

## SUPPORTING INFORMATION

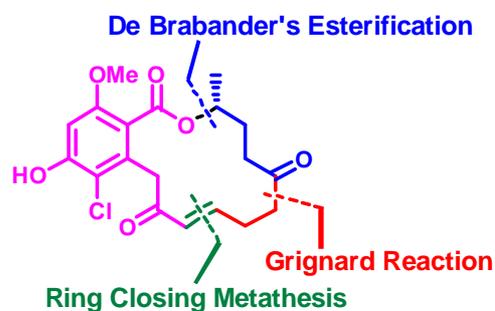
### Total Synthesis of Cryptosporiopsin A

Barla Thirupathi<sup>†</sup> and Debendra K. Mohapatra\*<sup>†</sup>

<sup>†</sup>Natural Products Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500  
007, INDIA.

Ph: 91-40-27193128; Fax: 91-40-27160512

E-mail: mohapatra@iict.res.in

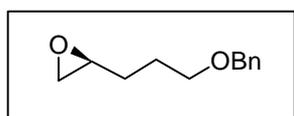


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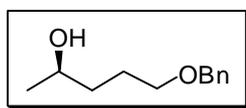
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## Experimental Section

**General Remarks:** Air and/or moisture sensitive reactions were carried out in anhydrous solvents under an atmosphere of argon in an oven or flame-dried glassware. All anhydrous solvents were distilled prior to use: THF, benzene, toluene, diethyl ether from Na and benzophenone;  $\text{CH}_2\text{Cl}_2$ , DMSO, DMF, hexane from  $\text{CaH}_2$ ; MeOH, EtOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using silica gel (60–120 mesh). Specific optical rotations  $[\alpha]_{\text{D}}$  are given in  $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$ . Infrared spectra were recorded in  $\text{CHCl}_3/\text{neat}$  (as mentioned) and reported in wave number ( $\text{cm}^{-1}$ ). TOF analyzer type was used for the HRMS measurement.  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shifts are reported 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.

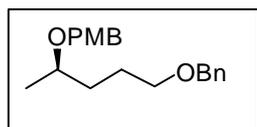


**(S)-2-(3-(Benzyloxy)propyl)oxirane (12):** A mixture of (*S,S*)-(-)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (0.26 g, 0.43 mmol), toluene (1.0 mL) and AcOH (0.1 mL, 1.73 mmol) was stirred for 1 h in open to the air at room temperature. The solvent was removed under reduced pressure and remaining brown residue was dried under high vacuum. Racemic epoxide (17.0 g, 86.75 mmol) was added in one portion and the mixture was cooled to 0 °C,  $\text{H}_2\text{O}$  (0.87 mL, 48.7 mmol) was added slowly and the reaction mixture was stirred for 36 h at room temperature. The product was purified by column chromatography on silica gel (ethyl acetate/hexane = 1:5) to afford **12** (7.65 g, 45%, 99% ee, HPLC).  $[\alpha]_{\text{D}}^{27} +5.6$  ( $c$  1.0,  $\text{CHCl}_3$ ); IR (KBr): 2929, 2836, 1630, 1347, 1210, 1109  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.40–7.20 (m, 5 H), 4.51 (s, 2H), 3.58–3.45 (m, 2H), 2.94 (m, 1H), 2.74 (t,  $J = 4.9$  Hz, 1H), 2.47 (dd,  $J = 5.1, 2.6$  Hz, 1H), 1.86–1.51 (m, 4H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.2, 129.2, 128.1, 127.3, 72.6, 69.5, 51.8, 46.8, 29.0, 25.9 ppm.

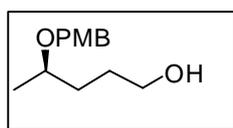


**(R)-5-(Benzyloxy)pentan-2-ol (13):** To a stirred suspension of  $\text{LiAlH}_4$  (1.62 g, 45.3 mmol) in anhydrous THF (20 mL) at 0 °C was added compound **12** (5.83 g, 30.2 mmol) in dry THF (20 mL). The reaction mixture was allowed to warm room temperature and stirred for 4 h. After completion of the reaction (monitored by TLC), it was quenched with saturated ammonium chloride solution (20 mL). The solid material was filtered through Celite pad and washed thoroughly with ethyl acetate (2 x 25 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 x 50 mL). The

combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , solvent removed under reduced pressure and the crude product on purification by silica gel column chromatography (ethyl acetate/hexane = 1:4) afforded **13** (4.9 g, 85%) as a viscous liquid.  $[\alpha]_{\text{D}}^{27} +8.5$  ( $c$  1.5,  $\text{CHCl}_3$ ); IR (KBr): 3379, 2954, 2931, 2857, 1643, 1372, 1253, 1067  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.40–7.26 (m, 5H), 4.51 (s, 2H), 3.80 (m, 1H), 3.51 (t,  $J$  = 6.0 Hz, 2H), 2.43 (bs, 1H), 1.66–1.75 (m, 2H), 1.44–1.75 (m, 2H), 1.18 (d,  $J$  = 6.0 Hz, 3H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 138.1, 128.3, 127.6, 127.5, 73.0, 70.5, 67.7, 36.5, 26.2, 23.4 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{12}\text{H}_{18}\text{O}_2$   $[\text{M} + \text{Na}]^+$ : 217.1204, found 217.1211.

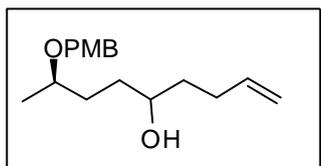


**(R)-1-((5-(Benzyloxy)pentan-2-yl)oxy)methyl-4-methoxybenzene (14):** To a solution of alcohol **13** (4.0 g, 20.61 mmol) in anhydrous THF (40 mL), NaH (1.73 g, 43.2 mmol, 60% in mineral oil) was added at 0 °C under nitrogen atmosphere and the mixture was allowed to stir for 30 min at the same temperature. 4-Methoxybenzyl bromide (5.3 g, 26.80 mmol) dissolved in anhydrous THF (50 mL) was added drop wise to the above reaction mixture. After completion of the reaction (monitored by TLC), it was carefully quenched with water (20 mL) at 0 °C and the reaction mixture was diluted with ethyl acetate (50 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 × 50 mL). The combined organic layer was washed with brine (2 × 100 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to dryness under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 1:10) to obtain **14** (5.82 g, 91%) as a colorless liquid.  $[\alpha]_{\text{D}}^{27} -5.6$  ( $c$  1.2,  $\text{CHCl}_3$ ); IR (KBr): 3030, 2935, 2857, 1733, 1611, 1512, 1456, 1247, 1174, 1099, 1033  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36–7.30 (m, 5H), 7.25 (d,  $J$  = 8.3 Hz, 2H), 6.85 (d,  $J$  = 8.3 Hz, 2H), 4.49 (s, 2H), 4.41 (AB<sub>q</sub>,  $J$  = 49.7, 11.3 Hz, 2H), 3.78 (s, 3H), 3.52–3.43 (m, 3H), 1.73–1.52 (m, 4H), 1.17 (d,  $J$  = 6.1 Hz, 3H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  158.9, 138.5, 130.9, 129.0, 128.2, 127.5, 127.3, 113.6, 74.1, 72.7, 70.3, 69.8, 55.1, 33.1, 25.7, 19.5 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{26}\text{O}_3$   $[\text{M} + \text{Na}]^+$ : 337.1774, found 337.1767.



**(R)-4-((4-Methoxybenzyl)oxy)pentan-1-ol (15):** To a suspension of Raney-Ni (W2) in ethanol (20 mL) was added a solution of compound **14** (3.21 g, 10.12 mmol) in ethanol (10 mL) under hydrogen atmosphere. The reaction mixture was stirred for 12 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was filtered through Celite and washed with ethanol

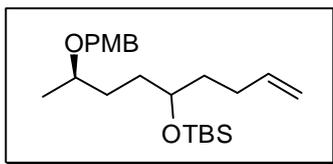
(2 x 20 mL). The filtrate was evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel (ethyl acetate/hexane = 1:3) to furnish **15** (2.01 g, 88%) as a colorless liquid.  $[\alpha]_D^{27} -14.4$  (*c* 1.8, CHCl<sub>3</sub>); IR (KBr): 3393, 2935, 2867, 1611, 1513, 1247, 1059, 1034 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.45 (AB<sub>q</sub>, *J* = 45.9, 11.1 Hz, 2H), 3.80 (s, 3H), 3.66–3.50 (m, 3H), 1.71–1.55 (m, 4H), 1.21 (d, *J* = 6.0 Hz, 3H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  159.1, 130.6, 129.3, 113.7, 74.4, 70.0, 62.9, 55.2, 33.3, 28.8, 19.4 ppm; HRMS (ESI): *m/z* calcd. for C<sub>13</sub>H<sub>21</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 225.1418, found 225.1420.



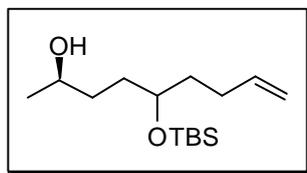
**(8R)-8-((4-Methoxybenzyl)oxy)non-1-en-5-ol (16):** To a stirred solution of primary alcohol **15** (1.5 g, 6.69 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL) at 0 °C, were added iodobenzenediacetate (BAIB) (3.22 g, 10.04 mmol) followed by TEMPO (0.11 g, 0.67 mmol). The reaction mixture was stirred at ambient temperature for 1 h. After complete consumption of the starting material (monitored by TLC), the reaction mixture was quenched with saturated solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (25 mL). The organic layer was separated and the aqueous layer extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> 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 (1.36 g) as a yellow liquid and used immediately for the next reaction.

To a solution of aldehyde (1.36 g, 5.94 mmol) in anhydrous THF (25 mL) was added 3-butenyl magnesium bromide (17.55 mL, 8.78 mmol, 0.5M in THF) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, allowed to warm to room temperature and stirred for additional 3 h at the same temperature. After completion of the reaction (monitored by TLC), it was quenched with saturated ammonium chloride solution (20 mL) and diluted with ethyl acetate (40 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 x 40 mL). The combined organic layer was washed with brine (2 x 100 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated under reduced pressure. The crude product was purified by flash column chromatography over silica gel (ethyl acetate/hexane = 1:6) to furnish the desired product **16** (1.41 g, 72% over two steps).  $[\alpha]_D^{27} -9.5$  (*c* = 1.5, CHCl<sub>3</sub>); IR (KBr): 3417, 2929, 2857, 1717, 1612, 1513, 1457, 1374, 1247, 1175, 1036 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.26 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.83 (m, 1H), 5.00 (AB<sub>q</sub>, *J* = 42.1, 17.8 Hz, 2H), 4.52 (dd, *J* = 11.3, 3.4 Hz, 1H), 4.38 (dd, *J* = 11.3, 1.5 Hz, 1H), 3.79 (s, 3H), 2.24–2.06 (m, 2H), 1.64–1.41 (m, 6H), 1.20 (d, *J* = 6.2 Hz, 3H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  =

159.0, 138.6, 130.6, 129.2, 114.5, 113.6, 74.6, 74.3, 71.1, 71.0, 69.9, 55.1, 36.5, 33.2, 32.7, 32.6, 30.0, 19.4 ppm; HRMS (ESI):  $m/z$  calcd. for  $C_{17}H_{26}O_3$   $[M + Na]^+$ : 301.1774; found: 301.1775.

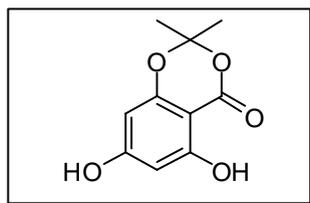


**tert-Butyl(((8R)-8-((4-methoxybenzyl)oxy)non-1-en-5-yl)oxy)dimethylsilane (17):** To a stirred solution of **16** (1.3 g, 4.67 mmol) in anhydrous  $CH_2Cl_2$  (30 mL), was added imidazole (0.66 g, 9.82 mmol) at 0 °C under nitrogen atmosphere. After 30 min, a solution of TBDMS-Cl (0.77 g, 5.1 mmol) dissolved in  $CH_2Cl_2$  (5 mL) was added dropwise. After completion of the reaction (monitored by TLC),  $H_2O$  (10 mL) was added to the reaction mixture and two layers were separated. The aqueous layer was extracted with  $CH_2Cl_2$  (3 × 25 mL). The combined organic layer was washed with brine (2 × 25 mL), dried over anhydrous  $Na_2SO_4$  and concentrated under reduced pressure to get the crude product, which on purification by flash column chromatography over silica gel (ethyl acetate/hexane = 1:19) to furnish the desired TBS-ether **17** (1.75 g, 96%) as a colorless liquid.  $[\alpha]_D^{27}$  -2.9 ( $c$  1.9,  $CHCl_3$ ), IR (KBr): 3075, 2953, 2932, 2857, 1641, 1513, 1614, 1373, 1249, 1173, 1249, 1077  $cm^{-1}$ ;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  7.42 (d,  $J$  = 8.8 Hz, 2H), 7.03 (d,  $J$  = 8.8 Hz, 2H), 5.98 (m, 1H), 5.12 (AB<sub>q</sub>,  $J$  = 38.0, 17.1 Hz, 1H), 4.65 (dd,  $J$  = 11.4, 3.0 Hz, 1H), 4.55 (dd,  $J$  = 11.4, 3.9 Hz, 1H), 3.96 (s, 3H), 3.82 (m, 1H), 3.64 (q,  $J$  = 11.7, 5.9 Hz, 1H), 2.30–2.17 (m, 2H), 1.84–1.50 (m, 6H), 1.34 (d,  $J$  = 6.2, 3H), 1.05 (s, 9H), 0.21 (s, 6H) ppm;  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta$  158.9, 138.9, 138.6, 131.1, 129.1, 126.9, 114.2, 113.6, 113.3, 74.6, 74.4, 71.8, 71.5, 69.8, 55.1, 40.1, 36.2, 32.6, 32.1, 31.8, 29.5, 27.4, 25.9, 22.8, 19.6, 18.1, -4.4 ppm; HRMS (ESI):  $m/z$  calcd for  $C_{23}H_{40}O_3Si$   $[M + Na]^+$ : 415.2639; found: 415.2644.

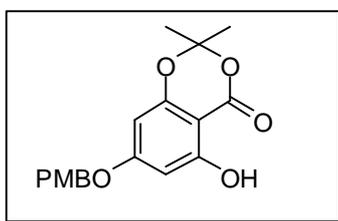


**(2R)-5-((tert-Butyldimethylsilyl)oxy)non-8-en-2-ol (10):** DDQ (694 mg, 3.06 mmol) was added to a stirred solution of PMB ether **17** (1.0 g, 2.55 mmol) in mixture of  $CH_2Cl_2:H_2O$  (9:1) (25 mL) at 0 °C. The reaction mixture was allowed to stir for 2 h at room temperature. After completion of 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 (50 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 = 1:6) to afford **10** (0.61 g, 89%) as a light yellow liquid.  $[\alpha]_D^{27} -3.5$  ( $c$  1.5,  $\text{CHCl}_3$ ); IR (KBr): 3363, 3078, 2954, 2931, 2958, 1642, 1463, 1252, 1219, 1065  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.81 (m, 1H), 4.97 (m, 2H), 3.82–3.67 (m, 2H), 2.15–1.98 (m, 2H), 1.62–1.44 (m, 6H), 1.18 (d,  $J = 6.2$  Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.6, 138.4, 114.3, 114.2, 71.6, 60.0, 67.8, 35.8, 35.5, 34.5, 34.3, 33.0, 32.4, 29.5, 29.4, 25.7, 23.3, 17.9, -4.6, -4.5 ppm; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{32}\text{O}_2\text{Si}$   $[\text{M} + \text{Na}]^+$ : 295.2063, found 295.2055.

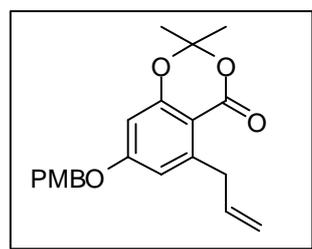


**5,7-Dihydroxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (18)**: To an ice-cold suspension of 2,4,6-trihydroxybenzoic acid monohydrate (10.0 g, 58.8 mmol) in trifluoroacetic acid (100 mL) was added trifluoroacetic anhydride (70 mL) and acetone (15 mL). The mixture was warmed slowly to room temperature and stirred for 12 h. The reaction mixture was concentrated under reduced pressure, poured into a saturated solution of aqueous  $\text{NaHCO}_3$  solution (200 mL) and extracted with ethyl acetate (3 x 200 mL). The combined extracts were washed with water (2 x 300 mL), brine (2 x 300 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude mass was purified by column chromatography over silica gel (ethyl acetate/hexane = 1:4) to afford **18** (6.79 g, 55%) as light yellow solid. Mp. 202–203 °C; IR (KBr): 3786, 3181, 2846, 2920, 1631, 1599, 1265, 1089  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz, acetone- $d_6$ ):  $\delta$  10.45 (s, 1H), 9.83 (s, 1H), 6.07 (d,  $J = 2.1$  Hz, 1H), 5.99 (d,  $J = 2.1$  Hz, 1H), 1.71 (s, 6H) ppm;  $^{13}\text{C}$  NMR (75 MHz, acetone- $d_6$ ):  $\delta$  68.2, 166.7, 164.9, 159.1, 108.5, 98.9, 97.2, 93.9, 26.6 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{10}\text{H}_{10}\text{O}_5$   $[\text{M} + \text{H}]^+$  211.0601, found 211.0601.



**5-Hydroxy-7-((4-methoxybenzyl)oxy)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (19)**: To a solution of compound **18** (4.5 g, 21.42 mmol) and 4-methoxy benzyl alcohol (3.10 g, 23.49 mmol) in  $\text{CH}_2\text{Cl}_2$  (45 mL) at 0 °C, was added triphenyl phosphine (6.16 g, 23.49 mmol) and DIAD (4.60 mL, 23.49 mmol). The reaction mixture was warmed to room temperature over 3 h. After completion of the reaction (monitored by TLC), it was quenched with water (30 mL). The organic layer was separated and

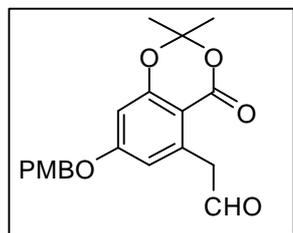
the aqueous layer extracted with  $\text{CH}_2\text{Cl}_2$  (2 x 50 mL). The combined organic layer was washed with water (100 mL), brine (100 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude mass was purified by column chromatography over silica gel (ethyl acetate/hexanes = 1:10) to give compound **19** (6.01, 85%) as a colorless liquid. IR (KBr): 3170, 2998, 2932, 1686, 1641, 1586, 1513, 1355, 1273, 1250, 1098, 1032  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.45 (s, 1H), 7.33 (d,  $J$  = 9.1 Hz, 2H), 6.92 (d,  $J$  = 9.1 Hz, 2H), 6.22 (d,  $J$  = 2.3 Hz, 1H), 6.06 (d,  $J$  = 2.3 Hz, 1H), 4.98 (s, 2H), 3.82 (s, 3H), 1.73 (s, 6H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  166.8, 165.1, 163.0, 159.7, 156.8, 129.3, 127.5, 114.1, 106.9, 96.5, 95.3, 93.1, 70.3, 55.3, 25.6 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{18}\text{H}_{18}\text{O}_6$  [ $\text{M} + \text{Na}$ ] $^+$  353.0995, found 353.0988.



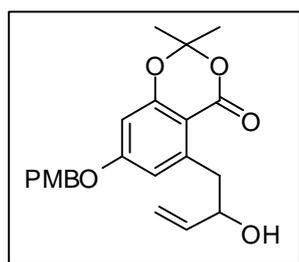
**5-Allyl-7-((4-methoxybenzyl)oxy)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (20):** To a stirred solution of compound **19** (4.0 g, 12.12) in pyridine (20 mL), was added triflic anhydride (2.25 mL, 13.33 mmol) at 0 °C and stirred the reaction mixture for 8 h at room temperature. After completion of the reaction (monitored by TLC), it was quenched with saturated  $\text{CuSO}_4$  solution (70 mL) and extracted with ethyl acetate (3 x 75 mL). The combined organic layer was washed with water (100 mL), brine (100 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude product was purified by flash column chromatography over silica gel (ethyl acetate/hexane = 1:5) to furnish the desired product which was used for next reaction without characterization.

A stirred solution of triflate (4.8 g, 10.38 mmol) in anhydrous DMF (40 mL), LiCl (0.47 g, 11.41 mmol),  $\text{Pd}(\text{PPh}_3)_4$  (0.12 g, 0.11 mmol) and allyltributyltin (3.55 mL, 11.41 mmol) were added at room temperature. The resulting mixture was heated to 80 °C and stirred for 4 h. After completion of the reaction (monitored by TLC), it was quenched with  $\text{H}_2\text{O}$  (100 mL) and extracted with ethyl acetate (3 x 70 mL). The combined organic layers were washed with water (150 mL), brine (150 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The crude mass was purified by column chromatography (ethyl acetate/hexane = 1:10) to obtain **20** (2.79 g, 76% over two steps) as a colorless liquid. IR (KBr): 2998, 2927, 2852, 1728, 1611, 1578, 1515, 1281, 1251, 1163, 1041  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34 (d,  $J$  = 8.3 Hz, 2H), 6.93 (d,  $J$  = 8.3 Hz, 2H), 6.58 (d,  $J$  = 2.3 Hz, 1H), 6.39 (d,  $J$  = 2.3 Hz, 1H), 6.02 (m, 1H), 5.10 (dd,  $J$  = 3.0, 1.5 Hz, 1H), 5.05 (dd,  $J$  = 3.0, 1.5 Hz, 1H), 4.99 (s,

2H), 3.83 (s, 3H), 1.69 (s, 6H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  164.1, 160.1, 159.7, 159.0, 147.1, 136.4, 129.4, 129.3, 127.7, 116.2, 113.7, 112.7, 104.9, 100.3, 70.1, 55.2, 38.4, 25.6 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{22}\text{O}_5$   $[\text{M} + \text{Na}]^+$  377.1359, found 377.1349.

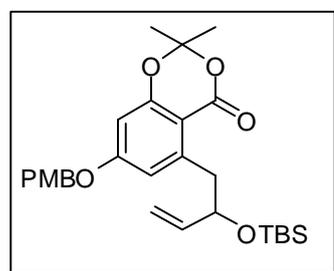


**2-(7-((4-Methoxybenzyl)oxy)-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxin-5-yl)acetaldehyde (21):** 2,6-Lutidine (0.3 mL, 2.82 mmol),  $\text{OsO}_4$  (2% in toluene, 7.0 mg, 0.0027 mmol), and  $\text{NaIO}_4$  (1.1 g, 5.50 mmol) were added to a stirred solution of compound **20** (0.48 g, 1.35 mmol) in dioxane and water (3:1, 20 mL). The reaction mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), it was quenched with water (25 mL) and diluted with  $\text{CH}_2\text{Cl}_2$  (50 mL). The organic layer was separated and the aqueous layer extracted with  $\text{CH}_2\text{Cl}_2$  (2 x 40 mL). The combined organic layer was washed with water (75 mL), brine (2 x 75 mL) and dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure and the crude mass was purified by silica gel chromatography (ethyl acetate/hexane = 1:5) to afford **21** (0.42, 89%) as a colorless viscous liquid. IR (KBr): 2924, 2853, 1720, 1610, 1583, 1641, 1377, 1251, 1166, 1036  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.78 (s, 1H), 7.32 (d,  $J = 8.7$  Hz, 2H), 6.92 (d,  $J = 8.7$  Hz, 2H), 6.49 (d,  $J = 2.4$  Hz, 1H), 6.46 (d,  $J = 2.4$  Hz, 1H), 4.98 (s, 2H), 4.11 (s, 2H), 3.81 (s, 3H), 1.70 (s, 6H) ppm;  $^{13}\text{C}$  NMR (75 MHz  $\text{CDCl}_3$ ):  $\delta$  198.1, 164.3, 160.6, 159.7, 159.0, 138.7, 129.3, 127.4, 114.7, 114.1, 105.5, 101.4, 70.2, 55.2, 49.1, 25.5 ppm.



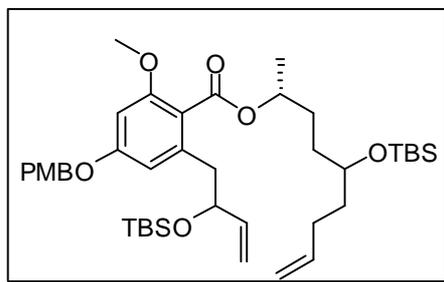
**5-(2-Hydroxybut-3-en-1-yl)-7-((4-methoxybenzyl)oxy)-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (22):** To a stirred solution of compound **21** (0.33 g, 0.92 mmol) in anhydrous THF (20 mL), was added vinyl magnesium bromide (1.01 mL, 1.01 mmol, 1M in THF) in THF at  $-78$  °C and stirred for 4 h. After completion of the reaction (monitored by TLC), it was quenched with saturated ammonium chloride solution (20 mL) and diluted with ethyl acetate (30 mL). The organic layer was separated and

the aqueous layer extracted with ethyl acetate (3 x 30 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by flash column chromatography over silica gel (ethyl acetate/hexane = 1:19) to furnish the desired allylic alcohol **22** (0.31 g, 87%): IR (KBr): 3447, 2997, 2928, 2852, 1722, 1611, 1576, 1515, 1284, 1250, 1163, 1055; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.32 (d, *J* = 8.3 Hz, 2H), 6.92 (d, *J* = 8.3 Hz, 2H), 6.57 (d, *J* = 2.3 Hz, 1H), 6.41 (d, *J* = 2.3 Hz, 1H), 5.96 (m, 1H), 5.25 (dd, *J* = 15.8, 1.5 Hz, 1H), 5.09 (dd, *J* = 15.8, 1.5 Hz, 1H), 4.98 (s, 2H), 4.37 (m, 1H), 3.81 (s, 3H), 3.31 (dd, *J* = 12.8, 4.5 Hz, 1H), 3.21 (dd, *J* = 12.8, 4.5 Hz, 1H), 2.76 (br s, 1H), 1.69 (s, 3H), 1.67 (s, 3H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 164.0, 161.6, 159.7, 159.0, 145.0, 140.5, 129.4, 127.5, 114.3, 114.1, 105.2, 101.4, 101.0, 73.7, 70.1, 55.3, 49.1, 41.8, 25.8, 25.3 ppm; HRMS (ESI): *m/z* calcd. for C<sub>22</sub>H<sub>24</sub>O<sub>6</sub> [M + H]<sup>+</sup> 385.1646, found 385.1644.

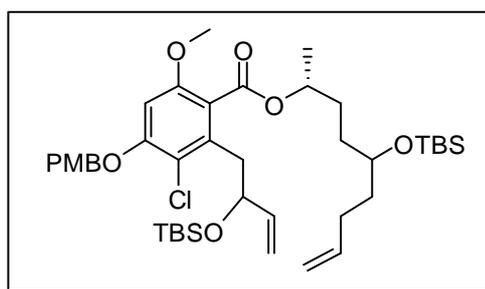


**5-(2-((tert-Butyldimethylsilyloxy)but-3-en-1-yl)-7-((4-methoxybenzyl)oxy)-2,2-dimethyl-4H-benzod[1,3]dioxin-4-one (9):** To a stirred solution of a compound **22** (0.6 g, 1.56 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (25 mL), was added imidazole (0.22 g, 3.28 mmol) at 0 °C under nitrogen atmosphere. After 10 min, a solution of TBDMS-Cl (0.24 g, 1.72 mmol) dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added dropwise. The reaction mixture was stirred at room temperature for 3 h. After completion of the reaction (monitored by TLC), it was quenched with water (30 mL) and two layers were separated. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 30 mL) and the combined organic layer was washed with brine (2 × 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by flash column chromatography over silica gel (ethyl acetate/hexane = 1:19) to obtain the desired TBS-ether **9** (0.36 g, 92%). IR (KBr): 2950, 2930, 2856, 1727, 1611, 1576, 1280, 1251, 1162, 1055 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.58 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 5.93 (m, 1H), 5.21 (dd, *J* = 16.9, 1.5 Hz, 1H), 4.97–5.05 (m, 3H), 4.43 (m, 1H), 3.83 (s, 3H), 3.52 (dd, *J* = 12.3, 3.0 Hz, 1H), 2.85 (dd, *J* = 12.3, 3.0 Hz, 1H), 1.70 (s, 3H), 1.68 (s, 3H), 0.83 (s, 9H), -0.11 (s, 3H), -0.25 (s, 3H) ppm; <sup>13</sup>C NMR (75 MHz CDCl<sub>3</sub>): δ 163.5, 160.2, 159.6, 158.8, 145.7, 141.4, 129.2, 127.7, 115.5, 114.0, 113.4, 104.9, 104.9, 100.9, 73.4, 69.9,

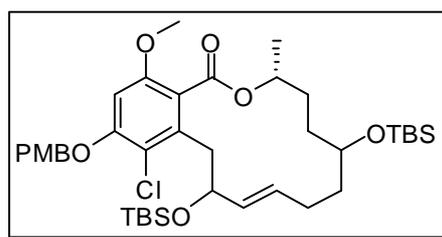
55.2, 43.6, 29.6, 25.8, 25.7, -4.8, -5.3 ppm; HRMS (ESI):  $m/z$  calcd. for  $C_{28}H_{38}O_6Si$   $[M + Na]^+$  521.2329, found 521.2319.



**(2R)-5-((tert-Butyldimethylsilyl)oxy)non-8-en-2-yl 2-(2-((tert-butylidimethylsilyl)oxy)but-3-en-1-yl)-6-methoxy-4-((4-methoxybenzyl)oxy)benzoate (23):** To a suspension of NaH (0.22 g, 5.5 mmol) (washed with hexane twice to remove mineral oil and dried) in dry THF (10 mL), alcohol **10** (0.14 g, 0.50 mmol) was added in THF (2 mL) at 0 °C under nitrogen atmosphere and stirred for 30 min. The 1,3-benzodioxin derivative **9** (0.23 g, 0.46 mmol) was added in THF (2 mL) to the reaction mixture at 0 °C. The suspension was stirred for 5 h at room temperature. The reaction mixture was again cooled to 0 °C and methyodide (0.07 mL, 1.10 mmol) was added. The reaction mixture warmed to room temperature and stirring was continued for 3 h. After completion of the reaction (monitored by TLC), it was quenched with cold water (15 mL) at 0 °C and diluted with ethyl acetate (25 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 x 30 mL). The combined organic layer was dried over anhydrous  $Na_2SO_4$  and solvent removed under reduced pressure. The crude mass was purified by silica gel chromatography (ethyl acetate/hexane = 1:16) to obtain **23** (0.28 g, 85%).  $[\alpha]_D^{27}^{-5.1}$  (c 1.0,  $CHCl_3$ ); IR (KBr): 2953, 2930, 2856, 1719, 1604, 1514, 1462, 1378, 1252, 1158, 1085  $cm^{-1}$ ;  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  7.34 (d,  $J = 8.5$  Hz, 2H), 6.92 (d,  $J = 8.5$  Hz, 2H), 6.47 (d,  $J = 2.1$  Hz, 1H), 6.41 (d,  $J = 2.1$  Hz, 1H), 5.88–5.76 (m, 2H), 5.21–5.09 (m, 2H), 5.04–4.92 (m, 5H), 4.37 (m, 1H), 3.82 (s, 3H), 3.77–3.72 (m, 4H), 2.82 (dd,  $J = 10.5, 5.6$  Hz, 1H), 2.64 (dd,  $J = 10.5, 5.6$  Hz, 1H), 2.04–2.12 (m, 2H), 1.59–1.67 (m, 2H), 1.50–1.57 (m, 2H), 1.31–1.37 (m, 3H), 1.25–1.29 (m, 2H), 0.90 (s, 9H), 0.85 (s, 9H), 0.05 (s, 6H), -0.10 (s, 3H), -0.20 (s, 3H) ppm;  $^{13}C$  NMR (75 MHz  $CDCl_3$ ):  $\delta$  167.9, 159.8, 157.8, 141.1, 138.7, 138.3, 129.3, 128.7, 128.3, 114.3, 114.0, 113.8, 113.3, 109.1, 97.8, 73.9, 73.8, 72.1, 71.8, 71.6, 71.2, 70.0, 55.8, 55.2, 42.6, 36.3, 32.7, 32.5, 31.9, 31.3, 29.6, 29.3, 25.9, 22.6, 20.1, 18.1, -4.4, -4.9, -5.2 ppm; HRMS (ESI):  $m/z$  calcd. for  $C_{41}H_{66}O_7Si_2$   $[M + H]^+$  727.4420, found 727.4421.

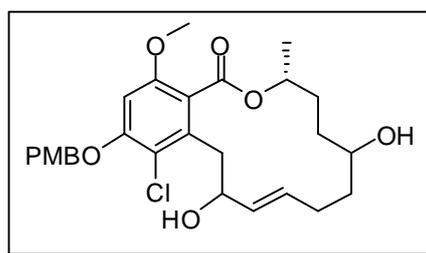


**(2R)-5-(tert-butyldimethylsilyloxy)non-8-en-2-yl 2-(2-(tert-butyldimethylsilyloxy)but-3-enyl)-3-chloro-6-methoxy-4-(4-methoxybenzyloxy)benzoate (8):** To a stirred solution of **23** (0.15 g, 0.20 mmol) in anhydrous chlorobenzene (5 mL), was added *N*-chlorosuccinimide (30 mg, 0.22 mmol). The reaction mixture was stirred at 80 °C for 12 h. After completion of the reaction (monitored by TLC), it was quenched with saturated NaHSO<sub>3</sub> solution (5 mL) and diluted ethyl acetate (15 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 x 15 mL). The combined organic layer was washed with brine (40 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated under reduced pressure and purified by flash chromatography (ethyl acetate/hexane = 1:19) to afford **8** (121 mg, 77%) as a colorless liquid.  $[\alpha]_D^{27} -3.5$  (*c* 1.2, CHCl<sub>3</sub>); IR (KBr): 2956, 2929, 2856, 1721, 1612, 1587, 1515, 1462, 1252, 1066 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.37 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.44 (s, 1H), 5.86–5.75 (m, 2H), 5.18–5.07 (m, 4H), 5.03–4.91 (m, 3H), 4.53 (m, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 3.68 (m, 1H), 3.10 (dd, *J* = 13.4, 5.4 Hz, 1H), 2.64 (dd, *J* = 13.4, 5.4 Hz, 1H), 2.10–2.04 (m, 2H), 1.66–1.50 (m, 2H), 1.35–1.26 (m, 5H), 0.90 (s, 9H), 0.80 (s, 9H), 0.04 (s, 6H), -0.09 (s, 3H), -0.15 (s, 3H) ppm; <sup>13</sup>C NMR (75 MHz CDCl<sub>3</sub>):  $\delta$  167.0, 159.5, 155.5, 140.9, 140.9, 139.2, 138.8, 135.8, 128.7, 128.2, 119.6, 119.4, 116.6, 116.5, 114.3, 114.0, 113.9, 113.7, 97.3, 73.1, 73.0, 72.3, 71.5, 71.1, 71.0, 56.1, 55.2, 39.4, 39.3, 36.3, 36.1, 32.7, 32.5, 32.4, 31.9, 31.4, 31.3, 29.6, 29.3, 28.9, 25.8, 25.8, 22.6, 20.0, 18.0, 14.1, -4.4, -4.9, -5.1 ppm; HRMS (ESI): *m/z* calcd. for C<sub>41</sub>H<sub>65</sub>O<sub>7</sub>ClSi<sub>2</sub> [M + H]<sup>+</sup> 761.4030, found 761.4034.

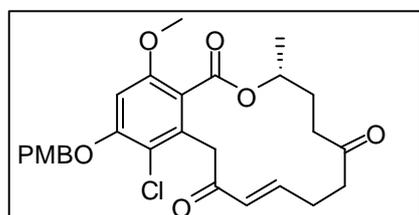


**(3R,E)-6,11-Bis((tert-butyldimethylsilyl)oxy)-13-chloro-16-methoxy-14-((4-methoxybenzyl)oxy)-3-methyl-3,4,5,6,7,8,11,12-octahydro-1H-benzo[c][1]oxacyclotetradecin-1-one (24):** To a solution of compound **8** (0.11 g, 0.14 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.01 M), was added Grubbs 2<sup>nd</sup> generation catalyst (13 mg, 0.014 mmol) at room temperature and degassed for 30 min with argon. The reaction mixture was refluxed for 24 h. After completion of the reaction (monitored by TLC), solvent was evaporated under reduced pressure. The crude mass was purified by silica gel chromatography (ethyl acetate/hexane =

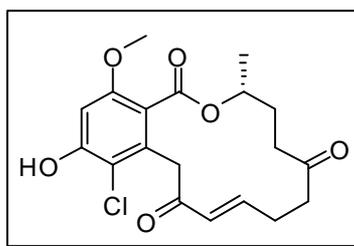
1:10) to afford **24** (0.078 g, 74%) as a light brown liquid.  $[\alpha]_D^{27} -1.2$  ( $c$  1.0,  $\text{CHCl}_3$ ); IR (KBr): 2955, 2928, 2855, 1720, 1588, 1462, 1254, 1070, 1035  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36 (d,  $J = 8.5$  Hz, 2H), 6.91 (d,  $J = 8.7$  Hz, 2H), 6.44 (s, 1H), 5.81 (m, 1H), 5.13–5.07 (m, 4H), 4.97 (m, 1H), 4.55 (m, 1H), 3.81 (s, 3H), 3.77–3.63 (m, 4H), 3.11 (m, 1H), 2.89 (m, 1H), 2.08–1.96 (m, 2H), 1.73–1.58 (m, 3H), 0.88 (s, 9H), 0.84–0.80 (m, 9H), 0.10–0.02 (m, 6H),  $-0.06$ – $-0.17$  (m, 6H) ppm;  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta = 167.4, 167.0, 159.5, 156.3, 155.5, 150.0, 140.9, 136.0, 131.6, 131.3, 128.8, 128.1, 119.1, 114.0, 97.3, 96.6, 73.9, 73.1, 71.8, 71.5, 71.0, 71.0, 56.2, 55.6, 55.3, 40.1, 39.5, 35.3, 33.8, 31.9, 29.6, 29.3, 29.1, 28.9, 28.1, 25.9, 22.7, 19.9, 18.1, -4.3, -4.5, -4.9, -5.1$  ppm; HRMS, (ESI)  $m/z$  calcd. for  $\text{C}_{39}\text{H}_{61}\text{O}_7\text{ClSi}_2$   $[\text{M} + \text{H}]^+$  733.3717, found 733.3722.



**(3R,E)-13-Chloro-6,11-dihydroxy-16-methoxy-14-((4-methoxybenzyl)oxy)-3-methyl-3,4,5,6,7,8,11,12-octahydro-1H-benzo[c][1]oxacyclotetradecin-1-one (7):** TBAF (0.4 mL, 1 M in THF, 0.4 mmol) was added to a stirred solution of compound **24** (70 mg, 0.09 mmol) in THF (5 mL) at 0 °C under argon atmosphere. The reaction mixture was stirred at room temperature for 4 h. After completion of the reaction (monitored by TLC), it was quenched with water (5 mL) and diluted with ethyl acetate (15 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 x 15 mL). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$  and solvent removed under reduced pressure. The crude mass was purified by silica gel chromatography (ethyl acetate/hexane = 1:1) to afford **7** (45 mg, 95%) as a colorless liquid.  $[\alpha]_D^{27} +4.5$  ( $c$  0.8,  $\text{CHCl}_3$ ); IR (KBr) 3447, 2927, 2856, 1715, 1629, 1400, 1251, 1071  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35 (d,  $J = 8.3$  Hz, 2H), 6.91 (d,  $J = 8.3$  Hz, 2H), 6.42 (m, 1H), 5.57 (m, 1H), 5.31 (m, 1H), 5.11(m, 1H), 4.99 (s, 2H), 4.38 (m, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.64 (m, 1H), 3.18–2.96 (m, 2H), 2.21–1.58 (m, 8H), 1.36 (d,  $J = 8.3$  Hz, 3H) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.1, 159.5, 156.8, 155.9, 136.9, 135.8, 131.9, 131.3, 128.8, 128.3, 127.9, 121.8, 119.3, 116.3, 114.1, 97.4, 82.0, 74.4, 71.0, 70.6, 70.2, 68.8, 67.2, 65.4, 56.3, 55.3, 45.8, 39.2, 36.3, 35.2, 34.0, 31.9, 31.3, 29.6, 29.3, 28.1, 26.2, 22.6, 20.5 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{33}\text{O}_7\text{Cl}$   $[\text{M} + \text{Na}]^+$  527.1807, found 527.1808.

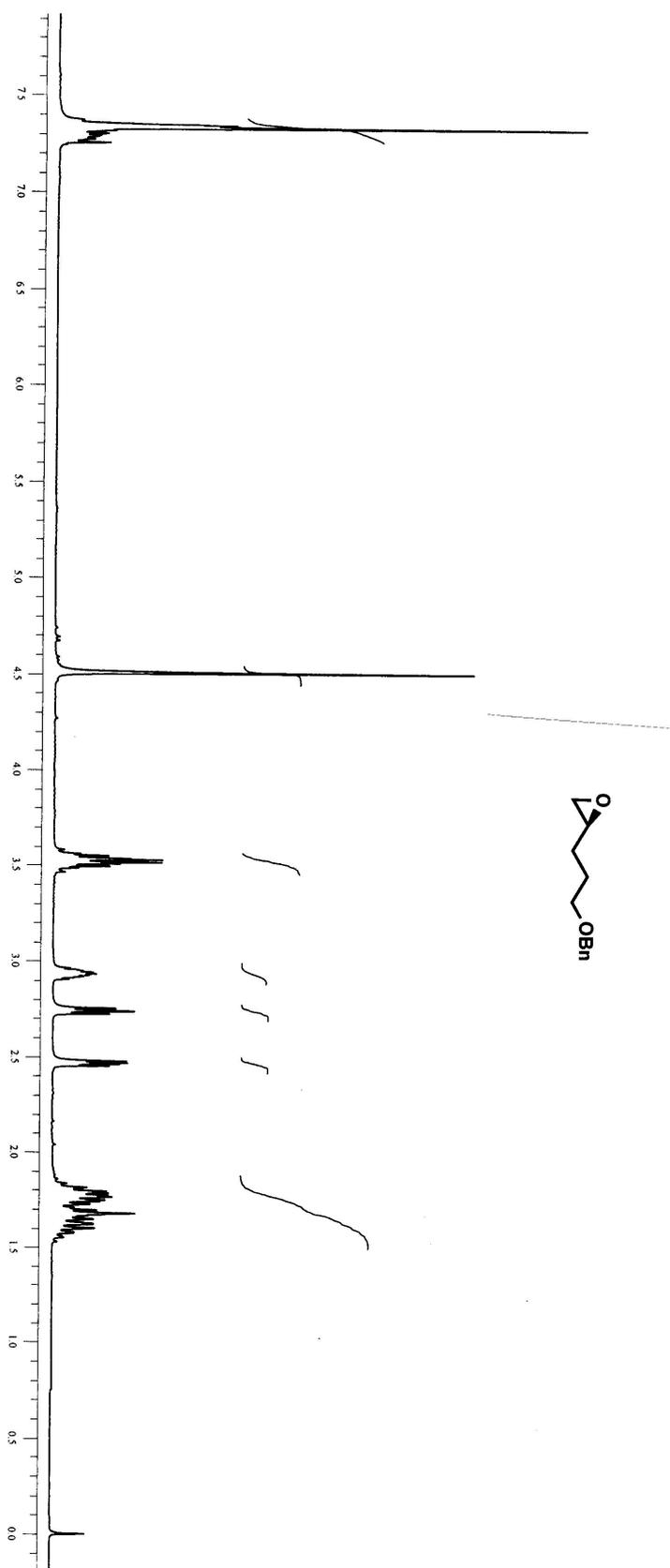


**(*R,E*)-13-Chloro-16-methoxy-14-((4-methoxybenzyl)oxy)-3-methyl-4,5,7,8-tetrahydro-1*H*-benzo[*c*][1]oxacyclotetradecine-1,6,11(3*H*,12*H*)-trione (25):** To a stirred solution of diol **7** (0.08 g, 0.16 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (8 mL), was added Dess–Martin periodinane (0.34 g, 0.8 mmol) at 0 °C under a nitrogen atmosphere and stirred for 3 h. After completion of the reaction (monitored by TLC), it was quenched with water (4 mL) and filtered through a small bed of Celite. The organic layer was separated and the aqueous layer extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 mL). The combined organic layer was washed with saturated aqueous sodium thiosulphate solution (2 × 25 mL), saturated aqueous NaHCO<sub>3</sub> solution (2 × 25) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Solvent was removed under reduced pressure and the crude product was purified by column chromatography over silica gel (ethyl acetate/hexane = 1:4) to afford compound **25** (70 mg, 92%) as a colorless liquid; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +7.1 (*c* 1.5, CHCl<sub>3</sub>); IR (KBr): 2923, 2852, 1712, 1589, 1460, 1333, 1251, 1067 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.38 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.93 (dt, *J* = 15.4, 6.2 Hz 1H), 6.52 (s, 1H), 6.05 (d, *J* = 15.7 Hz, 1H), 5.14 (m, 1H), 5.11 (s, 2H), 4.14 (d, *J* = 16.5 Hz, 1H), 3.97 (d, *J* = 16.5 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 2.61–2.39 (m, 6H), 1.94 (m, 1H), 1.73 (m, 1H), 1.32 (d, *J* = 6.1 Hz, 3H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  209.7, 194.5, 167.1, 159.6, 156.3, 156.0, 145.6, 132.7, 129.8, 128.8, 127.9, 114.1, 97.8, 71.6, 71.1, 56.3, 55.3, 42.8, 40.8, 39.5, 29.7, 28.9, 28.4, 20.0 ppm; HRMS (ESI): *m/z* calcd. for C<sub>27</sub>H<sub>29</sub>O<sub>7</sub>Cl [M + H]<sup>+</sup> 501.1674, found 501.1675.

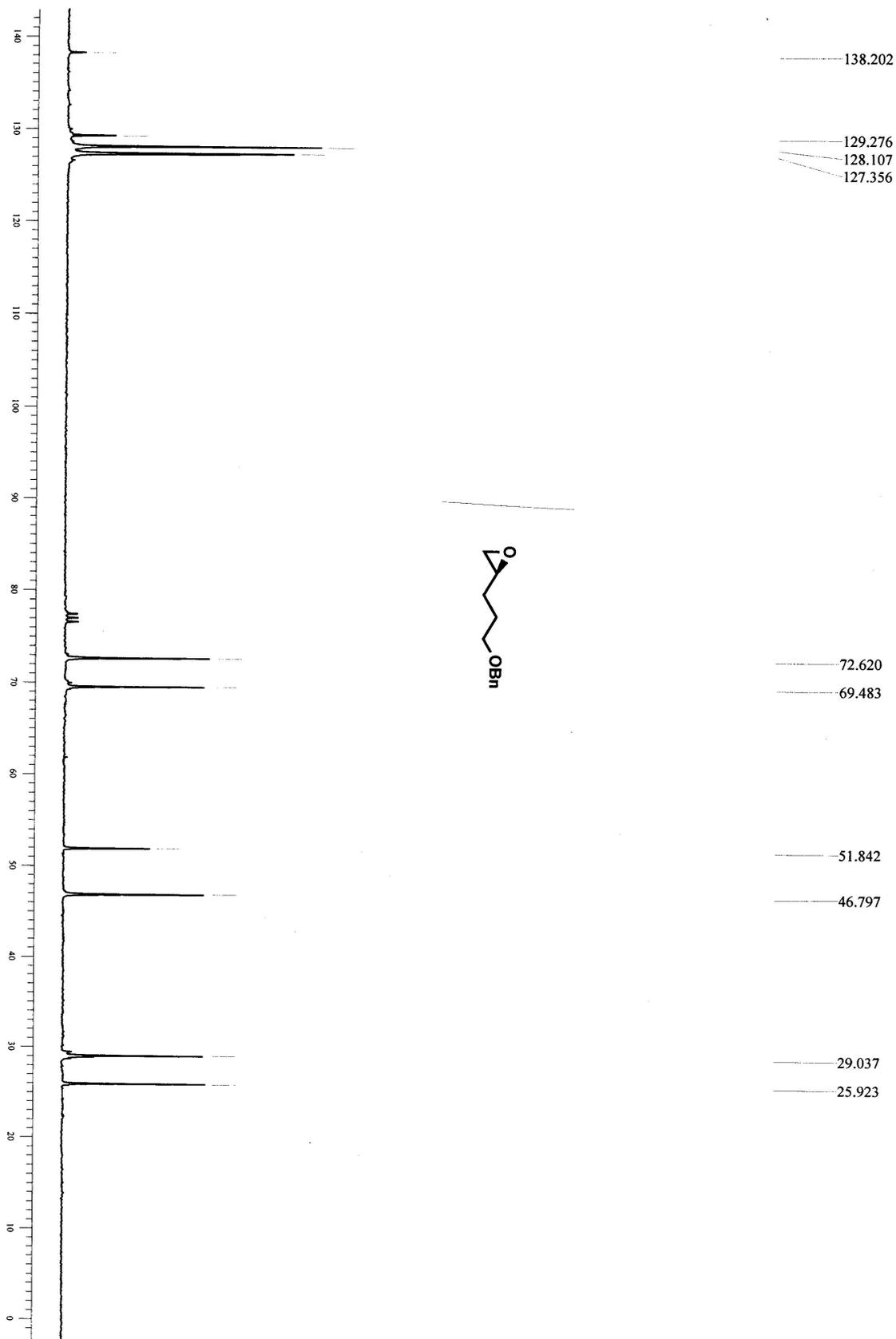


**(*R,E*)-13-Chloro-14-hydroxy-16-methoxy-3-methyl-4,5,7,8-tetrahydro-1*H*-benzo[*c*][1]oxacyclotetradecine-1,6,11(3*H*,12*H*)-trione (1):** To a stirred solution of compound **25** (28 mg, 0.056 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL), was added TiCl<sub>4</sub> (0.56 mL, 0.56 mmol, 1M in CH<sub>2</sub>Cl<sub>2</sub>) at 0 °C and the mixture was allowed to stir for 10 min at 0 °C. After completion of the reaction (monitored by TLC), it was quenched with a saturated solution of NaHCO<sub>3</sub> (5 mL). After separation of the two layers, the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 10 mL). The combined organic layer was washed with brine (2 × 30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate/hexane = 2:3) to afford **1** (18 mg,

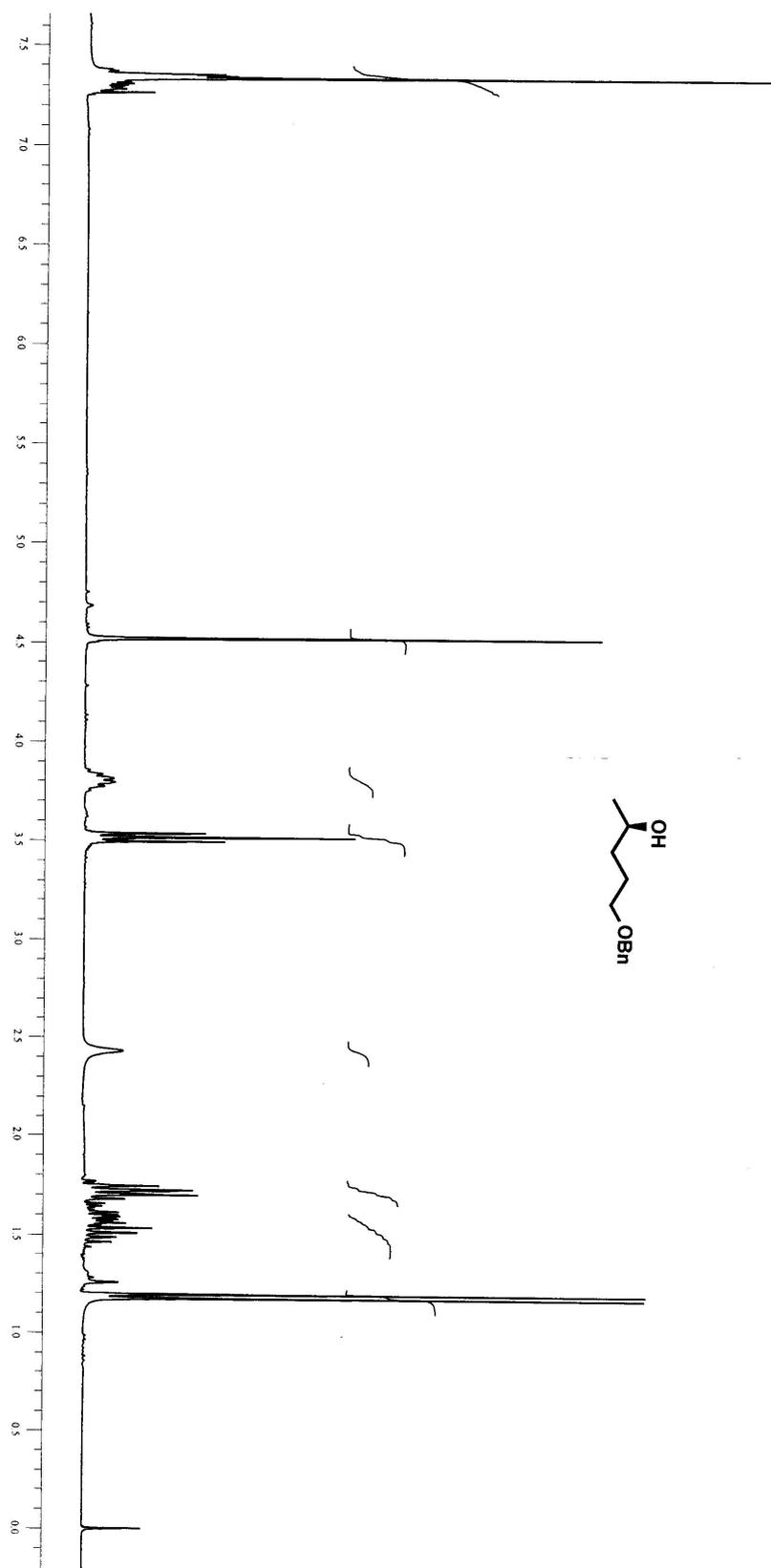
87%) as light yellow liquid.  $[\alpha]_{\text{D}}^{27} +9.7$  (*c* 1.05, MeOH); IR (neat): 3415, 2924, 2853, 1713, 1590, 1458, 1375, 1249, 1101, 1036  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.87 (dt,  $J = 15.4, 6.0$  Hz, 1H), 6.59 (s, 1H), 6.07 (d,  $J = 15.7$  Hz, 1H), 5.14 (m, 1H), 4.20 (d,  $J = 16.2$  Hz, 1H), 3.86 (d,  $J = 16.1$  Hz, 1H), 3.86 (d,  $J = 16.2$  Hz, 1H), 3.78 (s, 3H), 2.58–2.51 (m, 3H), 2.50–2.42 (m, 3H), 1.76–1.69 (m, 2H), 1.32 (d,  $J = 6.1$  Hz, 3H) ppm;  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ ):  $\delta$  10.64 (br s, 1H), 6.93 (dt,  $J = 15.7, 7.2$  Hz, 1H), 6.61 (s, 1H), 5.95 (d,  $J = 15.9$  Hz, 1H), 4.96 (m, 1H), 4.04 (d,  $J = 16.8$  Hz, 1H), 3.88 (d,  $J = 16.8$  Hz, 1H), 3.71 (s, 3H), 2.54–2.51 (m, 3H), 2.47–2.38 (m, 3H), 1.80–1.71 (m, 1H), 1.58–1.45 (m, 1H), 1.20 (d,  $J = 6.6$  Hz, 3H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ ):  $\delta$  210.3, 193.9, 166.3, 155.7, 155.0, 147.1, 132.1, 129.4, 116.2, 113.4, 99.2, 70.9, 55.9, 41.9, 40.2, 38.9, 22.8, 28.0, 19.9 ppm; HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{21}\text{O}_6\text{Cl}$   $[\text{M} + \text{Na}]^+$  403.0918, found 403.0911.



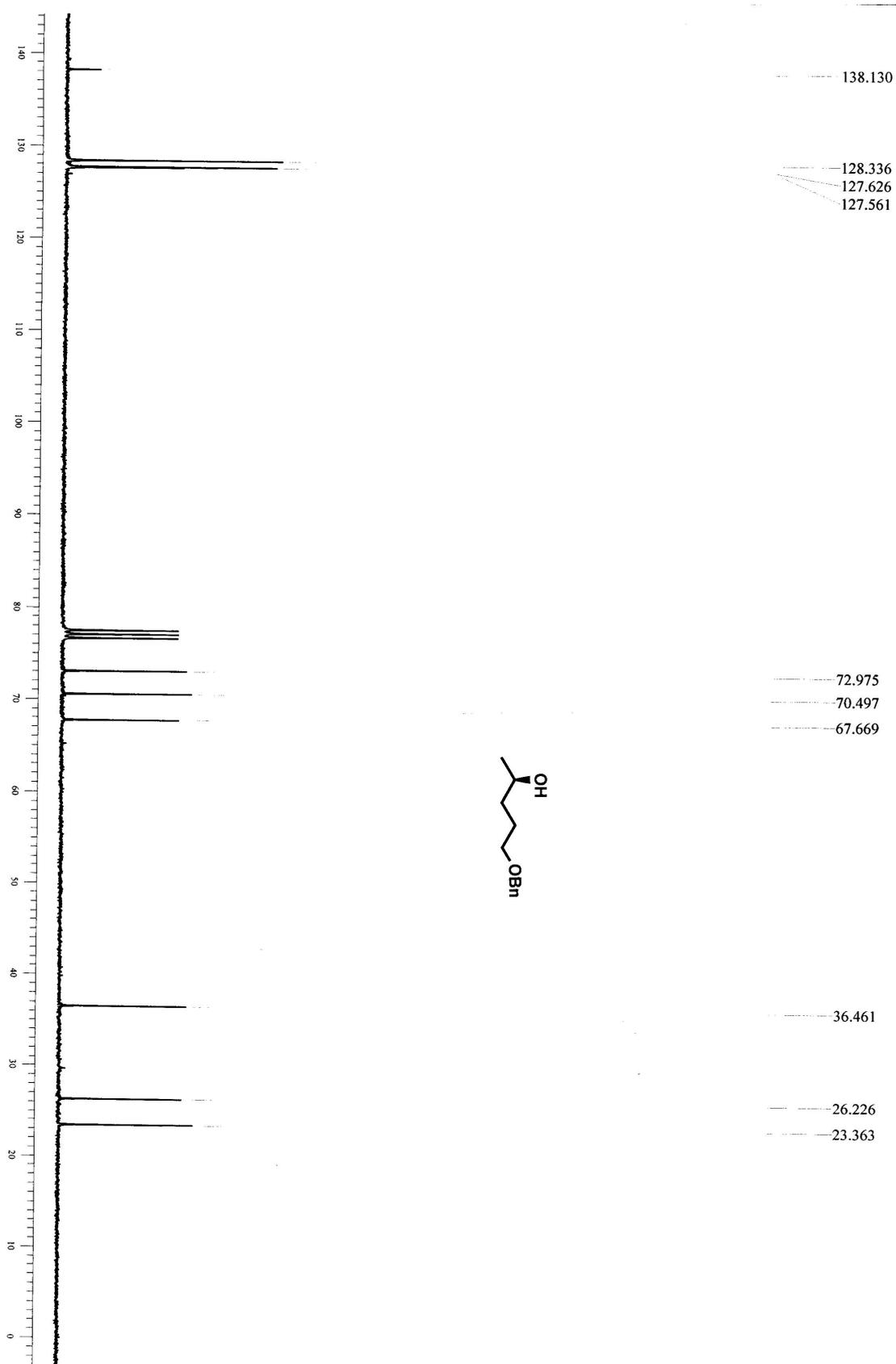
$^1\text{H}$  NMR of 12 (300 MHz,  $\text{CDCl}_3$ )



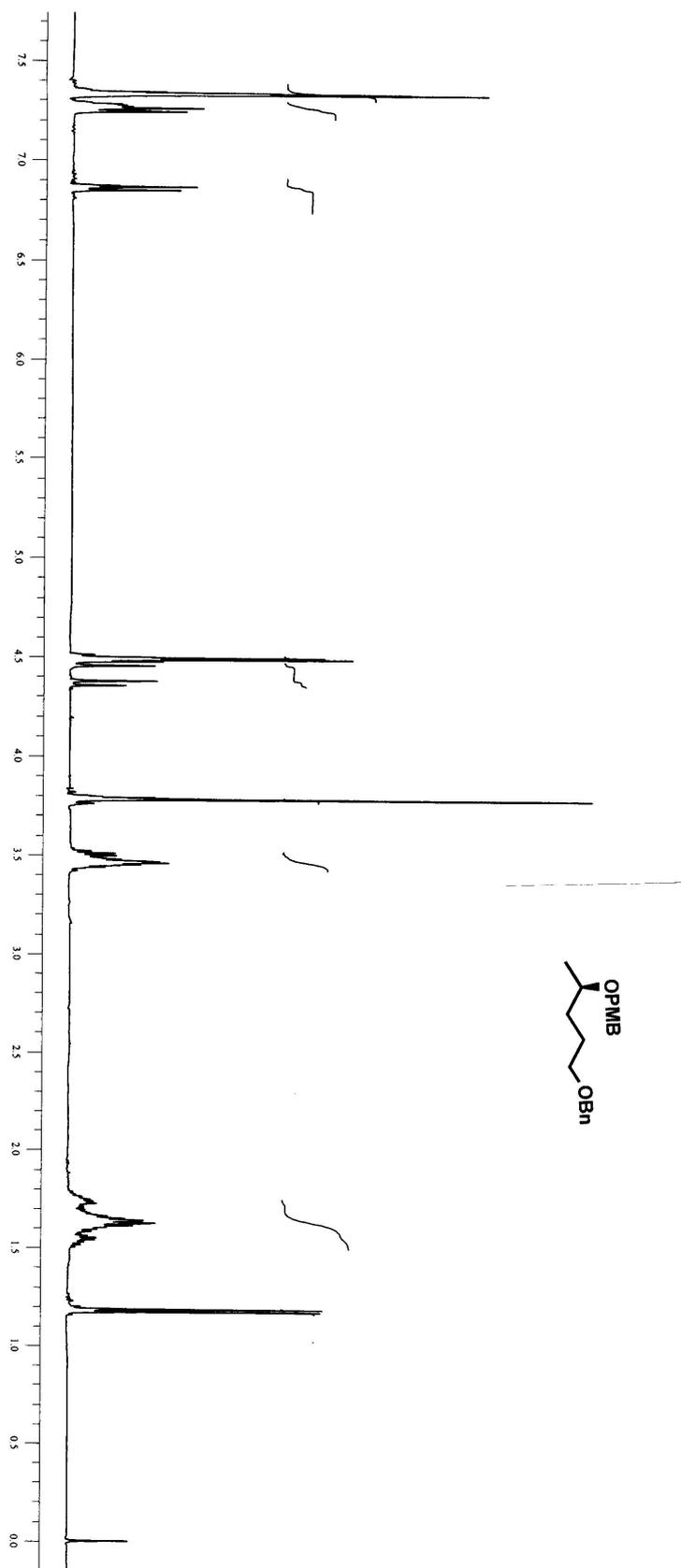
$^{13}\text{C}$  NMR of 12 (75 MHz,  $\text{CDCl}_3$ )



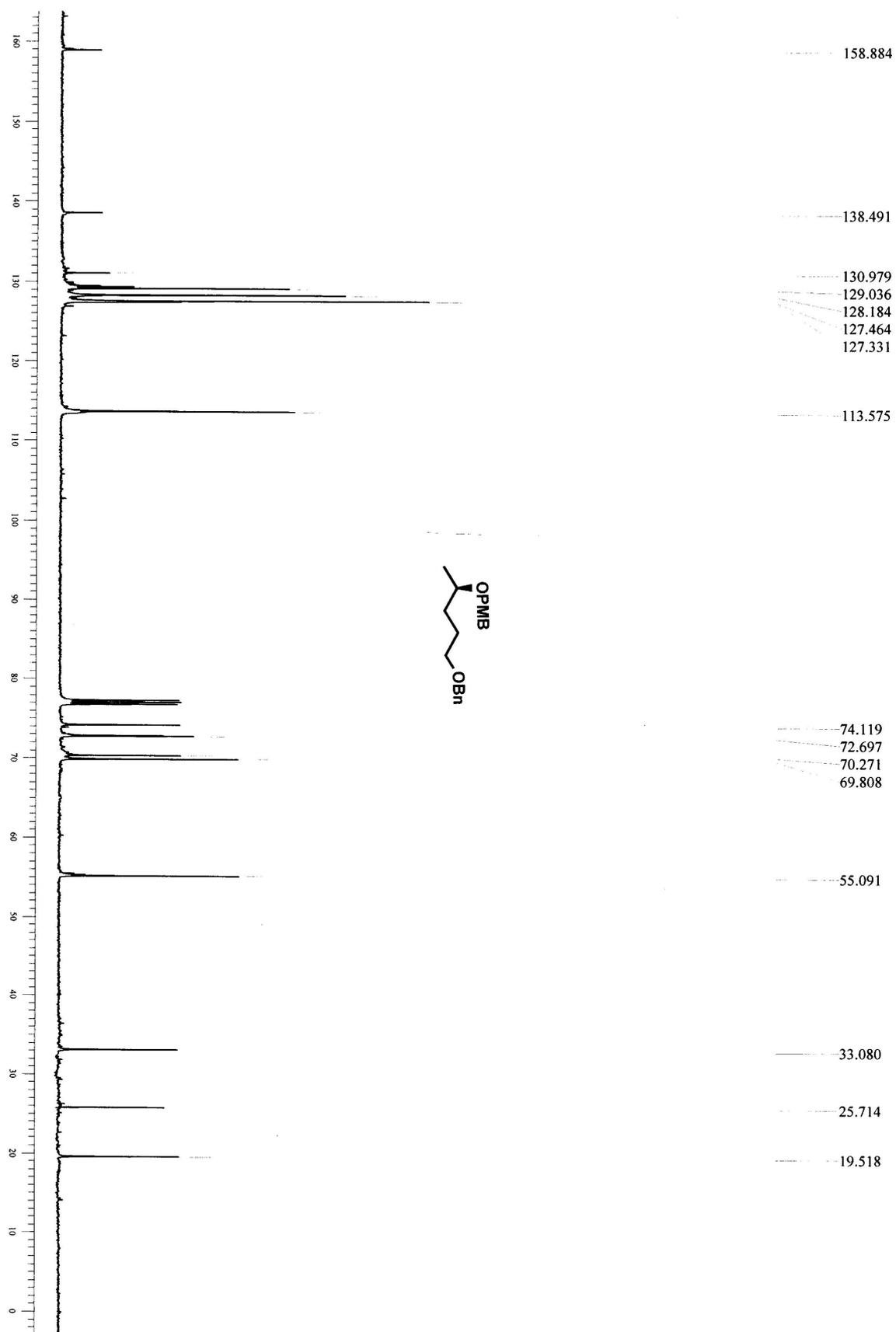
$^1\text{H}$  NMR of 13 (300 MHz,  $\text{CDCl}_3$ )

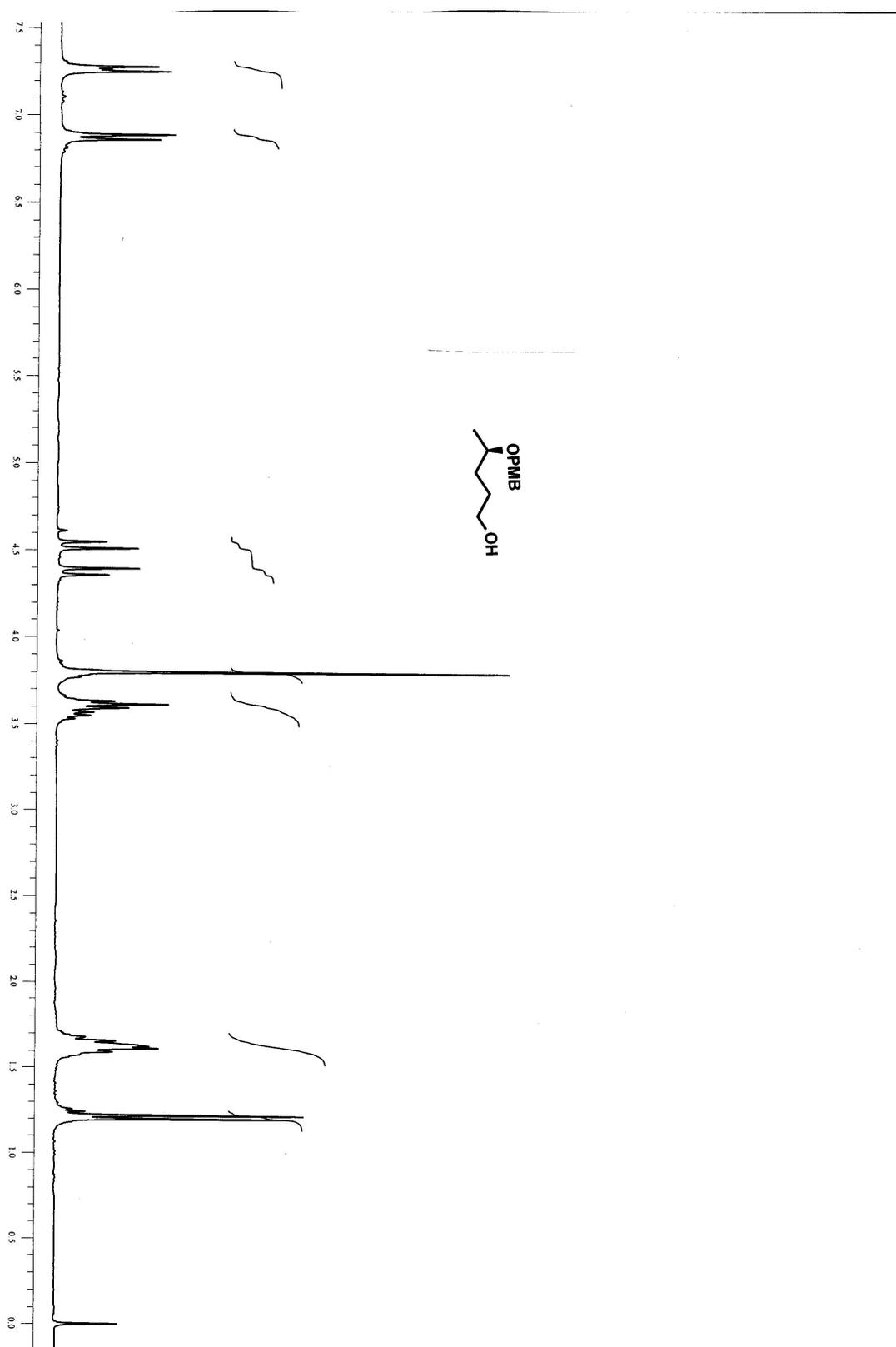


$^{13}\text{C}$  NMR of 13 (75 MHz,  $\text{CDCl}_3$ )

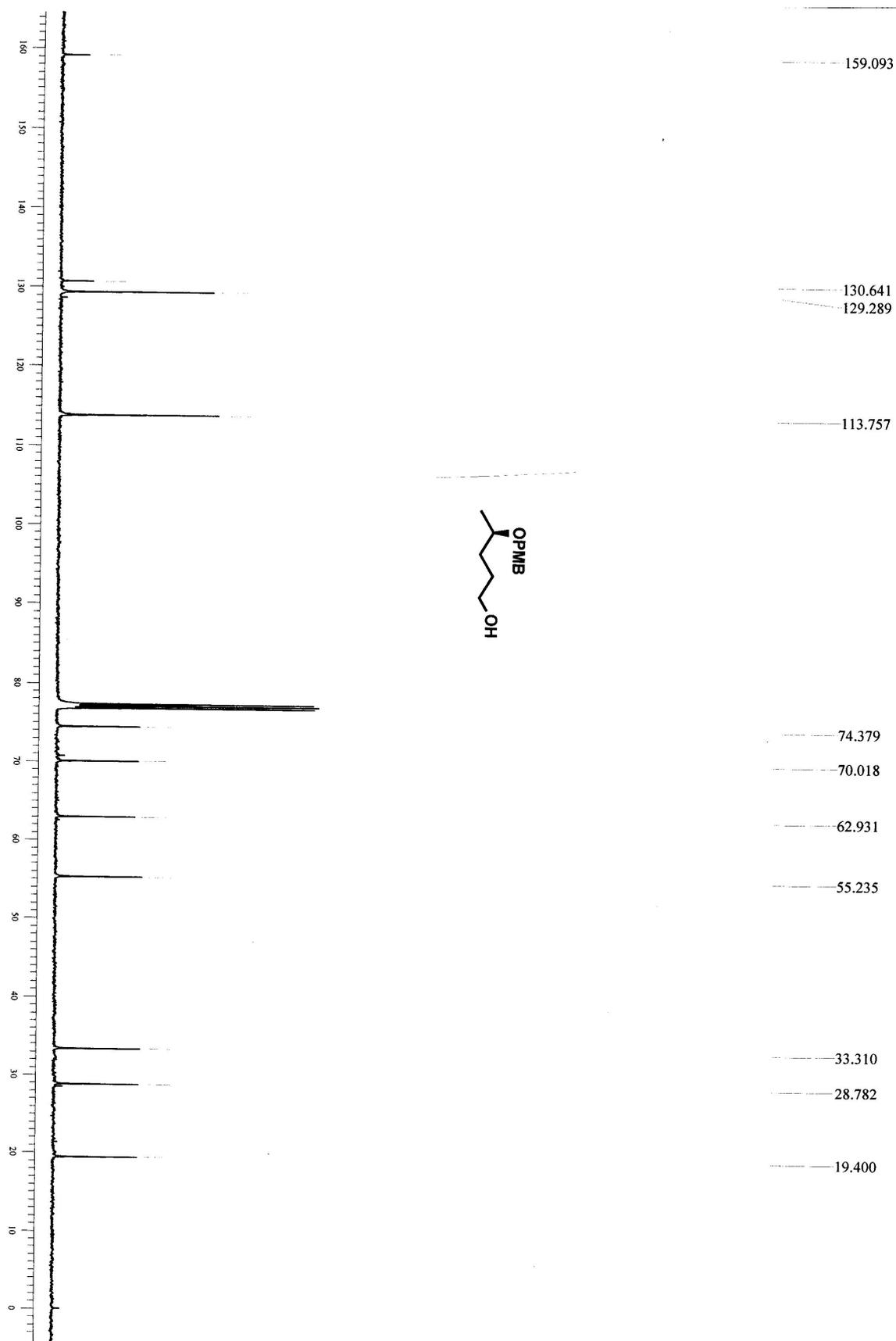


**<sup>1</sup>H NMR of 14 (300 MHz, CDCl<sub>3</sub>)**

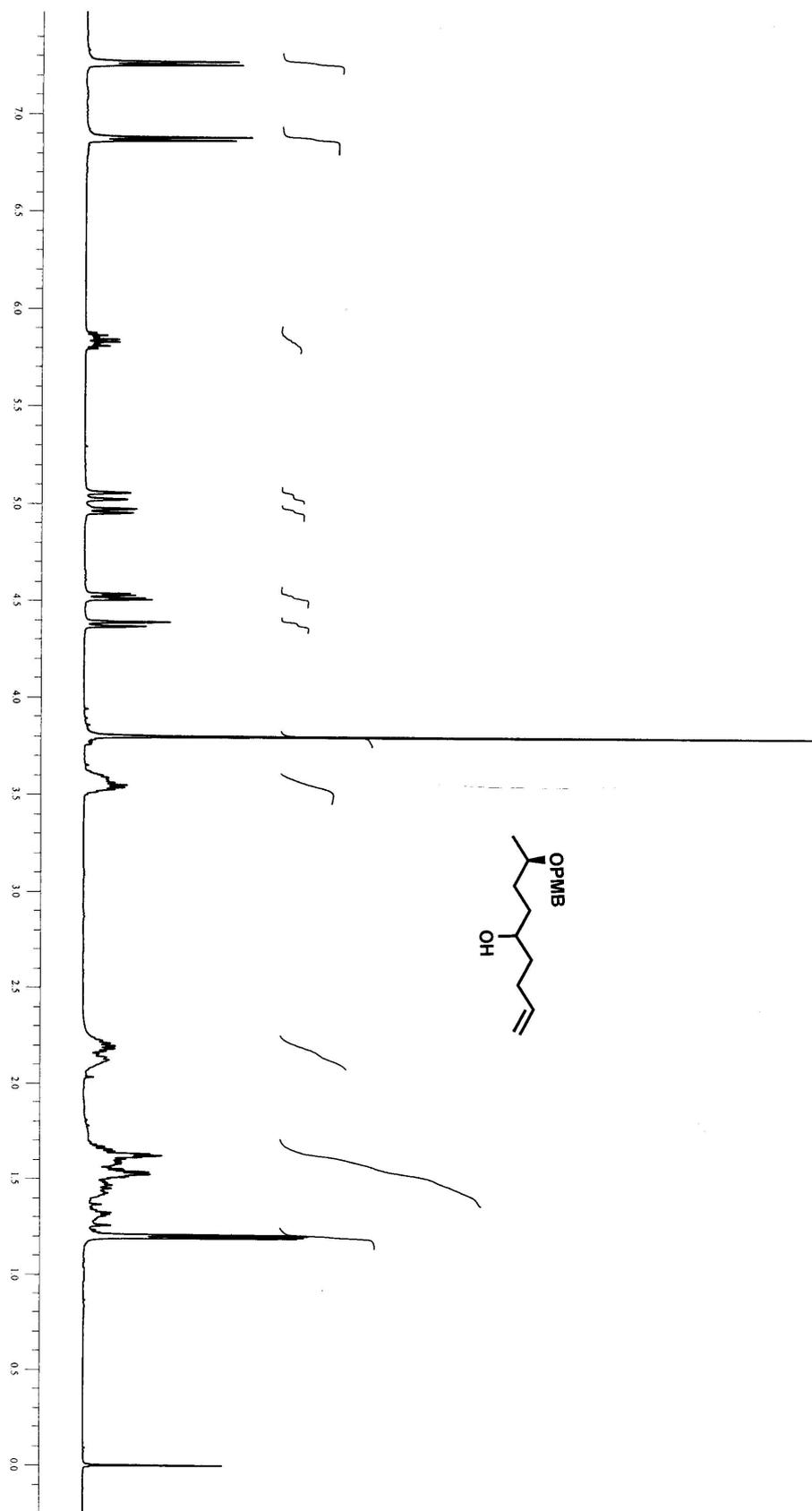




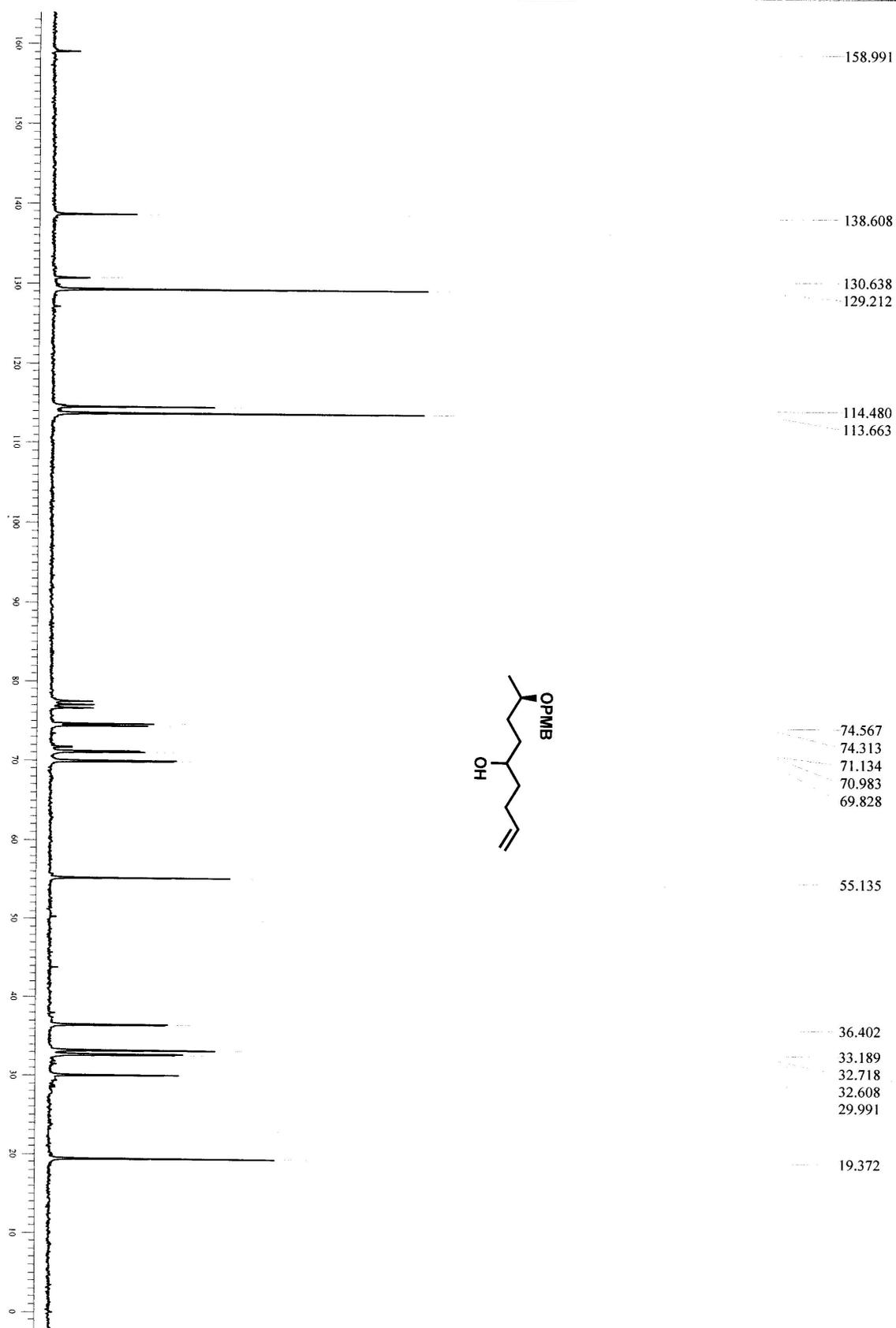
$^1\text{H}$  NMR of 15 (300 MHz,  $\text{CDCl}_3$ )

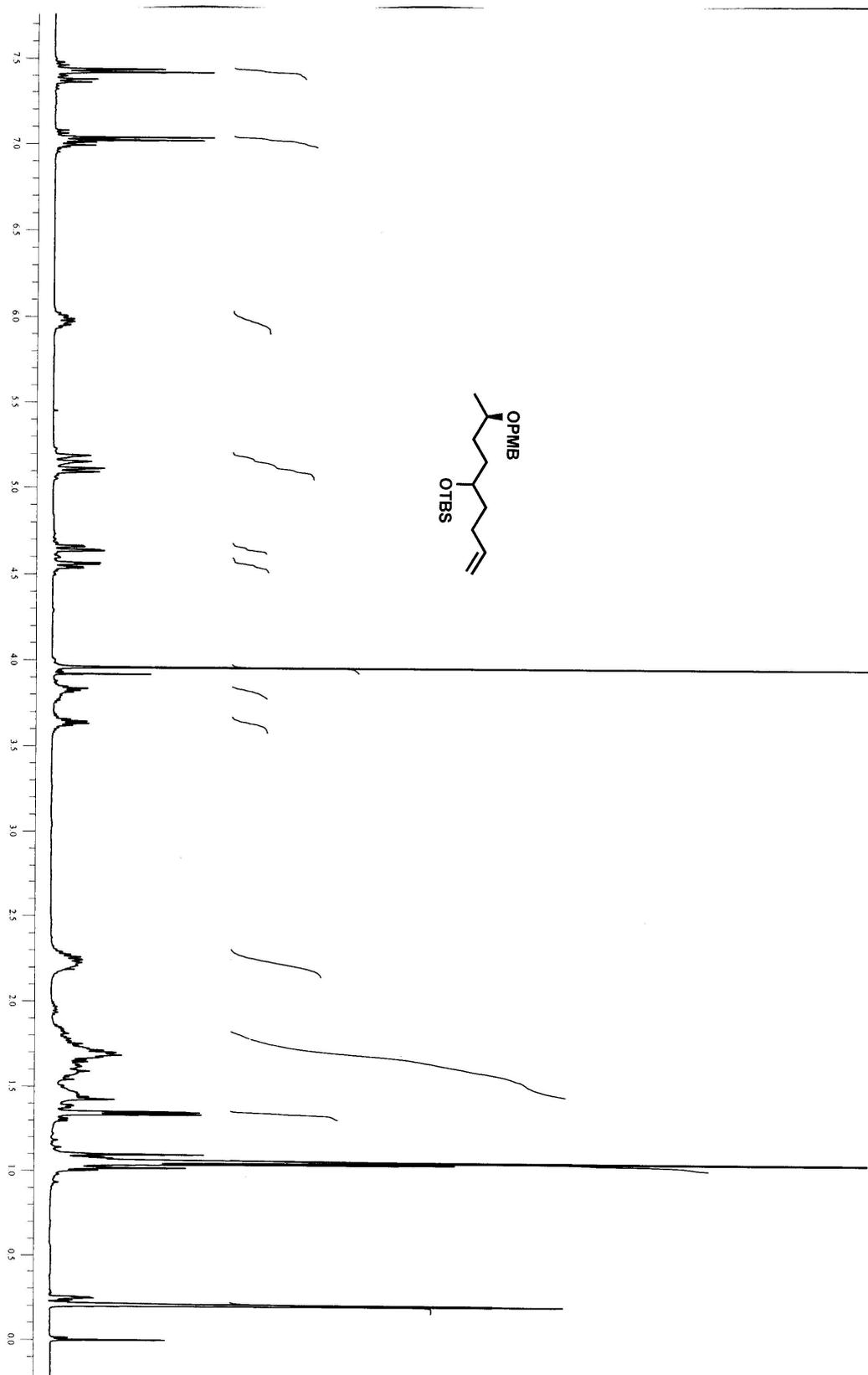


$^{13}\text{C}$  NMR of 15 (75 MHz,  $\text{CDCl}_3$ )

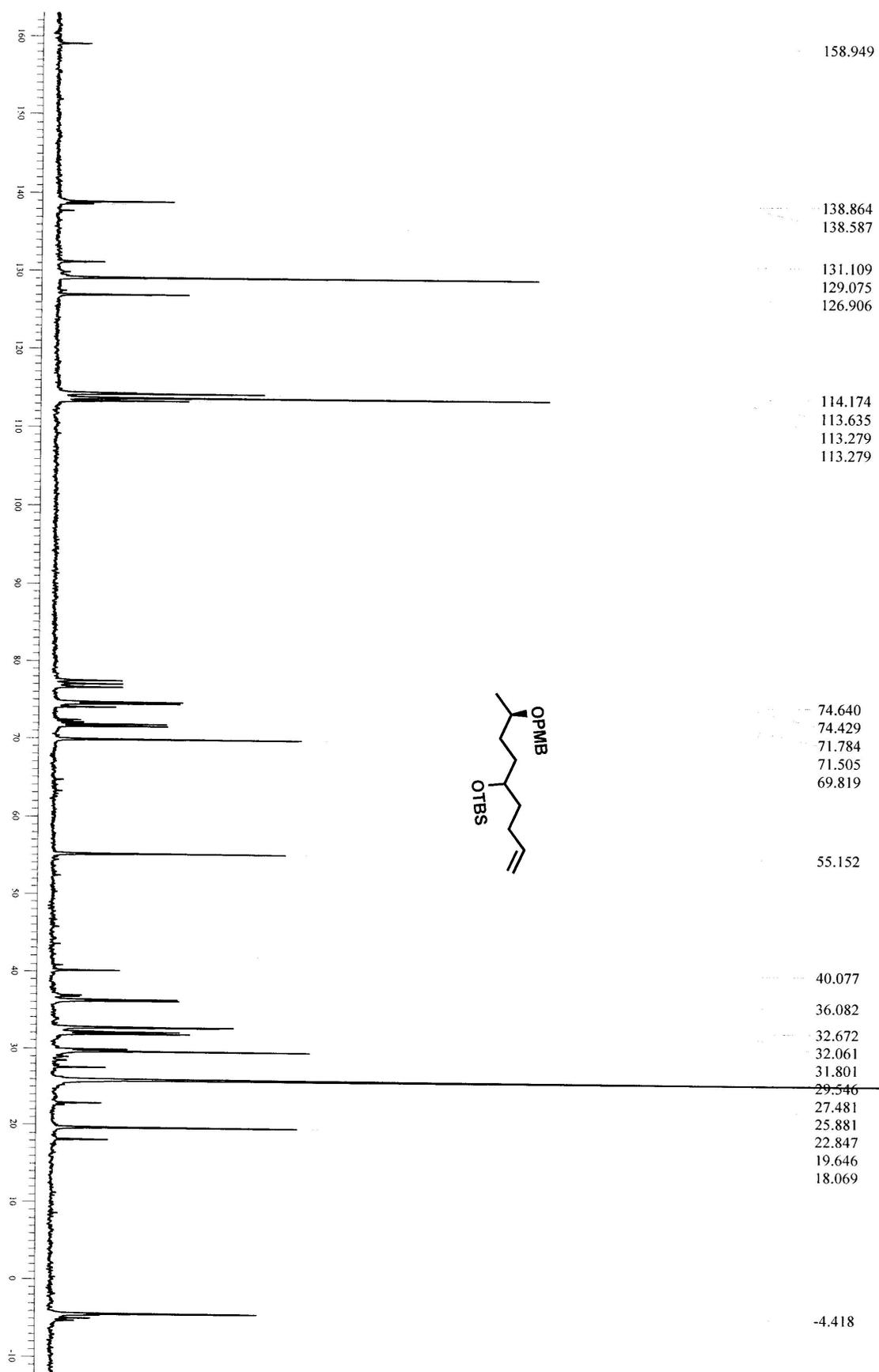


$^1\text{H}$  NMR of 16 (300 MHz,  $\text{CDCl}_3$ )

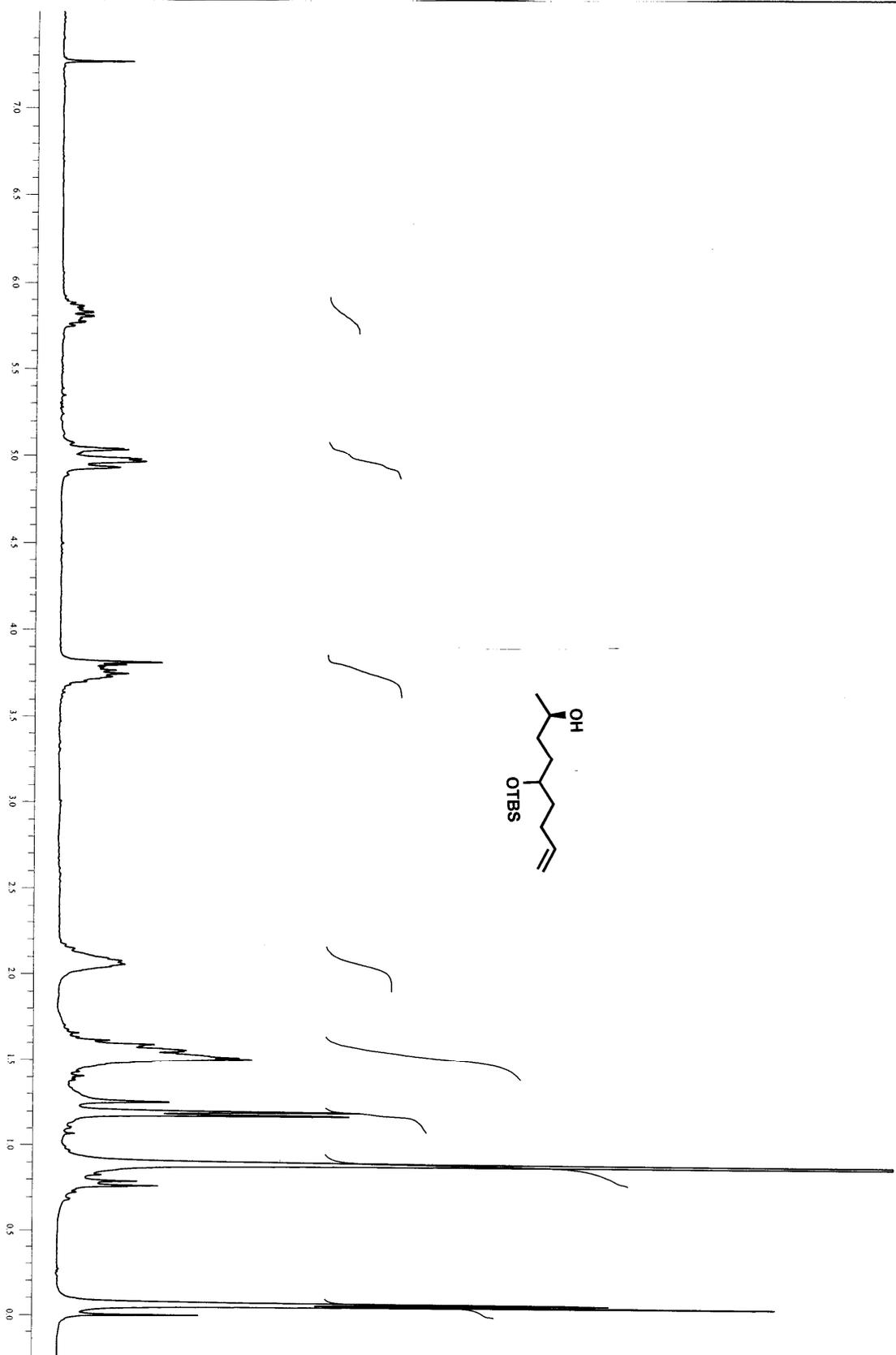




$^1\text{H}$  NMR of 17 (300 MHz,  $\text{CDCl}_3$ )

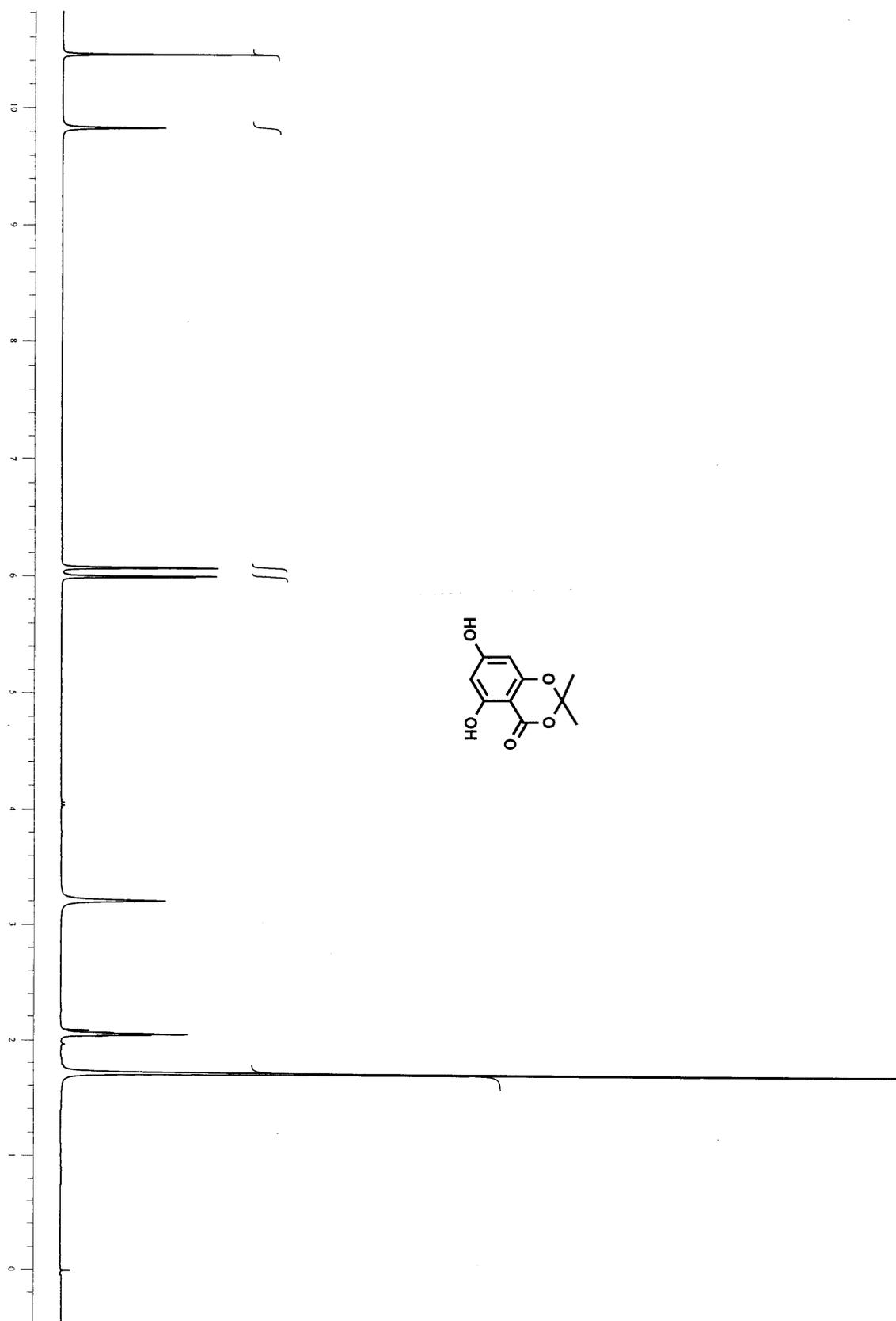


**<sup>13</sup>C NMR of 17 (75 MHz, CDCl<sub>3</sub>)**

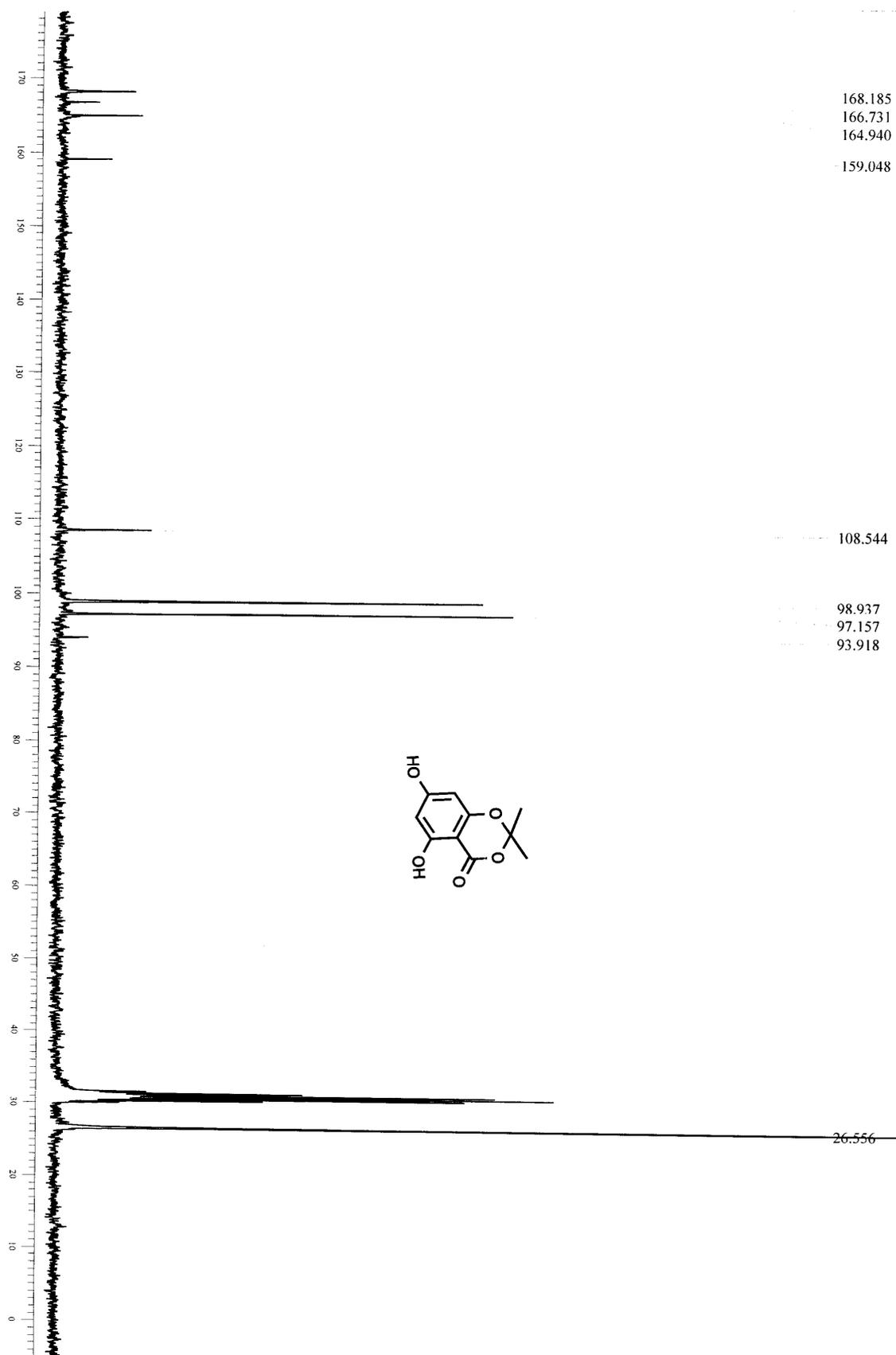


$^1\text{H}$  NMR of 10 (300 MHz,  $\text{CDCl}_3$ )

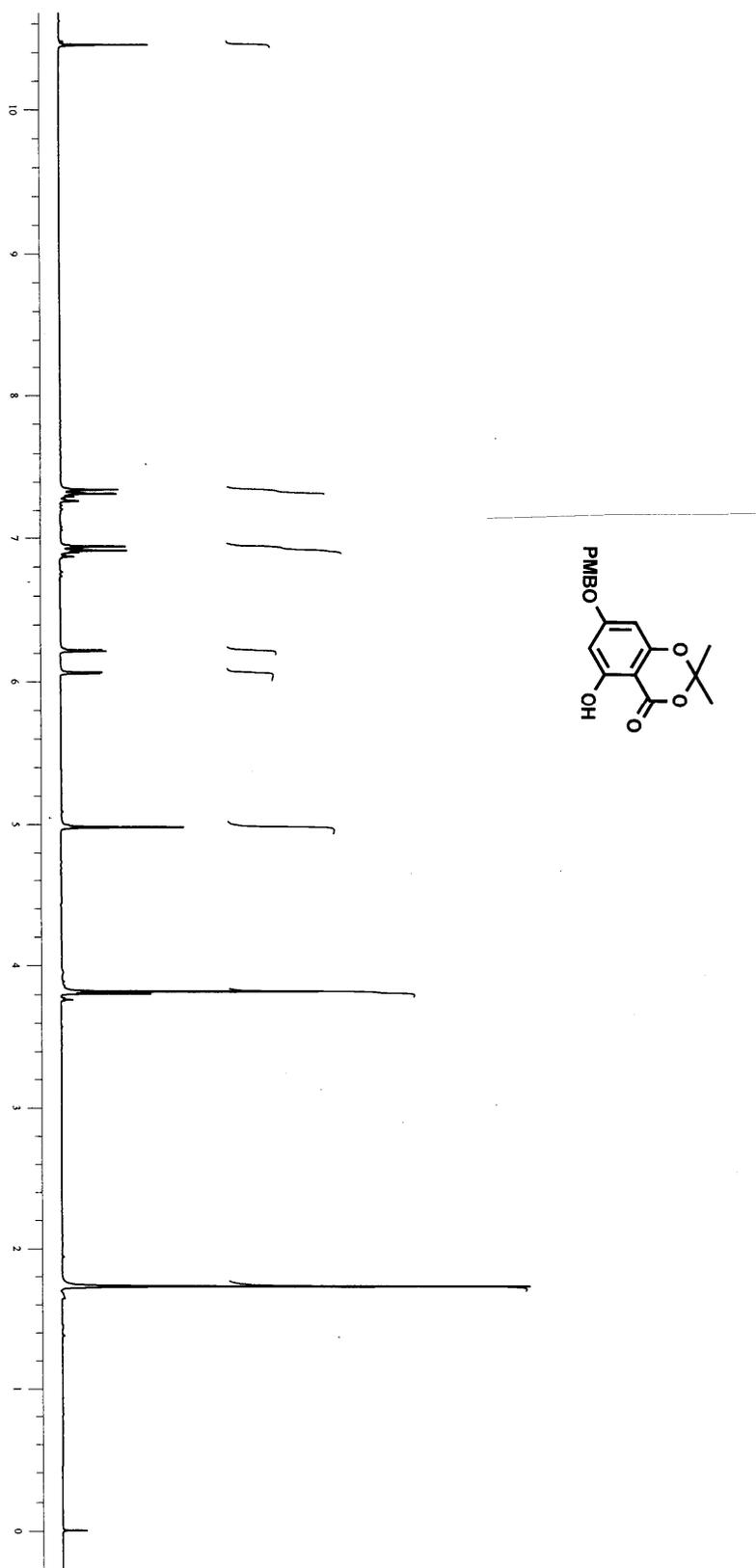




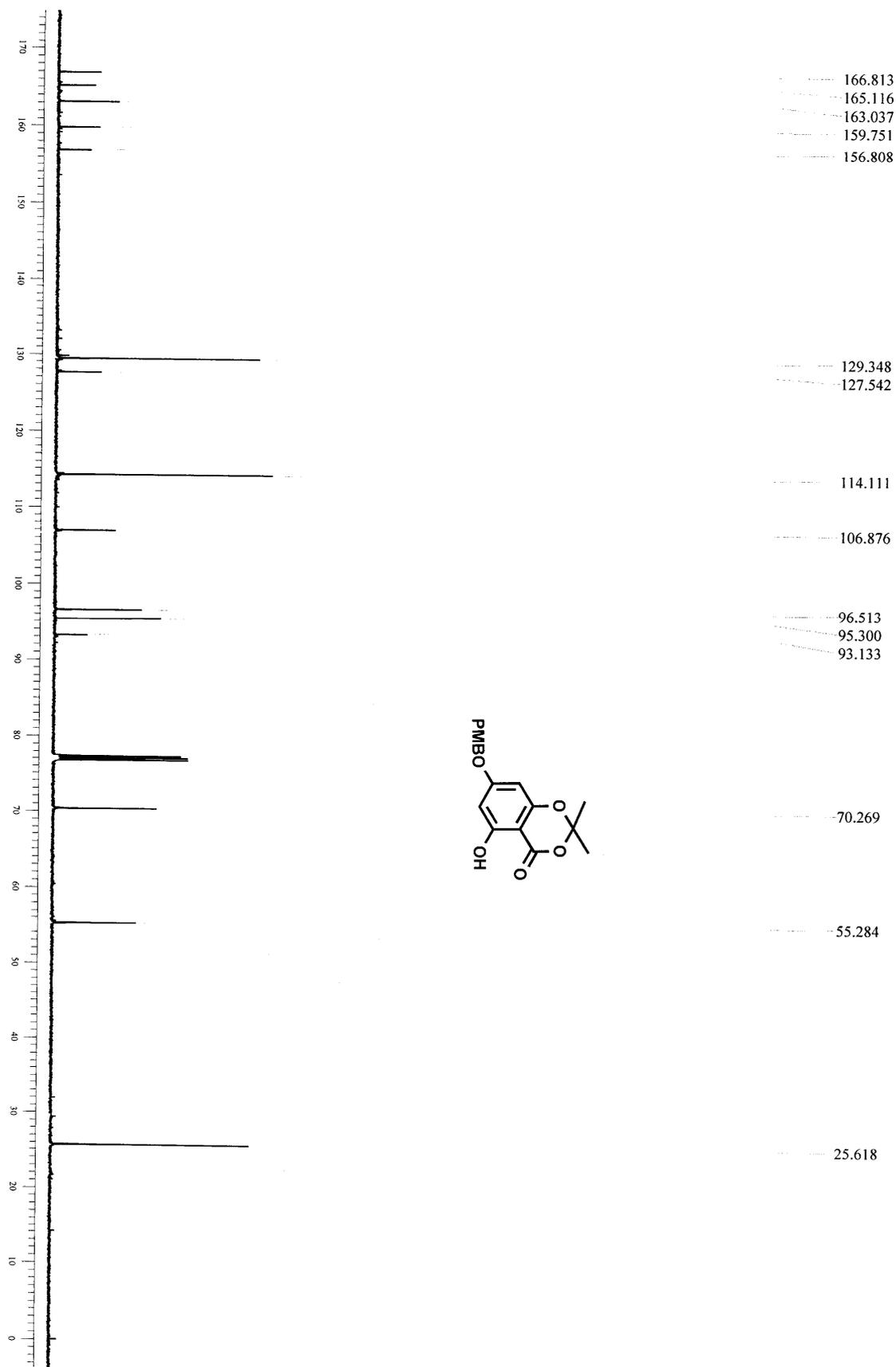
$^1\text{H}$  NMR of 18 (300 MHz, Acetone  $\text{d}_6$ )



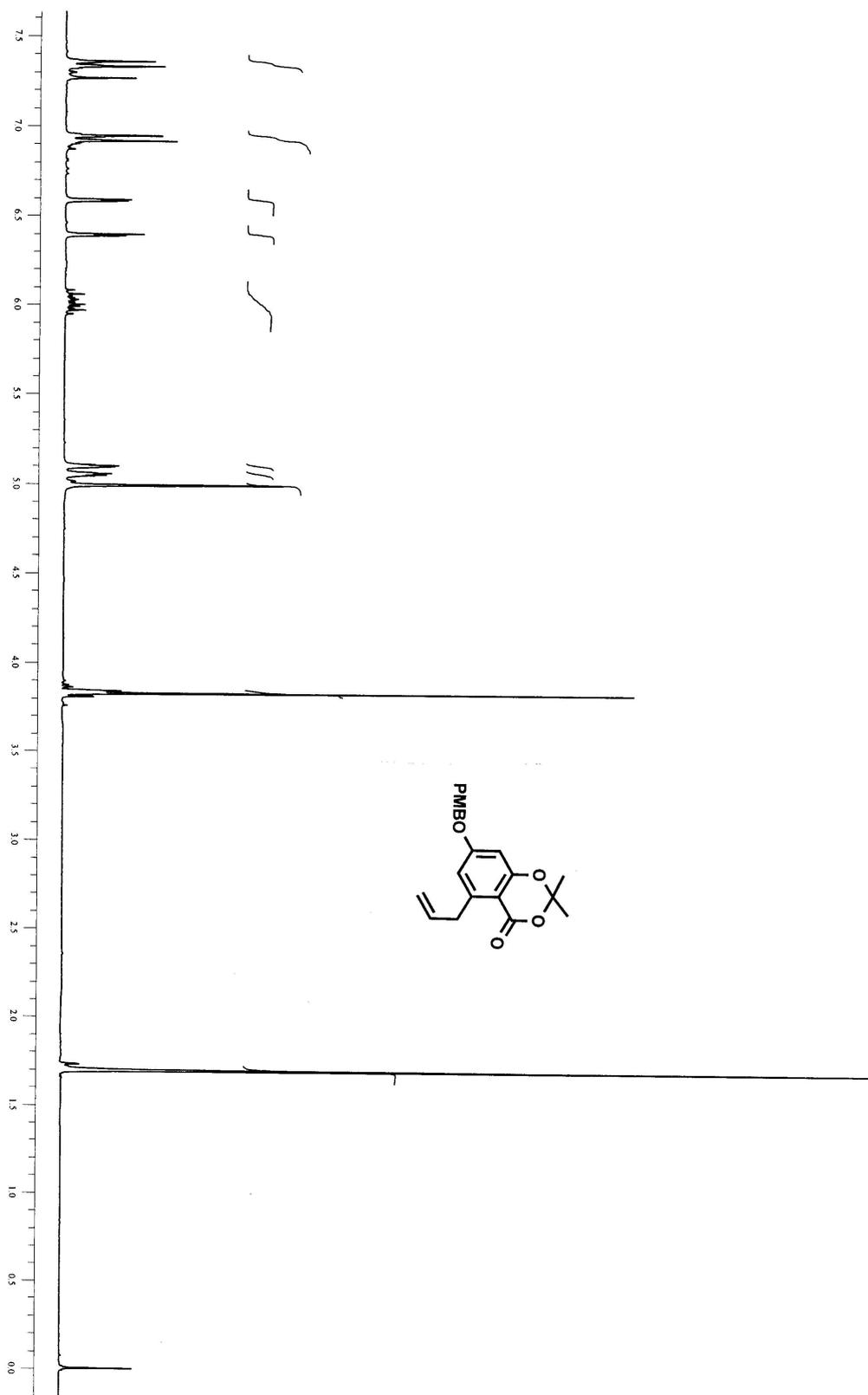
$^{13}\text{C}$  NMR of 18 (75 MHz, Acetone  $\text{d}_6$ )



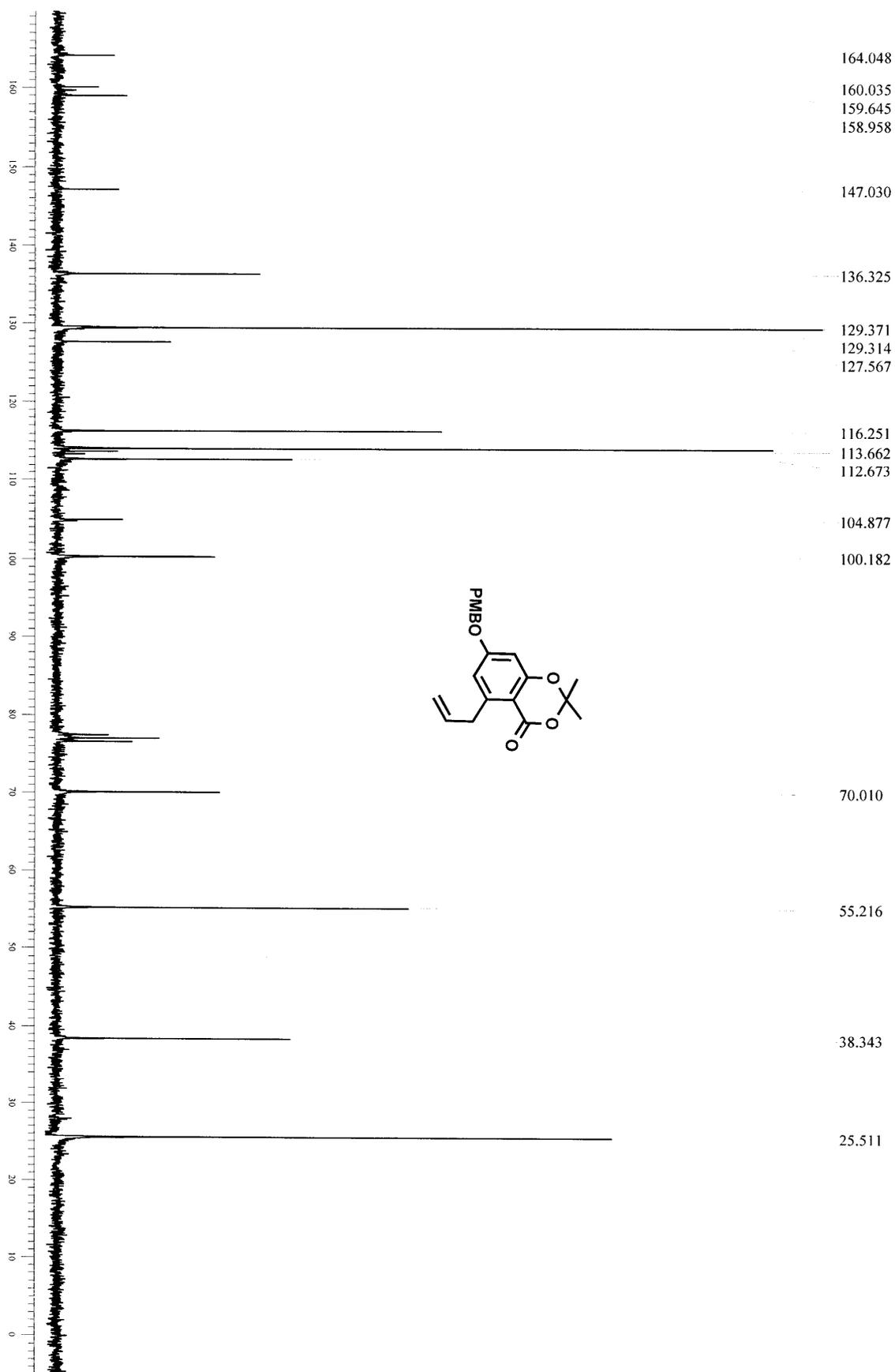
<sup>1</sup>H NMR of 19 (300 MHz, CDCl<sub>3</sub>)



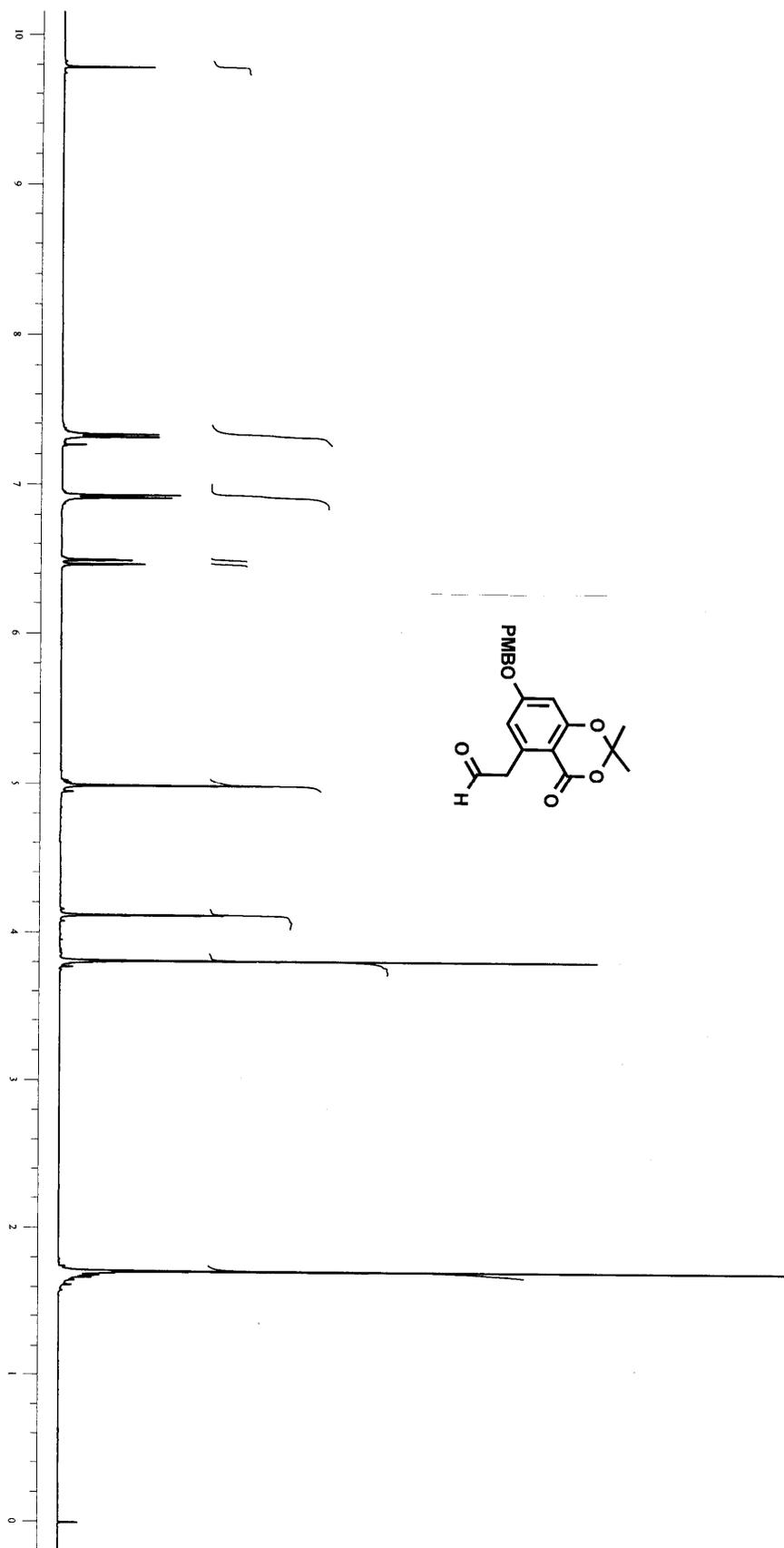
**<sup>13</sup>C NMR of 19 (75 MHz, CDCl<sub>3</sub>)**



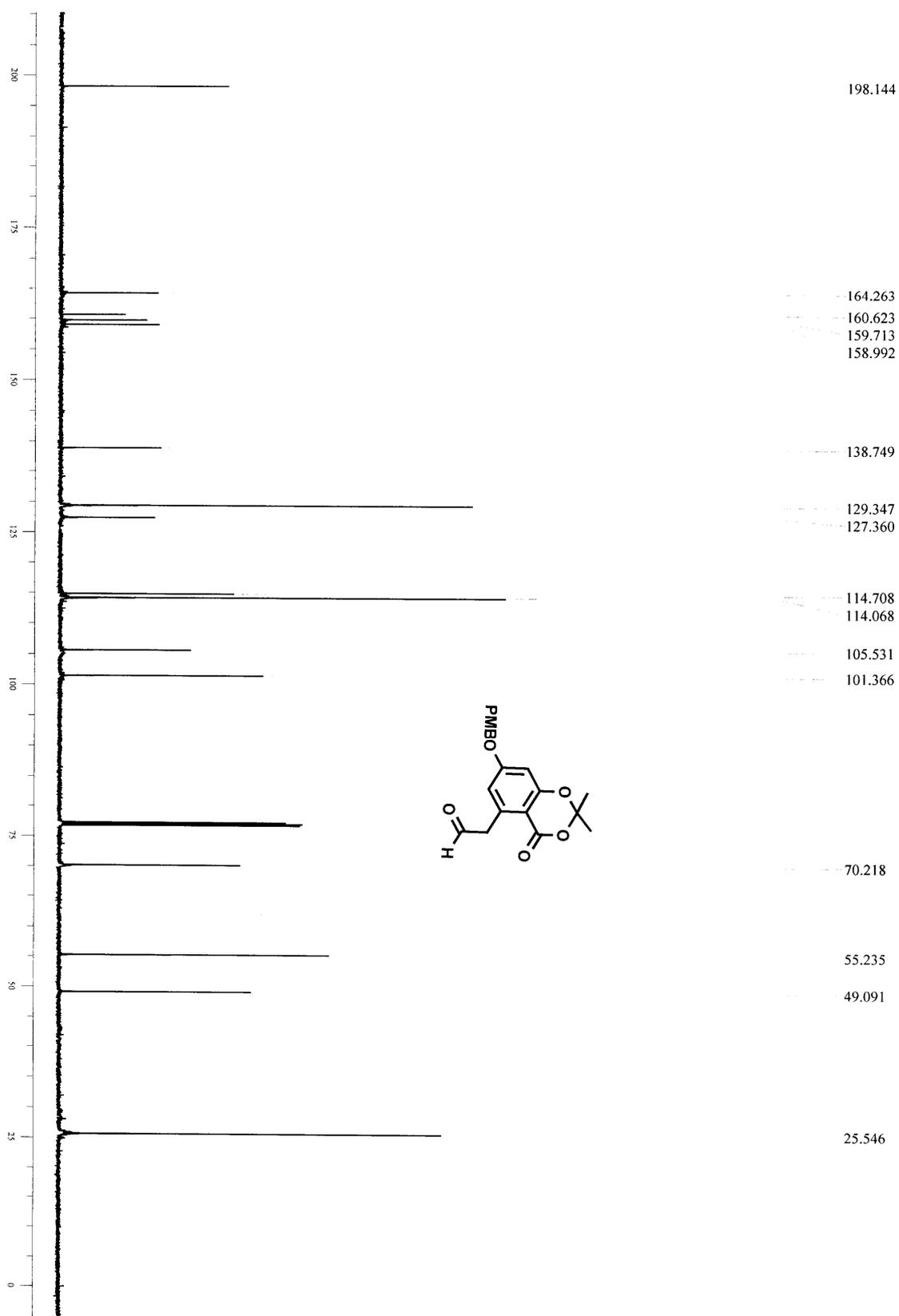
$^1\text{H}$  NMR of 20 (300 MHz,  $\text{CDCl}_3$ )



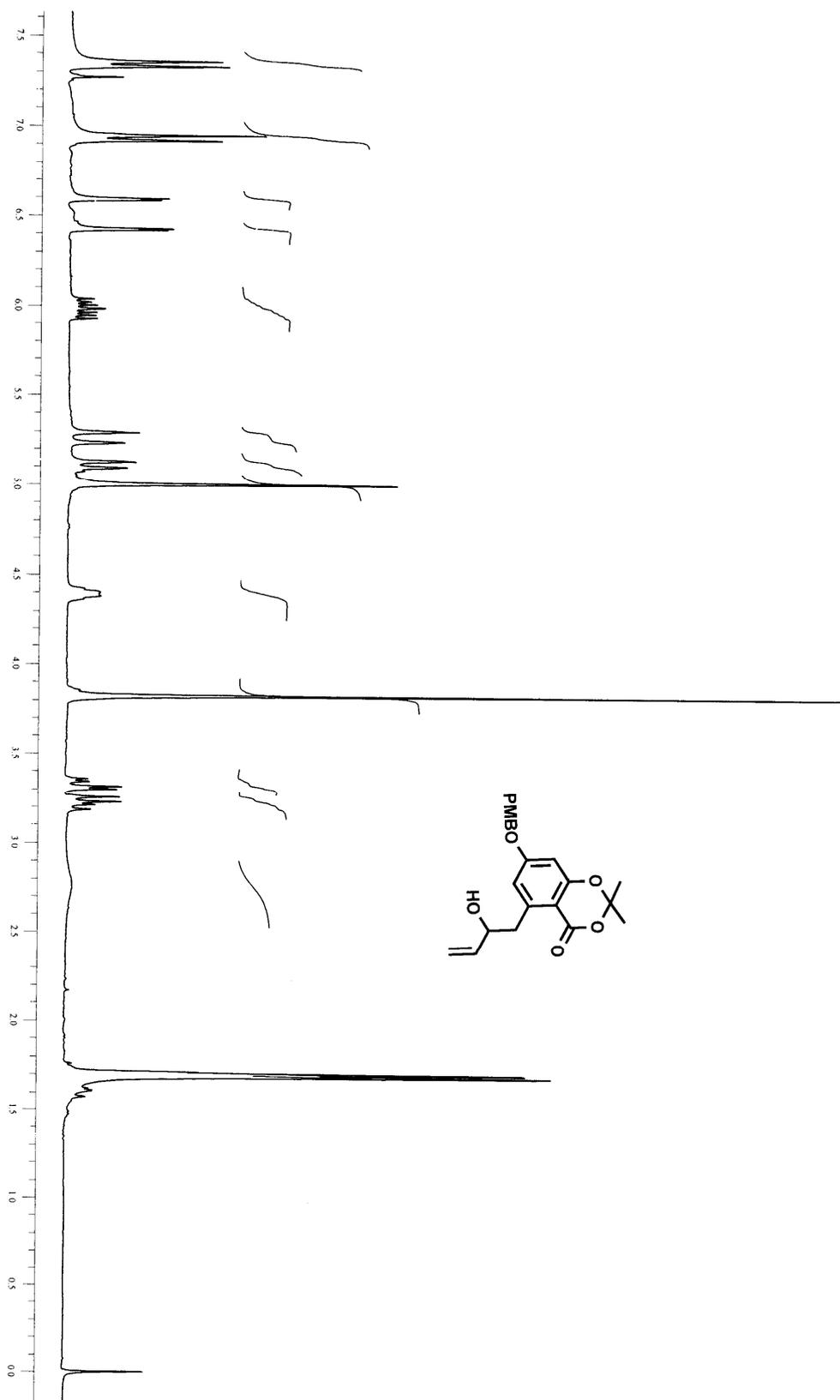
$^{13}\text{C}$  NMR of 20 (75 MHz,  $\text{CDCl}_3$ )



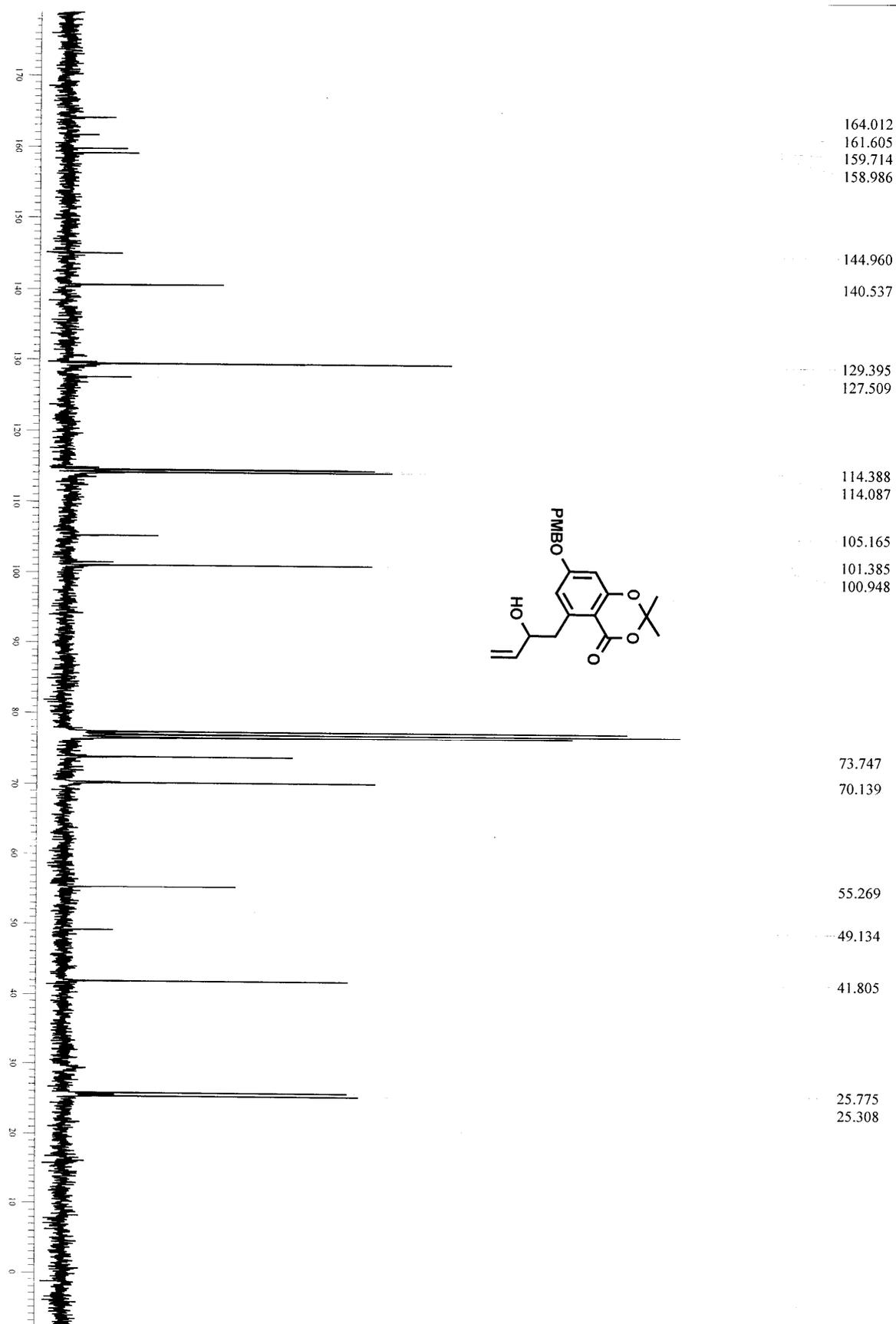
$^1\text{H}$  NMR of 21 (300 MHz,  $\text{CDCl}_3$ )



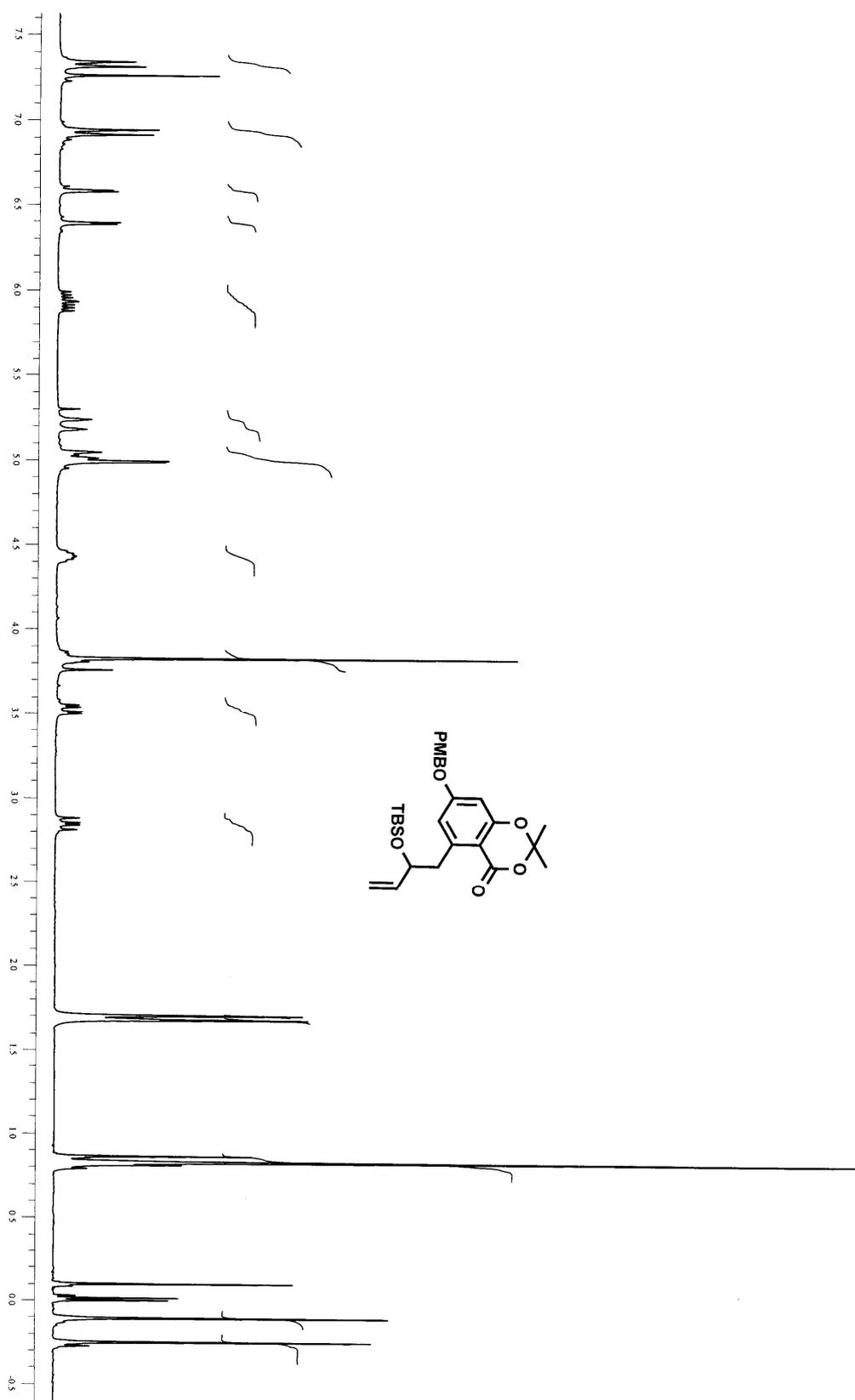
**<sup>13</sup>C NMR of 21 (75 MHz, CDCl<sub>3</sub>)**



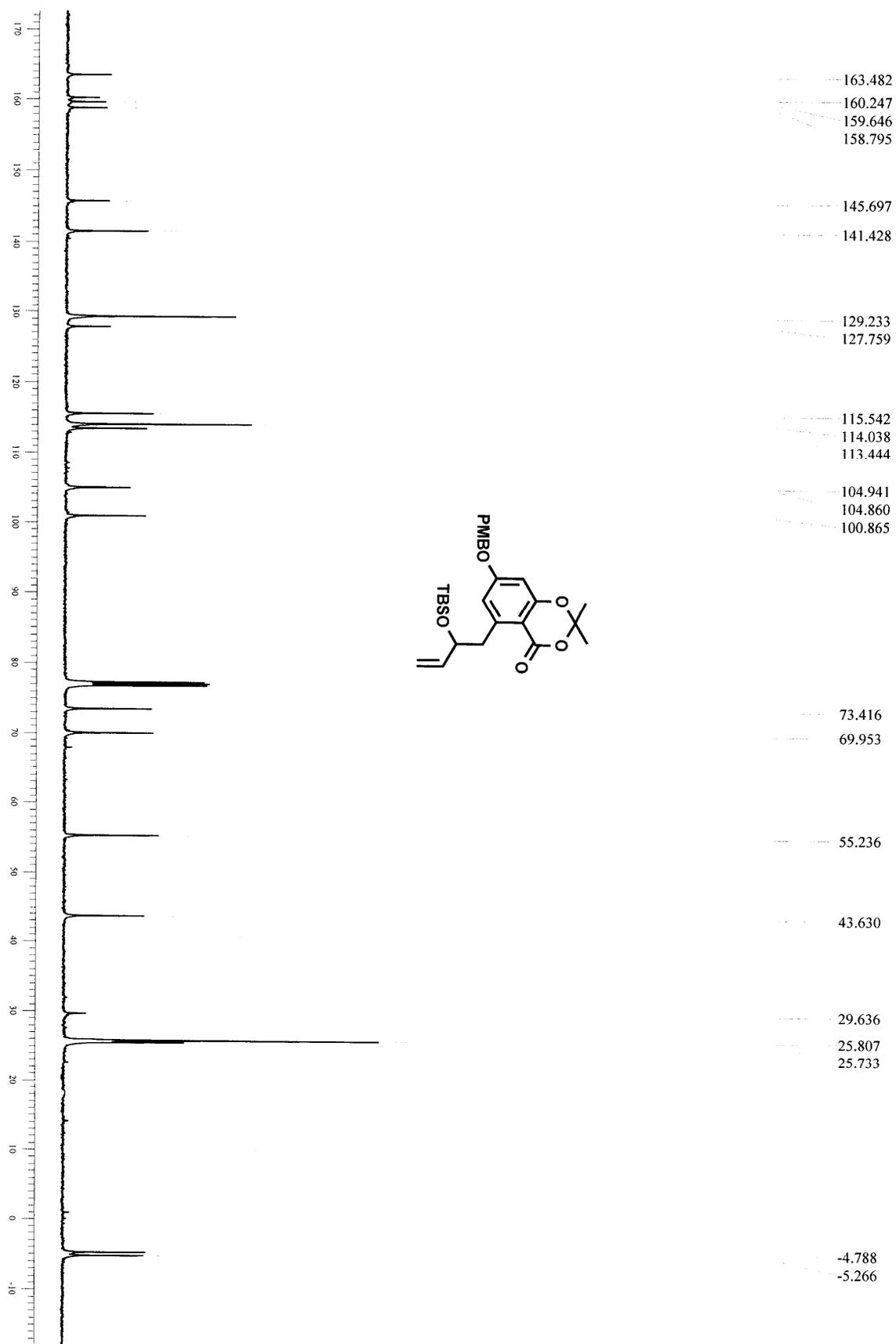
**$^1\text{H}$  NMR of 21 (300 MHz,  $\text{CDCl}_3$ )**

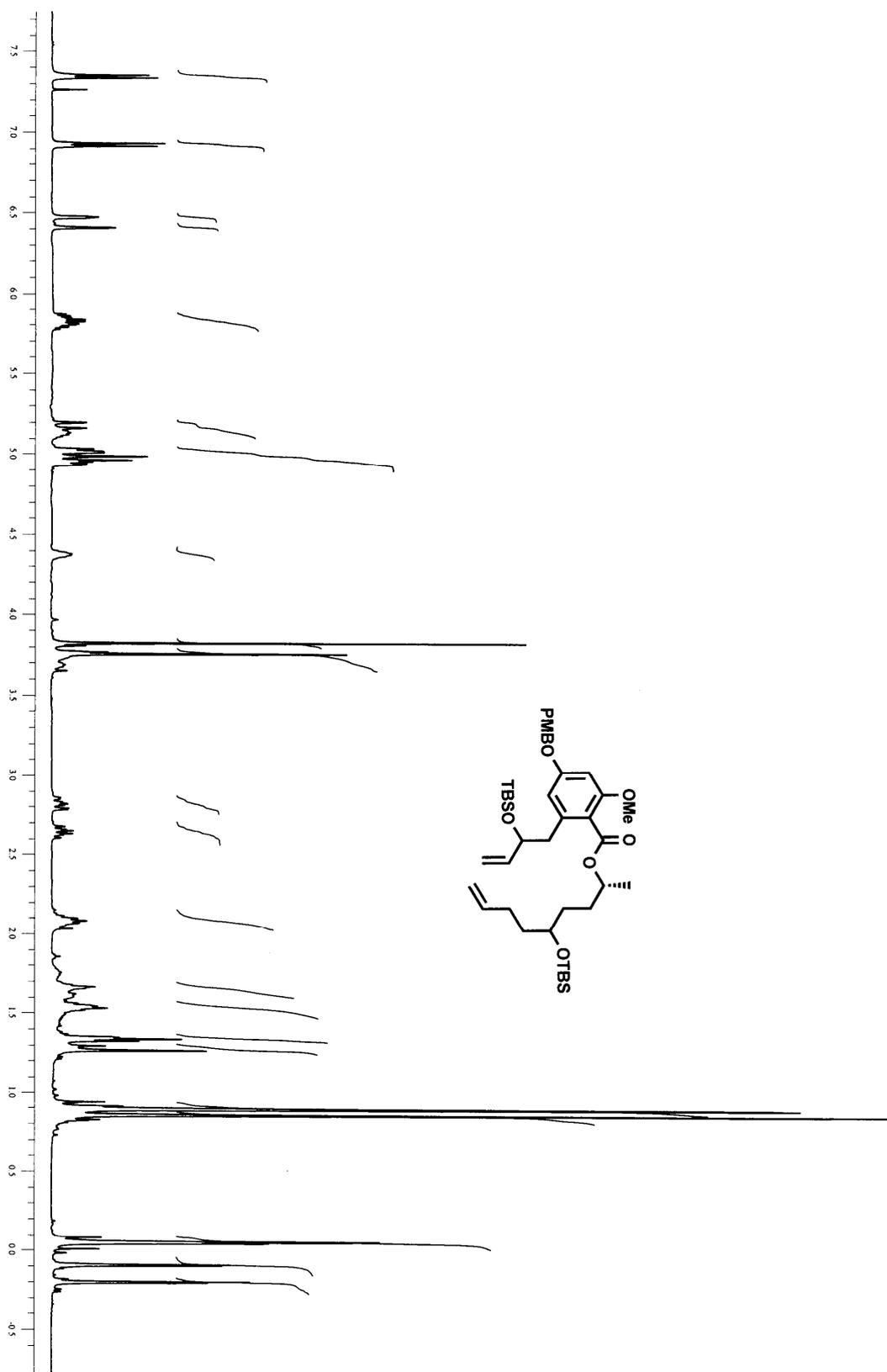


**<sup>13</sup>C NMR of 21 (75 MHz, CDCl<sub>3</sub>)**

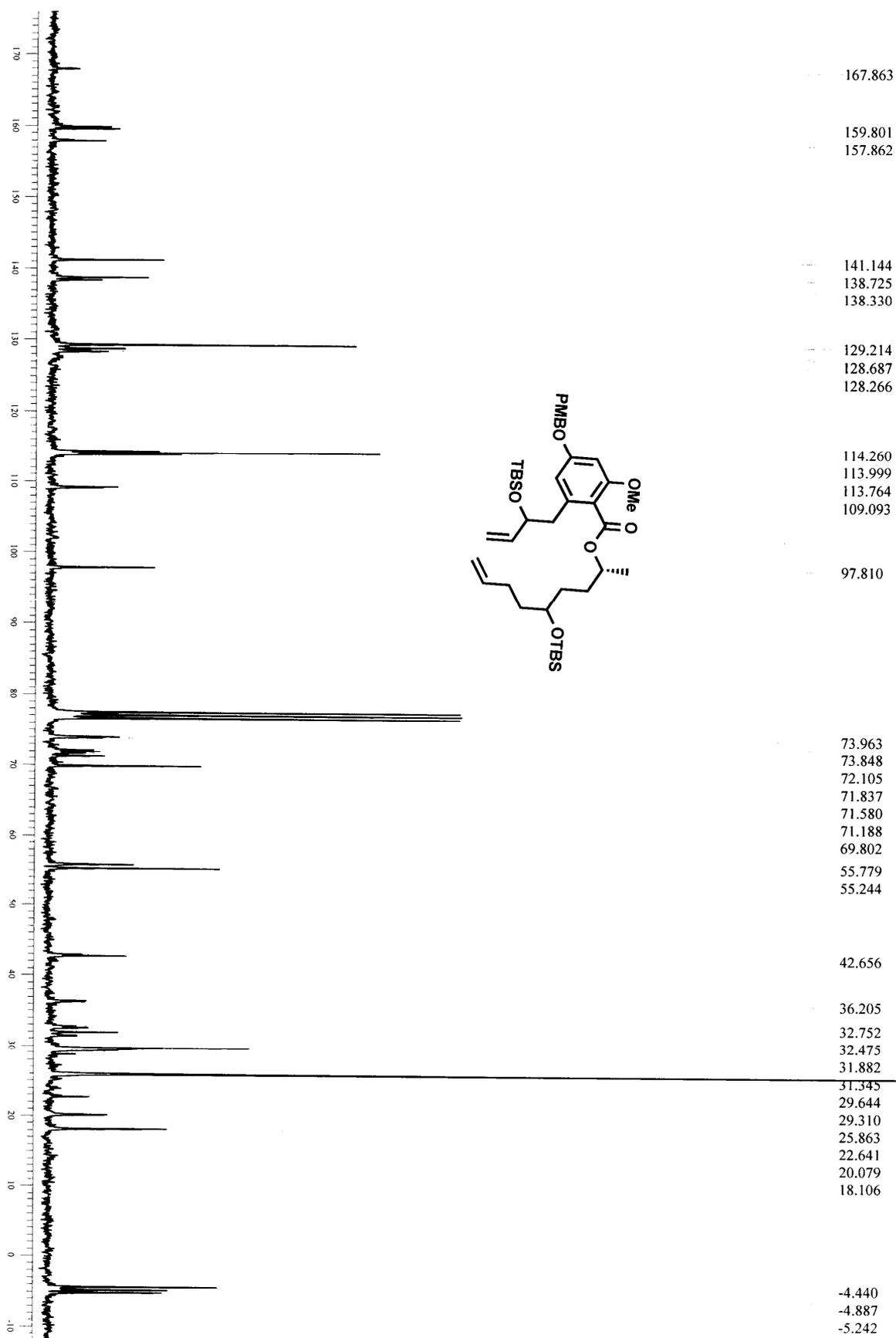


**<sup>1</sup>H NMR of 9 (300 MHz, CDCl<sub>3</sub>)**

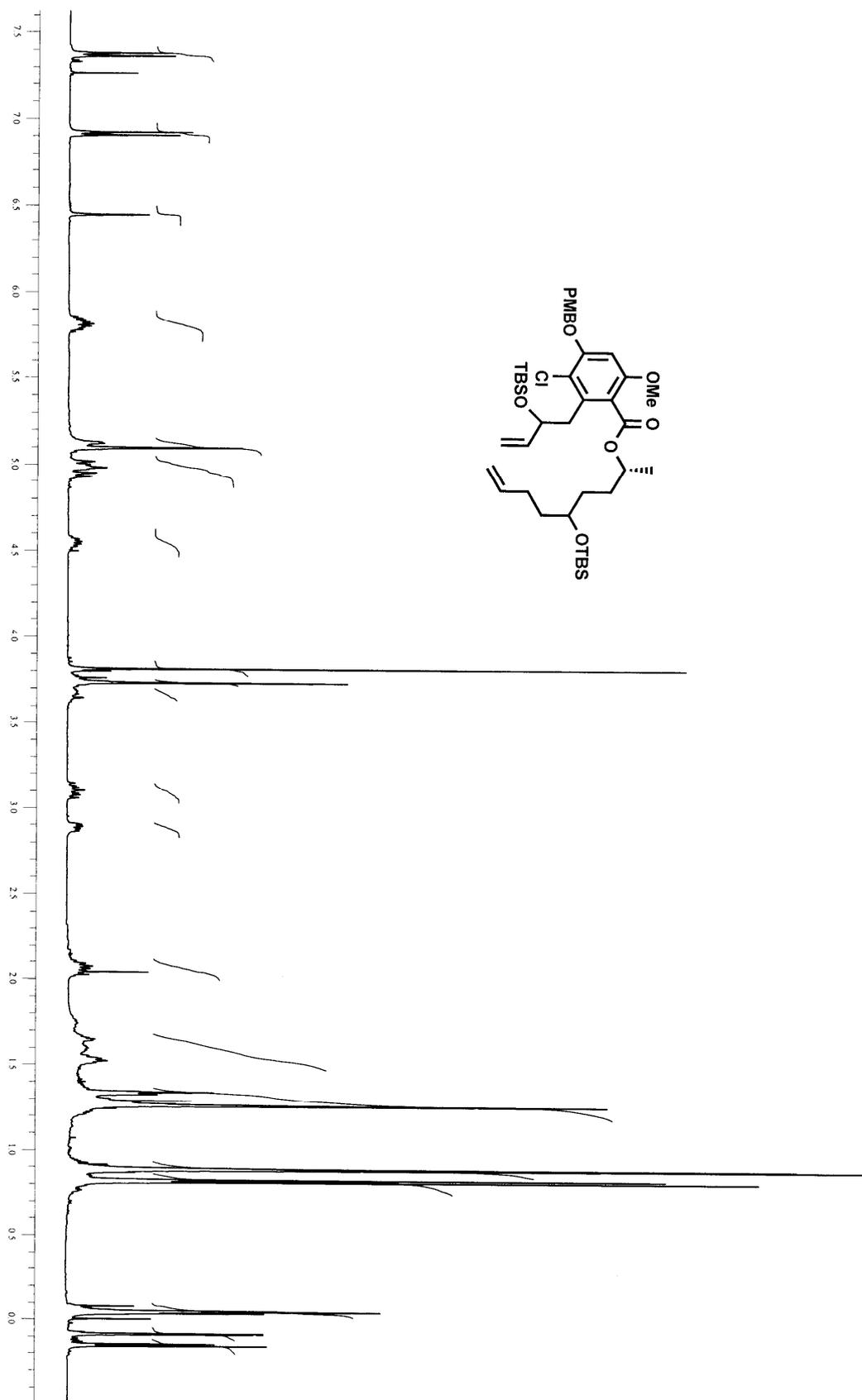




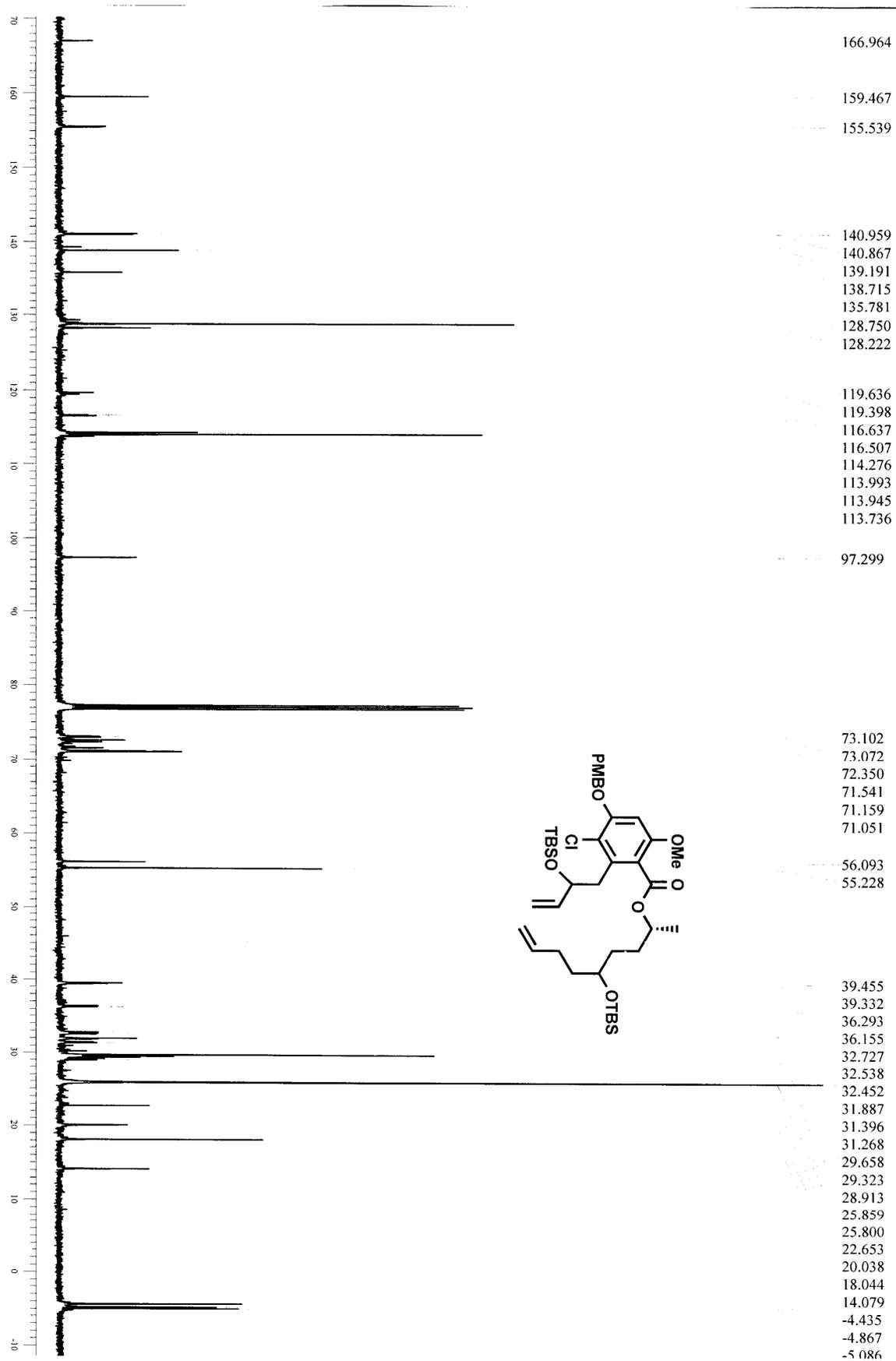
$^1\text{H}$  NMR of 23 (300 MHz,  $\text{CDCl}_3$ )



**<sup>13</sup>C NMR of 23 (75 MHz, CDCl<sub>3</sub>)**



$^1\text{H}$  NMR of 8 (300 MHz,  $\text{CDCl}_3$ )

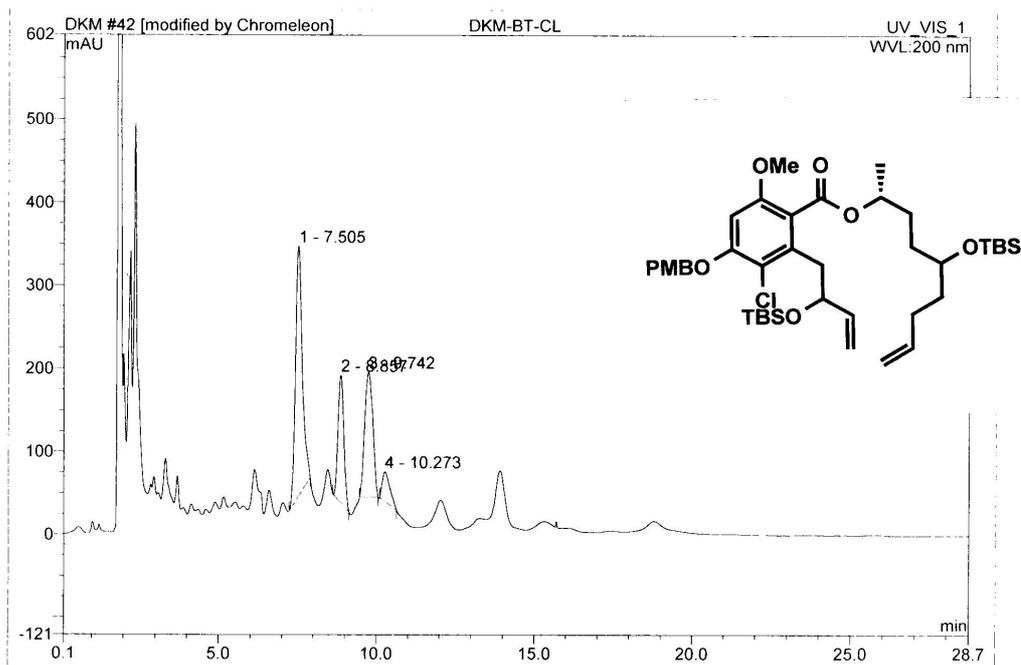


**<sup>13</sup>C NMR of 8 (75 MHz, CDCl<sub>3</sub>)**

Operator: Chromeleon Timebase: ANA\_PUMP Sequence: DKM

Page 1-1  
 12/3/2013 12:14 PM

42 DKM-BT-CL			
WATERS XSELECT 90%ACN IN WATER			
Sample Name:	DKM-BT-CL	Injection Volume:	10.0
Vial Number:	BA2	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	200
Control Program:	DKM	Bandwidth:	10
Quantif. Method:	DKM	Dilution Factor:	1.0000
Recording Time:	12/2/2013 16:57	Sample Weight:	1.0000
Run Time (min):	28.74	Sample Amount:	1.0000

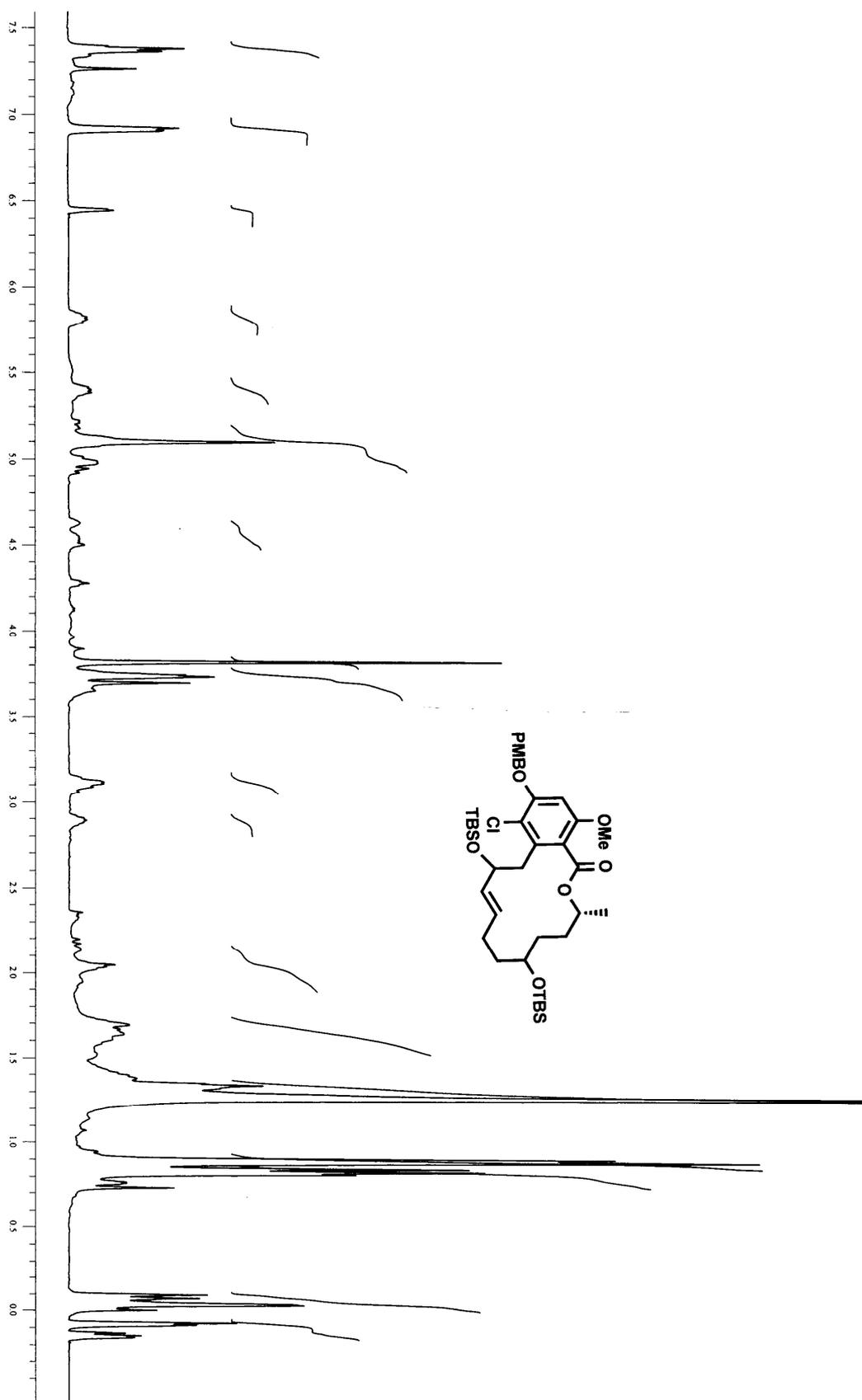


No.	Ret. Time min	Peak Name	Height mAU	Area mAU*min	Rel. Area %	Amount	Type
1	7.51	n.a.	302.099	76.237	46.28	n.a.	BMB*
2	8.86	n.a.	152.758	33.101	20.09	n.a.	BMB*
3	9.74	n.a.	150.534	45.426	27.57	n.a.	BMB*
4	10.27	n.a.	35.459	9.978	6.06	n.a.	BMB*
<b>Total:</b>			640.850	164.742	100.00	0.000	

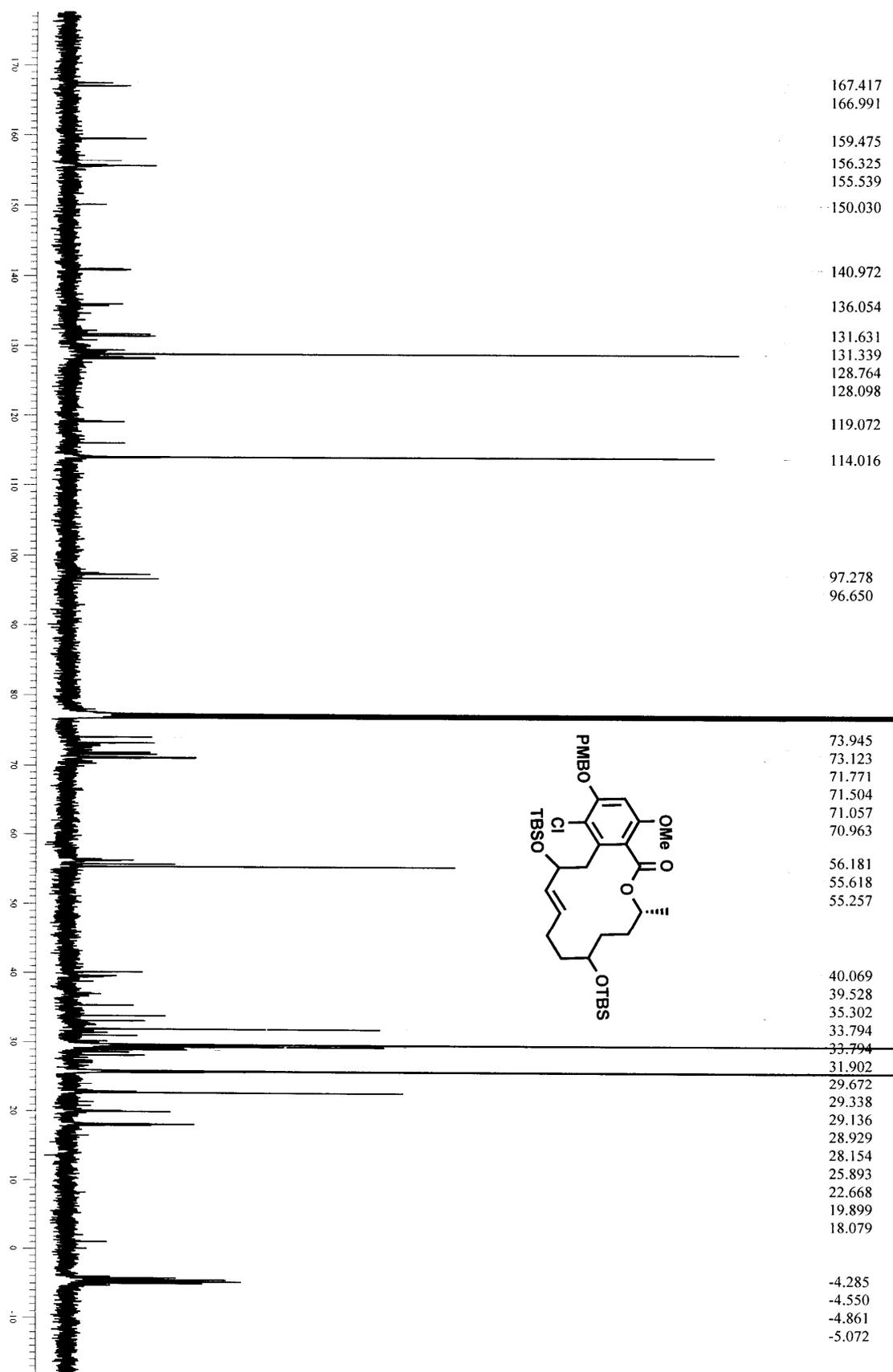
default for print/Integration

Chromeleon (c) Dionex 1996-2006  
 Version 6.80 SR13 Build 3967 (218758)

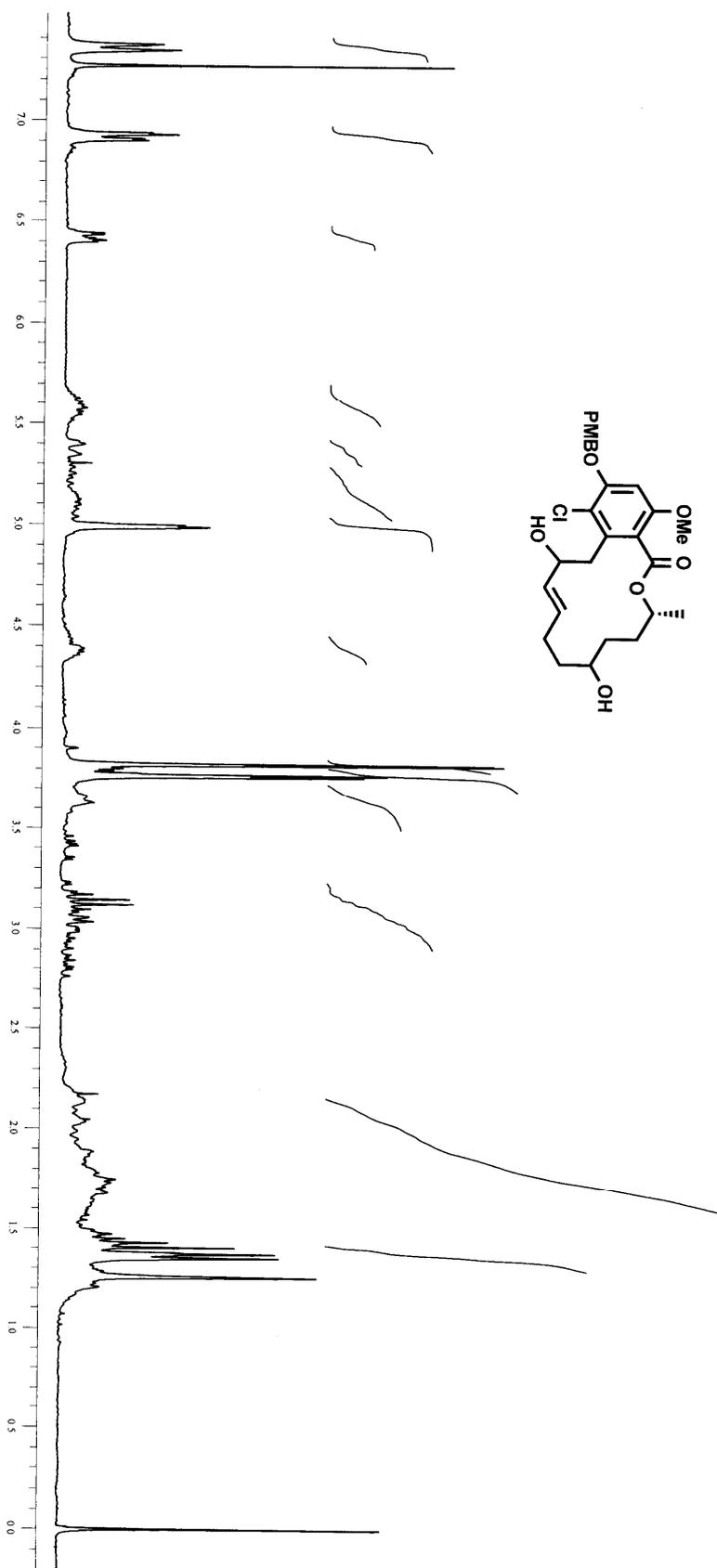
### HPLC Chromatogram of 8



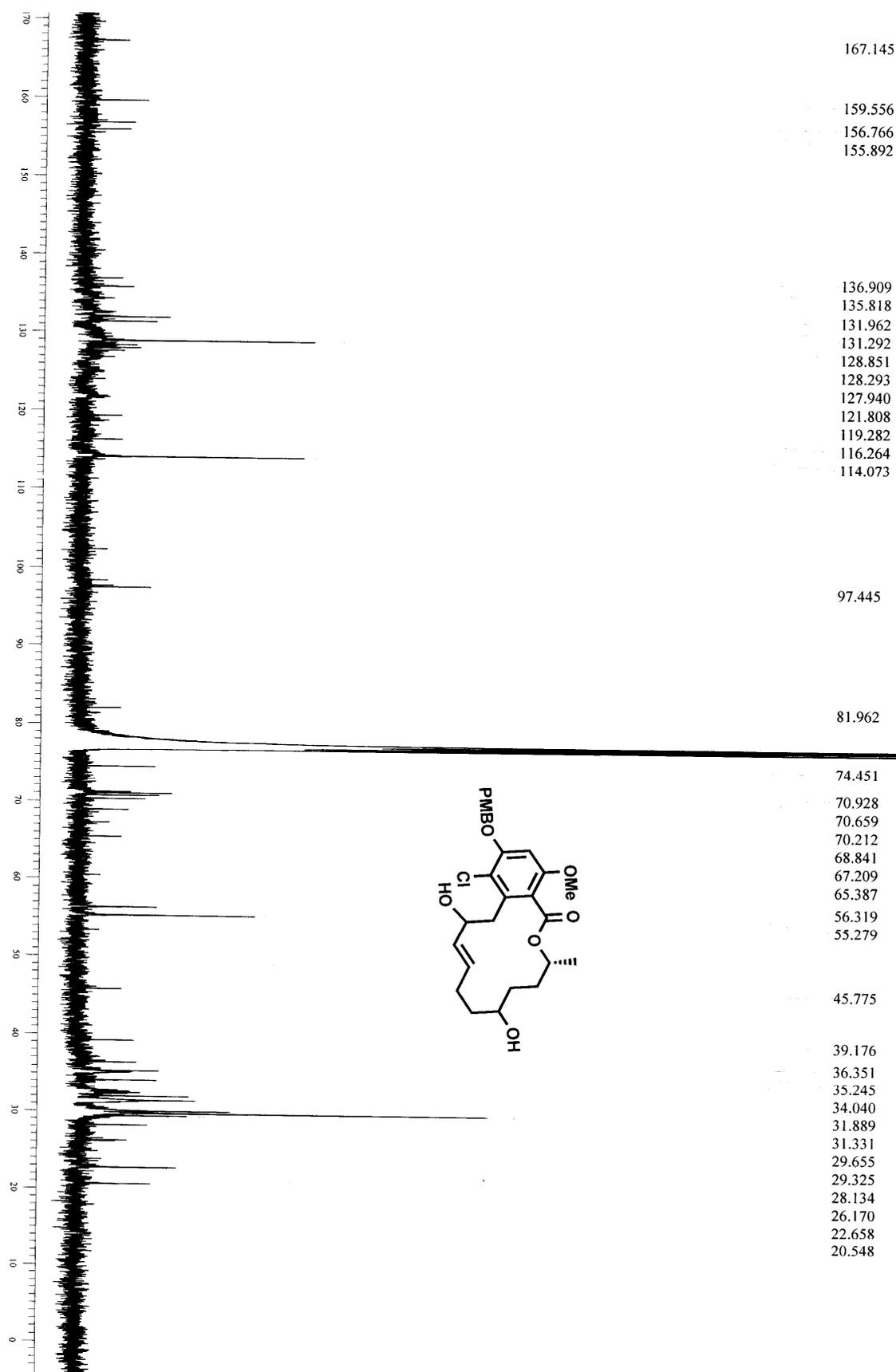
$^1\text{H}$  NMR of 24 (300 MHz,  $\text{CDCl}_3$ )



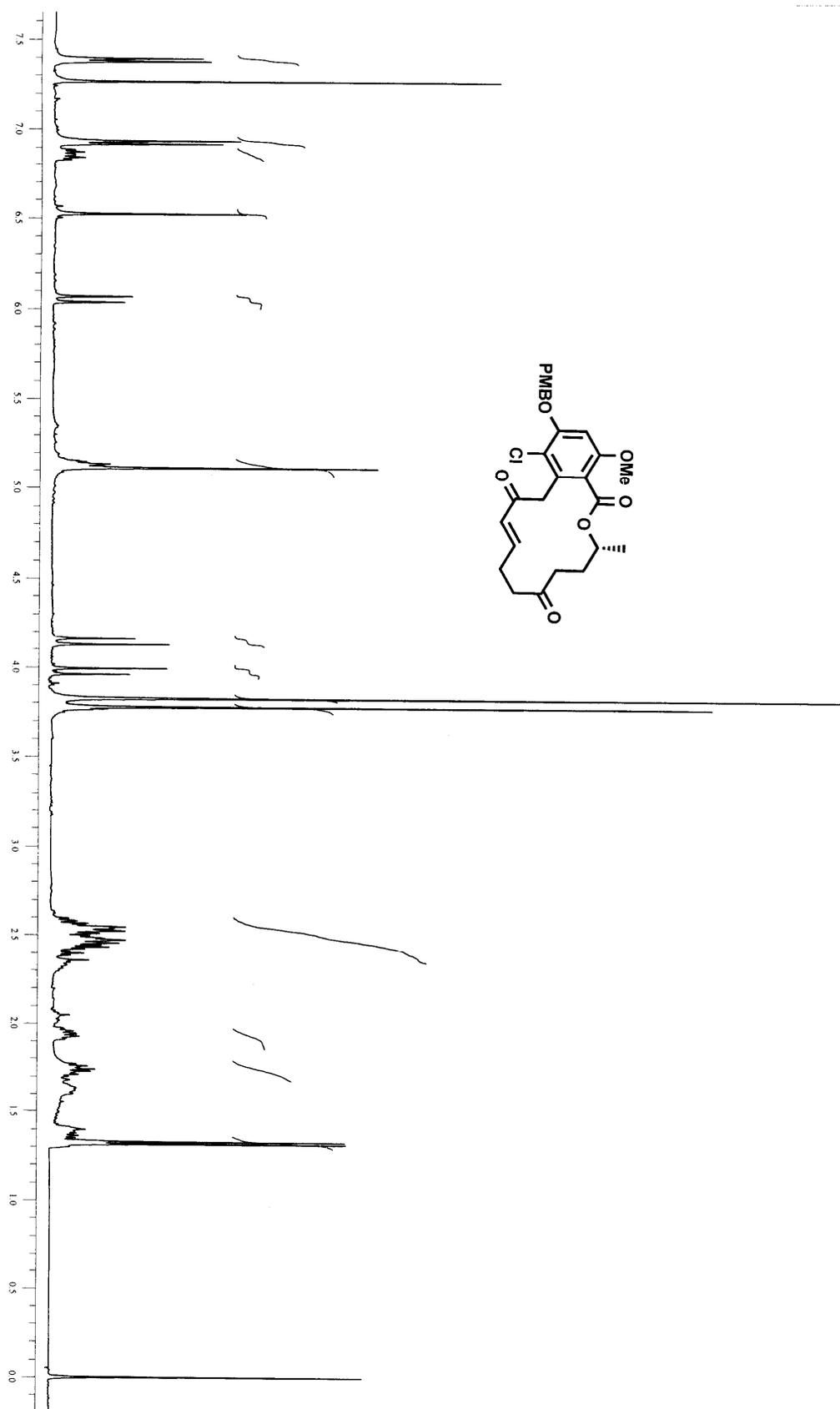
**<sup>13</sup>C NMR of 24 (75 MHz, CDCl<sub>3</sub>)**



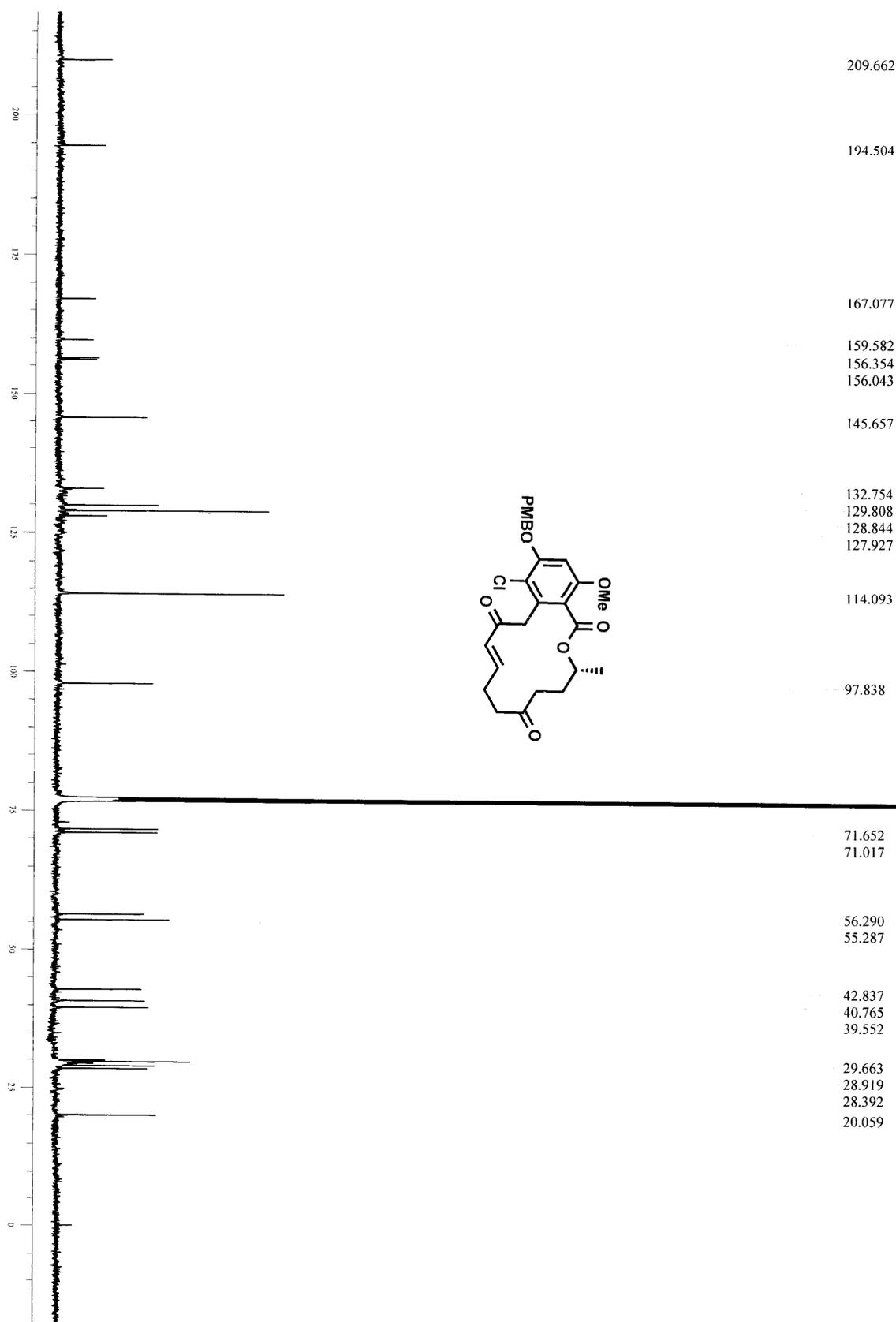
$^1\text{H}$  NMR of 7 (300 MHz,  $\text{CDCl}_3$ )



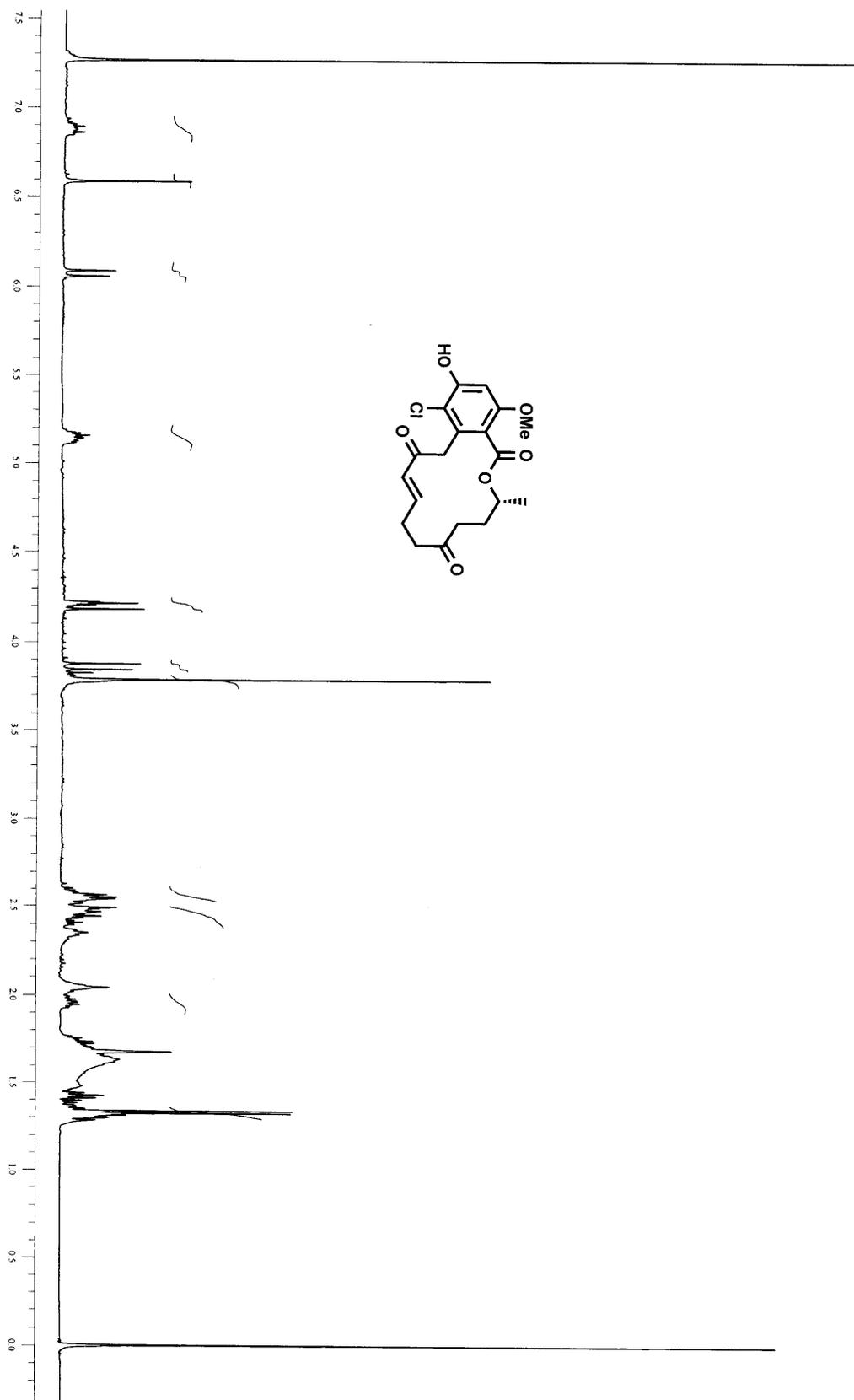
**<sup>13</sup>C NMR of 7 (75 MHz, CDCl<sub>3</sub>)**



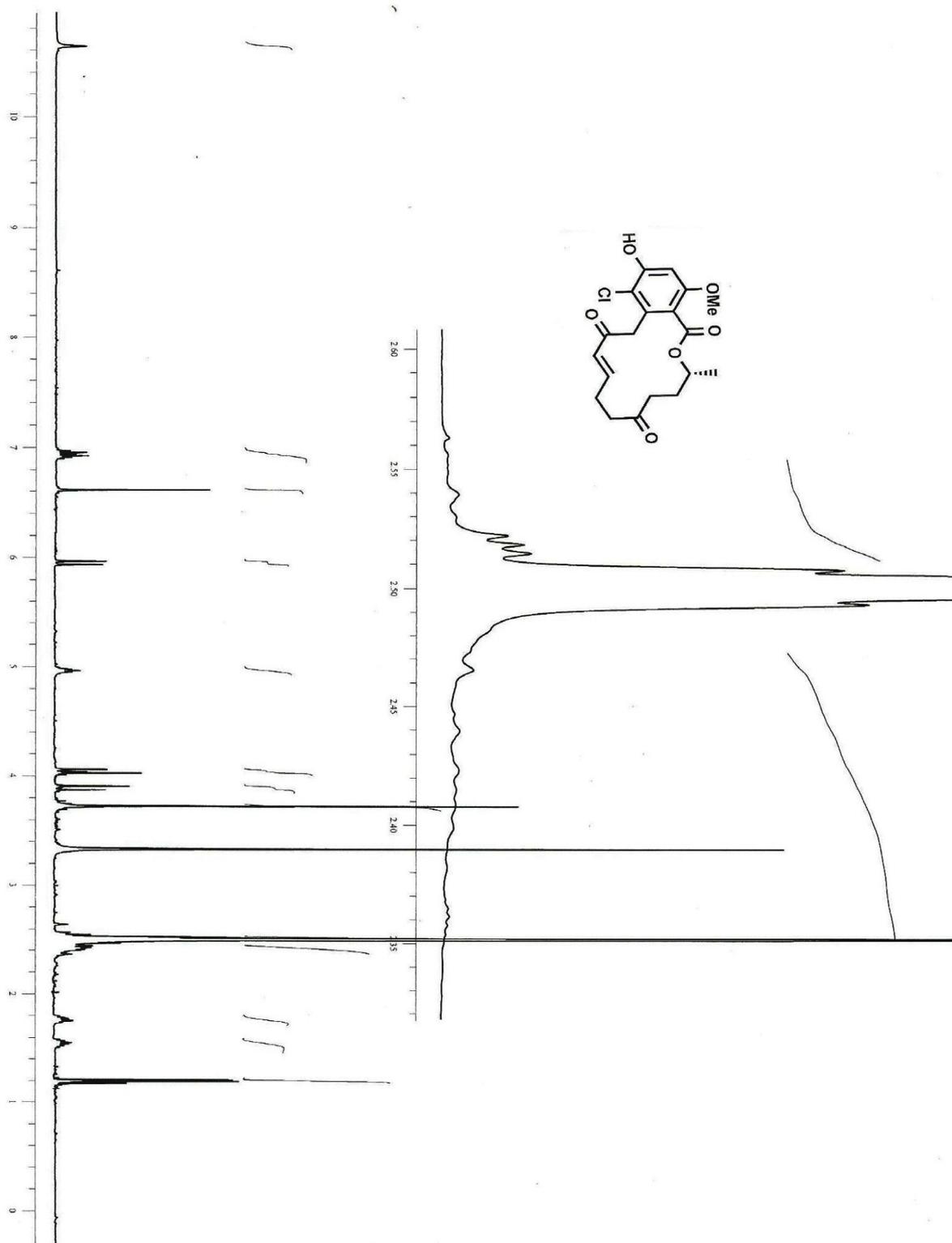
$^1\text{H}$  NMR of 25 (300 MHz,  $\text{CDCl}_3$ )



**<sup>13</sup>C NMR of 25 (75 MHz, CDCl<sub>3</sub>)**

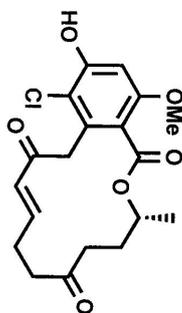
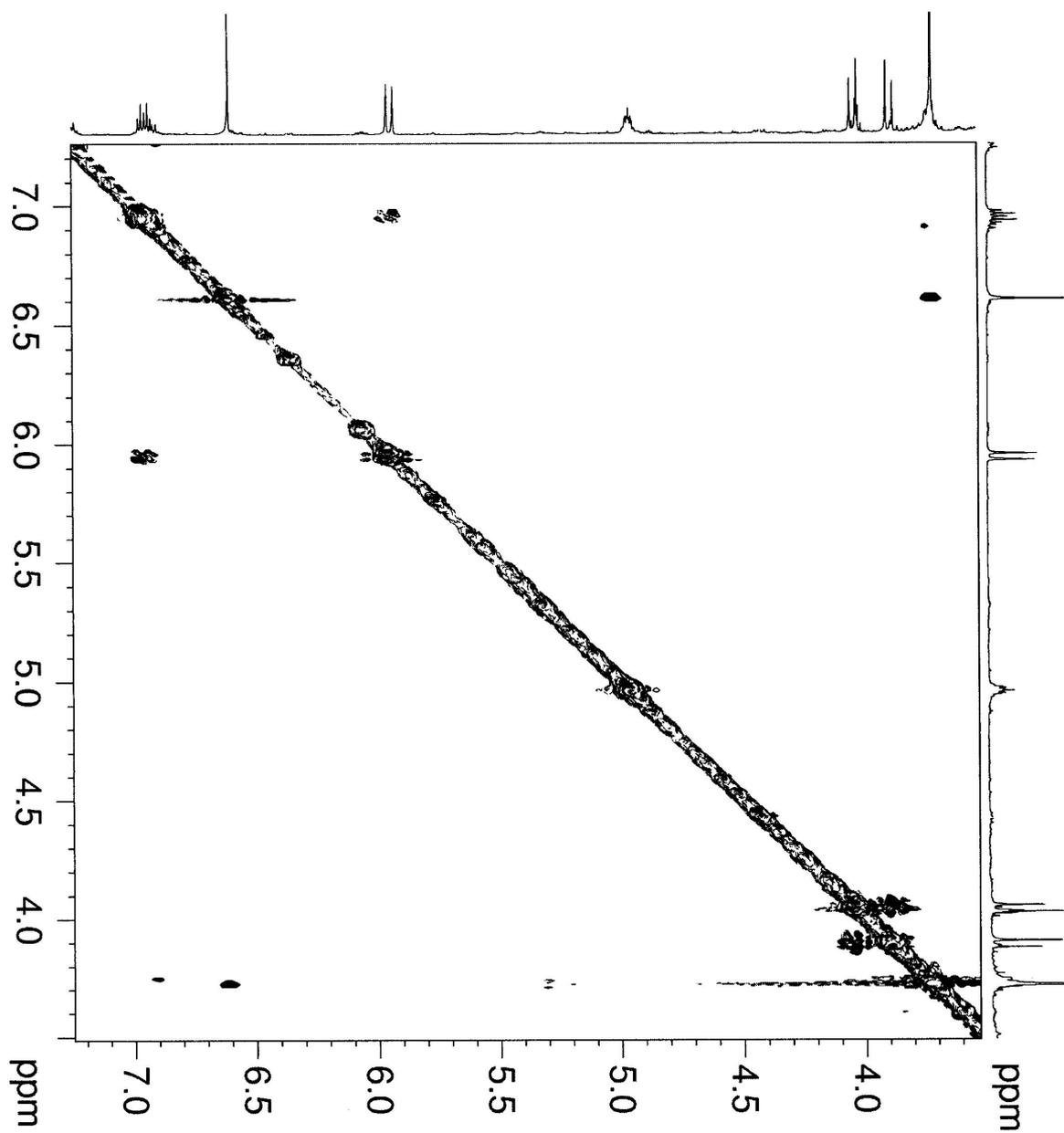


**<sup>1</sup>H NMR of 1 (300 MHz, CDCl<sub>3</sub>)**



$^1\text{H}$  NMR of 1 (300 MHz,  $\text{DMSO-}d_6$ )





NOE of 1 (500 MHz, DMSO d<sub>6</sub>)