Rhodium-Catalyzed Carbonylation of Spiropentanes

Takanori Matsuda, Tomoya Tsuboi, and Masahiro Murakami*

Department of Synthetic Chemistry and Biological Chemistry,

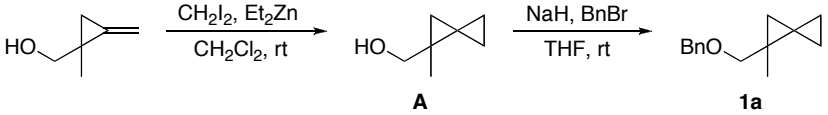
Kyoto University, Katsura, Kyoto 615-8510, Japan

Supporting Information

General. All reactions were carried out with standard Schlenk techniques under an argon, nitrogen or carbon monoxide atmosphere. Column chromatography was carried out on Kanto Silica Gel 60 N (spherical, neutral) (100–210 μm). Preparative thin-layer chromatography was performed on silica gel 60 PF_{254} (Merck). ^{1}H and ^{13}C NMR data were taken in $CDCl_3$ at 300.07 MHz and 75.46 MHz, respectively. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm. Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm.

Materials. (1-Methyl-2-methylenecyclopropyl)methanol, [1] 2-cyclopropylidene-2-phenylethanol, [2] 5-(4-*tert*-butylphenyl)spiro[2.3]hexane (**10**), [3] (3-bromopropyl)triphenylphosphonium bromide [4] were prepared according to the literature. *p*-Xylene was distilled over sodium–benzophenone ketyl. All other commercially available chemical resources were used as received without further purification.

Preparation of Spiropentanes 1



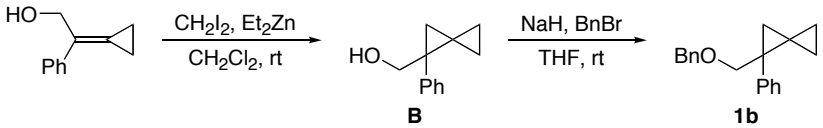
A **1a**

(1-Methylspiro[2.2]pent-1-yl)methanol (A). To a solution of CH_2I_2 (6.43 g, 24 mmol) in CH_2Cl_2 (70 mL) was added dropwise a solution of Et_2Zn in hexane (1.0 M, 12 mL, 12 mmol) at –20 °C. After stirring for 15 min, a solution of (1-methyl-2-methylenecyclopropyl)methanol (1.16 g, 11.9 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the reaction mixture. After being stirred overnight at room temperature, the reaction mixture was quenched with saturated NH_4Cl aqueous solution, diluted with 2.0 N HCl aqueous solution, and extracted with CH_2Cl_2. The

(1) Corlay, H.; Lewis, R. T.; Motherwell, W. B.; Shipman, M. *Tetrahedron* **1995**, *51*, 3303.
(2) Nemoto, H.; Ishibashi, H.; Nagamochi, M.; Fukumoto, K. *J. Org. Chem.* **1992**, *57*, 1707.
(3) Matsuda, T.; Shigeno, M.; Murakami, M. *Chem. Lett.* **2006**, *35*, 288.
(4) Siriwardana, A.; Nakamura, I.; Yamamoto, Y. *Tetrahedron Lett.* **2003**, *44*, 4547.

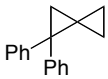
extract was washed with saturated $NaHCO_3$ aqueous solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (hexane:Et_2O = 2:1) to afford **A** (275 mg, 2.46 mmol, 21%).

1-(Benzyloxymethyl)-1-methylspiro[2.2]pentane (1a). To a suspension of NaH (37.2 mg, 1.55 mmol) in THF (10 mL) was added dropwise a solution of **A** (125 mg, 1.11 mmol) in THF (5 mL) at 0 °C. After stirring for 10 min, benzyl bromide (263 mg, 1.55 mmol) was added to the mixture. After being stirred overnight at room temperature, NaH (13.4 mg, 0.56 mmol) and benzyl bromide (96 mg, 0.56 mmol) was added again. After being stirred overnight at room temperature, the reaction mixture was quenched with water and extracted with Et_2O. The extract was dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel (hexane:AcOEt = 50:1, then 10:1) to afford **1a** (171 mg, 0.847 mmol, 76%): ^{1}H NMR δ 0.63-0.81 (m, 6H), 1.18 (s, 3H), 3.32 (d, J = 9.6 Hz, 1H), 3.38 (d, J = 9.6 Hz, 1H), 4.46 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 12.2 Hz, 1H), 7.26-7.35 (m, 5H); ^{13}C NMR δ 3.5, 4.6, 18.2, 19.2, 19.6, 19.8, 72.7, 77.6, 127.4, 127.5, 128.2, 138.8; HRMS (CI) calcd for $C_{14}H_{17}O$ 201.1279 ([M – H]$^+$), found 201.1282.



(1-Phenylspiro[2.2]pent-1-yl)methanol (B). To a solution of CH_2I_2 (1.37 g, 5.12 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of Et_2Zn in hexane (1.0 M, 2.56 mL, 2.56 mmol) at –20 °C and then stirred 15 min. To the reaction mixture was added dropwise a solution of cyclopropylidene-2-phenyl-1-ethanol (205 mg, 1.28 mmol) in CH_2Cl_2 (10 mL). After being stirred overnight at room temperature, the reaction mixture was quenched with saturated NH_4Cl aqueous solution, diluted with 2.0 N HCl aqueous solution, and extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ aqueous solution, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (hexane:AcOEt = 3:1) to afford **B** (132 mg, 0.759 mmol, 59%).

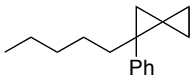
1-(Benzyloxymethyl)-1-phenylspiro[2.2]pentane (1b). To a suspension of NaH (73.4 mg, 3.06 mmol) in THF (20 mL) a solution of **B** (445 mg, 2.55 mmol) in THF (5 mL) was added dropwise at 0 °C. After being stirred for 10 min, benzyl bromide (523 mg, 3.06 mmol) was added. After being stirred for 11 h at room temperature, the reaction was quenched with water, extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel (hexane:AcOEt = 50:1, then 10:1) to afford **1b** (466 mg, 1.76 mmol, 69%): ^{1}H NMR δ 0.80-0.89 (m, 3H,), 0.98-1.03 (m, 1H,) 1.35 (d, J = 4.8 Hz, 1H), 1.36 (d, J = 5.1 Hz, 1H), 3.74 (d, J = 10.1 Hz, 1H), 3.78 (d, J = 10.1 Hz, 1H), 4.51 (d, J = 12.3 Hz, 1H), 4.57 (d, J = 12.3 Hz, 1H), 7.18-7.25 (m, 1H), 7.28-7.36 (m, 9H); ^{13}C NMR δ 5.1, 5.2, 20.9, 22.3, 28.0, 72.9, 76.4, 125.5, 127.3, 127.4, 127.6, 127.9, 128.2, 138.5, 142.8; HRMS (CI) calcd for $C_{19}H_{20}O$ (M^+) 264.1514, found 264.1516.



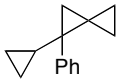
1,1-Diphenylspiro[2.2]pentane (1c).[5] ^{1}H NMR δ 1.06-1.07 (m, 2H), 1.09-1.11 (m, 2H),

(5) [128742-43-8].

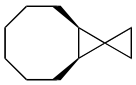
1.78-1.79 (m, 2H), 7.20-7.24 (m, 4H), 7.25-7.30 (m, 2H), 7.32-7.38 (m, 4H); ^{13}C NMR δ 7.0, 24.8, 25.0, 33.0, 125.7, 128.0, 128.4, 144.6; HRMS (CI) calcd for $C_{17}H_{16}$ (M^+) 220.1252, found 221.1254.



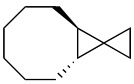
1-Pentyl-1-phenylspiro[2.2]pentane (1d). ^{1}H NMR δ 0.71-0.78 (m, 3H), 0.80-0.86 (m, 3H), 0.91-0.96 (m, 1H), 1.03 (d, J = 3.9 Hz, 1H), 1.02-1.36 (m, 7H), 1.45-1.54 (m, 1H), 1.75-1.87 (m, 1H), 7.14-7.19 (m, 3H), 7.26-7.31 (m, 2H); ^{13}C NMR δ 5.0, 5.8, 14.1, 20.1, 22.7, 22.8, 26.7, 28.8, 32.2, 38.2, 125.4, 127.9, 128.0, 144.6; HRMS (CI) calcd for $C_{16}H_{22}$ (M^+) 214.1722, found 214.1716.



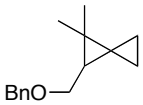
1-Cyclopropyl-1-phenylspiro[2.2]pentane (1e). ^{1}H NMR δ 0.13-0.20 (m, 1H), 0.37-0.44 (m, 1H), 0.47-0.58 (m, 2H), 0.64-0.71 (m, 1H), 0.74-0.80 (m, 1H), 0.86-0.96 (m, 2H), 1.08 (s, 2H), 1.27 (tt, J = 8.2, 5.2 Hz, 1H), 7.14-7.21 (m, 1H), 7.27-7.34 (m, 2H), 7.35-7.41 (m, 2H); ^{13}C NMR δ 2.8, 2.9, 4.9, 5.9, 15.6, 19.5, 21.8, 28.1, 125.2, 126.9, 127.8, 145.7; HRMS (CI) calcd for $C_{14}H_{16}$ (M^+) 184.1252, found 185.1248.



(1*RS*,8*SR*)-Spiro[bicyclo[6.1.0]nonane-9,1'-cyclopropane] (1f).[6] ^{1}H NMR δ 0.46-0.53 (m, 2H), 0.66-0.73 (m, 2H), 0.87-1.14 (m, 4H), 1.30-1.62 (m, 6H), 1.63-1.77 (m, 4H); ^{13}C NMR δ 1.1, 6.2, 20.4, 25.1, 26.7, 29.4; HRMS (CI) calcd for $C_{11}H_{19}$ ([M + H]$^+$) 151.1487, found 151.1489.

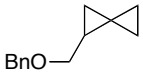


(1*RS*,8*RS*)-Spiro[bicyclo[6.1.0]nonane-9,1'-cyclopropane] (1g). ^{1}H NMR δ 0.52-0.60 (m, 2H), 0.65-0.73 (m, 4H), 0.81-0.95 (m, 2H), 1.24-1.36 (m, 2H), 1.42-1.56 (m, 2H), 1.84-2.05 (m, 6H); ^{13}C NMR δ 3.6, 16.8, 25.8, 28.8, 31.9 [overlapping]; HRMS (FAB) calcd for $C_{11}H_{19}$ (M^+) 150.1409, found 150.1411.



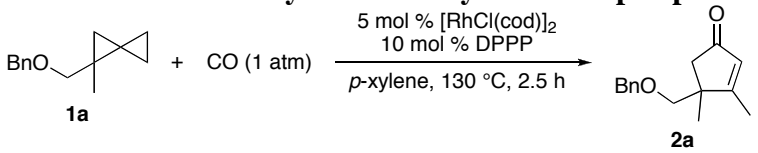
2-(Benzyloxymethyl)-1,1-dimethylspiro[2.2]pentane (1h). ^{1}H NMR δ 0.51-0.75 (m, 4H), 1.03 (s, 3H), 1.11 (s, 3H), 1.14 (t, J = 7.2 Hz, 1H), 3.47 (dd, J = 10.3, 7.7 Hz, 1H), 3.51 (dd, J = 10.3, 6.6 Hz, 1H), 4.50 (s, 2H), 7.27-7.36 (m, 5H); ^{13}C NMR δ 2.3, 4.3, 18.2, 18.9, 24.5, 24.9, 27.1, 70.3, 72.6, 127.4, 127.6, 128.3, 138.7; HRMS (EI) calcd for $C_{15}H_{20}O$ (M^+) 216.1514, found 216.1513.

(6) [305370-72-3].



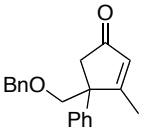
1-(Benzyloxymethyl)spiro[2.2]pentane (1i). ^{1}H NMR δ 0.62-0.80 (m, 5H), 1.03 (dd, J = 7.8, 4.2 Hz, 1H), 1.46 (ddd, J = 14.6, 7.1, 4.2 Hz, 1H), 3.42 (dd, J = 12.0, 6.6 Hz, 1H), 3.45 (dd, J = 12.0, 7.1 Hz, 1H), 4.48 (d, J = 12.2 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 7.25-7.38 (m, 5H); ^{13}C NMR δ 3.5, 5.4, 11.1, 13.5, 16.9, 72.6, 73.9, 127.4, 127.6, 128.2, 138.5; HRMS (CI) calcd for $C_{13}H_{15}O$ ([M – H]$^+$) 187.1123, found 188.1118.

General Procedure for Rhodium-Catalyzed Carbonylation of Spiropentanes

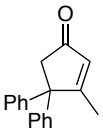


1a **2a**

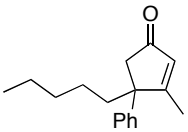
4-(Benzyloxymethyl)-3,4-dimethylcyclopent-2-enone (2a). To a mixture of $[RhCl(cod)]_2$ (4.9 mg, 9.9 μmol, 5 mol %) and $Ph_2P(CH_2)_3PPh_2$ (8.2 mg, 20 μmol, 10 mol %) under CO (1 atm) atmosphere, *p*-xylene (4.0 mL) was added. The solution was stirred for 5 min at 130 °C, then **1a** (40.5 mg, 0.200 mol) was added. After being stirred for 2.5 h at the same temperature, the reaction mixture was filtered through a pad of silica gel (AcOEt), and the filtrate was evaporated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 2:1) to afford **2a** (38.7 mg, 0.168 mmol, 84 %): ^{1}H NMR δ 1.17 (s, 3H), 1.99 (s, 3H), 2.13 (d, J = 18.3 Hz, 1H), 2.59 (d, J = 18.3 Hz, 1H), 3.33 (d, J = 8.9 Hz, 1H), 3.41 (d, J = 8.9 Hz, 1H), 4.50 (s, 2H), 5.89 (s, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR δ 14.6, 22.1, 47.1, 47.4, 73.3, 74.4, 127.5, 127.7, 128.4, 131.2, 137.9, 182.0, 207.6; HRMS (FAB) calcd for $C_{15}H_{19}O_2$ ([M + H]$^+$) 231.1385, found 231.1389.



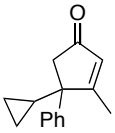
4-(Benzyloxymethyl)-3-methyl-4-phenylcyclopent-2-enone (2b). According to the general procedure, **2b** (48.2 mg, 82%) was obtained from **1b** (52.6 mg, 0.199 mmol). IR (neat) 1713, 1624 cm^{-1}; ^{1}H NMR δ 1.85 (s, 3H), 2.51 (d, J = 18.6 Hz, 1H), 2.90 (d, J = 18.6 Hz, 1H), 3.93 (d, J = 8.7 Hz, 1H), 3.97 (d, J = 8.7 Hz, 1H), 4.60 (d, J = 12.3 Hz, 1H), 4.65 (d, J = 12.3 Hz, 1H), 6.13 (s, 1H), 7.13-7.15 (m, 2H), 7.23-7.39 (m, 8H); ^{13}C NMR δ 15.5, 49.8, 54.8, 71.7, 73.6, 125.8, 127.0, 127.6, 127.8, 128.4, 128.8, 132.3, 137.6, 141.9, 180.5, 208.1; HRMS (FAB) calcd for $C_{20}H_{21}O_2$ ([M + H]$^+$) 293.1542, found 293.1536.



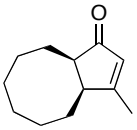
3-Methyl-4,4-diphenylcyclopent-2-enone (2c). According to the general procedure, **2c** (38.8 mg, 78%) was obtained from **1c** (44.2 mg, 0.201 mmol). ^{1}H NMR δ 1.94 (s, 3H), 3.11 (s, 2H), 6.12 (s, 1H), 7.19-7.21 (m, 4H), 7.25-7.36 (m, 6H); ^{13}C NMR δ 16.9, 55.1, 60.4, 126.8, 128.0, 128.5, 131.6, 143.9, 181.8, 207.4; HRMS (EI) calcd for $C_{18}H_{16}O$ (M^+) 248.1201, found 248.1201.



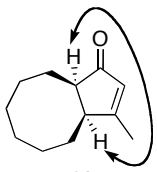
3-Methyl-4-pentyl-4-phenylcyclopent-2-enone (2d). According to the general procedure, **2d** (36.8 mg, 76%) was obtained from **1a** (42.5 mg, 0.198 mmol). ^{1}H NMR δ 0.90 (t, J = 7.1 Hz, 3H), 0.99-1.44 (m, 6H), 1.78 (s, 3H), 1.92 (dt, J = 4.8, 12.8 Hz, 1H), 2.14 (dt, J = 3.8, 12.8 Hz, 1H), 2.55 (d, J = 18.8 Hz, 1H), 2.64 (d, J = 18.8 Hz, 1H), 6.06 (s, 1H), 7.20-7.25 (m, 3H), 7.30-7.36 (m, 2H); ^{13}C NMR δ 14.0, 15.2, 22.5, 23.9, 32.4, 34.1, 50.9, 53.6, 125.9, 126.6, 128.6, 131.5, 144.3, 182.9, 208.6; HRMS (EI) calcd for $C_{17}H_{22}O$ (M^+) 242.1671 found 242.1676.



4-Cyclopropyl-3-methyl-4-phenylcyclopent-2-enone (2e). According to the general procedure, **2e** (33.8 mg, 82%) was obtained from **1e** (35.9 mg, 0.195 mmol). ^{1}H NMR δ 0.02-0.14 (m, 1H), 0.46-0.58 (m, 2H), 0.87-1.00 (m, 1H), 1.35-1.46 (m, 1H), 1.94 (d, J = 18.8 Hz, 1H), 1.94 (s, 3H), 2.11 (d, J = 18.8 Hz, 1H), 6.05 (s, 1H), 7.22-7.29 (m, 1H), 7.29-7.38 (m, 2H), 7.38-7.46 (m, 2H); ^{13}C NMR δ –0.3, 4.6, 14.7, 15.5, 45.6, 54.1, 126.4, 126.7, 128.7, 130.2, 145.0, 183.5, 208.2; HRMS (EI) calcd for $C_{15}H_{16}O$ (M^+) 212.1201, found 212.1191.

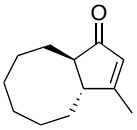


(1*SR*,5*RS*)-11-Methylbicyclo[6.3.0]undec-10-en-9-one (2f). According to the general procedure, **2f** (20.0 mg, 56%) was obtained from **1f** (30.1 mg, 0.200 mmol). ^{1}H NMR δ 1.24-1.85 (m, 11H), 2.07-2.14 (m, 4H), 2.29 (t, J = 6.9 Hz, 1H), 2.72 (t, J = 7.5 Hz, 1H), 5.88 (s, 1H); ^{13}C NMR δ 17.7, 23.5, 25.8, 25.9, 26.7, 30.1, 31.4, 50.4, 52.1, 128.9, 181.2, 211.3; HRMS (EI) calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1363.

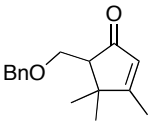


2f

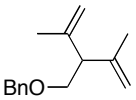
Figure 1. NOE Experiment of **2f**



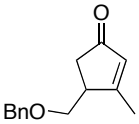
(1*RS*,5*RS*)-11-Methylbicyclo[6.3.0]undec-10-en-9-one (2g). According to the general procedure, **2g** (31.3 mg, 74%) was obtained from **1g** (35.9mg, 0.239 mmol). ^{1}H NMR δ 1.07-1.23 (m, 2H), 1.41-1.60 (m, 4H), 1.69-1.90 (m, 4H), 1.99-2.24 (m, 6H), 2.61-2.65 (m, 2H), 5.84 (s. 1H); ^{13}C NMR δ 17.2, 24.7, 24.8, 27.0, 27.3, 30.3, 32.1, 50.0, 51.9, 128.9, 180.6, 211.05; HRMS (EI) calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1358.



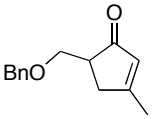
5-(Benzyloxymethyl)-3,4,4-trimethylcyclopent-2-enone (2h). According to the general procedure, **2h** (34.2 mg, 37%) and **7** (6.11 mg, 18%) were obtained from **1h** (34.2 mg, 0.158 mmol). **2h:** ^{1}H NMR δ 1.18 (s, 3H), 1.27 (s, 3H), 2.04 (s, 3H), 2.54 (dd, J = 9.8, 3.8 Hz, 1H), 3.60 (t, J = 9.8 Hz, 1H), 3.89 (dd, J = 9.8, 3.8 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 5.80 (s, 1H), 7.27-7.37 (m, 5H); ^{13}C NMR δ 14.4, 22.4, 26.9, 46.1, 58.2, 67.9, 73.2, 127.5 [overlapping], 128.2, 128.3, 138.2, 185.3, 206.7; HRMS (EI) calcd for $C_{16}H_{20}O_2$ (M^+) 244.1463, found 244.1460.



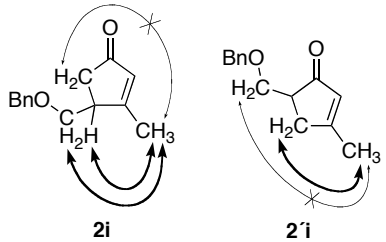
3-(Benzyloxymethyl)-2,4-dimethylpenta-1,4-diene (7). ^{1}H NMR δ 1.66 (s, 6H), 2.99 (t, J = 7.4 Hz, 1H), 3.60 (d, J = 7.4 Hz, 2H), 4.54 (s, 2H), 4.77 (s, 2H), 4.88 (s, 2H), 7.27-7.35 (m, 5H); ^{13}C NMR δ 21.0, 53.5, 70.3, 73.1, 111.8, 127.5, 127.7, 128.3, 138.4, 144.0; HRMS (EI) calcd for $C_{15}H_{20}O$ (M^+) 216.1514, found 216.1514.



4-(Benzyloxymethyl)-3-methylcyclopent-2-enone (2i). According to the general procedure **2i** (23.3 mg, 55%) and **2´i** (8.72 mg, 21%) were obtained from **1i** (36.7 mg, 0.195 mmol). **2i:** ^{1}H NMR δ 2.10 (s, 3H), 2.31 (dd, J = 18.4, 2.3 Hz, 1H), 2.54 (dd, J = 18.4, 6.6 Hz, 1H), 3.00 (br s, 1H), 3.53 (dd, J = 9.3, 5.7 Hz, 1H), 3.60 (dd, J = 9.3, 4.8 Hz, 1H), 4.49 (d, J = 12.3 Hz, 1H), 4.54 (d, J = 12.3 Hz, 1H), 5.96 (s, 1H), 7.24-7.38 (m, 5H); ^{13}C NMR δ 17.7, 39.7, 44.7, 70.3, 73.3, 127.6, 127.7, 128.4, 132.0, 137.7, 178.5, 208.5; HRMS (FAB) calcd for $C_{14}H_{17}O_2$ ([M + H]$^+$) 217.1229, found 217.1228.

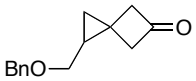


5-(Benzyloxymethyl)-3-methylcyclopent-2-enone (2´i). ^{1}H NMR δ 2.14 (s, 3H), 2.58-2.77 (m, 3H), 3.60-3.74 (m, 2H), 4.45-4.55 (m, 2H), 5.94 (s, 1H), 7.24-7.38 (m, 5H); ^{13}C NMR δ 19.6, 37.5, 47.4, 69.7, 73.2, 127.6 [overlapping], 128.3, 130.2, 138.1, 178.6, 209.4; HRMS (FAB) calcd for $C_{14}H_{17}O_2$ ([M + H]$^+$) 217.1229, found 217.1227.



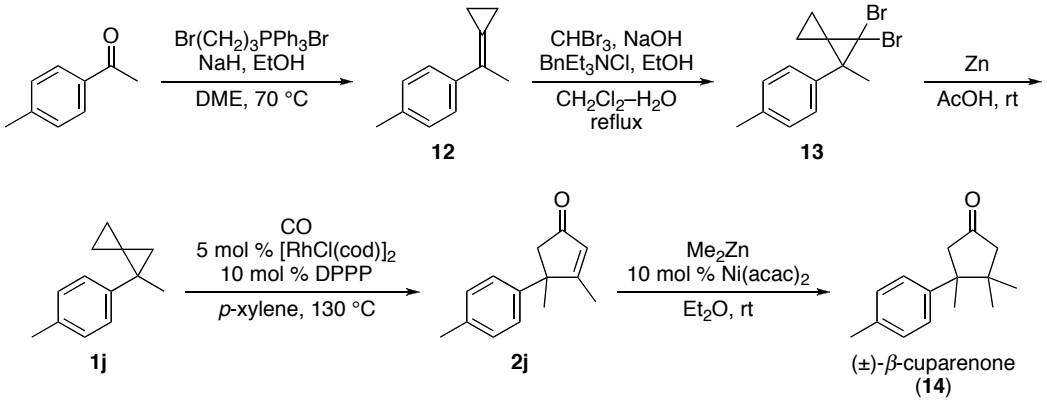
2i **2´i**

Figure 2. NOE Experiments of **2i** and **2´i**



1-(Benzyloxymethyl)spiro[2.3]hexan-5-one (8). ^{1}H NMR δ 0.59 (t, J = 5.2 Hz, 1H), 0.98 (dd, J = 8.9, 5.2 Hz, 1H), 1.43 (tt, J = 8.9, 5.5 Hz, 1H), 2.91-3.27 (m, 5H), 3.62 (dd, J = 10.1, 5.5 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 7.27-7.38 (m, 5H); ^{13}C NMR δ 15.2, 15.4, 20.5, 50.4, 54.4, 72.2, 72.8, 127.57, 127.63, 128.3, 138.0, 206.6; HRMS (CI) calcd for $C_{14}H_{16}O_2$ (M^+) 216.1150, found 216.1154.

Synthesis of (±)-β-Cuparenone (12)



[1-(4-Methylphenyl)ethylidene]cyclopropane (12).[7] To a suspension of NaH (1.03 g, 42.9 mmol) in 1,2-dimethoxyethane (30 mL) was added (3-bromopropyl)triphenylphosphonium bromide (10.0 g, 21.5 mmol) and EtOH (three drops), and the mixture was heated for 6 h at 60 °C. To the reaction mixture was added 4'-methylacetophenone (1.92 g, 14.3 mmol), and the mixture was heated for 20 h at 70 °C. The reaction mixture was quenched with water and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (hexane) to afford **12** (1.86 g, 11.8 mmol, 83%).

1,1-Dibromo-4-methyl-4-(4-methylphenyl)spiro[2.2]pentane (13). To a solution of NaOH (11.0 g, 275 mmol) in water (11.0 mL) was added successively $CHBr_3$ (3.9 mL, 45.0 mmol), benzyltriethylammonium chloride (42.1 mg, 0.185 mmol), a solution of **12** (1.61 g, 10.2 mmol) in CH_2Cl_2 (8 mL), and ethanol (220 μL). The mixture was refluxed for 4 h, and then stirred at room temperature for 15 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (hexane) to afford **13** (1.81 g, 5.48 mmol, 54%). ^{1}H NMR δ 1.08-1.16 (m, 1H), 1.25-1.40 (m, 2H), 1.67 (s, 3H), 1.73-1.81 (m, 1H), 2.36 (s, 3H), 7.17 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 10.7, 13.1, 21.2, 26.3, 36.0, 36.2, 48.3, 128.1, 128.7, 136.6, 139.2; HRMS (EI) calcd for $C_{13}H_{14}Br_2$ (M^+) 327.9462, found 327.9470.

1-Methyl-1-(4-methylphenyl)spiro[2.2]pentane (1j). A mixture of **13** (872 mg, 2.64 mmol),

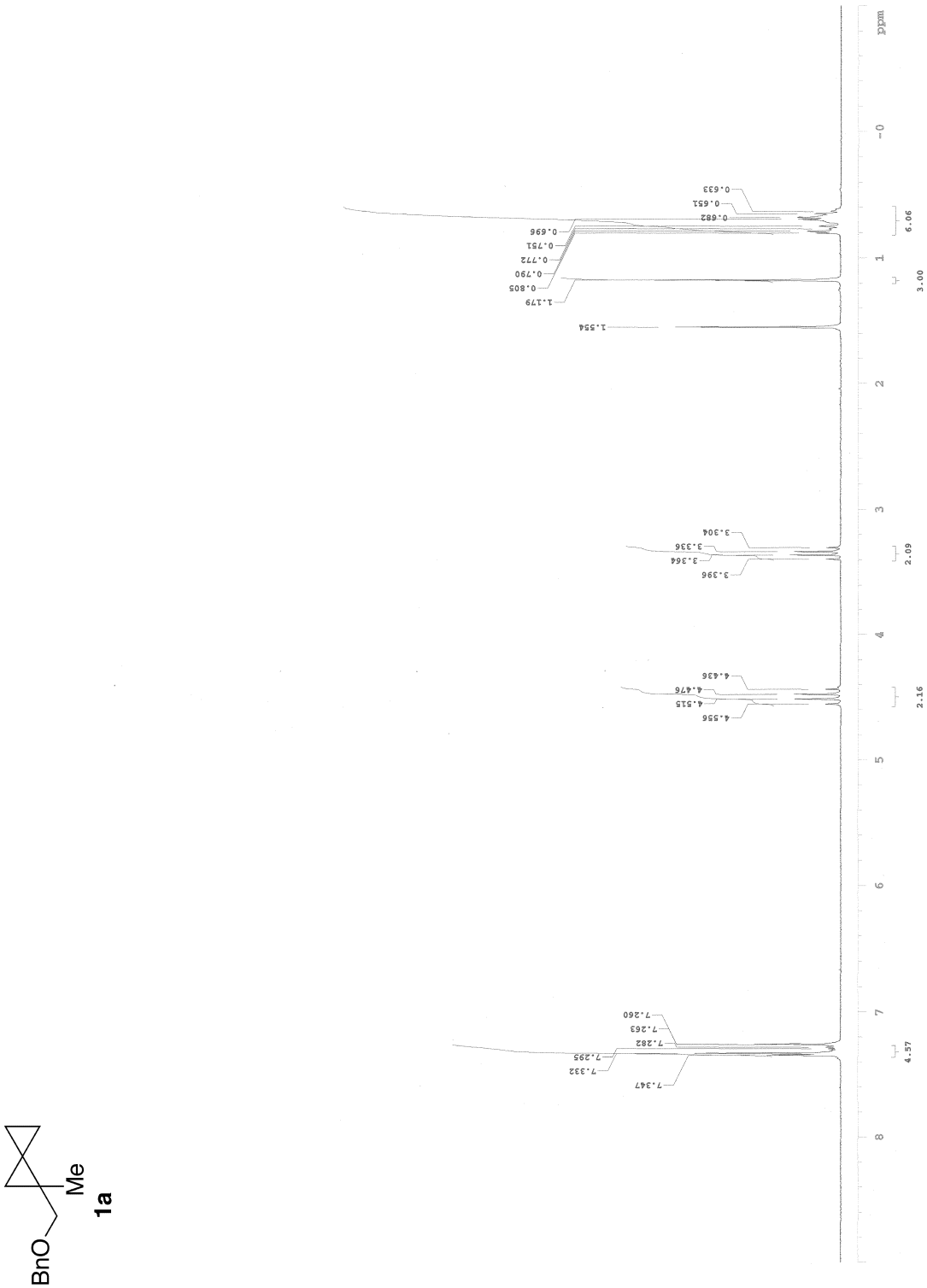
(7) [671782-19-7]

zinc powder (1.38 g, 21.1 mmol), and acetic acid (15 mL) was stirred at room temperature for 5 h. The reaction mixture was quenched with water, filtrated (Celite®, water and Et_2O), and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (hexane) to afford **1j** (254 mg, 1.47 mmol, 56%): ^{1}H NMR δ 0.71-0.94 (m, 4H), 1.11 (d, J = 4.1 Hz, 1H), 1.21 (d, J = 4.1 Hz, 1H), 1.44 (s, 3H), 2.31 (s, 3H), 7.07-7.14 (m, 4H); ^{13}C NMR δ 5.4, 6.4, 20.9, 22.5, 22.6, 23.4, 24.1, 125.8, 128.6, 134.4, 143.0; HRMS (EI) calcd for $C_{13}H_{16}$ (M^+) 172.1252, found 172.1253.

3,4-Dimethyl-4-(4-methylphenyl)cyclopent-2-enone (2j).[8] According to the general procedure, **2j** (71.8 mg, 82%) was obtained from **1j** (75.3 mg, 0.437 mmol). ^{1}H NMR δ 1.63 (s, 3H), 1.82 (s, 3H), 2.32 (s, 3H), 2.53 (d, J = 18.8 Hz, 1H), 2.65 (d, J = 18.8 Hz, 1H), 6.02 (s, 1H), 7.08-7.16 (m, 4H); ^{13}C NMR δ 14.9, 20.9, 23.7, 49.8, 54.3, 125.5, 129.3, 130.1, 136.2, 141.1, 184.6, 208.5; HRMS (EI) calcd for $C_{14}H_{16}O$ (M^+) 200.1201, found 200.1198.

(±)-β-Cuparenone (14).[9] To a mixture of **2j** (44.9 mg, 0.224 mmol) and $Ni(acac)_2$ (5.75 mg, 22.4 μmol) was added dropwise a solution of Me_2Zn in hexane (1.0 M, 2.5 mL) at 0 °C. After being stirred for 19 h at room temperature, the reaction mixture was quenched with saturated NH_4Cl aqueous solution and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 4:1) to afford **14** (36.5 mg, 0.169 mmol, 75 %): ^{1}H NMR δ 0.72 (s, 3H), 1.23 (s, 3H), 1.42 (s, 3H), 2.23 (d, J = 19.5 Hz, 1H), 2.30-2.37 (m, 5H), 3.13 (d, J = 18.3 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 20.8, 24.1, 24.4, 26.2, 41.8, 47.8, 50.7, 52.4, 126.5, 128.7, 135.8, 141.2, 218.3; HRMS (EI) calcd for $C_{15}H_{20}O$ (M^+) 216.1514, found 216.1511.

(8) [133321-75-2].
(9) [25090-79-3].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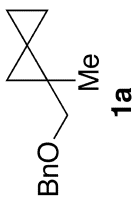
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Me

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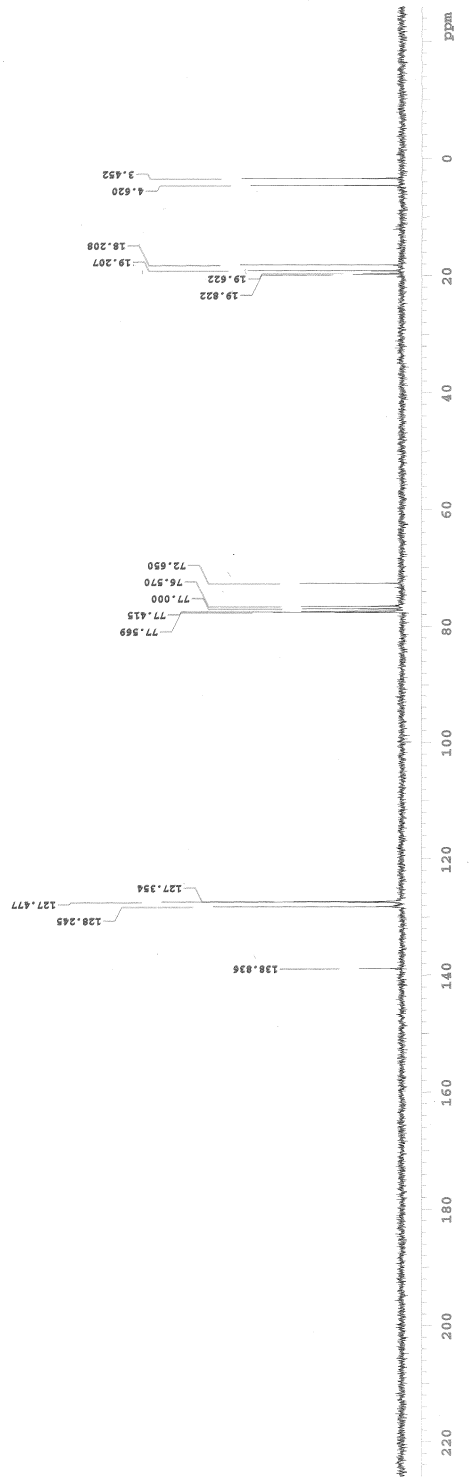
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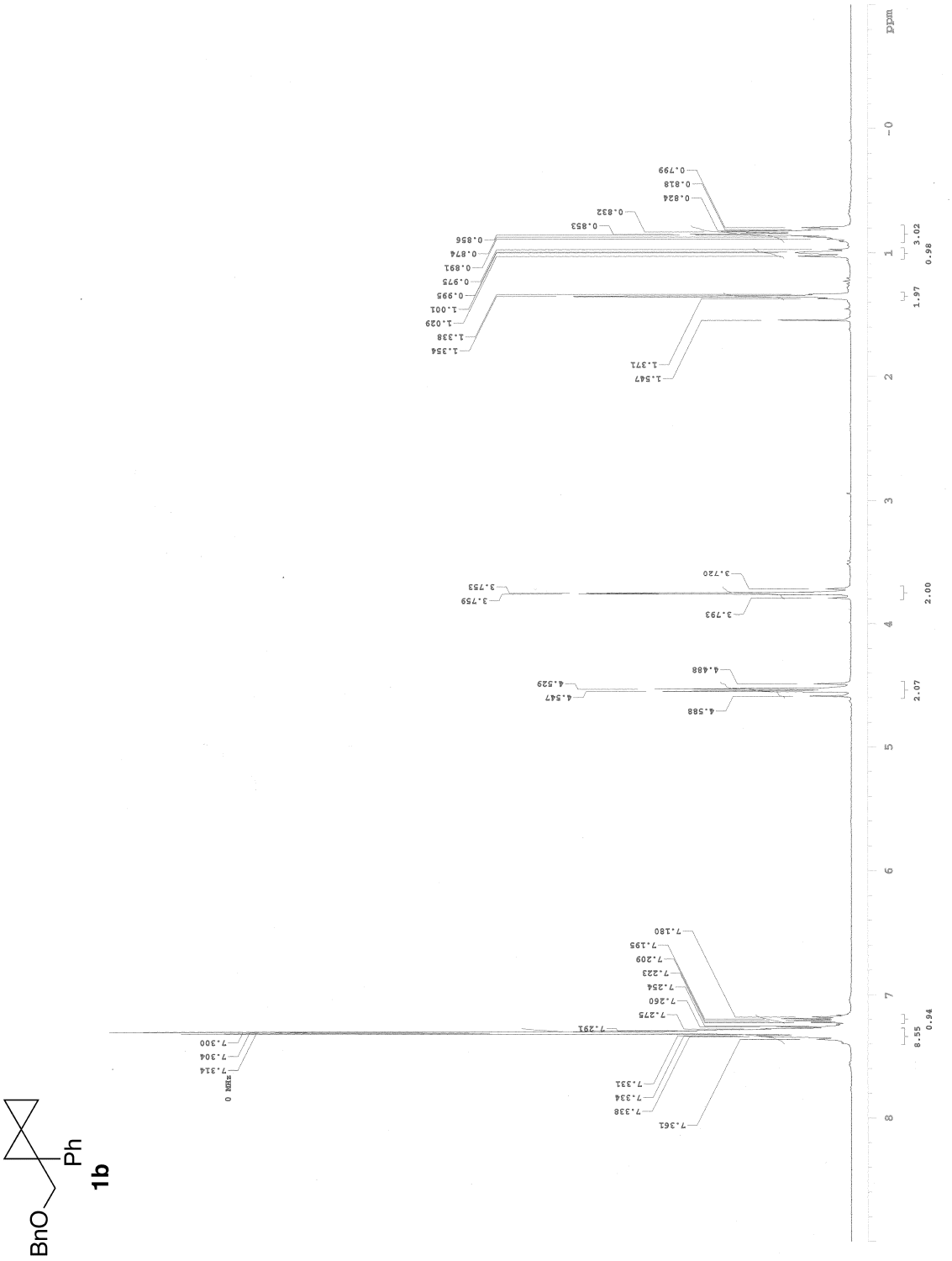
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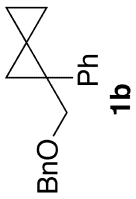
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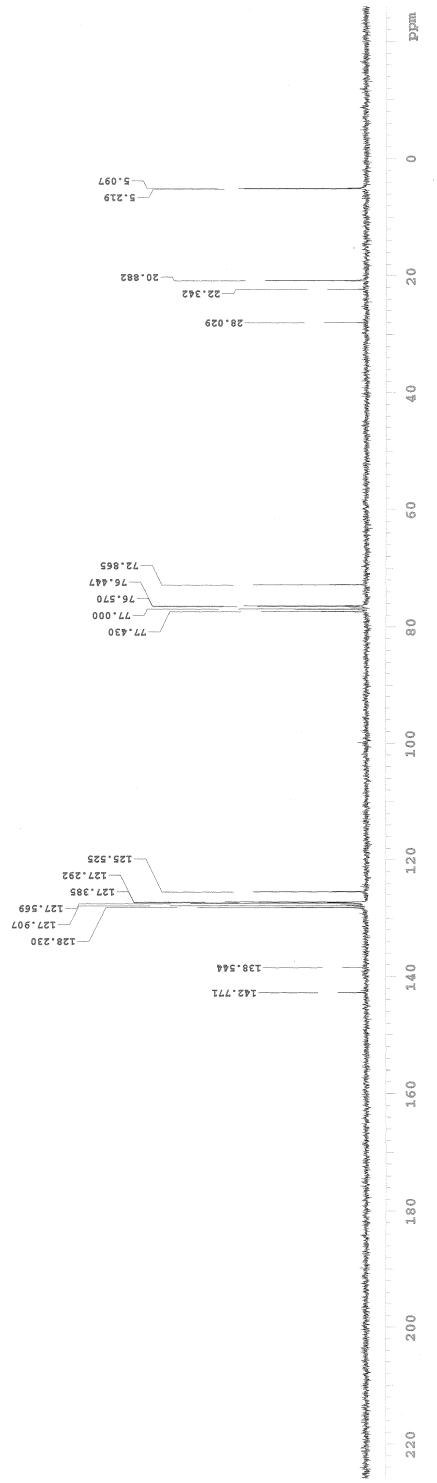
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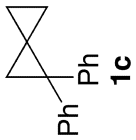
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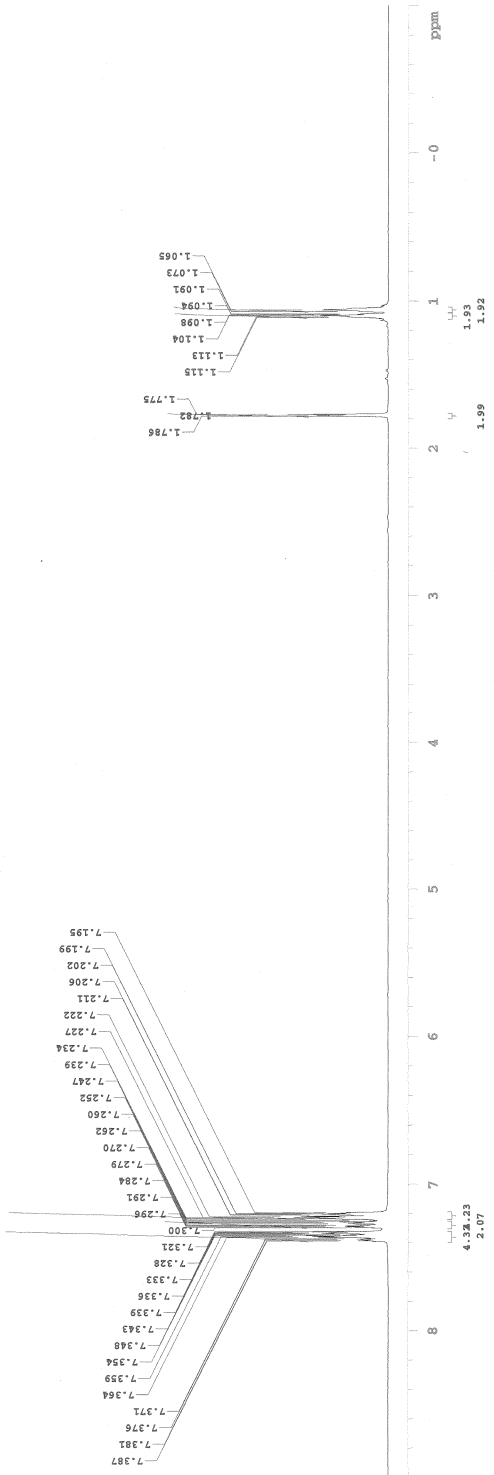
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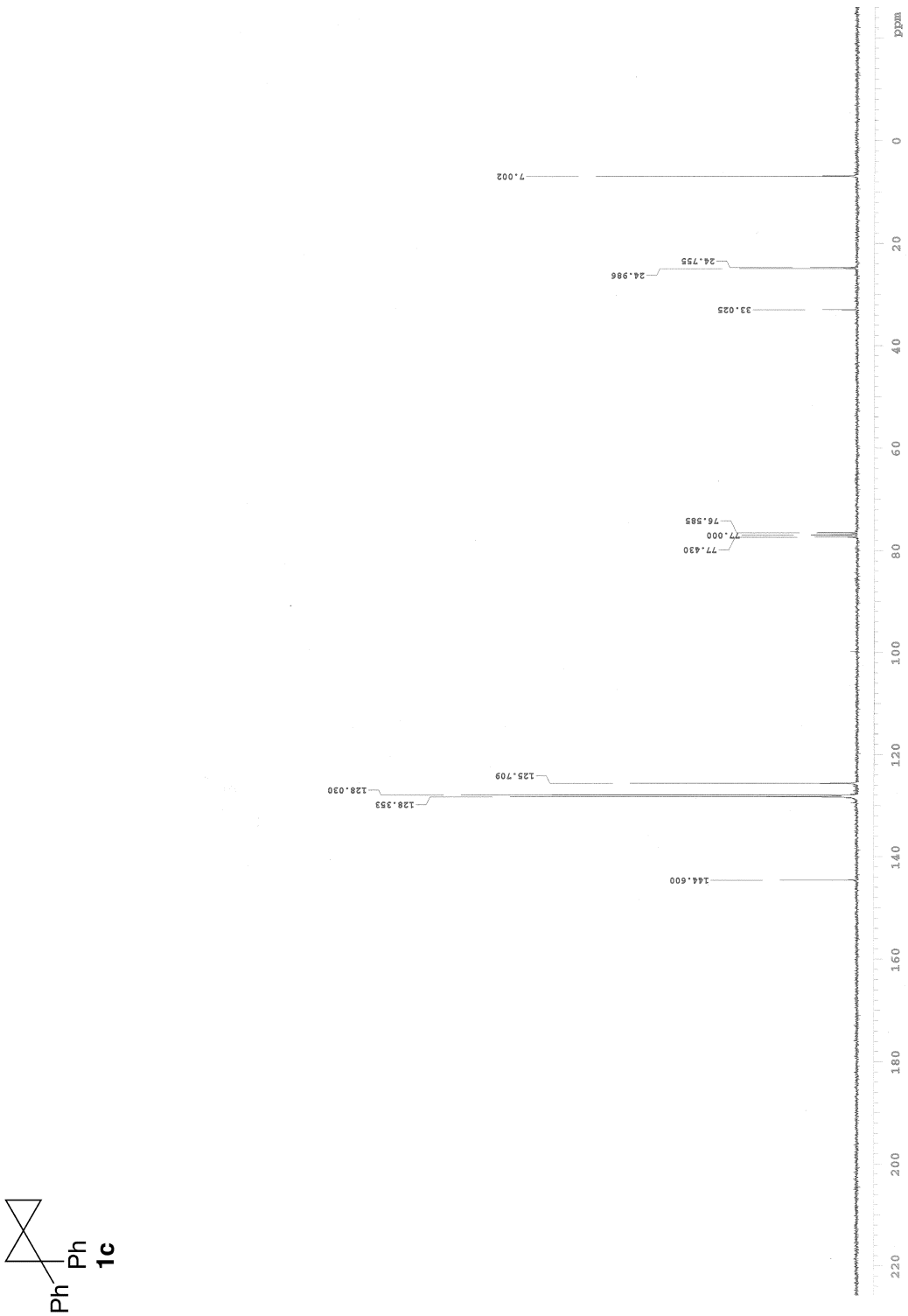
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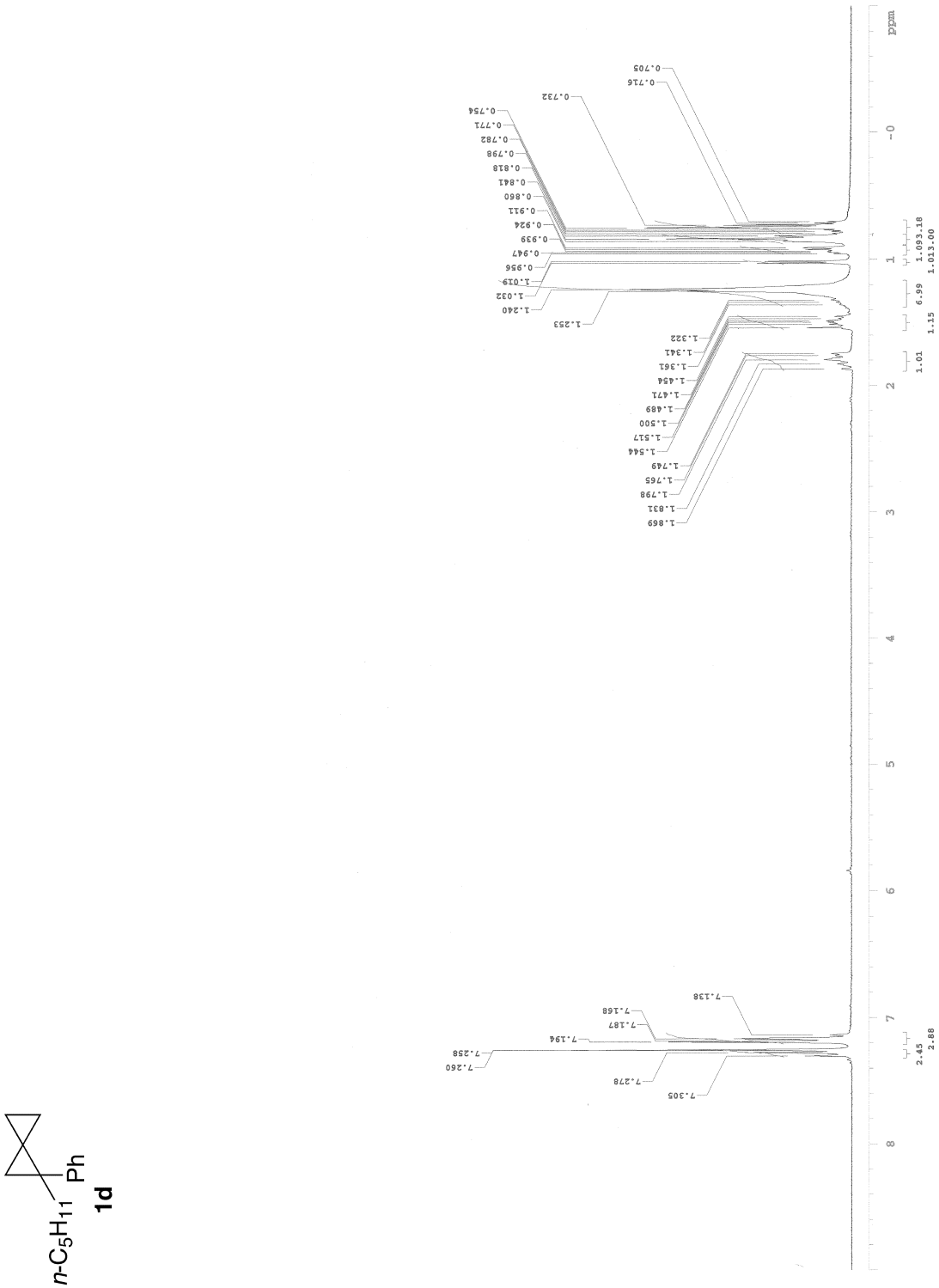
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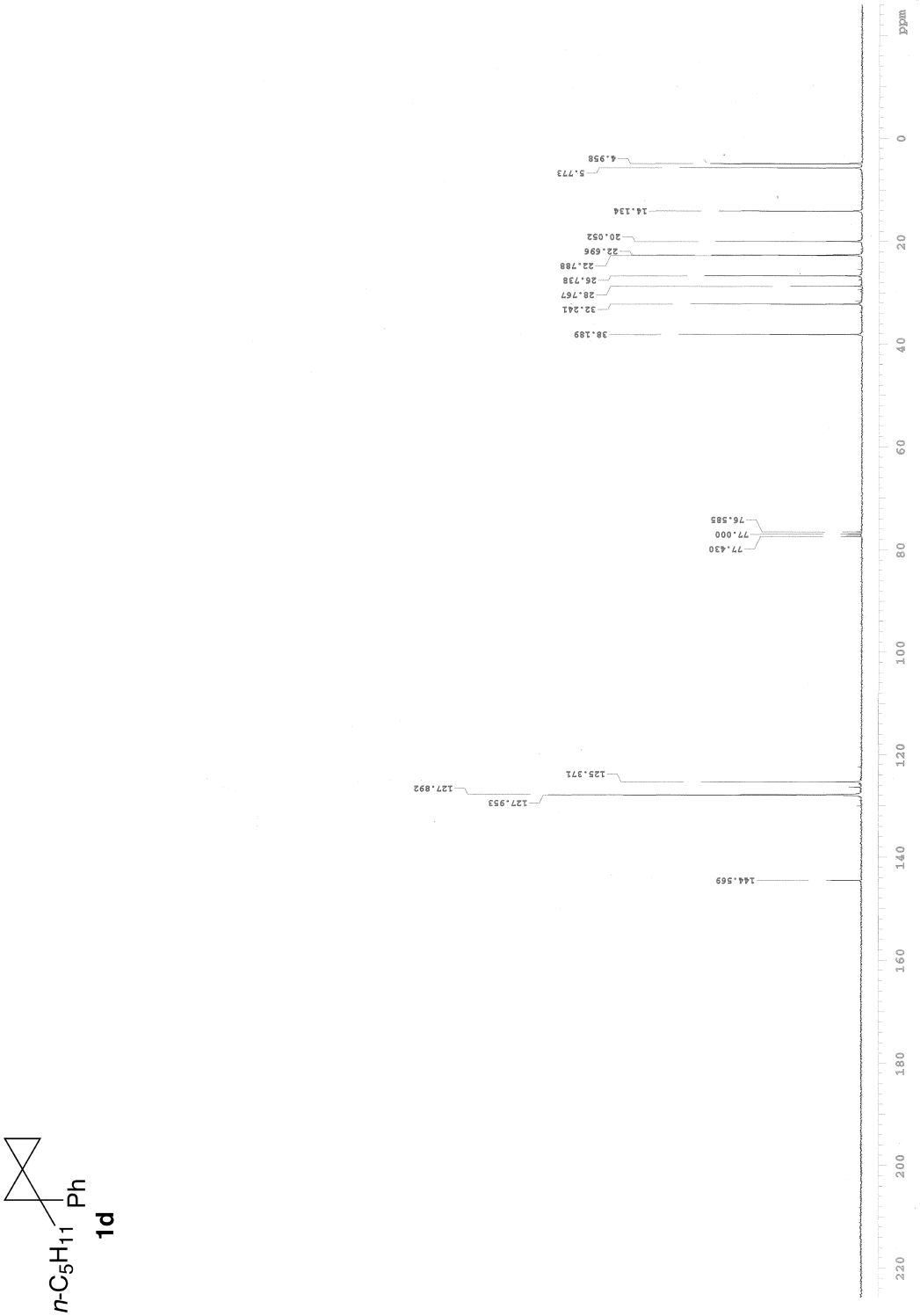
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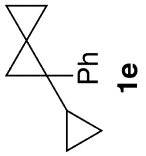
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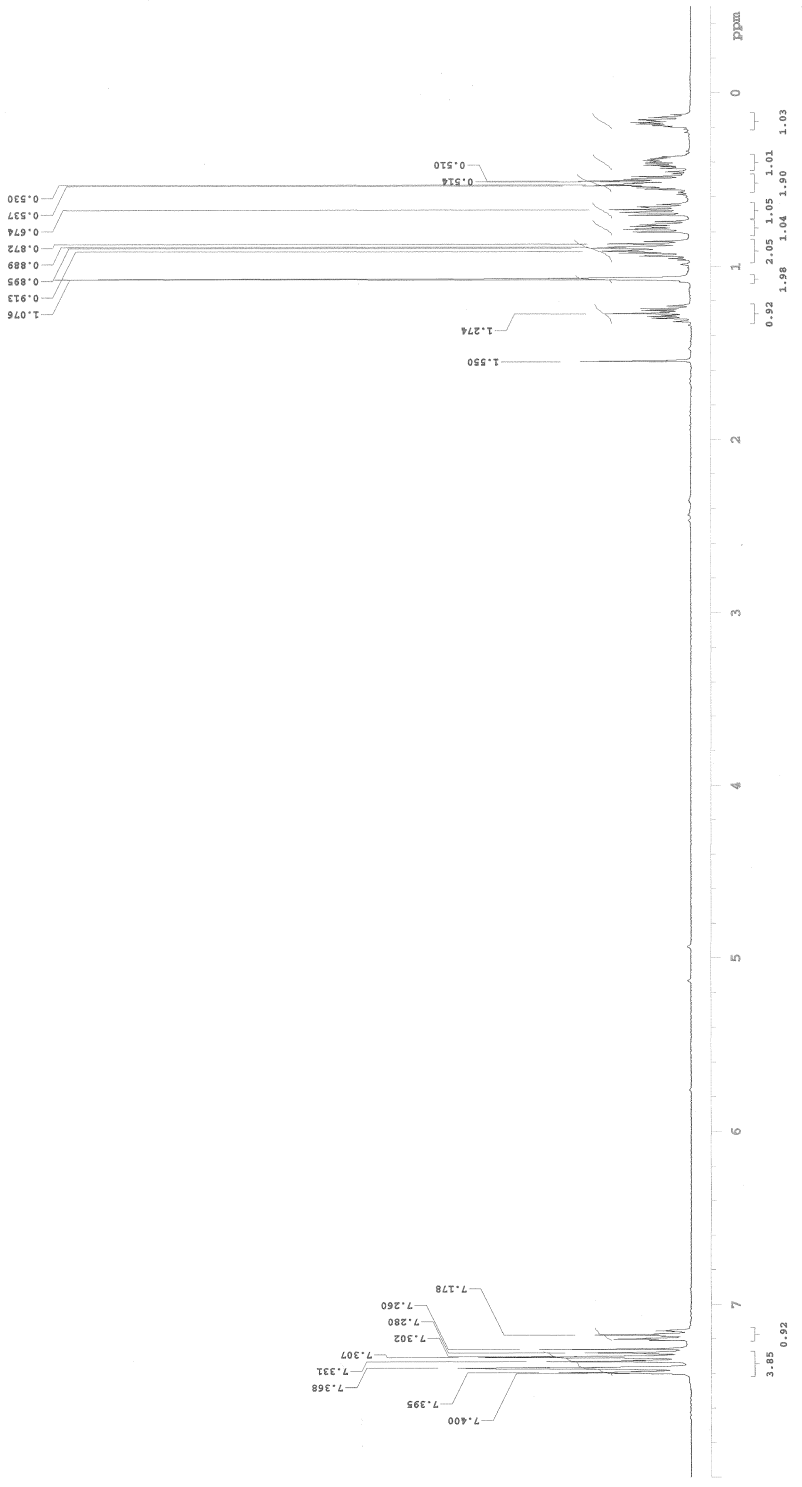
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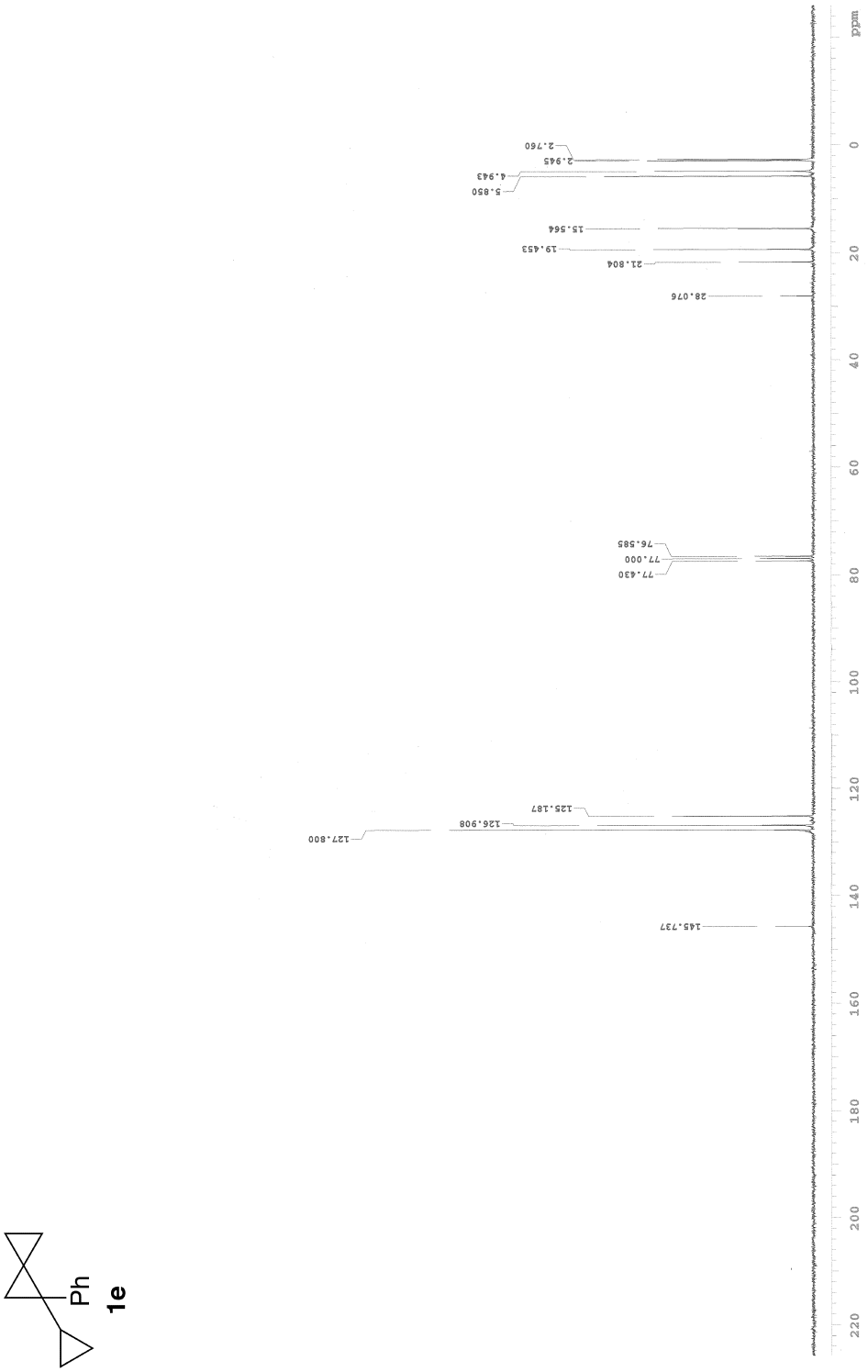
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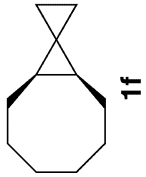
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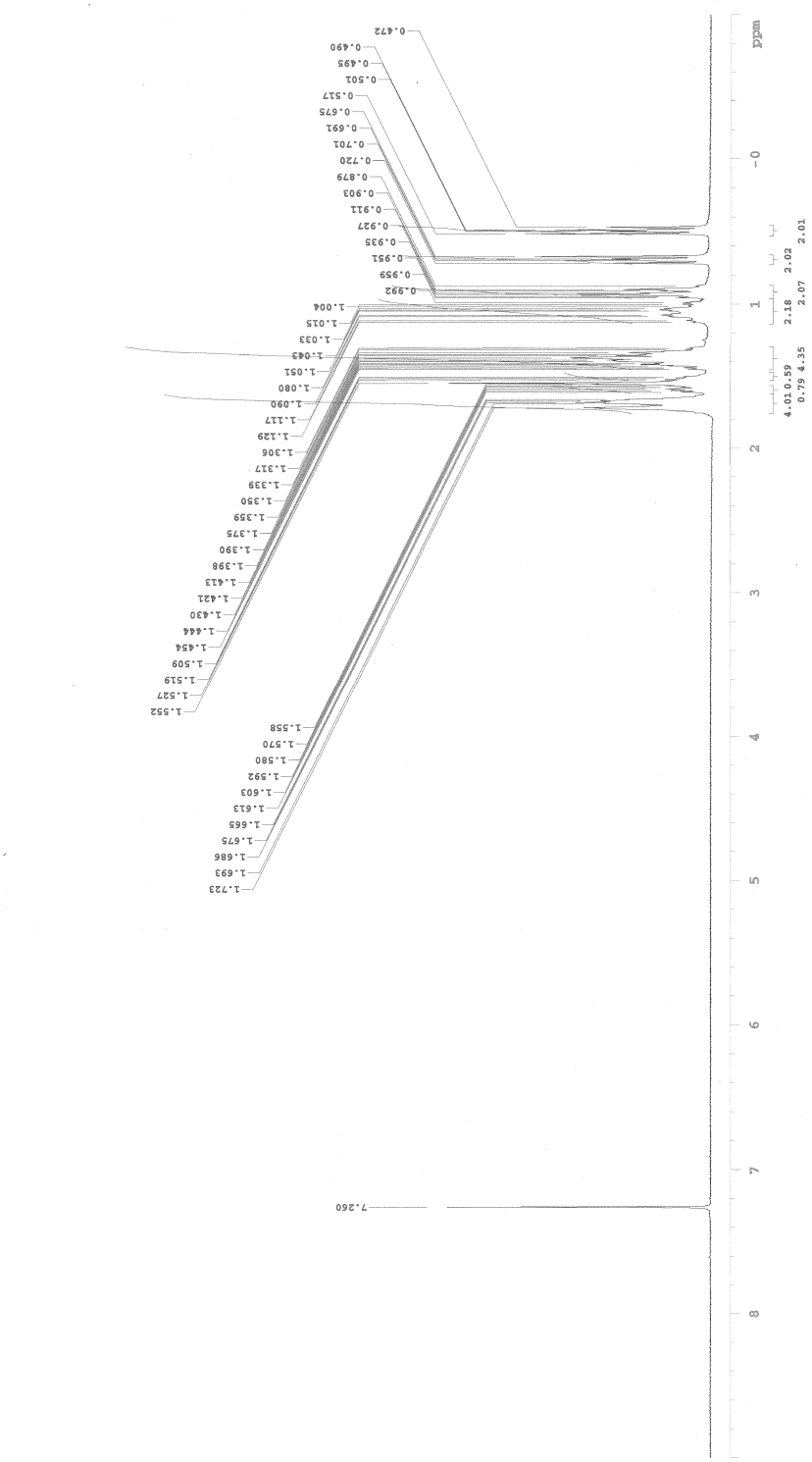
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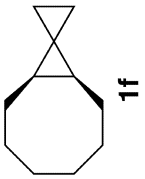
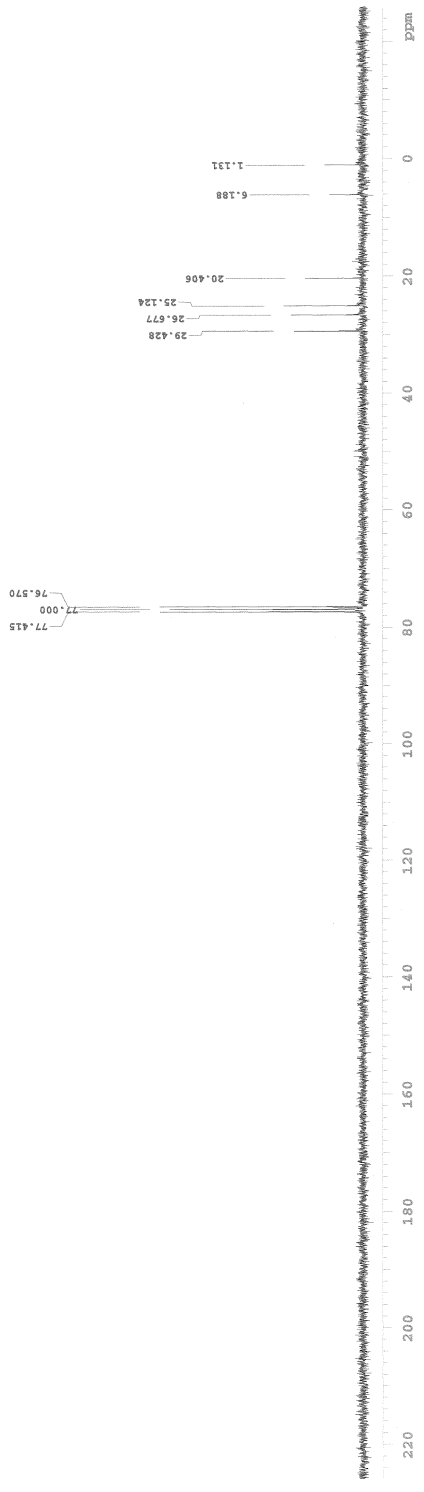
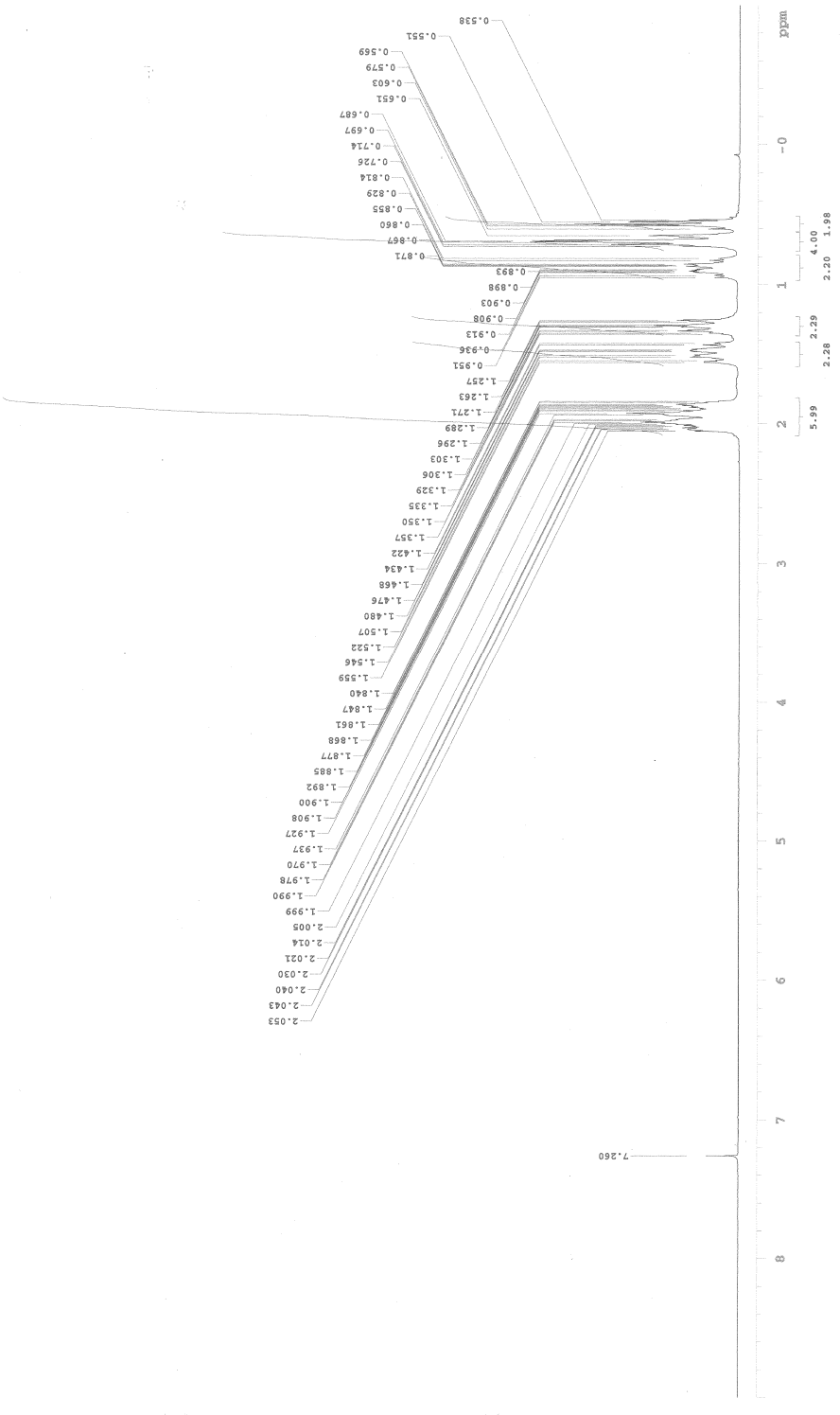
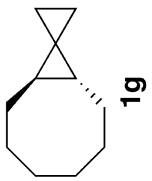
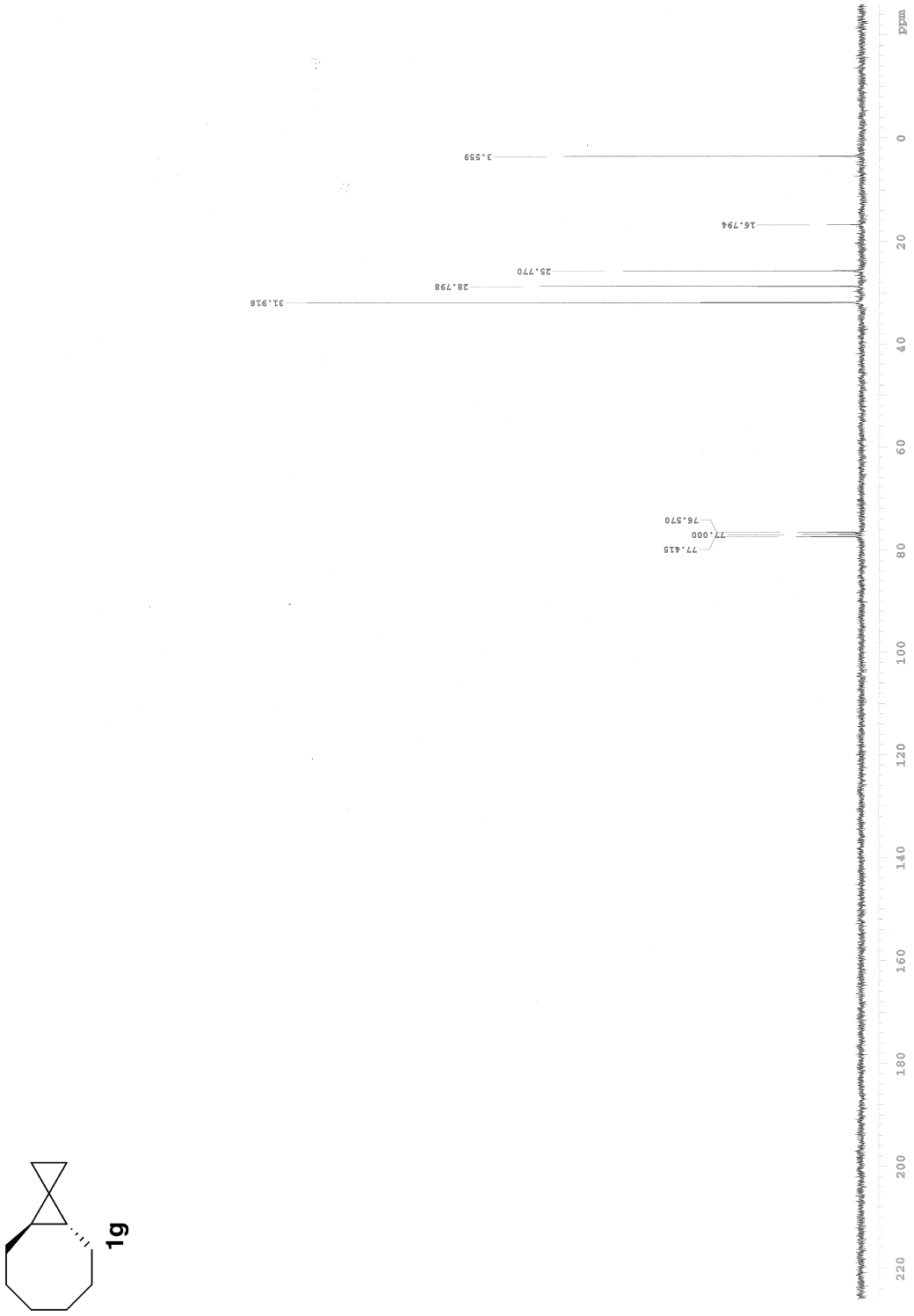
4.01 0.59
0.79 4.35
2.18
2.07
2.02
2.01

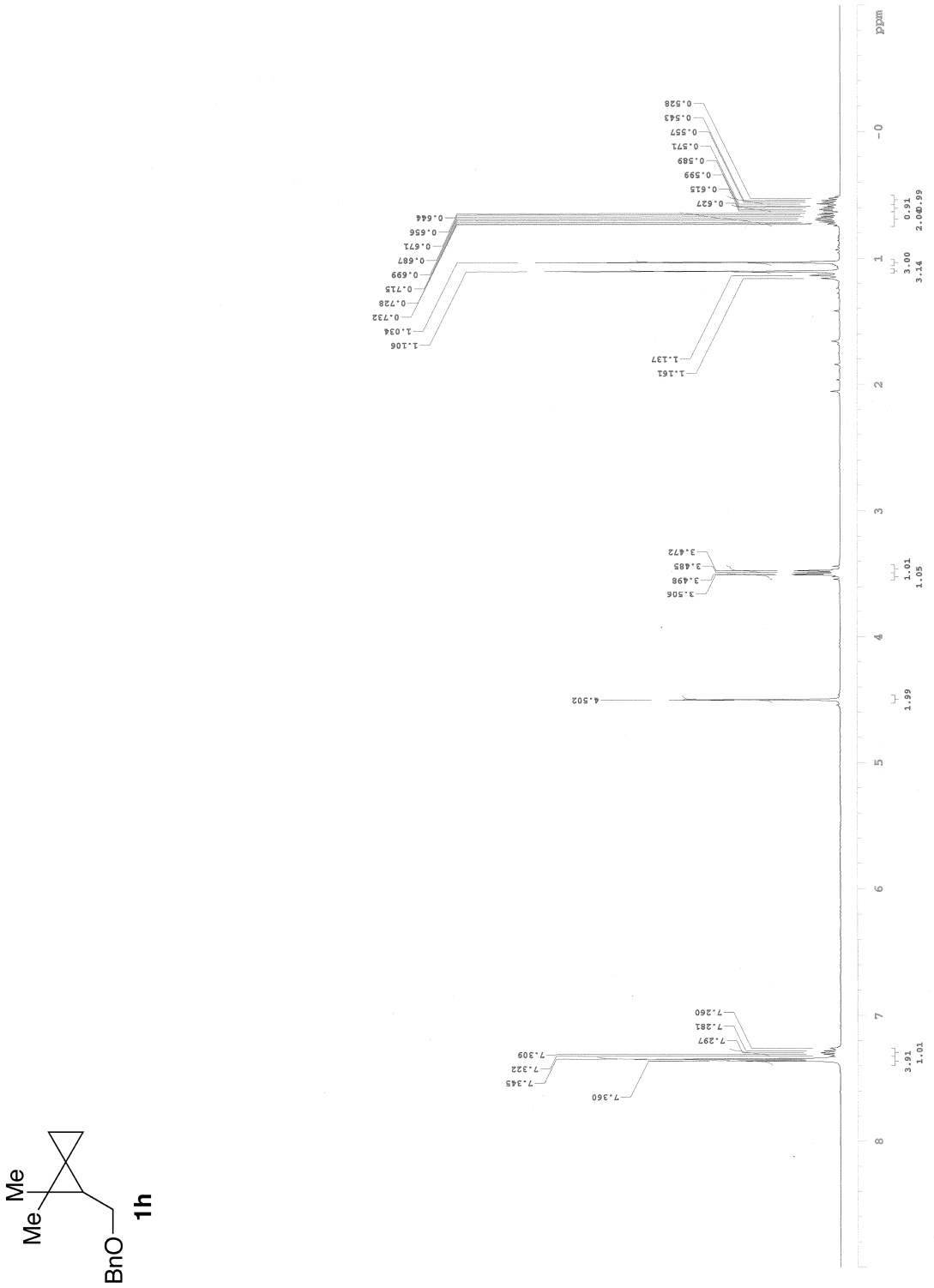

1f

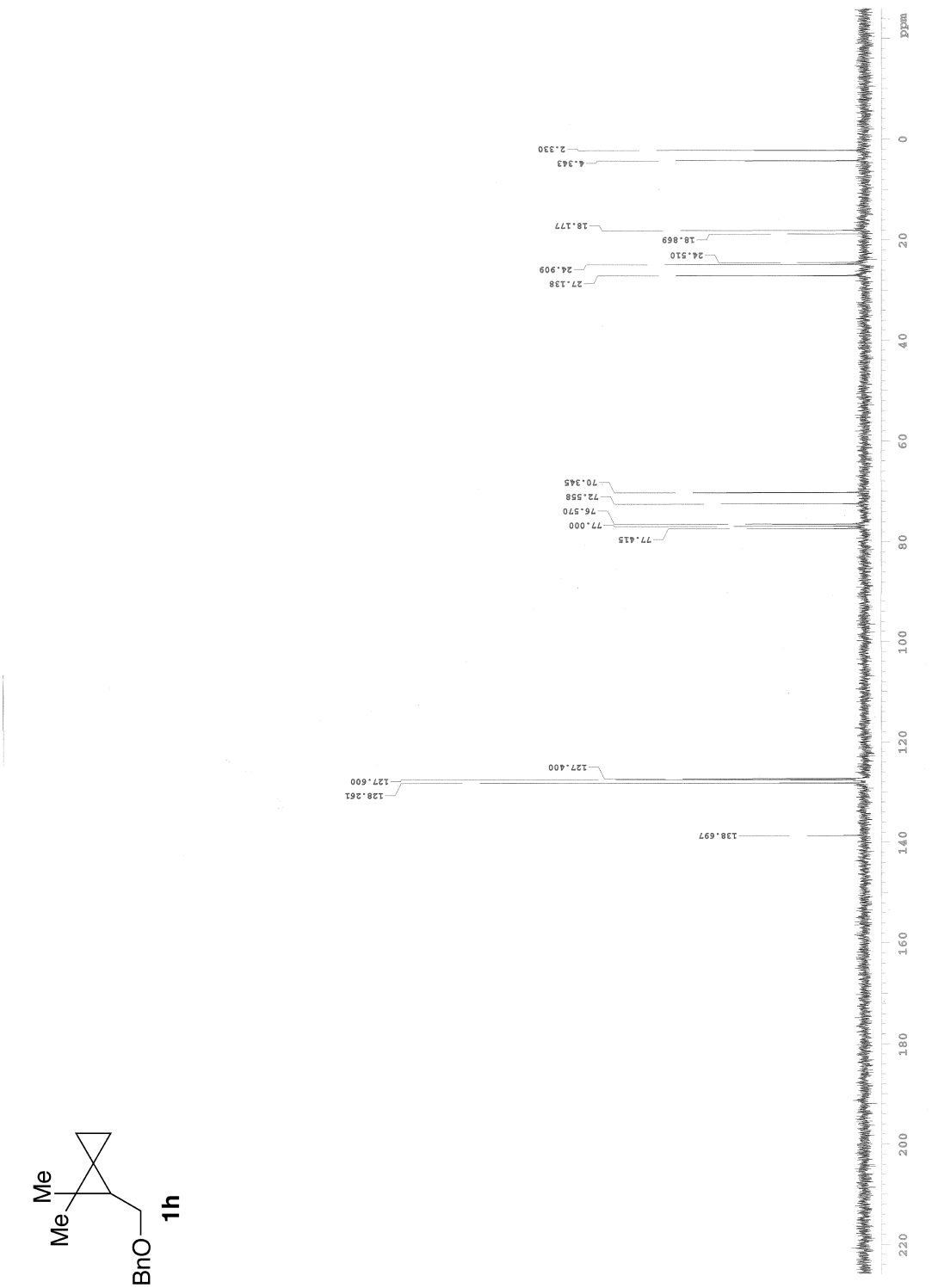

1.131
6.188
20.406
25.124
26.677
29.428
77.415
77.000
76.570
ppm
0
20
40
60
80
100
120
140
160
180
200
220

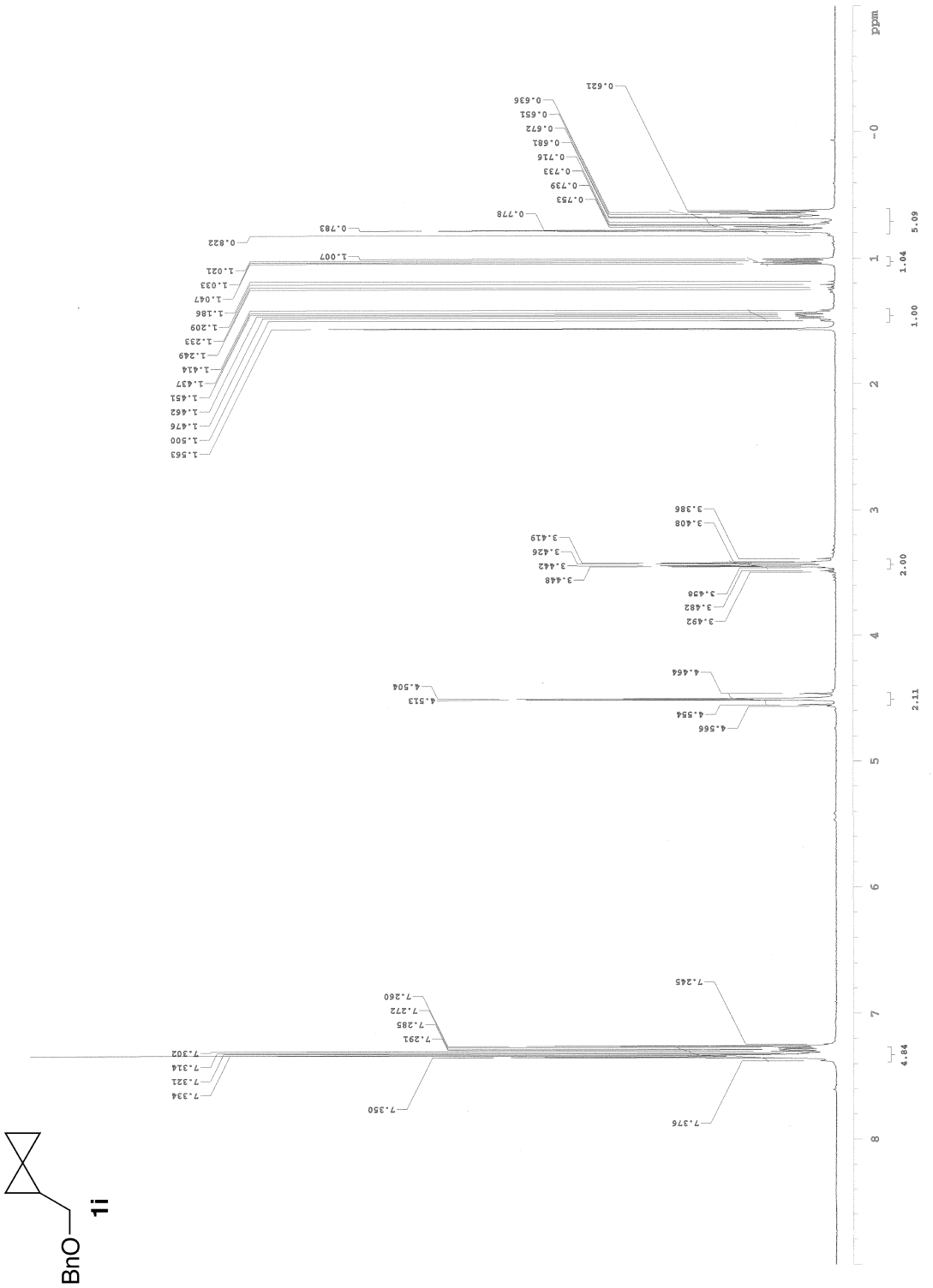

0.538
0.551
0.569
0.579
0.603
0.651
0.687
0.697
0.714
0.726
0.814
0.829
0.855
0.860
0.867
0.871
0.893
0.898
0.903
0.908
0.913
0.936
0.951
1.257
1.263
1.271
1.289
1.296
1.303
1.306
1.329
1.335
1.350
1.357
1.422
1.434
1.468
1.476
1.480
1.507
1.522
1.546
1.559
1.840
1.847
1.861
1.868
1.877
1.885
1.892
1.900
1.908
1.927
1.937
1.970
1.978
1.990
1.999
2.005
2.014
2.021
2.030
2.040
2.043
2.053
7.260
ppm
0
1
2
3
4
5
6
7
8
4.00
1.98
2.20
2.29
2.28
5.99

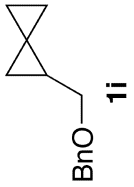

1g

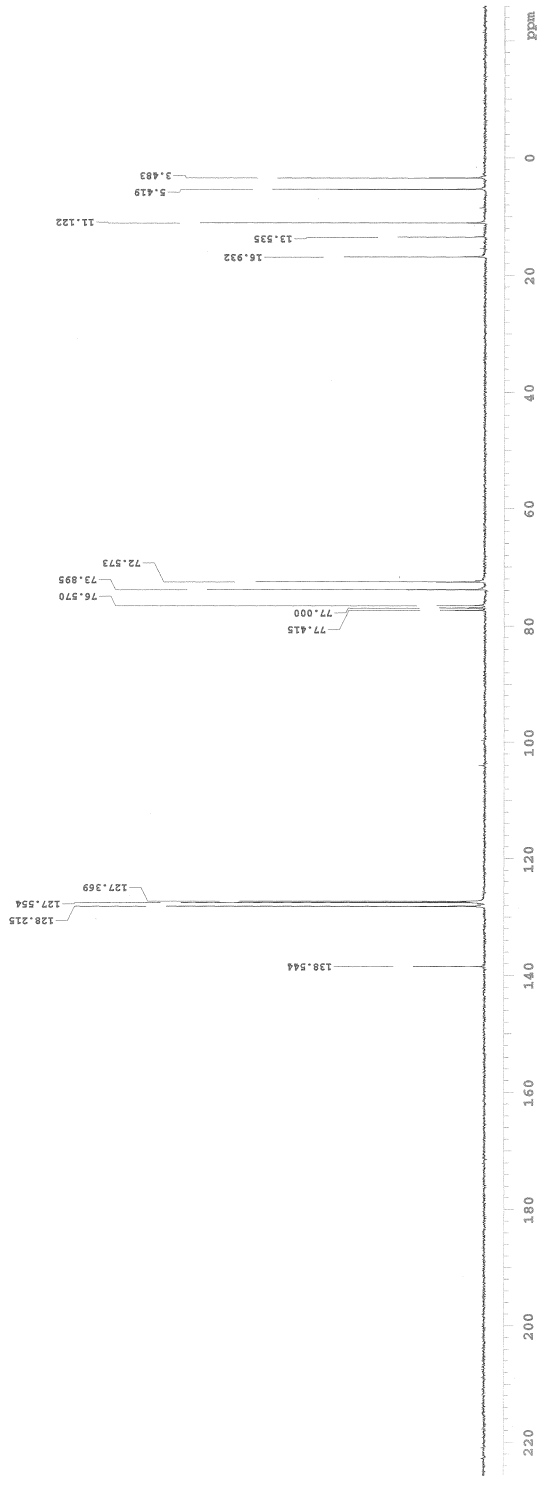

1g
3.559
16.794
25.770
28.798
31.918
76.570
77.000
77.415
0
20
40
60
80
100
120
140
160
180
200
220
ppm

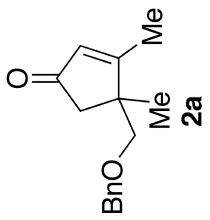

Me
Me
BnO
1h
ppm
0.528
0.543
0.557
0.571
0.589
0.599
0.615
0.627
0.644
0.656
0.671
0.687
0.699
0.715
0.728
0.732
1.034
1.106
1.137
1.161
3.472
3.485
3.498
3.506
4.502
7.260
7.281
7.297
7.309
7.322
7.345
7.360
0.91
2.00
2.99
3.00
3.14
1.01
1.05
1.99
3.91
1.01


Me
Me
BnO
1h
138.697
128.261
127.600
127.400
77.415
77.000
76.570
72.558
70.345
27.138
24.909
24.510
18.869
18.177
4.343
2.330
ppm
0
20
40
60
80
100
120
140
160
180
200
220

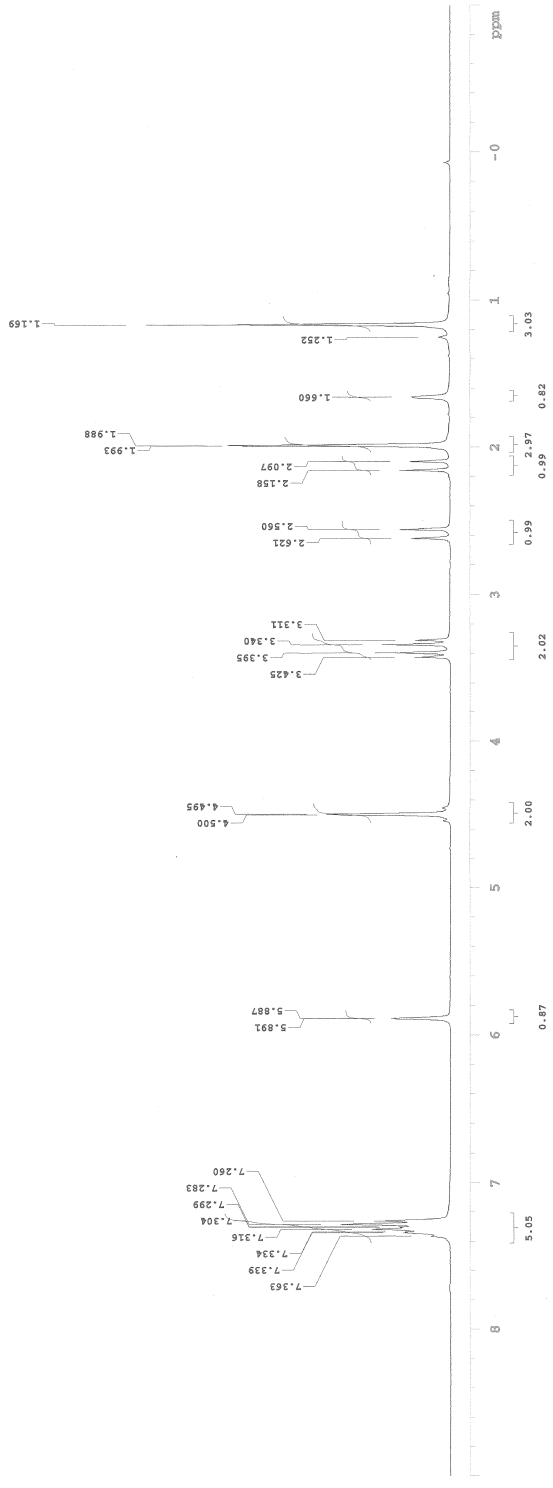

BnO
1i
ppm
7.376
7.350
7.334
7.321
7.314
7.302
7.291
7.285
7.272
7.260
7.245
4.564
4.554
4.513
4.504
3.492
3.482
3.456
3.448
3.442
3.426
3.419
3.408
3.386
1.563
1.500
1.476
1.462
1.451
1.437
1.414
1.249
1.233
1.209
1.186
1.047
1.033
1.021
1.007
0.822
0.783
0.778
0.753
0.739
0.733
0.716
0.682
0.672
0.651
0.636
0.621
5.09
1.04
1.00
2.00
2.11
4.84

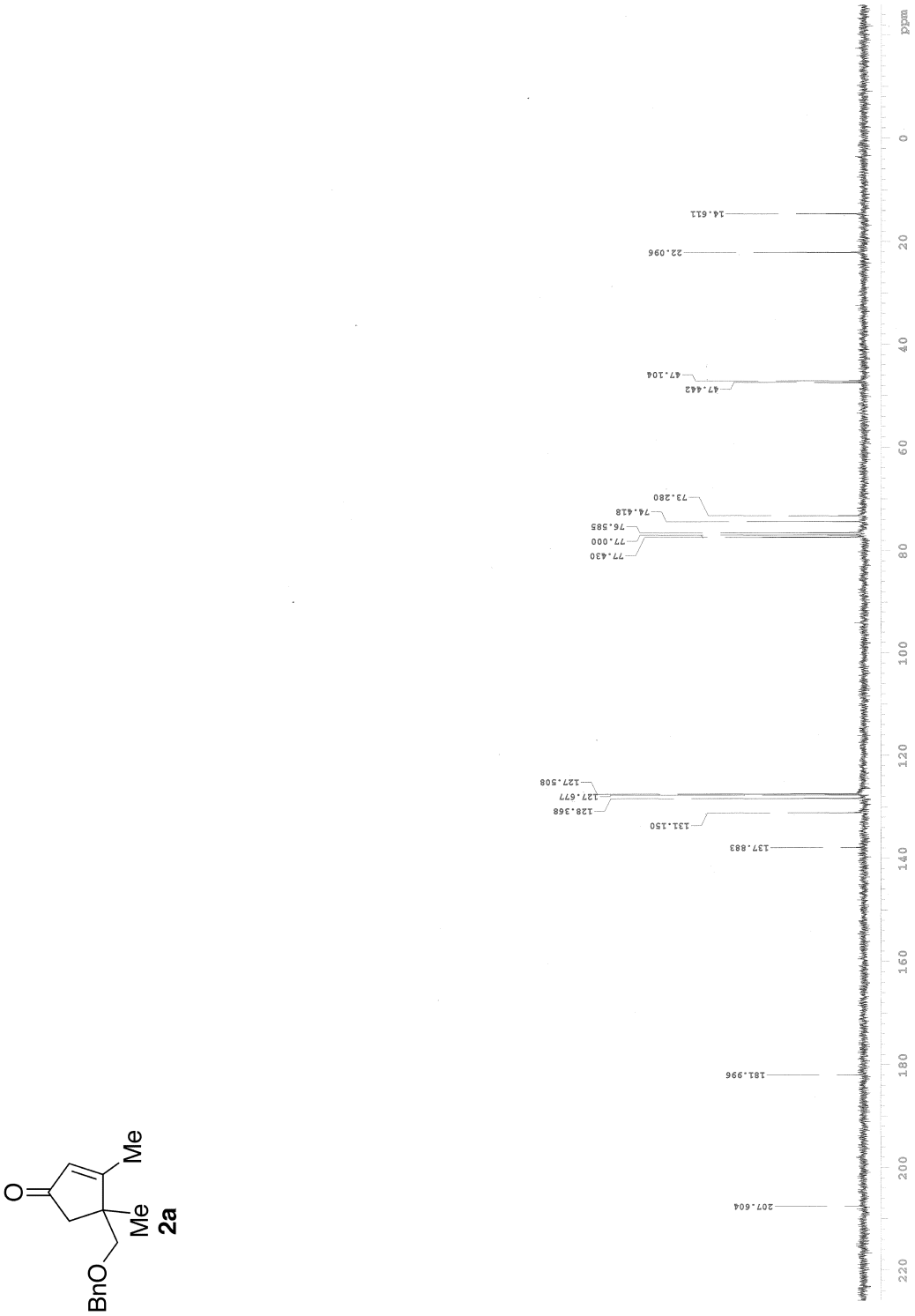

BnO
1i

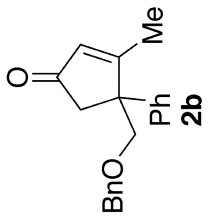

138.544
128.215
127.554
127.369
77.415
77.000
76.570
73.895
72.573
16.932
13.535
11.122
5.419
3.483
ppm
0
20
40
60
80
100
120
140
160
180
200
220


O
Me
Me
BnO

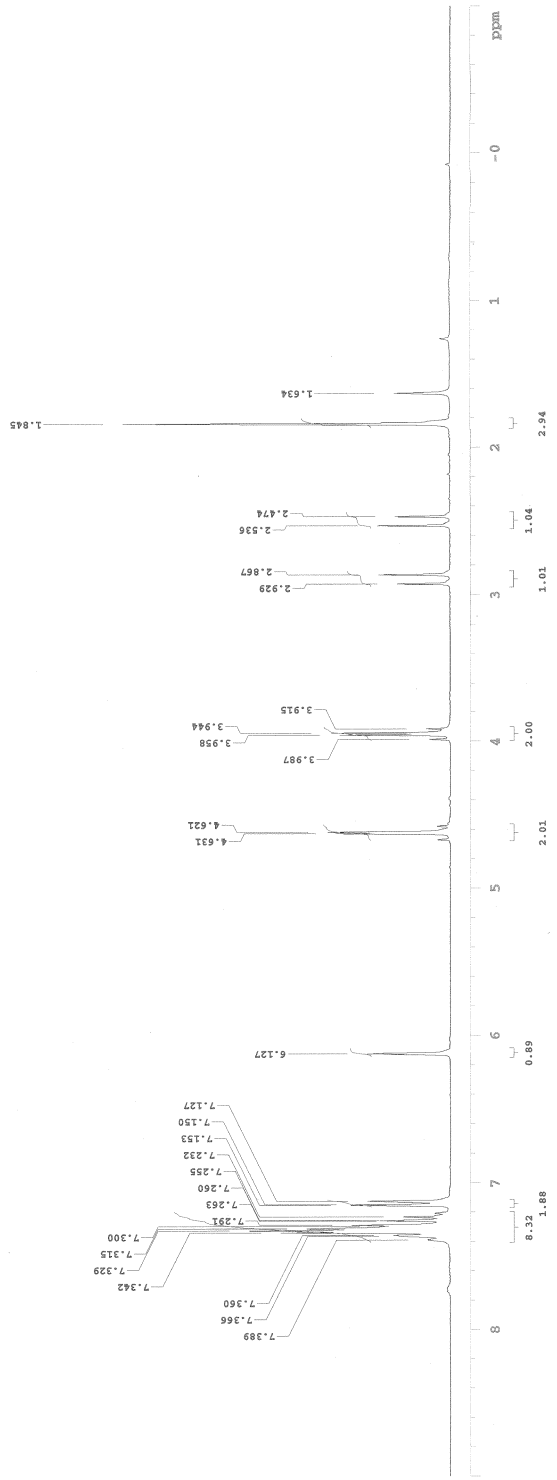
2a

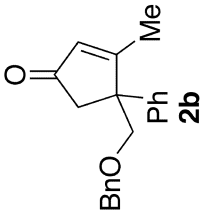

7.363
7.339
7.334
7.316
7.304
7.299
7.283
7.260
5.887
5.831
4.500
4.495
3.425
3.395
3.340
3.311
2.621
2.560
2.158
2.097
1.993
1.988
1.660
1.352
1.169
ppm
5.05
0.87
2.00
2.02
0.99
2.97
0.99
0.82
3.03


O
Me
Me
BnO
2a
207.604
181.996
137.883
131.150
128.368
127.677
127.508
77.430
77.000
76.585
74.418
73.280
47.442
47.104
22.096
14.611
ppm
0
20
40
60
80
100
120
140
160
180
200
220

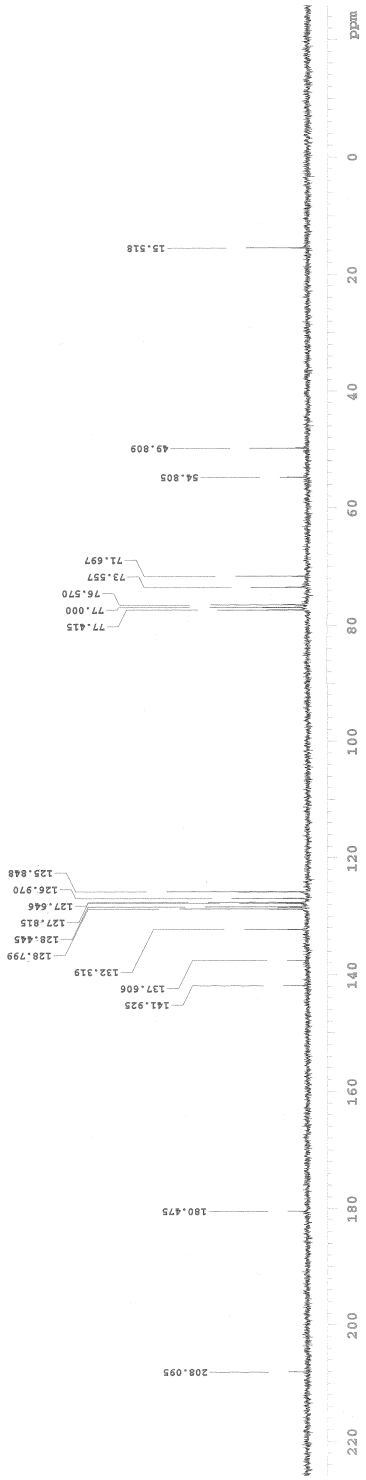

O
Me
Ph
BnO

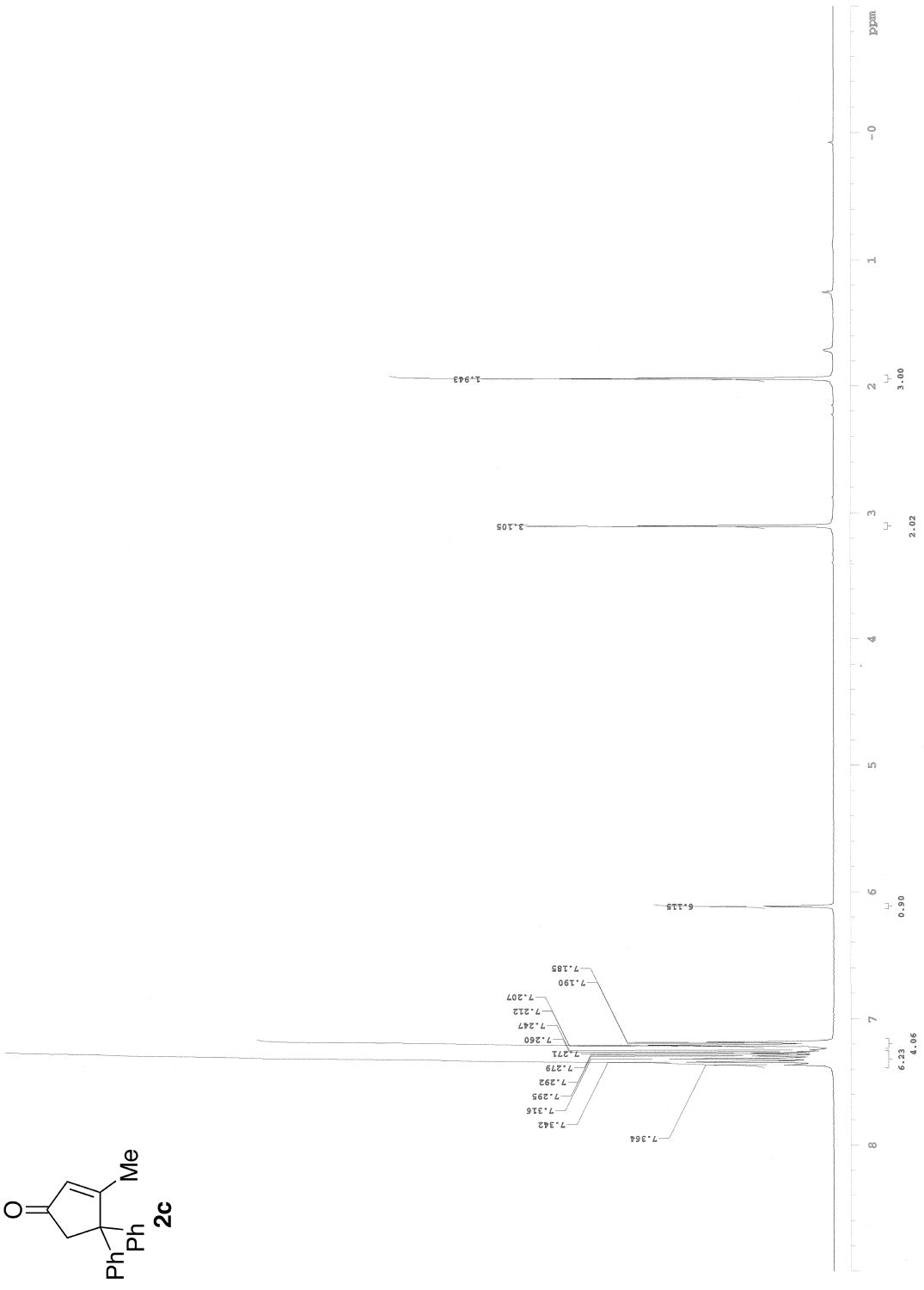
2b

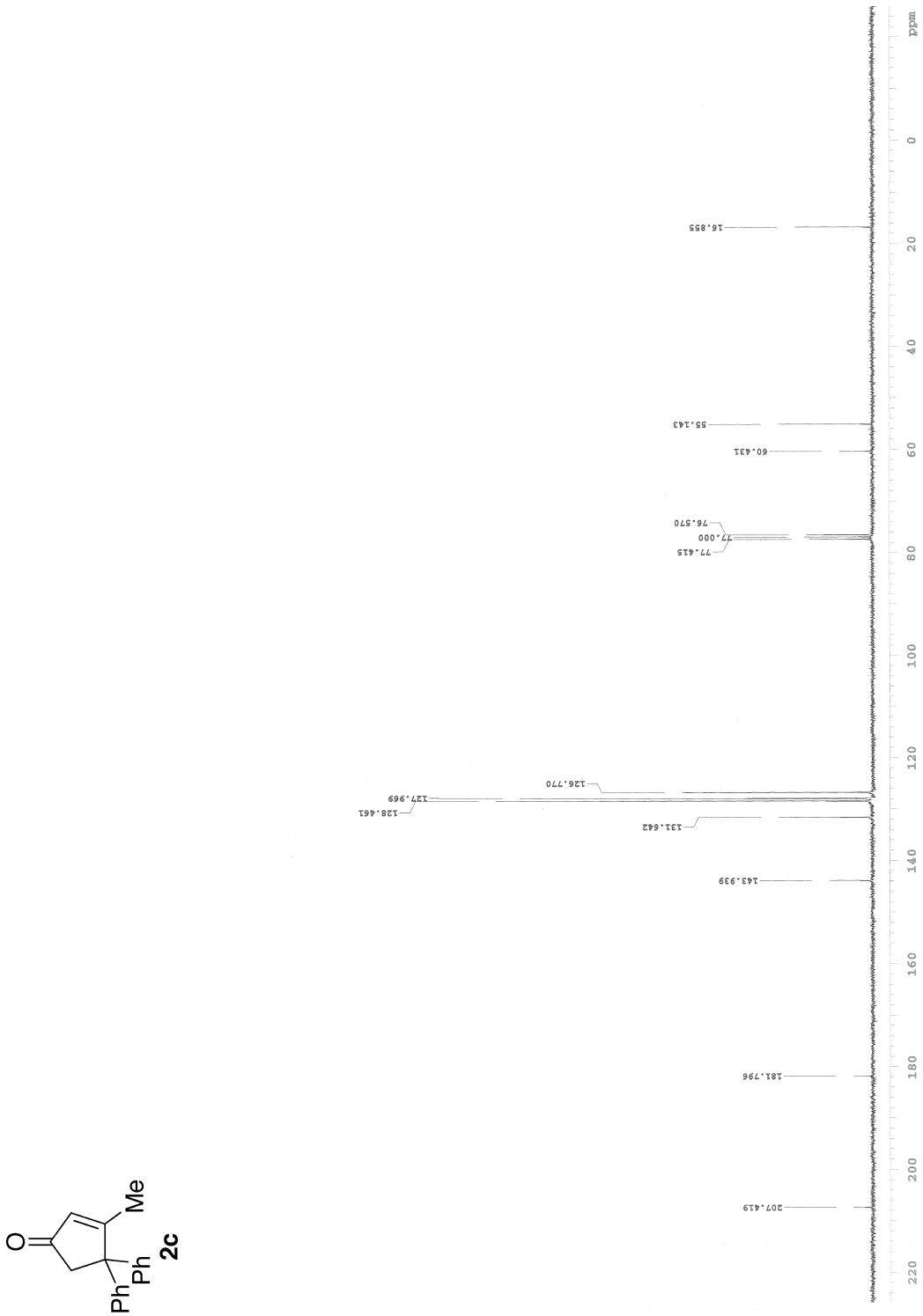

ppm
1.634
1.845
2.474
2.536
2.867
2.929
3.915
3.944
3.958
3.987
4.631
6.127
7.127
7.150
7.153
7.232
7.255
7.260
7.263
7.331
7.300
7.315
7.329
7.342
7.360
7.366
7.389
2.94
1.04
1.01
2.00
2.01
0.89
8.32
1.88

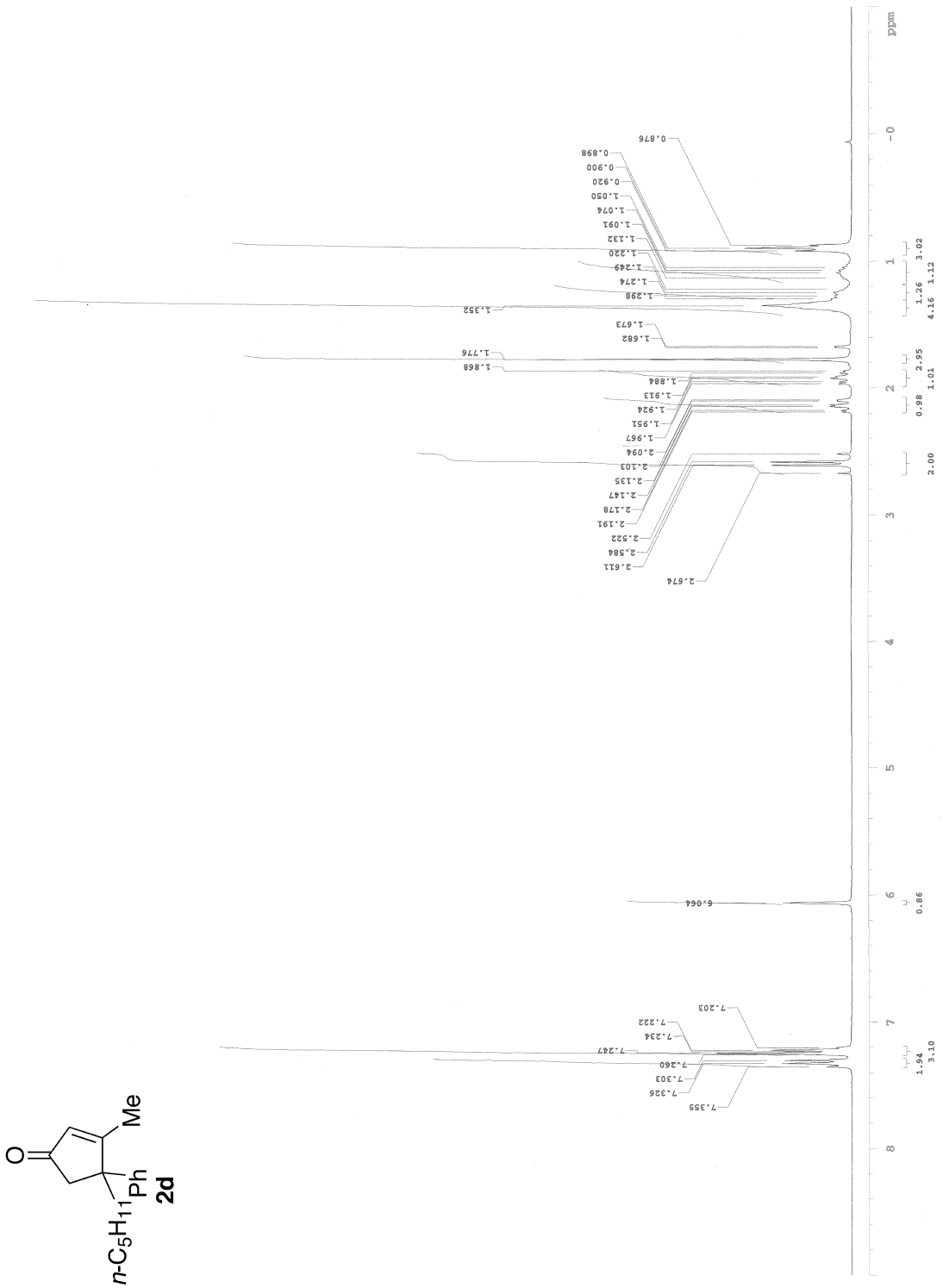

O
Me
Ph
BnO

2b


208.095
180.475
141.925
137.606
132.319
128.799
128.445
127.815
127.646
126.970
125.848
77.415
77.000
76.570
73.557
71.697
54.805
49.809
15.518
ppm
0
20
40
60
80
100
120
140
160
180
200
220


O
Me
Ph
Ph
2c
7.364
7.342
7.316
7.295
7.292
7.279
7.271
7.260
7.247
7.212
7.207
7.190
7.185
6.115
3.105
1.943
6.23
4.06
0.90
2.02
3.00
ppm


O
Me
Ph
Ph
2c
207.419
181.796
143.939
131.642
128.461
127.969
126.770
77.415
77.000
76.570
60.431
55.143
16.855
ppm
0
20
40
60
80
100
120
140
160
180
200
220


O
Me
Ph
n-C5H11
2d
ppm
0.876
0.898
0.900
0.920
1.050
1.074
1.091
1.132
1.220
1.249
1.274
1.298
1.352
1.673
1.682
1.776
1.868
1.884
1.913
1.924
1.951
1.967
2.094
2.103
2.135
2.147
2.178
2.191
2.522
2.584
2.611
2.674
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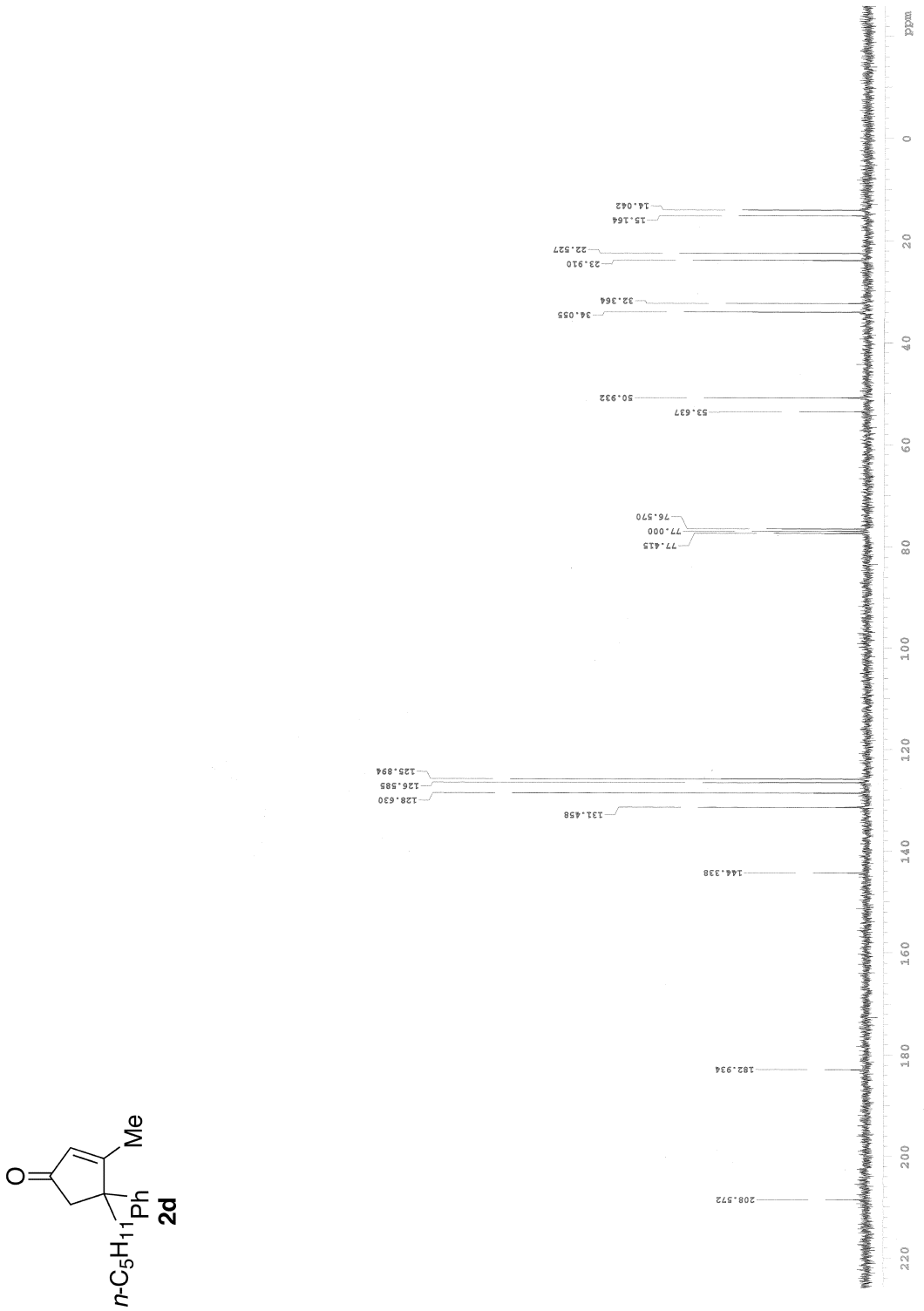
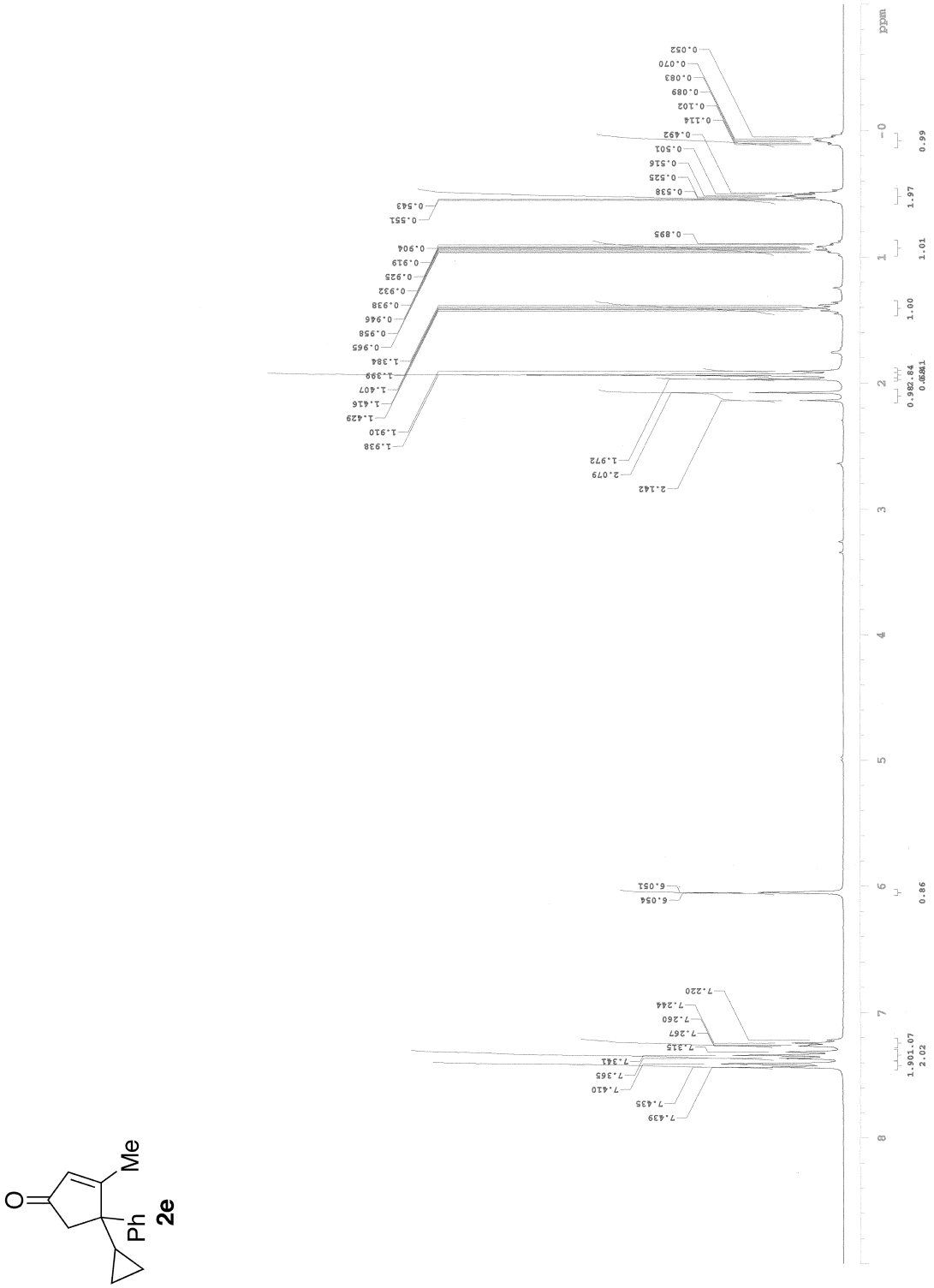
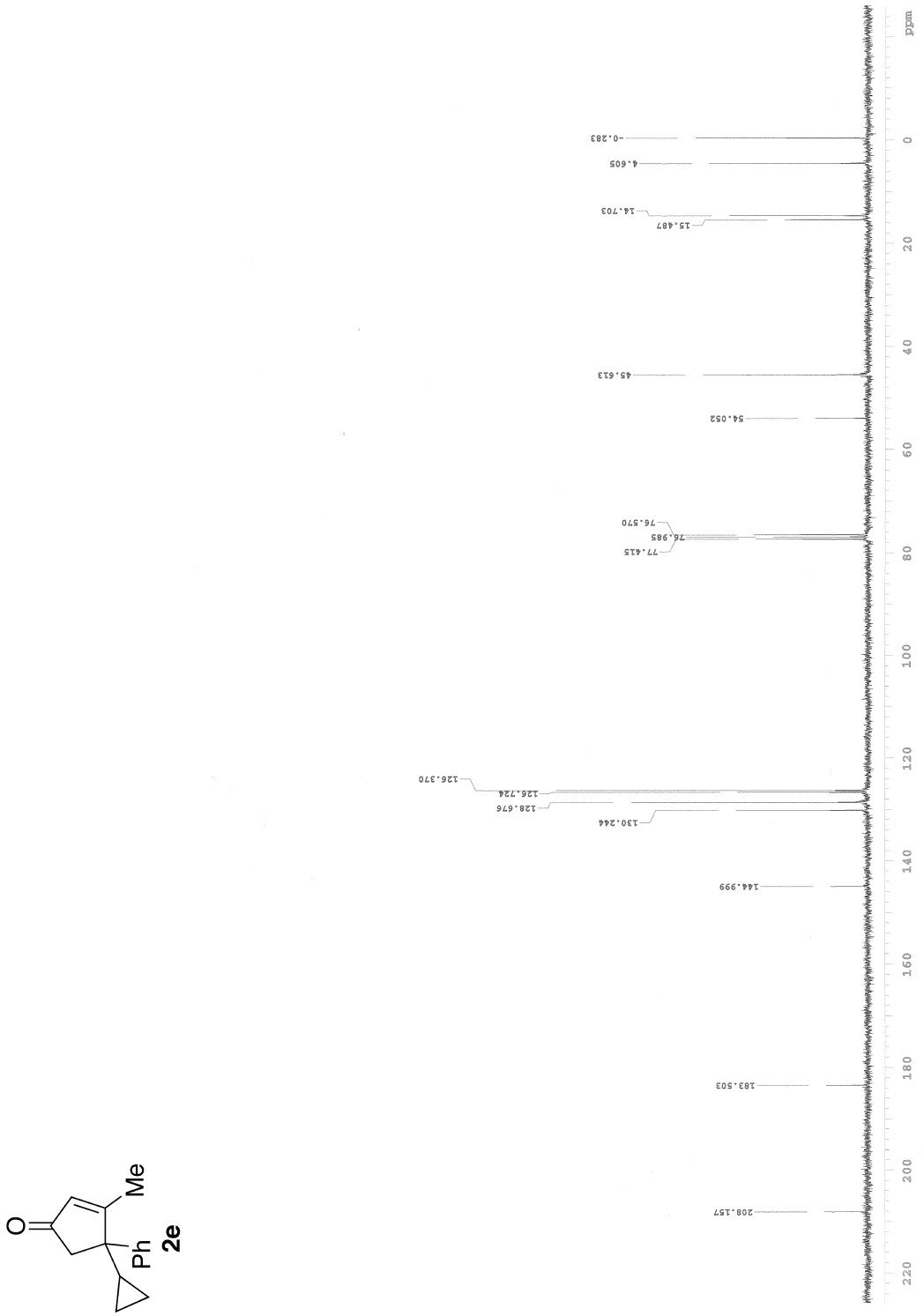
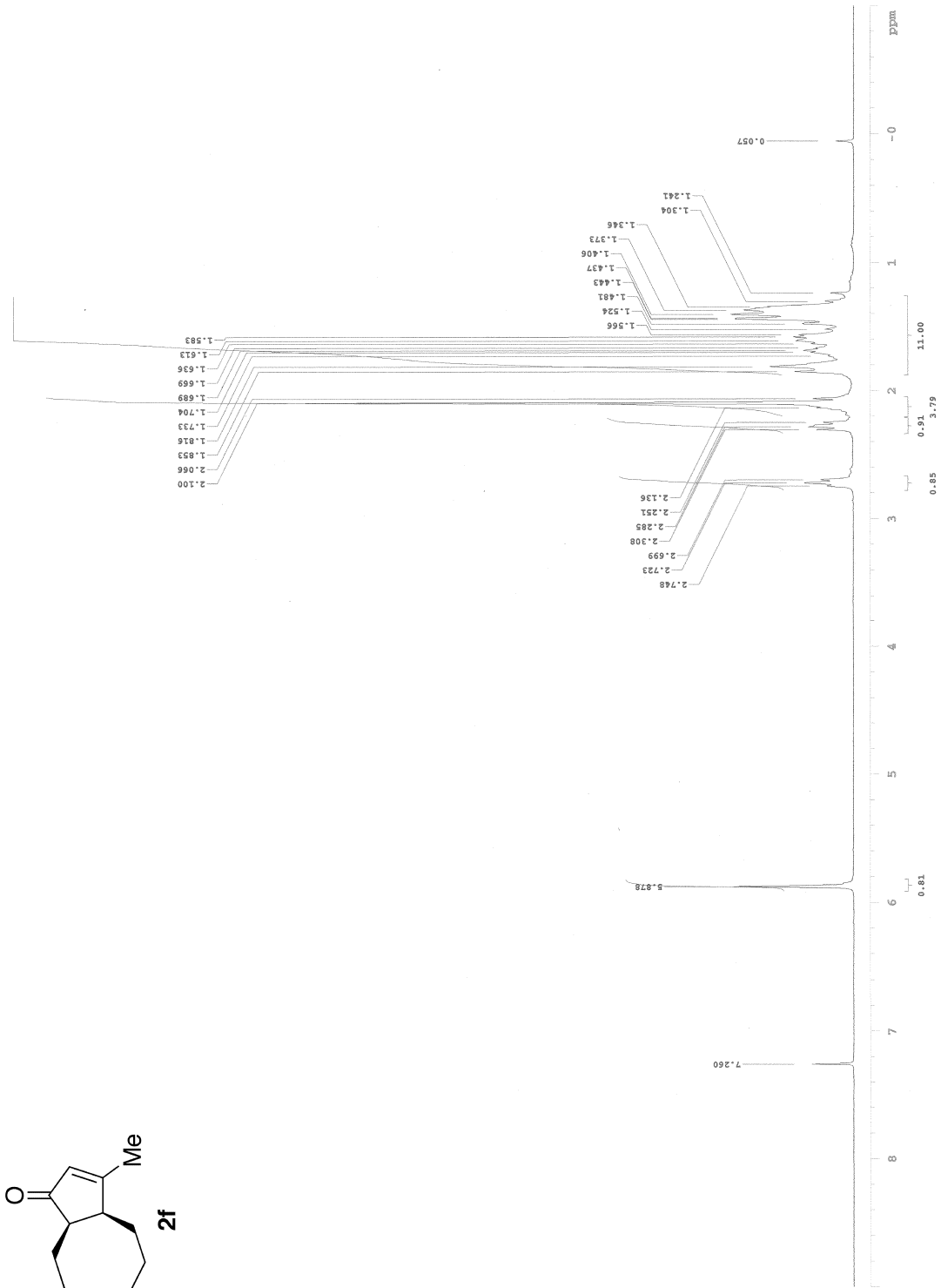
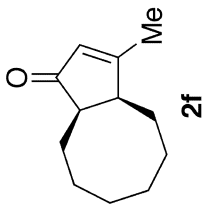
7.234
7.247
7.260
7.303
7.326
7.355


O
Me
Ph
n-C5H11
2d
208.572
182.934
144.338
131.458
128.630
126.585
125.894
77.415
77.000
76.570
53.637
50.932
34.055
32.364
23.910
22.527
15.164
14.042
ppm
0
20
40
60
80
100
120
140
160
180
200
220

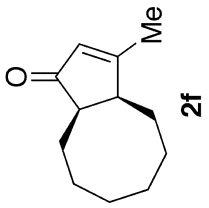

O
Me
Ph
2e


O
Me
Ph
2e
208.157
183.503
144.999
130.244
128.676
126.724
126.370
77.415
76.985
76.570
54.052
45.613
15.487
14.703
4.605
-0.283
ppm
0
20
40
60
80
100
120
140
160
180
200
220

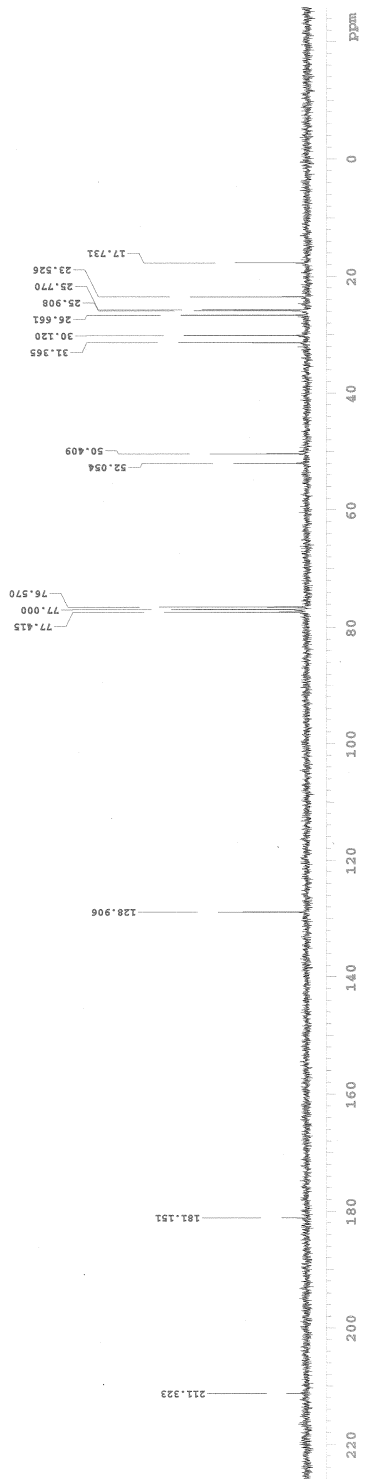

0.057
1.241
1.304
1.346
1.373
1.406
1.437
1.443
1.481
1.524
1.566
1.583
1.613
1.636
1.669
1.689
1.704
1.733
1.816
1.853
2.066
2.100
2.136
2.251
2.285
2.308
2.699
2.723
2.748
5.878
7.260
ppm
11.00
0.91
3.79
0.85
0.81

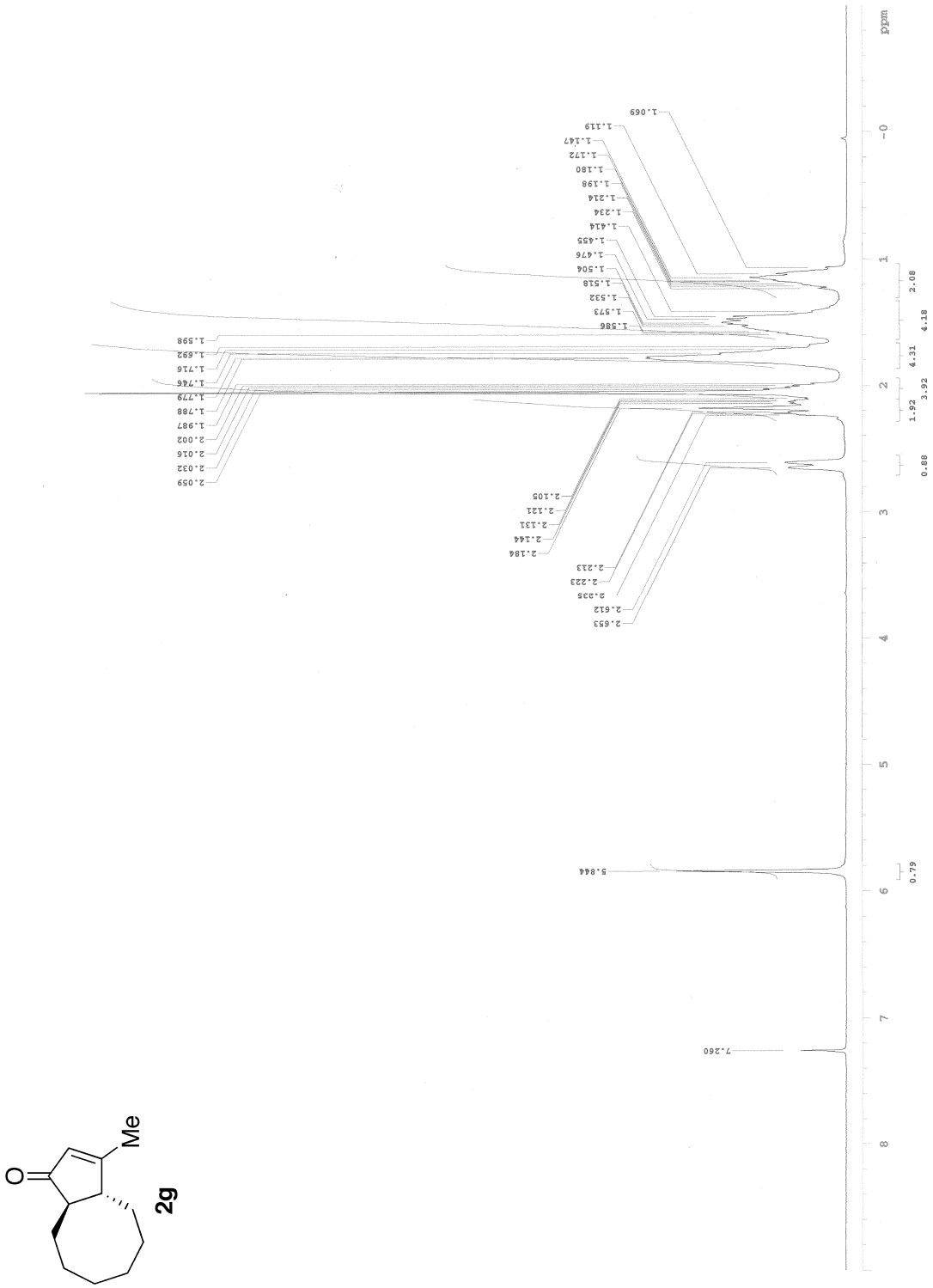

O
Me

2f


O
Me

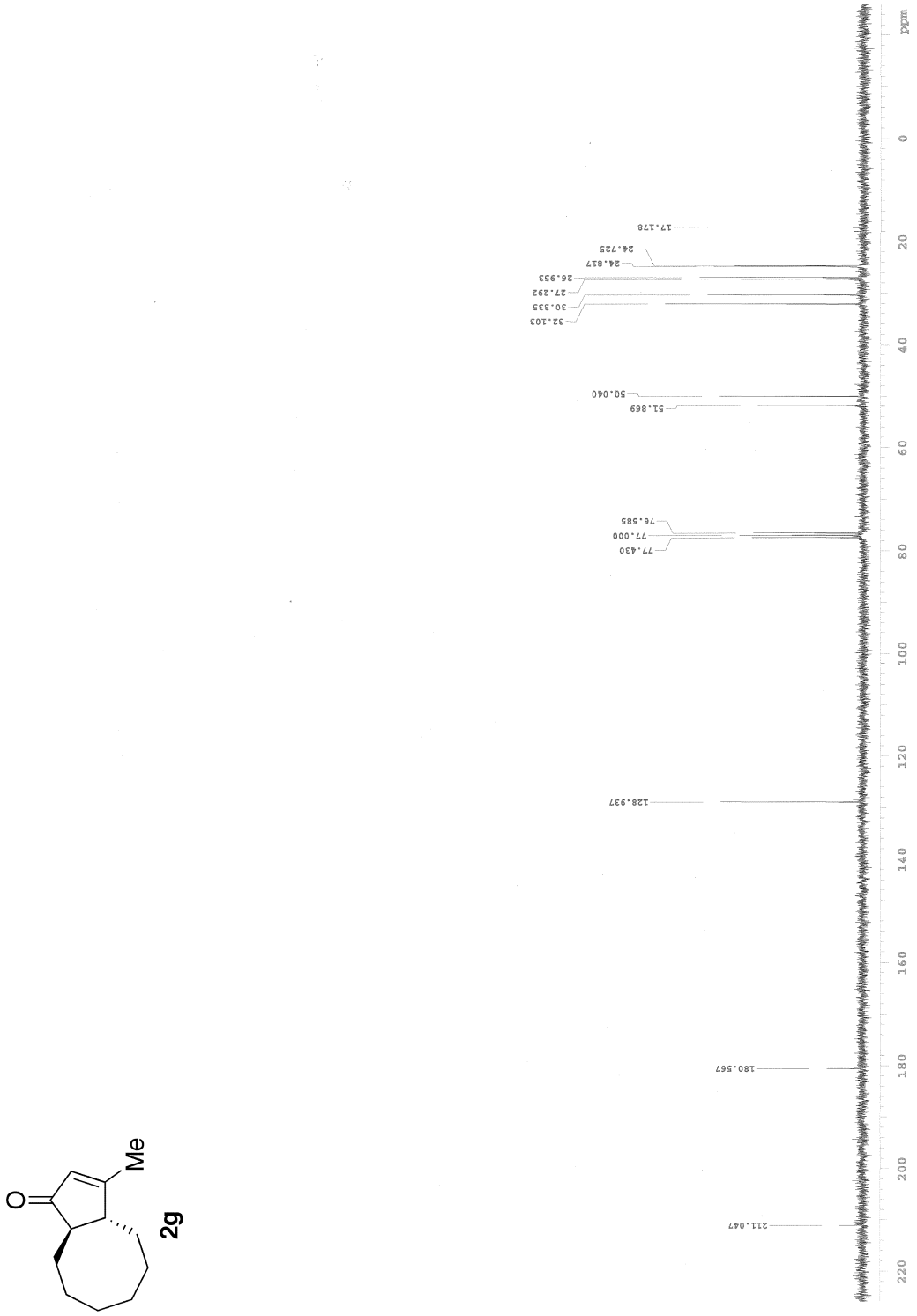
2f


211.323
181.151
128.906
77.415
77.000
76.570
52.054
50.409
31.365
30.120
26.661
25.908
25.770
23.526
17.731
ppm
0
20
40
60
80
100
120
140
160
180
200
220


1.069
1.119
1.147
1.172
1.180
1.198
1.314
1.334
1.414
1.455
1.476
1.504
1.518
1.532
1.573
1.586
1.598
1.692
1.716
1.746
1.779
1.788
1.987
2.002
2.016
2.032
2.059
2.105
2.121
2.131
2.144
2.184
2.213
2.223
2.335
2.612
2.653
5.844
7.260
ppm
0
1
2
3
4
5
6
7
8
2.08
4.18
4.31
1.92
3.92
0.88
0.79

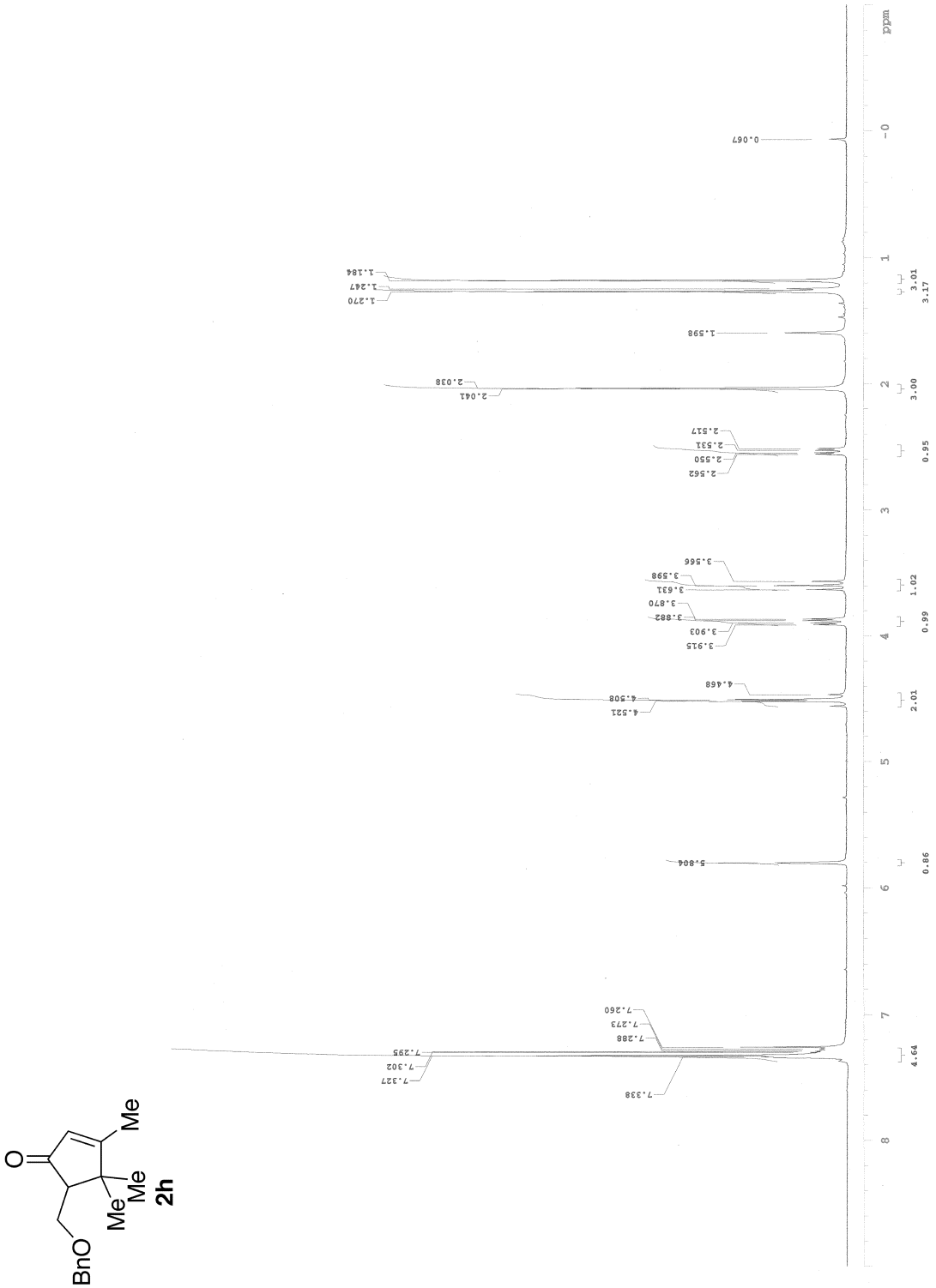
O
Me

2g


ppm
0
20
40
60
80
100
120
140
160
180
200
220
17.178
24.725
24.817
26.953
27.292
30.335
32.103
50.040
51.869
76.585
77.000
77.430
128.937
180.567
211.047

O
Me

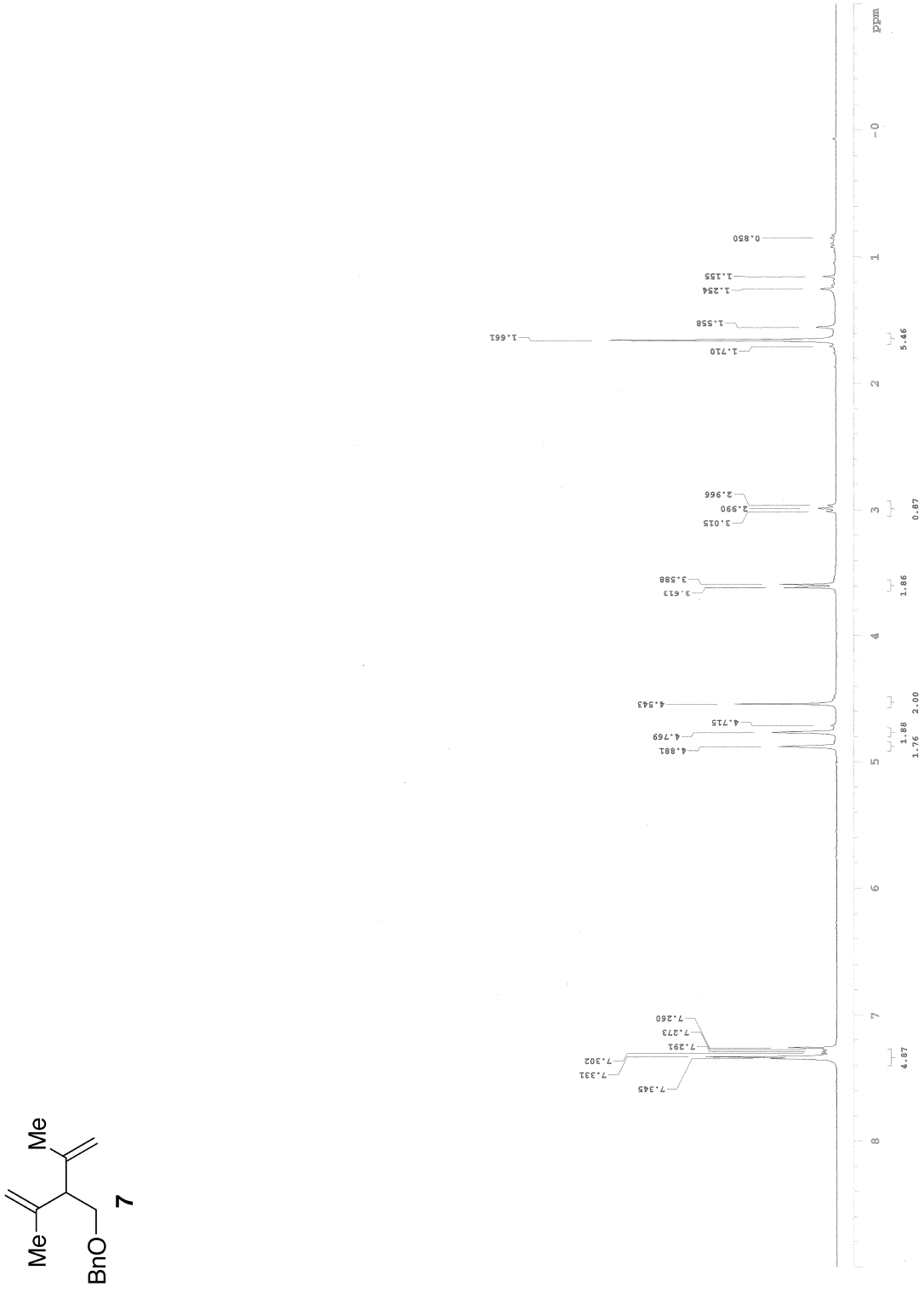
2g

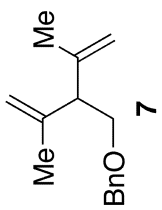

O
Me
Me
Me
BnO
2h
ppm
0.067
1.184
1.247
1.270
1.598
2.038
2.041
2.517
2.531
2.550
2.562
3.566
3.598
3.631
3.870
3.882
3.903
3.915
4.468
4.508
4.521
5.804
7.260
7.273
7.288
7.295
7.302
7.327
7.338
3.01
3.17
3.00
0.95
1.02
0.99
2.01
0.86
4.64

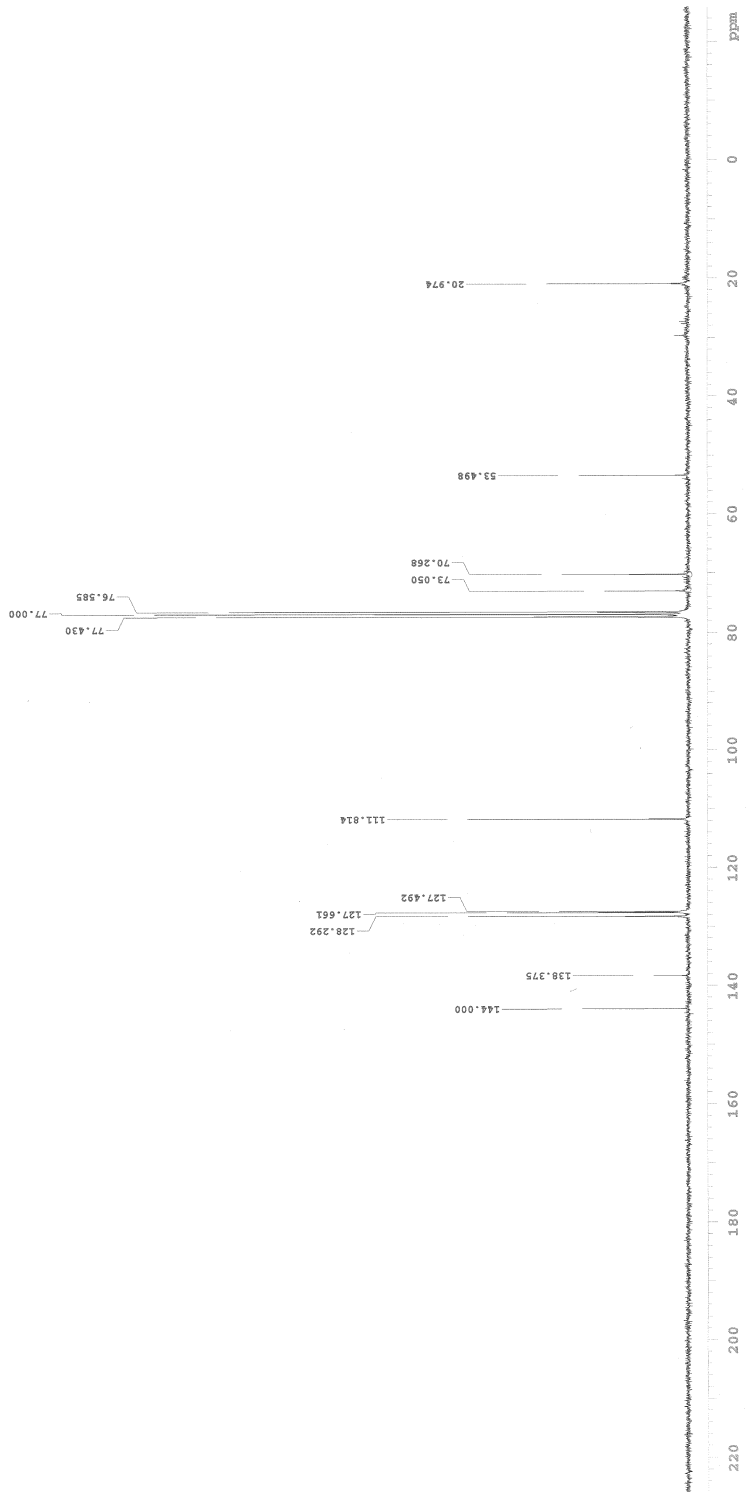

206.681
185.347
138.206
128.292
128.169
127.523
77.430
77.000
76.585
73.203
67.870
58.156
46.059
26.877
22.388
14.350
ppm
0
20
40
60
80
100
120
140
160
180
200
220

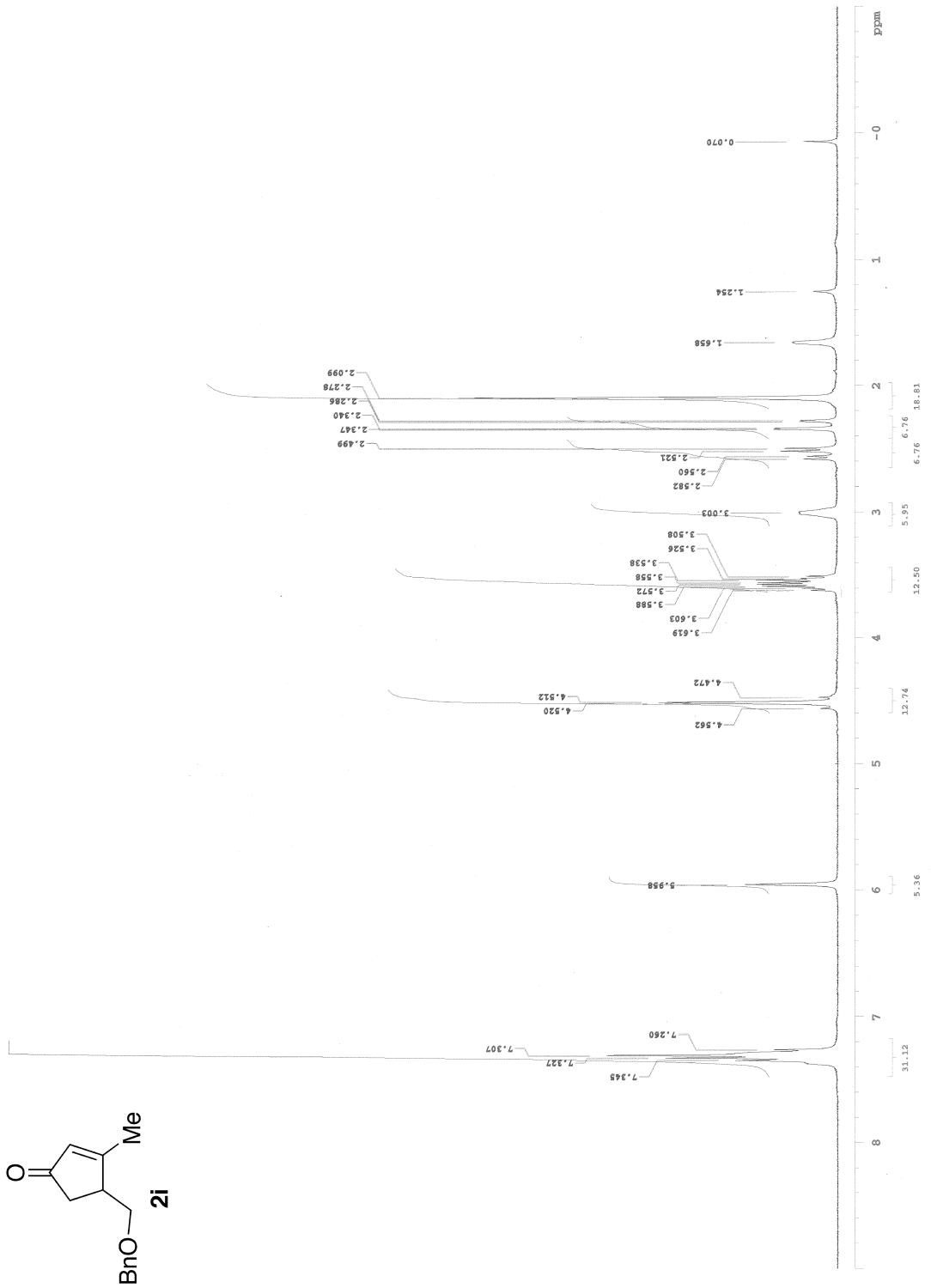
O
Me
Me
Me
BnO

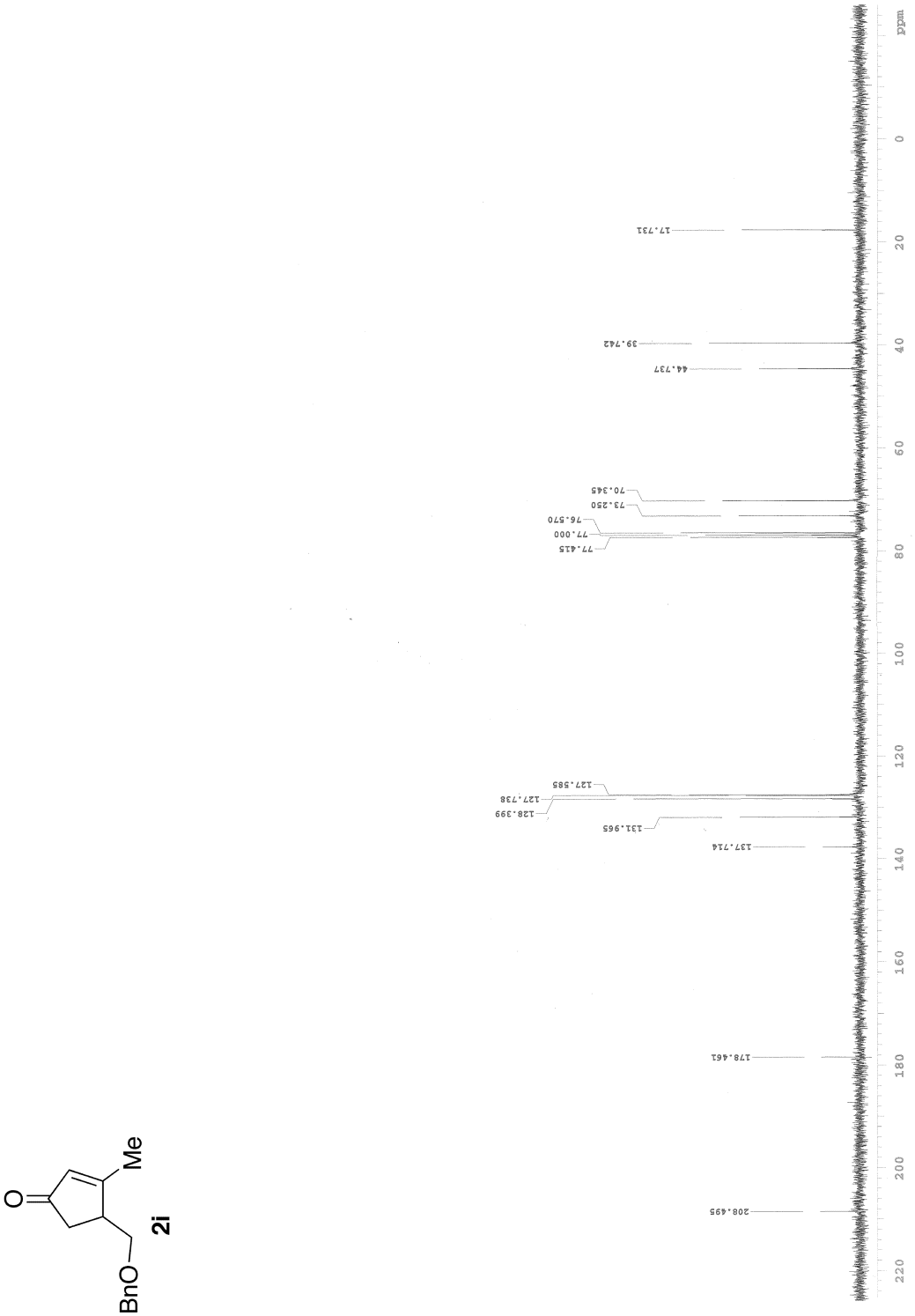
2h

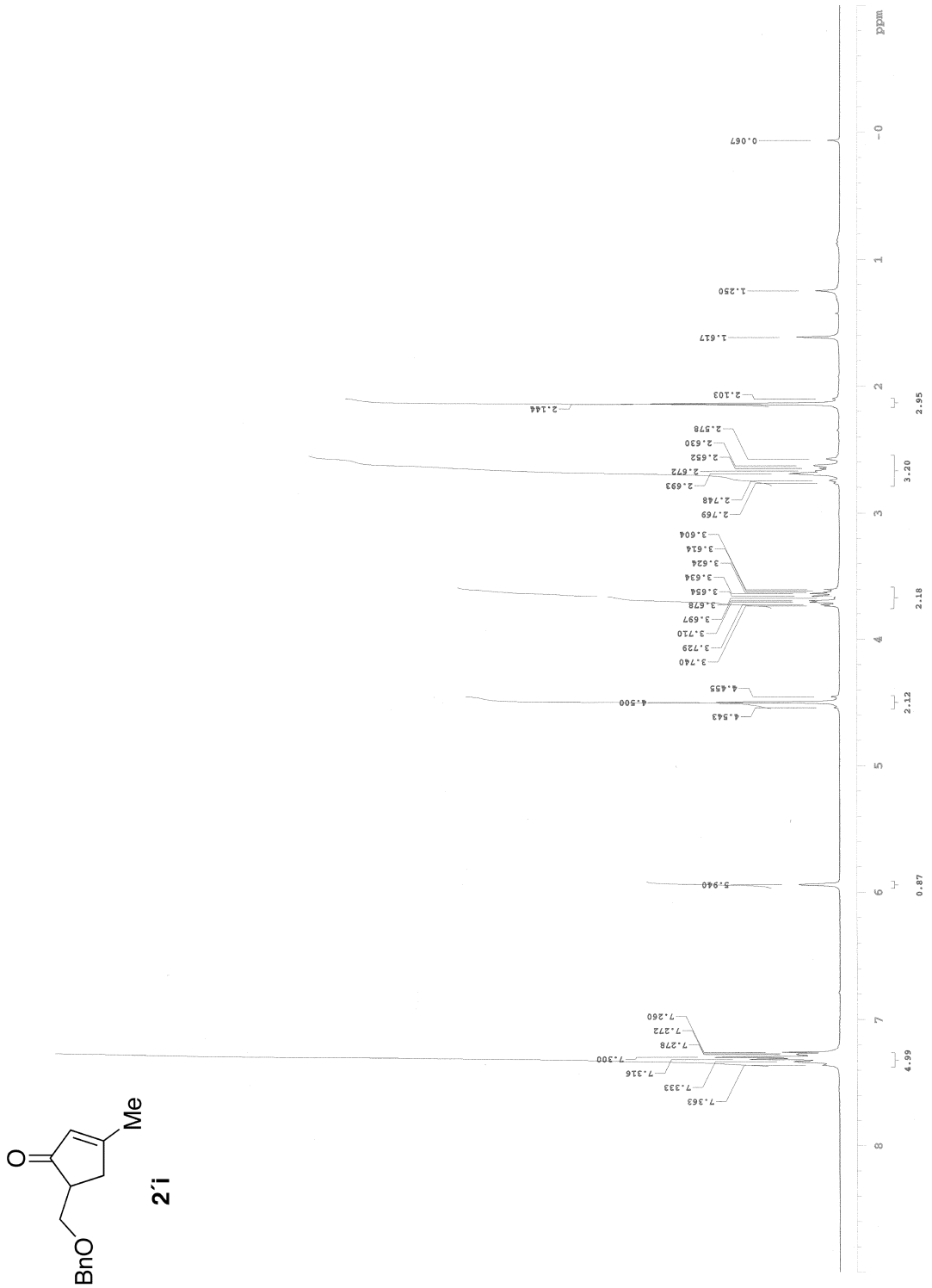

Me
Me
BnO
7
ppm
0.850
1.155
1.254
1.558
1.661
1.710
2.966
2.990
3.015
3.588
3.613
4.543
4.715
4.769
4.881
7.260
7.273
7.291
7.302
7.331
7.345
4.87
1.88
1.76
2.00
1.86
0.87
5.46

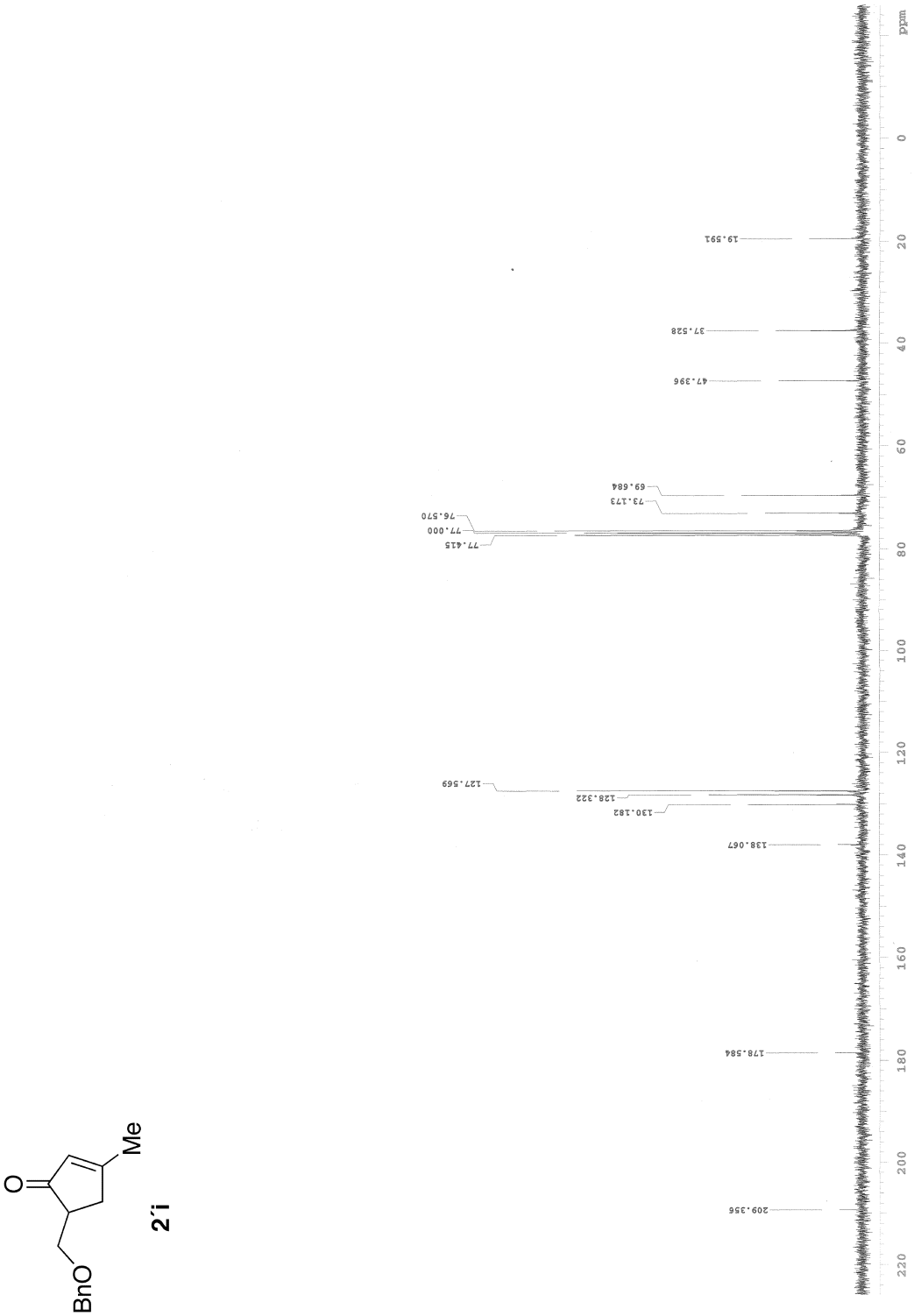

Me
Me
BnO
7

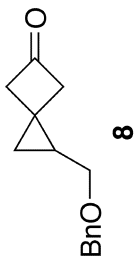

144.000
138.375
128.292
127.661
127.492
111.814
77.430
77.000
76.585
73.050
70.268
53.498
20.974
ppm
0
20
40
60
80
100
120
140
160
180
200
220


O
Me
BnO
2i
7.345
7.327
7.307
7.260
5.958
4.562
4.520
4.512
4.472
3.619
3.603
3.588
3.572
3.558
3.538
3.526
3.508
3.003
2.582
2.560
2.521
2.499
2.347
2.340
2.286
2.278
2.099
1.658
1.254
0.070
ppm
31.12
5.36
12.74
12.50
5.95
6.76
6.76
18.81

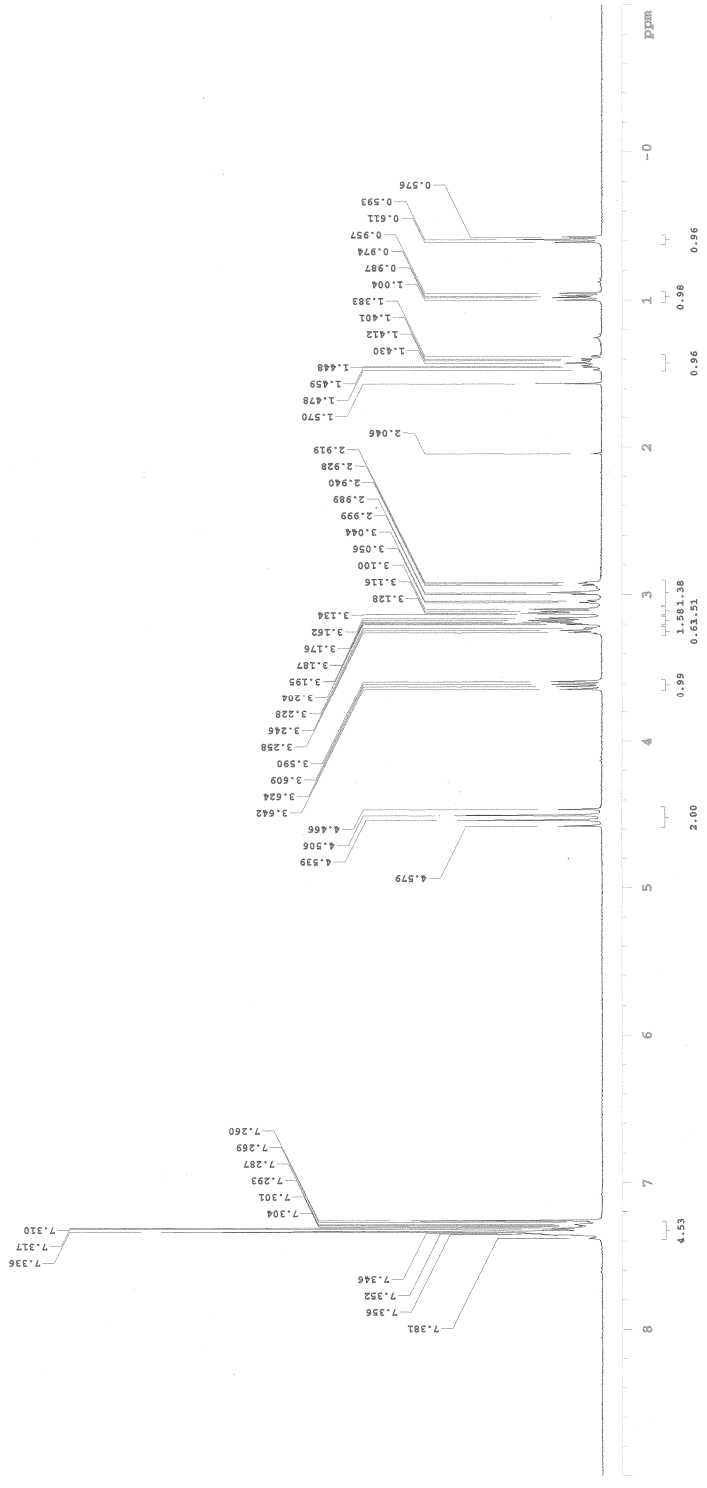

O
Me
BnO
2i
208.495
178.461
137.714
131.965
128.399
127.738
127.585
77.415
77.000
76.570
73.250
70.345
44.737
39.742
17.731
ppm

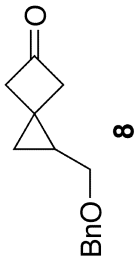

O
Me
BnO
2ĭ
7.363
7.333
7.316
7.300
7.278
7.272
7.260
5.940
4.543
4.500
4.455
3.740
3.729
3.710
3.697
3.678
3.654
3.634
3.624
3.614
3.604
2.769
2.748
2.693
2.672
2.652
2.630
2.578
2.144
2.103
1.617
1.250
0.067
ppm
4.99
2.12
0.87
2.18
3.20
2.95


O
Me
BnO
2´i
209.356
178.584
138.067
130.182
128.322
127.569
77.415
77.000
76.570
73.173
69.684
47.396
37.528
19.591
ppm
0
20
40
60
80
100
120
140
160
180
200
220

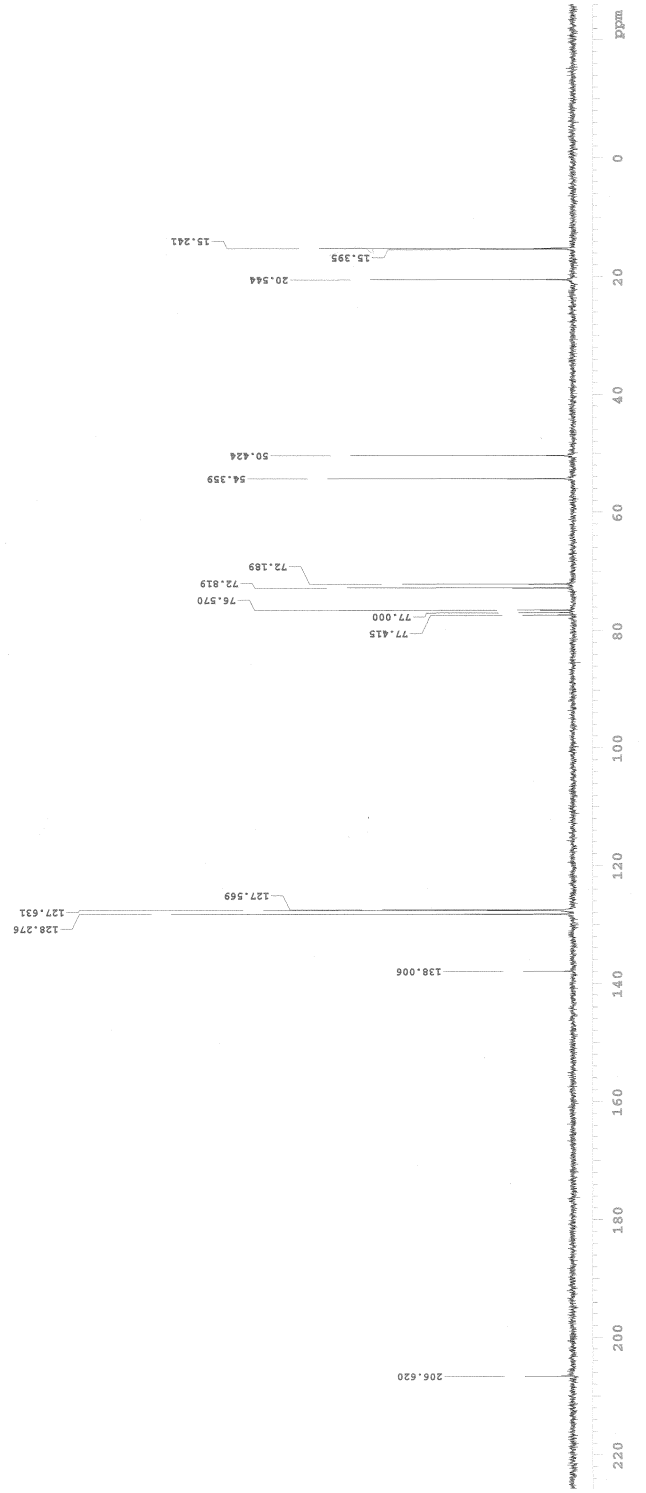

O
BnO

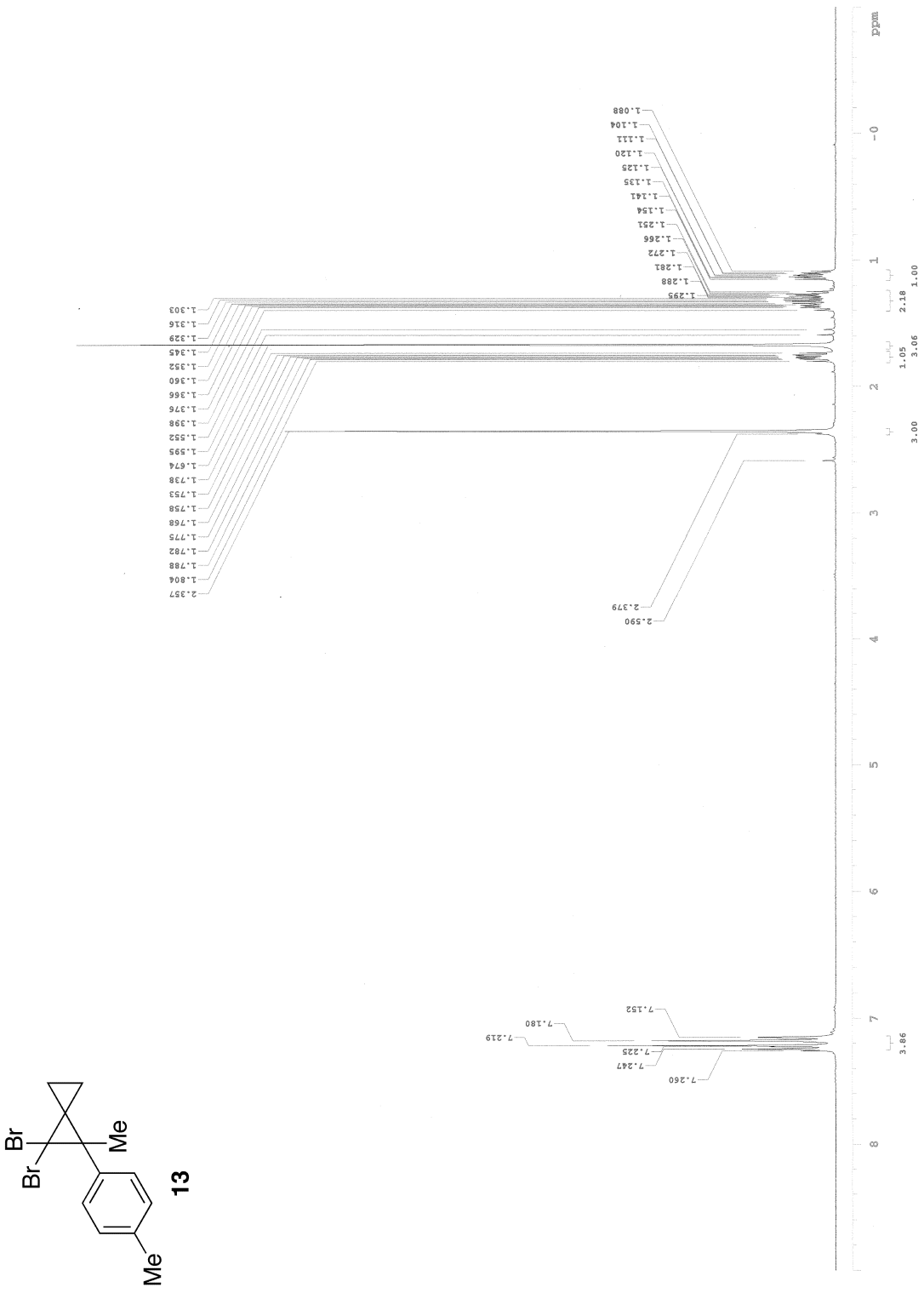
8

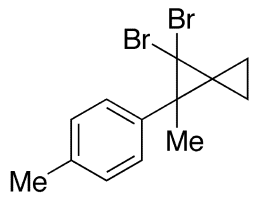

ppm
0.576
0.593
0.611
0.957
0.974
0.987
1.004
1.383
1.401
1.412
1.430
1.448
1.459
1.478
1.570
2.046
2.919
2.928
2.940
2.989
2.999
3.044
3.056
3.100
3.116
3.128
3.134
3.162
3.176
3.187
3.195
3.204
3.228
3.246
3.258
3.590
3.609
3.624
3.642
4.466
4.506
4.539
4.579
7.260
7.269
7.287
7.293
7.301
7.304
7.310
7.317
7.336
7.346
7.352
7.356
7.381
0.96
0.98
0.96
1.58
1.38
0.63
1.51
0.99
2.00
4.53


O
BnO

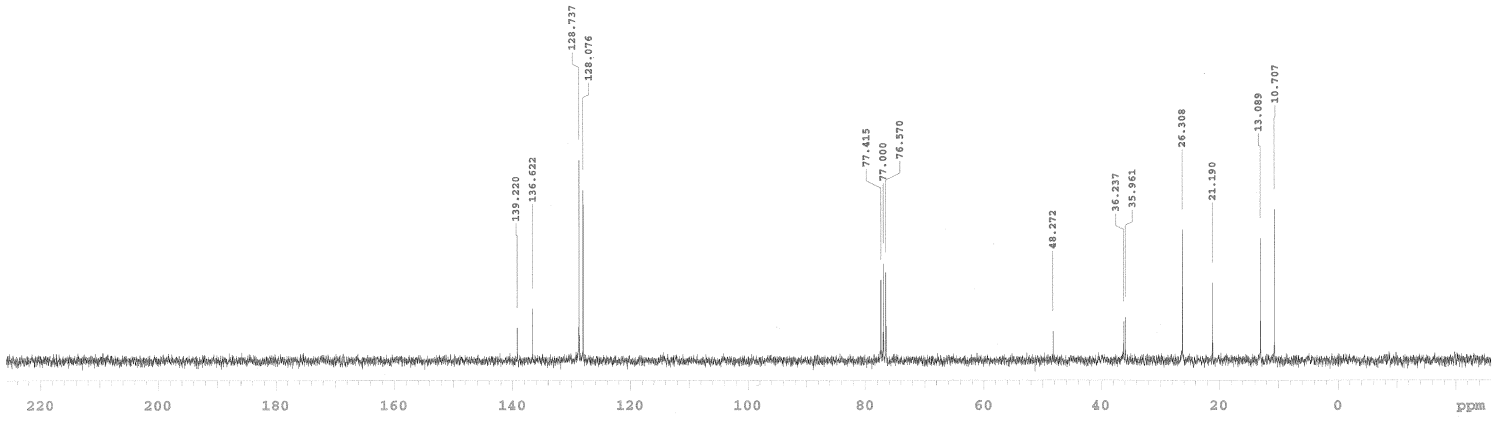
8

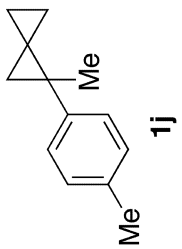

206.620
138.006
128.276
127.631
127.569
77.415
77.000
76.570
72.819
72.189
54.359
50.424
20.544
15.395
15.241
ppm
0
20
40
60
80
100
120
140
160
180
200
220


Br
Br
Me
Me
13
ppm
7.152
7.180
7.219
7.225
7.247
7.260
2.590
2.379
2.357
1.804
1.788
1.782
1.775
1.768
1.758
1.753
1.738
1.674
1.595
1.552
1.398
1.376
1.366
1.360
1.352
1.345
1.329
1.316
1.303
1.295
1.288
1.281
1.272
1.266
1.251
1.154
1.141
1.135
1.125
1.120
1.111
1.104
1.088
3.86
3.00
1.05
3.06
2.18
1.00

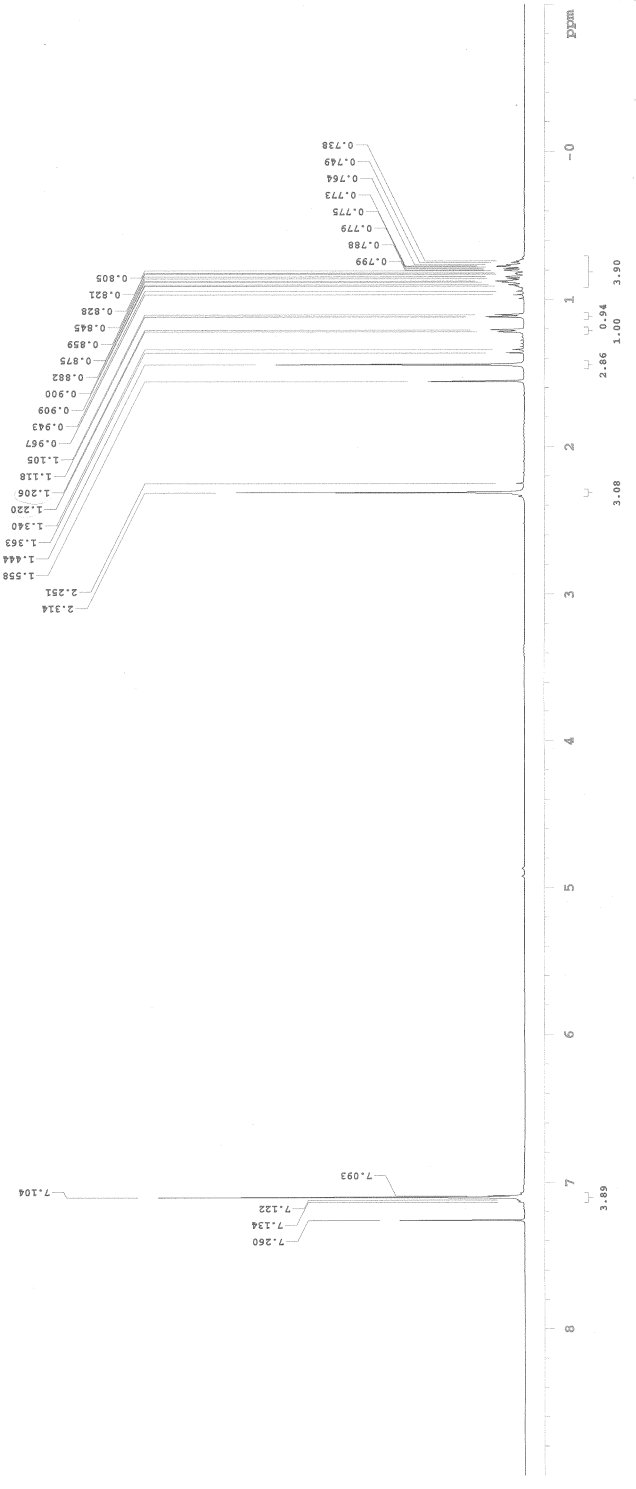

Br
Br
Me
Me

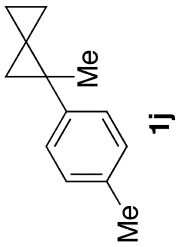
13


139.220
136.622
128.737
128.076
77.415
77.000
76.570
48.272
36.237
35.961
26.308
21.190
13.089
10.707
220
200
180
160
140
120
100
80
60
40
20
0
ppm

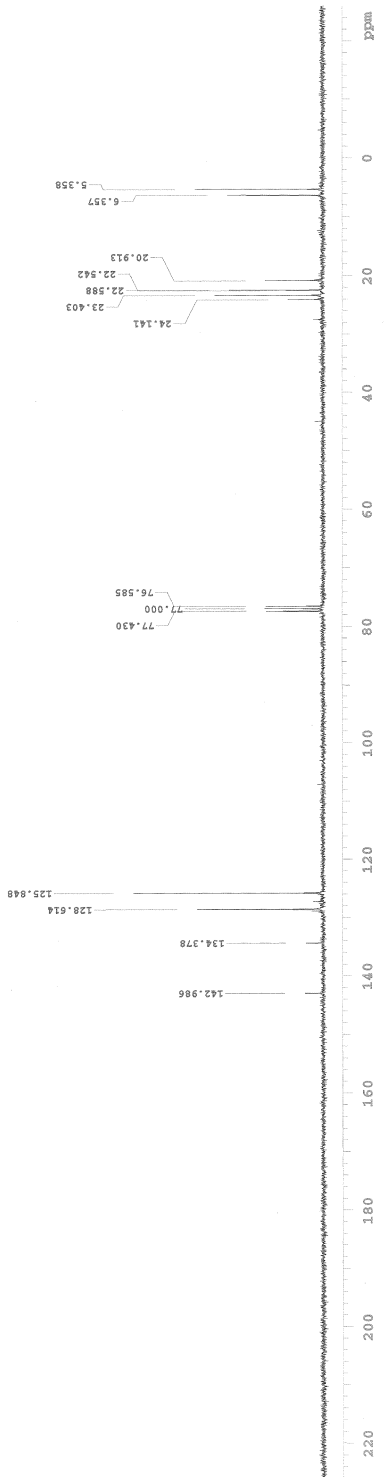

Me
Me

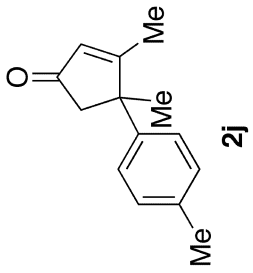
1j


ppm
0.738
0.749
0.764
0.773
0.775
0.779
0.788
0.799
0.805
0.821
0.828
0.845
0.859
0.875
0.882
0.900
0.909
0.943
0.967
1.105
1.118
1.206
1.220
1.340
1.363
1.444
1.558
2.251
2.314
7.093
7.104
7.122
7.134
7.260
3.89
3.08
2.86
0.94
1.00
3.90

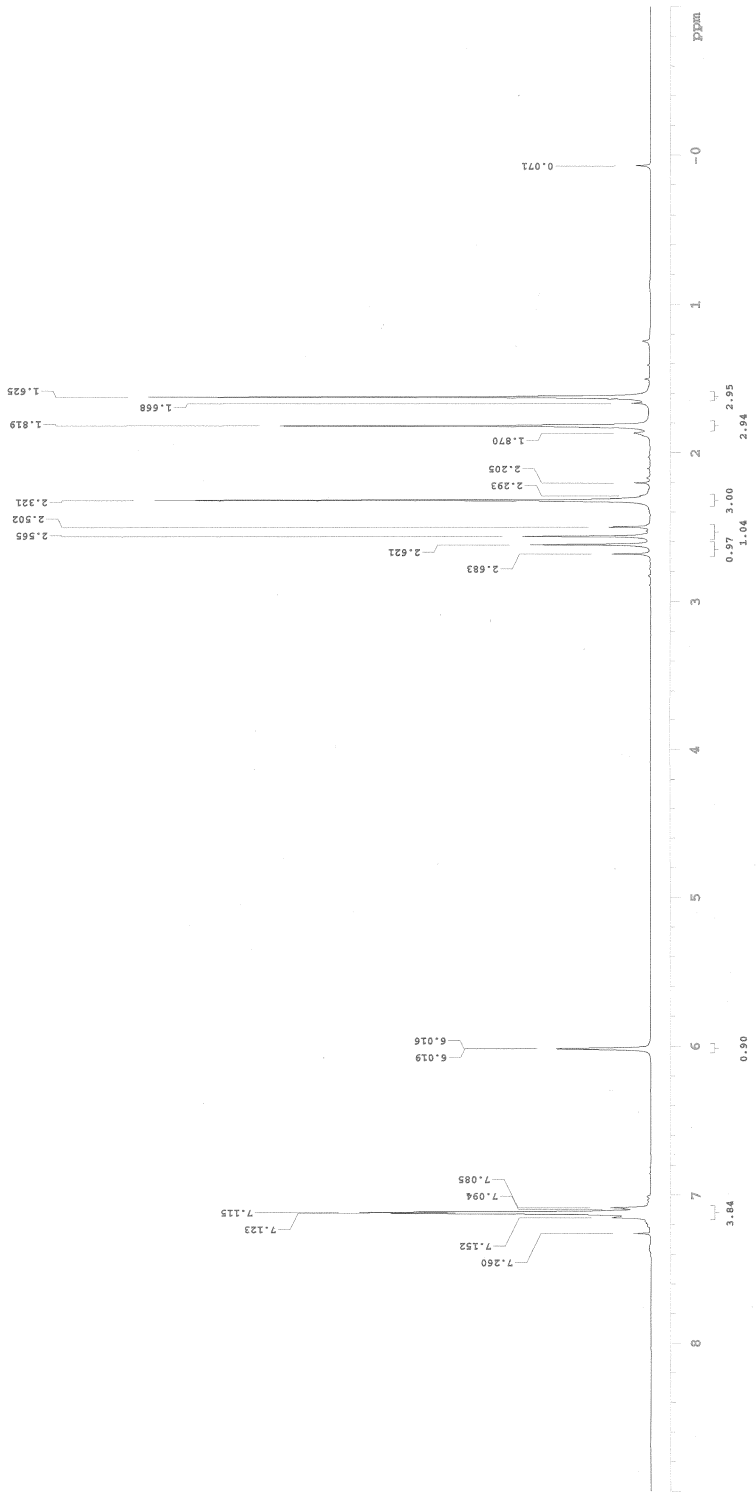

Me
Me

1j


5.358
6.357
20.913
22.542
22.588
23.403
24.141
76.585
77.000
77.430
125.848
128.614
134.378
142.986
ppm
0
20
40
60
80
100
120
140
160
180
200
220


O
Me
Me
Me

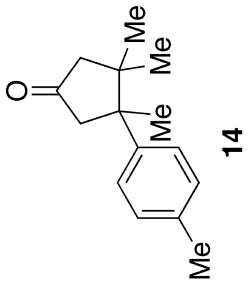
2j


ppm
0.071
1.625
1.668
1.819
1.870
2.205
2.293
2.321
2.502
2.565
2.621
2.683
6.016
6.019
7.085
7.094
7.115
7.123
7.152
7.260
2.95
2.94
3.00
1.04
0.97
0.90
3.84

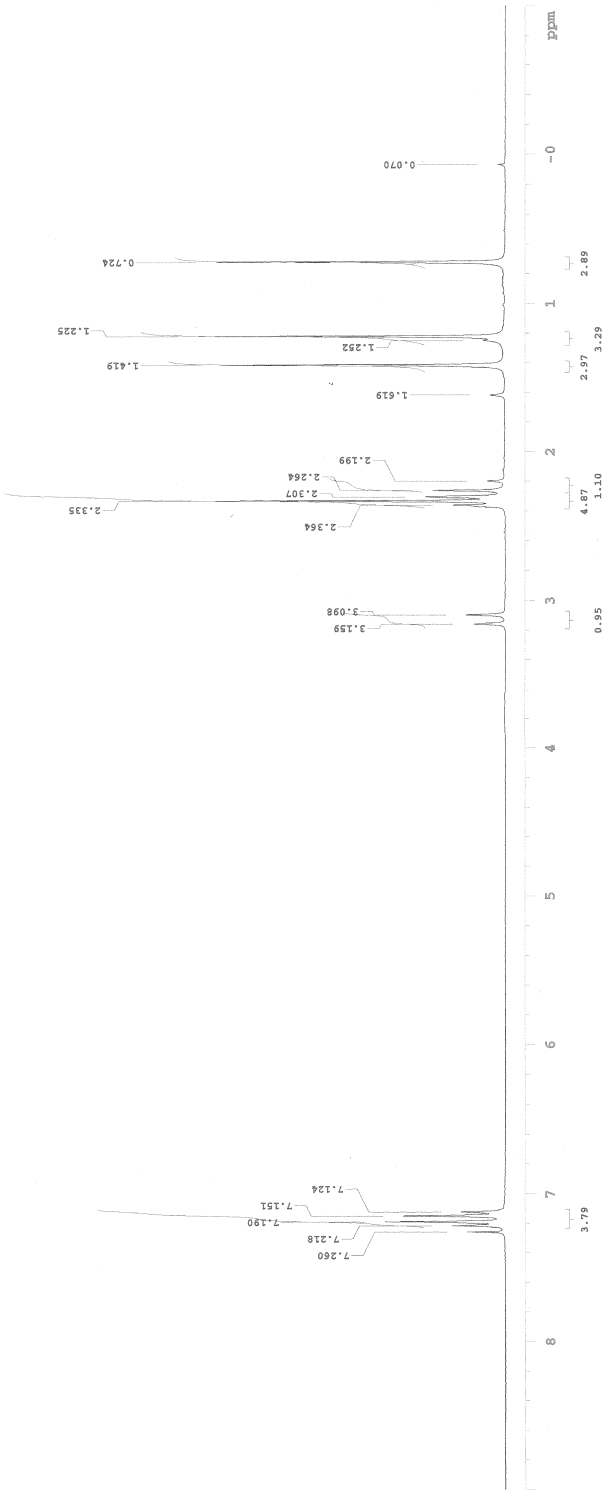
O
Me
Me
Me

2j

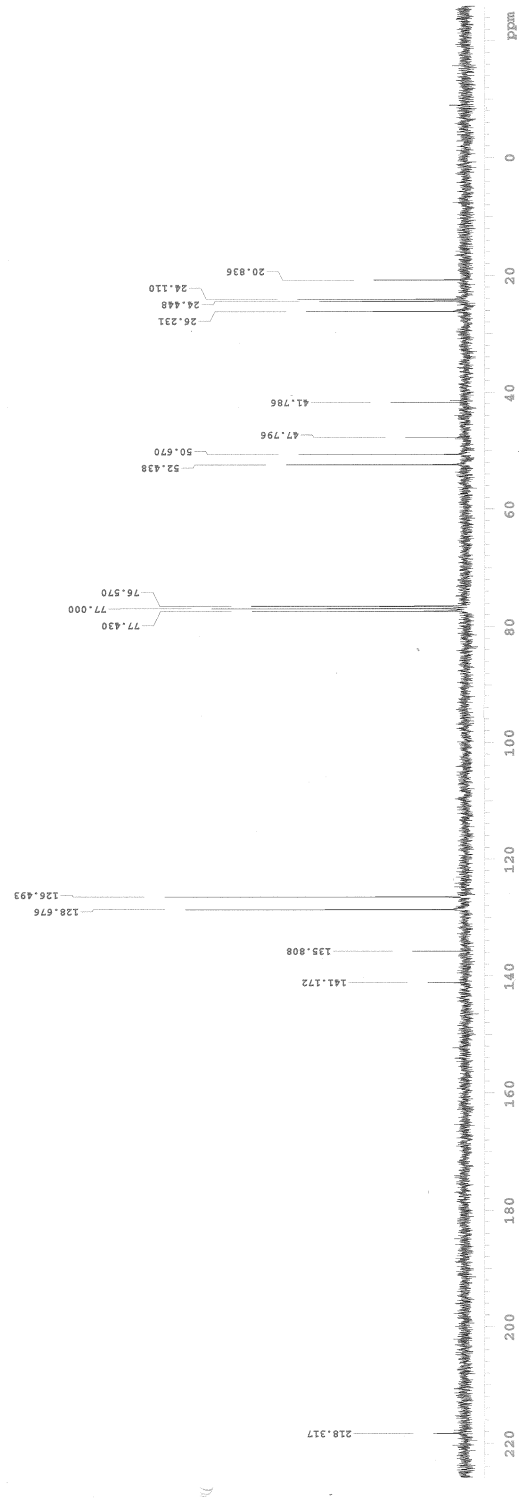
208.510
184.640
141.064
136.207
130.090
129.275
125.509
77.415
77.000
76.570
54.344
49.763
23.664
20.851
14.918
ppm


O
Me
Me
Me
Me

14


ppm
0.070
0.724
1.225
1.252
1.419
1.619
2.199
2.264
2.307
2.335
2.364
3.098
3.159
7.124
7.151
7.190
7.218
7.260
2.89
3.29
2.97
1.10
4.87
0.95
3.79


O
Me
Me
Me
Me
14


218.317
141.172
135.808
128.676
126.493
77.430
77.000
76.570
52.438
50.670
47.796
41.786
26.231
24.448
24.110
20.836
ppm