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Supporting Information

A New Method for the Preparation of Non-Terminal Alkynes: Application to the Total Syntheses of Tulearin A and C

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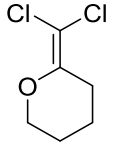
General. All reactions were carried out in flame-dried glassware under Argon. Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Fluka, Lancaster, Strem) were used as received. All solvents were purified by distillation over the drying agents indicated and were transferred under Argon: THF (Mg-anthracene), diethyl ether (Mg-anthracene), dichloromethane (CaH_2), acetonitrile (CaH_2), triethylamine (CaH_2), methanol (Mg), hexane (Na/K), toluene (Na/K). Flash chromatography: Merck silica gel 60 (230-400 mesh). IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200, MS (CI): Finnigan MAT 95, MS (ESI) ESQ 3000, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). NMR: Spectra were recorded on a Bruker AV 400 or AV 600 spectrometer in the solvents indicated; ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references ($CDCl_3$ δ_H = 7.24 ppm, δ_C = 77.0 ppm; C_6D_6 δ_H = 7.15 ppm, δ_C = 128.00 ppm; $CD_3(CO)CD_3$ δ_H = 2.04 ppm, δ_C = 29.80 ppm) and the chemical shifts converted to the TMS scale.

Where indicated, the signal assignments are unambiguous; the numbering scheme is arbitrary and shown in the inserts. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygpqf* and *cosydqtp*); HSQC (*hsqcedetgpsisp2.2*) optimized for $^{1}J_{C,H}$ = 145 Hz; HMBC (*hmbcetgpl3nd*) for correlations via $^{n}J_{C,H}$; HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms; NOESY (noesygpph).

The Experimental Part describing the total synthesis of tulearin C (2), including characterization data and copies of spectra, is contained in the Supporting Information of our Communication and therefore not duplicated herein.[1]

Preparation of Non-Terminal Alkynes by Reductive Alkylation

Representative Procedure for the Dichloro-Olefination of Lactones. Preparation of Compound 4.[2] A mixture of CCl_4 (88 mL, 140 g, 910 mmol) und THF (120 mL) was added dropwise over the course of 4



h to a refluxing solution of lactone **3** (3.52 mL, 3.80 g, 38.0 mmol) and PPh_3 (49.8 g, 152 mmol) in THF (500 mL). Once the addition was complete, the mixture was allowed to cool to ambient temperature. Water (300 mL) was added, the phases were separated, and the aqueous layer extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure to a total volume of ca. 60 mL. Pentane (250 mL) was added under vigorous stirring, the precipitate was filtered off, and the filtrate again reduced to a total volume of ca. 60 mL. This cycle of precipitation/evaporation was repeated three times before all volatile materials were evaporated and the solid residue subjected to flash chromatography (pentanes/Et_2O, 98:2) to furnish dichloro-olefin **4** in the form of a colorless syrup (5.87 g, 93%, ca. 95% pure). The product is only moderately stable but can be kept in a refrigerator under Ar for several days. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.02-3.96 (m, 2H), 2.48-2.43 (m, 2H), 1.76-1.72 ppm (m, 4H); ^{13}C NMR (100 MHz, C_6D_6): δ = 150.22, 103.90, 69.42, 25.62, 24.19, 21.22 ppm; IR (film): $\tilde{\nu}$ = 2947, 2871, 1630, 1439, 1340, 1277, 1256, 1238, 1068,

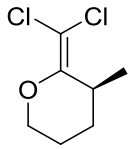
[1] K. Lehr, R. Mariz, L. Leseurre, B. Gabor, A. Fürstner, *Angew. Chem*. **2011**, *123*, 11575-11579; *Angew. Chem. Int. Ed*. **2011**, *50*, 11373-11377.

[2] M. Lakhrissi, Y. Chapleur, *J. Org. Chem*. **1994**, *59*, 5752-5757.

1050, 989, 956, 877, 684 cm^{-1}; MS (70 eV) *m/z* (%): 170 (6), 168 (34), 166 (55), 131 (27), 125 (23), 112 (66), 110 (100), 95 (40), 89 (13), 82 (21), 67 (37), 55 (46), 41 (55), 28 (45); HRMS (EI): *m/z* calcd. for $C_6H_8OCl_2$: 165.9952, found 165.9954.

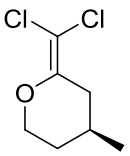
The following compounds were prepared analogously; because of their limited stability, most of the samples were only ca. 95% pure (NMR). They can usually be kept cold under Argon for several days

Compound S1.[3] Colorless oil (129 mg, 81%). $[\alpha]_D^{20}$ = +135 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$):



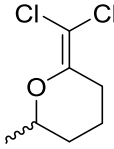
δ = 4.28-4.20 (m, 1H), 3.68 (dd, *J* = 11.6, 11.6 Hz, 1H), 3.05 (dddd, *J* = 5.4, 5.4, 5.3, 5.3 Hz, 1H), 2.10-1.96 (m, 1H), 1.81 (dddd, *J* = 13.2, 13.2, 4.7, 4.7 Hz, 1H), 1.66 (d, *J* = 12.3 Hz, 1H), 1.48 (d, *J* = 13.8 Hz, 1H), 1.19 ppm (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.51, 103.95, 70.42, 29.02, 28.12, 19.71, 17.12 ppm; IR (film): $\tilde{\nu}$ = 2939, 2871, 1730, 1625, 1463, 1375, 1340, 1275, 1249, 1178, 1133, 1072, 1010, 953, 919, 882, 850, 782, 664 cm^{-1}; MS (70 eV) *m/z* (%): 184 (8), 182 (47), 180 (73), 165 (24), 145 (27), 139 (60), 110 (52), 70 (75), 55 (100), 41 (60), 27 (25); HRMS (CI): *m/z* calcd. for $C_7H_{10}OCl_2$: 180.0109, found 180.0109.

Compound S2.[4] Colorless oil (1.11 g, 92%, contained traces of PPh_3) $[\alpha]_D^{20}$ = +128 (*c* = 1, $CHCl_3$); ^{1}H



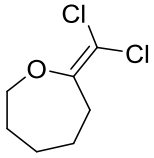
NMR (400 MHz, C_6D_6): δ = 3.73 (ddd, *J* = 11.0, 4.6, 2.9 Hz, 1H), 3.21 (td, *J* = 11.2, 3.1 Hz, 1H), 2.52 (ddd, *J* = 14.7, 4.5, 1.7 Hz, 1H), 1.35 (dd, *J* = 14.7, 11.4 Hz, 1H), 1.18-1.04 (m, 1H), 0.96-0.89 (m, 1H), 0.88-0.76 (m, 1H), 0.52 ppm (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 150.00, 104.17, 69.01, 33.84, 32.50, 28.18, 21.33 ppm; IR (film): $\tilde{\nu}$ = 2956, 2874, 1737, 1629, 1456, 1434, 1381, 1310, 1259, 1230, 1084, 1053, 996, 936, 843, 743, 695 cm^{-1}; MS (70 eV) *m/z* (%): 182 (18), 180 (27), 145 (7), 112 (21), 110 (47), 81 (12), 70 (20), 55 (100), 41 (27); HRMS (EI): *m/z* calcd. for $C_7H_{10}OCl_2$: 180.0109, found 180.0113.

Compound S3. Colorless oil (1.50 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.98 (s, 1H), 5.11 (ddd,



J = 4.3, 3.2, 0.8 Hz, 1H), 4.14-4.06 (m, 1H), 2.22.-2.04 (m, 2H), 1.89-1.82 (m, 1H), 1.63-1.51 (m, 1H) 1.36 ppm (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.95, 99.72, 72.87, 69.14, 28.29, 20.32, 19.79 ppm; IR (film): $\tilde{\nu}$ = 2974, 2940, 1445, 1386, 1224, 1087, 1040, 1009, 955, 888, 801, 766 cm^{-1}; MS (70 eV) *m/z* (%): 182 (19), 180 (30), 145 (23), 141 (17), 139 (28), 109 (15), 97 (42), 81 (32), 75 (21), 69 (56), 65 (28), 55 (100), 41 (56), 27 (27); HRMS (EI): *m/z* calcd. for $C_7H_{10}OCl_2$: 180.0109, found 180.0106.

2-(Dichlormethylen)oxepane (S4).[5] Colorless oil (1.60 g, 92%). ^{1}H NMR (400 MHz, C_6D_6): δ = 3.55-3.51



(m, 2H), 2.24-2.20 (m, 2H), 1.23-1.14 (m, 4H), 1.06-0.98 ppm (m, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ = 154.28, 101.78, 70.33, 30.24, 28.91, 28.81, 25.99 ppm; IR (film): $\tilde{\nu}$ = 2932, 2859, 1625, 1473, 1443, 1430, 1346, 1290, 1252, 1226, 1192, 1099, 1057, 1020, 927, 828, 733 cm^{-1}; MS (70 eV) *m/z* (%): 182 (11), 180 (17), 145 (14), 110 (15), 55 (100), 41 (16), 39 (17), 27 (11); HRMS (EI): *m/z* calcd. for $C_7H_{10}OCl_2$+Na^+: 180.0109, found 180.0111.

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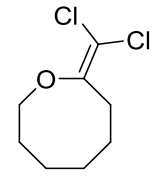
[3] L. Hoffmeister, P. Persich, A. Fürstner, *Chem. Eur. J.* **2014**, 20, 4396-4402.

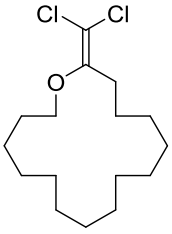
[4] K. Lehr, A. Fürstner, *Tetrahedron* **2012**, *68*, 7695-7700.

[5] M. Suda, A. Fukushima, *Tetrahedron Lett*. **1981**, *22*, 759-762.

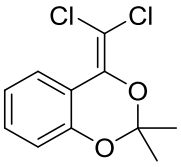
2-(Dichlormethylen)oxocane (S5). Colorless oil (568 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.17-4.13 (m, 2H), 2.56-2.51 (m, 2H), 1.74-1.55 ppm (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.80, 102.97, 68.50, 30.63, 27.15, 26.30, 25.94, 24.42 ppm; IR (film): $\tilde{\nu}$ = 2927, 2857, 1623, 1480, 1445, 1353, 1298, 1233, 1150, 1083, 1012, 916, 836, 742, 696 cm^{-1}; MS (70 eV) *m/z* (%): 196 (9), 194 (13), 138 (11), 110 (13), 69 (100), 68 (24), 55 (17), 41 (75), 39 (19), 29 (11), 27 (15); HRMS (EI): *m/z* calcd. for $C_8H_{12}OCl_2$: 194.0265, found 194.0263.



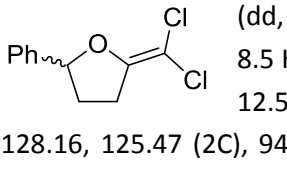
2-(Dichlormethylen)oxacyclohexadecane (S6). Colorless oil (380 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.79 (t, *J* = 6.1 Hz, 2H), 2.37 (dd, *J* = 7.3, 7.3 Hz, 2H), 2.09 (tt, *J* = 6.4, 6.4 Hz, 2H), 1.58-1.24 (m, 18H), 0.91-0.84 ppm (m, 4H); IR (film): $\tilde{\nu}$ = 2926, 2856, 1736, 1622, 1459, 1350, 1233, 1141, 1109, 1051, 1016, 985, 919, 736, 717, 665 cm^{-1}; MS (70 eV) *m/z* (%): 308 (10), 306 (16), 235 (4), 157 (5), 138 (24), 131 (40), 117 (14), 97 (26), 95 (14), 84 (15), 83 (36), 69 (61), 55 (100), 41 (78); HRMS (ESI): *m/z* calcd. for $C_{16}H_{28}Cl_2O$+Na$^+$: 329.1409, found 329.1412.



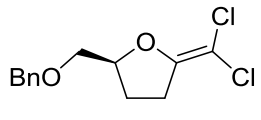
Compound S7. While solid (241 mg, 88%). mp = 66-67°C; ^{1}H NMR (400 MHz, C_6D_6): δ = 8.17 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.91 (ddd, *J* = 8.3, 7.3, 1.5 Hz, 1H), 6.79 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.68 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H), 1.30 ppm (s, 6H); ^{13}C NMR (100 MHz, C_6D_6): δ = 151.23, 141.38, 131.16, 127.01, 121.31, 117.76, 115.63, 107.79, 102.16, 24.79 ppm (2C); IR (film): $\tilde{\nu}$ = 1613, 1477, 1456, 1375, 1252, 1204, 1120, 1083, 986, 891, 824, 750, 703 cm^{-1}; MS (70 eV) *m/z* (%): 246 (20), 244 (31), 209 (12), 173 (9), 161 (7), 145 (8), 121 (100), 120 (79), 43 (22); HRMS (EI): *m/z* calcd. for $C_{11}H_{10}Cl_2O_2$: 244.0058, found 244.0060.



Compound 10.[2] Colorless oil (642 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41-7.29 (m, 5H), 5.45 (dd, *J* = 7.8, 6.6 Hz, 1H), 2.87 (ddd, *J* = 16.1, 8.5, 4.5 Hz, 1H), 2.77 (dd, *J* = 16.2, 8.5 Hz, 1H), 2.53 (dddd, *J* = 12.9, 8.2, 6.4, 4.8 Hz, 1H), 2.10 ppm (ddd, *J* = 16.8, 12.5, 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.67, 139.87, 128.58 (2C), 128.16, 125.47 (2C), 94.10, 85.73, 33.46, 29.66, ppm; IR (film): $\tilde{\nu}$ = 1666, 1604, 1495, 1452, 1433, 1372, 1324, 1292, 1218, 1202, 1178, 1079, 1054, 1017, 961, 901, 755, 732, 696 cm^{-1}; MS (70 eV) *m/z* (%): 232 (9), 230 (51), 228 (79), 195 (30), 193 (91), 157 (49), 129 (41), 117 (88), 115 (44), 105 (100), 91 (52), 77 (27), 51 (21); HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}OCl_2$+Na$^+$: 251.0001, found 250.9995.



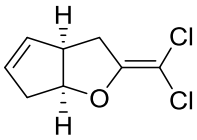
Compound S8. Colorless oil (417 mg, 62%). $[\alpha]_D^{20}$ = –14 (*c* = 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.24 (s, 2H), 4.08 (ddd, *J* = 11.3, 7.0, 4.5 Hz, 1H), 3.30 (s, 3H), 3.22-3.08 (m, 2H), 2.33 (ddd, *J* = 16.4, 8.9, 5.9 Hz, 1H), 2.13-2.03 (m, 1H), 1.44-1.27 ppm (m, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.86, 154.76, 130.51 (2C), 129.48, 114.13 (2C), 93.69, 84.02, 73.16, 71.03, 54.78, 29.51, 26.83 ppm; IR (film): $\tilde{\nu}$ = 2934, 2909, 2863, 2837, 1665, 1611, 1586, 1511, 1441, 1361, 1301, 1245, 1221, 1172, 1101, 1081, 1031, 980, 903, 738 cm^{-1}; MS (70 eV) *m/z* (%): 304 (3), 302 (4), 267 (3), 135 (2), 122 (9), 121 (100), 78 (5); HRMS (ESI): *m/z* calcd. for $C_{14}H_{16}O_3Cl_2$+Na$^+$: 325.0369, found 325.0370.



Compound S9. Colorless oil (210 mg, 88%). $[\alpha]_D^{20}$ = +16 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6): δ = 7.30-7.00 (m, 5H), 4.23 (s, 2H), 4.05 (tt, *J* = 6.9, 4.4 Hz, 1H), 3.16-3.04 (m, 2H), 2.31 (ddd, *J* = 15.5, 8.6, 6.2 Hz, 1H), 2.06

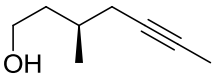
(ddd, *J* = 16.7, 9.1, 7.7 Hz, 1H), 1.41- 1.23 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.67, 138.59, 128.61 (2C), 127.85, 127.80 (2C), 93.78, 83.90, 73.38, 71.33, 29.48, 26.76 ppm; IR (film): $\tilde{\nu}$ = 2862, 1666, 1495, 1453 1362, 1221, 1209, 1119, 980, 902, 825, 734, 696 cm^{-1}; MS (70 eV) *m/z* (%): 272 (5), 205 (3), 151 (2), 117 (2), 105 (3), 91 (100), 77 (5), 65 (11), 51 (5), 39 (6); HRMS (ESI): *m/z* calcd. for $C_{13}H_{14}Cl_2O_2$+Na^+: 295.0269, found 295.0269.

Compound S10. Colorless oil (147 mg, 95%). $[\alpha]_D^{20}$ = –21 (*c* = 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6):



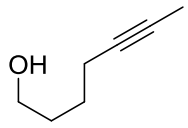
δ = 5.25 (ddd, *J* = 4.7, 4.6, 2.2 Hz, 1H), 4.99 (dtd, *J* = 4.4, 2.9, 1.7 Hz, 1H), 4.42 (t, *J* = 5.5 Hz, 1H), 2.64-2.52 (m, 1H), 2.40-2.30 (m, 2H), 2.23 (dd, J = 17.0, 8.9 Hz, 1H), 2.00 ppm (dddt, *J* = 18.0, 5.4, 2.9, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6): δ = 154.26, 131.52, 129.30, 93.49, 88.02, 48.83, 40.03, 34.82 ppm; IR (film): $\tilde{\nu}$ = 3727, 3420, 2058, 2937, 1430, 1362, 1215, 1171, 1056, 1013, 977, 901, 777, 699 cm^{-1}; MS (70 eV) *m/z* (%): 192 (18), 190 (27), 155 (28), 127 (10), 119 (13), 91 (22), 80 (100), 79 (75), 77 (19), 65 (10), 39 (20); HRMS (EI): *m/z* calcd. for $C_8H_8OCl_2$: 189.9952, found 189.9953.

Alkyne Formation: Representative Procedure for the Uncatalyzed Variant. Preparation of (*R*)-3-Methylhept-5-yn-1-ol (S11). MeLi (1.6 M in diethyl ether, 21 mL, 33 mmol) was slowly added to a solution of dichloro-olefin **S2** (1.20 g, 6.63 mmol) in Et_2O (50 mL) and the resulting mixture stirred for 2 d to room temperature. For work up, the mixture was cooled to 0°C and the reaction was carefully quenched with water (70 mL). The aqueous layer was extracted with diethyl ether (3 × 70 mL), the combined extracts were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentanes/diethyl ether, 1:1) afforded the title compound as a colorless liquid (750 mg, 90%).



$[\alpha]_D^{20}$ = +3.2 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.71 (dt, *J* = 10.9, 6.5 Hz, 1H), 3.67 (dt, *J* = 10.9, 6.5 Hz, 1H), 2.12-2.07 (m, 2H), 1.84-1.65 (m, 3H), 1.78 (t, *J* = 2.6 Hz, 3H), 1.55-1.42 (m, 2H), 0.98 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 77.53, 77.20, 61.03, 38.79, 29.58, 26.13, 19.65, 3.44 ppm; IR (film): $\tilde{\nu}$ = 3339, 2970, 2956, 2920, 2875, 1738, 1455, 1434, 1375, 1366, 1229, 1217, 1206, 1092, 1053, 1006, 962, 888, 842cm^{-1}; MS (70 eV) *m/z* (%): 111 (31), 98 (65), 97 (13), 93 (33), 91 (22), 84 (24), 83 (11), 82 (100), 81 (14), 80 (20), 79 (38), 77 (31), 71 (19), 67 (46), 55 (85), 54 (36), 53 (44), 43 (58), 41 (43); HRMS (CI): *m/z* calcd for $C_8H_{15}O$: 127.1124, found 127.1123.

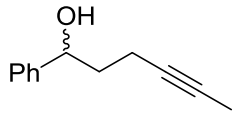
Alkyne Formation: Representative Procedure for the Copper-Catalyzed Variant. Preparation of Hept-5-yn-1-ol (5a, R = Me). MeLi (1.6 M in Et_2O, 3.7 mL, 5.4 mmol) was added at 0°C to a solution of dichloro-olefin **4** (300 mg, 1.80 mmol) and $Cu(acac)_2$ (47 mg, 0.18 mmol) in Et_2O (15 mL). The ice-bath was removed and the solution stirred for 4 h at ambient temperature. The reaction was carefully quenched with water (20 mL), the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 20 mL), the combined organic phases were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (pentanes/Et_2O, 1:1) to afford the title compound as a colorless oil (179 mg, 89%).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (t, *J* = 6.4 Hz, 2H), 2.20-2.14 (m, 2H), 1.71 (t, *J* = 2.6 Hz, 3H), 1.72-1.62 (m, 2H), 1.60-1.51 (m, 2H), 1.35 ppm (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.88, 75.82, 62.51, 31.87, 25.24, 18.48, 3.42 ppm; IR (film): $\tilde{\nu}$ = 3352, 2938, 2864, 1716, 1435, 1374, 1332, 1164, 1056, 1029, 980, 931, 893 cm^{-1}; MS (70 eV) *m/z* (%): 11 (2), 97 (18), 91 (8), 84 (53), 79 (38), 77 (27), 68 (100), 66 (46), 53 (42), 41 (40), 39 (37), 31 (35), 27 (27); HRMS (CI): *m/z* calcd. for

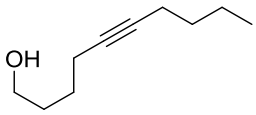
$C_7H_{12}O+NH_4^+$: 130.1232, found 130.1230. The data are in good accord with those previously described in the literature.[6]

Alkyne Formation: Representative Procedure for the Iron-Catalyzed Variant: Preparation of 1-Phenylhex-4-yn-1-ol (12). MeLi (1.6 M in Et_2O, 3.7 mL, 5.4 mmol) was added to a solution of the dichloro-olefin **10** (200 mg, 0.87 mmol), 1,2-diaminobenzene (24 mg, 0.22 mmol) and $Fe(acac)_3$ (15 mg, 0.04 mmol) in Et_2O (6 mL) and the mixture was stirred for 2 h at ambient temperature. The reaction was carefully quenched with water (15 mL), the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 15 mL), the combined organic phases were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (pentanes/Et_2O, 4:1) to afford the title compound as a colorless oil (129 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.27 (m, 5H), 4.85 (dd, J = 8.0, 5.1 Hz, 1H), 2.38-2.12 (m, 2H), 2.06-1.76 (m, 2H), 1.80 (t, J = 2.6 Hz, 3H), 1.25 ppm (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.23, 128.45 (2C), 127.57, 125.80 (2C), 78.42, 73.52, 65.83, 37.93, 15.46, 3.48 ppm; IR (film): $\tilde{\nu}$ = 3386, 2919, 1603, 1493, 1452, 1330, 1217, 1083, 1058, 1026, 1007, 912, 852, 752, 699, 666 cm^{-1}; MS (70 eV) *m/z* (%): 173 (8), 159 (41), 145 (12), 141 (32), 120 (14), 115 (16), 107 (79), 105 (65), 97 (22), 91 (15), 79 (100), 77 (63), 51 (24); HRMS (CI): *m/z* calcd. for $C_{12}H_{14}O+H^+$: 175.1123, found 175.1125. The data are in good accord with those previously described in the literature.[7]

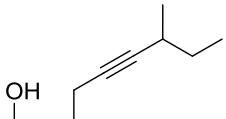


The following compounds were prepared analogously according to the method shown in Table 3:

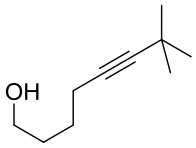
Dec-5-yn-1-ol (5b, R = *n*-Bu). Colorless oil (140 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (t, J = 6.4 Hz, 2H), 2.22-2.12 (m, 4H), 1.72-1.63 (m, 2H), 1.61-1.52 (m, 2H), 1.50-1.34 (m, 5H), 0.90 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.67, 79.68, 62.53, 31.88, 31.22, 25.36, 21.93, 18.53, 18.41, 13.61 ppm; IR (film): $\tilde{\nu}$ = 3328, 2932, 2863, 1456, 1433, 1378, 1331, 1250, 1164, 1056, 1030, 980, 930, 908, 729 cm^{-1}; MS (70 eV) *m/z* (%): 126 (4), 112 (4), 11 (19), 110 (30), 97 (37), 93 (30), 81 (42), 79 (100), 67 (60), 55 (50), 54 (52), 41 (56); HRMS (CI): *m/z* calcd. for $C_{10}H_{18}O+NH_4^+$: 172.1701, found 172.1701.



7-Methylnon-5-yn-1-ol (5c, R = *sec*-Bu). Colorless oil (78 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (t, J = 6.4 Hz, 2H), 2.36-2.25 (m, 1H), 2.19 (td, J = 6.9, 2.2 Hz, 2H), 1.70-1.61 (m, 3H), 1.60-1.51 (m, 2H), 1.48-1.31 (m, 2H), 1.10 (d, J = 6.9 Hz, 3H), 0.95 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 85.16, 79.90, 62.45, 31.82, 30.16, 27.52, 25.41, 21.03, 18.47, 11.73 ppm; IR (film): $\tilde{\nu}$ = 3340, 2964, 2931, 2872, 1455, 1377, 1336, 1056, 978 cm^{-1}; MS (70 eV) *m/z* (%): 125 (8), 110 (65), 97 (49), 81 (100), 67 (46), 55 (74); HRMS (CI): *m/z* calcd. for $C_{10}H_{18}O+H^+$: 155.1436, found 155.1737.



7,7-Dimethyloct-5-yn-1-ol (5d, R = *tert*-Bu). Colorless oil (152 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (t, J = 6.4 Hz, 2H), 2.18 (t, J = 6.9 Hz, 2H), 1.70-1.50 (m, 4H), 1.47 (br s, 1H), 1.19 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 89.43, 78.09, 62.53, 31.85, 31.36, 27.31, 25.40, 18.43 ppm (3C); IR (film): $\tilde{\nu}$ = 3325, 2967, 2866, 1456, 1361, 1265,

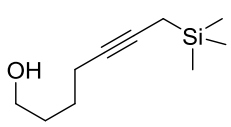


[6] J. Pornet, D. Damour, L. Miginiac, *Tetrahedron* **1986**, *42*, 2017-2014.

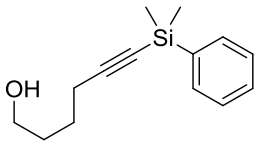
[7] H. Yanagisawa, K. Miura, M. Kitamura, K. Narasaka, K. Ando, *Bull. Chem. Soc. Jpn*. **2003**, *76*, 2009-2026.

1205, 1054, 905 cm^{-1}; MS (70 eV) *m/z* (%): 139 (4), 126 (5), 110 (88), 95 (100), 79 (49), 67 (39), 55 (60); HRMS (CI): *m/z* calcd. for $C_{10}H_{18}O+H^+$: 155.1436, found 184.1438.

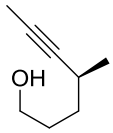
7-(Trimethylsilyl)hept-5-yn-1-ol (5e, R = CH_2SiMe_3).[6] Colorless oil (95 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (t, *J* = 6.4 Hz, 2H), 2.19 (tt, *J* = 6.9, 2.7 Hz, 2H), 1.73-1.63 (m, 2H), 1.60-1.51 (m, 3H), 1.42 (t, *J* = 2.7 Hz, 2H), 0.09 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.42, 77.81, 62.54, 31.92, 25.65, 18.69, 6.92, -2.08 ppm (3C); IR (film): $\tilde{\nu}$ = 3363, 2942, 1940, 1248, 1169, 1059, 844, 759, 697 cm^{-1}; MS (70 eV) *m/z* (%): 184 (4), 169 (6), 140 (8), 93 (11), 79 (47), 75 (70), 73 (100); HRMS (CI): *m/z* calcd. for $C_{10}H_{20}O$: 184.1283, found 184.1282.



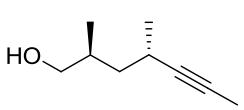
6-(Dimethyl(phenyl)silyl)hex-5-yn-1-ol (5f, R = $SiPhMe_2$). Colorless oil (248 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65-7.35 (m, 5H), 3.68 (t, *J* = 6.2 Hz, 2H), 2.33 (t, *J* = 6.8 Hz, 2H), 1.74-1.60 (m, 4H), 1.43 (br s, 1H), 0.39 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.58, 133.62 (2C), 129.24, 127.79 (2C), 109.03, 82.80, 62.39, 31.84, 24.87, 19.74, -0.64 ppm (2C); IR (film): $\tilde{\nu}$ = 3308, 2943, 2173, 1428, 1248, 1114, 1044, 813, 698 cm^{-1}; MS (70 eV) *m/z* (%): 217 (5), 199 (18), 161 (32), 137 (100), 75 (37); HRMS (CI): *m/z* calcd. for $C_{14}H_{20}OSi+H^+$: 233.1362, found 233.1360.



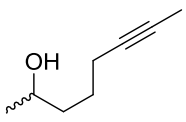
4-Methylhept-5-yn-1-ol (S12). Colorless oil (29 mg, 83%); ee = 94% [GC: 30 m BGB-178/BGB-15 G/615 column; temperature gradient: 60 °C, 1/min 120 °C 14/min, 220 °C; t_R (*major*): 39.4 min; t_R (*min*): 41.9 min; $[\alpha]_D^{20}$ = +22 (*c* = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.66 (t, *J* = 6.5 Hz, 2H), 2.39 (br s, 1H), 1.78 (d, *J* = 2.4 Hz, 3H), 1.77-1.58 (m, 2H), 1.53-1.36 (m, 3H), 1.14 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 83.52, 75.88, 62.82, 33.39, 30.63, 25.77, 21.47, 3.42 ppm; IR (film): $\tilde{\nu}$ = 3341, 2920, 2870, 1452, 1375, 1334, 1056, 1025, 983, 897 cm^{-1}; MS (70 eV) *m/z* (%): 111 (9), 98 (8), 82 (100), 67 (90), 41 (55); HRMS (CI): *m/z* calcd. for $C_8H_{14}O+H^+$: 127.1123, found 127.1122.



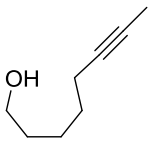
(2S*,4S*)-2,4-Dimethylhept-5-yn-1-ol (S13). Pale yellow oil (825 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.56 (dd, *J* = 10.7, 5.5 Hz, 1H), 3.46 (dd, *J* = 10.7, 6.1 Hz, 1H), 2.55-2.43 (m, 1H), 1.92-1.82 (m, 1H), 1.78 (d, *J* = 2.3 Hz, 3H), 1.47 (br s, 1H), 1.42 (ddd, *J* = 13.5, 6.1, 7.4 Hz, 1H), 1.33 (ddd, *J* = 13.5, 8.8, 6.3 Hz, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 84.1, 75.9, 67.7, 41.0, 33.7, 23.6, 21.7, 17.4, 3.6 ppm; IR (film): $\tilde{\nu}$ = 3324, 2965, 2919, 2873, 1453, 1375, 1335, 1042, 999, 978, 948 cm^{-1}; MS (EI): *m/z* (%): 125 (9), 109 (6), 107 (17), 98 (20), 93 (7), 91 (17), 83 (24), 82 (92), 81 (8), 80 (12), 79 (26), 77 (12), 71 (7), 69 (22), 68 (8), 67 (100), 66 (6), 65 (20), 58 (6), 57 (8), 55 (27), 53 (17), 51 (5), 43 (24), 41 (57), 39 (26), 31 (14), 29 (10), 27 (9); HRMS (CI): *m/z* calcd. for $C_9H_{17}O$: 141.1279 [M+H^+]; found: 141.1278.



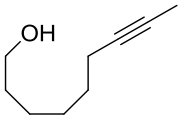
Oct-6-yn-2-ol (S14). Colorless oil (61 mg, 88%).^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87-3.78 (m, 1H), 2.19-2.13 (m, 1H), 1.77 (t, *J* = 2.6Hz, 3H), 1.64-1.44 (m, 6H), 1.20 ppm (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.95, 75.80, 67.74, 38.40, 25.24, 23.53, 18.68, 3.43 ppm; IR (film): $\tilde{\nu}$ = 3359, 2965, 2920, 2863, 1455, 1373, 1331, 1180, 1127, 1084, 1045, 990, 943, 861, 820 cm^{-1}; MS (70 eV) *m/z* (%): 111 (19), 93 (85), 84 (65), 79 (20), 77 (20), 71 (35), 67 (49), 66 (100), 55 (34), 54 (47), 53 (28), 45 (90), 43 (57), 41 (46), 27 (36); HRMS (CI): *m/z* calcd. for $C_8H_{14}O+H^+$: 127.1123, found 127.1122.



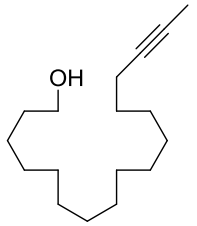
Oct-6-yn-1-ol (S15). Colorless oil (122 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (t, *J* = 6.5 Hz, 2H), 2.17-2.11 (m, 2H), 1.77 (t, *J* = 2.6 Hz, 3H), 1.62-1.33 ppm (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 79.04, 75.57, 62.89, 32.30, 28.80, 24.99, 18.69, 3.45 ppm; IR (film): $\tilde{\nu}$ = 3328, 2934, 2860, 1434, 1332, 1191, 1156, 1046, 1005, 956, 913, 732 cm^{-1}; MS (70 eV) *m/z* (%): 111 (7), 97 (22), 95 (21), 93 (100), 91 (37), 82 (28), 79 (77), 77 (34) 68 (100), 66 (90), 55 (92), 53 (76), 41 (95), 39 (81), 27 (56); HRMS (CI): *m/z* calcd. for $C_8H_{14}O+H^+$: 127.1123, found 127.1122.



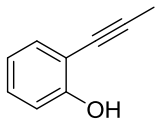
Non-7-yn-1-ol (S16). Colorless oil (30 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, *J* = 6.6 Hz, 2H), 2.13 (tq, *J* = 7.1, 2.5 Hz, 2H), 1.78 (t, *J* = 2.6 Hz, 3H), 1.62-1.32 ppm (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 79.20, 75.45, 62.96, 32.66, 28.97, 28.61, 25.28, 18.65, 3.45 ppm; IR (film): $\tilde{\nu}$ = 3315, 2931, 2858, 1457, 1330, 1231, 1150, 1072, 1054, 1031, 844, 720, 673, 662 cm^{-1}; MS (70 eV) *m/z* (%): 107 (10), 93 (21), 91 (11), 81 (18), 79 (39), 68 (100), 55 (30), 53 (51), 43 (16), 41 (72), 39 (30), 31 (27), 27 (29); HRMS (CI): *m/z* calcd. for $C_9H_{16}O+H^+$: 141.1279, found 141.1279.



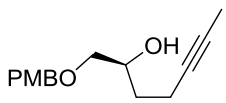
Heptadec-15-yn-1-ol (S17). (46 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, *J* = 6.6 Hz, 2H), 2.11 (tq, *J* = 7.2, 2.6 Hz, 1H), 1.78 (t, *J* = 2.6 Hz, 3H), 1.60-1.18 ppm (m, 26H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 79.43, 63.11, 32.81, 29.63 (2C), 29.62, 29.61, 29.60, 29.58, 29.53, 29.42, 29.18, 29.10, 28.91, 25.73, 18.73, 3.47 ppm; IR (film): $\tilde{\nu}$ = 3277, 2915, 2849, 1470, 1059, 1036, 1021, 993, 971, 719, 698 cm^{-1}; MS (70 eV) *m/z* (%): 149 (4), 135 (10), 109 (23), 95 (58), 81 (50), 68 (100), 55 (53), 41 (40); HRMS (EI): *m/z* calcd. for $C_{17}H_{32}O$: 252.2453, found 252.2451.



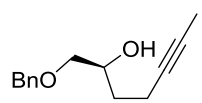
2-(Prop-1-yn-1-yl)phenol (S18). Colorless oil (33 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.19 (ddd, *J* = 7.8, 7.8, 1.6 Hz, 1H), 6.92 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.84 (ddd, *J* = 7.5, 7.5, 1.1 Hz, 1H), 5.79 (s, 1H), 2.14 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 156.56, 131.43, 129.58, 120.15, 114.32, 110.20, 93.26, 73.80, 4.57 ppm; IR (film): $\tilde{\nu}$ = 3500, 1578, 1485, 1286, 1234, 1177, 1032, 893, 823, 749 cm^{-1}; MS (70 eV) *m/z* (%): 133 (7), 132 (79), 131 (100), 103 (31), 77 (25), 51 (21); HRMS (EI): *m/z* calcd. for $C_9H_8O_2$: 132.0575, found 132.0575.



(*S*)-1-((4-Methoxybenzyl)oxy)hept-5-yn-2-ol (S19). Colorless oil (210 mg, 69%). $[\alpha]_D^{20}$ = -2.9 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 4.49 (s, 2H), 3.94 (ddt, *J* = 11.1, 7.4, 3.8 Hz, 1H), 3.81 (s, 3H), 3.49 (dd, *J* = 9.5, 3.1 Hz, 1H), 3.33 (dd, *J* = 9.2, 7.7 Hz, 1H), 2.40-2.20 (m, 3H), 1.76 (t, *J* = 2.3 Hz, 3H), 1.70-1.50 ppm (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.30, 130.05, 129.36 (2C), 113.84 (2C), 78.47, 76.03, 73.98, 73.03, 69.41, 55.27, 32.29, 15.06, 3.44 ppm; IR (film): $\tilde{\nu}$ = 3440, 2917, 2857, 1612, 1586, 1512, 1442, 1363, 1301, 1244, 1173, 1080, 1032, 914, 817, 757, 708 cm^{-1}; MS (ESIpos) *m/z* (%): 690 (20), 519 (100), 271 (32); HRMS (ESI): *m/z* calcd. for $C_{15}H_{20}O_3+Na^+$: 271.1305, found 271.1306.



(*S*)-1-(Benzyloxy)hept-5-yn-2-ol (S20). Colorless oil (28 mg, 70%). $[\alpha]_D^{20}$ = -14 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.7 (m, 5H), 4.56 (s, 2H), 4.00-3.93 (m, 1H), 3.53 (dd, *J* = 9.5, 3.3 Hz, 1H), 3.37 (dd, *J* = 9.5, 7.5 Hz, 1H), 2.38-2.25 (m, 2H), 1.76 (t, *J* = 2.6 Hz, 3H), 1.70-1.50 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.95, 128.44 (2C), 127.77, 127.71 (2C), 78.46, 76.08, 74.28, 73.38, 69.45, 32.28, 15.07, 3.45 ppm; IR (film):



$\tilde{\nu}$ = 3429, 2918, 2858, 1956, 1496, 1453, 1365, 1088, 1028, 736, 698 cm^{-1}; MS (70 eV) *m/z* (%): 203 (5), 157 (2), 148 (3), 143 (5), 107 (9), 97 (15), 91 (100), 79 (18), 65 (18), 53 (14), 41 (26); HRMS (ESI): *m/z* calcd. for $C_{14}H_{18}O_2$+Na^+: 241.1199, found 241.1195.

(1*S*,2*S*)-2-(But-2-yn-1-yl)cyclopent-3-en-1-ol (S21). Colorless oil (57 mg, 80%). $[\alpha]_D^{20}$ = –35 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.80-5.74 (m, 1H), 5.65-5.58 (m, 1H), 4.54-4.47 (m, 1H), 2.86-2.77 (m, 1H), 2.64 (dddt, *J* = 17.1, 6.4, 2.5, 2.0 Hz, 1H), 2.44-230 (m, 3H), 1.99 (br s, 1H), 1.78 ppm (t, *J* = 2.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.02, 129.00, 78.06, 76.58, 72.77, 49.26, 41.74, 17.73, 3.48 ppm; IR (film): $\tilde{\nu}$ = 3728, 3398, 2919, 2855, 1435, 1300, 1167, 1078, 1031, 985, 943, 855, 678 cm^{-1}; MS (70 eV) *m/z* (%): 136 (5), 135 (5), 118 (74), 117 (70), 91 (51), 83 (100), 55 (99); HRMS (EI): *m/z* calcd. for $C_9H_{12}O$: 136.0888, found 136.0887.

Intelligence Gathering

Macrocycle 45. TBAF (1 M in THF, 110 µL, 110 µmol) was added to a solution of alkenylsilane **44** (mixture of regioisomers, 10 mg, 14 µmol) in THF at 0°C. The resulting mixture was stirred at ambient temperature for 3 h and at 50°C for 5 h before the reaction was quenched with sat. aq. $NaHCO_3$ (5 mL). The aqueous layer was extracted with ethyl acetate (5 × 5 mL), the combined organic phases were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1) to give the title compound as a colorless syrup (8 mg, 78%, 3:1 *E*/*Z*). For the ^{1}H and ^{13}C NMR of the major *E*-isomer, see Table S-1; IR (film): $\tilde{\nu}$ = 2958, 2927, 2857, 1707, 1456, 1378, 1259, 1090, 1017, 965, 796, 756 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 514 (85), 499 (39), 456 (28), 367 (17), 244 (27), 164 (79), 107 (45), 93 (100), 81 (71), 43 (46); HRMS (ESI+): *m/z* calcd. for $C_{33}H_{54}O_4$+Na^+: 537.3914, found 537.3917.

Bicyclus 48. Trifluoroacetic acid (1.6 µL, 21 µmol) was added to a solution of compound **45** (3.7 mg, 6.9 µmol) in CH_2Cl_2 (1 mL) and the resulting mixture was stirred for 1 h. The reaction was quenched with sat. aq. $NaHCO_3$ (1 mL), the aqueous layer was extracted with Et_2O (5 x 1 mL), the combined organic phases were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromtography (hexanes/EtOAc, 2:1) to afford the title compound as a colorless oil (1.7 mg, 46%). For the ^{1}H and ^{13}C NMR spectra, see Table S-2; IR (film): $\tilde{\nu}$ = 2953, 2926, 2858, 1686, 1643, 1456, 1378, 1075, 1031, 963, 802, 752, 666 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 474 (38), 456 (10), 335 (13), 289 (100), 271 (17), 191 (11), 151 (13), 95 (22), 81 (9), 55 (22); HRMS (ESI+): *m/z* calcd. for $C_{30}H_{50}O_4$+Na^+: 497.3601, found 497.3602.

Table S-1. ^{1}H and ^{13}C NMR data (C_6D_6) of compound **45** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering is arbitrary as shown in the Insert.

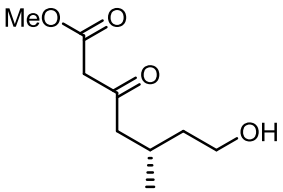
Nummer	δ_C [ppm]	Mult.	δ_H [ppm]	Mult.	Kuppl. [Hz]	Integ.
1	167.07	s				
2	129.43	s				
3	139.36	d	6.99	td	7.8, 1.6	1H
4	36.13	t	2.00	m		1H
			1.70	m		1H
5	32.22	d	1.37	m		1H
6	31.18	t	1.37	m		1H
			0.94	m		1H
7	30.97	t	1.71	m		1H
			1.43	m		1H
8	81.55	d	3.57	td	7.7, 4.4	1H
9	78.83	d	3.83	ddd	9.8, 8.0, 2.5	1H
10	34.05	t	1.63	m		1H
			1.48	m		1H
11	29.08	t	2.41	m		1H
			2.27	m		1H
12	130.87	d	5.52	ddd	15.2, 7.1, 6.0	1H
13	130.21	d	5.59	ddd	15.3, 7.0, 6.2	1H
14	40.49	t	1.92	m		1H
			1.78	m		1H
15	31.43	d	1.63	m		1H
16	42.16	t	2.03	ddd	14.2, 10.1, 3.5	1H
			1.13	ddd	14.1, 10.0, 3.5	1H
17	69.52	d	6.16	ddd	10.1, 8.9, 3.5	1H
18	129.45	d	5.51	d	9.2	1H
19	136.67	s				
20	134.56	d	6.11	dq	15.6, 0.9	1H
21	130.87	d	5.64	dt	15.5, 7.0	1H
22	32.22	t	2.00	dt		2H
23	29.51	t	1.30	m		2H
24	31.75	t	1.20	m		2H
25	22.91	t	1.23	m		2H
26	14.23	q	0.86	t	7.2	3H
27	12.79	q	1.84	dt		3H
28	20.54	q	0.76	d	6.6	3H
29	19.94	q	0.94	d	6.6	3H
30	13.34	q	1.97	d	1.1	3H
31						
32						
33	107.81	s				
34	27.75	q	1.45	s		3H
35	27.54	q	1.43	s		3H

Table S-2. ^{1}H and ^{13}C NMR data (C_6D_6) of compound **48** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering is arbitrary as shown in the Insert.

Nummer	δ_C [ppm]	Mult.	δ_H [ppm]	Mult.	Kuppl. [Hz]	Integ.
1	173.55	s				
2	128.12	s				
3	144.21	d	7.12	t	7.7	1H
4	36.51	t	1.96	m		1H
			1.82	m		1H
5	33.24	d	1.45	m		1H
6	32.9	t	1.48	m		2H
7	30.69	t	1.48	m		1H
			1.38	m		1H
8	74.30	d	3.45	m		1H
9	80.95	d	3.11	ddd	11.2, 6.4, 2.2	1H
10	28.37	t	1.41	m		1H
			1.28	m		1H
11	28.38	t	1.82	m		1H
			0.84	m		1H
12	46.1	d	0.84	m		1H
13	80.85	d	2.87	ddd	11.0, 9.0, 4.0	1H
14	41.00	t	1.8	m		1H
			1.03	dt	12.4, 11.3	1H
15	30.50	d	1.35	m		1H
16	41.68	t	1.49	m		1H
			0.72	dt	13.0, 11.8	1H
17	40.65	d	1.97	m		1H
18	134.06	d	5.11	d	9.6	1H
19	133.75	s				
20	135.52	d	6.24	d	15.6	1H
21	128.07	d	5.65	dt	15.5, 7.1	1H
22	33.38	t	2.14	q	7.3	2H
23	29.87	t	1.41	m		2H
24	31.84	t	1.28	m		2H
25	22.97	t	1.28	m		2H
26	14.27	q	0.88	t		3H
27	12.34	q	1.81	s		3H
28	19.56	q	0.79	d	6.4	3H
29	22.37	q	0.85	d	6.6	3H
30	13.31	q	1.76	d	1.2	3H

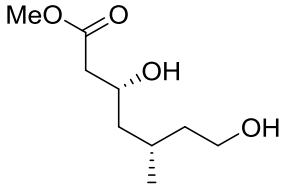
Total Synthesis of Tulearin A

Ketoester S23. *n*-Butyllithium (1.6 M in hexane, 6.6 mL, 11 mmol) was slowly added to a solution of diisopropylamine (1.6 mL, 12 mmol) in THF (9 mL) at -78 °C and the resulting mixture was stirred for 10 min at this temperature and for 5 min at 0 °C. Methyl acetate (0.73 mL, 9.2 mmol) was added dropwise at -78 °C to the solution of LDA thus formed and the mixture was stirred for 1 h at this temperature. A solution of lactone **19** (1.0 g, 8.8 mmol)[1] in THF (5 mL) was then added and stirring continued for 3 h at -78 °C. The reaction was quenched with acetic acid (1.5 mL) while cold, the resulting suspension was warmed to ambient temperature, diluted with diethyl ether (10 mL) and absorbed on silica gel (about 10 g), which was added on top of a silica gel column. The product was eluted with hexane/ethyl acetate (3:1) to give the title compound as a colorless oil (1.43 g, 87%). $[\alpha]_D^{20}$ = +47 (c = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.73 (d, *J* = 2.4 Hz, 1H), 3.96 (ddd, *J* = 13.0, 11.3, 2.4 Hz, 1H), 3.74 (s, 3H), 3.65 (ddd, *J* = 11.3, 4.9, 1.4 Hz, 1H), 2.59 (q, *J* = 15.4 Hz, 2H), 2.12-1.95 (m, 1H), 1.79 (ddd, *J* = 12.9, 3.8, 1.8 Hz, 1H), 1.54 (dddd, *J* = 13.1, 3.7, 3.6, 1.8 Hz, 1H), 1.28-0.94 (m, 2H), 0.90 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.92, 95.11, 61.35, 52.06, 45.08, 43.46, 33.83, 24.99, 22.24, ppm; IR (film): $\tilde{\nu}$ = 3466, 2952, 2929, 2873, 1736, 1718, 1439, 1357, 1212, 1171, 1090, 1044, 1018, 998, 853 cm^{-1}; MS (EI, 70eV) *m/z* (%): 188 (0.05), 170 (6), 155 (7), 143 (7), 119 (100), 115 (37), 101 (78), 69 (59), 55 (72), 42 (67); HRMS (EI) m/z calcd. for $C_9H_{16}O_4$: 188.1049, found 188.1051.

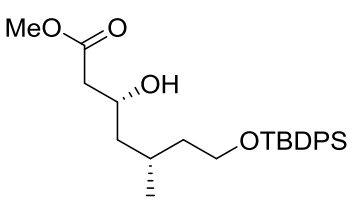


in equilibrium with hemiacetal

Diol S24. An autoclave was charged with $RuCl_3$ (45 mg, 0.22 µmol) and (*R*)-SYNPHOS (139 mg, 0.22 µmol) and put under an inert atmosphere by three vacuum/argon cycles. Methanol (41 mL) and β-ketoester **S23** (2.05 g, 10.9 mmol) were added. The autoclave was pressurized with hydrogen (10 bar) and the pressure was released. This purge cycle was repeated three times before the solution was stirred at 80 °C under hydrogen atmosphere (10 bar) for 24 h. For work up, the autoclave was vented at ambient temperature, the solvent was evaporated and the dark residue was purified by flash chromatography (hexane/ethyl acetate, 1:1 to 3:7) to give the title compound as a colorless oil (1.63 g, 79%). $[\alpha]_D^{20}$ = –6.6 (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.12-4.00 (m, 1H), 3.62 (s, 3H), 3.62-3.53 (m, 2H), 3.40 (br s, 1H), 2.59 (br s, 1H), 2.43-2.37 (m, 2H), 1.90-1.70 (m, 1H), 1.52 (ddd, *J* = 14.0, 10.1, 4.1 Hz, 1H), 1.43, (q, *J* = 6.6 Hz, 2H), 1.07 (ddd, *J* = 13.8, 9.5, 3.1 Hz, 1H), 0.88 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.44, 66.10, 60.37, 51.87, 43.42, 42.18, 40.30, 25.86, 19.83 ppm; IR (film): $\tilde{\nu}$ = 3355, 2954, 2929, 1733, 1438, 1280, 1166, 1053, 1007, 963, 859 cm^{-1}; MS (EI, 70eV) *m/z* (%): 191 (0.3), 154 (1), 142 (9), 130 (4), 116 (7), 103 (100), 99 (35), 74 (21), 71 (40), 43 (96); HRMS (ESI) m/z calcd. for $C_9H_{18}O_4$+Na^+: 213.1095, found 213.1097.

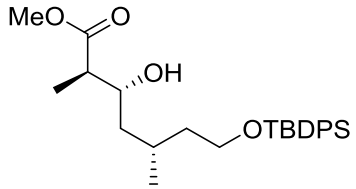


Alcohol S25. 4-(Dimethylamino)pyridine (52 mg, 0.43 mmol), triethylamine (1.37 mL, 9.85 mmol) and *tert*-butyl(chloro)diphenylsilane (2.44 mL, 9.43 mmol) were added to a solution of β-hydroxyester **S24** (1.63 g, 8.27 mmol) in dichloromethane (44 mL) and the resulting mixture was stirred for 16 h before the reaction was

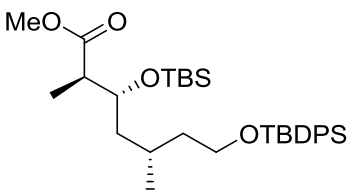


quenched with water (50 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL), the organic layer was dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexane/ethyl acetate 9:1) to give the title compound as a colorless oil (3.38 g, 92%). $[\alpha]_D^{20}$ = -5.0 (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.73-7.67 (m, 4H), 7.50-7.37 (m, 6H), 4.19-4.07 (m, 1H), 3.80-3.65 (m, 2H), 3.73 (s, 3H), 2.85 (br s, 1H), 2.51 (dd, *J* = 16.4, 3.7 Hz, 1H), 2.42 (dd, *J* = 16.4, 8.5 Hz, 1H), 1.97-1.82 (m, 1H), 1.70-1.39 (m, 3H), 1.17 (ddd, *J* = 13.8, 9.1, 3.9 Hz, 1H), 1.08 (s, 9H), 0.91 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 173.51, 135.70, 134.09, 129.66, 127.72, 65.89, 62.10, 51.82, 43.99, 41.84, 40.15, 26.98, 26.15, 19.46, 19.28 ppm; IR (film): $\tilde{\nu}$ = 3503, 2955, 2930, 2857, 1734, 1428, 1169, 1110, 1088, 997, 823 cm^{-1}; MS (EI, 70eV) *m/z* (%): 397 (2), 353 (3), 297 (17), 293 (96), 251 (38), 199 (100), 183 (19), 123 (18), 95 (39), 81 (15); HRMS (ESI) m/z calcd. for $C_{25}H_{36}O_4Si+Na^+$: 451.2275, found: 451.2274.

Alcohol S26. *n*-Butyllithium (1.6 M in hexane, 2.1 mL mL, 3.3 mmol) was added dropwise to a solution of diisopropylamine (0.47 mL, 3.3 mmol) in THF (3.3 mL) at -78 °C. The mixture was stirred for 30 min at ambient temperature. After cooling to -60 °C, a solution of alcohol **S25** (475 mg, 1.11 mmol) in THF (1 mL) was added dropwise. The mixture was warmed to -25 °C over 30 min. A solution of methyl iodide ((0.17 mL, 2.8 mmol) in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (0.5 mL, 4 mmol) was carefully added. The reaction mixture was warmed to 0 °C over 30 min and the reaction then quenched with water (20 mL). The aqueous phase was extracted with ethyl acetate (3 × 20 mL), the organic layer was dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexane/ethyl acetate 9:1) to give the title compound as a colorless oil (335 mg, 68%, 85:15 mixture of diastereomers). $[\alpha]_D^{20}$ = +0.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.70-7.65 (m, 4H), 7.68-7.64 (m, 4H), 7.45-7.34 (m,6H), 3.78-3.65 (m,3H), 3.70 (s, 3H), 2.54- 2.43 (m, 1H), 2.37 (dd, *J* = 24.6, 6.0 Hz, 1H), 1.97-1.80 (m, 1H), 1.68-1.38 (m, 3H), 1.28-1.15 (m, 1H) 1.19 (d, *J* = 7.2 Hz, 3H), 1.04 (s, 9H), 0.87 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 176.57, 135.75 (4C), 134.19 (2C), 129.68 (2C), 127.75 (4C), 71.34, 62.18, 51.82, 46.01, 42.33, 40.53, 27.02 (3C), 26.26, 19.33, 19.31, 14.43 ppm; IR (film): $\tilde{\nu}$ = 3469, 2954, 2932, 2857, 1734, 1722, 1472, 1461, 1428, 1389, 1259, 1195, 1172, 1111, 823, 738. 702 cm^{-1}; MS (EI, 70eV) *m/z* (%): 411 (1), 385 (1), 367 (3), 353 (6), 307 (100), 297 (12), 275 (8), 251 (18), 229 (9), 199 (88), 135 (13),109 (55), 99 (17), 81 (11); HRMS (ESI) m/z calcd. for $C_{26}H_{38}O_4Si+Na^+$: 465.2432, found: 465.2430.

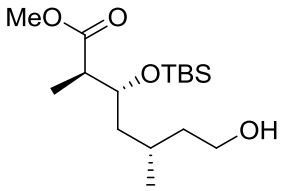


Protected Diol S27. 2,6-Lutidine (0.77 mL, 6.6 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.73 mL, 3.3 mmol) were added at 0 °C to a solution of the α-methyl-β-hydroxyester **S26** (730 mg, 1.65 mmol) in dichloromethane (24 mL). The solution was stirred for 3 h at ambient temperature before the reaction was quenched with methanol (2.4 mL). All volatile materials were evaporated under reduced pressure and the residue was purified by flash chromatography (hexane/ethyl acetate, 3:97) to give the title compound as a colorless oil (897 mg, 97%). $[\alpha]_D^{20}$ = +7.4 (c = 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$):



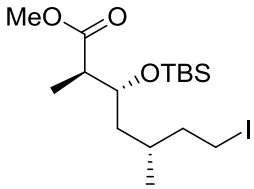
δ = 7.68-7.64 (m, 4H), 7.444-7.33 (m, 6H), 4.26- 4.00 (m, 1H), 3.73-3.61 (m 2H), 3.65 (s, 3H), 2.67 (qd, *J* = 7.1, 5.2 Hz, 1H), 1.84- 1.16 (m, 5H), 1.10 (d, J=7.10 Hz, 3H), 1.04 (s, 9H), 0.86 (s, 9H), 0.86-0.83 (m, 3H), 0.06 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.93, 135.73 (4C), 134.24 (2C), 129.64 (2C), 127.73 (4C), 71.11, 62.19, 51.59, 46.14, 40.93, 40.81, 27.02 (3C), 25.98 (3C), 25.85, 19.32, 19.27, 18.18, 10.68, -4.26, -4.49 ppm; IR (film): $\tilde{\nu}$ = 2955, 2930, 2858, 1742, 1472, 1428, 1388, 1361, 1254, 1195, 1111, 1051, 836, 775, 701 cm^{-1}; MS (EI, 70eV) *m/z* (%): 541 (2), 499 (100), 469 (5), 411 (7), 313 (6), 271 (8), 199 (15), 135 (18), 89 (19), 73 (29); HRMS (ESI) m/z calcd. for $C_{32}H_{52}O_4Si_2$+Na^+: 579.3302, found: 579.3302.

Alcohol S28. Acetic acid (180 mg, 0.17 mL, 3.0 mmol) and TBAF (1.0 M in THF, 3.0 mL, 3.0 mmol) were added to a solution of compound **S27** (1.39 g, 2.50 mmol) in DMF (47 mL) at 0 °C. The mixture was stirred for 24 h at ambient temperature before the reaction was quenched with water (3 mL) and extracted with *tert*-butyl methyl ether (3 × 3 mL). The combined organic phases were dried over Na_2SO_4 and the residue was purified by flash chromatography (hexane/ethyl acetate 9:1) to the title compound in the form of a colorless oil (630 mg, 80%). The minor C.2-isomer was separated at this stage by preparative HPLC (Nucleodur 250 × 40mm, 230 bar, 75 mL/min, acetonitrile/water 70:30).



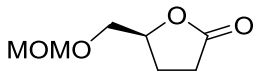
$[\alpha]_D^{20}$ = +3.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13-4.07 (m, 1H), 3.78- 3.59 (m, 5H), 2.73-2.63 (m, 1H), 1.77-1.64 (m, 1H), 1.58-1.38 (m, 3H), 1.25 (br s, 1H), 1.11 (d, *J* = 7.7 Hz, 3H), 1.02 (ddd, *J* = 13.3, 10.5, 2.7 Hz, 1H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.86, 71.00, 61.18, 51.65, 46.12, 40.95, 40.40, 25.86 (3C), 19.63, 18.16, 10.42, -4.36, -4.44 ppm; IR (film): $\tilde{\nu}$ = 3424, 2953, 2930, 2857, 1740, 1462, 1435, 1380, 1253, 1198, 1175, 1090, 1054, 911, 836, 775 cm^{-1}; MS (EI, 70eV) *m/z* (%): 261 (11), 243 (16), 211 (9), 199 (9), 169 (27), 155 (19), 137 (26), 109 (100), 99 (78), 89 (47), 75 (51), 57 (29), 43 (23), 31 (26); HRMS (ESI) m/z calcd. for $C_{16}H_{34}O_4Si$+Na^+: 341.2119, found: 341.2114.

Iodide 33b. Triphenylphosphine (115 mg, 440 µmol), iodine (112 mg, 440 µmol), and imidazole (45 mg, 0.66 mmol) were added to a solution of alcohol **S28** (70 mg, 220 µmol) in dichloromethane (2.0 mL) at 0 °C. The mixture was stirred for 1 h at ambient temperature before the reaction was quenched with water (4 mL). The aqueous phase was extracted with dichloromethane (3 × 4 mL), the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/methyl *tert*-butyl ether, 9:1) gave the title compound as a colorless oil (90 mg, 96%).



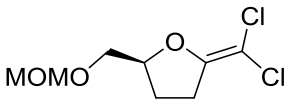
$[\alpha]_D^{20}$ = -6.5 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.10 (ddd, *J* = 9.1, 4.8, 2.2 Hz, 1H), 3.66 (s, 3H), 3.26-3.10 (m, 2H), 2.69 (qd, *J* = 8.9, 5.2 Hz, 1H), 1.90-1.60 (m, 3H), 1.53-1.45 (m, 1H), 1.11 (d, *J* = 7.1 Hz, 3H), 1.06-0.96 (m, 1H), 0.89 (s, 9H), 0.86 (d, *J* = 6.2 Hz, 3H), 0.09 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.77, 70.65, 51.68, 46.13, 41.98, 39.69, 30.21, 26.00 (3C), 18.41, 18.16, 10.32, 4.83, -4.29, -4.41 ppm; IR (film): $\tilde{\nu}$ = 2952, 2929, 2856, 1740, 1462, 1434, 1381, 1361, 1252, 1197, 1176, 1090, 1055, 1005, 912, 836, 807, 774, 729 cm^{-1}; MS (EI, 70eV) *m/z* (%): 143 (3), 371 (100), 341 (25), 315 (12), 231 (5), 185 (10), 173 (9), 145 (6), 109 (25), 99(20), 89 (92), 73 (35), 59 (11); HRMS (ESI) m/z calcd. for $C_{16}H_{33}O_3I$+Na^+: 451.1136, found: 451.1134.

(*S*)-5-((Methoxymethoxy)methyl)dihydrofuran-2(3*H*)-one (53). *N,N*-Diisopropylethylamine



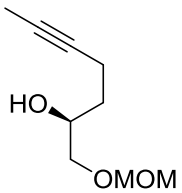
(1.7 g, 2.3 mL, 13 mmol) and chloromethyl methyl ether (0.7 g, 0.7 mL, 9 mmol) were added to a solution of (*S*)-(+)-dihydro-5-(hydroxymethyl)-2(3*H*)-furanone (0.50 g, 4.3 mmol) in dichloromethane (40 mL). The solution was stirred at reflux temperature for 12 h. After cooling to ambient temperature, the reaction was quenched with sat. aq. NH_4Cl (40 mL), the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 40 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (methyl *tert*-butyl ether) gave the title compound as a colorless oil (649 mg, 94%). $[\alpha]_D^{20}$ = –28 (*c* = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.72-4.61 (m, 1H), 4.64 (s, 2H), 3.75 (dd, *J* = 11.1, 3.3 Hz, 1H), 3.63 (dd, *J* = 11.1, 4.4 Hz, 1H), 3.36 (s, 3H), 2.62 (ddd, *J* = 17.7, 10.0, 6.4 Hz, 1H), 2.50 (ddd, *J* = 17.2, 10.0, 7.2 Hz, 1H), 2.31 (dddd, *J* = 12.9, 10.0, 7.8, 6.4 Hz, 1H), 2.12 (dddd, *J* = 13.0, 10.0, 7.2, 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.28, 96.77, 78.82, 69.14, 55.55, 28.50, 24.13 ppm; IR (film): $\tilde{\nu}$ = 2945, 1768, 1461, 1348, 1145, 1114, 1032, 942, 914, 803 cm^{-1}; MS (70 eV) *m/z* (%): 130 (18), 100 (28), 85 (75), 45 (100); HRMS (ESI): *m/z* calcd. for $C_7H_{12}O_4$+Na^+: 183.0628, found 183.0627.

(*S*)-2-(Dichloromethylene)-5-((methoxymethoxy)methyl)tetrahydrofuran (54). PPh_3 (9.8 g, 37 mmol) was added to a solution of lactone **53** (1.50 g, 9.4 mmol) in THF (200 mL). The



solution was stirred at reflux temperature while carbon tetrachloride (35 g, 22 mL, 220 mmol) was added dropwise over 4 h via a dropping funnel. Once the addition was complete the mixture was cooled to room temperature, the reaction was quenched with water (200 mL) and the aqueous layer extracted with dichloromethane (3 × 200 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (200 mL) and dried over Na_2SO_4. The solution was concentrated to about 40 mL before pentane (200 mL) was added under vigorous stirring. The resulting precipitate was filtered off and the filtrate was concentrated to about 40 mL. This cycle of precipitation/concentration was repeated three times. Purification of the residue by flash chromatography (pentane/methyl *tert*-butyl ether, 9:1 to 8:2) gave the title compound as a colorless oil (1.84 g, 87%). $[\alpha]_D^{20}$ = –10 (*c* = 1, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 4.34 (s, 2H), 4.03 (m, 1H), 3.26 (dd, *J* = 11.0, 3.9 Hz, 1H), 3.17 (dd, *J* = 11.1, 5.0 Hz, 1H), 3.10 (s, 3H), 2.35-2.25 (m, 1H), 2.07 (ddd, *J* = 16.7, 8.5, 8.5 Hz, 1H), 1.30 ppm (ddd, *J* = 7.9, 7.6, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ = 154.65, 96.56, 93.80, 83.68, 68.68, 54.94, 29.52, 26.62 ppm; IR (film): $\tilde{\nu}$ = 2938, 2889, 1666, 1457, 1439, 1214, 1146, 1114, 1033, 980, 903, 827, 739 cm^{-1}; MS (70 eV) *m/z* (%):228 (5), 226 (7), 140 (2), 138 (3), 89 (1), 87 (3), 71 (5), 45 (100); HRMS (ESI): *m/z* calcd. for $C_8H_{12}Cl_2O_3$+Na^+: 249.0056, found 249.0057.

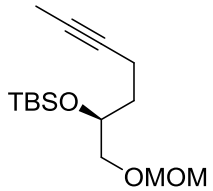
(*S*)-1-(Methoxymethoxy)hept-5-yn-2-ol (55). $Fe(acac)_3$ (148 mg, 0.418 mmol), *ortho*-



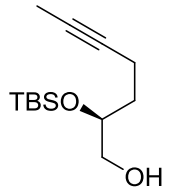
phenylenediamine (226 mg, 2.09 mmol), and MeLi (1.6 M in diethyl ether, 26 mL, 42 mmol) were successively added at 0°C to a solution of dichloro-olefin **54** (1.90 g, 8.37 mmol) in diethyl ether (60 mL). The cooling bath was removed and the mixture stirred for 1.5 h at ambient temperature. The mixture was cooled to 0°C and the reaction quenched with water (100 mL). The phases were separated, the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 100 mL), and the combined organic phases were dried over Na_2SO_4 and

concentrated. Purification of the residue by flash chromatography (pentane/*tert*-butyl methyl ether 1:1 to 0:1) gave the title compound as an oil (1.20 g, 83%). $[\alpha]_D^{20}$ = +12 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.65 (d, *J* = 6.5 Hz, 1H), 4.63 (d, *J* = 6.5 Hz, 1H), 3.89 (dddd, *J* = 7.3, 7.3, 5.6, 3.1 Hz, 1H), 3.60 (dd, *J* = 10.4, 3.1 Hz, 1H), 3.41 (dd, *J* = 10.3, 7.3 Hz, 1H), 3.37 (s, 3H), 2.69 (br s, 1H), 2.31- 2.24 (m, 2H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.70-1.55 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 97.14, 78.55, 76.22, 72.93, 69.65, 55.51, 32.43, 15.21, 3.54 ppm; IR (film): $\tilde{\nu}$ 3443, 2921, 1441, 1212, 1149, 1107, 1034, 917 cm^{-1}; MS (70 eV) *m/z* (%): 141 (5), 122 (4), 109 (10), 97 (32), 81 (14), 45 (100); HRMS (CI): *m/z* calcd. for $C_9H_{17}O_3$: 173.1178, found 173.1179.

Alkyne (S29). 2,6-Lutidine (1.4 g, 1.5 mL, 13 mmol) was added and a solution of alcohol **55** (1.10 g, 6.39 mmol) in dichloromethane (40 mL) prior to the addition of *tert*-butyldimethylsilyl trifluoromethanesulfonate (2.0 g, 1.7 mL, 7.7 mmol) at 0°C. The cooling bath was removed and the mixture stirred at ambient temperature for 1 h before the reaction was quenched with methanol (2 mL) and the mixture concentrated. Purification of the residue by flash chromatography (pentane/methyl *tert*-butyl ether, 99:1 to 8:2) gave the title compound as a colorless oil (1.65 g, 90%). $[\alpha]_D^{20}$ = –27 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (s, 1H), 4.61 (s, 1H), 3.92 (dddd, *J* = 7.8, 5.4, 5.4, 4.5 Hz, 1H), 3.44 (d, *J* = 5.40 Hz, 2H), 3.36 (s, 3H), 2.21 (m, 2H), 1.77 (t, *J* = 2.6 Hz, 3H), 1.77-1.64 (m, 1H), 1.63-1.56 (m, 1H), 0.89 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 96.89, 79.03, 75.90, 72.07, 70.26, 55.36, 33.98, 26.03 (3C), 18.31, 14.93, 3.58, -4.27, -4.70, ppm; IR (film): $\tilde{\nu}$ = 2928, 2857, 1472, 1252, 1151, 1111, 1043, 919, 833, 774 cm^{-1}; MS (70 eV) *m/z* (%): 211 (14), 197 (24), 145 (9), 123 (13), 93 (10), 89 (38), 73 (42), 59 (15), 45 (100); HRMS (ESIpos): *m/z* calcd. for $C_{15}H_{30}O_3Si$+Na: 309.1856, found 309.1854.

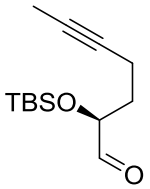


Alcohol S30. Bromo(dimethyl)borane (0.5 M in dichloromethane, 8.5 mL, 4.2 mmol)[8] was slowly added at –78°C to a solution of alkyne **S29** (810 mg, 2.83 mmol) in dichloromethane (15 mL). After 1.5 h at this temperature, the solution was transferred via cannula into a vigorously stirred mixture of THF (10 mL)/sat. aq. $NaHCO_3$ (15 mL). After stirring for 5 min, *tert*-butyl methyl ether (20 mL) was added, the phases were separated and the aqueous phase extracted with *tert*-butyl methyl ether (3 × 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/methyl *tert*-butyl ether, 99:1 to 8:2) gave the title compound as a colorless oil (610 mg, 90%). $[\alpha]_D^{20}$ = –15 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94-3.86 (m, 1H), 3.60 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.47 (dd, *J* = 11.2, 4.7 Hz, 1H), 2.17 (tq, *J* = 7.3, 2.5 Hz, 2H), 1.77 (t, *J* = 2.6 Hz, 3H), 1.76-1.60 (m, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.74, 76.15, 71.65, 66.27, 33.10, 25.98 (3C), 18.23, 14.97, 3.53, -4.43, -4.49 ppm; IR (film): $\tilde{\nu}$ = 3436, 2929, 2857, 1472, 1361, 1252, 1111, 1044, 938, 833, 774, 665 cm^{-1}; MS (70 eV) *m/z* (%): 211 (12), 185 (13), 167 (4), 101 (4), 93 (33), 75 (100), 59 (9), 41 (8); HRMS (ESIpos): *m/z* calcd. for $C_{13}H_{26}O_2Si$+Na: 265.1594, found 265.1593.

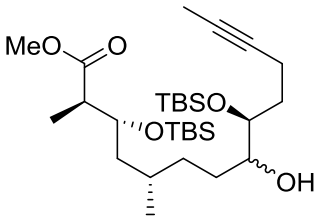


[8] Y. Guindon, H. E. Morten, C. Yoakim, *Tetrahedron Lett*. **1983**, *24*, 3969-3972; b) Y. Guidon, C. Yoakim, H. E. Morton, *J. Org. Chem*. **1984**, *49*, 3912-3920

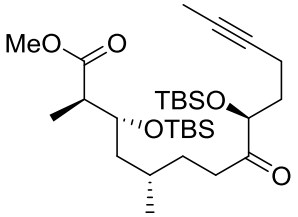
Aldehyde 56. *Method A:* Dess-Martin periodinane (1.57 g, 3.71 mmol) was added to a solution of alcohol **S30** (300 mg, 1.24 mmol) in dichloromethane (12 mL) and the mixture was stirred until TLC showed complete conversion (ca. 5 h). The reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The phases were separated, the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 10 mL), the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/*tert*-butyl methyl ether 99:1 to 9:1) gave the title aldehyde as a colorless oil (267, 90%). *Method B:* Alcohol **S30** (50 mg, 0.31 mmol) was dissolved in DMSO/dichloromethane (2:1, 2 mL) and the solution was cooled to 0 °C before triethylamine (104 mg, 1.44 mL, 1.03 mmol) and SO_3·pyridine (164 mg, 1.03) were successively added. The mixture was stirred for 3 h at 0 °C before the reaction was quenched with sat. aq. NH_4Cl (10 mL). *Tert*-butyl methyl ether (10 mL) was added, the phases were separated, the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 10 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography gave the title aldehyde as a colorless oil (46 mg, 93%). $[\alpha]_D^{20}$ = –34 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 9.41 (d, *J* = 1.2 Hz, 1H), 3.98 (ddd, *J* = 8.2, 4.3, 1.1 Hz, 1H), 2.21-2.14 (m, 2H), 1.72-1.50 (m, 2H), 1.51 (t, *J* = 2.6 Hz, 3H), 0.91 (s, 9H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 202.22, 78.33, 77.14, 76.76, 32.12, 25.93 (3C), 18.38, 14.69, 3.26, -4.49, -5.03 ppm; IR (film): $\tilde{\nu}$ = 2954, 2929, 2858, 1736, 1472, 1361, 1253, 1114, 1005, 969, 835, 776, 669 cm^{-1}; MS (70 eV) *m/z* (%): 211 (60), 197 (16), 183 (85), 155 (9), 129 (51), 89 (13), 73 (100), 59 (21), 45 (20); HRMS (ESIpos): *m/z* calcd. for $C_{13}H_{24}O_2Si$+Na: 263.1438, found 263.1435.



Alcohol 57. $CrCl_2$ (34 mg, 0.28 mmol) and cobalt(II)-phthalocyanin (8 mg, 0.01 mol) were suspended in degassed DMF (0.1 mL). A solution of aldehyde **56** (44 mg, 0.18 mmol) in degassed DMF (0.4 mL) and iodide **33b** (60 mg, 0.14 mmol) were successively added to the suspension. The mixture was stirred for 10 h before it was filtered through a pad of Celite (Ø = 1cm, height 4 cm) which was carefully rinsed with *tert*-butyl methyl ether (10 mL). Water (10 mL) was added to the combined filtrates and the phases were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 10 mL) and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography gave the title compound as a mixture of diastereomers (41 mg, 54%) which was used in the next step without detailed characterization.

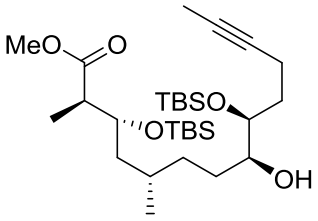


Ketone S31. Dess-Martin-Periodinane (57 mg, 0.14 mmol) was added to a solution of alcohol **57** (37 mg, 68 µmol) in dichloromethane (1 mL) at 0 °C before the mixture was stirred at ambient temperature for 1 h. Sat. aq. $NaHCO_3$ (5 mL) was added, the phases were separated, and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated. Purifcation of the residue by flash chromatography (pentane/methyl *tert*-butyl ether, 9:1) gave the title compound as a colorless oil (33 mg,



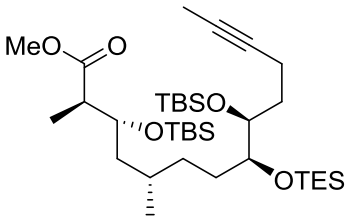
90%). $[\alpha]_D^{20}$ = –14 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.16-4.04 (m, 2H), 3.66 (s, 3H), 2.67 (qd, *J* = 7.0, 5.0 Hz, 1H), 2.58-2.49 (m, 2H), 2.30-2.15 (m, 2H), 1.80-1.70 (m, 2H), 1.75 (t, *J* = 2.5 Hz, 3H), 1.60-1.30 (m, 4H), 1.10 (d, *J* = 7.1 Hz, 3H), 1.03-0.82 (m,4H), 0.92 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.06 (s, 6H), 0.05 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.75, 174.79, 78.19, 77.36, 76.61, 70.95, 51.60, 46.14, 40.06, 35.43, 34.37, 31.25, 28.86, 25.96 (3C), 25.91 (3C), 19.39, 18.25, 18.16, 14.76, 10.45, 3.57, -4.37, -4.43, -4.76, -4.87 ppm; IR (film): $\tilde{\nu}$ = 2953, 29,29, 2857, 1738, 1472, 1462, 1435, 1361, 1252, 1197, 1096, 1053, 1023, 1005, 939, 908, 834, 804, 773, 732, 672, 663 cm^{-1}; MS (ESIpos) *m/z* (%): 841 (4), 661 (3), 564 (100); HRMS (ESI): *m/z* calcd. for $C_{29}H_{56}O_5Si_2$+Na^+: 563.3559, found 563.3555.

Alcohol S32. L-Selectride (1 M in THF, 0.41 mL 414 mmol) was added dropwise at -78 °C under vigorous stirring to a solution of ketone **S31** (112 mg, 207 mmol) in THF (2 mL). The solution was stirred for 2 h at -78 °C before the reaction was quenched at this temperature with sat. aq. NH_4Cl (3 mL). The phases were separated, the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 15 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/*tert*-butyl methyl ether, 9:1) gave the title compound as a diastereomerically pure colorless oil (89 mg, 79%).



$[\alpha]_D^{20}$ = –11 (*c* = 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.13-4.05 (m, 1H), 3.71-3.63 (m, 1H), 3.66 (s, 3H), 3.43-3.32 (m, 1H), 2.67 (qd, *J* =7.1, 5.2 Hz, 1H), 2.30-2.08 (m, 2H), 2.01 (br s, 1H), 1.79 (qdd, *J* =7.0, 6.9, 6.9 Hz, 1H), 1.77 (t, *J* = 2.5 Hz, 3H), 1.70-1.15 (m, 7H), 1.11 (d, *J* = 7.1 Hz, 3H), 0.99 (ddd, *J* = 13.6, 10.3, 2.8 Hz, 1H), 0.90 (s, 9H), 0.88 (s, 9H), 0.87 (d, *J* = 6.3 Hz, 3H), 0.12 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.89, 78.76, 76.12, 74.05, 73.16, 71.12, 51.57, 46.20, 40.53, 34.48, 33.01, 31.73, 29.08, 26.06 (3C), 25.97 (3C), 19.44, 18.27, 18.16, 14.88, 10.58, 3.54, -4.06, -4.33, -4.41, -4.44 ppm; IR (film): $\tilde{\nu}$ = 2952, 2929, 2857, 1736, 1472, 1462, 1385, 1361, 1252, 1198, 1055, 1023, 1005, 938, 909, 834, 804, 773, 733, 673, 663 cm^{-1}; MS (ESIpos) *m/z* (%): 663 (4), 581 (13), 565 (100); HRMS (ESI): *m/z* calcd. for $C_{29}H_{58}O_5Si_2$+Na^+: 565.3715, found 565.3719.

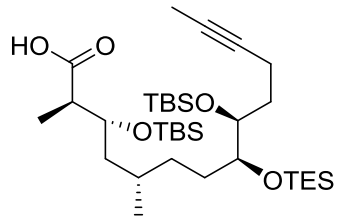
Ester S33. 2,6-Lutidine (16 mg, 17 µL, 150 µmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (19 mg, 17 µL, 74 µmol) were added to a solution of alcohol **S32** (16 mg, 29 µmol) in dichloromethane (1 mL) at 0 °C and the resulting mixture was stirred at this temperature for 1.5 h. The reaction was quenched with water (5 mL), the aqueous layer was extracted with dichloromethane (3 × 5 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/*tert*-butyl methyl ether 95:5) gave the title compound as a colorless oil (18 mg, 93%).



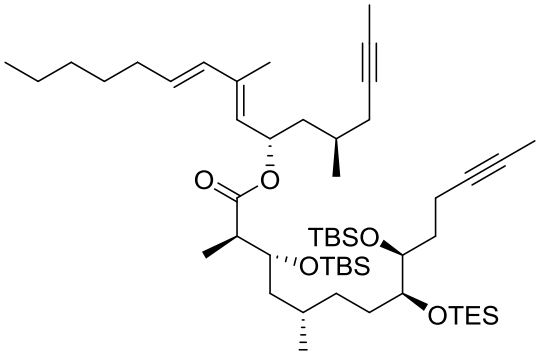
$[\alpha]_D^{20}$ = –16 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.12-4.02 (m, 1H), 3.72 (d, *J* = 9.6 Hz, 1H), 3.66 (s, 3H), 3.53 (d, *J* = 6.5 Hz, 1H), 2.66 (ddd, *J* = 13.8, 7.0, 6.8 Hz, 1H), 2.32-2.20 (m, 1H), 2.16-2.04 (m, 1H), 1.93-1.77 (m, 1H), 1.76 (t, *J* = 2.6 Hz, 3H), 1.68-1.15 (m, 6H), 1.14-1.04 (m, 1H), 1.10 (d, *J* = 7.1 Hz, 3H), 1.00-0.95 (m, 1H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.60 (q, *J* = 7.9 Hz, 6H), 0.09-

0.04 ppm (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.95, 79.36, 75.87, 75.85, 73.86, 71.19, 51.59, 46.20, 40.74, 35.67, 29.33 (2C), 27.72, 25.99 (3C), 25.97 (3C), 19.49, 18.16 (2C), 15.69, 10.56, 7.09 (3C), 5.28 (3C), 3.54, -4.11, -4.34, -4.42, -4.56 ppm; IR (film): $\tilde{\nu}$ = 2953, 2927, 2855, 1743, 1462, 1379, 1255, 1196, 1090, 1053, 1006, 912, 835, 806, 773, 742 cm^{-1}; MS (ESIpos) *m/z* (%): 965 (4), 737 (19), 679 (100), 625 (13); HRMS (ESI): *m/z* calcd. for $C_{35}H_{72}O_5Si_3$+Na^+: 679.4580, found 679.4586.

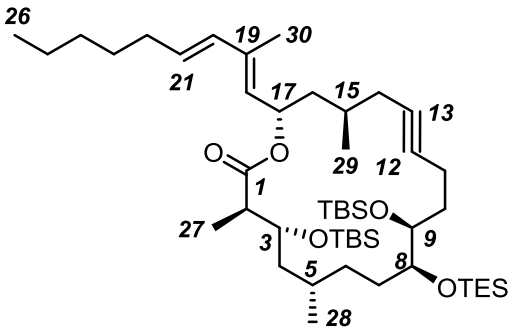
Acid 58. LiOH (5.8 mg, 0.24 mmol) was added to a solution of ester **S33** (16 mg, 24 µmol) in methanol/THF/water (4:4:2, 1 mL) at 0 °C and the mixture was stirred for 48 h at ambient temperature. Sat. aq. NH_4Cl (5 mL) and *tert*-butyl methyl ether (5 mL) were introduced and the phases separated. The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 5 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated. Purification of the residue by flash chromatography (pentane/*tert*-butyl methyl ether 9:1 to 8:2) gave the title compound as a colorless oil (10 mg, 64%). $[\alpha]_D^{20}$ = –3 (*c* = 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.92 (td, *J* = 6.3, 3.0 Hz, 1H), 3.74 (ddd, *J* = 10.2, 4.4, 2.0 Hz, 1H), 3.52 (ddd, *J* = 9.3, 4.4, 1.8 Hz, 1H), 2.68 (qd, *J* = 7.2, 3.0 Hz, 1H), 2.30-2.14 (m, 2H), 1.85-1.70 (m, 1H), 1.76 (t, *J* = 2.5 Hz, 3H), 1.70-1.05 (m, 9H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.00-0.85 (m, 3H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.92 (s, 9H), 0.87 (s, 9H), 0.60 (q, *J* = 7.7 Hz, 6H), 0.13 (s, 3H), 0.13 (s, 3H), 0.08 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.18 79.25, 75.94, 75.81, 73.75, 72.73, 44.90, 42.29, 33.98, 29.53, 29.32, 26.87, 25.97 (3C), 25.91 (3C), 20.08, 18.15, 18.11, 15.65, 14.25, 7.09 (3C), 5.29 (3C), 3.54, -4.16 (2C), -4.55, -4.58 ppm; IR (film): $\tilde{\nu}$ = 3727, 3629, 2951, 1711, 1541, 1472, 1257, 1090, 835, 773, 720, 698 cm^{-1}; MS (ESIpos) *m/z* (%): 681 (11), 665 (100), 565 (12); HRMS (ESI): *m/z* calcd. for $C_{34}H_{70}O_5Si_3$+Na^+: 665.4423, found 665.4429.



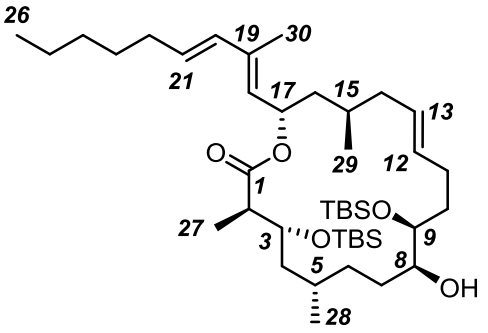
Ester 59. DMAP (1.4 mg, 11 µmol) and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (5.8 mg, 30 µmol) were added to a solution of acid **58** (6.5 mg, 10 µmol) and alcohol **25** (2.9 mg, 11 µmol)[1] in dichloromethane (0.5 mL) at 0 °C and the resulting mixture was stirred at ambient temperature for 16 h. The reaction was quenched with sat. aq. NH_4Cl (5 mL) and the organic layer extracted with *tert*-butyl methyl ether (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (pentane/*tert*-butyl methyl ether 95:5) to obtain the title compound (7.8 mg, 86%) as a colorless oil. $[\alpha]_D^{20}$ = +4 (*c* = 0.5, C_6H_6); ^{1}H NMR (400 MHz, C_6D_6): δ = 6.10 (d, *J* = 15.6 Hz, 1H), 6.05 (td, J = 8.7, 5.5 Hz, 1H), 5.64 (dt, *J* = 15.4, 7.0 Hz, 1H), 5.42 (d, *J* = 9.2 Hz, 1H), 4.40 (ddd, *J* = 9.4, 4.0, 2.4 Hz, 1H), 4.02 (ddd, *J* = 10.0, 4.3, 2.0 Hz, 1H), 3.78 (ddd, *J* = 9.4, 4.3, 2.0 Hz, 1H), 2.83 (qd, *J* = 7.0, 4.3 Hz, 1H), 2.40-2.22 (m, 2H), 2.17-1.74 (m, 10H), 1.93 (d, *J* = 1.0 Hz, 3H),1.73-1.17 (m, 11H), 1.60 (t, *J* = 2.5 Hz, 3H), 1.59 (t, *J* = 2.5 Hz, 3H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.16-0.95 (m, 7H), 1.08 (t, *J* = 7.9 Hz, 9H), 1.00 (s, 9H), 0.99 (s,



9H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.71 (q, *J* = 7.8 Hz, 6H), 0.19 (s, 3H), 0.18 (s, 3H), 0.16 (s, 3H), 0.13 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 172.89, 137.41, 134.52, 131.19, 79.44, 77.52, 77.11, 76.19, 76.14, 74.16, 71.52, 69.49, 46.82, 41.72, 40.63, 36.15, 33.28, 31.82, 29.73, 29.71, 29.60, 29.55, 28.20, 26.89, 26.17 (3C), 26.14 (3C), 22.96, 19.70, 19.67, 18.36, 18.31, 16.02, 14.26, 13.39, 10.28, 7.31 (3C), 5.65 (3C), 3.48, 3.39, 1.42, -3.94, -4.26, -4.39, -4.41 ppm; IR (film): $\tilde{\nu}$ = 2955, 2928, 2857, 1733, 1462, 1411, 1379, 1361, 1257, 1183, 1089, 1043, 1006, 963, 938, 909, 858, 835, 804, 773, 757, 725, 672, 664 cm^{-1}; MS (70 eV) *m/z* (%): 493 (1), 453 (3), 431 (3), 387 (2), 299 (2), 275 (3), 245 (100), 244 (44), 161 (36), 119 (41), 73 (21); HRMS (ESI): *m/z* calcd. for $C_{52}H_{98}O_5Si_3$+Na^+: 909.6614, found 909.6608.



Macrocycle 61. Ester **59** (52 mg, 59 µmol) was dissolved in toluene (26 mL) and molecular sieves (powdered, activated, 5 Å, 370 mg) were added. The suspension was first stirred for 15 min at room temperature before it was heated to 50 °C. At this temperature, a solution of complex **60** (4 mg, 3 µmol)[9] in toluene (3.3 mL) was introduced. The suspension was stirred for 15 min at 50 °C, before it was cooled to room temperature and filtered through a pad of Celite which was carefully rinsed with ethyl acetate. The combined filtrates were concentrated and the residue purified by flash chromatography (hexane/ethyl acetate 20:1) to obtain the title compound as a colorless oil (47 mg, 96%). $[\alpha]_D^{20}$ = +5 (*c* = 0.3, CH_2Cl_2); for the ^{1}H and ^{13}C NMR data, see Table S-3; IR (film): $\tilde{\nu}$ = 2956, 2928, 2856, 1732, 1462, 1379, 1257, 1186, 1089, 1050, 1017, 963, 938, 908, 834, 802, 773, 756 cm^{-1}; MS (ESIpos) *m/z* (%): 971.5 (3), 855.8 (100), 471.7 (3); HRMS (ESI): *m/z* calcd. for $C_{48}H_{92}O_5Si_3$+Na^+: 855.6145, found 855.6143. For the ^{1}H and ^{13}C NMR data of the ring expanded product formed upon storage of cycloalkyne **61** in a refrigerator, see Table S-4.



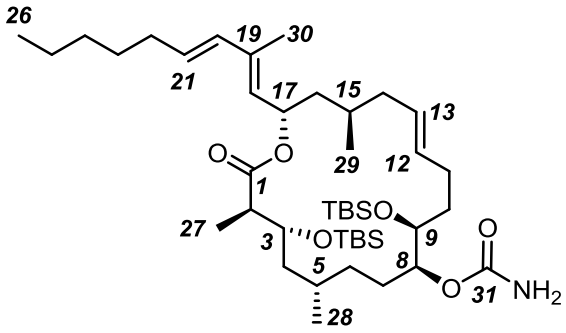
Alcohol 63. Triethoxysilane (freshly distilled, 2 µL, 1.8 mg, 11.2 µmol) and $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.2 mg, 0.4 µmol) were added at 0 °C to a solution of cycloalkyne **61** (3.1 mg, 3.7 µmol) in dichloromethane (1 mL). The solvent was largely removed by passing a gentle stream of argon over the solution and the remaining syrup was stirred for 30 min at ambient temperature. The residue was filtered through a pad of silica which was carefully rinsed with *tert*-butyl methyl ether (5 mL). The combined filtrates were concentrated and the residue dried in vacuo (1×10^{-3}mbar).

This residue was then dissolved in methanol (0.45 mL), water (0.1 mL) and THF (0.45 mL). AgF (1.9 mg, 15 µmol) was added and the suspension stirred in the dark overnight. The mixture was then filtered through a pad of silica (Ø = 1 cm, height = 1 cm) which was

[9] J. Heppekausen, R. Stade, A. Kondoh, G. Seidel, R. Goddard, A. Fürstner, *Chem. Eur. J.* **2012**, *18*, 10281-10299.

carefully rinsed with methyl *tert*-butyl ether. The combined filtrates were concentrated and the crude product was purified by flash chromatography (pentanes/methyl *tert*-butyl ether, 95:5 to 4:1) to obtain the title compound as a colorless oil (1.5 mg, 56%). $[\alpha]_D^{20}$ = –22 (*c* = 0.1, CH_2Cl_2); for the ^1H and ^{13}C NMR data, see Table S-5; IR (film): $\tilde{\nu}$ = 2956, 2929, 2857, 1733, 1463, 1379, 1253, 1060, 963, 836, 774, 719 cm^{-1}; MS (ESIpos) *m/z* (%): 743 (100), 441 (8); HRMS (ESI): *m/z* calcd. for $C_{42}H_{80}O_5Si_2+Na^+$: 743.5437, found 743.5447.

Carbamate S34. Trichloroacetyl isocyanate was added at –78 °C to a solution of alcohol **63** (4.3 mg, 6 µmol) in dichloromethane (1.2 mL). The resulting solution was stirred for 2 h at this temperature before methanol (0.5 mL) and solid sodium bicarbonate (5 mg, 60 µmol) were added. The resulting suspension was stirred at ambient temperature for 6 h before it was diluted with dichloromethane (2 mL). The reaction was quenched with water (2 mL), the aqueous phase was extracted with dichloromethane (3 x 1mL), the combined organic layers were dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on Florisil (hexanes/ethyl acetate, 9:1) to give the title compound as a colorless oil (2.3 mg, 50 %). $[\alpha]_D^{20}$ = –16 (c = 0.05, CH_2Cl_2); for the ^1H and ^{13}C NMR data, see Table S-6; IR (film): $\tilde{\nu}$ = 2956, 2924, 2853, 1728, 1633, 1468, 1379, 1258, 1087, 1021, 835, 799, 774 cm^{-1}; MS (ESIpos) m/z (%): 787 (100); 701 (6); 538 (4); HRMS (ESI): m/z calcd. for $C_{43}H_{81}NO_6Si_2+Na^+$: 786.5495, found 786.5502.



Tulearin A (1). Triethylamine (0.2 mL) and triethylamine trihydrofluoride (0.2 mL) were successively added to a solution of carbamate **S34** (2.3 mg. 3 µmol) in acetonitrile (0.5 mL). The resulting mixture was stirred for 20 h at 40 °C before the reaction was carefully quenched at ambient temperature with sat. aq. $NaHCO_3$ (1 mL). The aqueous phase was extracted with ethyl acetate (3 x 2 mL), the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on Florisil (hexanes/ethyl acetate, 1:10) to give tulearin A (**1**) as a colorless oil (1.1 mg, 68 %). $[\alpha]_D^{20}$ = –2.6 (c = 0.044, [D_6]-acetone); for the ^1H and ^{13}C NMR data, see Table S-7; IR (film): $\tilde{\nu}$ = 3411, 3228, 3207, 2955, 2926, 2870, 2856, 1708, 1604, 1457, 1380, 1324, 1261, 1171, 1132, 1047, 967, 945, 927, 864, 782 cm^{-1}; MS (ESIpos) *m/z* (%): 558 (100); HRMS (ESI): *m/z* calcd. for $C_{31}H_{53}O_6N+Na^+$: 558.37619, found 558.37651.

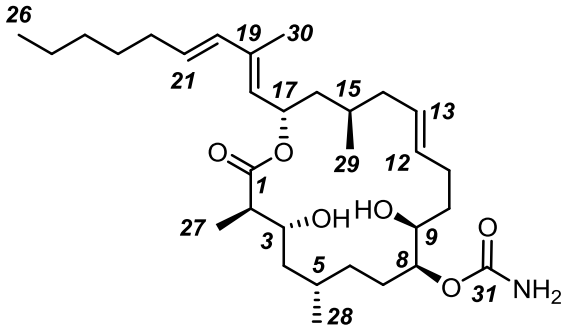
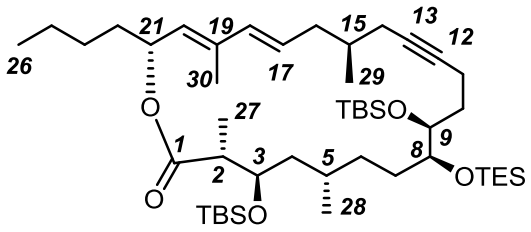


Table S-3. ^{1}H and ^{13}C NMR data (C_6D_6) of compound **61** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering scheme is shown in the Insert in the Text

Number	δ_C[ppm]	Multiplicity	δ_H[ppm]	Multiplicity	Coupling	Integration
1	172.49	s				
2	47.07	d	2.66	dq	7.1, 3.5	1H
3	71.05	d	4.24	dt	9.7, 3.2	1H
3-OTBS	26.16	q	1.00	s		9H
3-OTBS	18.44	s				
3-OTBS	- 4.01	q	0.13	s		3H
3-OTBS	- 4.15	q	0.10	s		3H
4	41.75	t	1.91	m		1H
4			1.43	m		1H
5	29.41	d	1.89	m		1H
6	33.47	t	1.72	m		1H
			1.41	m		1H
7	31.14	t	1.93	m		1H
7			1.74	m		1H
8	74.80	d	3.81	dt	7.4, 3.7	1H
8-OTES	7.29	q	1.04	t	8.0	9H
8-OTES	5.76	t	0.67	m		6H
9	73.34	d	4.07	td	6.4, 3.5	1H
9-OTBS	26.25	q	1.03	s		9H
9-OTBS	18.46	s				
9-OTBS	- 3.66	q	0.21	s		3H
9-OTBS	- 3.97	q	0.18	s		3H
10	33.00	t	1.98	m		1H
10			1.84	m		1H
11	15.46	t	2.43	m		1H
11			2.35	m		1H
12	81.52	s				
13	79.31	s				
14	27.00	t	2.01	m		2 H
15	29.80	d	1.87	m		1H
16	41.55	t	2.02	m		1H
16			1.17	m		1H
17	69.42	d	5.97	td	9.2, 5.2	1H
18	128.94	d	5.38	d	9.2	1H
19	137.09	s				
20	134.47	d	6.10	d	15.6	1H
21	131.08	d	5.64	dt	15.5, 6.9	1H
22	33.21	t	2.00	m		2H

23	29.47	t	1.30	quin		2H
24	31.74	t	1.20	m		2H
25	22.88	t	1.23	m		2H
26	14.19	q	0.85	t	7.1	3H
27	11.73	q	1.25	d	7.1	3H
28	18.71	q	1.08	d	6.7	3H
29	19.22	q	1.08	d	6.5	3H
30	13.32	q	1.93	d	1.2	3H

Table S-4. ^{1}H and ^{13}C NMR data (C_6D_6) of compound **62** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering scheme is shown in the Insert



Number	δ_C[ppm]	Multiplicity	δ_H[ppm]	Multiplicity	Coupling	Integration
1	172.25	s				
2	46.11	d	2.81	dq	4.2, 7.1	1H
3	70.42	d	4.48	ddd	10.7, 4.3, 1.5	1H
3-OTBS	26.16	q	1.00	s		9H
3-OTBS	18.39	s				
3-OTBS	- 4.67	q	0.08	s		3H*
3-OTBS	- 4.23	q	0.12	s		3H*
4	39.46	t	1.78	ddd	13.5, 10.6, 2.4	1H
4			1.14	m		1H
5	29.76	d	1.92	m		1H
6	34.92	t	1.55	m		2H
7	29.20	t	2.00	m		1H
7			1.68	m		1H
8	75.62	d	3.75	td	5.6, 3.7	1H
9	74.60	d	3.85	ddd	7.9, 4.4, 3.7	1H
9-OTBS	26.02	q	0.97	s		9H
9-OTBS	18.30	s				
9-OTBS	- 3.82	q	0.15	s		3H*
9-OTBS	- 4.05	q	0.14	s		3H*
10	32.97	t	2.17	m		1H
			1.88	m		1H
11	16.59	t	2.49	m		1H

			2.29	m		1H
12	81.82	s				
13	79.30	s				
14	25.46	t	2.11	ddt	16.4, 5.0, 2.2	1H
			1.96	m		1H
15	33.55	d	1.57	m		1H
16	38.97	t	2.43	dddd	13.8, 8.5, 7.1, 1.1	1H
			1.98	m		1H
17	129.13	d	5.61	ddd	15.4, 8.4, 6.2	1H
18	136.26	d	6.25	d	15.5	1H
19	137.51	s				
20	128.88	d	5.35	d	9.4	1H
21	71.52	d	5.79	dt	9.4, 6.8	1H
22	35.02	t	1.70	m		1H
			1.54	m		1H
23	25.24	t	1.32	m		2H
24	31.97	t	1.22	m		2H
25	22.88	t	1.23	m		2H
26	14.16	q	0.86	t	7.0	3H
27	9.15	q	1.30	d	7.1	3H
28	18.82	q	1.17	d	6.6	3H
29	20.05	q	0.90	d	6.7	3H
30	13.43	q	1.98	d	1.1	3H

*groups may be interchanged

Table S-5. ^{1}H and ^{13}C NMR data (C_6D_6) of compound **63** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering scheme is shown in the Insert in the Text

Number	δ_C[ppm]	Multiplicity	δ_H[ppm]	Multiplicity	Coupling	Integration
1	172.36	s				
2	46.98	d	2.50	dq	7.1, 3.5	1H
3	72.01	d	3.98	dt	10.1, 2.4	1H
3-OTBS	26.28	q	1.04	s		9H
3-OTBS	18.58	s				
3-OTBS	- 3.81	q	0.12	s		3H*
3-OTBS	- 3.84	q	0.12	s		3H*
4	44.06	t	1.82	m		1H
4			1.26	m		1H
5	29.56	d	1.73	m		1H
6	34.55	t	1.44	m		1H
6			1.31	m		1H
7	32.66	t	1.77	m		1H

7			1.56	m		1H
8	71.38	d	3.63	dddd	8.8, 7.1, 5.8, 2.4	1H
8-OH			2.36	d	8.7	1H
9	72.89	d	3.81	ddd	9.2, 3.8, 2.5	1H
9-OTBS	26.04	q	0.94	s		9H
9-OTBS	18.23	s				
9-OTBS	- 3.97	q	0.11	s		3H*
9-OTBS	- 4.32	q	0.12	s		3H*
10	32.43	t	1.96	m		1H
10			1.50	m		1H
11	29.02	t	2.11	m		2H
12	131.20	d	5.27	ddd	15.6, 7.8, 5.5	1H
13	130.55	d	5.35	ddd	15.6, 9.1, 5.5	1H
14	44.37	t	1.92	m		1H
14			1.65	dt	13.3, 9.1	1H
15	29.62	d	1.74	m		1H
16	42.64	t	1.84	m		1H
16			1.14	ddd	14.0, 11.0, 3.7	1H
17	69.34	d	5.95	ddd	10.9, 8.9, 3.6	1H
18	129.45	d	5.43	d	8.9	1H
19	136.38	s				
20	134.55	d	6.27	d	15.6	1H
21	130.84	d	5.65	dt	15.5, 6.9	1H
22	33.22	t	2.02	qd	7.3, 1.2	2H
23	29.51	t	1.32	m		2H
24	31.75	t	1.21	m		2H
25	22.90	t	1.23	m		2H
26	14.20	q	0.86	t	7.1	3H
27	13.74	q	1.18	d	7.1	3H
28	18.70	q	0.93	d	6.3	3H
29	18.11	q	0.99	d	6.5	3H
30	13.26	q	1.95	d	1.2	3H

* groups may be interchanged

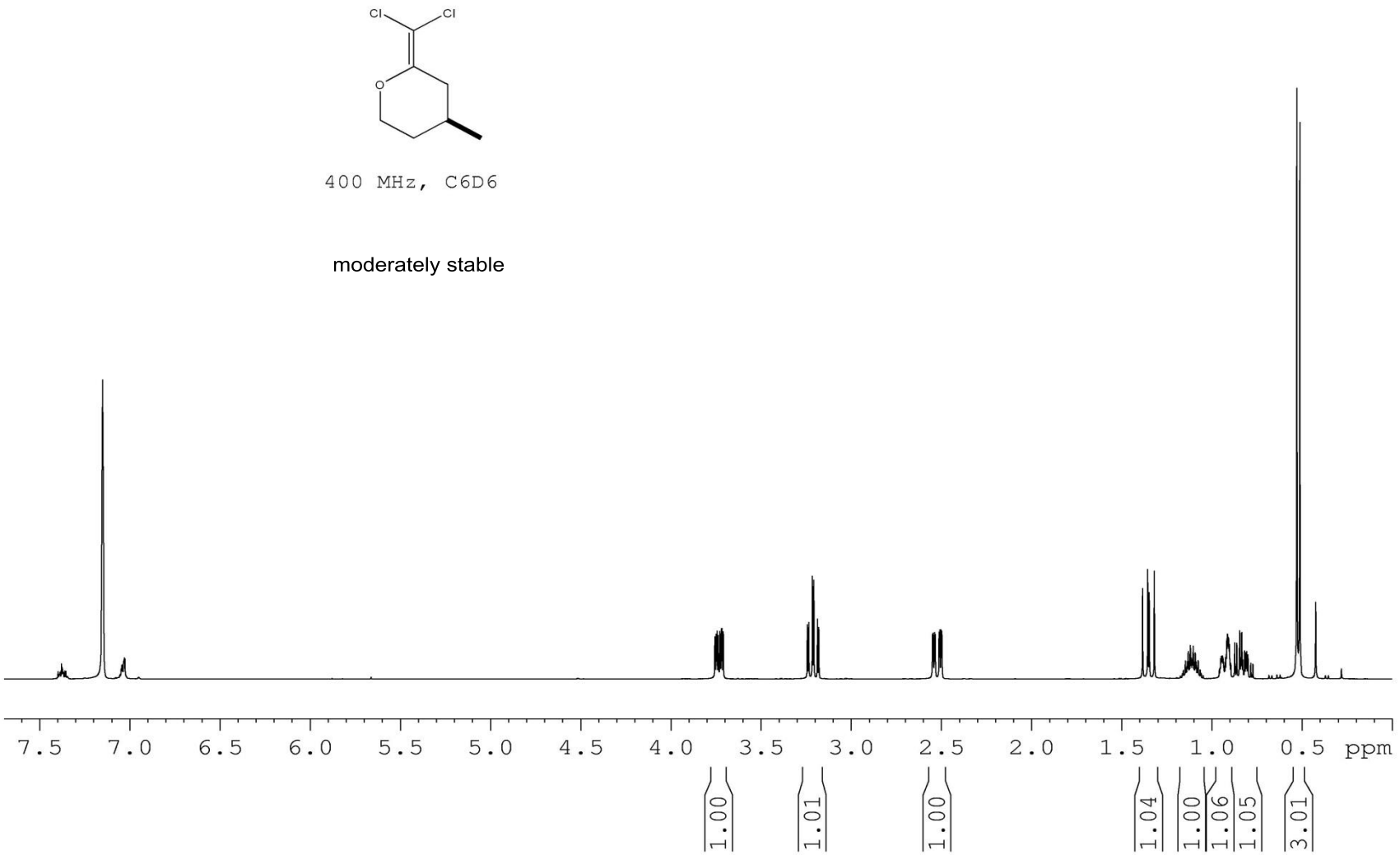
Table S-6. ^{1}H and ^{13}C NMR data (C_6D_6) of **S34** recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering scheme is shown in the Insert in the Text

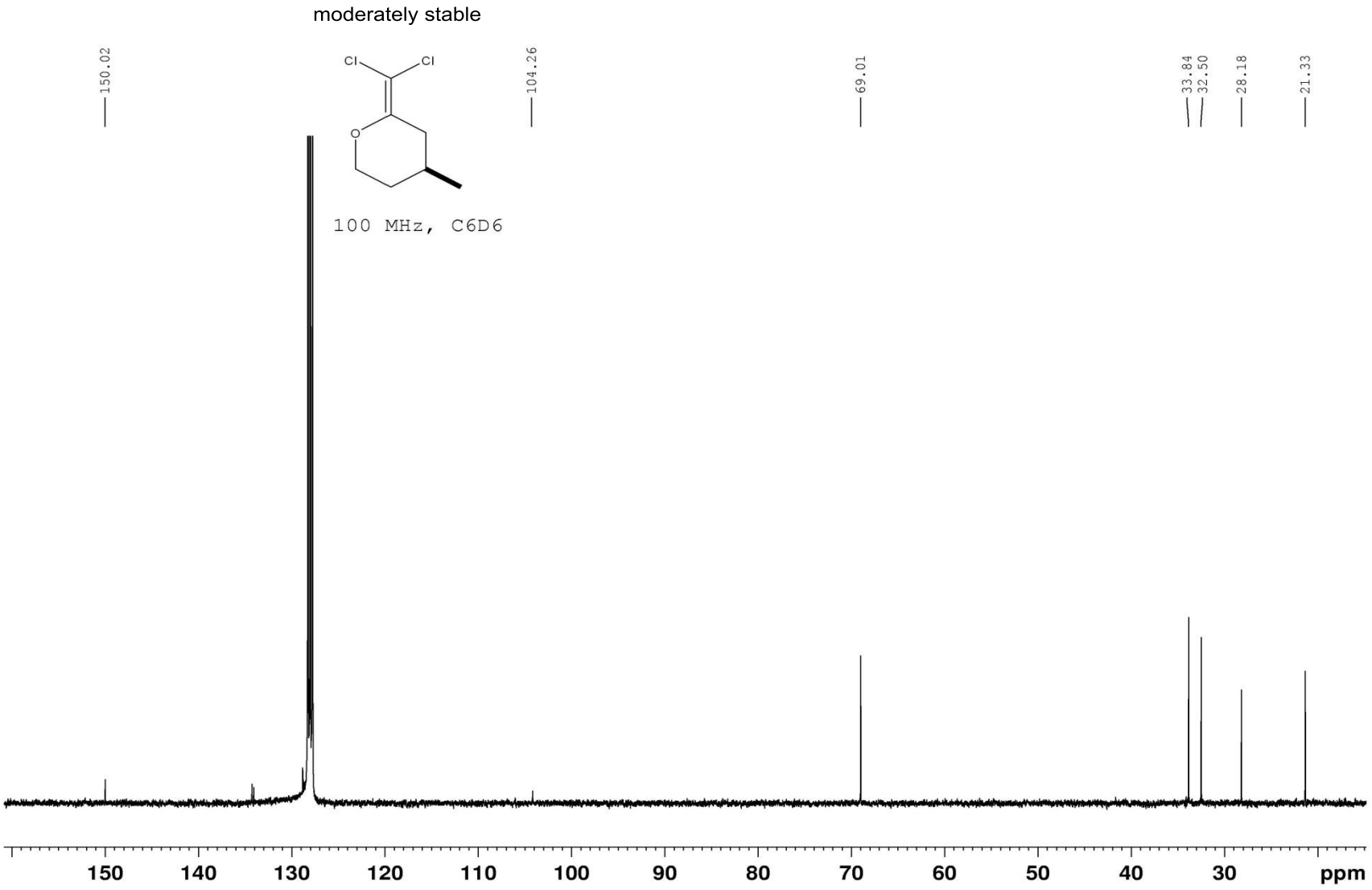
Number	δ_C[ppm]	Multiplicity	δ_H[ppm]	Multiplicity	Coupling	Integration
1	172.63	s				
2	46.94	d	2.61	dq	3.2, 7.1	1H
3	71.24	d	4.12	dt	9.7, 3.1	1H
3-OTBS	26.19	q	1.00	s		9H
3-OTBS	18.46	s				
3-OTBS	- 4.04	q	0.09	s		3H*
3-OTBS	- 4.09	q	0.11	s		3H*
4	41.98	t	1.80	m		1H
4			1.30	m		1H
5	29.35	d	1.76	m		1H
6	33.53	t	1.52	m		1H
6			1.34	m		1H
7	28.61	t	1.81	m		1H
7			1.77	m		1H
8	75.43	d	5.09	td	6.2, 3.8	1H
9	71.94	d	3.96	ddd	8.1, 4.9, 3.8	1H
9-OTBS	26.17	q	1.04	s		9H
9-OTBS	18.39	s				
9-OTBS	- 4.00	q	0.16	s		3H*
9-OTBS	- 4.18	q	0.19	s		3H*
10	32.67	t	1.84	m		1H
			1.62	m		1H
11	28.45	t	2.34	m		1H
			2.19	m		1H
12	131.66	d	5.37	ddd	15.3, 8.1, 5.3	1H
13	129.84	d	5.56	dt	15.3, 7.0	1H
14	40.84	t	1.89	m		1H
			1.77	m		1H
15	29.69	d	1.72	m		1H
16	42.16	t	1.88	m		1H
			1.17	m		1H
17	69.43	d	6.01	td	9.4, 4.4	1H
18	129.23	d	5.44	d	9.1	1H
19	136.7	s				
20	134.52	d	6.12	d	15.6	1H
21	130.98	d	5.65	dt	15.5, 6.9	1H
22	33.21	t	2.01	qd	7.3, 1.0	2H
23	29.49	t	1.31	m		2H
24	31.74	t	1.20	m		2H
25	22.89	t	1.23	m		2H
26	14.19	q	0.86	t	7.1	3H
27	12.25	q	1.22	d	7.1	3H
28	18.57	q	0.96	d	6.7	3H
29	18.80	q	0.99	d	6.4	3H
30	13.29	q	1.95	d	1.1	3H
31	156.44	s				
31-NH_2			3.67			2H

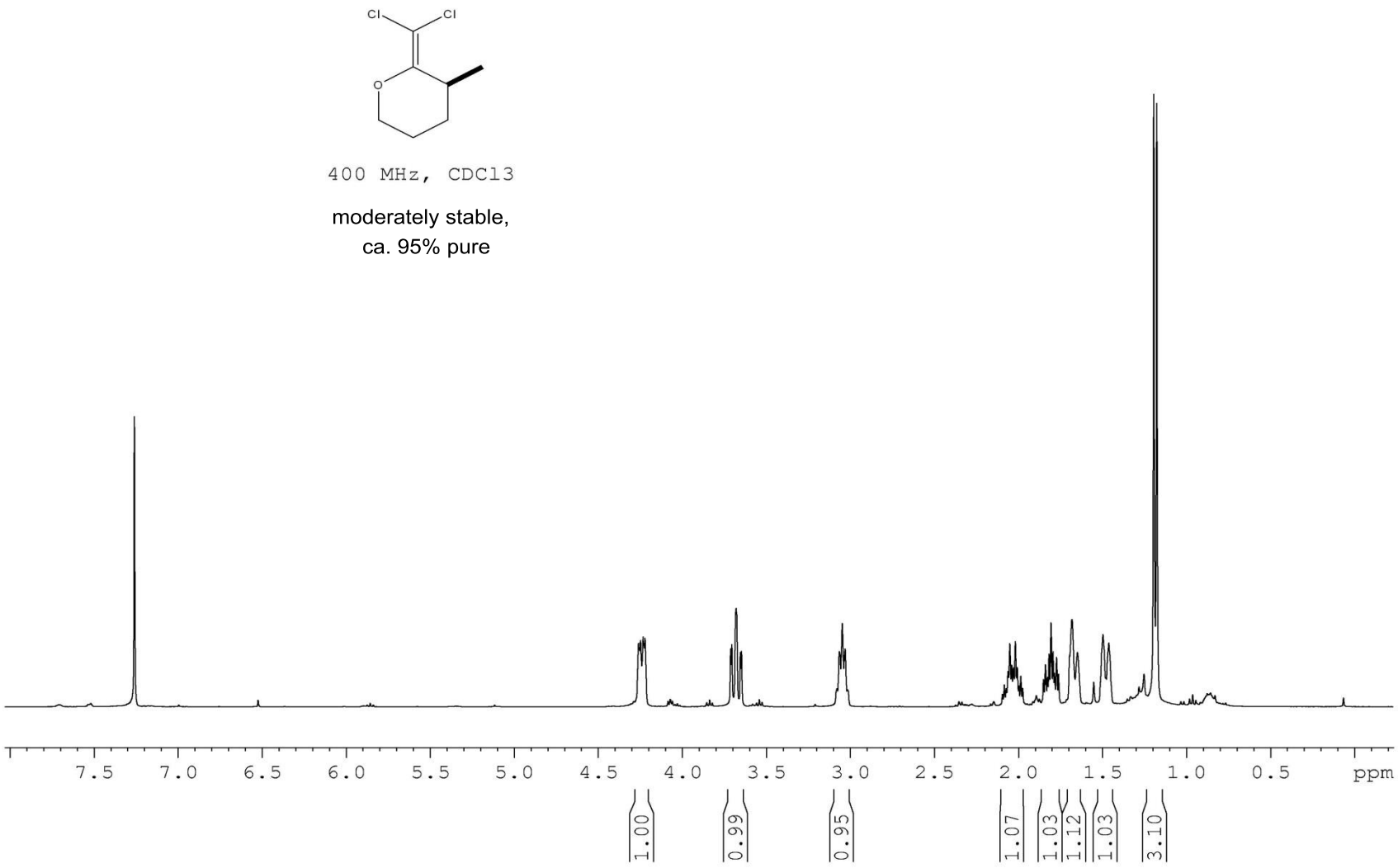
*groups may be interchanged

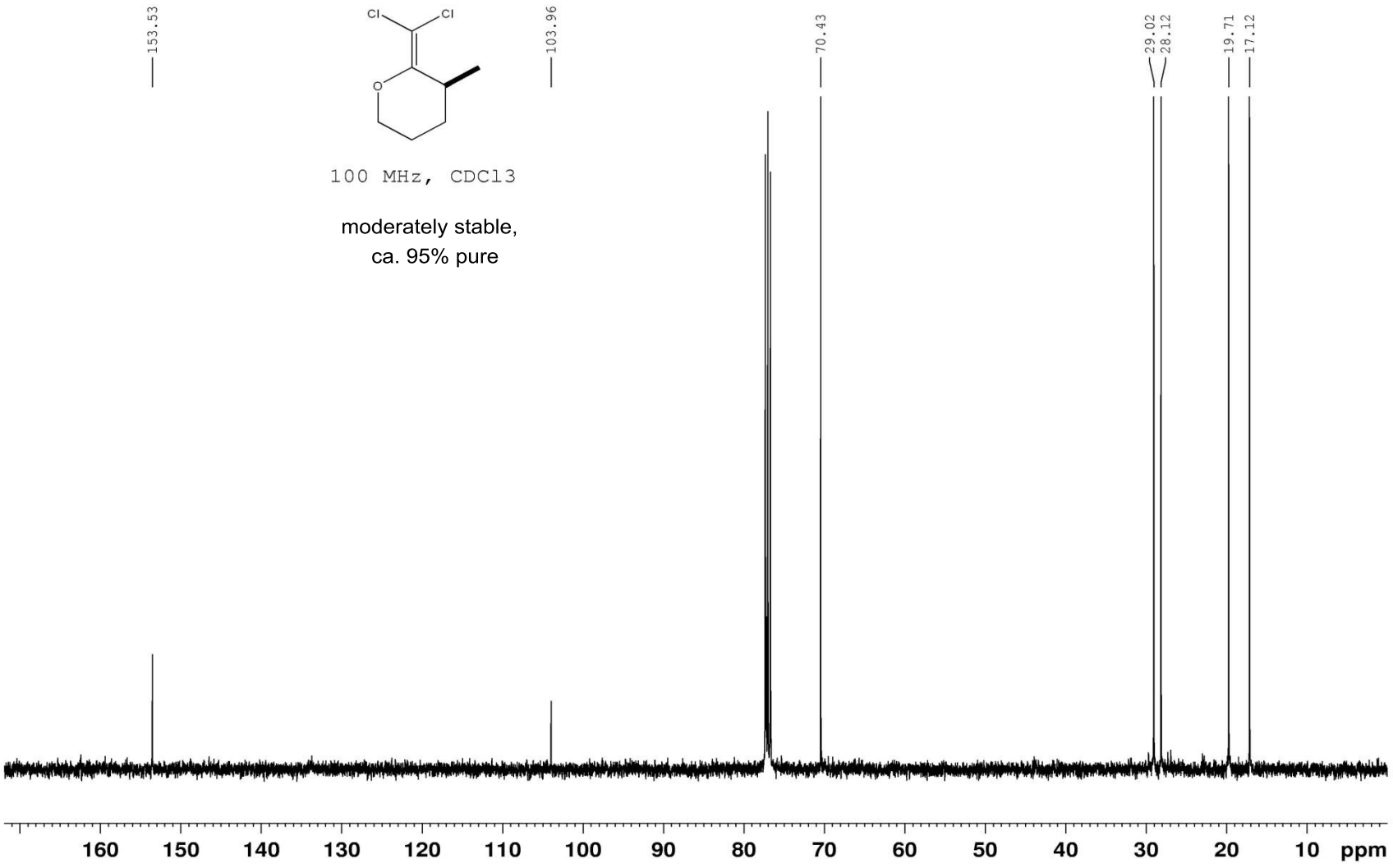
Table S-7. ^{1}H and ^{13}C NMR data ([D_6]-acetone) of tulearin A (**1**) recorded on a Bruker AV 600 spectrometer; the assignments are unambiguous; the numbering scheme is shown in the Insert in the Text

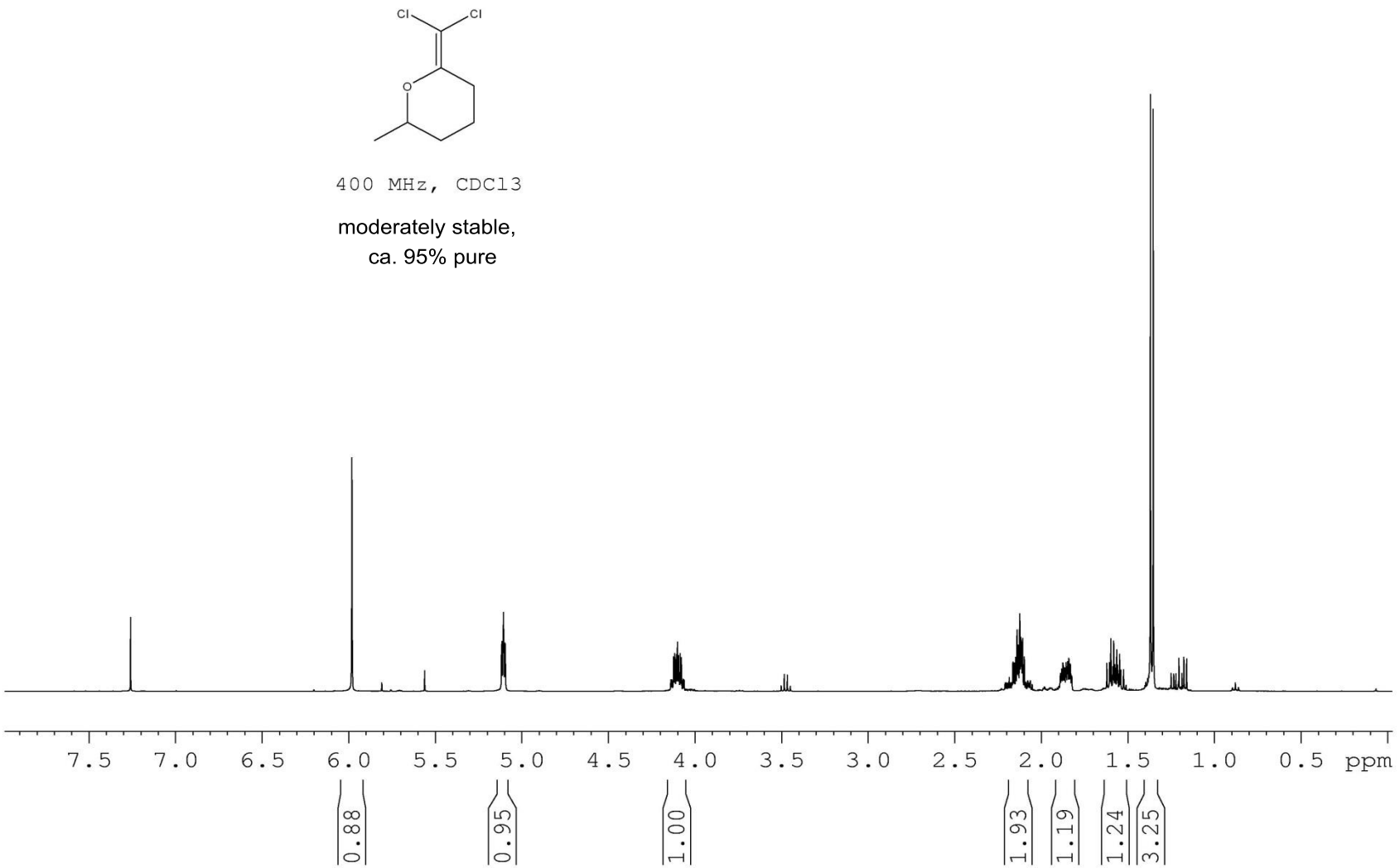
Number	δ_C[ppm]	Multiplicity	δ_H[ppm]	Multiplicity	Coupling	Integration
1	175.06	s				
2	46.58	d	2.49	dq	3.1, 7.1	1H
3	70.93	d	3.77	dddd	11.3, 7.9, 3.1, 2.4	1H
3-OH			3.36	d	7.8	1H
4	43.94	t	1.55	m		1H
4			1.18	m		1H
5	30.12		1.70	m		1H
6	34.53	t	1.32	m		1H
6			1.19	m		1H
7	29.39		1.62	m		2H
8	75.90	d	4.60	ddd	6.8, 5.5, 3.8	1H
9	70.03	d	3.69	qd	6.9, 3.8	1H
9-OH			3.39	d	7.1	1H
10	32.83	t	1.55	m		1H
			1.52	m		1H
11	28.80	t	2.14	m		2H
12	132.12	d	5.41	dt	15.4, 6.2	1H
13	130.69	d	5.44	ddd	15.4, 7.7, 5.9	1H
14	41.46	t	2.01	m		1H
			1.76	ddd	13.0, 9.2, 7.3	1H
15	30.47	d	1.62	m		1H
16	42.94	t	1.83	m		1H
			1.21	m		1H
17	69.69	t	5.77	ddd	10.4, 8.9, 3.8	1H
18	129.64	d	5.28	d	8.9	1H
19	136.76	s				
20	134.80	d	6.04	d	15.6	1H
21	131.40	d	5.75	dt	15.4, 7.0	1H
22	33.46	t	2.09	q	7.4	2H
23	29.87		1.40	quint	7.3	2H
24	32.15	t	1.29	m		2H
25	23.14	t	1.30	m		2H
26	14.25	q	0.87	t	7.0	3H
27	14.21	q	1.15	d	7.1	3H
28	18.74	q	0.90	d	6.7	3H
29	18.33	q	0.94	d	6.5	3H
30	13.11	q	1.83	d	1.2	3H
31	157.83	s				
31-NH_2			5.71			2H

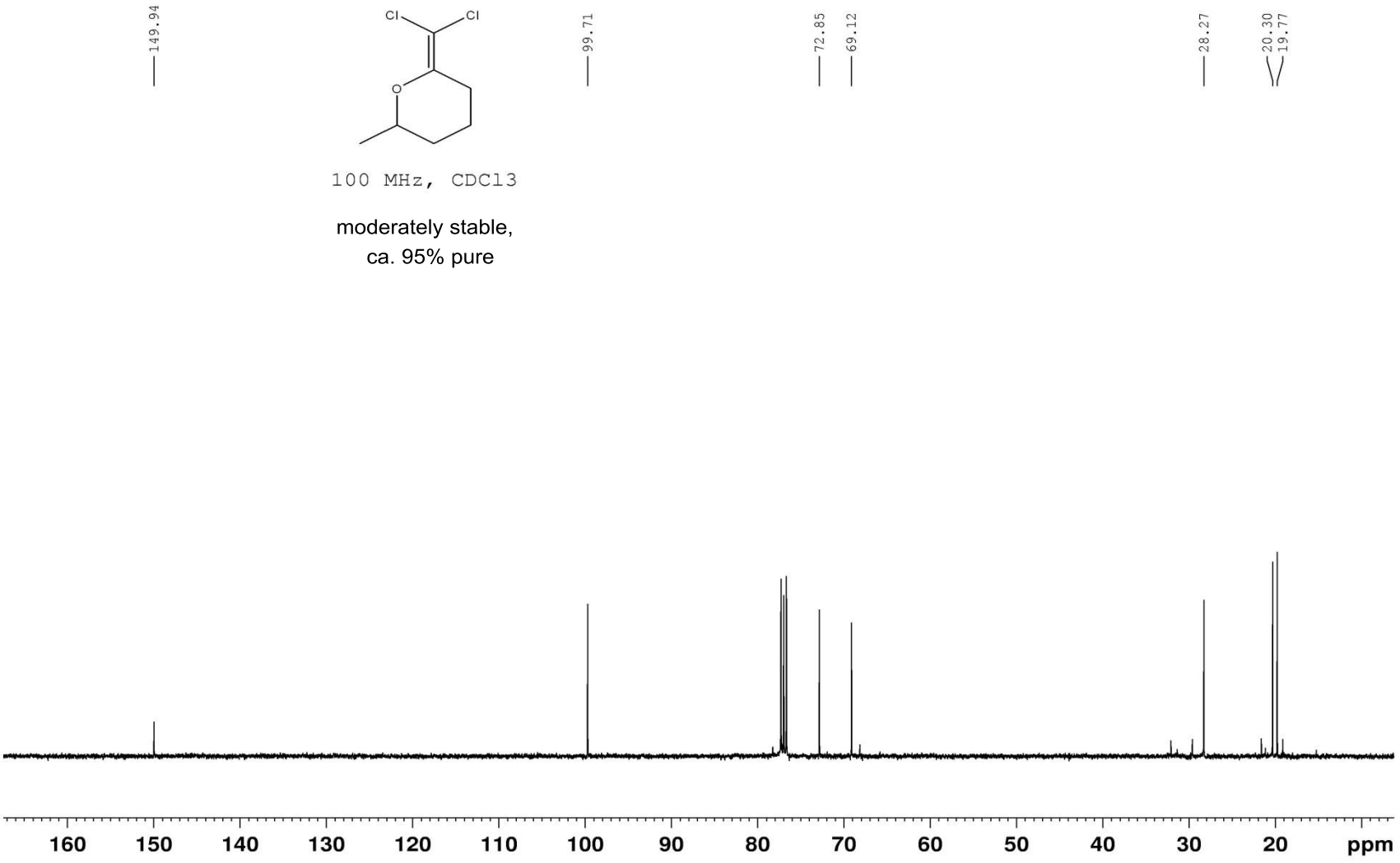

Cl
Cl
O
400 MHz, C6D6
moderately stable
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.01
1.00
1.04
1.00
1.06
1.05
3.01

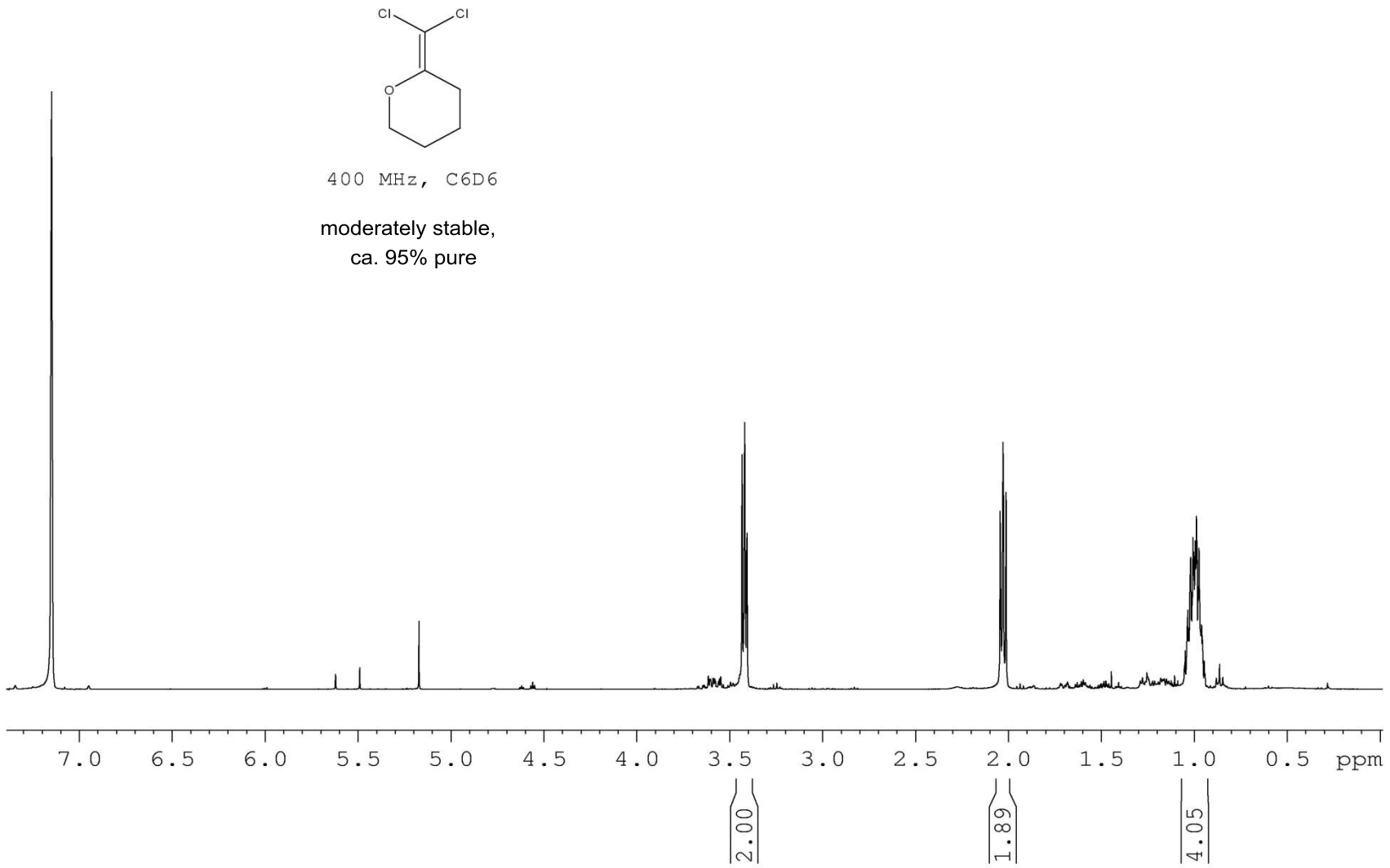

moderately stable
150.02
104.26
69.01
33.84
32.50
28.18
21.33
Cl
Cl
O
100 MHz, C6D6
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm


Cl
Cl
O
400 MHz, CDCl3
moderately stable,
ca. 95% pure
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.99
0.95
1.07
1.03
1.12
1.03
3.10

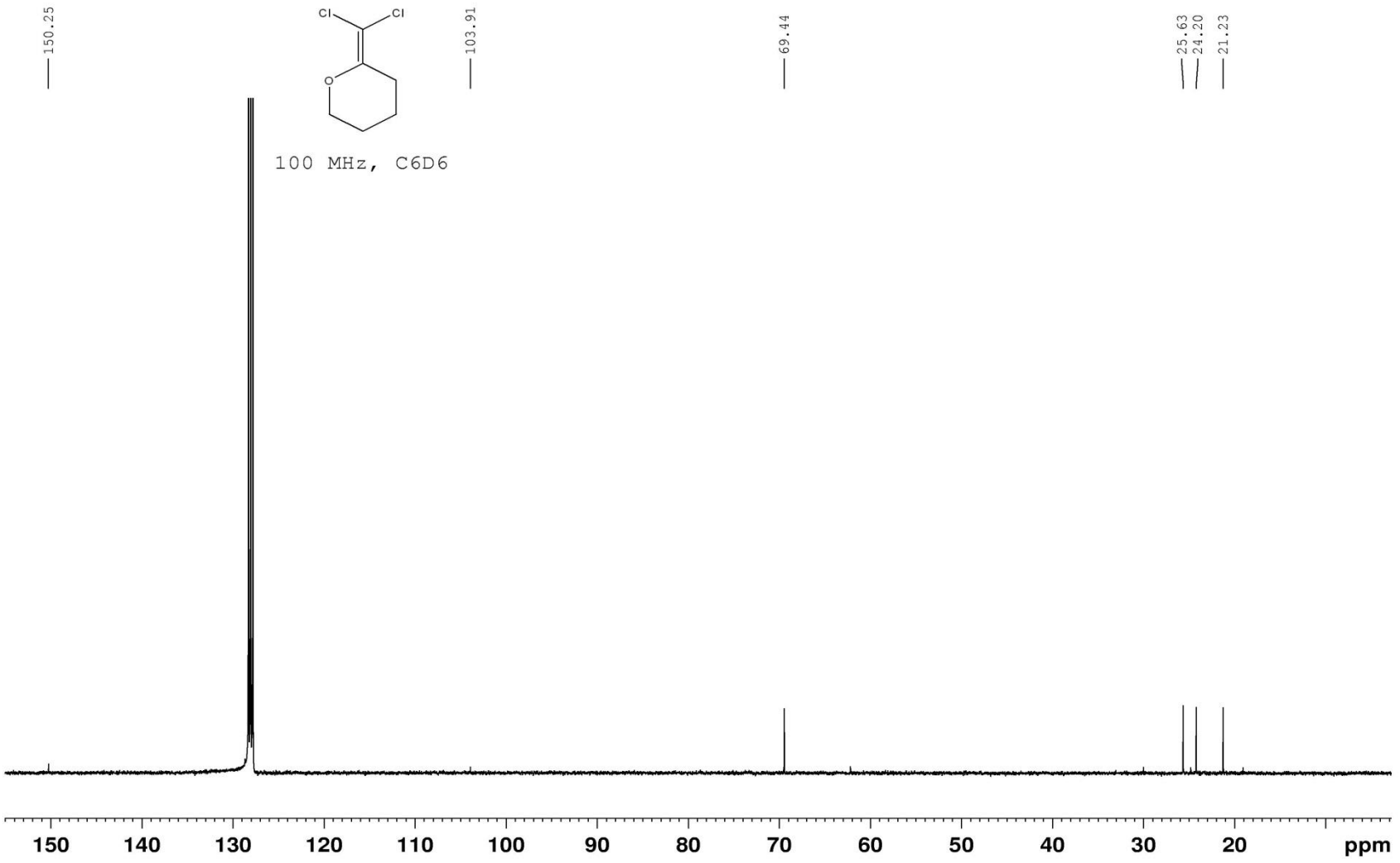

153.53
103.96
70.43
29.02
28.12
19.71
17.12
Cl
Cl
O
100 MHz, CDCl3
moderately stable,
ca. 95% pure
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

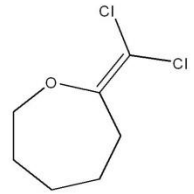

Cl
Cl
O
400 MHz, CDCl3
moderately stable,
ca. 95% pure
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.88
0.95
1.00
1.93
1.19
1.24
3.25


149.94
99.71
72.85
69.12
28.27
20.30
19.77
Cl
Cl
O
100 MHz, CDCl3
moderately stable,
ca. 95% pure
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


Cl
Cl
O
400 MHz, C6D6
moderately stable,
ca. 95% pure
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.89
4.05

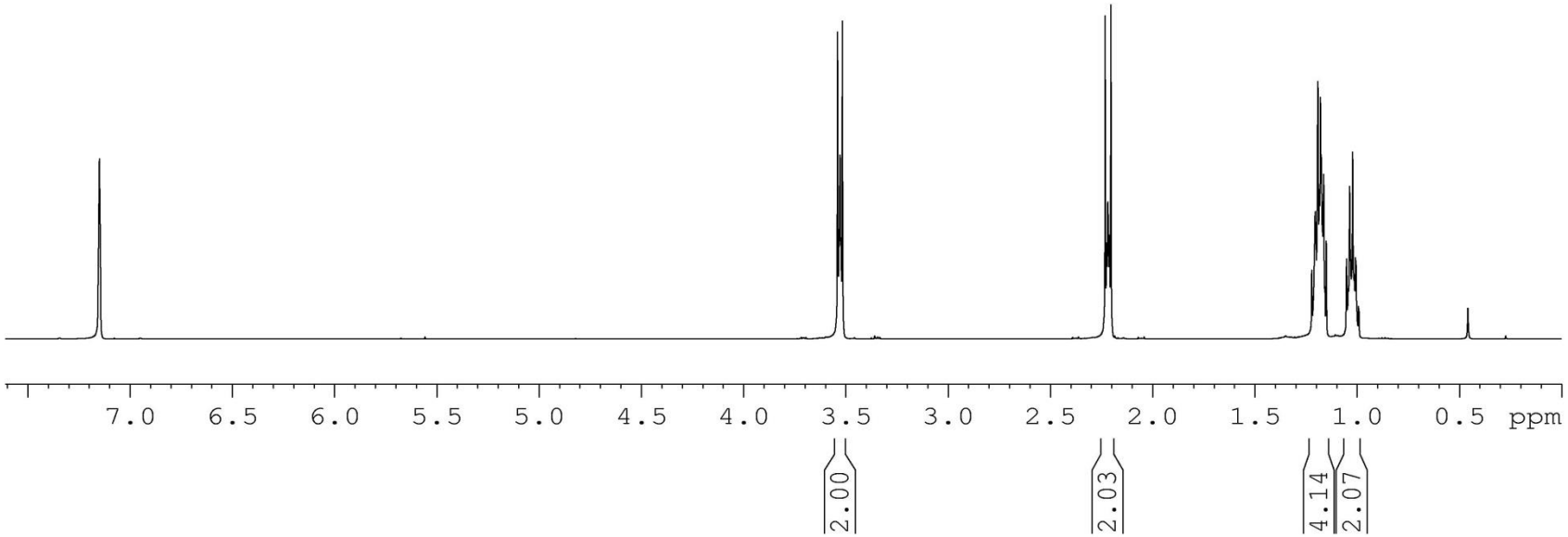
moderately stable,
ca. 95% pure

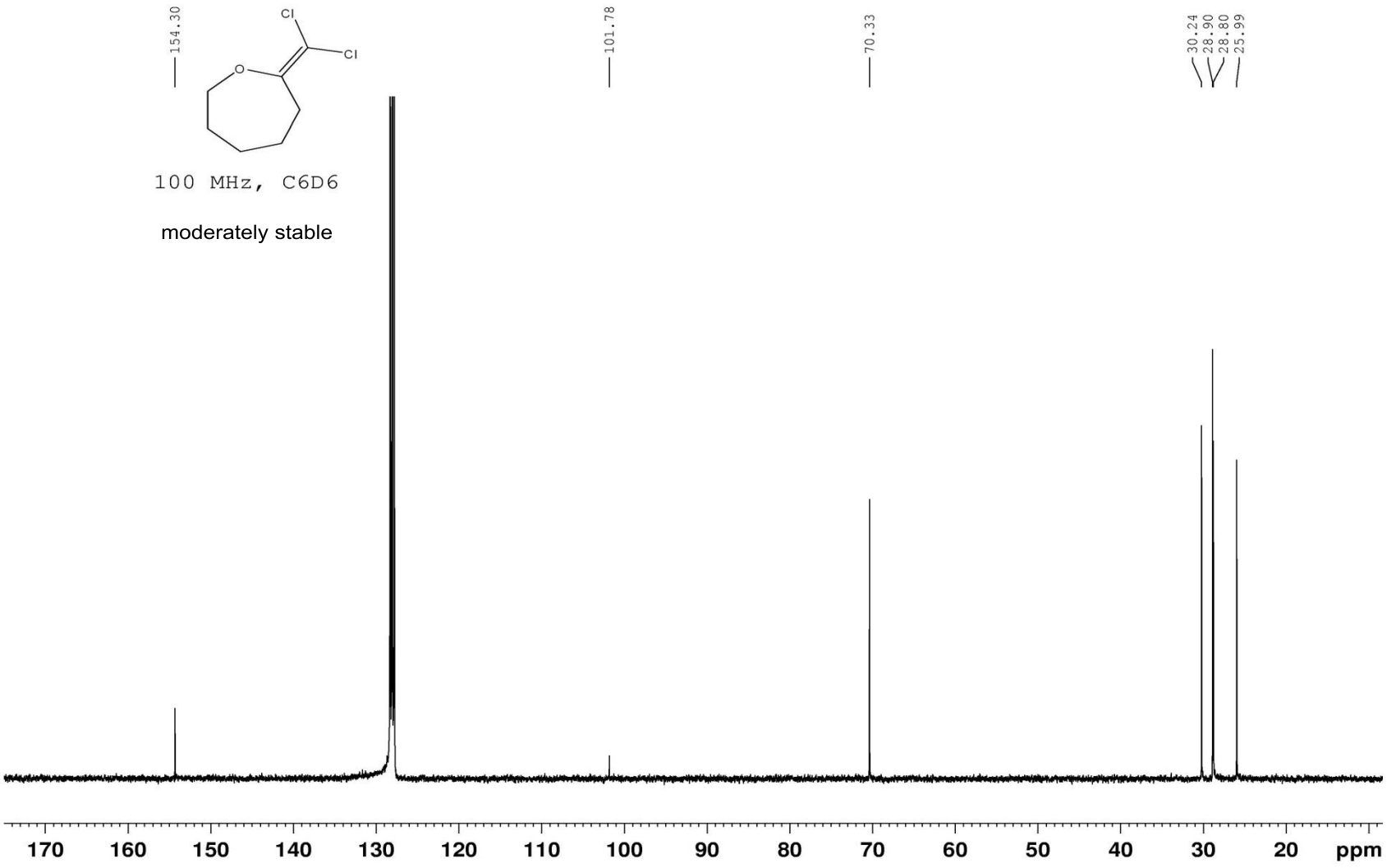


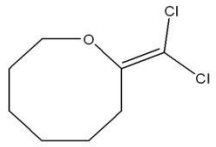


400 MHz, C6D6

moderately stable

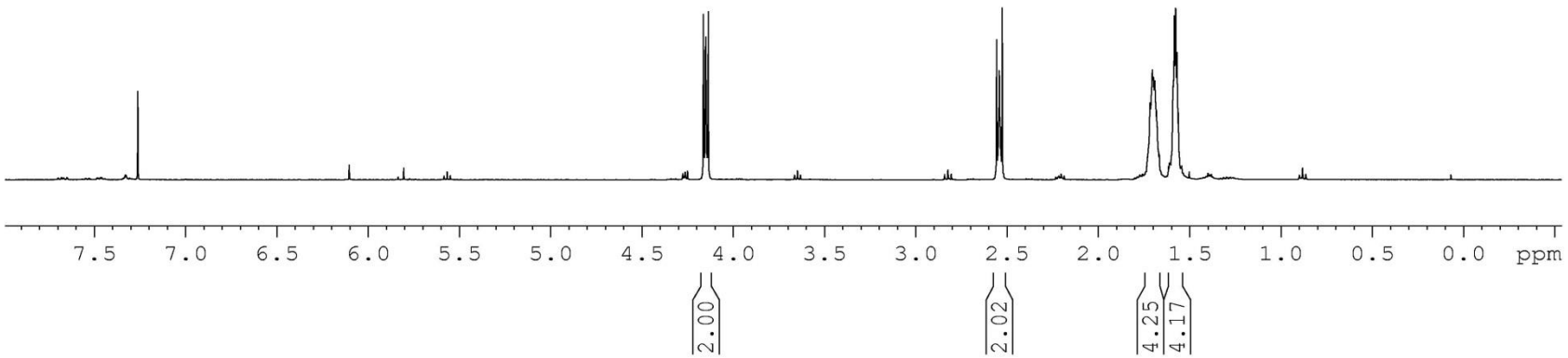


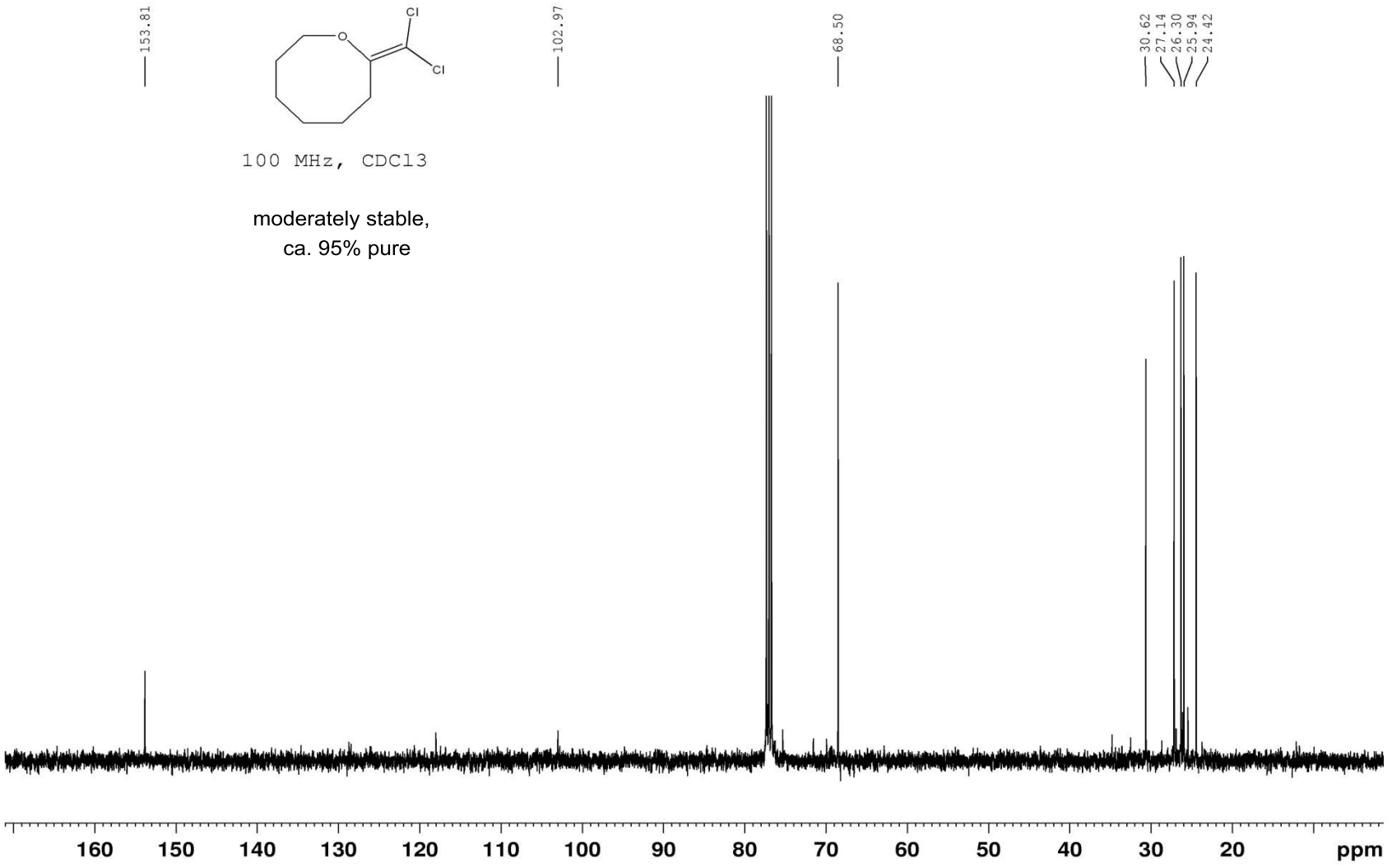

154.30
101.78
70.33
30.24
28.90
28.80
25.99
Cl
Cl
O
100 MHz, C6D6
moderately stable
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

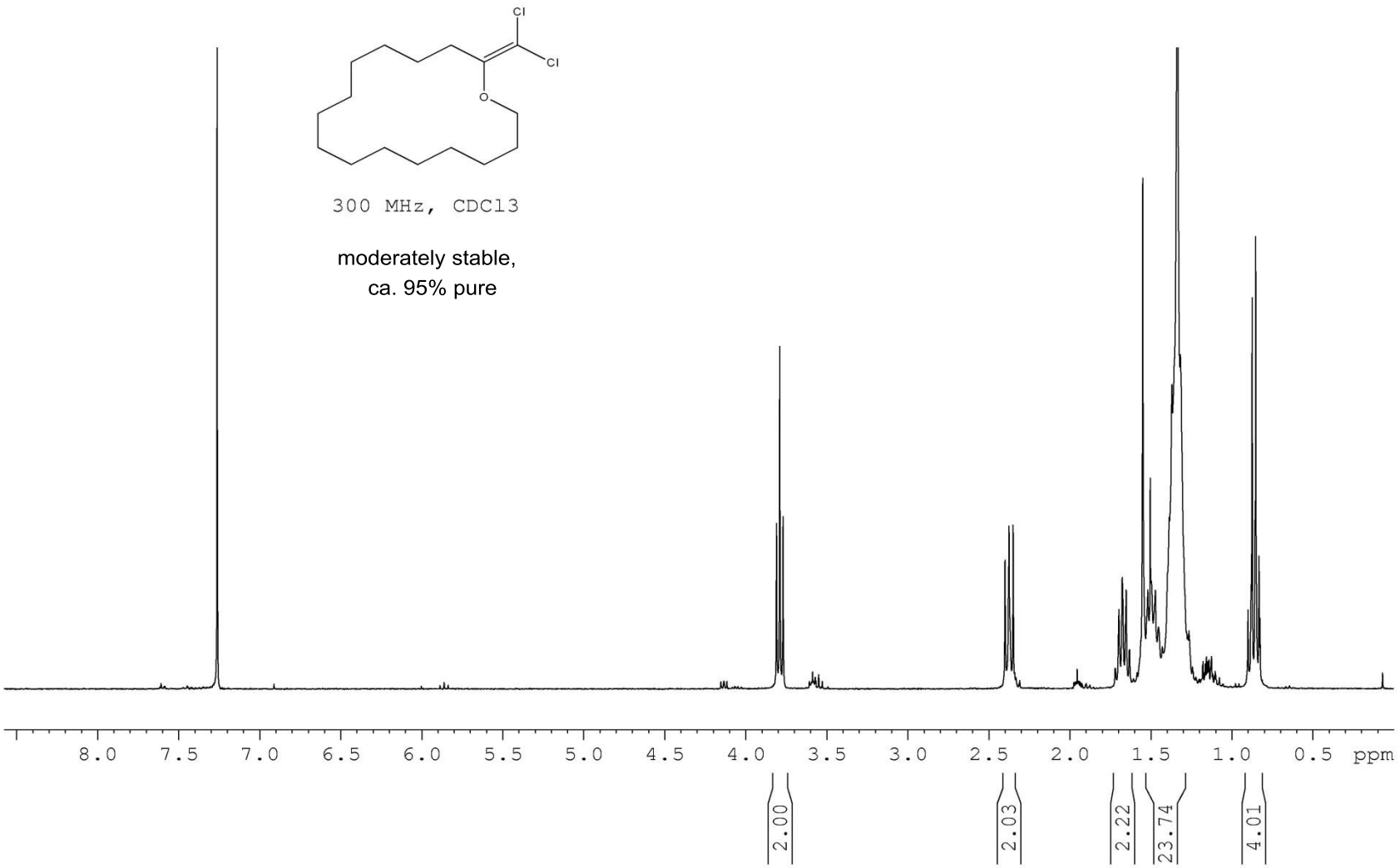


400 MHz, CDCl3

moderately stable,
ca. 95% pure

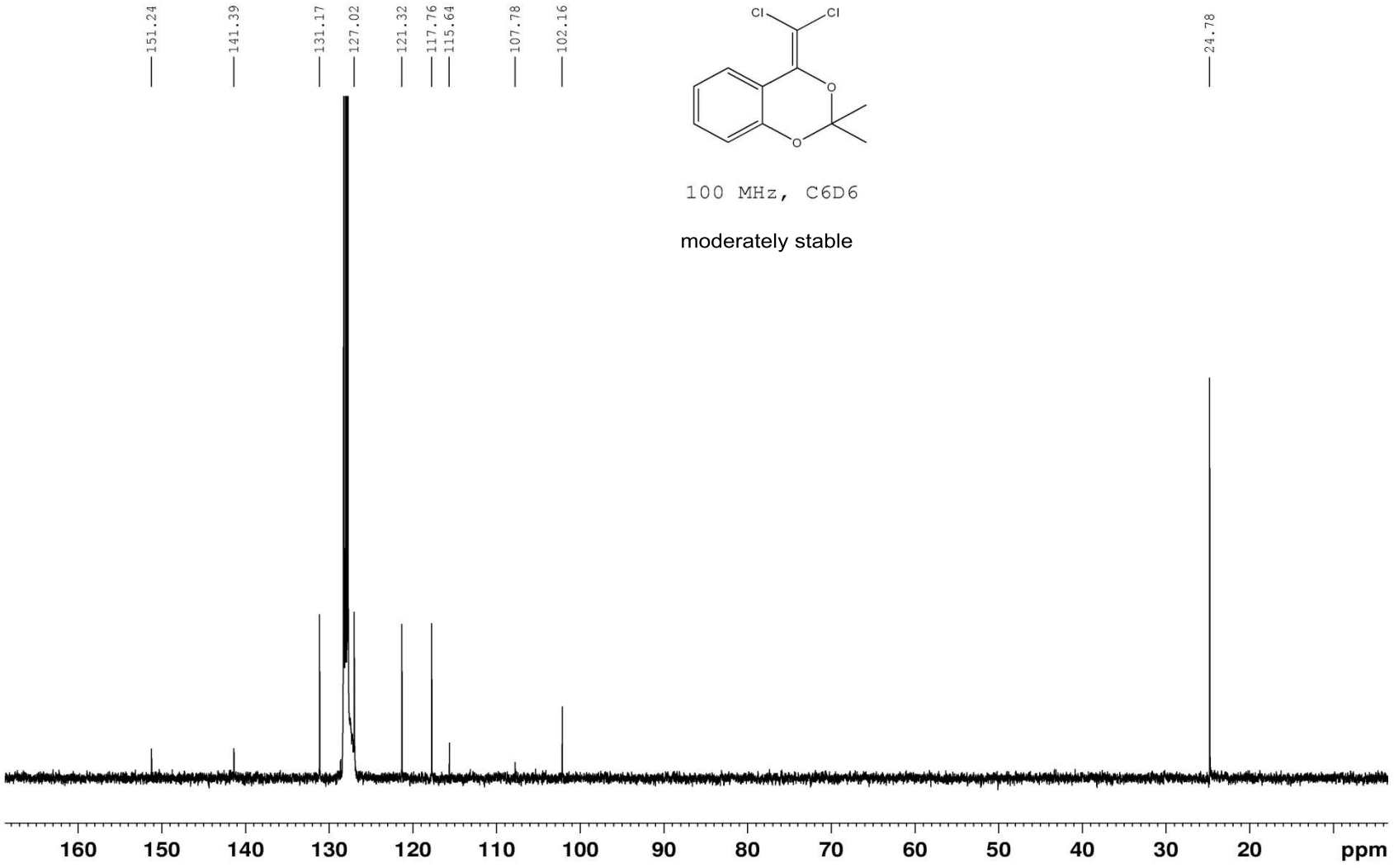


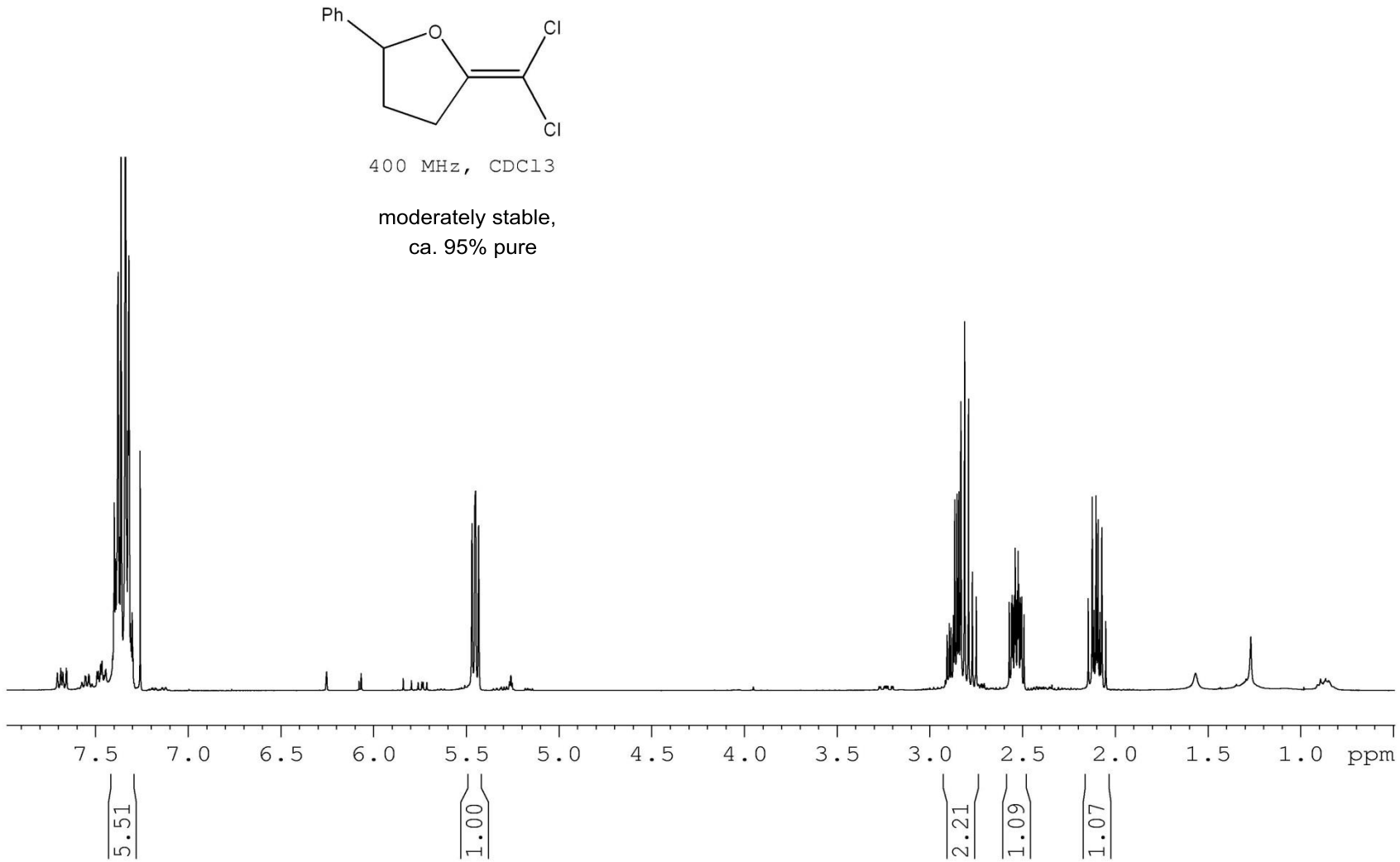

153.81
102.97
68.50
30.62
27.14
26.30
25.94
24.42
O
Cl
Cl
100 MHz, CDCl3
moderately stable,
ca. 95% pure
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

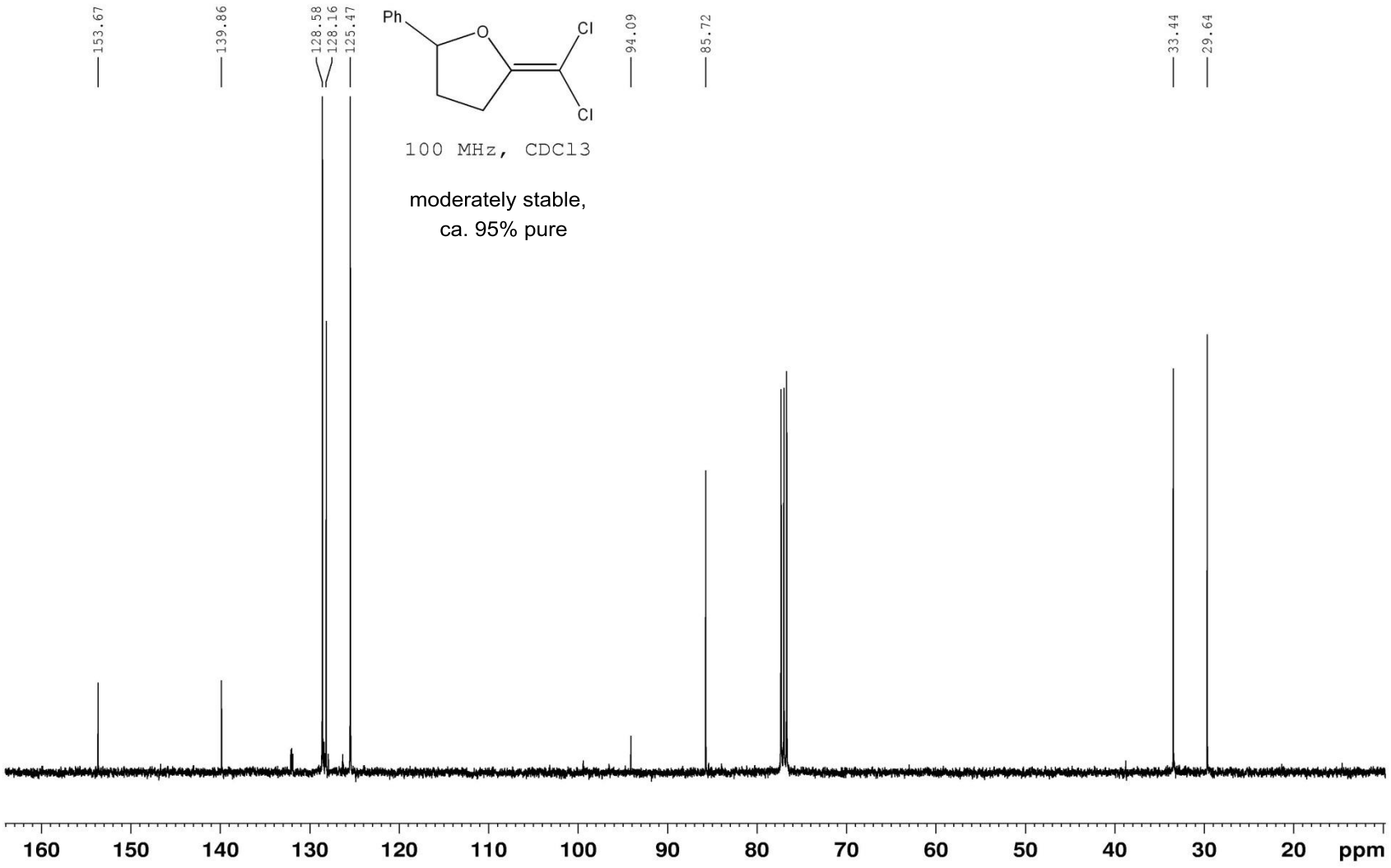

Cl
Cl
O
300 MHz, CDCl3
moderately stable,
ca. 95% pure
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
2.03
2.22
23.74
4.01

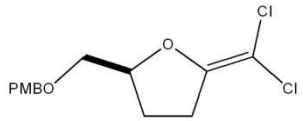
400 MHz, C6D6

moderately stable


151.24
141.39
131.17
127.02
121.32
117.76
115.64
107.78
102.16
24.78
Cl
Cl
O
O
100 MHz, C6D6
moderately stable
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

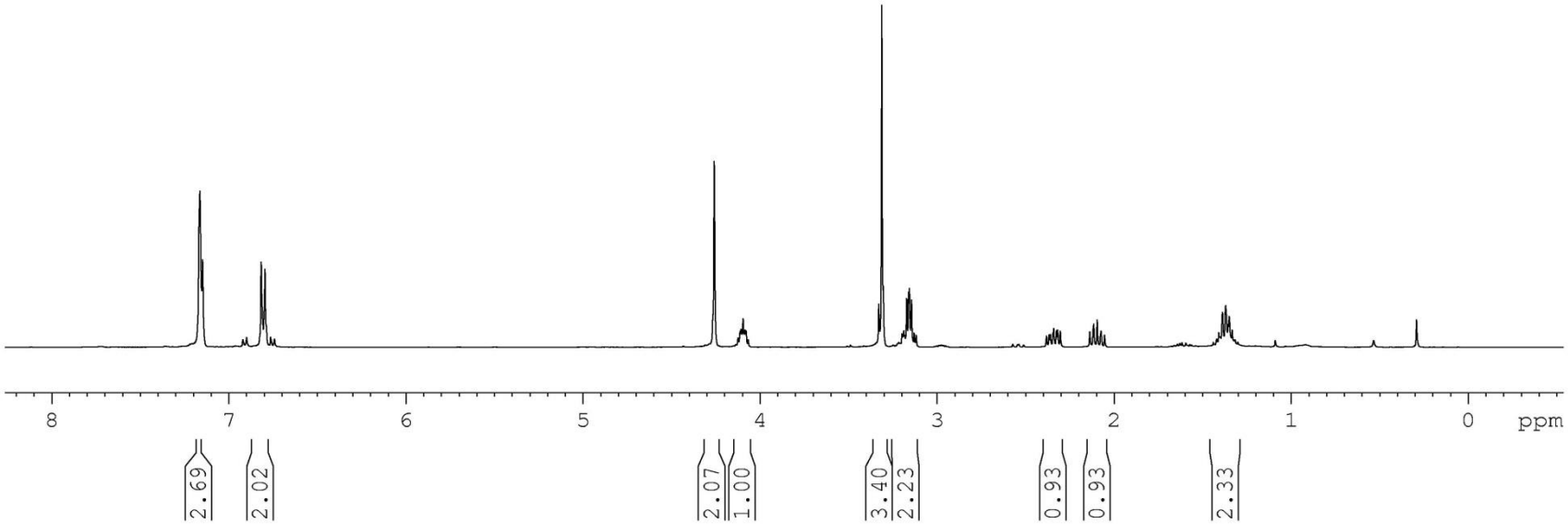

Ph
O
Cl
Cl
400 MHz, CDCl3
moderately stable,
ca. 95% pure
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
5.51
1.00
2.21
1.09
1.07

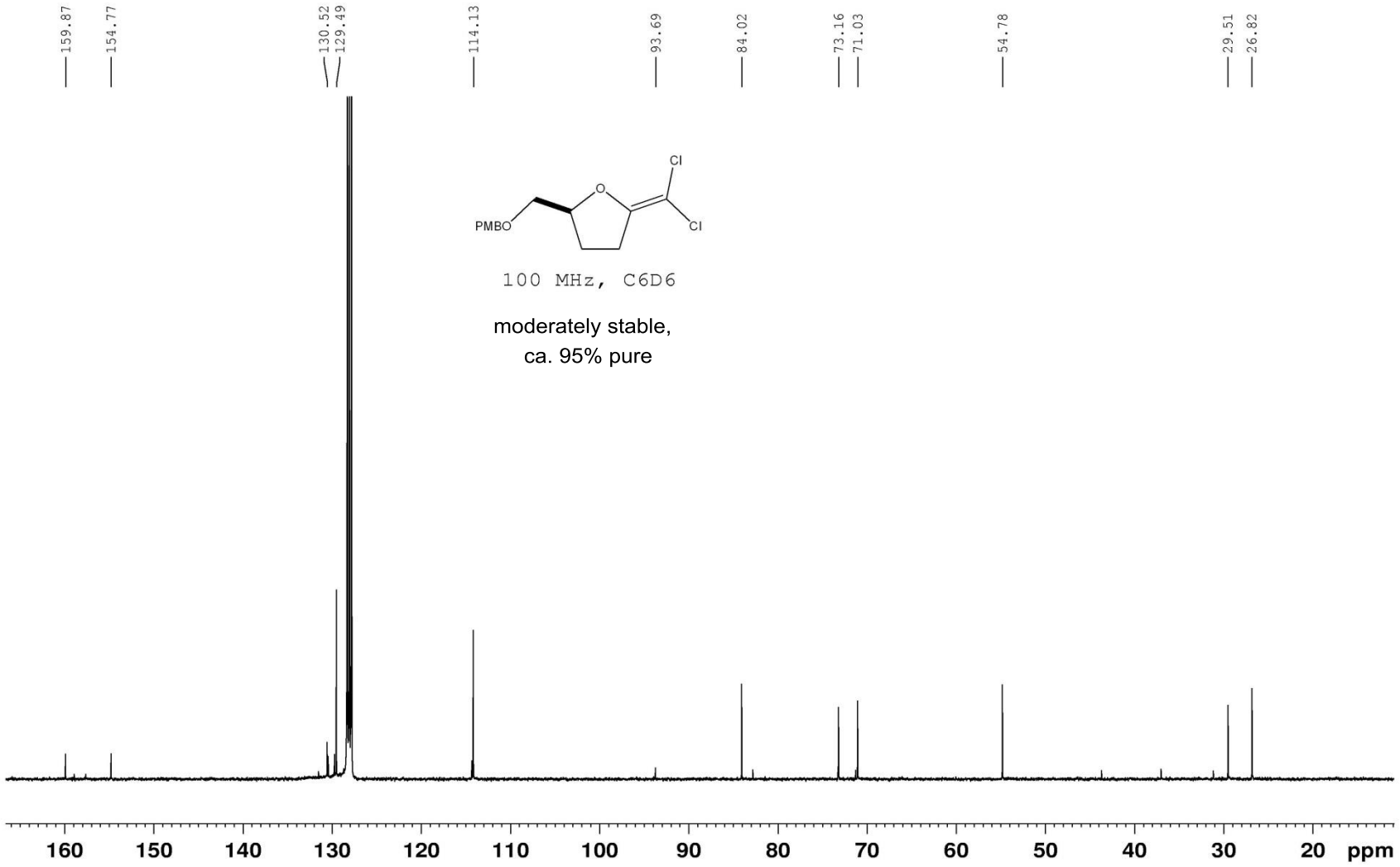

153.67
139.86
128.58
128.16
125.47
94.09
85.72
33.44
29.64
Ph
O
Cl
Cl
100 MHz, CDCl3
moderately stable,
ca. 95% pure
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

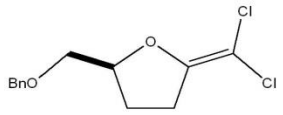


400 MHz, C6D6

moderately stable,
ca. 95% pure

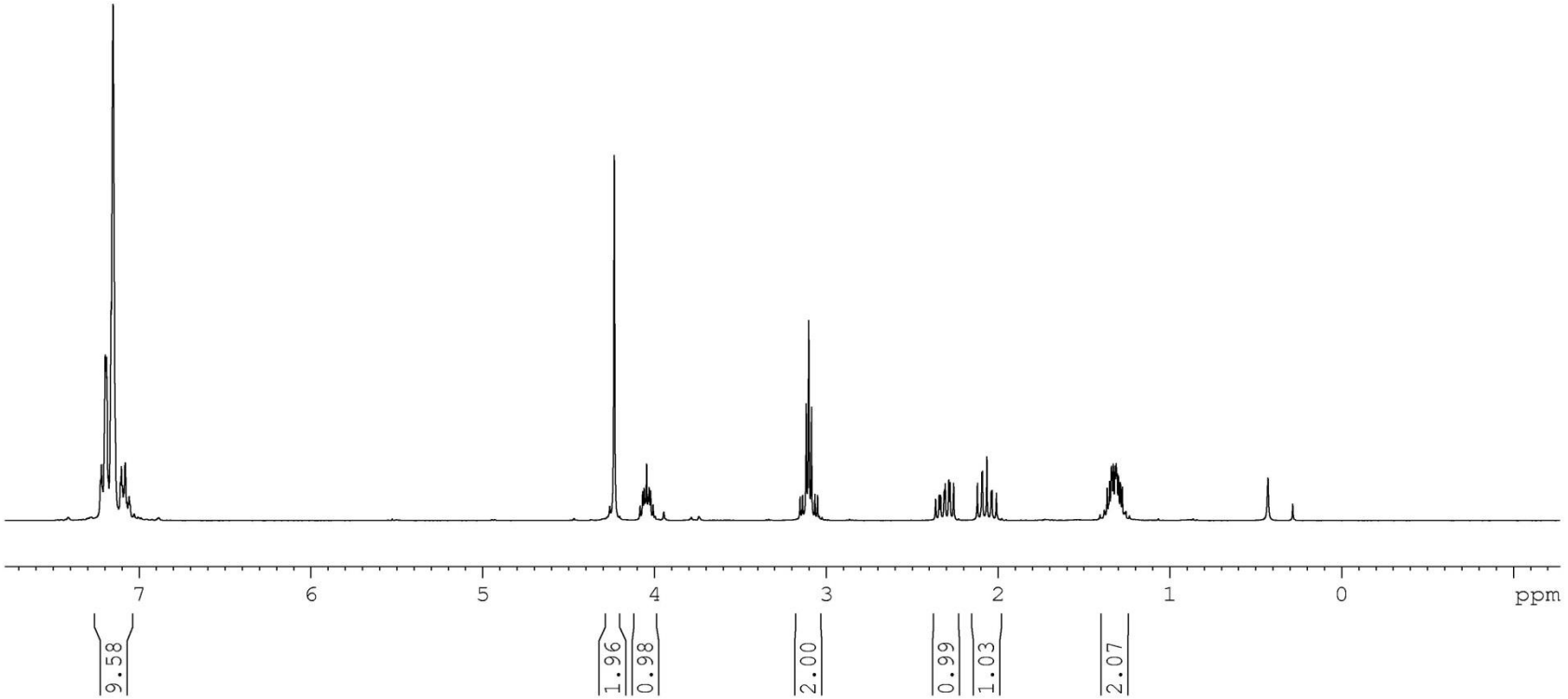


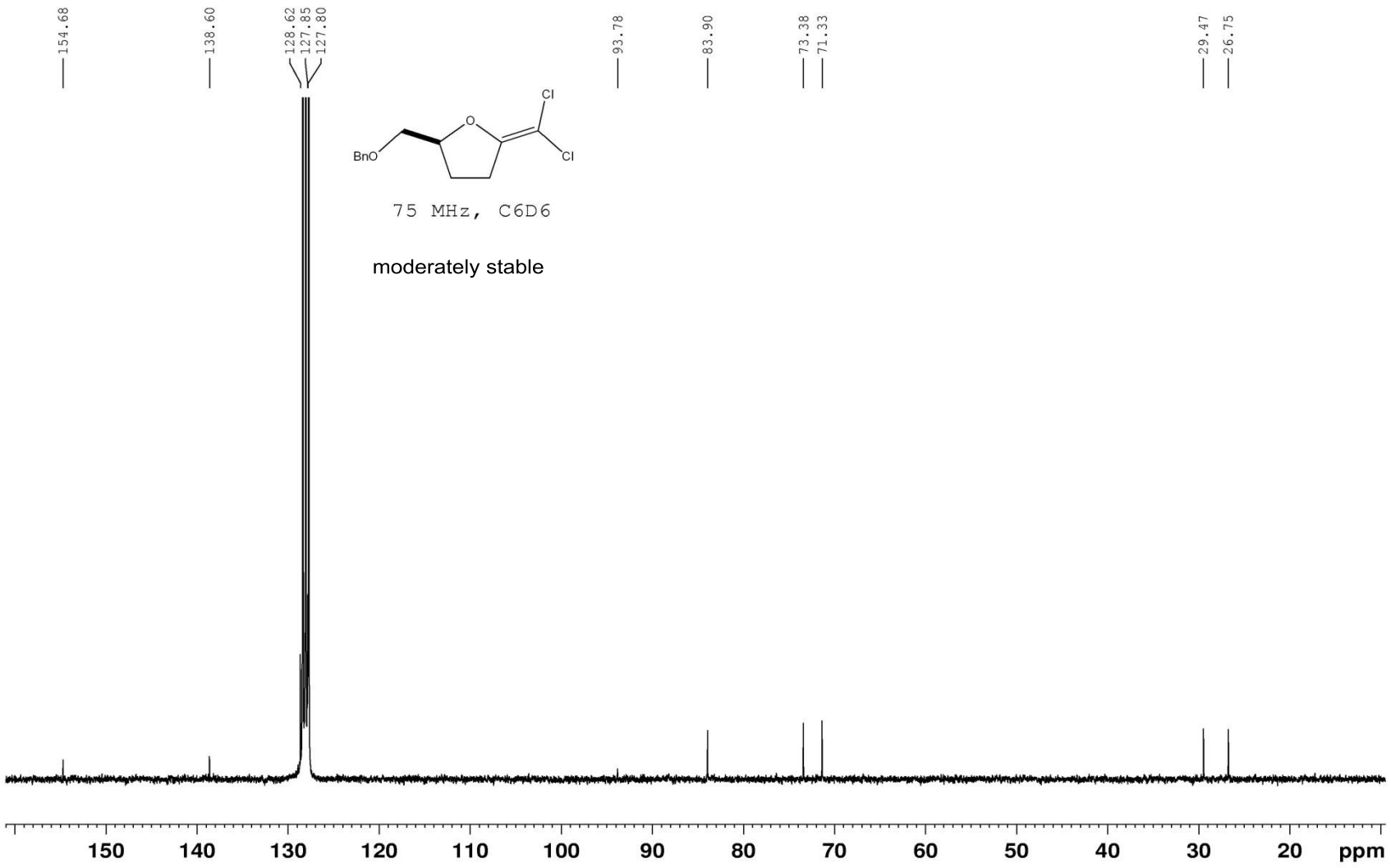

159.87
154.77
130.52
129.49
114.13
93.69
84.02
73.16
71.03
54.78
29.51
26.82
PMBO
O
Cl
Cl
100 MHz, C6D6
moderately stable,
ca. 95% pure
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

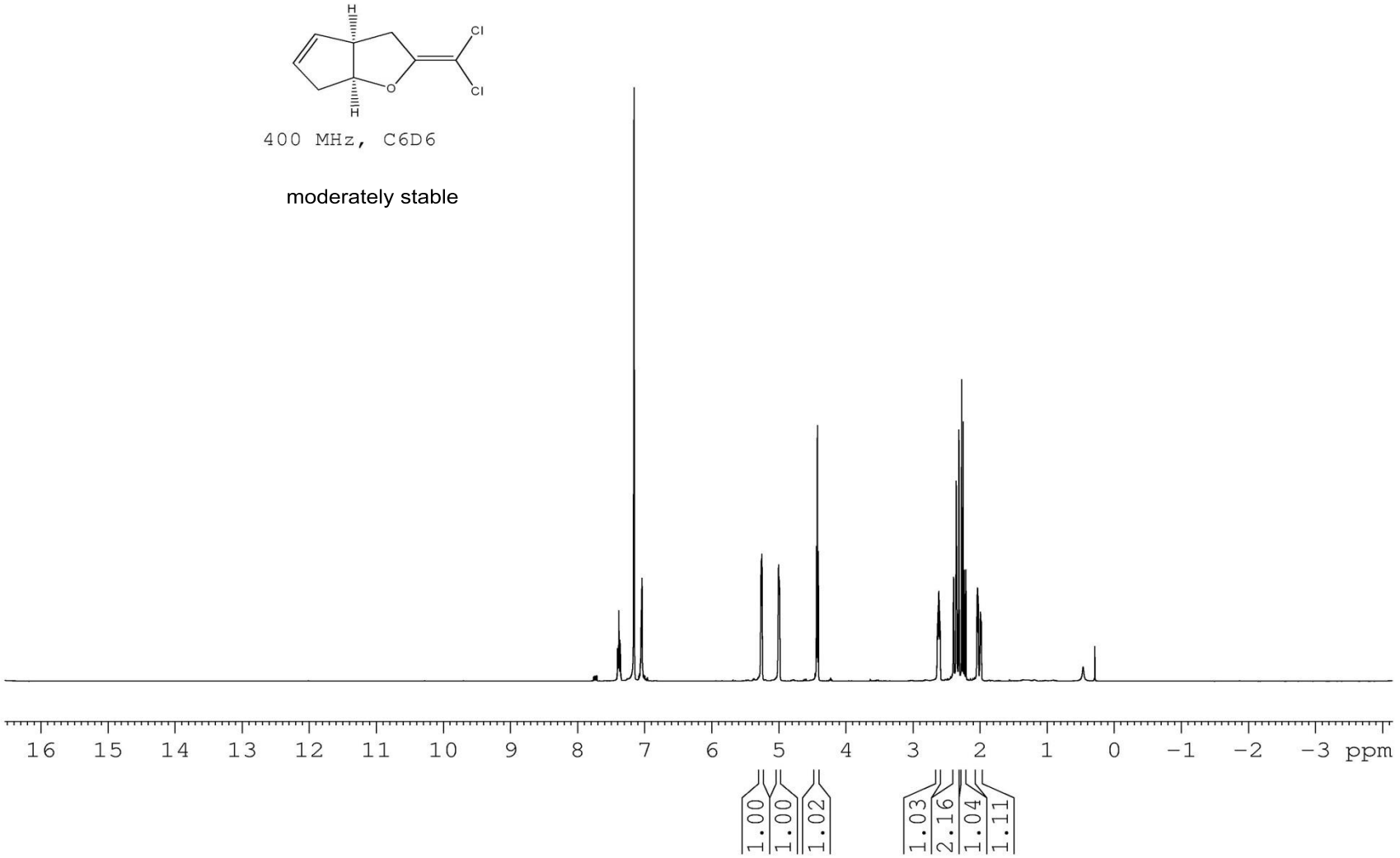


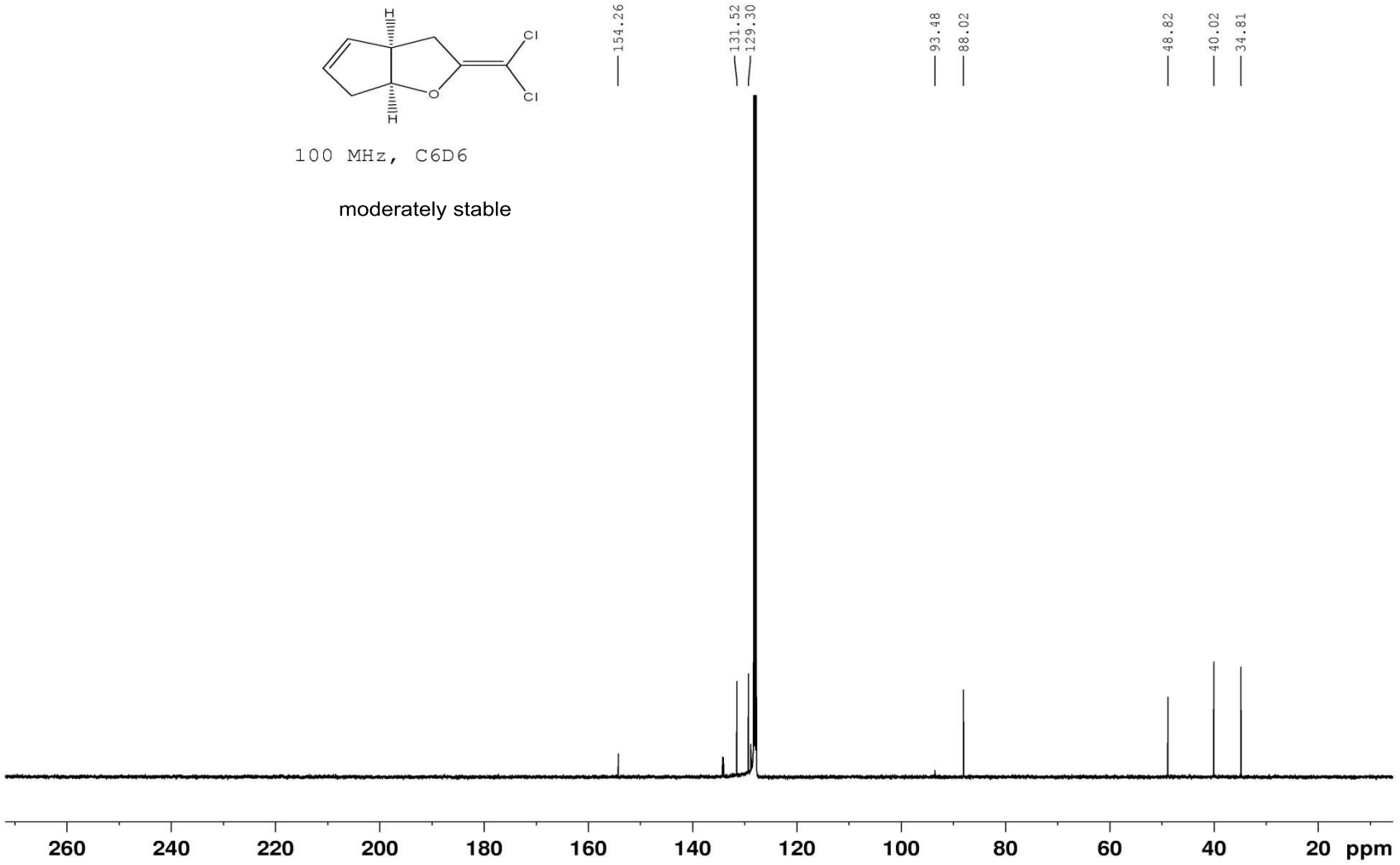
300 MHz, C6D6

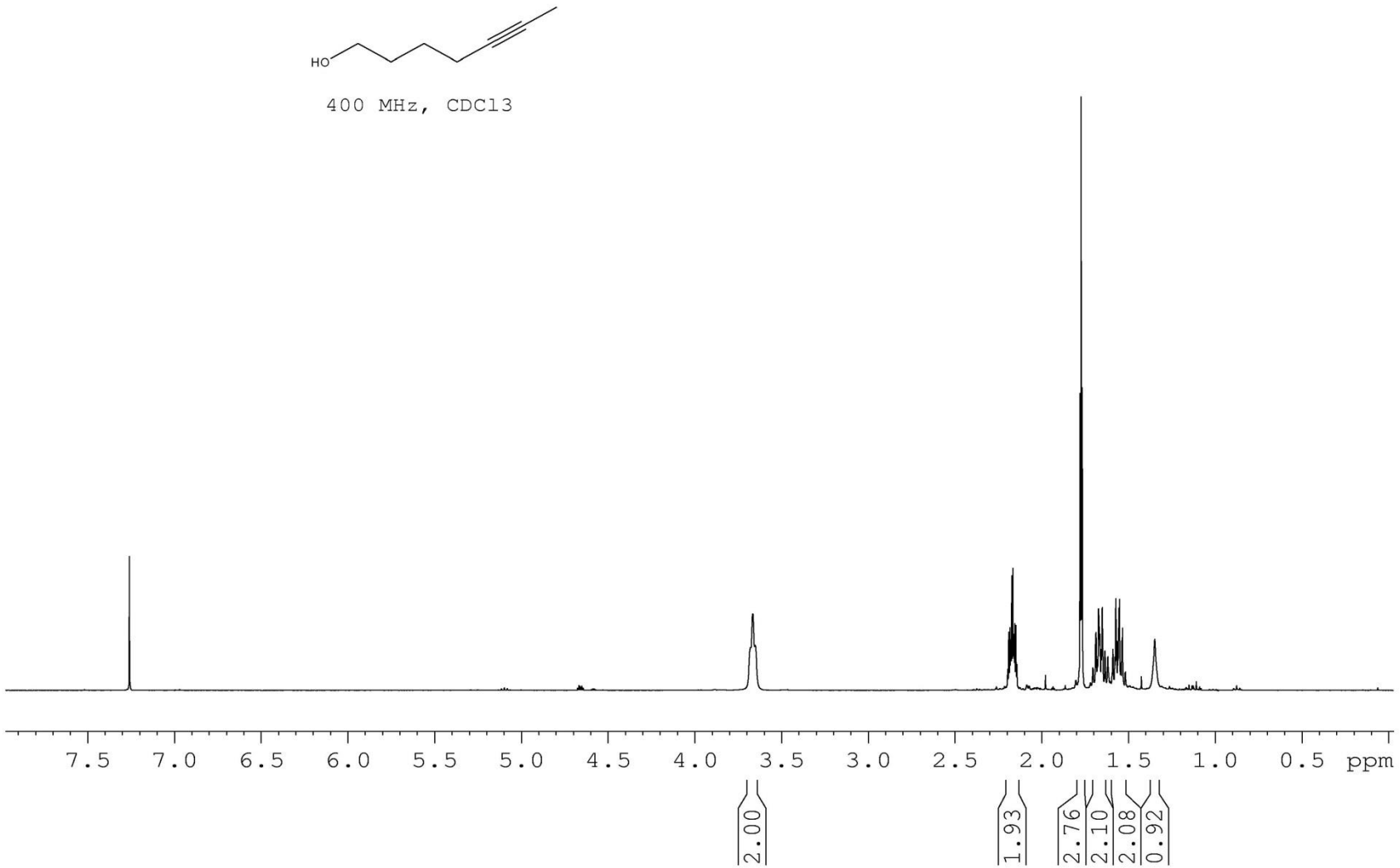
moderately stable

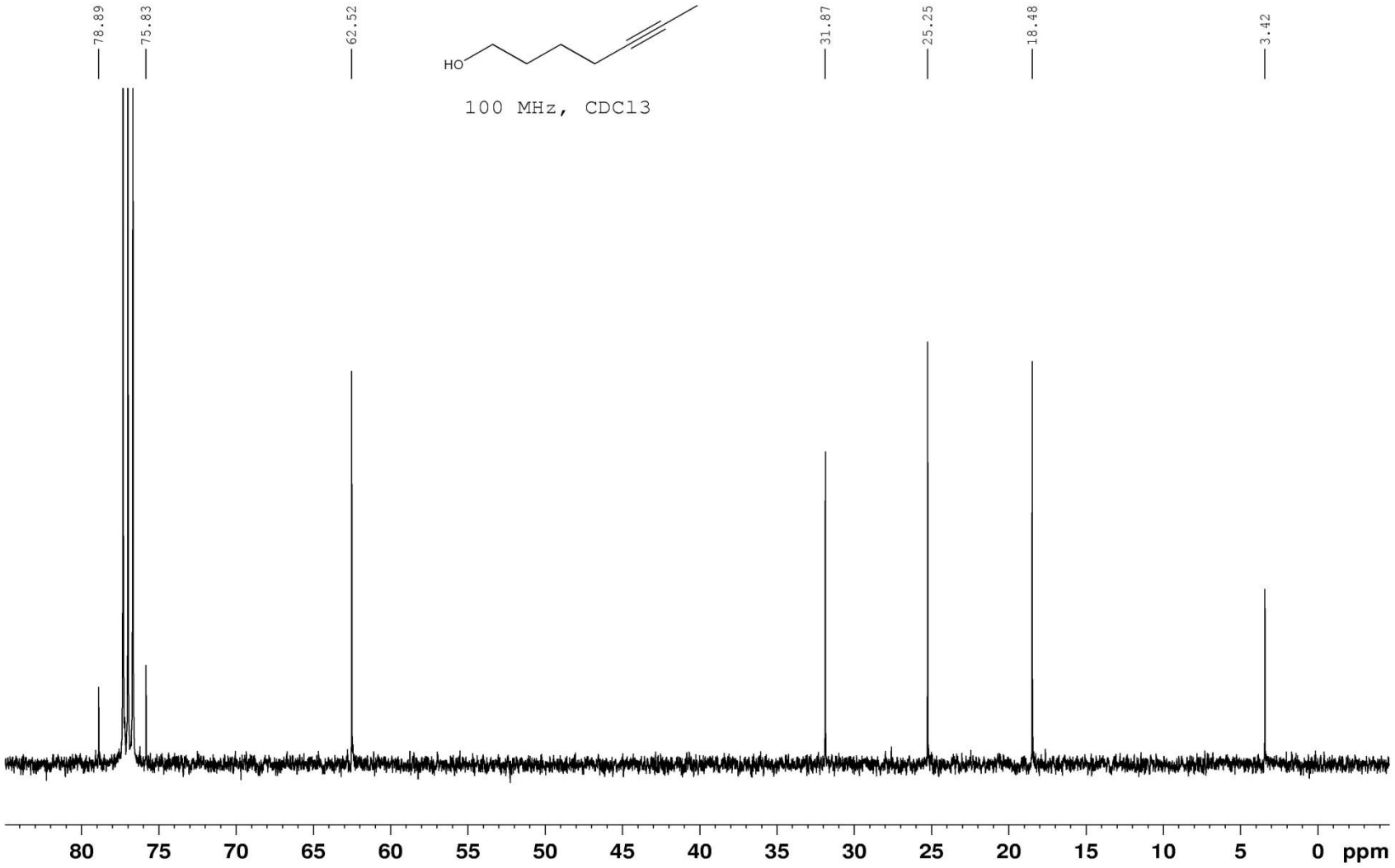


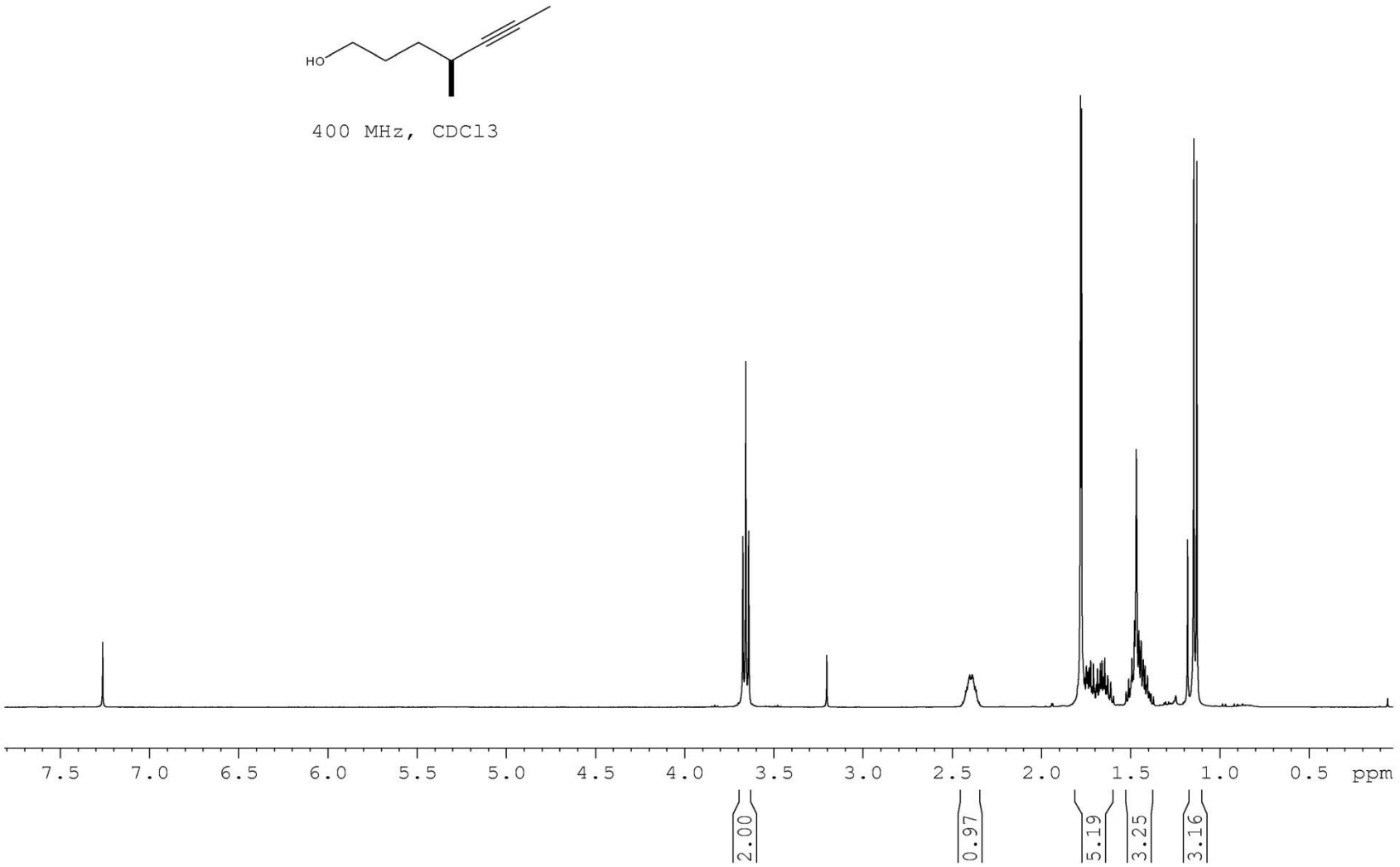

154.68
138.60
128.62
127.85
127.80
93.78
83.90
73.38
71.33
29.47
26.75
BnO
O
Cl
Cl
75 MHz, C6D6
moderately stable
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

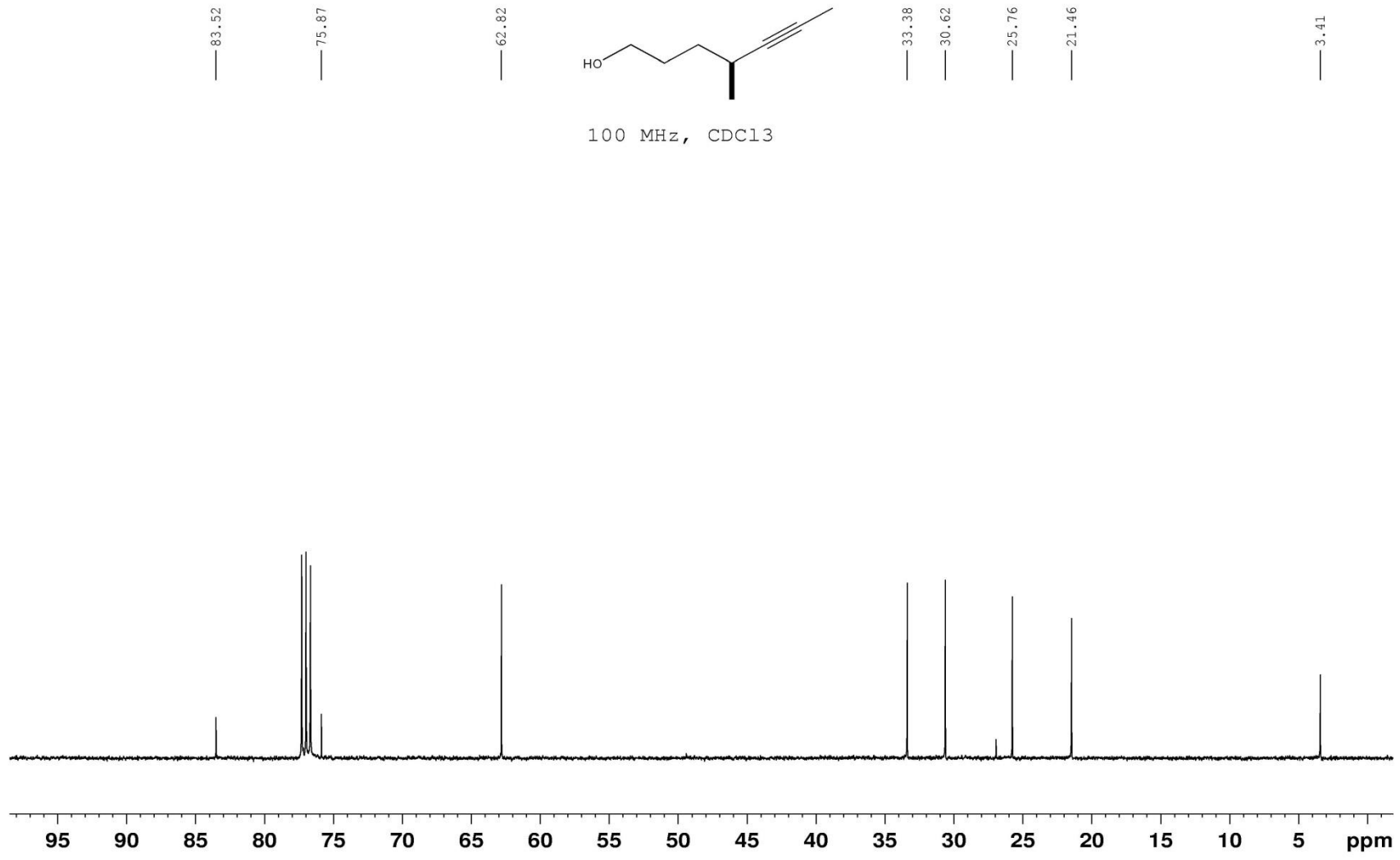

H
Cl
Cl
O
H
400 MHz, C6D6
moderately stable
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2 −3 ppm
1.00
1.00
1.02
1.03
2.16
1.04
1.11

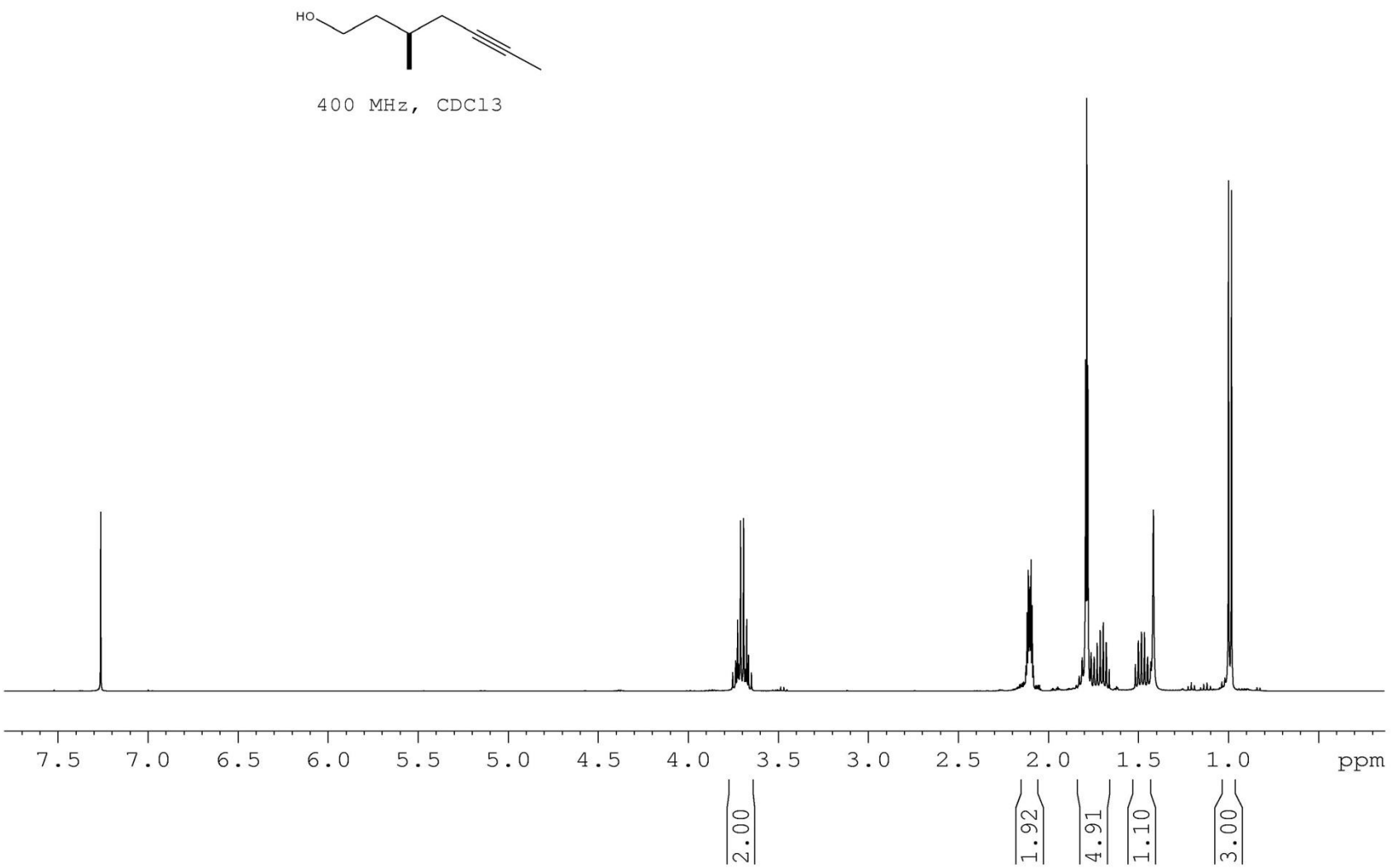

154.26
131.52
129.30
93.48
88.02
48.82
40.02
34.81
100 MHz, C6D6
moderately stable
260
240
220
200
180
160
140
120
100
80
60
40
20
ppm

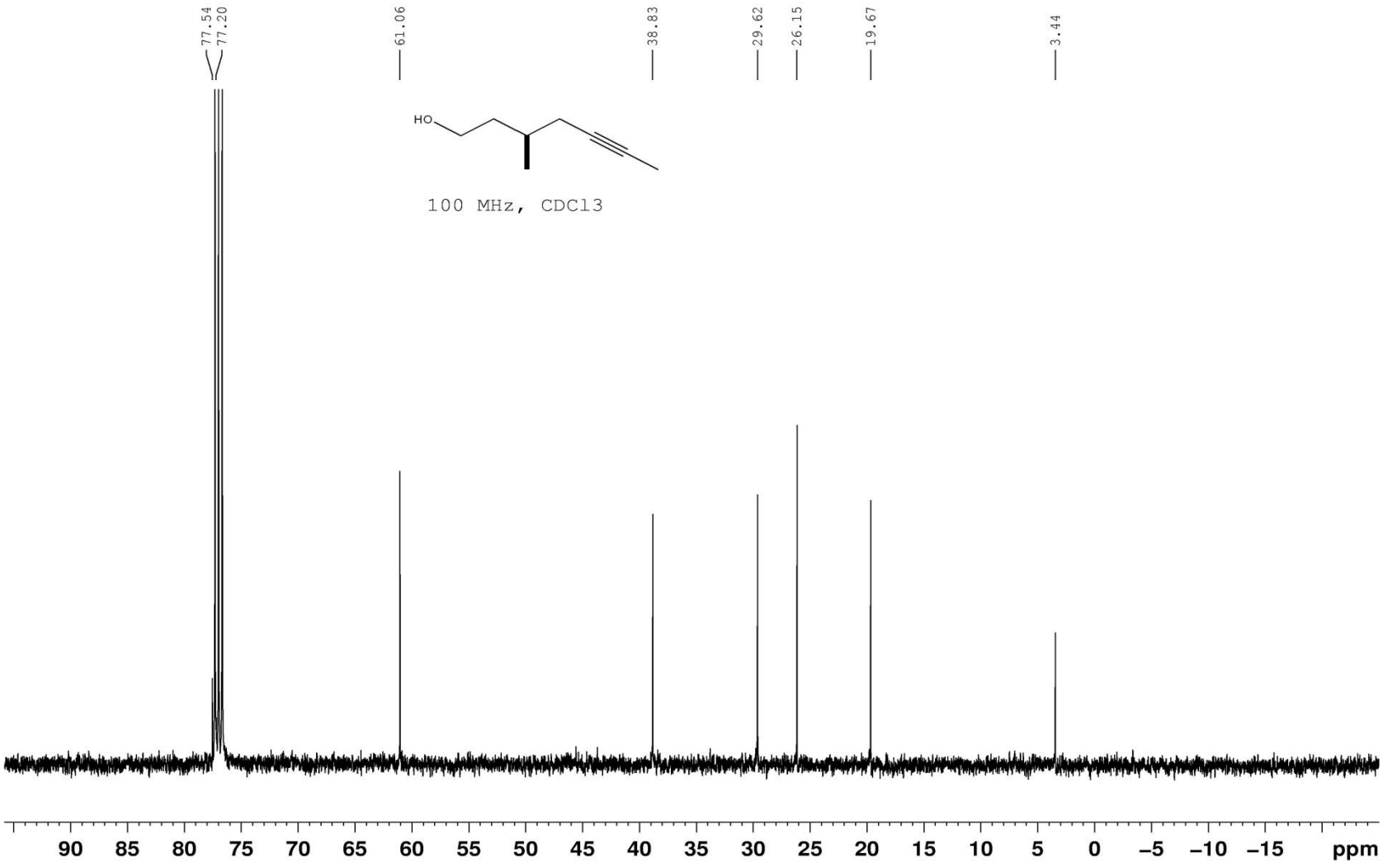

HO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.93
2.76
2.10
2.08
0.92

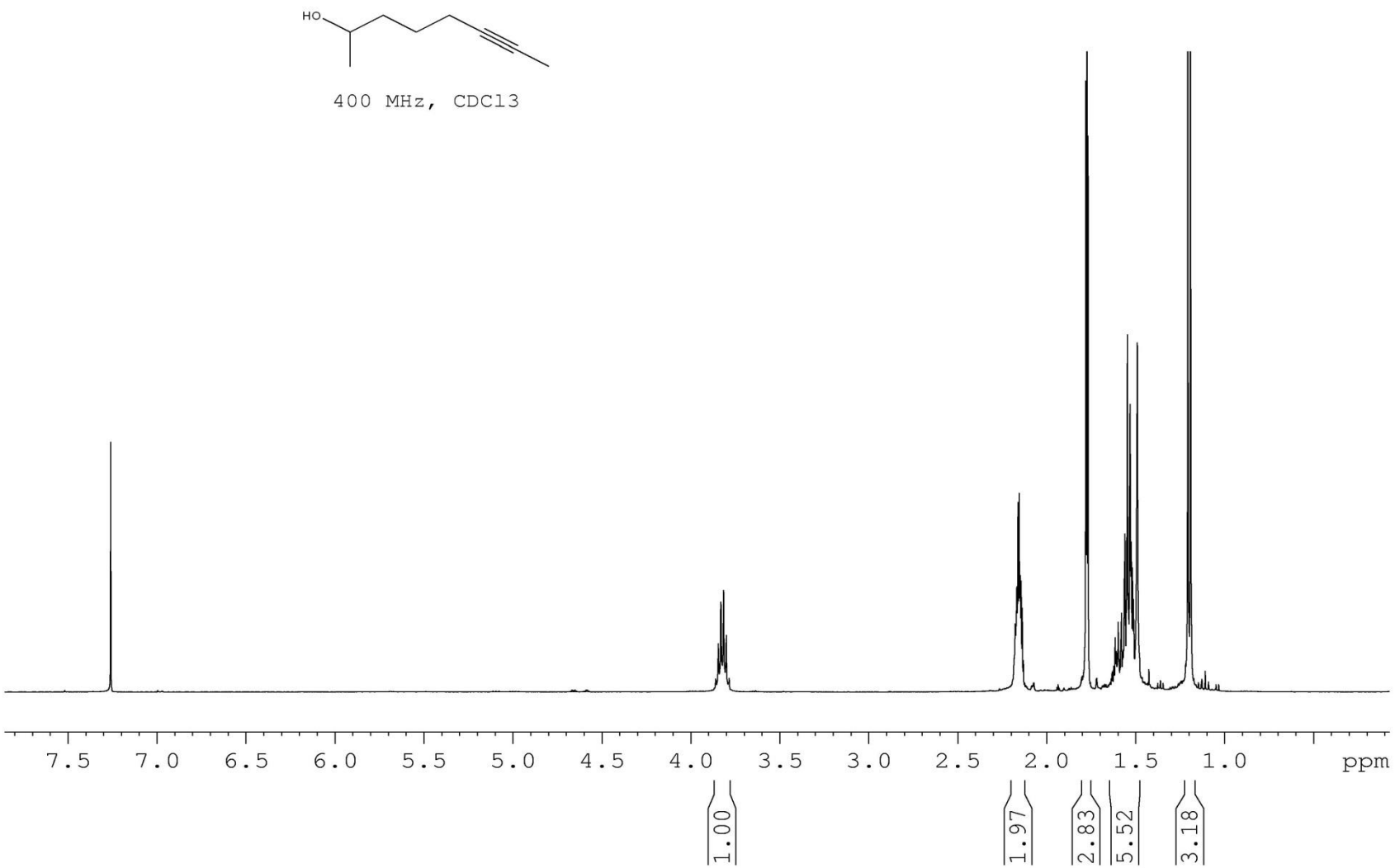

78.89
75.83
62.52
HO
31.87
25.25
18.48
3.42
100 MHz, CDCl3
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
ppm

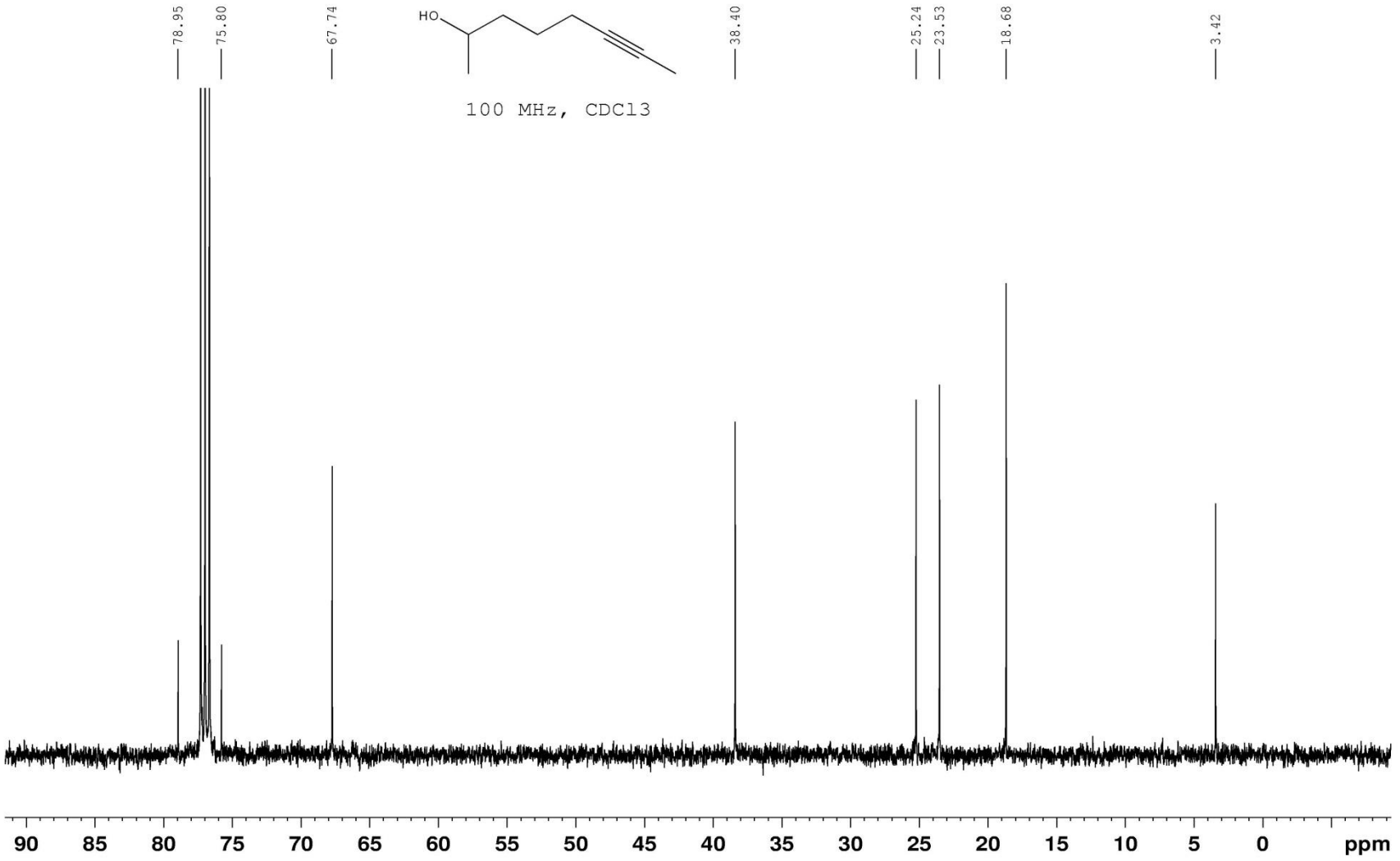

HO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
0.97
5.19
3.25
3.16

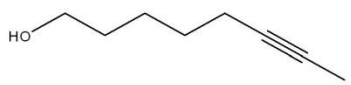

83.52
75.87
62.82
HO
33.38
30.62
25.76
21.46
3.41
100 MHz, CDCl3
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
ppm


HO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
1.92
4.91
1.10
3.00

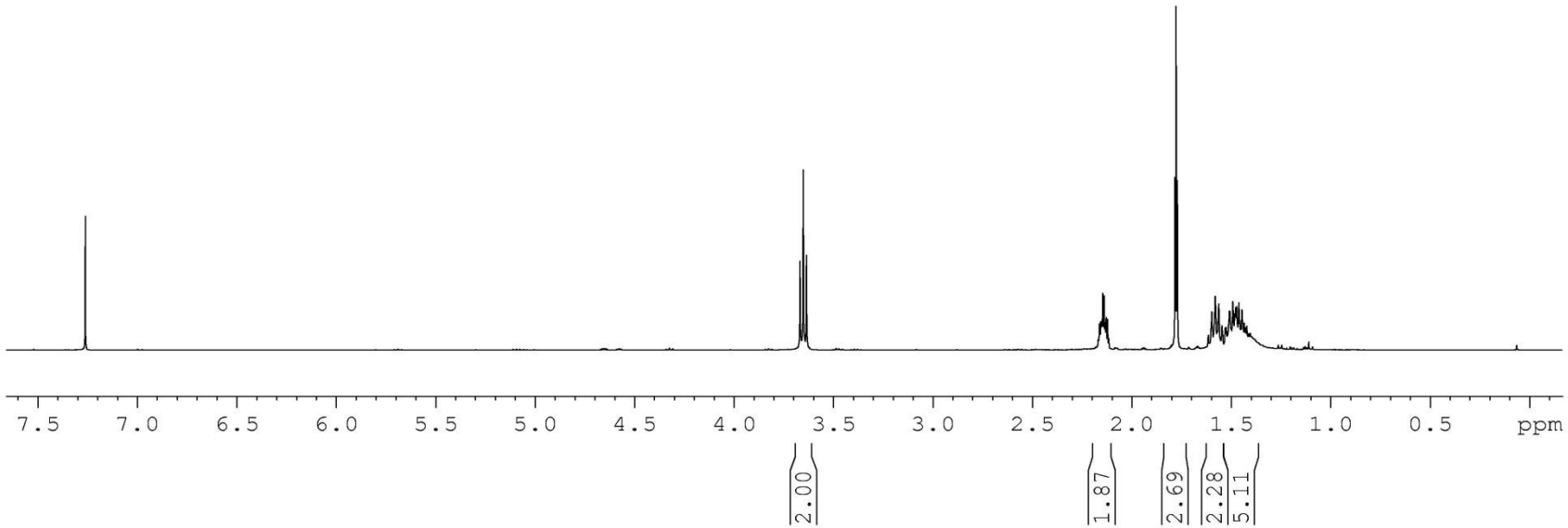

77.54
77.20
61.06
38.83
29.62
26.15
19.67
3.44
HO
100 MHz, CDCl3
90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 −5 −10 −15 ppm

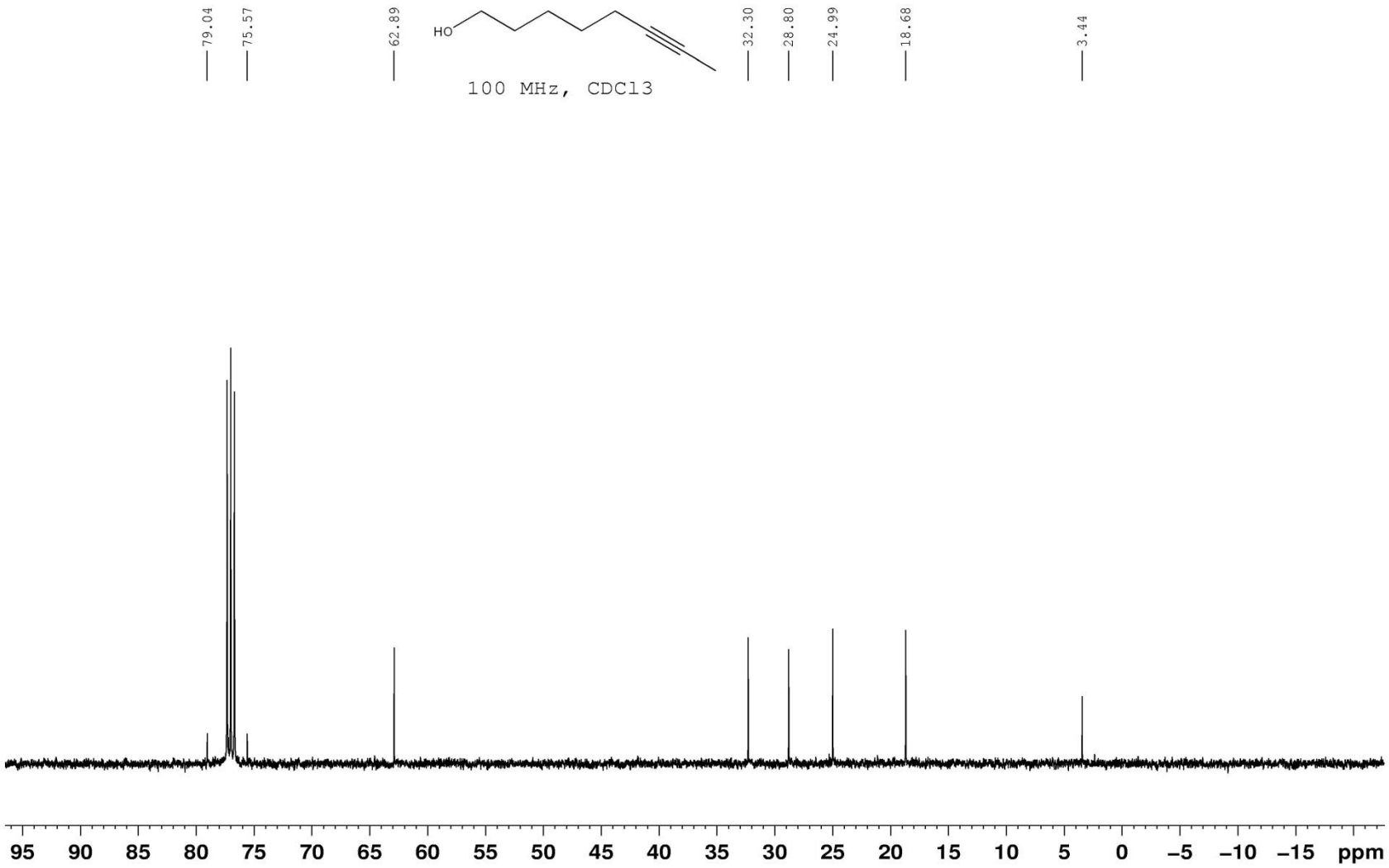

HO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.97
2.83
5.52
3.18

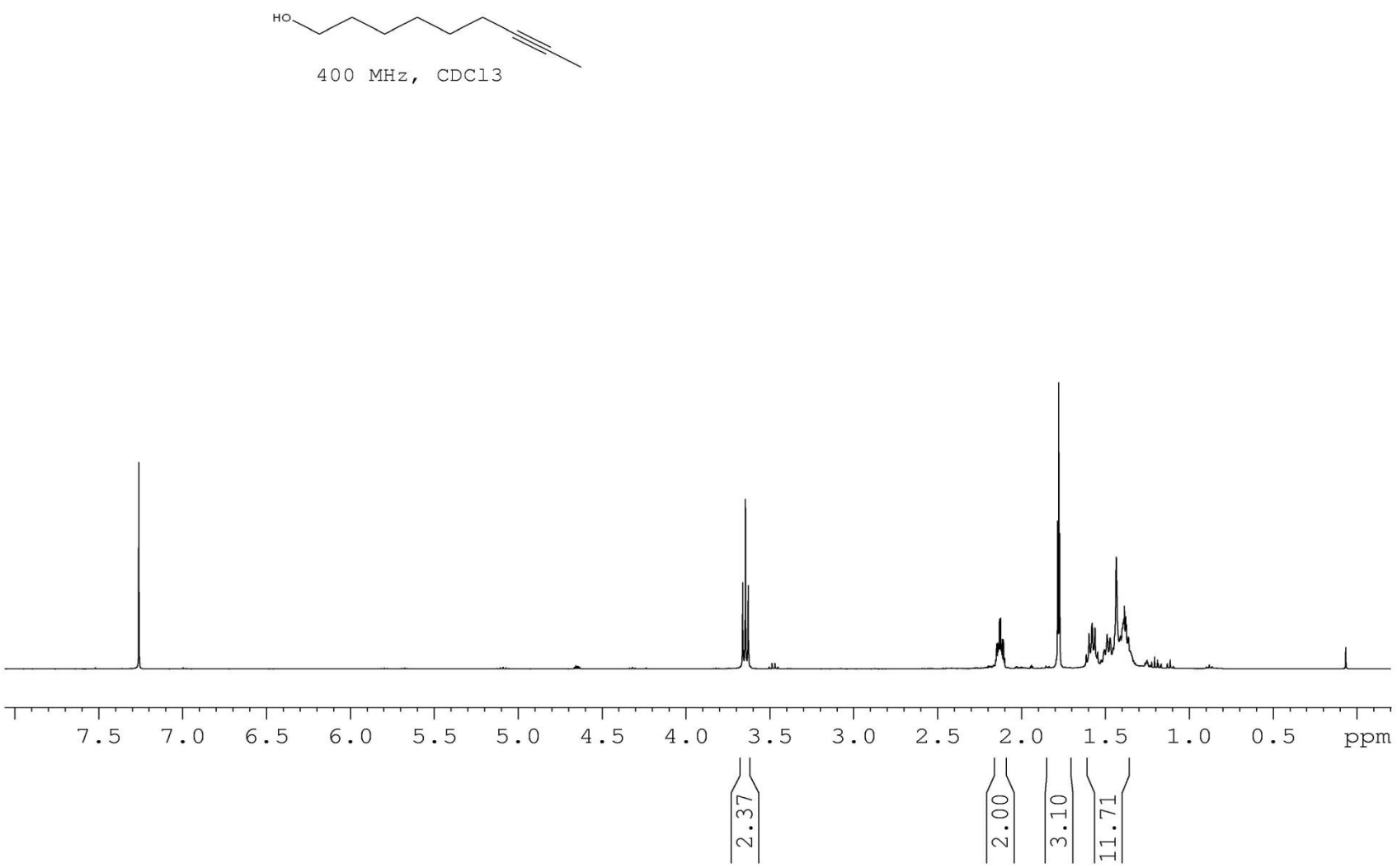

78.95
75.80
67.74
HO
38.40
25.24
23.53
18.68
3.42
100 MHz, CDCl3
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
ppm

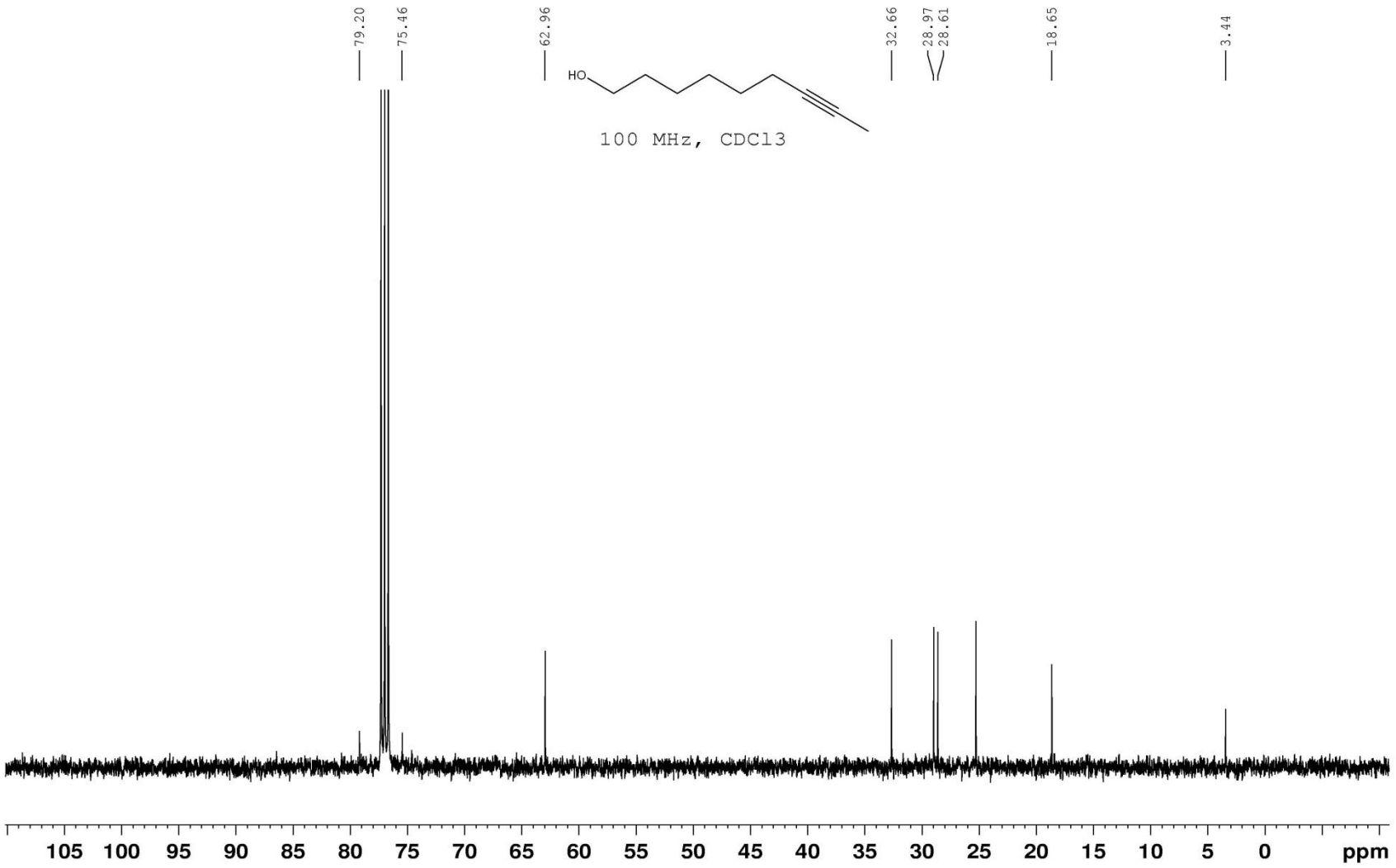


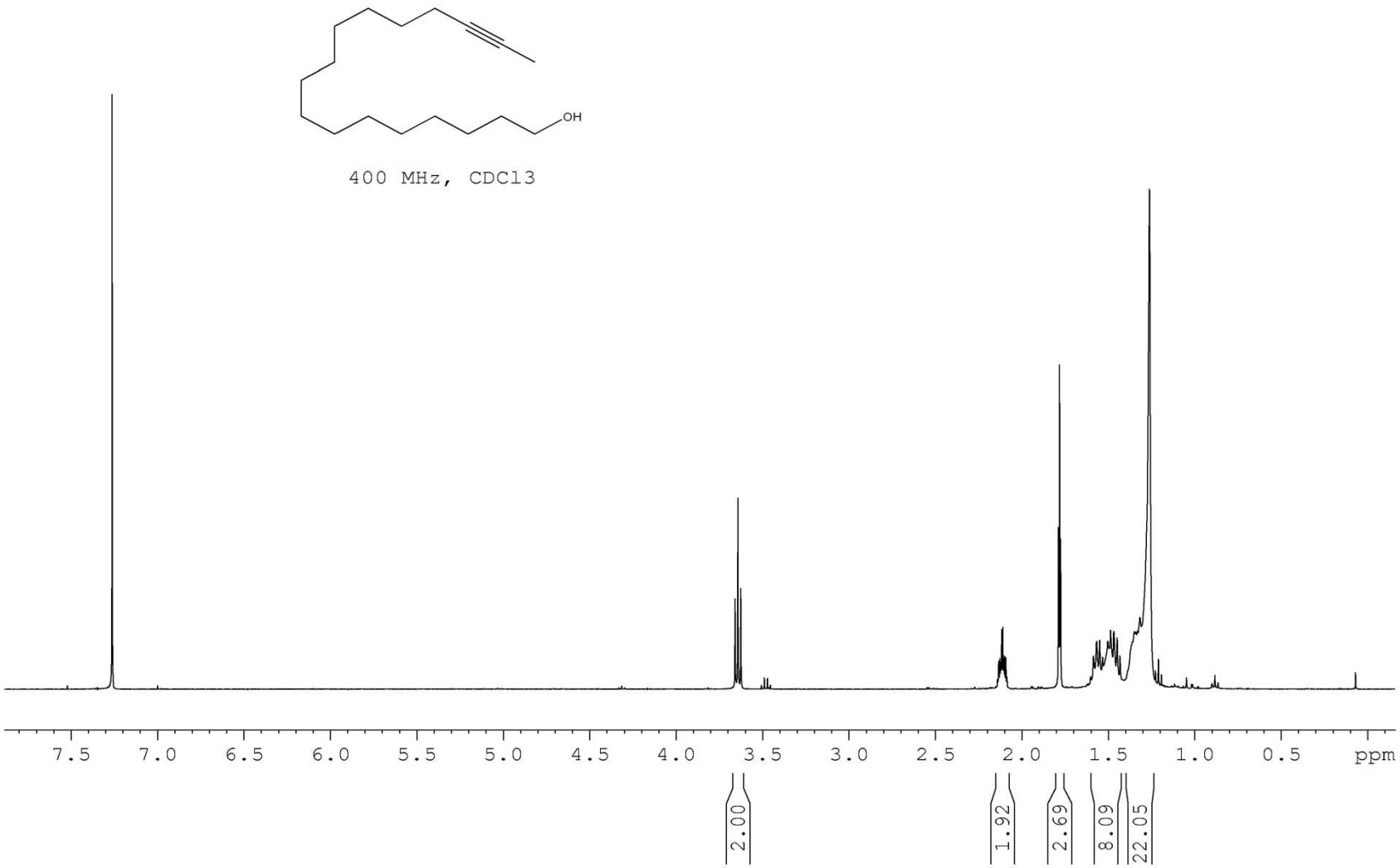
400 MHz, CDCl3

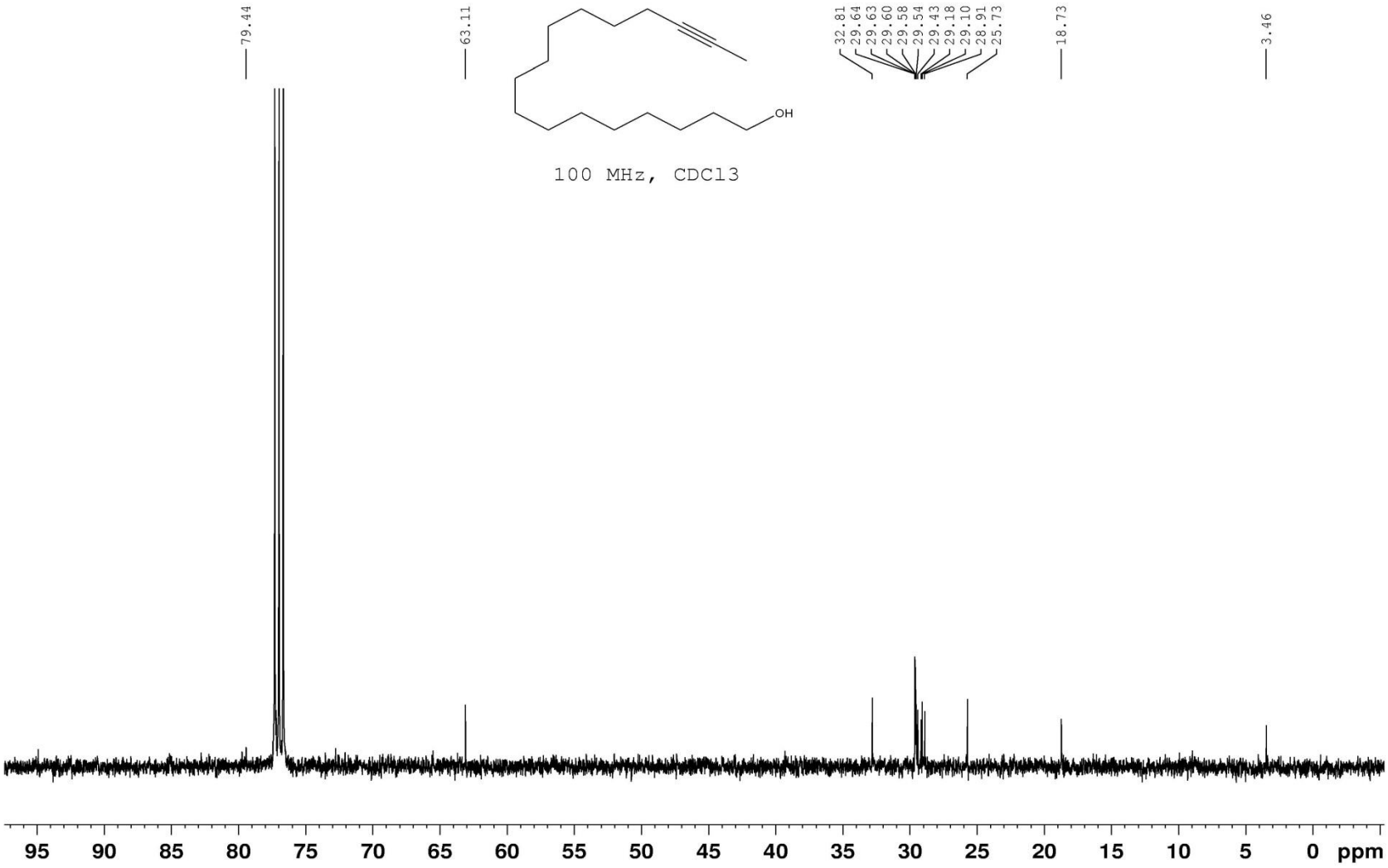


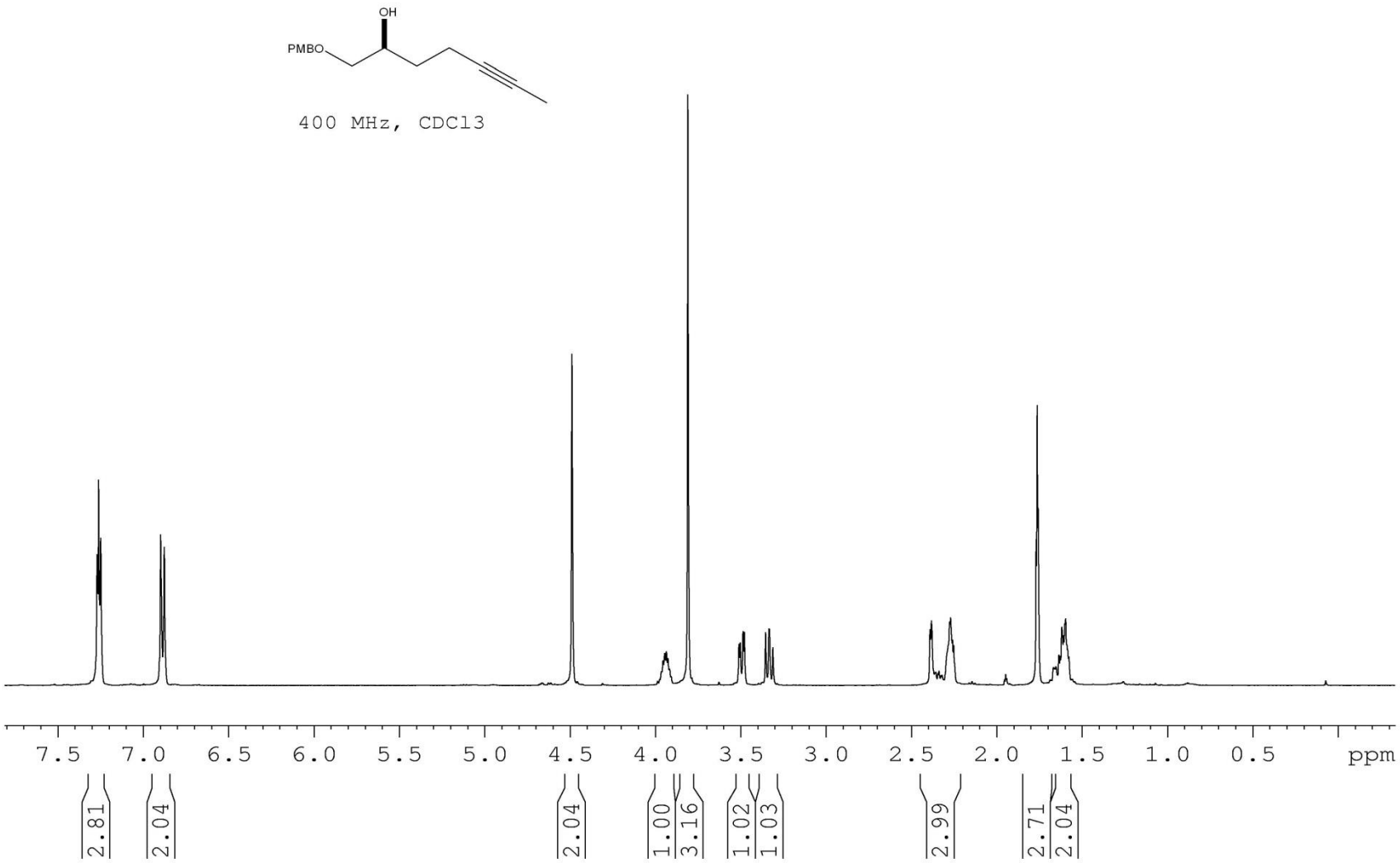

79.04
75.57
62.89
HO
32.30
28.80
24.99
18.68
3.44
100 MHz, CDCl3
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 −5 −10 −15 ppm

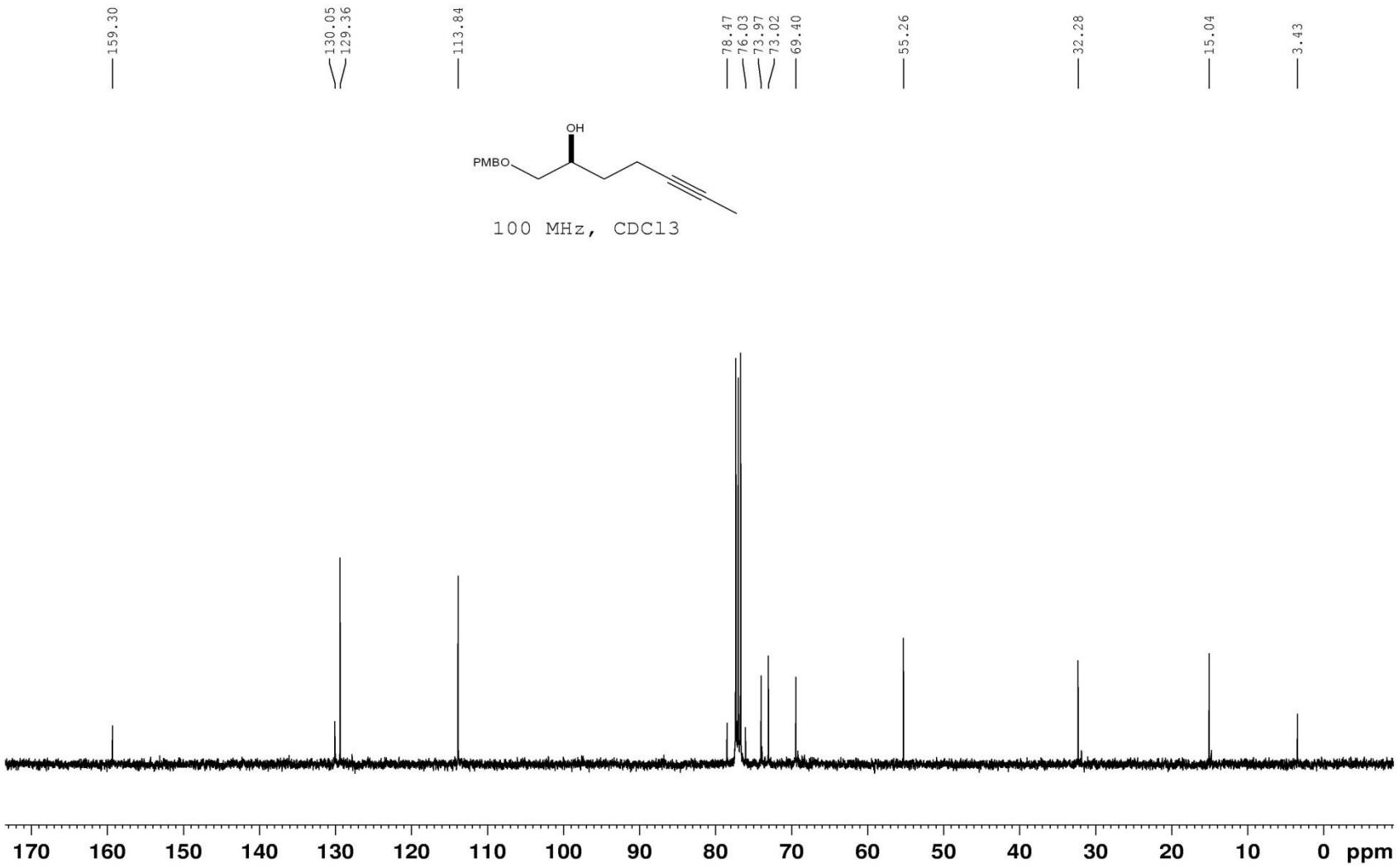

HO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.37
2.00
3.10
11.71

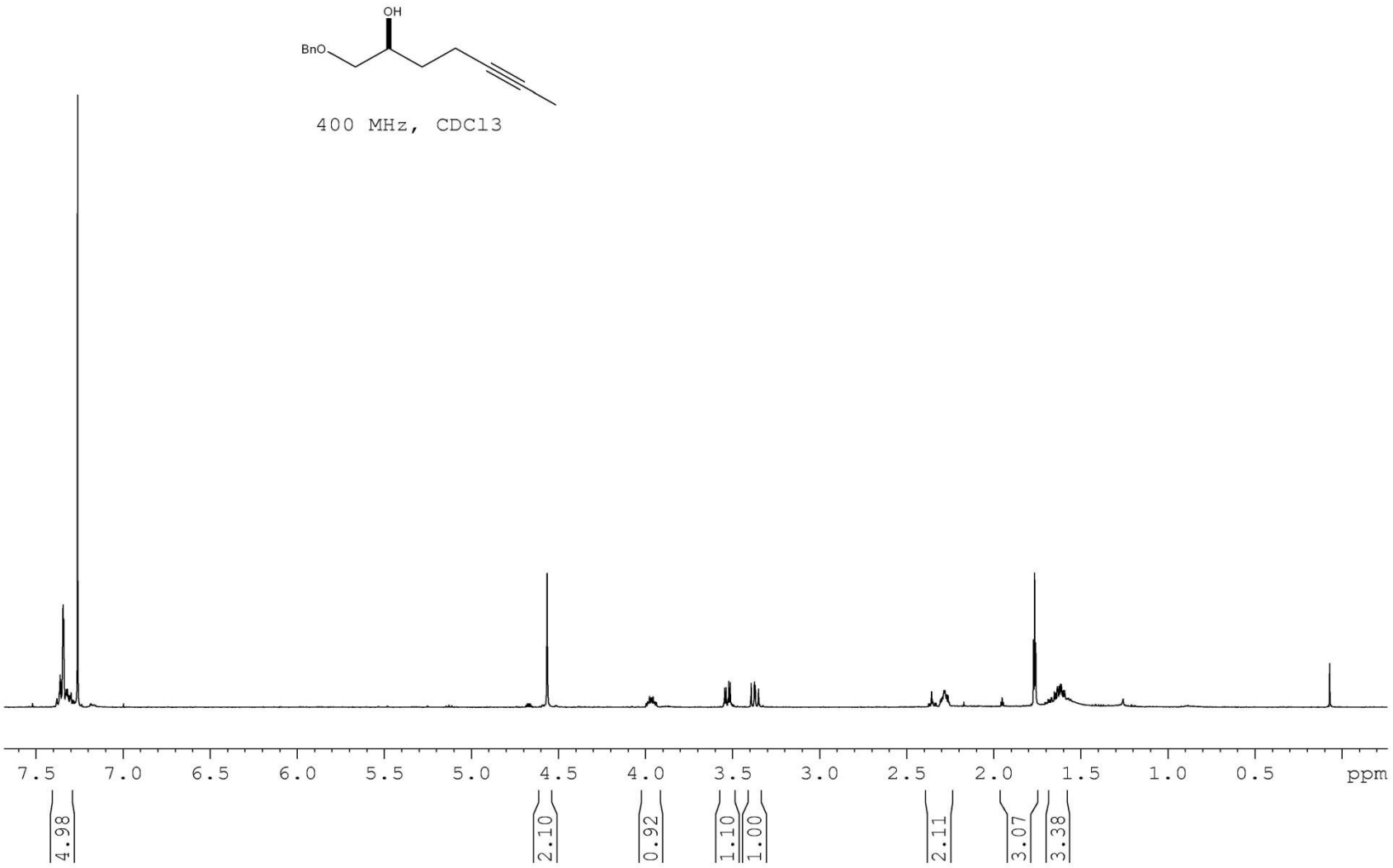

79.20
75.46
62.96
32.66
28.97
28.61
18.65
3.44
HO
100 MHz, CDCl3
105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 ppm

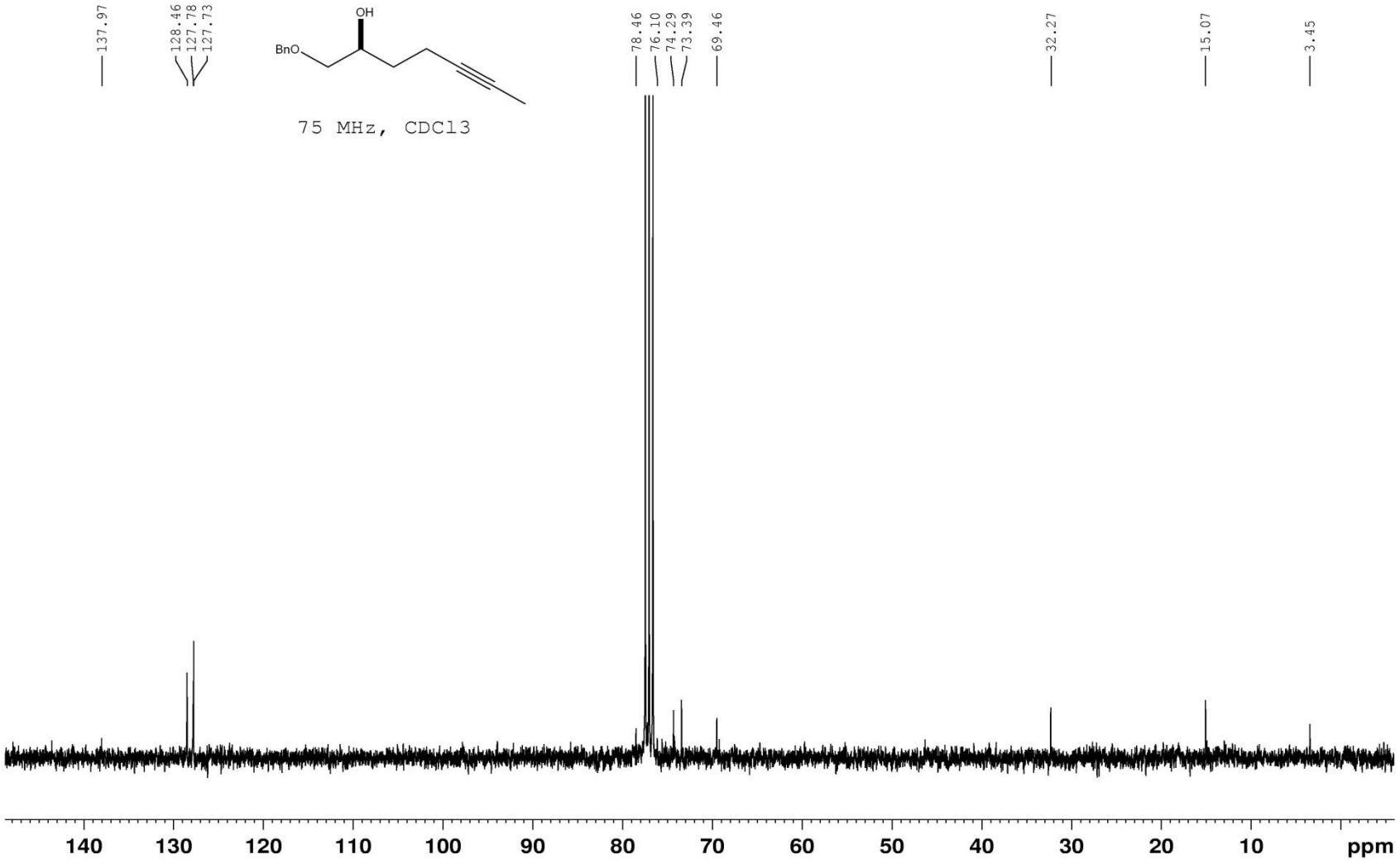

OH
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.92
2.69
8.09
22.05


79.44
63.11
32.81
29.64
29.63
29.60
29.58
29.54
29.43
29.18
29.10
28.91
25.73
18.73
3.46
OH
100 MHz, CDCl3
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 ppm


OH
PMBO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.81
2.04
2.04
1.00
3.16
1.02
1.03
2.99
2.71
2.04

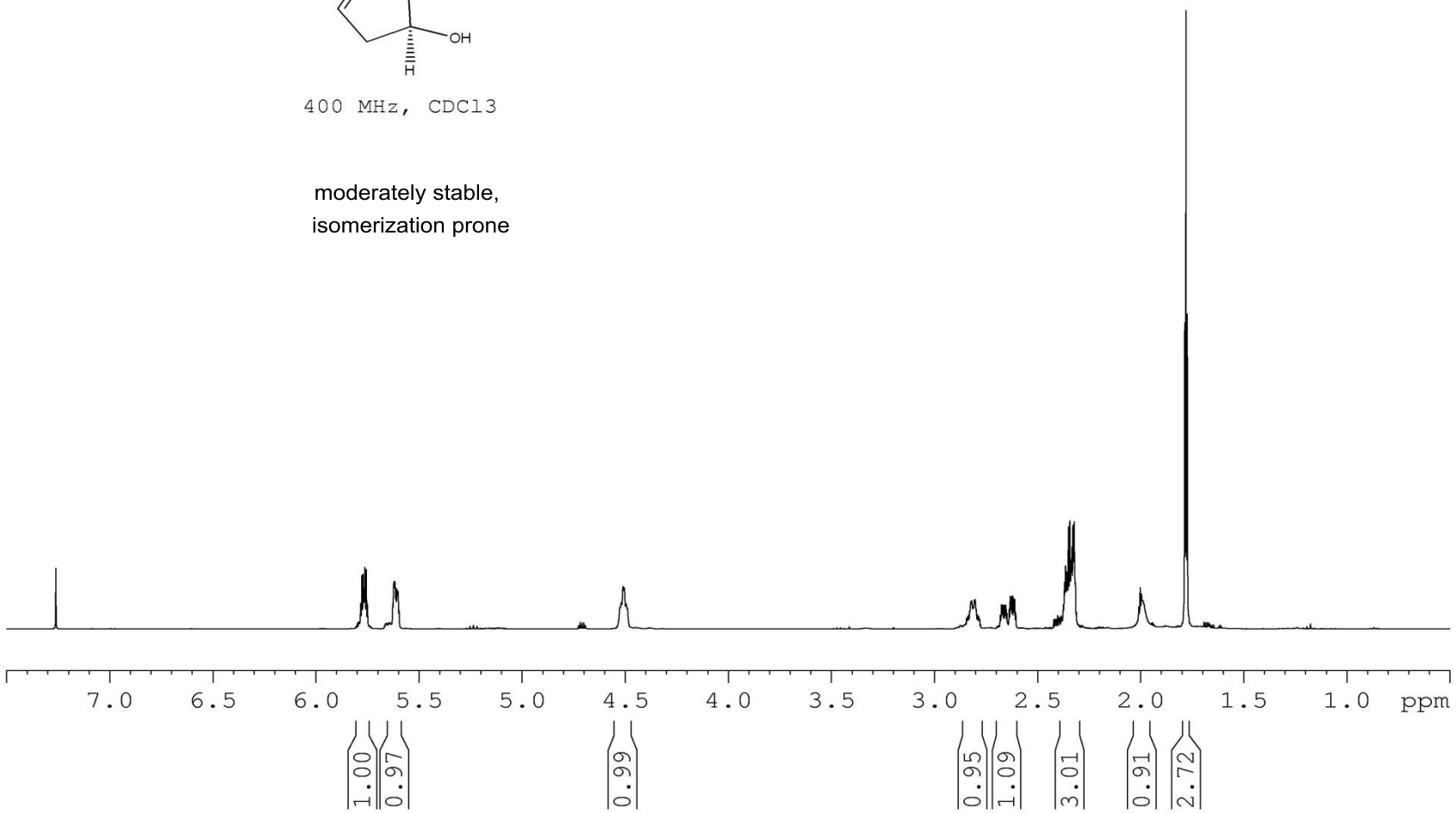

159.30
130.05
129.36
113.84
78.47
76.03
73.97
73.02
69.40
55.26
32.28
15.04
3.43
OH
PMBO
100 MHz, CDCl3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

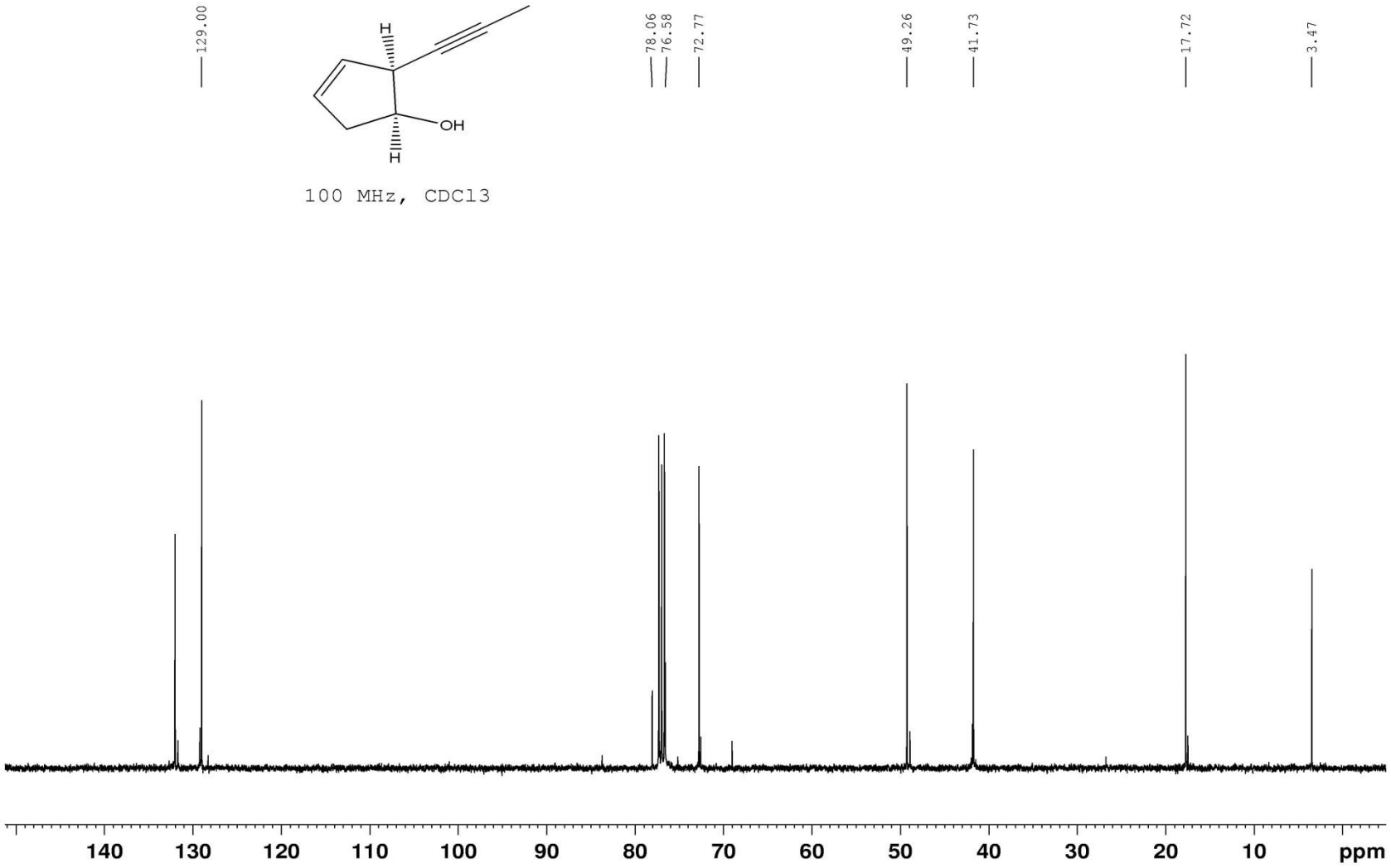

OH
BnO
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.98
2.10
0.92
1.10
1.00
2.11
3.07
3.38

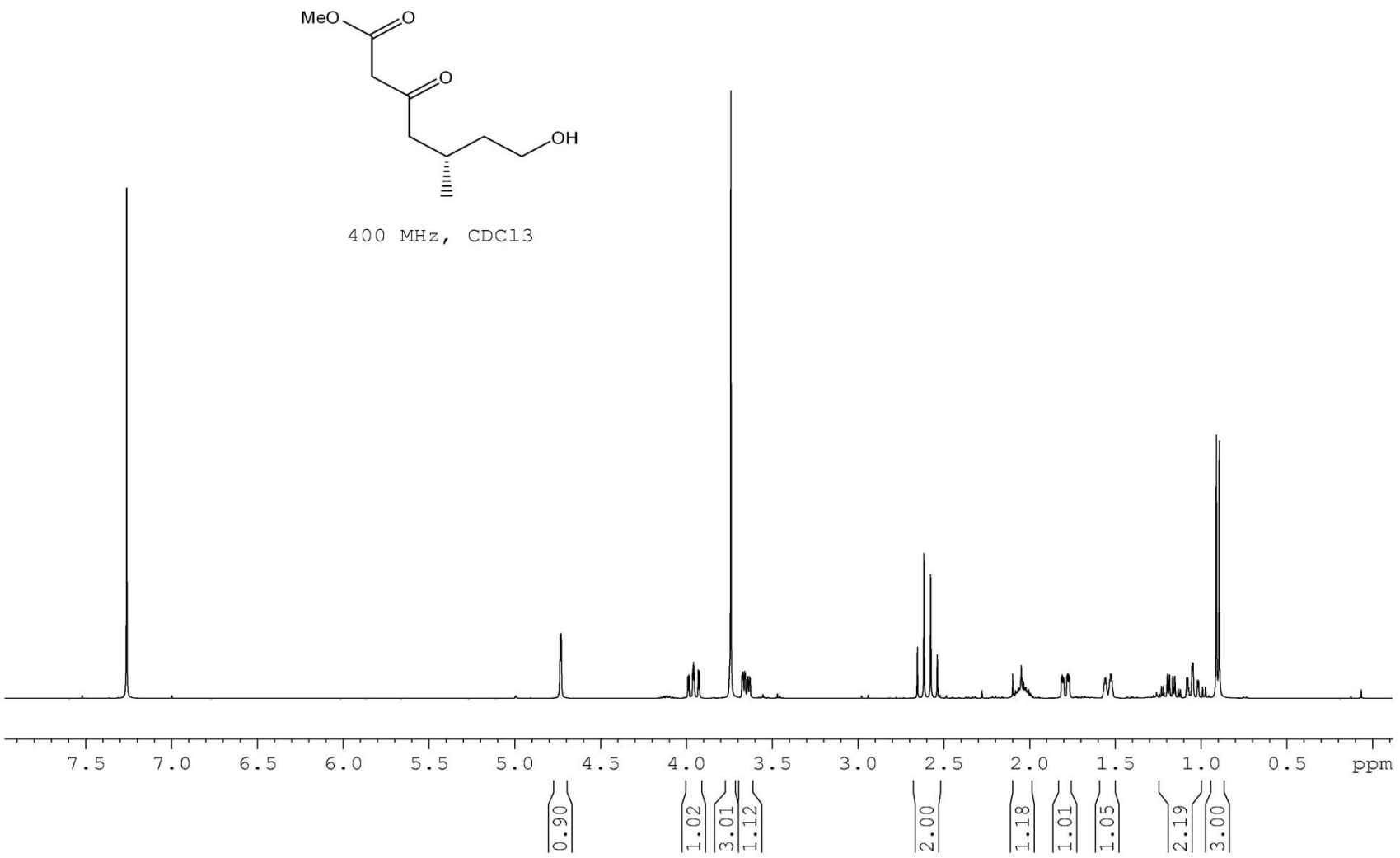

137.97
128.46
127.78
127.73
OH
BnO
75 MHz, CDCl3
78.46
76.10
74.29
73.39
69.46
32.27
15.07
3.45
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

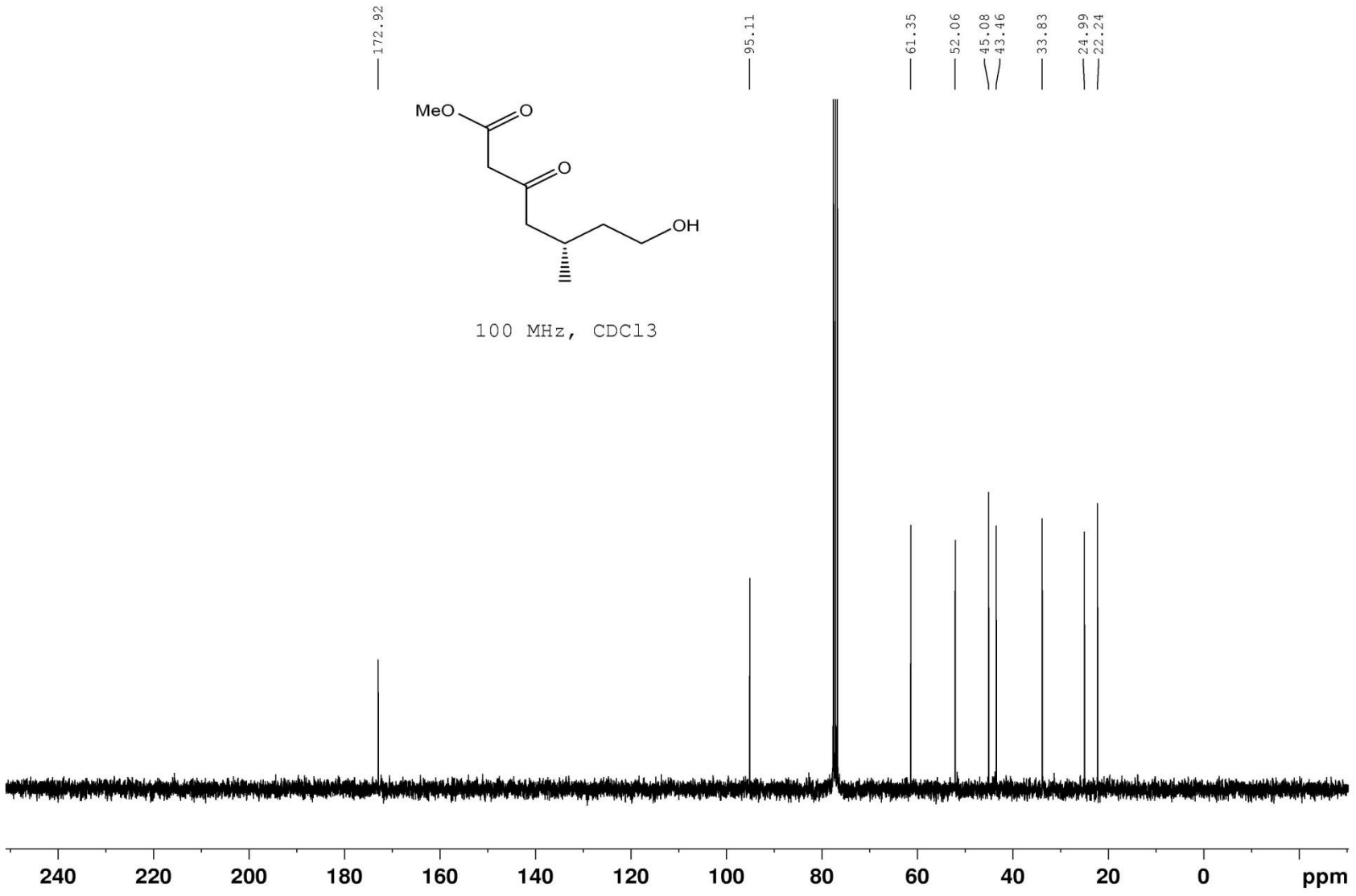
400 MHz, CDCl3

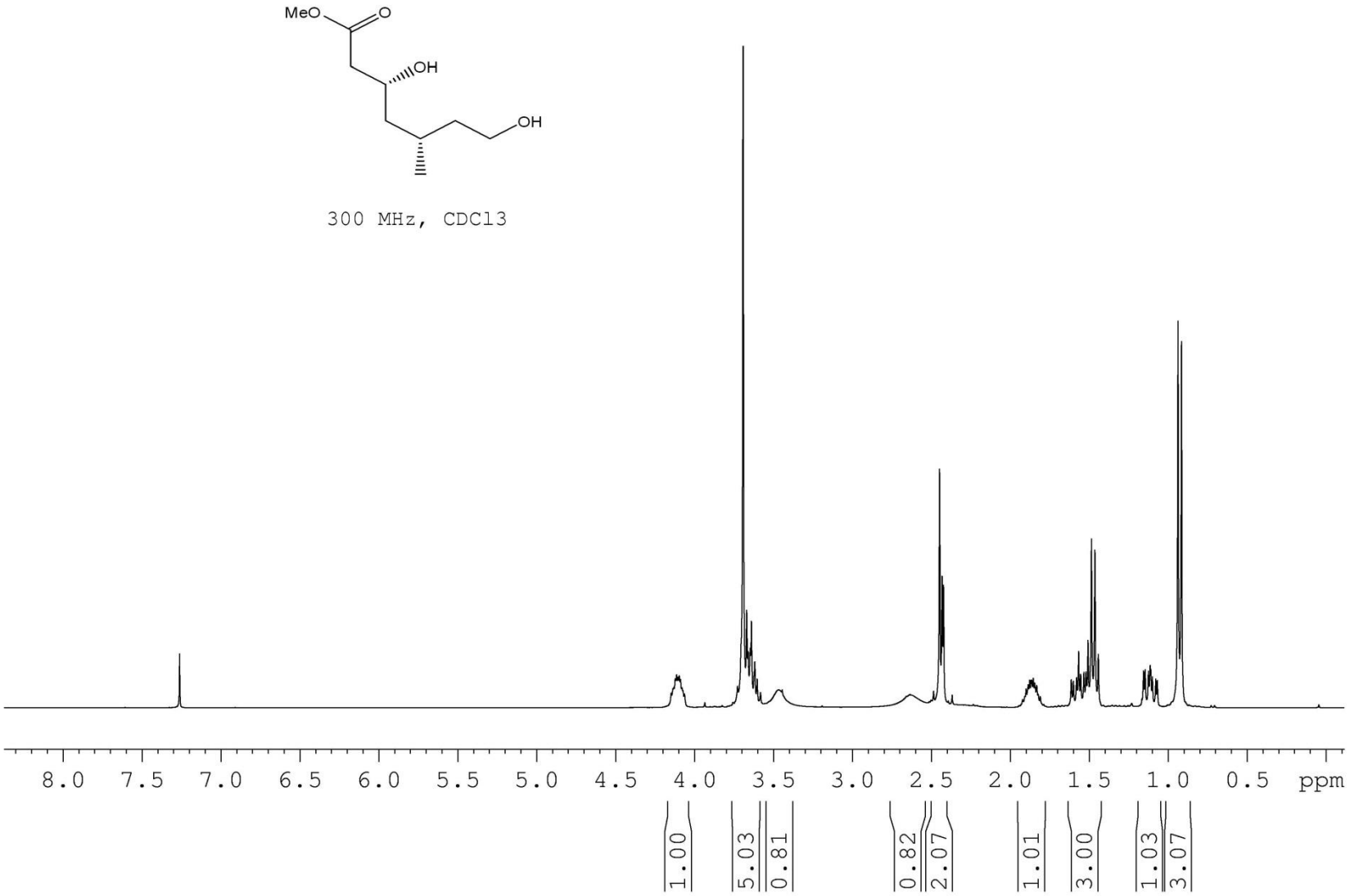
moderately stable,
isomerization prone

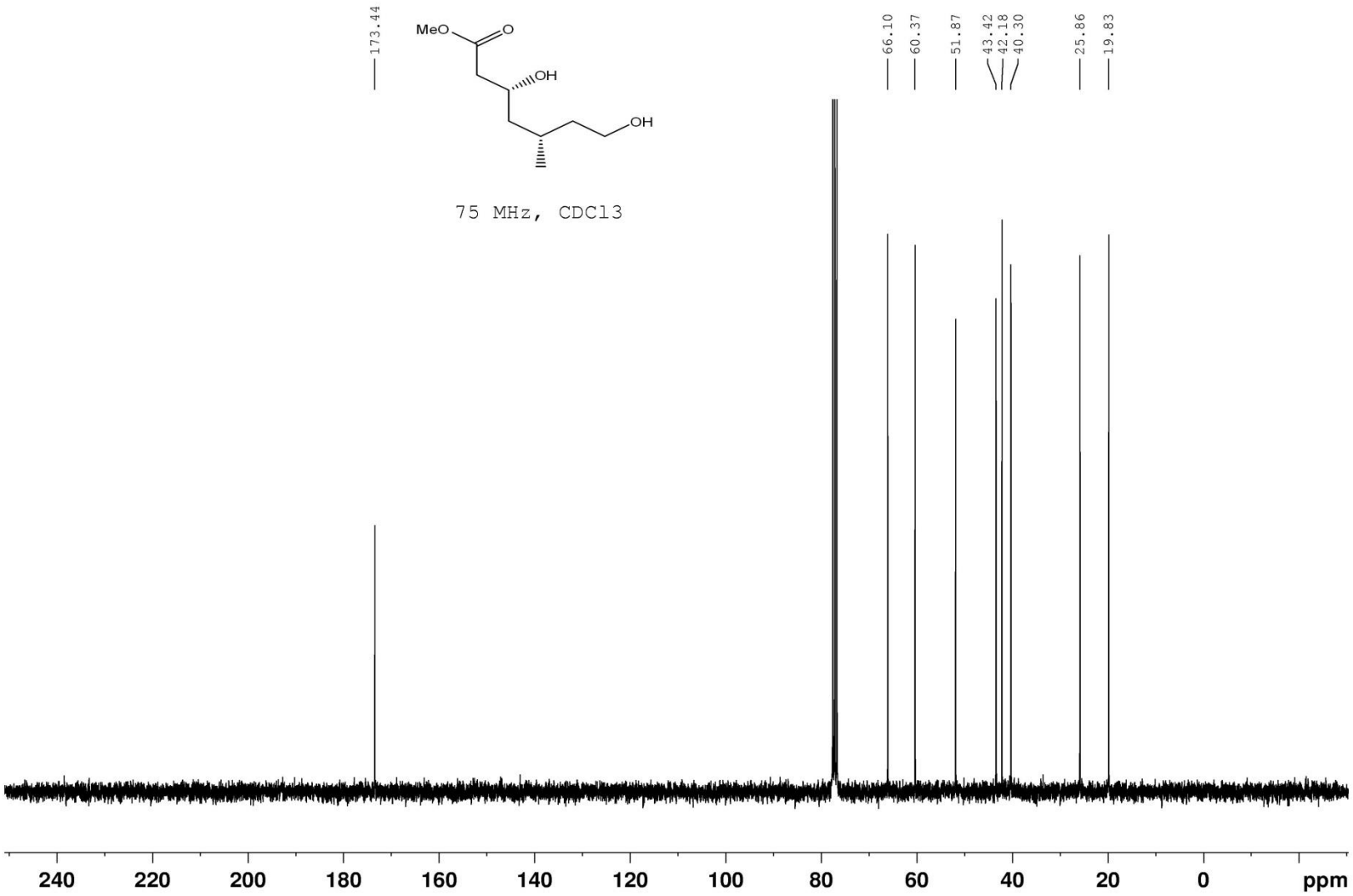


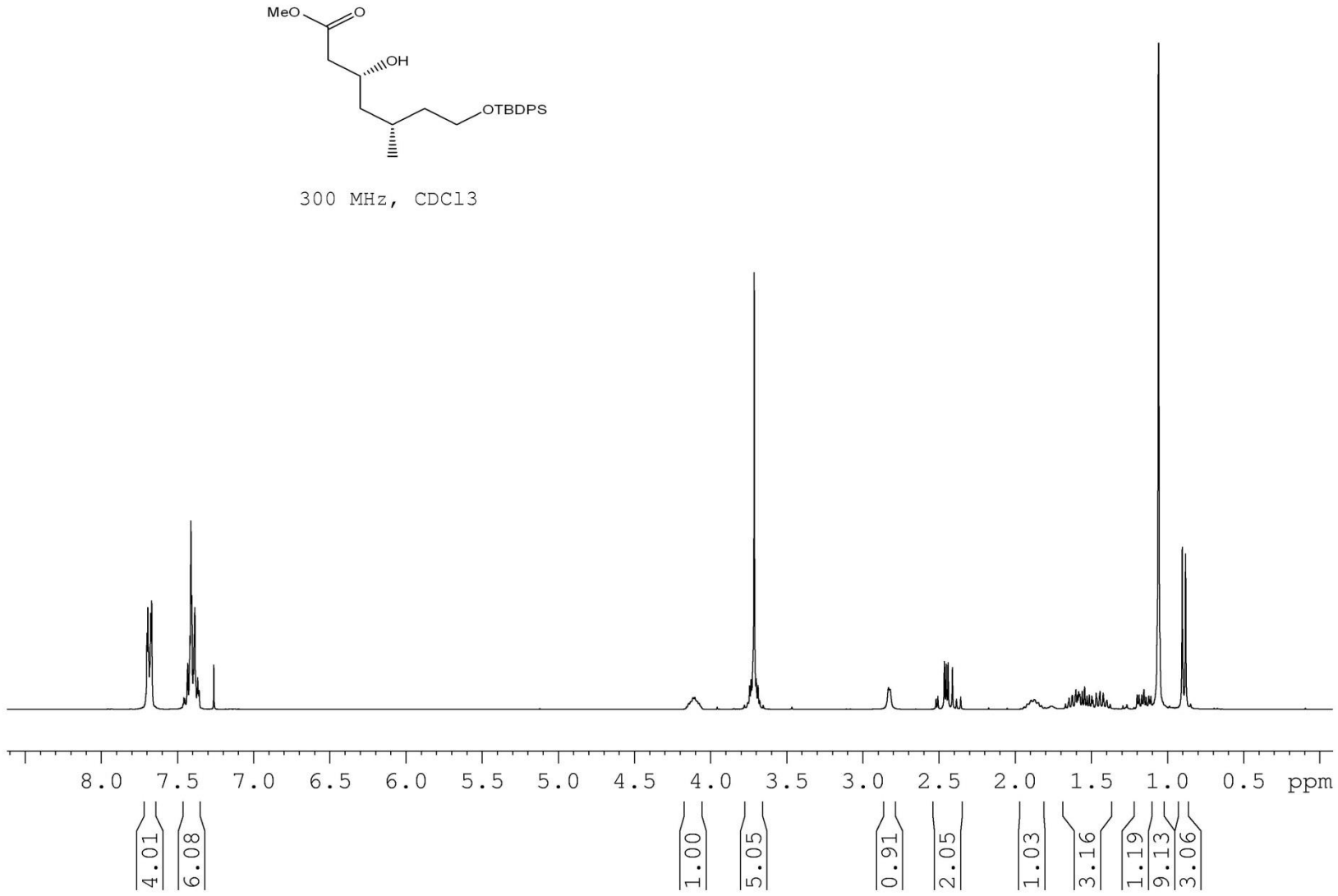

129.00
78.06
76.58
72.77
49.26
41.73
17.72
3.47
H
OH
H
100 MHz, CDCl3
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

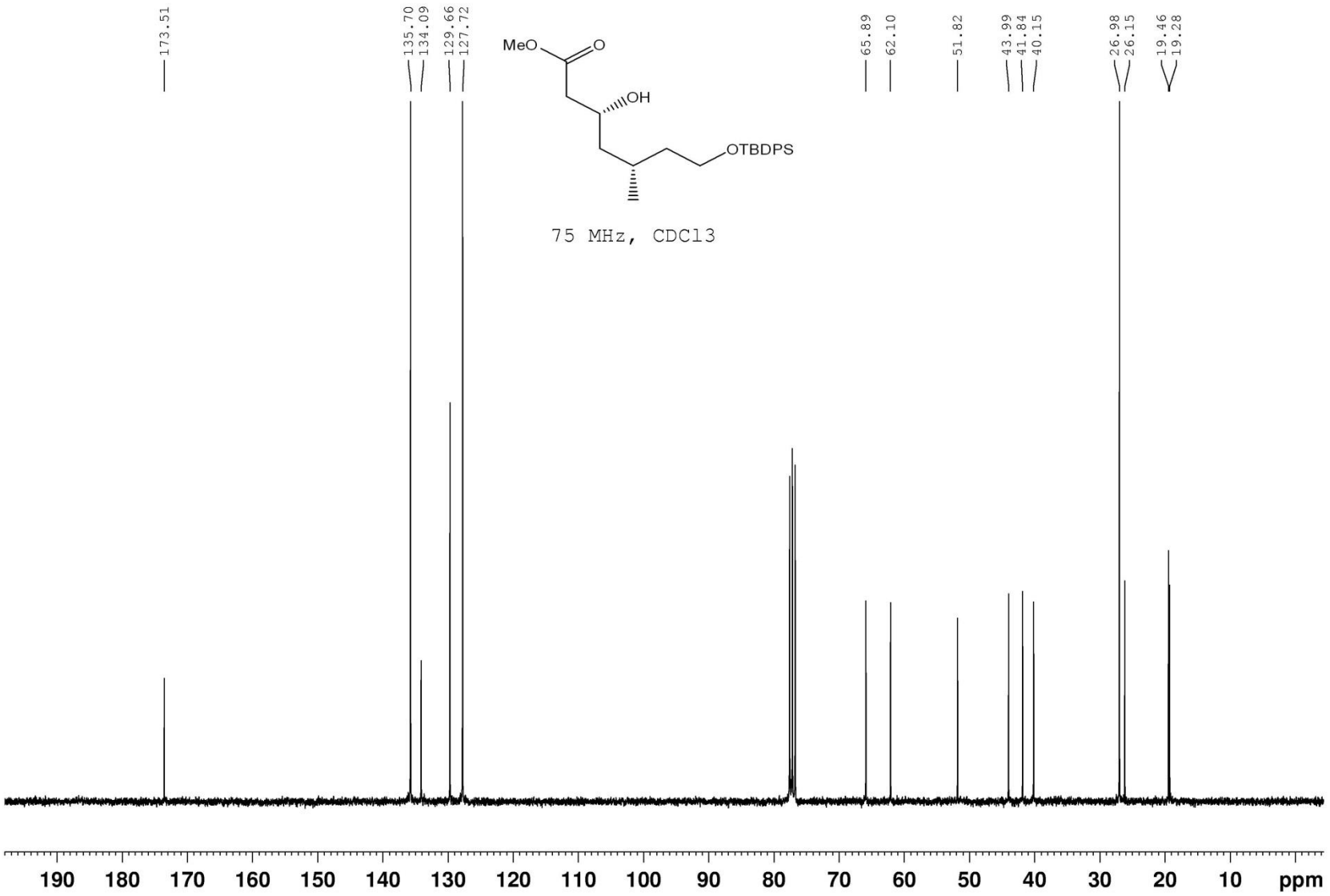

MeO
O
O
OH
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.90
1.02
3.01
1.12
2.00
1.18
1.01
1.05
2.19
3.00

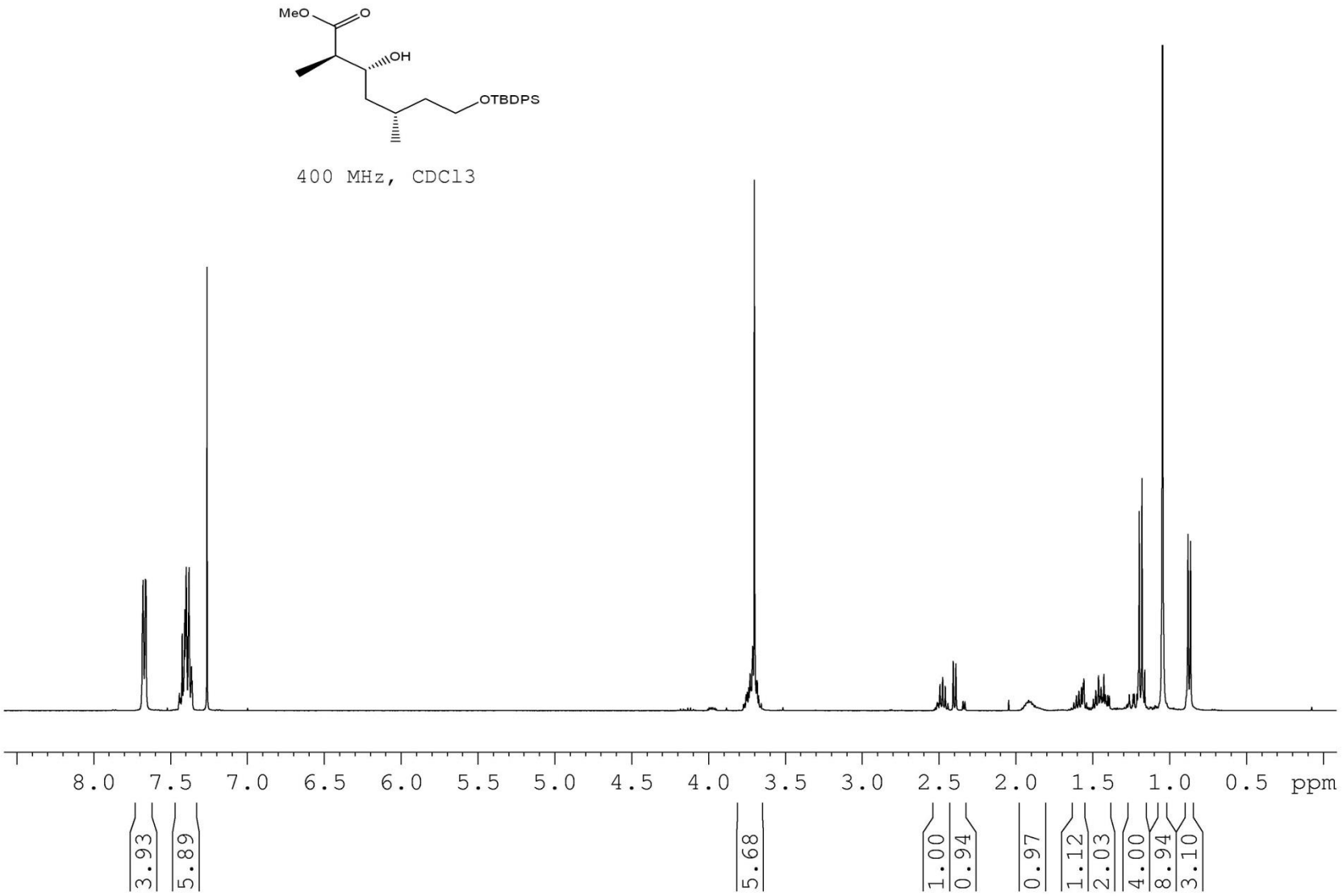

172.92
95.11
61.35
52.06
45.08
43.46
33.83
24.99
22.24
MeO
O
O
OH
100 MHz, CDCl3
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

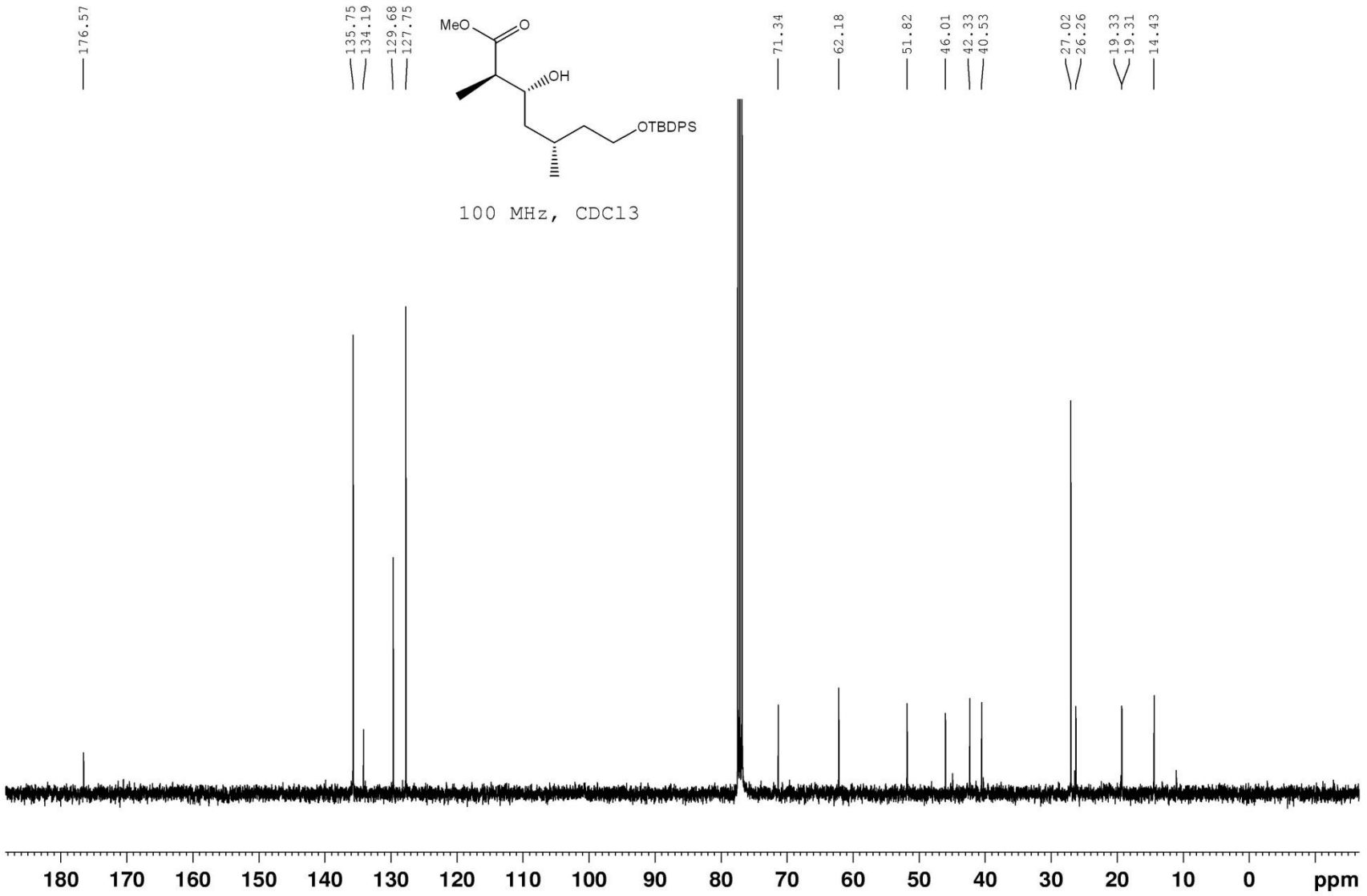

MeO
O
OH
OH
300 MHz, CDCl3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
5.03
0.81
0.82
2.07
1.01
3.00
1.03
3.07

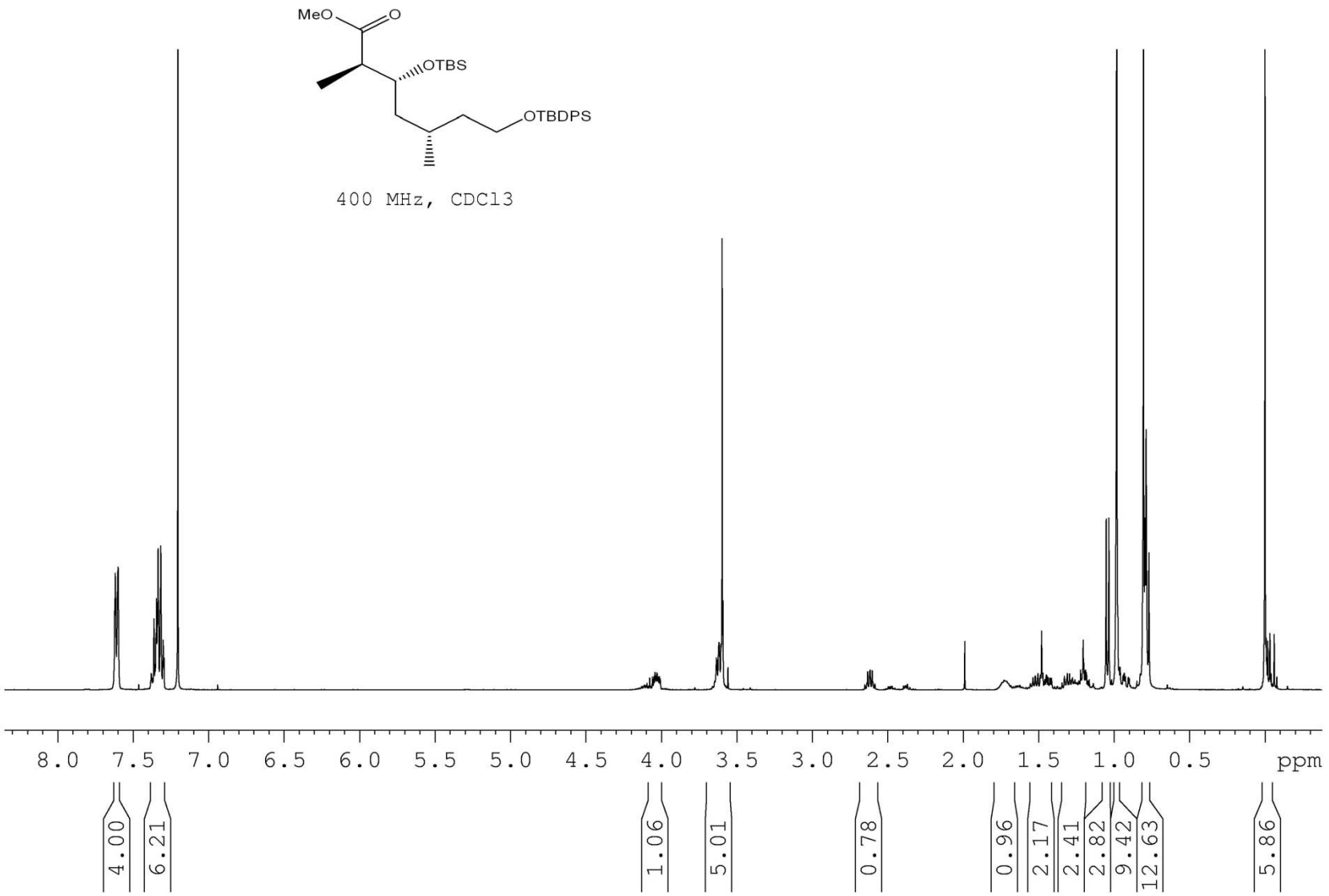

173.44
MeO
O
OH
OH
66.10
60.37
51.87
43.42
42.18
40.30
25.86
19.83
75 MHz, CDCl3
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

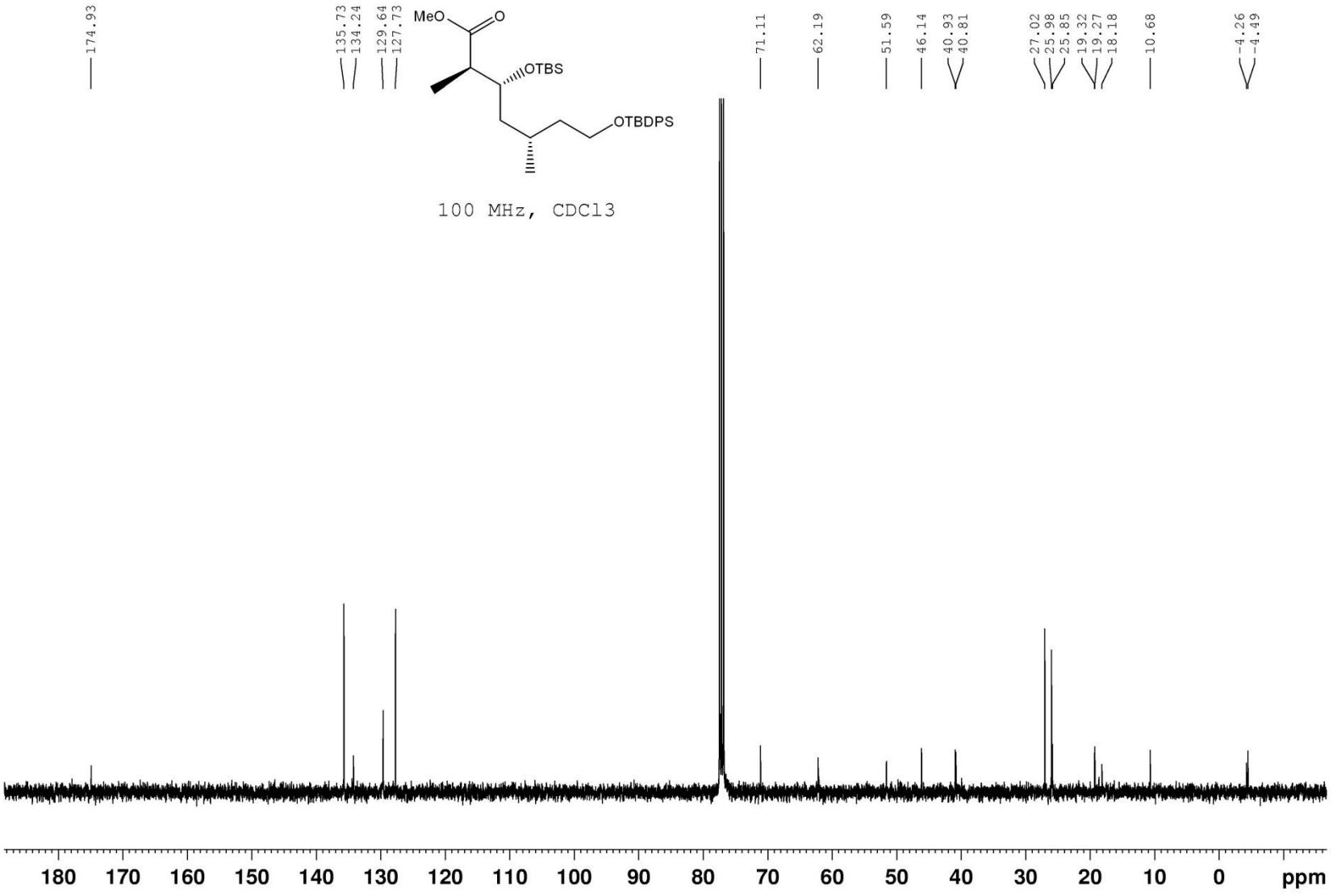

MeO
O
OH
OTBDPS
300 MHz, CDCl3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.01
6.08
1.00
5.05
0.91
2.05
1.03
3.16
1.19
9.13
3.06

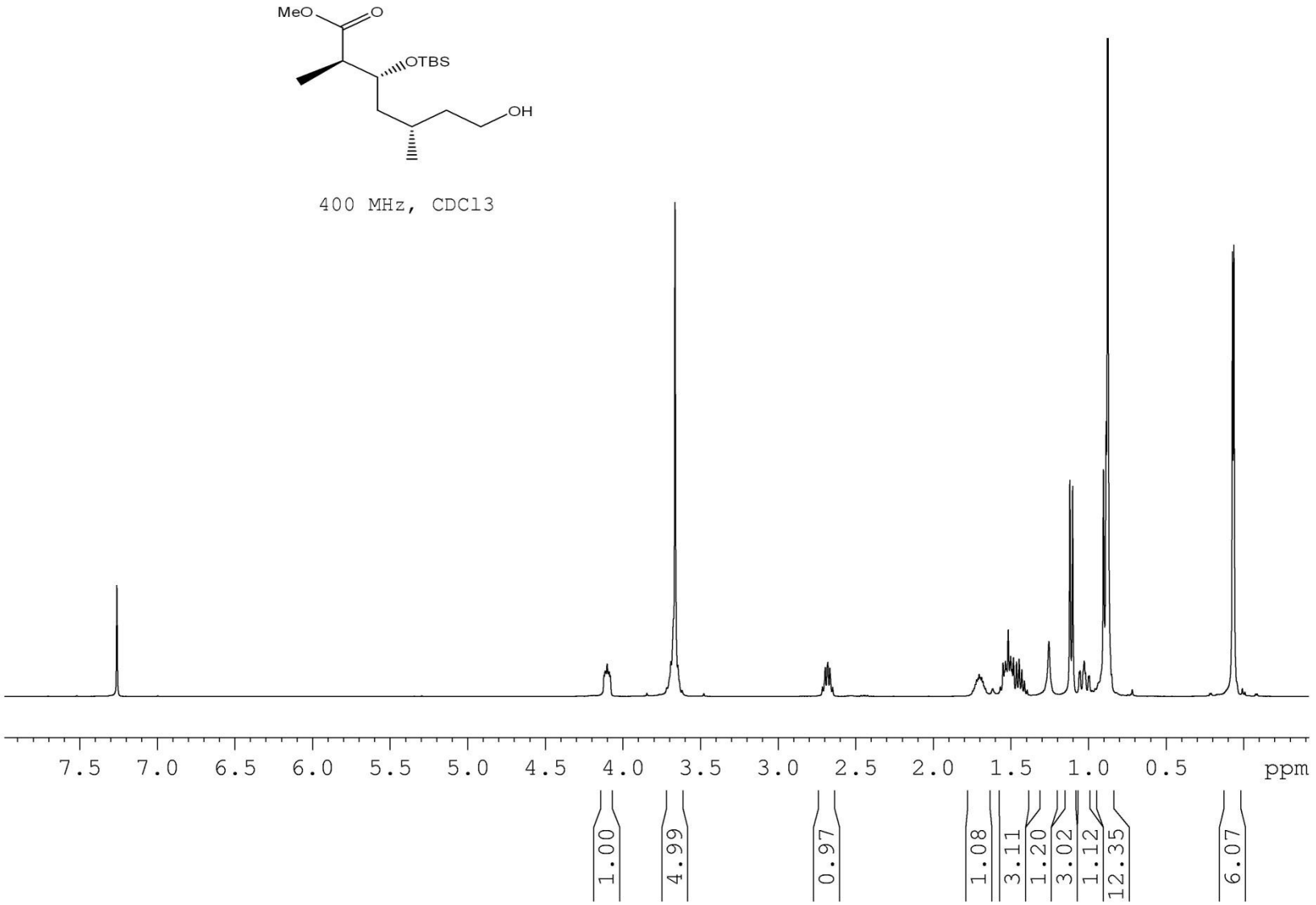

173.51
135.70
134.09
129.66
127.72
65.89
62.10
51.82
43.99
41.84
40.15
26.98
26.15
19.46
19.28
MeO
O
OH
OTBDPS
75 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

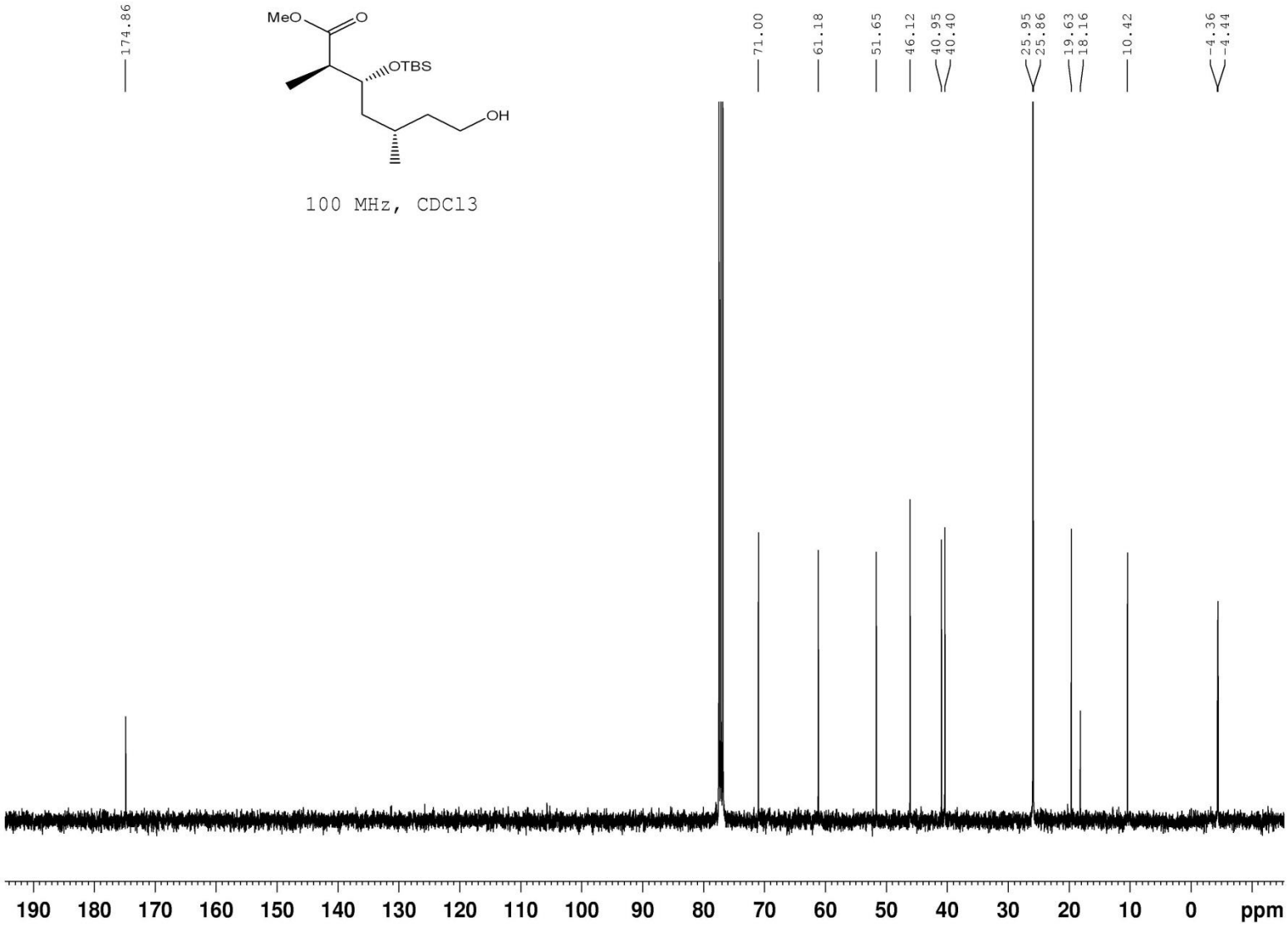

MeO
O
OH
OTBDPS
400 MHz, CDCl3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.93
5.89
5.68
1.00
0.94
0.97
1.12
2.03
4.00
8.94
3.10

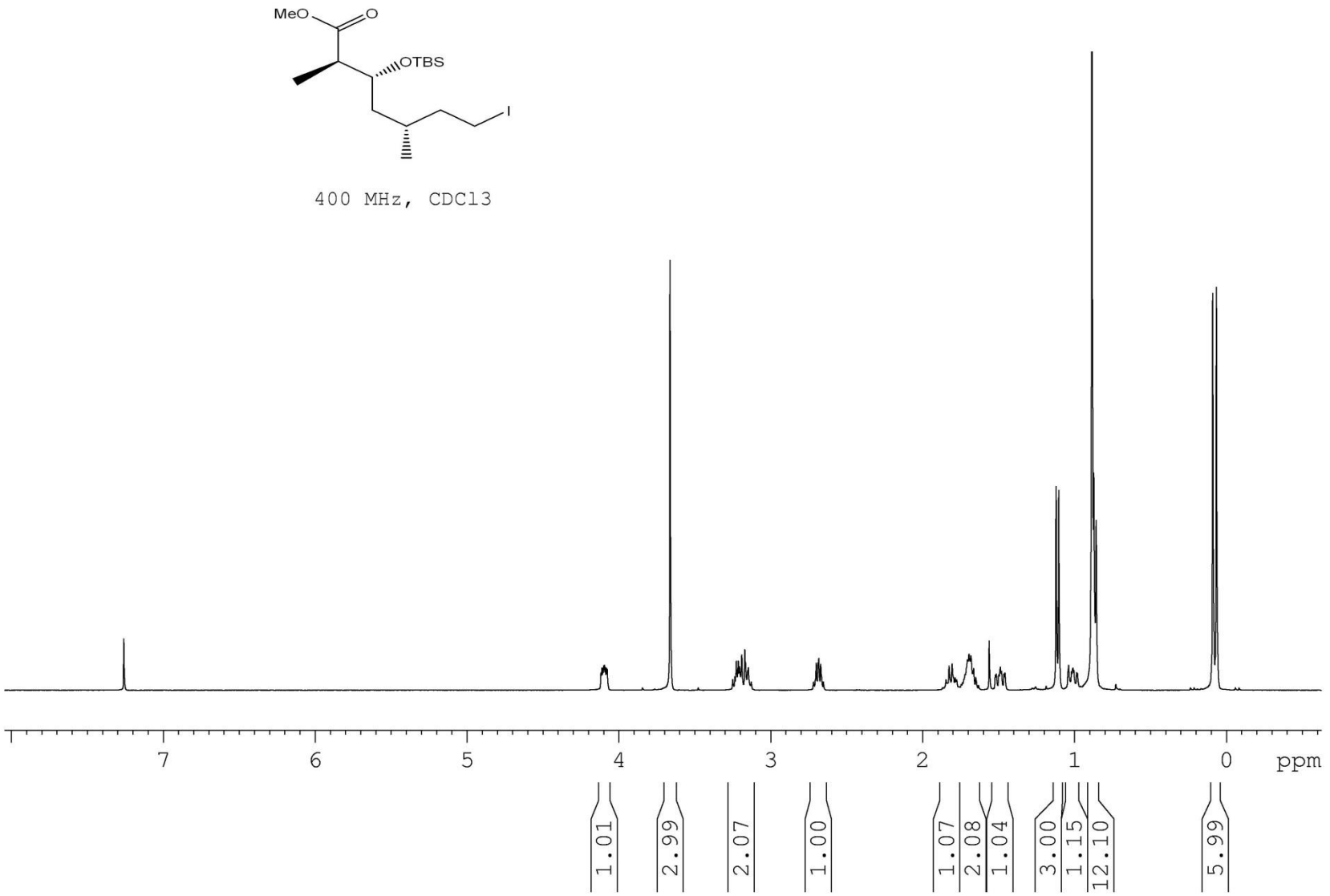

176.57
135.75
134.19
129.68
127.75
71.34
62.18
51.82
46.01
42.33
40.53
27.02
26.26
19.33
19.31
14.43
MeO
O
OH
OTBDPS
100 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

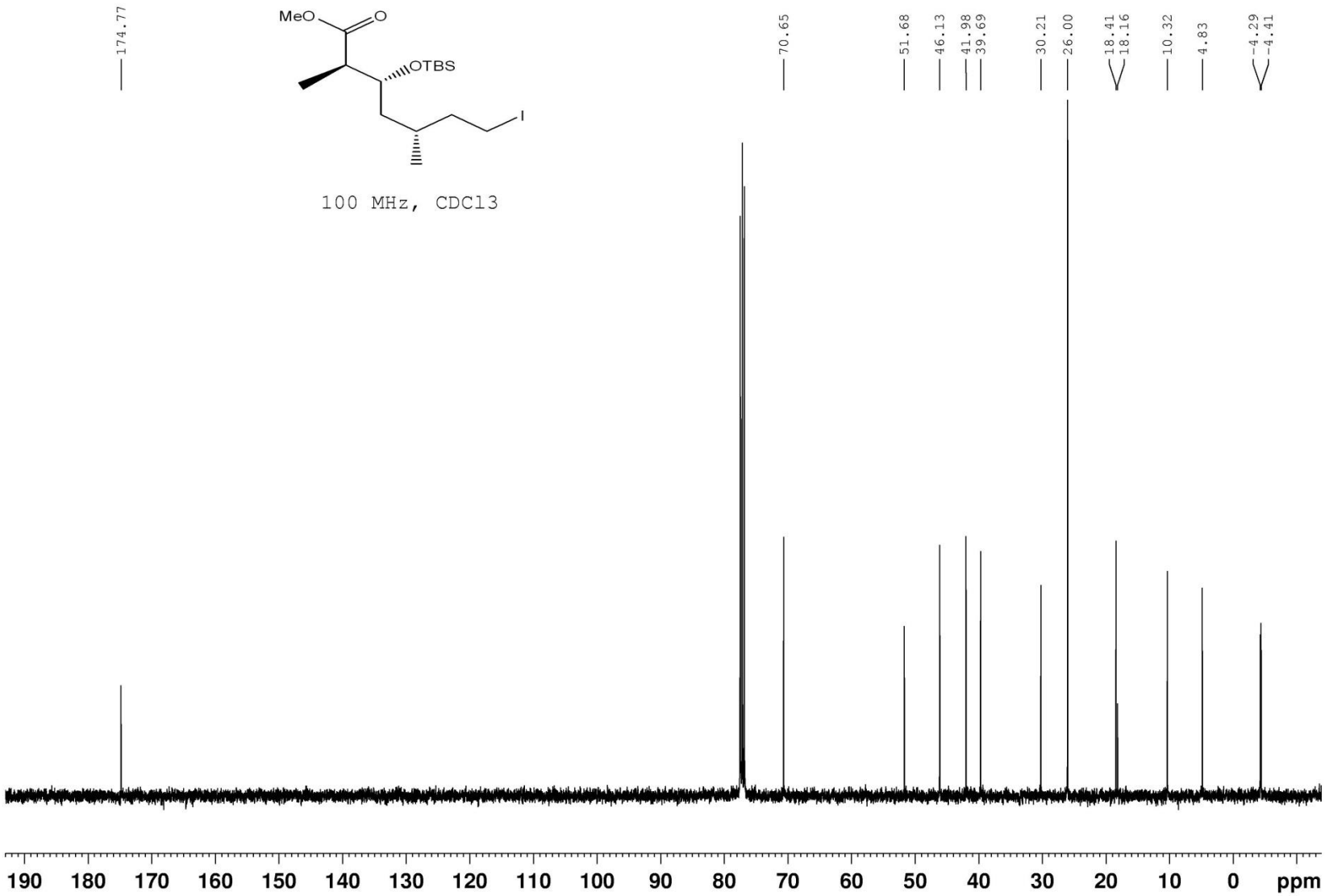

MeO
O
OTBS
OTBDPS
400 MHz, CDCl3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.00
6.21
1.06
5.01
0.78
0.96
2.17
2.41
2.82
9.42
12.63
5.86

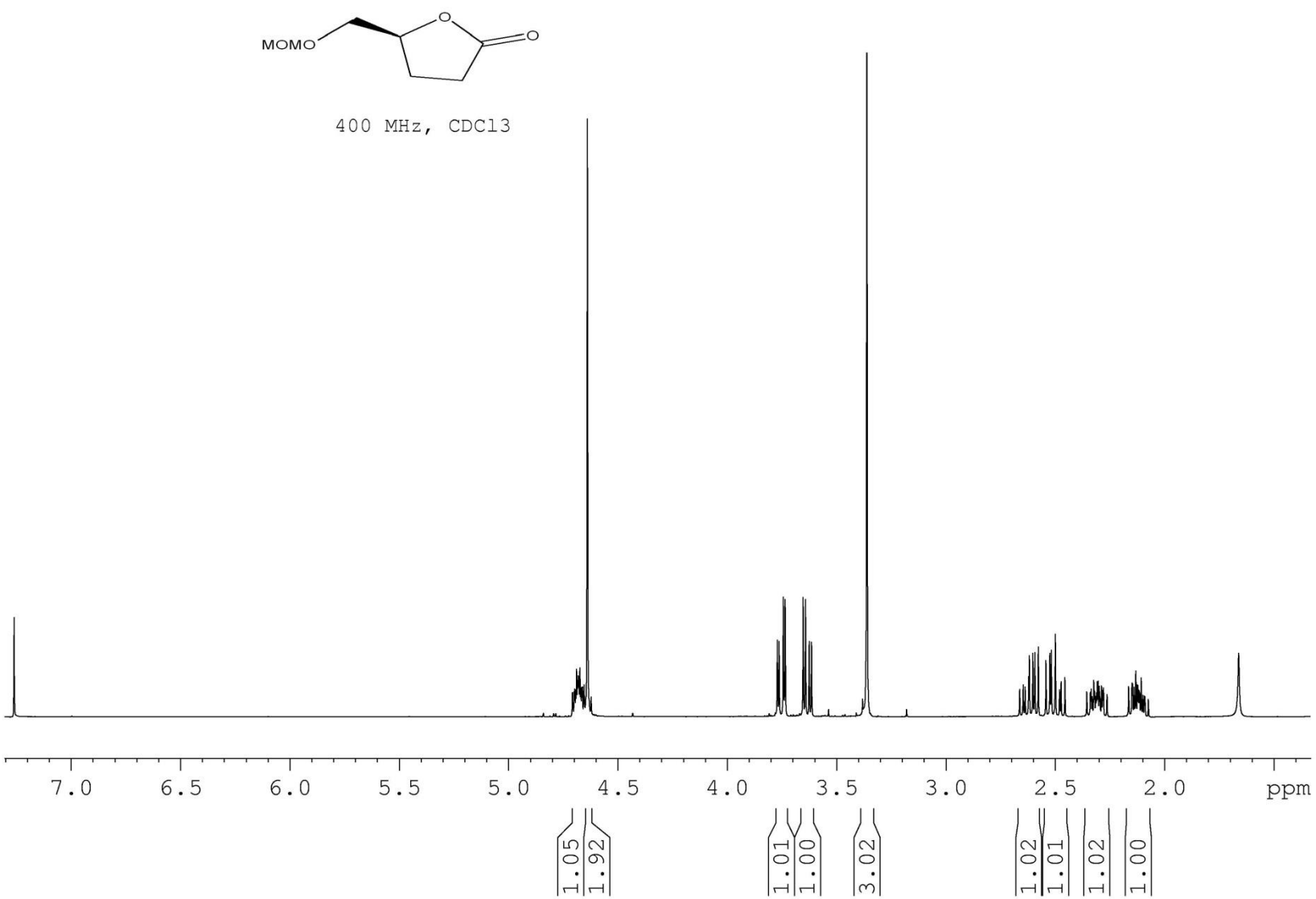

174.93
135.73
134.24
129.64
127.73
71.11
62.19
51.59
46.14
40.93
40.81
27.02
25.98
25.85
19.32
19.27
18.18
10.68
-4.26
-4.49
MeO
O
OTBS
OTBDPS
100 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

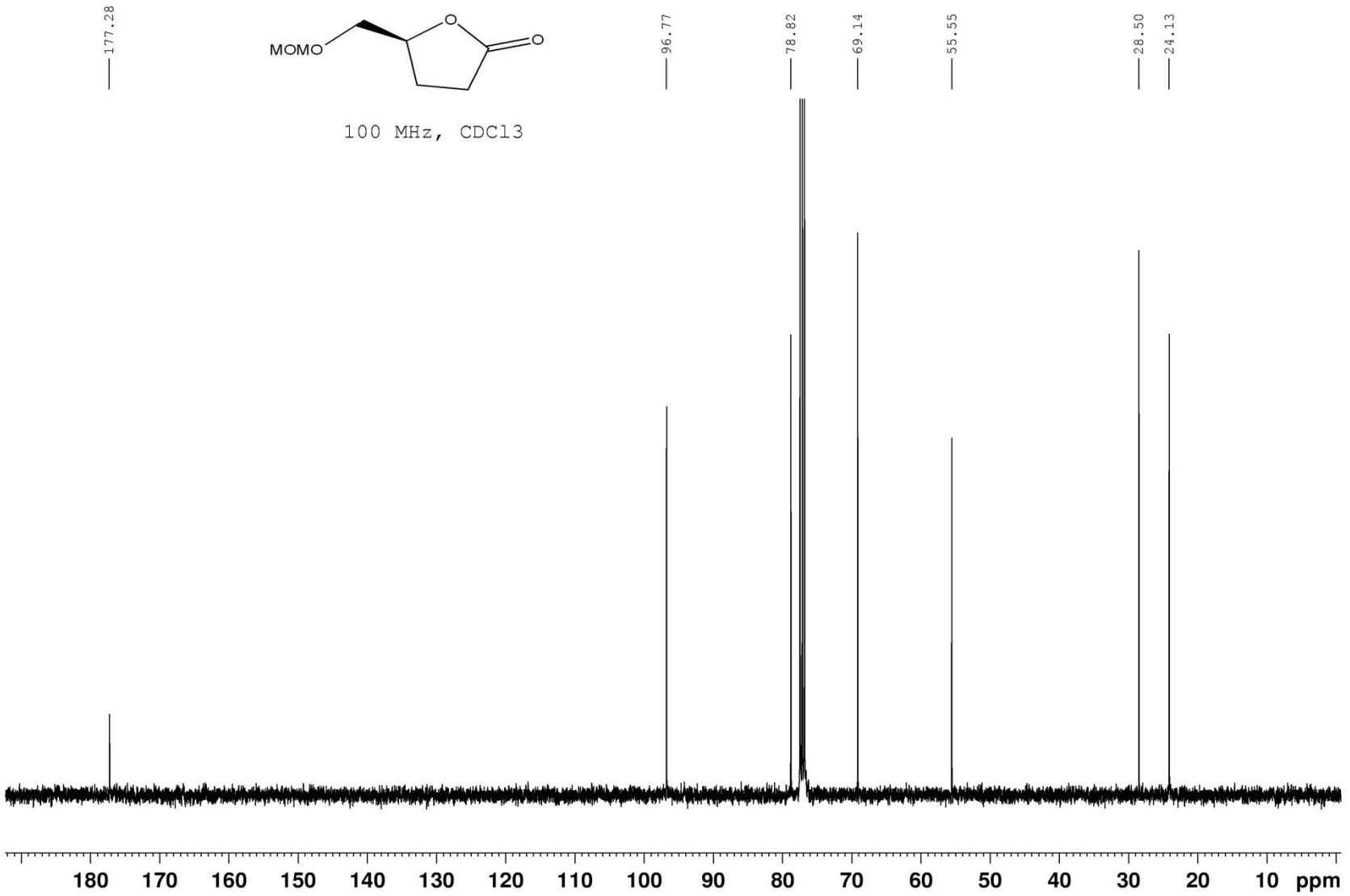

MeO
O
OTBS
OH
400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
4.99
0.97
1.08
3.11
1.20
3.02
1.12
12.35
6.07

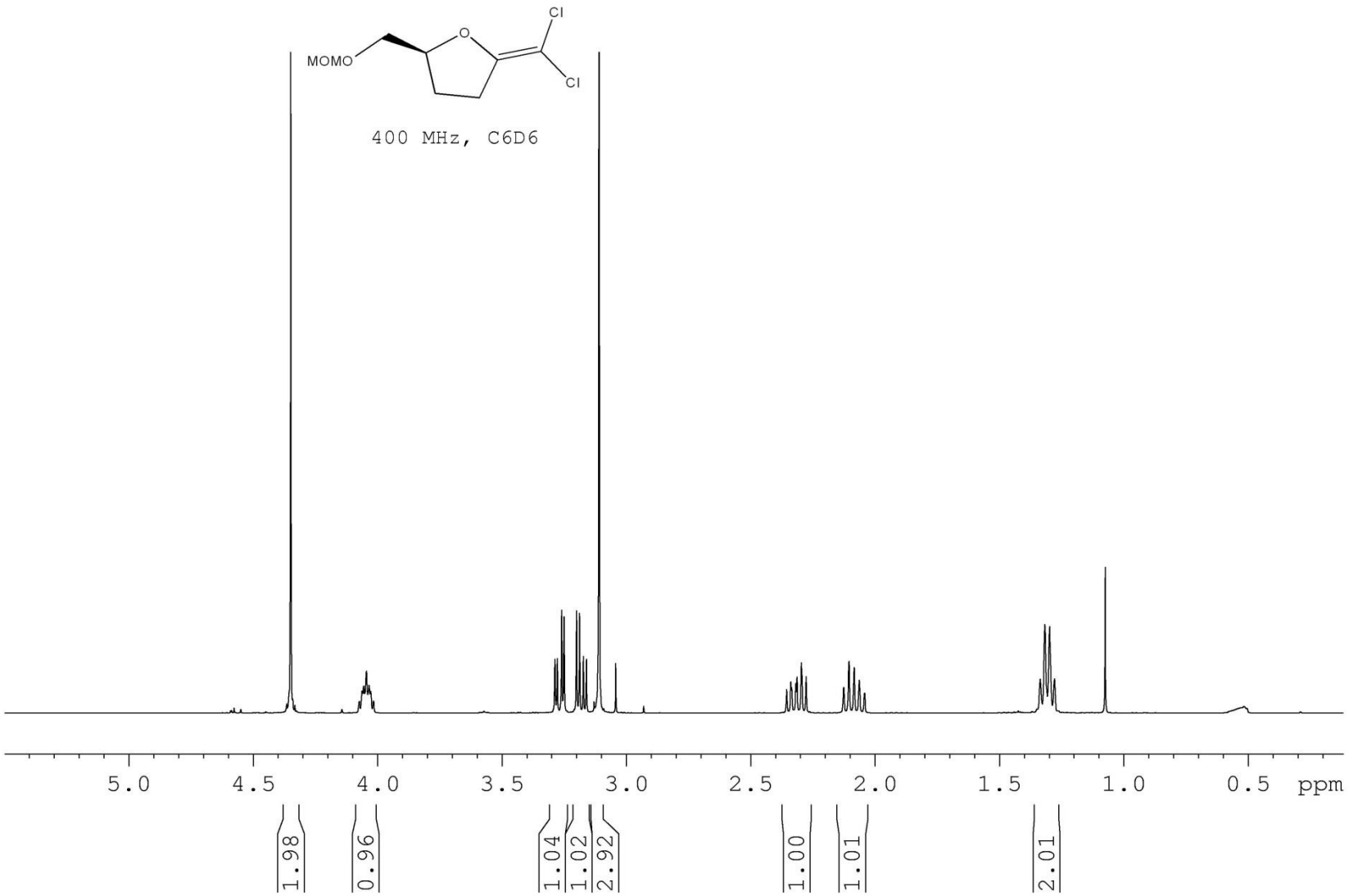

174.86
71.00
61.18
51.65
46.12
40.95
40.40
25.95
25.86
19.63
18.16
10.42
-4.36
-4.44
MeO
O
OTBS
OH
100 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

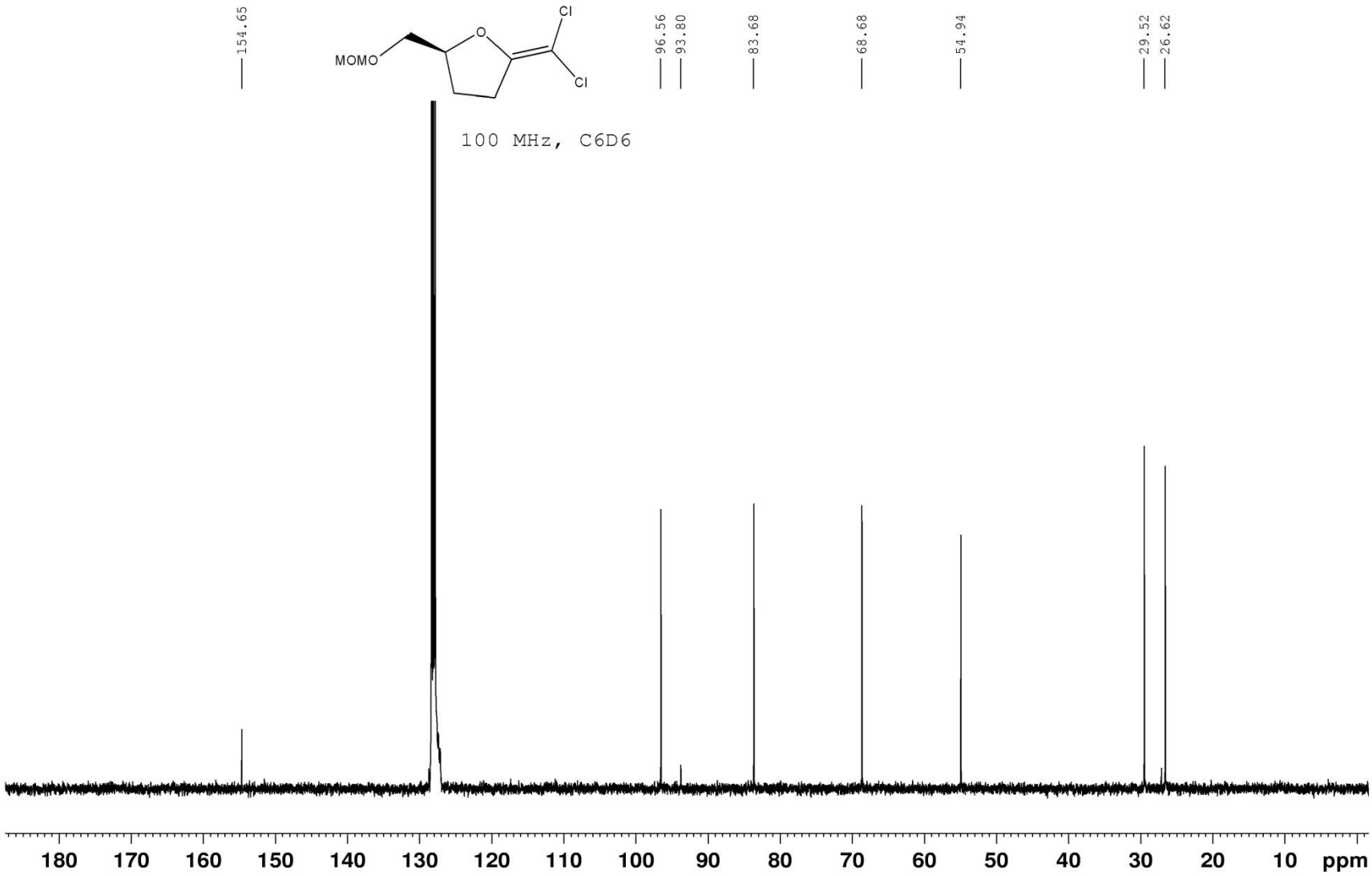

MeO
O
OTBS
I
400 MHz, CDCl3
7
6
5
4
3
2
1
0
ppm
1.01
2.99
2.07
1.00
1.07
2.08
1.04
3.00
1.15
12.10
5.99

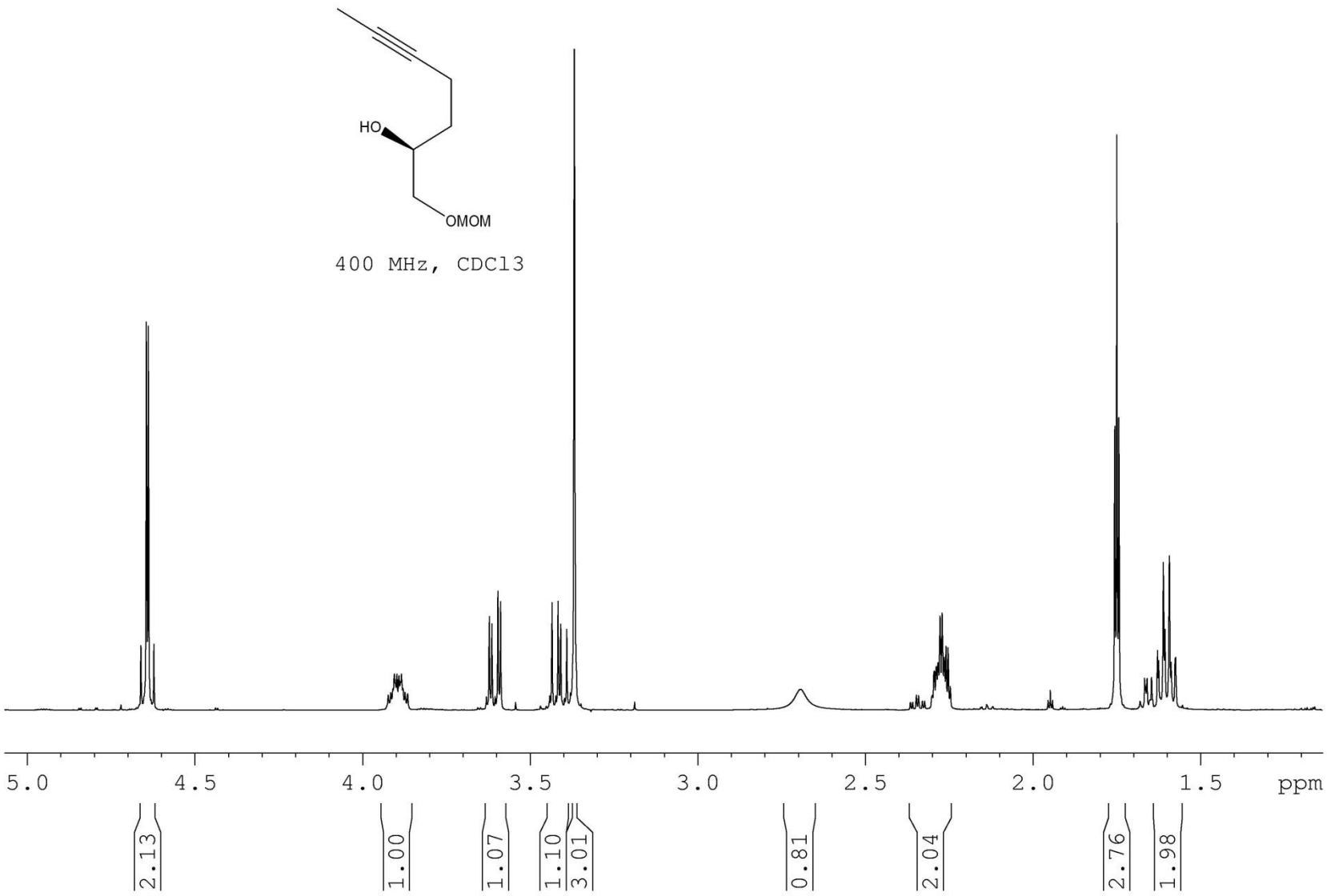

174.77
70.65
51.68
46.13
41.98
39.69
30.21
26.00
18.41
18.16
10.32
4.83
-4.29
-4.41
MeO
O
OTBS
I
100 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

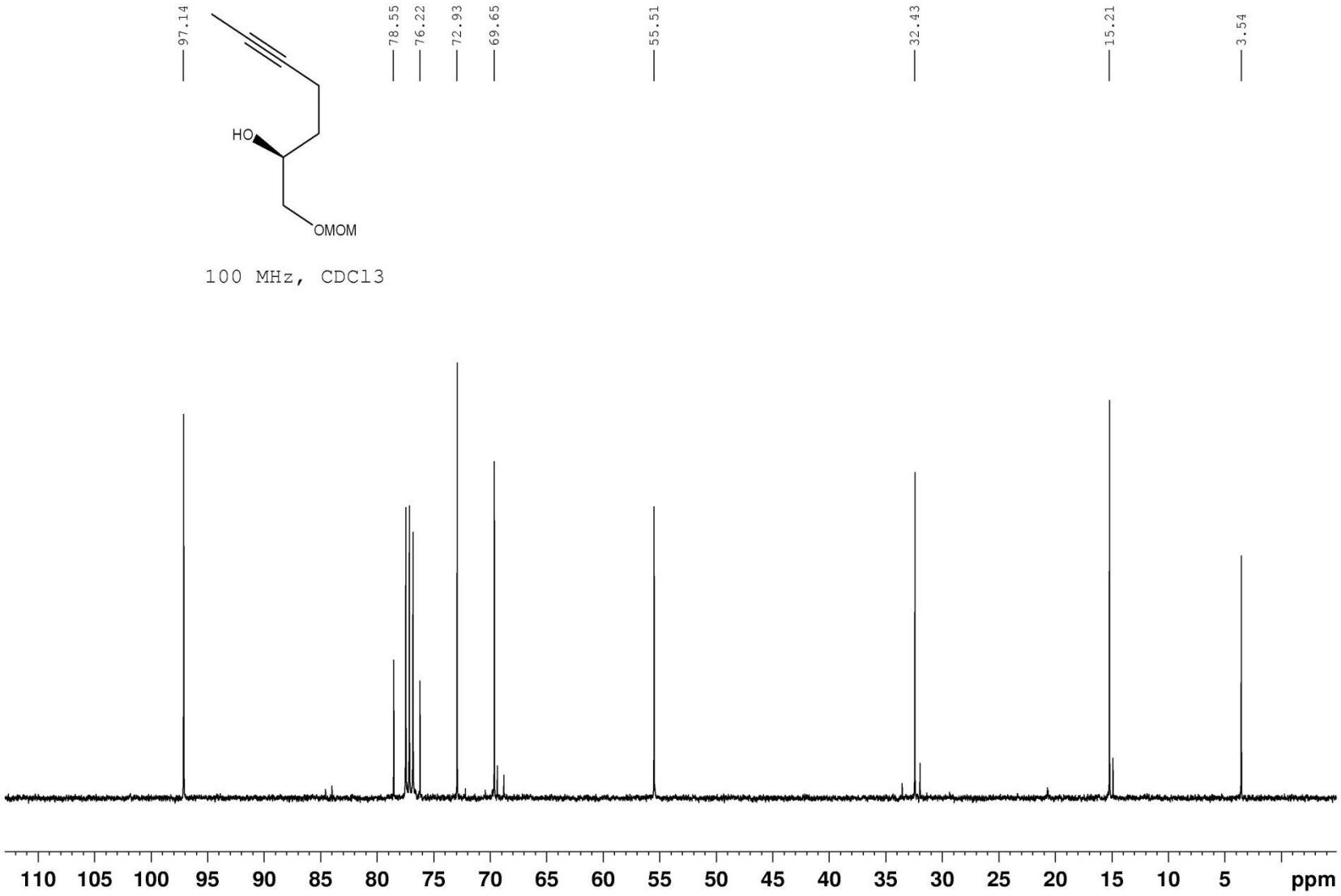

MOMO
O
O
400 MHz, CDCl3
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
1.05
1.92
1.01
1.00
3.02
1.02
1.01
1.02
1.00

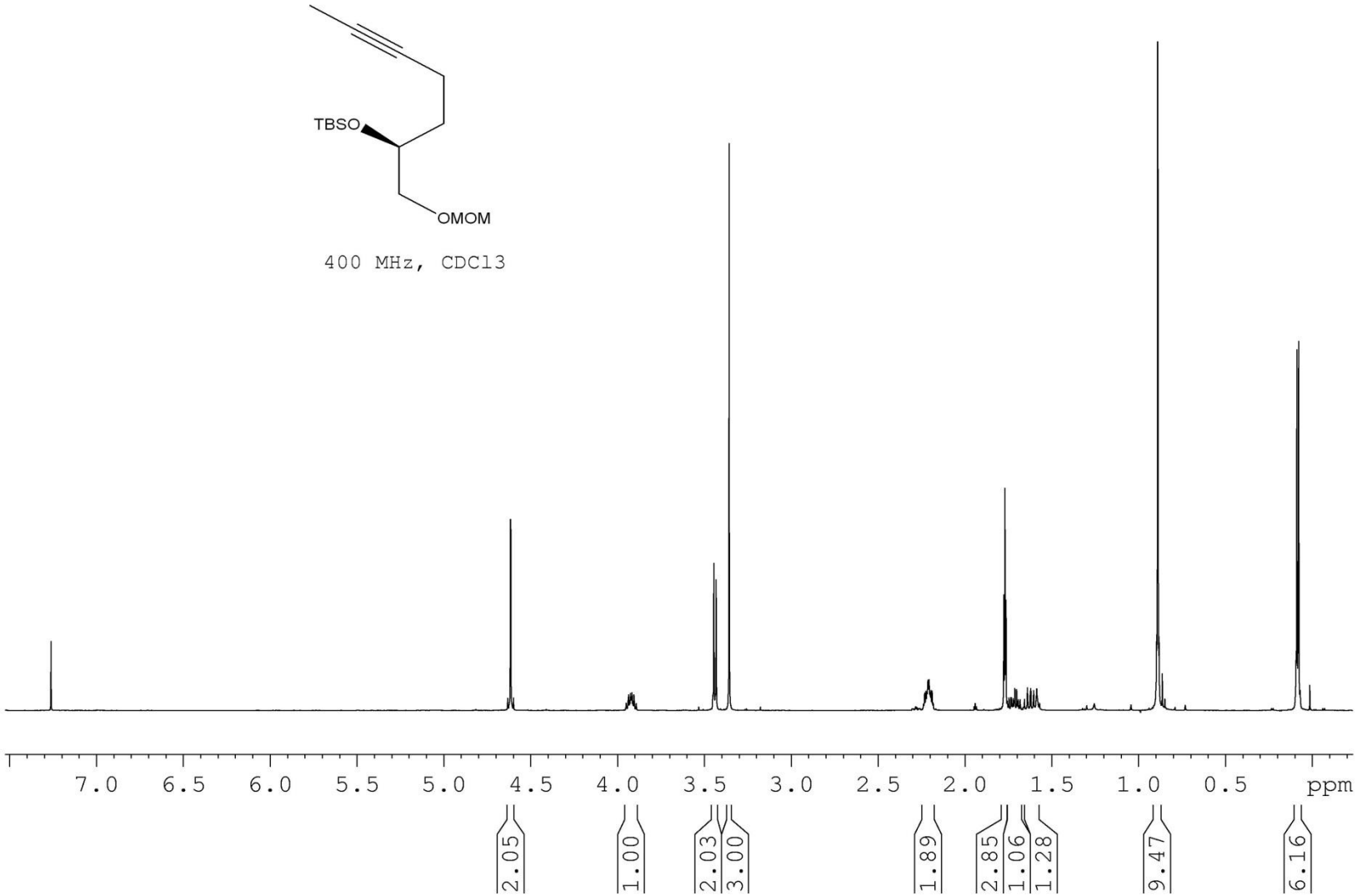

177.28
MOMO
O
O
96.77
78.82
69.14
55.55
28.50
24.13
100 MHz, CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

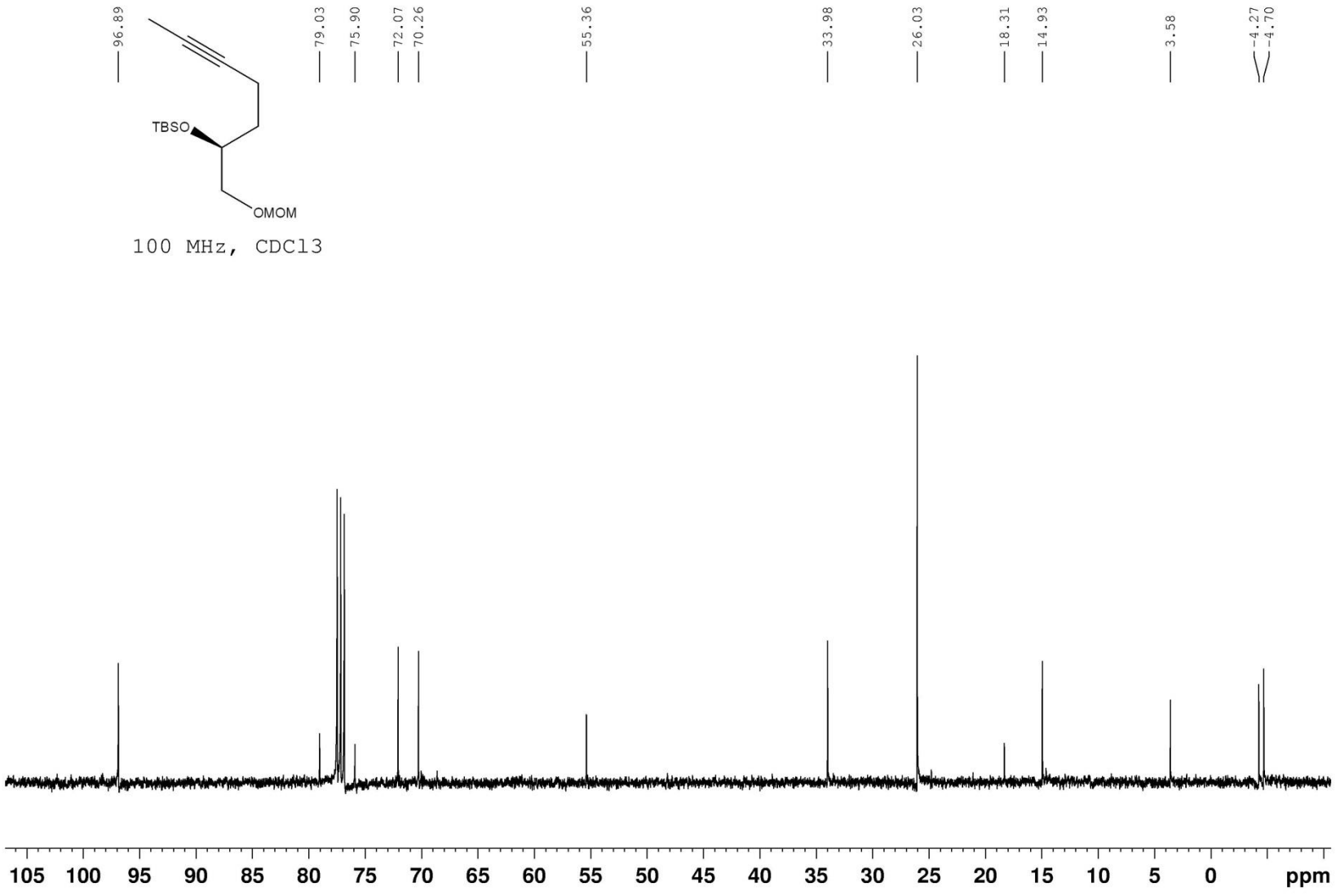

MOMO
O
Cl
Cl
400 MHz, C6D6
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.98
0.96
1.04
1.02
2.92
1.00
1.01
2.01

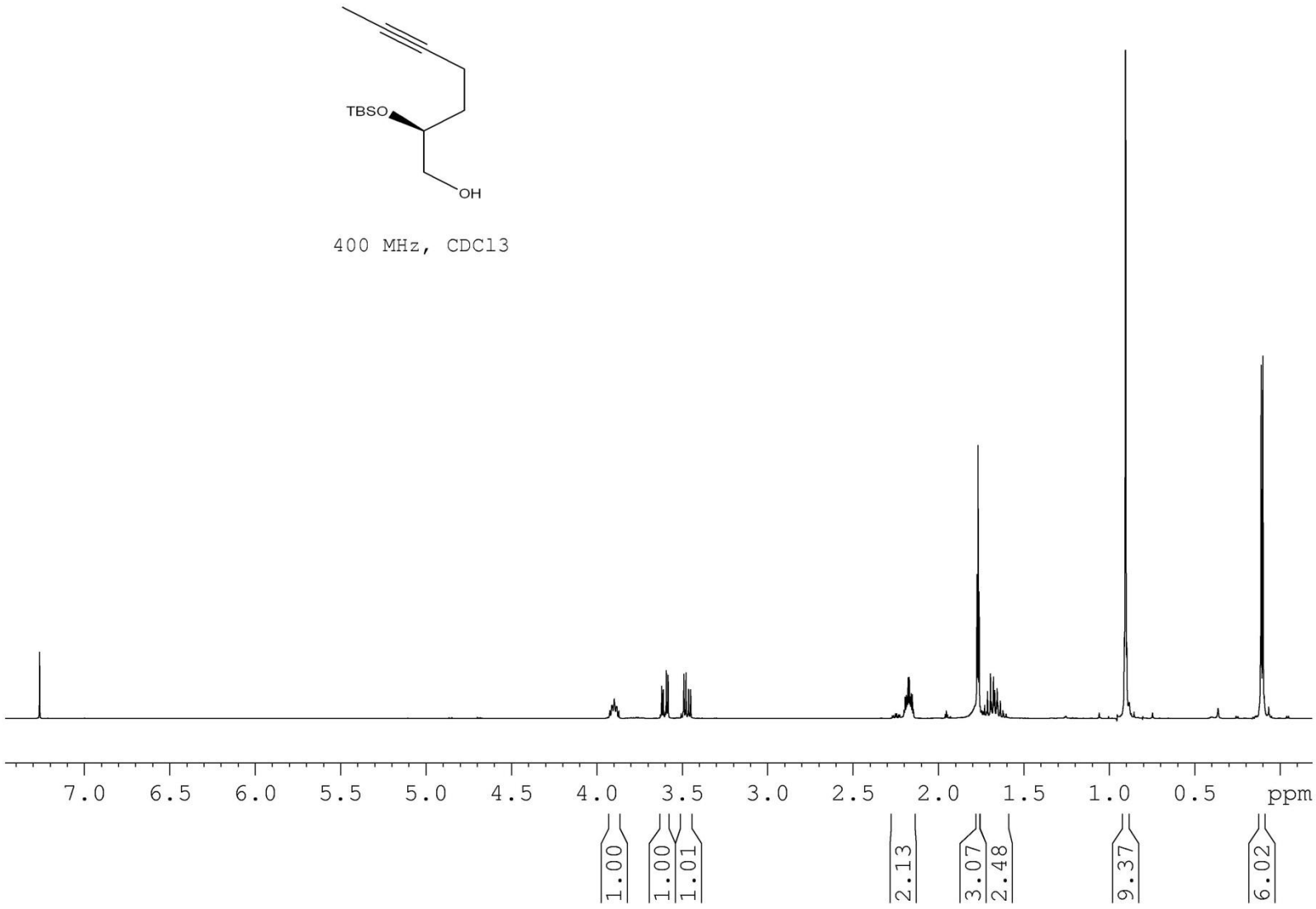

154.65
96.56
93.80
83.68
68.68
54.94
29.52
26.62
MOMO
O
Cl
Cl
100 MHz, C6D6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

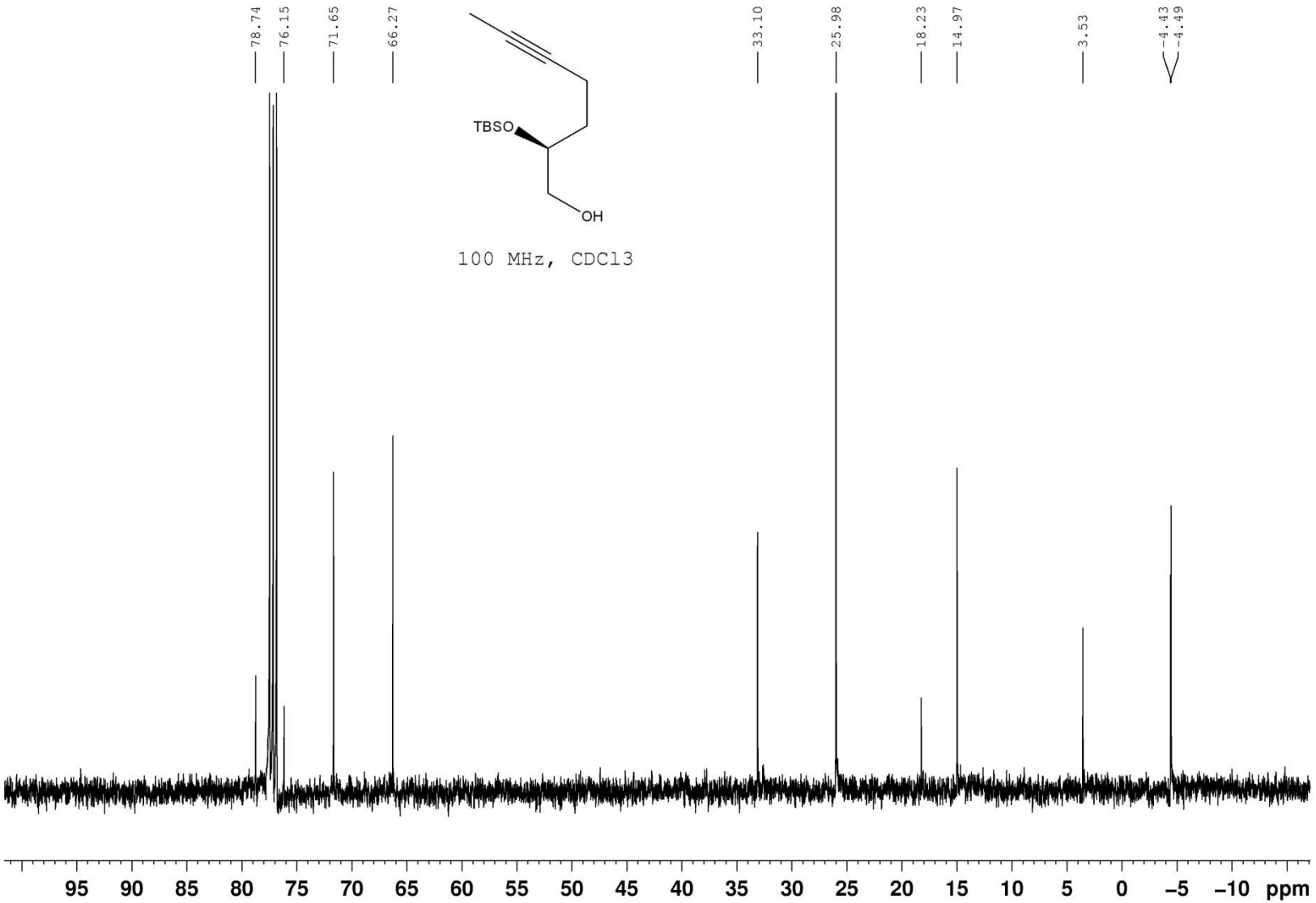

HO
OMOM
400 MHz, CDCl3
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
2.13
1.00
1.07
1.10
3.01
0.81
2.04
2.76
1.98

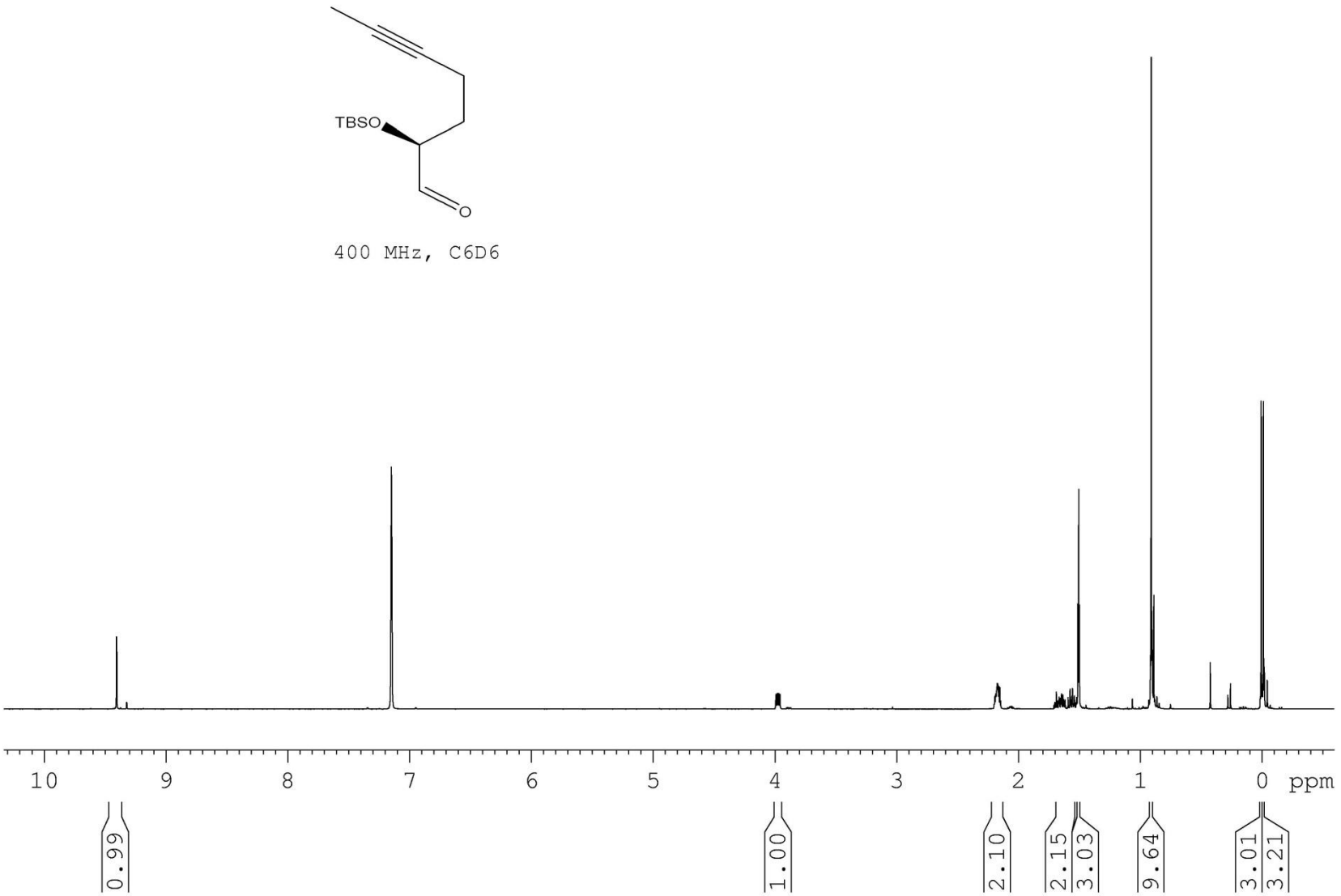

97.14
78.55
76.22
72.93
69.65
55.51
32.43
15.21
3.54
HO
OMOM
100 MHz, CDCl3
110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 ppm

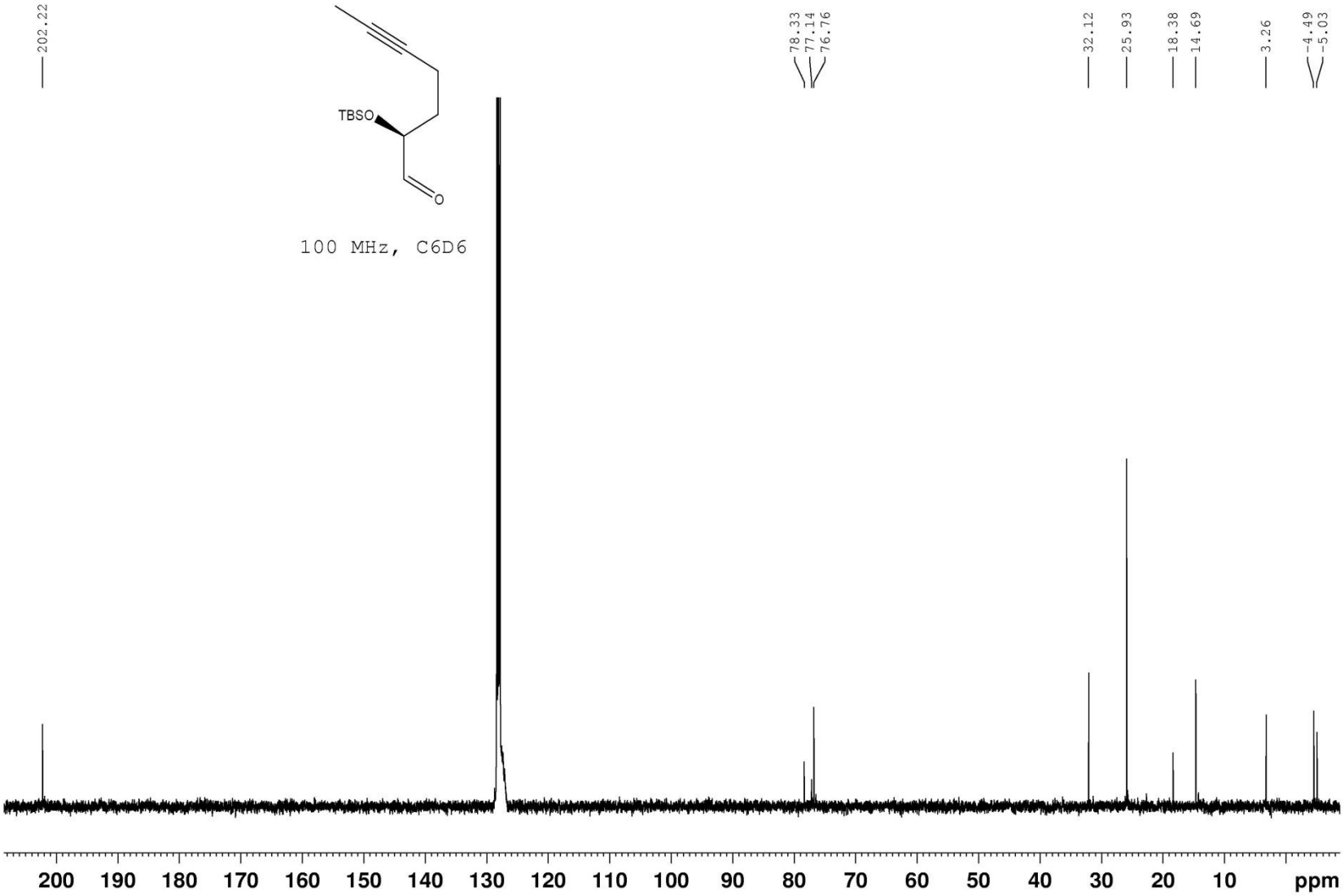

TBSO
OMOM
400 MHz, CDCl3
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.05
1.00
2.03
3.00
1.89
2.85
1.06
1.28
9.47
6.16

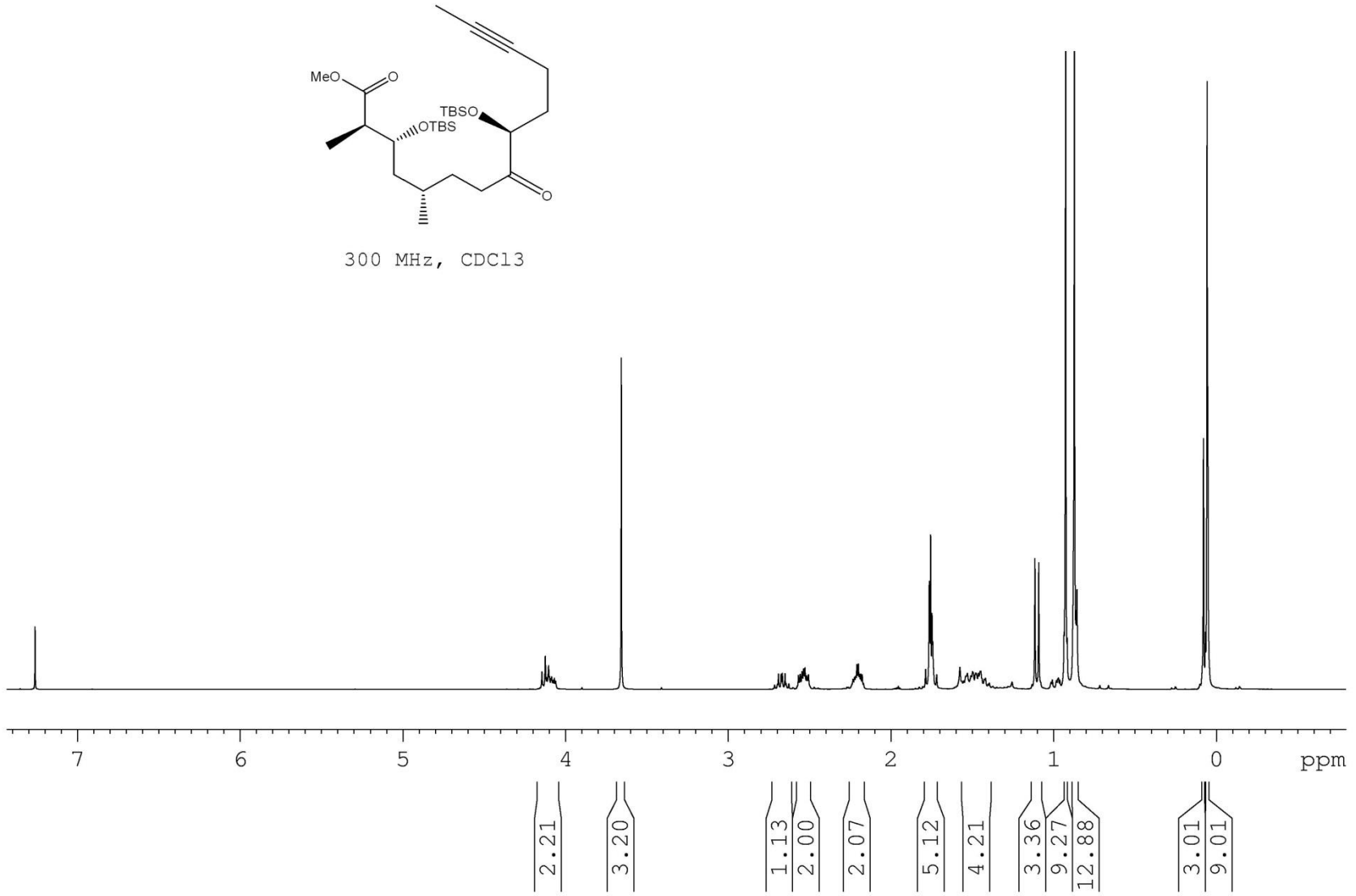

96.89
79.03
75.90
72.07
70.26
55.36
33.98
26.03
18.31
14.93
3.58
-4.27
-4.70
TBSO
OMOM
100 MHz, CDCl3
105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 ppm

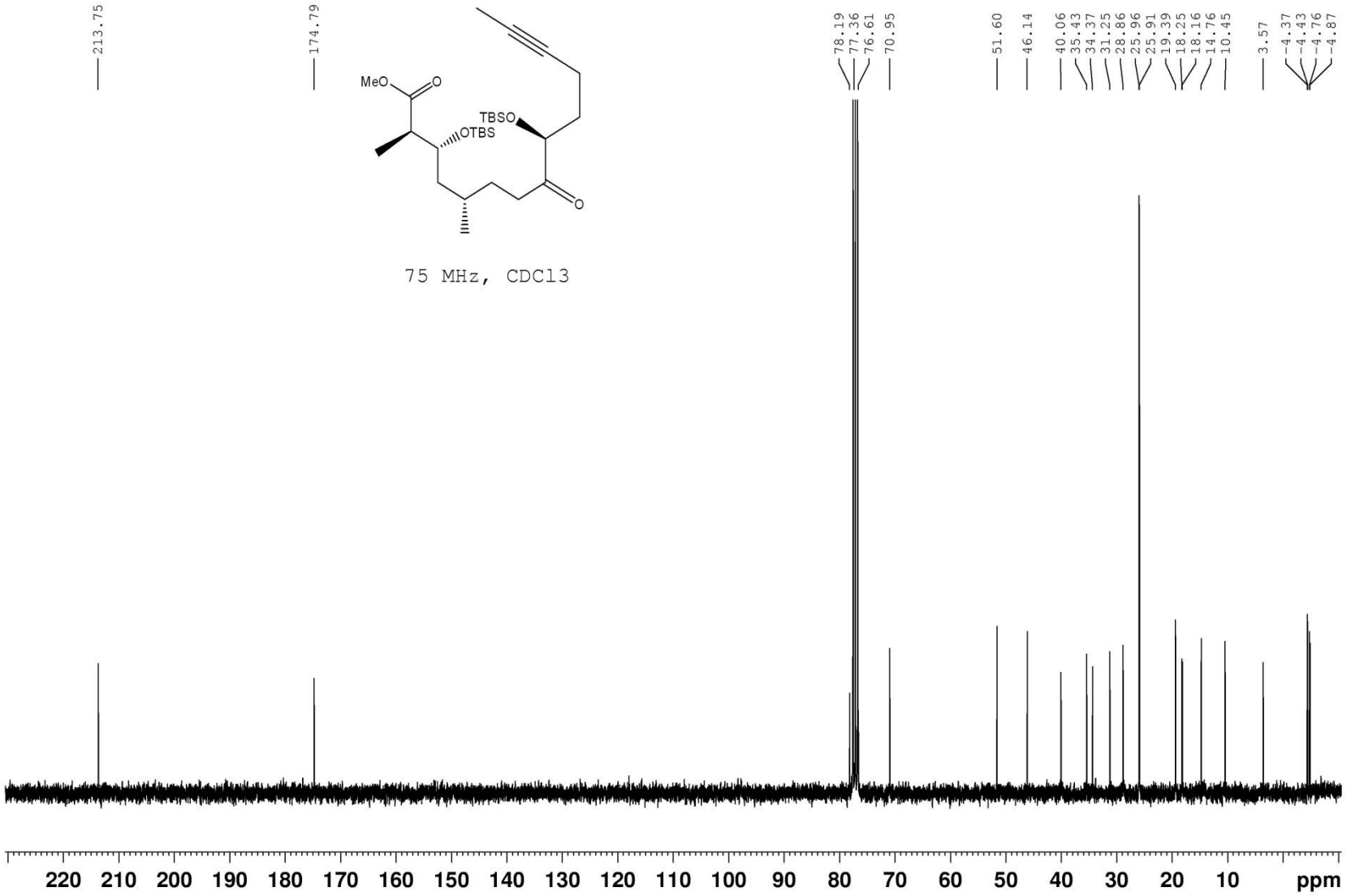

TBSO
OH
400 MHz, CDCl3
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.00
1.01
2.13
3.07
2.48
9.37
6.02

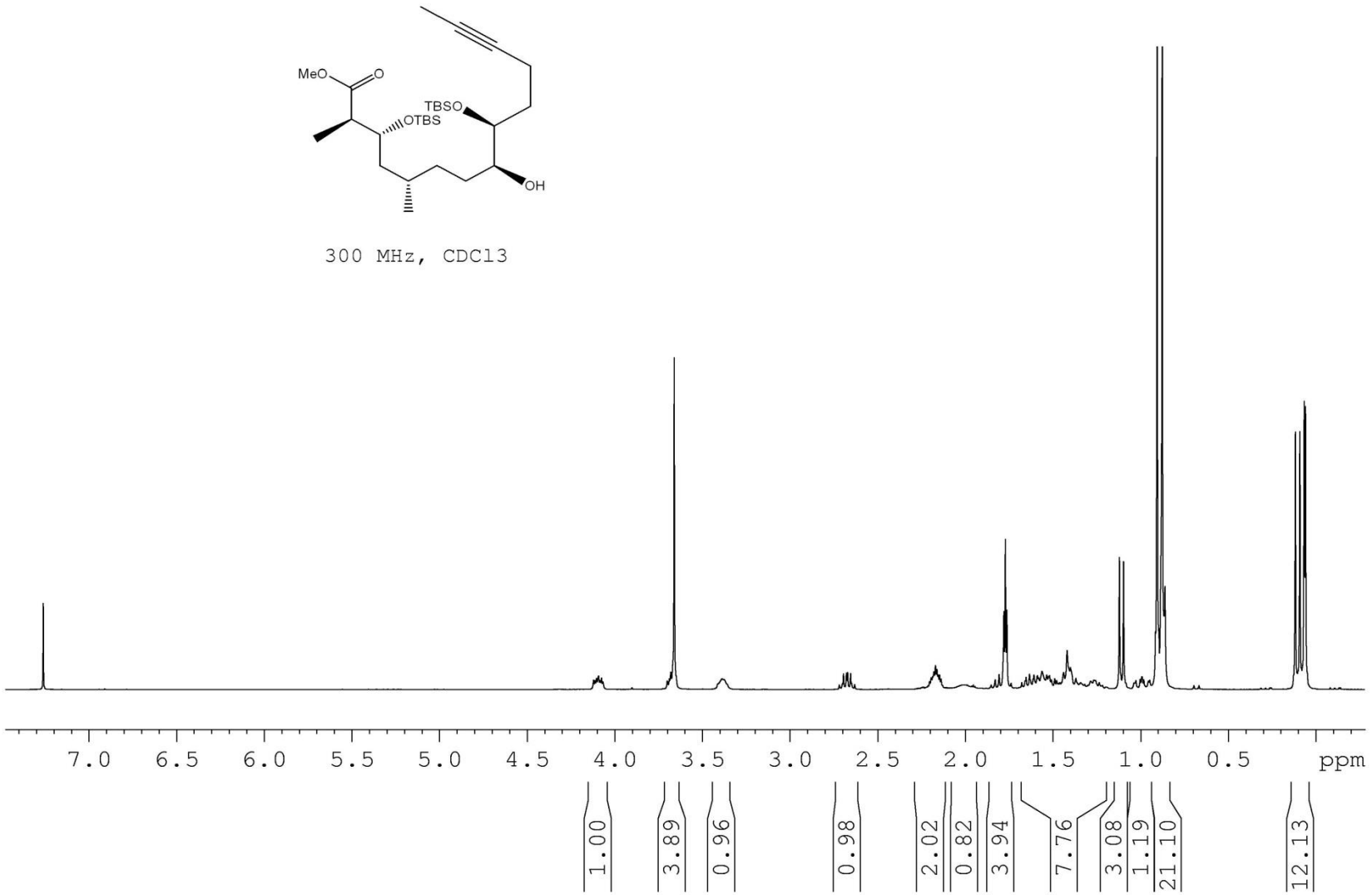

78.74
76.15
71.65
66.27
33.10
25.98
18.23
14.97
3.53
-4.43
-4.49
TBSO
OH
100 MHz, CDCl3
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 –5 –10 ppm

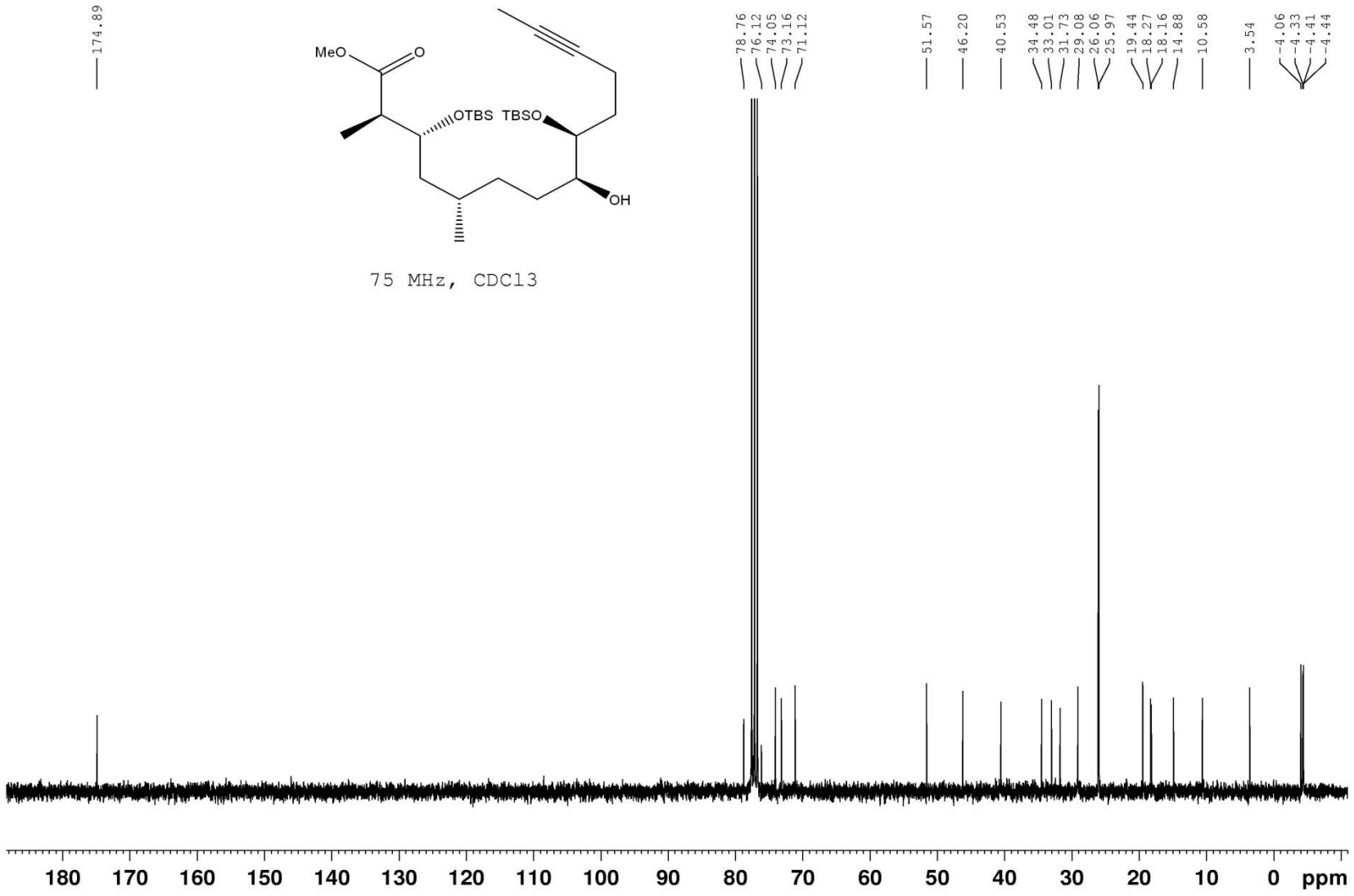

TBSO
O
400 MHz, C6D6
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
1.00
2.10
2.15
3.03
9.64
3.01
3.21

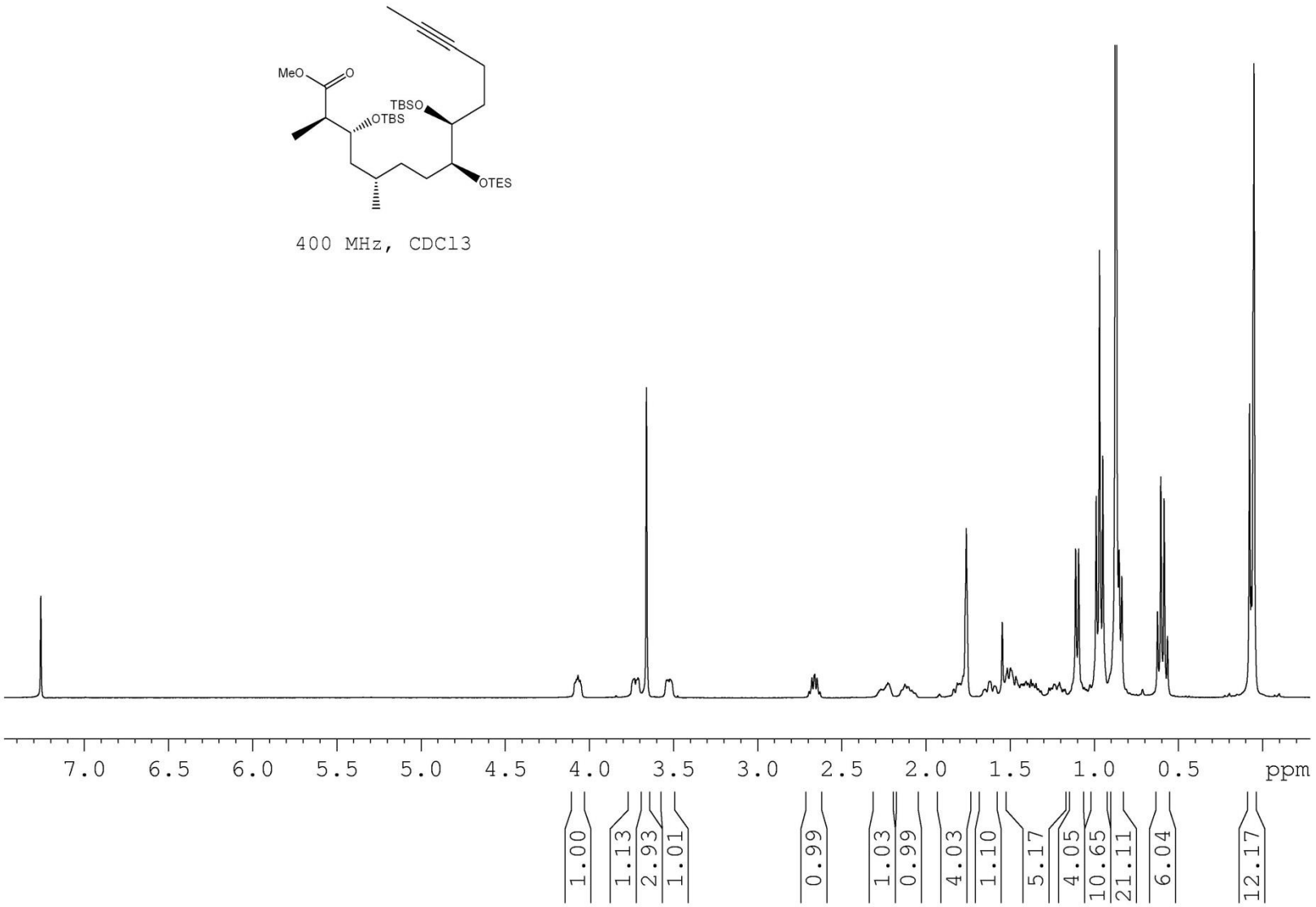

202.22
78.33
77.14
76.76
32.12
25.93
18.38
14.69
3.26
-4.49
-5.03
TBSO
O
100 MHz, C6D6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

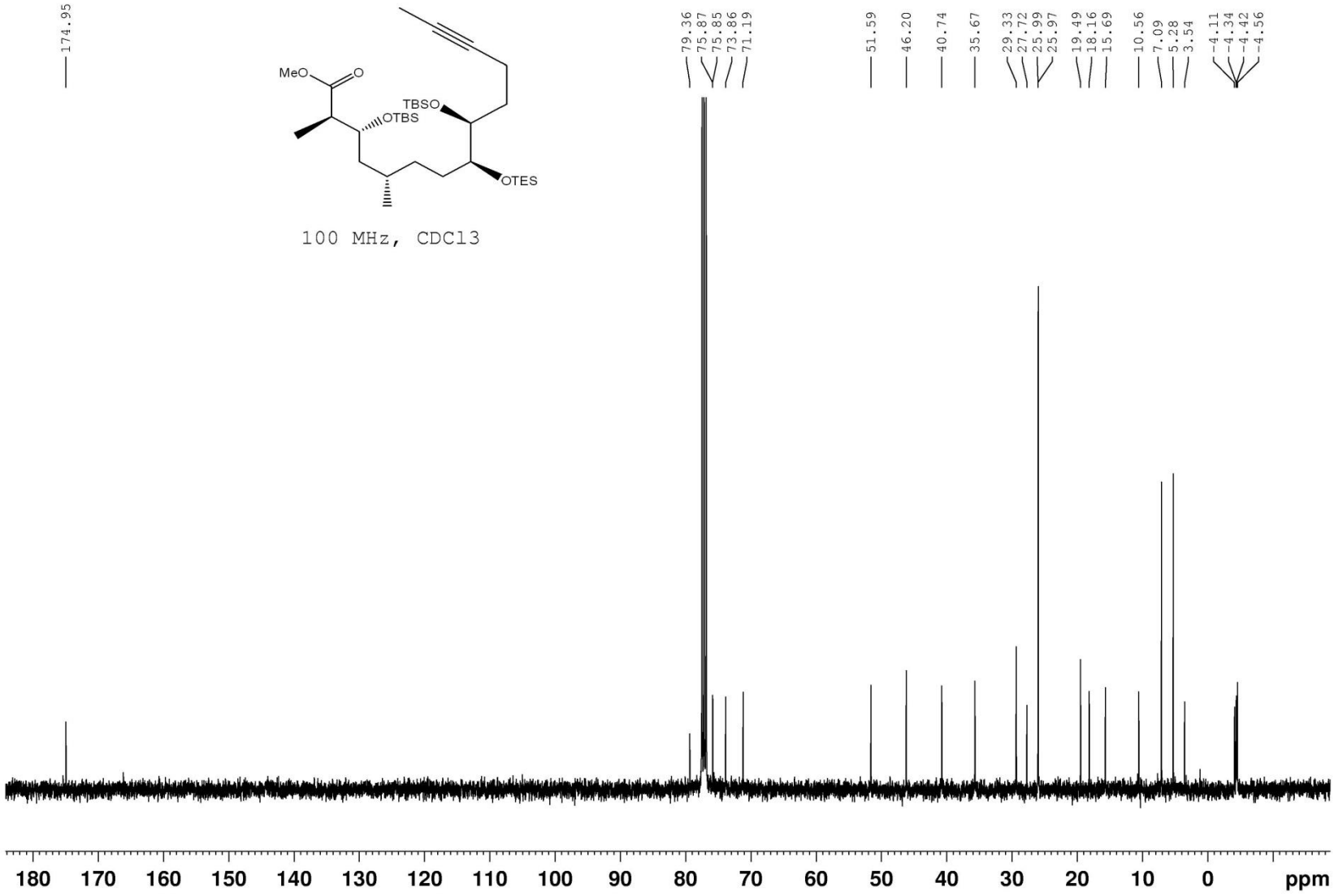

MeO
O
TBSO
OTBS
O
300 MHz, CDCl3
7
6
5
4
3
2
1
0
ppm
2.21
3.20
1.13
2.00
2.07
5.12
4.21
3.36
9.27
12.88
3.01
9.01

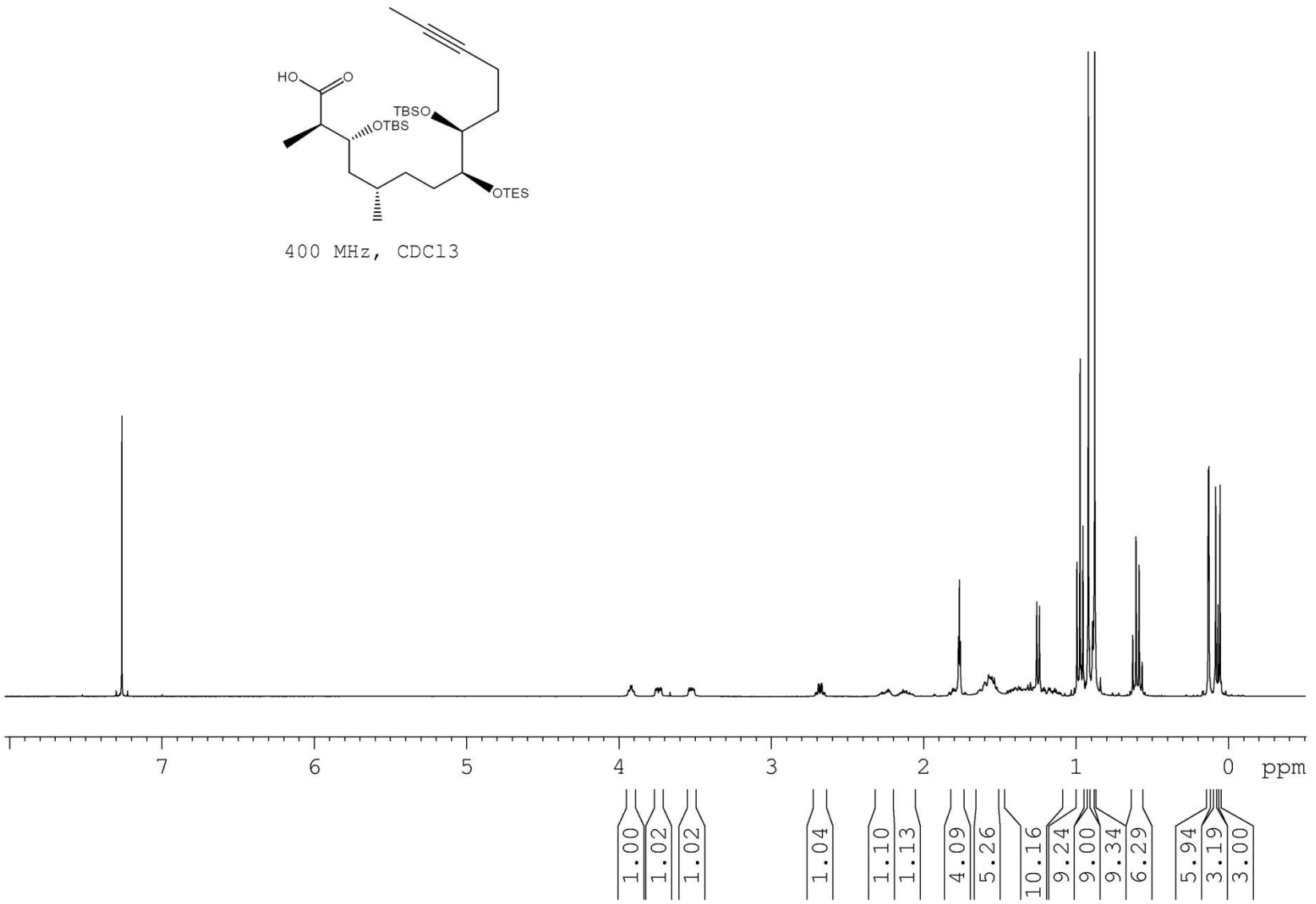

213.75
174.79
78.19
77.36
76.61
70.95
51.60
46.14
40.06
35.43
34.37
31.25
28.86
25.96
25.91
19.39
18.25
18.16
14.76
10.45
3.57
-4.37
-4.43
-4.76
-4.87
MeO
O
TBSO
OTBS
O
75 MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

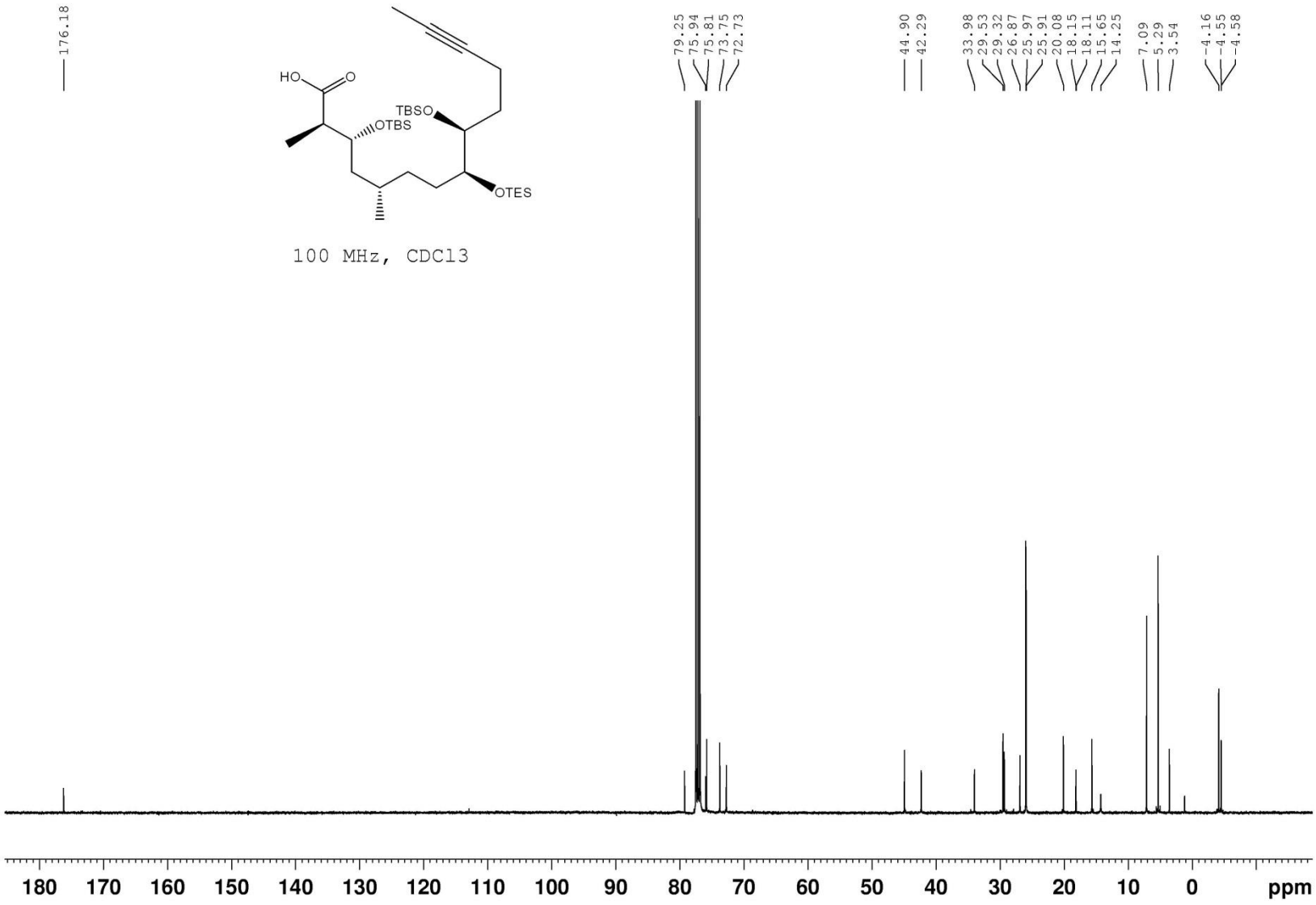

MeO
O
TBSO
OTBS
OH
300 MHz, CDCl3
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
3.89
0.96
0.98
2.02
0.82
3.94
7.76
3.08
1.19
21.10
12.13

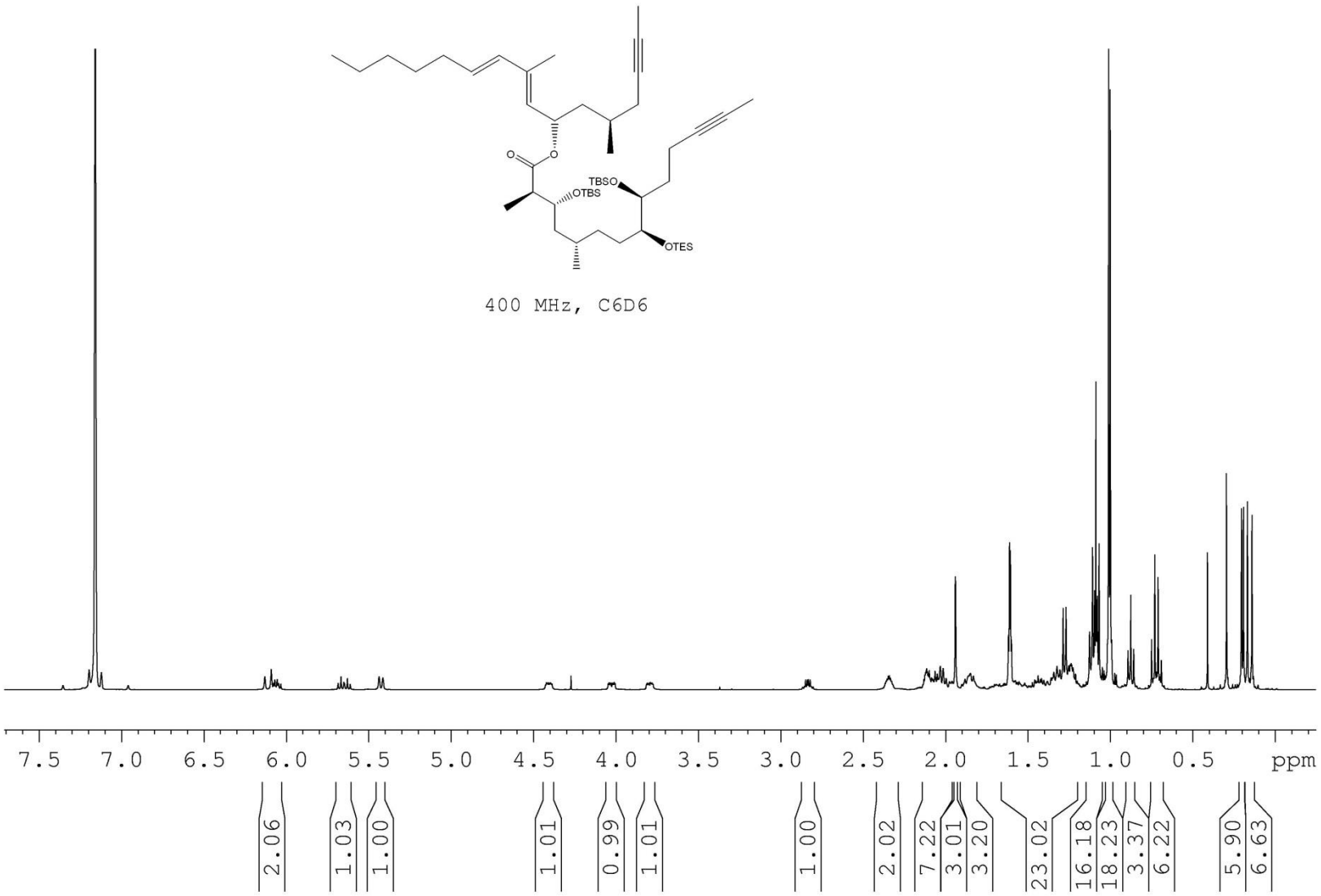

174.89
78.76
76.12
74.05
73.16
71.12
51.57
46.20
40.53
34.48
33.01
31.73
29.08
26.06
25.97
19.44
18.27
18.16
14.88
10.58
3.54
-4.06
-4.33
-4.41
-4.44
MeO
O
OTBS
TBSO
OH
75 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

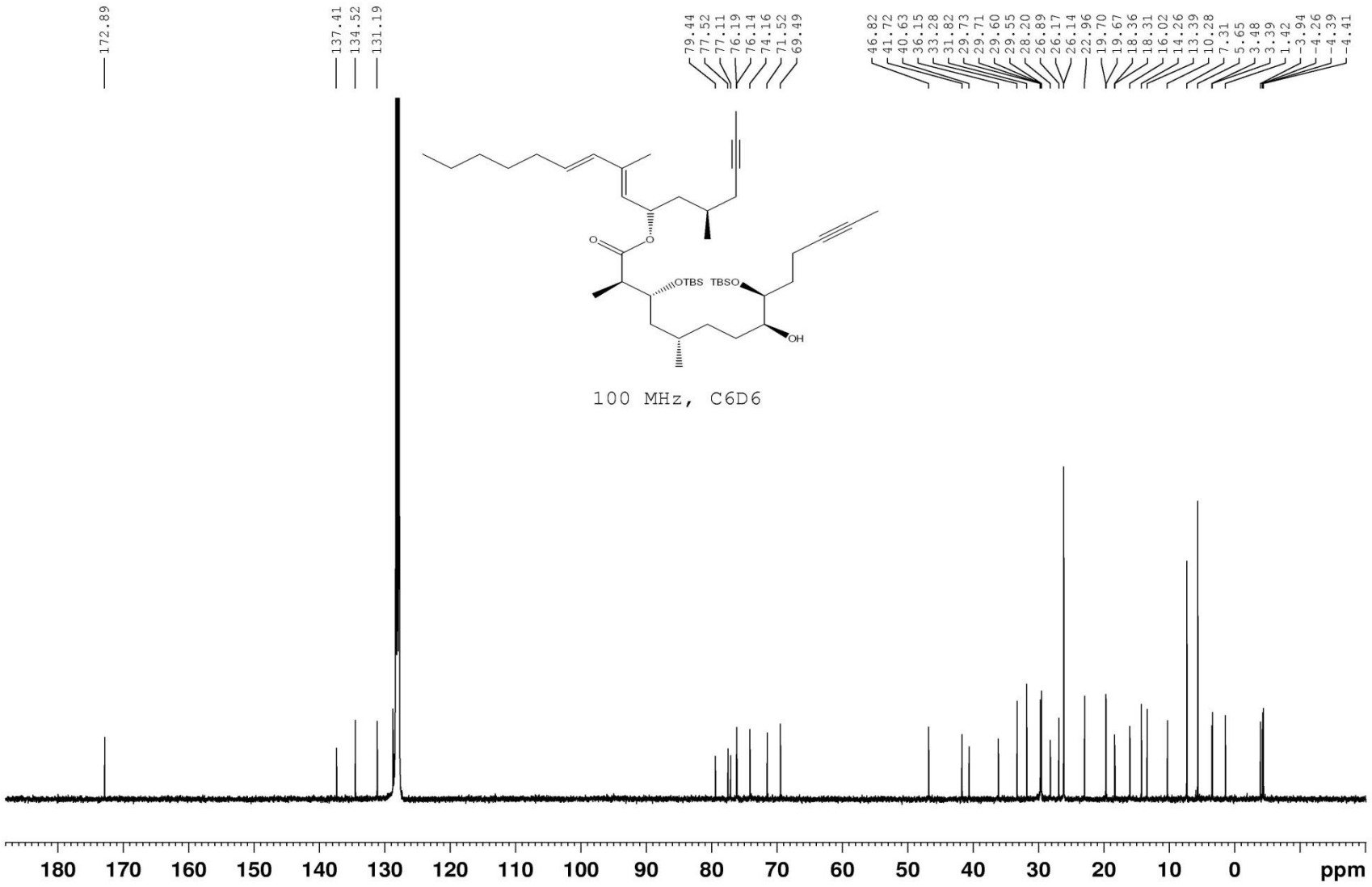

MeO
O
TBSO
OTBS
OTES
400 MHz, CDCl3
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.13
2.93
1.01
0.99
1.03
0.99
4.03
1.10
5.17
4.05
10.65
21.11
6.04
12.17

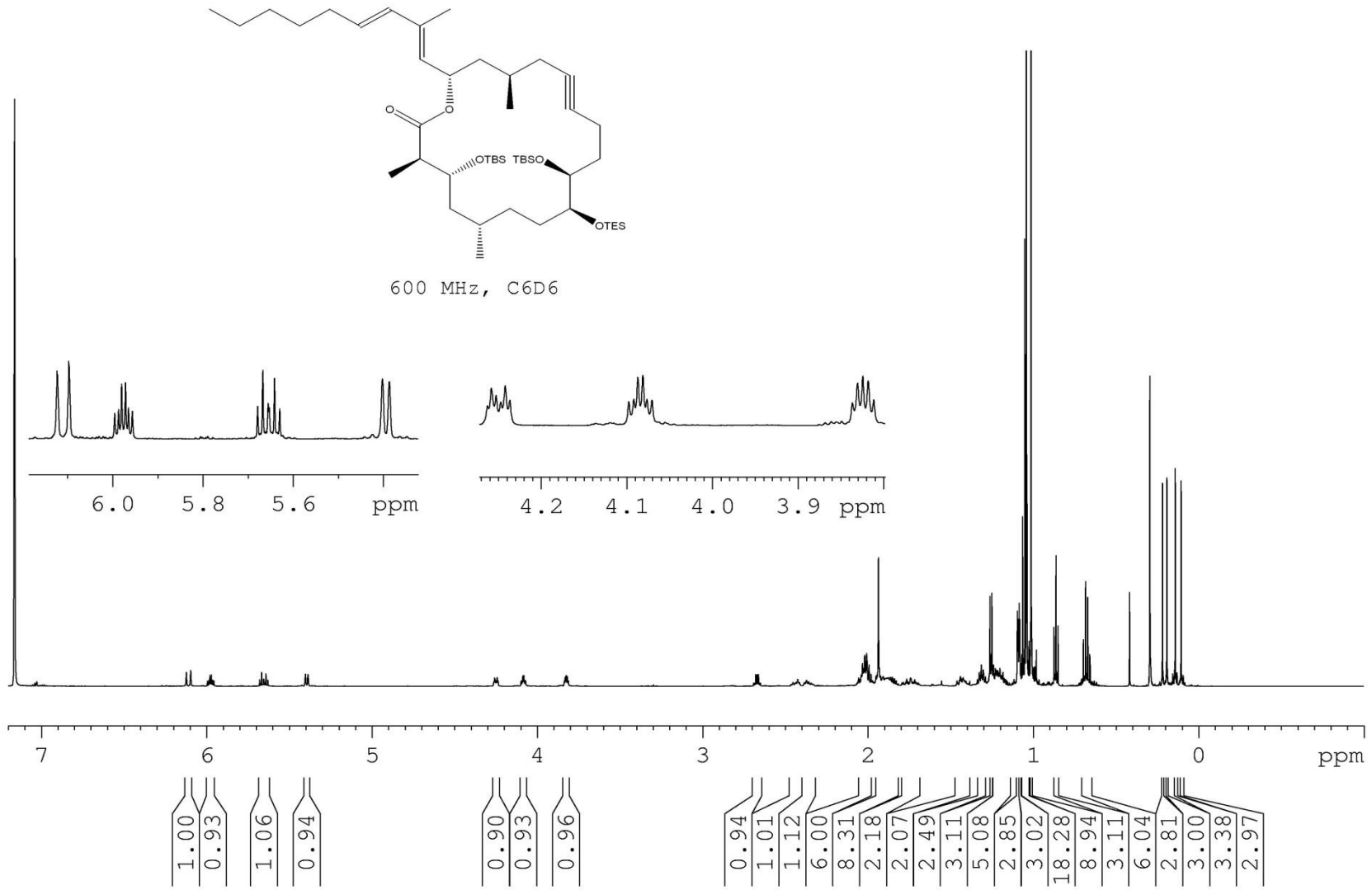

174.95
79.36
75.87
75.85
73.86
71.19
51.59
46.20
40.74
35.67
29.33
27.72
25.99
25.97
19.49
18.16
15.69
10.56
7.09
5.28
3.54
-4.11
-4.34
-4.42
-4.56
MeO
O
OTBS
TBSO
OTES
100 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

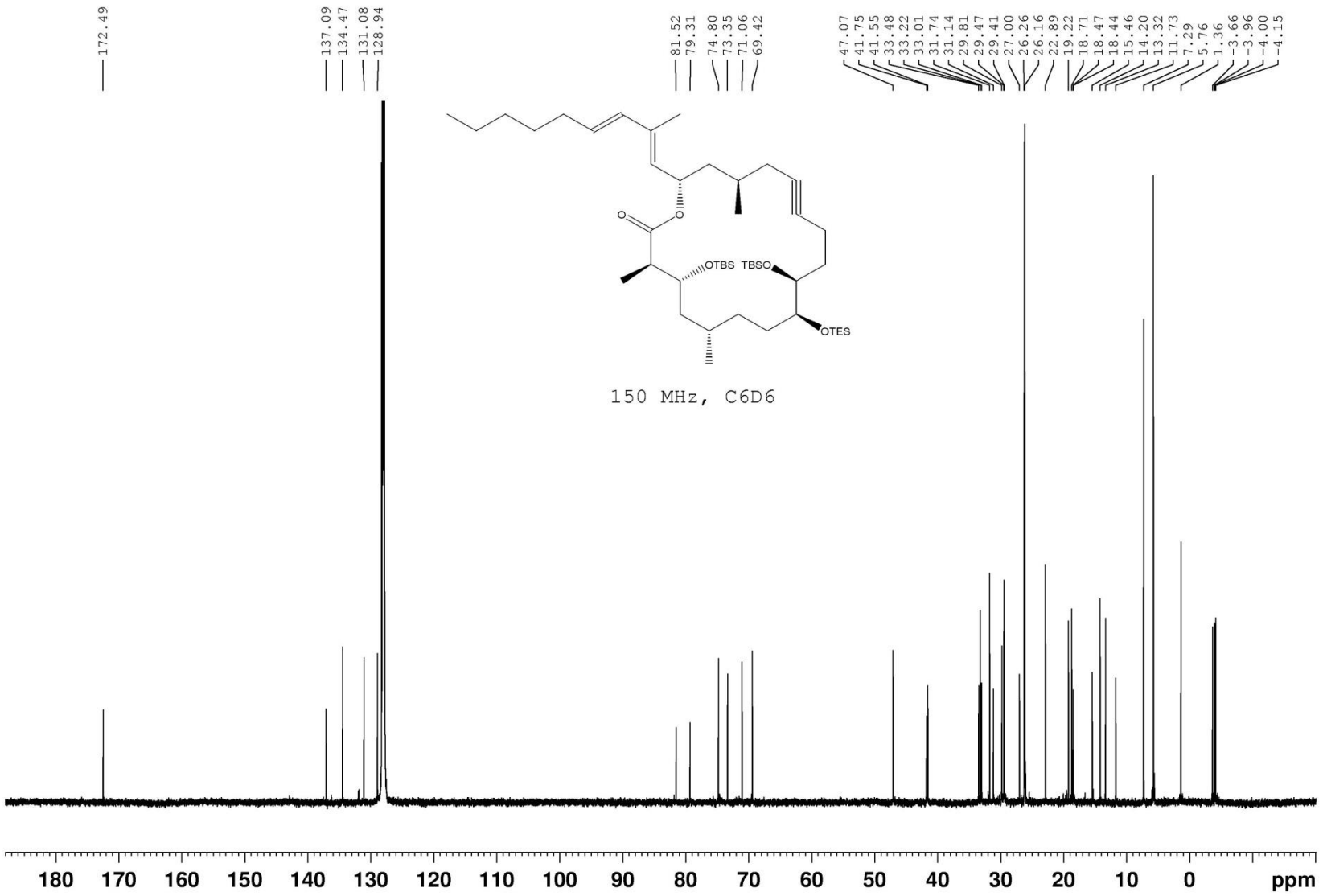

HO
O
TBSO
OTBS
OTES
400 MHz, CDCl3
7
6
5
4
3
2
1
0
ppm
1.00
1.02
1.02
1.04
1.10
1.13
4.09
5.26
10.16
9.24
9.00
9.34
6.29
5.94
3.19
3.00

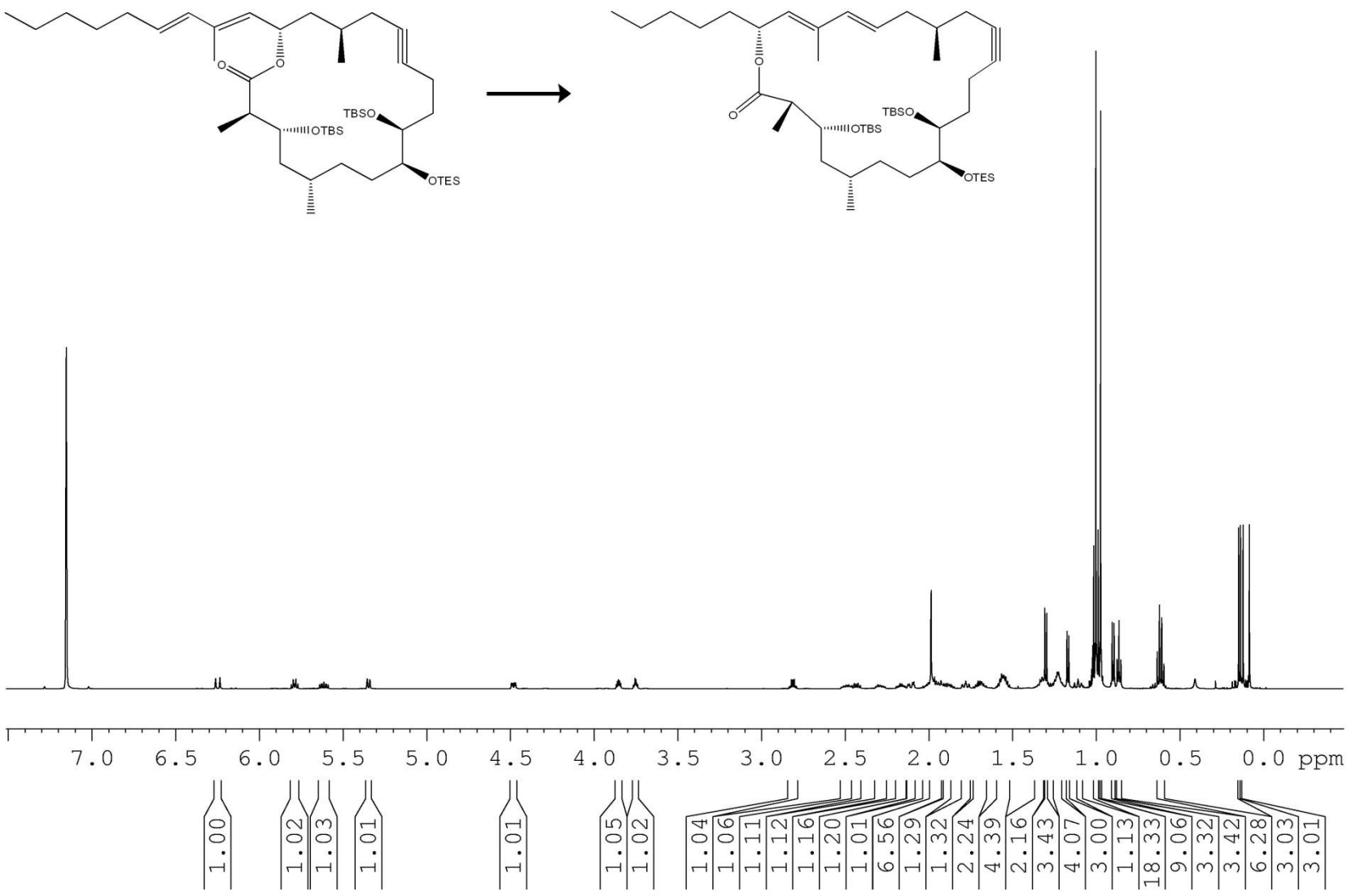

176.18
79.25
75.94
75.81
73.75
72.73
44.90
42.29
33.98
29.53
29.32
26.87
25.97
25.91
20.08
18.15
18.11
15.65
14.25
7.09
5.29
3.54
-4.16
-4.55
-4.58
HO
O
TBSO
OTBS
OTES
100 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

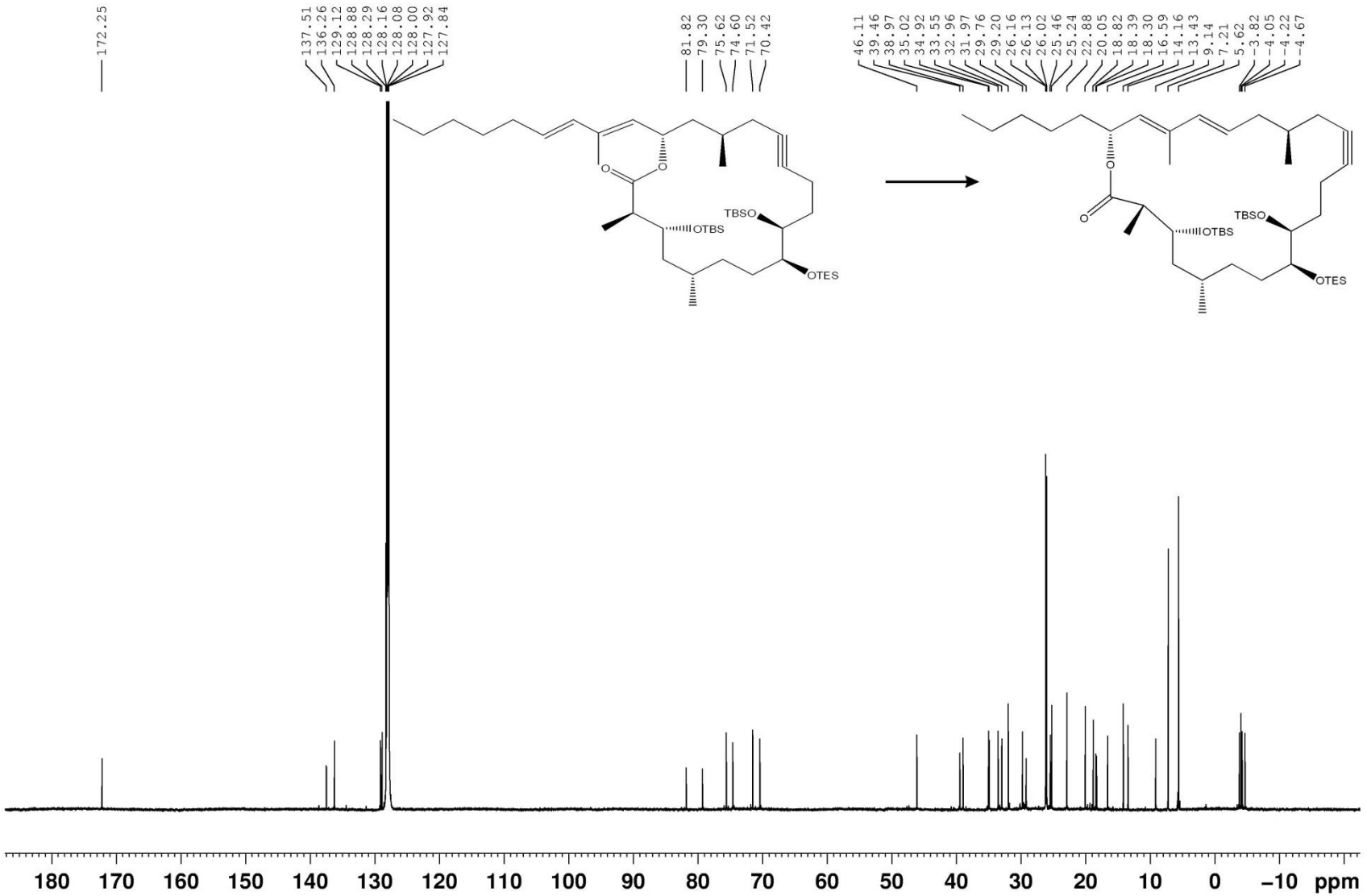

TBSO
OTBS
OTES
400 MHz, C6D6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.06
1.03
1.00
1.01
0.99
1.01
1.00
2.02
7.22
3.01
3.20
23.02
16.18
18.23
3.37
6.22
5.90
6.63

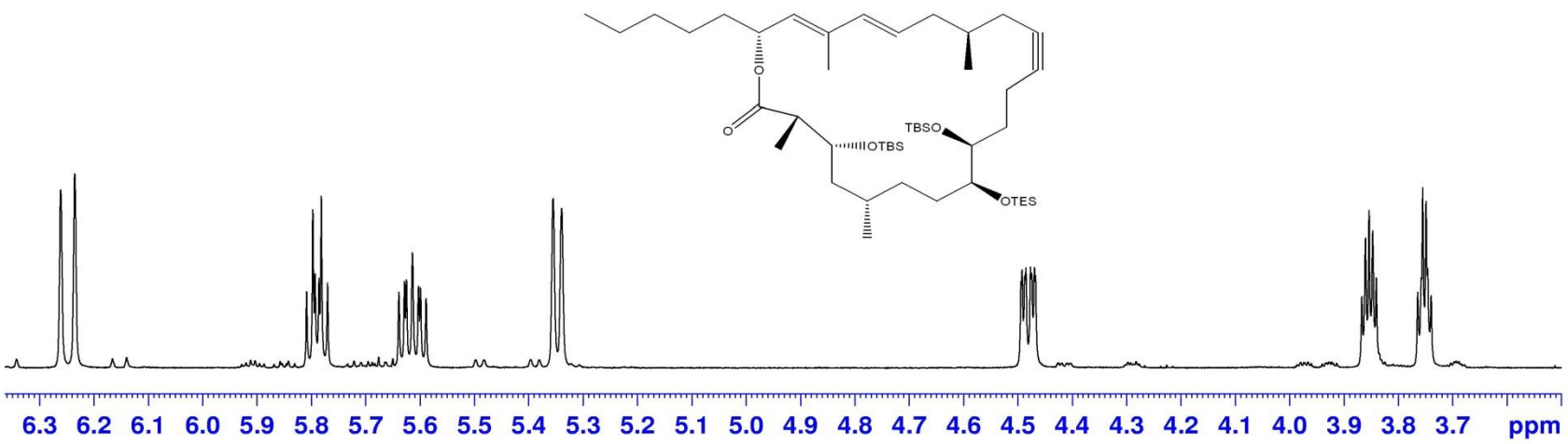

172.89
137.41
134.52
131.19
79.44
77.52
77.11
76.19
76.14
74.16
71.52
69.49
46.82
41.72
40.63
36.15
33.28
31.82
29.73
29.71
29.60
29.55
28.20
26.89
26.17
26.14
22.96
19.70
19.67
18.36
18.31
16.02
14.26
13.39
10.28
7.31
5.65
3.48
3.39
1.42
-3.94
-4.26
-4.39
-4.41
OTBS
TBSO
OH
100 MHz, C6D6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

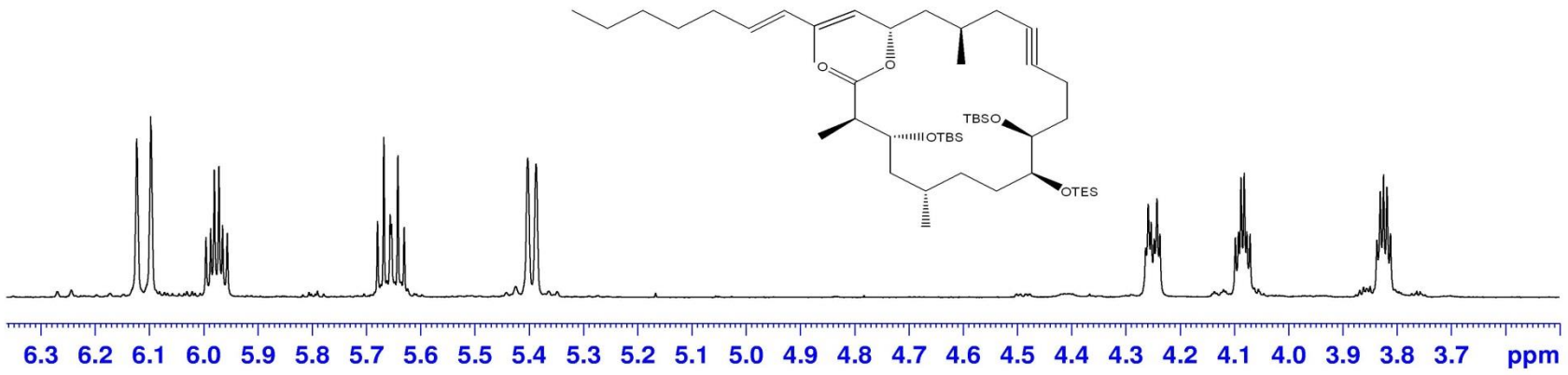

OTBS TBSO
OTES
600 MHz, C6D6
6.0 5.8 5.6 ppm
4.2 4.1 4.0 3.9 ppm
7 6 5 4 3 2 1 0 ppm
1.00 0.93 1.06 0.94 0.90 0.93 0.96 0.94 1.01 1.12 6.00 8.31 2.18 2.07 2.49 3.11 5.08 2.85 3.02 18.28 8.94 3.11 6.04 2.81 3.00 3.38 2.97

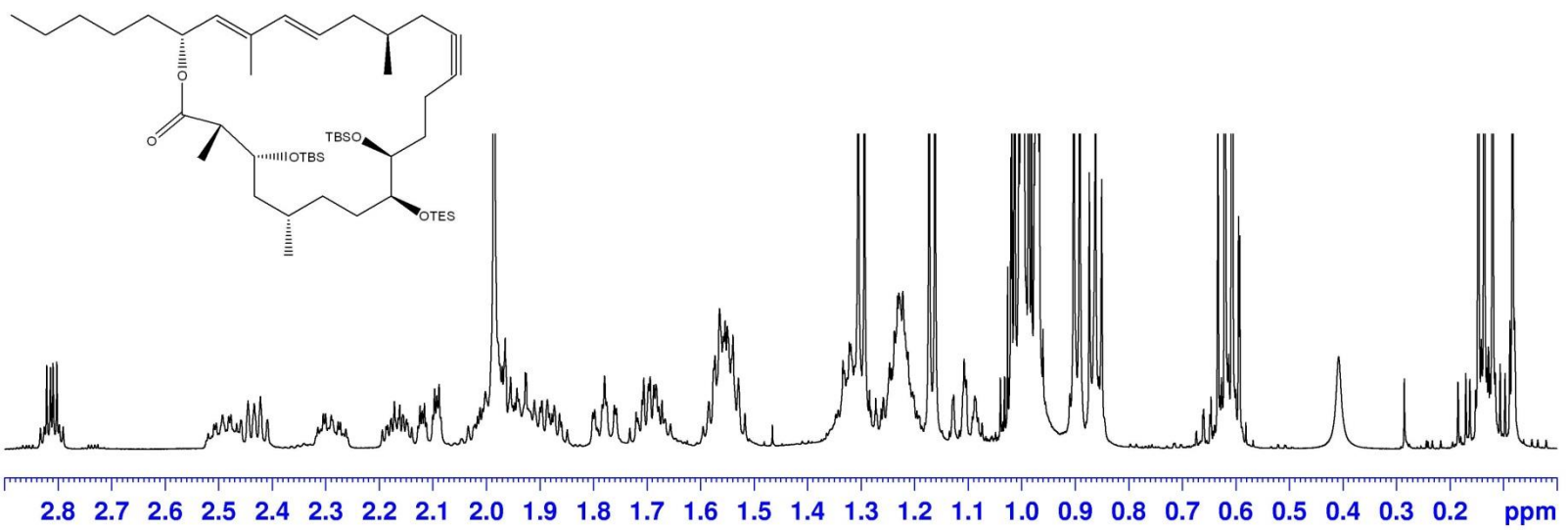

172.49
137.09
134.47
131.08
128.94
81.52
79.31
74.80
73.35
71.06
69.42
47.07
41.75
41.55
33.48
33.22
33.01
31.74
31.14
29.81
29.47
29.41
27.00
26.26
26.16
22.89
19.22
18.71
18.47
18.44
15.46
14.20
13.32
11.73
7.29
5.76
1.36
-3.66
-3.96
-4.00
-4.15
OTBS
TBSO
OTES
150 MHz, C6D6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

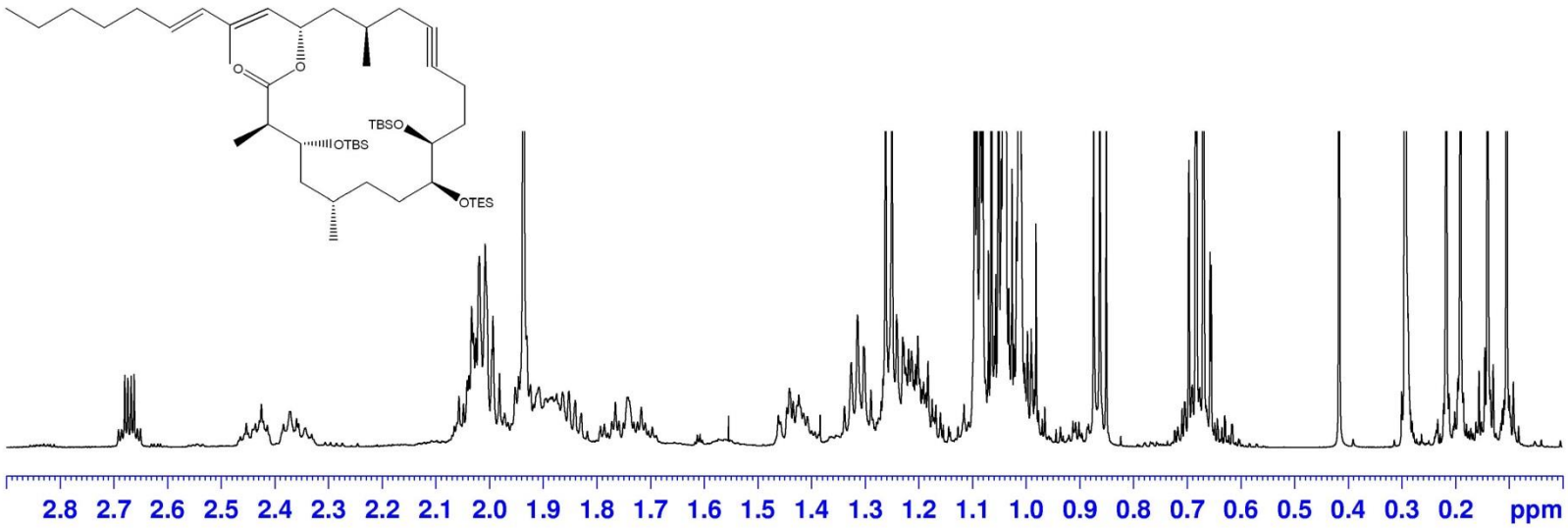

TBSO
OTBS
OTES
TBSO
OTBS
OTES
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.00
1.02
1.03
1.01
1.01
1.05
1.02
1.04
1.06
1.11
1.12
1.16
1.20
1.01
6.56
1.29
1.32
2.24
4.39
2.16
3.43
4.07
3.00
1.13
18.33
9.06
3.32
3.42
6.28
3.03
3.01

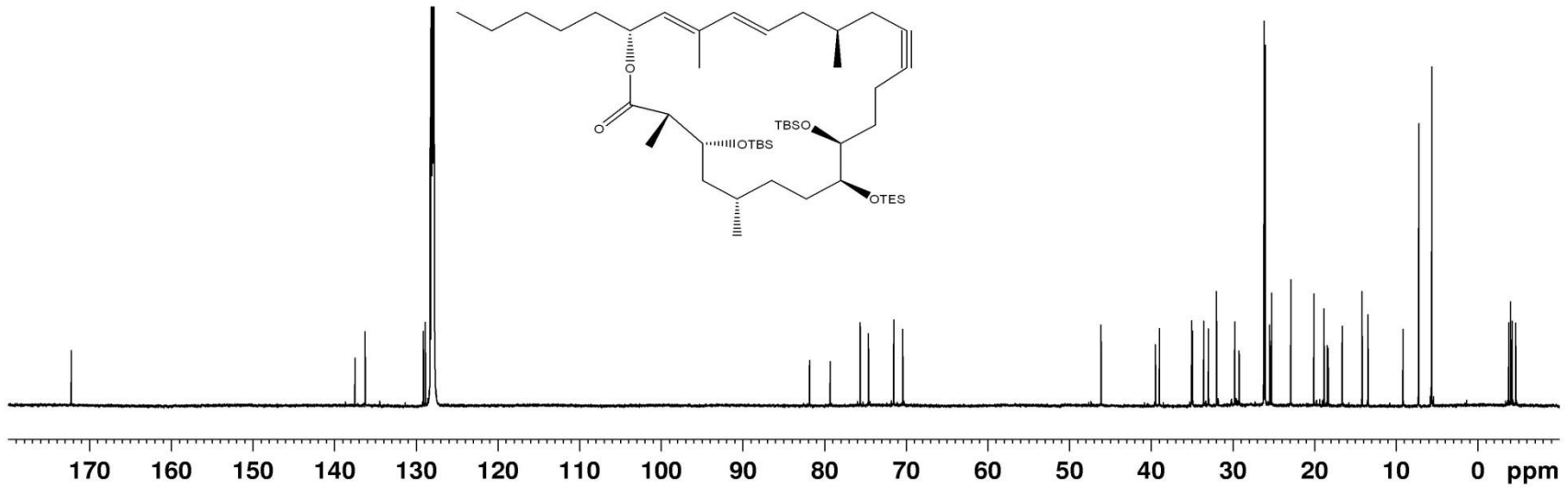

172.25
137.51
136.26
129.12
128.88
128.29
128.16
128.08
128.00
127.92
127.84
81.82
79.30
75.62
74.60
71.52
70.42
46.11
39.46
38.97
35.02
34.92
33.55
32.96
31.97
29.76
29.20
26.16
26.13
26.02
25.46
25.24
22.88
20.05
18.82
18.39
18.30
16.59
14.16
13.43
9.14
7.21
5.62
-3.82
-4.05
-4.22
-4.67
TBSO
OTBS
OTES
TBSO
OTBS
OTES
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

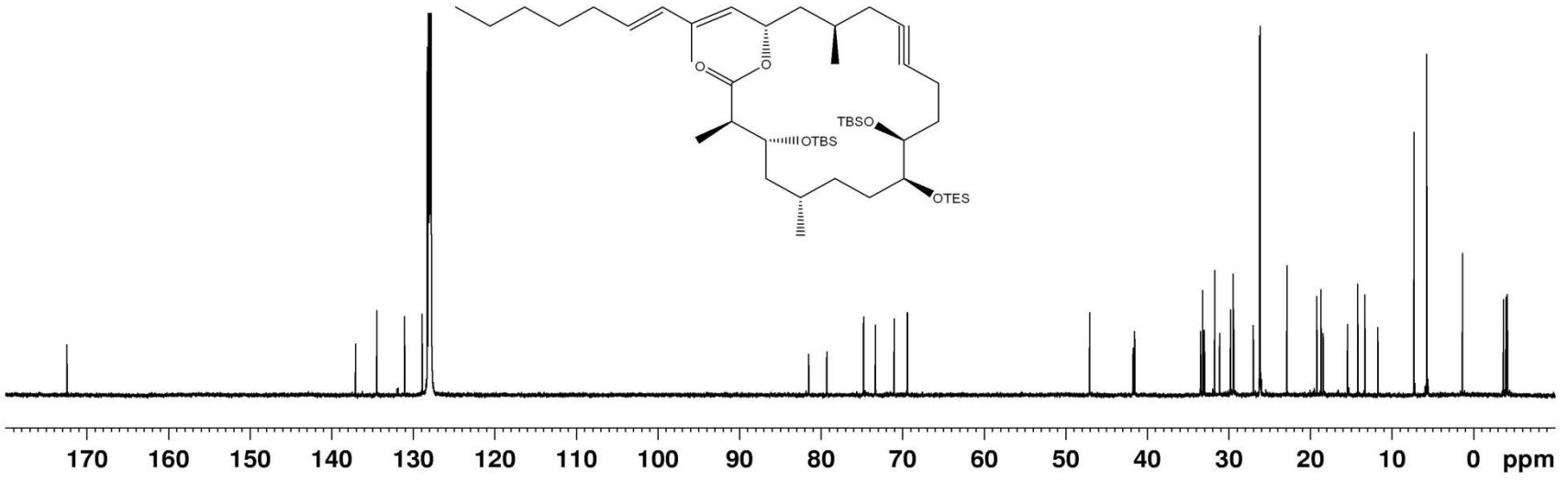

TBSO
OTBS
OTES
6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 ppm

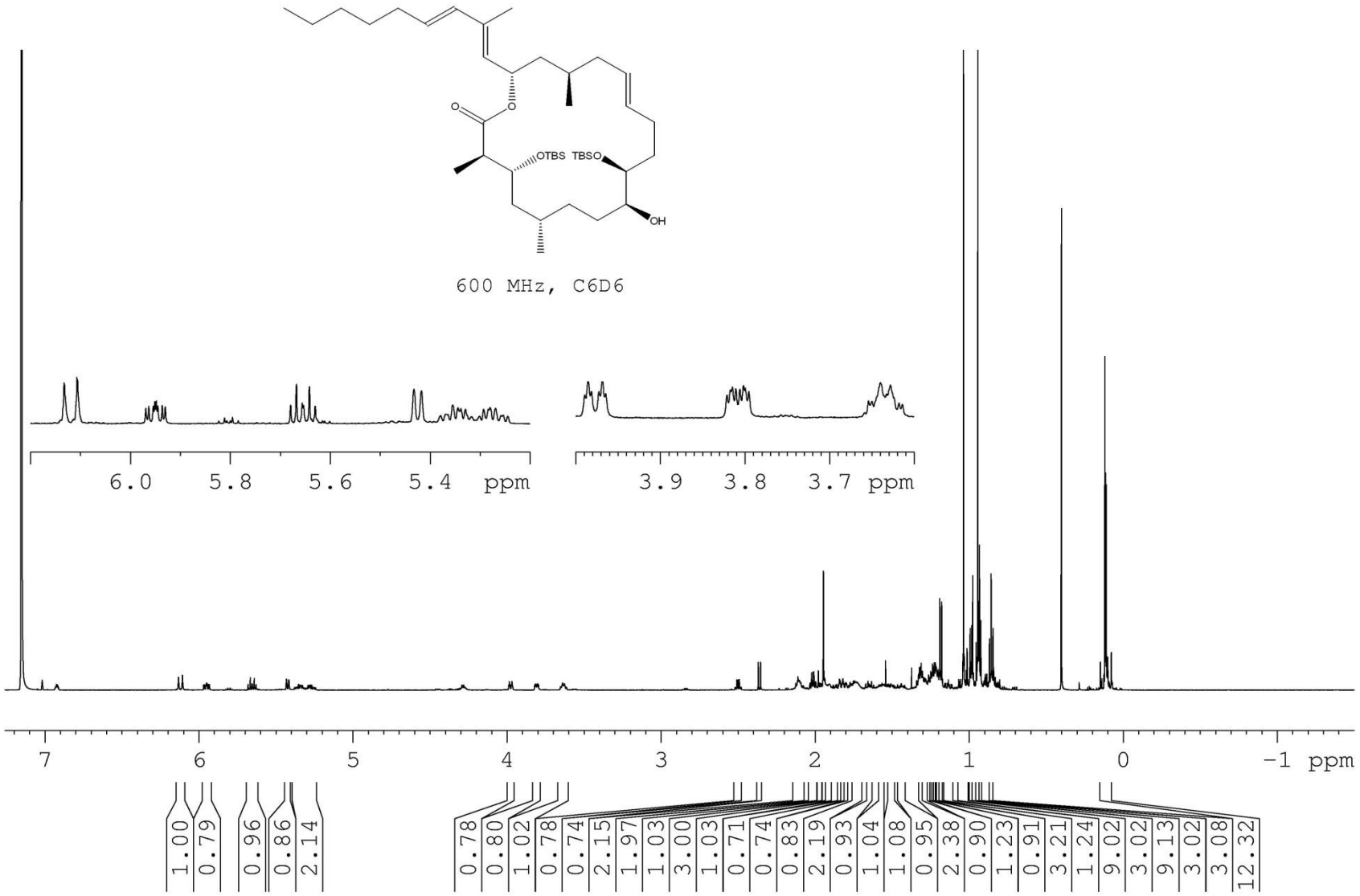

TBSO
OTBS
OTES
6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 ppm

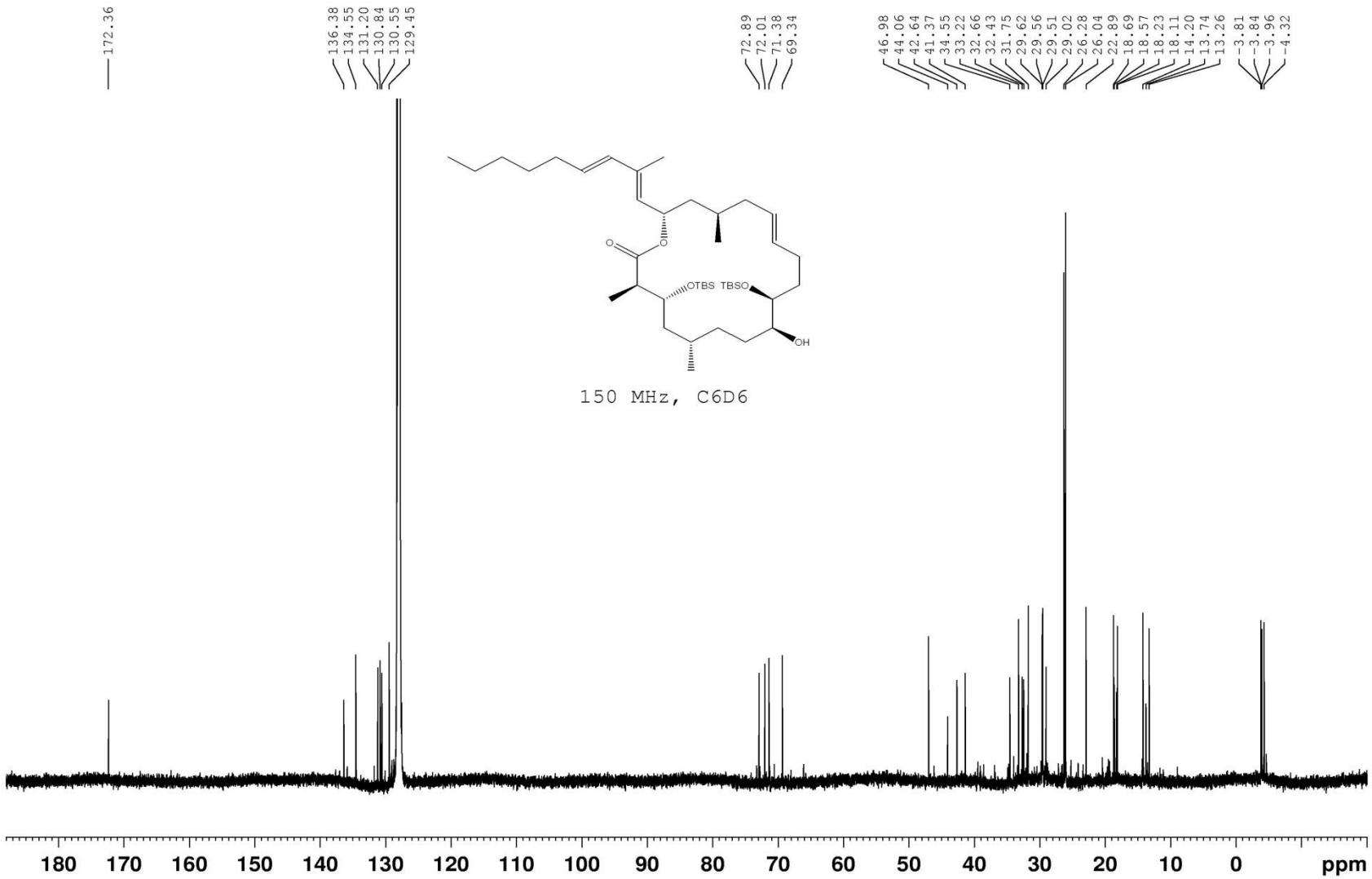

TBSO
OTBS
OTES
2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 ppm

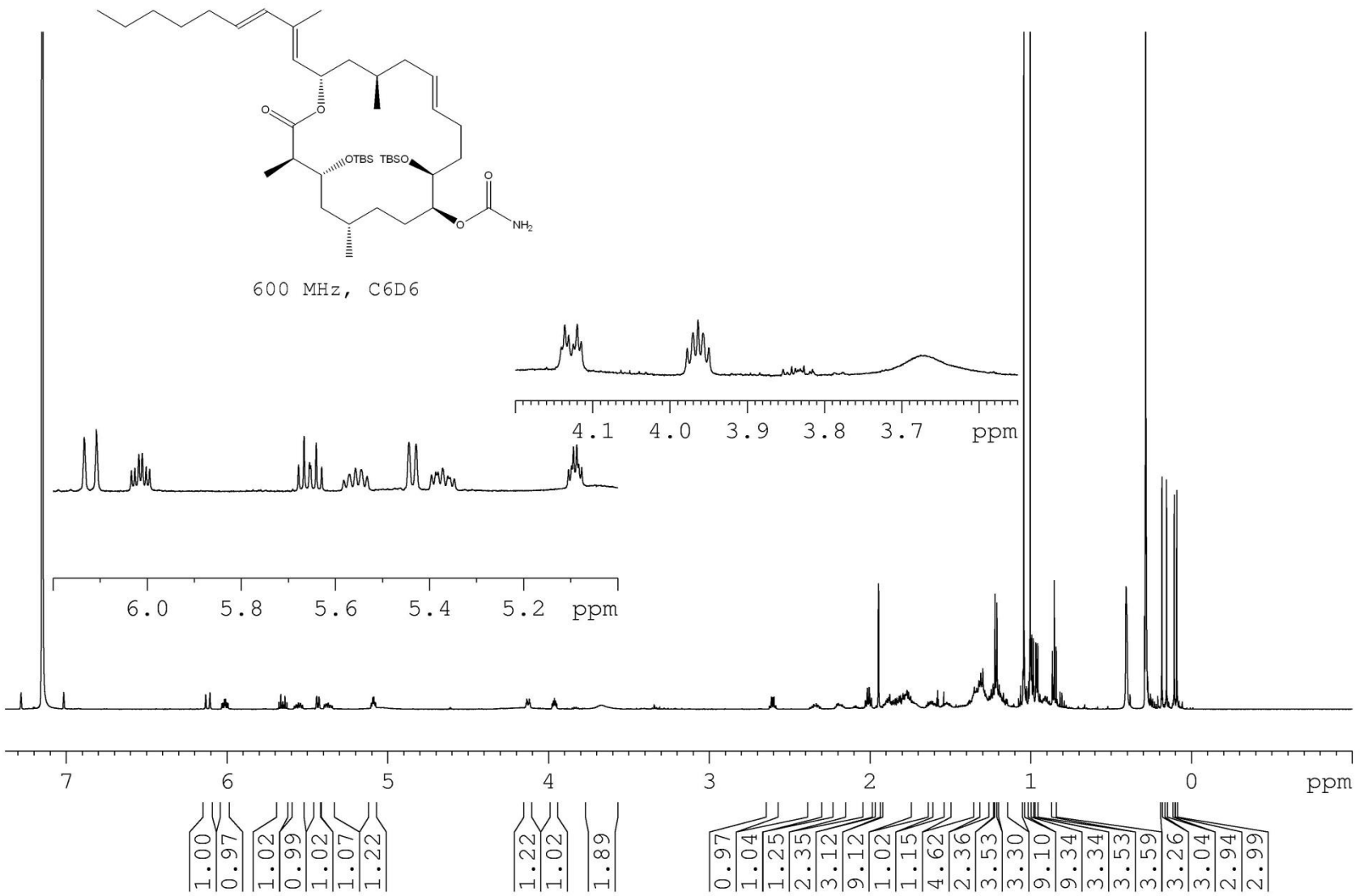

TBSO
OTBS
OTES
2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 ppm

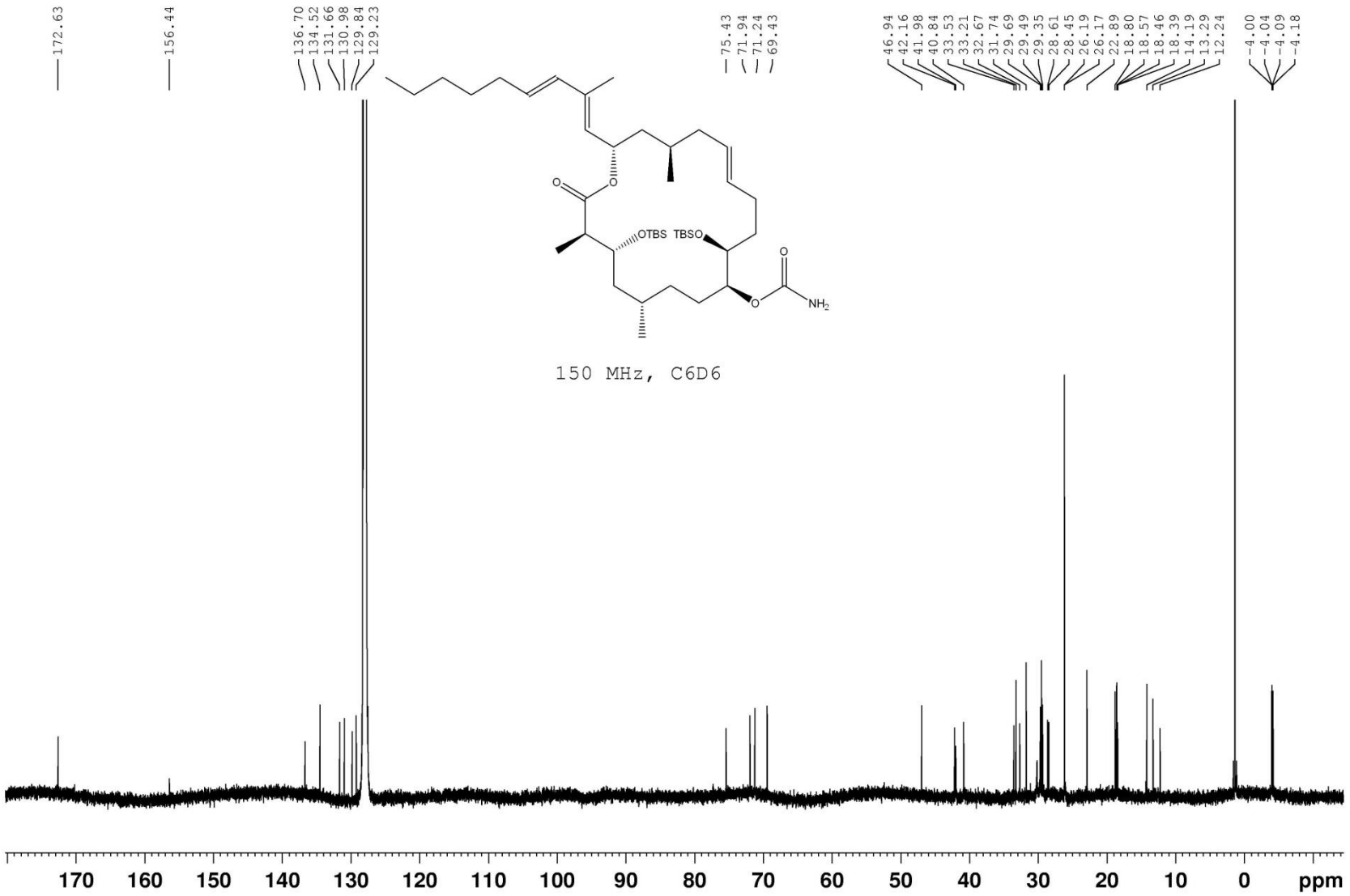

TBSO
OTBS
OTES
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

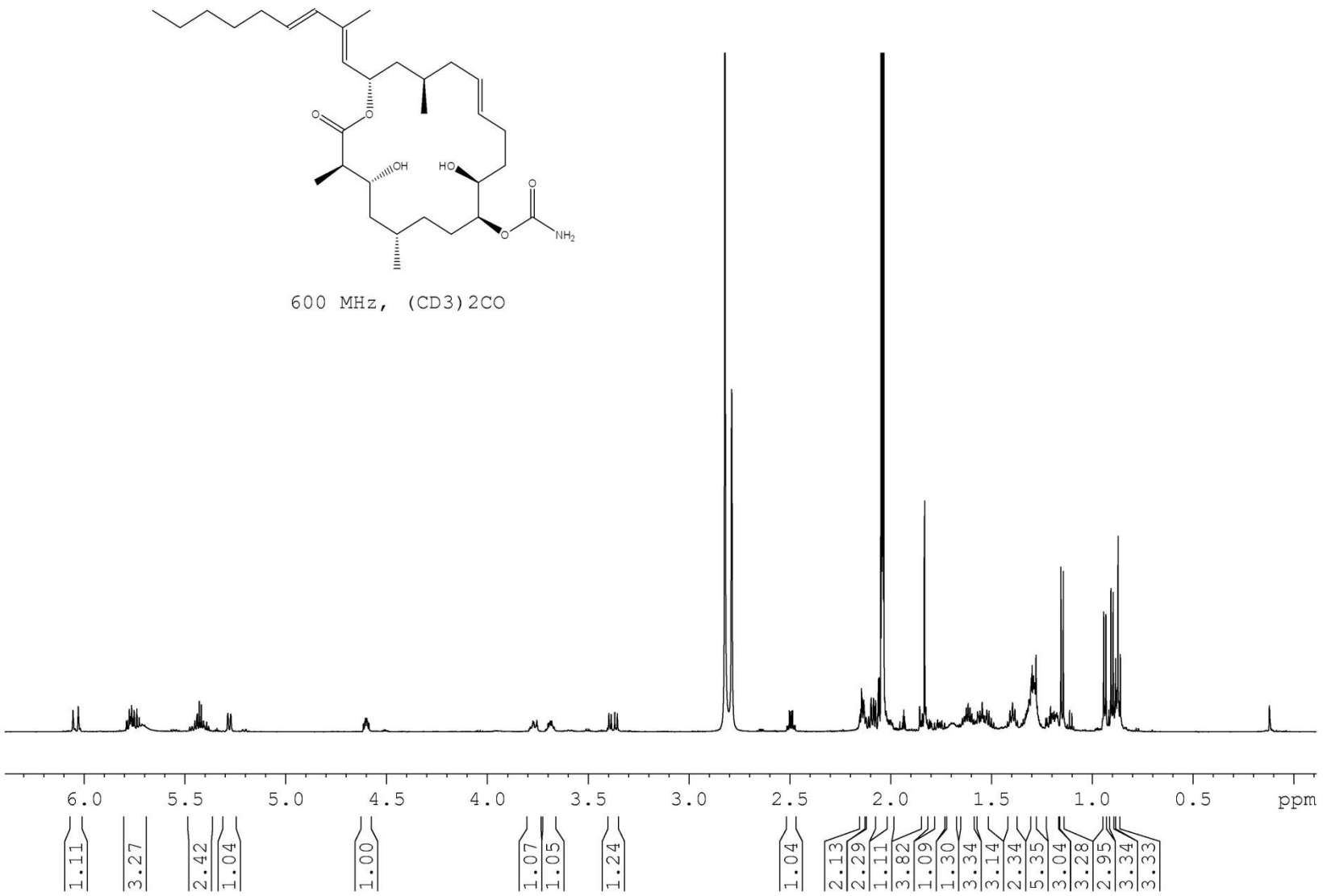

TBSO
OTBS
OTES
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

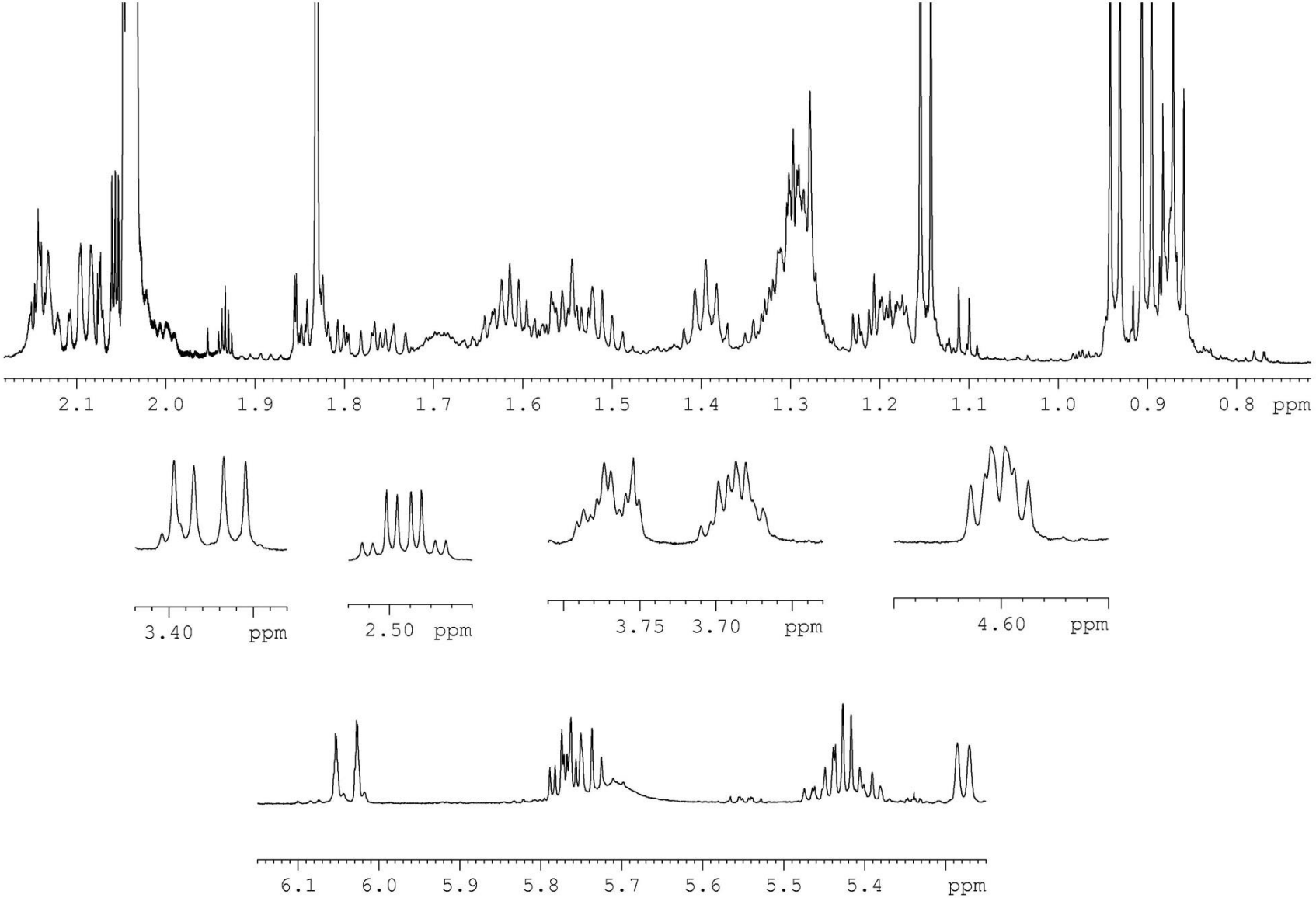

OTBS
TBSO
OH
600 MHz, C6D6
6.0
5.8
5.6
5.4
ppm
3.9
3.8
3.7
ppm
7
6
5
4
3
2
1
0
−1
ppm
1.00
0.79
0.96
0.86
2.14
0.78
0.80
1.02
0.78
0.74
2.15
1.97
1.03
3.00
1.03
0.71
0.74
0.83
2.19
0.93
1.04
1.08
0.95
2.38
0.90
1.23
0.91
3.21
1.24
9.02
3.02
9.13
3.02
3.08
12.32

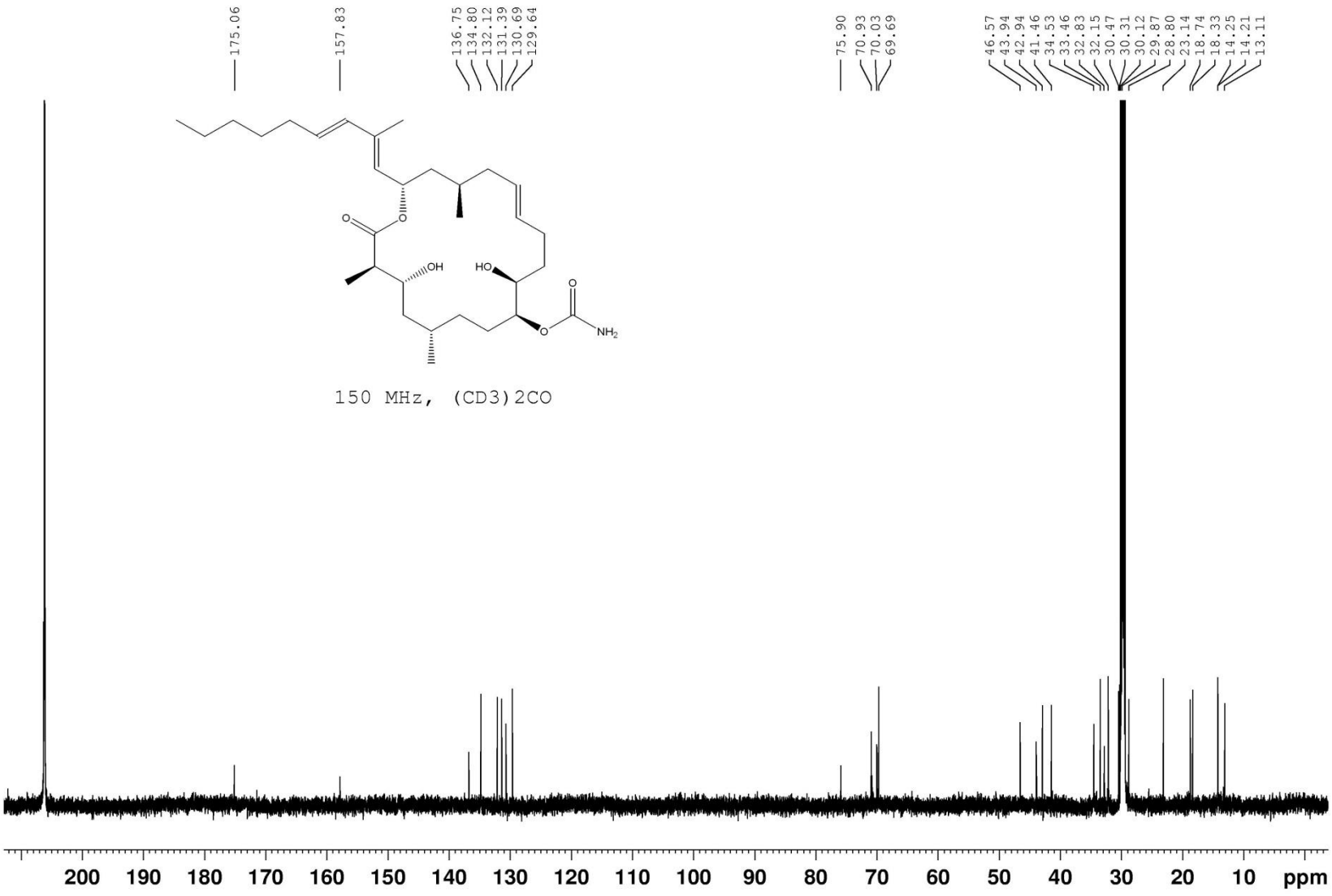

172.36
136.38
134.55
131.20
130.84
130.55
129.45
72.89
72.01
71.38
69.34
46.98
44.06
42.64
41.37
34.55
33.22
32.66
32.43
31.75
29.62
29.56
29.51
29.02
26.28
26.04
22.89
18.69
18.57
18.23
18.11
14.20
13.74
13.26
-3.81
-3.84
-3.96
-4.32
OTBS TBSO
OH
150 MHz, C6D6
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


OTBS TBSO
O
NH2
600 MHz, C6D6
4.1 4.0 3.9 3.8 3.7 ppm
6.0 5.8 5.6 5.4 5.2 ppm
7 6 5 4 3 2 1 0 ppm
1.00 0.97 1.02 0.99 1.02 1.07 1.22 1.22 1.02 1.89
0.97 1.04 1.25 2.35 3.12 9.12 1.02 1.15 4.62 2.36 3.53 3.30 9.10 9.34 3.34 3.53 3.59 3.26 3.04 2.94 2.99


172.63
156.44
136.70
134.52
131.66
130.98
129.84
129.23
75.43
71.94
71.24
69.43
46.94
42.16
41.98
40.84
33.53
33.21
32.67
31.74
29.69
29.49
29.35
28.61
28.45
26.19
26.17
22.89
18.80
18.57
18.46
18.39
14.19
13.29
12.24
-4.00
-4.04
-4.09
-4.18
OTBS
TBSO
O
NH2
150 MHz, C6D6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


600 MHz, (CD3)2CO
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.11
3.27
2.42
1.04
1.00
1.07
1.05
1.24
1.04
2.13
2.29
1.11
3.82
1.09
1.30
3.34
3.14
2.34
5.35
3.04
3.28
2.95
3.34
3.33

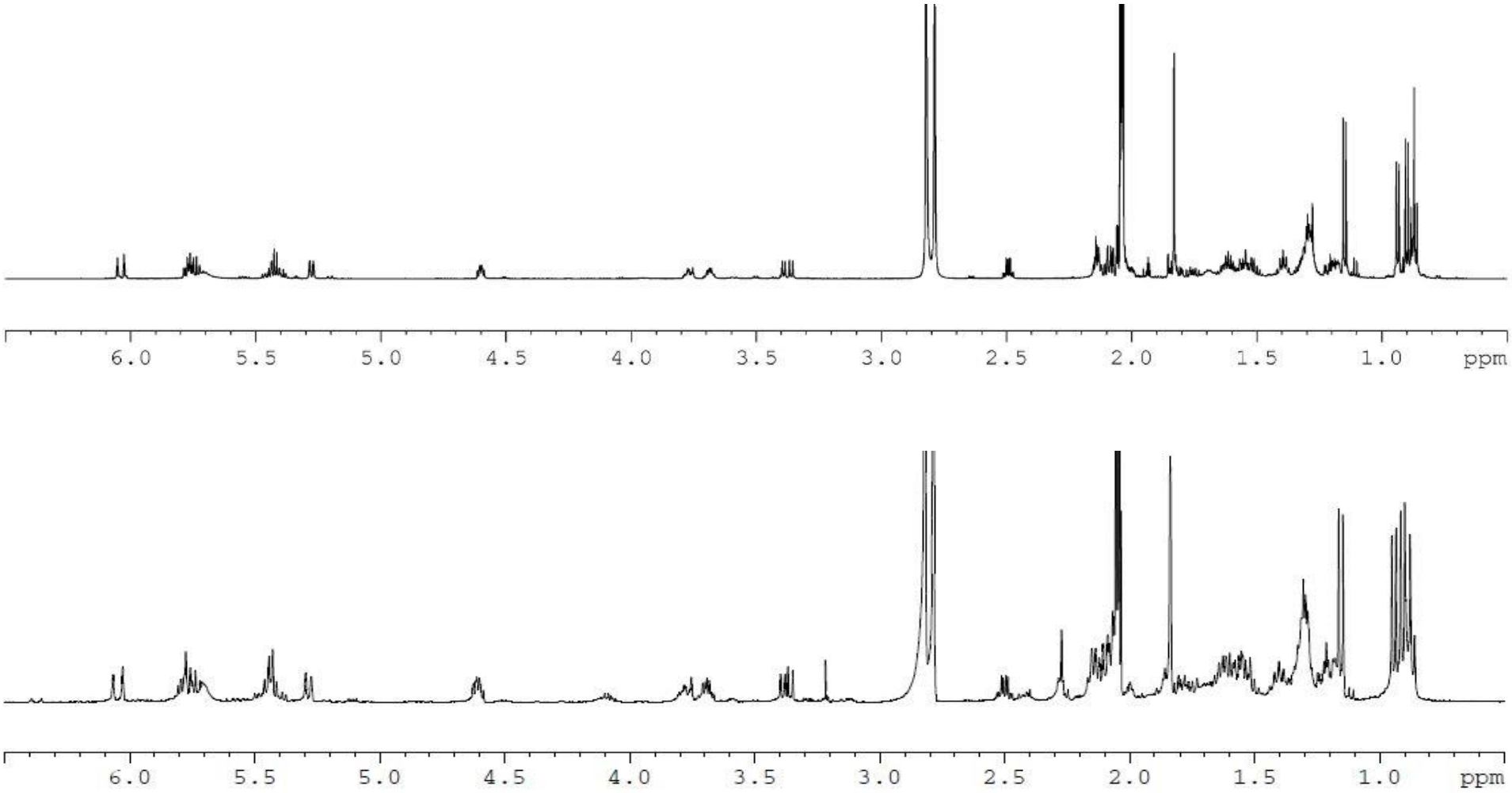

2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 ppm
3.40 ppm
2.50 ppm
3.75 3.70 ppm
4.60 ppm
6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 ppm


175.06
157.83
136.75
134.80
132.12
131.39
130.69
129.64
75.90
70.93
70.03
69.69
46.57
43.94
42.94
41.46
34.53
33.46
32.83
32.15
30.47
30.31
30.12
29.87
28.80
23.14
18.74
18.33
14.25
14.21
13.11
O
O
OH
HO
O
O
NH2
150 MHz, (CD3)2CO
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Comparison of the ^{1}H NMR spectra:

top: Synthetic tulearin A (600 MHz, $CD_3(CO)CD_3$)

bottom: Isolated tulearin A (500 MHz, $CD_3(CO)CD_3$) (A. Bishara, A. Rudi, M. Aknin, D. Neumann, N. Ben-Califa, Y. Kashman, *Org. Lett*. **2008**, *10*, 153)



Comparison of the ^{13}C NMR spectra:

top: Synthetic tulearin A (125 MHz, $CD_3(CO)CD_3$)

bottom: Isolated tulearin A (100 MHz, $CD_3(CO)CD_3$) (A. Bishara, A. Rudi, M. Aknin, D. Neumann, N. Ben-Califa, Y. Kashman, *Org. Lett*. **2008**, *10*, 153)