Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Stereoselective Total Synthesis of Dinemasone A by Double Intramolecular Hetero Michael addition (DIHMA)

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Experimental details

(*E*)-1,2-Bis((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)ethane (7)

A mixture of diol **6** (20.0 g, 76.34 mmol) and N, N-dimethylformamide dimethyl acetal (30 mL, 229.0 mmol) was heated at 55 °C for 3 h. The volatiles were evaporated, residue dissolved in Ac_2O (9.90 mL, 106.80 mmol) and heated at 130 °C for 3 h. The volatile components of the reaction mixture were evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 4% ethyl acetate in pet. ether) to afford **7** (15.3 g, 88%) as a colorless solid; m.p. 84 °C; $[\alpha]_D^{25}$ + 63.0 (*c* 0.8, $CHCl_3$); IR (neat): 3902, 3733, 3436, 2984, 2936, 2869, 1729, 1455, 1374, 1235, 1156, 1051, 788 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 298 K): δ 5.75 (m, 1H, olefinic), 4.47 (m, 1H, OCH), 4.05 (dd, 1H, *J* = 6.4, 7.9 Hz, OCH), 3.53 (t, 1H, *J* = 7.9 Hz, OCH), 1.40 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 130.7, 109.4, 75.9, 69.3, 26.6, 25.8; HRMS (ESI) *m/z* calculated for $C_{12}H_{20}O_4$ $(M+Na)^+$ 251.1247, found 251.1259.

(*S*, *E*)-4-((*S*)-2, 2-Dimethyl-1, 3-dioxolan-4-yl)but-3-ene-1,2-diol (8)

To a stirred solution of **7** (15.2 g, 66.6 mmol) in CH_3CN (225 mL) at 0 °C, $CuCl_2.2H_2O$ (6.9 g, 40.53 mmol) was added and stirred at room temperature for 30 min. Reaction mixture was quenched with aq. $NaHCO_3$ solution (25 mL), filtered through a pad of celite and washed with ethyl acetate (450 mL). Organic layer was dried (Na_2SO_4), evaporated solvent and purified the residue by column chromatography (60-120 mesh Silica gel, 50% ethyl acetate in pet. ether) to give **8** (6.8 g, 54%) as a yellow syrup; $[\alpha]_D^{25}$ +16.8 (*c* 0.15, $CHCl_3$); IR (neat): 3457, 2915, 2097, 1734, 1462, 1374, 1240, 864 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 298 K): δ 5.76 (m, 2H, olefinic), 4.48 (m, 1H, OCH), 4.20 (m, 1H, *J* = 3.4 Hz, OCH), 4.05 (m, 1H, OCH), 3.63-3.53 (m, 2H, OCH), 3.45 (m, 1H, OCH), 3.03 (bs, 1H, OH), 2.09 (m, 1H, OH), 1.40 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 132.7, 129.9, 109.4, 76.3, 72.1, 69.3, 66.1, 26.6, 25.8; HRMS (ESI) *m/z* calculated for $C_9H_{16}O_4$ $(M+Na)^+$ 211.0943, found 211.0946.

(*S*)-4-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)butane-1,2-diol (9)

A mixture of **8** (6.4 g, 34.04 mmol) and 10% Pd-C (cat.) in EtOAc (15 mL) was stirred at room temperature under hydrogen atmosphere for 4 h. The reaction mixture was filtered through a pad of celite and washed with ethyl acetate (100 mL). Solvent was evaporated

and residue purified by column chromatography (60-120 mesh Silica gel, 50% ethyl acetate in pet. ether) to furnish **9** (6.25 g, 97%) as a yellow syrup; $[\alpha]_D^{25}$ -26.4 (*c* 0.22, $CHCl_3$); IR (neat): 3448, 2936, 2016, 1735, 1645, 1456, 1373, 1219, 1056, 856 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 298K): δ 4.14-4.0 (m, 2H, OCH), 3.68 (m, 1H, OCH), 3.59 (dd, 1H, *J* = 3.0, 10.9 Hz, OCH), 3.50 (t, 1H, *J* = 7.2 Hz, OCH), 3.41 (m, 1H, OCH), 1.68 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.40 (s, 3H, CH_3), 1.35 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 108.8, 80.8, 76.0, 72.0, 69.4, 66.6, 30.0, 29.7, 26.8, 25.6; HRMS (ESI) *m/z* calculated for $C_9H_{18}O_4$ $(M+Na)^+$ 213.1103, found 213.1102.

***(S)*-4-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-hydroxybutyl4-methylbenzenesulfonate (10)**

To a stirred solution of the diol **9** (6.20 g, 32.57 mmol) in CH_2Cl_2 (60 mL) at 0 °C, Bu_2SnO (0.16 g, 0.65 mmol), Et_3N (4.54 mL, 32.63 mmol) and *p*-TsCl (6.21 g, 32.63 mmol) were added and stirred at room temperature for 30 min. The reaction mixture was filtered and the filtrate was washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 30% ethyl acetate in pet. ether) to give **10** (10.7 g, 93%) as a yellow syrup; $[\alpha]_D^{25}$ +0.2 (*c* 0.5 $CHCl_3$); IR (neat): 3444, 3018, 2985, 2924, 2853, 1742, 1597, 1454, 1359, 1241, 1174, 1056, 970, 813, 751, 666 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 298K): δ 7.8 (d, 2H, *J* = 8.3 Hz, ArH), 7.36 (d, 2H, *J* = 7.9 Hz, ArH), 4.11-3.88 (m, 4H, OCH), 3.51 (t, 1H, *J* = 6.8 Hz, OCH), 2.92 (d, 1H, *J* = 3.8 Hz, OCH), 2.46 (s, 3H, CH_3), 2.08 (m, 1H, OH), 1.70-1.52 (m, 4H, CH_2), 1.39 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): 145.0, 132.5, 129.9, 127.9, 109.1, 75.6, 73.8, 69.3, 69.1, 29.6, 29.3, 26.8, 25.6, 21.6; (ESIMS) *m/z* $(M+Na)^+$ calculated for $C_{16}H_{24}O_6S$ 367, found 367.

(*R*)-4-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)butan-2-ol (11)

A solution of tosylate **10** (10.2 g, 29.70 mmol) in THF (80 mL) was added to the stirred suspension of $LiAlH_4$ (1.12 g, 29.70 mmol) in THF (10 mL) at 0 °C. The reaction mixture was stirred at room temperature for 30 min and quenched with aq. Na_2SO_4 solution (30 mL). It was filtered through a pad of celite and washed with ethyl acetate (2 × 100 mL). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 30% ethyl acetate in pet. ether) to afford **11** (4.2 g, 81%) as a yellow

syrup; $[\alpha]_D^{25}$ -2.2 (*c* 0.7, $CHCl_3$); IR (neat): 3433, 2922, 1731, 1668, 1461, 1373, 1213, 1060, 968, 856, 770 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 298 K): δ 4.17-4.04 (m, 2H, OCH), 3.83 (sext, 1H, *J* = 6.0 Hz, OCH), 3.53 (t, 1H, *J* = 7.2 Hz, OCH), 1.66 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.42 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.20 (d, 3H, *J* = 6.0 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K):: δ 108.9, 72.6, 69.4, 67.9, 35.6, 30.1, 26.9, 25.7, 23.5; HRMS (ESI) *m/z* calculated for $C_9H_{18}O_3$ $(M+Na)^+$ 197.1135, found 197.1130.

(2*S*, 5*R*)-Hexane-1, 2, 5-triol (12)

To a stirred solution of **11** (3.7 g, 21.32 mmol) in CH_3CN (35 mL) at 0 °C, $CuCl_2.2H_20$ (4.34 g, 25.60 mmol) was added and stirred at room temperature for 30 min. Work up as described for **8** and purification of the residue by column chromatography (60-120 mesh Silica gel, ethyl acetate) furnished **12** (2.3 g, 82%) as a yellow syrup; $[\alpha]_D^{25}$ -51.3 (*c* 0.15, MeOH); IR (neat): 3372, 2916, 2360, 2098, 1732, 1648, 1457, 1322, 1050, 936 cm^{-1}; ^1H NMR (d_6-DMSO, 500 MHz, 298 K): δ 4.10 (dd, 2H, *J* = 14.0 Hz, 4.0 Hz), 3.90 (m, 1H), 3.60 (m, 1H), 3.44 (m, 1H), 3.35-3.31 (m, 1H), 3.27-3.22 (m, 1H), 1.45-1.33 (m, 4H, CH_2CH_2), 1.05 (d, 3H, *J* = 6.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$+d_6-DMSO, 75 MHz, 298 K): δ 71.2, 66.3, 65.6, 34.6, 28.9, 22.7; HRMS (ESI) *m/z* calculated for $C_6H_{15}O_3$ $(M+H)^+$ 135.1015, found 135.1019.

(*R*)-4-((4*S*)-2-Phenyl-1,3-dioxolan-4-yl)butan-2-ol (13)

To a solution of triol **12** (2.33 g, 17.39 mmol) in CH_2Cl_2 (15 mL) at 0 °C, benzaldehyde dimethyl acetal (3.12 mL, 20.80 mmol) and CSA (cat.) were added and stirred at room temperature for 5 h. Reaction mixture was neutralized with Et_3N (2 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 10% ethyl acetate in pet. ether) to give a diastereomeric mixture of **13** (3.3 g, 85%) as a yellow syrup; $[\alpha]_D^{25}$-14.5 (*c* 0.11, $CHCl_3$); IR (neat): 3447, 3031, 2926, 2857, 2361, 1949, 1731, 1460, 1364, 1252, 1051, 834 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.41 (m, 2H, ArH), 7.33 (m, 3H, ArH), 5.91 (s, 0.3 H, OCH), 5.76 (s, 0.7H, OCH), 4.21 (m, 1.5H, OCH), 4.08 (m, 0.5H, OCH), 3.82 (m, 1.2H, OCH), 3.66 (m, 0.8H, OCH), 1.76 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.18 (m, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 134.5, 129.7, 129.3, 129.1, 128.9, 128.3, 126.5, 126.3, 104.0, 103.1, 77.2, 76.4, 72.4, 70.7, 70.1, 68.3, 67.7, 66.7, 35.6, 35.4,

35.3, 30.0, 29.7, 23.7, 23.6, 23.5; HRMS (ESI) *m/z* calculated for $C_{13}H_{18}O_3$ $(M+Na)^+$ 245.1159, found 245.1150.

((*R*)-4-((4*S*)-2-Phenyl-1,3-dioxolan-4-yl)butan-2-yloxy)(*tert.*-butyl) dimethylsilane (14)

To a stirred solution of alcohol **13** (2.7 g, 12.20 mmol) in CH_2Cl_2 (20 mL) at 0 ºC, imidazole (2.5 g, 36.32 mmol) and TBDMS-Cl (2.2 g, 14.6 mmol) were added and stirred at room temperature for 2 h. Reaction mixture was diluted with $CHCl_3$ (100 ml), washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 5% ethyl acetate in pet. ether) to afford diastereomeric mixture of **14** (4.0 g, 96%) as a yellow syrup; $[\alpha]_D^{25}$ +9.0 (*c* 0.18, $CHCl_3$); IR (neat): 3037, 2950, 2858, 1952, 1809, 1727, 1604, 1462, 1371, 1219, 971 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.42 (m, 2H, ArH), 7.33 (m, 3H, ArH), 5.89 (s, 0.4 H, OCH), 5.74 (s, 0.6H, OCH), 4.17 (m, 1.5H, OCH), 4.05 (m, 0.5H, OCH), 3.84 (m, 1H, OCH), 3.66-3.55 (m, 1H, OCH), 1.77 (m, 1H, CH_2), 1.66-1.54 (m, 1H, CH_2), 1.41 (m, 2H, CH_2), 1.15 (m, 3 H, CH_3), 0.88 (s, 9H, $C(CH_3)_3$), 0.04 (m, 6H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 138.4, 129.2, 129.0, 128.3, 126.6, 126.3, 103.9, 103.1, 77.3, 76.4, 70.7, 70.1, 68.1, 35.3, 29.4, 29.2, 25.9, 23.7, -4.4, -4.7; HRMS (ESI) *m/z* calculated for $C_{19}H_{32}O_3Si$ $(M+Na)^+$ 359.2018 found 359.2014.

(2*S*,5*R*)-2-(Benzyloxy)-5-(*tert*.-butyldimethylsilyloxy)hexan-1-ol (15)

To a stirred solution of acetal **14** (3.8 g, 11.31 mmol) in CH_2Cl_2 (10 mL) at -40 ºC, DIBAL-H (11 mL, 22.61 mmol, 2M solution in toluene) was added dropwise and stirred for 1 h. Reaction mixture was treated sequentially with MeOH (30 mL) and saturated aq. sodium potassium tartarate solution (15 mL). It was filtered through a pad of celite and washed with ethyl acetate (100 mL). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 15% ethyl acetate in pet. ether) to furnish **15** (3.4 g, 90%) as a yellow syrup; $[\alpha]_D^{25}$ +22.2 (*c* 0.2, $CHCl_3$); IR (neat): 3406, 3063, 2922, 2562, 1962, 1711, 1455, 1278, 1065, 847 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.35-7.27 (m, 5H, ArH), 4.61 (d, 1H, *J* = 11.7 Hz, ArCH), 4.52 (d, 1H, *J* = 11.7 Hz, ArCH), 3.76 (m, 1H, OCH), 3.65 (m, 1H, OCH), 3.58-3.43 (m, 2H, OCH), 1.82-1.69 (m, 2H, CH_2), 1.55-1.37 (m, 2H, CH_2), 1.12 (d, 3H, *J* = 6.0 Hz, CH_3), 0.89 (s, 9H, $C(CH_3)_3$), 0.04 (d, 6H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 138.4, 128.5,

127.8, 79.6, 71.3, 68.4, 64.2, 35.0, 26.6, 25.9, 23.8, -4.4, -4.8; HRMS (ESI) *m/z* calculated for $C_{19}H_{34}O_3Si$ $(M+Na)^+$ 361.2157, found 361.2174.

((2*R*,5*S*)-5-(Benzyloxy)hept-6-yn-2-yloxy)(*tert*.-butyl)dimethylsilane (4)

To a stirred solution of **15** (2.0 g, 5.92 mmol) in CH_2Cl_2 (10 mL) at 0 °C, **Dess-Martin periodinane** (3.01 g, 7.10 mmol) was added and stirred at room temperature for 30 min. Reaction mixture was quenched with a 1:1 mixture of saturated solutions of $NaHCO_3$ and hypo (5 mL) and diluted with CH_2Cl_2 (100 mL). Organic layer was washed with water (40 mL), brine (40 mL) and dried (Na_2SO_4). Solvent was evaporated to afford *(2S,5R)-2-(benzyloxy)-5-(tert.-butyldimethylsilyloxy)hexanal* **16** (1.78 g; unstable during column chromatography) along with impurities as a yellow liquid, which was used as such for further reaction.

To a stirred and cooled (0 °C) solution of CBr_4 (4.4 g, 13.2 mmol) in CH_2Cl_2 (20 mL), Ph_3P (6.93 g, 26.45 mmol) was added and the resultant solution was stirred for 30 min. The reaction mixture was sequentially treated with Et_3N (4.40 mL, 31.78 mmol) followed by a solution of the above aldehyde **16** (1.78 g, 5.3 mmol) in CH_2Cl_2 (15 mL) at 0 °C and stirred for 3 h. The reaction mixture was quenched with aq. NH_4Cl (10 mL) solution and extracted with ethyl acetate (100 mL). The combined organic layers were washed with saturated aq. $NaHCO_3$ (50 mL) solution, brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated to give *((2R,5S)-5-(benzyloxy)-7,7-dibromohept-6-en-2-yloxy)(tert.-butyl) dimethylsilane* **17** (3.05 g; unstable during column chromatography) along with impurities, which was used for the next reaction without further purification; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ 7.33 (m, 5H, ArH), 6.40 (d, 1H, *J* = 8.5 Hz, olefinic), 4.59 (d, 1H, *J* = 11.9 Hz, ArCH), 4.41 (d, 1H, *J* = 11.9 Hz, ArCH), 4.06 (m, 1H, OCH), 3.79 (m, 1H, OCH), 2.03 (m, 1H, CH_2), 1.76 (m, 2H, CH_2), 1.55 (m, 1H, CH_2), 1.11 (d, 3H, *J* = 5.9 Hz, CH_3), 0.90 (s, 9H, $C(CH_3)_3$), 0.04 (s, 6H, $SiCH_3$); (ESIMS) *m/z* $(M+Na)^+$ calculated for $C_{20}H_{32}Br_2O_2Si$ 515, found 515.

A solution of the above dibromide **17** (3.0 g, 6.12 mmol) in THF (45 mL) was cooled to -78 °C and treated with *n*-BuLi (7.34 mL, 2.5 M in hexane, 18.2 mmol) and stirred for 1 h. The reaction mixture was quenched with aq. NH_4Cl solution (20 mL) and extracted with ethyl acetate (100 mL). Organic layers were washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by

column chromatography (60-120 mesh Silica gel, 4% ethyl acetate in pet. ether) to furnish **4** (1.61 g, 80%) as a yellow syrup; $[\alpha]_D^{25}$ -198.7 (*c* 0.19, $CHCl_3$); IR (neat): 3451, 2922, 2852, 1732, 1636, 1461, 1374, 1253, 1066, 833 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.31-7.27 (m, 5H, ArH), 4.79 (d, 1H, *J* = 12.1 Hz, ArCH), 4.47 (d, 1H, *J* = 12.1 Hz, ArCH), 4.02 (dt, 1H, *J* = 6.6, 2.2 Hz, OCH), 3.78 (sext, 1H, *J* = 5.9 Hz, OCH), 2.39 (d, 1H, *J* = 2.2 Hz, ≡CH), 1.83 (m, 1H, CH_2), 1.72 (m, 1H, CH_2), 1.72 (m, 2H, CH_2), 1.13 (d, 3H, *J* = 5.9 Hz, CH_3), 0.88 (s, 9H, $C(CH_3)_3$), 0.03 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 137.9, 128.3, 128.0, 127.6, 83.1, 73.8, 70.4, 68.4, 68.1, 34.9, 31.8, 25.9, 23.8, -4.4, -4.7; HRMS (ESI) *m/z* calculated for $C_{20}H_{32}O_2Si$ $(M+Na)^+$ 355.2057, found 355.2069.

(2*S*,3*R*)-3,4-Dihydroxybutan-2-yl benzoate (19)

To a stirred and cooled (0 °C) solution of **18**[16] (4.0 g, 45.45 mmol) in CH_2Cl_2 (40 mL), $Ti(O^iPr)_4$ (19.38 mL, 68.18 mmol) and benzoic acid (11.0 g, 90.9 mmol) were sequentially added and stirred at room temperature for 30 min. Solvent was evaporated and residue dissolved in ether (50 mL). The reaction mixture was treated with 5% aq. H_2SO_4 (25 mL) solution and stirred for 2 h until each layer was transparent. The aqueous layer was separated and extracted with ether (2 x 100 mL). Combined organic extracts were washed with brine (100 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 40% ethyl acetate in pet. ether) to afford **19** (7.26 g, 76%) as a yellow syrup; $[\alpha]_D^{25}$ +20.0 (*c* 0.1, $CHCl_3$); IR (neat): 3400, 3070, 2917, 2852, 2360,1970, 1720, 1602, 1450, 1280, 1120, 1070, 945 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 298K): δ 8.01 (m, 2H, ArH), 7.59-7.53 (m, 1H, ArH), 7.43 (m, 2H, ArH), 5.11 (quint, 1H, *J* = 6.4 Hz, OCH), 3.70-3.56 (m, 3H, *J* = 5.1 Hz, OCH), 2.65 (bs, 1H, OH), 2.46 (bs, 1H, OH), 1.45 (d, 3H, *J* = 6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 133.3, 129.7, 128.0 74.1, 71.4, 62.5, 16.4; HRMS (ESI) *m/z* calculated for $C_{11}H_{14}O_4$ $(M+Na)^+$ 233.0786, found 233.0789.

(1*S*)-1-((4*R*)-2-Phenyl-1,3-dioxolan-4-yl)ethyl benzoate (20)

To a stirred and cooled (0 °C) solution of diol **19** (6.2 g, 29.52 mmol) in CH_2Cl_2 (32 mL), benzaldehyde dimethyl acetal (5.31 mL, 35.42 mmol) and CSA (cat.) were added and stirred at room temperature for 5 h. Workup as described for **13** and purification of the residue by column chromatography (60-120 mesh Silica gel, 5% ethyl acetate in pet.

ether) furnished **20** (7.21 g, 82%) as a yellow syrup; $[\alpha]_D^{25}$ +71.5 (*c* 0.15, $CHCl_3$); IR (neat): 3316, 3065, 2915, 2851, 2362, 1966, 1720, 1601, 1455, 1378, 1175, 1026, 855 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 8.01 (m, 2H, ArH), 7.57-7.52 (m, 1H, ArH), 7.42 (m, 4H, ArH), 7.31 (m, 3H, ArH), 5.80 (s, 1H, OCH), 5.23 (quint, 1H, *J* = 6.1 Hz, OCH), 4.33 (m, 1H, OCH), 4.16-4.07 (m, 2H, OCH), 1.44 (d, 3H, *J* = 6.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 136.8, 133.1, 129.7, 129.4, 128.3, 126.7, 126.4, 104.6, 78.2, 71.2, 67.2, 65.3, 16.4; HRMS (ESI) *m/z* calculated for $C_{18}H_{18}O_4$ $(M+Na)^+$ 321.1100, found 321.1102.

(1*S*)-1-((4*R*)-2-Phenyl-1,3-dioxolan-4-yl)ethanol (21)

A solution of **20** (4.0 g, 13.42 mmol) in MeOH (20 mL) was treated with K_2CO_3 (5.64 g, 40.30 mmol) and stirred at room temperature for 30 min. MeOH was evaporated and residue extracted with EtOAc (4 x 50 mL). The combined organic layers were washed with water (50 mL), brine (50 mL) and dried (Na_2SO_4). Solvent was evaporated and residue purified by column chromatography (60-120 mesh Silica gel, 10% ethyl acetate in pet. ether) to give **21** (2.44 g, 94%) as a yellow syrup; $[\alpha]_D^{25}$ +51.0 (*c* 0.12, $CHCl_3$); IR (neat): 3462, 2915, 3036, 2359, 1961, 1729, 1456, 1375, 1309, 1219, 1072, 998 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.45 (m, 2H, ArH), 7.36 (m, 3H, ArH), 5.77 (s, 1H, OCH), 4.13 (m, 1H, OCH), 4.07 (m, 1H, OCH), 4.03-3.96 (m, 2H, OCH), 1.21 (d, 3H, *J* = 6.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 137.0, 129.5, 128.4, 126.5, 104.0, 80.3, 67.2, 65.7, 18.5; HRMS (ESI) *m/z* calculated for $C_{11}H_{14}O_3$ $(M+Na)^+$ 217.0848, found 217.0840.

***tert*.-Butyldimethyl((1*S*)-1-((4*R*)-2-phenyl-1,3-dioxolan-4-yl)ethoxy) silane (22)**

To a stirred solution of alcohol **21** (2.34 g 12.10 mmol) in CH_2Cl_2 (15 mL) at 0 ºC, imidazole (2.46 g, 36.20 mmol) and TBDMS-Cl (2.20 g, 14.47 mmol) were added and stirred at room temperature for 2 h. Work up as described for **14** and purification of residue by column chromatography (60-120 mesh Silica gel, 4% ethyl acetate in pet. ether) afforded **22** (3.53 g, 95%) as a yellow syrup; $[\alpha]_D^{25}$ +63.1 (*c* 0.1 $CHCl_3$); IR (neat): 3861, 3730, 3459, 3030, 2927, 2857, 1731, 1462, 1253, 994, 894, 583 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.43 (m, 2H, ArH), 7.34 (m, 3H, ArH), 5.71 (s, 1H, OCH), 4.02 (m, 1H, OCH), 3.90 (m, 1H, OCH), 3.79 (m, 2H, OCH), 1.25 (d, 3H, *J* = 6.1 Hz, CH_3), 0.88 (s, 9H, $C(CH_3)_3$) 0.07 (s, 3H, $SiCH_3$), 0.05 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$,

75 MHz, 298 K): δ 132.9, 129.2 128.2, 126.6, 104.3, 81.1, 69.6, 68.1, 25.7, 21.07, -4.1, -4.8; HRMS (ESI) *m/z* calculated for $C_{17}H_{28}O_3Si$ $(M+Na)^+$ 331.1709, found 331.1704.

(2*R*,3*S*)-2-(Benzyloxy)-3-(*tert.*-butyldimethylsilyloxy)butan-1-ol (23)

To a stirred solution of acetal **22** (3.0 g, 9.74 mmol) in CH_2Cl_2 (20 mL) at -40 ºC, DIBAL-H (9.80 mL, 19.40 mmol, 2 M solution in toluene) was added dropwise and stirred for 1 h. Workedup as described for **15** and purified the residue by column chromatography. First eluted (60-120 mesh Silica gel, 5% ethyl acetate in pet. ether) was **23a** (0.72 g, 24%) as a yellow syrup; $[\alpha]_D^{25}$ +5.9 (*c* 0.5 $CHCl_3$); IR (neat): 3439, 3018, 2954, 2928, 2886, 2856, 1723, 1497, 1454, 1372, 1254, 1214, 1088, 10005, 1027, 985, 916, 834, 751, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.36-7.29 (m, 5H, ArH), 4.58 (d, 1H, *J* = 11.7 Hz, ArCH), 4.51 (d, 1H, *J* = 11.7 Hz, ArCH), 3.83 (quint, 1H, *J* = 6.0 Hz, OCH), 3.66 (m, 1H, OCH), 3.60-3.47 (m, 2H, OCH), 2.39 (d, 1H, *J* = 3.7 Hz, OH), 1.15 (d, 3H, *J* = 6.1 Hz, CH_3), 0.87 (s, 9H, $C(CH_3)_3$), 0.06 (s, 3H, $SiCH_3$), 0.04 (s, 3H, $SiCH_3$); (ESIMS) *m/z* $(M+Na)^+$ calculated for $C_{17}H_{30}O_3Si$ 333, found 333.

Second eluted (60-120 mesh Silica gel, 7% ethyl acetate in pet. ether) was **23** (1.8 g, 58%) as a yellow syrup; $[\alpha]_D^{25}$ +30.6 (*c* 0.1, $CHCl_3$); IR (neat): 3459, 3030, 2927, 2857, 1731, 1462, 1364, 1253, 994, 894 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.31 (m, 5H, ArH), 4.66 (d, 1H, *J* = 11.7 Hz, ArCH), 4.60 (d, 1H, *J* = 11.7 Hz, ArCH), 3.94 (quint, 1H, *J* = 6.1 Hz, OCH), 3.70 (m, 2H, OCH), 3.25 (m, 1H, OCH), 2.07 (bs, 1H, OH), 1.22 (d, 3H, *J* = 6.1 Hz, CH_3), 0.90 (s, 9H, $C(CH_3)_3$), 0.09 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): δ 138.3, 128.4, 127.8, 127.7, 83.4, 72.4, 69.5, 61.4, 29.7, 25.8, 20.5, -4.5, -5.0; HRMS (ESI) *m/z* calculated for $C_{17}H_{30}O_3Si$ $(M+Na)^+$ 333.1854, found 333.1861.

(2*S*,3*S*)-2-(Benzyloxy)-3-(*tert.*-butyldimethylsilyloxy)butanal (3)

To a stirred and cooled (0 °C) solution of **23** (0.5 g, 1.6 mmol) in CH_2Cl_2 (5 mL), Dess-Martin periodinane (1.02 g, 2.41 mmol) was added and stirred at room temperature for 30 min. Work up as described for **16** and purification of residue by flash column chromatography (60-120 mesh Silica gel, 5% ethyl acetate in pet. ether) furnished **3** (0.46 g, 92%) as a yellow syrup; $[\alpha]_D^{25}$ -11.8 (*c* 0.5 $CHCl_3$); IR (neat): 3030, 2954, 2929, 2888, 2856, 1734, 1496, 1458, 1375, 1253, 1214, 1110, 1004, 832, 774, 738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ 9.71 (s, 1H, CHO), 7.36 (m, 5H, ArH), 4.71 (d, 1H, *J*

= 11.6 Hz, ArCH), 4.65 (d, 1H, *J* = 11.6 Hz, ArCH), 4.19 (m, 1H, OCH), 3.64 (dd, 1H, *J* = 2.4, 4.8 Hz, OCH), 1.27 (d, 3H, *J* = 5.9 Hz, CH_3), 0.90 (s, 9H, $C(CH_3)_3$), 0.11 (s, 3H, $SiCH_3$), 0.1 (s, 3H, $SiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K): 203.1, 128.4, 128.2, 128.0, 127.9, 87.2, 72.8, 69.5, 25.8, 25.6, 20.2, -4.7, -4.9; (ESIMS) *m*/*z* $(M+H)^+$ calculated for $C_{17}H_{29}O_3Si$ 309, found 309.

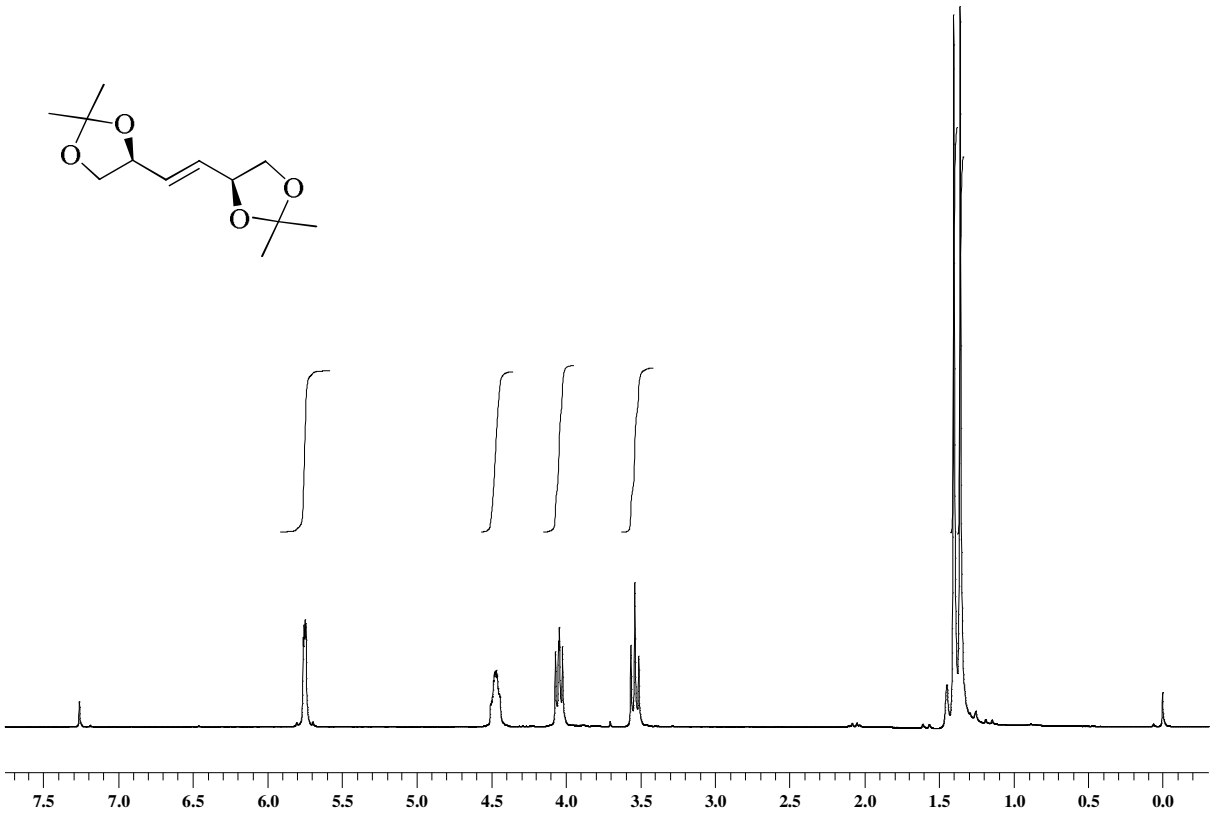

Figure 1. ^{1}H NMR Spectrum of 7 (300 MHz, $CDCl_3$, 298K).

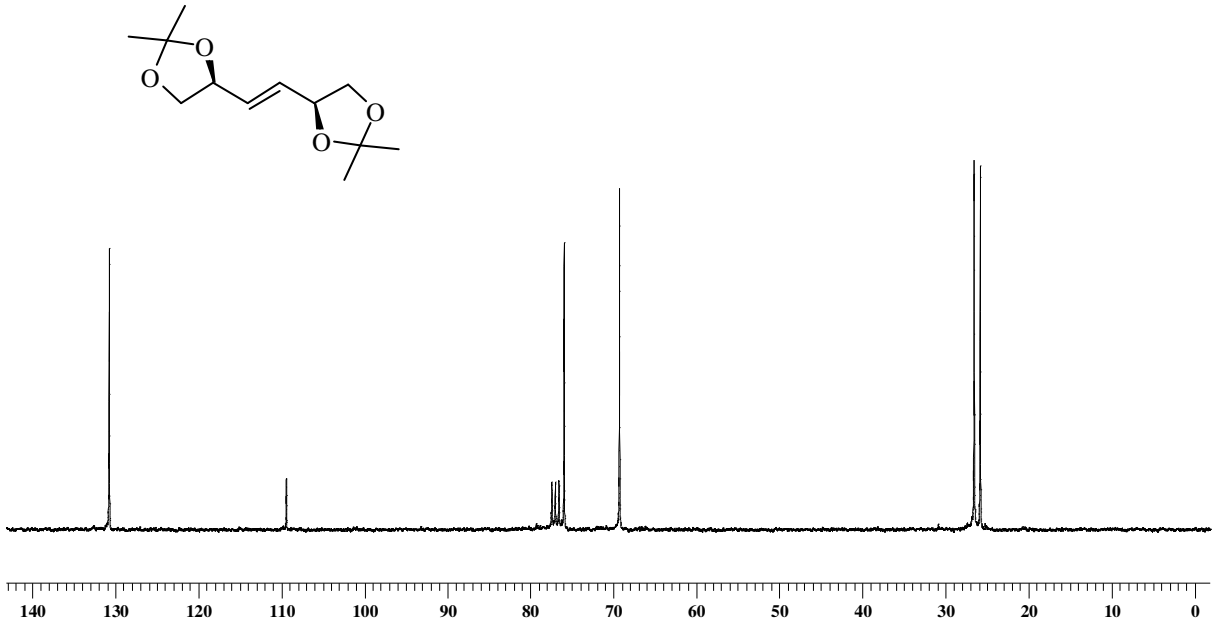

Figure 2. ^{13}C NMR Spectrum of 7 (75 MHz, $CDCl_3$, 298K).

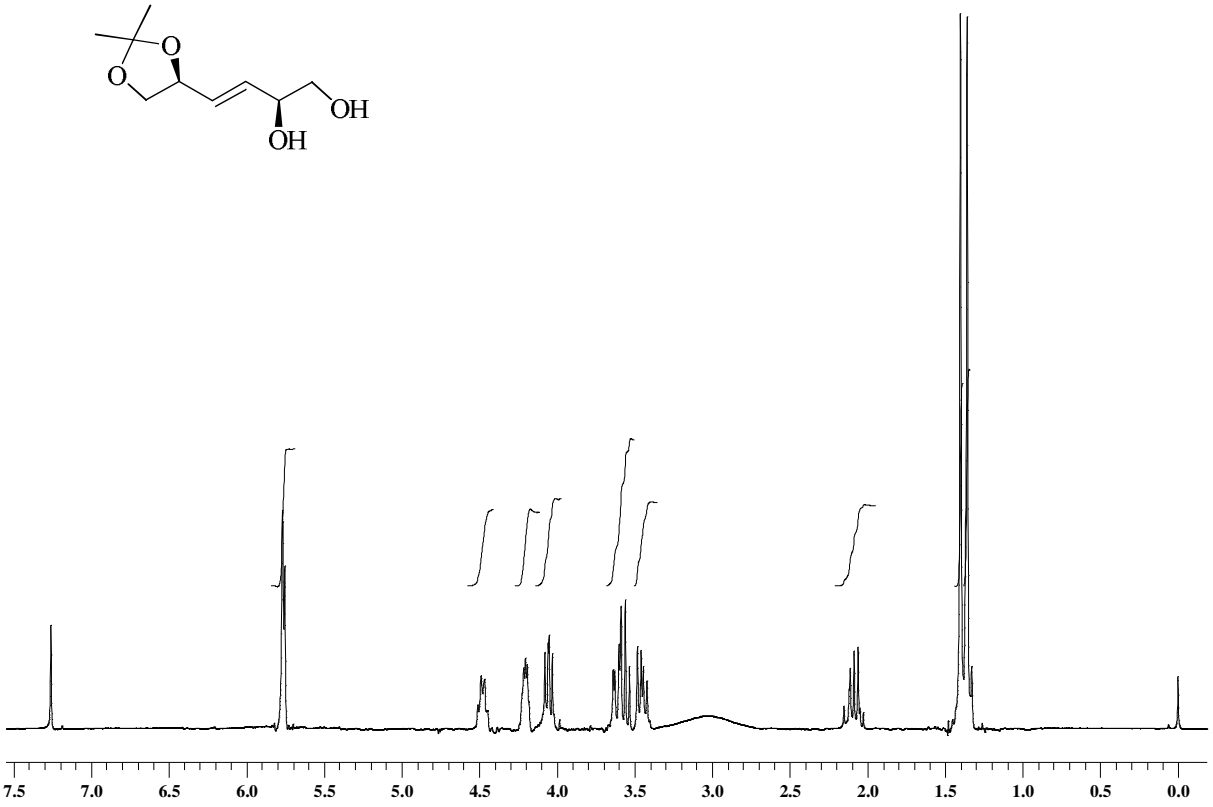

Figure 3. ^{1}H NMR Spectrum of 8 (300 MHz, $CDCl_3$, 298K).

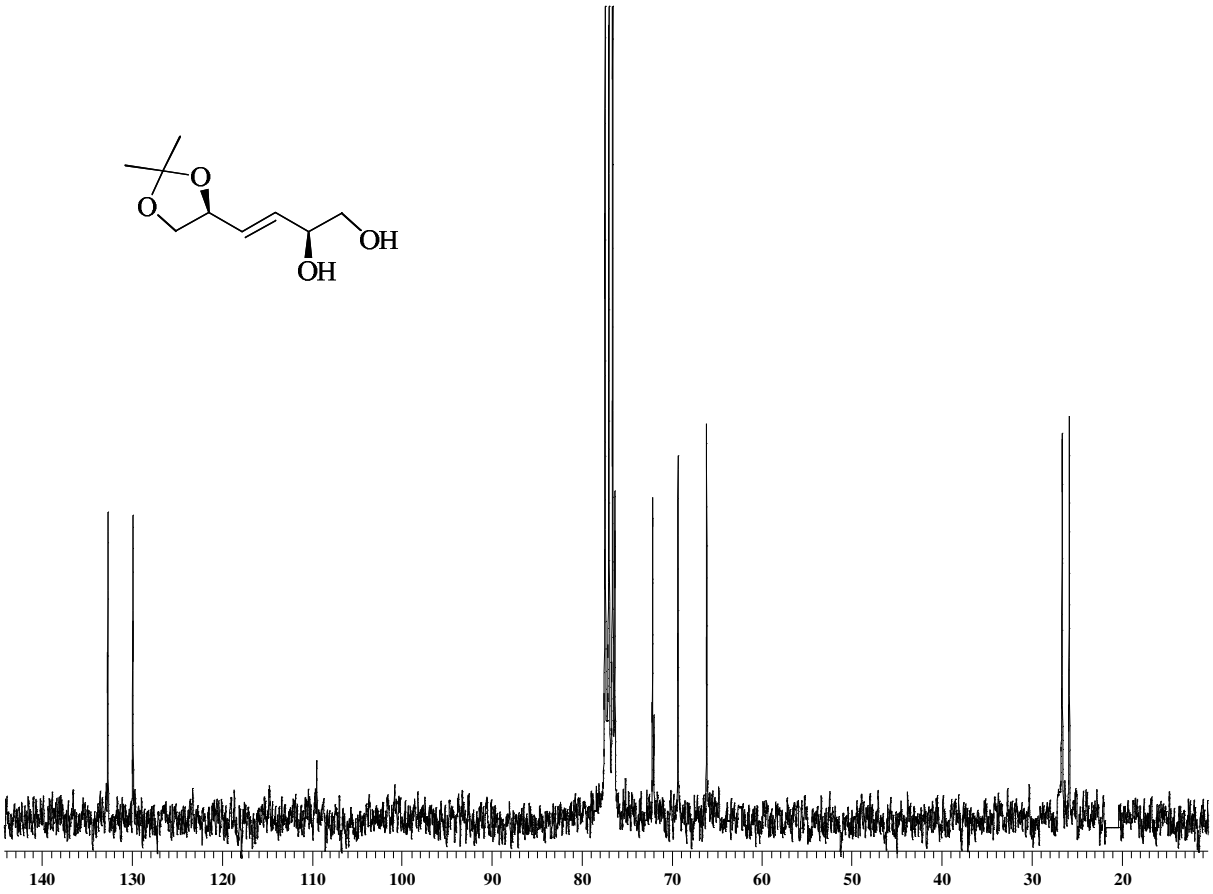

Figure 4. ^{13}C NMR Spectrum of 8 (75 MHz, $CDCl_3$, 298K).

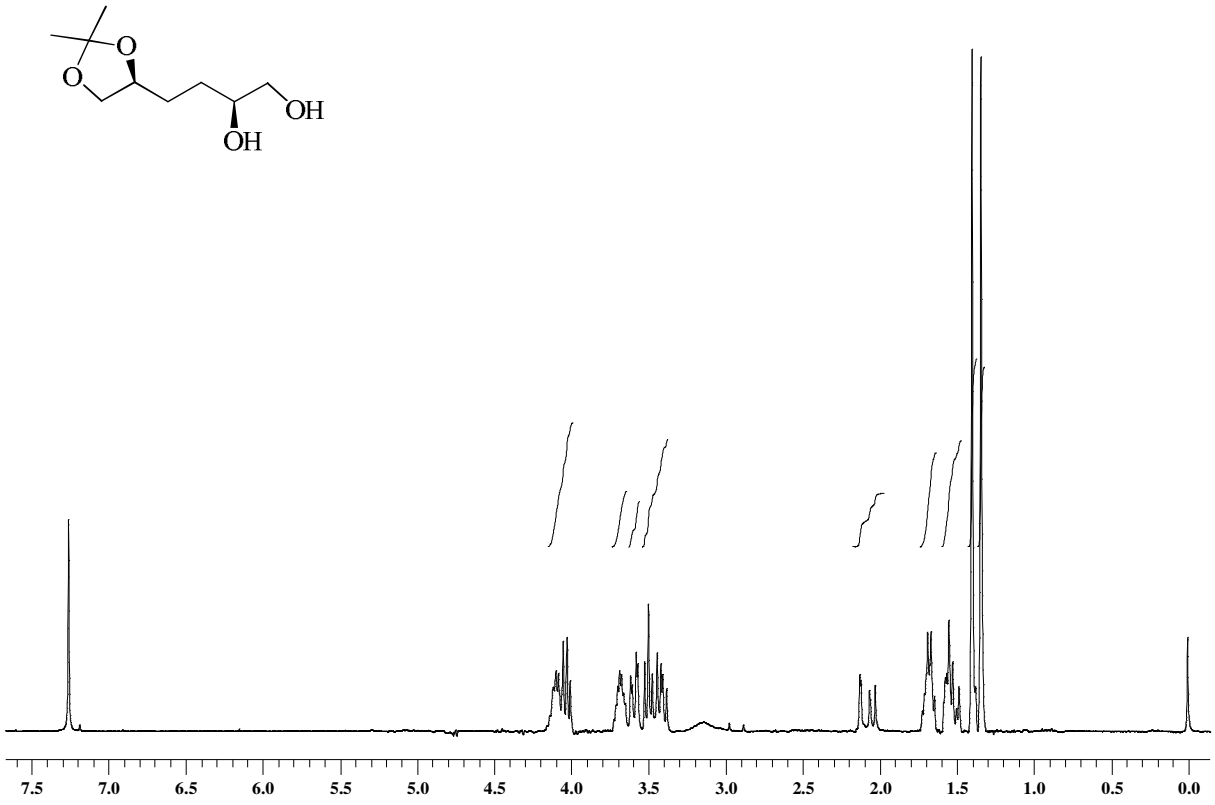

Figure 5. ^{1}H NMR Spectrum of 9 (300 MHz, $CDCl_3$, 298K).

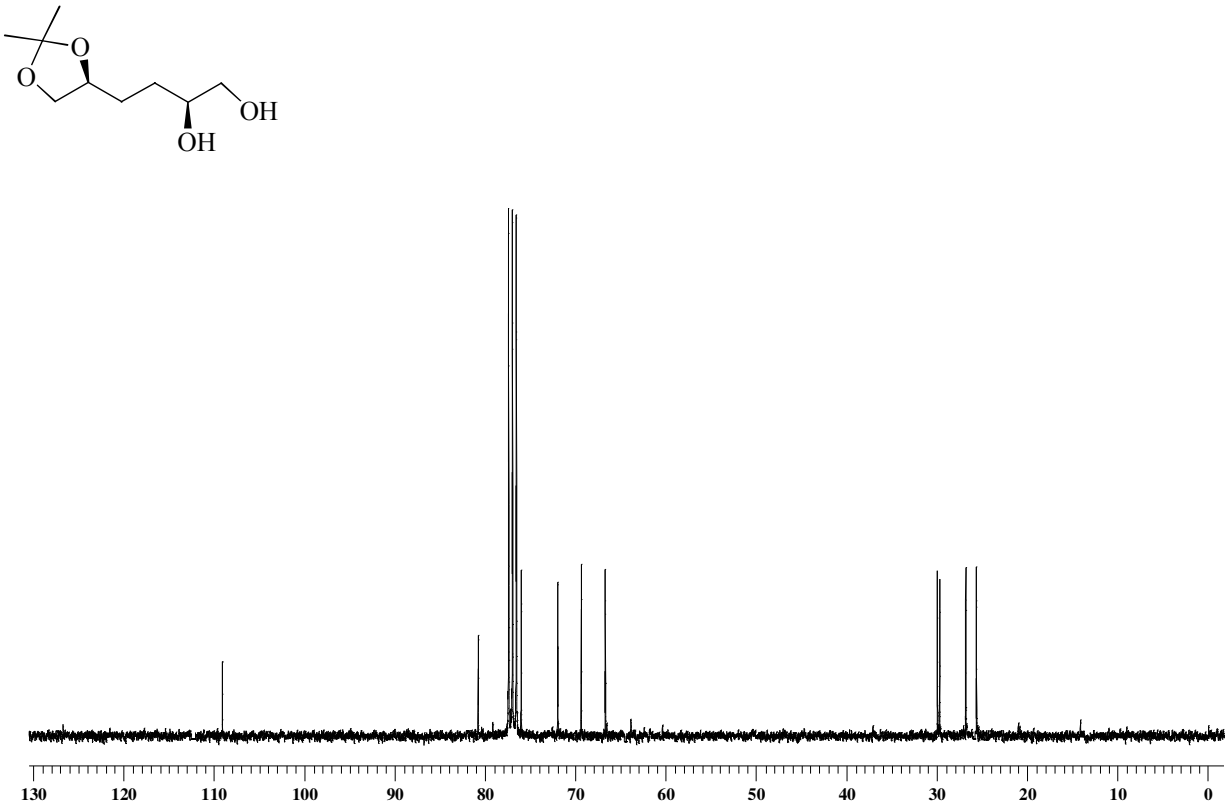

Figure 6. ^{13}C NMR Spectrum of 9 (75 MHz, $CDCl_3$, 298K).

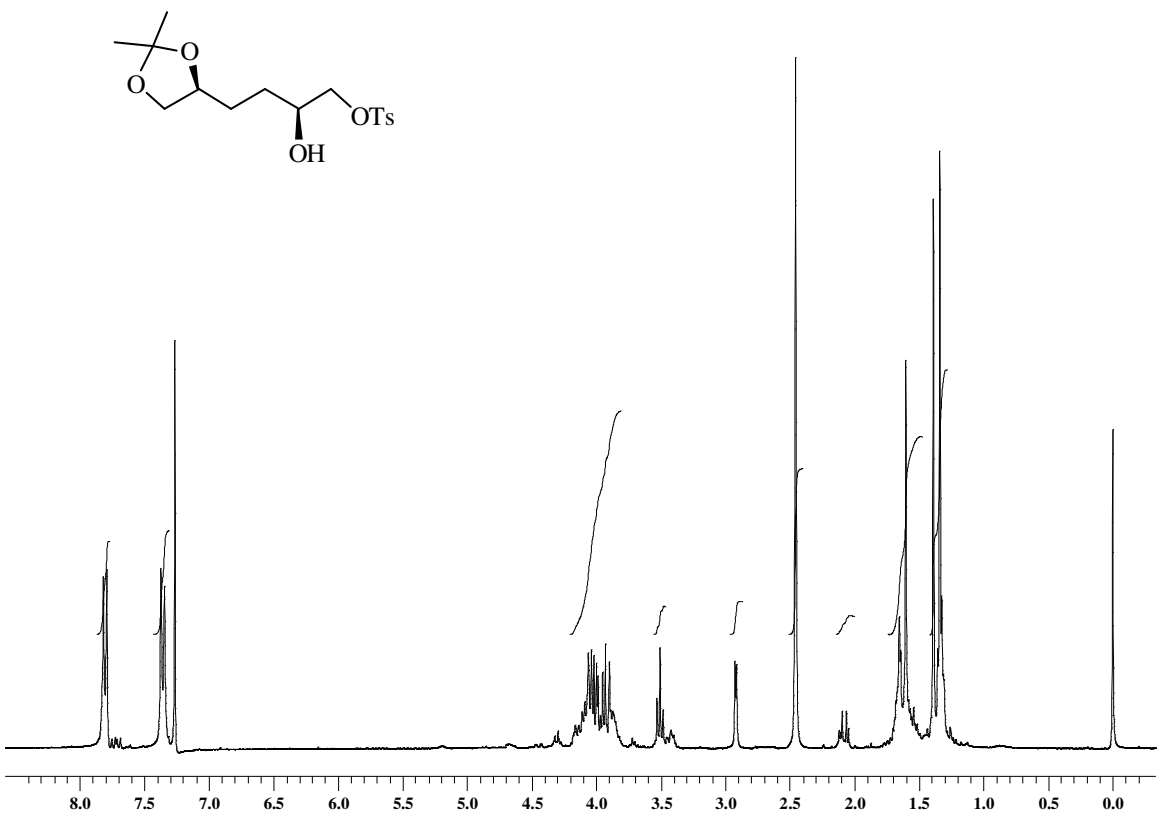

Figure 7. ^{1}H NMR Spectrum of 10 (300 MHz, $CDCl_3$, 298K).

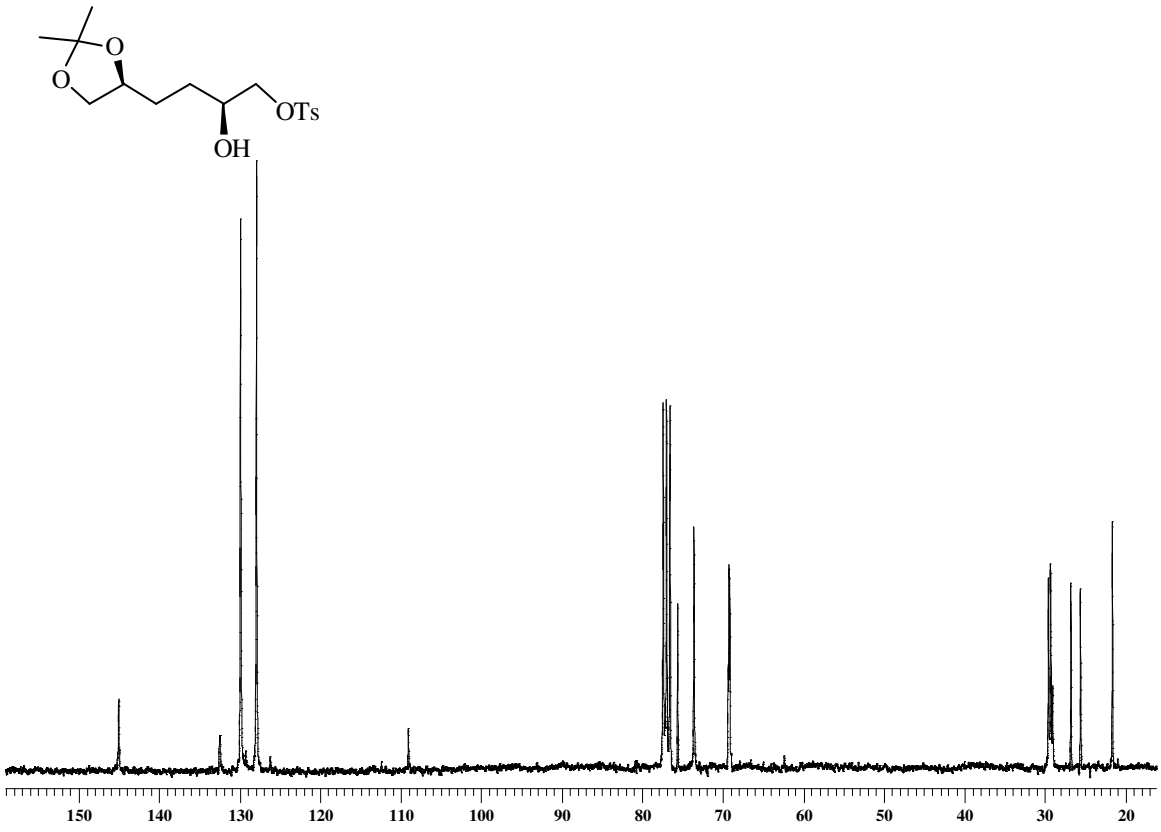

Figure 8. ^{13}C NMR Spectrum of 10 (75 MHz, $CDCl_3$, 298K).

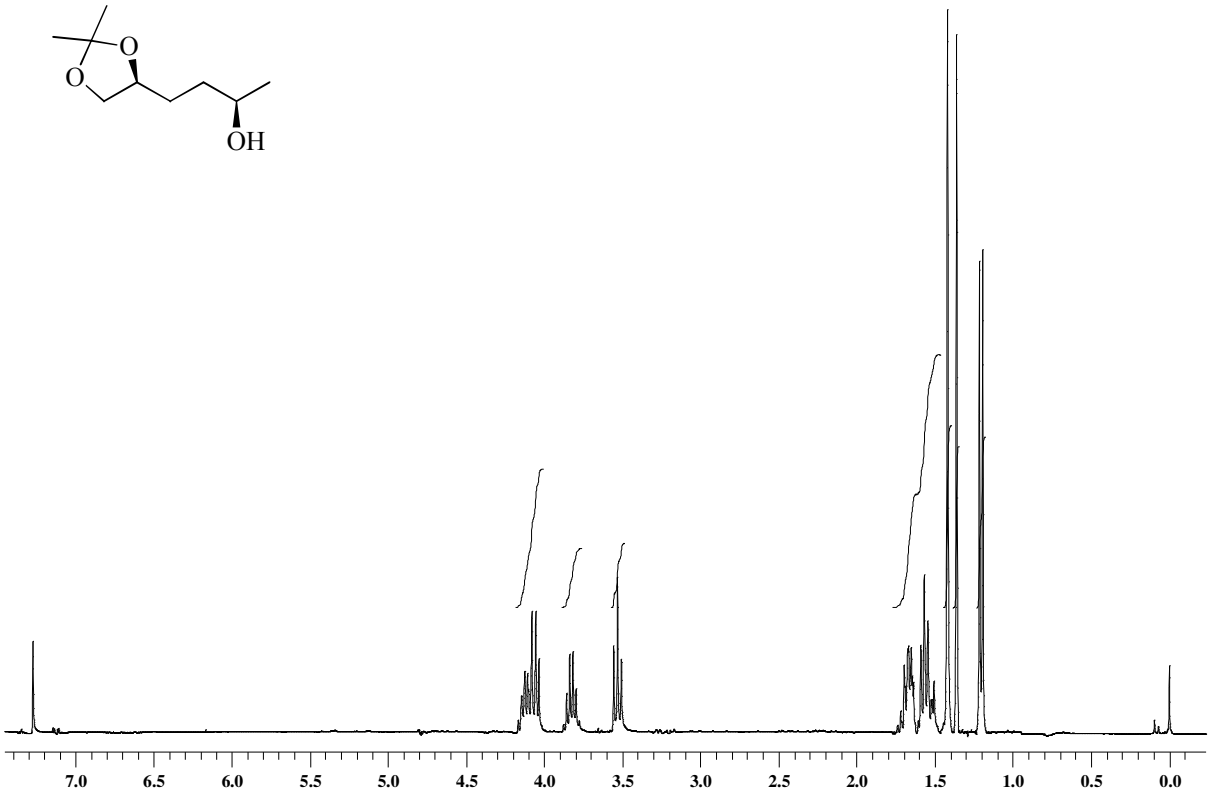

Figure 9. ^{1}H NMR Spectrum of 11 (300 MHz, $CDCl_3$, 298K).

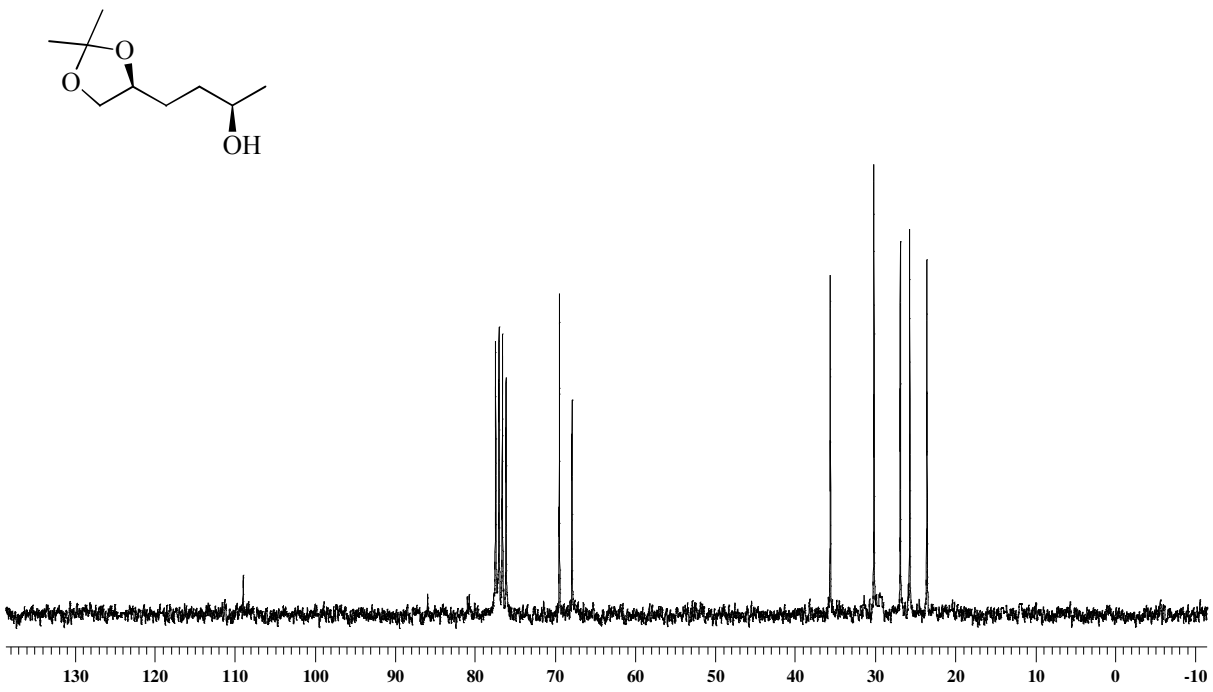

Figure 10. ^{13}C NMR Spectrum of 11 (75 MHz, $CDCl_3$, 298K).

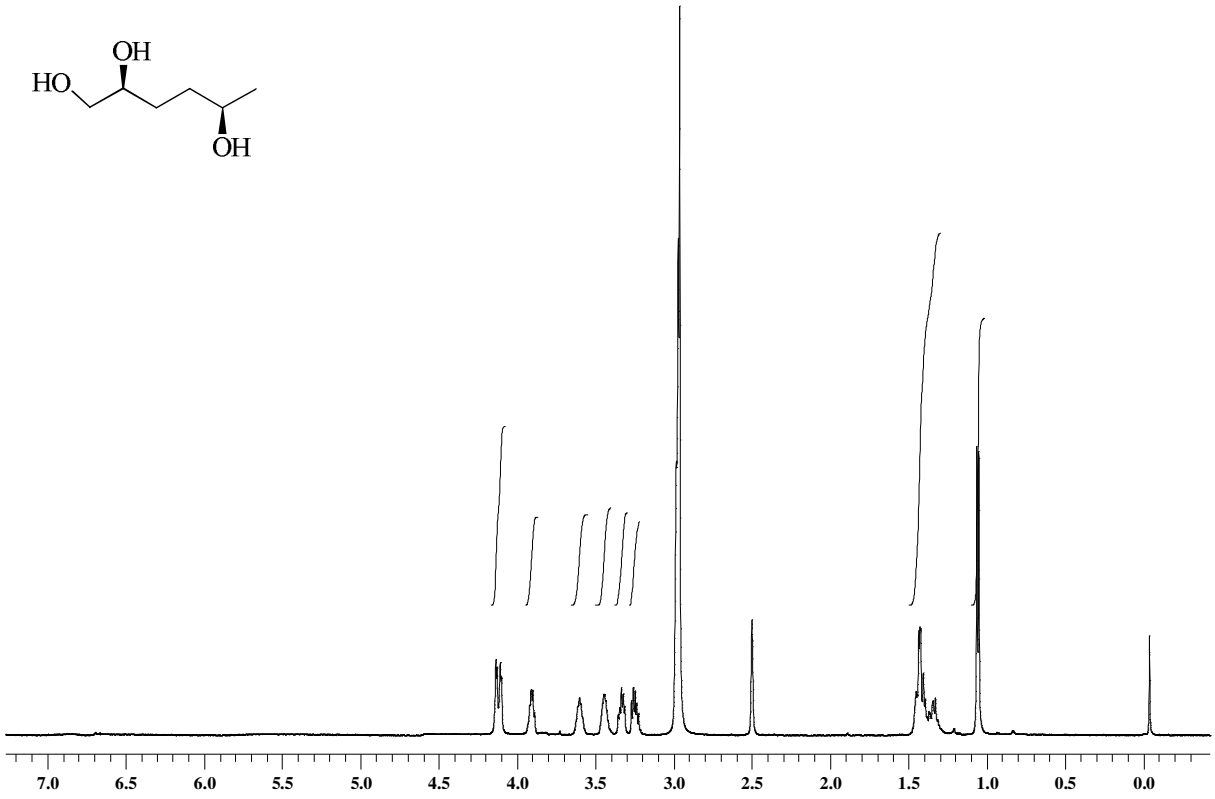

Figure 11. ^{1}H NMR Spectrum of 12 (500 MHz, d_6-DMSO, 298 K).

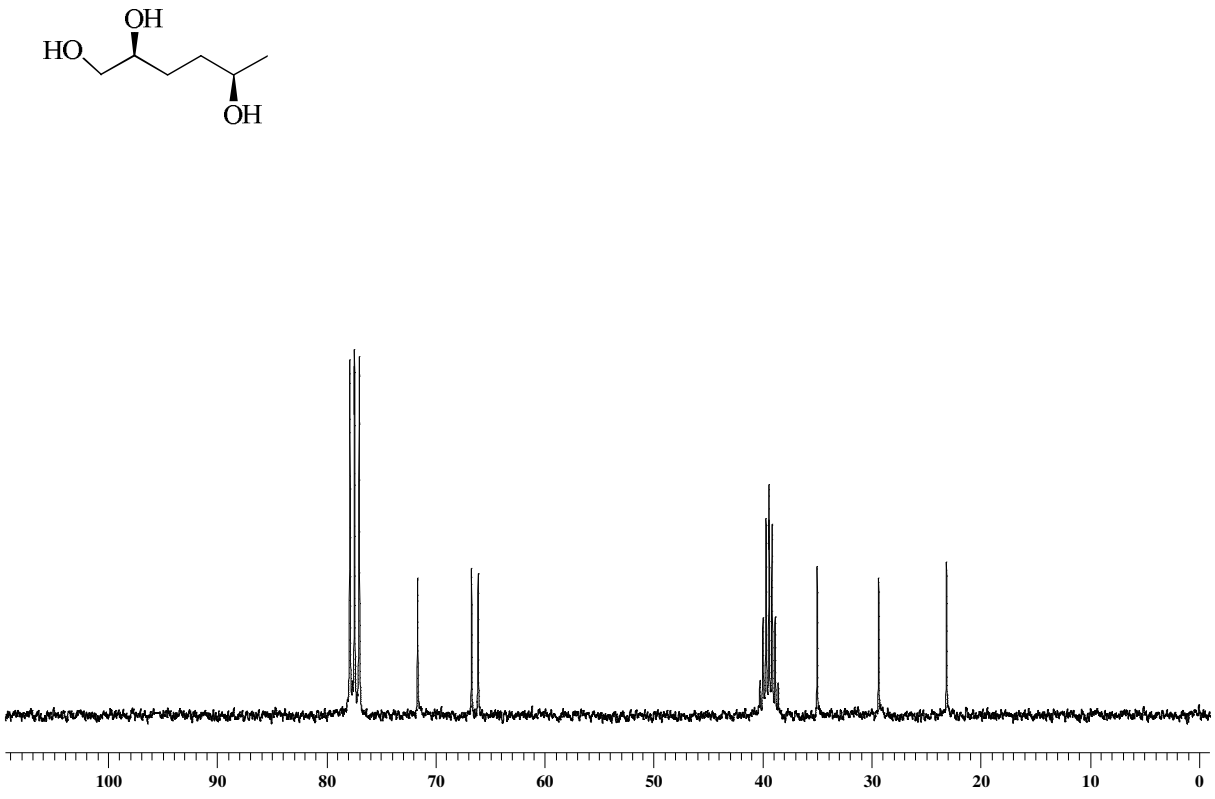

Figure 12. ^{13}C NMR Spectrum of 12 (75 MHz, d_6-DMSO+$CDCl_3$, 298K).

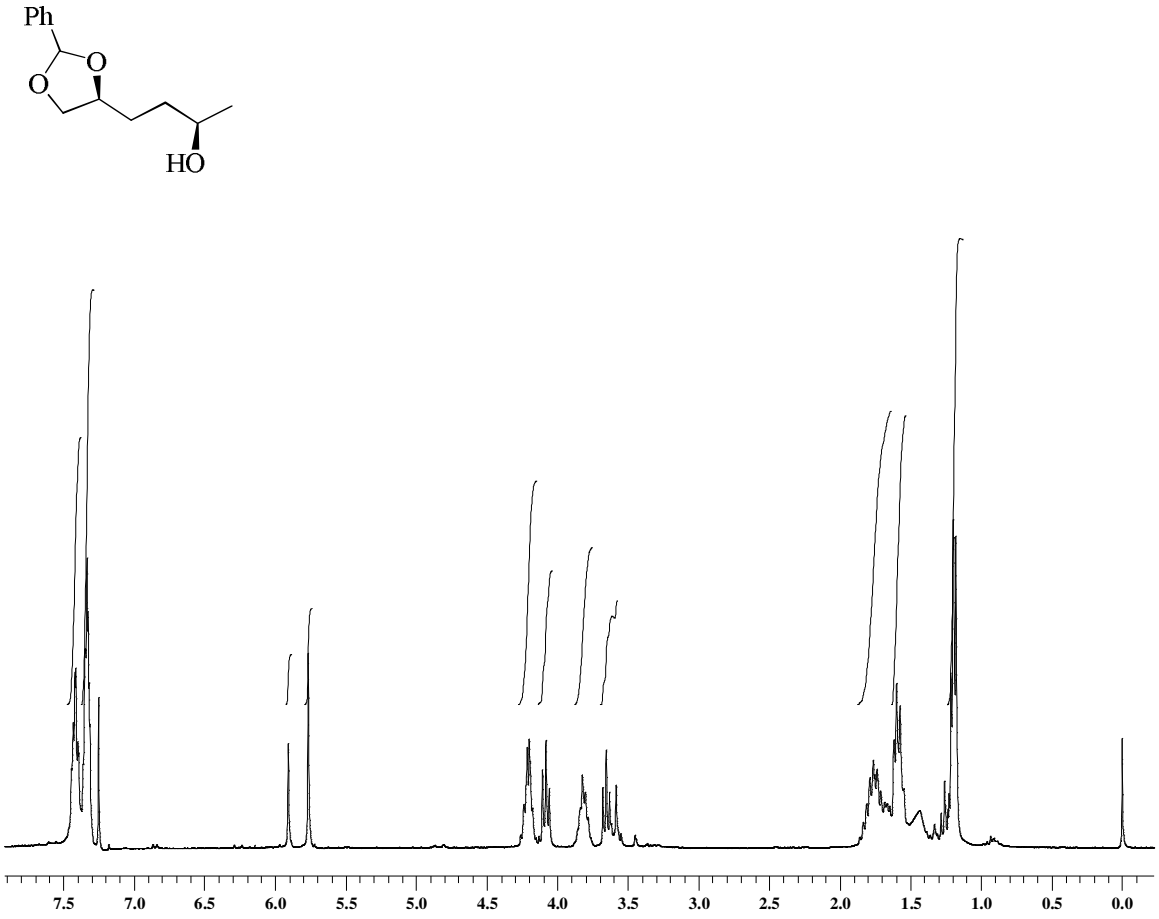

Figure 13. ^{1}H NMR Spectrum of 13 (300 MHz, $CDCl_3$, 298K).

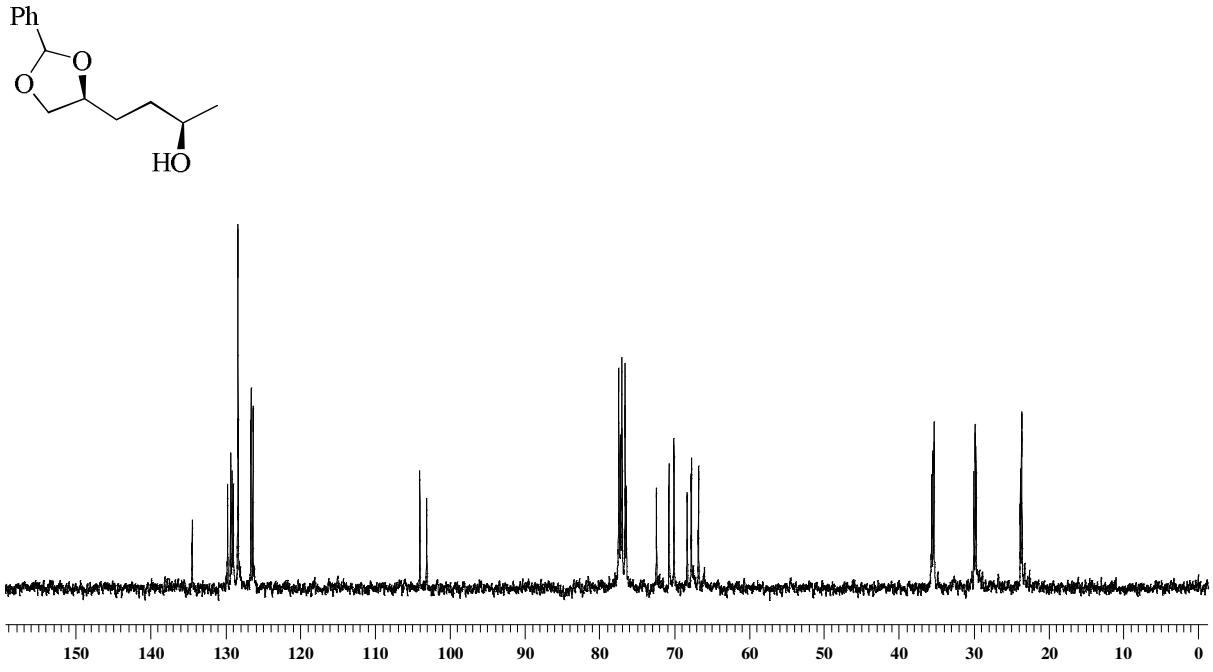

Figure 14. ^{13}C NMR Spectrum of 13 (75 MHz, $CDCl_3$, 298K).

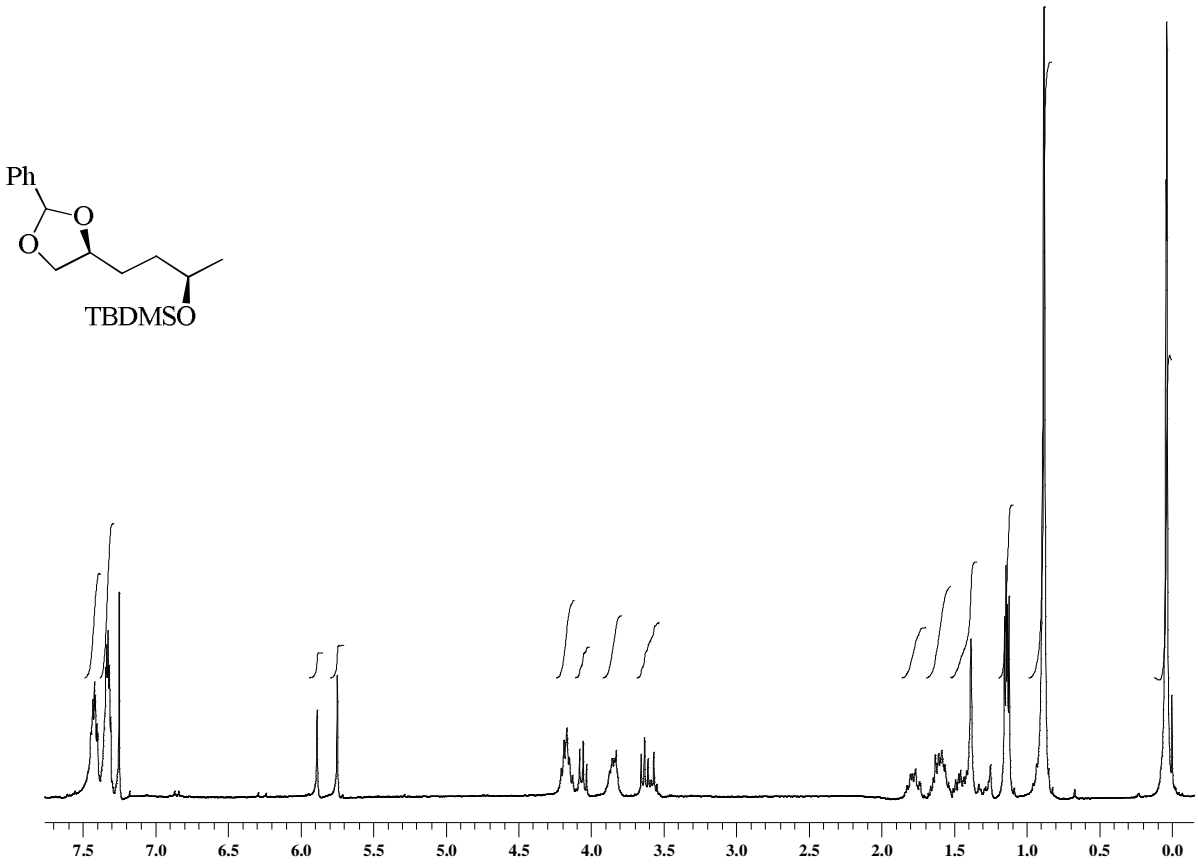

Figure 15. ^{1}**H NMR Spectrum of 14 (300 MHz, $CDCl_3$, 298K).**

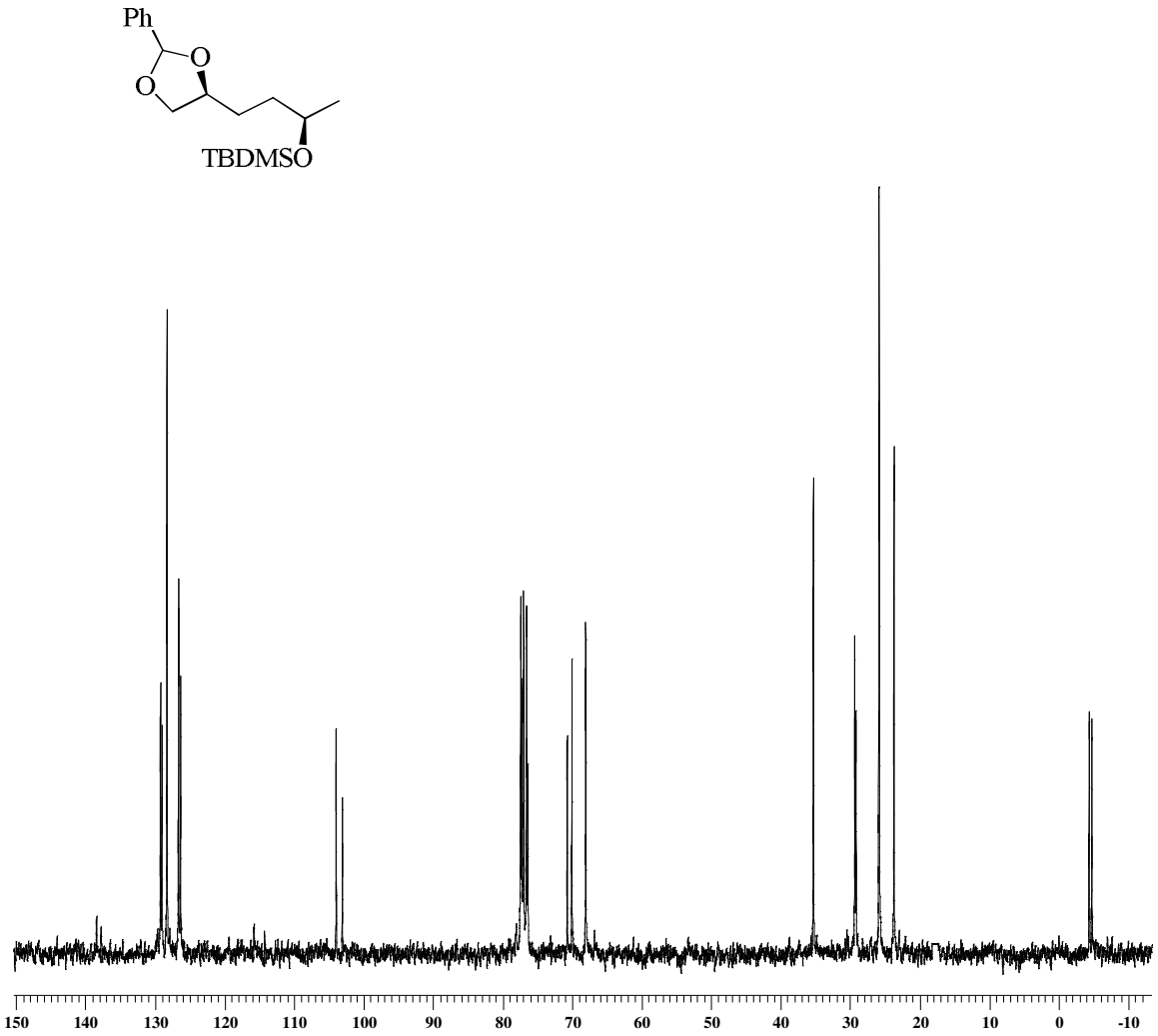

Figure 16.^{13}C NMR Spectrum of 14 (75 MHz, $CDCl_3$, 298K).

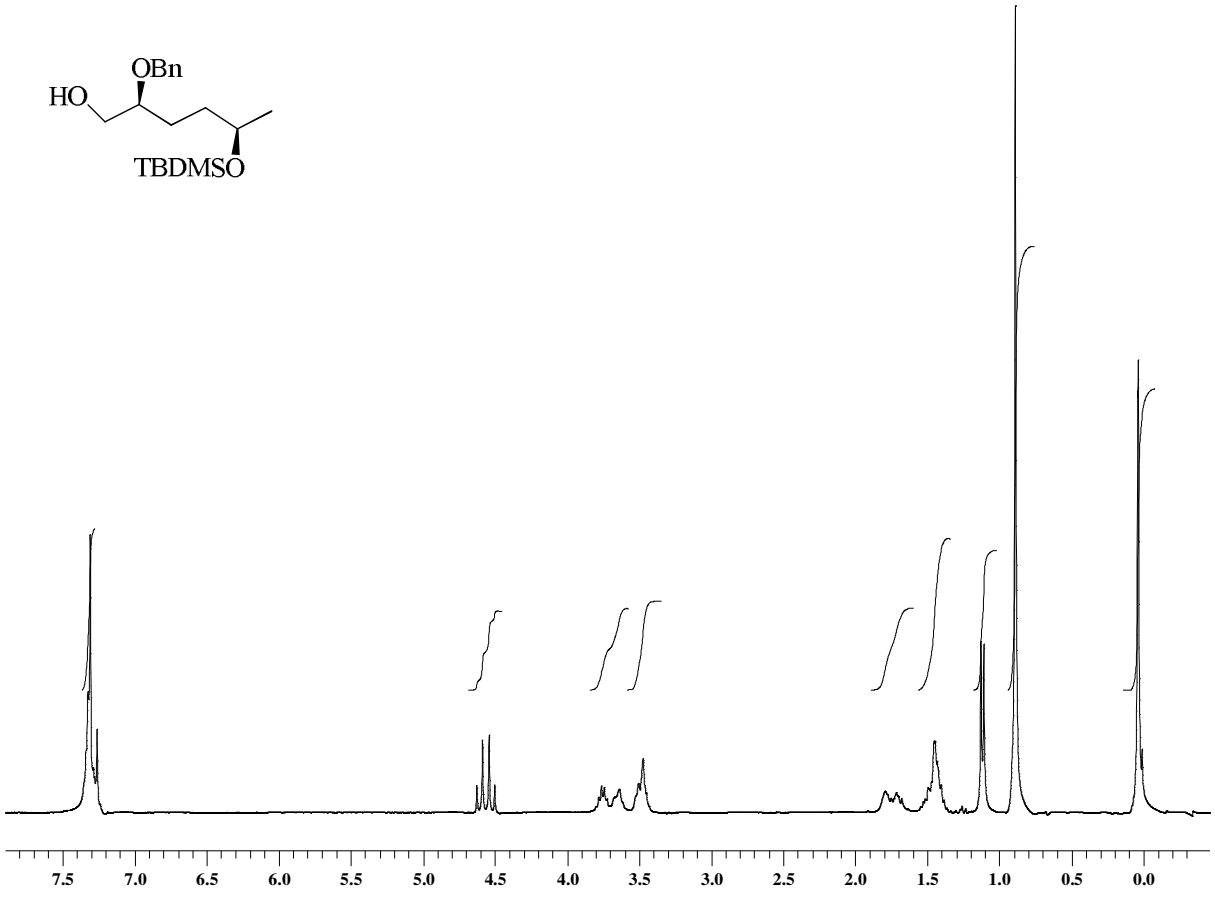

Figure 17. ^{1}H NMR Spectrum of 15 (300 MHz, $CDCl_3$, 298K).

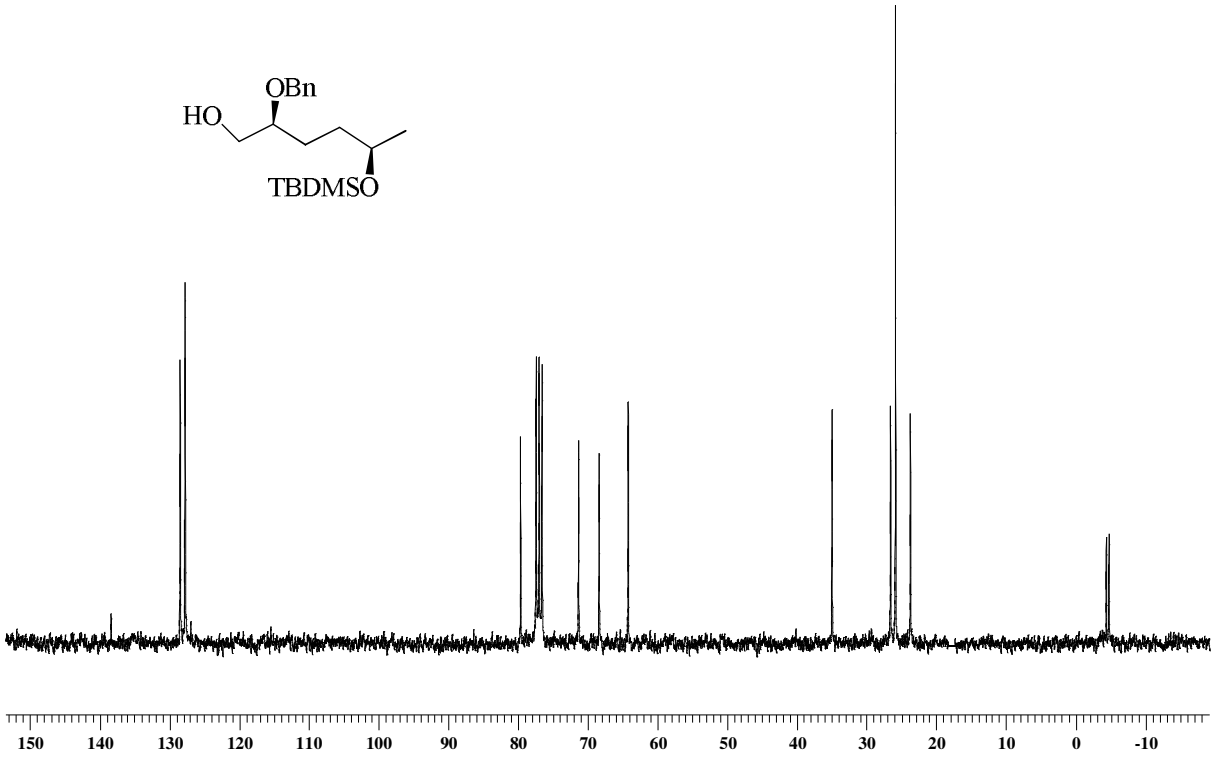

Figure 18. ^{13}C NMR Spectrum of 15 (75 MHz, $CDCl_3$, 298K).

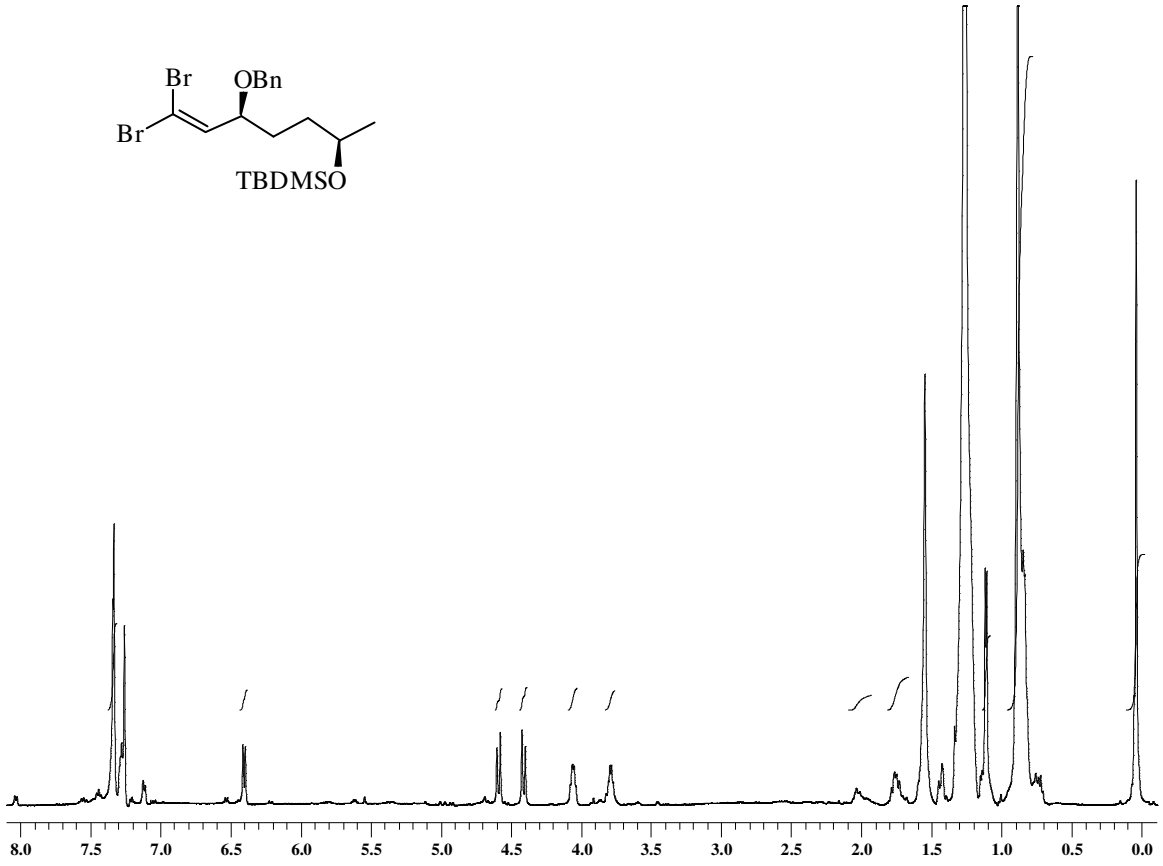

Figure 19. ^{1}H NMR Spectrum of 17 (300 MHz, $CDCl_3$, 298K).

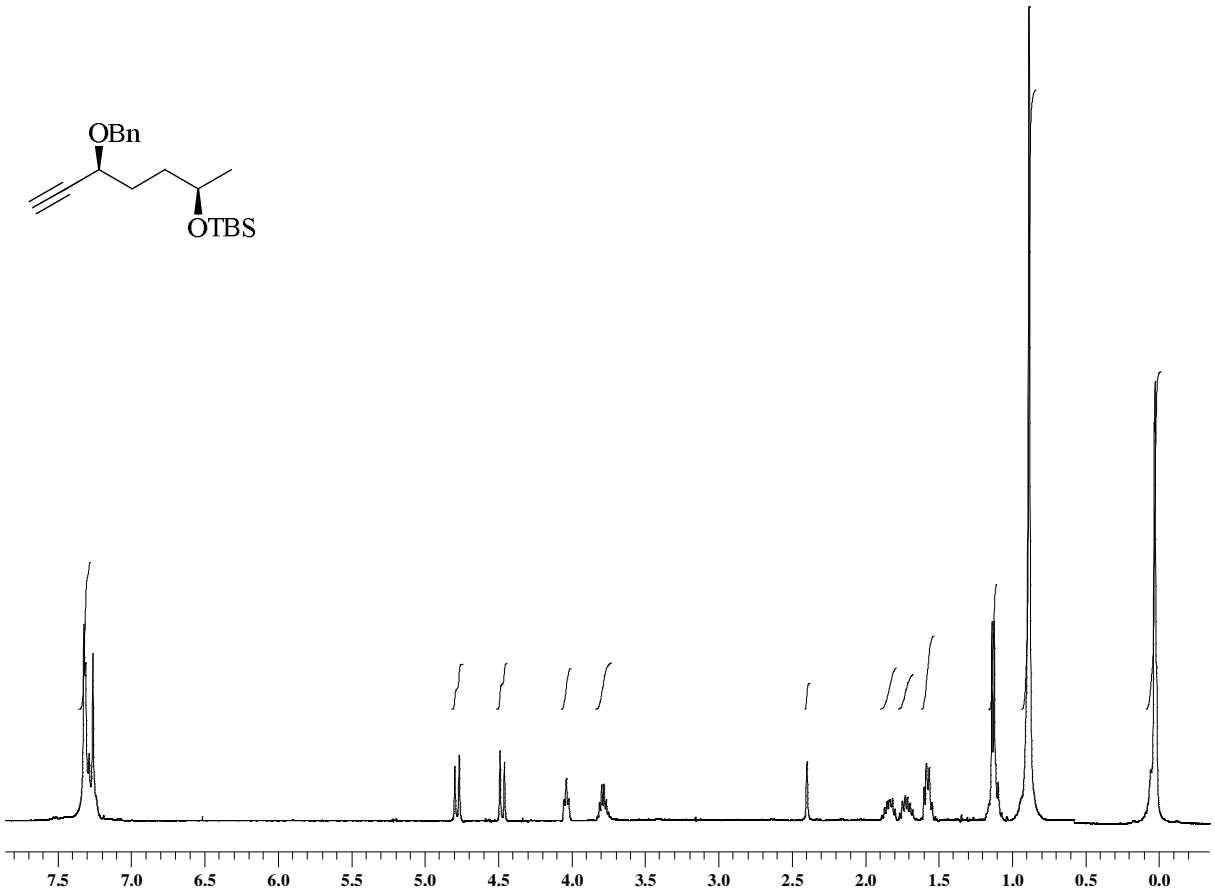

Figure 20. ^{1}H NMR Spectrum of 4 (300 MHz, $CDCl_3$, 298K).

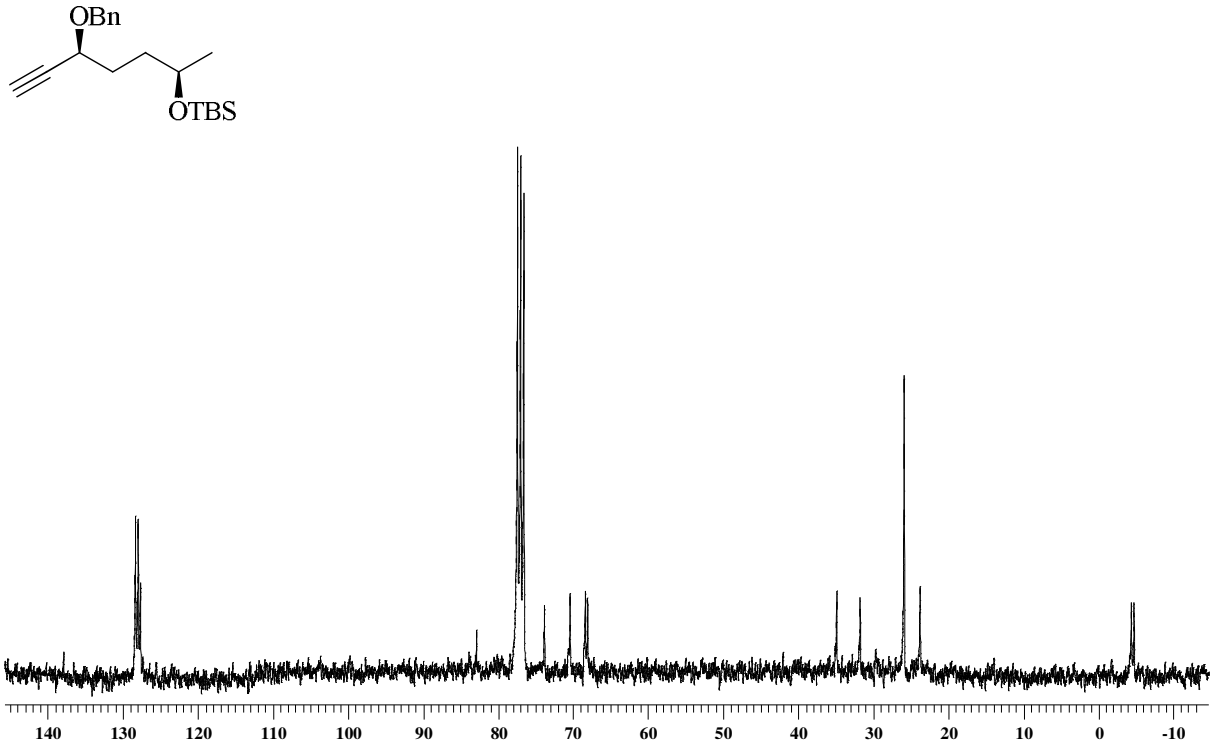

Figure 21. ^{13}C NMR Spectrum of 4 (75 MHz, $CDCl_3$, 298K).

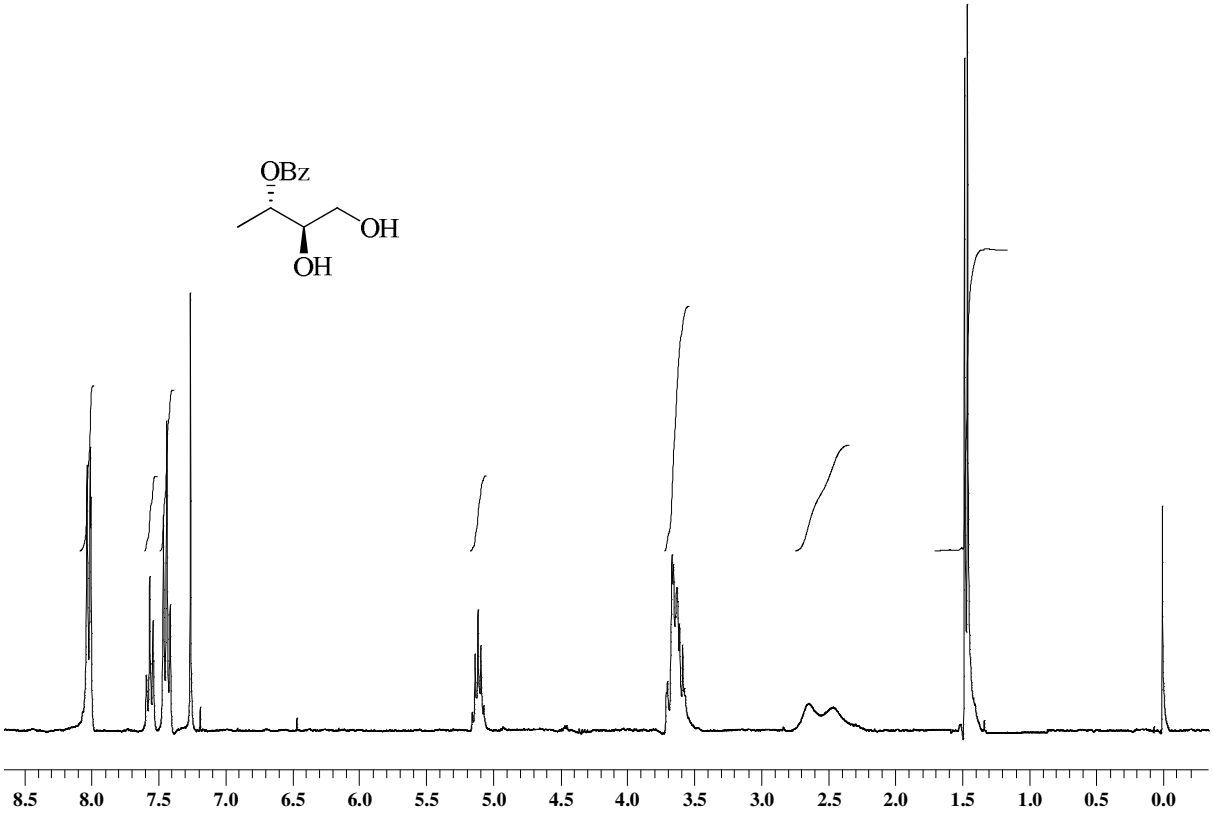

Figure 22. ^{1}H NMR Spectrum of 19 (300 MHz, $CDCl_3$, 298K).

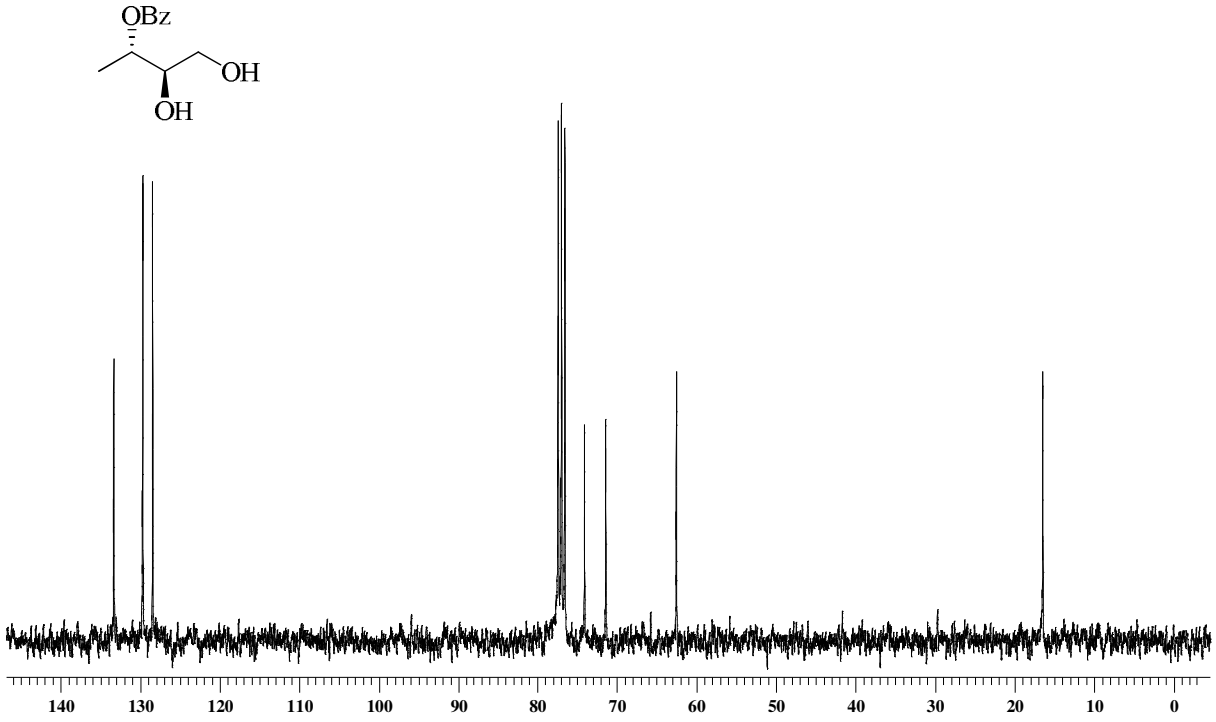

Figure 23. ^{13}C NMR Spectrum of 19 (75 MHz, $CDCl_3$, 298K).

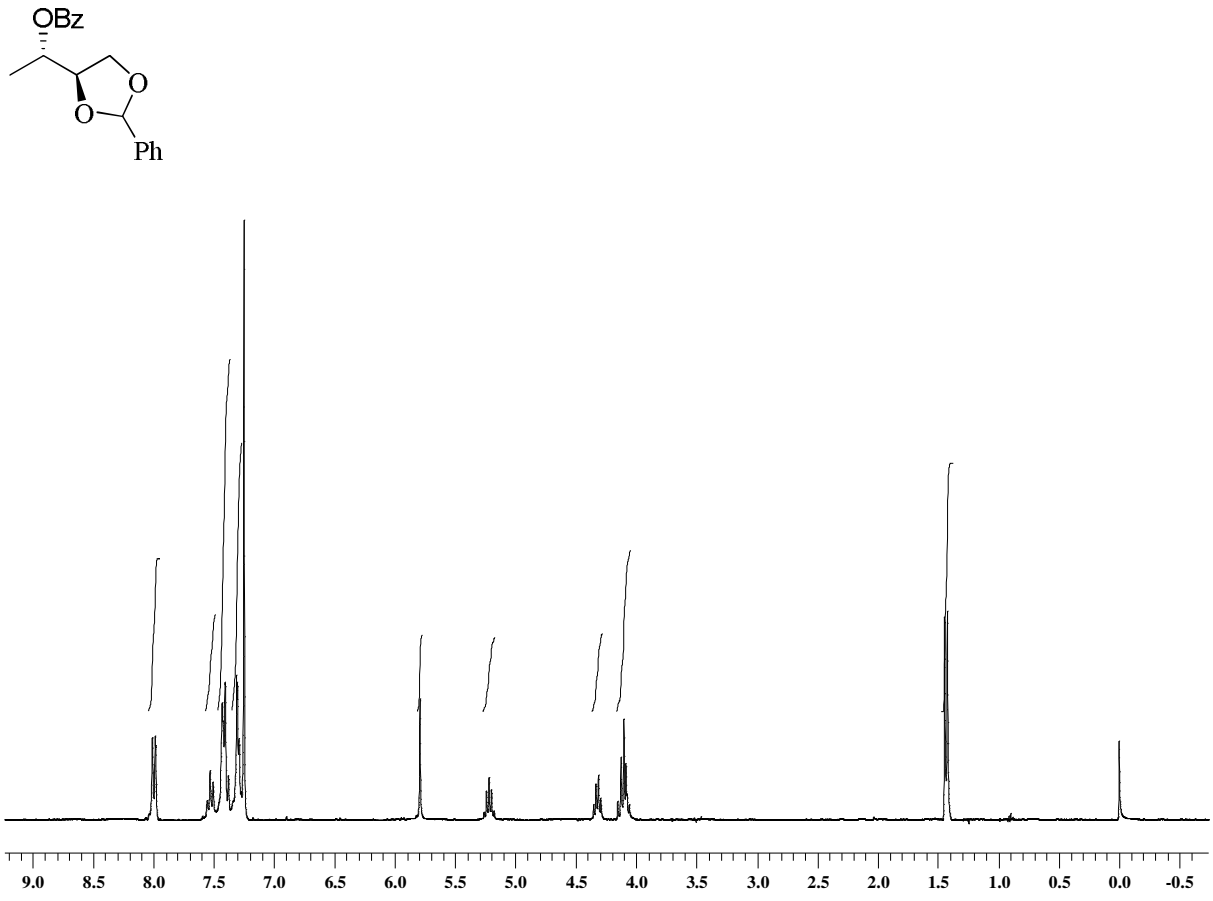

Figure 24. ^{1}H NMR Spectrum of 20 (300 MHz, $CDCl_3$, 298K).

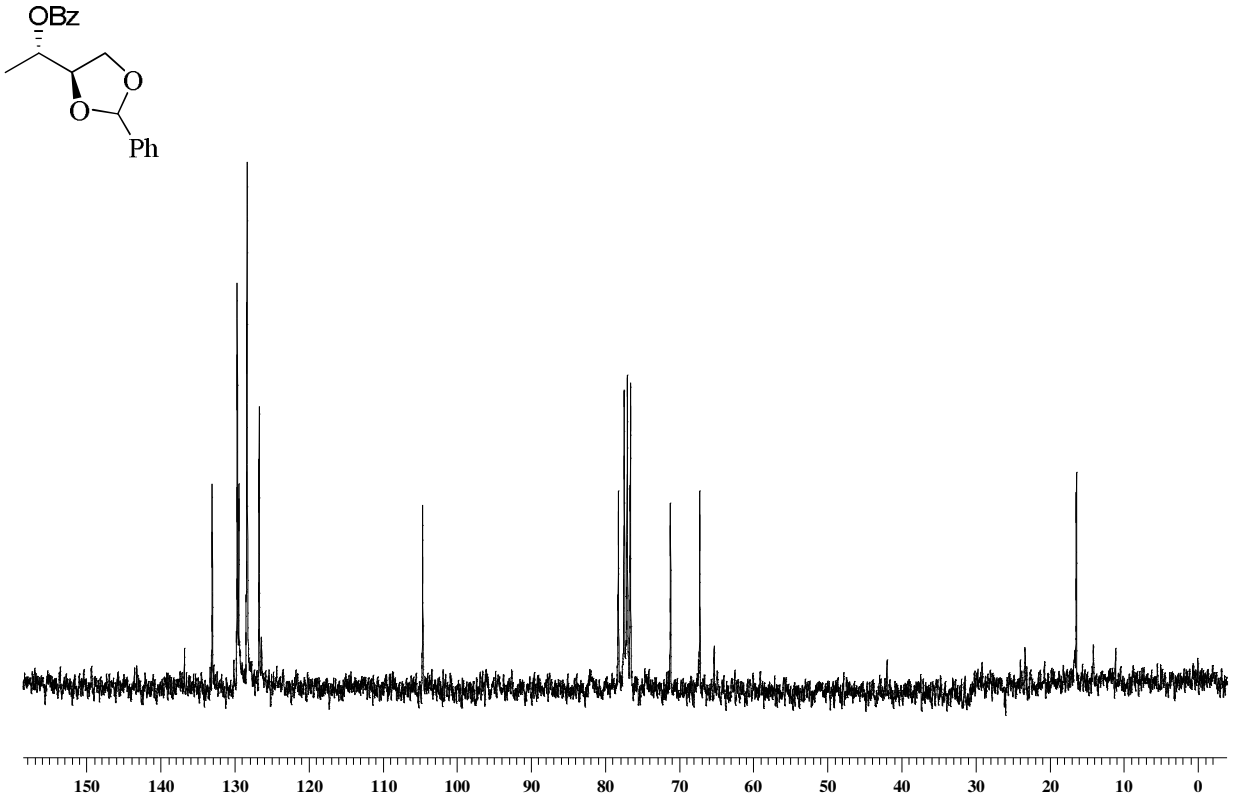

Figure 25. ^{13}C NMR Spectrum of 20 (75 MHz, $CDCl_3$, 298K).

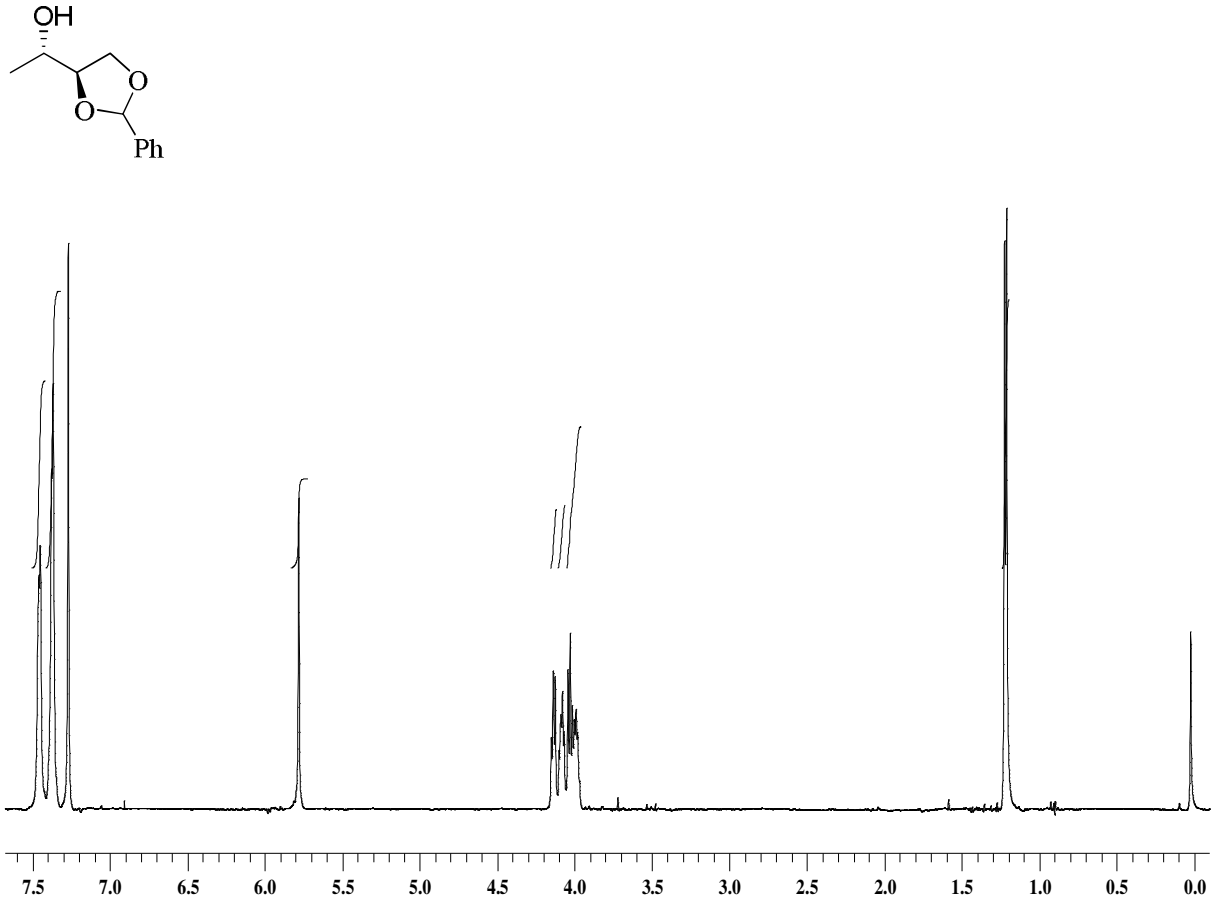

Figure 26. ^{1}H NMR Spectrum of 21 (300 MHz, $CDCl_3$, 298K).

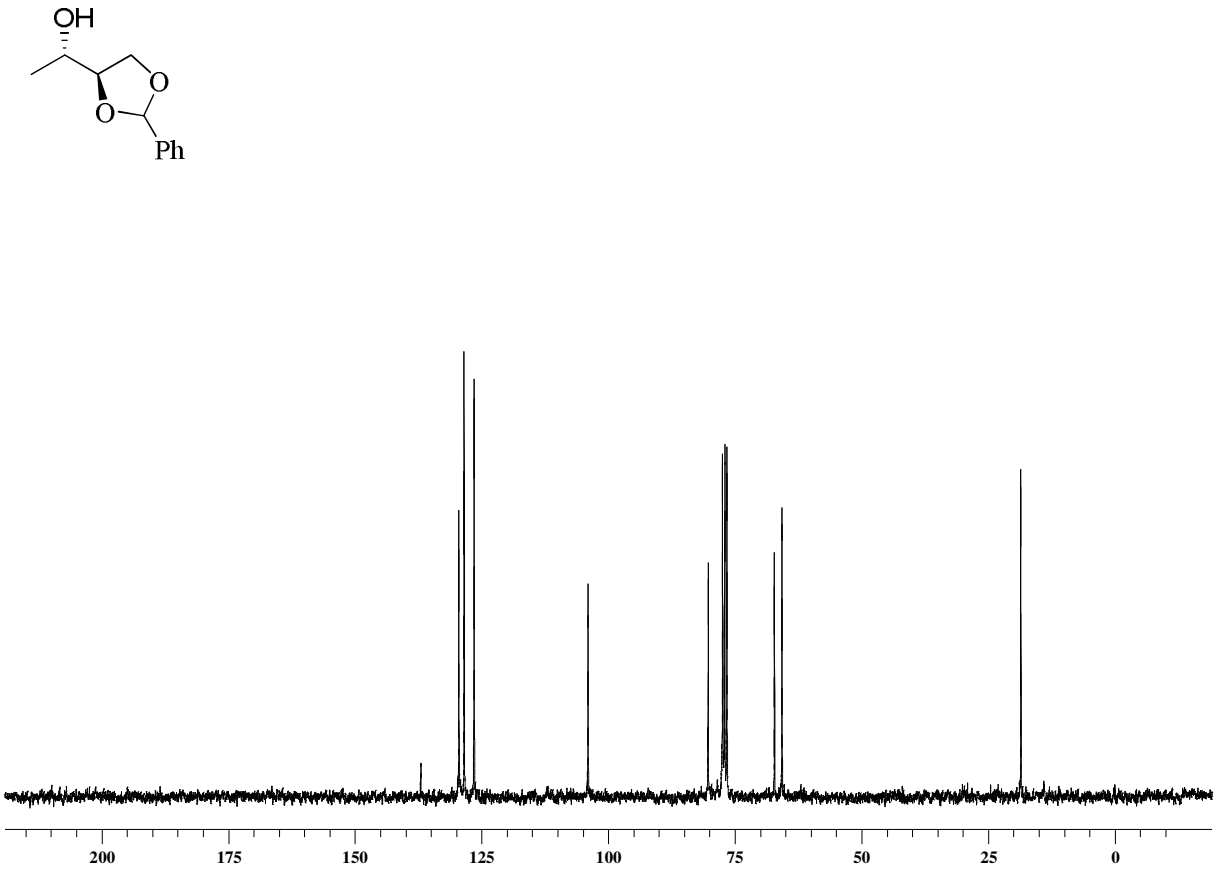

Figure 27. ^{13}C NMR Spectrum of 21 (75 MHz, $CDCl_3$, 298K).

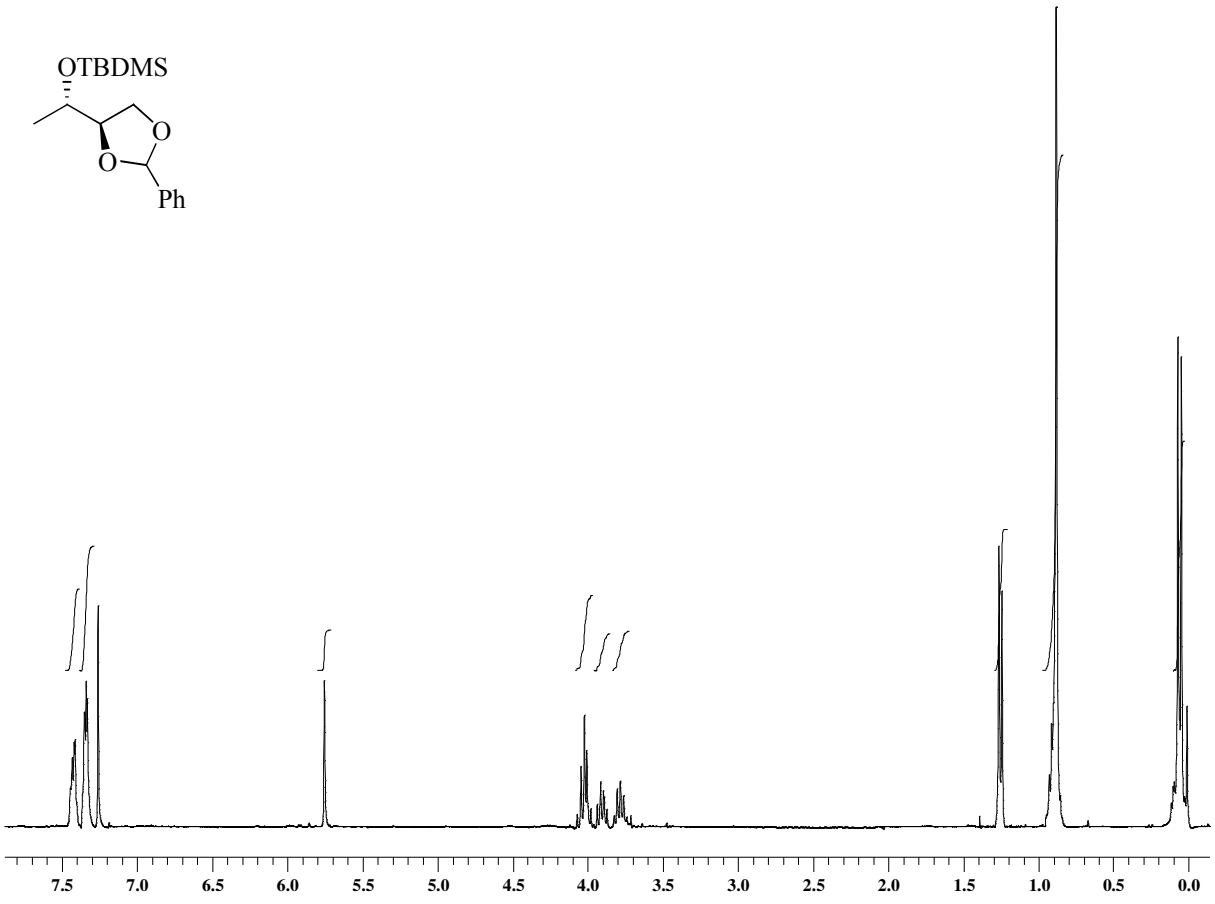

Figure 28. ^{1}H NMR Spectrum of 22 (300 MHz, $CDCl_3$, 298K).

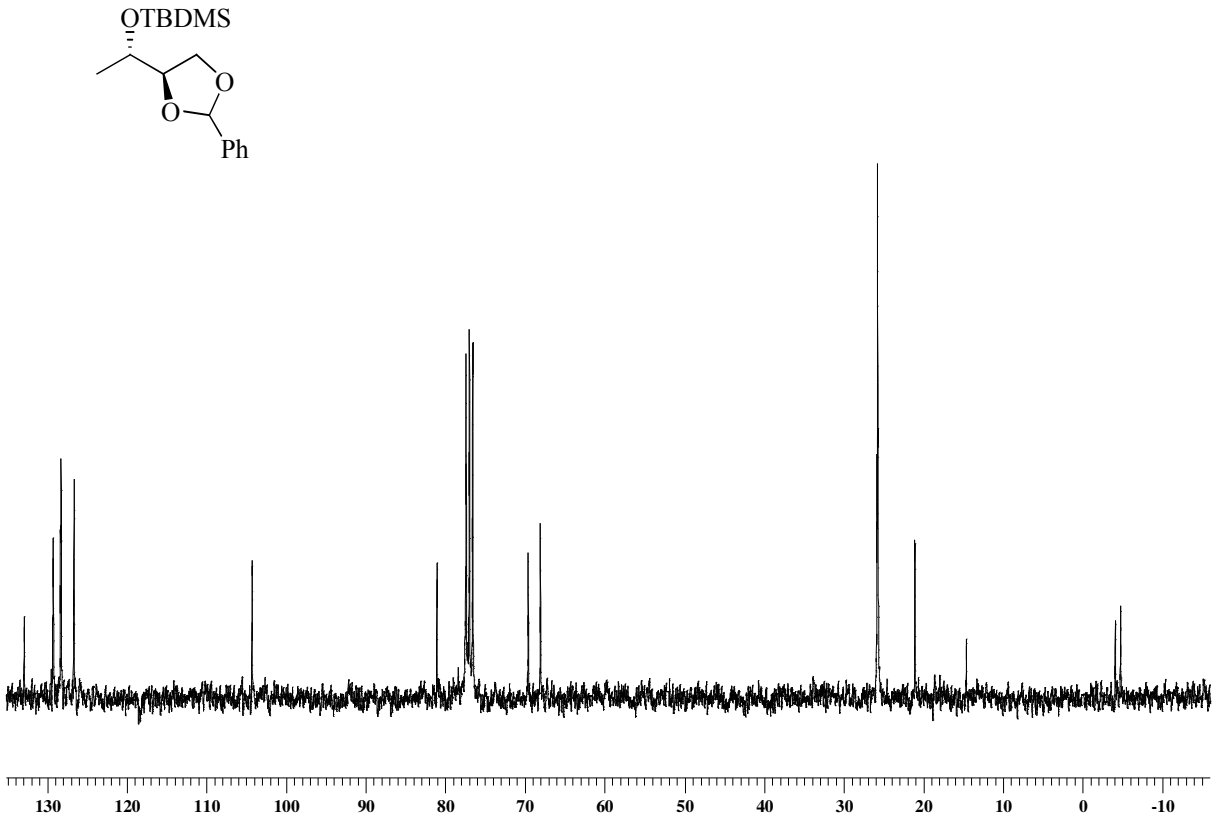

Figure 29. ^{13}C NMR Spectrum of 22 (75 MHz, $CDCl_3$, 298K).

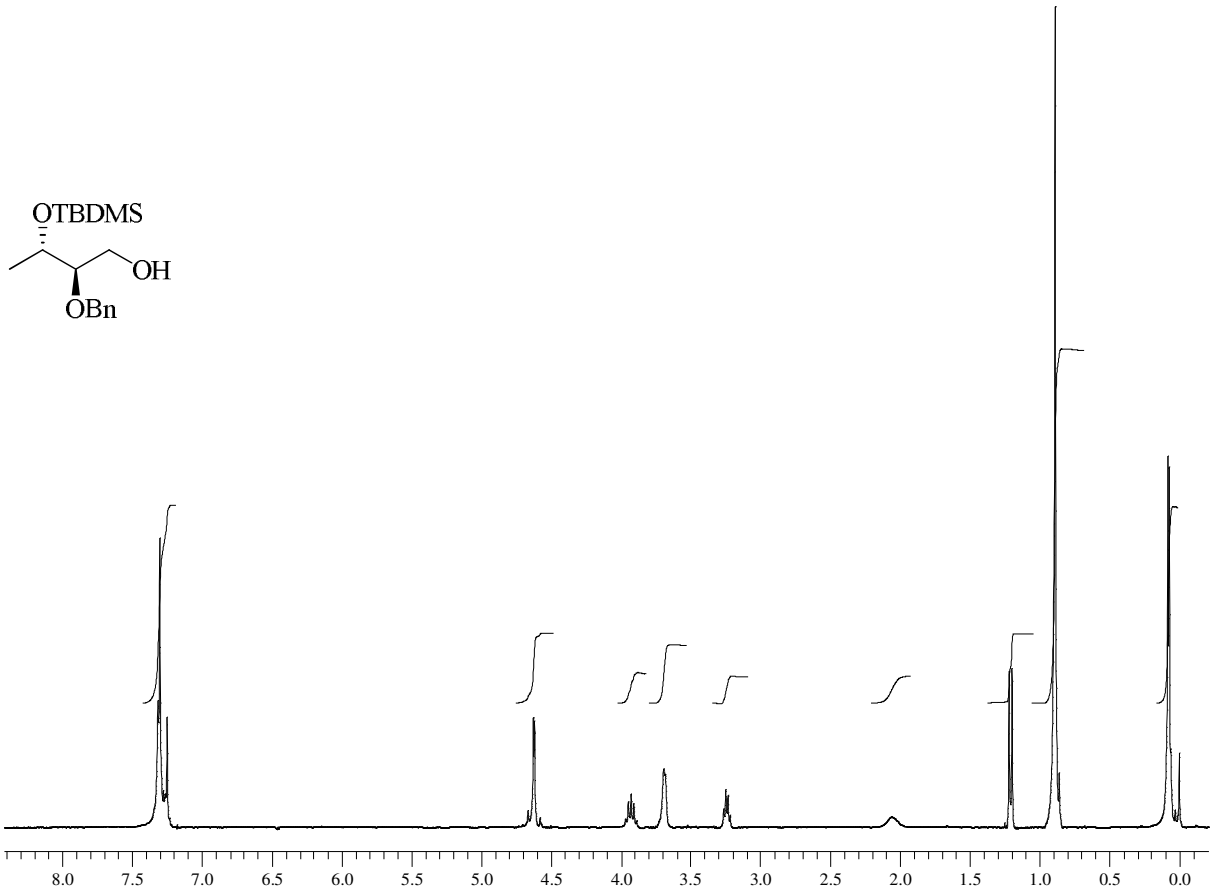

Figure 30. ^{1}H NMR Spectrum of 23 (300 MHz, $CDCl_3$, 298K).

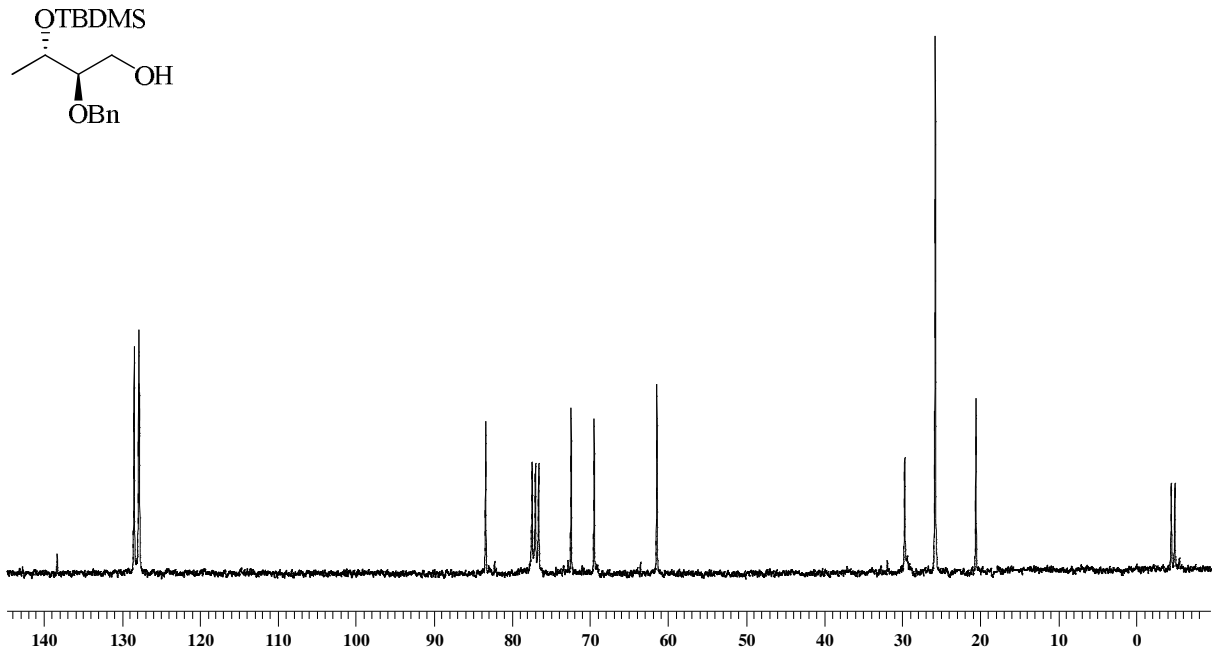

Figure 31. ^{13}C NMR Spectrum of 23 (75 MHz, $CDCl_3$, 298K).

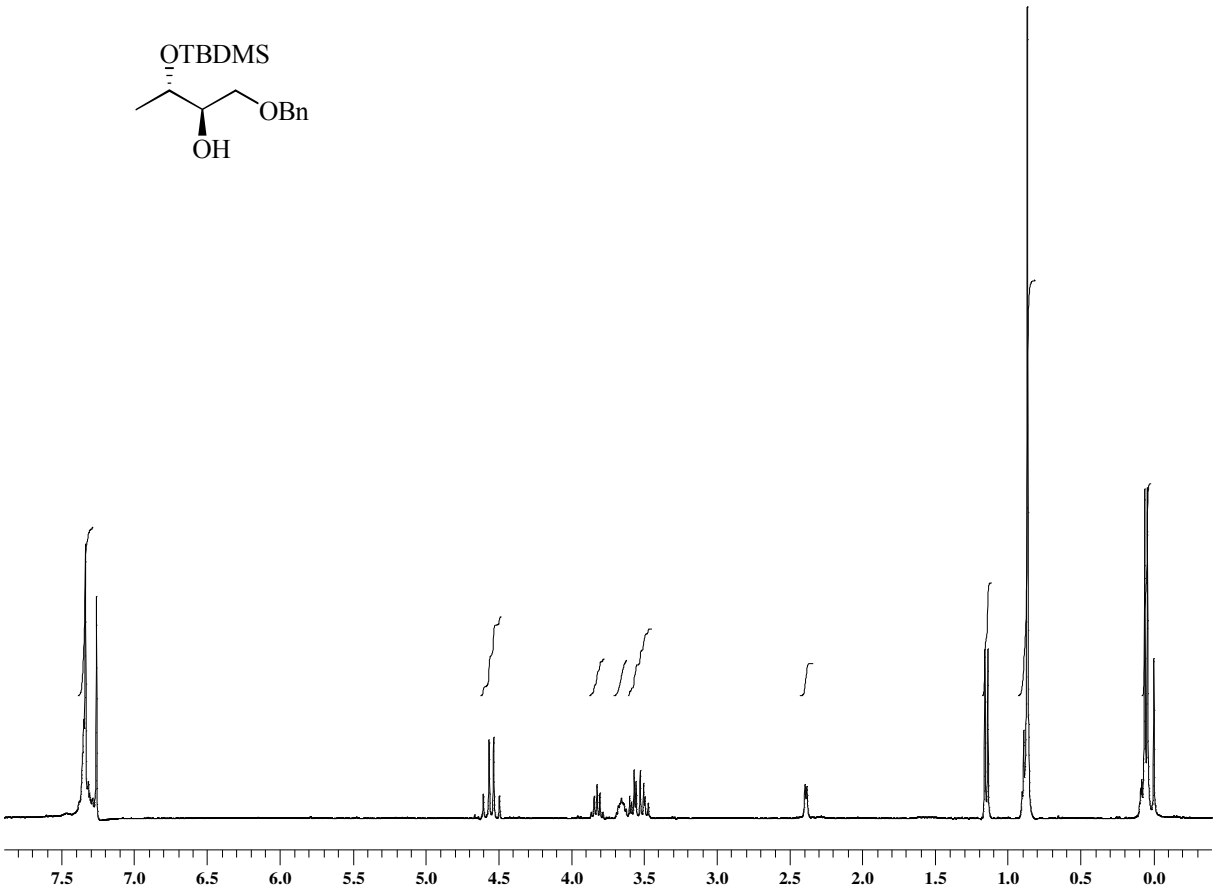

Figure 32. ^{1}H NMR Spectrum of 23a (300 MHz, $CDCl_3$, 298K).

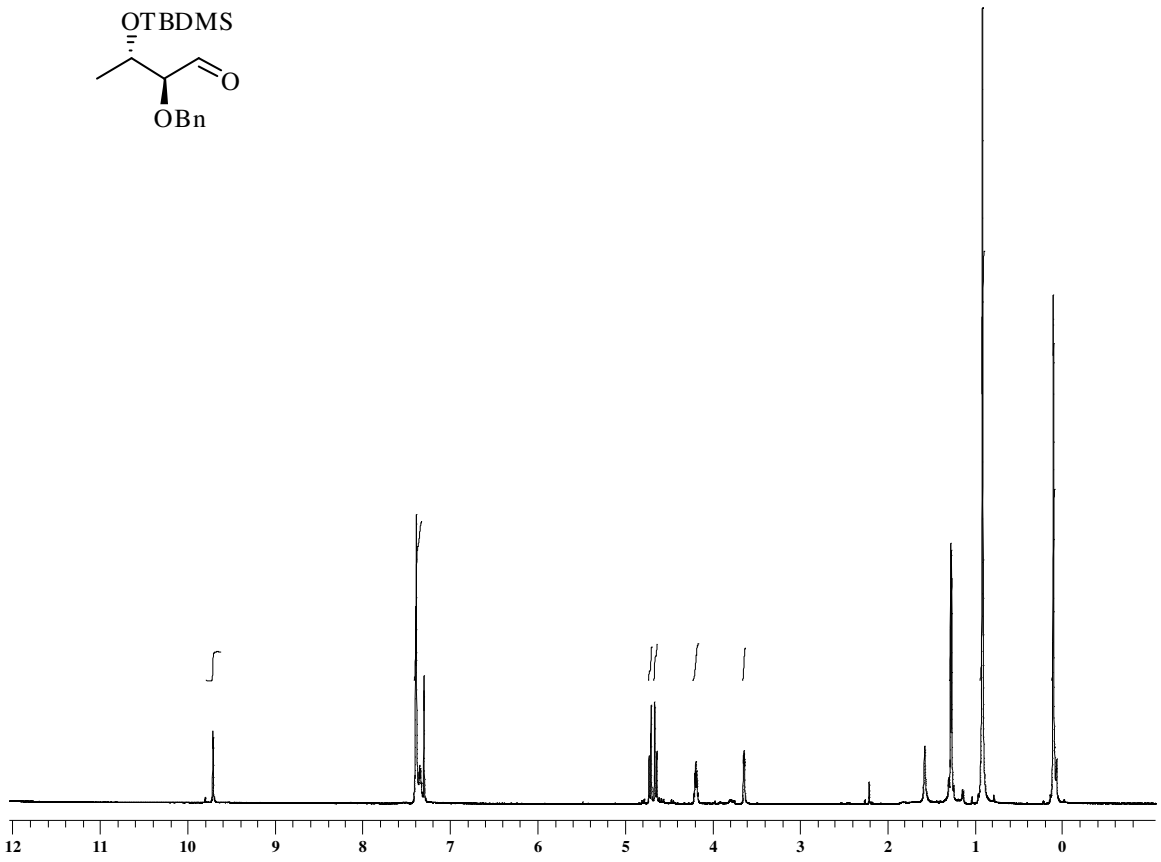

Figure 33. ^{1}H NMR Spectrum of 3 (500 MHz, $CDCl_3$, 298K).

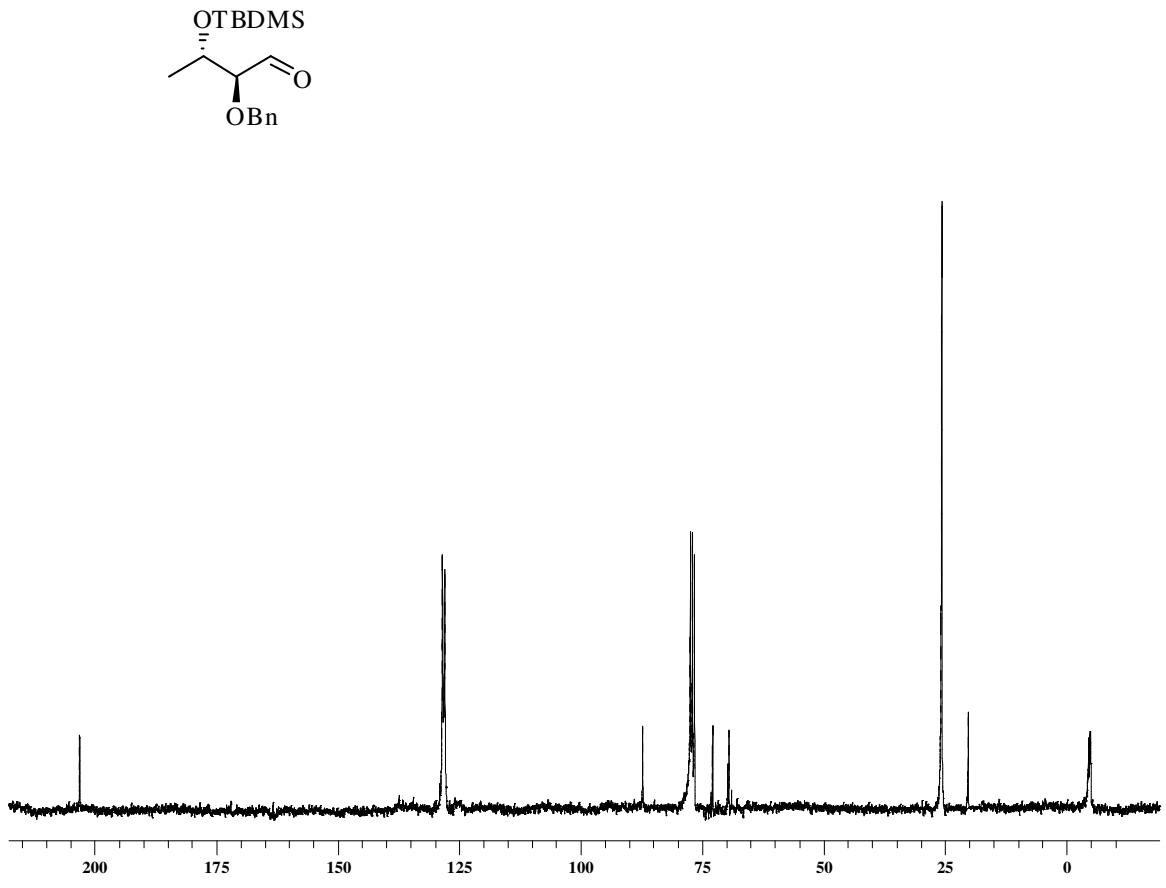

Figure 34. ^{13}C NMR Spectrum of 3 (75 MHz, $CDCl_3$, 298K).

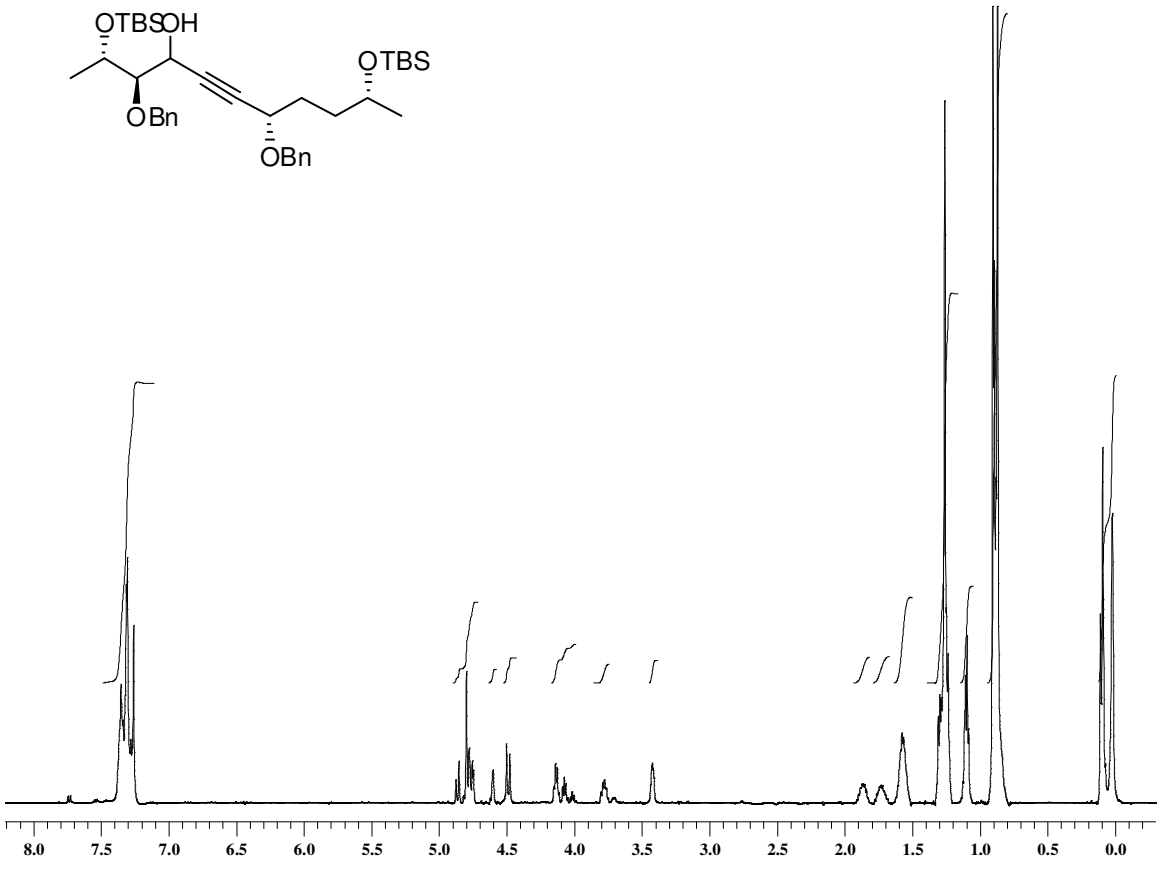

Figure 35. ^{1}H NMR Spectrum of 24 (500 MHz, $CDCl_3$, 298K).

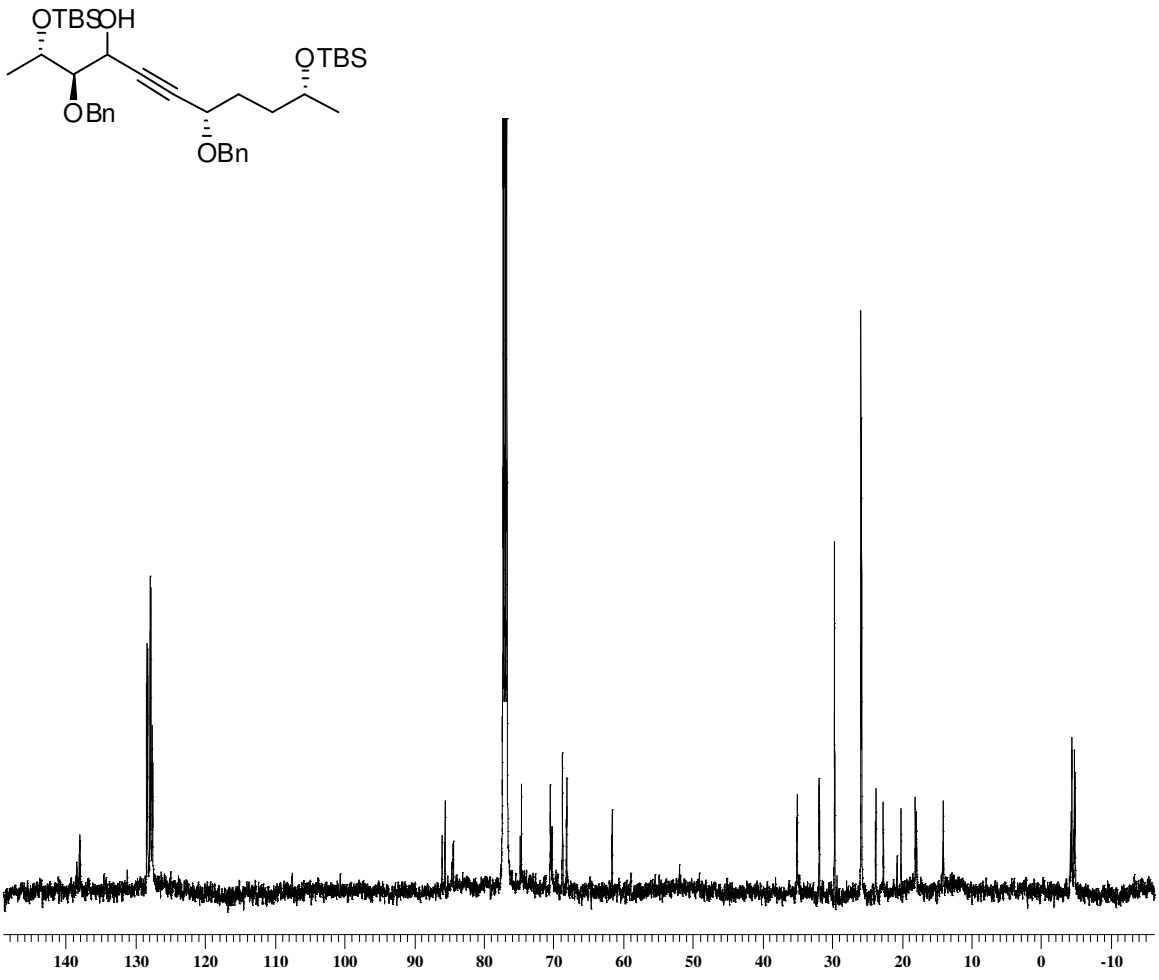

Figure 36. ^{13}C NMR Spectrum of 24 (125 MHz, $CDCl_3$, 298K).

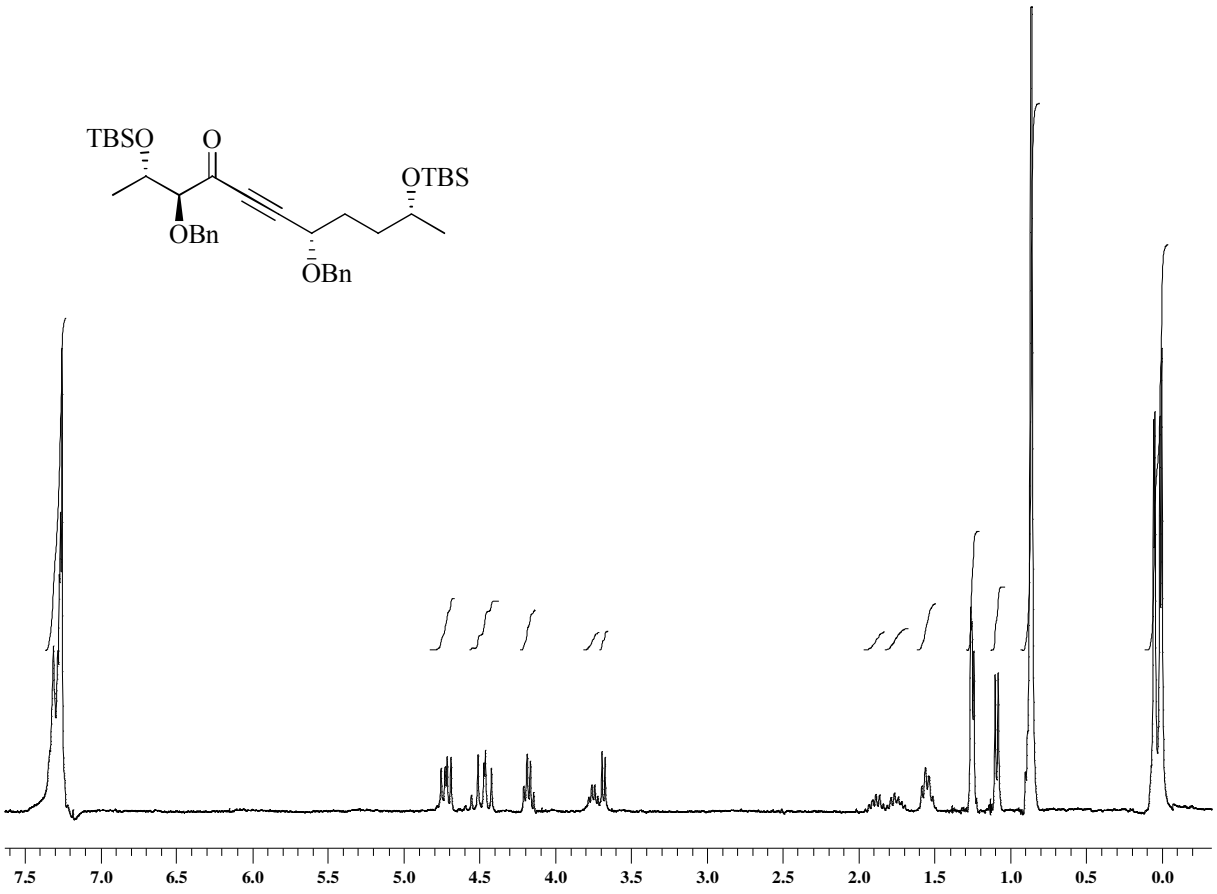

Figure 37. ^{1}H NMR Spectrum of 2 (300 MHz, $CDCl_3$, 298K).

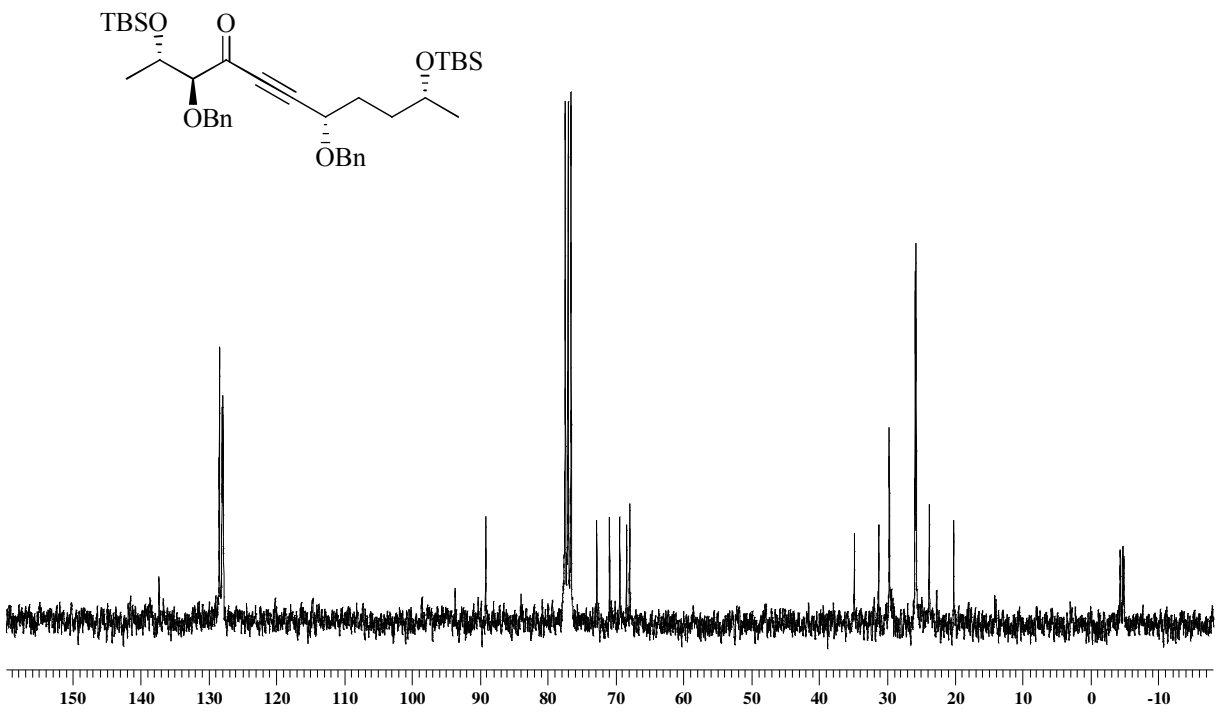

Figure 38. ^{13}C NMR Spectrum of 2 (75 MHz, $CDCl_3$, 298K).

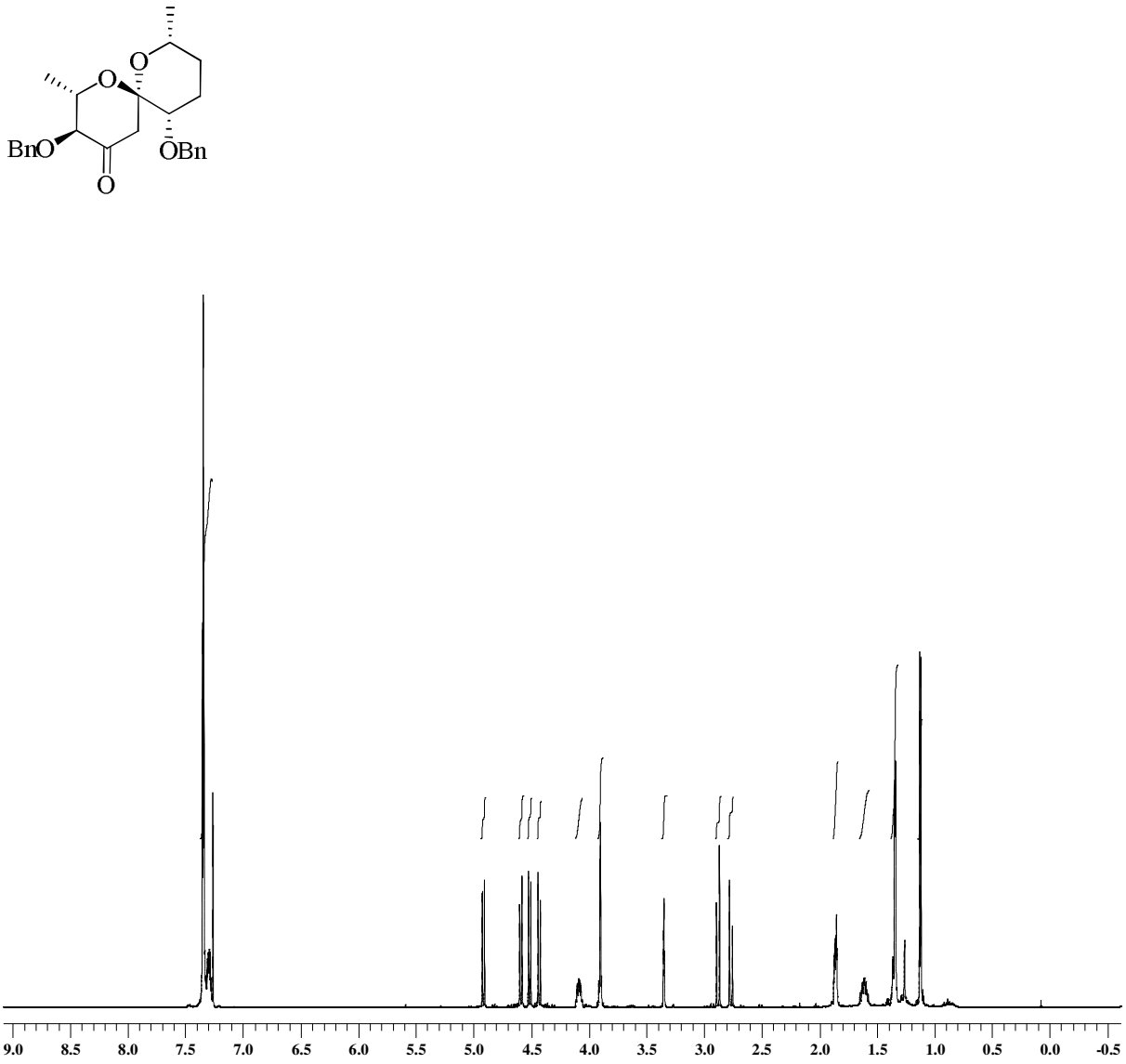

Figure 39. ^{1}H NMR Spectrum of 25 (600 MHz, $CDCl_3$, 298K).

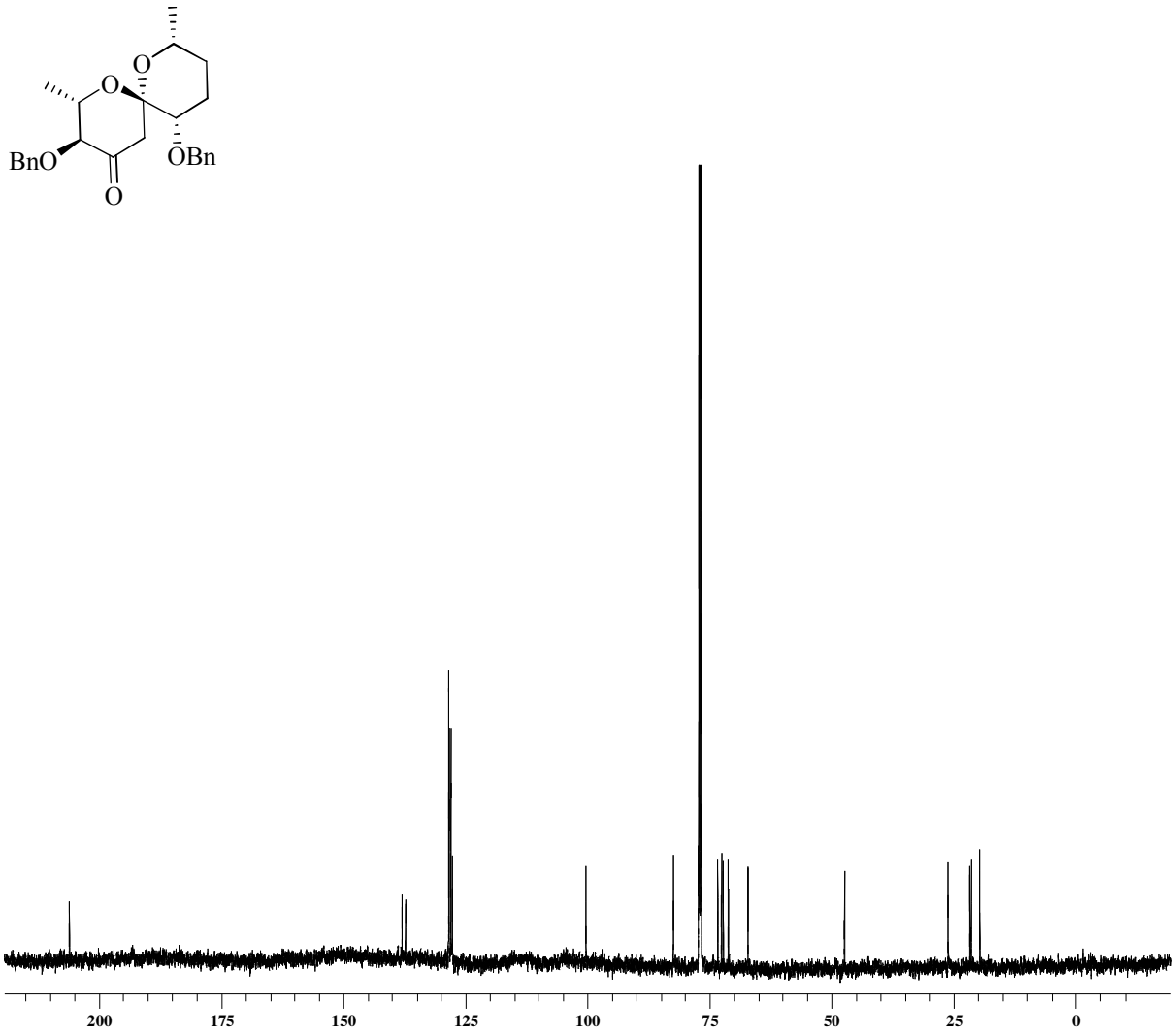

Figure 40. ^{13}C NMR Spectrum of 25 (150 MHz, $CDCl_3$, 298K).

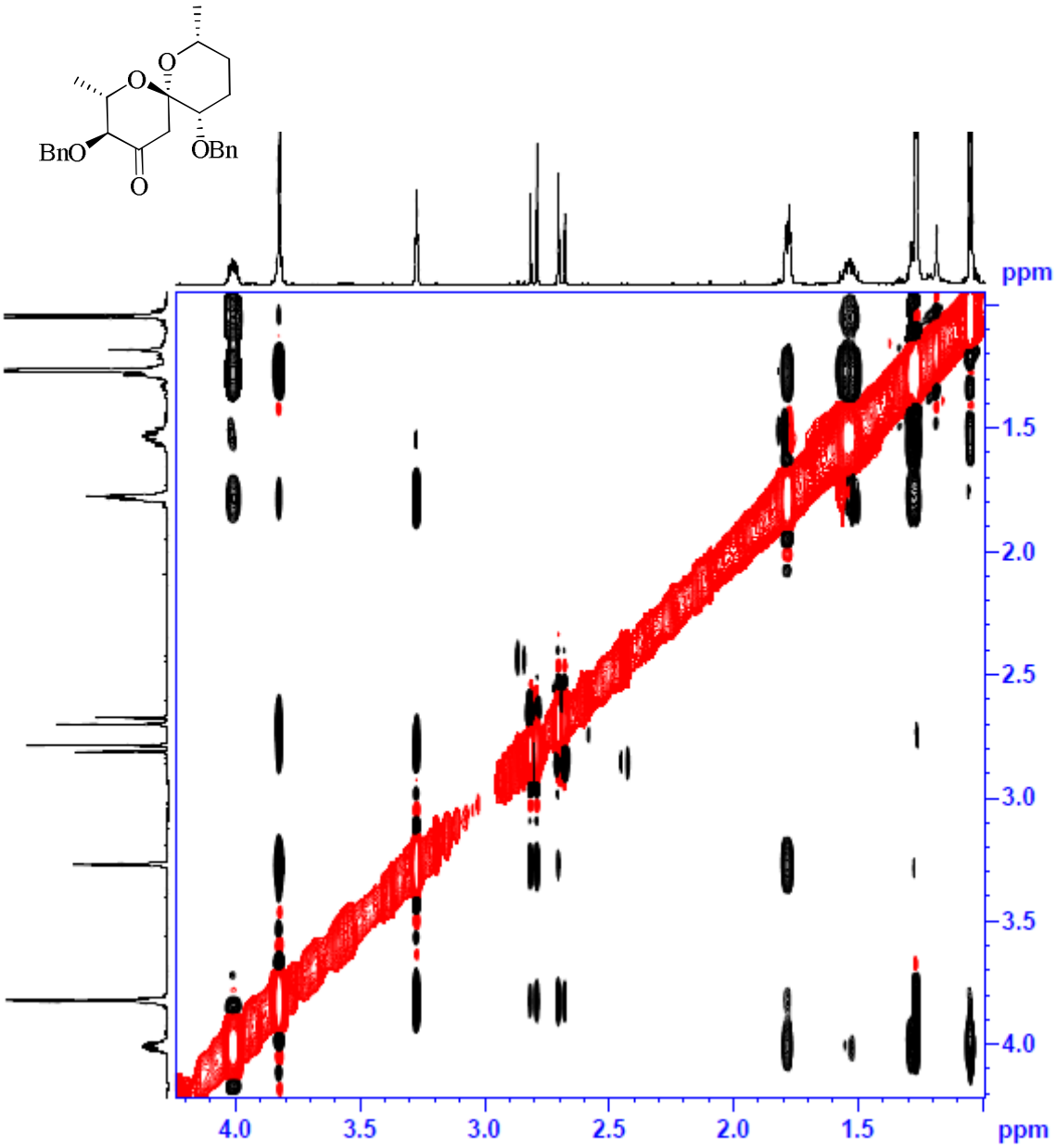

Figure 41. NOESY Spectrum of 25 (600 MHz, $CDCl_3$, 298K).

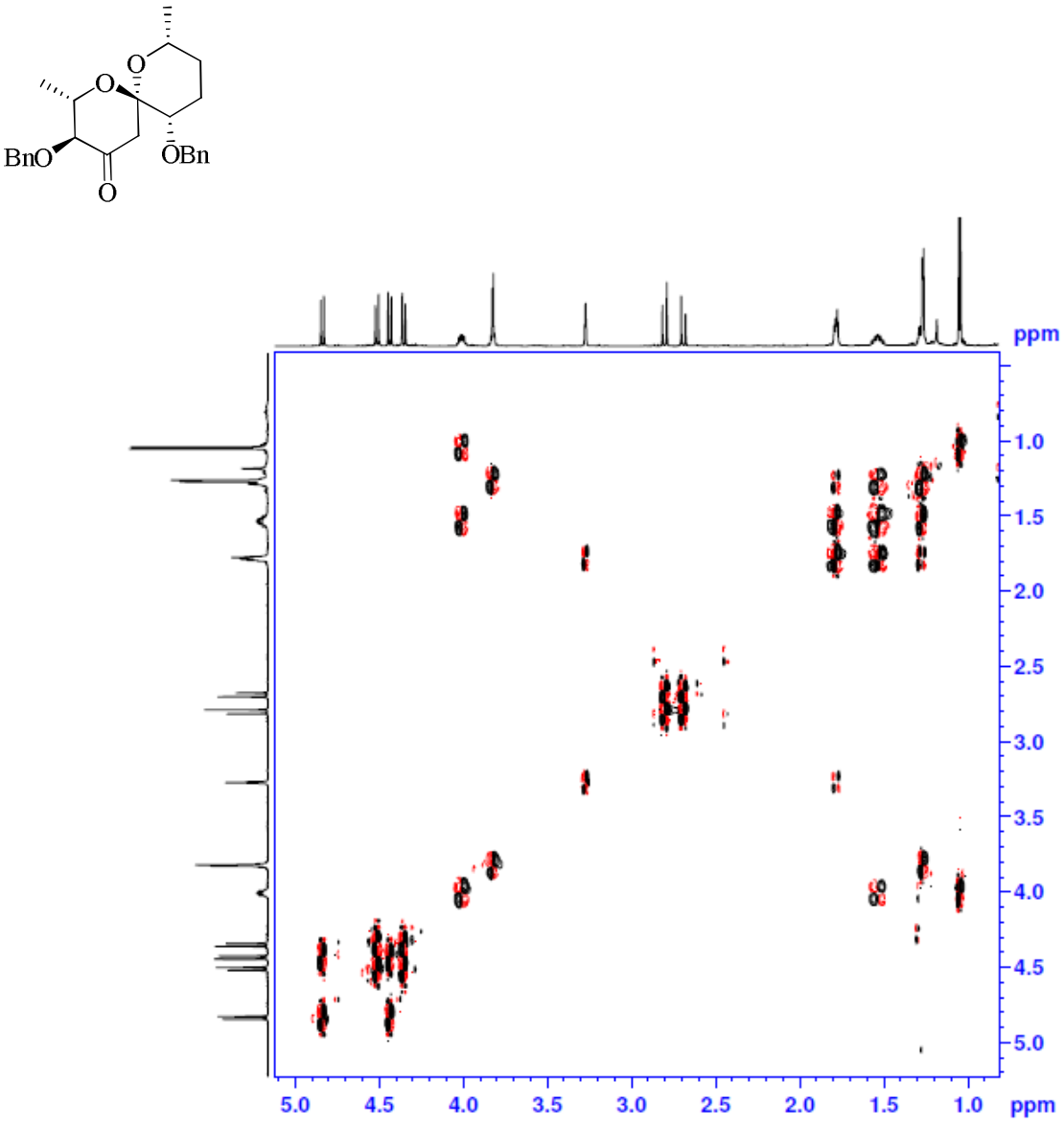

Figure S42. COSY Spectrum of 25 (600 MHz, $CDCl_3$, 298K).

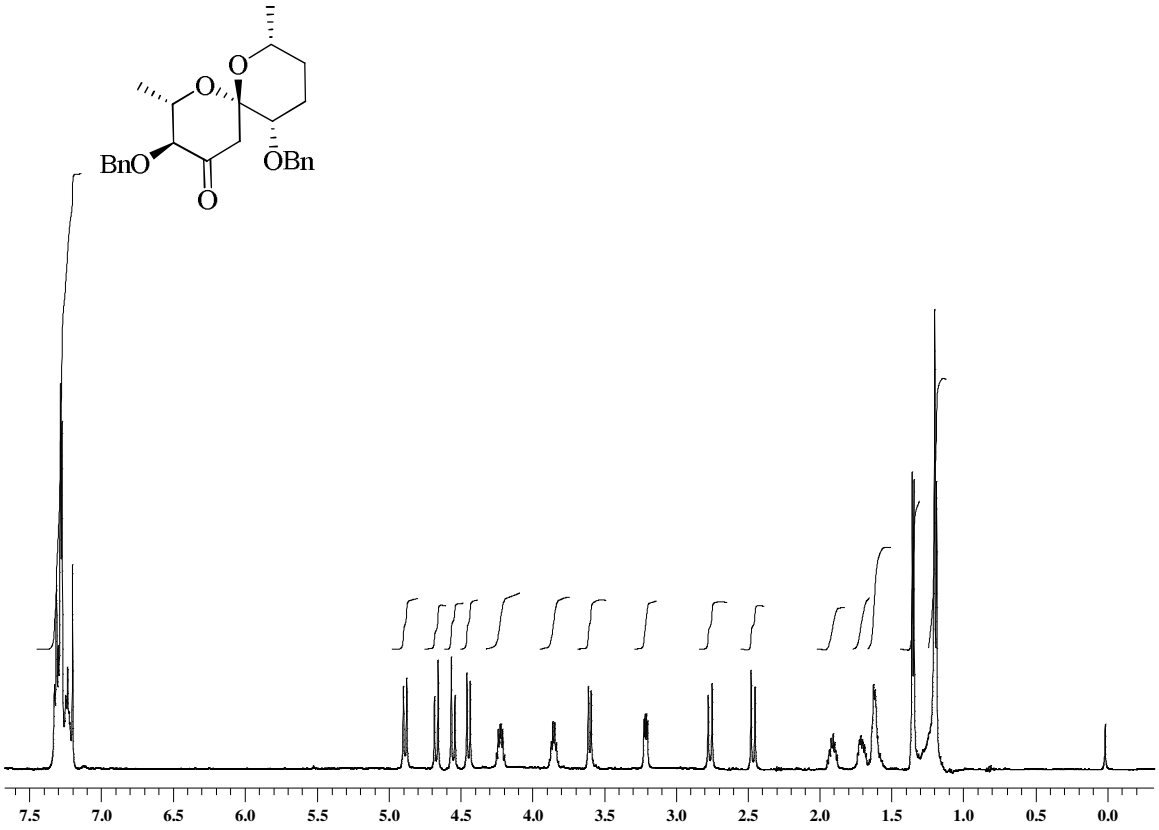

Figure 43. ^{1}H NMR Spectrum of 26 (500 MHz, $CDCl_3$, 298K).

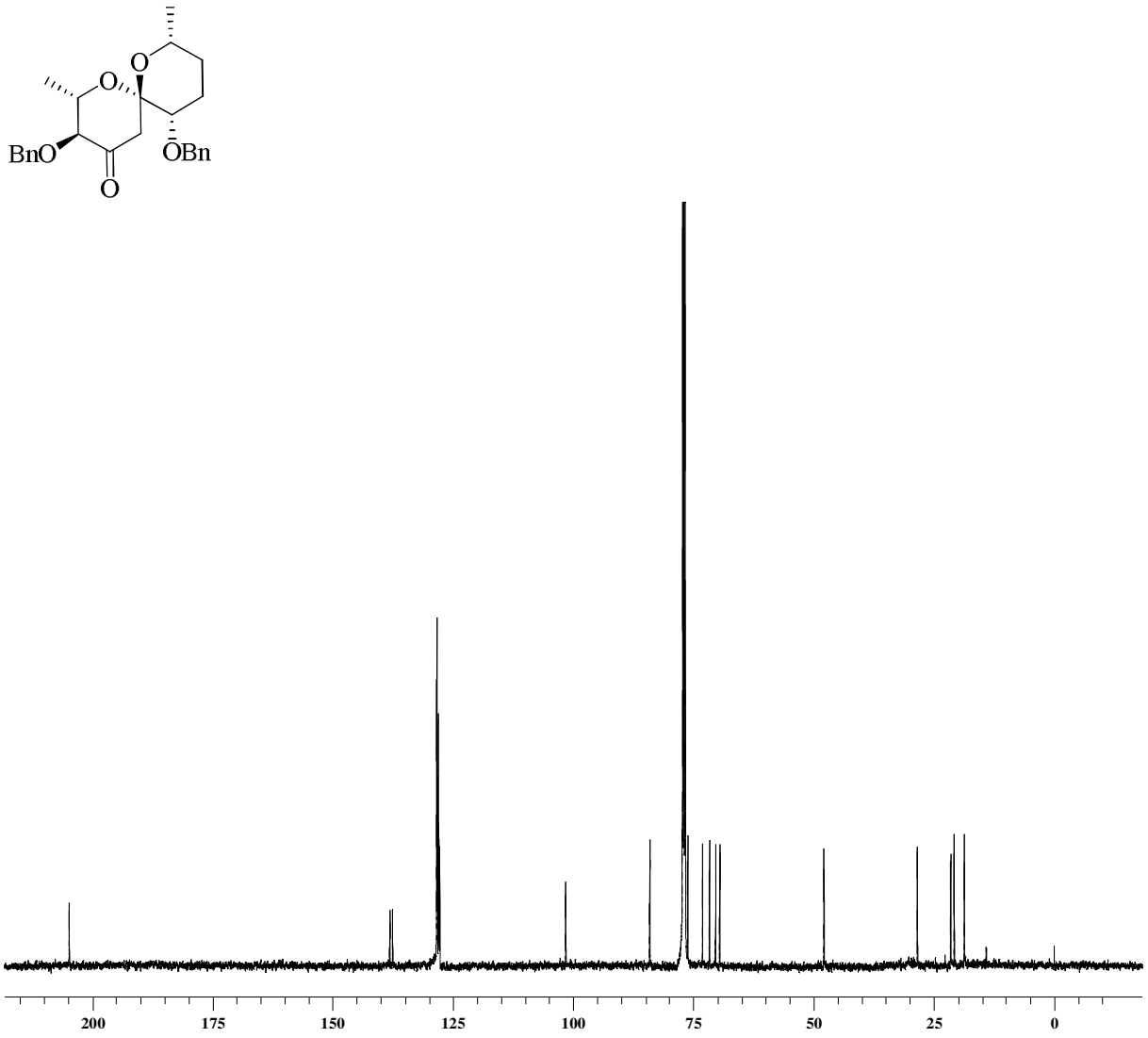

Figure 44. ^{13}C NMR Spectrum of 26 (125 MHz, $CDCl_3$, 298K).

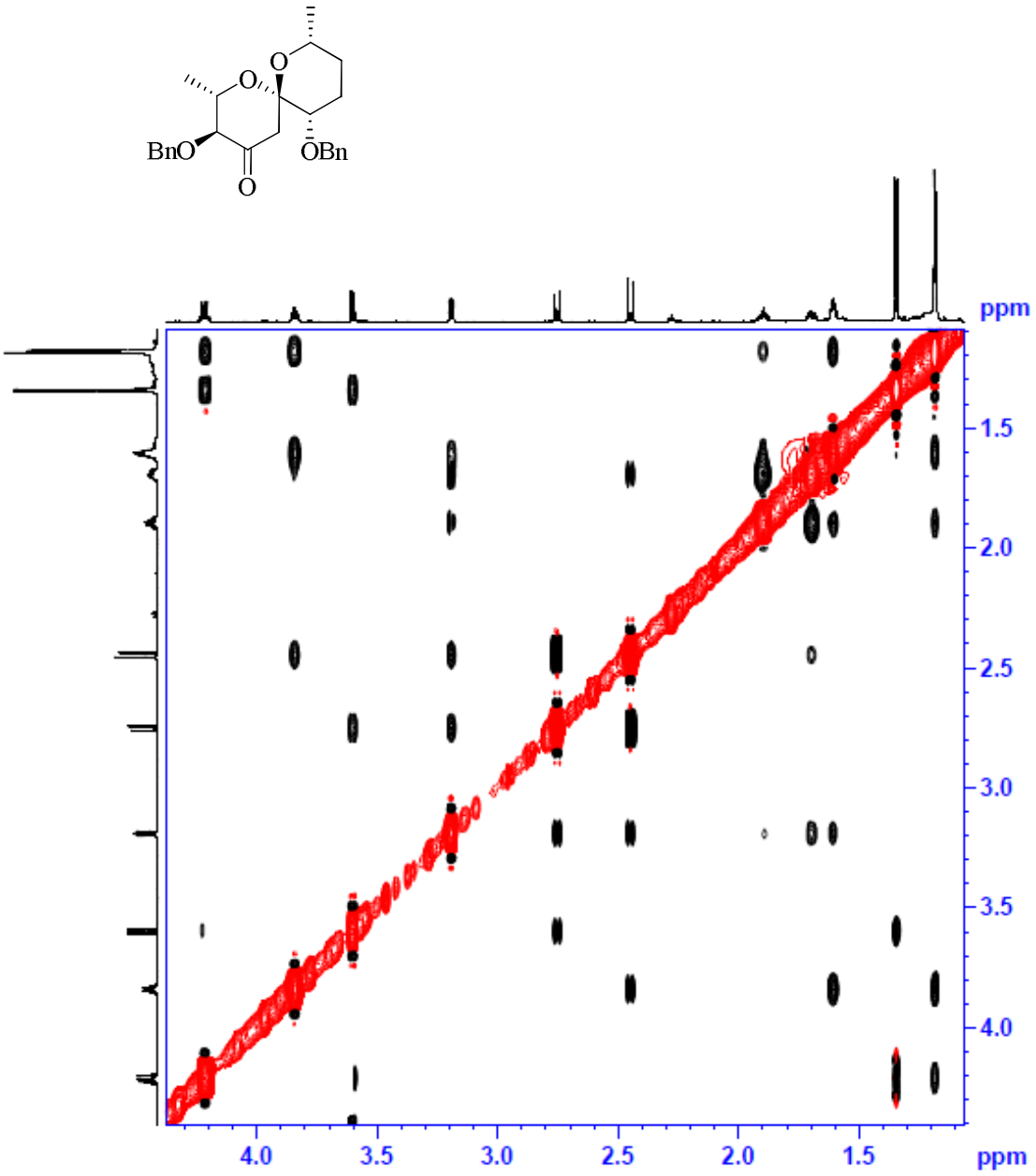

Figure 45. NOESY Spectrum of 26 (500 MHz, $CDCl_3$, 298K).

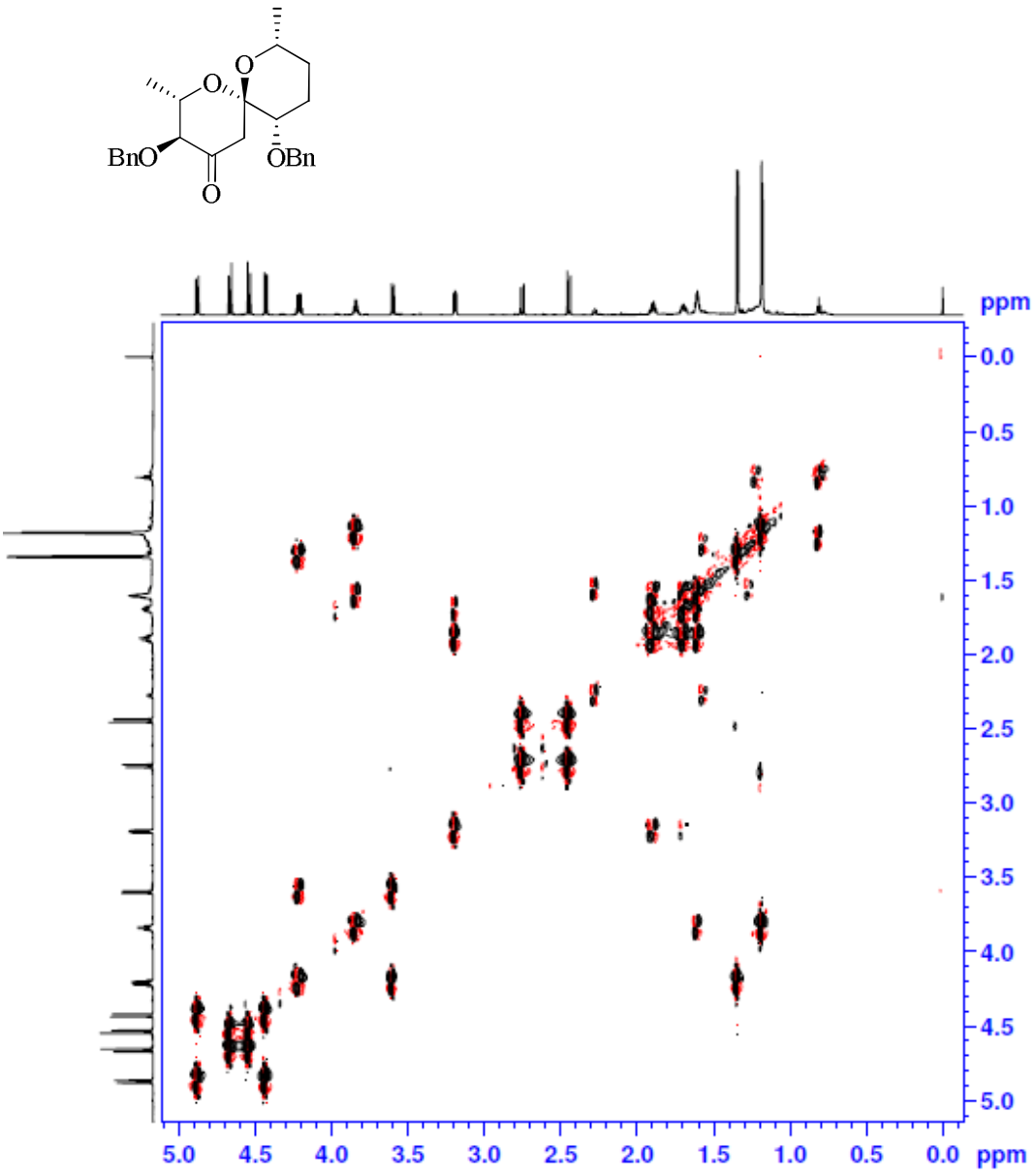

Figure S46. COSY Spectrum of 26 (500 MHz, $CDCl_3$, 298K).

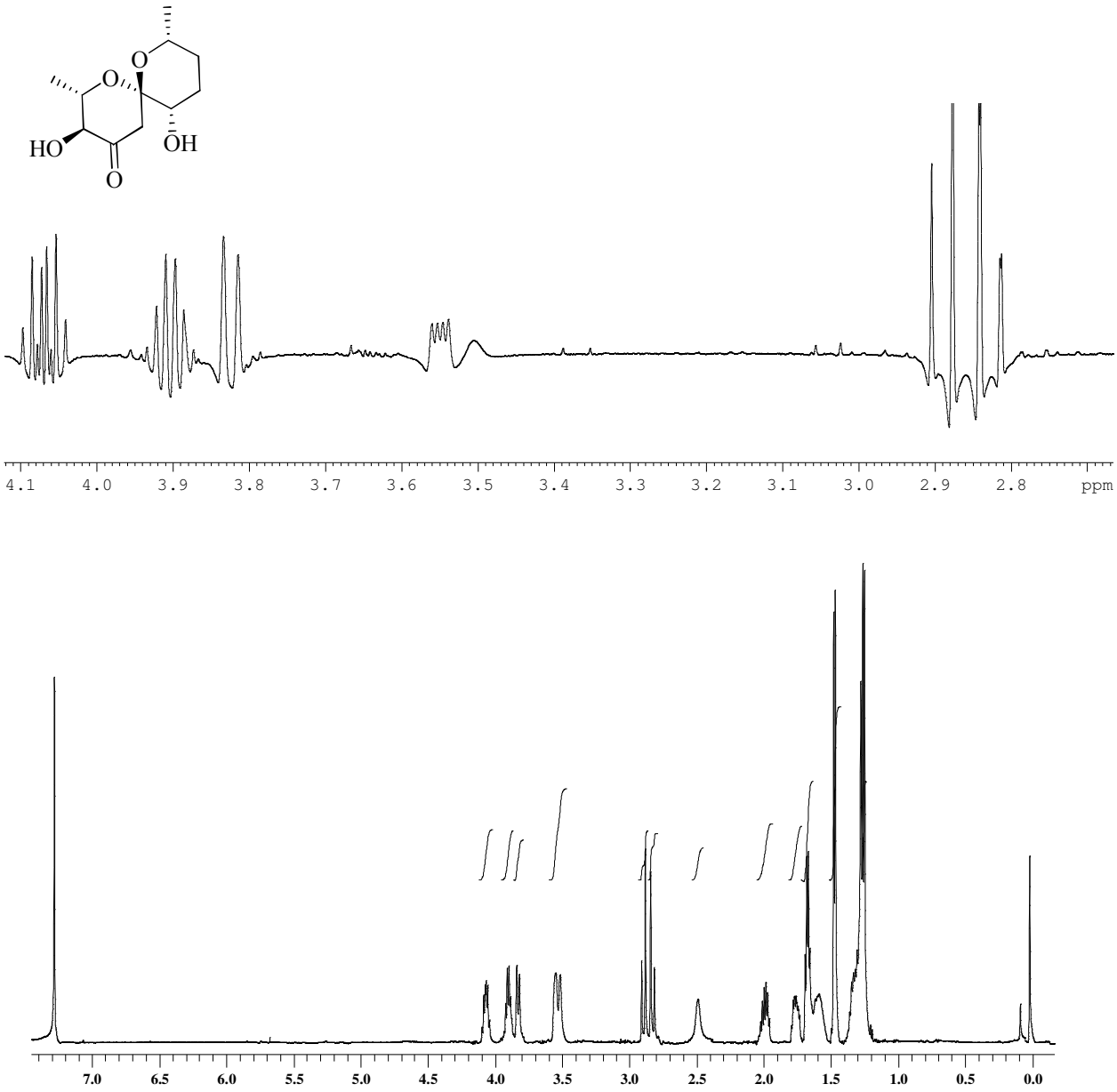

Figure S47. ^{1}H NMR Spectrum of 1 (500 MHz, $CDCl_3$, 298K).

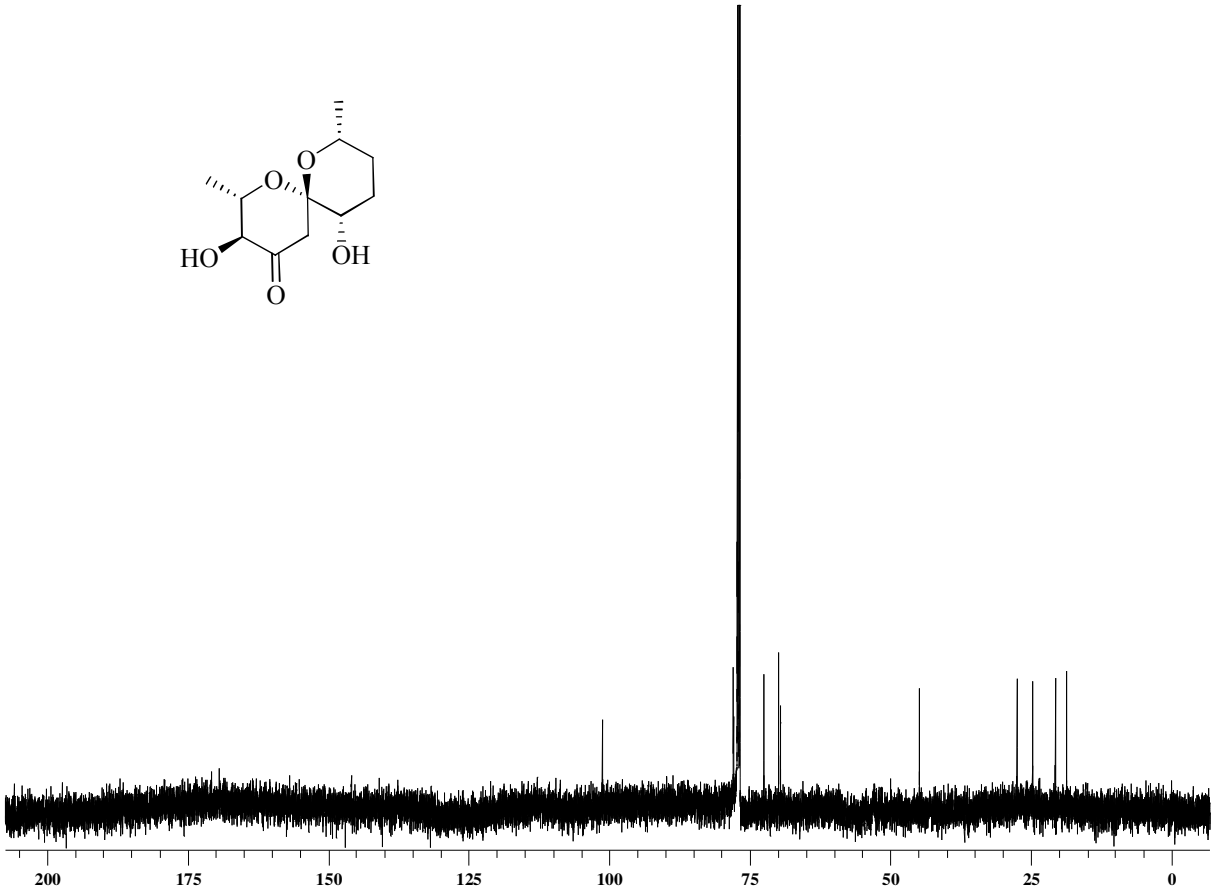

Figure 48. ^{13}C NMR Spectrum of 1 (125 MHz, $CDCl_3$, 298K).

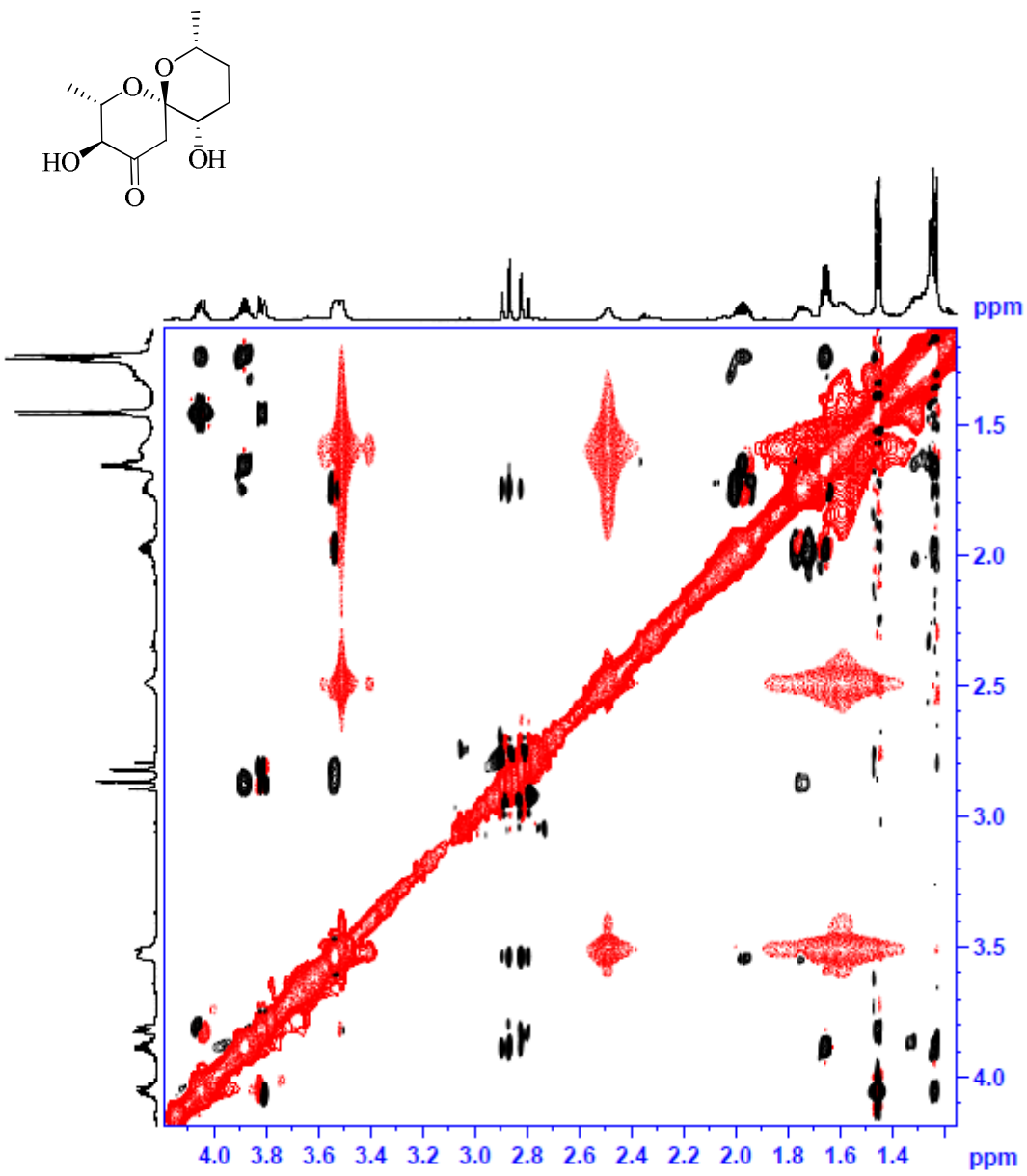

Figure 49. NOESY Spectrum of 1 (125 MHz, $CDCl_3$, 295 K).

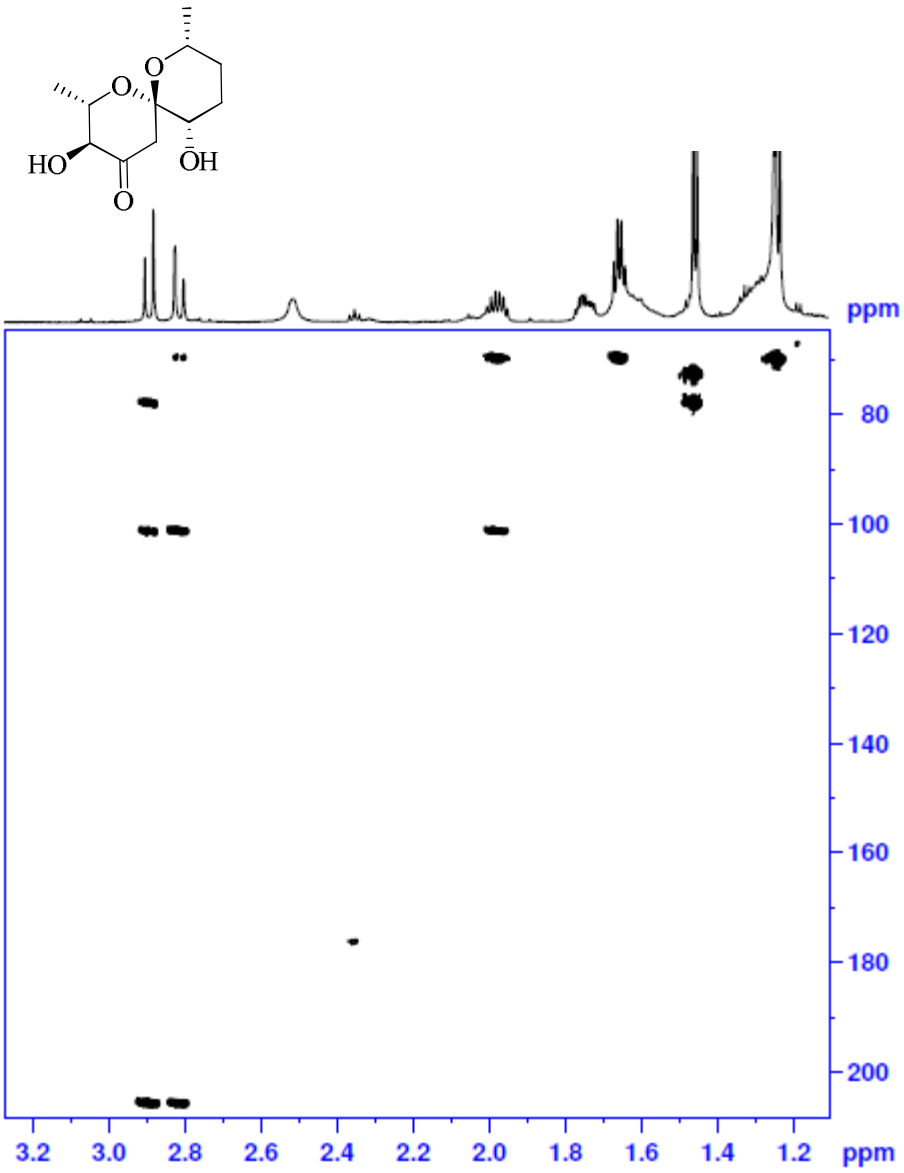

Figure S50. HMBC Spectrum of 1 (125 MHz, $CDCl_3$, 295 K).