Convenient Access to Bicyclic and Tricyclic Diazenes

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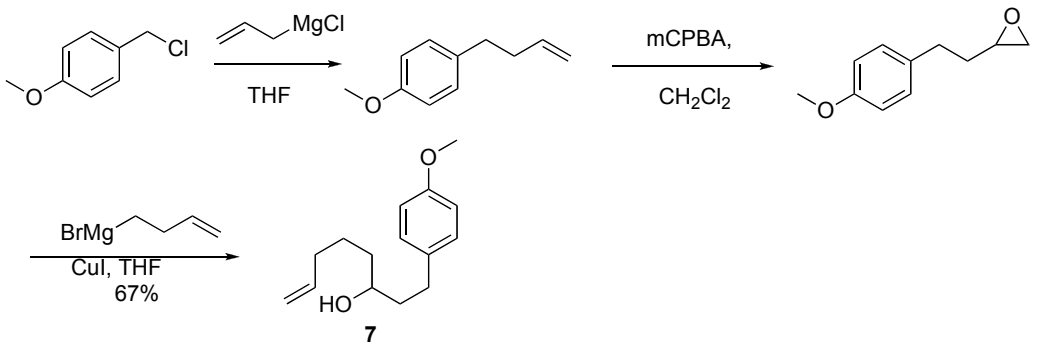
Supporting Information

Contents

General:

^{1}H NMR and ^{13}C NMR spectra were recorded, as solutions in deuteriochloroform ($CDCl_3$) unless otherwise indicated, at 400 MHz and 100 MHz, respectively. ^{13}C multiplicities were determined with the aid of a JVERT pulse sequence, differentiating the signals for methyl and methine carbons as "d" from methylene and quaternary carbons as "u". The infrared (IR) spectra were determined as neat oils. Rf values indicated refer to thin layer chromatography (TLC) on 2.5 x 10 cm, 250 μm analytical plates coated with silica gel GF, unless otherwise noted, and developed in the solvent system indicated. All glassware was oven dried and rinsed with dry solvent before use. THF and diethyl ether were distilled from sodium metal/benzophenone ketyl under dry nitrogen. MTBE is methyl tert-butyl ether and PE is petroleum ether. All reactions were conducted under N_2 and stirred magnetically.



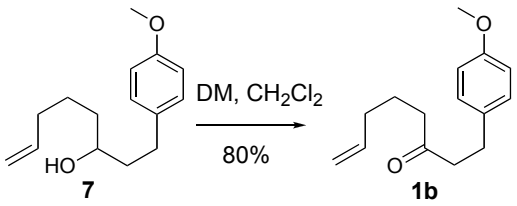
7

1-(4-Methoxyphenyl)oct-7-en-3-ol (7). To a stirred solution of *p*-methoxy benzyl chloride (3.28 g, 20.9 mmol) in dry THF (20 mL), was dropwise added allylmagnesium chloride (40 mmol) in THF over 5 min at 0℃. After stirring for 5 h at 60℃, the reaction mixture was quenched with methanol (3 mL). The mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated to give crude alkene (3.45 g).

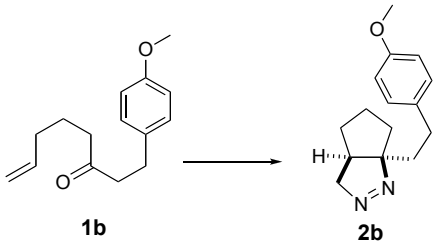
To a stirred solution of the above crude alkene in dry CH_2Cl_2 (50 mL) was added mCPBA (6.27g, 27.9 mmol) at rt. After stirring overnight at rt, the reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous $NaHSO_3$ and then with 1 M NaOH. The organic extracts were dried (Na_2SO_4) and concentrated to afford crude epoxide (3.41 g).

To a stirred solution of 4-butenyl magnesium bromide {freshly prepared with Mg (2.1 g, 87.5 mmol), 4-bromo-1-butene (7.15 g, 53.0 mmol) and I_2 in dry THF (30 mL)} in dry THF was added CuI (672 mg, 3.53 mmol) at 0℃. It was stirred for 5 min at 0℃ and then the solution of the above crude epoxide in THF (5 mL) was added. After stirring overnight at rt, the reaction mixture was quenched with saturated aqueous NH_4Cl (10

mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alcohol **7** (3.31 g, 67% yield from *p*-methoxy benzyl chloride) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.33; IR (cm^{-1}) 3380, 2929, 1510, 1240, 1034; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.75-5.85 (m 1H), 4.90-5.05 (q, 2H), 3.75 (s, 3H), 3.60 (s, 1H), 2.70 (m, 1H), 2.60 (m, 1H), 2.05 (m, 2H), 1.70 (m, 2H), 1.40-1.60 (m, 5H); ^{13}C NMR δ u 157.8, 134.2, 114.7, 39.4, 37.0, 33.7, 31.2, 24.9; d 138.7, 129.3, 113.9, 71.2, 55.3; HRMS calcd for $C_{15}H_{22}O_2$ (M^+) 234.1620, obsd 234.1618.

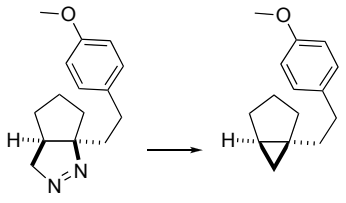


1-(4-Methoxyphenyl)oct-7-en-3-one (1b). To a stirred solution of the alcohol **7** (360 mg, 1.54 mmol) in dry CH_2Cl_2 (5 mL), was added Dess-Martin periodinane reagent (748 mg, 1.69 mmol) at 0℃. The reaction mixture was stirred for 15 min at 0℃ and then concentrated. The residue was chromatographed to yield ketone **1b** (286 mg, 80% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.53; IR (cm^{-1}) 1707, 1510, 1245; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.75 (m, 1H), 5.00 (q, 2H), 3.75 (s, 3H), 2.80 (m, 2H), 2.65 (m, 2H), 2.35 (t, J = 7.4 Hz, 2H), 2.00 (m, 2H), 1.65 (m, 2H); ^{13}C NMR δ u 210.2, 157.9, 133.2, 115.2, 44.6, 42.2, 33.1, 28.9, 22.7; d 138.0, 129.3, 113.9, 55.3; HRMS calcd for $C_{15}H_{21}O_2$ (MH^+) 233.1541, obsd 233.1551.



1b **2b**

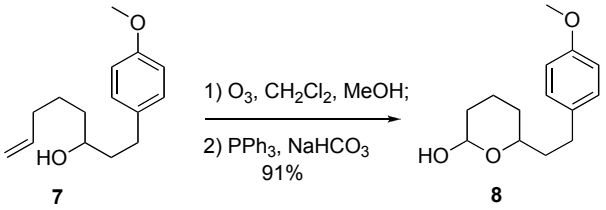
6a-(4-Methoxyphenethyl)-3,3a,4,5,6,6a-hexahydrocyclopenta[c]pyrazole (2b). Ketone **1b** (263 mg, 1.13 mmol) and tosylhydrazine (1.05 equiv, 223 mg, 1.20 mmol) were stirred in MeOH (4 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in toluene (3 mL), K_2CO_3 (6 equiv, 950 mg, 6.9 mmol) was added and the reaction mixture was heated in a sealed vial at 120℃ (oil bath) for 16 h. After cooling to rt, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield **2b** (211 mg, 76% yield) as a pale yellow oil: TLC R_f (5% MTBE/ CH_2Cl_2) = 0.40; IR (cm^{-1}) 2939, 1609, 1506, 1241; ^{1}H NMR δ 7.05 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 4.60 (dd, J = 9.2, 18.4 Hz, 1H), 4.35 (dd, J = 3.2, 18.4 Hz, 1H), 3.75 (s, 3H), 2.40-2.55 (m, 2H), 2.30 (m, 2H), 2.10 (m, 1H), 1.90 (m, 1H), 1.70 (m, 2H), 1.55 (m, 1H), 1.35 (m, 1H), 1.00 (m, 1H); ^{13}C NMR δ u 157.9, 133.8, 104.7, 85.8, 39.4, 36.3, 34.5, 30.4, 23.6; d 129.7, 113.9, 55.3, 37.8; HRMS calcd for $C_{15}H_{21}N_2O$ (MH^+) 245.1654, obsd 245.1663.



2b **3b**

1-(4-Methoxyphenethyl)bicyclo[3.1.0]hexane (3b). A solution of diazene **2b** (40 mg,

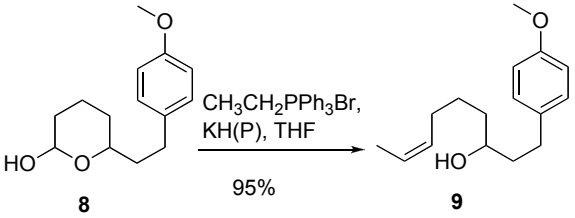
0.16 mmol) in dry toluene (6 mL) was photolyzed for 16 h at rt in a Rayonet apparatus (350 nm). The reaction mixture was concentrated and chromatographed to yield cyclopropane **3b** (26 mg, 72% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.80; IR (cm^{-1}) 2919, 1609, 1510, 1240; ^{1}H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 3.70 (s, 3H), 2.60 (t, J = 8.2 Hz, 2H), 2.30 (m, 1H), 1.50-1.90 (m, 6H), 1.20 (m, 1H), 0.95 (m, 1H), 0.30 (m, 1H), 0.20 (m, 1H); ^{13}C NMR δ u 157.6, 135.2, 38.6, 33.6, 31.3, 27.7, 24.2, 21.4, 12.2; d 129.2, 113.6, 55.3, 23.3; HRMS calcd for $C_{15}H_{20}O$ (M^+) 216.1514, obsd 216.1518.



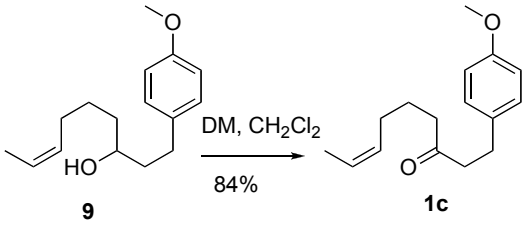
7 **8**

6-(4-Methoxyphenethyl)-tetrahydro-2H-pyran-2-ol (8). Ozone was passed through a stirred solution of alkene **7** (1.67 g, 7.13 mmol) in dry CH_2Cl_2 (5 mL) and MeOH (15 mL) at -78℃. After stirring at -78℃ for 10 min, the color of the reaction mixture changed to pale blue. N_2 was then passed through to remove the excess ozone. PPh_3 (3.2 g) and $NaHCO_3$ (3.2 g) were added at -78℃. The reaction mixture was warmed to rt and stirred for an additional hour. Then the mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield lactol **8** (1.52 g, 91% yield, a 3:2 mixture of two isomers) as a white solid: mp 85℃; TLC R_f (20% MTBE/PE) = 0.59; IR (cm^{-1}) 3400, 2929, 1609, 1506; ^{1}H NMR δ 7.10 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz,

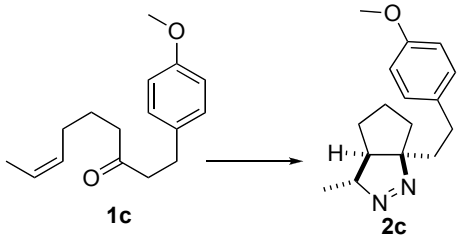
2H), 5.60 (m, 0.4H), 4.70 (m, 0.6H), 3.95 (m, 0.4H), 3.80 (s, 3H), 3.40 (m, 0.6H), 3.00 (d, J = 6.3 Hz, 0.6H), 2.70 (m, 1H), 2.60 (m, 1H), 2.45 (m, 0.4H), 1.75 (m, 2H), 1.45-1.70 (m, 4H), 1.15-1.35 (m, 2H); ^{13}C NMR δ u 157.7, 134.3, 38.1, 37.8, 32.9, 31.2, 30.8, 30.4, 29.8, 22.1, 17.4; d 129.3, 113.8, 96.5, 91.2, 75.4, 68.0, 55.3.



(Z)-1-(4-Methoxyphenyl)non-7-en-3-ol (9). To the mixture of ethyl triphenylphosphonium bromide (757 mg, 2.04 mmol) and KH (125 mg, 50% in paraffin, 1.56 mmol) was added dry THF (5 mL) at rt. After stirring at rt for 5 min, a solution of lactol **8** (241 mg, 1.02 mmol) in dry THF (1 ml) was added and the reaction mixture was stirred for another 30 min at rt.[3] The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alcohol **9** (240 mg, 95% yield, a ~ 5 : 1 *Z*/*E* mixture) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.24; IR (cm^{-1}) 3371, 2929, 1609, 1510; ^{1}H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.30-5.50 (m, 2H), 3.75 (s, 3H), 3.60 (bs, 1H), 2.75 (m, 1H), 2.60 (m, 1H), 2.05 (m, 2H), 1.70 (m, 2H), 1.55 (d, J = 6.6 Hz, 3H), 1.30-1.50 (m, 5H); ^{13}C NMR (major isomer) δ u 157.8, 134.2, 39.3, 37.1, 31.1, 26.8, 25.5; d 129.3, 128.5, 124.2, 113.9, 71.3, 55.3, 12.8; HRMS calcd for $C_{16}H_{24}O_2$ (M^+) 248.1776, obsd 248.1775.

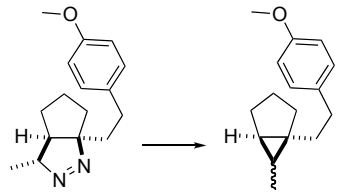


(Z)-1-(4-Methoxyphenyl)non-7-en-3-one (1c). To a solution of the alcohol **9** (203.8 mg, 0.82 mmol) in dry CH_2Cl_2 (3 mL), was added Dess-Martin periodinane reagent (398 mg, 0.90 mmol) at 0℃. The reaction mixture was stirred at 0℃ for 30 min and then concentrated. The residue was chromatographed to yield ketone **1c** (169 mg, 84% yield, a ~ 5 : 1 *Z*/*E* mixture) as a colorless oil: TLC R_f (20%MTBE/PE) = 0.59; IR (cm^{-1}) 2929, 1708, 1609, 1510; ^{1}H NMR δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 5.45 (m, 1H), 5.30 (m, 1H), 3.75 (s, 3H), 2.80 (t, *J* = 7.5 Hz, 2H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.00 (q, 2H), 1.65 (m, 2H), 1.55 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (major isomer) δ u 210.3, 157.9, 133.2, 44.6, 42.3, 28.9, 26.1, 23.5; d 129.6, 129.3, 124.8, 113.9, 55.2, 12.8; HRMS calcd for $C_{16}H_{22}O_2$ (M^+) 246.1620, obsd 246.1618.



6a-(4-Methoxyphenethyl)-3-methyl-3,3a,4,5,6,6a-hexahydrocyclopenta[c]pyrazole (2c). Ketone **1c** (78.5 mg, 0.32 mmol) and tosylhydrazine (1.05 equiv, 63 mg, 0.34 mmol) were stirred in MeOH (2 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in toluene (3 mL), K_2CO_3 (6 equiv, 263 mg, 1.9 mmol) was added and the reaction mixture was heated in a sealed vial

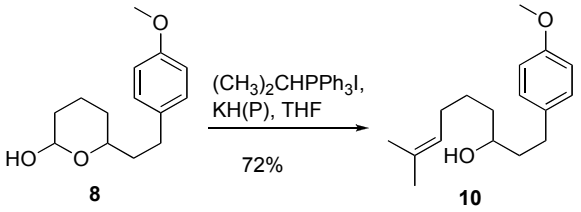
at 120℃ (oil bath) for 16 h. After cooling to rt, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield diazene **2c** (58 mg, 70% yield, a ~ 5:1 mixture of diastereomers) as a pale yellow oil: TLC R_f (5% MTBE/PE) = 0.41; IR (cm^{-1}) 2939, 1609, 1510, 1240; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 4.25-4.40 (m, 1H), 3.30 (s, 3H), 2.35-2.70 (m, 3H), 2.25 (m, 1H), 2.10 (m, 1H), 1.95 (m, 1H), 1.75 (m, 1H), 1.55-1.60 (m, 2H), 1.50 (d, J = 7.6 Hz, 3H), 1.40- 1.45 (m, 1H), 0.95 (m, 1H); ^{13}C NMR (major isomer) δ u 157.9, 134.0, 105.7, 40.7, 36.5, 30.4, 27.8, 23.7; d 129.1, 113.9, 86.2, 55.3, 41.7, 13.8; HRMS calcd for $C_{16}H_{23}N_2O$ (MH^+) 259.1810, obsd 259.1814.



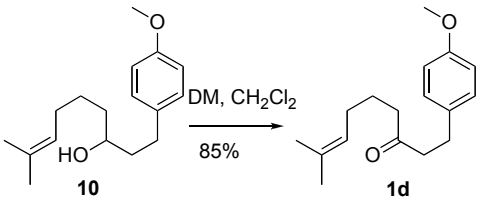
2c **3c**

1-(4-Methoxyphenethyl)-6-methylbicyclo[3.1.0]hexane (3c). A solution of diazene **2c** (45 mg, 0.17 mmol) in dry toluene (6 mL) was photolyzed for 24 h at rt in a Rayonet apparatus (350 nm). The reaction mixture was concentrated and chromatographed to yield cyclopropane **3c** (29 mg, 71% yield, a 1:1 mixture of diastereomers) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.75; IR (cm^{-1}) 2918, 1643, 1510, 1245; ^1H NMR δ 7.10 (m, 2H), 6.80 (m, 2H), 3.70 (s, 3H), 2.60 (m, 2H), 2.30 (m, 1H), 1.45-2.00 (m, 7H), 1.10-1.35 (m, 1H), 0.80-1.00 (m, 3H), 0.60 (m, 1H); ^{13}C NMR δ u 157.6, 135.4, 135.2, 40.7, 33.9, 33.7, 33.6, 33.5, 32.7, 32.1, 29.1, 28.0, 26.9, 25.0, 22.0; d 129.2, 113.7, 113.6, 55.3, 31.1, 28.2,

21.2, 16.8, 13.2, 8.1; HRMS calcd for C16H23O (MH^+) 231.1749, obsd 231.1750.

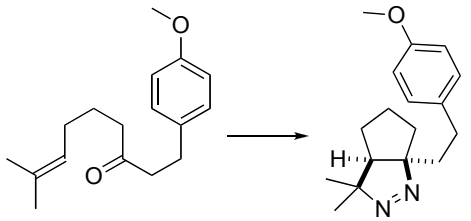


1-(4-Methoxyphenyl)-8-methylnon-7-en-3-ol (10). To the mixture of isopropyl triphenylphosphonium iodide (846 mg, 1.96 mmol) and KH (121 mg, 50% in paraffin, 1.51 mmol) was added dry THF (5 mL) at rt. After stirring at rt for 5 min, a solution of lactol **8** (220 mg, 0.93 mmol) in dry THF (1 ml) was added and the reaction mixture was stirred at reflux for 2 h. Then the mixture was quenched with saturated aqueous NH_4Cl (5 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alcohol **10** (177 mg, 72% yield) as a colorless oil: TLC R_f (5% MTBE/ CH_2Cl_2) = 0.52; IR (cm^{-1}) 3351, 2918, 1609, 1506, 1240; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.10 (m, 1H), 3.75 (s, 3H), 3.60 (bs, 1H), 2.70 (m, 1H), 2.60 (m, 1H), 1.95 (m, 2H), 1.70-1.80 (m, 2H), 1.65 (s, 3H), 1.55 (s, 3H), 1.30-1.50 (m, 5H); ^{13}C NMR δ u 157.7 134.3, 131.7, 39.3, 37.2, 31.2, 28.0, 25.9; d 128.3, 124.4, 113.8, 71.3, 55.3, 25.8, 17.7; HRMS calcd for $C_{17}C_{26}O_2$ (M^+) 262.1933, obsd 262.1925.



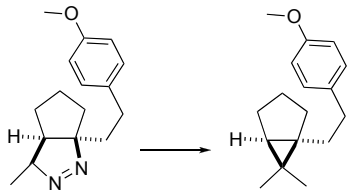
1-(4-Methoxyphenyl)-8-methylnon-7-en-3-one (1d). To a solution of the alcohol **10**

(162 mg, 0.62 mmol) in dry CH_2Cl_2 (3 mL), was added Dess-Martin periodinane reagent (302 mg, 0.68 mmol) at 0℃. The reaction mixture was stirred at 0℃ for 30 min and then concentrated. The residue was chromatographed to yield ketone **1d** (136 mg, 85% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.40; IR (cm^{-1}) 2929, 1708, 1511, 1447, 1245; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.05 (t, 1H), 3.75 (s, 3H), 2.80 (t, J = 7.5 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H), 2.35 (t, J = 7.5 Hz, 2H), 1.95 (q, 2H), 1.65 (s, 3H), 1.55-1.60 (m, 2H), 1.55 (s, 3H); ^{13}C NMR δ u 210.5, 157.9, 133.2, 132.4, 44.6, 42.4, 28.9, 27.4, 23.9; d 129.3, 123.8, 113.9, 55.2, 25.7, 17.7; HRMS calcd for $C_{17}H_{24}O_2$ (M^+) 260.1776, obsd 260.1771.



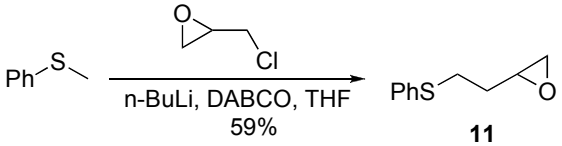
6a-(4-Methoxyphenethyl)-3,3-dimethyl-3,3a,4,5,6,6a-hexahydrocyclopenta[c]pyrazole (2d). Ketone **1d** (75 mg, 0.29 mmol) and tosylhydrazine (1.05 equiv, 58 mg, 0.31 mmol) were stirred in MeOH (2 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in toluene (3 mL), K_2CO_3 (6 equiv, 245 mg, 1.77 mmol) was added and the reaction mixture was heated in a sealed vial at 120℃ (oil bath) for 16 h. After cooling to rt, the reaction mixture was partitioned between CH_2Cl_2 (30 mL) and, sequentially, water (10 mL) and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield diazene **2d** (53 mg, 68% yield) as a pale

yellow oil: TLC R_f (5% MTBE/ CH_2Cl_2) = 0.40; IR (cm^{-1}) 2939, 1511, 1457, 1241; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H), 2.90 (m, 1H), 2.70 (m, 1H), 2.35 (m, 1H), 2.00 (m, 2H), 1.60-1.80 (m, 3H), 1.55 (m, 1H), 1.50 (m, 1H), 1.35 (s, 3H), 1.30 (s, 3H), 0.90 (m, 1H); ^{13}C NMR δ u 157.9, 134.1, 105.9, 91.1, 41.2, 35.9, 31.0, 29.6, 24.7; d 129.1, 113.9, 55.3, 48.4, 29.2, 21.9; HRMS calcd for $C_{17}H_{25}N_2O$ (MH^+) 273.1967, obsd 273.1968.



2d **3d**

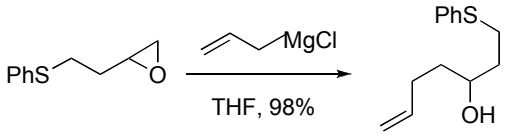
1-(4-Methoxyphenethyl)-6,6-dimethylbicyclo[3.1.0]hexane (3d). A solution of diazene **2d** (43 mg, 0.16 mmol) in dry toluene (6 mL) was photolyzed for 24 h at rt in a Rayonet apparatus (350 nm). The reaction mixture was concentrated and chromatographed to yield cyclopropane **3d** (29 mg, 74% yield) as a colorless oil: TLC R_f (2% MTBE/PE) = 0.47; IR (cm^{-1}) 2929, 1732, 1511, 1246; ^1H NMR δ 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H), 2.55 (m, 2H), 1.85 (m, 3H), 1.70 (m, 3H), 1.55 (m, 1H), 1.40 (m, 1H), 0.95 (s, 3H), 0.90 (s, 3H), 0.70 (d, J = 5.4 Hz, 1H); ^{13}C NMR δ u 157.6, 135.4, 38.3, 36.2, 34.3, 31.6, 27.6, 25.9, 23.4; d 129.2, 113.7, 55.3, 36.1, 23.9, 16.6; HRMS calcd for $C_{17}H_{25}O$ (MH^+) 245.1905, obsd 245.1905.



11

2-(2-(Phenylthio)ethyl)oxirane (11). To a stirred solution of DABCO (1.22 g, 10.9

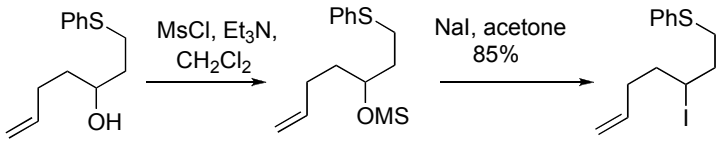
mmol) and thioanisole (13.2 g, 106 mmol) in dry THF (100 mL) was added n-BuLi (106 mmol, 43 mL, 2.46 M in Et_2O) at 0℃. [4]After stirring at room temperature for 2 h, the reaction mixture was cooled to -78℃. Then epichlorohydrin (19.6 g, 212 mmol) was added at -78℃ and the reaction mixture was slowly warmed to rt in 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (50 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the epoxide **11** (11.3 g, 59% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.57; IR (cm^{-1}) 2989, 2923, 1581, 1479; ^1H NMR δ 7.10-7.40 (m, 5H), 3.05 (m, 3H), 2.75 (m, 1H), 2.50 (m, 1H), 1.90 (m, 1H), 1.80 (m, 1H); ^{13}C NMR δ u 136.0, 47.2, 32.3, 30.2; d 129.4, 129.0, 126.2, 51.1; HRMS calcd for $C_{10}H_{12}OS$ (M^+) 180.0609, obsd 180.0607.



11 **12**

1-(Phenylthio)hept-6-en-3-ol (12). To a solution of epoxide **11** (9.1 g, 50.3 mmol) in dry THF (50 mL) was added allyl magnesium chloride (100 mmol, 50 mL, 2 M in THF) at 0℃.[5] The reaction mixture was stirred at 0℃ for 1 h and at rt for another 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (50 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the alcohol **12** (11.2 g, 98% yield) as a colorless oil: TLC R_f (20% MTBE/PE) =

0.32; IR (cm^{-1}) 3417, 2930, 2360, 1641; ^1H NMR δ 7.10-7.40 (m, 5H), 5.80 (m, 1H), 5.00 (q, 2H), 3.75 (bs, 1H), 3.00 (m, 2H), 2.10 (m, 3H), 1.75 (m, 2H), 1.50 (m, 2H); ^{13}C NMR δ u 136.4, 115.0, 36.5, 36.4, 30.1, 30.0; d 138.3, 129.1, 129.0, 126.0, 70.4; HRMS calcd for $C_{13}H_{18}OS$ (M^+) 222.1078, obsd 222.1072.

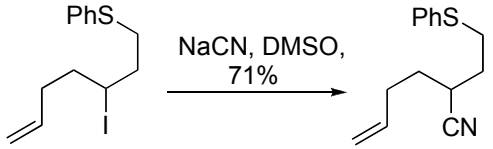


12 **13**

(3-Iodohept-6-enyl)(phenyl)sulfane (13). To a stirred solution of alcohol **12** (11.0 g, 50 mmol) in dry CH_2Cl_2 (50 mL) were sequentially added Et_3N (10.5 g, 103 mmol) and mesyl chloride (8.7 g, 76 mmol) at 0℃. After stirring at rt for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (30 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated to give the crude mesylate.

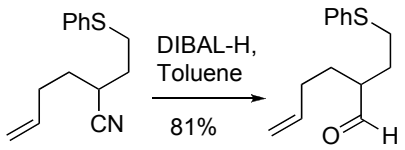
To a stirred solution of the above crude mesylate in acetone (100 mL) was added NaI (22.3 g, 149 mmol) at rt. The reaction mixture was stirred at reflux overnight. After cooling to rt, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (40 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the iodide **13** (14.3 g, 85% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.82; IR (cm^{-1}) 3072, 2923, 1581, 1437; ^1H NMR δ 7.05-7.30 (m, 5H), 5.65 (m, 1H), 4.95 (q, 2H), 4.10 (m, 1H), 3.10 (m, 1H), 2.90 (m, 1H), 2.15 (m, 1H), 2.05 (m,

2H), 1.85 (m, 2H), 1.65 (m, 1H); ^{13}C NMR δ u 134.7, 114.9, 38.5, 38.4, 32.7, 32.4; d 135.5, 128.8, 127.9, 125.2, 35.4; HRMS calcd for $C_{13}H_{17}SI$ (M+) 332.0096, obsd 332.0081.



13 **14**

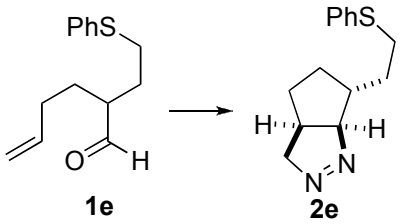
2-(2-(Phenylthio)ethyl)hex-5-enenitrile (14). To a solution of iodide **13** (2.4 g, 7.1 mmol) in DMSO (30 mL) was added NaCN (3.6 g, 73.5 mmol) at rt.[6] After stirring at rt overnight, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield nitrile **14** (1.2 g, 71% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.55; IR (cm^{-1}) 3074, 2931, 2238, 1641; ^{1}H NMR δ 7.20-7.50 (m, 5H), 5.85 (m, 1H), 5.05 (m, 2H), 3.20 (m, 1H), 3.00 (m, 1H), 2.85 (m, 1H), 2.15-2.45 (m, 2H), 1.55-2.00 (m, 4H); ^{13}C NMR δ u 134.6, 121.0, 116.2, 31.2, 30.9, 30.7, 29.4; d 135.8, 129.6, 128.8, 126.3, 27.7.



14 **1e**

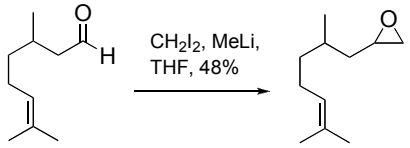
2-(2-(Phenylthio)ethyl)hex-5-enal (1e). To a stirred solution of nitrile **14** (1.0 g, 4.3 mmol) in dry toluene (25 mL) was added DIBAL-H (13 mmol, 13 mL, 1 M in pentane) at -78℃.[7] After stirring at -78℃ for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and then partitioned between CH_2Cl_2 and, sequentially, water

and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give aldehyde **1e** (817 mg, 81% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.62; IR (cm^{-1}) 3580, 2090, 1642; ^1H NMR δ 9.65 (s, 1H), 7.15-7.45 (m, 5H), 5.75 (m, 1H), 5.05 (q, 2H), 2.90 (m, 2H), 2.50 (m, 1H), 2.05 (m, 3H), 1.80 (m, 2H), 1.55 (m, 1H); ^{13}C NMR δ u 135.4, 115.4, 30.8, 30.6, 27.8, 27.6; d 203.6, 137.0, 129.5, 120.0, 125.8, 49.7; HRMS calcd for $C_{14}H_{18}OS$ (M^+) 234.1078, obsd 234.1078.



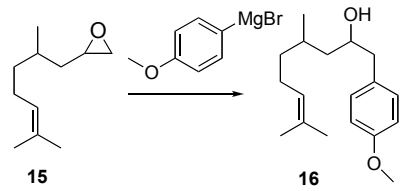
6-(2-(Phenylthio)ethyl)-3,3a,4,5,6,6a-hexahydrocyclopenta[c]pyrazole (2e). Aldehyde **1e** (110 mg, 0.47 mmol) and tosylhydrazine (1.07 equiv, 95 mg, 0.51 mmol) were stirred in MeOH (3 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in toluene (3 mL), K_2CO_3 (6 equiv, 395 mg, 2.9 mmol) was added and the reaction mixture was heated in a sealed vial at 120℃ (oil bath) for 13 h. After cooling to room temperature, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield diazene **2e** (105 mg, 91% yield, 6:1 mixture of two isomers based on ^1H NMR) as a pale yellow oil: TLC R_f (5% MTBE/ CH_2Cl_2) = 0.41; IR (cm^{-1}) 3056, 2947, 2863, 1582, 1478; ^1H NMR δ 7.10-7.50 (m, 5H), 4.20-5.00 (m, 3H), 3.05-3.40 (m, 2H), 2.40 (m, 2H), 1.60-2.05 (m, 3H), 1.50 (m, 1H), 1.30 (m, 1H), 1.05 (m, 1H); ^{13}C NMR(major isomer) δ u 136.5, 83.7,

33.9, 32.3, 32.2, 30.2; d 129.3, 129.0, 126.0, 100.2, 42.8, 34.0; HRMS calcd for $C_{14}H_{19}N_2S$ (MH^+) 247.1269, obsd 247.1269.



15

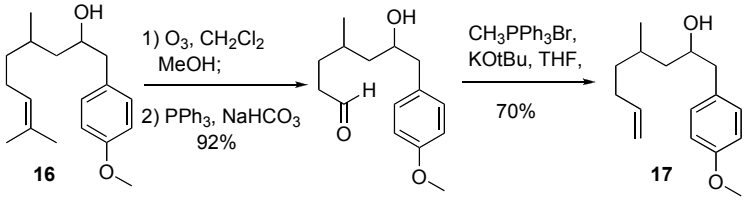
2-(2,6-Dimethylhept-5-enyl)oxirane (15). To a stirred solution of aldehyde (6.18 g, 40 mmol) and diiodomethane (17.7 g, 66 mmol) in THF(150 mL) was added dropwise methyl lithium (80 mmol) over 30 min at 0℃. The reaction mixture was stirred at 0℃ for 1 h and at rt for 3 h. Then resulting mixture was quenched with ice water and partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield epoxide **15** (3.22 g, 48% yield) as a colorless oil: TLC R_f (10% MTBE/PE) = 0.60; IR (cm^{-1}) 2957, 2091, 1643, 1457; ^{1}H NMR δ 5.05 (m, 1H), 2.90 (m, 1H), 2.75 (m, 1H), 2.60 (m, 1H), 2.00 (m, 2H), 1.70 (s, 3H), 1.60 (s, 3H), 1.10-1.55 (m, 4H), 0.90-1.05 (m, 4H); ^{13}C NMR δ u 131.3, 50.5, 47.5, 46.9, 39.8, 37.3, 36.9, 25.5, 25.4; d 124.5, 51.1, 51.0, 31.1, 30.6, 25.8, 20.1, 19.5, 17.8.



15 16

1-(4-Methoxyphenyl)-4,8-dimethylnon-7-en-2-ol (16). To a stirred solution of (*p*-methoxyphenyl)magnesium bromide {freshly prepared with Mg (2.42 g, 101 mmol), *p*-bromo anisole (10.7 g, 57.5 mmol) and I_2 in dry THF (30 mL)} in dry THF was added

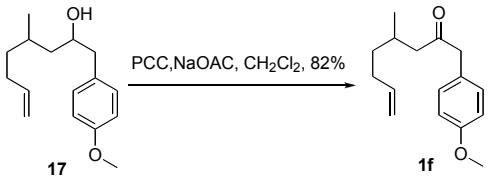
CuI (730 mg, 3.83 mmol) at 0℃. The mixture was stirred for 5 min at 0℃ and then the solution of epoxide **15** (3.2 g, 19 mmol) in dry THF (5 mL) was added dropwise over 5 min. After stirring overnight at rt, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alkene **16** (2.84 g, 54% yield, a 1:1 mixture of diastereomers) as a colorless oil: TLC R_f (20%MTBE/PE) = 0.42; IR (cm^{-1}) 3417, 2920, 1512, 1247; ^1H NMR δ 7.10 (m, 2H), 6.85 (m, 2H), 5.10 (m, 1H), 3.85 (bs, 1H), 3.75 (s, 3H), 2.50-2.80 (m, 2H), 1.95 (m, 2H), 1.65 (s, 3H), 1.60 (s, 3H), 1.10-1.55 (m, 6H), 0.90 (d, J = 6.7 Hz, 3H); ^{13}C NMR δ u 158.3, 131.3, 131.2, 130.6, 130.5, 44.3, 44.2, 43.9, 43.4, 37.9, 36.7, 25.5, 25.4; d 130.6, 130.4, 124.8,114.0, 70.8, 70.4, 55.3, 29.4, 29.0, 25.7, 20.3, 19.1, 17.8; HRMS calcd for $C_{18}H_{28}O_2(M^+)$ 276.2089, obsd 276.2084.



1-(4-Methoxyphenyl)-4-methyloct-7-en-2-ol (17). Ozone was passed through a stirred solution of alkene **16** (1.90 g, 6.88 mmol) in dry CH_2Cl_2 (5 mL) and MeOH (15 mL) at -78℃. After stirring at -78℃ for 8 min, the color of the reaction mixture changed to pale blue. N_2 was then passed through to remove the excess ozone. PPh_3 (3.8 g) and $NaHCO_3$ (3.8 g) were added at -78℃. The reaction mixture was warmed to rt and stirred for an additional hour. Then the mixture was partitioned between CH_2Cl_2 and, sequentially,

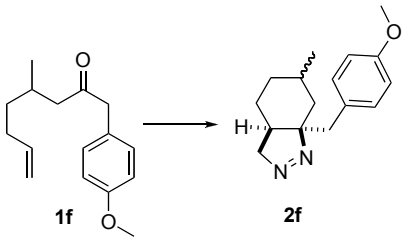
water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield aldehyde (1.58 g, 92% yield) as a colorless oil.

To the mixture of methyl triphenylphosphonium bromide (4.3 g, 12 mmol) and KO*t*Bu (1.0 g, 8.9 mmol) was added dry THF (15 mL) at rt. After stirring at rt for 30 min, a solution of aldehyde (758 mg, 3.03 mmol) in dry THF (2 ml) was added and the reaction mixture was stirred for another 3 h at rt. The reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) and then partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alkene **17** (525 mg, 70% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.44; IR (cm^{-1}) 2924, 1640, 1512, 1460; ^1H NMR δ 7.10 (m, 2H), 6.85 (m, 2H), 5.80 (m, 1H), 4.95 (q, 2H), 3.85 (bs, 1H), 3.80 (s, 3H), 2.75 (m, 1H), 2.55 (m, 1H), 2.05 (m, 2H), 1.65 (m, 1H), 1.35-1.55 (m, 3H), 1.10-1.25 (m, 2H), 0.90 (d, J = 6.7 Hz, 3H); ^{13}C NMR δ u 158.3, 130.5, 130.4, 114.3, 114.2, 44.3, 44.1, 43.9, 43.4, 37.0, 35.7, 31.3, 31.2; d 139.2, 139.1, 130.4, 114.0, 70.7, 70.4, 55.3, 29.2, 28.9, 20.2, 19.1; HRMS calcd for C16H24O2 (M+) 248.1776, obsd 248.1775.



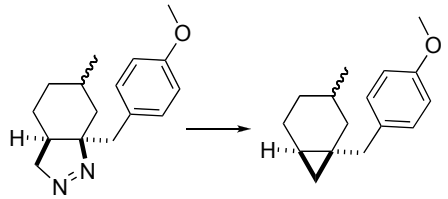
1-(4-Methoxyphenyl)-4-methyloct-7-en-2-one (1f). PCC (1.32 g, 6.12 mmol) and NaOAc (1.31 g) were suspended in dry CH_2Cl_2 (10 mL) at rt. After stirring for 5 min at

room temperature, alcohol **17** (505 mg, 2.04 mmol) was added in one portion. The reaction mixture was stirred at rt for 6 h. Et_2O (25 mL) was added and the mixture was stirred vigorously for 1 h at rt. The mixture was filtered with celite, the filtrate was concentrated and the residue was chromatographed to yield ketone **1f** (409 mg, 82% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.46; IR (cm^{-1}) 2927, 1709, 1609, 1512; ^1H NMR δ 7.10 (d, J = 8.3 Hz, 2H), 6.85 (d, J = 8.3 Hz, 2H), 5.75 (m, 1H), 4.95 (q, 2H), 3.80 (s, 3H), 3.60 (s, 2H), 2.40 (m, 1H), 2.25 (m, 1H), 2.00 (m, 3H), 1.30 (m 1H), 1.20 (m, 1H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR δ u 208.5, 158.6, 126.3, 114.1, 49.7, 49.1, 35.9, 31.2; d 138.7, 130.5, 113.7, 55.2, 28.6, 19.6; HRMS calcd for $C_{16}H_{22}O_2$ (M+) 246.1620, obsd 246.1623.



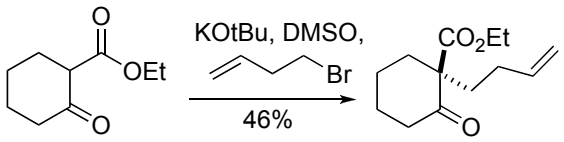
7a-(4-Methoxybenzyl)-6-methyl-3a,4,5,6,7,7a-hexahydro-3H-indazole (2f). Ketone **1f** (98 mg, 0.40 mmol) and tosylhydrazine (1.02 equiv, 77 mg, 0.41 mmol) were stirred in MeOH (2 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in dry toluene (2 mL), K_2CO_3 (6 equiv, 345 mg, 2.5 mmol) was added and the reaction mixture was heated in a sealed vial at 120℃ (oil bath) for 24 h. After cooling to rt, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the diastereomeric mixture of

diazenes **2f** (74 mg, 72% yield) as a pale yellow oil: TLC R_f (5% MTBE/ CH_2Cl_2) = 0.41; IR (cm^{-1}) 2923, 2862, 1611, 1511, 1455; ^1H NMR δ 6.95-7.10 (m, 2H), 6.80 (m, 2H), 4.25-4.40 (m, 1H), 3.50-3.80 (m, 4H), 2.50-3.00 (m, 2H), 1.20-2.00 (m, 6H), 0.90 (m, 3H), 0.45-0.80 (m, 1H); ^{13}C NMR δ u 158.4, 158.3, 129.4, 128.5, 92.4, 89.6, 82.8, 78.0, 43.3, 41.1, 40.0, 38.9, 30.3, 29.1, 28.7, 22.0; d 131.4, 131.3, 113.7, 113.6, 55.2, 33.5, 33.4, 27.2, 27.0, 22.6, 22.4; HRMS calcd for $C_{16}H_{23}N_2O$ (MH^+) 259.1810, obsd 259.1804.



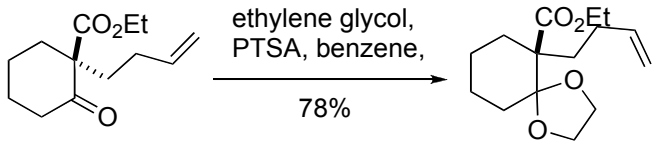
2f **3f**

1-(4-Methoxybenzyl)-3-methylbicyclo[4.1.0]heptane (3f). A solution of diazenes **2f** (53 mg, 0.21 mmol) in toluene was photolyzed for 24 h at rt in a Rayonet apparatus (350 nm). The reaction mixture was concentrated and chromatographed to yield the diastereomeric mixture of cyclopropanes **3f** (38 mg, 80% yield) as a colorless oil: TLC R_f (CH_2Cl_2) = 0.75; IR (cm^{-1}) 2913, 2849, 1611,1512, 1457; ^1H NMR δ 7.05-7.20 (m, 2H), 3.85 (s, 3H), 2.40-3.30 (m, 2H), 0.50-2.20 (m, 12H), 0.25 (m, 1H); ^{13}C NMR δ u 157.8, 133.0, 132.7, 46.3, 46.1, 38.3, 37.1, 31.7, 28.2, 24.5, 24.2, 17.3, 16.6; d 130.1, 130.0, 129.8, 129.3, 113.6, 113.5.113.4, 55.3, 55.2, 29.5, 29.3, 27.0, 26.7, 22.5, 22.4, 21.8, 18.4, 16.5; HRMS calcd for $C_{16}H_{22}O$ (M^+) 230.1671, obsd 230.1673.



18

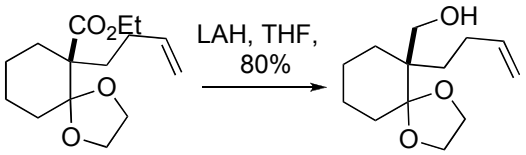
Ethyl 1-(but-3-enyl)-2-oxocyclohexanecarboxylate (18). The β-ketoester (5.16 g, 30.3 mmol) was added, over a period of 10 min, to a stirred solution of *t*-BuOK (3.04 g, 30.5 mmol) in dry DMSO (100 mL).[8] After 1.5 h, 4-bromo-1-butene (1.5 equiv, 6.03 g, 44.5 mmol) was added over a period of 5 min. After 20 h at rt, the reaction mixture was partitioned between Et_2O and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alkene **18** (3.12 g, 46% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.56; ^{1}H NMR δ 5.75 (m, 1H), 4.95 (q, 2H), 4.15 (m, 2H), 2.35-2.55 (m, 3H), 1.85-2.05 (m, 4H), 1.55-1.80 (m, 4H), 1.45-1.50 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR δ u 207.7, 171.8, 114.6, 61.1, 60.5, 41.0, 36.1, 33.8, 28.5, 27.6, 22.5; d 138.0, 14.1.



18 **19**

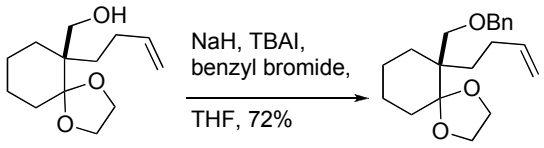
Ethyl 2-(but-3-enyl)-1,7-dioxospiro[5, 4]decan-2-carboxylate (19). A solution of ketone **18** (3.12 g, 13.9 mmol), ethylene glycol (4.45 g, 71.8 mmol), and p-toluenesulfonic acid (173 mg, 1.1 mmol) in benzene (150 mL) was heated under reflux for 12 h, using a Dean-Stark trap. Most of the solvent was then distilled off and the reaction mixture was partitioned between Et_2O (300 mL) and, sequentially, $NaHCO_3$ (100 mL) and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated.

The residue was chromatographed to yield ketal **19** (2.91g, 78% yield) as a colorless oil: TLC R_f (5% MTBE/CH_2Cl_2) = 0.61; IR (cm^{-1}) 1722, 1451, 1201, 1093; ^{1}H NMR δ 5.70 (m, 1H), 4.85 (q, 2H), 4.10 (m, 2H), 3.85 (m, 4H), 2.05 (m, 1H), 1.95 (m, 2H), 1.60-1.80 (m, 2H), 1.55 (m, 3H), 1.35-1.50 (m, 3H), 1.20—1.30 (m, 1H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ u 173.9, 114.4, 111.1, 64.8, 64.6, 60.3, 54.2, 32.1, 30.4, 29.6, 28.9, 23.1, 20.7; d 138.5, 14.3; HRMS calcd for $C_{15}H_{24}O_4Na$ (MNa^+) 291.1572, obsd 291.1570.



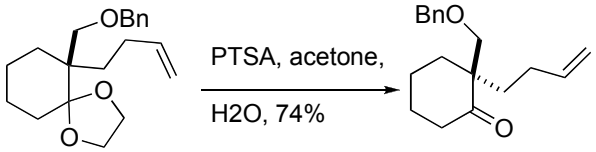
19 **20**

2-(Hydroxymethyl)-2-(but-3-enyl)-1,7-dioxospiro[5, 4]decane (20). $LiAlH_4$ (2.0 equiv, 422.6 mg, 11.1 mmol) was added in five portions, over a period of 5 min, to a solution of ester **19** (1.52 g, 5.65 mmol) in dry THF (20 mL) at 0℃ and the mixture was stirred at this temperature for 0.5 h and at rt for 7 h. Excess $LiAlH_4$ was destroyed with saturated aqueous NH_4Cl (30 mL) and the reaction mixture was partitioned between Et_2O and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield alcohol **20** (1.02 g, 80% yield) as a colorless oil: TLC R_f (5% MTBE/CH_2Cl_2) = 0.46; IR (cm^{-1}) 3538, 1702, 1451, 1083; ^{1}H NMR δ 5.75 (m, 1H), 5.00 (q, 2H), 3.90 (m, 4H), 3.75 (d, J = 10 Hz, 1H), 3.35 (d, J = 10 Hz, 1H), 2.70 (bs, 1H), 1.85-2.10 (m, 2H), 1.55-1.70 (m, 3H), 1.45-1.55 (m, 4H), 1.30-1.45 (m, 3H); ^{13}C NMR δ u 114.1,114.0, 65.0, 64.5, 64.1, 44.1, 30.1, 29.4, 28.7, 27.3, 23.2, 20.2; d 139.5; HRMS calcd for $C_{13}H_{23}O_3$ (MH^+) 227.1647, obsd 227.1650.



20 **21**

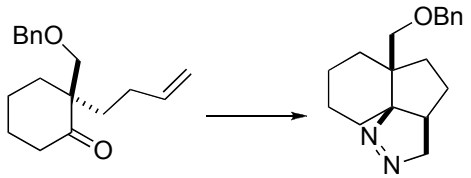
2-(Benzyloxymethyl)-2-(but-3-enyl)-1,7-dioxospiro[5, 4]decane (21). To a suspension of NaH (60%, 185 mg, 4.62 mmol) and TBAI (136 mg, 0.37 mmol) in THF (8 mL) was added a solution of alcohol **20** (805 mg, 3.56 mmol) in THF (1 mL) at 0℃. To this reaction mixture was added a solution of benzyl bromide (715 mg, 4.18 mmol) in DMF (1 mL) at 0℃, and the reaction mixture was stirred at rt for 12 h. The reaction was quenched with MeOH (0.1 mL). Then the reaction mixture was partitioned between EtOAc (90 mL) and, sequentially, saturated aqueous NH_4Cl (20 mL) and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield benzyl ether **21** (806 mg, 72% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.63; IR (cm^{-1}) 1717, 1638, 1451, 1088; ^1H NMR δ 7.10-7.35 (m, 5H), 5.75 (m, 1H), 4.85 (q, 2H), 4.40 (m, 2H), 3.80 (m, 4H), 3.45 (d, J = 9.2 Hz, 1H), 3.30 (d, J = 9.2 Hz, 1H), 1.90-2.10 (m, 2H), 1.70 (m, 1H), 1.25-1.65 (m, 9H); ^{13}C NMR δ u 138.9, 113.5, 112.3, 73.4, 71.8, 64.5, 44.9, 31.3, 31.2, 30.7, 28.6, 23.4, 20.4; d 140.3, 128.3, 127.8, 127.6; HRMS calcd for $C_{20}H_{28}O_3Na(MNa^+)$ 339.1936, obsd 339.1932.



21 **1g**

2-(Benzyloxymethyl)-2-(but-3-enyl)cyclohexanone (1g). A solution of ketal **21** (1.42 g, 4.49 mmol) and *p*-toluenesulfonic acid (74 mg, 0.47 mmol) in acetone/H_2O 2:1 (15 mL)

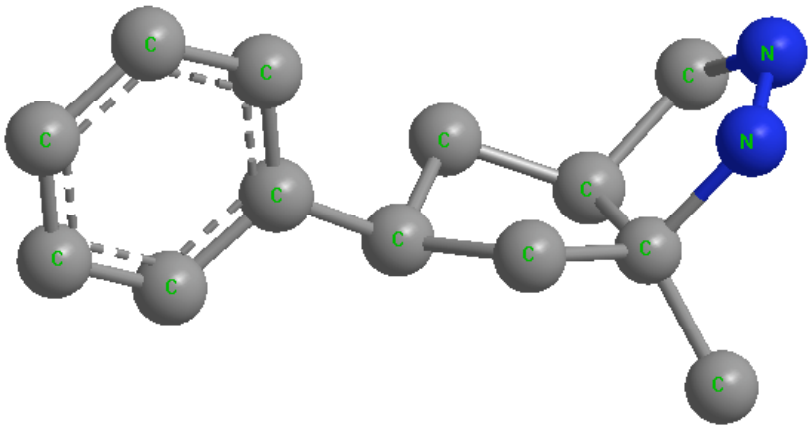
was heated under reflux for 4 h. After cooling to rt, the reaction mixture was partitioned between Et_2O and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield ketone **1g** (908 mg, 74% yield) as a colorless oil: TLC R_f (20% MTBE/PE) = 0.57; IR (cm^{-1}) 1702, 1447, 1098; ^1H NMR δ 7.10-7.35 (m, 5H), 5.70 (m, 1H), 4.85 (q, 2H), 4.45 (m, 2H), 3.50 (d, J = 9.8 Hz, 1H), 3.35 (d, J = 9.8 Hz, 1H), 2.30 (m, 1H), 2.20 (m, 1H), 1.80-1.95 (m, 3H), 1.50-1.80 (m, 7H); ^{13}C NMR δ u 214.2, 138.4, 114.6, 73.3, 72.7, 52.6, 39.5, 35.2, 32.4, 28.1, 27.1, 20.8; d 138.5, 128.3, 127.5; HRMS calcd for $C_{18}H_{24}O_4Na(MNa^+)$ 327.1572, obsd 327.1586.



1g **2g**

5a-(Benzyloxymethyl)-3a,4,5,5a,6,7,8,9-octahydro-3H-indeno[1-c]pyrazole (2g). Ketone **1g** (73 mg, 0.27 mmol) and tosylhydrazine (1.03 equiv, 55 mg, 0.29 mmol) were stirred in MeOH (2 mL) at rt overnight. The MeOH was removed under reduced pressure, the crude hydrazone was redissolved in toluene (2 mL), K_2CO_3 (6 equiv, 232 mg, 1.68 mmol) was added and the reaction mixture was heated in a sealed vial at 120℃ (oil bath) for 24 h. After cooling to rt, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, water and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield (52 mg, 68% yield) as a pale yellow oil: TLC R_f (5%MTBE/ CH_2Cl_2) = 0.50; IR (cm^{-1}) 2935, 2859, 1642, 1452; ^1H

NMR δ 7.20-7.40 (m, 5H), 4.45-4.65 (m, 3H), 4.35 (dd, *J* = 7.5, 17.9 Hz, 1H), 4.25 (d, *J* = 9.4 Hz, 1H), 3.75 (d, *J* = 9.4 Hz, 1H), 2.25 (t, *J* = 8.2 Hz, 1H), 2.10 (d, *J* = 12.4 Hz, 1H), 1.90-2.05 (m, 2H), 1.80 (m, 1H), 1.55 (m, 3H), 1.15-1.35 (m, 2H), 1.05 (m, 2H), 0.95 (m, 1H); ^{13}C NMR δ u 139.1, 105.6, 84.5, 73.7, 73.4, 48.1, 36.3, 30.9, 29.2, 26.8, 23.5, 21.4; d 128.3, 127.3, 127.0, 37.0; HRMS calcd for $C_{18}H_{25}N_2O$ (MH^+) 285.1967, obsd 285.1957.



X-ray of 2a

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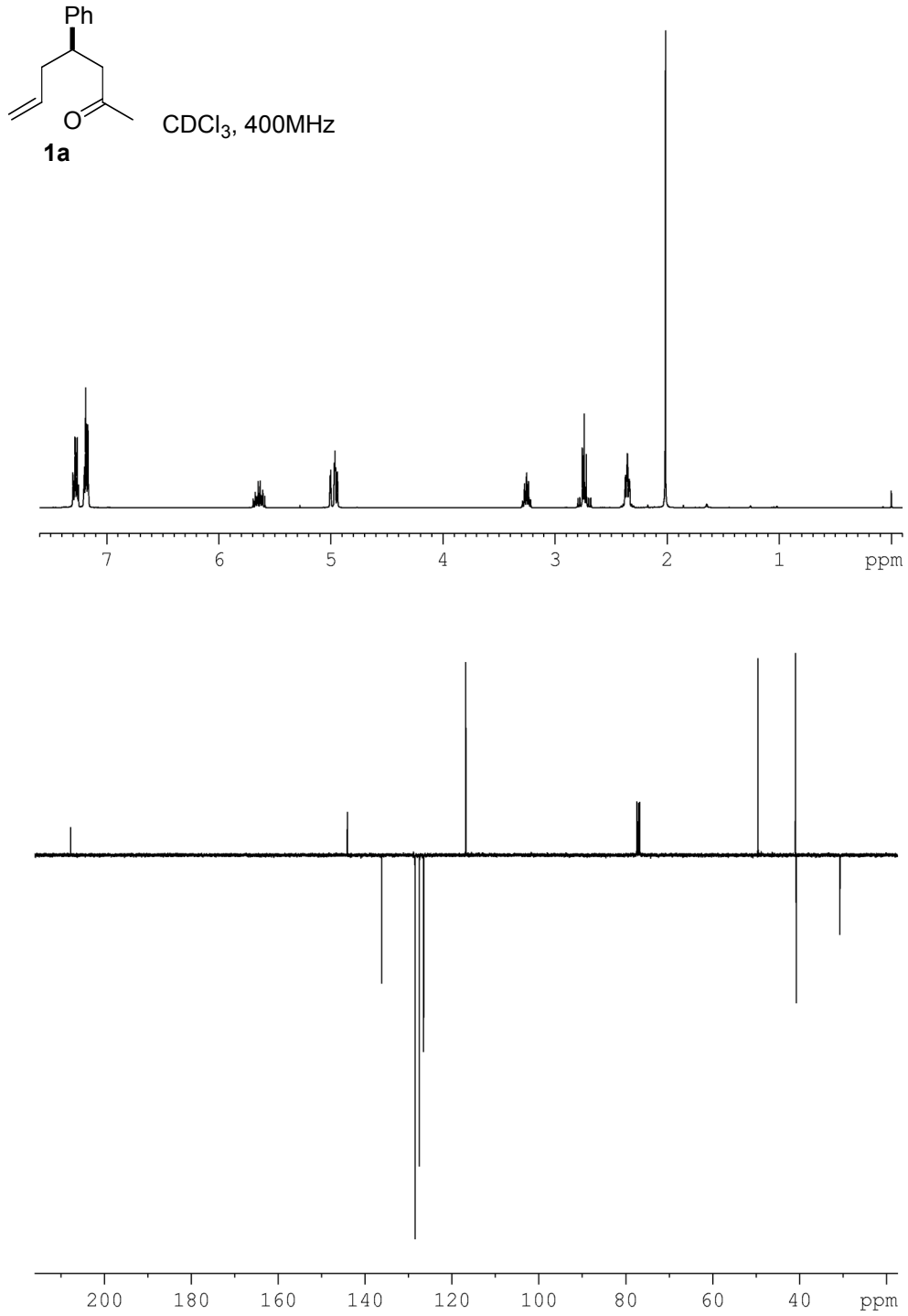
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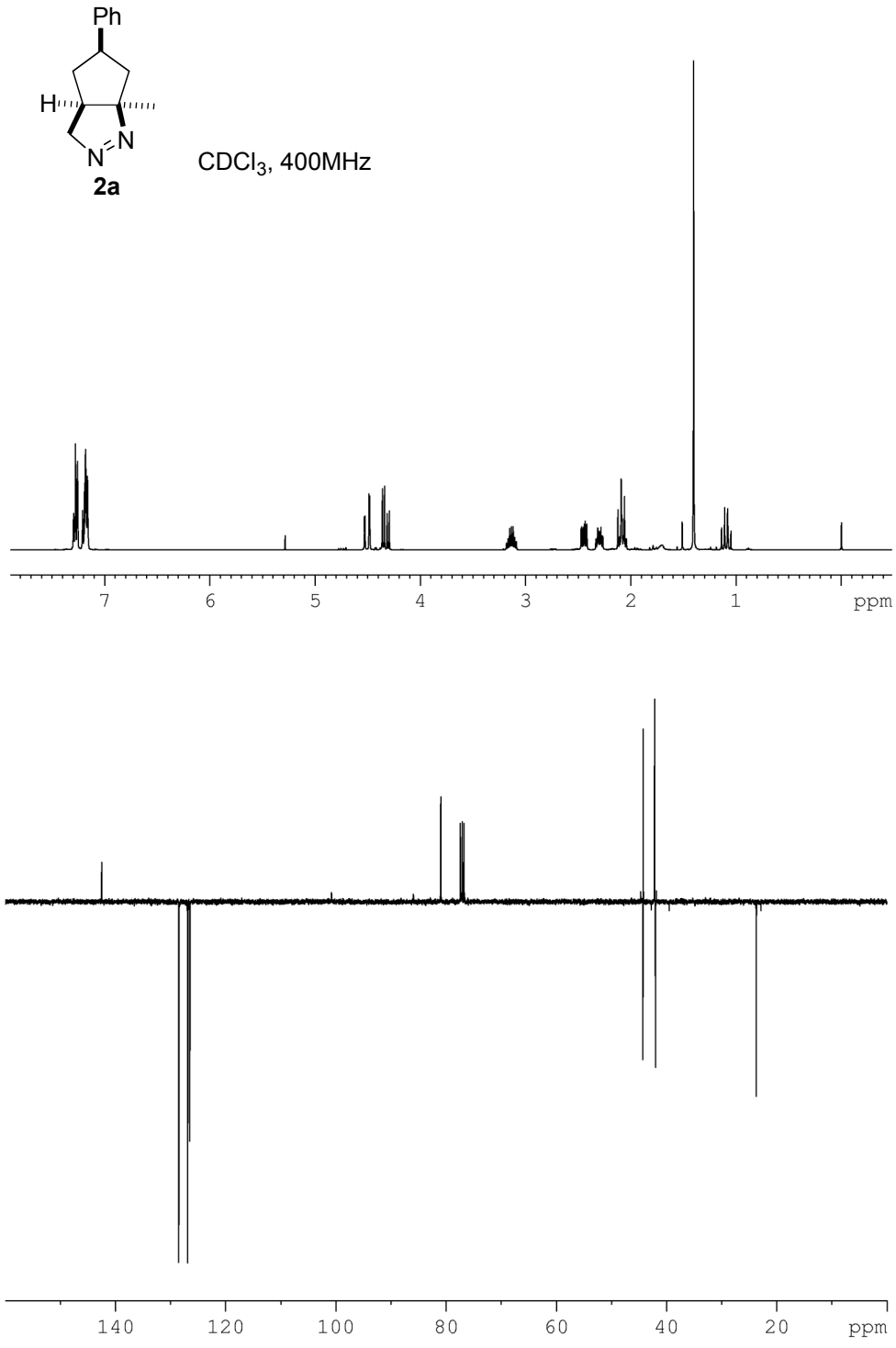
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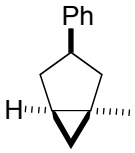

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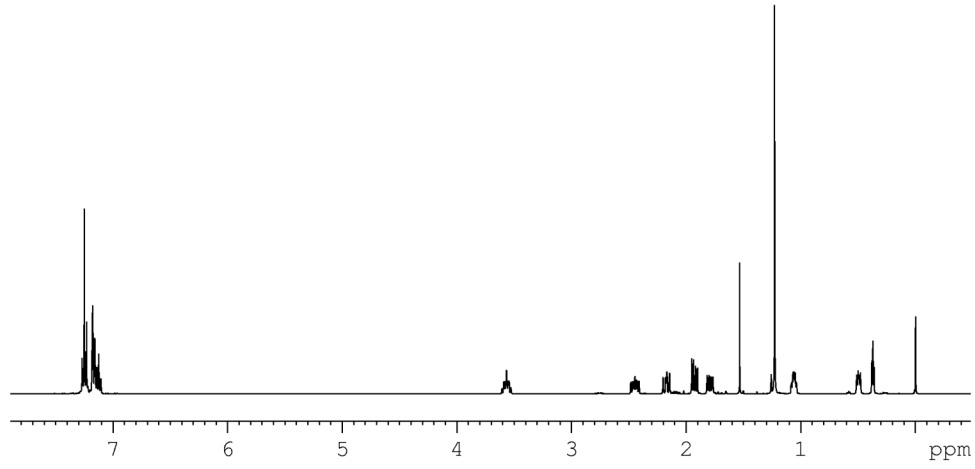

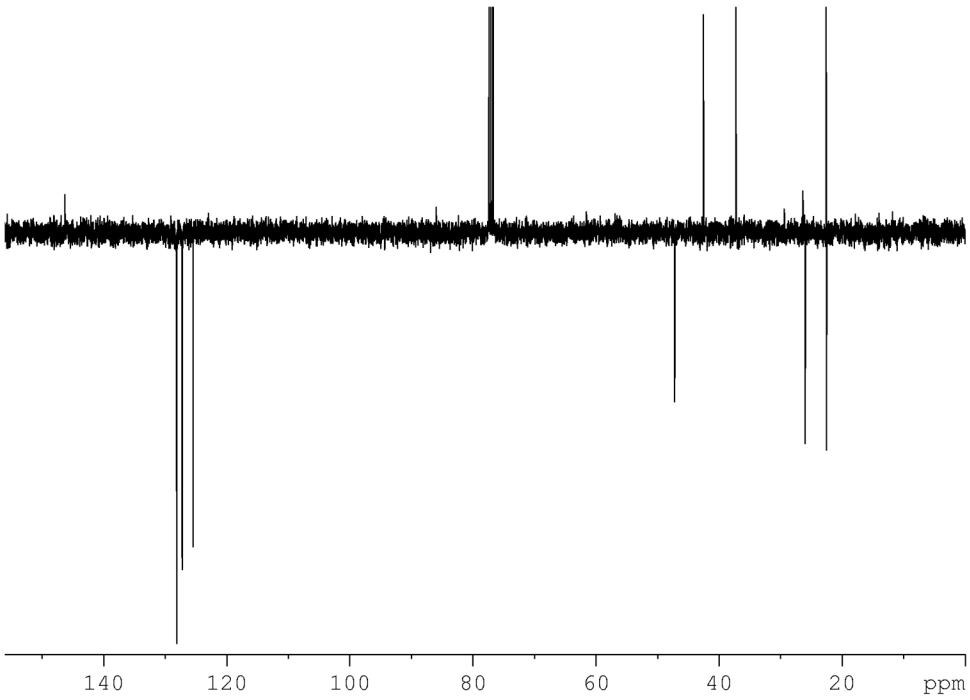

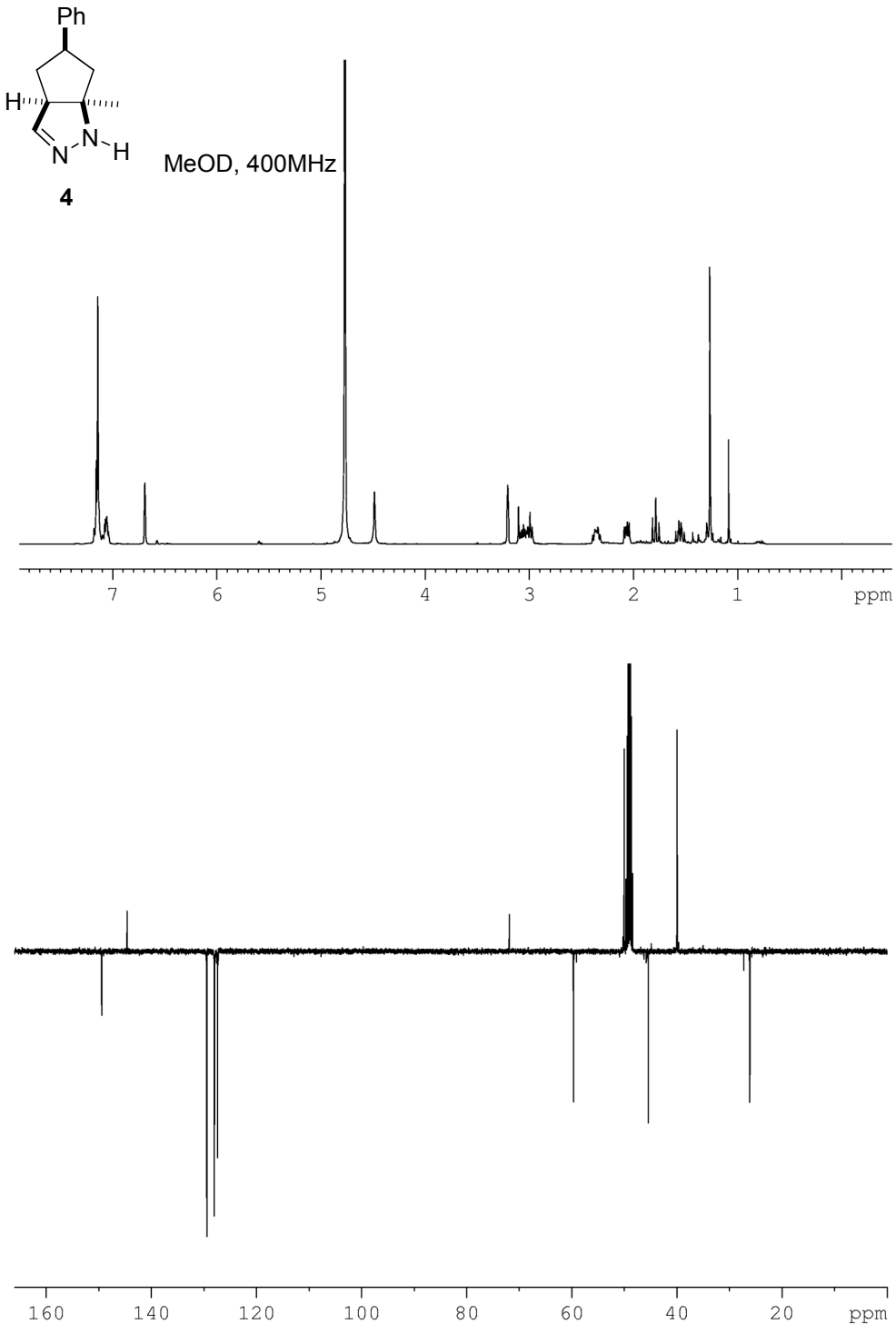
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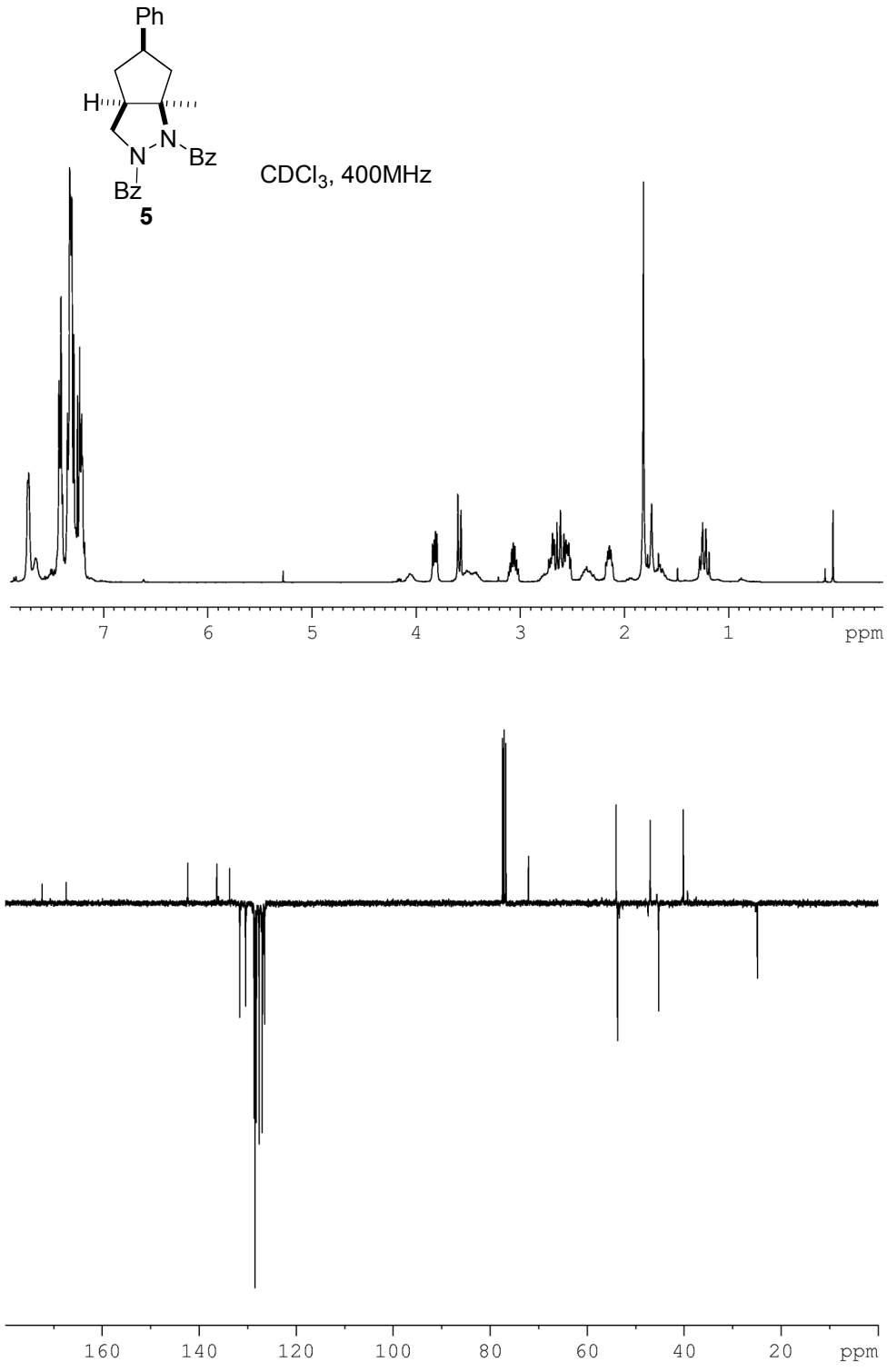
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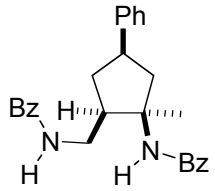

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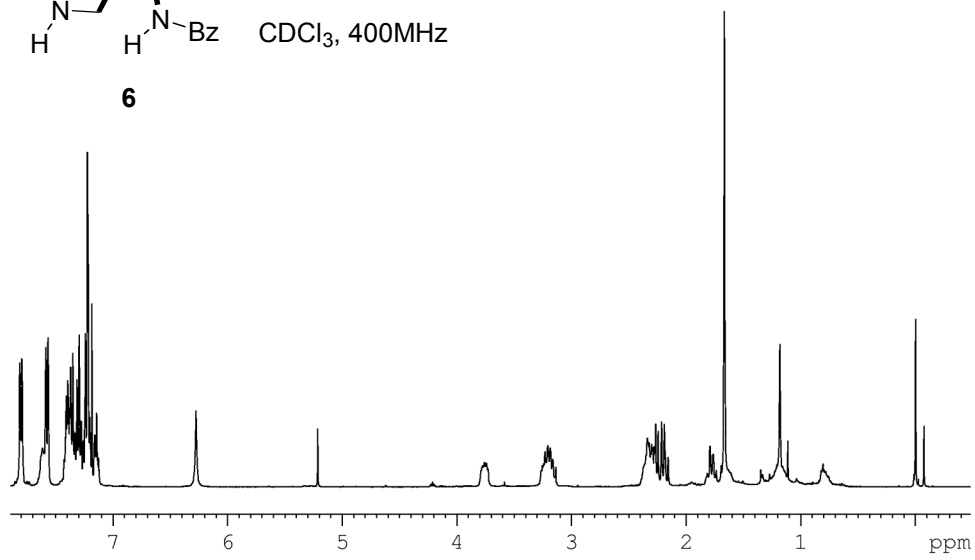

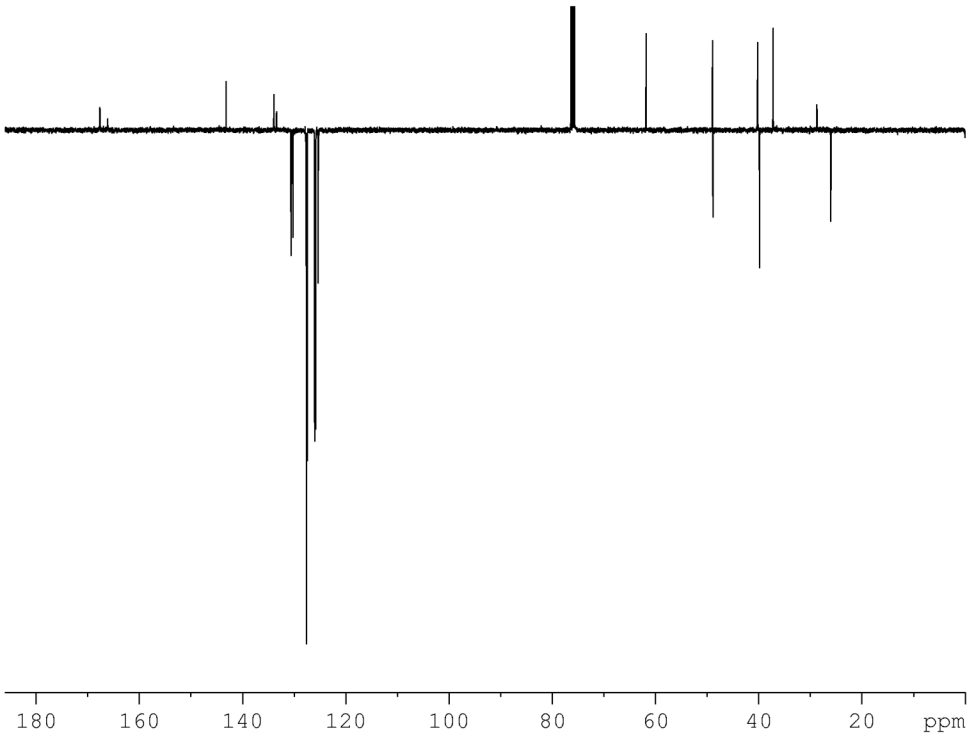

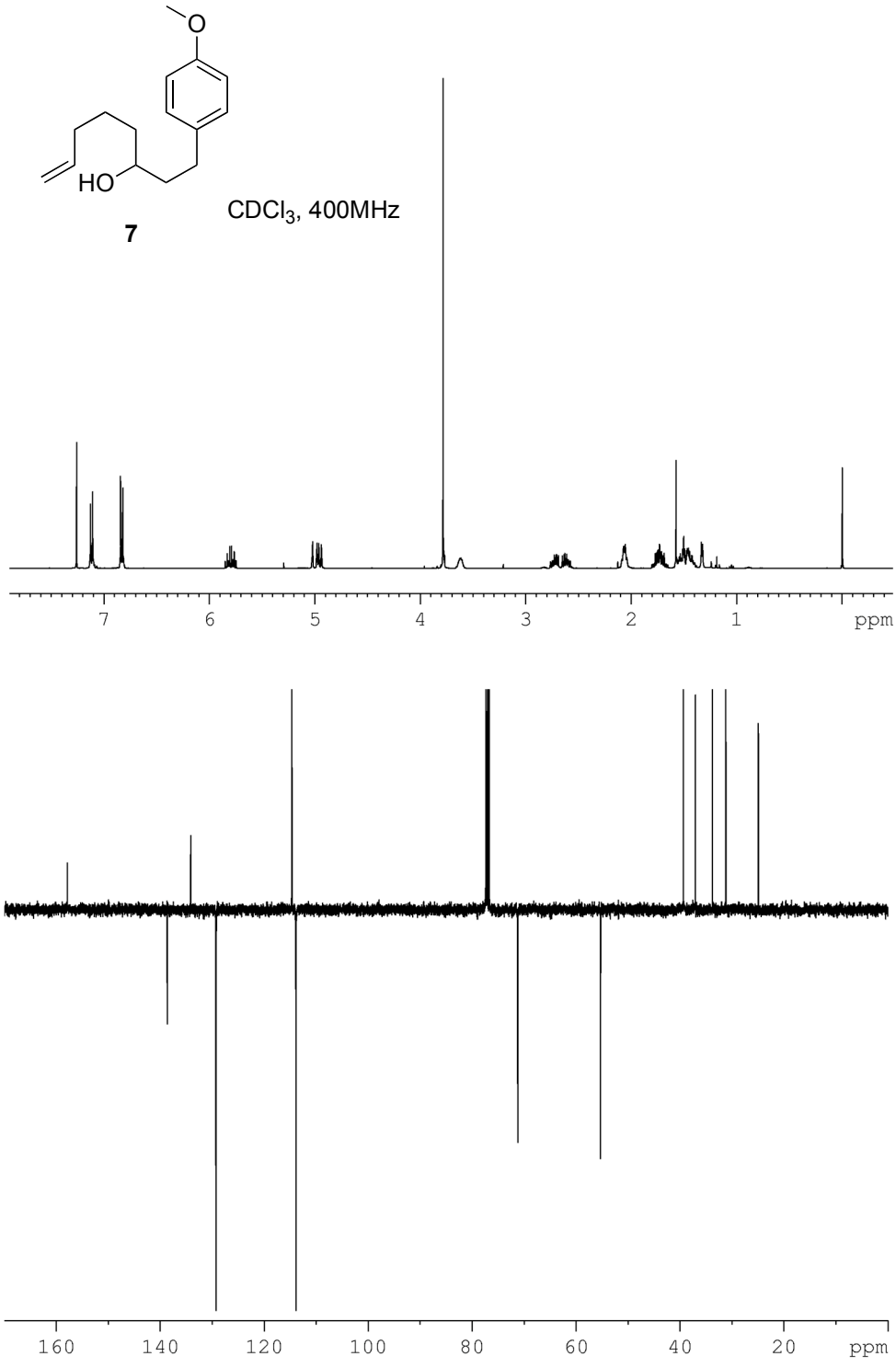
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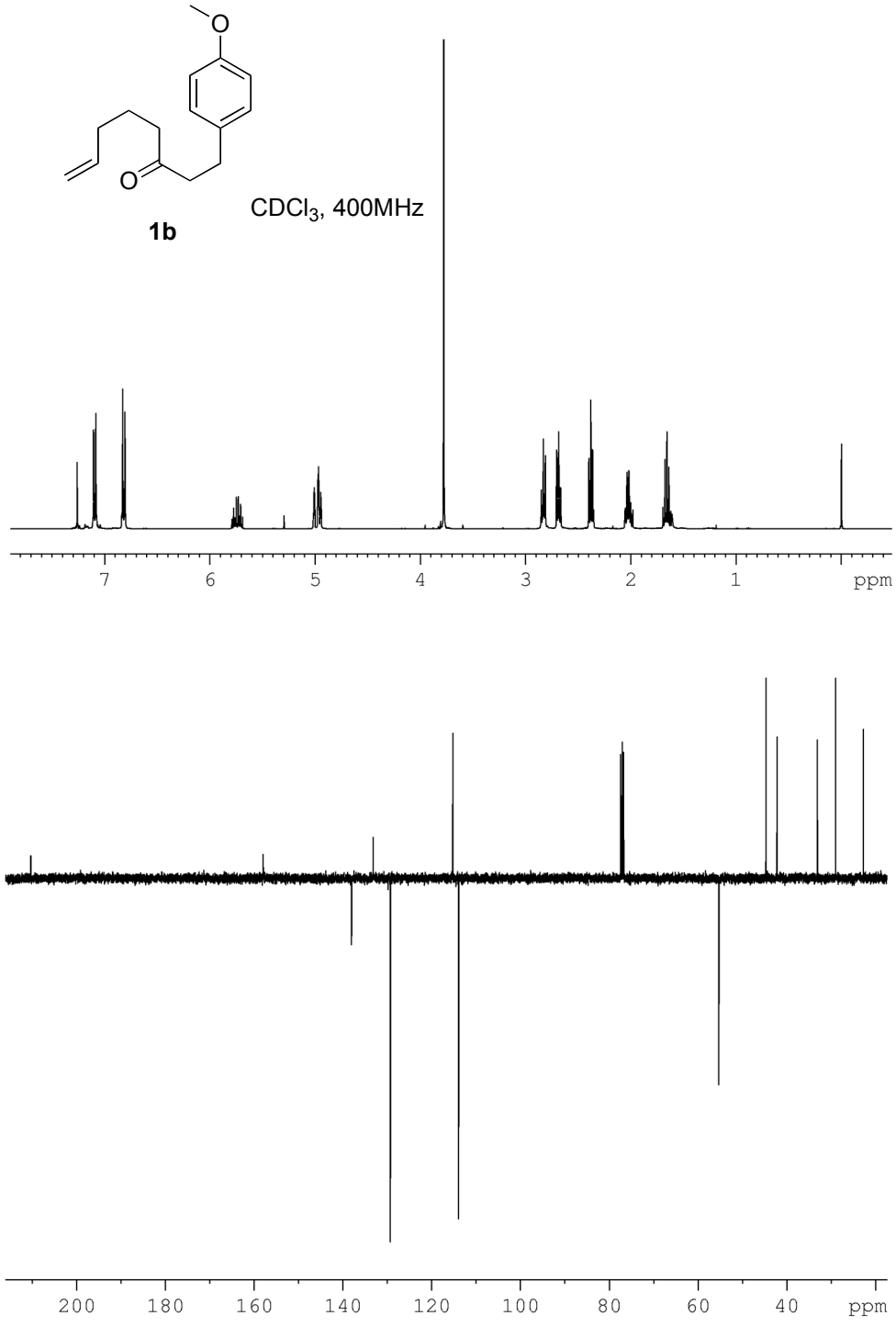
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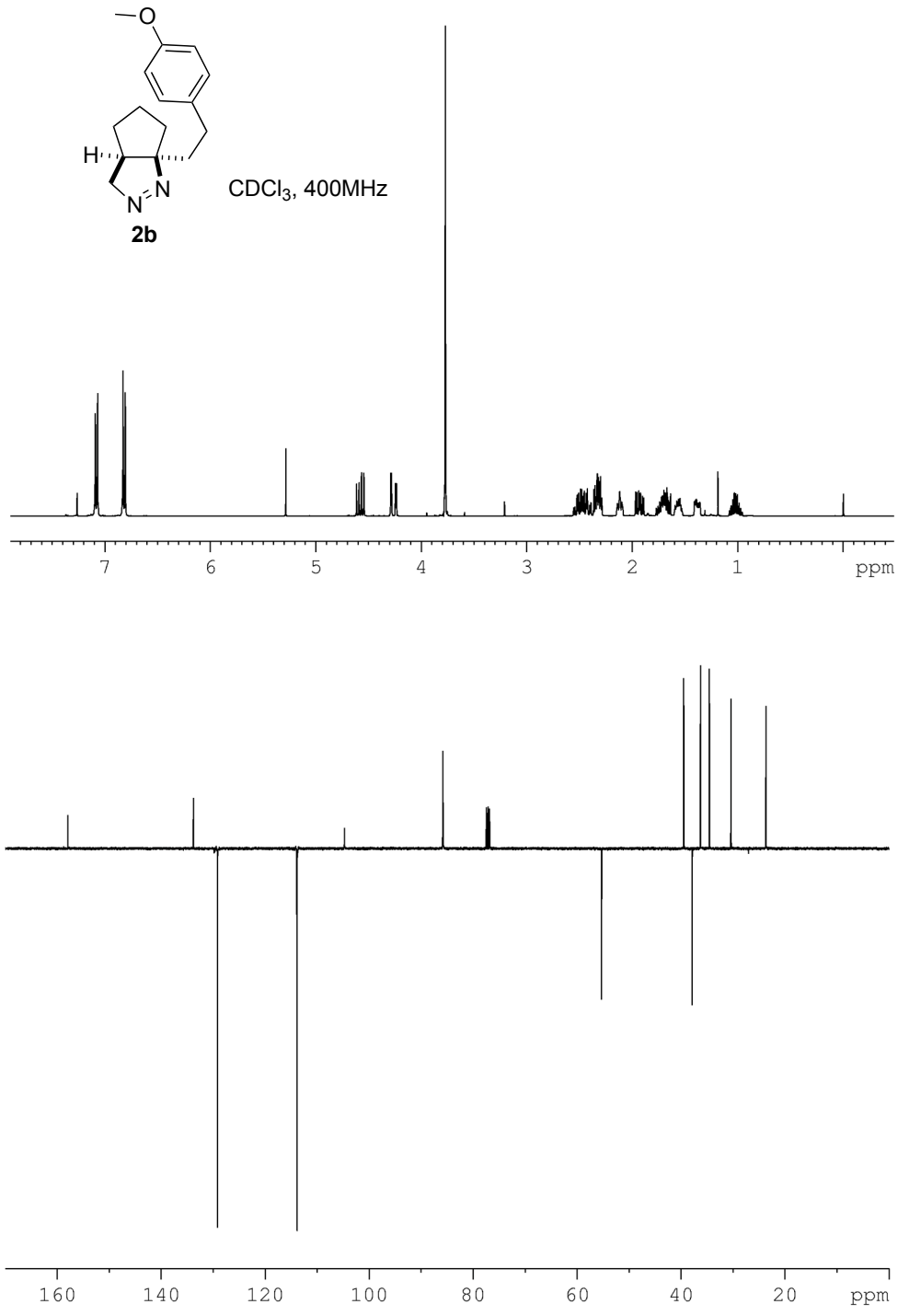
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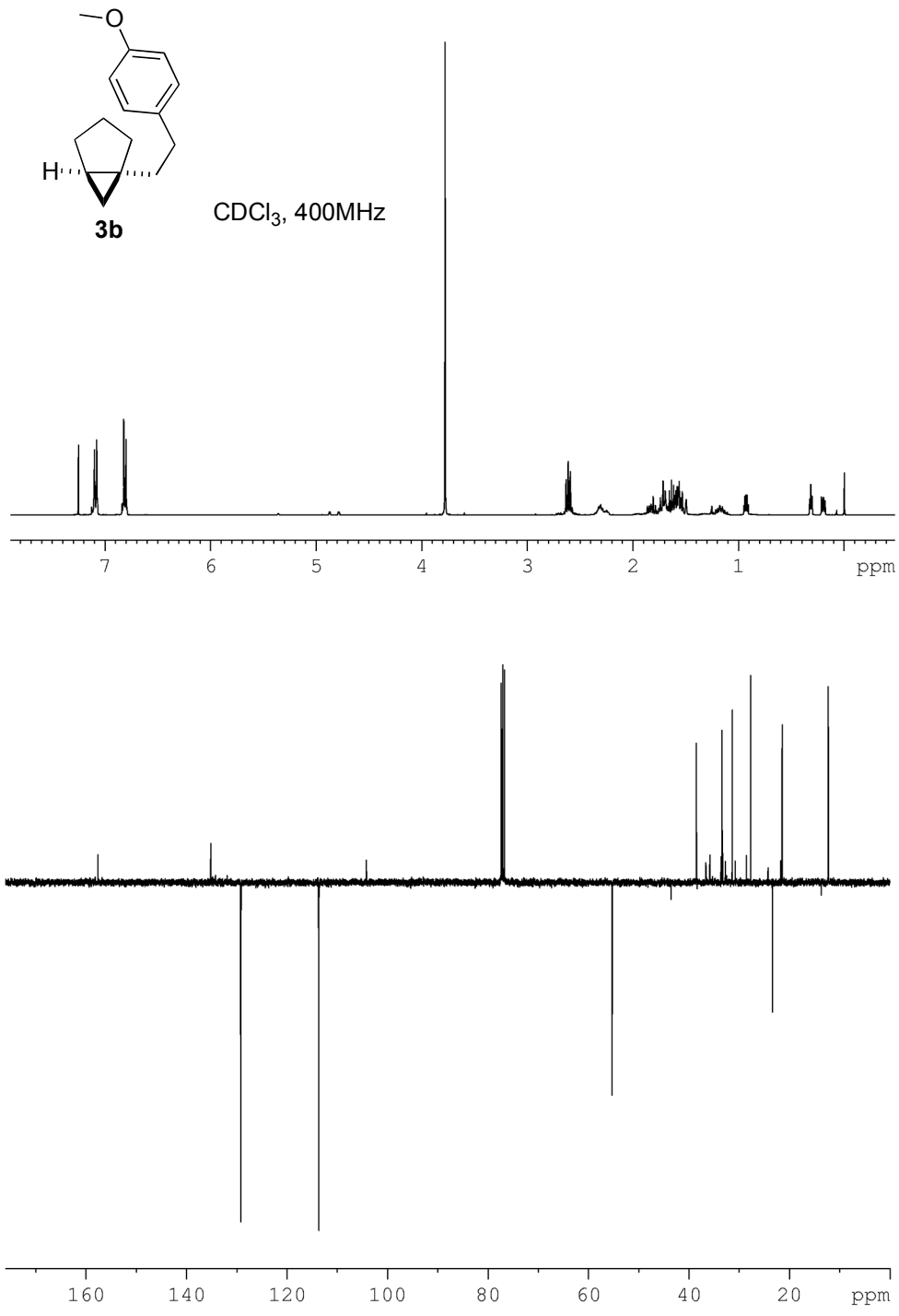
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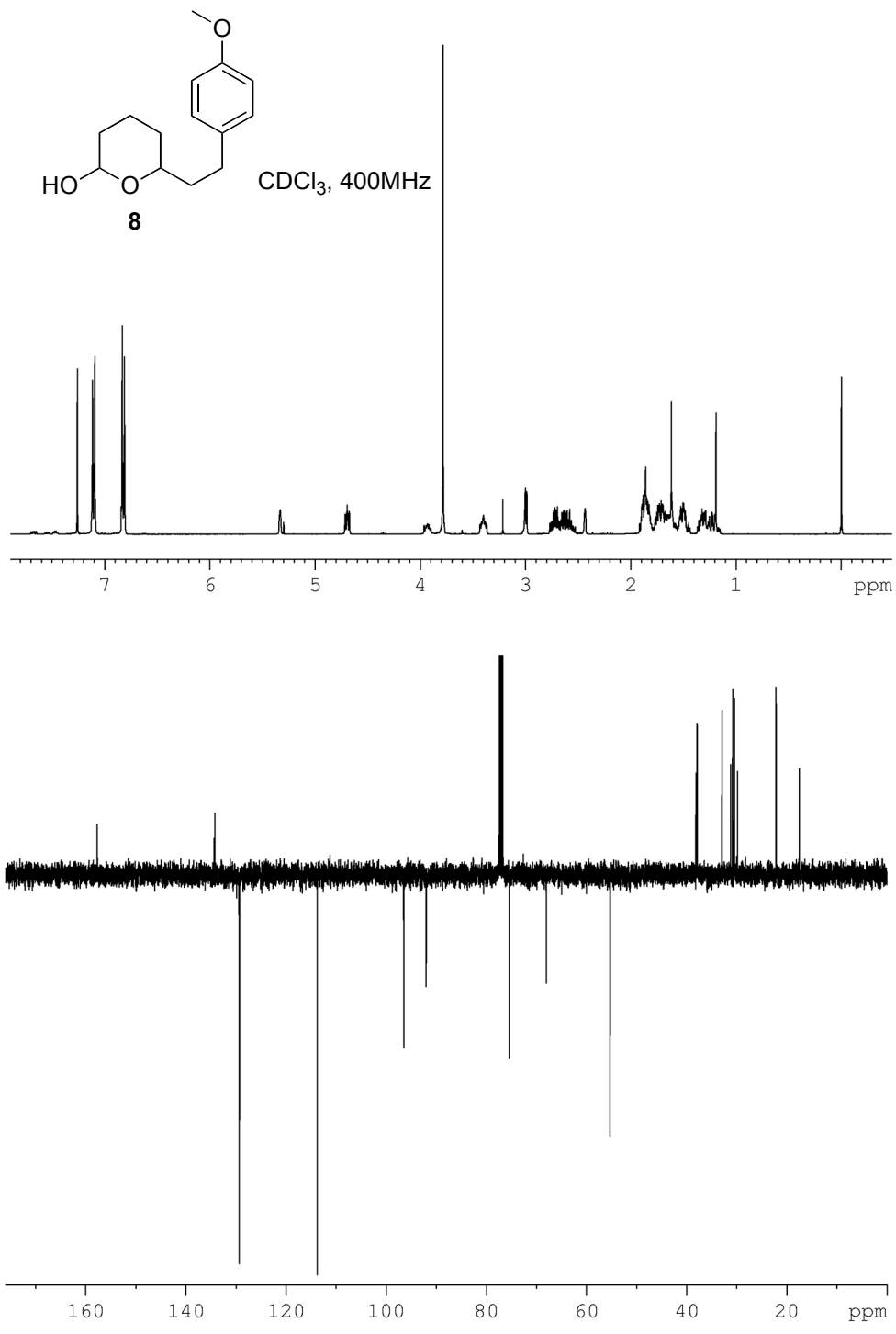
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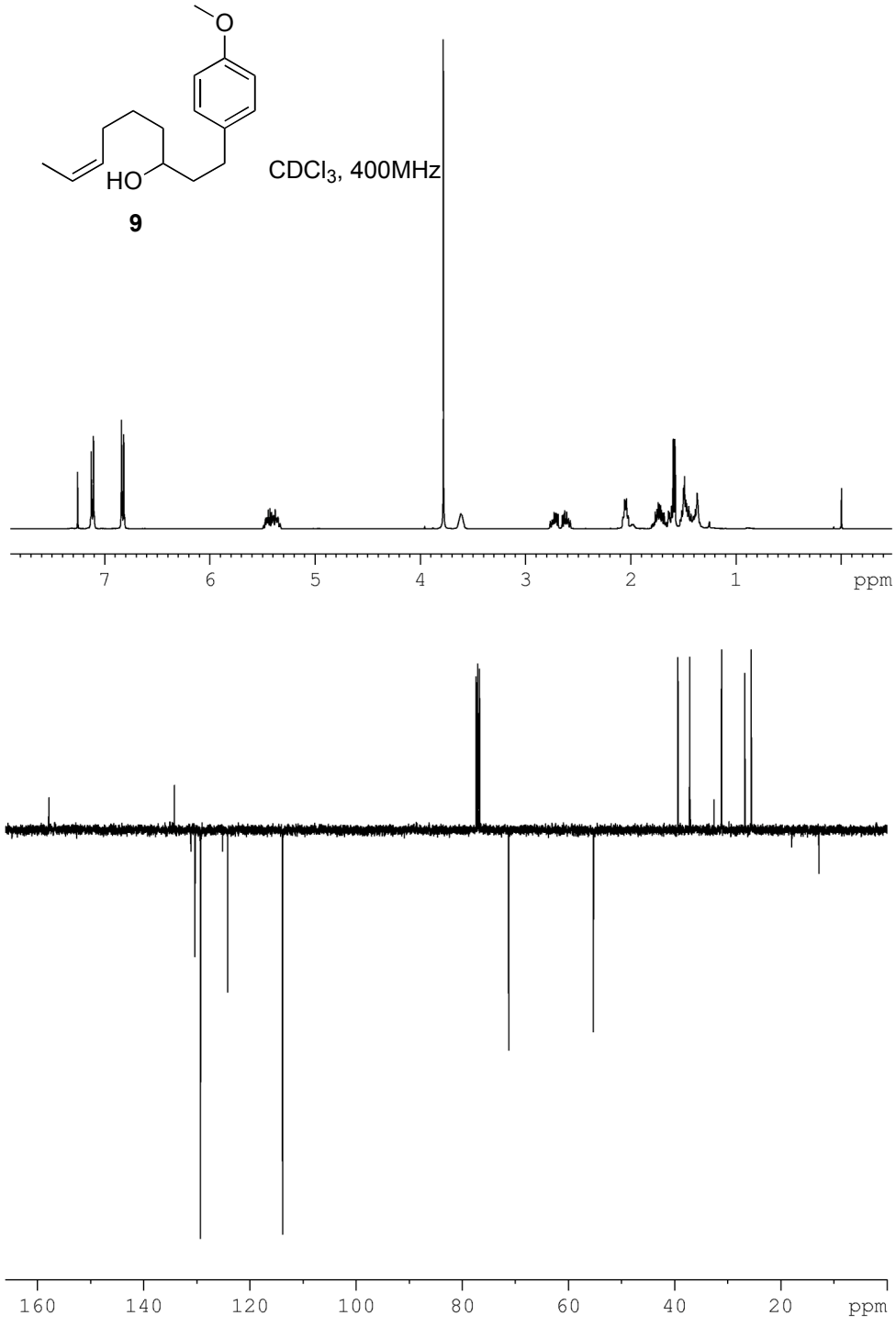

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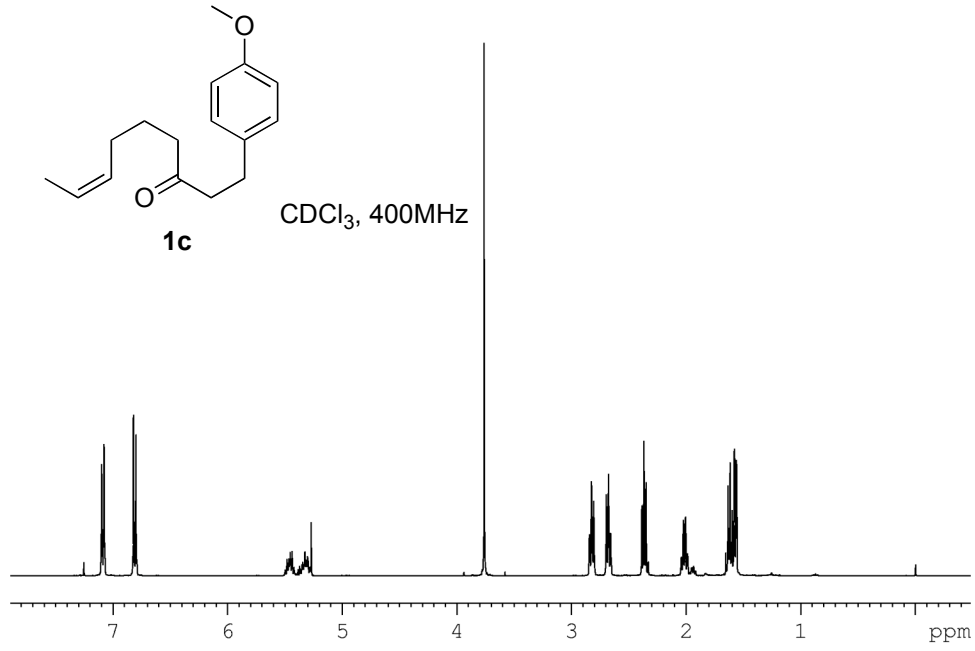
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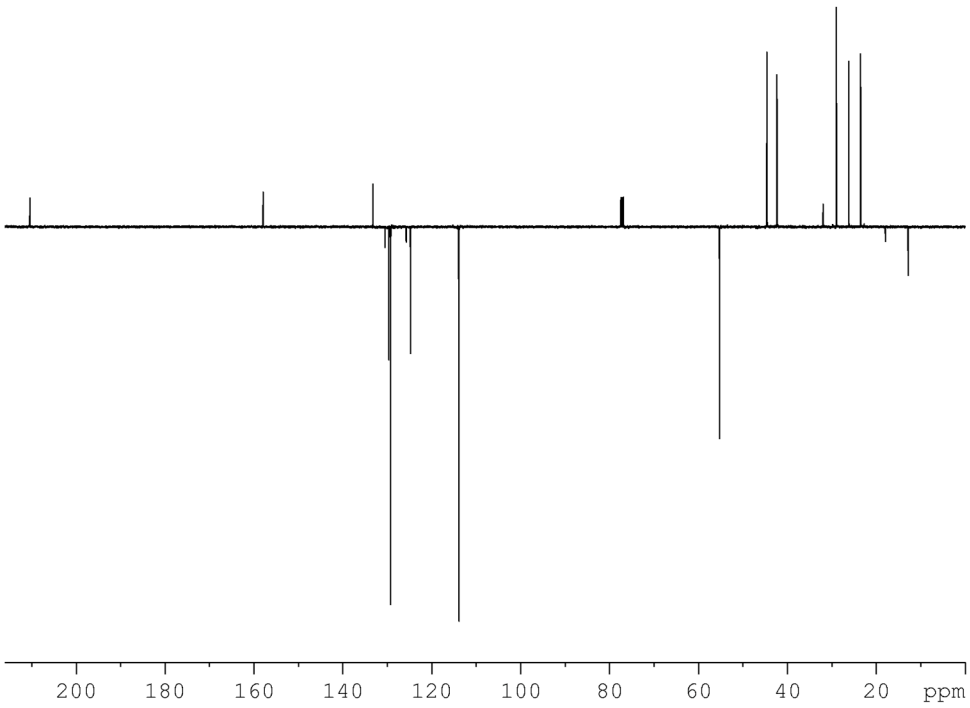
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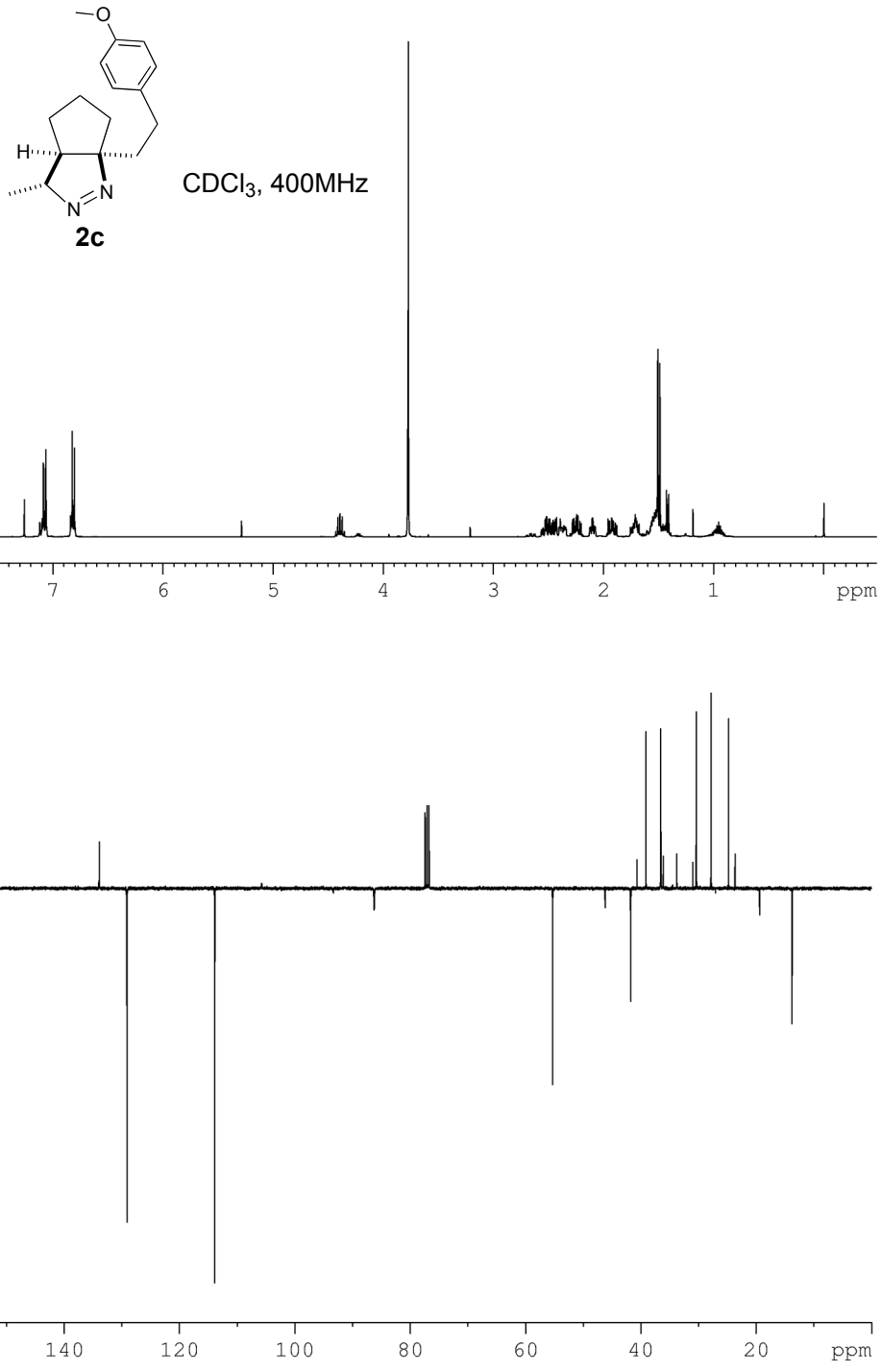
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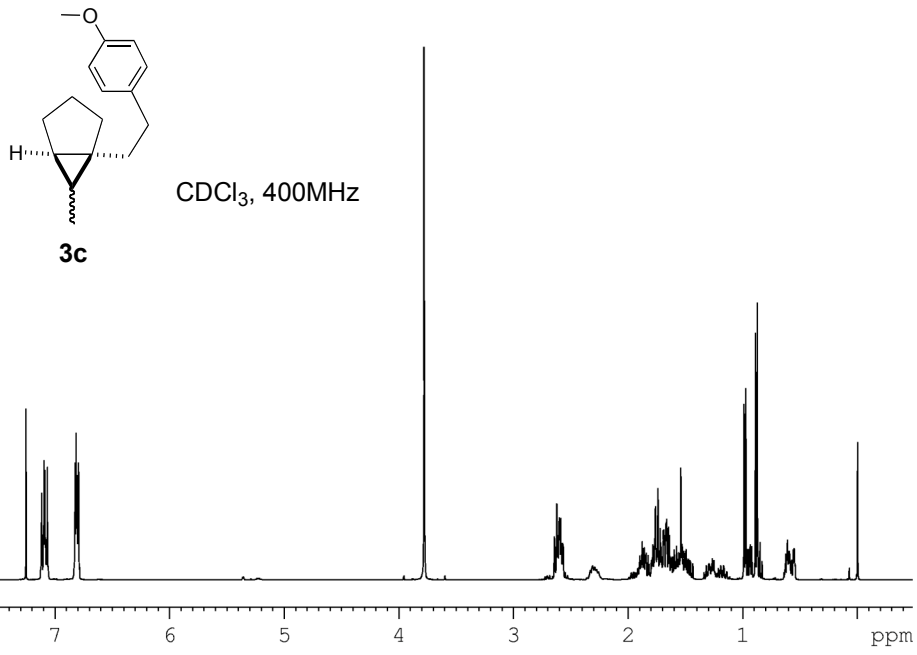

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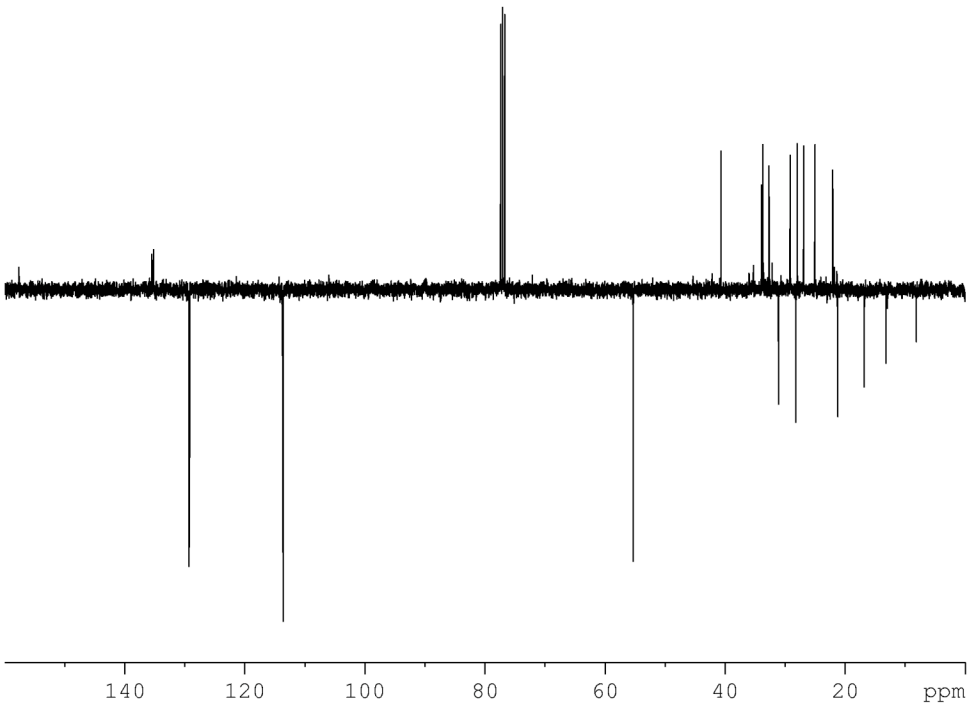

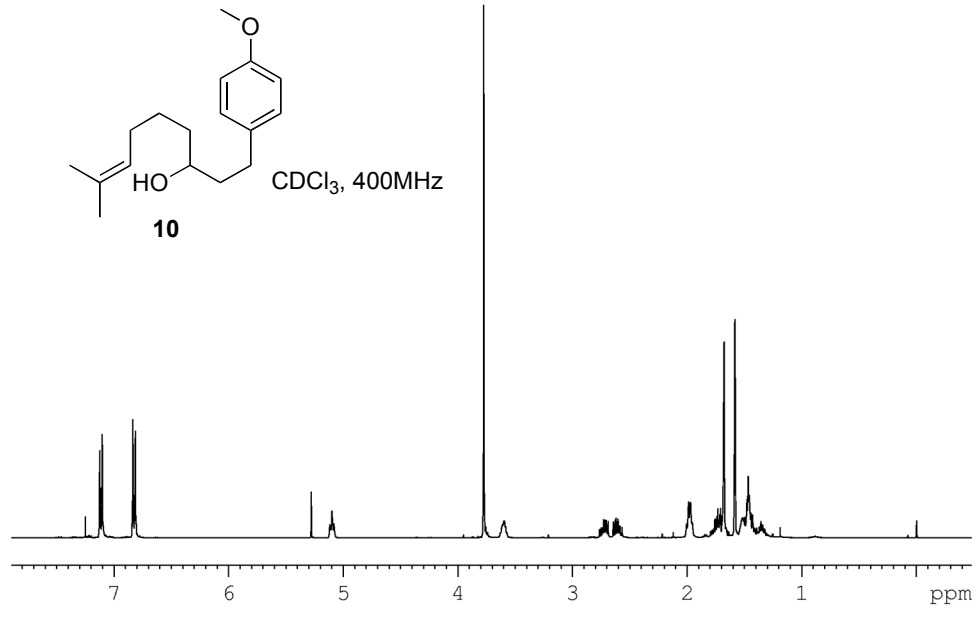
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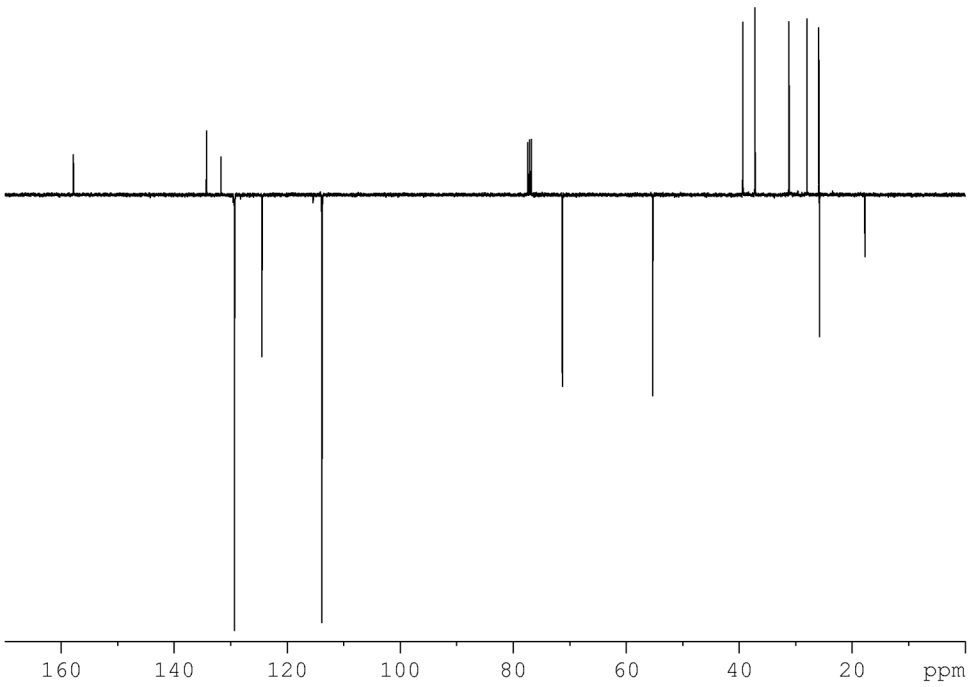
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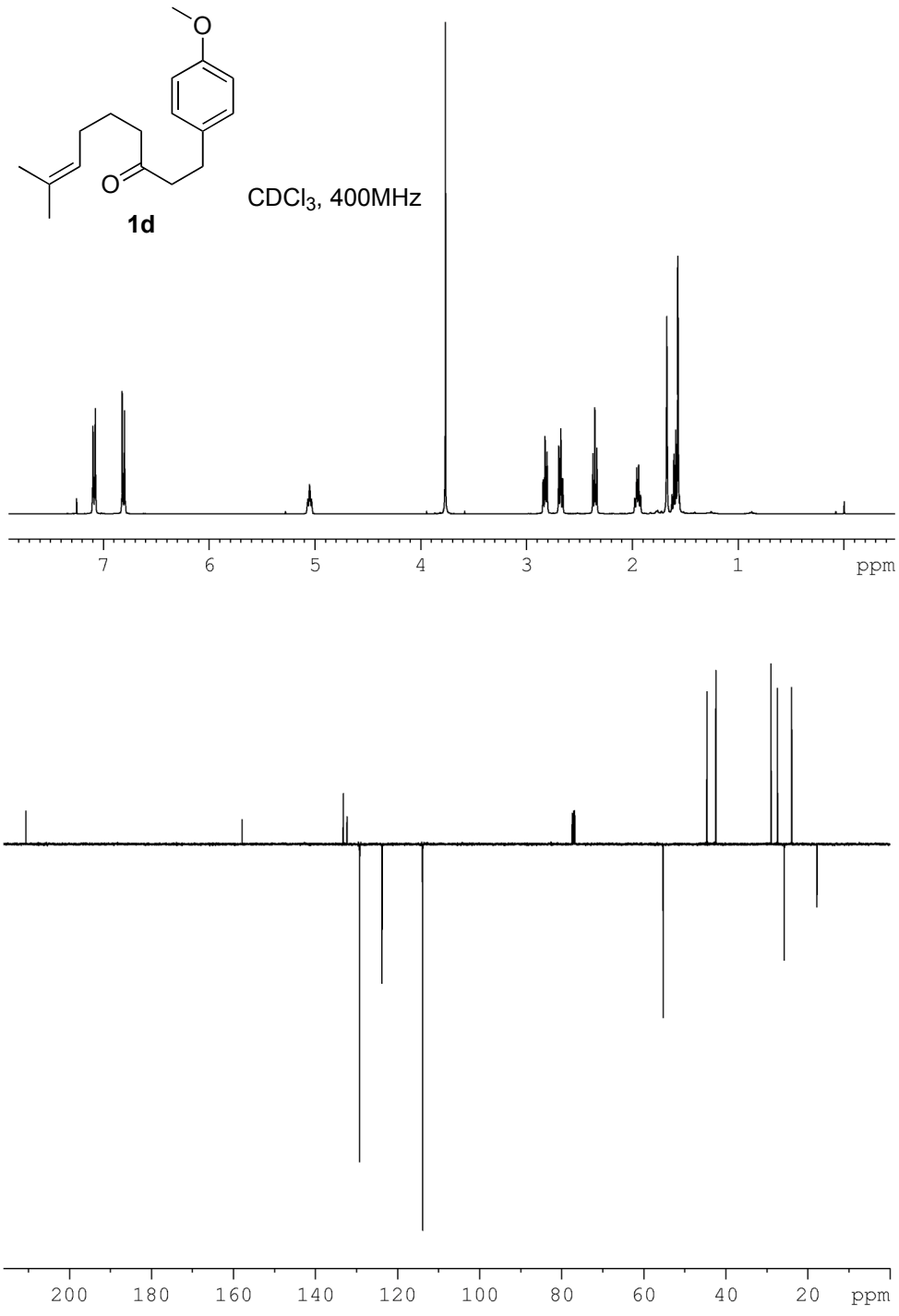
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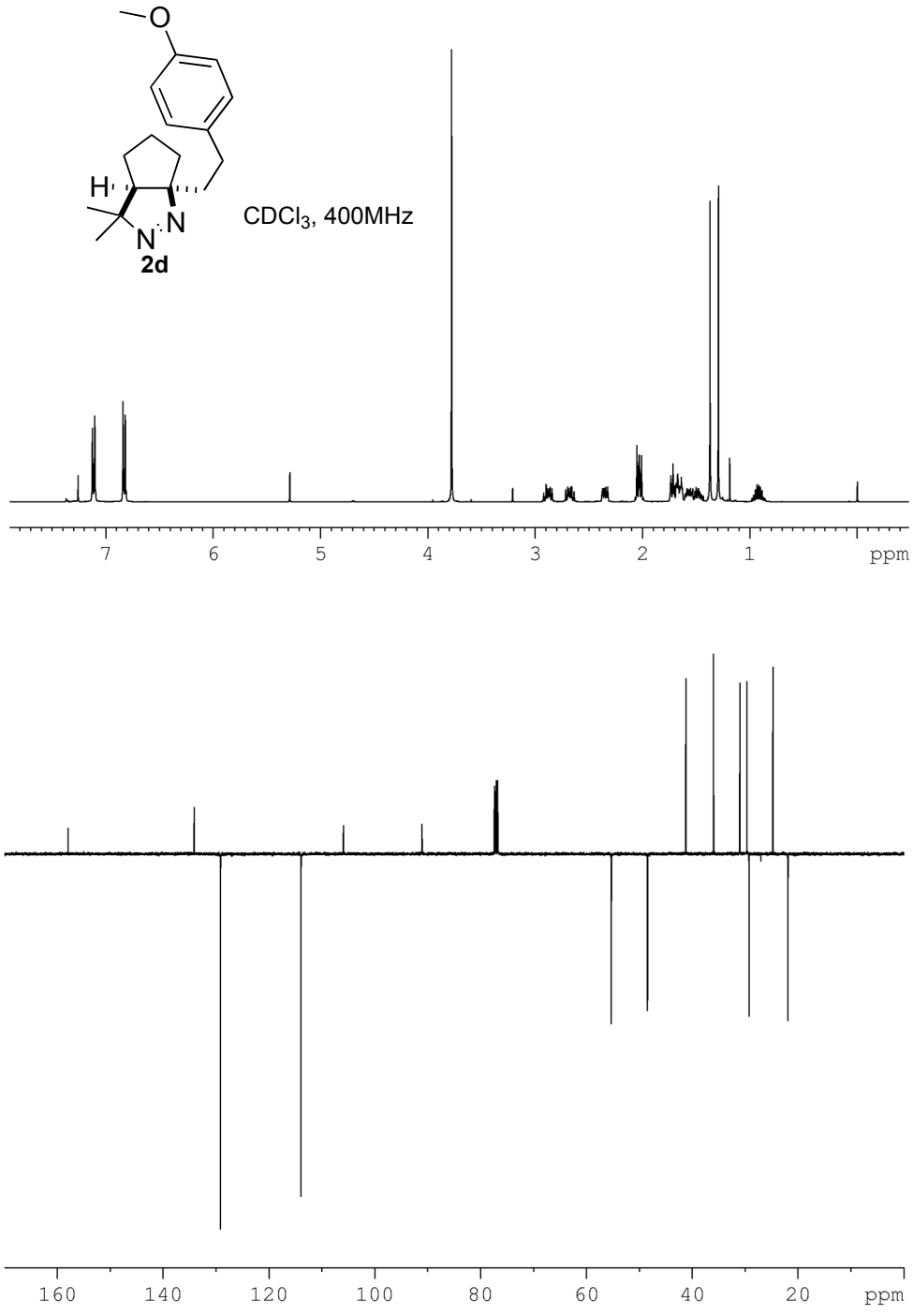
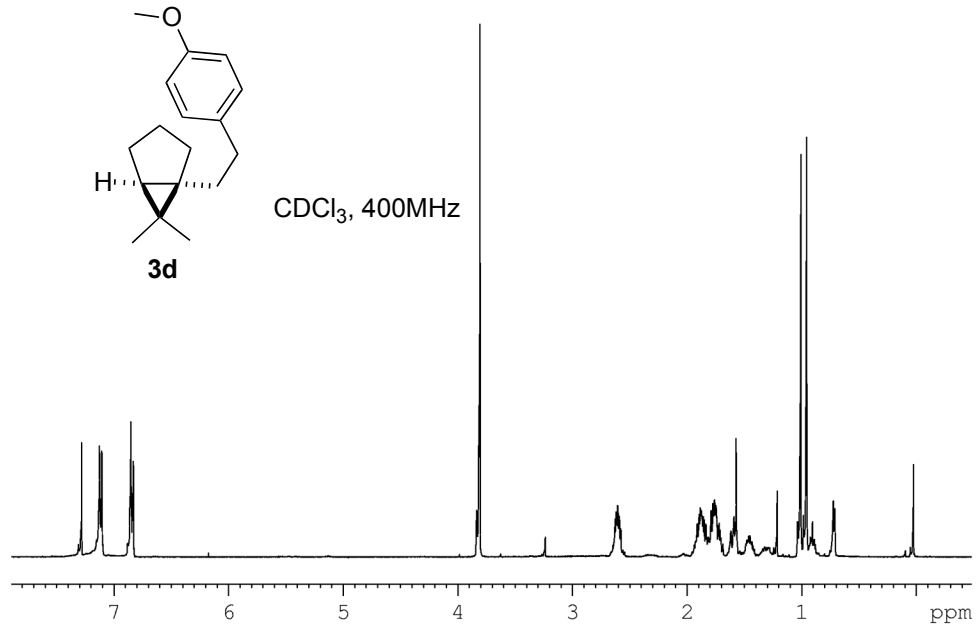
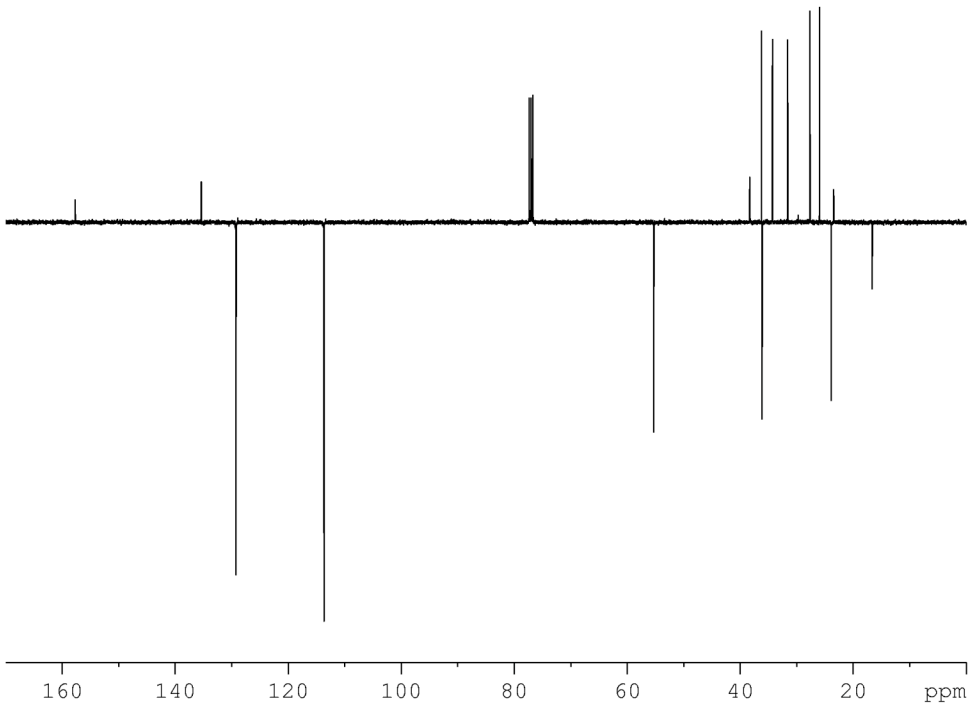
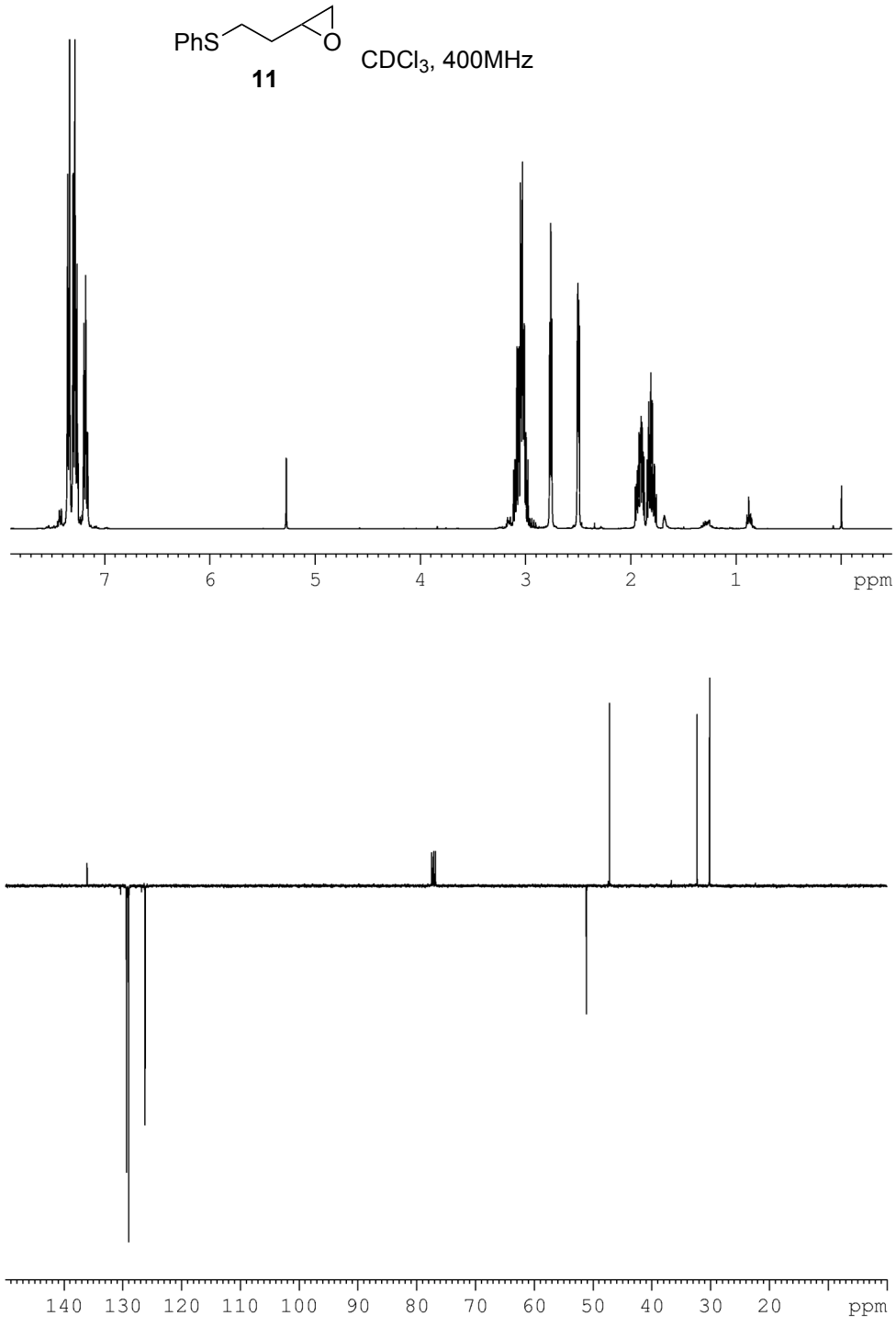

O
H
N
N
2d
CDCl3, 400MHz
7
6
5
4
3
2
1
ppm
160
140
120
100
80
60
40
20
ppm



3d




PhS
O
11
CDCl3, 400MHz
7
6
5
4
3
2
1
ppm
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130
120
110
100
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80
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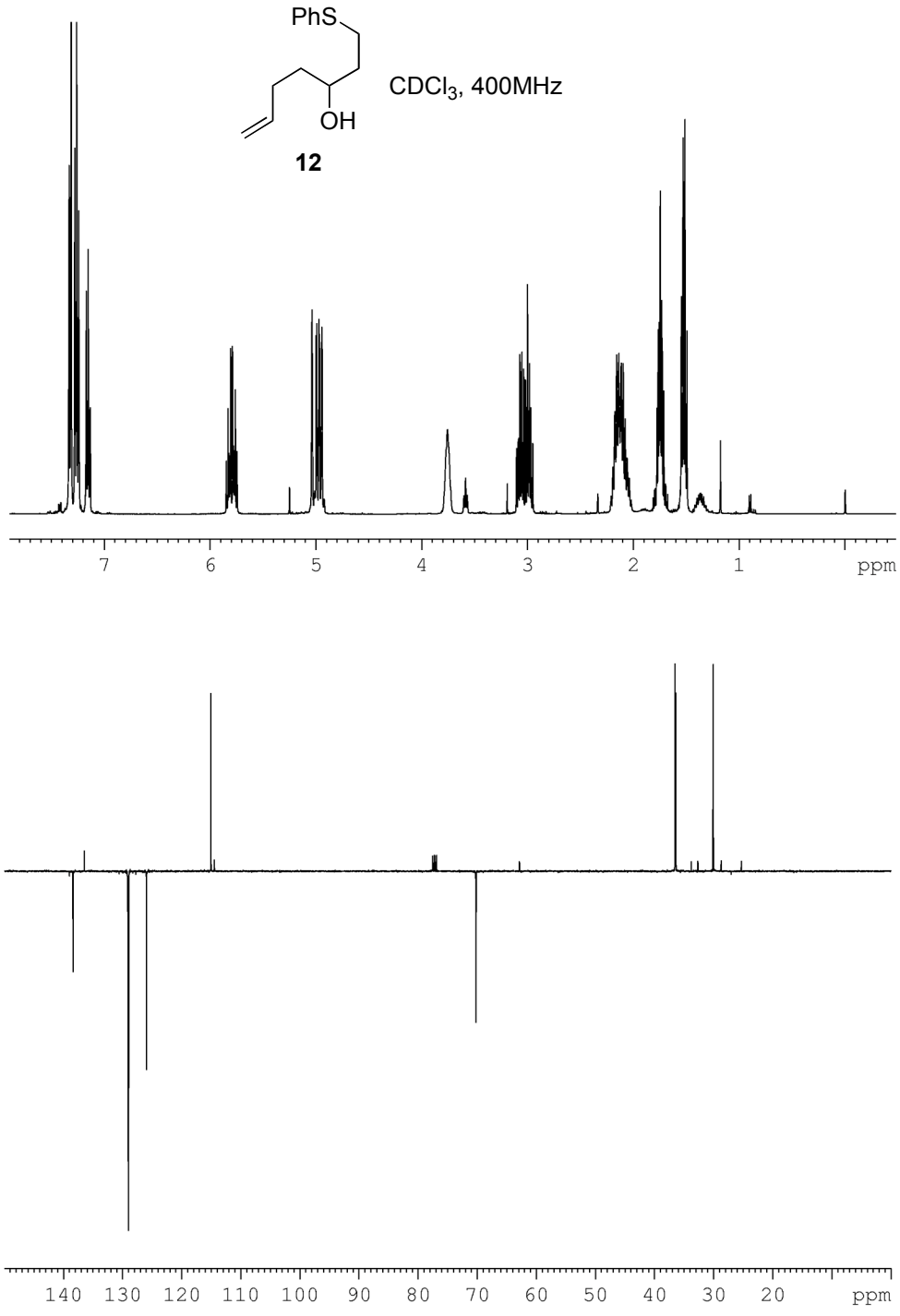
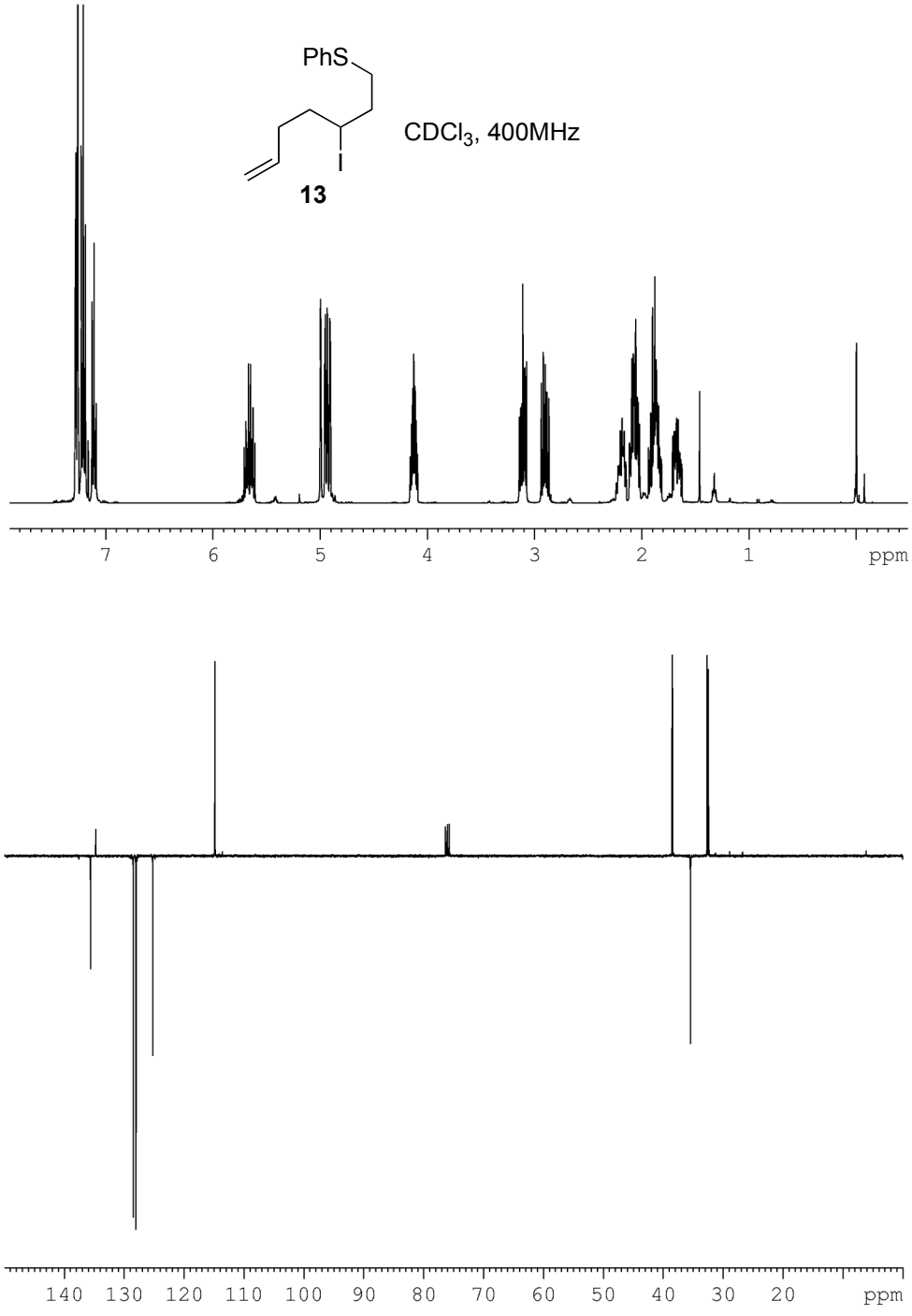
40
30
20
ppm


PhS
OH
CDCl3, 400MHz
12
7
6
5
4
3
2
1
ppm
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


PhS
I
13
CDCl3, 400MHz
7
6
5
4
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2
1
ppm
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120
110
100
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80
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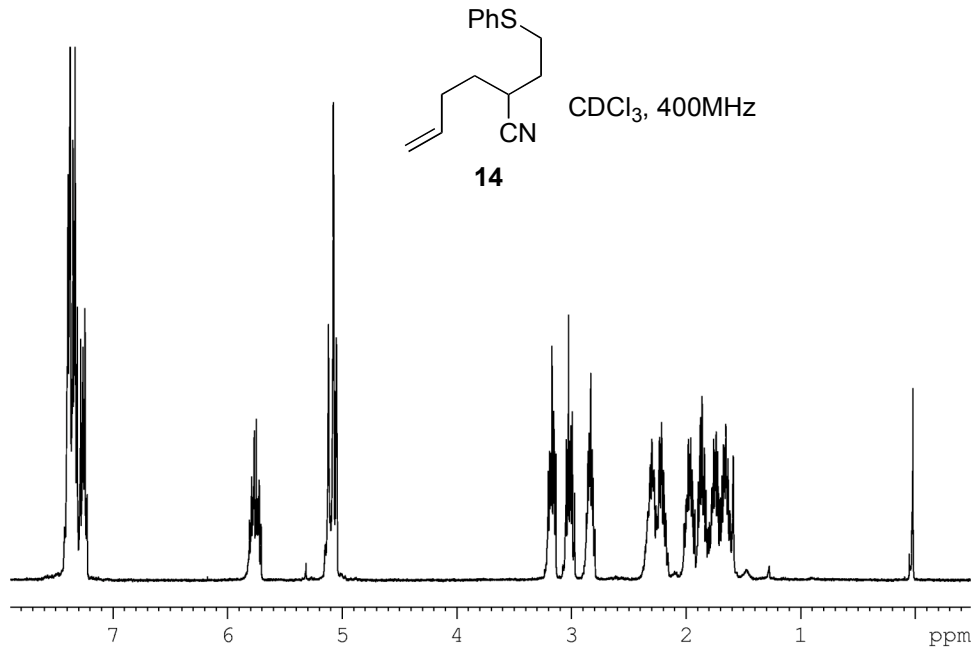
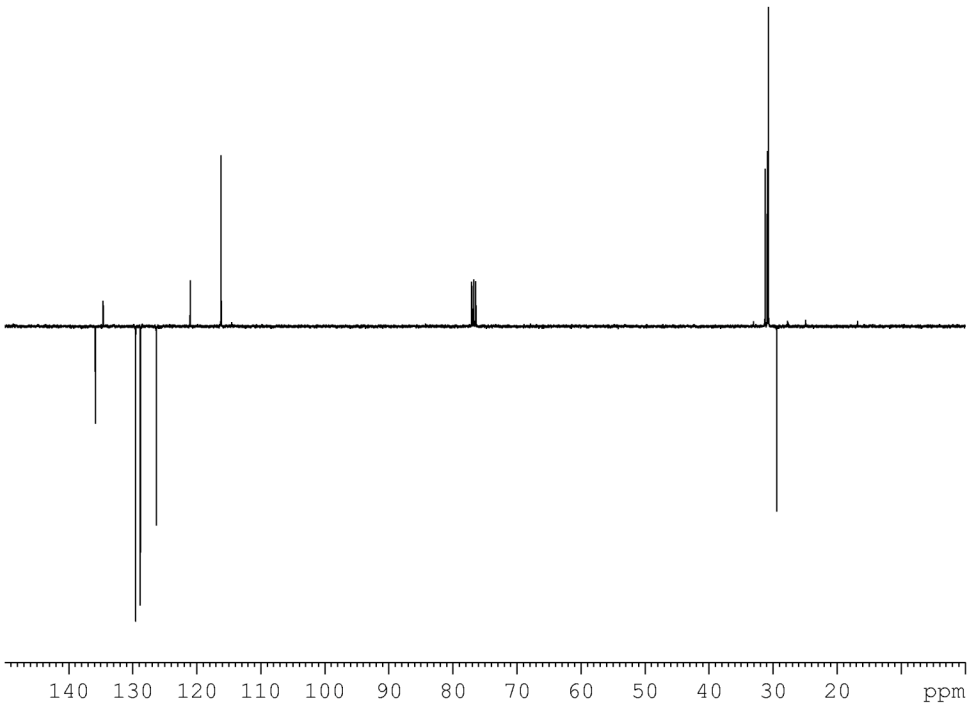
50
40
30
20
ppm


PhS
CN
CDCl3, 400MHz
14
7
6
5
4
3
2
1
ppm


140
130
120
110
100
90
80
70
60
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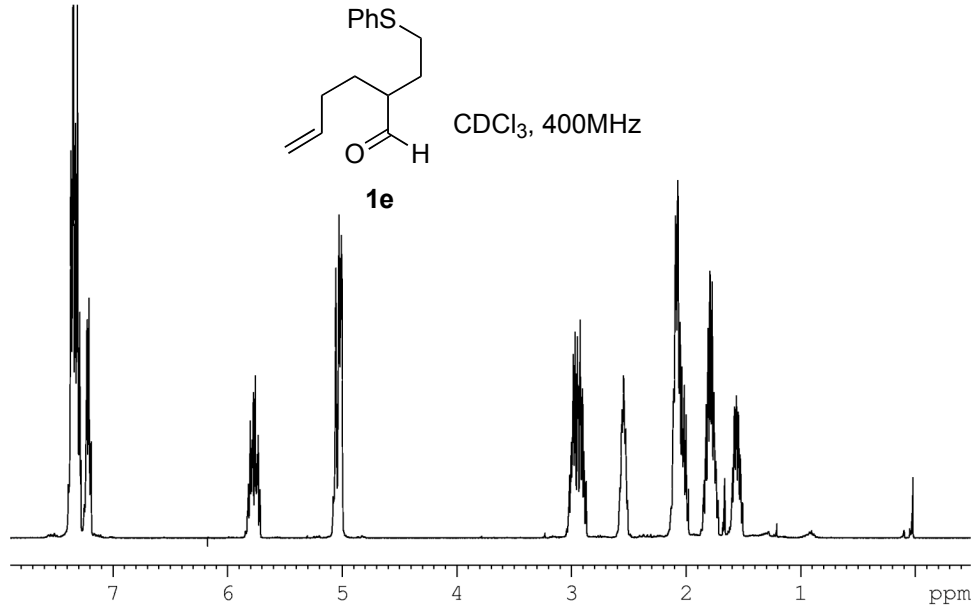
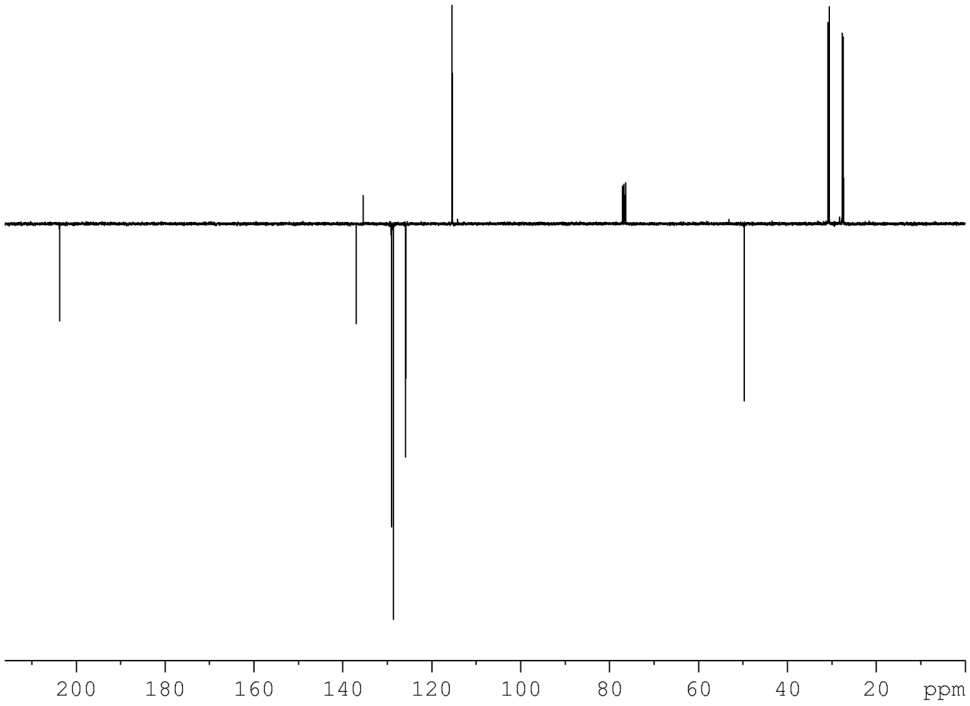
40
30
20
ppm


PhS
O
H
CDCl3, 400MHz
1e
7
6
5
4
3
2
1
ppm


200
180
160
140
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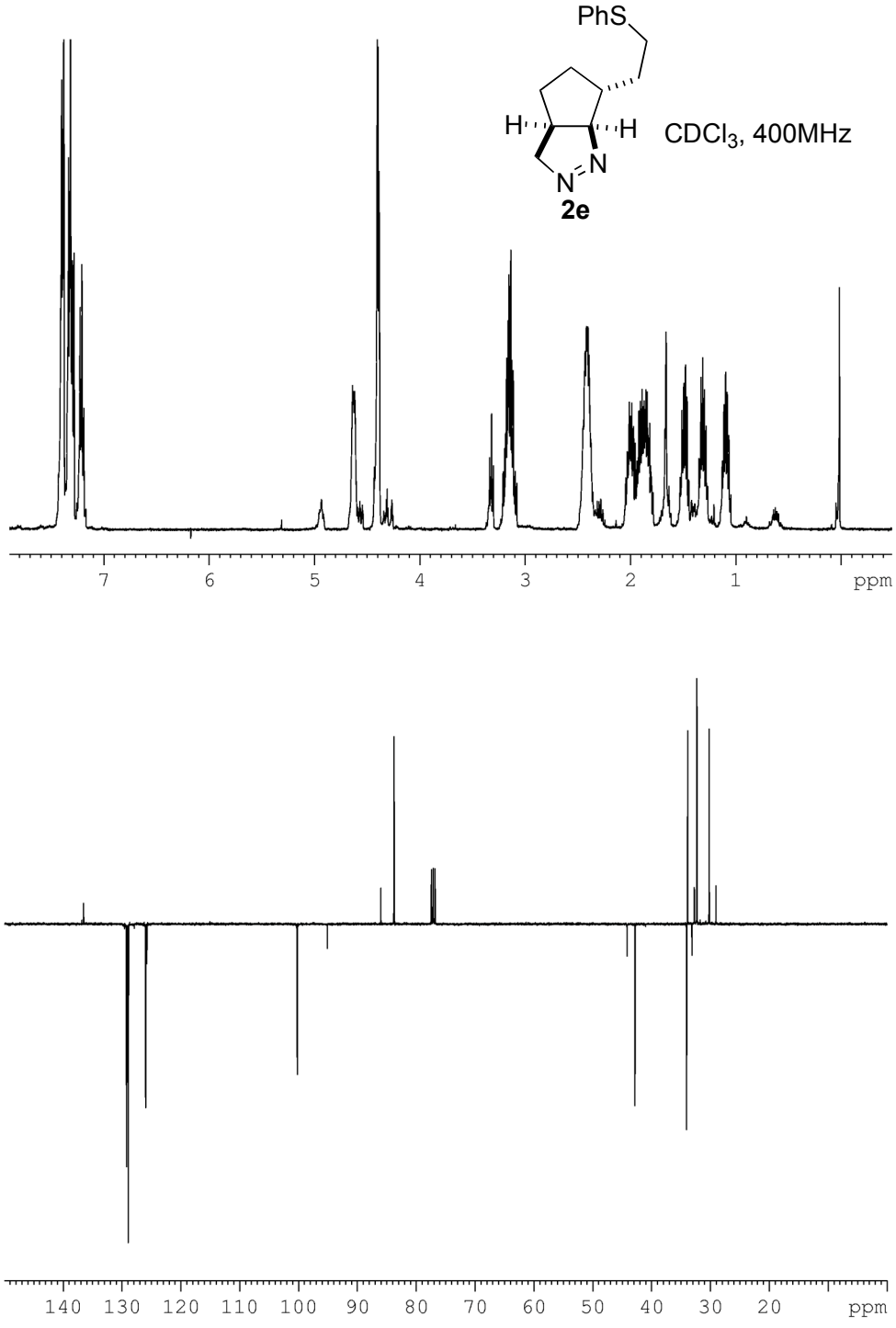
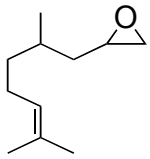
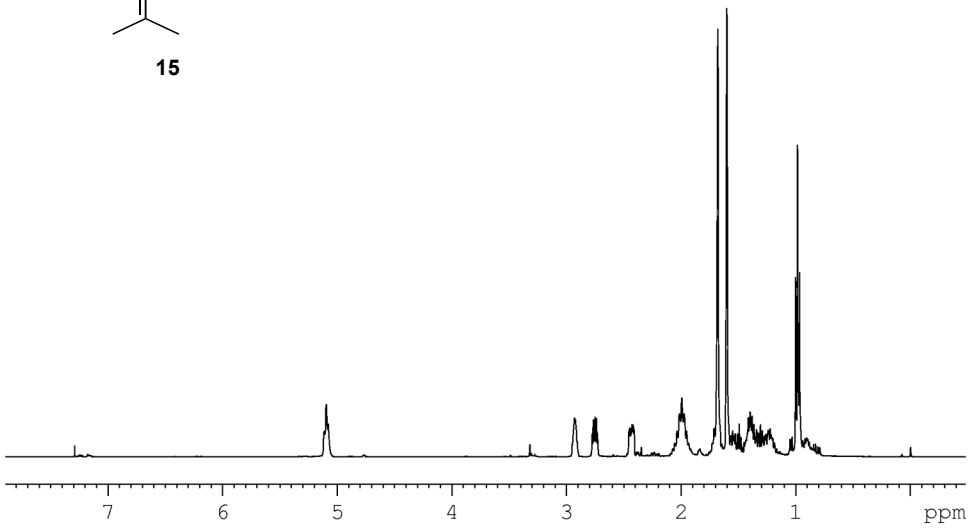
100
80
60
40
20
ppm

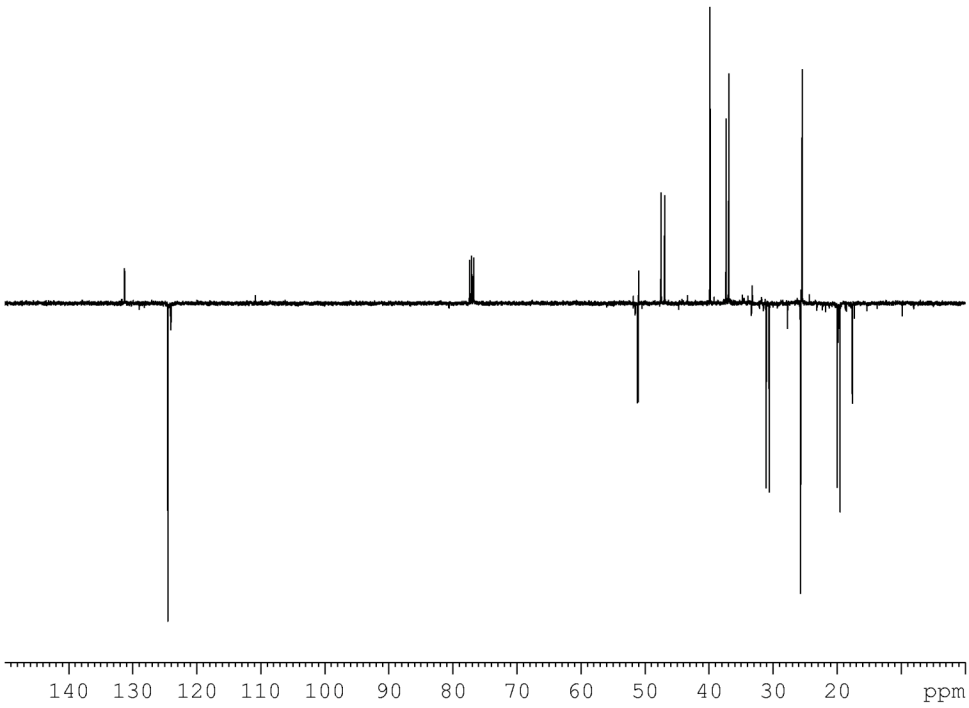

PhS
H
H
N
N
2e
CDCl3, 400MHz
7
6
5
4
3
2
1
ppm
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

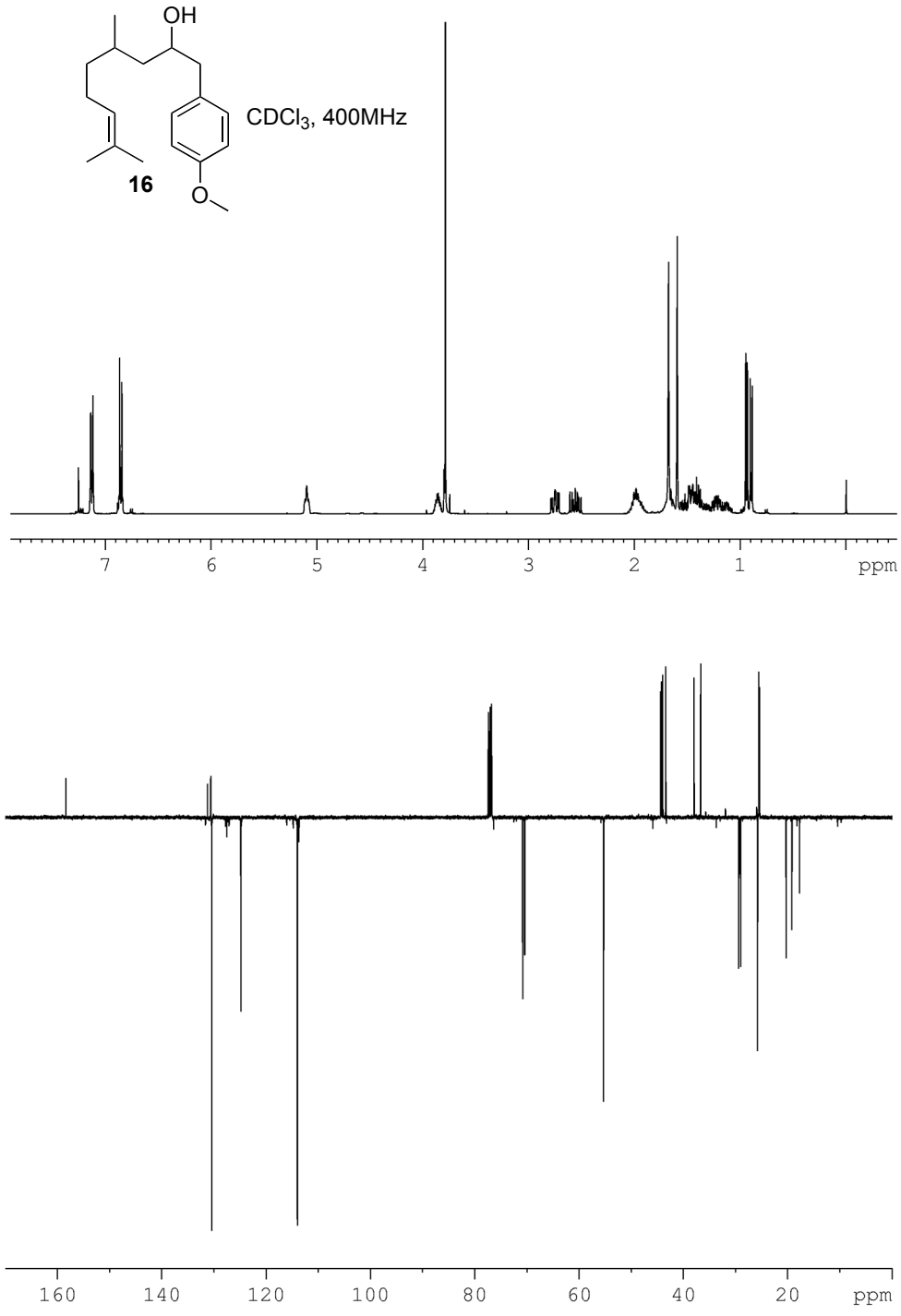


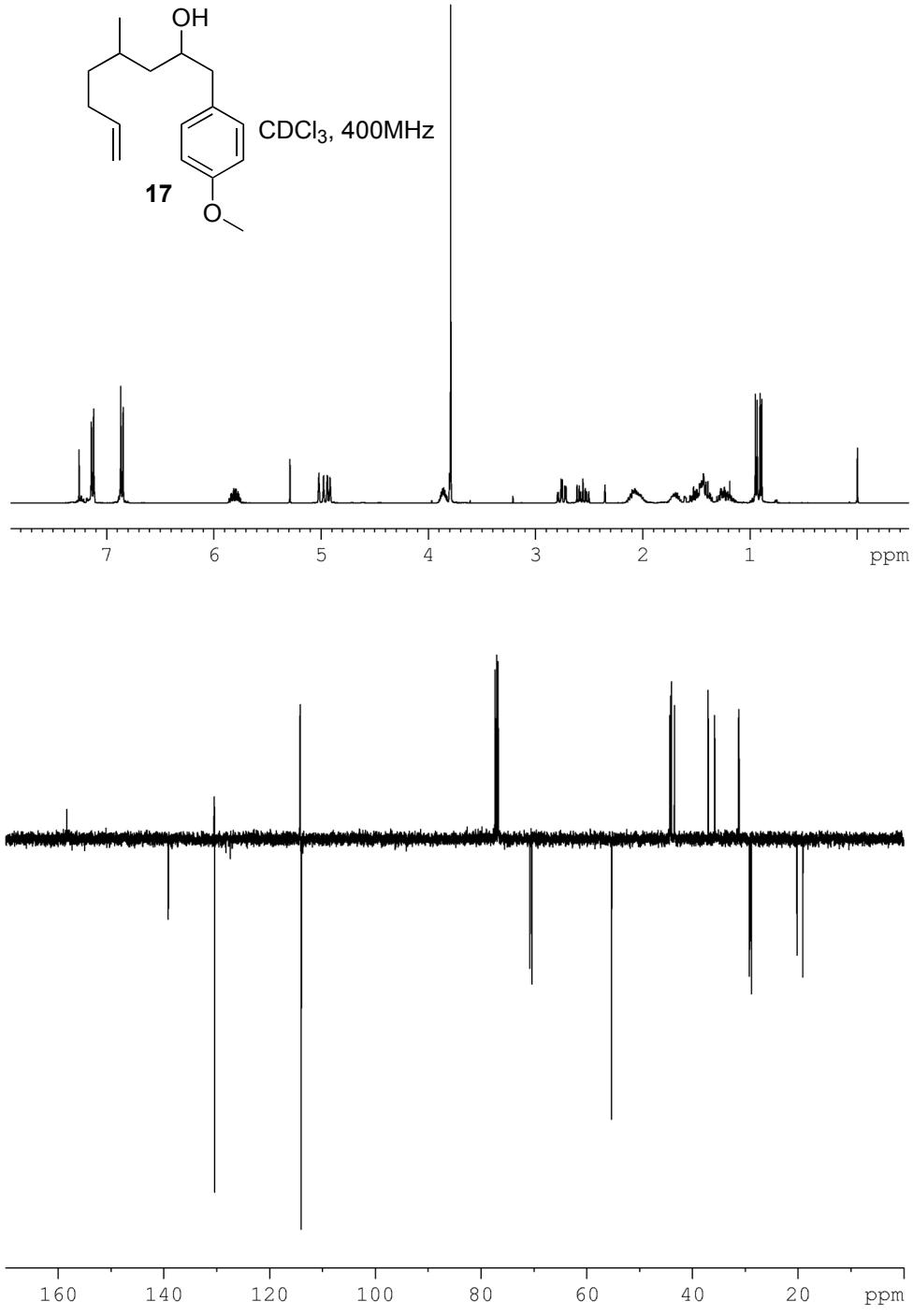
15

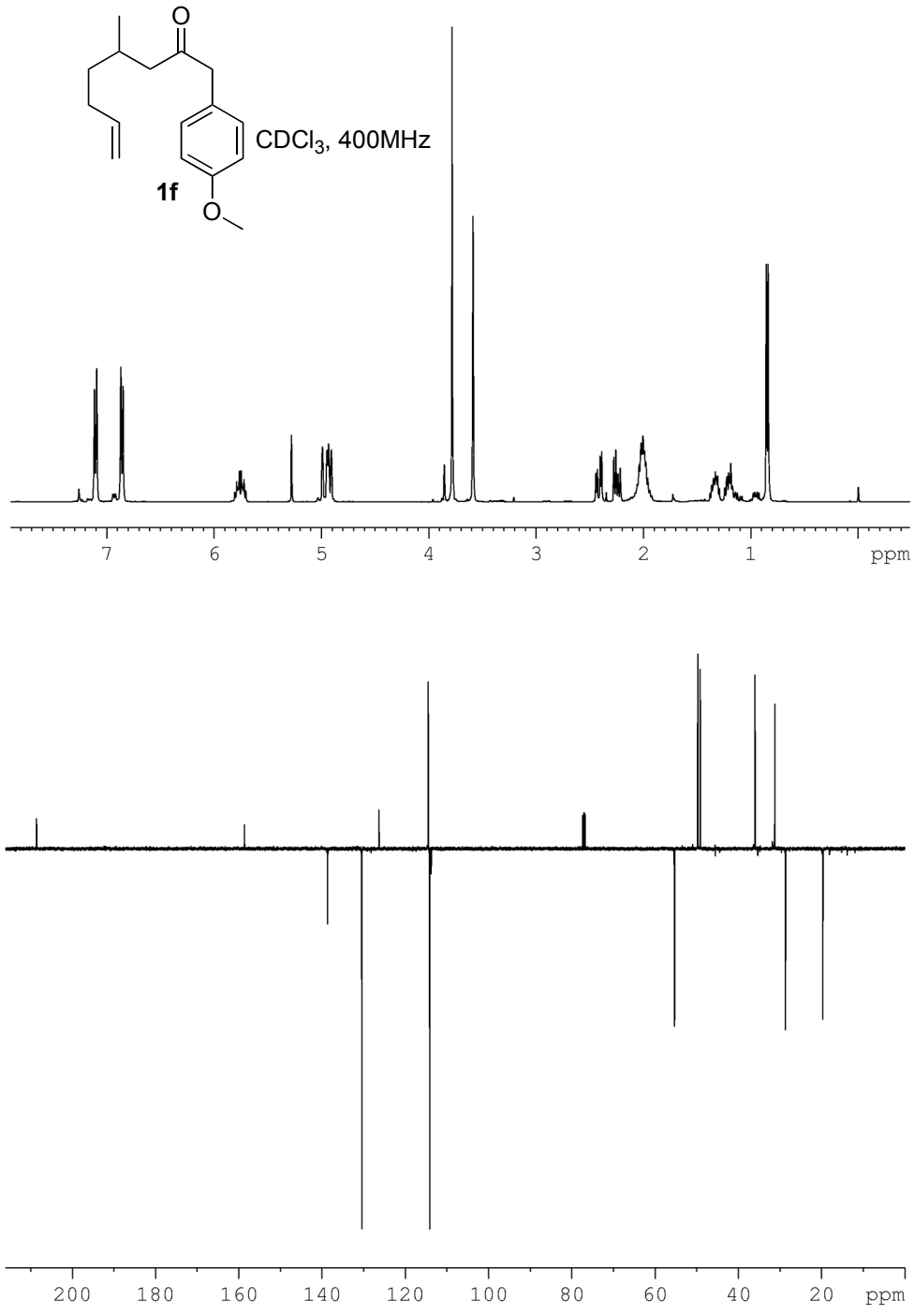
$CDCl_3$, 400MHz

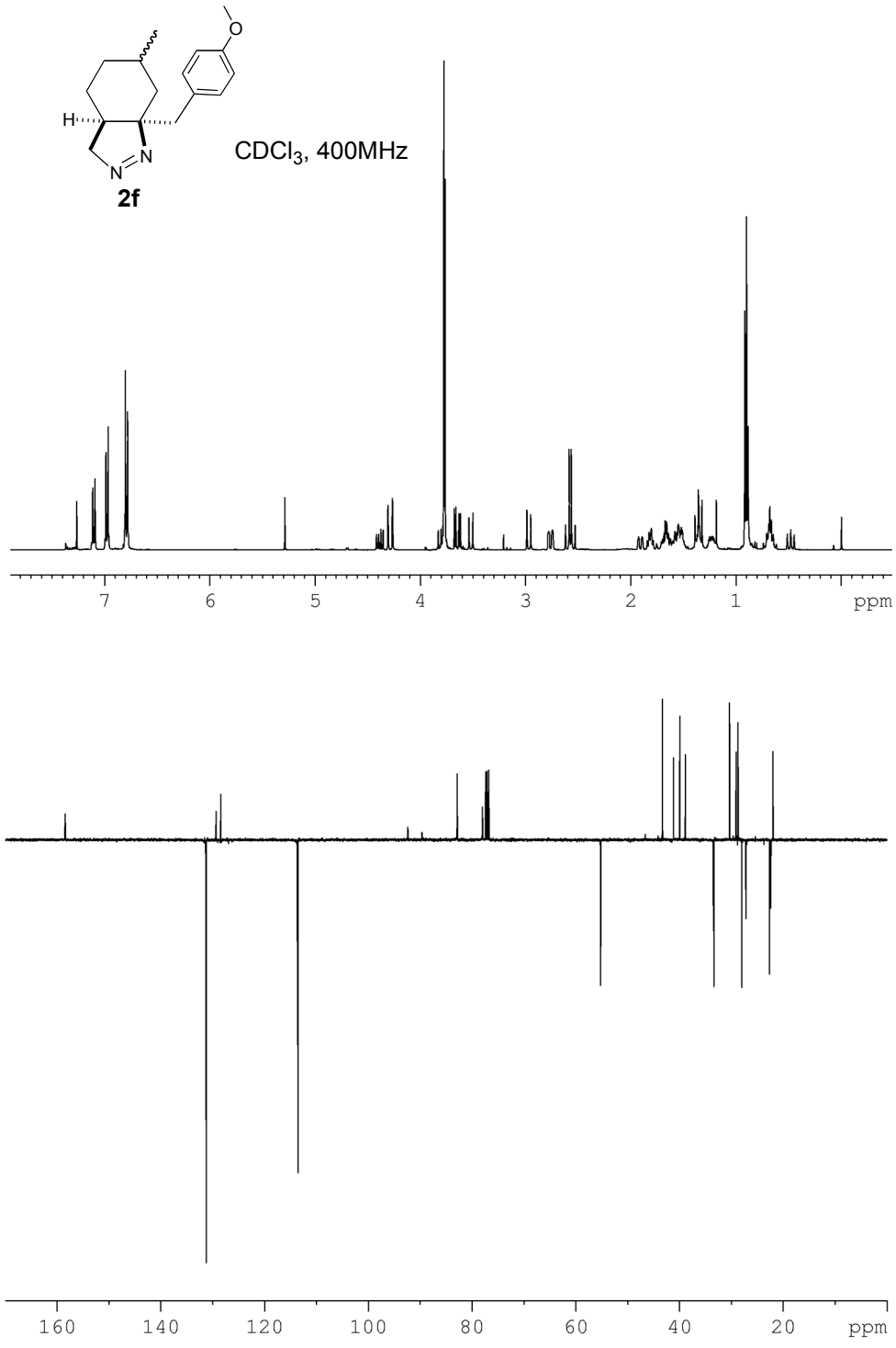


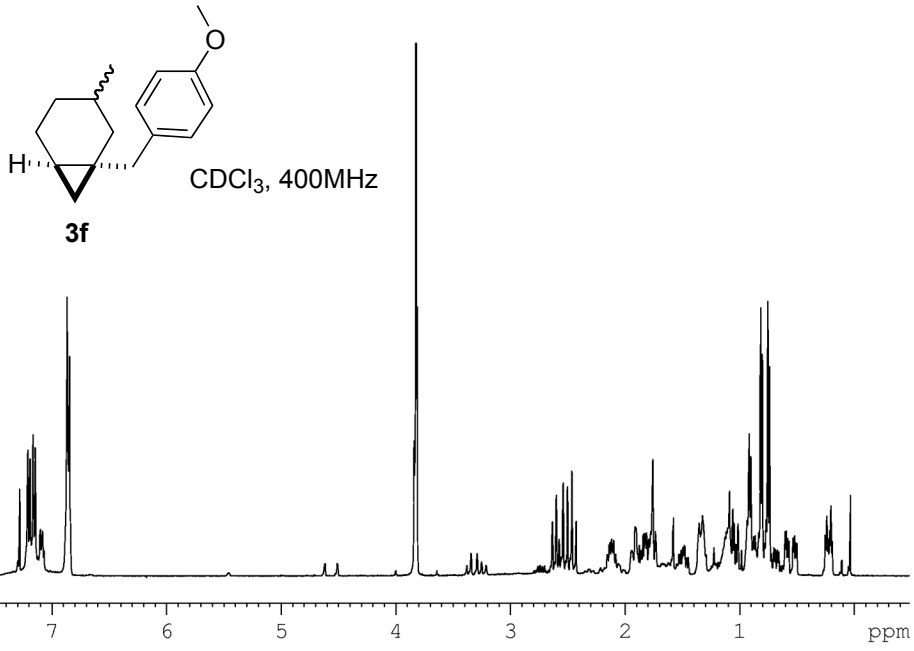


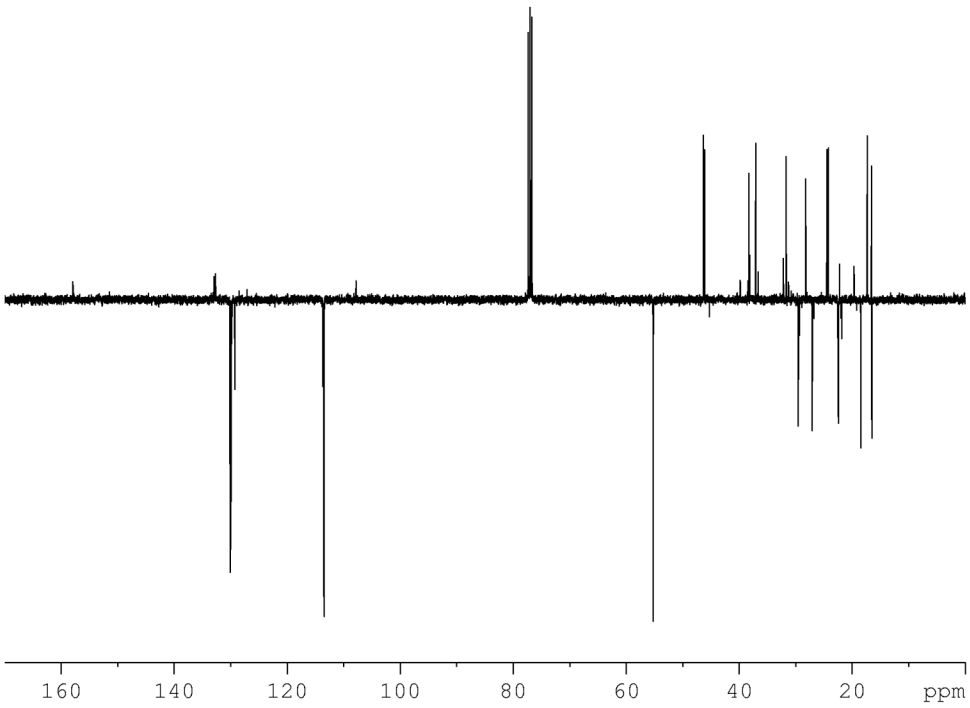

OH
CDCl3, 400MHz
16
O
7
6
5
4
3
2
1
ppm
160
140
120
100
80
60
40
20
ppm

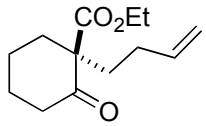

OH
CDCl3, 400MHz
17
O
7
6
5
4
3
2
1
ppm
160
140
120
100
80
60
40
20
ppm


O
CDCl3, 400MHz
1f
O
7
6
5
4
3
2
1
ppm
200
180
160
140
120
100
80
60
40
20
ppm


O
H
N
N
2f
CDCl3, 400MHz
7
6
5
4
3
2
1
ppm
160
140
120
100
80
60
40
20
ppm

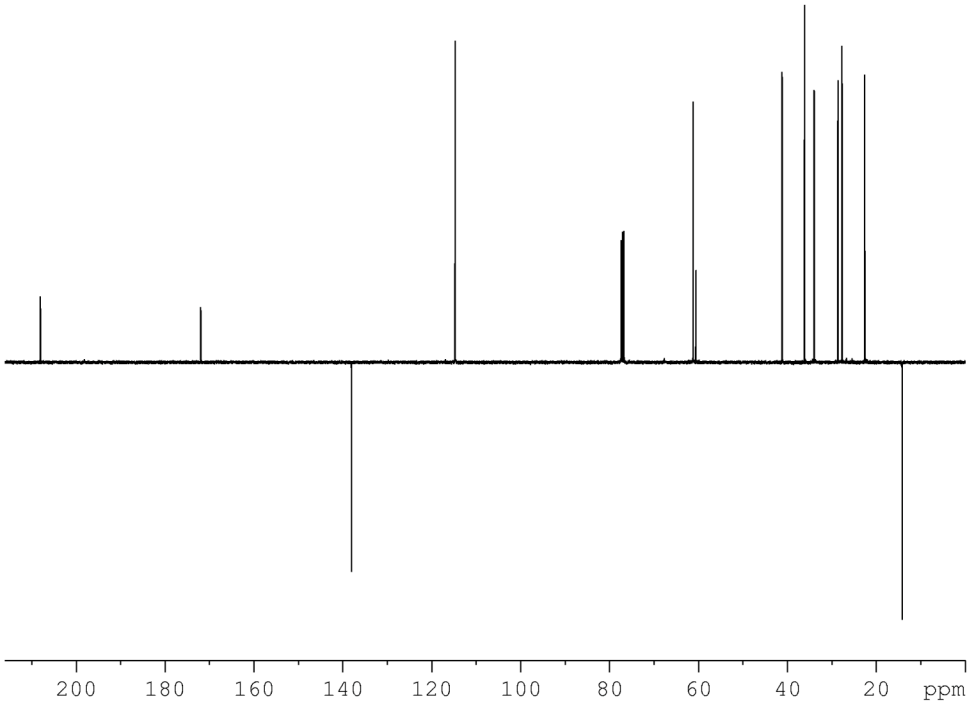

O
H
CDCl3, 400MHz
3f
7
6
5
4
3
2
1
ppm

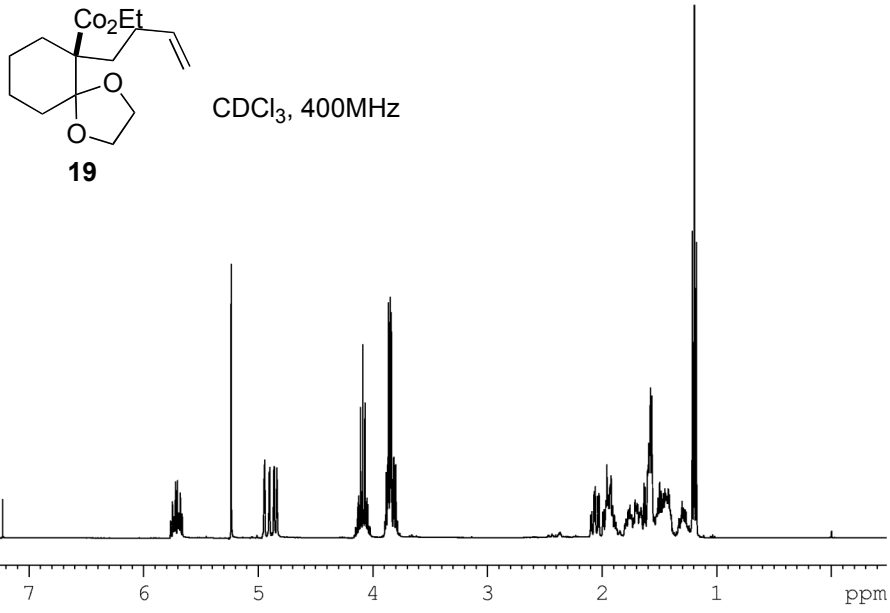

160
140
120
100
80
60
40
20
ppm

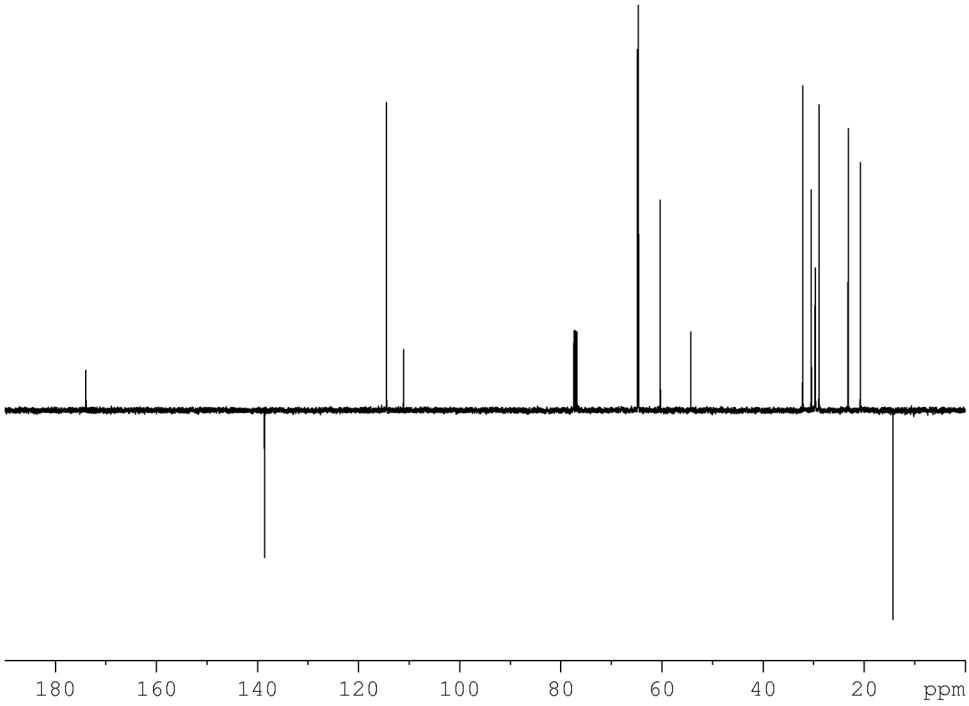


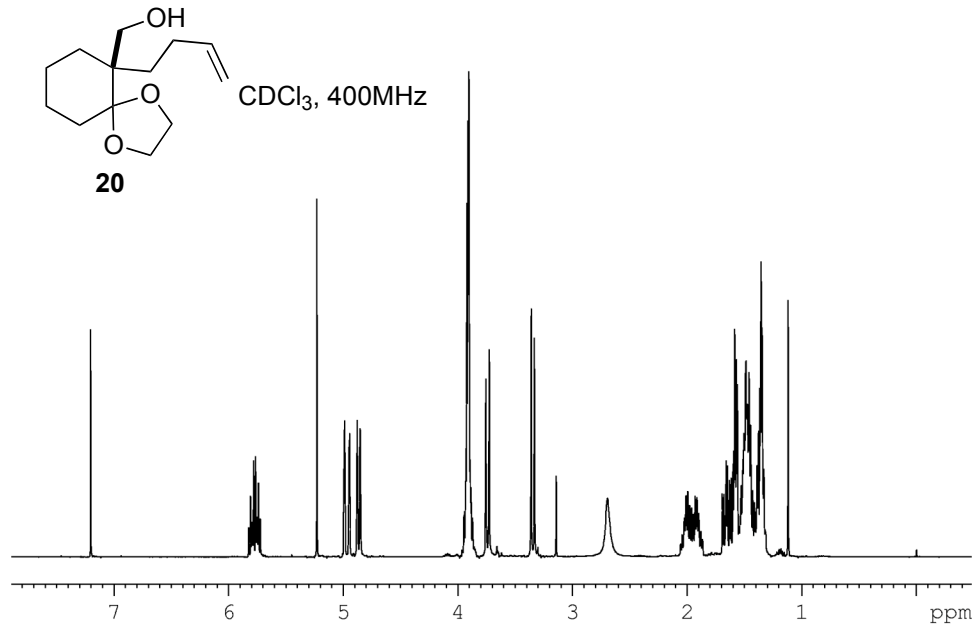
18

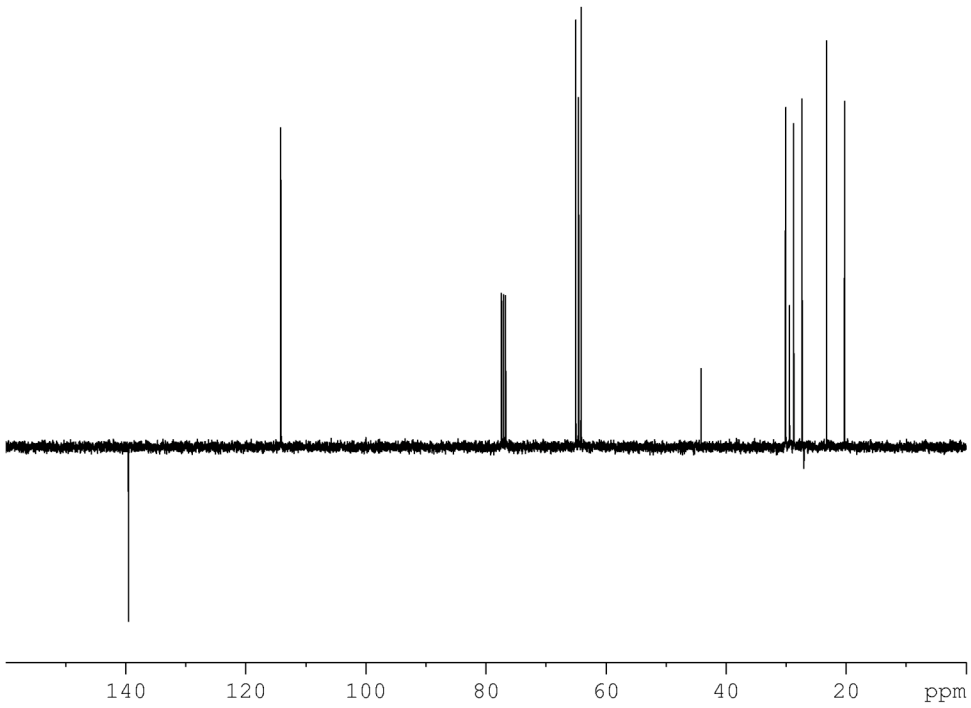
$CDCl_3$, 400MHz

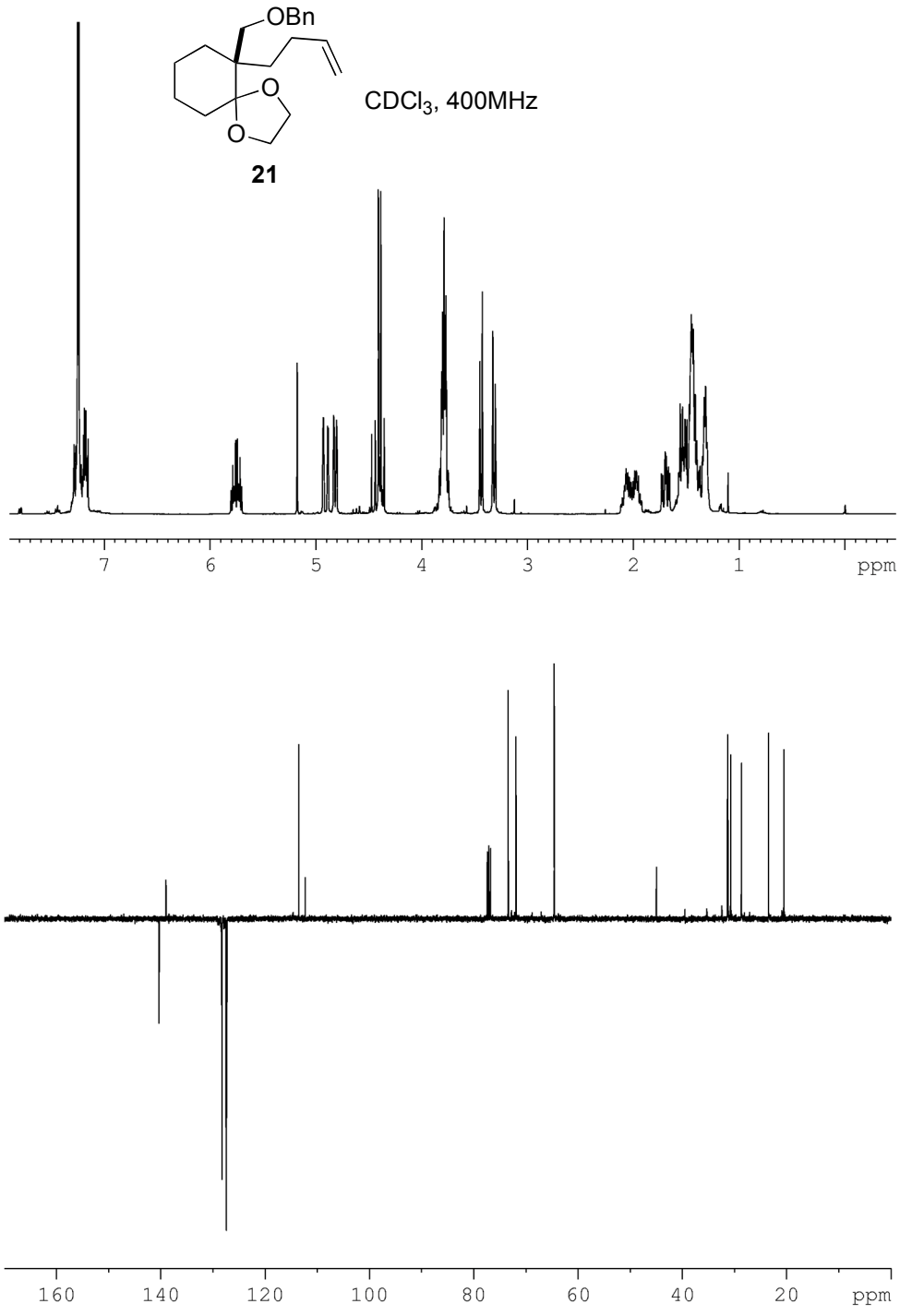


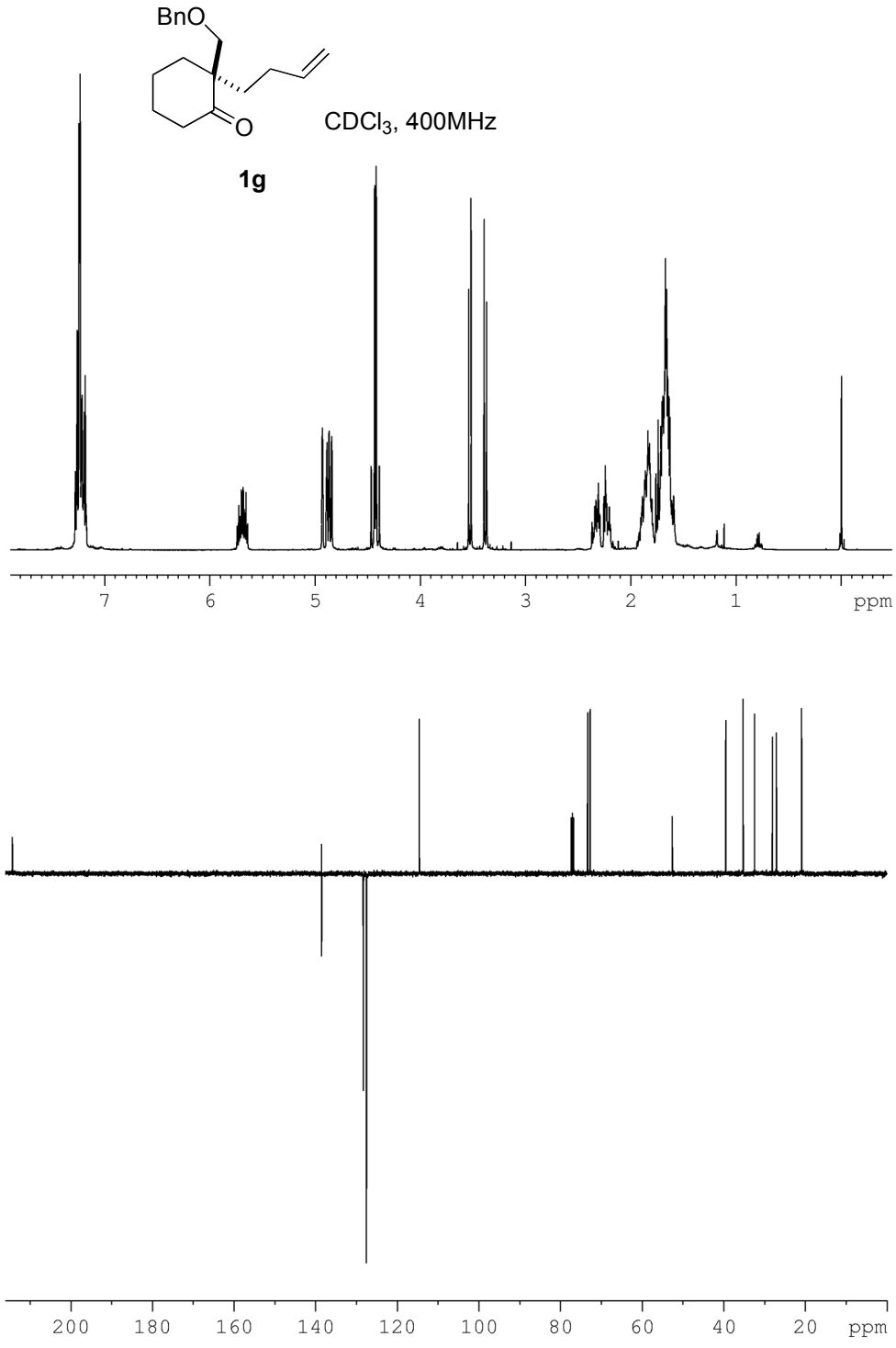

Co2Et
O
O
CDCl3, 400MHz
19
7
6
5
4
3
2
1
ppm

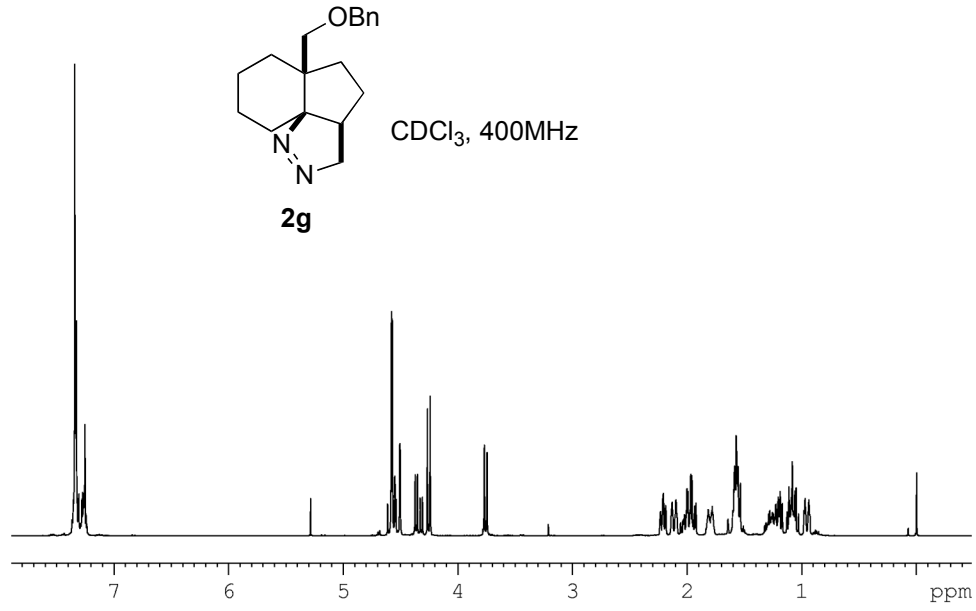

180
160
140
120
100
80
60
40
20
ppm

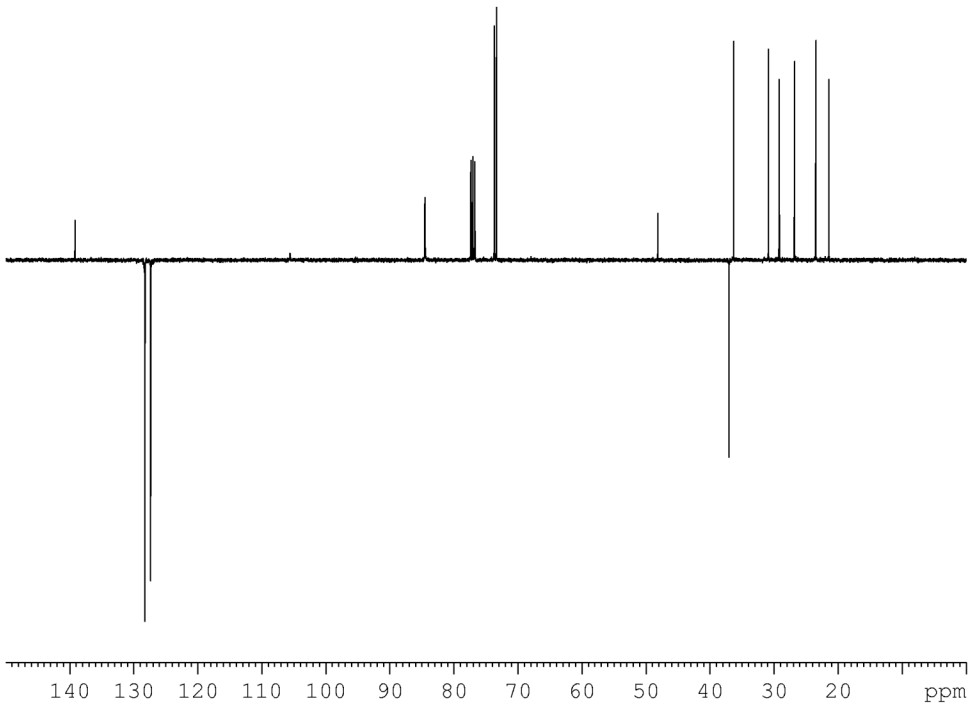

OH
O
O
CDCl3, 400MHz
20
7
6
5
4
3
2
1
ppm


140
120
100
80
60
40
20
ppm


OBn
O
O
21
CDCl3, 400MHz
7
6
5
4
3
2
1
ppm
160
140
120
100
80
60
40
20
ppm


BnO
O
CDCl3, 400MHz
1g
7
6
5
4
3
2
1
ppm
200
180
160
140
120
100
80
60
40
20
ppm


OBn
N
N
CDCl3, 400MHz
2g
7
6
5
4
3
2
1
ppm


140
130
120
110
100
90
80
70
60
50
40
30
20
ppm