CHEMISTRY
A EUROPEAN JOURNAL

Supporting Information

© Copyright Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2013

Formal Total Synthesis of the Algal Toxin (−)-Polycavernoside A

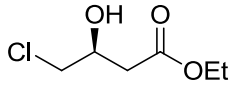
Lennart Brewitz, Josep Llaveria, Akira Yada, and Alois Fürstner*[a]

chem_201204551_sm_miscellaneous_information.pdf

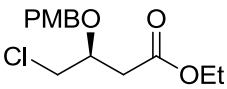
General. All reactions were carried out in flame-dried glassware under Argon unless stated otherwise. All solvents were purified by distillation over the indicated drying agents and were stored and transferred under Argon: THF (Mg-anthracene), diethyl ether (Mg-anthracene), dichloromethane (CaH_2), acetonitrile (molecular sieve 4 Å), methanol (Mg), ethanol (Mg), dimethylformamide (MS 4 Å), dimethylacetamide (CaH_2), pentane (Na/K), toluene (Na/K), triethylamine (MS 3 Å), pyridine (MS 4 Å), DBU (CaH_2). 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 DPX 300, AV 400, AV 500 or AV 600 spectrometer at 298 K (unless noted otherwise) in the solvents indicated; ^1H and ^{13}C chemical shifts (δ) are given in parts per million (ppm) relative to TMS, coupling constants (J) in Hertz (Hz). The solvent signals were used as references ($CDCl_3$: δ_H = 7.28 ppm, δ_C = 77.0 ppm; C_6D_6: δ_H = 7.15 ppm, δ_C = 128.0 ppm) and the chemical shifts converted to the TMS scale. Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Fluka, Strem) were used as received.

LiCl and LiBr were dried for 2 h at 160 °C under high vacuum. Zinc powder was dried at 90 °C for 1 h under high vacuum prior to use.

β-Hydroxyester 9a. A solution of $[RuCl_2((R)\text{-P-Phos})](DMF)_n$[1] (126 mg, 0.15 mmol) in ethanol (9 mL) and dichloromethane (1.2 mL) was added to a degassed (15 min with Argon) solution of ethyl 4-chloroacetoacetate (20 g, 123 mmol) in ethanol (45 mL) and dichloromethane (4.8 mL). The mixture was transferred via cannula into an autoclave and stirred for 14 h at 96 °C (outer temperature of autoclave) under hydrogen (35 bar). After cooling to room temperature and careful venting of the autoclave, the mixture was transferred into a flask and all volatile compounds were evaported. The crude prduct was purified by distillation (180 °C, 10 mbar) to obtain product **9a** (R = H) as a colorless oil (19.3 g, 94%, 96% *ee*) (GC-analysis on chiral stationary phase: 25 m LIPODEX A G 584 column; t_R (minor enantiomer): 29.59 min; t_R (major enantiomer): 29.09 min). All analytical and spectroscopic data matched those reported in the literature.[2] $[\alpha]_D^{25}$ = –18.4 (c = 7.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.26 (m, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.61 (m, 2H), 3.09 (brs, 1H), 2.63 (m, 2H), 1.29 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 67.9, 61.0, 48.1, 38.5, 14.1 ppm; IR (film): $\tilde{\nu}$ = 3456, 2984, 2908, 1720, 1373, 1304, 1187, 1153, 1028, 755 cm^{-1}; MS (EI): *m/z* (%): 167 (1), 139 (1), 121 (36), 117 (100), 113 (10), 89 (44), 79 (28), 71 (91), 60 (20), 43 (78), 29 (53); HRMS (CI): *m/z* calcd. for $C_6H_{12}O_3Cl$ $[M+H]^+$: 167.0475, found: 167.0475.



Ethylester 9b. A solution of copper(II) triflate (0.6 g, 1.7 mmol) in THF (7 mL) was added to a solution of the β-hydroxyester **9a** (10 g, 60 mmol) and *O*-*para*-methoxybenzyl-trichloroacetimidate (28 g, 99 mmol) in toluene

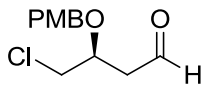


[1] C.-C. Pai, C.-W. Lin, C.-C. Lin, C.-C. Chen, A. S. C. Chan, W. T. Wong, *J. Am. Chem. Soc.* **2000**, *122*, 11513-11514.

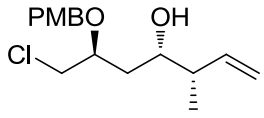
[2] Y. Yasohara, N. Kizaki, J. Hasegawa, M. Wada, M. Kataoka, S. Shimizu, *Tetrahedron: Asymmetry* **2001**, *12*, 1713-1718.

(500 mL) at –10 °C. The green suspension was stirred for 90 min while warming to 0 °C before the reaction was quenched with sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer extracted twice with ethyl acetate. The combined extracts were dried over Na_2SO_4, filtered, and evaporated. The crude material was filtrated through a pad of Celite, eluting with hexanes/dichloromethane (10:1). The combined filtrates were evaporated and the remaining syrup purified by flash chromatography (pentane/ethyl acetate, 15:1) to afford product **9b** as a pale green oil (14.1 g, 82%). $[\alpha]_D^{20}$ = –9.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (dt, *J* = 8.8, 2.4 Hz, 2H), 6.89 (dt, *J* = 8.7, 2.5 Hz, 2H), 4.61 (d, *J* = 11.0 Hz, 1H), 4.56 (d, *J* = 11.1 Hz, 1H), 4.17 (qd, *J* = 7.1, 0.8 Hz, 2H), 4.12 (m, 1H), 3.82 (s, 3H), 3.65 (dd, *J* = 11.4, 4.7 Hz, 1H), 3.60 (dd, *J* = 11.4, 5.8 Hz, 1H), 2.74 (dd, *J* = 16.0, 5.1 Hz, 1H), 2.64 (dd, *J* = 15.9, 7.5 Hz, 1H), 1.28 ppm (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 159.4, 129.8, 129.5, 113.8, 75.1, 72.1, 60.7, 55.3, 45.4, 37.9, 14.2 ppm; IR (film): $\tilde{\nu}$ = 2960, 2908, 2837, 1730, 1612, 1513, 1374, 1303, 1245, 1173, 1073, 1030, 820, 749 cm^{-1}; MS (EI): *m/z* (%): 286 (4), 251 (2), 137 (100), 121 (64), 109 (6); HRMS (ESI): *m/z* calcd. for $C_{14}H_{19}O_4ClNa$ $[M+Na]^+$: 309.0864, found: 309.0863.

Aldehyde 10. DIBAl-H (1 M in toluene, 24.2 mL, 24.2 mmol) was added over 30 min to a solution of ester **9b** (6.6 g, 23 mmol) in toluene (200 mL) at –78 °C. Once the addition was complete, stirring was continued for 35 min at this temperature before the reaction was carefully quenched by the addition of ethyl acetate. A saturated aq. solution of Rochelle's salt was added and the mixture stirred for 2 h at ambient temperature. The phases were separated and the aqueous layer extracted twice with ethyl acetate. The combined extracts were washed with water and brine, dried over Na_2SO_4, filtered, and evaporated. The crude material was purified by flash chromatography (pentane/ethyl acetate, 5:1) to give aldehyde **10** as an oil, which was directly used in the next step (4.9 g, 88%). $[\alpha]_D^{20}$ = –33.8 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (t, *J* = 1.5 Hz, 1H), 7.28 (dt, *J* = 8.6, 2.4 Hz, 2H), 6.91 (dt, *J* = 8.7, 2.5 Hz, 2H), 4.64 (d, *J* = 11.3 Hz, 1H), 4.54 (d, *J* = 11.1 Hz, 1H), 4.20 (ddd, *J* = 12.0, 6.0, 4.3 Hz, 1H), 3.83 (s, 3H), 3.67 (dd, *J* = 11.4, 4.3 Hz, 1H), 3.62 (dd, *J* = 11.5, 5.9 Hz, 1H), 2.82 ppm (dd, *J* = 6.0, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.9, 159.5, 129.6, 129.5, 113.9, 73.1, 71.8, 55.3, 46.6, 45.2 ppm; IR (film): $\tilde{\nu}$ = 2958, 2908, 2837, 2734, 1721, 1612, 1512, 1464, 1301, 1245, 1173, 1079, 1030, 818, 749 cm^{-1}; MS (EI): *m/z* (%): 242 (9), 215 (2), 163 (2), 137 (79), 121 (100), 109 (9), 77 (12); HRMS (ESI): *m/z* calcd. for $C_{12}H_{15}O_3ClNa$ $[M+Na]^+$: 265.0602, found: 265.0601.



Alcohol 11. A solution of crotyl silane **19**[3] (11.5 g, 20.2 mmol) in dichloromethane (20 mL) was added to a solution of aldehyde **10** (4.4 g, 18.1 mmol) in dichloromethane (150 mL) at 0 °C, followed by the addition of scandium triflate (413 mg, 0.8 mmol). The mixture was vigorously stirred at 0 °C for 1 h before it was concentrated under reduced pressure. The residue was diluted with diethyl ether (150 mL) and aq. HCl (1 M, 150 mL). After stirring for 90 min at ambient temperature, the resulting suspension was filtrated, the phases of the filtrate were separated, and the aqueous phase was extracted

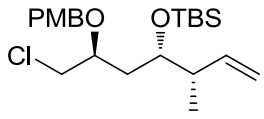


[3] B. M. Hackman, P. J. Lombardi, J. L. Leighton, *Org. Lett.* **2004**, *6*, 4375-4377.

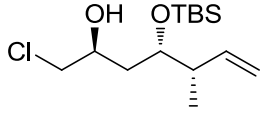
twice with diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated. Analysis of the crude material by GC showed a dr > 28:1 (30 m DB-1 0.25/0.25df G/575 column; t_R (minor diastereomer): 20.58 min; t_R (major diastereomer): 20.44 min)). Purification of the residue by flash chromatography (pentane/ethyl acetate, 5:1) furnished product **11** in diastereomerically pure form as a pale yellow oil (4.3 g, 78%). $[\alpha]_D^{20}$ = –51.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (dt, *J* = 8.6, 2.3 Hz, 2H), 6.91 (dt, *J* = 8.6, 2.5 Hz, 2H), 5.77 (m, 1H), 5.10 (m, 1H), 5.07 (m, 1H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.53 (d, *J* = 11.3 Hz, 1H), 3.94 (m, 1H), 3.83 (s, 3H), 3.72 (ddd, *J* = 10.1, 5.6, 2.1 Hz, 1H), 3.63 (s, 1H), 3.62 (d, *J* = 1.2 Hz, 1H), 2.26 (sext., *J* = 6.7 Hz, 1H), 1.91 (brs, 1H), 1.80 (ddd, *J* = 14.5, 8.5, 2.2 Hz, 1H), 1.65 (ddd, *J* = 14.5, 10.1, 3.3 Hz, 1H), 1.05 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 140.5, 129.9, 129.7, 115.5, 113.9, 75.9, 72.1, 71.0, 55.3, 46.0, 43.9, 36.5, 14.8 ppm; IR (film): $\tilde{\nu}$ = 3474, 2959, 2837, 1612, 1463, 1302, 1246, 1173, 1066, 1033, 999, 915, 820, 751 cm^{-1}; MS (EI): *m/z* (%): 298 (1), 263 (1), 242 (1), 224 (1), 137 (42), 121 (100); HRMS (ESI): *m/z* calcd. for $C_{16}H_{23}O_3ClNa$ $[M+Na]^+$: 321.1228, found: 321.1227.

Treatment of the white precipitate collected by filtration with NaOH allowed the diamine ligand to be recovered after chromatographic purification in > 90% yield.

Chloroolefin S-1. Imidazole (733 mg, 10.7 mmol), DMAP (22 mg, 0.18 mmol), and *tert*-butyldimethylsilyl chloride (1.08 g, 7.13 mmol) were added to a solution of alcohol **11** (1.05 g, 3.5 mmol) in dichloromethane (12 mL) at 0 °C. The mixture was stirred for 24 h while slowly warming to room temperature. The reaction was quenched with sat. aq. NH_4Cl and the aqueous layer extracted three times with dichloromethane. The combined extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 30:1) to afford product **S-1** as a colorless oil (1.27 g, 85%). $[\alpha]_D^{20}$ = –58.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (dt, *J* = 8.7, 2.4 Hz, 2H), 6.91 (dt, *J* = 8.7, 2.5 Hz, 2H), 5.96 (ddd, *J* = 17.2, 10.7, 6.3 Hz, 1H), 5.07 (dt, *J* = 10.7, 1.6 Hz, 1H), 5.03 (dt, *J* = 17.4, 1.7 Hz, 1H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.47 (d, *J* = 10.9 Hz, 1H), 3.86 (m, 1H), 3.83 (s, 3H), 3.78 (m, 1H), 3.65 (dd, *J* = 11.4, 5.1 Hz, 1H), 3.58 (dd, *J* = 11.4, 4.3 Hz, 1H), 2.39 (m, 1H), 1.73 (ddd, *J* = 14.4, 8.7, 3.0 Hz, 1H), 1.59 (ddd, *J* = 14.4, 9.0, 3.3 Hz, 1H), 0.98 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.08 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 140.1, 130.4, 129.1, 114.4, 113.9, 75.9, 73.0, 71.1, 55.3, 46.6, 42.9, 36.9, 26.0, 18.1, 14.4, –3.9, –4.4 ppm; IR (film): $\tilde{\nu}$ = 2956, 2930, 2885, 2857, 1613, 1513, 1463, 1302, 1247, 1172, 1073, 1036, 912, 832, 773 cm^{-1}; MS (EI): *m/z* (%): 357 (4), 251 (1), 221 (1), 137 (3), 121 (100); HRMS (ESI): *m/z* calcd. for $C_{22}H_{37}O_3SiClNa$ $[M+Na]^+$: 435.2093, found: 435.2095.

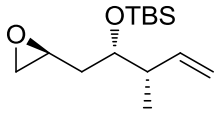


Alcohol S-2. DDQ (2.8 g, 12.3 mmol) was added to a solution of compound **S-1** (3.4 g, 8.2 mmol) in dichloromethane (not dried, 56 mL) and phosphate buffer (pH 7, 8.5 mL) at 0 °C. After stirring for 2 h at ambient temperature, the reaction was quenched with sat. aq. $NaHCO_3$ at 0°C. The resulting suspension was stirred for 2 h before it was diluted with water until all solids had dissolved. The aqueous phase was repeatedly extracted with dichloromethane, the combined extracts were dried over Na_2SO_4, filtered,

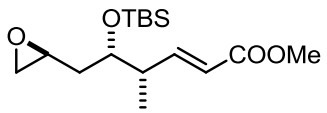


and evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 13:1) to afford product **S-2** as a colorless oil (2.4 g, 99%). $[\alpha]_D^{20}$ = –43.2 (*c* = 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (m, 1H), 5.09 (m, 1H), 5.05 (m, 1H), 4.10 (m, 1H), 3.87 (m, 1H), 3.56 (dd, *J* = 10.9, 4.4 Hz, 1H), 3.47 (dd, *J* = 10.9, 6.4 Hz, 1H), 3.10 (brs, 1H), 2.50 (m, 1H), 1.63 (m, 2H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.12 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.8, 115.0, 73.9, 68.4, 50.4, 42.8, 36.6, 25.9, 18.0, 16.1, –4.4, –4.5 ppm; IR (film): $\tilde{\nu}$ = 3446, 2956, 2930, 2887, 2858, 1640, 1472, 1376, 1254, 1072, 1004, 912, 833, 774 cm^{-1}; MS (EI): *m/z* (%): 237 (54), 217 (1), 193 (15), 179 (6), 159 (100), 141 (6), 125 (2), 115 (15), 101 (10), 55 (20), 43 (9); HRMS (ESI): *m/z* calcd. for $C_{14}H_{29}O_2SiClNa$ $[M+Na]^+$: 315.1518, found: 315.1517.

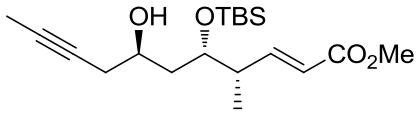
Epoxide 12. Potassium hydroxide (189 mg, 3.4 mmol) was added to a solution of alcohol **S-2** (0.82 g, 2.8 mmol) in ethanol (125 mL) at 0 °C. After stirring for 5 h at 0 °C and for additional 5 h at ambient temperature, the solvent was evaporated and the residue diluted with water. The aqueous phase was extracted three times with ethyl acetate, the combined extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 30:1) to obtain product **12** as a colorless oil (675 mg, 94%). $[\alpha]_D^{20}$ = –55.8 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.89 (ddd, *J* = 17.2, 10.6, 6.7 Hz, 1H), 4.99 (m, 2H), 3.76 (m, 1H), 2.88 (m, 1H), 2.42 (dd, *J* = 5.3, 3.9 Hz, 1H), 2.34 (m, 1H), 2.13 (dd, *J* = 5.3, 2.5 Hz, 1H), 1.60 (ddd, *J* = 14.1, 8.4, 4.2 Hz, 1H), 1.31 (ddd, *J* = 14.1, 7.4, 3.8 Hz, 1H), 0.98 (s, 9H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.09 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 140.7, 114.6, 74.1, 49.4, 47.4, 43.7, 37.1, 26.1, 18.3, 14.8, –4.3, –4.5 ppm; IR (film): $\tilde{\nu}$ = 2956, 2929, 2887, 2857, 1640, 1472, 1409, 1361, 1253, 1068, 906, 831, 773 cm^{-1}; MS (EI): *m/z* (%): 201 (49), 185 (1), 169 (1), 158 (6), 143 (45), 131 (5), 115 (68), 99 (11), 85 (14), 73 (100), 69 (23), 59 (27), 41 (13); HRMS (ESI): *m/z* calcd. for $C_{14}H_{28}O_2SiNa$ $[M+Na]^+$: 279.1751, found: 279.1750.



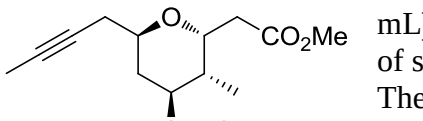
Compound 13. Methyl acrylate (0.72 mL, 8.0 mmol) and the Zhan-1B catalyst **20** (172 mg, 0.23 mmol) were added to a solution of olefin **12** (1.72 g, 6.7 mmol) in toluene (140 mL). The resulting mixture was stirred for 18 h at 70 °C while being constantly purged with argon. The solvent was removed under reduced pressure and the crude material (*E*/*Z* = 11:1) purified by flash chromatography (pentane/ethyl acetate, 15:1) to obtain product **13** as a single diastereomer in form of a colorless oil (1.59 g, 75%). $[\alpha]_D^{20}$ = –63.0 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.06 (dd, *J* = 15.9, 6.8 Hz, 1H), 5.86 (dd, *J* = 15.9, 1.5 Hz, 1H), 3.92 (q, *J* = 4.2 Hz, 1H), 3.75 (s, 3H), 3.01 (m, 1H), 2.82 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.58 (m, 1H), 2.49 (dd, *J* = 5.1, 2.7 Hz, 1H), 1.70 (ddd, *J* = 14.1, 8.5, 4.4 Hz, 1H), 1.47 (ddd, *J* = 14.2, 7.3, 3.6 Hz, 1H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.10 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 151.0, 121.0, 73.1, 51.4, 49.7, 47.8, 42.4, 36.8, 25.8, 18.0, 14.2, -4.4, -4.7 ppm; IR (film): $\tilde{\nu}$ = 2953, 2930, 2886, 2857, 1723, 1656, 1472, 1435, 1253, 1176, 1025, 833, 774 cm^{-1}; MS (EI): *m/z* (%): 283 (4), 257 (11), 225 (8), 201 (71), 111 (43), 99 (9), 89 (27), 73 (100), 59 (24), 41 (12); HRMS (ESI): *m/z* calcd. for $C_{16}H_{30}O_4SiNa$ $[M+Na]^+$: 337.1806, found: 337.1804.



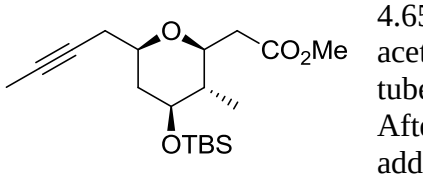
Alcohol 14. *n*BuLi (1.6 M in hexane, 0.74 mL, 1.19 mmol) was added to an excess of liquid propyne (ca 0.3 mL) in THF (2.5 mL) at –78 °C. After stirring for 30 min, boron trifluoride etherate (94 μL, 0.74 mmol) was introduced and stirring continued for 1 h at –78 °C before a solution of epoxide **13** (233 mg, 0.74 mmol) in THF (1 mL) was added via syringe. The mixture was stirred for an additional hour at –78 °C before the reaction was quenched with sat. aq. NH_4Cl. The aqueous phase was extracted three times with ethyl acetate, the combined extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 10:1) to give product **14** as a yellow oil (234 mg, 89%). $[\alpha]_D^{20}$ = –41.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (dd, *J* = 15.8, 7.4 Hz, 1H), 5.86 (dd, *J* = 15.9, 1.2 Hz, 1H), 3.93 (m, 2H), 3.75 (s, 3H), 2.64 (m, 2H), 2.29 (m, 2H), 1.80 (t, *J* = 1.5 Hz, 3H), 1.59 (m, 2H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.11 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 150.8, 121.1, 78.4, 75.1, 73.3, 66.9, 51.4, 42.0, 39.2, 28.2, 25.9. 18.0, 15.3, 3.5, –4.5 ppm; IR (film): $\tilde{\nu}$ = 3495, 2953, 2929, 2857, 1725, 1656, 1435, 1255, 1195, 1078, 1026, 836, 776 cm^{-1}; MS (EI): *m/z* (%): 323 (6), 297 (16), 257 (29), 241 (24), 217 (21), 183 (26), 173 (12), 159 (34), 145 (60), 133 (18), 109 (92), 89 (21), 73 (100), 55 (25), 43 (11); HRMS (ESI): *m/z* calcd. for $C_{19}H_{34}O_4SiNa$ $[M+Na]^+$: 377.2119, found: 377.2120.



***trans*-Pyrane 15.** KO*t*Bu (0.1 M in THF, 0.15 mL, 0.015 mmol) was added at –10 °C to a solution of compound **14** (53.1 mg, 0.15 mmol) in THF (5 mL). After 5 min, the reaction was quenched by the addition of silica and the suspension filtered using Et_2O as the eluent. The filtrate was evaporated and the crude product analyzed by NMR spectroscopy to determine the diastereomeric ratio (dr ≈ 10:1). The residue was then purified by flash chromatography (hexane/ethyl acetate, 10:1) to yield **15** as a yellow oil (31 mg, 58%). A second fraction was collected which consisted of the *cis*-isomer **17** (9%). Analytical and spectral data of **15**: $[\alpha]_D^{20}$ = +62.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.40 (dt, *J* = 10.7, 4.6 Hz, 1H), 3.78 (m, 1H), 3.67 (s, 3H), 3.58 (td, *J* = 8.8, 4.4 Hz, 1H), 2.59 (dd, *J* = 14.0, 10.7 Hz, 1H), 2.39 (m, 1H), 2.37 (m, 2H), 1.93 (dt, *J* = 13.1, 3.9 Hz, 1H), 1.78 (m, 1H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.41 (dt, *J* = 13.1, 9.2 Hz, 1H), 0.88 (s, 9H), 0.87 (s, 3H), 0.05 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 77.3, 75.5, 72.6, 70.2, 68.9, 51.7, 40.5, 37.9, 34.4, 25.8, 25.5, 18.0, 13.3, 3.5, –4.3, –4.8 ppm; IR (film): $\tilde{\nu}$ = 2932, 2928, 2857, 1744, 1437, 1256, 1086, 836, 776 cm^{-1}; MS (EI): *m/z* (%): 323 (2), 297 (29), 281 (4), 257 (18), 217 (16), 183 (100), 169 (58), 129 (17), 95 (29), 89 (12), 73 (54), 59 (18), 41 (9); HRMS (ESI): *m/z* calcd. for $C_{19}H_{34}O_4SiNa$ $[M+Na]^+$: 377.2119, found: 377.2122.

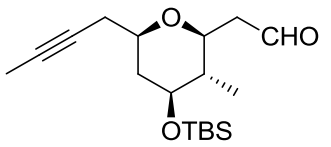


***cis*-Pyrane 17.** A Young-Schlenk tube was charged with dry lithium chloride (197 mg, 4.65 mmol), compound **14** (165 mg, 0.47 mmol), acetonitrile (10 mL) and DBU (0.7 mL, 4.70 mmol). The tube was sealed and the mixture stirred at 100 °C for 2 h. After cooling to room temperature, sat. aq. NH_4Cl was added to the bright pink suspension, the phases were



separated and the aqueous layer was extracted three times with ethyl acetate. The combined extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was analyzed by NMR to determine the diastereomeric ratio (dr ≥ 20:1). The crude material was then purified by flash chromatography (pentane/diethyl ether, 7:1) to obtain product **17** as a pale yellow oil (138 mg, 84%). $[\alpha]_D^{20}$ = +3.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.66 (s, 3H), 3.46 (ddd, *J* = 10.0, 9.2, 3.6 Hz, 1H), 3.41 (dddd, *J* = 11.4, 7.2, 5.6, 1.6 Hz, 1H), 3.33 (ddd, *J* = 10.6, 10.0, 4.6 Hz, 1H), 2.59 (dd, *J* = 15.0, 3.6 Hz, 1H), 2.40 (dd, *J* = 15.0, 9.2 Hz, 1H), 2.38 (ddq, *J* = 16.4, 5.2, 2.6 Hz, 1H), 2.19 (ddq, *J* = 16.4, 7.6, 2.6 Hz, 1H), 2.02 (ddd, *J* = 12.8, 4.6, 1.8 Hz, 1H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.30 (tq, *J* = 10.0, 7.0 Hz, 1H), 1.28 (ddd, *J* = 12.8, 11.4, 10.6 Hz, 1H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.05 ppm (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.2, 78.0, (77.2), 75.2, 74.2, 73.8, 51.6, 43.7, 40.6, 39.1, 25.9, 25.8, 18.0, 13.2, 3.5, –4.0, –4.7 ppm; IR (film): $\tilde{\nu}$ = 2955, 2929, 2857, 1744, 1472, 1473, 1251, 1152, 1079, 1001, 837, 774 cm^{-1}; MS (EI): *m/z* (%): 339 (2), 323 (7), 297 (100), 257 (2), 217 (94), 195 (11), 183 (49), 173 (8), 143 (19), 129 (14), 111 (27), 89 (25), 75 (73), 59 (20), 43 (14); HRMS (ESI): *m/z* calcd. for $C_{19}H_{34}O_4SiNa$ $[M+Na]^+$: 377.2119, found: 377.2122.

Aldehyde 7. DIBAl-H (1 M in toluene, 0.16 mL, 0.16 mmol) was added to a solution of methyl ester **17** (57 mg, 0.16 mmol) in toluene (1.6 mL) at –78 °C and the mixture was stirred until the starting material was consumed (ca. 25 min). The reaction was quenched with ethyl acetate before a sat. aq. solution of Rochelle's salt was introduced. The mixture was vigorously stirred for 2 h, at which point the layers could be separated. The aqueous phase was repeatedly extracted with ethyl acetate, the combined extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (pentane/diethyl ether, 5:1) to yield product **7** as a colorless oil (45 mg, 86%). $[\alpha]_D^{20}$ = +4.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.81 (dd, *J* = 3.0, 1.9 Hz, 1H), 3.55 (ddd, *J* = 10.1, 8.6, 3.5 Hz, 1H), 3.47 (m, 1H), 3.38 (ddd, *J* = 10.8, 9.6, 4.7 Hz, 1H), 2.62 (ddd, *J* = 16.1, 3.6, 1.8 Hz, 1H), 2.53 (ddd, *J* = 16.1, 8.6, 3.0 Hz, 1H), 2.41 (m, 1H), 2.25 (m, 1H), 2.05 (ddd, *J* = 12.7, 4.7, 1.9 Hz, 1H), 1.78 (t, *J* = 2.6 Hz, 3H), 1.36 (m, 2H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.09 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.9, 77.5, 76.8, 75.0, 74.3, 73.8, 47.0, 43.7, 40.6, 25.9. 25.8, 18.0, 13.1, 3.4, –4.0, –4.7 ppm; IR (film): $\tilde{\nu}$ = 2953, 2928, 2890, 2857, 2731, 1727, 1472, 1380, 1254, 1153, 1076, 835, 776 cm^{-1}; MS (EI): *m/z* (%): 267 (50), 249 (15), 223 (51), 205 (7), 173 (30), 143 (50), 129 (68), 101 (39), 93 (23), 75 (100), 67 (16), 59 (31), 43 (38); HRMS (ESI): *m/z* calcd. for $C_{18}H_{32}O_3SiNa$ $[M+Na]^+$: 347.2013, found: 347.2014.



Penten-3-yne (27). Vinyl bromide (5.7 mL, 80 mmol), $[(PPh_3)_2PdCl_2]$ (1.0 g, 1.2 mmol), and copper(I) iodide (0.46 g, 2.4 mmol) were added to degassed triethylamine (Argon, 30 min) (180 mL) at –78 °C in a thick-wall pressure Young-Schlenk tube.

In a separate flask, propyne (8.0 mL, 120 mmol) was condensed at –78°C and then transferred via canula into the pressure Young-Schlenk tube serving as the reaction flask. After complete addition, the flask was sealed, the cold bath removed and the mixture stirred for 12 h at ambient temperature. For work up, the reaction mixture was distilled

twice using a spinning-band distillation apperatus (bp 52-56 °C) to afford enyne **27** as a colorless oil (4.3 g, 81%). The analytical data were in reasonable agreement with those reported in literature.[4] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddq, J = 17.6, 10.9, 2.2 Hz, 1H), 5.56 (dd, J = 17.5, 2.1 Hz, 1H), 5.39 (dd, J = 10.9, 2.2 Hz, 1H), 1.96 ppm (d, J = 2.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 125.5, 117.6, 86.5, 78.5, 4.1 ppm; IR (film): $\tilde{\nu}$ = 2969, 2919, 2237, 1609, 1437, 1167, 974, 913 cm^{-1}; MS (GC-EI): *m/z* (%): 66 (100), 63 (16), 51 (6), 40 (26); HRMS (EI): *m/z* calcd. for C_5H_6 $[M]^+$: 66.0470, found: 66.0469.

(2*R*)-2-(Prop-1-yne-1-yl)oxirane (28). Sodium hypochlorite (140 mL, 88 mmol) and the (*S*,*S*)-Mn-salen complex **33** (1.3 g, 2.0 mmol) were added to a solution of penten-3-yne (3.0 g, 40 mmol) in dichloromethane (not dried, 40 mL) at 0 °C under air. The reaction was vigorously stirred for 6.5 h at this temperature before the mixture was diluted with dichloromethane. The phases were separated, and the aqueous phase was extracted twice with dichloromethane and twice with pentane. The combined organic extracts were dried over Na_2SO_4 and filtered through a short silica pad, which was rinsed with a pentane/dichloromethane mixture (1:1). The solvents of the combined filtrates were distilled off at ambient pressure and the remaining crude product was purified by distillation (60 $\rightarrow$ 15 mbar, 40 °C) to yield the corresponding epoxide which had an *ee* of ca. 50 % (GC-analysis on a chiral stationary phase: 30 m BGB-174/BGB-1701 0.25/0.25 column; t_R (minor enantiomer): 13.86 min; t_R (major enantiomer): 14.16 min).

Water (0.4 mL, 19 mmol) and the (*R*,*R*)-Co-salen complex **34**[5] (118 mg, 0.17 mmol) were added at 0 °C to a solution of the resulting epoxide in diethyl ether (not dried, 1.5 mL). The mixture was stirred at ambient temperature for 14 h. At this point, inspection by GC (see above) showed that an enantiomeric excess of > 99% had been reached. For work up, the mixture was diluted with diethyl ether, the phases were separated, and the aqueous phase extracted with diethyl ether (2 x). The combined extracts were dried over Na_2SO_4 and filtered, the solvents were carefully distilled off at ambient pressure, and the crude product purified by distillation (60 $\rightarrow$15 mbar, 40 °C) to afford epoxide **28** as a colorless oil (2.5 g, 73% over two steps, > 99% *ee*). $[\alpha]_D^{28}$ = –102 (c = 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (m, 1H), 2.89 (dd, J = 5.8, 4.0 Hz, 1H), 2.85 (dd, J = 5.9, 2.7 Hz, 1H), 1.86 ppm (d, J = 1.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.2, 75.9, 48.7, 40.0, 3.6 ppm; IR (film): $\tilde{\nu}$ = 3059, 2992, 2922, 2248, 1438, 1377, 1251, 1168, 1137, 976, 869, 788 cm^{-1}; HRMS (CI): *m/z* calcd. for C_5H_7O $[M+H]^+$: 83.0497, found: 83.0497.

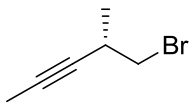
(2*S*)-2-Methylpent-3-yne-1-yl *para*-methylbenzenesulfonate (30). Methyllithium (1.6 M in diethyl ether, 30 mL, 48 mmol) and boron trifluoride etherate (3.0 mL, 24 mmol) were slowly added to a solution of the enantiopure epoxide **28** (1.0 g, 12 mmol) in diethyl ether (60 mL) at –78 °C. The mixture was stirred at this temperature until all starting material was consumed (90 min). Sat. aq. NH_4Cl was added at -78 °C and the phases were separated.

[4] C. J. Collins, M. Hanack, H. Stutz, G. Auchter, W. Schoberth, *J. Org. Chem.* **1983**, *48*, 5260-5268.
[5] L. P. C. Nielsen, C. P. Stevenson, D. G. Blackmond, E. N. Jacobsen, *J. Am. Chem. Soc.* **2004**, *126*, 1360-1362.

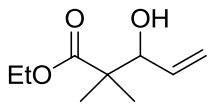
The aqueous phase was extracted with diethyl ether (2 x 20 mL), and the combined extracts were dried over Na_2SO_4 and filtered. The diethyl ether was distilled off very carefully to yield the corresponding crude primary alcohol **29**.

Triethylamine (1.8 mL, 13.2 mmol), tosyl chloride (2.5 g, 13.2 mmol) and DMAP (146 mg, 1.2 mmol) were successively added at 0 °C to a solution of this compound in dichloromethane (25 mL). The mixture was stirred at ambient temperature until all starting material was consumed (ca 6 h), before it was diluted with dichloromethane and extracted with sat. aq. NH_4Cl. The aqueous phase was extracted with diethyl ether (2 x), the combined organic layers were dried over Na_2SO_4 and filtered, and all volatile materials were evaporated. The crude product was purified by flash chromatography (hexane/ethyl acetate, 11:1) to yield tosylate **30** as a colorless oil (2.1 g, 70% over two steps). $[\alpha]_D^{20}$ = –2.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dt, *J* = 8.6, 1.9 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.01 (dd, *J* = 9.3, 5.8 Hz, 1H), 3.83 (dd, *J* = 9.4, 7.9 Hz, 1H), 2.73 (m, 1H), 2.47 (s, 3H), 1.74 (d, *J* = 2.3 Hz, 3H), 1.15 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 133.1, 129.8, 128.0, 78.3, 78.0, 73.1, 26.2, 21.6, 17.6, 3.4 ppm; IR (film): $\tilde{\nu}$ = 2979, 2921, 2884, 1598, 1457, 1359, 1189, 1177, 1097, 971, 836, 814 cm^{-1}; MS (EI): *m/z* (%): 185 (1), 173 (1), 155 (65), 139 (9), 91 (99), 80 (100), 67 (49), 53 (9), 41 (34); HRMS (ESI): *m/z* calcd. for $C_{13}H_{16}O_3SNa$ $[M+Na]^+$: 275.0712, found: 275.0712.

(4*S*)-5-Bromo-4-methylpent-2-yne (31). A solution of tosylate **30** (2.3 g, 9.1 mmol) in DMF (1.0 mL) was added to a solution of lithium bromide (1.6 g, 18.2 mmol) in DMF (4.0 mL) and the resulting mixture stirred for 12 h at 60 °C. For work up, pentane and water were added at room temperature, and the organic phase was extracted three times with pentane. The combined extracts were dried over Na_2SO_4 and filtered, and the pentane carefully distilled off (1 atm, 40 °C). The residue was purified by flash chromatography (pentane). After collection of the product-containing fractions, the pentane was carefully removed by distillation to furnish product **31** as a colorless oil (1.3 g, 86%, > 99% *ee*) (GC-analysis on a chiral stationary phase: 30 m BGB 176/BGB15 column; t_R (minor enantiomer): 19.09 min; t_R (major enantiomer): 18.66 min). $[\alpha]_D^{20}$ = –10.6 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.47 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.32 (dd, *J* = 9.6, 7.3 Hz, 1H), 2.79 (m, 1H), 1.82 (d, *J* = 2.3 Hz, 3H), 1.28 ppm (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.3, 77.8, 38.1, 28.9, 20.0, 3.5 ppm; IR (film): $\tilde{\nu}$ = 2975, 2920, 1454, 1431, 1374, 1290, 1223, 1191, 891 cm^{-1}; MS (GC-EI): *m/z* (%): 160 (9), 81 (100), 79 (19), 67 (35), 53 (19), 41 (49), 27 (10); HRMS (EI): *m/z* calcd. for C_6H_9Br $[M]^+$: 159.9888, found: 159.9889.

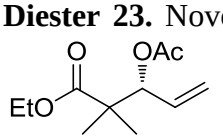


Ethyl 2,2-dimethyl-3-hydroxypent-4-enoate (22). *n*BuLi (1.6 M in hexane, 75 mL, 120 mmol) was added to a solution of diisopropylamine (17.0 mL, 120 mmol) in THF (240 mL) at -78 °C. After stirring for 40 min, a solution of ethyl isobutyrate (**21**) (13.4 mL, 100 mmol) in THF (20 mL) was added dropwise at the same temperature. After stirring for 30 min, acrolein (8.0 mL, 120 mmol) was slowly introduced while keeping the temperature at -78 °C. The reaction was quenched after 15 min by the addition of sat. aq. NH_4Cl, the phases were separated, and the aqueous layer was extracted three times with diethyl ether. The

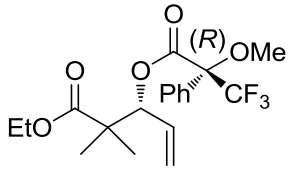


combined extracts were dried over Na_2SO_4, filtered, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate, 5:1) to furnish **22** as a pale yellow oil (16.2 g, 94%). All analytical data matched those reported in the literature.[6] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (ddd, J = 17.1, 10.5, 6.5 Hz, 1H), 5.33 (dt, J = 17.1, 1.4 Hz, 1H), 5.25 (ddd, J = 10.5, 1.3, 1.2 Hz , 1H), 4.15 (m, 3H), 2.72 (d, J = 6.1 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.22 (s, 3H), 1.19 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 136.2, 117.5, 77.9, 60.7, 46.5, 22.5, 19.9, 14.1 ppm; IR (film): $\tilde{\nu}$ = 3495, 2980, 2939, 2876, 1717, 1644, 1470, 1387, 1256, 1140, 1113, 1025, 924, 861 cm^{-1}; MS (EI): *m/z* (%): 286 (4), 251 (2), 137 (100), 121 (64), 109 (6), 77 (7); HRMS (CI): *m/z* calcd. for $C_9H_{17}O_3$ $[M+H]^+$: 173.1178, found: 173.1177.

Diester 23. Novozyme 435® (4.7 g) was added to a solution of the β-hydroxyester **22** (17.3 mL, 188 mmol) in toluene (100 mL) and the resulting mixture gently stirred at 70 °C for 6 days. The mixture was filtered, all volatile compounds were evaporated, and the residue was purified by flash chromatography (hexane/ethyl acetate, 8:1→6:1) to yield **23** as a colorless oil (6.7 g, 33%, 98% *ee*) (GC-analysis on a chiral stationary phase: 25 m LIPODEX G column; t_R (minor enantiomer): 25.82 min; t_R (major enantiomer): 26.29 min). $[\alpha]_D^{20}$ = +25.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddd, J = 17.2, 10.5, 6.5 Hz, 1H), 5.52 (dt, J = 6.8, 1.0 Hz, 1H), 5.31 (m, 1H), 5.28 (m, 1H), 4.15 (m, 2H), 2.06 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.22 (s, 3H), 1.17 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 169.7, 132.3, 119.3, 78.4, 60.7, 45.9, 21.4, 20.9, 20.3, 14.1 ppm; IR (film): $\tilde{\nu}$ = 2983, 2941, 1733, 1645, 1470, 1370, 1228, 1136, 1024, 990, cm^{-1}; MS (EI): *m/z* (%): 169 (5), 158 (10), 141 (4), 125 (4), 116 (100), 99 (16), 88 (23), 82 (10), 70 (7), 43 (55); HRMS (ESI): *m/z* calcd. for $C_{11}H_{18}O_4Na$ $[M+Na]^+$: 237.1097, found: 237.1099.



(*R*)-Mosher Ester S-3. Potassium carbonate (180 mg, 1.3 mmol) was added to a solution of diester **23** (55.4 mg, 0.26 mmol) in ethanol (1.3 mL) and the resulting mixture stirred at 50 °C for 18 h. Water was added and the aqueous layer extracted with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered and evaporated, and the residue was purified by flash chromatography (hexane/ethyl acetate, 5:1) to yield the corresponding β-hydroxy ester (38 mg, 84%).



(*S*)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid chloride (13.1 µL, 70 µmol) was added to a solution of this compound (8.6 mg, 50 µmol) in pyridine (0.5 mL) at 0 °C. The mixture was stirred at ambient temperature for 7 h. Water was added and the aqueous layer extracted with diethyl ether. The combined extracts were washed with aq. HCl (1 M), dried over $MgSO_4$, filtered and evapoprated, and the residue was purified by flash chromatography (hexane/ethyl acetate, 10:1) to give the desired Mosher ester in quantitative yield.

(*S*)-Mosher Ester S-4. Prepared analogously with (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid chloride as the reagent.

---

[6] P. de A. Amaral, J. Petrignet, N. Gouault, T. Augustini, F. Lohézic-Ledévéhat, A. Cariou, R. Grée, V. L. Eifler-Lima, M. David, *J. Braz. Chem. Soc.* **2009**, *20*, 1687-1697.

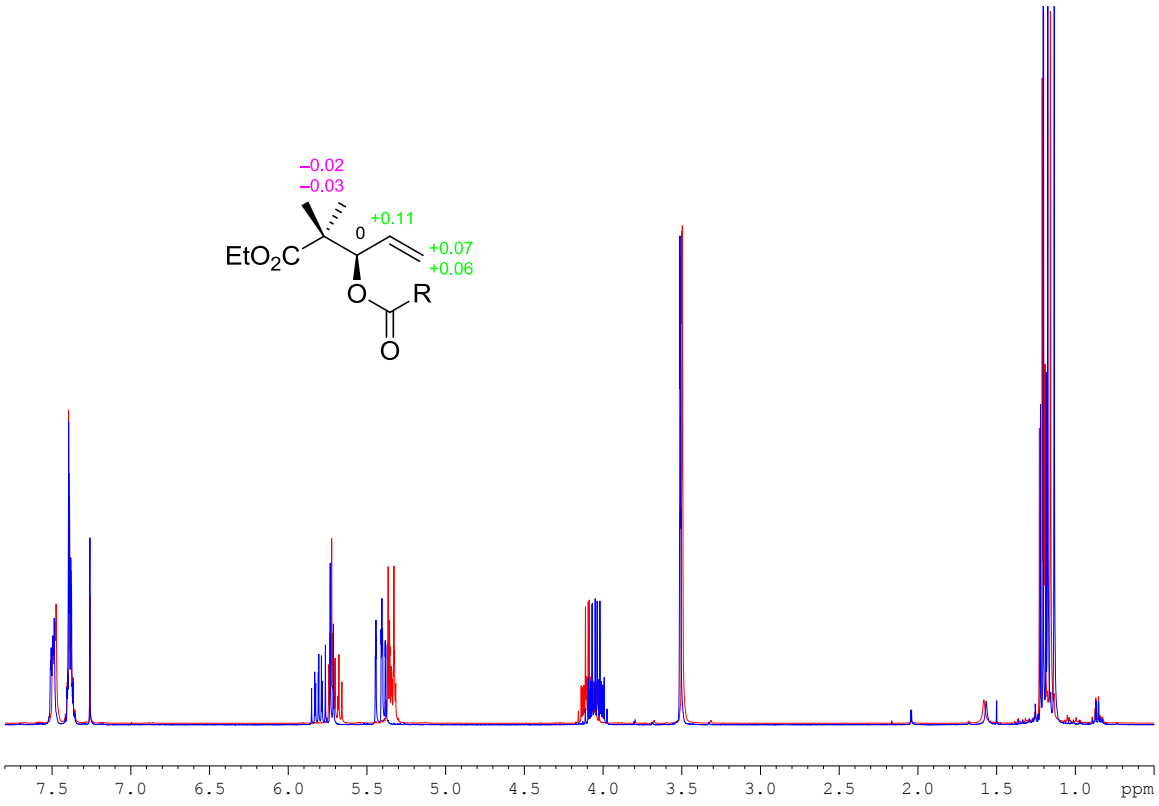
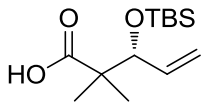


Figure S1. Superposition of the ^{1}H NMR spectra of the two Mosher esters derived from **23**. The two methyl singlets are shifted upfield and the three alkene protons are shifted downfield in **(*S*)-S-4** (blue) relative to the signals in **(*R*)-S-3** (red). This pattern confirms the (*R*)-configuration of the secondary alcohol in **23.**[7]

Acid 24. Aq. NaOH (4 M, 30 mL) was added to a solution of diester **23** (3.5 g, 20.3 mmol) in methanol (not dried, 30 mL) under air at 0 °C. The cold bath was removed and the mixture stirred at room temperature until all starting material was consumed (2 h). The solution was diluted with water and the aqueous layer washed three times with diethyl ether before it was carefully acidified using concentrated aq. HCl. The aqueous phase was extracted three times with diethyl ether, the combined extracts were dried over Na_2SO_4, filtered and evaporated to yield the crude (*R*)-β-hydroxy acid, which was used in the next step without further purification. $[\alpha]_D^{20}$ = +14.8 (*c* = 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = ≈ 7 (br., 1H), 5.89 (ddd, *J* = 17.2, 10.4, 6.7 Hz, 1H), 5.34 (ddd, *J* = 17.1, 1.5, 1.4 Hz, 1H), 5.27 (ddd, *J* = 10.4, 1.3, 1.2 Hz, 1H), 4.23 (ddd, *J* = 6.7, 1.1, 1.0 Hz, 1H), 1.24 (s, 3H), 1.20 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.9, 135.6, 118.2, 77.8, 46.5, 22.6, 19.5 ppm; IR (film): $\tilde{\nu}$ = 3386, 3080, 2981, 2942, 2880, 1697, 1472, 1260, 1115, 1038, 992, 926, 854 cm^{-1}; MS (EI): *m/z* (%): 126 (2), 111 (1), 99 (1), 88 (100), 73 (53), 70 (35), 57 (32), 55 (10), 43 (17), 29 (17); HRMS (CI): *m/z* calcd. for $C_7H_{13}O_3$ $[M+H]^+$: 145.0865, found: 145.0864.

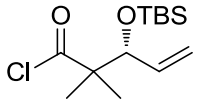
[7] T. R. Hoye, C. S. Jeffrey, F. Shao, *Nat. Protoc.* **2007**, *2*, 2451-2458.

Imidazole (3.1 g, 44.7 mmol) and *tert*-butyldimethylsilyl chloride (6.7 g, 44.7 mmol) were added to a solution of the crude acid in DMF (40.6 mL) at 0 °C. The mixture was stirred at ambient temperature for 12 h before it was partitioned between ethyl acetate and sat. aq. NH_4Cl. The aqueous layer was was extracted three times with ethyl acetate, the combined organic phases were dried over Na_2SO_4, filtered, and evaporated to yield a mixture of the corresponding mono- and bis-silylated compound which was used as such in the next step. Analytical data for the bis-silylated acid: $[\alpha]_D^{20}$ = +3.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.78 (ddd, *J* = 17.4, 10.2, 7.3 Hz, 1H), 5.18 (ddd, *J* = 17.1, 1.9, 1.0 Hz, 1H), 5.15 (ddd, *J* = 10.2, 1.8, 0.9 Hz, 1H), 4.29 (d, *J* = 7.6 Hz, 1H), 1.17 (s, 3H), 1.06 (s, 3H), 0.96 (s, 9H), 0.90 (s, 9H), 0.27 (s, 3H), 0.26 (s, 3H), 0.06 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.0, 137.9, 116.9, 78.8, 49.0, 25.8, 25.6, 21.4, 20.3, 18.1, 17.7, –3.9, –4.9, –4.9, –5.0 ppm; IR (film): $\tilde{\nu}$ = 2956, 2931, 2887, 2859, 1721, 1643, 1471, 1252, 1150, 1081, 837, 825, 790, 774 cm^{-1}; MS (EI): *m/z* (%): 357 (4), 315 (95), 245 (3), 189 (7), 171 (100), 147 (50), 133 (5), 115 (10), 73 (72); HRMS (ESI): *m/z* calcd. for $C_{19}H_{40}O_3Si_2Na$ $[M+Na]^+$: 395.2408, found: 395.2412.

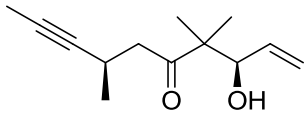


K_2CO_3 (8.4 g, 53.4 mmol) was added to a solution of this mixture in methanol/water/THF (1/1/2, 80 mL) and the resulting mixture stirred until all starting material was consumed (ca. 2 h). For work up, it was diluted with diethyl ether and extracted three times with water. The combined aqueous phases were acidified with citric acid and extracted three times with diethyl ether. The combined extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (hexane/ethyl acetate, 5:1) to yield product **24** as a colorless oil (3.5 g, 67% over three steps). $[\alpha]_D^{20}$ = +16.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.78 (ddd, *J* = 16.6, 10.9, 7.9 Hz, 1H), 5.28 (m, 1H), 5.24 (m, 1H), 4.12 (d, *J* = 7.9 Hz, 1H), 1.24 (s, 3H), 1.15 (s, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.2, 136.9, 117.9, 79.2, 47.7, 25.7, 21.8, 19.8, 18.0, –4.0, –5.3 ppm; IR (film): $\tilde{\nu}$ = 3100, 2956, 2930, 2888, 2858, 1702, 1472, 1283, 1256, 1084, 835, 775 cm^{-1}; MS (EI): *m/z* (%): 243 (1), 201 (52), 171 (48), 143 (15), 131 (16), 115 (7), 99 (9), 81 (12), 75 (100); HRMS (ESI): *m/z* calcd. for $C_{13}H_{26}O_3SiNa$ $[M+Na]^+$: 281.1543, found: 281.1543.

Acid Chloride 25. Oxalyl chloride (0.4 mL, 4.0 mmol) was slowly added to a solution of acid **24** (206 mg, 0.8 mmol) in dichloromethane (12 mL) at 0 °C. The mixture was stirred for 12 h at ambient temperature before all volatile compounds were removed under reduced pressure to yield product **25** as a yellow oil, which was used in the next step without purification (quant. by NMR). Characteristic data: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.73 (ddd, *J* = 17.1, 10.4, 7.7 Hz, 1H), 5.30 (d, *J* = 6.9 Hz, 1H), 5.27 (s, 1H), 4.45 (d, *J* = 7.7 Hz, 1H), 1.68 (brs, 1H), 1.27 (s, 3H), 1.19 (s, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.04 ppm (s, 3H).



β-Hydroxy-ketone 6. Iodine (13 mg, 0.05 mmol) was added to a suspension of dried zinc powder (98 mg, 1.5 mmol) in degassed (10 min argon purge) dimethylacetamide (1.0 mL) at room temperature. The reaction was stirred until the initial yellow color had faded away (ca 5 min). At this point, bromide **31** (181 mg, 1.0 mmol) was added via syringe and the resulting suspension stirred for

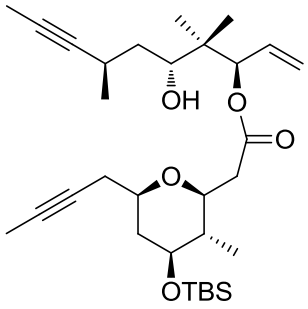


12 h at 75 °C. After the mixture had reached ambient temperature, the conversion was checked by NMR.

In a separate Schlenk tube, lithium chloride (76 mg, 1.8 mmol) and copper(I) cyanide (80.5 mg, 0.9 mmol) were dissolved in THF (1.0 mL). To the resulting clear greenish solution was added the suspension of the organozinc compound **32** at –30 °C via syringe. The mixture was stirred at 0 °C for 10 min before it was cooled back to –30 °C and a solution of the freshly prepared acid chloride **25** (0.8 mmol) in THF (0.3 mL) was introduced. The mixture was stirred at -30 °C until the conversion ceased (ca. 6 h). For work up, sat. aq. NH_4Cl and diethyl ether were added and the organic phase was separated. The aqueous layer was extracted with diethyl ether, the combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (pentane/diethyl ether, 100:1) to yield the corresponding O-TBS-protected β-hydroxyketone along with some minor impurities.

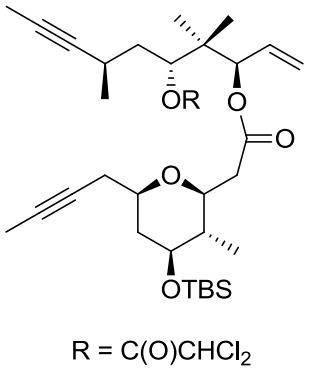
Trifluoroacetic acid (0.3 mL, 4.0 mmol) was added at 0 °C to a solution of this crude material in dichloromethane (25 mL, not dried). The mixture was stirred at ambient temperature for 3 h before sat. aq. $NaHCO_3$ was carefully introduced. The aqueous phase was extracted three times with dichloromethane, the combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (pentane/ethyl acetate, 15:1 to 10:1, Merck silica gel 50 mesh) to yield β-hydroxyketone **6** as a colorless oil (165 mg, 67% over 2 steps). $[\alpha]_D^{20}$ = +1.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.68 (ddd, *J* = 17.0, 10.6, 6.3 Hz , 1H), 5.13 (ddd, *J* = 17.1, 1.8, 1.6 Hz, 1H), 5.00 (ddd, *J* = 10.5, 1.9, 1.3 Hz, 1H), 4.09 (d, *J* = 6.1 Hz, 1H), 3.20 (m, 1H), 2.66 (dd, *J* = 17.4, 6.4 Hz, 1H), 2.28 (dd, *J* = 17.3, 7.5 Hz, 1H), 1.99 (brs, 1H), 1.52 (d, *J* = 2.3 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 3H), 0.85 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 212.5, 137.1, 116.7, 83.8, 77.5, 75.7, 51.2, 45.8, 21.7, 21.5, 21.3, 18.6, 3.2 ppm; IR (film): $\tilde{\nu}$ = 3514, 2971, 2921, 2876, 1700, 1466, 1365, 1271, 1106, 1036, 994, 928 cm^{-1}; MS (EI): *m/z* (%): 208 (1), 190 (2), 175 (6), 168 (3), 152 (77), 137 (48), 123 (6), 109 (18), 85 (15), 82 (92), 70 (22), 67 (100), 57 (12), 43 (47), 29 (10); HRMS (EI): *m/z* calcd. for $C_{13}H_{20}O_2$ $[M]^+$: 208.1463, found: 208.1461.

Ester 5a. SmI_2 (0.1 M in THF, 0.44 mL, 0.044 mmol) was added to a solution of freshly prepared aldehyde **7** (37.0 mg, 0.11 mmol) and ketone **6** (18.3 mg, 0.09 mmol) in THF (0.75 mL) at –50 °C. The blue mixture was stirred for 1 h before sat. aq. $NaHCO_3$ solution was added at -50 °C. The mixture was extracted three times with ethyl acetate, the combined extracts were dried over Na_2SO_4, filtered and evaporated. LC analysis of the crude product showed a dr ≈ 12:1 (50 mm Zorbax Eclipse Plus C18 column, 1.8 μm/3.0 mm; acetonitrile/water (90/10): 0.5 mL/min; 308 K; t_R (minor diastereomer): 3.45 min; t_R (major diastereomer): 3.68 min). The residue was purified by flash chromatography (pentane/diethyl ether, 8:1) and HPLC (150 mm Kromasil C18 Classic column, 5 μm/30 mm; acetonitrile/water (95/5): 30 mL/min; 308 K; UV detection at 210 nm; t_R (minor diastereomer): 12.6 min; t_R (major diastereomer): 13.1 min) to afford product **5a** as a single diastereomer in form of a pale yellow oil (32 mg, 68%). $[\alpha]_D^{20}$ = +3.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ =



5.77 (ddd, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.69 (d, *J* = 6.9 Hz, 1H), 5.24 (d, *J* = 16.3 Hz, 1H), 5.08 (dd, *J* = 10.2, 1.4 Hz, 1H), 3.64 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.48 (td, *J* = 9.5, 3.4 Hz, 1H), 3.37 (m, 1H), 3.17 (ddd, *J* = 10.5, 9.8, 4.7 Hz, 1H), 3.04 (d, *J* = 4.4 Hz, 1H), 2.88 (m, 1H), 2.56 (m, 1H), 2.39 (dd, *J* = 14.9, 3.5 Hz, 1H), 2.35 (m, 1H), 2.31 (dd, *J* = 15.0, 9.0 Hz, 1H), 2.10 (ddd, *J* = 12.7, 4.8, 1.7 Hz, 1H), 1.85 (ddd, *J* = 13.8, 10.4, 5.3 Hz, 1H), 1.56 (m, 1H), 1.55 (d, *J* = 2.3 Hz, 3H), 1.51 (t, *J* = 2.5 Hz, 3H), 1.48 (m, 1H), 1.26 (m, 1H), 1.25 (d, *J* = 6.8 Hz, 3H), 0.96 (s, 9H), 0.89 (s, 3H), 0.86 (s, 3H), 0.71 (d, *J* = 6.6 Hz, 3H), 0.04 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 171.0, 134.0, 118.5, 85.0, 79.1, 78.4, 77.7, 76.3, 75.6, 74.4, 74.2, 72.7, 43.8, 41.4, 41.1, 39.6, 39.2, 26.4, 26.0, 23.8, 20.9, 19.0, 18.3, 18.2, 13.3, 3.3, (3.3), –3.8, –4.7 ppm; IR (film): $\tilde{\nu}$ = 3535, 2960, 2928, 2857, 1736, 1468, 1373, 1252, 1084, 834, 772 cm^{-1}; MS (EI): *m/z* (%): 532 (2), 475 (4), 380 (3), 341 (34), 283 (100), 265 (5), 241 (7), 209 (17), 183 (16), 149 (24), 121 (36), 93 (19), 82 (46), 43 (20); HRMS (ESI): *m/z* calcd. for $C_{31}H_{52}O_5SiNa$ $[M+Na]^+$: 555.3476, found: 555.3472.

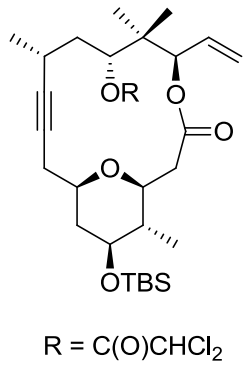
Diyne (5b). Dichloroacetic anhydride (26 µL, 0.17 mmol) was added to a solution of compound **5a** (46 mg, 0.09 mmol) in dichloromethane (2.0 mL) and pyridine (0.2 mL) at 0 °C and the mixture was stirred for 15 min. For work up, all volatile materials were evaporated and the crude material purified by flash chromatography (pentane/ethyl acetate, 16:1) to afford product **5b** as a colorless oil (53 mg, 94%). $[\alpha]_D^{20}$ = +2.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.67 (ddd, *J* = 17.4, 10.4, 6.8 Hz, 1H), 5.66 (s, 1H), 5.39 (d, *J* = 6.9 Hz, 1H), 5.27 (m, 1H), 5.24 (m, 1H), 5.06 (ddd, *J* = 10.4, 1.5, 1.0 Hz, 1H), 3.52 (ddd, *J* = 10.1, 8.5, 3.7 Hz, 1H), 3.41 (m, 1H), 3.22 (ddd, *J* = 10.6, 9.6, 4.8 Hz, 1H), 2.55 (m, 2H), 2.51 (dd, *J* = 15.1, 3.8 Hz, 1H), 2.44 (dd, *J* = 15.1, 8.5 Hz, 1H), 2.35 (m, 1H), 2.14 (ddd, *J* = 12.5, 4.7, 1.9 Hz, 1H), 2.00 (ddd, *J* = 14.7, 10.6, 4.8 Hz, 1H), 1.64 (ddd, *J* = 14.6, 9.0, 1.7 Hz, 1H), 1.56 (d, *J* = 2.3 Hz, 3H), 1.51 (t, *J* = 2.5 Hz, 3H), 1.48 (m, 1H), 1.35 (m, 1H), 1.20 (d, *J* = 6.8 Hz, 3H), 0.96 (s, 9H), 0.88 (s, 3H), 0.88 (s, 3H), 0.79 (d, *J* = 6.7 Hz, 3H), 0.05 (s, 3H), 0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 170.1, 164.3, 133.0, 119.5, 83.6, 78.6, 78.3, 77.7, 77.6, 76.2, 75.6, 74.4, 74.3, 65.3, 43.9, 41.5, 41.1, 39.7, 37.6, 26.4, 26.0, 23.4, 20.9, 19.4, 19.3, 18.2, 13.3, 3.4, 3.3, –3.8, –4.6 ppm; IR (film): $\tilde{\nu}$ = 2956, 2928, 2857, 1760, 1742, 1470, 1371, 1276, 1250, 1163, 1086, 836, 774 cm^{-1}; MS (EI): *m/z* (%): 585 (21), 551 (2), 515 (4), 393 (13), 341 (4), 303 (39), 223 (6), 175 (100), 149 (41), 121 (45), 93 (29), 75 (32); HRMS (ESI): *m/z* calcd. for $C_{33}H_{52}Cl_2O_6SiNa$ $[M+Na]^+$: 665.2802, found: 665.2799.



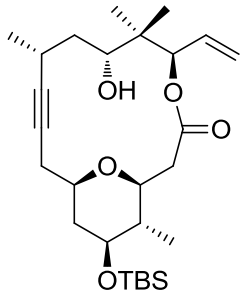
Macrocycle S-5. The molybdenum ate-complex **38** (7.1 mg, 0.004 mmol)[8] was added to a suspension of diyne **5b** (53 mg, 0.082 mmol) and powdered molecular sieves (MS 5 Å, 200 mg) in toluene (160 mL) and the resulting mixture stirred at 80 °C for 3 h. For work up, the mixture was filtered through a plug of silica, the filtrate was evaporated and the residue purified by flash chromatography (pentane/ethyl acetate, 16:1) to yield product **3b** as a white foam (44 mg, 91%). $[\alpha]_D^{20}$ = +19.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz,

[8] The catalyst was prepared according to: J. Heppekausen, R. Stade, A. Kondoh, G. Seidel, R. Goddard, A. Fürstner, *Chem. Eur. J.* **2012**, *18*, 10281-10299.

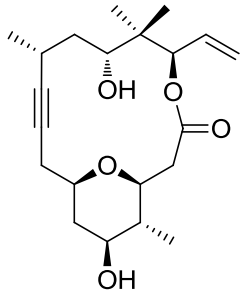
C_6D_6): δ = 6.75 (brs, 1H), 5.77 (d, J = 6.8 Hz, 1H), 5.66 (ddd, J = 17.0, 10.2, 6.8 Hz, 1H), 5.22 (ddd, J = 16.9, 1.4, 1.1 Hz, 1H), 5.13 (brs, 1H), 5.05 (ddd, J = 10.4, 1.6, 1.0 Hz, 1H), 3.68 (td, J = 10.4, 1.2 Hz, 1H), 3.39 (brm, 1H), 3.09 (ddd, J = 10.6, 9.6, 4.8 Hz, 1H), 2.48 (dd, J = 15.3, 10.5 Hz, 1H), 2.40 (m, 1H), 2.34 (dd, J = 15.3, 1.5 Hz, 1H), 2.26 (ddd, J = 16.9, 11.1, 3.1 Hz, 1H), 2.09 (brm, 1H), 1.95 (dd, J = 16.8, 2.9 Hz, 1H), 1.53 (ddd, J = 12.5, 4.7, 1.9 Hz, 1H), 1.39 (d, J = 13.5 Hz, 1H), 1.28 (m, 1H), 1.18 (m, 1H), 1.05 (m, 6H), 0.95 (s, 9H), 0.70 (d, J = 6.6 Hz, 3H), 0.54 (s, 3H), –0.02 (s, 3H), –0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 171.0, 164.8, 133.7, 118.6, 86.1 (br), 82.6 (br), 78.9, 78.0 (br), 75.8, 74.2, 73.8, 65.9, 43.3, 42.5, 41.2, 38.5, 36.5, 26.8, 26.0, 24.8, 23.0, 22.5 (br), 19.0, 18.1, 13.3, –3.9, –4.7 ppm; IR (film): $\tilde{\nu}$ = 2960, 2932, 2857, 1760, 1732, 1472, 1308, 1167, 1078, 985, 858 cm^{-1}; MS (EI): *m/z* (%): 531 (7), 461 (2), 403 (7), 385 (2), 329 (2), 303 (2), 269 (3), 241 (3), 229 (8), 203 (11), 157 (28), 95 (100), 73 (36), 55 (22); HRMS (ESI): *m/z* calcd. for $C_{29}H_{46}Cl_2O_6SiNa$ $[M+Na]^+$: 611.2333, found: 611.2336.



Compound 4b. Potassium carbonate (25 mg, 0.18 mmol) was added to a solution of macrocycle **S-5** (43 mg, 0.07 mmol) in methanol (2 mL) and the resulting mixture stirred at 40 °C for 90 min before it was diluted with water. The aqueous phase was carefully extracted with ethyl acetate, the combined extracts were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 12:1) to yield product **4b** as a colorless oil (28 mg, 80%). $[\alpha]_D^{20}$ = +62.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.82 (m, 2H), 5.14 (m, 1H), 5.05 (m, 1H), 4.29 (dd, J = 9.6, 5.1 Hz, 1H), 4.05 (d, J = 4.7 Hz, 1H), 3.50 (td, J = 10.2, 2.7 Hz, 1H), 3.22 (tt, J = 11.1, 2.0 Hz, 1H), 3.03 (ddd, J = 10.8, 9.7, 4.8 Hz, 1H), 2.79 (m, 1H), 2.27 (dd, J = 14.4, 10.1 Hz, 1H), 2.18 (m, 2H), 1.93 (dt, J = 16.7, 1.9 Hz, 1H), 1.67 (ddt, J = 13.7, 5.9, 1.5 Hz, 1H), 1.60 (d, J = 7.2 Hz, 3H), 1.47 (m, 2H), 1.13 (m, 2H), 0.95 (s, 9H), 0.90 (s, 3H), 0.89 (s, 3H), 0.67 (d, J = 6.5 Hz, 3H), 0.01 (s, 3H), –0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 174.0, 134.2, 118.5, 84.9, 79.4, 79.2, 78.8, 74.6, 73.9, 71.8 (br), 43.5, 42.2, 42.1, 39.5, 35.3, 26.6, 26.0, 25.8, 22.9, 18.4, 18.1, 18.1 (br), 13.4, –3.9, –4.6 ppm; IR (film): $\tilde{\nu}$ = 3523, 2956, 2928, 2857, 1712, 1643, 1470, 1371, 1306, 1250, 1195, 1080, 1066, 921, 856, 832, 774 cm^{-1}; MS (EI): *m/z* (%): 421 (6), 379 (4), 339 (18), 321 (2), 297 (5), 247 (6), 223 (16), 177 (14), 155 (9), 95 (40), 82 (100), 75 (40), 43 (24); HRMS (ESI): *m/z* calcd. for $C_{27}H_{46}O_5SiNa$ $[M+Na]^+$: 501.3008, found: 501.3010.

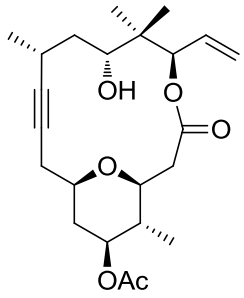


Diol S-6. Trifluoroacetic acid (21.5 µL, 0.29 mmol) was added to a solution of macrocycle **4b** (28 mg, 0.06 mmol) in dichloromethane (not dried, 8.0 mL) and the resulting mixture stirred at 40 °C for 2 h before sat. aq. $NaHCO_3$ was introduced. The aqueous phase was extracted three times with dichloromethane, the combined extracts were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 1:1) to yield product **S-6** as a white solid (16 mg, 76%). $[\alpha]_D^{20}$ = +65.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.81 (m, 1H), 5.76 (m, 1H), 5.14 (m,

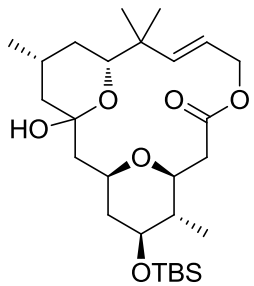


1H), 5.04 (m, 1H), 4.27 (d, *J* = 9.3 Hz, 1H), 4.01 (brs, 1H), 3.45 (td, *J* = 9.7, 3.6 Hz, 1H), 3.20 (tt, *J* = 11.0, 2.1 Hz, 1H), 2.77 (m, 2H), 2.22 (m, 2H), 2.16 (ddd, *J* = 16.7, 10.6, 1.3 Hz, 1H), 1.95 (dt, *J* = 16.7, 1.9 Hz, 1H), 1.66 (ddd, *J* = 13.7, 6.0, 1.8 Hz, 1H), 1.57 (d, *J* = 7.2 Hz, 3H), 1.47 (ddd, *J* = 13.5, 9.8, 3.2 Hz, 1H), 1.22 (ddd, *J* = 12.3, 4.7, 2.0 Hz, 1H), 0.94 (m, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.83 (m, 2H), 0.65 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 173.9, 134.1, 118.5, 84.9, 79.3, 79.2, 78.9, 74.7, 72.5, 71.9 (br), 43.2, 42.2, 41.5, 39.4, 35.3, 26.6, 25.8, 22.9, 18.4, 18.1 (br), 12.8 ppm; IR (film): $\tilde{\nu}$ = 3507, 3420, 2972, 2932, 2876, 1710, 1643, 1472, 1373, 1304, 1189, 1094, 996, 921, 739 cm^{-1}; MS (EI): *m/z* (%): 307 (1), 283 (7), 265 (4), 247 (2), 223 (3), 205 (1), 177 (2), 155 (5), 137 (4), 109 (3), 95 (18), 82 (100), 67 (20), 55 (9), 43 (14); HRMS (ESI): *m/z* calcd. for $C_{21}H_{32}O_5Na$ $[M+Na]^+$: 387.2142, found: 387.2146.

Acetate 4a. Pyridine (26.7 µL, 0.33 mmol) and acetic anhydride (15.5 µL, 0.16 mmol) were subsequently added to a solution of macrocycle **S-6** (12 mg, 0.03 mmol) in dichloromethane (1.2 mL) and the resulting mixture stirred for 4 h at 40 °C. After cooling to room temperature, all volatile compounds were evaporated and the residue was purified by flash chromatography (hexane/ethyl acetate, 4:1) to yield product **4a** as a colorless oil (13 mg, 97%). $[\alpha]_D^{20}$ = +61.7 (*c* = 1.0, $CHCl_3$) ($[\alpha]_D^{20}$ = +90.9 (*c* = 1.00, $CHCl_3$) of a sample with a *dr* = 5.5:1, cf. ref. 9]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.90 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.50 (d, *J* = 6.8 Hz, 1H), 5.27 (m, 1H), 5.24 (m, 1H), 4.62 (td, *J* = 10.7, 4.8 Hz, 1H), 3.89 (brd, *J* = 9.1 Hz, 1H), 3.69 (td, *J* = 10.4, 2.1 Hz, 1H), 3.62 (m, 1H), 3.55 (brs, 1H), 2.70 (m, 1H), 2.69 (dd, *J* = 14.4, 2.2 Hz, 1H), 2.49 (dd, *J* = 14.4, 10.5 Hz, 1H), 2.27 (t, *J* = 1.9 Hz, 1H), 2.26 (d, *J* = 1.5 Hz, 1H), 2.05 (s, 3H), 2.02 (ddd, *J* = 12.3, 4.8, 2.0 Hz, 1H), 1.69 (ddd, *J* = 13.8, 5.5, 2.0 Hz, 1H), 1.55 (m, 1H), 1.41 (ddd, *J* = 13.7, 9.5, 4.0 Hz, 1H), 1.28 (d, *J* = 7.3 Hz, 3H), 1.27 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 3H), 0.80 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 170.6, 133.4, 118.7, 85.0, 79.1, 78.7, 78.5, 74.7, 74.4, 72.1 (br), 41.8, 39.8, 39.3, 37.4, 35.2, 26.1, 25.1, 22.2, 21.1, 18.3, 18.1 (br), 13.0 ppm; IR (film): $\tilde{\nu}$ = 3519, 2968, 2932, 2876, 1738, 1714, 1643, 1373, 1308, 1238, 1199, 1103, 1032, 973, 923 cm^{-1}; MS (EI): *m/z* (%): 349 (1), 325 (8), 307 (2), 289 (1), 265 (6), 247 (2), 223 (6), 205 (2), 177 (4), 155 (5), 137 (2), 109 (3), 95 (16), 82 (100), 67 (15), 43 (24); HRMS (ESI): *m/z* calcd. for $C_{23}H_{34}O_6Na$ $[M+Na]^+$: 429.2248, found: 429.2250.



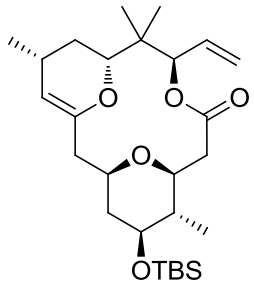
Hemiketal 37. A solution of macrocycle **4b** (3.0 mg, 6 µmol) in diethyl ether (0.3 mL) was added via syringe to a solution of $[PtCl_2(C_2H_4)]_2$ (0.4 mg, 0.6 µmol) in diethyl ether (0.1 mL). After stirring for 30 min, the solution was filtrated through a pad of Celite, eluting with diethyl ether. The combined filtrates were evaporated and the residue was purified by flash column chromatography (pentane/ethyl acetate, 12:1) to yield product **37** as a single diastereomer in form of a colorless oil (2.3 mg, 77%). $[\alpha]_D^{20}$ = –18.0 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6): δ = 5.99 (dt, *J* = 16.1, 1.7 Hz, 1H), 5.55 (dt, *J* = 16.1, 4.5 Hz, 1H), 5.05 (ddd, *J* = 13.5, 4.4, 1.5 Hz, 1H),



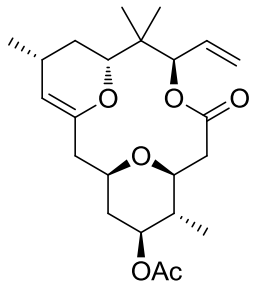
[9] S. K. Woo, E. Lee, *J. Am. Chem. Soc.* **2010**, *132*, 4564-4565.

4.15 (d, *J* = 2.6 Hz, 1H), 4.05 (ddd, *J* = 11.4, 2.8, 2.1 Hz, 1H), 4.00 (dd, *J* = 11.7, 1.6 Hz, 1H), 3.94 (ddd, *J* = 13.6, 4.5, 1.7 Hz, 1H), 3.53 (ddd, *J* = 11.2, 10.1, 1.8 Hz, 1H), 3.09 (ddd, *J* = 10.7, 9.4, 4.9 Hz, 1H), 2.38 (dd, *J* = 13.1, 1.8 Hz, 1H), 2.12 (m, 1H), 2.11 (dd, *J* = 13.1, 11.2 Hz, 1H), 1.84 (dd, *J* = 14.3, 11.2 Hz, 1H), 1.84 (ddd, *J* = 12.7, 4.0, 1.3 Hz, 1H), 1.59 (ddd, *J* = 12.6, 4.9, 2.0 Hz, 1H), 1.46 (m, 1H), 1.44 (dd, *J* = 14.2, 2.9 Hz, 1H), 1.34 (q, *J* = 11.6 Hz, 1H), 1.17 (m, 1H), 1.11 (s, 3H), 0.97 (s, 9H), 0.85 (m, 4H), 0.84 (m, 3H), 0.80 (m, 1H), 0.68 (d, *J* = 6.7 Hz, 3H), 0.01 (s, 3H), –0.01 ppm (s, 3H); ^{13}C NMR (150 MHz, C_6D_6): δ = 170.1, 141.7, 120.1, 96.0, 79.9, 75.9, 73.7, 72.6, 63.8, 47.5, 45.1, 43.7, 42.7, 39.6, 38.4, 33.9, 26.8, 26.0, 23.8, 22.7, 20.9, 18.1, 13.3, –3.9, –4.6 ppm; IR (film): $\tilde{\nu}$ = 3515, 2956, 2928, 2857, 1746, 1670, 1470, 1373, 1250, 1187, 1084, 1074, 1010, 860, 838, 772 cm^{-1}; MS (EI): *m/z* (%): 478 (5), 439 (12), 415 (27), 329 (4), 265 (11), 243 (9), 195 (14), 135 (42), 113 (17), 82 (100), 75 (31); HRMS (ESI): *m/z* calcd. for $C_{27}H_{48}O_6SiNa$ [M+Na]$^+$: 519.3112, found: 519.3109.

Enol ether 3b. The gold complex **40** (1.9 mg, 0.003 mmol) was added to a suspension of



alcohol **4b** (12 mg, 0.025 mmol) and powdered molecular sieves (MS 4 Å, 20 mg) in dichloromethane (1.2 mL) and the resulting mixture was stirred for 90 min. The reaction was quenched with triethylamine, all volatile materials were evaporated, and the residue was purified by flash chromatography (pentane/ethyl acetate, 24:1) to yield product **3b** as a colorless oil (8 mg, 67%). $[\alpha]_D^{20}$ = +5.4 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, 328 K, C_6D_6): δ = 5.82 (ddd, *J* = 17.2, 10.5, 6.9 Hz, 1H), 5.56 (d, *J* = 7.0 Hz, 1H), 5.33 (ddd, *J* = 17.1, 1.8, 1.2 Hz, 1H), 5.16 (ddd, *J* = 10.5, 1.8, 1.0 Hz, 1H), 4.32 (t, *J* = 1.7 Hz, 1H), 3.77 (dd, *J* = 11.4, 0.9 Hz, 1H), 3.30 (ddd, *J* = 10.6, 10.1, 3.9 Hz, 1H), 3.24 (dtd, *J* = 11.0, 5.4, 2.6 Hz, 1H), 3.17 (td, *J* = 9.9, 5.2 Hz, 1H), 2.37 (dd, *J* = 11.4, 4.0 Hz, 1H), 2.30 (m, 1H), 2.22 (t, *J* = 11.2 Hz, 1H), 2.20 (m, 1H), 1.85 (dd, *J* = 13.6, 5.2 Hz, 1H), 1.71 (ddt, *J* = 12.7, 6.1, 1.4 Hz, 1H), 1.59 (m, 1H), 1.55 (m, 1H), 1.35 (m, 1H), 1.21 (m, 1H), 1.08 (s, 3H), 0.96 (s, 9H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.77 (s, 3H), 0.68 (d, *J* = 6.6 Hz, 3H), 0.04 (s, 3H), 0.03 ppm (s, 3H); ^{13}C NMR (150 MHz, 328 K, C_6D_6): δ = 171.0, 153.2, 135.1, 117.9, 104.5, 81.3 (br), 78.6, 77.6 (br), 74.9 (br), 74.8, 45.0, 41.2, 41.0, 39.8, 39.5, 32.4, 28.8, 26.0, 22.1, 21.0 (br), 19.2, 18.2, 12.8, –3.8, –4.5 ppm; IR (film): $\tilde{\nu}$ = 2956, 2928, 2853, 1740, 1726, 1670, 1470, 1369, 1252, 1086, 836, 774 cm^{-1}; MS (EI): *m/z* (%): 478 (30), 421 (13), 395 (13), 321 (3), 285 (4), 243 (14), 203 (11), 177 (12), 155 (31), 110 (23), 95 (100), 73 (48), 55 (31); HRMS (ESI): *m/z* calcd. for $C_{27}H_{46}O_5SiNa$ [M+Na]$^+$: 501.3008, found: 501.3011.

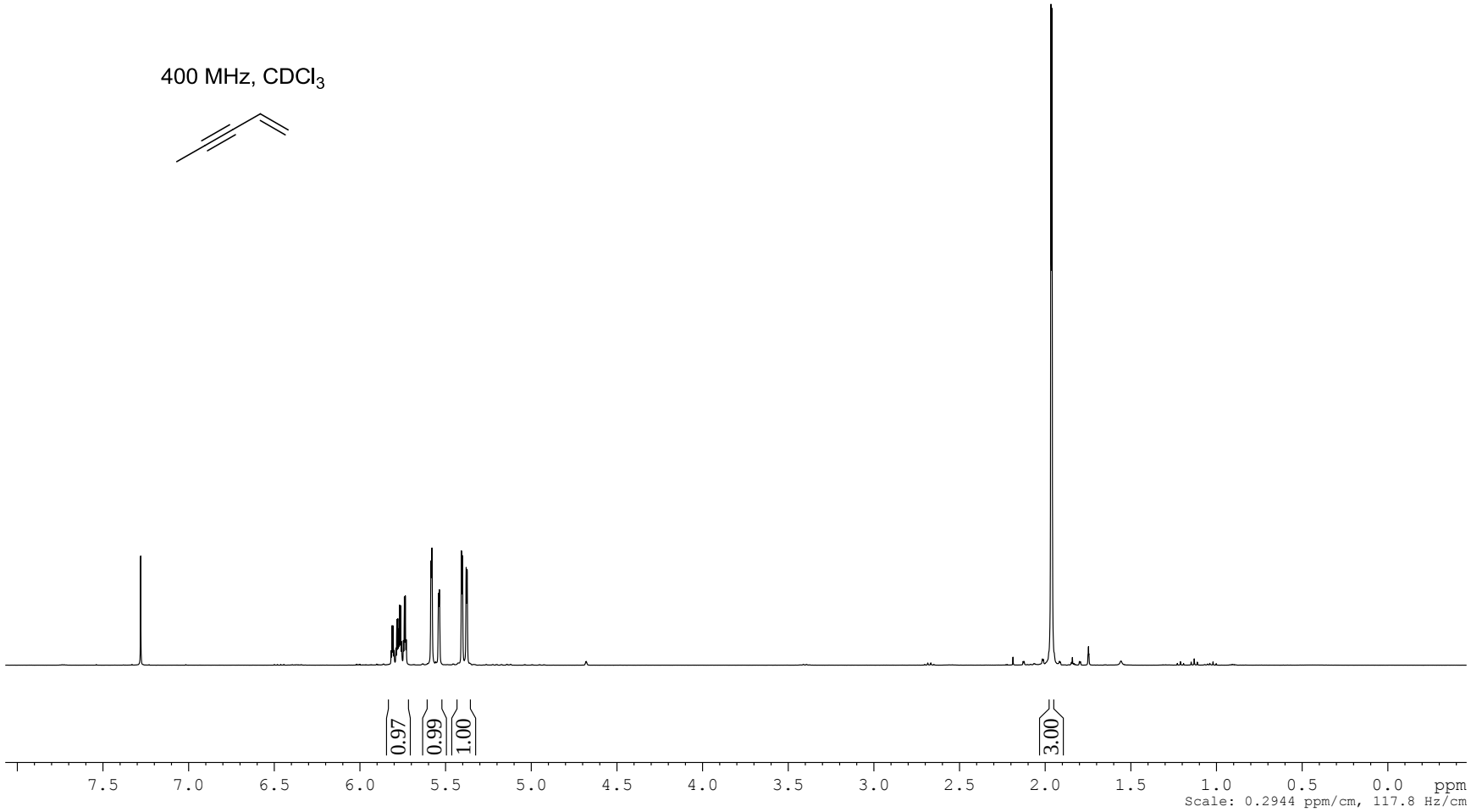


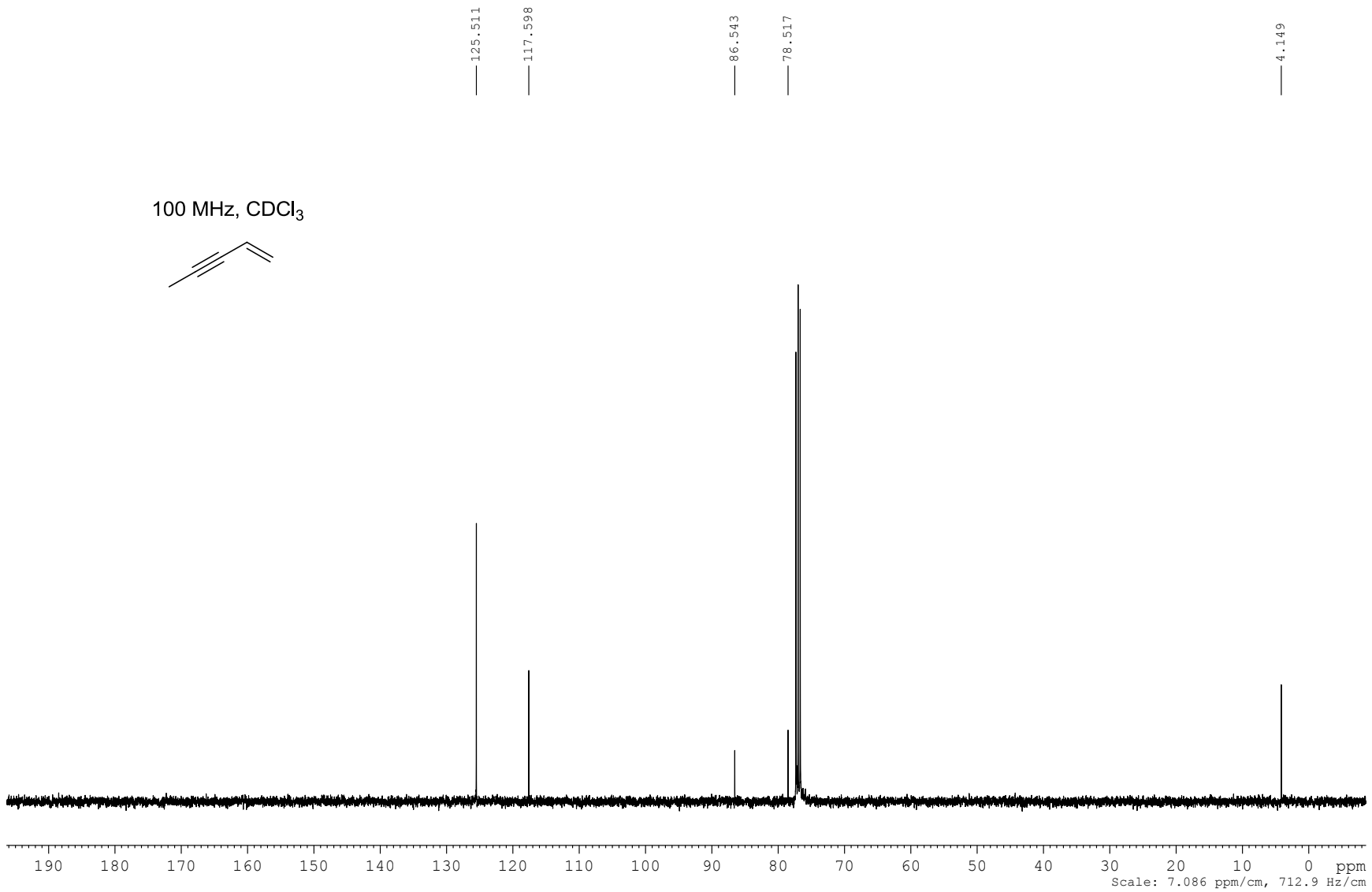
Enol ether 3a. The gold complex **40** (2.3 mg, 0.003 mmol) was added to a suspension of alcohol **4a** (13 mg, 0.03 mmol) and powdered molecular sieves (MS 4 Å, 20 mg) in dichloromethane (1.3 mL) and the resulting mixture was stirred for 60 min. The reaction was quenched with triethylamine, all volatile materials were evaporated, and the residue was purified by flash chromatography (hexane/ethyl acetate, 7:1) to yield product **3a** as a colorless oil (11 mg, 84%). $[\alpha]_D^{20}$ = +16.2 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (600 MHz, 328 K, C_6D_6): δ = 5.81 (ddd, *J* = 17.2, 10.4, 6.9 Hz, 1H), 5.52 (d, *J* = 7.0 Hz, 1H), 5.31 (ddd, *J* = 17.2, 1.8, 1.2 Hz, 1H), 5.16 (ddd, *J* = 10.5, 1.8, 1.0 Hz, 1H),

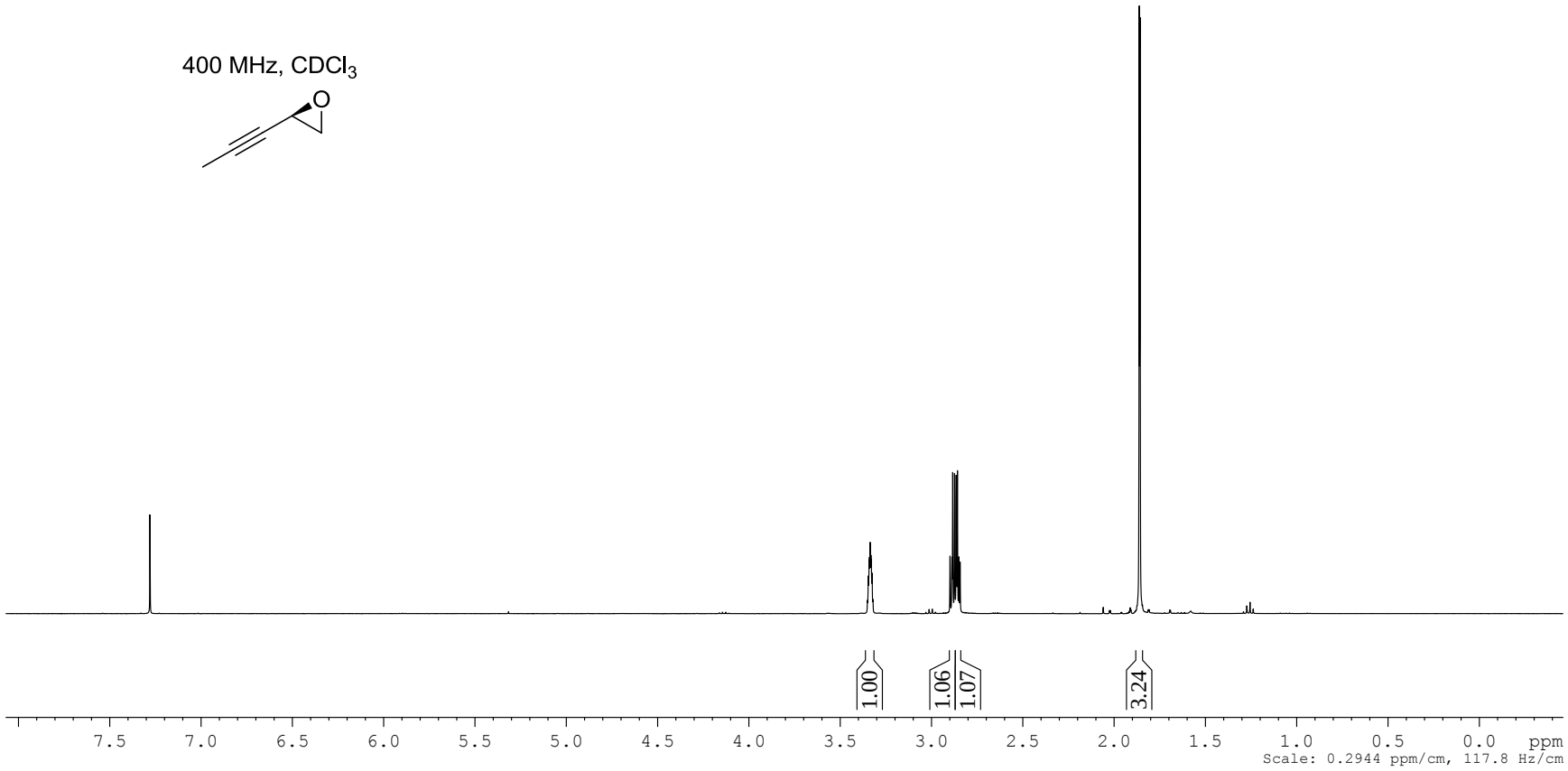
4.57 (td, *J* = 10.7, 4.7 Hz, 1H), 4.26 (t, *J* = 1.7 Hz, 1H), 3.73 (dd, *J* = 11.2, 1.1 Hz, 1H), 3.29 (ddd, *J* = 10.6, 10.1, 4.0 Hz, 1H), 3.18 (dtd, *J* = 11.3, 5.3, 2.0 Hz, 1H), 2.33 (dd, *J* = 11.6, 4.0 Hz, 1H), 2.30 (m, 1H), 2.16 (t, *J* = 11.1 Hz, 1H), 2.11 (dd, *J* = 13.4, 5.3 Hz, 1H), 1.75 (m, 1H), 1.71 (m, 2H), 1.69 (s, 3H), 1.42 (q, *J* = 11.5 Hz, 1H), 1.33 (m, 1H), 1.28 (m, 1H), 1.06 (s, 3H), 0.79 (d, *J* = 7.0 Hz, 3H), 0.75 (s, 3H), 0.56 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, 328 K, C_6D_6): δ = 170.5, 169.5, 152.9, 135.0, 118.0, 104.6, 81.2, 78.4, 77.7, 75.5, 74.8, 41.9, 40.9, 39.8, 39.1, 36.8, 32.3, 28.8, 22.1, 21.0, 20.6, 19.2, 12.2 ppm; IR (film): $\tilde{\nu}$ = 2952, 2928, 2849, 1738, 1670, 1639, 1433, 1365, 1236, 1165, 1092, 981 cm^{-1}; MS (EI): *m/z* (%): 406 (40), 391 (10), 363 (6), 323 (78), 309 (5), 263 (4), 215 (4), 177 (11), 155 (35), 137 (12), 110 (46), 95 (100), 81 (18), 69 (42), 55 (28), 43 (71); HRMS (ESI): *m/z* calcd. for $C_{23}H_{34}O_6Na$ $[M+Na]^+$: 429.2248, found: 429.2248.

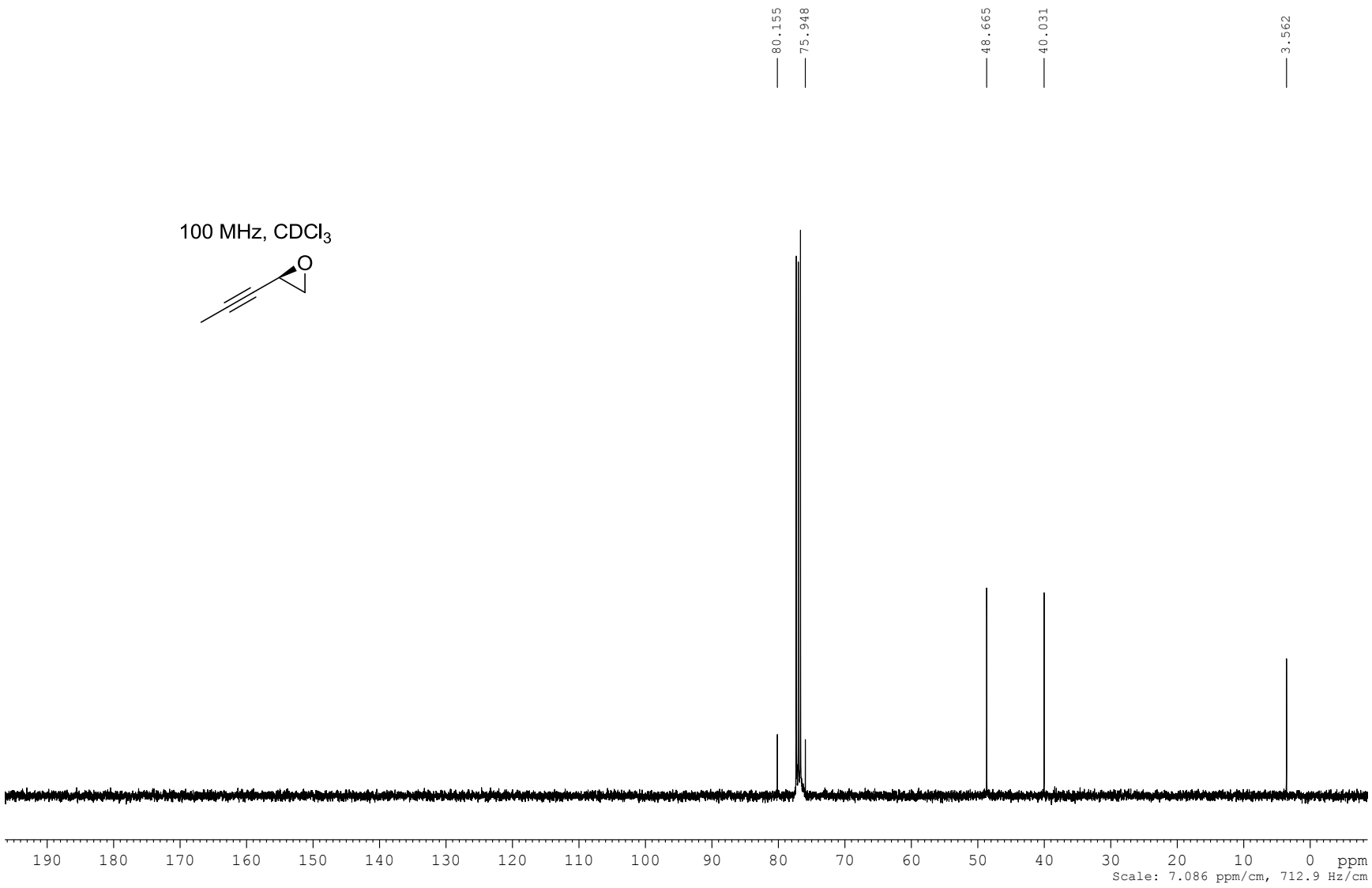
Table S-1. Comparison of the ^{13}C NMR data of compound **4a** (100 MHz, $CDCl_3$); δ (ppm)

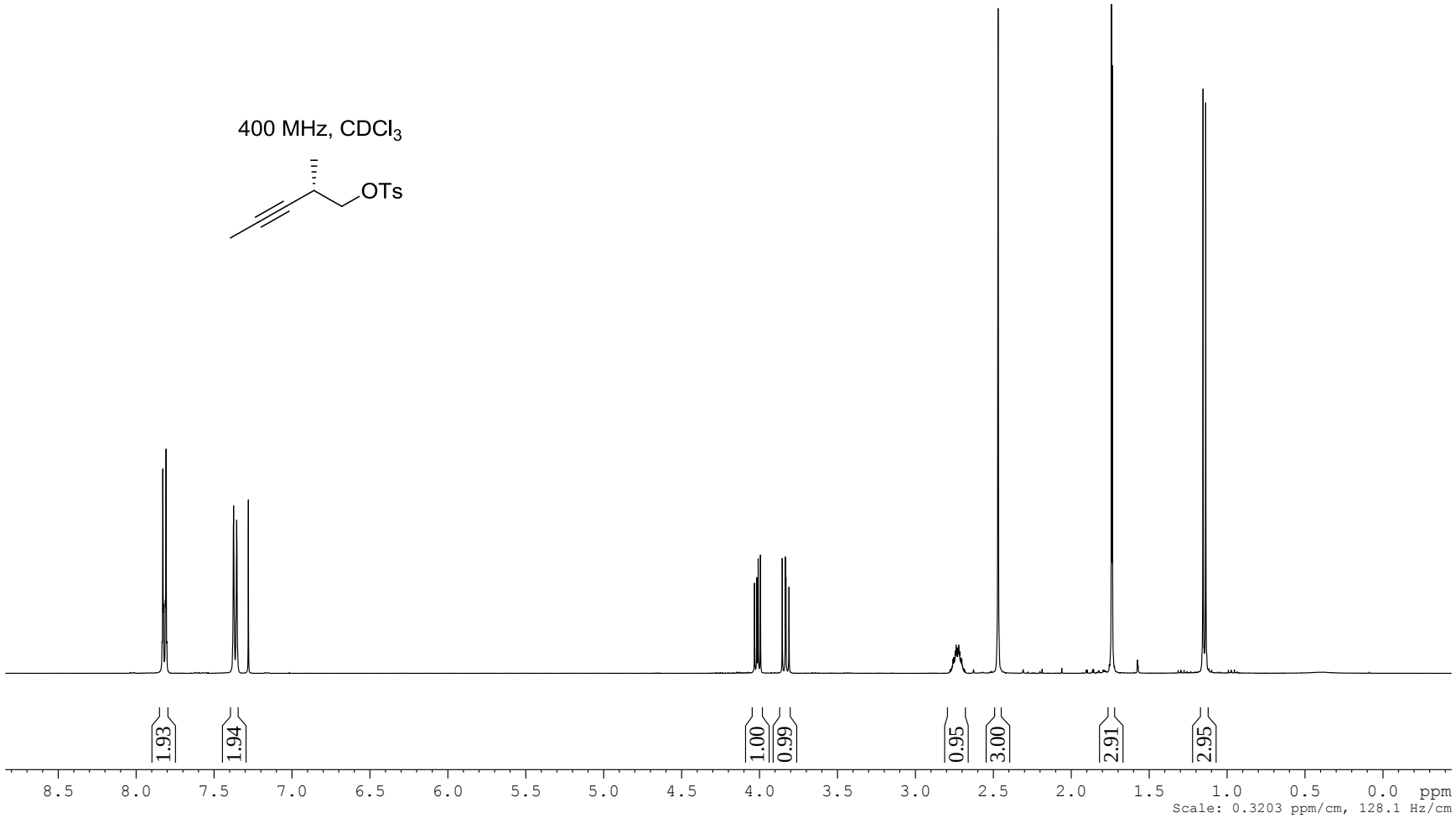
Literature data, ref.[9]	**Recorded data**
173.5	173.4
170.7	170.6
133.5	133.4
118.8	118.7
85.1	85.0
79.2	79.1
78.8	78.7
78.6	78.5
74.8	74.7
74.5	74.4
-	72.1 (br)
41.9	41.8
39.9	39.8
39.4	39.3
37.6	37.4
35.2	35.2
26.2	26.1
25.2	25.1
22.4	22.2
21.2	21.1
18.4	18.3
-	18.1 (br)
13.2	13.0

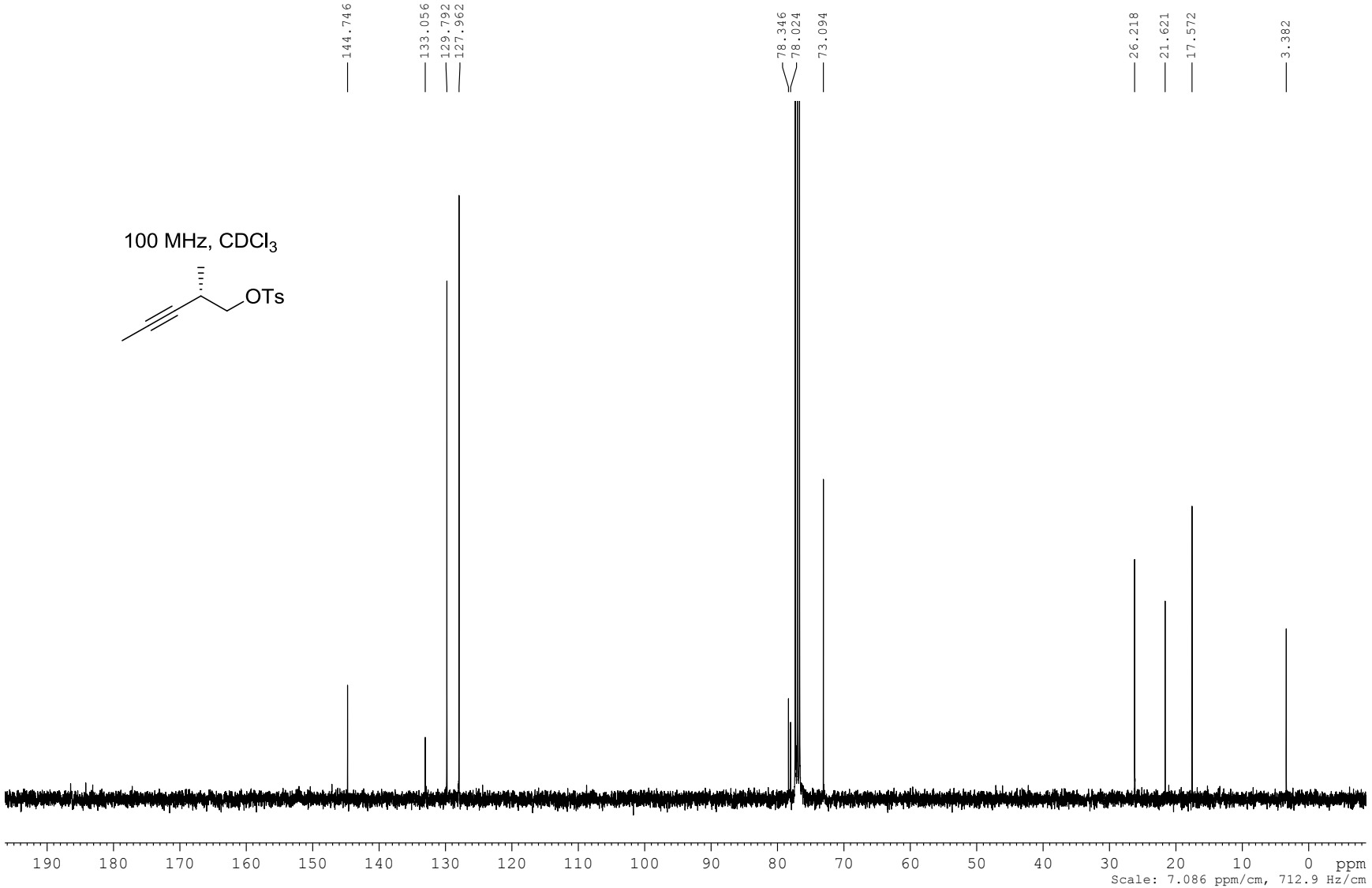

400 MHz, CDCl3
0.97
0.99
1.00
3.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

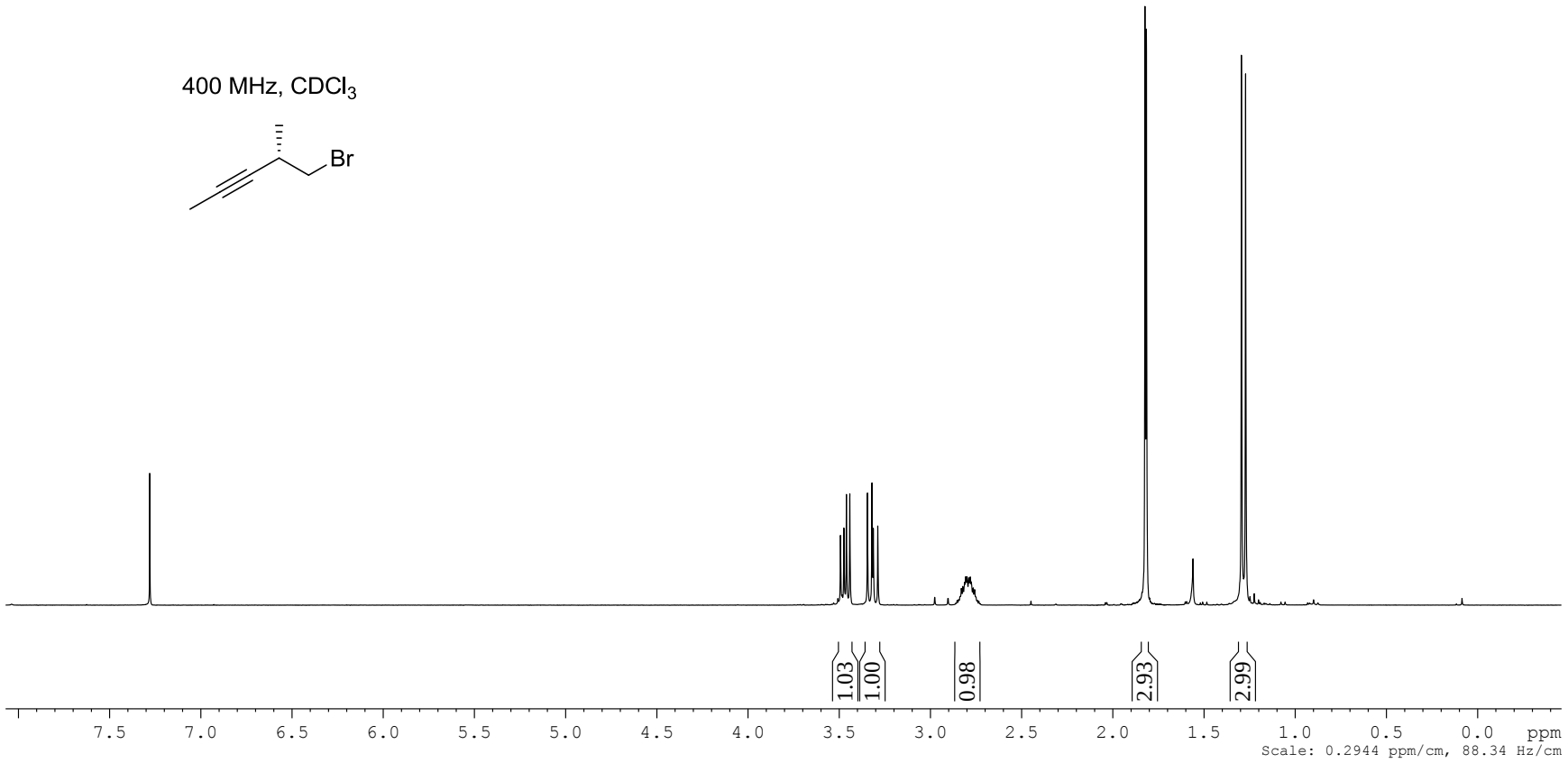

125.511
117.598
86.543
78.517
4.149
100 MHz, CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

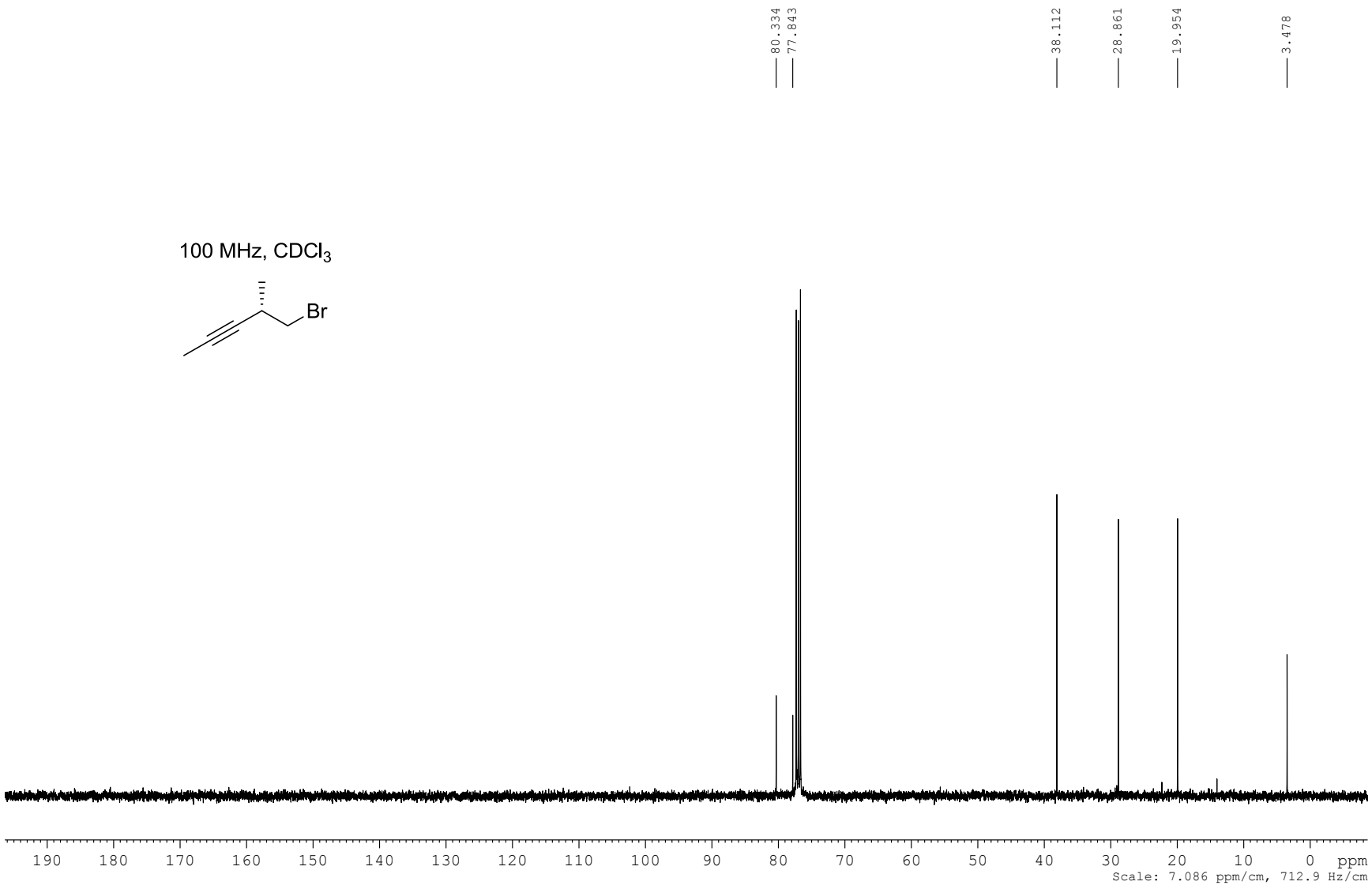

400 MHz, CDCl3
O
1.00
1.06
1.07
3.24
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

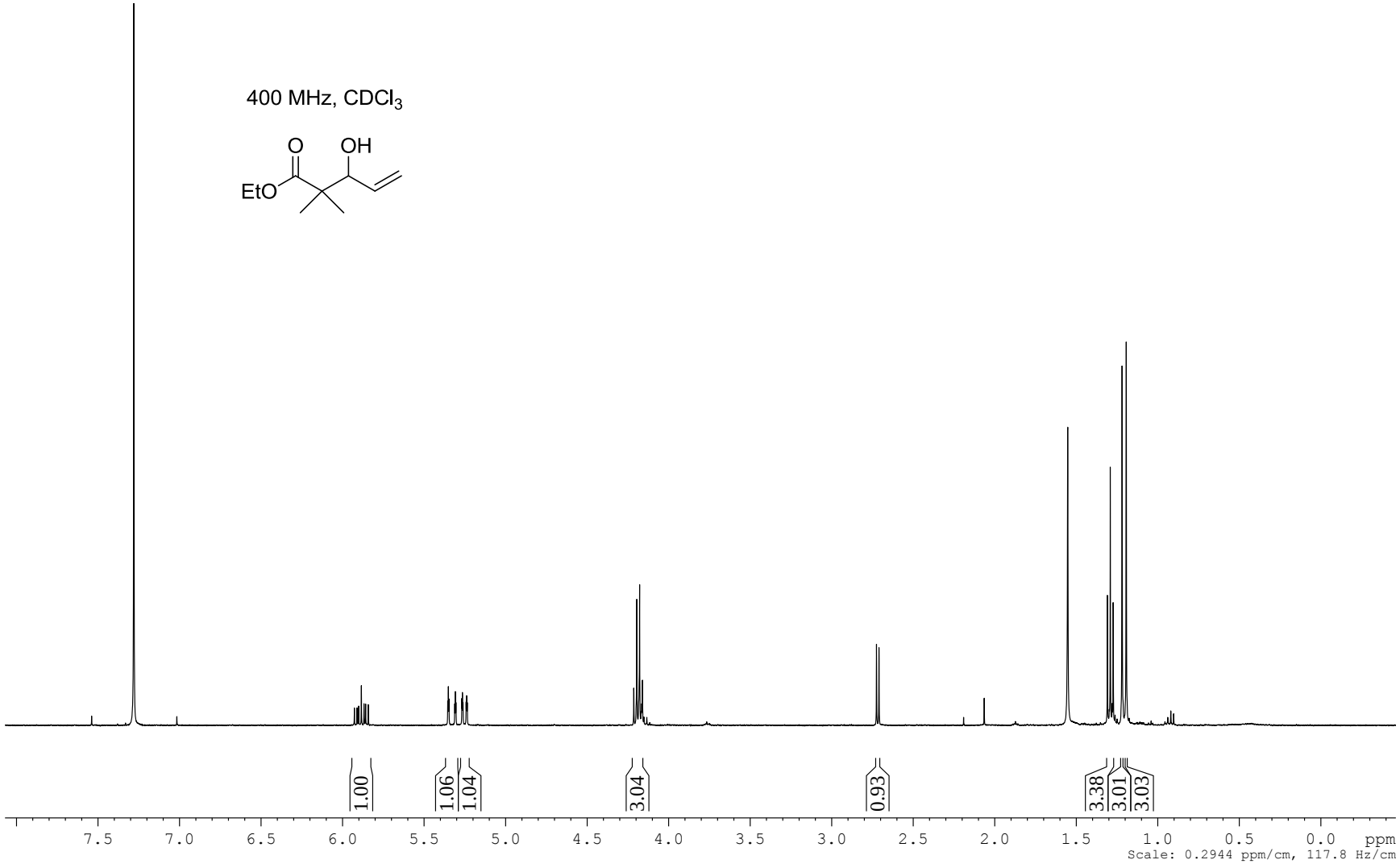

80.155
75.948
48.665
40.031
3.562
100 MHz, CDCl3
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

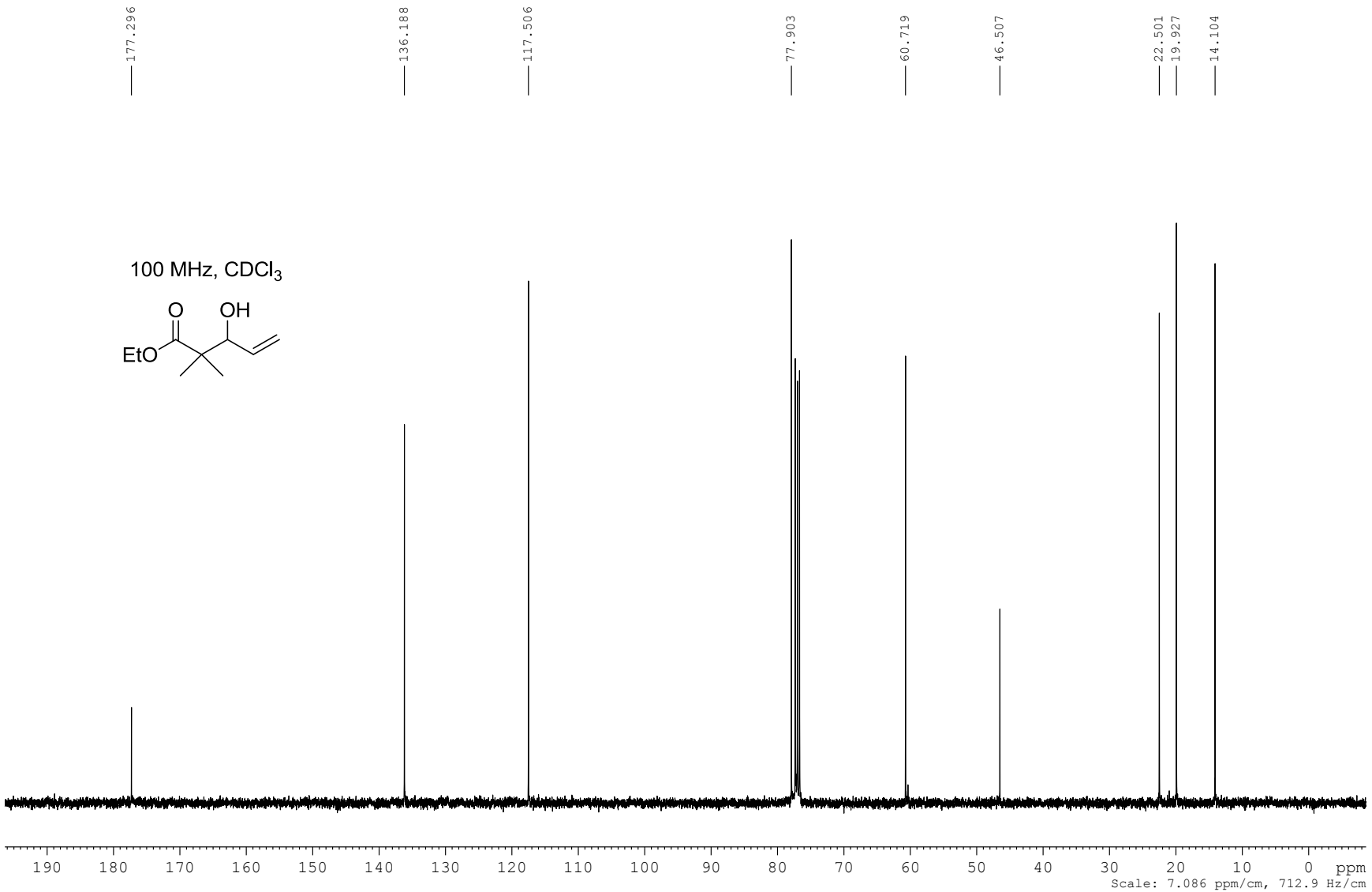

400 MHz, CDCl3
OTs
1.93
1.94
1.00
0.99
0.95
3.00
2.91
2.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.3203 ppm/cm, 128.1 Hz/cm

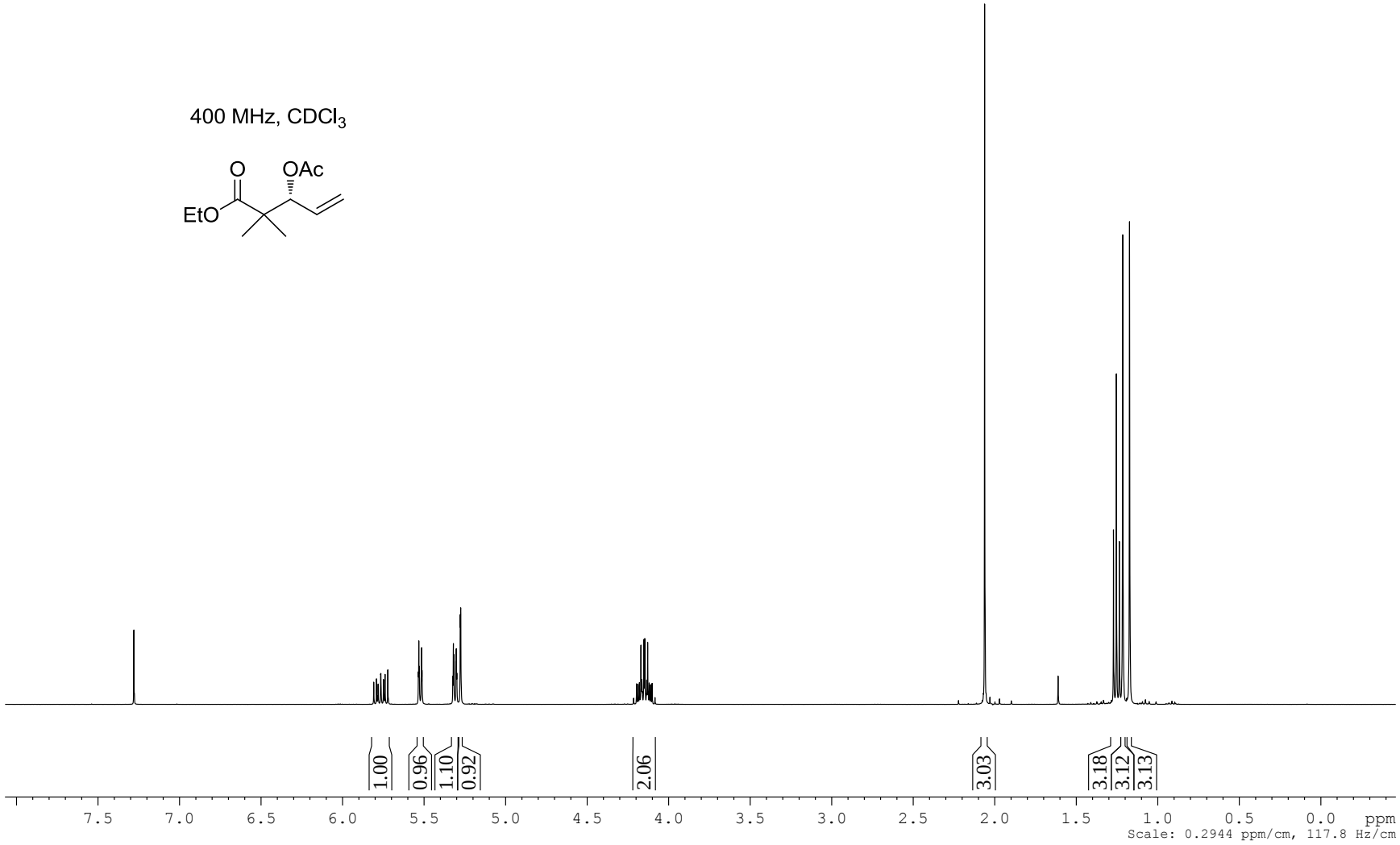

144.746
133.056
129.792
127.962
78.346
78.024
73.094
26.218
21.621
17.572
3.382
100 MHz, CDCl3
OTs
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

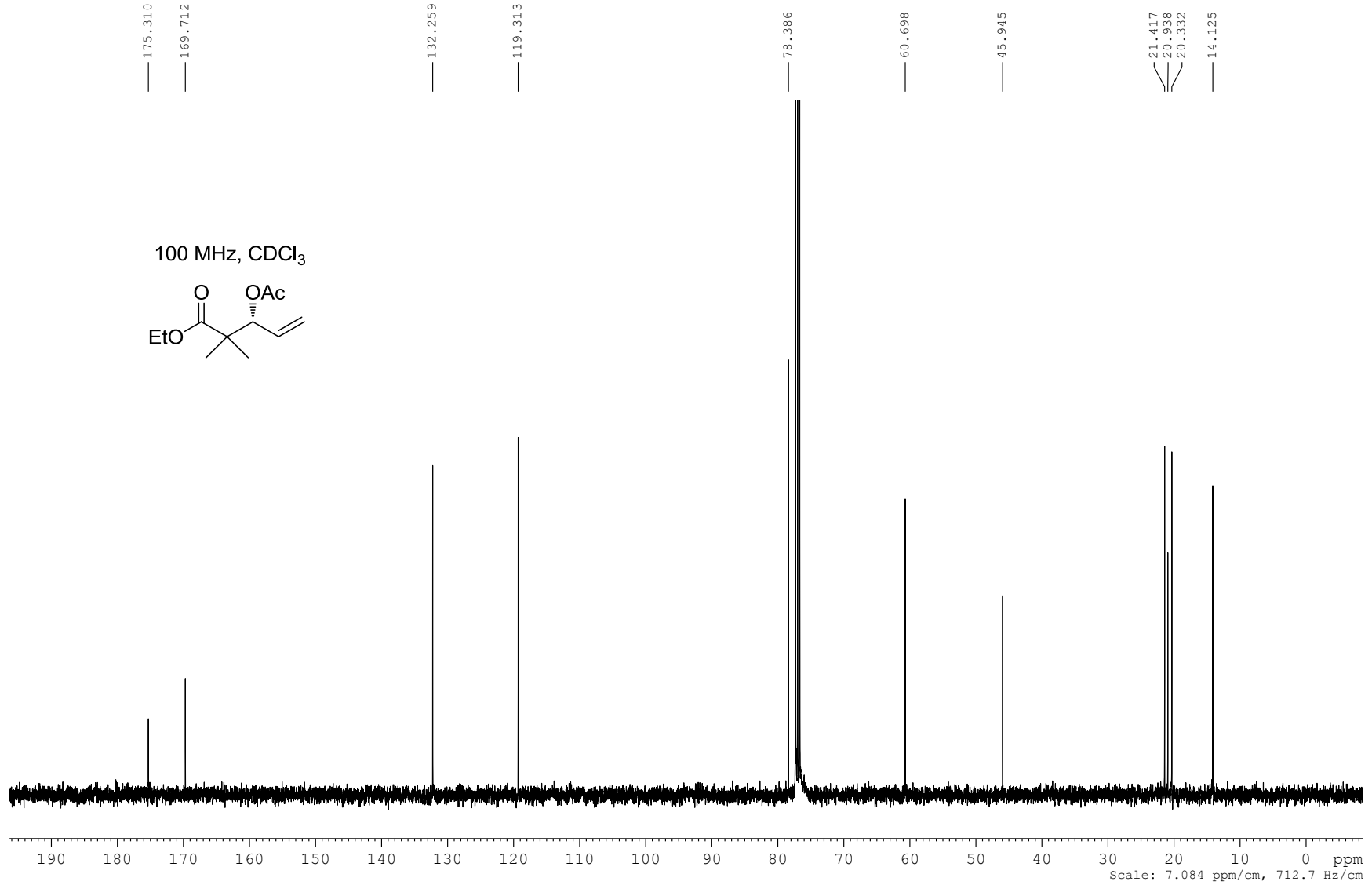

400 MHz, CDCl3
Br
1.03
1.00
0.98
2.93
2.99
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 88.34 Hz/cm


80.334
77.843
38.112
28.861
19.954
3.478
100 MHz, CDCl3
Br
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

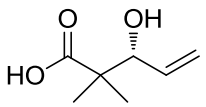

400 MHz, CDCl3
O
OH
EtO
1.00
1.06
1.04
3.04
0.93
3.38
3.01
3.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

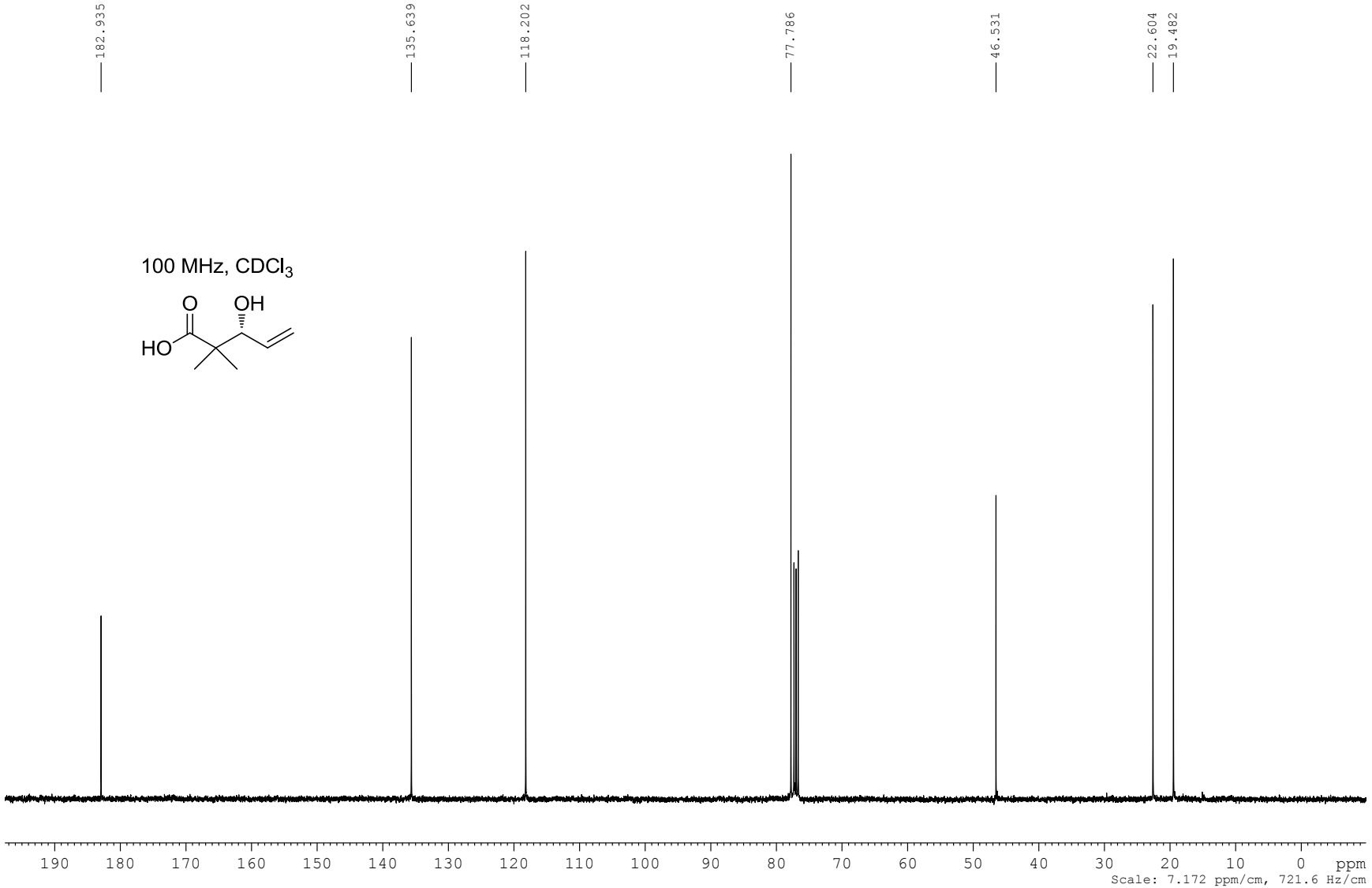

177.296
136.188
117.506
77.903
60.719
46.507
22.501
19.927
14.104
100 MHz, CDCl3
O
OH
EtO
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm


400 MHz, CDCl3
O
OAc
EtO
1.00
0.96
1.10
0.92
2.06
3.03
3.18
3.12
3.13
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
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

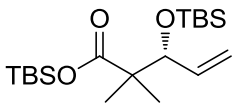

175.310
169.712
132.259
119.313
78.386
60.698
45.945
21.417
20.938
20.332
14.125
100 MHz, CDCl3
O
OAc
EtO
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.084 ppm/cm, 712.7 Hz/cm

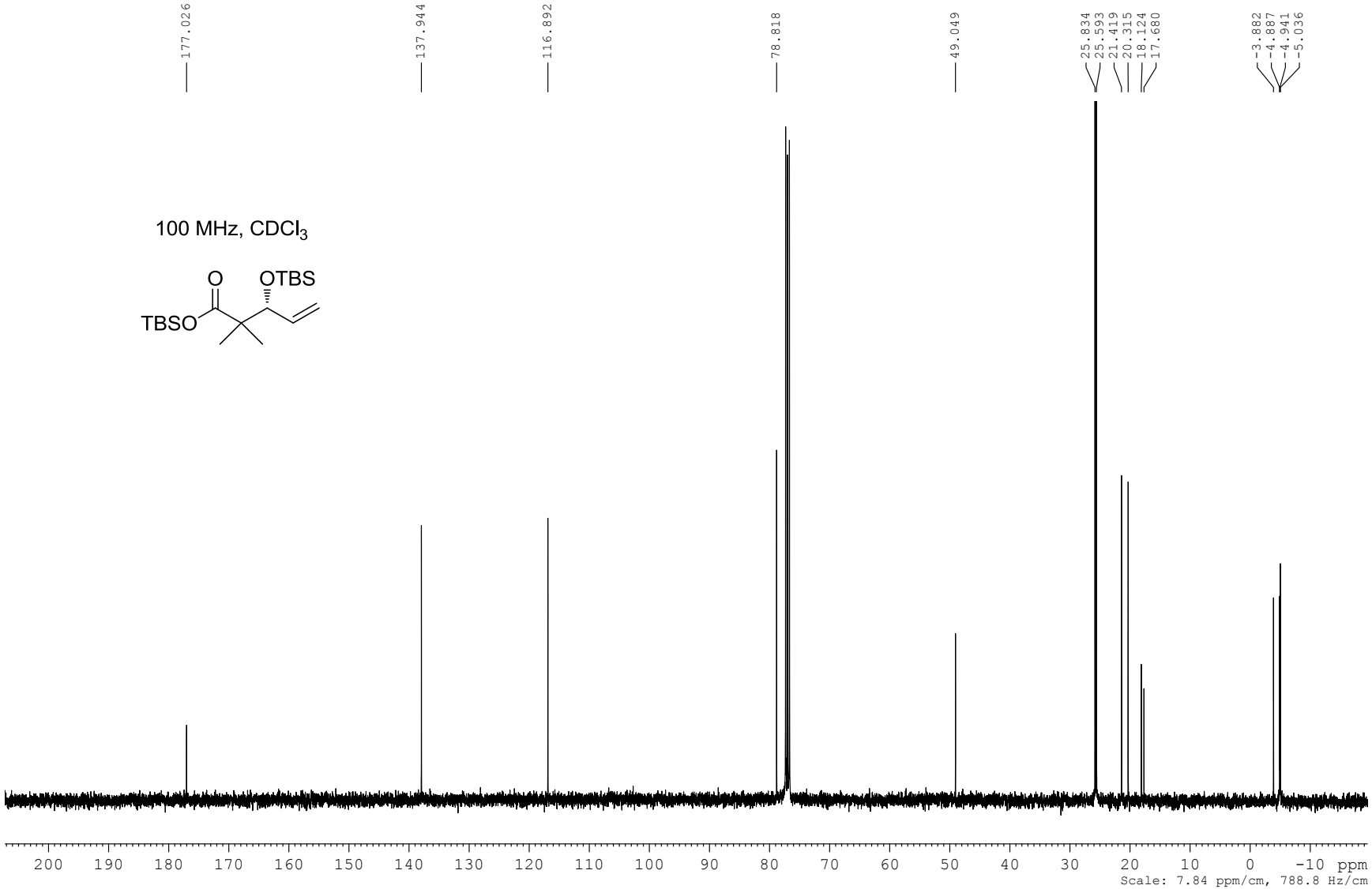
400 MHz, $CDCl_3$

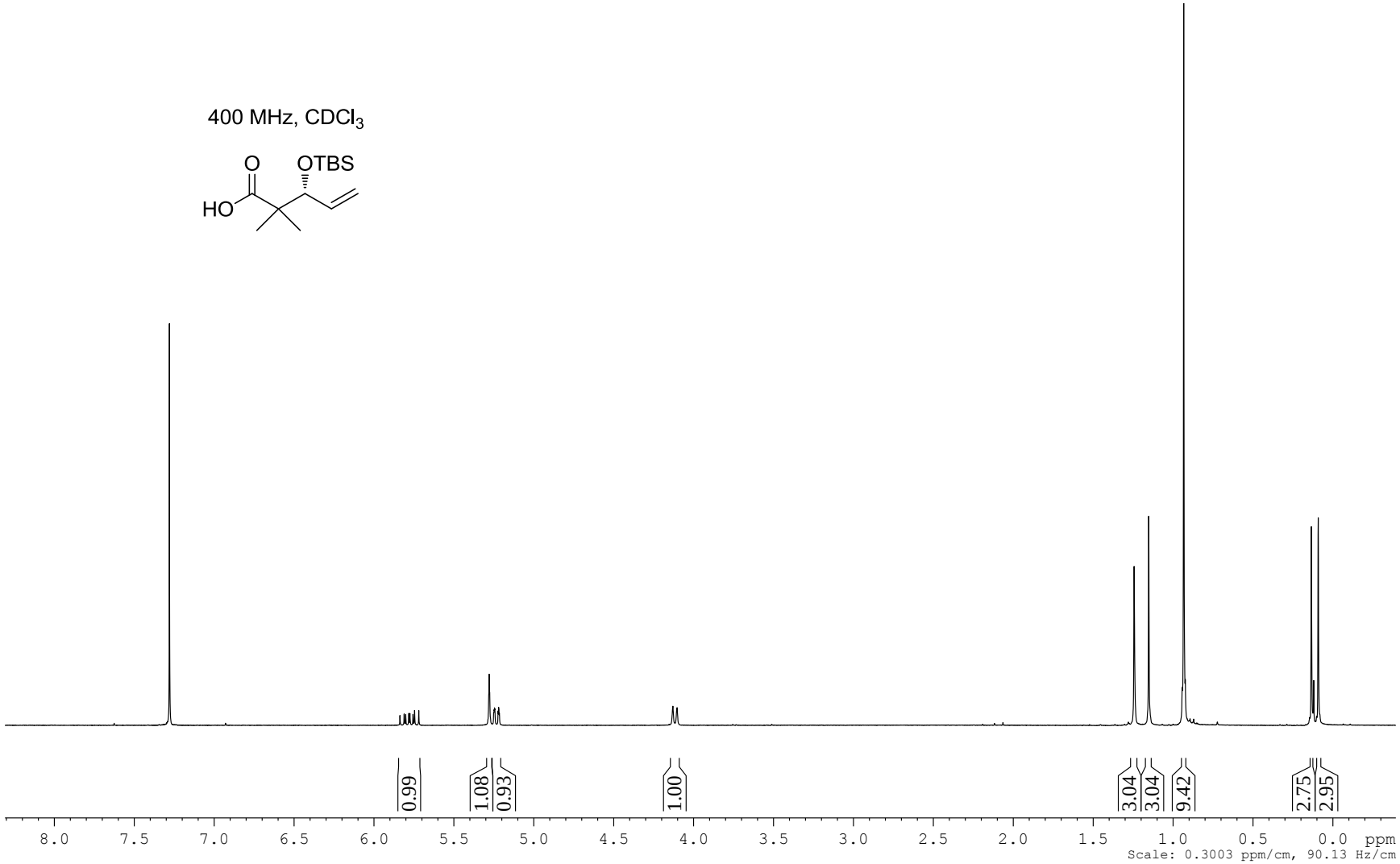


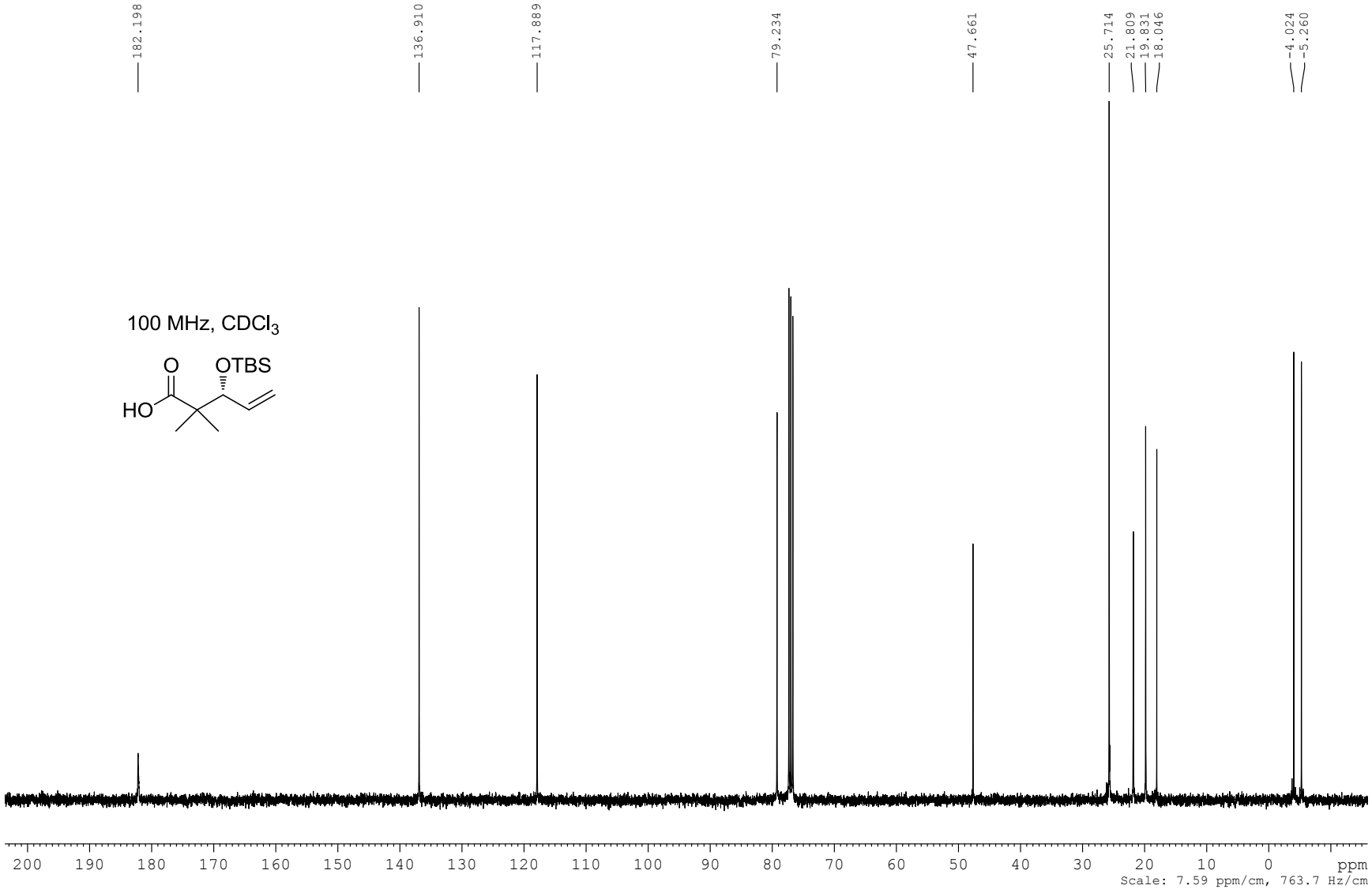

182.935
135.639
118.202
77.786
46.531
22.604
19.482
100 MHz, CDCl3
O
OH
HO
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.172 ppm/cm, 721.6 Hz/cm

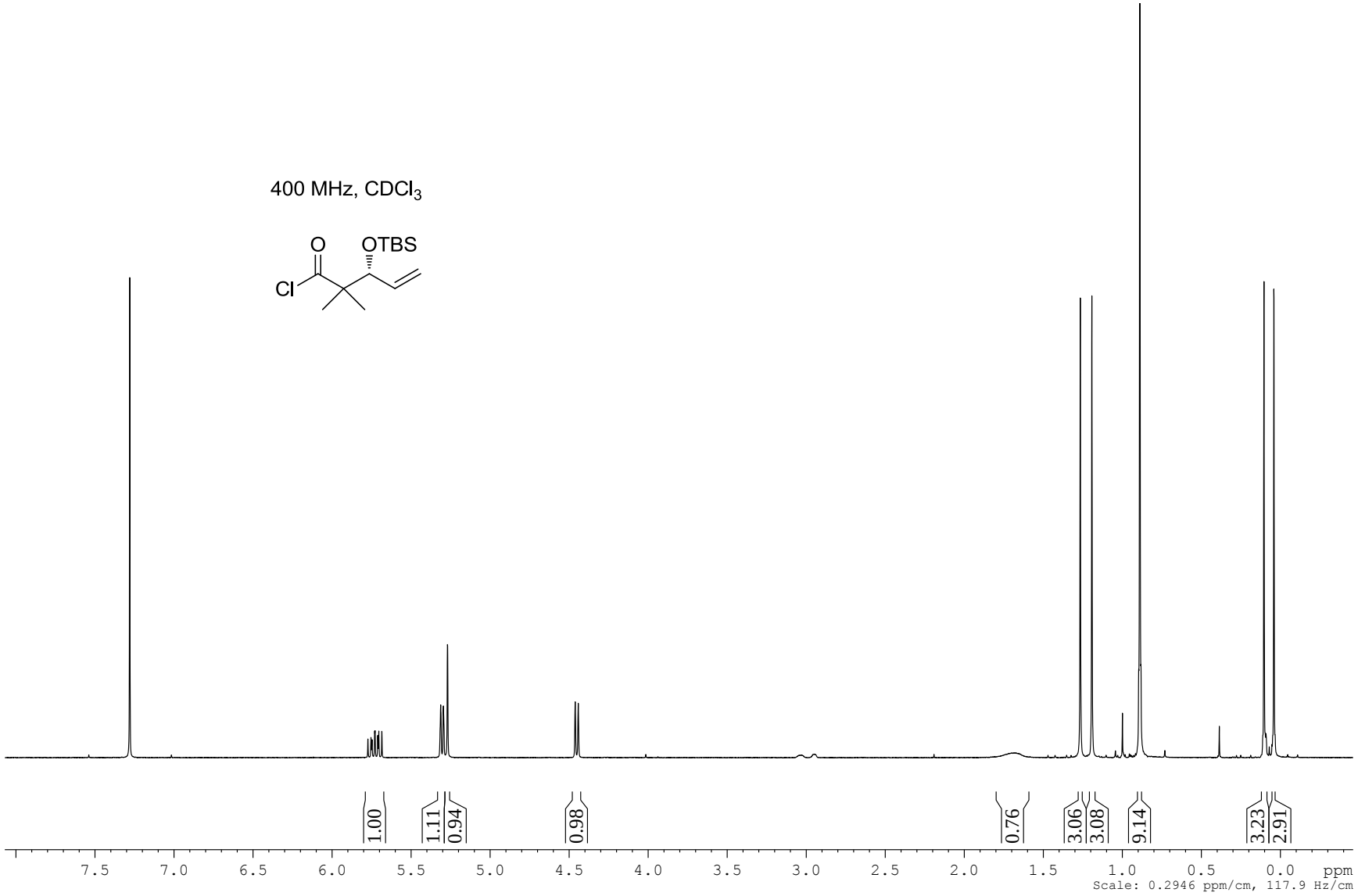
400 MHz, $CDCl_3$

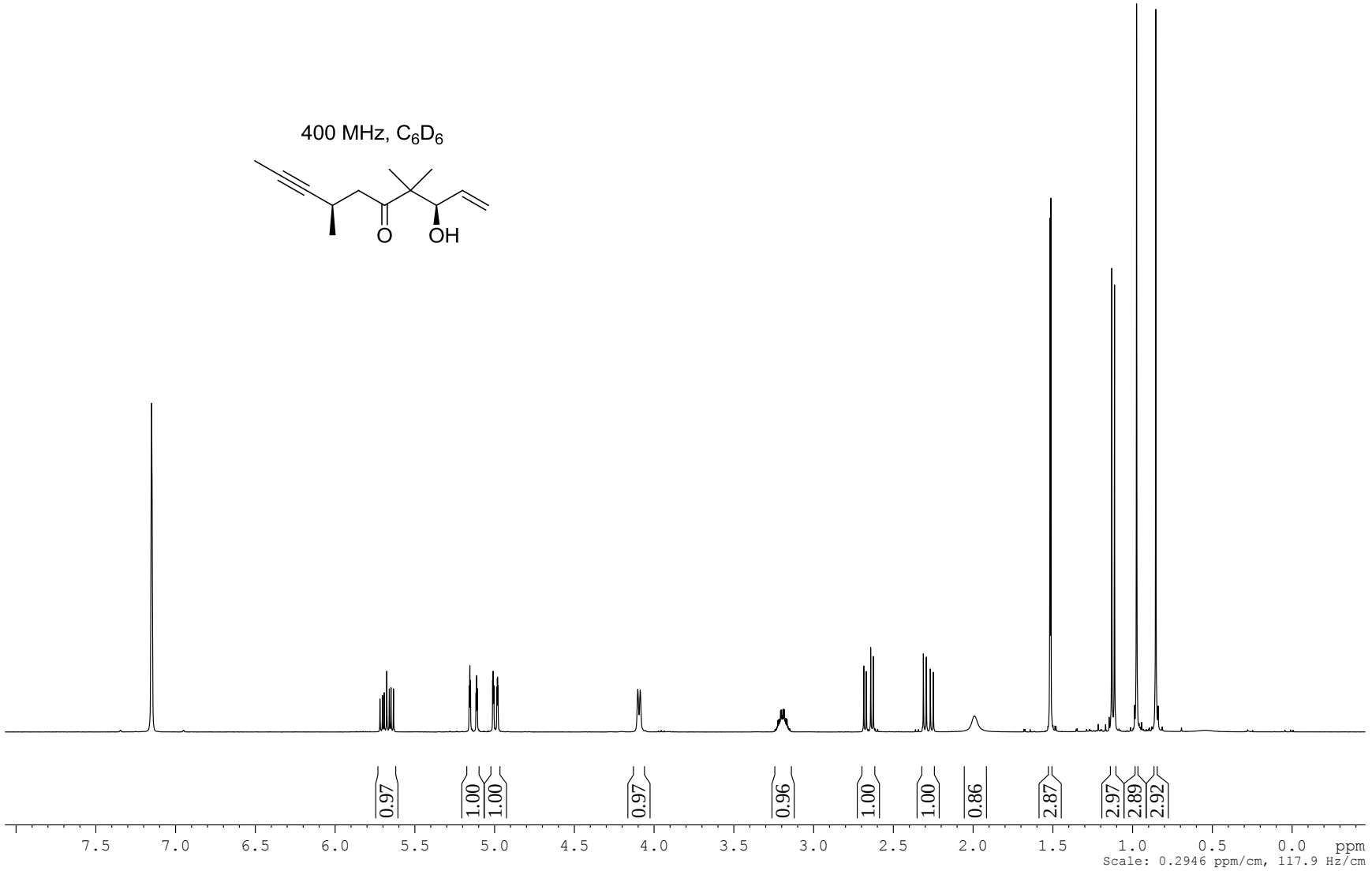


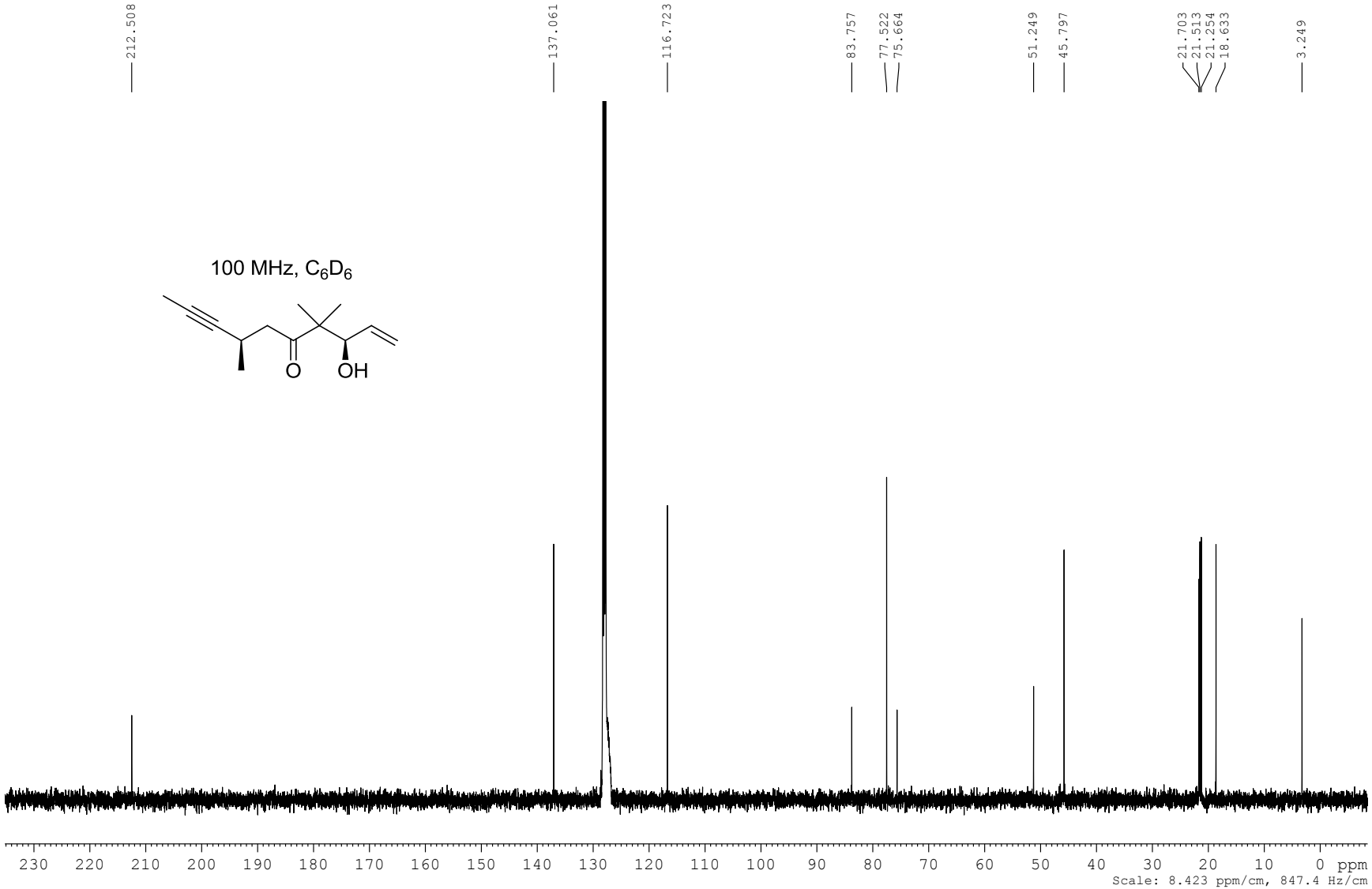

177.026
137.944
116.892
78.818
49.049
25.834
25.593
21.419
20.315
18.124
17.680
-3.882
-4.887
-4.941
-5.036
100 MHz, CDCl3
O
OTBS
TBSO
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm
Scale: 7.84 ppm/cm, 788.8 Hz/cm

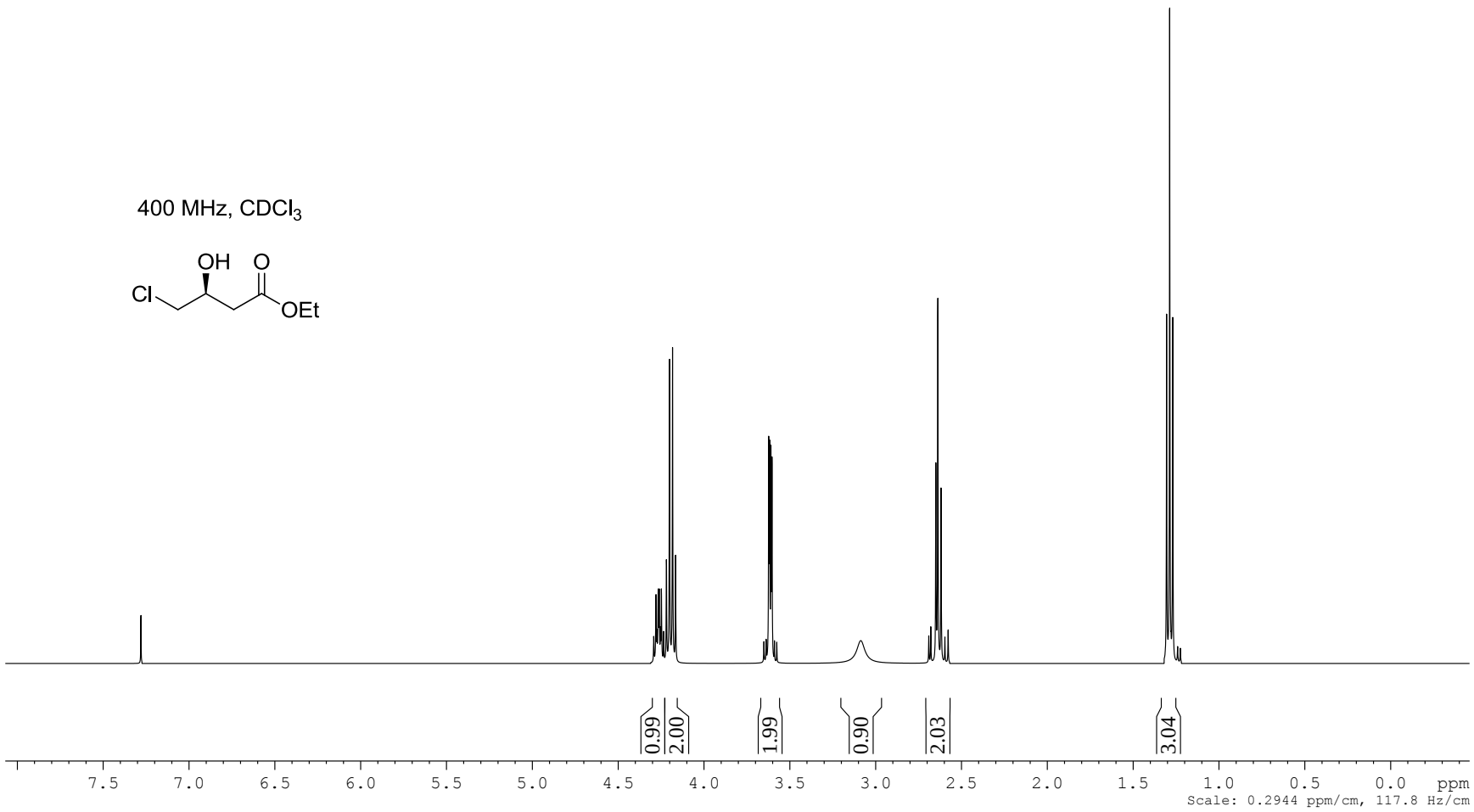

400 MHz, CDCl3
O
OTBS
HO
0.99
1.08
0.93
1.00
3.04
3.04
9.42
2.75
2.95
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.3003 ppm/cm, 90.13 Hz/cm

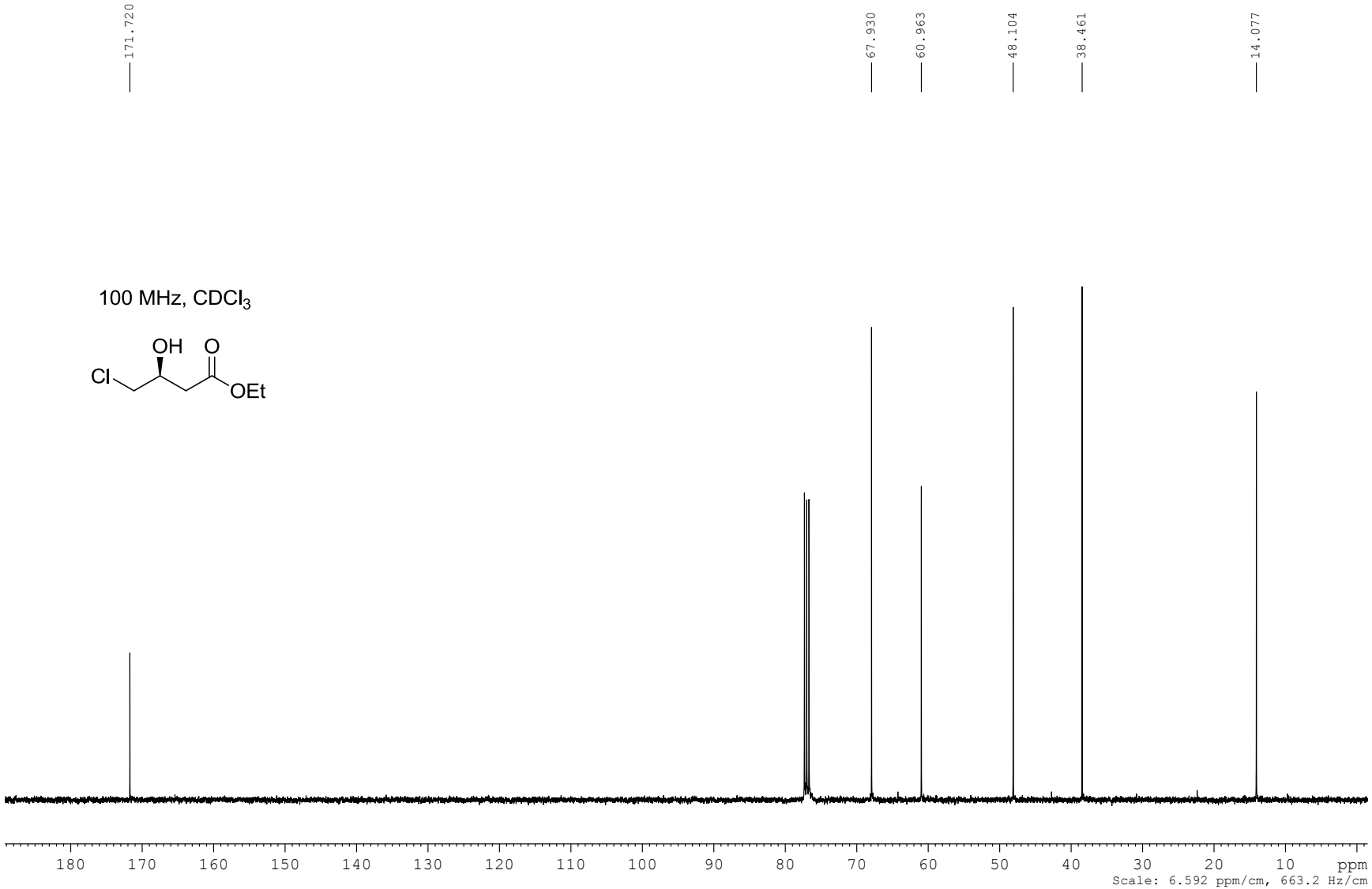

182.198
136.910
117.889
79.234
47.661
25.714
21.809
19.831
18.046
4.024
-5.260
100 MHz, CDCl3
O
OTBS
HO
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.59 ppm/cm, 763.7 Hz/cm

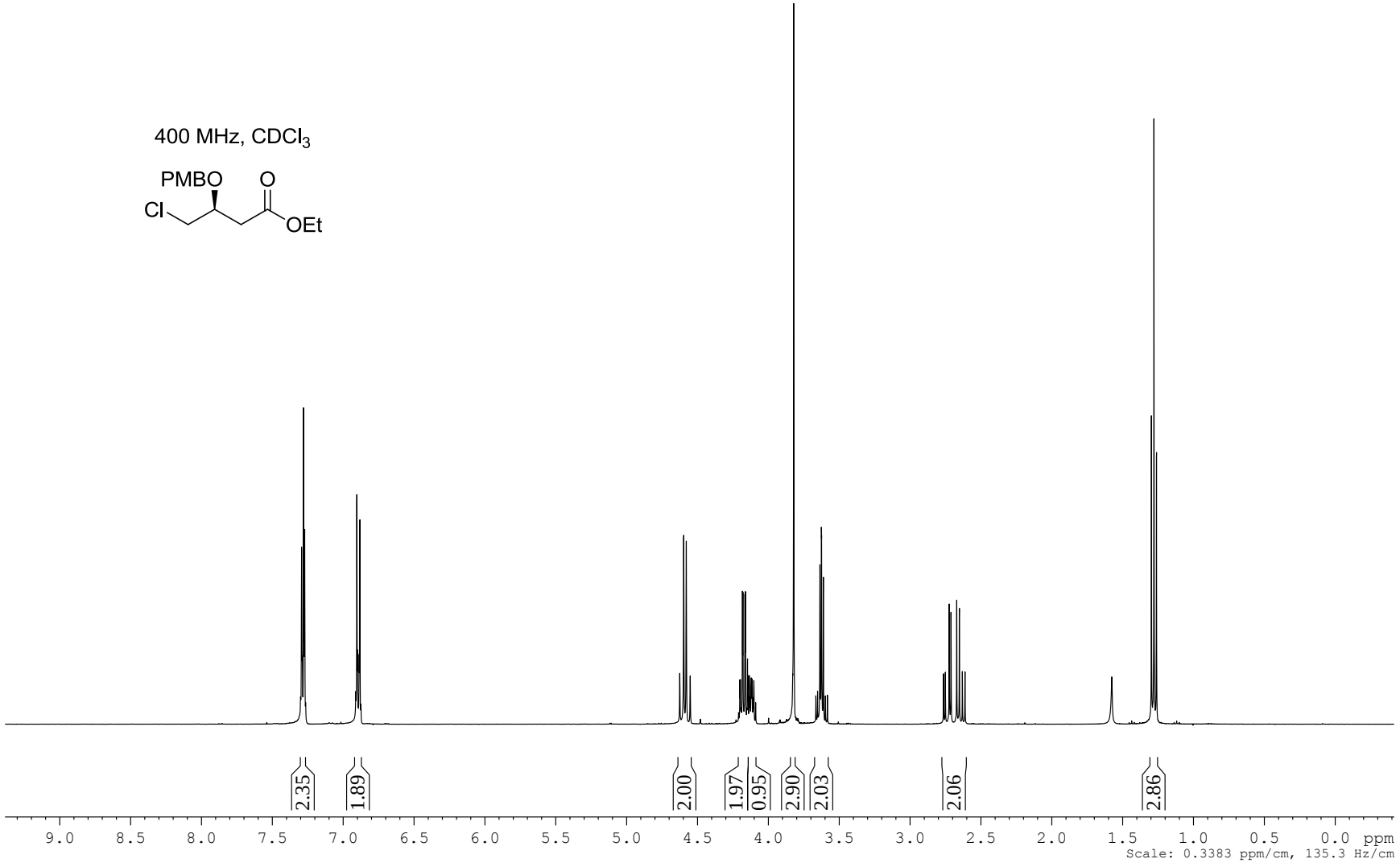

400 MHz, CDCl3
O
OTBS
Cl
1.00
1.11
0.94
0.98
0.76
3.06
3.08
9.14
3.23
2.91
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

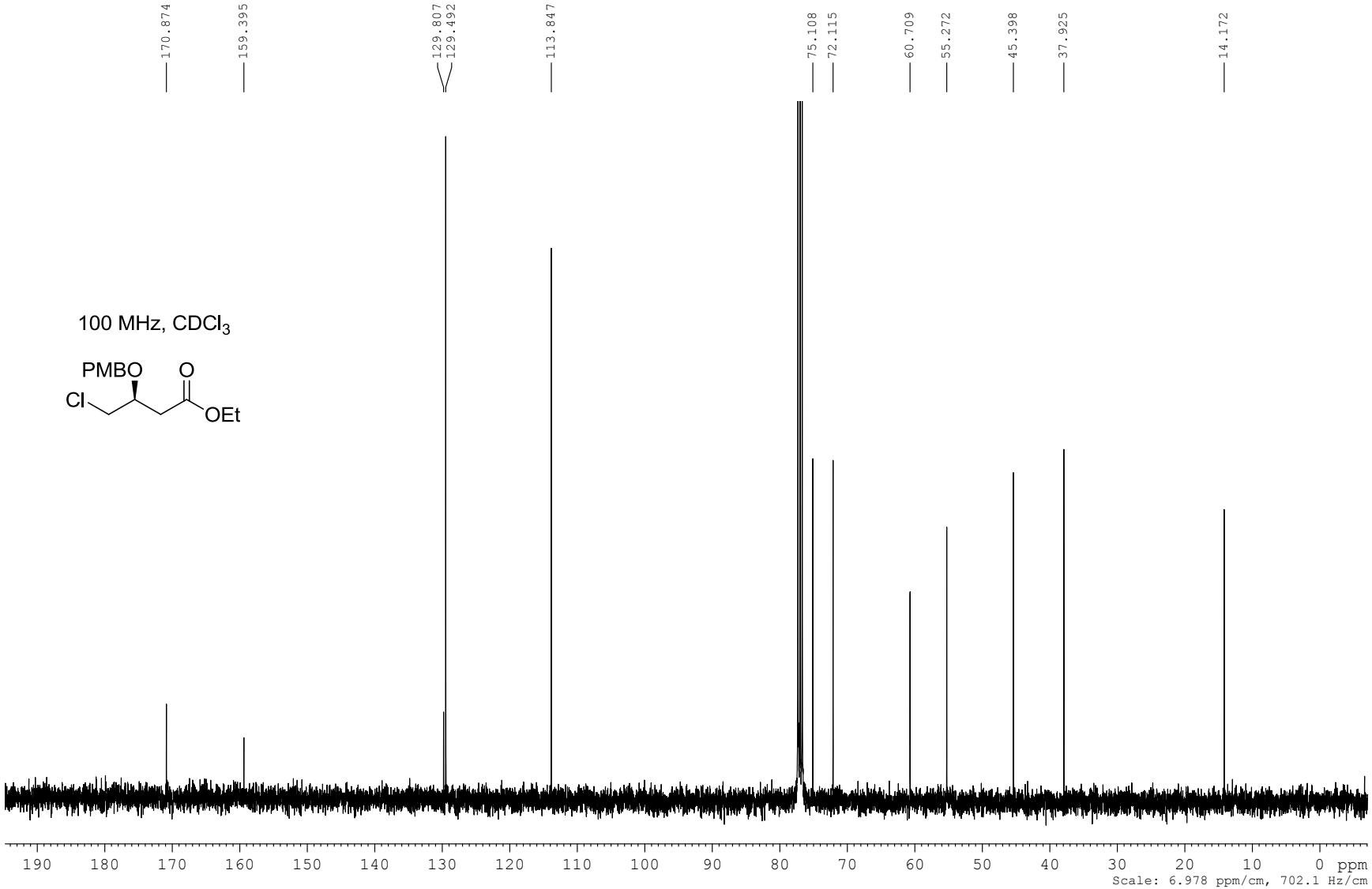

400 MHz, C6D6
O
OH
0.97
1.00
1.00
0.97
0.96
1.00
1.00
0.86
2.87
2.97
2.89
2.92
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm


212.508
137.061
116.723
83.757
77.522
75.664
51.249
45.797
21.703
21.513
21.254
18.633
3.249
100 MHz, C6D6
O
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 8.423 ppm/cm, 847.4 Hz/cm

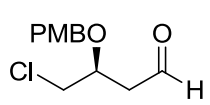

400 MHz, CDCl3
OH
O
Cl
OEt
0.99
2.00
1.99
0.90
2.03
3.04
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

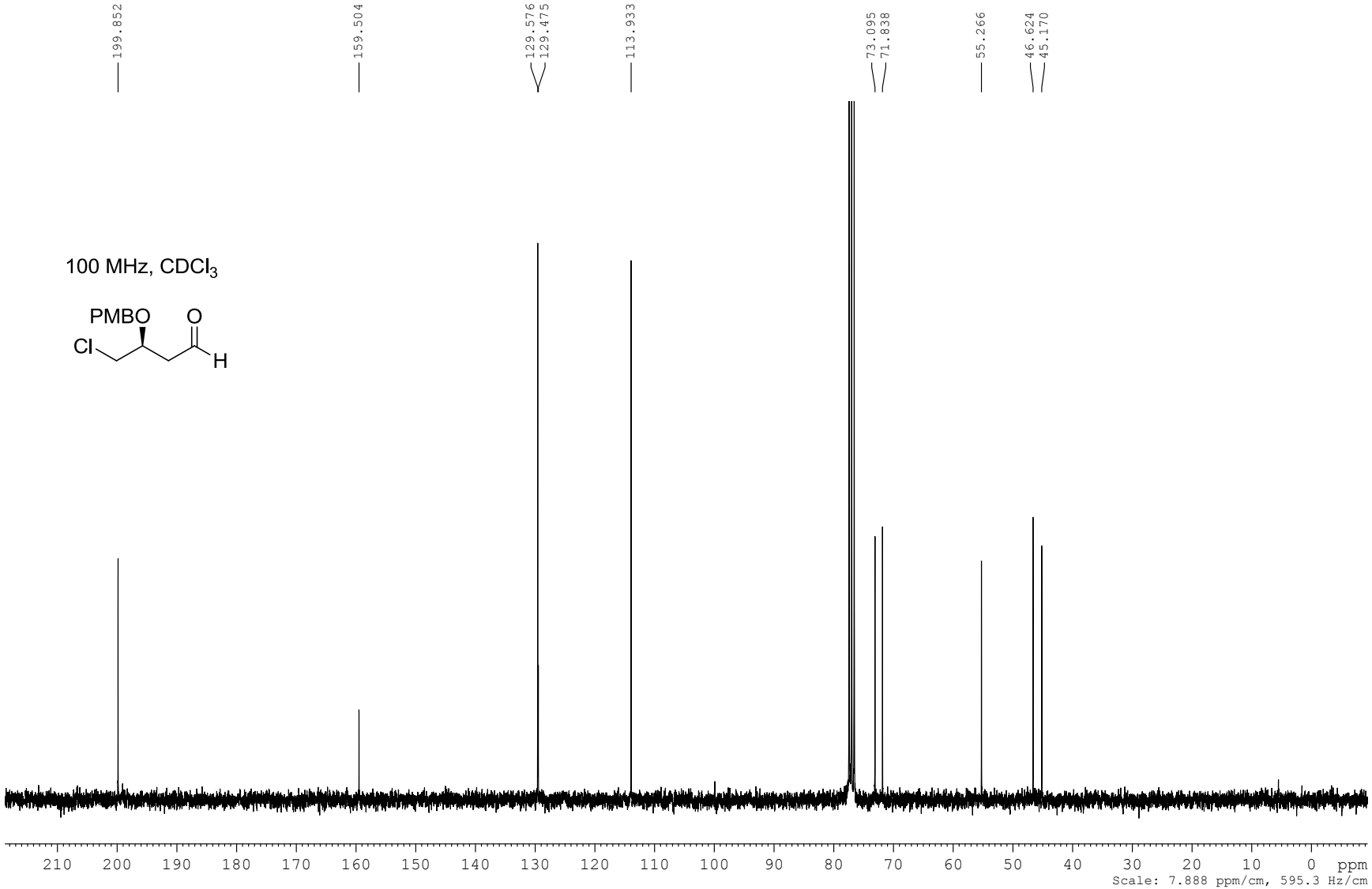

171.720
67.930
60.963
48.104
38.461
14.077
100 MHz, CDCl3
OH
O
Cl
OEt
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Scale: 6.592 ppm/cm, 663.2 Hz/cm

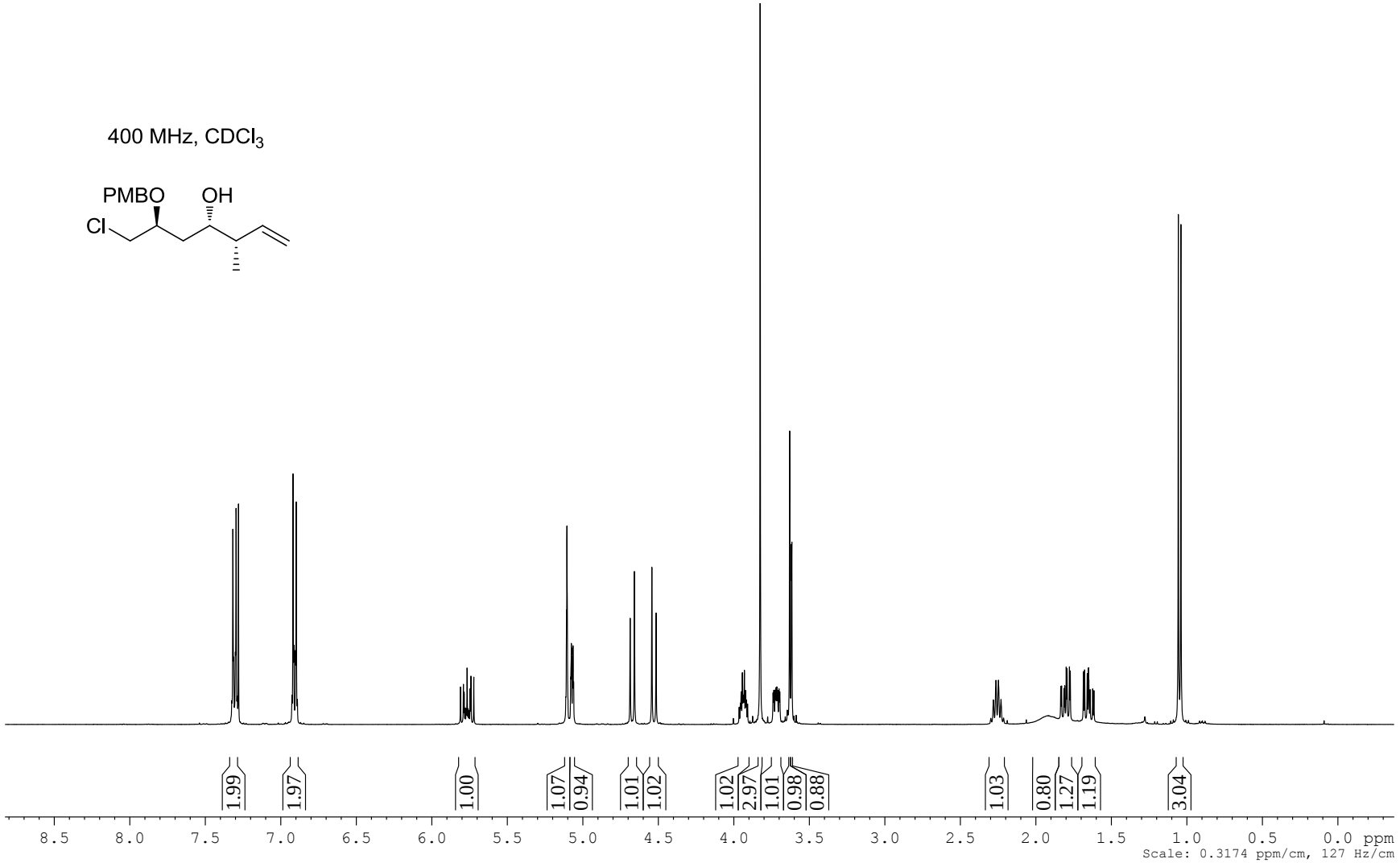

400 MHz, CDCl3
PMBO
O
Cl
OEt
2.35
1.89
2.00
1.97
0.95
2.90
2.03
2.06
2.86
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
Scale: 0.3383 ppm/cm, 135.3 Hz/cm

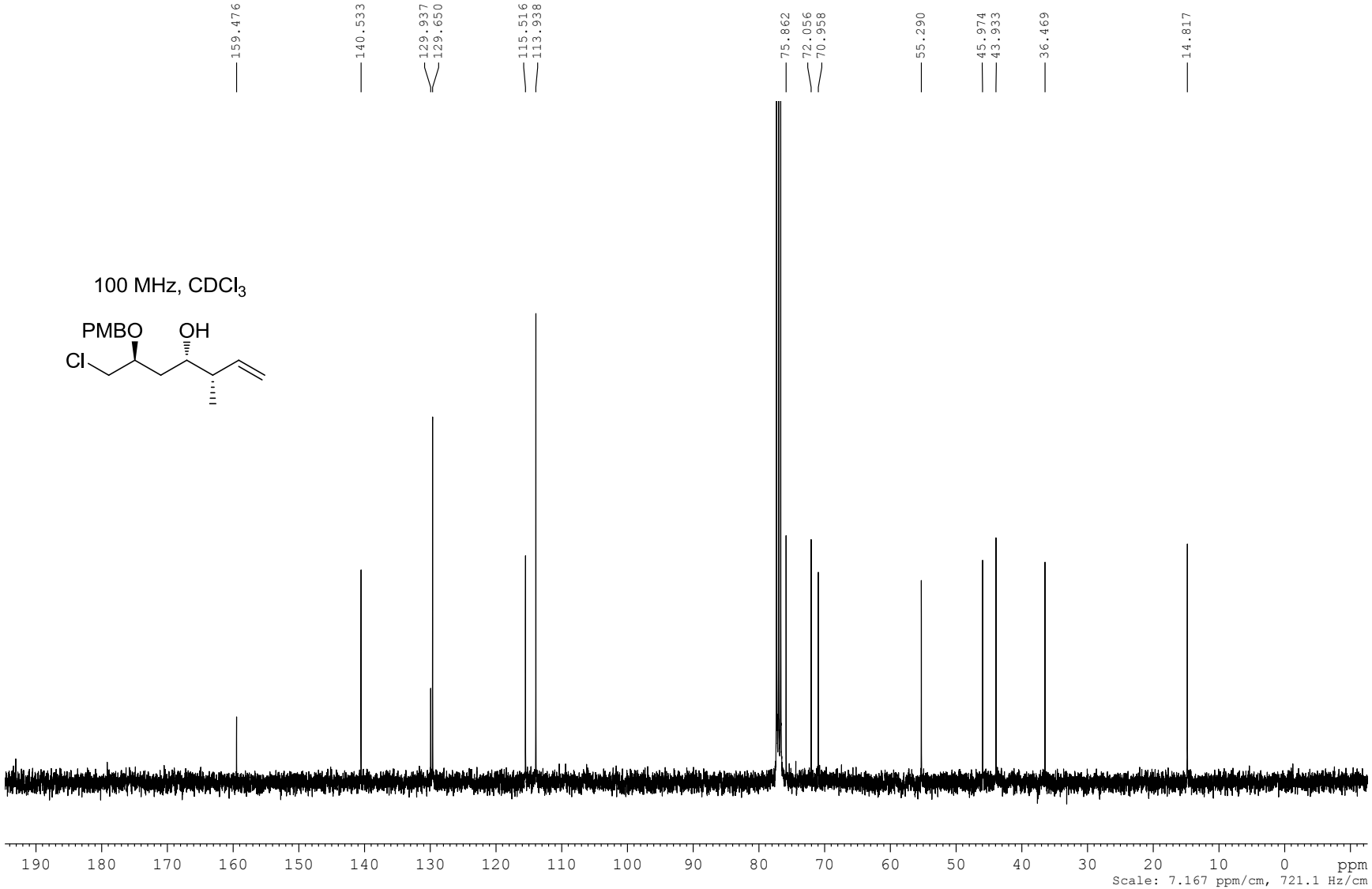

170.874
159.395
129.807
129.492
113.847
75.108
72.115
60.709
55.272
45.398
37.925
14.172
100 MHz, CDCl3
PMBO
O
Cl
OEt
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 6.978 ppm/cm, 702.1 Hz/cm

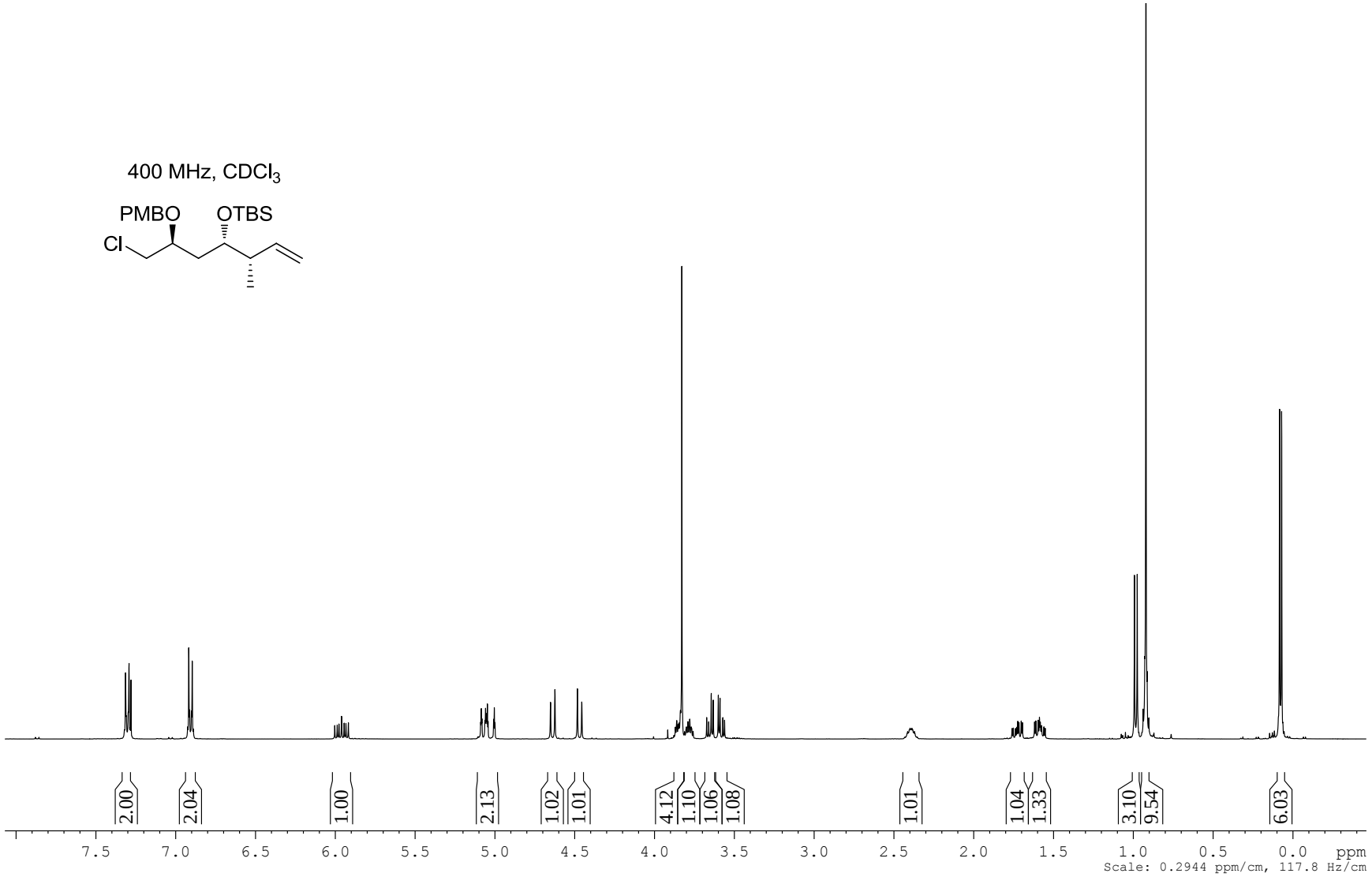
400 MHz, $CDCl_3$

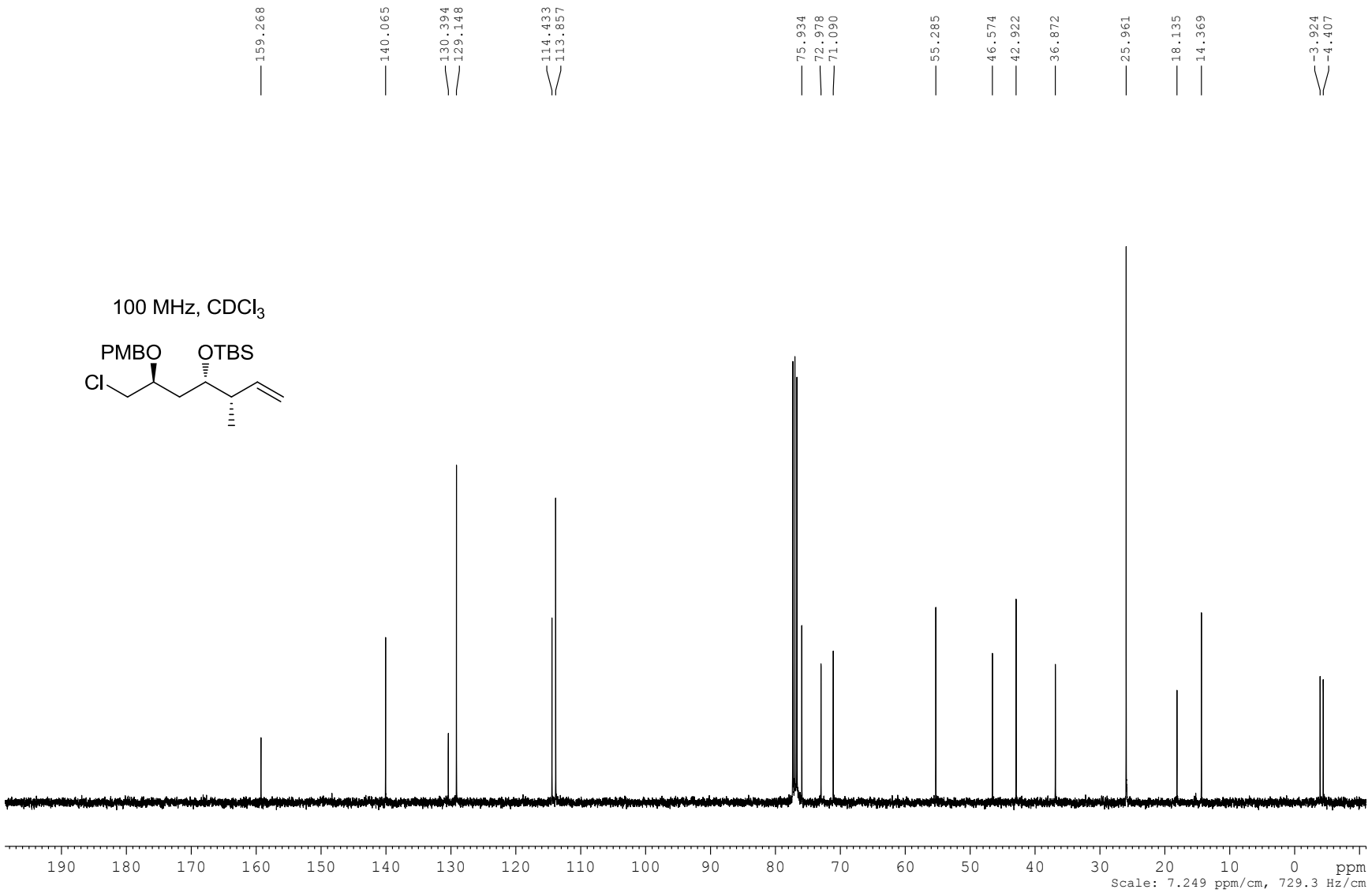


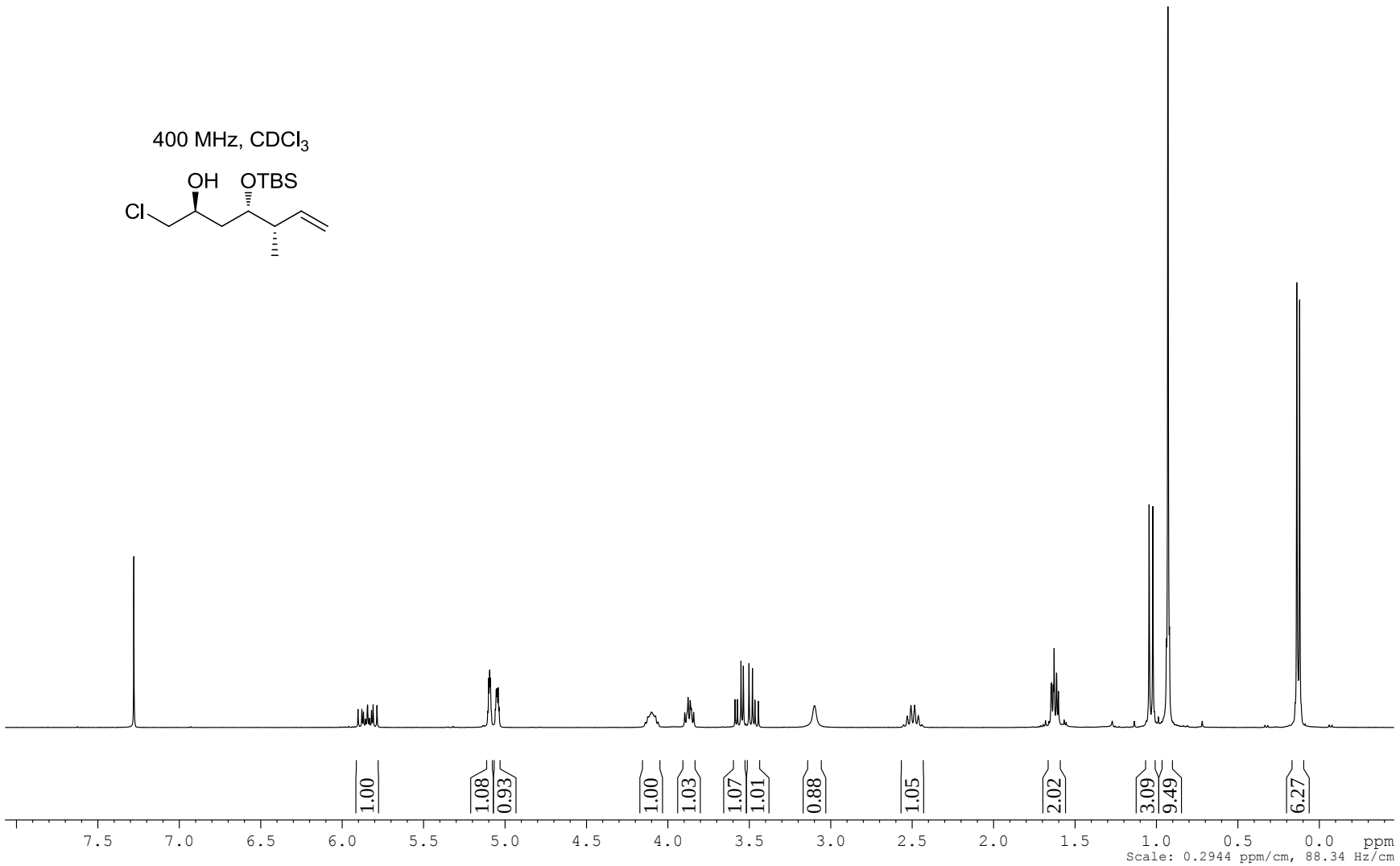

199.852
159.504
129.576
129.475
113.933
73.095
71.838
55.266
46.624
45.170
100 MHz, CDCl3
PMBO
O
Cl
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.888 ppm/cm, 595.3 Hz/cm

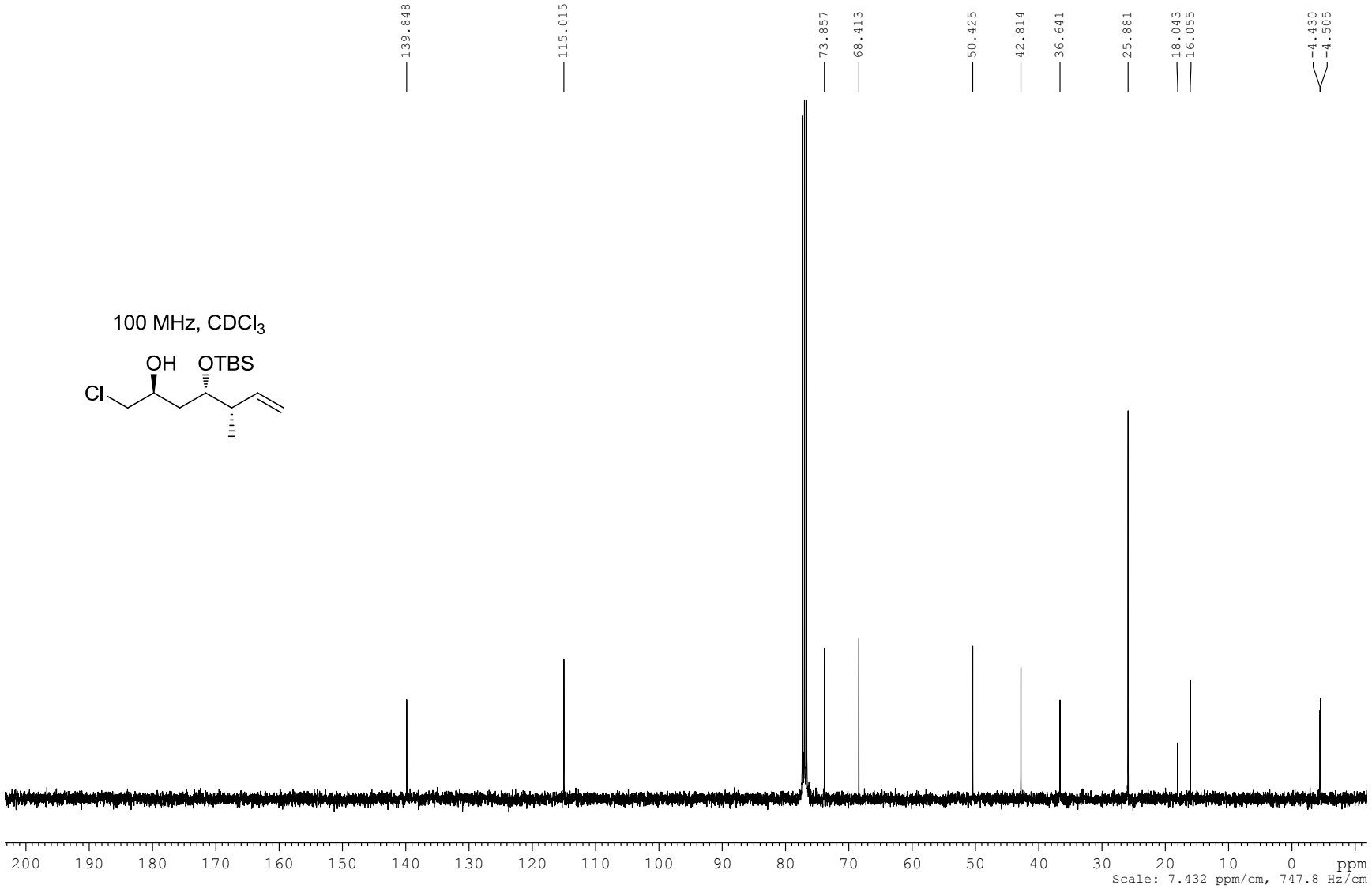

400 MHz, CDCl3
PMBO
OH
Cl
1.99
1.97
1.00
1.07
0.94
1.01
1.02
1.02
2.97
1.01
0.98
0.88
1.03
0.80
1.27
1.19
3.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
Scale: 0.3174 ppm/cm, 127 Hz/cm

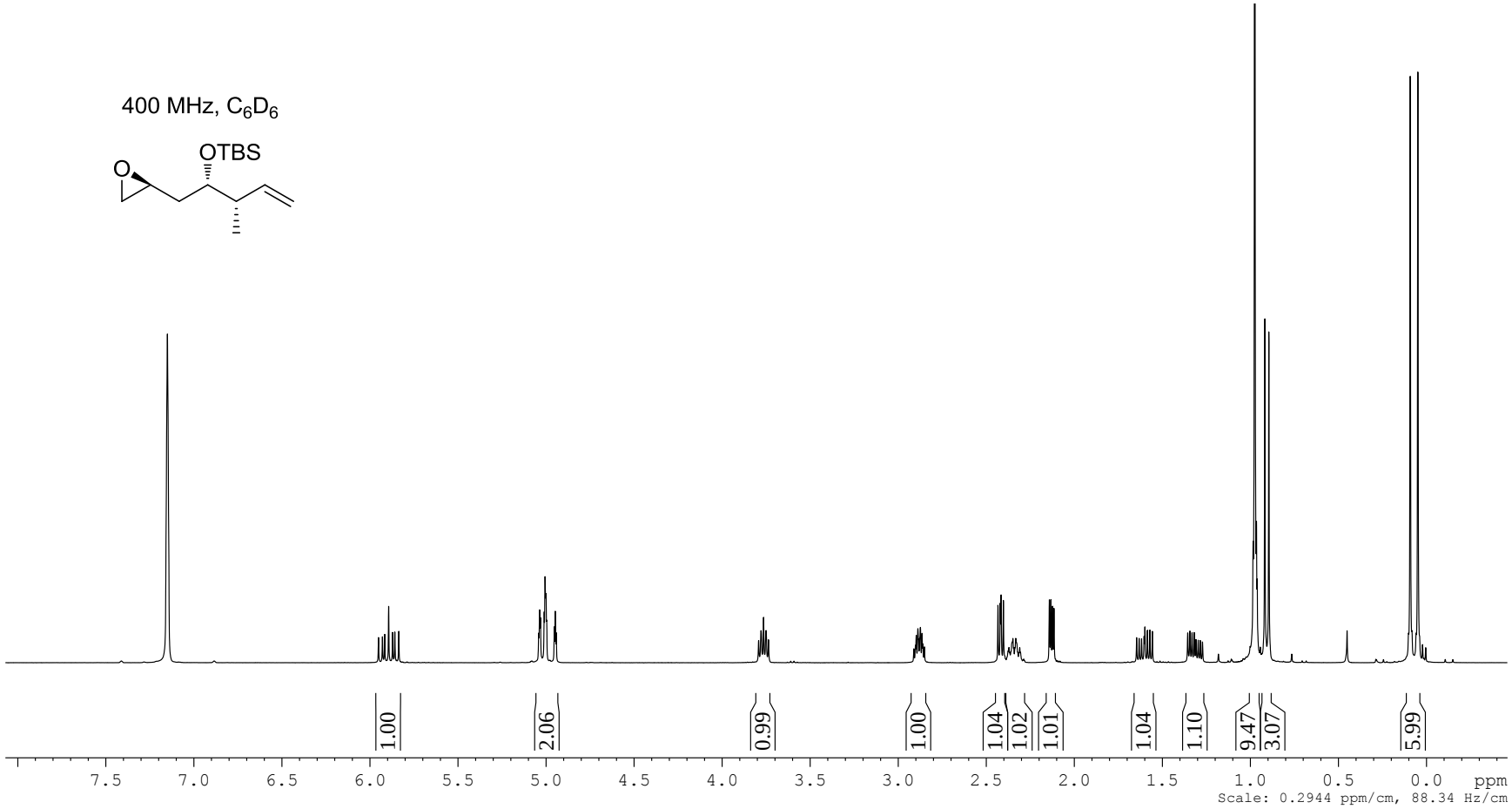

159.476
140.533
129.937
129.650
115.516
113.938
75.862
72.056
70.958
55.290
45.974
43.933
36.469
14.817
100 MHz, CDCl3
PMBO
OH
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.167 ppm/cm, 721.1 Hz/cm

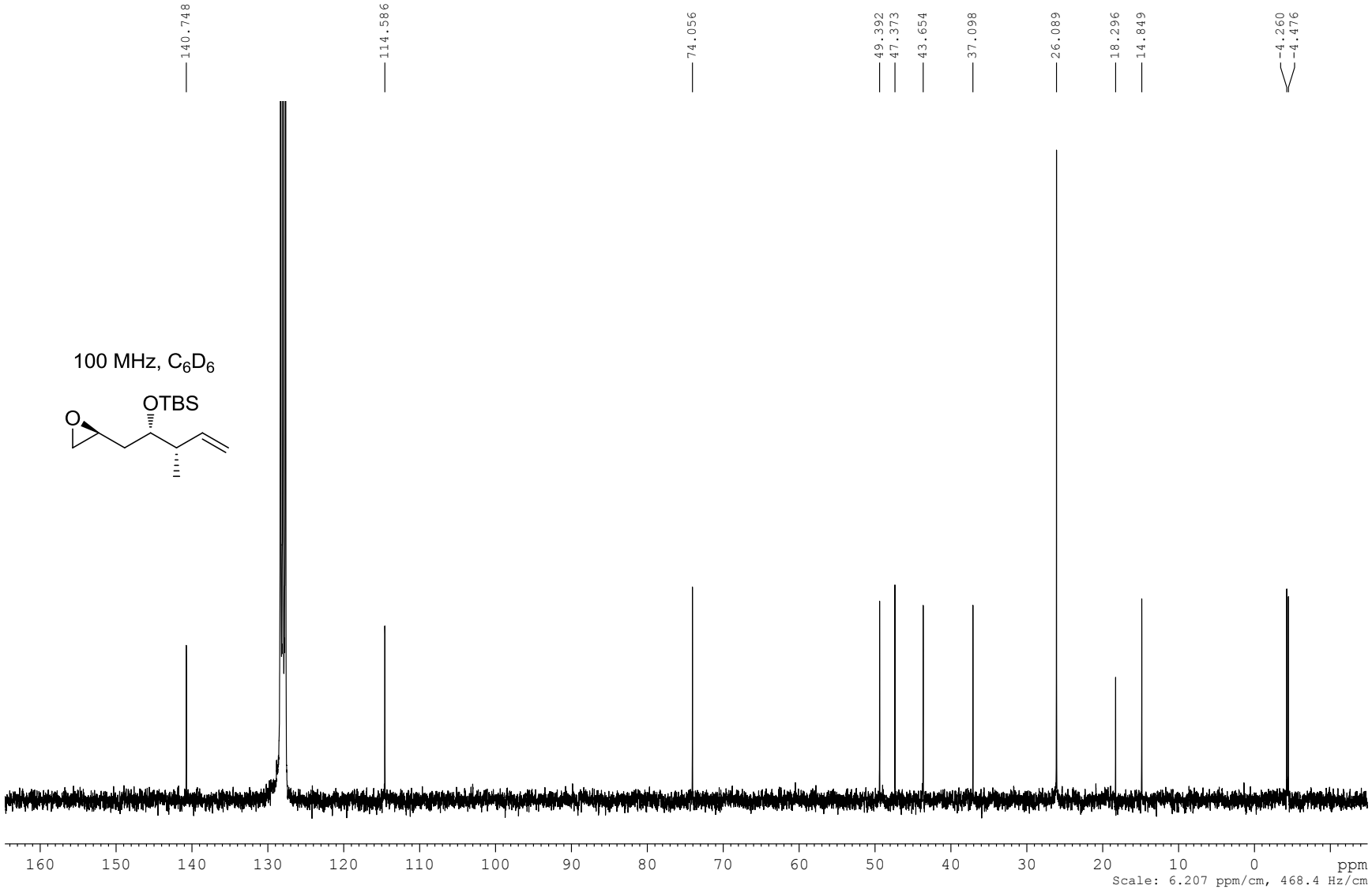

400 MHz, CDCl3
PMBO
OTBS
Cl
2.00
2.04
1.00
2.13
1.02
1.01
4.12
1.10
1.06
1.08
1.01
1.04
1.33
3.10
9.54
6.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

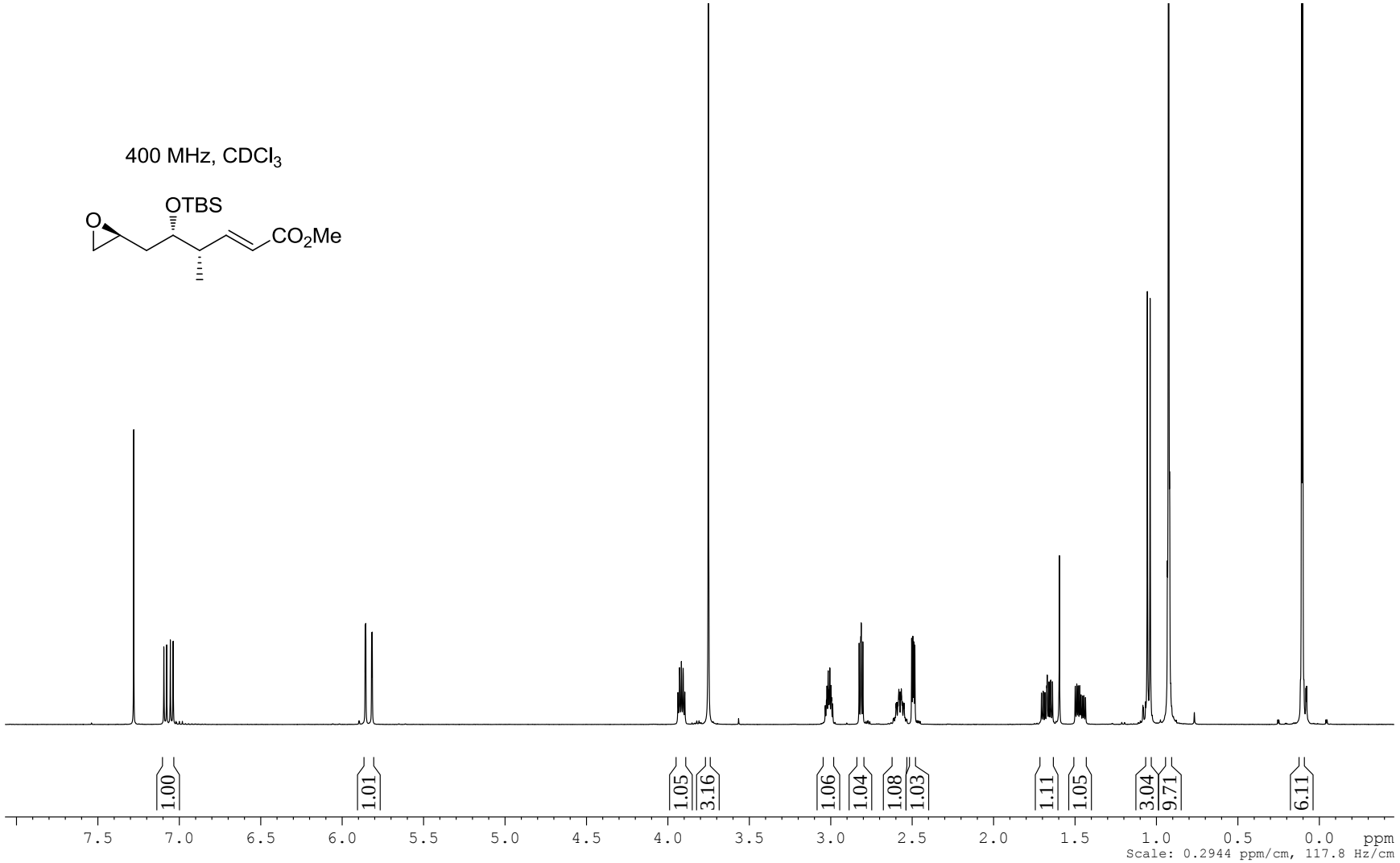

159.268
140.065
130.394
129.148
114.433
113.857
75.934
72.978
71.090
55.285
46.574
42.922
36.872
25.961
18.135
14.369
-3.924
-4.407
100 MHz, CDCl3
PMBO
OTBS
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.249 ppm/cm, 729.3 Hz/cm

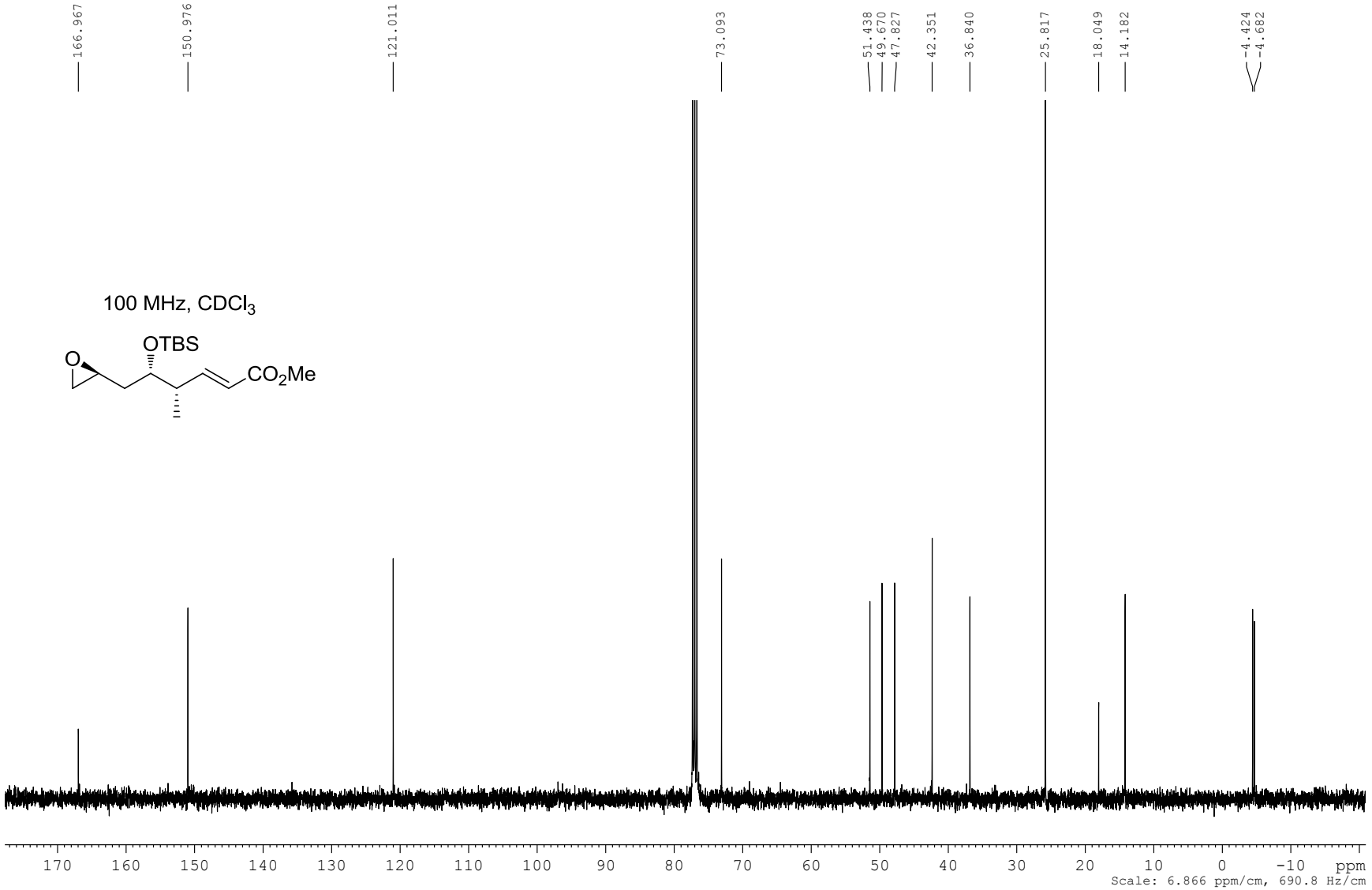

400 MHz, CDCl3
OH
OTBS
Cl
1.00
1.08
0.93
1.00
1.03
1.07
1.01
0.88
1.05
2.02
3.09
9.49
6.27
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 88.34 Hz/cm

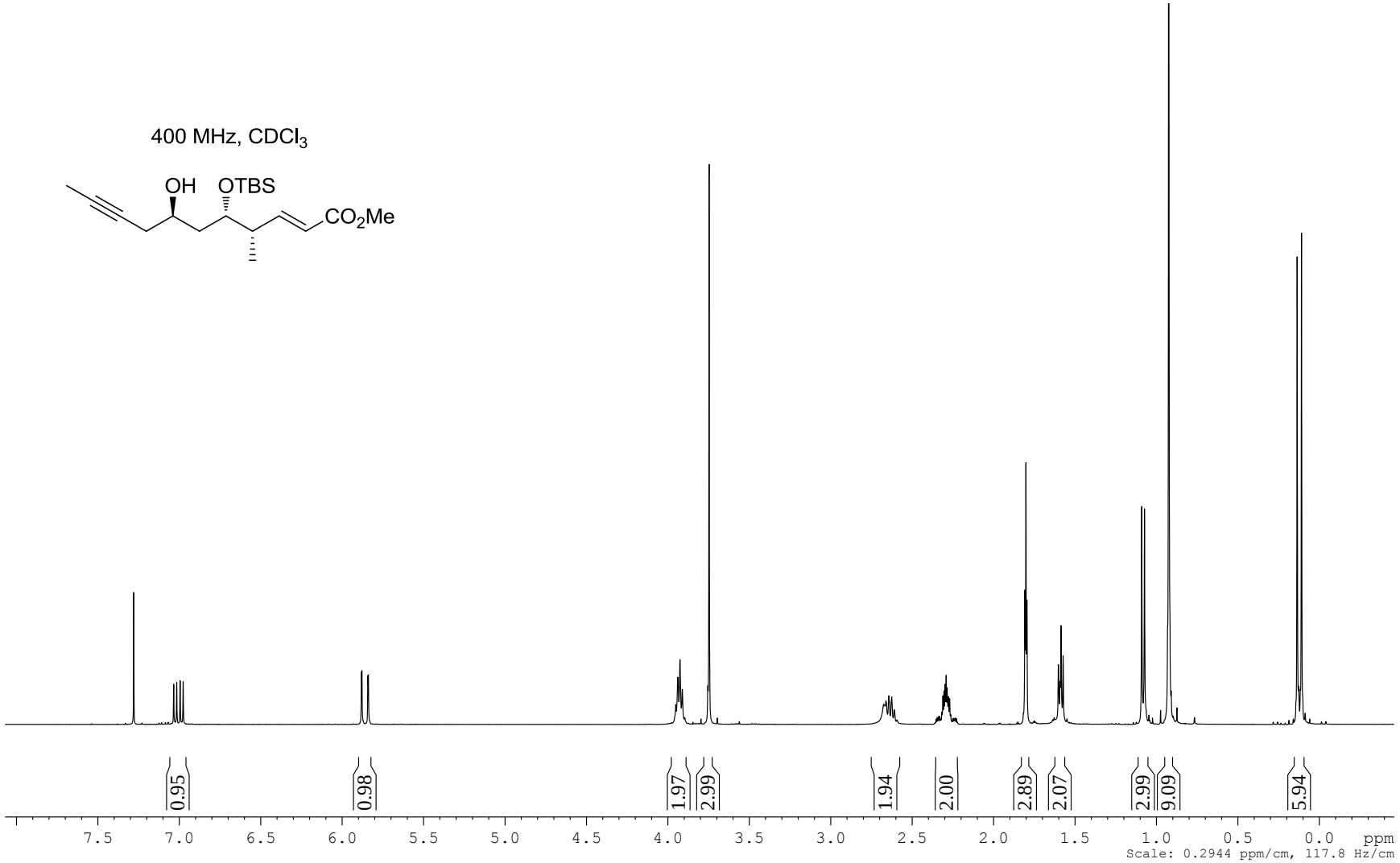

139.848
115.015
73.857
68.413
50.425
42.814
36.641
25.881
18.043
16.055
-4.430
-4.505
100 MHz, CDCl3
OH
OTBS
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.432 ppm/cm, 747.8 Hz/cm

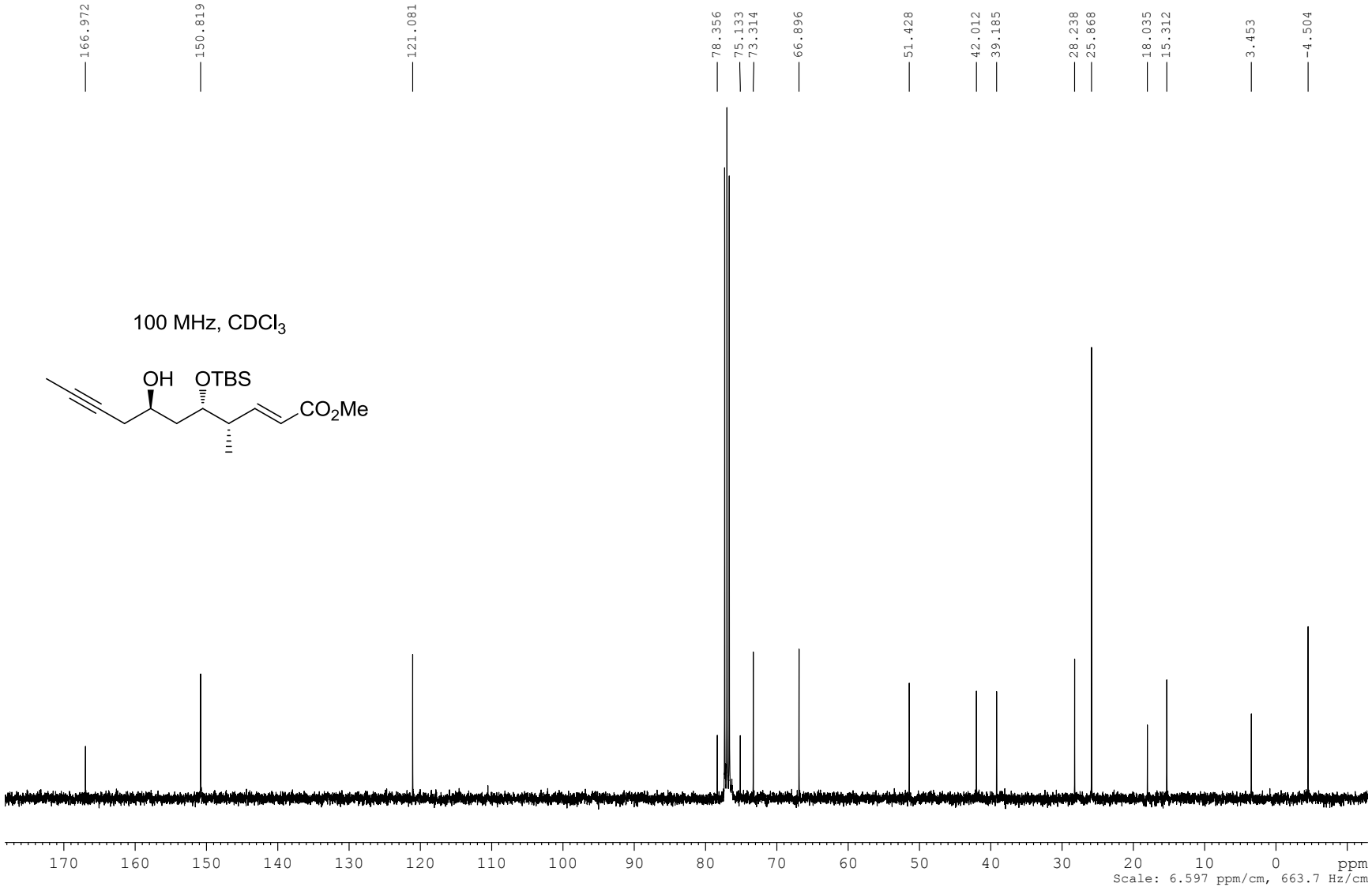

400 MHz, C6D6
OTBS
O
1.00
2.06
0.99
1.00
1.04
1.02
1.01
1.04
1.10
9.47
3.07
5.99
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 88.34 Hz/cm

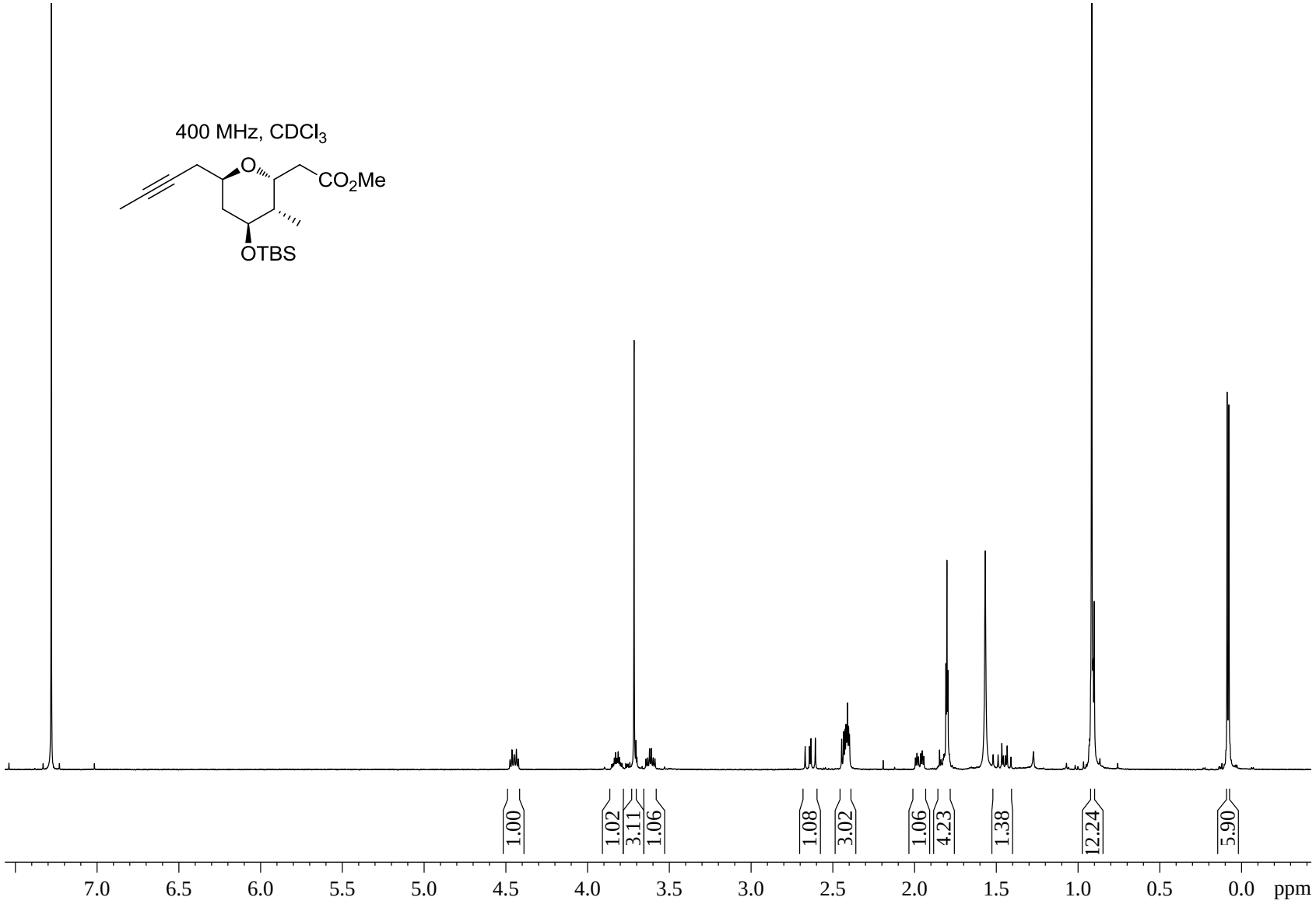

140.748
114.586
74.056
49.392
47.373
43.654
37.098
26.089
18.296
14.849
-4.260
-4.476
100 MHz, C6D6
OTBS
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 6.207 ppm/cm, 468.4 Hz/cm

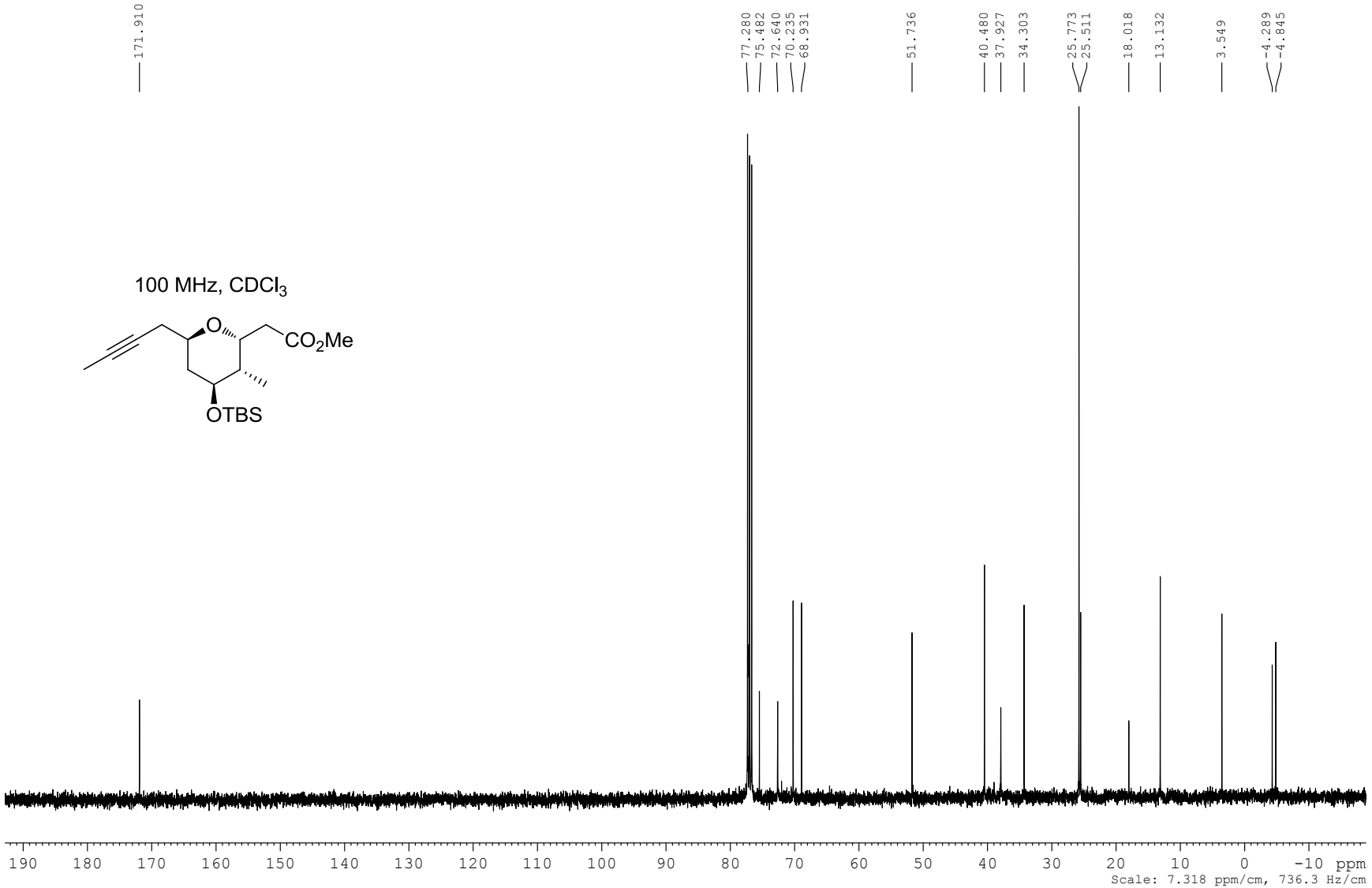

400 MHz, CDCl3
OTBS
O
CO2Me
1.00
1.01
1.05
3.16
1.06
1.04
1.08
1.03
1.11
1.05
3.04
9.71
6.11
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

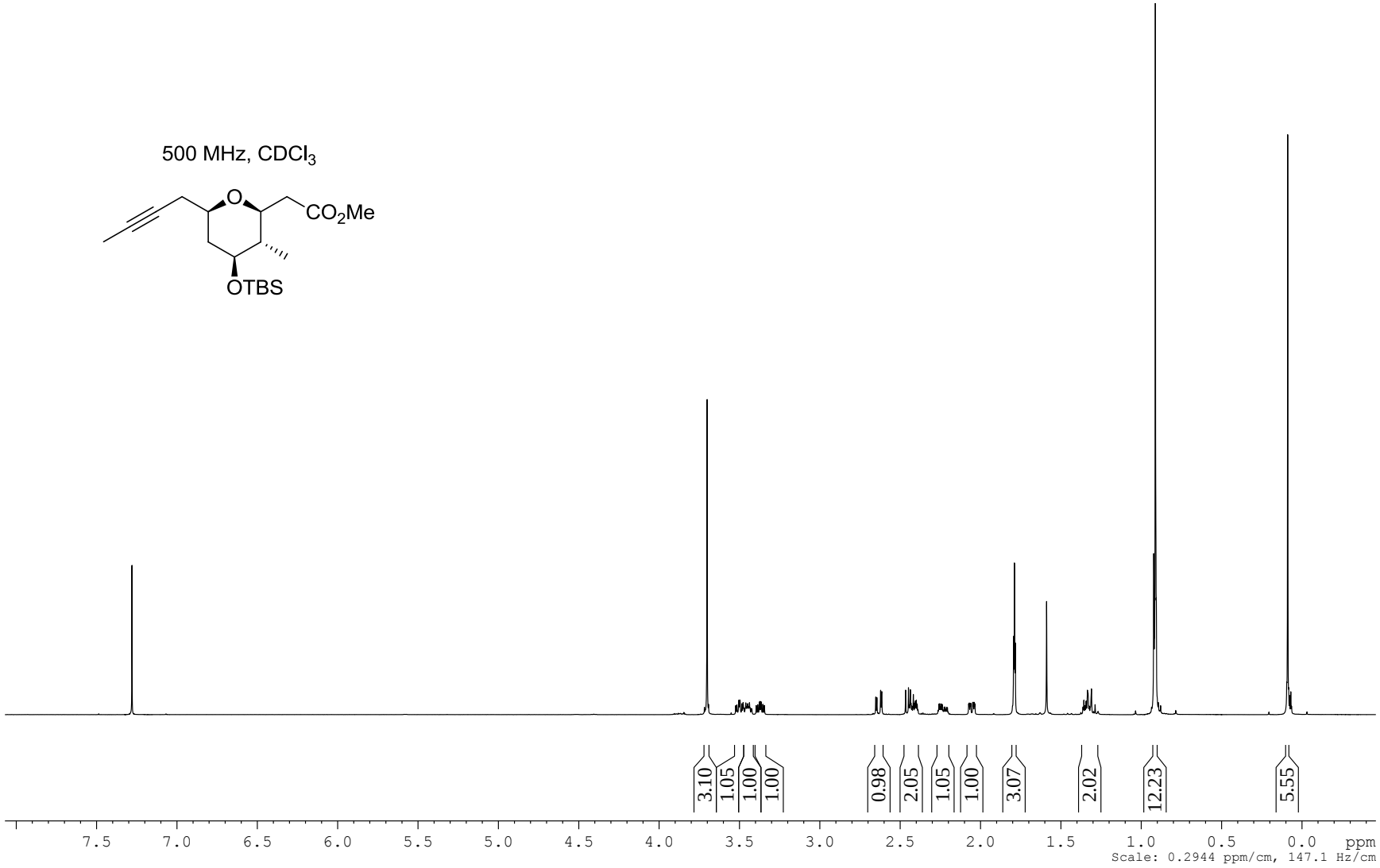

166.967
150.976
121.011
73.093
51.438
49.670
47.827
42.351
36.840
25.817
18.049
14.182
-4.424
-4.682
100 MHz, CDCl3
OTBS
O
CO2Me
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm
Scale: 6.866 ppm/cm, 690.8 Hz/cm

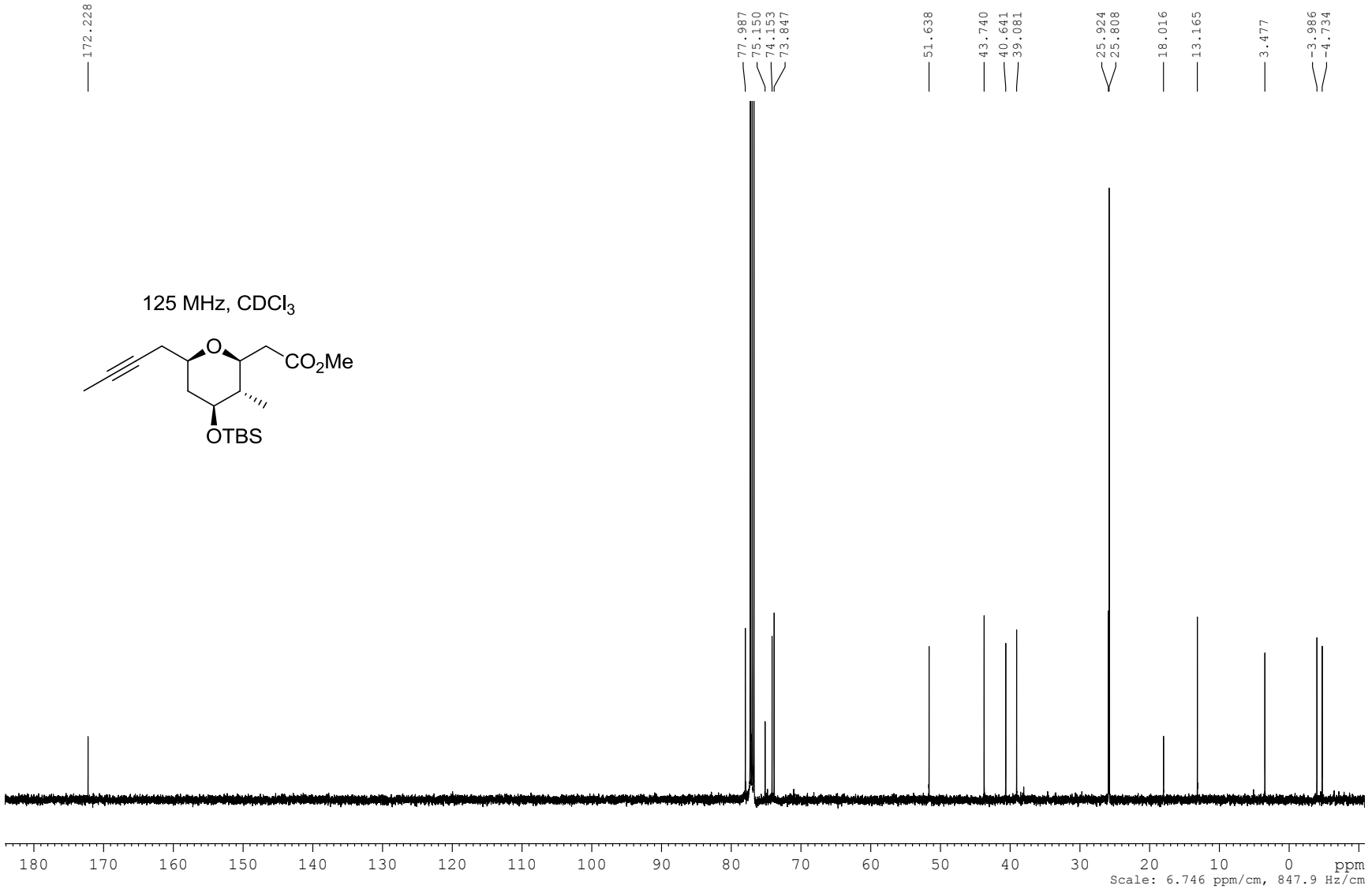

400 MHz, CDCl3
OH
OTBS
CO2Me
0.95
0.98
1.97
2.99
1.94
2.00
2.89
2.07
2.99
9.09
5.94
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

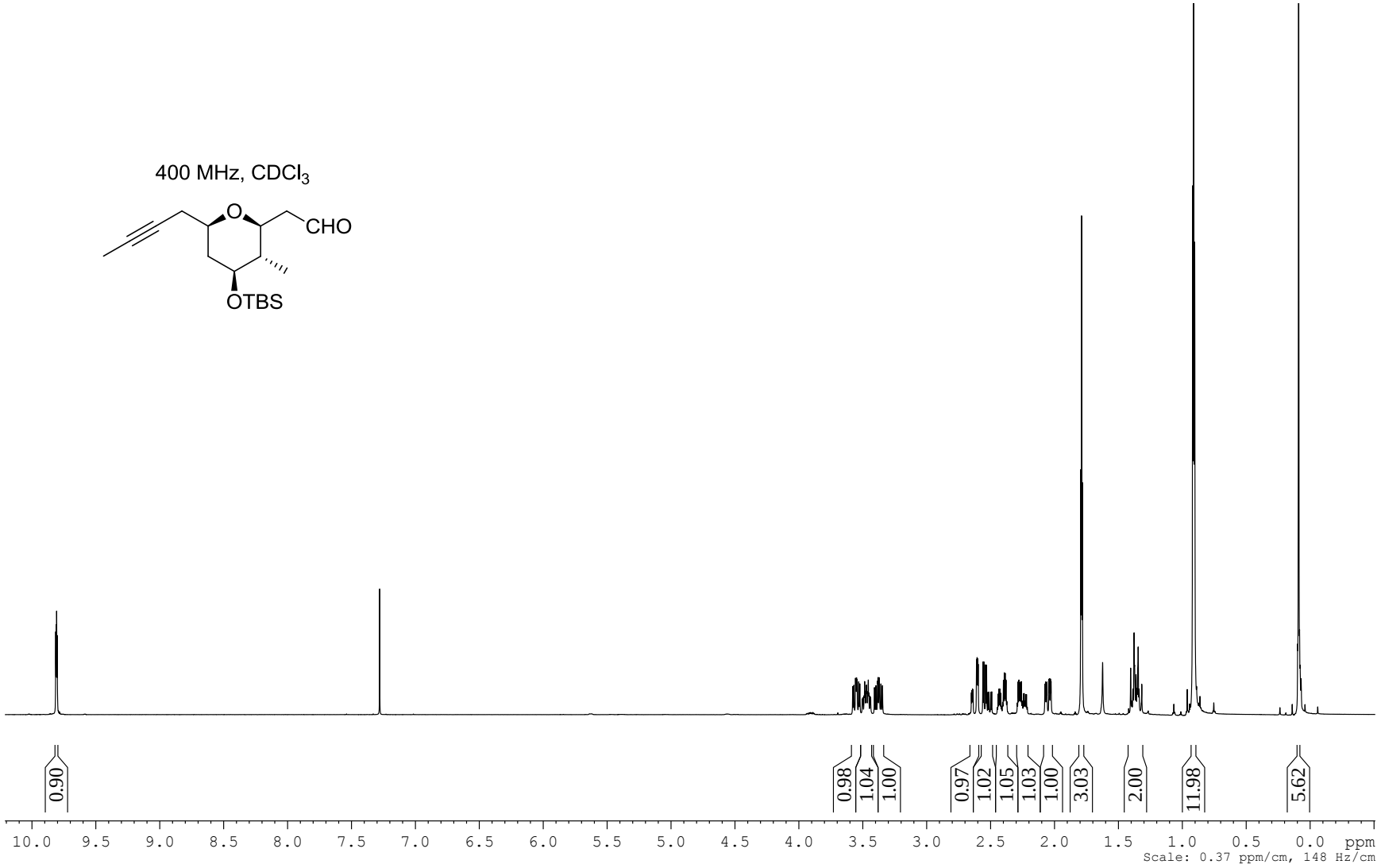

166.972
150.819
121.081
78.356
75.133
73.314
66.896
51.428
42.012
39.185
28.238
25.868
18.035
15.312
3.453
-4.504
100 MHz, CDCl3
OH
OTBS
CO2Me
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 6.597 ppm/cm, 663.7 Hz/cm

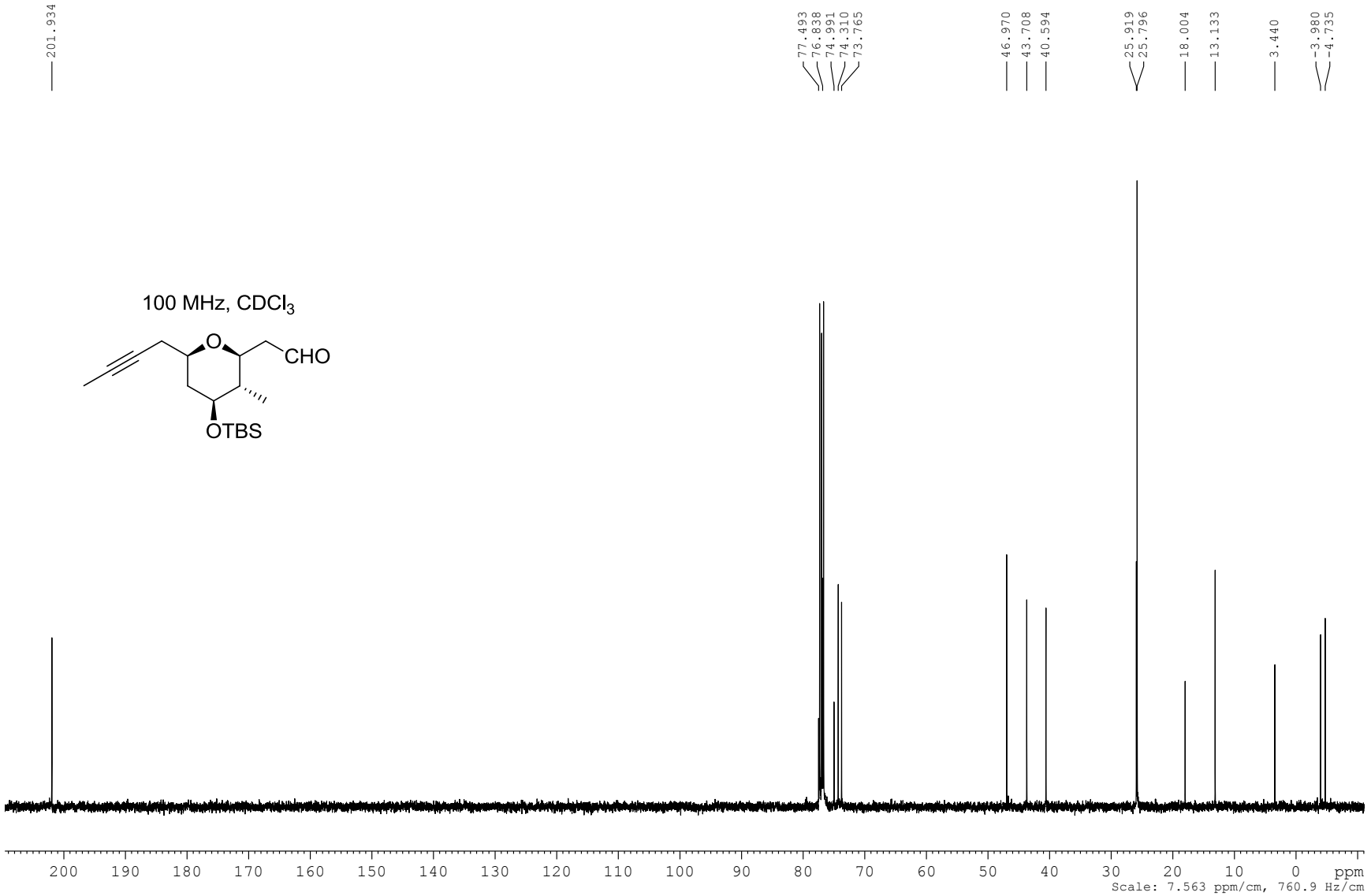

400 MHz, CDCl3
O
CO2Me
OTBS
1.00
1.02
3.11
1.06
1.08
3.02
1.06
4.23
1.38
12.24
5.90
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

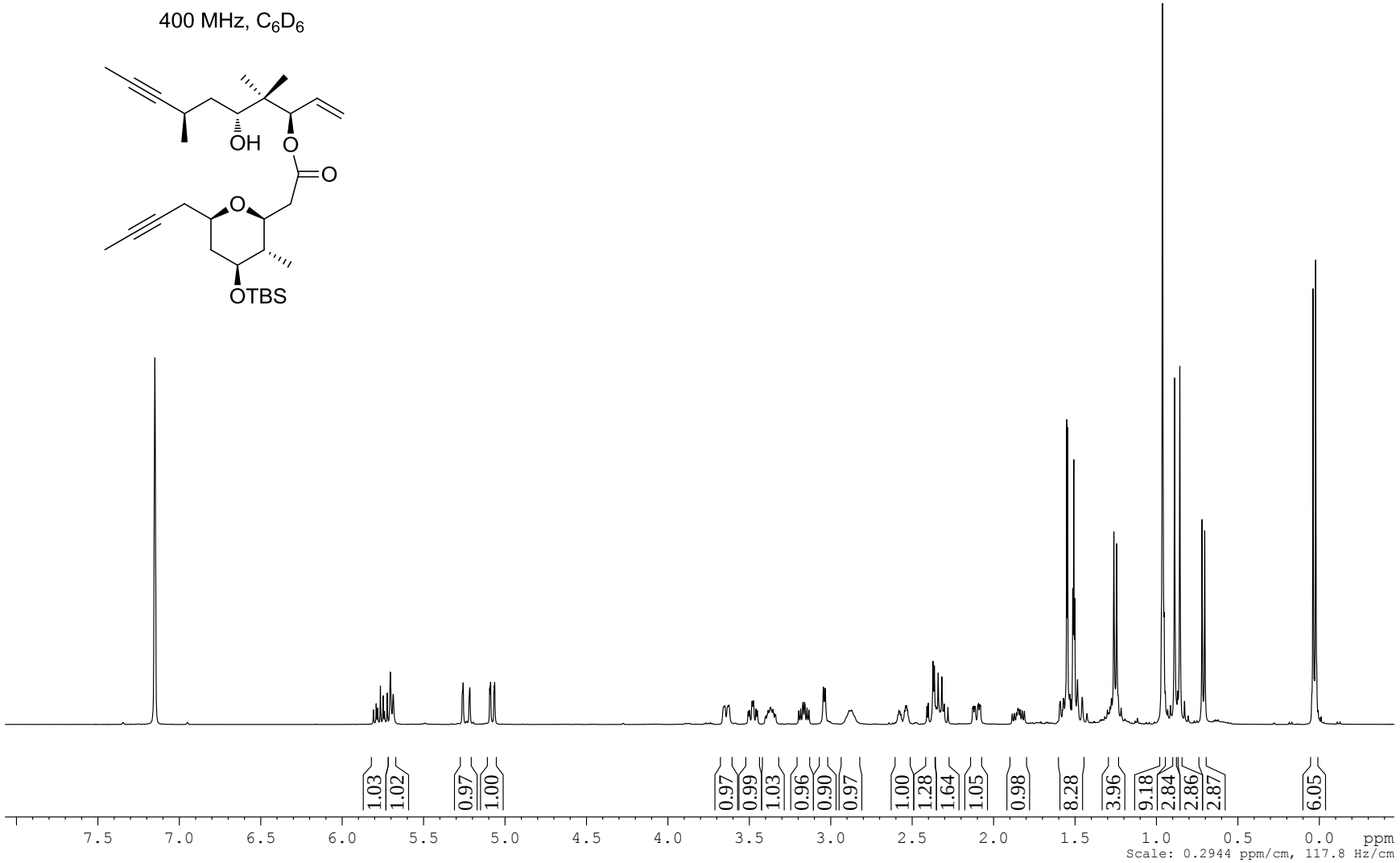

171.910
77.280
75.482
72.640
70.235
68.931
51.736
40.480
37.927
34.303
25.773
25.511
18.018
13.132
3.549
-4.289
-4.845
100 MHz, CDCl3
O
CO2Me
OTBS
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm
Scale: 7.318 ppm/cm, 736.3 Hz/cm

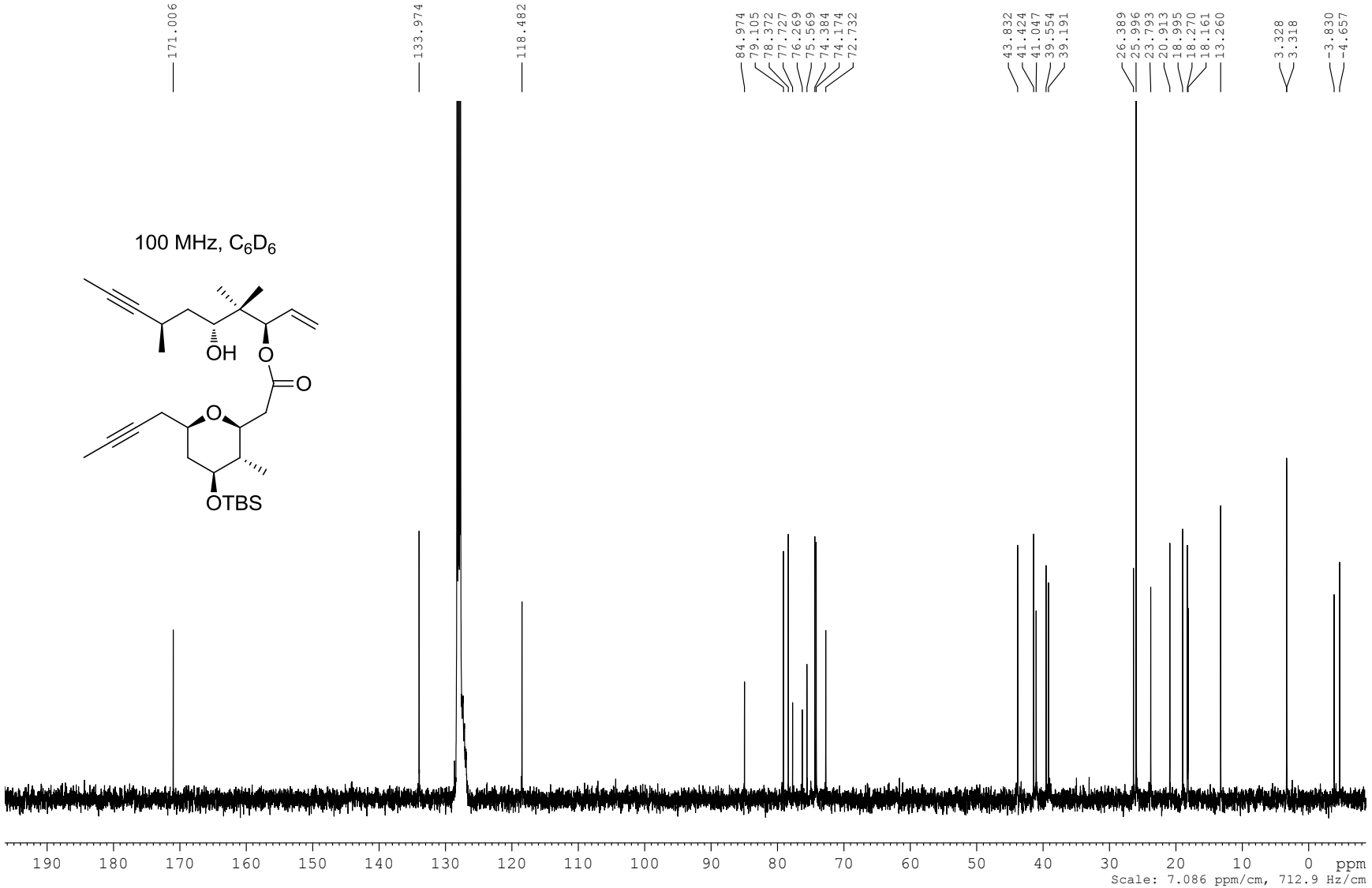

500 MHz, CDCl3
O
CO2Me
OTBS
3.10
1.05
1.00
1.00
0.98
2.05
1.05
1.00
3.07
2.02
12.23
5.55
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 147.1 Hz/cm

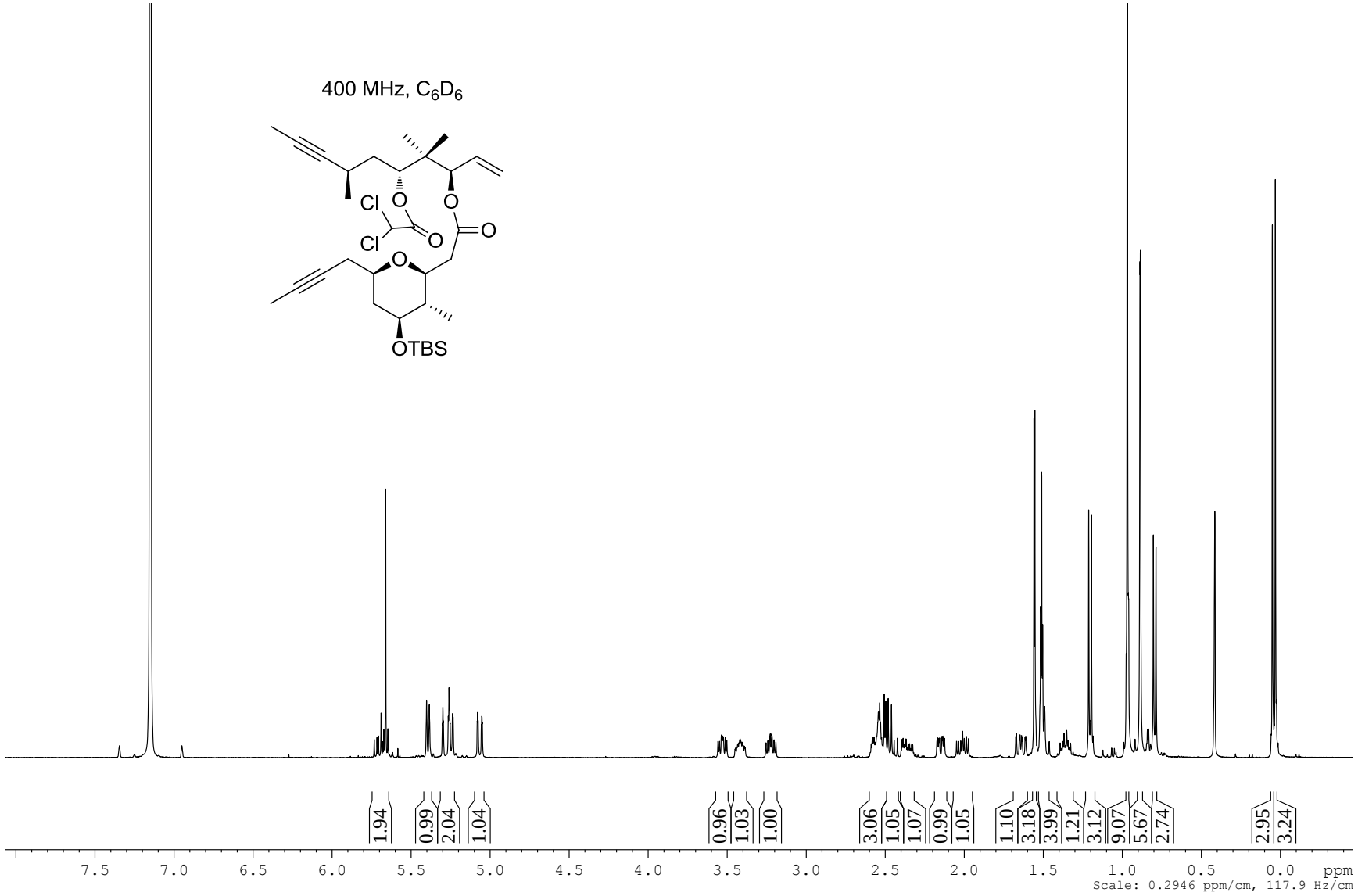

172.228
77.987
75.150
74.153
73.847
51.638
43.740
40.641
39.081
25.924
25.808
18.016
13.165
3.477
-3.986
-4.734
125 MHz, CDCl3
O
CO2Me
OTBS
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 6.746 ppm/cm, 847.9 Hz/cm

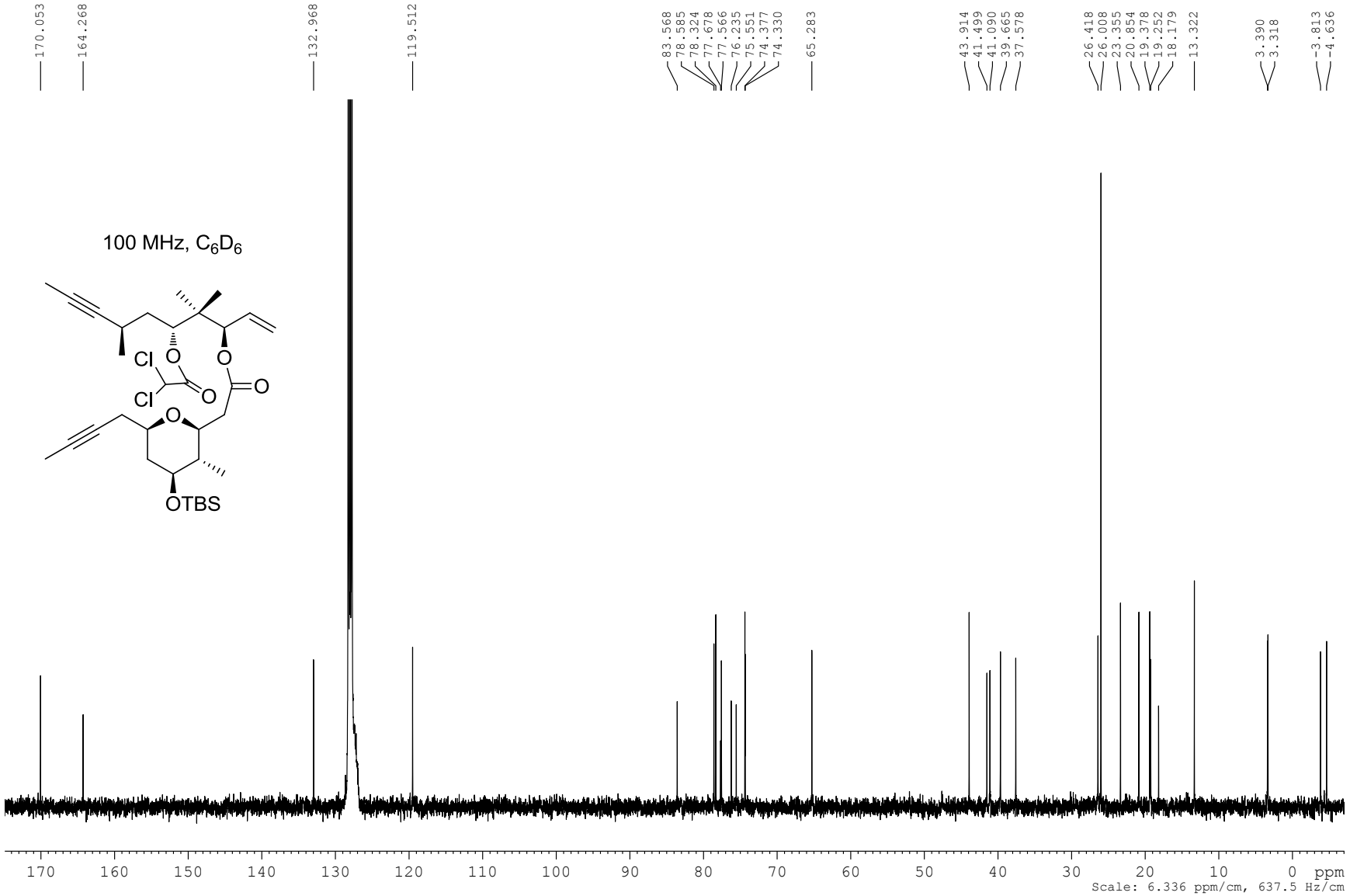

400 MHz, CDCl3
O
CHO
OTBS
0.90
0.98
1.04
1.00
0.97
1.02
1.05
1.03
1.00
3.03
2.00
11.98
5.62
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
Scale: 0.37 ppm/cm, 148 Hz/cm

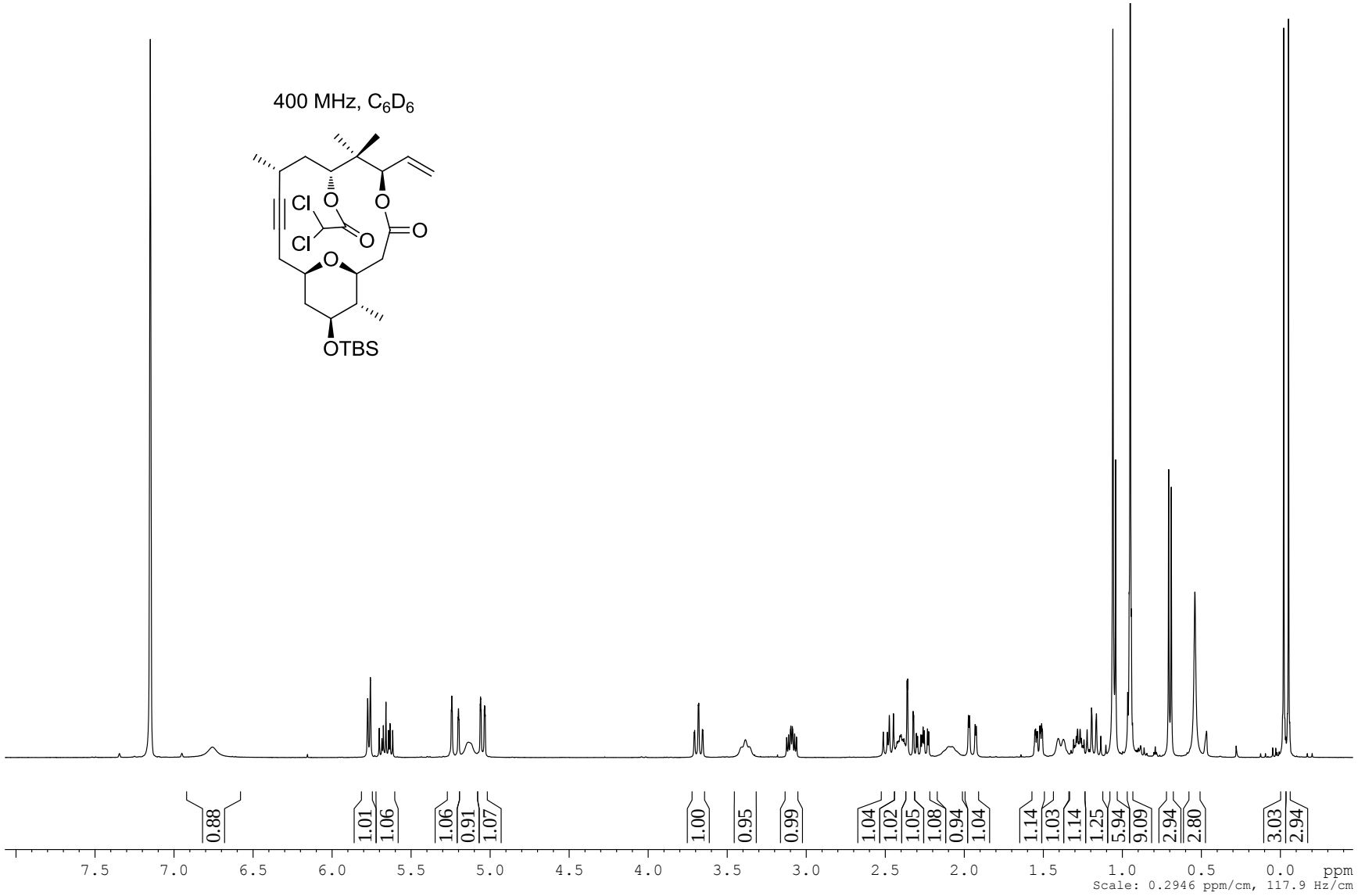

201.934
77.493
76.838
74.991
74.310
73.765
46.970
43.708
40.594
25.919
25.796
18.004
13.133
3.440
-3.980
-4.735
100 MHz, CDCl3
O
CHO
OTBS
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.563 ppm/cm, 760.9 Hz/cm

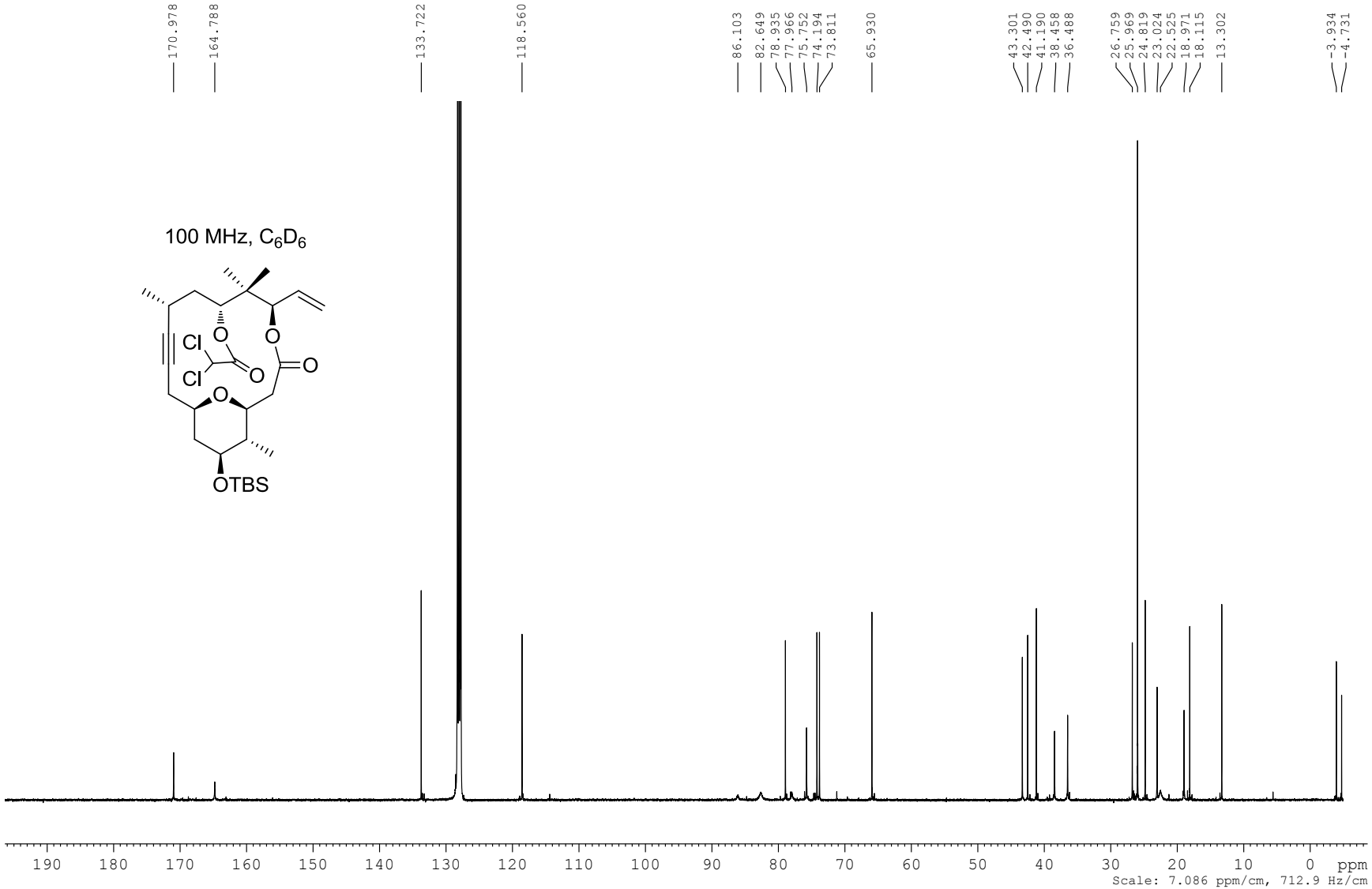

400 MHz, C6D6
OH
O
O
O
OTBS
1.03
1.02
0.97
1.00
0.97
0.99
1.03
0.96
0.90
0.97
1.00
1.28
1.64
1.05
0.98
8.28
3.96
9.18
2.84
2.86
2.87
6.05
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2944 ppm/cm, 117.8 Hz/cm

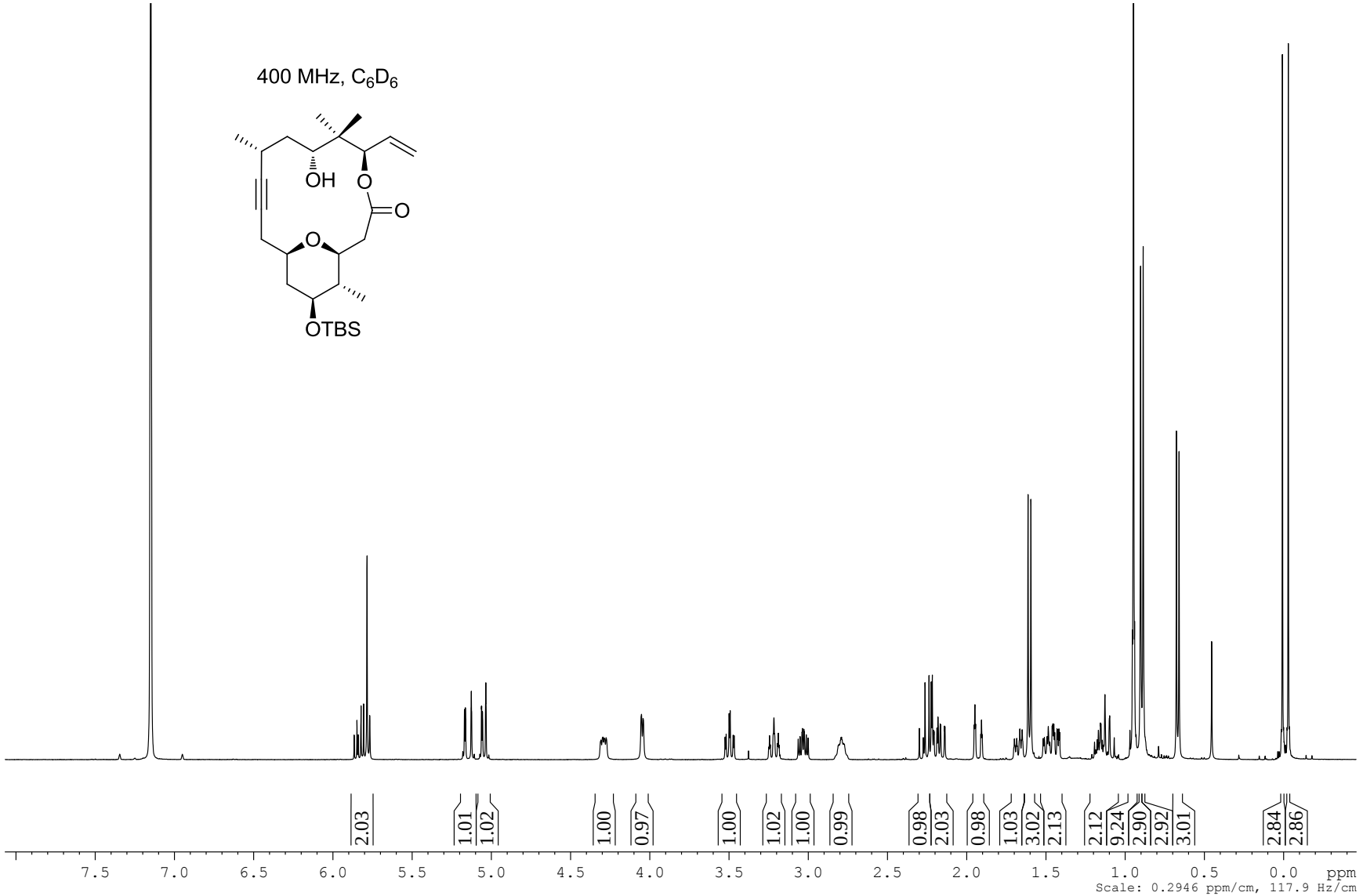

171.006
133.974
118.482
84.974
79.105
78.372
77.727
76.269
75.569
74.384
74.174
72.732
43.832
41.424
41.047
39.554
39.191
26.389
25.996
23.793
20.913
18.995
18.270
18.161
13.260
3.328
3.318
-3.830
-4.657
100 MHz, C6D6
OH
O
O
O
OTBS
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

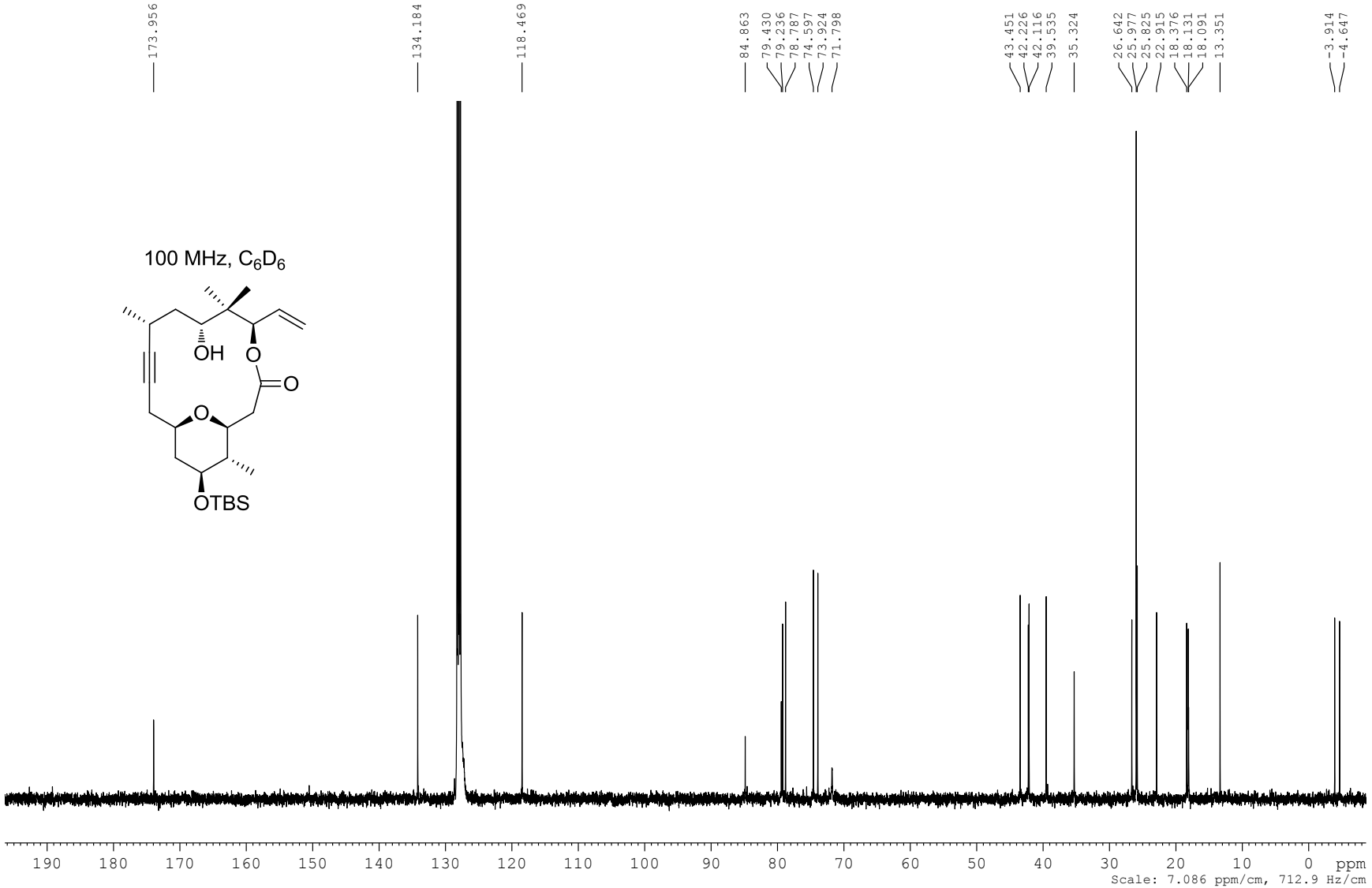

400 MHz, C6D6
Cl
Cl
O
O
O
O
O
OTBS
1.94
0.99
2.04
1.04
0.96
1.03
1.00
3.06
1.05
1.07
0.99
1.05
1.10
3.18
3.99
1.21
3.12
9.07
5.67
2.74
2.95
3.24
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

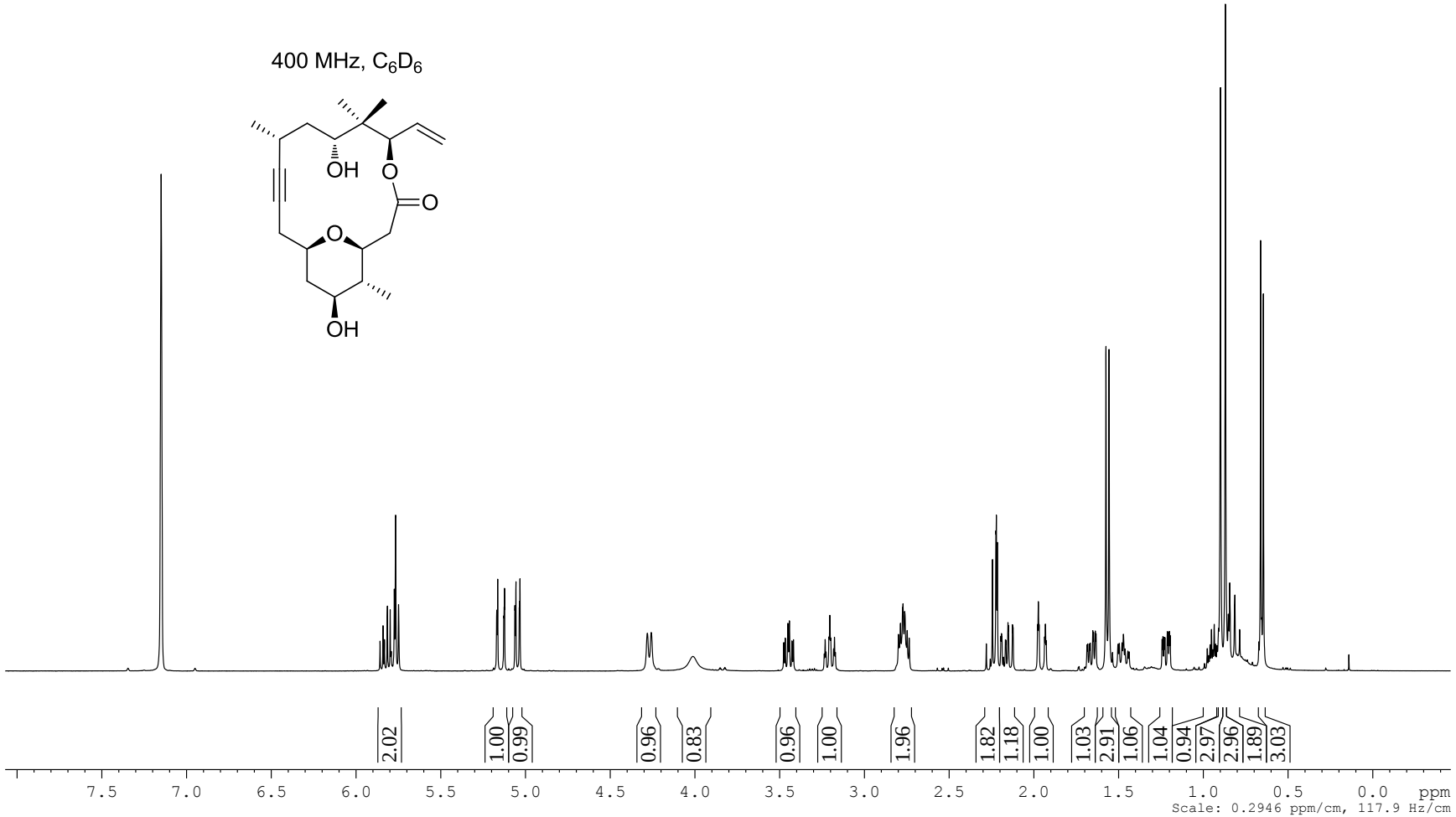

170.053
164.268
132.968
119.512
83.568
78.585
78.324
77.678
77.566
76.235
75.551
74.377
74.330
65.283
43.914
41.499
41.090
39.665
37.578
26.418
26.008
23.355
20.854
19.378
19.252
18.179
13.322
3.390
3.318
-3.813
-4.636
100 MHz, C6D6
Cl
Cl
O
O
O
O
O
O
OTBS
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 6.336 ppm/cm, 637.5 Hz/cm

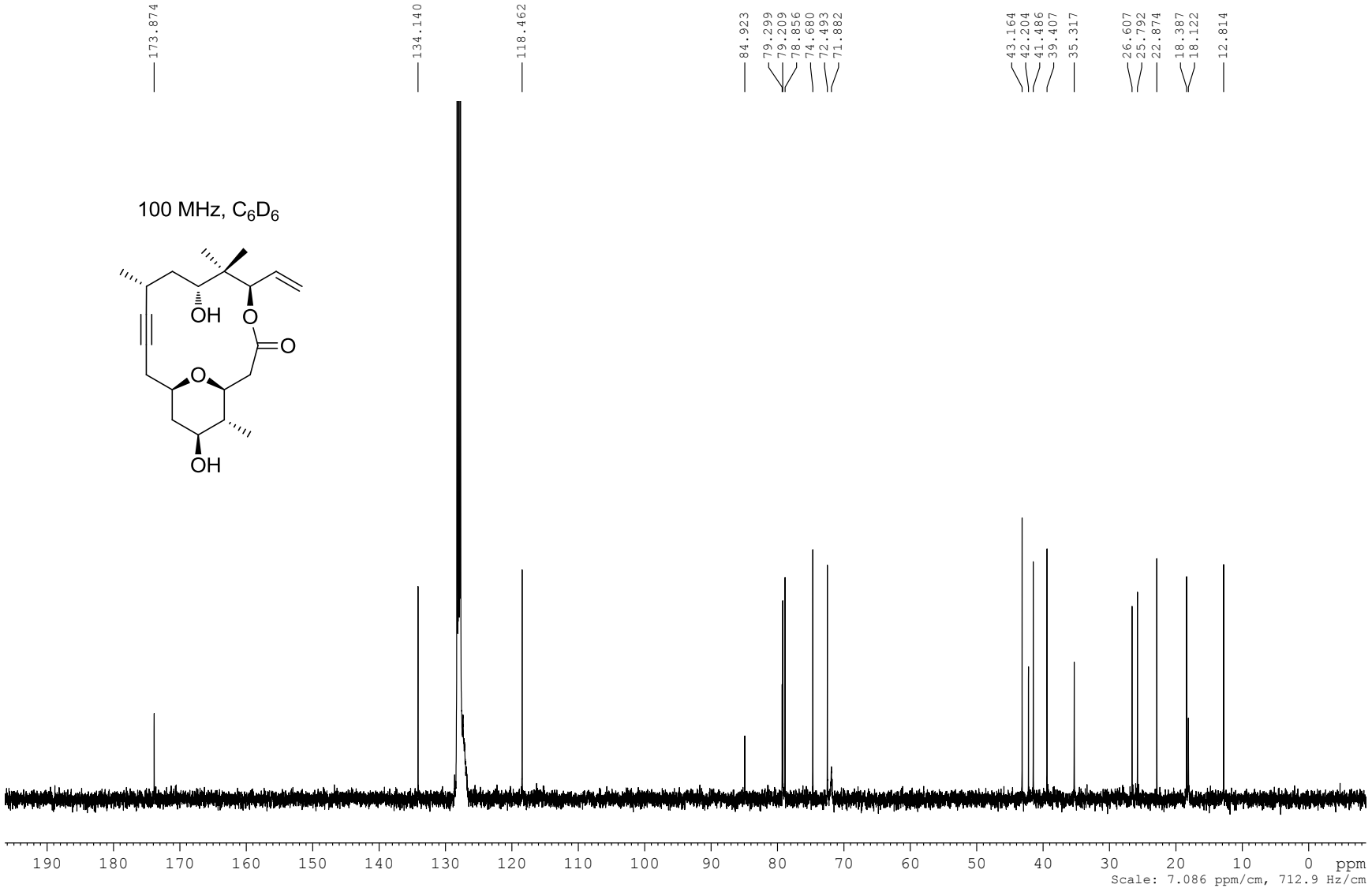

400 MHz, C6D6
Cl
Cl
O
O
O
O
O
O
OTBS
0.88
1.01
1.06
1.06
0.91
1.07
1.00
0.95
0.99
1.04
1.02
1.05
1.08
0.94
1.04
1.14
1.03
1.14
1.25
5.94
9.09
2.94
2.80
3.03
2.94
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

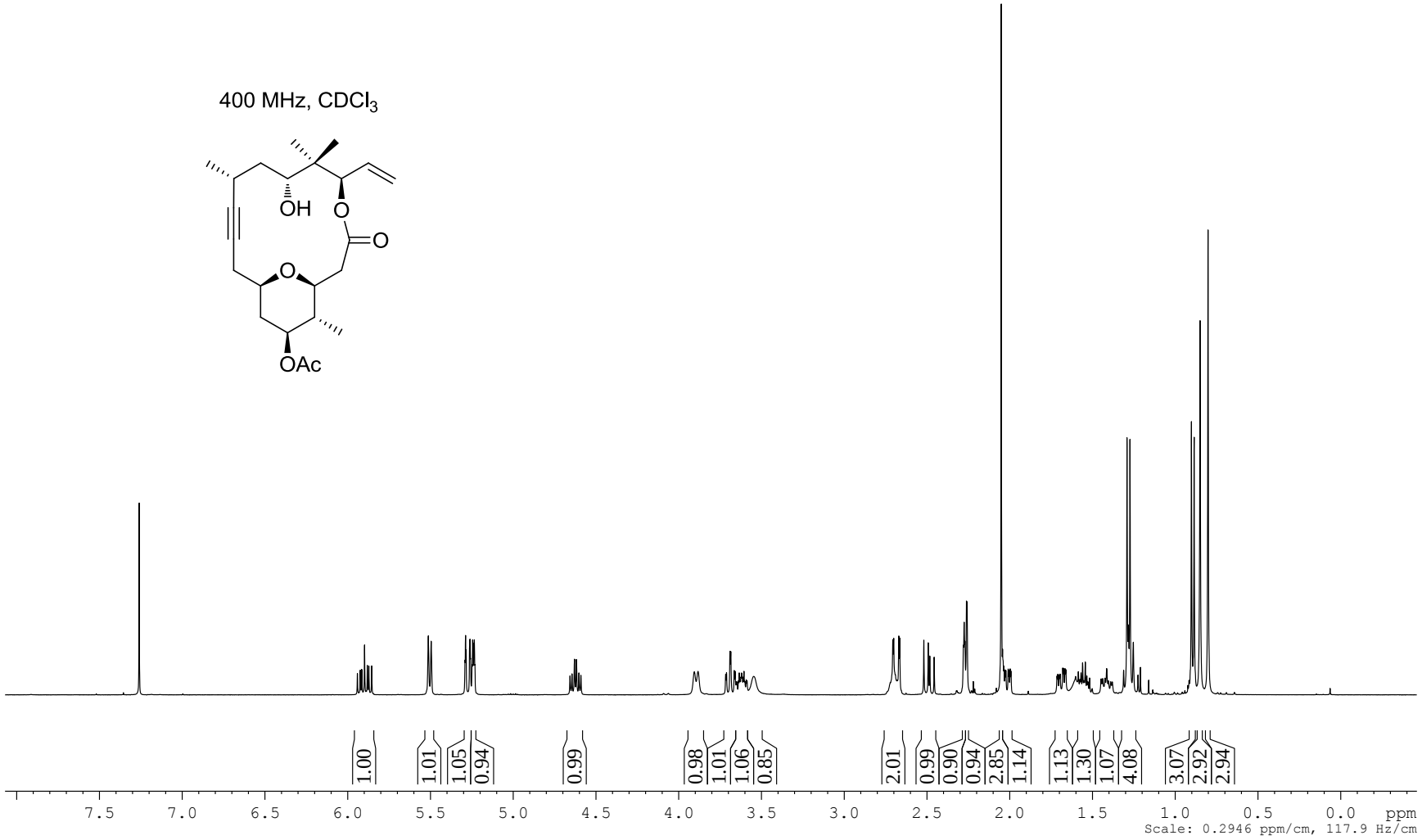

170.978
164.788
133.722
118.560
86.103
82.649
78.935
77.966
75.752
74.194
73.811
65.930
43.301
42.490
41.190
38.458
36.488
26.759
25.969
24.819
23.024
22.525
18.971
18.115
13.302
-3.934
-4.731
100 MHz, C6D6
Cl
Cl
O
O
O
O
O
OTBS
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

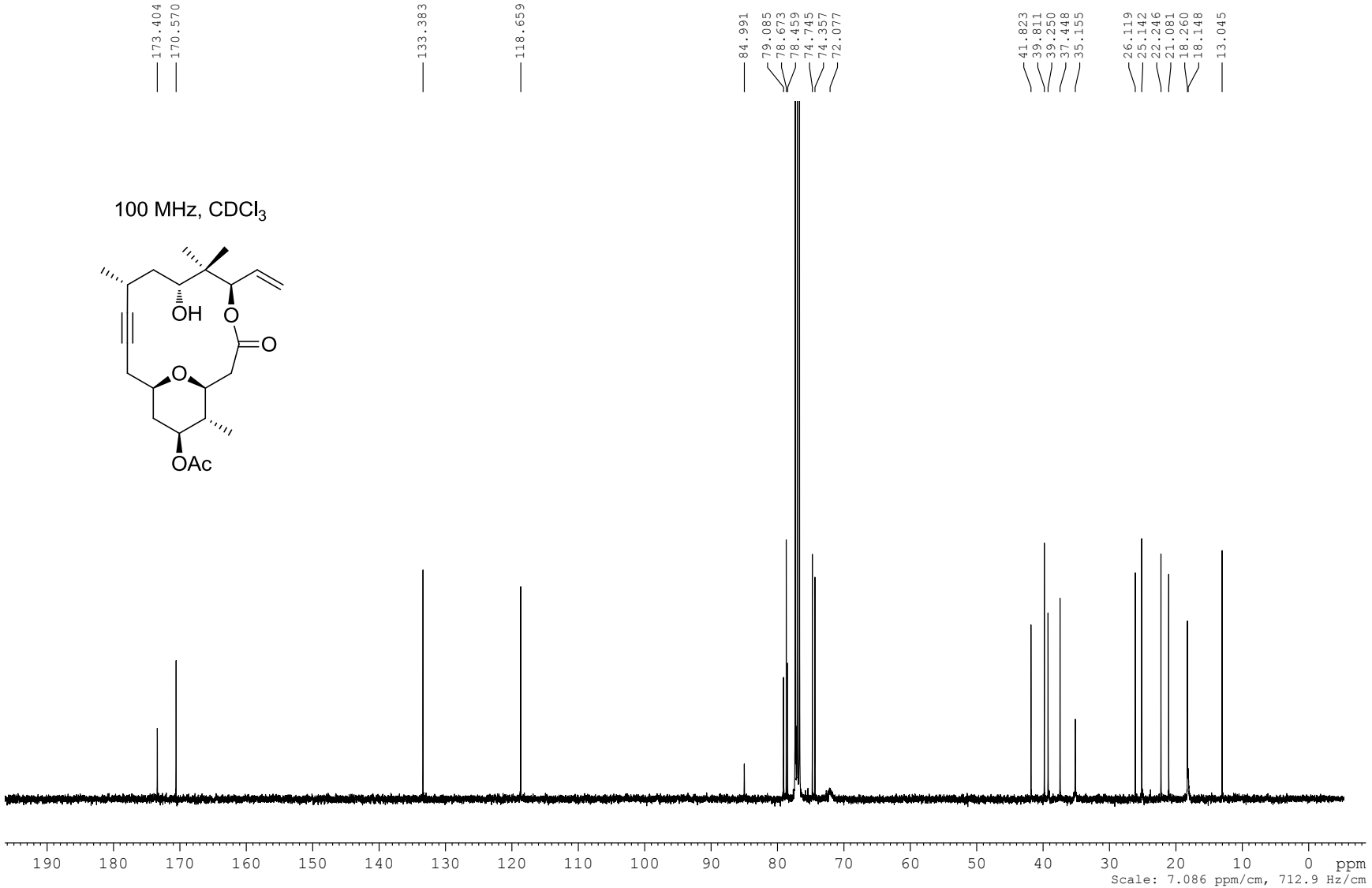

400 MHz, C6D6
OH
O
O
O
OTBS
2.03
1.01
1.02
1.00
0.97
1.00
1.02
1.00
0.99
0.98
2.03
0.98
1.03
3.02
2.13
2.12
9.24
2.90
2.92
3.01
2.84
2.86
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

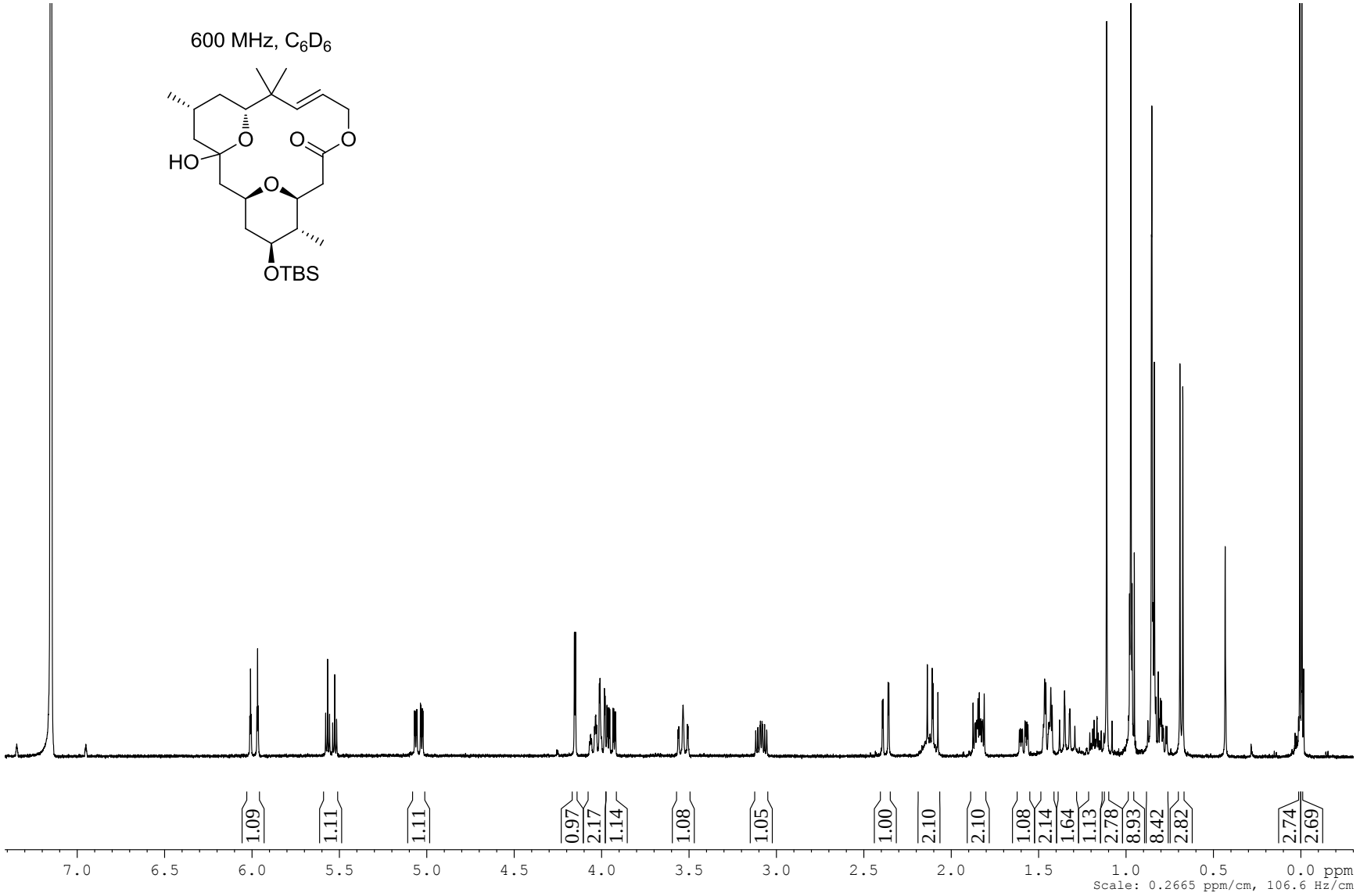

173.956
134.184
118.469
84.863
79.430
79.236
78.787
74.597
73.924
71.798
43.451
42.226
42.116
39.535
35.324
26.642
25.977
25.825
22.915
18.376
18.131
18.091
13.351
-3.914
-4.647
100 MHz, C6D6
OH
O
O
O
OTBS
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

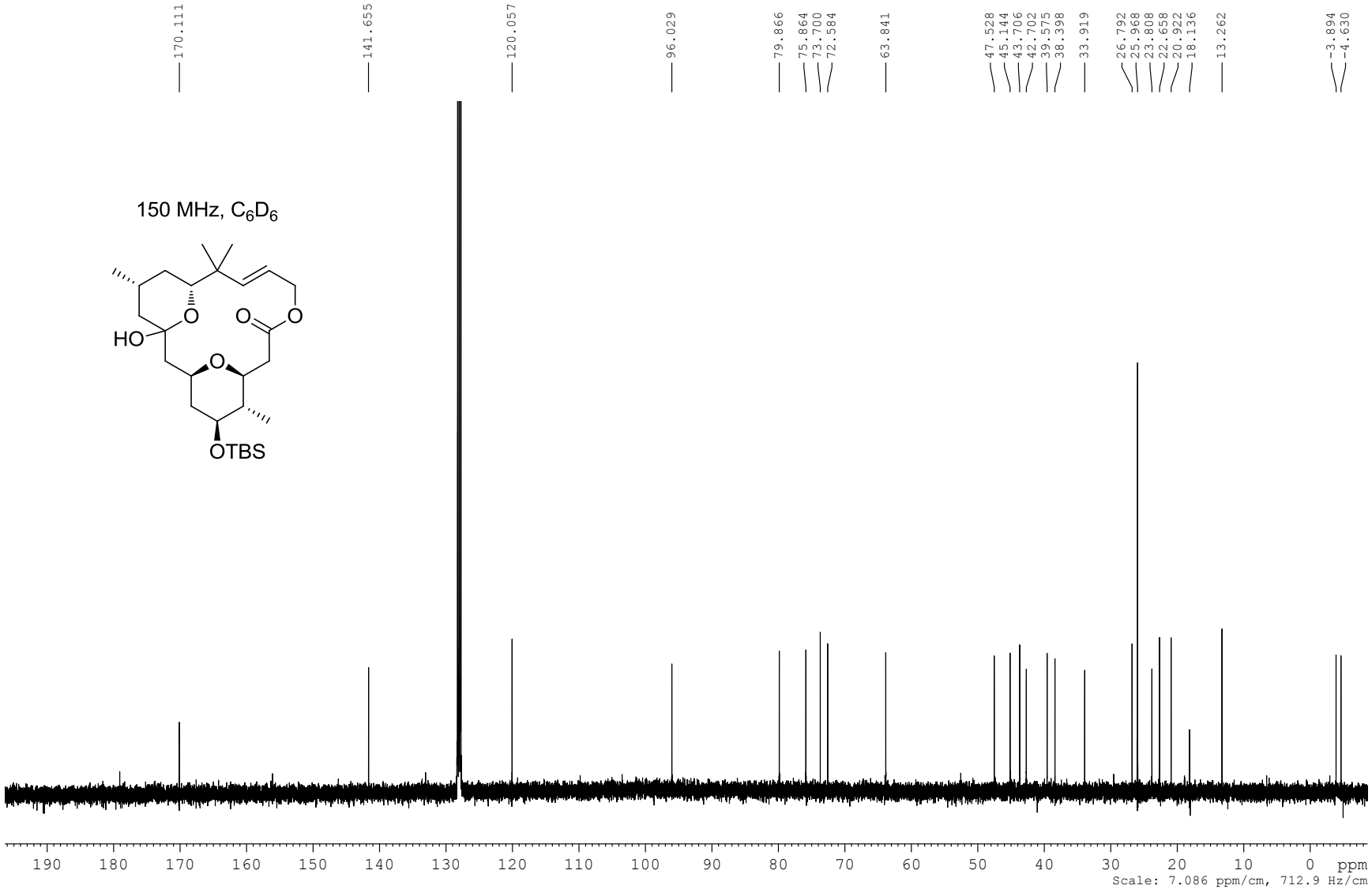

400 MHz, C6D6
OH
O
O
O
OH
2.02
1.00
0.99
0.96
0.83
0.96
1.00
1.96
1.82
1.18
1.00
1.03
2.91
1.06
1.04
0.94
2.97
2.96
1.89
3.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

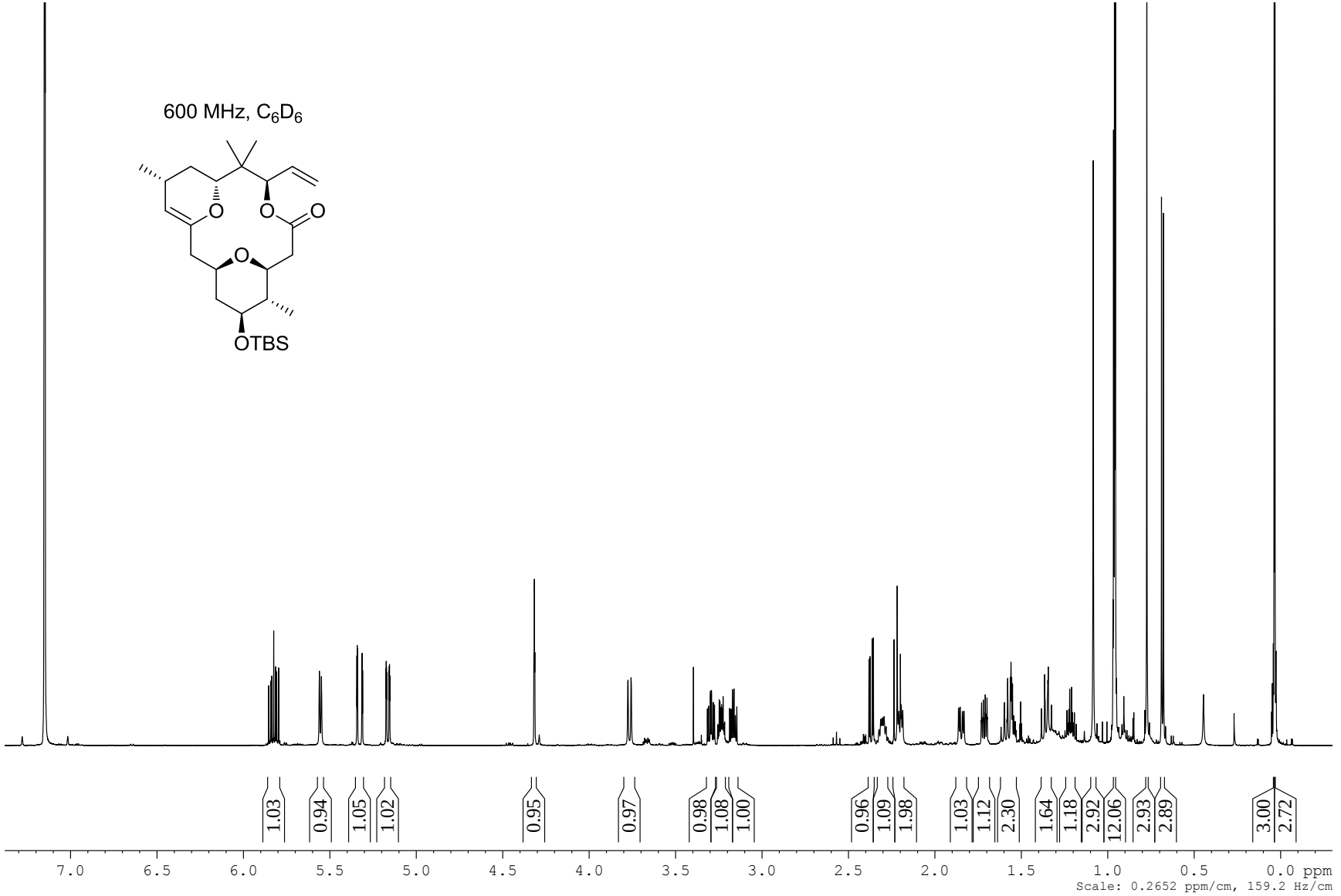

173.874
134.140
118.462
84.923
79.299
79.209
78.856
74.680
72.493
71.882
43.164
42.204
41.486
39.407
35.317
26.607
25.792
22.874
18.387
18.122
12.814
100 MHz, C6D6
OH
O
O
O
OH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

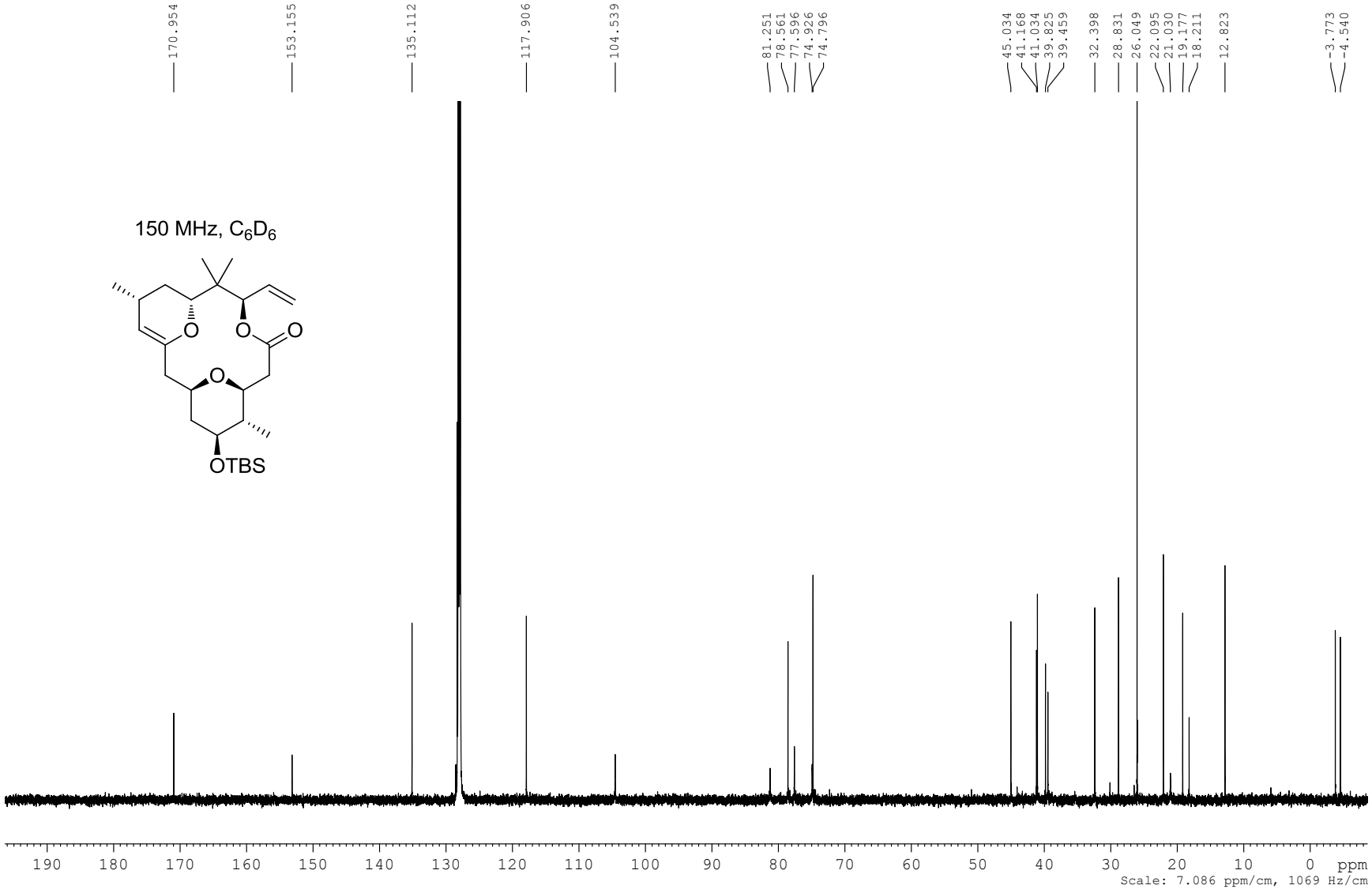

400 MHz, CDCl3
OH
O
O
O
O
OAc
1.00
1.01
1.05
0.94
0.99
0.98
1.01
1.06
0.85
2.01
0.99
0.90
0.94
2.85
1.14
1.13
1.30
1.07
4.08
3.07
2.92
2.94
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Scale: 0.2946 ppm/cm, 117.9 Hz/cm

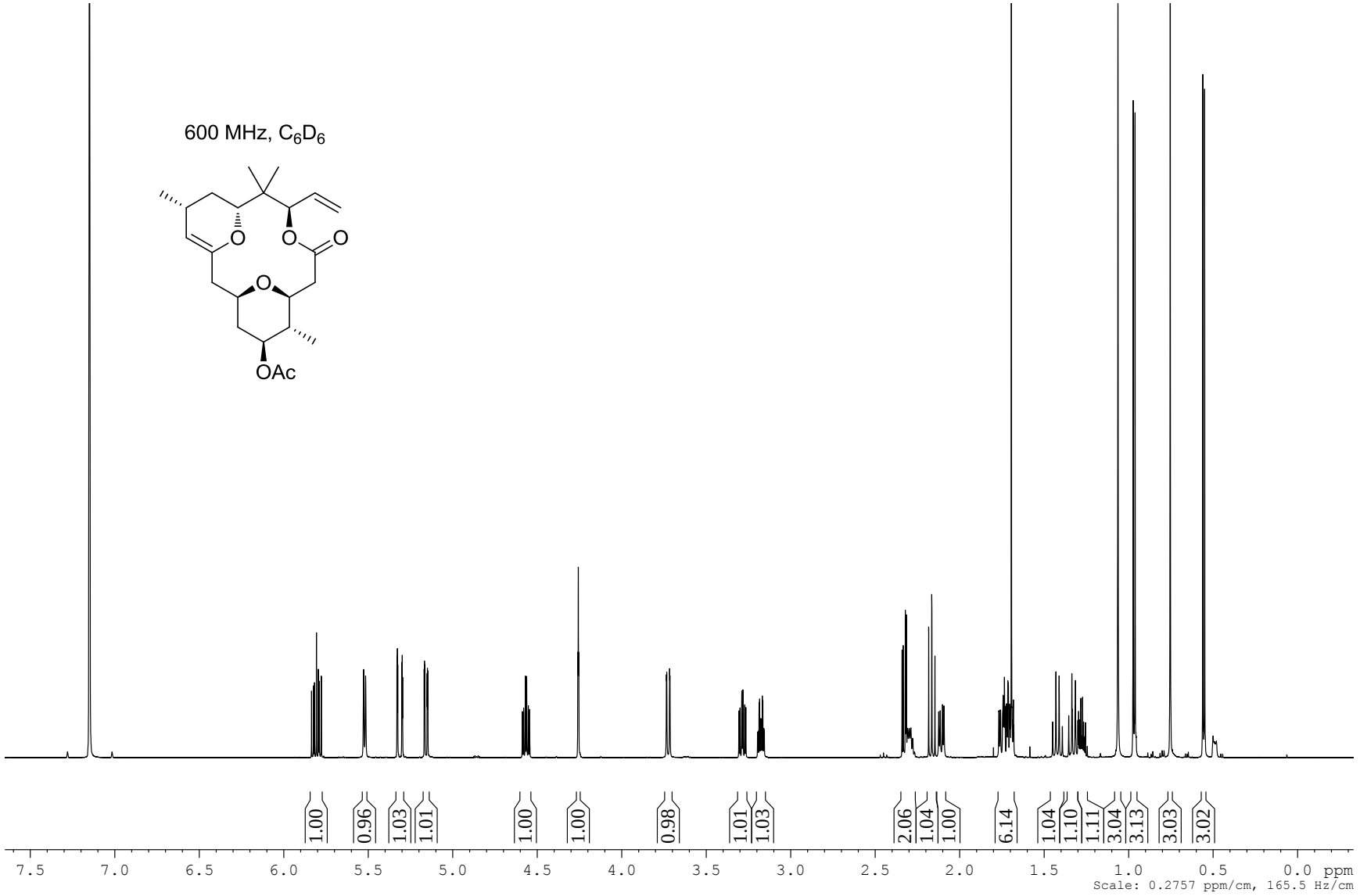

173.404
170.570
133.383
118.659
84.991
79.085
78.673
78.459
74.745
74.357
72.077
41.823
39.811
39.250
37.448
35.155
26.119
25.142
22.246
21.081
18.260
18.148
13.045
100 MHz, CDCl3
OH
O
O
O
O
OAc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm

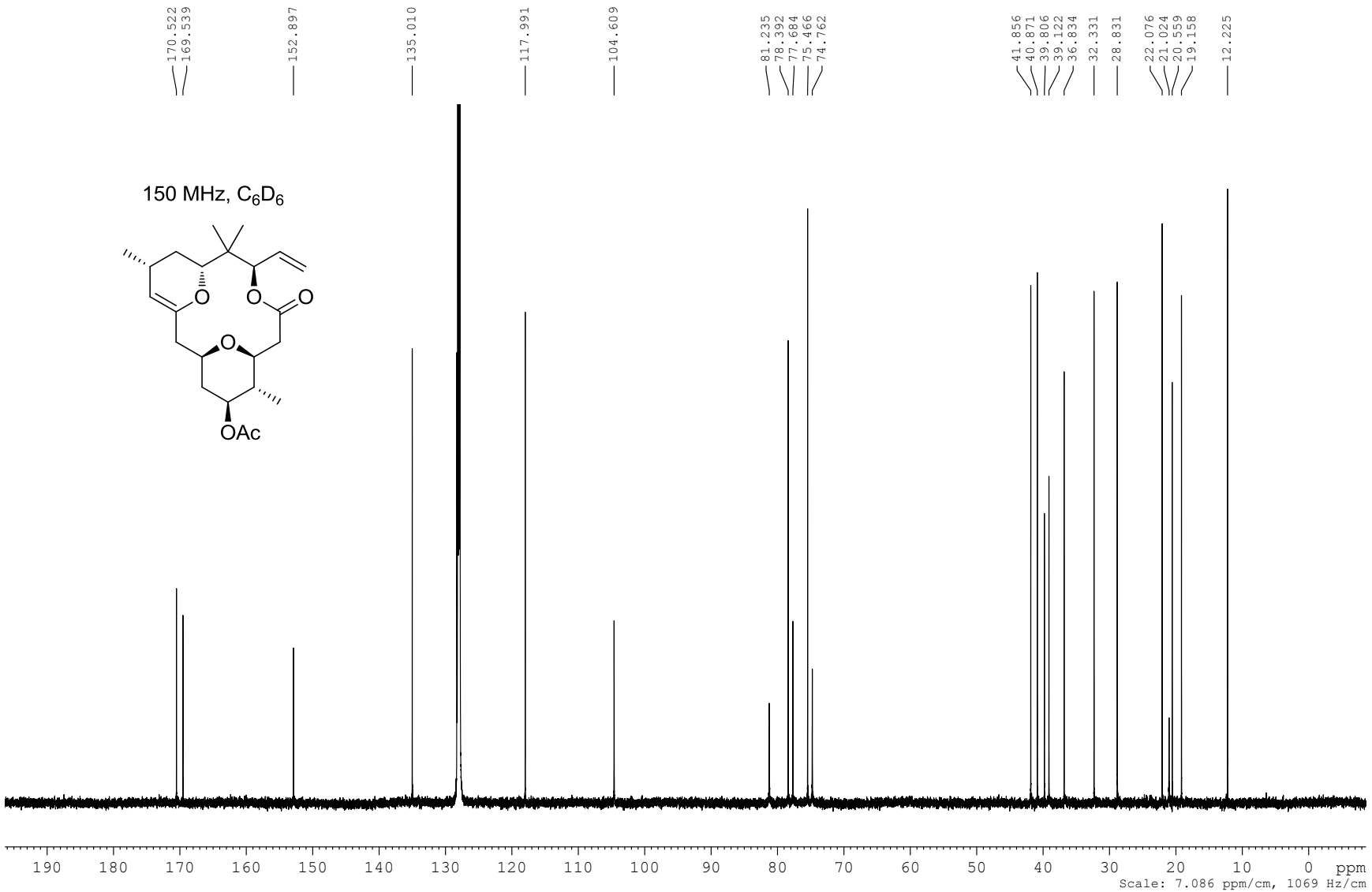

600 MHz, C6D6
HO
O
O
O
O
O
OTBS
1.09
1.11
1.11
0.97
2.17
1.14
1.08
1.05
1.00
2.10
2.10
1.08
2.14
1.64
1.13
2.78
8.93
8.42
2.82
2.74
2.69
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
Scale: 0.2665 ppm/cm, 106.6 Hz/cm


170.111
141.655
120.057
96.029
79.866
75.864
73.700
72.584
63.841
47.528
45.144
43.706
42.702
39.575
38.398
33.919
26.792
25.968
23.808
22.658
20.922
18.136
13.262
-3.894
-4.630
150 MHz, C6D6
HO
O
O
O
O
OTBS
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 7.086 ppm/cm, 712.9 Hz/cm


600 MHz, C6D6
OTBS
1.03
0.94
1.05
1.02
0.95
0.97
0.98
1.08
1.00
0.96
1.09
1.98
1.03
1.12
2.30
1.64
1.18
2.92
12.06
2.93
2.89
3.00
2.72
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
Scale: 0.2652 ppm/cm, 159.2 Hz/cm


170.954
153.155
135.112
117.906
104.539
81.251
78.561
77.596
74.926
74.796
45.034
41.168
41.034
39.825
39.459
32.398
28.831
26.049
22.095
21.030
19.177
18.211
12.823
-3.773
-4.540
150 MHz, C6D6
O
O
O
O
OTBS
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 1069 Hz/cm


600 MHz, C6D6
O
O
O
O
OAc
1.00
0.96
1.03
1.01
1.00
1.00
0.98
1.01
1.03
2.06
1.04
1.00
6.14
1.04
1.10
1.11
3.04
3.13
3.03
3.02
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
0.0 ppm
Scale: 0.2757 ppm/cm, 165.5 Hz/cm


170.522
169.539
152.897
135.010
117.991
104.609
81.235
78.392
77.684
75.466
74.762
41.856
40.871
39.806
39.122
36.834
32.331
28.831
22.076
21.024
20.559
19.158
12.225
150 MHz, C6D6
O
O
O
O
OAc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 7.086 ppm/cm, 1069 Hz/cm