Stereoselective Synthesis of the Macrocyclic Core (C7-C19) of Carolacton

Gangavaram V. M. Sharma* and Sheri Venkata Reddy*

Organic and Biomolecular Chemistry Division, CSIR-Indian Institute of Chemical Technology

Hyderabad-500 007, India.

Contents **P. No.**

((2*R*,3*R*)-3-(4-(*tert*.-Butyldiphenylsilyloxy)butyl)oxiran-2-yl)methanol (10)

To a stirred mixture of (-)-DIPT (1.24 g, 5.32 mmol) in CH_2Cl_2 (30 mL) at -20 °C containing molecular seives 4 Å (2.0 g), $Ti(O^iPr)_4$ (0.76 mL, 2.66 mmol) and cumene hydroperoxide (4.90 mL, 31.90 mmol) were sequentially added and stirred for 20 min. A solution of allylic alcohol **9a** (9.0 g, 26.62 mmol) in CH_2Cl_2 (60 mL) was added and stirred for 5 h at -20 °C. The reaction mixture was quenched with 10% NaOH in brine solution (45 mL) and stirred for 3 h. It was filtered through a pad of celite and washed with CH_2Cl_2 (200 mL). The organic layer was dried (Na_2SO_4), evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 12% ethyl acetate in pet. ether) to furnish **10** (8.2 g, 87%) as a yellow oil. $[\alpha]_D^{25}$ +38.1 (*c* 0.73, $CHCl_3$); IR (neat): 3450, 3073, 2932, 2859, 1585, 1472, 1427, 1109, 824, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.65-7.59 (m, 4H), 7.39-7.30 (m, 6H), 3.88-3.80 (m, 1H), 3.68-3.61 (m, 2H), 3.60-3.51 (m, 1H), 2.90-2.85 (m, 1H), 2.83-2.79 (m, 1H), 1.62-1.47 (m, 6H), 1.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5, 133.9, 129.5, 127.6, 63.5, 61.6, 58.4, 55.9, 32.1, 31.6, 31.2, 26.8, 22.2; HRMS (ESI): *m/z* calculated for $C_{23}H_{32}O_3NaSi$ $(M+Na)^+$ 407.2018, found 407.2011.

(2*S*,3*S*)-7-(*tert*.-Butyldiphenylsilyloxy)-3-methylheptane-1,2-diol (11)

To a stirred solution of **10** (8.0 g, 22.47 mmol) in dry hexane (80 mL), Me_3Al (33.7 mL, 67.4 mmol, 2 M in toluene) was added at 0 °C and allowed to stir for 10 min. Reaction mixture was quenched with sat. NH_4Cl solution (15 mL) and extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 15% ethyl acetate in pet. ether) to afford **11** (6.70 g, 80%) as a colourless oil. $[\alpha]_D^{25}$ -11.6 (*c* 0.25, $CHCl_3$); IR (neat): 3393, 3071, 2932, 2863, 1462, 1427, 1248, 1109, 824, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.66-7.59 (m, 4H), 7.39-7.30 (m, 6H), 3.67-3.60 (m, 3H), 3.46-3.40 (m, 2H), 2.39-2.04 (bs, 2H), 1.63-1.41 (m, 6H), 1.33-1.23 (m, 1H), 1.04 (s, 9H), 0.86 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5, 134.0, 129.5, 127.5, 64.5, 63.8, 35.0, 32.7, 32.0, 26.8, 23.1, 19.2, 15.1; HRMS (ESI): *m/z* calculated for $C_{24}H_{37}O_3Si$ $(M+H)^+$ 401.2511, found 401.2508. The diastereomeric ratio was measured by HPLC {column: XDB-C 18, 20% water in acetonitrile, flow rate: 1 mL/min, 254 nm, tr (major) = 6.367 min, tr (minor) = 7.261 min}.

(*S*,*E*)-Ethyl 8-(*tert*.-butyldiphenylsilyloxy)-2,4-dimethyloct-2-enoate (12)

To a cooled (0 ^{o}C) solution of **11** (6.70 g, 18.01 mmol) in H_2O:acetone (1:9, 35 mL), $NaIO_4$ (5.89 g, 27.02 mmol) was added and stirred at room temperature for 1 h. Acetone was removed under reduced pressure below 30 ^{o}C and extracted with CH_2Cl_2 (2 x 75 mL). It was washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated under reduced pressure to give aldehyde, which was used as such for further reaction.

To a solution of the above aldehyde (6.0 g, 16.21 mmol) in dry toluene (30 mL) at reflux, $Ph_3P{=}C(Me)CO_2Me$ (6.45 g, 17.83 mmol) was added and stirred at reflux for 1.5 h. The reaction mixture was cooled to room temperature and filtered through a pad of Celite using EtOAc (100 mL), solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 3% ethyl acetate in pet. ether) to furnish ester **12** (6.5 g, 88%) as a yellow oil. $[\alpha]_D^{25}$ +22.7 (*c* 0.57, $CHCl_3$); IR (neat): 3073, 2953, 2932, 2863, 1711, 1649, 1460, 1427, 1387, 1370, 1248, 1190, 1109, 1030, 824, 737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.58 (m, 4H), 7.41-7.29 (m, 6H), 6.46 (d, 1H, *J* = 10.0 Hz), 4.16 (q, 2H, *J* = 7.2, 14.4 Hz), 3.61 (t, 2H, *J* = 6.4 Hz), 2.51-2.39 (m, 1H), 1.81 (s, 3H), 1.58-1.46 (m, 2H), 1.36-1.23 (m, 7H), 1.03 (s, 9H), 0.99 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.5, 148.5, 147.9, 135.5, 134.0, 129.5, 127.6, 63.7, 60.4, 36.5, 33.2, 32.6, 26.8, 23.7, 20.0, 19.2, 14.3, 12.5; HRMS (ESI): *m/z* calculated for $C_{28}H_{41}O_3Si$ $(M+H)^+$ 453.2819, found 453.2820.

(*S*,*E*)-8-(*tert*.-Butyldiphenylsilyloxy)-2,4-dimethyloct-2-en-1-ol (13)

To a stirred solution of **12** (6.5 g, 14.31 mmol) in dry CH_2Cl_2 (50 mL), DIBAL-H (20.3 mL, 28.63 mmol, 20% solution in hexane) was added at 0 ºC and stirred at the same temperature for 2 h. Methanol (10 mL) was added to the reaction mixture at this temperature and stirred for 10 min. The reaction mixture was diluted with EtOAc (20 mL), aq. potassium sodium tartarate (5 mL) and stirred vigorously at room temperature for an additional 1 h. It was filterd through celite and the filtrate dried (Na_2SO_4). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 7% ethyl acetate in pet. ether) to furnish **13** (5.0 g, 85%) as colourless syrup. $[\alpha]_D^{25}$ +17.6 (*c* 0.62,

$CHCl_3$); IR (neat): 2938, 2861, 1649, 1462, 1427, 1111, 1015, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.66-7.59 (m, 4H), 7.41-7.30 (m, 6H), 5.11 (d, 1H, *J* = 10.6 Hz), 3.93 (s, 2H), 3.62 (t, 2H, *J* = 6.4 Hz), 2.40-2.27 (m, 1H), 1.64 (s, 3H), 1.59-1.46 (m, 2H), 1.38-1.15 (m, 4H), 1.03 (s, 9H), 0.91 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5, 134.1, 132.8, 129.5, 127.5, 69.0, 63.9, 37.2, 32.7, 32.0, 26.8, 23.7, 21.0, 19.2, 13.8; HRMS (ESI): *m/z* calculated for $C_{26}H_{39}O_2Si$ $(M+H)^+$ 411.27138, found 411.27133.

***tert*.-Butyl((5*S*,6*S*)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-7-enyloxy)diphenyl-silane (16)**

To a cooled (0 °C) solution of **15** (3.7 g, 8.98 mmol) in dry THF (20 mL), NaH (1.08 g, 26.9 mmol, 60% in wax) was added and stirred for 30 min. A solution of PMBBr (1.98 g, 9.87 mmol) [prepared from *p*-methoxybenzylalcohol (1.36 g, 9.85 mmol) with PBr_3 (0.46 mL, 4.90 mmol) in ether] in dry THF (10 mL) was added and stirred at room temperature for 6 h. The reaction mixture was treated with aq. NH_4Cl (10 mL) and extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with water (2 x 30 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated under reduced pressure and purified the residue by column chromatography (60-120 mesh Silica gel, 3% ethyl acetate in pet. ether) to give **16** (4.2 g, 88%) as a yellow liquid. $[\alpha]_D^{25}$ -55.74 (*c* 0.49, $CHCl_3$); IR (neat): 3069, 2932, 2857, 1645, 1616, 1514, 1458, 1248, 1109, 824, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.83-7.59 (m, 4H), 7.40-7.29 (m, 6H), 7.15 (d, 2H, *J* = 8.5 Hz), 6.77 (d, 2H, *J* = 8.5 Hz), 4.97 (s, 1H), 4.83 (s, 1H), 4.38 (d, 1H, *J* = 11.5 Hz), 4.08 (d, 1H, *J* = 11.5 Hz), 3.76 (s, 3H), 3.66-3.57 (m, 2H), 3.24 (d, 1H, *J* = 9.07), 1.74-1.46 (m, 2H), 1.65 (s, 3H), 1.31-1.19 (m, 3H), 1.03 (s, 9H), 0.94-0.81 (m. 2H), 0.70 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 143.7, 135.6, 134.2, 131.0, 129.4, 127.5, 114.9, 113.6, 87.8, 69.6, 64.1, 55.2, 34.9, 33.1, 32.5, 26.9, 22.9, 19.2, 16.6, 15.7; HRMS (ESI): *m/z* calculated for $C_{34}H_{46}O_3NaSi$ $(M+Na)^+$ 553.3113, found 553.3096.

(5*S*,6*S*)-6-(4-Methoxybenzyloxy)-5,7-dimethyloct-7-en-1-ol (8)

To a stirred solution of **16** (4.2 g, 7.89 mmol) in anhydrous THF (4 mL), TBAF (8.7 mL, 8.68 mmol, 1.0 M solution in THF) was added at 0 ^oC and stirred at room temperature for 3 h. The reaction mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried (Na_2SO_4). Solvent was evaporated and purified the residue

by column chromatography (60-120 mesh Silica gel, 15% ethyl acetate in pet. ether) to afford **8** (2.0 g, 86%) as a colorless oil. $[\alpha]_D^{25}$ -88.76 (*c* 0.93, $CHCl_3$); IR (neat): 3414, 2936, 1711, 1613, 1514, 1462, 1377, 1300, 1250, 1173, 1069, 1036, 901, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, 2H, *J* = 8.7 Hz), 6.81 (d, 2H, *J* = 8.7 Hz), 4.99 (s, 1H), 4.84 (s, 1H), 4.40 (d, 1H, *J* = 11.3 Hz), 4.09 (d, 1H, *J* = 11.3 Hz), 3.78 (s, 3H), 3.62-3.51 (m, 2H), 3.26 (d, 1H, *J* = 9.07), 1.65 (s, 3H), 1.59-1.00 (m, 6H), 0.72 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 143.5, 130.8, 129.4, 115.0, 113.6, 87.6, 69.5, 62.8, 55.2, 34.7, 33.0, 32.4, 22.7, 16.5, 15.7; HRMS (ESI): *m/z* calculated for $C_{18}H_{29}O_3$ $(M+H)^+$ 293.2116, found 293.2126.

(7*S*,8*S*,*E*)-Methyl 8-(4-methoxybenzyloxy)-7,9-dimethyldeca-2,9-dienoate (17)

To a solution of oxalyl chloride (0.92 mL, 7.48 mmol) in dry CH_2Cl_2 (4 mL) at -78 °C, dry DMSO (1.2 mL, 14.96 mmol) was added dropwise and stirred for 10 min. A solution of **8** (2.0 g, 6.80 mmol) in dry CH_2Cl_2 (10 mL) was added and stirred for 3 h at -78 °C. It was quenched with Et_3N (5.7 mL, 40.81 mmol) and diluted with CH_2Cl_2 (20 mL). The reaction mixture was washed with water (10 mL), brine (10mL) and dried (Na_2SO_4). Solvent was evaporated to furnish the corresponding aldehyde (1.9 g) as a pale yellow liquid, which was used directly for the next step without further purification.

A solution of the above aldehyde (1.9 g, 6.50 mmol) in benzene (10 mL) was added to a solution of (methoxycarbonylmethylene)triphenyl phosphorane (2.5 g, 7.21 mmol) in benzene (10 mL) at reflux. After 5 h, solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 3% ethyl acetate in pet. ether) to give **17** (2.1 g, 93%) as a colorless oil. $[\alpha]_D^{25}$ -81.3 (*c* 0.755, $CHCl_3$); IR (neat): 3441, 2944, 1721, 1651, 1607, 1514, 1456, 1437, 1256, 1165, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.16 (d, 2H, *J* = 8.7 Hz), 6.97-6.86 (m, 1H), 6.80 (d, 2H, *J* = 8.7 Hz), 5.76 (d, 1H, *J* = 15.5 Hz), 4.99 (s, 1H), 4.84 (s, 1H), 4.40 (d, 1H, *J* = 11.3 Hz), 4.08 (d, 1H, *J* = 11.3 Hz), 3.79 (s, 3H), 3.71 (s, 3H), 3.24 (d, 1H, *J* = 9.07), 2.25-2.09 (m, 2H), 1.65 (s, 3H), 1.48-1.24 (m, 4H), 1.17-1.04 (m, 1H), 0.72 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 159.0, 149.8, 143.4, 130.8, 129.5, 120.7, 115.1, 113.6, 87.4, 69.5, 55.2, 51.3, 34.7, 32.6, 32.4, 25.1, 16.5, 15.8; HRMS (ESI): *m/z* calculated for $C_{21}H_{30}O_4Na$ $(M+Na)^+$ 369.2041, found 369.2059.

(7*S*,8*S*,*E*)-8-(4-Methoxybenzyloxy)-7,9-dimethyldeca-2,9-dien-1-ol (**18**)

To a stirred solution of **17** (2.1 g, 6.03 mmol) in dry CH_2Cl_2 (20 mL), DIBAL-H (8.6 mL, 12.06 mmol, 20% solution in hexane) was added at 0 ºC and stirred at the same temperature for 4 h. Work up as described for **13** and purification of the residue by column chromatography (60-120 mesh Silica gel, 12% ethyl acetate in pet. ether) afforded **18** (1.8 g, 91%) as colorless syrup. $[\alpha]_D^{25}$ -89.4 (*c* 0.59, $CHCl_3$); IR (neat): 3437, 2934, 1715, 1612, 1514, 1462, 1250, 1171, 1034, 824 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, 2H, *J* = 8.7 Hz), 6.81 (d, 2H, *J* = 8.7 Hz), 5.63-5.55 (m, 2H), 4.99 (s, 1H), 4.83 (s, 1H), 4.39 (d, 1H, *J* = 11.3 Hz), 4.08 (d, 1H, *J* = 11.3 Hz), 4.04-3.99 (m, 2H), 3.79 (s, 3H), 3.25 (d, 1H, *J* = 9.1 Hz), 2.05-1.92 (m, 2H), 1.77-1.54 (m, 1H), 1.65 (s, 3H), 1.46-1.20 (m, 4H), 0.70 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 143.5, 133.4, 130.9, 129.5, 128.8, 115.0, 113.6, 87.6, 69.5, 63.8, 55.2, 34.6, 32.5, 32.2, 26.0, 16.5, 15.8; HRMS (ESI): *m/z* calculated for $C_{20}H_{31}O_3$ $(M+H)^+$ 319.22677, found 319.22675.

((2*S*,3*S*)-3-((4*S*,5*S*)-5-(4-Methoxybenzyloxy)-4,6-dimethylhept-6-enyl)oxiran-2-yl)methanol (**19**)

To a stirred mixture of (+)-DIPT (0.26 g, 1.13 mmol) in CH_2Cl_2 (5 mL) at -20 °C containing molecular seives 4 Å (0.5 g), $Ti(O^iPr)_4$ (0.16 mL, 0.57 mmol) and cumene hydroperoxide (1.0 mL, 6.75 mmol) were added sequentially and stirred for 20 min. A solution of allylic alcohol **18** (1.8 g, 5.62 mmol) in CH_2Cl_2 (10 mL) was added and stirred for 5 h at -20 °C. Work up as described for **10** and purification of the residue by column chromatography (60-120 mesh Silica gel, 20% ethyl acetate in pet. ether) gave **19** (1.7 g, 90%) as a yellow oil. $[\alpha]_D^{25}$ -119.16 (*c* 0.44, $CHCl_3$); IR (neat): 3468, 3069, 2934, 2863, 1717, 1649, 1612, 1514, 1460, 1375, 1300, 1248, 1175, 1069, 1036, 897, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, 2H, *J* = 8.7 Hz), 6.81 (d, 2H, *J* = 8.7 Hz), 5.00 (s, 1H), 4.84 (s, 1H), 4.40 (d, 1H, *J* = 11.7 Hz), 4.09 (d, 1H, *J* = 11.7 Hz), 3.82-3.75 (m, 1H), 3.79 (s, 3H), 3.59-3.50 (m, 1H), 3.26 (d, 1H, *J* = 9.1 Hz), 2.88-2.78 (m, 2H), 1.80-1.05 (m, 7H), 1.66 (s, 3H), 0.72 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 143.4, 130.8, 129.5, 115.1, 113.6, 87.5, 69.5, 61.7, 58.6, 56.0, 55.2, 34.5, 32.3, 31.7, 22.8, 16.5, 15.7; HRMS (ESI): *m/z* calculated for $C_{20}H_{30}O_4Na$ $(M+Na)^+$ 357.2041, found 357.2057. The diastereomeric ratio was measured by HPLC {column: XDB-C 18, 15% water in acetonitrile, flow rate: 1 mL/min, 254 nm, tr(major) = 6.311 min, tr(minor) = 8.014 min}.

(2*R*,3*R*,7*S*,8*S*)-8-(4-Methoxybenzyloxy)-3,7,9-trimethyldec-9-ene-1,2-diol (20)

To a stirred solution of **19** (1.7 g, 5.06 mmol) in dry hexane (20 mL), Me_3Al (7.6 mL, 15.17 mmol, 2 M in toluene) was added at 0 ^oC and allowed to stir for 10 min. Work up as described for **11** and purification of the residue by column chromatography (60-120 mesh Silica gel, 22% ethyl acetate in pet. ether) furnished **20** (1.4 g, 79%) as a colourless oil. $[\alpha]_D^{25}$ -65.0 (*c* 0.63, $CHCl_3$); IR (neat): 3395, 2921, 2852, 1612, 1514, 1463, 1214, 1037, 822, 752, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, 2H, *J* = 8.3 Hz), 6.18 (d, 2H, *J* = 8.3 Hz), 4.99 (s, 1H), 4.84 (s, 1H), 4.40 (d, 1H, *J* = 11.7 Hz), 4.09 (d, 1H, *J* = 11.7 Hz), 3.79 (s, 3H), 3.61 (m, 1H), 3.48-3.38 (m, 2H), 3.26 (d, 1H, *J* = 9.1 Hz), 1.65 (s, 3H), 1.75-1.38 (m, 5H), 1.31-1.23 (m, 1H), 1.18-1.0 (m, 2H), 0.85 (d, 3H, *J* = 6.4 Hz), 0.70 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 143.5, 130.8, 129.5, 115.1, 113.6, 87.7, 76.1, 69.6, 64.5, 55.2, 36.2, 34.7, 33.1, 32.8, 23.9, 16.5, 15.9, 15.2; HRMS (ESI): *m/z* calculated for $C_{21}H_{34}O_4Na$ $(M+Na)^+$ 373.2354, found 373.2356. The diastereomeric ratio was measured by HPLC {column: XDB-C 18, 20% water in acetonitrile, flow rate: 1 mL/min, 254 nm, tr (major) = 7.286 min, tr (minor) = 6.878 min}.

1-Methoxy-4-(((3*S*,4*S*,8*R*)-2,4,8-trimethyldeca-1,9-dien-3-yloxy)methyl)benzene (21)

To a stirred solution of **20** (1.40 g, 3.98 mmol) in dry CH_2Cl_2 (20 mL), Ph_3P (4.17 g, 15.90 mmol), imidazole (1.08 g, 15.90 mmol) and I_2 (3.0 g, 11.93 mmol) were added at 0 ^oC and allowed to stir for 30 min. The reaction mixture was quenched with sat. NaOH (5 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 3% ethyl acetate in pet. ether) to give **21** (0.80 g, 63%) as a colourless oil. $[\alpha]_D^{25}$ -81.12 (*c* 0.32,5 $CHCl_3$); IR (neat): 3451, 2924, 2856, 1615, 1513, 1456, 1247, 1072, 905, 818, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.20 (d, 2H, *J* = 8.3 Hz), 6.82 (d, 2H, *J* = 8.3 Hz), 5.72-5.58 (m, 1H), 5.03-4.83 (m, 4H), 4.41 (d, 1H, *J* = 11.7 Hz), 4.11 (d, 1H, *J* = 11.7 Hz), 3.80 (s, 3H), 3.26 (d, 1H, *J* = 9.1 Hz), 2.15-2.02 (m, 1H), 1.76-1.55 (m, 6H), 1.35-1.15 (m, 4H), 0.99 (d, 3H, *J* = 6.8 Hz), 0.72 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 145.0, 143.7, 131.0, 129.5, 115.0, 113.6, 112.2, 87.8, 69.6, 55.2, 37.8, 37.1, 34.8, 32.9, 24.3, 20.3, 16.6, 15.8; HRMS (ESI): *m/z* calculated for $C_{21}H_{33}O_2Na$ $(M+H)^+$ 314.24751, found 314.24765.

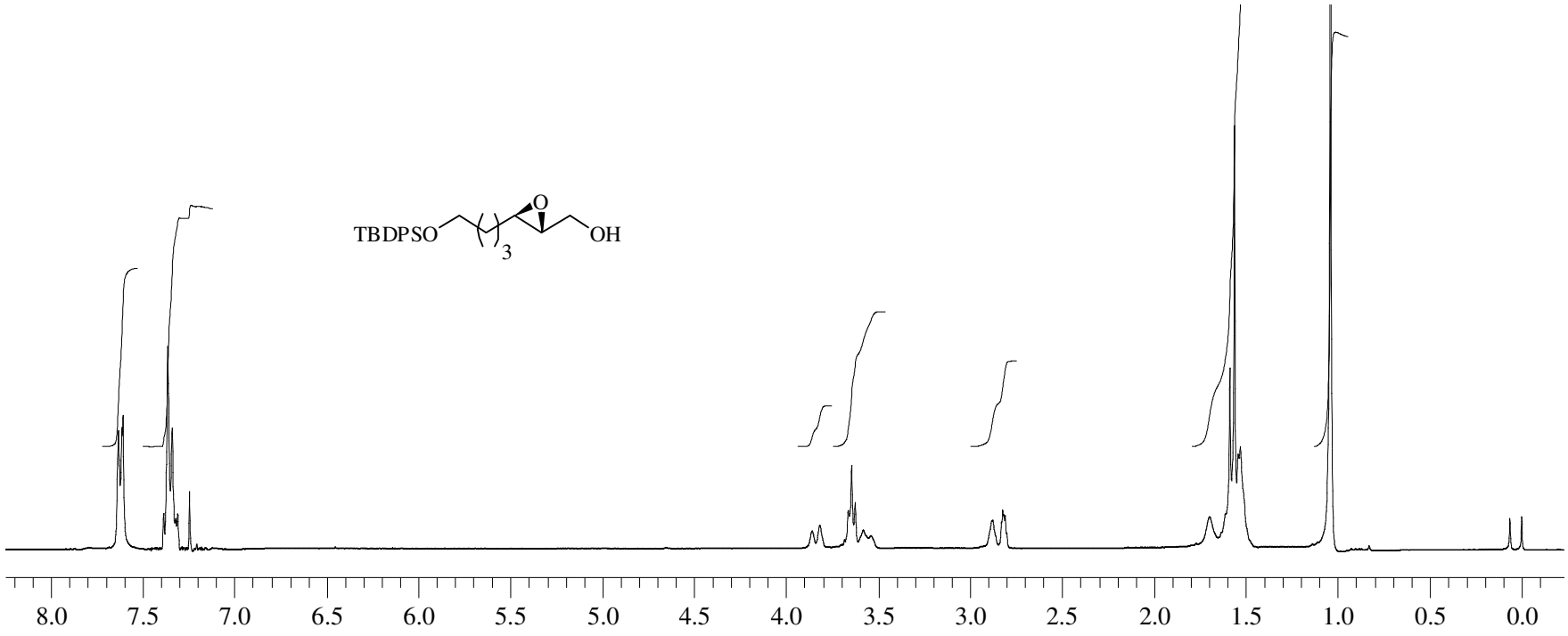


Figure 1: ^{1}H NMR Spectrum of compound **10** ($CDCl_3$, 300 MHz).

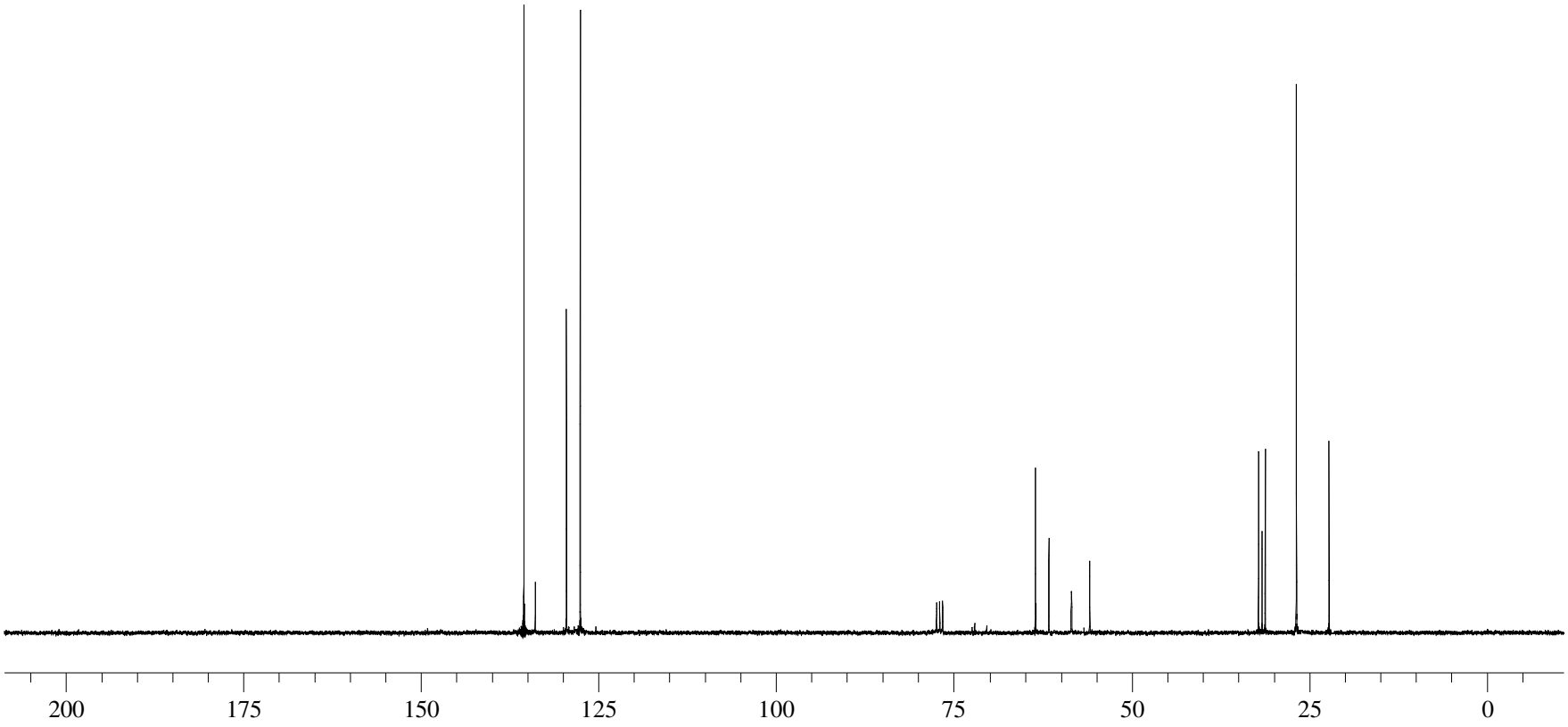


Figure 2: ^{13}C NMR Spectrum of compound **10** ($CDCl_3$, 125 MHz).

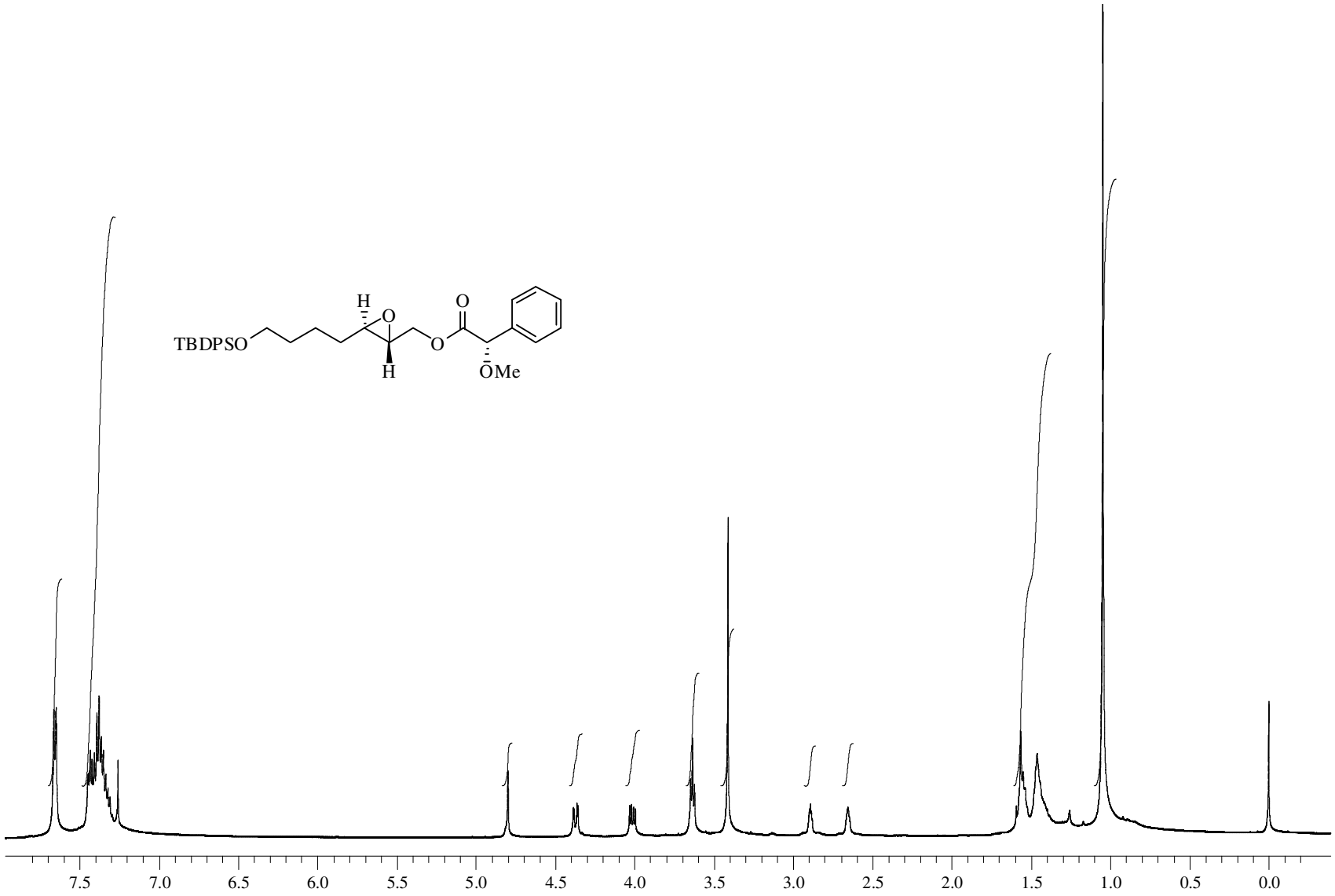


Figure 2a: ^{1}H NMR Spectrum of (*S*)-Moscher ester of **10** (500 MHz, $CDCl_3$)

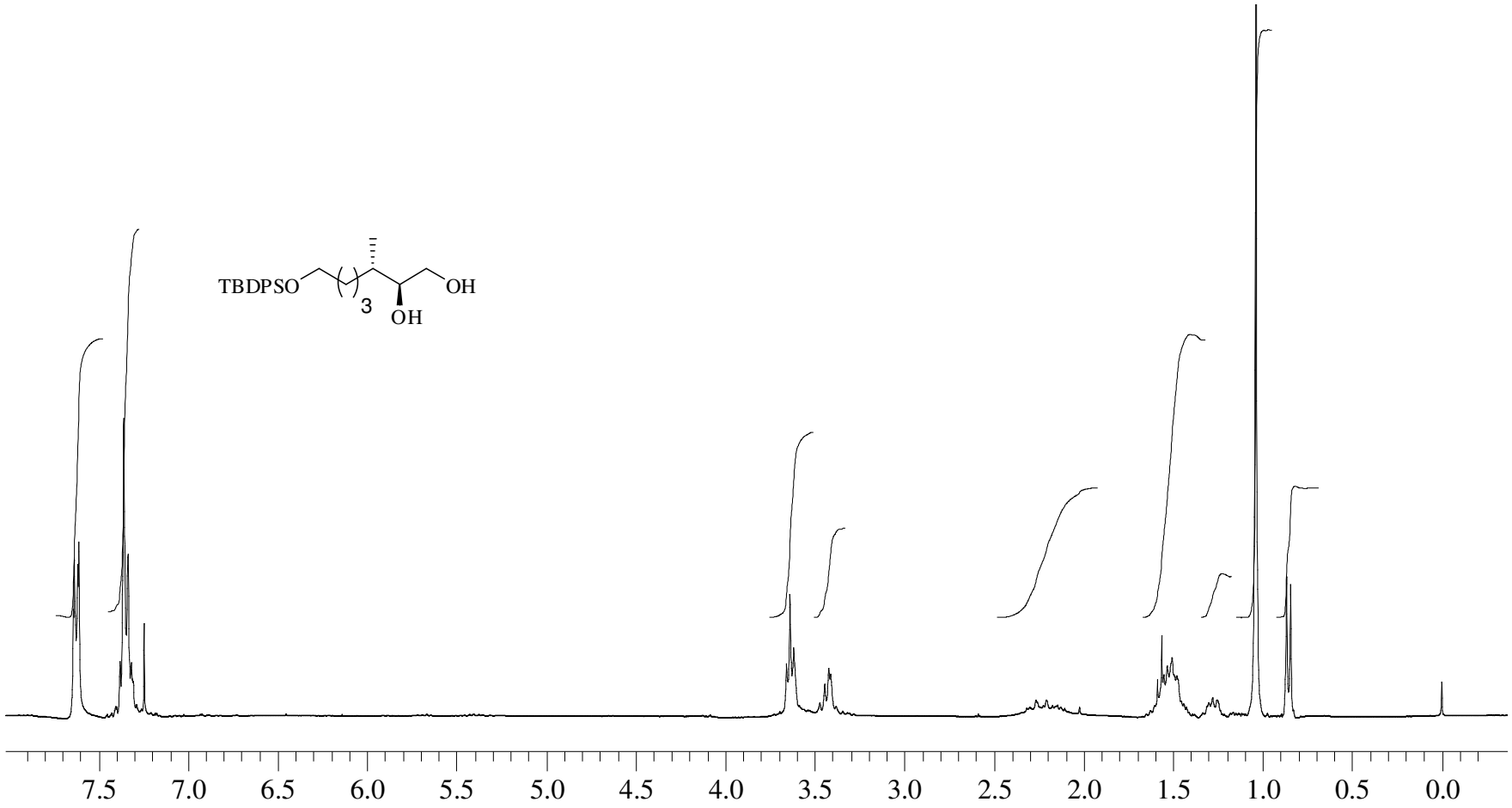


Figure 3: ^{1}H NMR Spectrum of compound **11** ($CDCl_3$, 300 MHz).

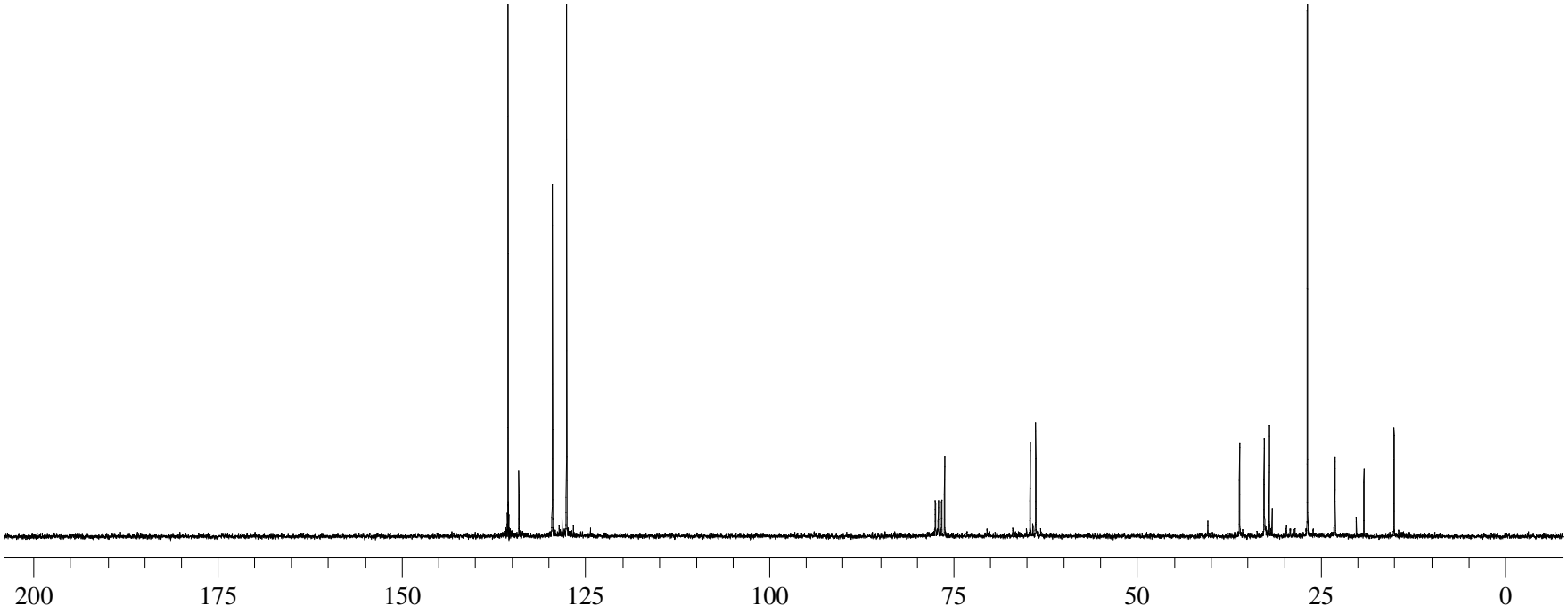
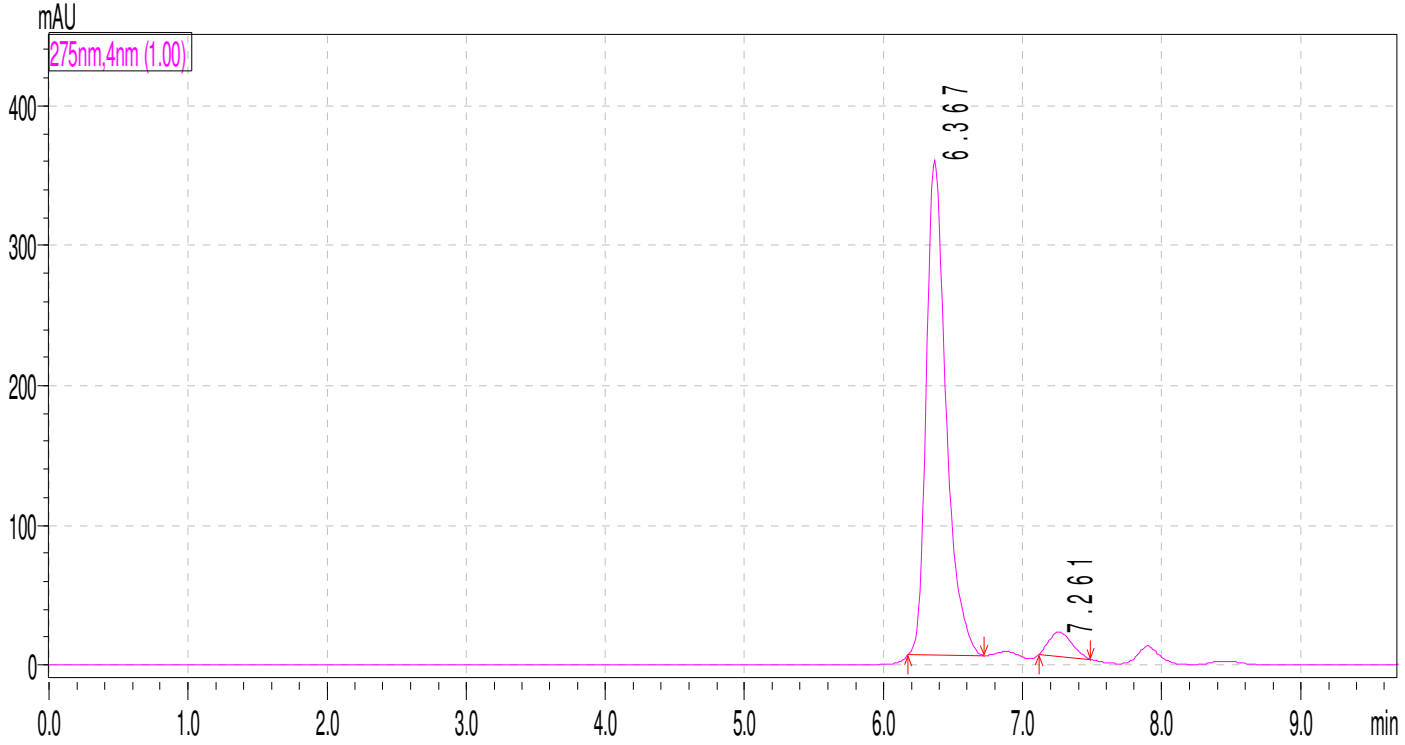


Figure 4: ^{13}C NMR Spectrum of compound **11** ($CDCl_3$, 125 MHz).



Peak	Ret. Time	Area	Height	Area%
1	6.367	3483736	354032	94.578
2	7.261	199728	17448	5.422
Total		3683464	371480	100.000

Figure 4a: HPLC Spectrum of compound **11**

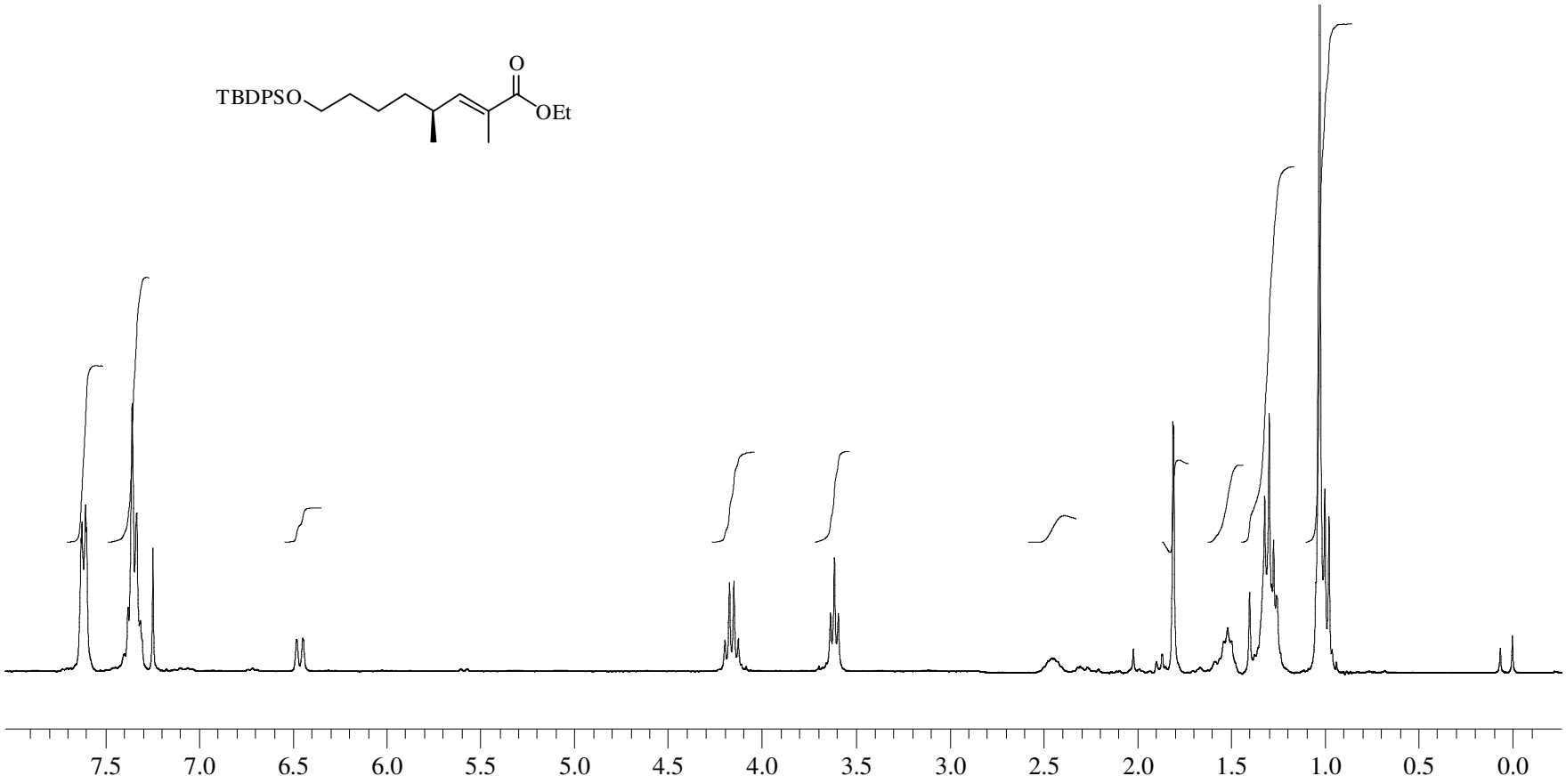


Figure 5: ^{1}H NMR Spectrum of compound **12** ($CDCl_3$, 300 MHz).

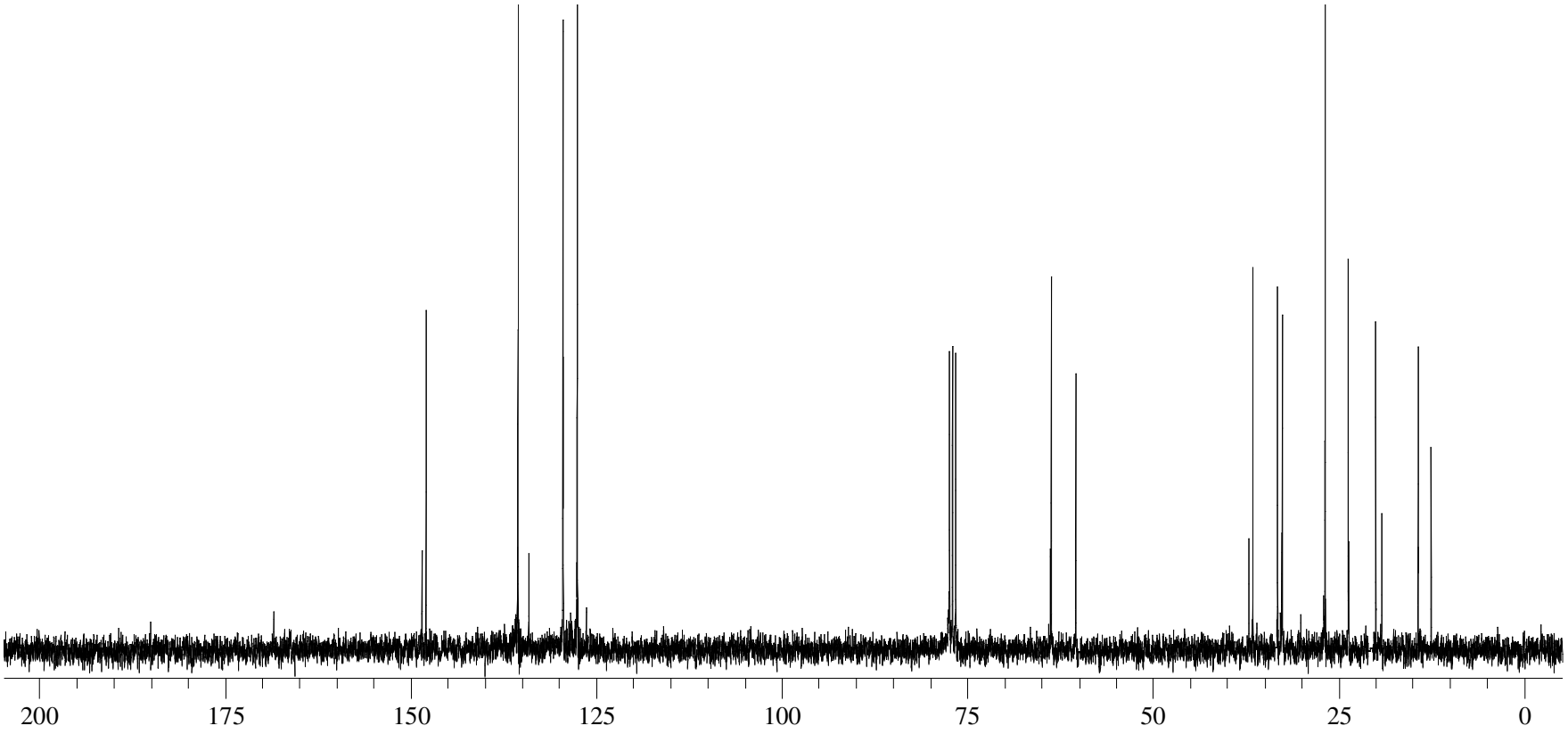


Figure 6: ^{13}C NMR Spectrum of compound **12** ($CDCl_3$, 125 MHz).

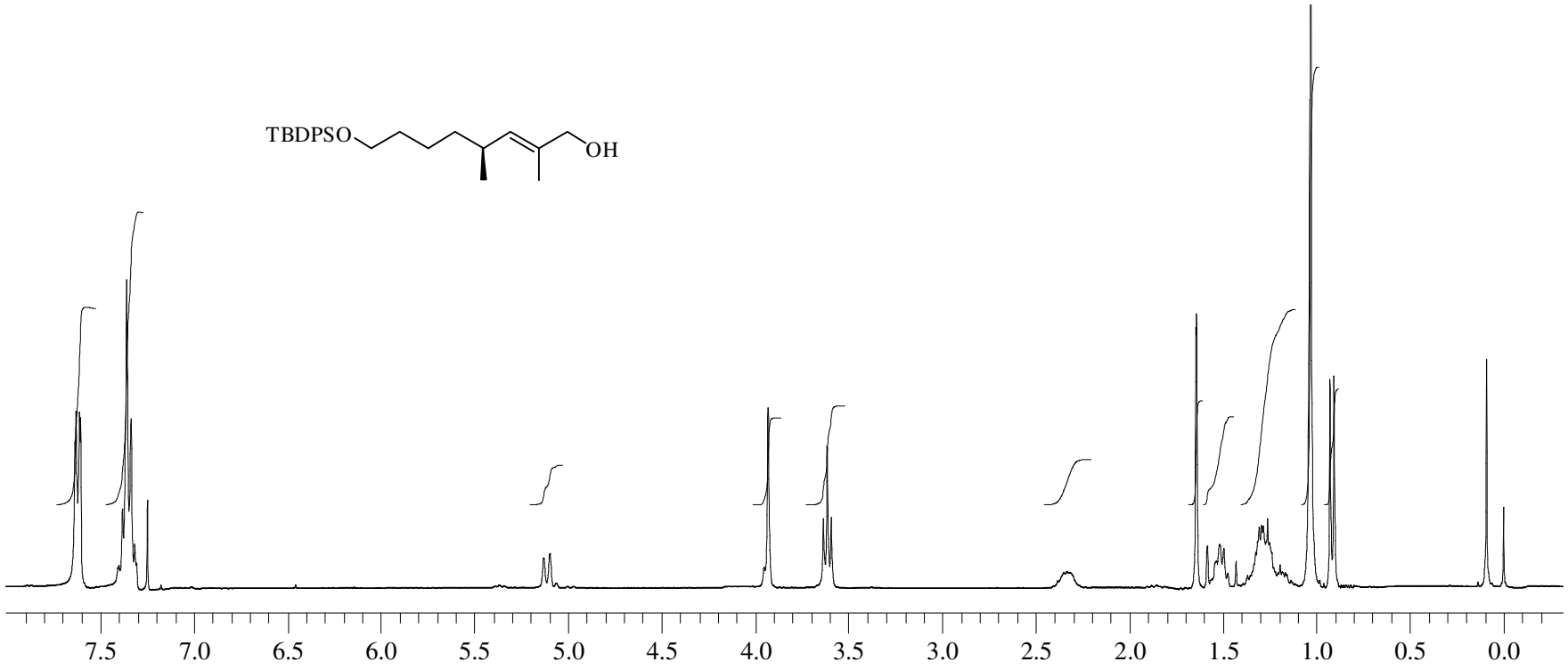


Figure 7: ^{1}H NMR Spectrum of compound **13** ($CDCl_3$, 300 MHz).

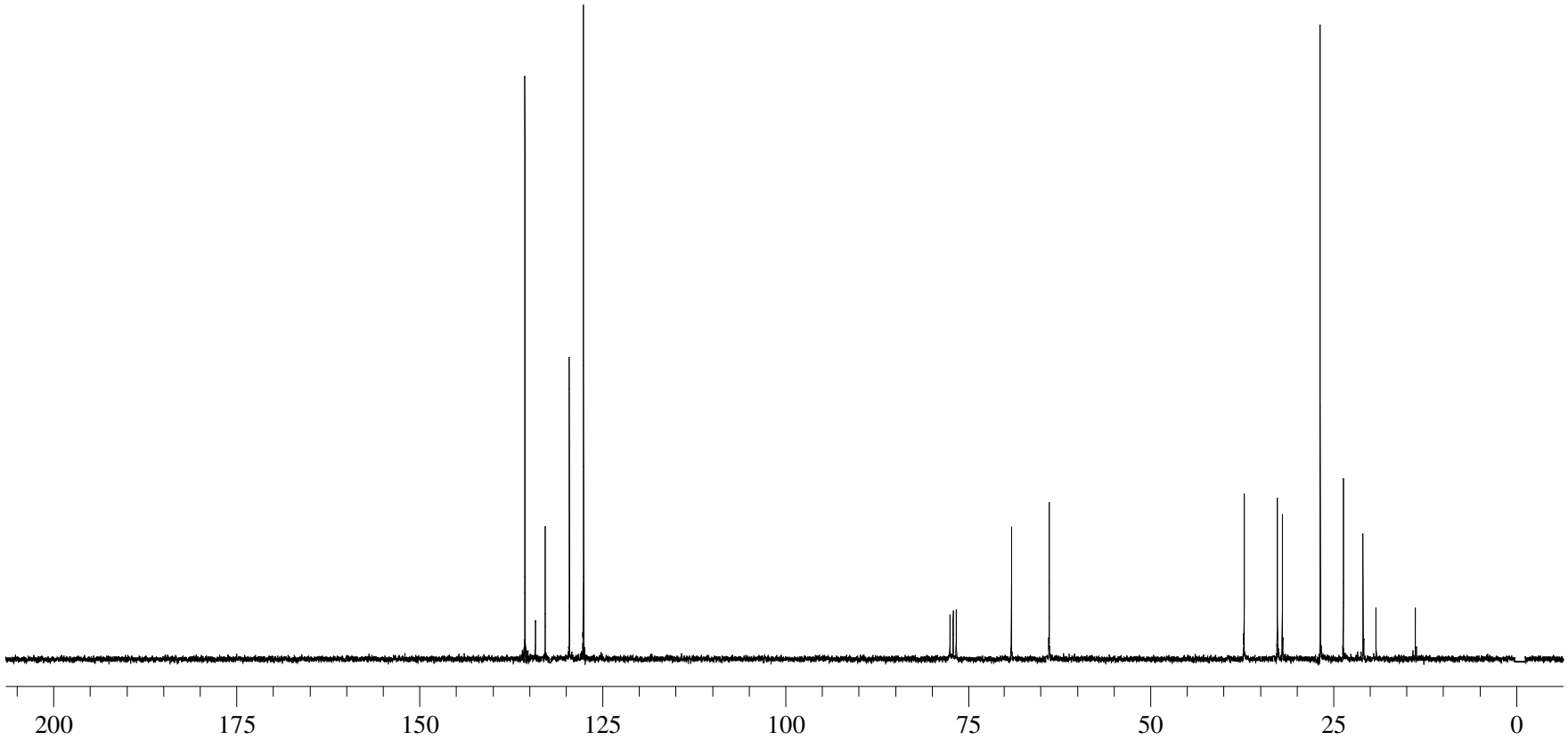


Figure 8: ^{13}C NMR Spectrum of compound **13** ($CDCl_3$, 125 MHz).

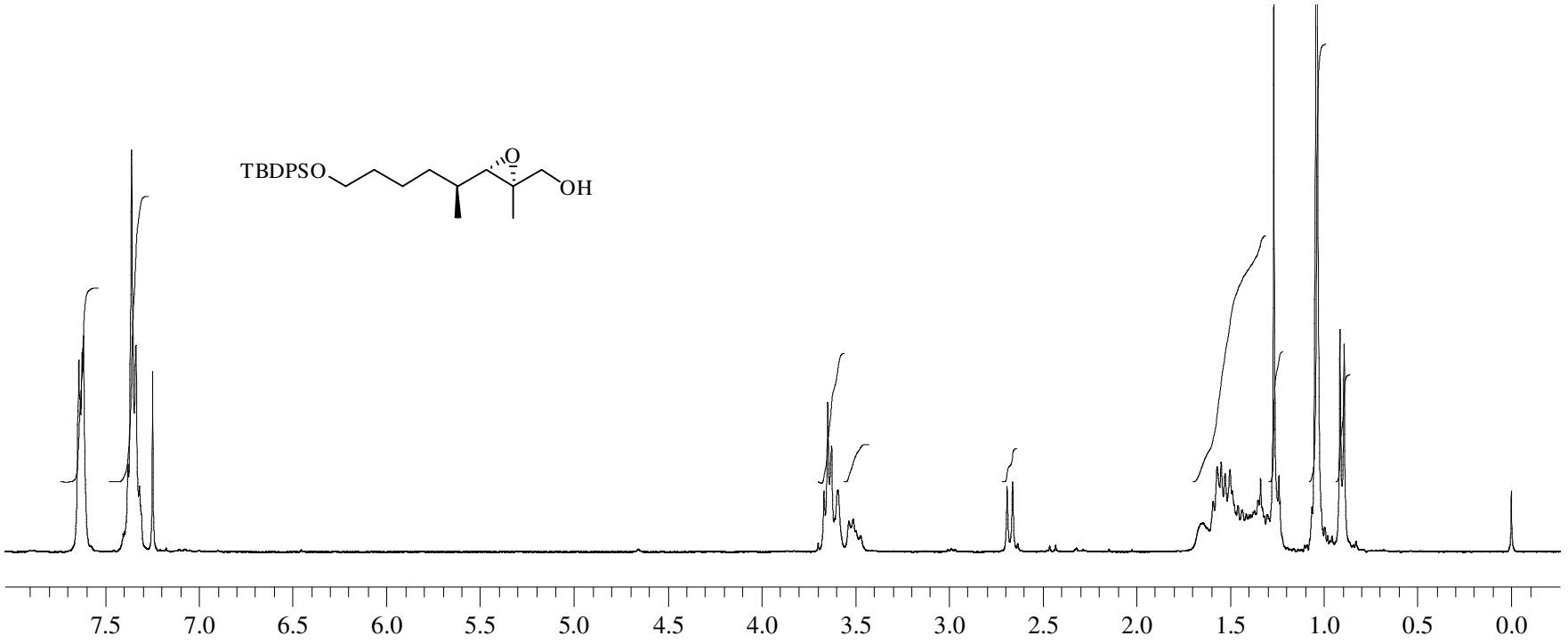


Figure 9: ^{1}H NMR Spectrum of compound **14** ($CDCl_3$, 300 MHz).

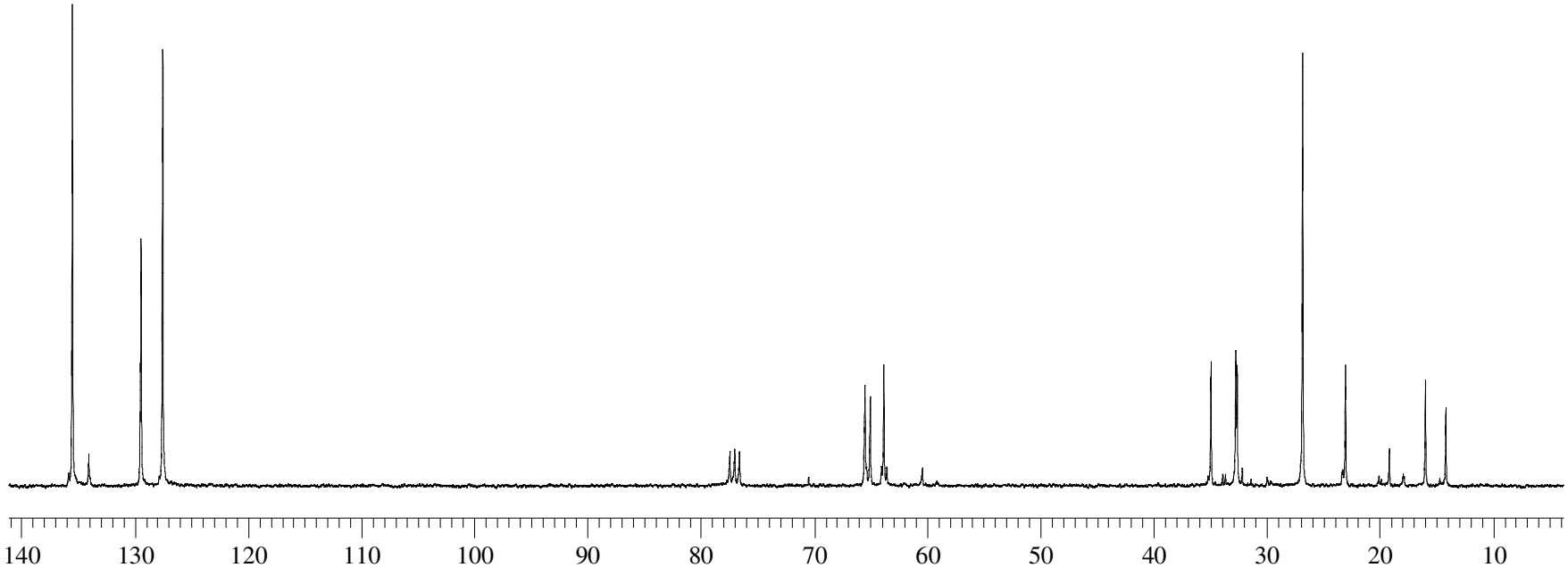
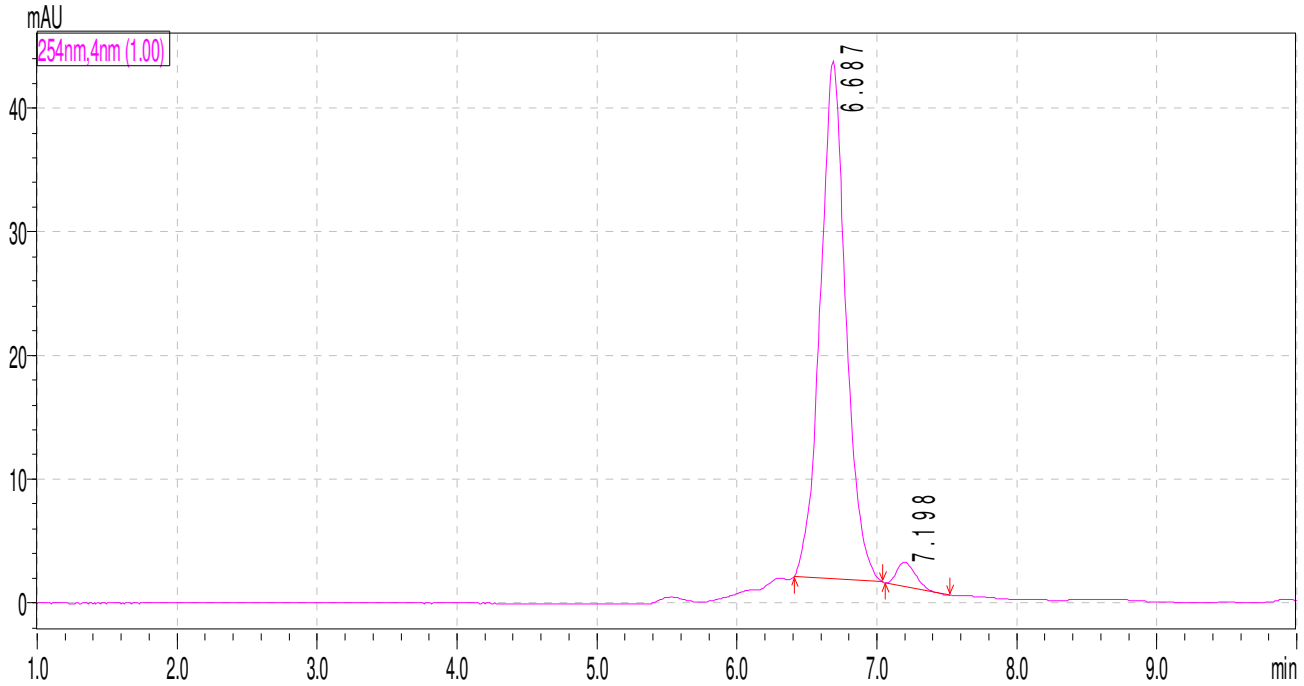


Figure 10: ^{13}C NMR Spectrum of compound **14** ($CDCl_3$, 125 MHz).



Peak	Ret. Time	Area	Height	Area%
1	6.687	533553	41817	96.730
2	7.198	18036	1982	3.270
Total		551590	43798	100.000

Figure 10a: HPLC Spectrum of compound **14**

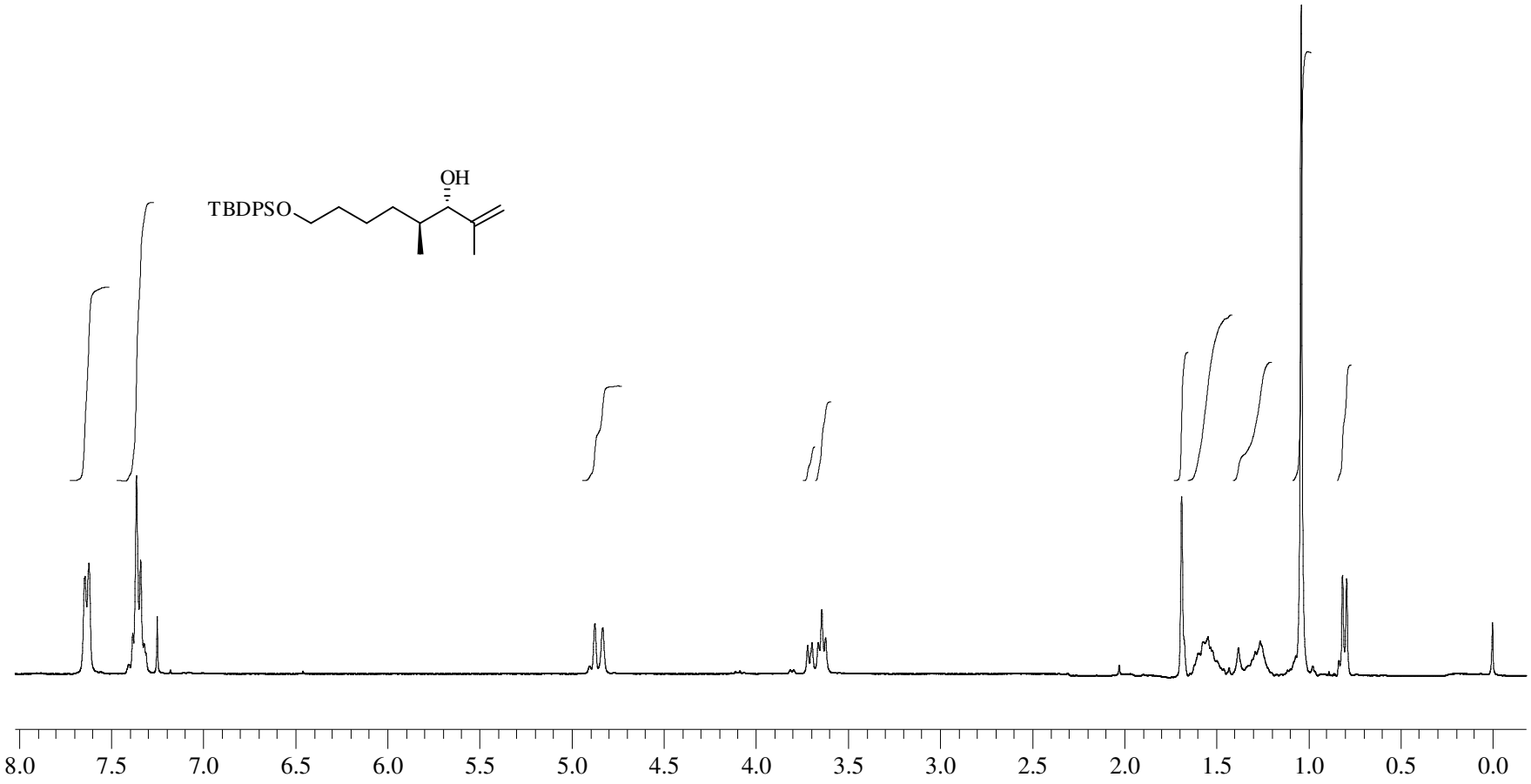


Figure 11: ^{1}H NMR Spectrum of compound **15** ($CDCl_3$, 300 MHz).

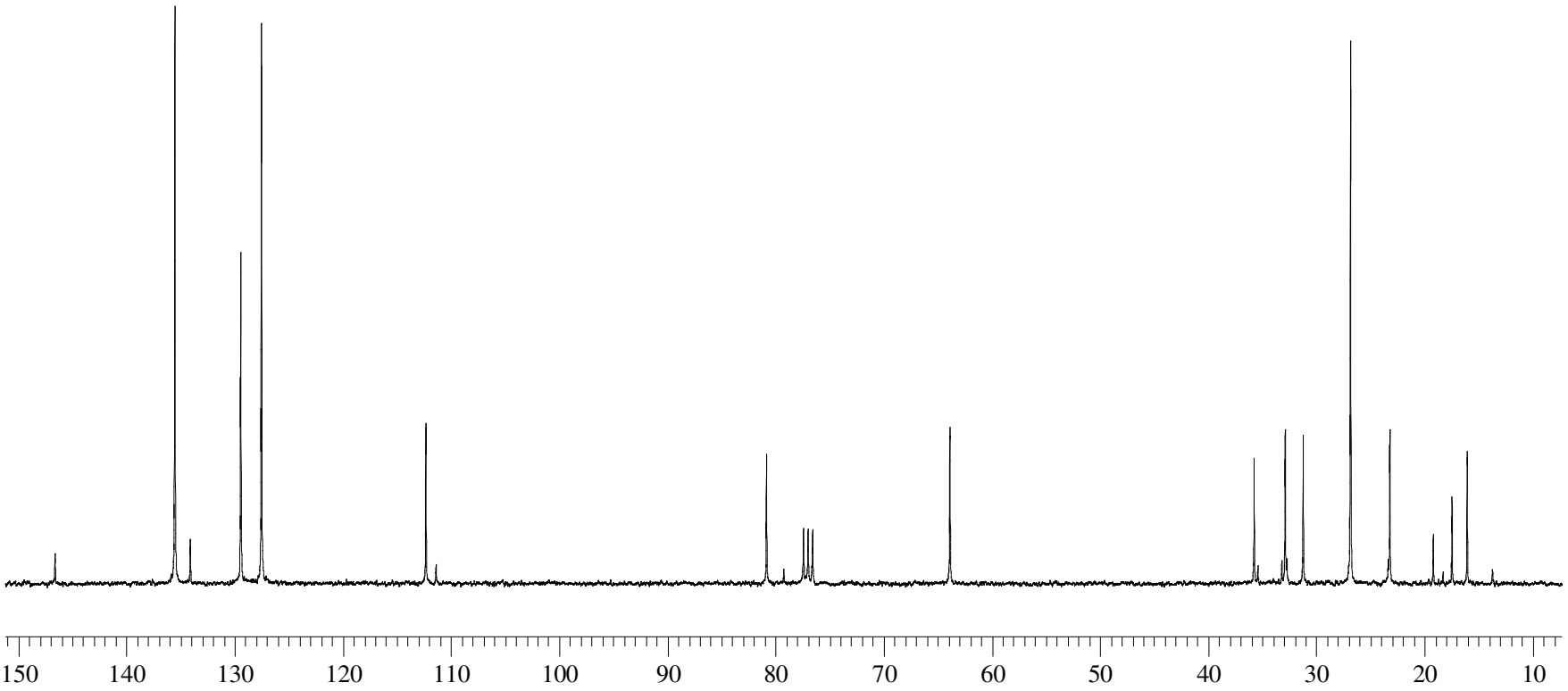


Figure 12: ^{13}C NMR Spectrum of compound **15** ($CDCl_3$, 125 MHz).

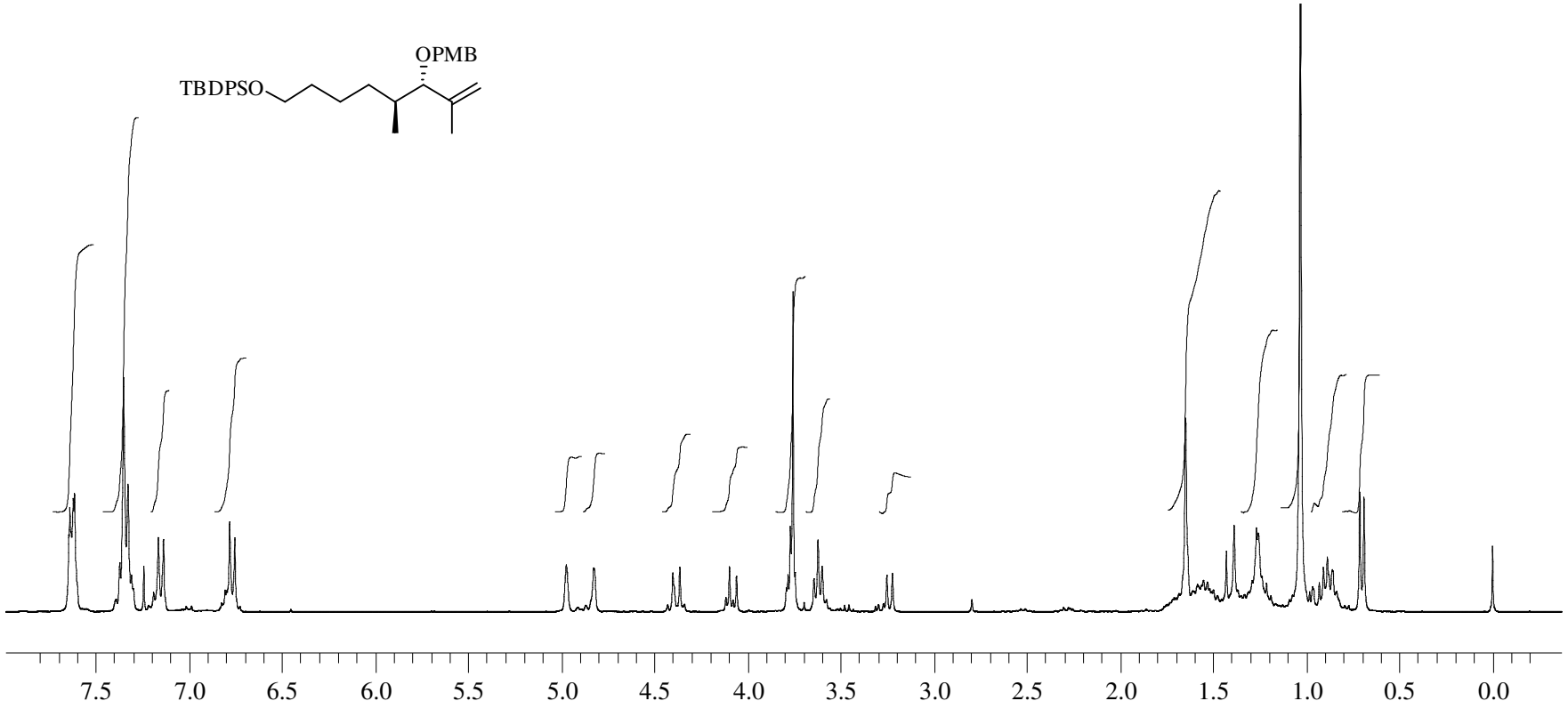


Figure 13: ^{1}H NMR Spectrum of compound **16** ($CDCl_3$, 300 MHz).

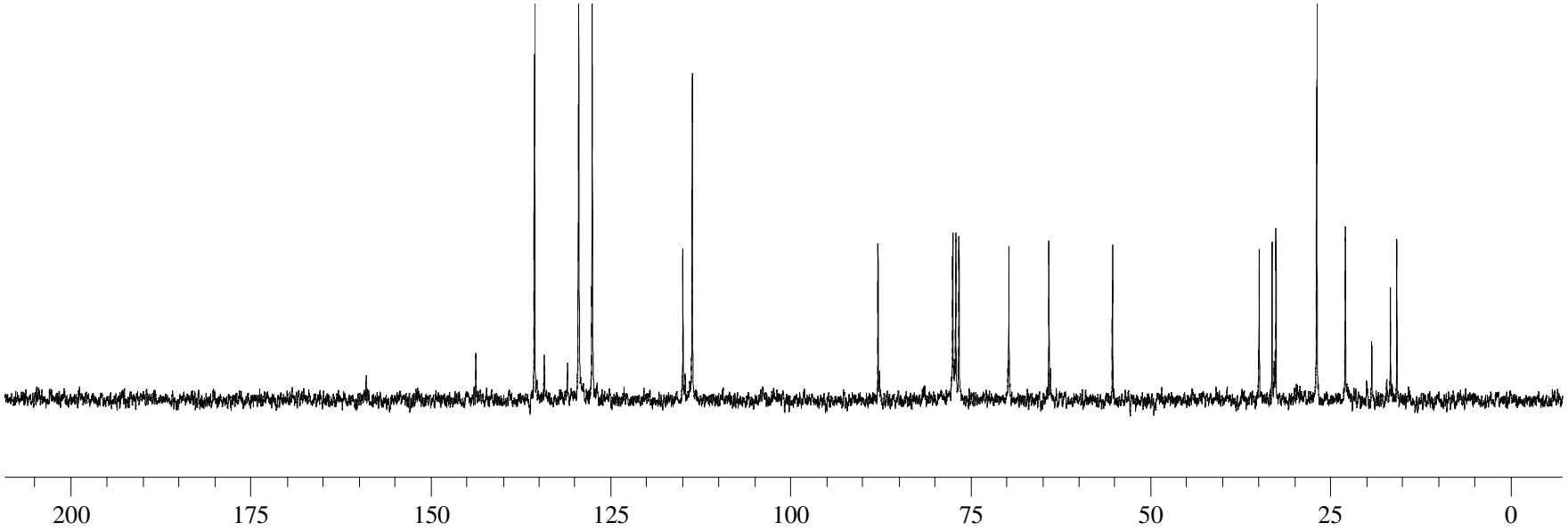


Figure 14: ^{13}C NMR Spectrum of compound **16** ($CDCl_3$, 125 MHz).

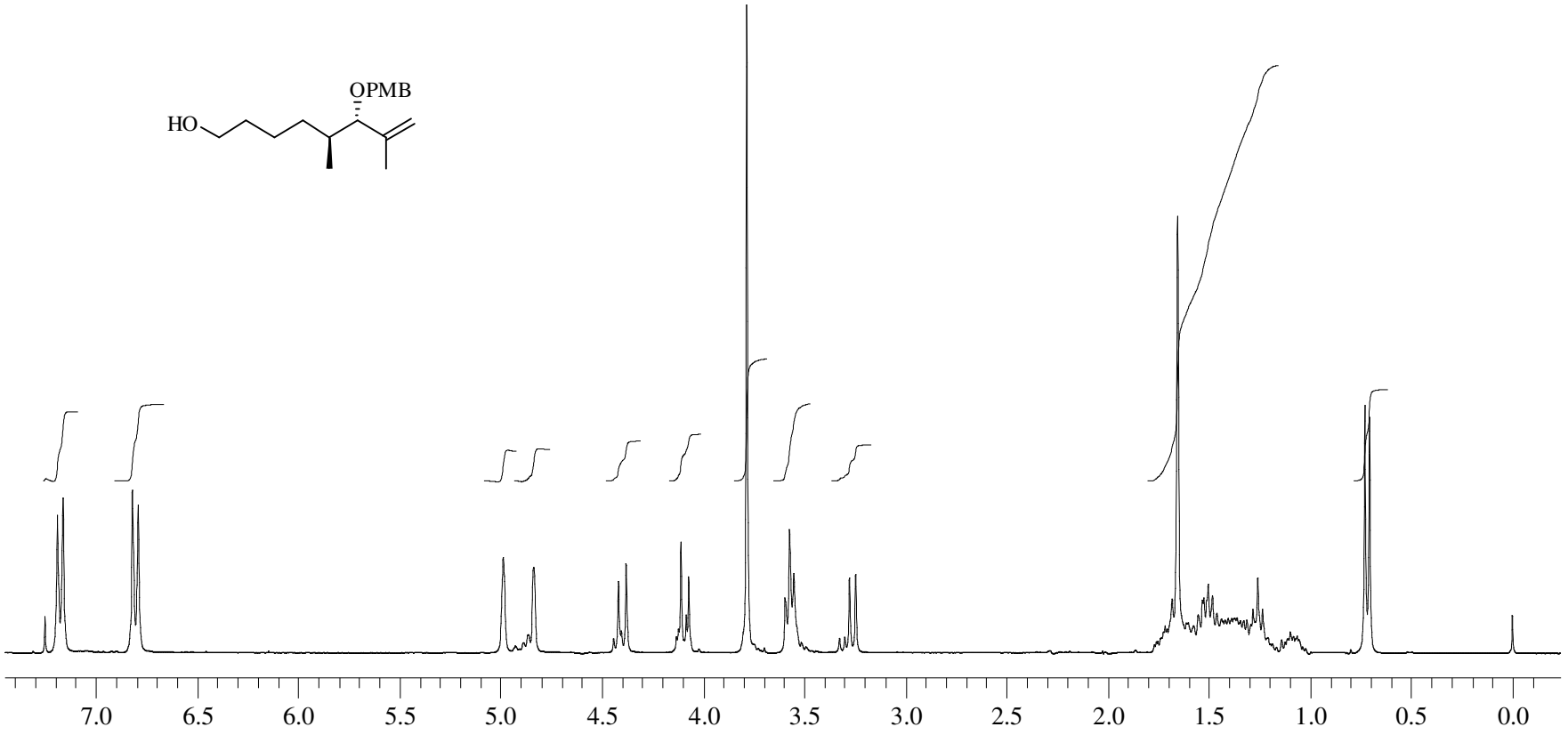


Figure 15: ^{1}H NMR Spectrum of compound **8** ($CDCl_3$, 300 MHz).

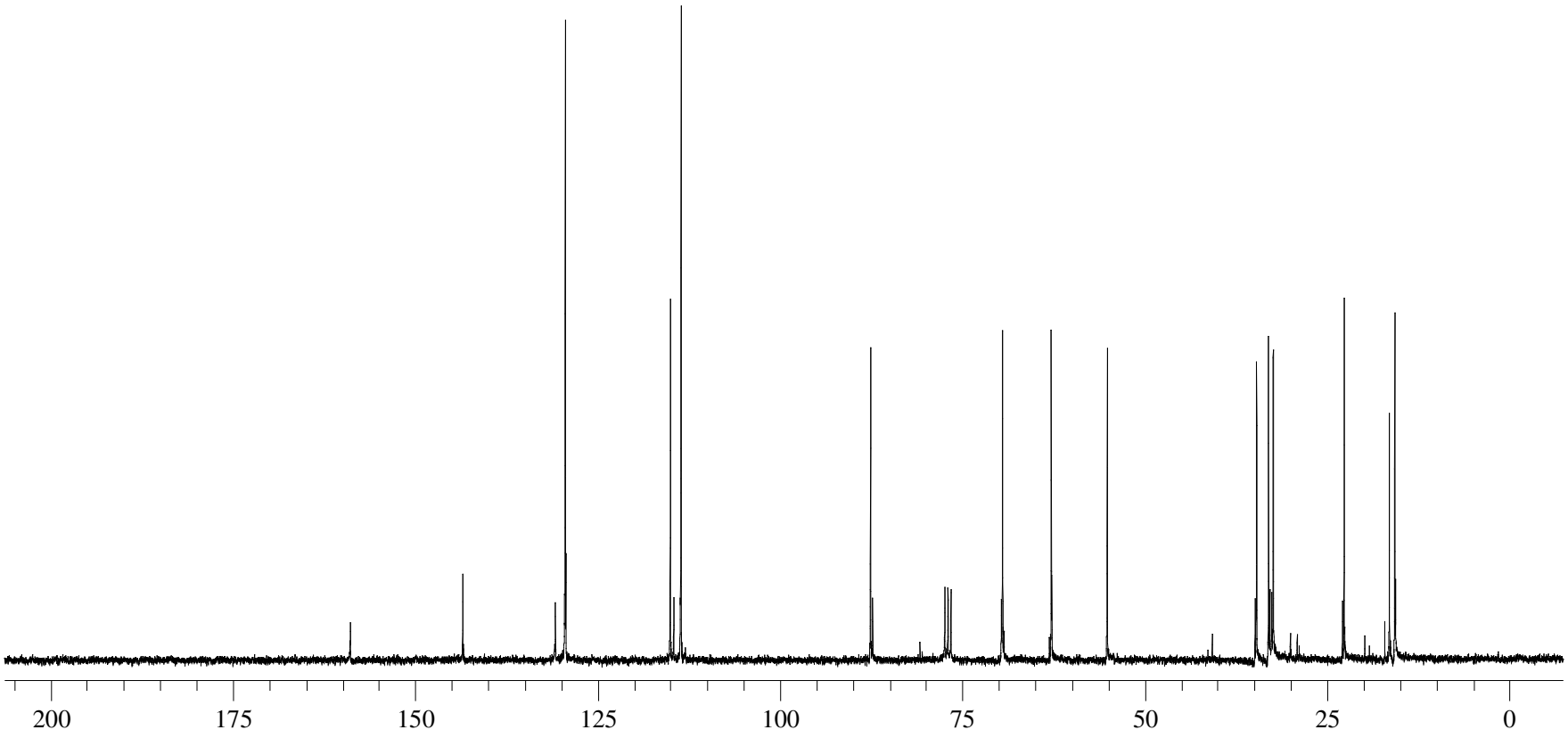


Figure 16: ^{13}C NMR Spectrum of compound **8** ($CDCl_3$, 125 MHz).

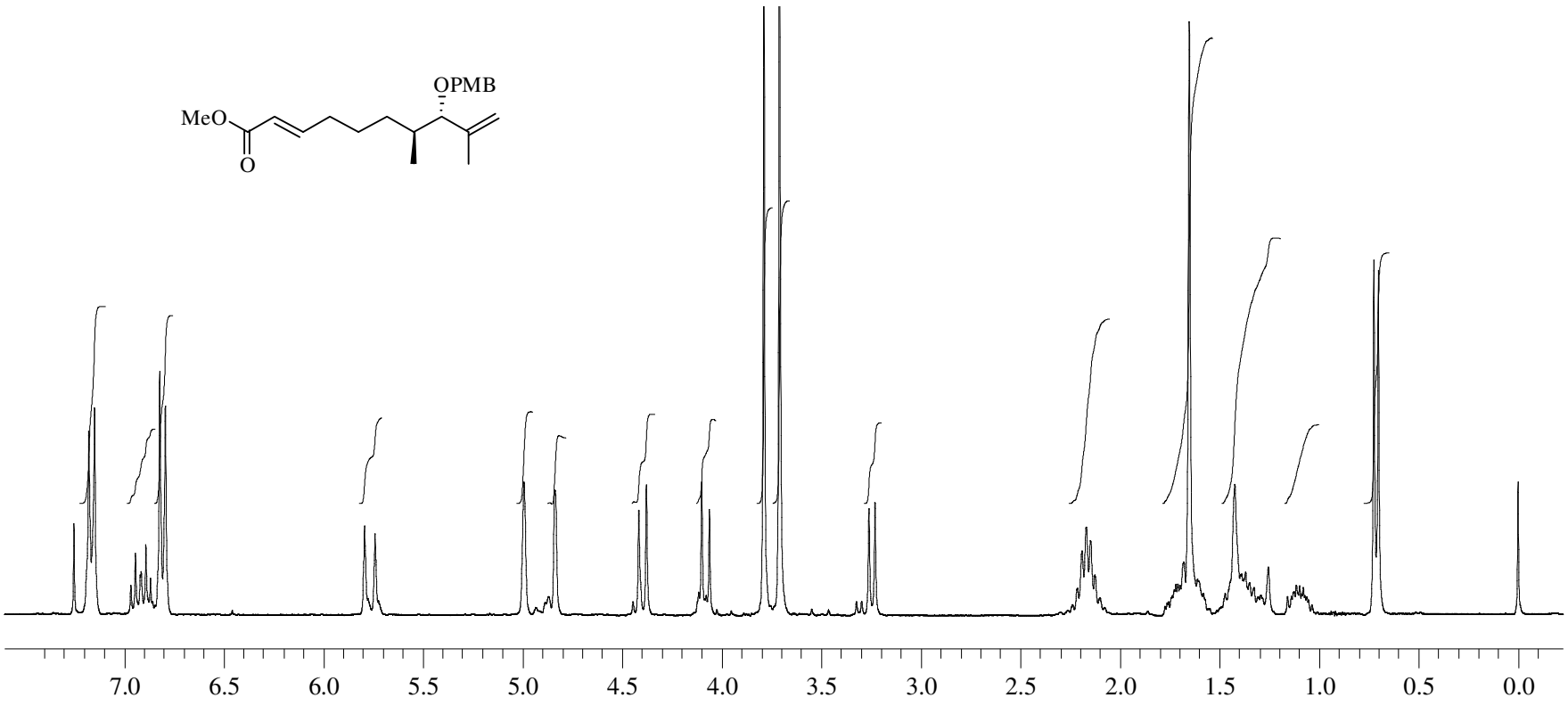


Figure 17: ^{1}H NMR Spectrum of compound **17** ($CDCl_3$, 300 MHz).

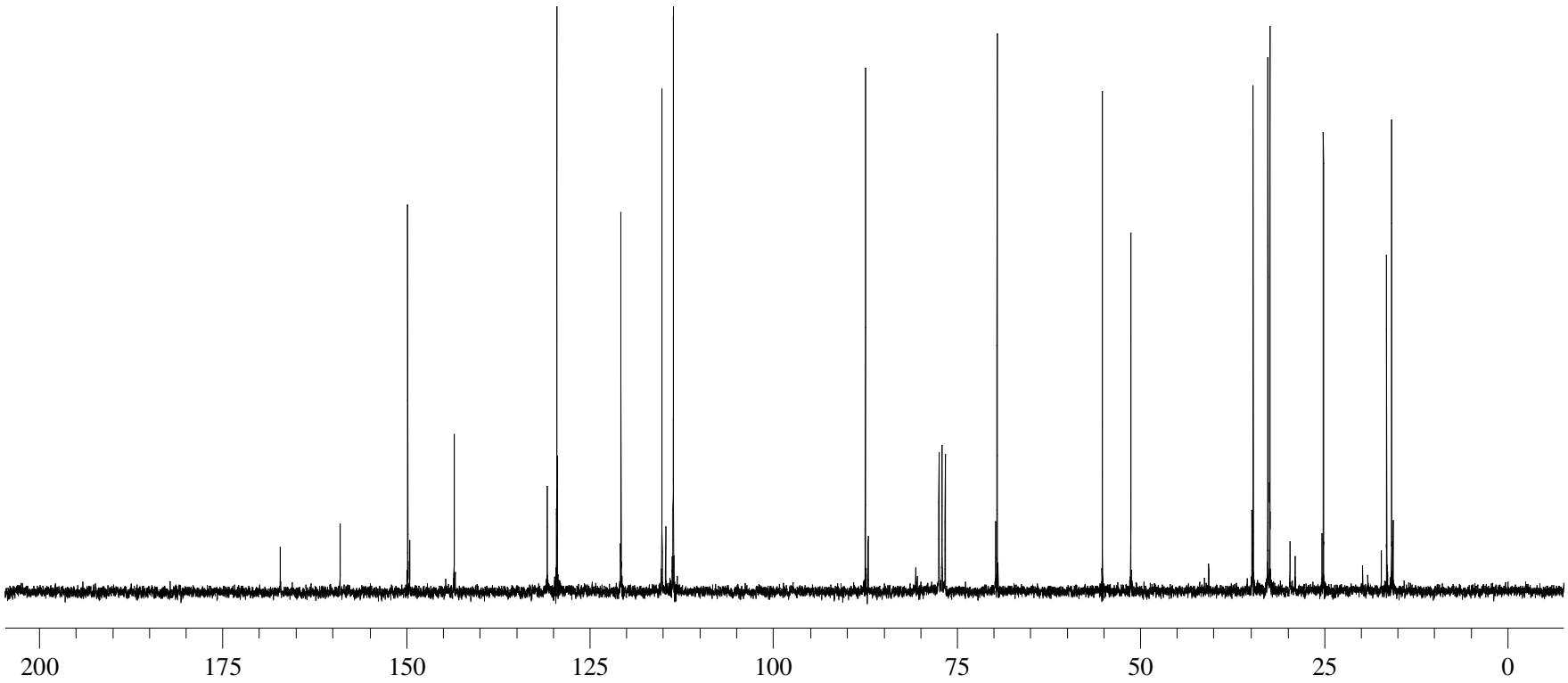


Figure 18: ^{13}C NMR Spectrum of compound **17** ($CDCl_3$, 125 MHz).

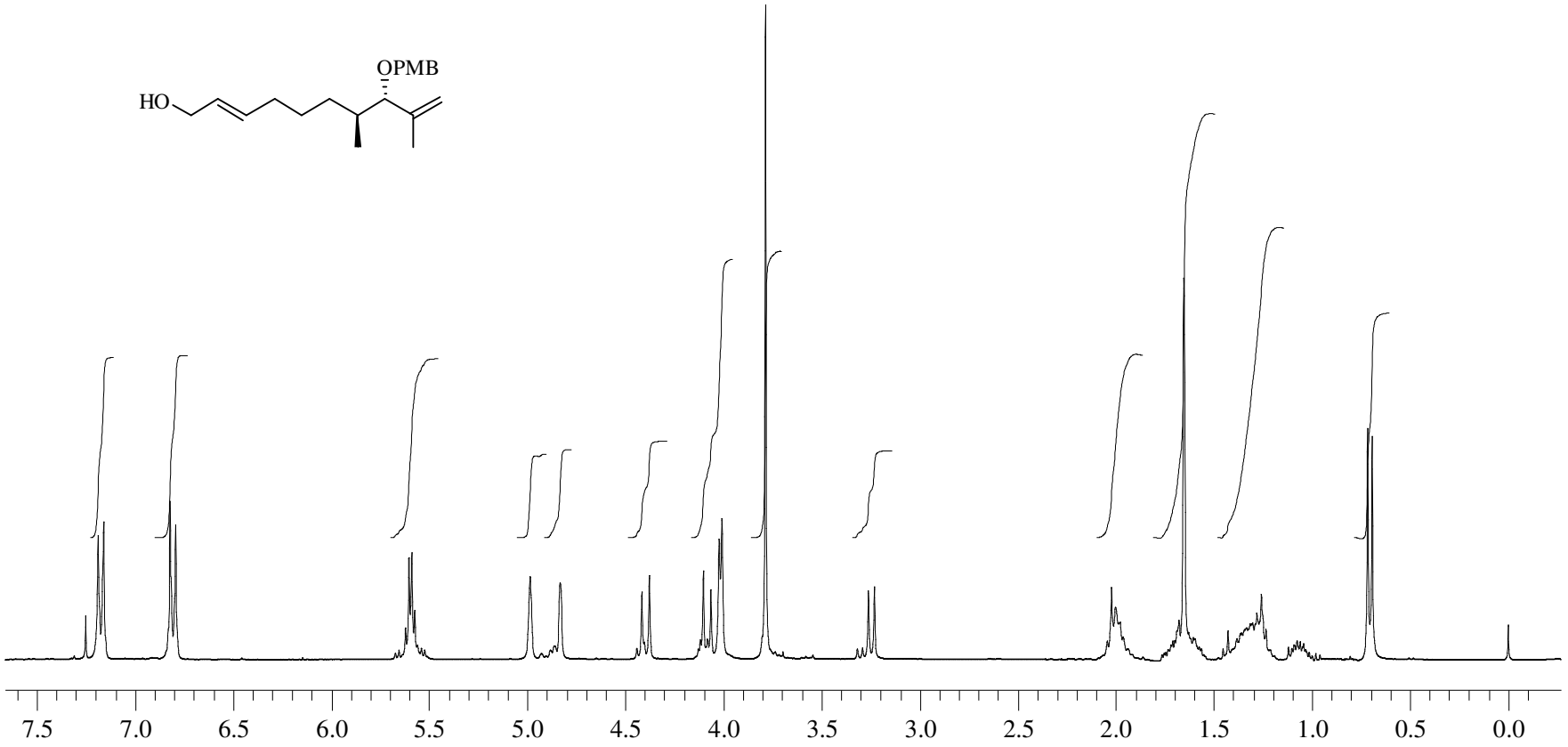


Figure 19: ^{1}H NMR Spectrum of compound **18** ($CDCl_3$, 300 MHz).

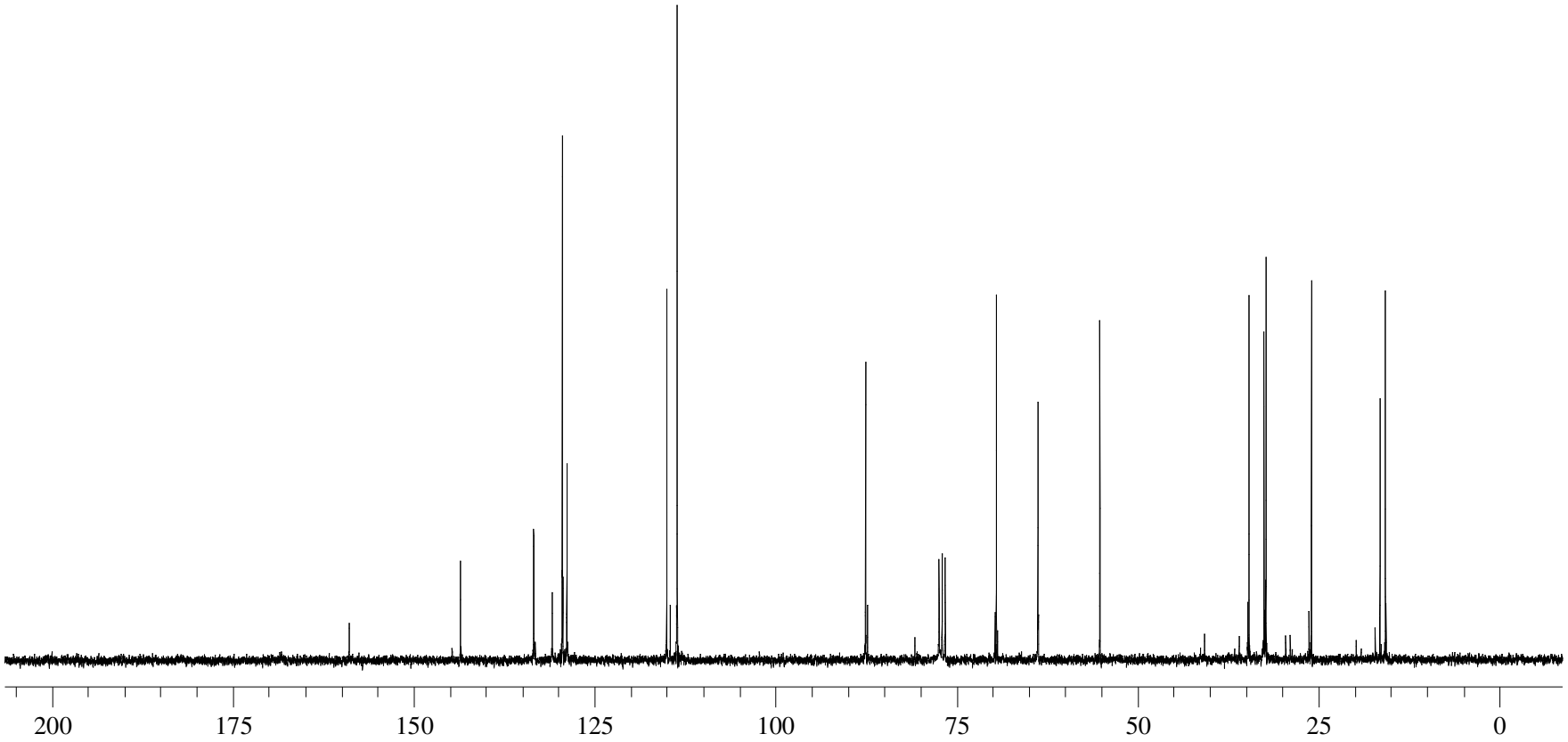


Figure 20: ^{13}C NMR Spectrum of compound **18** ($CDCl_3$, 125 MHz).

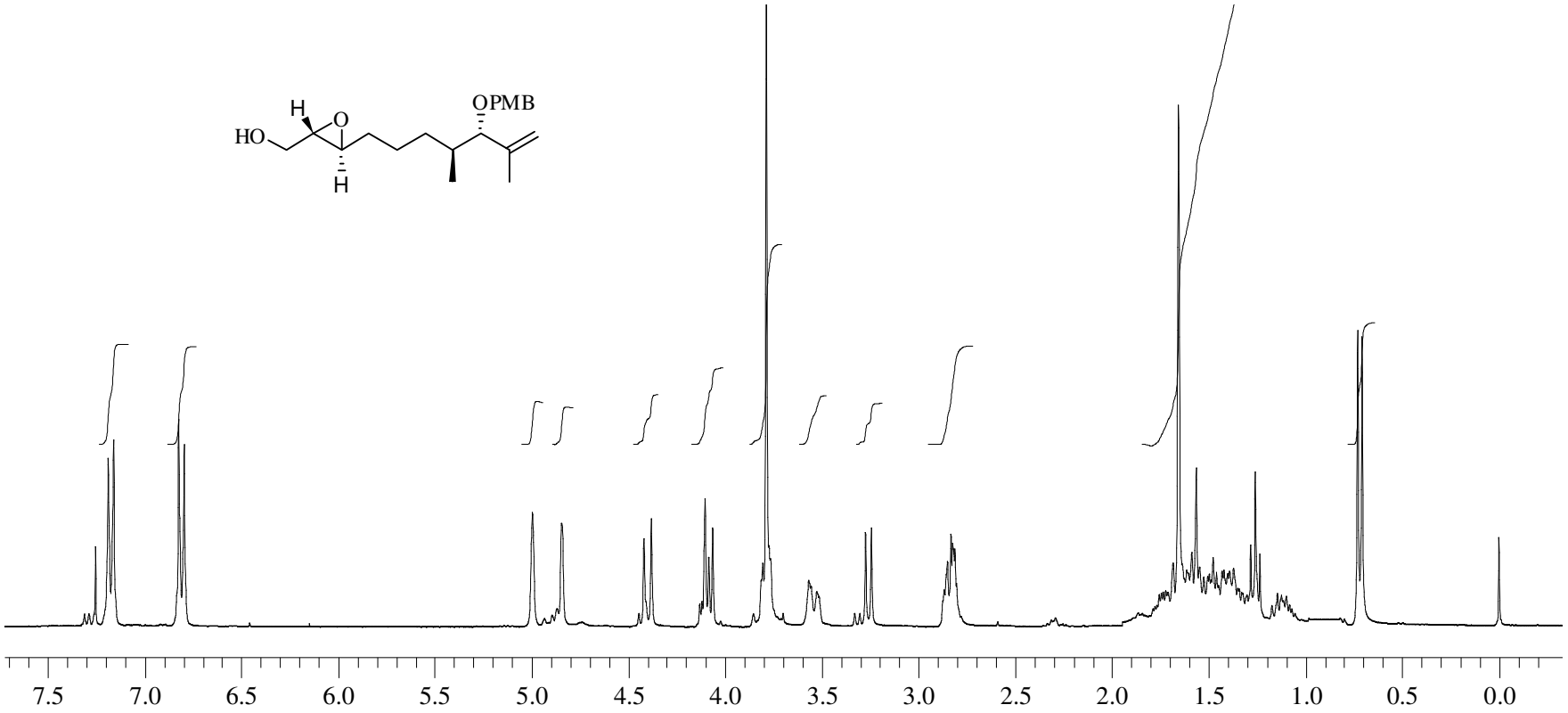


Figure 21: ^{1}H NMR Spectrum of compound **19** ($CDCl_3$, 300 MHz).

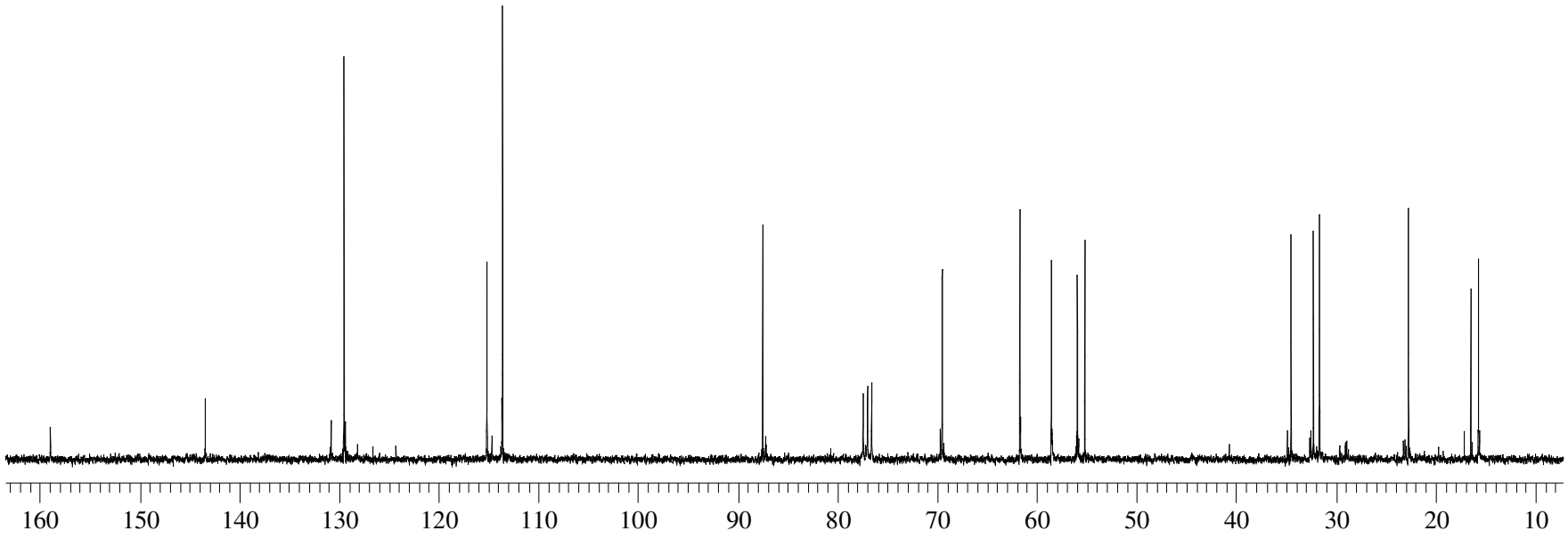
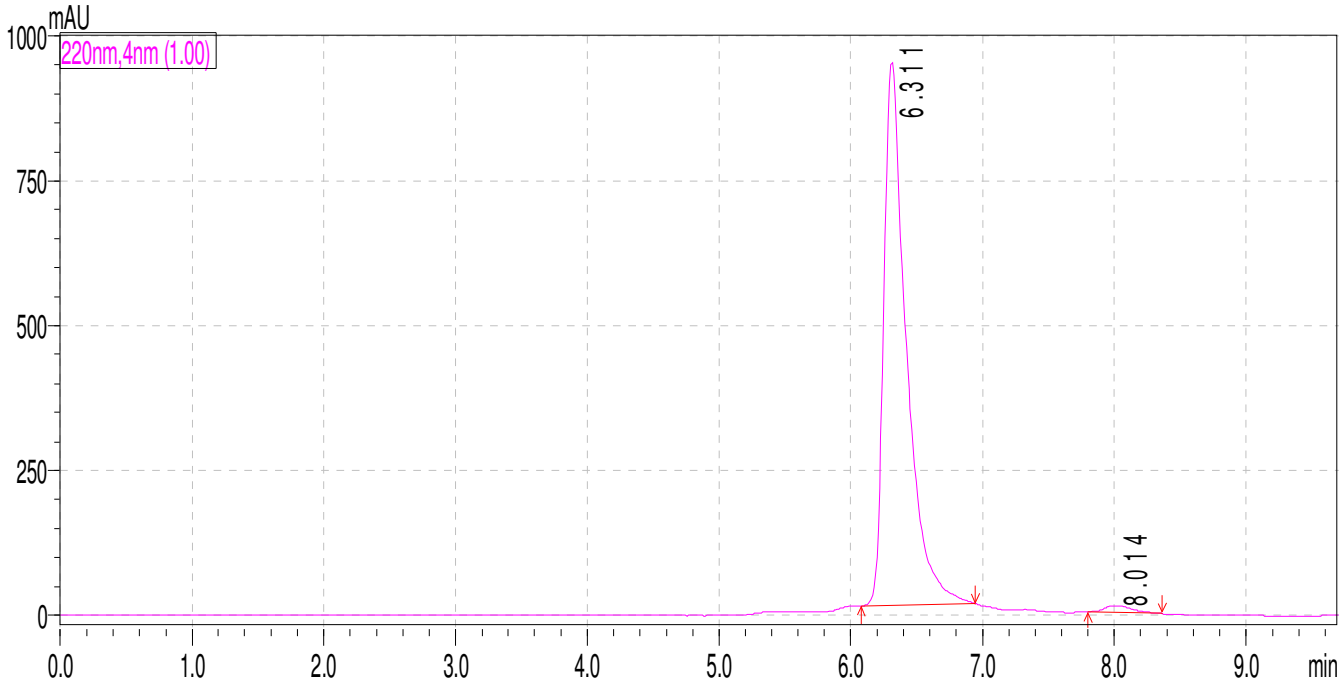


Figure 22: ^{13}C NMR Spectrum of compound 1**9** ($CDCl_3$, 125 MHz).



Peak	Ret. Time	Area	Height	Area%
1	6.311	11145891	936881	98.396
2	8.014	181740	12510	1.604
Total		11327631	949391	100.000

Figure 22a: HPLC Spectrum of compound **19**

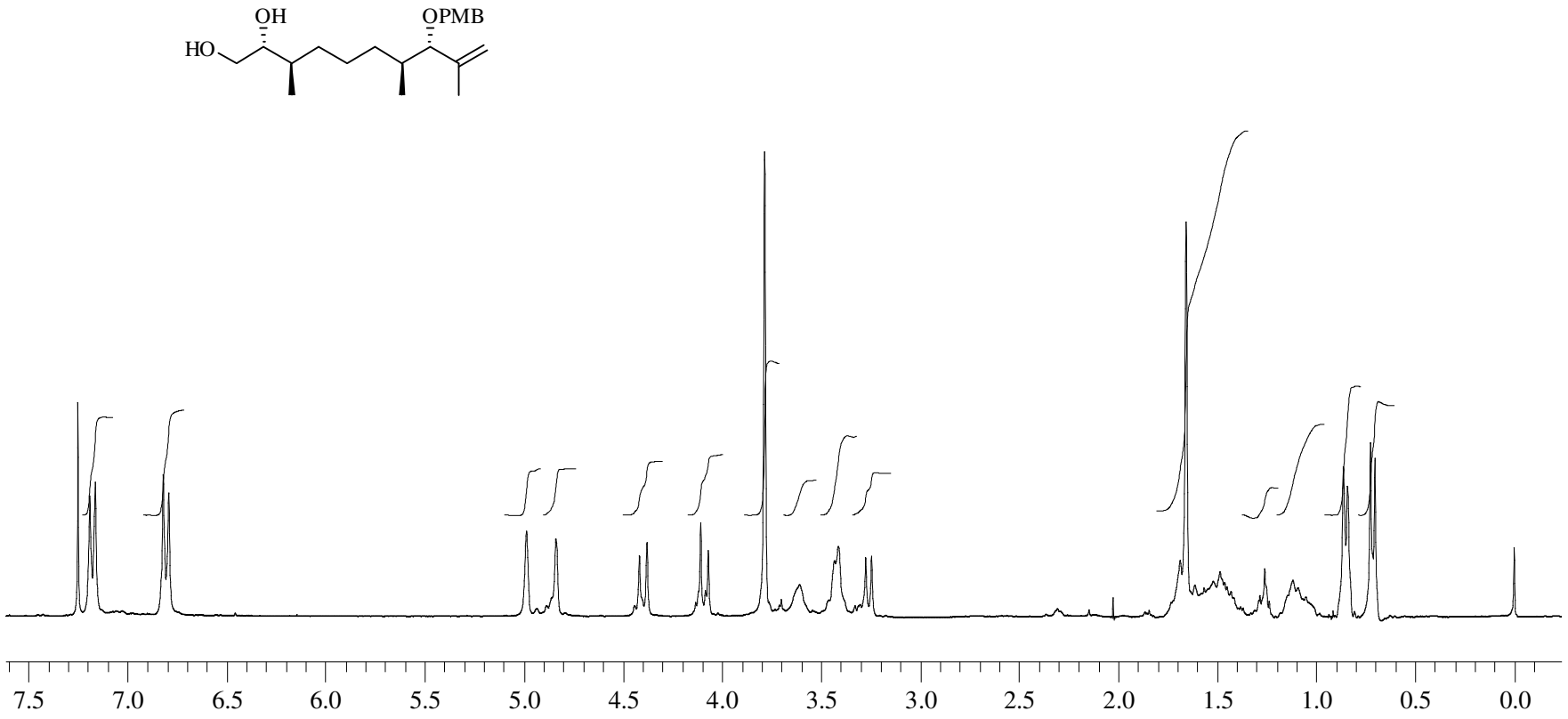


Figure 23: ^{1}H NMR Spectrum of compound **20** ($CDCl_3$, 300 MHz).

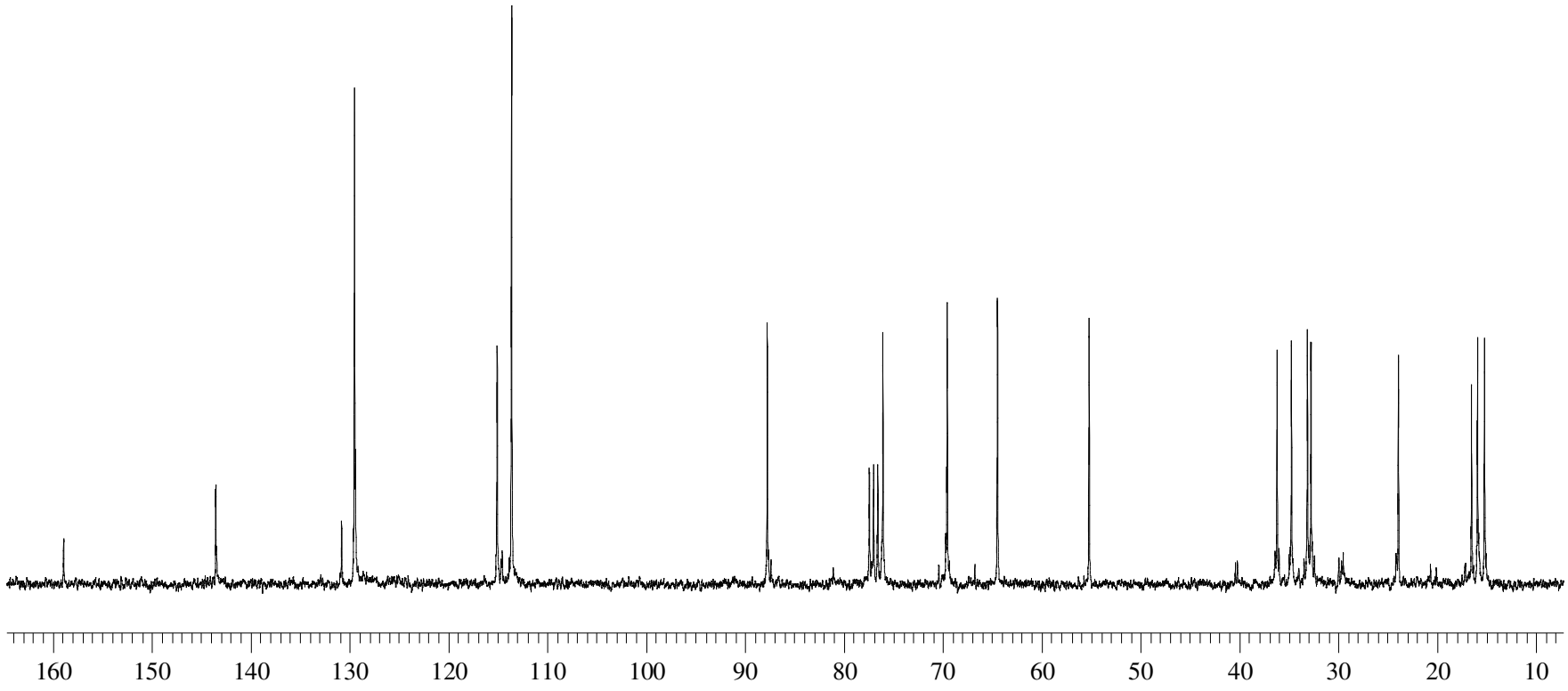
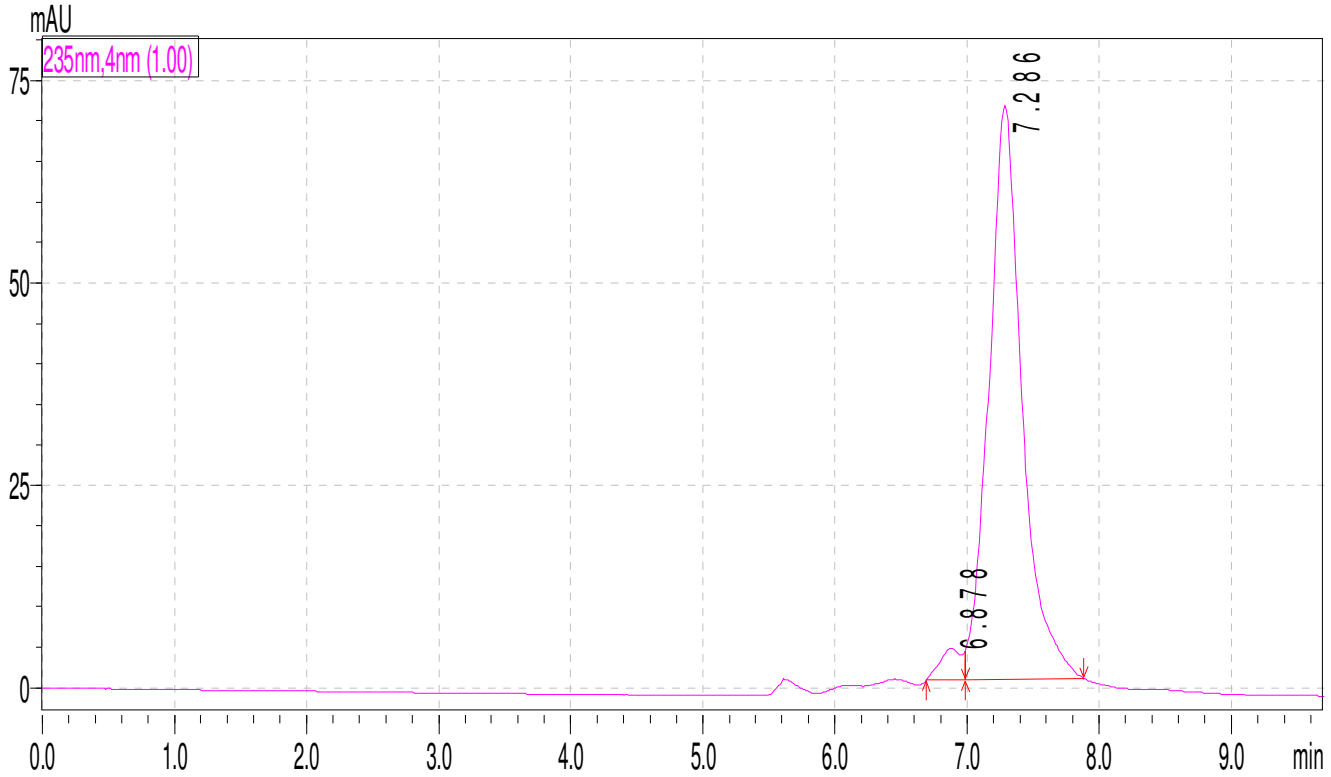


Figure 24: ^{13}C NMR Spectrum of compound **20** ($CDCl_3$, 125 MHz).



Peak	Ret. Time	Area	Height	Area%
1	6.878	46826	3900	3.651
2	7.286	1235586	70800	96.349
Total		1282412	74700	100.000

Figure 24a: HPLC Spectrum of compound **20**

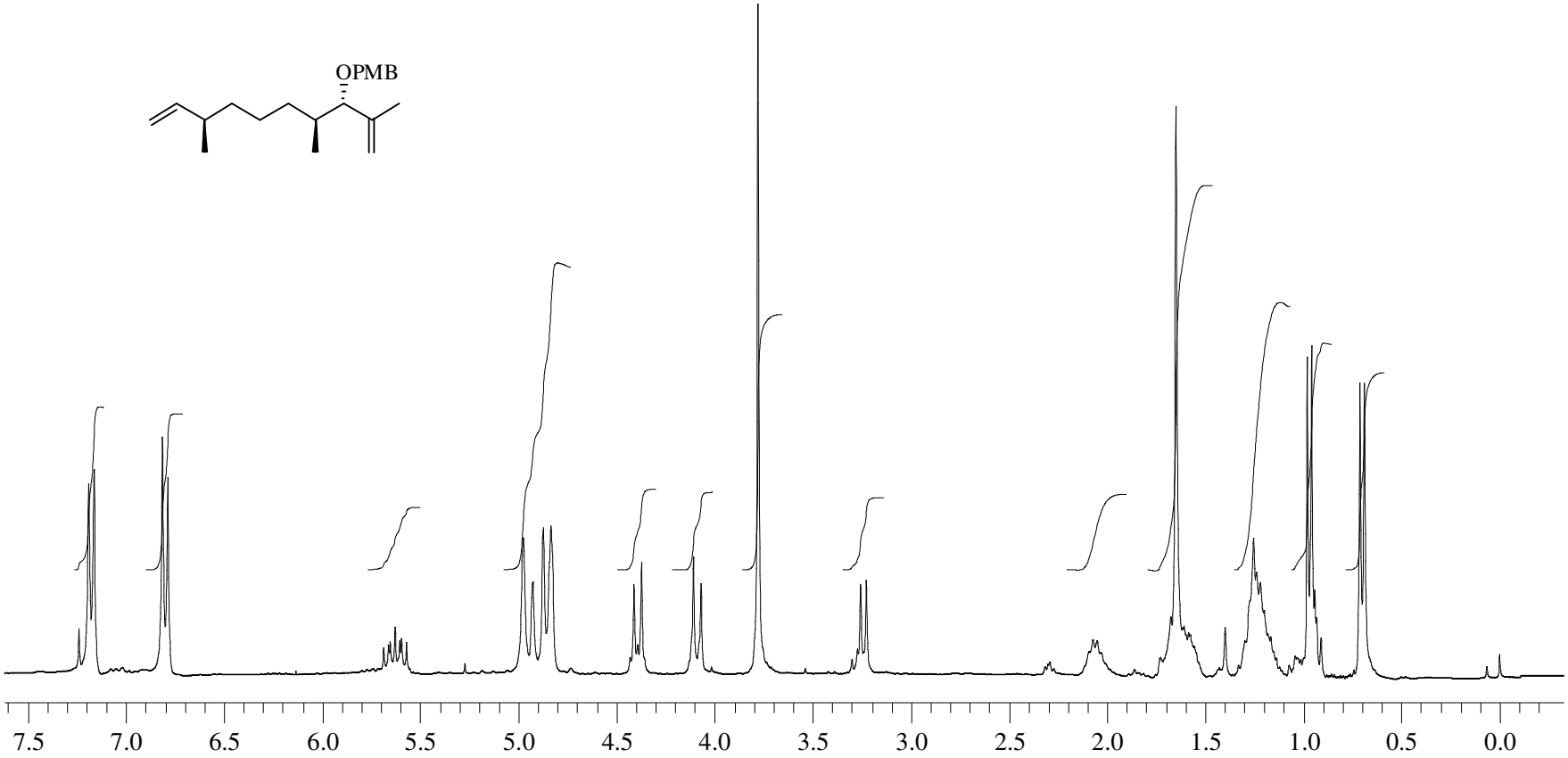


Figure 25: ^{1}H NMR Spectrum of compound **21** ($CDCl_3$, 300 MHz).

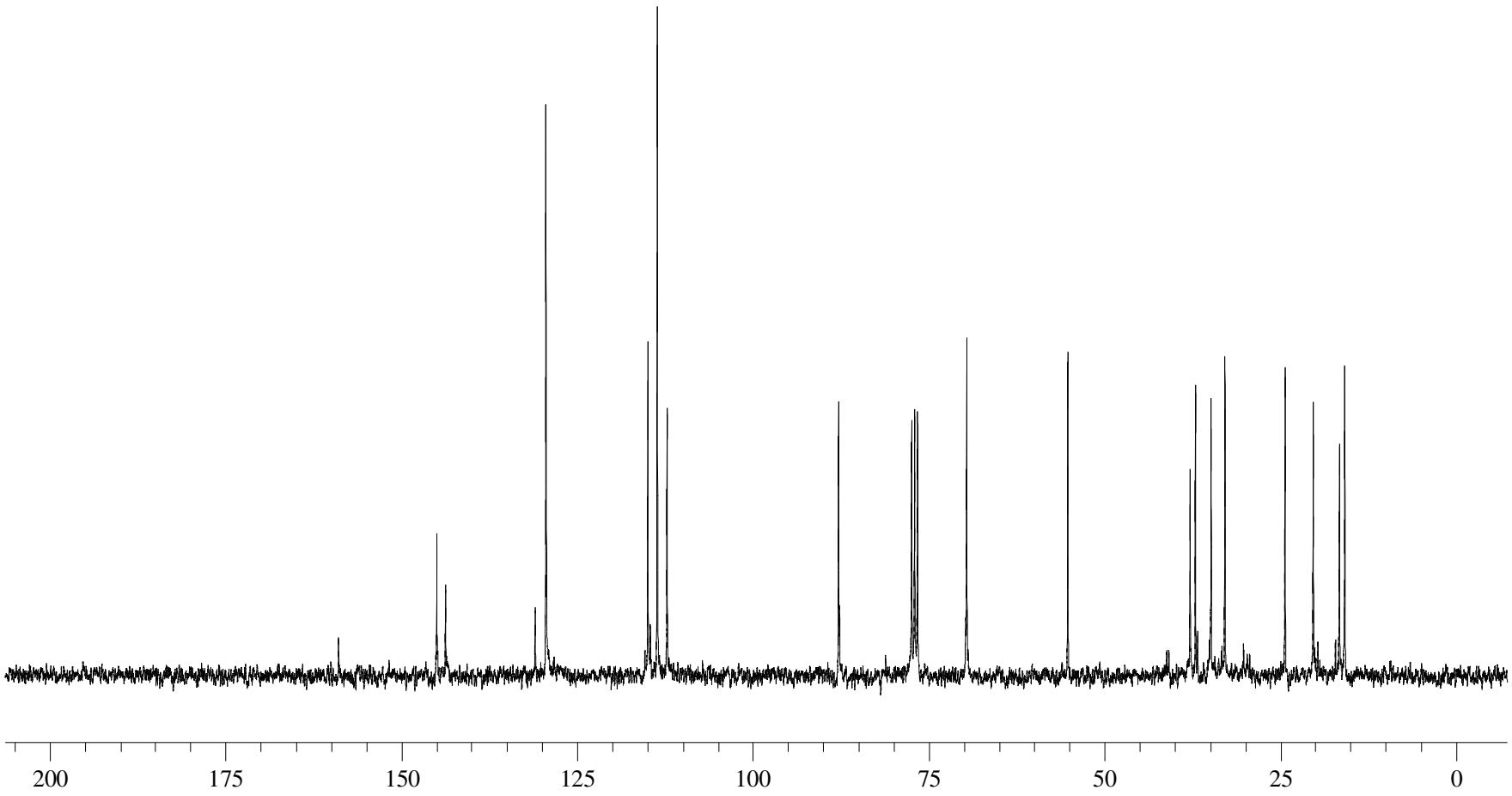


Figure 26: ^{13}C NMR Spectrum of compound **21** ($CDCl_3$, 125 MHz).

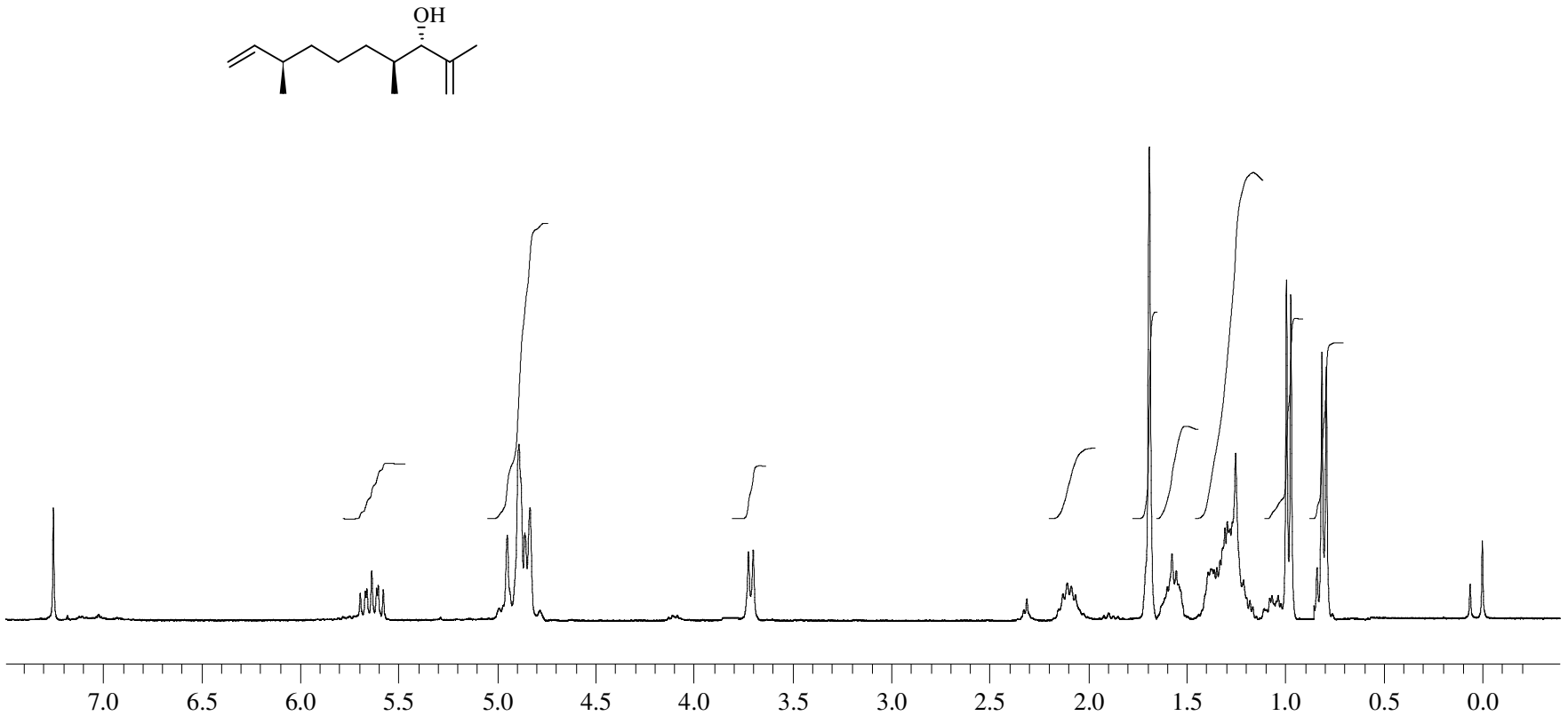


Figure 27: ^{1}H NMR Spectrum of compound **6** ($CDCl_3$, 300 MHz).

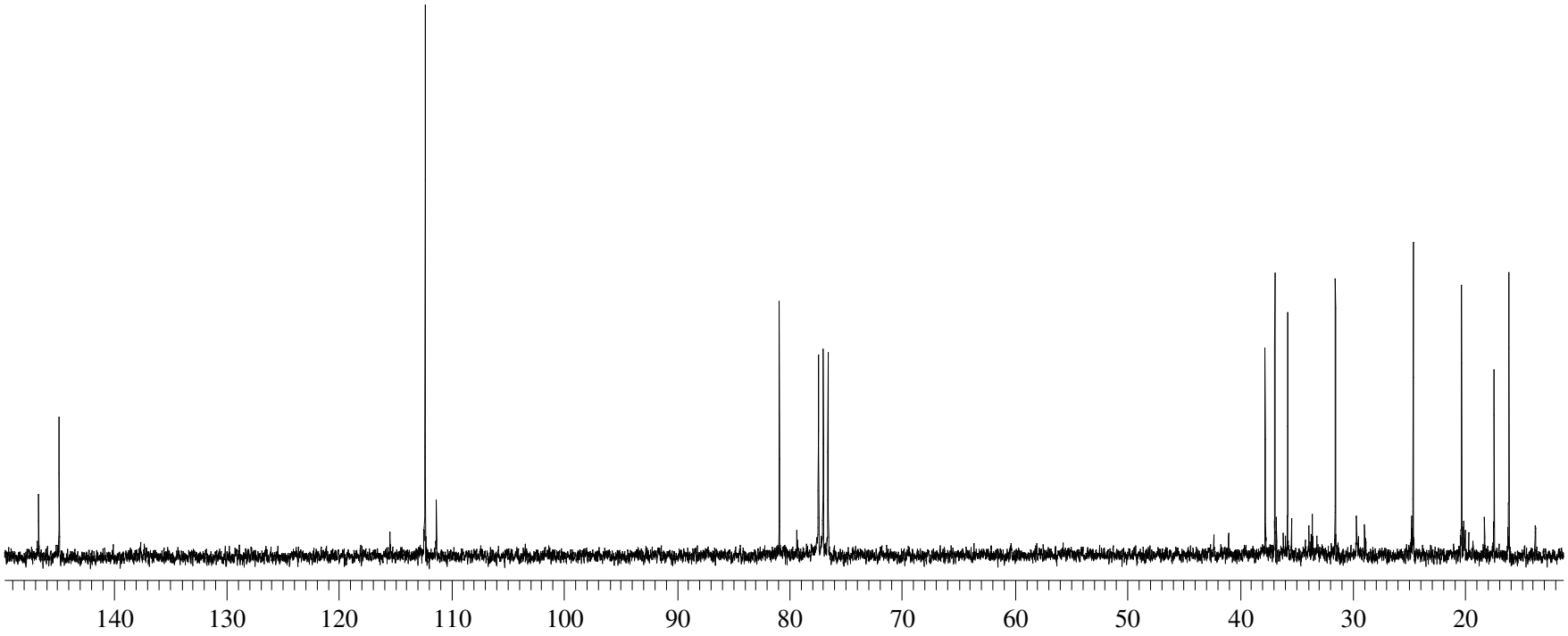


Figure 28: ^{13}C NMR Spectrum of compound **6** ($CDCl_3$, 125 MHz).

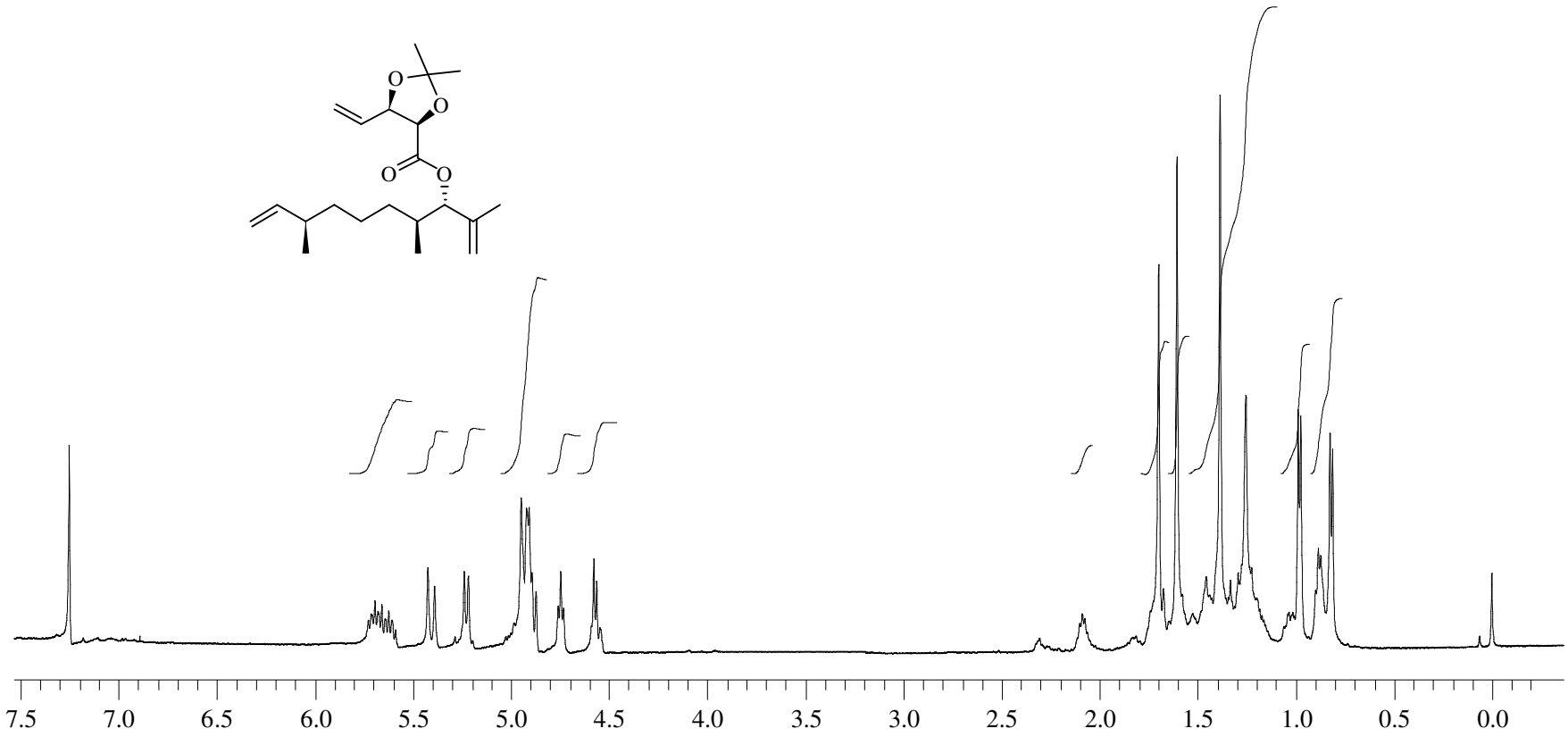


Figure 29: ^{1}H NMR Spectrum of compound **4** ($CDCl_3$, 300 MHz).

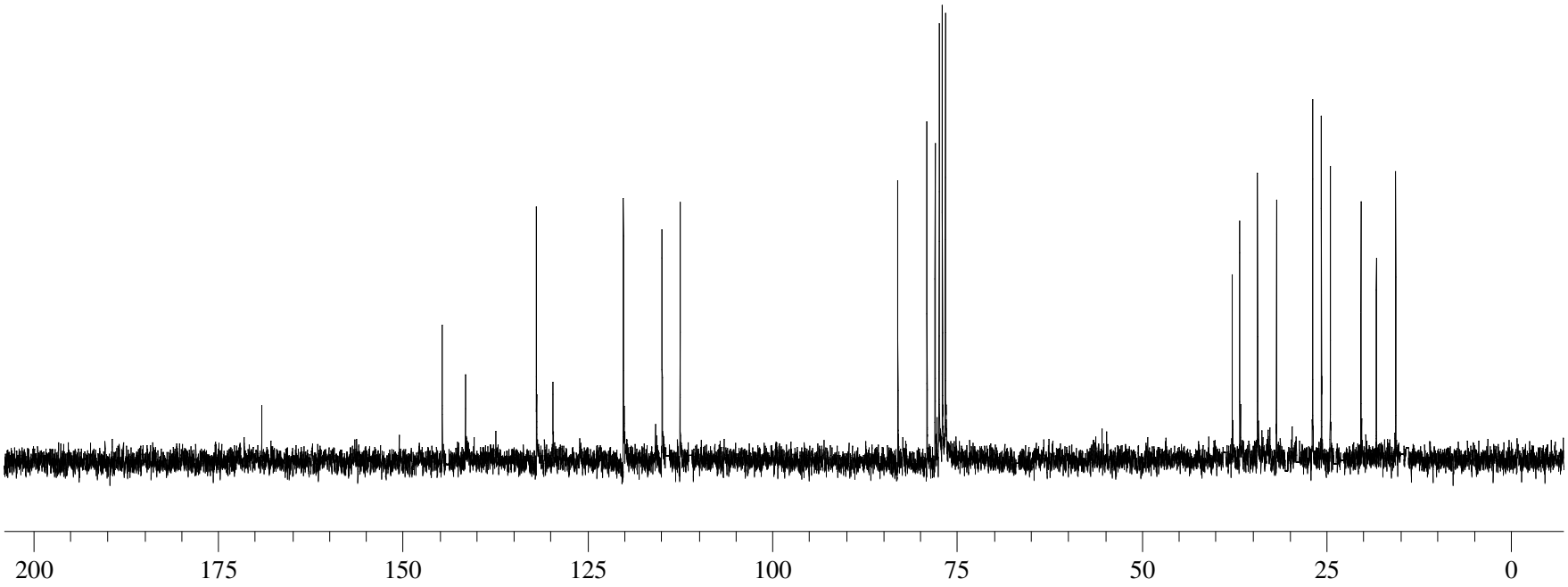


Figure 30: ^{13}C NMR Spectrum of compound **4** ($CDCl_3$, 125 MHz).

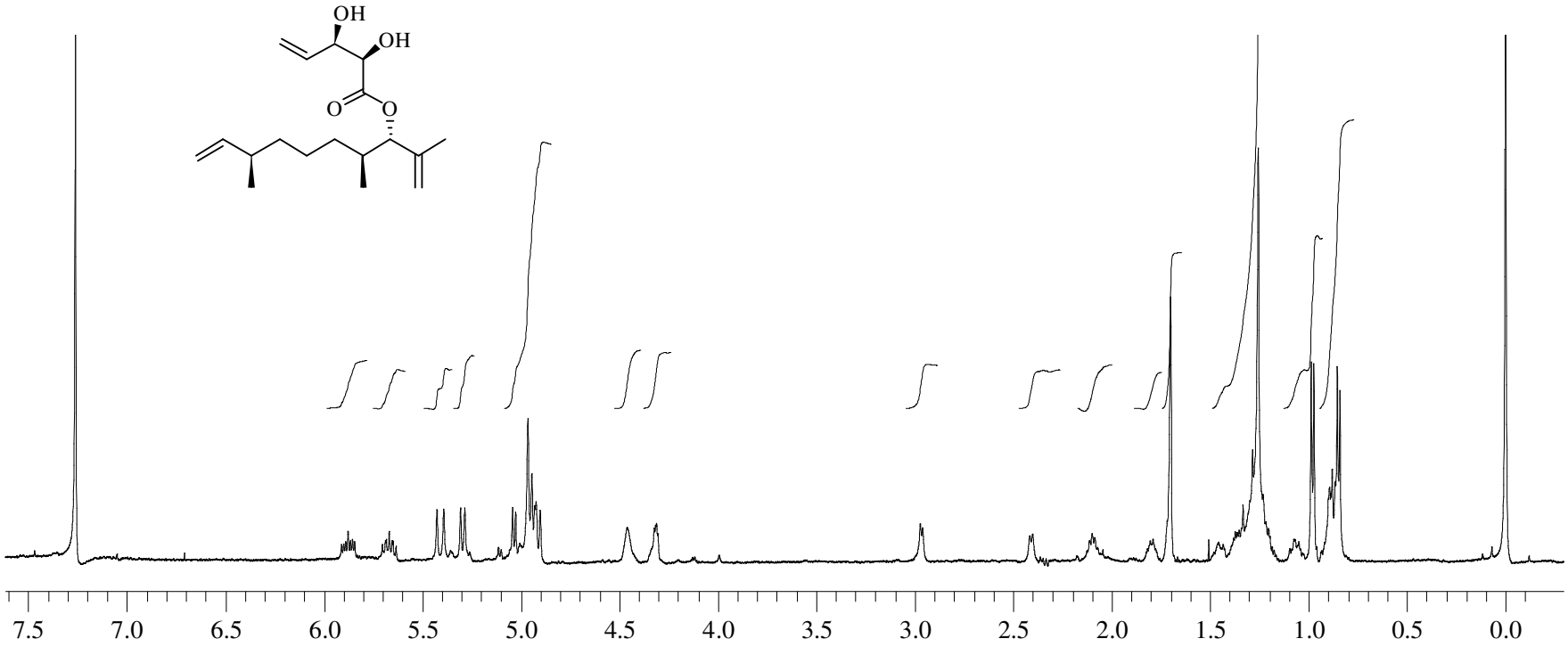


Figure 31: ^{1}H NMR Spectrum of compound **23** ($CDCl_3$, 300 MHz).

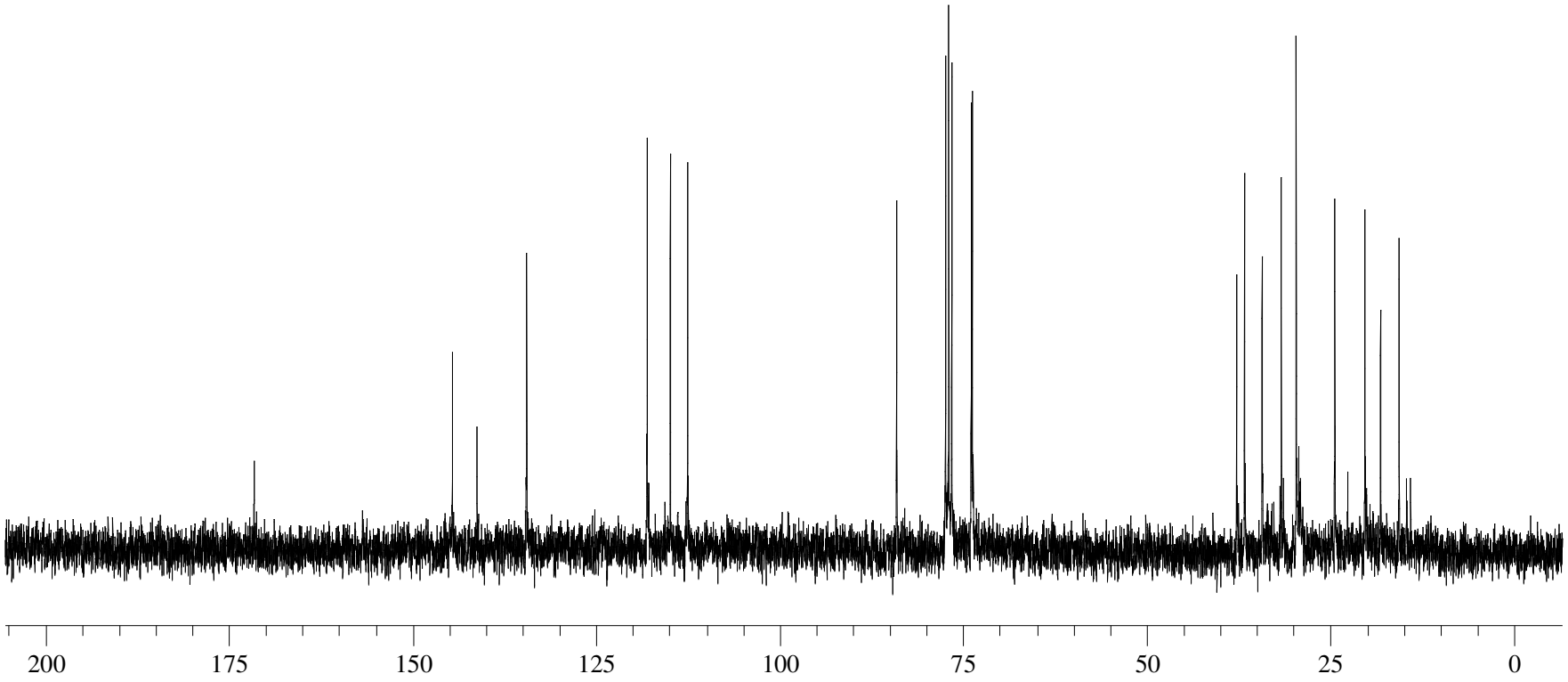


Figure 32: ^{13}C NMR Spectrum of compound **23** ($CDCl_3$, 125 MHz).

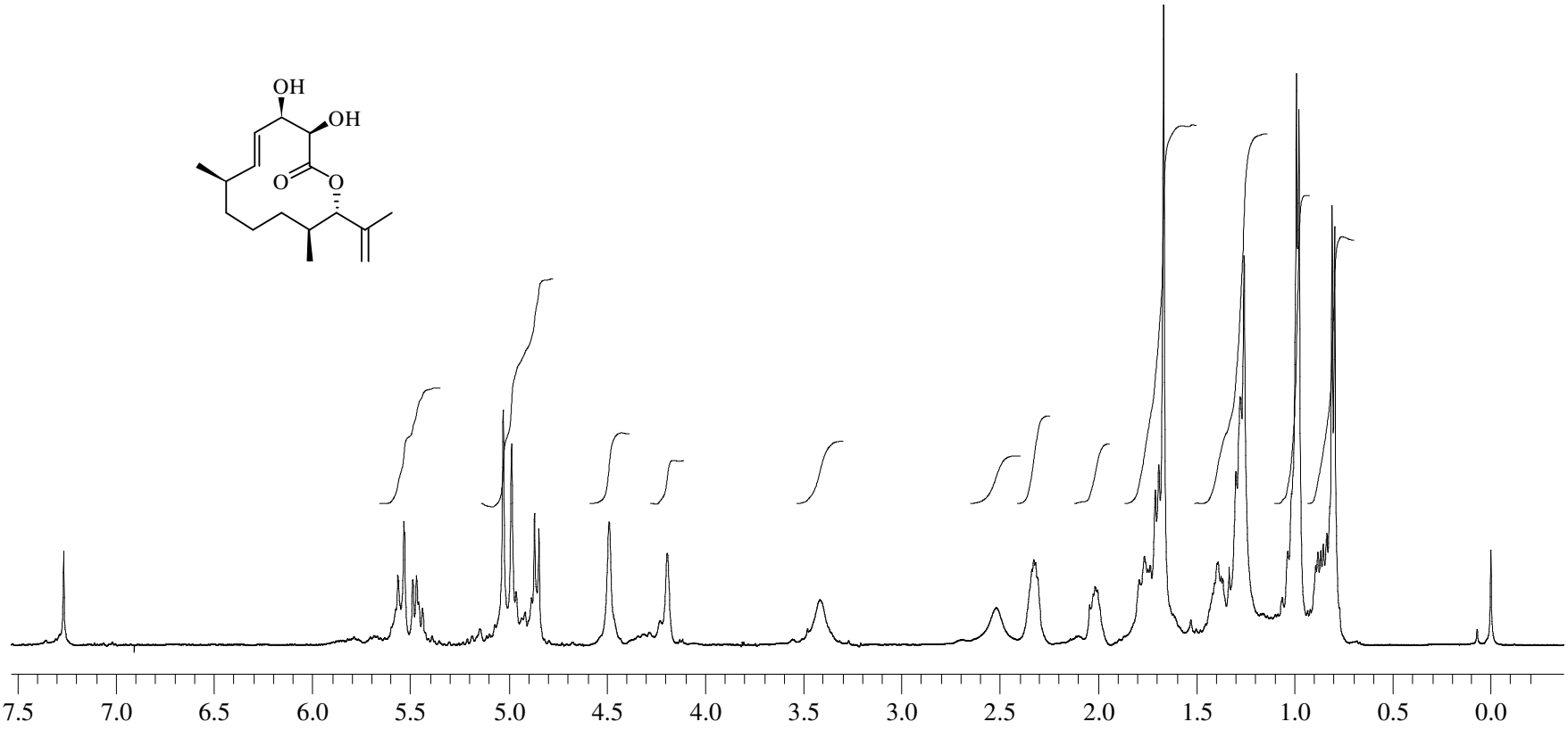


Figure 33: ^{1}H NMR Spectrum of compound **2** ($CDCl_3$, 300 MHz).

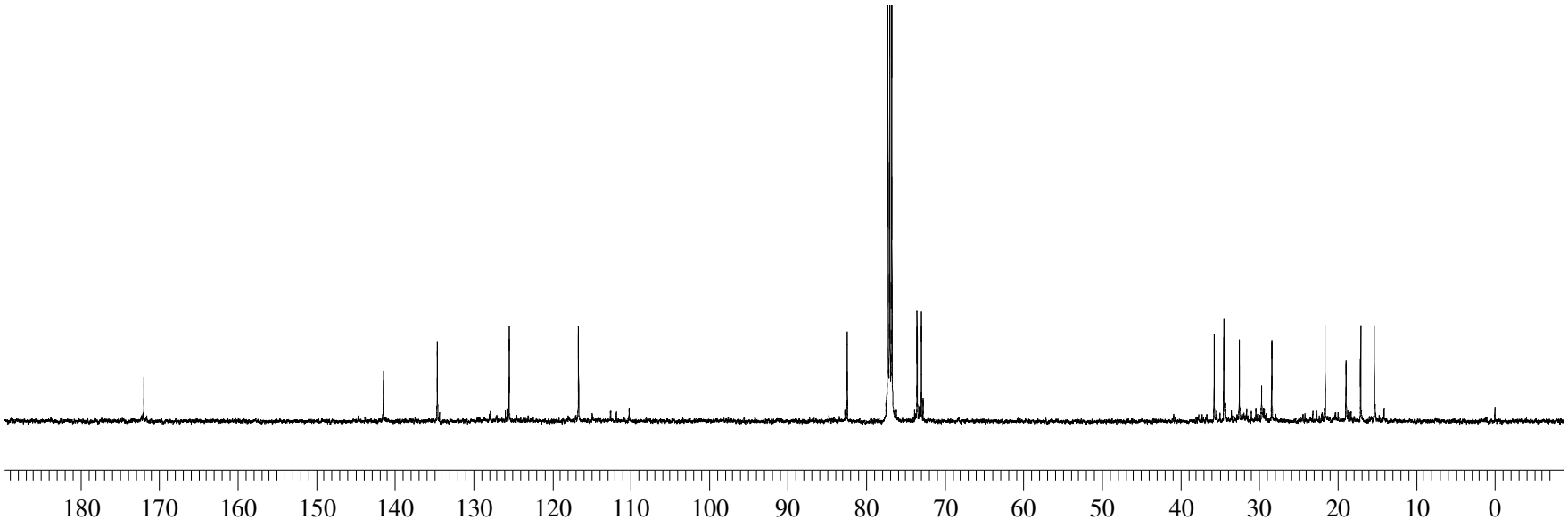


Figure 34: ^{13}C NMR Spectrum of compound **2** ($CDCl_3$, 125 MHz).