Supporting Information For

Copper(I)-Catalyzed Intramolecular [2 + 2] Cycloaddition of 1,6-Enyne Derived Ketenimine: An Efficient Construction of Strained and Bridged 7-Substituted-3-heterobicyclo[3.1.1]heptan-6-one

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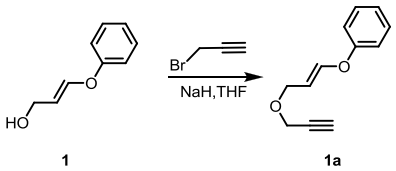
1. General information

All reactions were carried out under standard conditions using flame-dried glassware and monitored by thin layer chromatography on gel F_{254} plates. All solvents were freshly distilled under standard conditions. The silica gel (200–300 meshes) was used for column chromatography, and the petroleum is distilled in the range of was 60–90 °C. All other reagents were commercially available. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or acetone-d_6 solution on BRUKER AVANCE III 400 MHz instruments and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard. IR spectra were recorded on NEXUS spectrometer. Low resolution mass spectra (MS) were measured on TRACE DSQ spectrometer and signals were given in m/z with relative intensity (%) in brackets. High resolution mass spectra (HRMS) were obtained by means of the ESI or EI techniques. The diastereomeric ratios of the products **11d**, **12d**, **13d** and **15d** were determined by NMR and the relative configuration of all products were assigned according to the X-ray structure of **1d**, **4d**, **12d** and **13d**.

2. Preparation and spectroscopic data of substrates

Compounds **1**–**4**[1], **5a**[2], **7a**[3], **8**[4], **9a**[5] and **10a**[6] were synthesized according to the previously reported procedure in literatures.

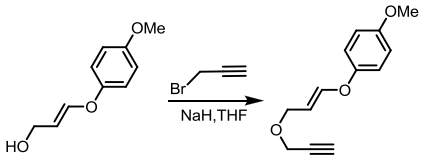
Preparation of substrate 1a



1 **1a**

Under Ar atmosphere, NaH (480 mg, 1.2 equiv, 12 mmol, 60%) was added slowly to the solution of the compound **1**[1] (1.501 g, 10 mmol) in dry THF (15 mL) at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (1.1 equiv, 0.46 mL, 11 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (8 h) by TLC monitoring. Then the reaction mixture was treated slowly with H_2O (20 mL), and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15:1) provided **1a** as colorless oil (1.505 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (m, 2H), 7.09–7.05 (m, 1H), 7.01–6.98 (m, 2H), 6.72 (d, *J* = 12.0 Hz, 1H), 5.44–5.38 (dt, *J* = 7.6 Hz, 12.0 Hz, 1H), 4.15 (d, *J* = 2.4 Hz, 2H), 4.09–4.06 (dd, *J* = 0.8 Hz, 7.6 Hz, 2H), 2.44 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6 (C), 146.8 (CH), 129.6 (CH), 123.2 (CH), 117.0 (CH), 106.9 (CH), 79.6 (C), 74.5 (CH), 66.0 (CH_2), 56.2 (CH_2); IR ν (cm^{-1}) 3293, 2857, 1073; MS (EI) m/z (%) 188 (M^+, 1), 133 (21), 121 (37), 77 (100), 67 (27), 55 (16); HRMS (EI) calcd. For $C_{12}H_{12}O_2$ $[M+H]^+$: 188.0837, Found: 188.0834.

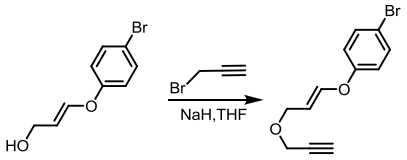
Preparation of substrate 2a



2 2a

Following the procedure of the substrate **1a** described above, the substrate **2a** was synthesized from compound **2**[1] (1.801 g, 10 mmol). Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15: 1) provided **2a** (2.137 g) as yellow oil in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96–6.93 (m, 2H), 6.86–6.83 (dd, *J* = 3.2Hz, 10.4 Hz, 2H), 6.67 (d, *J* = 12.4 Hz, 1H), 5.34–5.27 (dt, *J* = 7.6 Hz, 12.0 Hz, 1H), 4.16 (d, *J* = 2.4 Hz, 2H), 4.06 (d, *J* = 7.6 Hz, 2H), 3.77 (s, 3H), 2.44 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7 (C), 150.4 (C), 148.4 (CH), 118.6 (CH), 114.6 (CH), 105.5 (CH), 79.7 (C), 74.4 (CH), 66.2 (CH_2), 56.2 (CH_2), 55.6 (CH_3); IR ν (cm^{-1}) 2843, 1671, 1071; MS (EI) m/z (%) 218 (M^+, 44), 163 (18), 151 (20), 124 (100), 67 (29), 55 (15); HRMS (EI) calcd. For $C_{13}H_{14}O_3$ $[M]^+$: 218.0943, Found: 218.0942.

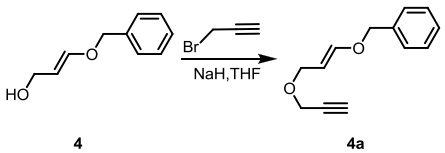
Preparation of substrate 3a



3 3a

Following the procedure of the substrate **1a** described above, the substrate **3a** was synthesized from compound **3**[1] (2.280 g, 10 mmol). Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15:1) provided **3a** (2.207 g) as yellow oil in 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.39 (m, 2H), 6.89–6.86 (m, 2H), 6.68–6.64 (dd, *J* = 1.2 Hz, 12.4 Hz, 1H), 5.47–5.40 (dt, *J* = 7.2 Hz, 12.0 Hz, 1H), 4.16 (m, 2H), 4.09–4.07 (dd, *J* = 0.8 Hz, 7.2 Hz, 2H), 2.46 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6 (C), 146.1 (CH), 132.5 (CH), 118.7 (CH), 115.7 (C), 107.9 (CH), 79.5 (C), 74.6 (CH), 65.8 (CH_2), 56.4 (CH_2); IR ν (cm^{-1}) 2855, 1674, 1070; MS (EI) m/z (%) 266 (M^+, 5), 199 (48), 131 (100), 104 (23), 95 (67), 67 (86); HRMS (EI) calcd. For $C_{12}H_{11}BrO_2$ $[M]^+$: 265.9942, Found: 265.9945.

Preparation of substrate 4a

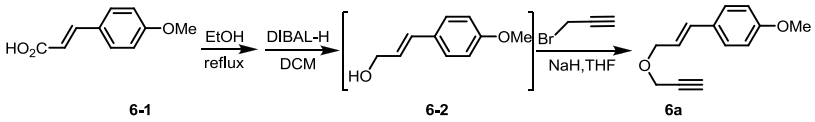


4 4a

Following the procedure of the substrate **1a** described above, the substrate **4a** was synthesized from compound **4**[1] (1.641 g, 10 mmol). Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15:1) provided **4a** (1.643 g) as yellow oil in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.30 (m, 5H), 6.67 (d, *J* = 12.4 Hz, 1H), 5.03–4.97 (dt, *J* = 7.6 Hz, 12.4 Hz, 1H), 4.83 (s, 2H), 4.08 (d, *J* = 2.4 Hz, 2H), 3.96 (d, *J* = 7.6 Hz, 2H), 2.90 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7 (CH), 138.2 (C), 129.3 (CH), 128.7 (CH), 128.5 (CH), 101.0 (CH), 81.2 (C), 75.5 (CH), 71.9 (CH_2), 67.4 (CH_2), 56.3 (CH_2); IR ν (cm^{-1}) 3291,

2860, 1071; MS (EI) m/z (%) 202 (M^+, < 1%), 155 (2), 129 (3), 92 (9), 91 (100), 65 (9); HRMS (ESI) calcd. for $C_{13}H_{14}O_2$ $[M+Na]^+$: 225.0886, Found: 225.0881.

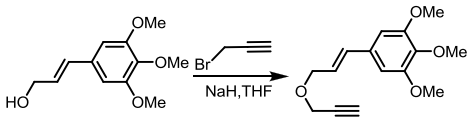
Preparation of substrate 6a



6-1 **6-2** **6a**

Acid **6-1** (0.450 g) and H_2SO_4 (0.25 mL) was stirred in ethanol (25 mL) under reflux condition for 8 h. Then the reaction system was cooled to rt and saturated $NaHCO_3$ (8 mL) was added for the removal of the acid. The ethanol was removed under reduce pressure and the reaction mixture was extracted with ethyl acetate (10 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was dissolved in CH_2Cl_2, (10 mL). Under Ar atmosphere, DIBAL-H (1 M in toluene, 2.0 equiv, 5.0 mL) was added slowly to the above solution at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 2 h. The system was quenched by the addition of saturated Rochelle's salt solution (10 mL). After 1 h, the reaction mixture was diluted with ethyl acetate (15 mL) and water (15 mL). The organic layer was separated and aqueous phase was extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford crude **6-2**. Under Ar atmosphere, NaH (1.2 equiv, 240 mg) was added slowly to the solution of crude product **6-2** in dry THF (15 mL) at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (1.1 equiv, 0.22 mL) was added. Then, the cold bath was removed and the new reaction system was stirred at rt until **6-2** disappeared completely (8 h) by TLC monitoring. This reaction was treated with H_2O (20 mL) and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15: 1) provided **6a** (369 mg) as yellow oil in 78% yield (for three steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.29 (m, 2H), 6.85–6.82 (m, 2H), 6.57 (d, *J* = 15.6 Hz, 1H), 6.16–6.08 (dt, *J* = 6.4 Hz, 16.0 Hz, 1H), 4.20–4.18 (dd, *J* = 1.2Hz, 6.4 Hz, 2H), 4.17 (d, *J* = 2.4 Hz, 2H), 3.77 (s, 3H), 2.45 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3 (C), 133.0 (CH), 129.2 (C), 127.6 (CH), 122.6 (CH), 113.9 (CH), 79.7 (C), 74.3 (CH), 70.2 (CH_2), 56.7 (CH_2), 55.1 (CH_3); IR ν (cm^{-1}) 3288. 2936, 1103; MS (EI) m/z (%) 202 (M^+, 6), 172 (100), 157 (38), 135 (100), 105 (60), 77 (35); HRMS (ESI) calcd. for $C_{13}H_{14}O_2$ $[M+H]^+$: 203.1067, Found: 203.1070.

Preparation of substrate 8a

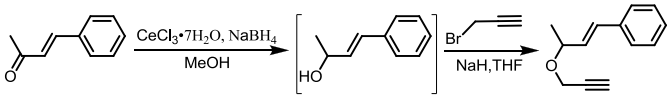


8 **8a**

Under Ar atmosphere, NaH (1.2 equiv, 480 mg, 60%) was added slowly to the solution of **8**[4] (2.441 g, 10 mmol) in dry THF (20 mL) at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (2 equiv, 1.6 mL, 20 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (8 h) by TLC monitoring. The system was treated with H_2O (15 mL) and aqueous phase was extracted

with ethyl acetate (20 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15: 1) provided **8a** (1.841 g) as yellow oil 70%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59–6.50 (m, 3H), 6.20-6.11 (m, 1H), 4.21–4.15 (m, 4H), 3.83–3.80 (m, 9H), 2.44 (t, *J* = 2.4 Hz , 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2 (C), 137.9 (C), 133.1 (C), 132.1 (CH), 124.5 (CH), 103.6 (CH), 79.6 (C), 74.4 (CH), 69.9 (CH_2), 60.7 (CH_3), 56.9 (CH_2), 55.9 (CH_3); IR ν (cm^{-1}) 3282, 2939, 1078; MS (EI) m/z (%) 262 (M^+, 8), 208 (2), 201 (100), 151 (6), 77 (7), 55 (3); HRMS (ESI) calcd. for $C_{15}H_{18}O_4$ $[M+H]^+$: 263.1278, Found: 263.1279.

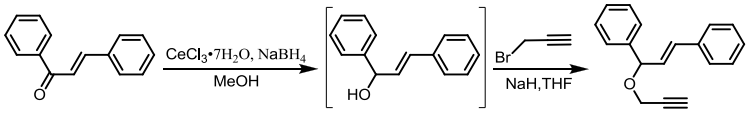
Preparation of substrate 11a



11-1 **11-2** **11a**

Under Ar atmosphere, compound **11-1** (1.461 g, 10 mmol) was dissolved in methanol (30 mL), then $CeCl_3$•$7H_2O$ (1.2 equiv, 4.470 g, 12 mmol) and $NaBH_4$ (1.2 equiv, 0.456 mg, 12 mmol) were added slowly to the solution at 0 °C. After 30 min, the reaction was quenched by sluggish addition of H_2O (20 ml), extracted with ethyl acetate (30 mL × 3), dried over $MgSO_4$, and concentrated under reduced pressure to give crude product **11-2**. Under Ar atmosphere, the crude product **11-2** was dissolved in dry THF (25 mL) and then NaH (1.2 equiv, 480 mg, 12 mmol) was added slowly to this system at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and 3-bromoprop-1-yne (2.0 equiv, 1.56 mL, 20 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely by TLC monitoring. H_2O (20 mL) was added dropwise to the mixture, and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15: 1) provided **11a** (1.488 g) as yellow oil in 80% yield (for two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.19 (m, 5H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.07–6.01 (dd, *J* = 8.0 Hz, *J* = 16.0 Hz,1H), 4.25–4.03 (m, 3H), 2.40 (t, *J* = 2.4 Hz, 1H), 1.35 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.2 (C), 132.2 (CH), 130.2 (CH), 128.4 (CH), 127.7 (CH), 126.4 (CH), 80.1 (C), 75.3 (CH), 73.9 (CH), 55.0 (CH_2), 21.4 (CH_3); IR ν (cm^{-1}) 3296, 2976, 1076; MS (EI) m/z (%) 186 (M+, <1 %), 131 (29), 91 (34), 77 (16), 55 (5), 43 (100); HRMS (ESI) calcd. for $C_{13}H_{14}O$ $[2M+H]^+$: 373.2162, Found: 373.2173.

Preparation of substrate 12a

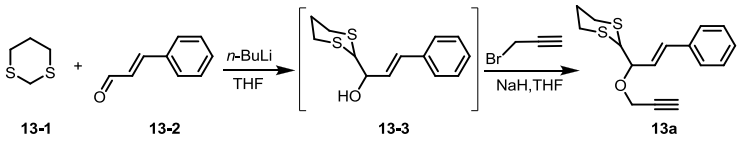


12-1 **12-2** **12a**

Following the procedure of the substrate **11a** above, the substrate **12a** was synthesized from compound **12-1** (2.801 g, 10 mmol) in one-pot process. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1–15:1) provided **12a** (1.861 g) as yellow oil in 75% yield (for two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.20 (m, 10H), 6.66 (d, *J* = 16.0 Hz, 1H), 6.31–6.26 (dd, *J* = 7.2 Hz, 16.0 Hz, 1H), 5.20 (d, *J* = 6.8 Hz, 1H), 4.24–4.12 (dq, *J* =

2.4 Hz, 15.6 Hz, 2H), 2.44 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2 (C), 136.4 (C), 132.3 (CH), 129.1 (CH), 128.6 (CH), 128.5 (CH), 127.9 (CH), 127.8 (CH), 127.1 (CH), 126.6 (CH), 80.9 (CH), 79.8 (CH), 74.4 (C), 55.3 (CH_2) IR ν (cm^{-1}) 3292, 3029, 1068; MS (EI) m/z (%) 248 (M^+, 1), 142 (21), 115 (22), 106 (8), 105 (100), 77 (28); HRMS (EI) calcd. for $C_{18}H_{16}O$ $[M]^+$: 248.1201, Found: 248.1201.

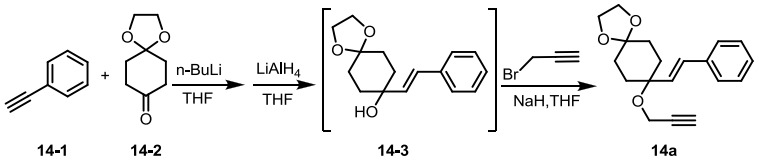
Preparation of substrate 13a



13-1 13-2 13-3 13a

Compound **13**–**1** (1.803 g, 15 mmol) was dissolved in THF (15 mL) under Ar atmosphere, *n*-BuLi (2.4 M, 1.1 equiv, 6.9 mL) was added dropwise to the solution at –78 °C. After 15 min, cinnamaldehyde **13**–**2** (1.1 equiv, 2.10 mL, 16.5 mmol) was added to the solution and the resulting mixture was stirred at –78 ℃ for 50 min. The reaction mixture was quenched with water (20 mL), extracted with ethyl acetate (30 mL × 3), dried over $MgSO_4$, and concentrated under reduced pressure to afford crude compound **13-3**. Under Ar atmosphere, the crude compound **13-3** was dissolved directly in dry THF (20 mL), and then NaH (2.0 equiv, 1.20 g) was added slowly to this system at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (2.0 equiv, 2.4 mL) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely by TLC monitoring. H_2O (20 mL) was added dropwise to the mixture, and the aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30:1-15: 1) provided **13a** (3.804 g) as yellow oil in 81% yield (for two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.24 (m, 5H), 6.68 (d, *J* = 16.0 Hz, 1H), 6.20–6.14 (dd, *J* = 8.4 Hz, 16.0 Hz, 1H), 4.41–4.37 (dd, *J* = 6.0 Hz, 8.4 Hz, 1H), 4.32–4.27 (m, 2H), 4.15–4.11 (dd, *J* = 2.0 Hz, 16.0 Hz, 1H), 2.92–2.80 (m, 4H), 2.46 (t, *J* = 2.4 Hz, 1H), 2.11–2.03 (m, 1H), 1.96–1.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 135.6 (C), 135.5 (CH), 128.4 (CH), 128.1 (CH), 126.7 (CH), 124.9 (CH), 81.2 (CH), 79.2 (CH), 74.8 (C), 55.4 (CH_2), 51.4 (CH), 29.9 (CH_2), 29.8 (CH_2), 25.8 (CH_2); IR ν (cm^{-1}) 3287, 2899, 1071; MS (EI) m/z (%) 290 (M^+, <1%), 171 (16), 131 (12), 119 (100), 115 (8), 77 (4); HRMS (ESI) calcd. for $C_{16}H_{18}OS_2$ $[M+Na]^+$: 313.0691, Found: 313.0692.

Preparation of substrate 14a

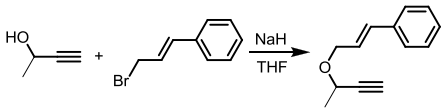


14-1 14-2 14-3 14a

Under Ar atmosphere, compound **14**–**1** (1.2 equiv, 1.2 mL, 10.9 mmol) was dissolved in dry THF (15 mL), *n*-BuLi (1.2 equiv, 2.4 M, 4.6 mL) was added dropwise to the solution at –78 °C. The mixture was stirred for 15 min at –78 °C, then compound **14**–**2** (1.420 g, 9.1 mmol) was added slowly. The reaction was monitored by TLC until the substrate disappeared completely (15 min).

The system was quenched by the addition of water (20 mL), the organic layer was separated and aqueous phase was extracted with ethyl acetate (25 mL × 3). The combined organic layer was washed with brine (25 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was dissolved in dry THF, $LiAlH_4$ (2.2 equiv, 0.760 g) was added sluggishly to the solution at 0 °C under Ar atmosphere. The mixture was stirred until the substrate disappeared completely by TLC monitoring, and the system was quenched by the addition of ethyl acetate (5 mL) as well as dilution with H_2O (20 mL) at 0 °C. The organic layer was separated and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic layer was washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford crude product **14-3**. Under Ar atmosphere, NaH (1.2 equiv, 0.439 g, 10.9 mmol) was added slowly to the solution of crude product **14-3** in dry THF at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (1.2 equiv, 0.85 mL, 10.9 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (6 h) by TLC monitoring. H_2O (20 mL) was added slowly to the reaction mixture, and aqueous phase was extracted with Ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$ and filtered. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30: 1-15: 1) provided **14a** (976 mg) as white solid in 36% yield (for three steps). m.p. 66–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.22 (m, 5H), 6.55 (d, *J* = 16.4 Hz, 1H), 6.14 (d, *J* = 16.4 Hz, 1H), 4.02 (d, *J* = 2.4 Hz, 2H), 3.98–3.90 (m, 4H), 2.40 (t, *J* = 2.4 Hz, 1H), 2.01–1.95 (m, 4H), 1.87–1.79 (m, 2H), 1.63–1.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4 (C), 132.8 (CH), 130.6 (CH), 128.5 (CH), 127.7 (CH), 126.4 (CH), 108.4 (C), 81.1 (C), 76.3 (CH), 73.3 (C), 64.2 (CH_2), 64.1 (CH_2), 50.7 (CH_2), 31.9 (CH_2), 30.2 (CH_2); IR ν (cm^{-1}) 3284, 2934, 1444; MS (EI) m/z (%) 298 (M^+, < 1), 199 (8), 156(12), 142 (67), 101 (100), 99 (56); HRMS (EI) calcd. for $C_{19}H_{22}O3$ $[M]^+$: 298.1569, Found: 298.1568.

Preparation of substrate 15a



15-1 **15-2** **15a**

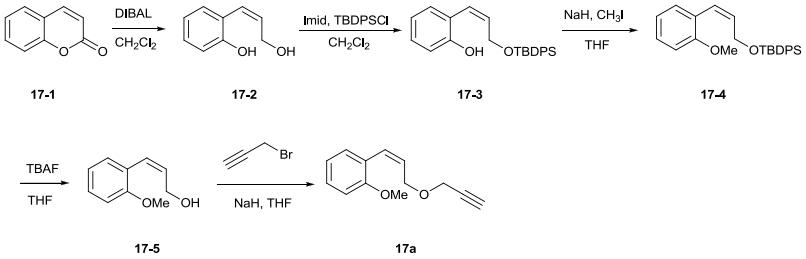
Under Ar atmosphere, NaH (1.2 equiv, 0.480 g, 12.0 mmol) was added slowly to the solution of compound **15**–**1** (0.78 mL, 10.0 mmol) in dry THF at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then compound **15–2** (1.1 equiv, 2.167g, 11.0 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (8 h) by TLC monitoring. H_2O was added dropwise to the mixture, and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried ($MgSO_4$) and filtered. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 90:1–40: 1) provided the **15a** (1.451 g) as yellow liquid in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.27 (m, 2H), 7.24–7.23 (m, 2H), 7.22–7.20 (m, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.31–6.24 (m, 1H), 4.42–4.38 (ddd, *J* = 1.6 Hz, 5.6 Hz, 12.4 Hz, 1H), 4.27–4.21 (dq, *J* = 2.0 Hz, 6.8 Hz, 1H), 4.15–4.10 (ddd, *J* = 1.6 Hz, 6.8 Hz, 12.8 Hz, 1H), 2.44 (d, *J* = 2.0 Hz, 1H), 1.47 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.6 (C), 132.9 (CH), 128.5 (CH), 127.6 (CH), 126.5 (CH), 125.5 (CH), 83.7 (C), 73.0 (CH), 69.1 (CH_2), 64.2 (CH), 22.0 (CH_3); IR ν (cm^{-1}) 3291, 2988, 1103; MS (EI) m/z (%) 186 (M^+, <1%), 129 (22), 115 (38),

91(100), 77 (8), 57 (2); HRMS (ESI) calcd. for $C_{13}H_{14}O$ $[2M+H]^+$: 373.2162, Found: 373.2165.

Preparation of substrate 16a

The substrate **16a**[7] was synthesized according to the previously reported procedure in literature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.78–5.68 (m, 1H), 5.32–5.23 (m, 2H), 4.09 (d, *J* = 2.4 Hz, 2H), 3.83 (d, *J* = 6.4 Hz, 2H), 2.43 (s, 3H), 2.01 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5 (C), 135.9 (C), 131.8 (CH), 129.4 (CH), 127.7 (CH), 120,0 (CH_2), 76.4 (C), 73.7 (CH), 48.9 (CH_2), 35.7 (CH_2), 21.5 (CH_3).

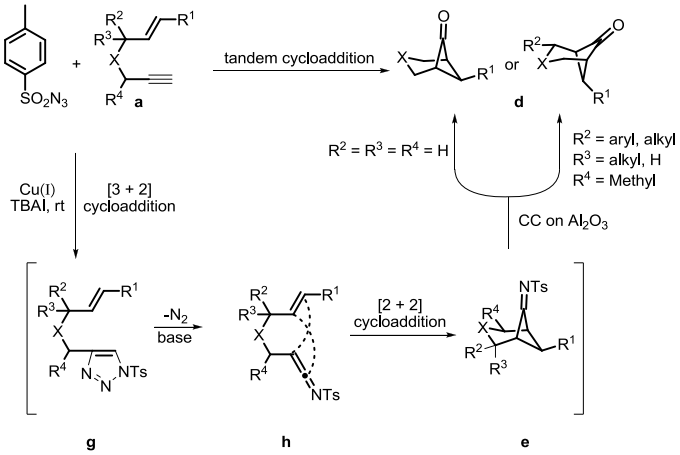
Preparation of substrate 17a



The compound **17-1** (1.462 g, 10 mmol) was dissolved in CH_2Cl_2, (10 mL). Under Ar atmosphere, DIBAL-H (1 M in toluene, 2.0 equiv, 20 mL) was added slowly to the above solution at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 2 h. The system was quenched by the addition of saturated Rochelle's salt solution (10 mL). After 1 h, the reaction mixture was diluted with ethyl acetate (15 mL) and water (15 mL). The organic layer was separated and aqueous phase was extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford crude **17-2**. Under Ar atmosphere, iminazole (2.2 equiv, 1.498 g) was added slowly to the solution of crude product **17-2** in dry THF (15 mL) at 0 °C. The mixture was stirred vigorously at 0 °C for 5 min, and then TBDPSCl (1.1 equiv, 1.8 mL) was added. Then, the cold bath was removed and the new reaction system was stirred at rt until **17-2** disappeared completely (10 h) by TLC monitoring. This reaction was treated with H_2O (20 mL) and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum provided crude product **17-3** (2.456 g). Under Ar atmosphere, NaH (1.2 equiv, 200 mg, 8.3 mmol) was added slowly to the solution of compound **17-3** (2.456 g, 6.9 mmol) in dry THF at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then compound CH_3I (1.1 equiv, 0.4 mL, 7.6 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (8 h) by TLC monitoring. H_2O was added dropwise to the mixture, and aqueous phase was extracted with ethyl acetate (30 mL × 3). The combined organic phase was washed with brine, dried ($MgSO_4$), filtered and concentrated under vacuum provided crude product **17-4**. Then crude compound **17-4** was treated directly with $(Bu)_4NF•3H_2O$ (3.602 g, 13.6 mmol, 2.0 equiv) in THF. The new reaction system was stirred at rt until **17-4** disappeared completely (2 h) by TLC monitoring and concentrated under vacuum. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether = 10/1) afforded compound **17-5** (512

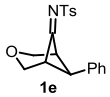
mg) in 31% yield for four steps). Under Ar atmosphere, NaH (1.2 equiv, 90 mg, 3.74 mmol) was added slowly to the solution of crude product **17-5** (512 mg, 3.12 mmol) in dry THF at 0 °C. The mixture was stirred vigorously at 0 °C for 30 min, and then 3-bromoprop-1-yne (1.2 equiv, 0.30 mL, 3.74 mmol) was added. The cold bath was removed and the reaction was stirred at rt until the substrate disappeared completely (6 h) by TLC monitoring. H_2O (20 mL) was added slowly to the reaction mixture, and aqueous phase was extracted with Ethyl acetate (20 mL × 3). The combined organic phase was washed with brine, dried over $MgSO_4$ and filtered. Column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 30: 1-15: 1) provided **17a** (976 mg) as white solid in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.15 (m, 2H), 6.93–6.84 (m, 2H), 6.77 (d, *J* = 11.6 Hz, 1H), 5.89–5.83 (dt, *J* = 6.8 Hz, 11.6 Hz, 1H), 4.25–4.23 (dd, *J* = 1.6 Hz, 6.8 Hz, 2H), 4.12 (d, *J* = 2.4 Hz, 2H), 3.79 (s, 3H), 2.45 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9 (C), 130.0 (CH), 128.8 (CH), 128.2 (CH), 127.4 (CH), 125.2 (C), 120.0 (CH), 110.2 (CH), 79.7 (C), 74.3 (CH), 66.6 (CH_2), 57.2 (CH_2), 55.2 (CH_3); IR ν (cm^{-1}) 3290. 2936, 2947; MS (EI) m/z (%) 202 (M^+, 2), 172 (61), 157 (48), 135 (100), 105 (61), 77 (44); HRMS (ESI) calcd. for $C_{13}H_{14}O_2$ $[M+Na]^+$: 225.0886, Found: 225.0888.

3. The typical procedure and the spectroscopic data of products



To a solution of **a** (1.0 equiv) and TsN_3 (1.5 equiv) in CH_2Cl_2 or toluene, were added CuI (0.2 equiv), K_2CO_3 (1.2 equiv) and TBAI (0.1 equiv) and stirred at rt. After completed conversion of **a** by TLC monitoring, the reaction mixture was concentrated under reduced pressure and chromatographied on neutral Al_2O_3 column to remove $TsNH_2$ and give the pure products **d**.

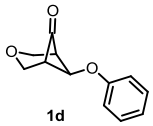
Synthesis of compound 1e



1e

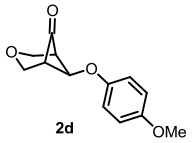
After completed conversion of **1a** to **1e**, the reaction mixture was concentrated under reduced pressure. Compound **1e** was obtained by column chromatography on silica gel (eluting with ethyl acetate/petroleum ether 15:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.31–7.25 (m, 4H), 7.03–6.99 (m, 1H), 6.79–6.76 (dd, *J* = 0.8 Hz, 8.4 Hz, 2H), 4.93 (s, 1H), 4.59–4.55 (m, 3H), 4.41–4.38 (dd, *J* = 2.0 Hz, 9.6 Hz, 1H), 3.38–3.31 (m, 1H), 2.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5 (C), 156.3 (C), 144.5 (C), 136.2 (C), 129.7 (CH), 129.7 (CH), 127.5 (CH), 122.0 (CH), 115.3 (CH), 74.8 (CH_2), 74.7 (CH_2), 59.3 (CH), 57.6 (CH), 21.6 (CH_3).

Synthesis of product 1d



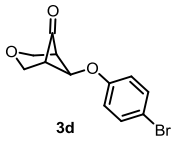
According to typical procedure described above, **1a** (83 mg, 0.44 mmol) gave the product **1d** (65 mg) in 72% yield in DCM at rt for 8 h (eluting with ethyl acetate/petroleum ether 25:1). Light yellow solid; m.p. 119–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.27 (m, 2H), 7.01–6.98 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 4.83 (s, 1H), 4.56 (d, *J* = 10.4 Hz, 2H), 4.46 (d, *J* = 10.0 Hz, 2H), 3.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5 (C), 156.4 (C), 129.6 (CH), 121.7 (CH), 115.3 (CH), 74.3 (CH_2), 72.2 (CH), 63.7 (CH); IR ν (cm^{-1}) 2961, 1795, 1228; MS (EI) m/z (%) 204 (M^+, 9), 176 (5), 110 (94), 94 (34), 77 (44), 55 (100); HRMS (ESI) calcd. for $C_{12}H_{12}O_3$ $[M+H]^+$: 205.0859, Found: 205.0857.

Synthesis of product 2d



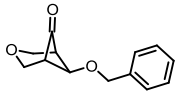
According to typical procedure described above, **2a** (135 mg, 0.62 mmol) gave the product **2d** (107 mg) in 74% yield in DCM at rt for 4 h (eluting with ethyl acetate/petroleum ether 25:1). White solid; m.p. 87–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85–6.80 (m, 4H), 4.78 (s, 1H), 4.53 (d, *J* = 10.0 Hz, 2H), 4.45 (d, *J* = 10.0 Hz, 2H), 3.76 (s, 3H), 3.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7 (C), 154.6 (C), 150.3 (C), 116.6 (CH), 114.7 (CH), 74.3 (CH_2), 72.9 (CH), 63.7 (CH_3), 55.6 (CH); IR ν (cm^{-1}) 2865, 1791, 1085; MS (EI) m/z (%) 234 (M^+, 20), 135 (2), 124 (100), 109 (22), 81 (12), 55 (20) . HRMS (EI) calcd. for $C_{13}H_{14}O_4$ $[M]^+$: 234.0892 , Found: 234.0893.

Synthesis of product 3d



According to typical procedure described above, **3a** (150 mg, 0.56 mmol) gave the product **3d** (108 mg) in 69% yield in DCM at rt for 12 h (eluting with ethyl acetate/petroleum ether 25:1). White solid; m.p. 115–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 4.81 (s, 1H), 4.57 (d, *J* = 10.4 Hz, 2H), 4.47 (d, *J* = 10.4 Hz, 2H), 3.30 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2 (C), 155.5 (C), 132.5 (CH), 117.1 (CH), 114.1 (C), 74.3 (CH_2), 72.5 (CH), 63.7 (CH); IR ν (cm^{-1}) 2925, 1794, 1079; MS (EI) m/z (%) 282 (M^+, 9), 172 (22), 117 (8), 110 (72), 82 (64), 55 (100). HRMS (EI) calcd. for $C_{12}H_{11}BrO_3$ $[M]^+$: 281.9892, Found: 281.9893.

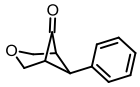
Synthesis of product 4d



4d

According to typical procedure described above, **4a** (89 mg, 0.44 mmol) gave the product **4d** (47 mg) in 45% yield in toluene at rt for 48 h (eluting with ethyl acetate/petroleum ether 25:1). Light yellow solid; m.p. 47–55 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.26 (m, 5H), 4.56 (s, 2H), 4.41 (s, 4H), 4.25 (s, 1H), 3.21 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.7 (C), 137.0 (C), 128.6 (CH), 128.0 (CH), 127.8 (CH), 74.5 (CH_2), 74.3 (CH), 71.0 (CH_2), 63.6 (CH); IR ν (cm^{-1}) 2925, 1791, 1091; MS (EI) m/z (%) 218 (M^+, <1), 149 (1), 127 (11), 91 (100), 77 (2), 69 (2); HRMS (ESI) calcd. for $C_{13}H_{14}O_3$ $[M+NH_4]^+$: 236.1281, Found: 236.1279.

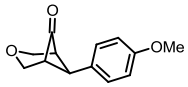
Synthesis of product 5d



5d

According to typical procedure described above, **5a** (52 mg, 0.30 mmol) gave the product **5d** (28 mg) as a colorless liquid in 50% yield in DCM at rt for 8 h (eluting with ethyl acetate/petroleum ether 20:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.23 (m, 5H), 4.58 (d, *J* = 9.2 Hz, 2H), 4.42 (d, *J* = 10.0 Hz, 2H), 3.68 (s, 1H), 3.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4 (C), 139.8 (C), 128.9 (CH), 127.1 (CH), 126.9 (CH), 75.5 (CH_2), 64.9 (CH), 38.0 (CH); IR ν (cm^{-1}) 2858, 1780, 1106; MS (EI) m/z (%) 188 (M^+, 1), 131 (21), 115 (28), 77 (14), 57 (12), 44 (100); HRMS (ESI) calcd. for $C_{12}H_{12}O_2$ $[M+Na]^+$: 211.0730, Found: 211.0732.

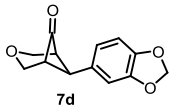
Synthesis of product 6d



6d

According to typical procedure described above, **6a** (60 mg, 0.30 mmol) gave the product **6d** (48 mg) in 73% yield in DCM at rt for 24 h (eluting with ethyl acetate/petroleum ether 20:1). Yellow solid; m.p. 49–52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 4.57–4.55 (m, 2H), 4.40 (d, *J* = 10.0 Hz, 2H), 3.78 (s, 3H), 3.62 (s, 1H), 3.20 (d, *J* = 0.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5 (C), 158.6 (C), 131.7 (C), 127.9 (CH), 114.2 (CH), 75.4 (CH_2), 64.9 (CH_3), 55.2 (CH), 37.3 (CH); IR ν (cm^{-1}) 2860, 1783, 1251; MS (EI) m/z (%) 218 (M^+, 41), 190 (63), 159 (100), 115 (45), 103 (38), 77 (33); HRMS (ESI) calcd. for $C_{13}H_{14}O_3$ $[M+H]^+$: 219.1016, Found: 219.1008.

Synthesis of product 7d

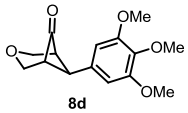


7d

According to typical procedure described above, **7a** (85 mg, 0.39 mmol) gave the product **7d** (63 mg) in 70% yield in DCM at rt for 40 h (eluting with ethyl acetate/petroleum ether 20:1). White solid; m.p. 128–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76–6.66 (m, 3H), 5.94 (s, 2H), 4.55 (d, *J* = 10.0 Hz, 2H), 4.40 (d, *J* = 10.0 Hz, 2H), 3.60 (s, 1H), 3.19 (s, 2H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 207.2 (C), 148.1 (C), 146.7 (C), 133.5 (C), 119.8 (CH), 108.5 (CH), 107.5 (CH), 101.1 (CH_2), 75.4 (CH_2), 65.0 (CH), 37.8 (CH); IR ν (cm^{-1}) 2924, 1776, 1032; MS (EI) m/z (%) 232 (M^+, 60), 204 (32), 200 (100), 143 (16), 89 (26), 77 (29); HRMS (ESI) calcd. for $C_{13}H_{12}O_4$ $[M+H]^+$: 233.0808, Found: 233.0803.

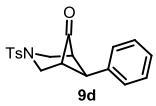
Synthesis of product 8d



8d

According to typical procedure described above, **8a** (115 mg, 0.44 mmol) gave the product **8d** (92 mg) in 75% yield in DCM at rt for 24 h (eluting with ethyl acetate/petroleum ether 15: 1). Light yellow solid; m.p. 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.44 (s, 2H), 4.57 (d, *J* = 9.2 Hz, 2H), 4.41 (d, *J* = 9.6 Hz, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 3.60 (s, 1H), 3.24 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.2 (C), 153.4 (C), 137.1 (C), 135.5 (C), 103.9 (CH), 75.3 (CH_2), 64.9 (CH_3), 60.7 (CH_3), 56.0 (CH), 38.3 (CH); IR ν (cm^{-1}) 2853, 1778, 1124; MS (EI) m/z (%) 278 (M^+, 96), 250 (72), 219 (92), 189 (100), 176 (62), 77 (26); HRMS (ESI) calcd. for $C_{15}H_{18}O_5$ $[M+H]^+$: 279.1227, Found: 279.1223.

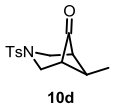
Synthesis of product 9d



9d

According to typical procedure described above, **9a** (245 mg, 0.75 mmol) gave the product **9d** (210 mg) in 78% yield in DCM at rt for 8 h (eluting with ethyl acetate/petroleum ether 15: 1). White solid; m.p. 162–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.30–7.22 (m, 3H), 7.12 (d, *J* = 7.2 Hz, 2H), 4.16–4.13 (dd, *J* =1.6 Hz, 11.6 Hz, 2H), 3.93 (d, *J* = 10.4 Hz, 2H), 3.24 (s, 1H), 3.20 (d, *J* = 0.8 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.4 (C), 143.9 (C), 138.8 (C), 133.9 (C), 129.8 (CH), 128.8 (CH), 127.2 (CH), 127.1 (CH), 126.5 (CH), 60.5 (CH), 53.8 (CH_2), 40.0 (CH), 21.4 (CH_3); IR ν (cm^{-1}) 2860, 1788, 1160; MS (EI) m/z (%) 341 (M^+, 1), 183(6), 158 (89), 115 (69), 77 (41), 43 (100); HRMS (ESI) calcd. for $C_{19}H_{19}NO_3S$ $[M+NH_4]^+$: 359.1424, Found: 359.1430.

Synthesis of product 10d

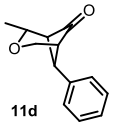


10d

According to typical procedure described above, **10a** (100 mg, 0.38 mmol) gave the product **10d** (33 mg) in 31% yield in DCM at rt for 20 h (eluting with ethyl acetate/petroleum ether 15: 1). White solid; m.p. 48–51 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 3.96–3.92 (dd, *J* = 1.6 Hz, 11.2 Hz, 2H), 3.82 (d, *J* = 10.0 Hz, 2H), 2.75 (s, 2H), 2.44 (s, 3H), 2.16–2.11 (q, *J* = 6.8 Hz, 1H), 1.14 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1 (C), 143.9 (C), 134.0 (C), 129.8 (CH), 127.2 (CH), 60.4 (CH), 53.0 (CH_2), 30.1 (CH), 21.5(CH_3), 16.8 (CH_3); IR ν (cm^{-1}) 2926, 1788, 1164; MS (EI) m/z (%) 279 (M^+, <1%), 155 (60), 124 (8), 96 (18), 91 (100), 55 (38); HRMS (ESI) calcd. for $C_{14}H_{17}NO_3S$ $[M+H]^+$:

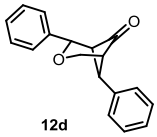
280.1002, Found: 280.1007.

Synthesis of product 11d



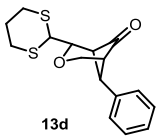
According to typical procedure described above, **11a** (400 mg, 2.15 mmol) gave the compound **11d** (288 mg, colorless liquid) as a mixture of two diastereoisomers (dr = 17:1, dr value analyzed by NMR) in 61% yield in DCM at rt for 24 h (eluting with ethyl acetate/petroleum ether 25: 1). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.34–7.23 (m, 5H), 4.50–4.46 (dd, *J* = 5.2 Hz, 9.6 Hz, 1H), 4.44–4.39 (q, *J* = 6.0 Hz, 1H), 4.21 (d, *J* = 10.0 Hz, 1H), 3.71 (s, 1H), 3.23–3.19 (dd, *J* = 5.2 Hz, 8.8 Hz, 1H), 3.03 (d, *J* = 9.2 Hz, 1H), 1.38 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3 (C), 139.7 (C), 128.8 (CH), 127.1 (CH), 126.9 (CH), 80.3 (CH), 72.9 (CH_2),70.1 (CH), 64.3 (CH), 33.2 (CH), 20.8 (CH_3); IR ν (cm^{-1}) 2926, 1782, 1112; MS (EI) m/z (%) 202 (M^+, 1), 158 (100), 115 (77), 91 (62), 77 (29),51 (14); HRMS (ESI) calcd. For $C_{13}H_{14}O_2$ $[M+NH_4]^+$: 220.1332, Found: 220.1327.

Synthesis of product 12d



According to typical procedure described above, **12a** (390 mg, 1.57 mmol) gave the compound **12d** (305 mg) as a single product in 69% yield in DCM at rt for 24 h (eluting with ethyl acetate/petroleum ether 25: 1). White solid; m.p. 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.14 (m, 10H), 5.38 (s, 1H), 4.72–4.68 (dd, *J* = 4.4 Hz, 9.6 Hz, 1H), 4.42 (d, *J* = 10.0 Hz, 1H), 3.83 (s, 1H), 3.37–3.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1 (C), 140.2 (C), 139.3 (C), 128.8 (CH), 128.7 (CH), 128.1 (CH), 127.0 (CH), 127.0 (CH), 125.4 (CH), 84.8 (CH), 73.4 (CH_2), 70.9 (CH), 64.0 (CH), 33.5 (CH); IR ν (cm^{-1}) 2924, 1770, 1098; MS (EI) m/z (%) 264 (M^+, 2), 235 (5), 158 (80), 130 (100), 105 (69), 77 (48); HRMS (ESI) calcd. For $C_{18}H_{16}O_2$ $[M+NH_4]^+$: 282.1489, Found: 282.1494.

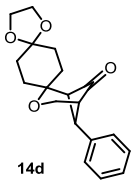
Synthesis of product 13d



According to typical procedure described above, **13a** (105 mg, 0.36 mmol) gave the compound **13d** (72 mg) as a single product in 61% yield in DCM at rt for 16 h (eluting with ethyl acetate/petroleum ether 25: 1). White solid; m.p. 109–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.23 (m, 5H), 4.59–4.55 (dd, *J* = 4.8 Hz, 10.0 Hz, 1H), 4.42 (d, *J* = 4.8 Hz, 1H), 4.30–4.26 (m, 2H), 3.99 (s, 1H), 3.47 (d, *J* = 8.8 Hz, 1H), 3.28–3.25 (m, 1H), 2.99–2.82 (m, 4H), 2.15–2.09 (m, 1H), 2.01–1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6 (C), 138.9 (C), 128.8 (CH),

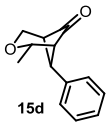
127.1 (CH), 127.0 (CH), 84.9 (CH), 72.7 (CH_2), 68.0 (CH), 63.2 (CH), 51.1 (CH), 33.9 (CH), 29.8 (CH_2), 29.7 (CH_2), 25.7 (CH_2); IR ν (cm^{-1}) 2897, 1778, 1105; MS (EI) m/z (%) 306 (M^+, 2), 187 (2), 159 (1), 119 (100), 91 (7), 77 (3); HRMS (ESI) calcd. For $C_{16}H_{18}O_2S_2$ $[M+Na]^+$: 329.0640 Found: 329.0638.

Synthesis of product 14d



According to typical procedure described above, **14a** (138 mg, 0.46 mmol) gave the compound **14d** (90 mg) in 62% yield in DCM at rt for 8 h (eluting with ethyl acetate/petroleum ether 25: 1). Light yellow solid; m.p. 65–68 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.30 (m, 2H), 7.26–7.22 (m, 3H), 4.45–4.42 (dd, *J* = 4.8 Hz, 10.0 Hz, 1H), 4.28–4.26 (d, *J* = 10.0 Hz, 1H), 3.97–3.90 (m, 4H), 3.72 (s, 1H), 3.22–3.19 (dd, *J* = 4.8 Hz, 8.8, 1H), 3.06 (d, *J* = 8.8 Hz, 1H), 2.22–2.17 (m, 1H),1.99–1.60 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.2 (C), 139.6 (C), 128.8 (CH), 127.0 (CH), 126.9 (CH), 108.2 (C), 84.5 (C), 73.0 (CH), 70.3 (CH_2), 64.6 (CH), 64.3 (CH_2), 64.2 (CH_2), 35.7 (CH), 33.8 (CH_2), 30.6 (CH_2), 30.5 (CH_2), 30.2 (CH_2); IR ν (cm^{-1}) 2932, 1766, 1100; MS (EI) m/z (%) 314 (M^+, 2), 286 (2), 158 (100), 130 (100), 103 (9), 55 (24); HRMS (ESI) calcd. For $C_{19}H_{22}O_4$ $[M+H]^+$: 315.1591, Found: 315.1589.

Synthesis of product 15d



According to typical procedure described above, **15a** (63 mg, 0.34 mmol) gave the product **15d** (45 mg) as a mixture of two diastereoisomers (dr = 4:1, dr value analyzed by NMR) in 61% total yield in DCM at rt for 52 h (spectroscopic data of **15d,** please see above spectroscopic data of **11d**).

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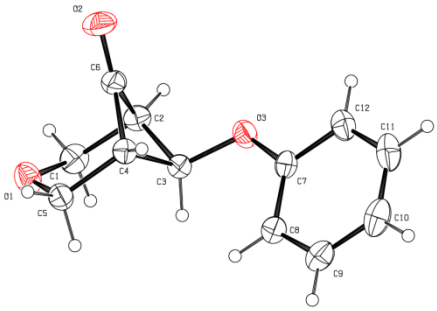
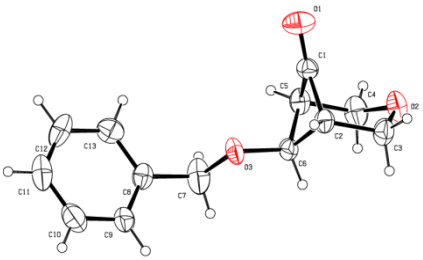
4. ORTEPS drawing of 1d, 4d, 12d and 13d from X-ray crystallographic analysis



CCDC code: 855318
1d (relative configuration)



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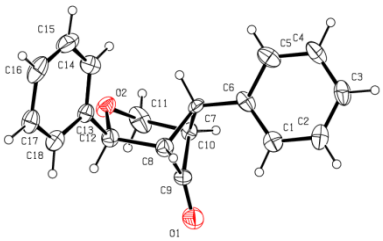
4d (relative configuration)



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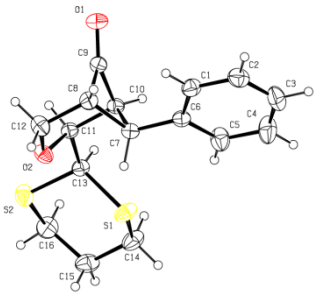
12d (relative configuration)



CCDC code: 855320
13d (relative configuration)

5. Reference

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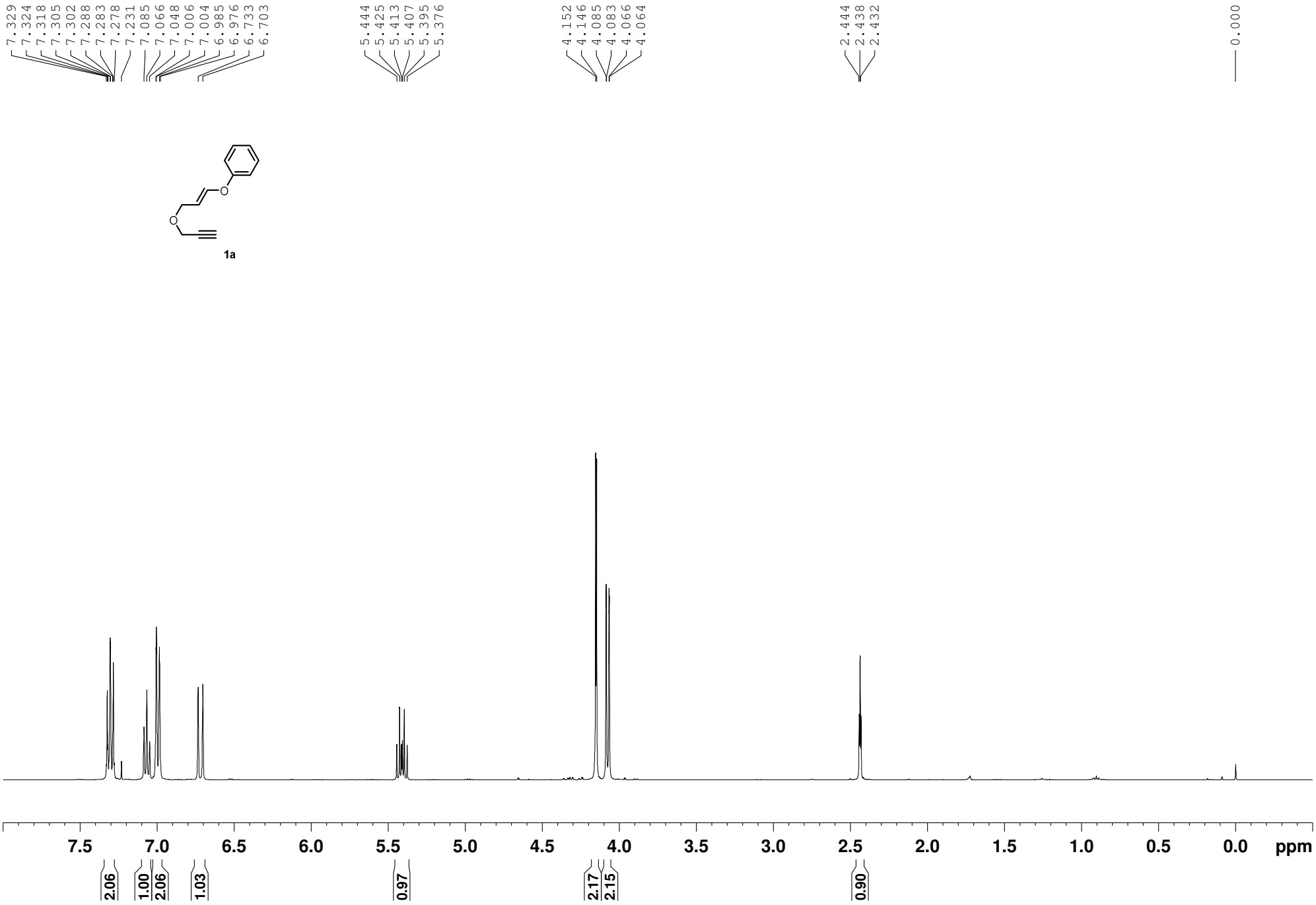

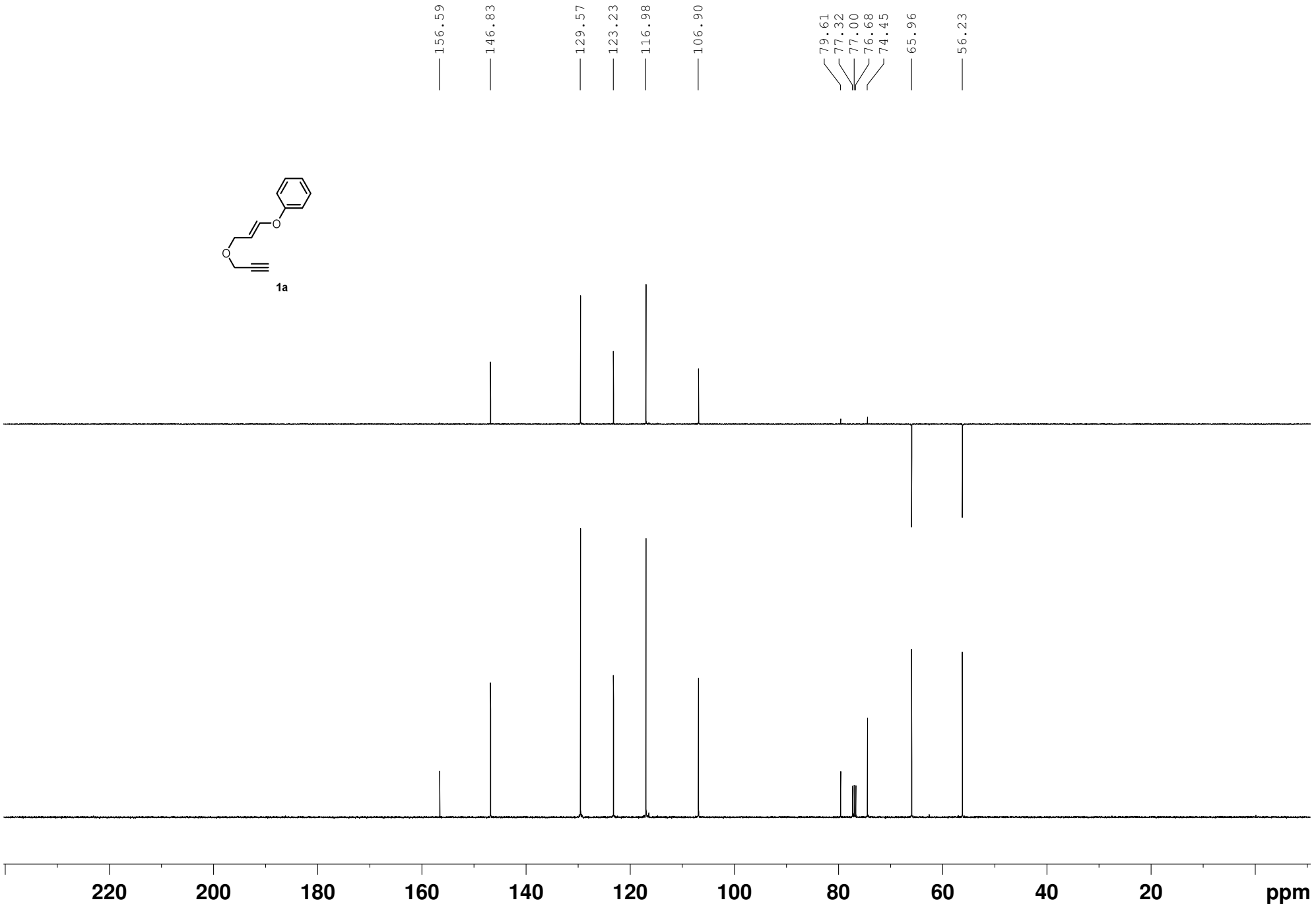

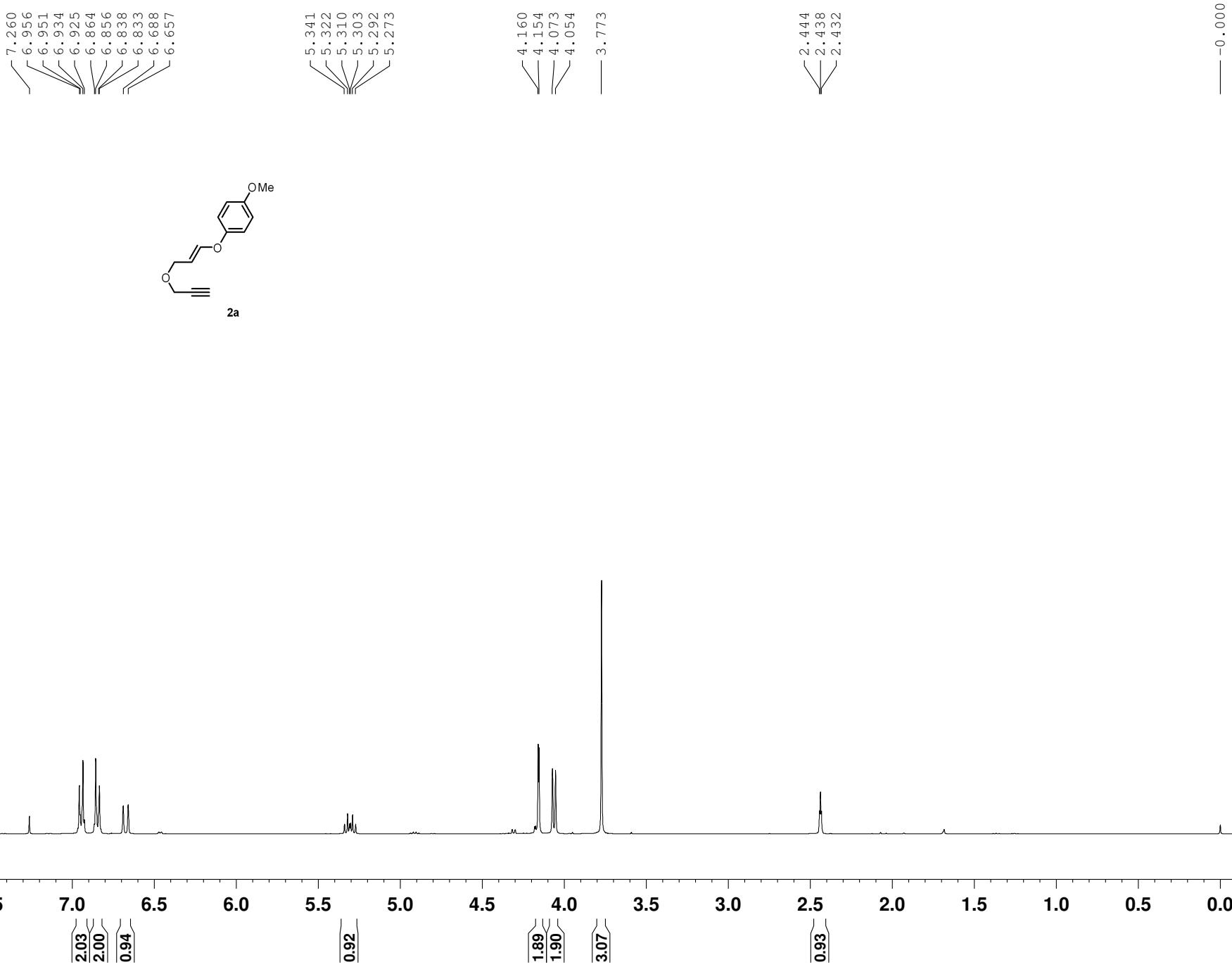

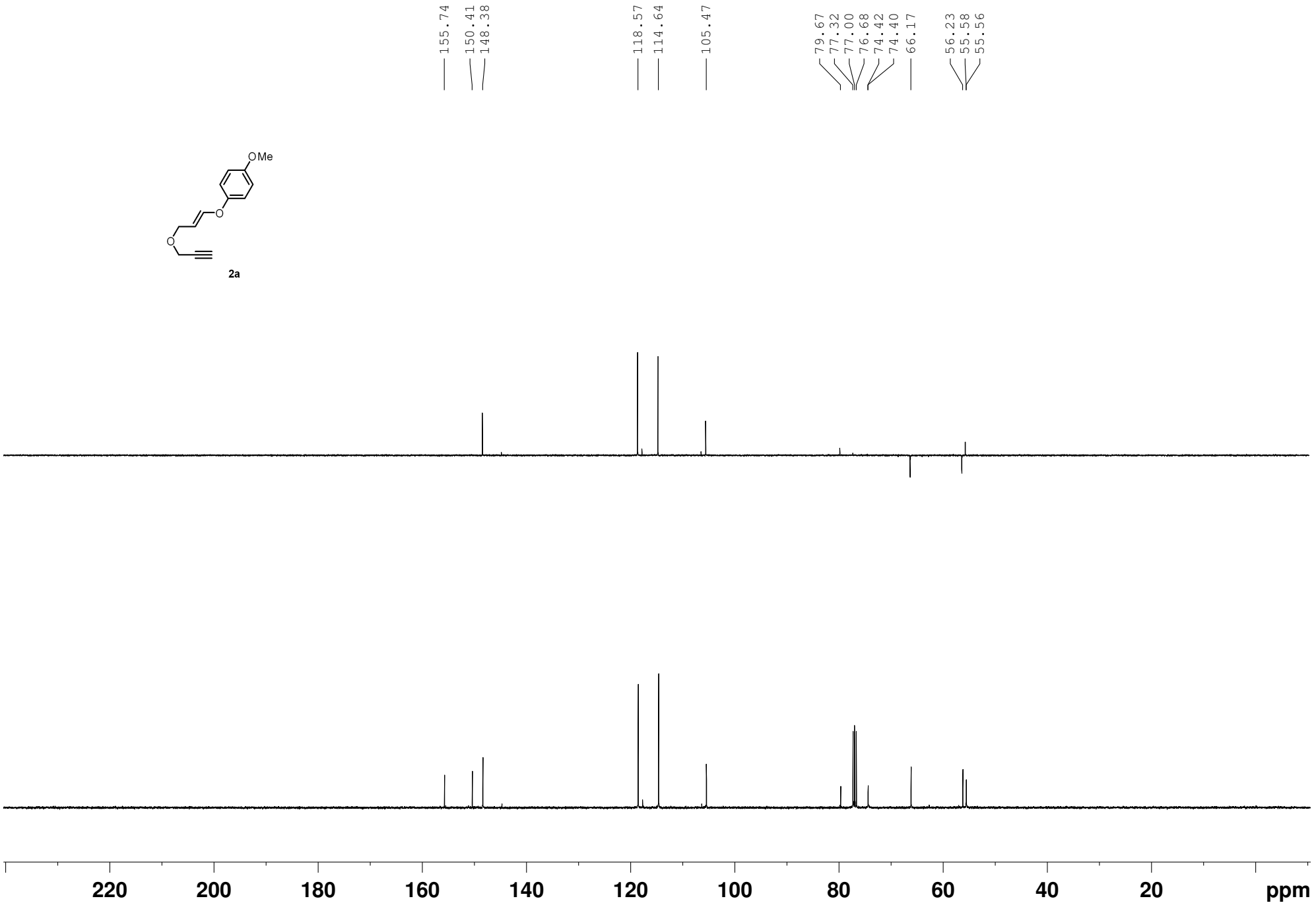

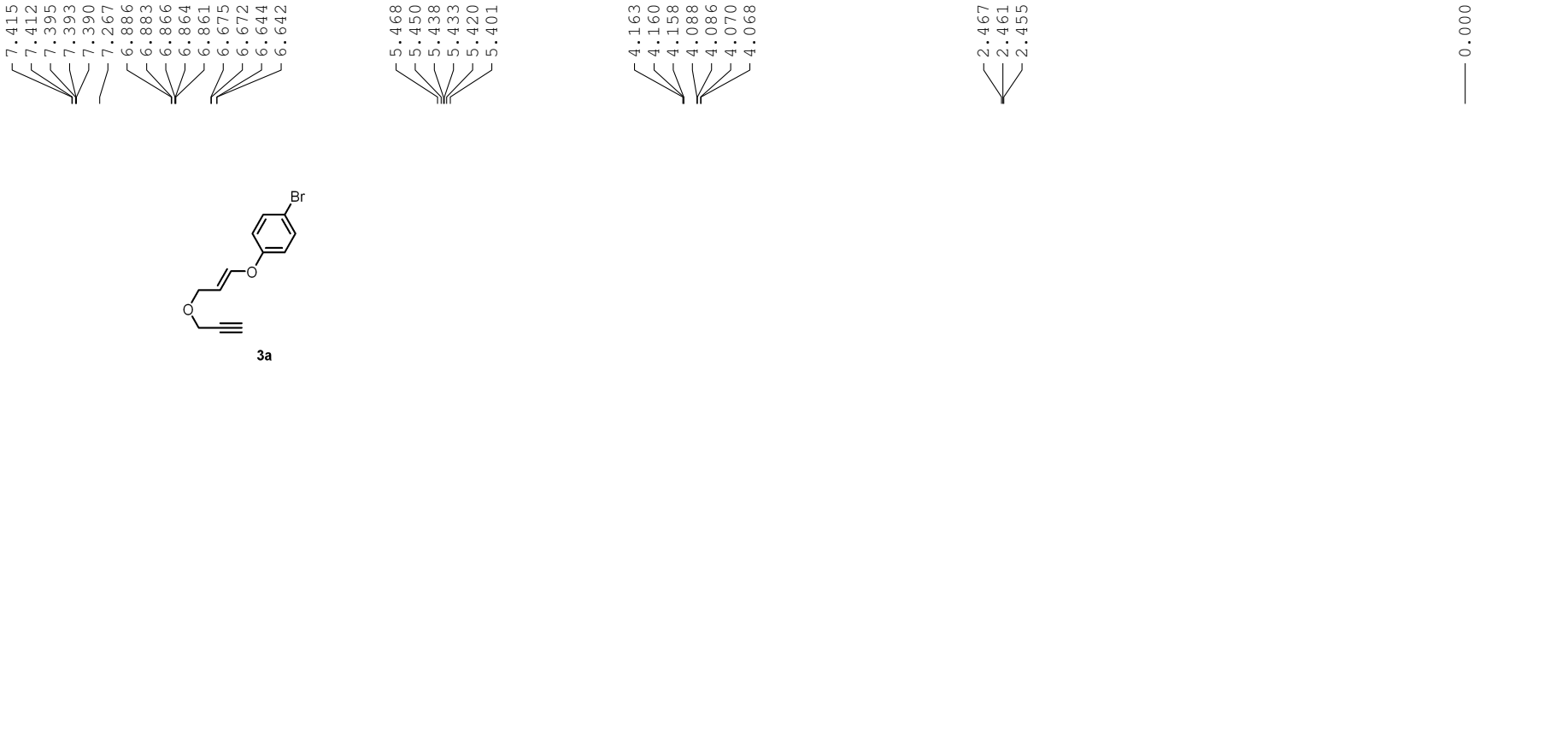

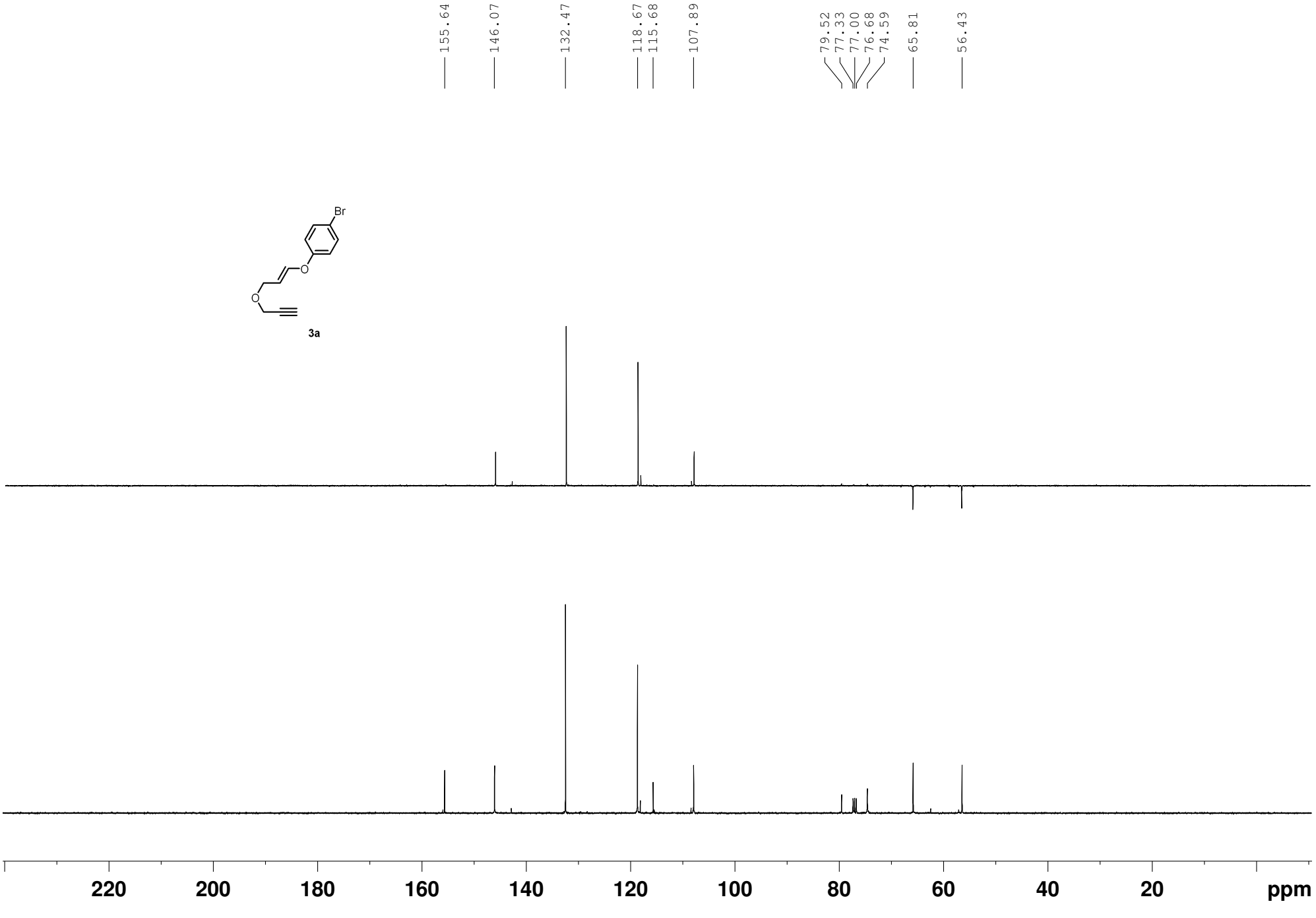

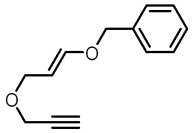

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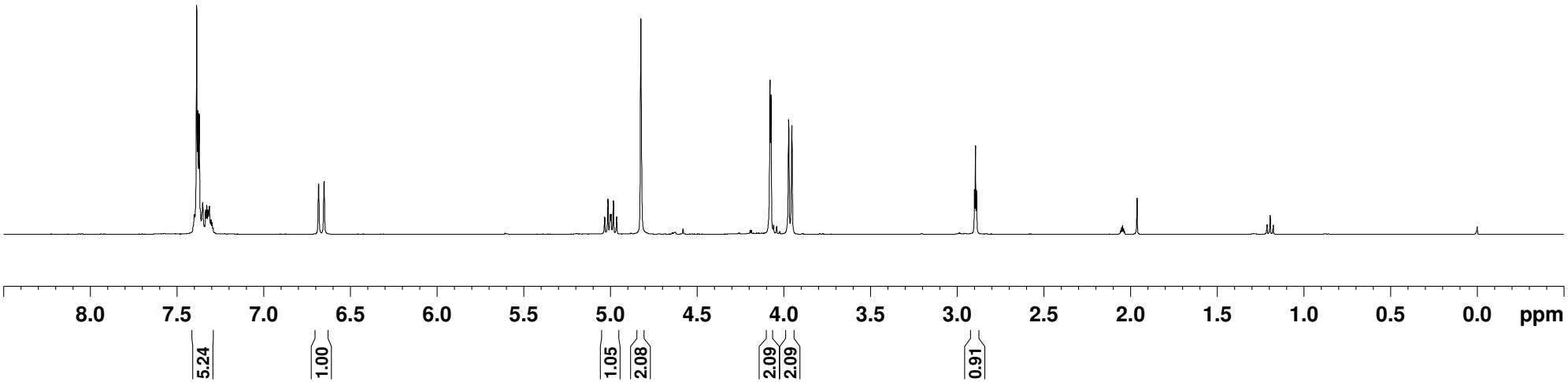

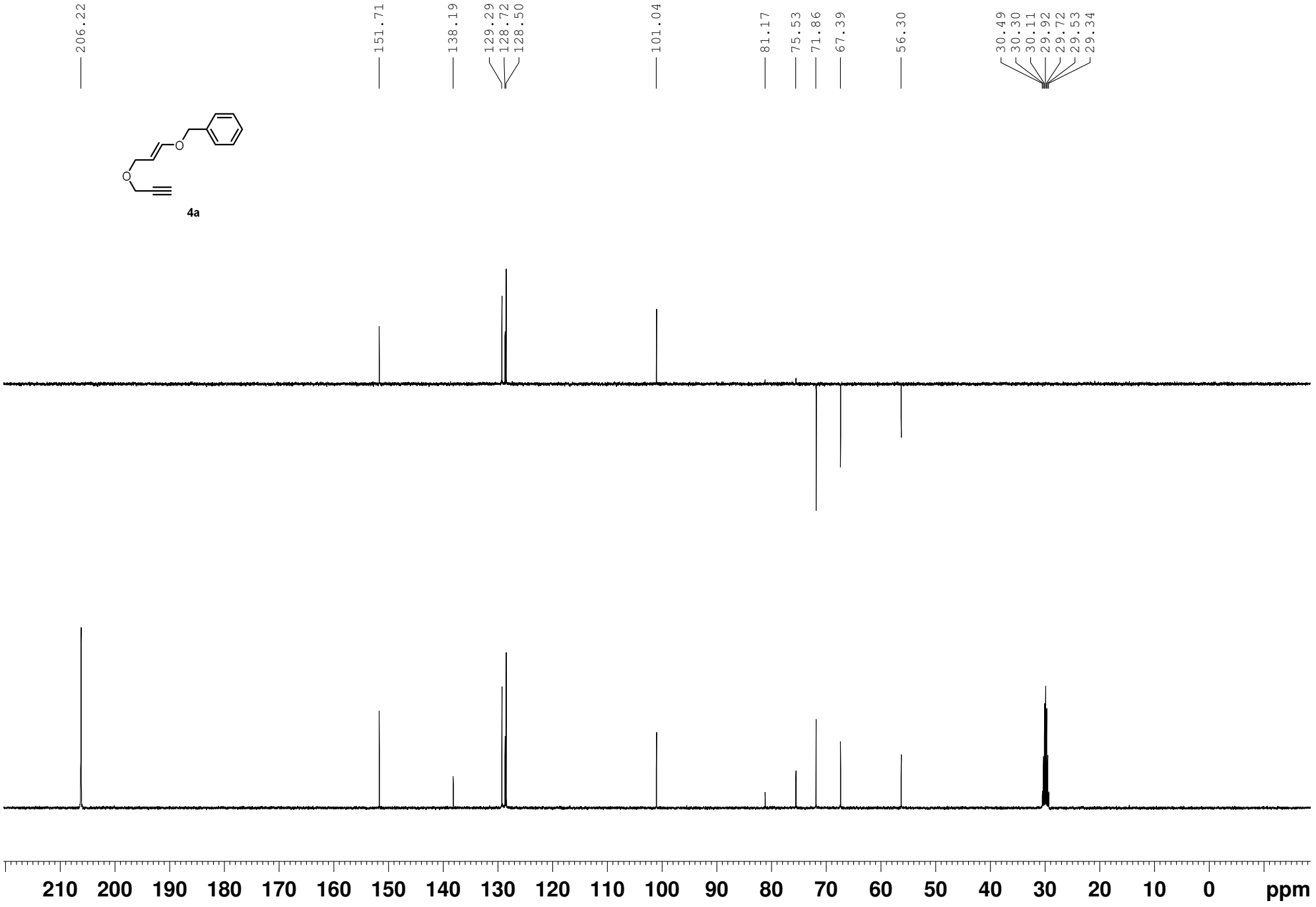

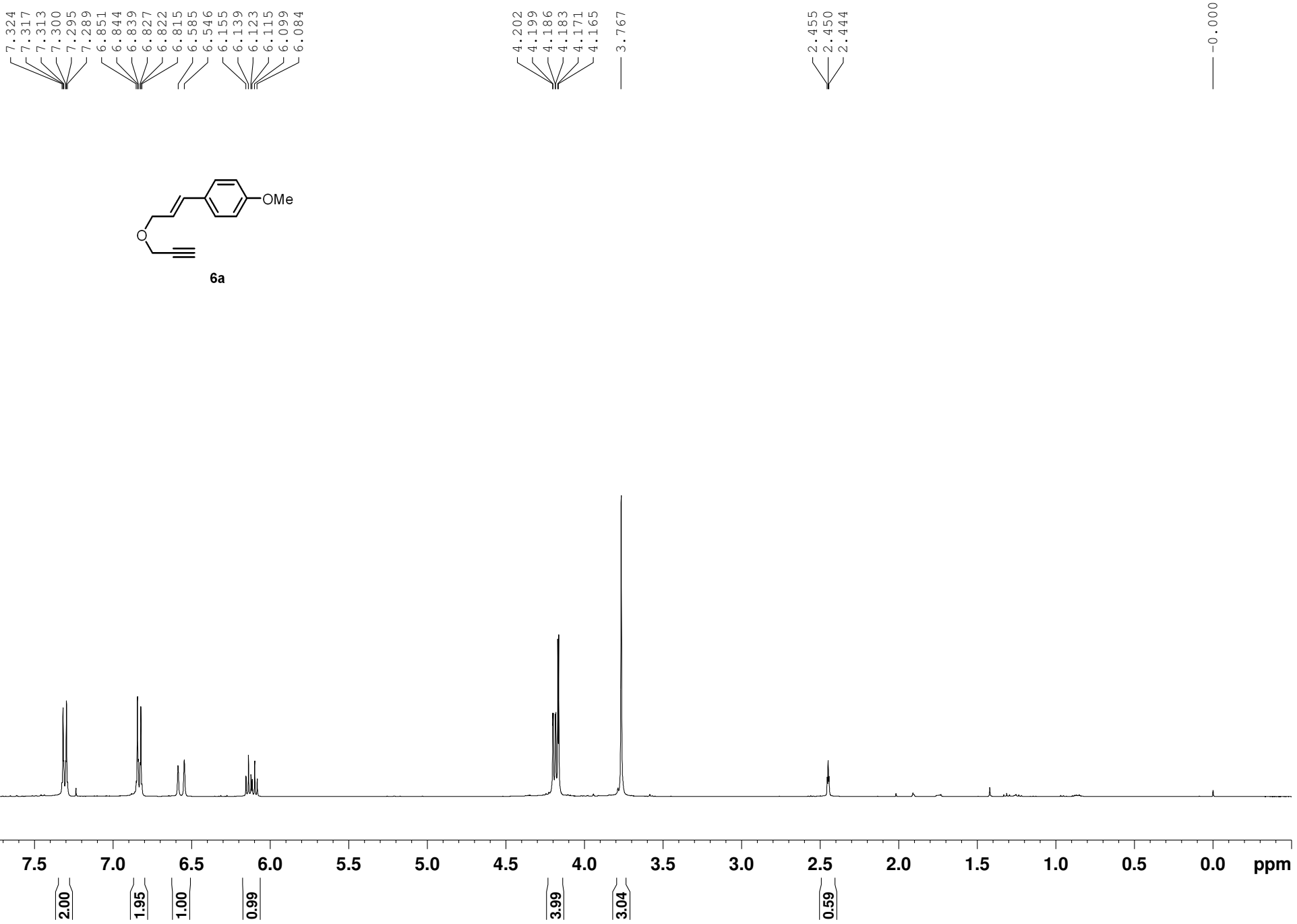

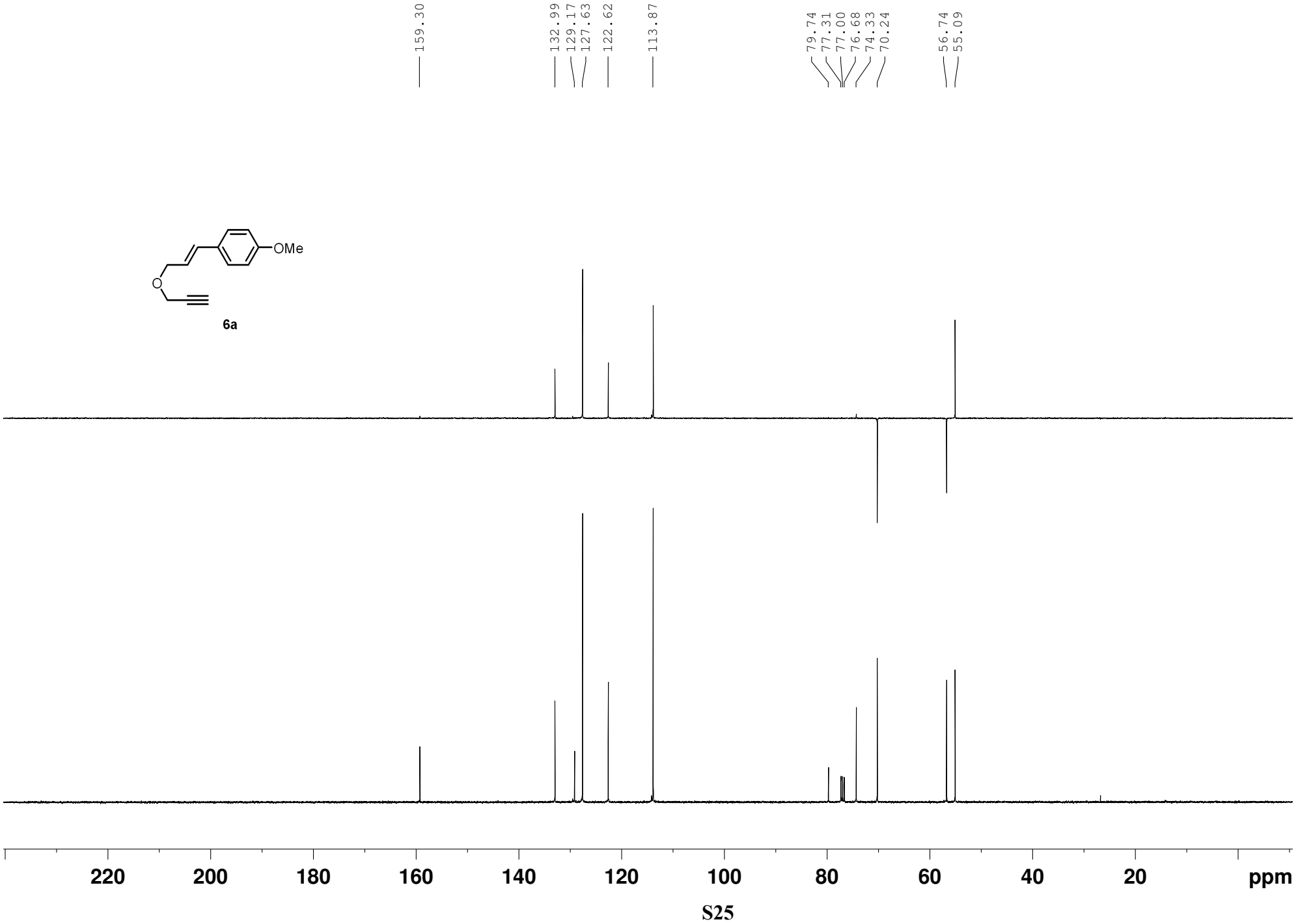

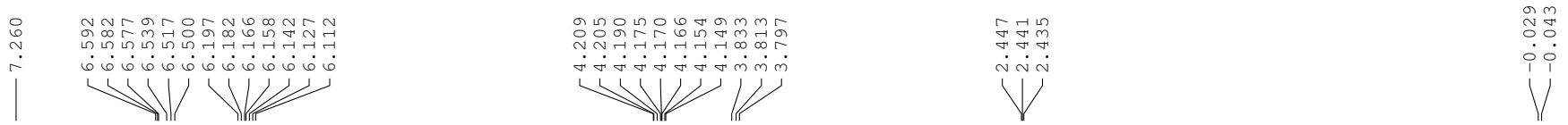

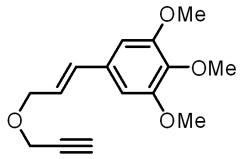

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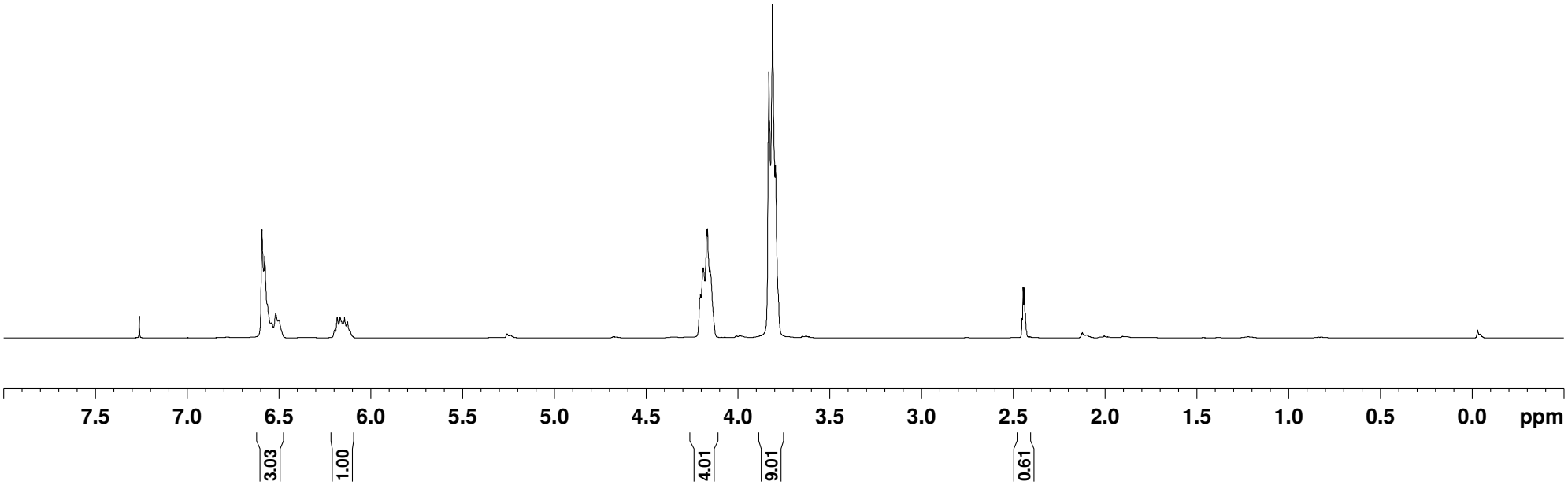
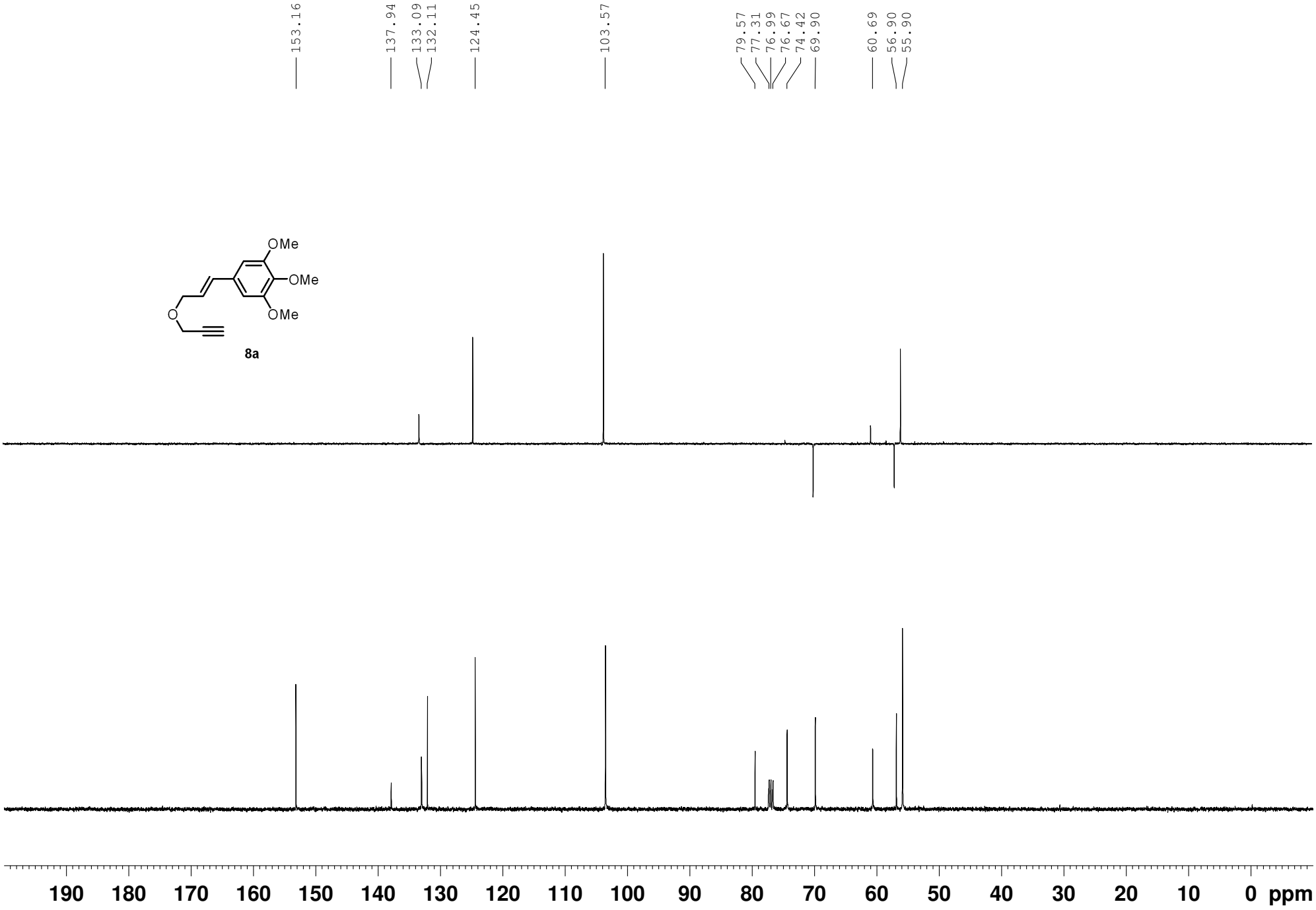
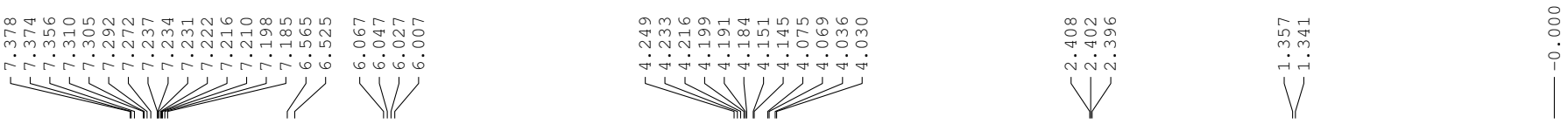
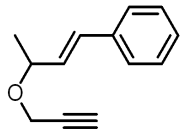
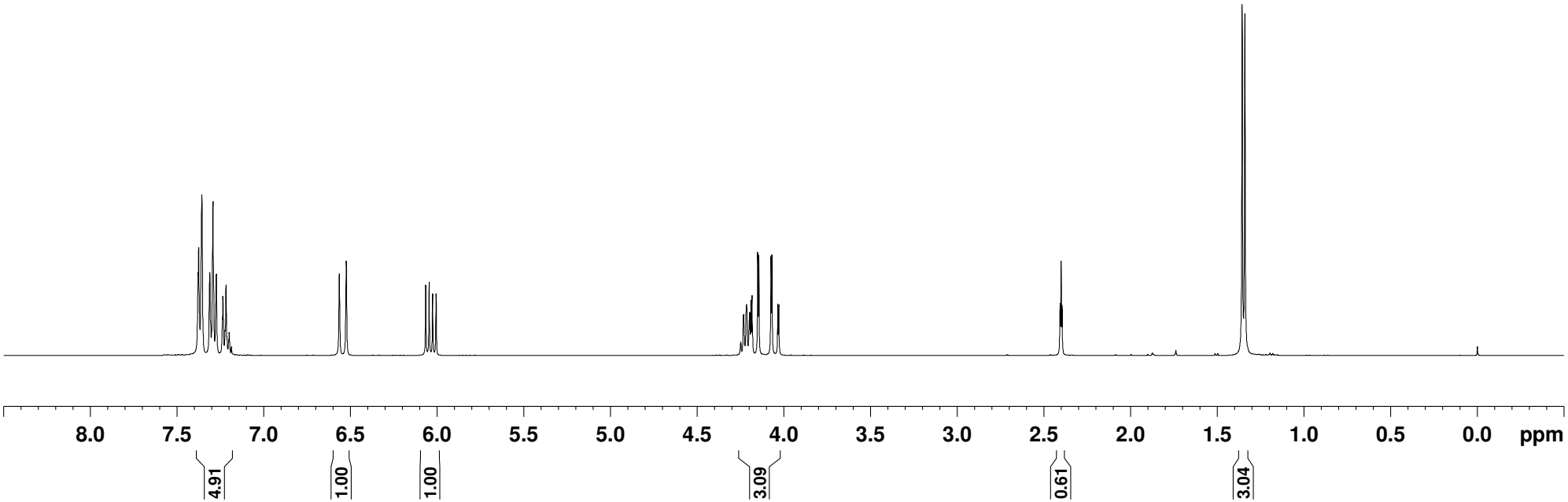


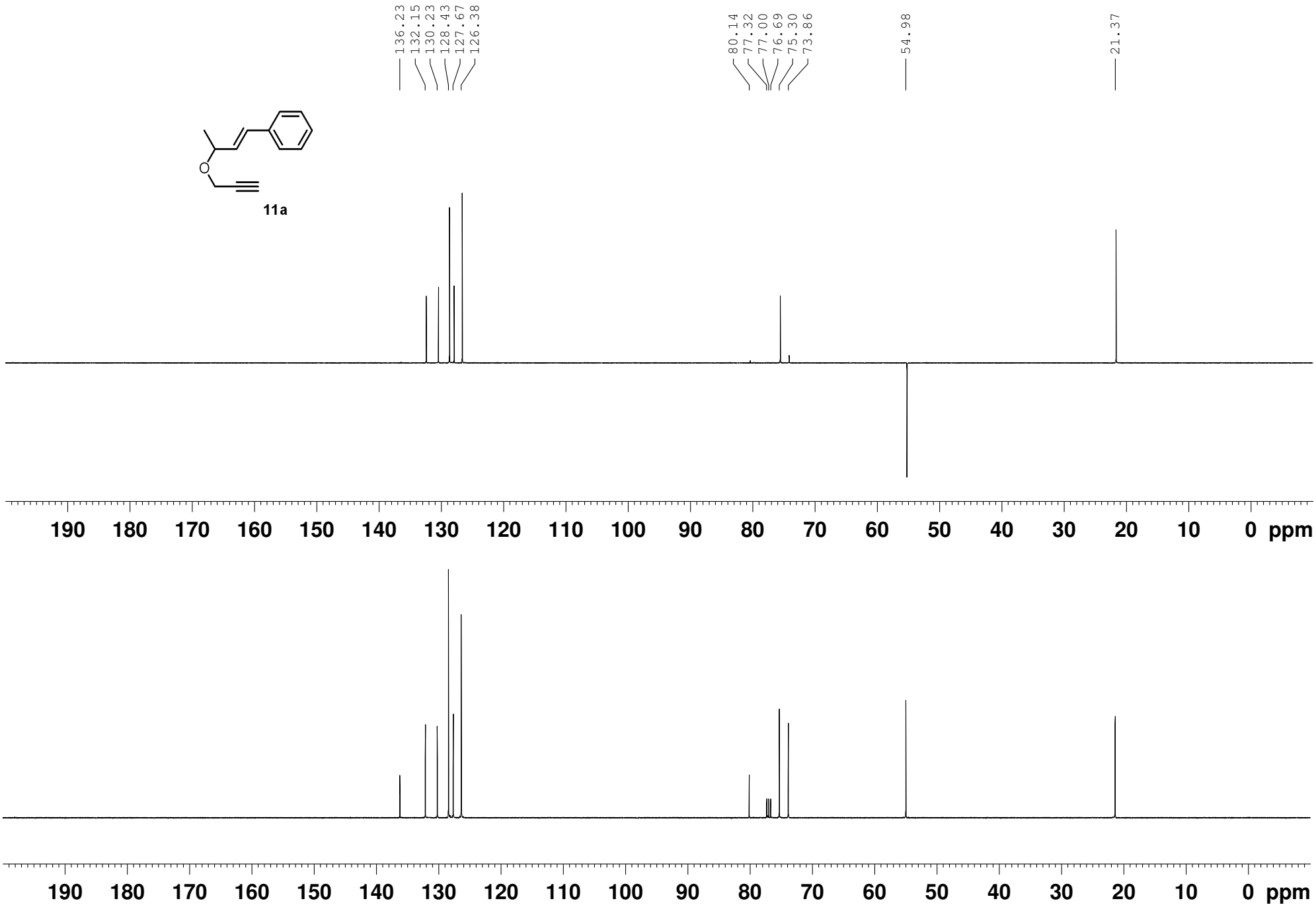


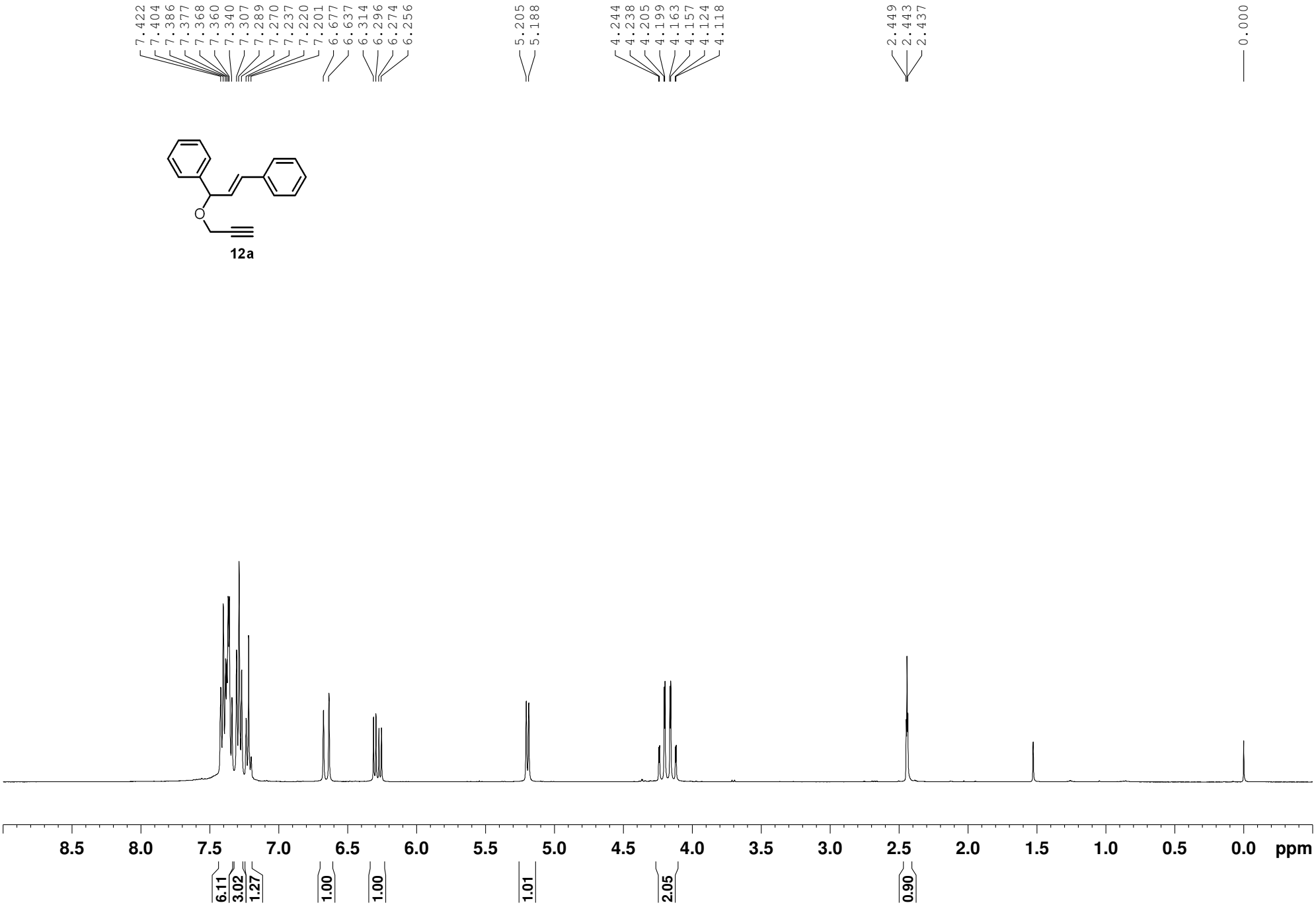


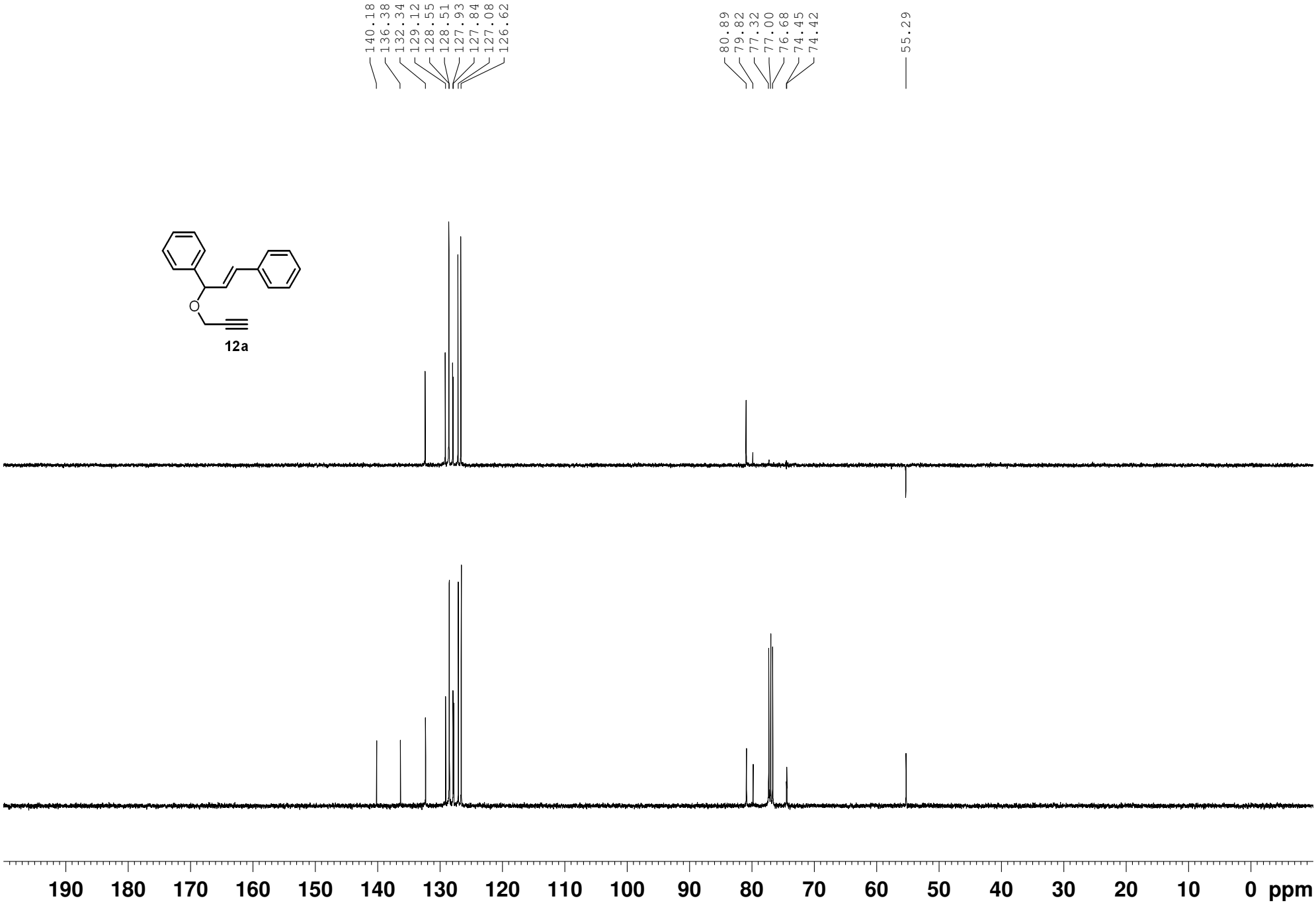


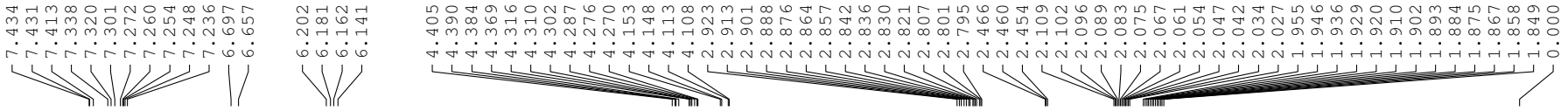
11a

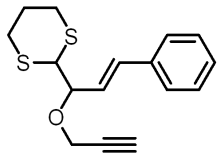




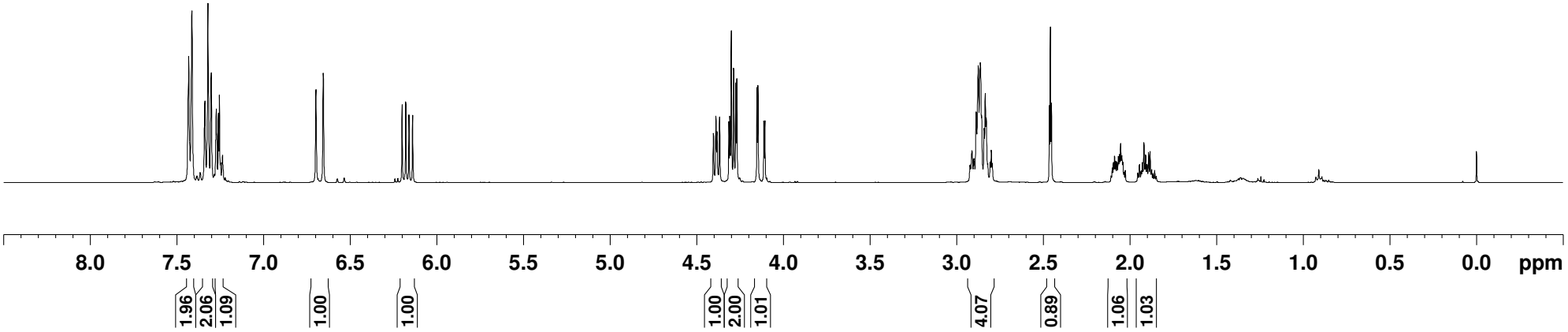


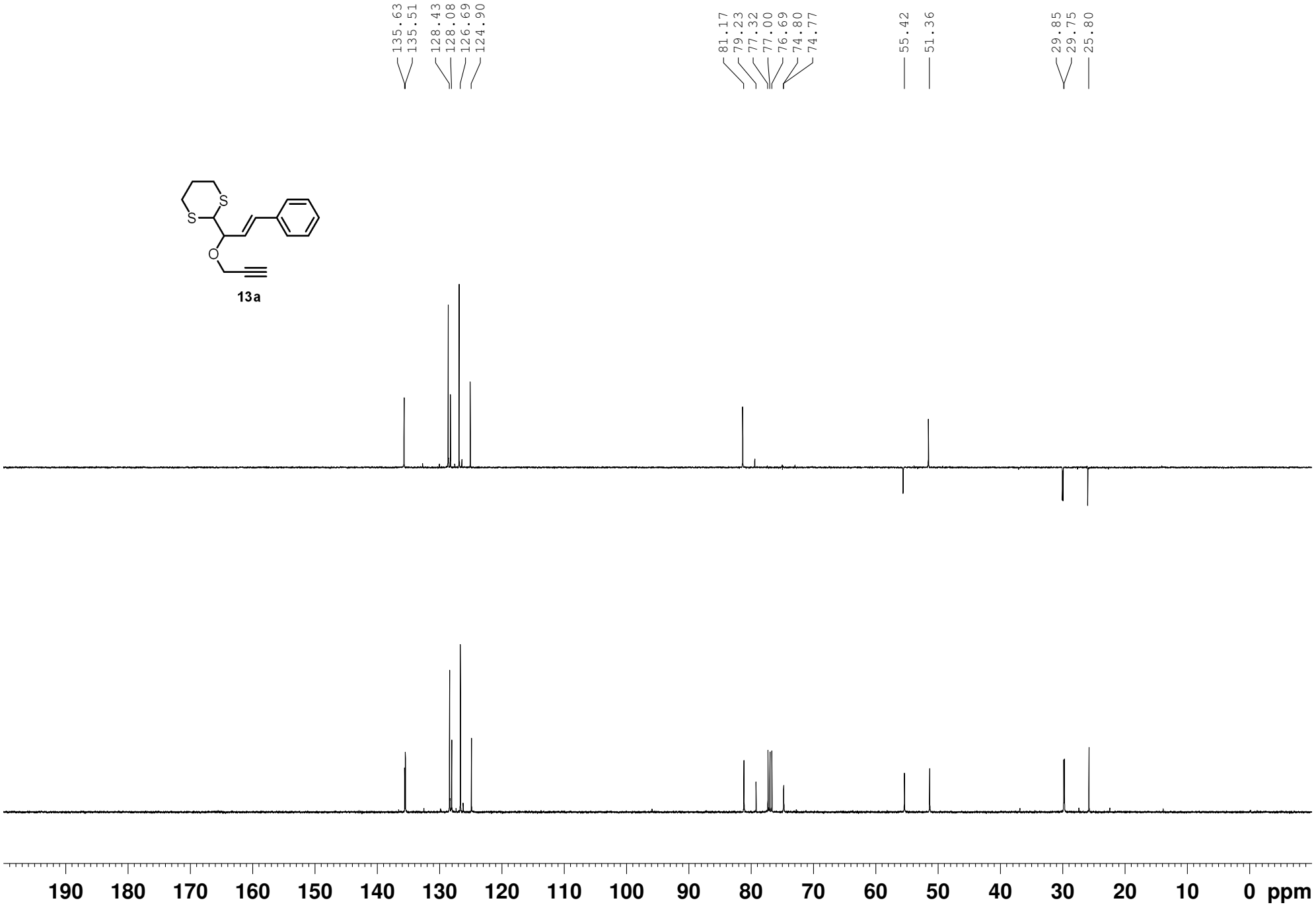


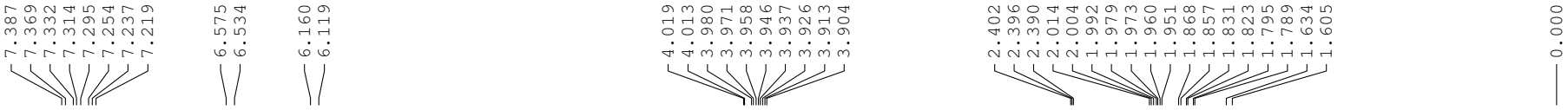


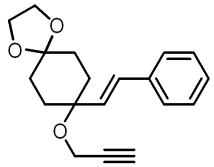


13a









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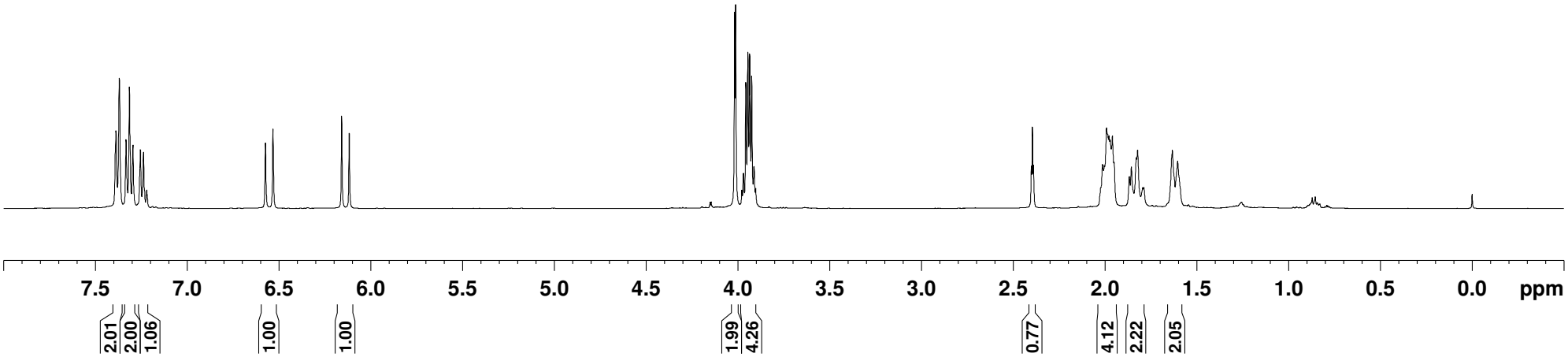

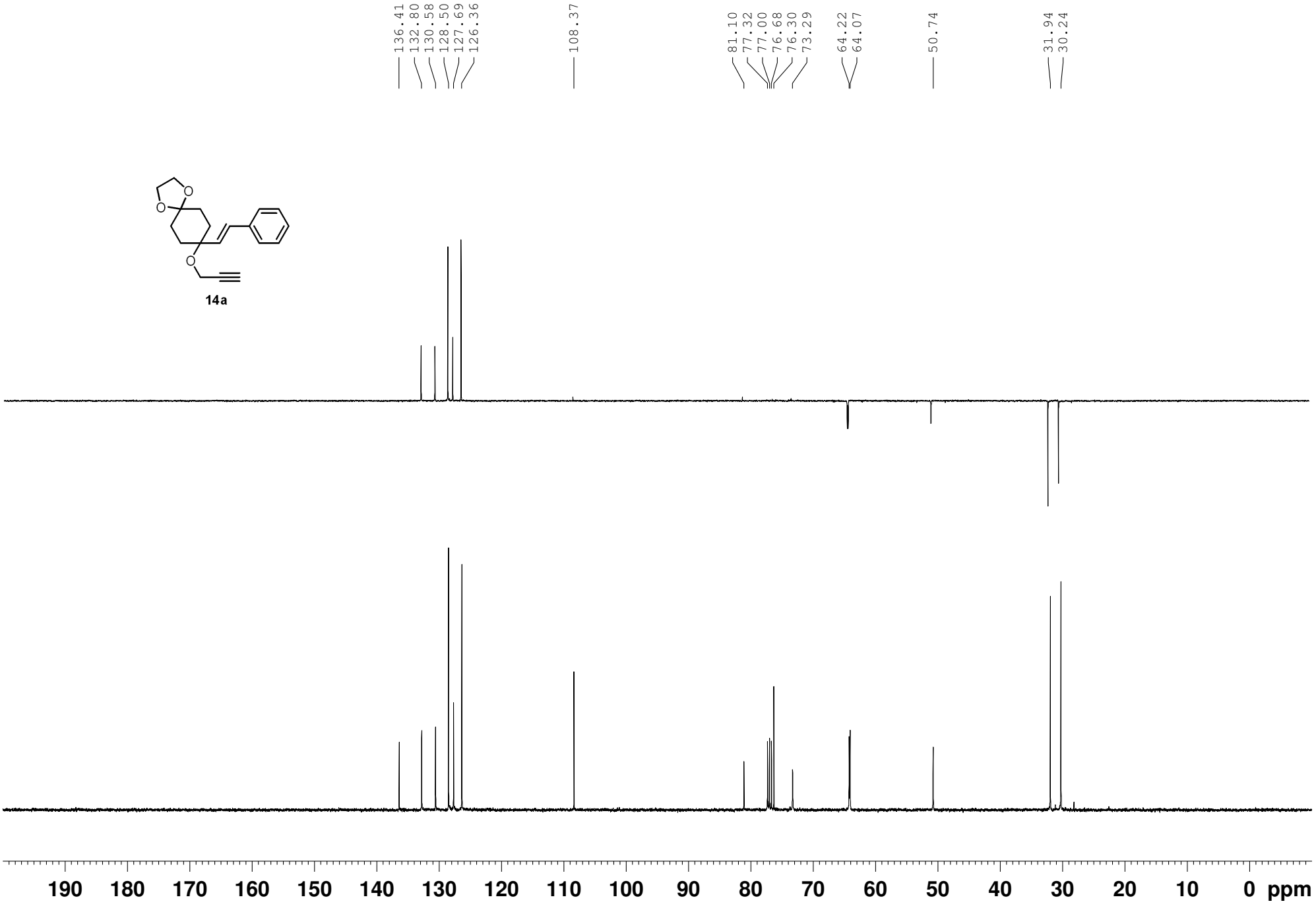

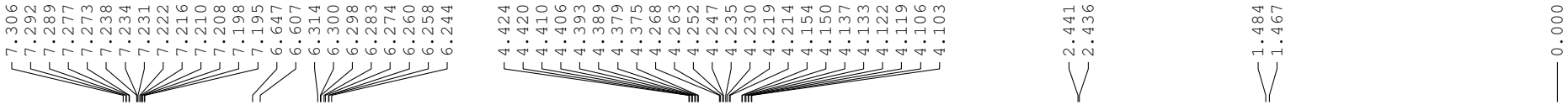
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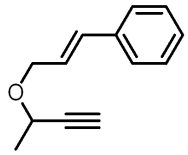

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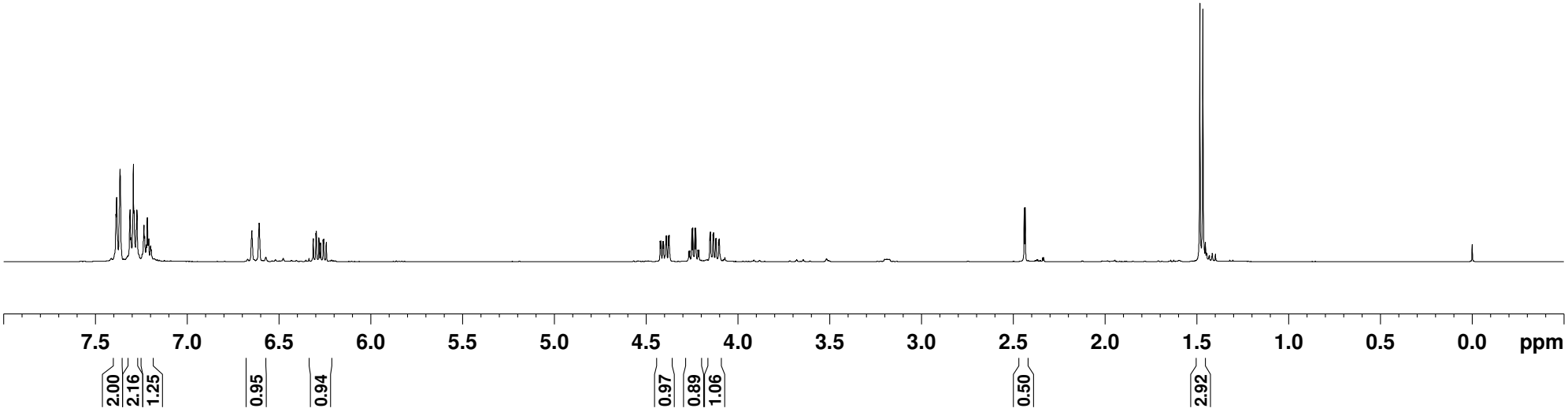
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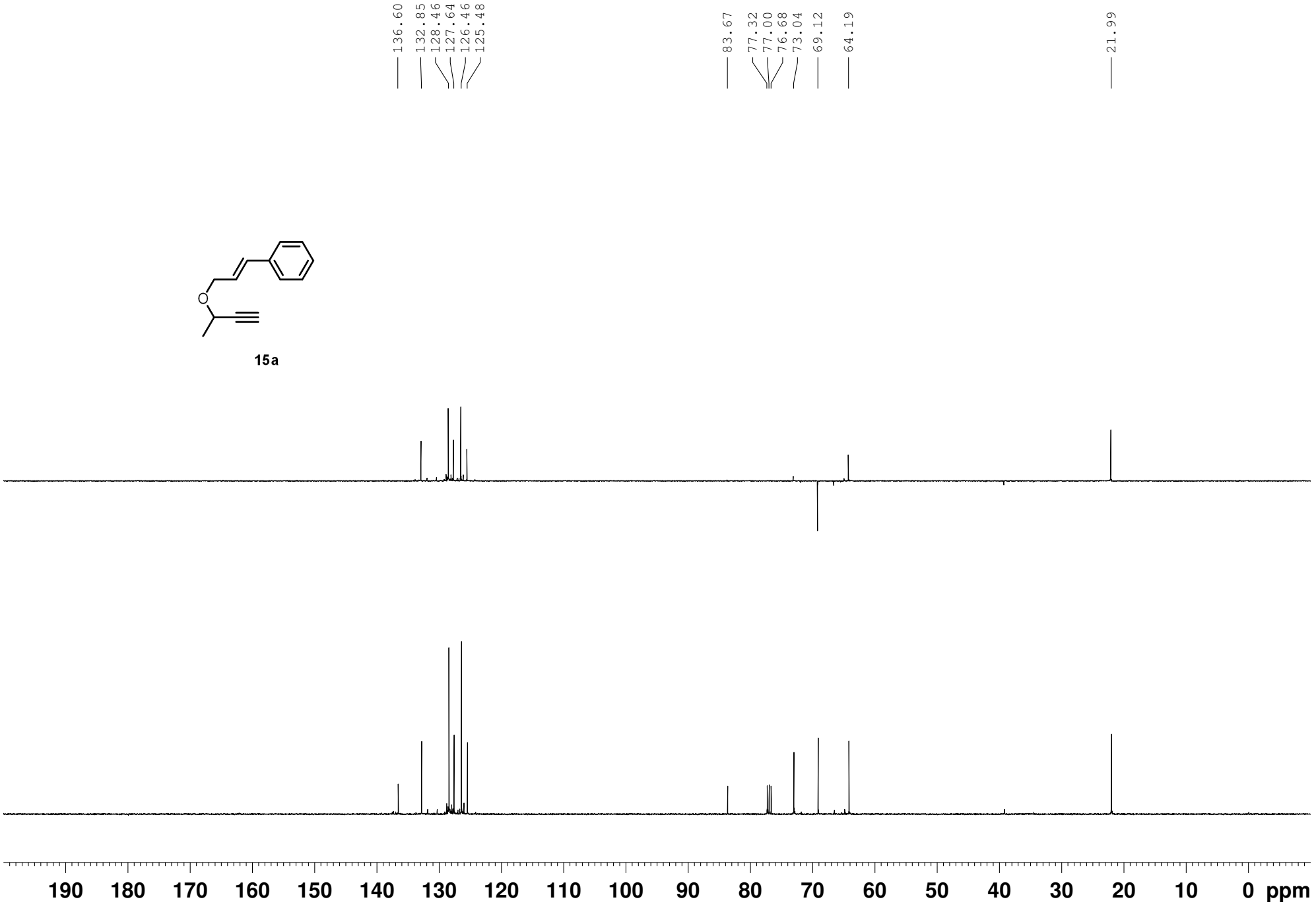

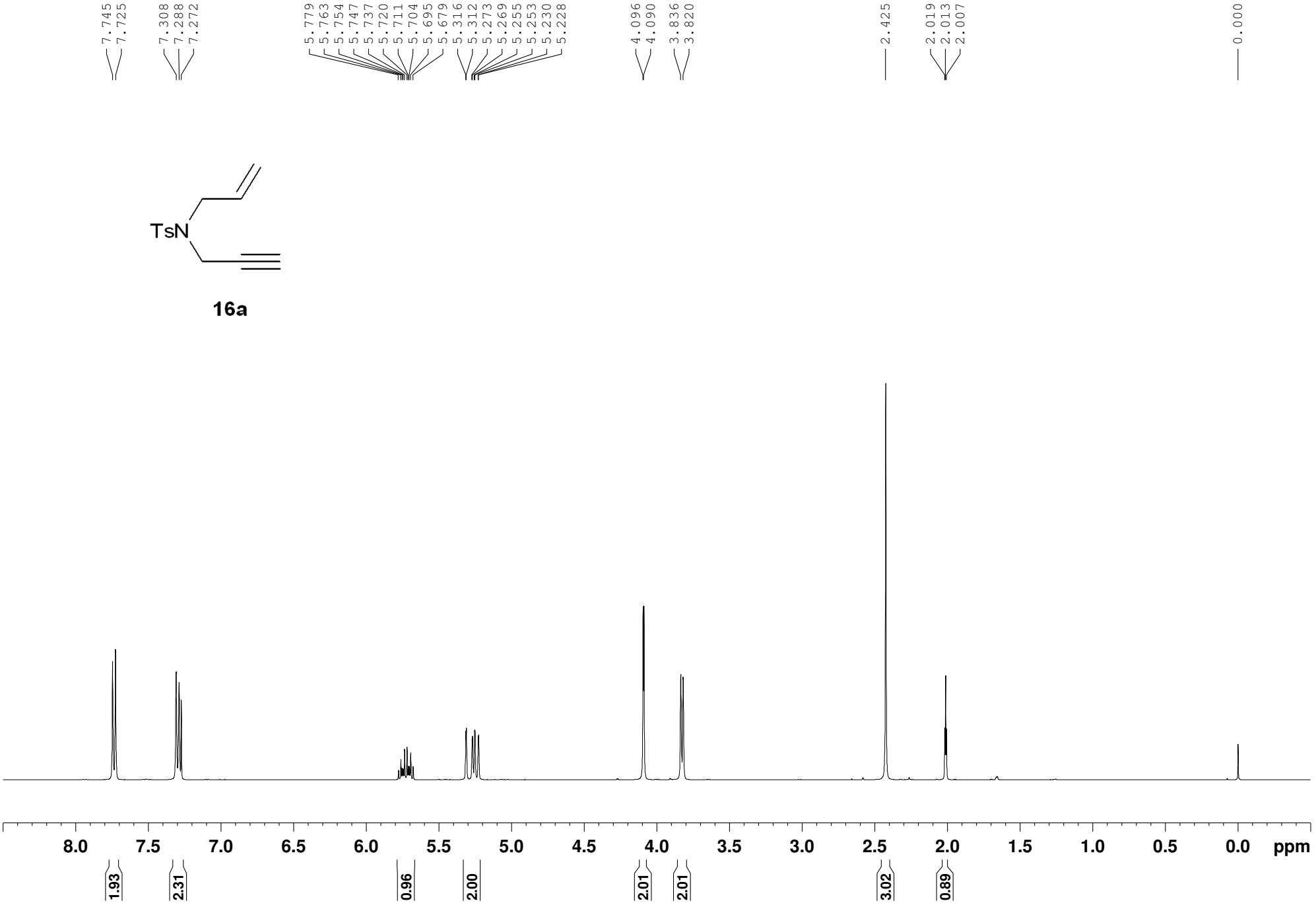

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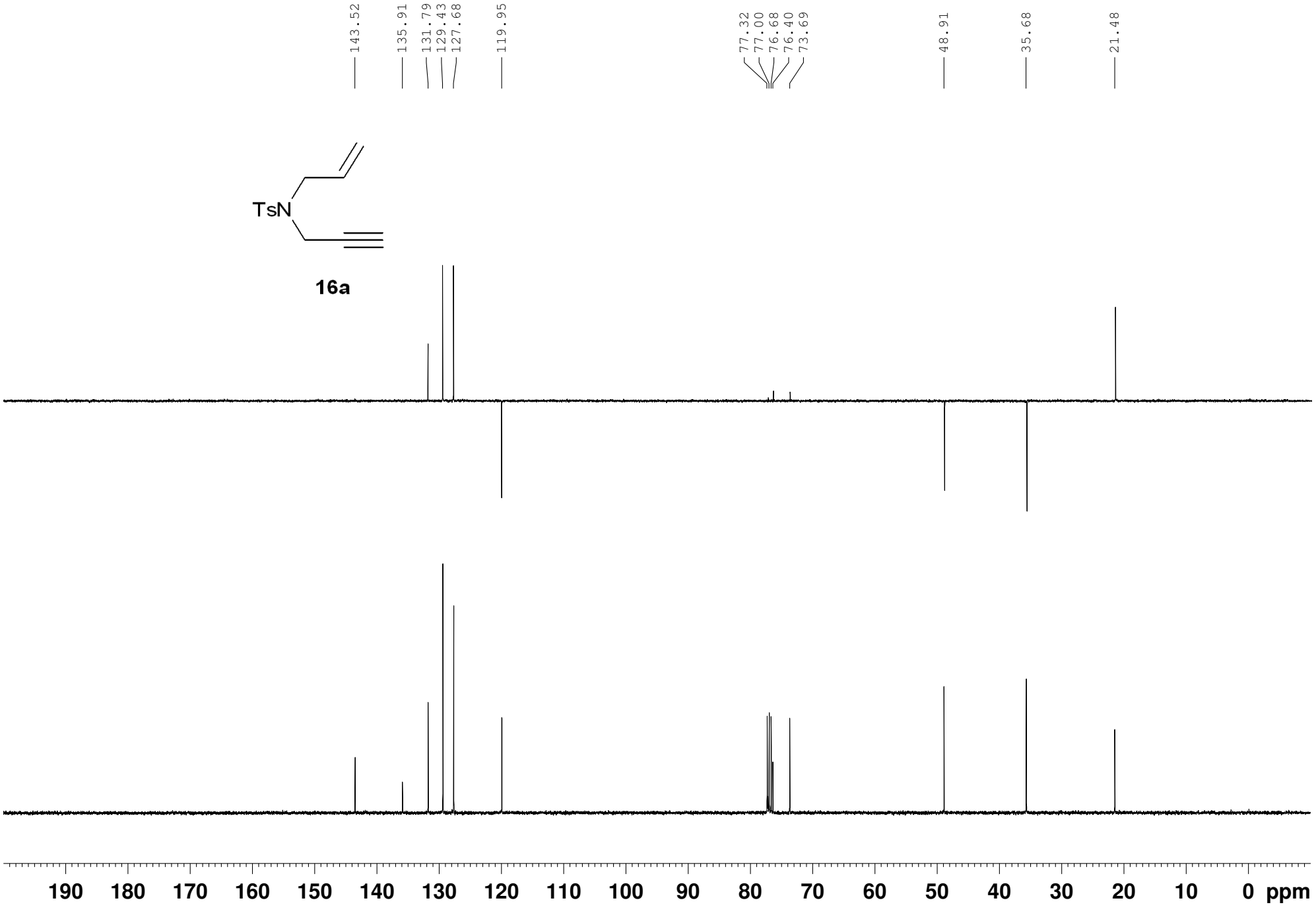

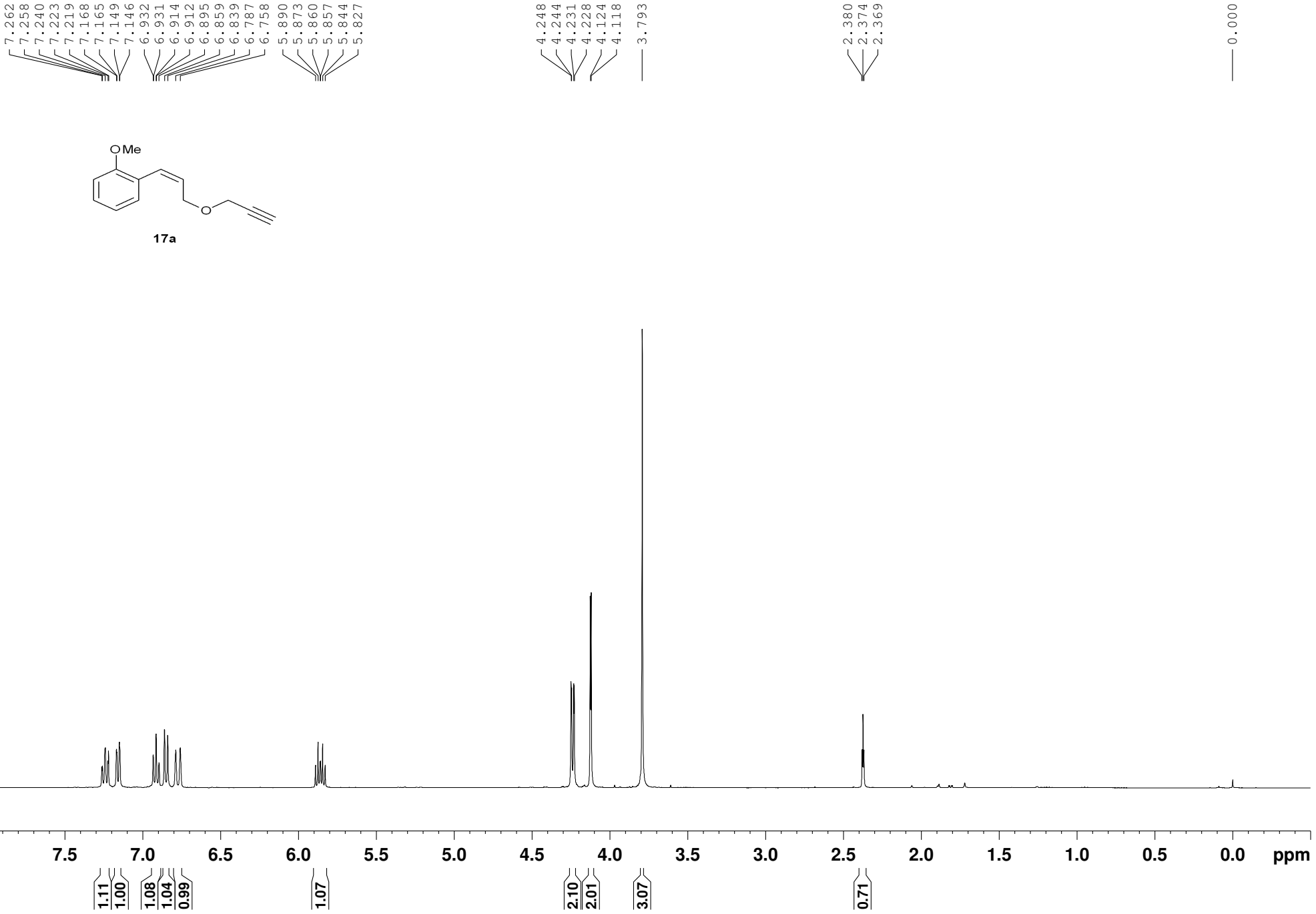
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OMe
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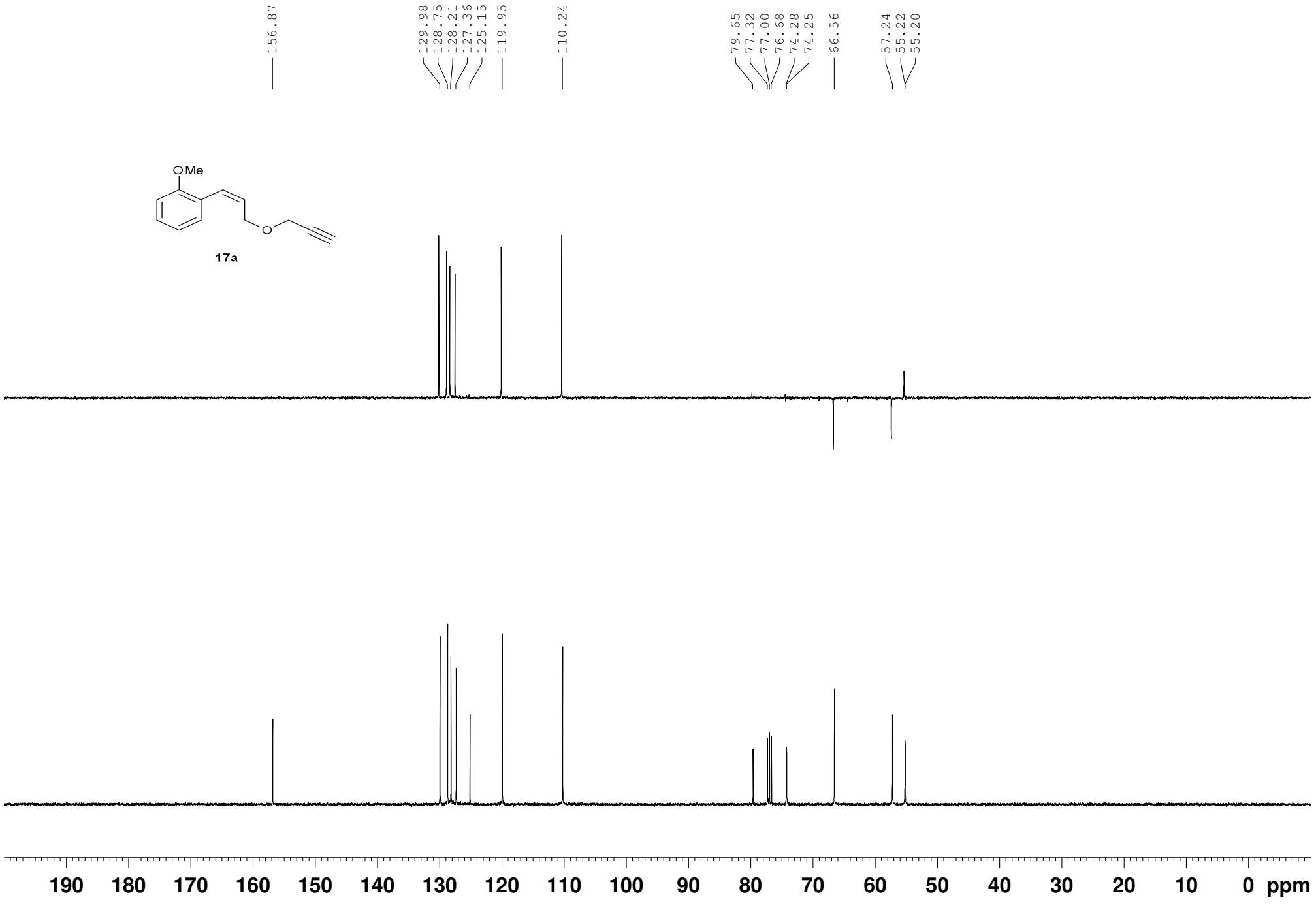

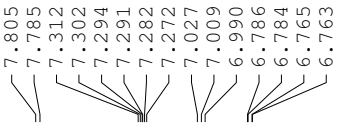

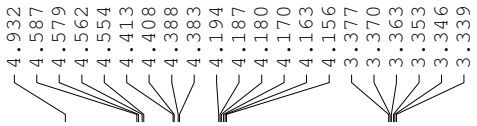

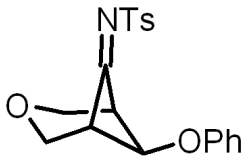

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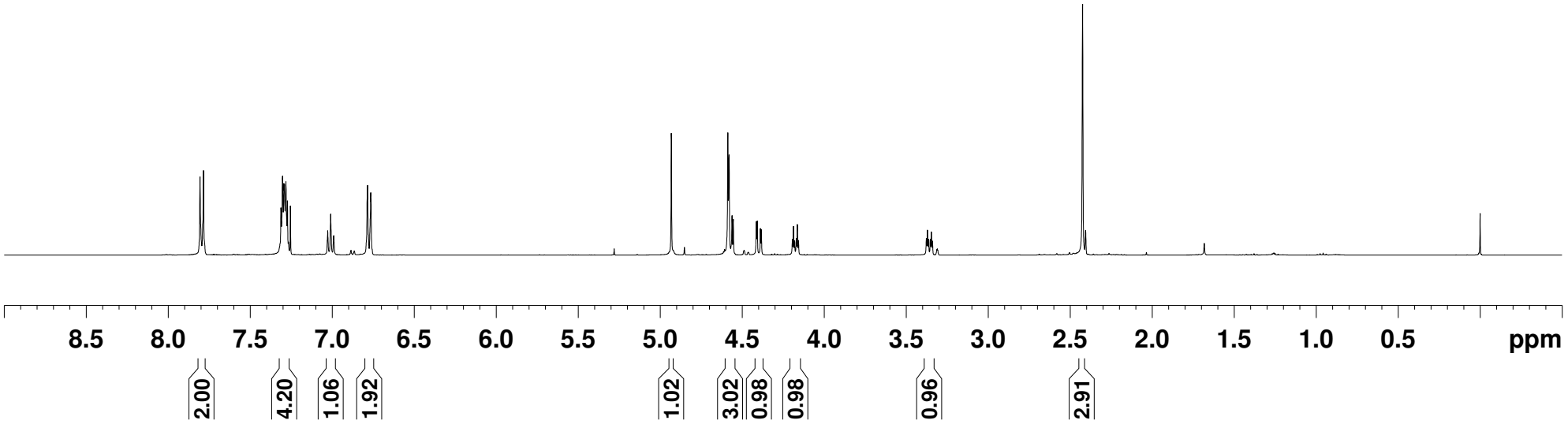

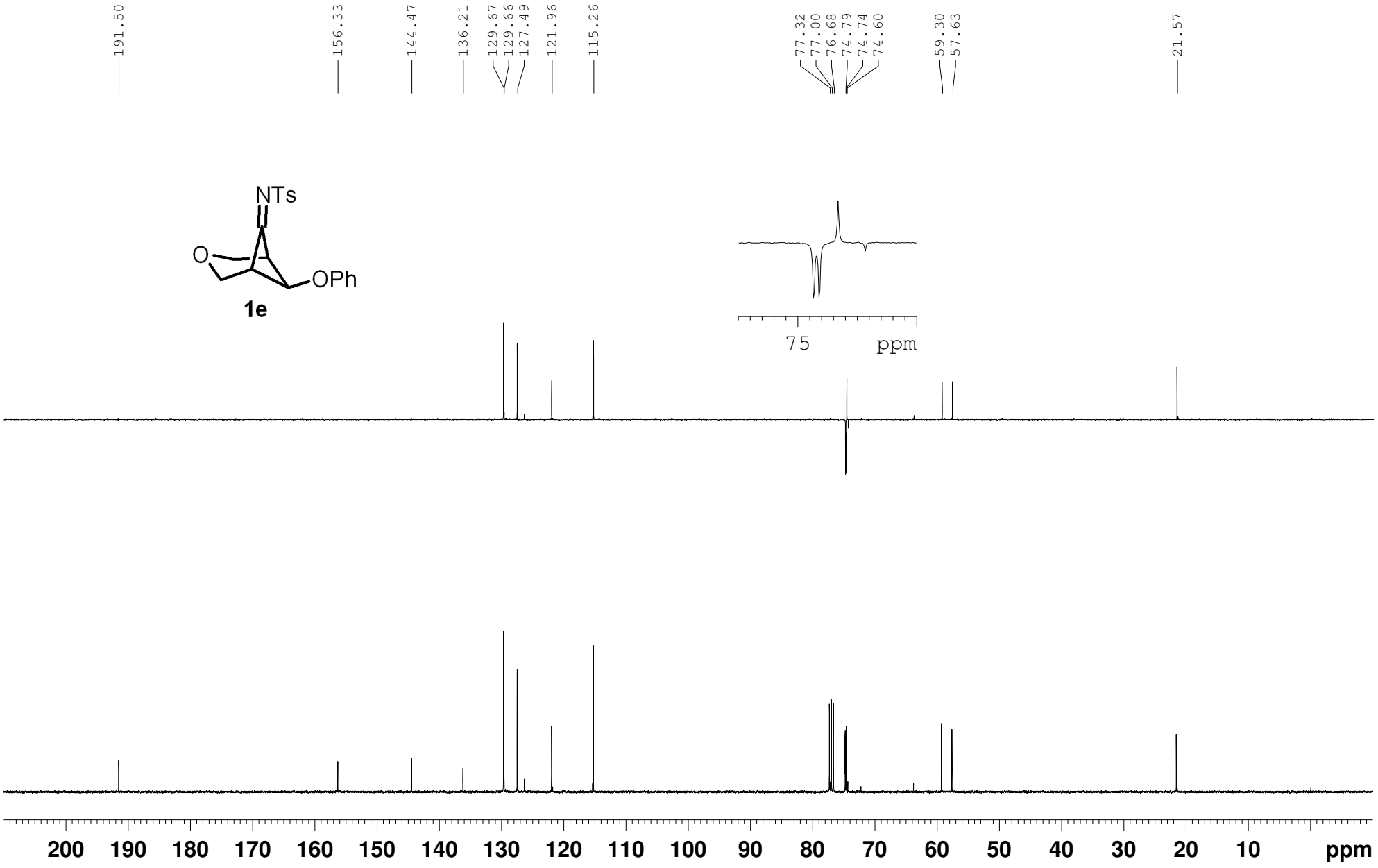

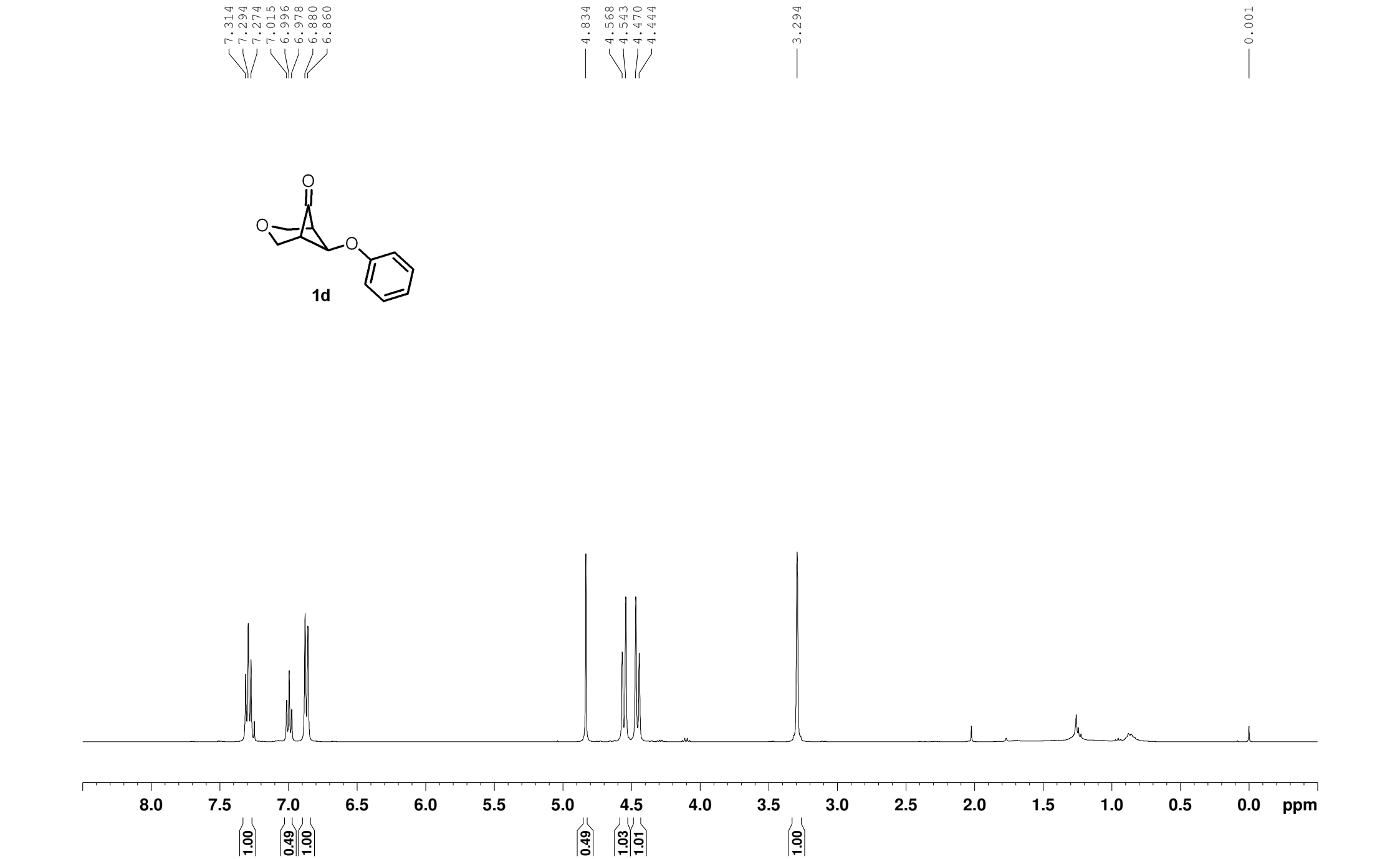

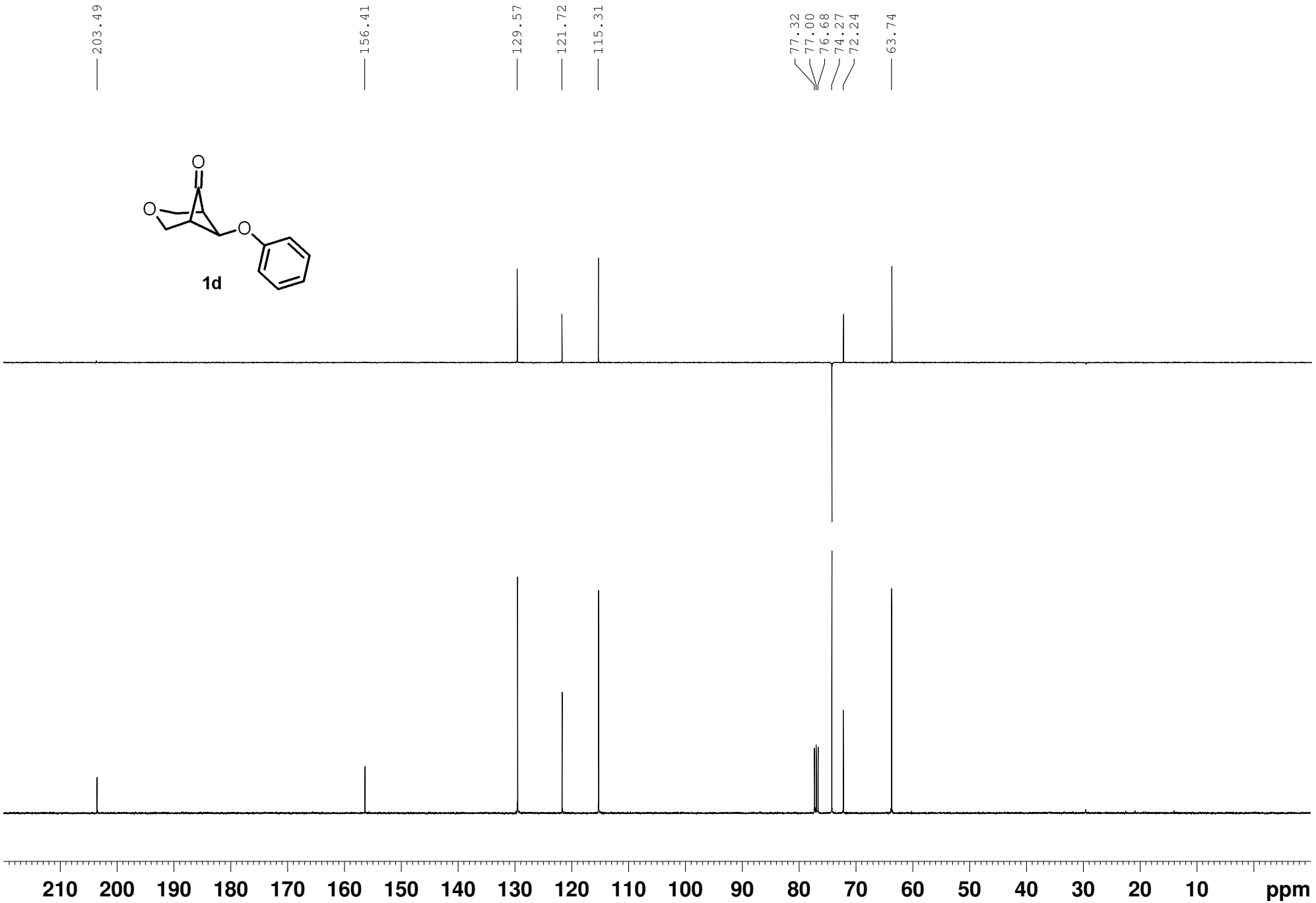

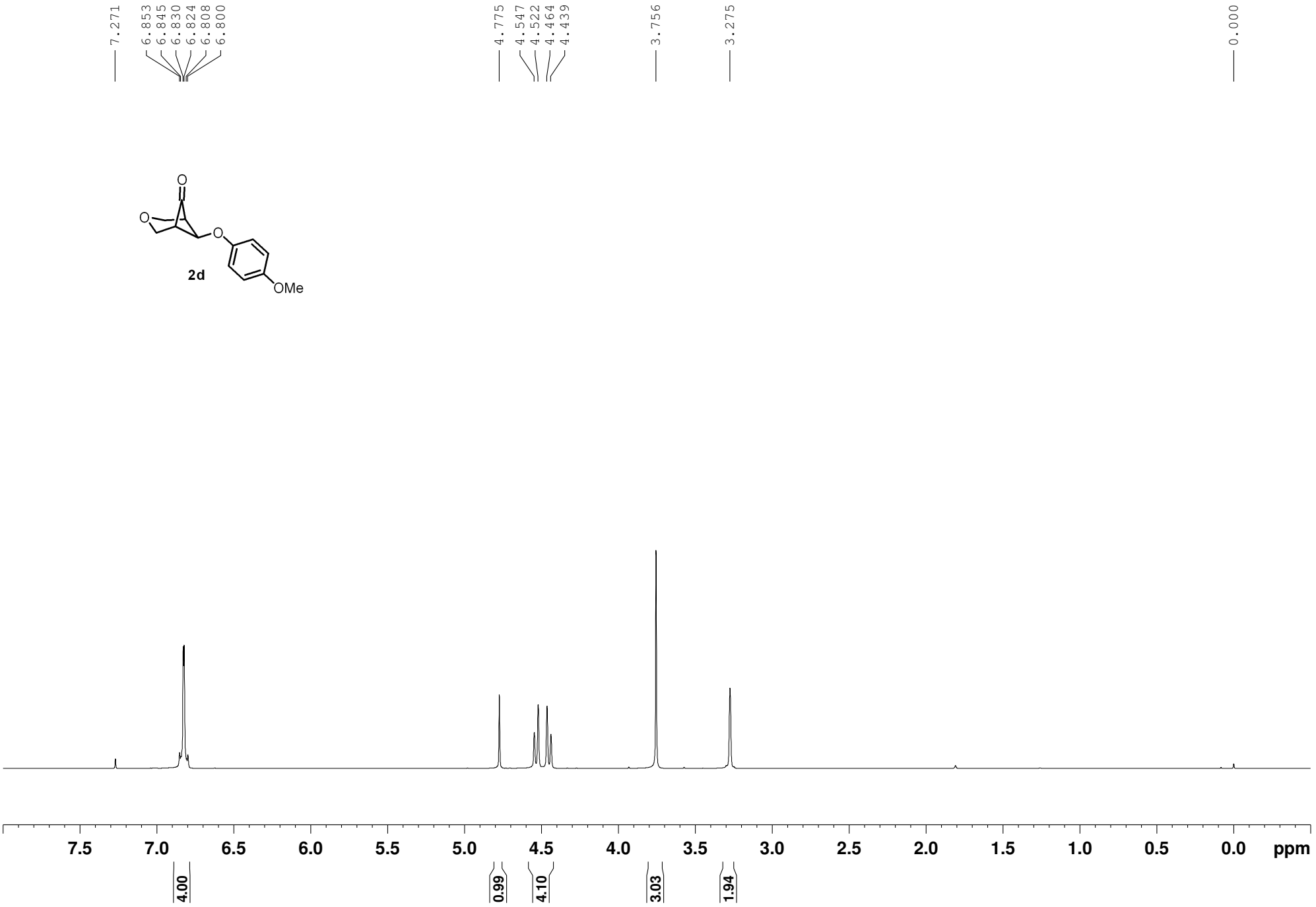

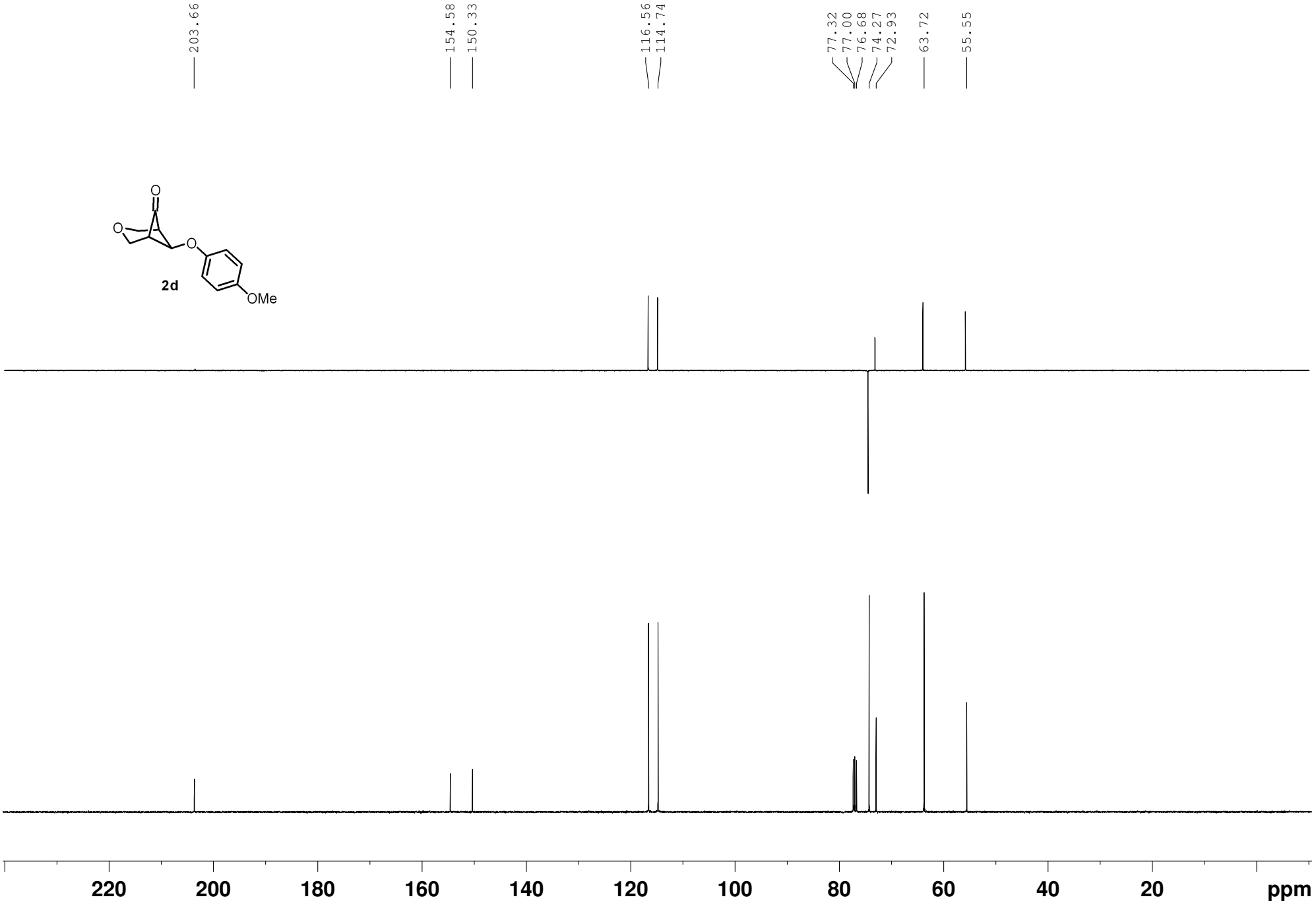

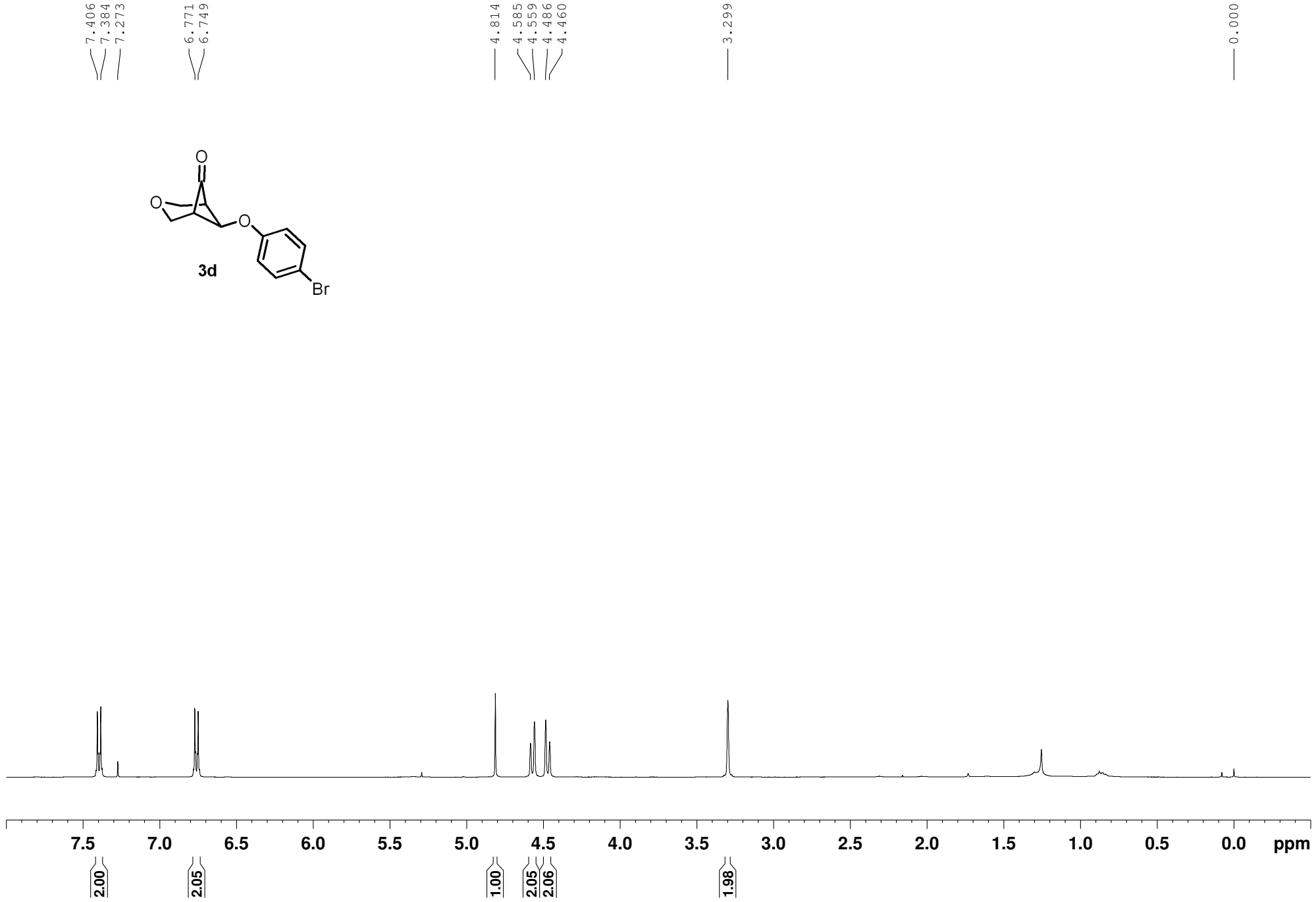
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O
Br
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6.5
6.0
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5.0
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3.0
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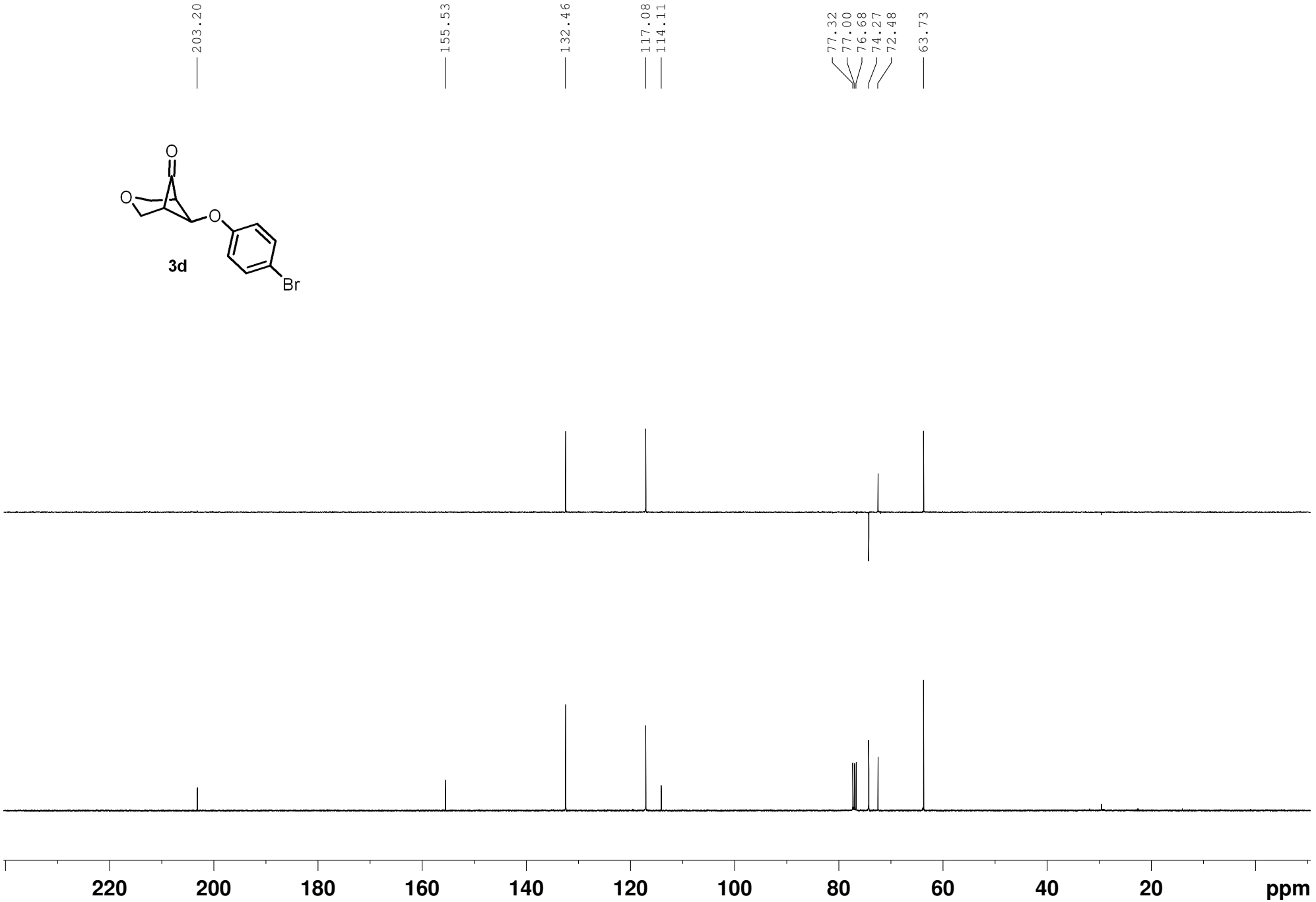
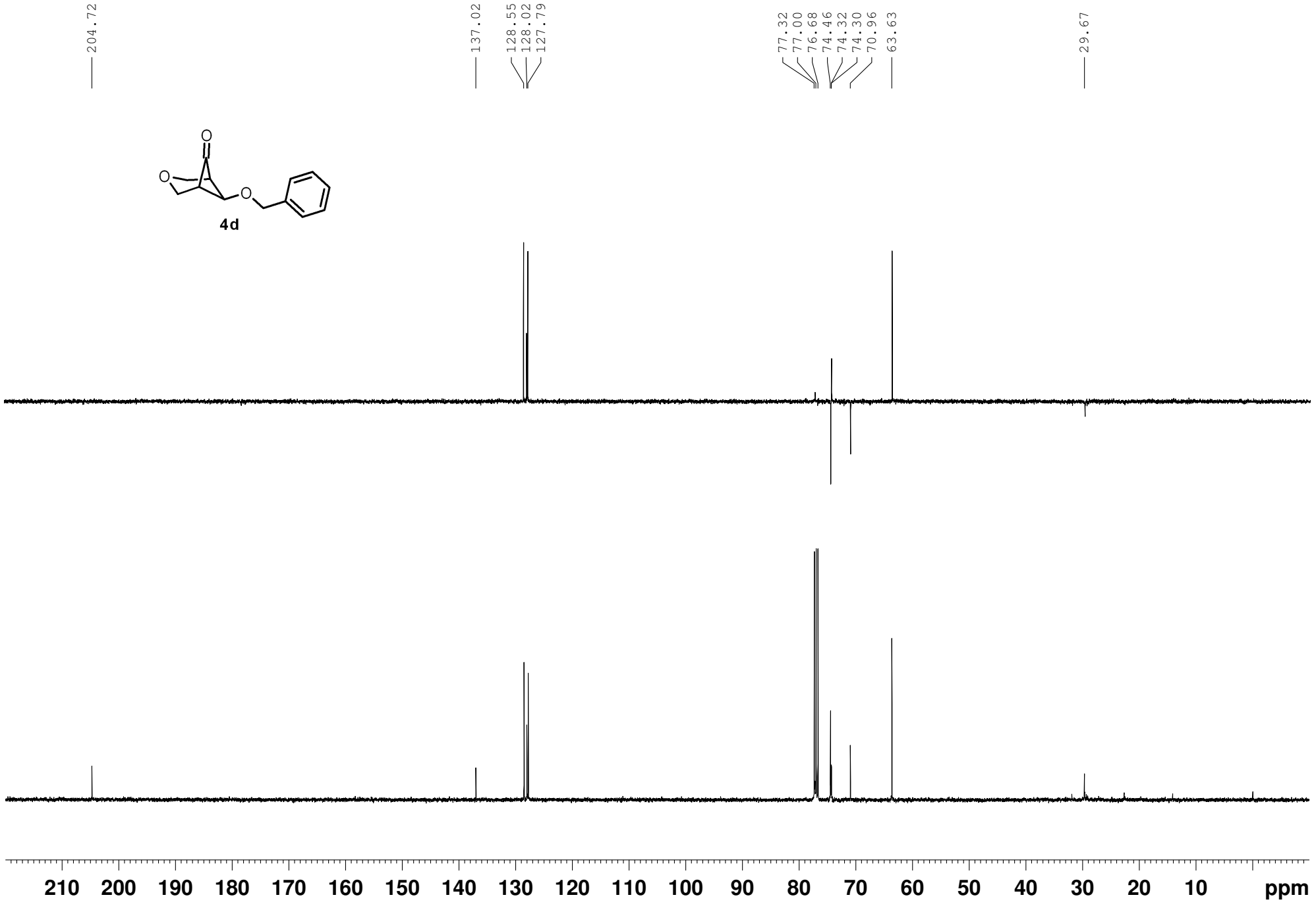
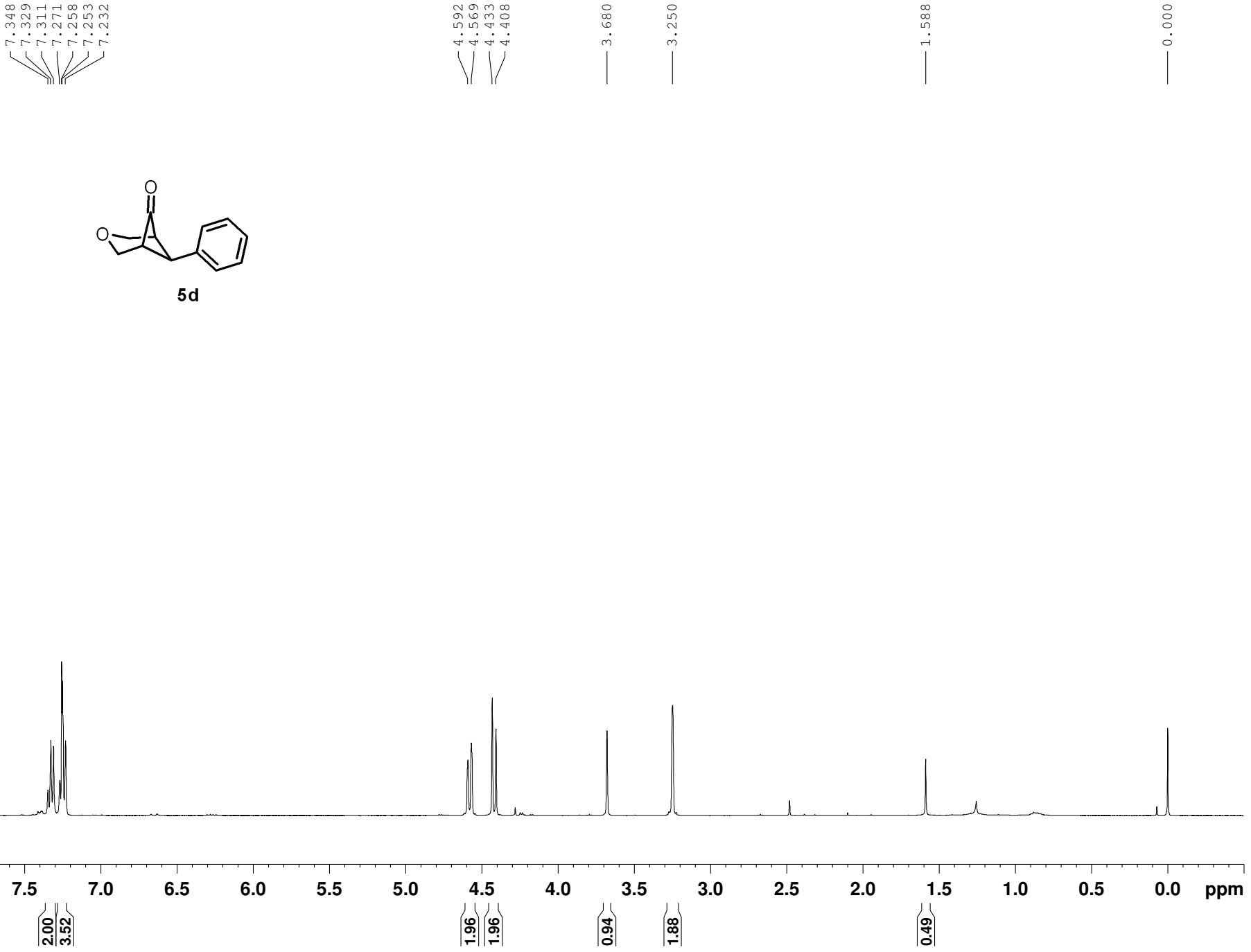
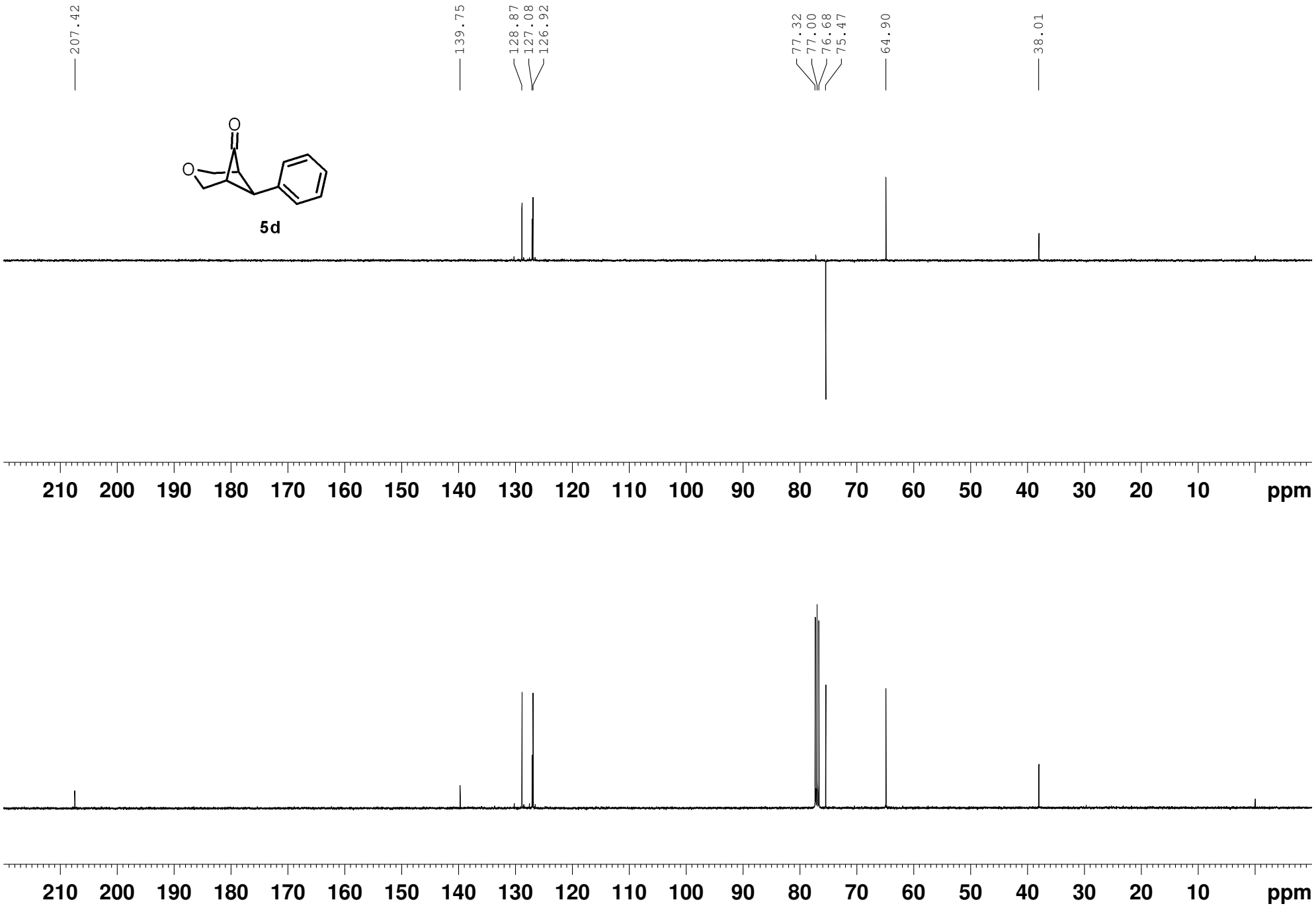
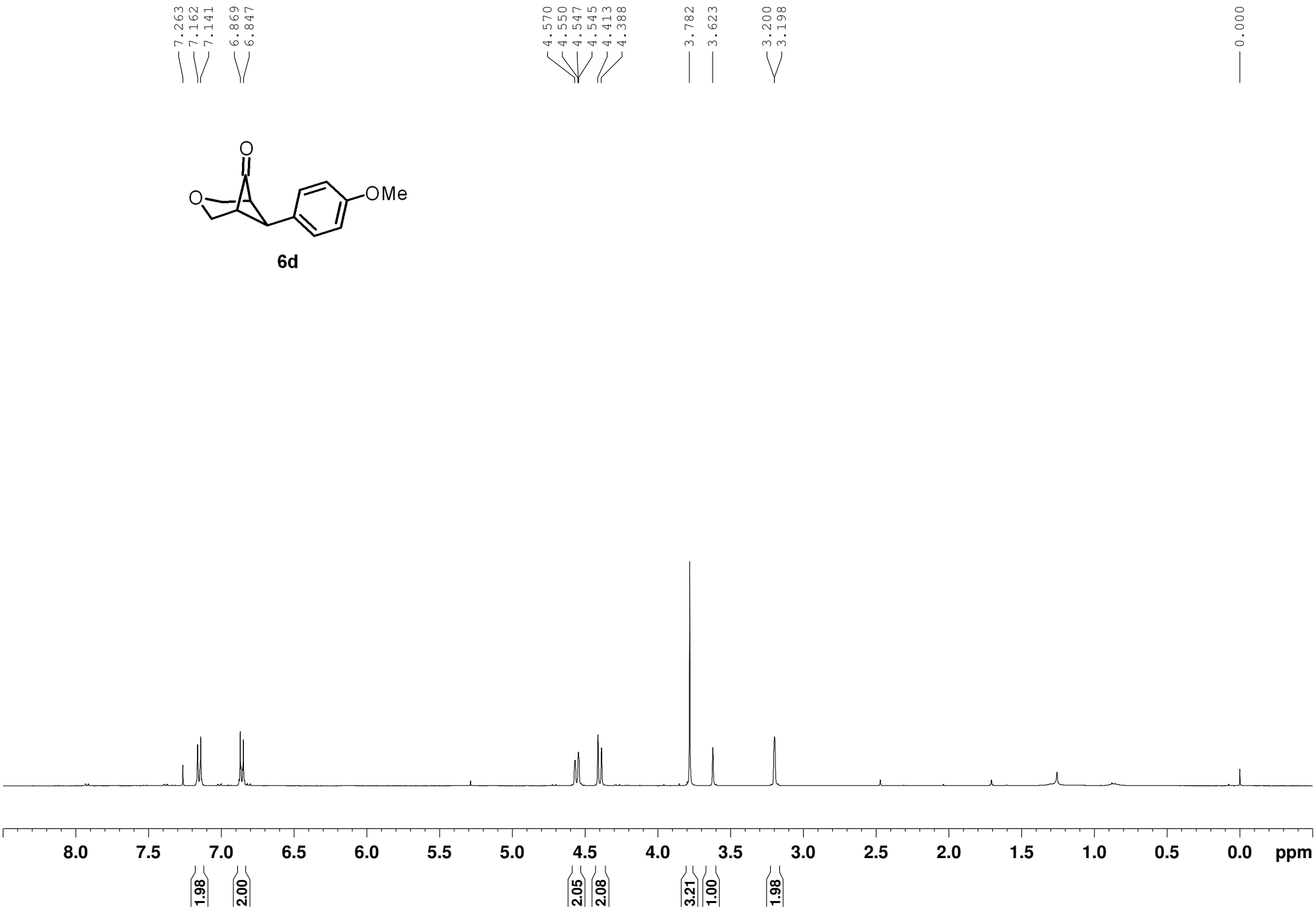


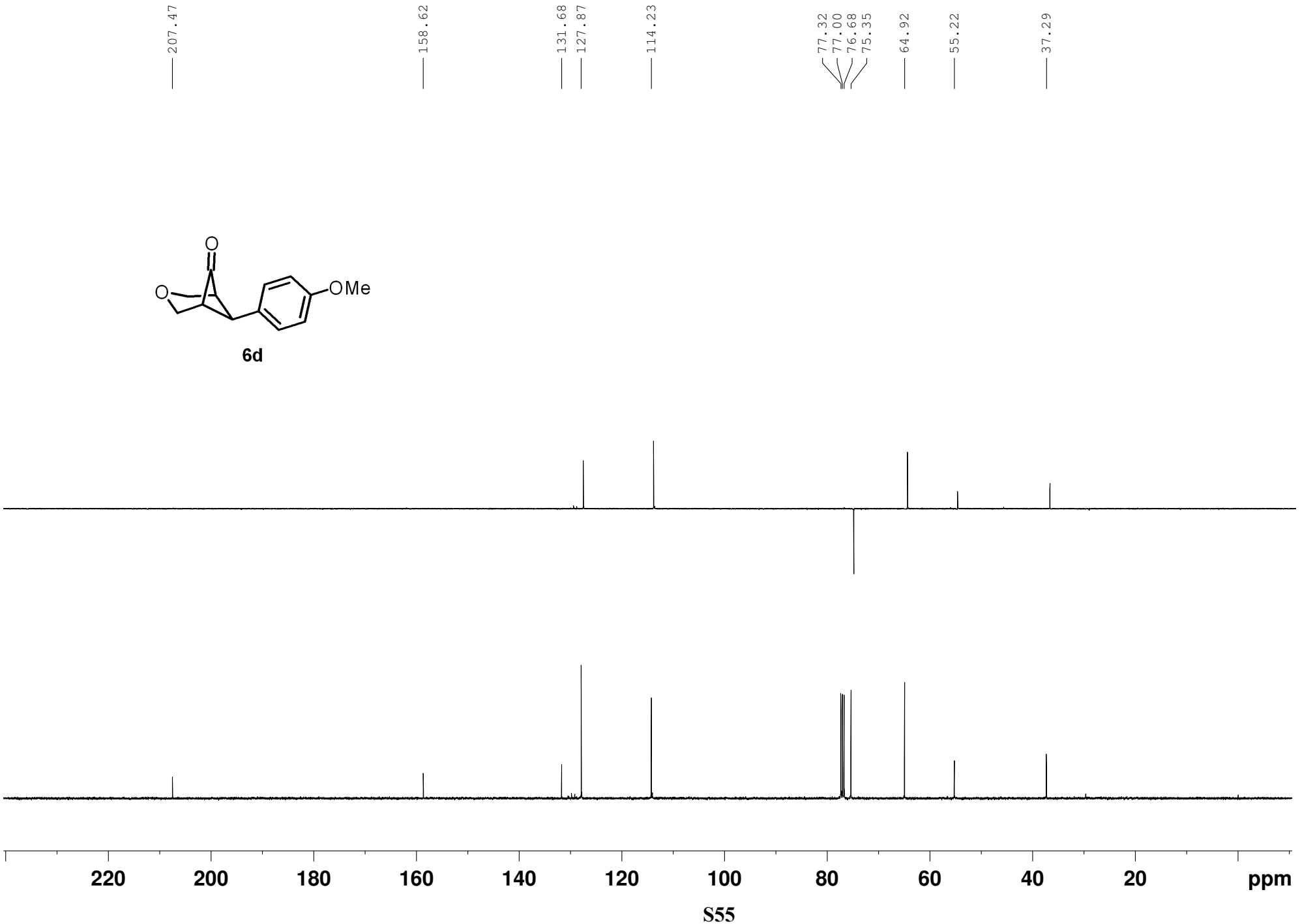
4d



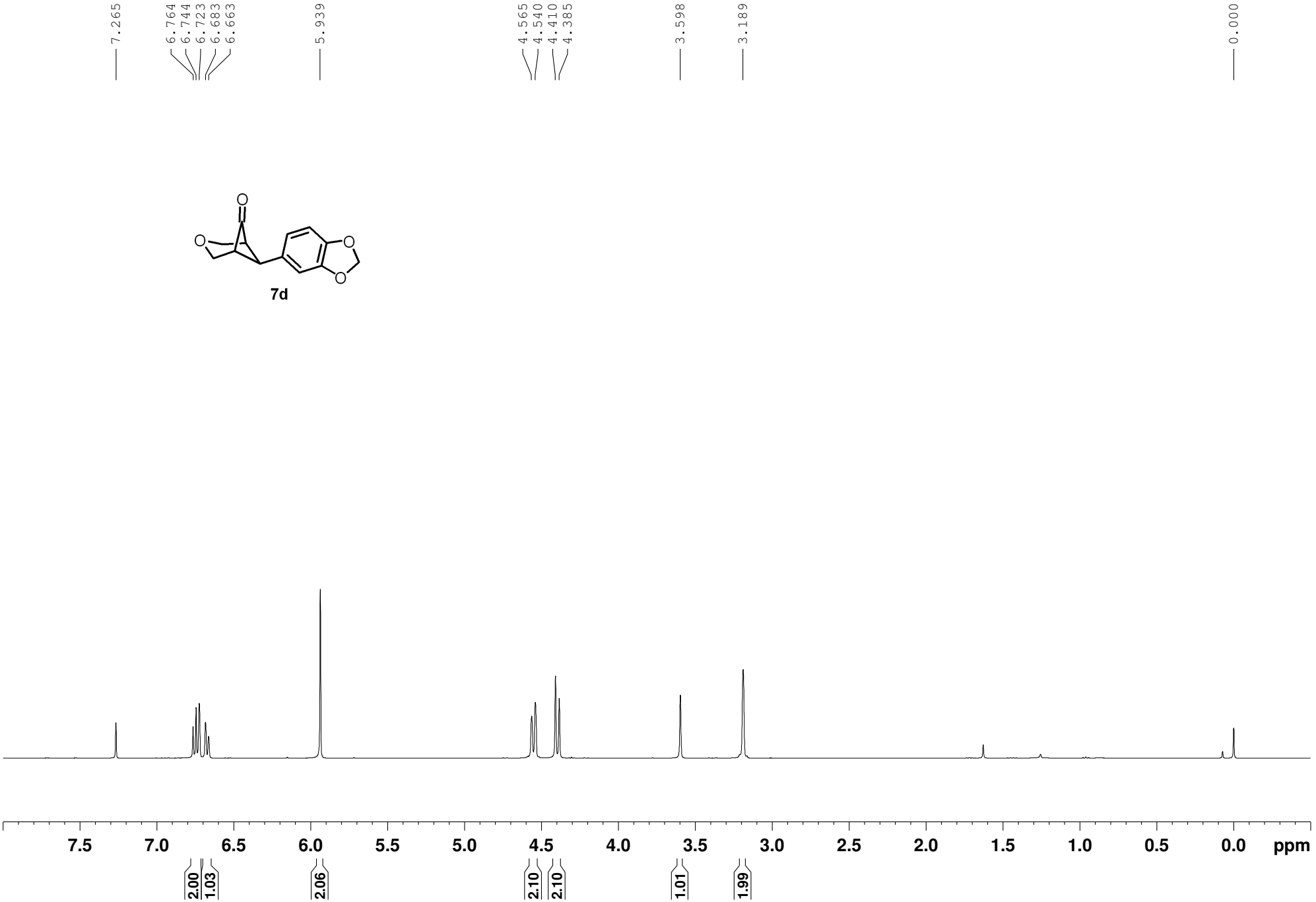


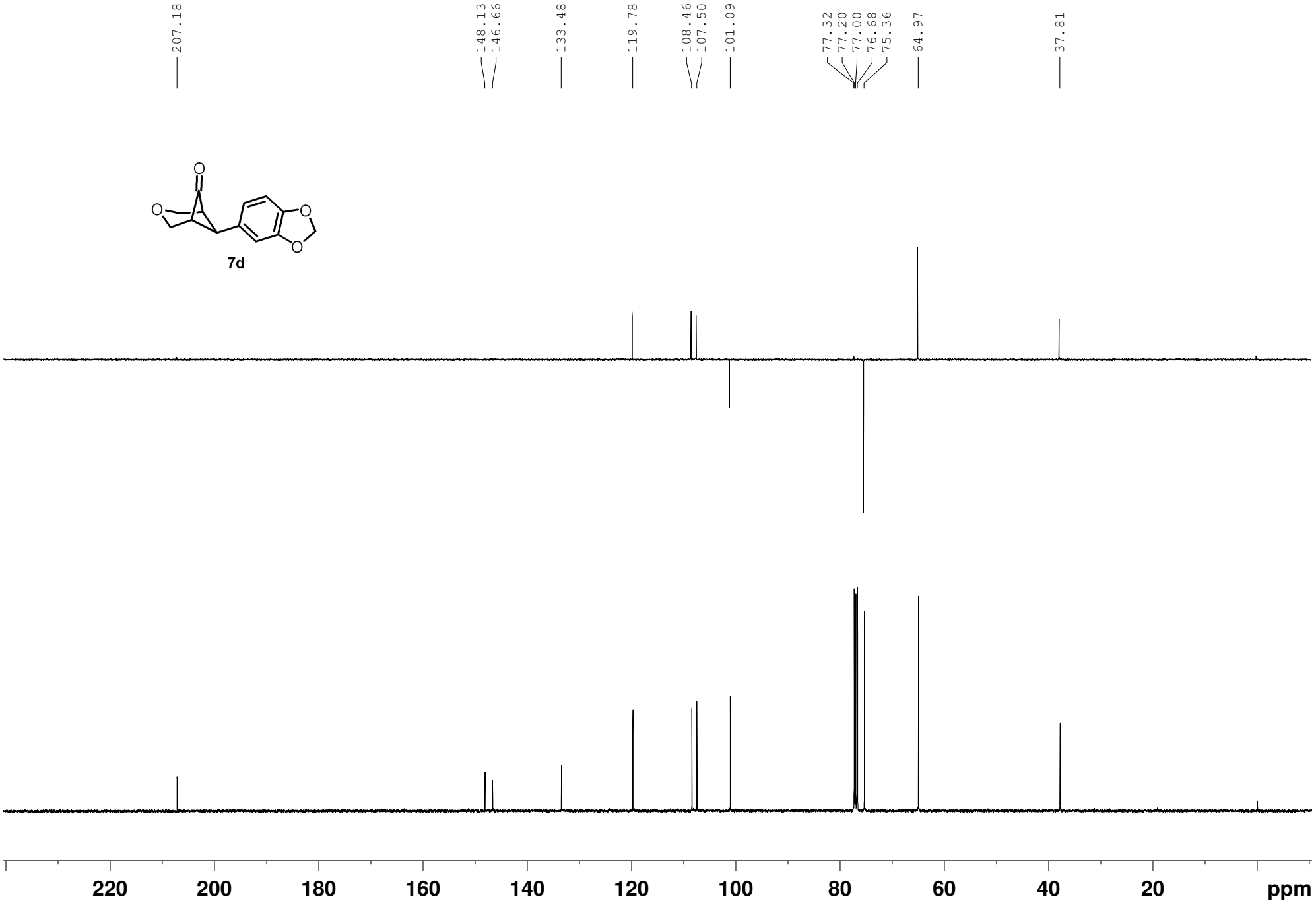


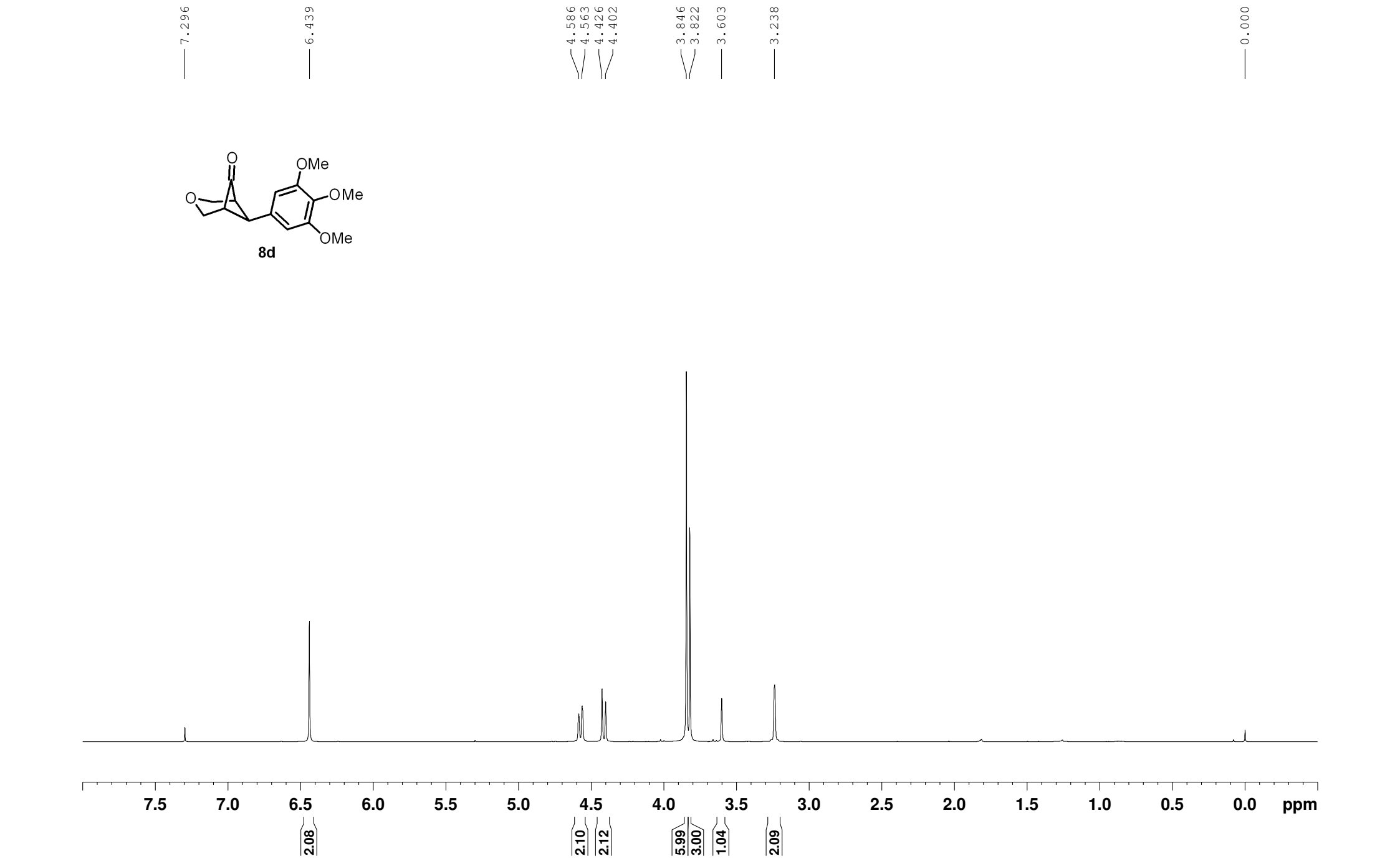


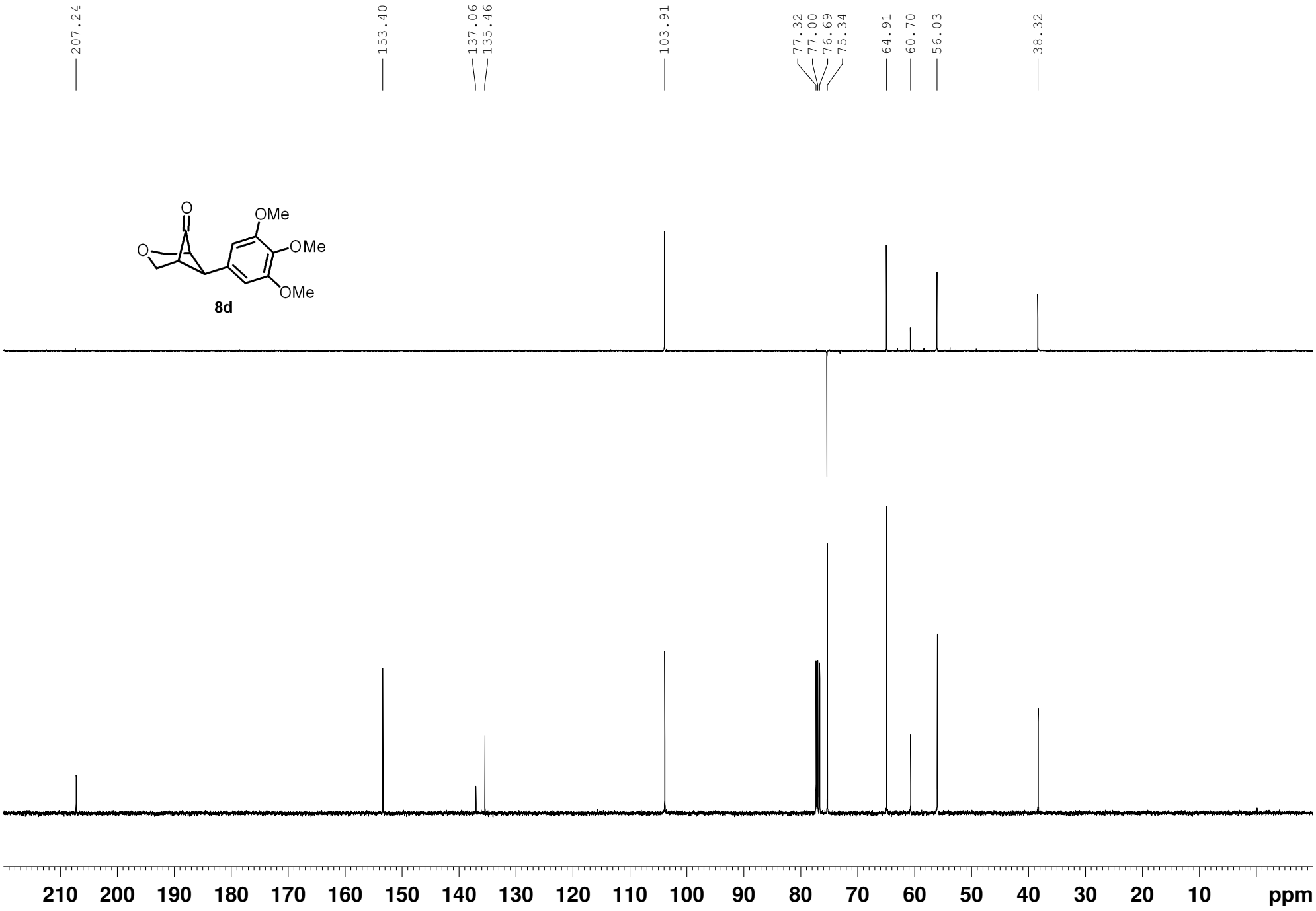


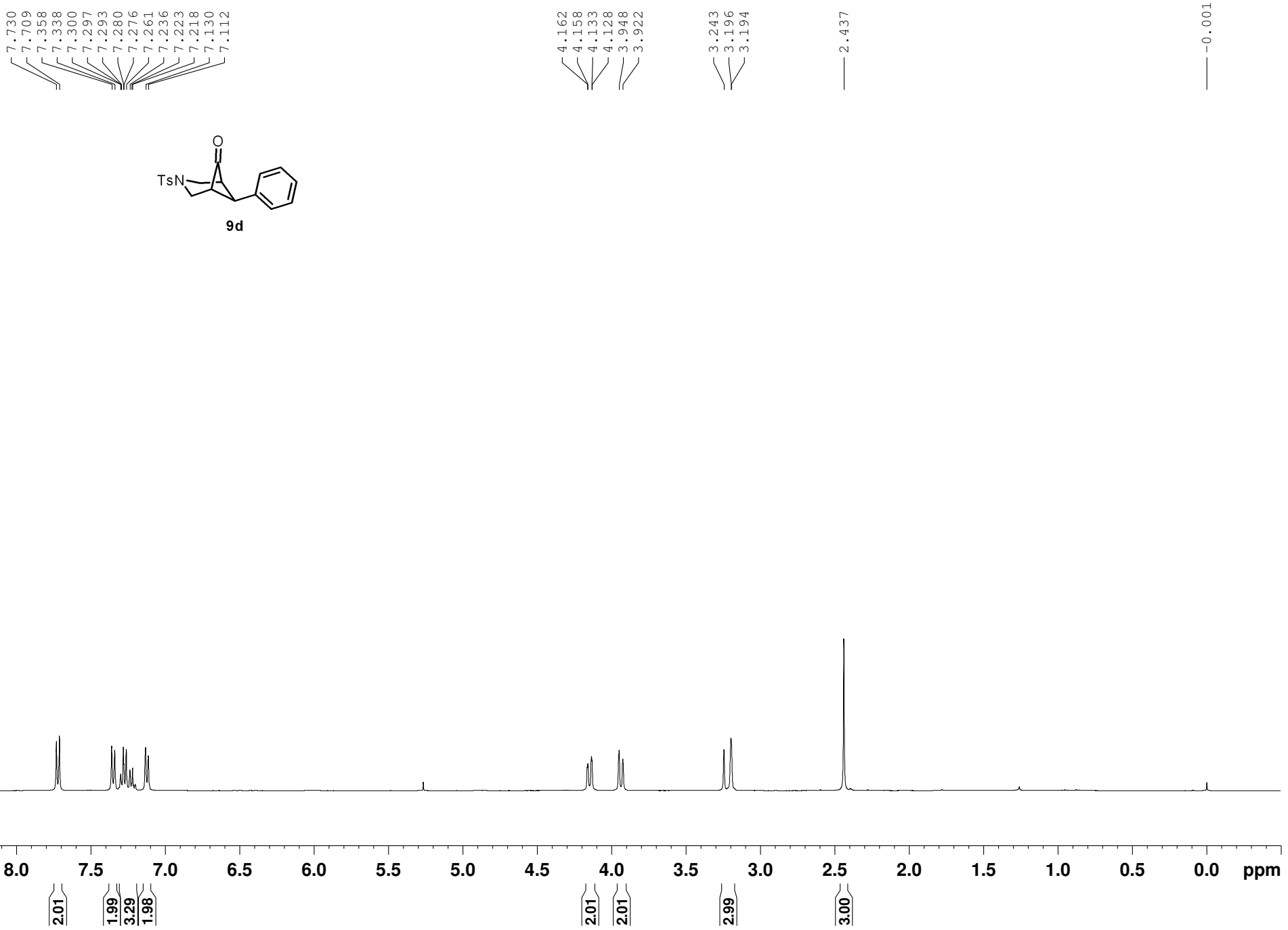
6d

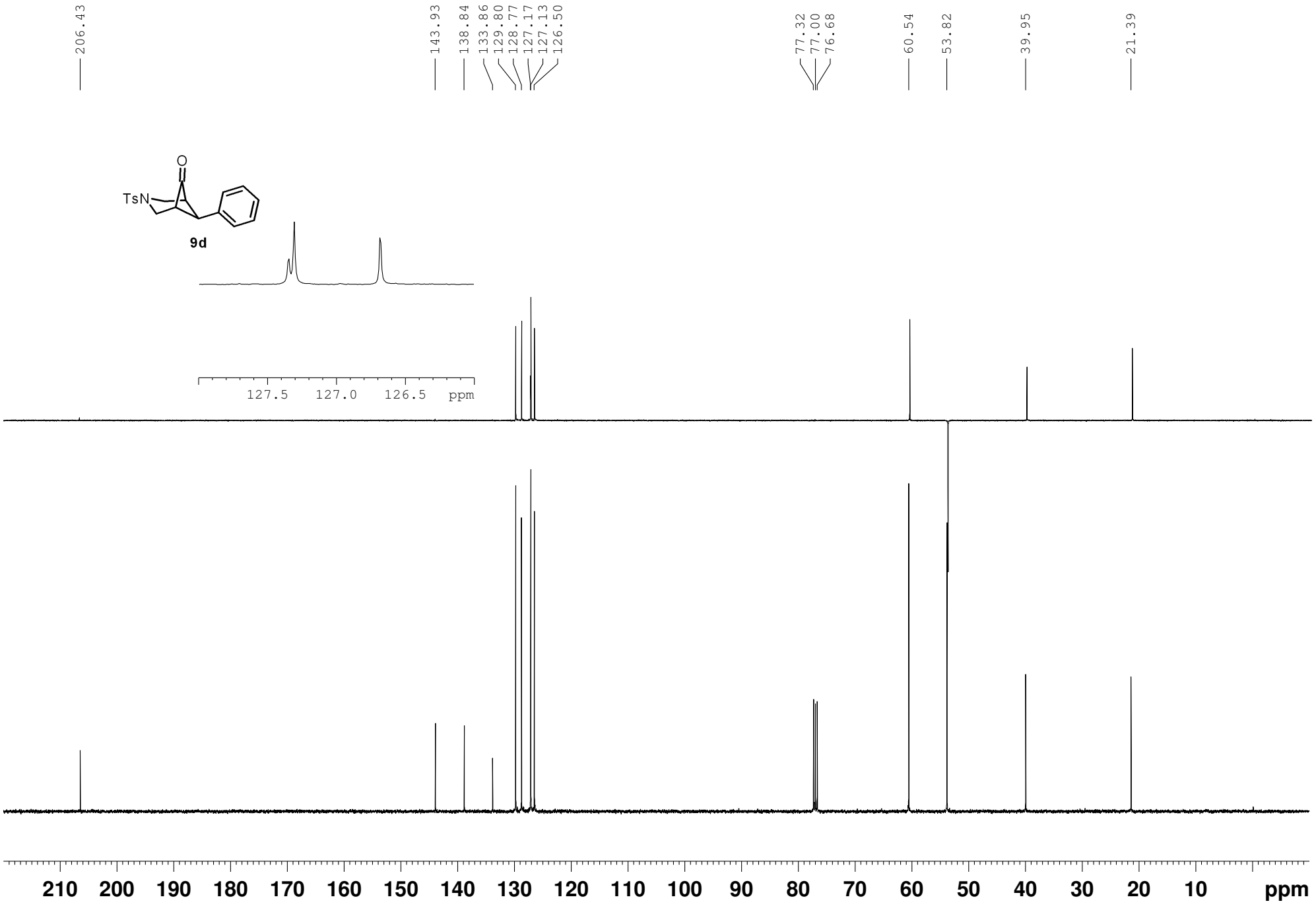


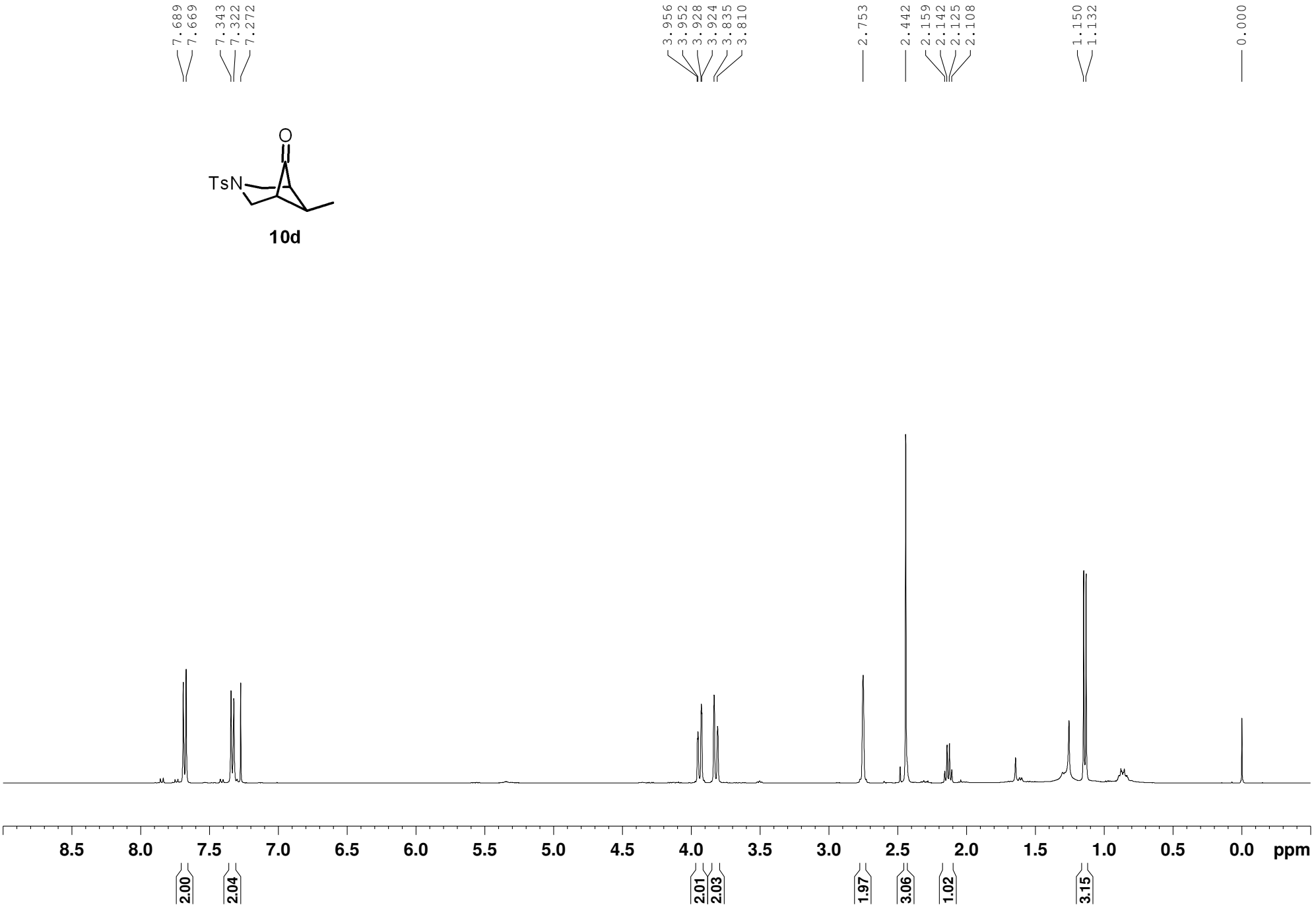












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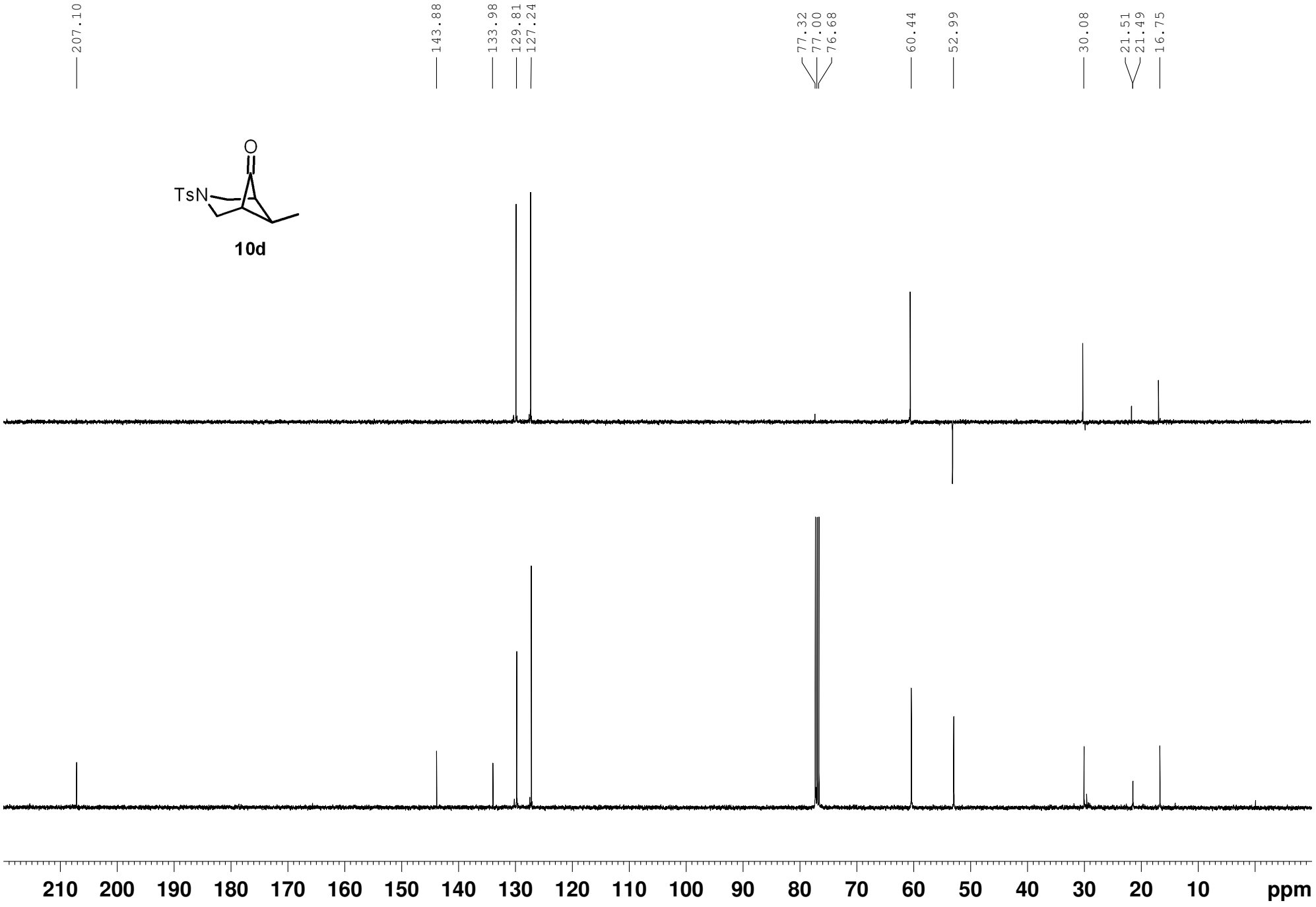

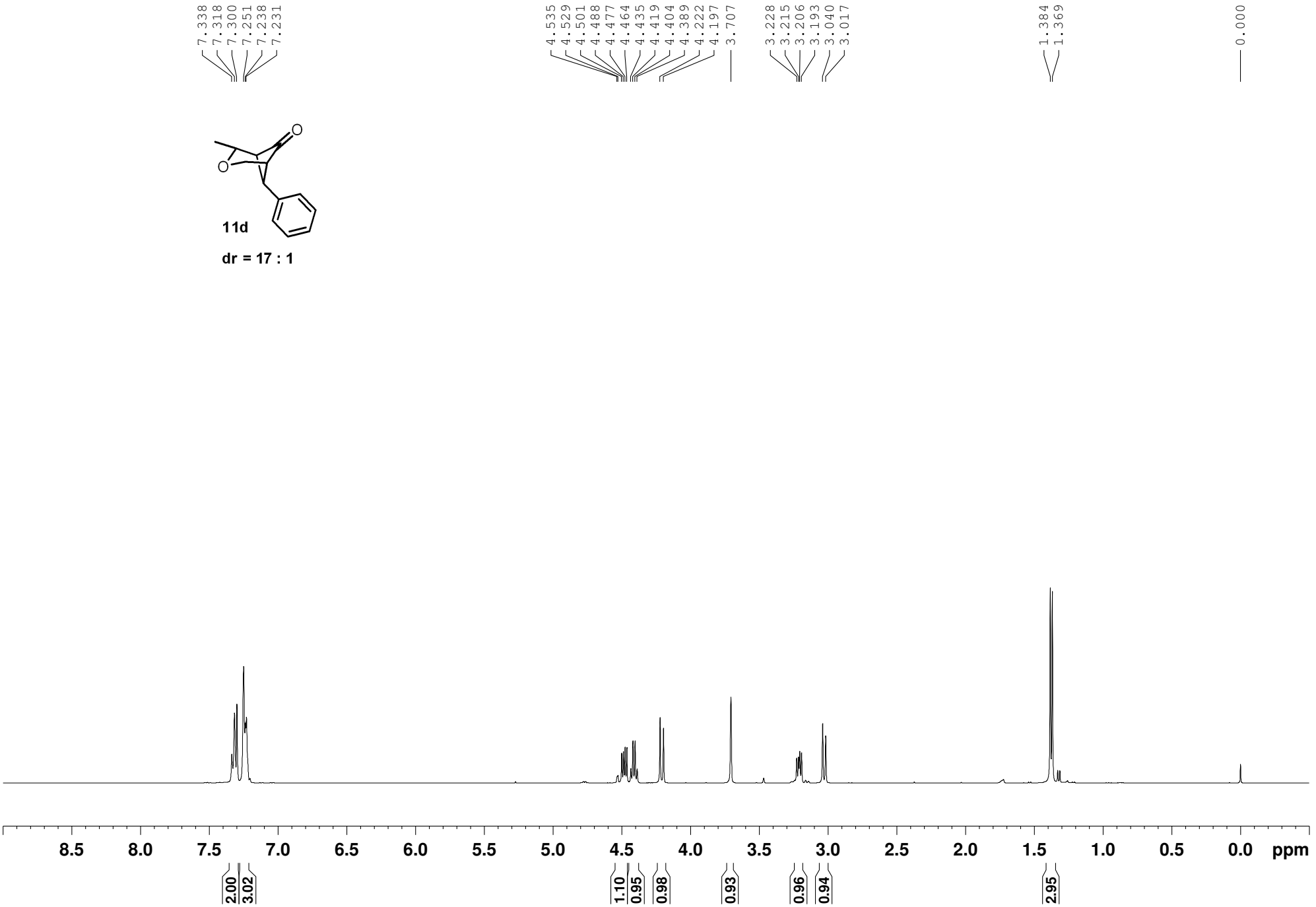

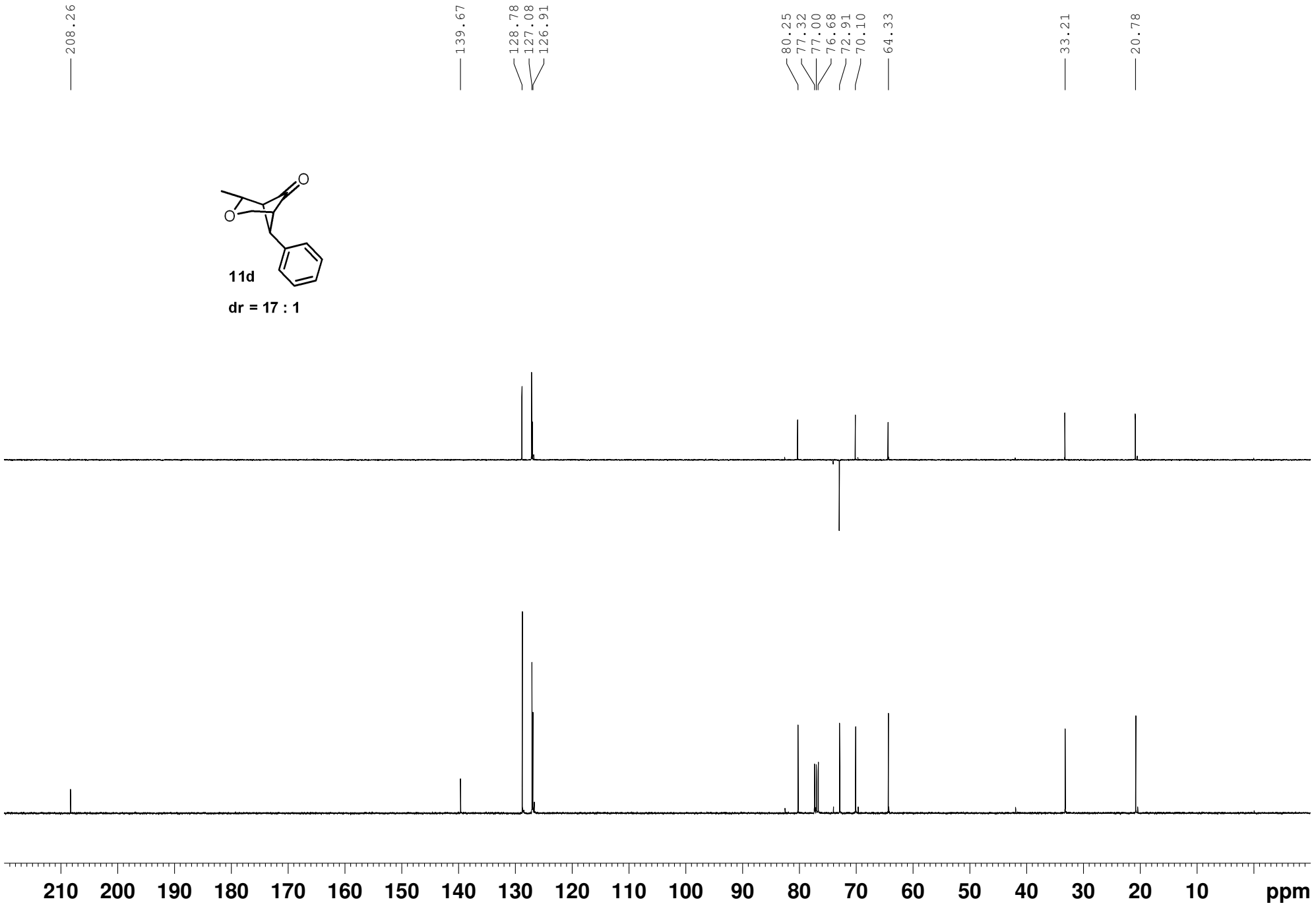

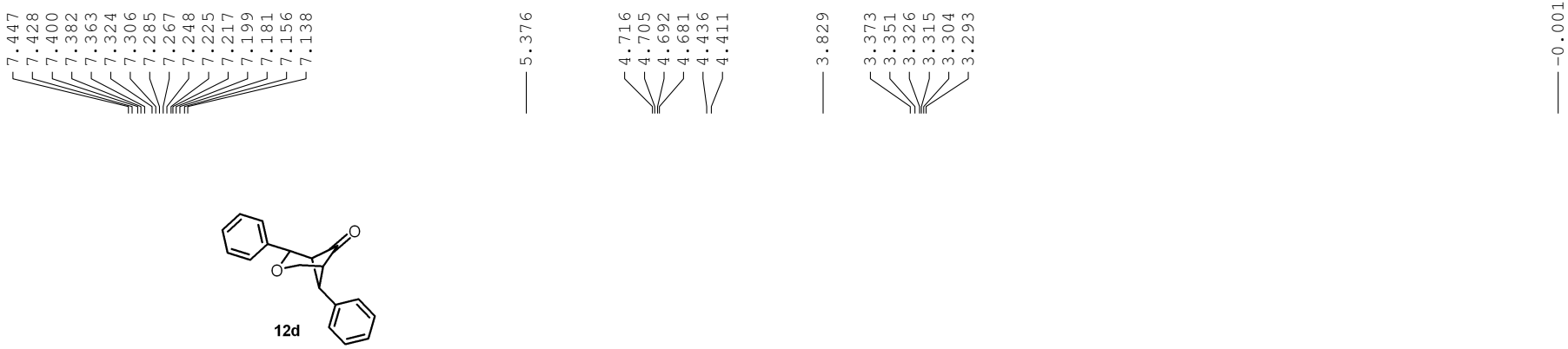

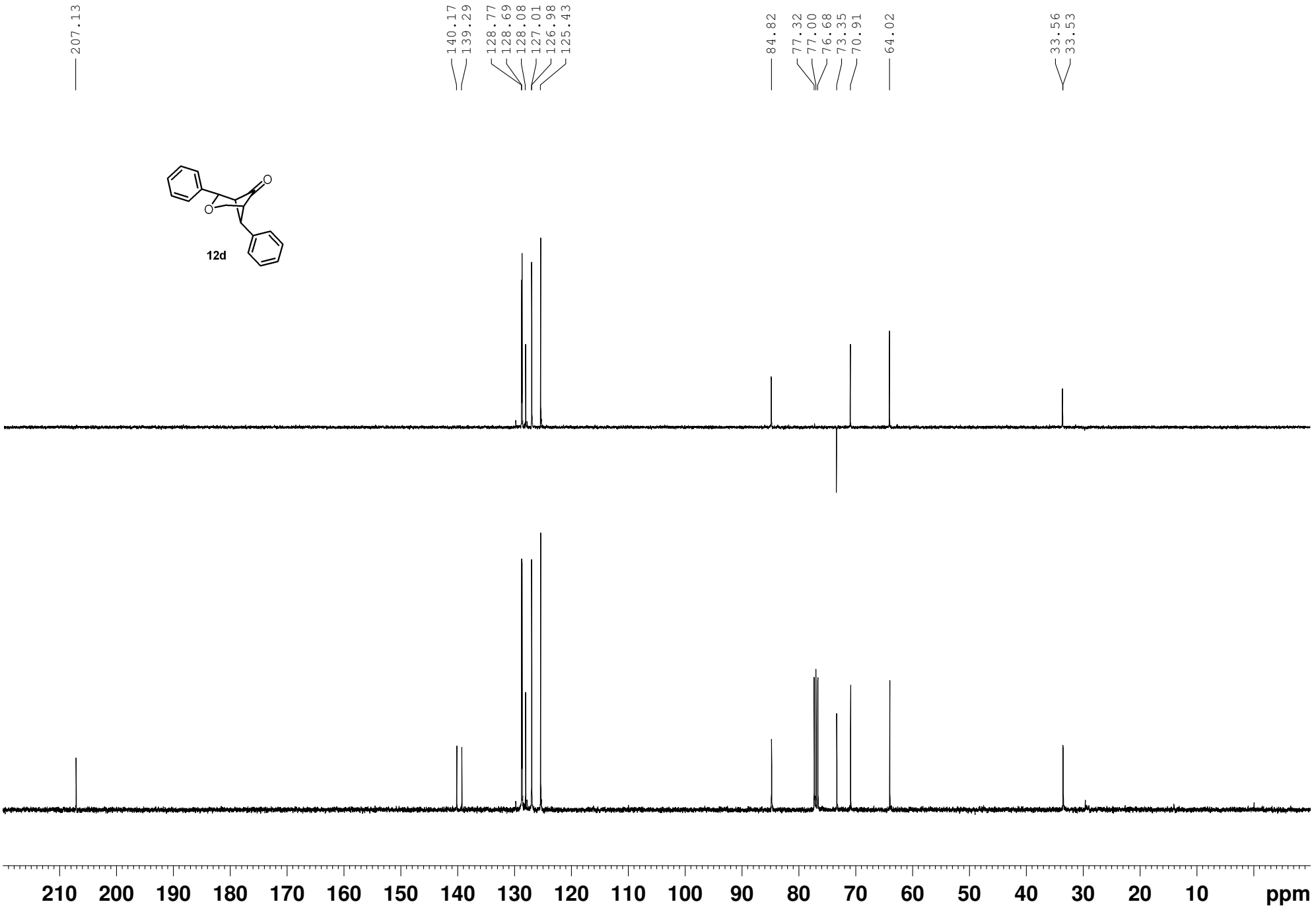

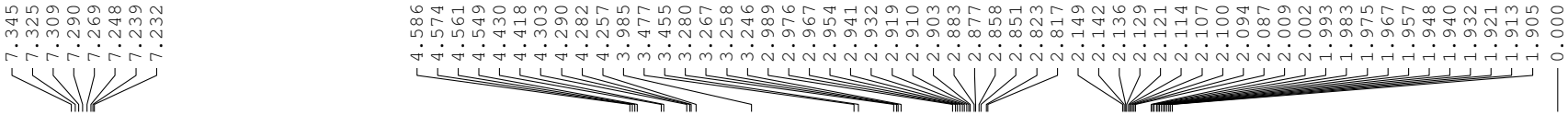

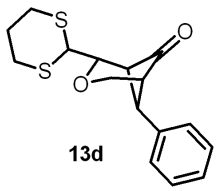

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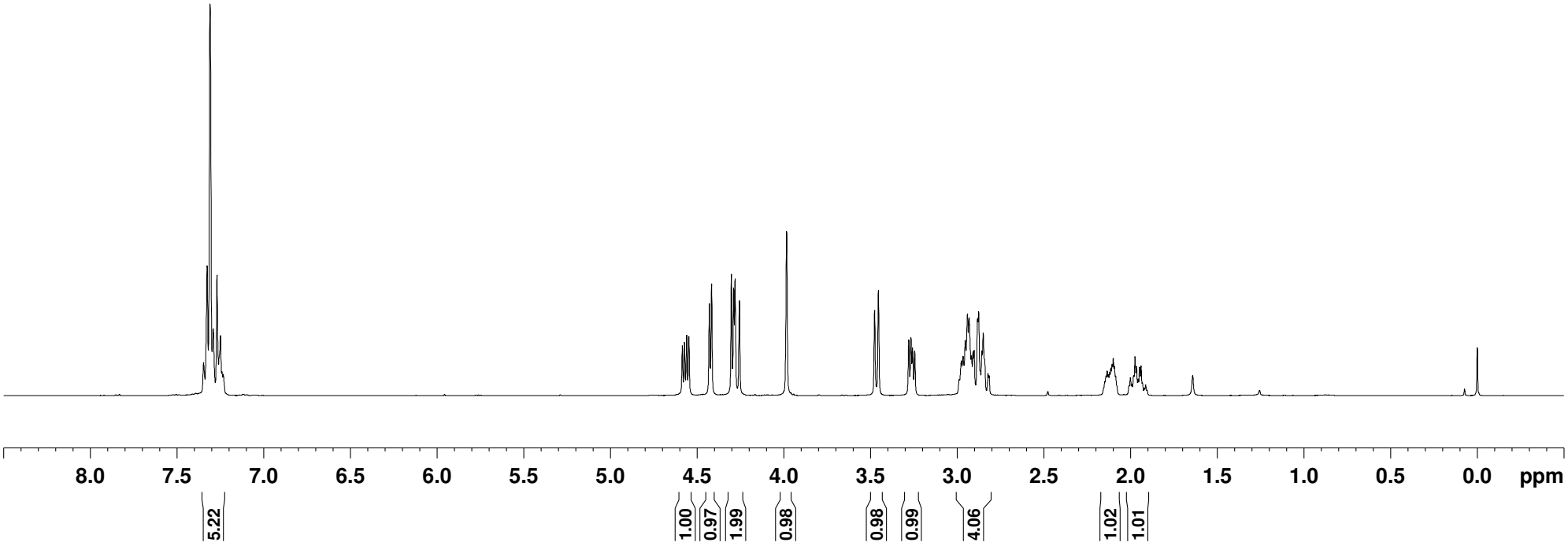

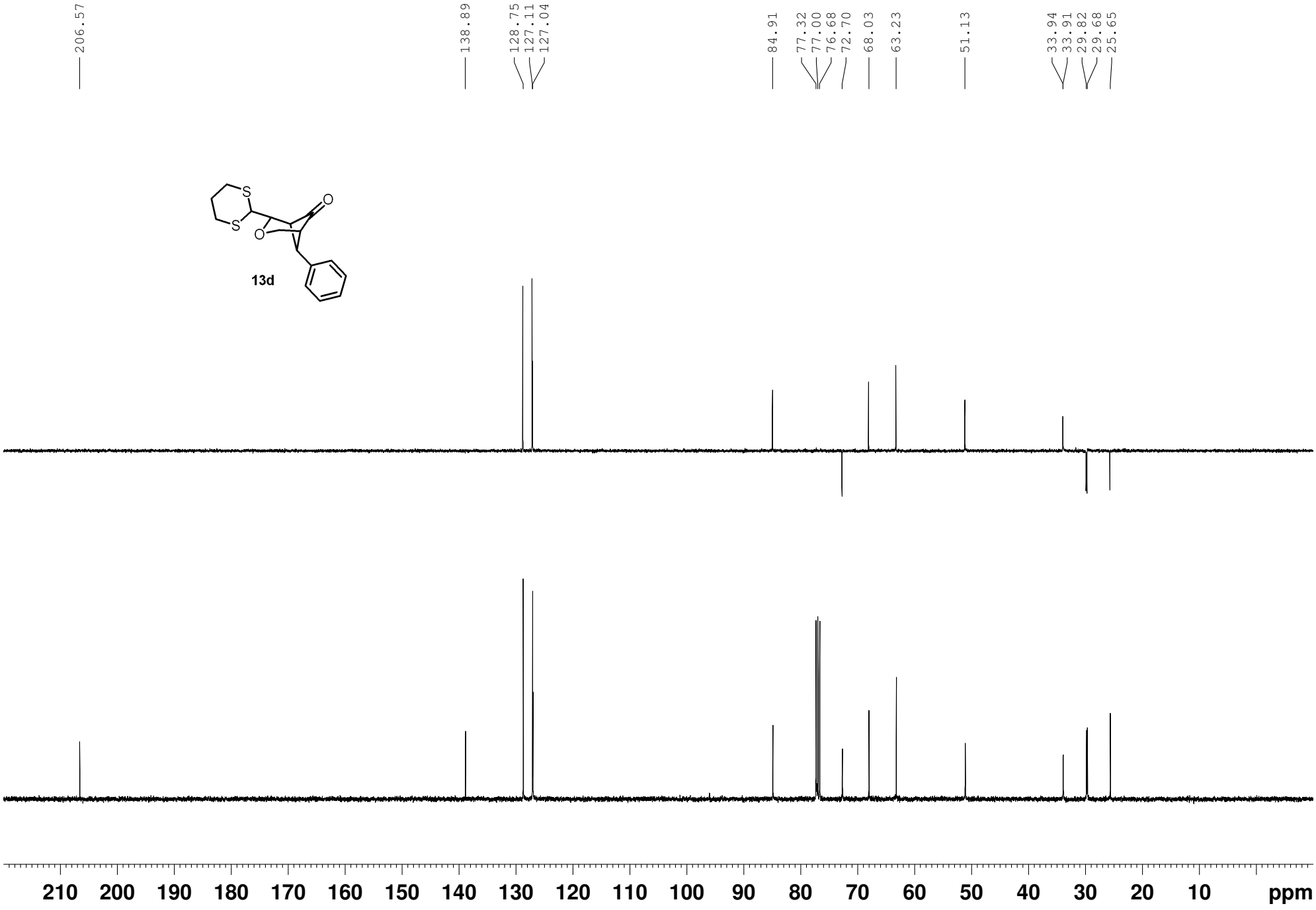

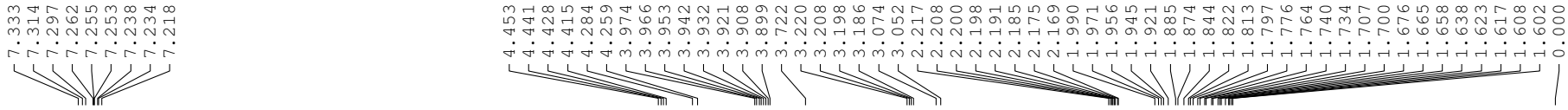

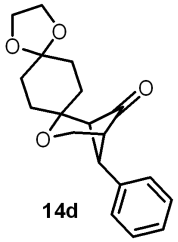

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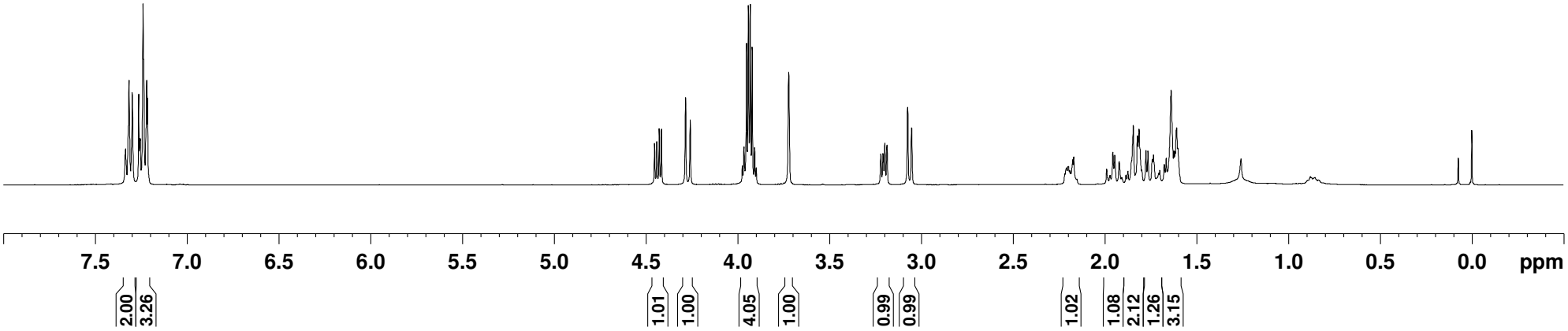

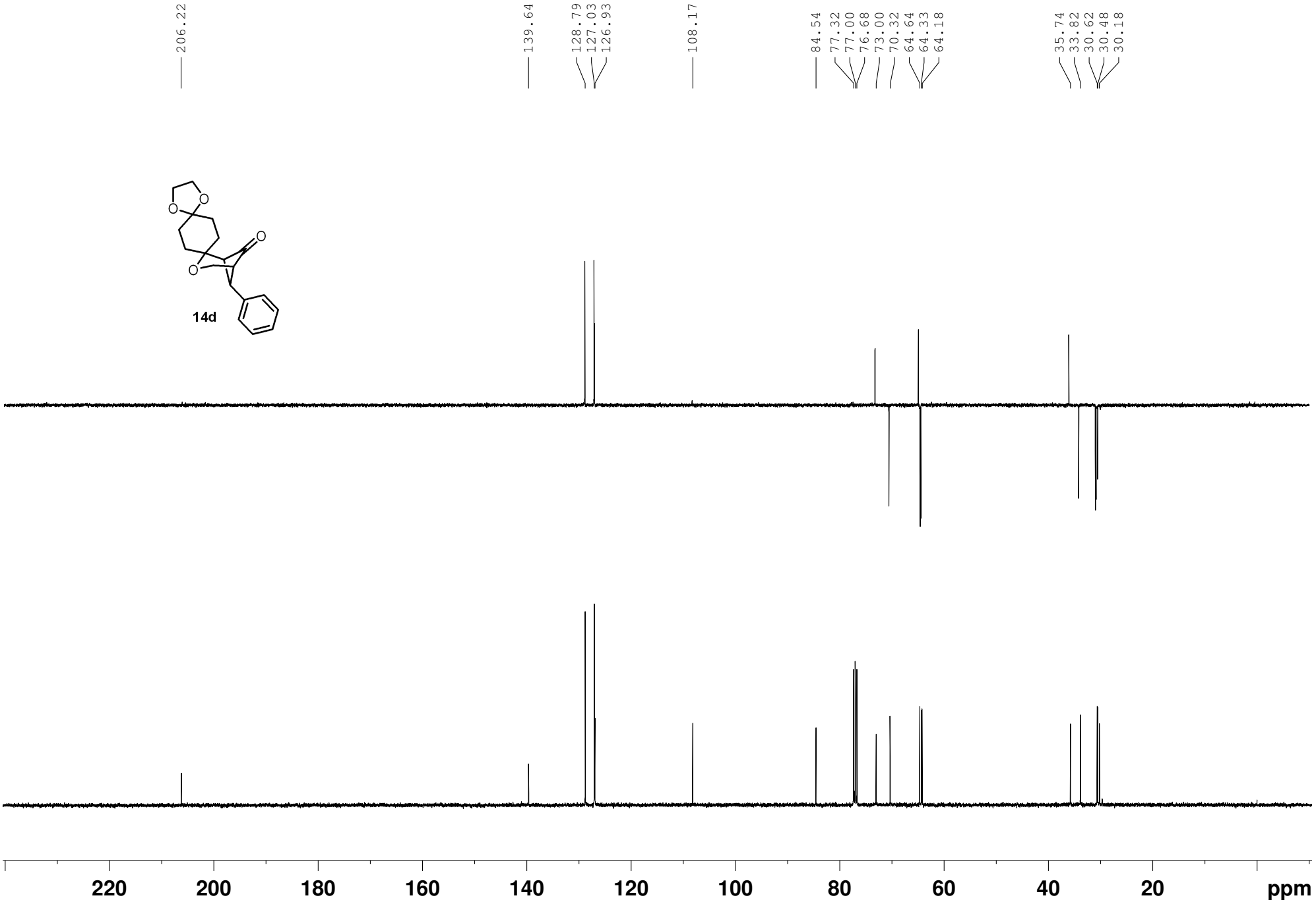

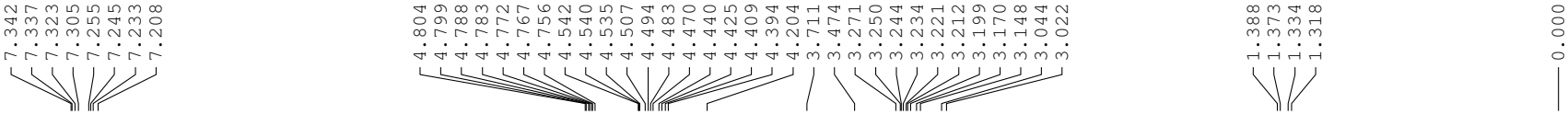

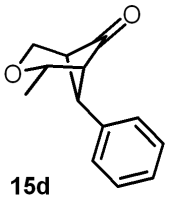

15d

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