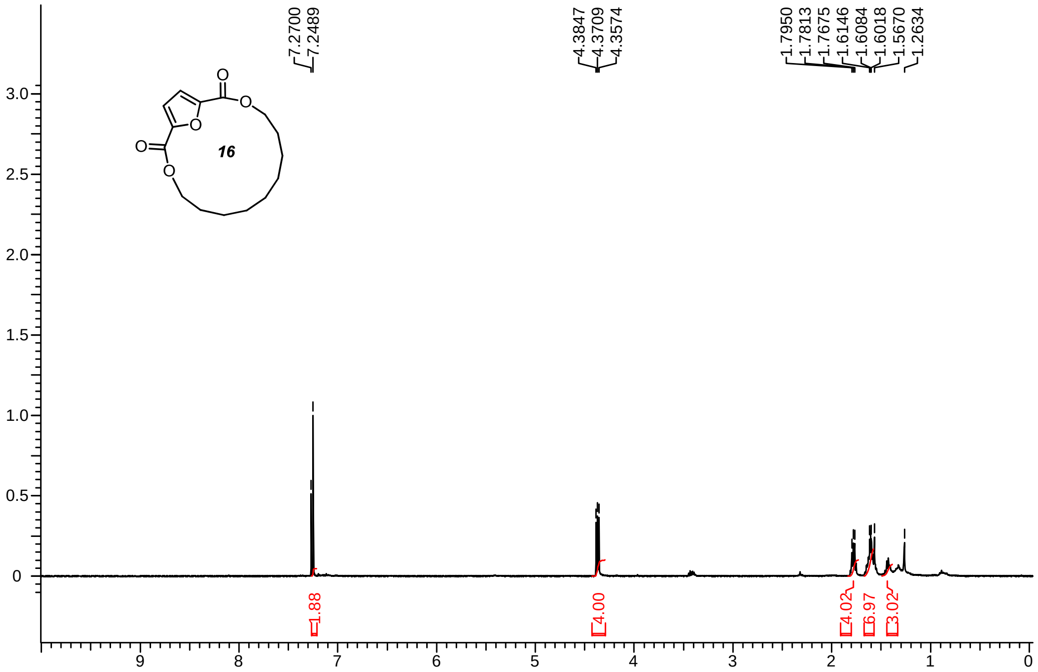

166.6235
77.4061
77.3141
77.0000
76.6782
65.6457
41.8110
29.1926
28.7942
28.3499
28.2732
27.7829
25.8063
19.0795
27
( )5
( )5
O
O
O
O
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0

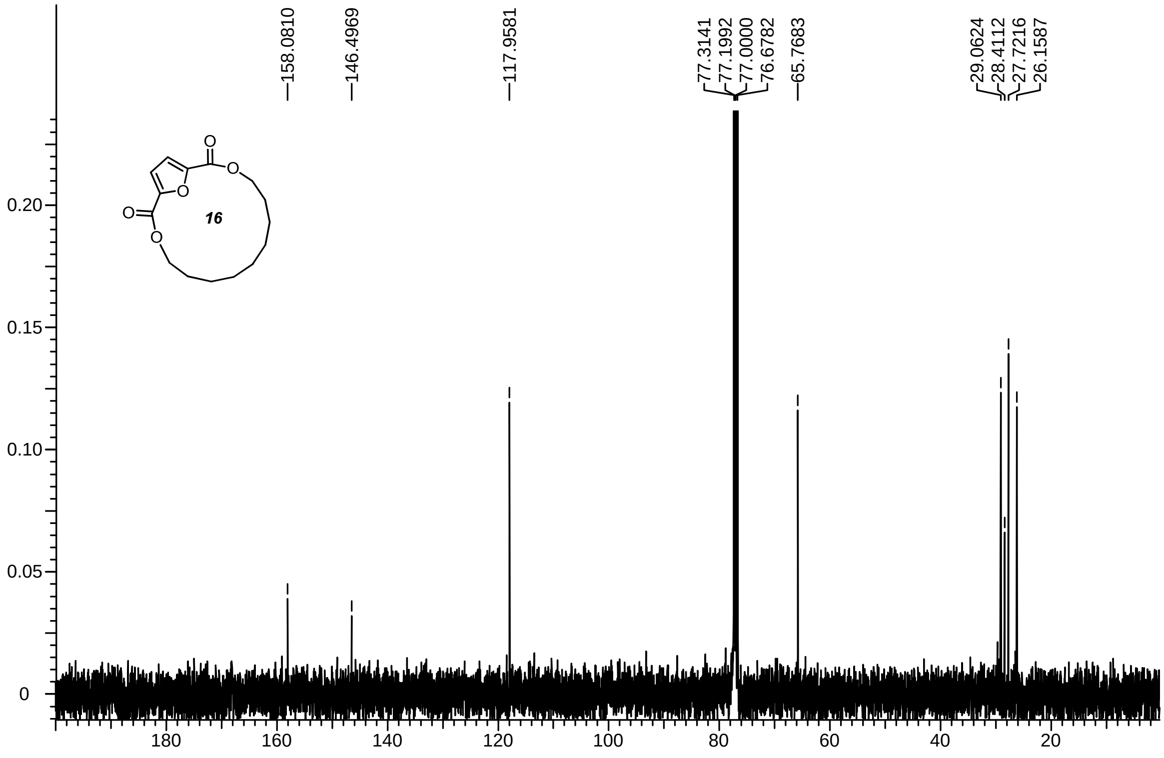
Compound 9


8.7618
8.2559
8.2516
8.2364
8.2323
7.5928
7.5733
7.2700
4.4071
4.3941
4.3803
1.8186
1.8049
1.7911
1.6621
1.6451
1.6275
1.6110
1.6002
1.5929
O
O
O
O
16
3.0
2.5
2.0
1.5
1.0
0.5
0
1.12
2.00
1.04
4.05
14.42
9
8
7
6
5
4
3
2
1

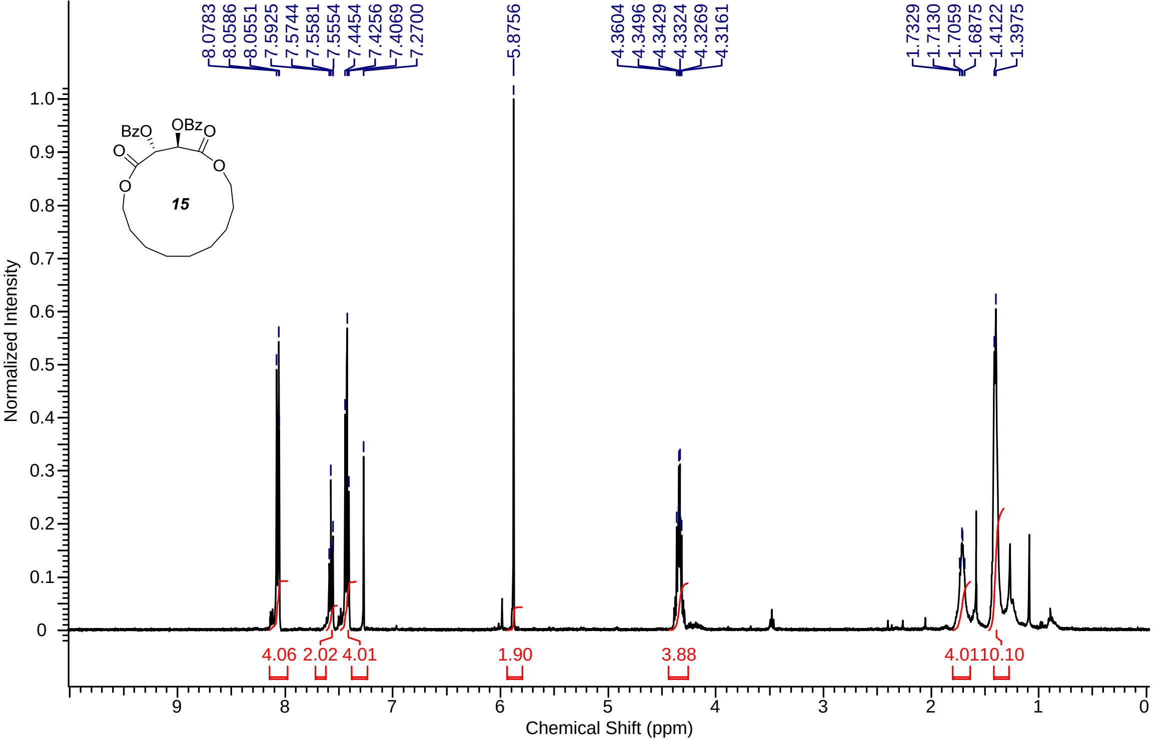

165.5356
133.6640
130.9059
128.8450
77.3141
77.0000
76.6782
65.2780
28.8938
28.3882
28.0817
26.1664
O
O
O
O
16
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20

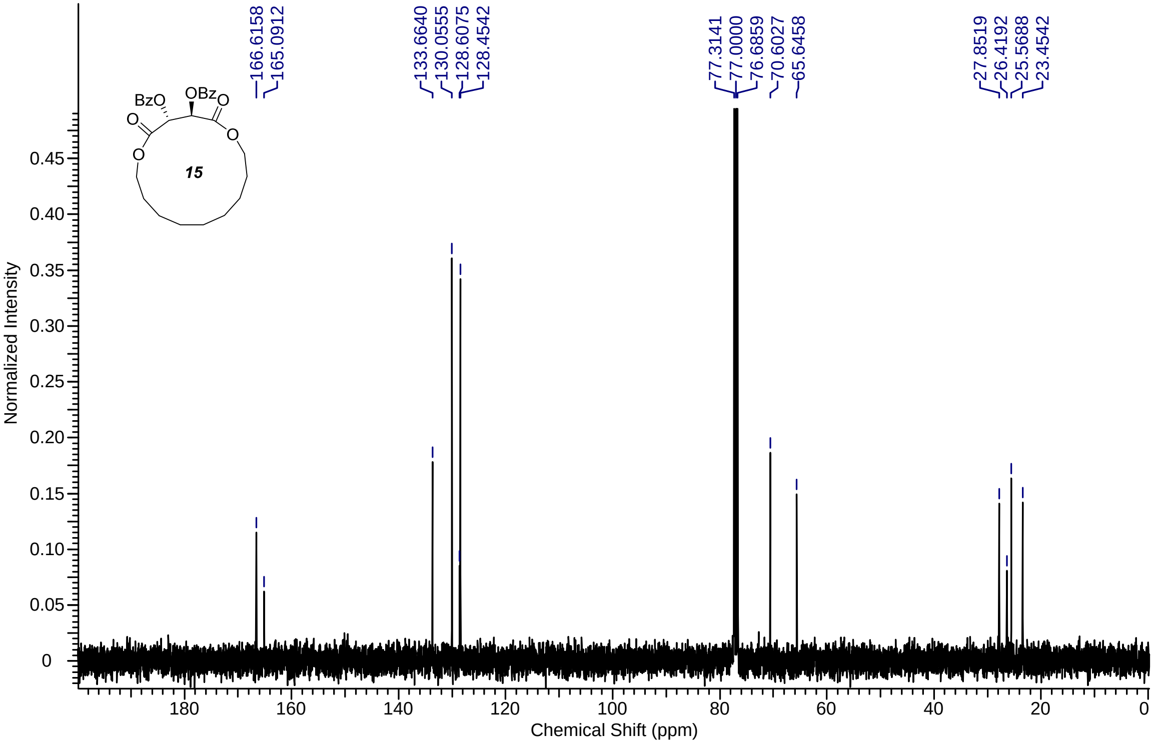
Compound 10


7.2700
7.2489
4.3847
4.3709
4.3574
1.7950
1.7813
1.7675
1.6146
1.6084
1.6018
1.5670
1.2634
O
O
O
O
O
16
3.0
2.5
2.0
1.5
1.0
0.5
0
1.88
4.00
4.02
6.97
3.02
9
8
7
6
5
4
3
2
1
0

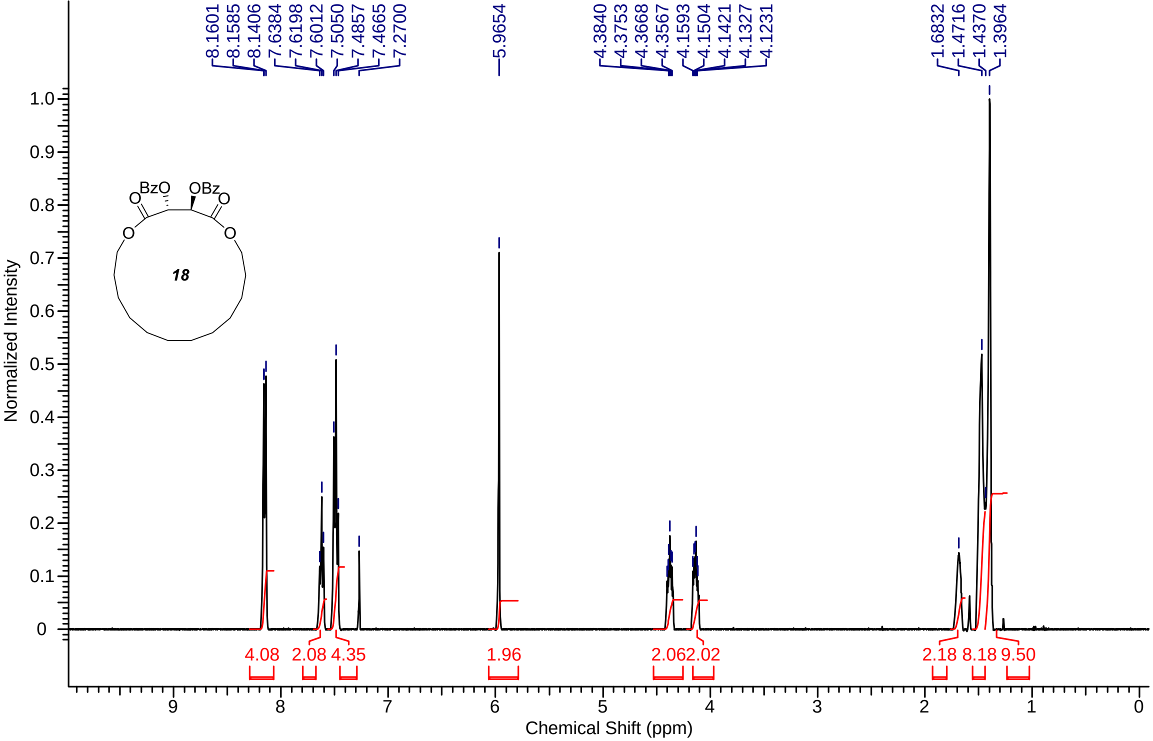

158.0810
146.4969
117.9581
77.3141
77.1992
77.0000
76.6782
65.7683
29.0624
28.4112
27.7216
26.1587
O
O
O
O
O
16
0.20
0.15
0.10
0.05
0
180
160
140
120
100
80
60
40
20

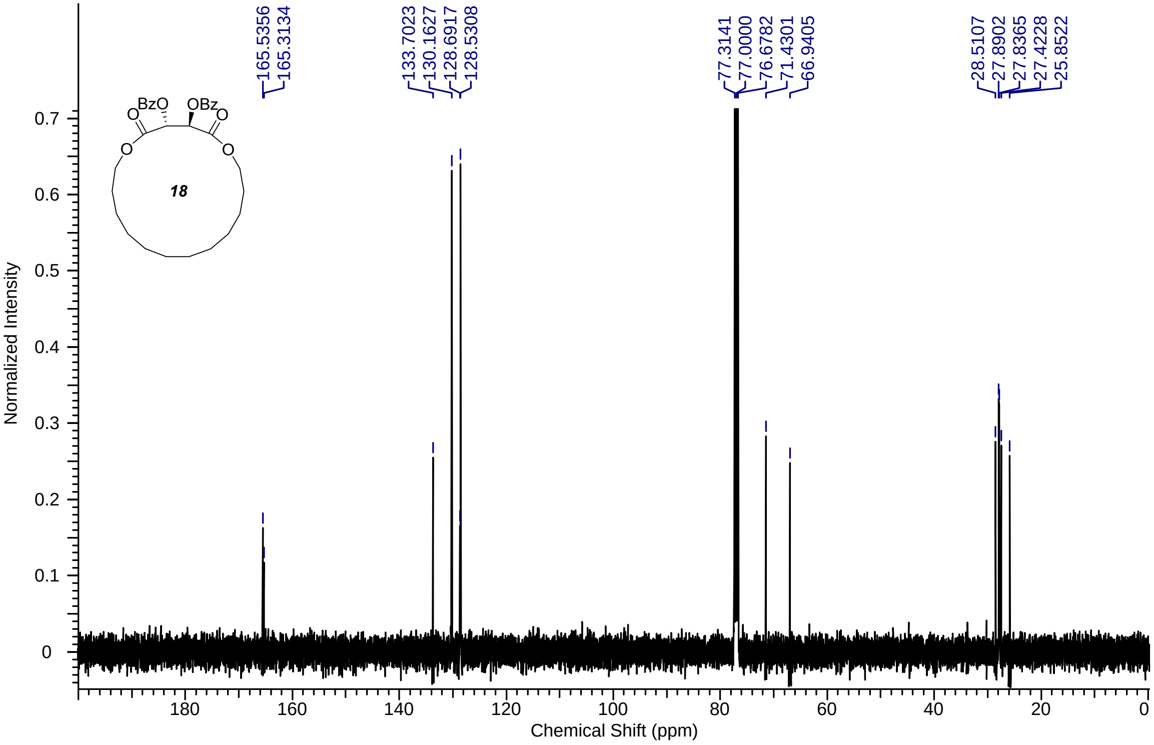
Compound 11


8.0783
8.0586
8.0551
7.5925
7.5744
7.5581
7.5554
7.4454
7.4256
7.4069
7.2700
5.8756
4.3604
4.3496
4.3429
4.3324
4.3269
4.3161
1.7329
1.7130
1.7059
1.6875
1.4122
1.3975
BzO
OBz
O
O
O
O
15
4.06
2.02
4.01
1.90
3.88
4.01
10.10
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

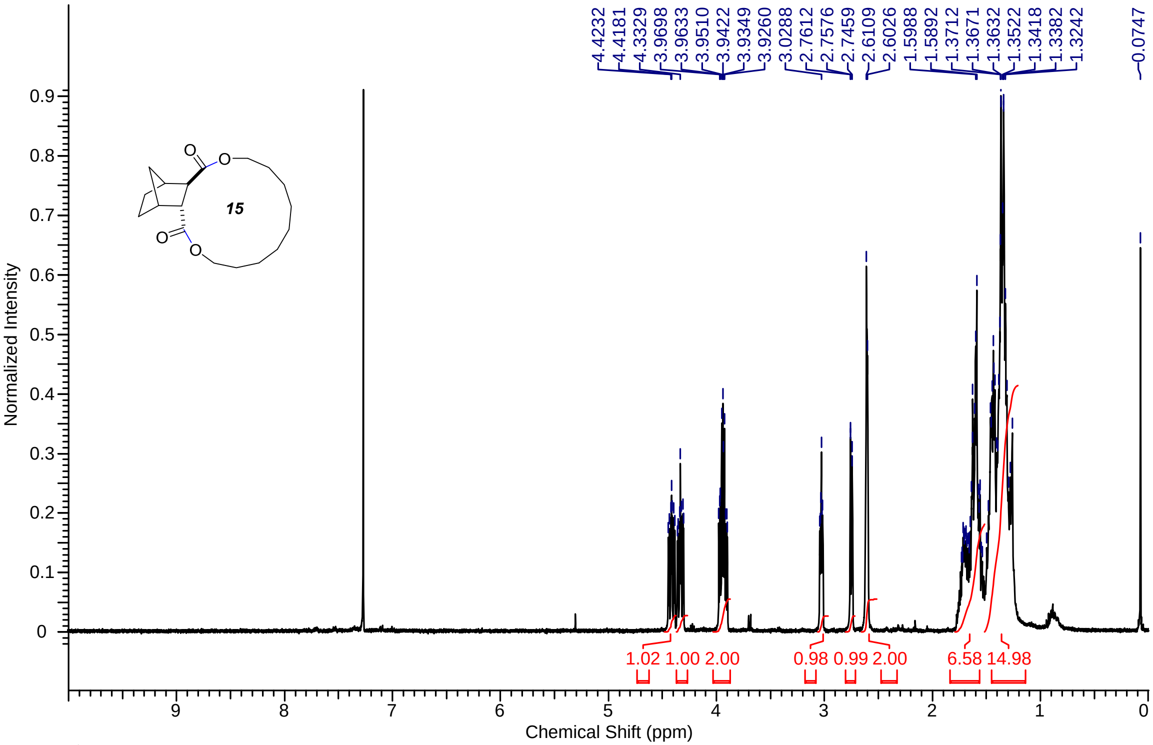

166.6158
165.0912
133.6640
130.0555
128.6075
128.4542
77.3141
77.0000
76.6859
70.6027
65.6458
27.8519
26.4192
25.5688
23.4542
BzO
OBz
O
O
O
O
15
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

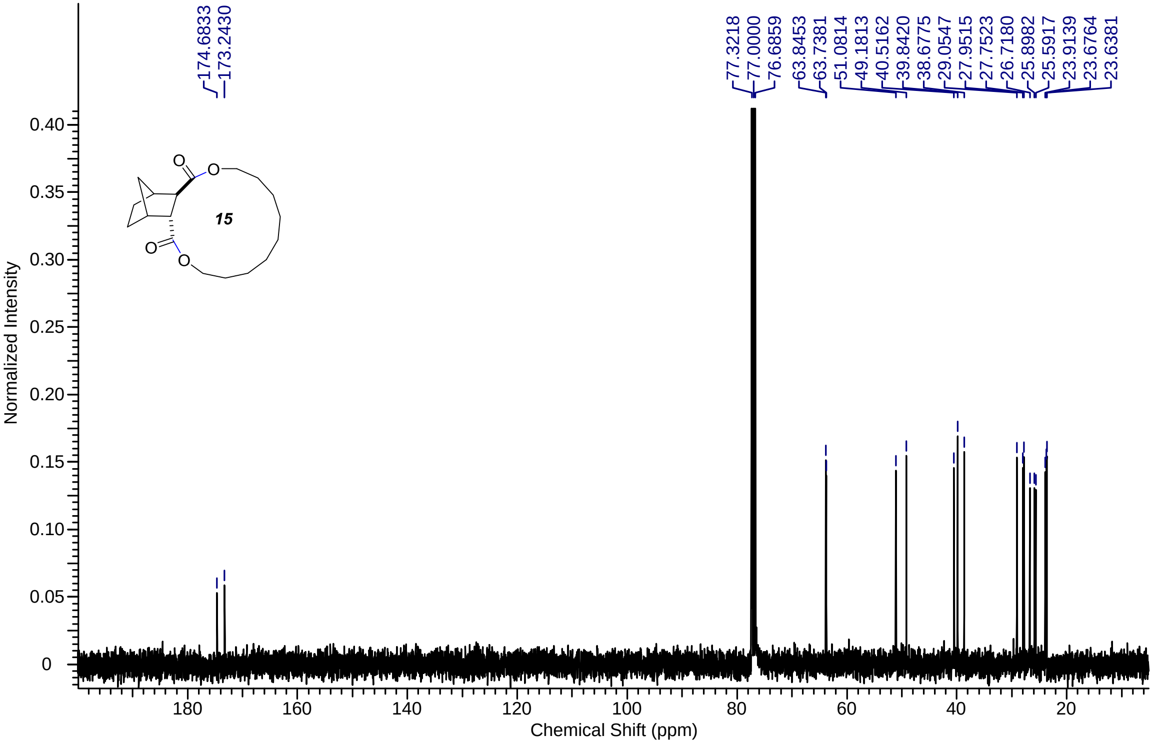
Compound 12


8.1601
8.1585
8.1406
7.6384
7.6198
7.6012
7.5050
7.4857
7.4665
7.2700
5.9654
4.3840
4.3753
4.3668
4.3567
4.1593
4.1504
4.1421
4.1327
4.1231
1.6832
1.4716
1.4370
1.3964
BzO
OBz
O
O
O
O
18
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
4.08
2.08
4.35
1.96
2.06
2.02
2.18
8.18
9.50
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

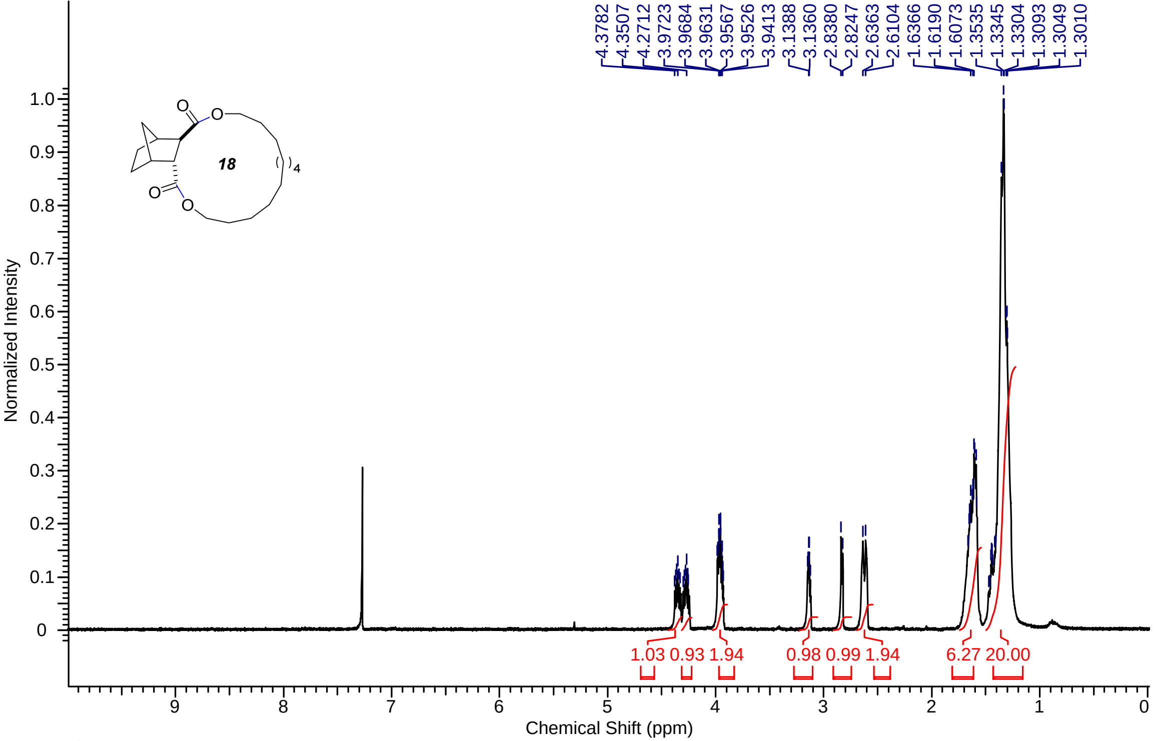

165.5356
165.3134
133.7023
130.1627
128.6917
128.5308
77.3141
77.0000
76.6782
71.4301
66.9405
28.5107
27.8902
27.8365
27.4228
25.8522
BzO
OBz
O
O
O
O
18
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

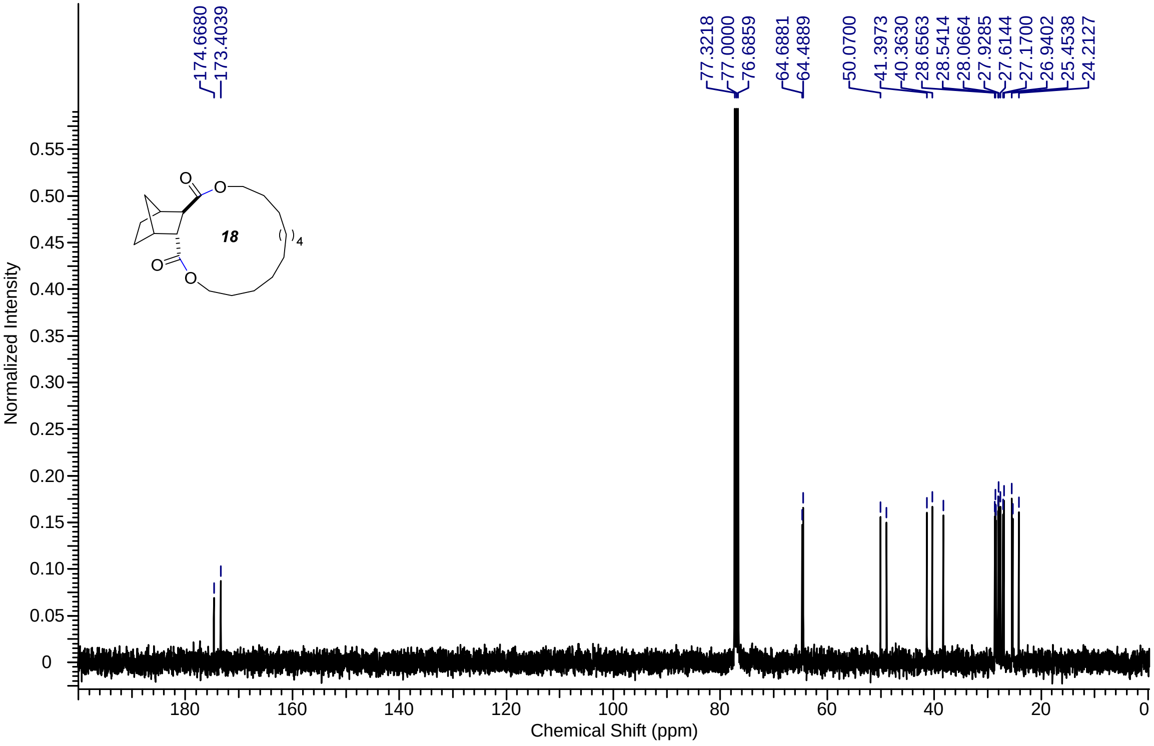
Compound 13


4.4232
4.4181
4.3329
3.9698
3.9633
3.9510
3.9422
3.9349
3.9260
3.0288
2.7612
2.7576
2.7459
2.6109
2.6026
1.5988
1.5892
1.3712
1.3671
1.3632
1.3522
1.3418
1.3382
1.3242
0.0747
O
O
O
O
15
1.02
1.00
2.00
0.98
0.99
2.00
6.58
14.98
Normalized Intensity
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

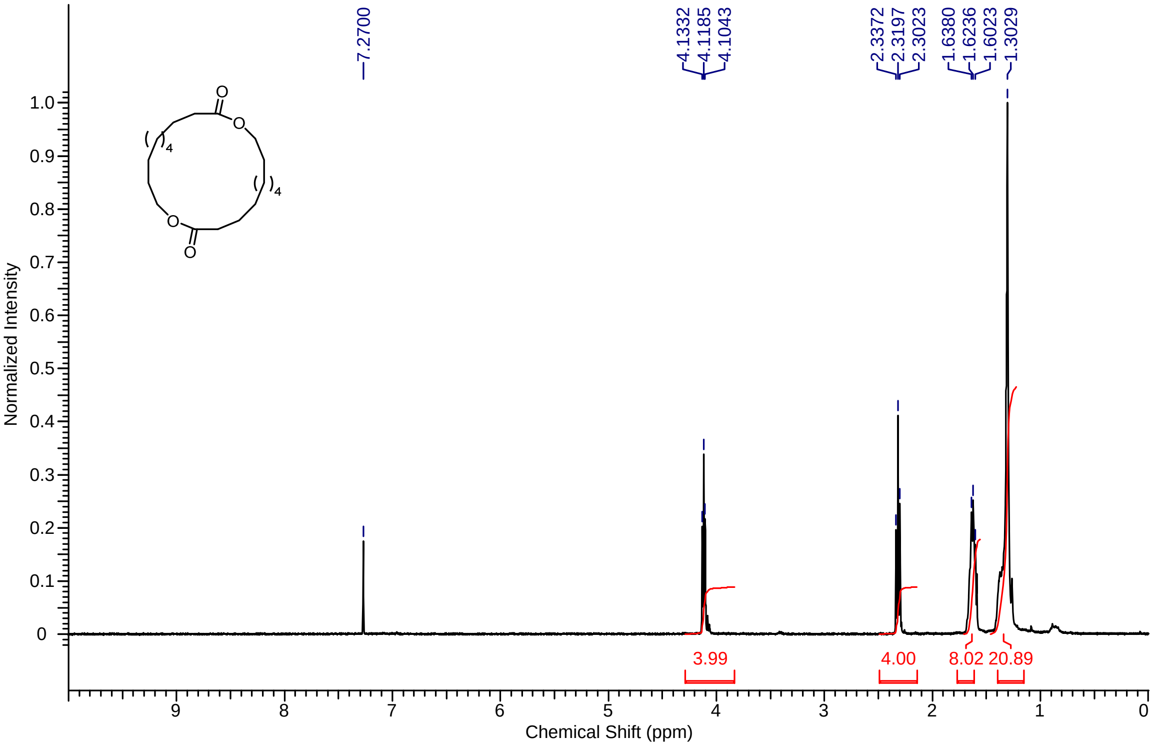

174.6833
173.2430
77.3218
77.0000
76.6859
63.8453
63.7381
51.0814
49.1813
40.5162
39.8420
38.6775
29.0547
27.9515
27.7523
26.7180
25.8982
25.5917
23.9139
23.6764
23.6381
O
O
O
O
15
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)

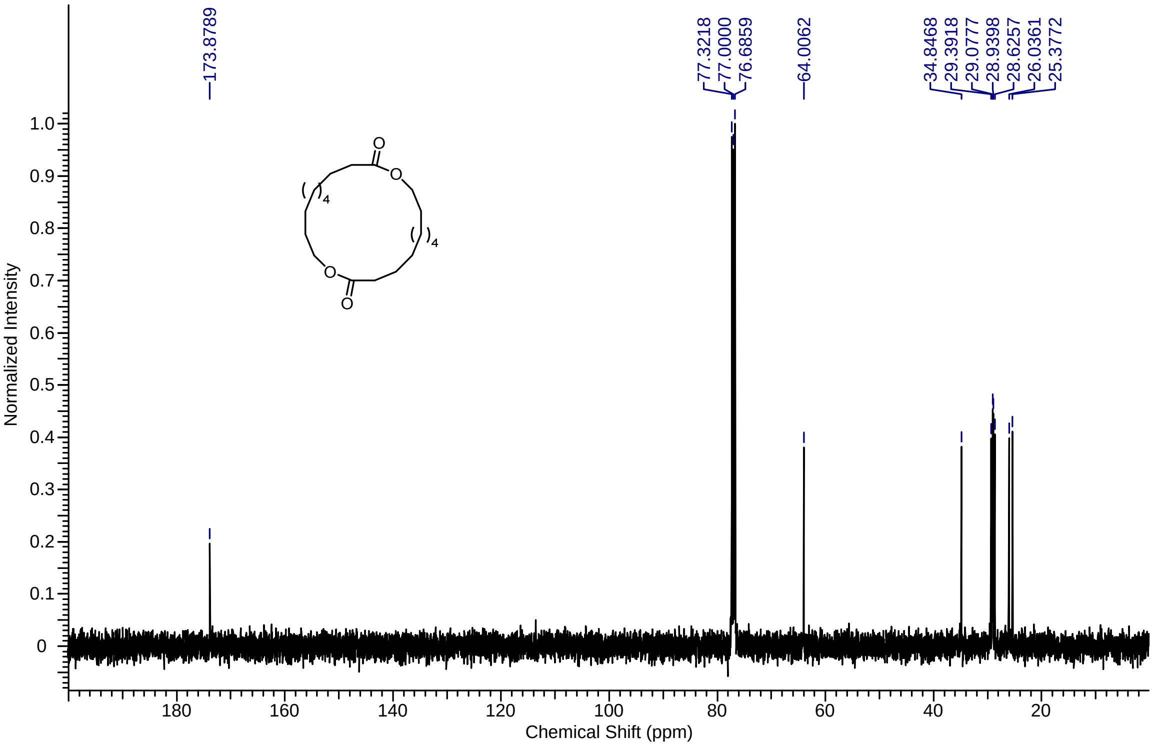
Compound 14


4.3782
4.3507
4.2712
3.9723
3.9684
3.9631
3.9567
3.9526
3.9413
3.1388
3.1360
2.8380
2.8247
2.6363
2.6104
1.6366
1.6190
1.6073
1.3535
1.3345
1.3304
1.3093
1.3049
1.3010
O
O
O
O
18
( )4
1.03
0.93
1.94
0.98
0.99
1.94
6.27
20.00
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

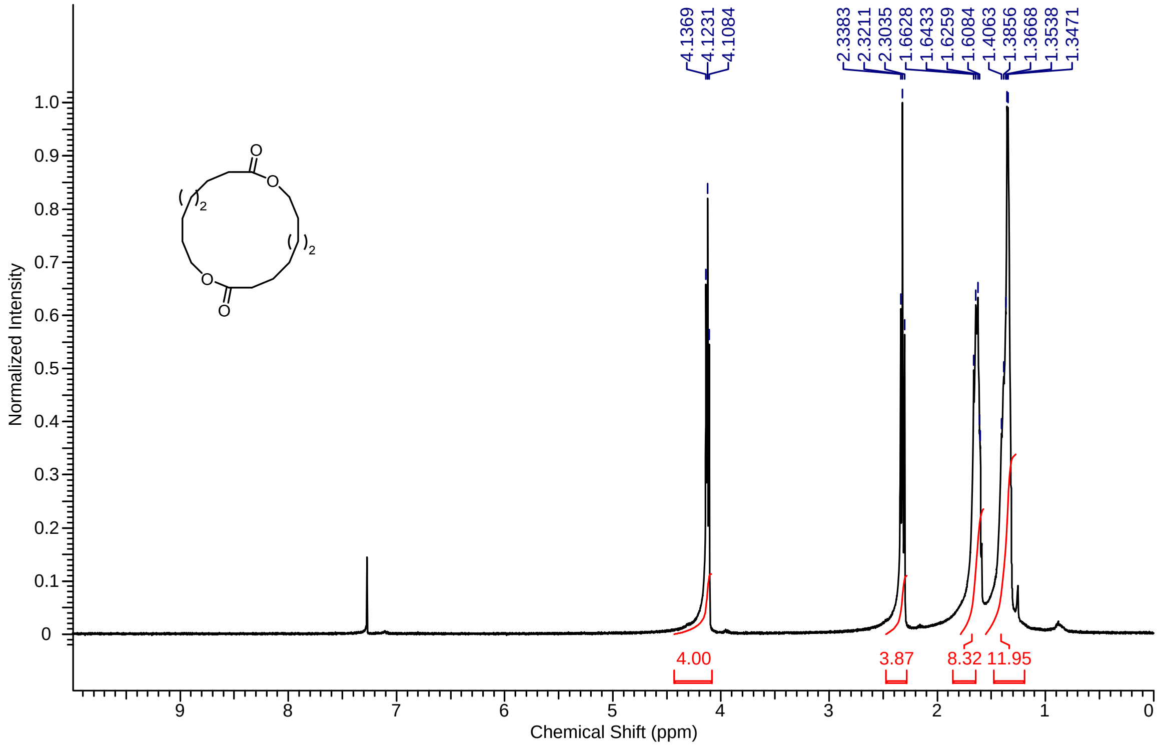

174.6680
173.4039
77.3218
77.0000
76.6859
64.6881
64.4889
50.0700
41.3973
40.3630
28.6563
28.5414
28.0664
27.9285
27.6144
27.1700
26.9402
25.4538
24.2127
O
O
O
O
18
( )4
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

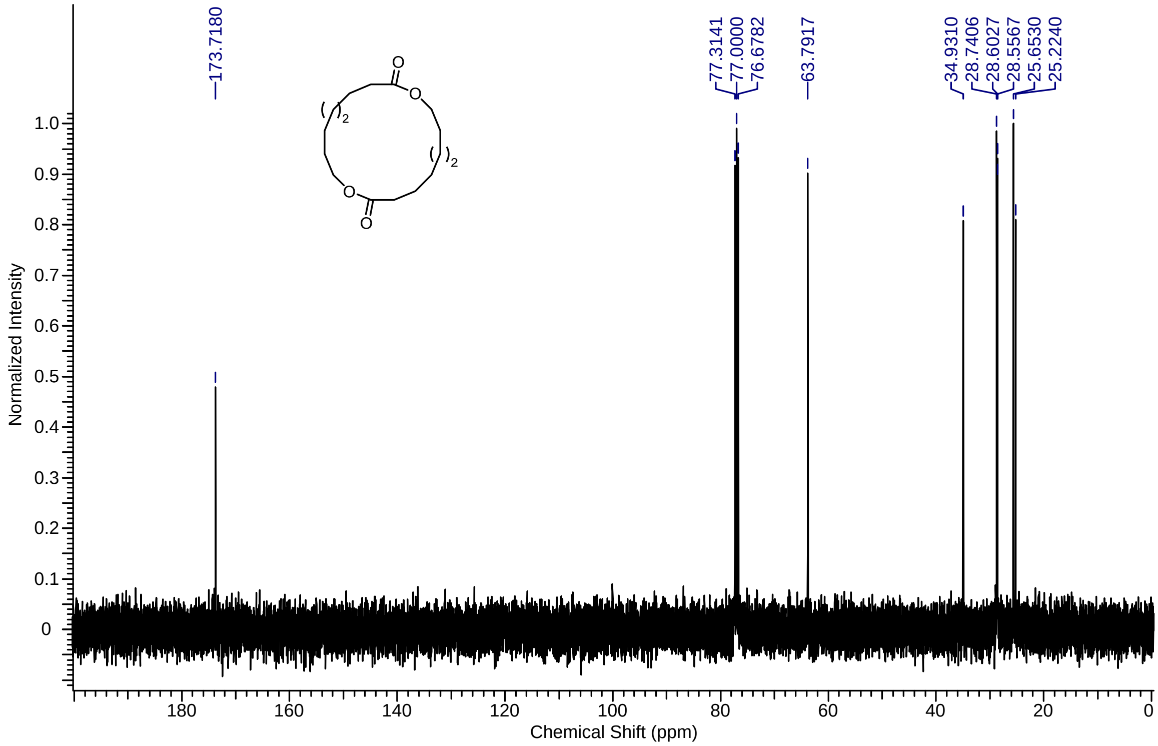
Compound 16


7.2700
4.1332
4.1185
4.1043
2.3372
2.3197
2.3023
1.6380
1.6236
1.6023
1.3029
3.99
4.00
8.02
20.89
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)
O
O
O
O
( )4
( )4

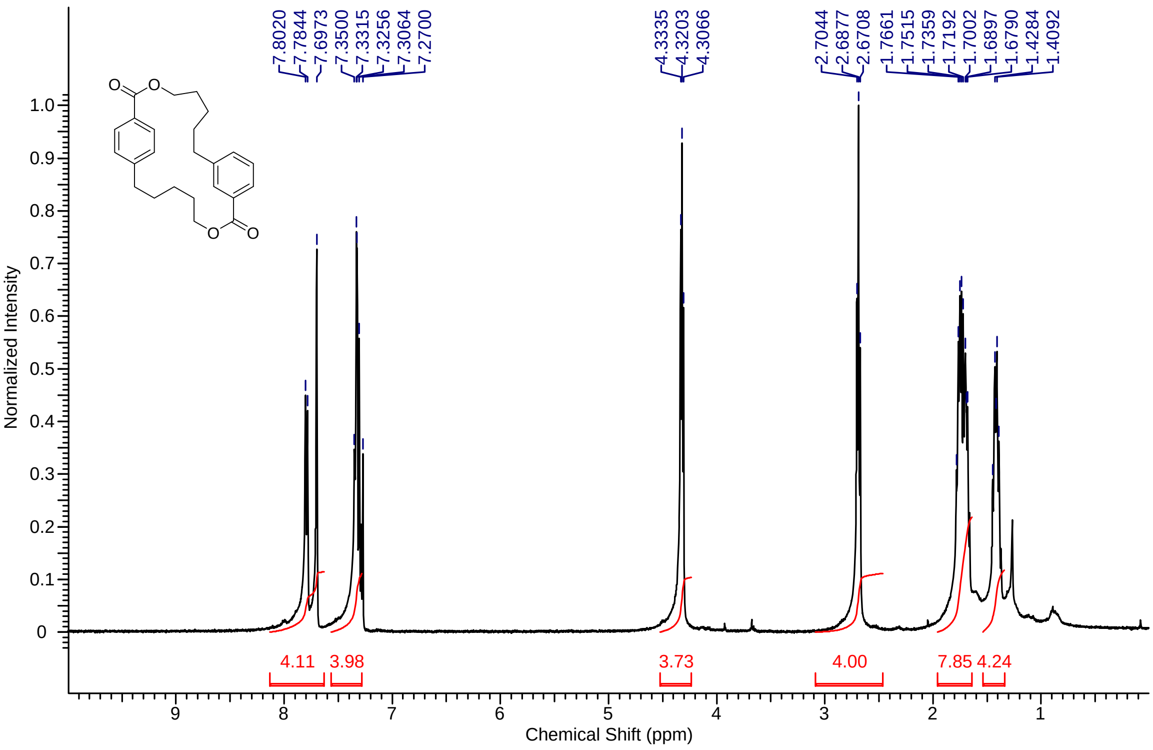

173.8789
77.3218
77.0000
76.6859
64.0062
34.8468
29.3918
29.0777
28.9398
28.6257
26.0361
25.3772
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)
O
O
O
O
( )4
( )4

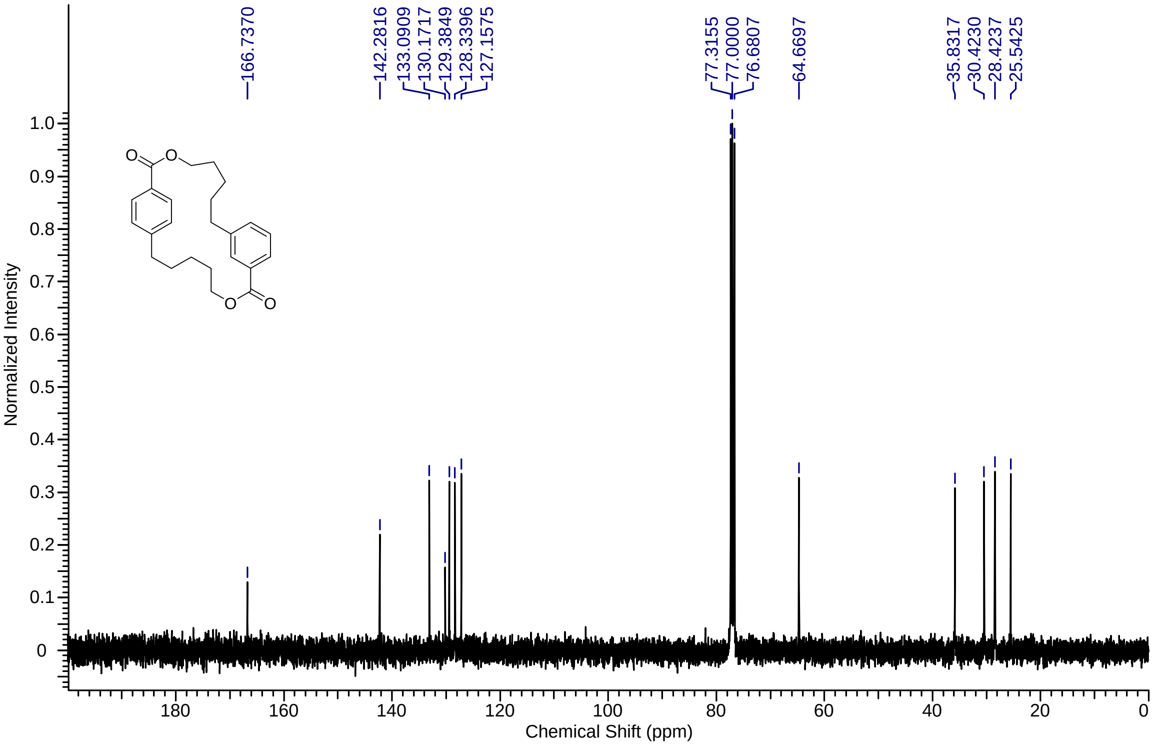
Compound 17


4.1369
4.1231
4.1084
2.3383
2.3211
2.3035
1.6628
1.6433
1.6259
1.6084
1.4063
1.3856
1.3668
1.3538
1.3471
O
O
O
O
( )2
( )2
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
4.00
3.87
8.32
11.95
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

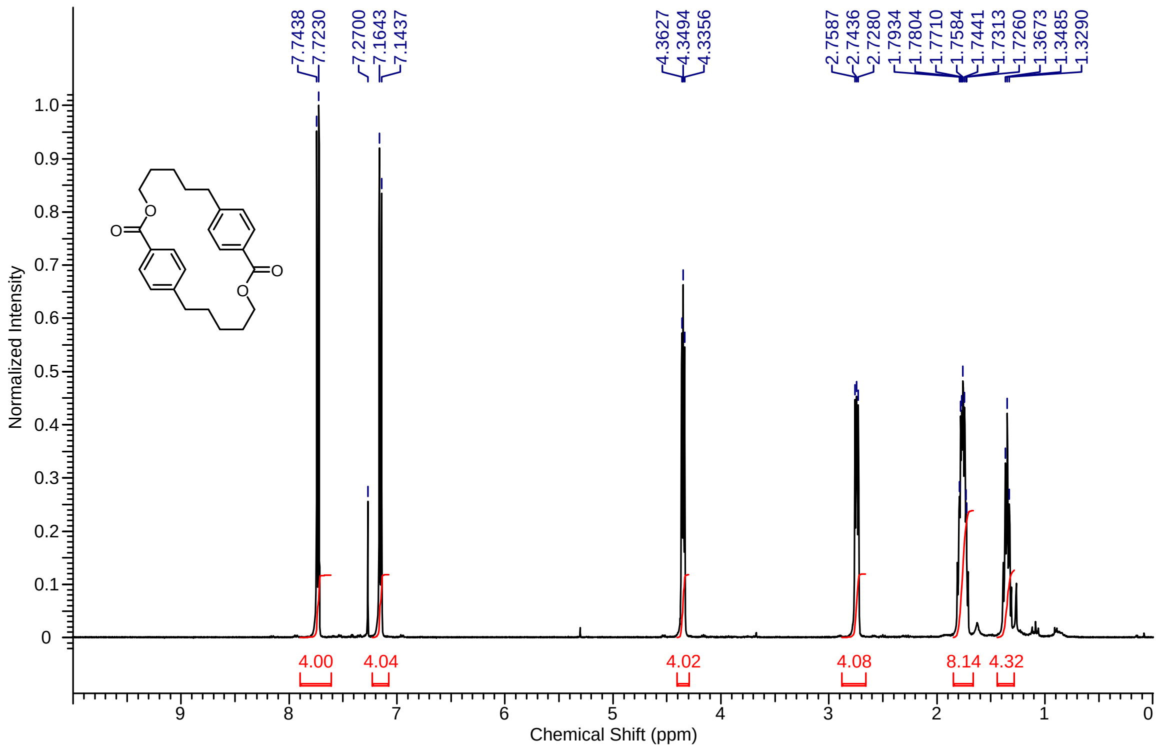

173.7180
77.3141
77.0000
76.6782
63.7917
34.9310
28.7406
28.6027
28.5567
25.6530
25.2240
O
O
O
O
( )2
( )2
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

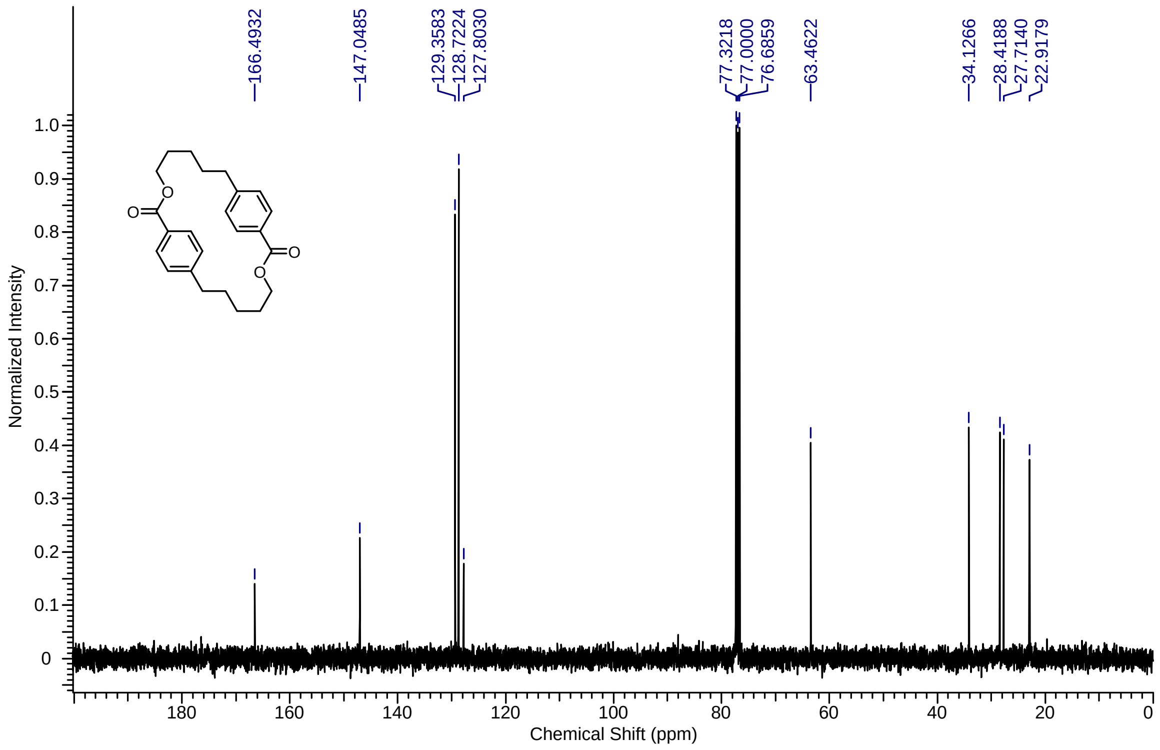
Compound 18


7.8020
7.7844
7.6973
7.3500
7.3315
7.3256
7.3064
7.2700
4.3335
4.3203
4.3066
2.7044
2.6877
2.6708
1.7661
1.7515
1.7359
1.7192
1.7002
1.6897
1.6790
1.4284
1.4092
O
O
O
O
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
4.11
3.98
3.73
4.00
7.85
4.24
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)


166.7370
142.2816
133.0909
130.1717
129.3849
128.3396
127.1575
77.3155
77.0000
76.6807
64.6697
35.8317
30.4230
28.4237
25.5425
O
O
O
O
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

Compound 19


7.7438
7.7230
7.2700
7.1643
7.1437
4.3627
4.3494
4.3356
2.7587
2.7436
2.7280
1.7934
1.7804
1.7710
1.7584
1.7441
1.7313
1.7260
1.3673
1.3485
1.3290
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
O
O
O
O
4.00
4.04
4.02
4.08
8.14
4.32
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


166.4932
147.0485
129.3583
128.7224
127.8030
77.3218
77.0000
76.6859
63.4622
34.1266
28.4188
27.7140
22.9179
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
O
O
O
O
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)