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Supporting Information

A convergent approach for the synthesis of C14–C26 fragment of anti-cancer drug eribulin mesylate

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Experimental procedures and analytical data for intermediates:

(***S***,***E***)-3-(but-2-enoyl)-4-phenyloxazolidin-2-one (11)[1]

To a solution of crotonic acid (6.8 g, 70.60 mmol) in dry THF (50 mL) at 0 ºC was added pivaloyl chloride (8.5 g, 70.60 mmol) followed by the slow addition of NMM (N-methylmorpholine, 7.1 g, 70.60 mmol) in dry THF (400 ml). After stirring for 45 min at 0 ºC, the temperature was lowered to -78 ºC. In a separate RBF, (*S*)-4-phenyloxazolidin-2-one **13** (11.52 g, 70.60 mmol) was dissolved in dry THF (400 mL). The resulting solution was cooled to -78 ºC, n-BuLi (1.6 M in hexane, 53 mL, 84.72 mmol) was added slowly. After stirring for 30 min, this solution was slowly cannulated to the above mixed anhydride solution. After stirring for 1 h at -78 ºC, the cooling bath was removed and stirring was continued for 30 min at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl (100 mL). The aqueous layer was extracted with ethyl acetate (3×100mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent concentrated under reduced pressure and the crude residue was purified by column chromatography to give the compound **11** (15.0 g, 92% yield) as a brown oil. R_f = 0.4 (40% EtoAc in Hexane). $[\alpha]_D^{20}$ +106.00 (*c* 1, $CHCl_3$). NMR data consistent with previous report[1].

IR (neat): $\tilde{\nu}$ = 2924, 1777, 1689, 1638, 1385, 1339, 1233, 1201, 1127, 1062, 970, 925, 762, 710 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.35 (m, 2H), 7.34–7.31 (m, 2H), 7.30 (m, 1H), 7.26–7.25 (m, 1H), 7.14–7.05 (m, 1H) 5.48 (dd, *J* = 8.4, 3.6 Hz, 1H), 4.69 (t, *J* = 8.8 Hz, 1H), 4.27 (dd, *J* = 8.8, 4.0 Hz, 1H), 1.93 (dd, *J* = 6.8, 1.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.5, 153.7, 147.3, 139.1, 129.1, 128.6, 125.9, 121.7, 69.9, 57.7, 18.5.

MS (ESI): *m*/*z* = 254 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{13}H_{13}NO_3Na$ $[M+Na]^+$ is 254.0793, found 254.0798.

(***R***)-3-Methylhex-5-en-1-ol (9)

Compound **10** (15.0 g, 54.94 mmol) was dissolved in anhydrous Et_2O (300 mL) under argon atmosphere and cooled to 0 °C. Absolute ethanol (3.9 mL, 65.93 mmol) was added followed by the slow addition of $LiBH_4$ (1.45 g, 65.93 mmol). The reaction was allowed to warm to room temperature overnight under argon. The reaction was quenched by slow addition of 1.0 M NaOH (300 mL) and allowed to stir until both layers were clear. The aqueous layer was separated and extracted with Et_2O (3×50 mL), all the organic layers were combined, washed with brine (100 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude residue was purified by using silica gel chromatography to give alcohol **9** as pale oil (5.63 g, 90% yield). R_f = 0.5 (40% EtoAc in Hexane). $[\alpha]_D^{20}$ −0.20 (*c* 1, $CHCl_3$).

IR (neat): $\tilde{\nu}$ = 2926, 2859, 1734, 1459, 1261, 1084, 806, 758, 570 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.83–5.68 (m, 1H), 5.03–4.93 (m, 2H), 3.72–3.58 (m, 2H), 2.06 (ddd, *J* = 13.6, 6.8, 5.6 Hz, 1H), 1.91 (dt, *J* = 14.4, 7.2 Hz, 2H), 1.62 (ddd, *J* = 15.4, 11.6, 6.2 Hz, 2H), 1.36 (dd, *J* = 13.2, 5.8 Hz, 1H), 0.89 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.1, 115.8, 60.8, 41.4, 39.2, 29.4, 19.4.

MS (ESI): *m*/*z* = 137 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_7H_{14}ONa$ $[M+Na]^+$ is 137.0942, found 137.0948.

(*S*)-5-((tert-Butyldiphenylsilyl)oxy)-3-methylpentanal (13)

i) To a stirred solution of alcohol **9** (4.0 g, 35.08 mmol) in dry CH_2Cl_2 (80 mL) at 0 °C, imidazole (5.96 g, 87.72 mmol), TBDPSCl (14.42 g, 52.62 mmol), and catalytic amount of DMAP (0.42 g, 3.50 mmol) were added under N_2 atmosphere and stirred for 6 h. The mixture was warmed to room temperature, diluted with H_2O (50 mL), and aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to afford the crude product. The crude product was purified by silica gel column chromatography to afford olefin compound as a colorless oil (11.7 g, 95% yield). R_f = 0.7 (5% EtoAc in Hexane). $[\alpha]_D^{20}$ −2.20 (*c* 1, $CHCl_3$).

IR (neat): $\tilde{\nu}$ = 3065, 2929, 2861, 1468, 1434, 1106, 1000, 913, 824, 744, 705, 614, 548 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69–7.66 (m, 4H), 7.43–7.35 (m, 6H), 5.84–5.67 (m, 1H), 5.02–4.91 (m, 2H), 3.77–3.60 (m, 2H), 2.10–1.99 (m, 1H), 1.93–1.83 (m, 1H), 1.79–1.58 (m, 2H), 1.43–1.32 (m, 1H), 1.05 (s, 9H), 0.85 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.4, 135.6, 134.1, 129.5, 127.6, 115.6, 62.1, 41.4, 39.1, 29.4, 26.9, 19.5, 19.2.

MS (ESI): *m*/*z* = 353 $[M+H]^+$.

HRMS (ESI): calcd. for $C_{23}H_{33}OSi$ $[M+H]^+$ is 353.2301, found 353.2302.

ii) To a solution of olefin obtained above (6.0 g, 17.04 mmol) in CH_2Cl_2 (60 ml), cooled at −78 °C, ozone was bubbled until the solution turned to light blue in colour. To this cold solution, triphenylphosphine (6.7 g, 25.56 mmol) was added and stirring was maintained at room temperature for 5 h. The solvent was evaporated under the reduced pressure and the residue was purified by silica gel column chromatography to afford aldehyde **13** (5.52 g; 92% yield) as a colorless oil. R_f = 0.4 (5% EtoAc in Hexane). $[\alpha]_D^{20}$ −4.70 (*c* 1, $CHCl_3$). NMR data consistent with previous report[2]

IR (neat): $\tilde{\nu}$ = 2937, 2864, 1726, 1468, 1428, 1104, 1006, 742, 704, 614 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.72 (s, 1H), 7.67 (d, *J* = 6.8 Hz, 4H), 7.40 (dd, *J* = 15.8, 8.6 Hz, 6H), 3.71 (t, *J* = 6.2 Hz, 2H), 2.40 (dd, *J* = 15.8, 3.6 Hz, 1H), 2.33–2.15 (m, 2H), 1.60 (dd, *J* = 11.8, 8.0 Hz, 1H), 1.49 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.06 (s, 9H), 0.94 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.9, 135.5, 133.8, 129.6, 127.6, 61.5, 50.8, 39.2, 26.8, 25.0, 20.0, 19.2.

MS (ESI): *m*/*z* = 377 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{22}H_{31}O_2Si$ $[M+H]^+$ is 355.2093, found 355.2085.

(4*R*,6*S*)-4-((tert-Butyldimethylsilyl)oxy)-8-((tert-butyldiphenylsilyl)oxy)-6-methyloctan-1-ol (14)

i) To a stirred solution of alcohol **8** (2.0 g, 5.05 mmol) in dry CH_2Cl_2 (40 mL), 2,6-lutidine (0.87 mL, 7.57 mmol) and TBSOTf (1.4 mL, 6.06 mmol) were added sequentially at 0 °C and allowed to stir at same temperature. After completion of the reaction in 2 h, (as monitored by TLC) the reaction was quenched with saturated aqueous NH_4Cl, the aqueous layer was extracted with CH_2Cl_2. Combined organic layers were washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4. Solvent was concentrated under reduced pressure to afford crude product which was then purified by using silica gel column chromatography to afford TBS ether[10] as a light yellow oil (2.46 g, 96% yield). $R_f = 0.8$ (10% EtoAc in Hexane). $[\alpha]_D^{20}$ −7.70 (*c* 1, $CHCl_3$). NMR data consistent with previous report[2]

IR (neat): $\tilde{\nu}$ = 3064, 2932, 2860, 1467, 1432, 1255, 1102, 999, 915, 832, 776, 702, 614 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.58 (m, 4H), 7.49–7.30 (m, 6H), 5.92–5.71 (m, 1H), 5.03 (qd, *J* = 2.4, 1.2 Hz, 1H), 5.00 (dd, *J* = 2.4, 1.2 Hz, 1H), 3.81–3.73 (m, 1H), 3.72–3.62 (m, 2H), 2.28–2.08 (m, 2H), 1.87–1.55 (m, 2H), 1.49–1.32 (m, 2H), 1.30–1.13 (m, 1H), 1.05 (s, 9H), 0.88 (s, 9H), 0.84 (t, *J* = 6.8 Hz, 3H), 0.05 (dd, *J* = 6.8, 3.8 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.6, 135.4, 134.1, 129.5, 127.6, 116.6, 70.2, 62.1, 44.7, 41.7, 39.9, 26.9, 26.2, 25.9, 20.2, 19.2, 18.1, -4.3, -4.4.

MS (ESI): *m*/*z* = 533 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{31}H_{51}O_2Si_2$ $[M+H]^+$ is 511.3428, found 511.3423.

ii) To a stirred solution of alkene obtained above (1.0 g, 1.96 mmol) in dry THF (10 mL) at 0 °C, a solution of borane dimethylsulfide (2.0 N solution in THF) (1.5 mL, 2.94 mmol) was added dropwise and allowed to stir for 6 h at room temperature. Then the reaction mixture was again cooled to 0 °C and treated with 2N NaOH solution (2 mL) and H_2O_2 (1 mL) dropwise and stirred for 2 h at room temperature. After completion of the reaction (20 h), (monitored by TLC), reaction mixture was diluted with water and extracted with ethyl acetate (3×20 mL). The organic layers were combined, washed with brine (40 mL) and dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography to afford alcohol **14** (0.84 g, 82% yield) as a light yellow oil. $R_f = 0.4$ (10% EtoAc in Hexane). $[\alpha]_D^{20}$ +0.7 (*c* 1, $CHCl_3$).

IR (neat): $\tilde{\nu}$ = 3396, 2927, 2858, 1465, 1431, 1385, 1254, 1102, 831, 774, 738, 701, 613 cm^{-1}.

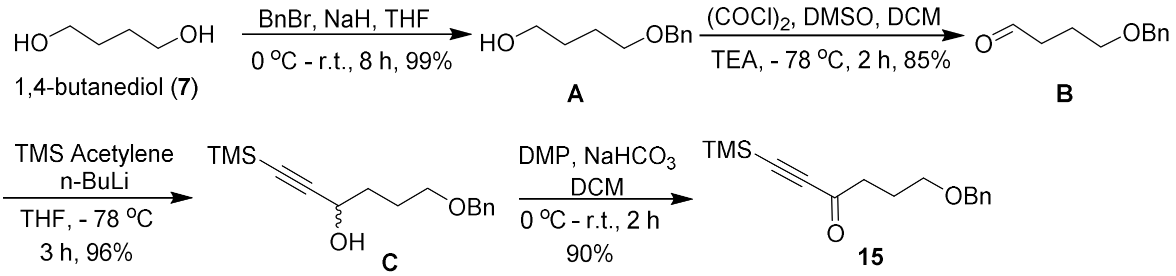
^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 7.8, 1.6 Hz, 4H), 7.47–7.34 (m, 6H), 3.89–3.78 (m, 1H), 3.76–3.53 (m, 4H), 2.21 (br, 1H), 1.64–1.47 (m, 6H), 1.41–1.21 (m, 3H), 1.06 (s, 9H), 0.90 (s, 9H), 0.84 (d, *J* = 6.4 Hz, 3H), 0.07 (d, *J* = 5.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.5, 134.0, 129.5, 127.6, 70.2, 63.2, 61.9, 44.1, 40.3, 33.0, 27.9, 26.9, 26.3, 25.9, 19.8, 19.2, 18.1, -4.4, -4.5.

MS (ESI): *m*/*z* = 551 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{31}H_{53}O_3Si_2$ $[M+H]^+$ is 529.3533, found 529.3528.

Scheme for compound 15



4-(Benzyloxy)butan-1-ol (A)

Sodium hydride (1.1 g, 27.5 mmol, 60% in mineral oil) was added slowly to the solution of 1,4-butanediol **7** (5.0 g, 55.45 mmol) in dry THF (25 mL) at 0 ºC. Benzyl bromide (3.16 g, 18.48 mmol) was added dropwise at the same temperature. The reaction mixture was allowed to stirr at room temperature for 8 h. Then the reaction was quenched with aqueous ammonium chloride (20 mL). The aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were collected, washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by using silica gel column chromatography to give compound **A** (3.3 g, 99% yield) as a colorless oil. R_f = 0.4 (30% EtoAc in Hexane). NMR data consistent with previous report[3]

IR (neat): $\tilde{v}$ = 3378, 2939, 2862, 1452, 1363, 1205, 1095, 1061, 998, 736, 698, 612 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.25 (m, 5H), 4.52 (s, 2H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.52 (t, *J* = 5.8 Hz, 2H), 2.43 (br, 1H), 1.76–1.62 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.1, 128.3, 127.6, 127.6, 73.0, 70.3, 62.6, 30.0, 26.6.

MS (ESI): *m*/*z* = 203 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{11}H_{16}O_2Na$ $[M+Na]^+$ is 203.1048, found 203.1056.

4-(Benzyloxy)butanal (B)

Oxalyl chloride (3.06 g, 24 mmol) was dissolved in dry DCM (45 mL) and cooled to -78 °C. DMSO (3.51 g, 45 mmol) was added and stirred for 10 min. at same temperature. A solution of 4-(benzyloxy)butan-1-ol (**A**) (2.7 g, 15 mmol) in dry DCM (30 mL) was added to the reaction mixture dropwise over 15 min at -78 °C. The reaction mixture was stirred at -78 °C for 30 min followed by dropwise addition of triethylamine (6.7 g, 75 mmol). The reaction mixture was allowed to warm up to room temperature and stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were collected, washed with brine (30 mL), and dried over anhydrous Na_2SO_4. Solvent was concentrated under reduced pressure to afford crude product as a yellow oil. The crude product was further purified by using silica gel column chromatography to give aldehyde **19** (2.3 g, 85% yield) as a colorless oil. R_f = 0.6 (30% EtoAc in Hexane). NMR data consistent with previous report[3]

IR (neat): ṽ = 2930, 2859, 1682, 1452, 1363, 1100, 1027, 993, 738, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.77 (t, *J* = 1.6 Hz, 1H), 7.32 (m, 5H), 4.49 (s, 2H), 3.50 (t, *J* = 6.0 Hz, 2H), 2.54 (td, *J* = 7.2, 1.6 Hz, 2H), 1.98–1.90 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.2, 138.2, 128.3, 127.5, 72.9, 69.0, 40.8, 22.5.

MS (ESI): *m*/*z* = 201 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{11}H_{14}O_2Na$ $[M+Na]^+$ is 201.0891, found 201.0899.

6-(Benzyloxy)-1-(trimethylsilyl)hex-1-yn-3-ol (c)

To a solution of (trimethylsilyl)acetylene (1.43 mL, 10.11 mmol) in dry THF (20 mL) was slowly added n-BuLi (2.5 M in hexane, 4.0 mL, 10.11 mmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. To the resulting mixture was added a solution of aldehyde **B** (1.50 g, 8.42 mmol) in THF (15 mL) at the same temperature, and the mixture was warmed to 0 °C over a period of 3 h. The reaction was quenched by addition of a saturated aqueous NH_4Cl solution (25 mL), and the aqueous layer was extracted with EtOAc (3×20 mL). The organic layer was washed with brine (25 mL) and dried over anhydrous Na_2SO_4. After the solvent was evaporated under the reduced pressure the residue was purified by using silica gel column chromatography to afford racemic alcohol **C** (2.22 g, 96%) as a colorless liquid. R_f = 0.3 (30% EtoAc in Hexane). $[\alpha]_D^{20}$ +0.01 (*c* 1, $CHCl_3$).

IR (neat): ṽ = 2956, 2924, 2856, 1251, 1094, 1020, 841, 758, 737, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 5H), 4.52 (d, *J* = 2.4 Hz, 2H), 4.40 (d, *J* = 5.6 Hz, 1H), 3.55–3.48 (m, 2H), 2.84 (d, *J* = 5.6 Hz, 1H), 1.89–1.73 (m, 4H), 0.17 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.0, 128.4, 127.6, 127.6, 106.7, 89.1, 72.8, 70.0, 62.4, 35.0, 25.4, -0.1.

MS (ESI): *m*/*z* = 299 $[M+Na]^+$.

HRMS (ESI): calcd. for $C_{16}H_{24}NaO_2Si$ $[M+Na]^+$ is 299.1443, found 299.1448.

6-(Benzyloxy)-1-(trimethylsilyl)hex-1-yn-3-one (15)

To a stirred solution of racemic propargylic alcohol (**C**) (2.0 g, 7.24 mmol) in dry CH_2Cl_2 (50 mL) was added $NaHCO_3$ (60 mg, 0.72 mmol), Dess-Martin periodinane (3.68 g, 8.68 mmol) sequentially at 0 °C and the reaction mass was allowed to stir for 4 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (30 mL) and saturated aqueous $Na_2S_2O_3$ solution (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3×25 mL) and combined organic layers were washed with water (25 mL), brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was concentrated under reduced pressure to afford crude product which was further purified with silica gel column chromatography to afford ketone **15** (1.8 g, 90% yield) as a colourless liquid. R_f = 0.5 (30% EtOAc in Hexane). NMR data consistent with previous report[4]

IR (neat): ṽ = 1675, 1360, 1251, 1101, 1067, 843, 760, 737, 698 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.02 (m, 5H), 4.49 (s, 2H), 3.50 (t, *J* = 6.0 Hz, 2H), 2.69 (t, *J* = 7.0 Hz, 2H), 2.16–1.82 (m, 2H), 0.24 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$): δ = 187.3, 138.3, 128.3, 127.5, 102.0, 97.7, 72.8, 68.9, 42.0, 24.0, -0.8.

MS (ESI): *m*/*z* = 297 [M+Na]$^+$.

HRMS (ESI): calcd. for $C_{16}H_{22}NaO_2Si$ [M+Na]$^+$ is 297.1287, found 297.1289.

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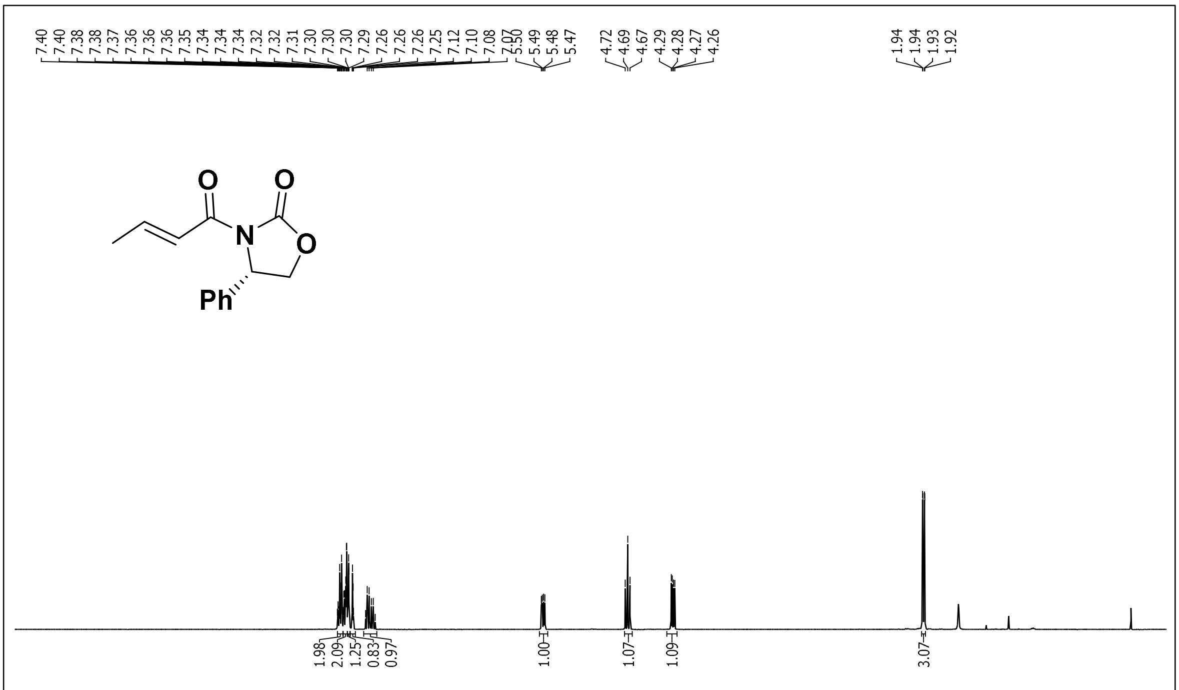
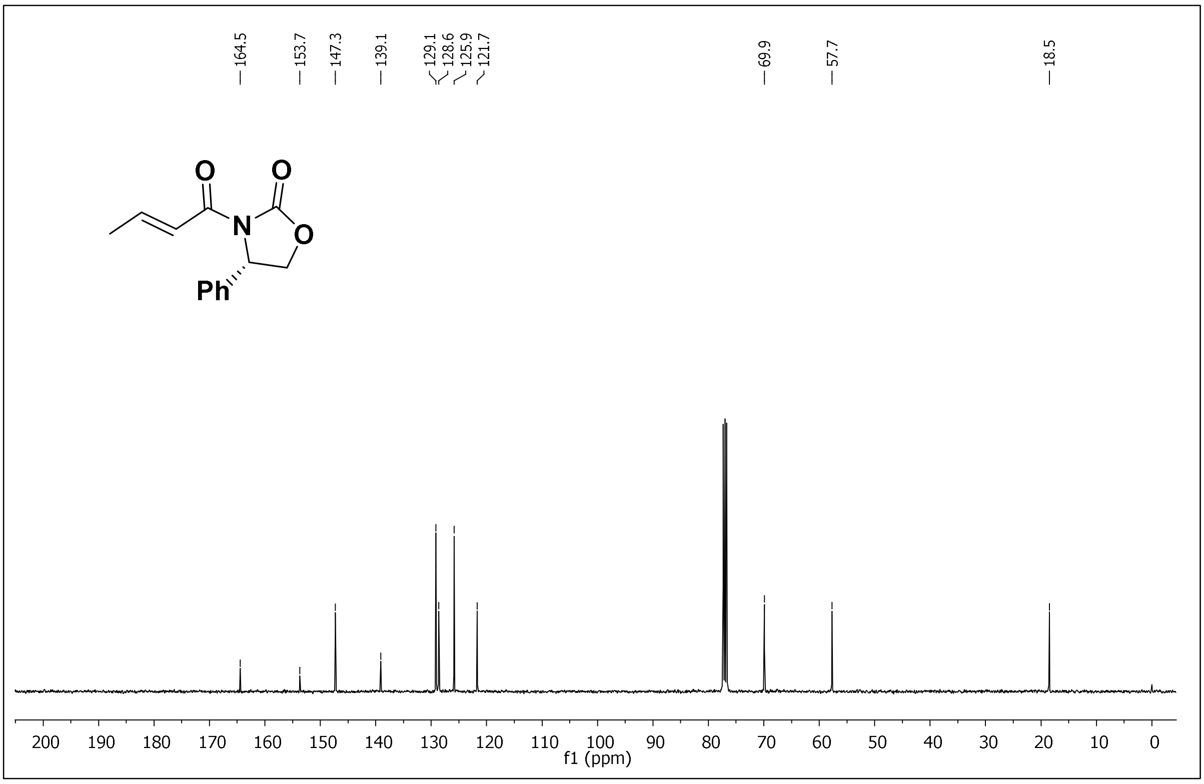


^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 11



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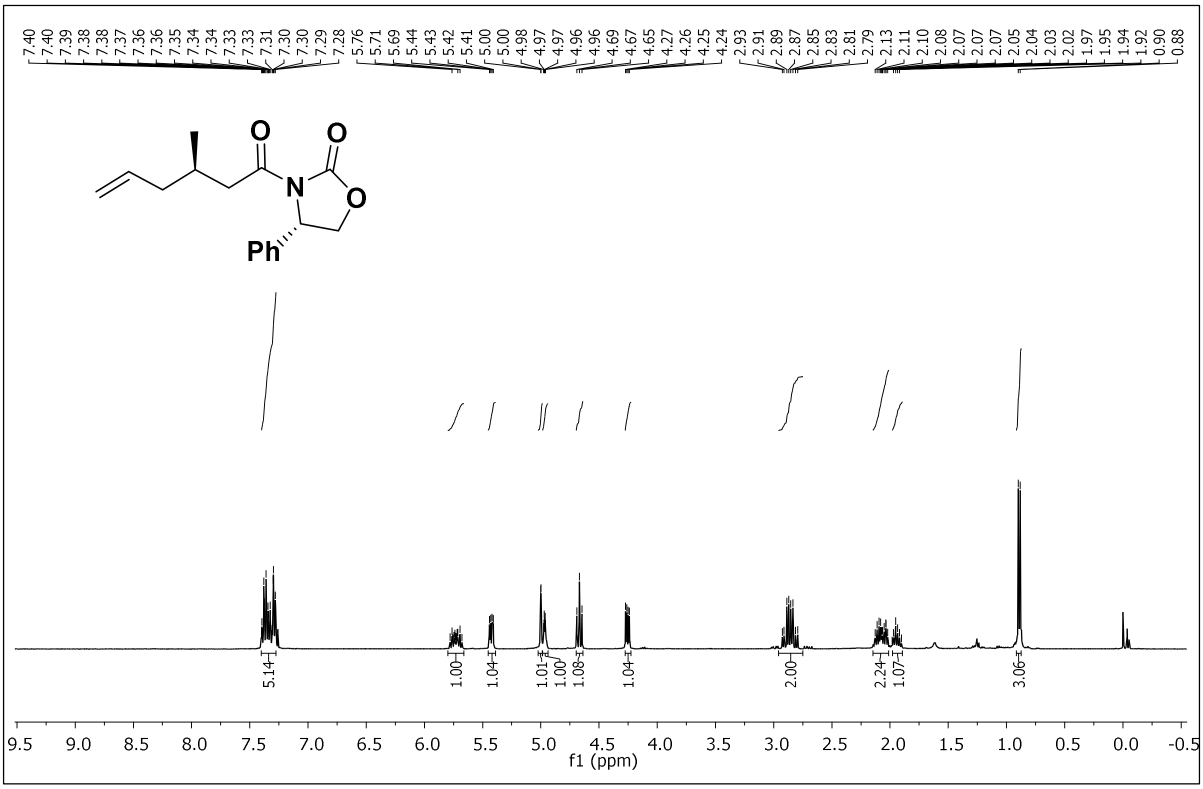
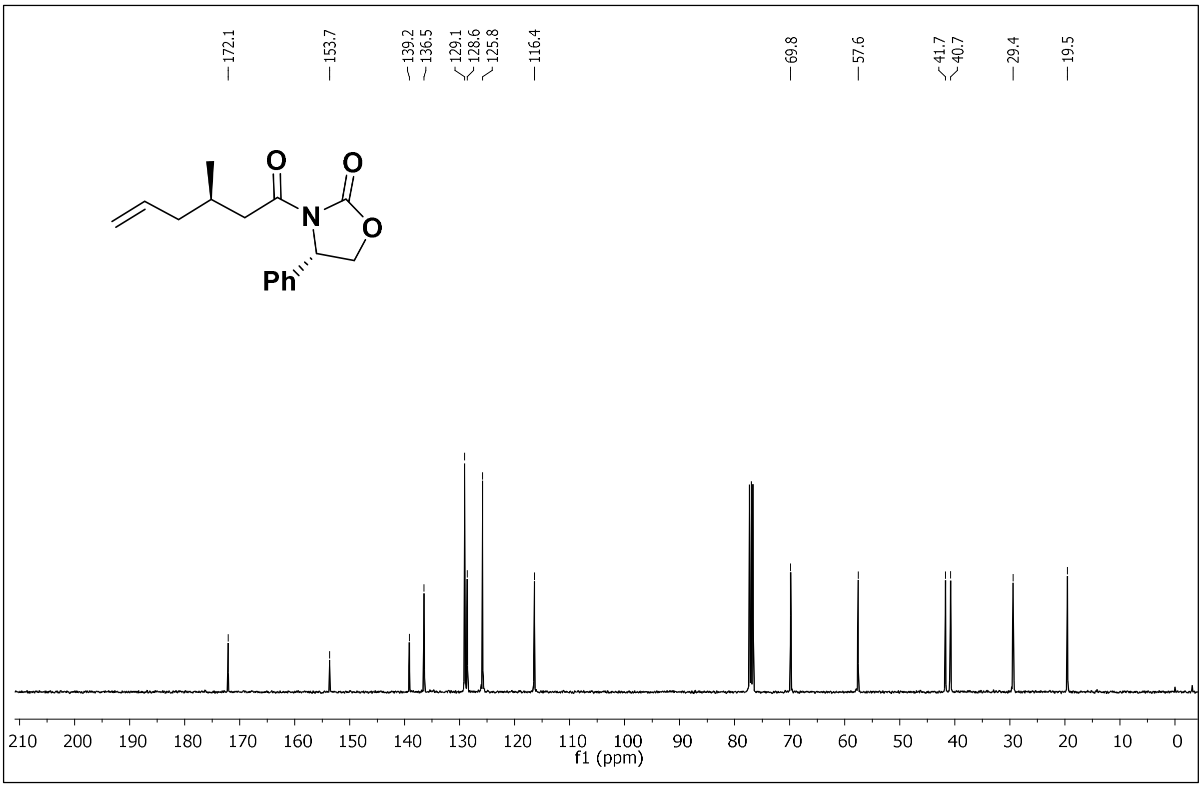


^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 10



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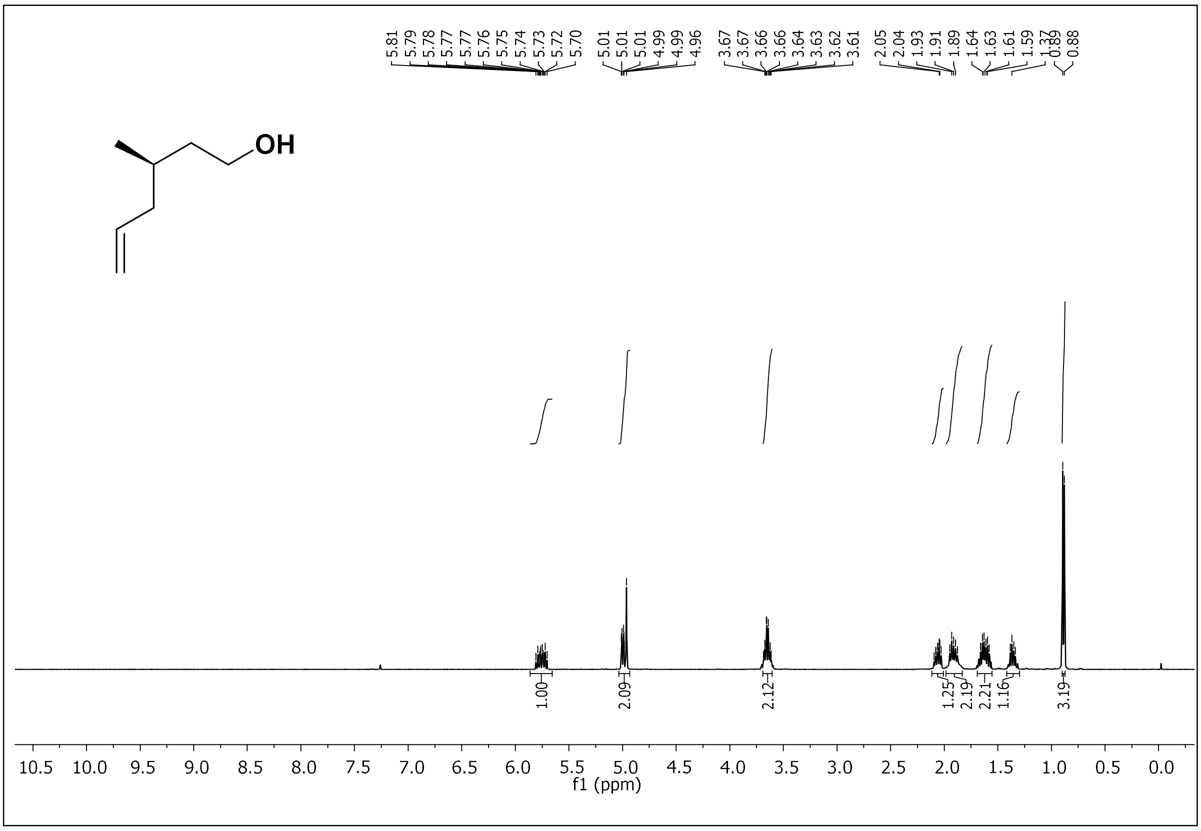
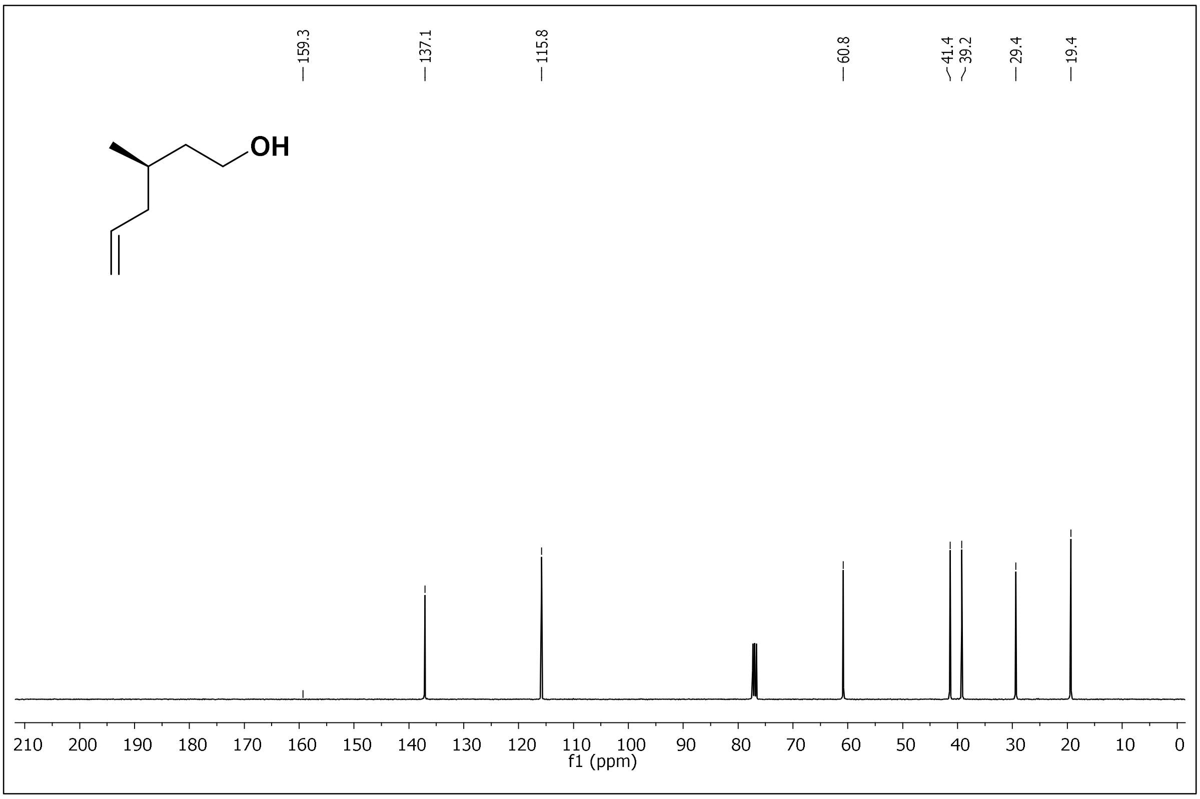
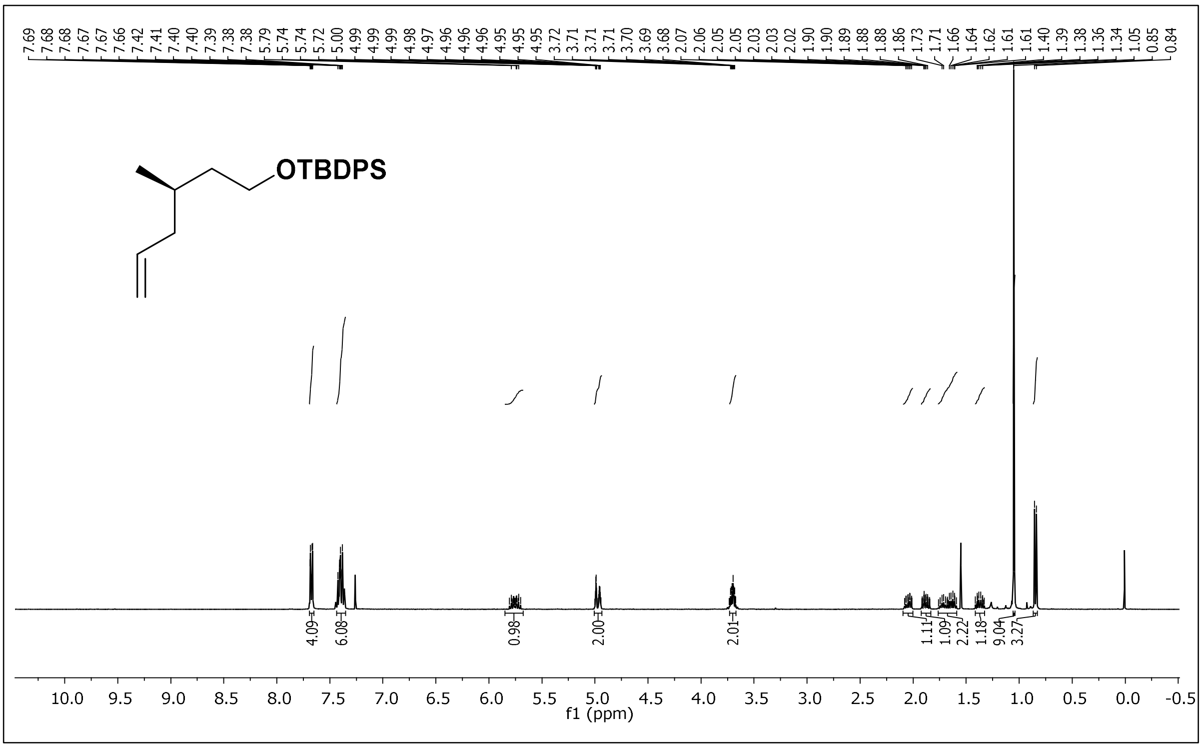


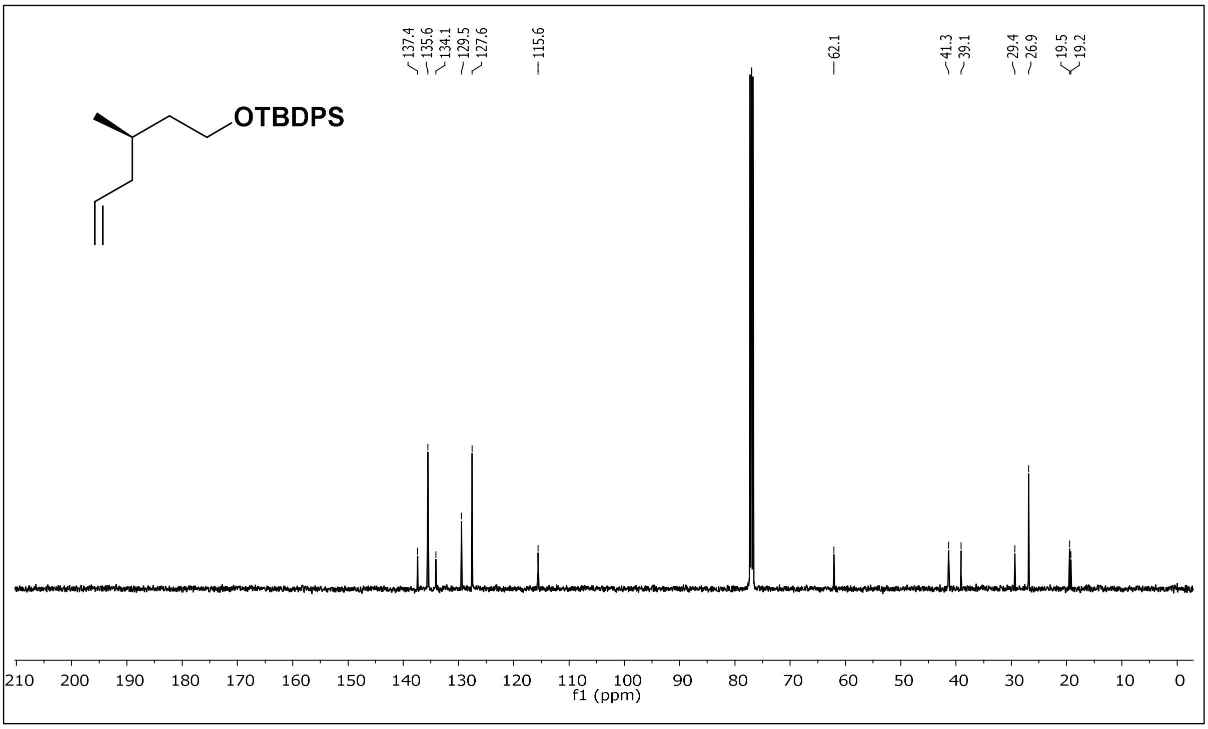
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 9



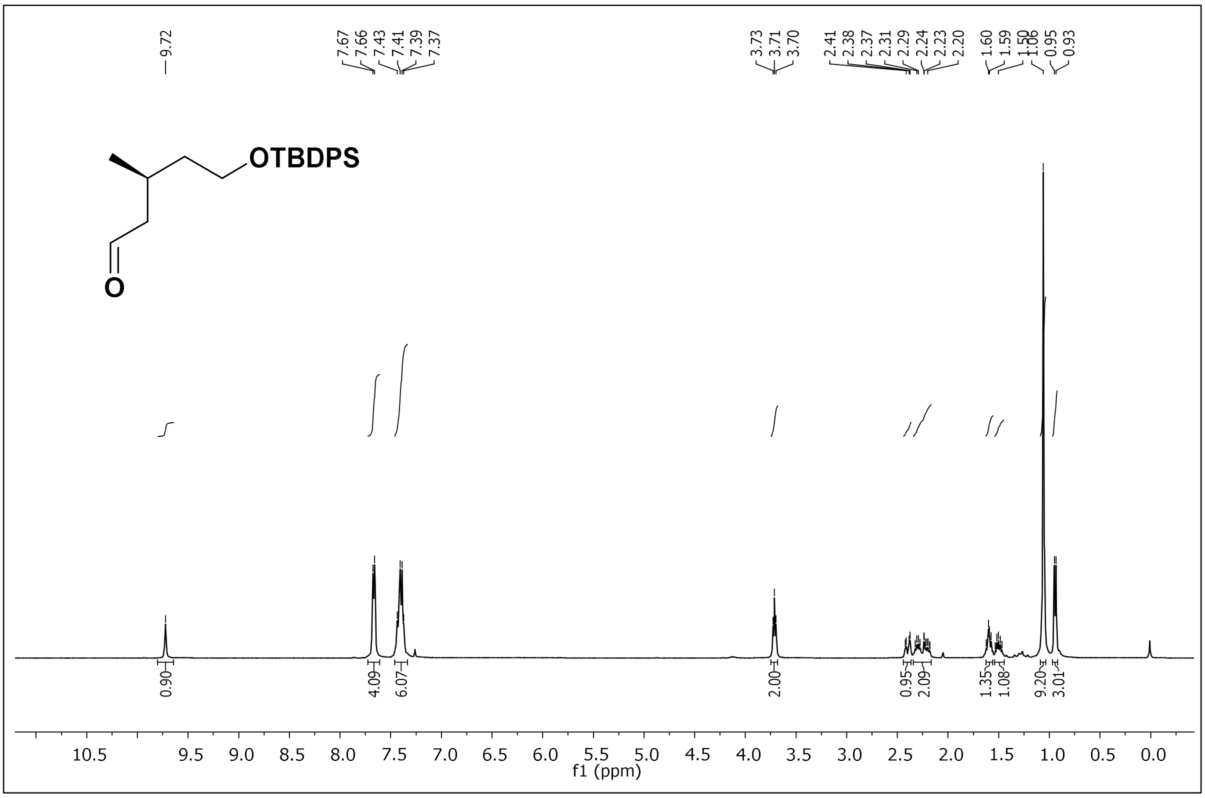
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 9



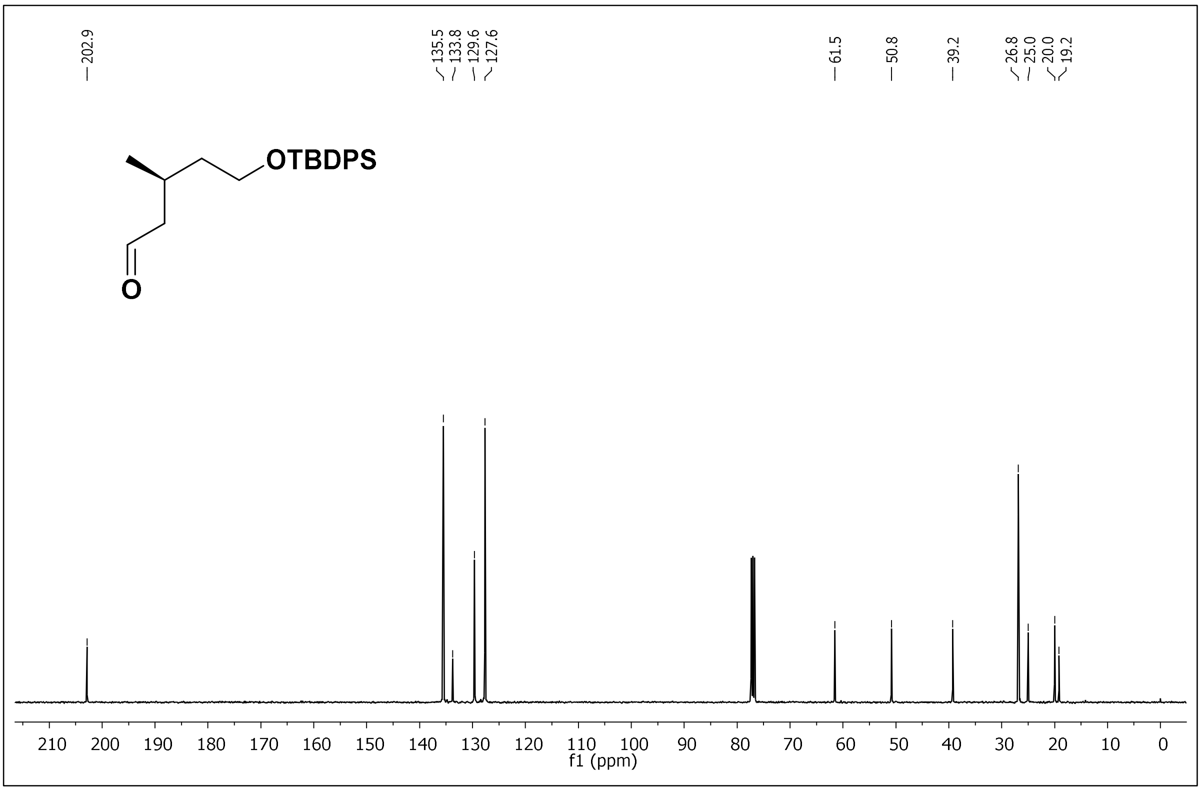
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of TBSether



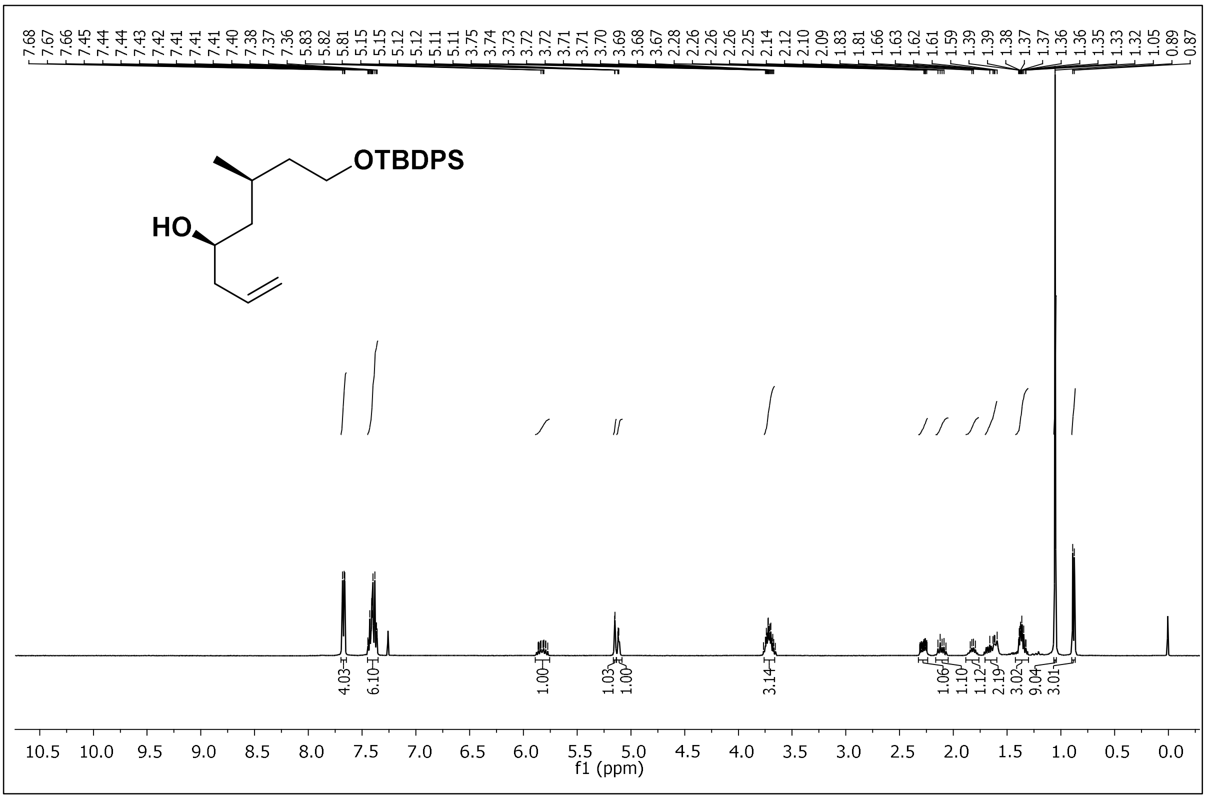
^{13}C NMR (126 MHz, CDCl$_3$) of spectrum of TBSether



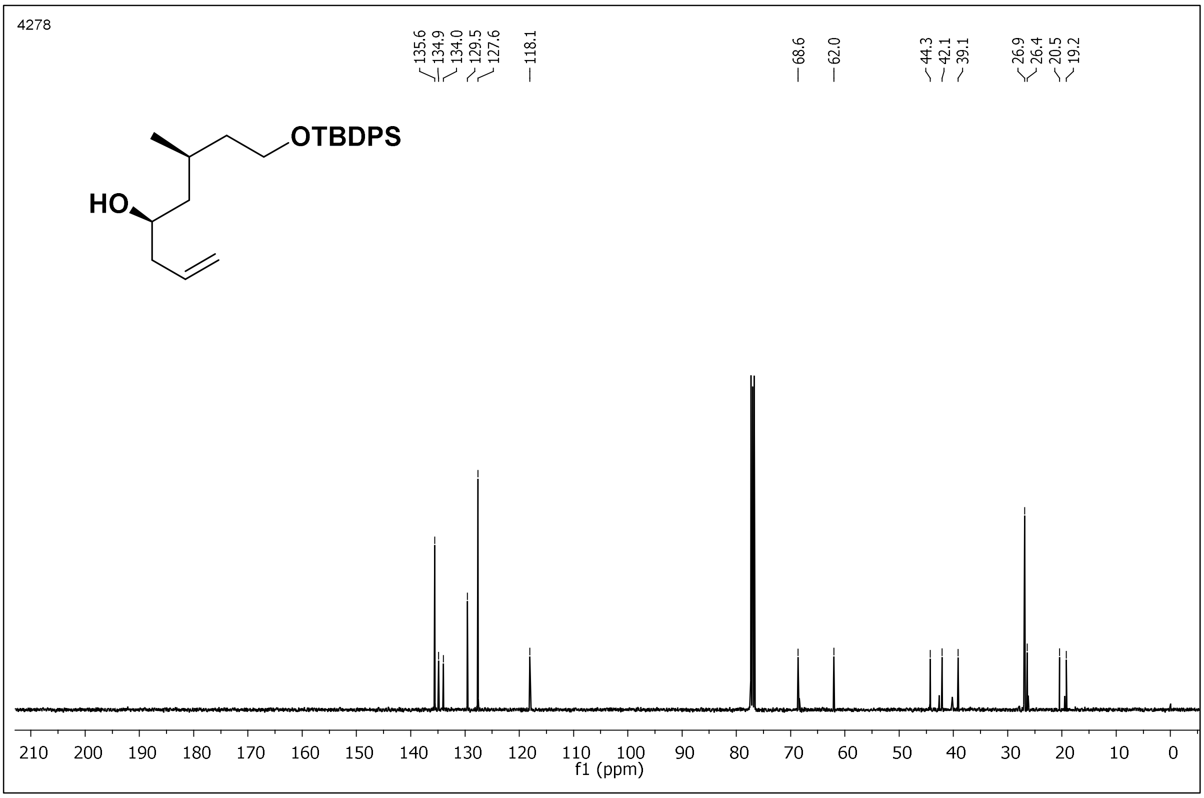
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 13



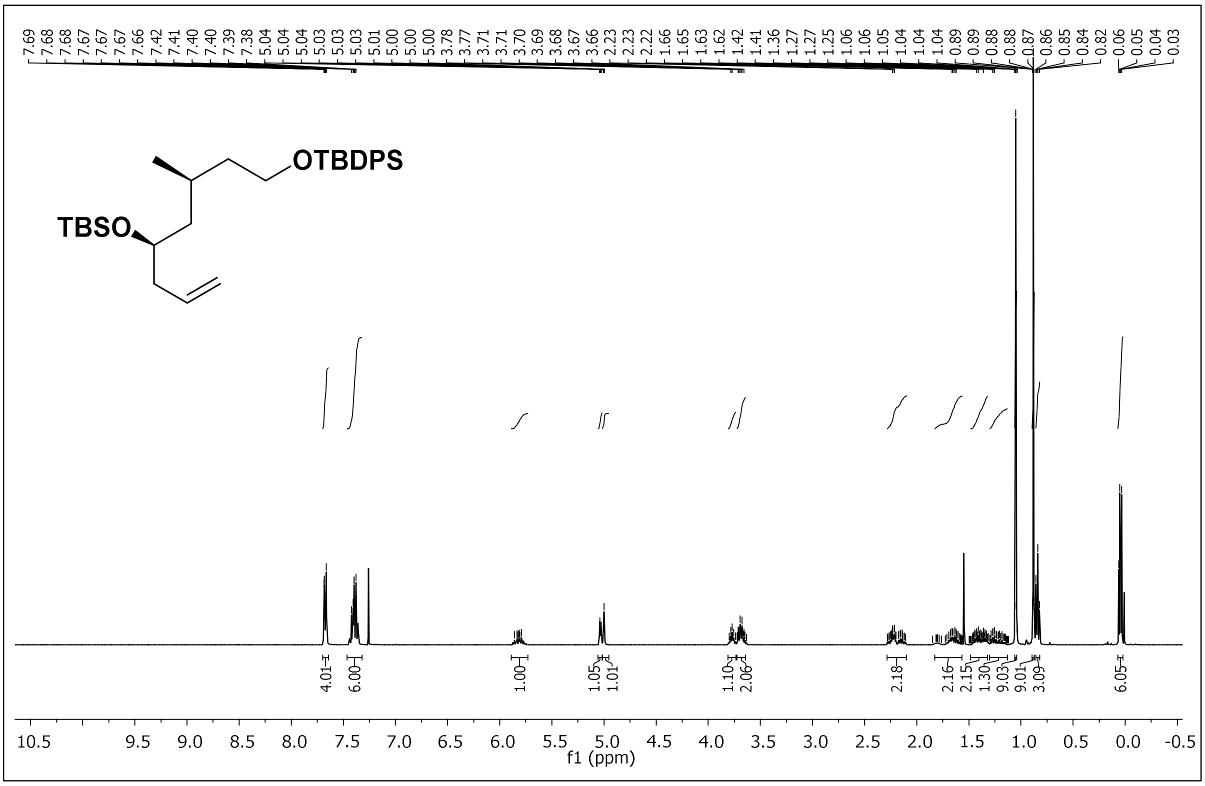
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 13



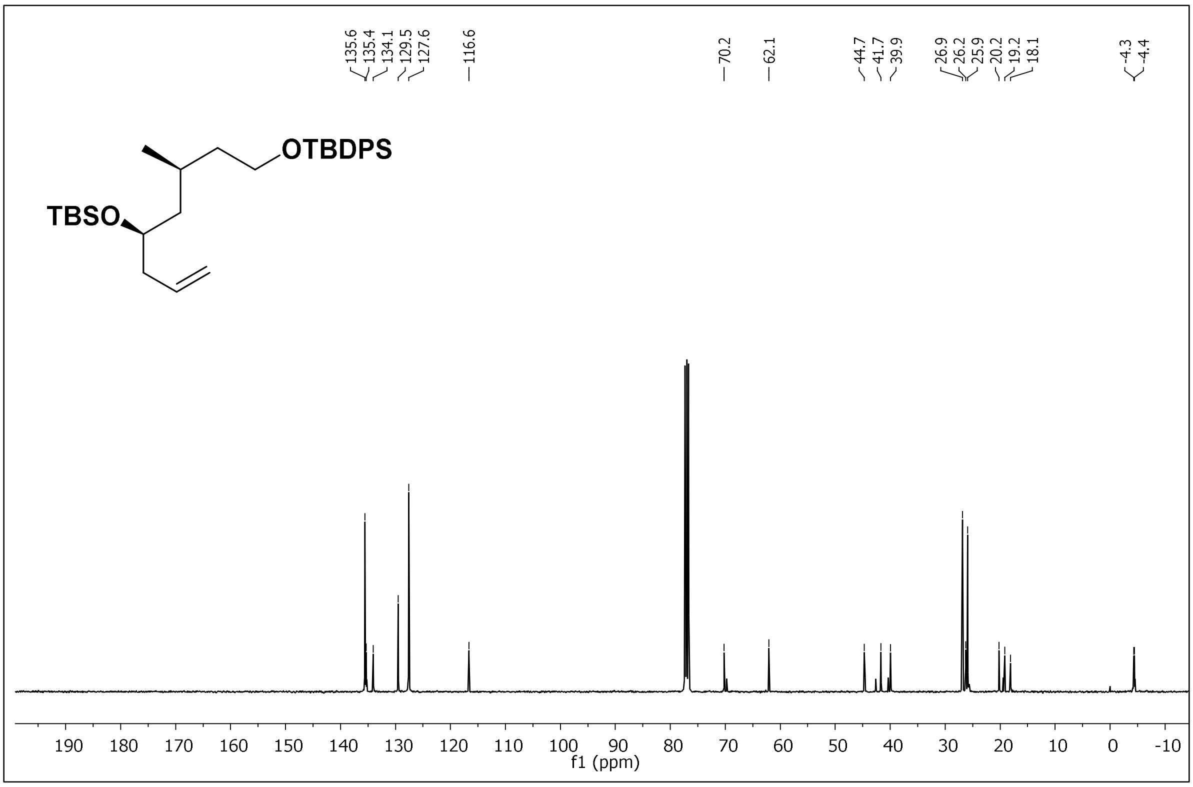
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 8



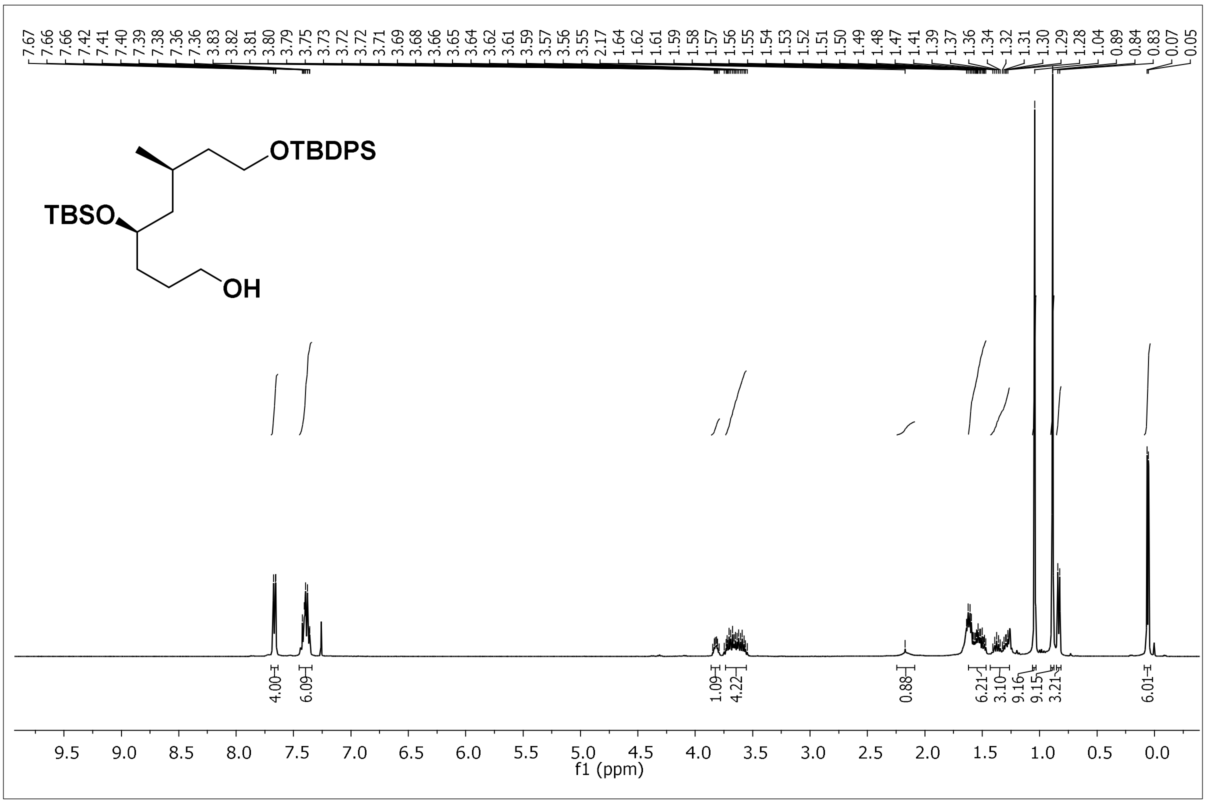
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 8



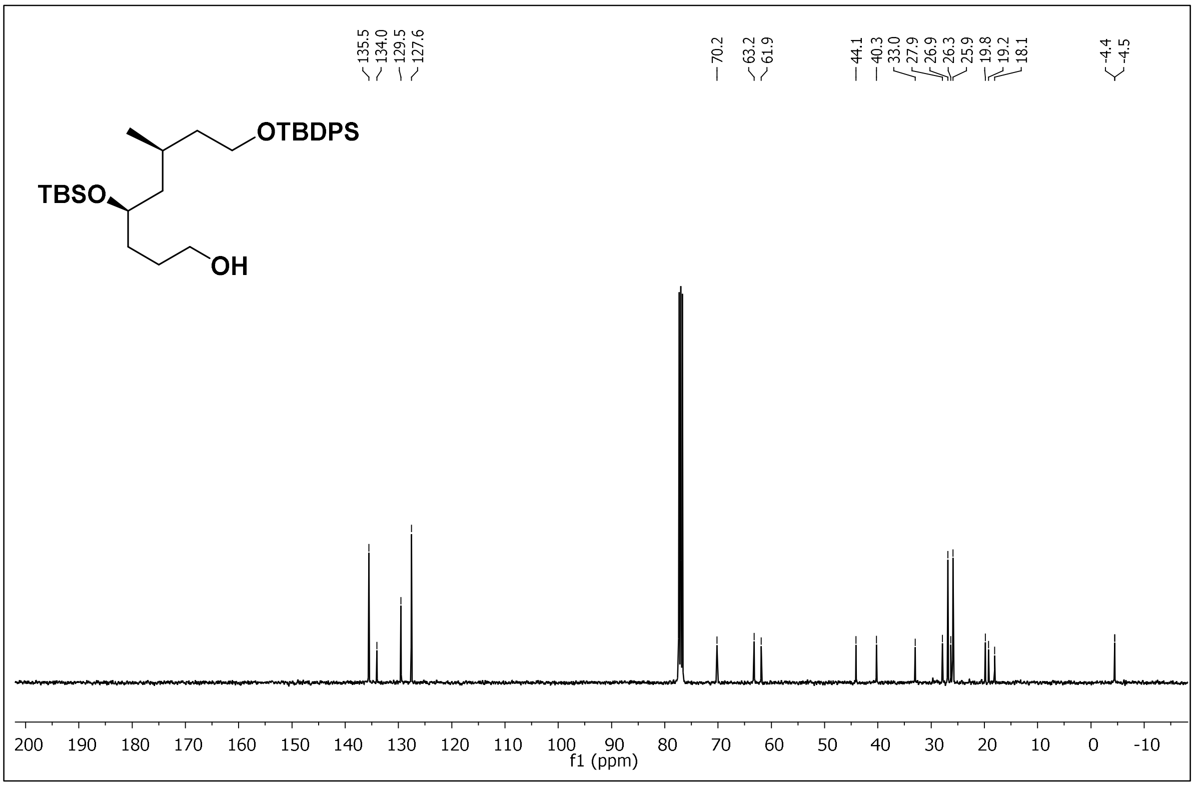
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of dislyl ether



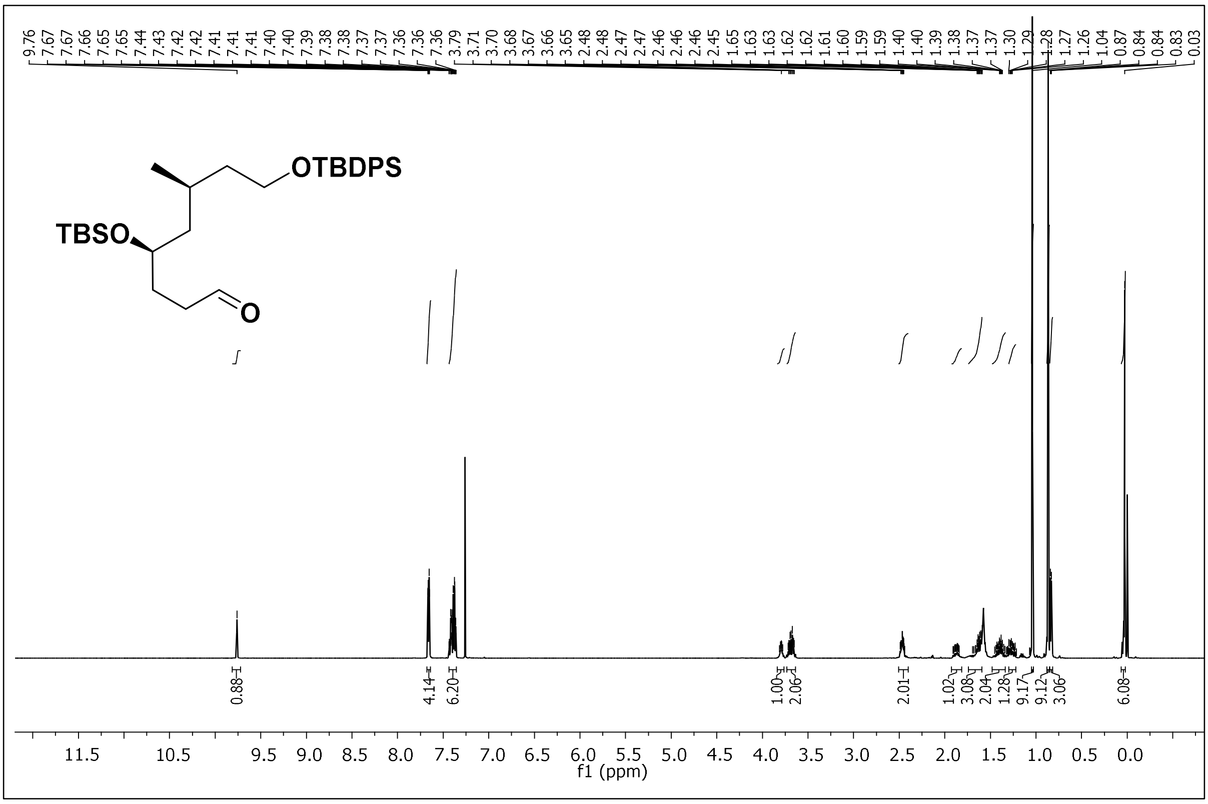
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of dislyl ether



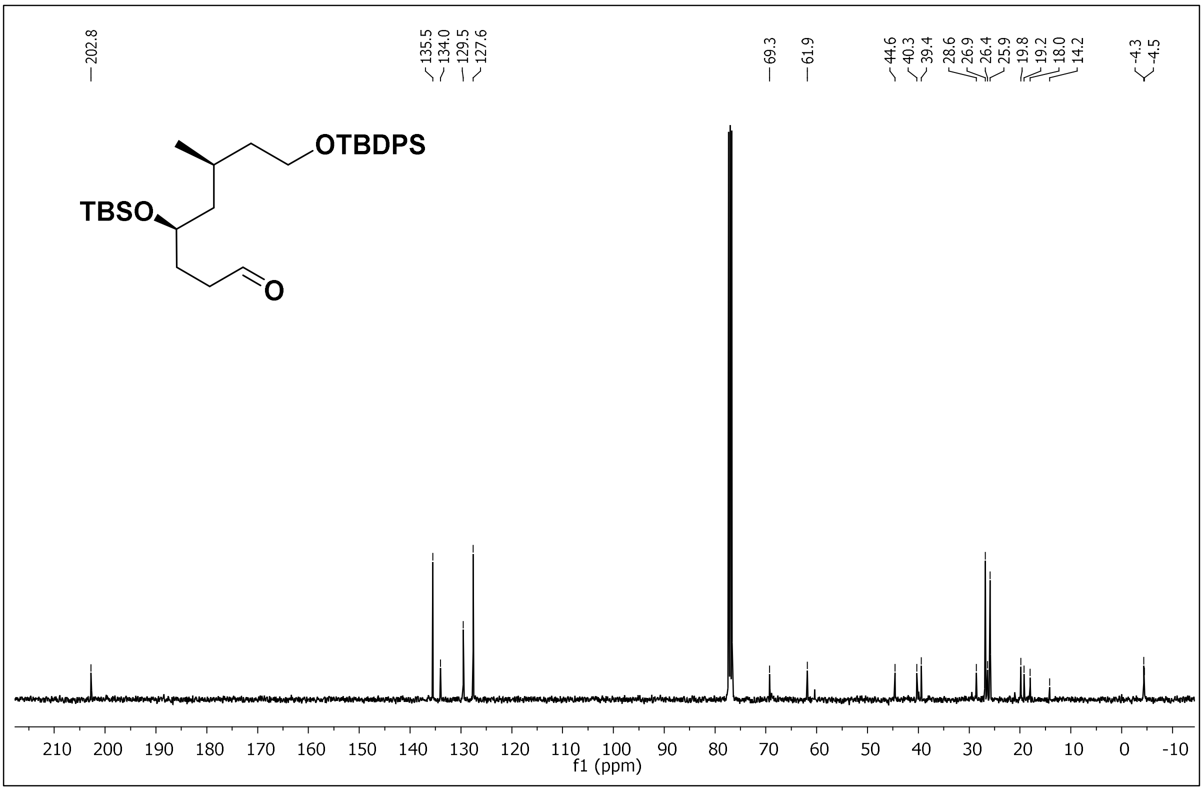
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 14



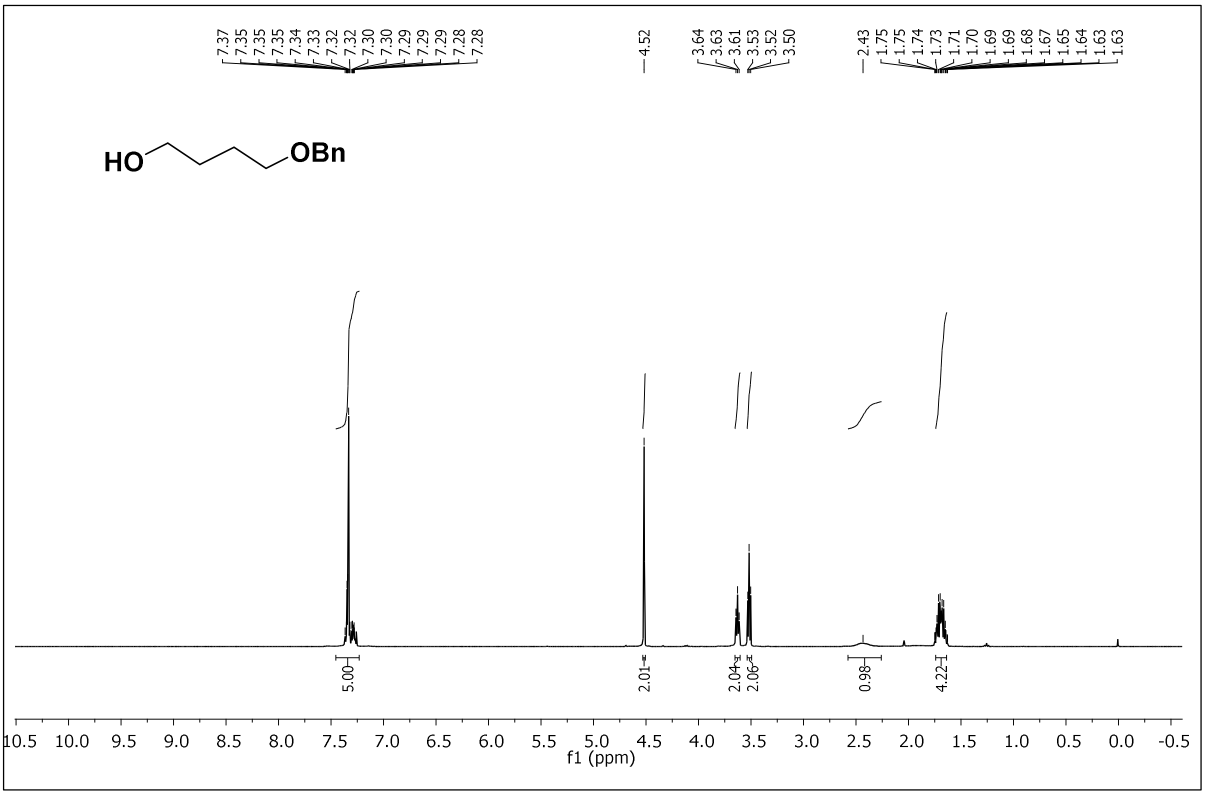
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 14



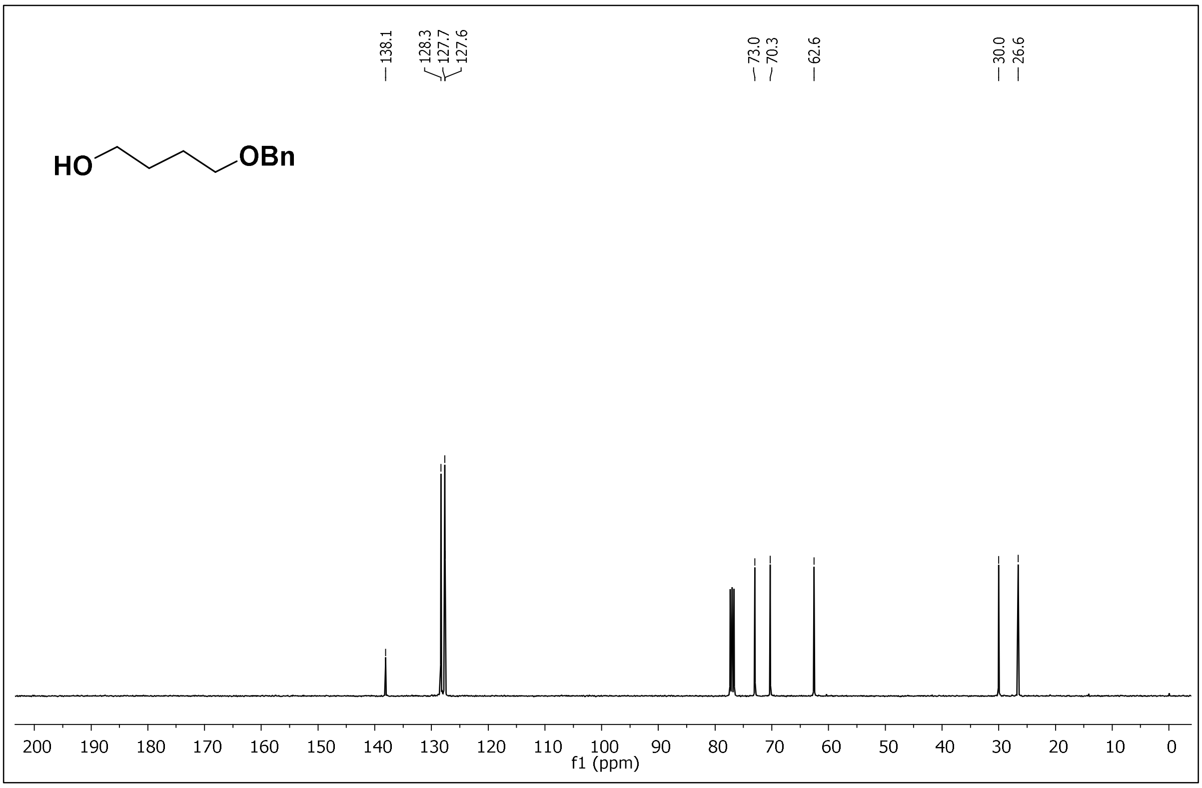
^{1}H NMR (500 MHz, CDCl$_3$) spectrum of compound 5



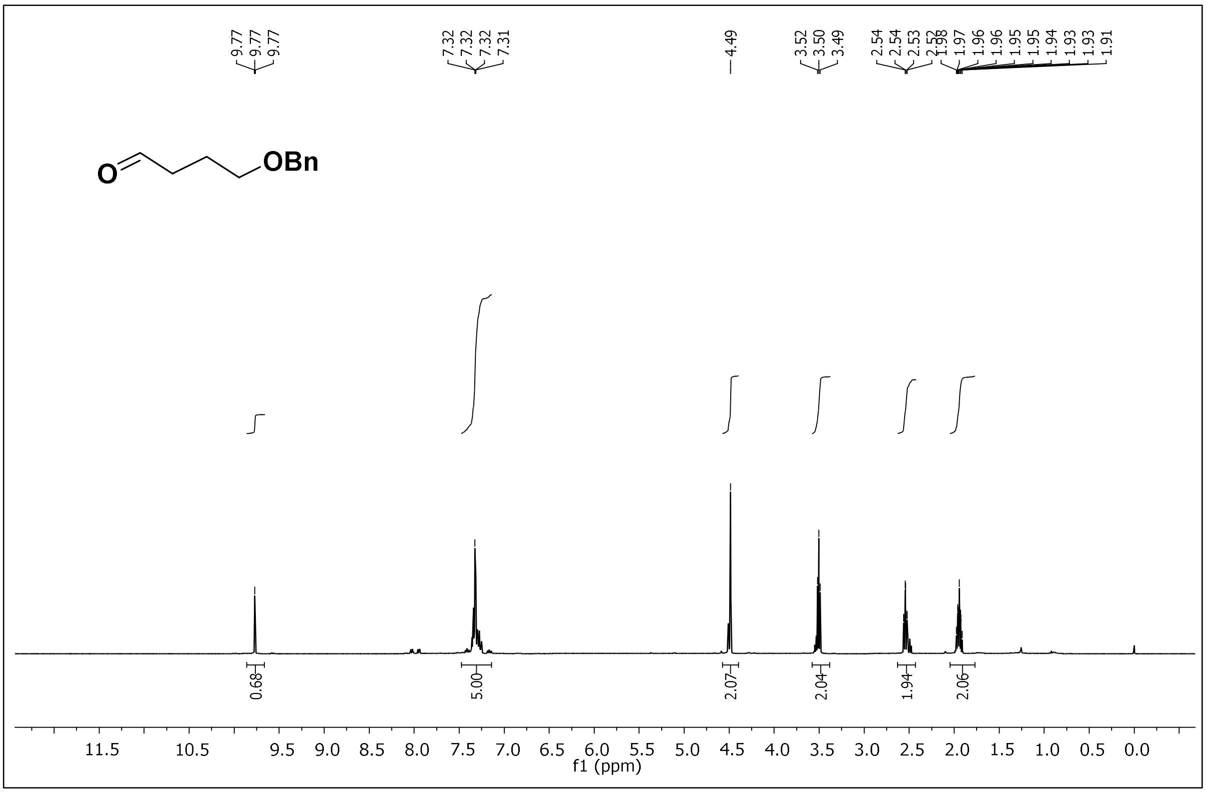
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 5



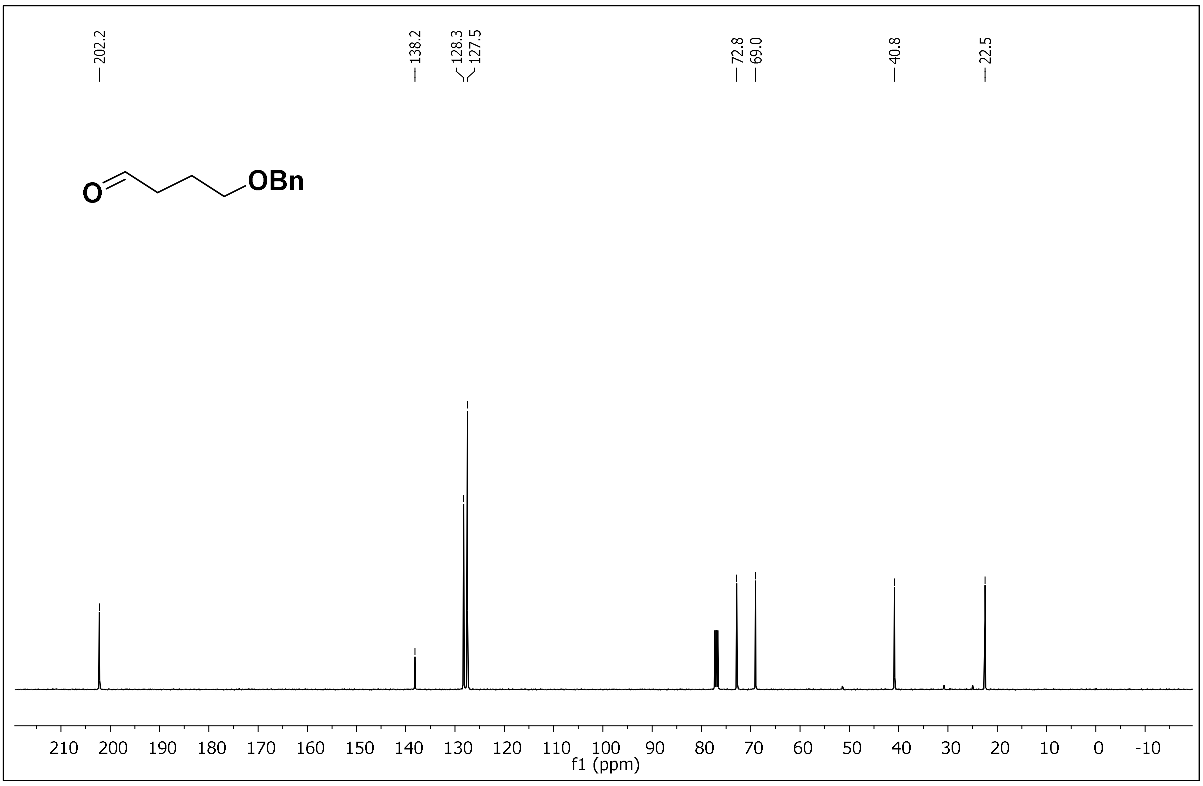
^{1}H NMR (400 MHz, CDCl$_3$) of spectrum compound A



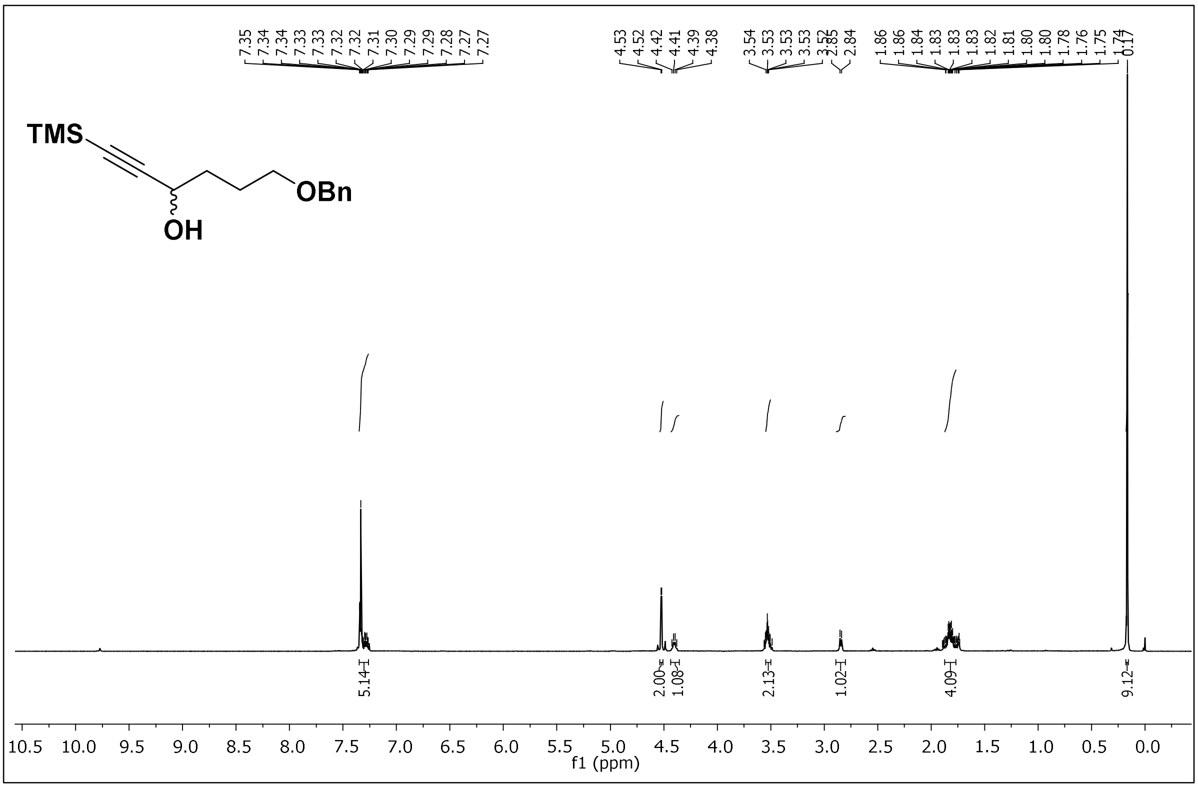
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound A



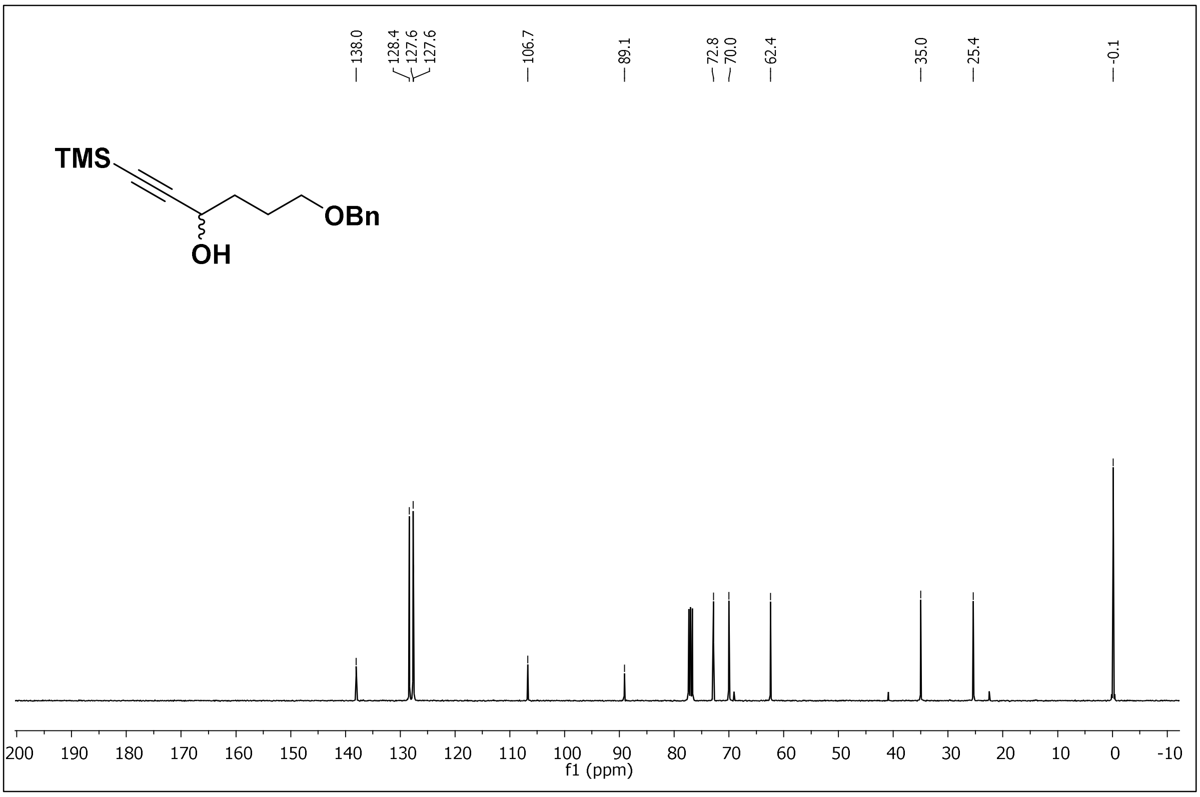
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound B



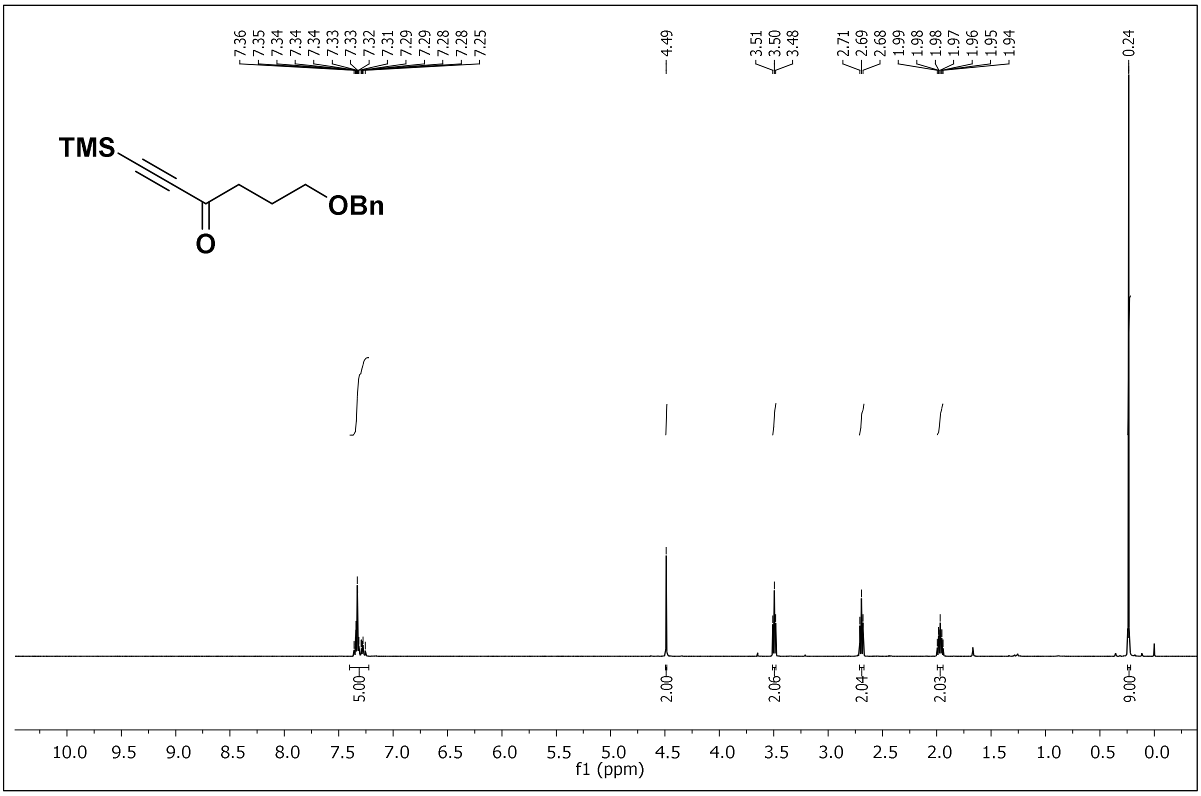
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound B



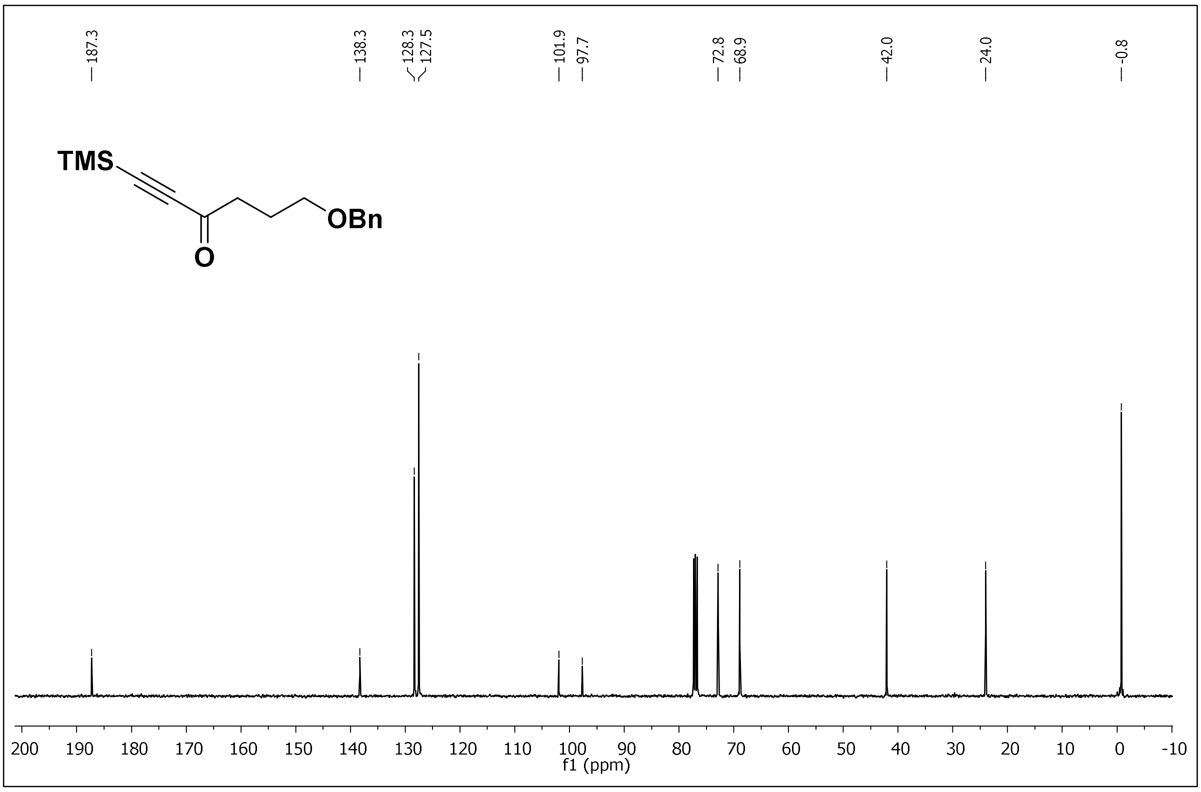
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound C



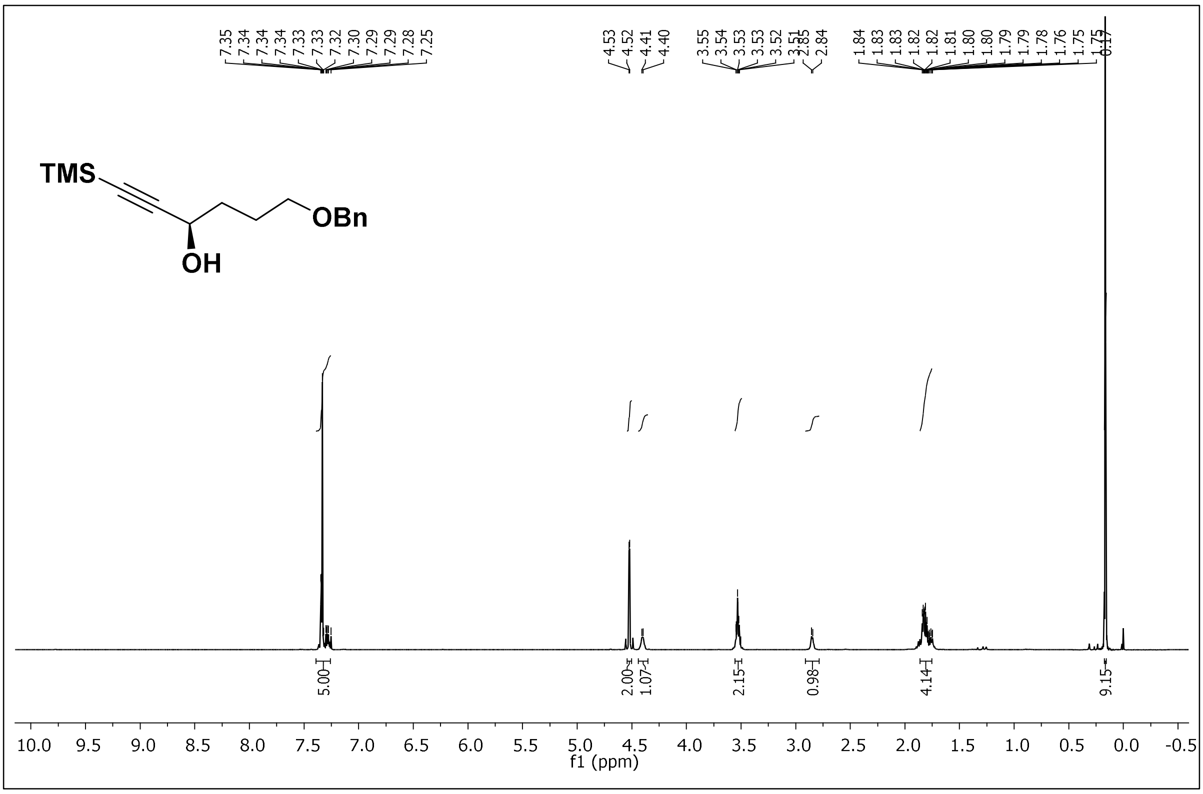
^{13}C NMR (101 MHz, CDCl3) spectrum of compound C



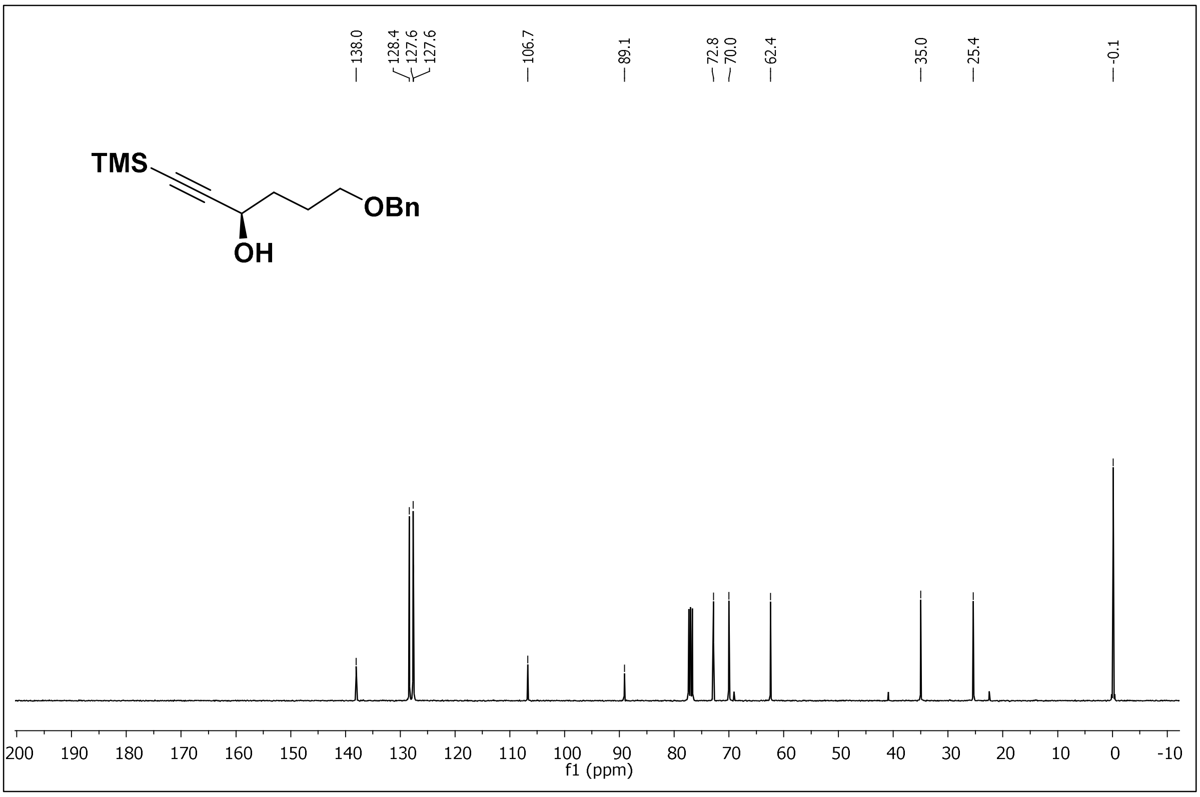
^{1}H NMR (500 MHz, CDCl$_3$) spectrum of compound 15



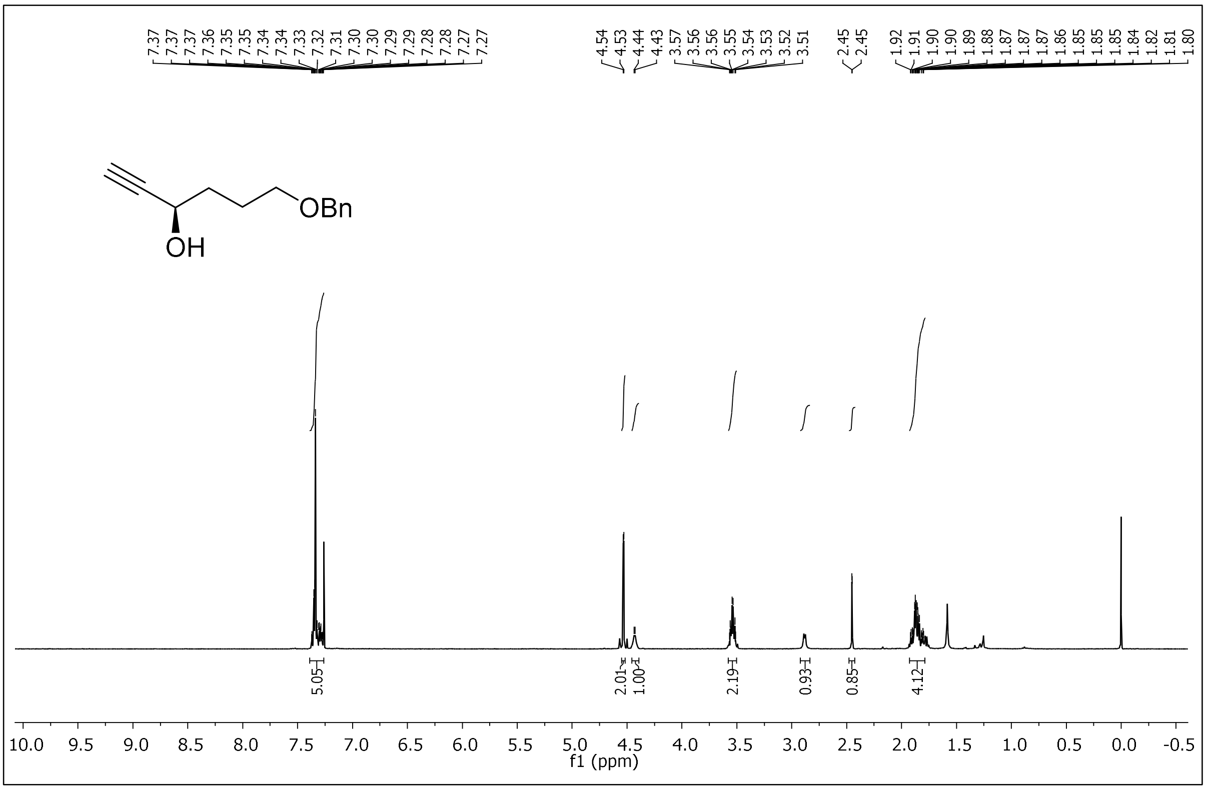
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 15



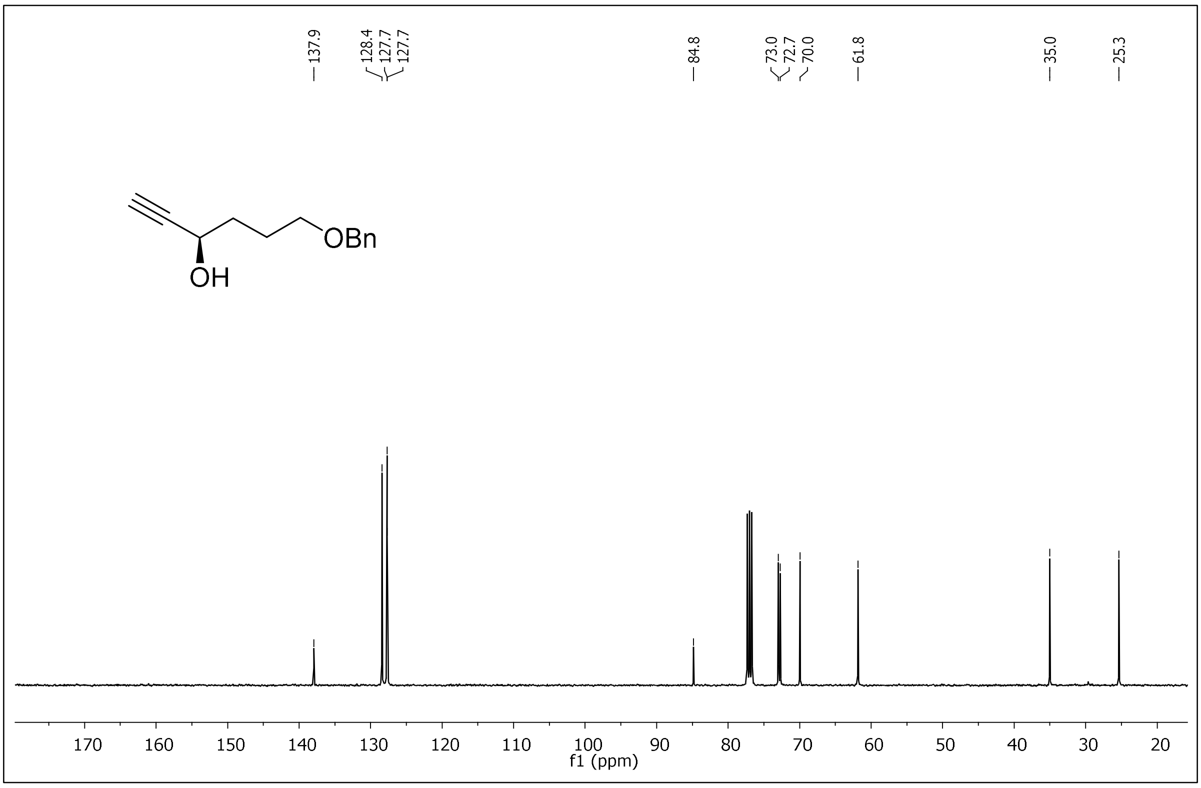
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 16



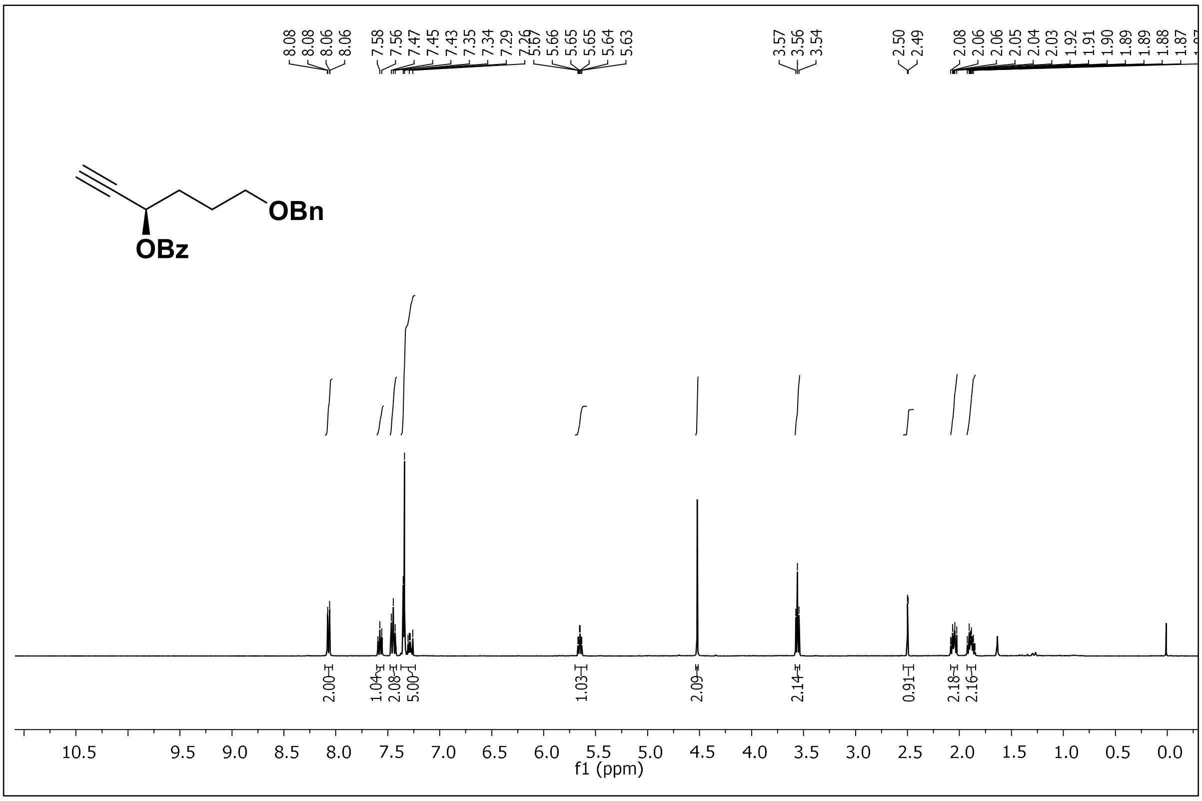
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 16



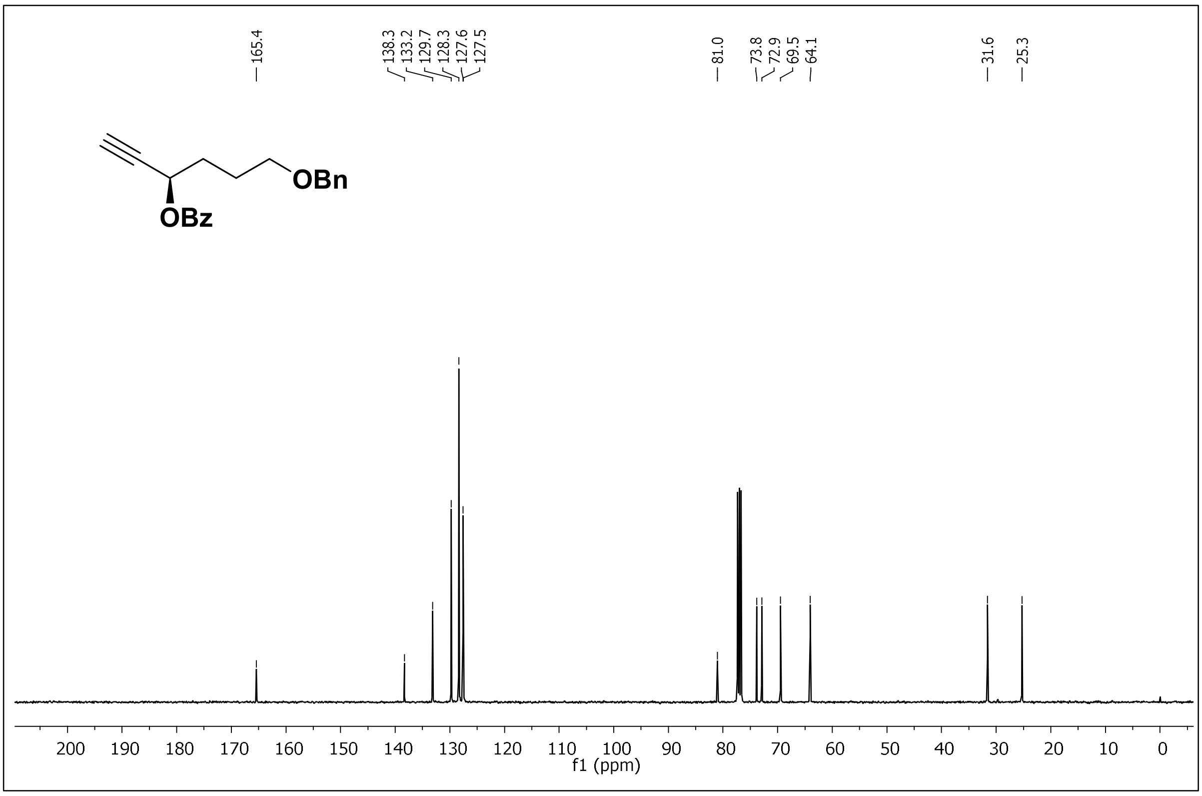
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 17



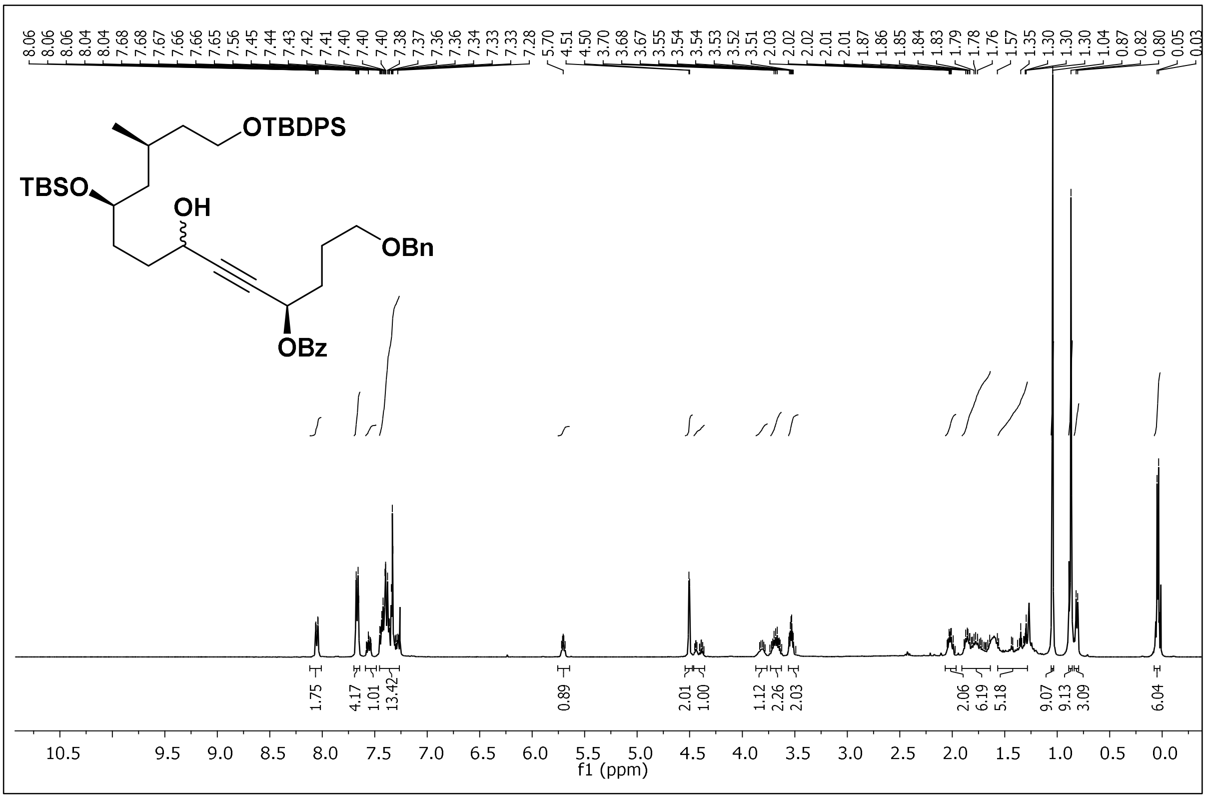
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 17



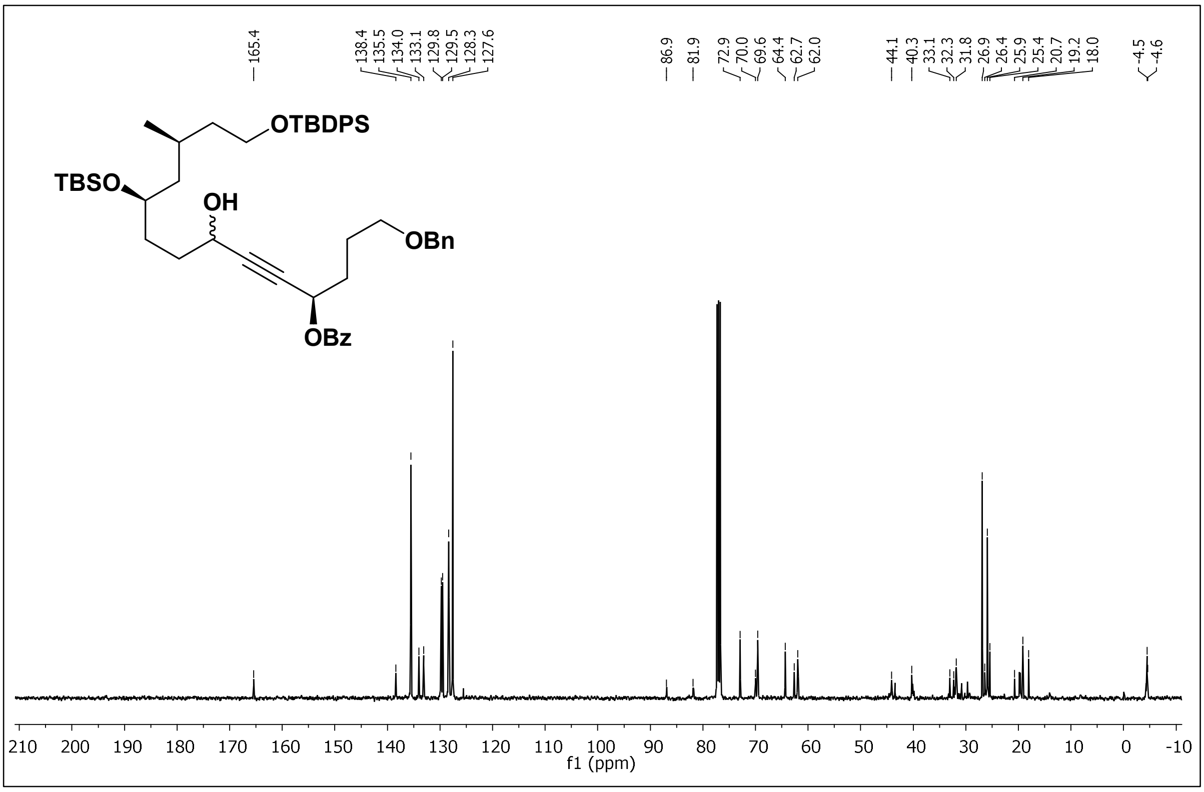
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 6



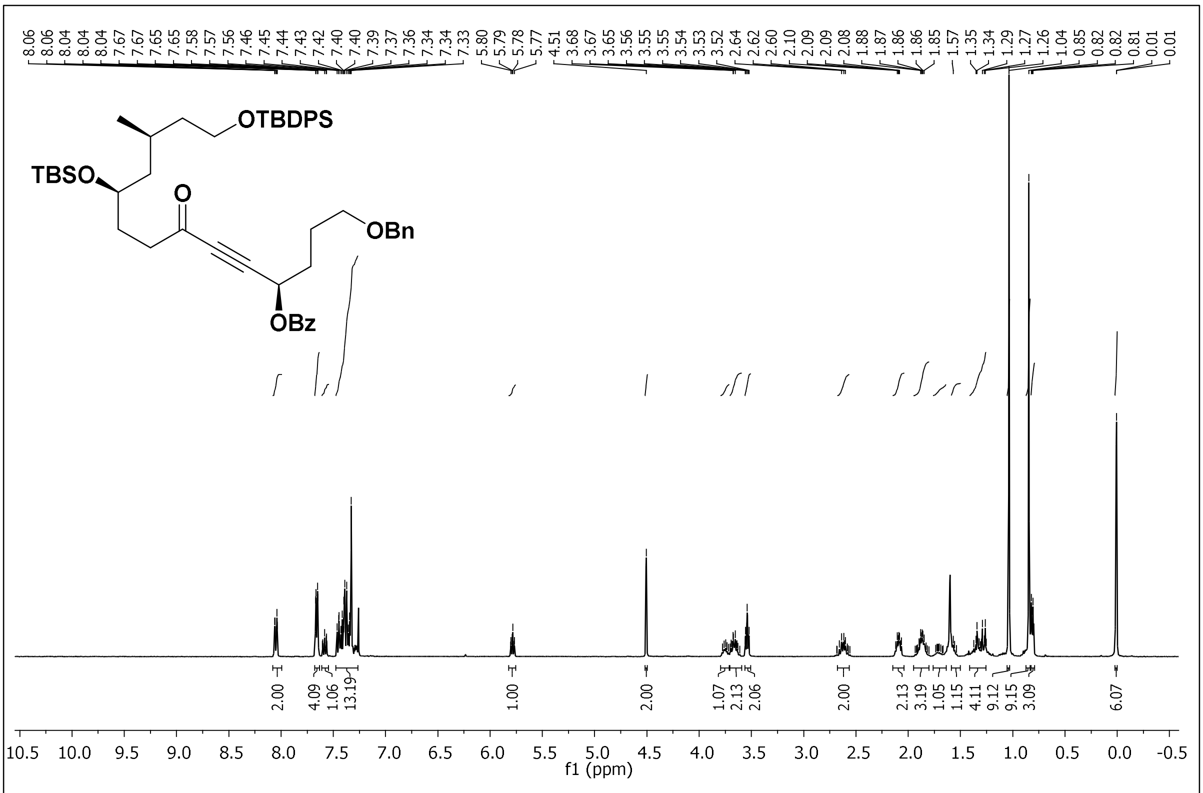
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 6



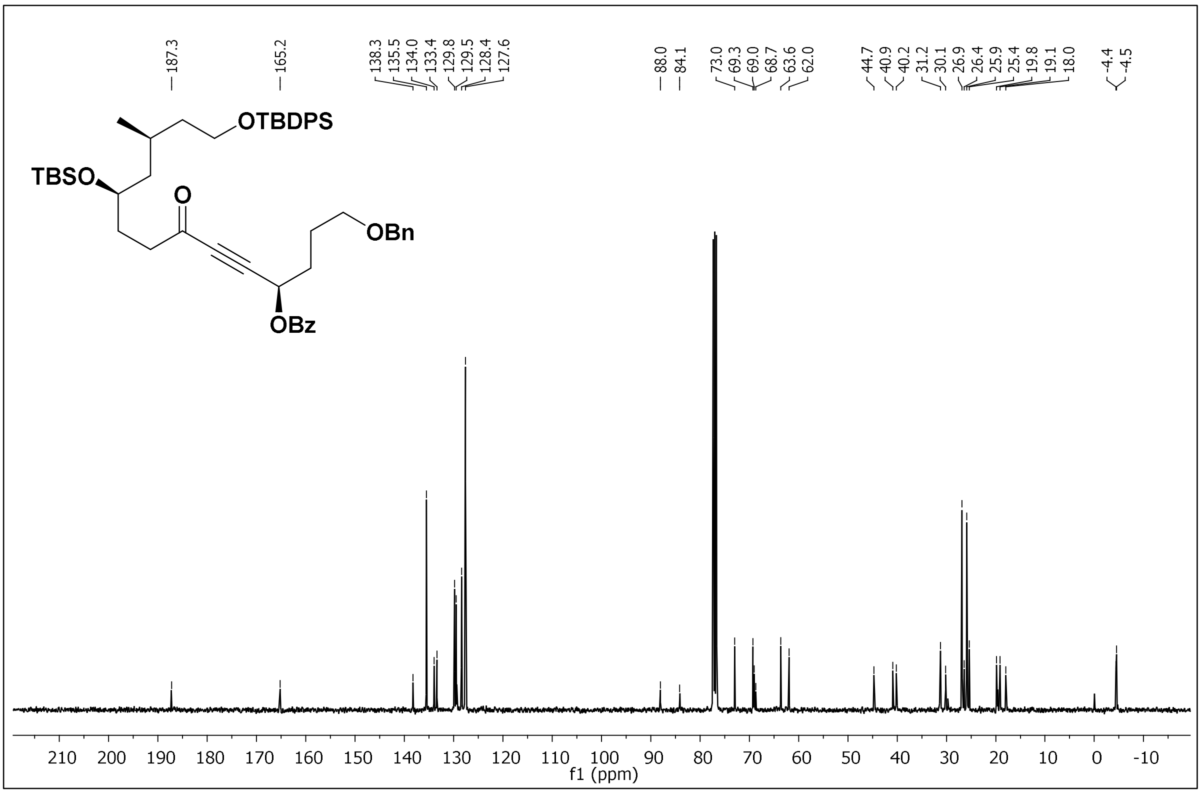
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 4a



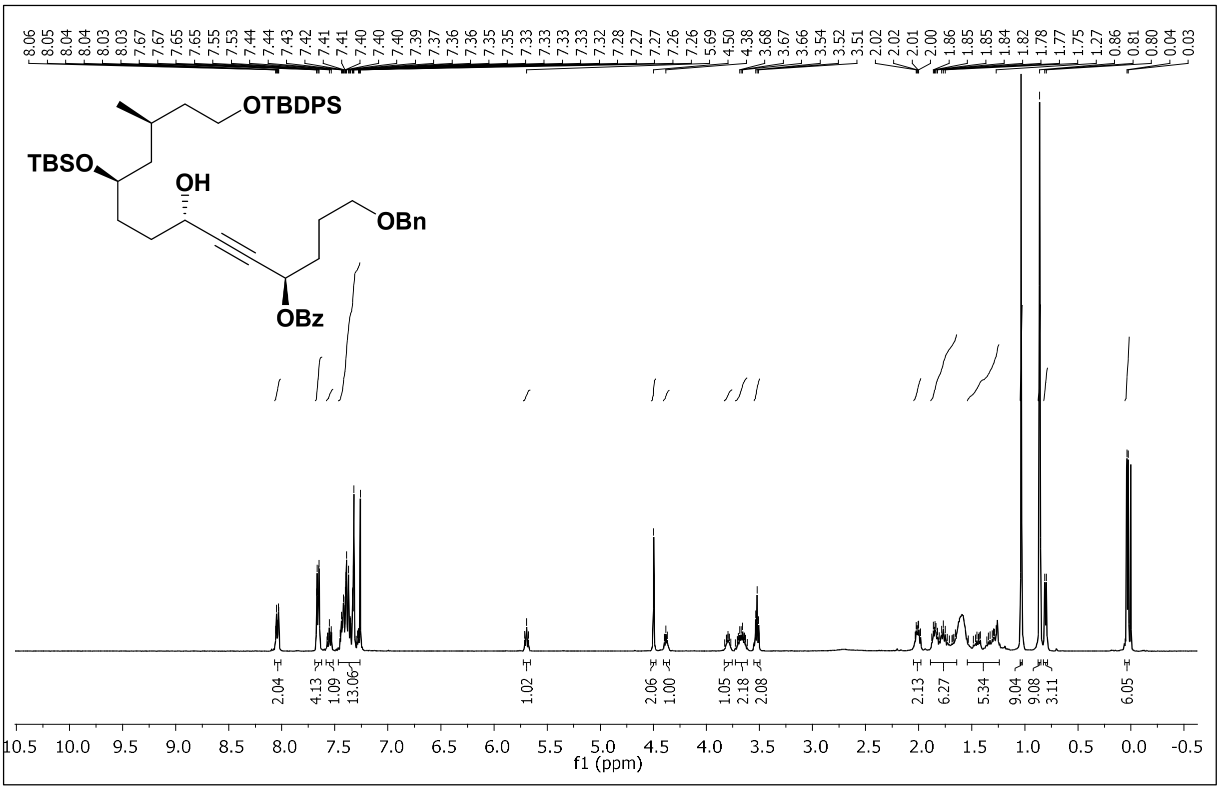
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 4a



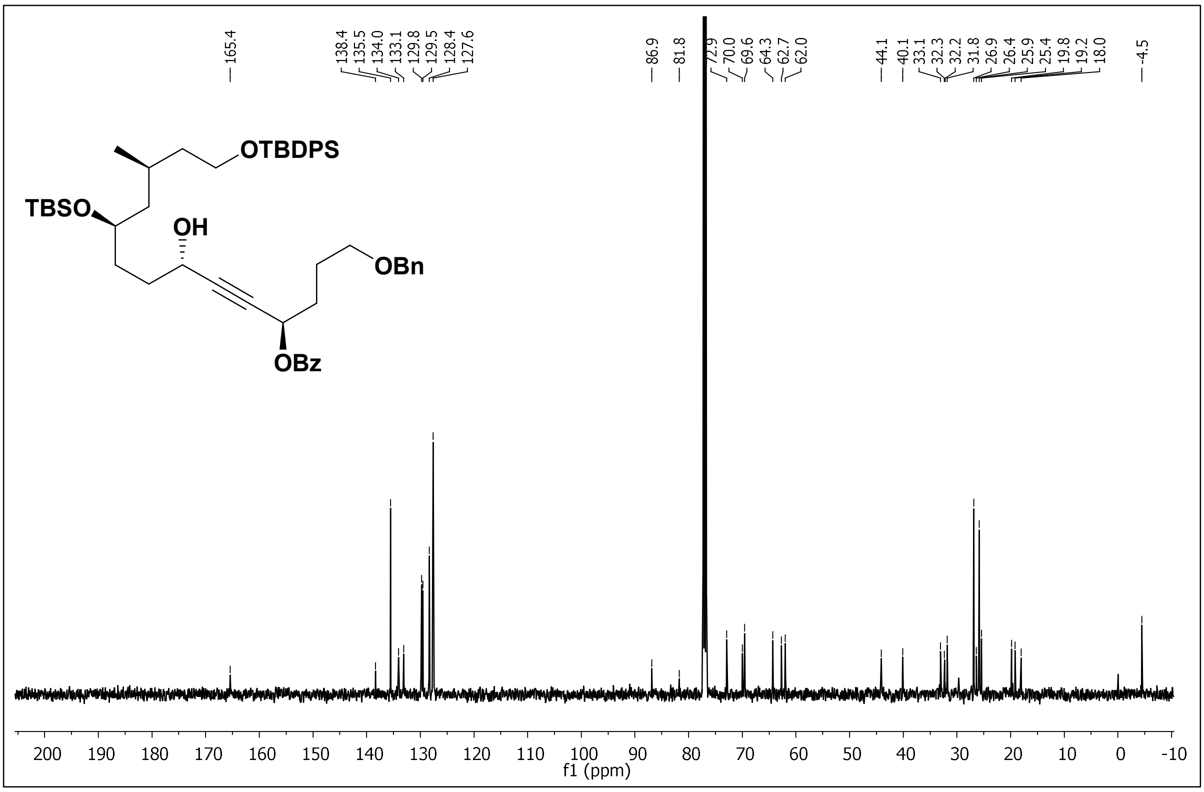
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 18



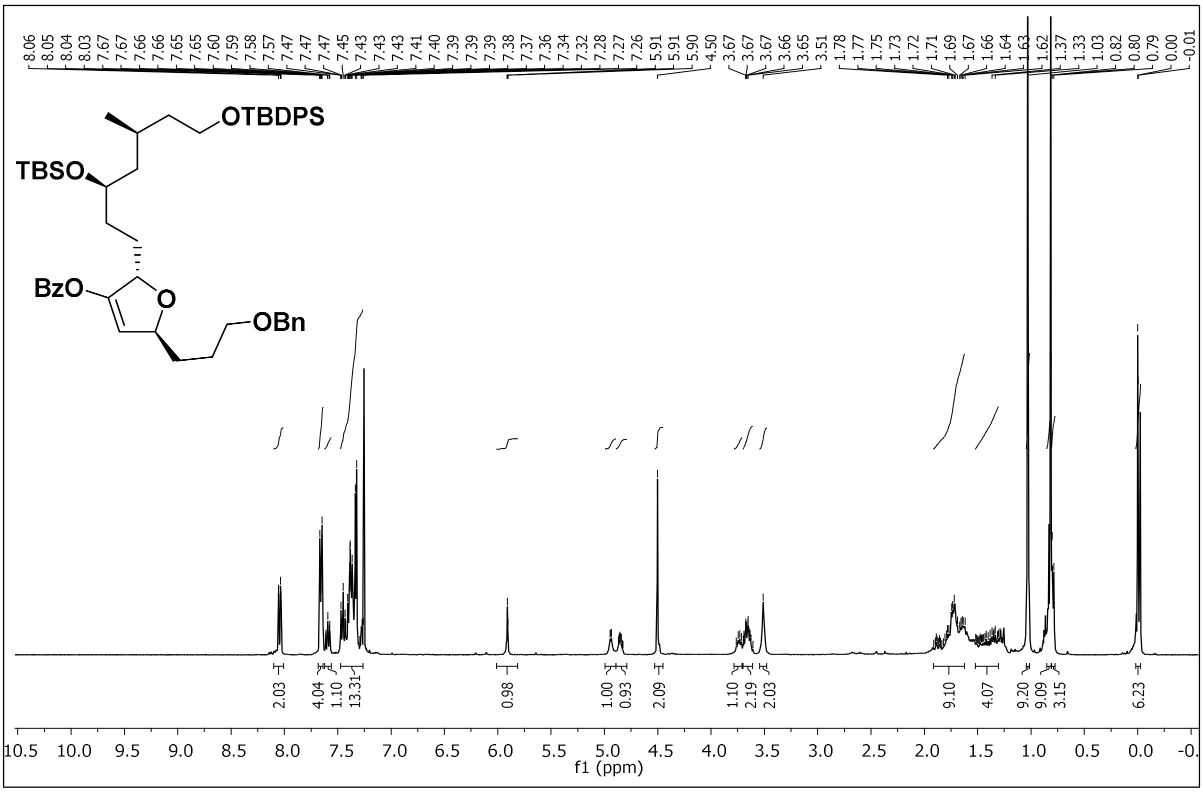
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 18



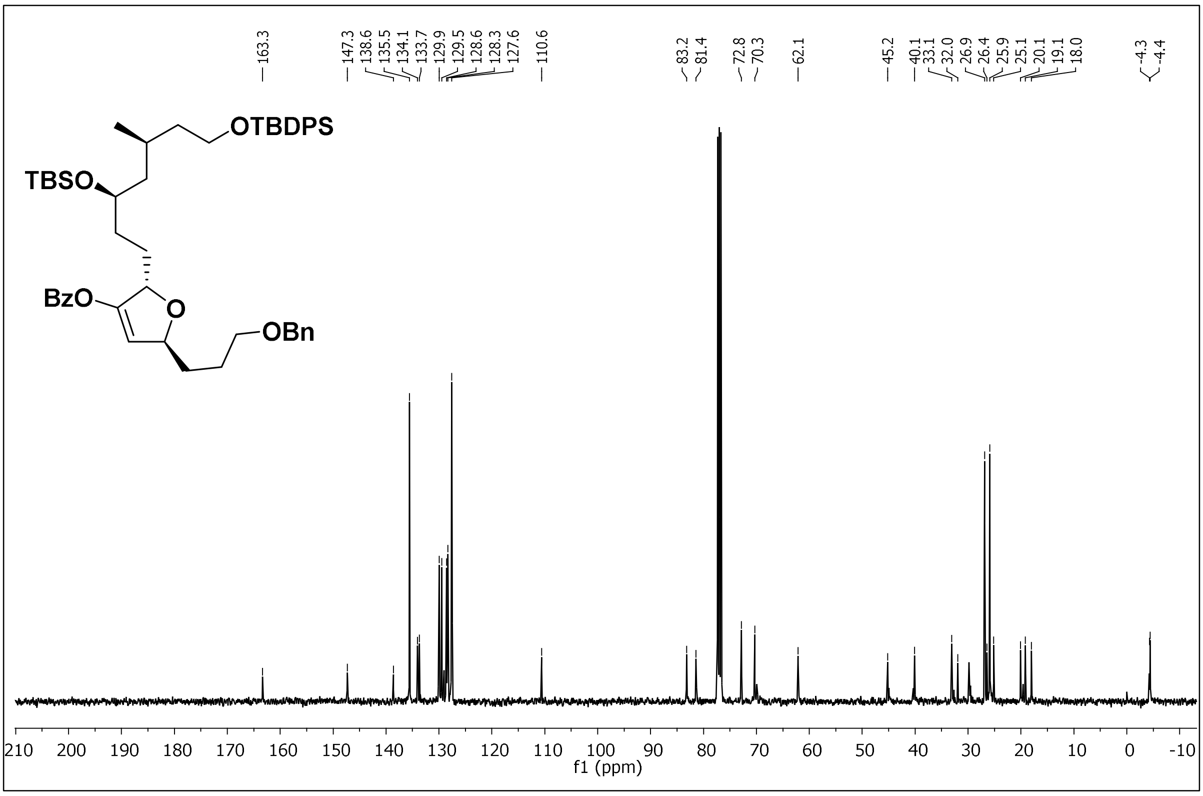
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 4



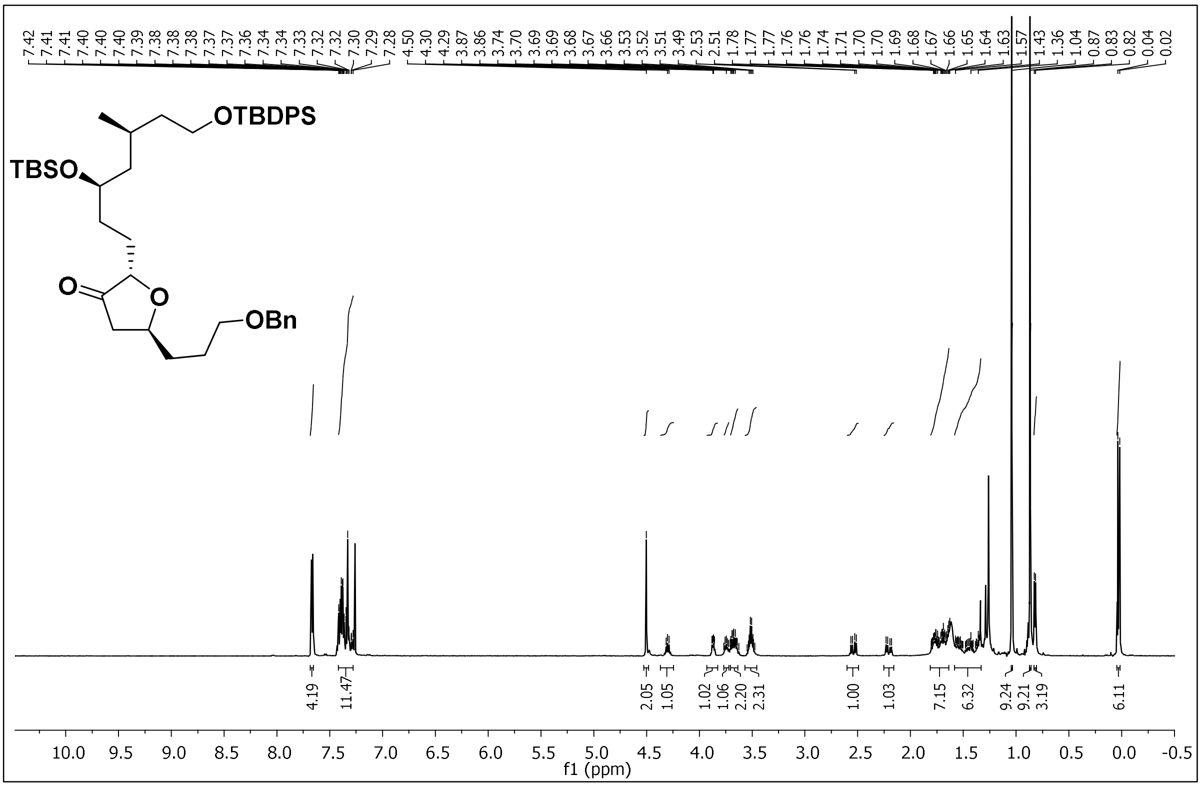
^{13}C NMR (126 MHz, CDCl$_3$) spectrum of compound 4



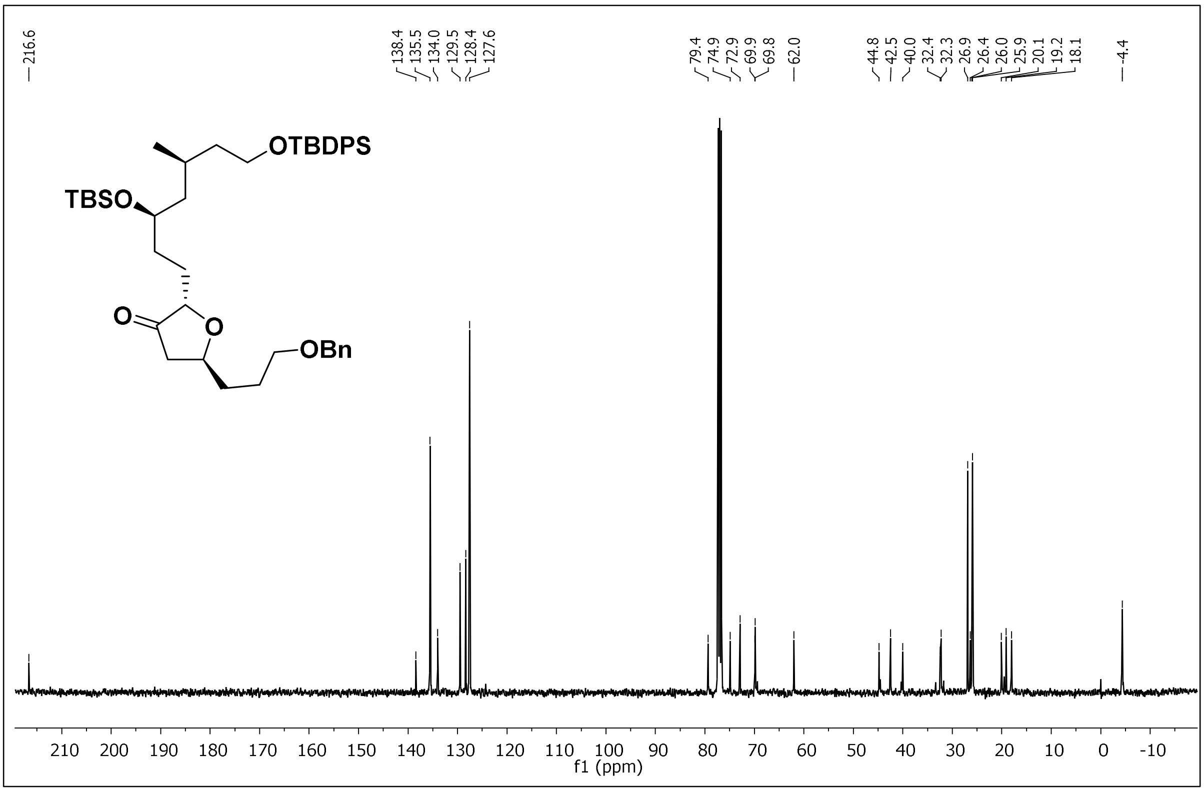
^{1}H NMR (400 MHz, CDCl$_3$) spectrum of compound 3



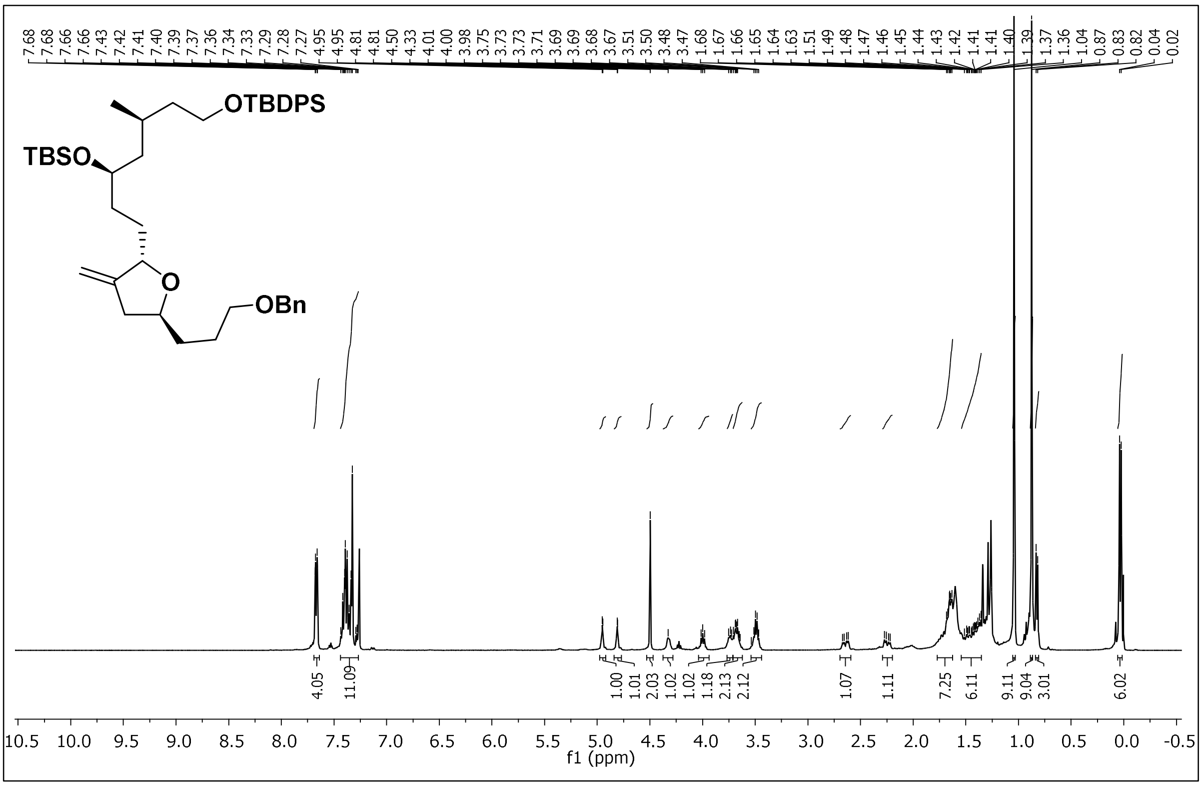
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 3



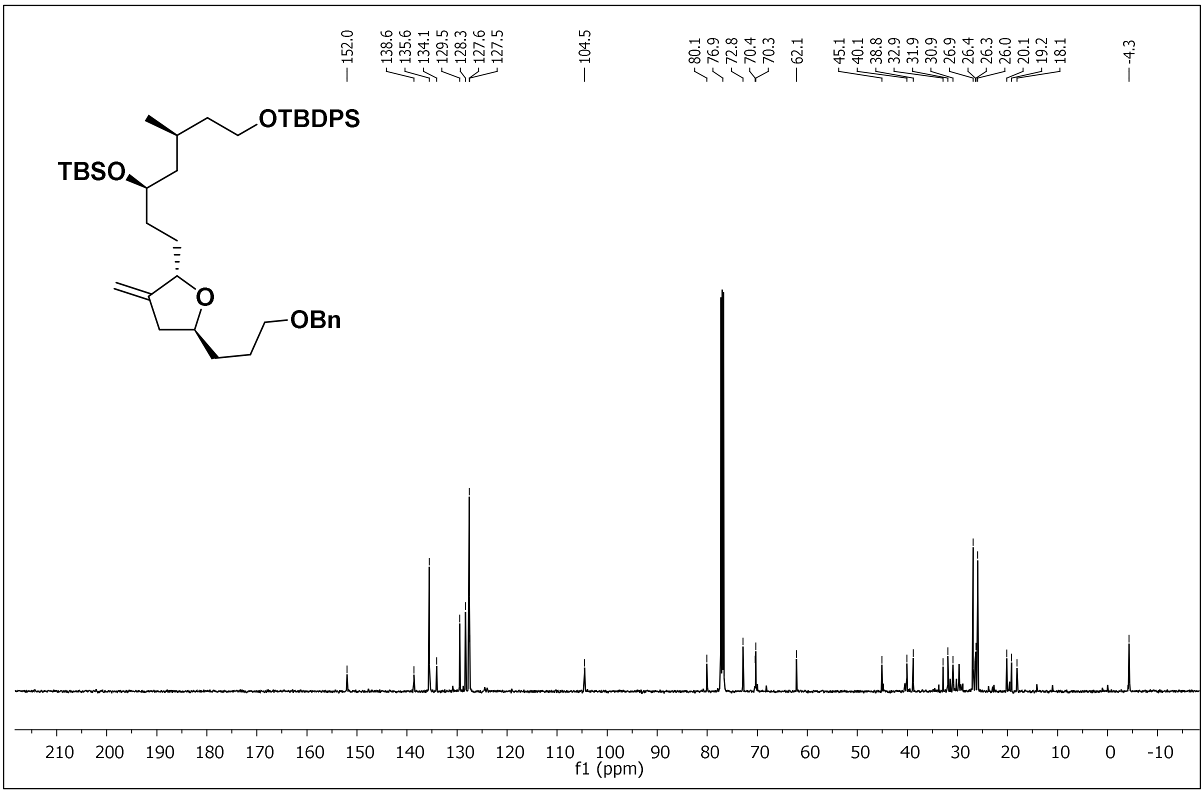
^{1}H NMR (500 MHz, CDCl$_3$) spectrum of compound 20



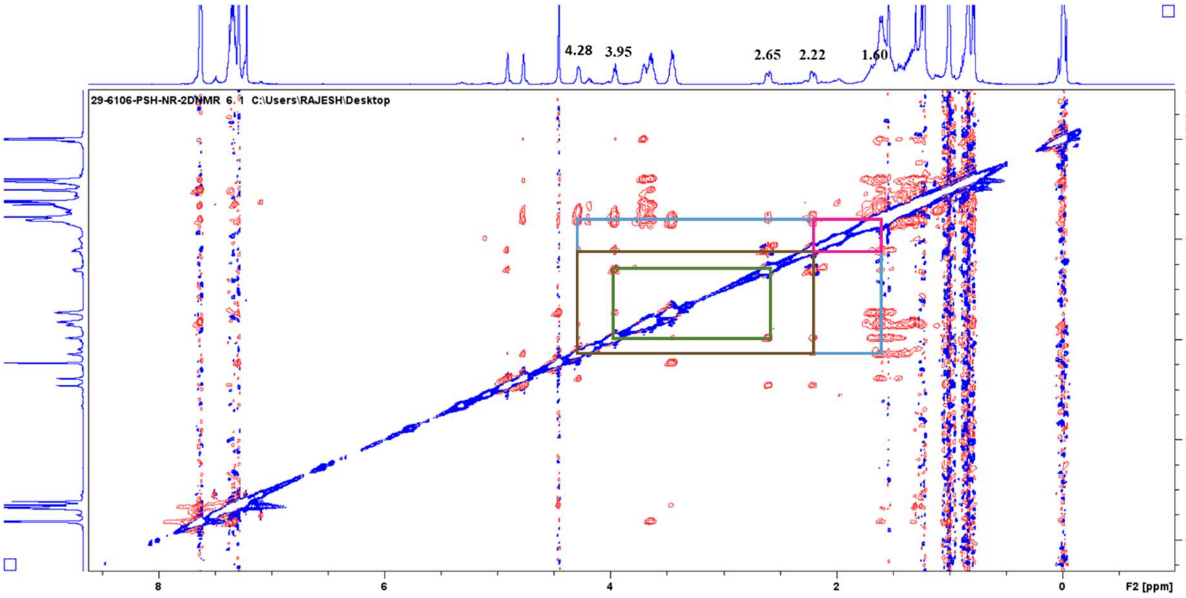
^{13}C NMR (101 MHz, CDCl$_3$) spectrum of compound 20



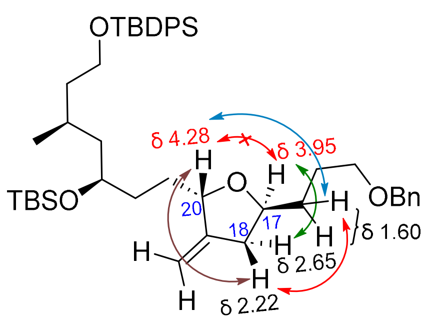
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 2



^{13}C NMR (126 MHz, $CDCl_3$) spectrum of compound 2



2D NOESY correlations in compound **2**



2D NOESY correlations in **2**