

A One-step, Versatile Synthesis of Dibenzo [n.2.2] Macrobicyclic Compounds via a Conformation-Directed Macrocyclization Reaction

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Materials and Methods: All reactions were carried out in flame-dried glassware under Ar. The solvents used were purified prior to use by distillation over the drying agents indicated: THF and Et₂O from Na/benzophenone; CH₂Cl₂, 1,2-dichloroethane, pyridine and DMF from CaH₂. Most *bis*-electrophiles were purchased from commercial sources, distilled under reduced pressure and stored over molecular sieves under an atmosphere of argon. 1,20-Dibromoicosane was prepared by Kolbe's electrolysis of 11-bromoundecanoic acid in methanol,¹ and 2,2'-*bis*(chloromethyl)-1,1'-biphenyl was prepared according to the literature.² Column chromatography was performed using 230-400 mesh silica gel. Melting points were measured using a B-565 Büchi apparatus. ¹H and ¹³C NMR spectra were recorded on Bruker DPX 250, Varian Mercury 300 and Varian Inova 500 spectrometers in the solvents indicated. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (CDCl₃: δ_{H} 7.26 and δ_{C} 77.0 ppm, CD₂Cl₂: δ_{H} 5.32 and δ_{C} 54.0 ppm, THF-D₈: δ_{H} 3.58 and δ_{C} 67.57 ppm). Coupling constants (*J*) are given in Hz. Infrared (IR) spectra were recorded on a Bruker FT-IR IFS-66V or MIDAC FT-IR Grams-386 spectrometer and are reported in frequency of absorption (cm⁻¹). Only selected IR peaks are reported. High-resolution mass spectra were obtained from a Bruker Microtof mass spectrometer (ESI) or a Micromass Autospec mass spectrometer (EI). Elemental analyses were recorded on a Fisons EA1108 analyzer.

Experimental Procedures

Diisopropyl anthracene-9,10-dicarboxylate (1a). A suspension of 9,10-anthracenedicarboxylic acid³ (1.5 g, 5.63 mmol) and benzyltriethylammonium chloride (12 mg, 0.05 mmol) in 1,2-dichloroethane (20 mL) was heated to reflux and treated with SOCl₂ (1 mL, 14 mmol). The reaction mixture was heated to reflux for 12 h, filtered hot, and the filtrate was concentrated. The residue was dried under vacuum in the presence of NaOH pellets for 4 h. Anhydrous isopropanol (20 mL) and pyridine (1 mL, 12.4 mmol) were added and the solution was heated to 90 °C overnight. The mixture was cooled to rt, concentrated to one-third the original volume, and CH₂Cl₂ (30 mL) was added. The solution was washed with HCl 2M (3 x 10 mL), H₂O (2 x 10 mL) and brine (10 mL), and the organic layer was dried and concentrated. Recrystallization from CH₂Cl₂/hexane afforded **1a** (1.48 g, 75% yield) as yellow crystals, mp 149-151 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CDCl₃) δ 8.03 (m, 4H), 7.56 (m, 4H), 5.62 (hept, *J* = 6.3 Hz, 2H), 1.53 (d, *J* = 6.3 Hz, 12H); ¹³C NMR (62.9 MHz, CDCl₃) δ 168.7, 130.9, 127.4, 126.8, 125.2, 69.8, 22.0; IR (KBr) 1713 cm⁻¹. Anal. Calcd for C₂₂H₂₂O₄: C, 75.41; H, 6.33. Found: C, 75.02; H, 6.51.

Dimethyl anthracene-9,10-dicarboxylate⁴ (1b): BuLi (40.9 mL, 65.5 mmol) was slowly added during 30 min to a suspension of 9,10-dibromoanthracene (10.0 g, 29.8 mmol) in Et₂O (100 mL) at rt and, after being stirred for 10 more min, the reaction mixture was cooled at – 78 °C. A 50 mL Et₂O solution of dimethyl carbonate (10 mL, 119 mmol) was added dropwise, and the reaction was stirred for 6 h while slowly warmed to 0 °C, quenched with deoxygenated acetic acid (3.9 mL, 68.5 mmol) and the resulting solid was filtered and washed with cold Et₂O. Recrystallization from hot MeOH afforded 3.5 g of **1b** (40%), mp 183-185 °C (MeOH); ¹H NMR (300 MHz, CDCl₃) δ 7.99 (m, 4H), 7.56 (m, 4H), 4.19 (s, 6H); ¹³C NMR (62.9 MHz, CDCl₃) δ 169.4, 130.5, 127.5, 126.8, 125.2, 52.7; IR (KBr) 1715 cm⁻¹. Anal. Calcd for C₁₈H₁₄O₄: C, 73.46; H, 4.79. Found: C, 73.37; H, 4.75.

Preparation of Compounds 2-16.

General Me₃SnLi Procedure (A). A solution of Me₃SnLi in THF was prepared by adding MeLi (280 μL, 0.44 mmol) to a solution of Me₆Sn₂ (91 μL, 0.44 mmol) in THF (2 mL) at 0 °C. After 15 min, the solution of Me₃SnLi was cooled to –78 °C and treated with a solution of anthracene **1a** (70 mg, 0.2 mmol) in THF (2 mL), stirred for 1 h, and treated with the corresponding electrophile (0.44 mmol). The reaction mixture was stirred overnight while slowly warming to room temperature. The reaction was quenched with pH 7.0 phosphate buffer (0.5 mL) and partitioned between CH₂Cl₂ (10 mL) and phosphate buffer (10 mL). The aqueous phase was extracted with CH₂Cl₂, and the combined organic phase was washed with brine, dried and concentrated. The residue was crystallized from CH₂Cl₂/hexane.

Diisopropyl 9,10-dihydro-9,10-propanoanthracene-9,10-dicarboxylate (2a). 72 mg, 92% yield; mp 218-220 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.26 (m, 4H), 7.08 (m, 4H), 5.36 (hept, *J* = 6.3 Hz, 2H), 1.89 (t, *J* = 6.6 Hz, 4H), 1.33 (d, *J* = 6.3 Hz, 12H), 1.11 (quint, *J* = 6.6 Hz, 2H); ¹³C NMR (62.9 MHz, CD₂Cl₂) δ 174.2, 140.4, 127.5, 125.3, 69.7, 56.8, 32.6, 22.2, 22.0; IR (KBr) 1716 cm⁻¹. HRMS (ESI): calcd. for C₂₅H₂₈O₄Na [M + Na]⁺ 415.1880, found 415.1879.

Diisopropyl 9,10-dihydro-9,10-butanoanthracene-9,10-dicarboxylate (3a). 43 mg, 53% yield; mp 212-214 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.29 (m, 4H), 7.08 (m, 4H), 5.28 (hept, *J* = 6.3 Hz, 2H), 2.18 (br s, 4H), 1.22 (d, *J* = 6.3 Hz, 12H), 0.90 (br s, 4H); ¹³C NMR (62.9 MHz, CD₂Cl₂) δ 175.6, 138.8, 127.8, 126.3, 69.5, 56.8, 46.2, 24.2, 21.6; IR(KBr) 1716 cm⁻¹. HRMS (ESI): calcd for C₂₆H₃₀O₄Na [M + Na]⁺ 429.2036, found: 429.2040.

Diisopropyl 9,10-dihydro-11-vinyl-9,10-ethanoanthracene-9,10-dicarboxylate (12a). 74 mg, 92% yield; mp 103.5-105.5 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.93 (m, 1H),

7.38 (m, 2H), 7.20 (m, 5H), 5.45 (m, 2H), 4.96 (m, 3H), 3.08 (m, 1H), 2.34 (dd, $J = 10.3, 13.0$ Hz, 1H), 1.71 (dd, $J = 4.2, 13.0$ Hz, 1H), 1.48 (d, $J = 6.3$ Hz, 9H), 1.40 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (62.9 MHz, CD_2Cl_2) δ 171.5, 170.8, 142.1, 141.6, 141.5, 140.0, 137.8, 127.0, 126.8, 126.7, 126.5, 126.2, 123.1, 123.0, 122.7, 116.7, 69.9, 69.5, 59.3, 55.7, 45.4, 38.5, 22.43, 22.39, 22.37, 22.2; IR (KBr) 1723 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{26}\text{H}_{28}\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 427.1880, found 427.1877.

General Li/C₁₀H₈ Procedure (B). Lithium wire coated with mineral oil (25 mg, 3.40 mmol) was hammered into a sheet and cut into thin strips. The strips were rinsed with hexanes and added to a dry round-bottomed flask. To this was added naphthalene (100 mg, 0.80 mmol) and THF (1 mL) and the mixture was sonicated for 90 min. The dark purple solution was transferred via cannula to a vessel under Ar, and the excess lithium was washed with THF (1 mL). The vessel was cooled to $-78\text{ }^\circ\text{C}$ and a solution of **1b** (100 mg, 0.34 mmol) in THF (1 mL) was added. After 1.5 h, a solution of the *bis*-electrophile (0.36 mmol) in THF or in DMF was added, and the resulting mixture was stirred for 18 h while slowly warming to room temperature. The reaction was quenched with deoxygenated acetic acid (50 μL , 0.87 mmol), pH 7 phosphate buffer (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (10 mL). The organic phase was dried and concentrated. The residue was crystallized from a suitable solvent or purified by column chromatography.

Dimethyl 9,10-dihydro-9,10-propanoanthracene-9,10-dicarboxylate (2b). Following procedure B, 300 mg of **1b** (1.02 mmol) and 1,3-dibromopropane (114 μL , 1.12 mmol) in THF (2 mL) afforded 325 mg (95% yield) of **2b** after crystallization from CH_2Cl_2 /hexane, mp $244\text{--}245\text{ }^\circ\text{C}$; ^1H NMR (250 MHz, CDCl_3) δ 7.29 (m, 4H), 7.04 (m, 4H), 3.95 (s, 6H), 2.00 (t, $J = 6.6$ Hz, 4H), 1.19 (quint, $J = 6.5$ Hz, 2H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 175.2, 139.7, 127.3, 124.8, 56.9, 52.3, 32.1, 21.7; IR (KBr) 1729 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{21}\text{H}_{20}\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 359.1254, found 359.1249. Anal. Calcd for $\text{C}_{21}\text{H}_{20}\text{O}_4$: C, 74.98; H, 5.99. Found: C, 74.95; H, 6.19.

Dimethyl 9,10-butano-9,10-dihydroanthracene-9,10-dicarboxylate (3b). Following procedure B, 100 mg of **1b** (0.34 mmol) and 1,4-dibromobutane (42 μL , 0.35 mmol) in DMF (4 mL) afforded 62 mg (52% yield) of **3b** after column chromatography (SiO_2 , CHCl_3 /hexane (1:1) to CHCl_3); mp $170.2\text{--}171.1\text{ }^\circ\text{C}$ (CH_2Cl_2 /hexane); ^1H NMR (250 MHz, CD_2Cl_2) δ 7.31 (m, 4H), 7.04 (m, 4H), 3.74 (s, 6H), 2.19 (br s, 4H), 1.04–0.74 (br s, 4H); ^{13}C NMR (75.45 MHz, CDCl_3) δ 176.3, 137.8, 127.5, 125.6, 56.3, 52.4, 45.2, 23.5; IR (KBr) 1731 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{22}\text{H}_{22}\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 373.1410, found 373.1421.

Dibenzobicyclo[6.2.2]dodecane 5b. General procedure B was followed using 1,6-dibromohexane (55 μL , 0.36 mmol) in DMF (4 mL) as the electrophile at $-78\text{ }^\circ\text{C}$. The reaction mixture was slowly

warmed to rt and then stirred at 30 °C for a total of 48 h. Quenching and work-up as described afforded 53 mg (41% yield) of **5b** after column chromatography (SiO₂, CHCl₃/toluene 1:15); mp 225.7-227.6 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.31 (m, 4H), 7.18 (m, 4H), 3.54 (s, 6H), 2.50 (t, *J* = 5.6 Hz, 4H), 1.08 (br s, 4H), 0.64 (br s, 4H); ¹³C NMR (62.9 MHz, CDCl₃) δ 176.7, 136.8, 127.7, 126.9, 54.1, 52.9, 42.0, 24.8, 19.9; IR (KBr) 1729 cm⁻¹. HRMS (ESI): calcd. for C₂₄H₂₆O₄Na [M + Na]⁺ 401.1723, found 401.1727.

Dibenzobicyclo[7.2.2]tridecane 6b. General procedure B was followed using 1,7-dibromoheptane (64 μL, 0.37 mmol) in DMF (2 mL) as the electrophile. The reaction mixture was stirred overnight from -78 °C to rt and then at 30 °C for 2 days. Quenching and work-up as described afforded **6b** as a solid after addition of hexane to the crude reaction residue (96 mg, 72% yield); mp 257-259 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.18 (s, 8H), 3.31 (s, 6H), 2.22 (m, 4H), 0.74 (br s, 6H), 0.38 (br s, 4H); ¹³C NMR (75.45 MHz, CDCl₃) δ 175.8, 135.5, 127.4, 126.2, 53.4, 52.0, 43.6, 29.4, 29.2, 23.2; IR (KBr) 1729 cm⁻¹. HRMS (ESI): calcd. for C₂₅H₂₈O₄Na [M + Na]⁺ 415.1880, found 415.1876.

Dibenzobicyclo[9.2.2]pentadecane 7b. General procedure B was followed using 1,9-dibromononane (71 μL, 0.35 mmol) in DMF (4 mL) as the electrophile. The reaction mixture was stirred overnight from -78 °C to rt and then at 30 °C for 2 days. Quenching and work-up gave a solid residue that was sonicated with MeOH for 10 min, the suspension was centrifuged and the supernatant liquid was discarded. The process was repeated twice to give **7b** as a colorless solid (95 mg, 66% yield), mp 91.4-91.9 °C; ¹H NMR (500 MHz, CD₂Cl₂) δ 7.23 (s, 8H), 3.39 (s, 6H), 2.29 (m, 4H), 1.02-0.81 (m, 10H), 0.46 (br s, 4H); ¹³C NMR (75.45 MHz, CDCl₃) δ 175.9, 135.6, 127.4, 126.3, 53.5, 52.2, 43.6, 29.8, 29.3, 23.3; IR (KBr) 1728 cm⁻¹. Anal. Calcd for C₂₇H₃₂O₄·1/4H₂O: C, 76.30; H, 7.71. Found: C, 76.24; H, 7.93.

Dibenzobicyclo[10.2.2]hexadecane 8b. Following the same procedure as for **7b** except using 1,10-dibromodecane (80 μL, 0.35 mmol) in DMF (4 mL) as the electrophile, 104 mg (70% yield) of **8b** were obtained as a colorless solid, mp 109.8-111.1 °C; ¹H NMR (500 MHz, CD₂Cl₂) δ 7.24 (s, 8H), 3.40 (s, 6H), 2.31 (m, 4H), 0.93 (m, 12H), 0.49 (br s, 4H); ¹³C NMR (75.45 MHz, CDCl₃) δ 175.9, 135.6, 127.4, 126.3, 53.5, 52.2, 43.6, 29.8, 29.4, 23.3. IR (KBr) 1730 cm⁻¹. Anal. Calcd for C₂₈H₃₄O₄·1/4H₂O: C, 76.59; H, 7.92. Found: C, 76.31; H, 8.03.

Dibenzobicyclo[11.2.2]heptadecane 9b. Following the same procedure as for **7b** but using 1,11-dibromoundecane (82 μL, 0.35 mmol) in DMF (4 mL), **9b** (110 mg, 72% yield) was obtained as a solid, mp 94.5-96.9 °C; ¹H NMR (250 MHz, CD₂Cl₂) δ 7.27 (s, 8H), 3.43 (s, 6H), 2.34 (m, 4H), 0.94 (br s, 14 H), 0.52 (br s, 4H); ¹³C NMR (75.45 MHz, CDCl₃) δ 175.9, 135.6, 127.4, 126.3,

53.5, 52.1, 43.7, 29.8, 29.4, 23.3; IR (KBr) 1730 cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{36}\text{O}_4$: C, 77.64; H, 8.09. Found: C, 77.68; H, 8.10.

Dibenzobicyclo[12.2.2]octadecane 10b. General procedure B was followed using 1,12-dibromododecane (115 mg, 0.35 mmol) in DMF (4 mL) as the electrophile. The reaction mixture was stirred at room temperature for 42 h. Quenching and work-up were performed as described and 121 mg of **10b** (77% yield) were isolated after column chromatography (SiO_2 , CHCl_3 :hexane 1/1), mp 139-141 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.26 (s, 8H), 3.43 (s, 6H), 2.34 (m, 4H), 0.94 (d, $J = 13.7$ Hz, 16H), 0.52 (br s, 4H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 175.9, 135.6, 127.4, 126.3, 53.6, 52.2, 43.7, 29.8, 29.4, 23.3; IR (KBr) 1730 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{30}\text{H}_{38}\text{O}_4\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 485.2662, found 485.2683.

Dibenzobicyclo[20.2.2]hexacosane 11b. Following the same procedure as for **7b** but using 1,20-dibromoicosane (155 mg, 0.35 mmol) in DMF (4 mL) as the electrophile, **11b** (119 mg, 61% yield) was obtained as a colorless solid, mp 125.9-127.2 $^\circ\text{C}$; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.29 (s, 8H), 3.46 (s, 6H), 2.37 (m, 4H), 1.33-0.96 (m, 32H), 0.56 (br s, 4H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 176.0, 135.7, 127.4, 126.4, 53.6, 52.2, 43.7, 29.9, 29.7, 29.6, 29.5, 23.4; IR (KBr) 1732 cm^{-1} . HRMS (EI): calcd. for $\text{C}_{38}\text{H}_{55}\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 575.4100, found 575.4078.

Dimethyl 12-vinyl-9,10-dihydro-9,10-ethanoanthracene-9,10-dicarboxylate (12b). Following the procedure B except using 1,4-dichlorobutene (38 μL , 0.36 mmol) in THF (1 mL) afforded 89 mg (75% yield) of **12b** after crystallization from CH_2Cl_2 /hexane, mp 100-101 $^\circ\text{C}$ (CH_2Cl_2 /hexane); ^1H NMR (250 MHz, CDCl_3) δ 7.81 (m, 1H), 7.29-7.04 (m, 6H), 6.96 (m, 1H), 5.05-4.72 (m, 3H), 4.00 (s, 3H), 3.94 (s, 3H), 3.04 (ddd, $J = 10.4, 7.6, 4.2$ Hz, 1H), 2.31 (dd, $J = 12.9, 10.3$ Hz, 1H), 1.69 (dd, $J = 12.9, 4.3$ Hz, 1H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 172.1, 171.5, 141.1, 140.6, 140.3, 139.3, 136.7, 126.6, 126.4, 126.3, 126.2, 125.6, 122.5, 122.4, 122.1, 116.5, 59.6, 55.6, 52.2, 51.7, 44.9, 37.8; IR (KBr) 1727 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{22}\text{H}_{20}\text{O}_4\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 371.1254, found 371.1240.

Dimethyl 5,6,11,12-tetrahydro-5,12-[1,2]benzenodibenzo[*a,e*][8]annulene-5,12-dicarboxylate (13b). Following the procedure B, 56 mg of **1b** (0.18 mmol) and *o*-dichloroxylylene (**17**, 35 μg , 0.20 mmol) in THF (1 mL) afforded 69 mg (96% yield) of **13b** after crystallization from CH_2Cl_2 /hexane, mp 255-257 $^\circ\text{C}$ (CH_2Cl_2 /hexane); ^1H NMR (250 MHz, CD_2Cl_2) δ 7.13 (m, 4H), 6.89 (m, 4H), 6.81 (s, 4H), 3.86 (s, 6H), 3.62 (s, 4H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 175.7, 139.8, 139.7, 130.9, 126.9, 126.1, 125.5, 58.2, 52.7, 47.4; IR (KBr) 1727 cm^{-1} . HRMS (ESI): calcd for $\text{C}_{26}\text{H}_{23}\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 399.1591, found 399.1588. Anal. Calcd for $\text{C}_{26}\text{H}_{22}\text{O}_4$: C, 78.37; H, 5.57. Found: C, 77.97; H, 5.78.

Dimethyl 4,5,10,11-tetrahydro-5,10-[1,2]benzenobenzo[6,7]cyclonona[1,2,3-*de*]naphthalene-5,10-dicarboxylate (14b). 100 mg of **1b** (0.34 mmol) and 1,8-*bis*(bromomethyl)naphthalene **18** (115 mg, 0.37 mmol) in THF (4 mL) afforded 94 mg (61% yield) of **14b** after crystallization from CH₂Cl₂/hexane, mp 287.6-290.1 °C; ¹H NMR (300 MHz, CD₂Cl₂) δ 7.41 (m, 6H), 7.17 (m, 4H), 6.51 (m, 2H), 6.20 (m, 2H), 4.70 (d, *J* = 15.4, 2H), 3.85 (d, *J* = 15.4, 2H), 3.85 (s, 6H); ¹³C NMR (62.9 MHz, CDCl₃) δ 176.0, 140.1, 136.8, 135.3, 134.5, 132.6, 130.5, 129.0, 127.2, 127.1, 125.34, 125.31, 124.4, 58.7, 52.7, 45.1; IR (KBr) 1734 cm⁻¹. HRMS (ESI): calcd. for C₃₀H₂₄O₄Na [M + Na]⁺ 471.1567, found 471.1569.

Dimethyl 9,10,15,16-tetrahydro-10,15-[1,2]benzenotribenzo[*a,c,g*][10]annulene-10,15-dicarboxylate (15b). Following the procedure B except using 2,2'-*bis*(chloromethyl)-1,1'-biphenyl (**19**, 94 mg, 0.37 mmol) in DMF (4 mL) provided 77 mg (48% yield) of **15b** after crystallization from Et₂O/hexane, mp 182-183 °C (CH₂Cl₂/hexane); ¹H NMR (250 MHz, CDCl₃) δ 7.11-6.78 (m, 14H), 6.67 (m, 2H), 4.37 (d, *J* = 13.9 Hz, 2H), 3.58 (s, 6H), 3.15 (d, *J* = 13.9 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃) δ 176.7, 142.1, 139.3, 137.0, 133.8, 133.5, 128.4, 128.3, 127.3, 126.5, 126.3, 125.1, 56.2, 53.1, 45.5; IR (KBr) 1726 cm⁻¹. HRMS (ESI): calcd. for C₃₂H₂₆O₄Na [M + Na]⁺ 497.1723, found 497.1719.

Dimethyl 6,7,12,13-tetrahydro-7,12-[1,2]benzenotribenzo[*b,f,j*][1] oxacycloundecine-7,12-dicarboxylate (16b). Following the procedure B and using 2,2-oxi-*bis*[(chloromethyl)benzene] (**20**, 104 mg, 0.39 mmol) in DMF (1.7 mL) as the electrophile provided 67 mg (40% yield) of **16b** after column chromatography (SiO₂, CH₂Cl₂:hexane 1:1), mp 268-269 °C (CH₂Cl₂/MeOH); ¹H NMR (250 MHz, CD₂Cl₂) δ 7.25 (dd, *J* = 7.3, 1.8 Hz, 2H), 7.07 (m, 4H), 7.01-6.81 (m, 8H), 6.38 (dd, *J* = 7.9, 1.2 Hz, 2H), 3.61 (s, 6H), 3.38 (br s, 4H); ¹³C NMR (62.9 MHz, CDCl₃) δ 176.4, 156.3, 135.9, 134.0, 128.1, 128.0, 126.7, 122.8, 118.2, 55.4, 53.0, 45.7; IR (CHCl₃) 1723 cm⁻¹. HRMS (ESI): calcd. for C₃₂H₂₆O₅Na [M + Na]⁺ 513.1672, found 513.1657. Anal. Calcd for C₃₂H₂₆O₅: C, 78.35; H, 5.34. Found: C, 78.04; H, 5.32.

2,2'-oxy-*bis*[(chloromethyl)benzene] (20). To a stirred suspension of [oxybis(2,1-phenylene)]dimethanol⁵ (565 mg, 2.45 mmol) in CH₂Cl₂ (12 mL) was slowly added SOCl₂ (1 mL) at rt. The resulting mixture was stirred for 2.5 h at rt. The mixture was partitioned between sat NaHCO₃ (15 mL) and CH₂Cl₂ (10 mL). The organic layer was washed with pH 7.0 buffer (10 mL) and water (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was distilled under vacuum (90 °C, 0.1 mm Hg) to yield the product as a white solid that was recrystallized from hexane (610 mg, 93% yield), mp 81-83 °C (hexane); ¹H NMR (250 MHz, CDCl₃) δ 7.47 (dd, *J* = 7.5, 1.6 Hz, 2H), 7.26 (td, *J* = 7.9, 1.7 Hz, 2H), 7.11 (td, *J* = 7.5, 1.1 Hz,

2H), 6.82 (dd, $J = 8.1, 0.9$ Hz, 2H), 4.71 (s, 4H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 154.7, 131.0, 130.1, 128.5, 123.9, 118.3, 41.1. Anal. Calcd for $\text{C}_{14}\text{H}_{12}\text{Cl}_2\text{O}$: C, 62.94; H, 4.53. Found: C, 62.68; H, 4.54.

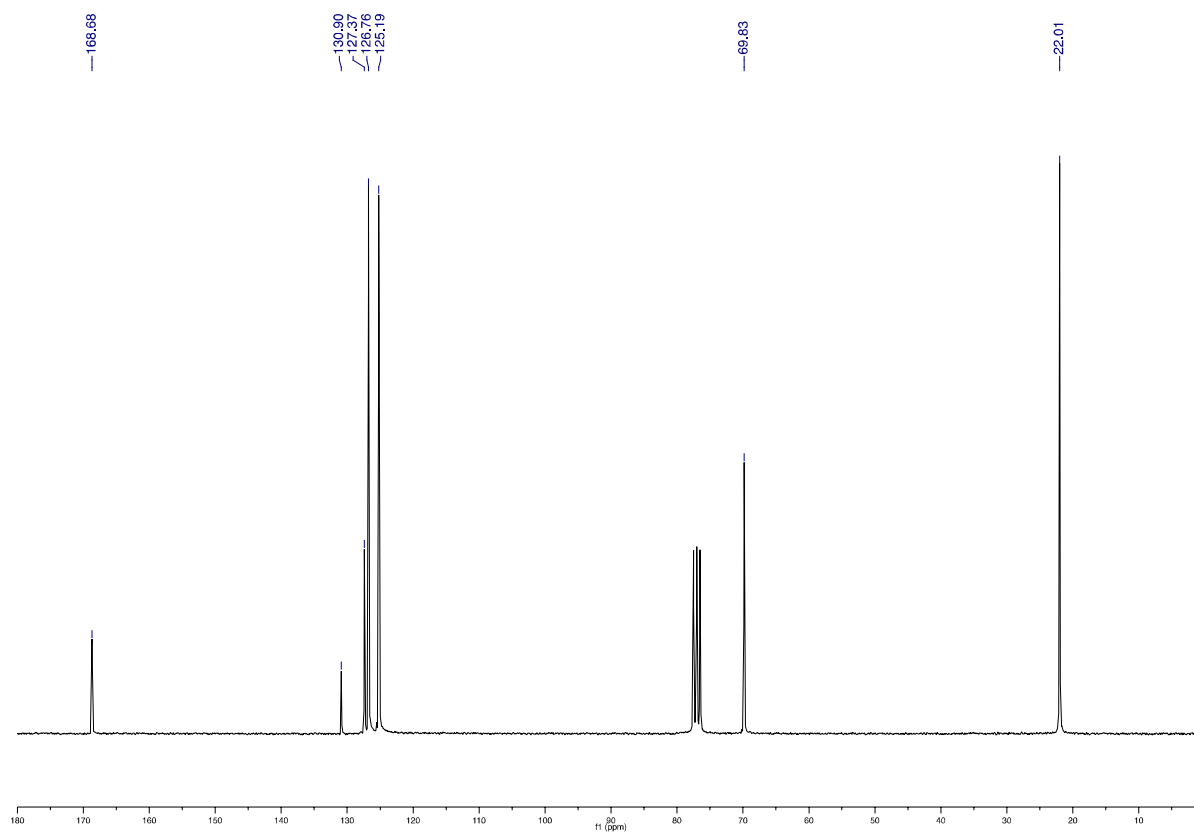
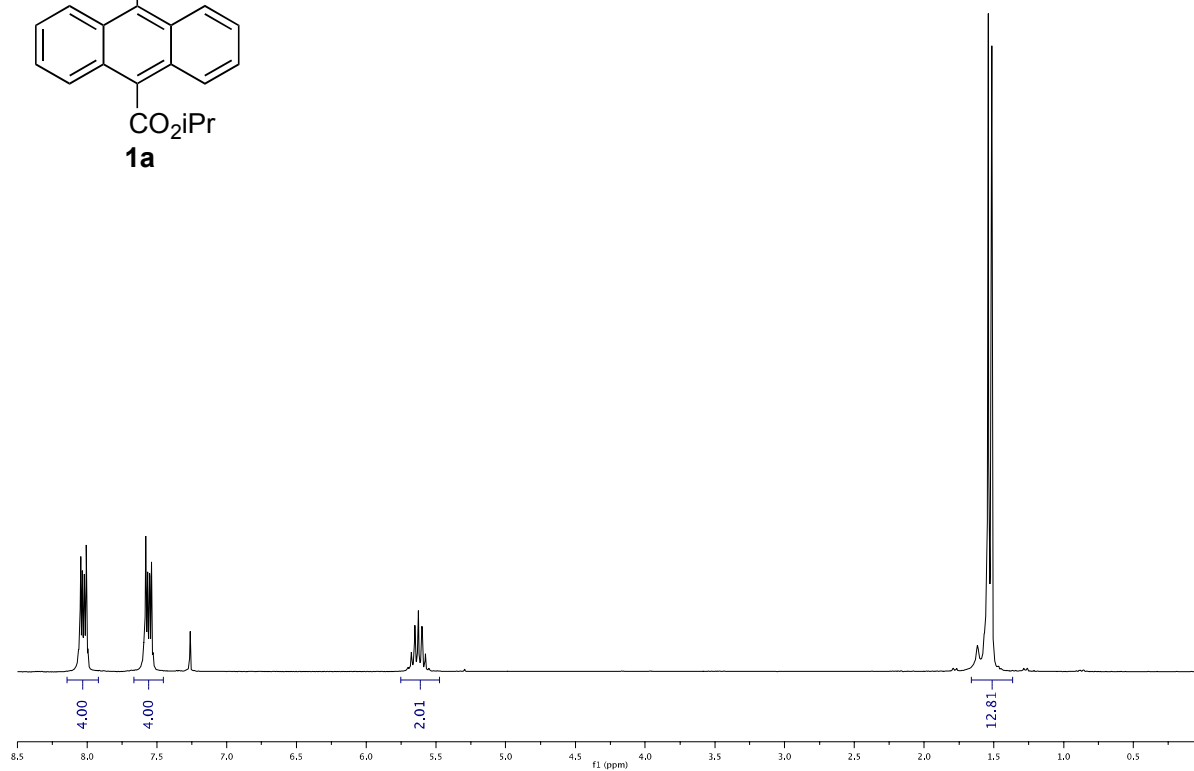
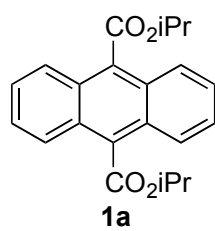
Dimethyl 9,10-dihydro-9-propyl-anthracene-9,10-dicarboxylate (25). General procedure B was followed except using 1-iodopropane (35 μL , 0.34 mmol) as the electrophile. The reaction mixture was stirred for 2 h while warming to rt and then stirred for an additional 18 h. Quenching and work-up as described followed by column chromatography (SiO_2 , CH_2Cl_2) provided 80 mg of **25** (70% yield), mp 152.2-152.9 $^\circ\text{C}$ ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$); ^1H NMR (500 MHz, THF-D_8 , 195 K) δ 7.44 (m, 2H), 7.30 (quint, $J = 7.1$ Hz, 4H), 7.16 (m, 2H), 5.29 (s, 1H), 3.58 (s, 3H), 3.42 (s, 3H), 2.15 (m, 2H), 0.99 (m, 2H), 0.72 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (125.8 MHz, THF-D_8 , 195 K) δ 176.1, 173.3, 137.8, 132.5, 130.1, 128.7, 127.9, 127.8, 56.0, 53.0, 52.8, 50.2, 46.1, 19.1, 15.1; IR (CHCl_3) 1730.7 cm^{-1} . HRMS (ESI): calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_4\text{Na} [\text{M} + \text{Na}]^+$ 361.1410, found 361.1411.

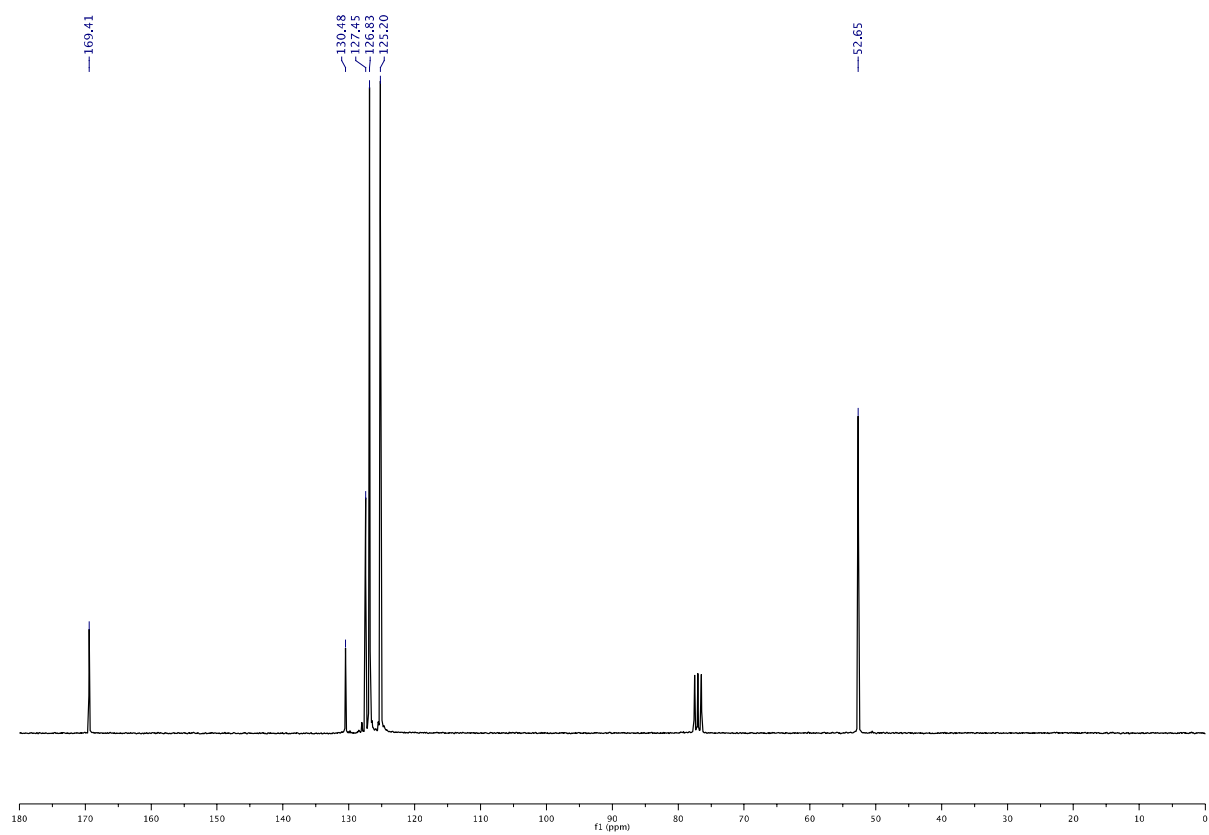
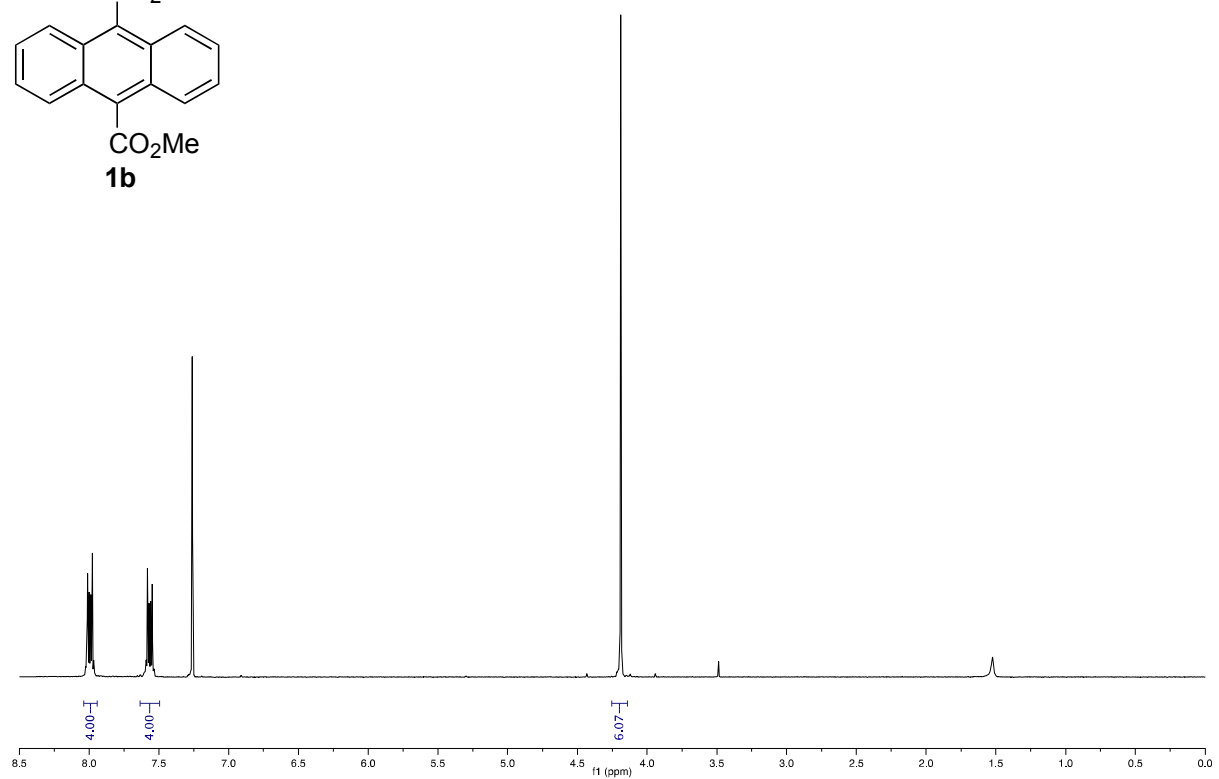
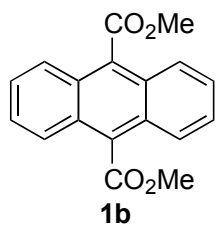
Preparation of the NMR samples: THF-D_8 was dried from CaH_2 by sonication (30 min) and then centrifuged under Ar atmosphere. A stock solution of lithium diisopropylamide was prepared by adding BuLi (330 μL , 0.50 mmol) to a 0 $^\circ\text{C}$ solution of dry diisopropylamine (70 μL , 0.50 mmol) in anhydrous THF-D_8 (0.40 $\square\text{L}$) and stirring for 30 min at 0 $^\circ\text{C}$.

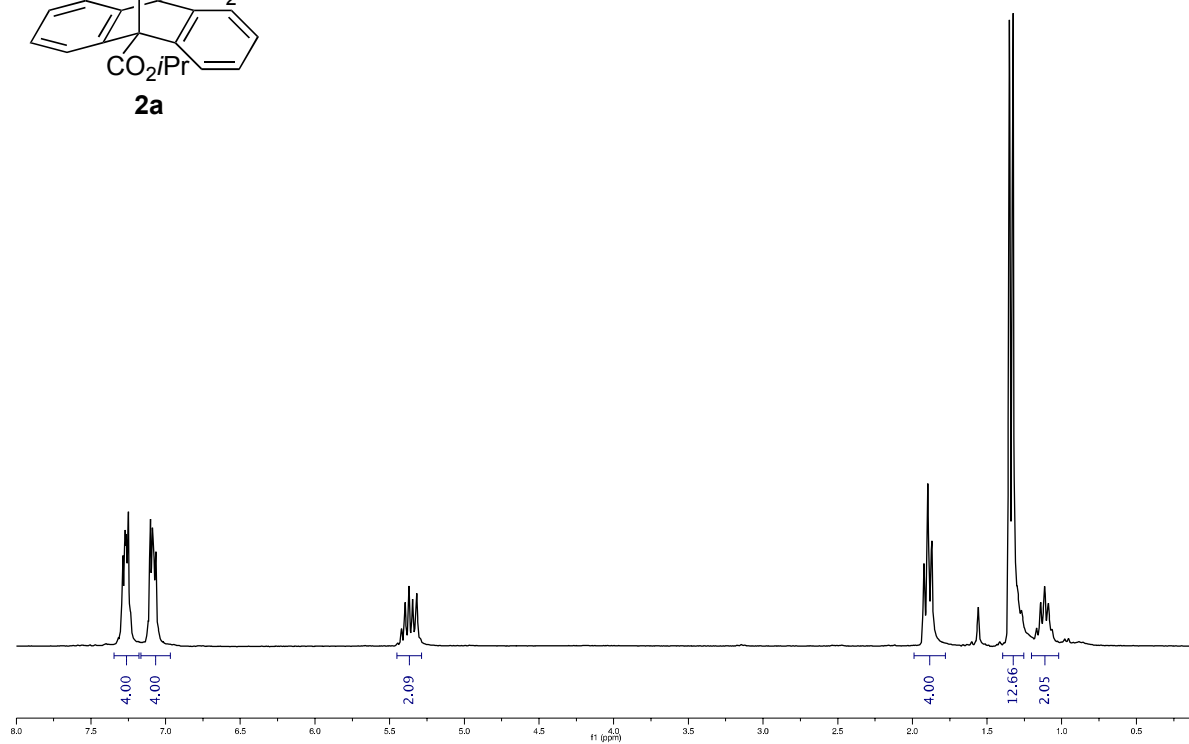
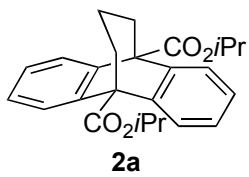
An NMR tube (with J Young valve) was flame-dried and cooled under Ar. The NMR tube was placed in a $-78\text{ }^\circ\text{C}$ dry ice/acetone bath under positive Ar pressure, and charged with LDA solution (160 μL , 0.10 mmol) followed by a solution of **25** (30 mg, 0.089 mmol) in THF-D_8 (0.7 $\square\text{L}$), sealed under a high pressure of Ar and kept at $-78\text{ }^\circ\text{C}$.

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1. Woolford, R. G. *Can. J. Chem.* **1962**, *40*, 1846-1850.
2. Puckette, T. A.; Devon, T. J.; Phillips, G. W.; Stavinoha, J. L. U.S. Patent 4 879 416, 1989.
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5. Preparation of (oxybis(2,1-phenylene))dimethanol: (a) Shapiro, R.; Slobodin, D. *J. Org. Chem.* **1969**, *34*, 1165-1168. (b) Martínez-Otero, D.; Alvarado-Rodríguez, J. G.; Cruz-Borbolla, J.; Andrade-López, N.; Pandiyan, T.; Moreno-Esparza, R.; Flores-Alamo, M.; Cantillo-Castillo, J. *Polyhedron* **2012**, *33*, 367-377.







— 174.22

— 140.39

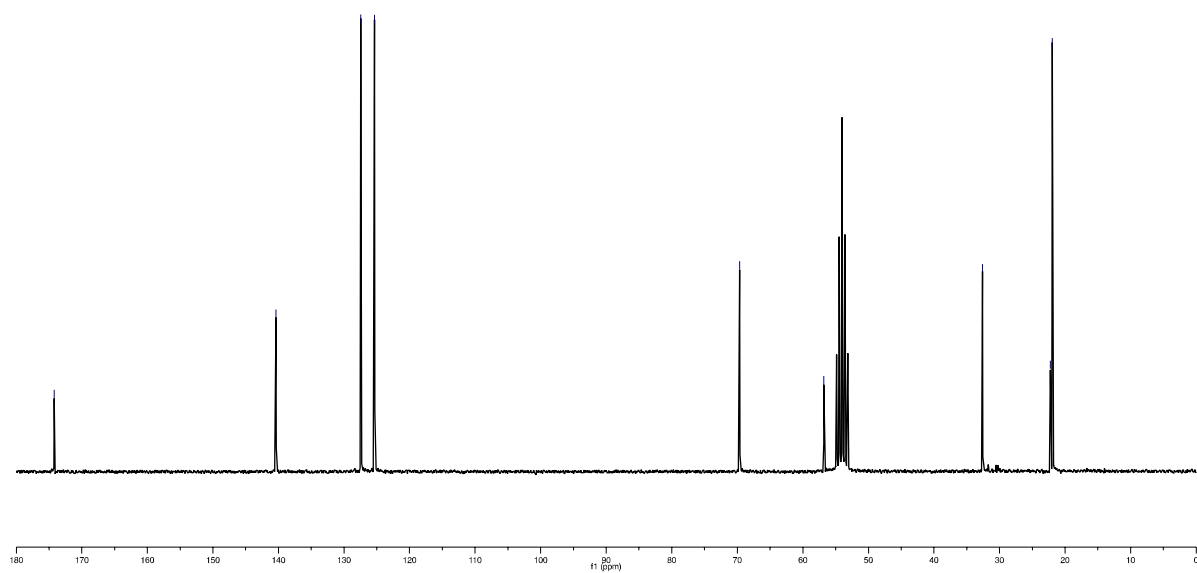
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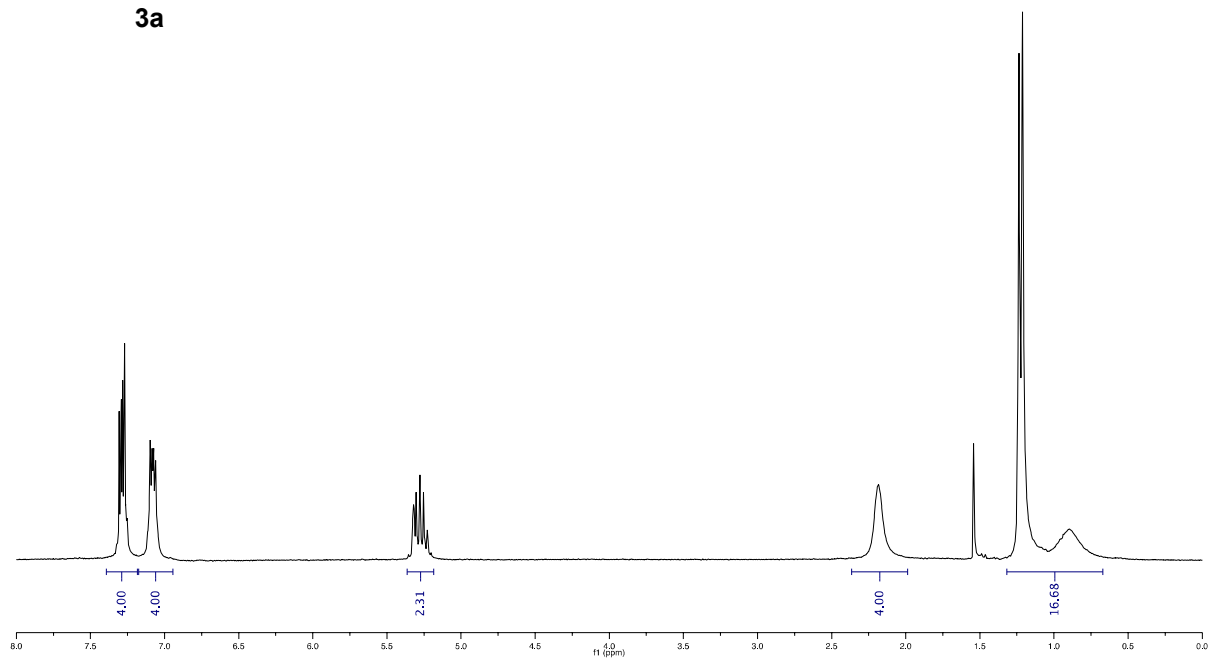
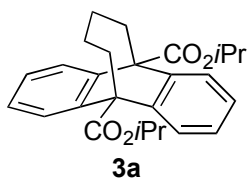
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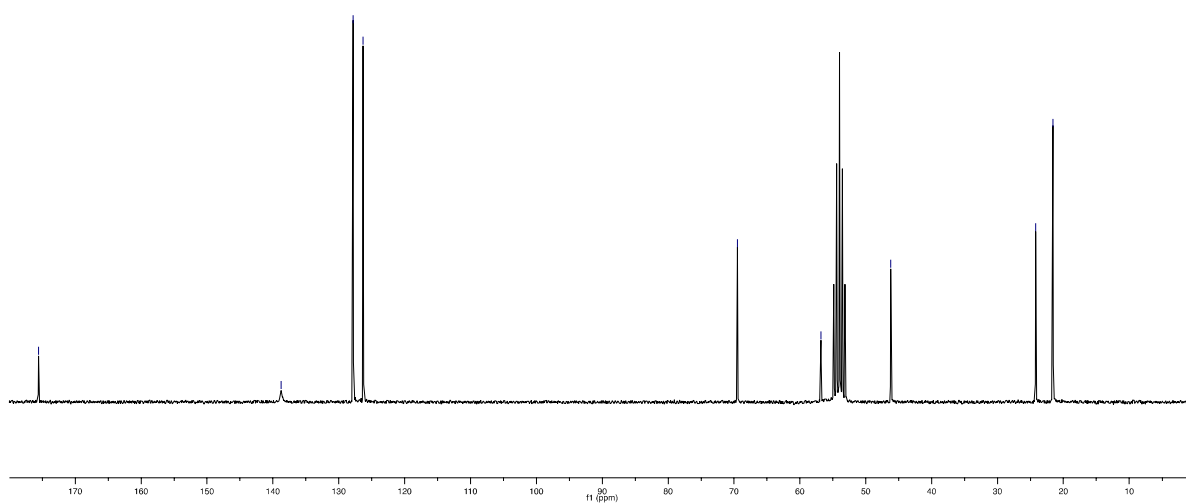
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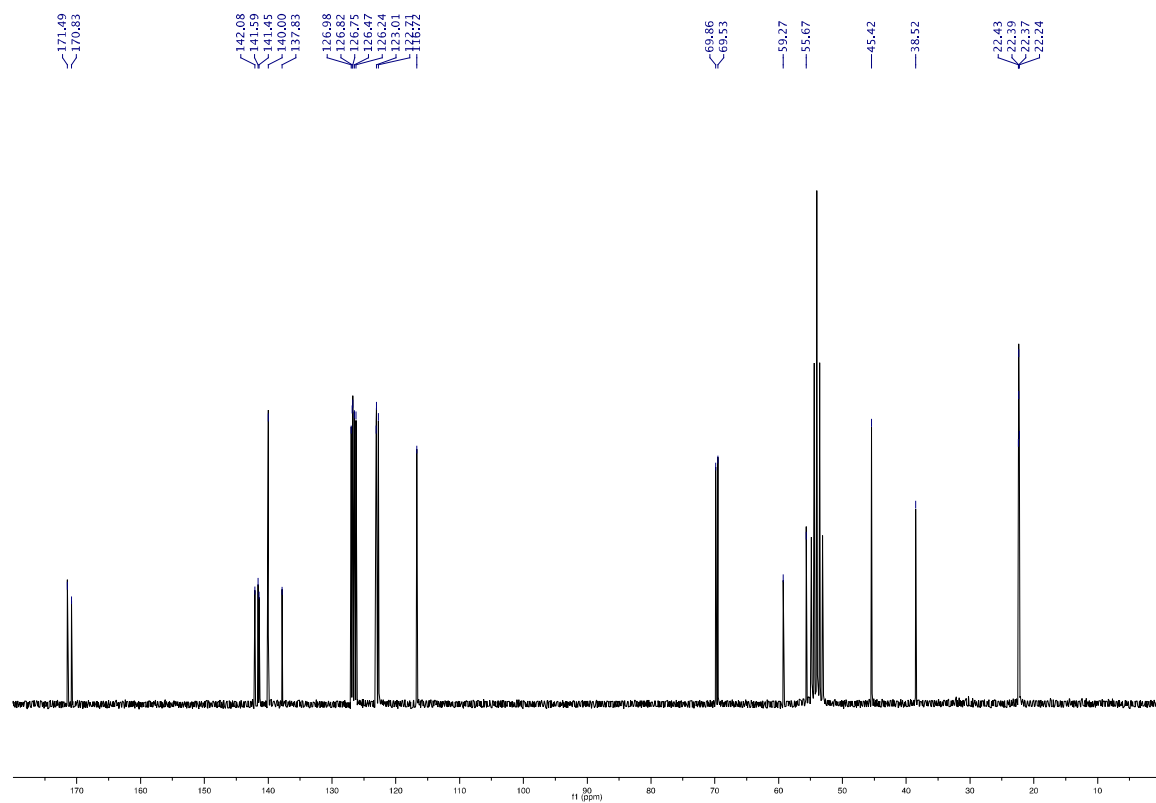
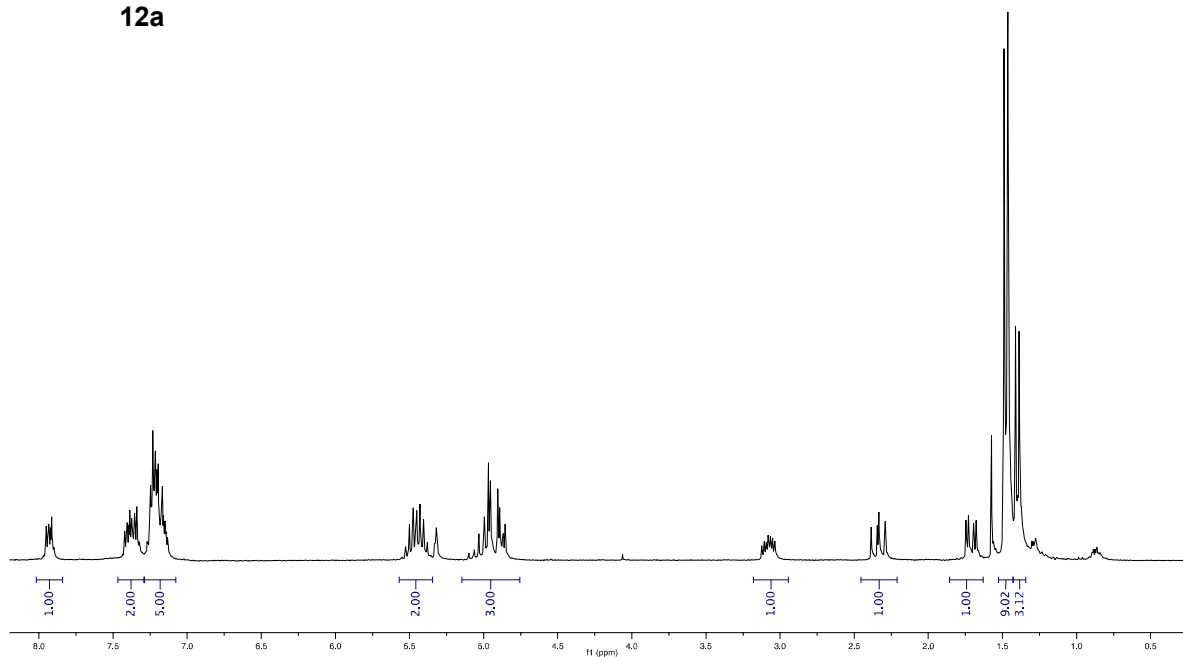
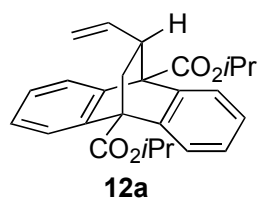
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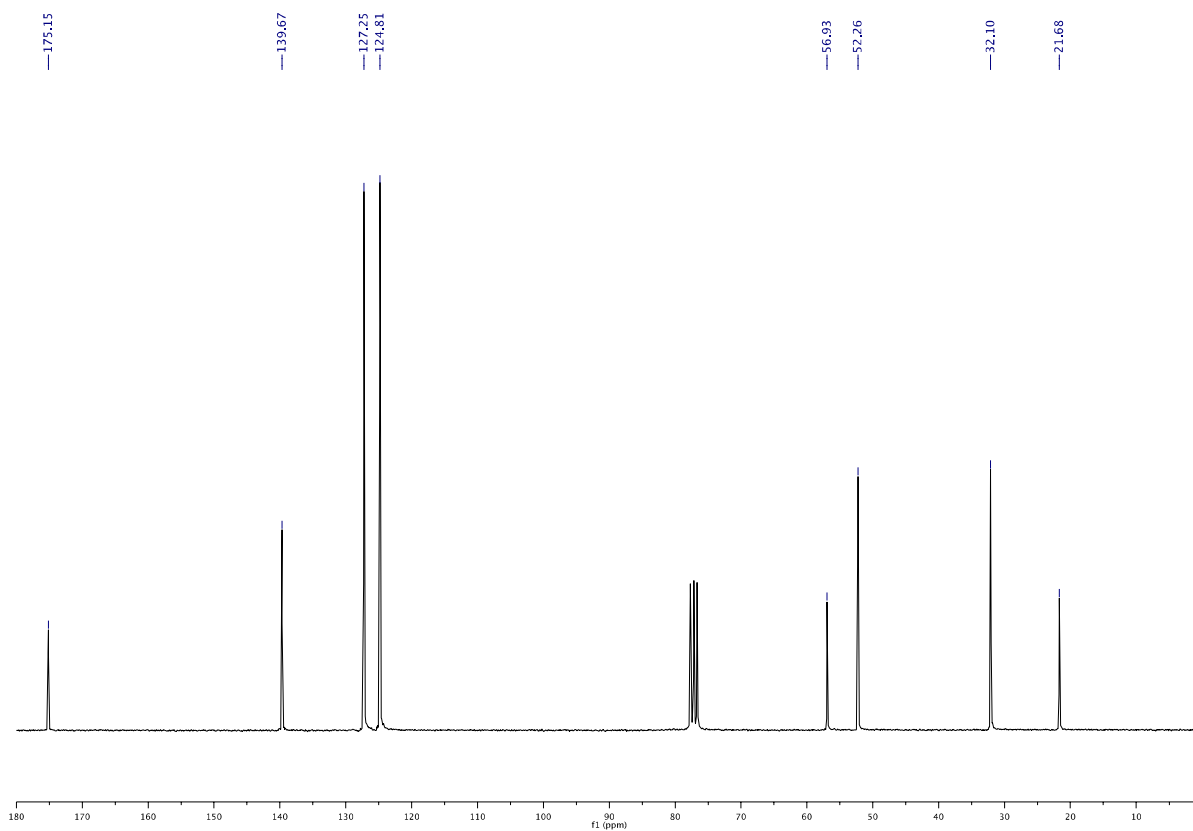
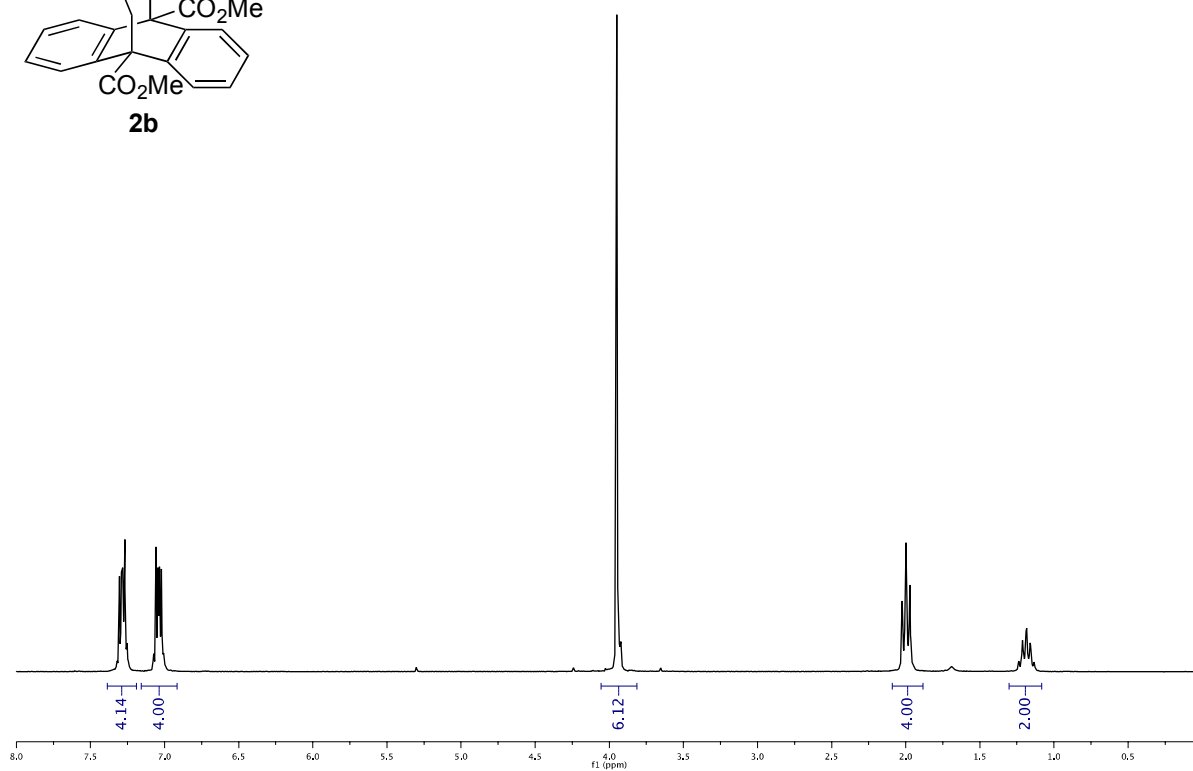
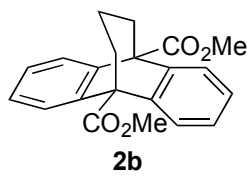


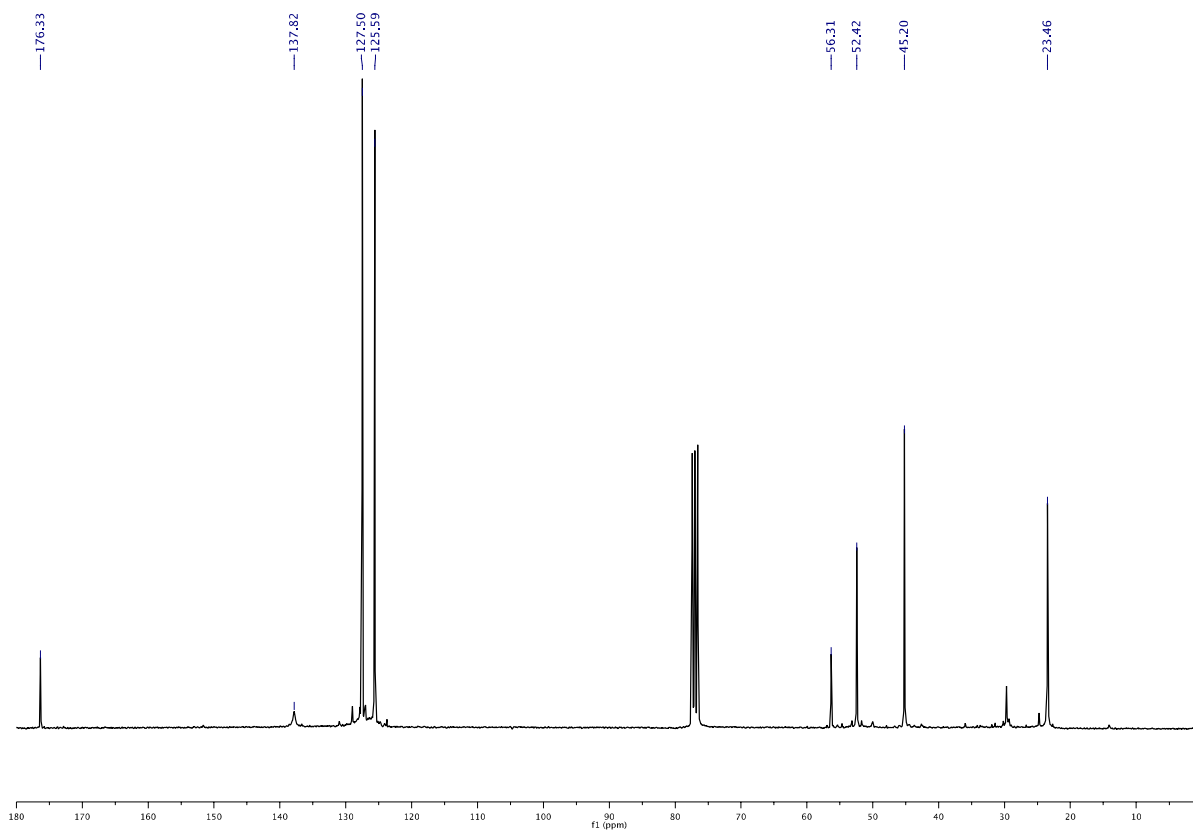
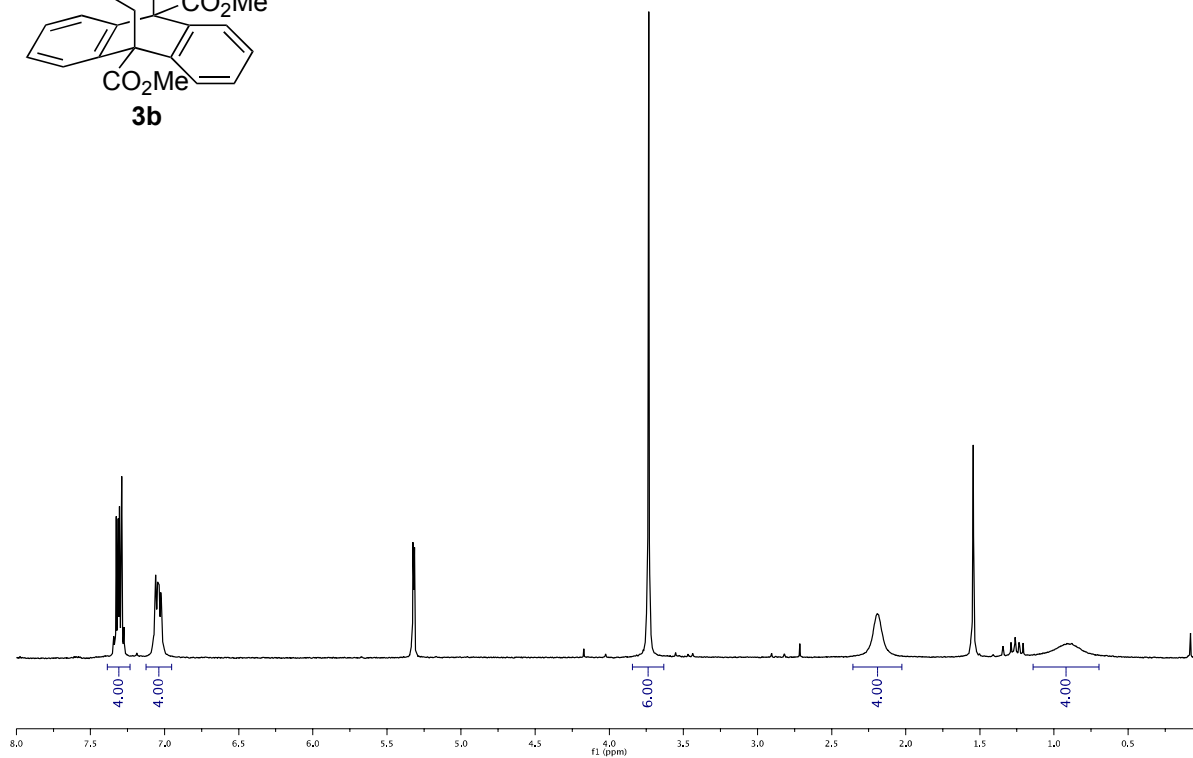
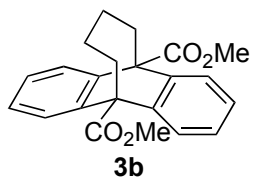


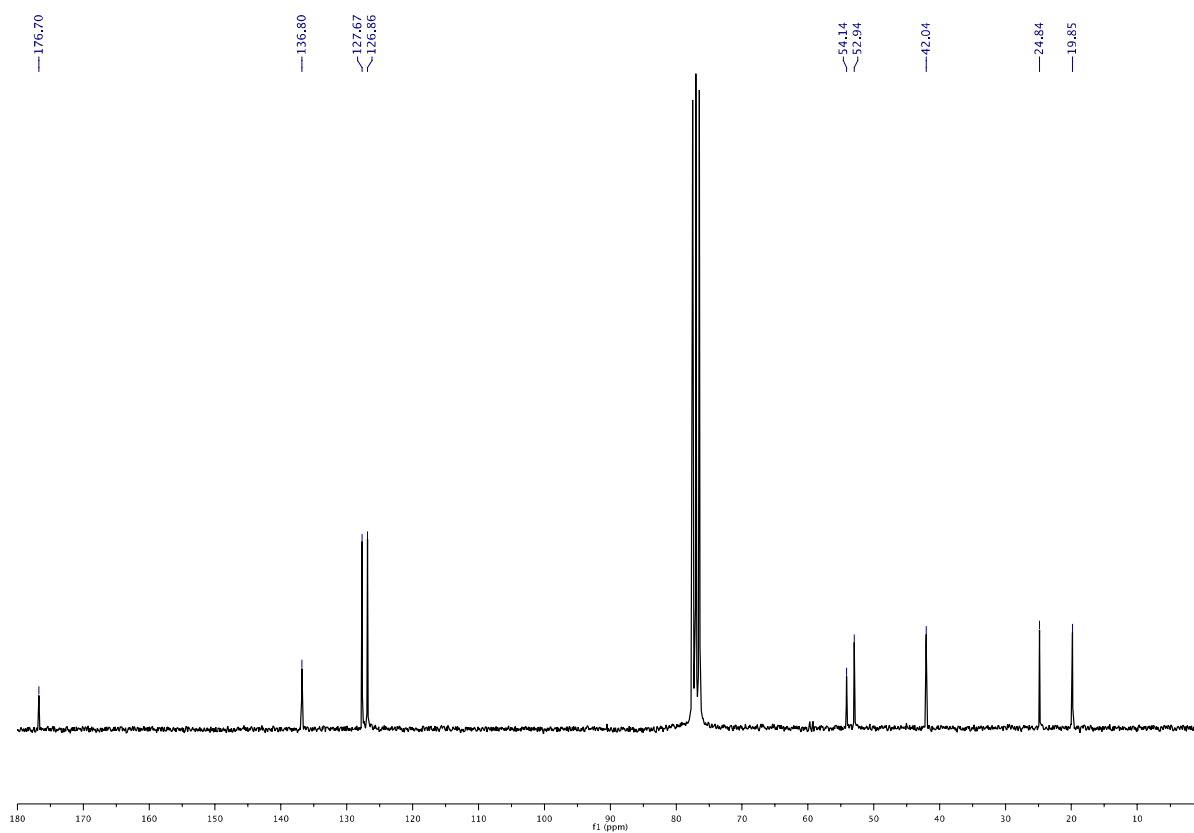
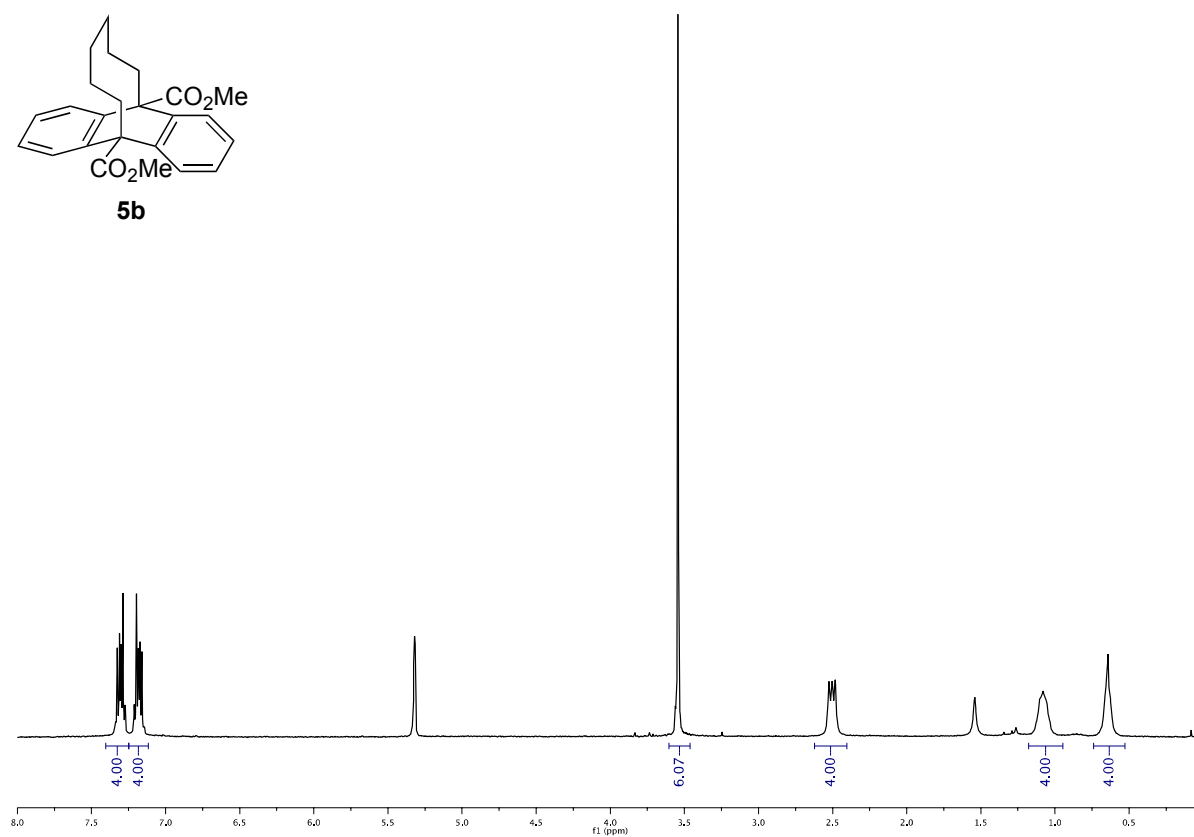
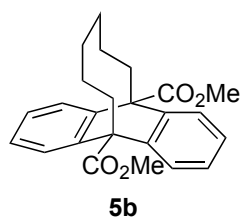
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 — 138.75
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 — 56.80
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 — 21.59

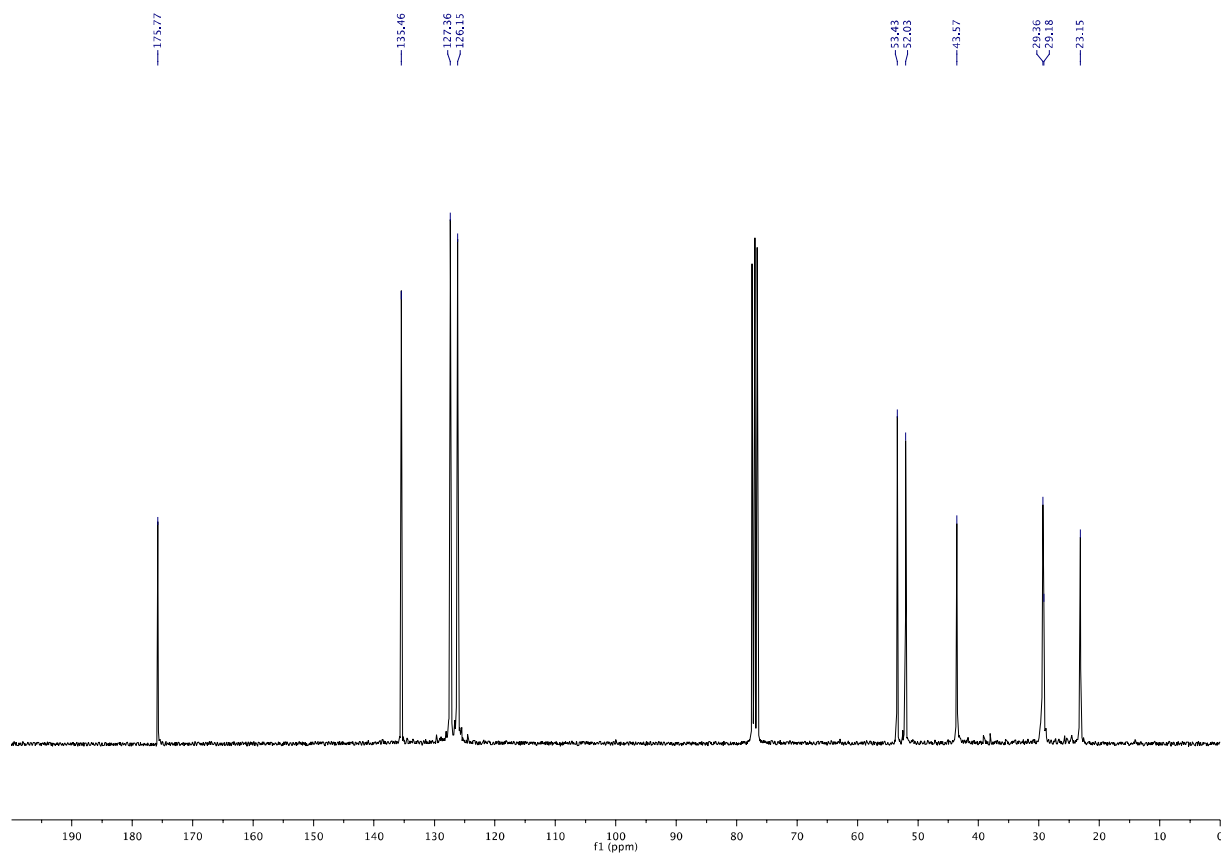
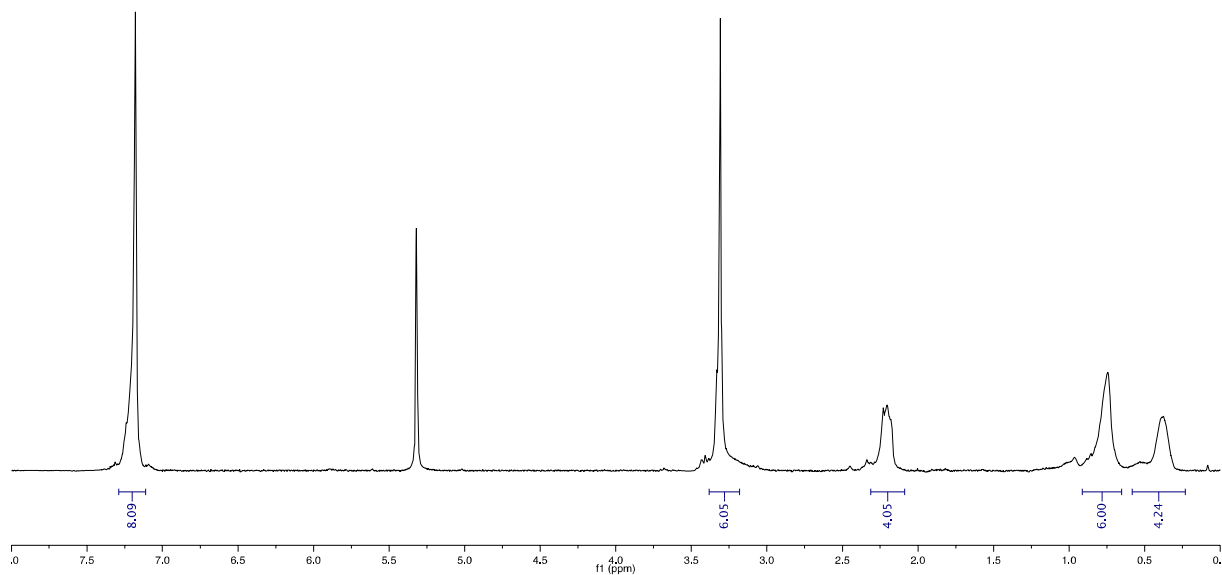
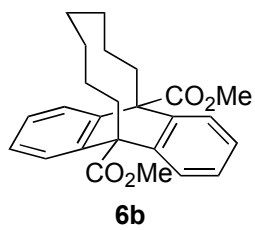


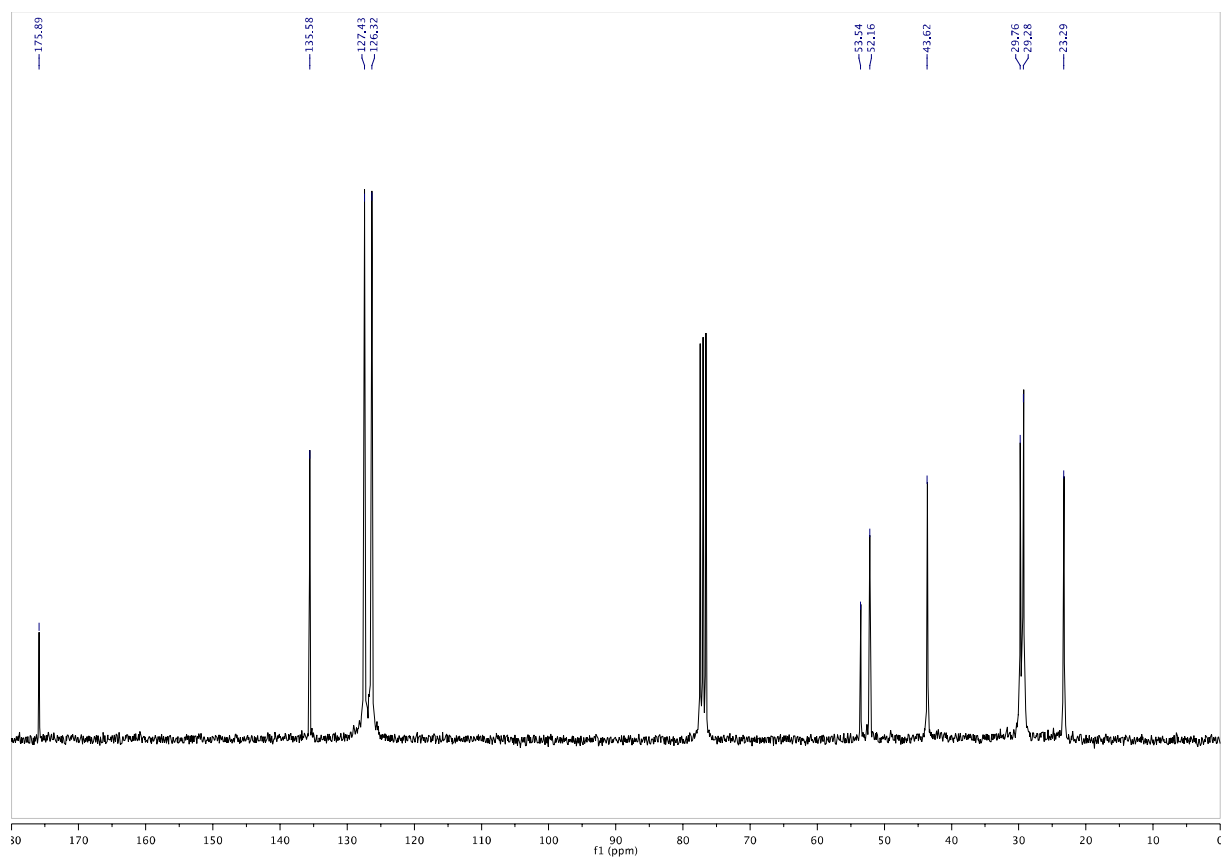
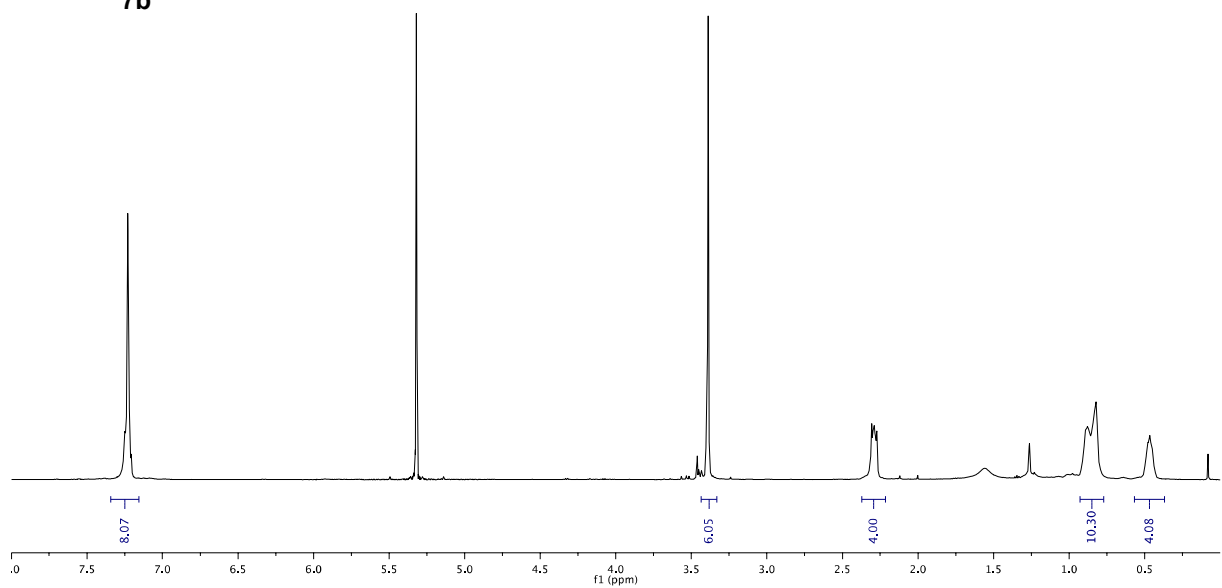
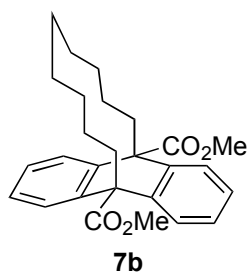


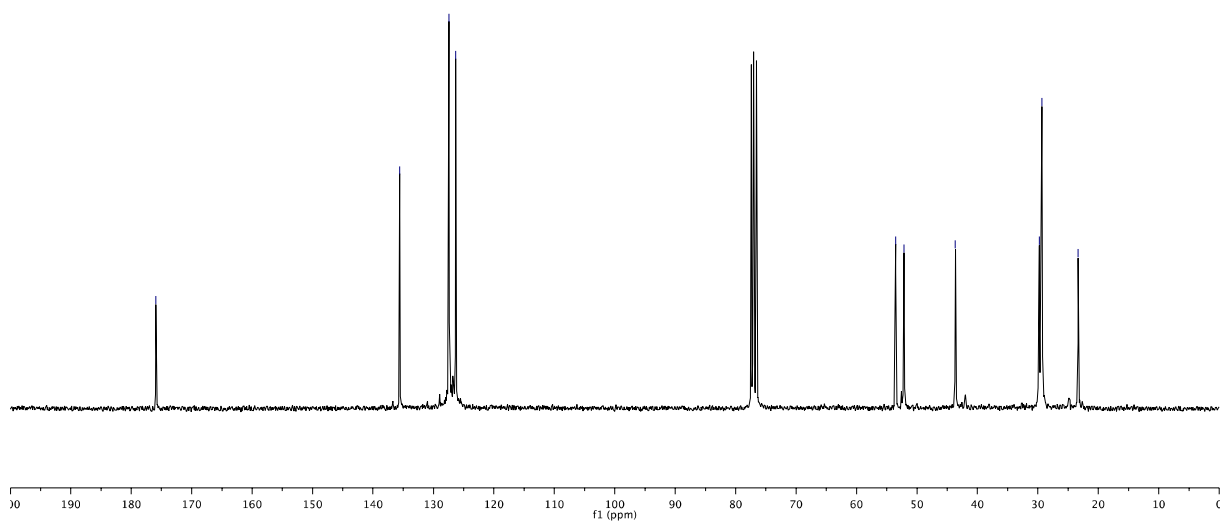
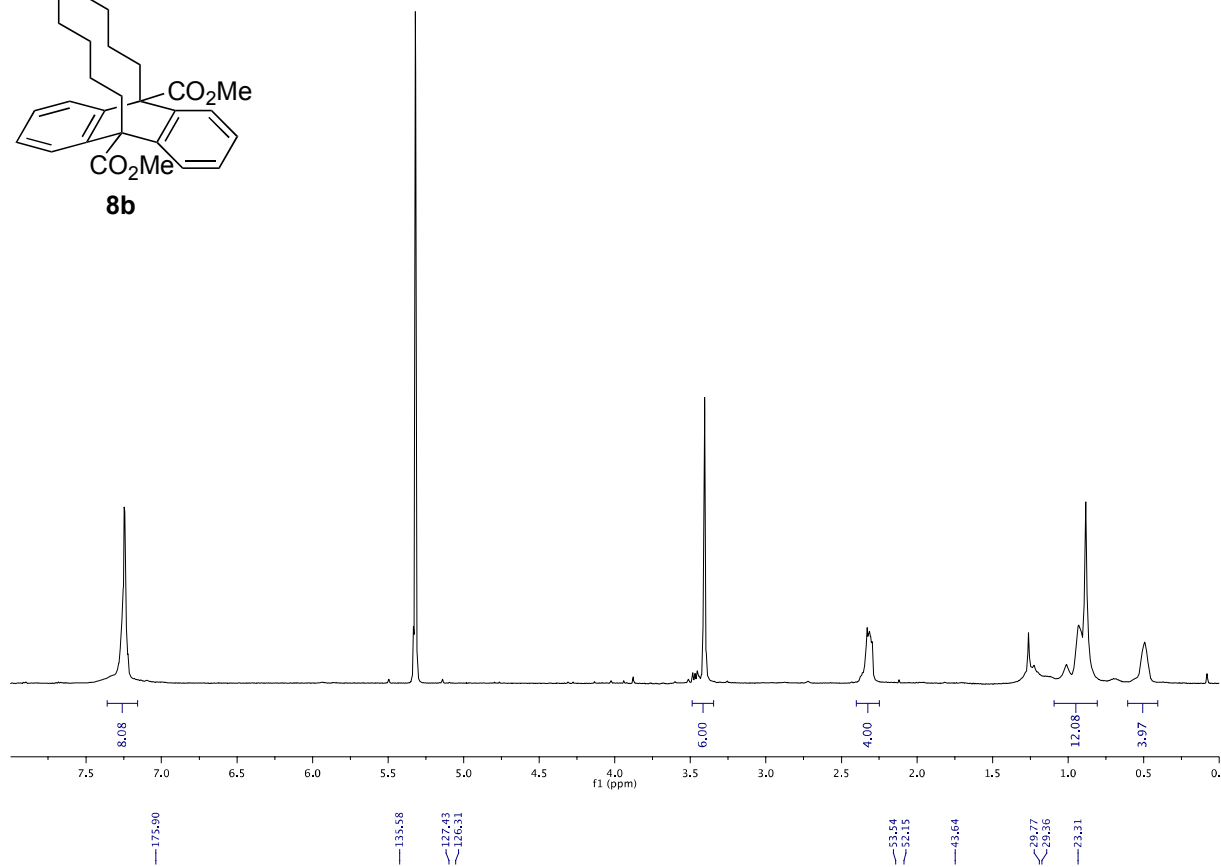
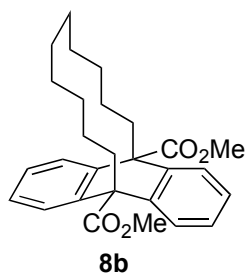


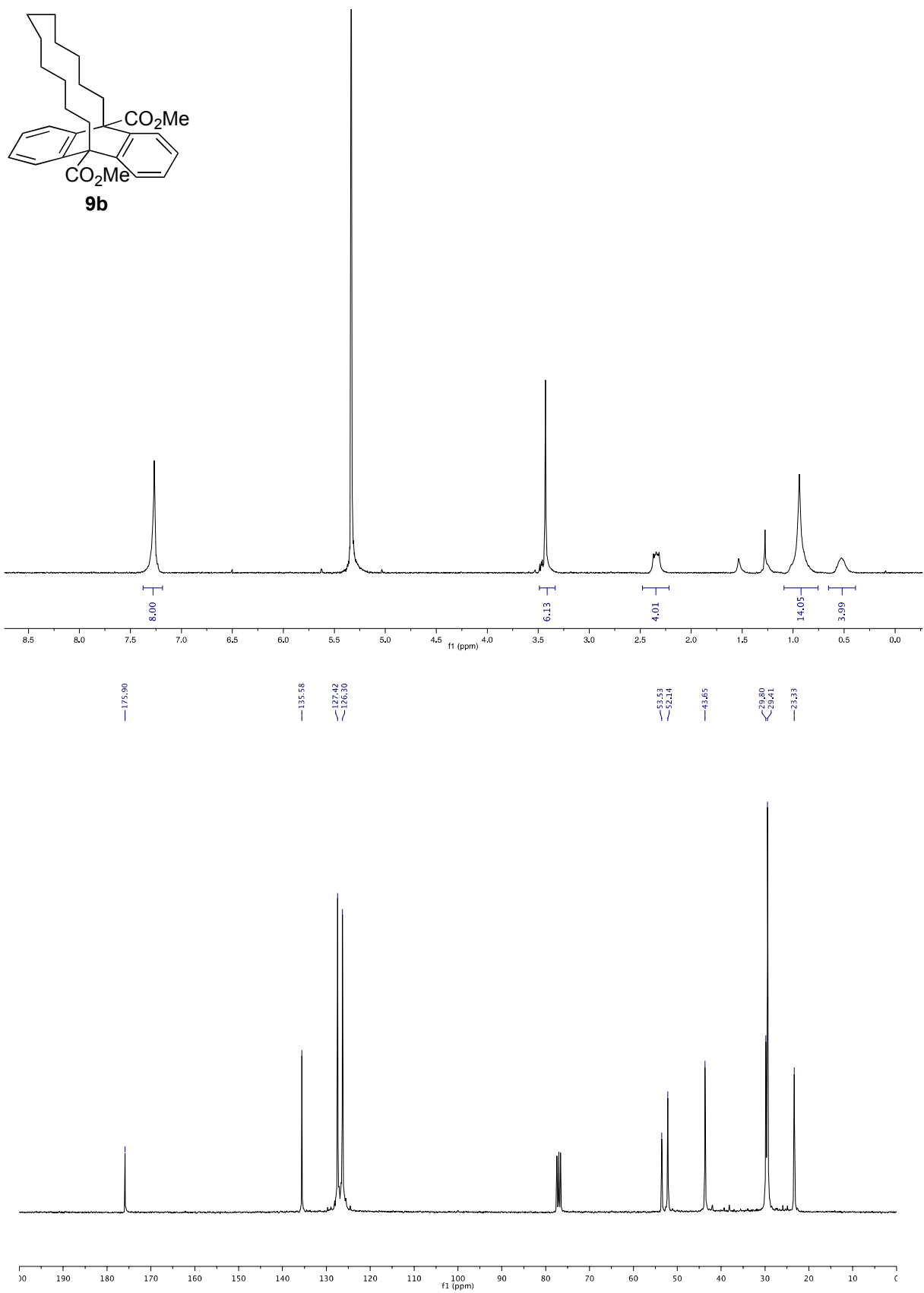


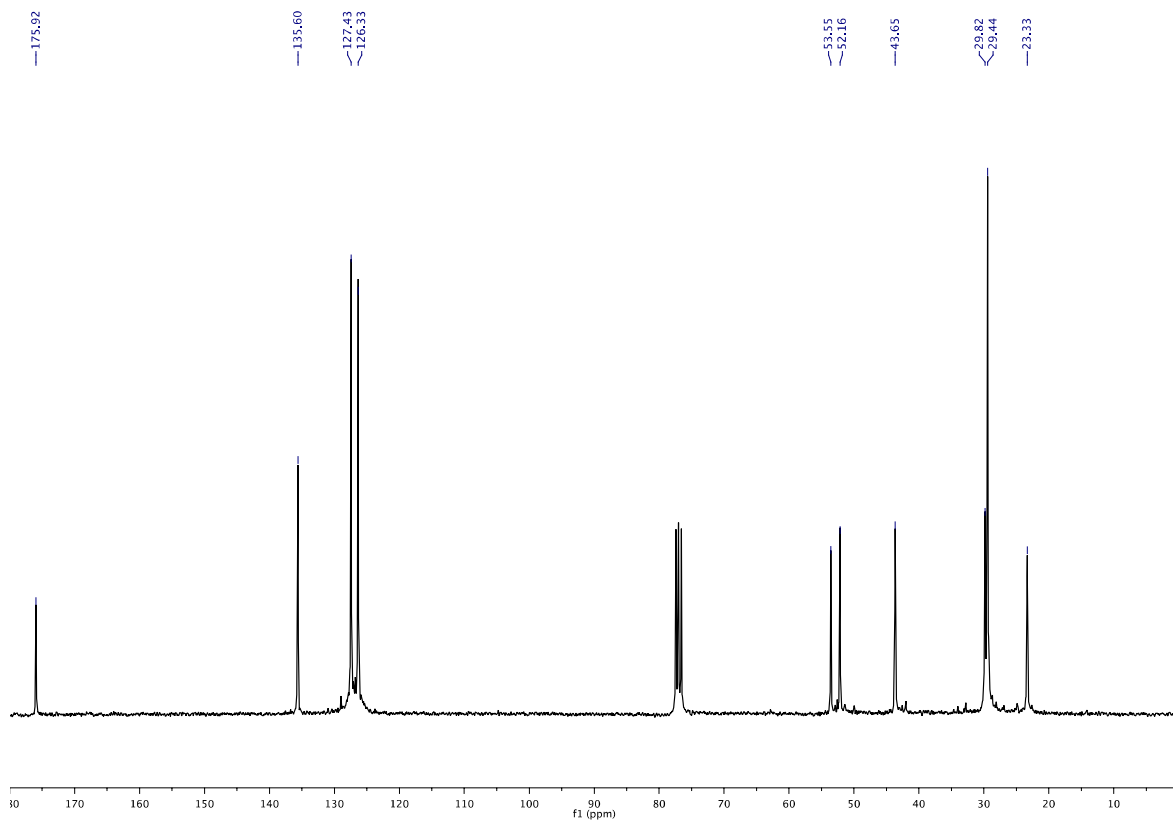
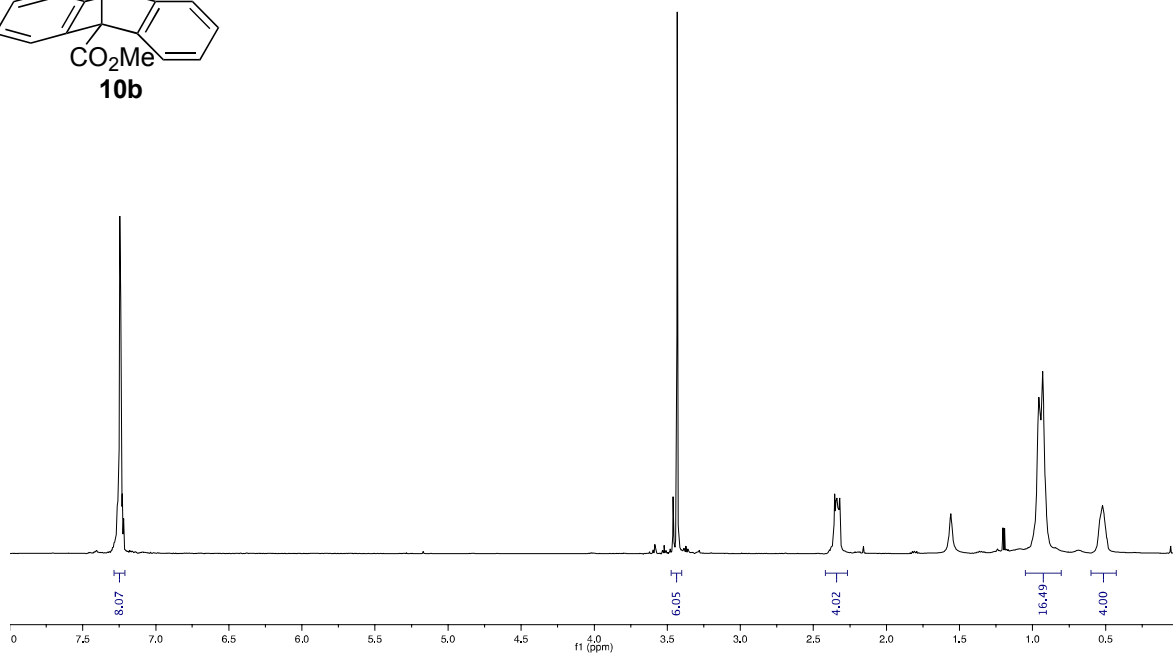
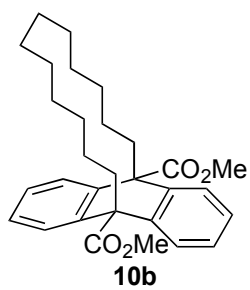


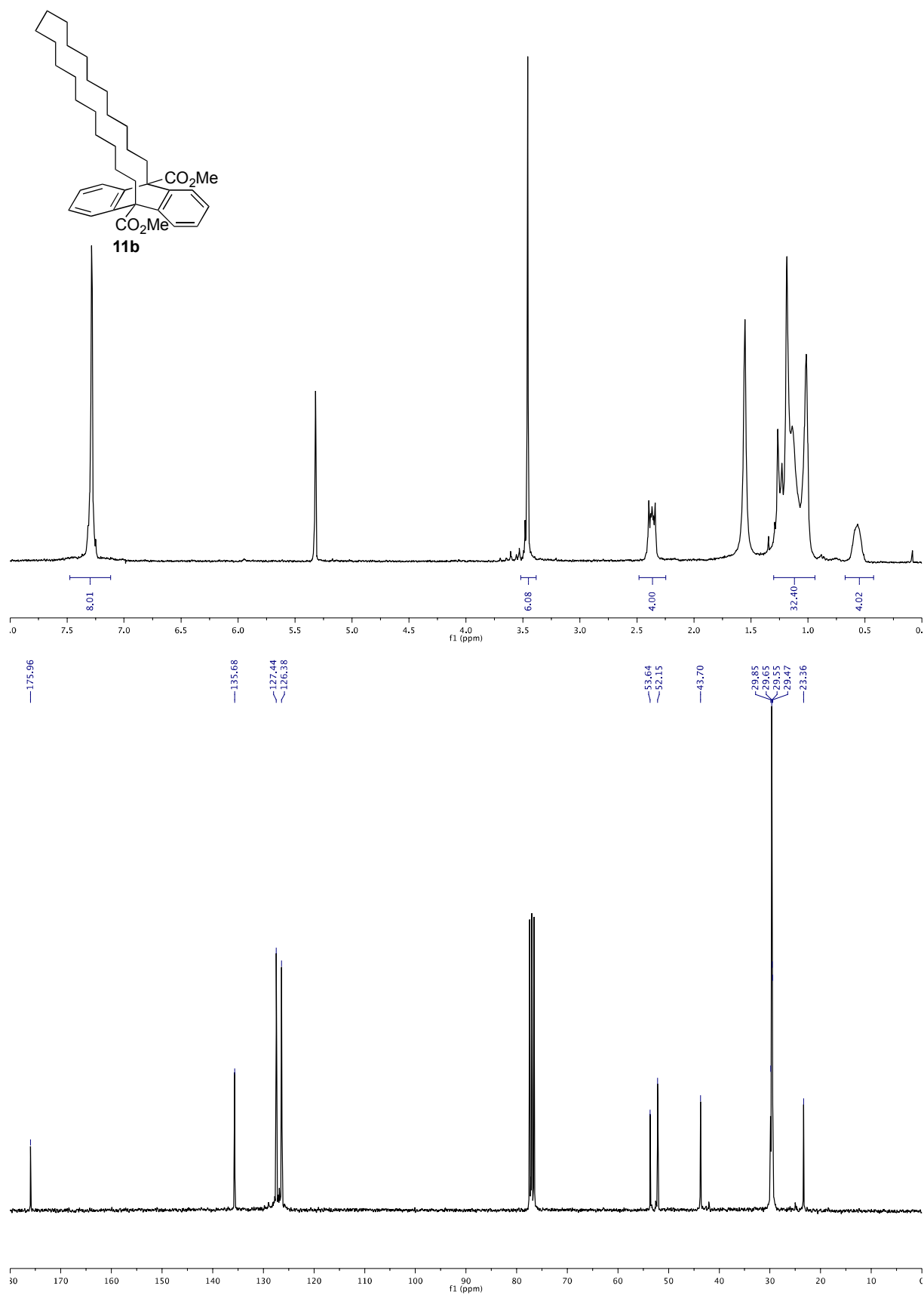


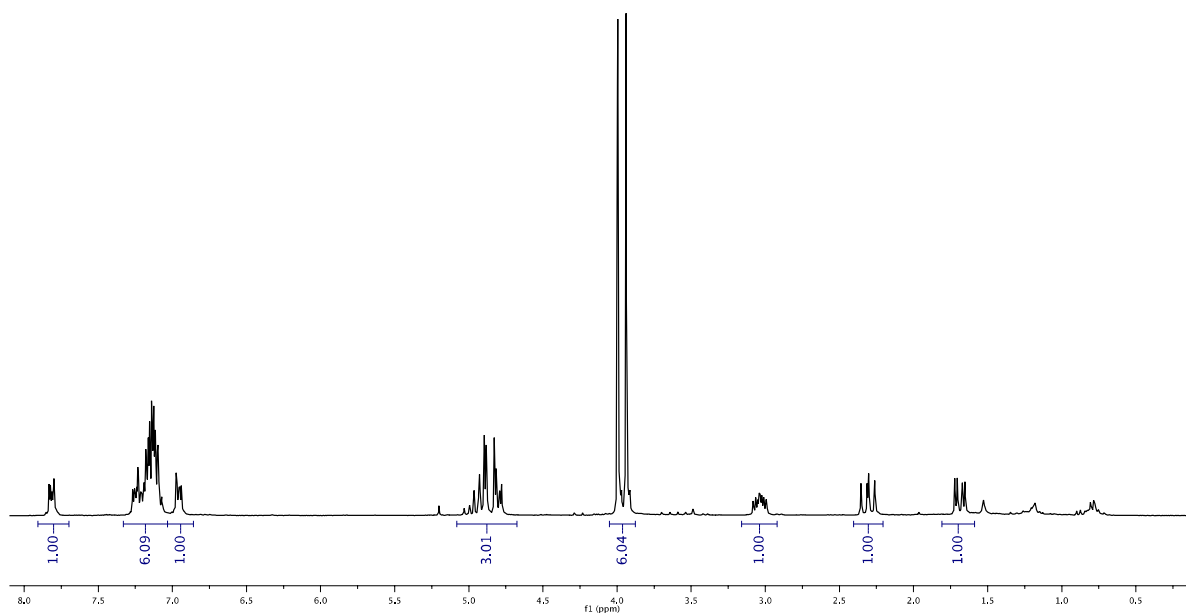
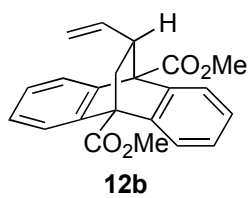








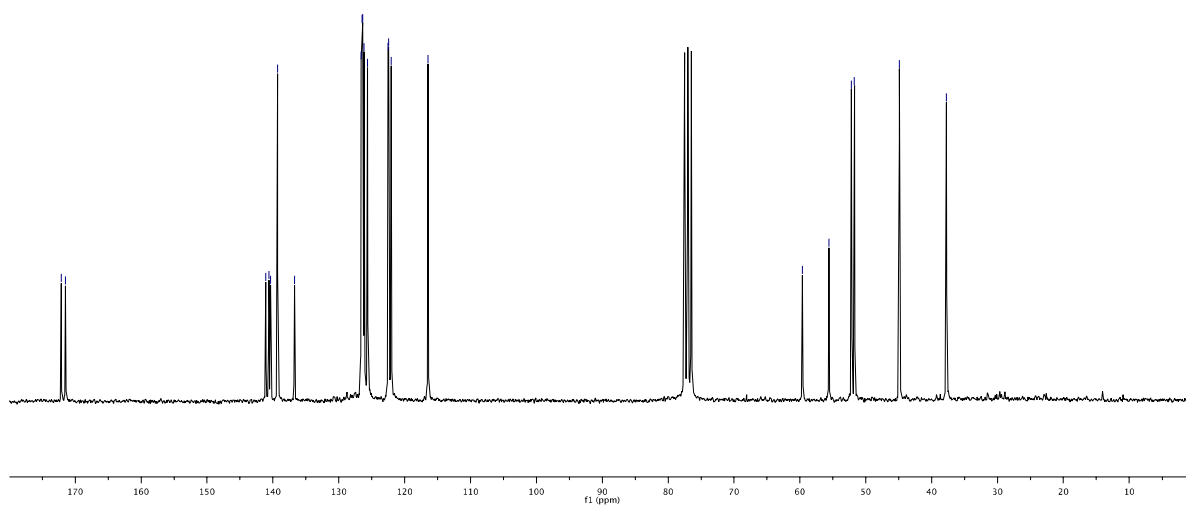


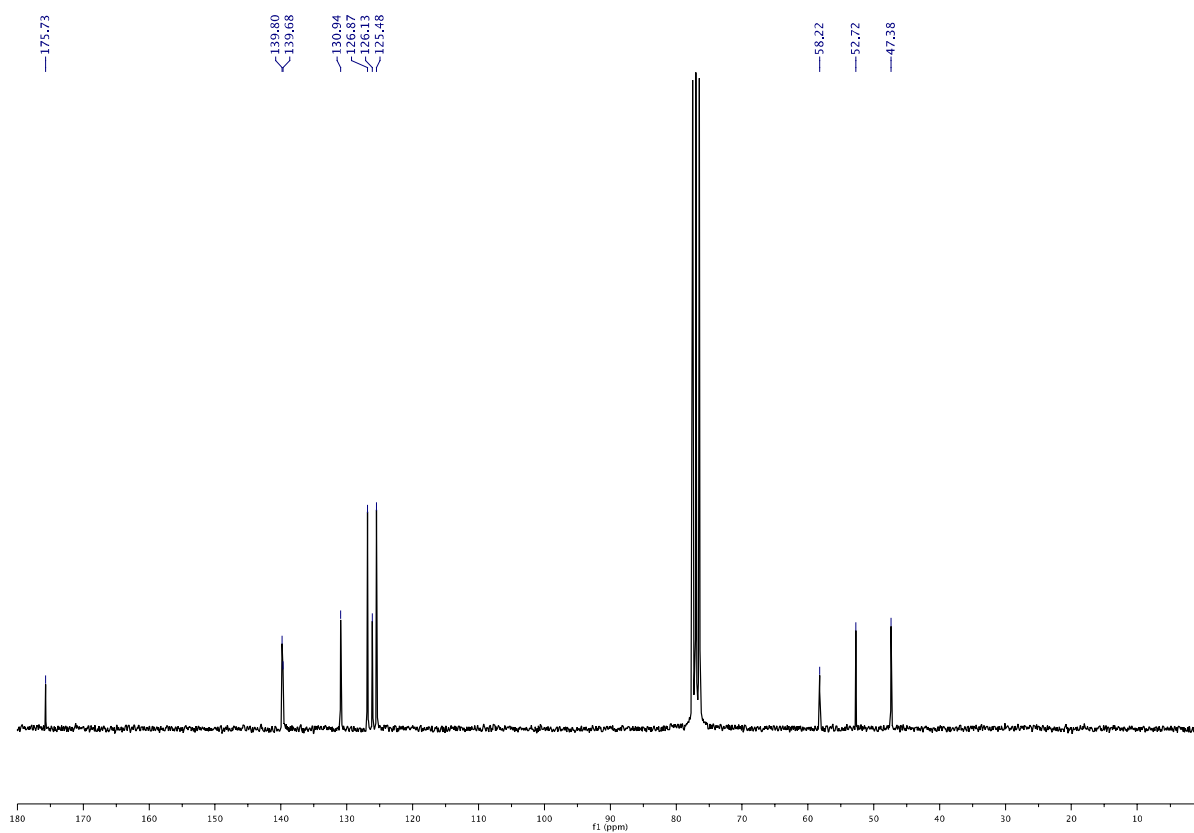
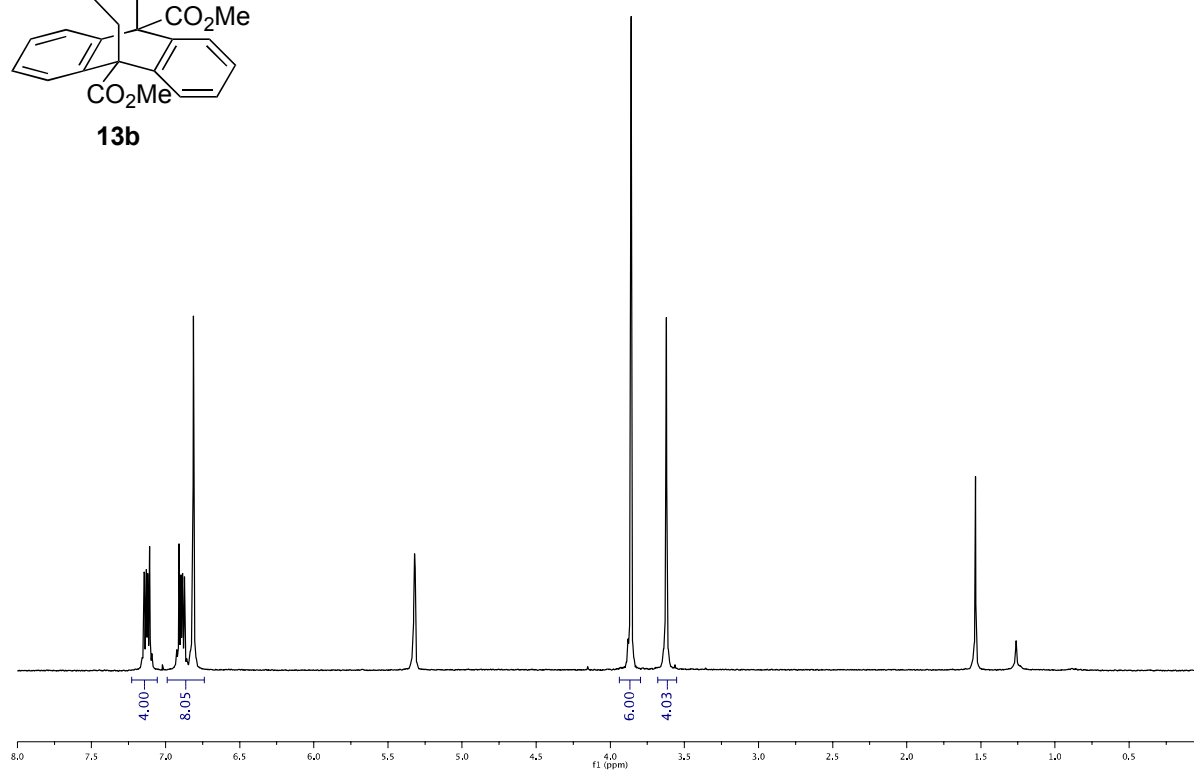
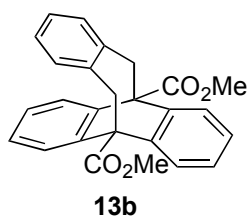


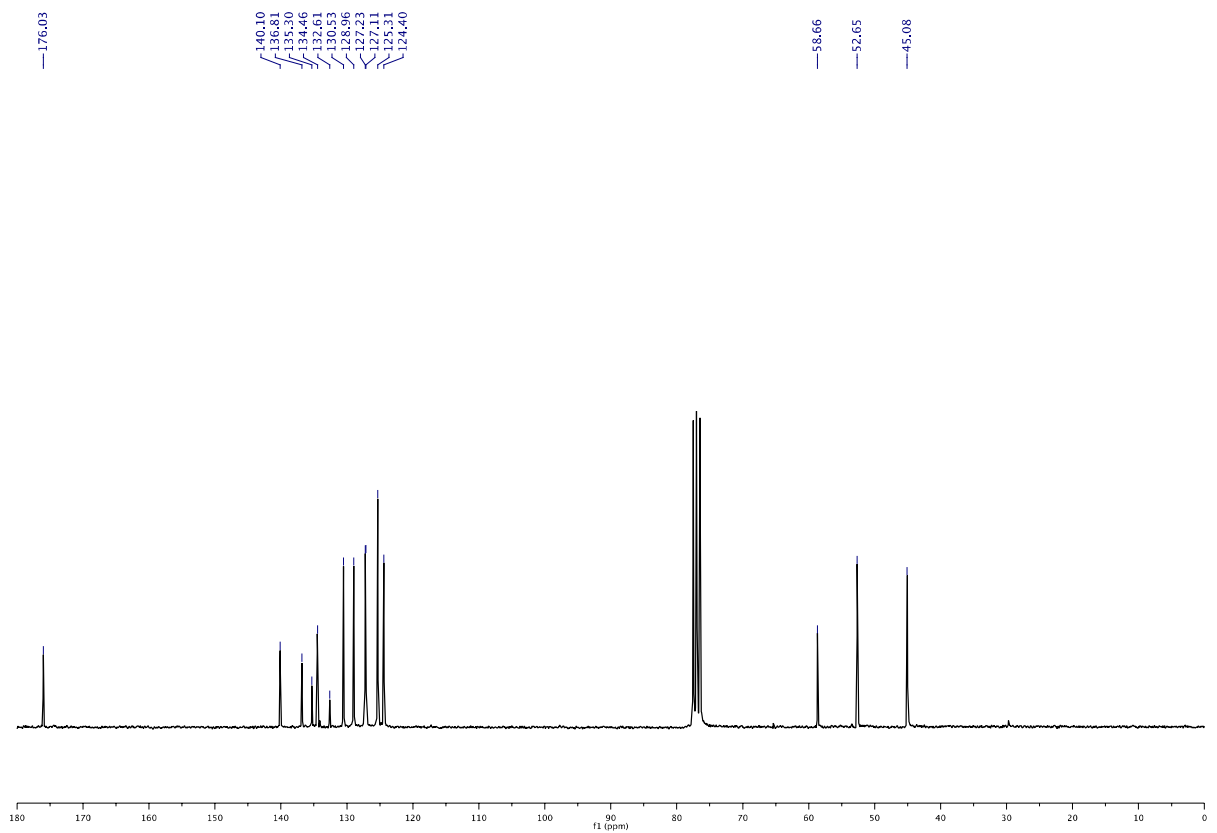
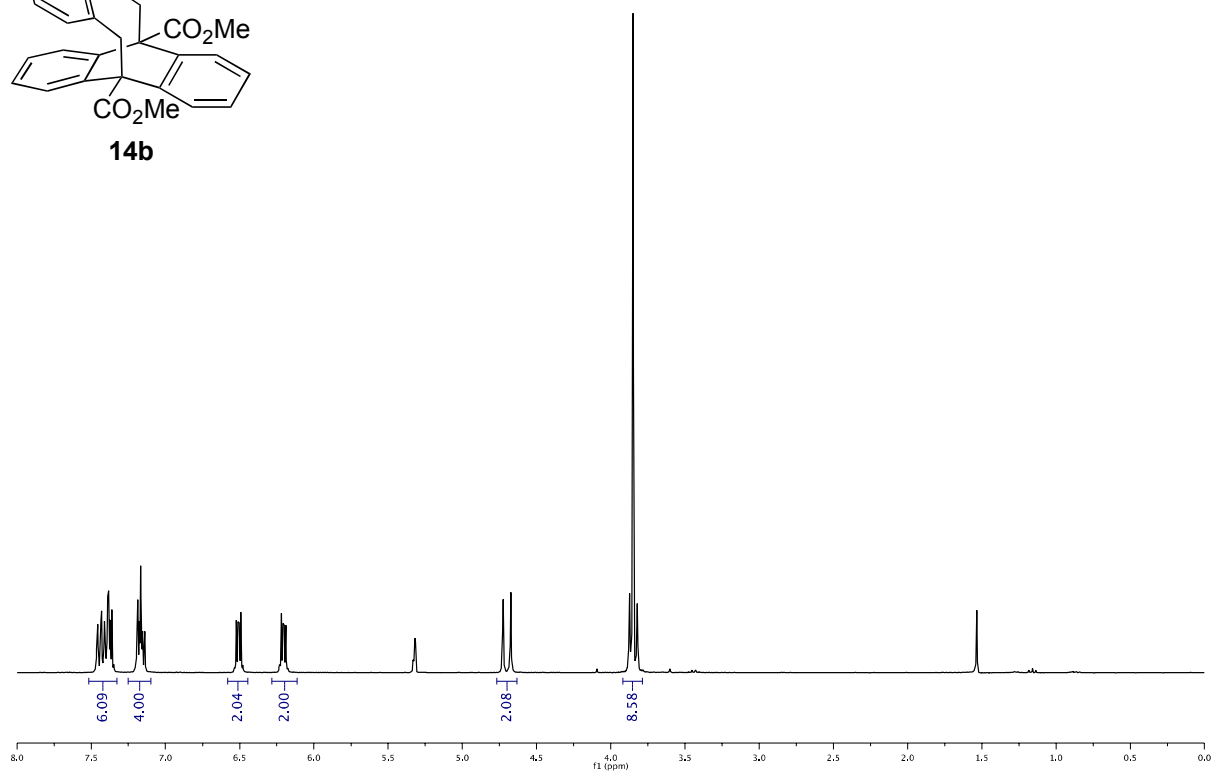
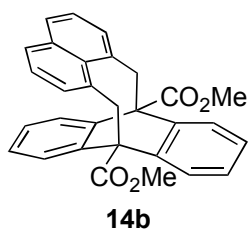
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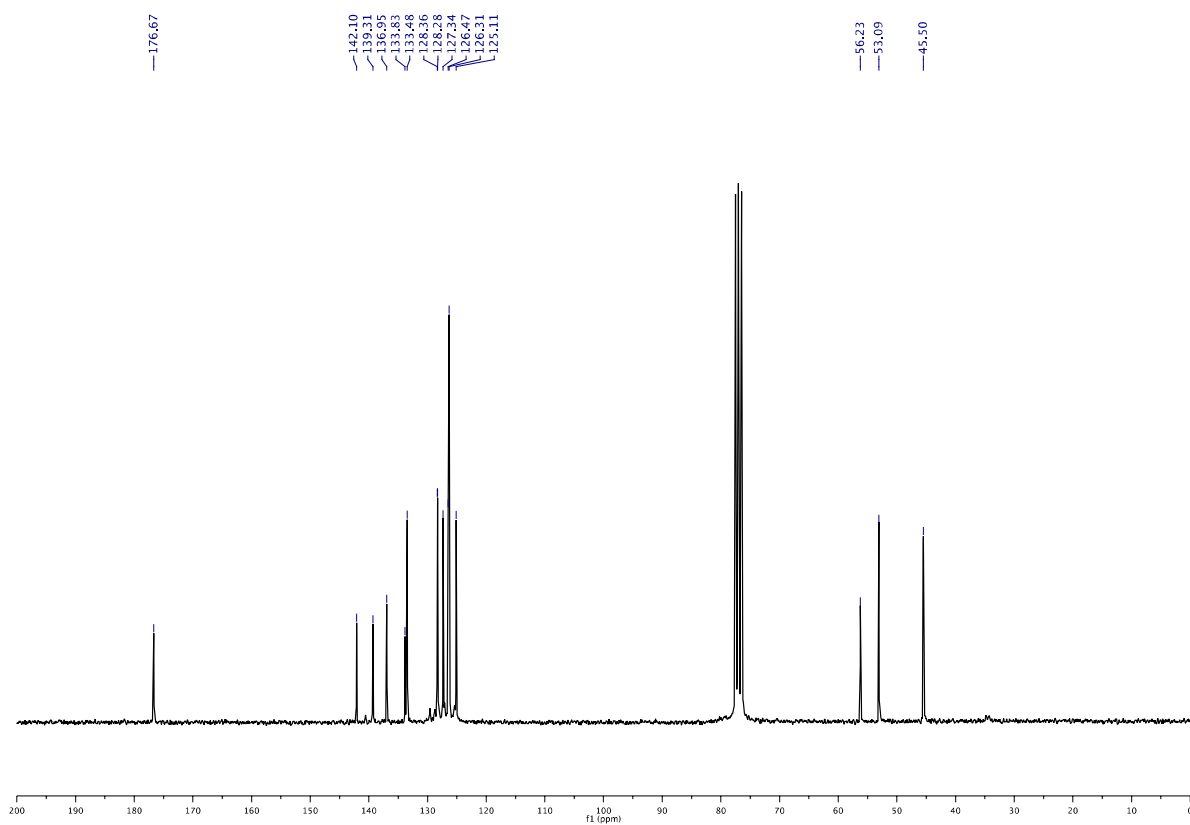
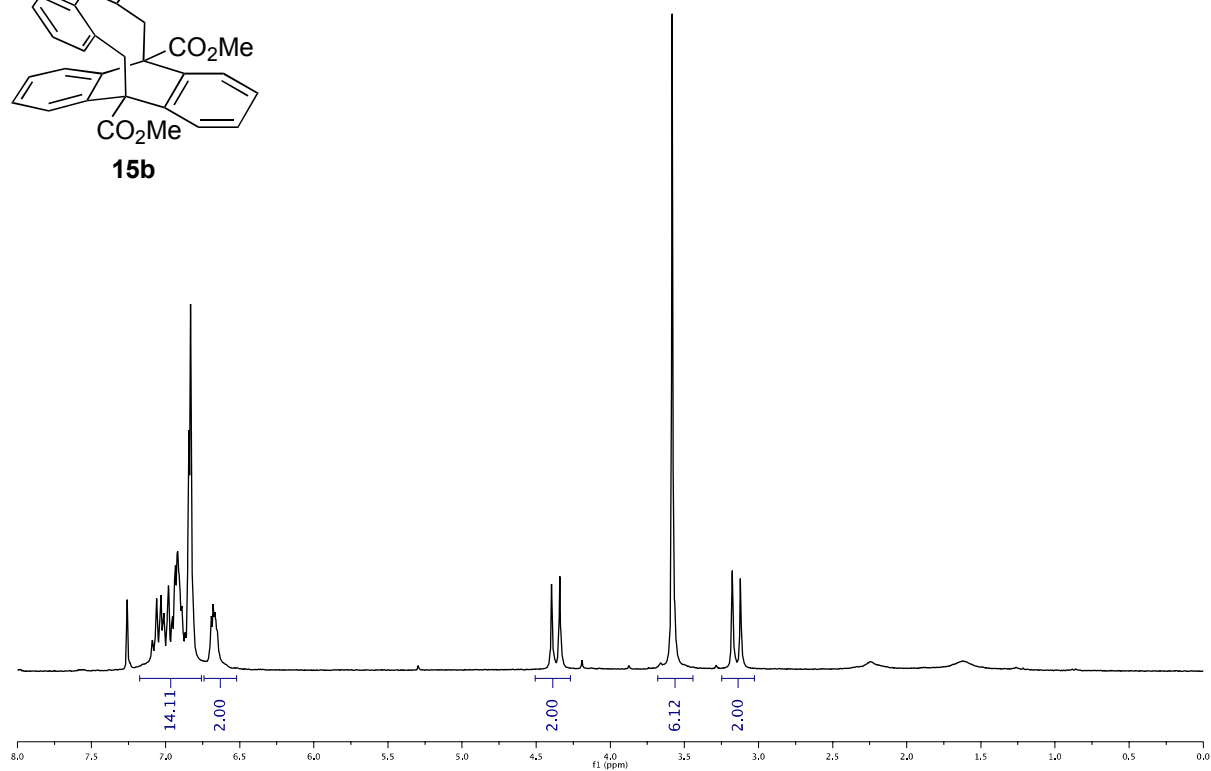
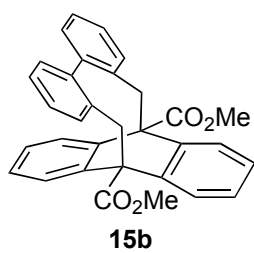
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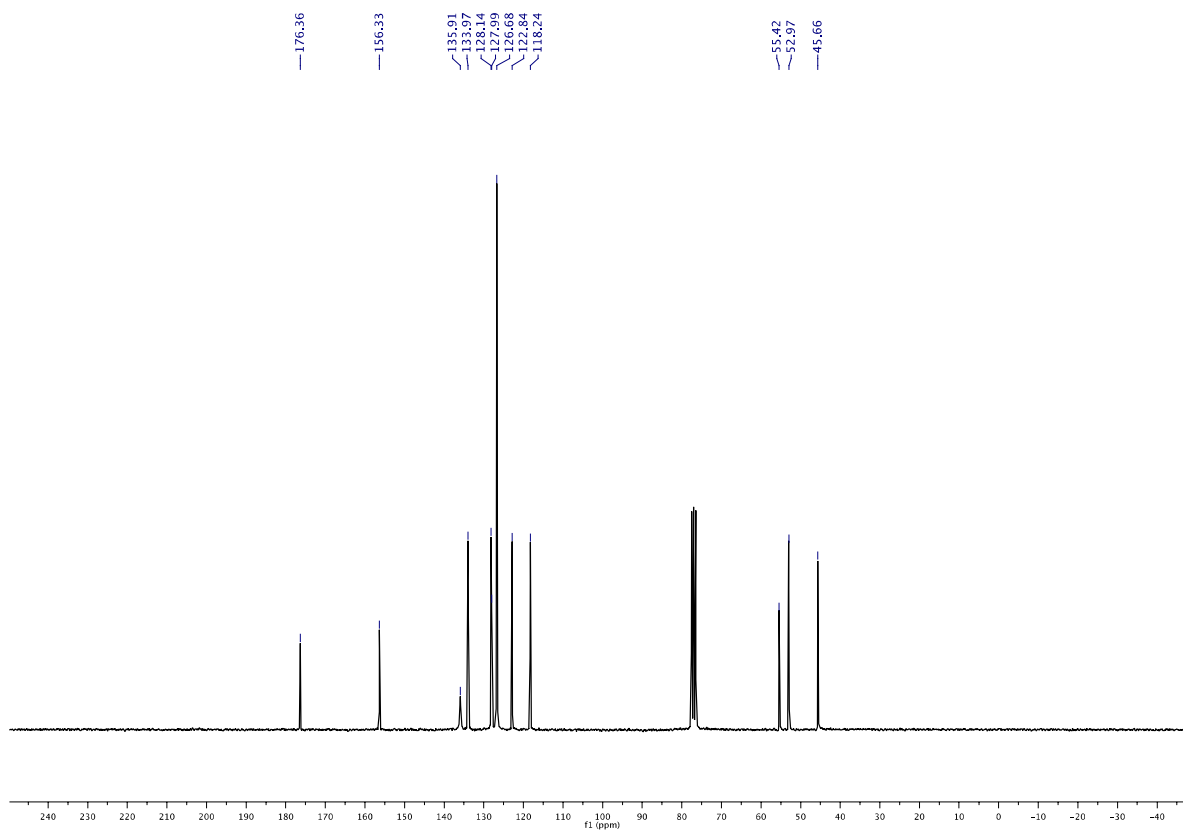
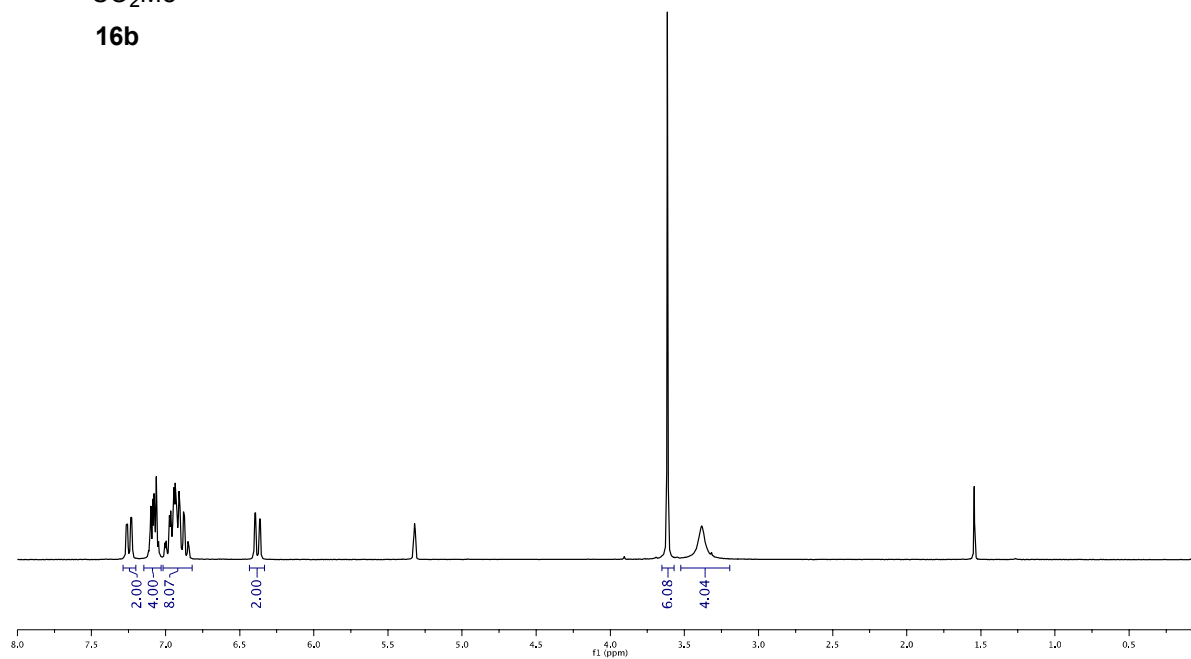
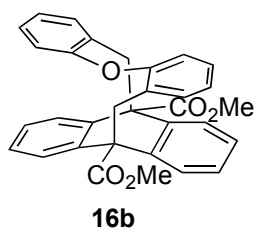
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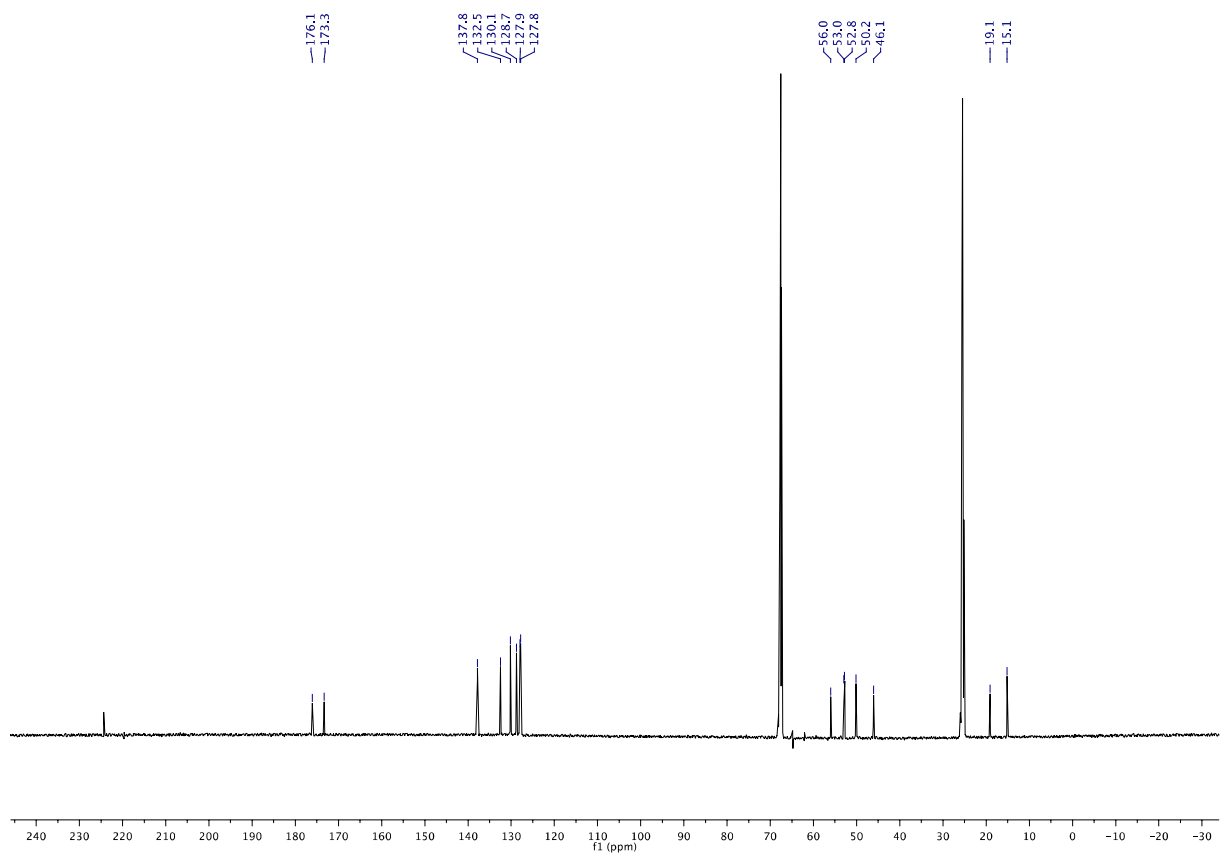
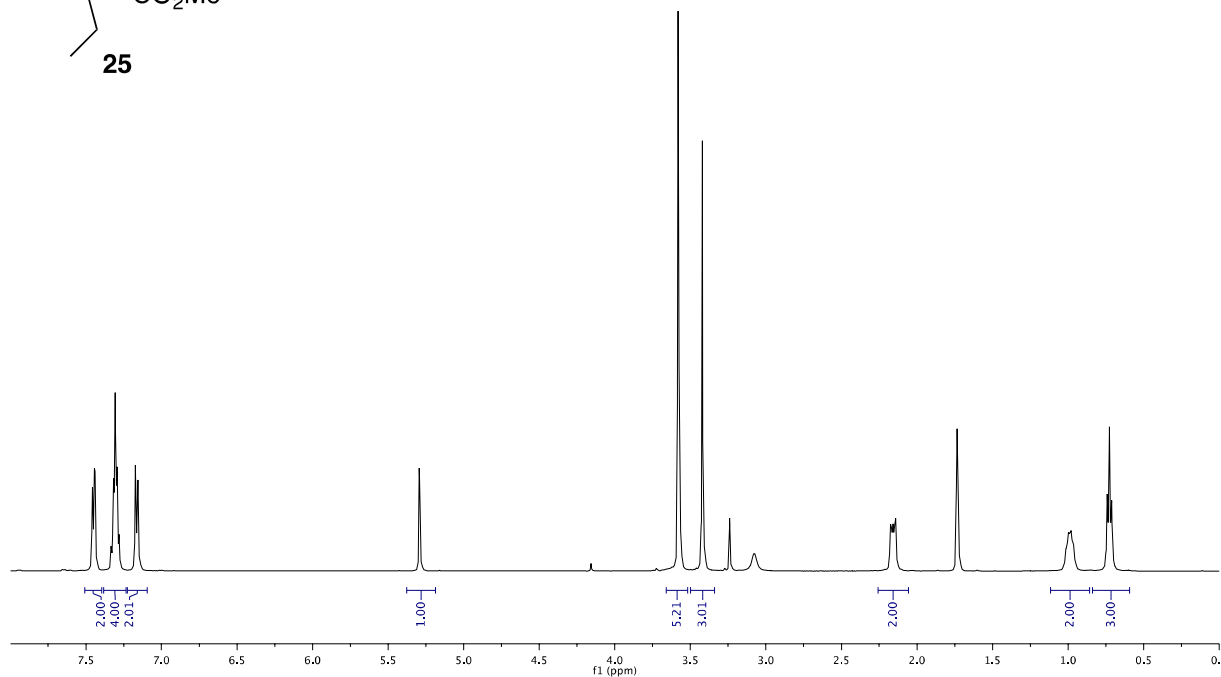
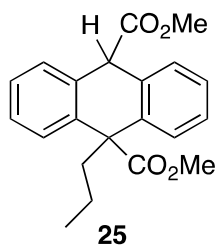


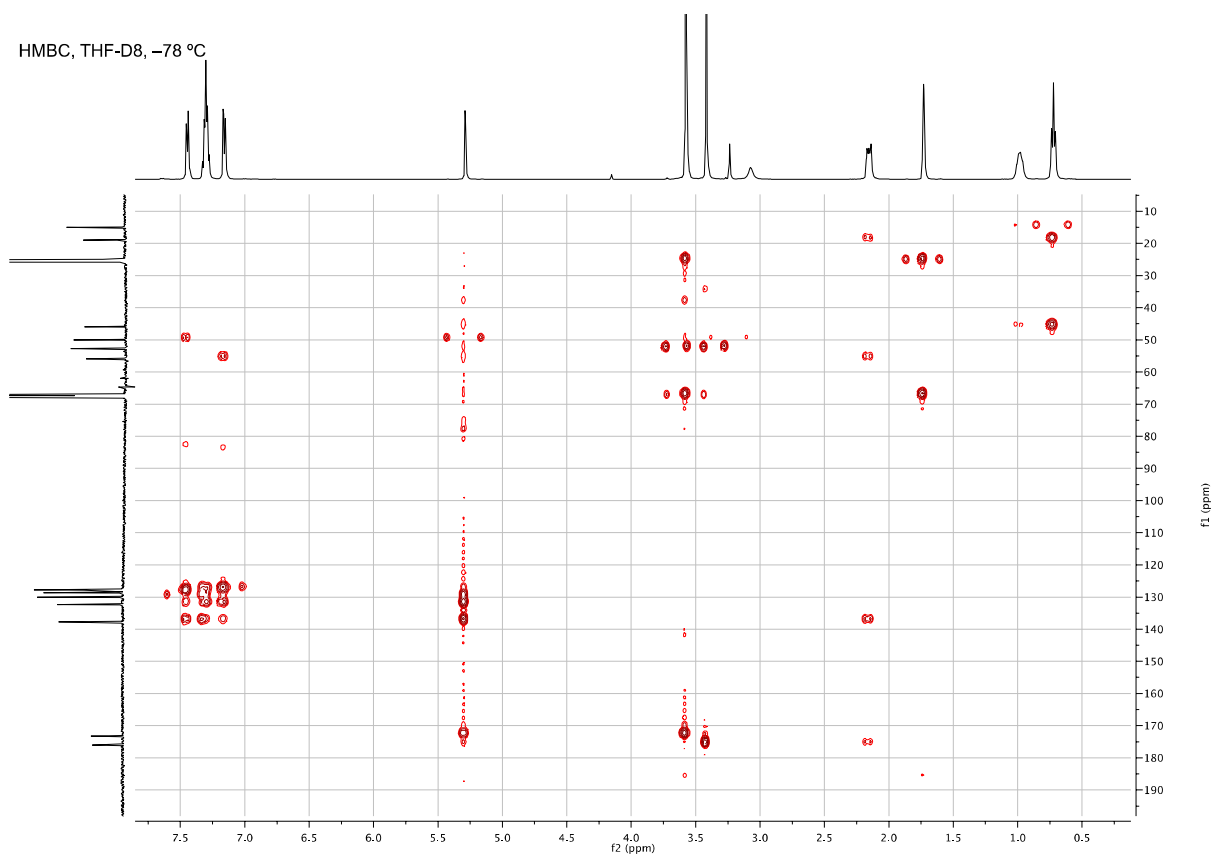
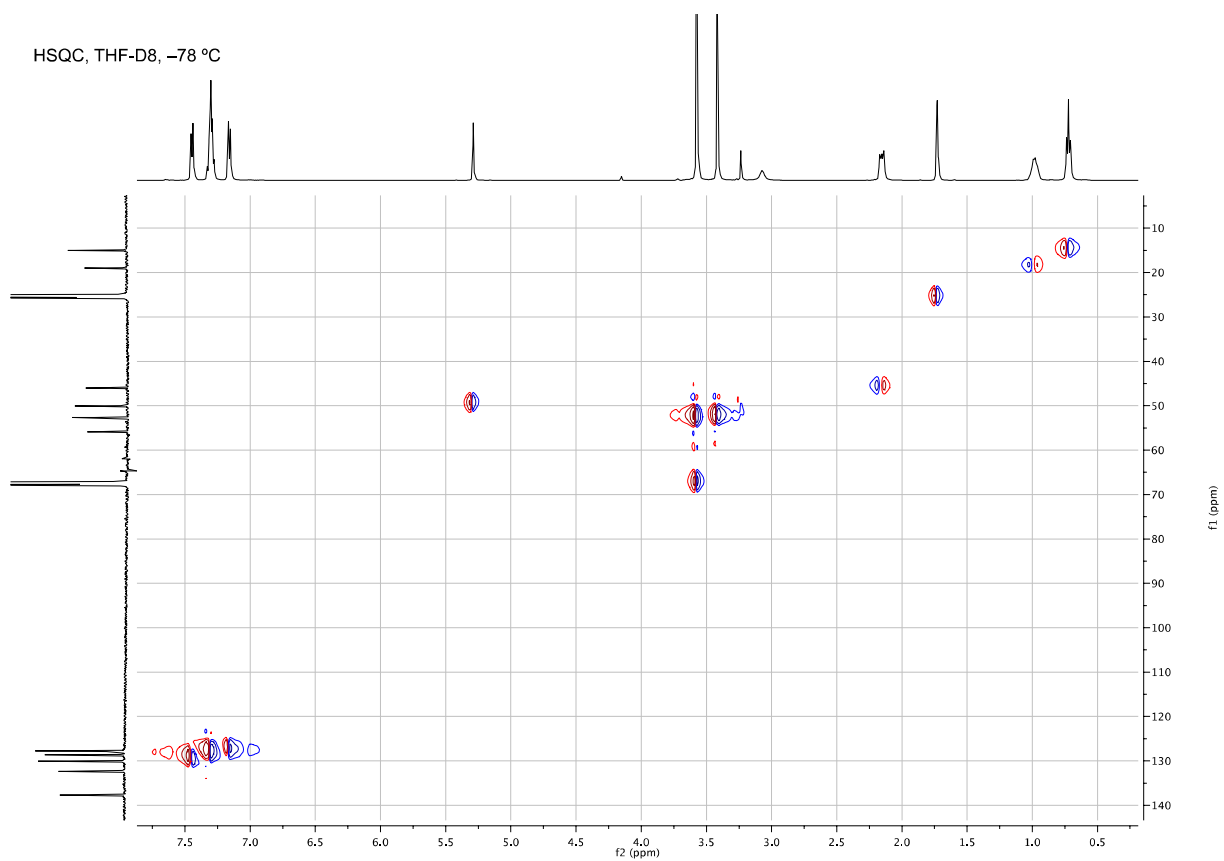


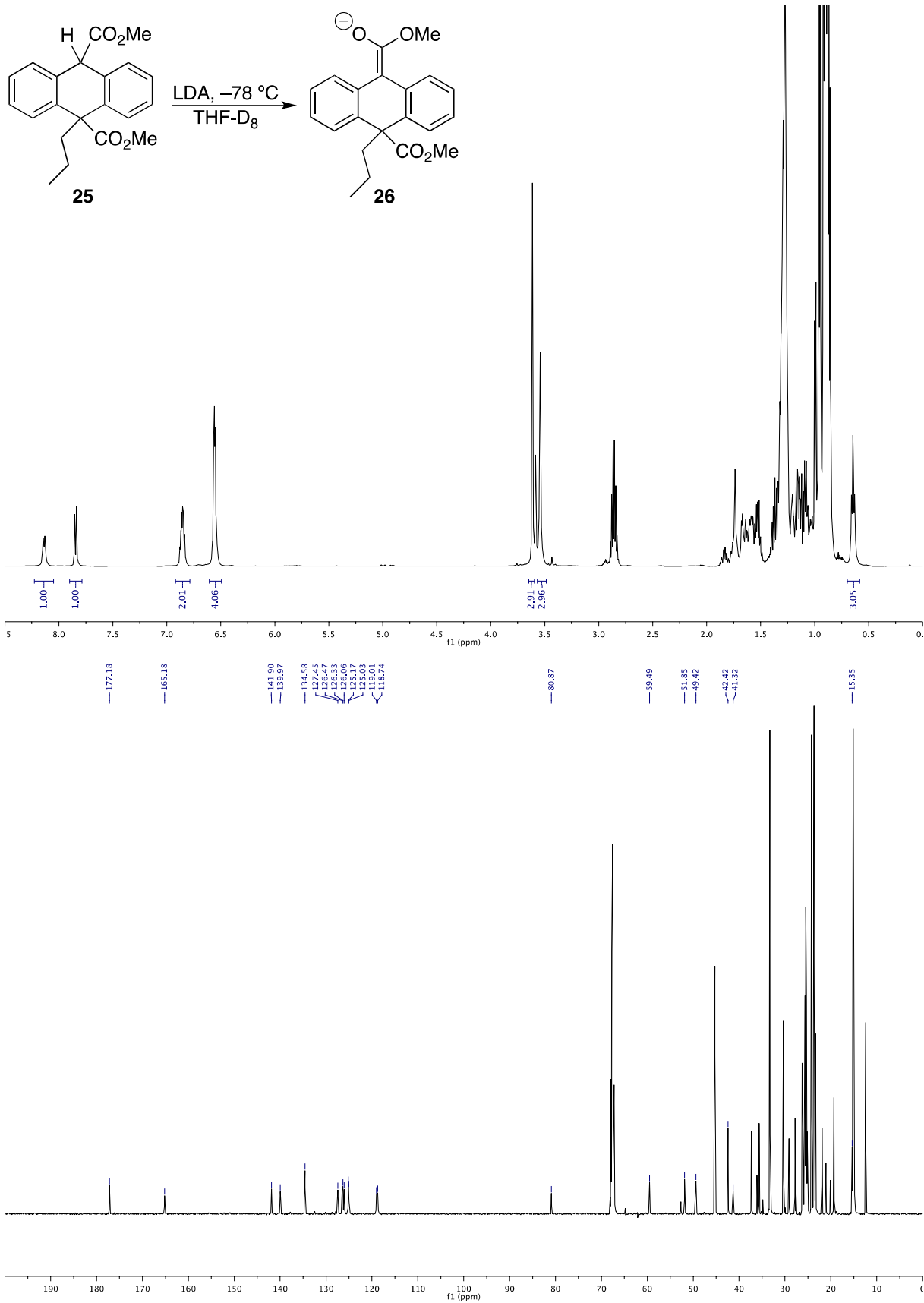




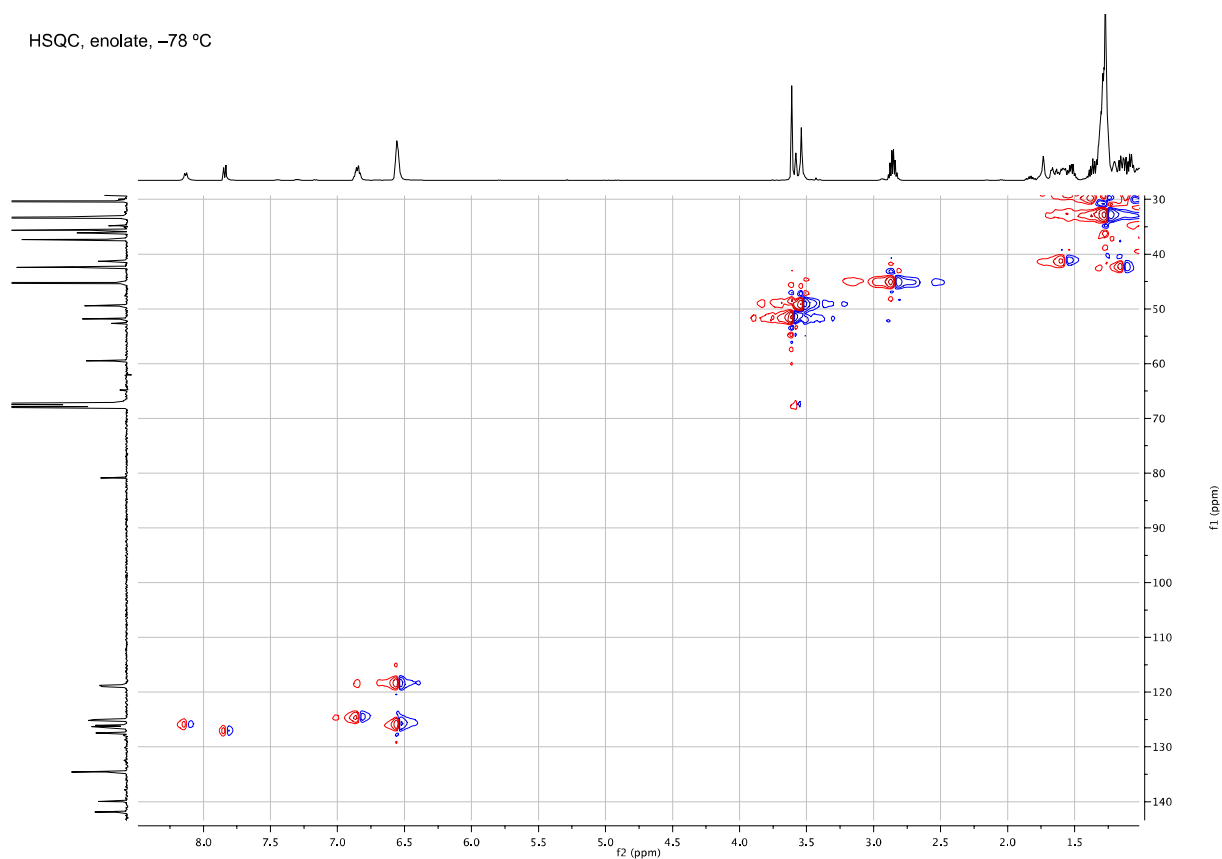




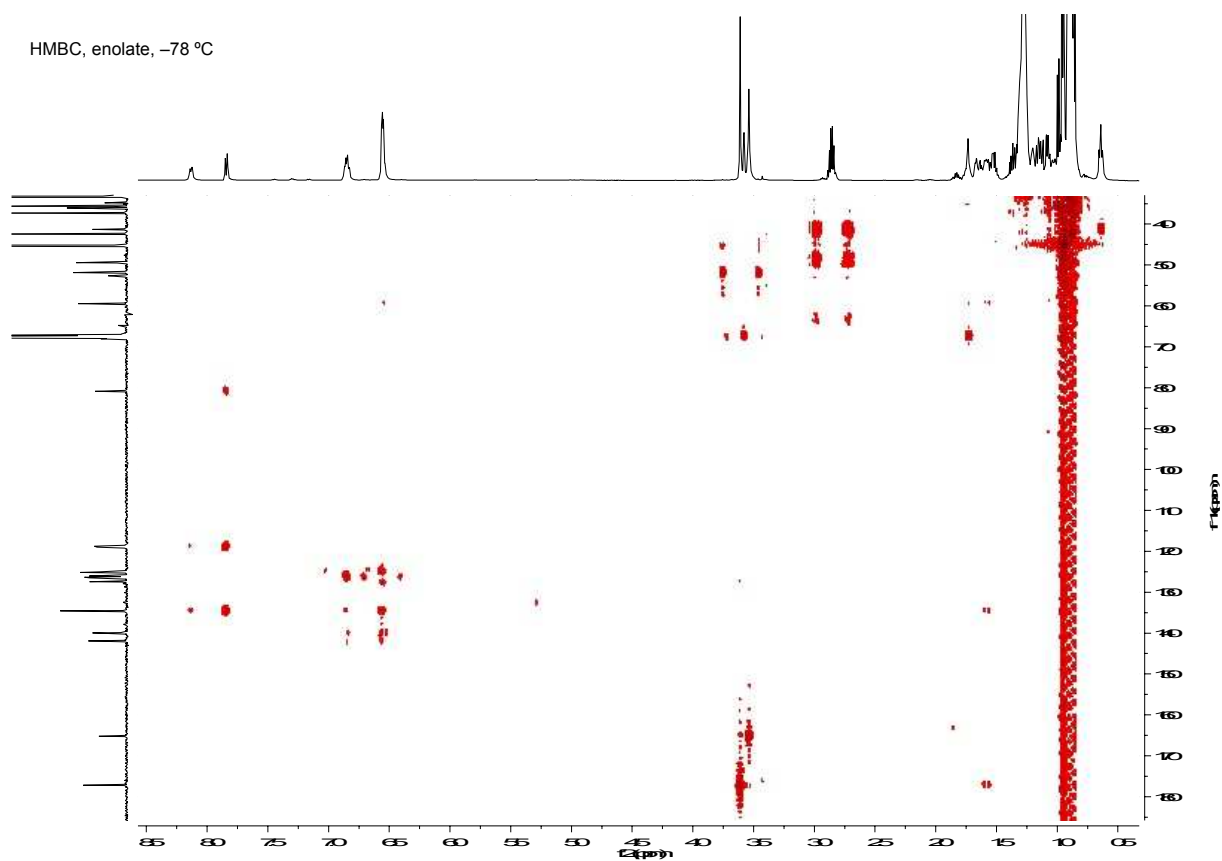




HSQC, enolate, -78 °C



HMBC, enolate, -78 °C



1D-NOESY (-78 °C)

