

Bleach/Acetic Acid Promoted Chlorinative Ring Expansion of [2.2.1] and [2.2.2] Bicycles

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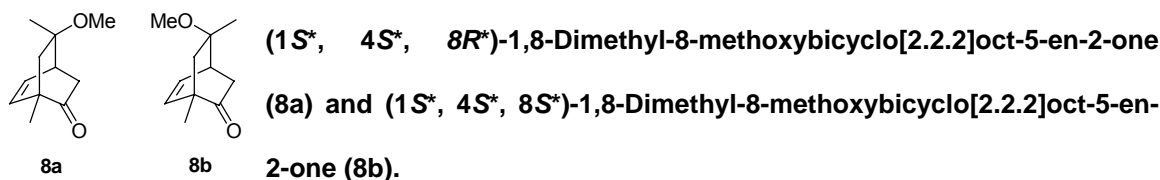
Supporting Information

Instrumental and Materials.

All air or moisture sensitive reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere unless otherwise noted. All commercial reagents were used without purification. All solvents were reagent grade. Diethyl ether and THF were freshly distilled from sodium/benzophenone under nitrogen. Except as otherwise noted, all reactions were magnetically stirred and monitored by thin-layer chromatography with 0.25 mm precoated silica gel plates or capillary GC with a fused silica column. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 mesh ASTM). High performance liquid chromatography (HPLC) was performed with Ranin component analytical semiprep system. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Melting points were determined on a Thomas-Hoover Apparatus, uncorrected. Infrared spectra were recorded on a Nicolet IR/42 spectrometer. Proton and carbon NMR spectra were recorded on a Varian Gemini 300, or VXR 500 spectrometer. Chemical shifts for ^1H NMR and ^{13}C NMR are reported in parts per million (ppm) relative to CDCl_3 ($\delta = 7.24$ ppm for ^1H NMR or $\delta = 77.0$ ppm for ^{13}C NMR). Optical rotations were measured with a Perkin-Elmer Model 341 polarimeter. High

resolution mass spectra (HRMS) data were obtained at either the Michigan State University Mass Spectrometry Service Center or at the Mass Spectrometry Laboratory of the University of South Carolina, Department of Chemistry and Biochemistry. GC/MS were performed with a fused silica column (30 m by 0.25 mm i.d.).

Experimental:



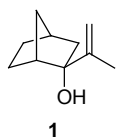
A solution containing 28.98 g (133.1 mmol) bromocarvone (prepared according to the procedure of Srikrishna, see reference following spectral data), in 300 mL ^tBuOH and 350 mL THF was chilled to 0 °C, and 17.50 g (155.9 mmol, 1.17 eq.) of ^tBuOK was added in portions. Upon complete addition of the base the reaction was stirred at 0 °C for 10 minutes and then warmed to room temperature and stirred for 18 hrs. The reaction was then poured into 300 mL of acidic brine (150 mL 3% HCl_{aq} / 150 mL brine). The aqueous mixture was partitioned with 150 mL Et₂O and separated. The ethereal solution was washed two additional times with 300 mL acidic brine. The ethereal layer was dried with Na₂SO₄, filtered and concentrated. The resultant brown oil was purified *via* flash chromatography (180 g; 230-400 mesh; 4:1 hexanes/ethyl acetate) to yield 9.67 g (40 %) of **8a** as a clear oil and 6.67 g (28 %) of **8b**.

8a: R_f = 0.53 (4:1 Hex/EtOAc); [α]_D²⁰ = -383.8 (c 1.49, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 6.41 (t, *J* = 7.5 Hz, 1 H), 5.81 (d, *J* = 8.1 Hz, 1 H), 3.15 (s, 3 H), 2.88 (m, 1 H), 2.50 (dd, *J* = 18.0, 3.3 Hz, 1 H), 1.84 (dt, *J* = 18.3, 3.3 Hz, 1 H), 1.73 (dd, *J* = 13.5, 3.3 Hz, 1 H), 1.42 (dd, *J* = 13.8, 3.3 Hz, 1 H), 1.23 (s, 3 H), 1.12 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 212.9 (C), 135.7 (CH), 134.4 (CH), 78.8 (C), 50.2 (C), 49.6 (CH₃), 45.9 (CH₂), 41.5 (CH), 34.6 (CH₂), 24.8 (CH₃), 17.1 (CH₃); IR (neat) 3090 (w), 2970 (m), 2930 (m), 2828 (w), 1724 (s), 1454 (w), 1371 (w), 1082 (m), 754 (w) cm⁻¹; LRMS (EI) *m/z* 180.6 (M⁺).

8b: $R_f = 0.333$ (4:1 Hex/EtOAc); $[\alpha]_D^{20} = -377.9$ (c 1.72, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.42 (t, $J = 8.1$ Hz, 1 H), 5.88 (d, $J = 8.1$ Hz, 1 H), 3.13 (s, 3 H), 2.97 (m, 1 H), 2.05 (m, 2 H), 1.61 (ABq, $J = 15.0$ Hz, 2 H), 1.32 (s, 3 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 212.8 (C), 135.7 (CH), 134.4 (CH), 78.8 (C), 50.2 (C), 49.6 (CH_3), 45.9 (CH_2), 41.5 (CH), 34.6 (CH_2), 24.8 (CH_3), 17.2 (CH_3); IR (neat) 3090 (w), 2970 (m), 2933 (m), 2826 (w), 1724 (s), 1452 (w), 1375 (w), 1132 (m), 1080 (m), 1012 (w), 920 (w), 848 (w), 748 (m) cm^{-1} ; LRMS (EI) m/z 180.0 (M^+).

For original synthesis see: Srikrishna, A., Sharma, V. R., Danielloss, J., Hemamalini, P. *J. Chem. Soc. Perkin Trans. I* **1996**, 1305-1311.

Typical substrate synthesis (1, 9a/b, 12a/b): A vinyl magnesium bromide/THF, for **12a/b**, (1.0 M, 3.00 eq) or isopropenyl magnesium bromide/THF, for **1** and **9a/b**, (0.5 M, 3.00 eq) solution was chilled to 0 °C prior to the dropwise addition of [2.2.2]-ketone **8a** (1.00 eq), or norcamphor for **1**, in THF (~2.0 M). After complete addition the reaction was stirred at 0 °C for 0.5 hrs and then warmed to reflux (80 °C). Reflux was maintained until the reaction was judged complete by TLC (3-6 hrs). The reaction was then cooled to 0 °C and quenched with an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat})}$. After partitioning with Et_2O and separation, the ethereal layer was washed two times with an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat})}$ and once with H_2O . The combined aqueous layers were extracted two times with Et_2O . The combined ethereal layers were dried over MgSO_4 , filtered, and concentrated. The crude residue was purified via flash alumina chromatography with hexanes/ethyl acetate as the eluent (30 g alumina per 1 g compound; 150 mesh; basic Activity III).

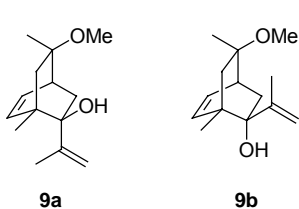


(1R*, 2R*, 4S*)-2-Isopropenyl-bicyclo[2.2.1]heptan-2-ol (1).

1: $R_f = 0.40$ (5:1 Hex/EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 4.85 (s, 1 H), 4.72 (d, $J = 3.9$ Hz, 1 H), 2.35 (m, 1 H), 2.14 (m, 1 H), 1.98 (d, $J = 0.9$, 1 H), 1.86 (m, 2 H), 1.76 (s, 3 H), 1.46 (d, $J =$

9.9 Hz, 1 H), 1.37-1.18 (series of m, 4 H), 1.12 (dd, $J = 13.2, 3.3$ Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.8 (C), 108.8 (CH_2), 80.8 (C), 44.6 (CH), 43.7 (CH_2), 38.7 (CH_3), 36.8 (CH), 28.6 (CH_2), 21.9 (CH_2), 18.4 (CH_2); IR (neat) 3366 (br s), 2088 (w), 2968 (s), 2872 (s), 1643 (m), 1454 (s), 1373 (m), 1307 (s), 1163 (s), 1147 (s), 1026 (s), 993 (s), 897 (s), 868 (m), 734 (m) cm^{-1} ; HRMS (EI) m/z 152.1198 [M^+] calcd. for $\text{C}_{10}\text{H}_{16}\text{O}$: 152.1201].

For previous synthesis see: Johnson, C. R.; Herr, R. W. *J. Org. Chem.* **1973**, 38, 3153-3159.



(1S*, 2R*, 4S*, 8R*)-1,8-dimethyl-2-isopropenyl-8-

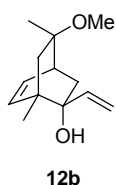
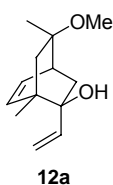
methoxybicyclo[2.2.2]oct-5-en-2-ol (9a) and (1S*, 2S*, 4S*, 8R*)-

1,8-dimethyl-2-isopropenyl-8-methoxybicyclo[2.2.2]oct-5-en-2-ol (9b).

9a: $R_f = 0.42$ (5:1 Hex/EtOAc); $[\alpha]_{546}^{20} = -50.1$ (c 0.63, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.11 (t, $J = 6.6$ Hz, 1 H), 5.94 (d, $J = 7.2$ Hz, 1 H), 5.11 (d, $J = 2.4$ Hz, 1 H), 4.78 (AB_q, $J = 2.4, 1.2$ Hz, 1 H), 3.19 (s, 3 H), 2.68 (m, 1 H), 2.24 (d, $J = 13.8$ Hz, 1 H), 1.98 (d, $J = 13.8$ Hz, 1 H), 1.76 (dd, $J = 14.4, 3.3$ Hz, 1 H), 1.66 (dd, $J = 13.8, 2.4$ Hz, 1 H), 1.58 (s, 3 H), 1.38 (s, 1 H), 1.11 (s, 3 H), 0.94 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 148.7 (C), 141.5 (CH), 131.7 (CH), 111.6 (CH_2), 78.7 (C), 77.6 (C), 49.8 (CH_3), 47.3 (CH_2), 43.7 (C), 40.6 (CH), 30.3 (CH_2), 24.7 (CH_3), 21.5 (CH_3), 18.7 (CH_3); IR (neat) 3493 (m), 3040 (w), 2961 (s), 2872 (m), 1680 (w), 1620 (w), 1452 (s), 1371 (s), 1101 (s), 1062 (s), 918 (m), 904 (m), 879 (w), 736 (m) cm^{-1} ; HRMS (EI) m/z 222.1622 [M^+] calcd. for $\text{C}_{14}\text{H}_{22}\text{O}_2$: 222.1620].

9b: $R_f = 0.21$ (5:1 Hex/EtAc); $[\alpha]_{546}^{20} = -81.0$ (c 0.65, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.33 (t, $J = 6.9$ Hz, 1 H), 5.83 (d, $J = 7.8$ Hz, 1 H), 5.20 (d, $J = 1.8$ Hz, 1 H), 4.99 (t, $J = 1.8$ Hz, 1 H), 3.10 (s, 3 H), 2.54 (m, 1 H), 2.53 (d, $J = 12.6$ Hz, 1 H), 1.86 (d, $J = 14.1$ Hz, 1 H), 1.82 (s, 3 H), 1.21 (s, 1 H), 1.14 (d, $J = 14.4$ Hz, 1 H), 1.12 (d, $J = 13.8$ Hz, 1 H), 1.07 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.1 (C), 138.0 (CH), 135.0 (CH), 114.0 (CH_2), 79.8 (C), 79.4 (C), 49.2

(CH₃), 45.8 (C), 41.4 (CH₂), 41.0 (CH), 40.9 (CH₂), 24.9 (CH₃), 22.1 (CH₃), 19.5 (CH₃); IR (neat) 3501 (br m), 3090 (w), 2966 (s), 2932 (s), 2878 (m), 2826 (m), 1697 (m), 1664 (s), 1454 (s), 1367 (s), 1101 (s), 1072 (s), 939 (m), 810 (w), 690 (w) cm⁻¹; HRMS (EI) *m/z* 222.1624 [M⁺] calcd. for C₁₄H₂₂O₂: 222.1620].

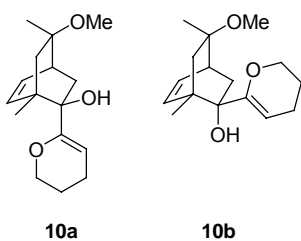


(1S*, 2S*, 4S*, 8R*)-1,8-dimethyl-2-ethenyl-8-methoxybicyclo[2.2.2]oct-5-en-2-ol (12a) and (1S*, 2R*, 4S*, 8R*)-1,8-dimethyl-2-ethenyl-8-methoxybicyclo[2.2.2]oct-5-en-2-ol (12b).

12a: *R*_f = 0.42 (5:1 Hex/EtOAc); [α]_D²⁰ = -40.0 (c 1.19, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 6.17 (t, *J* = 6.9 Hz, 1 H), 5.86 (d, *J* = 8.1 Hz, 1 H), 5.53 (dd, *J* = 16.8, 10.5 Hz, 1 H), 5.17 (dd, *J* = 17.1, 2.1 Hz, 1 H), 4.92 (dd, *J* = 10.8, 2.1 Hz, 1 H), 3.17 (s, 3 H), 2.85 (s, 1 H), 2.61 (m, 1 H), 1.92 (d, *J* = 14.1 Hz, 1 H), 1.82 (dd, *J* = 13.8, 3.0 Hz, 1 H), 1.47 (dd, *J* = 14.1, 2.4 Hz, 1 H), 1.09 (s, 3 H), 0.98 (d, *J* = 13.5 Hz, 1 H) 0.94 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 144.2 (CH), 139.7 (CH), 133.5 (CH), 110.8 (CH₂), 78.4 (C), 75.5 (C), 49.6 (CH₃), 45.7 (CH₂), 43.2 (C), 40.7 (CH₂), 40.1 (CH), 24.5 (CH₃), 18.8 (CH₃); IR (neat) 3439 (br s), 3092 (w), 3042 (w), 2934 (s), 2831 (m), 1650 (w), 1454 (m), 1367 (m), 1116 (s), 1062 (s), 1003 (m), 918 (m), 844 (w), 740 (w-m) cm⁻¹; HRMS (EI) *m/z* 208.1465 [(M⁺), calcd. for C₁₃H₂₀O₂: 208.1463].

12b: *R*_f = 0.33 (5:1 Hex/EtOAc); [α]_D²⁰ = -97.3 (c 1.25, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 6.37 (t, *J* = 7.8 Hz, 1 H), 6.07 (dd, *J* = 17.7, 11.1 Hz, 1 H), 5.89 (d, *J* = 7.8 Hz, 1 H), 5.31 (dd, *J* = 17.7, 2.1 Hz, 1 H), 5.11 (dd, *J* = 10.5, 1.5 Hz, 1 H), 3.14 (s, 3 H), 2.57 (m, 1 H), 2.34 (dd, *J* = 13.8, 2.1 Hz, 1 H), 1.60 (d, *J* = 13.8 Hz, 1 H), 1.51 (s, 1 H), 1.19 (dd, *J* = 13.5, 3.3 Hz, 1 H), 1.09 (s, 3 H), 1.01 (d, *J* = 14.4 Hz, 1 H), 1.00 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 140.7 (CH), 137.9 (CH), 134.5 (CH), 113.2 (CH₂), 79.6 (C), 78.9 (C), 49.3 (CH₃), 44.3 (CH₂), 43.4 (C), 40.3 (CH), 39.4 (CH₂), 24.7 (CH₃), 18.1 (CH₃); HRMS (EI) *m/z* 208.1461 [(M⁺), calcd. for C₁₃H₂₀O₂: 208.1463].

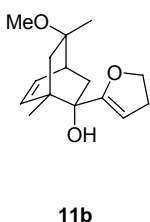
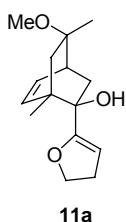
Typical substrate synthesis (10a/b, 11a/b): A solution of (5.00 eq) dihydrofuran, for **11a/b**, or dihydropyran, for **10a/b**, in 15 mL THF (1.8 M) was chilled to $-78\text{ }^{\circ}\text{C}$ prior to the dropwise addition of (5.05 eq) a *t*-BuLi/pentane (1.7 M) solution. After 15 min the reaction temperature was raised to $0\text{ }^{\circ}\text{C}$ for 45 min. Subsequent cooling to $-78\text{ }^{\circ}\text{C}$ was followed by the dropwise addition of (1.00 eq) **8a** or **8b** (1.1 M) in THF. After 15 min the reaction temperature was raised to $0\text{ }^{\circ}\text{C}$ and stirred for 5 hrs. The reaction was quenched with the addition of an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat.})}$ and partitioned with Et_2O . After separation, the ethereal layer was washed two times with an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat.})}$. The combined aqueous layers were extracted two times with Et_2O . The combined ethereal layers were washed once with brine and then dried over MgSO_4 , filtered, and concentrated. The residue was purified *via* flash alumina chromatography with hexanes/ethyl acetate as the eluent (30 g alumina per 1 g compd; 150 mesh; basic Activity III).



(**1S***, **2R***, **4S***, **8R***)-2-(2,3)-dihydropyranyl-8-methoxy-1,8-dimethyl-bicyclo[2.2.2]oct-5-en-2-ol (**10a**) and (**1S***, **2S***, **4S***, **8R***)-2-(2,3)-dihydropyranyl-8-methoxy-1,8-dimethyl-bicyclo[2.2.2]oct-5-en-2-ol (**10b**).

10a: $R_f = 0.50$ (5:1 Hex/EtOAc); $[\alpha]_{546}^{20} = -51.0$ (*c* 0.19, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.07 (t, $J = 7.5$ Hz, 1 H), 5.93 (d, $J = 7.8$ Hz, 1 H), 4.96 (t, $J = 3.6$ Hz, 1 H), 3.88 (m, 2 H), 3.61 (s, 1 H), 3.21 (s, 3 H), 2.64 (m, 1 H), 2.02 (m, 2 H), 1.96 (d, $J = 13.8$ Hz, 1 H), 1.74 (m, 4H), 1.12 (s, 3 H), 0.96 (s, 3 H), 0.95 (d, $J = 13.8$ Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 152.7 (C), 138.2 (CH), 132.3 (CH), 98.8 (CH), 79.5 (C), 78.1 (C), 65.9 (CH_2), 49.1 (CH_3), 44.4 (C), 42.1 (CH_2), 40.6 (CH), 37.4 (CH_2), 24.9 (CH_3), 22.1 (CH_2), 20.2 (CH_2), 19.4 (CH_3); IR (neat) 3543 (br s), 3050 (w), 2937 (s), 2874 (m), 2830 (m), 1714 (s), 1458 (m), 1369 (m), 1284 (w), 1105 (s), 1066 (s), 796 (m), 680 (m) cm^{-1} ; HRMS (EI) m/z 264.1719 [M^+] calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_3$: 264.1725].

10b: R_f = 0.30 (5:1 Hex/EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.25 (t, J = 7.8 Hz, 1 H), 5.82 (d, J = 7.8 Hz, 1 H), 5.19 (t, J = 3.9 Hz, 1 H), 3.95 (t, J = 5.4 Hz, 2 H), 3.15 (s, 3 H), 2.52 (m, 1 H), 2.40 (dd, J = 14.4, 1.8 Hz, 1 H), 2.04 (m, 2 H), 1.85 (d, J = 13.8 Hz, 1 H), 1.77 (m, 2 H), 1.37 (s, 1 H), 1.30 (dd, J = 14.4, 3.3 Hz, 1 H), 1.08 (s, 3 H), 0.98 (s, 3 H), 0.82 (d, J = 13.8 Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 155.6 (C), 140.2 (CH), 134.5 (CH), 95.8 (CH), 80.1 (C), 78.6 (C), 66.4 (CH_2), 49.2 (CH_3), 45.3 (C), 42.2 (CH_2), 40.8 (CH), 37.6 (CH_2), 25.3 (CH_3), 22.9 (CH_2), 20.3 (CH_2), 19.9 (CH_3); IR (neat) 3439 (br s), 3044 (w), 2934 (s), 2872 (s), 2826 (m), 1709 (s), 1458 (s), 1365 (s), 1255 (m), 1085 (s), 1066 (s), 987 (w), 846 (w), 734 (m) cm^{-1} ; HRMS (EI) m/z 264.1739 [M^+] calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_3$: 264.1725].



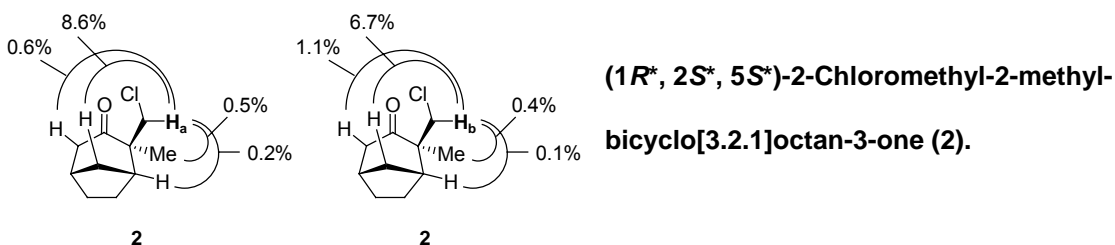
(1S*, 2R*, 4S*, 8S*)-1,8-dimethyl-2-(2,3)-dihydrofuryl-8-methoxybicyclo[2.2.2]oct-5-en-2-ol (11a) and (1S*, 2S*, 4S*, 8S*)-1,8-dimethyl-2-(2,3)-dihydrofuryl-8-methoxybicyclo[2.2.2]oct-5-en-2-ol (11b).

11a: R_f = 0.15 (4:1 Hex/EtOAc); $[\alpha]_{546}^{20}$ = -67.0 (c 0.32, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.39 (ABq, J = 8.1, 1.5 Hz, 1 H), 5.97 (d, J = 8.1 Hz, 1 H), 4.92 (t, J = 2.4 Hz, 1 H), 4.32 (t, J = 9.6 Hz, 2 H), 3.09 (s, 3 H), 2.68 (m, 1 H), 2.62 (td, J = 9.3, 2.7 Hz, 2 H), 2.23 (dd, J = 15.0, 1.5 Hz, 1 H), 2.04 (s, 1 H), 1.82 (d, J = 14.1 Hz, 1 H), 1.35 (s, 3 H), 1.21 (d, J = 9.3 Hz, 1 H), 1.13 (d, J = 9.3 Hz, 1 H), 1.09 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.4 (C), 136.1 (CH), 133.9 (CH), 97.2 (CH), 79.5 (C), 76.5 (C), 70.2 (CH_2), 48.9 (CH_3), 43.7 (CH_2), 43.4 (C), 39.9 (CH), 38.6 (CH_2), 29.9 (CH_2), 21.1 (CH_3), 19.3 (CH_3); IR (neat) 3466 (br m), 3090 (w), 2936 (s), 2872 (s), 2824 (m), 1707 (m), 1680 (w), 1456 (s), 1136 (s), 1080 (s), 970 (s), 941 (s), 830 (w), 731 (s) cm^{-1} ; HRMS (EI) m/z 250.1568 [M^+], calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_3$: 250.1569].

11b: R_f = 0.31 (4:1 Hex/EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 6.30 (t, J = 7.2 Hz, 1 H), 5.85 (d, J = 8.1 Hz, 1 H), 5.08 (t, J = 2.4 Hz, 1 H), 4.32 (dt, J = 9.3, 3.3 Hz, 2 H), 3.17 (s, 3 H), 2.65 (series

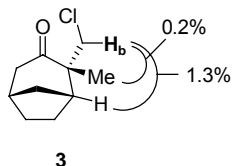
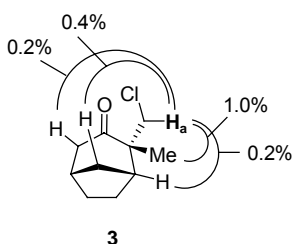
of m, 2 H), 2.55 (m, 1 H), 2.49 (dd, $J = 13.8, 2.1$ Hz, 1 H), 1.86 (d, $J = 13.8$ Hz, 1 H), 1.63 (d, $J = 14.7$ Hz, 1 H), 1.38 (dd, $J = 14.4, 3.3$ Hz, 1 H), 1.22 (s, 1 H), 1.11 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.7 (C), 137.6 (CH), 133.0 (CH), 97.7 (CH), 79.3 (C), 76.1 (C), 69.8 (CH_2), 49.2 (CH_3), 44.0 (CH_2), 42.5 (CH), 40.4 (CH_2), 38.5 (C), 30.5 (CH_2), 24.8 (CH_3), 19.4 (CH_3); IR (neat) 3468 (br s), 3061 (m), 2974 (s), 1710 (m), 1651 (s), 1456 (s), 1365 (s), 1163 (s), 1070 (s), 1008 (s), 939 (s), 852, (m), 733 (s) cm^{-1} ; HRMS (EI) m/z 250.1572 [M^+], calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_3$: 250.1569].

Typical one-carbon expansion procedure (2-7, 13-20, 22a/b): A solution of bicyclo[3.2.1]octan-3-one (1.00 eq) in CCl_4 (0.6 M) was chilled to 0 °C. After 10 min. at 0 °C, AcOH (1.95 eq) was added rapidly to the CCl_4 solution. This solution was stirred at 0 °C for an additional 5 min. and then added rapidly to a 0 °C solution of NaOCl (0.75 M 1.19 eq) in H_2O (same volume as CCl_4). The biphasic reaction was vigorously stirred for 6 hrs at 0 °C. The reaction was then poured into a cold solution of 3% K_2CO_3 in H_2O and partitioned with the addition of room temperature CH_2Cl_2 . After separation the organic layer was washed three times with a cold solution of 3% K_2CO_3 in H_2O . The combined aqueous washes were extracted three times with ambient CH_2Cl_2 . The combined CH_2Cl_2 layers were then dried over MgSO_4 , filtered, and concentrated. The residual was purified *via* flash chromatography (10 g SiO_2 per 1 g compd) with hexanes/ethyl acetate as the eluent.



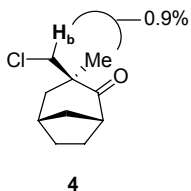
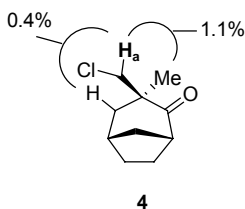
2: $R_f = 0.73$ (5:1 Hex/EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 3.71 (d, $J = 6.6$ Hz, 1 H), 3.52 (d, $J = 6.6$ Hz, 1 H), 2.49 (m, 2 H), 2.36 (m, 1 H), 2.21 (dm, $J = 15.0$ Hz, 1 H), 2.13 (d, $J = 12.5$ Hz, 1 H),

1.72-1.63 (series of m, 3 H), 1.52 (m, 1 H), 1.39 (m, 1 H), 1.15 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 212.0 (C), 54.9 (C), 50.7 (CH_2), 47.7 (CH_2), 43.6 (CH), 36.0 (CH_2), 33.7 (CH_2), 28.5 (CH), 25.0 (CH_2), 18.7 (CH_3); IR (neat) 2957 (s), 2878 (s), 1709 (s), 1462 (s), 1377 (s), 1290 (s), 1084 (m), 1041 (m), 964 (w), 916 (w), 881 (m), 733 (s) cm^{-1} ; HRMS (EI) m/z 186.0807 [(M^+) calcd. for $\text{C}_{10}\text{H}_{15}\text{O}^{35}\text{Cl}$: 186.0811].



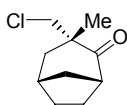
(1*R*^{*}, 2*R*^{*}, 5*S*^{*})-2-Chloromethyl-2-methyl-bicyclo[3.2.1]octan-3-one (3).

3: R_f = 0.61 (5:1 Hex/EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 3.78 (d, J = 7.2 Hz, 1 H), 3.68 (d, J = 6.9 Hz, 1 H), 2.61 (dm, J = 9.6 Hz, 1 H), 2.51 (series of m, 2 H), 2.12 (series of m, 2 H), 1.77-1.52 (series of m, 4H), 1.23 (m, 1 H), 1.26 (s, 3 H); ^1H NMR (500 MHz, C_6D_6) δ 3.86 (d, J = 11.7 Hz, 1 H), 3.66 (d, J = 11.7 Hz, 1 H), 2.30 (t, J = 4.4 Hz, 1 H), 2.10 (dd, J = 12.6 Hz, J = 4.4 Hz, 1 H), 1.91 (t, J = 4.4 Hz, 1 H), 1.86 (d, J = 3.8 Hz, 1 H), 1.56 (d, J = 12.0 Hz, 1 H), 1.28 (m, 3 H), 1.04 (m, 1 H), 1.00 (m, 1 H), 0.96 (d, J = 0.9 Hz, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 214.3 (C), 53.0 (C), 50.1 (CH), 47.3 (CH_2), 41.7 (CH), 35.6 (CH), 33.6 (CH_2), 28.2 (CH_2), 24.8 (CH_2), 22.0 (CH_3); IR (neat) 2953 (s), 2878 (ms), 1703 (s), 1460(m), 1288 (m), 1066 (m), 981 (w), 887 (w), 713 (m) cm^{-1} ; HRMS (EI) m/z 186.0808 [(M^+) calcd. for $\text{C}_{10}\text{H}_{15}\text{O}^{35}\text{Cl}$: 186.0811].



(1*R*^{*}, 3*R*^{*}, 5*S*^{*})-3-Chloromethyl-3-methyl-bicyclo[3.2.1]octan-2-one (4).

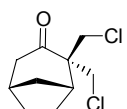
4: $R_f = 0.61$ (5:1 Hex/EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 3.82 (d, $J = 6.3$ Hz, 1 H), 3.10 (d, $J = 6.3$ Hz, 1 H), 2.77 (t, $J = 3.0$ Hz, 1 H), 2.49 (m, 1 H), 2.32 (dd, $J = 8.4, 2.7$ Hz, 1 H), 1.94 (series of m, 4 H), 1.69 (series of m, 2 H), 1.58 (dt, $J = 8.4, 1.5$ Hz, 1 H), 1.20 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 214.8 (C), 53.1 (CH_2), 50.8 (CH), 47.7 (C), 40.8 (CH_2), 34.7 (CH), 34.3 (CH_2), 28.7 (CH_2), 28.3 (CH_3), 28.1 (CH_2); IR (neat) 2955 (s), 2876 (s), 1709 (s), 1448 (s), 1288 (s), 1068 (m), 960 (m), 918 (m), 736 (s) cm^{-1} ; HRMS (EI) m/z 186.0801 [(M^+) calcd. for $\text{C}_{10}\text{H}_{15}\text{O}^{35}\text{Cl}$: 186.0811].



(1*R, 3*S**, 5*S**)-3-Chloromethyl-3-methyl-bicyclo[3.2.1]octan-2-one (4).**

5

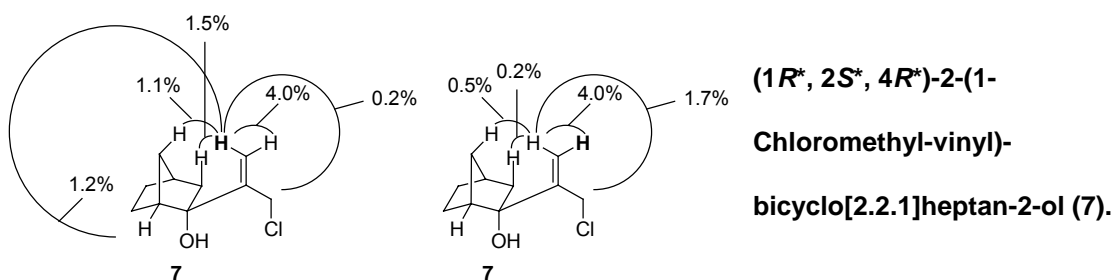
Compound 5 was never isolated in pure form and as a result spectral information is not available. It's isolation as a mixture with other regio and diastereomers allowed for its identification due to its inherent signature ^1H NMR signals and 1-D NOE correlations. See Johnson, C. R.; Herr, R. W. *J. Org. Chem.* **1973**, 38, 3153-3159.



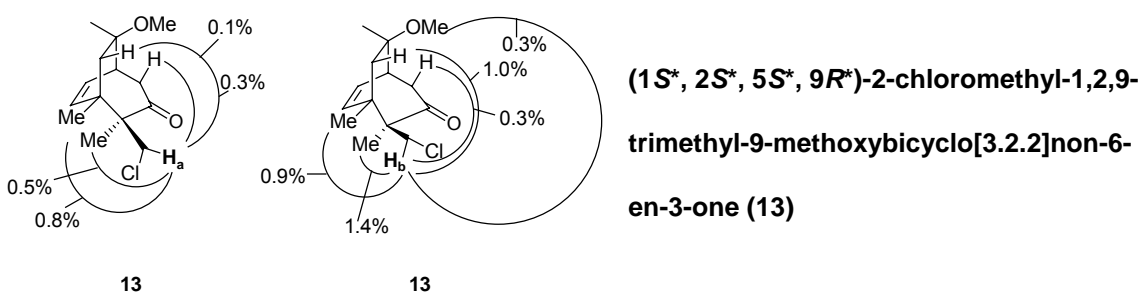
(1*R, 5*S**)-2,2-Bis-chloromethyl-bicyclo[3.2.1]octan-3-one (6).**

6

6: $R_f = 0.59$ (5:1 Hex/EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 4.18 (d, $J = 7.5$ Hz, 1 H), 4.00 (dd, $J = 6.9, 0.9$ Hz, 1 H), 3.85 (d, $J = 6.9$ Hz, 1 H), 3.64 (dd, $J = 7.2, 0.9$ Hz, 1 H), 2.59 (m, 3 H), 2.24 (dt, $J = 8.7, 1.8$ Hz, 1 H), 2.13 (d, $J = 7.5$ Hz, 1 H), 1.71 (m, 2 H), 1.58 (m, 2 H), 1.40 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.1 (C), 57.7 (C), 47.8 (CH_2), 45.0 (CH_2), 44.8 (CH_2), 40.9 (CH), 36.4 (CH), 33.6 (CH_2), 27.6 (CH_2), 25.2 (CH_2); IR (neat) 2959 (s), 2880 (m), 1714 (s), 1460 (m), 1439 (m), 1288 (m), 1190 (w), 1097 (w), 870 (w), 787 (s), 761 (s) cm^{-1} ; HRMS (EI) m/z 220.0426 [(M^+) calcd. for $\text{C}_{10}\text{H}_{14}\text{O}^{35}\text{Cl}_2$: 220.0422].

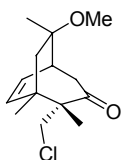


7: R_f = 0.45 (5:1 Hex/EtOAc); ^1H NMR (500 MHz, CDCl_3) δ 5.33 (s, 1 H), 5.26 (s, 1 H), 4.24 (d, J = 12.5 Hz, 1 H), 4.20 (d, J = 12.5 Hz, 1 H), 2.44 (m, 1 H), 2.38 (br s, 1 H), 2.23 (m, 1 H), 2.04 (dm, J = 5.1 Hz, 2 H), 1.60 (series of m, 2 H), 1.42 (dt, J = 7.5, 2.7 Hz, 1 H), 1.36 (series of m, 1 H), 1.30 (dp, J = 6.0, 1.2 Hz, 1 H), 1.22 (dd, J = 7.8, 2.1 Hz, 1 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 150.22 (C), 114.2 (CH_2), 81.0 (C), 45.7 (CH), 45.0 (CH_2), 44.8 (CH_2), 38.7 (CH_2), 37.0 (CH), 28.6 (CH_2), 21.9 (CH_2); IR (neat) 3428 (br m), 2959 (s), 2872 (m), 1690 (w), 1610 (w), 1454 (m), 1309 (m), 1163 (m), 1026 (m), 958 (m), 912 (m), 788 (s), 761 (s) cm^{-1} ; HRMS (EI) m/z 186.0815 [(M^+) calcd. for $\text{C}_{10}\text{H}_{15}\text{O}^{35}\text{Cl}$: 186.0811].



13: R_f = 0.83 (5:1Hex/EtOAc); $[\alpha]_{546}^{20}$ = -60.0 (c 0.10, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.20 (AB_q , J = 8.8, 1.3 Hz, 1 H), 5.82 (d, J = 8.8 Hz, 1 H), 3.87 (d, J = 11.0 Hz, 1 H), 3.77 (d, J = 11.4 Hz, 1 H), 3.17 (s, 3 H), 2.94 (dd, J = 15.9, 3.9 Hz, 1 H), 2.63 (d, J = 15.4 Hz, 1 H), 2.54 (m, 1 H), 2.32 (dd, J = 15.9, 3.9 Hz, 1 H), 1.25 (d, J = 15.4 Hz, 1 H), 1.19 (s, 3 H), 1.15 (s, 3 H), 1.06 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 209.9 (C), 139.8 (CH), 132.7 (CH), 78.3 (C), 58.1 (C), 49.3 (CH_3), 47.2 (CH_2), 45.9 (CH_2), 40.8 (CH_2), 40.0 (CH), 39.4 (C), 27.1 (CH_3), 24.6 (CH_3), 21.2 (CH_3); IR (neat) 3034 (m), 2932 (s), 2828 (m), 1701

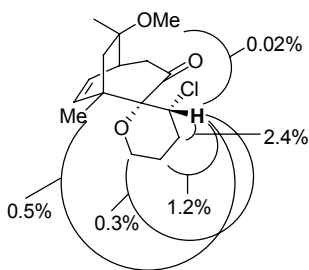
(s), 1458 (s), 1371 (s), 1277 (m), 1140 (s), 1064 (s), 916 (m), 738 (s), 680 (s) cm^{-1} ; HRMS (EI) m/z 256.1238 $[(M^+)]$; calcd. for $\text{C}_{14}\text{H}_{21}\text{O}_2^{35}\text{Cl}$: 256.7680].



14

(1S*, 2R*, 5S*, 9R*)-2-chloromethyl-1,2,9-trimethyl-9-methoxybicyclo[3.2.2]non-6-en-3-one (14).

14: R_f = 0.42 (5:1Hex/EtOAc); $[\alpha]_{546}^{20}$ = -48.0 (c 0.02, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.29 (ABq, J = 8.7, 0.9 Hz, 1 H), 5.90 (d, J = 9.0 Hz, 1 H), 3.64 (d, J = 3.0 Hz, 2 H), 3.15 (s, 3 H), 2.82 (dd, J = 15.6, 5.1 Hz, 1 H), 2.57 (m, 1 H), 2.37 (dd, J = 15.6, 2.7 Hz, 1 H), 2.06 (d, J = 15.3 Hz, 1 H), 1.16 (s, 3 H), 1.15 (s, 3 H), 1.12 (d, J = 15.6 Hz, 1 H), 1.07 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 212.3 (C), 135.7 (CH), 134.4 (CH), 78.8 (C), 56.9 (C), 50.3 (CH_3), 49.6 (CH_2), 45.9 (CH_2), 41.6 (CH), 40.8 (CH_2), 34.6 (C), 29.6 (CH_3), 24.8 (CH_3), 22.6 (CH_3); IR (neat) 3093 (w), 2986 (s), 2804 (s), 2777 (s), 1728 (s), 1705 (m), 1458 (s), 1383 (s), 1298 (m), 1116 (s), 1076 (s), 935 (m), 844 (m), 752 (m) cm^{-1} ; HRMS (EI) m/z 256.1233 $[(M^+)]$; calcd. for $\text{C}_{14}\text{H}_{21}\text{O}_2^{35}\text{Cl}$: 256.7680].

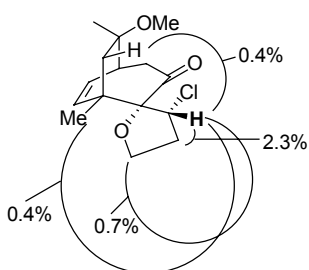


15

(1S*, 2R*-(3R*), 5S*, 9R*)-2-(3-chloro)-spiropyranyl-1,9-dimethyl-9-methoxybicyclo[3.2.2]non-6-en-3-one (15).

15: R_f = 0.08 (5:1Hex/EtOAc); $[\alpha]_{546}^{20}$ = +24.0 (c 0.20, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.16 (t, J = 6.6 Hz, 1 H), 6.02 (d, J = 6.6 Hz, 1 H), 4.96 (dd, J = 8.7, 3.8 Hz, 1 H), 3.65 (t, J = 5.5 Hz, 2 H), 3.21 (s, 3 H), 2.75 (m, 1 H), 1.95 (dd, J = 13.7, 3.3 Hz, 1 H), 1.93 (d, J = 14.2 Hz, 1 H), 1.86-1.75 (series of m, 3 H), 1.70 (dd, J = 13.7, 2.7 Hz, 1 H), 1.62 (m, 1 H), 1.13 (s, 3 H), 0.97 (s, 3 H),

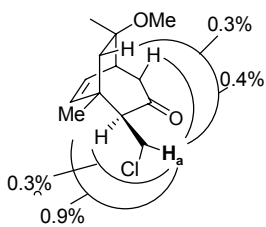
0.94 (d, $J = 14.2$ Hz, 1 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 208.0 (C), 140.1 (CH), 131.3 (CH), 82.3 (C), 78.3 (C), 61.9 (CH_2), 57.4 (C), 49.7 (CH_3), 46.2 (CH_2), 43.7 (C), 42.2 (CH_2), 40.3 (CH), 29.1 (CH_2), 29.0 (CH_2), 24.4 (CH_3), 18.5 (CH_3); IR (neat) 3049 (w), 2932 (s), 1724 (s), 1643 (w), 1460 (s), 1367 (s), 1334 (s), 1286 (s), 1224 (s), 1169 (s), 1105 (s), 1062 (s), 910 (s), 846 (m), 756 (m), 731 (m), 704 (m), 667 (s) cm^{-1} ; HRMS (EI) m/z 298.1244 [M^+]; calcd. for $\text{C}_{16}\text{H}_{23}\text{O}_3^{35}\text{Cl}$: 298.8047].



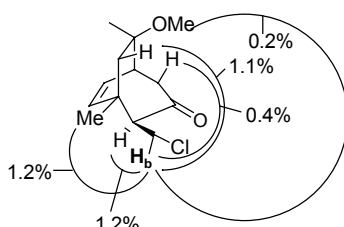
(1S*, 2R*, 5S*, 9S*)-2-(3-chloro)-spirofuranyl-1,9-dimethyl-9-methoxybicyclo[3.2.2]non-6-en-3-one (16).

16

16: $R_f = 0.56$ (4:1 Hex/EtOAc); $[\alpha]_{546}^{20} = -91.0$ (c 0.16, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.32 (AB_q , $J = 8.3, 1.9$ Hz, 1 H), 5.82 (d, $J = 7.3$ Hz, 1 H), 4.06 (m, 2 H), 3.03 (s, 3 H), 3.00 (t, $J = 5.8$ Hz, 1 H), 2.71 (dd, $J = 7.3, 2.9$ Hz, 2 H), 2.65 (m, 1 H), 2.42 (dd, $J = 14.1, 7.3$ Hz, 1 H), 2.33 (dd, $J = 15.1, 2.44$ Hz, 1 H), 1.91 (d, $J = 14.6$ Hz, 1 H), 1.33 (d, $J = 14.6$ Hz, 1 H), 1.29 (s, 3 H), 1.06 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (75 MHz, CDCl_3) δ 208.5 (C), 135.2 (CH), 133.4 (CH), 111.6 (C), 85.4 (CH), 67.9 (C), 65.7 (CH_2), 43.8 (CH_3), 38.4 (CH_2), 37.2 (CH_2), 34.9 (C), 33.7 (CH), 25.9 (CH_2), 24.4 (CH_3), 19.0 (CH_3); IR (neat) 3110 (w), 2932 (s), 1721 (m), 1705 (m), 1454 (s), 1369 (s), 1300 (s), 1242 (s), 1217 (s), 1174 (s), 1082 (s), 925 (s), 879 (s), 781 (m), 756 (m), 734 (mw), 677 (mw) cm^{-1} ; HRMS (EI) m/z 284.1205 [M^+]; calcd. for $\text{C}_{15}\text{H}_{21}\text{O}_3^{35}\text{Cl}$: 284.1179].



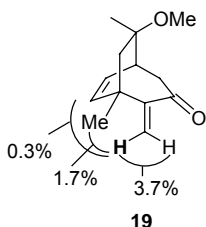
18



18

(1*S*^{*}, 2*S*^{*}, 5*S*^{*}, 9*R*^{*})-2-chloromethyl-1,9-dimethyl-9-methoxybicyclo[3.2.2]non-6-en-3-one (18).

18: $R_f = 0.33$ (5:1Hex/EtOAc); $[\alpha]_{546}^{20} = -49.4$ (c 0.68, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.28 (AB_q, $J = 7.8, 1.2$ Hz, 1 H), 5.83 (d, $J = 9.0$ Hz, 1 H), 3.74 (dd, $J = 11.4, 4.2$ Hz, 1 H), 3.49 (dd, $J = 11.4, 8.4$ Hz, 1 H), 3.15 (s, 3 H), 2.79 (dd, $J = 15.9, 5.4$ Hz, 1 H), 2.64 (m, 1 H), 2.59 (dd, $J = 8.4, 4.2$ Hz, 1 H), 2.19 (dd, $J = 13.2, 2.4$ Hz, 1 H), 1.94 (d, $J = 14.4$ Hz, 1 H), 1.43 (d, $J = 15.0$ Hz, 1 H), 1.23 (s, 3 H), 1.17 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (75 MHz, CDCl_3) δ 208.5 (C), 136.1 (CH), 133.6 (CH), 78.5 (C), 66.6 (CH), 49.7 (CH₂), 49.3 (CH₃), 42.6 (CH₂), 41.3 (CH₂), 40.3 (CH), 36.5 (C), 29.6 (CH₃), 26.9 (CH₃); IR (neat) 3070 (w), 2961 (s), 2928 (s), 2855 (m), 1684 (s), 1599 (m), 1462 (s), 1371 (s), 1257 (m), 1134 (s), 1064 (s), 765 (m) cm^{-1} ; HRMS (EI) m/z 242.1163 [M^+]; calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_2^{35}\text{Cl}$: 242.1074].

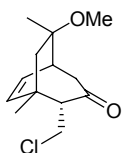


19

(1*S*^{*}, 5*S*^{*}, 9*R*^{*})-1,9-dimethyl-9-methoxy-2-methylenebicyclo[3.2.2]non-6-en-3-one (19).

19: $R_f = 0.40$ (5:1 Hex/EtOAc); $[\alpha]_D^{20} = -53.5$ (c 1.05, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.21 (AB_q, $J = 8.1, 1.2$ Hz, 1 H), 5.82 (d, $J = 0.9$ Hz, 1 H), 5.77 (d, $J = 8.7$ Hz, 1 H), 5.15 (d, $J = 0.6, 1$ H), 3.16 (s, 3 H), 2.99 (dd, $J = 18.0, 3.6$ Hz, 1 H), 2.59 (m, 1 H), 2.27 (dd, $J = 18.3, 4.2$ Hz, 1 H), 1.99 (d, $J = 14.4$ Hz, 1 H), 1.57 (d, $J = 14.1$ Hz, 1 H), 1.25 (s, 3 H), 1.23 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (75 MHz, CDCl_3) δ 202.2 (C), 154.4 (C), 137.4 (CH), 132.6 (CH), 116.9 (CH₂), 78.1 (C), 49.6 (CH₂), 49.3 (CH₃), 42.2 (CH₂), 40.0 (CH), 38.2 (C), 26.8 (CH₃), 26.4 (CH₃); IR (neat) 3040 (m), 2970 (s), 2965 (s), 2860 (m), 1710 (m), 1684 (s),

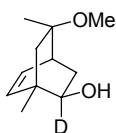
1599 (s), 1450 (s), 1371 (s), 1136 (s), 1064 (s), 960 (m), 765 (m) cm^{-1} ; HRMS (EI) m/z 206.1298 $[(M^+)]$; calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_2$: 206.1307].



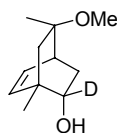
20

(1*S*^{*}, 2*R*^{*}, 5*S*^{*}, 9*R*^{*})-2-chloromethyl-1,9-dimethyl-9-methoxybicyclo[3.2.2]non-6-en-3-one (20).

20: R_f = 0.26 (5:1Hex/EtOAc); $[\alpha]_{546}^{20}$ = -20.0 (c 0.14, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 6.28 (AB_q, J = 8.7, 1.1 Hz, 1 H), 5.84 (d, J = 9.3 Hz, 1 H), 3.74 (dd, J = 11.5, 3.9 Hz, 1 H), 3.50 (dd, J = 11.5, 8.2 Hz, 1 H), 3.16 (s, 3 H), 2.78 (dd, J = 15.3, 4.9 Hz, 1 H), 2.65 (m, 1 H), 2.60 (dd, J = 7.7, 3.3 Hz, 1 H), 2.19 (dd, J = 15.9, 2.7 Hz, 1 H), 1.93 (d, J = 14.2 Hz, 1 H), 1.35 (d, J = 14.3 Hz, 1 H), 1.18 (s, 3 H), 1.17 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 224.1 (C), 136.8 (CH), 132.2 (CH), 78.3 (C), 78.0 (CH), 50.0 (CH_3), 49.7 (CH_2), 41.0 (CH), 34.5 (CH_2), 29.9 (CH_2), 28.0 (CH_3), 24.3 (C), 22.6 (CH_3); IR (neat) 3023 (w), 2918 (s), 2849 (s), 1724 (w), 1603 (w), 1462 (m), 1379 (m), 1120 (ms), 1074 (m), 935 (w), 844 (w), 758 (m) cm^{-1} ; HRMS (EI) m/z 242.1087 $[(M^+)]$; calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_2^{35}\text{Cl}$: 242.1074].



21a



21b

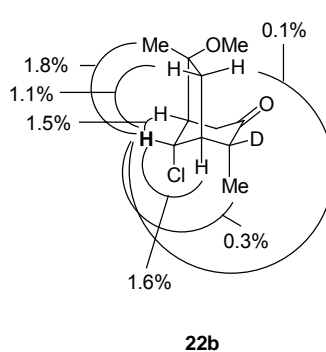
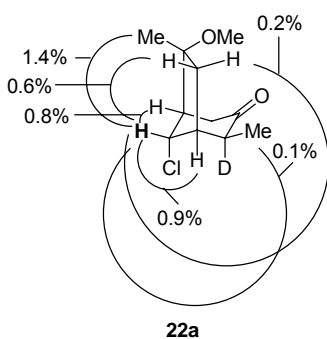
(1*S*^{*}, 2*R*^{*}, 4*S*^{*}, 8*R*^{*})-8-methoxy-1,8-dimethylbicyclo[2.2.2]oct-5-en-2-ol (21a) and (1*S*^{*}, 2*S*^{*}, 4*S*^{*}, 8*R*^{*})-8-methoxy-1,8-dimethylbicyclo[2.2.2]oct-5-en-2-ol (21b).

A solution of **8a** (1.00 eq) in 30 mL 95% EtOH (0.37 M) was cooled to 0 °C after which LiAlD_4 (1.00 eq), was added in one portion. The reaction was stirred at 0 °C for 30 min., then warmed to room temperature and stirred for 16 hrs. The reaction was then quenched with an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat})}$ and partitioned with Et_2O . After separation the ethereal phase was washed two times with an aqueous solution of $\text{NH}_4\text{Cl}_{(\text{sat})}$. The combined aqueous layer were extracted

two consecutive times with Et₂O. The combined ethereal layers were dried over MgSO₄, filtered, and concentrated. The crude residue was purified *via* flash alumina chromatography with hexanes/ethyl acetate (10:1) as the eluent (30 g alumina per 1 g compd; 150 mesh; basic Activity III) to afford a 1:1 mixture of carbinols in 67 % yield.

21a: ¹H NMR (300 MHz, CDCl₃) δ 6.19 (AB_q, *J* = 8.1 Hz, *J* = 1.2 Hz, 1 H), 5.77 (d, *J* = 8.1 Hz, 1 H), 3.17 (s, 3 H), 2.53 (m, 1 H), 2.48 (d, *J* = 14.4 Hz, 1 H), 1.87 (s, 1 H), 1.67 (m, 1 H), 1.61 (dd, *J* = 13.5, 2.7 Hz, 1 H), 1.16 (s, 3 H), 1.10 (s, 3 H), 0.86 (dd, *J* = 13.5, 2.7 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 134.9 (CH), 134.5 (CH), 78.9 (C), 77.5 (CD), 49.4 (CH₃), 42.7 (CH₂), 40.5 (C), 39.4 (CH), 33.5 (CH₂), 24.6 (CH₃), 21.2 (CH₃); IR (neat) 3433 (br s), 3040 (m), 2934 (s), 2870 (s), 2826 (m), 1458 (s), 1385 (s), 1325 (m), 1280 (m), 1221 (m), 1145 (s), 1109 (s), 1076 (s), 947 (m), 920 (m), 890 (m), 723 (s), 700 (m), 673 (m) cm⁻¹; HRMS (EI) *m/z* 183.1342 [(M⁺); calcd. for C₁₁H₁₇DO₂: 183.1369].

21b: ¹H NMR (300 MHz, CDCl₃) δ 6.33 (t, *J* = 7.2 Hz, 1 H), 5.85 (d, *J* = 7.8 Hz, 1 H), 3.13 (s, 3 H), 2.53 (m, 1 H), 1.83 (s, 1 H), 1.72 (m, 1 H), 1.61 (dd, *J* = 13.5, 2.7 Hz, 1 H), 1.29 (d, *J* = 13.5 Hz, 1 H), 1.12 (s, 3 H), 1.08 (s, 3 H), 0.97 (d, *J* = 13.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 138.8 (CH), 134.3 (CH), 78.8 (C), 76.4 (CD), 49.5 (CH₃), 46.6 (CH₂), 40.8 (C), 39.5 (CH), 34.0 (CH₂), 24.3 (CH₃), 21.1 (CH₃); HRMS (EI) *m/z* 183.1378 [(M⁺); calcd. for C₁₁H₁₇DO₂: 183.1369].

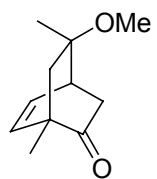


(1*R*^{*}, 2*S*^{*}, 5*S*^{*}, 6*S*^{*}, 8*R*^{*})-2-deutero-8-Chloro-6-methoxy-2,6-dimethyl-bicyclo[3.2.1]octan-3-one (22a) and (1*R*^{*}, 2*R*^{*}, 5*S*^{*}, 6*S*^{*}, 8*R*^{*})-2-deutero-8-Chloro-6-methoxy-2,6-dimethyl-bicyclo[3.2.1]octan-3-one (22b).

Use of the typical one-carbon expansion procedure provided 40 % **22a** and 20 % **22b** after purification of the crude reaction mixture *via* flash chromatography with hexanes/ethyl acetate (10:1) as the eluent (15 g alumina per 1 g compd).

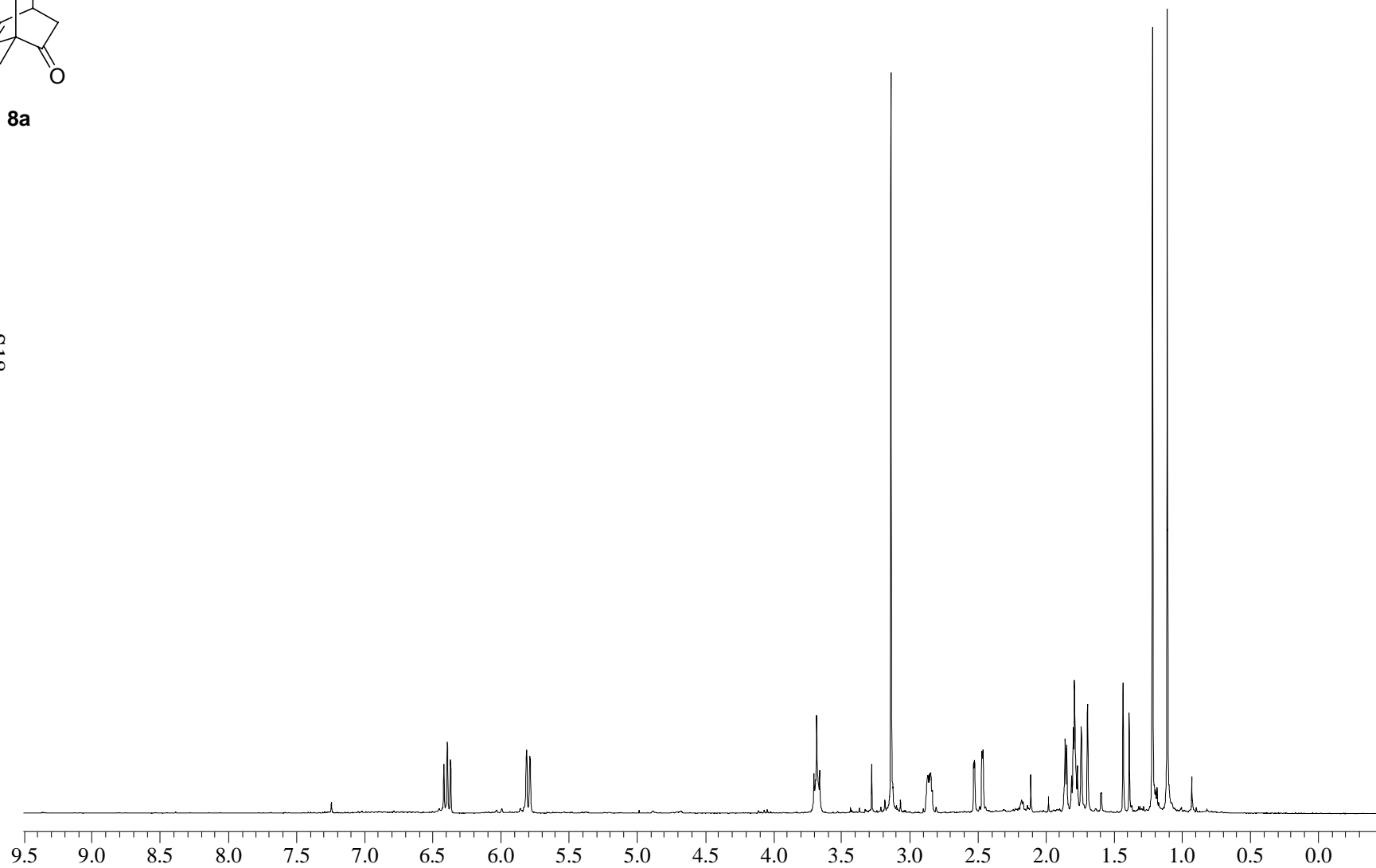
22a: $R_f = 0.56$ (4:1 Hex/EtOAc); $[\alpha]_{546}^{20} = +40.0$ (c 0.23, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 4.40 (dt, $J = 4.5, 1.5$ Hz, 1 H), 3.12 (s, 3 H), 2.71 (dd, $J = 15.9, 3.9$ Hz, 1 H), 2.51 (ddd, $J = 16.2, 3.0, 1.5$ Hz, 1 H), 2.43 (m, 1 H), 2.31 (m, 1 H), 1.81 (d, $J = 14.4$ Hz, 1 H), 1.64 (dd, $J = 14.4, 6.6$ Hz, 1 H), 1.32 (s, 3 H), 1.00 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (75 MHz, CDCl_3) δ 209.7 (C), 80.7 (C), 61.2 (CH), 51.1 (CH), 50.9 (CH_3), 48.5 (CD), 45.5 (CH), 38.6 (CH_2), 37.6 (CH_2), 25.8 (CH_3), 11.8 (CH_3); IR (neat) 2974 (s), 2937 (s), 1714 (s), 1450 (s), 1412 (m), 1379 (s), 1323 (m), 1226 (s), 1153 (s), 1078 (s), 918 (s), 852 (m), 798 (m), 733 (s) cm^{-1} ; HRMS (EI) m/z 217.7186 [(M^+) ; calcd. for $\text{C}_{11}\text{H}_{16}\text{DO}_2^{35}\text{Cl}$: 217.7192].

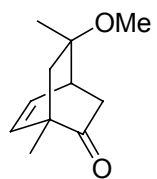
22b: $R_f = 0.31$ (5:1 Hex/EtOAc); $[\alpha]_{546}^{20} = +18.0$ (c 0.08, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 4.26 (t, $J = 3.3$ Hz, 1 H), 3.14 (s, 3H), 2.78 (dd, $J = 10.8, 2.7$ Hz, 1 H), 2.68 (ddd, $J = 10.8, 1.5, 0.6$ Hz, 1 H), 2.45 (m, 1 H), 2.39 (m, 1 H), 1.83 (m, 2 H), 1.34 (s, 3 H), 1.32 (s, 3 H); For 1-D NOE correlations see scheme shown above; ^{13}C NMR (125 MHz, CDCl_3) δ 208.5 (C), 80.0 (C), 59.4 (CH), 50.9 (CH_3), 50.4 (CH), 49.3 (CD), 45.0 (CH_2), 44.6 (CH), 37.1 (CH_2), 26.0 (CH_3), 19.8 (CH_3); IR (neat) 2970 (s), 2937 (s), 1709 (s), 1454 (m), 1377 (m), 1325 (m), 1226 (m), 1167 (m), 1084 (m), 1064 (s), 929 (m), 790 (m) cm^{-1} ; HRMS (EI) m/z 217.7190 [(M^+) ; calcd. for $\text{C}_{11}\text{H}_{16}\text{DO}_2^{35}\text{Cl}$: 217.7192].



8a

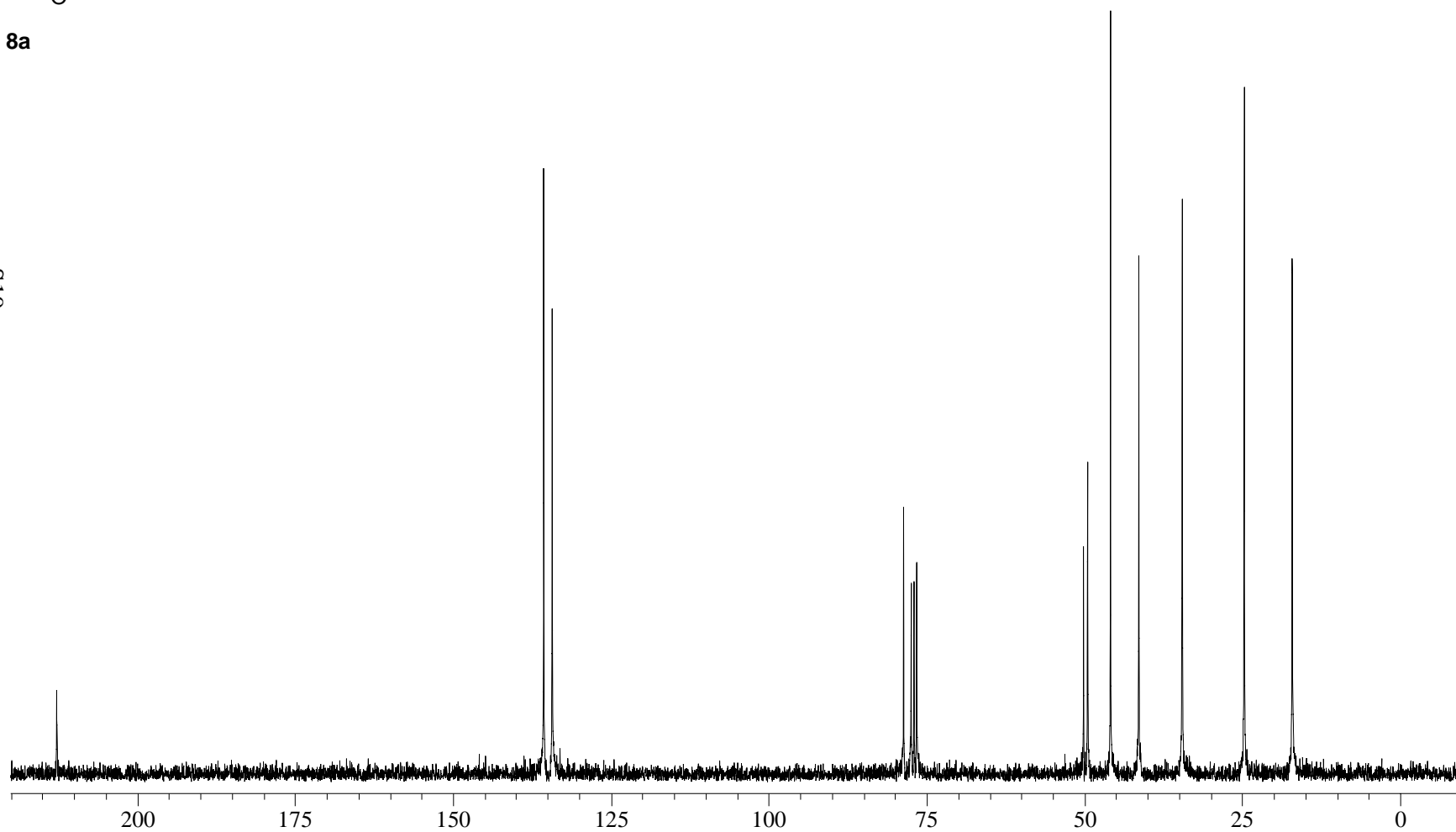
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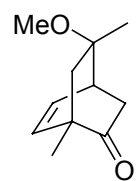




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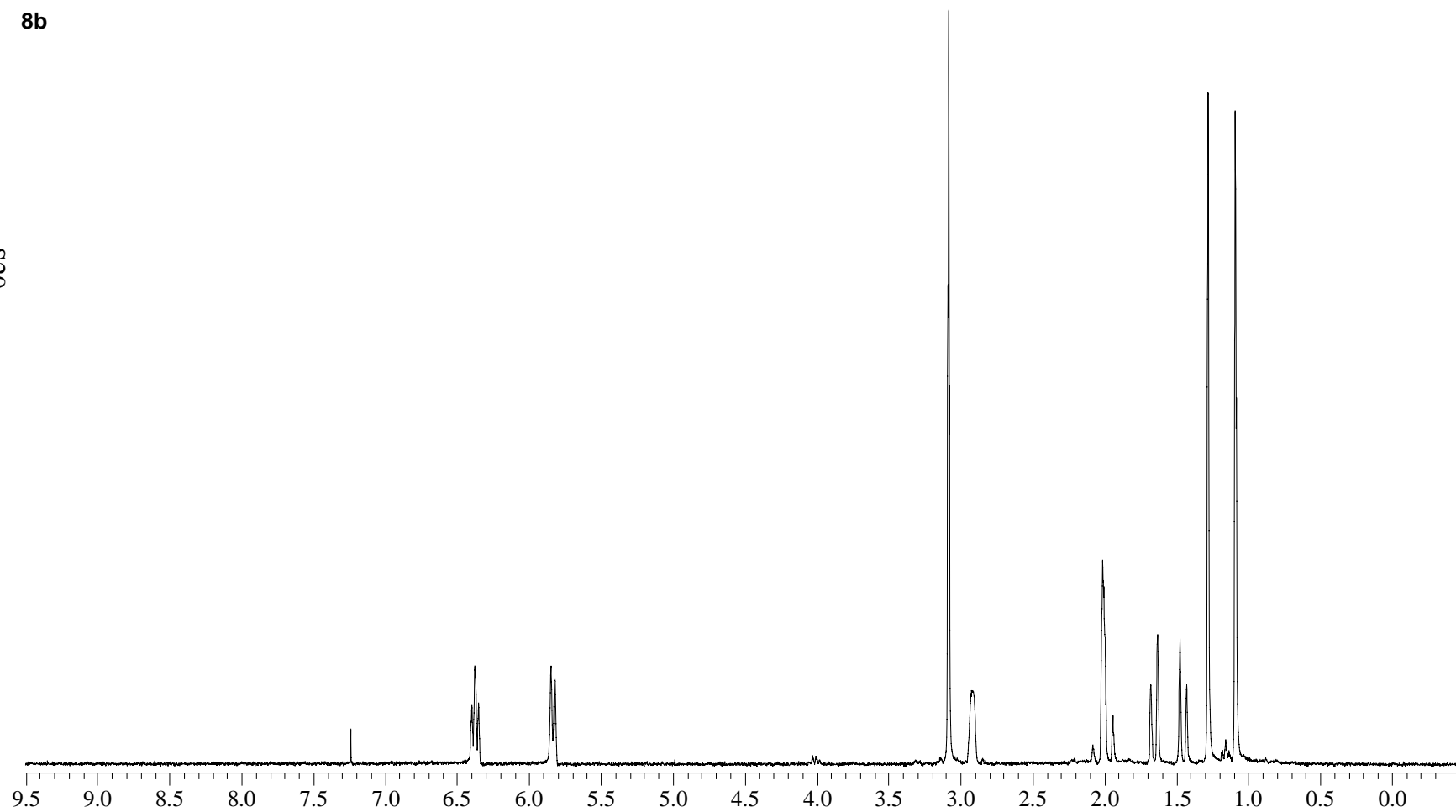
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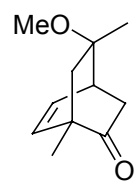




8b

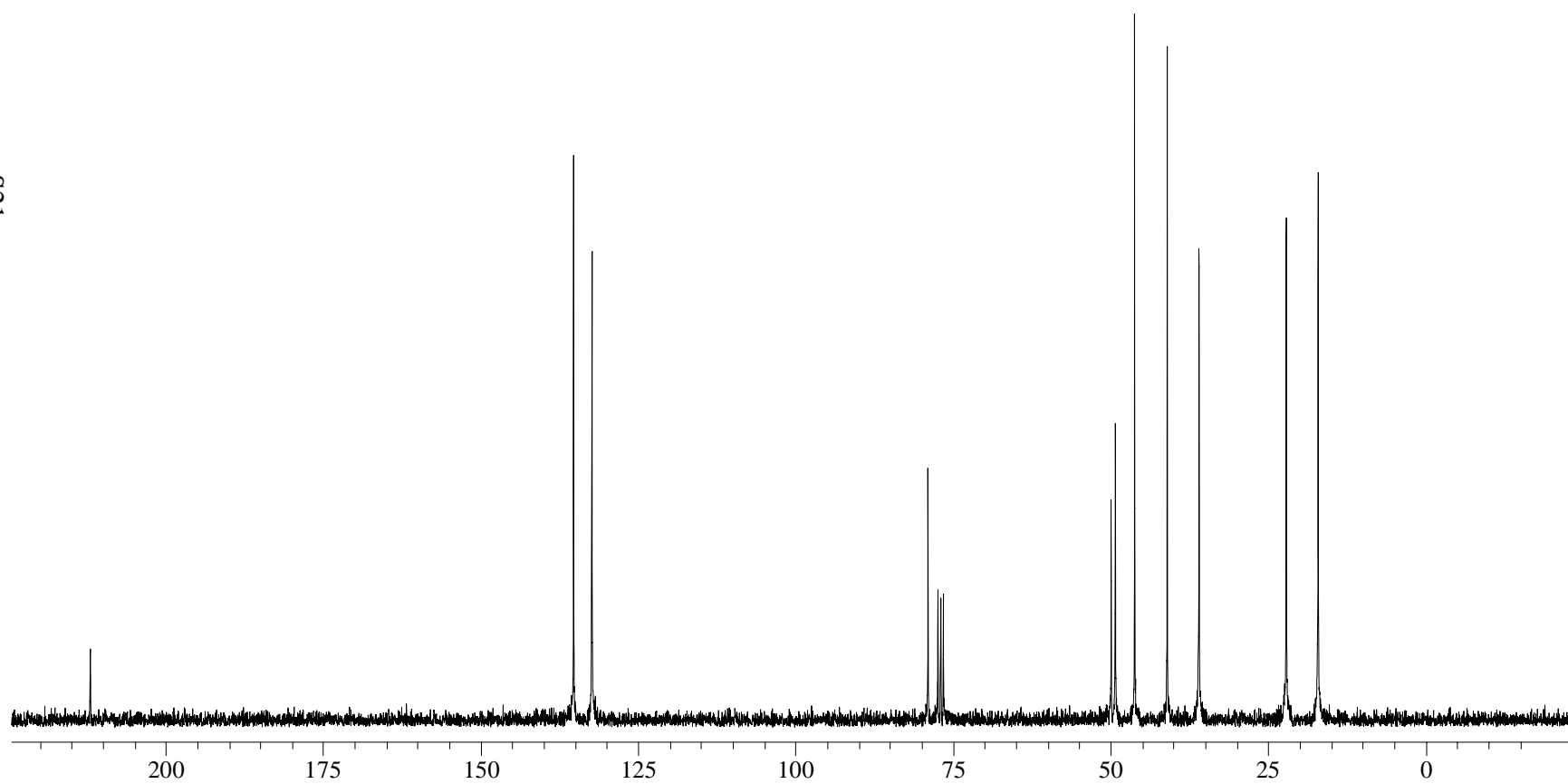
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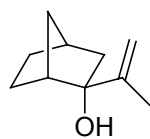




8b

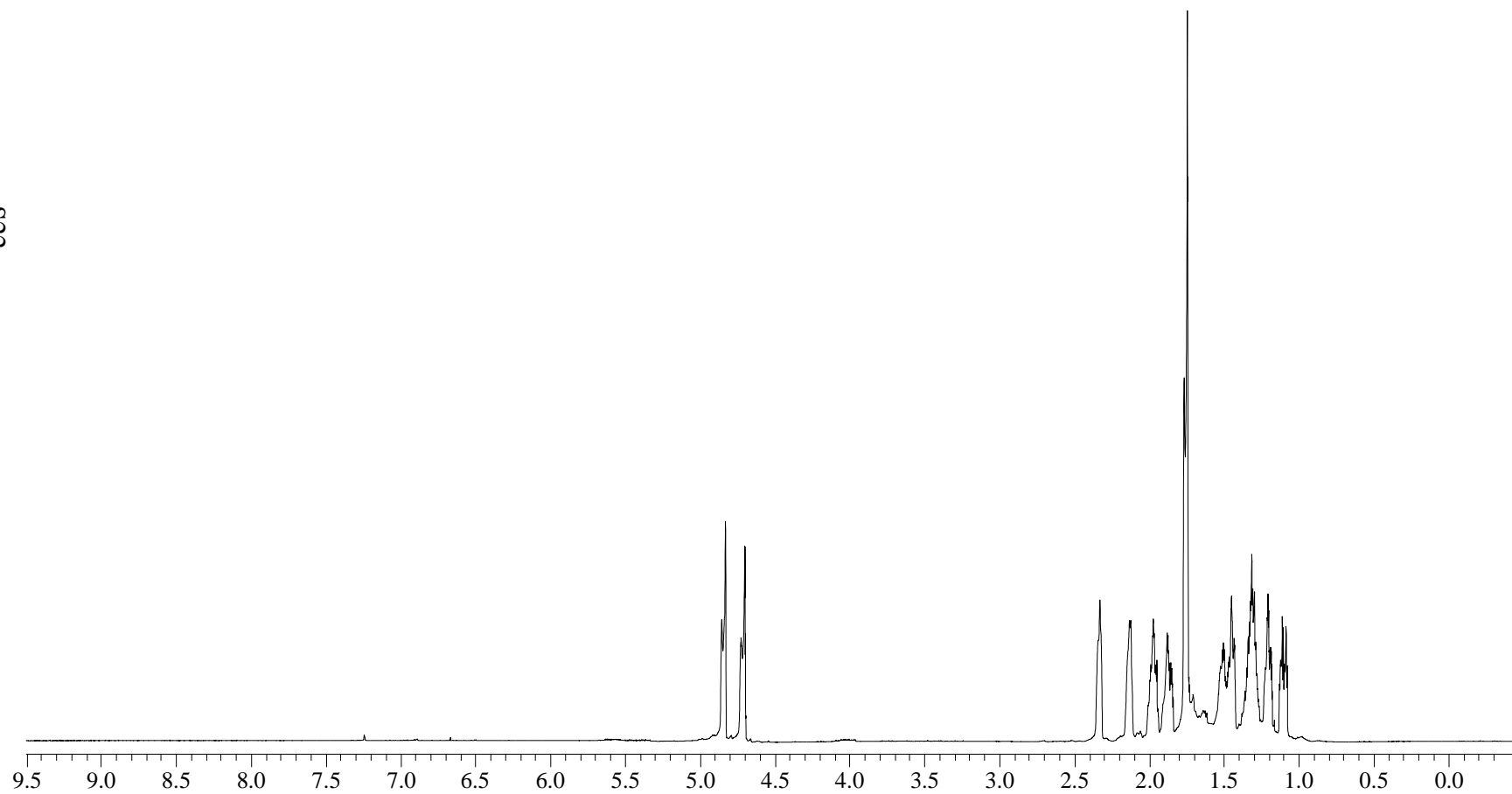
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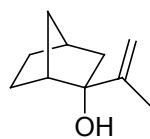




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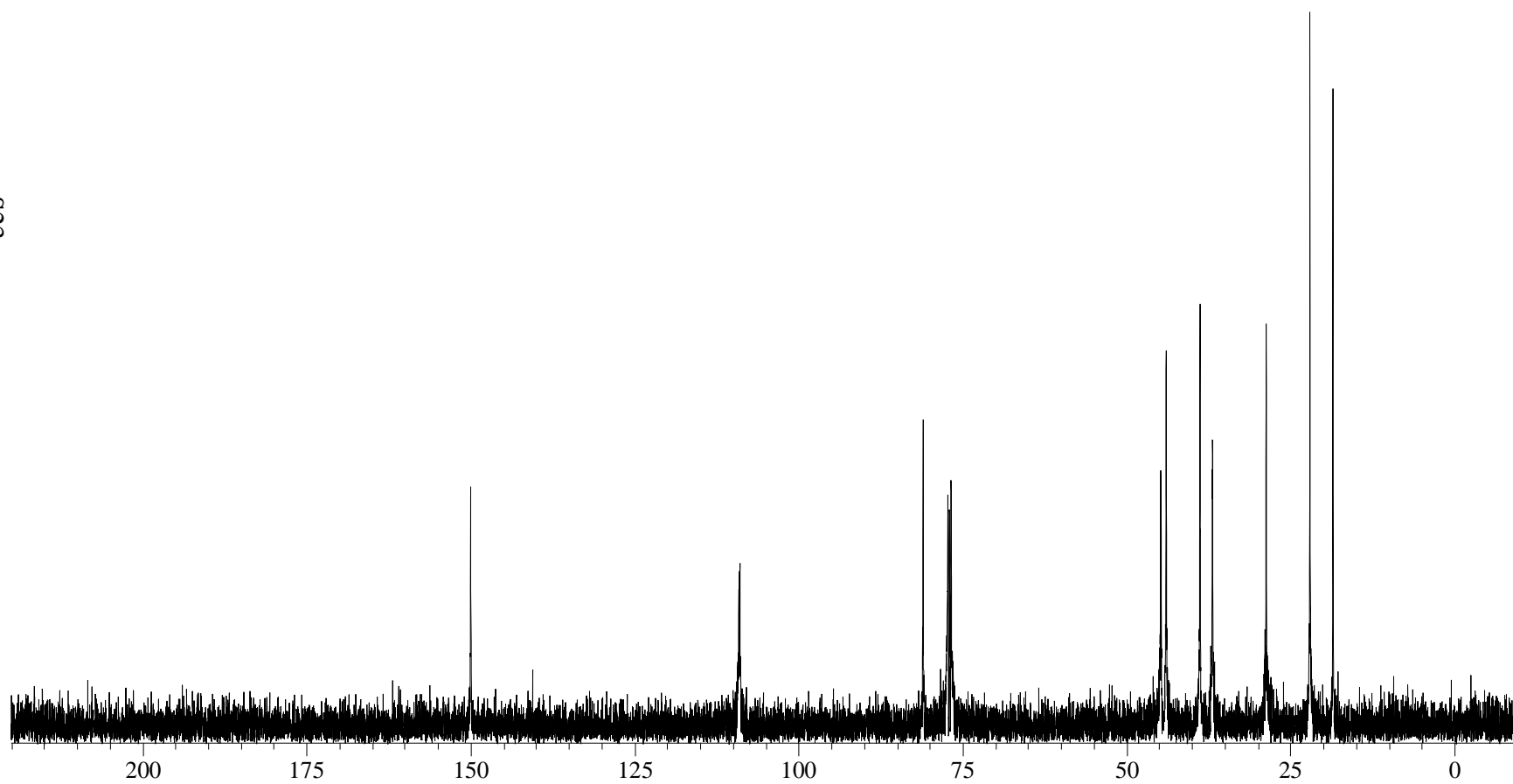
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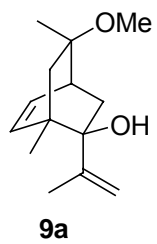




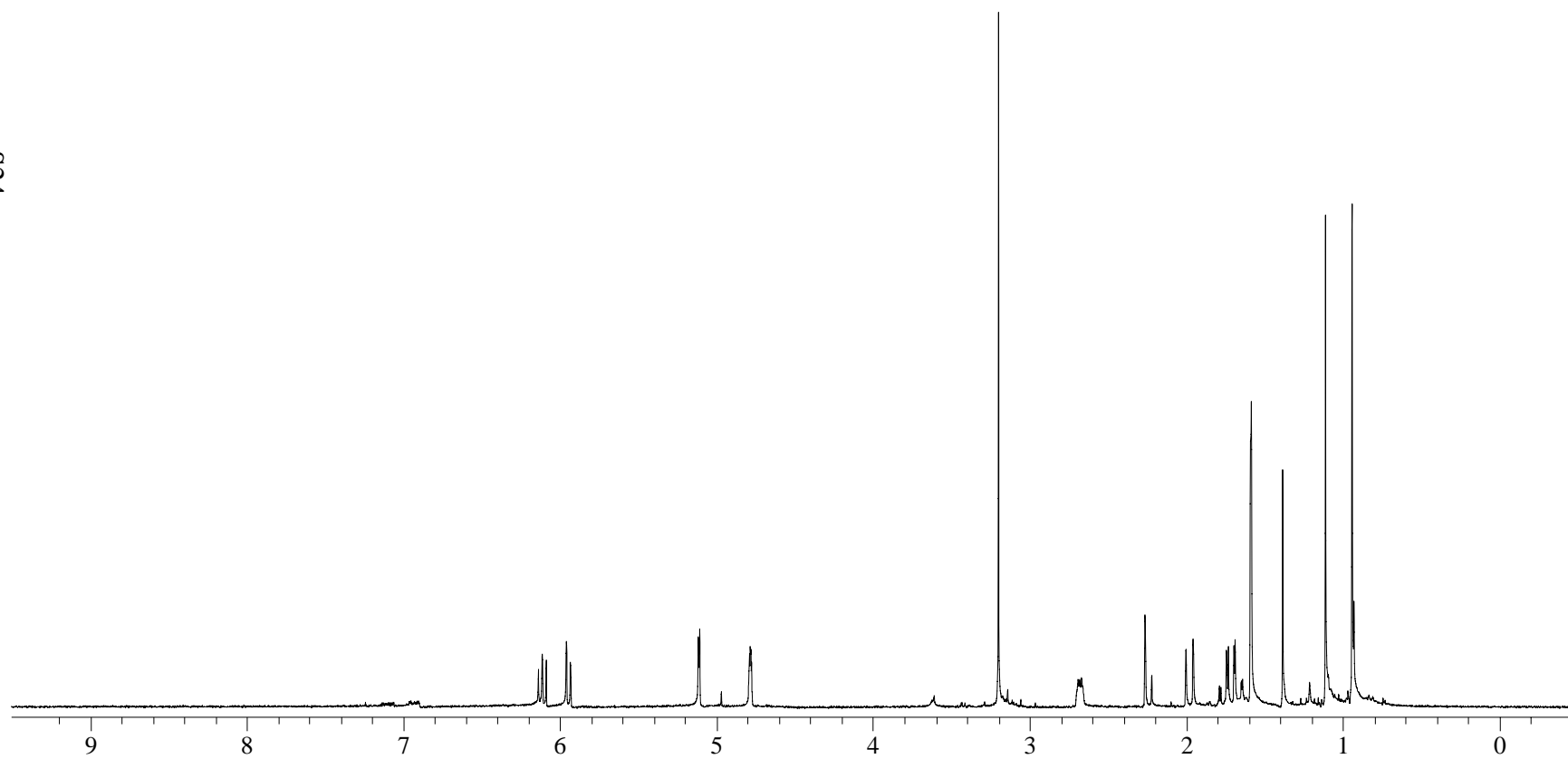
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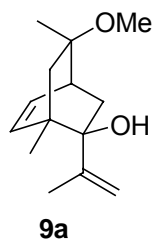
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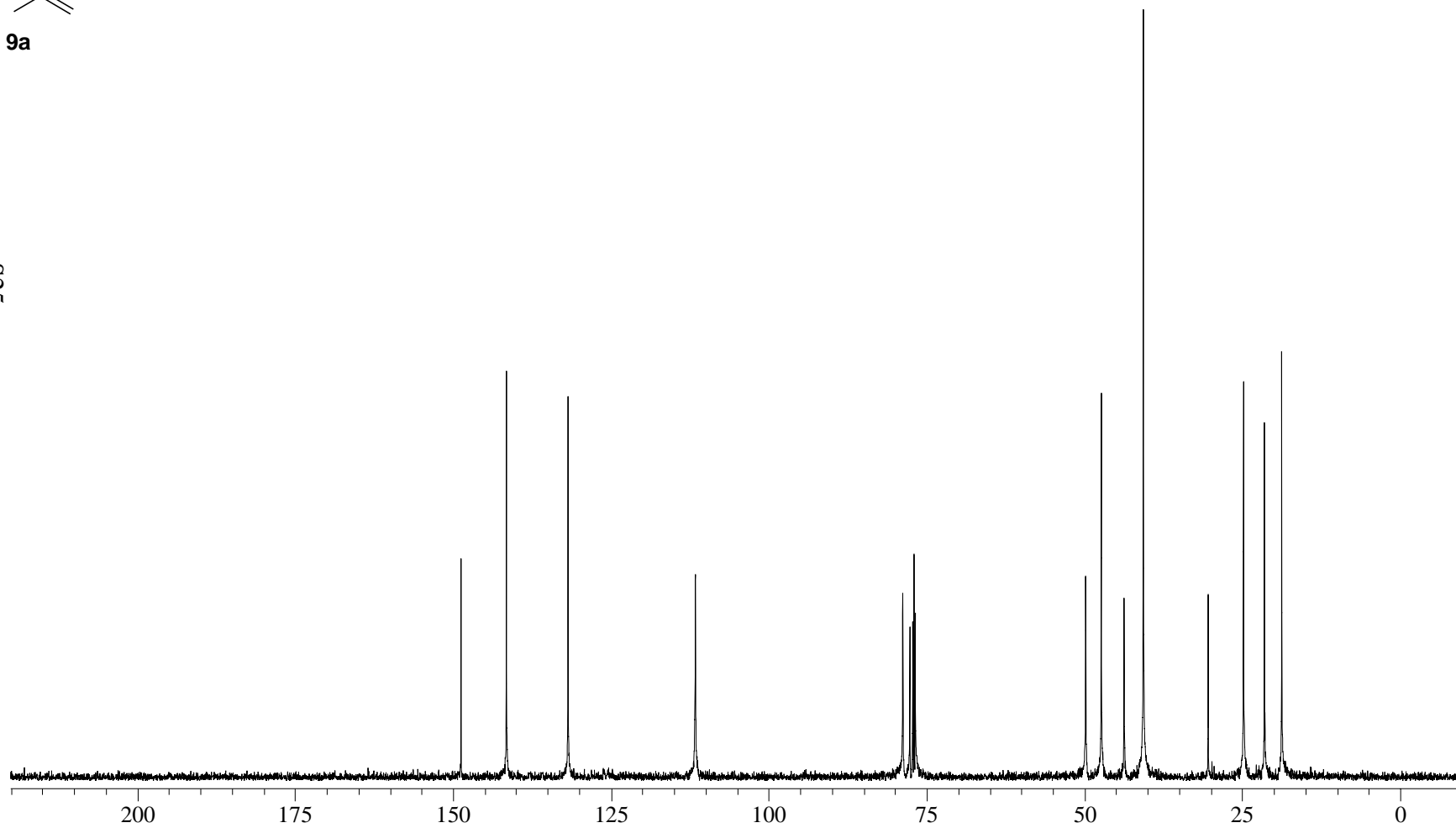


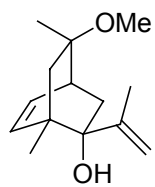
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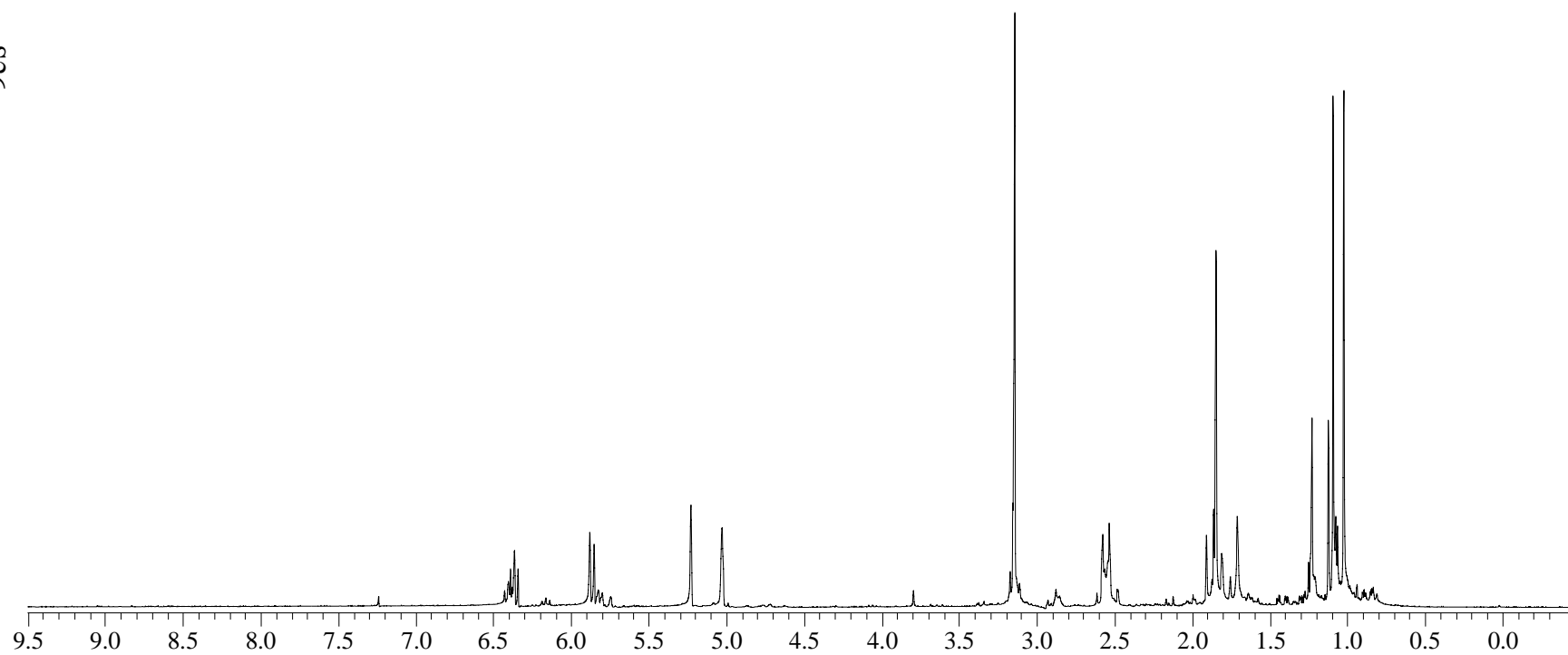
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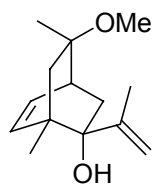




9b

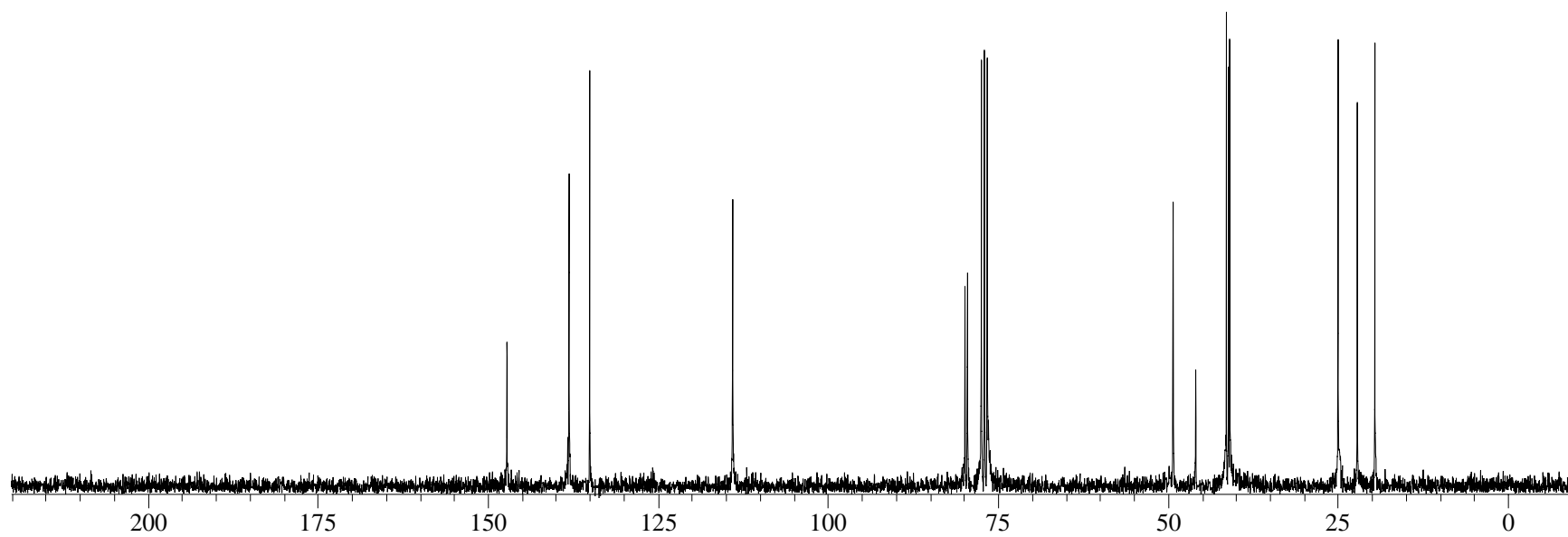
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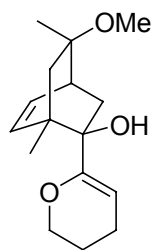




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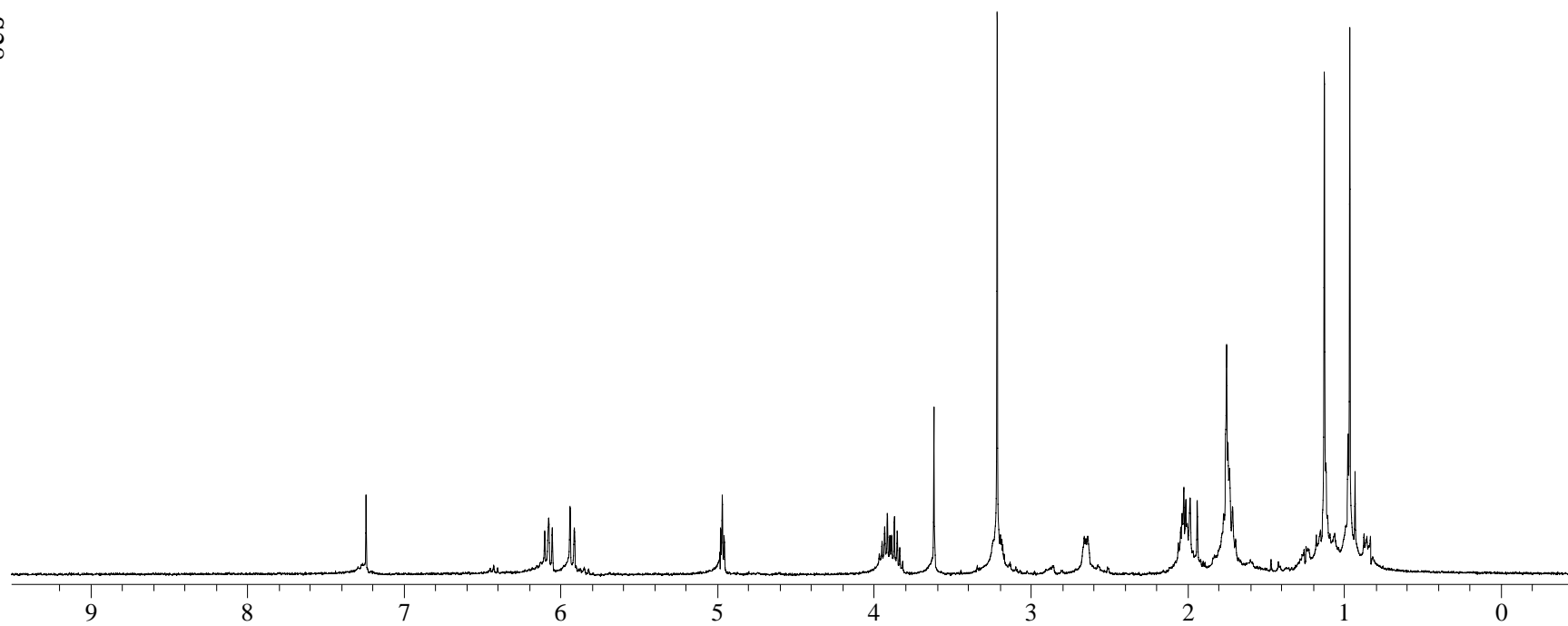
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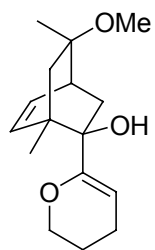




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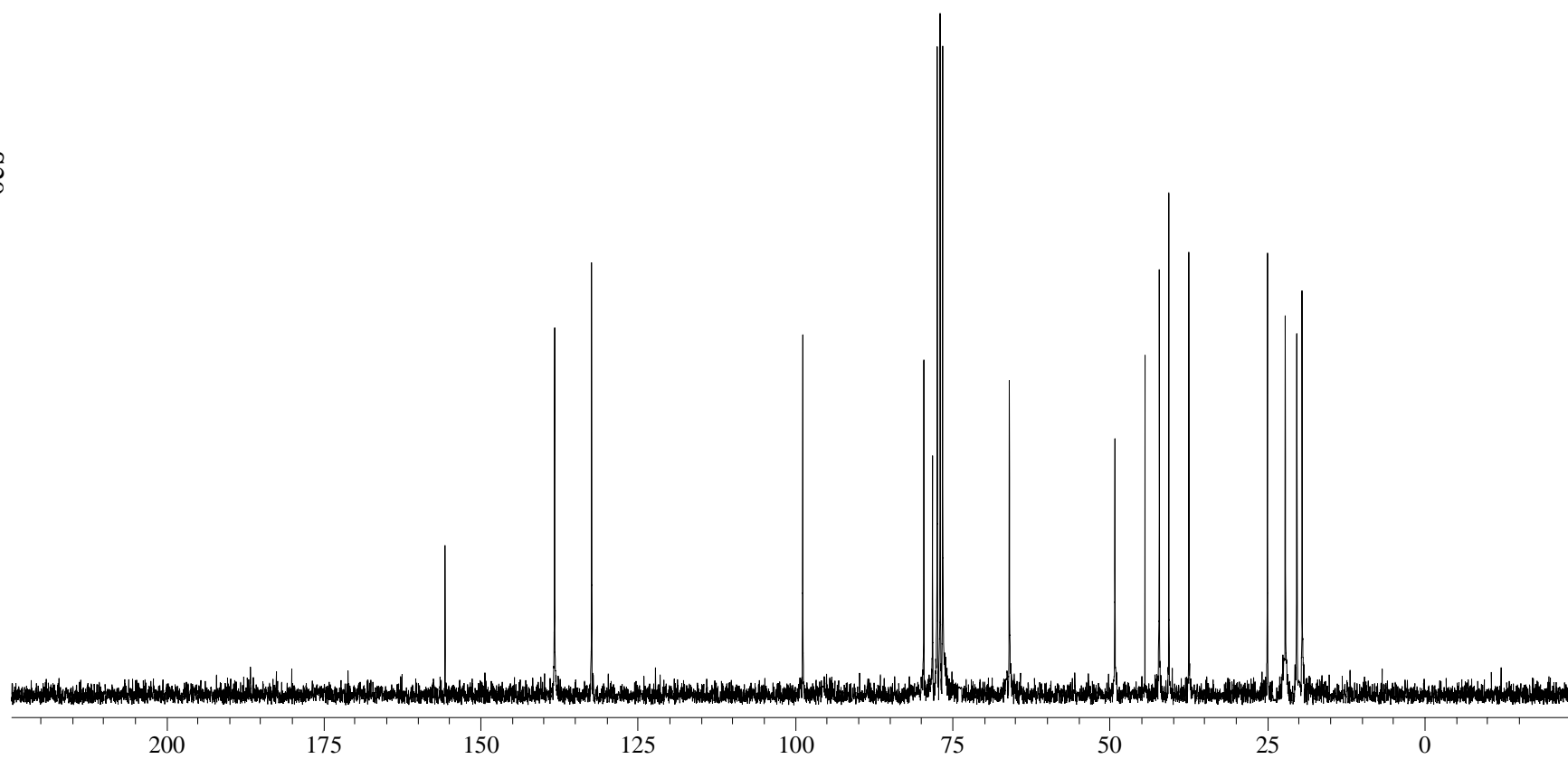
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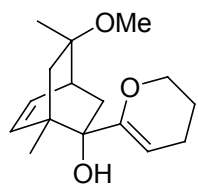




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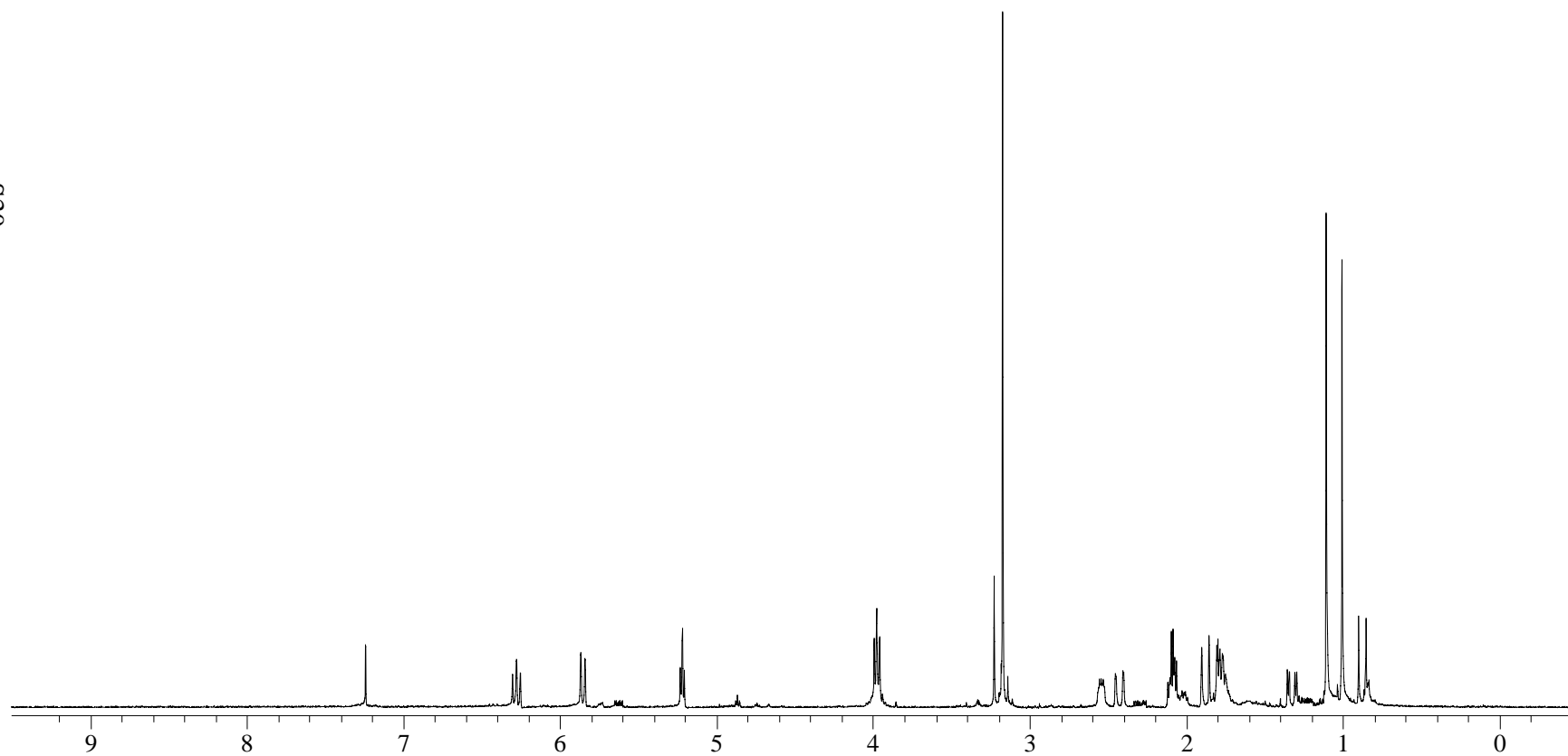
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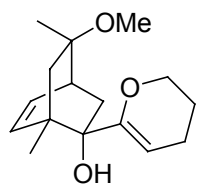




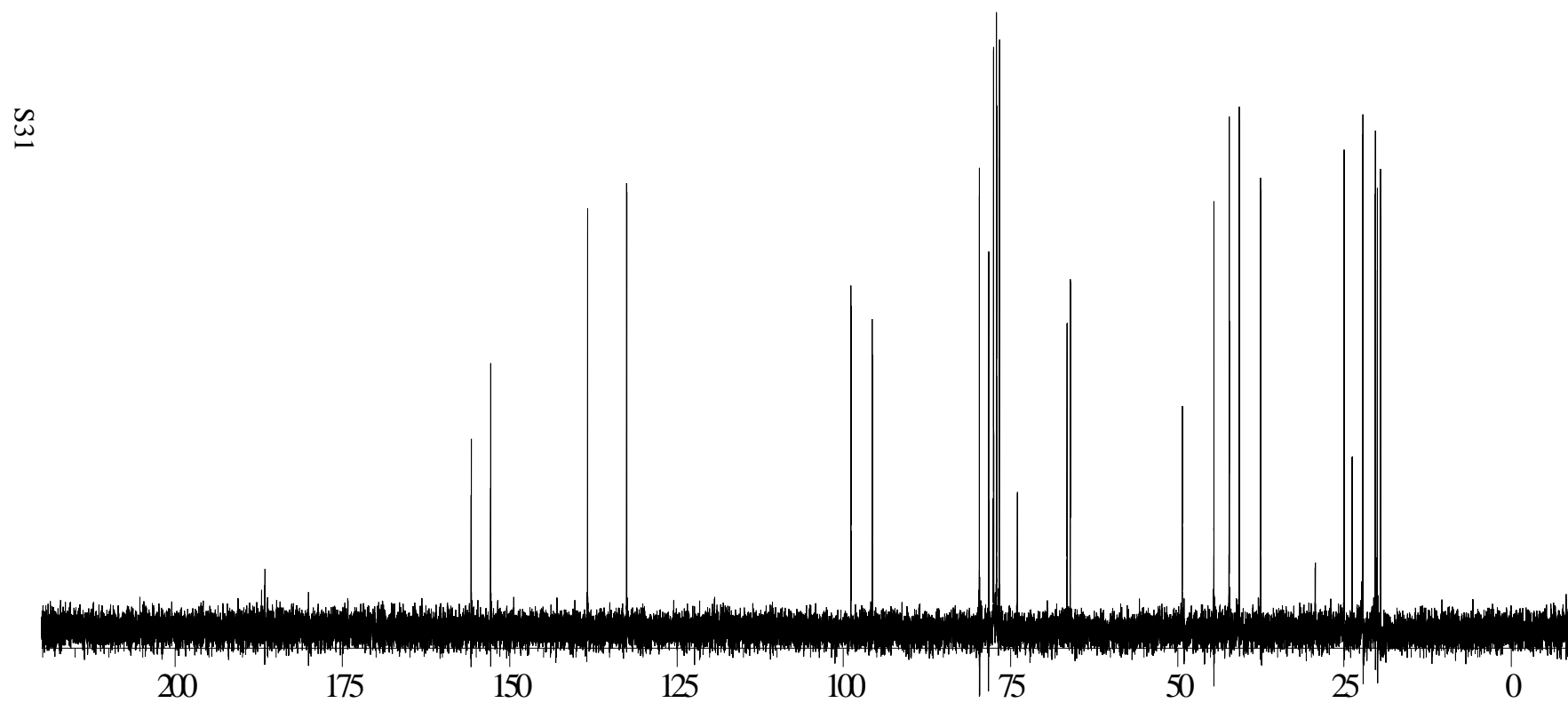
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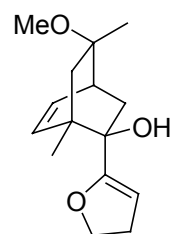
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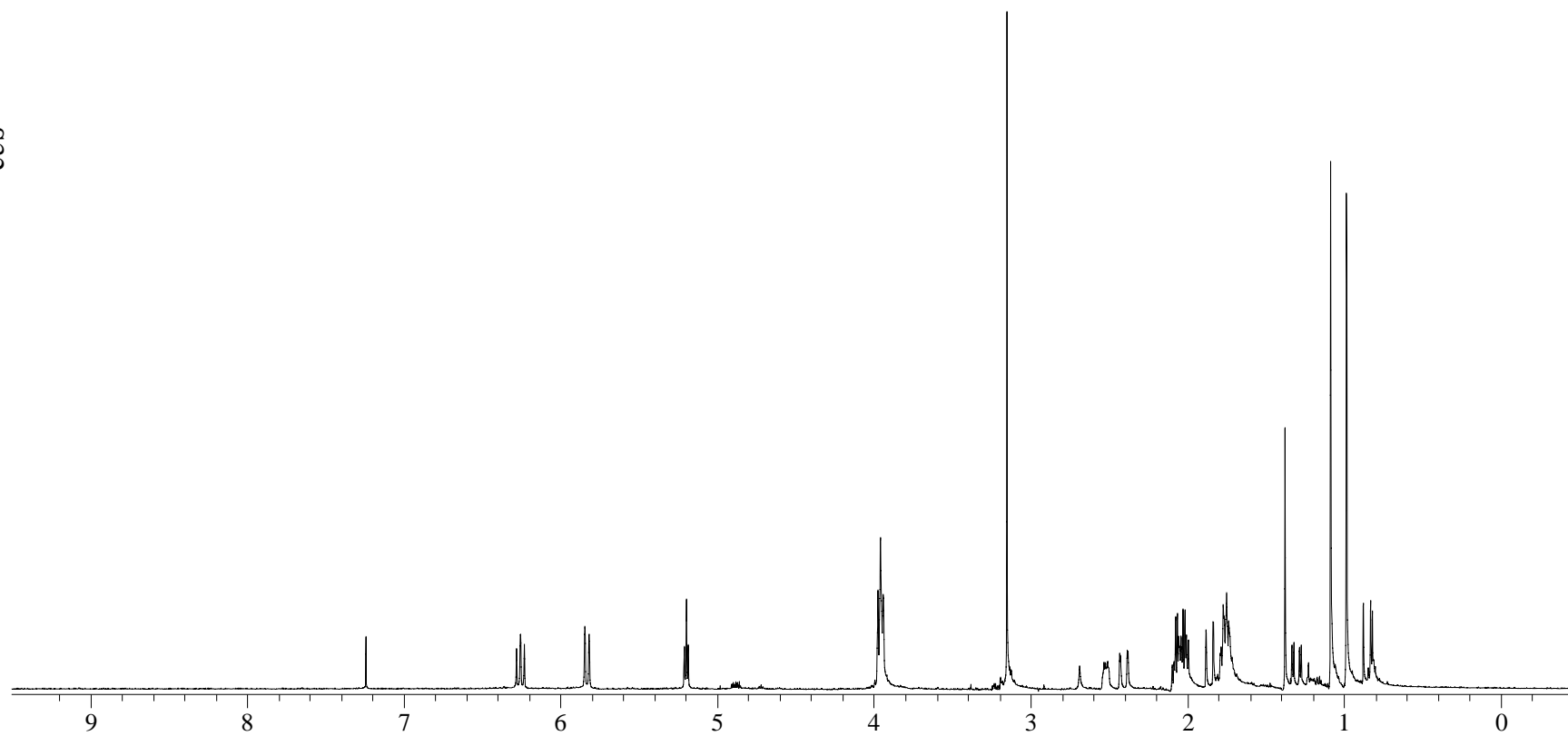
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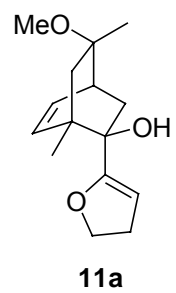




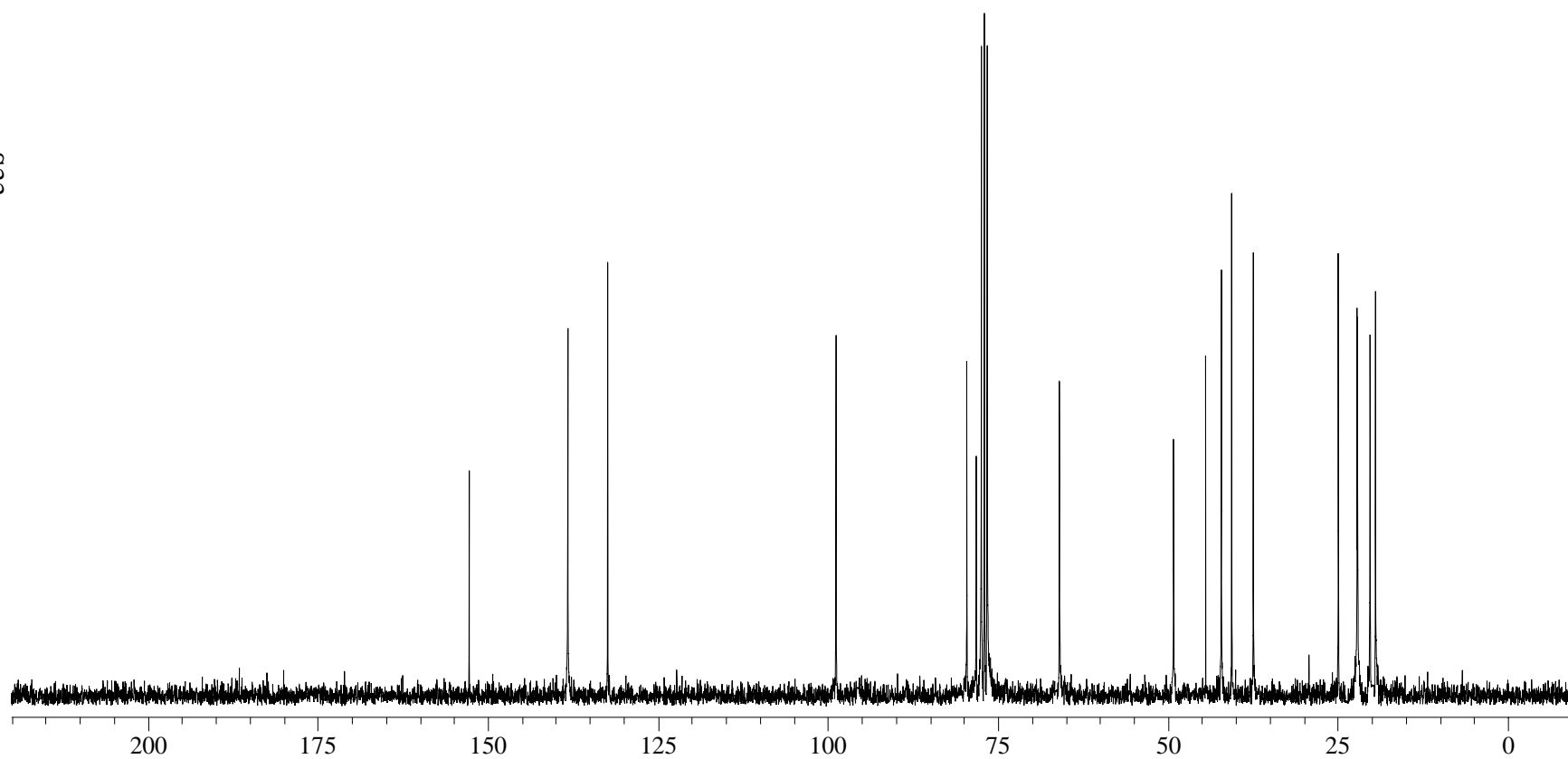
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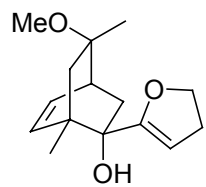
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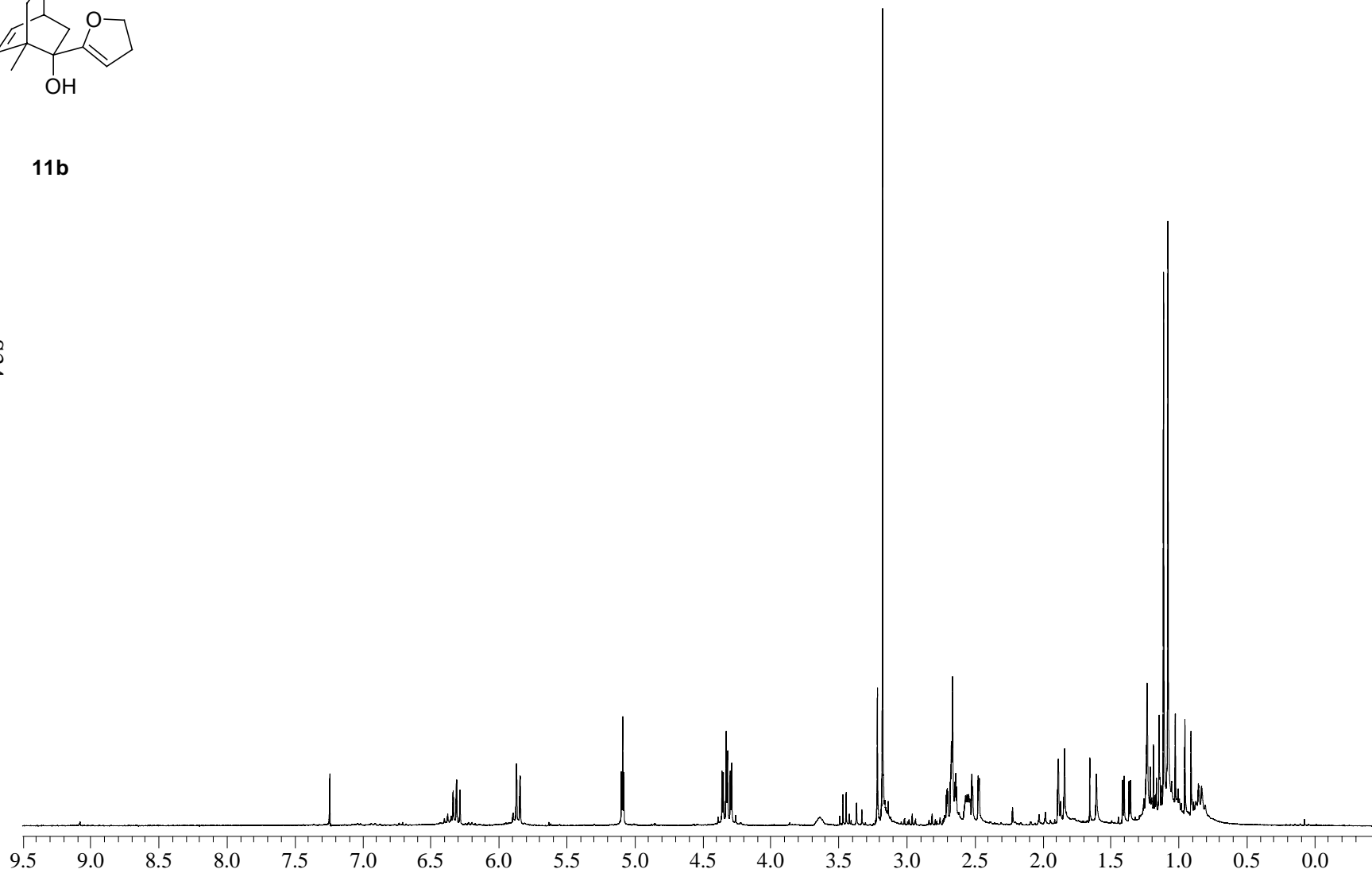
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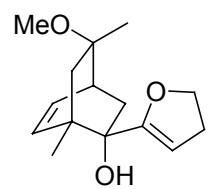




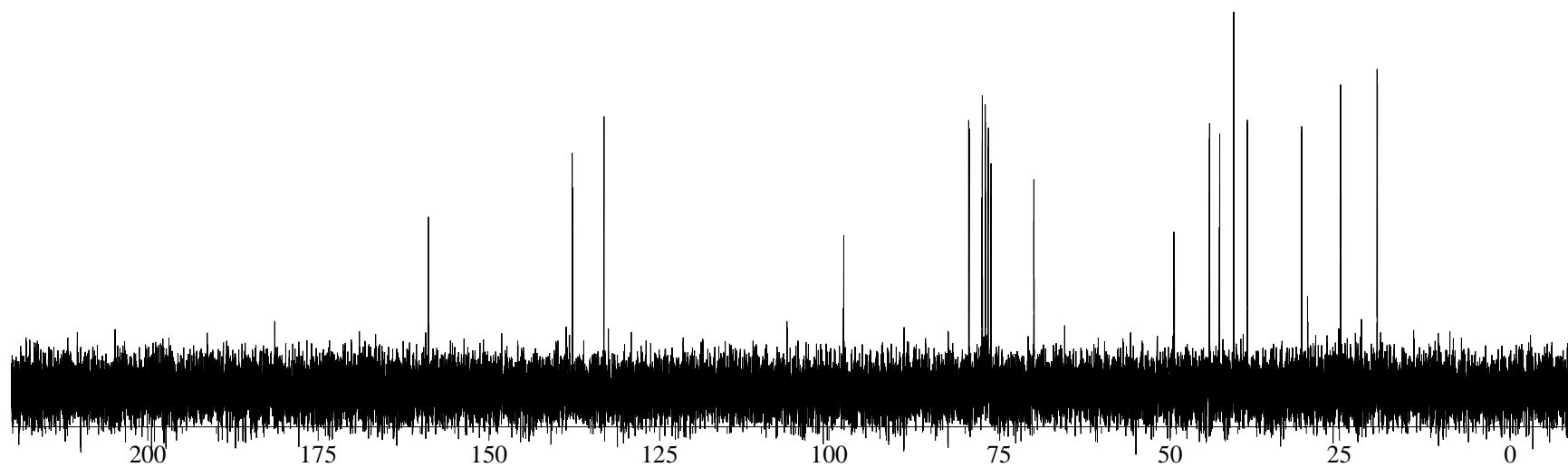
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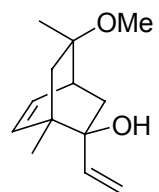
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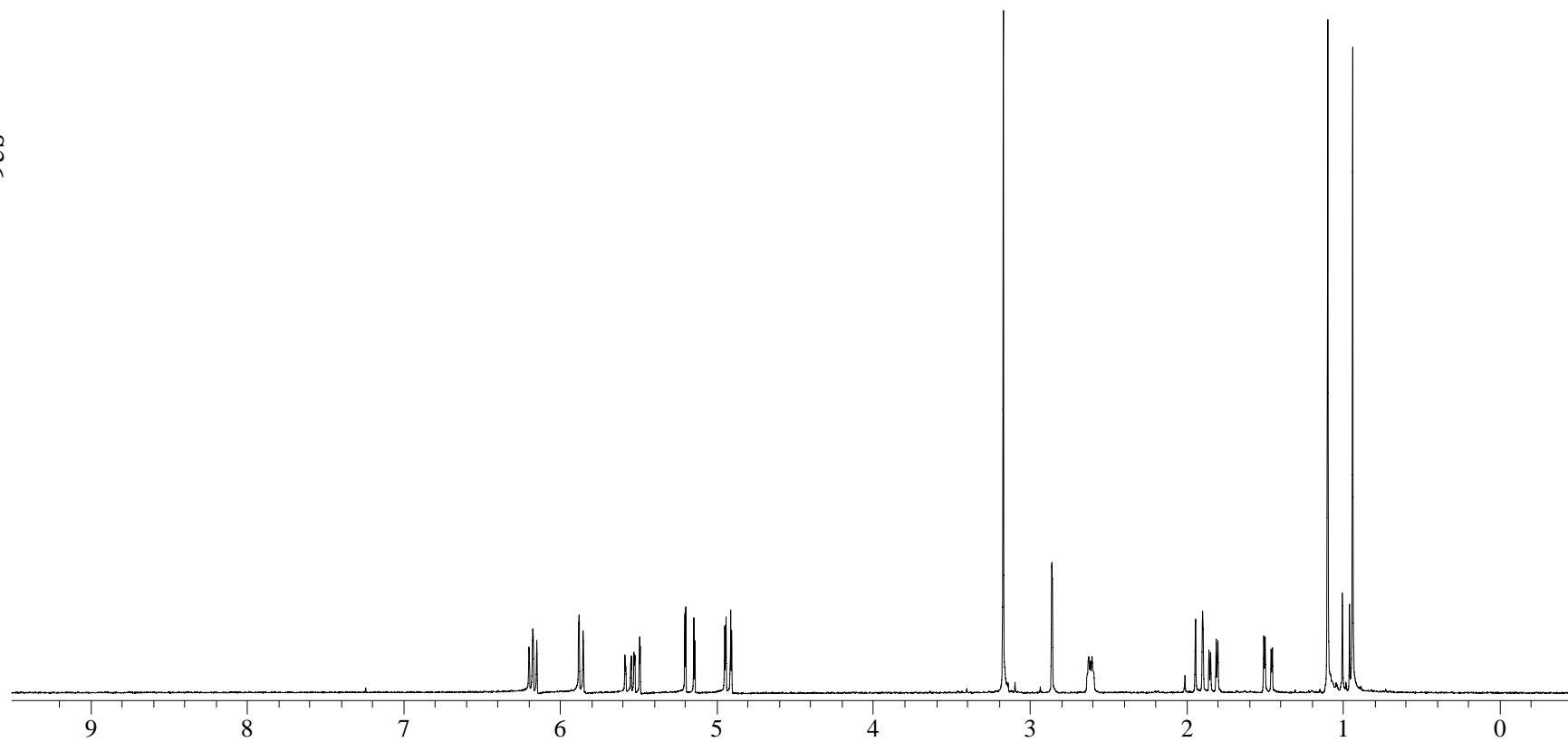
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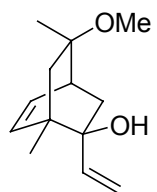




12a

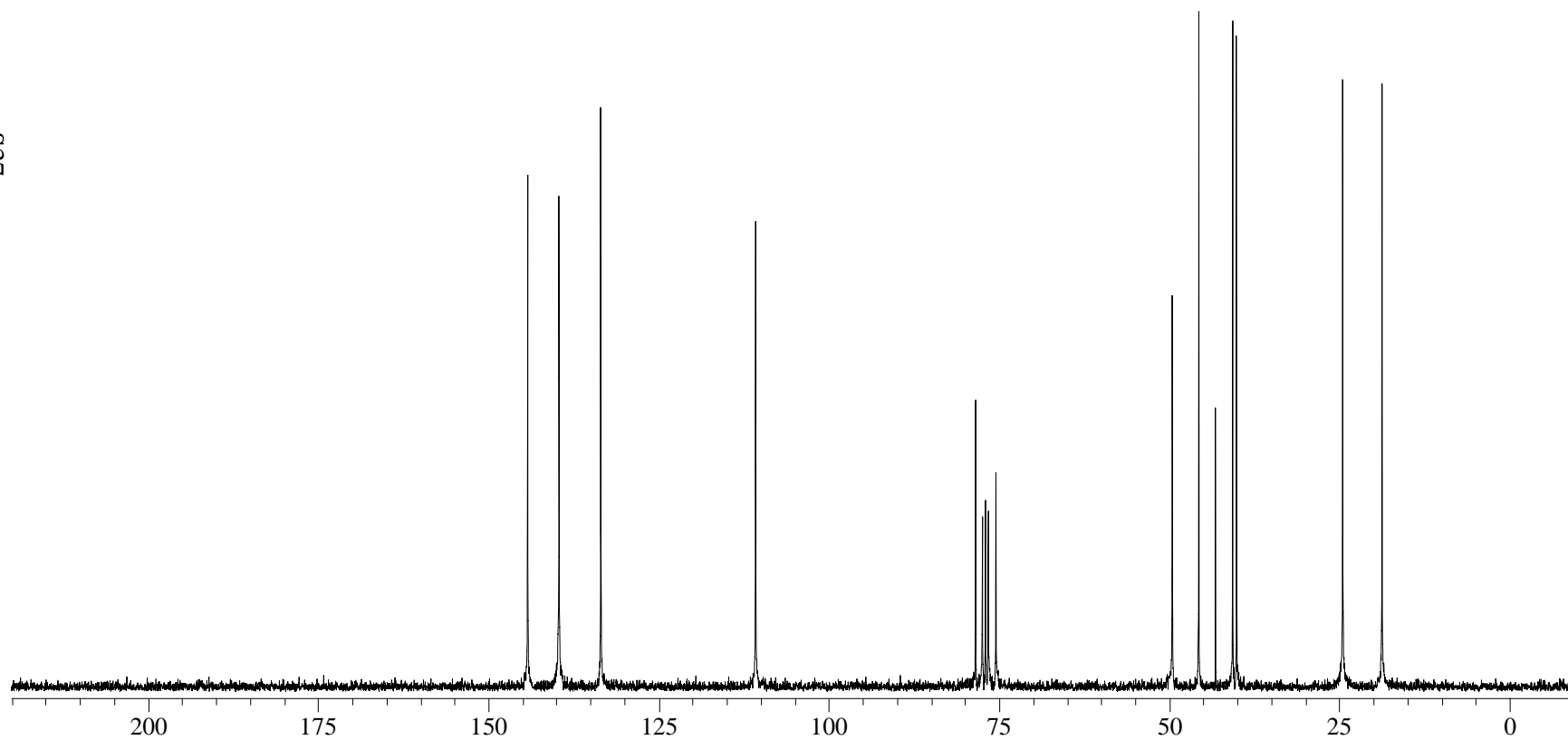
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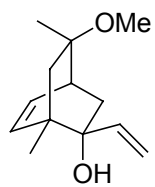




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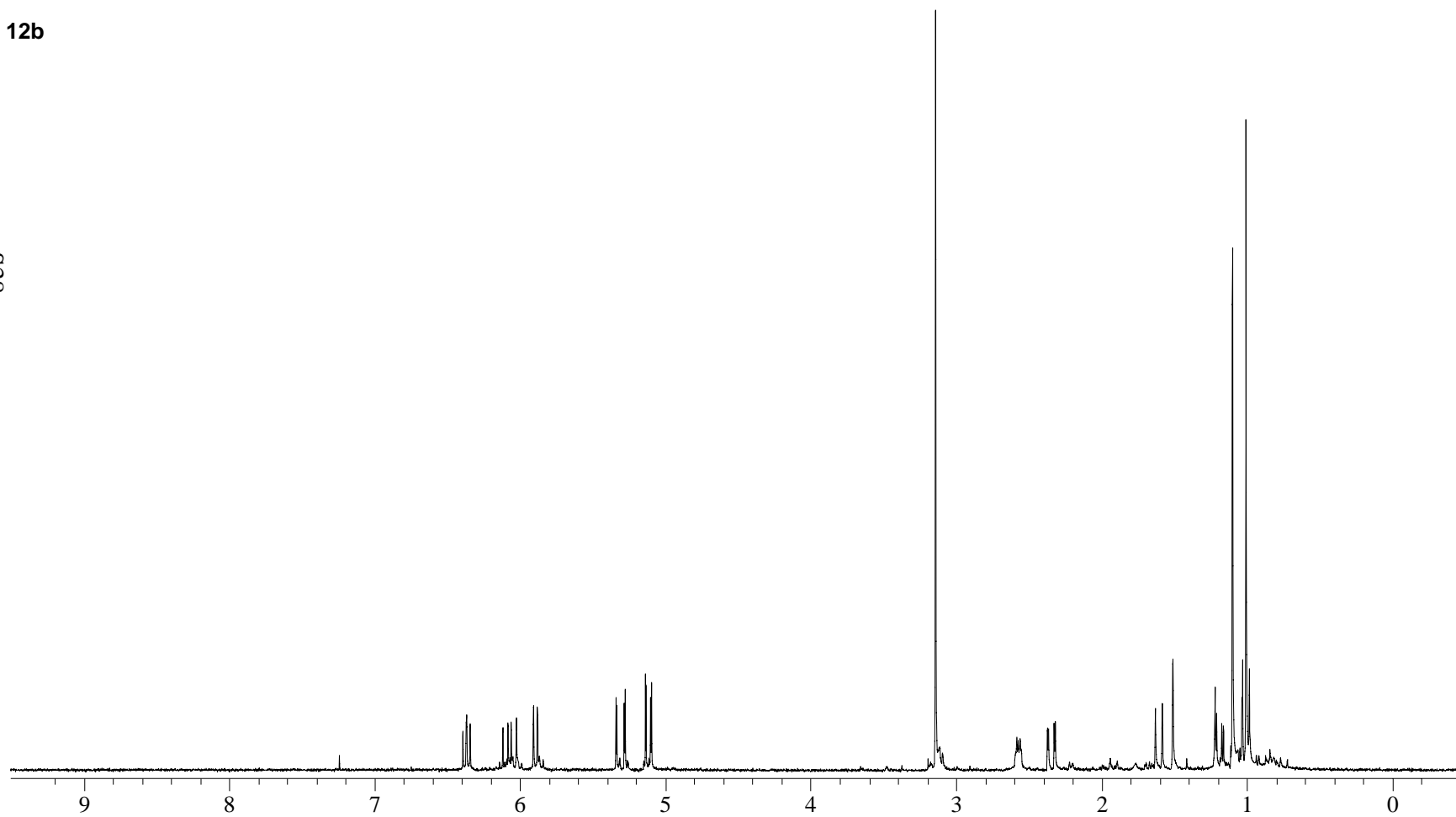
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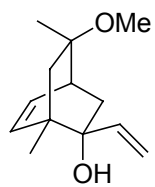




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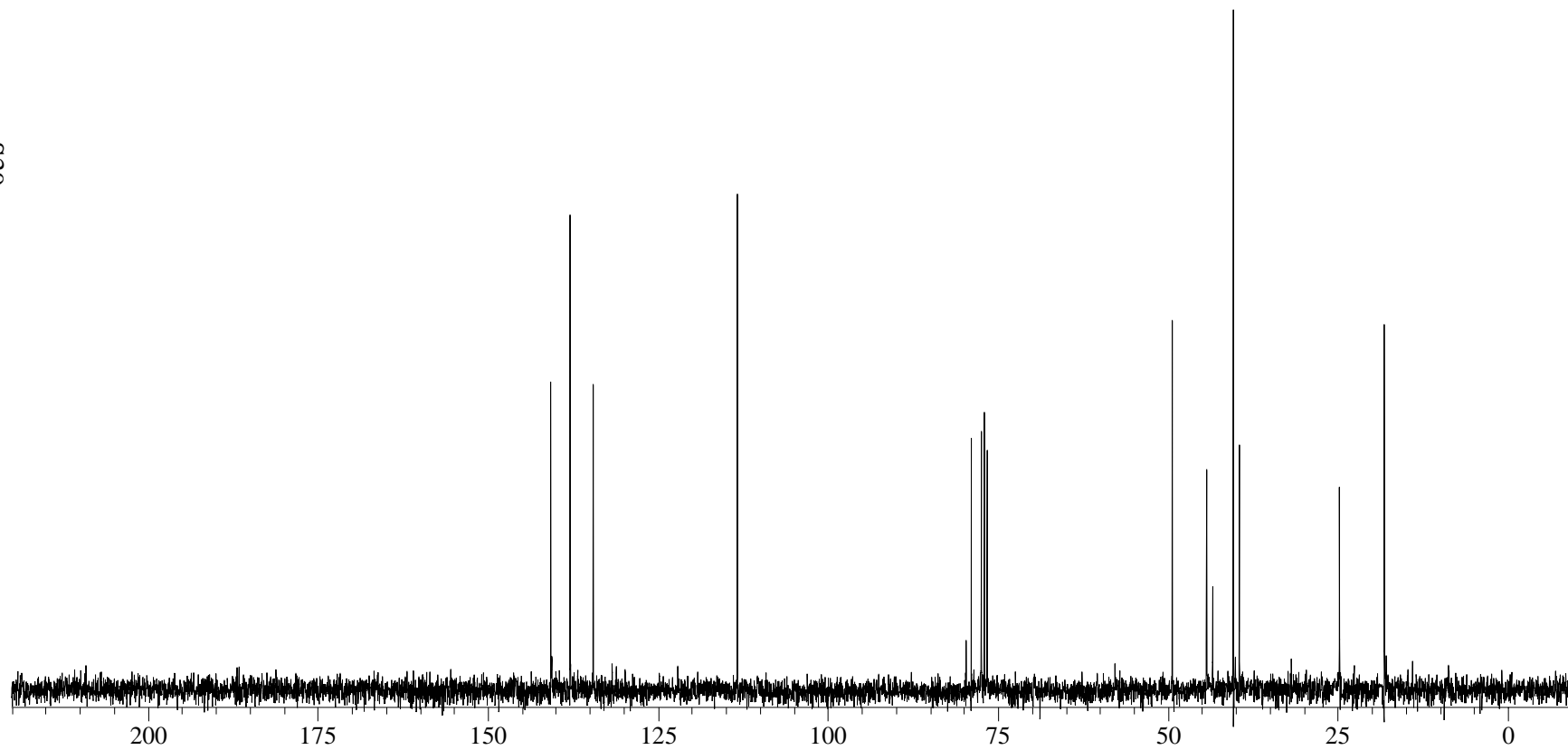
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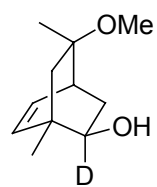




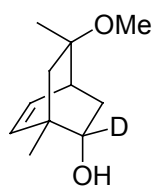
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S39



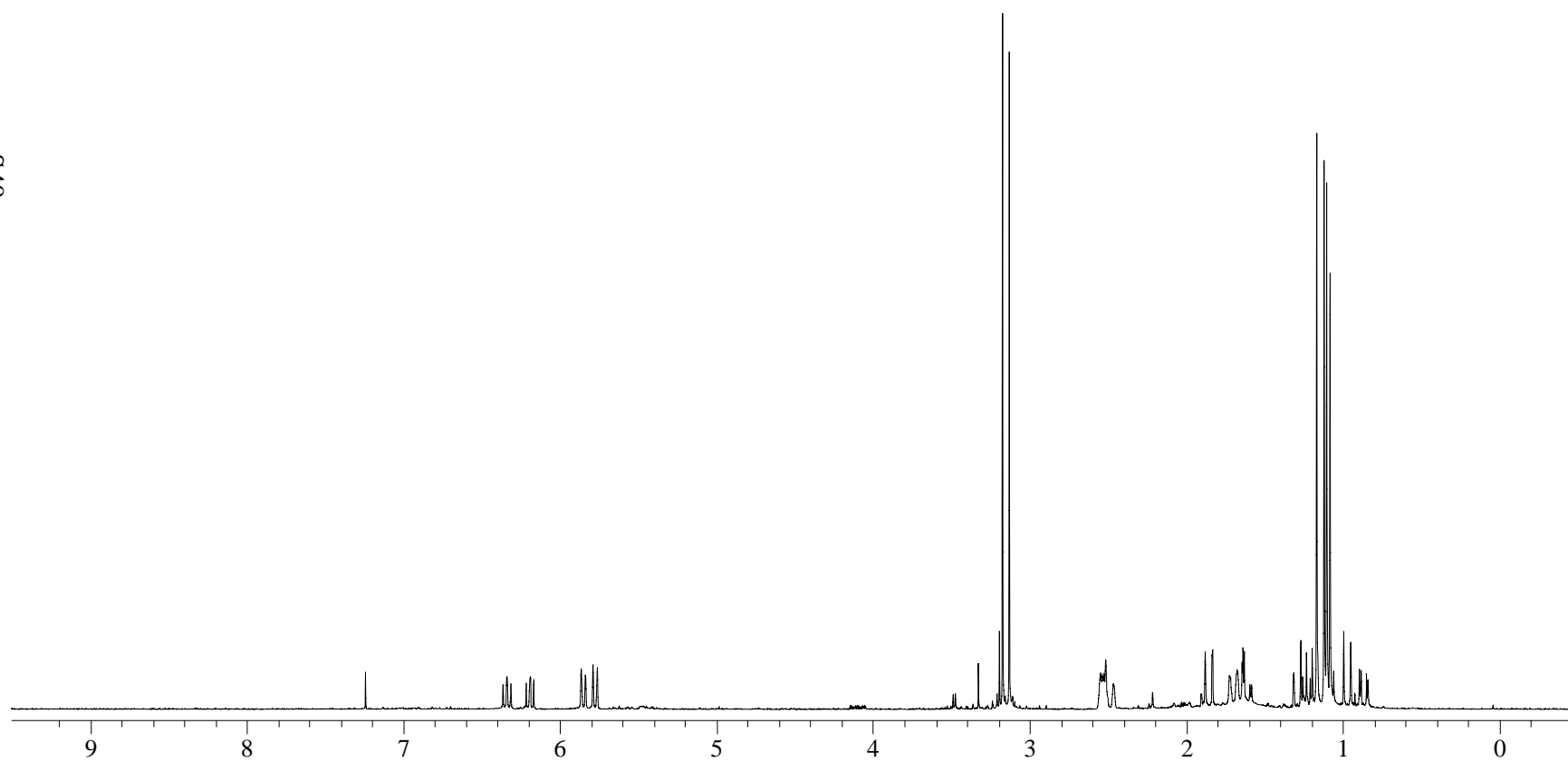


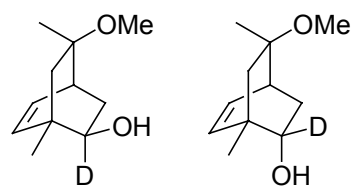
21a



21b

S40

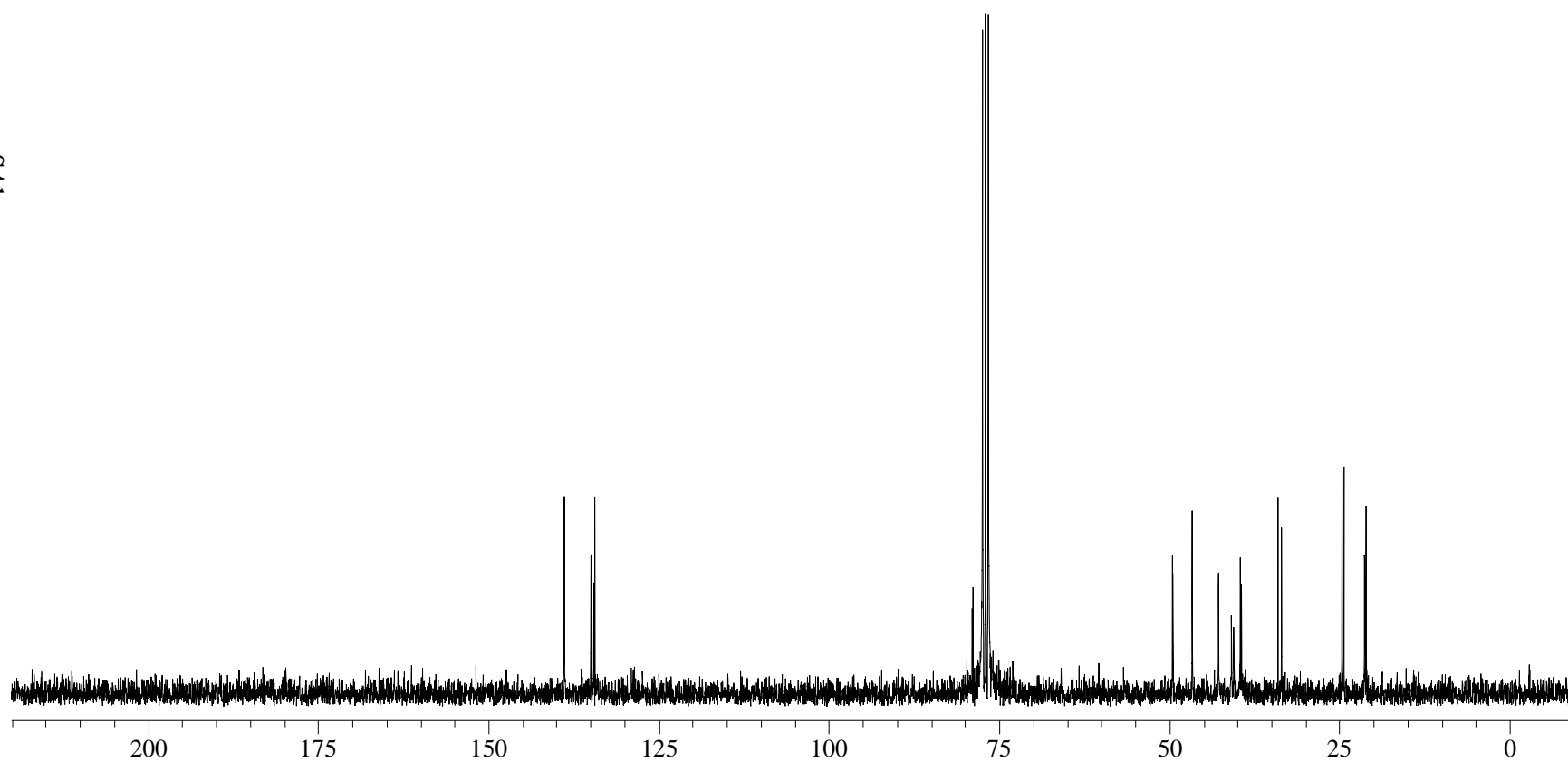


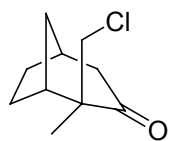


21a

21b

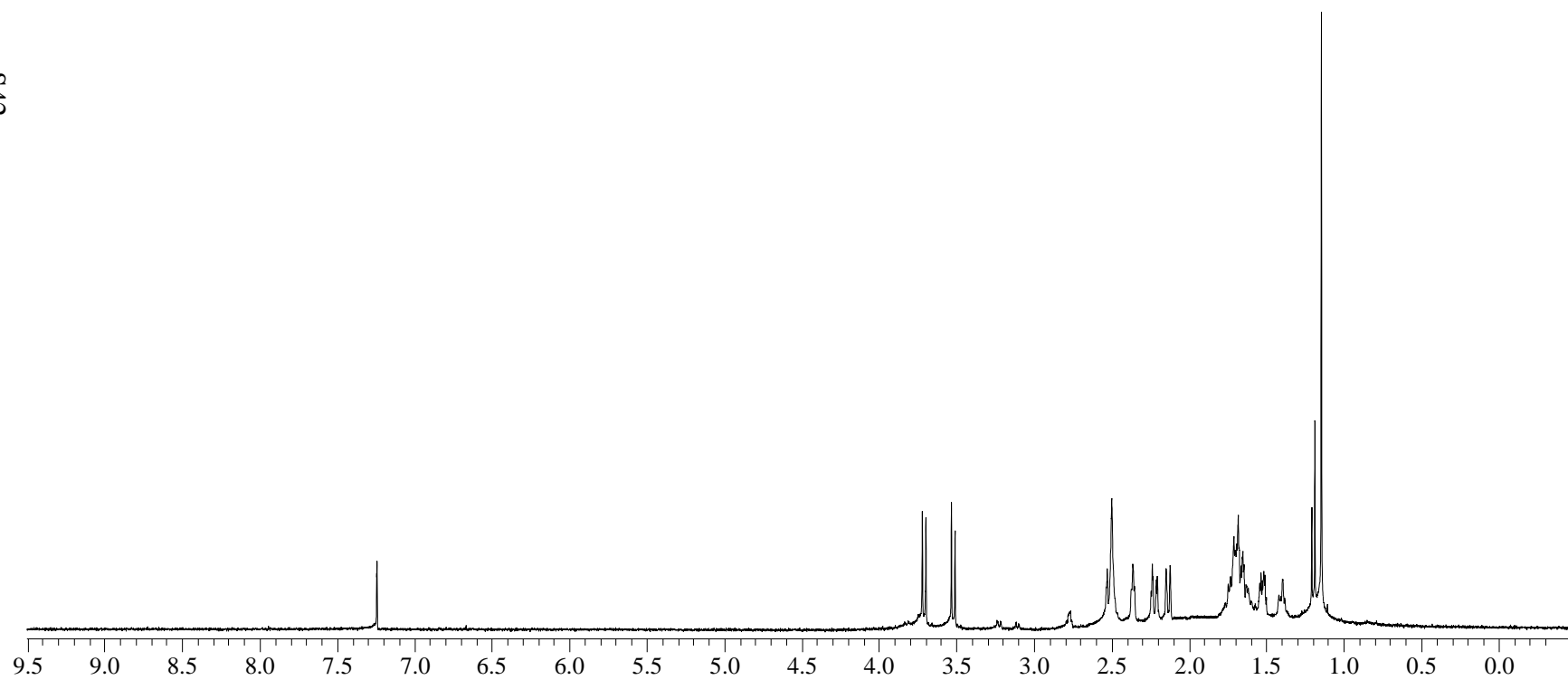
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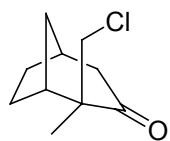




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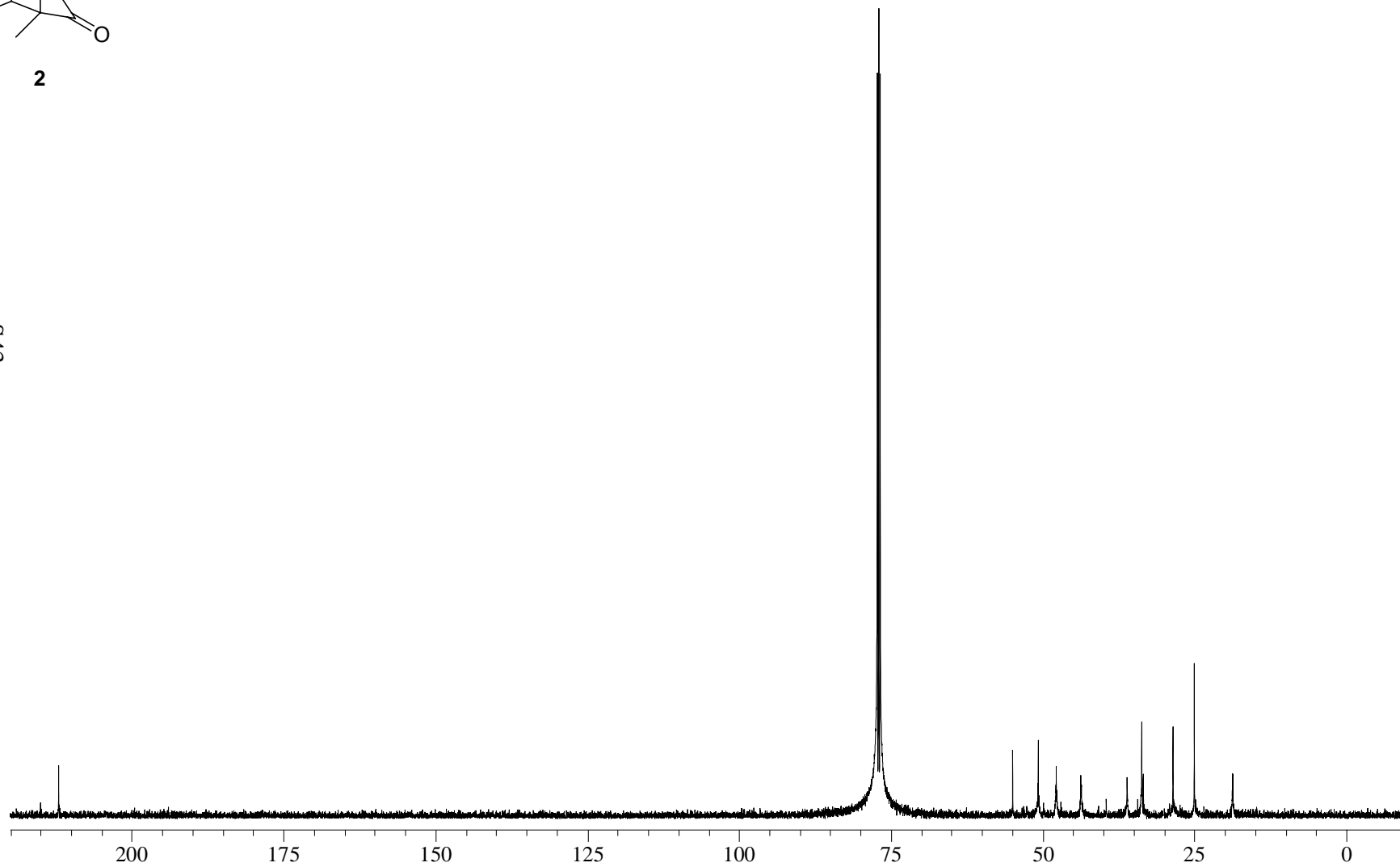
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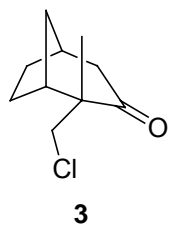




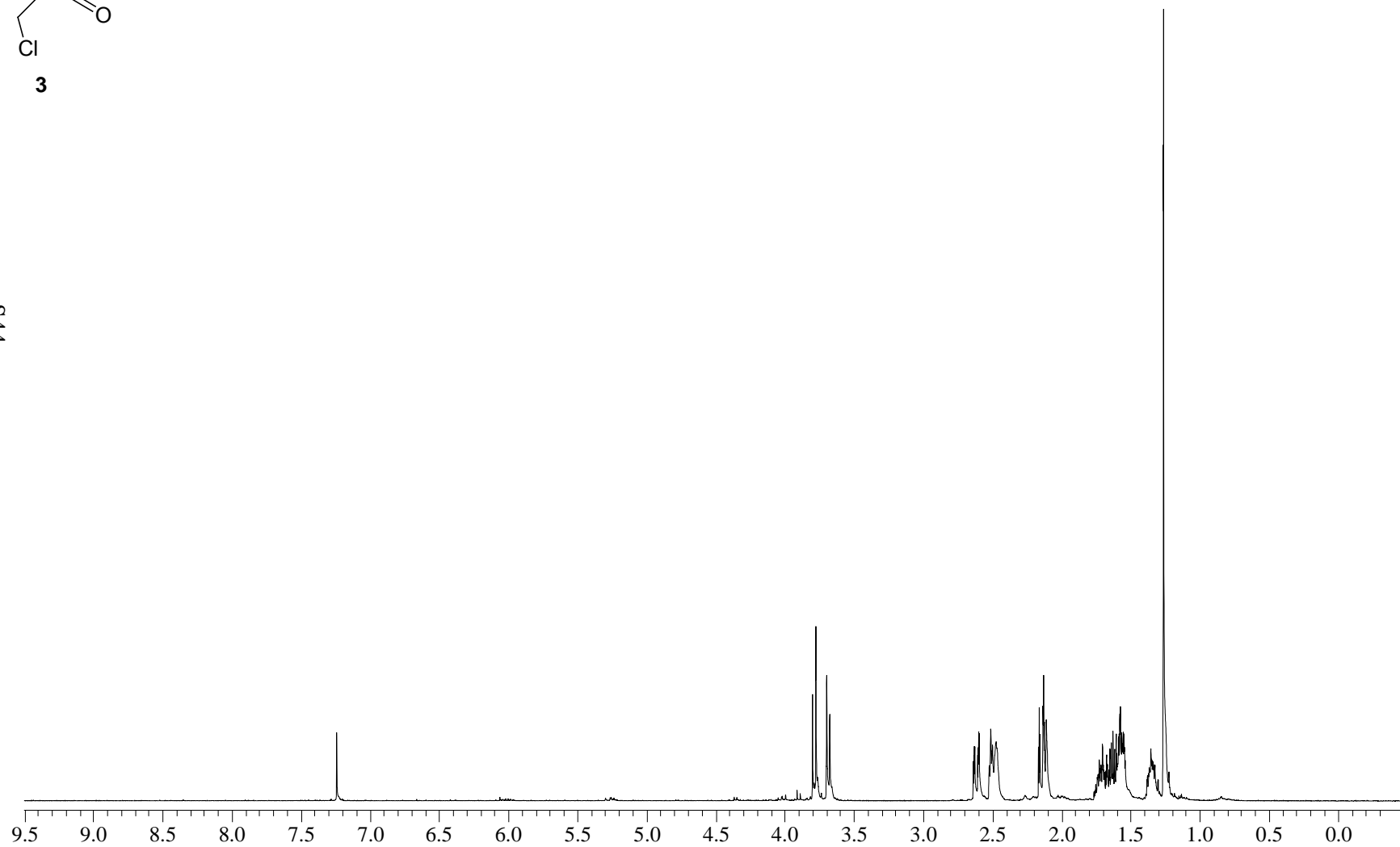
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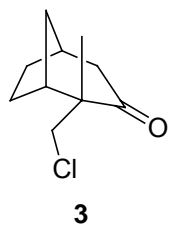
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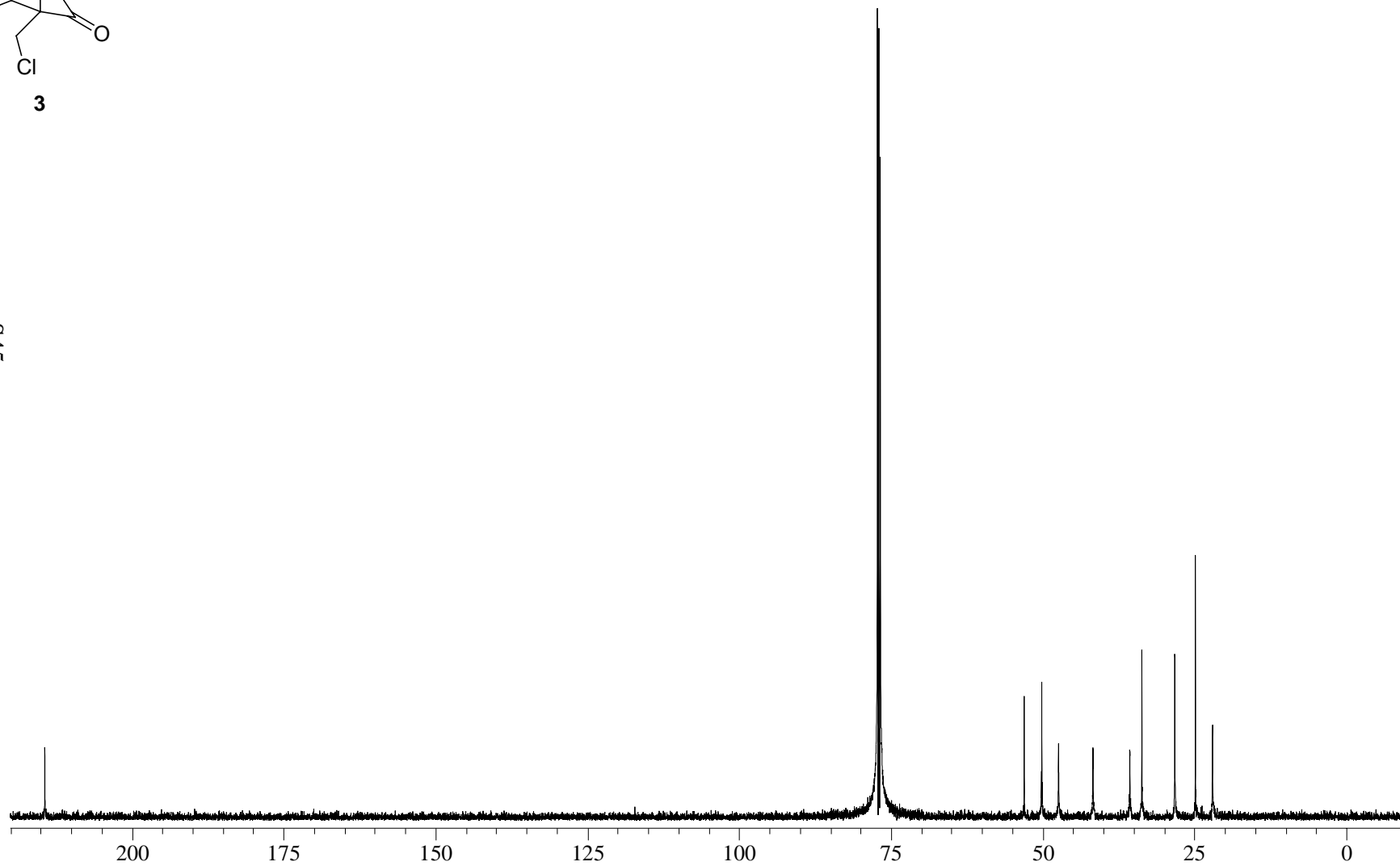


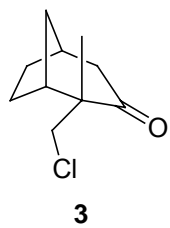
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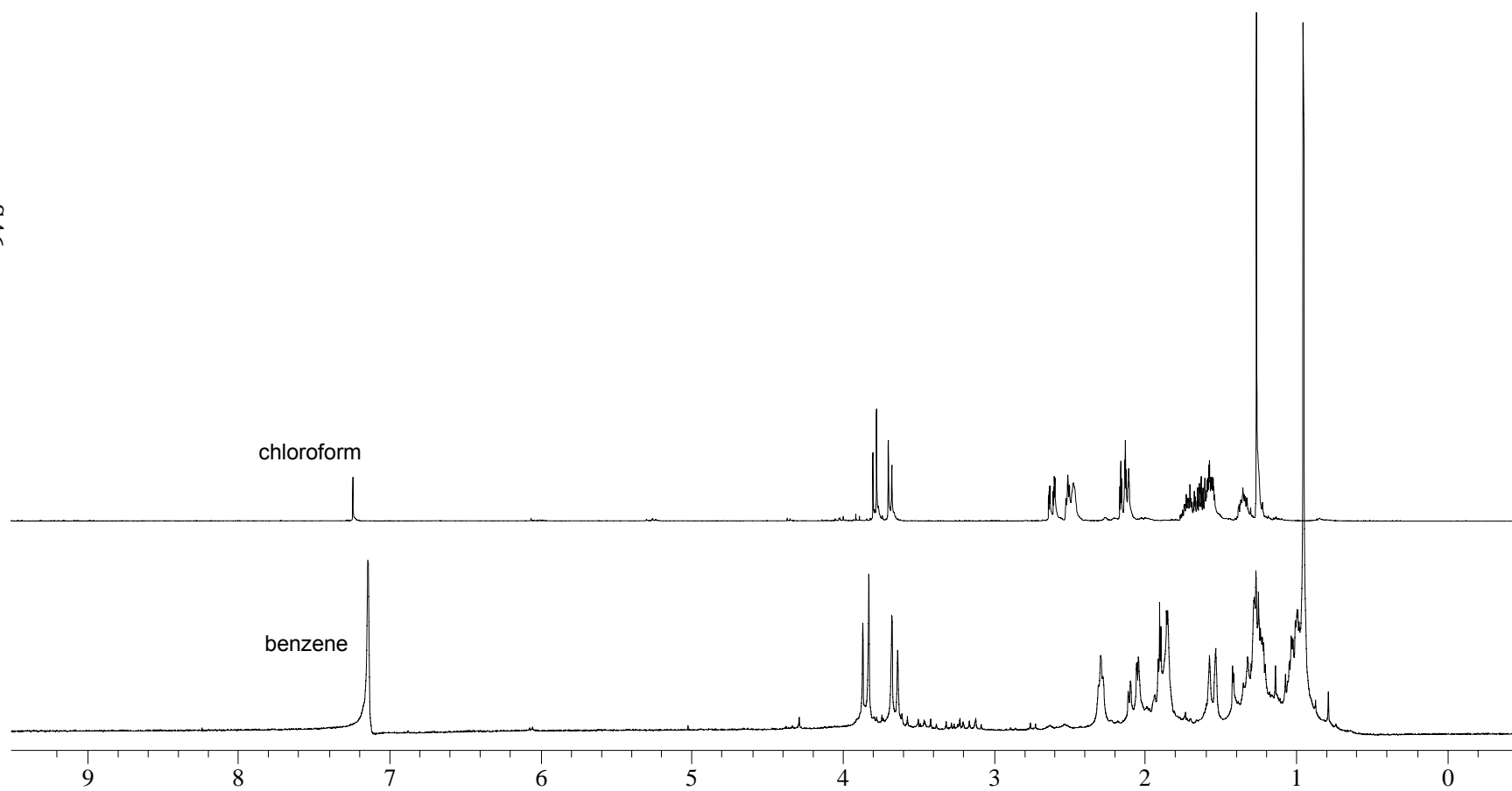


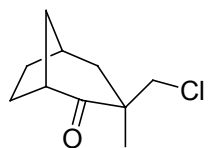
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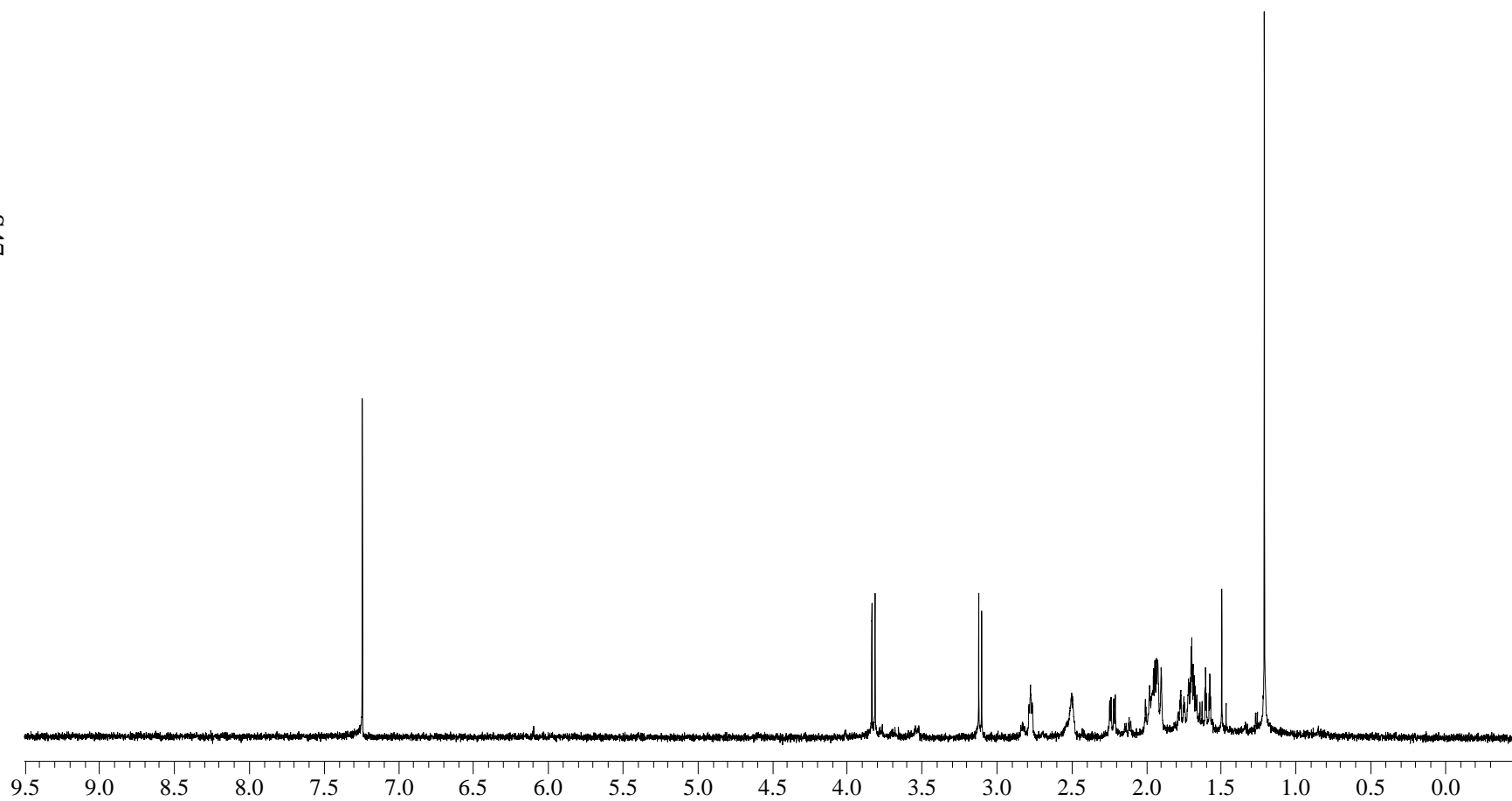
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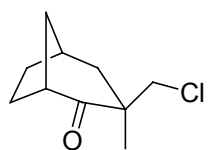




4

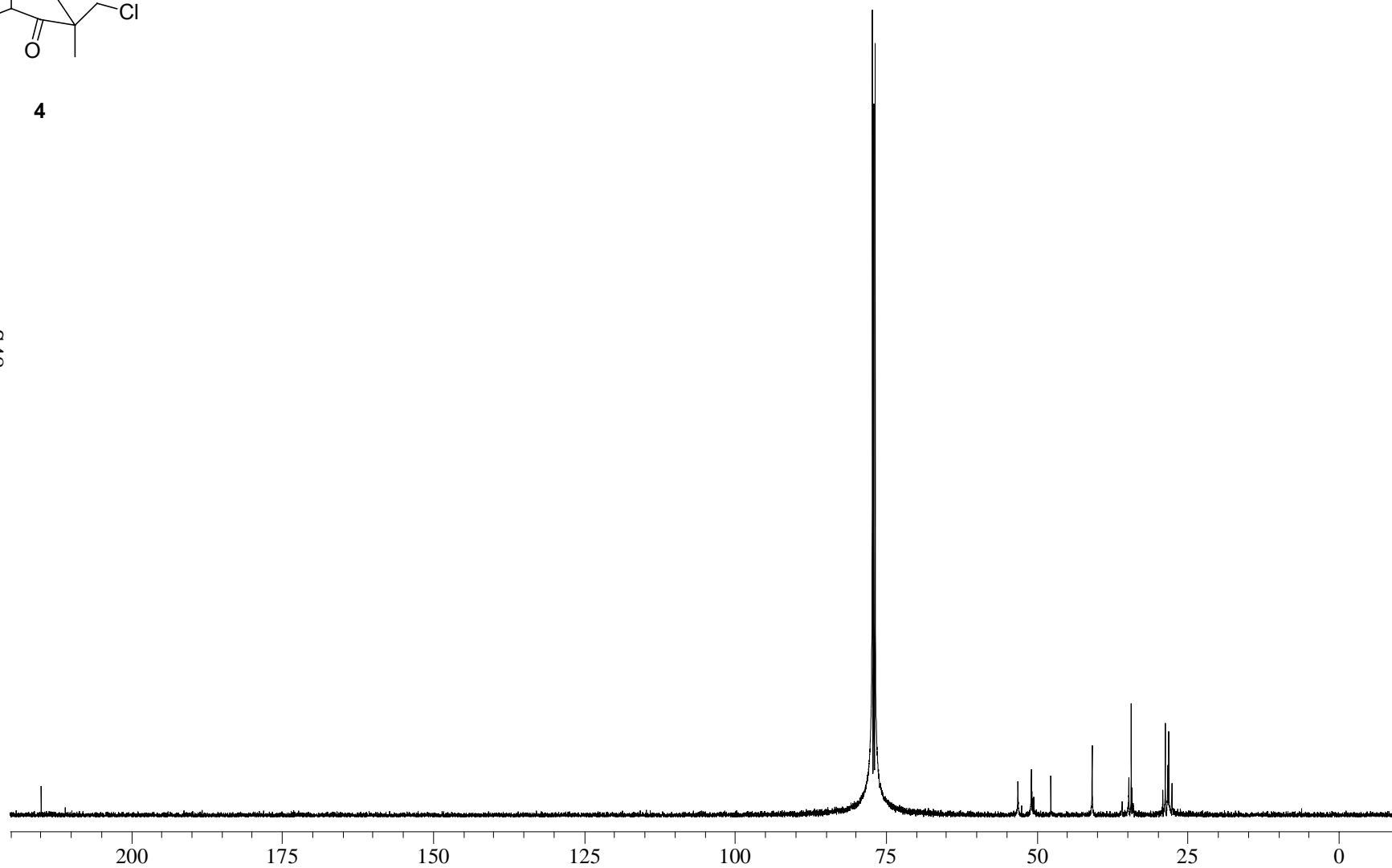
S47

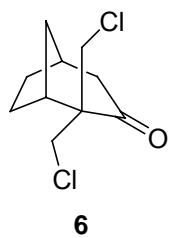




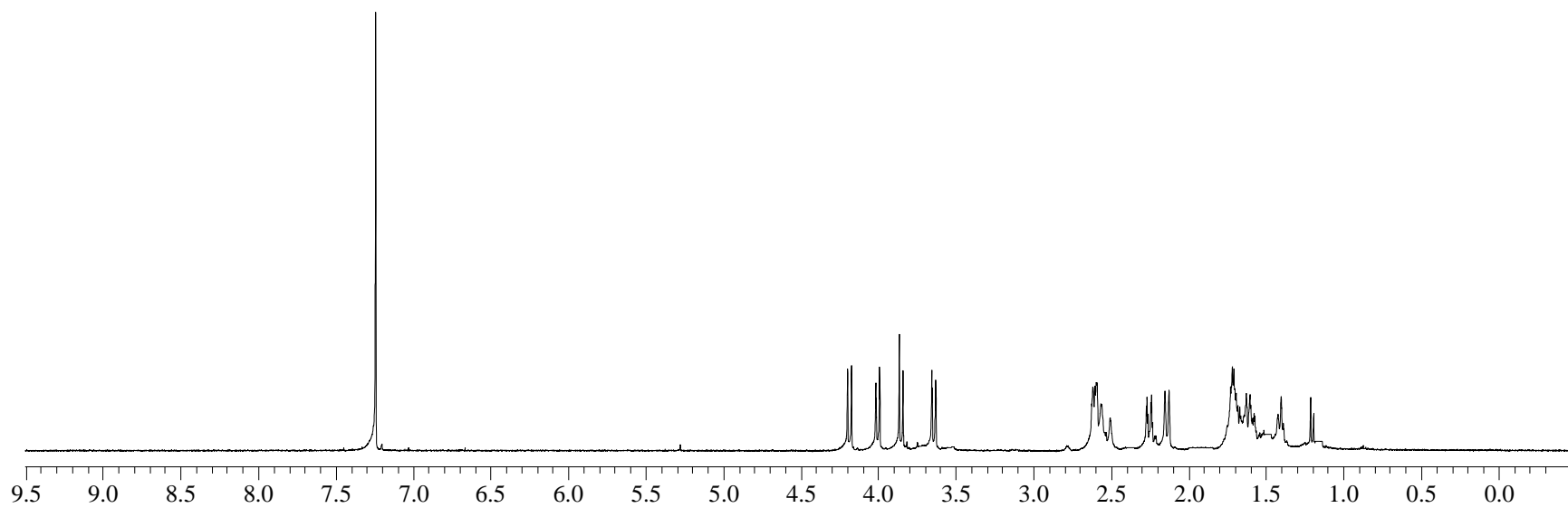
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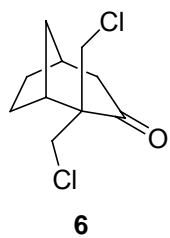
S48



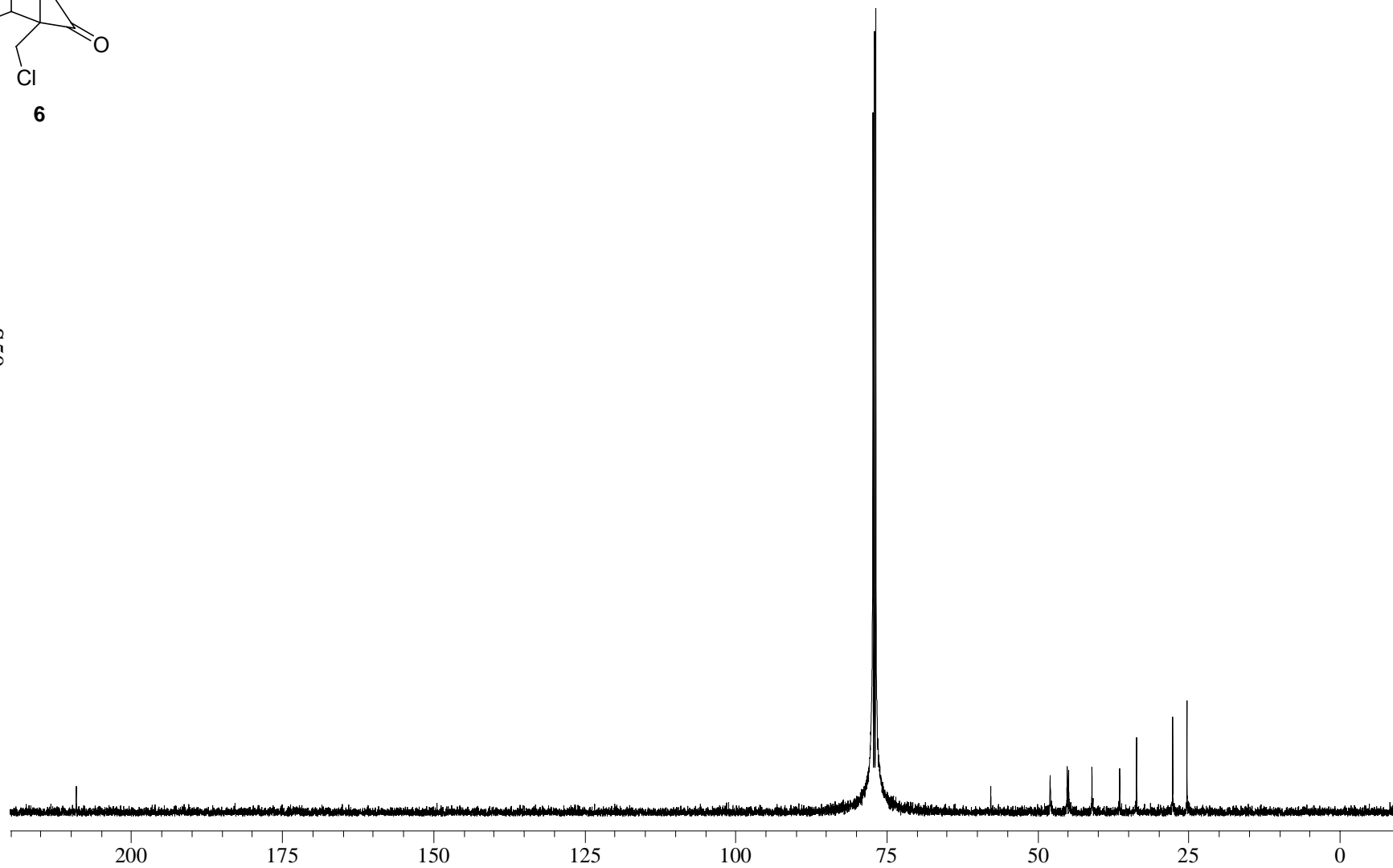


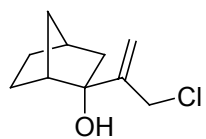
S49





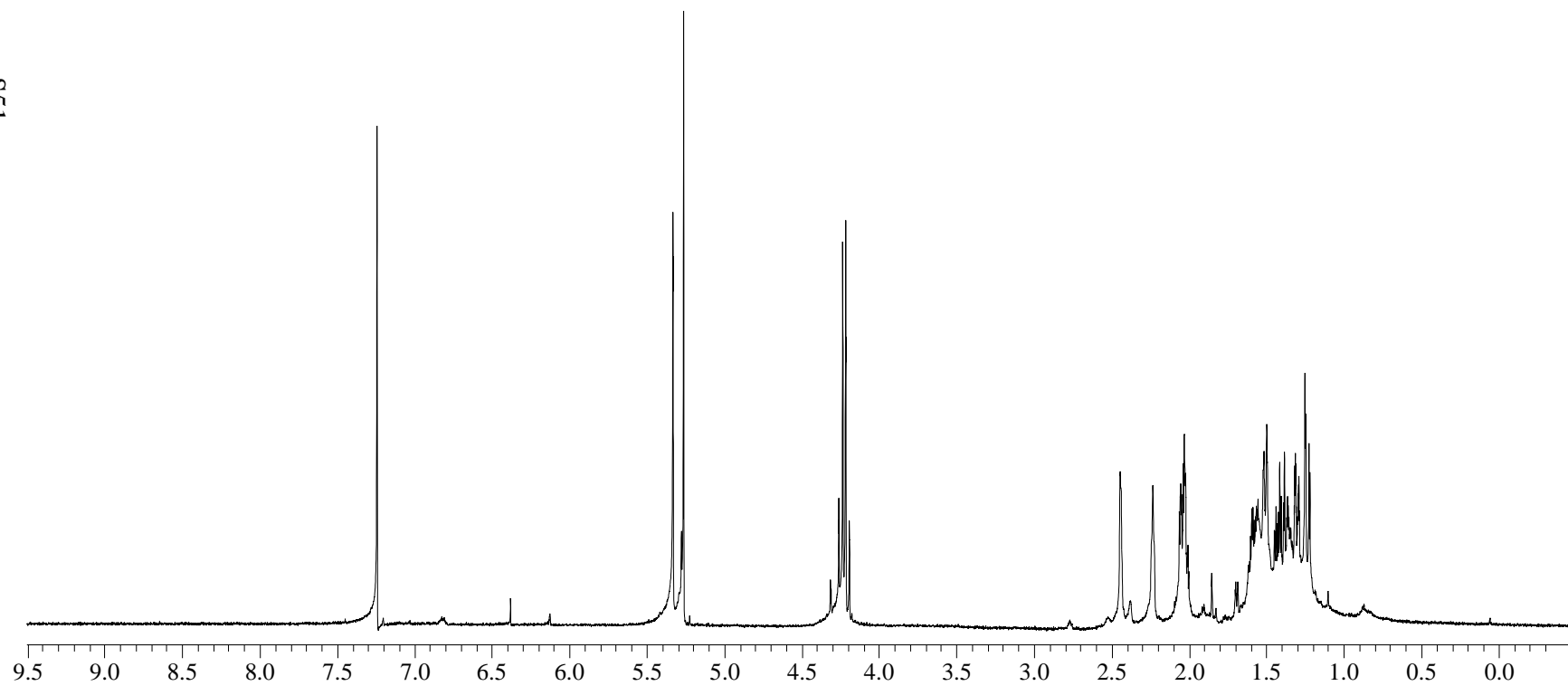
S50

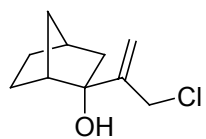




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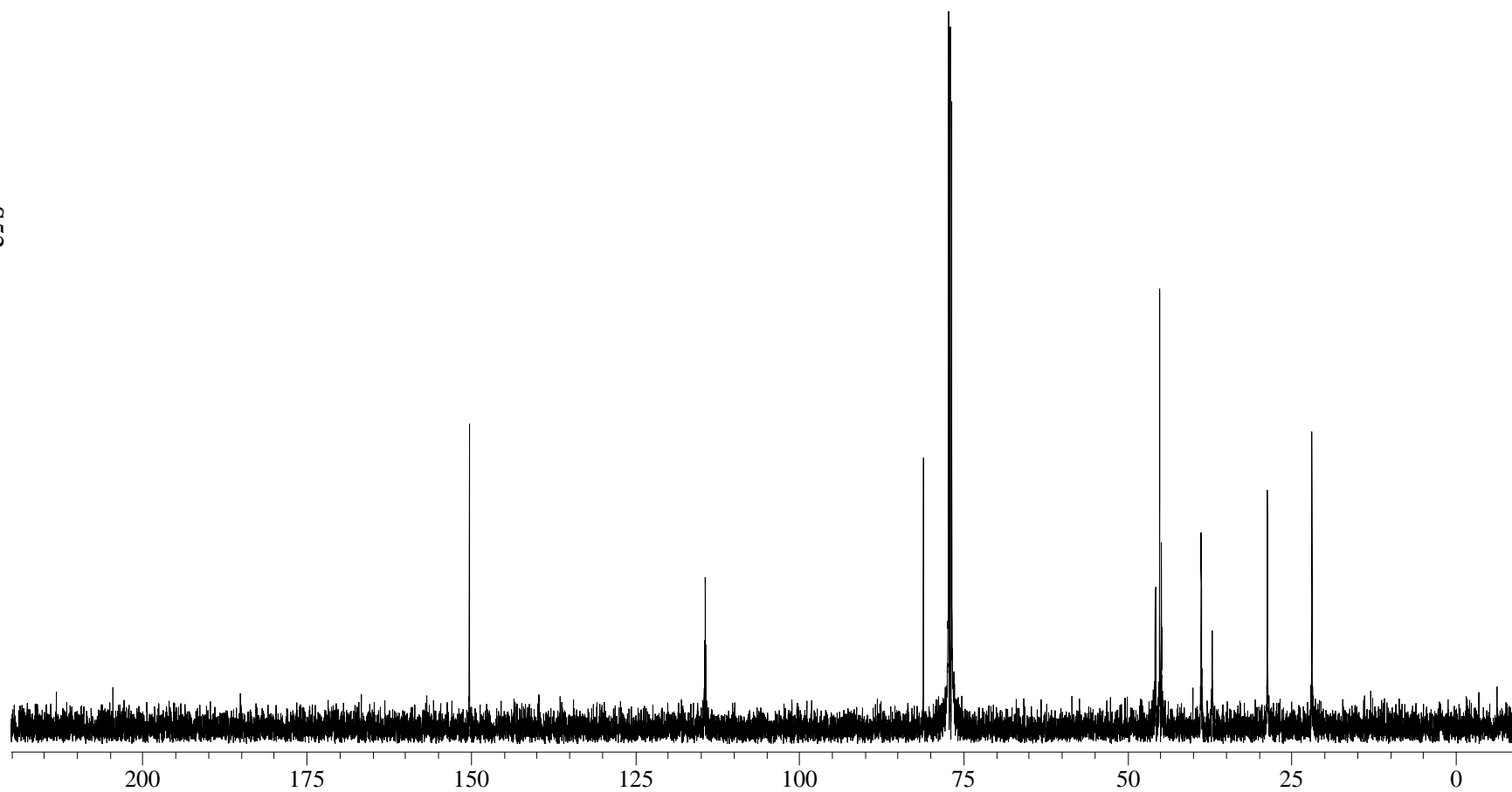
S51

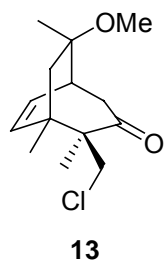




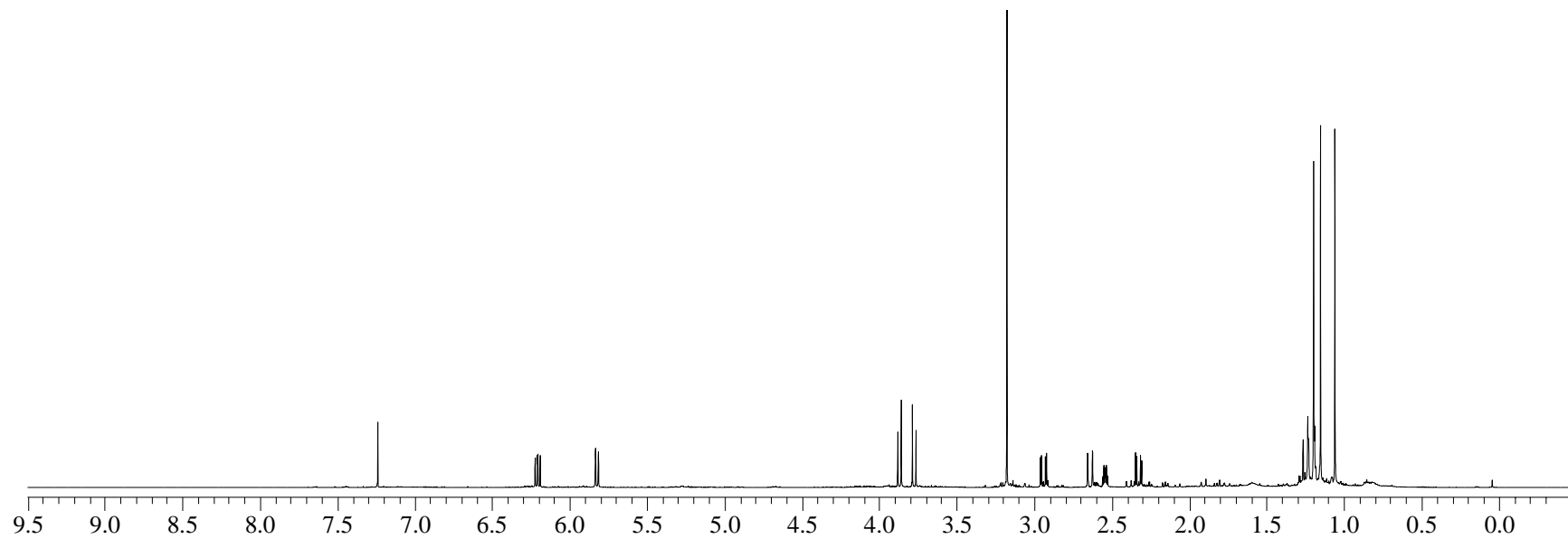
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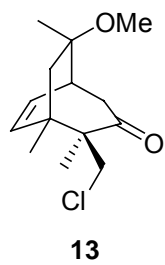
§ 52



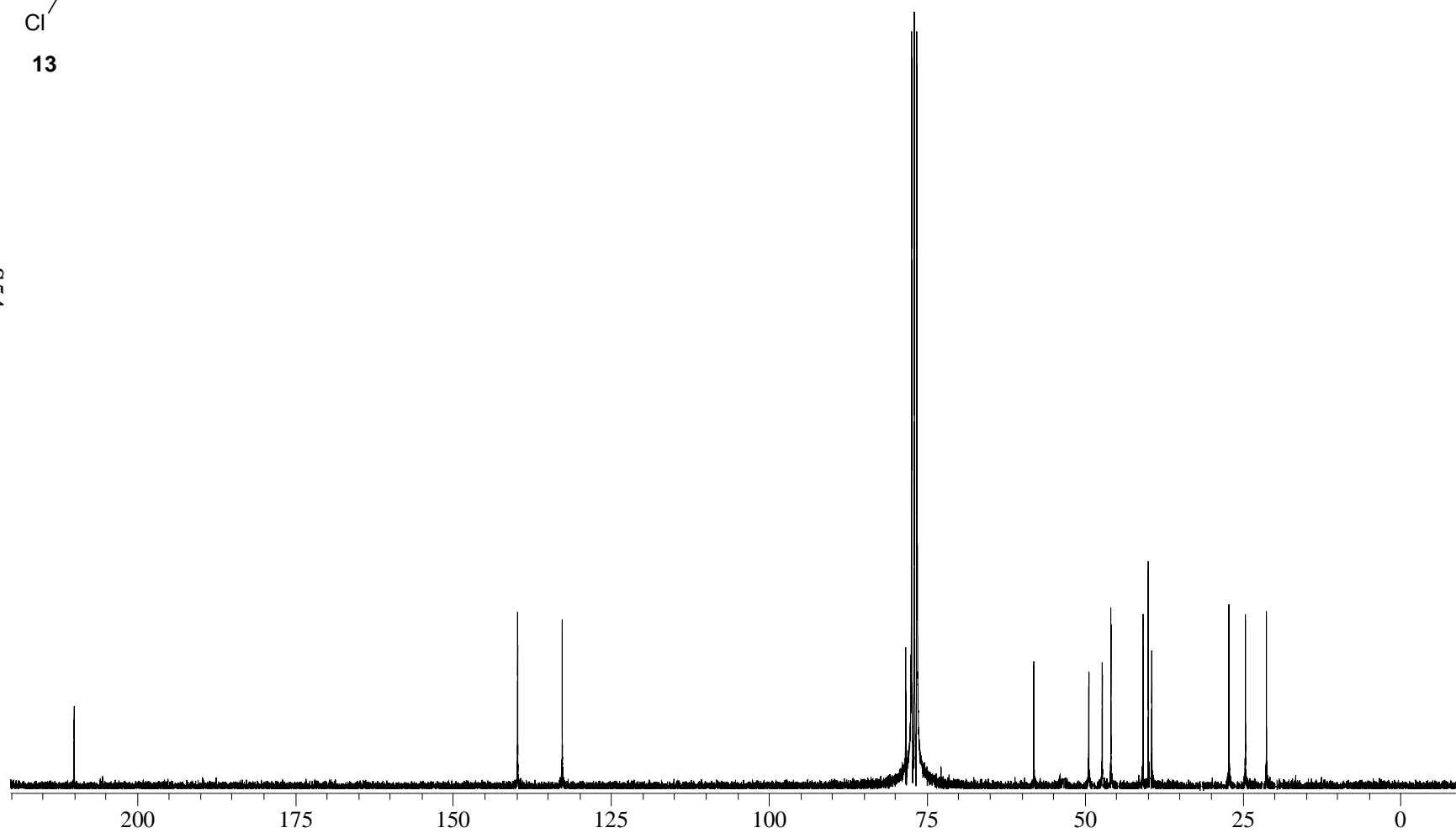


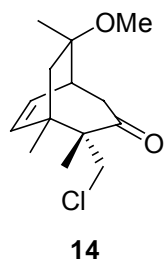
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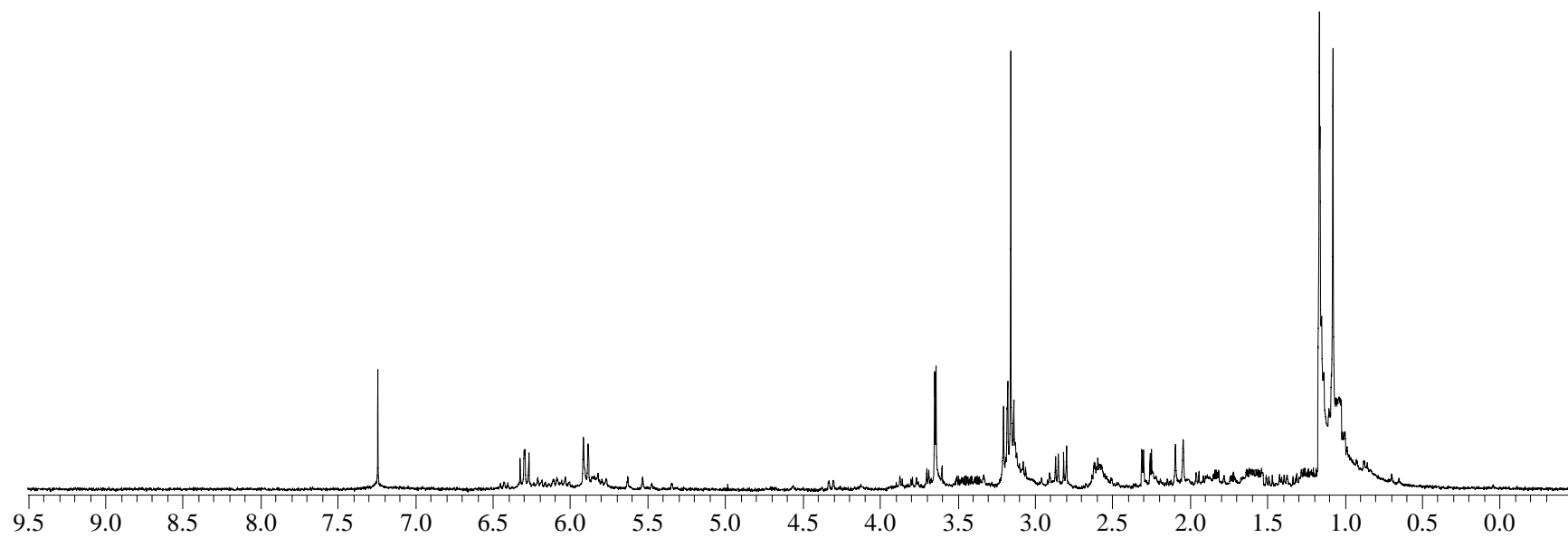


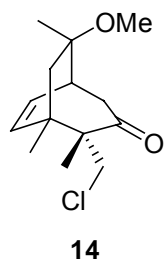
S54



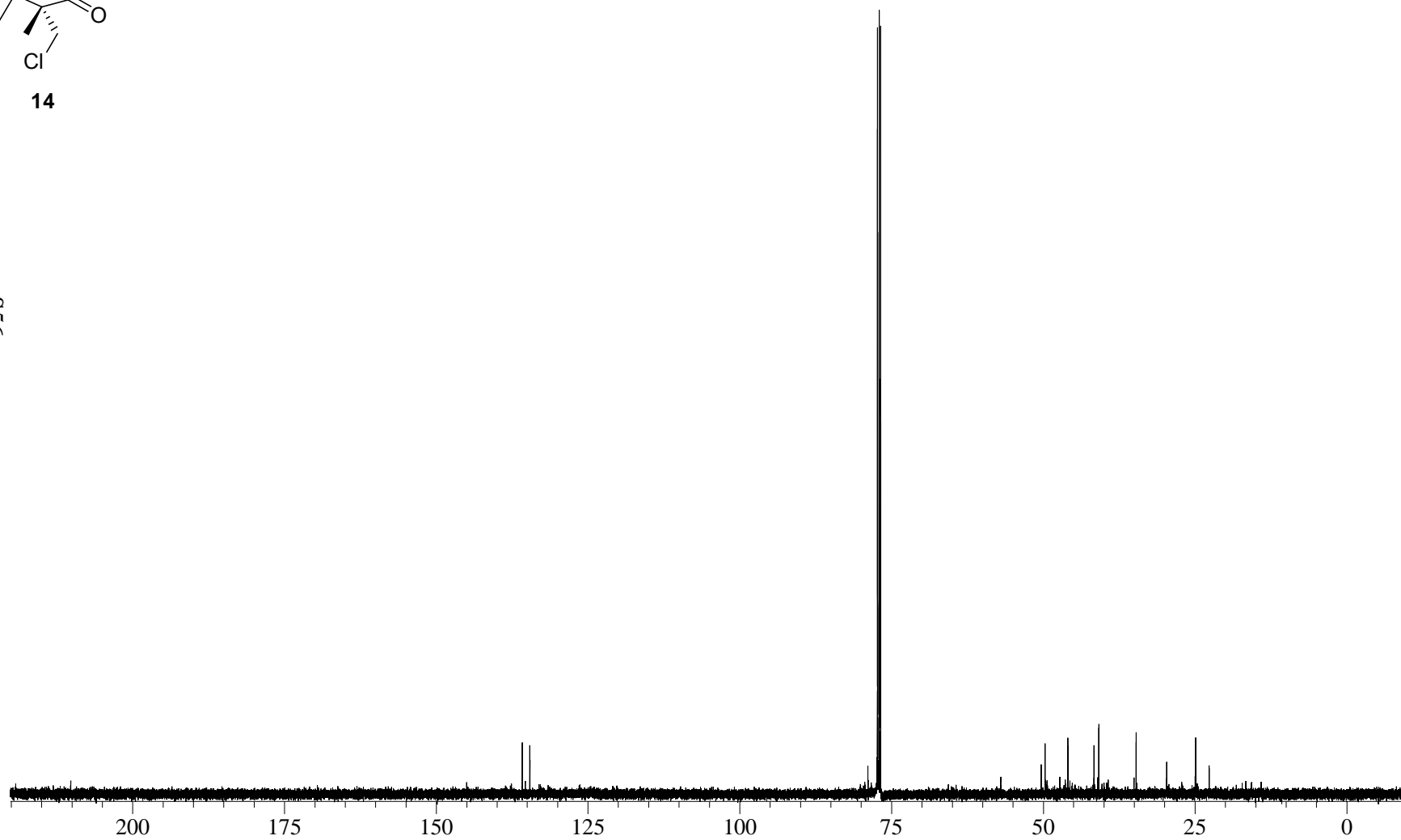


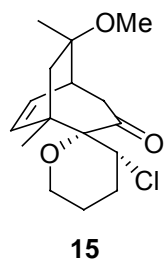
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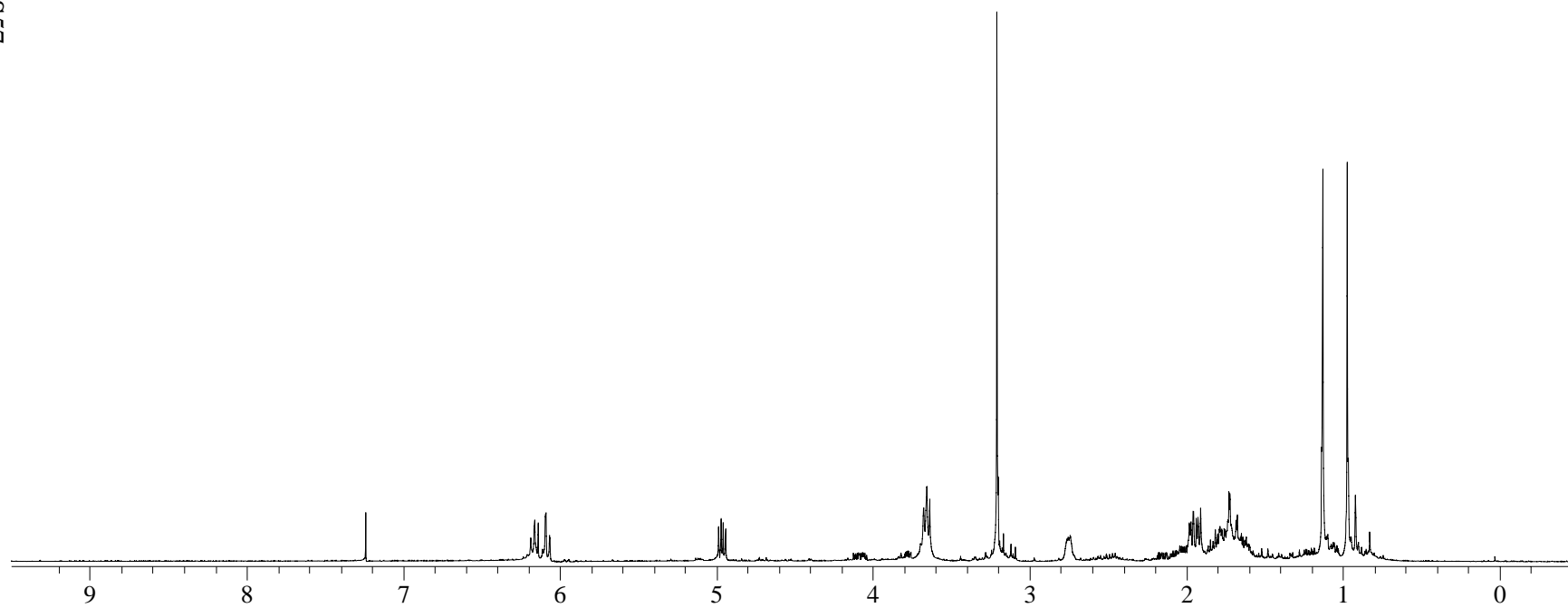


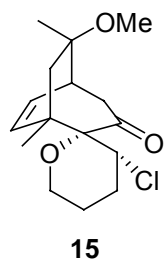
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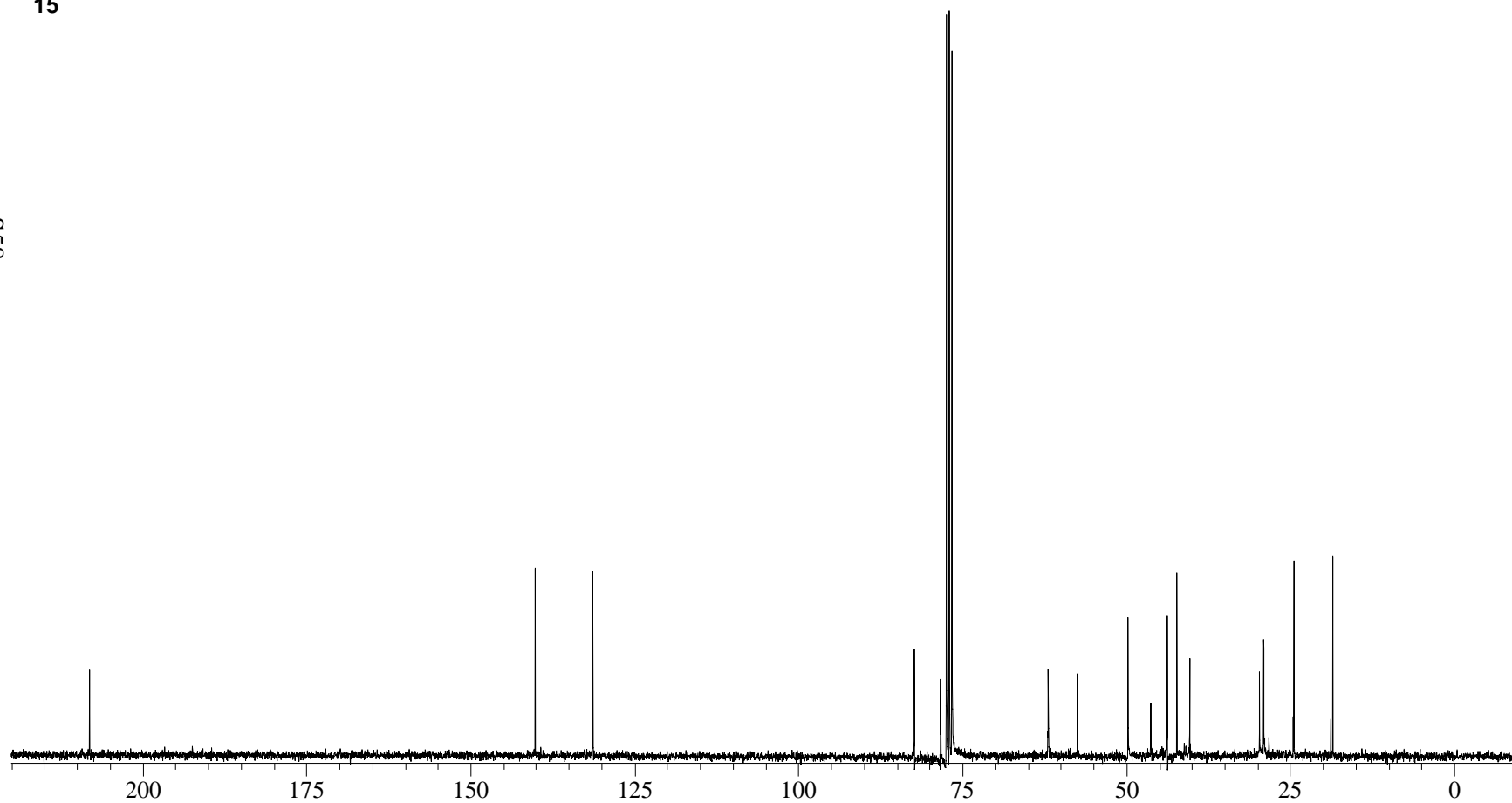


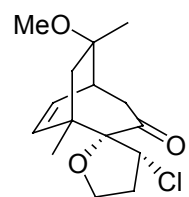
S57





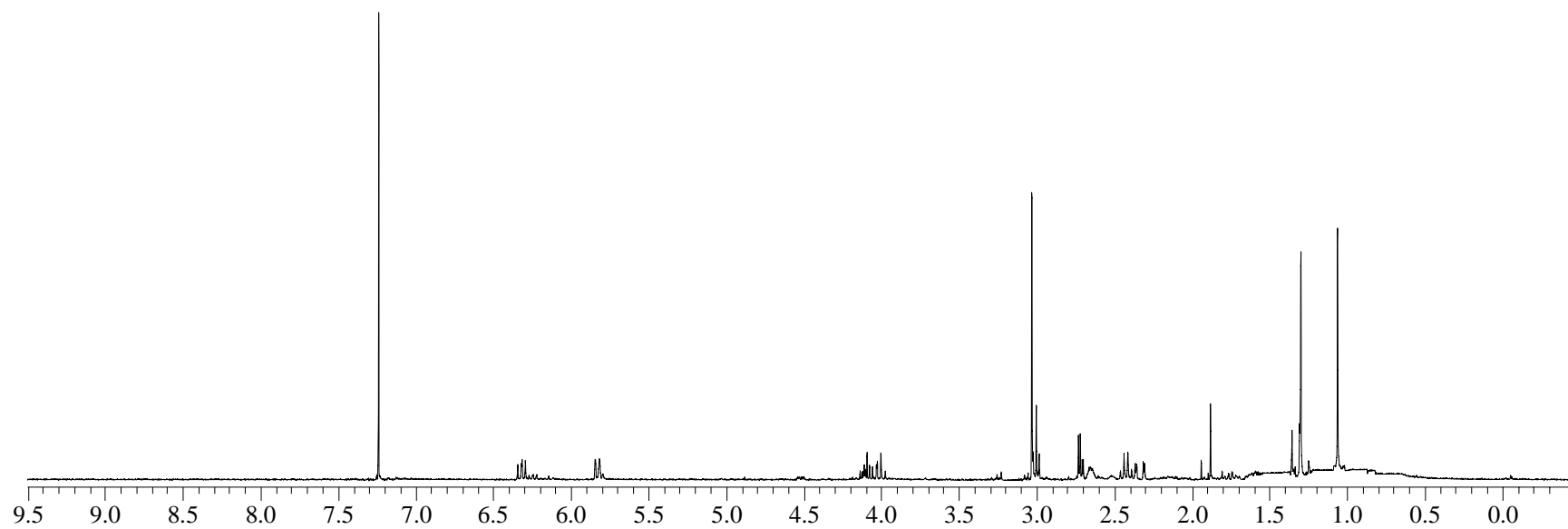
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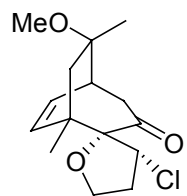




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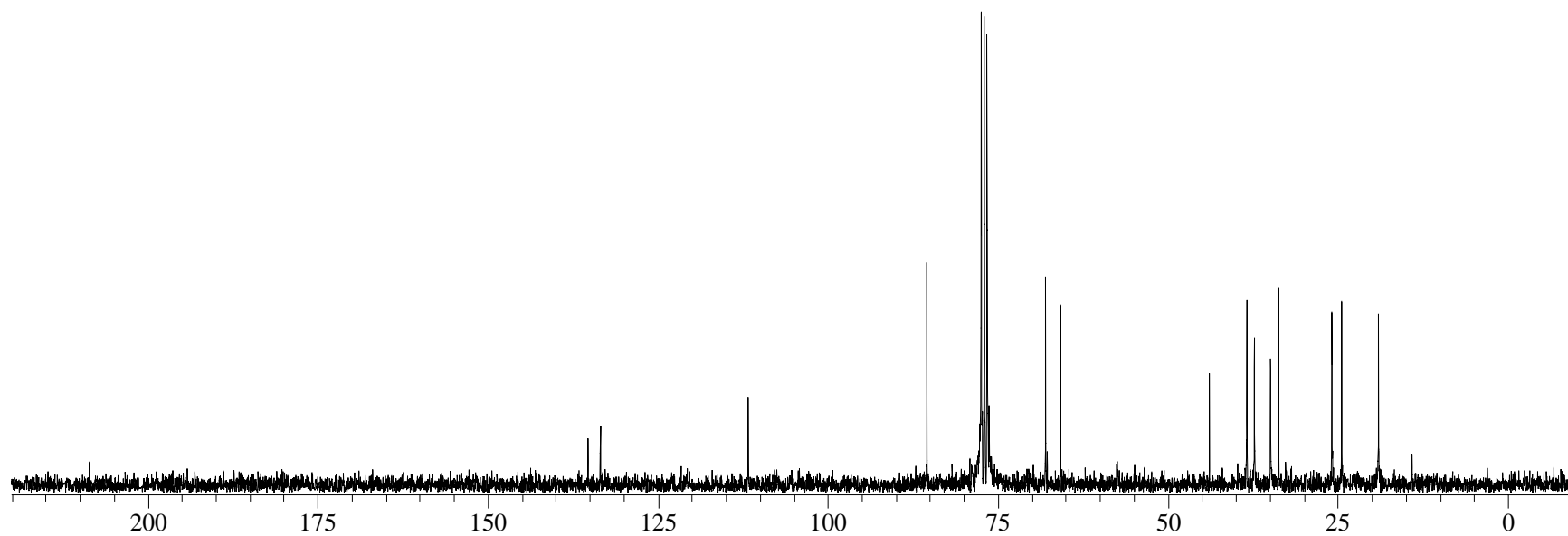
659

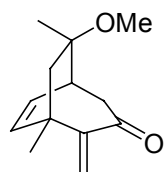




16

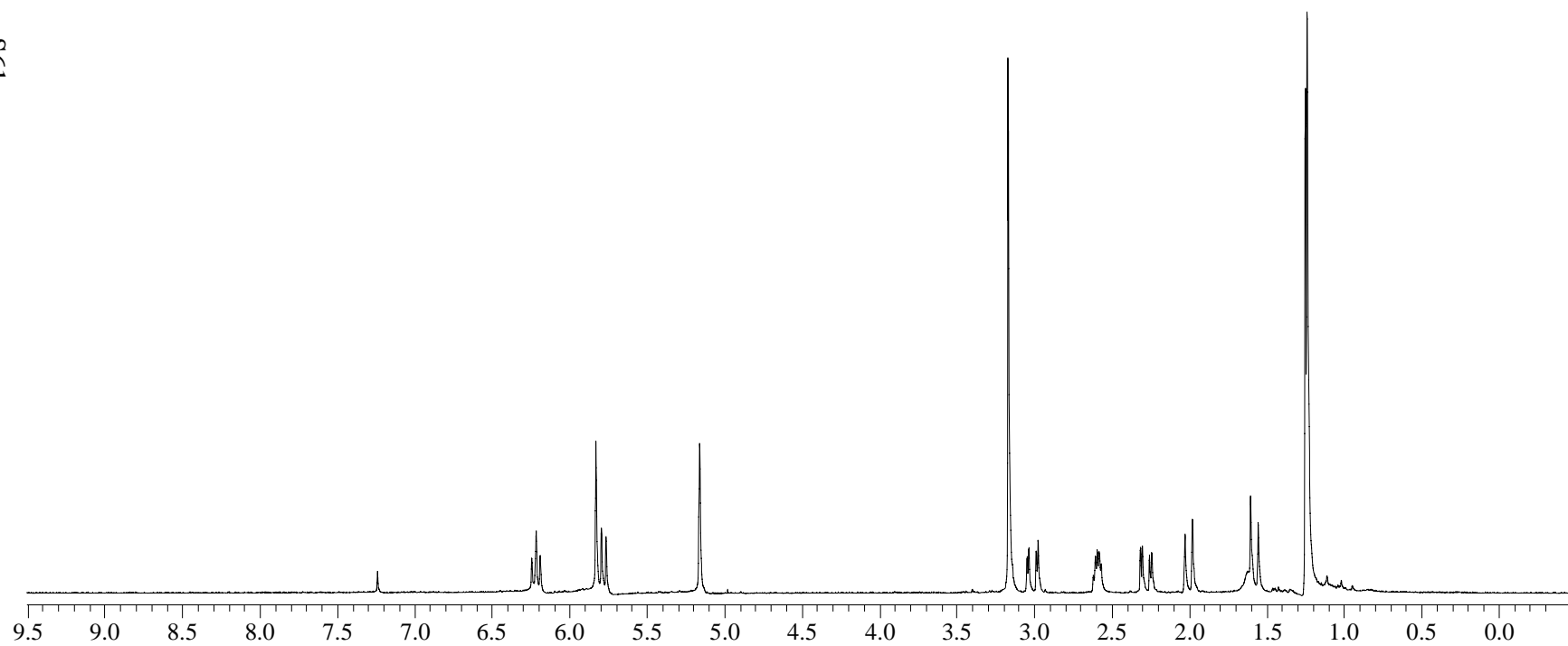
S60

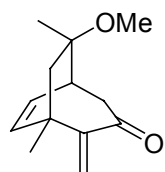




19

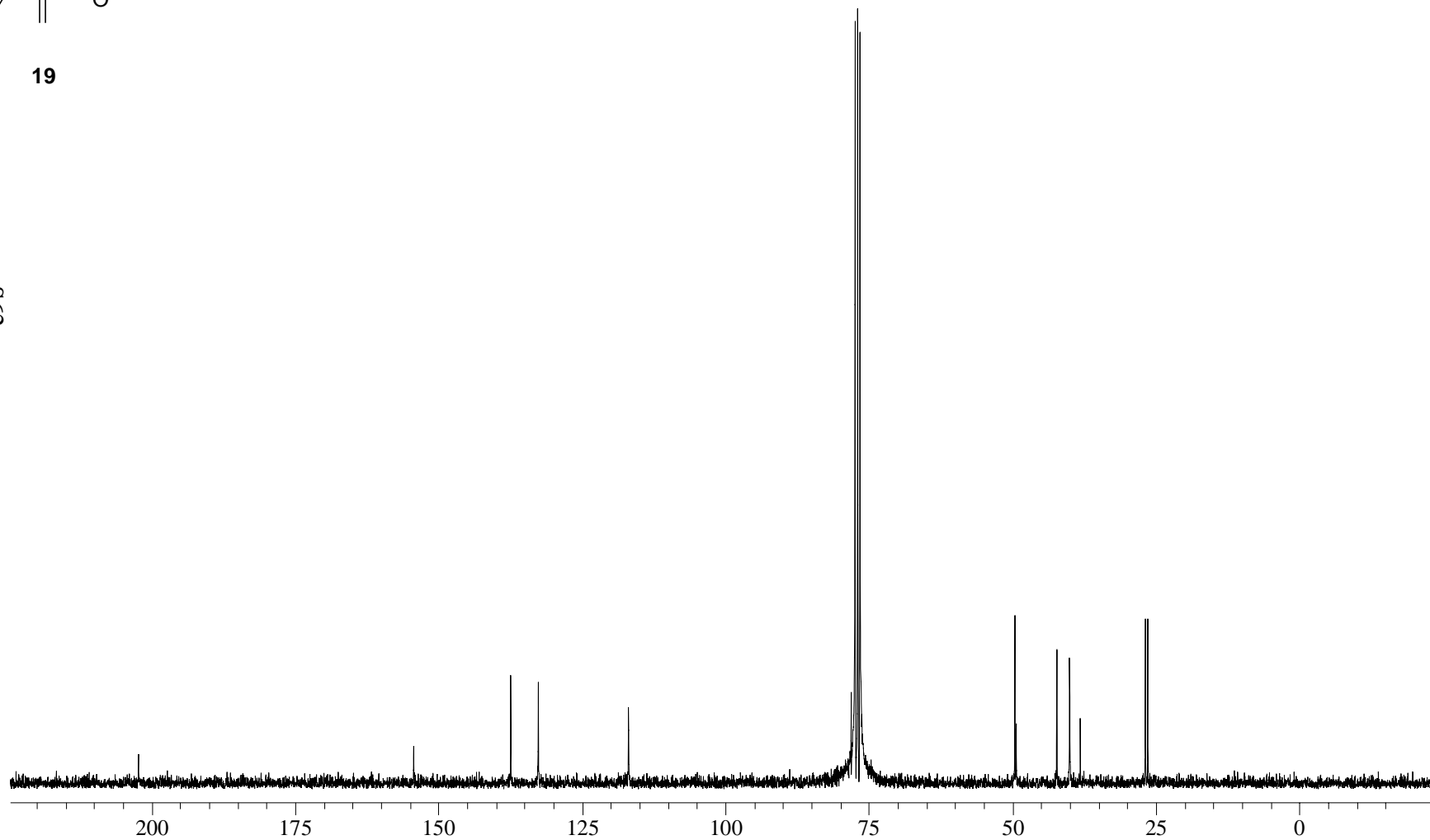
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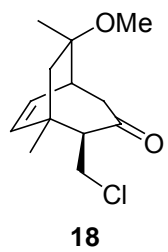




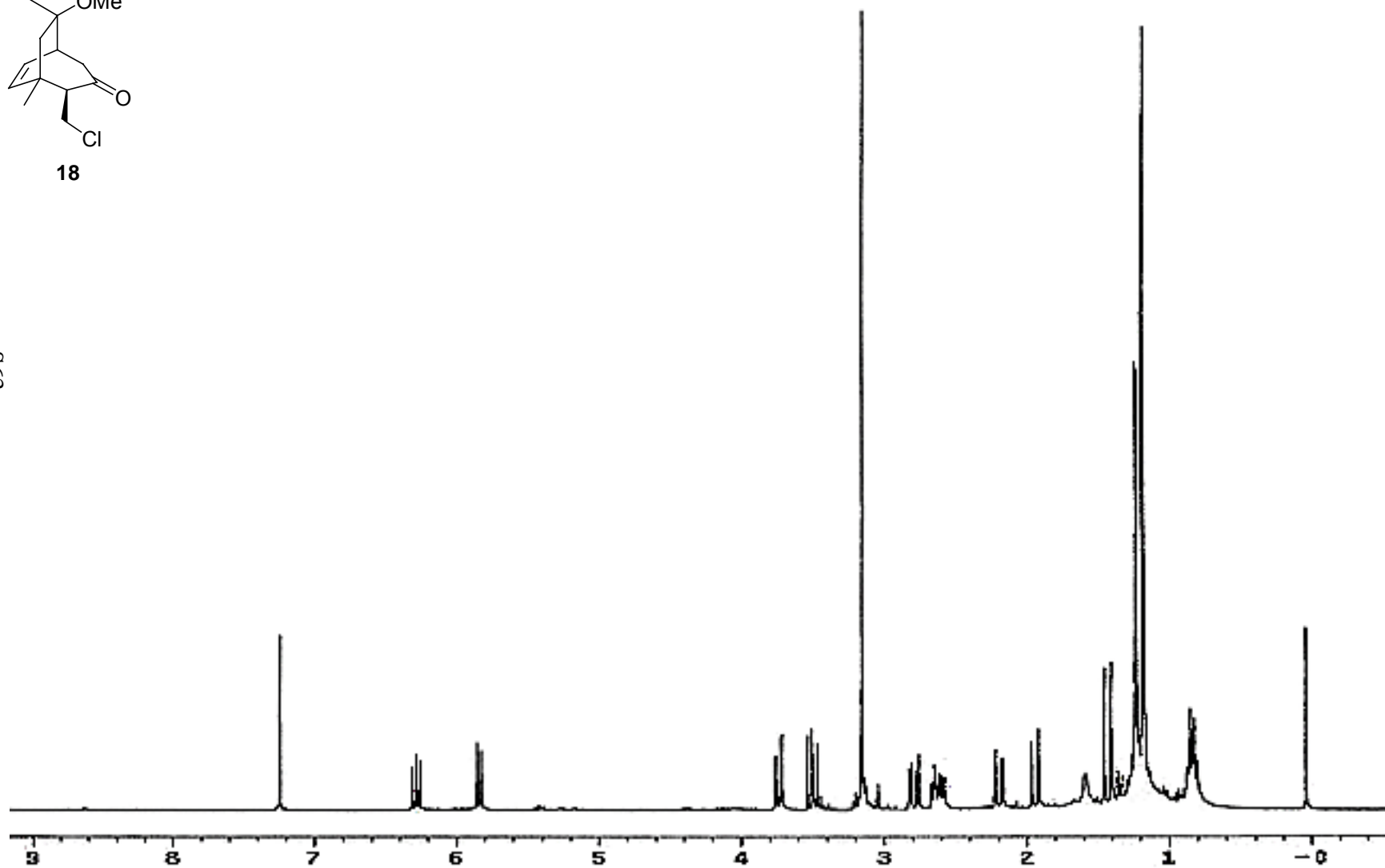
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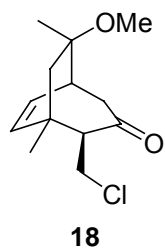
S62



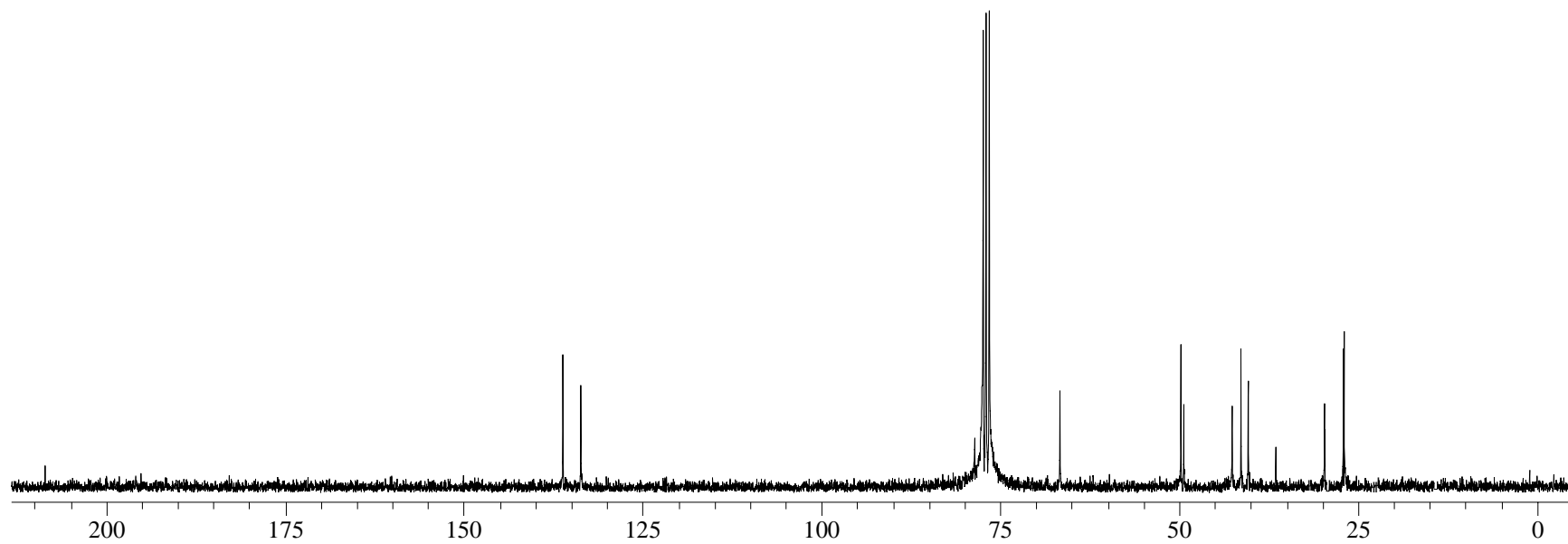


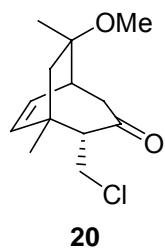
S63



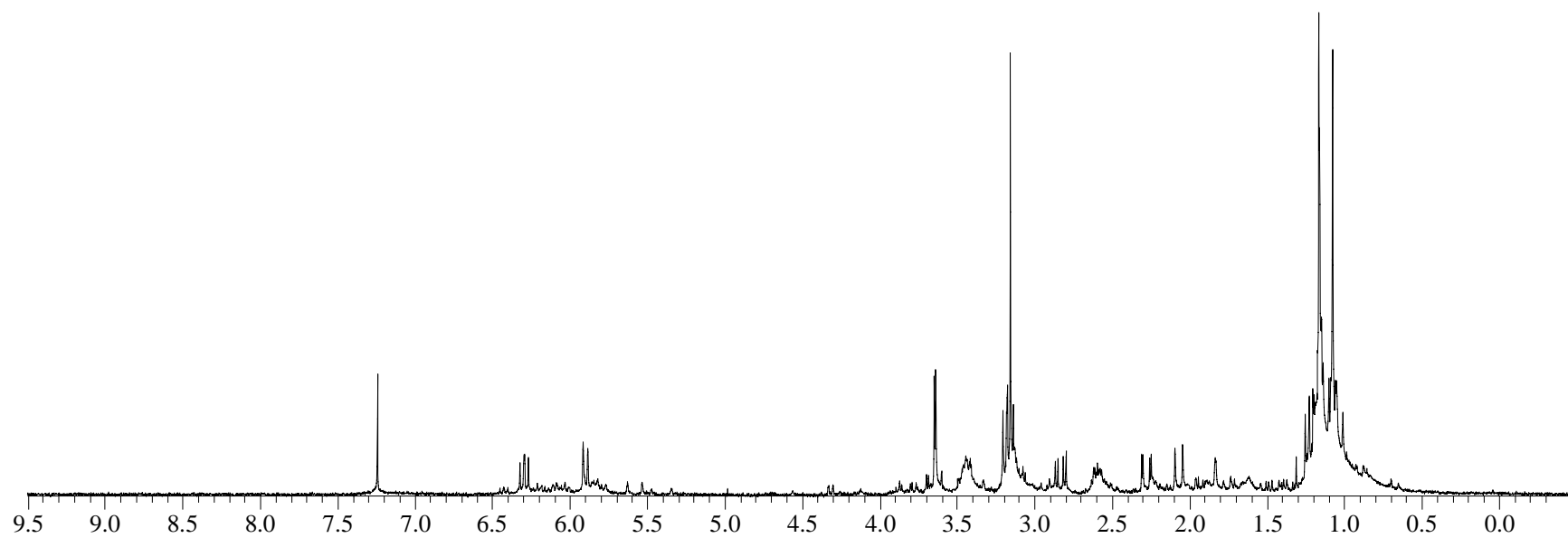


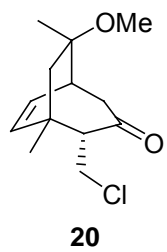
S64



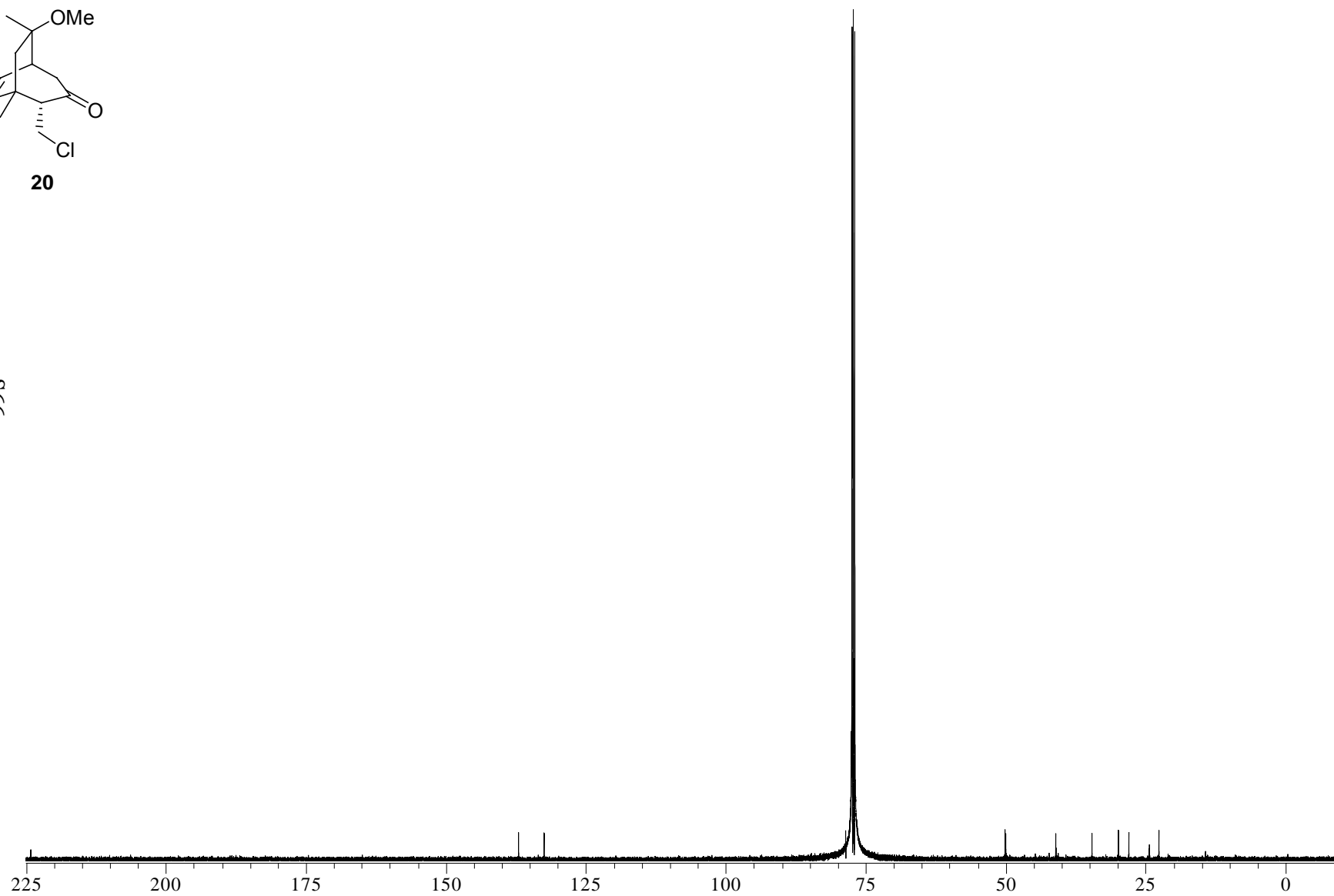


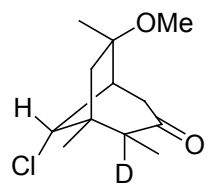
S65





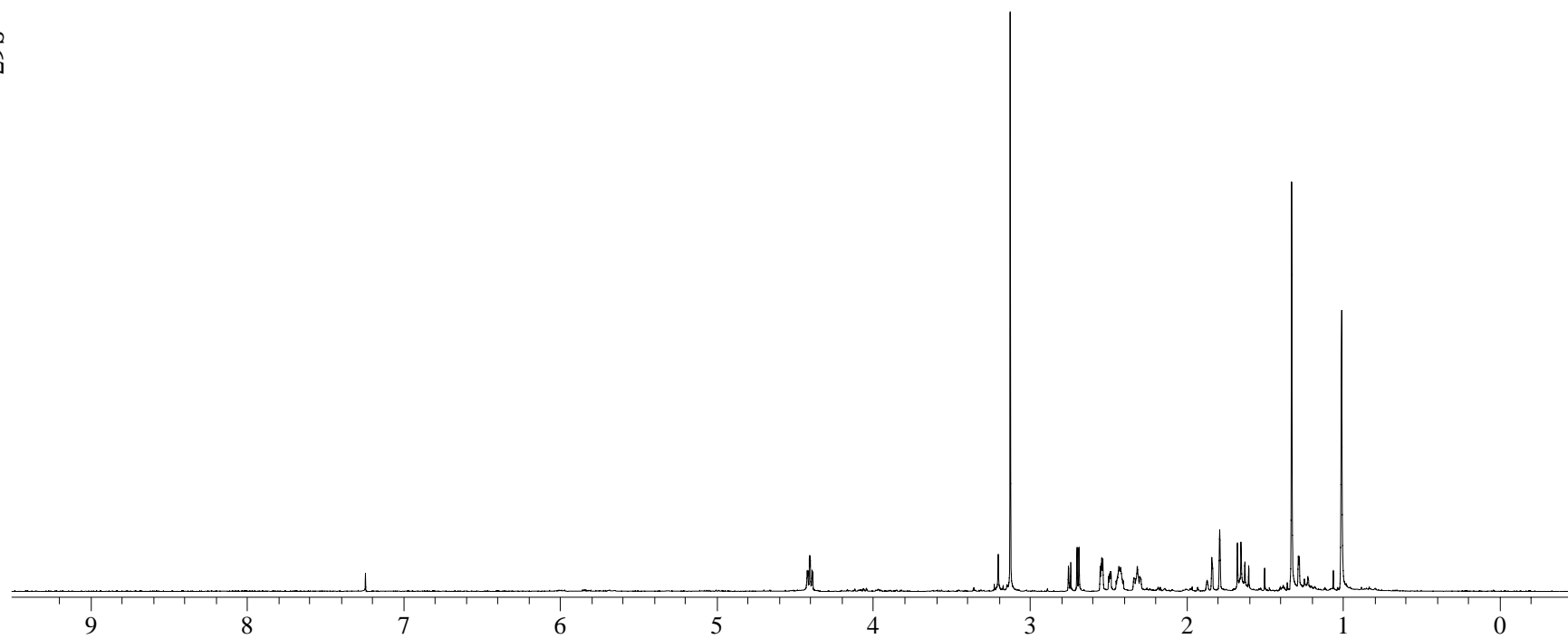
99S

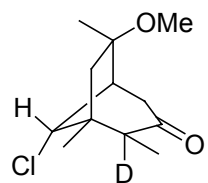




22a

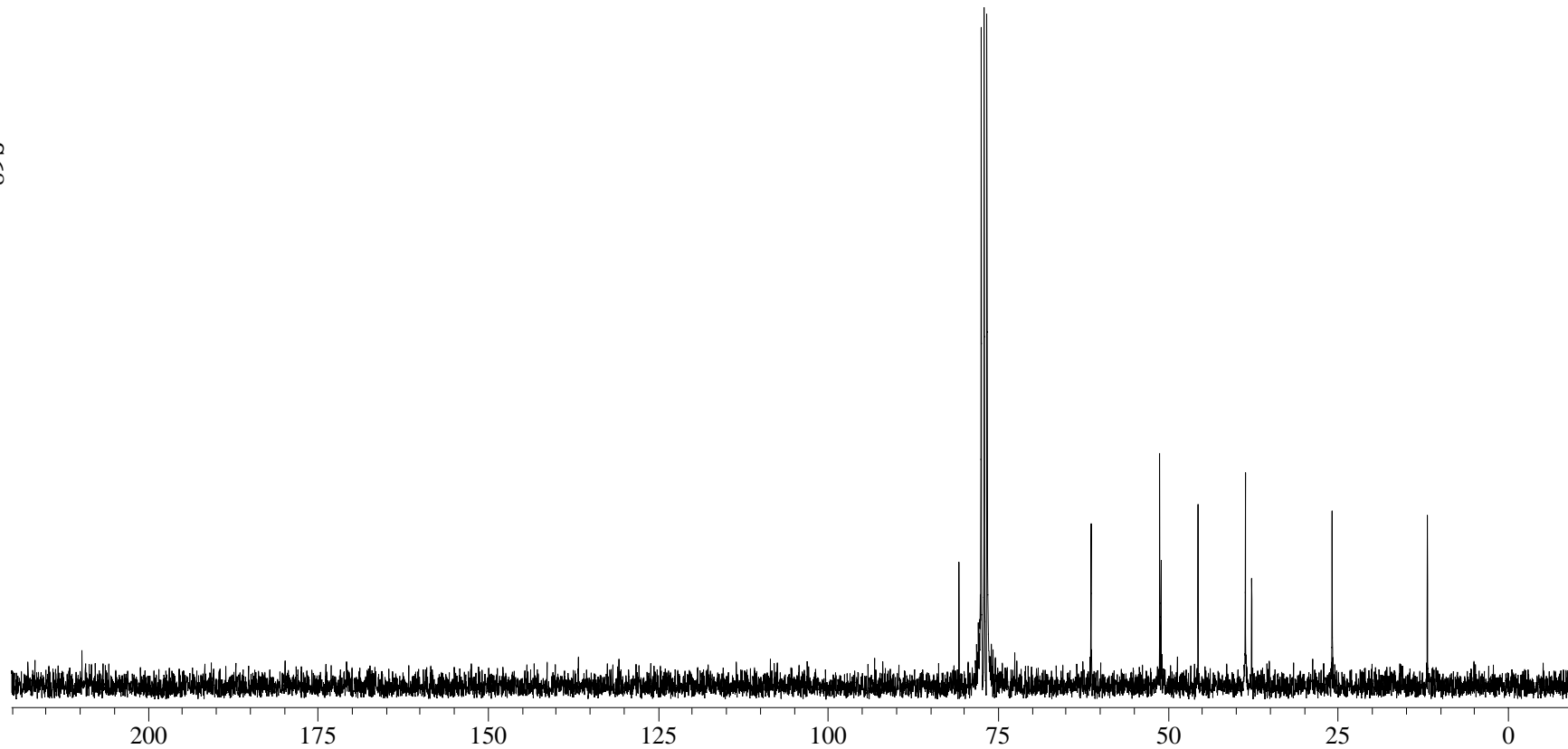
S67

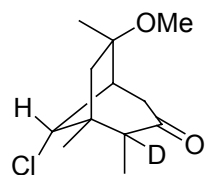




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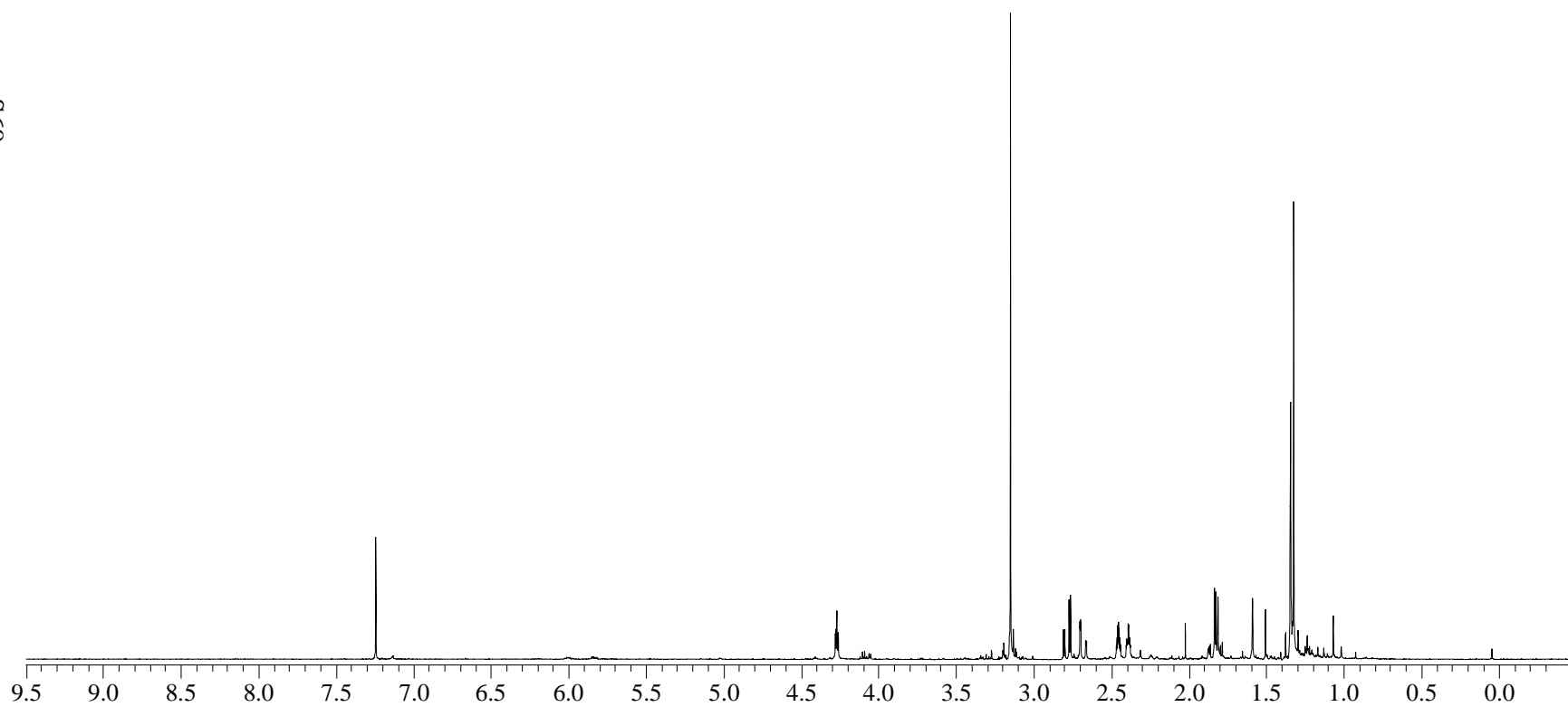
89S

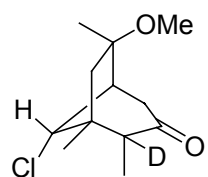




22b

695





22b

S70

