

Supporting Information for

Competition Between Alkenes in the Intramolecular Ketene–Alkene [2+2]–Cycloaddition: What Does It Take to Win?

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I General Experimental Details

All required fine chemicals were used directly without purification unless mentioned. Compounds lacking experimental details were prepared according to the literature as cited and are in agreement with published spectra. THF and Et₂O were distilled from Na and benzophenone at atmospheric pressure. CH₂Cl₂, benzene, toluene and diisopropylamine were distilled from CaH₂ at atmospheric pressure. Infrared spectra were recorded with a FT-IR spectrometer by applying substrates as thin films onto a KBr plate. ¹H (300 MHz) NMR and ¹³C (75 MHz) NMR spectra are given in ppm as referenced to CDCl₃ (7.26 ppm for ¹H NMR and 77.0 ppm for ¹³C NMR) and were measured with a 300 MHz NMR spectrometer. For the determination of the ratios of **24/25a-e**, the ¹H NMR spectra were recorded with a relaxation delay of 4 sec.¹ 2D experiments (COSY, NOESY, TOCSY, HSQC and HMBC) were measured with a 600 MHz NMR spectrometer. ¹H NMR coupling constants are reported in hertz and refer to apparent multiplicities and not true coupling constants. 230-400 Mesh silica gel was used for column chromatography, while 250 μm silica gel plates were used for TLC analysis. All reactions were conducted under nitrogen or argon in flame-dried glassware and concentrations were performed under reduced pressure using a rotary evaporator.

II Procedures and Spectroscopic Data of Compounds 2, 7, 8, 10, 11, 15, 20, 22-25.

2-(Pent-4-en-1-yn-1-yl)oct-7-enoic acid (2). *n*-BuLi (2.38 M in hexanes, 8.0 mL, 19 mmol) was added to a solution of *i*-Pr₂NH (2.7 mL, 19 mmol) in THF (20 mL) at 0°C. After 30 min at 0°C, a precooled (0°C) solution of **1** (1.00 g 7.80 mmol) in THF (7 mL) and DMPU (1.9 mL) was added. The solution was stirred 1 h at rt, cooled to 0°C, then 6-iodohex-1-ene (1.30 mL, 9.4 mmol) was added. After 2 h at rt, H₂O was added THF was evaporated under reduced pressure. The aqueous phase was extracted with Et₂O and the combined organic layers were dried over anhyd. MgSO₄, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography (94:5:1 hexanes-EtOAc-AcOH) to give 1.00 g (60 %) of pure **2** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.86–5.72 (m, 2H), 5.04 – 4.92 (m, 4H), 2.39 – 2.31 (m, 1H), 2.11 – 2.01 (m, 4H), 1.70 – 1.60 (m, 2H), 1.58 – 1.28 (m, 8H); ¹³C

NMR (75 MHz, CDCl_3) δ 181.9, 138.7, 138.3, 114.7, 114.4, 45.2, 33.5, 31.9, 28.7, 26.7, 26.5; IR (film) ν 3081, 2980, 2931, 2856, 1703, 1288, 1235, 909 cm^{-1} ; MS (CI) m/z 211 (35) [MH^+], 193 (18), 165 (13), 141 (15), 124 (29); HRMS (EI) calcd for $\text{C}_{13}\text{H}_{23}\text{O}_2$ (MH^+) 211.1698, found 211.1702.

2-Hexylhept-6-enoic acid (7). Following the procedure used to form **2**, a solution of **1** (1.00 g, 7.8 mmol) in THF (7 mL) and DMPU (1.9 mL) was treated with LDA [prepared from *n*-BuLi (2.38 M in hexanes, 8.0 mL, 19.0 mmol) and *i*-Pr₂NH (2.7 mL, 19.2 mmol) in THF (20 mL)] and 1-iodohexane (1.22 mL, 8.9 mmol) in THF (11 mL) to give, after purification by flash chromatography (94:5:1 hexanes–EtOAc–AcOH), 1.00 g (59 %) of pure **7** as a colorless oil: ¹H NMR (300 MHz, CDCl_3) δ 5.78 (ddt, J =17.0, 10.5, 6.5 Hz, 1H), 5.00 (dd, J =19.0, 1.5 Hz, 1H), 4.95 (d, J =9.0 Hz, 1H), 2.41 – 2.31 (m, 1H), 2.11 – 2.02 (m, 2H), 1.70 – 1.27 (m, 14H), 0.89 – 0.85 (m, 3H); ¹³C NMR (75 MHz, CDCl_3) δ 183.3, 138.2, 114.7, 45.4, 33.6, 32.2, 31.5, 29.2, 27.2, 26.5, 22.5, 14.0; IR (film) ν 3081 (br), 2935, 2860, 2684, 1703, 1456, 1288, 1231, 904 cm^{-1} ; MS (CI) m/z 230 (100) [MNH_4^+], 213 (30) [MH^+], 195 (15), 141 (4), 126 (7); HRMS (CI) calcd for $\text{C}_{13}\text{H}_{25}\text{O}_2$ (MH^+) 213.1854, found 213.1849.

1-Hexylbicyclo[3.2.0]heptan-7-one (8) from 5 Pd/C (5 % w/w, 2 mg) was added to a solution of **5** (30 mg,) in EtOAc (3 mL). The flask was purged with H₂ then the suspension was stirred for 2 h at rt. The flask was purged with N₂, then the suspension was filtered on Celite and the filtrate was concentrated under reduced pressure. The crude material was purified by flash chromatography (19:1 hexanes–EtOAc) to give 28.5 g (95 %) of pure **8**. **1-Hexylbicyclo[3.2.0]heptan-7-one (8) from 7.** Following the procedure used to form **5**, **7** (400 mg, 1.9 mmol) was treated with oxalyl chloride (830 μL , 9.5 mmol) in toluene (2.0 mL) then with Et₃N (1.6 mL, 11 mmol) in toluene (33 mL) to give, after purification by flash chromatography (19:1 hexanes–EtOAc), 313 mg (85 %) of pure **8** as a colorless oil: ¹H NMR (300 MHz, CDCl_3) δ 3.02 (dd, J =18.5, 9.0 Hz, 1H), 2.50 – 2.45 (m, 1H), 2.34 (dd, J =18.5, 5.0 Hz, 1H), 1.92 (dd, J =21.5, 6.0 Hz, 1H), 1.79 – 1.19 (m, 15H), 0.82 – 0.78 (m, 3H); ¹³C NMR (75 MHz, CDCl_3) δ 218.2, 75.9, 49.2, 35.2, 33.8, 33.1, 32.6, 31.6, 29.7, 25.5, 24.9, 22.5, 14.0; IR (film) ν 2949 (br), 2856, 1770, 1465, 1386, 1076 cm^{-1} ; MS (EI) m/z 194 (2) [M^+], 152 (48), 123 (11), 110 (14), 95 (41), 82 (100); HRMS (EI) calcd for $\text{C}_{13}\text{H}_{22}\text{O}$ (M^+) 194.1671, found 194.1673.

2-Pentyloct-7-enoic acid (10). Following the procedure used to form **2**, a solution of **9** (1.00 g, 7.7 mmol) in THF (7 mL) and DMPU (1.9 mL) was treated with LDA [prepared from *n*-BuLi (2.38 M in hexanes, 8.0 mL, 19.0 mmol) and *i*-Pr₂NH (2.7 mL, 19.2 mmol) in THF (20 mL)] and 6-iodohex-1-ene (1.22 mL, 8.8 mmol) in THF (11 mL) to give, after purification by flash chromatography (94:5:1 hexanes–EtOAc–AcOH), 1.13 g (67 %) of pure **10** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 5.79 (ddt, *J*=17.0, 10.5, 6.5 Hz, 1H), 4.98 (dd, *J*=17.0, 1.5 Hz, 1H), 4.93 (dd, *J*=10.5, 1.5 Hz, 1H), 2.41 – 2.29 (m, 1H), 2.08 – 2.01 (m, 2H), 1.69 – 1.28 (m, 14H), 0.90 – 0.85 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 183.3, 138.4, 114.3, 45.5, 33.5, 32.1, 31.9, 28.7, 26.9, 26.7, 22.4, 13.9; IR (film) ν 3081, 2936, 2856, 1703, 1465, 1231, 909 cm⁻¹; MS (CI) *m/z* 240 (14) [MNH₄⁺], 213 (31) [MH⁺], 155 (8), 124 (19); HRMS (CI) calcd for C₁₃H₂₅O₂ (MH⁺) 213.1854, found 213.1851.

1-Pentylbicyclo[4.2.0]octan-8-one (11). Following the procedure used to form **5**, **10** (1.79 g, 8.4 mmol) was treated with oxalyl chloride (3.7 mL, 42 mmol) in toluene (8 mL) then with Et₃N (5 mL, 35.9 mmol) in toluene (141 mL) to give, after purification by flash chromatography (19:1 hexanes–EtOAc), 175 mg (1.1 %) of pure **8** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 2.98 (dd, *J*=17.0 Hz, 9.5 Hz, 1H), 2.79 (dd, *J*=17.0 Hz, 7.0 Hz, 1H), 2.27–2.18 (m, 1H), 1.86–1.69 (m, 2H), 1.53–1.19 (m, 14H), 0.85 (t, *J*=6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 214.0, 63.7, 48.1, 36.4, 32.4, 28.4, 27.3, 26.0, 24.4, 22.5, 21.2, 20.5, 14.0; IR (film) ν 2927, 2856, 1774, 1456, 1165, 1068 cm⁻¹; MS (EI) *m/z* 194 (1) [M⁺], 152 (55), 96 (100), 81 (83), 67 (42), 55 (20), 41 (26); HRMS (EI) calcd for C₁₃H₂₂O 194.1671, found 194.1666.

(E)-5-Phenylpent-4-en-1-ol (15). DIBALH (1.0 M in CH₂Cl₂, 53 mL, 53 mmol) was added to a precooled (–78°C) solution of ester **14** (2.7 g, 13 mmol) in THF (130 mL). After 4 h at –78°C, acetone (52 mL) was added and the solution was allowed to warm to rt. A saturated aq solution of potassium and sodium tartrate (160 mL) was added and the mixture was vigorously stirred overnight. THF was evaporated under reduced pressure and the aqueous phase was extracted with Et₂O. The combined organic layers were dried over anhyd. MgSO₄, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography (13:1 hexanes–EtOAc) to give 2.11 g (100 %) of

pure **15** as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.60–7.17 (m, 5H), 6.43 (d, $J=16.0$ Hz, 1H), 6.23 (dt, $J=16.0$, 7.0 Hz, 1H), 3.72 (t, $J=7.0$ Hz, 2H) 2.32 (q, $J=7.0$ Hz, 2H), 1.76 (qn, $J=7.0$ Hz, 2H), 1.39 (br s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 130.4, 130.0, 128.4, 127.0, 125.9, 62.4, 32.2, 29.3; MS (EI) m/z 162 (34) [M^+], 143 (23), 129 (100), 115 (60), 91 (48); HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{O}$ 162.1045, found 162.1054.²

(E)-2,2-Dimethyl-5-(5-phenylpent-4-enyl)-[1,3]dioxane-4,6-dione (20). A solution of DMSO (3.41 mL, 48 mmol) in CH_2Cl_2 (7 mL) was added to a solution of oxalyl chloride (2.09 mL, 24 mmol) in CH_2Cl_2 (54 mL) at -78°C . After 5 min at -78°C , a precooled (-78°C) solution of **15** (3.81 g, 20 mmol) in CH_2Cl_2 (13 mL) was added and the reaction mixture was stirred 15 min at -78°C then 1 h at -40°C . A solution of Et_3N (13.9 mL, 100 mmol) in CH_2Cl_2 (13 mL) was added and the reaction mixture was allowed to warm to rt over 4h. H_2O was added and the aqueous phase was extracted with CH_2Cl_2 . The combined organic layers were washed with 1 N HCl, brine, dried over anhyd. MgSO_4 , filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography (9:1 to 5:1 hexanes–EtOAc) to give 3.26 g (87 %) of pure aldehyde as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 9.83 (s, 1H), 7.36–7.18 (m, 5H), 6.44 (d, $J=16.0$ Hz, 1H), 6.21 (dt, $J=16.0$, 6.5 Hz, 1H), 2.64–2.54 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 201.7, 137.2, 131.1, 128.5, 128.1, 127.2, 126.0, 43.3, 25.5; IR (film) ν 3028, 2913, 2830, 2724, 1717, 970 cm^{-1} ; MS (EI) m/z 160 (38) [M^+], 115 (57), 104 (100), 91 (46); HRMS (EI) calcd for $\text{C}_{11}\text{H}_{12}\text{O}$ 160.0888, found 160.0886.³ Following the procedure used to form **13**, the previously prepared aldehyde (1.43 g, 8.9 mmol) was treated with $\text{BH}_3\cdot\text{HNMe}_2$ complex (530 mg, 9.0 mmol) in MeOH (7 mL) to give 1.28 g (49%) of pure **20** (without purification) as a white solid: m.p. 78–82 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 7.36–7.26 (m, 4H), 7.21–7.17 (m, 1H), 6.42 (d, $J=16.0$ Hz, 1H), 6.20 (dt, $J=16.0$, 7.0 Hz, 1H), 3.54 (t, $J=5.0$ Hz, 2H), 2.29 (q, $J=7.0$ Hz, 2H), 1.77 (s, 3H), 1.76 (s, 3H), 1.71 – 1.61 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.4, 137.6, 130.6, 129.6, 128.4, 127.0, 126.0, 104.5, 46.1, 32.8, 28.4, 26.9, 26.0; IR (film) ν 3028, 2944, 2869, 1783, 1743, 1293 cm^{-1} ; MS (CI) m/z 306 (100) [MNH_4^+], 248 (50), 230 (92), 204 (72), 184 (52), 130 (52); HRMS (CI) calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4\cdot\text{NH}_4^+$ 306.1705, found 306.1700.

(E)-5-(p-Methoxyphenyl)pent-4-en-1-ol (22a). PPh₃ (1.05 g, 4.0 mmol) was added to a solution of palladium (II) acetate (200 mg, 0.89 mmol) in THF (15 mL) at rt. After 20 min at rt, NaOH (3.0 g, 75 mmol), THF (25 mL) and a solution of 4-iodoanisole (5.27 g, 23 mmol) in THF (25 mL) were added at rt, followed by the addition of **21** (7.85 g, 25 mmol). After stirring at reflux overnight, the solution was allowed to cool to rt, then 3N HCl (40 mL) was added (the solution became black). After 4 h at rt, benzene was added followed by 1N NaOH (until pH = 7). The layers were separated and the organic phase was washed with 1N NaOH (until the aq phase remains colorless), brine, dried over anhyd. MgSO₄, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography (9:1 hexanes–EtOAc) to give 2.23 g (52 %) of pure **22a** as an orange solid: m.p. 72.5–74°C; ¹H NMR (300 MHz, CDCl₃) δ 7.27 (d, *J*=8.5 Hz, 2H), 6.84 (d, *J*=8.5 Hz, 2H), 6.35 (d, *J*=16.0 Hz, 1H), 6.12 (dt, *J*=16.0, 7.0 Hz, 1H), 3.80 (s, 3H), 3.70 (t, *J*=7.0 Hz, 2H), 2.29 (q, *J*=7.0 Hz, 2H), 1.74 (qn, *J*=7.0 Hz, 2H), 1.40 (br s, 1H); MS (EI) *m/z* 192 (83) [M⁺], 147 (100), 121 (76), 115 (23); HRMS (EI) calcd for C₁₂H₁₆O₂ 192.1150, found 192.1153.^{1b}

(E)-5-(p-Tolyl)pent-4-en-1-ol (22b). Following the procedure used to form **22a**, NaOH (3.0 g, 75 mmol) and THF (25 mL) were added to a solution of PPh₃ (1.05 g, 4 mmol) and palladium (II) acetate (0.2 g, 0.9 mmol) in THF (25 mL), followed by a solution of 4-iodotoluene (4.9 g, 22.5 mmol) in THF (25 mL) then addition of **21** (7.85 g, 24.7 mmol) and 3N HCl (40 mL) to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 2.06 g (52 %) of pure **22b** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.27 (d, *J*=8.5 Hz, 2H), 7.13 (d, *J*=8.5 Hz, 2H), 6.42 (d, *J*=16.0 Hz, 1H), 6.20 (dt, *J*=16.0, 7.0 Hz, 1H), 3.70 (t, 7.0 Hz, 2H), 2.36 (s, 3H), 2.31 (q, *J*=7.0 Hz, 2H), 2.28 (s, 1H), 1.76 (qn, *J*=7.0 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 136.7, 134.8, 130.2, 129.2, 129.0, 125.8, 62.2, 32.3, 29.3, 21.2; IR (film) ν 3307 (br), 3028, 2940, 2874, 966 cm⁻¹; MS (EI) *m/z* 176 (61) [M⁺], 143 (100), 131 (91), 115 (59), 105 (63); HRMS (EI) calcd for C₁₂H₁₆O 176.1201, found 176.1203.^{2b}

(E)-5-(p-Chlorophenyl)pent-4-en-1-ol (22c). Following the procedure used to form **22a**, NaOH (3.1 g, 78 mmol) and THF (25 mL) were added to a solution of PPh₃ (970 mg, 3.7 mmol) and palladium (II) acetate (210 mg, 0.93 mmol) in THF (15 mL), followed by a solution of 4-chloriodobenzene (4.7 g, 20 mmol) in THF (25 mL) then addition of **21** (8.25 g, 22 mmol) and 3N HCl (30 mL) to give, after

purification by flash chromatography (1:0 to 4:1 CH₂Cl₂–MeOH), 3.2 g (82 %) of pure **22c** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.24 (s, 4H), 6.35 (d, *J*=16.0 Hz, 1H), 6.19 (dt, *J*=16.0, 7.0 Hz, 1H), 3.69 (t, *J*=7.0 Hz, 2H), 2.29 (q, *J*=7.0 Hz, 2H), 1.91 (br s, 1H), 1.74 (qn (*J*=7.0 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 136.1, 132.4, 130.8, 129.1, 128.6, 127.1, 62.2, 32.1, 29.3; IR (film) ν 3378 (br), 3032, 2934, 2868, 1646, 1491, 1094, 1059 cm⁻¹; MS (EI) *m/z* 196 (35) [M⁺], 151 (22), 143 (100), 128 (64), 115 (79); HRMS (EI) calcd for C₁₁H₁₃ClO 196.0655, found 196.0658.

(E)-5-(*p*-Trifluoromethylphenyl)pent-4-en-1-ol (22d). Following the procedure used to form **22a**, NaOH (2.4 g, 60 mmol) and THF (20 mL) were added to a solution of PPh₃ (730 mg, 2.8 mmol) and palladium (II) acetate (160 mg, 0.72 mmol) in THF (15 mL), followed by a solution of 4-iodo(trifluoromethyl)benzene (4.9 g, 18 mmol) in THF (20 mL) then addition of **21** (6.27 g, 20 mmol) and 3N HCl (40 mL) to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 4.0 g (97 %) of pure **22d** as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.54 (d, *J*=8.5 Hz, 2H), 7.42 (d, *J*=8.5 Hz, 2H), 6.45 (d, *J*=16.0 Hz, 1H), 6.34 (dt, *J*=16.0, 7.0 Hz, 1H), 3.72 (t, *J*=7.0 Hz, 2H), 2.35 (q, *J*=7.0 Hz, 2H), 1.77 (qn, *J*=7.0 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 141.1, 132.9, 129.1, 28.9, 128.5, 126.0, 125.4, 62.1, 32.0, 29.3; IR (film) ν 3333 (br), 2944, 2878, 1615, 1324, 1121, 1068 cm⁻¹; MS (EI) *m/z* 230 (30) [M⁺], 212 (40), 197 (55), 143 (100); HRMS (EI) calcd for C₁₂H₁₃F₃O 230.0918, found 230.0924.

(E)-5-(*p*-Nitrophenyl)pent-4-en-1-ol (22e). Following the procedure used to form **22a**, NaOH (3.1 g, 78 mmol) and THF (25 mL) were added to a solution of PPh₃ (970 mg, 3.7 mmol) and palladium (II) acetate (210 mg, 0.93 mmol) in THF (15 mL), followed by a solution of 4-iodonitrobenzene (4.9 g, 20 mmol) in THF (25 mL) then addition of **21** (7.0 g, 22 mmol) and 3N HCl (30 mL) to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 3.09 g (75 %) of pure **22e** as an orange solid: m.p. 53 – 54°C; ¹H NMR (300 MHz, CDCl₃) δ 8.14 (d, *J*=9.0 Hz, 2H), 7.44 (d, *J*=8.0 Hz, 2H), 6.52–6.39 (m, 2H), 3.72 (t, *J*=6.5 Hz, 2H), 2.37 (q, *J*=6.5 Hz, 2H), 1.77 (qn, *J*=6.5 Hz, 2H), 1.52 (br s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 146.4, 144.2, 135.7, 128.5, 126.4, 123.9, 62.0, 31.8, 29.4; IR (film) ν 3543, 2939, 2884, 1593, 1506, 1340 cm⁻¹; MS (EI) *m/z* 207 (18) [M⁺], 172 (30), 128 (100), 115 (91); HRMS (EI) calcd for C₁₁H₁₃NO₃ 207.0895, found 207.0898.

(4*E*,6*E*)-7-(*p*-Methoxyphenyl)-2-(5-phenylpent-4-enyl)hept-6-enoic acid (23a). Following the procedure used to form **16**, **22a** (700 mg, 3.64 mmol) was treated with I₂ (924 mg, 3.64 mmol), PPh₃ (944 mg, 3.60 mmol) and imidazole (298 mg, 4.37 mmol) in CH₂Cl₂ (10 mL) to give, after purification by flash chromatography (49:1 hexanes–EtOAc), 1.0 g (91 %) of pure iodide as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.34 (d, *J*=8.5 Hz, 2H), 6.91 (d, *J*=8.5 Hz, 2H), 6.45 (d, *J*=16 Hz, 1H), 6.05 (dt, *J*=16.0, 7.0 Hz, 1H), 3.82 (s, 3H), 3.25 (t, *J*=7.0 Hz, 2H), 2.34 (q, *J*=7.0 Hz, 2H), 2.01 (qn, *J*=7.0 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 158.9, 130.8, 130.3, 127.3, 126.1, 114.1, 55.4, 33.7, 33.1, 6.9; IR (film) ν 3033, 2997, 2925, 2834, 1608, 1510, 1463, 1441, 1248 cm⁻¹; MS (EI) *m/z* 302 (20) [M⁺], 147 (40), 84 (100); HRMS (EI) calcd for C₁₂H₁₅IO 302.0168, found 302.0177. Following the procedure used to form **16**, the previously prepared iodide (220 mg, 0.69 mmol) was treated with Cs₂CO₃ (346 mg, 1.06 mmol) and **20** (153 mg, 0.53 mmol) in MeCN (1.5 mL) to give, after purification by flash chromatography (20:1 hexanes–EtOAc), 170 mg (67%) of pure branched Meldrum's acid as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.35–7.20 (m, 7H), 6.84 (d, *J*=9.0 Hz, 2H), 6.35 (t, *J*=16.0 Hz, 2H), 6.13 (dt, *J*=16.0, 7.0 Hz, 1H), 5.98 (dt, *J*=16.0, 7.5 Hz, 1H), 3.80 (s, 3H), 2.21 (qn, *J*=7.0 Hz, 4H), 2.10–2.04 (m, 4H), 1.74 (s, 6H), 1.54–1.42 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 158.8, 137.4, 130.9, 130.2, 129.0, 128.5, 127.1, 126.8, 126.0, 113.9, 105.5, 55.3, 54.6, 38.9, 32.7, 29.8, 25.5, 25.4; IR (film) ν 3028, 2935, 2838, 1774, 1748, 1509, 1249 cm⁻¹; MS (CI) *m/z* 480 (38) [MNH₄⁺], 462 (25) [M⁺], 405 (55), 378 (53), 361 (100), 253 (90), 121 (73); HRMS (EI) calcd for C₂₉H₃₄O₅ 462.2406, found 462.2397. Following the procedure used to form **17**, the previously prepared branched Meldrum's acid (170 mg, 0.37 mmol) was heated in THF (1.2 mL) and H₂O (0.6 mL), to give, after purification by flash chromatography (14:1 hexanes–EtOAc), 102 mg (73%) of pure **23a** as a white solid: m.p. 80 – 84.5°C : ¹H NMR (300 MHz, CDCl₃) δ 7.36–7.19 (m, 7H), 6.84 (d, *J*=9.0 Hz, 2H), 6.36 (t, *J*=16.0 Hz, 2H), 6.20 (dt, *J*=16.0, 8.0 Hz, 1H), 6.05 (dt, *J*=16.0, 7.0 Hz, 1H), 3.81 (s, 3H), 2.44–2.40 (m, 1H), 2.22 (qn, *J*=6.5 Hz, 4H), 1.73–1.66 (m, 2H), 1.66–1.45 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 182.5, 158.7, 137.7, 130.5, 130.2, 129.6, 128.4, 128.0, 127.0, 126.9, 125.9, 113.9, 113.6, 55.3, 45.2, 32.8, 31.6, 27.1, 27.0; IR (film) ν 3449,

3024, 2931, 2856, 1703, 1646, 1606, 1509, 1244 cm^{-1} ; MS (EI) m/z 378 (88) [M^+], 173 (17), 147 (100), 121 (43), 91 (28); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{30}\text{O}_3$ 378.2195, found 378.2185.

(4*cE*,6*E*)-2-(5*c*-Phenylpent-4*c*-enyl)-7-(*p*-tolyl)hept-6-enoic acid (23b). Following the procedure used to form **16**, **22b** (1.21 g, 6.8 mmol) was treated with I_2 (1.78 g, 7.0 mmol), PPh_3 (1.78 g, 6.7 mmol) and imidazole (570 mg, 8.4 mmol) in CH_2Cl_2 (84 mL) to give, after purification by flash chromatography (49:1 hexanes–EtOAc), 1.63 g (82 %) of pure iodide as a colorless oil ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, $J=7.5$ Hz, 2H), 7.13 (d, $J=7.5$ Hz, 2H), 6.44 (d, $J=16.0$ Hz, 1H), 6.11 (dt, $J=16.0, 7.0$ Hz, 1H), 3.24 (t, $J=7.0$ Hz, 2H), 2.37–2.29 (m, 5H), 2.00 (qn, $J=7.0$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 136.9, 134.7, 131.2, 129.2, 127.2, 125.9, 33.5, 32.9, 21.2, 6.5; IR (film) ν 3019, 2931, 2838, 1514, 1434, 1213, 966 cm^{-1} ; MS (EI) m/z 286 (37) [M^+], 131 (100), 115 (29), 105 (21), 91 (21); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{15}\text{I}$ 286.0218, found 283.0221. Following the procedure used to form **16**, the previously prepared iodide (1.63 g, 5.7 mmol) was treated with Cs_2CO_3 (3.29 g, 11 mmol) and **20** (1.25 g, 3.8 mmol) in MeCN (6 mL) to give, after purification by flash chromatography (13:1 hexanes–EtOAc), 1.36 g (80 %) of pure branched Meldrum's acid as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.23 (m, 7H), 7.15 (d, $J=8.5$ Hz, 2H), 6.43 (d, $J=16.0$ Hz, 1H), 6.41 (d, $J=16.0$ Hz, 1H), 6.23 – 6.08 (m, 2H), 2.38 (s, 3H), 2.28 – 2.23 (m, 4H), 2.16 – 2.09 (m, 4H), 1.75 (s, 6H), 1.55 – 1.30 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 137.5, 136.7, 134.7, 131.0, 130.0, 129.3, 129.0, 128.6, 128.0, 127.1, 126.1, 105.5, 54.7, 38.9, 29.8, 25.4, 21.2, 14.3; IR (film) ν 3028, 2927, 2856, 1774, 1739, 1266, 966 cm^{-1} ; MS (CI) m/z 464 (100) [MNH_4^+], 406 (15), 389 (21), 362 (43), 345 (78); HRMS (CI) calcd for $\text{C}_{29}\text{H}_{38}\text{NO}_4$ (MNH_4^+) 464.2801, found 464.2807. Following the procedure used to form **17**, the previously prepared branched Meldrum's acid (1.0 g, 2.2 mmol) was heated in THF (7.3 mL) and H_2O (3.6 mL), to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 553 mg (70 %) of pure **23b** as a white solid: m.p. 90 – 93°C; ^1H NMR (300 MHz, CDCl_3) δ 12.05 (br s, 1H), 7.47 – 7.26 (m, 7H), 7.21 (d, $J=7.5$ Hz, 2H), 6.50 (d, $J=16.0$ Hz, 1H), 6.47 (d, $J=16.0$ Hz, 1H), 6.35 – 6.20 (m, 2H), 2.61 – 2.48 (m, 1H), 2.44 (s, 3H), 2.37 – 2.29 (m, 4H), 1.90 – 1.81 (m, 2H), 1.77 – 1.56 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 183.3, 137.8, 136.7, 135.0, 130.3, 129.3, 128.6, 127.0, 126.1, 126.0, 45.4, 32.9, 31.7, 27.2, 21.3; IR

(film) ν 3024, 2943, 2856, 2662, 1699, 1452, 962, 732 cm^{-1} ; MS (EI) m/z 362 (16) [M^+], 157 (16), 143 (19), 131 (26), 84 (100); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{30}\text{O}_2$ 362.2246, found 362.2240.

(4*E*,6*E*)-7-(*p*-Chlorophenyl)-2-(5*c*-phenylpent-4*c*-enyl)hept-6-enoic acid (23c). Following the procedure used to form **16**, **22c** (800 mg, 4.1 mmol) was treated with I_2 (1.03 g, 4.1 mmol), PPh_3 (1.06 g, 4.0 mmol) and imidazole (333 mg, 4.9 mmol) in CH_2Cl_2 (10 mL) to give, after purification by flash chromatography (32:1 hexanes–EtOAc), 1.0 g (80 %) of pure iodide as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.27 (s, 4H), 6.40 (d, $J=16.0$ Hz, 1H), 6.13 (dt, $J=16.0, 7.0$ Hz, 1H), 3.23 (t, $J=7.0$ Hz, 2H), 2.33 (q, $J=7.0$ Hz, 2H), 1.99 (qn, $J=7.0$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 135.9, 132.6, 130.1, 129.0, 128.6, 127.2, 33.5, 32.7, 6.2; IR (film) ν 3025, 2930, 2837, 1489, 1216, 1092, 967 cm^{-1} ; MS (EI) m/z 306 (41) [MH^+], 151 (100), 125 (34), 115 (80); HRMS (EI) calcd for $\text{C}_{11}\text{H}_{12}\text{ClI}$ 305.9672, found 305.9675. Following the procedure used to form **16**, the previously prepared iodide (461 mg, 1.5 mmol) was treated with Cs_2CO_3 (1.27 g, 3.9 mmol) and **20** (375 mg, 1.3 mmol) in MeCN (3 mL) to give, after purification by flash chromatography (13:1 hexanes–EtOAc), 410 mg (67%) of pure branched Meldrum's acid as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.35 – 7.18 (m, 9H), 6.38 (d, $J=16.5$ Hz, 1H), 6.33 (d, $J=16.0$ Hz, 1H), 6.18 – 6.05 (m, 2H), 2.27 – 2.18 (m, 4H), 2.13 – 2.05 (m, 4H), 1.74 (s, 6H), 1.58 – 1.45 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 137.4, 135.9, 132.6, 131.0, 129.7, 128.9, 128.5, 127.3, 127.1, 126.0, 105.6, 54.5, 38.8, 32.7, 29.8, 25.3; IR (film) ν 3028, 2938, 2860, 1770, 1739, 1266, 1200, 967 cm^{-1} ; MS (CI) m/z 484 (87) [MNH_4^+], 409 (20), 365 (100), 347 (43); HRMS (CI) calcd for $\text{C}_{28}\text{H}_{35}\text{NClO}_4$ (MNH_4^+) 484.2254, found 484.2258. Following the procedure used to form **17**, the previously prepared branched Meldrum's acid (300 mg, 0.64 mmol) was heated in THF (2.1 mL) and H_2O (1.0 mL), to give, after purification by flash chromatography (13:1 hexanes–EtOAc), 153 mg (62%) of pure **23c** as a white solid: m.p. 103 – 107°C; ^1H NMR (300 MHz, CDCl_3) δ 7.36 – 7.19 (m, 9H), 6.40 (d, $J=16.0$ Hz, 1H), 6.34 (d, $J=17.0$ Hz, 1H), 6.25 – 6.12 (m, 2H), 2.50 – 2.39 (m, 1H), 2.29 – 2.17 (m, 4H), 1.81 – 1.46 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3) δ 182.8, 137.6, 136.1, 132.4, 131.0, 130.2, 129.1, 128.5, 127.1, 126.9, 125.9, 45.3, 32.8, 31.6, 29.7, 26.9; IR (film) ν 3028, 2933, 2856, 1699, 1487, 1090,

962 cm^{-1} ; MS (EI) m/z 382 (40) [M^+], 177 (44), 143 (92), 117 (100); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{27}\text{ClO}_2$ 382.1699, found 382.1704.

(4*cE*,6*E*)-2-(5*c*-Phenylpent-4*c*-enyl)-7-(*p*-trifluoromethylphenyl)hept-6-enoic acid (23d). Following the procedure used to form **16**, **22d** (600 mg, 2.6 mmol) was treated with I_2 (660 mg, 2.6 mmol), PPh_3 (680 mg, 2.6 mmol) and imidazole (210 mg, 3.1 mmol) in CH_2Cl_2 (35 mL) to give, after purification by flash chromatography (49:1 hexanes–EtOAc), 840 mg (95 %) of pure iodide as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.56 (d, $J=8.0$ Hz, 2H), 7.43 (d, $J=8.0$ Hz, 2H), 6.50 (d, $J=16.0$ Hz, 1H), 6.28 (dt, $J=16.0$, 7.0 Hz, 1H) 3.24 (t, $J=7.0$ Hz, 2H), 2.37 (q, $J=7.0$ Hz, 2H), 2.02 (qn, $J=7.0$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 140.9, 131.2, 130.1, 128.6, 126.4, 126.2, 125.5, 122.5, 33.6, 32.6, 6.2; IR (film) ν 3024, 2935, 2838, 1616, 1165, 1122 cm^{-1} ; MS (EI) m/z 340 (39) [M^+], 185 (32), 159 (18), 84 (100); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{12}\text{F}_3\text{I}$ 339.9936, found 339.9938. Following the procedure used to form **16**, the previously prepared iodide (800 mg, 2.3 mmol) was treated with Cs_2CO_3 (1.86 g, 5.7 mmol) and **20** (557 mg, 1.9 mmol) in MeCN (5 mL) to give, after purification by flash chromatography (19:1 hexanes–EtOAc), 426 mg (45%) of pure branched Meldrum's acid as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.54 (d, $J=8.0$ Hz, 2H), 7.41 (d, $J=8.0$ Hz, 2H), 7.35 – 7.20 (m, 5H), 6.40 (d, $J=16.0$ Hz, 1H), 6.37 (d, $J=15.5$ Hz, 1H), 6.22 (dt, $J=15.5$, 7.0 Hz, 1H), 6.12 (dt $J=16.0$, 7.0 Hz, 1H), 2.23 (qn, $J=7.0$ Hz, 4H), 2.10 – 2.04 (m, 4H), 1.74 (s, 6H), 1.55 – 1.43 (m, 4H). Following the procedure used to form **17**, the previously prepared branched Meldrum's acid (426 mg, 0.85 mmol) was heated in THF (3.0 mL) and H_2O (1.5 mL), to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 100 mg (28%) of pure **23d** as a white solid: m.p. 89 – 92°C; ^1H NMR (300 MHz, CDCl_3) δ 7.53 (d, $J=8.0$ Hz, 2H), 7.40 (d, $J=8.0$ Hz, 2H), 7.35 – 7.20 (m, 5H), 6.44 – 6.16 (m, 4H), 2.51 – 2.29 (m, 1H), 2.32 – 2.18 (m, 4H), 1.71 – 1.50 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3) δ 182.3, 141.1, 137.6, 133.0, 130.2, 130.1, 129.1, 128.9, 128.5, 126.9, 126.0, 125.9, 125.4, 122.4, 45.2, 32.8, 31.6, 27.0, 26.8; IR (film) ν 3033, 2931, 2860, 1703, 1319, 1160, 1116, 1068 cm^{-1} ; MS (EI) m/z 416 (100) [M^+], 211 (40), 143 (36), 117 (70); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{27}\text{F}_3\text{O}_2$ 416.1963, found 416.1959.

(4*E*,6*E*)-7-(*p*-Nitrophenyl)-2-(5-phenylpent-4-enyl)hept-6-enoic acid (23e). Following the procedure used to form **16**, **22e** (800 mg, 3.9 mmol) was treated with I₂ (1.0 g, 3.9 mmol), PPh₃ (1.01 mg, 3.9 mmol) and imidazole (320 mg, 4.7 mmol) in CH₂Cl₂ (10 mL) to give, after purification by flash chromatography (32:1 hexanes–EtOAc), 1.03 g (82 %) of pure iodide as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 8.15 (d, *J*=9.0 Hz, 2H), 7.45 (d, *J*=9.0 Hz, 2H), 6.52 (d, *J*=16.0 Hz, 1H), 6.37 (dt, *J*=16.0, 7.0 Hz, 1H), 3.23 (t, *J*=7.0 Hz, 2H), 2.40 (q, *J*=7.0 Hz, 2H), 2.02 (qn, *J*=7.0 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 146.6, 143.8, 133.7, 129.5, 126.4, 124.0, 33.7, 32.3, 5.9; IR (film) ν 3077, 3033, 2931, 2838, 1593, 1514, 1341 cm⁻¹; MS (EI) *m/z* 317 (32) [M⁺], 155 (14), 116 (100); HRMS (EI) calcd for C₁₁H₁₂NO₂I 316.9913, found 316.9920. Following the procedure used to form **16**, the previously prepared iodide (1.00 g, 3.2 mmol) was treated with Cs₂CO₃ (1.8 g, 5.4 mmol) and **20** (780 mg, 2.7 mmol) in MeCN (4 mL) to give, after purification by flash chromatography (19:1 hexanes–EtOAc), 890 mg (77 %) of pure branched Meldrum's acid as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 8.14 (d, *J*=9.0 Hz, 2H), 7.44 (d, *J*=9.0 Hz, 2H), 7.34-7.17 (m, 5H), 6.49-6.27 (m, 3H), 6.11 (dt, *J*=16.0 Hz, 7.0 Hz, 1H), 2.30-2.18 (m, 4H), 2.09-2.03 (m, 4H), 1.74 (s, 6H), 1.56-1.43 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 169.3, 146.6, 143.8, 137.3, 134.2, 131.0, 129.2, 128.8, 128.5, 127.1, 126.5, 126.0, 124.0, 123.5, 105.7, 54.5, 38.8, 38.6, 32.7, 29.9, 29.8, 25.2, 24.9; IR (film) ν 3028, 2997, 2936, 2860, 1774, 1739, 1597, 1518, 1346, 1266, 1204, 970, 909, 732 cm⁻¹; MS (EI) *m/z* 495 (20) [MNH₄⁺], 448 (15), 420 (27), 376 (100), 358 (30), 346 (16), 189 (20), 130 (28); HRMS (CI) calcd for C₂₈H₃₅N₂O₆ (MNH₄⁺) 495.2495, found 495.2487. Following the procedure used to form **17**, the previously prepared branched Meldrum's acid (750 mg, 1.7 mmol) was heated in THF (5.5 mL) and H₂O (2.7 mL), to give, after purification by flash chromatography (9:1 hexanes–EtOAc), 400 mg (61 %) of pure **23e** as a yellow solid: m.p. 84 – 86°C; ¹H NMR (300 MHz, CDCl₃) δ 8.14 (d, *J*=9.0 Hz, 2H), 7.43 (d, *J*=9.0 Hz, 2H), 7.34-7.19 (m, 5H), 6.47-6.35 (m, 3H), 6.18 (dt, *J*=16.0 Hz, 7.0 Hz, 1H), 2.44-2.41 (m, 1H), 2.31-2.20 (m, 4H), 1.78-1.47 (m, 8H); ¹³C NMR (75 MHz, CDCl₃) δ 182.7, 146.4, 144.2, 137.6, 135.6, 130.3, 130.1, 128.5, 126.9, 126.4, 126.0, 123.9, 45.3, 33.0, 32.8, 31.6, 27.0, 26.7; IR (film) ν 3024, 2935 (br), 2856, 1699,

1509, 1341, 966, 728, 697 cm^{-1} ; MS (EI) m/z 393 (15) [M^+], 143 (25), 117 (100), 91 (48); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{27}\text{NO}_4$ 393.1940, found 393.1945.

(E)-7-(*p*-Methoxyphenyl)-1-(5*o*-phenylpent-4-enyl)bicyclo[3.1.1]heptan-6-one (24a) and (E)-1-[5*o*-(*p*-methoxyphenyl)pent-4-enyl]-7-phenylbicyclo[3.1.1]heptan-6-one (25a). Following the procedure used to form **5**, **23a** (50 mg, 0.13 mmol) was treated with oxalyl chloride (50 μL , 0.65 mmol) in toluene (1 mL) then with Et_3N (110 μL , 0.8 mol) in toluene (3 mL) to give a 3.2:1.0 mixture of **24a** and **25a** determined by ^1H NMR on the crude material. After purification by flash chromatography (19:1 hexanes–EtOAc), 9 mg (20 %) an inseparable mixture of **24a** and **25a** was obtained as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.29–7.12 (m, 5H), 7.06 (d, $J=9.0$ Hz, 2H), 6.81 (d, $J=9.0$ Hz, 2H), 6.21 (d, $J=16.0$ Hz, 1H), 5.92 (dt, $J=15.5$ Hz, 7.0 Hz, 1H), 3.80 (s, 3H, 25a), 3.75 (s, 3H, 24a), 3.17 (t, $J=3.5$ Hz, 1H, 25a), 3.12 (t, $J=3.5$ Hz, 1H, 24a), 3.04 (s, 1H, 25a), 3.00 (s, 1H, 24a), 2.53–2.42 (m, 3H), 2.28–2.19 (m, 1H), 2.02–1.83 (m, 3H), 1.76–1.63 (m, 1H), 1.47–1.38 (m, 1H), 1.29–1.08 (m, 3H) ; ^{13}C NMR (75 MHz, CDCl_3) δ 216.2, 158.3, 137.7, 132.1, 130.2, 130.0, 129.3, 128.4, 127.5, 126.9, 126.7, 125.8, 113.8, 70.5, 60.6, 55.1, 47.2, 40.0, 34.6, 33.1, 28.8, 22.9, 22.7, 18.4; IR (film) ν 2935, 2860, 1770, 1514, 1249, 1028 cm^{-1} ; MS (EI) m/z 360 (45) [M^+], 269 (17), 229 (25), 199 (47), 160 (50), 148 (75), 121 (100), 91 (48); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{28}\text{O}_2$ 360.2089, found 360.2095.

(E)-1-(5*o*-Phenylpent-4-enyl)-7-(*p*-tolyl)bicyclo[3.1.1]heptan-6-one (24b) and (E)-7-phenyl-1-(5*o*-(*p*-tolyl)pent-4-enyl)bicyclo[3.1.1]heptan-6-one (25b). Following the procedure used to form **5**, **23b** (180 mg, 0.50 mmol) was treated with oxalyl chloride (220 μL , 2.5 mmol) in toluene (2 mL) then with Et_3N (420 μL , XX mol) in toluene (10 mL) to give a 2.4:1.0 mixture of **24b** and **25b** determined by ^1H NMR on the crude material. After purification by flash chromatography (19:1 hexanes–EtOAc), 141 mg (82 %) an inseparable mixture of **24b** and **25b** was obtained as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.31 – 7.03 (m, 9H), 6.22 (d, $J=16.0$ Hz, 1H **24b**), 6.19 (d, $J=16.0$ Hz, 1H **25b**), 5.98 – 5.84 (m, 2H), 3.18 (t, $J=3.5$ Hz, 1H **25b**), 3.15 (t, $J=3.5$ Hz, 1H **24b**), 3.06 (s, 1H **25b**), 3.02 (s, 1H **24b**), 2.55 – 2.43 (m, 3H), 2.33 (s, 3H **25b**), 2.30 (s, 3H **24b**), 2.29 – 2.21 (m., 1H), 2.04 – 1.85 (m, 3H), 1.80 –

1.65 (m, 1H), 1.51 – 1.09 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 216.2, 216.0, 140.2, 137.8, 137.0, 136.4, 136.2, 134.9, 130.3, 130.0, 129.8, 129.2, 129.0, 128.5, 128.4, 127.4, 126.7, 125.8, 70.7, 70.5, 60.4, 48.1, 47.7, 40.1, 34.7, 33.1, 28.9, 22.8, 21.0, 18.4; IR (film) ν 3024, 2939, 2865, 1765, 1518, 1447, 970, 732, 692 cm^{-1} ; MS (EI) m/z 344 (74) [M^+], 253 (14), 239 (18), 183 (53), 144 (61), 132 (100); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{28}\text{O}$ 344.2140, found 344.2133.

(*E*)-7-(*p*-Chlorophenyl)-1-(5*ċ*-phenylpent-4*ċ*-enyl)bicyclo[3.1.1]heptan-6-one (24c) and (*E*)-1-[5*ċ*-(*p*-chlorophenyl)pent-4*ċ*-enyl]-7-phenylbicyclo[3.1.1]heptan-6-one (25c). Following the procedure used to form **5**, **23c** (85 mg, 0.22 mmol) was treated with oxalyl chloride (100 μL , 1.1 mmol) in toluene (2 mL) then with Et_3N (190 μL , XX mol) in toluene (10 mL) to give a 1.0:1.3 mixture of **24c** and **25c** determined by ^1H NMR on the crude material. After purification by flash chromatography (19:1 hexanes– EtOAc), 47 mg (56 %) an inseparable mixture of **24c** and **25c** was obtained as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.36 – 7.06 (m, 9H), 6.22 (d, $J=15.5$ Hz, 1H **25c**), 6.14 (d, $J=16.0$ Hz, 1H, **24c**), 5.95 – 5.81 (m, 2H), 3.17 (t, $J=3.5$ Hz, 1H **25c**), 3.12 (t, $J=3.5$ Hz, 1H **24c**), 3.05 (s, 1H **25c**), 3.02 (s, 1H **24c**), 2.54 – 2.43 (m, 3H), 2.29 – 2.21 (m, 1H), 2.01 – 1.64 (m, 4H), 1.50 – 1.09 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 216.0, 215.5, 140.1, 138.8, 137.6, 136.2, 132.5, 132.3, 131.0, 130.2, 130.0, 128.8, 128.6, 128.4, 127.5, 127.1, 126.8, 126.7, 125.8, 70.8, 70.6, 60.6, 60.4, 48.0, 47.4, 40.0, 35.6, 33.1, 28.8, 22.7, 18.3; IR (film) ν 3033, 2937, 2860, 1770, 1483, 1452, 1085, 970, 842, 736, 697 cm^{-1} ; MS (EI) m/z 364 (47) [M^+], 273 (12), 239 (20), 200 (35), 169 (70), 130 (100); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{25}\text{ClO}$ 364.1594, found 364.1601.

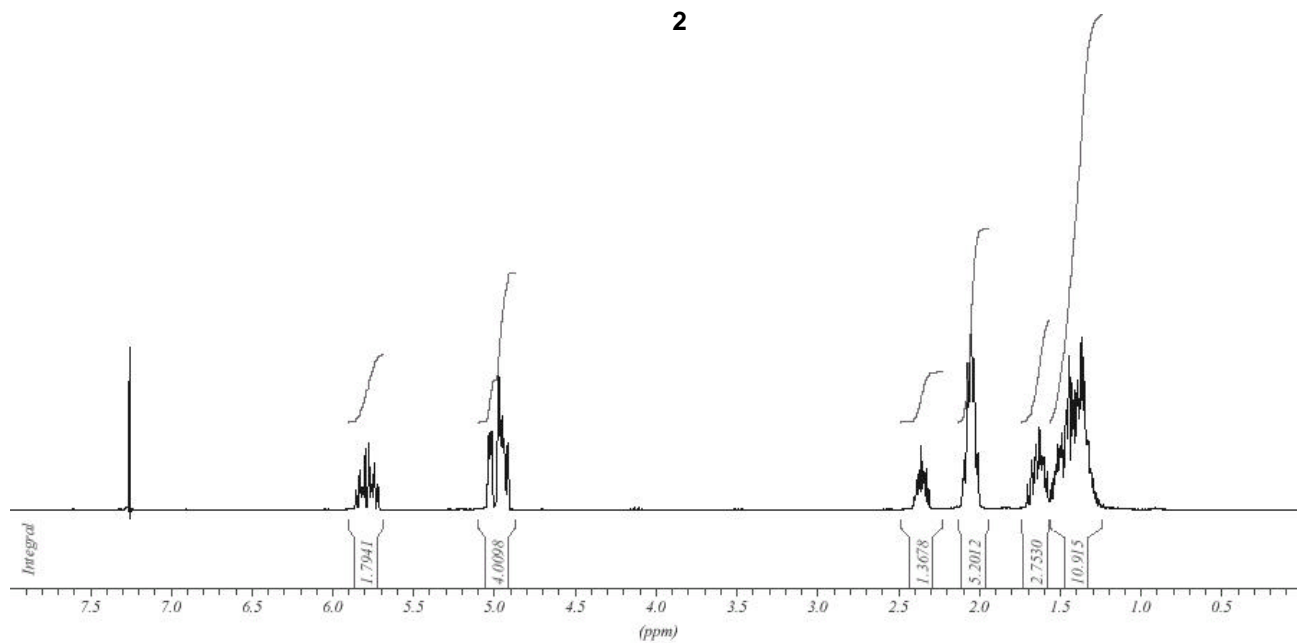
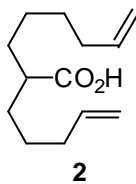
(*E*)-1-(5*ċ*-Phenylpent-4*ċ*-enyl)-7-(*p*-trifluoromethylphenyl)bicyclo[3.1.1]heptan-6-one (24d) and (*E*)-7-phenyl-1-[5*ċ*-(*p*-trifluoromethylphenyl)pent-4*ċ*-enyl]bicyclo[3.1.1]heptan-6-one (25d). Following the procedure used to form **5**, **23d** (42 mg, 0.1 mmol) was treated with oxalyl chloride (44 μL , 0.5 mmol) in toluene (1 mL) then with Et_3N (84 μL , 0.6 mol) in toluene (2 mL) to give a 1.0:4.1 mixture of **24d** and **25d** determined by ^1H NMR on the crude material. After purification by flash chromatography (19:1 hexanes– EtOAc), 15 mg (38 %) an inseparable mixture of **24d** and **25d** was obtained as a colorless

oil: ^1H NMR (300 MHz, CDCl_3) δ 7.55-7.49 (m, 2H), 7.39-7.12 (m, 7H), 6.21 (d, $J=15.5$ Hz, 1H), 5.97 (dt, $J=16.0$ Hz, 7.5 Hz, 1H), 3.18 (t, $J=3.5$ Hz, 2H), 3.11 (s, 1H 24c), 3.04 (s, 1H 25c), 2.55-2.43 (m, 3H), 2.31-2.22 (m, 1H), 2.04-1.88 (m, 3H), 1.80-1.33 (m, 2H), 1.30-1.08 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 216.0, 141.1, 140.1, 133.1, 129.9, 128.9, 128.4, 127.9, 127.5, 126.8, 126.7, 126.0, 125.8, 125.3, 70.5, 60.4, 48.0, 47.9, 40.1, 34.6, 33.1, 29.7, 28.8, 22.8, 22.5, 18.3; IR (film) ν 3098, 2935, 2865, 1761, 1615, 1319, 1165, 1121, 1068 cm^{-1} ; MS (EI) m/z 398 (24) [M^+], 169 (41), 129 (67), 118 (100), 91 (54); HRMS (EI) calcd for $\text{C}_{25}\text{H}_{25}\text{F}_3\text{O}_2$ 398.1857, found 398.1865.

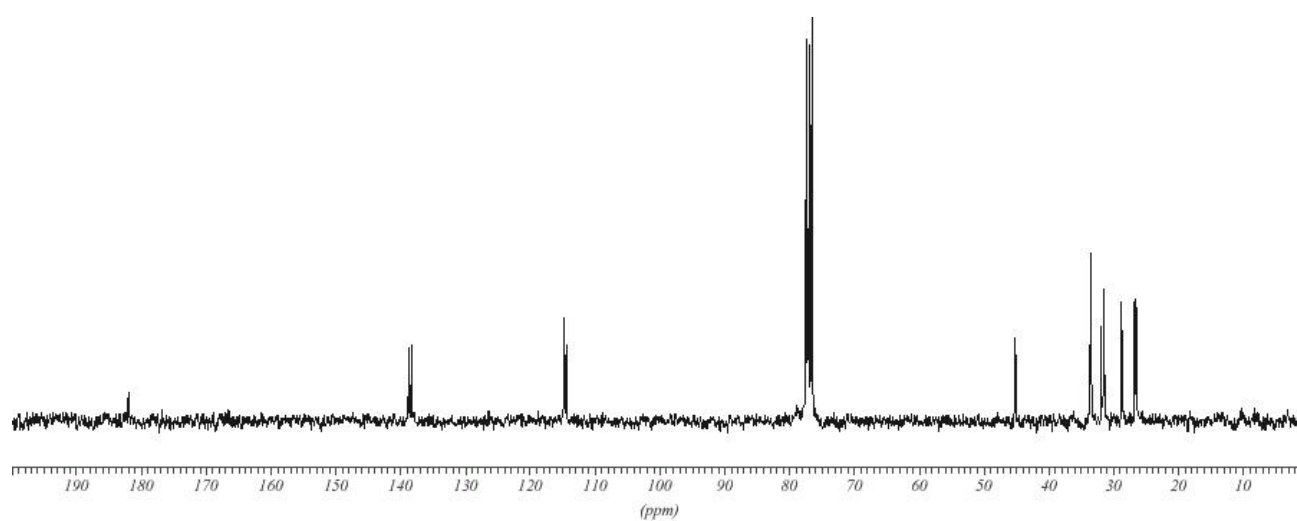
(*E*)-7-(*p*-Nitrophenyl)-1-(5*c*-phenylpent-4*c*-enyl)bicyclo[3.1.1]heptan-6-one (24e) and (*E*)-1-[5*c*-(*p*-nitrophenyl)pent-4*c*-enyl]-7-phenylbicyclo[3.1.1]heptan-6-one (25e). Following the procedure used to form **5**, **23e** (210 mg, 0.53 mmol) was treated with oxalyl chloride (230 μL , 2.6 mmol) in toluene (2 mL) then with Et_3N (450 μL , 3.2 mol) in toluene (10 mL) to give a 1.0:9.0 mixture of **24e** and **25e** determined by ^1H NMR on the crude material. After purification by flash chromatography (19:1 hexanes–EtOAc), 12 mg (6 %) of **24e** and 116 mg (58 %) of **25e** were obtained as a yellow oil. **24e**: ^1H NMR (300 MHz, CDCl_3) δ 7.32 – 7.16 (m, 9H), 6.18 (d, $J=15.5$ Hz, 1H), 5.85 (dt, $J=15.5$, 7.0 Hz, 1H), 3.20 – 3.12 (m, 1H), 3.16 (s, 1H), 2.55 – 2.46 (m, 3H), 2.34 – 2.25 (m, 1H), 2.05 – 1.68 (m, 4H), 1.58 – 1.07 (m, 4H); IR (film) ν 3024, 2933, 2865, 1765, 1597, 1514, 1341, 856, 750, 692 cm^{-1} ; MS (EI) m/z 375 (13) [M^+], 245 (64), 130 (100), 118 (77), 91 (69); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{25}\text{NO}_3$ 375.1834, found 375.1841. **25e**: ^1H NMR (300 MHz, CDCl_3) δ 8.12 (d, $J=8.5$ Hz, 2H), 7.23 – 7.12 (m, 7H), 6.24 (d, $J=16.0$, 1H), 6.05 (dt, $J=16.0$, 6.5 Hz, 1H), 3.18 – 3.15 (m, 1H), 3.05 (s, 1H), 2.55 – 2.42 (m, 3H), 2.30 – 2.21 (m, 1H), 2.05 – 1.87 (m, 3H), 1.75 – 1.63 (m, 1H), 1.51 – 1.44 (m, 1H), 1.29 – 1.08 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 215.9, 146.4, 144.2, 140.1, 136.2, 135.7, 129.2, 128.4, 127.5, 127.2, 126.7, 126.4, 123.8, 123.4, 70.5, 66.4, 48.0, 40.0, 34.6, 33.2, 29.1, 28.8, 22.3, 18.3; IR (film) ν 3033, 2937, 2865, 1761, 1593, 1518, 1337, 732, 701 cm^{-1} ; MS (EI) m/z 375 (15) [M^+], 169 (29), 141 (18), 129 (47), 118 (100), 91 (71); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{25}\text{NO}_3$ 375.1834, found 375.1841.

III ^1H and ^{13}C -NMR Spectra of Compounds 2, 5, 7, 8, 10, 11, 14, 16, 17, 19, 20, 22b–25.

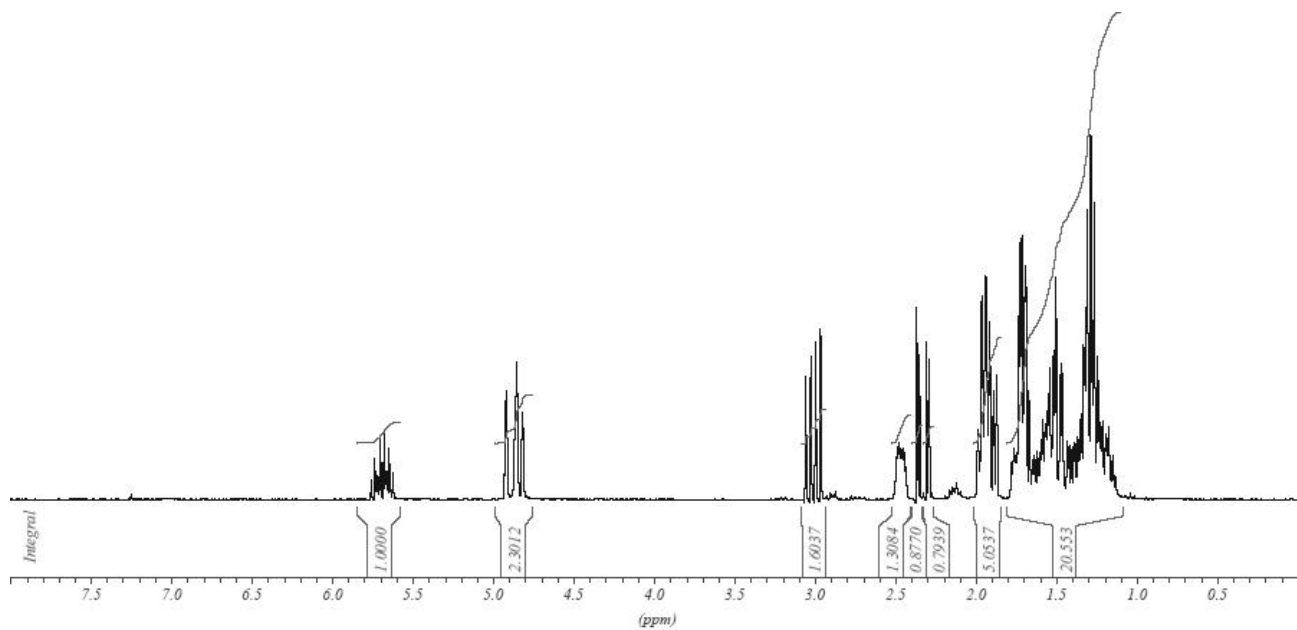
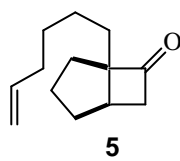
RMN ^1H spectrum



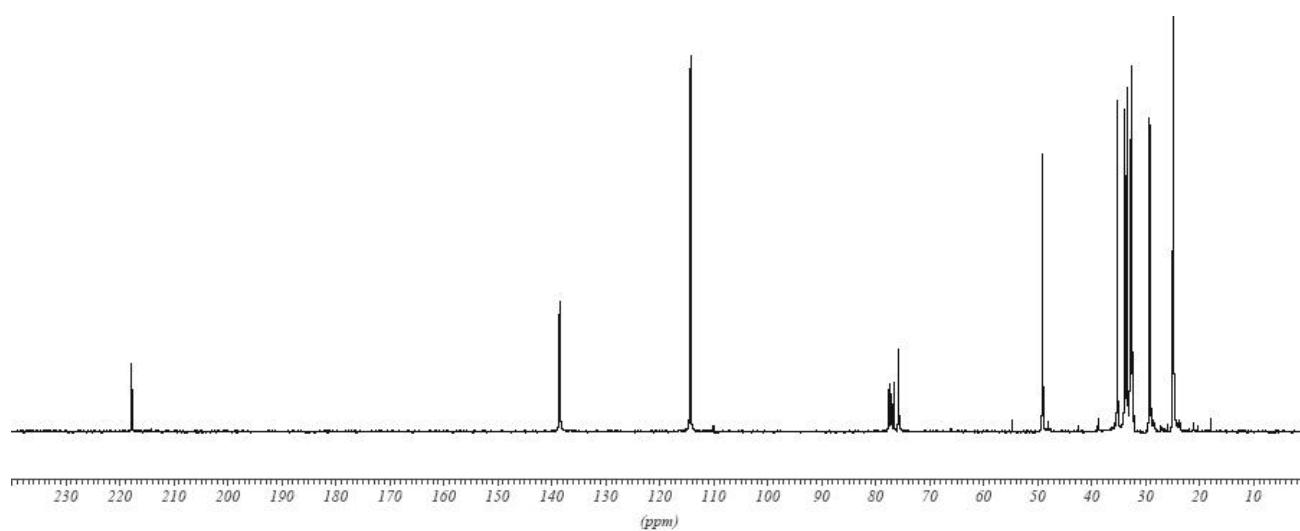
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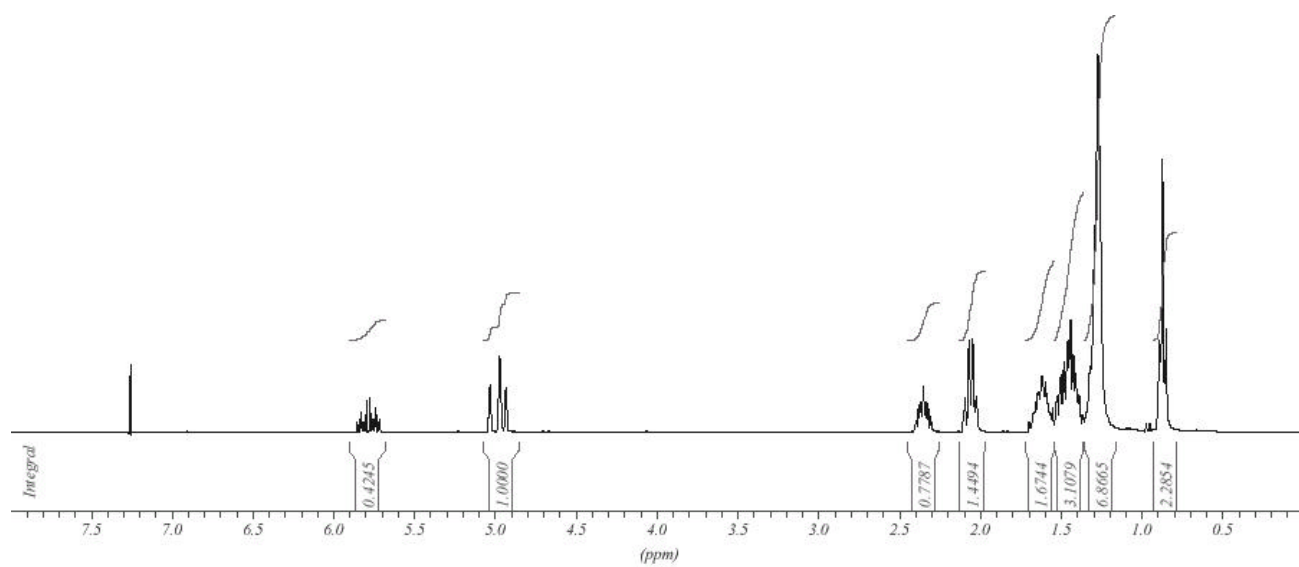
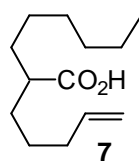
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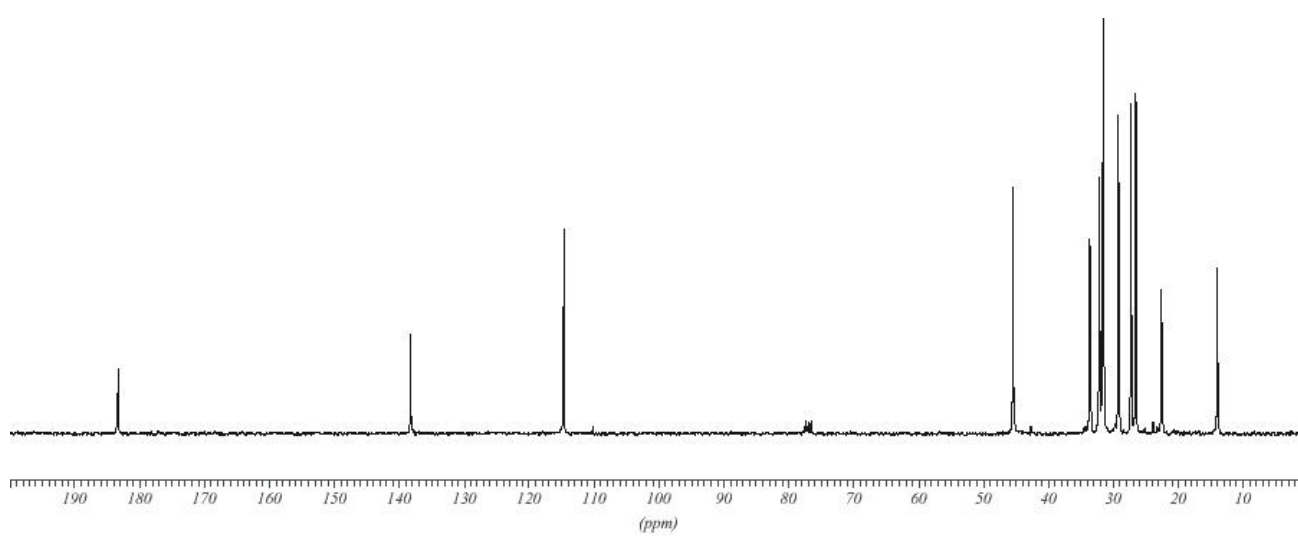
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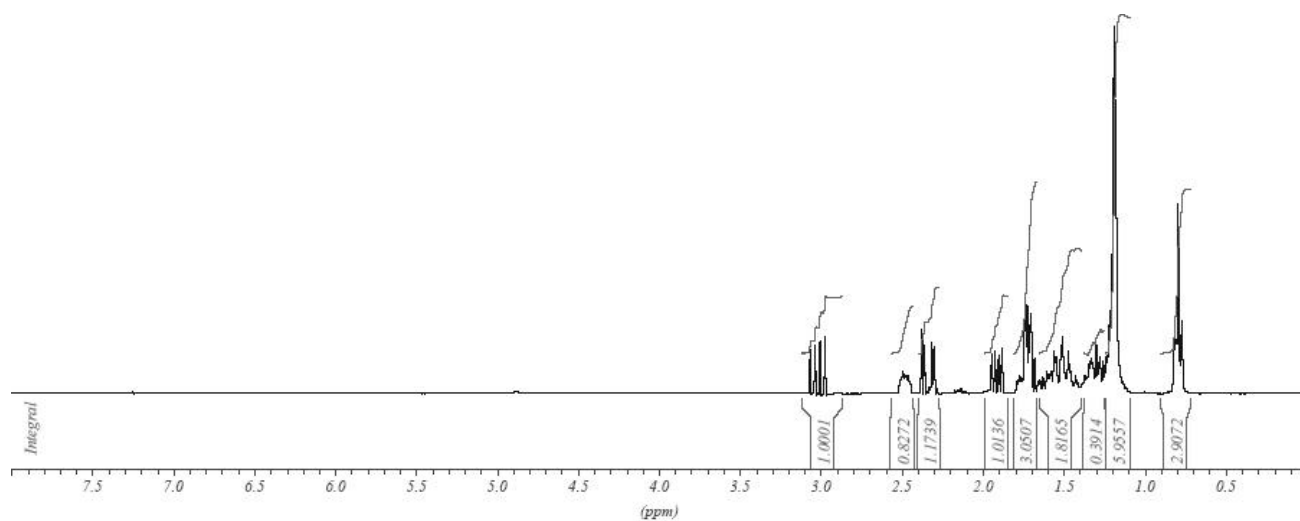
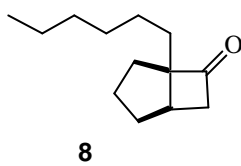
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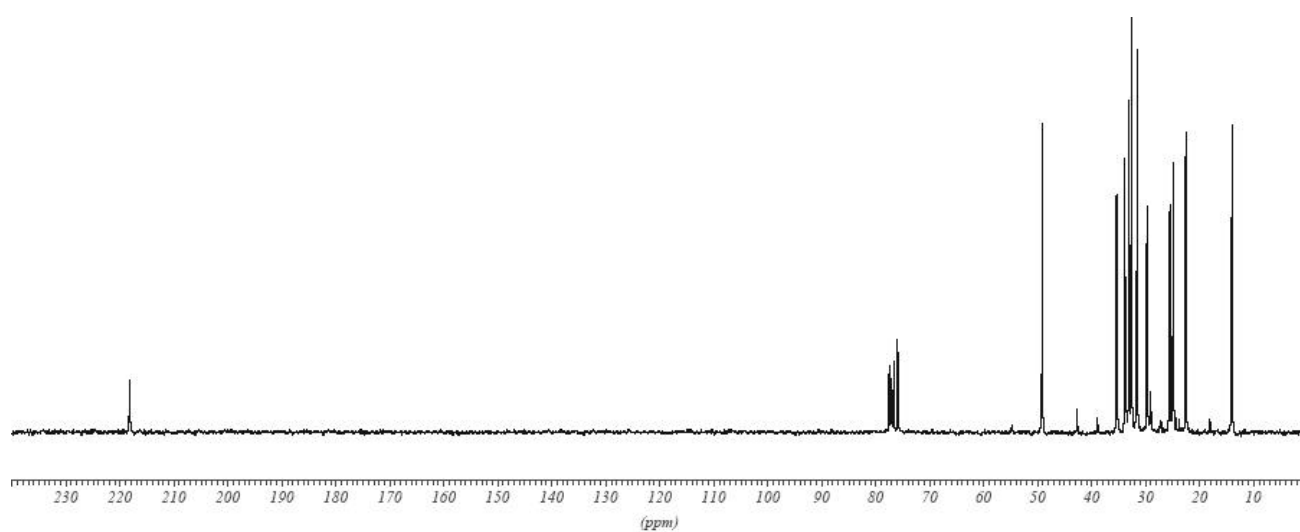
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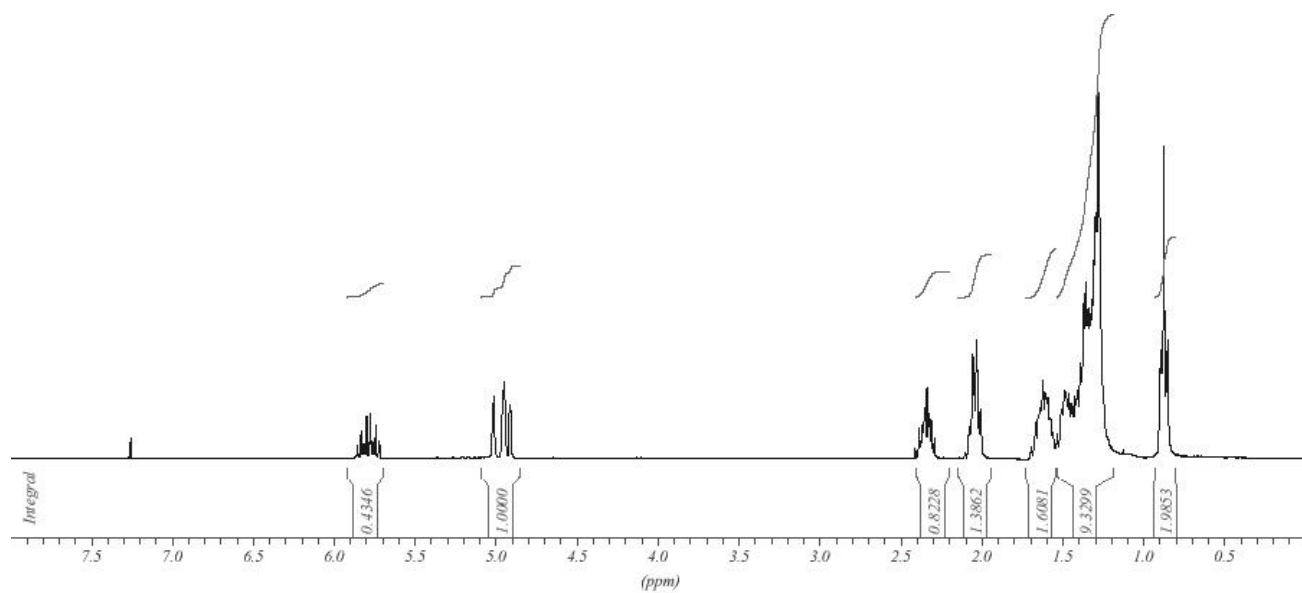
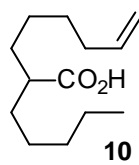
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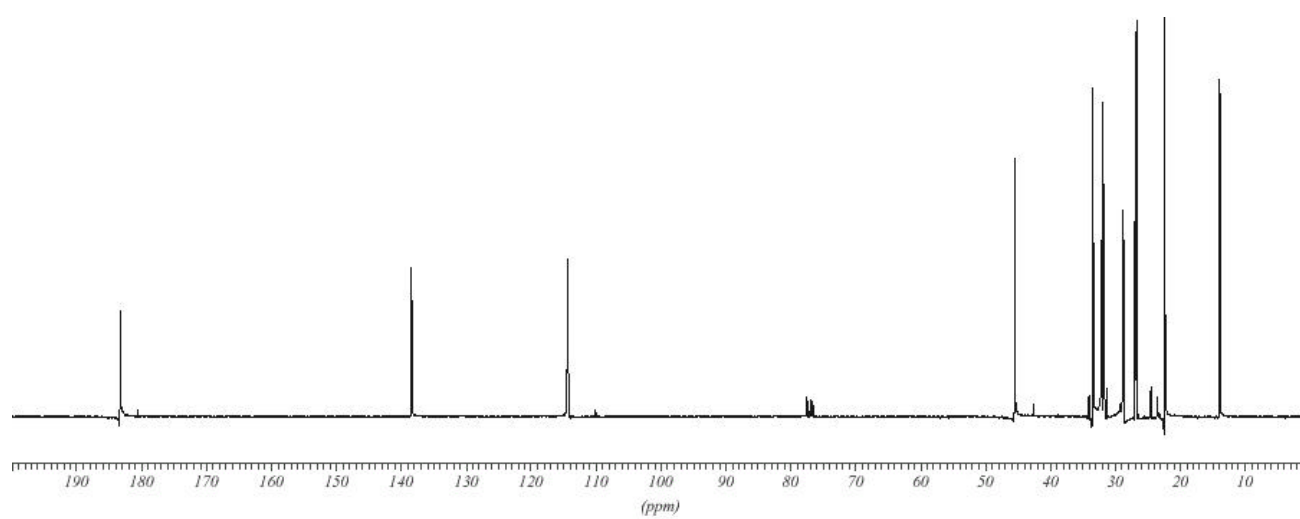
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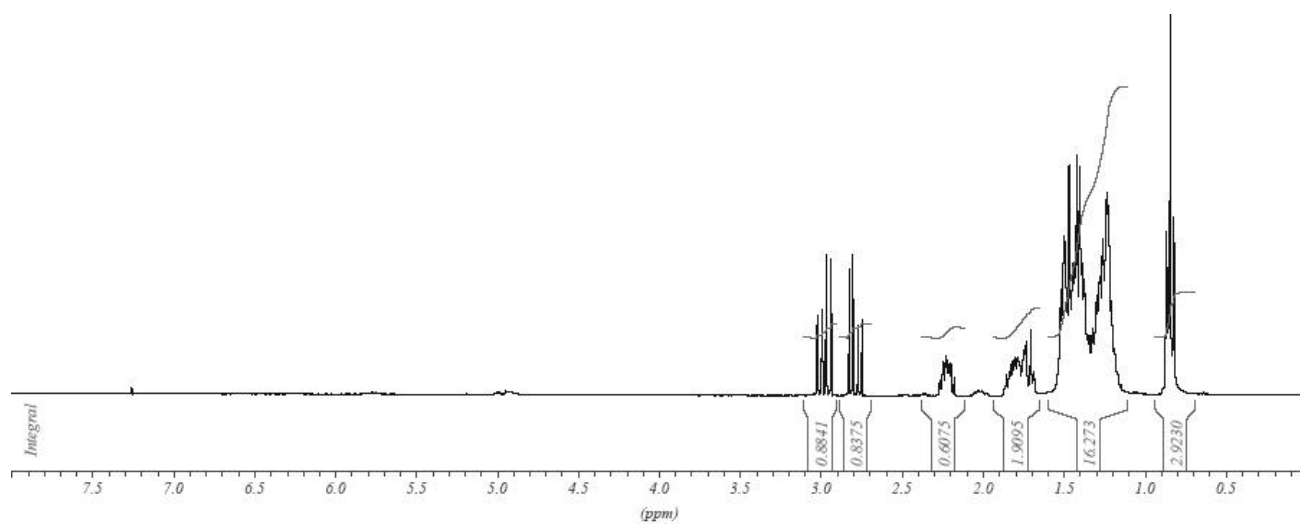
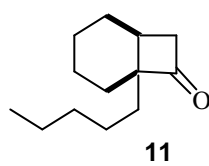
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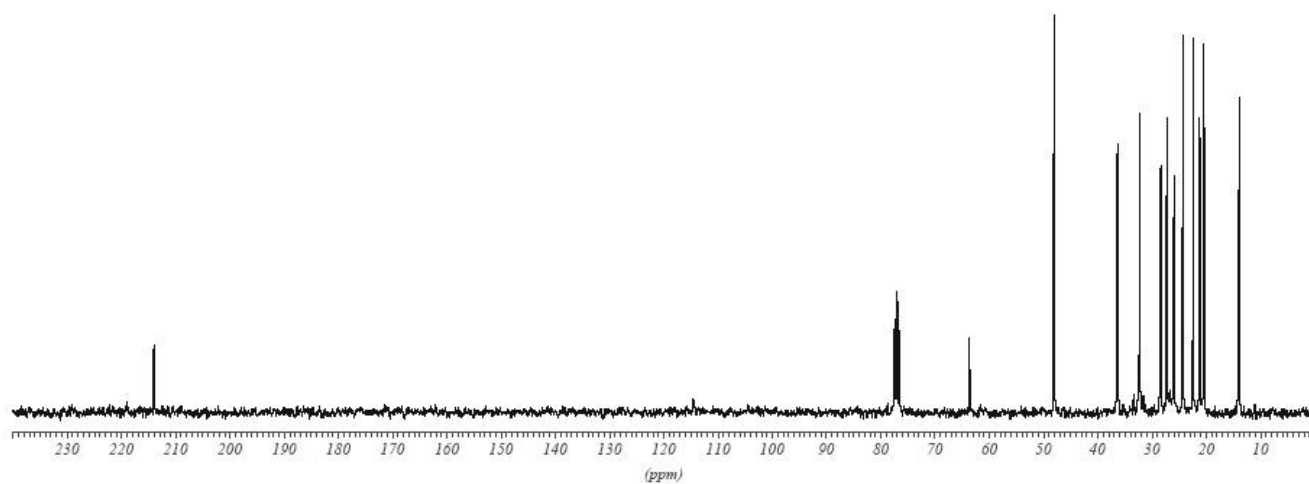
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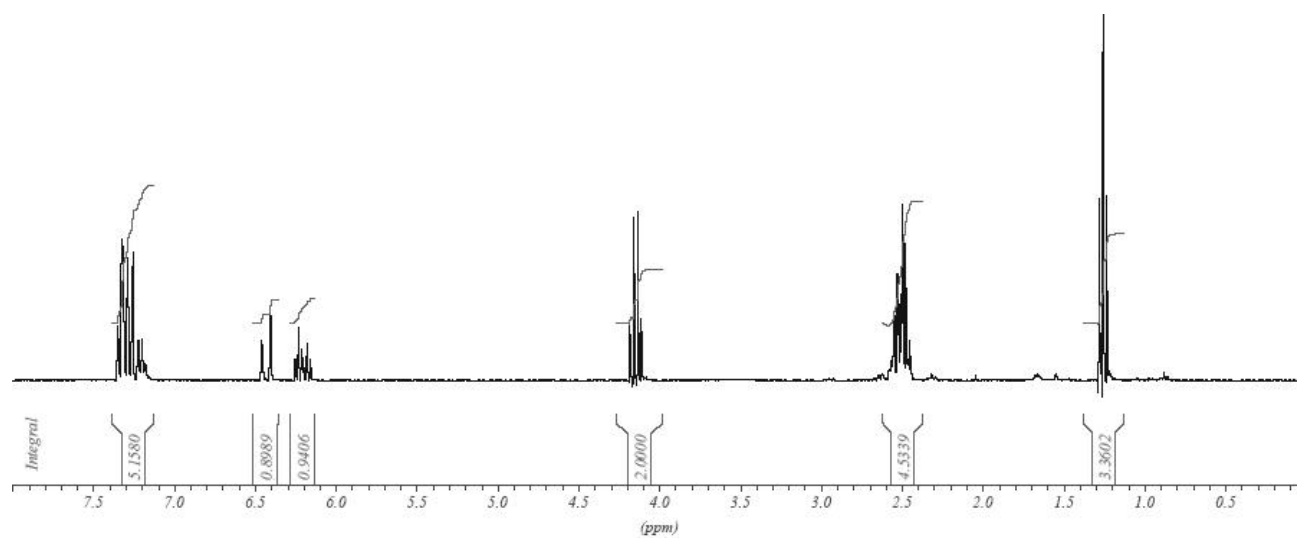
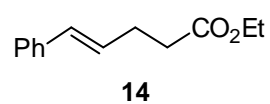
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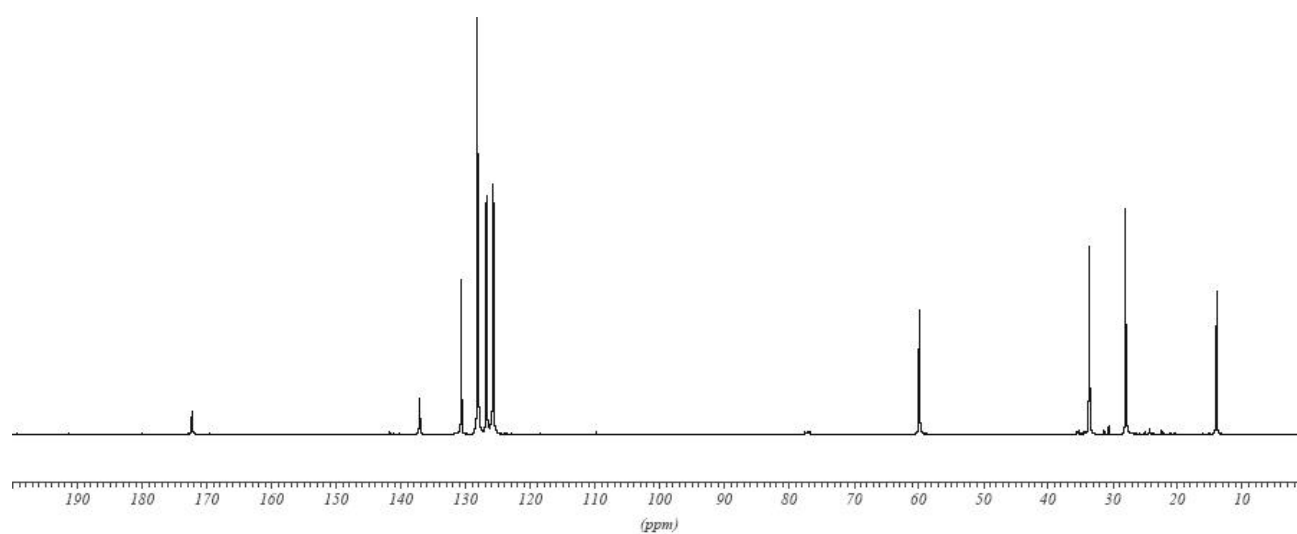
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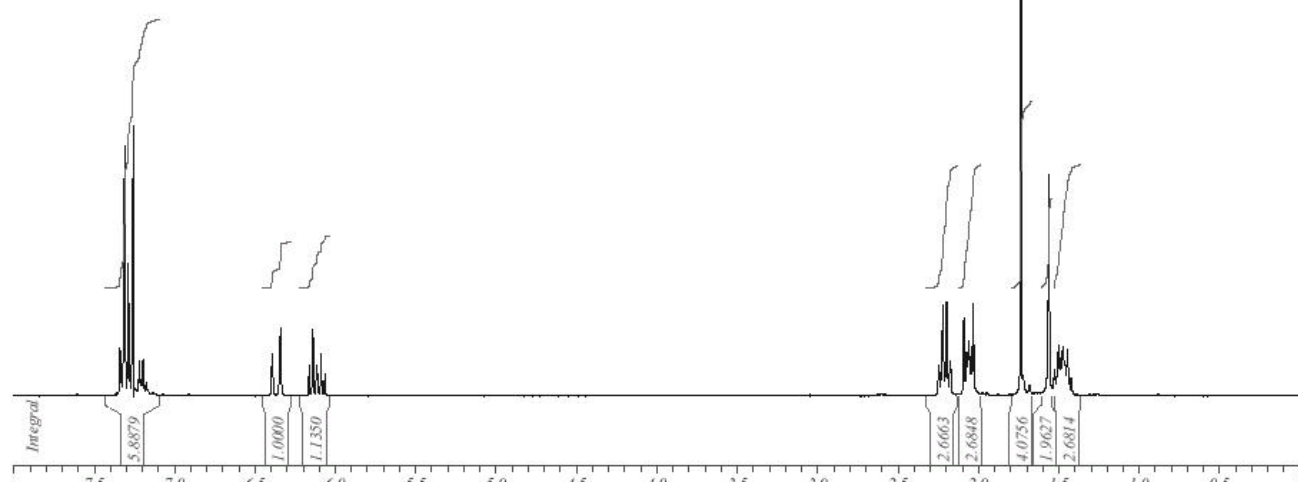
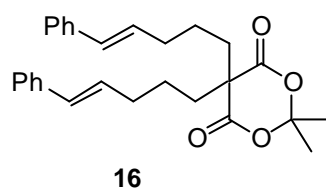
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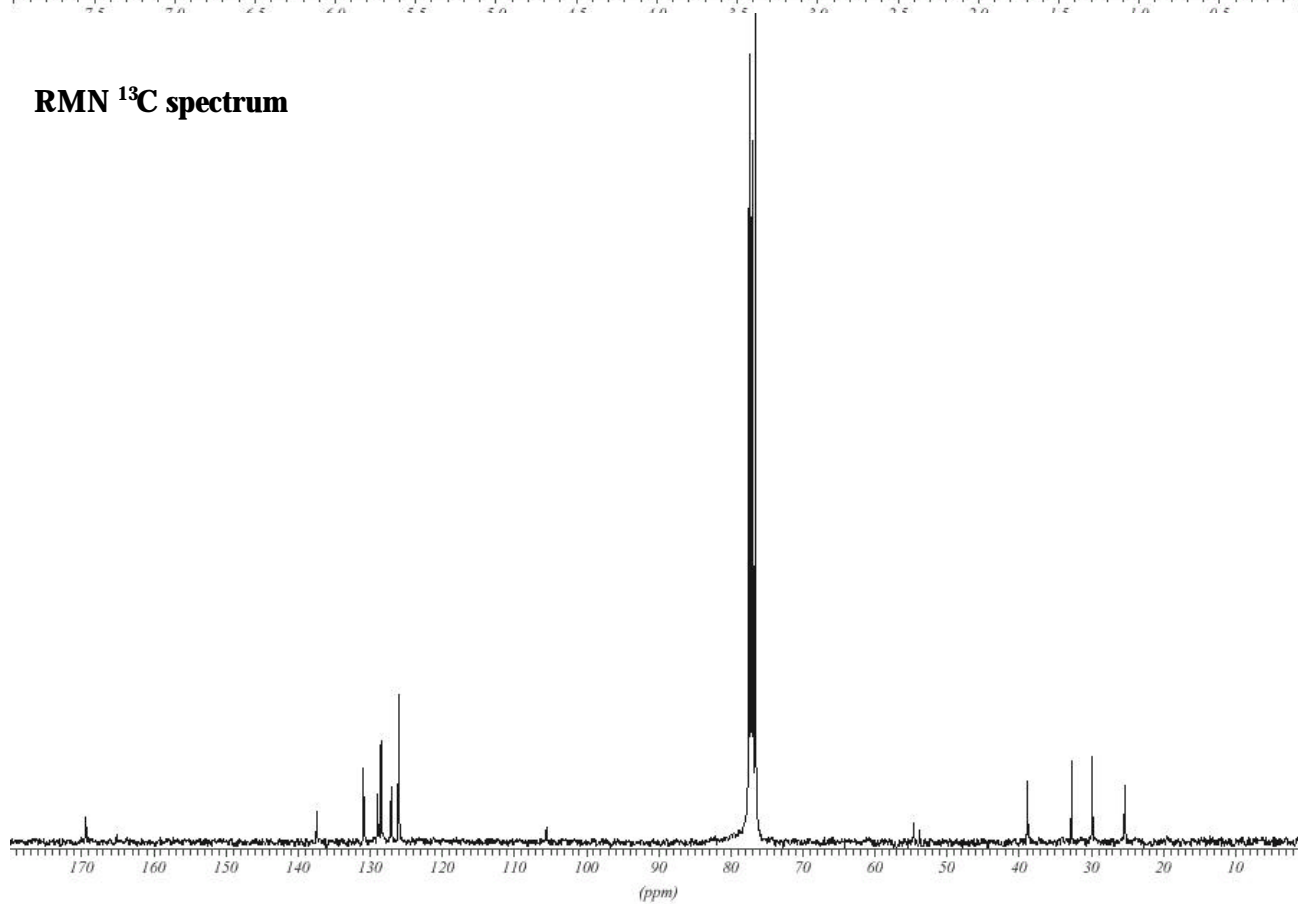
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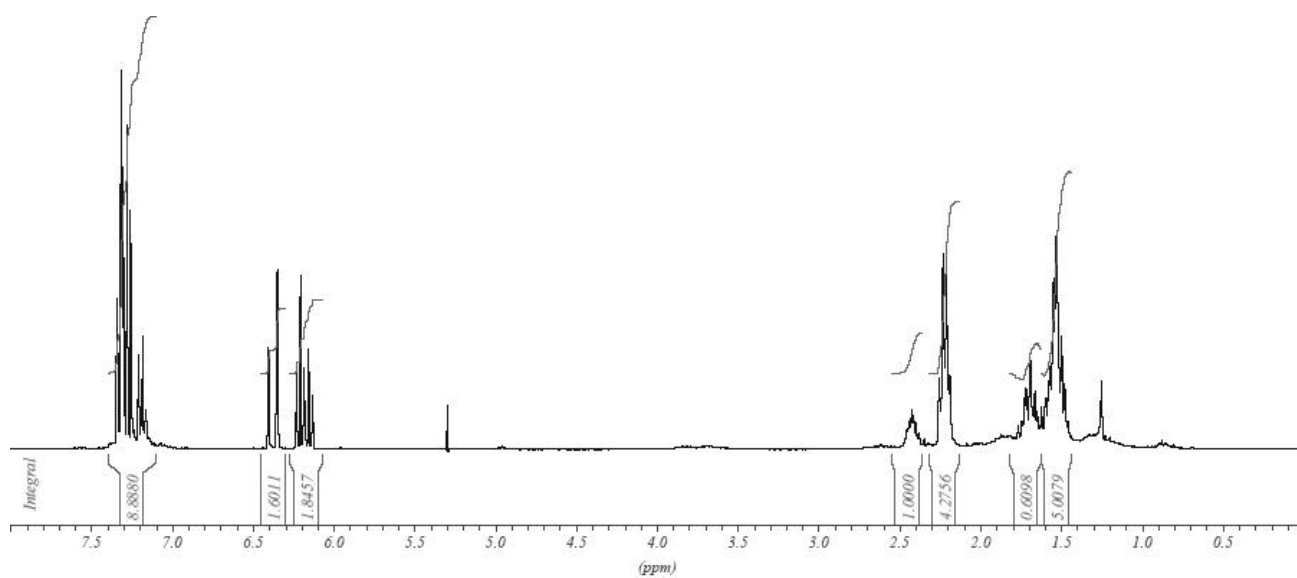
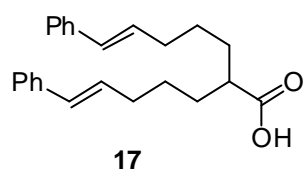
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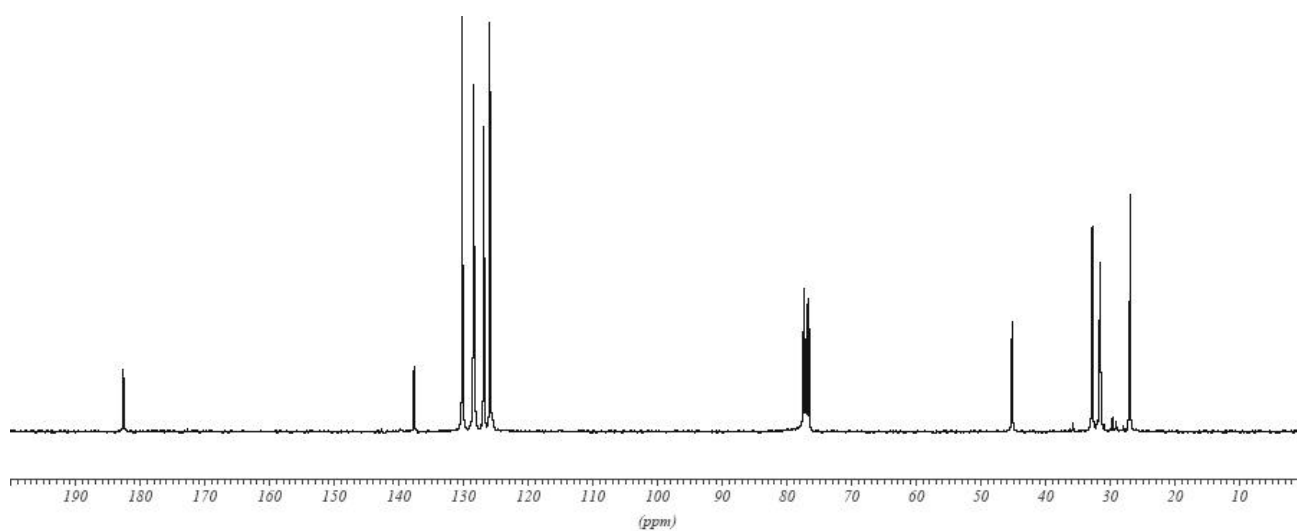
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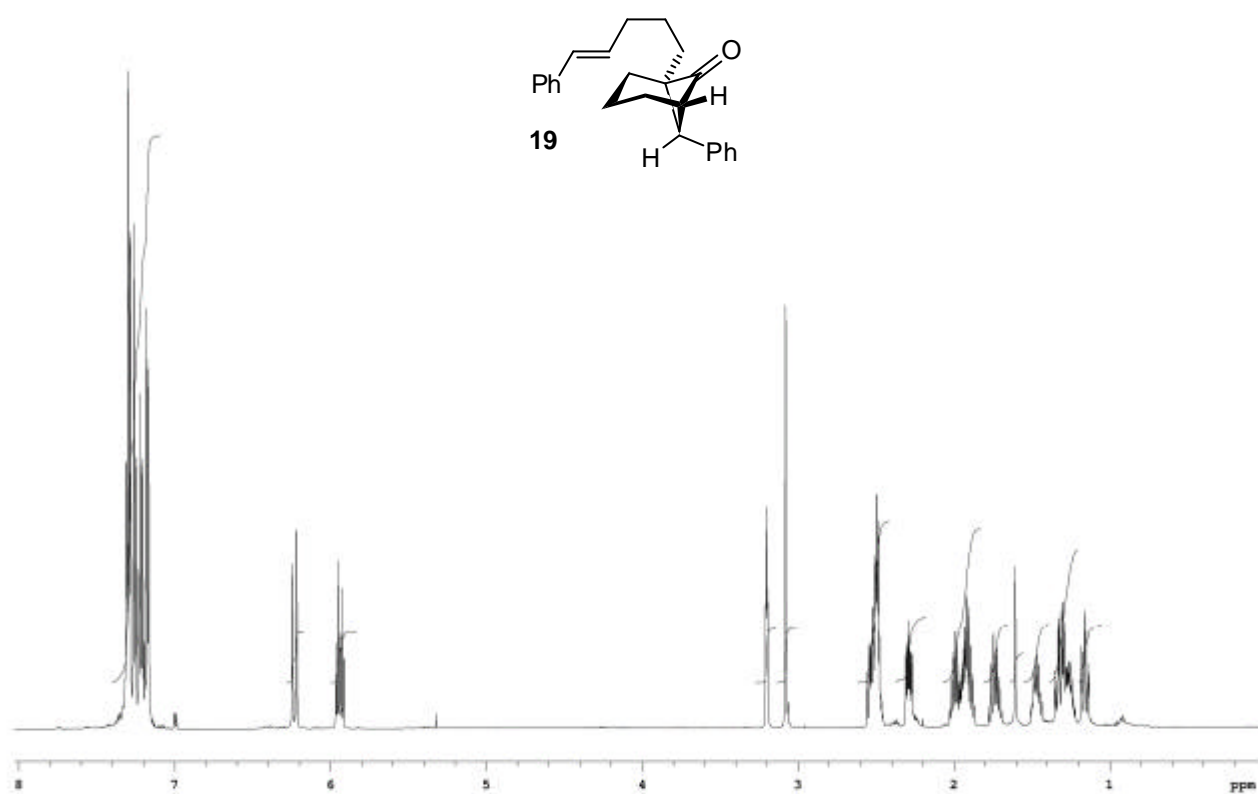
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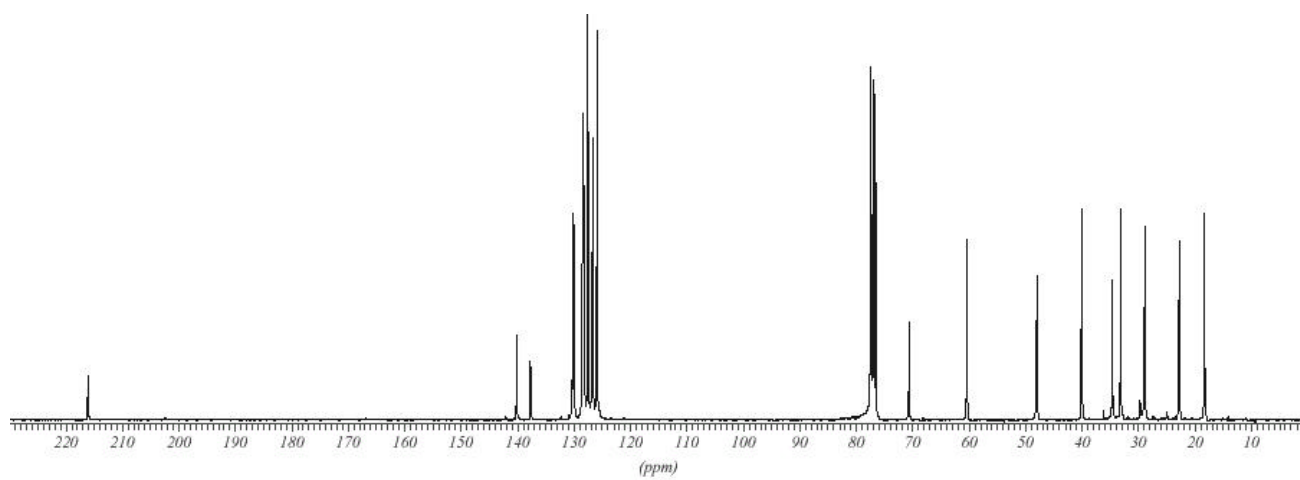
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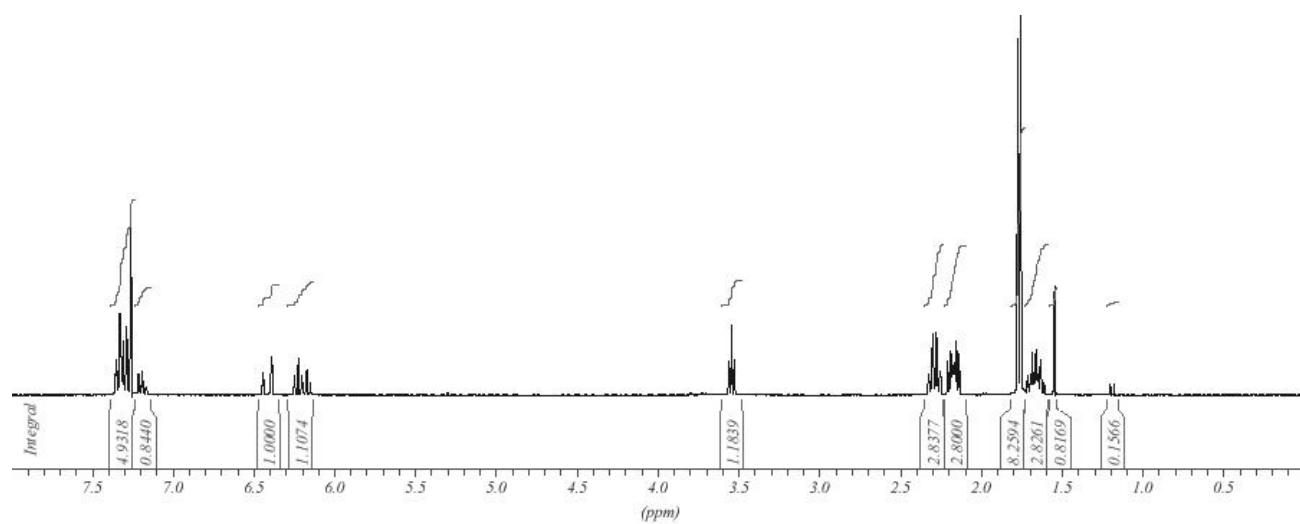
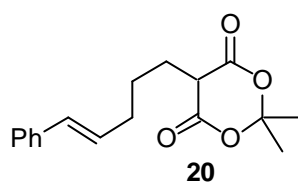
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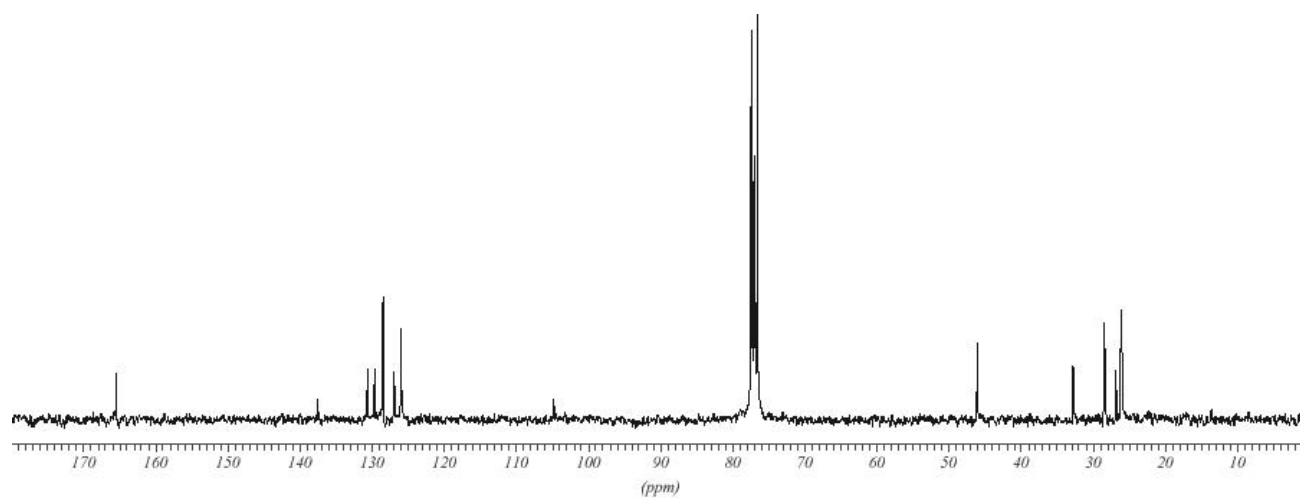
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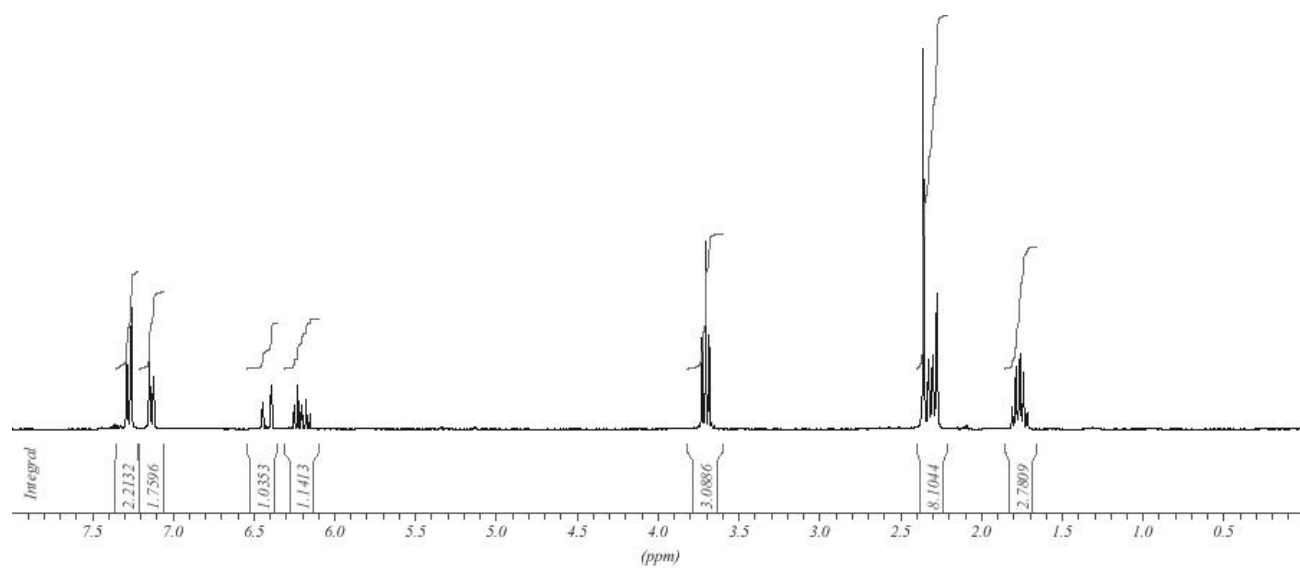
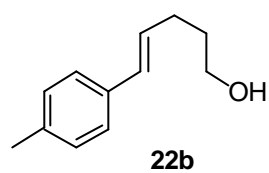
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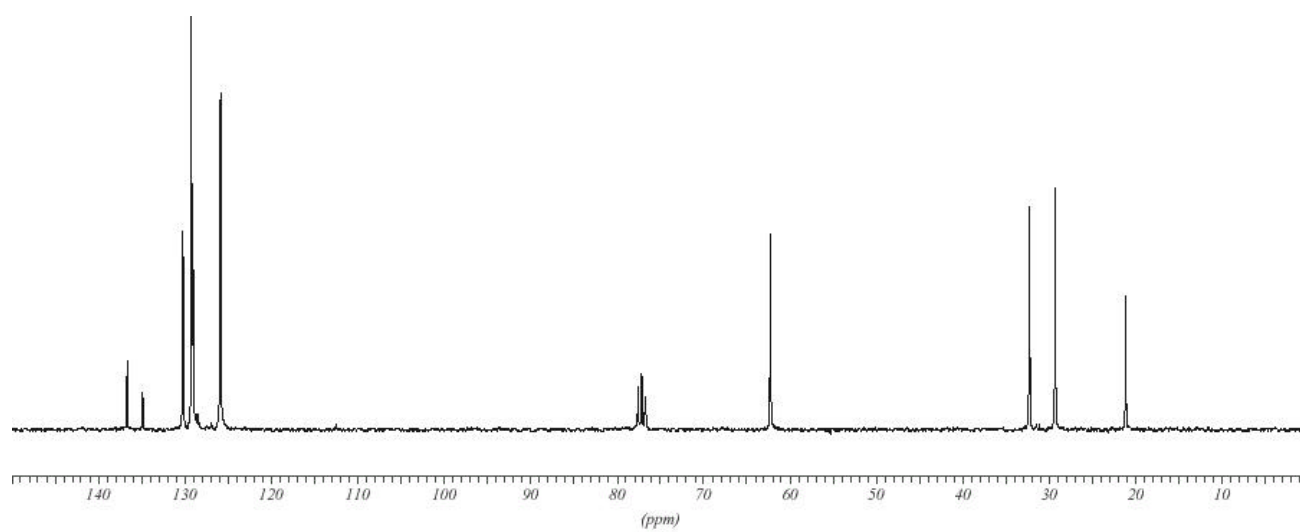
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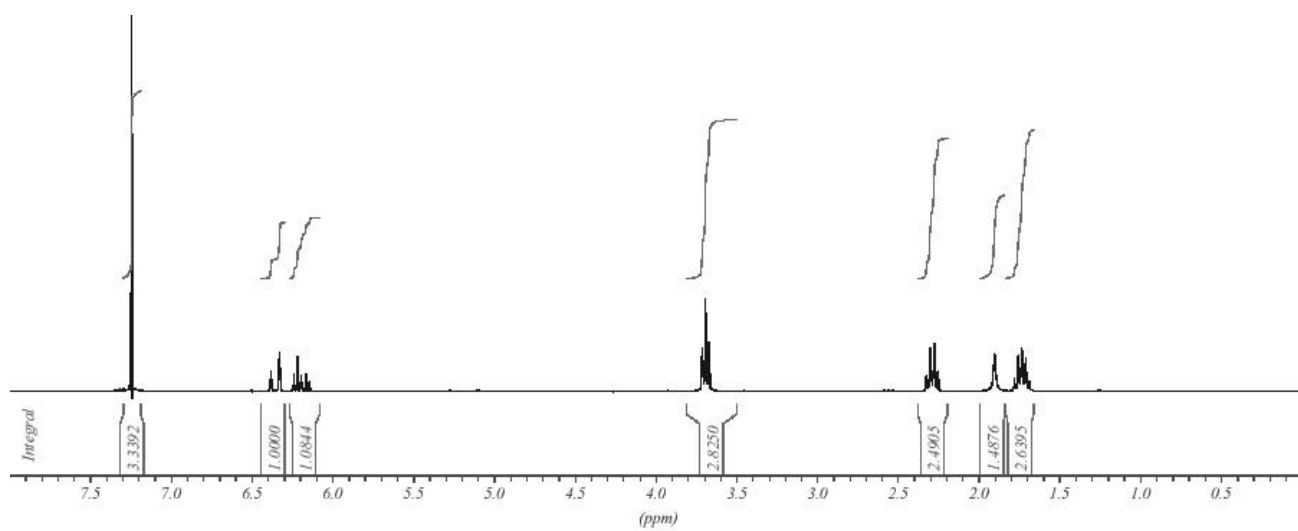
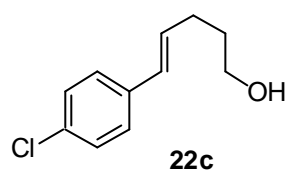
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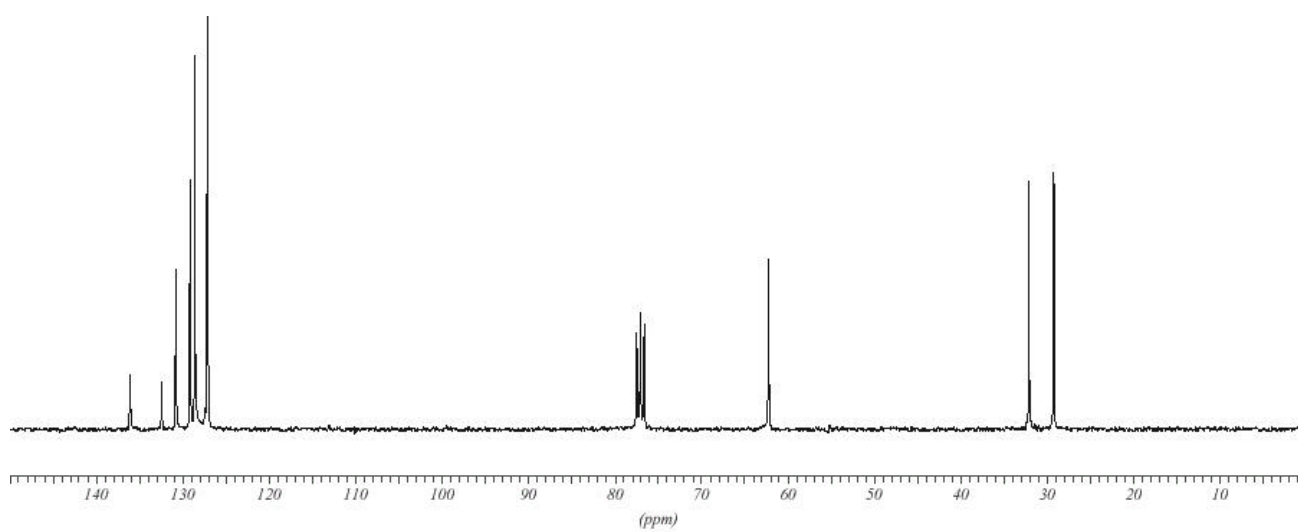
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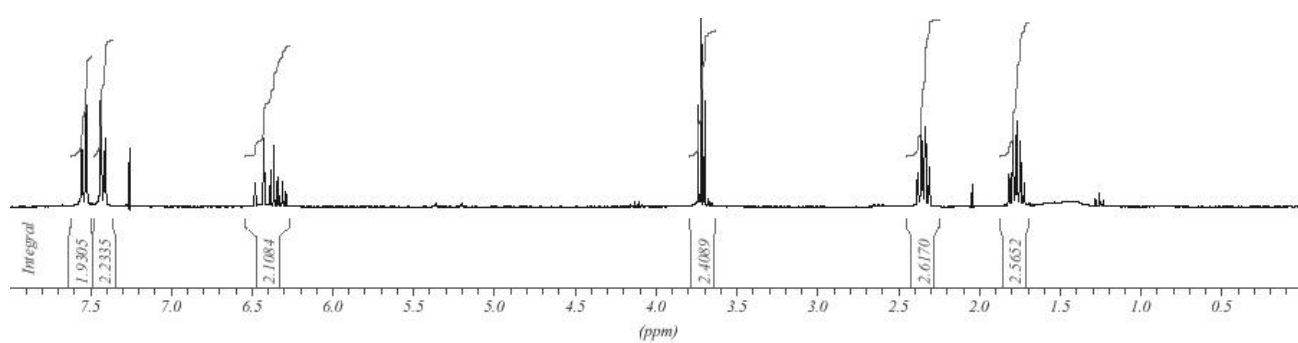
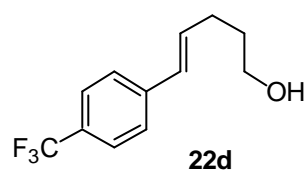
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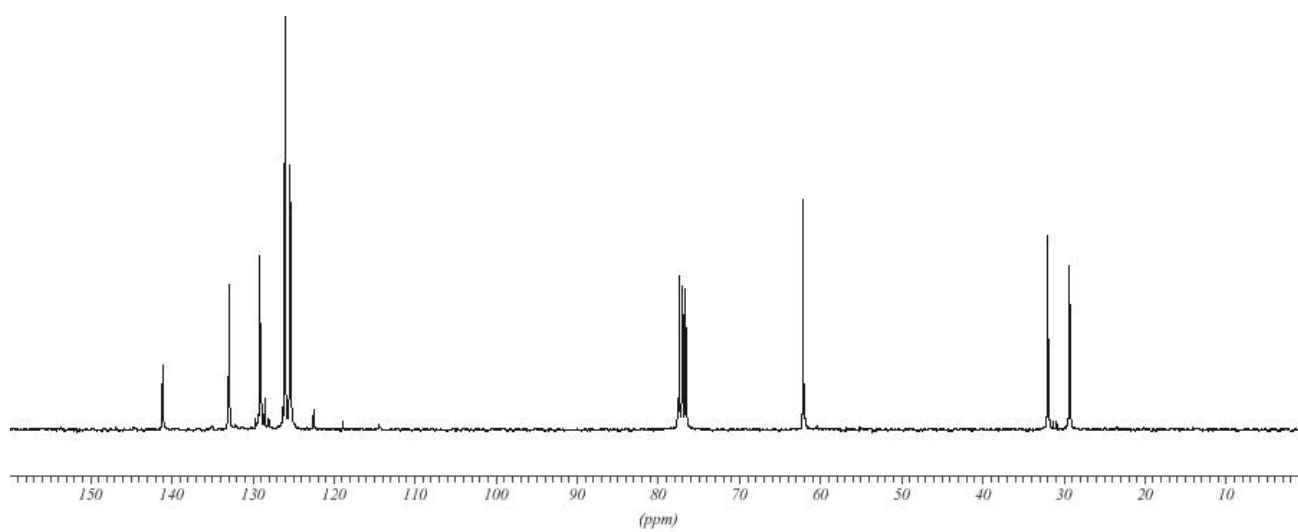
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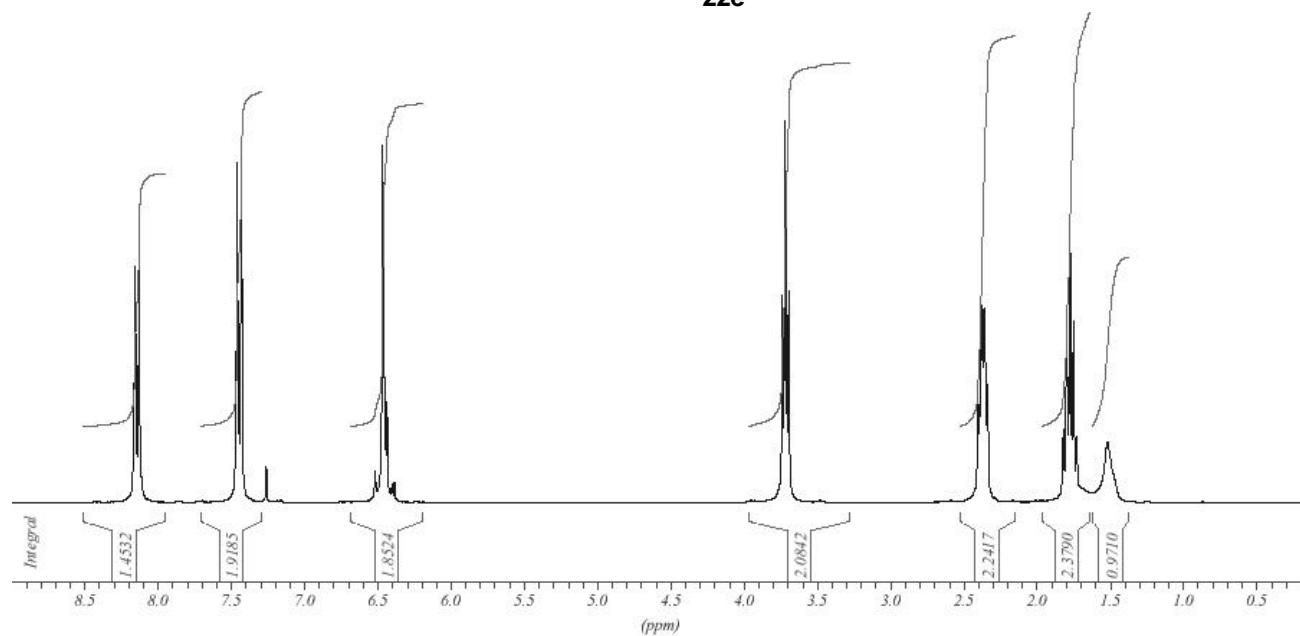
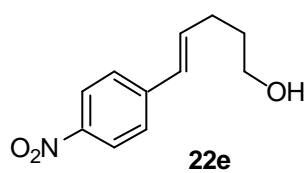
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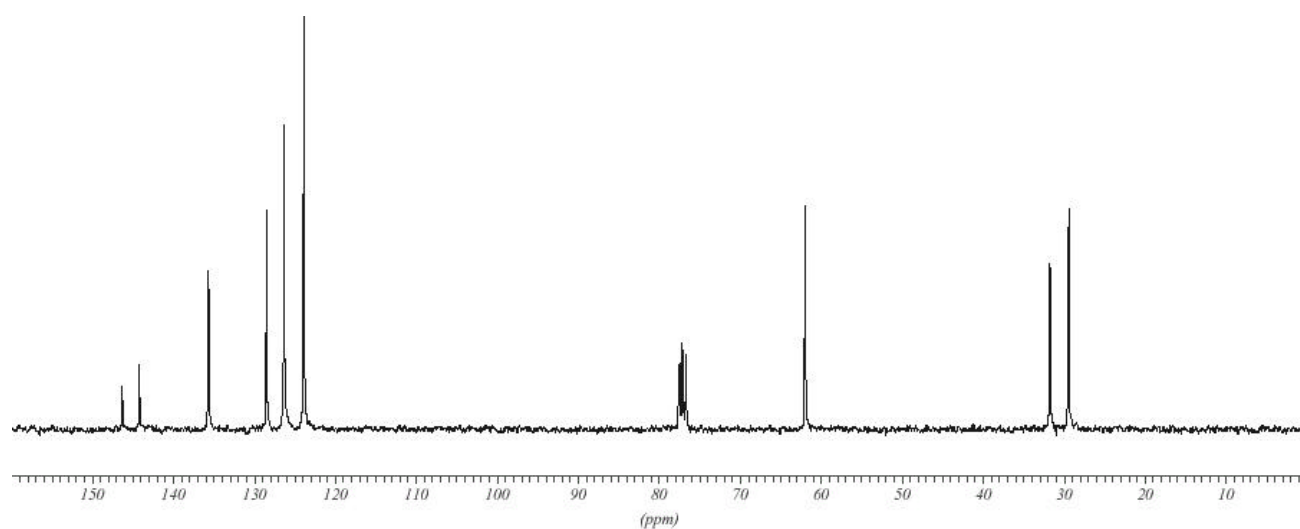
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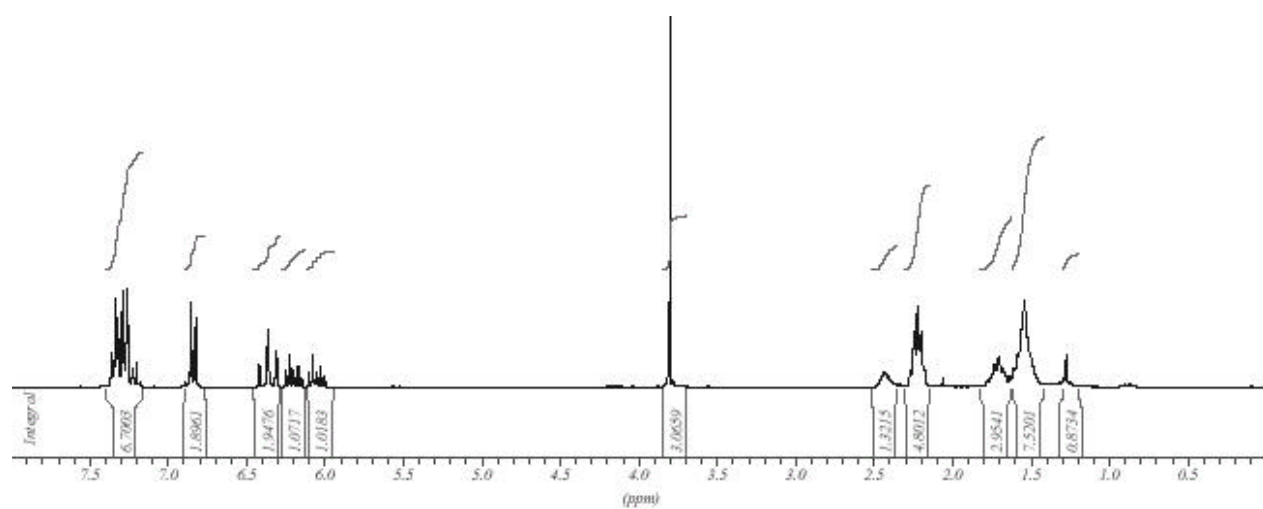
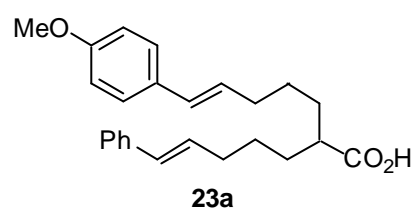
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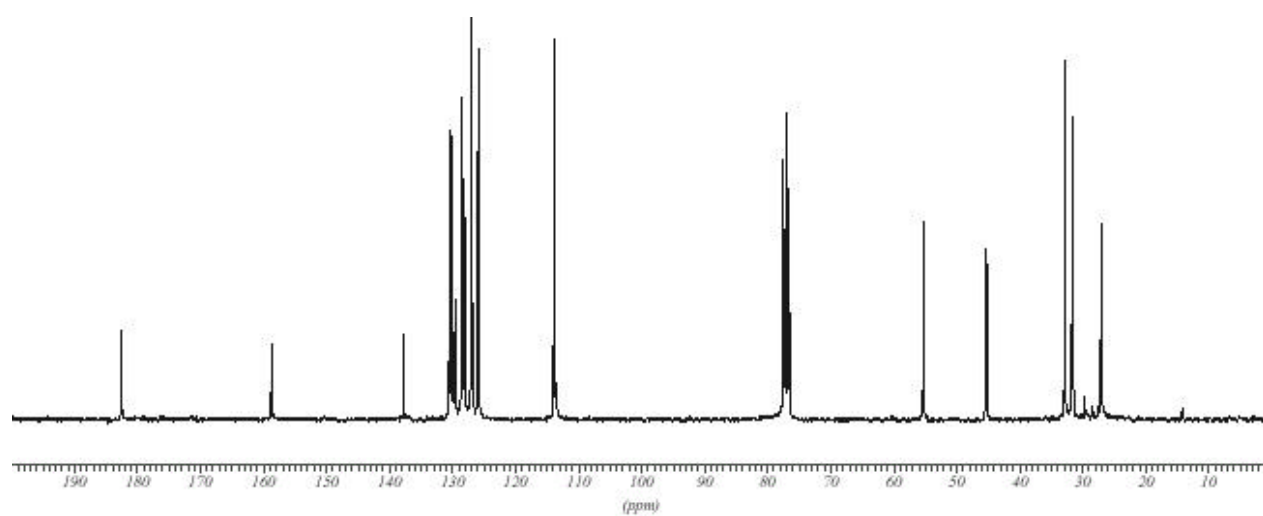
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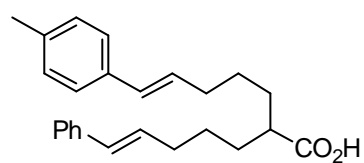
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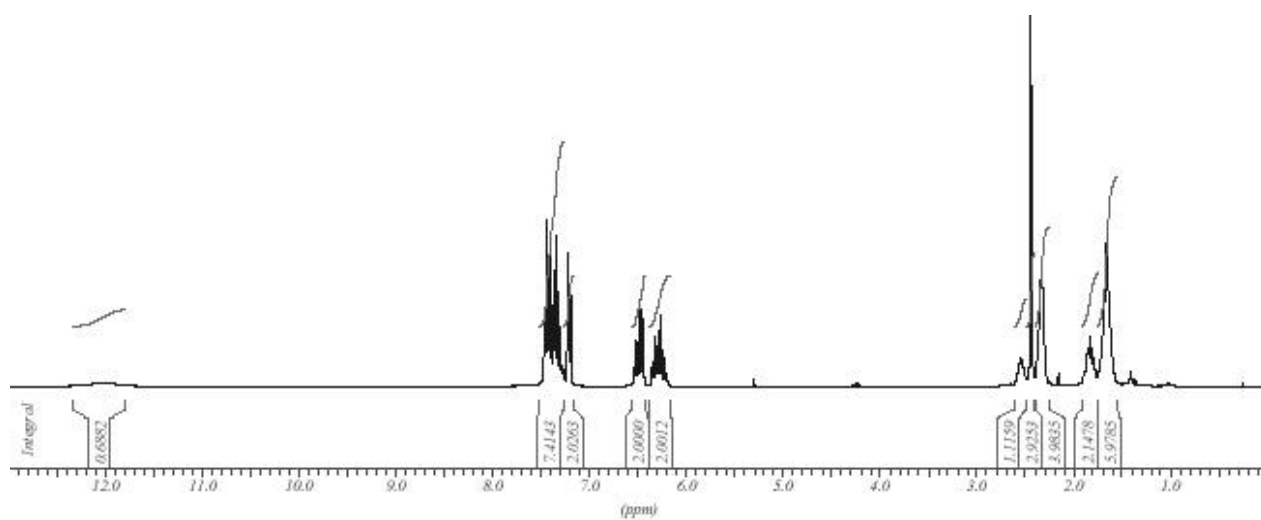
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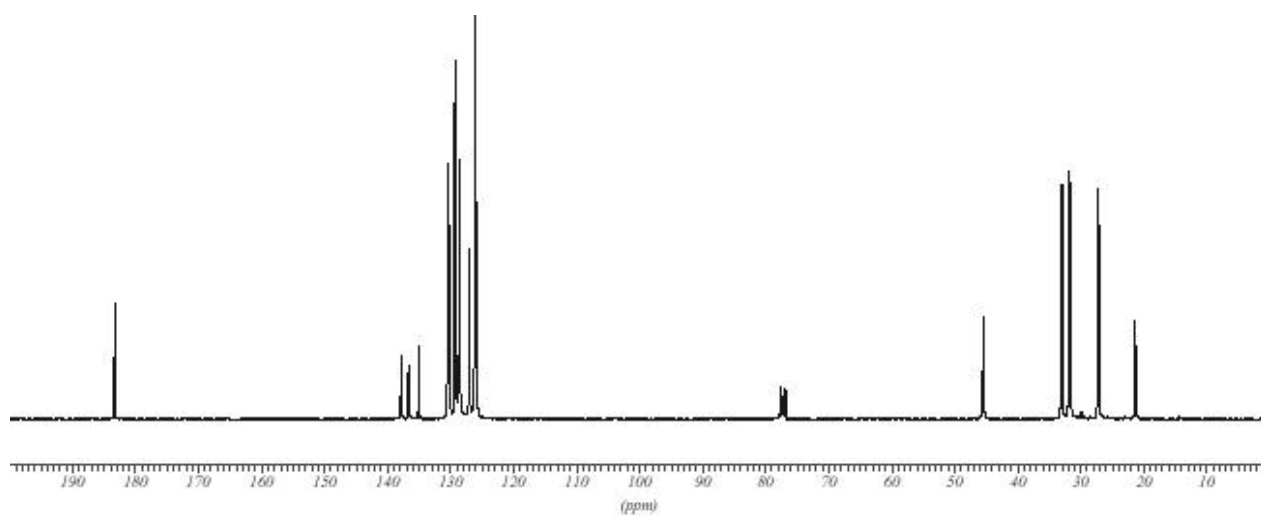
RMN ^1H spectrum



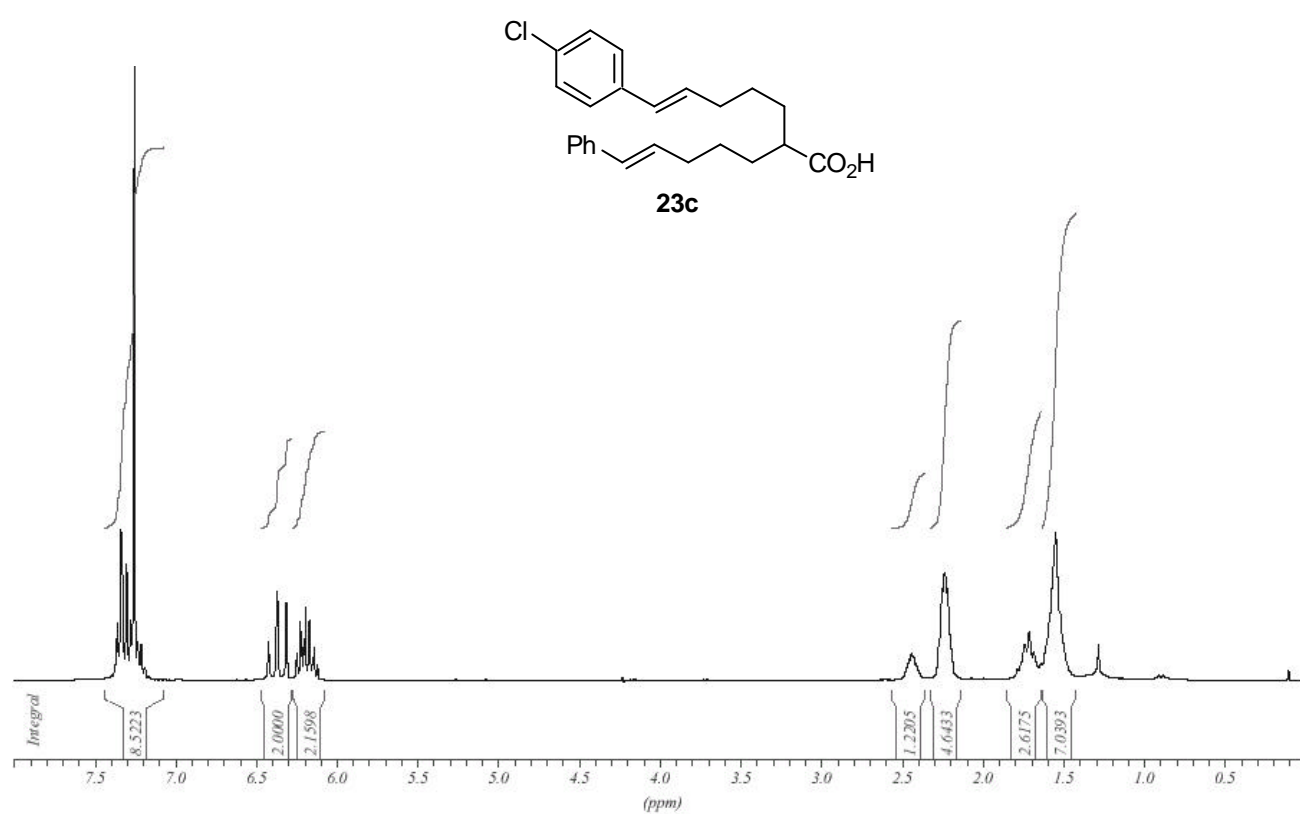
23b



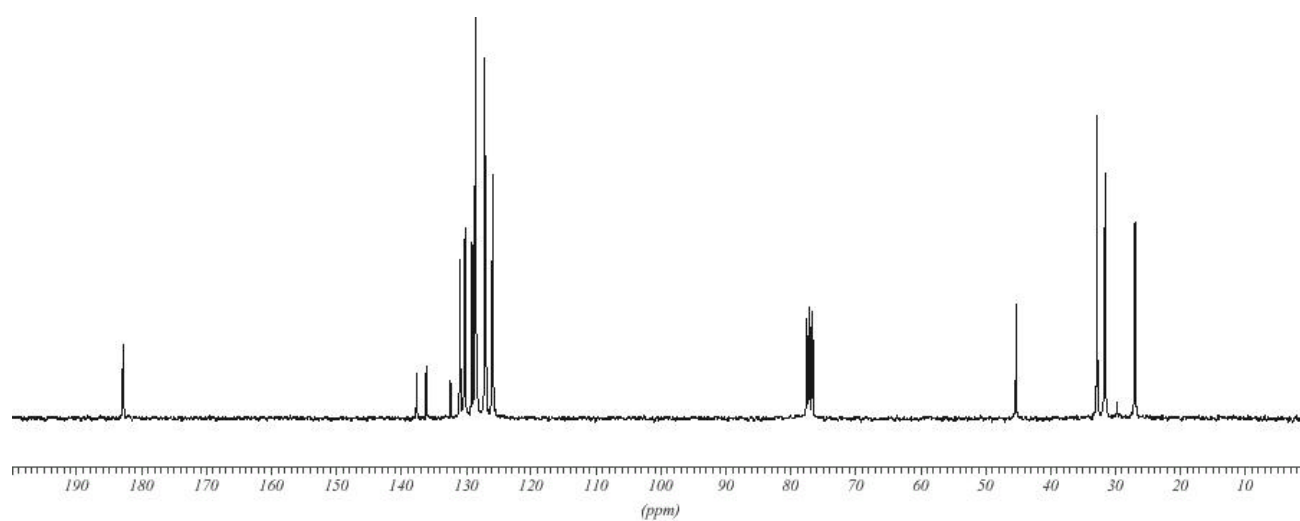
RMN ^{13}C spectrum



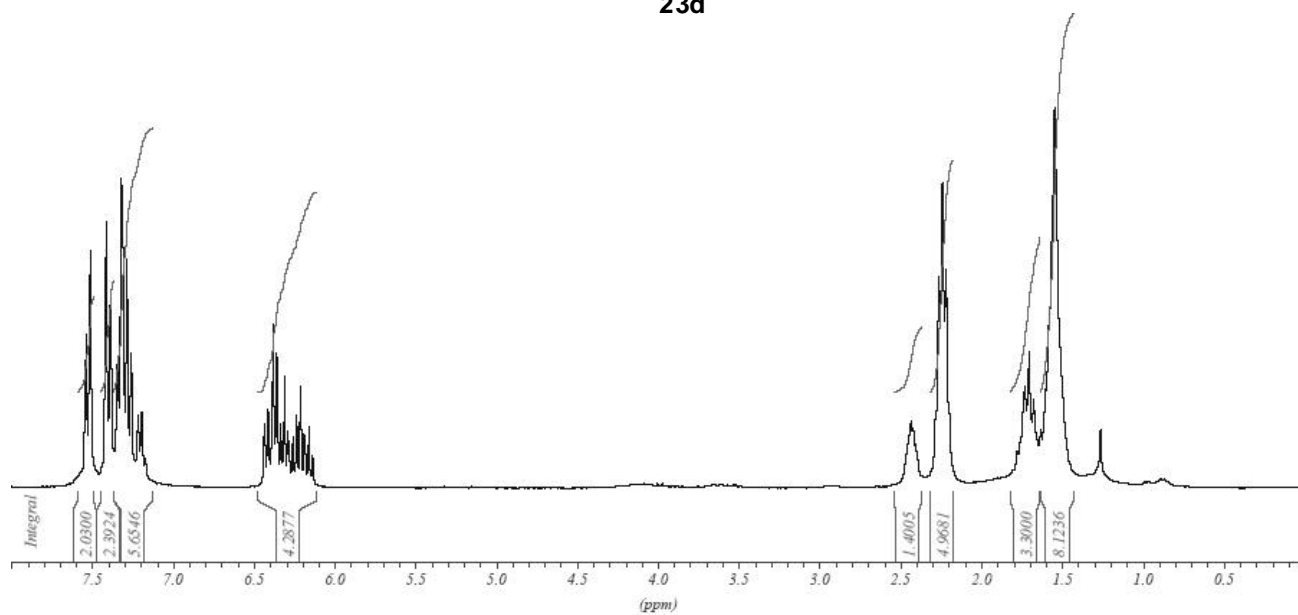
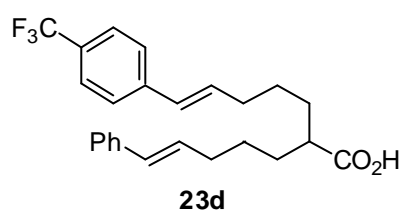
RMN ^1H spectrum



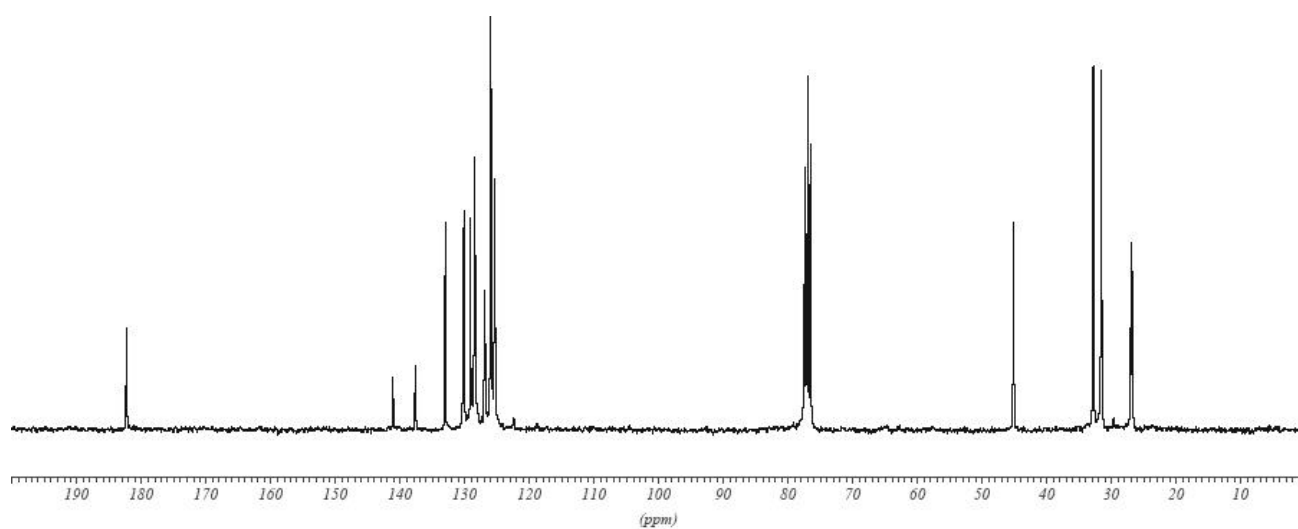
RMN ^{13}C spectrum



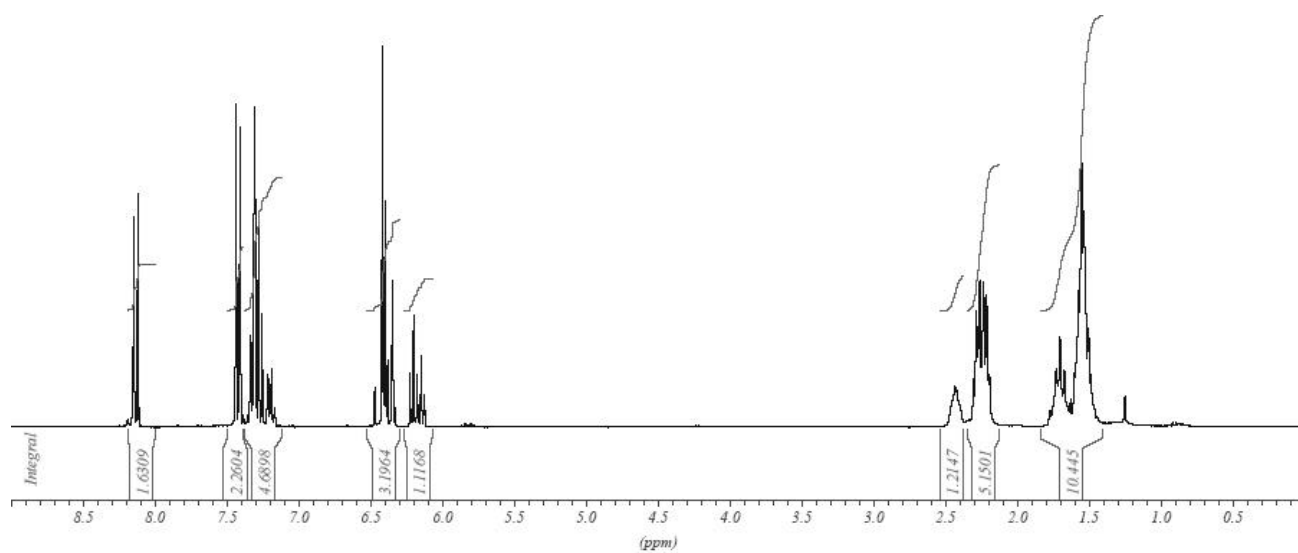
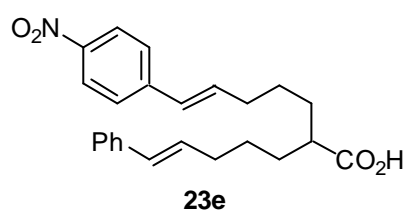
RMN ^1H spectrum



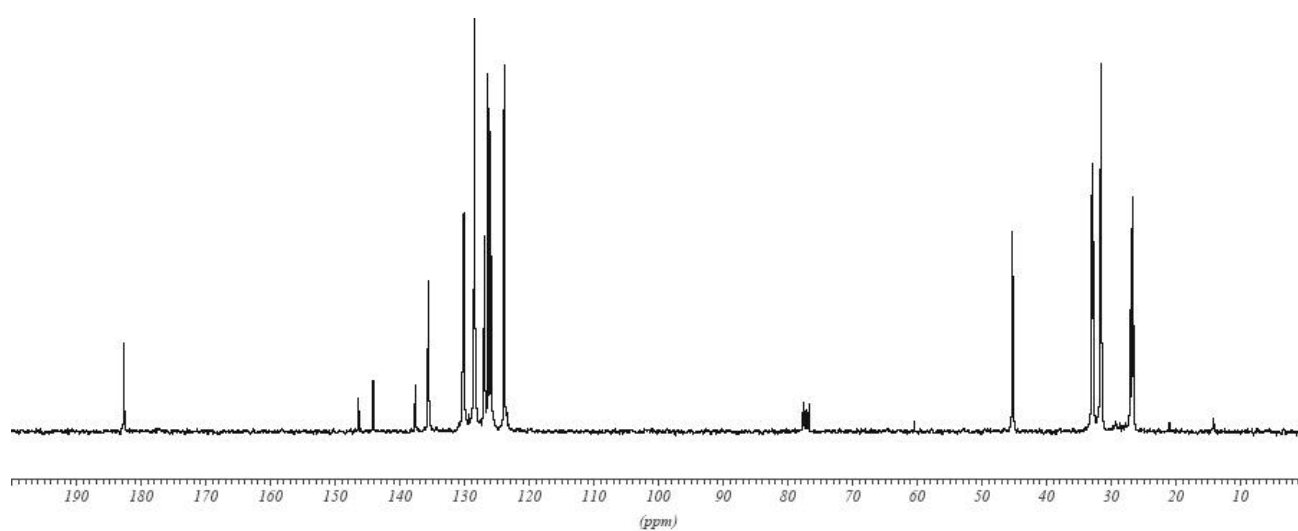
RMN ^{13}C spectrum



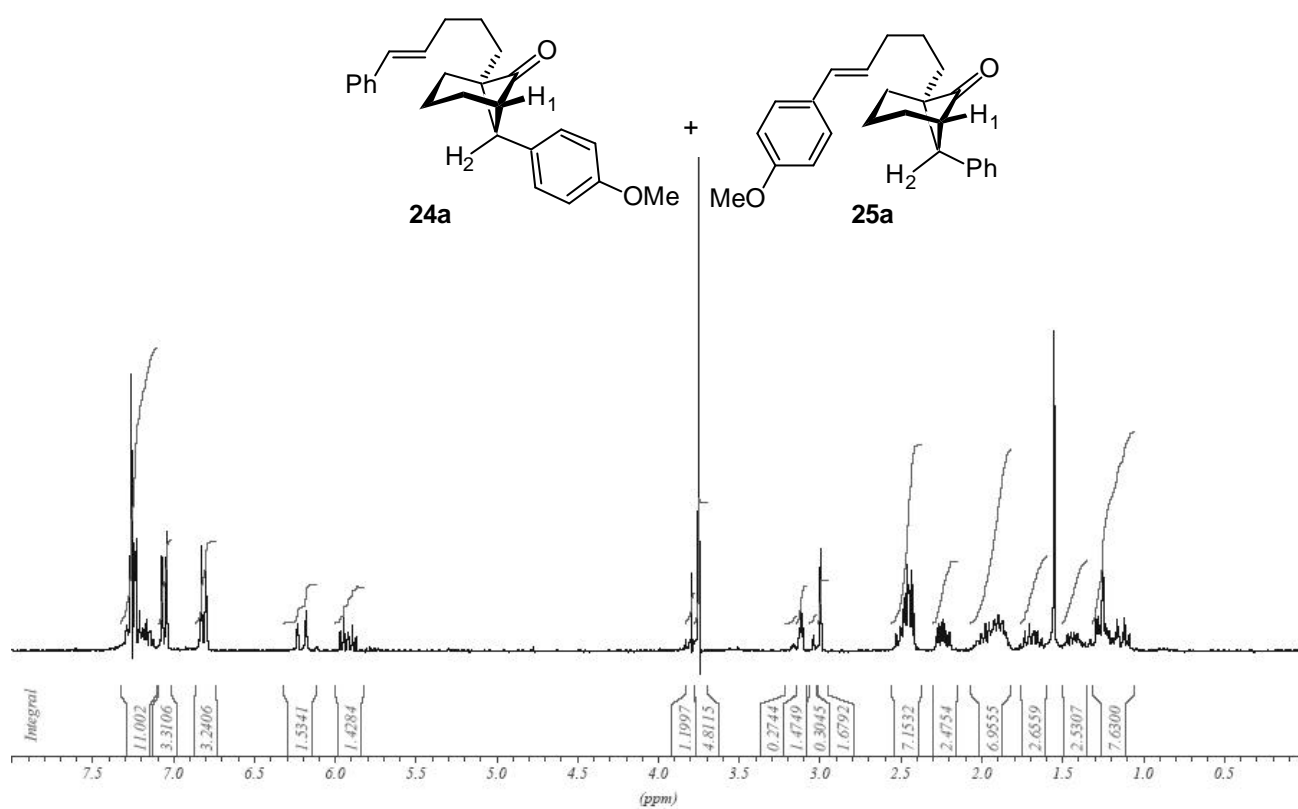
RMN ^1H spectrum



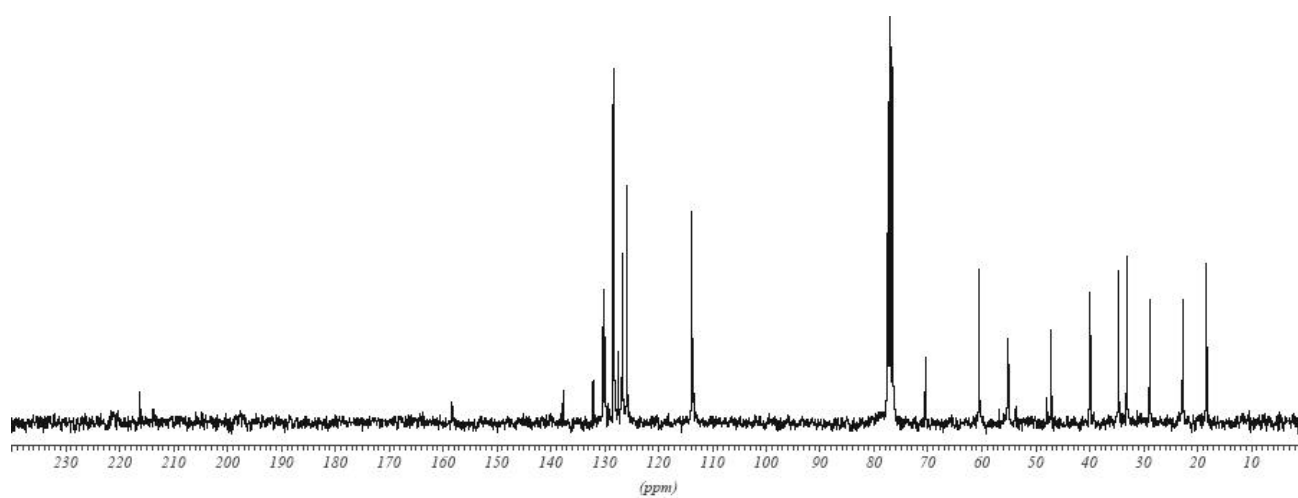
RMN ^{13}C spectrum



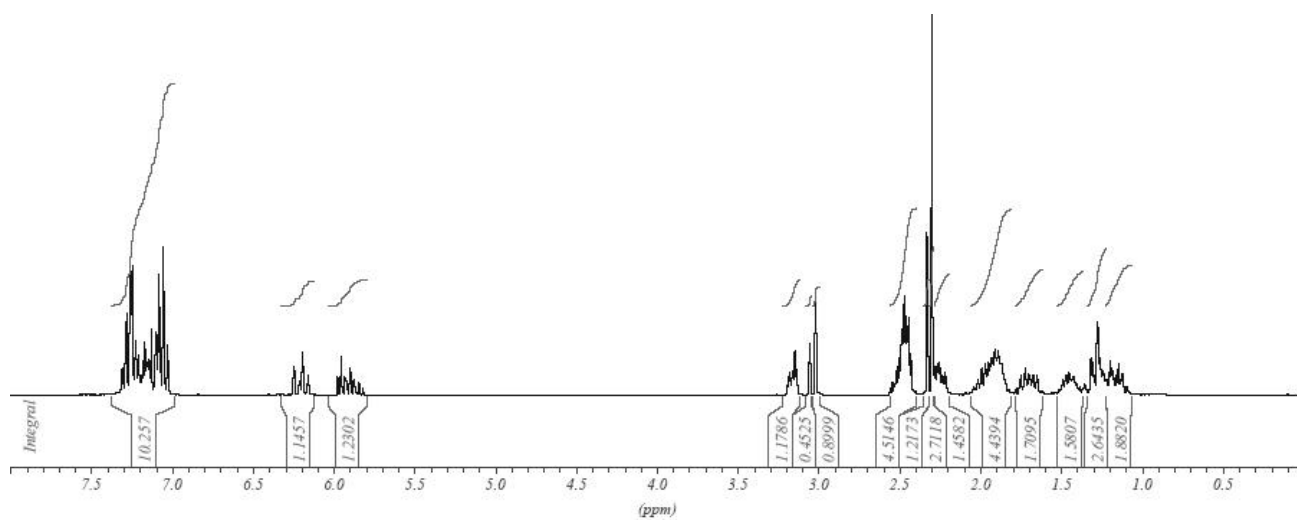
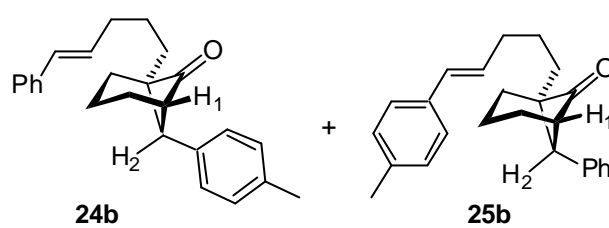
RMN ^1H spectrum



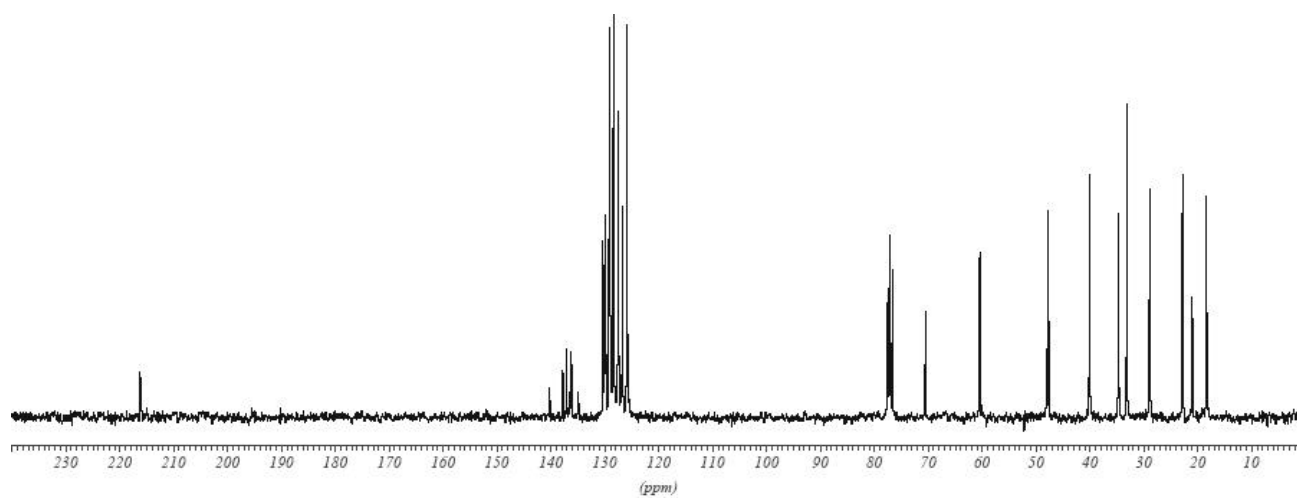
RMN ^{13}C spectrum



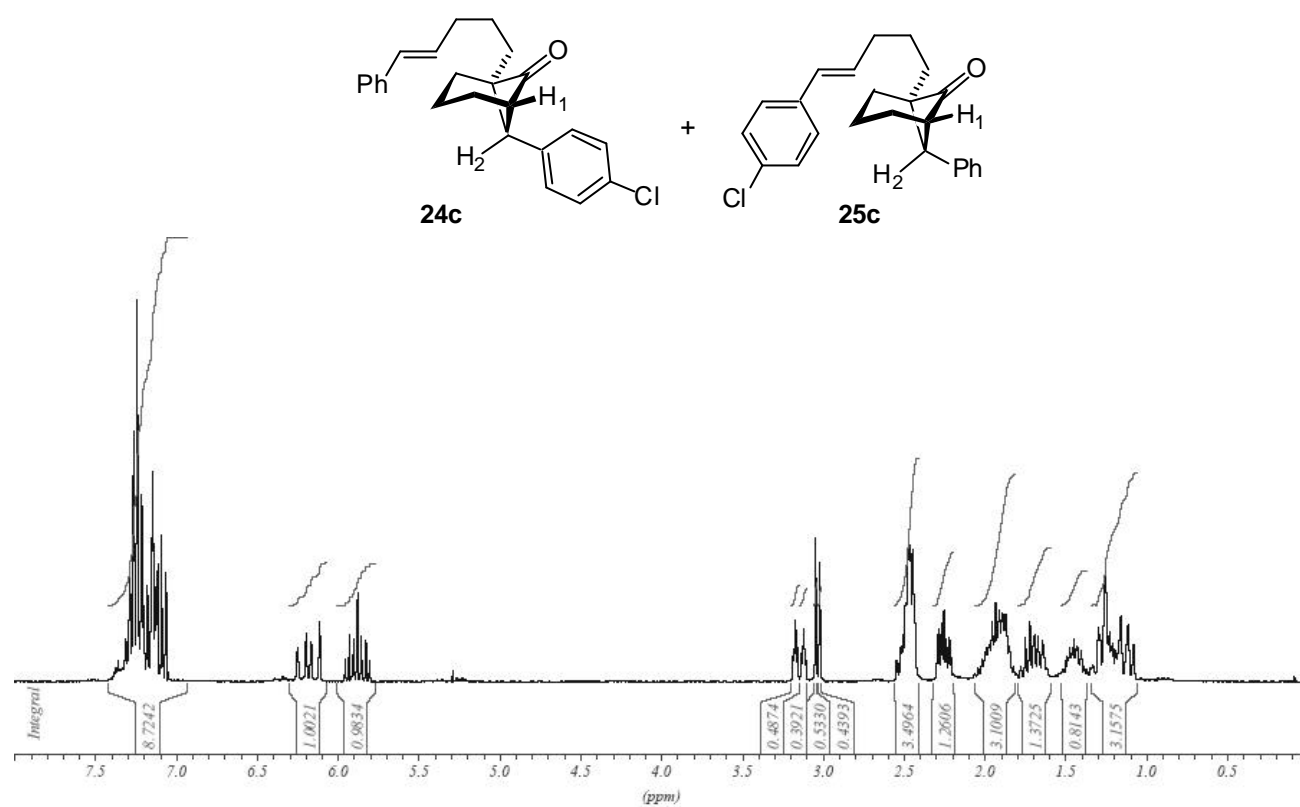
RMN ^1H spectrum



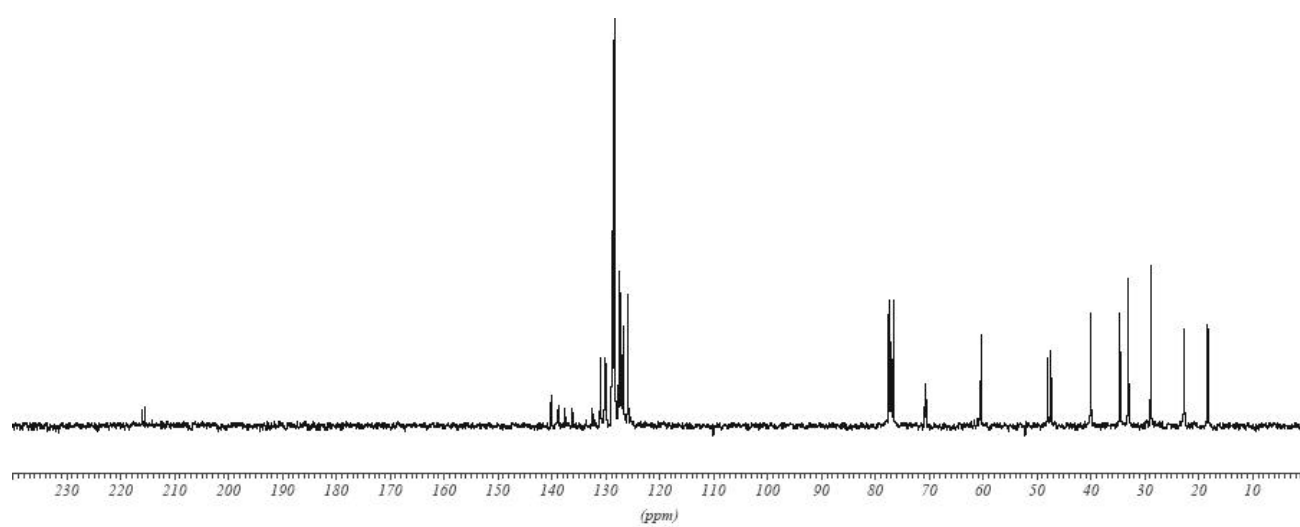
RMN ^{13}C spectrum



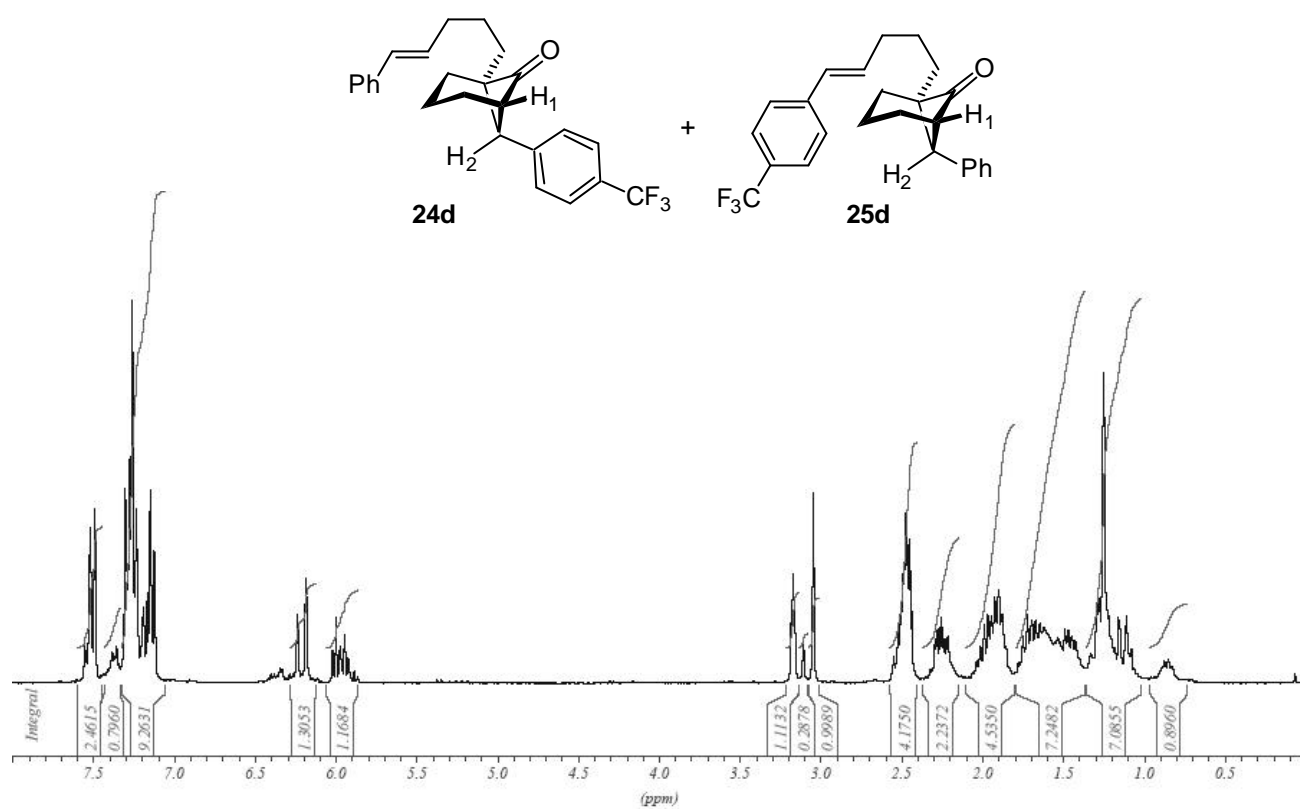
RMN ^1H spectrum



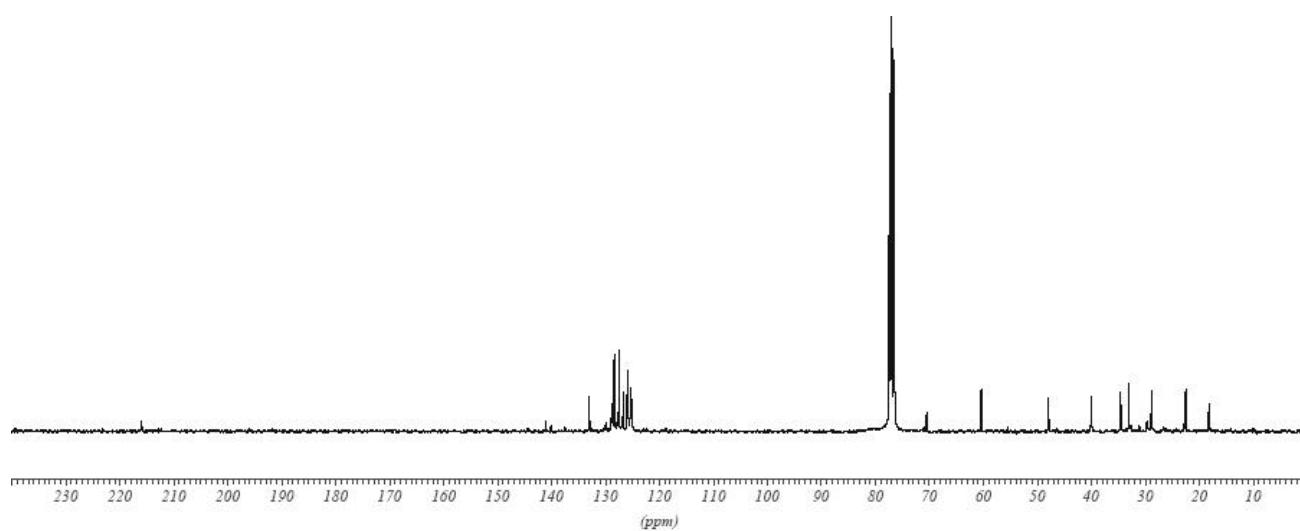
RMN ^{13}C spectrum



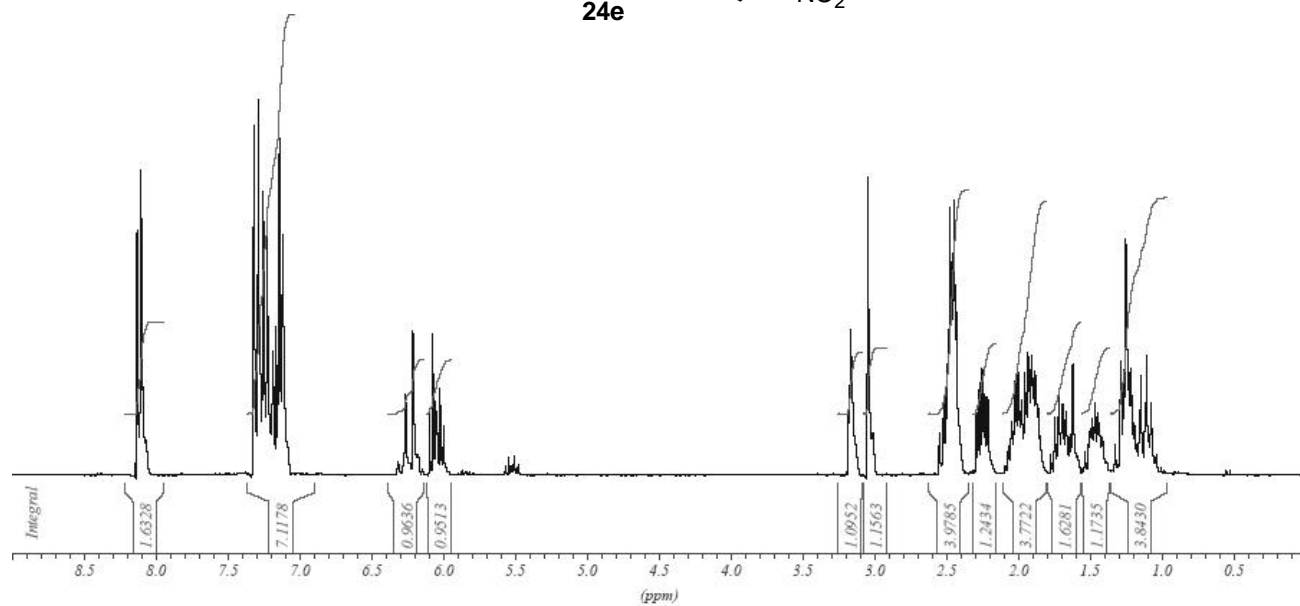
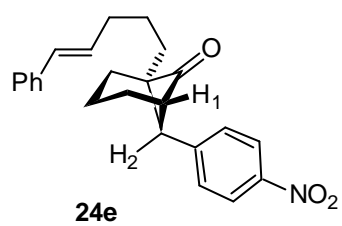
RMN ^1H spectrum



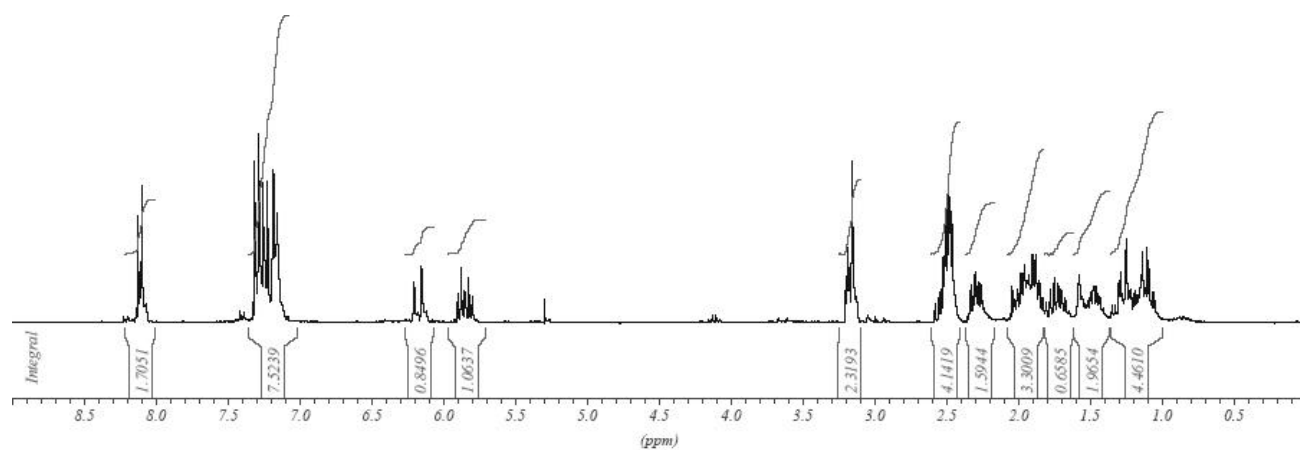
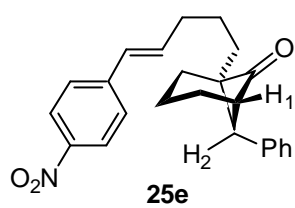
RMN ^{13}C spectrum



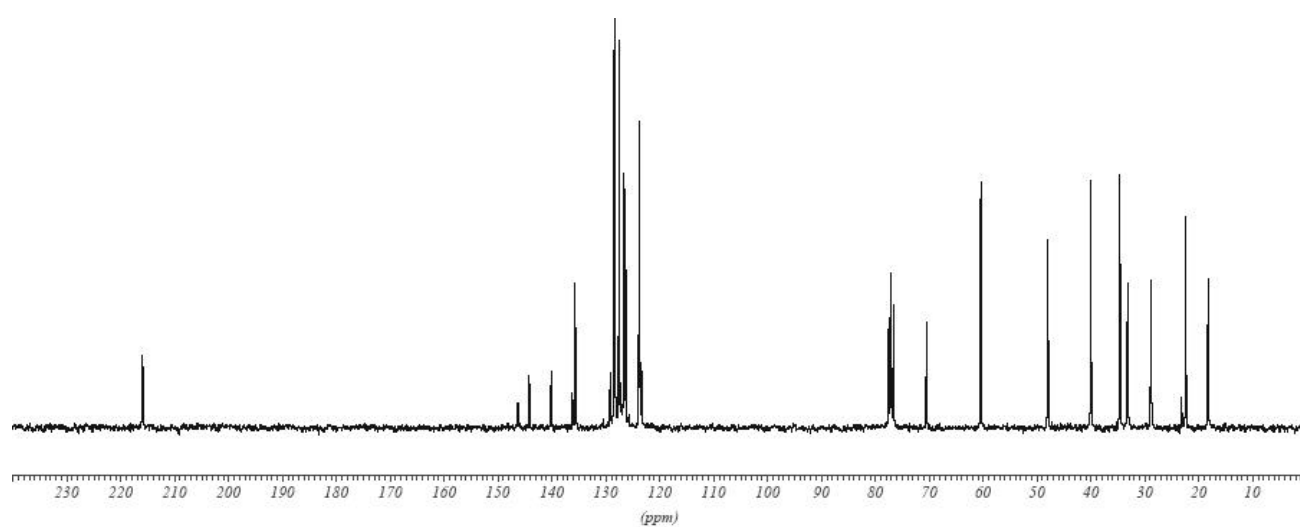
RMN ^1H spectrum



RMN ^1H spectrum

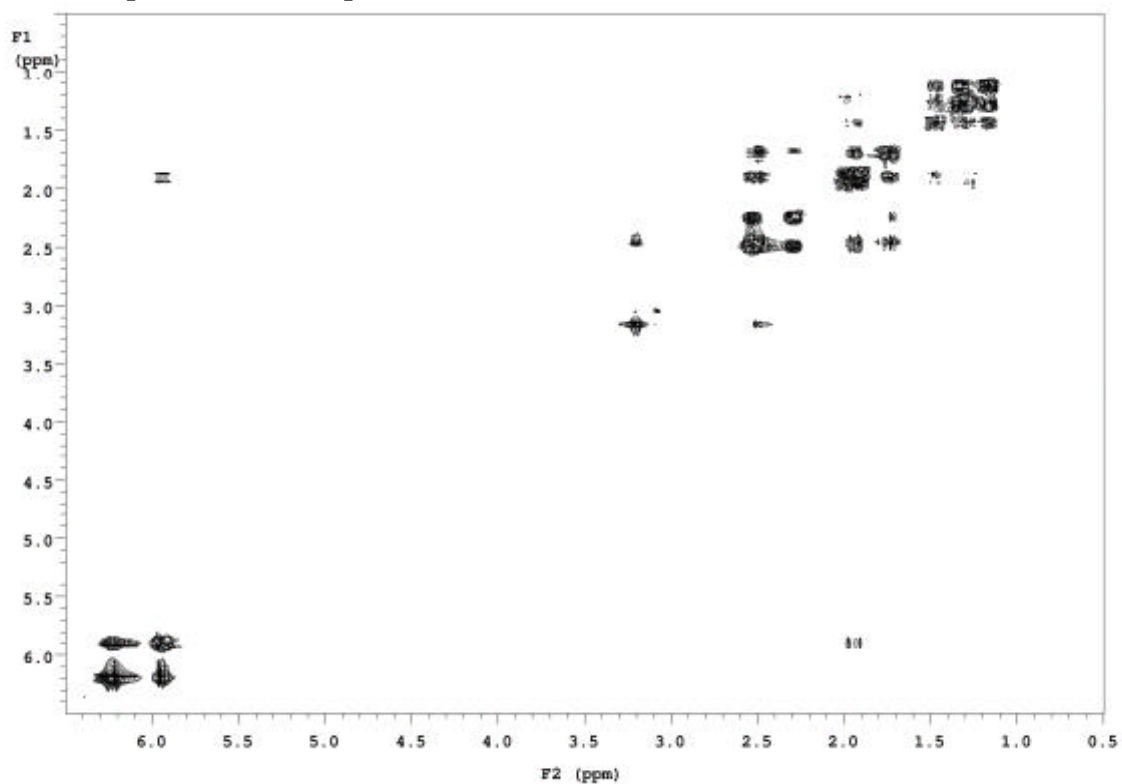


RMN ^{13}C spectrum

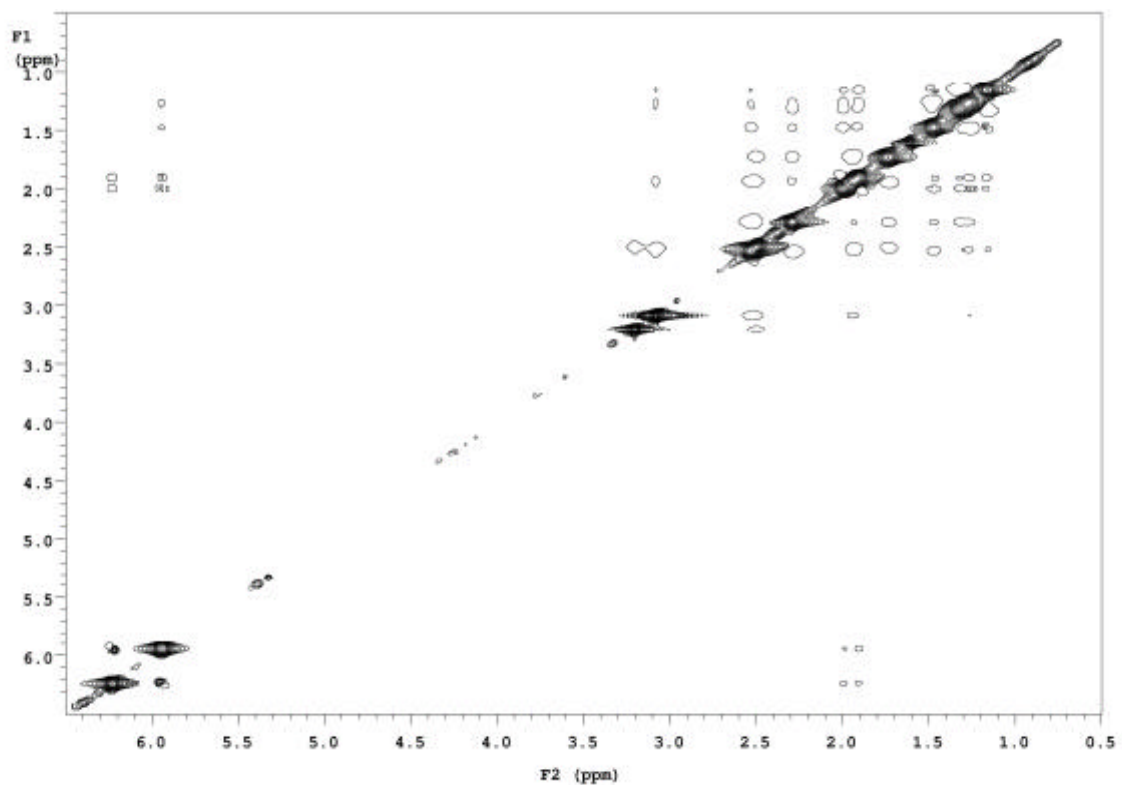


IV COSY, NOESY, TOCSY, HSQC and HMBC Spectra of Compound 19.

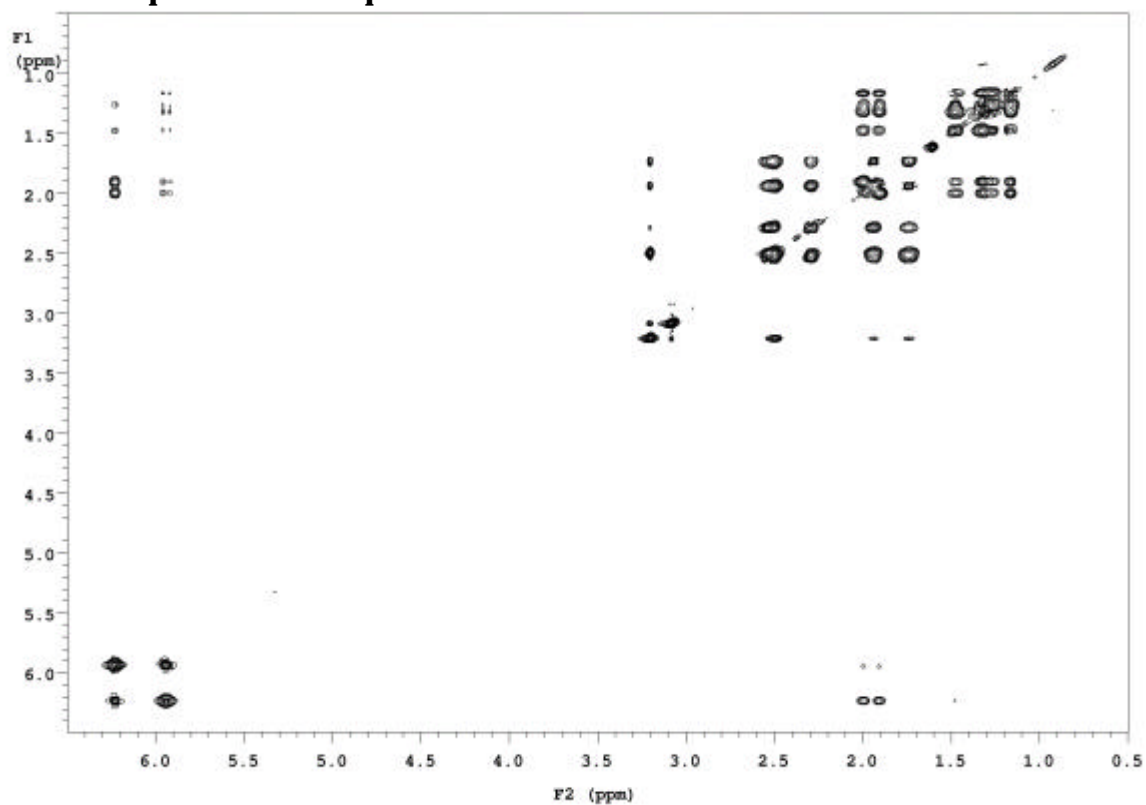
COSY Spectrum of Compound 19.



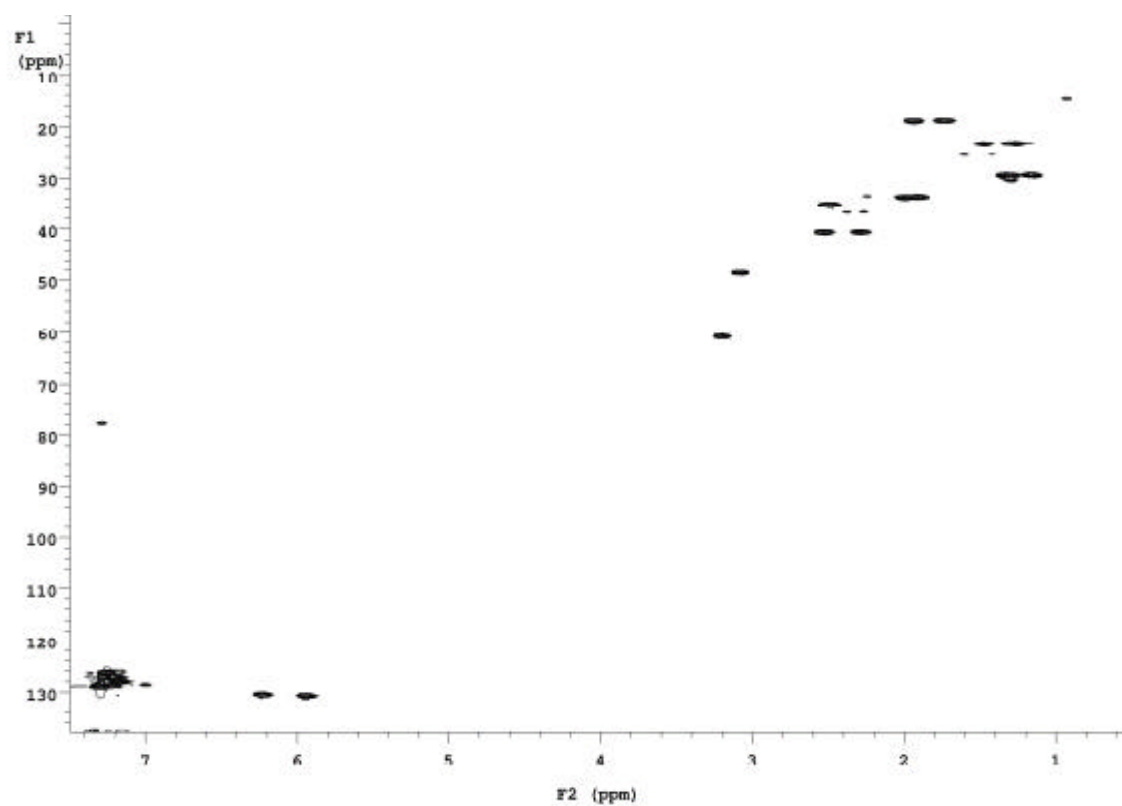
NOESY Spectrum of Compound 19.



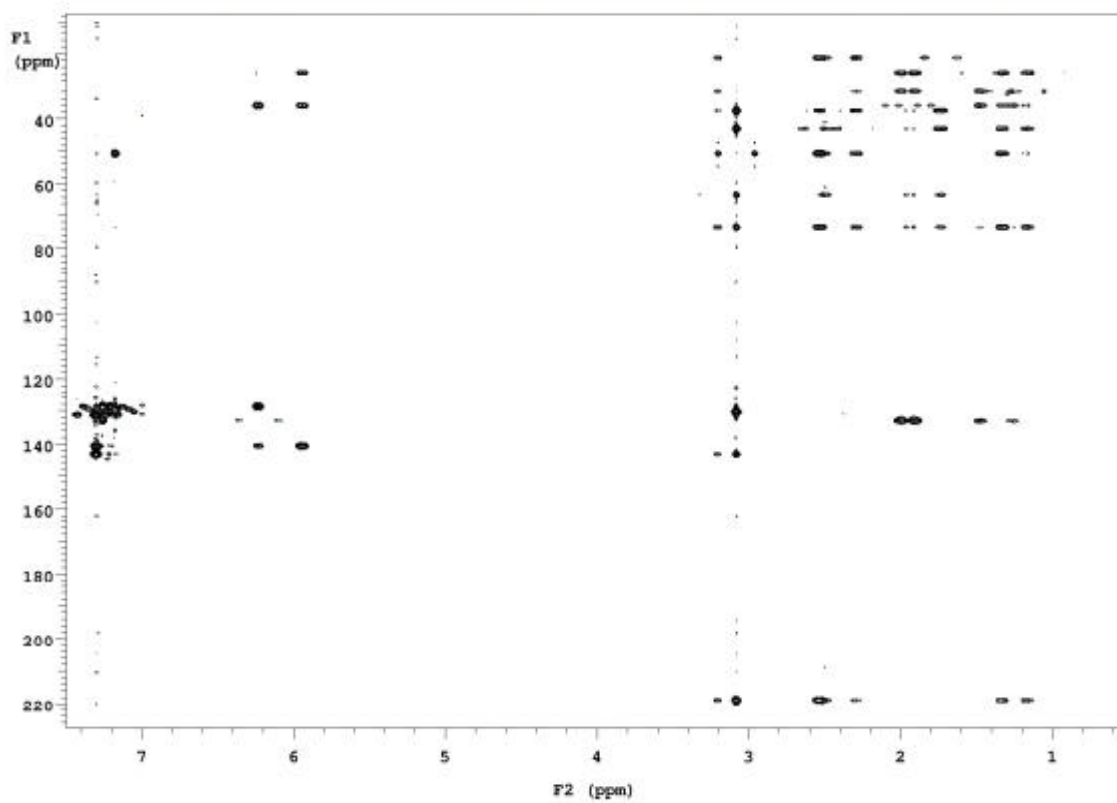
TOCSY Spectrum of Compound 19.



HSQC Spectrum of Compound 19.

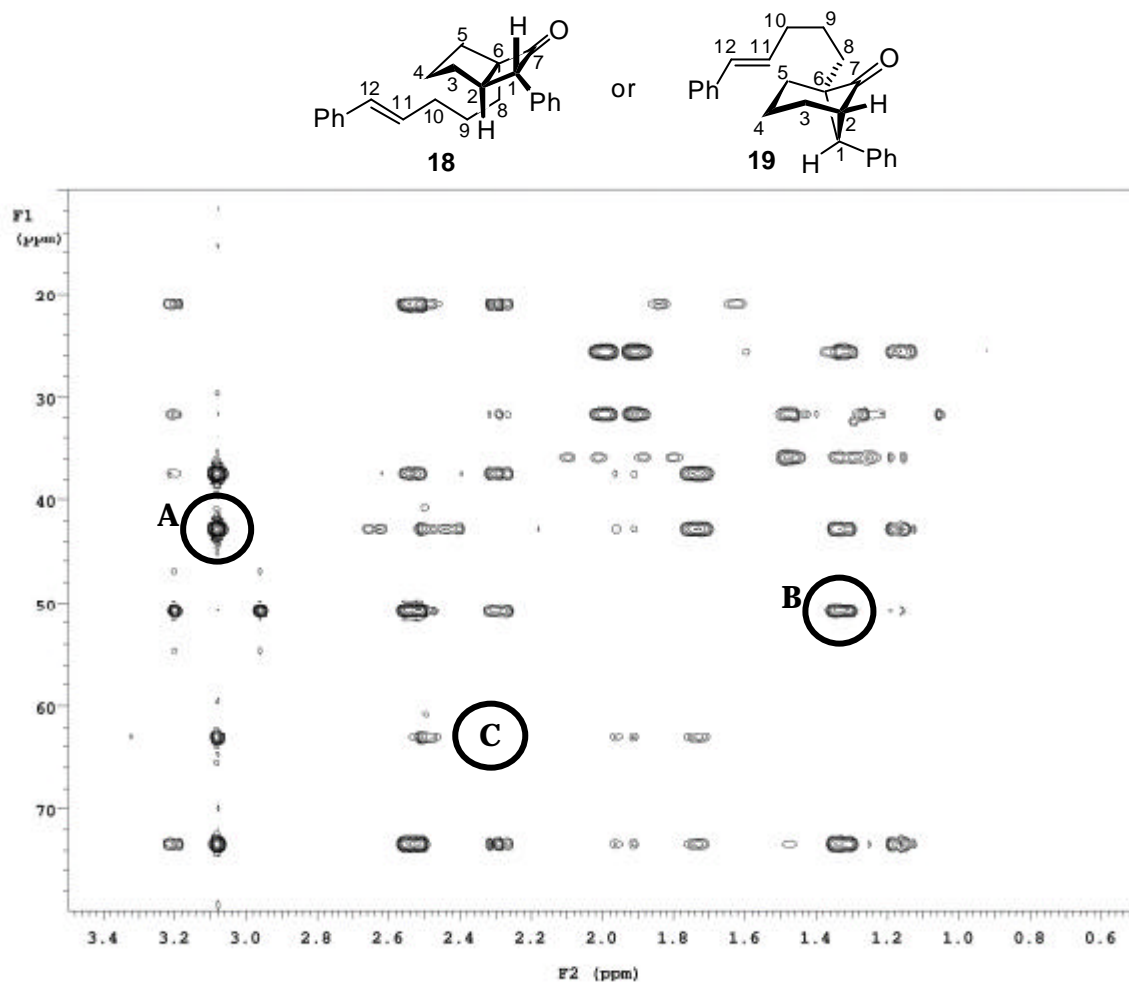


HMBC Spectrum of Compound 19.



V Proof of Structure of Compound 19.

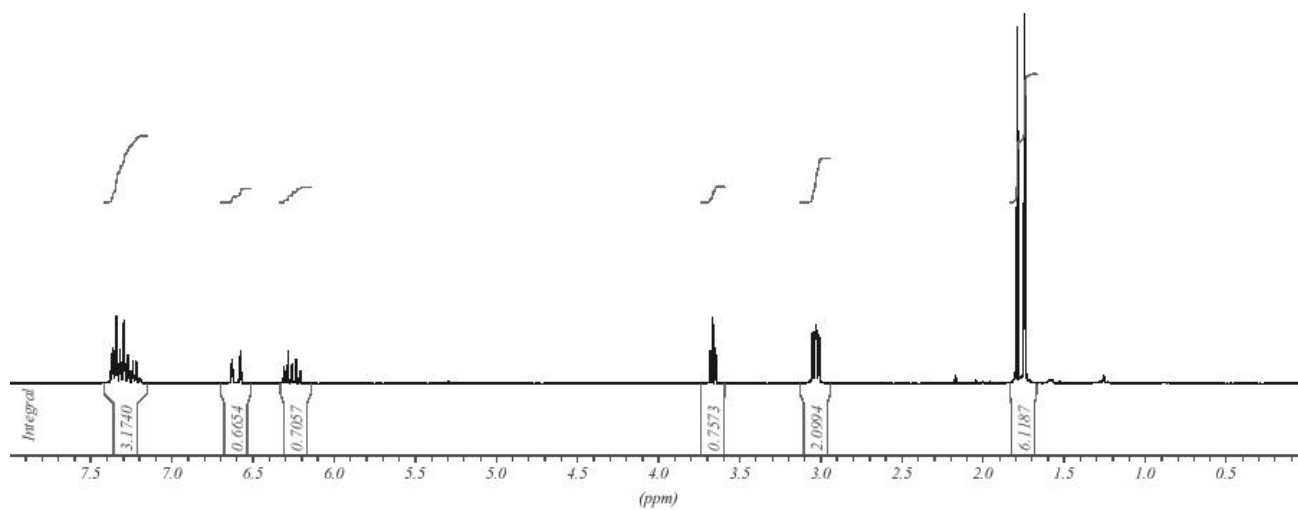
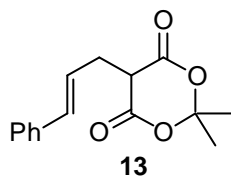
Enlarged Portion of the HMBC Spectrum of Cycloadduct 19 (or 18).



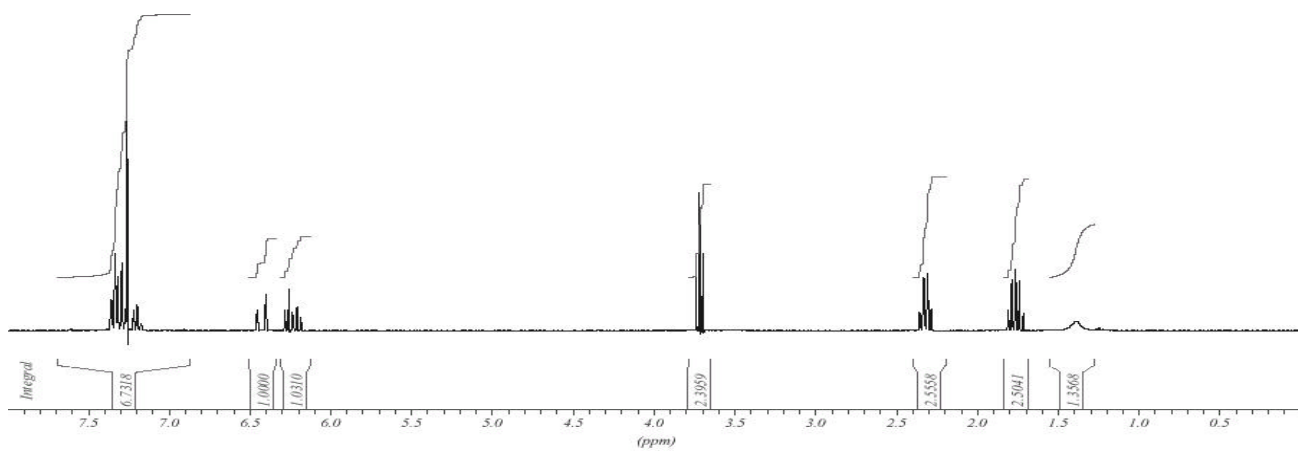
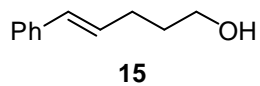
This enlarged portion of the HMBC spectrum of the cycloadduct **19** (or **18**) is depicting three pieces of evidence on the structure of the compound : **(A)** the coupling between the C1 proton (3.04 ppm) and the C5 carbon (40 ppm), **(B)** the coupling between the C8 proton (1.28 ppm) and the C1 carbon (48 ppm) and **(C)** the absence of coupling between the C5 proton (2.25 ppm) and the C2 carbon (61 ppm).⁴ This information allowed us to unambiguously assign the structure as being **19**.

VI Proof of Identity of the Reported Compounds 13,⁵ 15,^{2b} 21,⁶ 22a.^{2b}

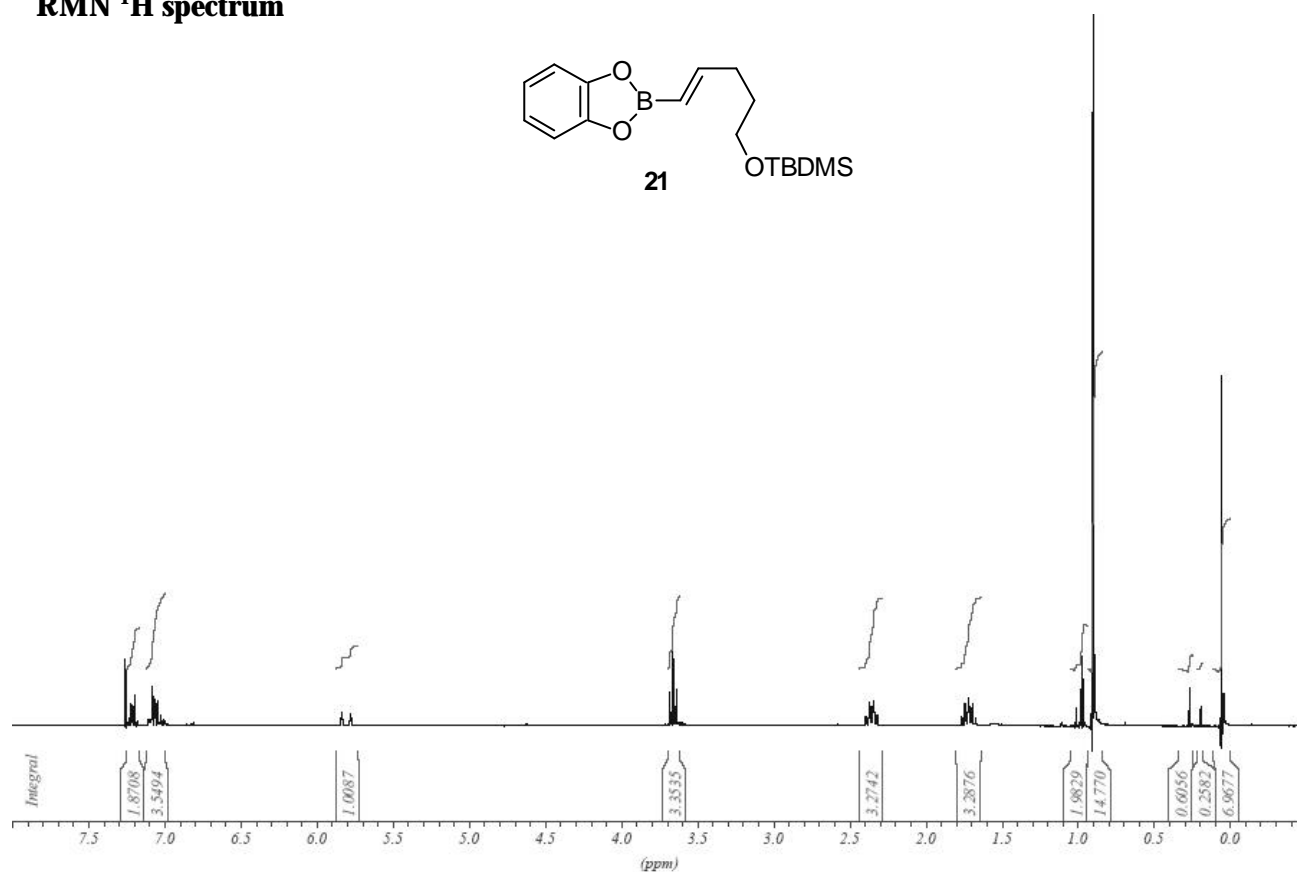
RMN ¹H spectrum



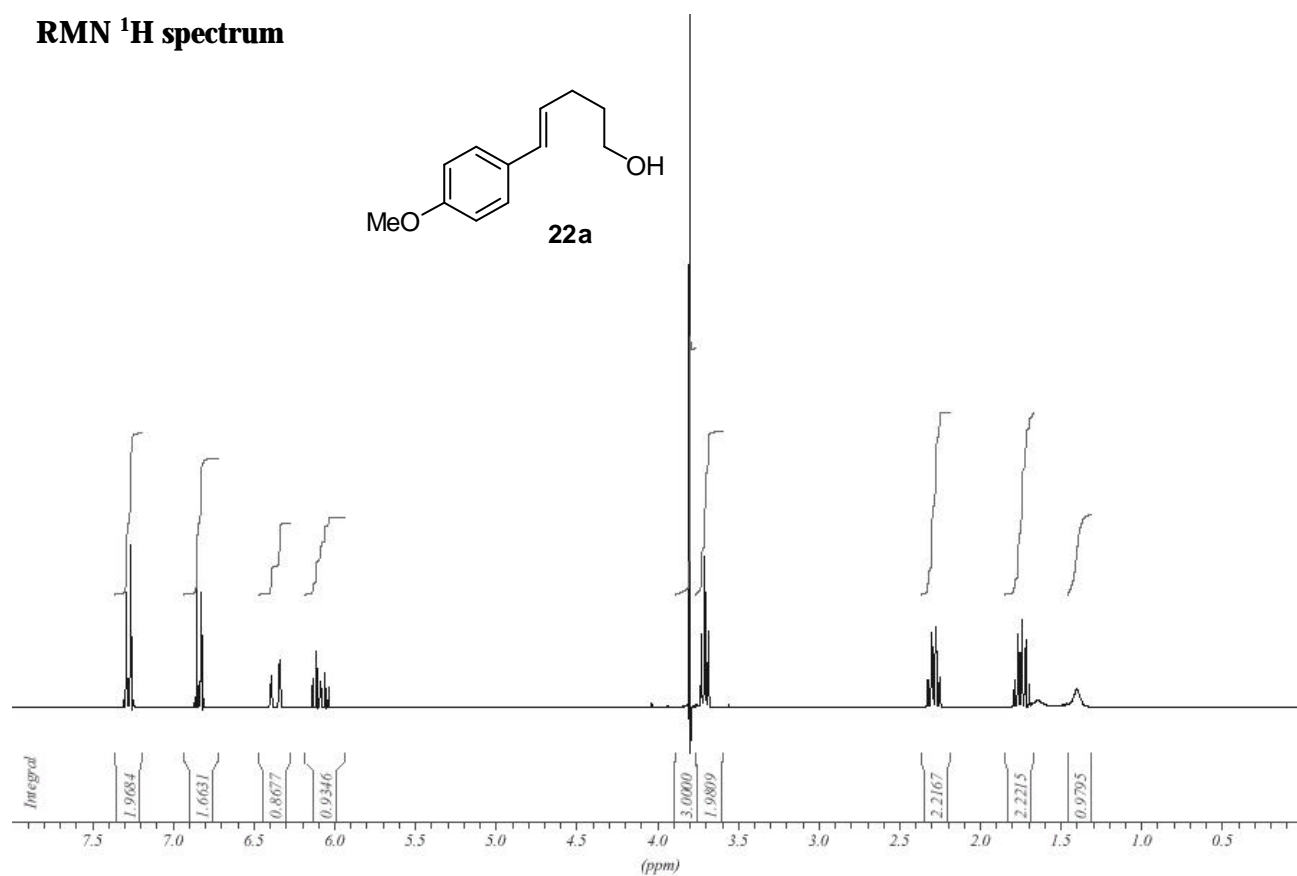
RMN ¹H spectrum



RMN ¹H spectrum

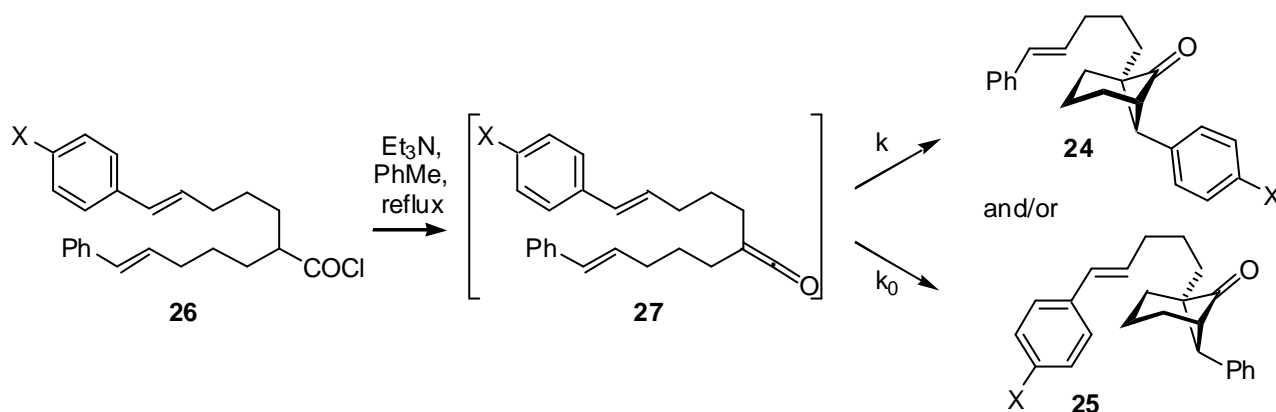


RMN ¹H spectrum



VII Detailed Calculation for the Determination of the Cycloadducts **24**/**25** Ratios.⁷

Since the ketene formation from **27**, as well as the [2+2]-cycloadditions to give the mixture of **24** and **25** are irreversible, we could write:



where k and k_0 are rate constants for ketene cycloaddition with a *p*-substituted styrene and with a non-substituted styrene respectively. The time dependent variation of the concentration of **27** is given by:

$$\frac{d[\mathbf{27}_{(t)}]}{dt} = -k[\mathbf{27}_{(t)}] - k_0[\mathbf{27}_{(t)}] = -(k + k_0)[\mathbf{27}_{(t)}]$$

$$\int_0^t \frac{d[\mathbf{27}_{(t)}]}{[\mathbf{27}_{(t)}]} = -(k + k_0) \int_0^t dt$$

$$\ln[\mathbf{27}_{(t)}] - \ln[\mathbf{27}_{(0)}] = -(k + k_0)t$$

$$[\mathbf{27}_{(t)}] = [\mathbf{27}_{(0)}]e^{-(k + k_0)t}$$

The time dependent variation of the concentration of **24** is given by:

$$\frac{d[\mathbf{24}_{(t)}]}{dt} = k[\mathbf{27}_{(t)}] = k[\mathbf{27}_{(0)}]e^{-(k + k_0)t}$$

$$\int_0^t d[\mathbf{24}_{(t)}] = k[\mathbf{27}_{(0)}] \int_0^t e^{-(k + k_0)t} dt$$

$$[\mathbf{24}_{(t)}] - [\mathbf{24}_{(0)}] = \frac{-k[\mathbf{27}_{(0)}]e^{-(k + k_0)t}}{k + k_0} + \frac{k[\mathbf{27}_{(0)}]e^{-(k + k_0)0}}{k + k_0}$$

Since $[\mathbf{24}_{(0)}] = 0$,

$$[\mathbf{24}_{(t)}] = \frac{k[\mathbf{27}_{(0)}]}{k + k_0} \{1 - e^{-(k + k_0)t}\}$$

The time dependent variation of the concentration of **25** is given by:

$$\frac{d[25_{(t)}]}{dt} = k_0[27_{(0)}] = k_0[27_{(0)}]e^{-(k+k_0)t}$$

$$\int_0^t d[25_{(t)}] = k_0[27_{(0)}] \int_0^t e^{-(k+k_0)t} dt$$

$$[25_{(t)}] - [25_{(0)}] = -\frac{k_0 d[27_{(0)}]e^{-(k+k_0)t}}{k+k_0} + \frac{k_0 d[27_{(0)}]e^{-(k+k_0)0}}{k+k_0}$$

Since $[25_{(0)}] = 0$,

$$[25_{(t)}] = \frac{k_0[27_{(0)}]\{1 - e^{-(k+k_0)t}\}}{k+k_0}$$

The ratio of cycloadducts **24** and **25** is given by:

$$\frac{[24_{(t)}]}{[25_{(t)}]} = \frac{\frac{k[27_{(0)}]\{1 - e^{-(k+k_0)t}\}}{k+k_0}}{\frac{k_0[27_{(0)}]\{1 - e^{-(k+k_0)t}\}}{k+k_0}}$$

$$\frac{[24_{(t)}]}{[25_{(t)}]} = \frac{k}{k_0}$$

References and Footnotes.

¹ A series of ¹H NMR were recorded at different relaxation delay (1 to 7 sec) and we found that a relaxation delay of over 3 sec gave consistent ratios when we integrated the H₁ and H₂ protons of **24/25a-e**.

² The characterization is identical to the one reported for the same compound, but prepared through another route. See: a) Kruse, C.G.; Janse, C.V.; Dert, V.; van der Den, A. *J. Org. Chem.* **1979**, *44*, 2916 – 2920. b) Senda, Y.; Kanto, H.; Itoh, H. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1143 – 1146.

³ The characterization is identical to the one reported for the same compound, but prepared through another route. See: Meyers, A.I.; Durandetta, J.L. *J. Org. Chem.* **1975**, *40*, 2021 – 2025.

⁴ A correlation spot between the C2 carbon and the proton at 2.45 ppm is seemingly due to the C3 protons rather than to the other C5 proton.

⁵ The characterization is identical to the one reported for the same compound, but prepared through another route. See: Prat, M.; Moreno-Mañas, M.; Ribas, J. *Tetrahedron* **1988**, 44, 7205 – 7212.

⁶ The characterization is identical to the one reported for the same compound, but prepared through another route. See: Muir, J.C.; Pattenden, G.; Ye, T. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2243 – 2250.

⁷ a) Logan, S. *Introduction à la cinétique chimique*, Dunod, Paris, 1998, pp. 47 – 50. b) Schaal, R. *Chemical Kinetics of Homogeneous Systems*, D. Riedel Publishing Company, Dordrecht, 1974, pp. 30 – 32.