SUPPORTING INFORMATION

Carbohydrate-based first stereoselective total synthesis of bioactive cytospolide P

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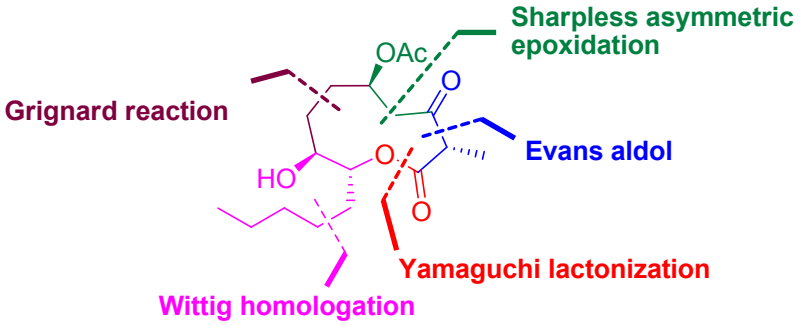
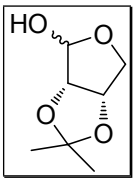


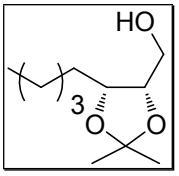
Experimental Section

General remarks: Air and/or moisture sensitive reactions were carried out in anhydrous solvents under an atmosphere of argon/nitrogen in an oven or flame-dried glassware. All anhydrous solvents were distilled prior to use: THF, benzene, toluene, diethyl ether from Na and benzophenone ketyl; CH_2Cl_2, DMS, from CaH_2; MeOH, from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using silica gel (60–120 and 100-200 mesh). Specific optical rotations were measured with digital polarimeter by using 1 mL cell with 1 dm path length and $[\alpha]_D^{20}$ values given in 10^{-1} degcm^{2}g^{-1}. Infrared spectra were recorded in KBr pellet (as mentioned) and reported in wave number (cm^{-1}). Mass analysis was carried out on ESI mode, TOF analyzer type was used for the HRMS measurement. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations were used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.



(3a*S*,6a*S*)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (6):

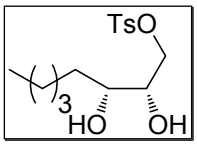
This compound was prepared as reported standard procedures from D-ribose; spectral data are in agreement with the literature values.[6]



((4*S*,5*R*)-2,2-dimethyl-5-propyl-1,3-dioxolan-4-yl)methanol (7): *n*-Butylphosphonium bromide (70 g, 123.51 mmol) was suspended in dry tetrahydrofuran (250 mL) at –78 ^{0}C under nitrogen atmosphere. *n*-Butyllithium (1.7 M in *n*-hexane, 76 mL, and 122.53 mmol) was added drop wise to the solution. The reaction mixture was stirred for 30 min at same temperature, a solution of lactol **6** (10 g, 62.52 mmol) in dry THF (50 mL) was added drop wise, stirring was continued for 2 h at -78 ^{0}C. The unreacted *n*-butylphosphonium bromide salt was filtered off, and the reaction mixture was extracted with ethyl acetate (2 X 100 ml). The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate/hexane,1:9) afforded olefin compound (9.6 g, 78%) as pale yellow oil. $[\alpha]_D^{20}$ –41.08 (*c* 2.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (t, *J* = 6.79 Hz, 3H), 1.40 (s, 3H), 1.44 (m, 2H), 1.50 (s, 3H), 2.07 (m, 2H), 3.55 (d, *J* = 5.28 Hz, 2H), 4.21 (q, *J* = 6.04 Hz, 1H), 5.00 (t, *J* = 8.30 Hz, 1H), 5.47 (m, 1H), 5.70 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.6, 22.5, 25.2, 27.8, 29.8, 62.1, 72.8, 78.3, 108.5, 124.3, 135.2 ppm;

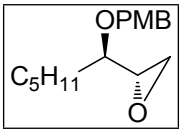
Pd/C (10% w/w, 750 mg) was added to a solution of compound (9.4 g, 47 mmol) in EtOH (45 mL) and the reaction mixture was stirred for 12 h under hydrogen atmosphere. After completion of the reaction (TLC), catalyst was filtered off and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (ethyl acetate/hexanes, 0.9:9.1) obtained alcohol compound **7** (9.2 g, 97%) as pale yellow oil. $[\alpha]_D^{20}$ –25.85 (*c* 2.0, $CHCl_3$); IR (KBr) 3447, 2932, 2865, 1461, 1375, 1217, 1167, 1043 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.01 (t, *J* = 6.51 Hz, 3H), 1.47-1.41 (m, 6H), 1.45 (s, 3H), 1.55 (s, 3H), 1.70-1.59 (m, 2H),

1.92 (s, 1H), 3.66 (m, 2H), 4.20 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 22.4, 25.5, 26.3, 28.2, 28.7, 31.7, 61.7, 77.9, 107.9 ppm; ESI (MS): 225 $[M+H]^+$.



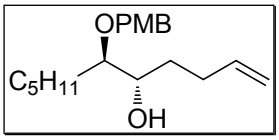
(2*S*,3*R*)-2,3-dihydroxyhexy*l* 4-methylbenzenesulfonate (8): TsCl (10.2 g, 53.52 mmol) was added to a solution of alcohol **7** (9 g, 44.51 mmol) in dry CH_2Cl_2 (180 mL) at 0 ^{0}C, followed by Et_3N (12.02 g, 111.38 mmol) and DMAP (0.27 g, 2.22 mmol) were added at the same temperature. The reaction mixture was warmed to room temperature for 14 h. After completion the reaction (TLC), the reaction mixture was washed with ice-water (2 x 70 mL), followed by brine solution (100 mL) and the reaction mixture were extracted with ethyl acetate (2 X 100 ml). The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate/hexane, 0.2:9.8) furnished tosylated compound (13.2 g, 83%) as pale yellow oil. $[\alpha]_D^{20}$ –20.13 (*c* 0.7, $CHCl_3$); IR (KBr) 2928, 1361, 1171, 981 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, *J* = 6.79 Hz, 3H), 1.28-1.22 (m, 5H), 1.28 (s, 3H), 1.30 (s, 3H), 1.47-1.34 (m, 3H), 2.44 (s, 3H), 3.88 (dd**,** *J* = 16.6, 9.8 Hz,1H), 4.01 (dd, *J* = 15.5, 10.1 Hz, 1H), 4.22-4.06 (m, 2H), 7.35 (d, *J* = 8.31 Hz, 2H), 7.80 (d, *J* = 8.31 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 21.5, 22.4, 25.3, 26.2, 27.9, 28.5, 31.6, 68.1, 74.7, 108.4, 127.9, 129.8, 132.6, 144.9 ppm; ESI (MS): 379 $[M+H]^+$.

TsOH (0.31 g, 1.82 mmol) was added to a solution of tosylated compound (13 g, 36.51 mmol) in MeOH (300 mL) at 0 ^{0}C. The reaction mixture was stirred for 12 h at room temperature. After completion of the reaction (TLC), the solvent was removed under reduced pressure, and the resulting residue was purified by silica gel column chromatography (ethyl acetate/hexane, 2:8) obtained diol **8** (9.81 g, 89%) as colourless solid. $[\alpha]_D^{20}$ +1.24 (*c* 1.1, $CHCl_3$); IR (KBr) 3546, 3325, 2927, 2855, 1364, 1173, 1071, 982 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 6.61 Hz, 3H), 1.52-1.24 (m, 8H), 2.45 (s, 3H), 3.80-3.63 (m, 2H), 4.22-4.09 (m, 2H), 7.36 (d, *J* = 8.12 Hz, 2H), 7.80 (d, *J* = 8.12 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 21.6, 22.4, 25.3, 31.6, 32.3, 71.2, 72.0, 72.2, 127.9, 129.9, 132.3, 145.1 ppm; HRMS (ESI): calcd. for ($C_{15}H_{24}O_5NaS$) $[M+Na]^+$ 339.1240, found 339.1236.

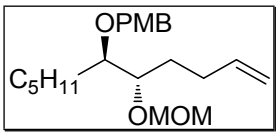


Synthesis of (*S*)-2-((*R*)-1-((4-methoxybenzyl)oxy)hexyl)oxirane (9): To a stirred solution of diol **8** (10 g, 33.11 mmol) in MeOH (220 mL), K_2CO_3 (4.8 g, 36.22 mmol) was added at 0^0C and the reaction mixture was stirred for 2 h at same temperature. The solid was removed by filtration and the filtrate was extracted with diethyl ether (3 x 60 mL). Organic extract was washed with brine (1 X 20 mL), the combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane, 0.5:9.5) afforded epoxy alcohol (3.96 g, 82%) as colorless liquid. $[\alpha]_D^{20}$ +11.54 (*c* 1.3, $CHCl_3$); IR (KBr) 3443, 2930, 2862, 1254, 1072, 945 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, *J* = 6.8 Hz, 3H), 1.65-1.29 (m, 8H), 2.74 (dd, *J* = 5.28, 3.77 Hz, 1H), 2.82 (t, *J* = 4.74 Hz, 1H), 3.03 (dd, *J* = 9.8, 3.0 Hz, 1H), 3.85 (dt, *J* = 6.79, 3.77 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.8, 22.4, 24.8, 31.7, 33.3, 43.4, 54.5, 68.5 ppm.

In the next step, to a stirred suspension of NaH (60%, 3.32 g, 83.33 mmol) in dry THF (40 mL) was added a solution of epoxy alcohol (10 g, 69.44 mmol) in anhydrous THF (120 mL) drop wise over a period of 10 min at 0 ^{0}C. The reaction mixture was stirred for 1 h at same temperature, then freshly prepared *p*-methoxybenzyl bromide (16.7 g, 83.33 mmol) was added at 0 ^{0}C over a period of 10 min, followed by addition of TBAI (1.28 g, 3.47 mmol) and the reaction mixture was warmed to room temperature until complete conversion of the starting material (TLC). Then cold water (20 mL) was added and the layers were separated, aqueous layer was extracted with ethyl acetate (2 x 80 mL). The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,0.3:9.7) to afforded *p*-methoxybenzyl ether compound **9** (14.66 g, 80%) as colorless liquid. $[\alpha]_D^{20}$ +13.5 (*c* 4.1, $CHCl_3$); IR (KBr) 2930, 2860, 1612, 1513, 1248, 1084, 1036, 822 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 6.98 Hz, 3H), 1.23-1.65 (m, 8H), 2.69-2.72 (dd, *J* = 2.64, 5.28 Hz, 1H), 2.77-2.80 (dd, *J* = 3.96, 5.28 Hz, 1H), 2.90-2.94 (m, 1H), 3.24 (q, *J* = 5.47 Hz, 1H), 3.80 (s, 3H), 4.46 (d, *J* = 11.33 Hz, 1H), 4.58 (d, *J* = 11.33 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 1H), 7.25 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 22.5, 24.7, 31.7, 32.7, 45.5, 53.5, 55.1, 71.8, 77.6, 113.6, 129.2, 130.6, 159.1 ppm; HRMS (ESI): calcd. for $C_{16}H_{24}O_3Na$ $[M+Na]^+$ 287.1623, found 287.1617.

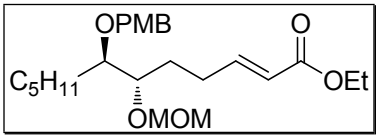


Synthesis of (5*S*,6*R*)-6-((4-methoxybenzyl)oxy)undec-1-en-5-ol (10): CuBr (352 mg, 2.46 mmol) was added to a stirred solution of epoxide **9** (13 g, 49.24 mmol) in dry THF (100 mL) at 0 ^{0}C, and followed by 73 mL 1.0 M solution of ally magnesium bromide in Et_2O was added drop wise. After addition was complete, the reaction mixture was stirred for 2 hours at the same temperature. The reaction was quenched with sat. aq. NH_4Cl (100 ml) and the mixture was stirred for 20 minutes at 0 ^{0}C, and the layers were separated, aqueous layer was extracted with ethyl acetate (3 x 40 mL). The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane, 0.5:9.5) to afford secondary alcohol **10** (13.10 g, 87%) as pale yellow oil. $[\alpha]_D^{20}$ +8.85 (*c* 1.3, $CHCl_3$); IR (KBr) 3445, 2932, 2857, 1612, 1513, 1249, 1094, 1033, 803 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 6.98 Hz, 3H), 1.23-1.68 (m, 10H), 2.04-2.16 (m, 1H), 2.22-2.34 (m, 1H), 3.31-3.36 (m, 1H), 3.76-3.80 (m, 1H), 3.82 (s, 3H), 4.46 (d, *J* = 11.33 Hz, 1H), 4.53 (d, *J* = 11.33 Hz, 1H), 4.98 (dd, *J* = 1.51, 10.19 Hz, 1H), 5.04 (dd, *J* = 1.51, 16.99 Hz, 1H), 5.77-5.90 (m, 1H), 6.88 (d, *J* = 8.68 Hz, 1H), 7.25 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 22.5, 25.3, 28.7, 30.3, 31.1, 31.9, 55.1, 71.1, 71.5, 81.7, 113.7, 114.7, 129.3, 130.5, 138.3, 159.1 ppm; HRMS (ESI): calcd. for $C_{19}H_{30}O_3Na$ $[M+Na]^+$ 329.2095, found 329.2087.

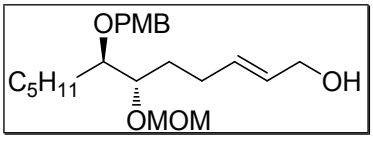


Synthesis of 1-methoxy-4-((((5*S*,6*R*)-5-(methoxymethoxy)undec-1-en-6-yl)oxy)methyl) benzene (5): Diisopropyl ethyl amine (20.27 g, 156.88 mmol) was added to a stirred solution of alcohol **10** (12 g, 39.22 mmol) in dry CH_2Cl_2 (80 mL) at 0^{0}C, followed by MOMCl (6.31 mL,78.44 mmol) was added slowly at the same temperature. The reaction was warmed to room temperature for 8 h. After completion of the reaction (TLC), quench with ice water (30 mL), extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts weredried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,0.4:9.6) afforded compound **5** (11.66 g, 85%) as pale yellow oil. R_f = 0.5 ethyl acetate hexane, 1:9). $[\alpha]_D^{20}$ +0.08 (*c* 1.2, $CHCl_3$); IR (KBr)

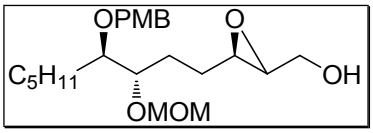
2931, 2860, 1513, 1247, 1093, 1035, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, J = 7.17 Hz, 3H), 1.20-1.60 (m, 9H), 1.68-1.76 (m, 1H), 2.06-2.14 (m, 1H), 2.22-2.28 (m, 1H), 3.37-3.43 (m, 1H), 3.40 (s, 3H), 3.70-3.73 (m, 1H), 3.79 (s, 3H), 4.42 (d, J = 11.13 Hz, 1H), 4.63 (d, J = 11.13 Hz, 1H), 4.64 (d, J = 6.86 Hz, 1H), 4.78 (d, J = 6.86 Hz, 1H), 4.98 (dd, J = 1.98, 10.52 Hz, 1H), 5.05 (dd, J = 1.67, 15.56 Hz, 1H), 5.79-5.87 (m, 1H), 6.88 (d, J = 8.68 Hz, 1H), 7.25 (d, J = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.0, 22.5, 25.7, 29.9, 30.1, 30.4, 31.8, 55.1, 55.7, 71.7, 77.9, 80.5, 96.2, 113.6, 114.7, 129.4, 130.8, 138.4, 159.0 ppm; HRMS (ESI): calcd. for $C_{21}H_{34}O_4Na$ $[M+Na]^+$ 373.2348, found 373.2356.



Synthesis of (6*S*,7*R*,*E*)-ethyl 7-((4-methoxybenzyl)oxy)-6-(methoxymethoxy)dodec-2-enoate (11): A solution of olefin compound **5** (11 g, 31.43 mmol) in CH_2Cl_2 (120 mL) was cooled to -78 ^{0}C, then it was bubbled with ozone until the color began to turn blue. The excess of ozone was removed by bubbling argon through the solution. The reaction was quenched with PPh_3 (8.23 g, 31.43 mmol) at –78 ^{0}C and the mixture was warmed to room temperature for 1 h. The solvent was evaporated to dryness to afford the carbaldehyde. The crude aldehyde was taken in benzene and $Ph_3P{=}CHCO_2Et$ (13.12 g, 37.71 mmol) was added at room temperature. After stirring for 2 h, the solvent was concentrated in vacuo and purified by column chromatography (ethyl acetate hexane, 0.5:9.5) afforded pure (*E*)-α,β-unsaturated ester **11** (10.87 g, 82% yield from two steps) as pale yellow oil. $[\alpha]_D^{20}$ –3.07 (*c* 2.7, $CHCl_3$); IR (KBr) 3450, 2931, 1719, 1651, 1251, 1096, 1035, 771 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, J = 7.17 Hz, 3H), 1.20-1.62 (m, 12H), 1.75-1.82 (m, 1H), 2.21-2.29 (m, 1H), 2.35-2.43 (m, 1H), 3.37-3.44 (m, 1H), 3.40 (s, 3H), 3.65-3.68 (m, 1H), 3.80 (s, 3H), 4.18 (q, J = 7.17 Hz, 2H), 4.44 (d, J = 11.13 Hz, 1H), 4.61 (d, J = 11.13 Hz, 1H), 4.63 (d, J = 7.62 Hz, 1H), 4.78 (d, J = 6.86 Hz, 1H), 5.84 (d, J = 15.56 Hz, 1H), 6.86 (d, J = 8.68 Hz, 1H), 6.98 (td, J = 6.86, 15.71 Hz, 1H), 7.26 (d, J = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 14.2, 22.5, 25.5, 28.5, 28.9, 30.5, 31.8, 55.6, 55.8, 60.1, 71.8, 78.1, 80.2, 96.2, 113.6, 121.4, 129.3, 130.6, 148.7, 159.0, 166.5 ppm; HRMS (ESI): calcd. for $C_{24}H_{38}O_6Na$ $[M+Na]^+$ 445.2556, found 445.2560.

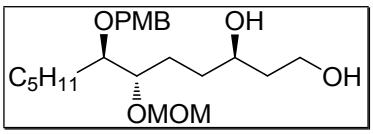


Synthesis of (6*S*,7*R*,*E*)-7-((4-methoxybenzyl)oxy)-6-(methoxymethoxy)dodec-2-en-1-ol (12): DIBAL-H (1.76 M in toluene, 29.61 mL, 52.14 mmol) was added to a solution of ester **11** (10 g, 23.7 mmol) in CH_2Cl_2 (110 mL) at –20 ^{0}C slowly drop wise for 20 min. After the mixture was stirred for 45 min., the reaction was quenched with a solution of sat. sodium potassium tartarate (40 mL) and the mixture were allowed to room temperature for 1 h. The layers were separated, extracted with EtOAc (2 X 50 mL). The combined organic extracts weredried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,1.5:8.5) afforded allylic alcohol **12** (7.20 g, 78%) as pale yellow oil. R_f = 0.2 ethyl acetate hexane, 2:8). $[\alpha]_D^{20}$ –0.20 (*c* 0.5, $CHCl_3$); IR (KBr) 3422, 2932, 2859, 1612, 1513, 1248, 1094, 1034, 821 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 7.17 Hz, 3H), 1.20-1.59 (m, 8H), 1.70 (m, 2H), 2.10 (m, 1H), 2.28 (m, 1H), 3.41 (m, 1H), 3.39 (s, 3H), 3.70 (m, 1H), 3.79 (s, 3H), 4.09 (m, 2H), 4.44 (d, *J* = 11.13 Hz, 1H), 4.62 (d, *J* = 11.13 Hz, 1H), 4.63 (d, *J* = 6.86 Hz, 1H), 4.77 (d, *J* = 6.86 Hz, 1H), 5.64-5.73 (m, 2H), 6.86 (d, *J* = 8.68 Hz, 1H), 6.98 (td, *J* = 6.86, 15.71 Hz, 1H), 7.25 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.0, 22.6, 25.7, 28.7, 30.1, 30.4, 31.9, 55.2, 55.7, 63.5, 71.7, 78.0, 80.5, 96.1, 113.7, 129.4, 130.8, 132.5, 159.1 ppm; HRMS (ESI): calcd. for $C_{22}H_{36}O_5Na$ $[M+Na]^+$ 403.2456, found 403.2455.

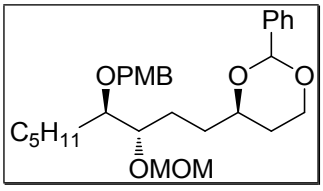


Synthesis of ((3*R*)-3-((3*S*,4*R*)-4-((4-methoxybenzyl)oxy)-3-(methoxymethoxy)nonyl) oxiran-2-yl)methanol (13): 4-Å molecular sieves powder (4.0 g) and CH_2Cl_2 (60 mL) were taken in a two-necked 250-mL round bottomed flask, the suspension was cooled to –20 ^{0}C, Ti(O*i*Pr)$_4$ (1.04 g, 3.68 mmol) and D-(–) DIPT (0.86 g, 3.68 mmol) were subsequently added with stirring and the resulting mixture was stirred for 0.5 h at –20 ^{0}C. Compound **12** (7 g, 18.42 mmol) in anhydrous CH_2Cl_2 (30 mL) was added, the resulting mixture was stirred for another 0.5 h at same temperature followed by the addition of TBHP (4.1 M solution in toluene, 6.73 mL,27.63 mmol) was added and the resulting mixture was stirred at the same temperature for 3 h. It was then warmed to 0 ^{0}C, quenched with 1.0 mL of water, and stirred for 1 h, after that 30% aqueous NaOH solution (1.0 mL) was added and the reaction mixture was stirred vigorously for another 0.5 h at room temperature. The resulting mixture was then filtered through celite, rinsing with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel

column chromatography (ethyl acetate hexane,1.8:8.2) to afford epoxy alcohol **13** (6.33 g, 87%) as pale yellow oil. $[\alpha]_D^{20}$ +6.39 (*c* 2.3, $CHCl_3$); IR (KBr) 3449, 2925, 2855, 1612, 1094, 1034, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 7.17 Hz, 3H), 1.23-1.87 (m, 11H), 2.03-2.09 (m, 1H), 2.91-2.98 (m, 1H), 3.35-3.45 (m, 1H), 3.42 (s, 3H), 3.58-3.74 (m, 2H), 3.80 (s, 3H), 3.83-3.90 (m, 1H), 4.44 (d, *J* = 11.14 Hz, 1H), 4.60 (d, *J* = 11.13 Hz, 1H), 4.63 (d, *J* = 6.79 Hz, 1H), 4.76 (d, *J* = 6.79 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 1H), 7.26 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 22.4, 25.5, 26.9, 228.2, 30.4, 31.8, 55.1, 55.7, 55.9, 58.5, 61.6, 71.7, 78.30, 80.3, 96.1, 113.5, 129.3, 130.7, 158.9 ppm; HRMS (ESI): calcd. for $C_{22}H_{36}O_6Na$ $[M+Na]^+$ 419.2399, found 419.2404.

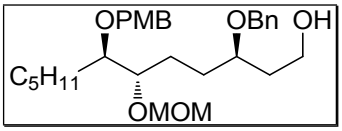


Synthesis of (3*R*,6*S*,7*R*)-7-((4-methoxybenzyl)oxy)-6-(methoxymethoxy)dodecane-1,3-diol: Red-Al (7.06 mL, 3.2 M solution in toluene, 22.73 mmol) was added to a solution of epoxy alcohol **13** (6 g, 15.15 mmol) in anhydrous THF (70 mL) at 0 ^0C over period of 30 min. After stirring 2 h at the same temperature, sat. aq. NH_4Cl solution was added. The organic layer was washed with brine, The combined organic extracts were dried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane, 3:7) obtained diol (5.48 g, 91%) as colour less oil. $[\alpha]_D^{20}$ +7.3 (*c* 1.3, $CHCl_3$); IR (KBr) 3421, 2931, 2865, 1613, 1513, 1093, 1034, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 7.17 Hz, 3H), 1.22-1.71 (m, 14H), 3.40 (s, 3H), 3.42 (m, 1H), 3.70 (m, 1H), 3.80 (s, 3H), 3.83-3.90 (m, 3H), 4.44 (d, *J* = 11.14 Hz, 1H), 4.60 (d, *J* = 11.13 Hz, 1H), 4.65 (d, *J* = 6.79 Hz, 1H), 4.78 (d, *J* = 6.79 Hz, 1H), 6.87 (d, *J* = 8.68 Hz, 1H), 7.26 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.0, 22.6, 25.6, 26.8, 30.4, 31.9, 34.0, 38.4, 55.2, 55.8, 71.8, 78.9, 80.5, 96.3, 113.7, 129.4, 130.7, 159.1 ppm; HRMS (ESI): calcd. for $C_{22}H_{38}O_6Na$ $[M+Na]^+$ 421.2554, found 421.2560.



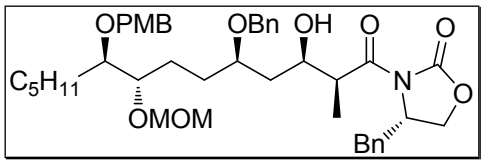
Synthesis of (4*R*)-4-((3*S*,4*R*)-4-((4-methoxybenzyl)oxy)-3-(methoxymethoxy)nonyl)-2-phenyl-1,3-dioxane (14): A catalytic amount of PPTS was added to a solution of diol

compound (5.30 g, 13.32 mmol) in anhydrous CH_2Cl_2 (60 mL) at 0 ^{0}C and followed by benzyl dimethyl acetal (2.42 g, 15.98 mmol) was added. After stirring 2 h at the same temperature, sat. aq. $NaHCO_3$ solution was added. The organic layer was washed with brine, The combined organic extracts weredried over Na_2SO_4, organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,1:9) afforded benzylidene acetal compound **14** (5.37 g, 83%) as colour less oil. $[\alpha]_D^{20}$ +6.86 (*c* 0.7, $CHCl_3$); IR (KBr) 2924, 2853, 1614, 1513, 1460, 1104, 1033, 766 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, *J* = 7.17 Hz, 3H), 1.22-1.86 (m, 14H), 3.40 (s, 3H), 3.42 (m, 1H), 3.38-3.44 (m, 1H), 3.68-3.72 (m, 1H), 3.79 (s, 3H), 3.81-3.83 (m, 1H), 3.93-3.98 (td, *J* = 2.59, 12.35 Hz, 1H), 4.25-4.28 (dd, *J* = 4.73,11.13 Hz, 1H), 4.42 (d, *J* = 11.13 Hz, 1H), 4.60 (d, *J* = 11.13 Hz, 1H), 4.64 (d, *J* = 6.71 Hz, 1H), 4.78 (d, *J* = 6.79 Hz, 1H), 5.50 (s, 1H), 6.86 (d, *J* = 8.68 Hz, 1H), 7.24-7.37 (m, 5H), 7.49 (d, *J* = 8.68 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.1, 22.6, 25.7, 26.4, 30.4, 31.4, 31.9, 32.6, 55.2, 55.8, 67.0, 71.8, 77.5, 78.6, 80.6, 96.2, 101.1, 113.7, 125.9, 128.1, 128.6, 129.4, 130.8, 138.8, 159.1 ppm; HRMS (ESI): calcd. for $C_{29}H_{42}O_6Na$ $[M+Na]^+$ 509.2867, found 509.2873.



Synthesis of (3*R*,6*S*,7*R*)-3-(benzyloxy)-7-((4-methoxybenzyl)oxy)-6-(methoxymethoxy) dodecan-1-ol (4): DIBAL- H (1.76 M in toluene, 7.46 mL, 13.13 mmol) was added to a solution of benzyl acetal compound **14** (2.9 g, 5.97 mmol) in CH_2Cl_2 (50 mL) at –20 ^{0}C slowly drop wise over period of 30 min .The mixture was stirred at same temperature for 2 h. After monitoring with TLC, the reaction was quenched with aq. MeOH (1 mL) at 0 ^{0}C. Then sat. sol. of sodium potassium tartrate (20 mL) was added, extracted with CH_2Cl_2 (2 X 30 mL). The organic layer was washed with brine (20 mL) and H_2O (20 mL), The combined organic extracts were dried over Na_2SO_4, solvent was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,1:9) gave alcohol **4** (2.50 g, 86%) as colour less oil. $[\alpha]_D^{20}$ –14.44 (*c* 2.5, $CHCl_3$); IR (KBr) 3448, 2930, 2859, 1513, 1093, 1034, 771 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 7.17 Hz, 3H), 1.25-1.86 (m, 14H), 2.36 (brs, 1H), 3.39 (s, 3H), 3.42 (m, 1H), 3.62-3.83 (m, 4H), 3.79 (s, 3H), 4.43 (d, *J* = 11.33 Hz, 1H), 4.48 (d, *J* = 11.33 Hz, 1H), 4.58 (d, *J* = 9.07 Hz, 1H), 4.60 (d, *J* = 6.79 Hz, 1H), 4.64 (d, *J* = 9.06 Hz, 1H), 4.78 (d, *J* = 6.79 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 2H), 7.24-7.34 (m, 7H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.1, 22.6, 25.6, 26.3, 29.9, 30.5, 31.9, 35.9,

55.2, 55.8, 60.6, 71.0, 71.8, 78.5, 78.9, 80.6, 96.3, 113.7, 127.7, 127.8, 128.4, 129.4, 130.7, 138.3, 159.1 ppm; HRMS (ESI): calcd. for $C_{29}H_{44}O_6Na$ $[M+Na]^+$ 511.3023, found 511.3030.

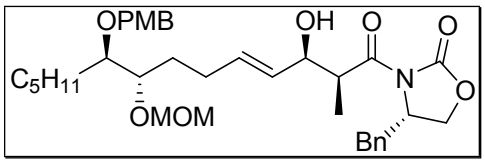


Synthesis of (*S*)-4-benzyl-3-((2*S*,3*R*,5*R*,8*S*,9*R*)-5-(benzyloxy)-3-hydroxy-9-((4-methoxybenzyl)oxy)-8-(methoxymethoxy)-2-methyltetradecanoyl)oxazolidin-2-one (16): Dess–Martin periodinane (1.30 g, 3.07 mmol) was added to a stirred solution of alcohol **4** (1 g, 2.05 mmol) in dry CH_2Cl_2 (25 mL) at 0 ^{0}C, the reaction was warmed to room temperature for 1 h. After completion of the reaction (TLC), quenched with by addition of sat. aq. $Na_2S_2O_3$ (15 mL) followed by sat. aq. $NaHCO_3$ (15 mL) at 0 ^{0}C, stirring was continued until clear solution formed. The mixture was diluted with CH_2Cl_2 (20 mL), washed with sat. aq. brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give the crude aldehyde **15**, which was used for next step without further purification or characterization. To a stirred solution of (S)-1-(4-benzyl-2-oxazolidin-3-yl)propan-1-one (0.687 g, 2.60 mmol) in DCM (26 mL, 1M with respect to zolidinone) at 0^{0}C was added $TiCl_4$ (0.55 g, 2.60 mmol) was added drop wise to form an orange slurry. After stirring 25 min, *i*Pr_2NEt (0.38 g, 2.86 mmol) was added drop wise. The resultant dark red solution was allowed to stir for 45 min at 0 °C and then NMP (0.51 g, 5.19 mmol) was added, stirring was continued further 15 min. The reaction was cooled to –78 °C, to a solution of above aldehyde (0.84 g, 1.73 mmol) in 10 mL DCM was added. The reaction was stirred for 2 h at -78 °C, warmed to 0 °C for 1 h and quenched with sat. aq. NH_4Cl (20 mL) solution. The reaction mixture was extracted with CH_2Cl_2 (2 X 20 mL) and the combined organic extracts were dried over Na_2SO_4. The organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,1:3) furnished syn Evans aldol adduct **16** (1.03 g, 83%, for two steps, >20:1 d.r.) as colourless oil. $[\alpha]_D^{20}$ –12.10 (*c* 1.1, $CHCl_3$); IR (KBr) 3447, 2922, 2852, 1779, 1741, 1460, 1096, 1033, 771 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 7.17 Hz, 3H), 1.20-1.88 (m, 17H), 2.73-2.78 (m, 1H), 3.26 (dd, *J* = 3.20, 13.24 Hz, 1H), 3.39 (s, 3H), 3.42 (dd, *J* = 3.20, 13.24 Hz, 1H), 3.59-3.74 (m, 1H), 3.78 (s, 3H), 3.79-3.85 (m, 1H), 4.09-4.13 (dd, *J* = 7.17, 14.34 Hz, 1H), 4.15-4.18 (dd, *J* = 7.17, 13.54 Hz, 1H), 4.43 (d, *J* = 8.68 Hz, 1H), 4.45 (d, *J* = 8.68 Hz, 1H), 4.60 (d, *J* = 11.13 Hz, 1H), 4.62 (d, *J* = 11.13 Hz, 1H), 4.64 (d, *J* = 7.06 Hz, 1H), 4.65-4.68 (m, 1H), 4.78 (d, *J*

= 7.06 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 2H), 7.19-7.34 (m, 12H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.1, 14.1, 22.6, 25.6, 25.7, 29.8, 30.4, 31.9, 37.7, 38.0, 42.9, 55.3, 55.8, 60.0, 66.0, 70.7, 70.9, 71.8, 78.8, 78.9, 80.6, 96.3, 113.7, 127.3, 127.6, 127.8, 128.4, 128.9, 129.4, 129.4, 130.8, 135.2, 138.1, 153.1, 159.1, 175.9 ppm; HRMS (ESI): calcd. for $C_{42}H_{57}O_9NNa$ $[M+Na]^+$ 742.3939, found 742.3925.

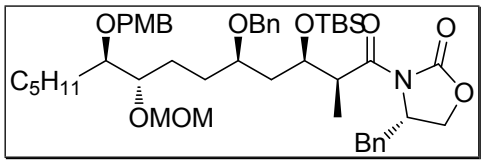
Table 1. Optimization conditions for Evans aldol reaction.

Lewis acid/equiv.	Base/ equiv.	Reaction conditions to form enolate complex	Yields (%)	
			16	**17**
Bu_2BOTf/1.2	DIPEA/1.3	5 min., 0 ^{0}C/30 min.	25	0
$TiCl_4$/1.2	DIPEA/1.3	5 min., 0 ^{0}C/20 min.	58	22
$TiCl_4$/1.1	DIPEA/1.2	15 min., 0 ^{0}C/30 min.	72	10
$TiCl_4$/1.0	DIPEA/1.1	25 min., 0 ^{0}C/45 min.	83	trace

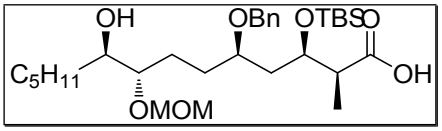


Synthesis of (*S*)-4-benzyl-3-((2*S*,3*R*,8*S*,9*R*,*E*)-3-hydroxy-9-((4-methoxybenzyl)oxy)-8-(methoxymethoxy)-2-methyltetradec-4-enoyl)oxazolidin-2-one (17):

$[\alpha]_D^{20}$ +59.46 (*c* 2.4, $CHCl_3$); IR (KBr) 3447, 2957, 2925, 2854, 1737, 1651, 1259, 1095, 1028, 802 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 7.17 Hz, 3H), 1.20-1.72 (m, 13H), 2.19-2.33 (m, 2H), 2.76-2.81 (m, 1H), 3.24 (dd, *J* = 3.20, 13.24 Hz, 1H), 3.39 (s, 3H), 3.42 (dd, *J* = 3.20, 13.24 Hz, 1H), 3.68-3.79 (m, 1H), 3.79 (s, 3H), 3.84-3.88 (m, 1H), 4.15-4.18 (dd, *J* = 7.17, 14.34 Hz, 1H), 4.19-4.24 (dd, *J* = 7.17, 13.54 Hz, 1H), 4.42 (d, *J* = 11.29, 1H), 4.45 (m, 1H), 4.61 (d, *J* = 11.29 Hz, 1H), 4.64 (d, *J* = 6.86 Hz, 1H), 4.68-4.72 (m, 1H), 4.77 (d, *J* = 6.86 Hz, 1H), 5.50-5.55 (dd, *J* = 6.10, 15.41 Hz, 1H), 5.74-5.79 (dt, *J* = 15.41, 7.32 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 1H), 7.20(d, *J* = 8.68 Hz, 1H), 7.25-7.35 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.29, 14.05, 22.60, 25.71, 28.74, 30.13, 30.42, 31.88, 37.73, 42.73, 55.10, 55.21, 55.76, 66.12, 71.73, 72.58, 78.02, 80.58, 96.17, 113.66, 125.20, 127.39, 128.93, 129.32, 129.43,130.85, 132.77, 134.98, 153.48, 159.04, 176.61ppm; HRMS (ESI): *m/z* calcd. for $C_{35}H_{49}O_8NNa$ $[M+Na]^+$ 634.3357, found 634.3350.

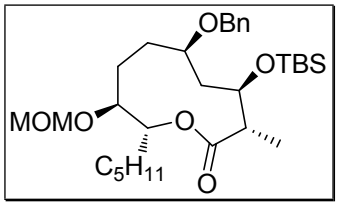


(*S*)-4-benzyl-3-((2*S*,3*R*,5*R*,8*S*,9*R*)-5-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-9-((4-methoxybenzyl)oxy)-8-(methoxymethoxy)-2-methyltetradecanoyl)oxazolidin-2-one (18): 2,6-Lutidine (0.45 g, 4.17 mmol) and TBSOTf (0.55 g, 2.08 mmol)were added to solution of alcohol **16** (1.0 g, 1.39 mmol) in anhydrous CH_2Cl_2 (15 mL) at –78 ^{0}C, after stirring for 2 h at the same temperature, the reaction was warmed to 0 ^{0}C for 1 h and quenched by using phosphate buffer. The reaction mixture was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4. The organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate/hexane, 1:9) to afford silylether **18** (1.05 g, 92%) as colourless oil. $[\alpha]_D^{20}$ –15.30 (*c* 1.7, $CHCl_3$); IR (KBr) 2919, 2845, 1780, 1740, 1459, 1093, 1028, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 3H), 0.042 (s, 3H), 0.87 (t, *J* = 7.17 Hz, 3H), 0.90 (s, 9H), 1.20-2.05 (m, 17H), 2.67 (m, 1H), 3.17 (dd, *J* = 2.89, 13.27 Hz, 1H), 3.31 (m, 1H), 3.37 (s, 3H), 3.40 (dd, *J* = 2.89, 13.27 Hz, 1H), 3.68 (m, 1H), 3.78 (m, 4H), 3.86 (m, 1H), 4.09-4.13 (dd, *J* = 7.17, 14.34 Hz, 1H), 4.15-4.18 (dd, *J* = 7.17, 13.54 Hz, 1H), 4.43 (d, *J* = 8.68 Hz, 1H), 4.45 (d, *J* = 8.68 Hz, 1H), 4.60 (d, *J* = 11.13 Hz, 1H), 4.62 (d, *J* = 11.13 Hz, 1H), 4.64 (d, *J* = 7.06 Hz, 1H), 4.65-4.68 (m, 1H), 4.78 (d, *J* = 7.06 Hz, 1H), 6.86 (d, *J* = 8.68 Hz, 2H), 7.19-7.34 (m, 12H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ –4.8, –4.1, 14.1, 14.3, 17.9, 22.6, 25.7, 25.8, 25.9, 29.3, 29.9, 30.4, 31.9, 37.6, 39.8, 42.9, 55.2, 55.7, 65.6, 69.5, 70.9, 71.7, 74.6, 78.72, 80.7, 96.2, 113.6, 127.1, 127.2, 127.2, 128.1, 128.8, 129.4, 129.4, 130.9, 135.4, 139.3, 152.7, 159.0, 175.4 ppm; HRMS (ESI): calcd. for $C_{48}H_{71}O_9NNaSi$ $[M+Na]^+$ 856.4785, found 856.4790.



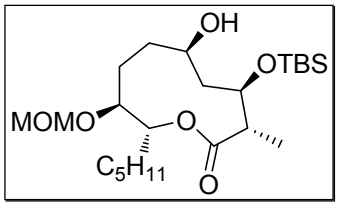
(2*S*,3*R*,5*R*,8*S*,9*R*)-5-(benzyloxy)-3-((ter-butyldimethylsilyl)oxy)-9-hydroxy-8-(methoxymethoxy)-2-methyltetradecanoic acid (3): DDQ (0.32 g, 1.44 mmol) was added in one portion to a solution of silyl ether compound **18** (0.8 g, 0.96 mmol) in CH_2Cl_2 (13.5 mL) and aqueous pH 7.0 buffer (1.5 mL) at 0 ^{0}C. After stirring 1 h at the same temperature, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (5 mL). The mixture was diluted with CH_2Cl_2 (15 mL), the layers were separated, and the aqueous layer was extracted

with CH_2Cl_2 (2×10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel ethyl acetate hexanes, 1.5:8.5) furnished a pale yellow liquid. R_f = 0.5 ethyl acetate hexane, 3:7). The compound was used for the next step without further characterization. 30% aq. H_2O_2 (0.35 mL, 3.36 mmol) was added to a solution of alcohol (0.3 g, 0.42 mmol) in THF–water (4:1, 10 mL) at 0 ^{0}C, followed by a solution of $LiOH{\cdot}H_2O$ (0.07 g, 1.68 mmol) in water (0.4 mL) at 0 ^{0}C was added and stirring was continued for 5 h at same temperature. To the reaction sat. aq. Na_2SO_3 (2 mL) was added, and stirring continued at 0 ^{0}C for 30 min. The mixture was then adjusted to pH 3 with 1 N HCl, extracted with ethyl acetate (2 X 10 mL) and the combined organic extracts were dried over Na_2SO_4. The organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,1:3) to afford *seco* acid **3** (0.21 g, 87%, from two steps) as colourless oil. $[\alpha]_D^{20}$ +4.75 (*c* 2.4, $CHCl_3$); IR (KBr) 3447, 2930, 2856, 1711, 1461, 1095, 1033, 836, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 6H), 0.86 (s, 9H), 0.88 (t, *J* = 7.17 Hz, 3H), 1.10-1.11 (d, *J* = 7.09 Hz, 3H), 1.24-1.88 (m, 14H), 2.57-2.62 (m, 1H), 3.41 (s, 3H), 3.48 (m, 2H), 3.59-3.63 (m, 1H), 4.27 (m, 1H), 4.49 (d, *J* = 11.44 Hz, 1H), 4.52 (d, *J* = 11.44 Hz, 1H), 4.63 (d, *J* = 6.86 Hz, 1H), 4.73 (d, *J* = 6.86 Hz, 1H), 7.27-7.35 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ –4.9, –4.3, 10.5, 14.0, 22.6, 25.6, 25.7, 29.6, 30.3, 31.6, 31.9, 39.2, 44.2, 55.8, 70.3, 70.9, 72.9, 75.7, 84.0, 97.1, 127.6, 127.9, 128.3, 138.1, 179.1 ppm; HRMS (ESI): calcd. for $C_{30}H_{54}O_7NaSi$ $[M+Na]^+$ 577.3525, found 577.3531.

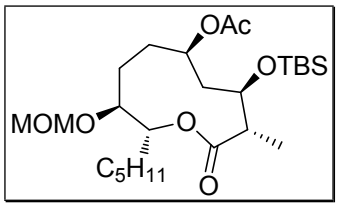


(3*S*,4*R*,6*R*,9*S*,10*R*)-6-(benzyloxy)-4-((tert-butyldimethylsilyl)oxy)-9-(methoxymethoxy)-3-methyl-10-pentyloxecan-2-one (2): Triethylamine (0.09 g, 0.90 mmol) was added to a stirred solution of *seco* acid **3** (0.1 mg, 0.18 mmol) in THF (5 mL) at 0 ^{0}C followed by the addition of 2,4,6-trichlorobenzoyl chloride (0.11 g, 0.45 mmol). The stirring was continued at 0 ^{0}C for 1 h and then warmed to room temperature for 1h. The reaction mixture was diluted with toluene (10 mL). To a solution of DMAP (0.395 g, 3.23 mmol) in toluene (40 mL) was added the resulting mixture drop wise over 8h by syringe pump at 60 ^{0}C under argon. After the addition, the mixture was stirred for another 15 min. The toluene was evaporated under reduced pressure, and the residue was diluted with EtOAc (10 mL), was neutralized with sat.

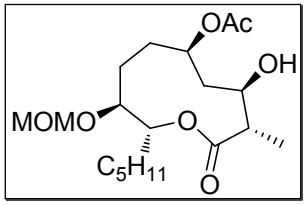
aq. NH_4Cl, and the solution was extracted with EtOAc (2 X 10 mL). The combined organic extracts were dried over Na_2SO_4, the organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate hexane,0.6:9.4) afforded lactone **2** (0.07 g, 76%) as a colourless oil. $[\alpha]_D^{20}$ +7.67 (*c* 0.6, $CHCl_3$); IR (KBr) 2944, 2927, 1735, 1243, 1072, 1032, 856 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.89 (m, 12H), 1.18 (d, *J* = 6.79 Hz, 3H), 1.23-1.87 (m, 12H), 2.04 (m, 2H), 2.71 (m, 1H), 3.41 (s, 3H), 3.63 (m, 2H), 4.23 (m, 1H), 4.50 (d, *J* = 11.44 Hz, 1H), 4.52 (d, *J* = 11.44 Hz, 1H), 4.58 (d, *J* = 6.86 Hz, 1H), 4.75 (d, *J* = 6.86 Hz, 1H), 4.96 (td, *J* = 8.30, 3.02 Hz, 1H), 7.27-7.35 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ –4.7, –4.7, 8.4, 14.0, 17.9, 22.5, 24.1, 24.6, 25.7, 26.9, 29.7, 31.8, 32.8, 36.3, 46.0, 55.9, 68.5, 69.9, 78.9, 95.1, 127.5, 128.3, 138.7, 173.0 ppm; HRMS (ESI): calcd. for $C_{30}H_{52}O_6NaSi$ $[M+Na]^+$ 559.3432, found 559.3425.



(3*S*,4*R*,6*R*,9*S*,10*R*)-4-((*tert*-butyldimethylsilyl)oxy)-6-hydroxy-9-(methoxymethoxy)-3-methyl-10-pentyloxecan-2-one (19): Pd/C (10% w/w, 20 mg) was added to a solution of compound **2** (0.06 g, 0.11 mmol) in EtOAc (3 mL) and the reaction mixture was stirred for 4 h under an atmosphere of hydrogen. After completion of reaction (TLC), catalyst was filtered off and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (ethyl acetate hexanes, 1:4) to give alcohol **19** (0.04 g, 97%) as colourless oil. $[\alpha]_D^{20}$ +5.14 (*c* 0.7, $CHCl_3$); IR (KBr) 3453, 2954, 2930, 2857, 1735, 1253, 1059, 1034, 823 cm^{-1}.^1H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.88(t, *J* = 6.86 Hz, 3H), 0.90 (s, 9H), 1.23 (d, *J* = 7.01 Hz, 3H), 1.25-1.30 (m, 6H), 1.54 (m, 2H), 1.64 (m, 2H), 1.75 (m, 1H), 1.78 (m, 1H), 1.89-1.94 (m, 2H), 2.58 (qd, *J* = 7.01, 9.61 Hz, 1H), 3.38 (s, 3H), 3.44 (t, *J* = 9.00 Hz, 1H), 3.51 (dt, *J* = 9.46, 3.35 Hz, 1H), 4.02 (m, 1H), 4.58 (d, *J* = 7.01 Hz, 1H), 4.70 (d, *J* = 7.01 Hz, 1H), 4.96 (td, *J* = 8.30, 3.02 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ –4.4, –3.9, 13.9, 15.9, 17.9, 22.5, 23.9, 24.6, 25.8, 30.2, 31.6, 32.7, 43.1, 50.4, 55.9, 68.9, 71.8, 75.8, 78.6, 95.2, 173.8 ppm; HRMS (ESI): calcd. for $C_{23}H_{46}O_6NaSi$ $[M+Na]^+$ 469.2955, found 469.2954.

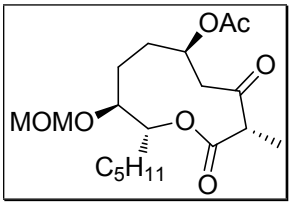


(3*S*,4*R*,6*R*,9*S*,10*R*)-4-((*tert*-butyldimethylsilyl)oxy)-9-(methoxymethoxy)-3-methyl-2-oxo-10-pentyloxecan-6-yl acetate (20): Triethylamine (0.011 g, 0.11 mmol) was added to a stirred solution of alcohol **19** (0.04 g, 0.09 mmol) in dry CH_2Cl_2 (2 mL) at 0 °C, followed by the addition of DMAP (4-(*N*,*N*-dimethylamino)pyridine, Cat.) and Ac_2O (0.013 g, 0.11 mmol) at the same temperature. After completion of the reaction (TLC), then quenched with sat. aq. NH_4Cl solution (3 mL) at 0 °C. The resulting solution was extracted with CH_2Cl_2 (2 X 5 mL). The combined extracts were washed with water (5 mL), a sat. aq. solution of $NaHCO_3$ (5 mL), dried with anhydrous Na_2SO_4, the organic layer was concentrated in a rotary evaporator and purified by silica gel column chromatography (ethyl acetate/hexane, 0.5:9.5) through a short pad of silica gel to give **20** (0.04 g, 93%) as a colorless oil; $[\alpha]_D^{20}$ +4.0 (*c* 0.3, $CHCl_3$). IR (KBr) 2930, 2859, 1737, 1461, 1246, 1100, 1035, 840 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 3H), 0.12 (s, 3H), 0.87(t, *J* = 6.86 Hz, 3H), 0.89 (s, 9H), 1.24 (d, *J* = 7.01 Hz, 3H), 1.25-1.30 (m, 6H), 1.52 (m, 2H), 1.59 (m, 2H), 1.78 (m, 2H), 1.89-1.94 (m, 2H), 2.01 (s, 3H), 2.58 (qd, *J* = 7.01, 9.61 Hz, 1H), 3.38 (s, 3H), 3.44 (t, *J* = 9.00 Hz, 1H), 3.56 (dt, *J* = 9.46, 3.35 Hz, 1H), 4.56 (d, *J* = 7.01 Hz, 1H), 4.70 (d, *J* = 7.01Hz, 1H), 4.96 (td, *J* = 8.30, 3.02 Hz, 1H), 5.09 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ –4.6, –4.1, 13.9, 16.1, 17.9, 21.2, 22.4, 24.6, 25.7, 28.2, 31.6, 32.6, 39.9, 50.6, 55.9, 71.6, 71.7, 75.9, 78.5, 95.3, 170.3, 173.7 ppm;

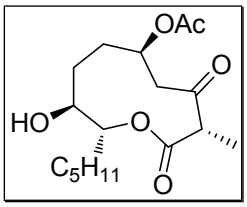


(3*S*,4*R*,6*R*,9*S*,10*R*)-4-Hydroxy-9-(methoxymethoxy)-3-methyl-2-oxo-10-pentyloxecan-6-yl acetate (21): Tetrabutylammoniumfluoride (1 M solution in THF, 0.12 mL, 122.95 μmol) was added to a stirred solution of silyl ether **20** (0.040 g, 81.97 μmol) in anhydrous THF (2 mL) at 0 °C. The reaction mixture was warmed to room temperature for 5h and quenched with water (2 mL), and the resulting solution was extracted with EtOAc (10 mL). The combined extracts were washed with brine (5 mL), dried with anhydrous Na_2SO_4, filtered and

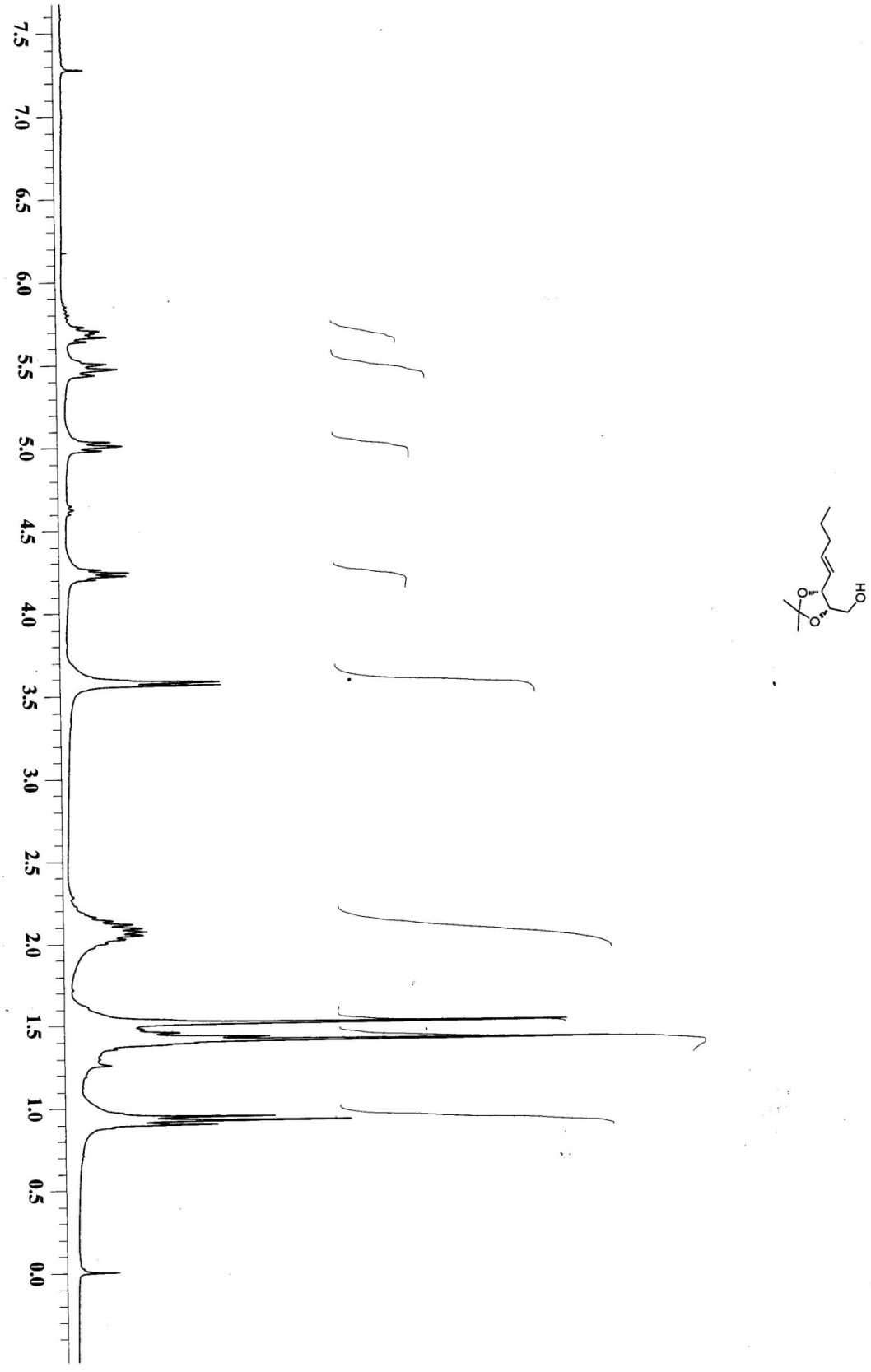
concentrated *in vacuo*. The residue was purified by column chromatography (ethyl acetate/hexane, 1.6:8.4) afforded **21** as a colour less solid (0.028 g, 95%), m.p 42-44 ^{0}C; $[\alpha]_D^{20}$ +27.7 (*c* 1.0, $CHCl_3$); IR (KBr) 3407, 2954, 2925, 2854, 1725, 1462, 1255, 1095, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 6.86 Hz, 3H), 1.25-1.30 (m, 6H), 1.33 (d, *J* = 7.01 Hz, 3H), 1.46-1.65 (m, 4H), 1.71 (m, 1H), 1.80 (m, 1H), 1.91-1.99 (m, 2H), 2.01 (s, 3H), 2.56 (qd, *J* = 7.01, 9.61 Hz, 1H), 3.38 (s, 3H), 3.45 (t, *J* = 9.00 Hz, 1H), 3.66 (dt, *J* = 9.46, 3.35 Hz, 1H), 4.56 (d, *J* = 7.01Hz, 1H), 4.70 (d, *J* = 7.01Hz, 1H), 4.94 (td, *J* = 8.30, 3.02 Hz, 1H), 4.98 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.9, 15.5, 21.3, 22.4, 24.4, 25.0, 27.9, 31.6, 32.5, 39.9, 49.5, 55.9, 71.1, 72.4, 76.1, 78.2, 95.2, 170.8, 173.5 ppm; HRMS (ESI): calcd. for $C_{19}H_{34}O_7Na$ $[M+Na]^+$ 397.2196, found 397.2201.



(3*S*,6*R*,9*S*,10*R*)-9-(methoxymethoxy)-3-methyl-2,4-dioxo-10-pentyloxecan-6-yl acetate (22): Dess–Martin periodinane (0.044 g, 100.26 µmol) was added to a stirred solution of alcohol **21** (0.025 g, 66.84 µmol) in dry CH_2Cl_2 (3 mL) at 0 ^{0}C, the reaction was warmed to room temperature for 1 h. After completion of the reaction (TLC), quenched with by addition of sat. aq. $Na_2S_2O_3$ (5 mL) followed by sat. aq. $NaHCO_3$ (5 mL) at 0 ^{0}C, stirring was continued until clear solution formed. The mixture was diluted with CH_2Cl_2 (10 mL), washed with sat. aq. brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Recrystallization in ethyl acetate/hexanes, 1:10 gave **22** (0.022 g, 92%) as a colourless solid. m.p 66-68 ^{0}C. $[\alpha]_D^{20}$ –44.25 (*c* 0.4, $CHCl_3$); IR (KBr) 2927, 2857, 1739, 1710, 1236, 1105, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87 (t, *J* = 6.86 Hz, 3H), 1.28 (m, 6H), 1.33 (d, *J* = 7.01 Hz, 3H), 1.38 (m, 1H), 1.50-1.98 (m, 5H), 2.01 (s, 3H), 2.59 (dd, *J* = 15.10, 5.28 Hz, 1H), 3.13 (dd, *J* = 15.10, 11.0 Hz, 1H), 3.38 (s, 3H), 3.41 (dt, *J* = 9.46, 3.35 Hz, 1H), 3.47 (q, *J* = 6.79 Hz, 1H), 4.56 (d, *J* = 7.01Hz, 1H), 4.69 (d, *J* = 7.01 Hz, 1H), 4.98 (dt, *J* = 8.30, 3.02 Hz, 1H), 5.38 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 11.2, 13.9, 21.1, 22.4, 24.4, 24.8, 26.9, 31.5, 32.3, 41.9, 55.6, 55.9, 69.9, 77.5, 77.7, 95.1, 170.0 (2C), 201.2 ppm; HRMS (ESI): calcd. for $C_{19}H_{32}O_7Na$ $[M+Na]^+$ 395.2040, found 395.2041.



(3*S*,6*R*,9*S*,10*R*)-9-hydroxy-3-methyl-2,4-dioxo-10-pentyloxecan-6-yl acetate (1): $BF_3 \cdot Et_2O$ (0.4 mL, 403.20 μmol) was added to a solution of lactone **22** (0.015 g, 40.32 μmol) in dimethyl sulphide (2 mL) at –10 ^{0}C. The reaction mixture was stirred at the same temperature for 30 min, quenched with sat. aq. $NaHCO_3$ solution and extract with diethyether (2 X 5 mL). The combined extracts were washed with brine (5 mL), dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by recrystallization (ethyl acetate hexane, 1:4) afforded **1** (0.012 g, 92%) as a colour less solid. m.p. 100-101 ^{0}C R_f = 0.2 ethyl acetate hexane, 3:7). $[\alpha]_D^{20}$ –97.30 (*c* 0.2, $CHCl_3$); IR (KBr) 3416, 2968, 2936, 1857, 1737, 1705, 1460, 1244, 1074, 1032 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.87 (t, *J* = 6.86 Hz, 3H), 1.28 (m, 6H), 1.33 (d, *J* = 7.01 Hz, 3H), 1.38 (m, 1H), 1.50-1.84 (m, 4H), 2.01 (s, 3H), 2.06 (m, 1H), 2.59 (dd, *J* = 15.10, 5.28 Hz, 1H), 3.13 (dd, *J* = 15.10, 11.0 Hz, 1H), 3.38 (s, 3H), 3.47 (q, *J* = 6.79 Hz, 1H), 3.54 (brt, 1H), 4.89 (dt, *J* = 8.30, 3.02 Hz, 1H), 5.38 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.1, 13.9, 21.1, 22.4, 24.5, 26.8, 28.7, 31.5, 32.7, 41.8, 55.7, 69.9, 73.2, 79.4, 170.1, 170.2, 201.2 ppm; HRMS (ESI): calcd. for $C_{17}H_{28}O_6Na$ $[M+Na]^+$ 351.1778, found 351.1784.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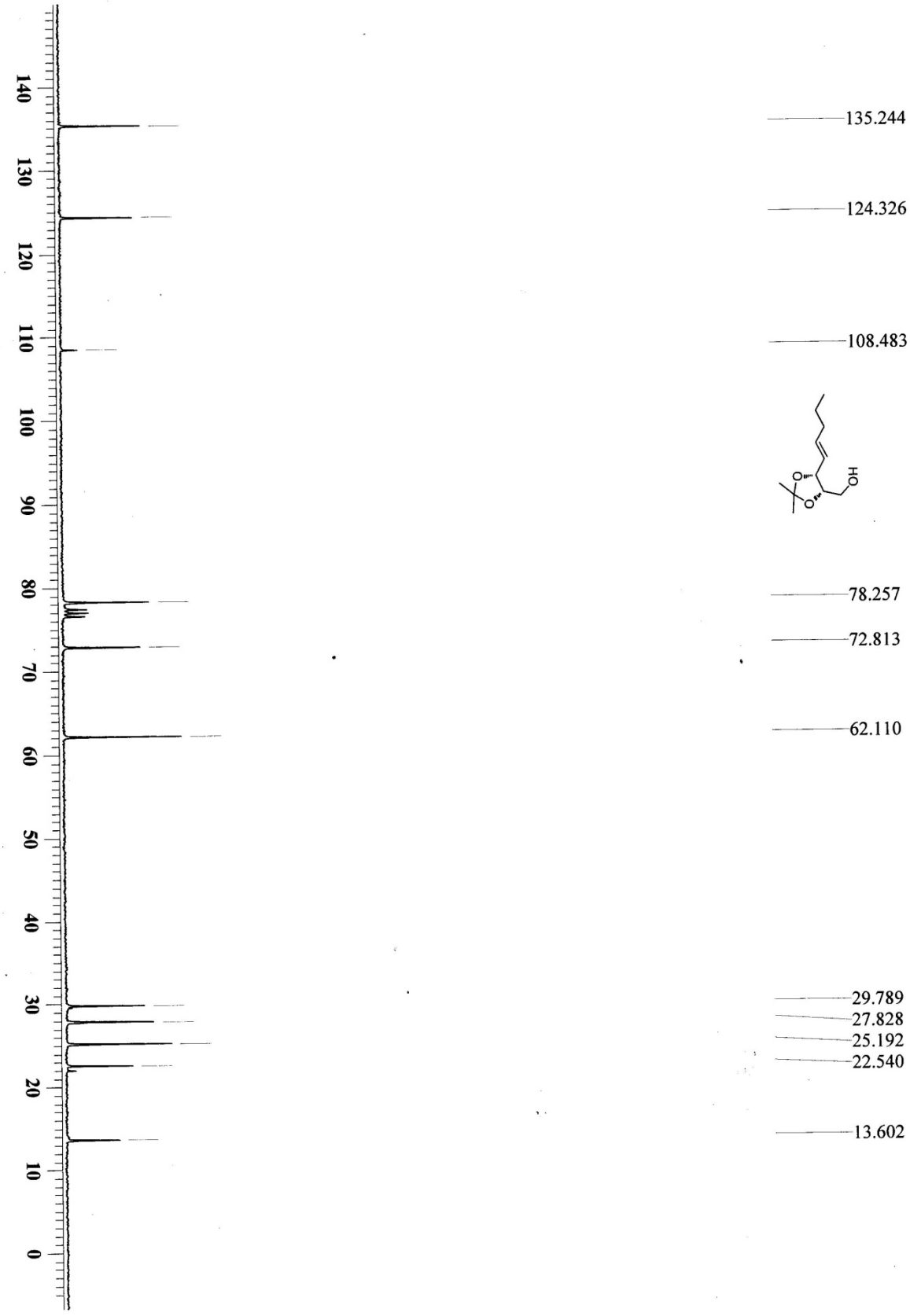
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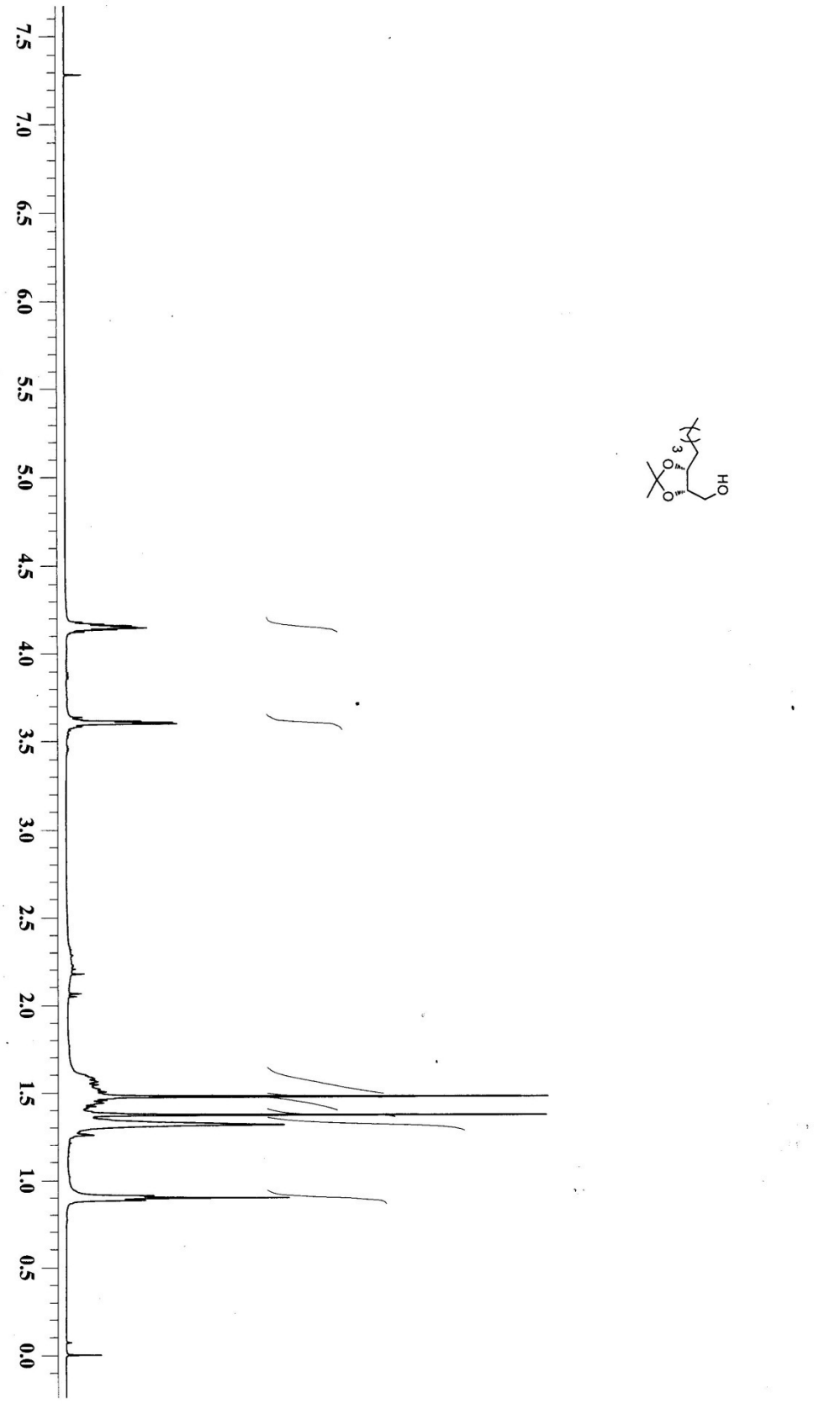
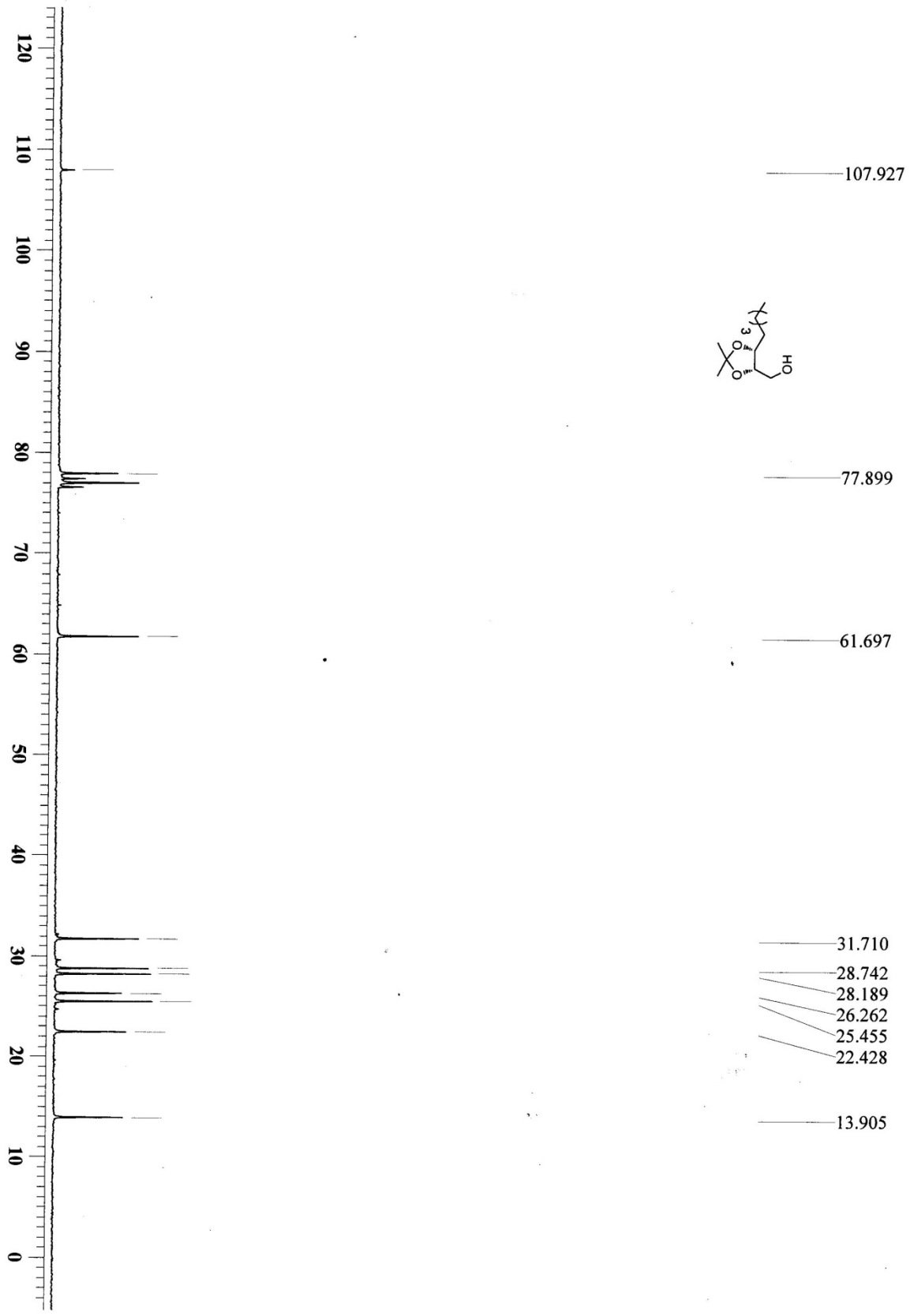
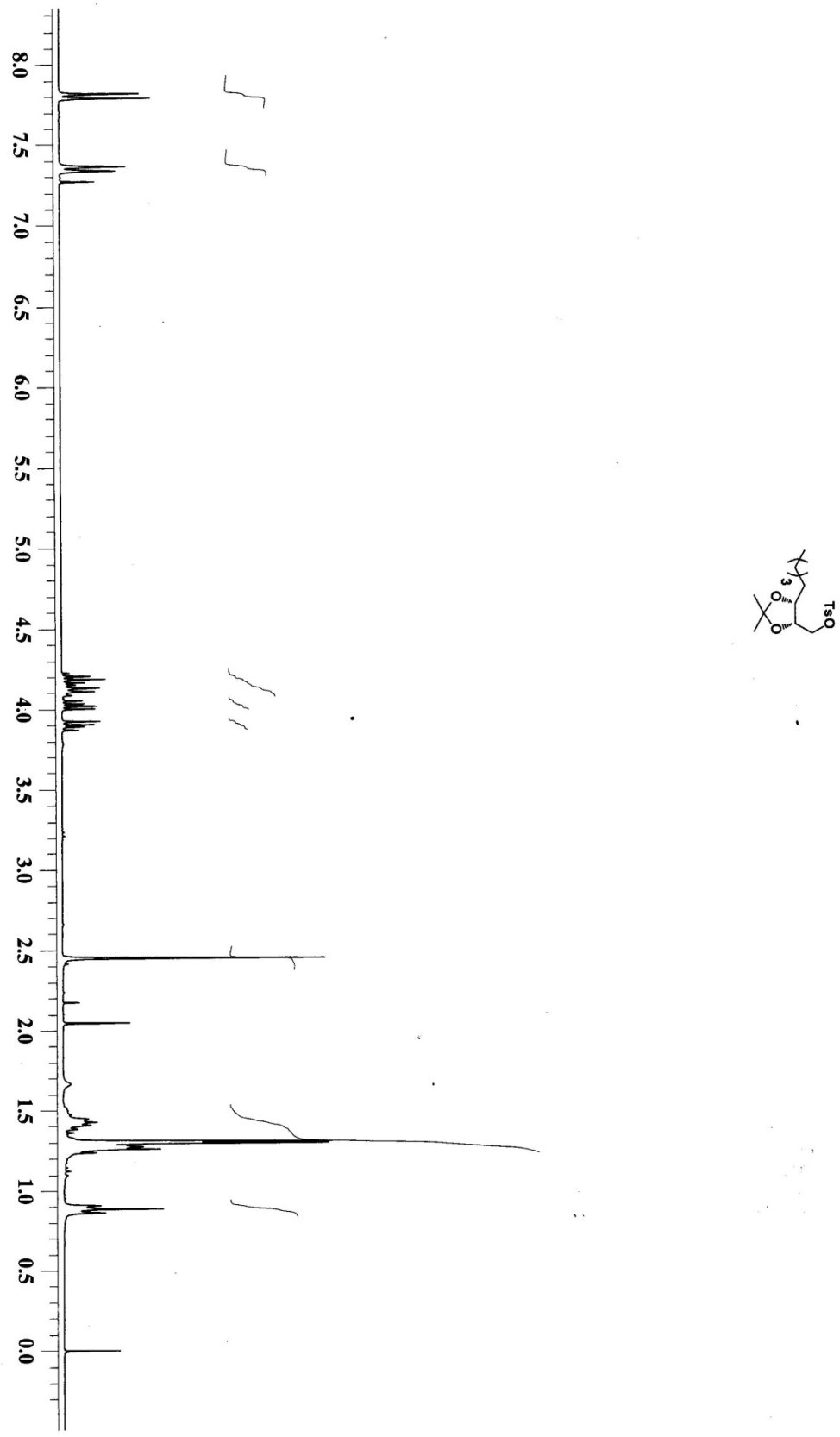


^{1}H-NMR of Compound 7



^{13}C-NMR of Compound 7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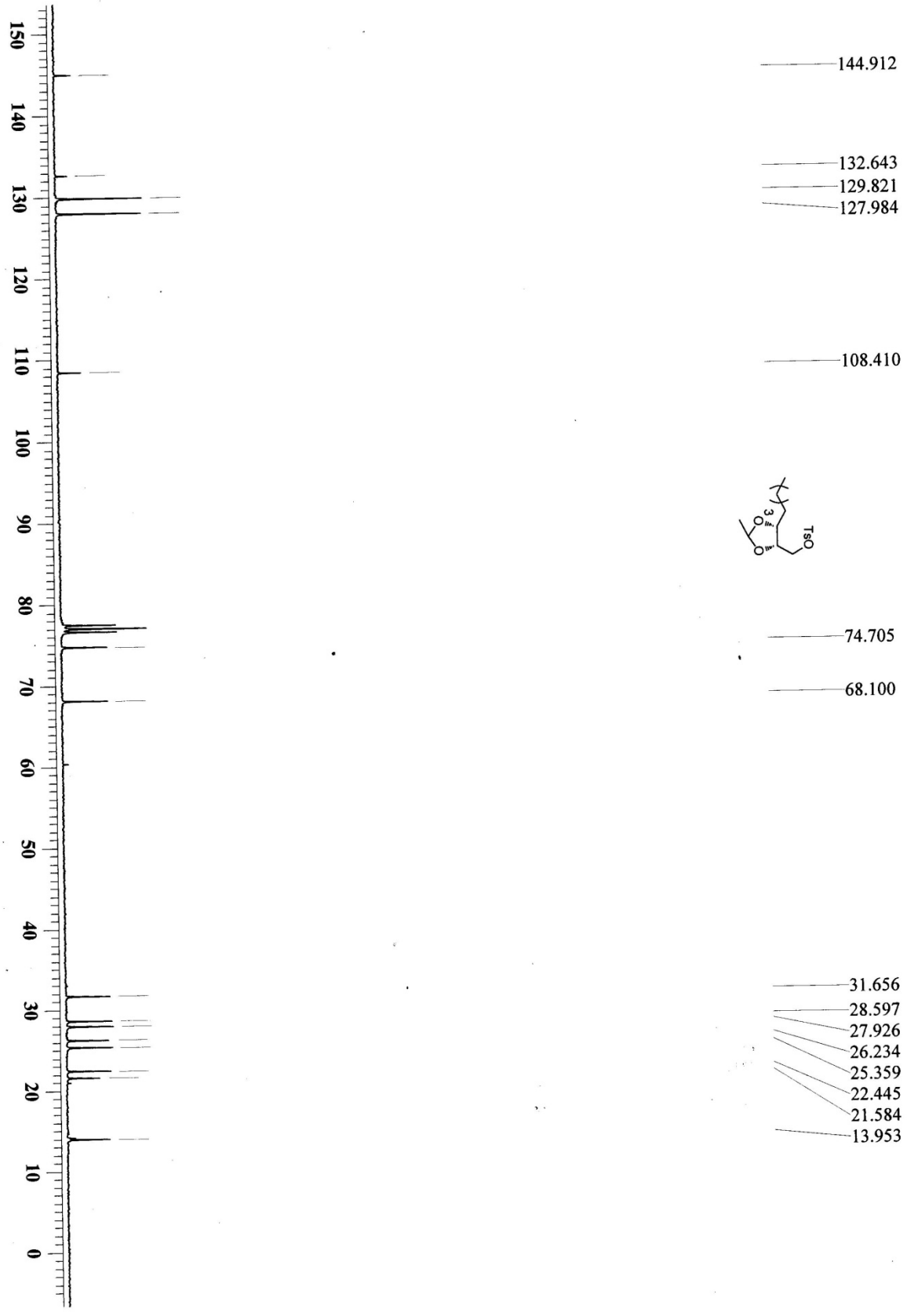
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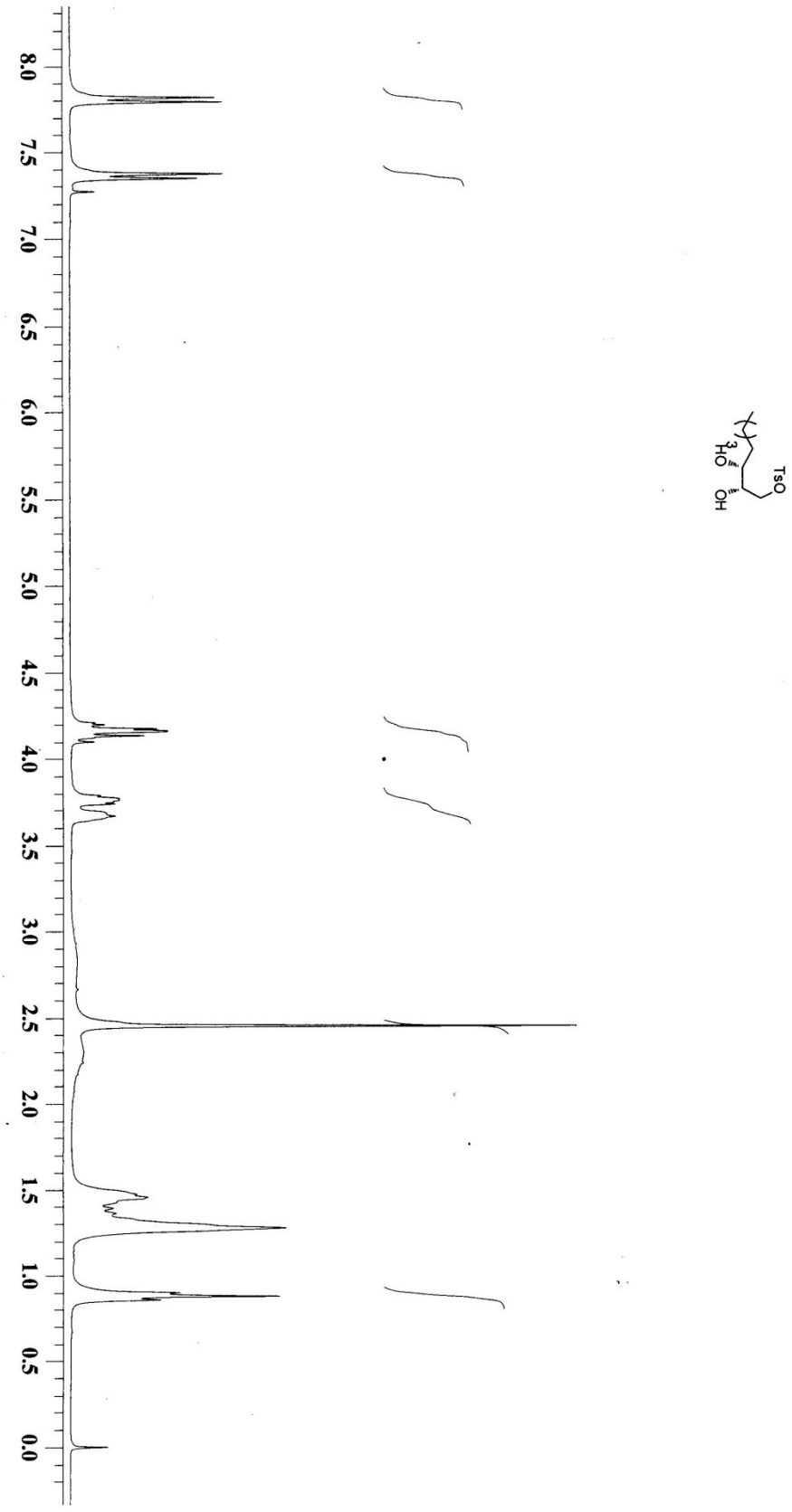
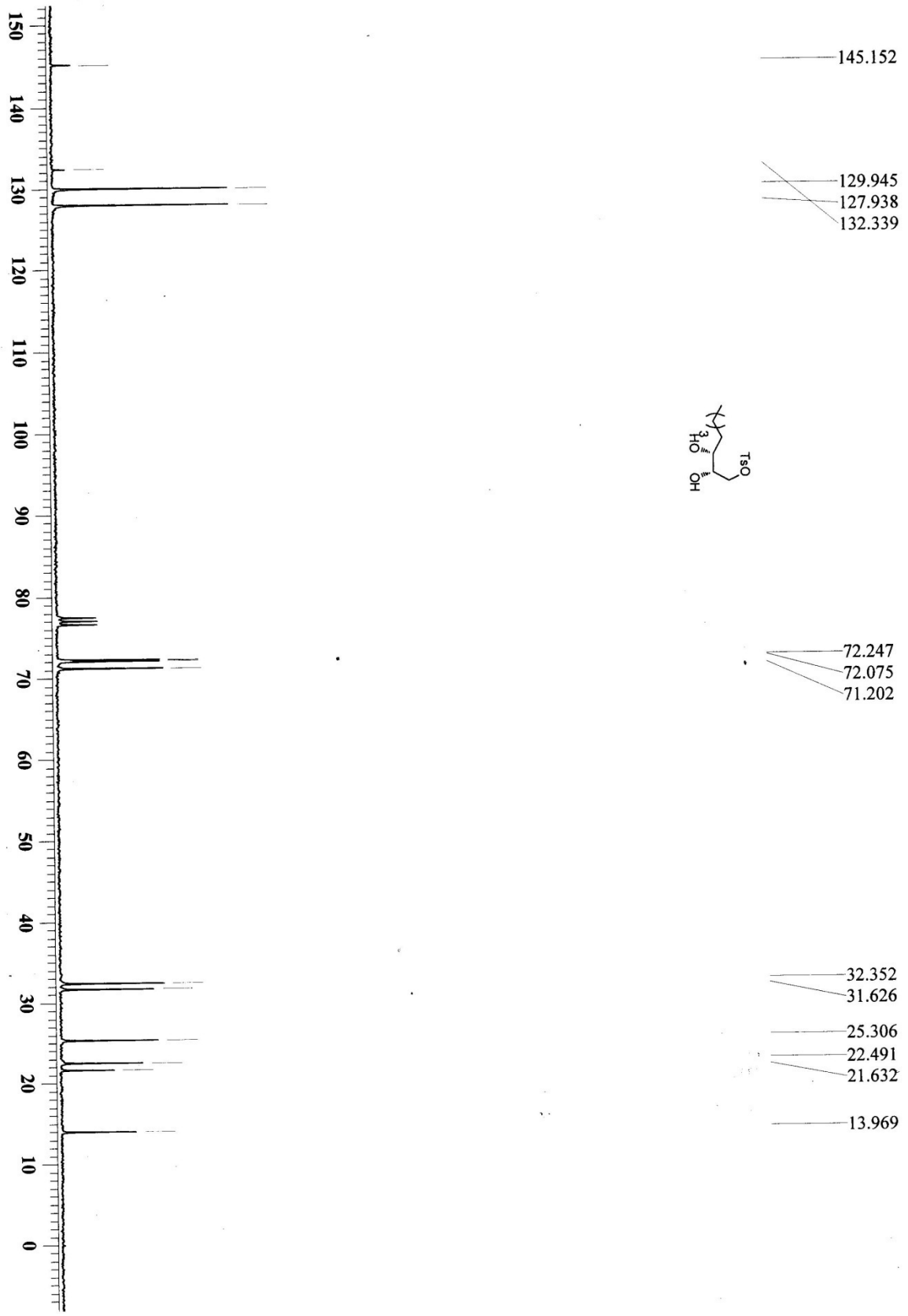
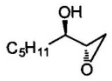


^{1}H-NMR of Compound 8



^{13}C-NMR of Compound 8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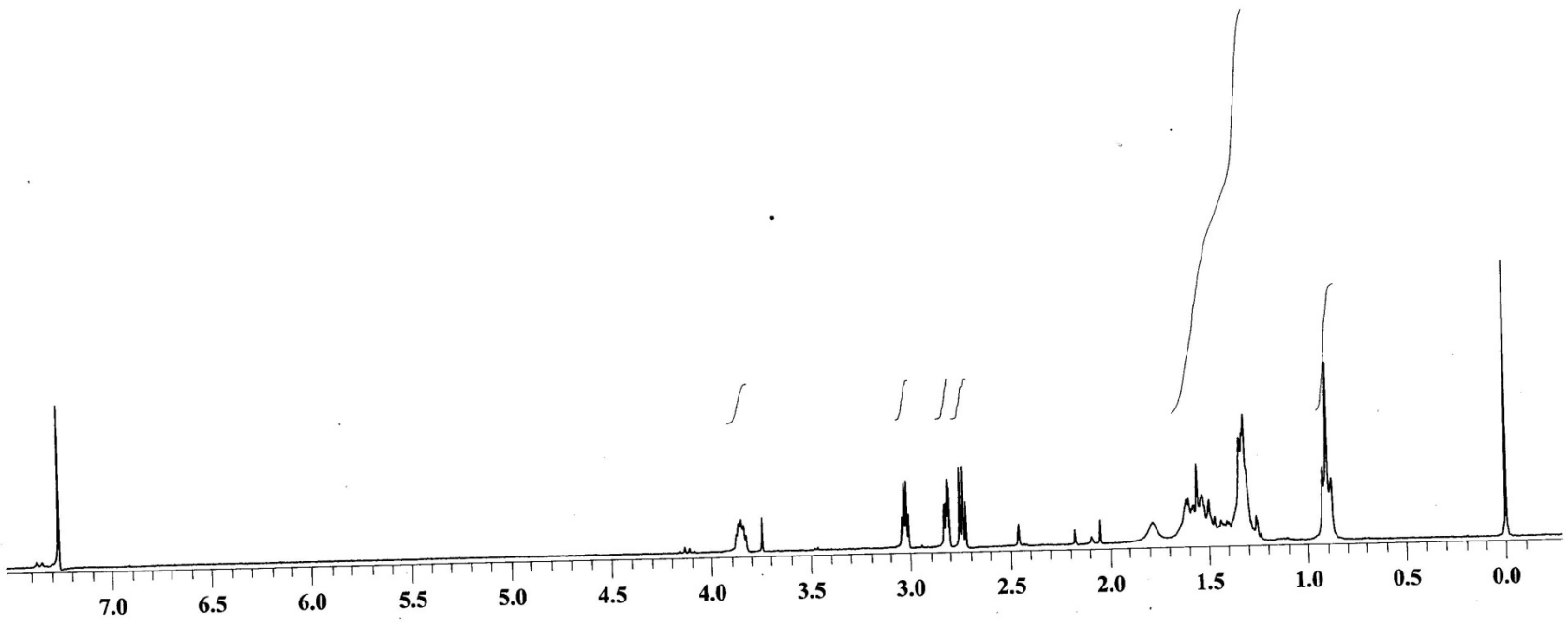
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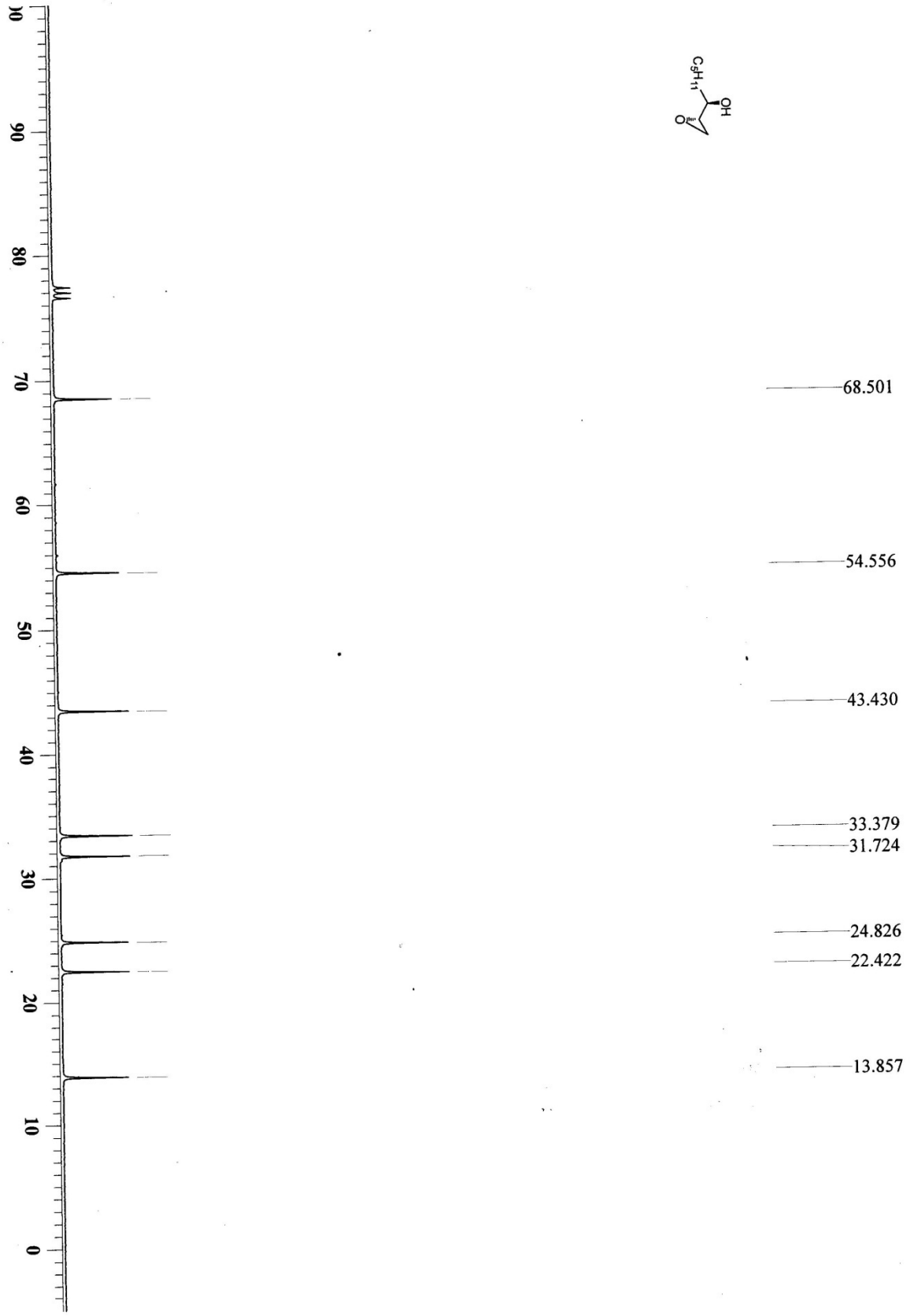
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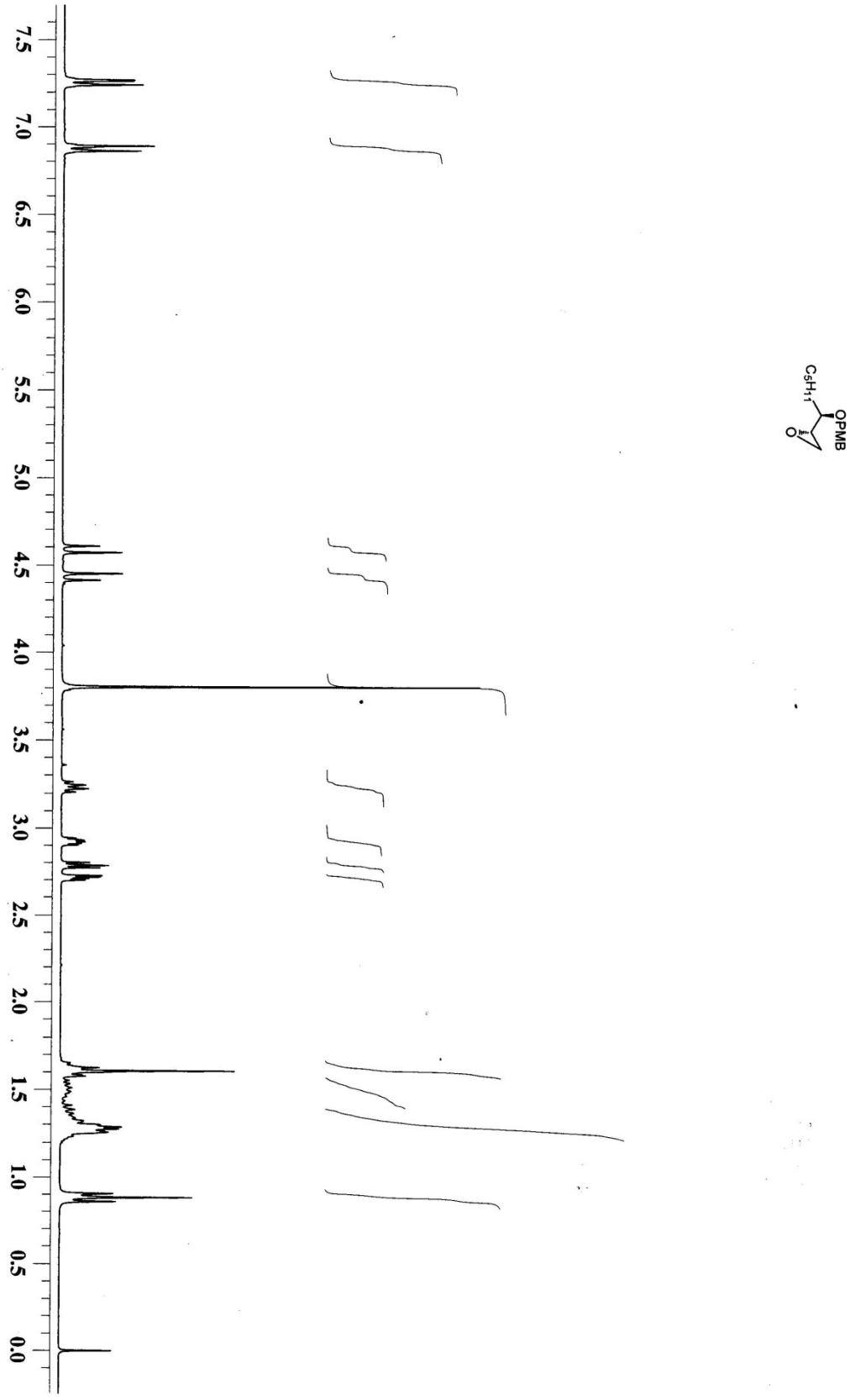
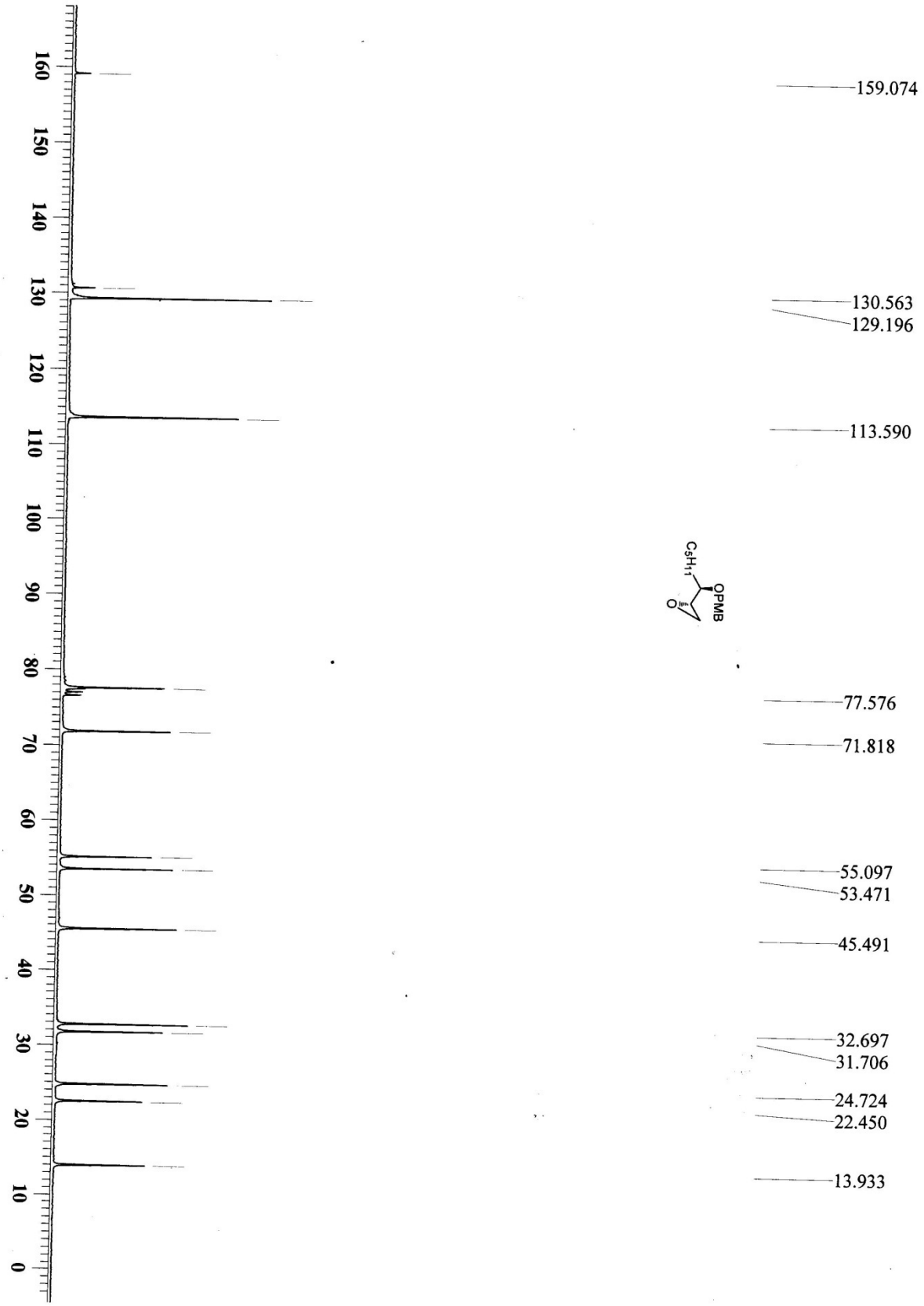
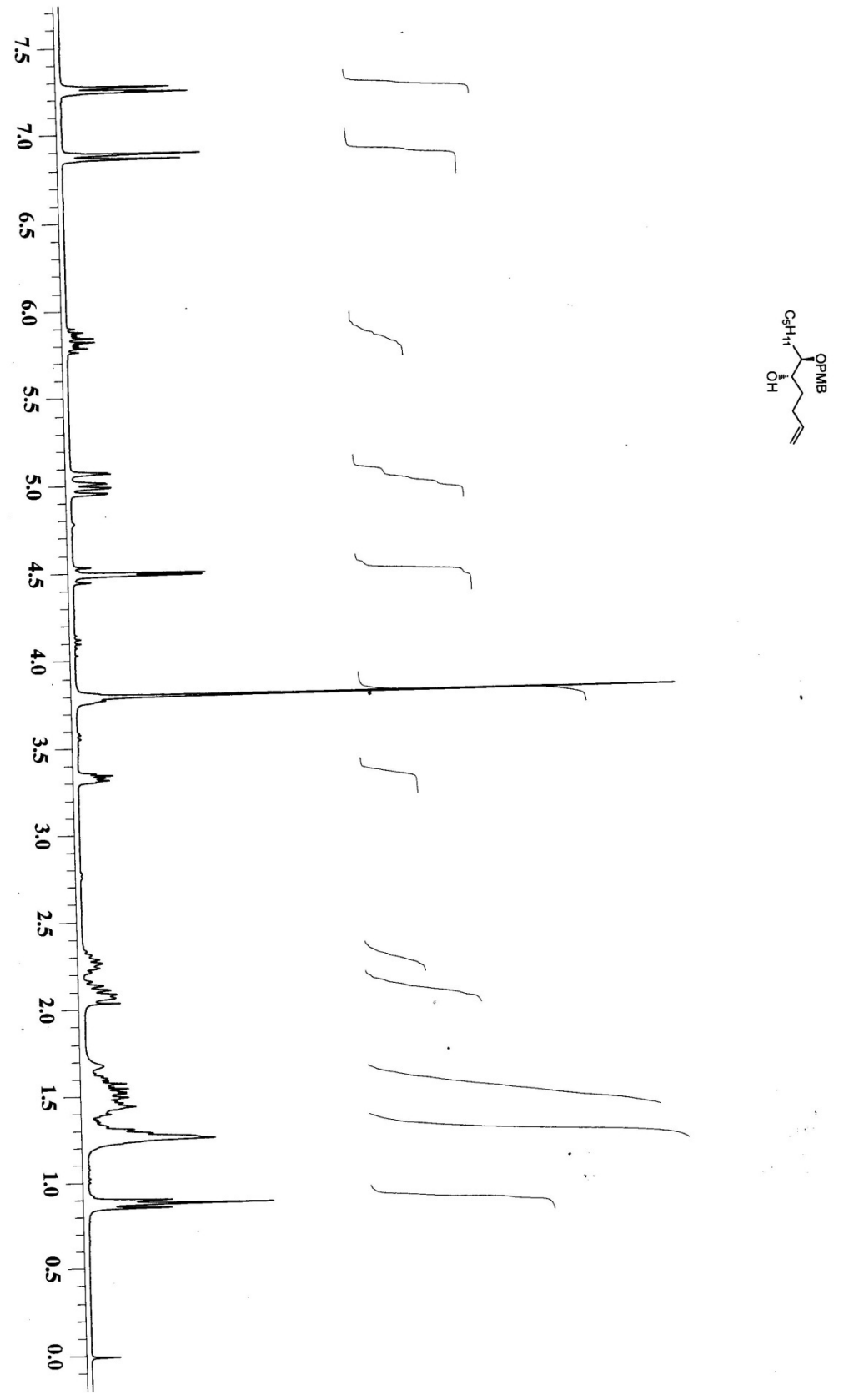
22.422
13.857



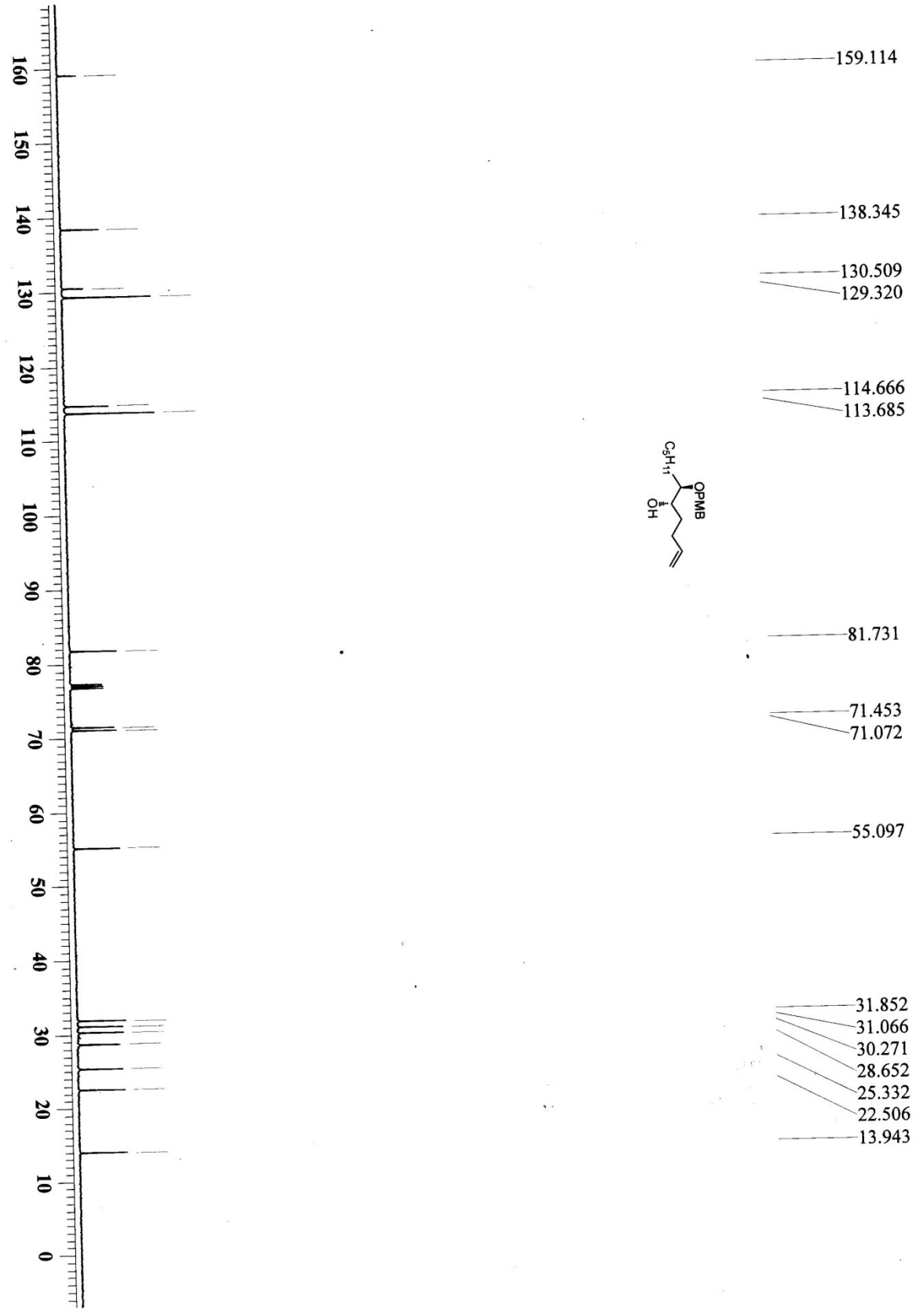
^{1}H-NMR of Compound 9



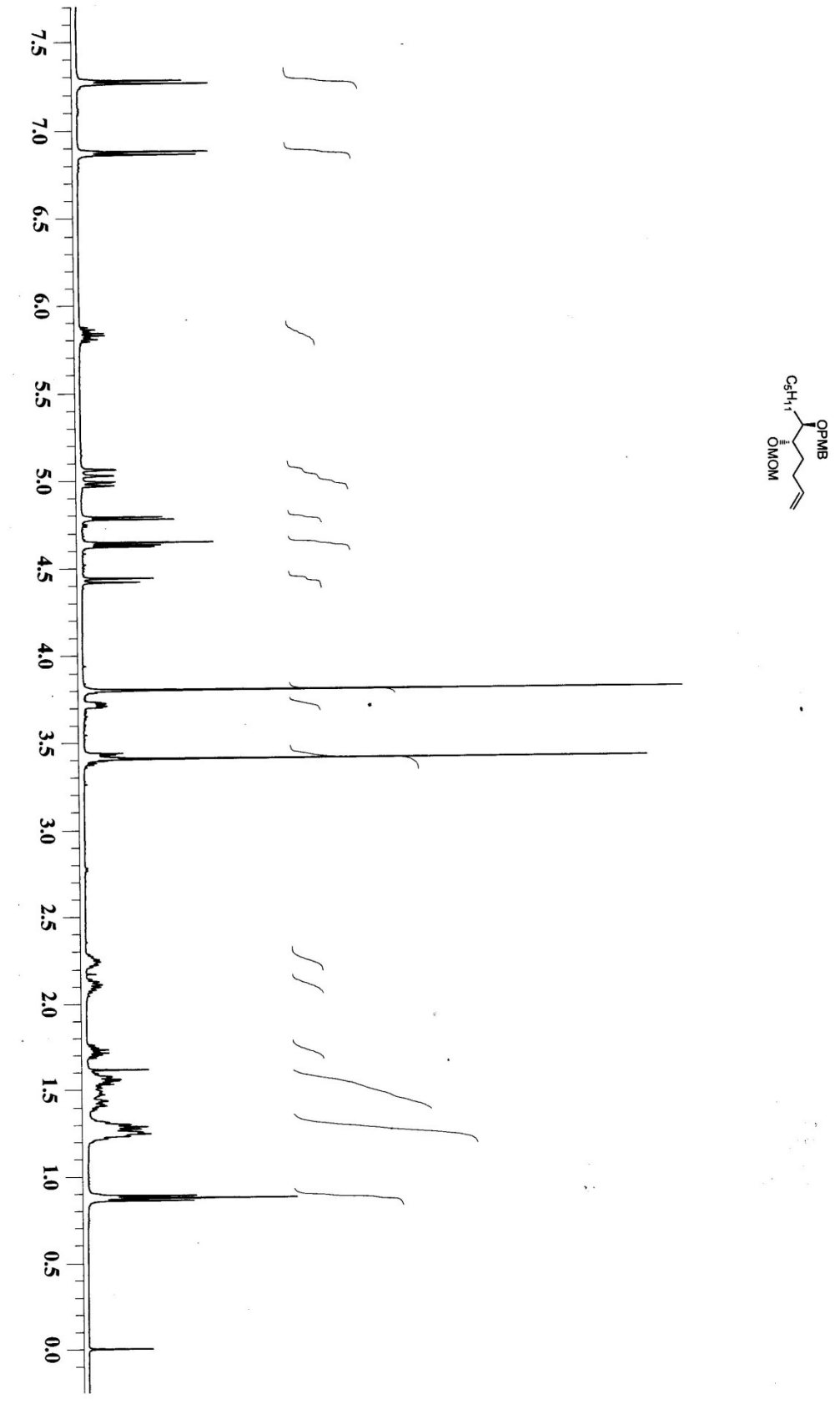
^{13}C-NMR of Compound 9



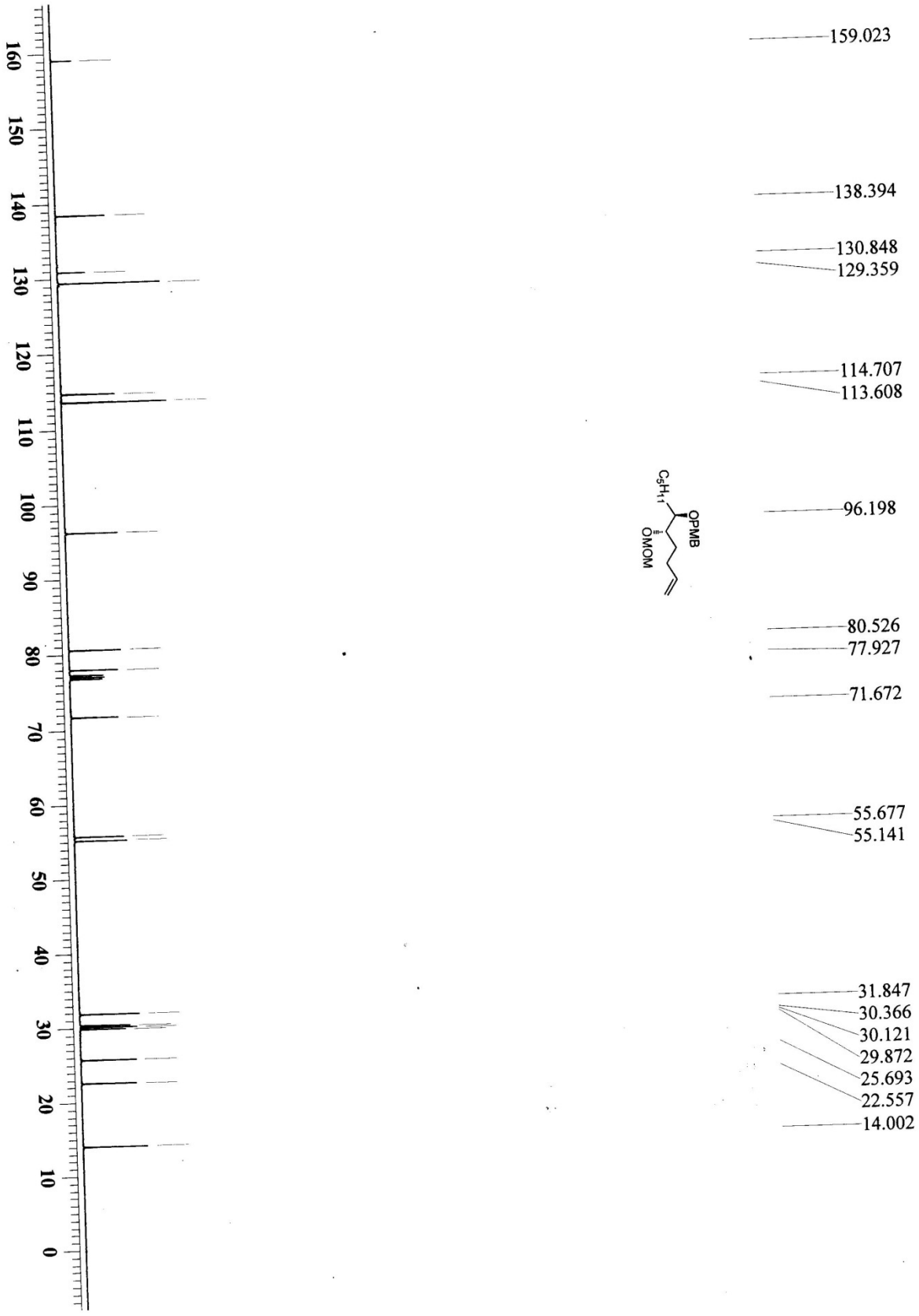
^{1}H-NMR of Compound 10



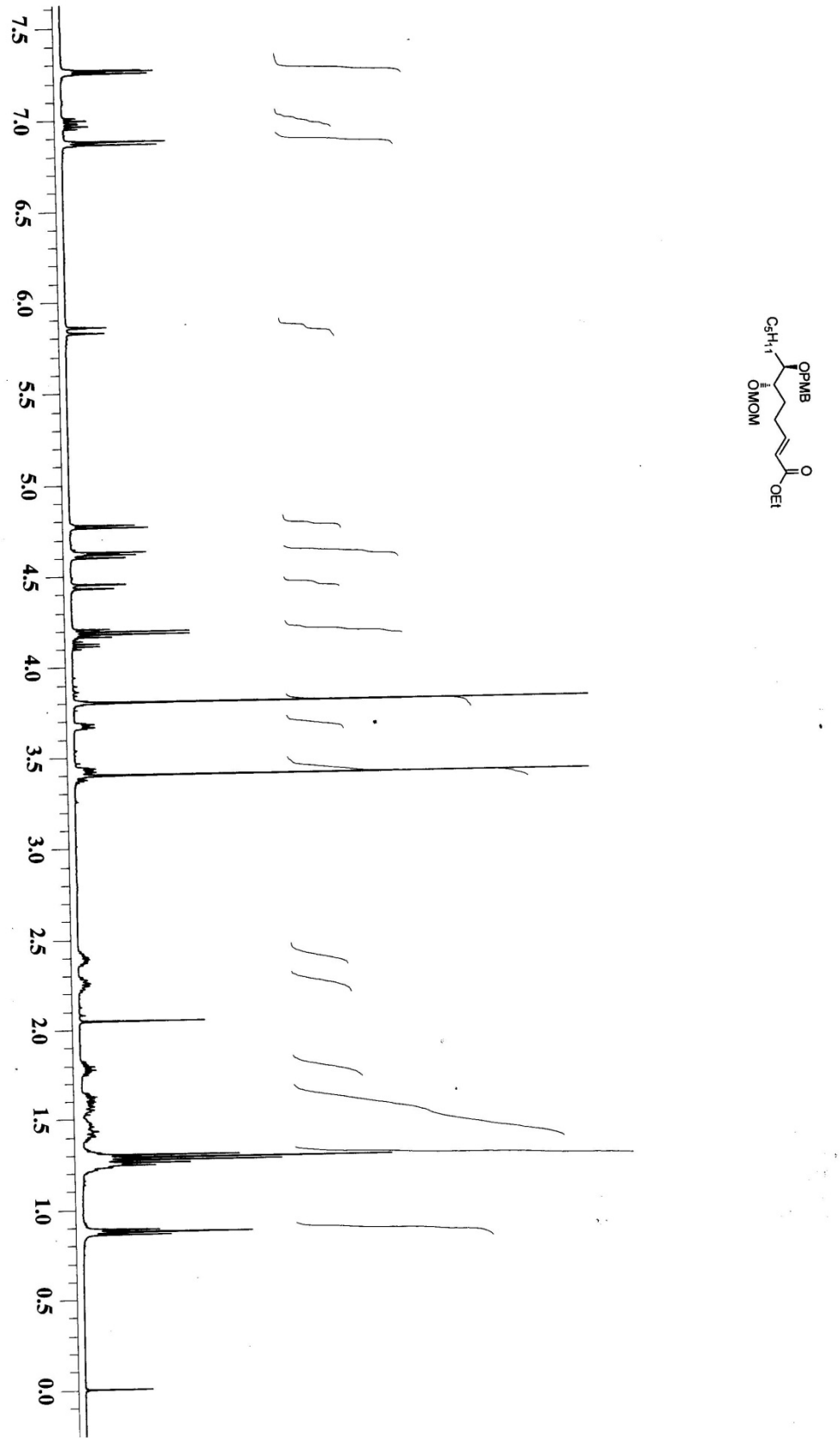
^{13}C-NMR of Compound 10



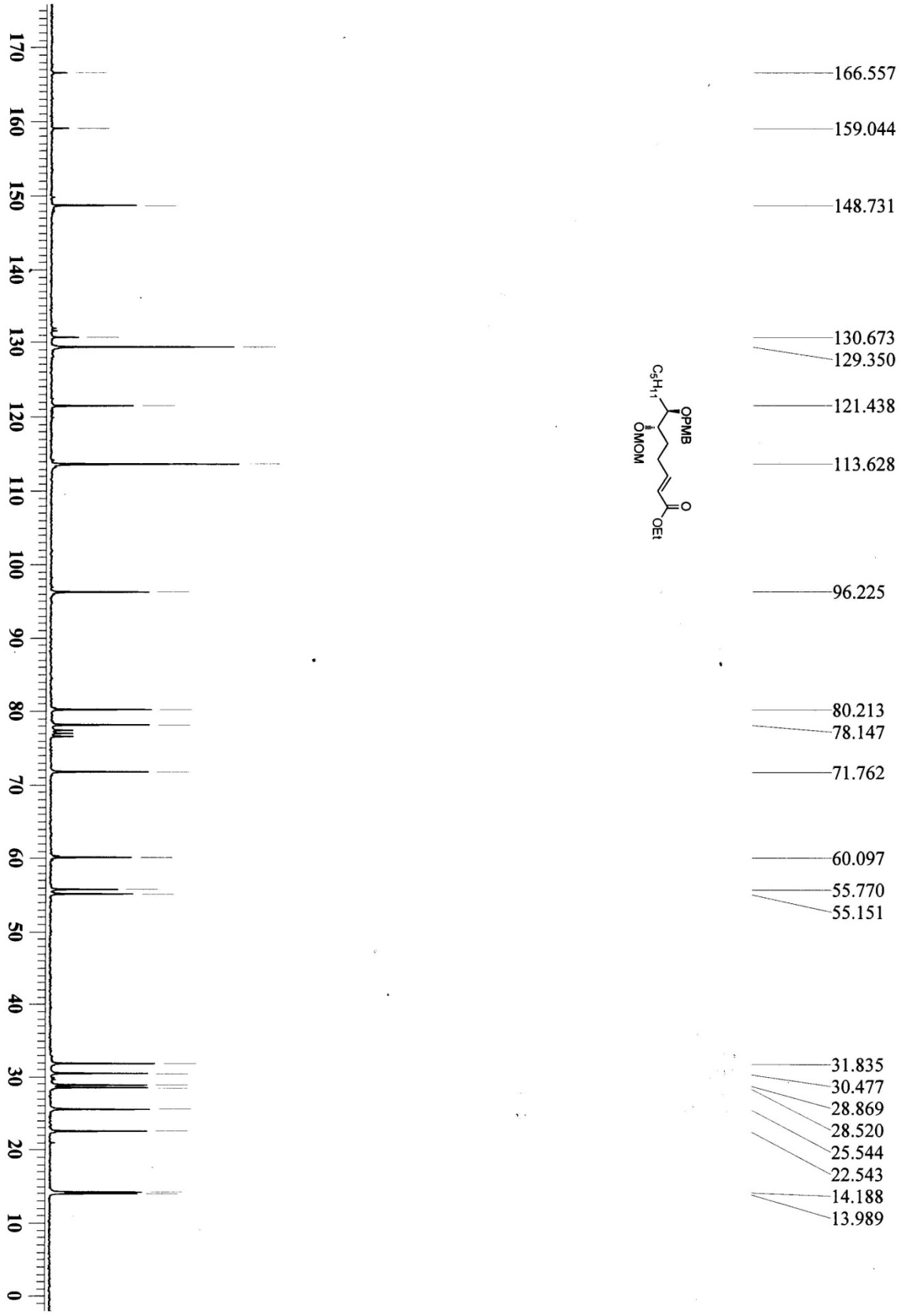
^{1}H-NMR of Compound 5



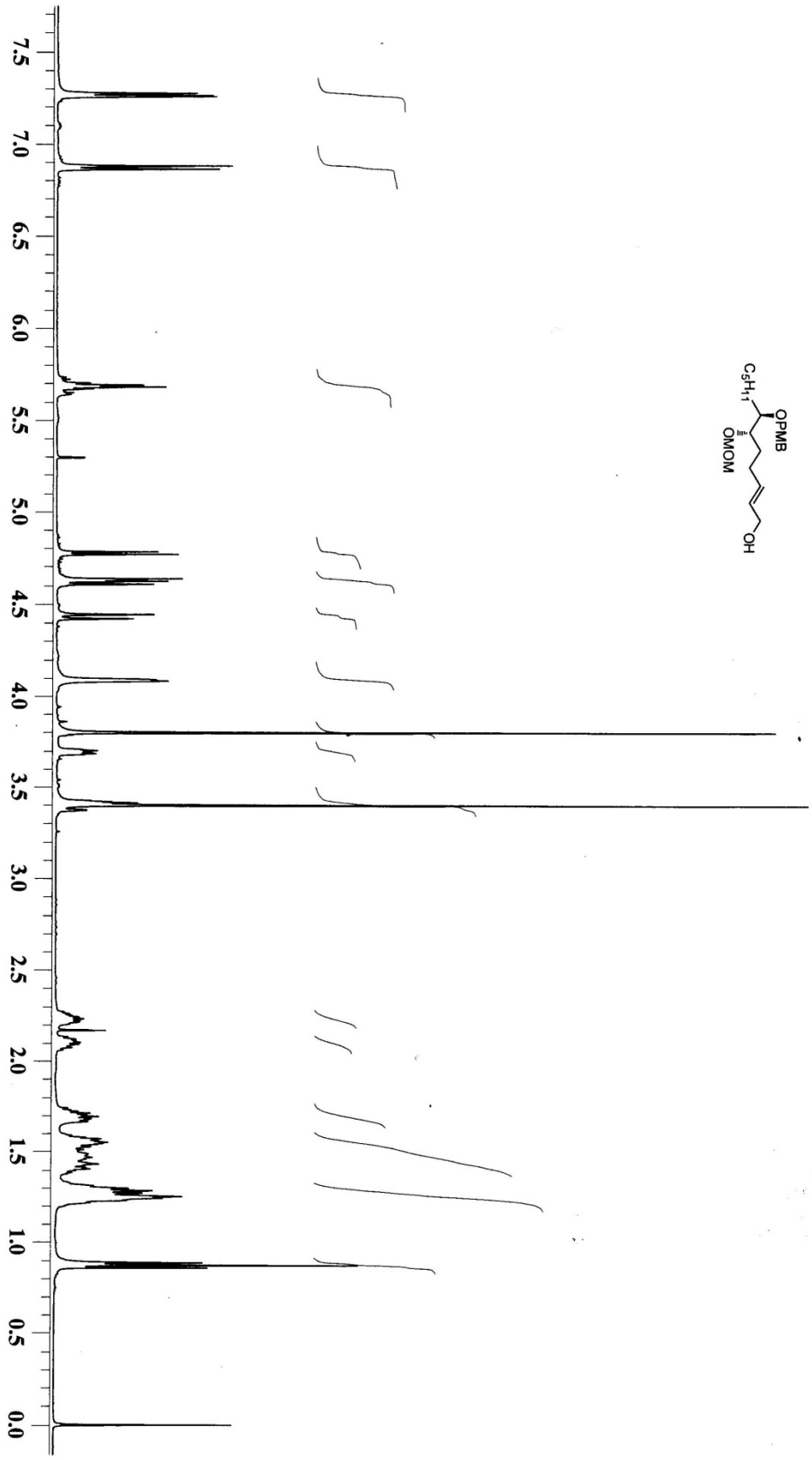
^{13}C-NMR of Compound 5



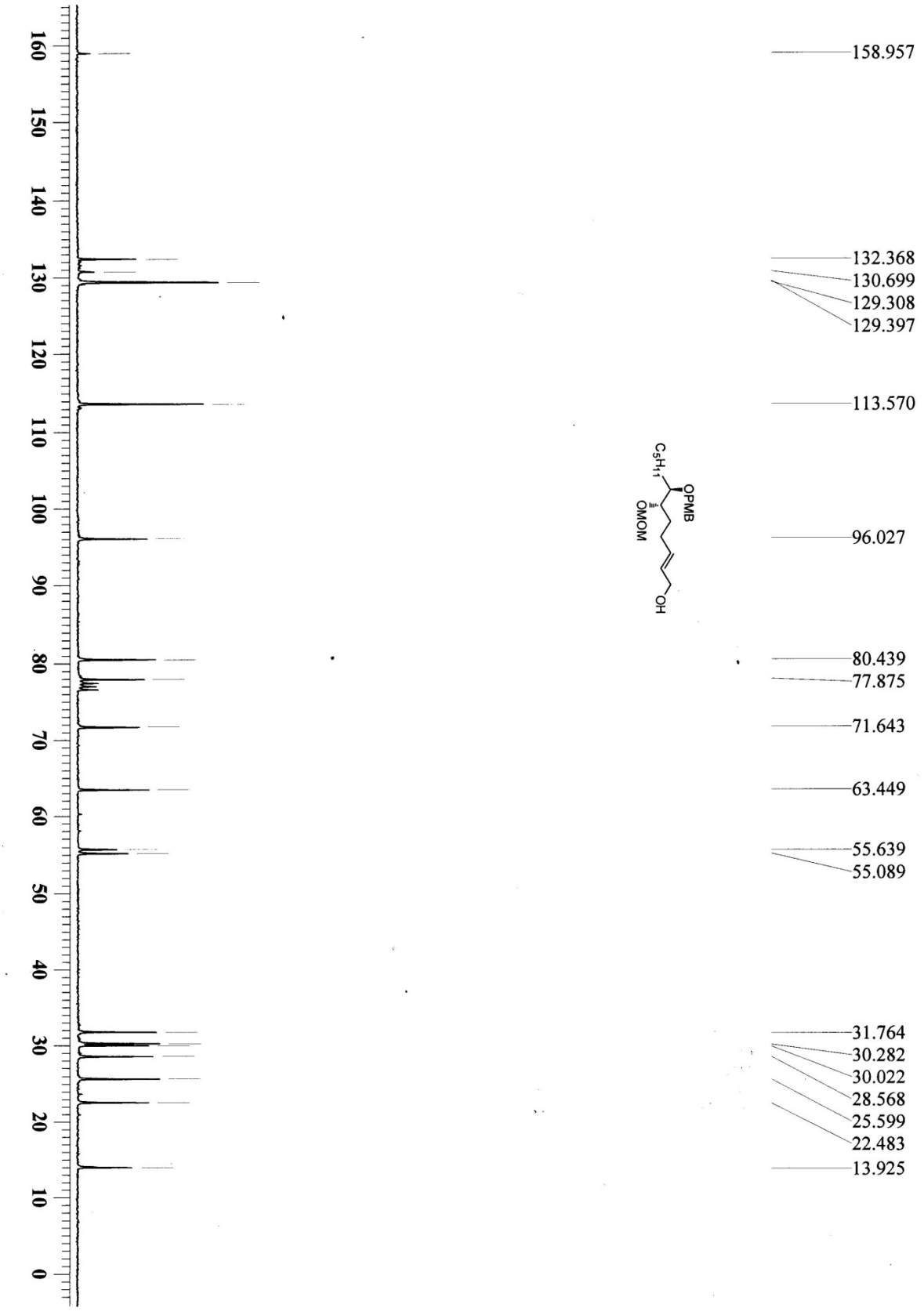
^{1}H-NMR of Compound 11



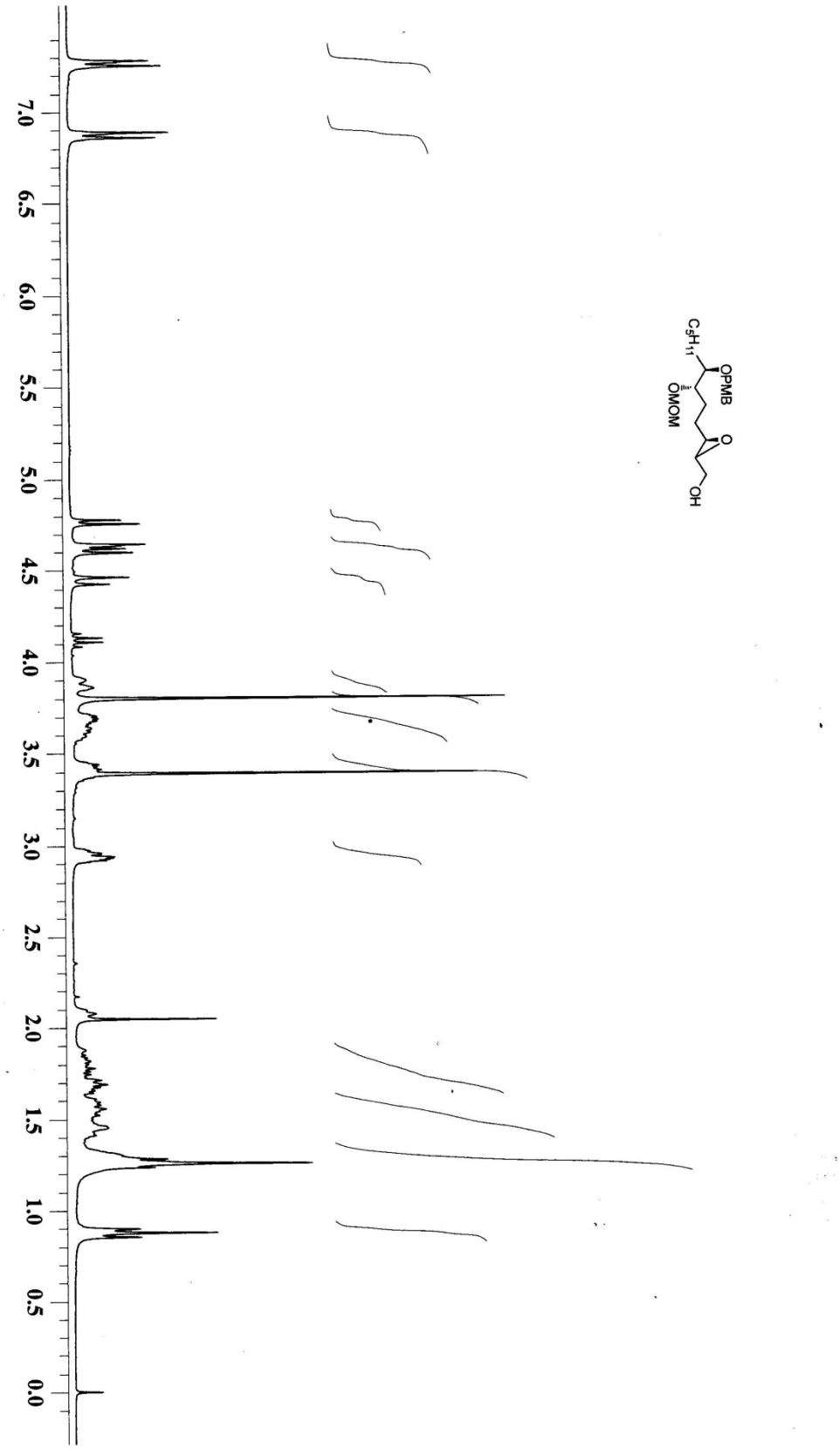
^{13}C-NMR of Compound 11



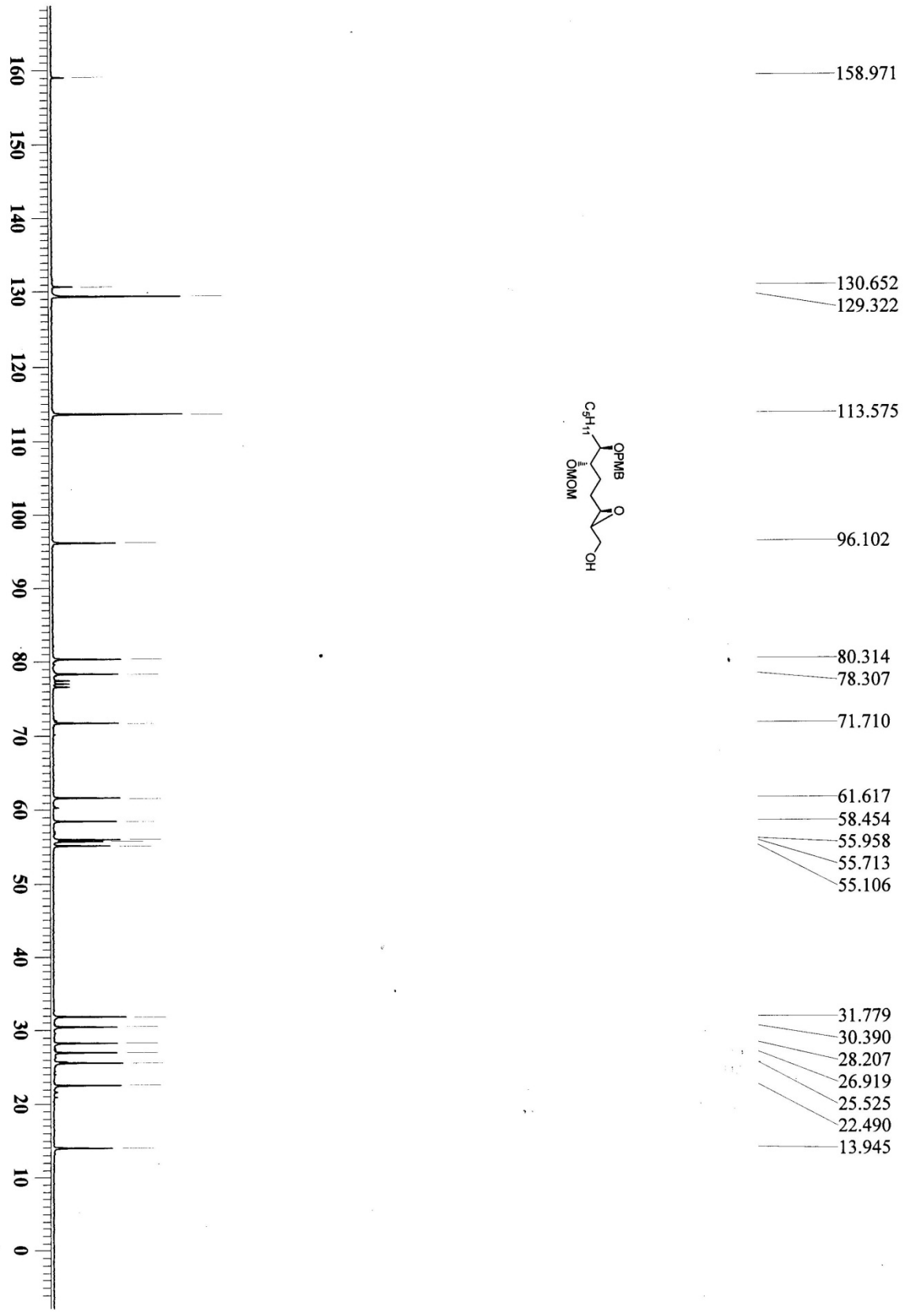
^{1}H-NMR of Compound 12



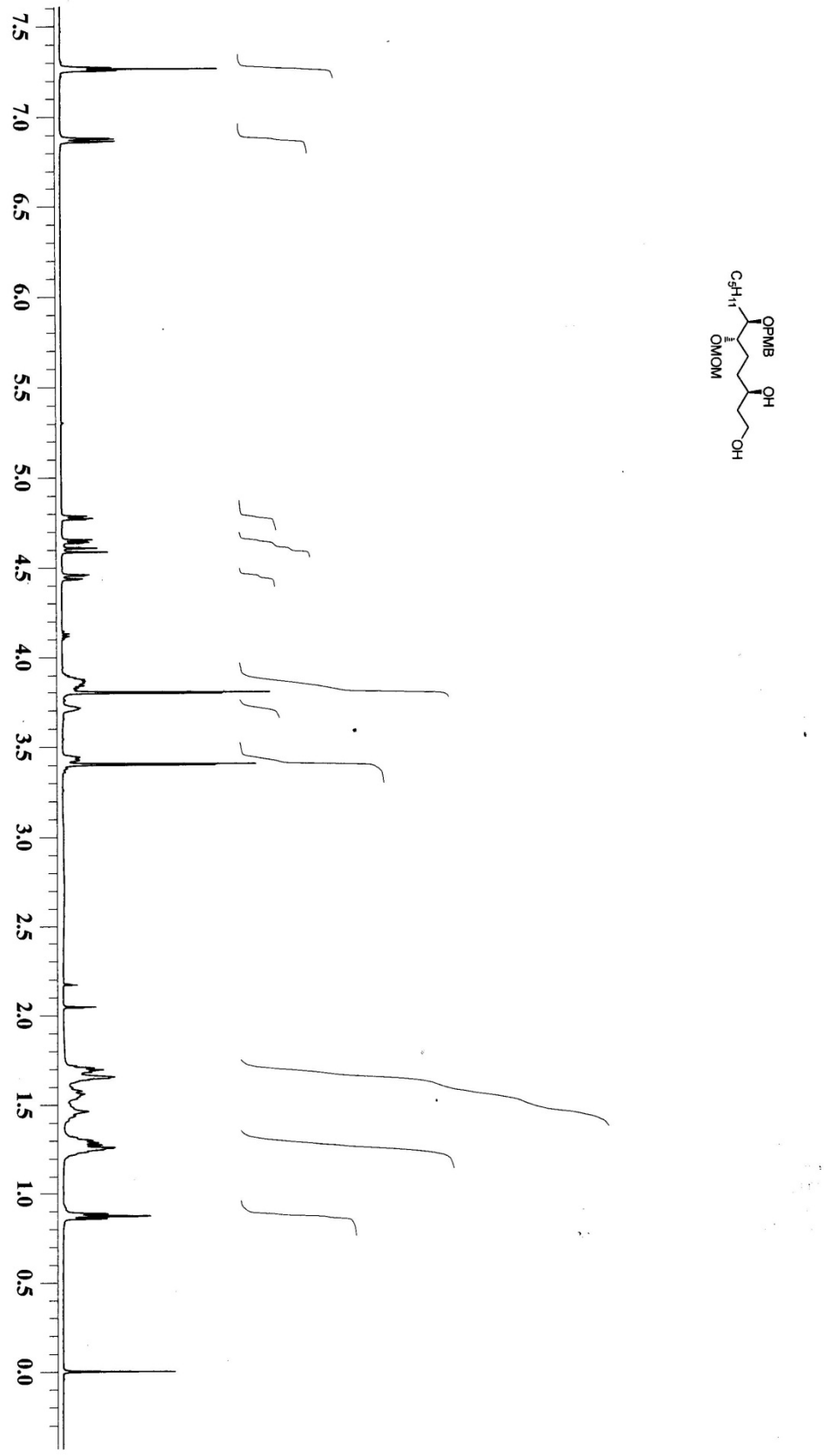
^{13}C-NMR of Compound 12



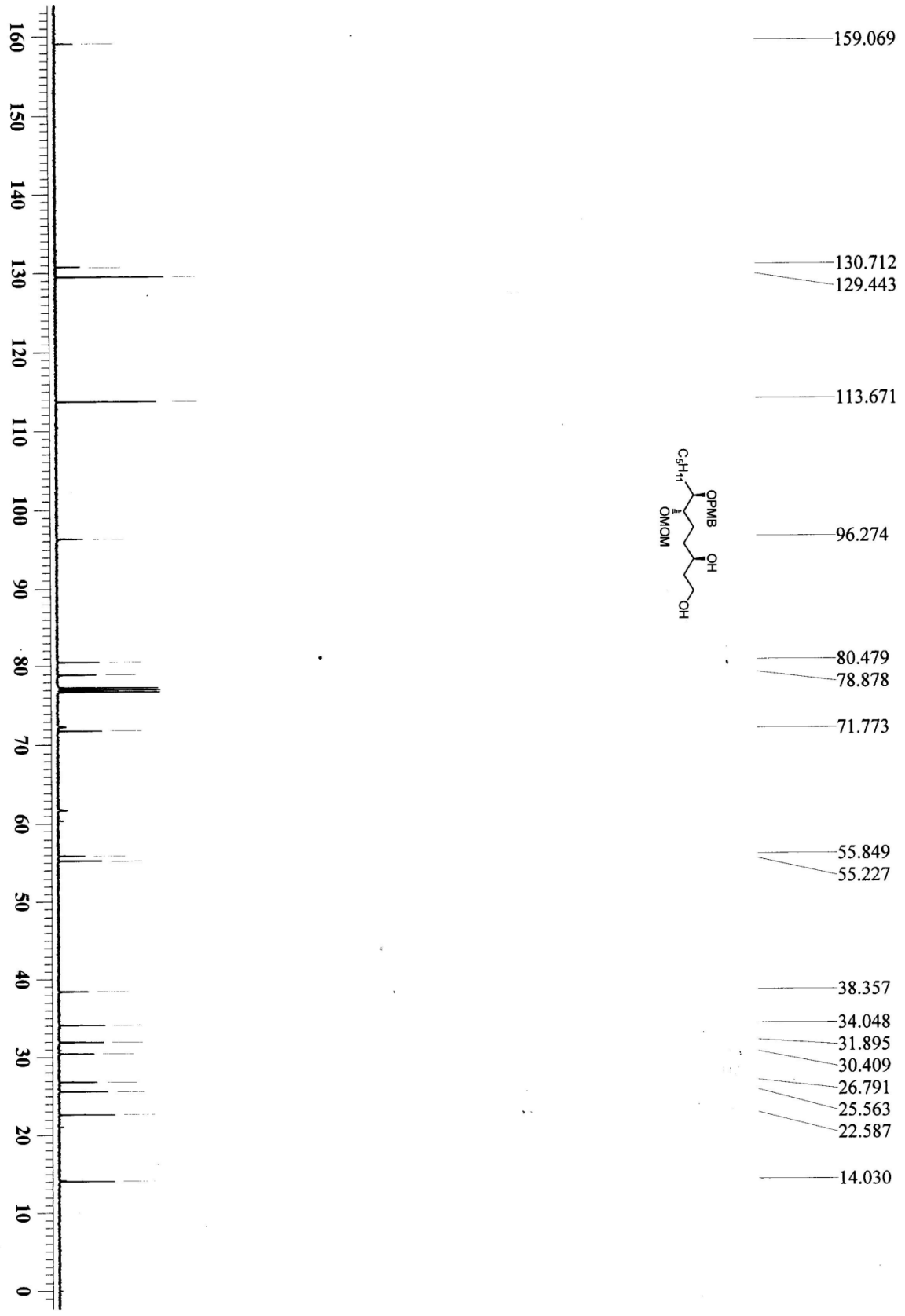
^{1}H-NMR of Compound 13



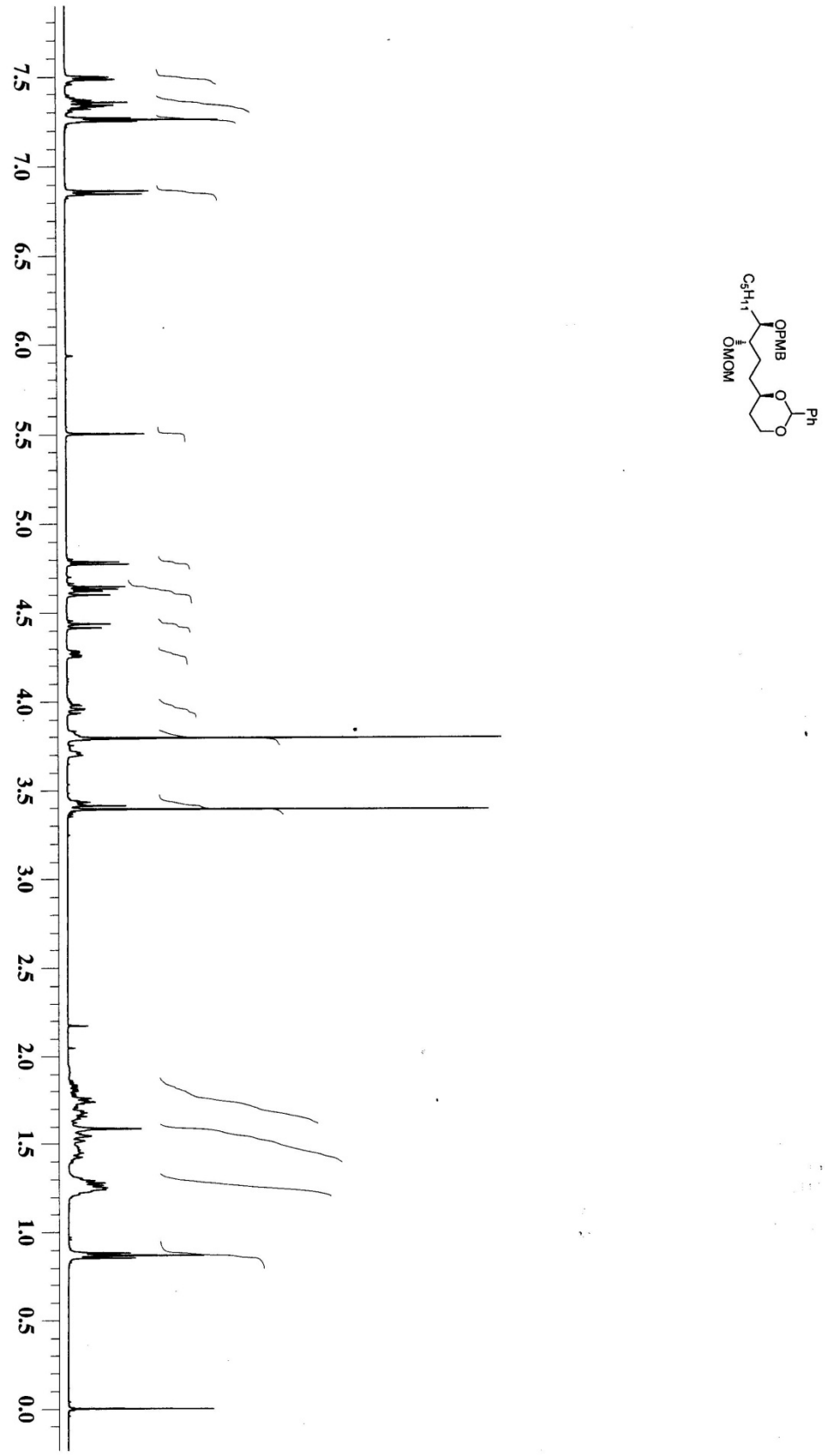
^{13}C-NMR of Compound 13



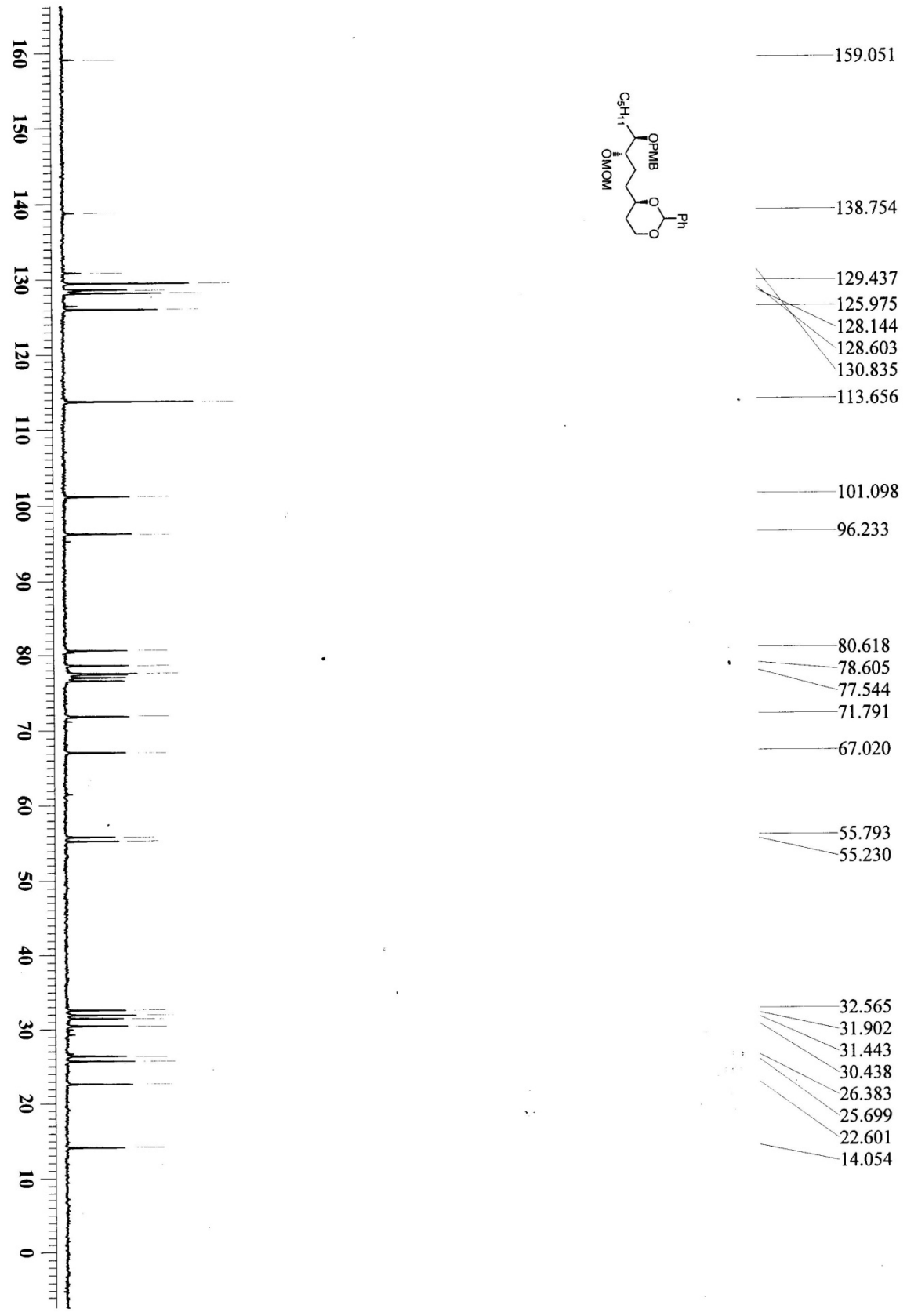
^{1}H-NMR of Compound diol



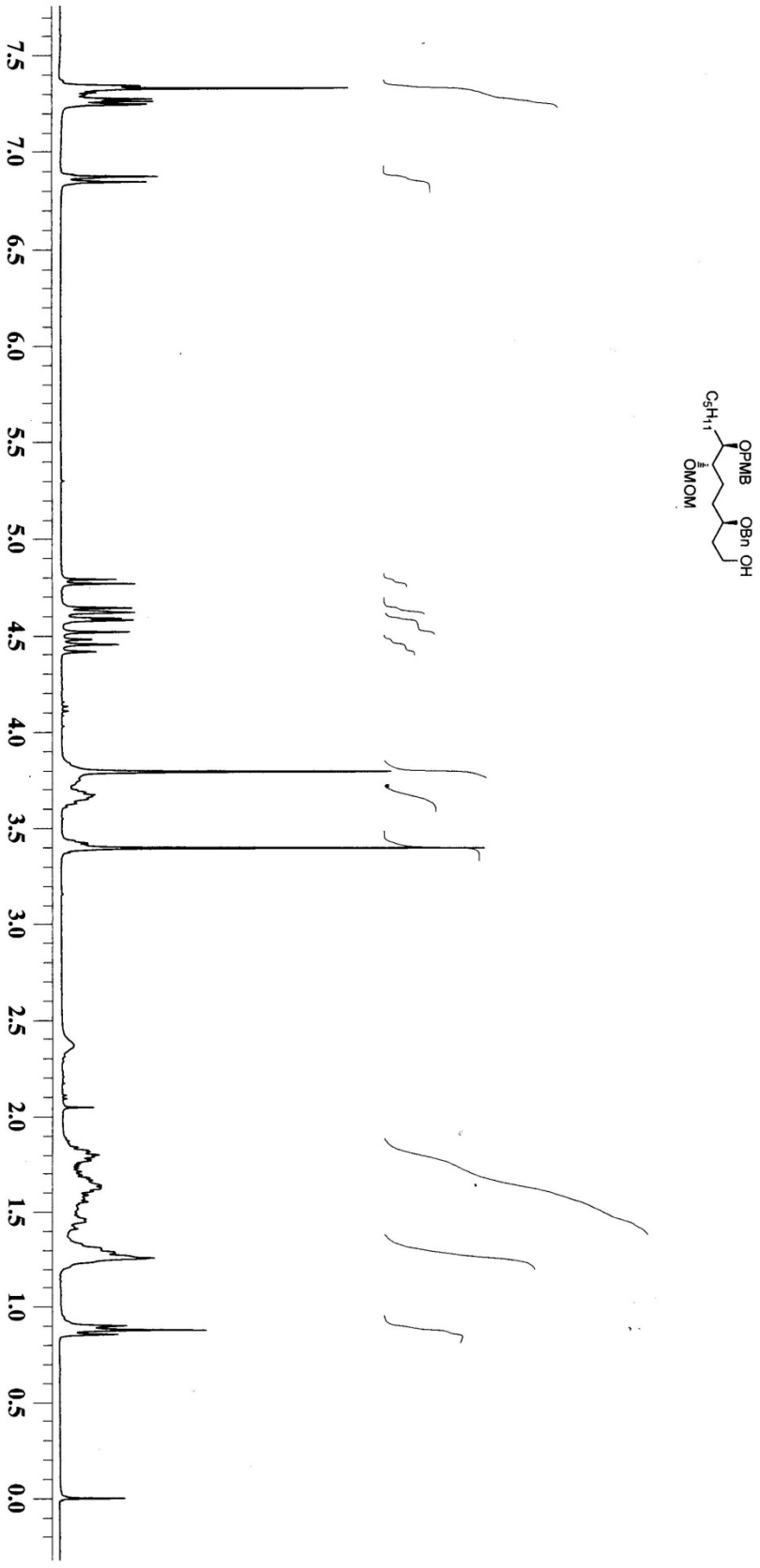
^{13}C-NMR of Compound diol



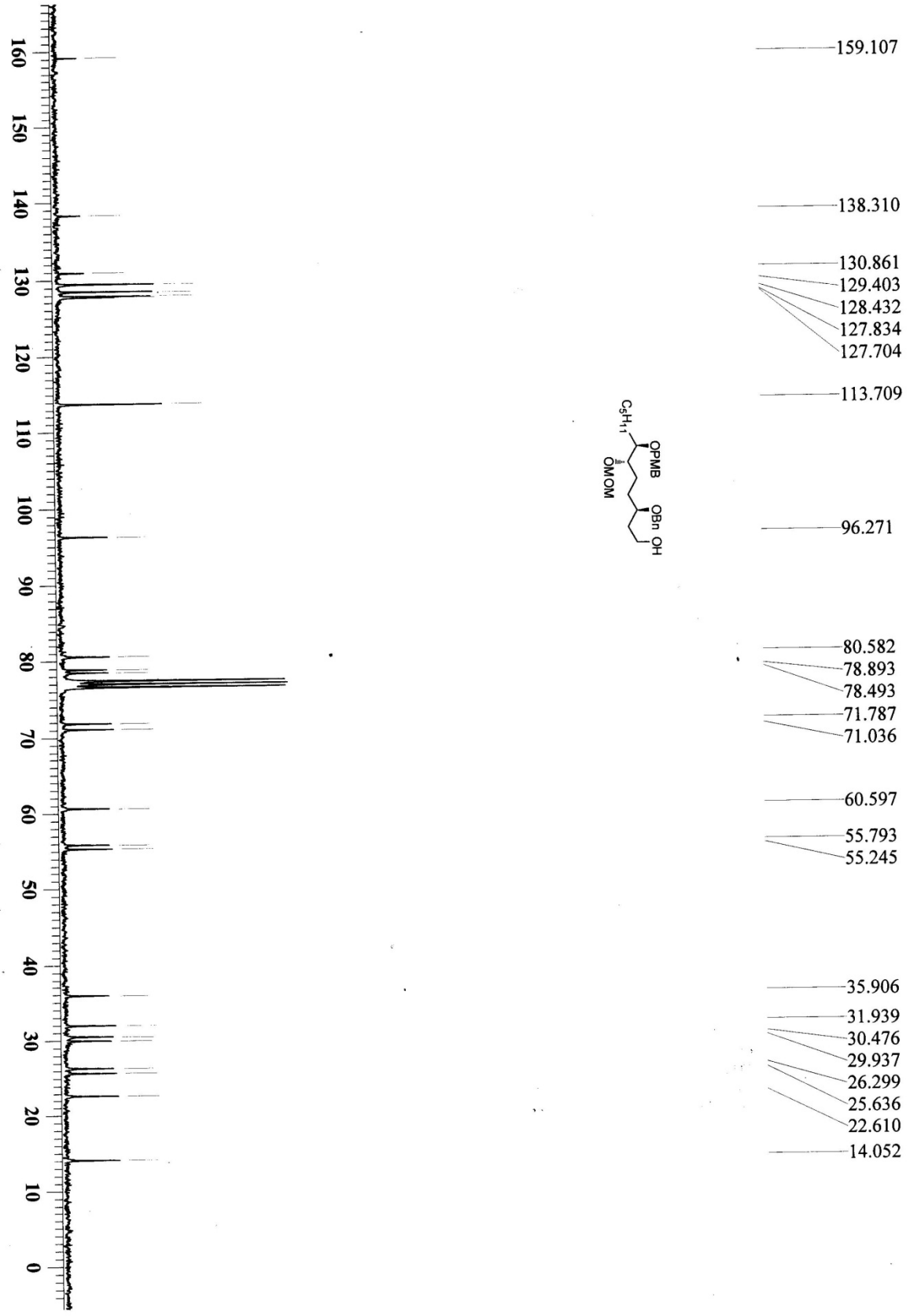
^{1}H-NMR of Compound 14



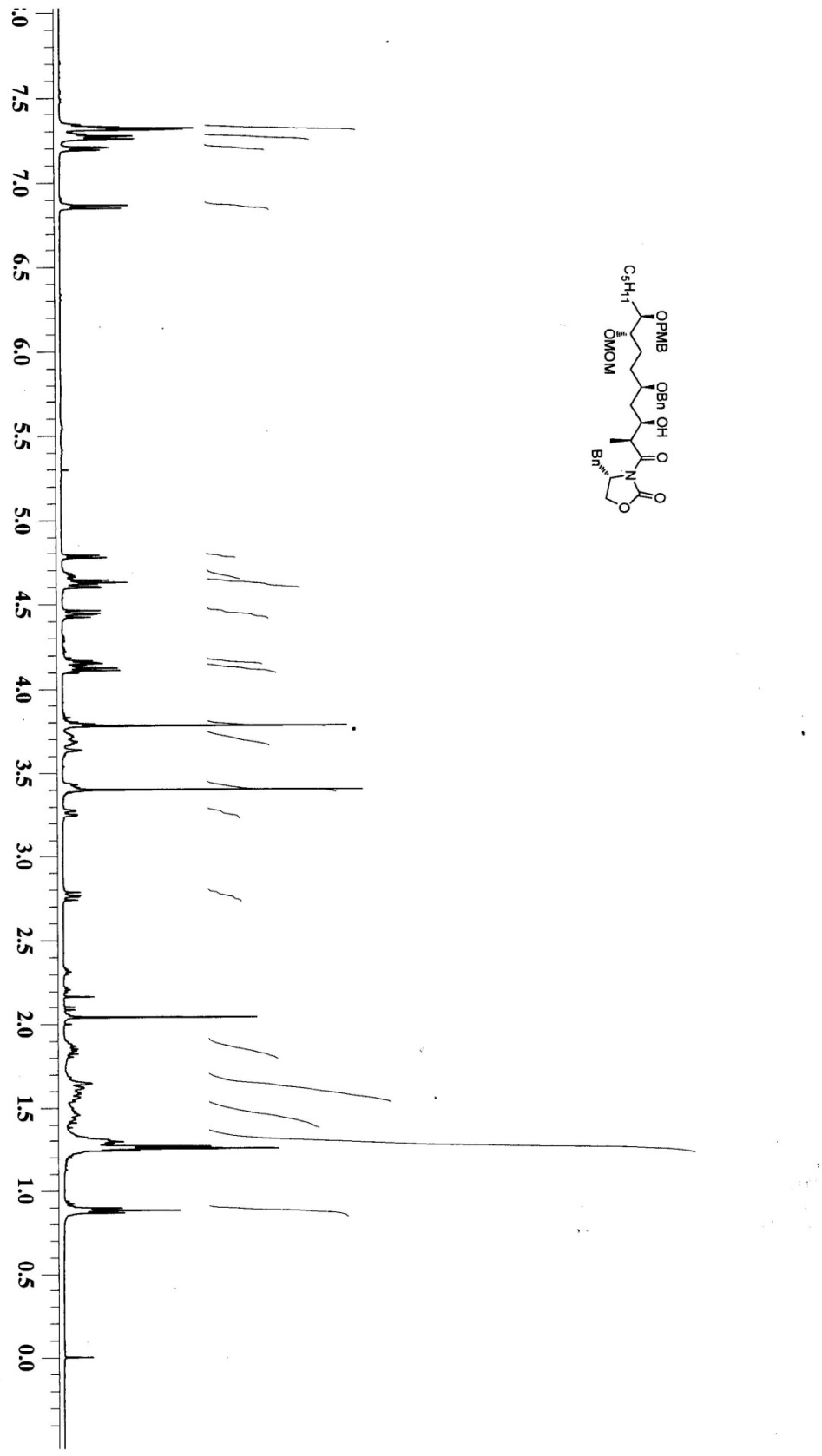
^{13}C-NMR of Compound 14



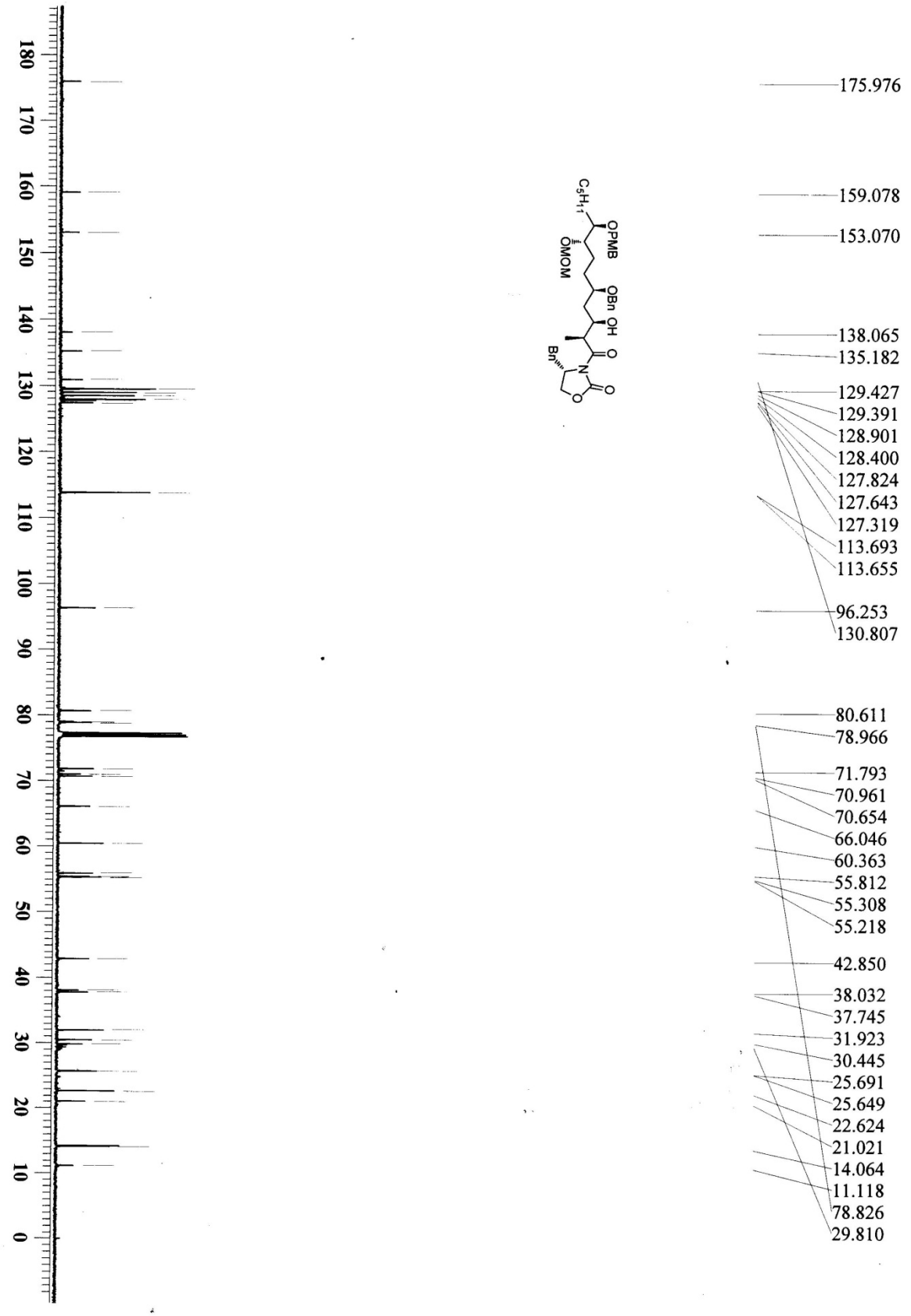
^{1}H-NMR of Compound 4



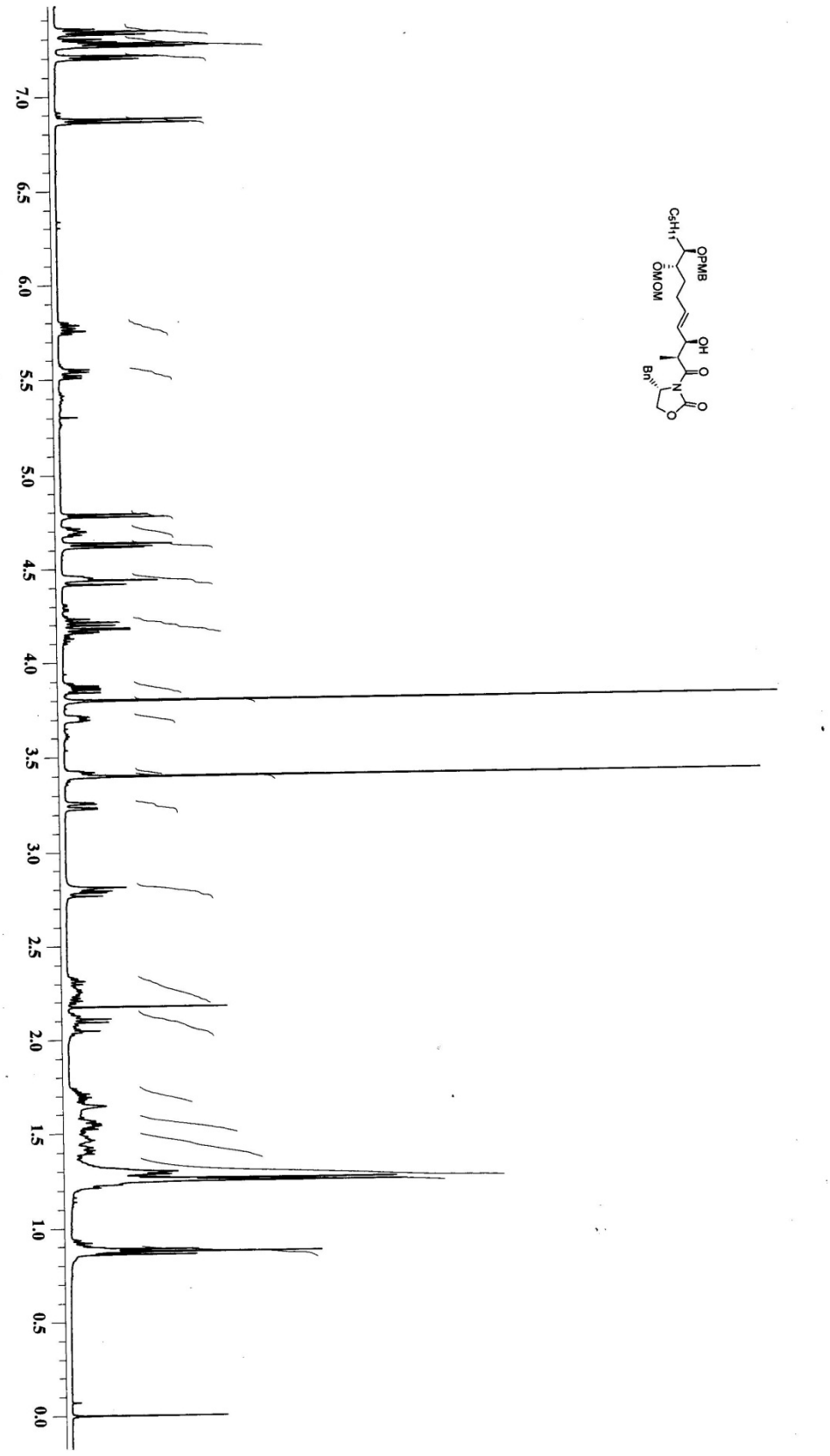
^{13}C-NMR of Compound 4



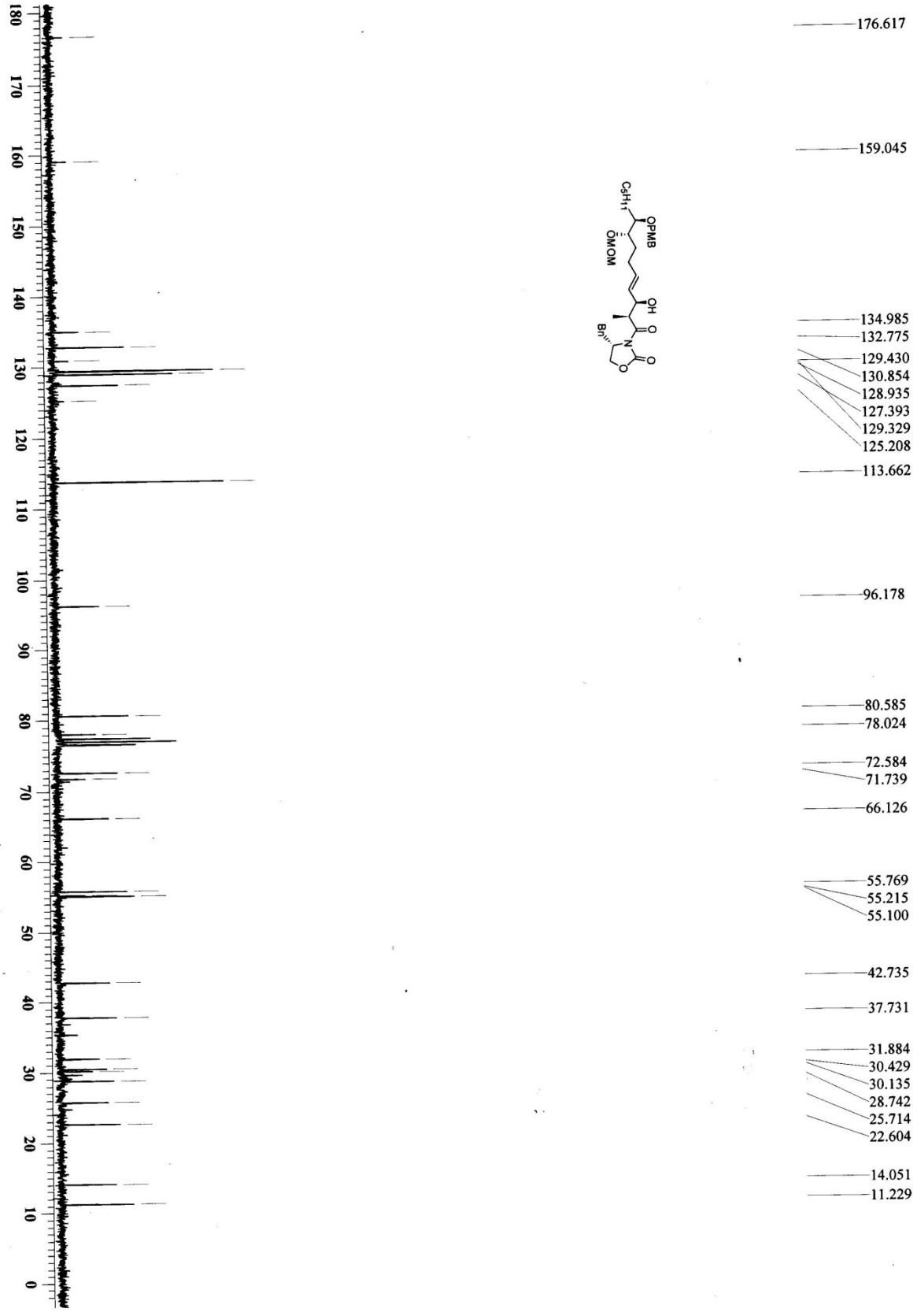
^{1}H-NMR of Compound 16



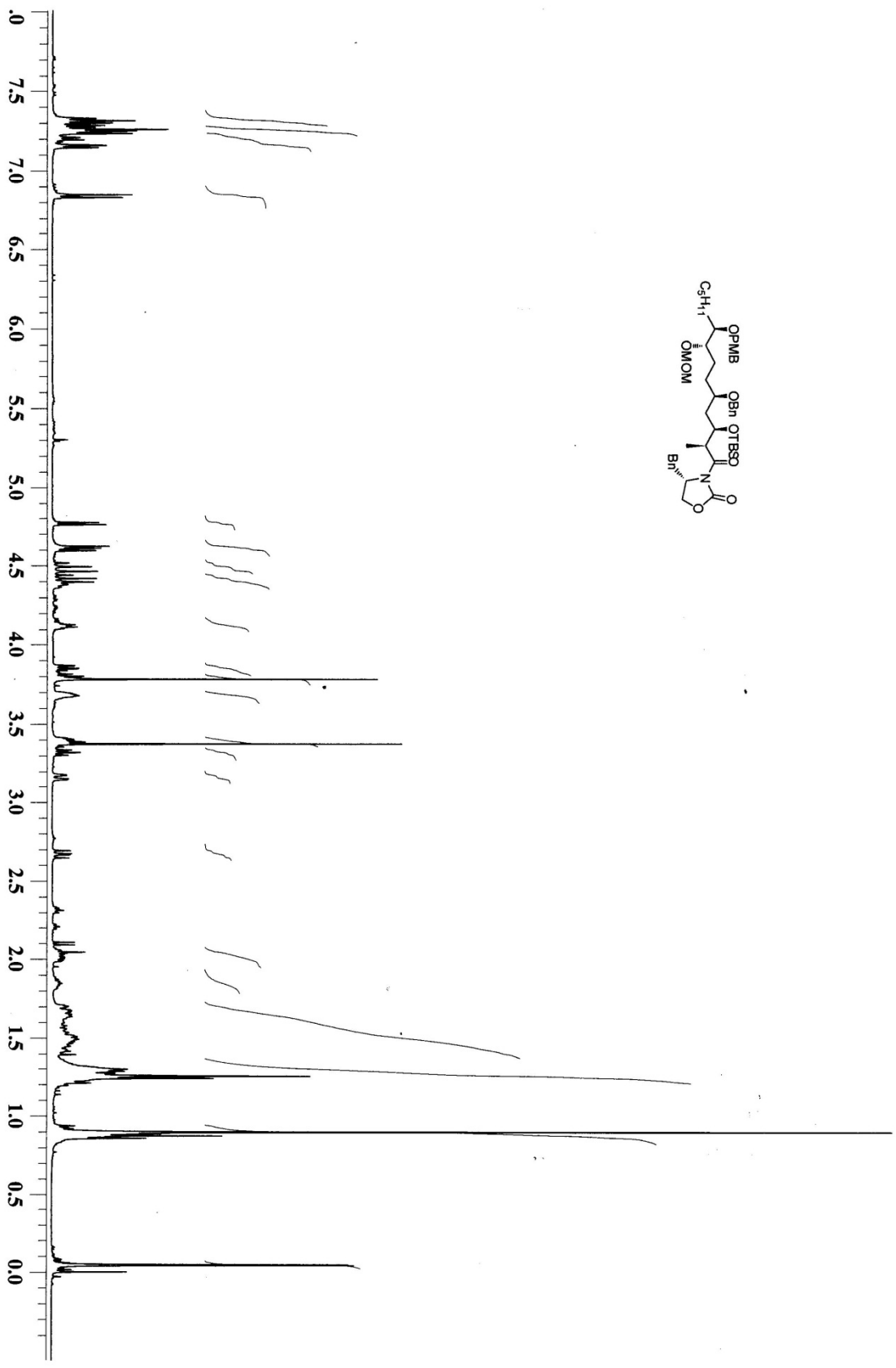
^{13}C-NMR of Compound 16



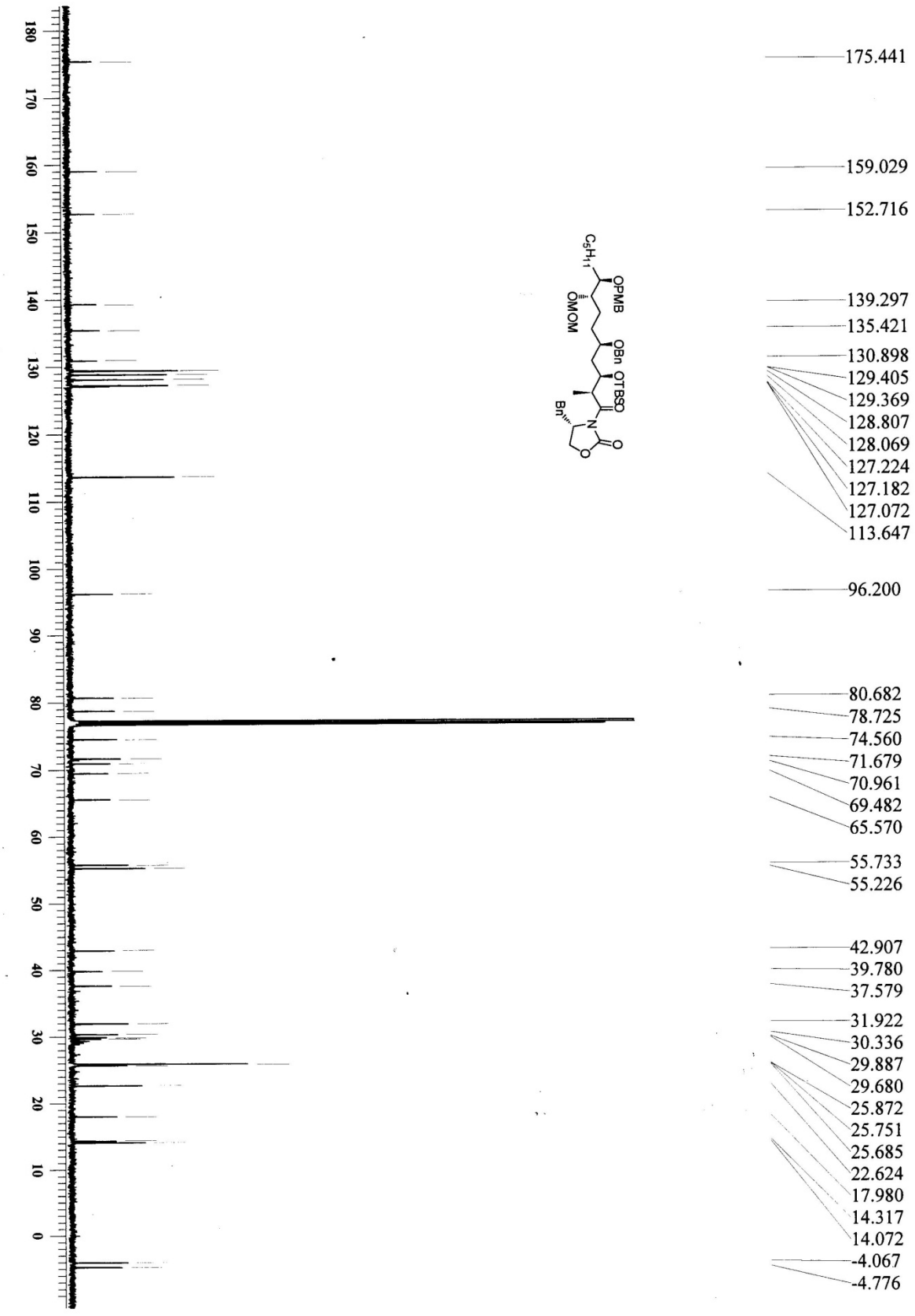
^{1}H-NMR of Compound 17



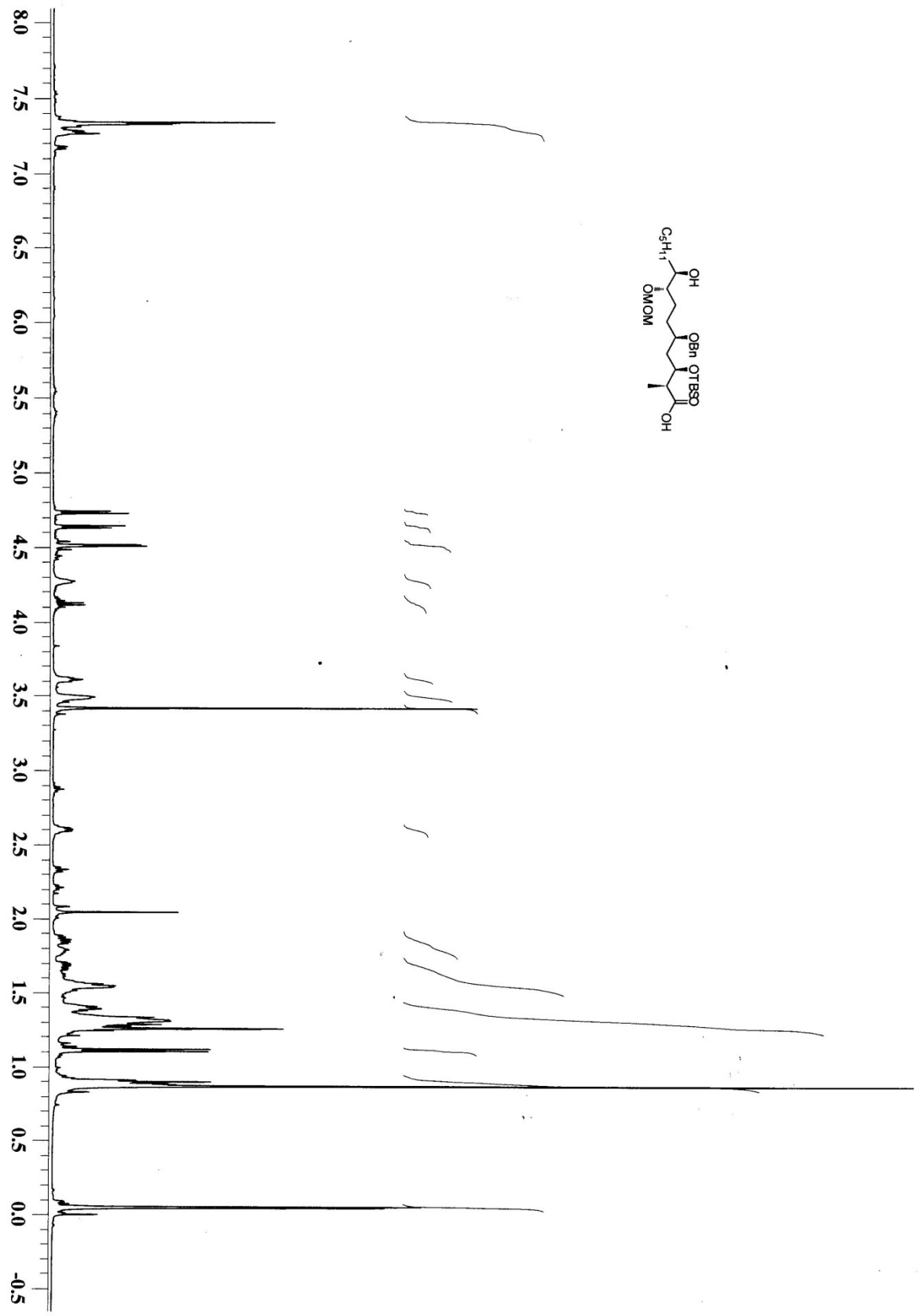
^{13}C-NMR of Compound 17



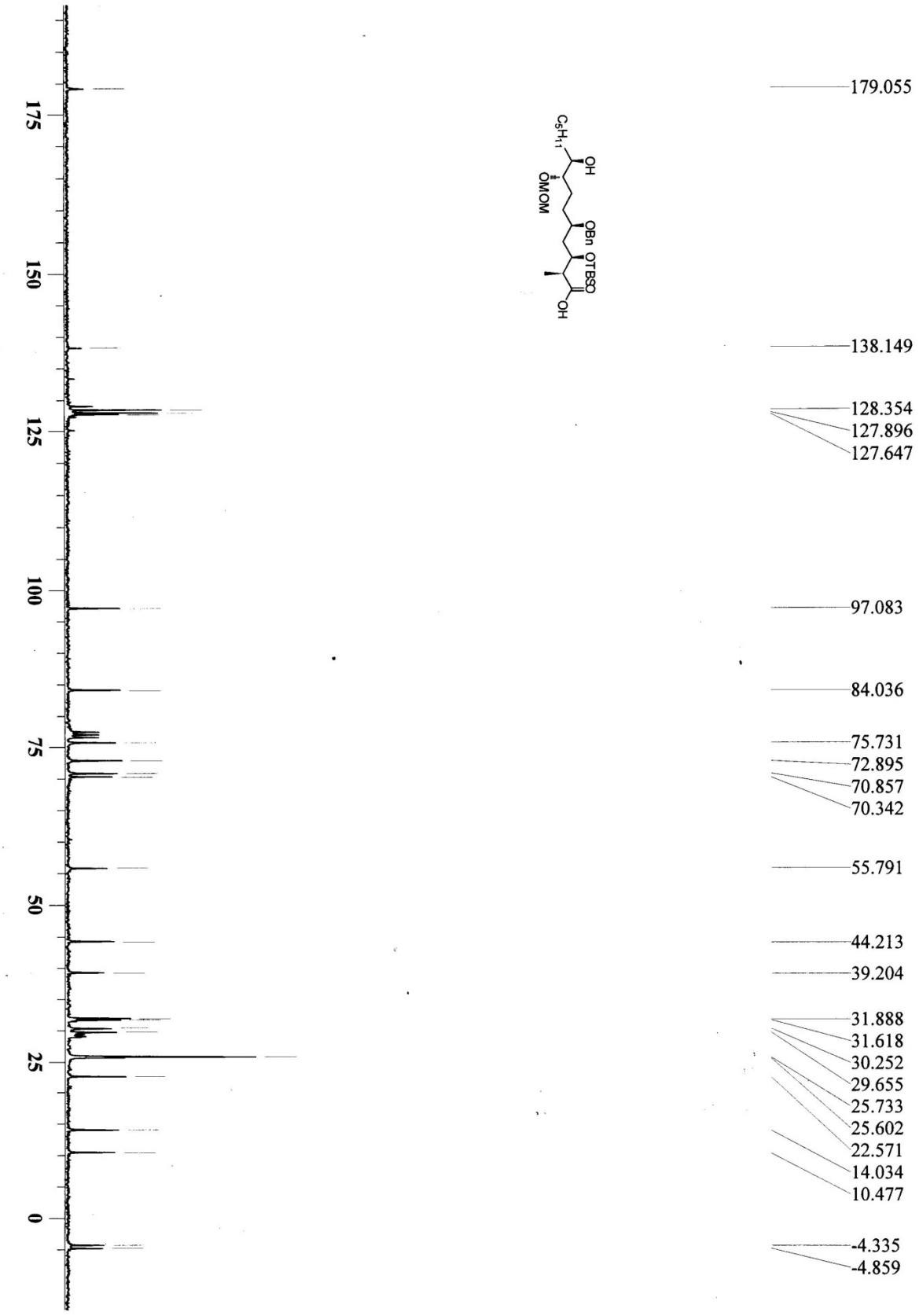
^{1}H-NMR of Compound 18



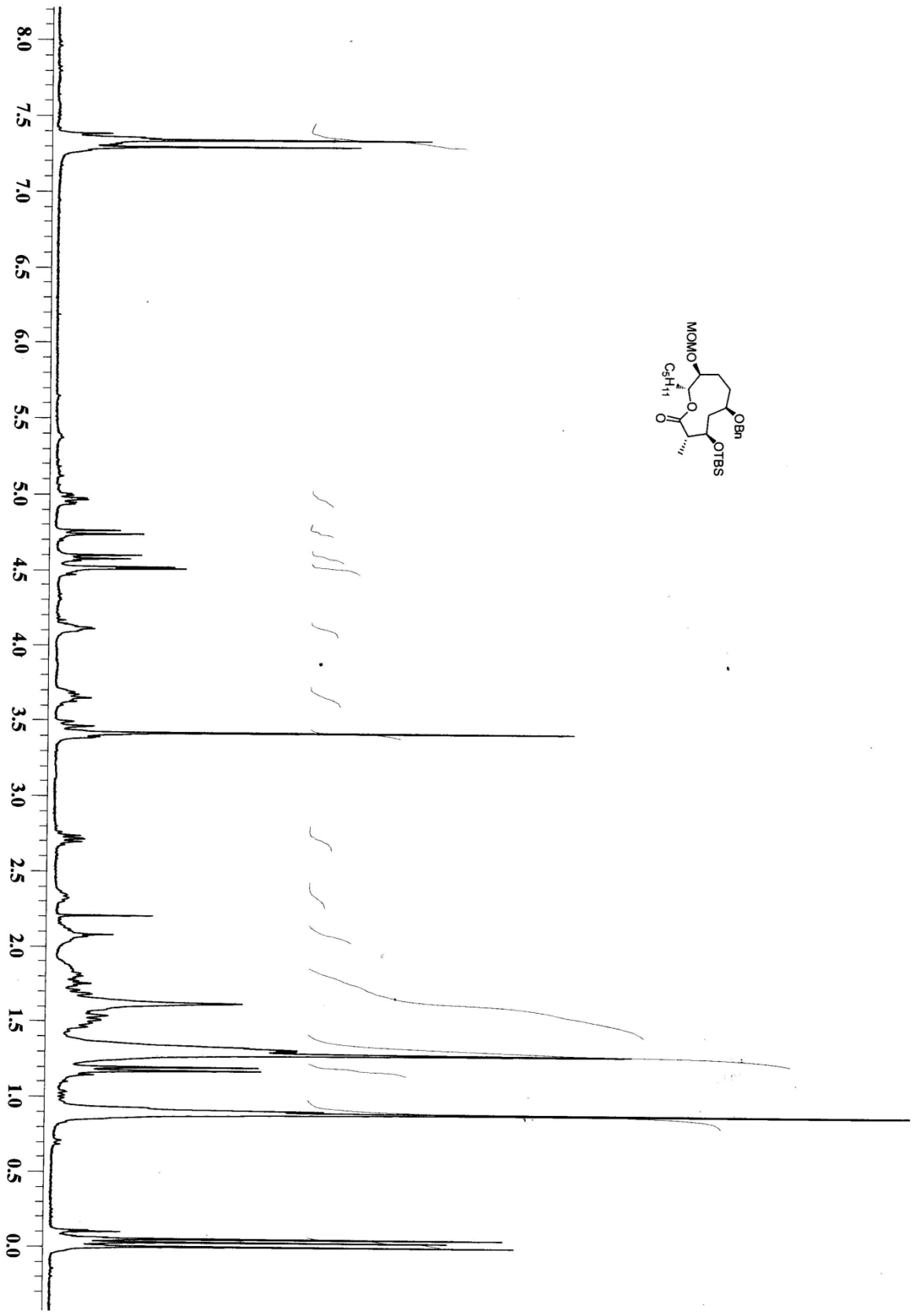
^{13}C-NMR of Compound 18



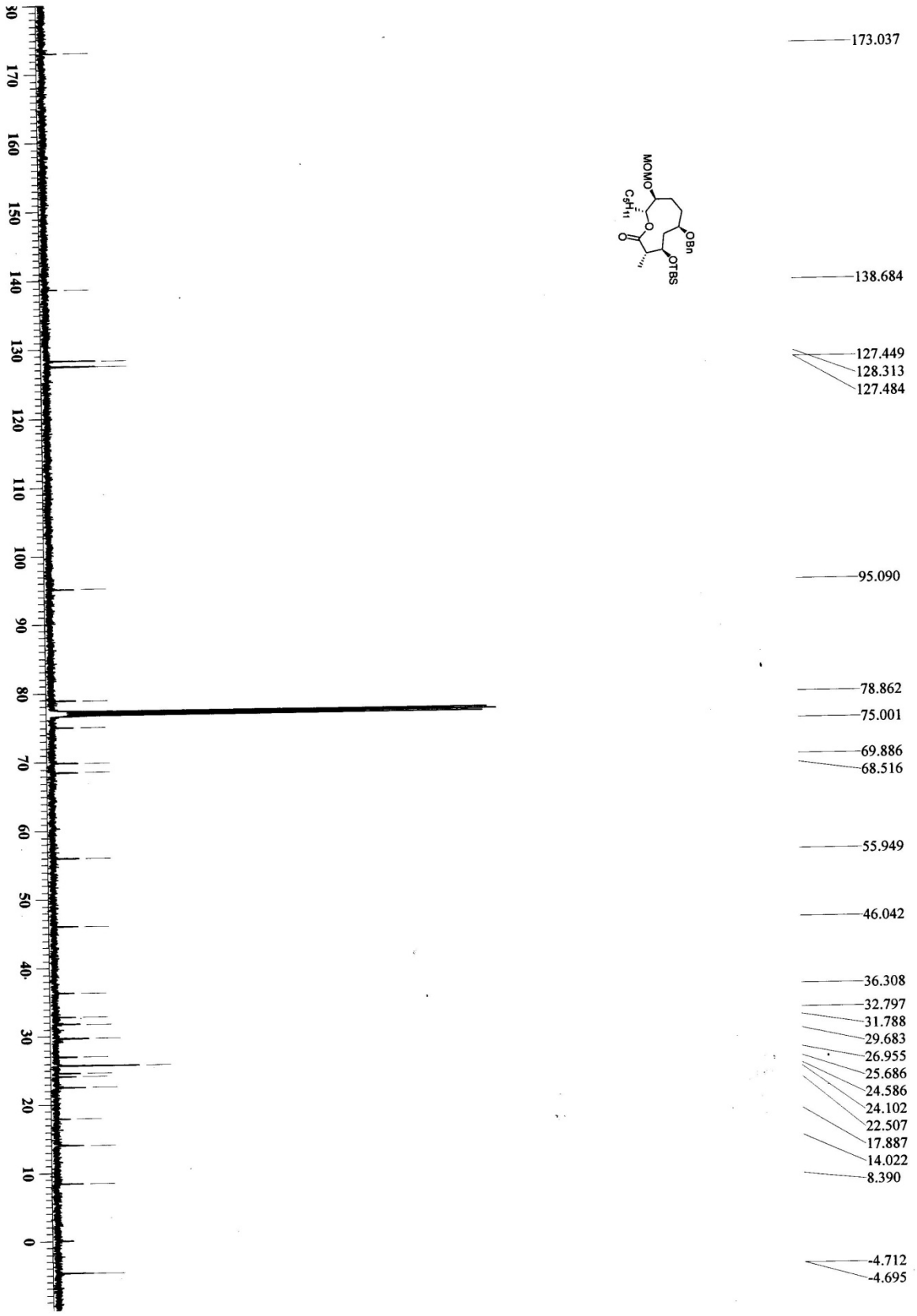
[1]H-NMR of Compound 3



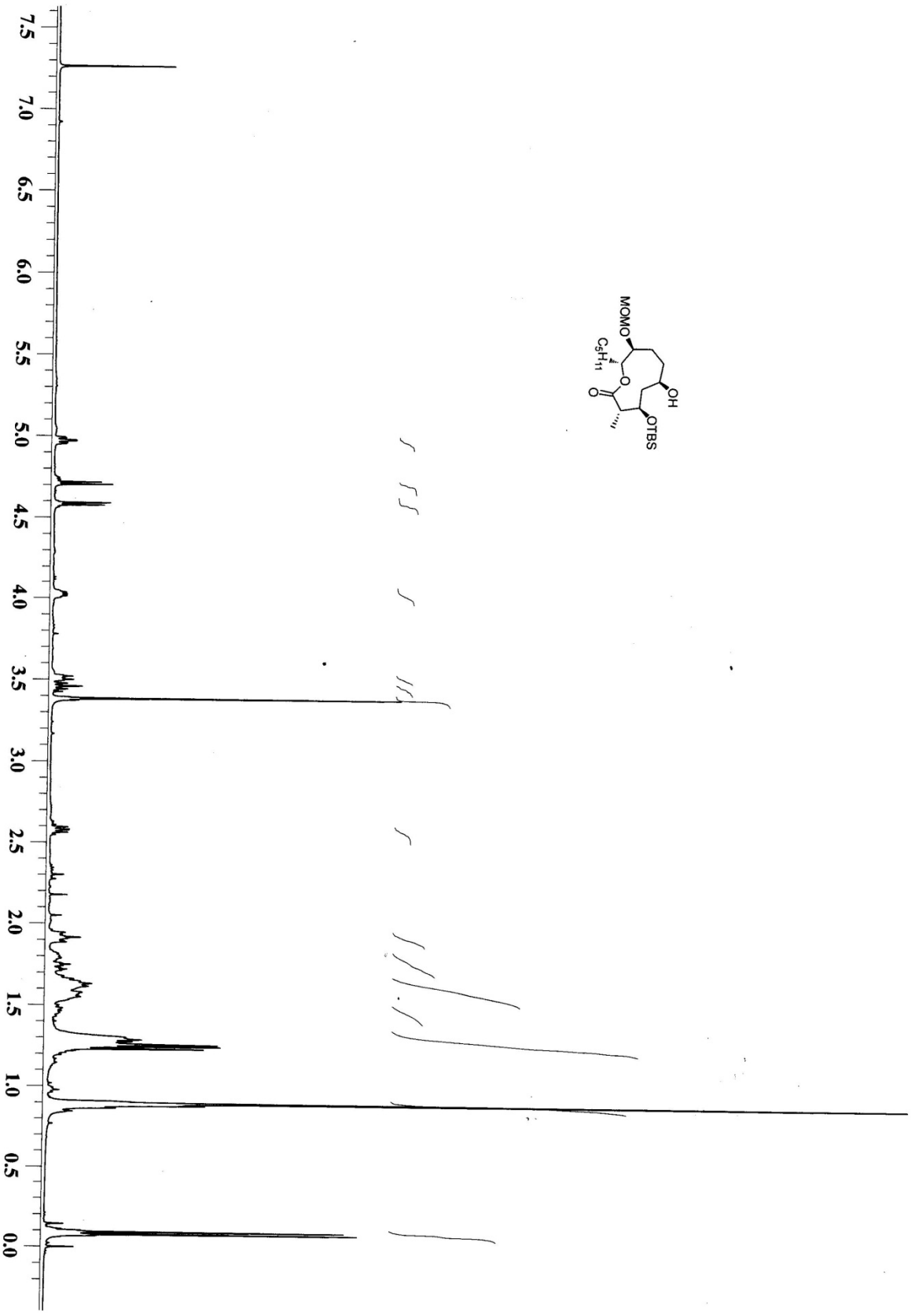
^{13}C-NMR of Compound 3



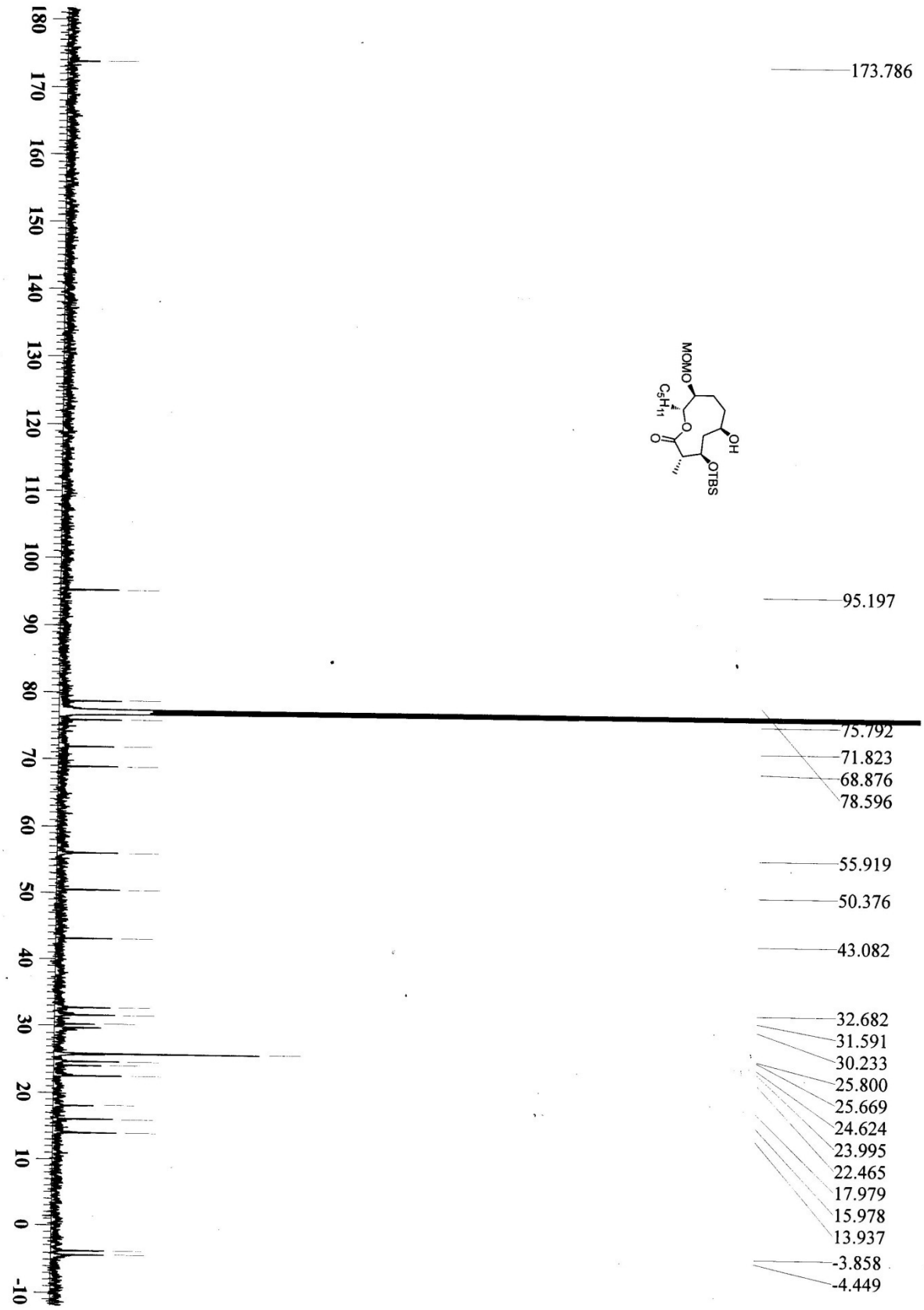
^{1}H-NMR of Compound 2



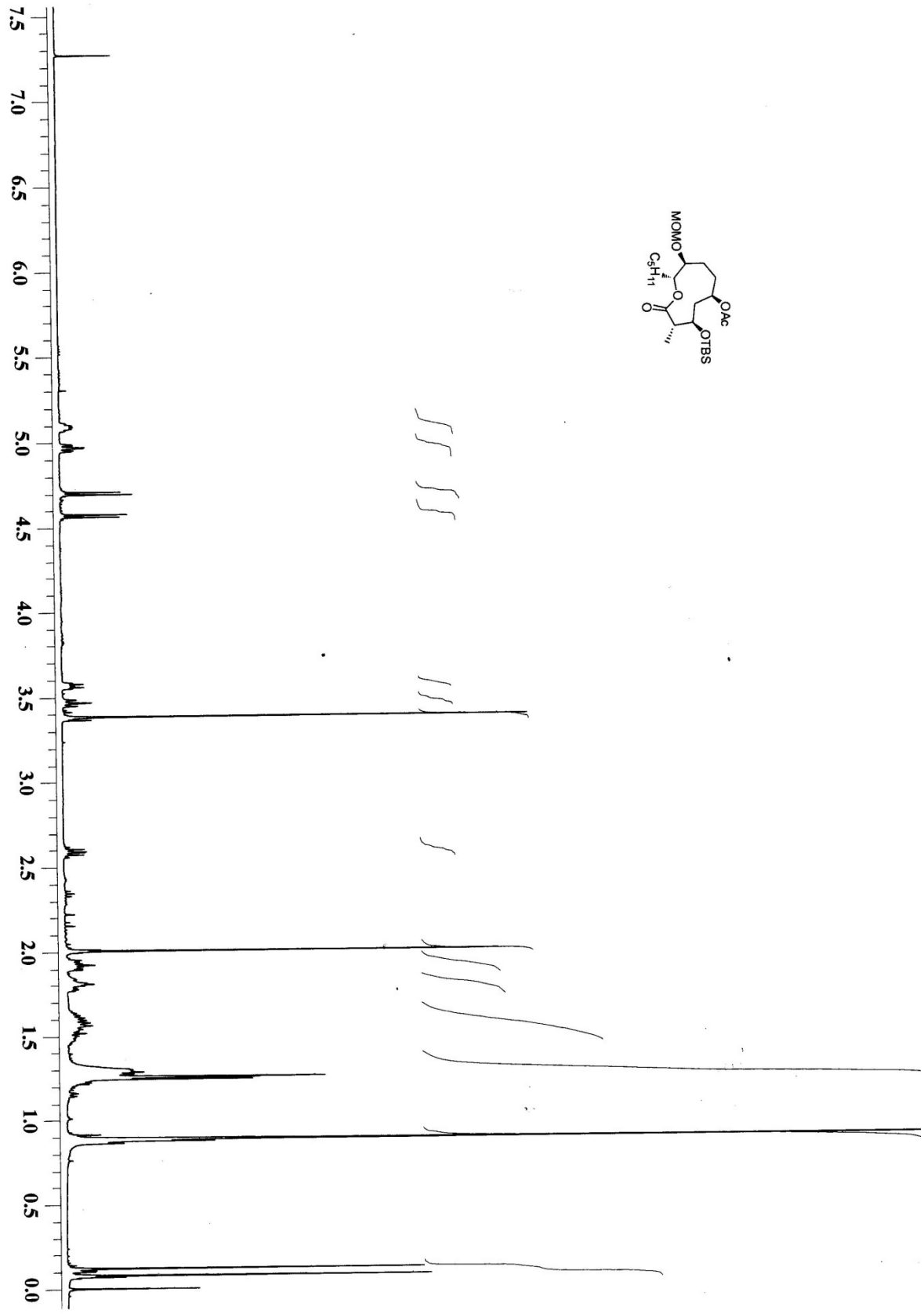
^{13}C-NMR of Compound 2



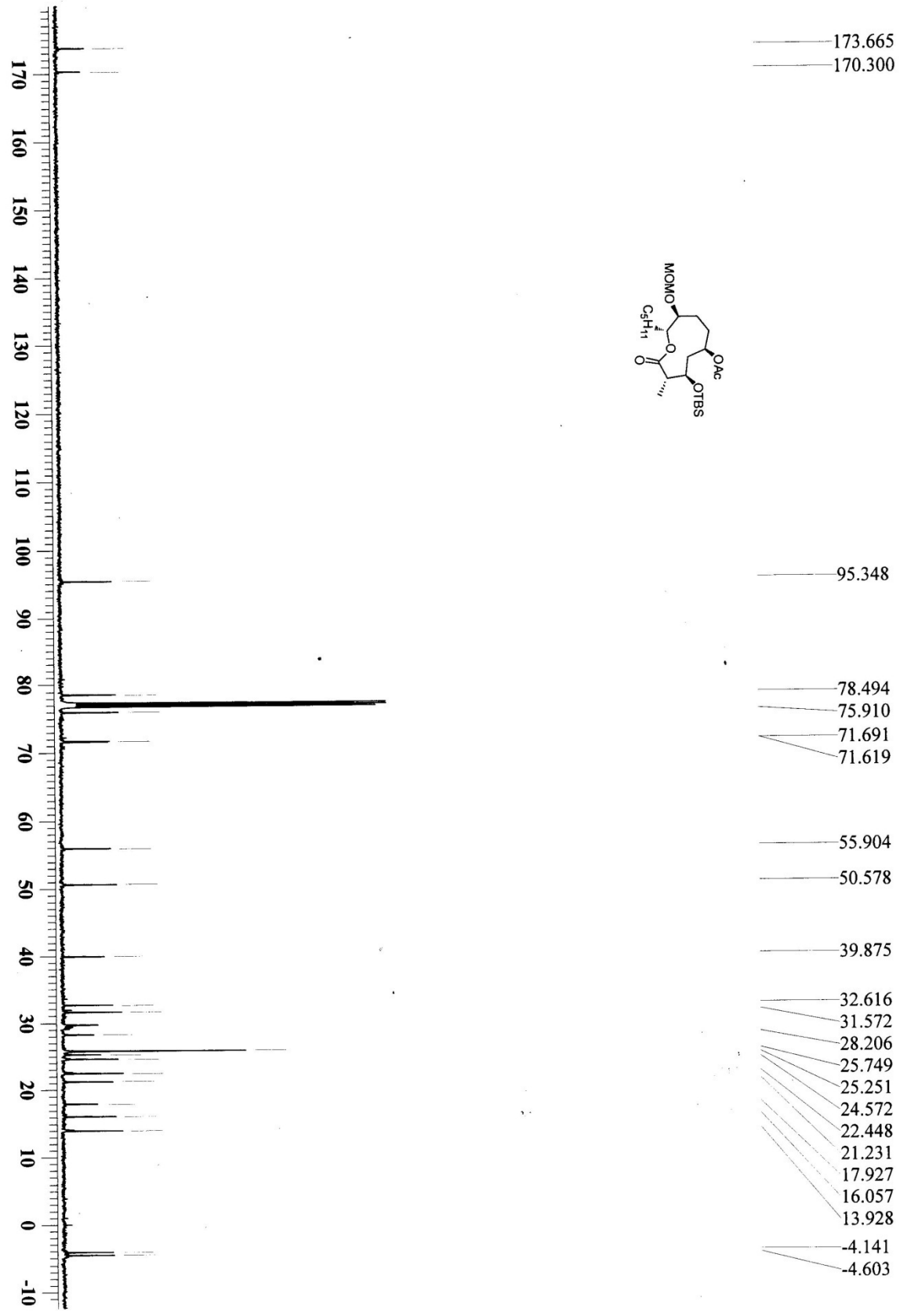
^{1}H-NMR of Compound 19



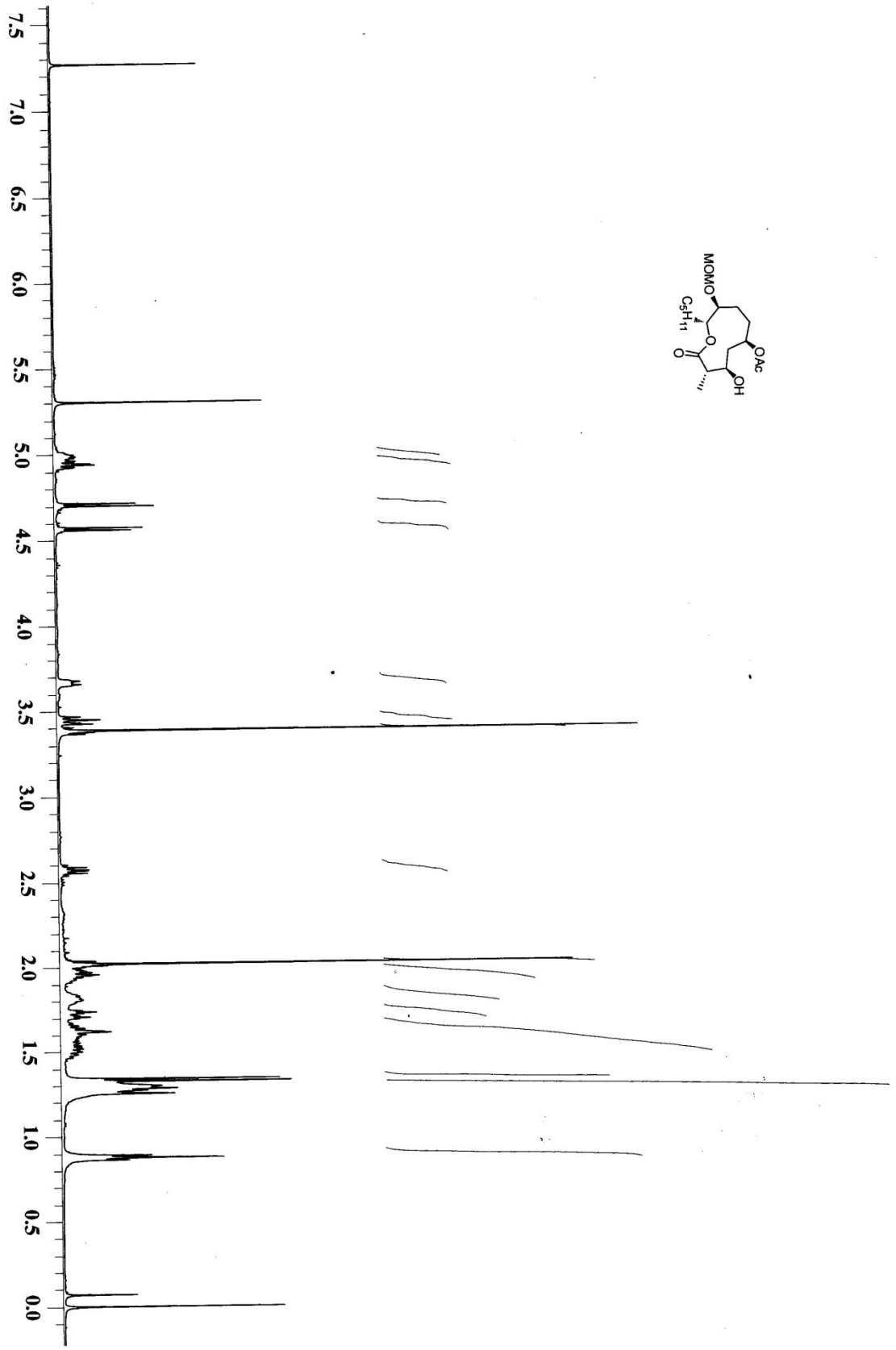
^{13}C-NMR of Compound 19



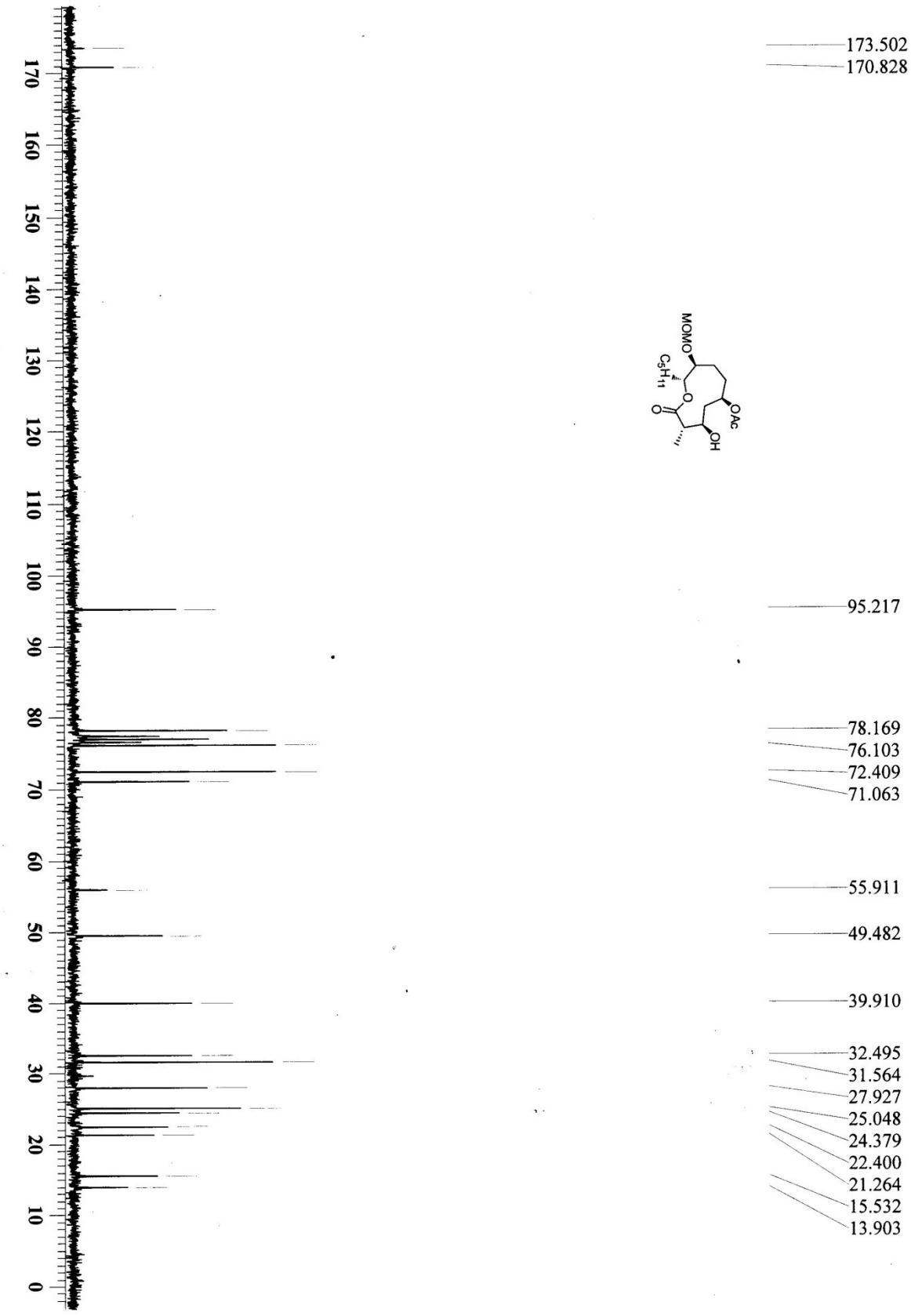
^{1}H-NMR of Compound 20



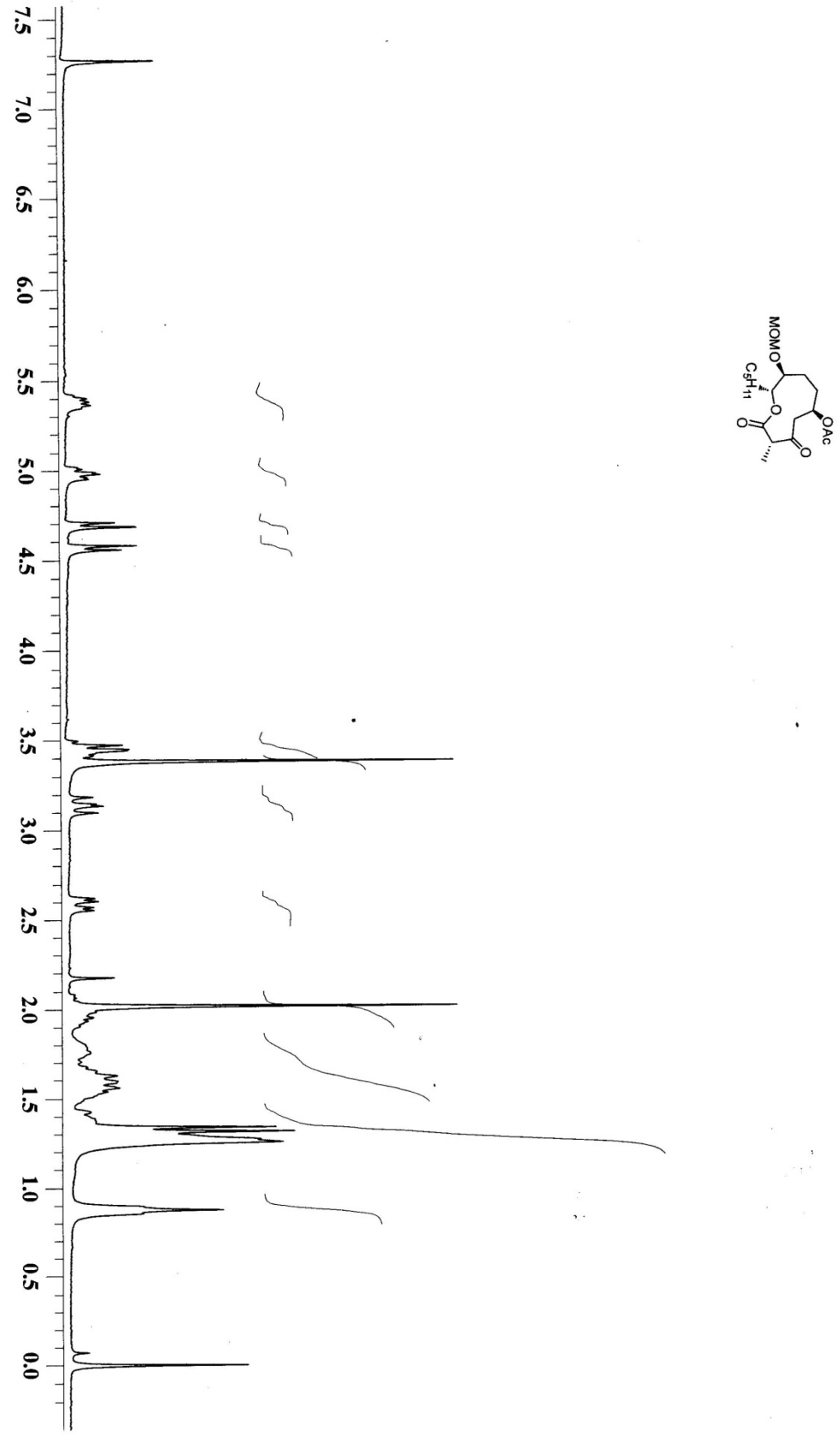
^{13}C-NMR of Compound 20



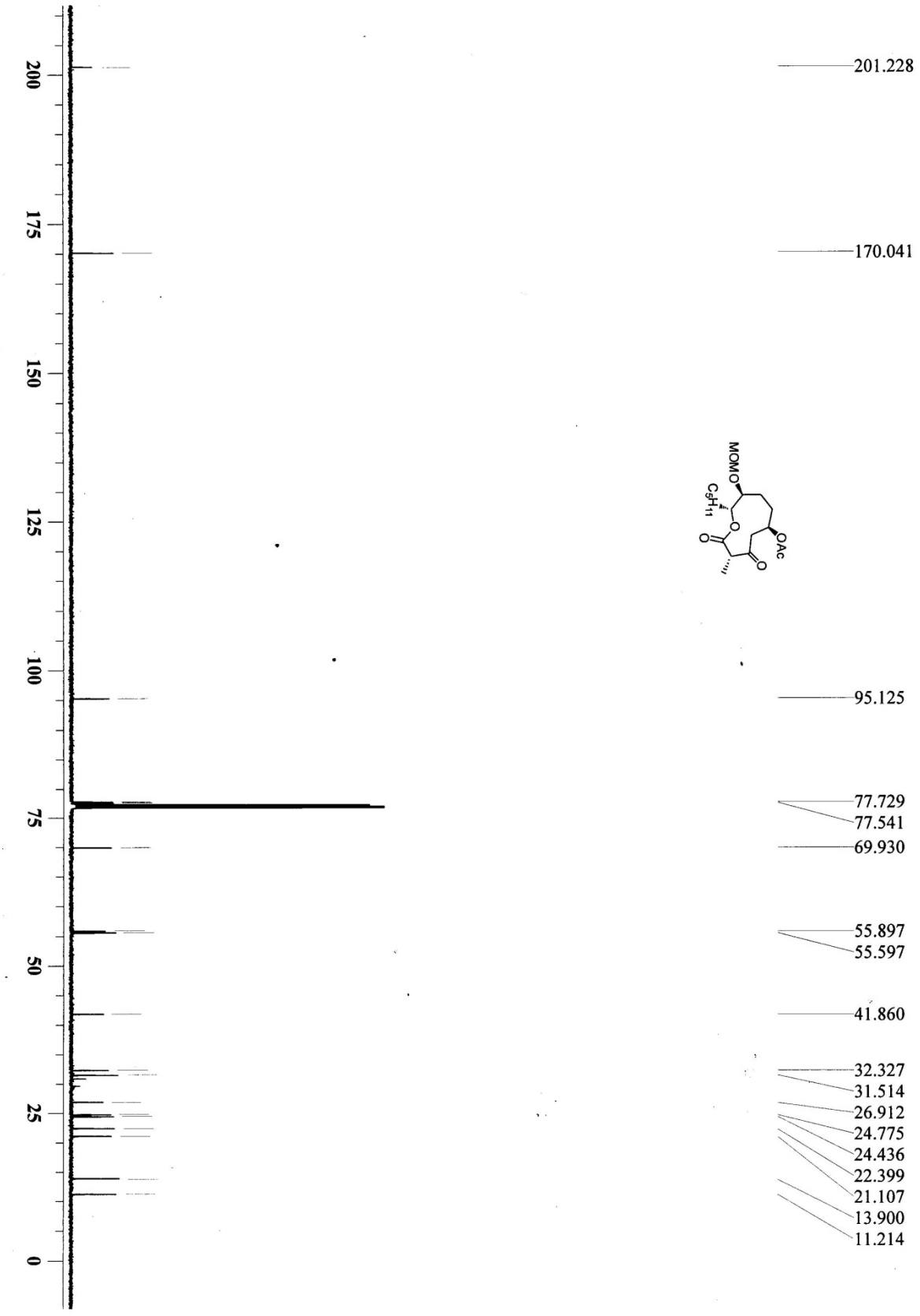
^{1}H-NMR of Compound 21



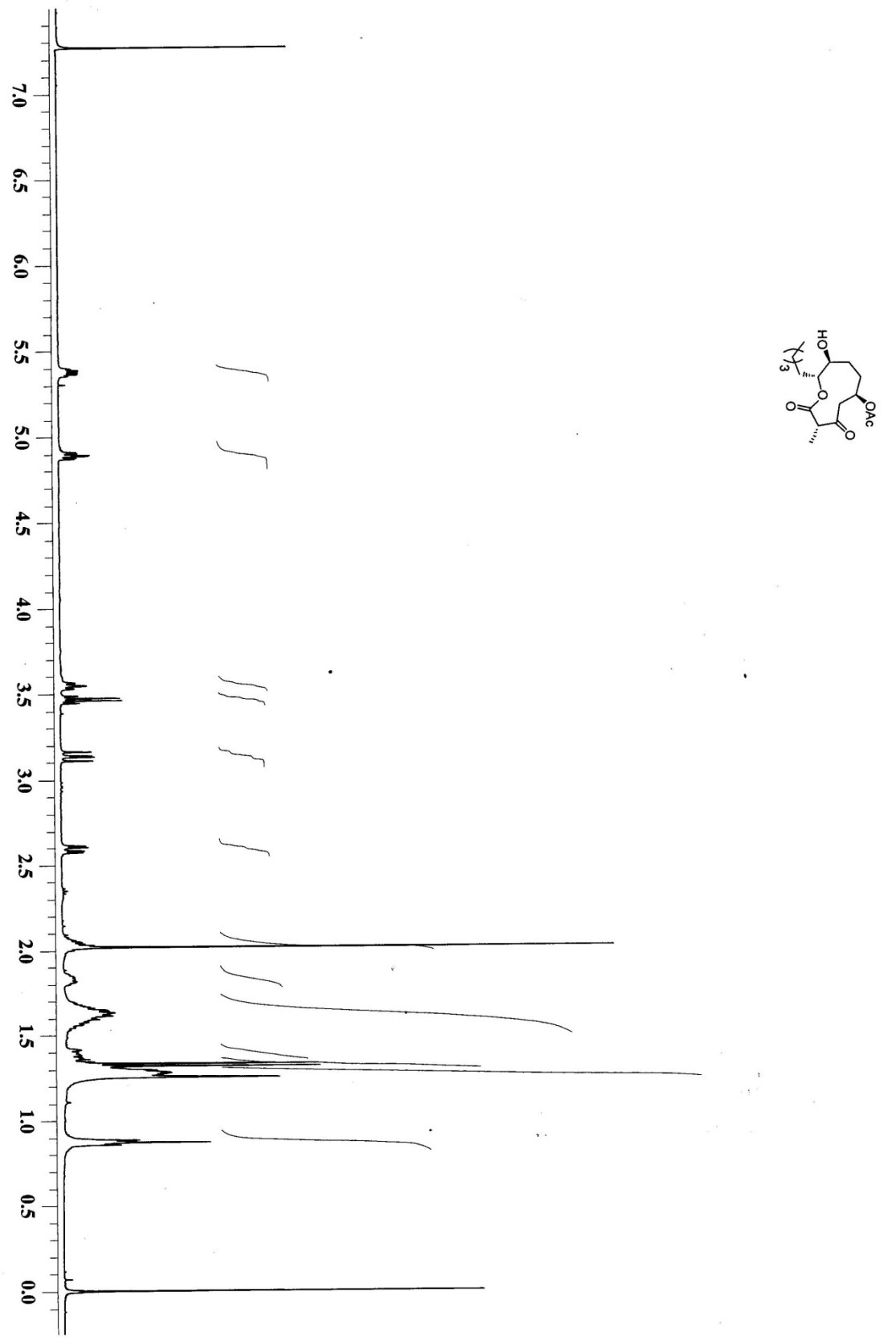
^{13}C-NMR of Compound 21



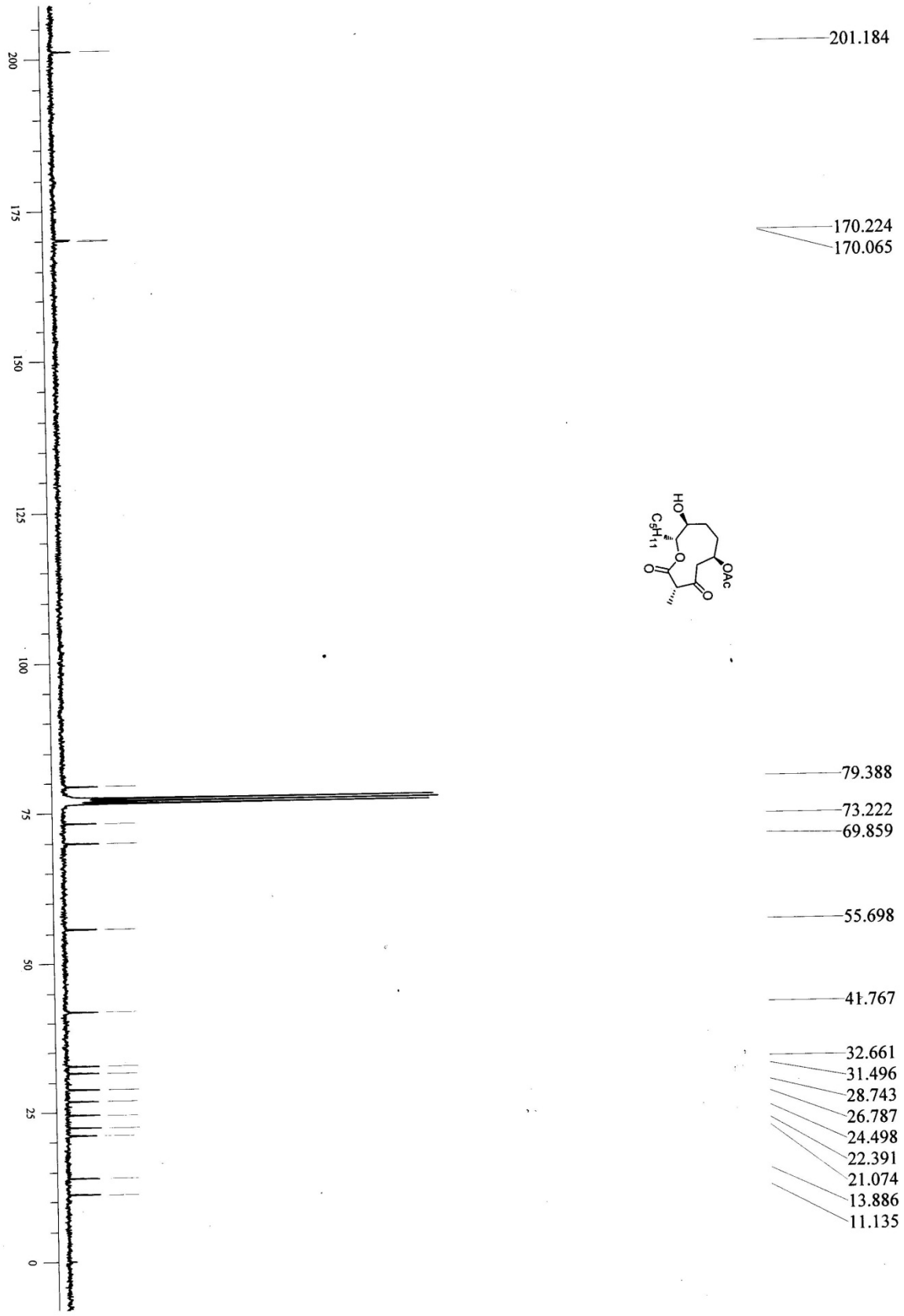
^{1}H-NMR of Compound 22



^{13}C-NMR of Compound 22



^{1}H-NMR of Compound 1 (cytospolide P, 500MHz)



^{13}C-NMR of Compound 1 (cytospolide P, 75 MHz)