



Supporting Information

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## Total Syntheses of Amphidinolide H and G

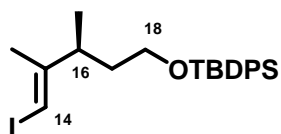
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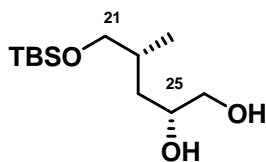
**General.** NMR spectra were recorded with a Bruker DPX 300, AV 400, or DMX 600 spectrometer in the solvents indicated; chemical shifts ( $\delta$ ) are given in ppm relative to TMS, coupling constants ( $J$ ) in Hertz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ( $\text{CDCl}_3$ :  $\delta_{\text{C}} = 77.0$  ppm; residual  $\text{CHCl}_3$  in  $\text{CDCl}_3$ :  $\delta_{\text{H}} = 7.24$  ppm;  $\text{CD}_2\text{Cl}_2$ :  $\delta_{\text{C}} = 53.8$  ppm; residual  $\text{CH}_2\text{Cl}_2$  in  $\text{CD}_2\text{Cl}_2$ :  $\delta_{\text{H}} = 5.32$  ppm). **Where indicated, the signal assignments are unambiguous**; the numbering scheme is arbitrary and is shown in the inserts. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygs* and *cosydqtp*); HSQC (*invietgssi*) optimized for  $^1J(\text{C,H}) = 145$  Hz; HMBC (*inv4gslplrnd*) for correlations via  $^nJ(\text{C,H})$ ; HSQC-TOCSY (*invietgsm1*) using an MLEV17 mixing time of 120 ms. IR: Nicolet FT-7199 spectrometer, wavenumbers ( $\tilde{\nu}$ ) in  $\text{cm}^{-1}$ . MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: Finnigan MAT 95, accurate mass determination: Bruker APEX III FT-MS (7 T magnet).

**Negishi carboalumination: Preparation of vinyl iodide 25.** A solution of  $\text{AlMe}_3$  (2.0 M in heptane, 21.2 mL, 42.4 mmol) was added to a suspension of  $\text{Cp}_2\text{ZrCl}_2$  (4.64 g, 15.9 mmol) in 1,2-dichloroethane (70 mL). After stirring for 0.5 h, a solution of alkyne **24** (3.56 g, 10.57 mmol) in 1,2-dichloroethane (15 mL) was added dropwise. The resulting yellow solution was stirred for 24 h at ambient temperature before the mixture was cooled to  $-20^\circ\text{C}$  and a solution of iodine (16.10 g, 63.5 mmol) in THF (60 mL) was slowly added. After stirring for 20 min at  $-20^\circ\text{C}$  and 30 min at  $0^\circ\text{C}$ , the reaction was carefully quenched with water (10 mL). A sat. aq.  $\text{Na}_2\text{SO}_3$  solution was then added and the layers were separated. The aqueous phase was extracted twice with  $\text{CH}_2\text{Cl}_2$  (40 mL each), the combined organic extracts were washed with brine, dried over  $\text{MgSO}_4$  and evaporated. Purification of the residue by flash chromatography (hexanes:*tert*-butyl methyl ether, 30:1) afforded vinyl iodide **25** as a colorless oil (5.06 g, 94%).  $[\alpha]_{\text{D}}^{20} = +12.8$  ( $c = 0.71$ ,  $\text{CHCl}_3$ ),  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.67\text{--}7.63$  (m, 4H), 7.43–7.36 (m, 6H), 5.91 (br s, 1H), 3.59–3.55 (m, 2H), 2.67 (q,  $J = 9.2$  Hz, 1H), 1.69 (d,  $J = 1.2$  Hz, 3H), 1.64–1.52 (m, 2H), 1.04 (s,



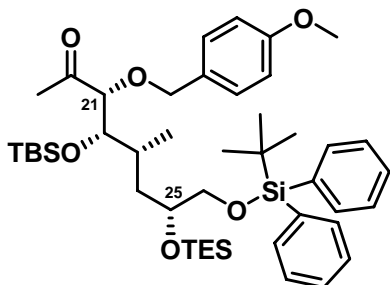
9H), 0.99 (d,  $J = 9.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 151.7, 135.7, 134.0, 129.7, 127.8, 75.4, 61.8, 39.9, 37.7, 27.0, 20.5, 19.6, 19.3$ . IR (film):  $\tilde{\nu} = 3070, 2959, 2930, 1427, 1104, 699$ . HRMS (ESI+):  $m/z$ : calcd for:  $\text{C}_{23}\text{H}_{31}\text{IOSi}+\text{Na}$ : 501.1083; found: 501.1081, ( $\text{M}+\text{Na}^+$ ).

**Regioselective Epoxide Opening: Diol 8.** A solution of DIBAL (1.0 M in hexanes, 123 mL) was added dropwise to a solution of epoxide **7** (7.6 g, 30.84 mmol) in toluene (25 mL) at  $-78^\circ\text{C}$  over the course of 1 h. The temperature was then raised to  $-40^\circ\text{C}$  and stirring continued for 4 h before the reaction was carefully quenched at  $-60^\circ\text{C}$  with a solution of *t*BuOH in THF (1:1, 25 mL). The resulting mixture was poured into an ice-



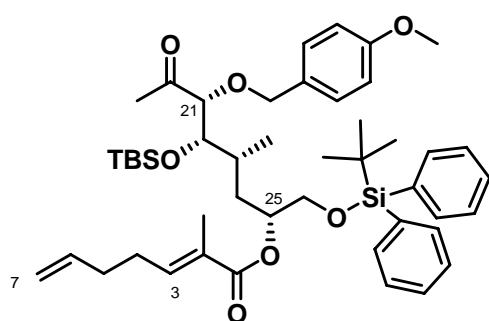
cold solution of Rochelle's salt (85g in 250 mL water) and vigorously stirred for 2 h until a clear separation of the phases was reached. The aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were dried over  $\text{Na}_2\text{SO}_4$  and evaporated, and the residue was purified by flash chromatography (hexanes:EtOAc, 1:1) to give product **8** as a colorless oil.  $[\alpha]_D^{20} = +3.1$  ( $c = 0.43, \text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.79\text{-}3.70$  (m, 1H), 3.59-3.51 (m, 2H), 3.44-3.35 (m, 2H), 1.86-1.74 (m, 1H), 1.48-1.32 (m, 2H), 0.89 (s, 9H), 0.88 (d,  $J = 6.7$  Hz, 3H), 0.06 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 71.1, 69.5, 67.5, 39.4, 34.2, 26.0, 18.4, 18.0,  $-5.3, -5.4$ . IR (film):  $\tilde{\nu} = 3350, 2929, 2857, 1471, 1251, 1077, 832, 773$ . HRMS (ESI+):  $m/z$ : calcd for:  $\text{C}_{12}\text{H}_{28}\text{O}_3\text{Si}+\text{Na}$ : 271.1699; found: 271.1698 ( $\text{M}+\text{Na}^+$ ).

**Methyl ketone 15.** MeLi (1.6 M in  $\text{Et}_2\text{O}$ , 10.9 mL, 17.6 mmol) was added to a suspension of CuI (1.7 g, 8.79 mmol) in  $\text{Et}_2\text{O}$  (7.0 mL) at  $-20^\circ\text{C}$ . After stirring for 35 min, the resulting colorless solution was cooled to  $-60^\circ\text{C}$  before a solution of thioester **14** (1.2 g, 1.43 mmol) in  $\text{Et}_2\text{O}$  (5 mL) was slowly added *via* cannula. Once the addition was complete, the mixture was allowed to slowly warm to  $-20^\circ\text{C}$  over a period of 2 h. The reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) at  $-10^\circ\text{C}$ , the resulting mixture warmed to ambient temperature and stirred



for 1 h. The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 10 mL), the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and evaporated, and the crude product purified by flash chromatography, (hexanes:EtOAc, 9:1) to give ketone **15** as a colorless oil (1.0 g, 89%).  $[\alpha]_D^{20} = +35.5$  ( $c = 0.5, \text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.57$  (m, 4H), 7.37-7.27 (m, 6H), 7.16 (d,  $J = 8.4$  Hz, 2H), 6.78 (d,  $J = 8.4$  Hz, 2H), 4.37 (d,  $J = 11.2$  Hz, 1H), 4.26 (d,  $J = 11.3$  Hz, 1H), 3.73 (br.s, 3H), 3.68 (m, 1H), 3.63 (d,  $J = 7$  Hz, 1H), 3.56 (m, 1H), 3.48 (dd,  $J = 9.8, 4.5$  Hz, 1H), 3.30 (dd,  $J = 9.8, 8.1$  Hz, 1H), 2.0 (s, 3H), 1.82 (tdd,  $J = 11.4, 2.01, 1.8$  Hz, 1H), 1.52 (m, 1H), 1.26 (tdd,  $J = 11.4, 2.5, 1.5$  Hz, 1H), 0.97 (s, 9H), 0.81 (s, 9H), 0.79 (d,  $J = 6.7$  Hz, 3H), 0.71 (t,  $J = 7.8$  Hz, 9H), 0.33 (q,  $J = 7.8$  Hz, 6H),  $-0.01$  (s, 3H),  $-0.06$  (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 209.6, 158.9, 135.3, 135.2, 133.2, 129.3, 129.3, 129.2, 127.2, 113.3, 89.9, 77.5, 72.2, 70.0, 67.8, 54.9, 40.7, 31.0, 26.5, 26.0, 25.8, 25.4, 18.8, 18.1, 11.8, 6.4, 4.5, -4.1, -4.9$ . IR (film):  $\tilde{\nu} = 2954, 2858, 1715, 1613, 1515, 1462, 1428, 1388, 1249, 1111, 1037, 1066, 832, 777, 739, 702\text{ cm}^{-1}$ ; HRMS (ESI+):  $m/z$ : calcd for:  $\text{C}_{45}\text{H}_{72}\text{O}_3\text{Si}_5+\text{Na}$ : 815.45290; found: 815.45302 ( $\text{M}+\text{Na}^+$ ).

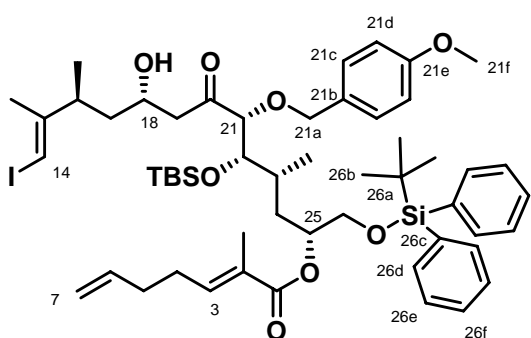
**Methyl ketone 17.** A solution of pyridinium *p*-toluenesulfonate (251 mg, 1 mmol) and **15** (1g,



1.26 mmol) in EtOH (3 mL) was stirred for 1 h before the reaction was quenched with a sat. aq. NaHCO<sub>3</sub> (5 mL). A standard extractive work up followed by flash chromatography (hexanes:*tert*-butyl methyl ether, 12:1) of the crude product gave the TES-deprotected alcohol as a colorless oil (480 mg, 56%).

DCC (365 mg, 1.77 mmol) was added to a solution of this alcohol (480 mg, 0.70 mmol) and DMAP (72 mg, 0.59 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) at 0°C. The mixture was stirred for 30 min before acid **16** (393 mg, 2.8 mmol) was introduced and stirring continued for 12 h. For work up, all volatile materials were evaporated, the product adsorbed on silica and purified by flash chromatography (hexanes:*tert*-butyl methyl ether, 12:1) to give product **17** as a colorless oil (405 mg, 75%).  $[\alpha]_D^{20} = +11.5$  ( $c = 0.5$ , CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 7.63$  (m, 4H), 7.43-7.32 (m, 6H), 7.20 (d,  $J = 8.4$  Hz, 2H), 6.82 (d,  $J = 8.4$  Hz, 2H), 6.75 (td,  $J = 6.9$ , 1.3 Hz, 1H), 5.82 (ddt,  $J = 17.3$ , 10.4, 6.6 Hz, 1H), 5.10 (m, 1H), 5.03 (ddt,  $J = 17.1$ , 1.8, 1.4 Hz, 1H), 4.98 (ddt,  $J = 10.4$ , 1.4, 1.2 Hz, 1H), 4.38 (d,  $J = 11.6$  Hz, 1H), 3.78 (br.s, 5H), 3.72 (d,  $J = 5.7$  Hz, 1H), 3.66 (d,  $J = 4.8$  Hz, 2H), 2.25 (td,  $J = 7.2$ , 6.9 Hz, 2H), 2.18 (td,  $J = 6.8$ , 6.61 Hz, 2H), 2.09 (s, 3H), 1.94 (3d,  $J = 14.2$ , 9.8, 4.2 Hz, 1H), 1.82 (s(d),  $J = 1.0$  Hz, 3H), 1.59 (m, 2H), 1.01 (s, 9H), 0.87 (s, 9H), 0.86 (d,  $J = 6.7$  Hz, 3H), 0.02 (s, 3H), -0.03 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 210.1$ ; 167.3, 159.0, 141.9, 137.2, 135.2, 133.0, 129.3, 129.0, 127.8, 127.3, 114.9, 113.4, 87.6, 76.6, 72.1, 71.8, 65.4, 54.9, 34.5, 32.5, 32.1, 27.8, 26.8, 26.3, 25.6, 18.83, 18.0, 13.4, 12.1, -4.5, -5.0. IR (film):  $\tilde{\nu} = 3072$ , 2955, 2930, 2857, 1710, 1648, 1613, 1514, 1471, 1462, 1462, 1388, 1249, 1111, 1035, 913, 834, 740 cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>):  $m/z$ : calcd for: C<sub>47</sub>H<sub>68</sub>O<sub>7</sub>Si<sub>2</sub>+Na: 823.4396; found: 823.4398 (M+Na<sup>+</sup>).

**Aldol adduct 42.** A solution of LDA (1 M in THF, 0.19 mL, 0.16 mmol) was added to a

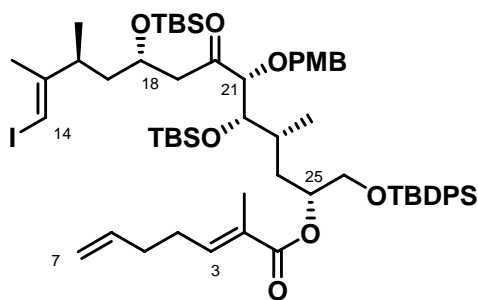


solution of methyl ketone **17** (100 mg, 0.13 mmol) in THF (0.5 mL) at -78°C. After stirring for 2 h, a pre-cooled solution of vinyl aldehyde **26** (40 mg, 0.17 mmol) was added via cannula at -78°C. Stirring was continued for 45 min at this temperature before the reaction was quenched with aq. buffer (pH = 7, 10 mL). The mixture was extracted with EtOAc (3 x 5 mL), the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and

evaporated. Purification of the residue by flash chromatography (hexanes:*tert*-butyl methyl ether, 4:1) gave aldol **42** as a colorless oil (90 mg, 70%, *dr* >10:1).  $[\alpha]_D^{20} = +5$  ( $c = 0.2$ , CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta = 7.78$  (m, 4H, H26d), 7.26 (m, 6H, H26e, H26f), 7.18 (d,  $J = 8.5$  Hz, 2H, H21c), 6.98 (tq,  $J = 7.3$ , 1.4 Hz, 1H, H3), 6.75 (d,  $J = 8.5$  Hz, 2H, H21d), 5.86 (s(q),  $J = 0.8$ , 1H, H14), 5.69 (ddt,  $J = 17.0$ , 10.4, 6.3 Hz, 1H, H6), 5.43 (m, 1H, H25), 4.98 (ddt,  $J = 17.7$ , 1.7, 1.6 Hz, 1H, H7<sub>Z</sub>), 4.95 (ddt,  $J = 10.2$ , 1.8, 1.2 Hz, 1H, H7<sub>E</sub>), 4.29 (d,  $J = 11.2$  Hz, 1H, H21a), 4.24 (d,  $J = 11.2$  Hz, 1H, H21a'), 4.08 (m, 1H, H18), 4.01 (dd,  $J = 6.1$ , 3.2 Hz, 1H, H22), 3.82 (dd,  $J = 10.8$ , 4.2 Hz, 1H, H26a), 3.82 (d,  $J = 6.1$  Hz, 1H, H21), 3.79

(dd,  $J = 10.8, 5.5$  Hz, 1H, H26b), 3.26 (s, 3H, H21f), 2.86 (d,  $J = 3.3$  Hz, 1H, OH), 2.71 (dd,  $J = 18.2, 9.2$  Hz, 1H, H19a), 2.61 (ddq,  $J = 9.2, 6.8, 5.5$  Hz, 1H, H16), 2.51 (dd,  $J = 18.2, 2.4$  Hz, 1H, H19b), 2.14 (3d,  $J = 14.2, 9.8, 4.2$  Hz, 1H, H24a), 2.06 (m, 2H, H4), 2.01 (m, 2H, H5), 1.90 (s, 3H, H27), 1.86 (m, 1H, H23), 1.68 (s(d),  $J = 1.0$  Hz, 3H, H30), 1.68 (3d,  $J = 14.2, 9.3, 3.4$  Hz, 1H, H24b) 1.52 (3d,  $J = 13.7, 9.5, 5.5$  Hz, 1H, H17a), 1.16 (s, 9H, H26b), 1.11 (3d,  $J = 13.6, 9.2, 3.6$  Hz, 1H, H17b), 1.06 (d,  $J = 6.7$  Hz, 3H, H32), 0.99 (s, 9H, H22b), 0.90 (d,  $J = 6.8$  Hz, 3H, H31), 0.12 (s, 3H, H22c), 0.15 (s, 3H, H22d);  $^{13}\text{C}$  NMR (100 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta = 212.8$  (s, C20), 167.6 (s, C1), 160.1 (s, C21e), 152.7 (s, C15), 141.6 (d, C3), 137.7 (d, C6), 136.0 (d, C26d), 135.9 (d, C26e), 133.8 (2s, C26c), 130.0 (d, C21d), 129.6 (s, C21b), 128.7 (s, C2), 115.4 (t, C7), 114.2 (d, C21d), 88.0 (d, 21), 77.0 (d, C22), 75.6 (d, C14), 73.0 (t, C21a), 72.9 (d, C25), 66.4 (t, C26), 65.2 (d, C18), 54.8 (q, C21f), 47.2 (t, C19), 42.2 (t, C17), 39.5 (d, C16), 35.4 (t, C24), 33.8 (d, C23), 32.8 (t, C5), 28.4 (t, C4), 27.0 (q, C26b), 26.4 (q, C22b), 21.3 (q, C30), 19.5 (s, C26a), 18.6 (s, C22a), 18.5 (q, C31), 14.6 (q, C32), 12.8 (q, C27),  $-3.7$  (q, C22c),  $-4.3$  (q, C22d); IR (film)  $\tilde{\nu} = 3480, 2930, 2857, 1708, 1613, 1514, 1462, 1428, 1388, 1250, 1115, 1036, 834, 777, 741, 702$   $\text{cm}^{-1}$ ; HRMS (ESI<sup>+</sup>):  $m/z$ : calcd for:  $\text{C}_{54}\text{H}_{79}\text{O}_8\text{Si}_2\text{I}+\text{Na}$ : 1061.42504; found: 1061.42498 ( $\text{M}+\text{Na}^+$ ).

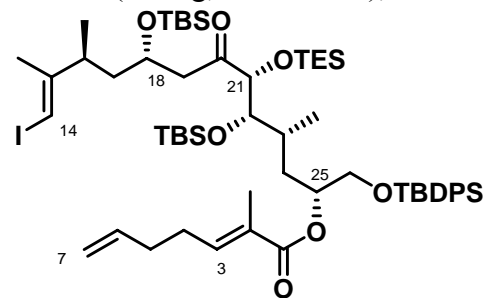
**Compound 43.** A precooled solution of TBSOTf (39.6 mg, 34.5  $\mu\text{L}$ , 0.15 mmol) and 2,6-lutidine (27.8 mg, 31  $\mu\text{L}$ , 0.26 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.5 mL) was added to a solution of **42** (130 mg, 0.13 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.8 mL) at  $0^\circ\text{C}$  and the resulting mixture was slowly warmed to ambient temperature. After stirring for 1 h, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (5 mL), the mixture extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL), and the combined organic phases were dried over  $\text{Na}_2\text{SO}_4$  and evaporated.



Purification of the residue by flash chromatography (hexanes:*tert*-butyl methyl ether, 11:1) gave product **43** as a light yellow oil (112 mg, 79%).  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta = 7.78$  (m, 4H), 7.31 (d,  $J = 8.2$  Hz, 2H), 7.24 (m, 6H), 6.99 (tq,  $J = 7.1, 1.4$  Hz, 1H), 6.78 (d,  $J = 8.5$  Hz, 2H), 6.06 (s, 1H), 5.71 (ddt,  $J = 17.0, 10.7, 6.2$  Hz, 1H), 5.43 (m, 1H), 4.97 (m, 2H), 4.55 (d,  $J = 11.1$  Hz, 1H), 4.39 (m, 1H), 4.29 (d,  $J = 10.9$  Hz, 1H), 4.04 (dd,  $J = 10.8, 3.3$  Hz, 1H), 3.89 (d,  $J = 5.8$  Hz, 1H), 3.81 (dd,  $J = 10.8, 5.5$  Hz, 1H), 3.27 (s, 3H), 3.26 (m, 1H), 3.25 (m, 1H), 2.59 (dd,  $J = 18.2, 7.7$  Hz, 1H), 2.54 (ddq,  $J = 9.8, 6.7, 5.5$  Hz, 1H), 2.15 (m, 1H), 2.09 (m, 2H), 2.01 (m, 2H), 1.92 (s(d),  $J = 1.3$  Hz, 3H), 1.76 (s(d),  $J = 1.01$  Hz, 3H), 1.74 (m, 1H), 1.68-1.65 (m, 2H), 1.17 (s, 9H), 1.08 (d,  $J = 6.8$  Hz, 3H), 1.0 (s, 9H), 0.99 (d,  $J = 6.8$  Hz, 3H), 0.93 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.05 (s, 3H); IR (film)  $\tilde{\nu} = 2926, 2855, 1713, 1613, 1515, 1462, 1428, 1361, 1250, 1112, 1084, 1039, 1005, 914, 834, 775, 701$   $\text{cm}^{-1}$ .

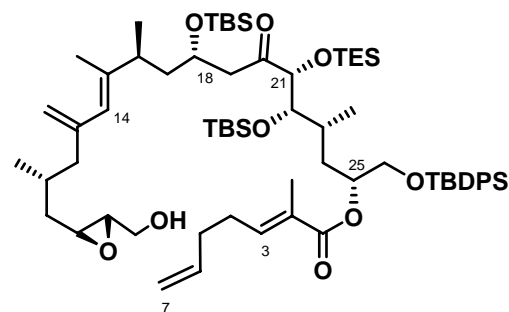
**Compound 44.** DDQ (66 mg, 0.29 mmol) was added to a solution of **43** (110 mg, 97  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (2 mL). After stirring for 2 h, the reaction was quenched with sat. aq.  $\text{NaHCO}_3$  (5 mL) / ice, the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL), and the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and evaporated. Purification of the residue by flash chromatography (hexanes:*tert*-butyl methyl ether, 9:1) gave the corresponding alcohol as a colorless oil (61 mg, 62%).

DMAP (13 mg, 0.10 mmol), imidazole (21.8 mg, 0.32 mmol) and TESCOI (48.2 mg, 53  $\mu$ L, 0.32 mmol) were added to a solution of this alcohol (100 mg, 96.8  $\mu$ mol) in DMF (4 mL) and the resulting mixture was stirred at 45°C for 3 d. The reaction was quenched with sat. aq. NH<sub>4</sub>Cl (20 mL), the aqueous phase extracted with EtOAc (4 x 10 mL), the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated, and the residue was purified by flash chromatography (hexanes:*tert*-butyl methyl ether,



20:1) to give product **44** as a colorless oil (86 mg, 79%). <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  = 7.81 (m, 4H), 7.26 (m, 6H), 7.01 (tq,  $J$  = 7.1, 1.5 Hz, 1H), 6.01 (s, 1H), 5.71 (ddt,  $J$  = 16.7, 10.8, 6.6 Hz, 1H), 5.50 (m, 1H), 4.97 (m, 2H), 4.36 (m, 1H), 4.30 (d,  $J$  = 4.6 Hz, 1H), 3.89 (m, 3H), 3.09 (dd,  $J$  = 18.4, 4.5 Hz, 1H), 2.74 (dd,  $J$  = 18.4, 7.6 Hz, 1H), 2.64 (m, 1H), 2.12-2.06 (m, 5H), 1.94 (s, 3H), 1.76 (s(d),  $J$  = 1.0 Hz, 3H), 1.67 (m, 1H), 1.57 (m, 2H), 1.19 (s, 9H), 1.0 (s, 9H), 0.99 (d,  $J$  = 6.8 Hz, 3H), 0.97 (d,  $J$  = 6.8 Hz, 3H), 0.93 (s, 9H), 0.89 (t,  $J$  = 7.8 Hz, 9H), 0.56 (q,  $J$  = 7.8 Hz, 6H), 0.19 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.09 (s, 3H).

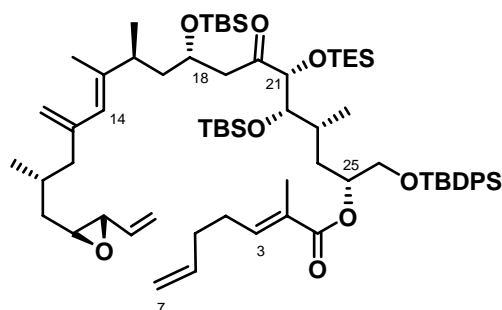
**Stille Coupling: Compound 45.** A degassed solution of stannane **34** (51 mg, 113  $\mu$ mol) and vinyl iodide **44** (65 mg, 57  $\mu$ mol) in DMF (0.6 mL) was added to a Schlenk tube containing flame-dried [Ph<sub>2</sub>PO<sub>2</sub>]<sup>-</sup>[NBu<sub>4</sub>]<sup>+</sup> (105 mg, 230  $\mu$ mol). Copperthiophene carboxylate complex (CuTC, 33 mg, 170  $\mu$ mol) was then introduced followed by Pd(PPh<sub>3</sub>)<sub>4</sub> (46 mg, 40  $\mu$ mol). The resulting mixture was stirred for 30 min before the reaction was quenched with water (1 mL). The aqueous phase was extracted with Et<sub>2</sub>O (2 x 2 mL), the combined organic layers were



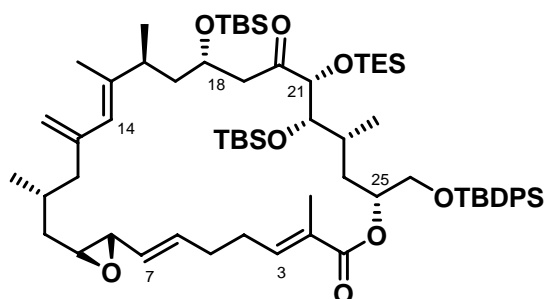
dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated, and the residue was purified by flash chromatography (hexanes:*tert*-butyl methyl ether, 4:1) to afford product **45** as a pale yellow oil (58.6 mg, 89%). [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +12.3 ( $c$  = 0.4, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  = 7.81 (tt,  $J$  = 1.8, 6.6 Hz, 4H), 7.26 (m, 6H), 7.01 (tq,  $J$  = 7.4, 1.1 Hz, 1H), 5.78 (s, 1H), 5.70 (ddt,  $J$  = 16.9, 10.3, 6.4 Hz, 1H), 5.53 (m, 1H), 5.02 (ddt,  $J$  = 17.7, 1.7, 1.4 Hz, 1H), 4.98 (ddt,  $J$  = 11.0, 1.8, 1.2 Hz, 1H), 4.96 (s, 1H), 4.94 (s, 1H), 4.42 (m, 1H), 4.34 (d,  $J$  = 4.6 Hz, 1H), 3.96 (dd,  $J$  = 4.5, 4.3 Hz, 1H), 3.89 (dd,  $J$  = 10.7, 5.5 Hz, 2H), 3.51 (ddd,  $J$  = 12.1, 5.4, 2.9 Hz, 1H), 3.34 (ddd,  $J$  = 12.3, 6.8, 4.7 Hz, 1H), 3.15 (dd,  $J$  = 17.7, 5.2 Hz, 1H), 2.85 (dd,  $J$  = 18.2, 7.2 Hz, 1H), 2.81 (ddd,  $J$  = 7.2, 6.4, 2.1 Hz, 1H), 2.58 (ddd,  $J$  = 7.2, 6.7, 2.7 Hz, 1H), 2.52 (dq,  $J$  = 13.8, 6.7 Hz, 1H), 2.16 (m, 1H), 2.14 (m, 1H), 2.08 (m, 3H), 2.04 (m, 2H), 1.94 (s(d),  $J$  = 0.9 Hz, 3H), 1.94 (m, 1H), 1.84 (s(d),  $J$  = 1.3 Hz, 3H), 1.81 (m, 1H), 1.78 (m, 1H), 1.71 (m, 1H), 1.55 (m, 1H), 1.36 (ddd,  $J$  = 13.2, 8.4, 4.0 Hz, 1H), 1.18 (s, 9H), 1.10 (m, 1H), 1.08 (d,  $J$  = 6.7 Hz, 3H), 1.06 (d,  $J$  = 6.8 Hz, 3H), 1.03 (s, 9H), 1.02 (s, 9H), 0.89 (t,  $J$  = 7.8 Hz, 9H), 0.86 (d,  $J$  = 6.7 Hz, 3H), 0.7 (q,  $J$  = 7.8 Hz, 6H), 0.45 (s, 3H), 0.20 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H); <sup>13</sup>C NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  = 208.1, 167.5, 144.8, 143.2, 141.4, 137.8, 136.0, 135.9, 133.8, 129.9, 125.6, 115.3, 114.9, 81.8, 78.6, 72.5, 66.9, 66.3, 62.0, 58.8, 54.3, 48.7, 46.3, 39.8, 39.0, 35.8, 32.9, 32.4, 30.2, 30.0, 29.6, 28.4, 28.3, 28.2, 28.1, 26.0, 26.6, 26.3, 22.7, 19.7, 19.5, 19.4, 18.5, 18.4,

18.3, 18.2, 17.3, 16.3, 16.2, 16.1, 15.6, 15.0, 13.9, 13.7, 12.9, 10.0, 7.2, 5.4, -3.8, -4.1, -4.3, -4.5; IR (film)  $\tilde{\nu}$  = 3390, 2927, 2876, 1711, 1608, 1514, 1462, 1425, 1390, 1252, 11125, 834, 702, 691  $\text{cm}^{-1}$ ; HRMS (ESI<sup>+</sup>):  $m/z$ : calcd for:  $\text{C}_{67}\text{H}_{114}\text{O}_9\text{Si}_4+\text{Na}$ : 1197.74376; found: 1197.74369 ( $\text{M}+\text{Na}^+$ ).

**Vinyl epoxide 46.** A mixture containing compound **45** (45 mg, 38  $\mu\text{mol}$ ) and  $\text{NaHCO}_3$  (32 mg, 380  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (0.5 mL) was stirred for 0.5 h before Dess-Martin periodinane (21 mg, 49  $\mu\text{mol}$ ) was introduced. Stirring was continued for 1.5 h at 0°C before the solvent was removed under reduced pressure and the residue was suspended in pentane (3 mL). The precipitates were filtered off through a pad of Florisil which was carefully rinsed with  $\text{Et}_2\text{O}$  (5 x 5 mL). Evaporation of the combined filtrates gave the corresponding epoxy-aldehyde as a pale yellow oil, which was immediately used in the next step.



A solution of  $\text{NaHMDS}$  in THF (1 M, 95  $\mu\text{L}$ , 0.40 mmol) was added dropwise to a suspension of (methyl) triphenylphosphonium bromide (53 mg, 95  $\mu\text{mol}$ ) in THF (0.5 mL) at 0°C. The resulting yellow suspension was stirred for 45 min at this temperature before a solution of the crude aldehyde prepared above in THF (0.2 mL) was slowly added. After stirring for 1 h, the reaction was quenched with sat. aq.  $\text{NH}_4\text{Cl}$ , the aqueous phase was extracted with  $\text{EtOAc}$  (2 x 3 mL), the combined organic extracts were dried over  $\text{Na}_2\text{SO}_4$  and evaporated, and the residue was purified by flash chromatography (hexanes:*tert*-butyl methyl ether, 15:1) to afford product **46** as a colorless oil (28 mg, 65% over 2 steps).  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  = 7.67 (m, 4H), 7.13 (m, 6H), 6.89 (tq,  $J$  = 7.4, 1.1 Hz, 1H), 5.65 (s, 1H), 5.57 (ddt,  $J$  = 16.9, 10.3, 6.4 Hz, 1H), 5.39 (m, 3H), 5.15 (3d,  $J$  = 17.5, 1.7, 0.5 Hz, 1H), 4.86 (m, 4H), 4.30 (m, 1H), 4.21 (d,  $J$  = 6.3 Hz, 1H), 3.82 (dd,  $J$  = 4.5, 4.3 Hz, 1H), 3.76 (dd,  $J$  = 10.7, 5.5 Hz, 2H), 3.0 (dd,  $J$  = 14.4, 4.8 Hz, 1H), 2.76 (dd,  $J$  = 13.2, 2.4 Hz, 1H), 2.69 (dd,  $J$  = 7.8, 2.2 Hz, 1H), 2.58 (ddd,  $J$  = 6.8, 5.7, 2.2 Hz, 1H), 2.39 (m, 1H), 2.16-1.98 (m, 7H), 1.94 (m, 1H), 1.91 (s(d),  $J$  = 0.9 Hz, 3H), 1.81 (s, 3H), 1.80 (m, 1H), 1.79 (m, 2H), 1.71 (m, 1H), 1.55 (m, 1H), 1.18 (s, 9H), 1.13 (m, 1H), 1.08 (d,  $J$  = 6.8 Hz, 3H), 1.06 (d,  $J$  = 6.8 Hz, 3H), 1.03 (s, 9H), 1.0 (s, 9H), 0.98 (d,  $J$  = 6.7 Hz, 3H), 0.87 (t,  $J$  = 7.8 Hz, 9H), 0.8 (q,  $J$  = 7.8 Hz, 6H), 0.45 (s, 3H), 0.20 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H).



**Compound 47.** Ruthenium complex **38** (1.0 mg, 1.6  $\mu\text{mol}$ ) was added to a solution of compound **46** (19 mg, 16  $\mu\text{mol}$ ) in  $\text{C}_6\text{H}_6$  (20 mL) and the resulting mixture was stirred at 20°C for 2 h. The reaction was quenched with ethyl vinyl ether (20  $\mu\text{L}$ , 216  $\mu\text{mol}$ ) and stirring was continued 10 min before all volatile materials were evaporated under reduced pressure at 20°C. The crude product was then adsorbed onto Celite and purified by flash chromatography (hexanes:*tert*-butyl methyl ether, 15:1) to afford **47** as a yellow oil (12 mg, 68%).  $^1\text{H}$  NMR (400 MHz,

C<sub>6</sub>D<sub>6</sub>):  $\delta$  = 7.80 (m, 4H), 7.24 (m, 6H), 6.92 (tq,  $J$  = 7.2, 1.1 Hz, 1H), 5.68 (s, 1H), 5.77 (m, 1H), 5.51 (m, 1H), 5.17 (dd,  $J$  = 16.7, 8.3 Hz, 1H), 5.06 (d,  $J$  = 1.6 Hz, 1H), 5.06 (d,  $J$  = 1.6 Hz, 1H), 4.92 (d,  $J$  = 1.7 Hz, 1H), 4.50 (d,  $J$  = 3.1 Hz, 1H), 4.22 (m, 1H), 3.96 (dd,  $J$  = 9.8, 4.1 Hz, 1H), 3.88 (m, 3H), 3.0 (m, 2H), 2.92 (dd,  $J$  = 16.1, 2.8 Hz, 1H), 2.86 (dd,  $J$  = 16.8, 4.6 Hz, 1H), 2.58 (3d,  $J$  = 16.8, 6.7, 3.2 Hz, 1H), 2.39 (m, 1H), 2.22 (m, 2H), 2.18 (m, 1H), 1.92 (m, 2H), 1.90 (s, 3H), 1.81 (m, 1H), 1.79 (m, 2H), 1.76 (s, 3H), 1.71 (m, 1H), 1.60 (m, 1H), 1.21 (s, 9H), 1.07 (m, 1H), 1.06 (d,  $J$  = 6.8 Hz, 3H), 1.04 (d,  $J$  = 6.8 Hz, 3H), 1.01 (s, 9H), 1.0 (s, 9H), 0.98 (d,  $J$  = 6.7 Hz, 3H), 0.89 (t,  $J$  = 7.8 Hz, 9H), 0.81 (q,  $J$  = 7.6 Hz, 6H), 0.3 (s, 3H), 0.16 (s, 3H), 0.14 (s, 3H), 0.10 (s, 3H).

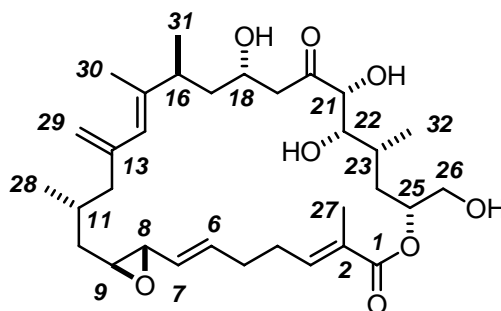
**Amphidinolide H.** A solution of TASF (16.4 mg, 59.3  $\mu$ mol) in aq. DMF (0.2 mL + 4  $\mu$ L H<sub>2</sub>O) was added to a solution of compound **47** (12 mg, 9.9  $\mu$ mol) in THF (2 mL) at 0°C. The mixture was slowly warmed to ambient temperature over a period of 30 min and stirring was continued for 2h. For work up, the mixture was extracted with cold (5°C) buffer solution (pH 7, 3 x 2 mL), the aqueous phases were extracted with EtOAc (2 x 1 mL), the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated, and the residue was purified by flash chromatography (EtOAc/hexane, 9:1) to afford compound **1** as a white solid (3 mg, 55%). HRMS (ESI+):  $m/z$ : calcd for: C<sub>32</sub>H<sub>50</sub>O<sub>8</sub>+Na: 585.33979; found: 585.33996 (M+Na<sup>+</sup>).

A solution of **amphidinolide H** in acidic CDCl<sub>3</sub> equilibrates with **amphidinolide G** by transesterification (cf. spectra) as previously reported in the literature.<sup>1</sup> The two isomers can be separated by preparative HPLC.

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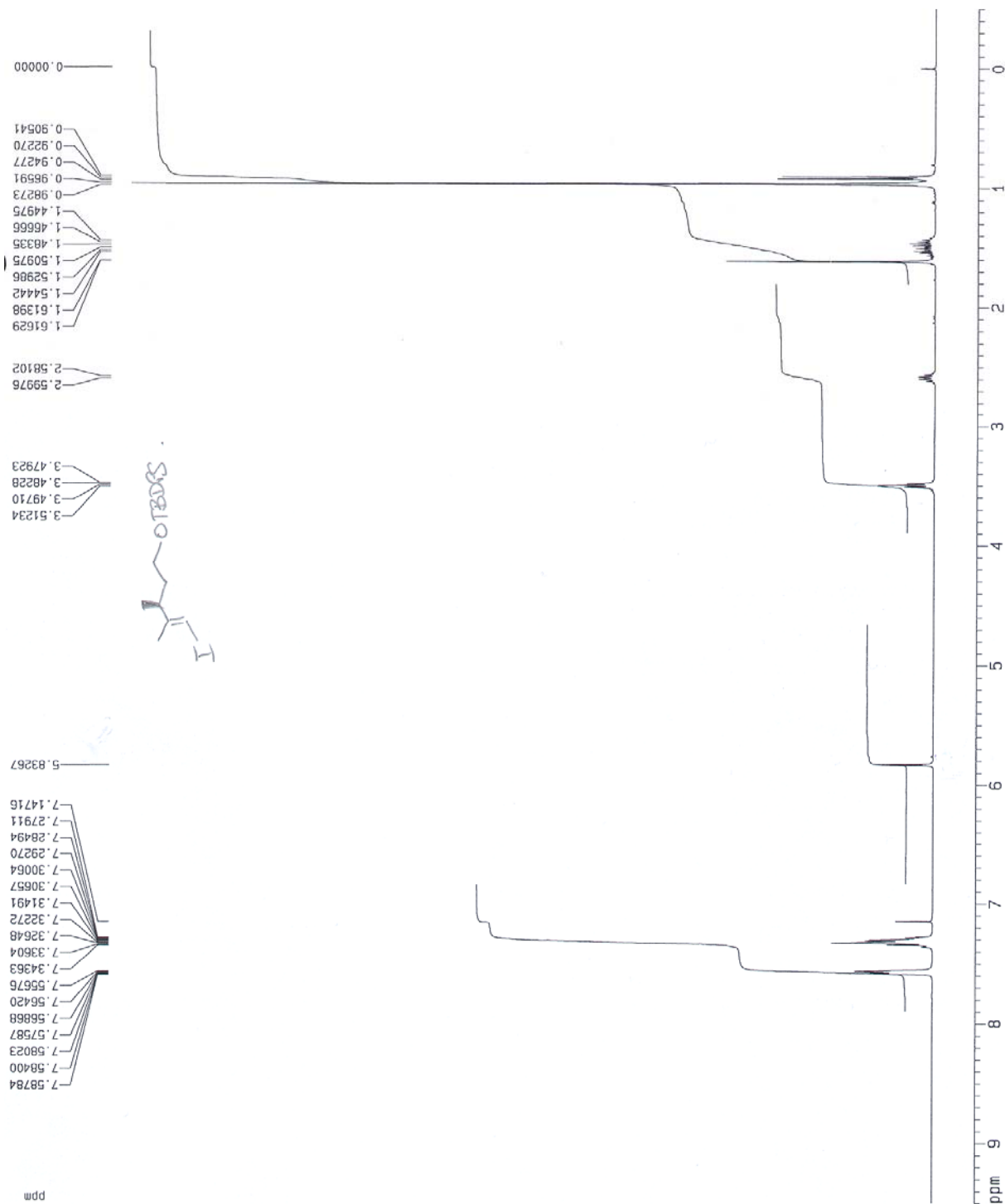
<sup>1</sup> See the Supporting Information of the following paper: Kobayashi, J.; Shimbo, K.; Sato, M.; Shiro, M.; Tsuda, M. *Org. Lett.* **2000**, 2, 2805-2807.



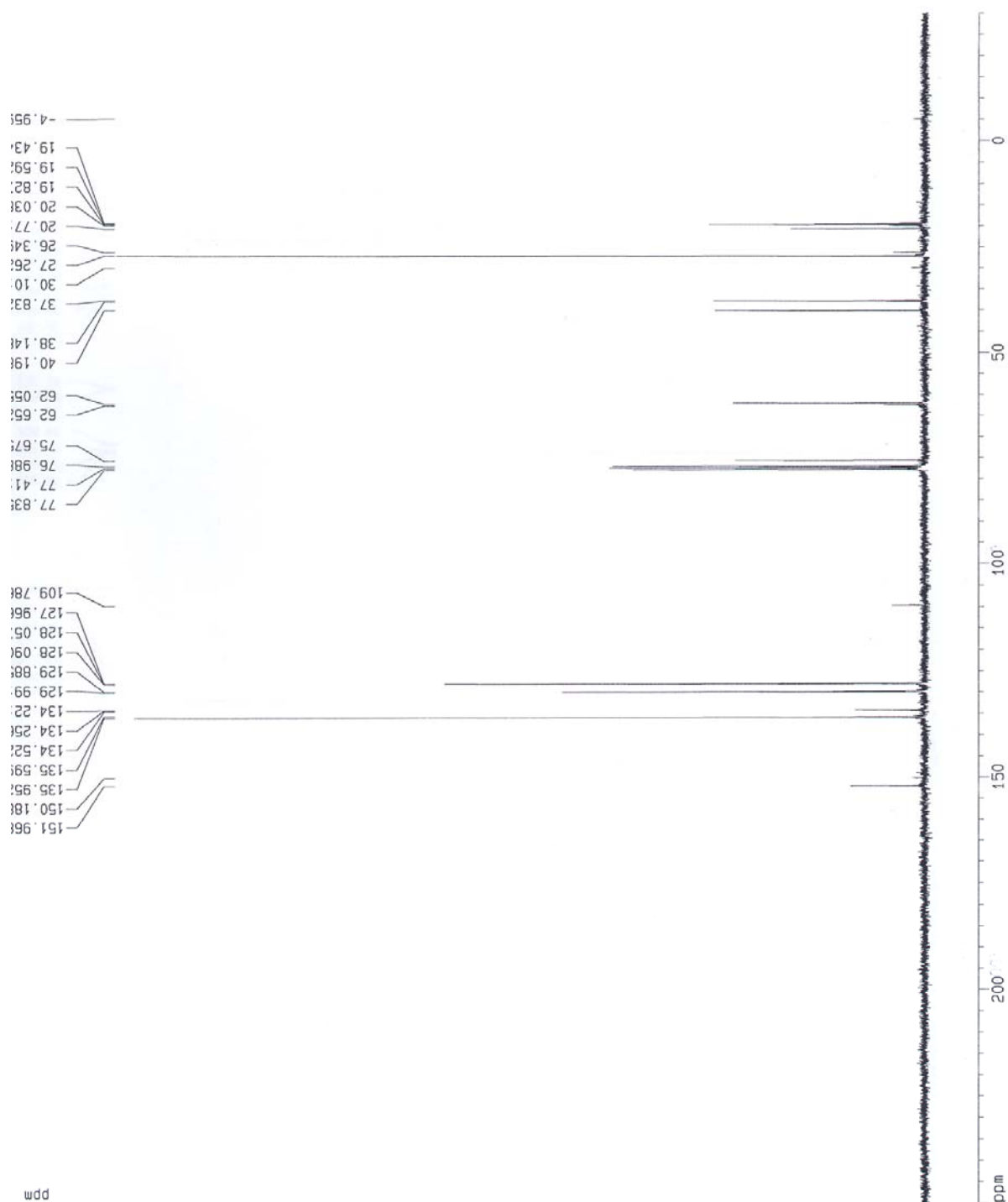
Table 1. Comparison between reported  $^{13}\text{C}$  NMR data ( $\text{CDCl}_3$ ) and the data recorded for synthetic **1**.

Position	Synthetic 1	Literature data <sup>2</sup>
1	168.7	168.7
2	127.9	127.9
3	141.0	141
4	30.9	30.9
5	27.0	26.9
6	135.7	135.7
7	128.6	128.6
8	60.4	60.3
9	59.5	59.5
10	39.8	39.8
11	29.1	29.1
12	47.2	47.1
13	144.2	144.1
14	126.1	126.1
15	141.7	141.7
16	40.8	40.7
17	40.9	40.9
18	67.6	67.5
19	45.2	45.2
20	212.2	212.2
21	77.7	77.7
22	75.4	75.4
23	33.0	33
24	33.4	33.5
25	73.4	73.4
26	66.2	66.1
27	12.6	12.5
28	18.0	18
29	114.7	114.7
30	14.1	13.1
31	20.3	20.3
32	15.6	15.6

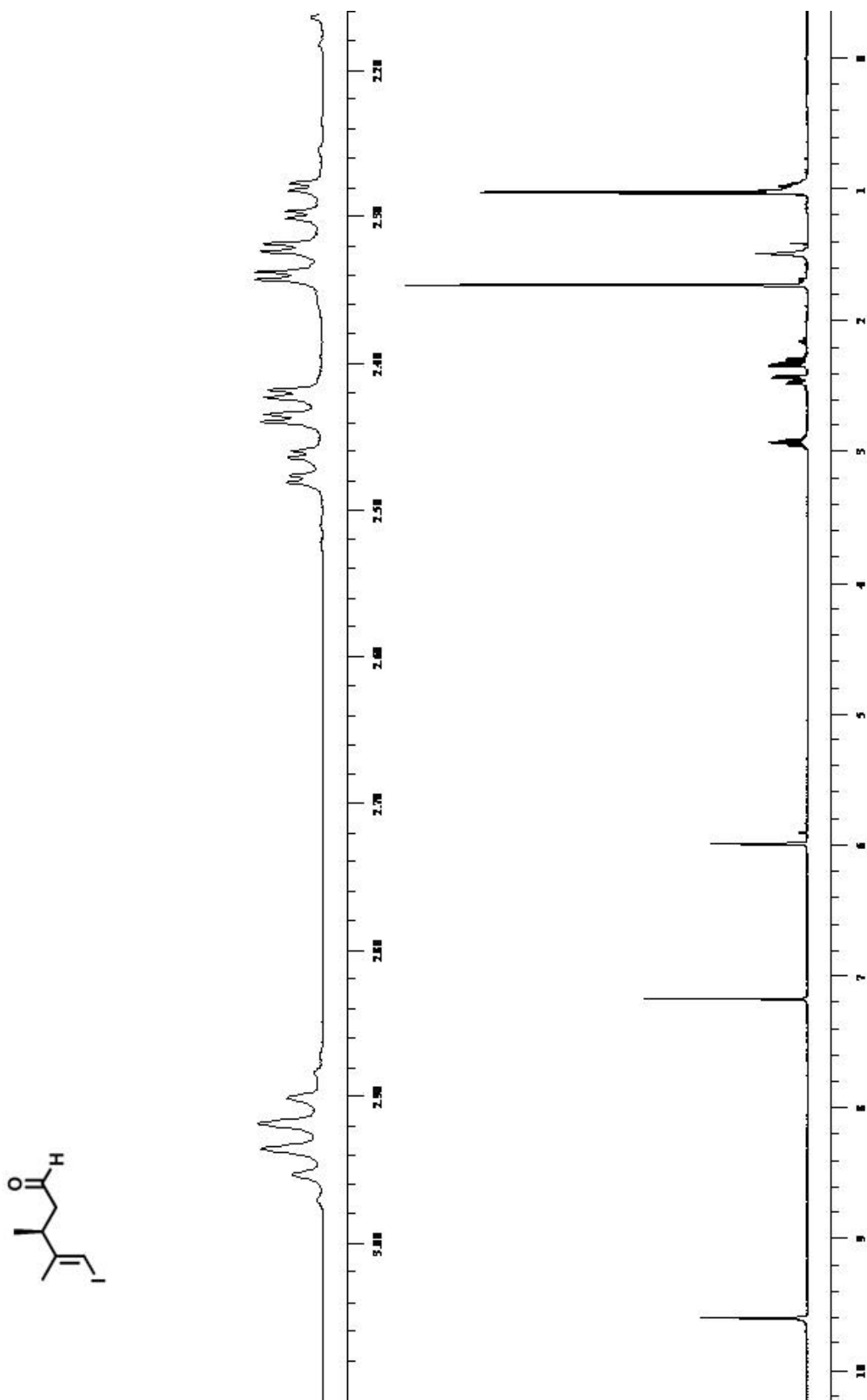
<sup>2</sup> Kobayashi, J. ; Shigemori, H.; Ishibashi, M.; Yamasu, T.; Hirota, H.; Sasaki, T. *J. Org. Chem.* **1991**, *56*, 5221-5224.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **25**.

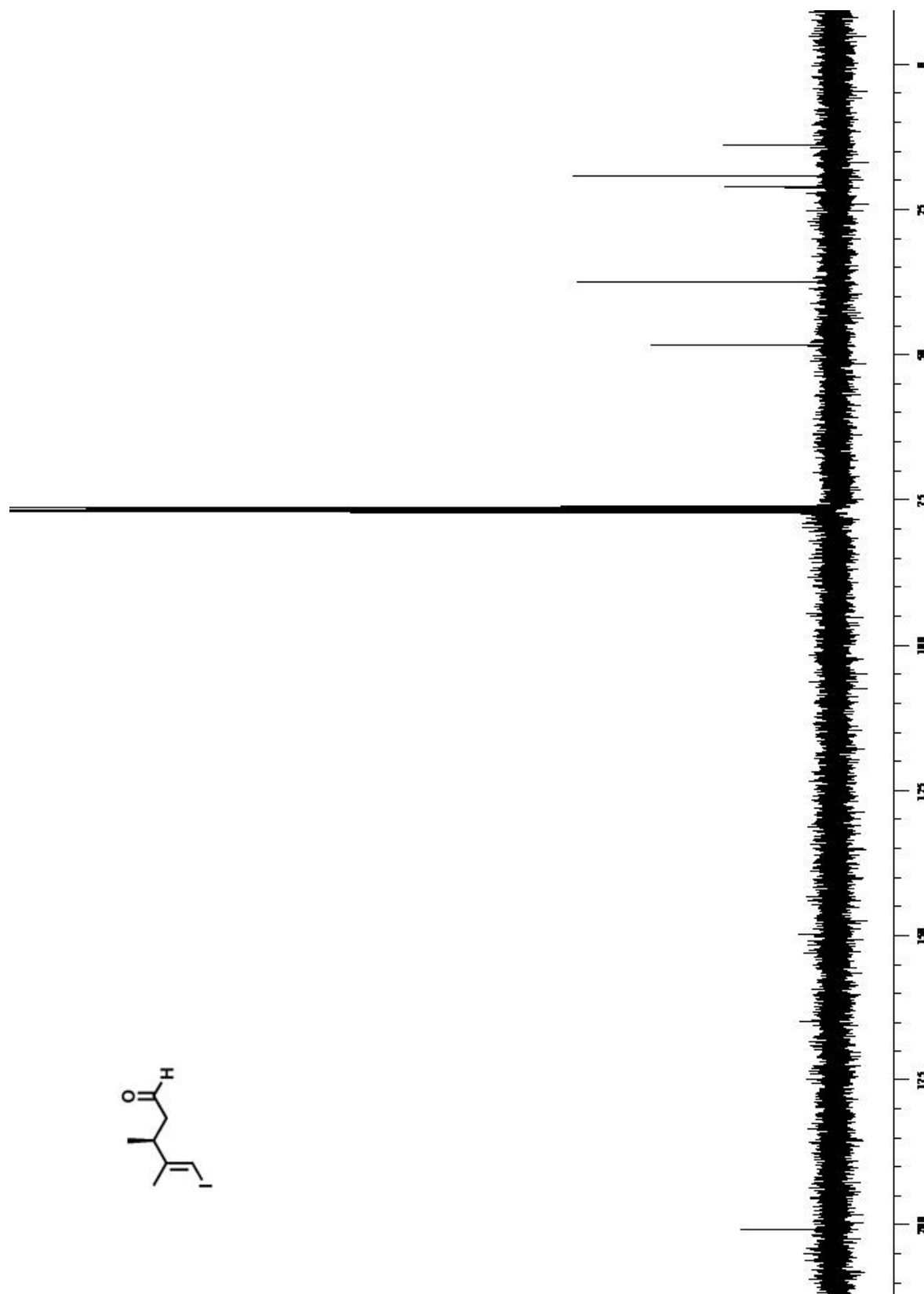
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **25**.



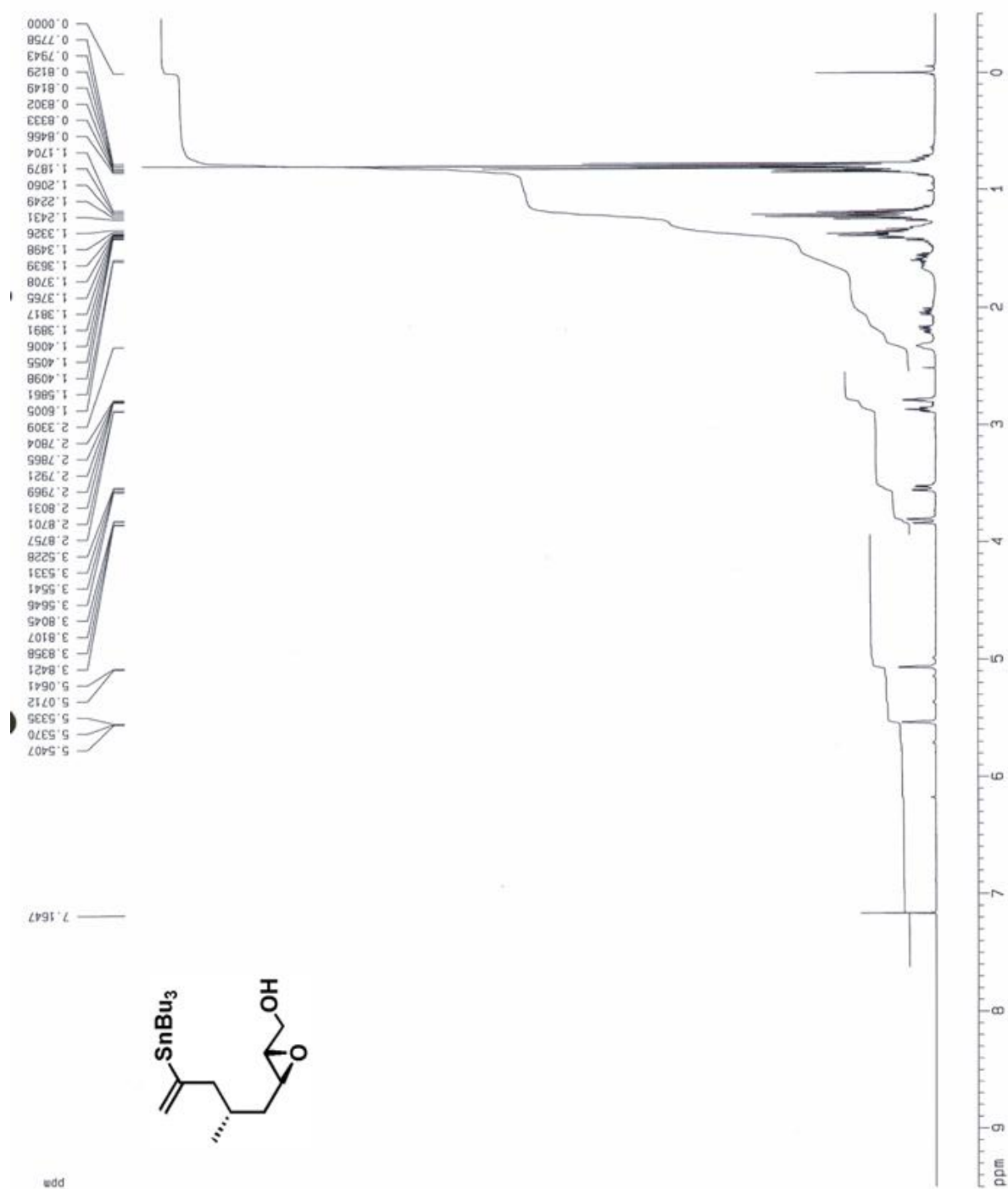
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **26**.



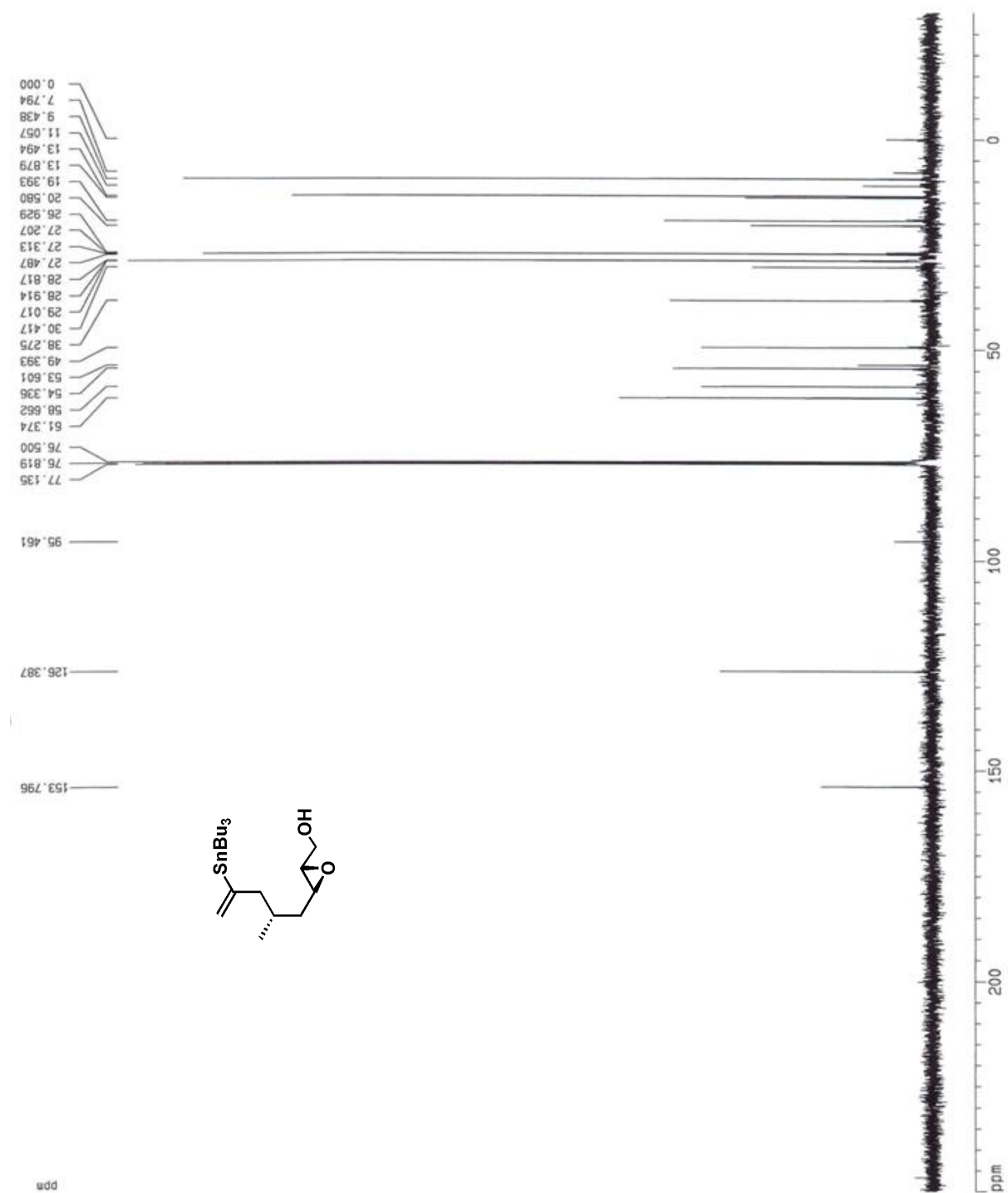
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **26**.



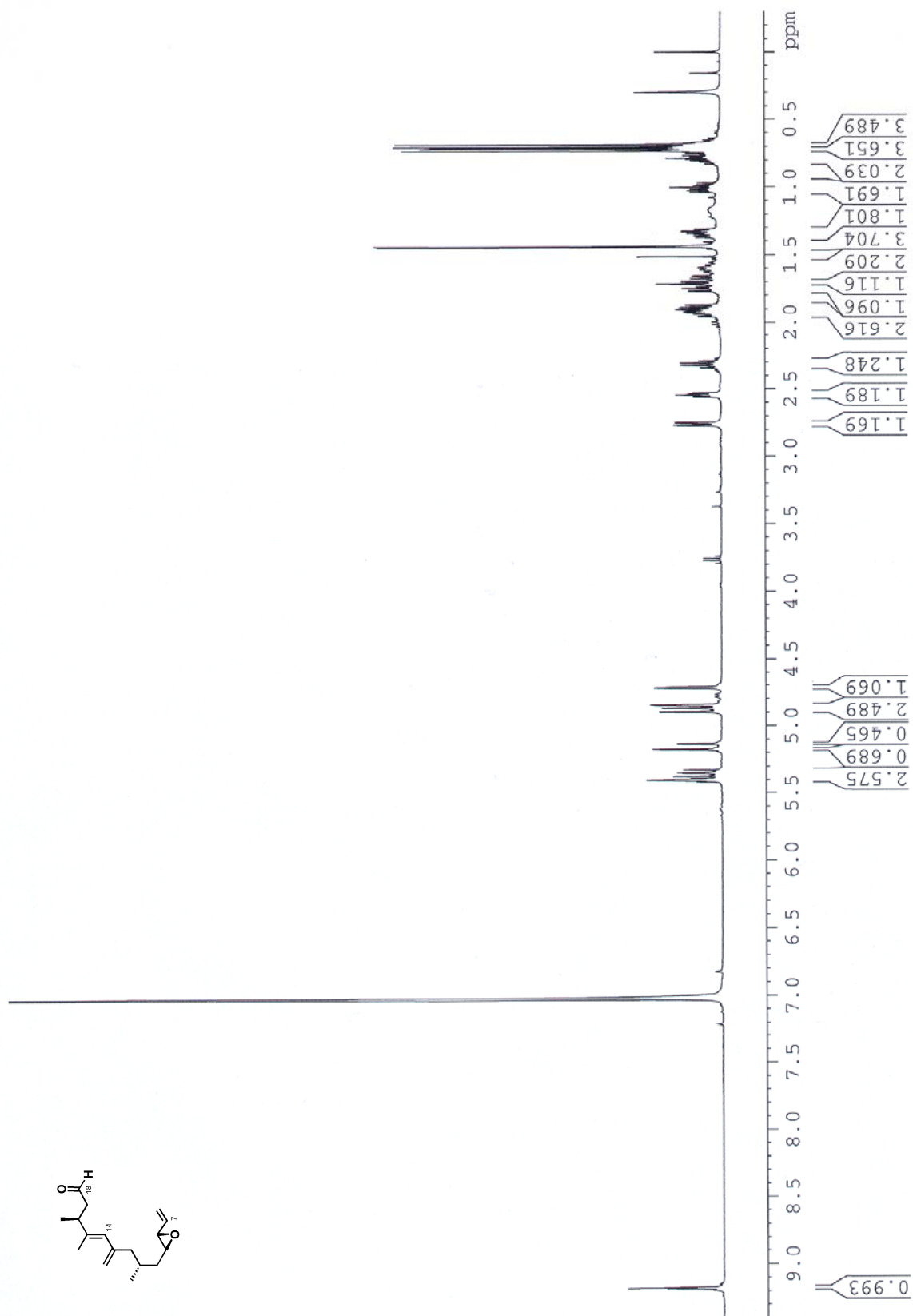
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **34**.



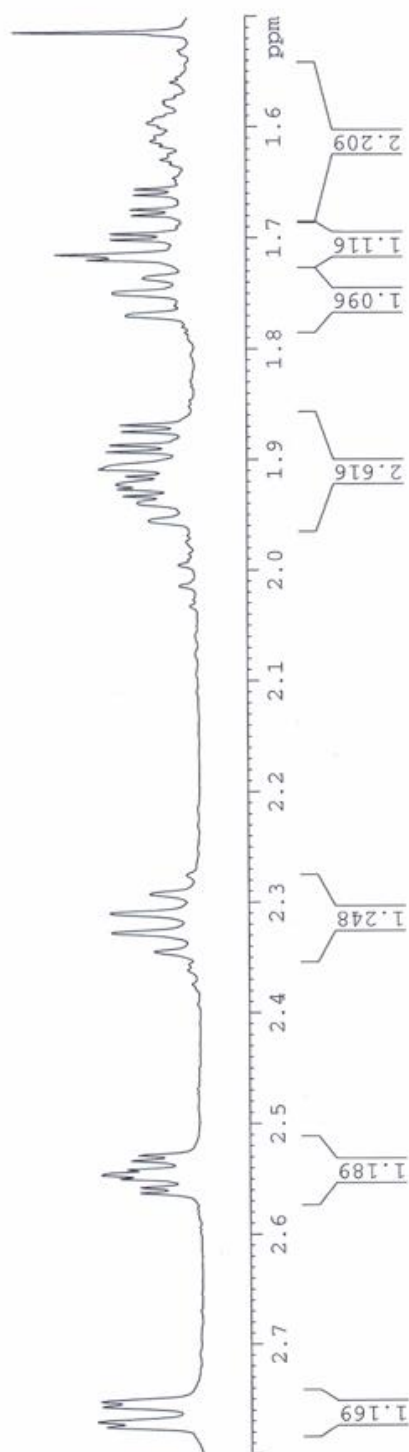
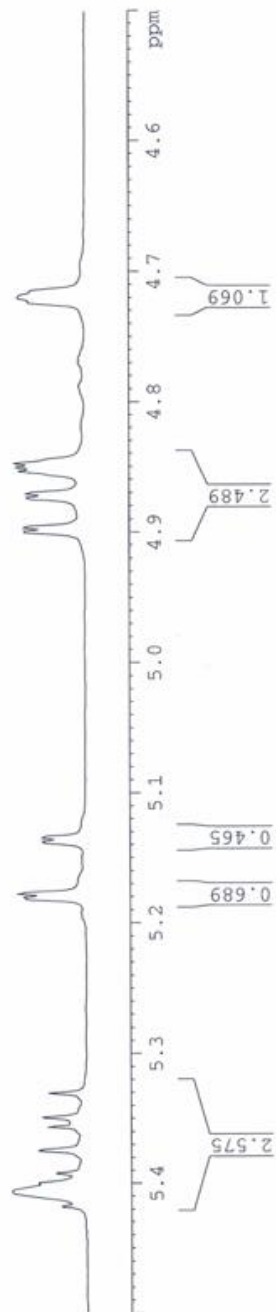
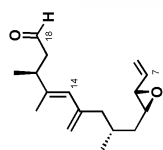
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **34**.



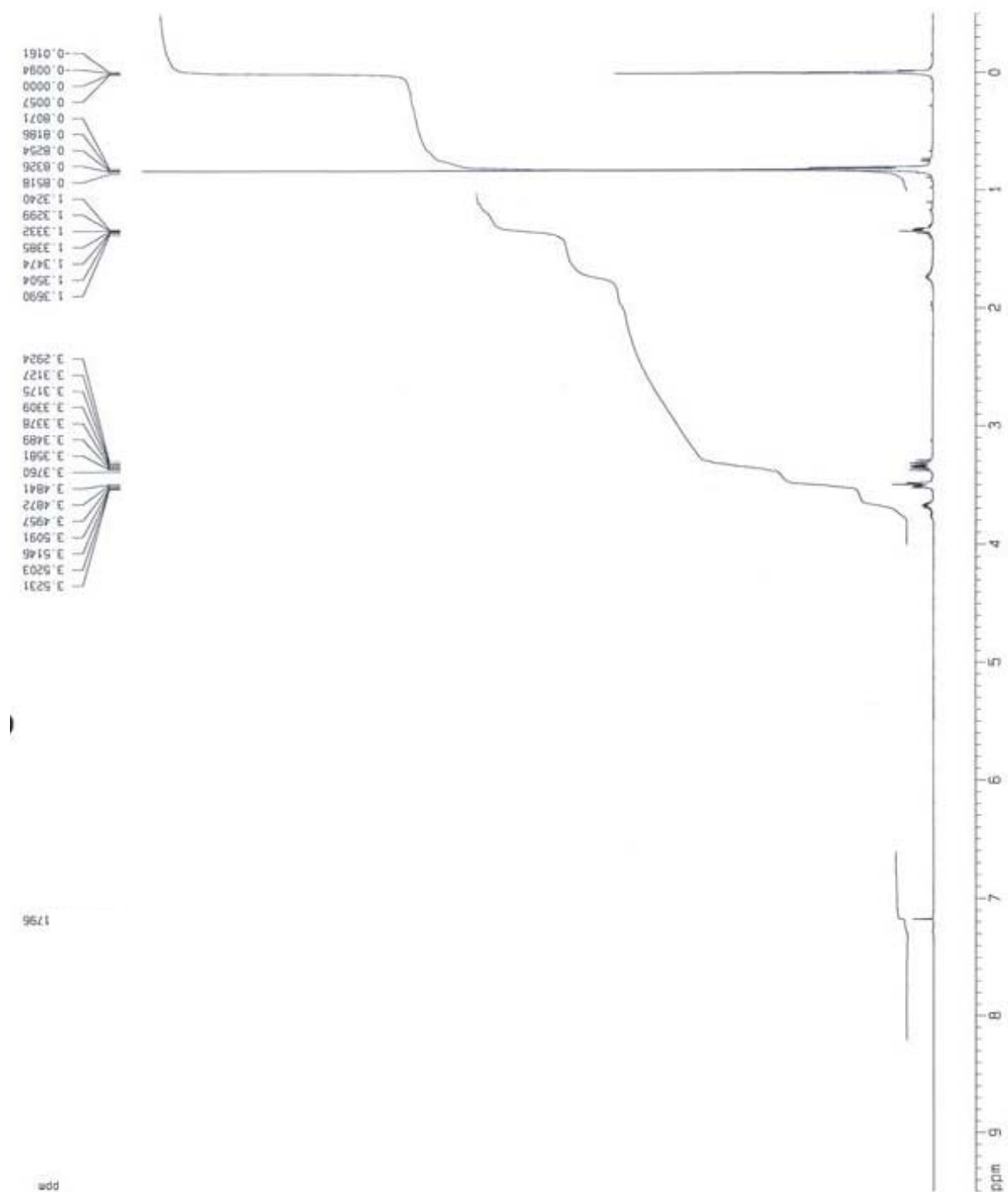
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **36**.

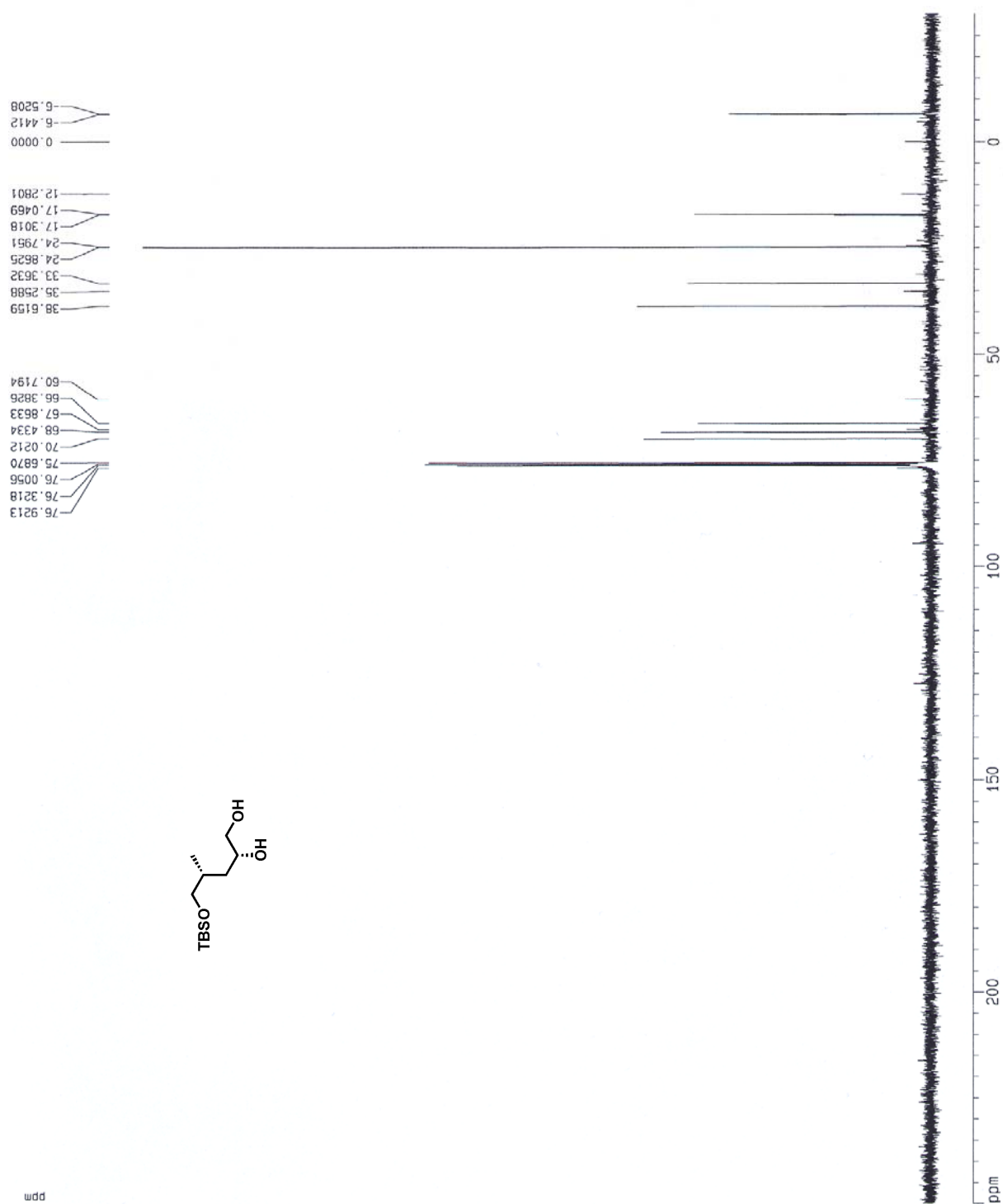




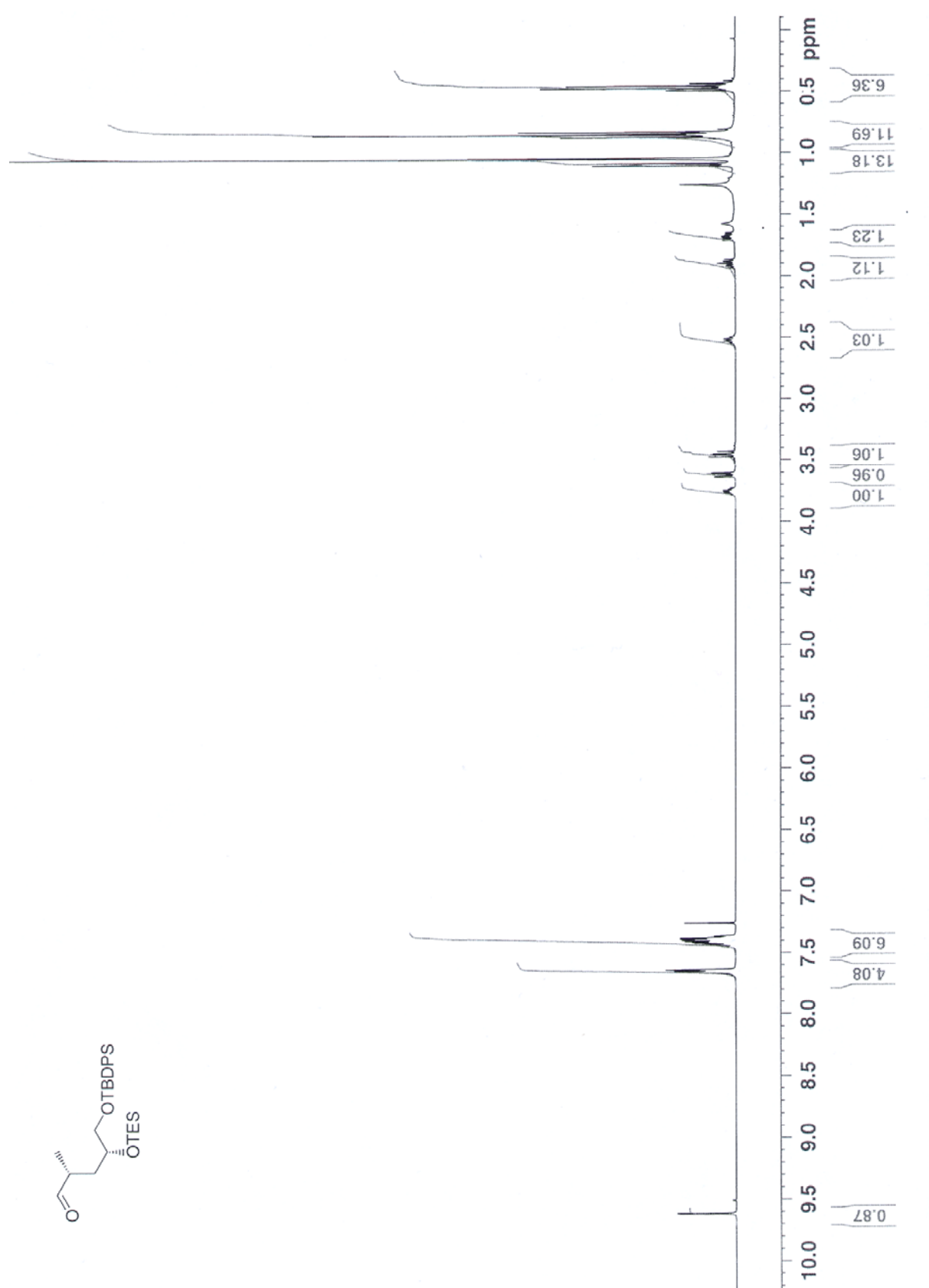
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **36**.

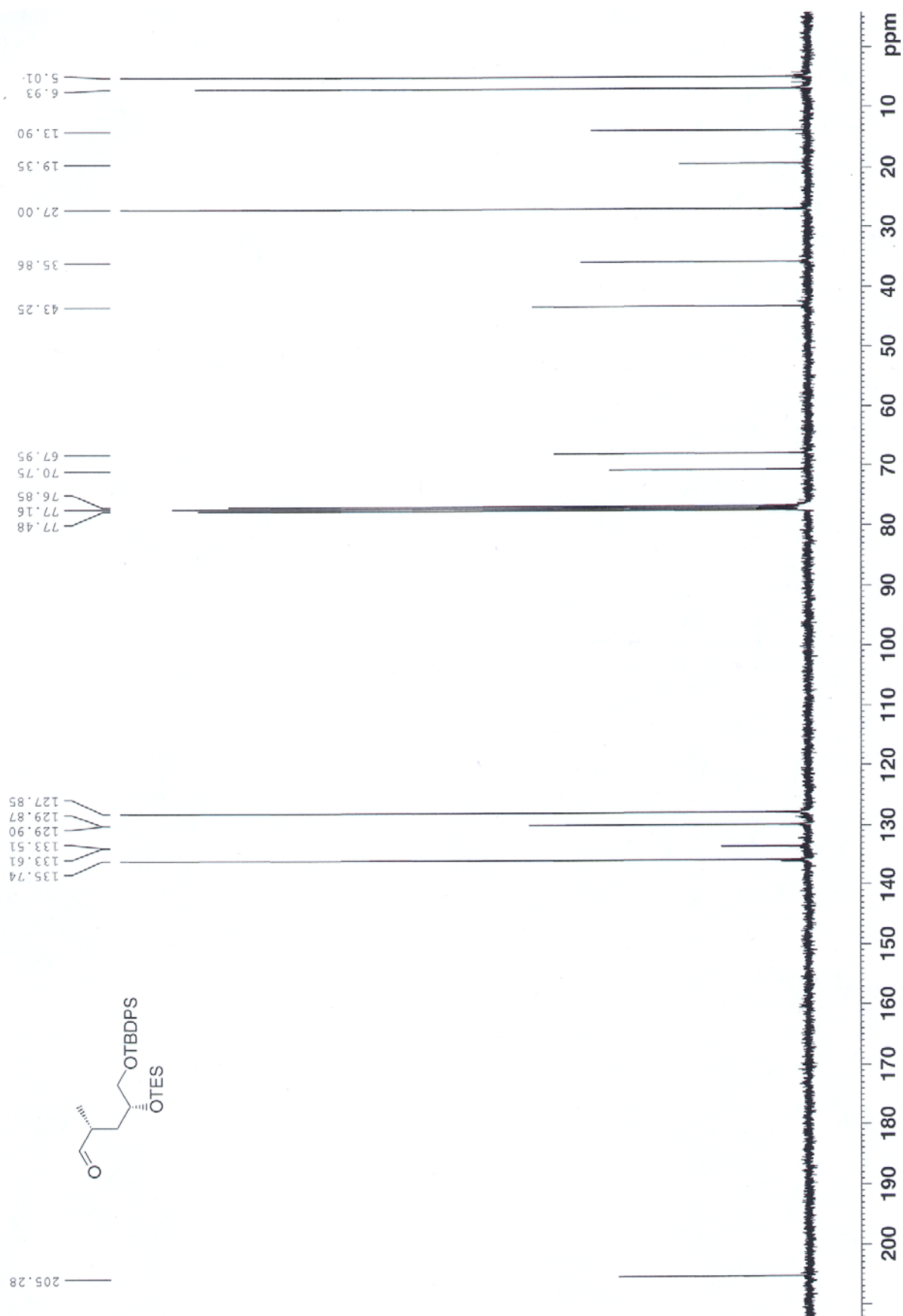
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **8**.

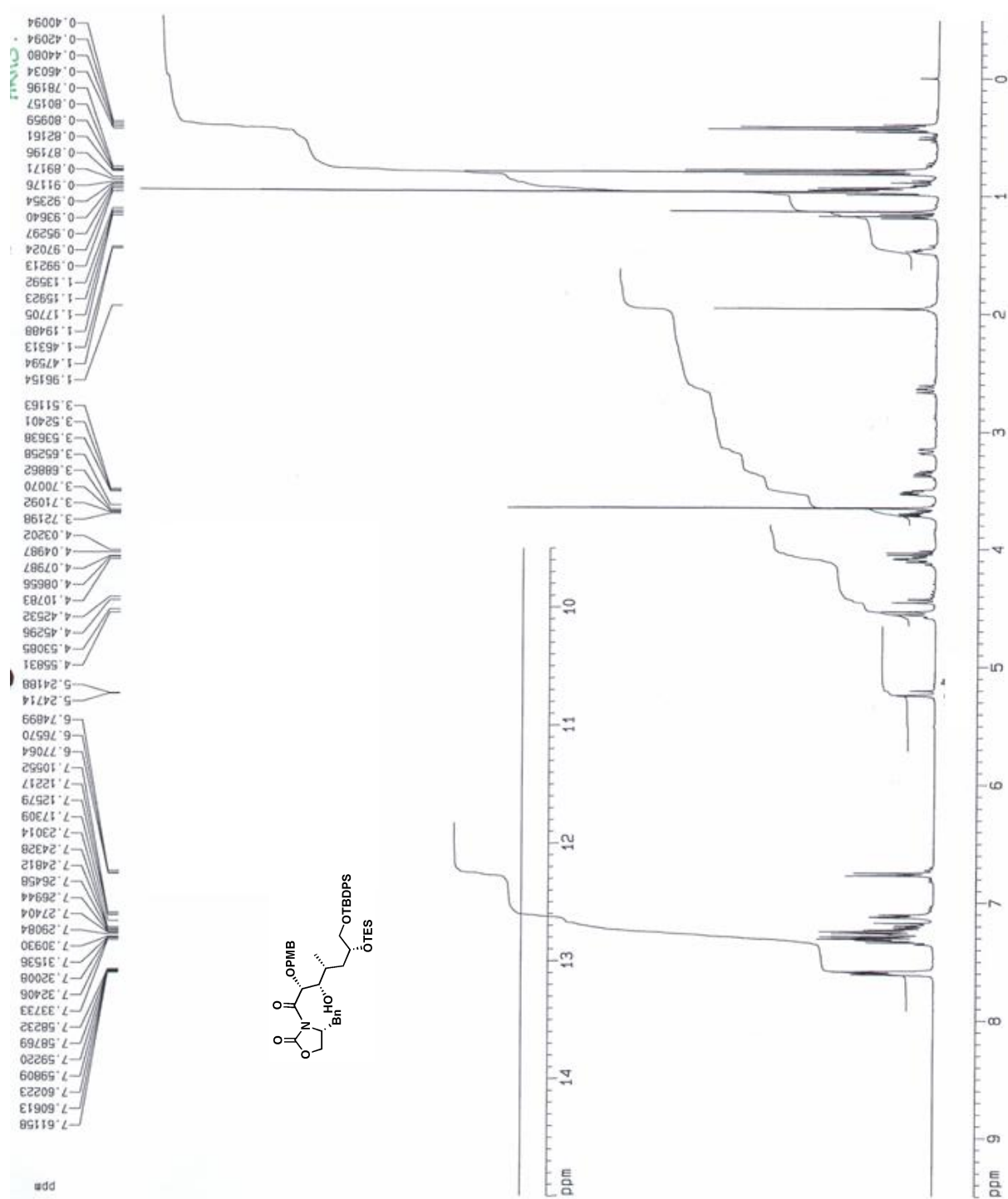


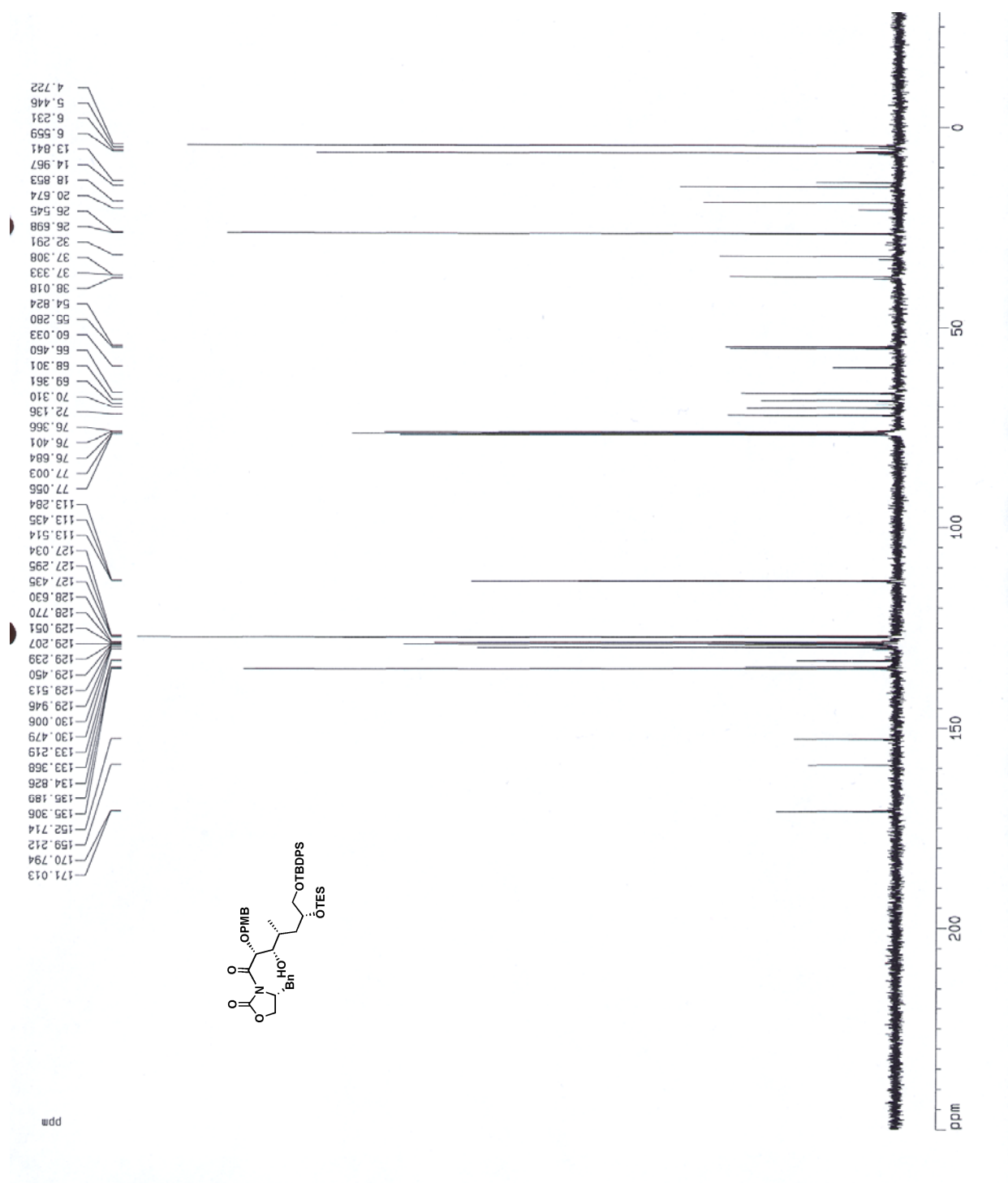
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **8**.

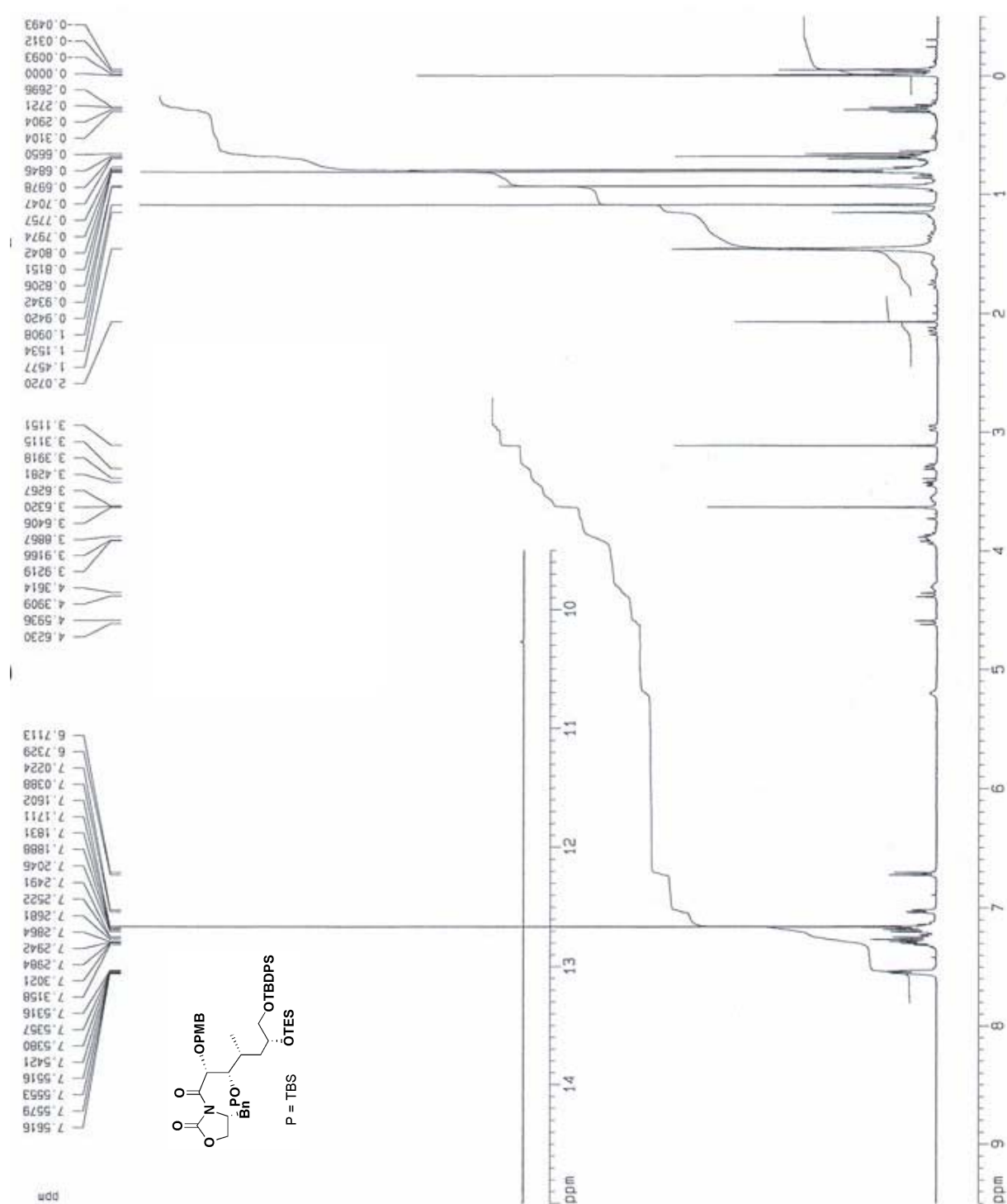
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **10**.



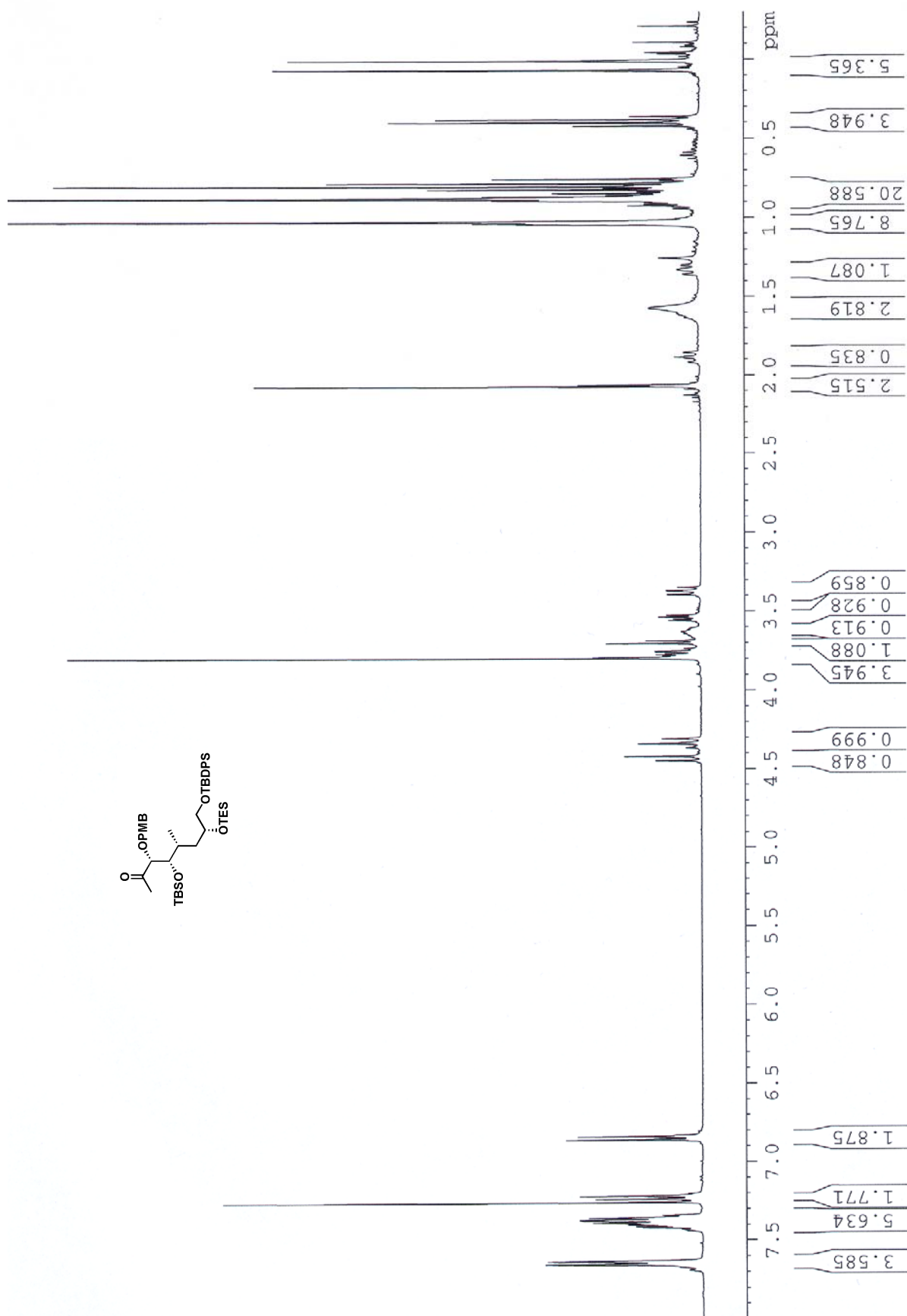
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **10**.

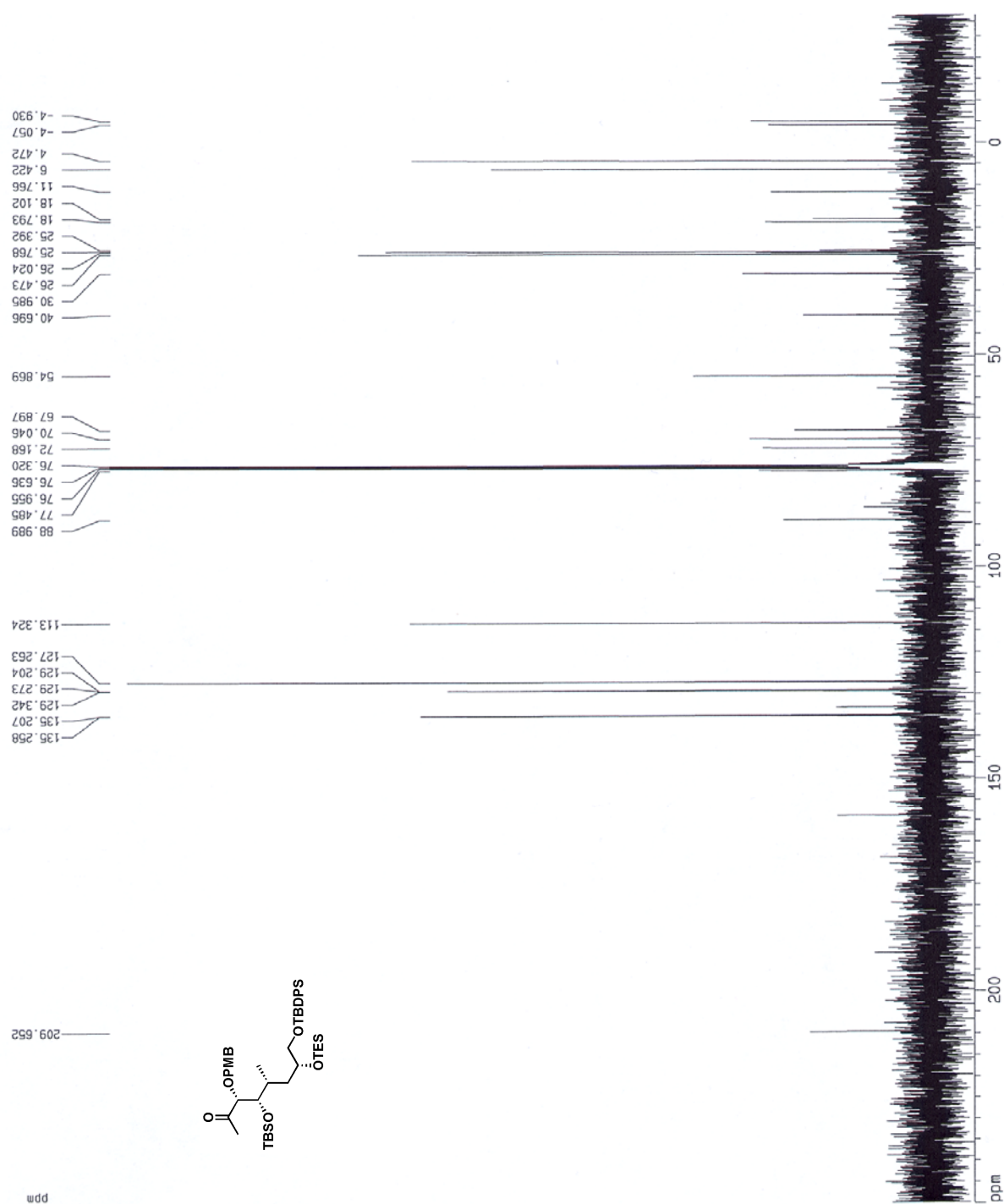
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **12**.

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **12**.

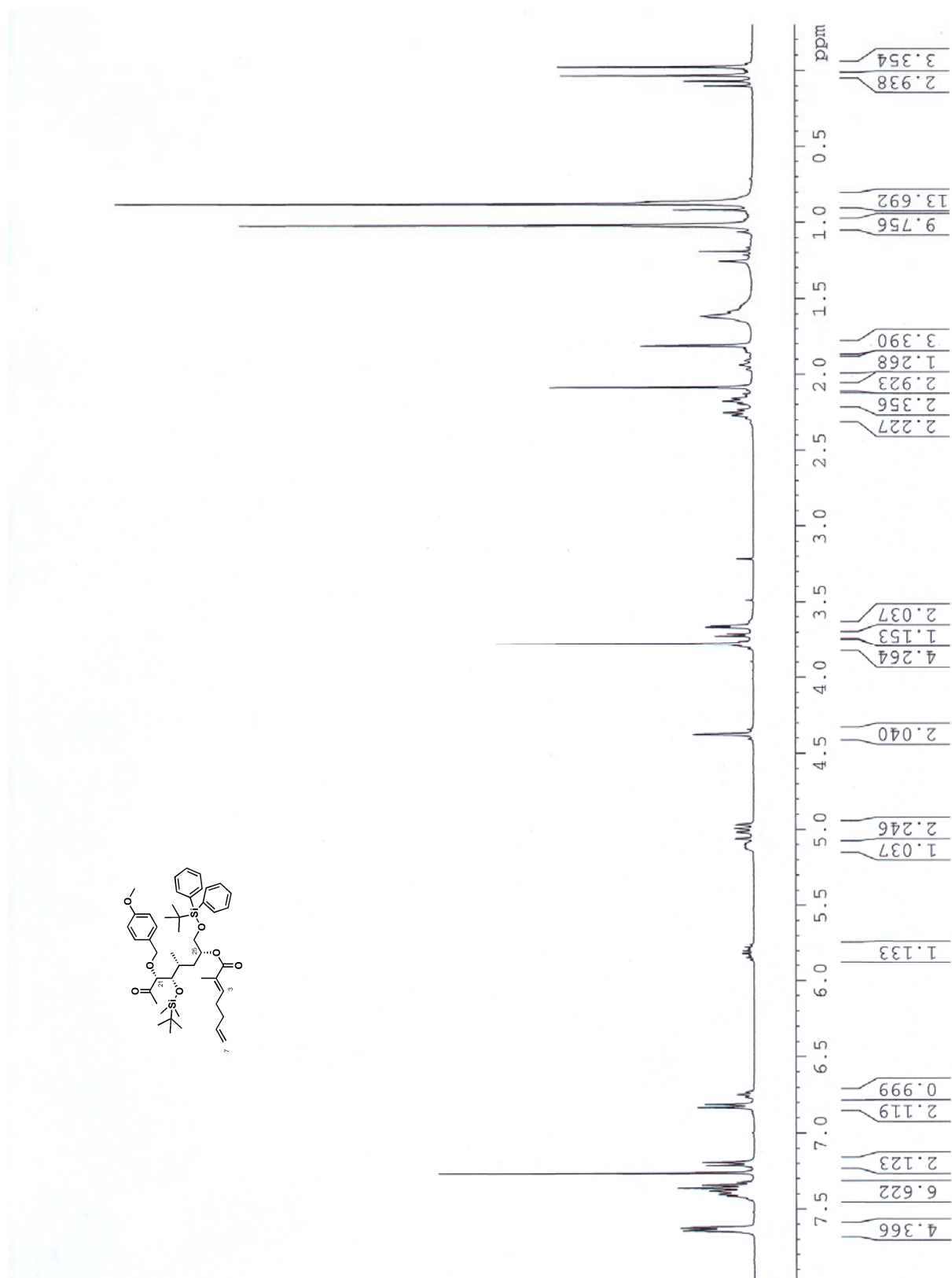
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **13**.



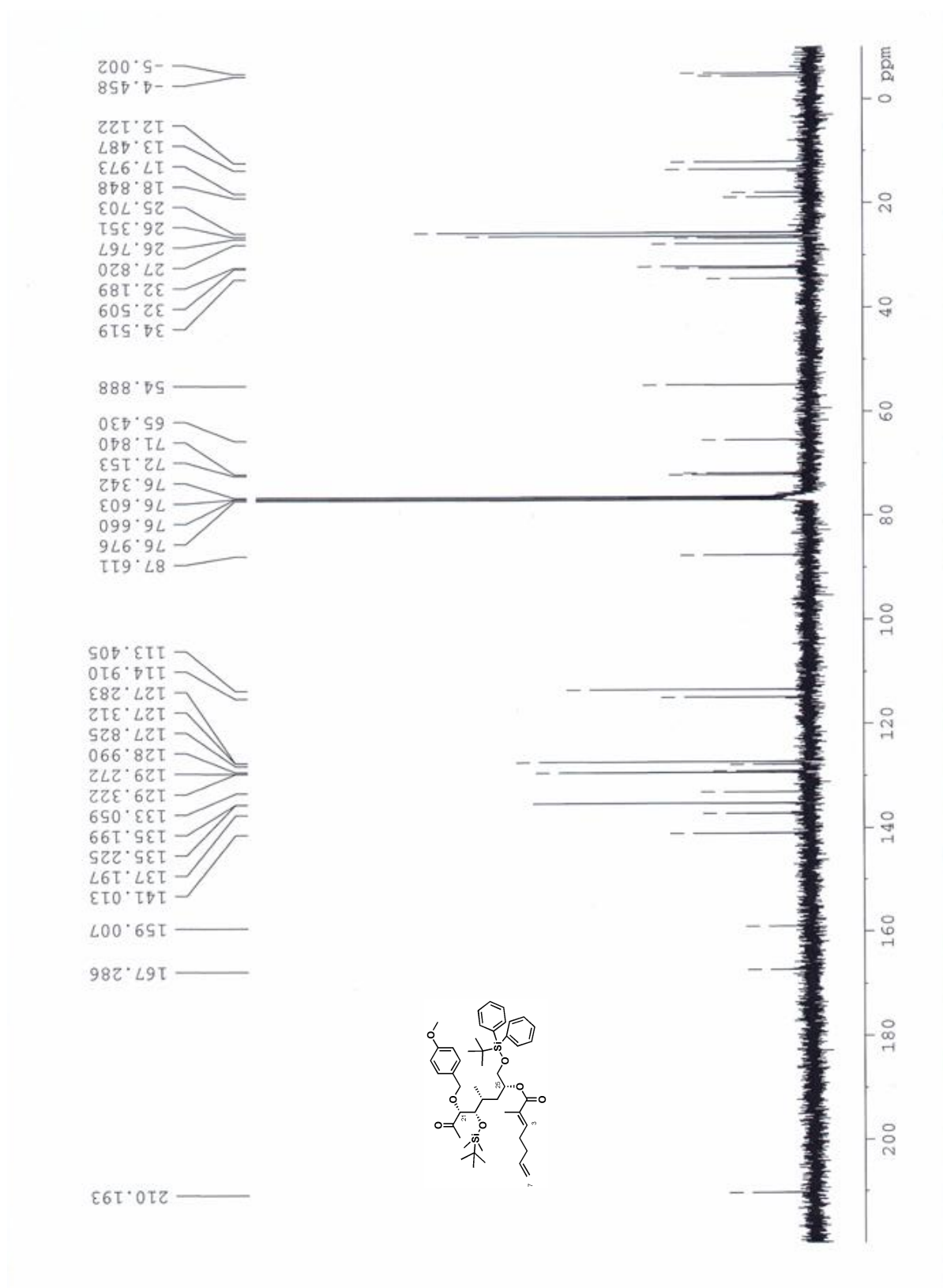
<sup>1</sup>H NMR (CDCl<sub>3</sub>) of compound **15**.

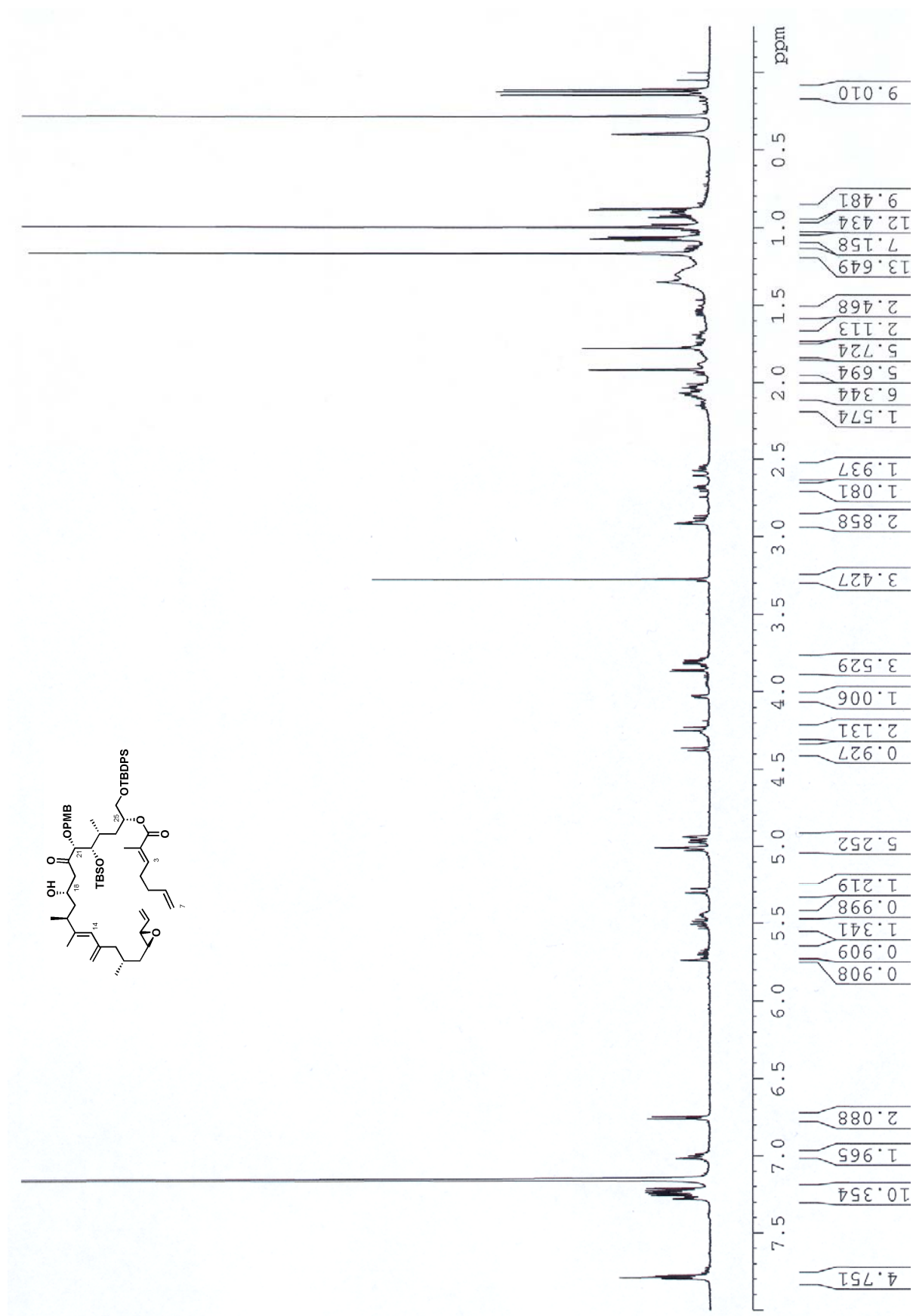
$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **15**.

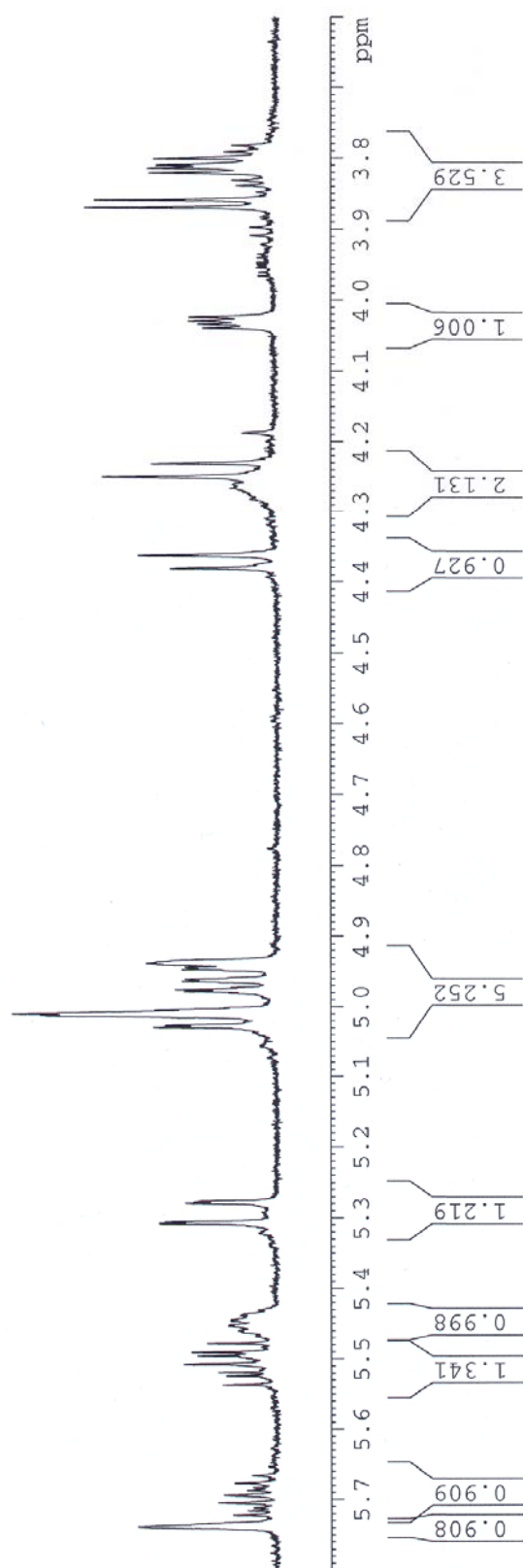
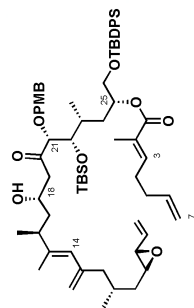
$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **17**.

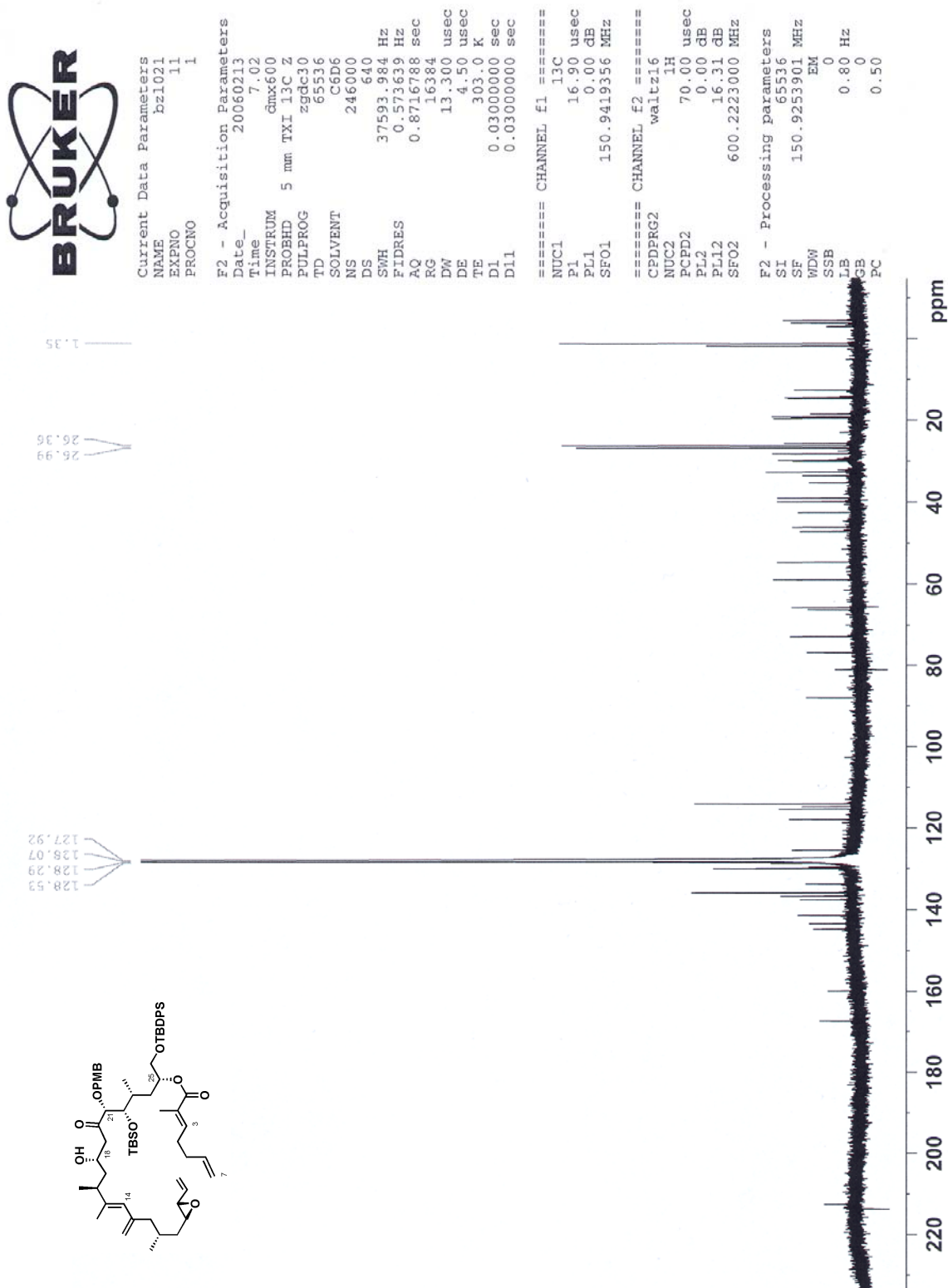


$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **17**.

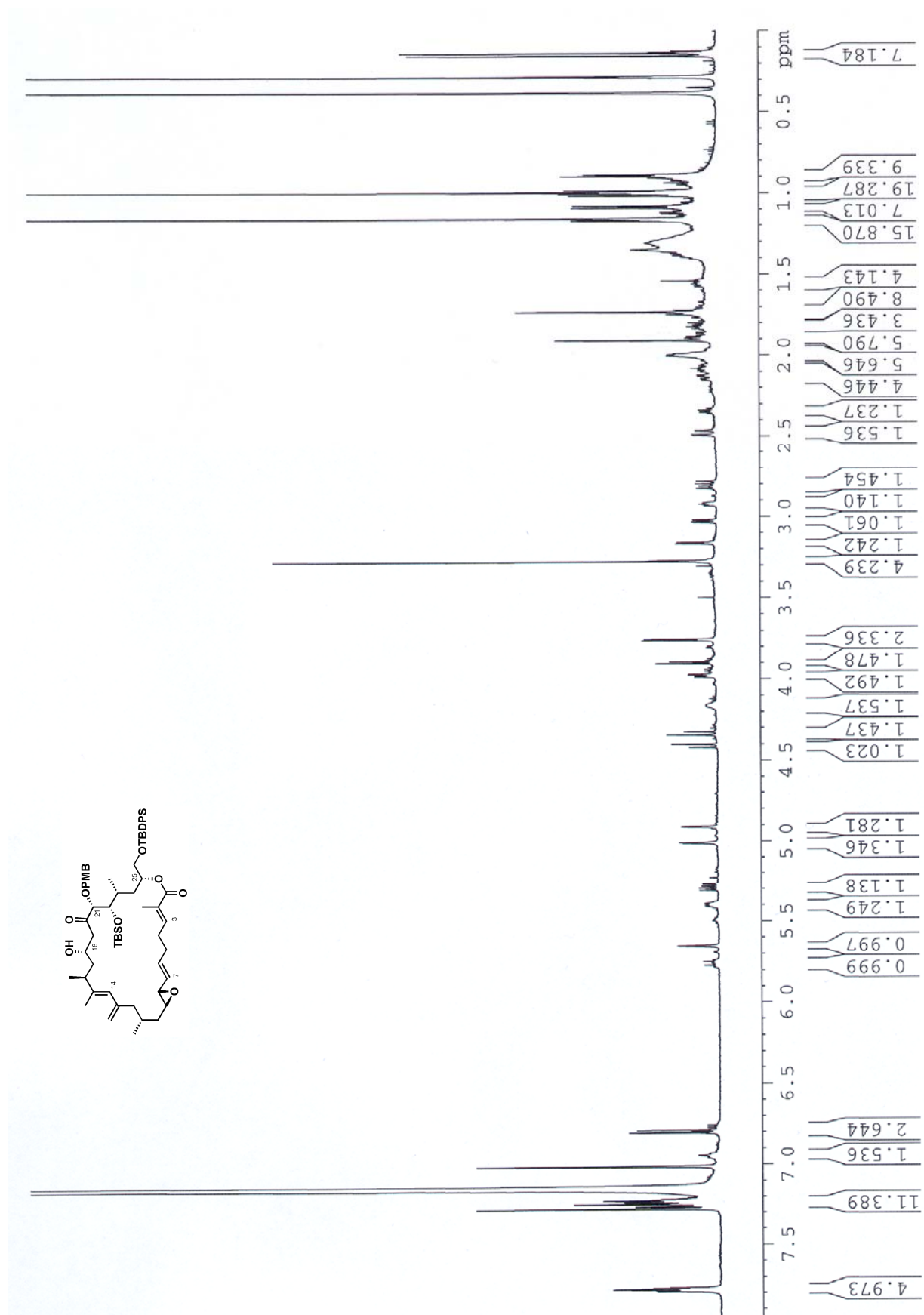


$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **37**.

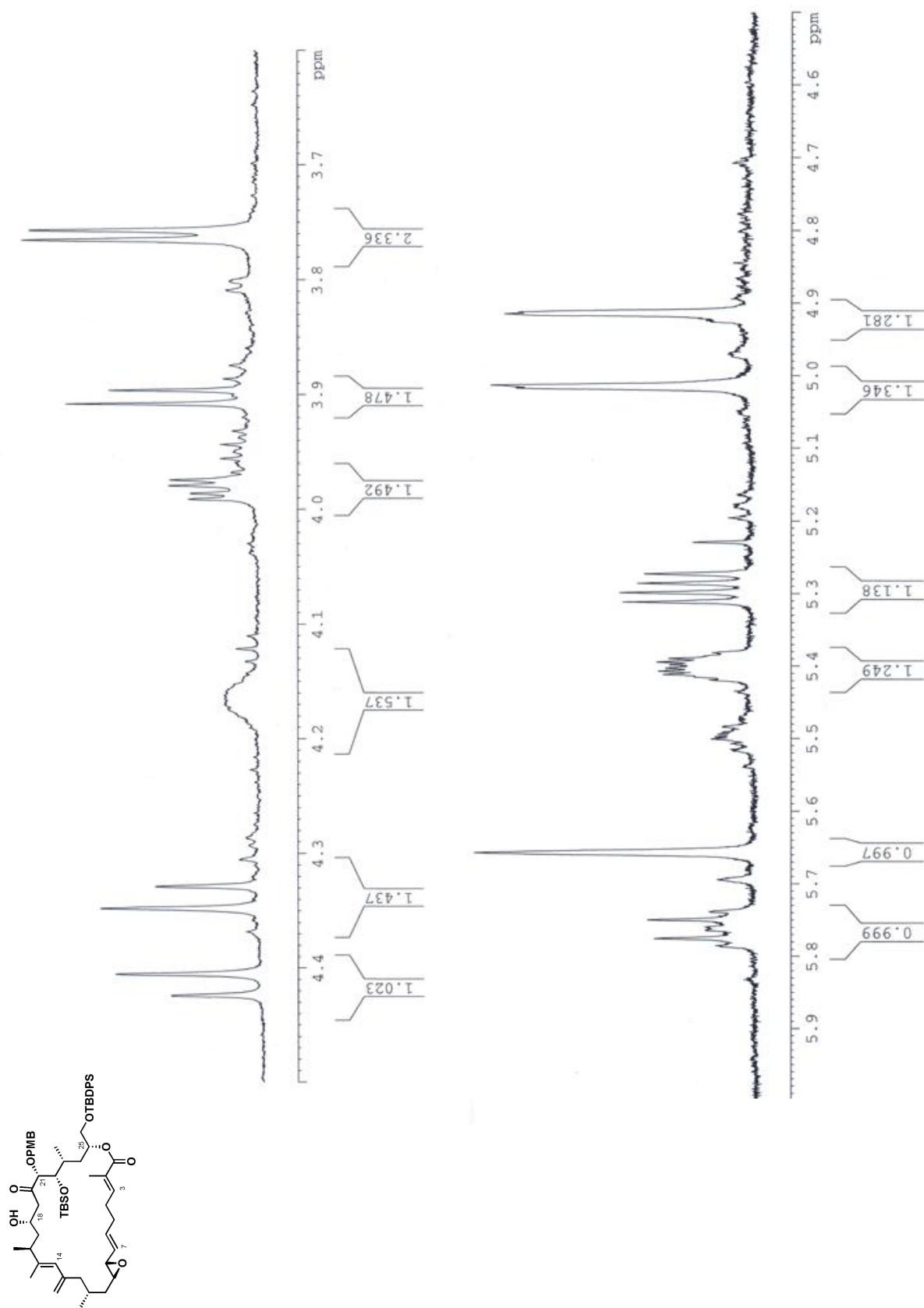
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **37**.

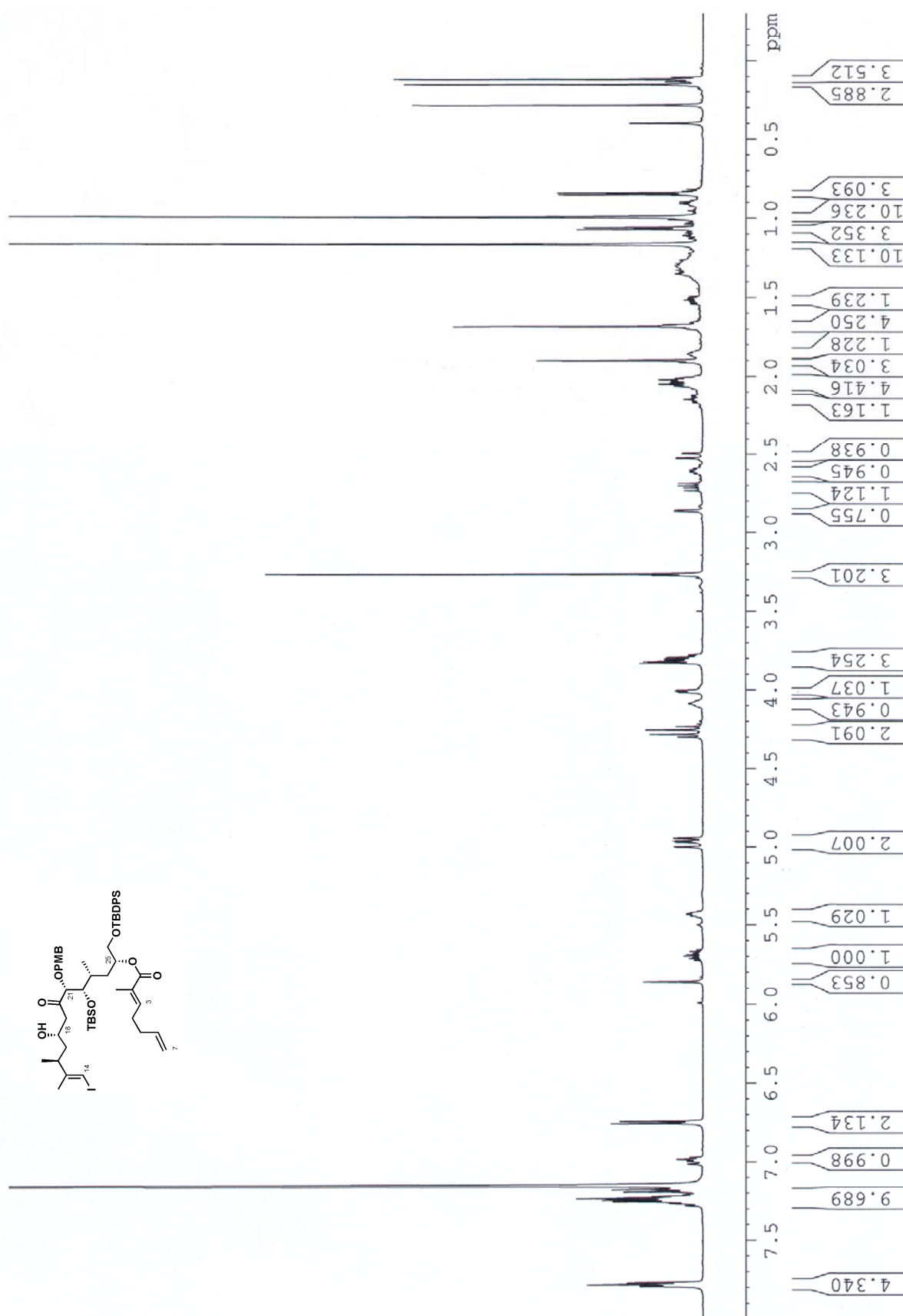
$^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **37**.

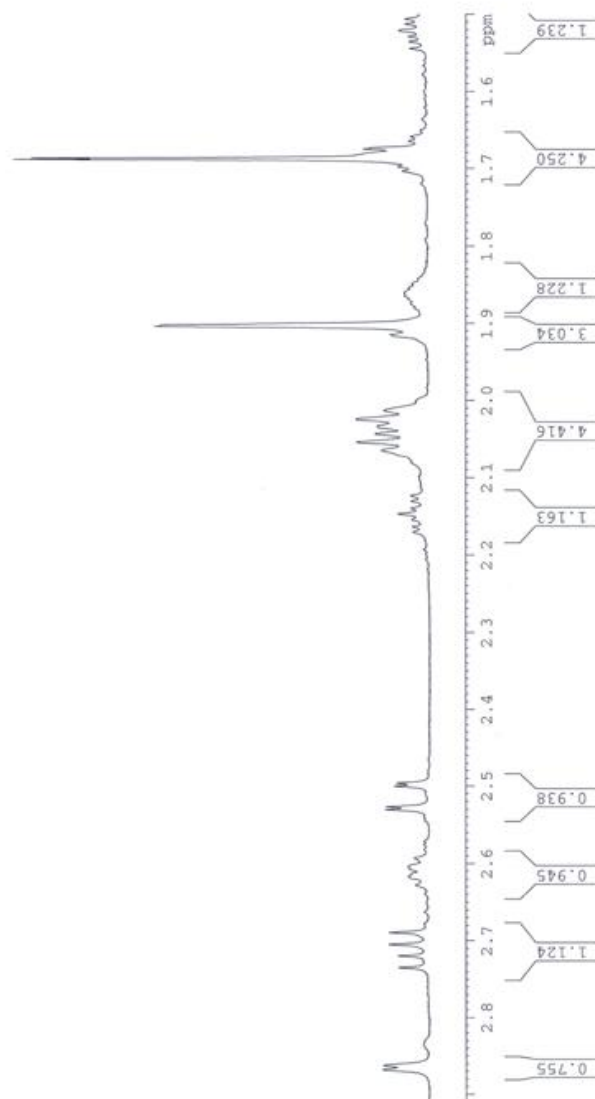
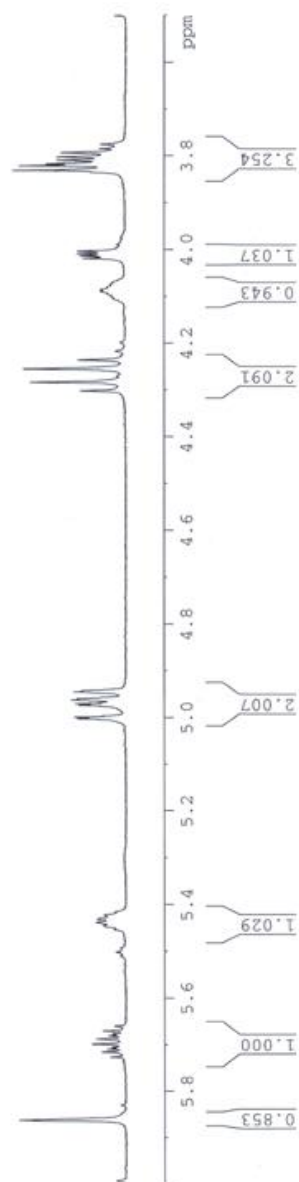
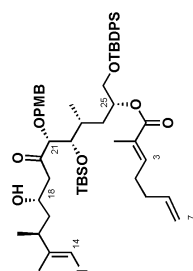


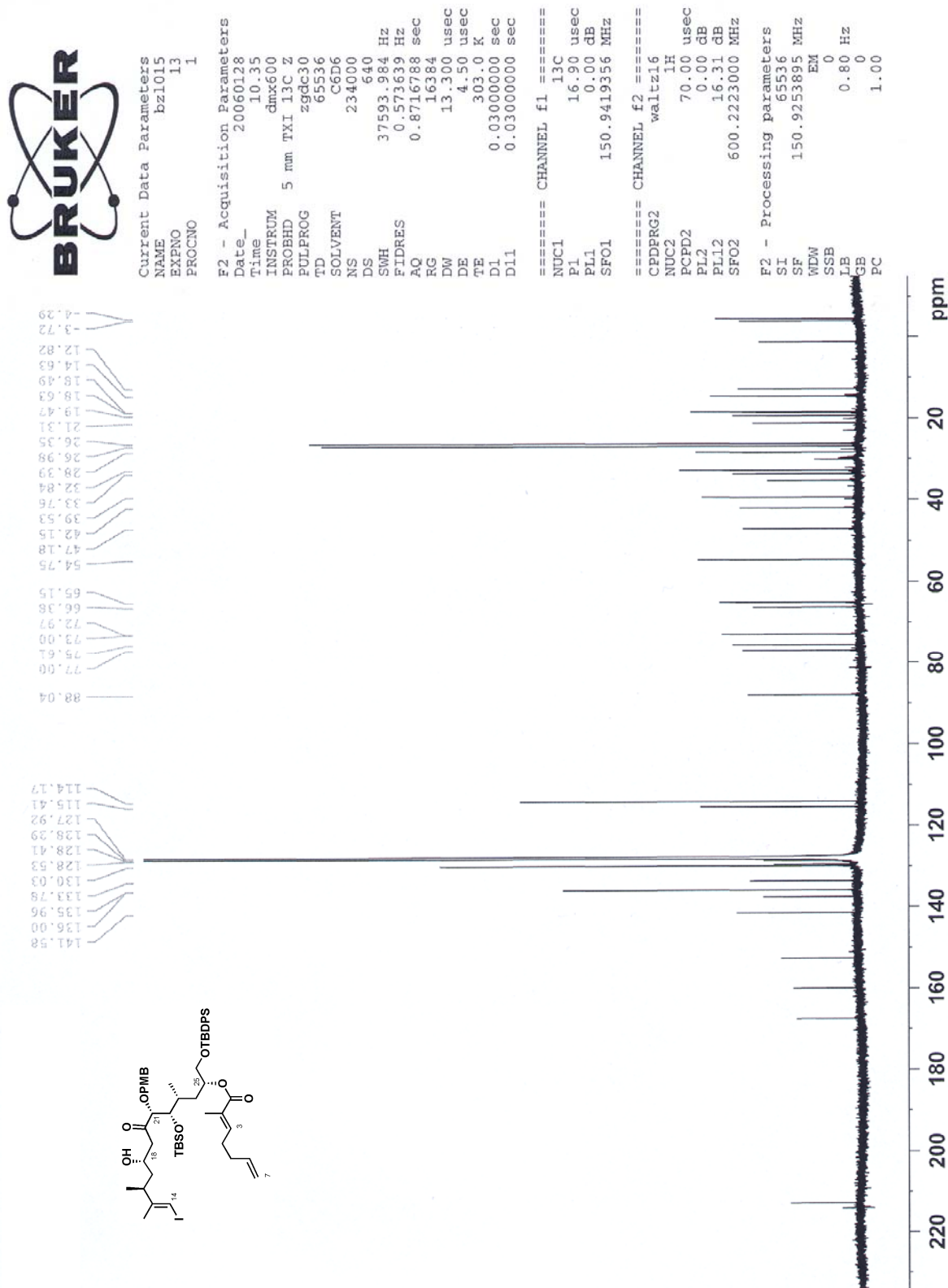
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **39**.

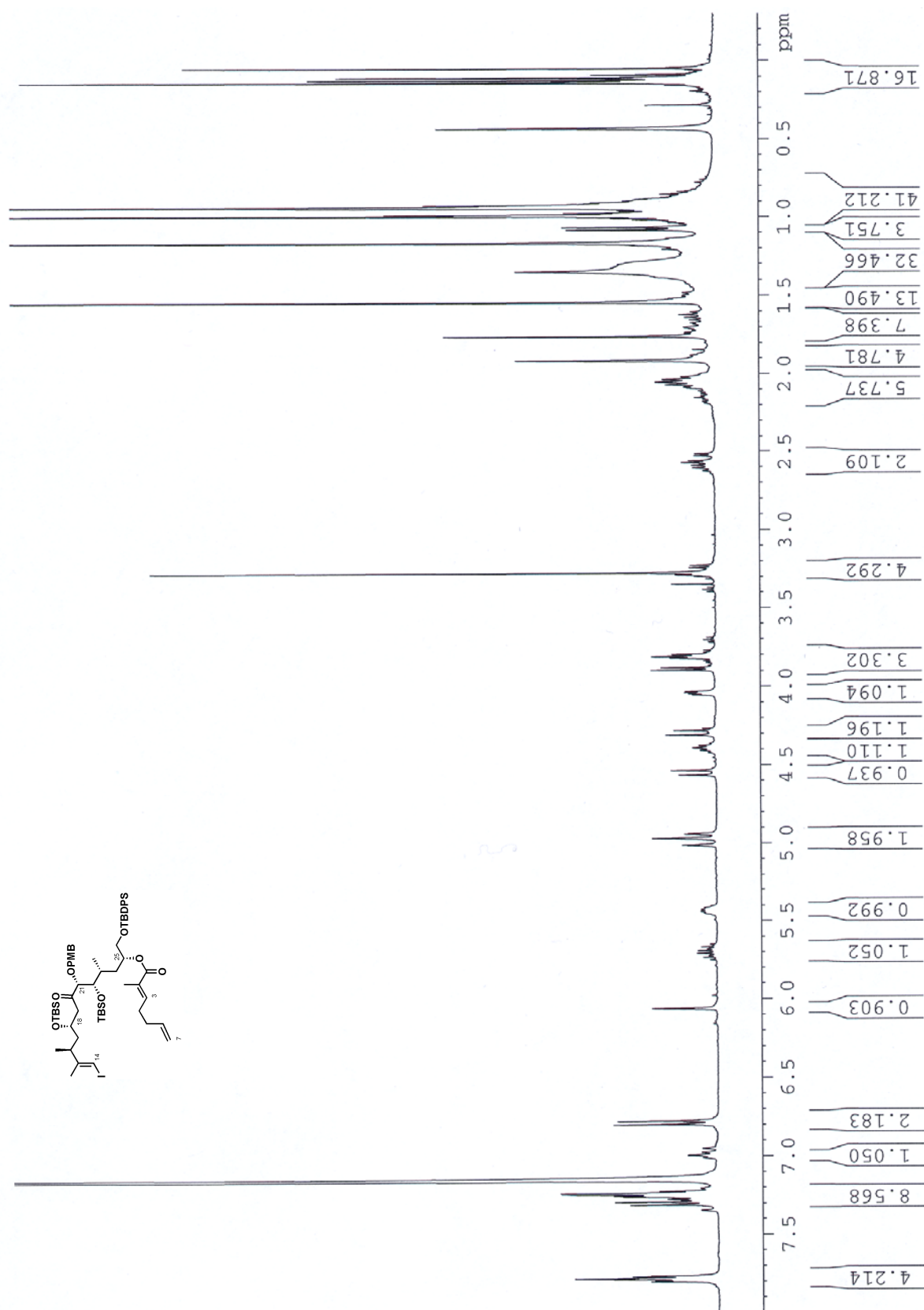


$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **39** (crude)

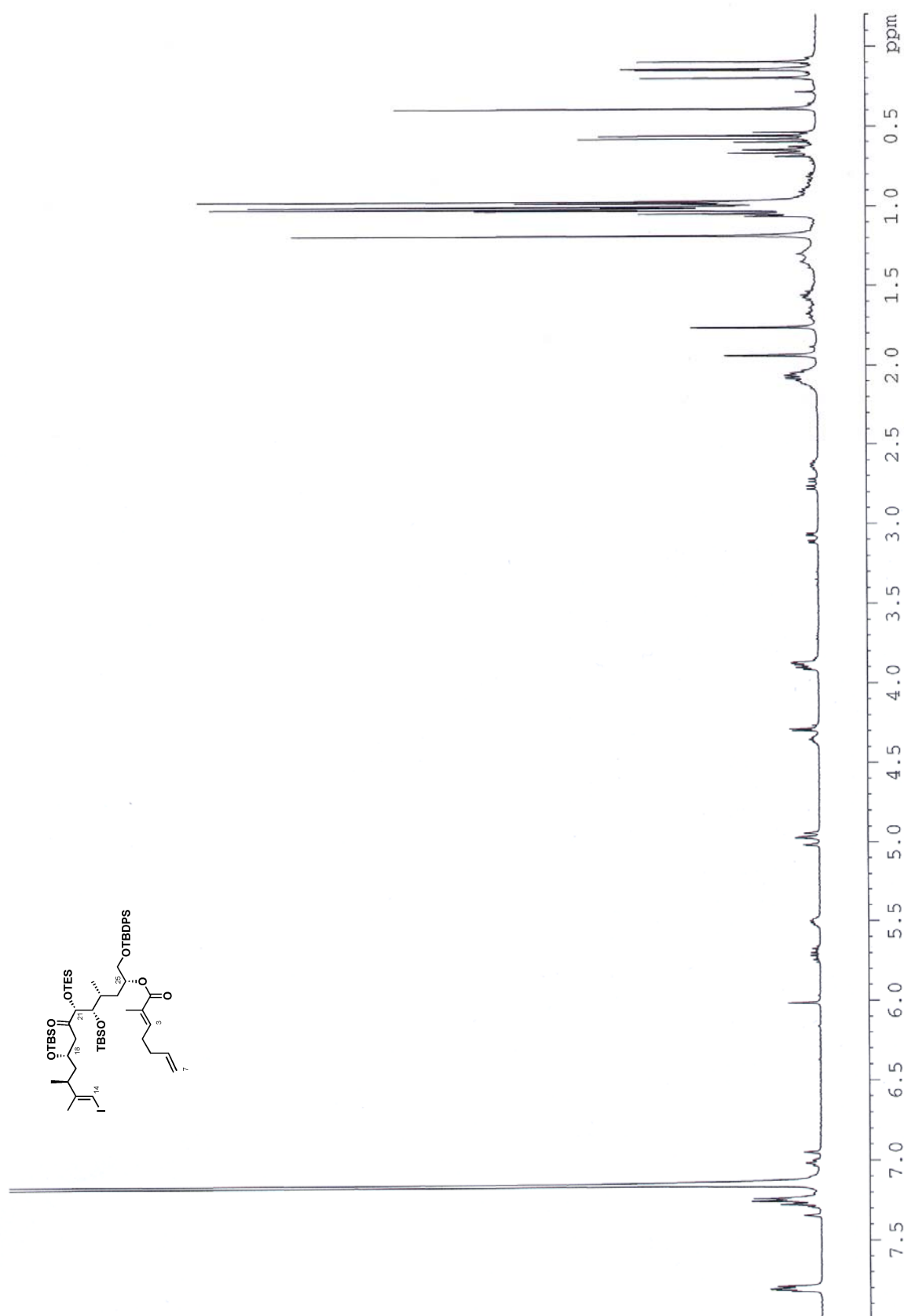
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **42**.

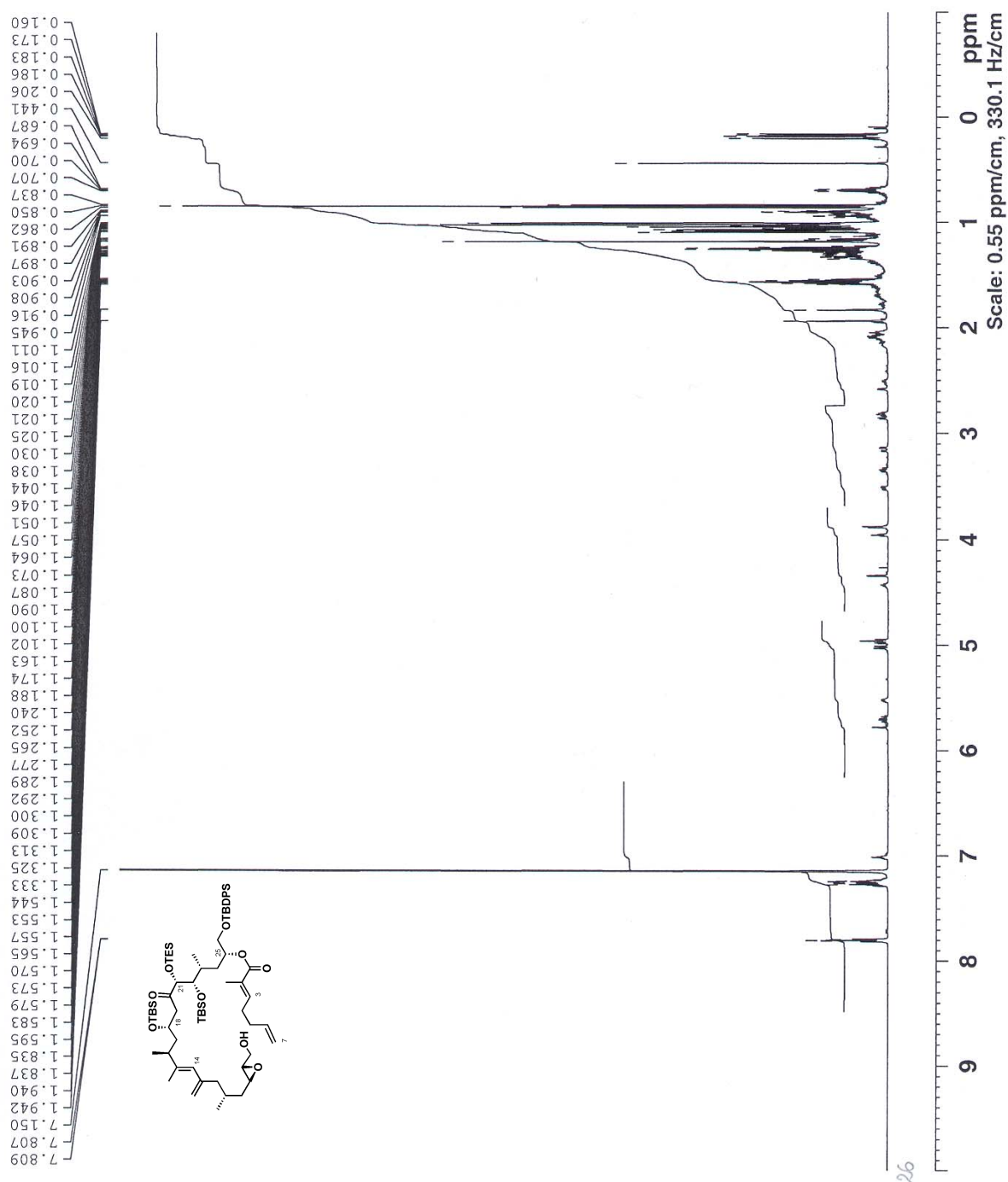
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **42**.

$^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **42**.

$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **43**.

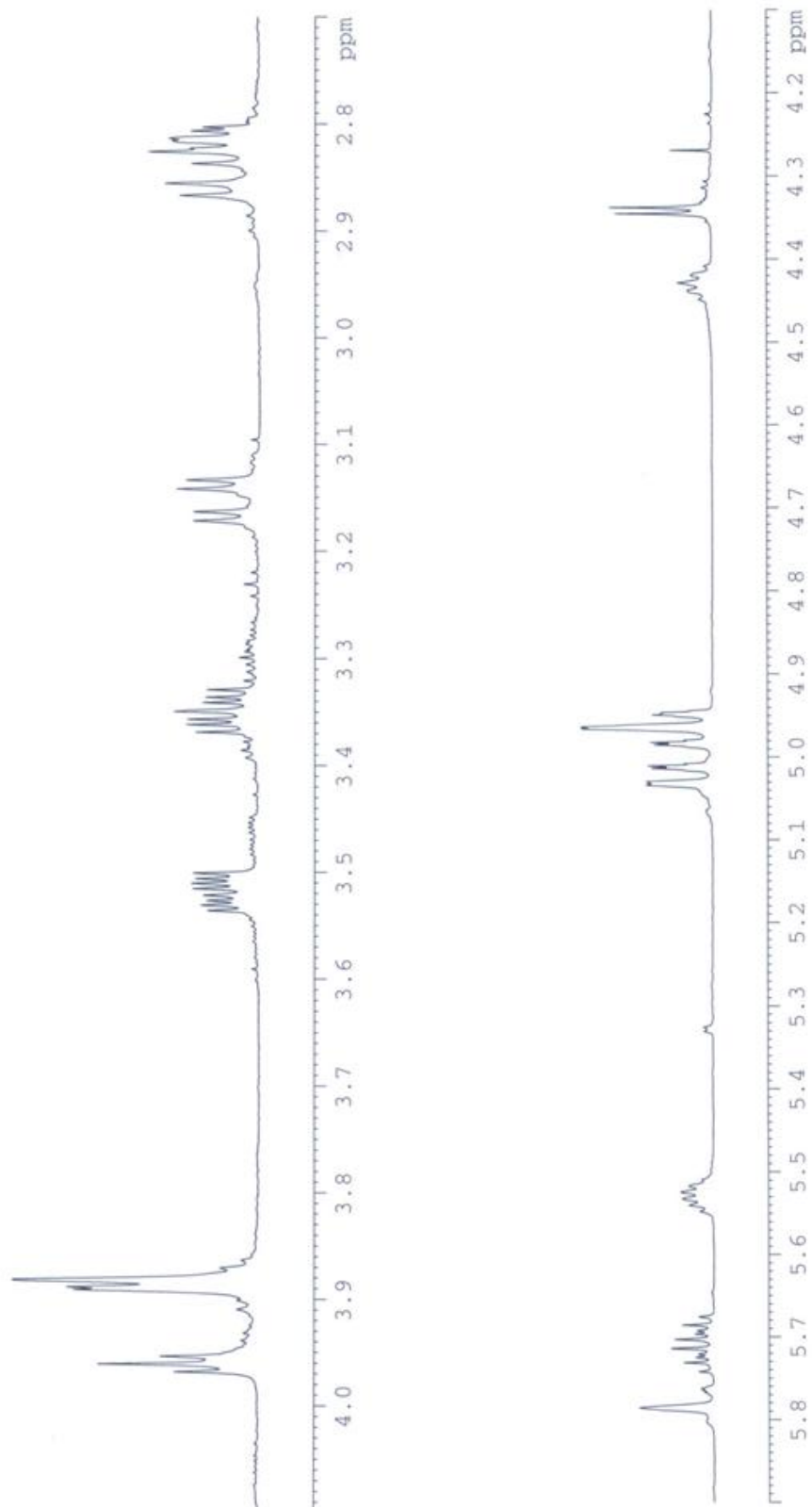
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **44**.



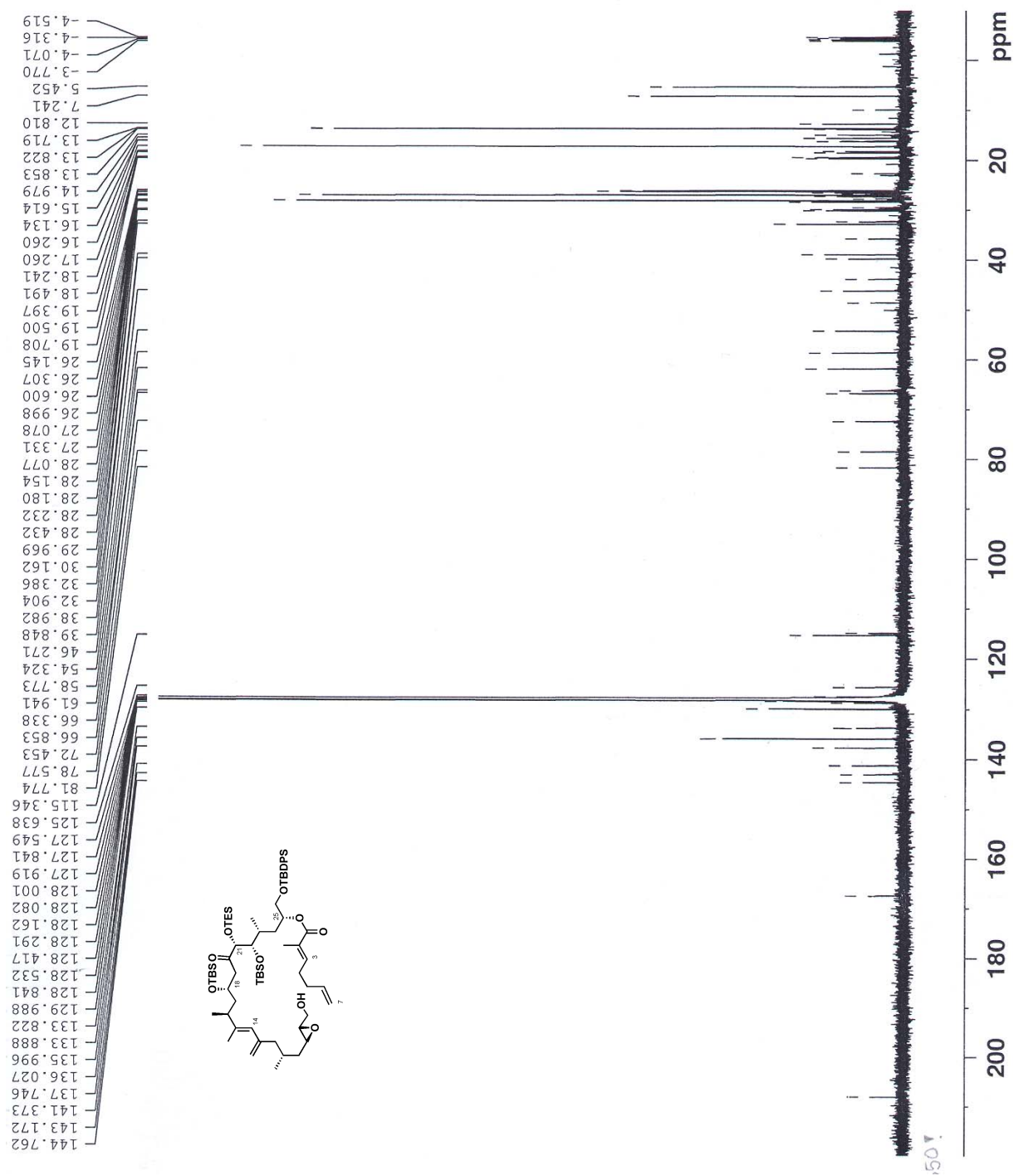
$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **45**.



$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **45**.

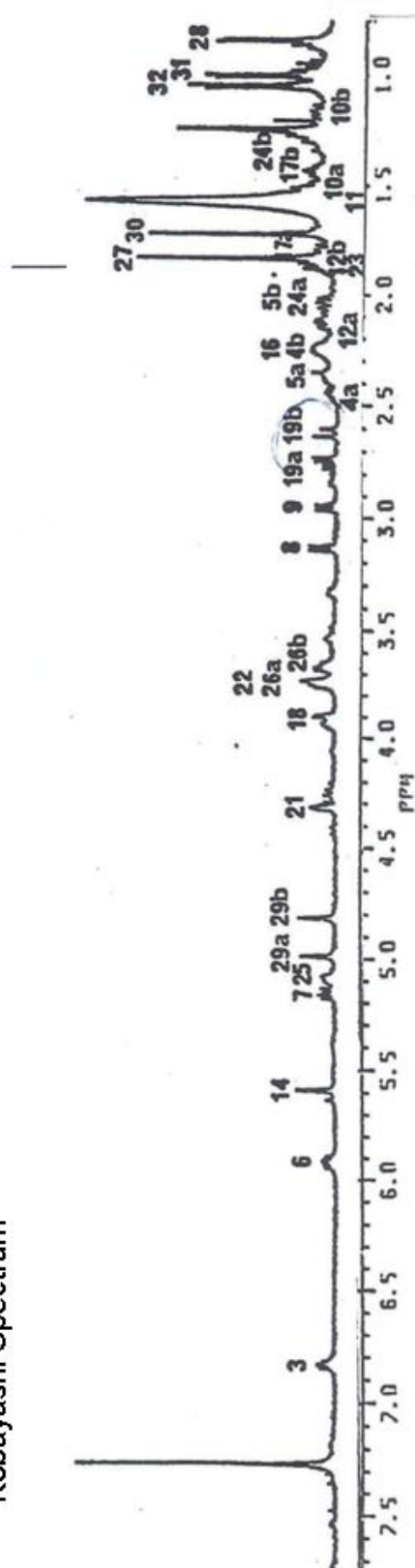




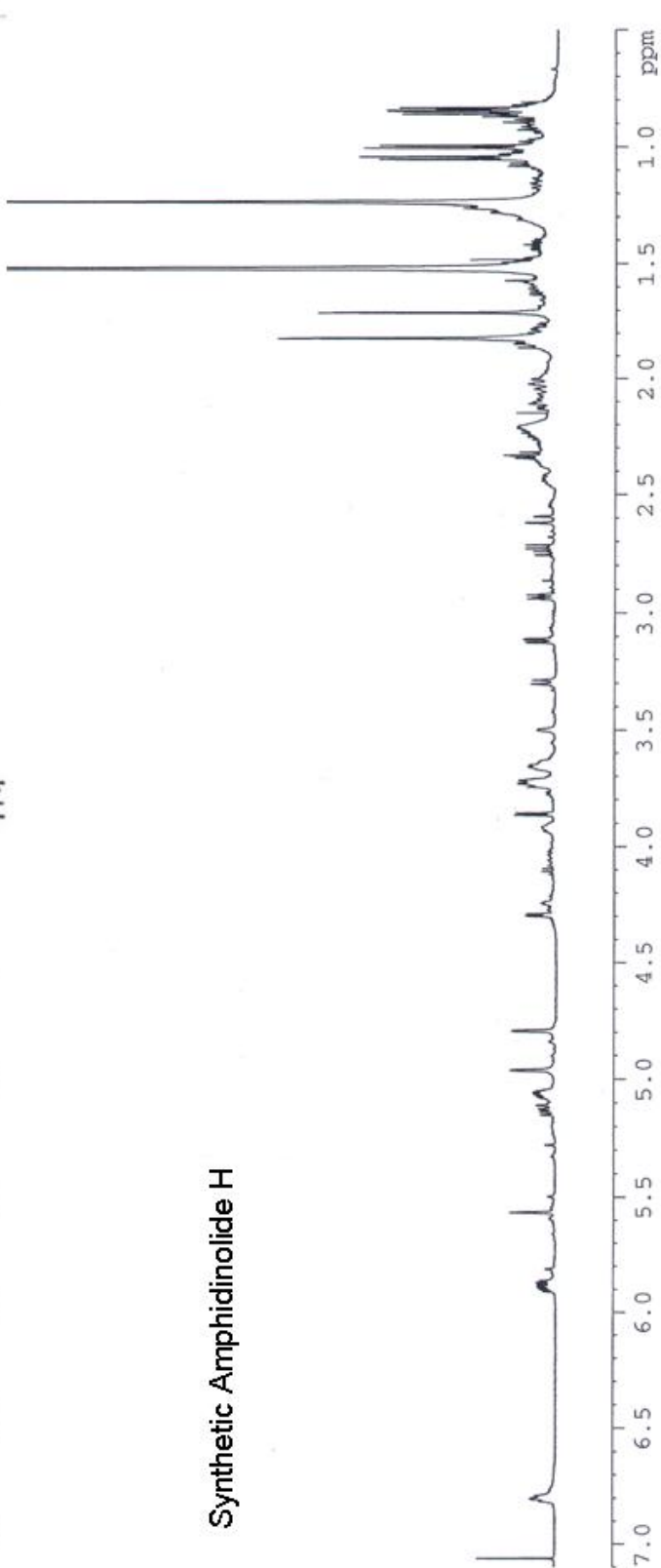
$^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ ) of compound **45**.

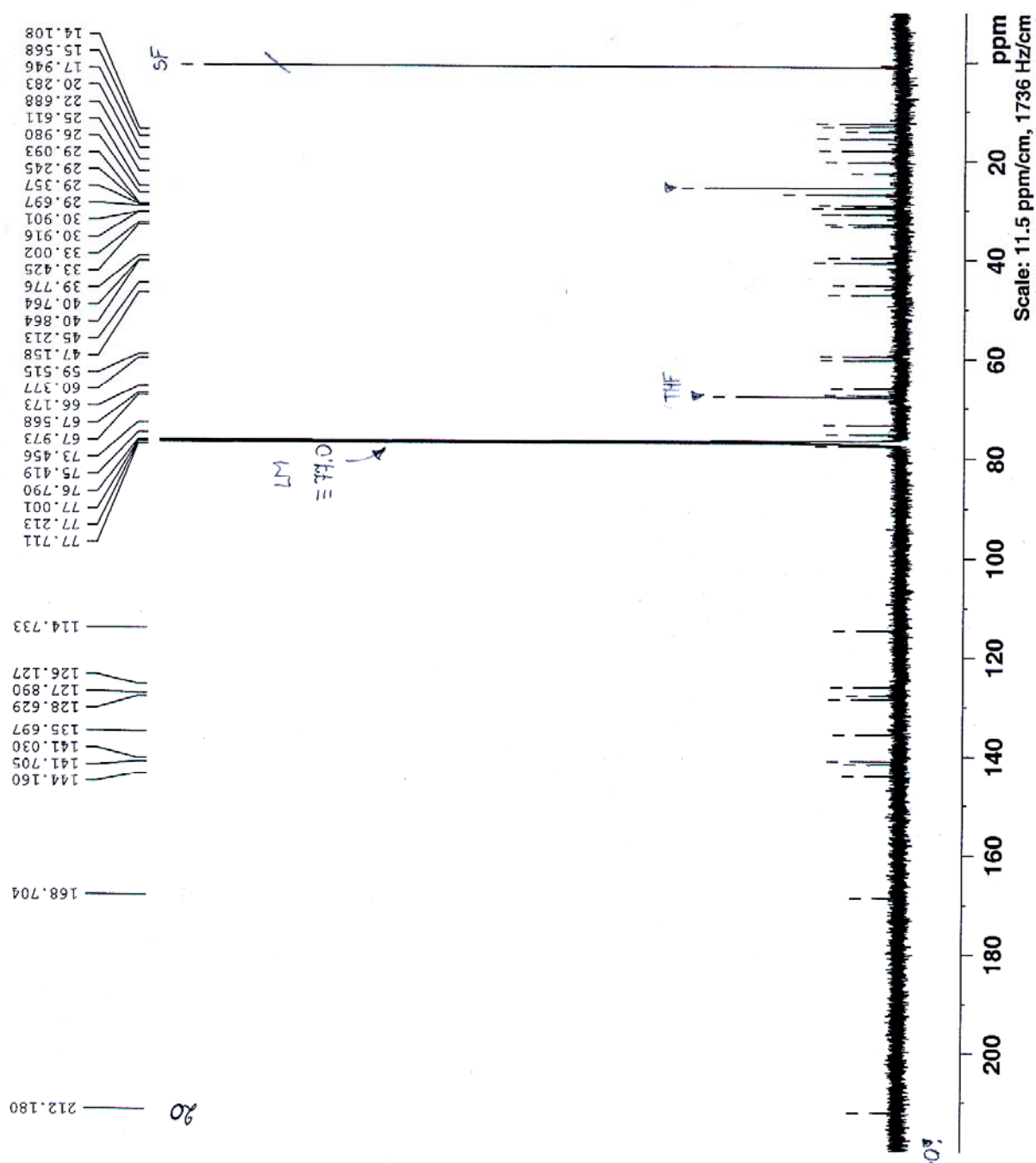
Comparison of  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) of compound **1**.

Kobayashi Spectrum

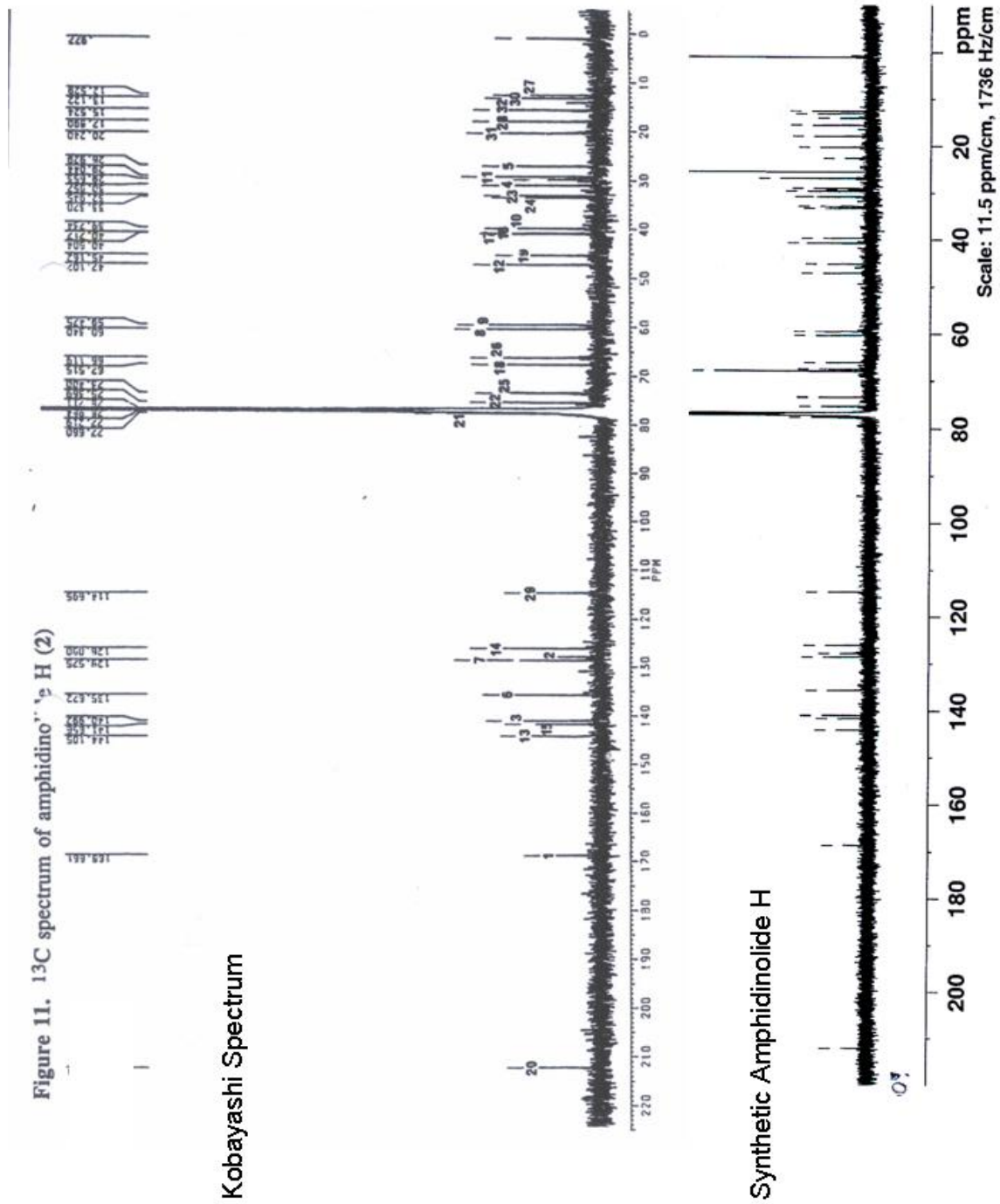


Synthetic Amphidinolide H

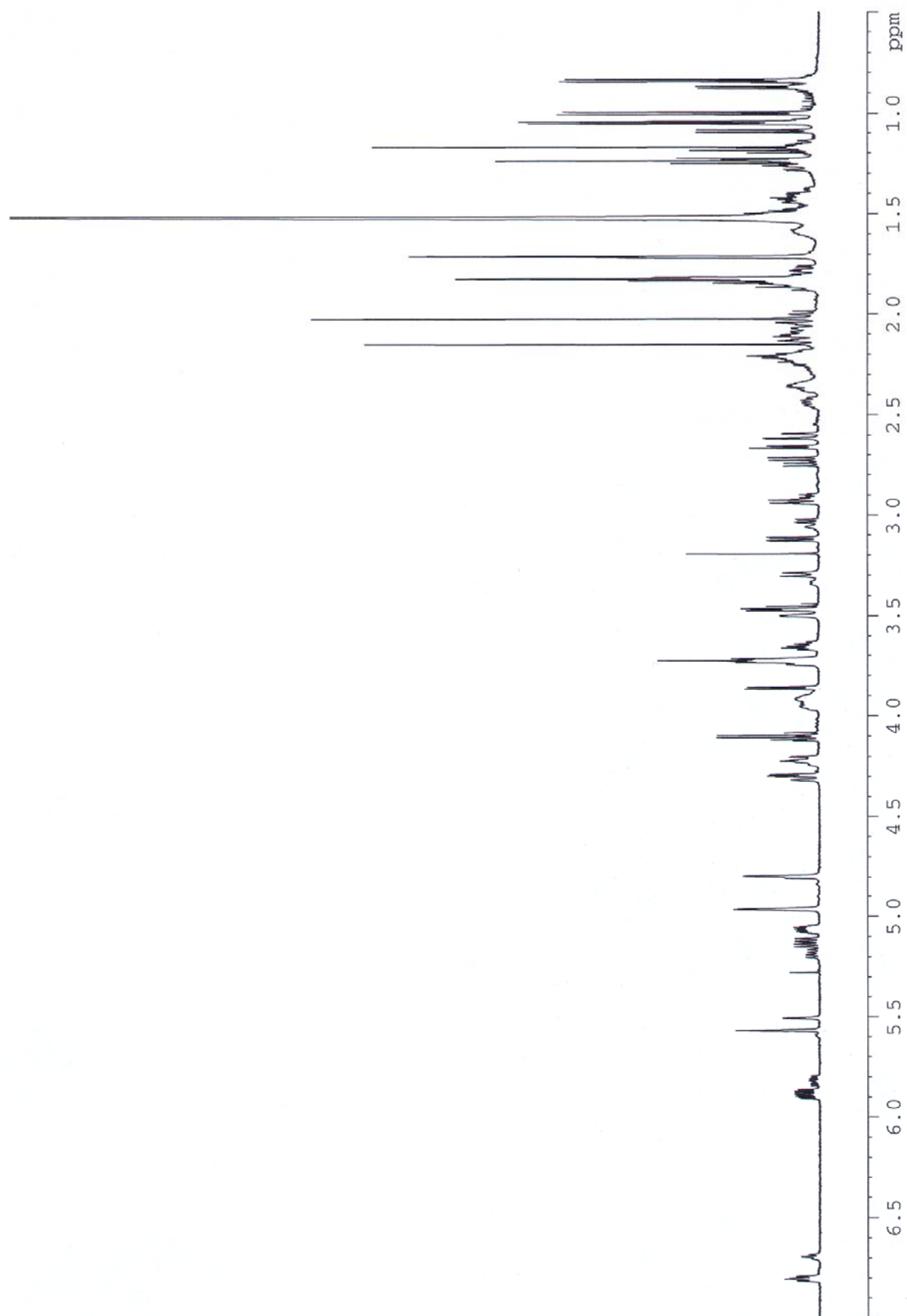


$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **1**.

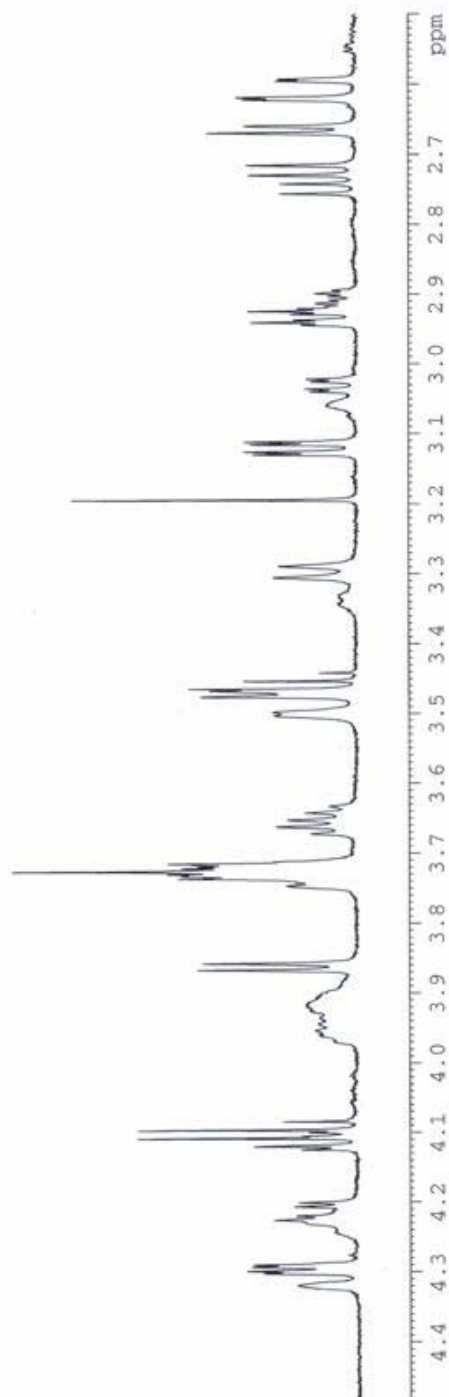
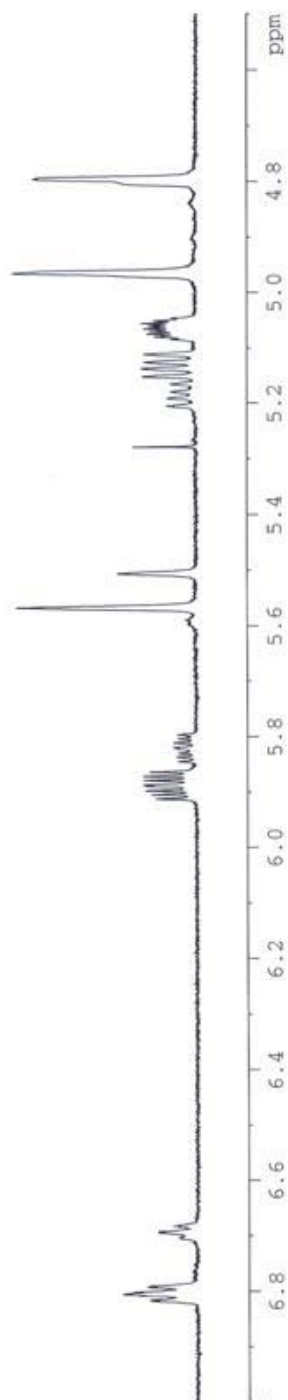
Comparison of  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) of compound **1**.



$^1\text{H}$  NMR ( $\text{CDCl}_3$ )-Equilibration between Amphidinolide H and G.



$^1\text{H}$  NMR ( $\text{CDCl}_3$ )- Equilibration between Amphidinolide H and G.



$^1\text{H}$  NMR ( $\text{CDCl}_3$ ) spectra of the equilibrium mixture of Amphidinolide H/G and of amphidinolide G (ca. 90%) isolated from this mixture by chromatography.

