Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information

Ring-Closing Metathesis (RCM) Based Synthesis of the Macrolactone Core of Amphidinolactone A

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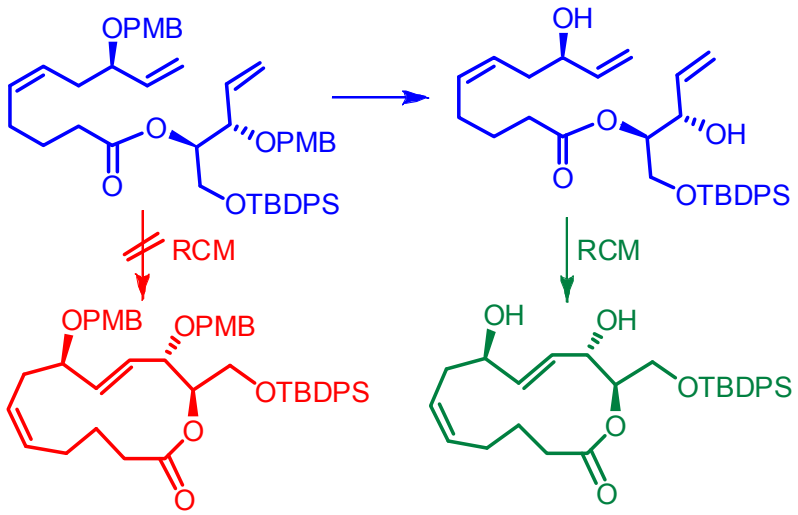
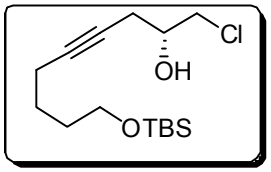


CONTENTS

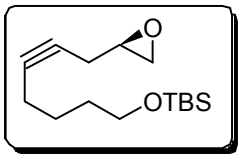
General Experimental Procedures: All reactions were performed under inert atmosphere, if argon mentioned. All glassware apparatus used for reactions are perfectly oven/flame dried. Anhydrous solvents were distilled prior to use: THF, toluene and *t*-butyl methyl ether from Na and benzophenone; CH_2Cl_2, DMSO from CaH_2; MeOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using silica gel (60–120 mesh) unless otherwise mentioned. Analytical thin layer chromatography (TLC) was run on Merck silica gel 60 F254 precoated plates (250 μm thickness).Specific optical rotations $[\alpha]_D$ were measured on a Perkin-Elmer 343 polarimeter and given in 10^{-1} $degcm^2g^{-1}$. Infrared spectra were recorded in $CHCl_3$/neat (as mentioned) and reported in wave number (cm^{-1}). Mass spectral data were obtained using MS (EI) ESI, HRMS mass spectrometers. ^1H NMR spectra were recorded at 200, 300, 400, 500 and ^{13}C NMR spectra 50, 75, 100 MHz in $CDCl_3$ solution unless otherwise mentioned, chemical shifts are in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.



(*R*)-9-(*tert*-Butyldimethylsilyloxy)-1-chlorononon-4-yn-2-ol (11). A flame-dried 250 mL two necked round bottom flask was charged with TBS protected 5-hexyne 1-ol **10** (3.0 g, 14.12 mmol) in THF (100 mL) and cooled to −78 °C. To this solution, *n*-BuLi (2.5M in hexanes, 5.64 mL, 14.12 mmol) was added drop-wise via syringe, warmed slowly to 0

^{o}C. During this period, the reaction mixture turned to dark red in color. After 30 min, (*R*)-epichlorohydrin **8** (1.1 g, 11.29 mmol) was slowly added followed by $BF_3.OEt_2$ (1.43 mL, 11.29 mmol) at −78 °C and stirred for an additional 30 min. The reaction was then quenched with saturated $NaHCO_3$ (50 mL), diluted with ethyl acetate (50 mL), and warmed to room temperature. The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 x 60 mL). The combined organic layer was washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/hexane = 1:19) provided the desired secondary alcohol **11** (3.96 g, 92%) as a colorless oil.

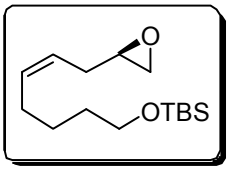
$[\alpha]_D^{25}$ −5.0 (*c* 0.9, $CHCl_3$); IR (neat) 3416, 2933, 2859, 1466, 1432, 1254, 1102, 833, 776 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (m, 1 H), 3.73-3.56 (m, 4 H), 2.55-2.48 (m, 2 H), 2.32-2.15 (m, 2 H), 1.65-1.50 (m, 4 H), 0.91 (s, 9 H), 0.05 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 83.6, 74.6, 67.0, 62.6, 48.3, 31.9, 25.9, 25.3, 24.7, 18.5, 18.3, −5.3 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{29}ClNaO_2Si$ $[M + Na]^+$ 327.1518; found 327.1509.



(*R*)-*tert*-Butyldimethyl-(7-(oxiran-2-yl)hept-5-ynyloxy)silane (12). To a suspension of NaH (0.69 g, 28.78 mmol, 60% w/v dispersion in mineral oil) in dry THF (25 mL), was added dropwise a solution of chlorohydrins **11** (3.5 g, 11.51 mmol) in dry THF (50 mL) under N_2 atmosphere at 0 ^{o}C. The reaction mixture was allowed to stir at room temperature for 30 min. After completion of the reaction (monitored by TLC), it was quenched with ice cold water (50 mL) at 0 ^{o}C. The organic layer was separated and the

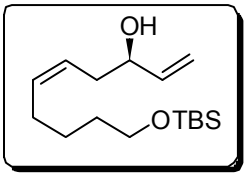
aqueous layer extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent evaporated under reduced pressure. The crude mass was purified by silica gel chromatography (ethyl acetate/hexane = 1:49) to afford the epoxide **12** (2.70 g, 91%) as a light yellow liquid.

$[\alpha]_D^{25}$ −9.2 (*c* 0.8, $CHCl_3$); IR (neat) 3051, 2933, 2859, 1741, 1613, 1467, 1392, 1252, 1102, 996, 838, 776 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.62 (t, *J* = 5.8 Hz, 2 H), 3.07 (m, 1 H), 2.78 (t, *J* = 4.7 Hz, 1 H), 2.65 (m, 1 H), 2.57 (m, 1 H), 2.44 (m, 1 H), 2.23-2.14 (m, 2 H), 1.70-1.48 (m, 4 H), 0.9 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.5, 74.2, 62.7, 50.3, 46.4, 31.9, 25.9, 25.2, 22.5, 18.5, 18.3, −5.3; HRMS (ESI): *m/z* calcd for $C_{15}H_{28}NaO_2Si$ $[M + Na]^+$ 291.1751; found 291.1739.



(*R*,*Z*)-*tert*-Butyldimethyl-(7-(oxiran-2-yl)hept-5-enyloxy)silane (13). Lindlar catalyst (Pd/C on $CaCO_3$,) (10 mol%) was added to a stirred solution of alkyne **12** (2.5 g, 9.32 mmol)) in benzene (10 mL) followed by catalytic amount of quinoline (0.02 mL, 0.093 mmol) at room temperature under hydrogen atmosphere. The mixture was vigorously stirred for 3 h at room temperature. After complete consumption of the starting material (monitored by TLC), the black reaction mass was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and purification of the crude product by silica gel column chromatography (ethyl acetate/hexane = 1:49) to yield the desired *Z*-olefin **13** (2.41 g, 96%).

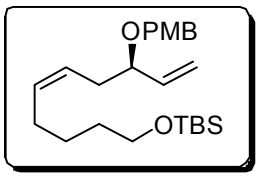
$[\alpha]_D^{25}$ −5.5 (*c* 1.35, $CHCl_3$); IR (neat) 2932, 2858, 1742, 1467, 1389, 1253, 1101, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.53 (m, 1 H), 5.41 (m, 1 H), 3.62 (t, *J* = 6.4 Hz, 2 H), 2.95 (m, 1 H), 2.74 (t, *J* = 4.5 Hz, 1 H), 2.51 (m, 1 H), 2.38 (m, 1 H), 2.26 (m, 1 H), 2.06 (q, *J* = 7.2 Hz, 2 H), 1.58-1.47 (m, 2 H), 1.46-1.35 (m, 2 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.9, 123.2, 63.0, 51.6, 46.5, 32.4, 30.1, 27.1, 25.9, 25.8, 18.3, −5.3; HRMS (ESI): *m/z* calcd for $C_{15}H_{30}NaO_2Si$ $[M + Na]^+$ 293.1907; found 293.1893.



(*R*,*Z*)-10-(*tert*-Butyldimethylsilyloxy)deca-1,5-dien-3-ol (14). To a stirred solution of trimethylsulfonium iodide (predried by azeotropic method using dry toluene) (4.53 g, 22.2 mmol) in THF (30 mL) was cooled to −20 °C, added *n*-BuLi (7.4 mL, 2.5M in hexane, 18.5 mmol) and stirred for 30 min. After stirring the reaction mixture for 30 min at −20 °C, the epoxide **13** (2.0 g, 7.4 mmol) in THF (20 mL) was added *via* syringe over 20 min at the same temperature. After complete addition, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature over 30 min. After stirring at room temperature for 2 h, the reaction was quenched with saturated ammonium chloride (40 mL) water and diluted with diethyl ether (60 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether (2x 50 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel

(ethyl acetate/hexane = 1:19) to obtain the secondary allylic alcohol **14** (1.79 g, 85%) as colorless syrup.

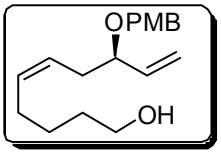
$[\alpha]_D^{25}$ +9.7 (*c* 0.8, $CHCl_3$); IR (neat): 3410, 3011, 2932, 2858, 1466, 1389, 1253, 1101, 837, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.85 (m, 1 H), 5.53 (m, 1 H), 5.37 (m, 1 H), 5.22 (d, *J* = 16.8 Hz, 1 H), 5.09 (d, *J* = 10.3 Hz, 1 H), 4.11 (q, *J* = 6.0, 12.2 Hz, 1 H), 3.58 (t, *J* = 6.2 Hz, 2 H), 2.28 (t, *J* = 6.7 Hz, 2 H), 2.12 (q, *J* = 6.9, 13.9 Hz, 2 H), 1.57-1.35 (m, 4 H), 0.88 (s, 9 H), 0.03 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.5, 133.0, 124.5, 114.5, 72.4, 63.0, 35.0, 32.3, 27.1, 25.9, 18.3, -5.3 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{32}NaO_2Si$ $[M + Na]^+$ 307.2064; found 307.2051.



(*R*,*Z*)-*tert*-Butyl(8-(4-methoxybenzyloxy)deca-5,9-dienyloxy)dimethylsilane. To a suspension of NaH (0.28 g, 7.04 mmol, 60% w/v dispersion in mineral oil) in dry THF (25 mL) was added dropwise a solution of resulting allylic alcohol **14** (1.0 g, 3.52 mmol) at 0 °C and continued the stirring for the next 45 min at room temperature. At 0 °C, freshly prepared *p*-methoxy benzyl bromide (0.71 g, 3.52 mmol) was added and stirred further for 4 h at room temperature with frequent monitoring of the progress of the reaction by TLC. The reaction mixture was quenched with crushed ice flakes until a clear solution (biphasic) was formed. The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (2 x 70 mL), brine (100 mL), and dried over anhydrous Na_2SO_4. Solvent was

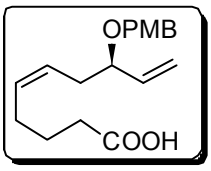
removed under reduced pressure and the crude was purified by column chromatography on silica gel (ethyl acetate/hexane = 1:49) to afford the PMB-ether (1.29 g, 91%) as a colorless liquid.

$[\alpha]_D^{25}$ +11.7 (*c* 1.1, $CHCl_3$); IR (neat): 2933, 2857, 1613, 1513, 1464, 1301, 1249, 1174, 1099, 835, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.21 (d, *J* = 9.0 Hz, 2 H), 6.82 (d, *J* = 9.0 Hz, 2 H), 5.73 (m, 1 H), 5.48-5.32 (m, 2 H), 5.24-5.14 (m, 2 H), 4.51 (d, *J* = 11.3 Hz, 1 H), 4.47 (d, *J* = 11.3 Hz, 1 H), 3.79 (s, 3 H), 3.71 (q, *J* = 6.9, 14.5 Hz, 1 H), 3.58 (t, *J* = 6.0 Hz, 2 H), 2.43-2.19 (m, 2 H), 2.08-2.01 (m, 2 H), 1.54-1.30 (m, 4 H), 0.90 (s, 9 H), 0.04 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9, 138.6, 131.6, 130.7, 129.1, 125.0, 117.1, 113.6, 80.0, 69.6, 63.0, 55.1, 33.4, 32.4, 27.1, 25.9, −5.3 ppm; HRMS (ESI): *m/z* calcd for $C_{24}H_{40}NaO_3Si$ $[M + Na]^+$ 427.2639; found 427.2623.



(*R*,*Z*)-8-(4-Methoxybenzyloxy)deca-5,9-dien-1-ol (15). To a stirred solution of TBS ether (1.0 g, 2.47 mmol) in MeOH (20 mL) was added *p*-TsOH (catalytic) at 0 °C and the resulting solution was stirred for 1 h at ambient temperature. The reaction mixture was quenched with aqueous $NaHCO_3$ (20 mL). MeOH was removed under reduced pressure, the residue extracted with EtOAc (3 x 50 mL), the combined organic layer washed with brine (50 mL), dried over Na_2SO_4, and evaporated to dryness which on silica gel column chromatography (EtOAc/hexane: 1/7) furnished the desired primary alcohol **15** (0.64 g, 89%) as a viscous colorless liquid.

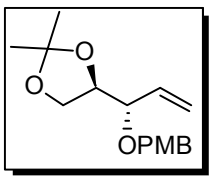
$[\alpha]_D^{25}$ +19.3 (*c* 0.9, $CHCl_3$); IR (neat): 3406, 3074, 2933, 2861, 1612, 1513, 1459, 1301, 1247,1175, 1037, 821,774 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.21 (d, *J* = 8.3 Hz, 2 H), 6.81 (d, *J* = 8.3 Hz, 2 H), 5.72 (m, 1 H), 5.47-5.3 (m, 2 H), 5.24-5.12 (m, 2 H), 4.50 (d, *J* = 11.5 Hz, 1 H), 4.25 (d, *J* = 11.5 Hz, 1 H), 3.78 (s, 3 H), 3.69 (q, *J* = 6.9, 13.9 Hz, 1 H), 3.53 (t, *J* = 6.2 Hz, 2 H), 2.36 (m, 1 H), 2.22 (m, 1 H), 2.08-1.97 (m, 2 H), 1.56-1.32 (m, 4 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 138.5, 131.4, 130.6, 129.2, 125.3, 117.2, 113.6, 79.9, 69.7, 62.7, 55.2, 33.4, 32.2, 27.0, 25.6 ppm; HRMS (ESI): *m/z* calcd for $C_{18}H_{26}NaO_3$ $[M + Na]^+$ 313.1774; found 313.1794.



(*R*,*Z*)-8-(4-Methloxy)deca-5,9-dienoioxybenzyc acid (6). To a stirred solution of primary alcohol **15** (0.35 g, 1.21 mmol) in CH_2Cl_2 (30 mL) at 0 °C, were added iodobenzenediacetate (0.43 g, 1.33 mmol) followed by TEMPO (0.04 g, 0.24 mmol) and allowed to stir at ambient temperature for 30 min. After complete consumption of the starting material (monitored by TLC), the reaction mixture was quenched with saturated solution of $Na_2S_2O_3$ (20 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporation of solvent led to crude aldehyde which was passed through a small pad of silica gel (ethyl acetate/hexane = 1:4) to afford the corresponding aldehyde (0.32 g, 94%) as a thick viscous liquid and used immediately for the next reaction.

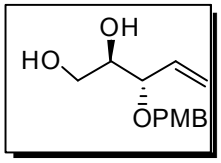
To a solution of resulting aldehyde (0.32 g, 1.04 mmol) in *tert*-butyl alcohol (10 mL), 2-methyl-2-butene (0.5 mL, 1.04 mmol, 2M solution in THF) was added at room temperature. Sodium dihydrogenphosphate (0.49 g, 3.12 mmol) and sodium chlorite (0.14 g, 1.56 mmol) were dissolved in water (5 mL) to make a clear solution which was subsequently added to the above mentioned reaction mixture at 0 ^{o}C. It was allowed to stir for further 3 h at room temperature. The reaction mixture was extracted with EtOAc (3 x 20 mL), the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexane: 3/7) to afford the corresponding acid **6** (0.29 g, 93%) as a colorless oil.

$[\alpha]_D^{25}$ +5.5 (*c* 1.1, $CHCl_3$); IR (neat): 3450, 3009, 2937, 2862,1706, 1609, 1513, 1420, 1248, 1172, 1034, 821 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (d, *J* = 8.5 Hz, 2 H), 6.8 (d, *J* = 8.7 Hz, 2 H), 5.72 (m, 1 H), 5.47-5.33 (m, 2 H), 5.24-5.12 (m, 2 H), 4.49 (d, *J* = 11.7 Hz, 1 H), 4.25 (d, *J* = 11.7, 1 H), 3.77 (s, 3 H), 3.69 (q, *J* = 6.6, 13.9 Hz, 1 H), 2.45-2.17 (m, 4 H), 2.07 (m, 1 H), 1.73-1.61 (m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 158.9, 138.4, 130.3, 129.2, 126.1, 117.2, 113.6, 79.8, 69.6, 55.1, 33.4, 33.3, 26.6, 24.6 ppm; HRMS (ESI): *m/z* calcd for $C_{18}H_{24}NaO_4$ $[M + Na]^+$ 327.1203; found 327.1182.



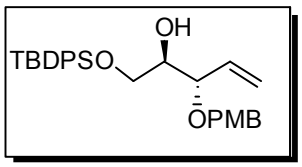
(*R*)-4-((*S*)-1-(4-Methoxybenzyloxy)allyl)-2,2-dimethyl-1,3-dioxolane (19): To a suspension of NaH (0.3 g, 7.56 mmol, 60% w/v dispersion in mineral oil) in dry THF (25 mL) was added dropwise a solution of secondary allylic alcohol **18** (1.2 g, 7.56 mmol) at

0 ^{o}C and continued the stirring for the next 45 min at room temperature. At 0 ^{o}C, freshly prepared *p*-methoxy benzyl bromide (1.53 g, 7.56 mmol) was added and stirred further for 4 h at room temperature with frequent monitoring of the progress of reaction by TLC. The reaction mixture was quenched by small crushed ice flakes until a clear solution (biphasic) had formed. The combined organic layers were washed with water, brine and dried over anhydrous Na_2SO_4. After removing the volatiles under reduced pressure, crude *p*-methoxy benzyl ether was purified by column chromatography on silica gel (ethyl acetate/hexane = 1:49) to afford the pure product **19** (1.9 g, 92%) as a colorless liquid. $[\alpha]_D^{25}$ +12.5 (*c* 1.0, $CHCl_3$); IR (neat) 3070,2985, 2926, 1727, 1639, 1427, 1249, 1115, 1066, 821 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.6 Hz, 2 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 5.77 (m, 1 H), 5.40-5.27 (m, 2 H), 4.54 (d, *J* = 11.5 Hz, 1 H), 4.30 (d, *J* = 11.3 Hz, 1 H), 4.4-3.6 (m, 2 H), 3.79 (s, 3 H), 3.76 (m, 1 H), 3.67 (m,1 H), 1.36 (s, 3 H) 1.31 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 135.2, 130.1, 129.4, 119.6, 113.7, 109.4, 80.6, 77.5, 70.1, 66.8, 55.2, 26.5, 25.2 ppm; MS (ESI) ($C_{16}H_{22}O_4$): m/z 301 $[M + Na]^+$.



(2*R*,3*S*)-3-(4-Methoxybenzyloxy)pent-4-ene-1,2-diol (20): To a solution of **19** (1.5 g, 5.39 mmol) in methanol (50 mL), CSA (cat.) was added at 0 ^{o}C and stirred at room temperature for 2 h after which it was quenched with Et_3N (3 mL), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography (Silica gel, ethyl acetate/hexane = 2:3) to give **20** (1.1 g, 87%).

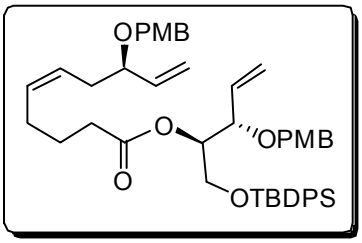
$[\alpha]_D^{25}$ +25.4 (*c* 0.42, $CHCl_3$); IR (neat): 3408,2924, 1612, 1513, 1301, 1248, 1176, 1035, 932,821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.5 Hz, 2 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 5.79 (m, 1 H), 5.39-5.27 (m, 2 H), 4.53 (d, *J* = 11.3 Hz, 1 H), 4.27 (d, *J* = 11.3 Hz, 1 H), 3.84 (m, 1 H), 3.78 (s, 3 H), 3.66-3.57 (m, 3 H) 2.89 (br s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 134.9, 129.8, 129.4, 120.0, 113.8, 81.6, 73.1, 70.2, 63.2, 55.2; HRMS (ESI): *m/z* calcd for $C_{13}H_{18}NaO_4$ $[M + Na]^+$ 261.1097; found 261.1115.



(2*R*,3*S*)-1-(*tert*-Butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)pent-4-en-2-ol (7): To a stirred solution of diol **20** (1.0 g, 4.2 mmol) in CH_2Cl_2 (50 mL) under nitrogen atmosphere at room temperature, was added TBDPSCl (1.12 mL, 4.2 mmol) and imidazole (0.57 g, 8.4 mmol). The reaction mixture was stirred at room temperature for 3 h. After completion (monitored by TLC), the reaction was quenched with water (20 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel column chromatography to give **7** (1.78 g, 89%) as colorless viscous liquid.

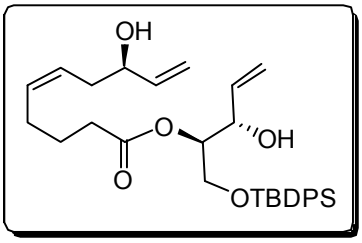
$[\alpha]_D^{25}$ +6.4 (*c* 0.5, $CHCl_3$); IR (neat) 3453, 2932, 2859, 1613, 1513, 1426, 1301, 1247, 1109, 1069, 930, 820, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.68-7.61 (m, 4 H), 7.46-7.32 (m, 6 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 6.82 (d, *J* = 8.6 Hz, 2 H), 5.84 (m, 1 H), 5.39-5.27 (m, 2 H), 4.52 (d, *J* = 11.3 Hz, 1 H), 4.26 (d, *J* = 11.3 Hz, 1 H), 3.79 (s, 3 H),

3.77-3.73 (m, 3 H) 2.45 (br s, 1 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 135.5, 135.2, 133.2, 130.2, 129.7, 129.3, 127.7, 119.5, 113.7, 80.3, 73.5, 70.0, 64.4, 55.2, 26.8, 19.2; HRMS (ESI): *m/z* calcd for $C_{29}H_{36}NaO_4Si$ $[M + Na]^+$ 499.2275; found 499.2252.



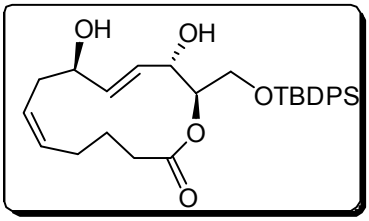
(*R*,*Z*)-((2*R*,3*S*)-1-(*tert*-Butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)pent-4-en-2-yl)-8-(4-methoxybenzyloxy)deca-5,9-dienoate (4). To a stirred solution of acid **6** (0.28 g, 0.92 mmol) in CH_2Cl_2 (15 mL) at 0 ^oC, Et_3N (0.30 mL, 1.68 mmol) followed by EDCI (0.24 g, 1.26 mmol) and DMAP (0.84 mmol, 0.09 g) were added and stirred for 30 min. Alcohol **7** (0.4 g, 0.84 mmol) was dissolved in CH_2Cl_2 (10 mL) and slowly added to the resulting reaction mixture at the same temperature and then allowed to stir for 12 h at room temperature. After completion of the reaction (monitored by TLC), it was quenched with water (20 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2 x 25 mL). The combined organic layer was dried over Na_2SO_4 and the solvent evaporated under reduced pressure to give a colorless oil which on purification by silica gel column chromatography (ethyl acetate/hexane = 3:97) furnished the desired coupled product **4** (0.576 g, 90%, based on the starting alcohol) as a colorless liquid. $[\alpha]_D^{25}$ +17.4 (*c* 0.48, $CHCl_3$); IR (neat) 2923, 2855, 1738, 1612, 1512, 1462, 1381, 1245, 1107, 1069, 929, 819, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, *J* = 6.9 Hz, 4 H),

7.43-7.29 (m, 6 H), 7.20 (d, *J* = 8.7 Hz, 2 H), 7.12 (d, *J* = 8.5 Hz, 2 H), 6.81 (d, *J* = 8.7 Hz, 2 H), 6.77 (d, *J* = 8.5 Hz, 2 H), 5.78-5.64 (m, 2 H), 5.44-5.35 (m, 2 H), 5.31-5.14 (m, 4 H), 5.04 (q, *J* = 5.8, 9.6 Hz, 1 H), 4.5 (d, *J* = 11.5 Hz, 2 H), 4.26 (d, *J* = 11.7 Hz, 2 H), 3.98 (t, *J* = 6.9 Hz, 1 H),3.85 (m, 1 H), 3.78 (s, 6 H), 3.71 (m, 2 H), 2.40-2.14 (m, 4 H), 2.08-1.98 (m, 2 H), 1.68-1.54 (m, 2 H), 1.02 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.7, 159.0, 138.6, 135.6, 135.5, 135.0, 130.5, 129.6, 129.2, 127.6, 126.0, 119.6, 117.3, 113.7, 79.9, 78.4, 74.7, 70.1, 69.7, 62.2, 55.2,33.9, 33.4, 29.7, 26.7, 24.7, 19.2 ppm; HRMS (ESI): *m/z* calcd for $C_{47}H_{58}NaO_7Si$ $[M + Na]^+$ 785.3844; found 785.3847.



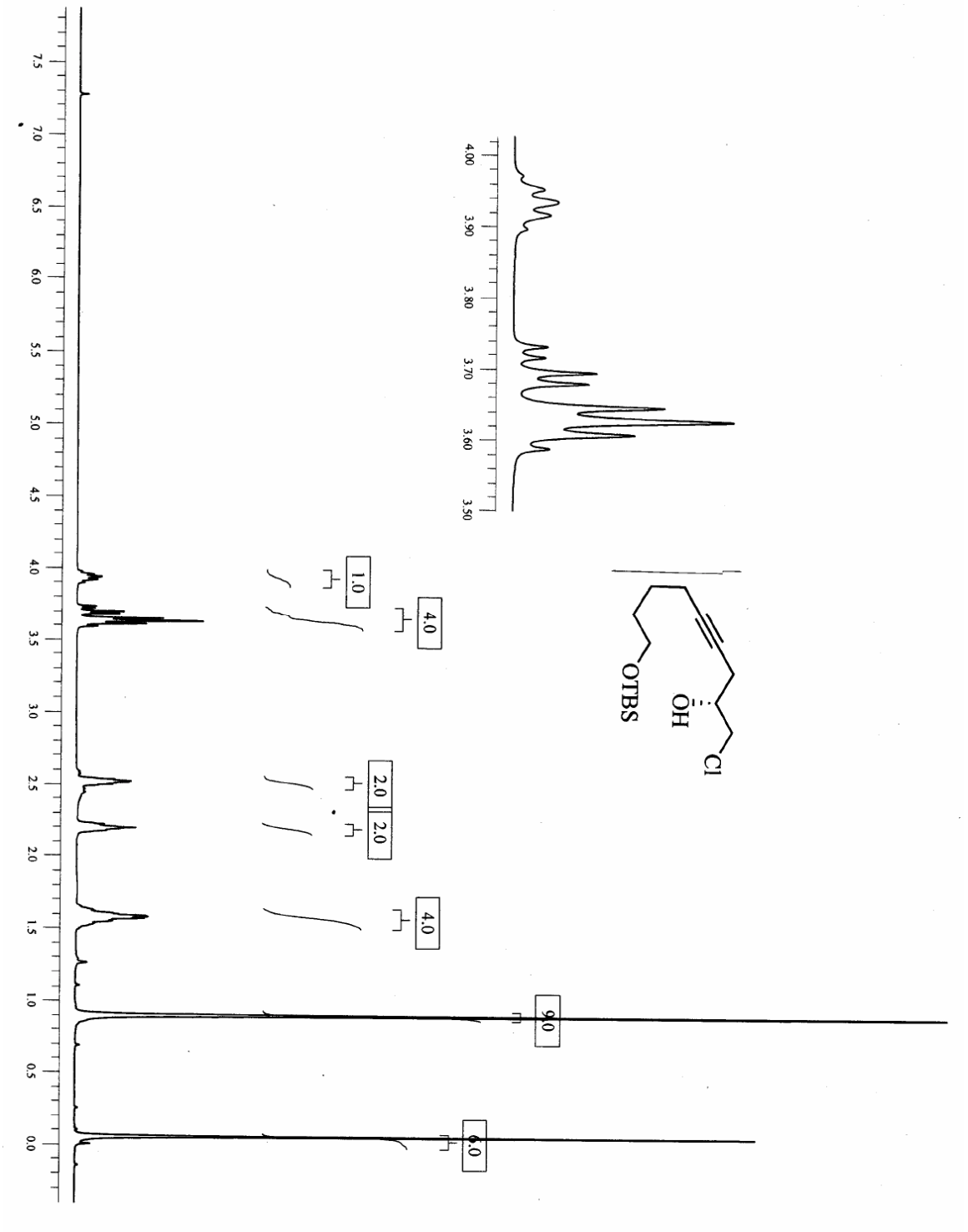
(*R*,*Z*)-((2*R*,3*S*)-1-(*tert*-Butyldiphenylsilyloxy)-3-hydroxypent-4-en-2-yl)-8-hydroxydeca-5,9-dienoate (5). To a stirred solution of di-PMB ether **4** (255 mg, 0.33 mmol) in CH_2Cl_2 (15 mL), was added DDQ (227 mg, 1.0 mmol) at pH7 with phosphate buffer solution (1.6 mL) at 0 ^oC. The reaction mixture was allowed to stir for 2 h at room temperature. After completion of the reaction (monitored by TLC), it was quenched with saturated $NaHCO_3$ (10 mL) solution. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was washed with brine (40 mL), dried over anhydrous Na_2SO_4 and evaporated to give the crude product which on purification by silica gel column chromatography (ethyl acetate/hexane = 1:5) to afford the desired diol **5** (162 mg, 93%) as a colorless viscous liquid.

$[\alpha]_D^{25}$ −7.5 (*c* 1.4, $CHCl_3$); IR (neat): 3446, 2927, 2856, 1728, 1637, 1426, 1218, 1111, 768, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.70-7.61 (m, 4 H), 7.46-7.34 (m, 6 H), 5.93-5.76 (m, 2 H), 5.60-5.34 (m, 3 H), 5.28-5.08 (m, 3 H), 4.93 (q, *J* = 4.5, 9.1 Hz, 1 H), 4.42 (t, *J* = 4.5 Hz, 2 H), 4.12 (q, *J* = 6.8, 12.1 Hz, 1 H), 3.92 (dd, *J* = 5.3, 11.3 Hz, 1 H), 3.77 (dd, *J* = 3.8, 11.3 Hz, 1 H), 2.41-2.20 (m, 4 H), 2.17-2.15 (m, 3 H), 1.77-1.63 (m, 2 H), 1.05 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.2, 140.3, 136.3, 135.6, 135.5, 132.6, 131.8, 129.9, 127.8, 125.8, 117.0, 114.8, 75.5, 73.1, 72.4, 63.1, 35.1, 33.6, 26.7, 26.6, 24.6, 19.1 ppm; HRMS (ESI): *m/z* calcd for $C_{31}H_{42}NaO_5Si$ $[M + Na]^+$ 545.2694; found 545.2712.

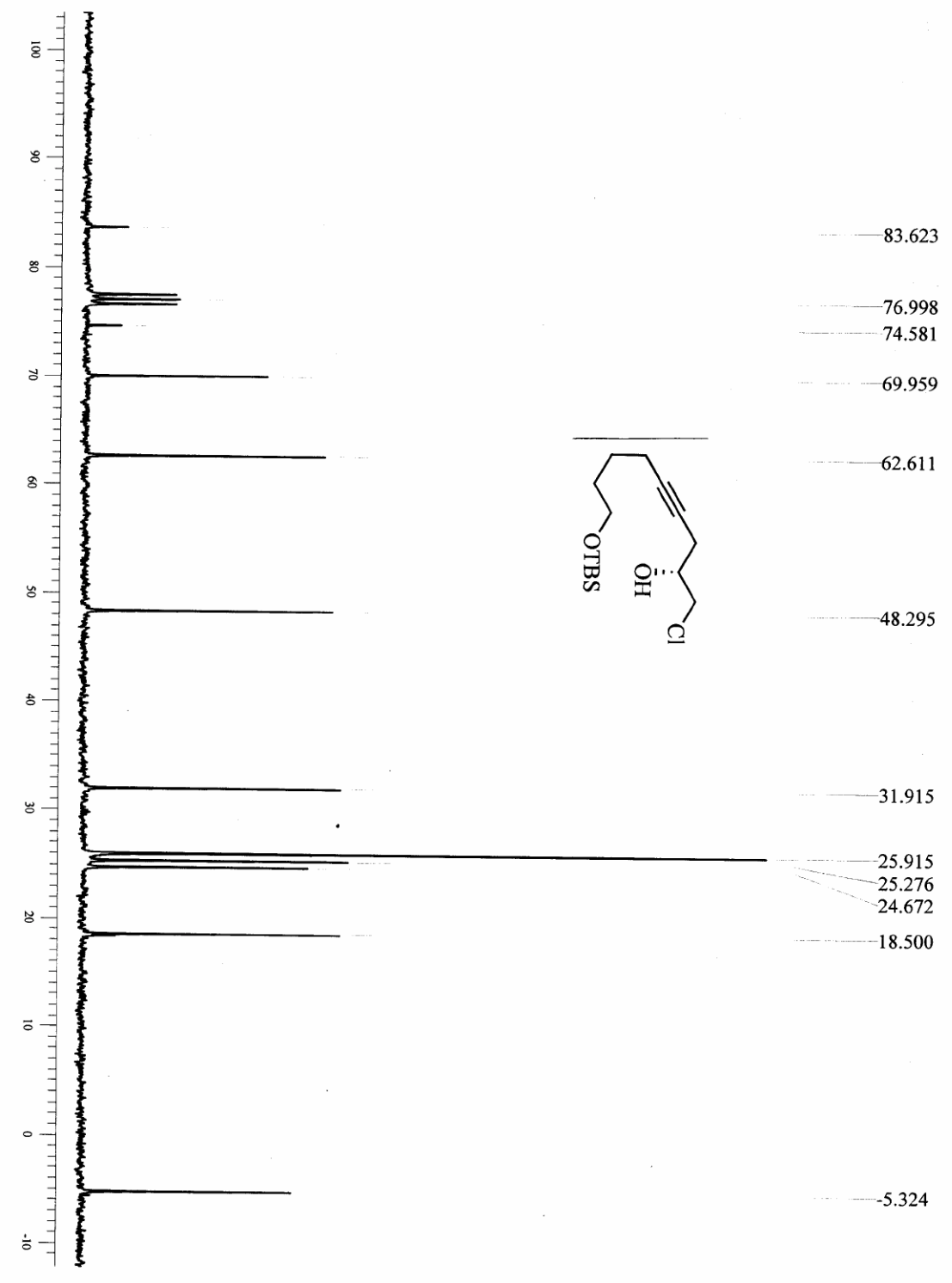


(6*Z*,9*R*,10*E*,12*S*,13*R*)-13-((*tert*-Butyldiphenylsilyloxy)methyl)-9,12-dihydroxyoxacyclotri-deca-6,10-dien-2-one (3). Grubbs second generation catalyst (16 mg, ca. 0.02 mmol) was dissolved in dry, deoxygenated CH_2Cl_2 (200 mL) under argon atmosphere. After the solution was heated to reflux, diene **5** (0.1 g, 0.2 mmol) was added slowly via syringe (30 min) in dry, deoxygenated CH_2Cl_2 (30 mL) to the reaction mixture. The reaction mixture was then stirred at reflux for an additional 8 h. After completion of the reaction (monitored by TLC), solvent was evaporated under reduced pressure. Purification of the crude residue by silica gel column chromatography (ethyl acetate/hexane = 3:7) afforded **3** (71 mg, 76%) (single stereoisomer) as a colorless viscous oil.

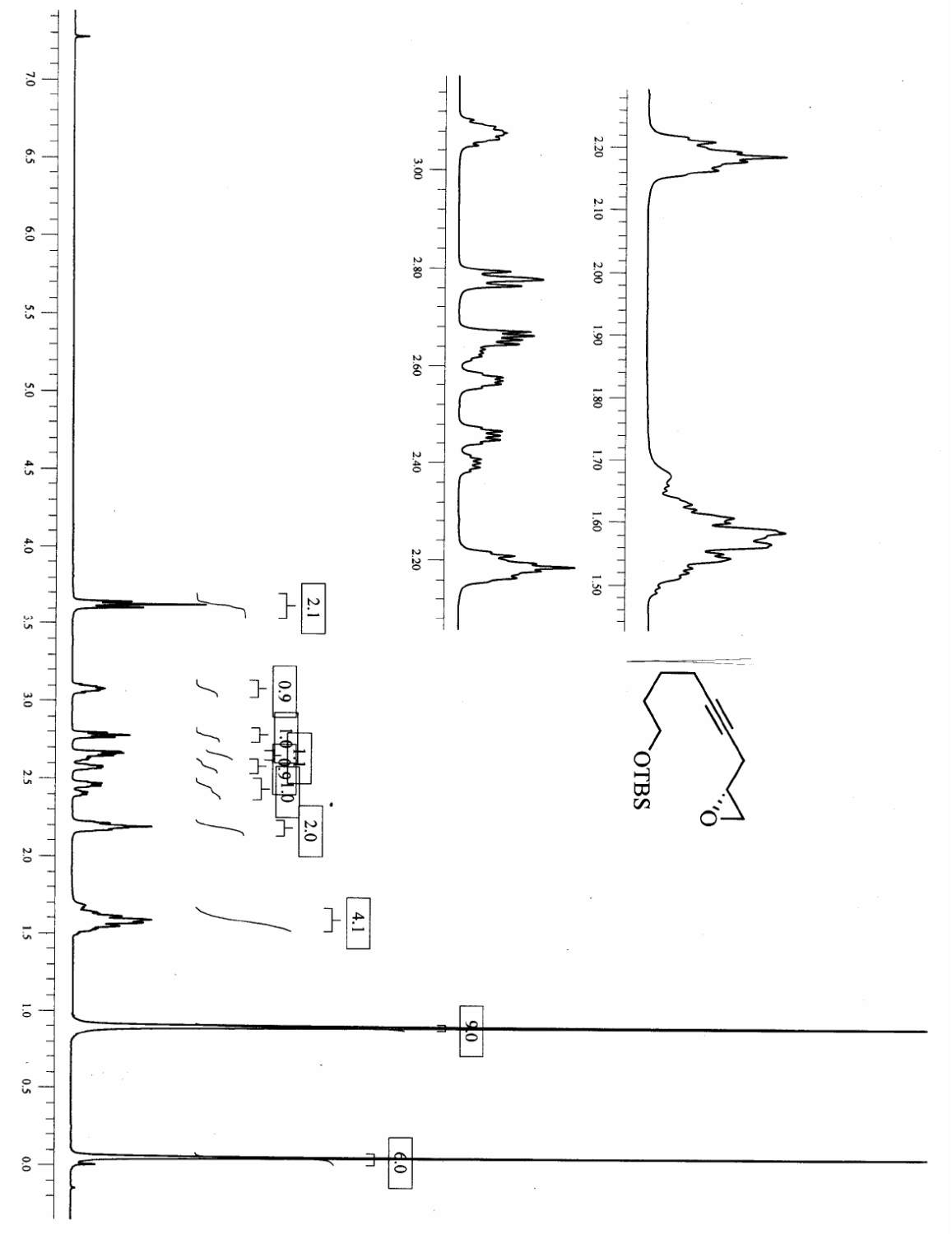
$[\alpha]_D^{25}$ −12.5 (*c* 0.8, $CHCl_3$); IR (neat): 3421, 2926, 2855, 1733, 1463, 1428, 1379, 1110, 1035, 969, 767, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.69-7.62 (m, 4 H), 7.48-7.35 (m, 6 H), 5.66 (dd, *J* = 7.7 Hz, 15.7 Hz, 1 H), 5.60-5.46 (m, 2 H), 5.23 (q, *J* = 6.2, 10.9 Hz, 1 H), 4.8 (m, 1 H), 4.40-4.26 (m, 2 H), 3.99-3.78 (m, 2 H), 2.47-2.12 (m, 6 H), 2.20-1.82 (m, 2 H), 1.06 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.6, 135.9, 135.6, 131.3, 131.1, 130.4, 129.9, 127.8, 126.6, 124.4, 74.9, 73.6, 72.6, 63.9, 35.1, 32.5, 26.7, 25.7, 22.9, 19.2 ppm; HRMS (ESI): *m/z* calcd for $C_{29}H_{38}NaO_5Si$ $[M + Na]^+$ 517.2381; found 517.2400.



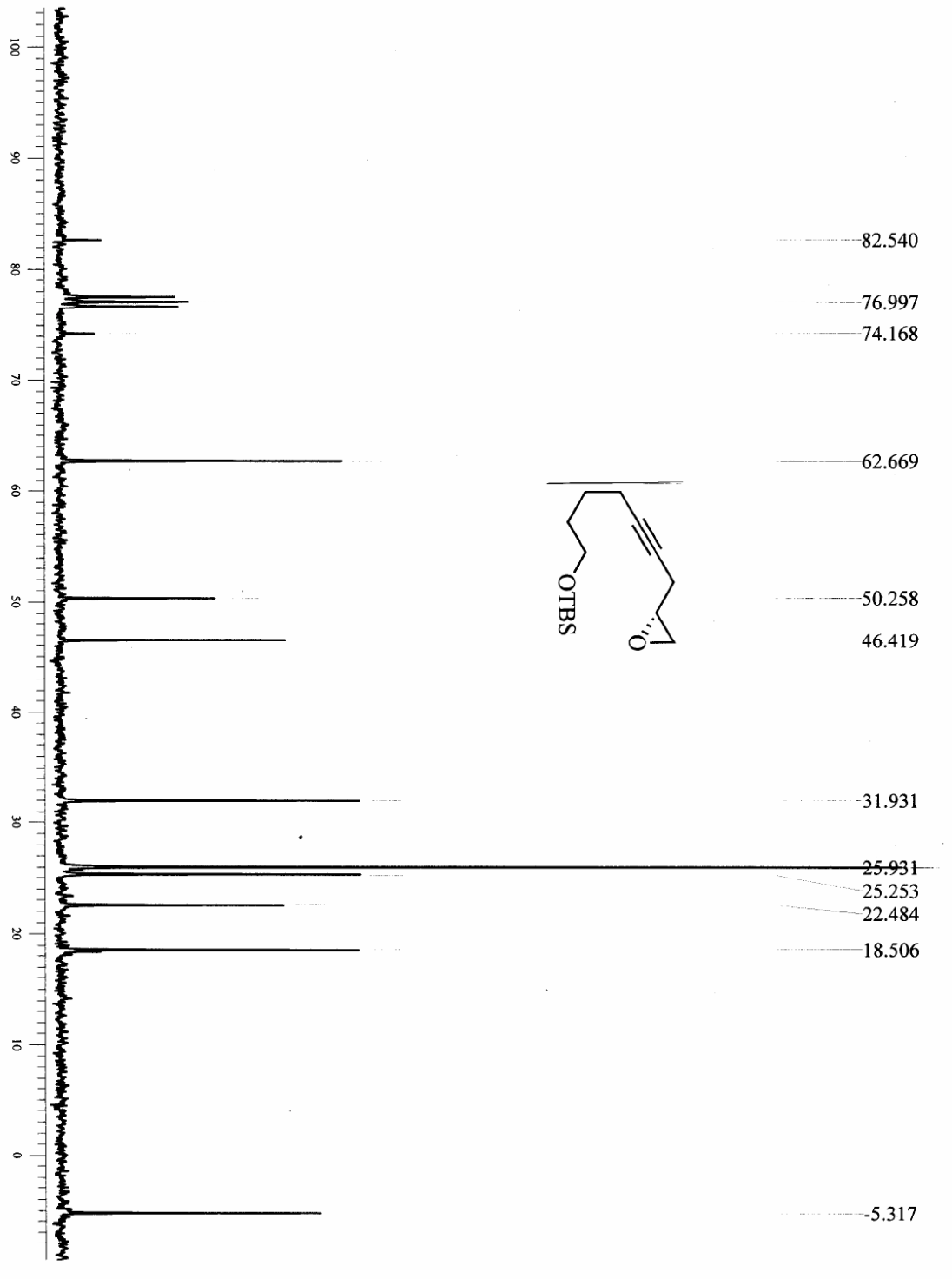
^{1}H NMR of 11 (300 MHz, $CDCl_3$)



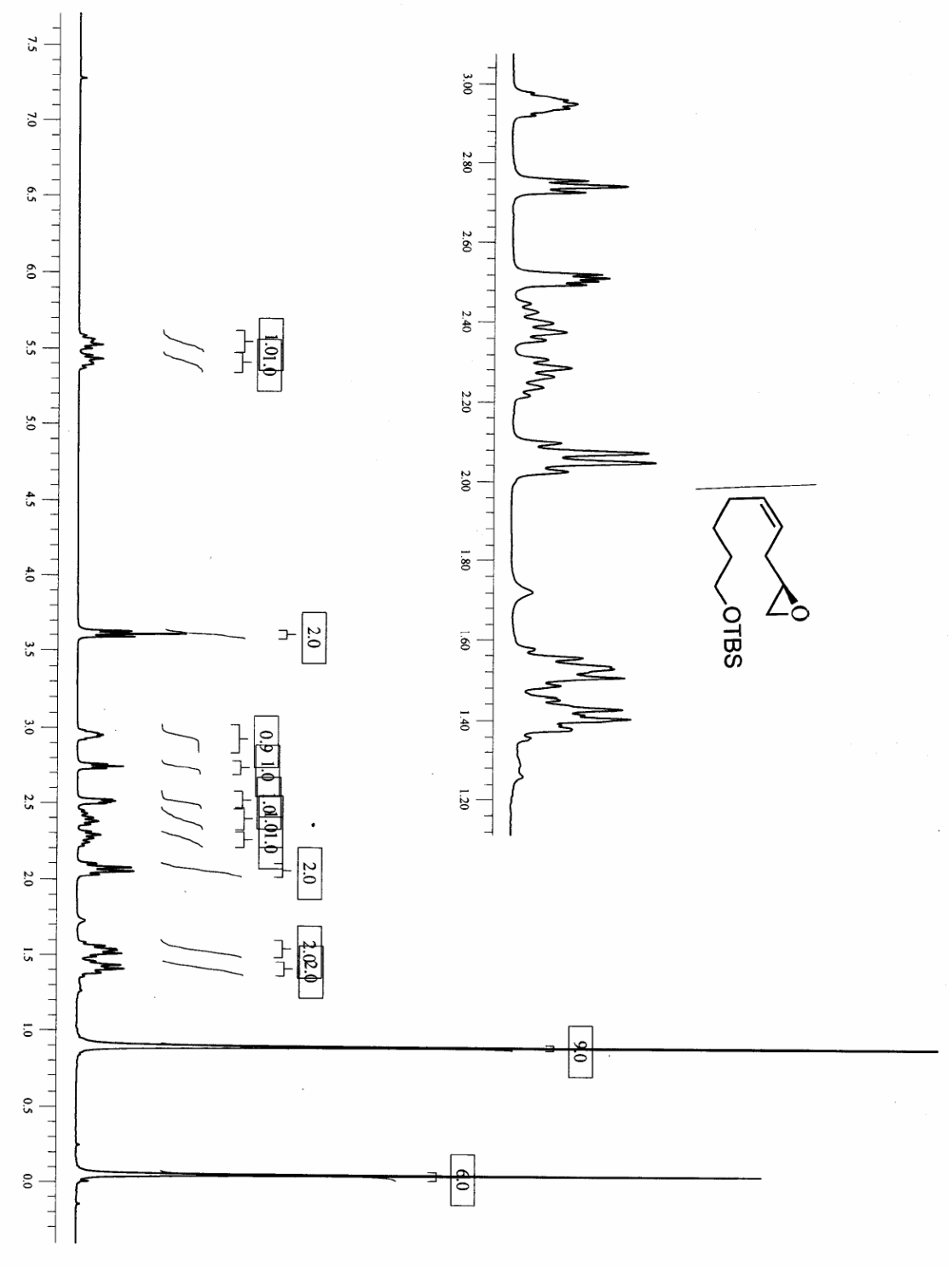
^{13}C NMR of 11 (75 MHz, $CDCl_3$)



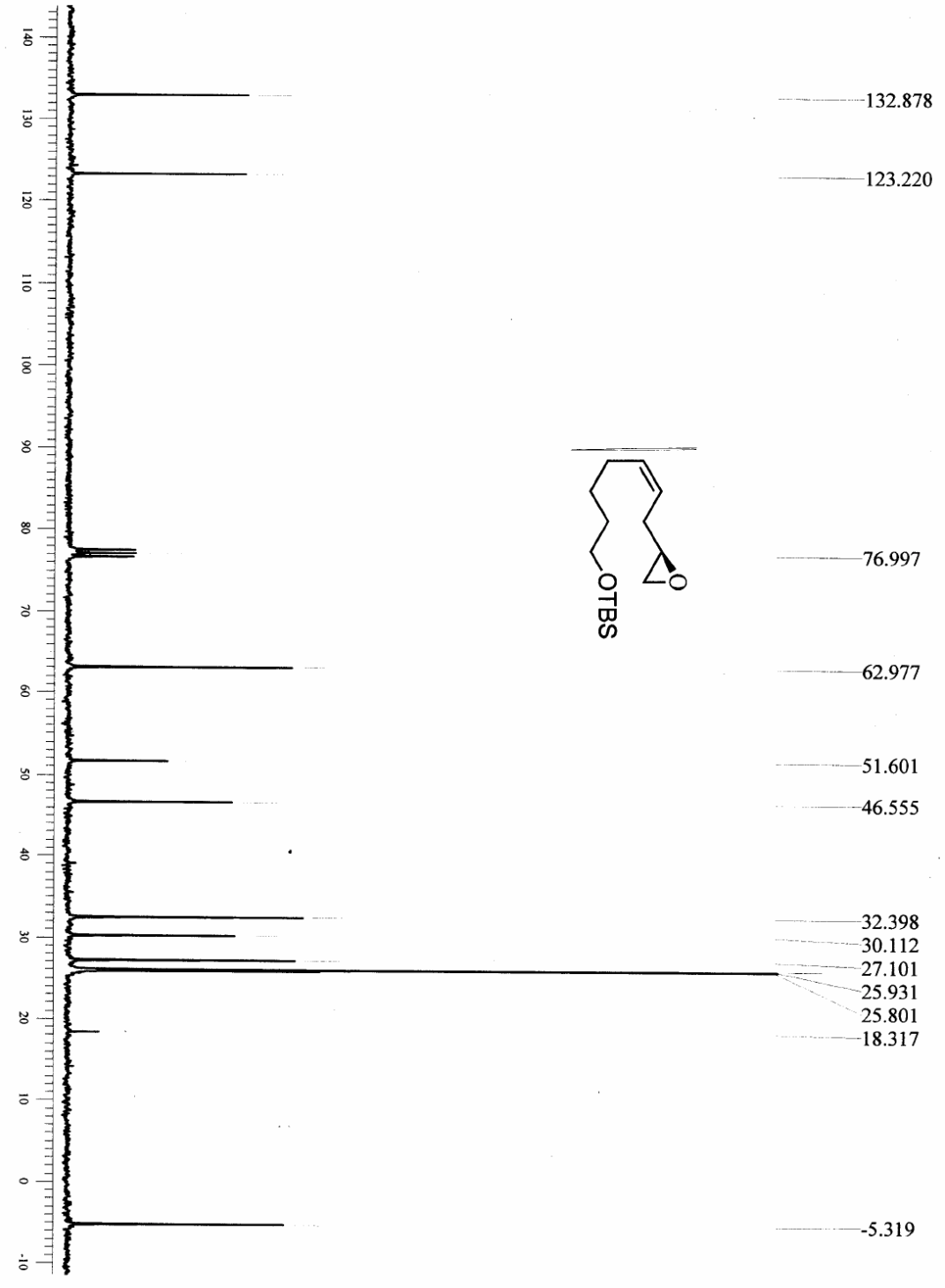
^{1}H NMR of 12 (300 MHz, $CDCl_3$)



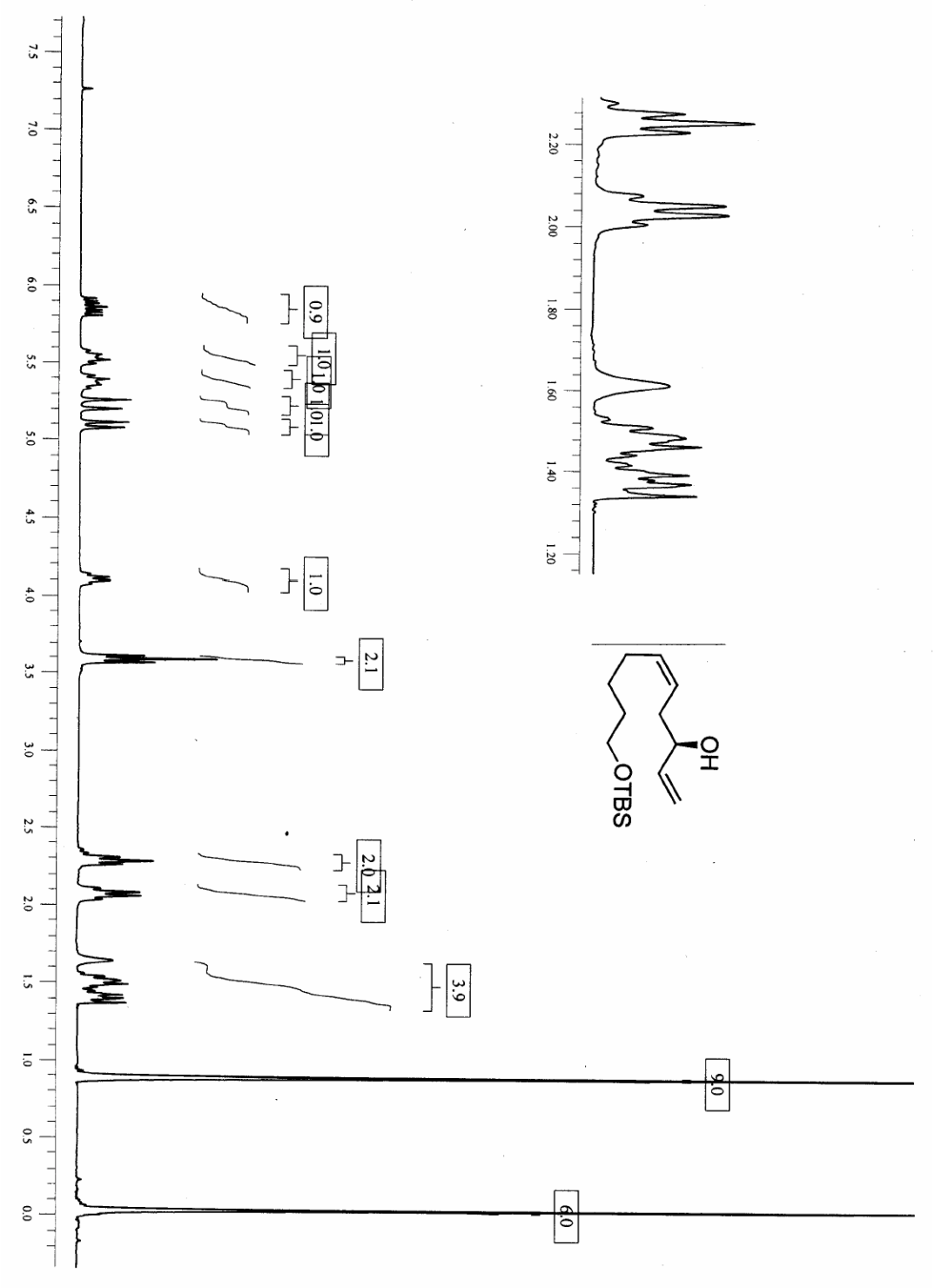
^{13}C NMR of 12 (75 MHz, $CDCl_3$)



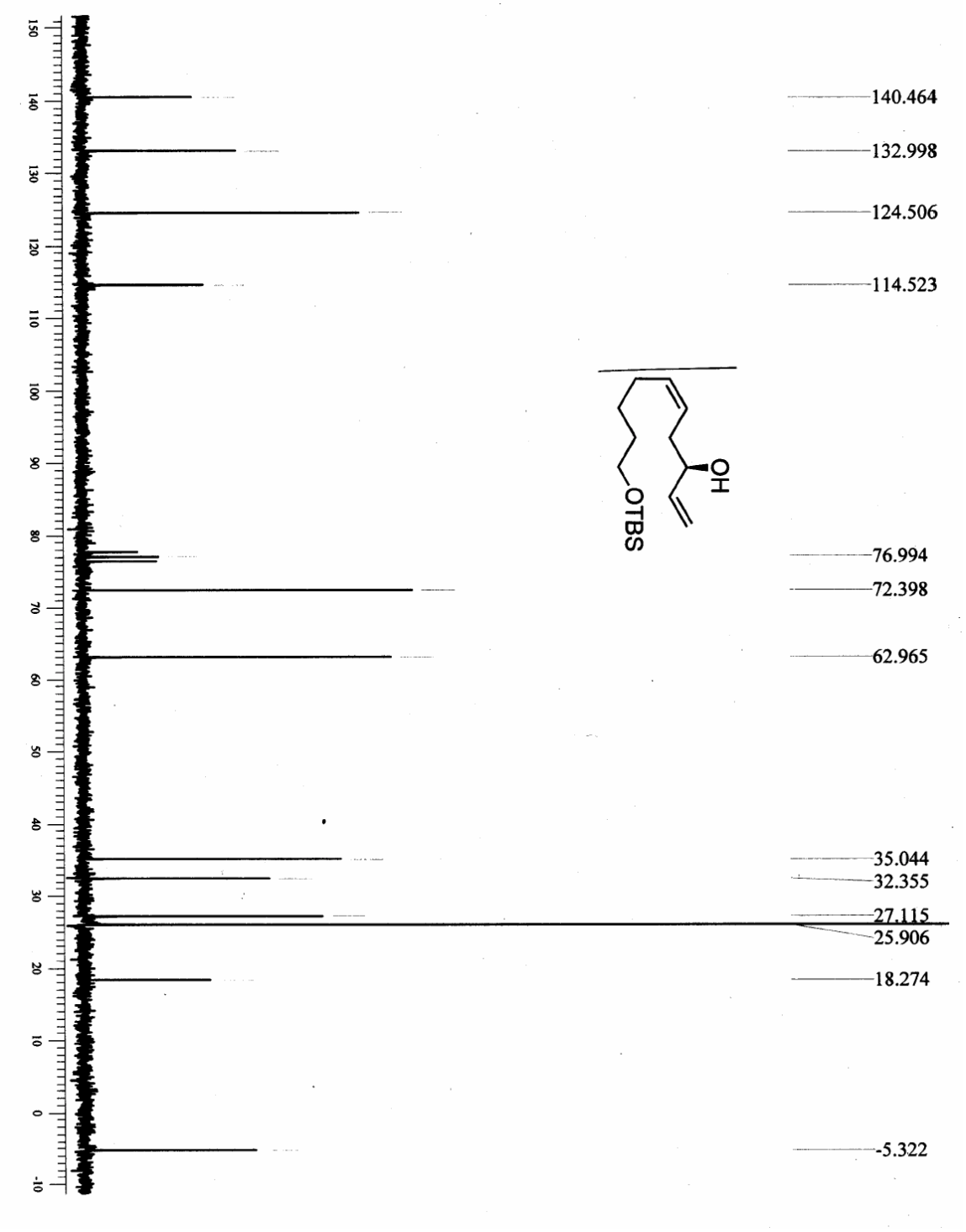
^{1}H NMR of 13 (300 MHz, $CDCl_3$)



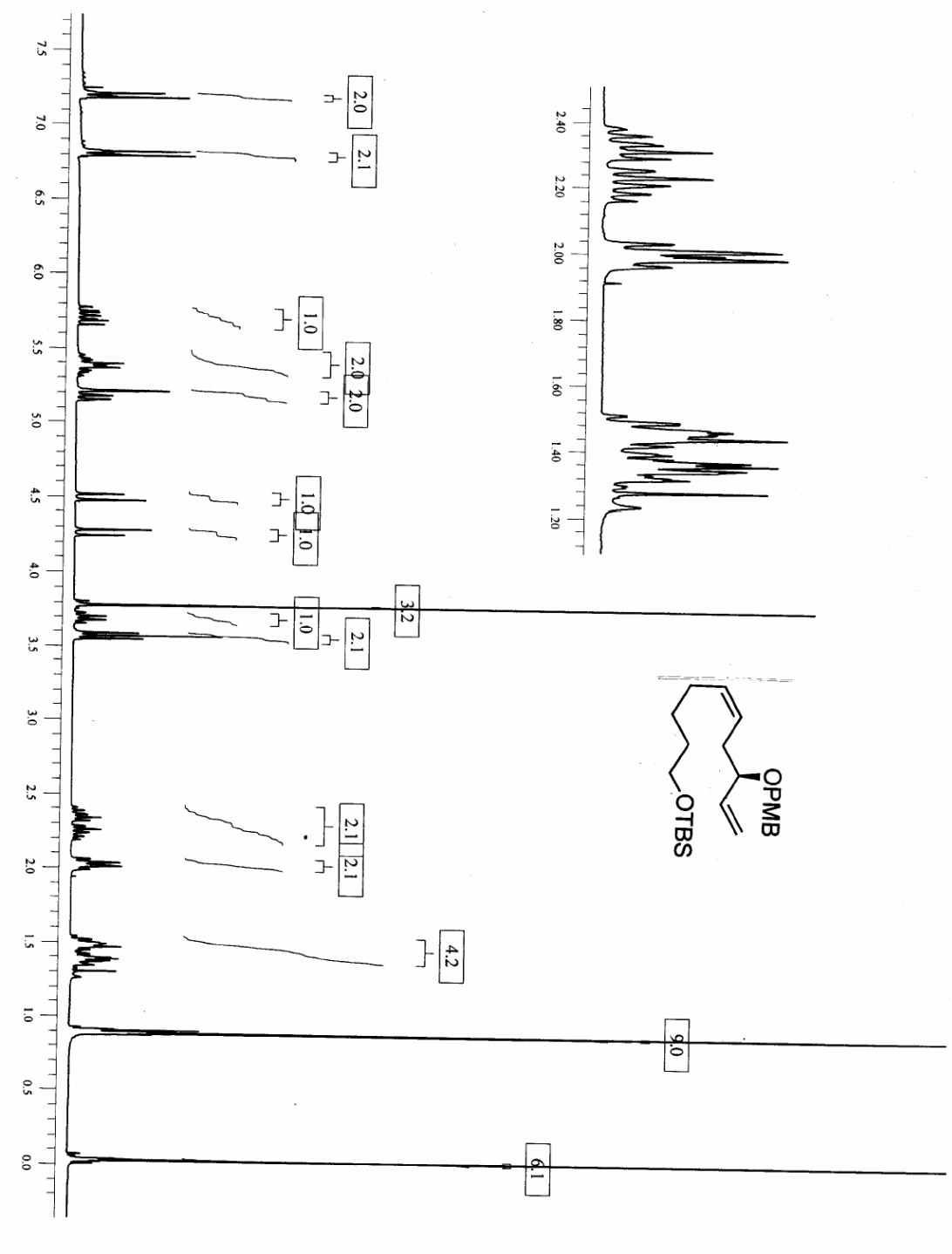
^{13}C NMR of 13 (75 MHz, $CDCl_3$)



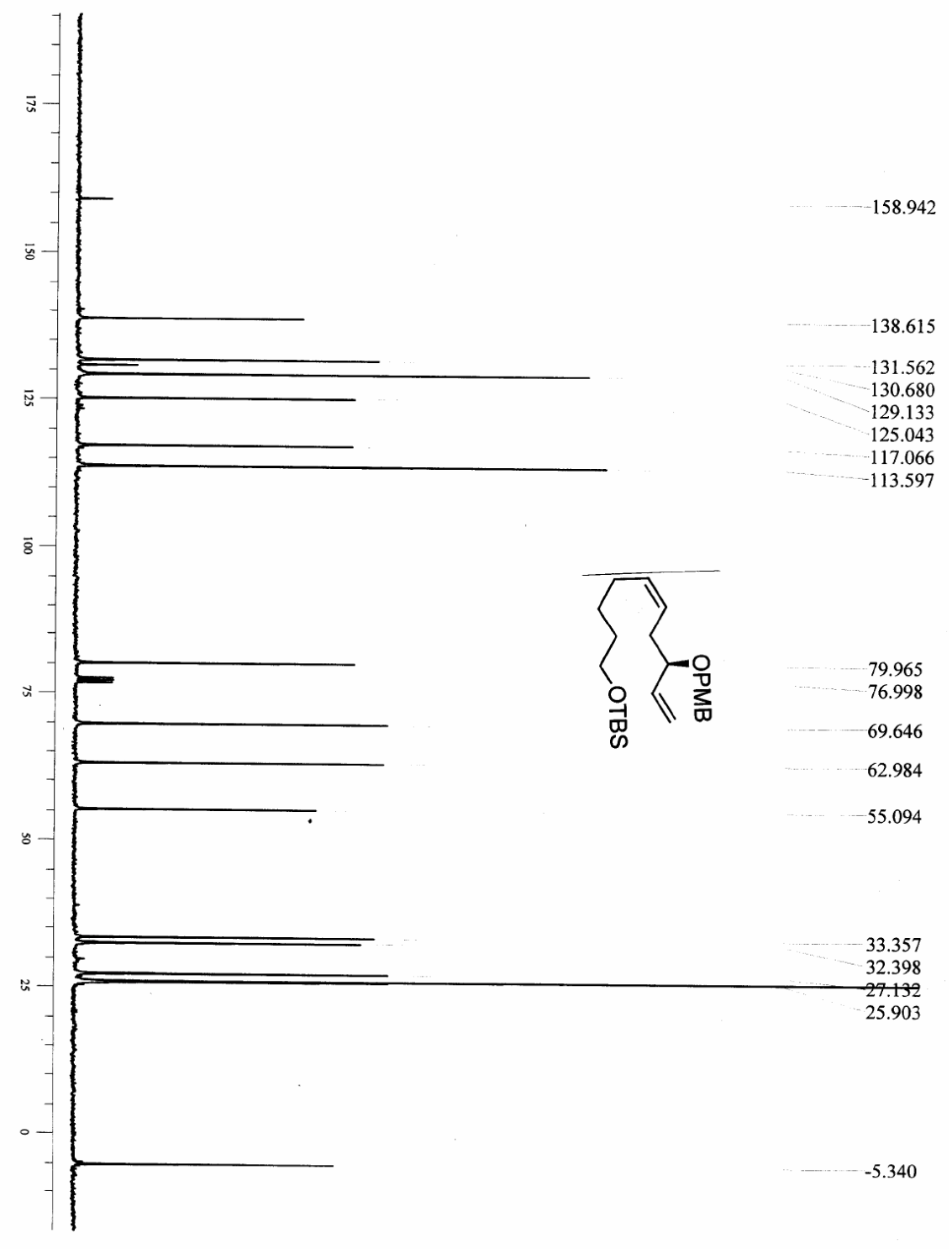
^{1}H NMR of 114 (300 MHz, $CDCl_3$)



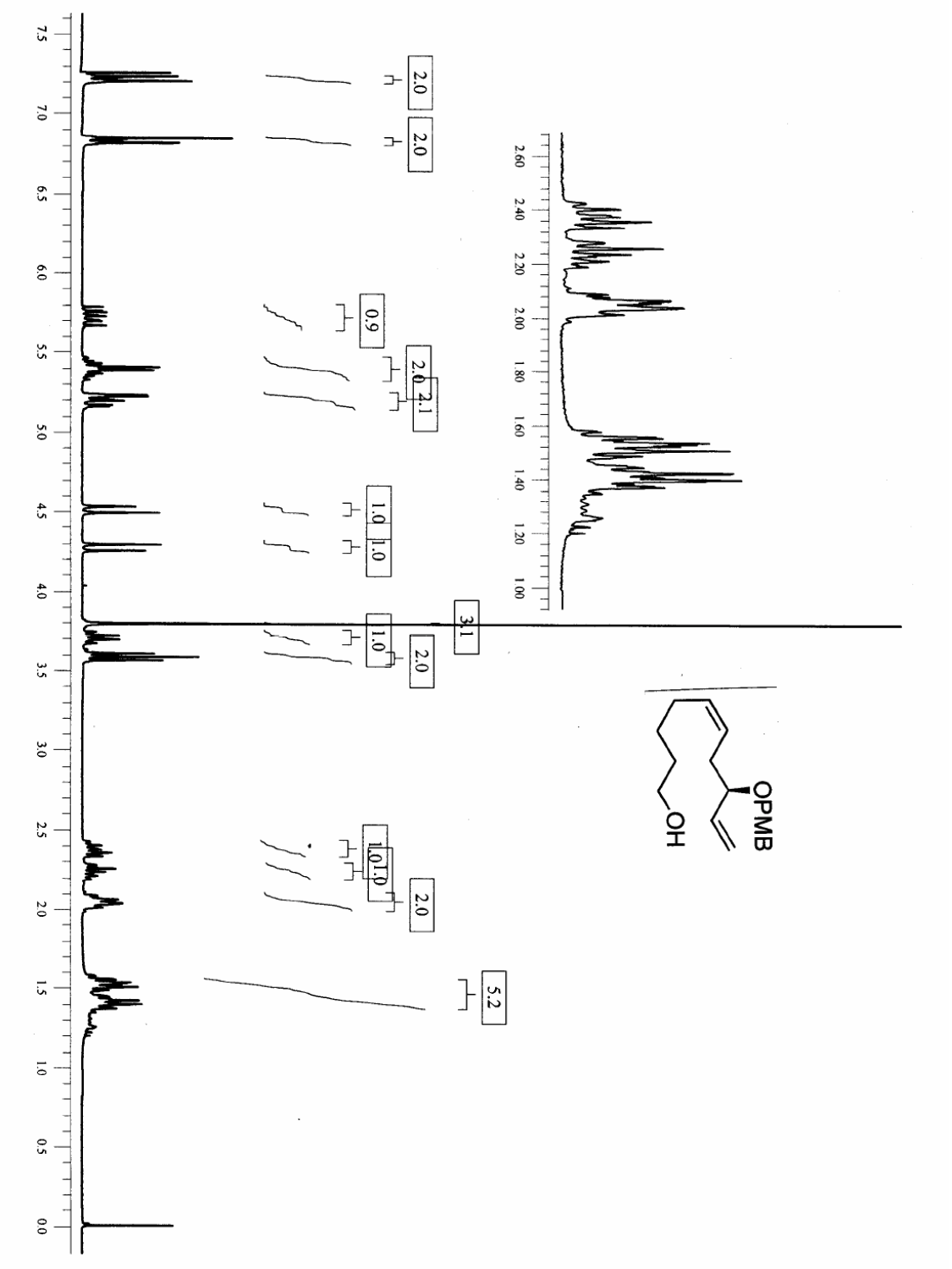
^{13}C NMR of 14 (75 MHz, $CDCl_3$)



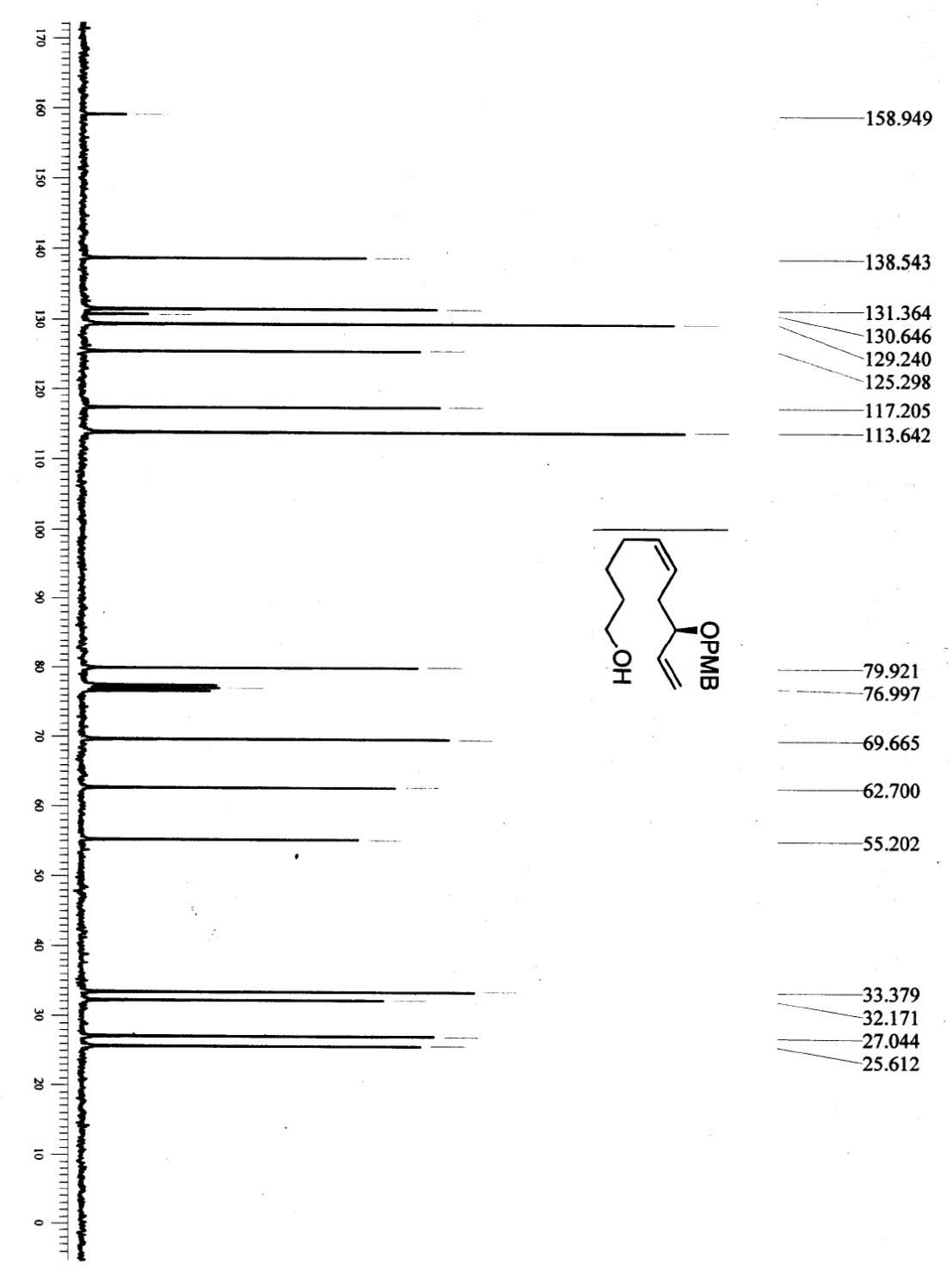
^{1}H NMR of PMB protected compound (300 MHz, $CDCl_3$)



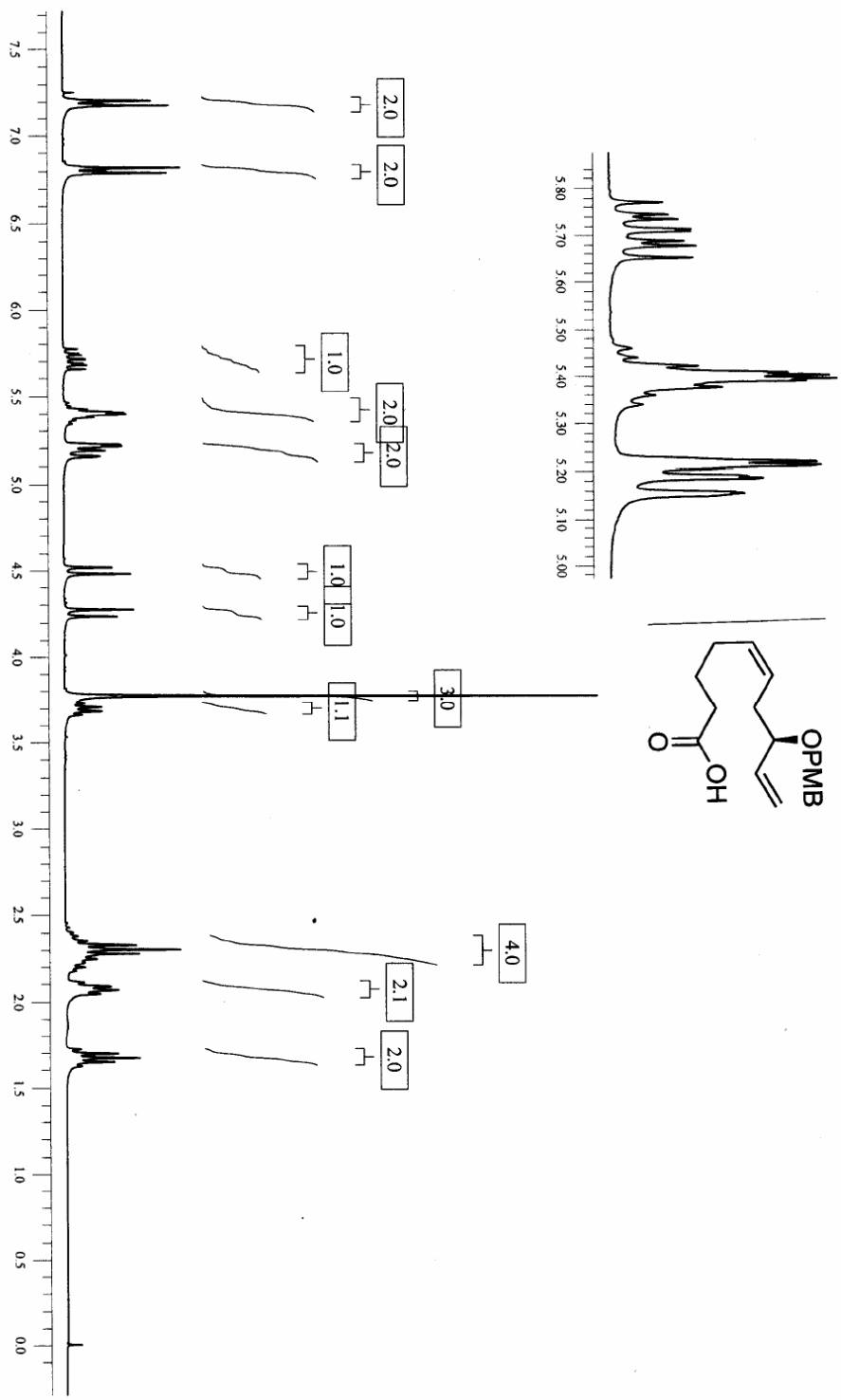
^{13}C NMR of PMB protected compound (75 MHz, CDCl



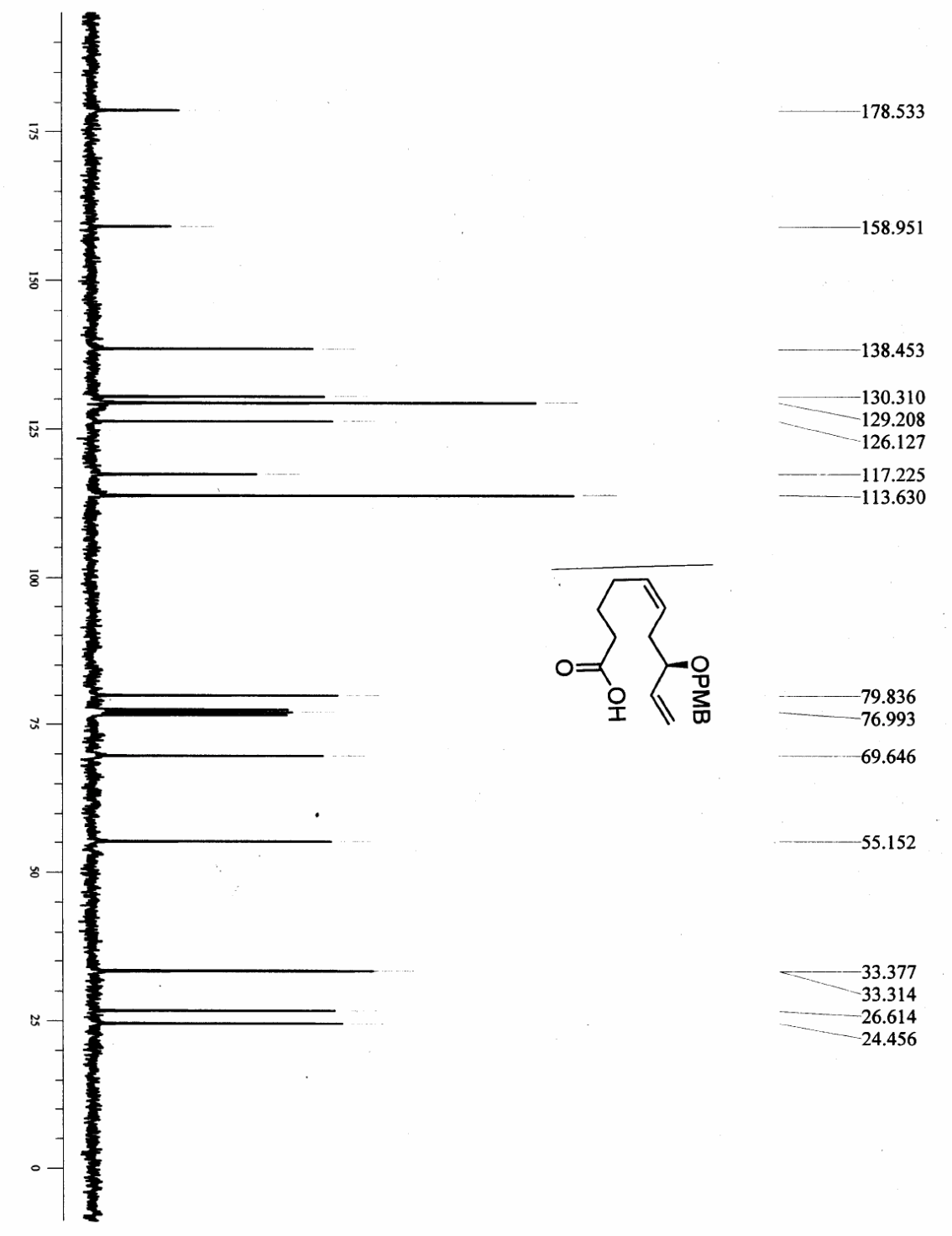
^{1}H NMR of 15 (300 MHz, $CDCl_3$)



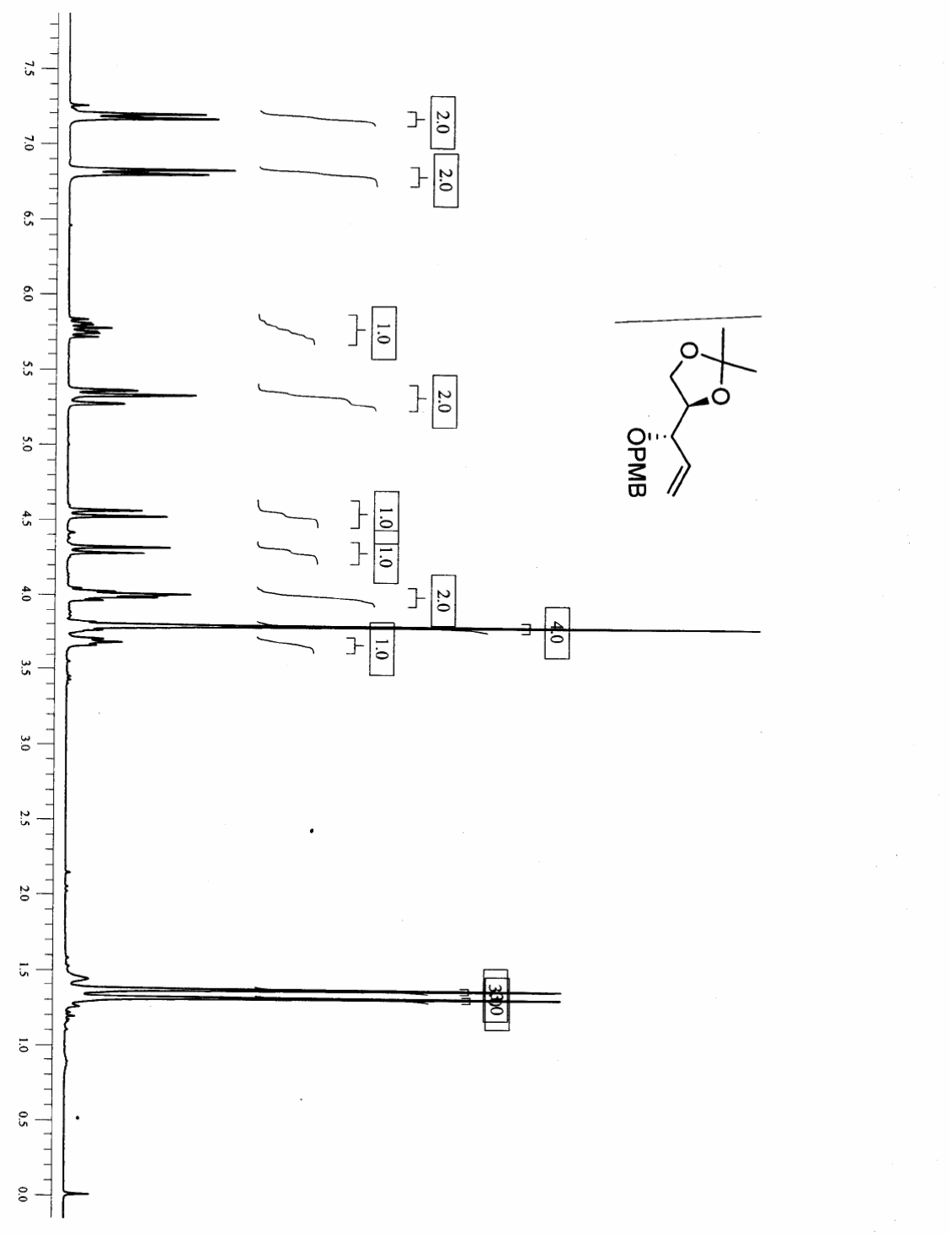
^{13}C NMR of 15 (75 MHz, $CDCl_3$)



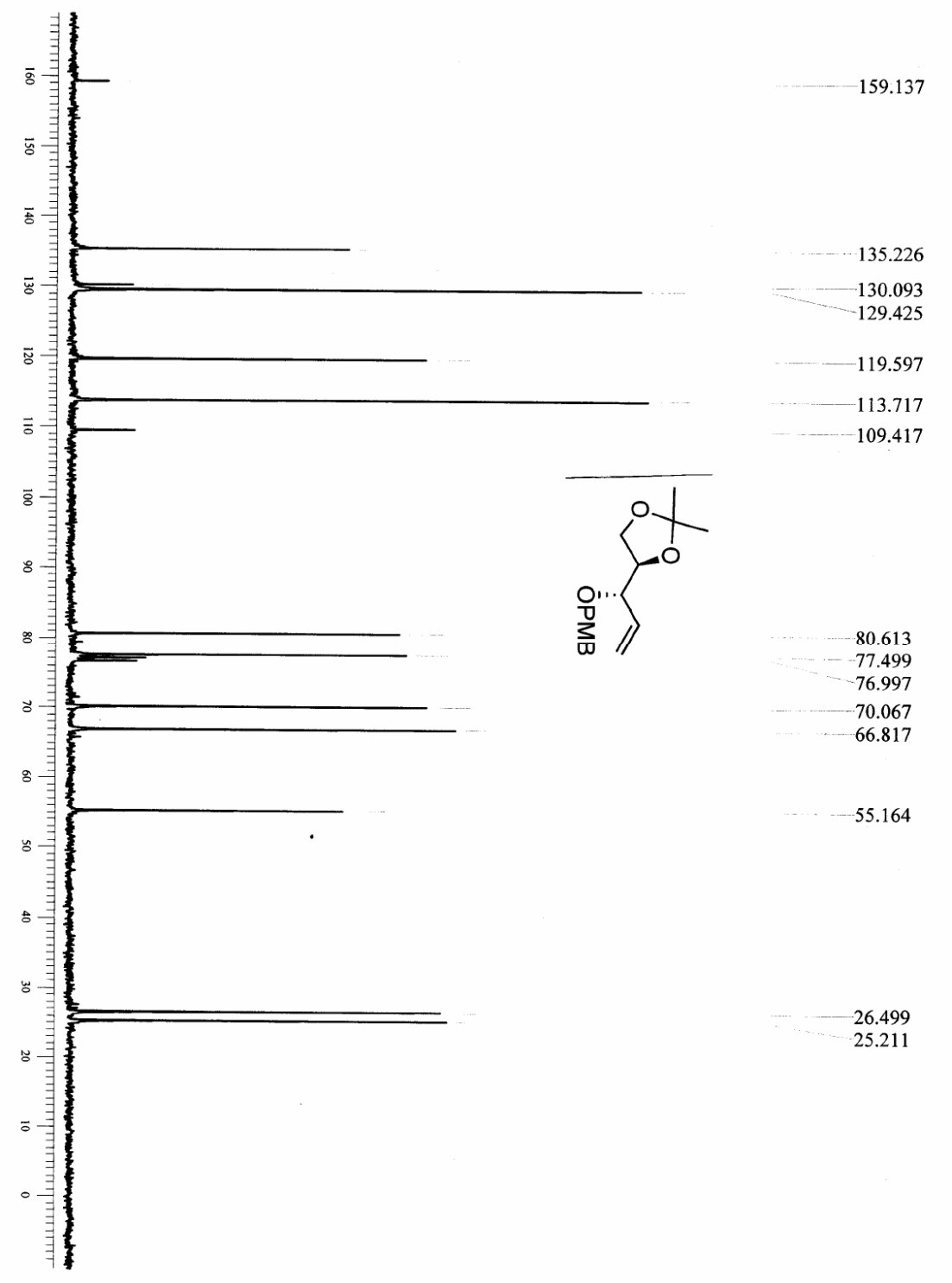
^{1}H NMR of 6 (300 MHz, $CDCl_3$)



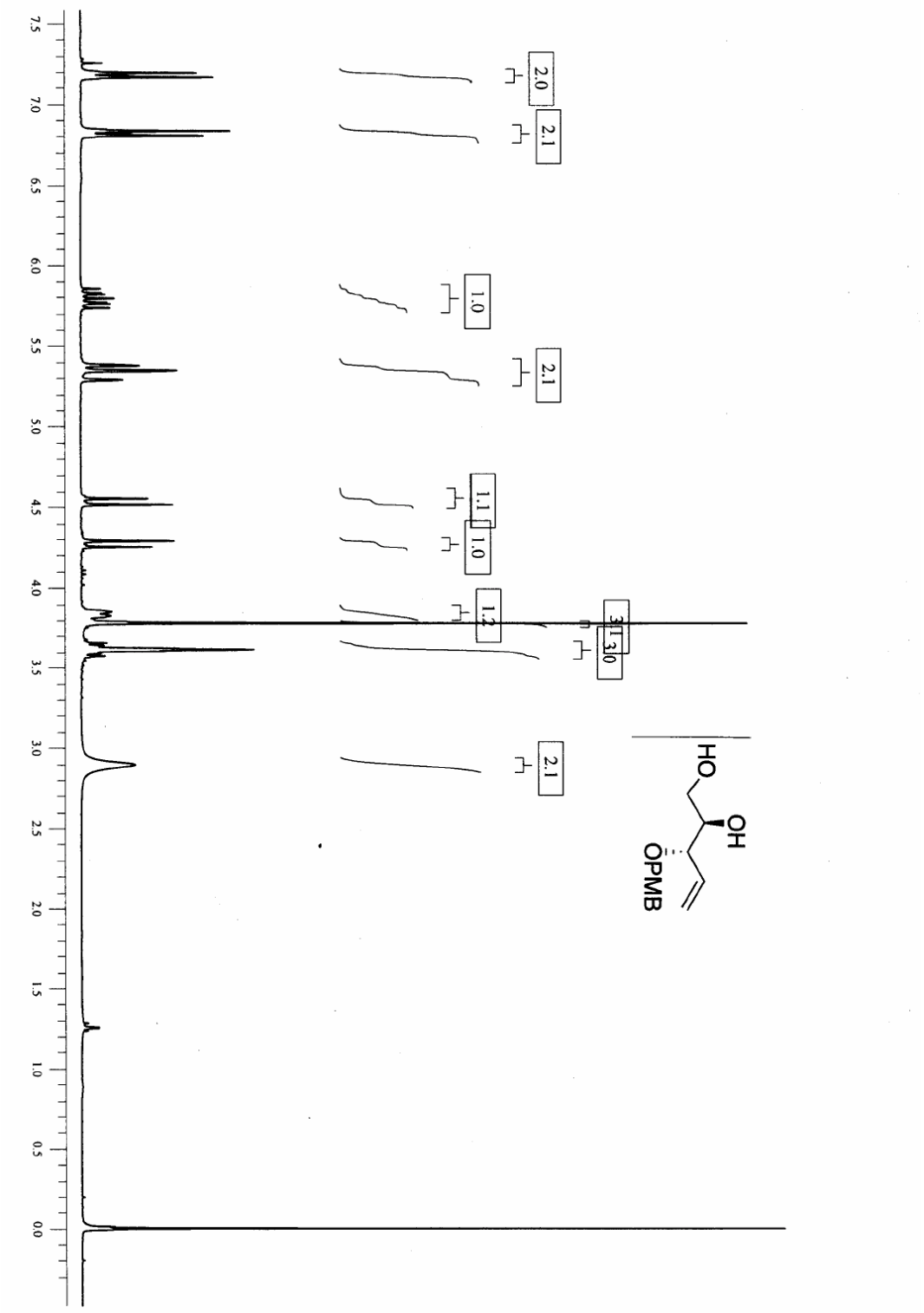
^{13}C NMR of 6 (75 MHz, $CDCl_3$)



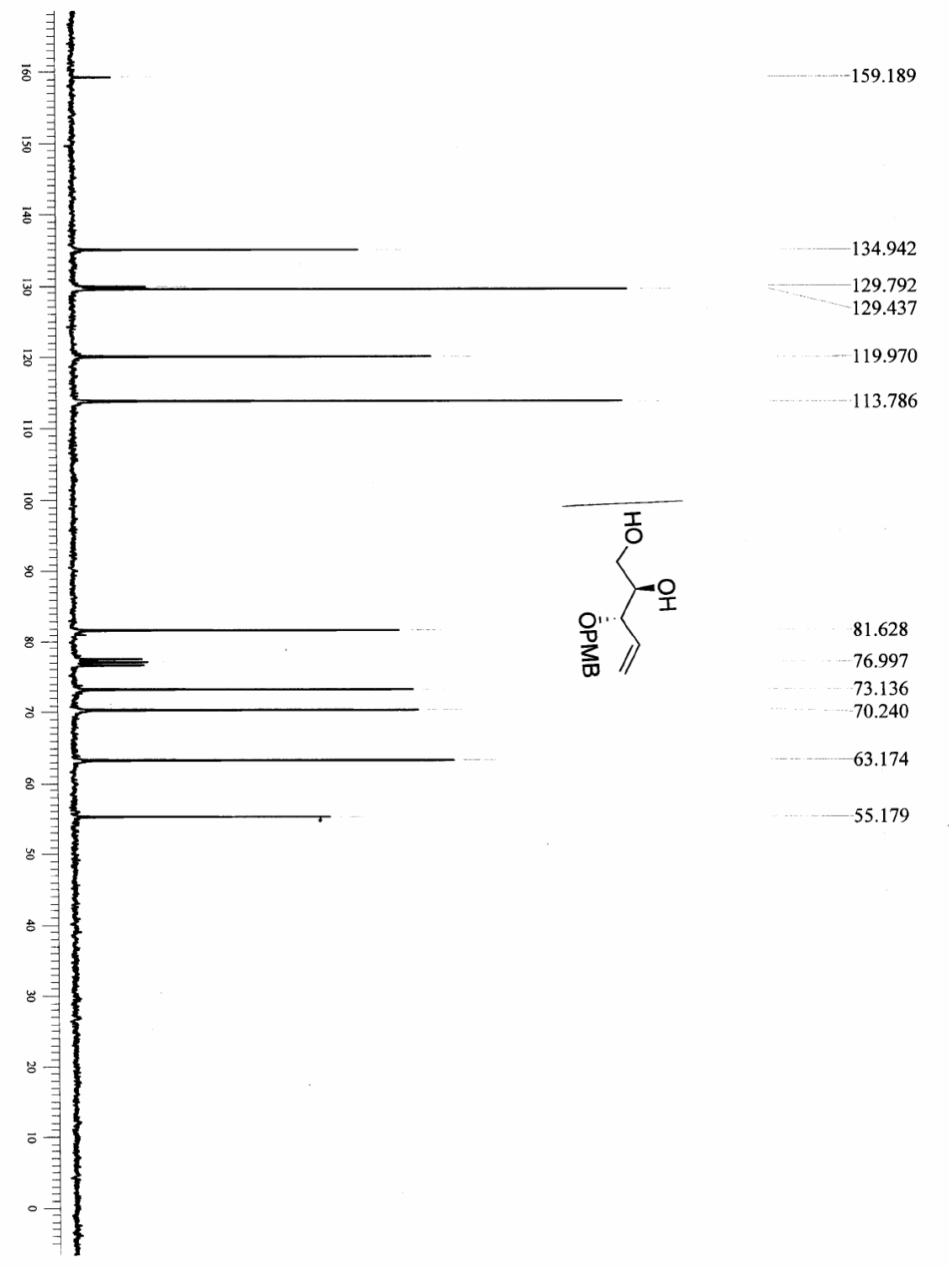
^{1}H NMR of 19 (300 MHz, $CDCl_3$)



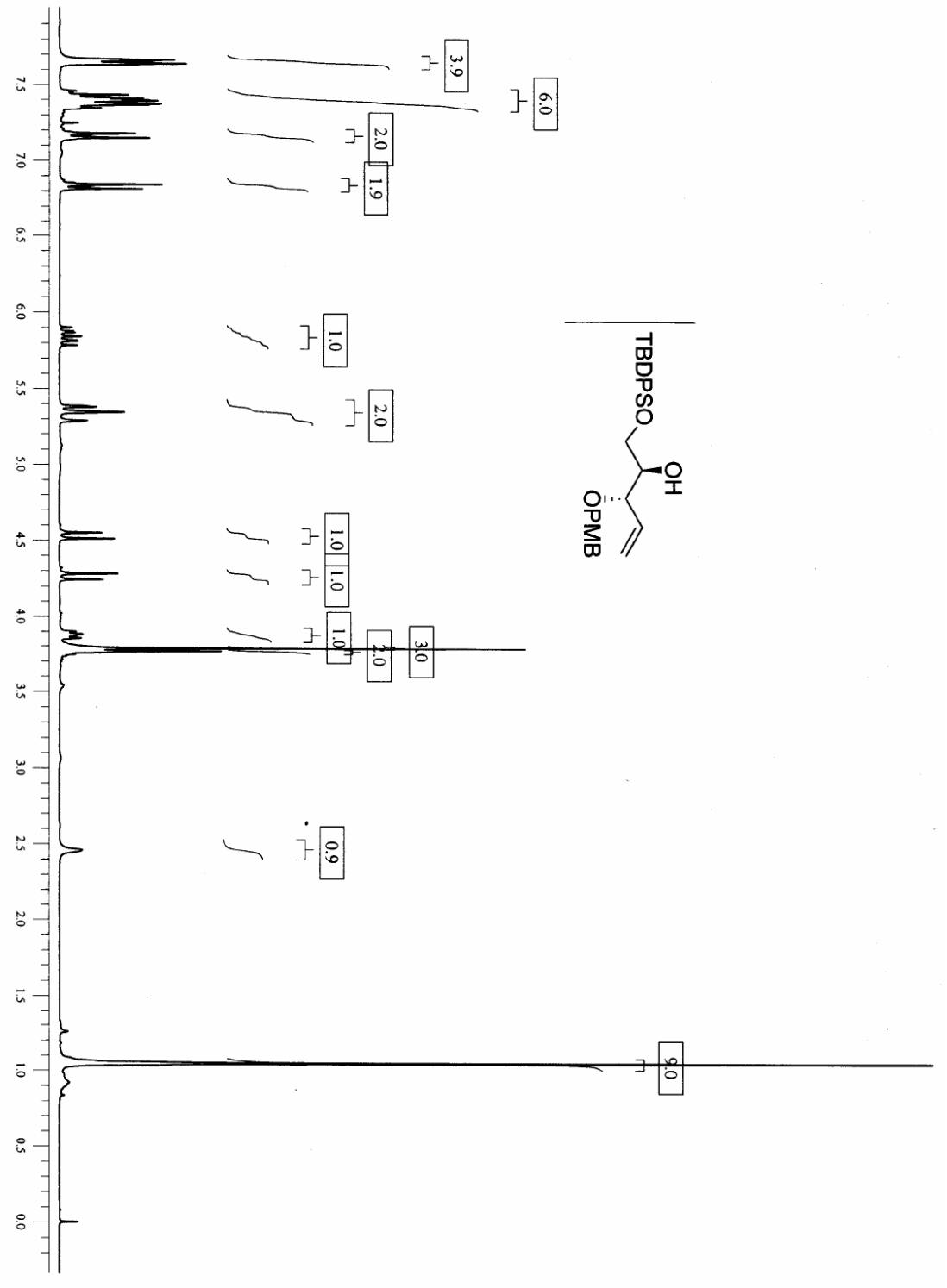
^{13}C NMR of 19 (75 MHz, $CDCl_3$)



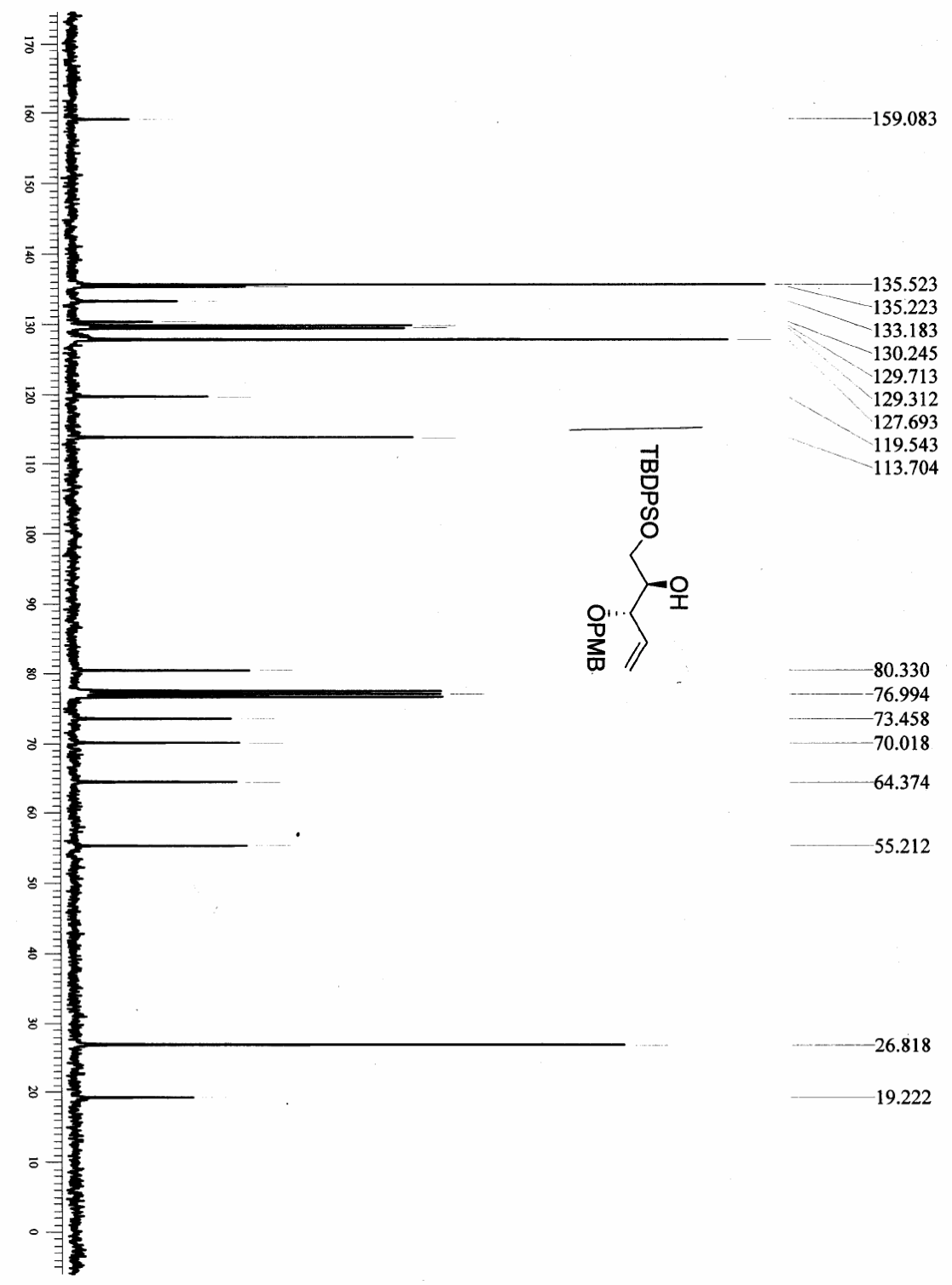
^{1}H NMR of 20 (300 MHz, $CDCl_3$)



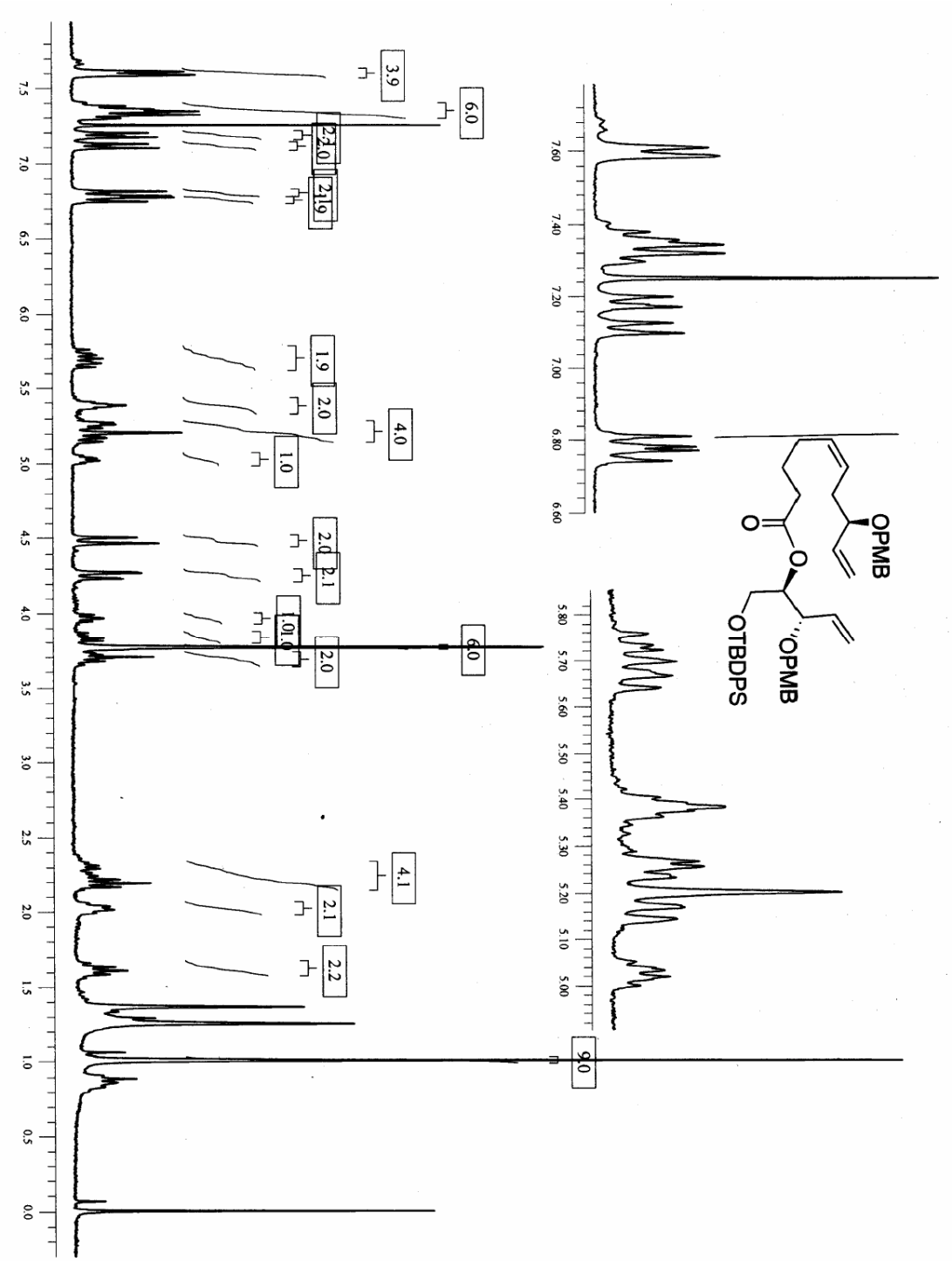
^{13}C NMR of 20 (75 MHz, $CDCl_3$)



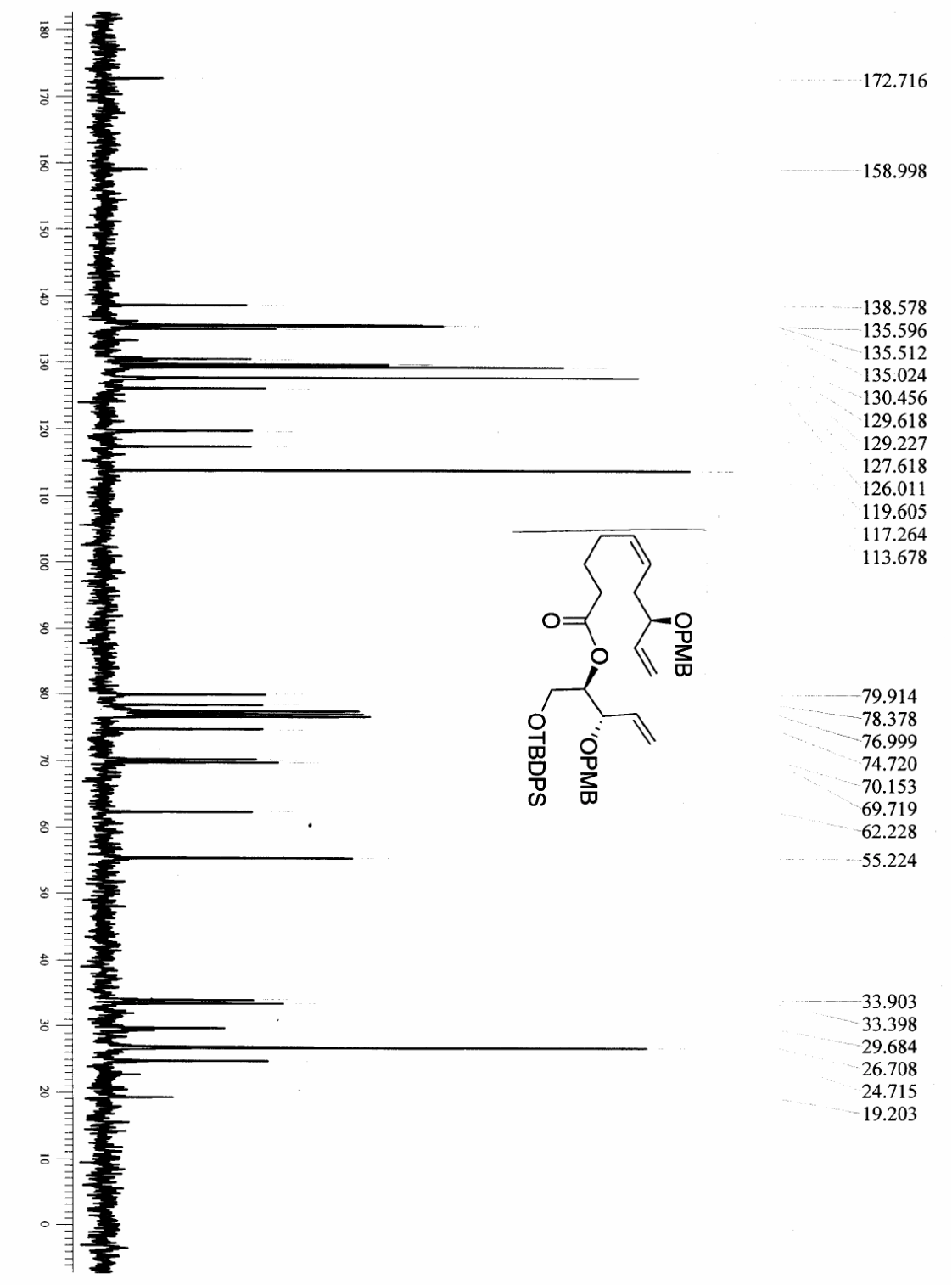
^{1}H NMR of 7 (300 MHz, $CDCl_3$)



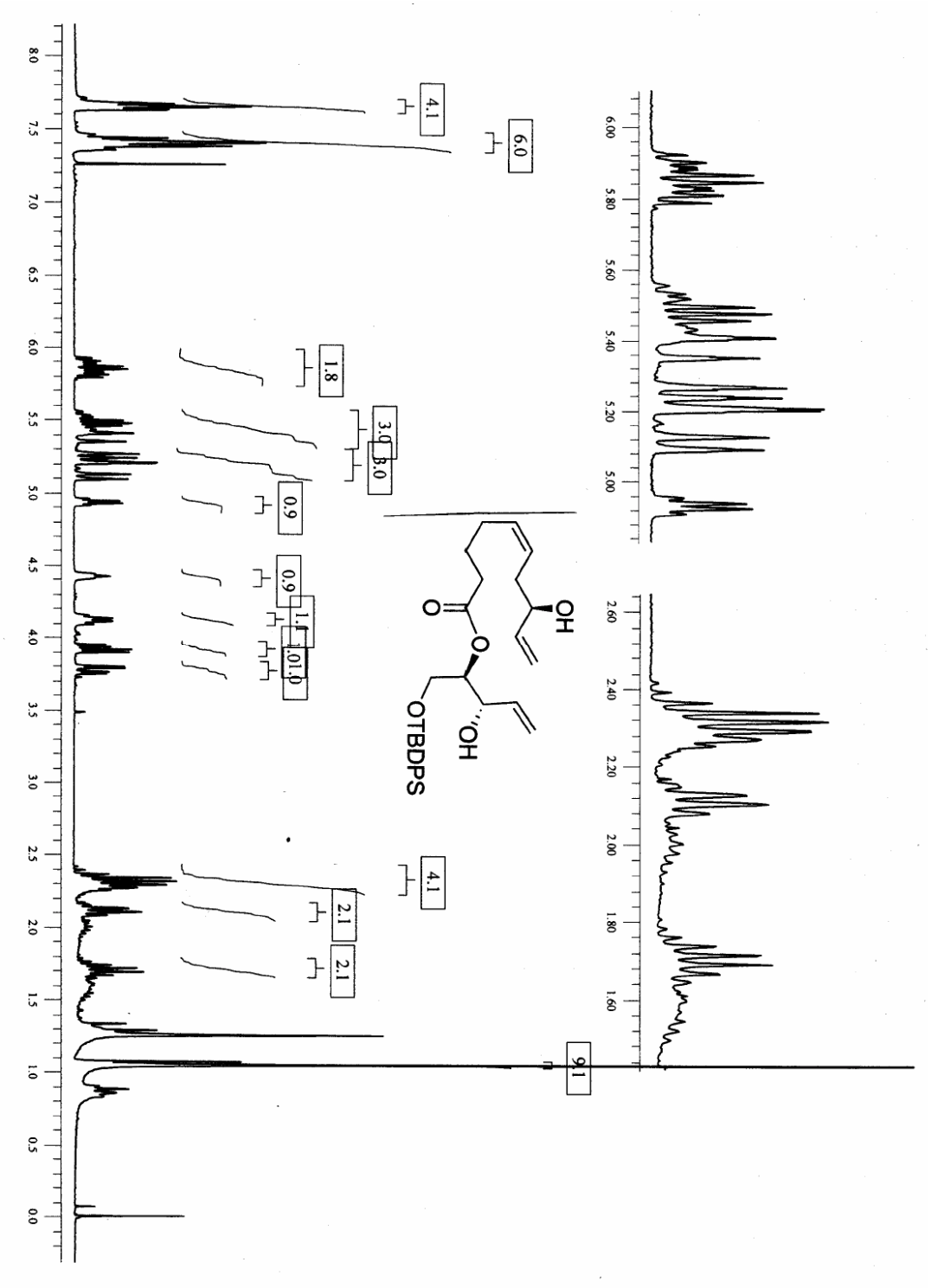
^{13}C NMR of 7 (75 MHz, $CDCl_3$)



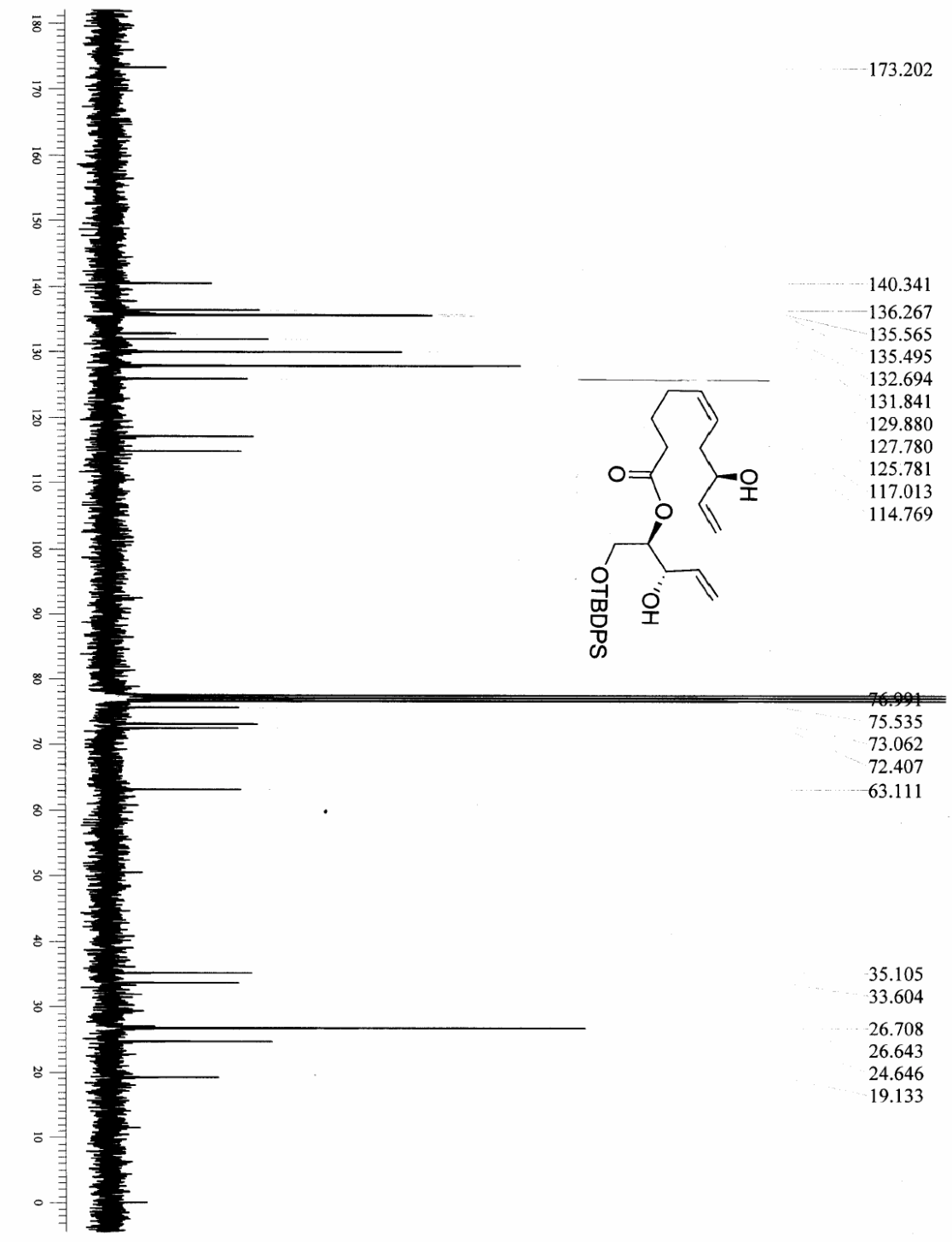
^{1}H NMR of 4 (300 MHz, $CDCl_3$)



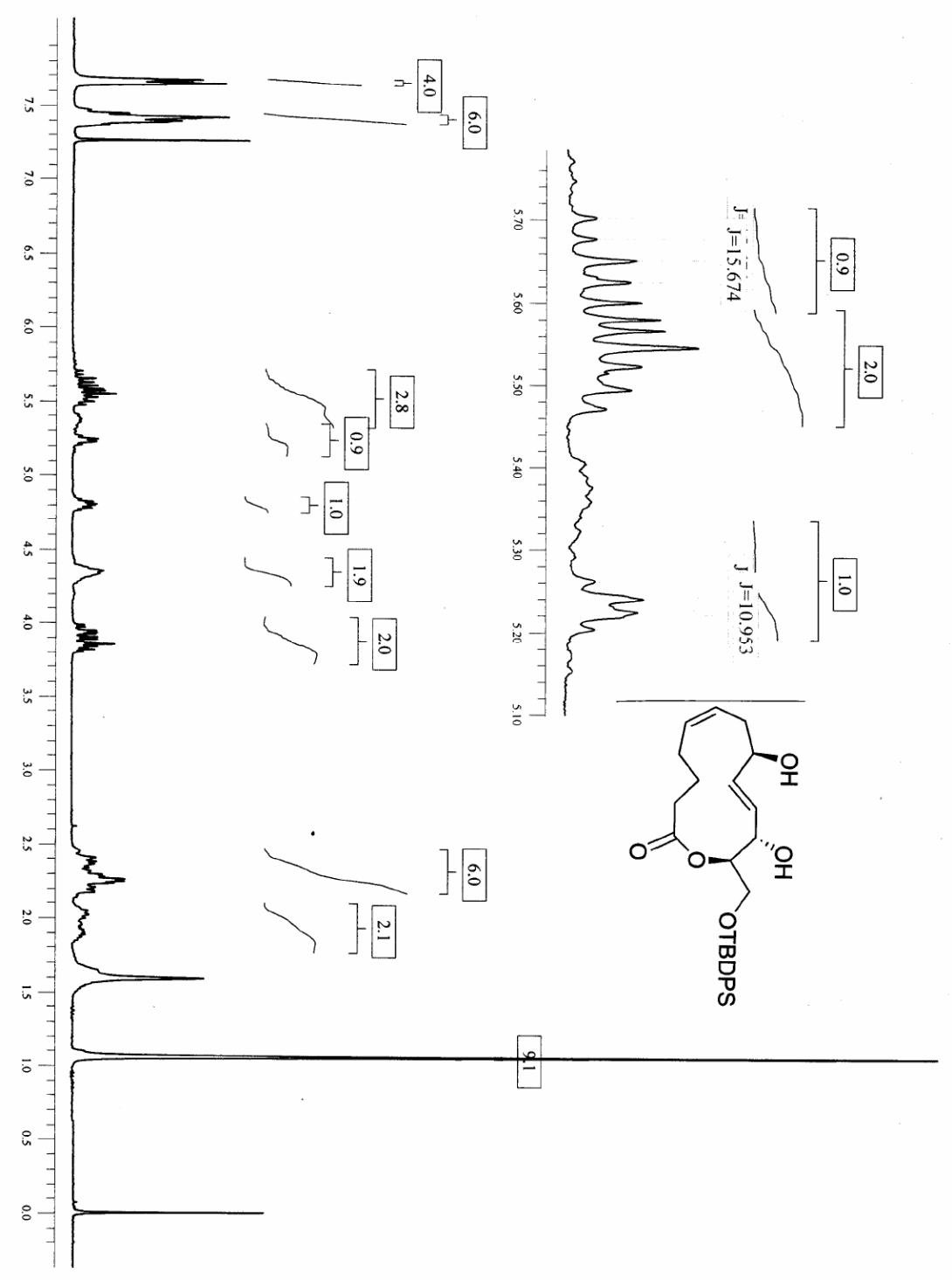
^{13}C NMR of 4 (75 MHz, $CDCl_3$)



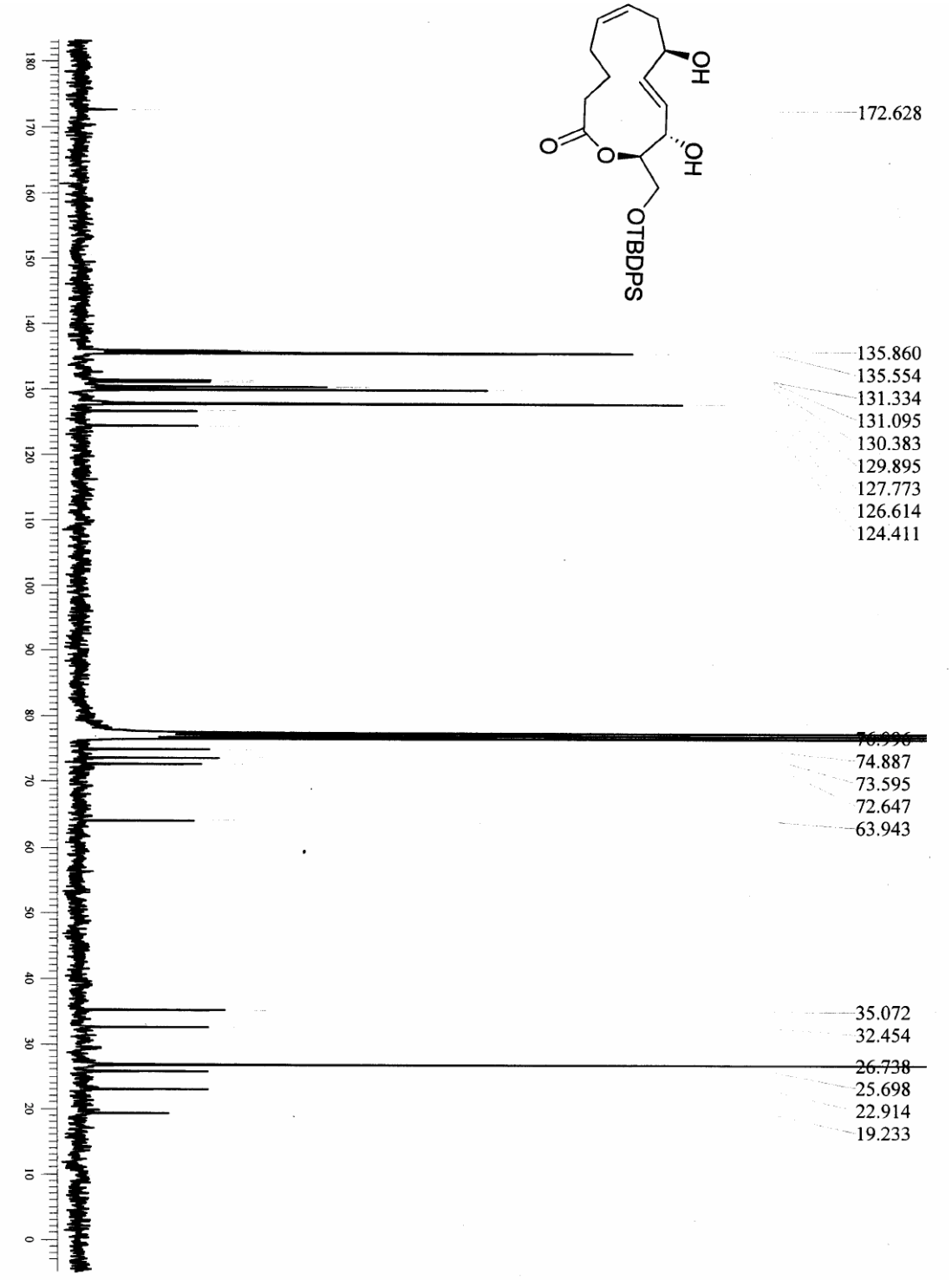
^{1}H NMR of 5 (300 MHz, $CDCl_3$)



^{13}C NMR of 5 (75 MHz, $CDCl_3$)



^{1}H NMR of 3 (300 MHz, $CDCl_3$)



^{13}C NMR of 3 (75 MHz, $CDCl_3$)