Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Stereochemical Aspects in tricho-Acorenol Biosynthesis

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Supplementary Information

GENERAL METHODS

Chemicals were purchased from Acros Organics (Geel, Belgium) or Sigma Aldrich Chemie GmbH (Steinheim, Germany) and used without further purification. All non-aqueous reactions were performed under an inert atmosphere (N_2) in flame-dried flasks. Solvents were purified by distillation and dried according to standard methods. Thin-layer chromatography was performed with 0.2 mm precoated plastic sheets Polygram® Sil G/UV254 (Machery-Nagel). Column chromatography was carried out using Merck silica gel 60 (70-200 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker DRX-400 (400 MHz) and AV III-400 (400 MHz) spectrometers, and were referenced against TMS (δ = 0.00 ppm) for ^{1}H-NMR and $CDCl_3$ (δ = 77.01 ppm) for ^{13}C-NMR. IR spectra were recorded with a Bruker Tensor 27 ATR (attenuated total reflectance). Specific rotations were measured using a Dr. Kernchen Propol Digital Automatic Polarimeter. GC/MS analyses of synthetic compounds were carried out with a HP6890 gas chromatograph connected to an HP5973 mass selective detector fitted with a BPX-5 fused silica capillary column (25 m, 0.25 mm i. d., 0.25 µm film). Instrumental parameters were (1) inlet pressure, 77.1 kPa, He 23.3 mL min^{-1}, (2) injection volume, 2 µL, (3) transfer line, 300 °C, and (4) electron energy 70 eV. The GC was programmed as follows: 5 min at 50 °C increasing at 10 °C min^{-1} to 320 °C, and operated in split mode (20:1, 60 s valve time). The carrier gas was He at 1 mL min^{-1}. Retention indices (*I*) were determined from a homologous series of *n*-alkanes (C_8-C_{38}). Highly polar compounds were derivatised in microreactions with *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (MSTFA) prior to GC/MS analysis.

CULTURE CONDITIONS

Trichoderma harzianum 714 was a kind gift of Gabriele König (Bonn). The fungus was cultivated for 10 days at 28 °C in liquid BM-ASW medium before three pieces of mycelium were transferred onto agar plates and incubation was continued for 2-3 days at 28 °C. BM-ASW: 20 g malt extract, 1000 mL artificial sea water (23.5 g NaCl, 10.6 g MgCl2 x 6H_2O, 3.92 g Na_2SO_4, 1.47 g $CaCl_2$ x 2H_2O, 0.66 g KCl, 0.19 g $NaHCO_3$, 0.10 g KBr, 0.04 g $SrCl_2$ x 6H_2O, 0.03 g H_3BO_3, 1 L H_2O).

COLLECTION OF VOLATILES

The volatile material from the agar plate cultures was collected by use of the closed-loop stripping analysis technique (CLSA). In a closed vessel an air stream was pumped over the agar plate and the emitted volatiles were trapped on charcoal filters (Chromtech GmbH, Idstein, Precision Char Coal Filter 5 mg). After 18-24 h the filter was eluted with ~50 µL dichloromethane, immediately analysed by GC/MS and the rest of the extract stored at -80 °C.[1]

GC/MS

GC/MS analyses of headspace extracts were carried out on an Agilent 7890A connected with an Agilent 5975C inert mass detector fitted with a HP5-MS fused silica capillary column (30 m, 0.25 mm i. d., 0.25 µm film, Agilent). GC conditions were as follows: inlet pressure 77.1 kPa, He 23.3 mL min^{-1}, injection volume 1.5 µL, transfer line 300 °C, electron energy 70 eV. The operation mode was splitless (60 s valve time) and the carrier gas was He at 1.2 mL min^{-1}. The GC was programmed as follows: 5 min at 50 °C increasing with 5 °C min^{-1} to 320 °C.

SYNTHESIS

((But-3-yn-1-yloxy)methyl)benzene (14). A suspension of NaH (1.64 g, 42.8 mmol, 3.0 eq.) in 35 mL of abs. THF was cooled to 0 °C. Homopropargylic alcohol **13** (1.0 g, 14.3 mmol, 1.0 eq.) was added dropwise and stirred for 10 min at 0 °C. Benzyl bromide (7.33 g, 42.9 mmol, 3.0 eq.) and abs. DMF (3.3 mL, 42.8 mmol, 3.0 eq.) were added slowly and stirring was continued for 10 min at 0 °C and 3 h at room temperature. The reaction mixture was quenched by the addition of sat. NH_4Cl solution and extracted three times with diethyl ether. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography with hexane/ethyl acetate (20:1) yielded **14** (2.1 g, 13.1 mmol, 92%) as colourless liquid; ν_{max}/cm^{-1} 3295 (m), 3064 (w), 2863 (m), 1496 (w), 1453 (m), 1362 (m), 1098 (s), 736 (s), 697 (s), 635 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.24 (m, 5H, Ph), 4.55 (s, 2H, CH_2), 3.59 (t, 2H, *J* = 6.9 Hz, CH_2), 2.49 (dt,

2H, J = 7.0, 2.8 Hz, CH_2), 1.99 (t, 1H, J = 2.6 Hz, CH) ppm; δ_C (100 MHz, $CDCl_3$) 138.0 (C_q), 128.4 (2x CH), 127.7 (3x CH), 81.3 (C_q), 72.9 (CH_2), 69.3 (C_q), 68.1 (CH_2), 19.8 (CH_2) ppm; *m/z* (%) 160 (2) $[M]^+$, 159 (15), 145 (3), 129 (7), 115 (4), 105 (21), 91 (100), 77 (14), 65 (21), 51 (12), 39 (17); *I* 1277. NMR spectroscopic data are in agreement with those reported previously.[2]

5-(Benzyloxy)pent-2-yn-1-ol (15). According to Ganem et al.,[3] compound **14** (2.1 g, 13.1 mmol, 1.0 eq.) was dissolved in 40 mL of abs. THF and cooled to -78 °C. A 1.6 m solution of *n*-BuLi (8.2 mL, 13.1 mmol, 1.0 eq.) in hexane was added and stirred for 2 h at -78 °C. In one portion *p*-formaldehyde (600 mg, 20.0 mmol, 1.5 eq.) was added and stirring was continued for 30 min at -78 °C and over night at room temperature. After addition of H_2O it was extracted thrice with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (2:1) yielded the alcohol **15** (1.66 g, 8.74 mmol, 67%) as colourless oil; ν_{max}/cm^{-1} 3386 (br), 3030 (w), 2865 (w), 1453 (w), 1095 (s), 1011 (s), 735 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.25 (m, 5H, Ph), 4.55 (s, 2H, CH_2), 4.22 (br s, 2H, CH_2), 3.58 (t, 2H, J = 7.0 Hz, CH_2), 2.53 (tt, 2H, J = 6.8, 2.2 Hz, CH_2), 1.97 (br s, 1H, OH); δ_C (100 MHz, $CDCl_3$) 137.9 (C_q), 128.4 (2x CH), 127.7 (3x CH), 83.0 (C_q), 79.5 (C_q), 72.9 (CH_2), 68.2 (CH_2), 51.2 (CH_2), 20.1 (CH_2); *m/z* (%) 190 (<1) $[M]^+$, 189 (1), 171 (15), 159 (42), 141 (3), 129 (13), 105 (7), 91 (100), 77 (9), 65 (20), 51 (7), 39 (10); *I* 1694. NMR spectroscopic data are in agreement with those reported previously, only the chemical shift of the aromatic quarternary carbon in ^{13}C-NMR was reported to be 128.2 instead of 137.9.[3] This is likely a typo (should be corrected to 138.2). The remaining difference of ca. 0.3 ppm occurs also for all other peaks, likely due to wrong referencing of the ^{13}C NMR spectrum.

(*Z*)-5-(Benzyloxy)-3-iodopent-2-en-1-ol (16a). According to Ganem et al.,[3] a solution of **15** (1.61 g, 8.47 mmol, 1.0 eq.) in 35 mL abs. THF was cooled to 0 °C. A 3.5 m solution of RedAl® (4.1 mL, 14.1 mmol, 1.7 eq.) in toluene was added dropwise. The reaction was stirred for 3 h at room temperature after which it was cooled to -78 °C. *N*-iodosuccinimide (3.4 g, 15.3 mmol, 1.8 eq.) in 15 mL of abs. THF was added slowly and stirring was continued for 30 min at -78 °C. After warming up to 0 °C it was quenched by the addition of a sat. Na/K-tartrate solution. It was extracted three times with diethyl ether, dried over $MgSO_4$ and concentrated under reduced pressure. Colum chromatography with hexane/ethyl acetate (2:1) yielded vinyl iodide **16a** (2.47 g, 7.76 mmol, 92%) as yellow oil; ν_{max}/cm^{-1} 3380 (br), 3029 (w), 2860 (w), 1453 (w), 1361 (w), 1205 (w), 1095 (s), 1022 (s), 735 (s), 696 (s); δ_H (400 MHz, $CDCl_3$) 7.33 – 7.26 (m, 5H, Ph), 5.93 (tt, 1H, J = 5.8, 1.3 Hz, CH), 4.52 (s, 2H, CH_2), 4.17 (d, 2H, J = 5.8 Hz, CH_2), 3.62 (t, 2H, J = 6.4 Hz, CH_2), 2.79 (dt, 2H, J = 6.4, 1.1 Hz, CH_2), 1.93 (br s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.0 (C_q), 135.8 (CH), 128.4 (2x CH), 127.7 (2x CH), 127.6 (CH), 105.0 (C_q), 73.0 (CH_2), 68.6 (CH_2), 67.2 (CH_2), 45.2 (CH_2) ppm; *m/z* (%) 318 (<1) $[M]^+$, 227 (4), 191 (1), 173 (6), 143 (5), 128 (3), 107 (8), 91 (100), 77 (5), 65 (12), 51 (3), 39 (4); *I* 2014. NMR spectroscopic data are in agreement with those reported previously, only the peak in the ^{13}C-NMR spectrum at 127.7 ppm is missing in the earlier report, and a consistent difference of ca. 0.4 ppm occurs for all ^{13}C-NMR peaks, likely due to wrong referencing of the spectrum.[3]

[2-^{2}H]-(*Z*)-5-(Benzyloxy)-3-iodopent-2-en-1-ol (16b). To a suspension of $LiAlD_4$ (350 mg, 8.3 mmol, 1.7 eq.) in 25 mL abs. THF was added **15** (950 mg, 5.0 mmol, 1.0 eq.). The mixture was stirred for 4 h at room temperature and then cooled to -78 °C. *N*-iodosuccinimide (4.0 g, 18.0 mmol, 3.6 eq.) in 20 mL of THF was added dropwise and stirring was continued for 30 min at -78 °C and over night at room temperature. It was quenched by the addition of sat. Na/K-tartrate solution and extracted three times with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (2:1) yielded vinyl iodide **16b** (1.04 g, 3.26 mmol, 65%) as yellow oil; ν_{max}/cm^{-1} 3385 (br), 3029 (w), 2860 (w), 1634 (w), 1360 (w), 1206 (w), 1091 (s), 1024 (s), 736 (s), 696 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.25 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 4.14 (s, 2H, CH_2), 3.61 (t, 2H, J = 6.4 Hz, CH_2), 2.77 (t, 2H, J = 6.3 HZ, CH_2), 2.26 (br s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.1 (C_q), 135.8 (C^2H, t, J = 23.9 Hz), 128.5 (2x CH), 127.9 (2x CH), 127.8 (CH), 104.9 (C_q), 73.1 (CH_2), 68.7 (CH_2), 67.2 (CH_2), 45.2 (CH_2) ppm; *m/z* (%) 219 (<1) $[M]^+$, 228 (7), 210 (3), 192 (12), 174 (10), 144 (5), 128 (3), 107 (18), 91 (100), 77 (15), 65 (31), 51 (14), 39 (16); *I* 2013.

General Procedure for the Preparation of 17a-d. According to Ganem et al.,[2] CuI (5.2 eq.) was suspended in abs. THF to a final concentration of 0.78 M. It was cooled to 0 °C and a solution of MeLi (1.6 M, 10.0 eq.) in Et_2O was added (compounds **17a**/**b**). For compounds **17c**/**d** [$^2H_3$]MeLi (0.5 M, 10.0 eq.) was used. By use of a syringe pump, vinyl iodides **16a-d** (1.0 eq.) in abs. THF (0.5 M) were added. The reaction mixture was stirred for 6 h at 0 °C after which it was quenched by pouring into an ice-cold sat. NH_4Cl solution. It was extracted three times with diethyl ether, dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (2:1) yielded **17a-d** as colourless oils.

(*E*)-5-(Benzyloxy)-3-methylpent-2-en-1-ol (17a). Yield (1.3 g, 6.3 mmol, 83%); ν_{max}/cm^{-1} 3364 (br), 3063 (w), 2860 (w), 1495 (w), 1362 (w), 1093 (s), 996 (s), 737 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.25 (m, 5H, Ph), 5.46 (tq, 1H, J = 6.9 Hz, 1.3 Hz, CH), 4.51 (s, 2H, CH_2), 4.13 (d, 2H, J = 6.9 Hz, CH_2), 3.56 (t, 2H, J = 6.9 Hz, CH_2), 2.34 (t, 2H, J = 6.8 Hz, CH_2), 1.68 (s, 3H, CH_3), 1.60 (br s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.3 (C_q), 136.5 (C_q), 128.3 (2x CH), 127.6 (2x CH), 127.5 (CH), 125.1 (CH), 72.8 (CH_2), 68.6 (CH_2), 59.2 (CH_2), 39.4 (CH_2), 16.4 (CH_2) ppm; *m/z* (%) 206 (<1) $[M]^+$,

187 (3), 173 (2), 161 (2), 143 (9), 129 (4), 120 (6), 115 (8), 107 (18), 97 (13), 91 (100), 82 (16), 77 (15), 65 (27), 57 (7), 51 (7), 41 (19); *I* 1758. NMR spectroscopic data are in agreement with those reported previously.[3]

[2-^{2}H]-(*E*)-5-(Benzlyoxy)-3-methylpent-2-en-1-ol (17b). Yield (534 mg, 2.58 mmol, 82%); ν_{max}/cm^{-1} 3377 (br), 3063 (w), 2859 (w), 1496 (w), 1362 (w), 1095 (s), 988 (s), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.27 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 4.14 (s, 2H, CH_2), 3.57 (t, 2H, *J* = 6.9 Hz, CH_2), 2.34 (t, 2H, *J* = 6.9 Hz, CH_2), 1.69 (s, 3H, CH_3), 1.49 (s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.3 (C_q), 136.5 (C_q), 128.3 (2x CH), 127.6 (2x CH), 127.5 (CH), 124.7 (C^2H, t, *J* = 23.8 Hz), 72.9 (CH_2), 68.6 (CH_2), 59.1 (CH_2), 39.4 (CH_2), 16.4 (CH_3) ppm; *m/z* (%) 207 (<1) $[M]^+$, 188 (3), 174 (1), 144 (4), 130 (3), 116 (1), 105 (1), 98 (4), 91 (100), 77 (17), 65 (14), 51 (18), 39 (15); *I* 1753.

[6,6,6-$^2H_3$]-(*E*)-5-(Benzyloxy)-3-methylpent-2-en-1-ol (17c). Yield (470 mg, 2.25 mmol, 55%); ν_{max}/cm^{-1} 3383 (br), 3063 (w), 2859 (w), 1453 (w), 1361 (w), 1092 (s), 999 (s), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.25 (m, 5H, Ph), 5.46 (t, 1H, *J* = 6.9 Hz, CH), 4.51 (s, 2H, CH_2), 4.13 (d, 2H, *J* = 6.8 Hz, CH_2), 3.56 (t, 2H, *J* = 6.9 Hz, CH_2), 2.34(t, 2H, *J* = 6.8 Hz, CH_2), 1.60 (br s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.3 (C_q), 136.3 (C_q), 128.4 (2x CH), 127.6 (2x CH), 127.5 (CH), 125.2 (CH), 77.8 (CH_2), 68.6 (CH_2), 59.1 (CH_2), 39.3 (CH_2), 15.6 (C^2H_3, *J* = 19.5 Hz) ppm; *m/z* (%) 209 (<1) $[M]^+$, 190 (2), 173 (1), 164 (1), 120 (2), 105 (6), 100 (4), 91 (100), 85 (4), 77 (15), 65 (23), 51 (9), 41 (9); *I* 1754.

[2,6,6,6-$^2H_4$]-(*E*)-5-(Benzyloxy)-3-methylpent-2-en-1-ol (17d). Yield (892 mg, 4.25 mmol, 85%); ν_{max}/cm^{-1} 3383 (br), 3063 (w), 2859 (w), 1453 (w), 1361 (w), 1092 (s), 999 (s), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.26 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 4.12 (s, 2H, CH_2), 3.56 (t, 2H, *J* = 6.8 Hz, CH_2), 2.33 (t, 2H, *J* = 6.8 Hz, CH_2), 1.74 (s, 1H, OH) ppm; δ_C (100 MHz, $CDCl_3$) 138.3 (C_q), 136.3 (C_q), 128.3 (2x CH), 127.6 (2x CH), 127.6 (CH), 124.8 (C^2H, t, *J* = 23.3 Hz), 72.8 (CH_2), 68.5 (CH_2), 59.1 (CH_2), 39.3 (CH_2), 15.6 (C^2H_3, *J* = 19.5 Hz) ppm; *m/z* (%) 210 (<1) $[M]^+$, 191 (3), 174 (2), 164 (2), 144 (4), 119 (7), 107 (17), 101 (9), 91 (100), 77 (22), 65 (37), 51 (12), 39 (12); *I* 1750.

General Procedure for the Preparation of 18a-d. Molecular sieve (1.0 g/10 mmol starting material) was placed in a flask and abs. CH_2Cl_2 (0.2 M referred to **17**) were added. It was cooled to -10 °C and subsequently (-)-diisopropyl-D-tartrate (0.12 eq.), Ti(O^iPr)$_4$ (0.1 eq.) and cumene hydroperoxide (1.0 eq.) were added. It was stirred for further 10 min at -10 °C. The reaction mixture was cooled to -23 °C and compound **17a-d** (1.0 eq.) in abs. CH_2Cl_2 (2 M) were added dropwise. After stirring at this temperature over night, 1 – 2 mL of H_2O were added and stirring was continued for 30 min. The mixture was filtered over Celite®, dried and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (1:1) yielded epoxides **18a-d** as colourless oils.

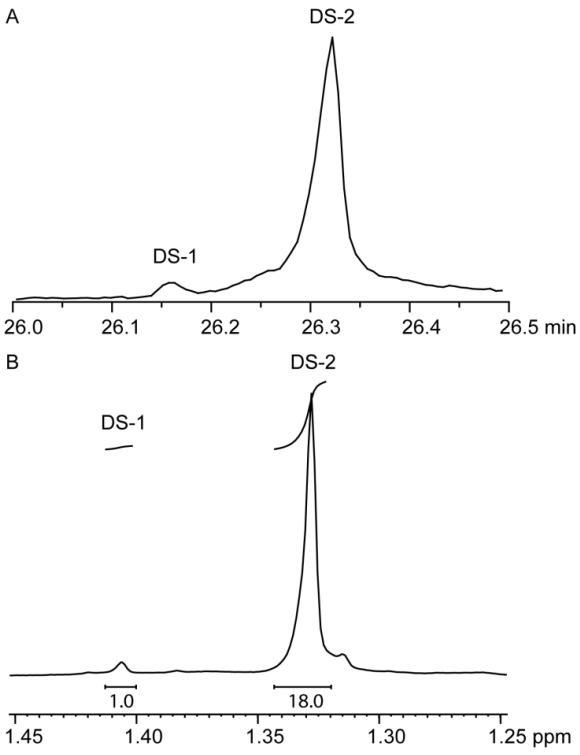

Figure 1 Results of the Mosher analysis of **18a**. Analysis by (a) gas chromatography; (b) ^{1}H-NMR spectroscopy.

Determination of the enantiomeric excess of the epoxidation step. For the determination of the enantiomeric excess of the epoxidation reaction a Mosher analysis was carried out. Following the reported procedure[4] the derivatisation was performed with compound **18a**. The product of the reaction was analysed by NMR and GC/MS (Figure 1).

The peaks in GC corresponding to the diastereomers (DS-1 and DS-2) of the product of the derivatisation reaction (Figure 1A) as well as the peaks corresponding to the methyl group of **18a** in 1H-NMR (Figure 1B) were integrated and compared. The enantiomeric excess of the epoxidation was calculated to be ~95% by both analytical methods which is in good agreement with a report on a reaction performed with the same starting material but targettinge the opposite enantiomer that yielded 94% *ee*.[5]

((2*R*,3*R*)-3-(2-(Benzyloxy)ethyl)-3-methyloxiran-2-yl)methanol (18a). Yield (1.66 g, 7.48 mmol, 84%); $a_D^{22.6}$ = +0.6 (*c* = 1.65 in CH_2Cl_2); ν_{max}/cm^{-1} 3418 (br), 3063 (w), 2864 (w), 1453 (w), 1364 (w), 1204 (w), 1096 (s), 1027 (s), 863 (w), 738 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.37 – 7.28 (m, 5H, Ph), 4.51 (d, 1H, *J* = 11.9 Hz, CH_2), 4.47 (d, 1H, *J* = 11.9 Hz, CH_2), 3.82 – 3.79 (m, 1H, CH_2), 3.68 – 3.63 (m, 1H, CH_2), 3.61 – 3.54 (m, 2H, CH_2), 3.04 (dd, 1H, *J* = 6.6, 4.3 Hz, CH), 2.28 (br s, 1H, OH), 1.96 (dt, *J* = 14.3, 5.9 Hz, 1H, CH_2), 1.85 – 1.76 (m, 1H, CH_2), 1.31 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 138.1 (C_q), 128.4 (2x CH), 127.7 (CH), 127.6 (2x CH), 73.1 (CH_2), 66.4 (CH_2), 62.9 (CH), 61.2 (CH_2), 59.7 (C_q), 38.3 (CH_2), 17.2 (CH_3) ppm; *m*/*z* (%, MSTFA) 294 (<1) $[M]^+$, 195 (4), 173 (28), 160 (9), 143 (16), 129 (10), 113 (15), 103 (18), 91 (100), 85 (15), 73 (55), 65 (26), 59 (15), 43 (18); *I* (MSTFA) 1909. NMR spectroscopic data are in agreement with those reported previously.[5]

[2-^{2}H]-((2*R*,3*R*)-3-(2-(Benzyloxy)ethyl)-3-methyloxiran-2-yl)methanol (18b). Yield (1.03 g, 4.62 mmol, 88%); $a_D^{24.7}$ = –0.4 (*c* = 1.05 in CH_2Cl_2); ν_{max}/cm^{-1} 3408 (br), 3063 (w), 2866 (w), 1495 (w), 1364 (w), 1203 (w), 1096 (s), 1026 (s), 738 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.37 – 7.26 (m, 5H, Ph), 4.51 (d, 1H, *J* = 11.9 Hz, CH_2), 4.47 (d, 1H, *J* = 11.9 Hz, CH_2), 3.82 – 3.79 (m, 1H, CH_2), 3.67 – 3.64 (m, 1H, CH_2), 3.59 – 3.54 (m, 2H, CH_2), 2.13 (br s, 1H, OH), 1.96 (dt, *J* = 14.3, 5.9 Hz, 1H, CH_2), 1.83 – 1.76 (m, 1H, CH_2), 1.31 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 138.1 (C_q), 128.4 (2x CH), 127.7 (CH), 127.6 (2x CH), 73.0 (CH_2), 66.4 (CH_2), 62.4 (C^2H, t, *J* = 24.8 Hz), 61.1 (CH_2), 59.6 (C_q), 38.2 (CH_2), 17.2 (CH_3) ppm; *m*/*z* (%, MSTFA) 295 (<1) $[M]^+$, 195 (3), 174 (19), 161 (5), 144 (8), 130 (5), 114 (7), 103 (10), 91 (100), 73 (38), 65 (17), 59 (6), 43 (10); *I* (MSTFA) 1908.

[6,6,6-^{2}H$_3$]-((2*R*,3*R*)-3-(2-(Benzyloxy)ethyl)-3-methyloxiran-2-yl)methanol (18c). Yield (1.46 g, 6.49 mmol, 76%); $a_D^{24.4}$ = +1.2 (*c* = 5.90 in CH_2Cl_2); ν_{max}/cm^{-1} 3419 (br), 3031 (w), 2922 (w), 1497 (w), 1364 (w), 1098 (s), 1027 (s), 798 (w), 735 (s), 698 (s); δ_H (400 MHz, $CDCl_3$) 7.36 – 7.26 (m, 5H, Ph), 4.51 (d, 1H, *J* = 11.9 Hz, CH_2), 4.47 (d, 1H, *J* = 11.9 Hz, CH_2), 3.81 – 3.79 (m, 1H, CH_2), 3.67 – 3.61 (m, 1H, CH_2), 3.59 – 3.52 (m, 2H, CH_2), 3.03 (dd, 1H, *J* = 6.4, 4.4 Hz, CH), 2.3 (br s, 1H, OH), 1.96 (dt, *J* = 14.3, 5.9 Hz, 1H, CH_2), 1.83 – 1.76 (m, 1H, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 138.1 (C_q), 128.4 (2x CH), 127.6 (CH), 127.5 (2x CH), 73.0 (CH_2), 66.4 (CH_2), 62.8 (CH), 61.2 (CH_2), 59.5 (C_q), 38.2 (CH_2), 16.4 (C^2H_3, *J* = 19.5 Hz) ppm; *m*/*z* (%, MSTFA) 297 (<1) $[M]^+$, 195 (4), 176 (27), 163 (10), 146 (13), 129 (10), 116 (17), 103 (21), 91 (100), 73 (61), 65 (23), 59 (12), 46 (14); *I* (MSTFA) 1905.

[2,6,6,6-^{2}H$_4$]-((2*R*,3*R*)-3-(2-(Benzyloxy)ethyl)-3-methyloxiran-2-yl)methanol (18d). Yield (1.3 g, 5.8 mmol, 86%); $a_D^{24.6}$ = +0.6 (*c* = 0.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3419 (br), 3031 (w), 2922 (w), 1497 (w), 1364 (w), 1098 (s), 1027 (s), 798 (w), 735 (s), 698 (s); δ_H (400 MHz, $CDCl_3$) 7.37 – 7.26 (m, 5H, Ph), 4.51 (d, 1H, *J* = 11.9 Hz, CH_2), 4.47 (d, 1H, *J* = 11.9 Hz, CH_2), 3.81 (dd, 1H, *J* = 12.3, 4.8 Hz, CH_2), 3.66 (d, 1H, *J* = 12.1 Hz, CH_2), 3.59 – 3.54 (m, 2H, CH_2), 2.01 (br s, 1H, OH), 1.96 (dt, 1H, *J* = 14.2, 5.9 Hz, CH_2), 1.83 – 1.76 (m, 1H, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 138.1 (C_q), 128.4 (2x CH), 127.7 (CH), 127.6 (2x CH), 73.0 (CH_2), 66.4 (CH_2), 62.4 (C^2H, t, *J* = 26.1 Hz), 61.1 (CH_2), 59.5 (C_q), 38.2 (CH_2), 16.4 (C^2H_3, *J* = 19.3 Hz) ppm; *m*/*z* (%, MSTFA) 294 (<1) $[M]^+$, 195 (4), 177 (21), 163 (6), 147 (8), 130 (6), 117 (12), 103 (15), 91 (100), 73 (49), 59 (8), 46 (12); *I* (MSTFA) 1904.

General Procedure for the Preparation of 19a-d. A suspension of $LiAlD_4$ (1.0 eq.) in 40 mL abs. Et_2O (0.2 M) was cooled to 0 °C (Compounds **19a**/**c**). For the preparation of compounds **19b**/**d** $LiAlH_4$ was used. The epoxides **18a-d** (1.0 eq.) in 10 mL of abs. THF (1 M) were added dropwise and the reaction stirred for 3 h at 0 °C. It was quenched by the addition of H_2O and extracted three times with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (1:1) yielded diols **19a-d** as colourless oils.

[2-^{2}H]-(2*S*,3*R*)-5-(Benzyloxy)-3-methylpentane-1,3-diol (19a). Yield (1.52 g, 6.76 mmol, 90%); $a_D^{22.6}$ = –2.1 (*c* = 1.05 in CH_2Cl_2); ν_{max}/cm^{-1} 3362 (br), 3064 (w), 2872 (w), 1454 (w), 1366 (w), 1091 (s), 4126 (s), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.38 – 7.26 (m, 5H, Ph), 4.54 (d, 1H, *J* = 12.0 Hz, CH_2), 4.51 (d, 1H, *J* = 12.1 Hz, CH_2), 3.92 – 3.80 (m, 2H, CH_2), 3.79 – 3.71 (m, 2H, CH_2), 3.50 (br s, 2H, 2x OH), 2.01 (ddd, 1H, *J* = 14.5, 11.9, 7.6 Hz, CH_2), 1.81 (br m, 1H, CH), 1.70 (ddd, 1H, *J* = 14.5, 5.7, 4.2 Hz, CH_2), 1.26 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 137.5 (C_q), 128.5 (2x CH), 127.9 (CH), 127.7 (2x CH), 73.8 (C_q), 73.5 (CH_2), 67.2 (CH_2), 59.5 (CH_2), 42.0 (C^2HH, t, 19.1 Hz), 40.2 (CH_2), 26.5 (CH_3) ppm; *m*/*z*

(%, MSTFA) 369 (<1) $[M]^+$, 251 (15), 234 (37), 218 (2), 188 (3), 179 (2), 160 (10), 147 (24), 133 (7), 117 (5), 103 (34), 91 (100), 73 (54), 65 (11), 45 (9); *I* (MSTFA) 1966.

[2-^{2}H]-(2*R*,3*R*)-5-(Benzyloxy)-3-methylpentane-1,3-diol (19b). Yield (890 mg, 3.96 mmol, 86%); $a_D^{24.6}$ = –4.5 (*c* = 1.00 in CH_2Cl_2); ν_{max}/cm^{-1} 3362 (br), 3064 (w), 2872 (w), 1454 (w), 1366 (w), 1091 (s), 4126 (s), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.38 – 7.28 (m, 5H, Ph), 4.54 (d, 1H, *J* = 12.2 Hz, CH_2), 4.51 (d, 1H, *J* = 12.2 Hz, CH_2), 3.91 (dd, 1H, *J* = 11.4, 3.6 Hz, CH_2), 3.82 (dd, 1H, *J* = 11.2, 6.3 Hz, CH_2), 3.78 – 3.70 (m, 2H, CH_2), 3.49 (br s, 2H, 2x OH), 2.01 (ddd, 1H, *J* = 14.7, 11.7, 8.3 Hz, CH_2), 1.71 (ddd, 1H, *J* = 14.7, 5.8, 4.4 Hz, CH_2), 1.63 (ddd, 1H, *J* = 8.1, 5.7, 1.8 Hz, CH_2), 1.27 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 137.5 (C_q), 128.5 (2x CH), 127.9 (CH), 127.8 (2x CH), 73.8 (C_q), 73.5 (CH_2), 67.3 (CH_2), 59.5 (CH_2), 41.9 (C^2HH, t, *J* = 19.8 Hz), 40.2 (CH_2), 26.5 (CH_3) ppm; *m*/*z* (%, MSTFA) 369 (<1) $[M]^+$, 251 (24), 234 (48), 218 (3), 188 (6), 179 (4), 171 (2), 160 (16), 147 (28), 133 (9), 117 (7), 103 (48), 91 (100), 73 (61), 65 (14), 45 (14); *I* (BPX-5, MSTFA) 1966.

[2,6,6,6-^{2}H$_4$]-(2*S*,3*R*)-5-(Benzyloxy)-3-methylpentane-1,3-diol (19c). Yield (1.17 g, 5.12 mmol, 79%); $a_D^{24.3}$ = –2.4 (*c* = 3.40 in CH_2Cl_2); ν_{max}/cm^{-1} 3374 (br), 1365 (w), 1093 (s), 1026 (s), 737 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.37 – 7.28 (m, 5H, Ph), 4.53 (d, 1H, *J* = 12.2 Hz, CH_2), 4.50 (d, 1H, *J* = 12.2 Hz, CH_2), 3.92 – 3.78 (m, 2H, CH_2), 3.77 – 3.69 (m, 2H, CH_2), 3.55 (s, 2H, 2x OH), 2.04 – 1.95 (m, 1H, C^2HH), 1.79 (br m, 1H, CH_2), 1.70 (ddd, 1H, *J* = 14.7, 5.8, 4.5 Hz, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 137.5 (C_q), 128.5 (2x CH), 127.9 (CH), 127.7 (2x CH), 73.6 (C_q), 73.5 (CH_2), 67.2 (CH_2), 59.5 (CH_2), 41.9 (C^2HH, t, *J* = 18.3 Hz), 40.2 (CH_2) ppm; *m*/*z* (%, MSTFA) 372 (<1) $[M]^+$, 254 (42), 237 (72), 218 (6), 191 (15), 179 (11), 163 (38), 147 (68), 133 (27), 119 (18), 103 (78), 91 (100), 73 (85), 65 (25), 59 (13), 46 (13); *I* (MSTFA) 1960.

[2,6,6,6-^{2}H$_4$]-(2*R*,3*R*)-5-(Benzyloxy)-3-methylpentane-1,3-diol (19d). Yield (1.1 g, 4.8 mmol, 83%); $a_D^{24.6}$ = –3.5 (*c* = 1.15 in CH_2Cl_2); ν_{max}/cm^{-1} 3374 (br), 1365 (w), 1093 (s), 1026 (s), 737 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 7.37 – 7.29 (m, 5H, Ph), 4.54 (d, 1H, *J* = 12.1 Hz, CH_2), 4.50 (d, 1H, *J* = 12.1 Hz, CH_2), 3.90 (dd, 1H, *J* = 11.2, 4.0 Hz, CH_2), 3.82 (dd, 1H, *J* = 11.5, 6.8 Hz, CH_2), 3.77 – 3.70 (m, 2H, CH_2), 3.39 (s, 2H, 2x OH), 1.99 (ddd, 1H, *J* = 14.8, 12.3, 7.4 Hz, CH_2), 1.70 (ddd, 1H, *J* = 14.7, 5.8, 4.6 Hz, CH_2), 1.62 (ddd, 1H, *J* = 8.0, 3.7, 1.8, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 137.5 (C_q), 128.5 (2x CH), 127.9 (CH), 127.7 (2x CH), 73.6 (C_q), 73.5 (CH_2), 67.2 (CH_2), 59.5 (CH_2), 41.9 (C^2HH, t, *J* = 19.4 Hz), 40.2 (CH_2), 25.8 (C^2H_3, *J* = 17.2 Hz) ppm; *m*/*z* (%, MSTFA) 372 (<1) $[M]^+$, 254 (10), 237 (27), 218 (1), 191 (3), 179 (2), 163 (10), 147 (29), 133 (7), 119 (5), 103 (38), 91 (100), 73 (55), 59 (4); *I* (BPX-5, MSTFA) 1961.

Spectroscopic data for the unlabelled compound are reported in reference (6).

General Procedure for the Preparation of 20a-d. IBX (1.2 eq.) was dissolved in abs. DMSO (0.1 M) and compounds **19a-d** (1.0 eq.) were added. The reaction mixture was stirred over night at room temperature and then partitioned between diethyl ether and a sat. solution of $NaHCO_3$. It was extracted three times with diethyl ether, dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography with hexane/ethyl acetate (1:1) yielded aldehydes **20a-d** as colourless oils.

[2-^{2}H]-(2*R*,3*R*)-5-(Benzyloxy)-3-hydroxy-3-methylpentanal (20a). Yield (1.3 g, 5.83 mmol, 86%); $a_D^{23.8}$ = –1.4 (*c* = 1.10 in CH_2Cl_2); ν_{max}/cm^{-1} 3412 (br), 3063 (w), 2870 (w), 1712 (m), 1454 (w) 1736 (m), 1094 (s), 1026 (m), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 9.87 (d, 1H, *J* = 2.3 Hz, CHO), 7.38 – 7.30 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 3.84 (br s, 1H, OH), 3.75 (ddd, 1H, *J* = 9.9, 7.4, 4.5 Hz, CH_2), 3.69 (ddd, 1H, *J* = 10.0, 6.9, 4.5 Hz, CH_2), 2.61 (q, 1H, *J* = 2.3 Hz, C^2HH), 1.92 (ddd, 1H, *J* = 14.8, 7.3, 4.5 Hz, CH_2), 1.84 (ddd, 1H, *J* = 14.9, 6.8, 4.4 Hz, CH_2), 1.31 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 203.1 (CHO), 137.4 (C_q), 128.5 (2x CH), 128.0 (CH), 127.8 (2x CH), 73.6 (CH_2), 71.6 (C_q), 67.0 (CH_2), 54.2 (C^2HH, t, *J* = 19.1 Hz), 40.3 (CH_2), 27.6 (CH_3) ppm; *m*/*z* (%, MSTFA) 295 (<1) $[M]^+$, 228 (43), 205 (10), 184 (8), 160 (10), 145 (3), 134 (9), 118 (5), 107 (13), 91 (100), 73 (37), 65 (15), 51 (8), 43 (20); *I* (MSTFA) 2142.

[2-^{2}H]-(2*S*,3*R*)-5-(Benzyloxy)-3-hydroxy-3-methylpentanal (20b). Yield (734 mg, 3.29 mmol, 87%); $a_D^{24.5}$ = –3.2 (*c* = 1.40 in CH_2Cl_2); ν_{max}/cm^{-1} 3412 (br), 3063 (w), 2870 (w), 1712 (m), 1454 (w) 1736 (m), 1094 (s), 1026 (m), 736 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 9.92 (d, 1H, *J* = 2.5 Hz, CHO), 7.39 – 7.35 (m, 5H, Ph), 4.56 (s, 2H, CH_2), 3.77 (br s, 1H, OH), 3.67 (ddd, 1H, *J* = 9.8, 7.3, 4.4 Hz, CH_2), 3.61 (ddd, 1H, *J* = 9.9, 6.8, 4.5 Hz, CH_2), 2.41 (q, 1H, *J* = 2.3 Hz, C^2HH), 1.84 (ddd, 1H, *J* = 14.8, 7.2, 4.4 Hz, CH_2), 1.77 (ddd, 1H, J = 14.8, 6.7, 4.5 Hz, CH_2), 1.24 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 203.1 (CHO), 137.4 (C_q), 128.5 (2x CH), 127.9 (CH), 127.8 (2x CH), 73.5 (CH_2), 71.5 (C_q), 67.0 (CH_2), 54.2 (C^2HH, t, *J* = 19.7 Hz), 40.3 (CH_2), 27.6 (CH_3) ppm; *m*/*z* (%, MSTFA) 295 (<1) $[M]^+$, 228 (43), 205 (10), 184 (8), 160 (10), 145 (3), 134 (9), 118 (5), 107 (13), 91 (100), 73 (37), 65 (15), 51 (8), 43 (20); *I* (MSTFA) 2142.

[2,6,6,6-^{2}H$_4$]-(2*R*,3*R*)-5-(Benzyloxy)-3-hydroxy-3-methyl-pentanal (20c). Yield (915 mg, 4.05 mmol, 79%); $a_D^{24.3}$ = –1.8 (*c* = 1.60 in CH_2Cl_2); ν_{max}/cm^{-1} 3414 (br), 3063 (w), 2865 (w), 1716 (w), 1453 (w), 1366 (w), 1095 (s), 1026 (m), 734 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 9.86 (d, 1H, *J* = 2.6 Hz, CHO), 7.37 – 7.28 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 3.84 (br s, 1H, OH), 3.74 (ddd, 1H, *J* = 9.8, 7.2, 4.4 Hz, CH_2), 3.68 (ddd, 1H, *J* = 9.9, 6.8, 4.5 Hz, CH_2), 2.61 (q, 1H, *J* = 2.2 Hz, CH_2), 1.91 (ddd, 1H, *J* = 14.8, 7.2, 4.5 Hz, CH_2), 1.84 (ddd, 1H, *J* = 14.8, 6.7, 4.4 Hz, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 203.1 (CHO),

137.4 (C_q), 128.5 (2x CH), 127.9 (CH), 127.8 (2x CH), 73.5 (CH_2), 71.4 (C_q), 67.0 (CH_2), 54.2 (C^2HH, t, J = 19.4 Hz), 40.3 (CH_2), 26.7 (C^2H_3, J = 19.5 Hz); *m/z* (%, MSTFA)298 (<1) $[M]^+$, 228 (35), 208 (8), 184 (9), 163 (11), 134 (12), 107 (14), 91 (100), 73 (39), 46 (21) ppm; *I* (MSTFA) 2138.

[2,6,6,6-$^2H_4$]-(2*S*,3*R*)-5-(Benzyloxy)-3-hydroxy-3-methyl-pentanal (20d). Yield (920 mg, 4.1 mmol, 85%); $\alpha_D^{24.6}$ = –0.9 (*c* = 2.20 in CH_2Cl_2); ν_{max}/cm^{-1} 3414 (br), 3063 (w), 2865 (w), 1716 (w), 1453 (w), 1366 (w), 1095 (s), 1026 (m), 734 (s), 697 (s); δ_H (400 MHz, $CDCl_3$) 9.86 (d, 1H, J = 2.3 Hz, CHO), 7.37 – 7.27 (m, 5H, Ph), 4.51 (s, 2H, CH_2), 3.83 (br s, 1H, OH), 3.74 (ddd, 1H, J = 9.9, 7.3, 4.5 Hz, CH_2), 3.68 (ddd, 1H, J = 9.8, 6.8, 4.5 Hz, CH_2), 2.48 (q, 1H, J = 2.3 Hz, C^2HH), 1.91 (ddd, 1H, J = 14.8, 7.2, 4.5 Hz, CH_2), 1.84 (ddd, 1H, J = 14.8, 6.6, 4.4 Hz, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 203.1 (CHO), 137.4 (C_q), 128.5 (2x CH), 127.9 (CH), 127.8 (2x CH), 73.5 (CH_2), 71.4 (C_q), 67.0 (CH_2), 54.1 (C^2HH, t, J = 19.6 Hz), 40.3 (CH_2), 26.7 (C^2H_3, J = 19.8 Hz) ppm; *m/z* (%, MSTFA) 298 (<1) $[M]^+$, 228 (32), 208 (9), 184 (10), 163 (11), 148 (3), 134 (14), 107 (13), 91 (100), 73 (40), 46 (19); *I* (MSTFA) 2138.

General Procedure for the Preparation of 22a-d. Aldehydes **20a-d** (1.0 eq.) were dissolved in ^{t}BuOH (0.2 M) and 2-methyl-2-butene (10.0 eq.) was added. Slowly a solution of $NaClO_2$ (1.25 eq.) in sat. NaH_2PO_4 buffer (1.3 M) was added. The reaction mixture was stirred for 3 h at room temperature. For work-up it was diluted with H_2O and extracted three times with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The acid was obtained as yellow oil that was used without further purification in the next step. The crude material was dissolved in Et_2O (0.1 M) and 5%-Pd/C (0.05 eq.) was added. The reaction mixture was stirred under an atmosphere of H_2 (40 bar) at 40 °C. After 4 h the reaction mixture was filtered over a small plug of silica gel. Removal of the solvent under reduced pressure yielded pure mevalonolactones **22a-d** as colourless oils.

[2-^{2}H]-(3*R*,4*R*)-4-Hydroxy-4-methyltetrahydro-2*H*-pyran-2-one (22a). Yield (400 mg, 3.03 mmol, 69%); $\alpha_D^{24.5}$ = –2.4 (*c* = 0.65 in CH_2Cl_2); ν_{max}/cm^{-1} 3418 (br), 2972 (w), 2930(w), 1704 (s), 1473 (w), 1407 (m), 1262 (m), 1225 (m), 1157 (m), 1069 (s), 912 (m), 755 (m); δ_H (400 MHz, $CDCl_3$) 4.61 (ddd, 1H, J = 11.3, 8.6, 6.2 Hz, CH_2), 4.35 (ddd, 1H, J = 11.3, 5.1, 4.1 Hz, CH_2), 2.95 (br s, 1H, OH), 2.49 (t, 1H, J = 2.5 Hz, C^2H), 1.93 – 1.90 (m, 2H, CH_2), 1.39 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 171.0 (CO), 67.9 (C_q), 66.1 (CH_2), 44.2 (C^2HH, t, J = 20.6 Hz), 35.7 (CH_2), 29.5 (CH_3) ppm; *m/z* (%, MSTFA) 203 (<1) $[M]^+$, 188 (14), 158 (7), 145 (100), 115 (50), 101 (14), 75 (54), 59 (9), 43 (27); *I* (MSTFA) 1385.

[2-^{2}H]-(3*S*,4*R*)-4-Hydroxy-4-methyltetrahydro-2*H*-pyran-2-one (22b). Yield (195 mg, 1.49 mmol, 45%); $\alpha_D^{23.5}$ = –4.1 (*c* = 0.70 in CH_2Cl_2); ν_{max}/cm^{-1} 3418 (br), 2972 (w), 2930(w), 1704 (s), 1473 (w), 1407 (m), 1262 (m), 1225 (m), 1157 (m), 1069 (s), 912 (m), 755 (m); δ_H (400 MHz, $CDCl_3$) 4.61 (ddd, 1H, J = 11.3, 9.1, 5.7 Hz, CH_2), 4.35 (ddd, 1H, J = 11.4, 5.2, 4.2 Hz, CH_2), 2.65 (br m, 1H, C^2HH), 2.64 (br s, 1H, OH), 1.94 – 1.90 (m, 2H, CH_2), 1.40 (s, 3H, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 170.7 (CO), 68.1 (C_q), 66.0 (CH_2), 44.3 (C^2HH, t, J = 19.4 Hz), 35.8 (CH_2), 29.6 (CH_3) ppm; *m/z* (%, MSTFA) 203 (<1) $[M]^+$, 188 (14), 158 (7), 145 (100), 115 (50), 101 (14), 75 (54), 59 (9), 43 (27); *I* (MSTFA) 1385.

[2,6,6,6-$^2H_4$]-(3*R*,4*R*)-4-Hydroxy-4-methyltetrahydro-2*H*-pyran-2-one (22c). Yield (330 mg, 2.5 mmol, 59%); $\alpha_D^{24.4}$ = –3.8 (*c* = 3.20 in CH_2Cl_2); ν_{max}/cm^{-1} 3415 (br), 2975 (w), 1711 (s), 1476 (w), 1408 (m), 1264 (m), 1220 (s), 1077 (s), 959 (m), 916 (m), 752 (m); δ_H (400 MHz, $CDCl_3$) 4.61 (ddd, 1H, J = 11.3, 8.8, 6.1 Hz, CH_2), 4.37 – 4.31 (m, 1H, CH_2), 2.76 (br s, 1H, OH), 2.50 – 2.49 (m, 1H, CH), 1.93 – 1.89 (m, 2H, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 171.0 (C_q), 67.8 (C_q), 66.1 (CH_2), 44.2 (C^2HH, t, J = 20.7 Hz), 35.7 (CH_2) ppm; *m/z* (%, MSTFA) 206 (<1) $[M]^+$, 191 (10), 161 (5), 148 (100), 118 (45), 101 (11), 73 (42), 59 (14), 46 (24); *I* (MSTFA) 1380.

[2,6,6,6-$^2H_4$]-(3*S*,4*R*)-4-Hydroxy-4-methyltetrahydro-2*H*-pyran-2-one (22d). Yield (313 mg, 2.3 mmol, 59%); $\alpha_d^{24.5}$ = –3.7 (*c* = 0.60 in CH_2Cl_2); ν_{max}/cm^{-1} 3415 (br), 2975 (w), 1711 (s), 1476 (w), 1408 (m), 1264 (m), 1220 (s), 1077 (s), 959 (m), 916 (m), 752 (m); δ_H (400 MHz, $CDCl_3$) 4.64 – 4.47 (m, 1H, CH_2), 4.37 – 4.32 (m, 1H, CH_2), 2.41 (br s, 1H, OH), 2.65 – 2.64 (m, 1H, CH), 1.93 – 1.89 (m, 2H, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 170.7 (C_q), 67.9 (C_q), 66.0 (CH_2), 44.3 (C^2HH, t, J = 18.6 Hz), 35.8 (CH_2) ppm; *m/z* (%, MSTFA) 206 (<1) $[M]^+$, 191 (11), 161 (6), 148 (100), 118 (44), 101 (13), 73 (48), 59 (14), 46 (25); *I* (MSTFA) 1380.

Several deuterated isotopomers have previously been synthesised in our own group and all spectrsocopic data were in agreement with the reported data.[7] Spectroscopic data for the unlabelled compound are also available in reference (8).

LITERATURE

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NMR SPECTRA OF SYNTHETIC COMPOUNDS

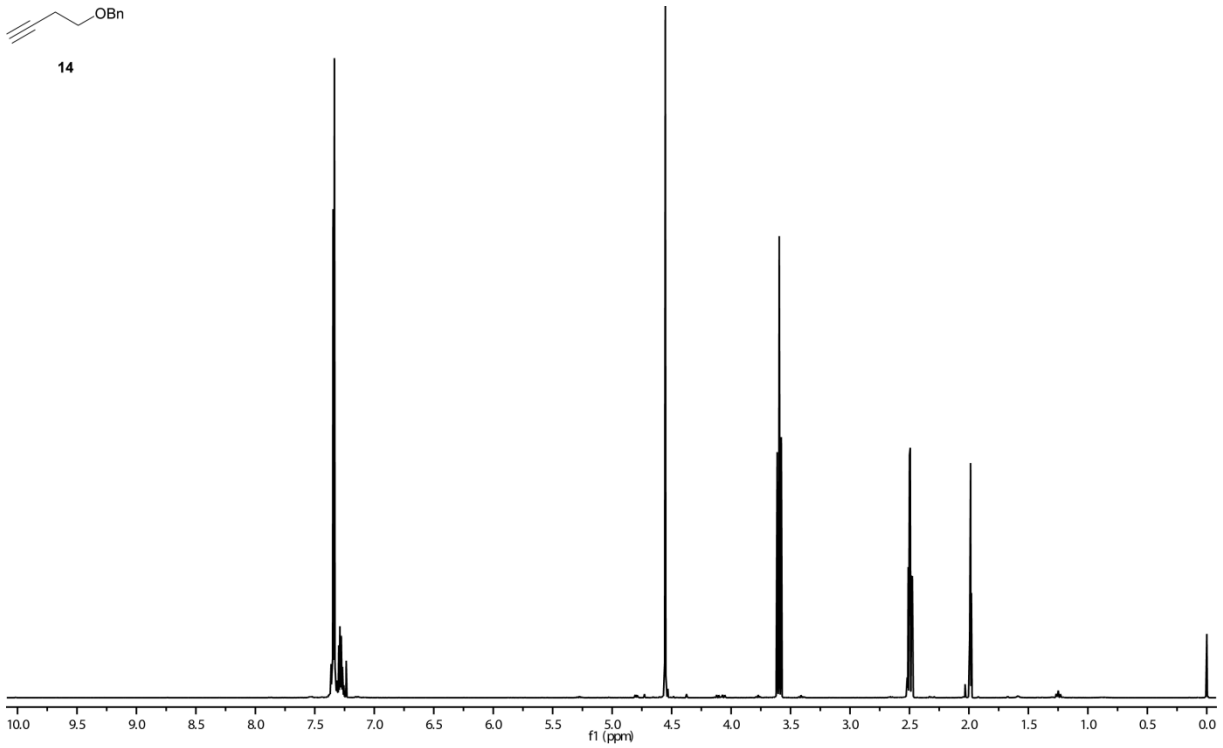


Figure 2 ^{1}H-NMR spectrum of compound **14**.

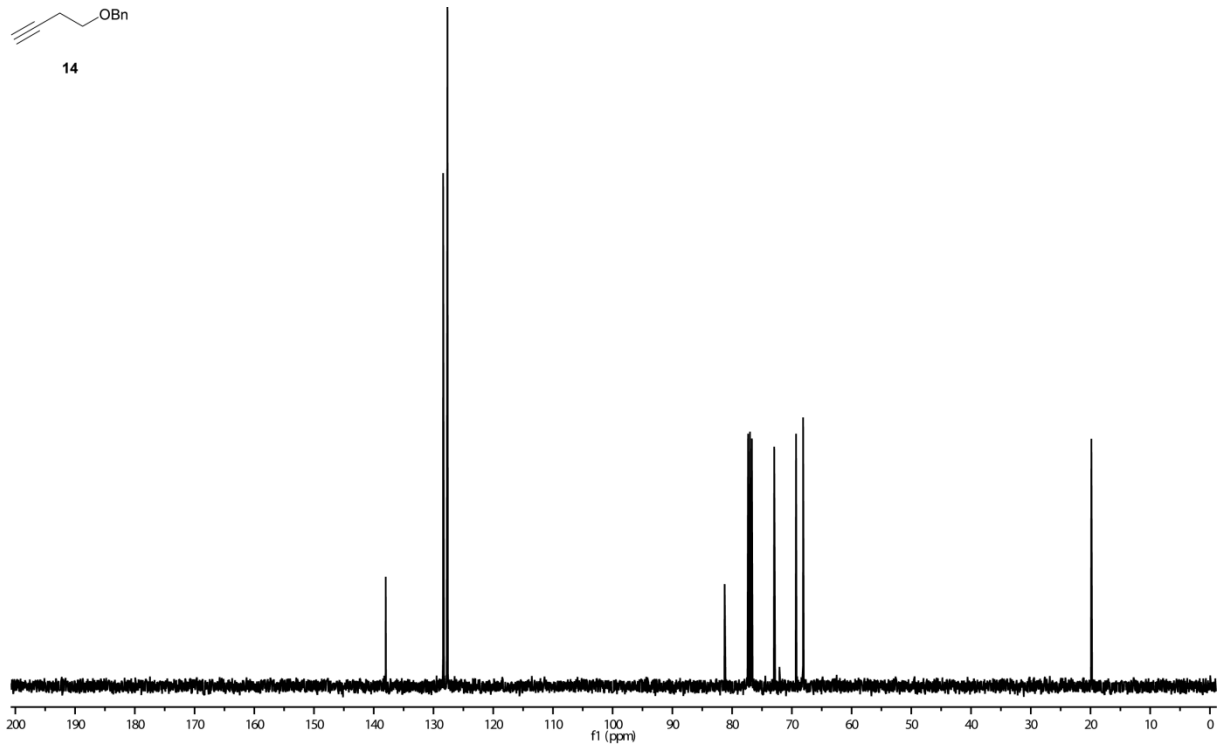


Figure 3 ^{13}C-NMR spectrum of compound **14**.

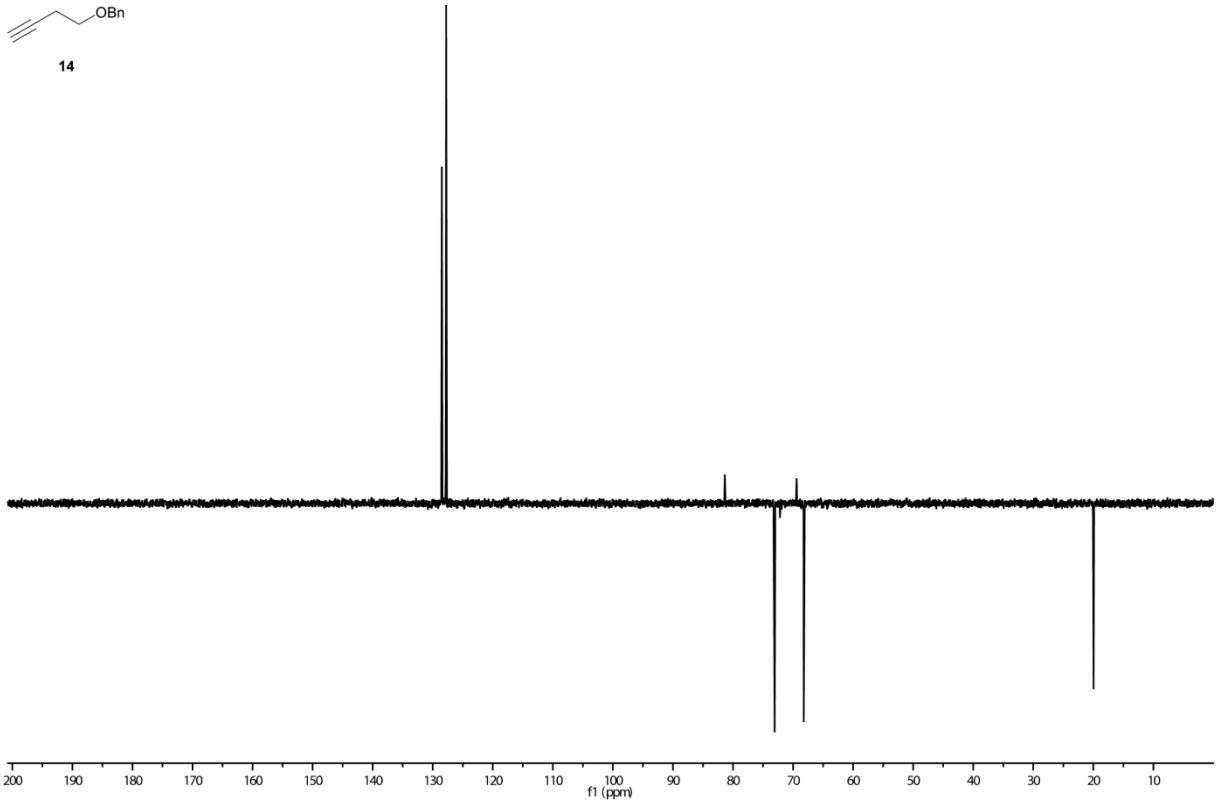


Figure 4 DEPT spectrum of compound **14**.

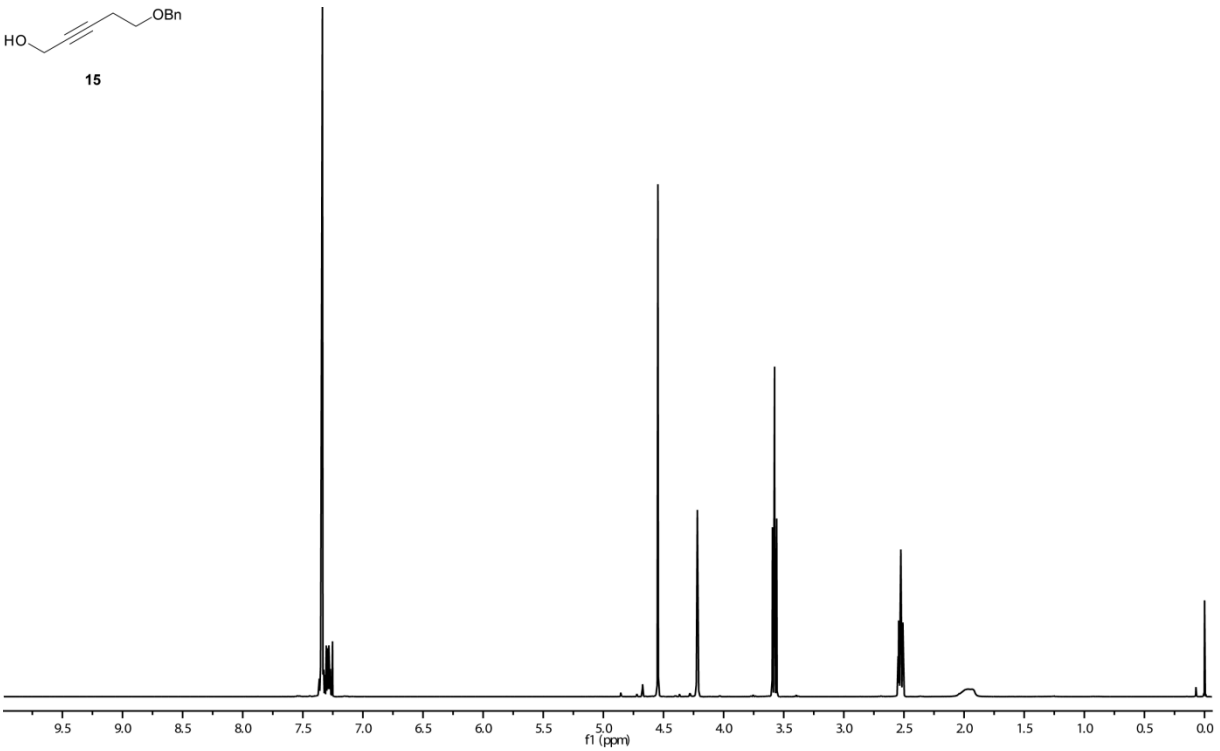


Figure 5 ^{1}H-NMR spectrum of compound **15**.

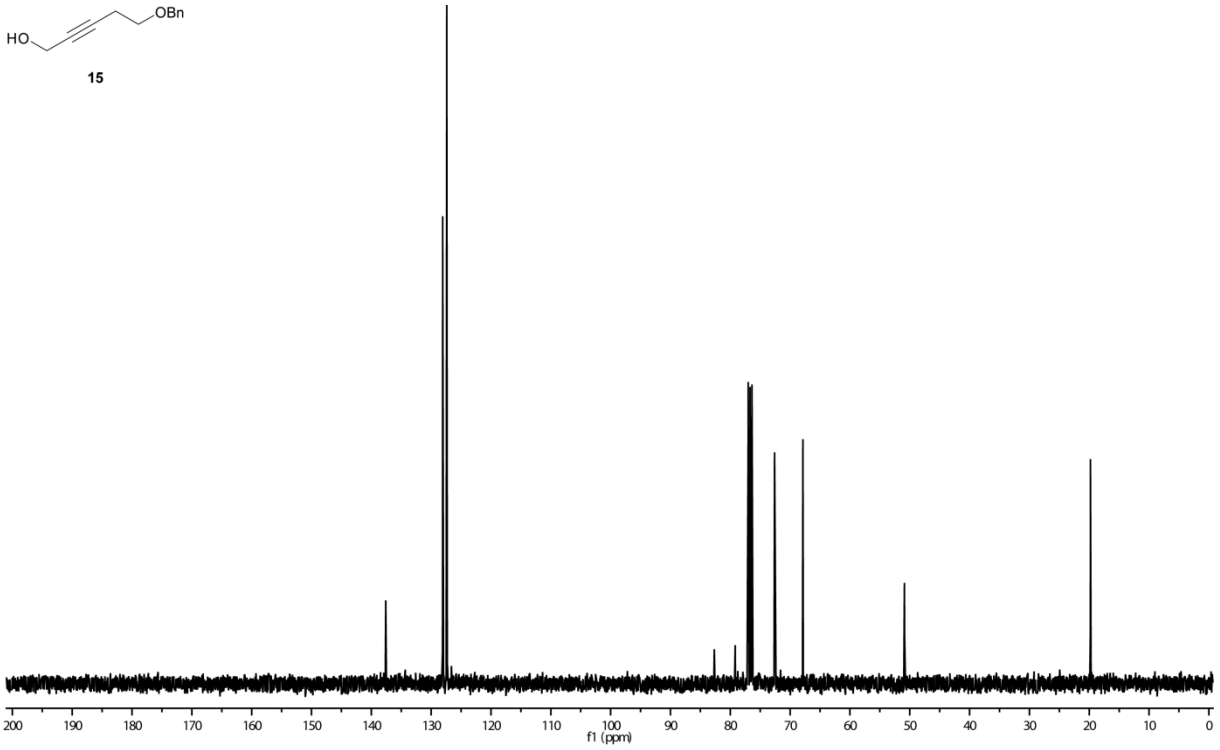


Figure 6 ^{13}C-NMR spectrum of compound **15**.

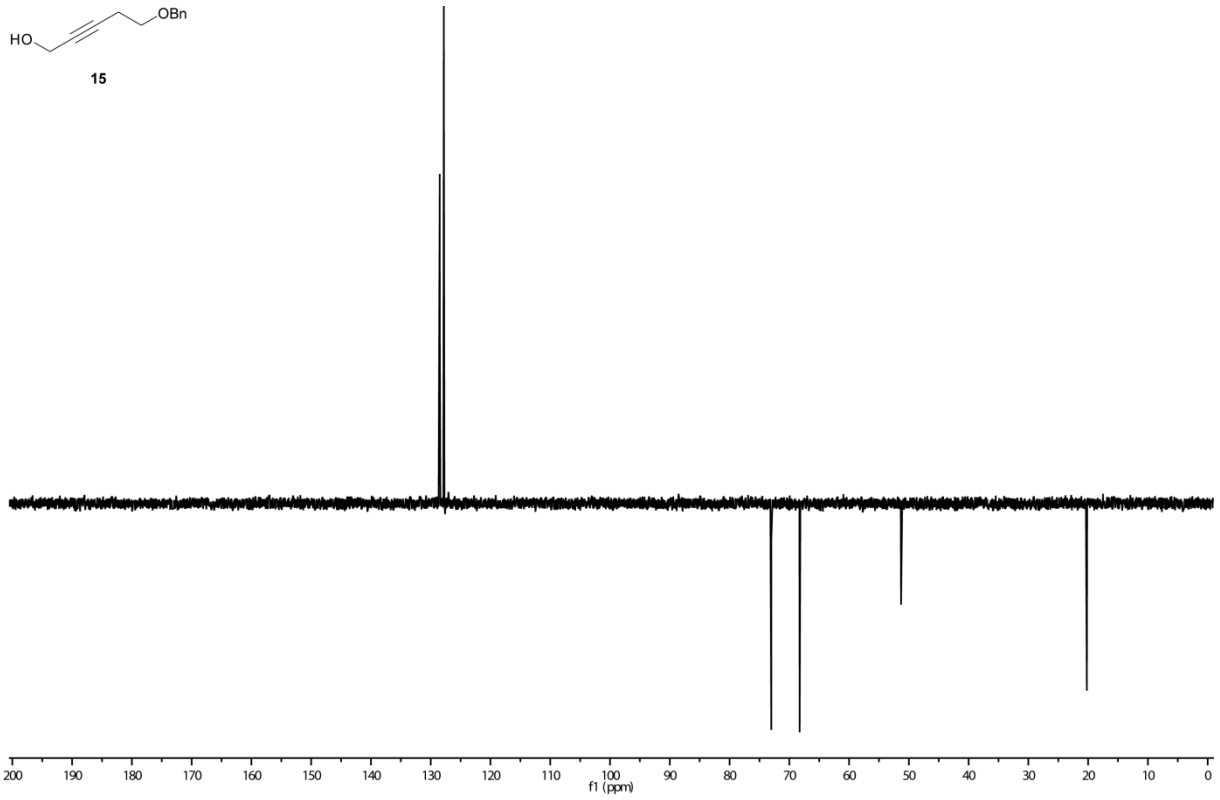


Figure 7 DEPT spectrum of compound **15**.

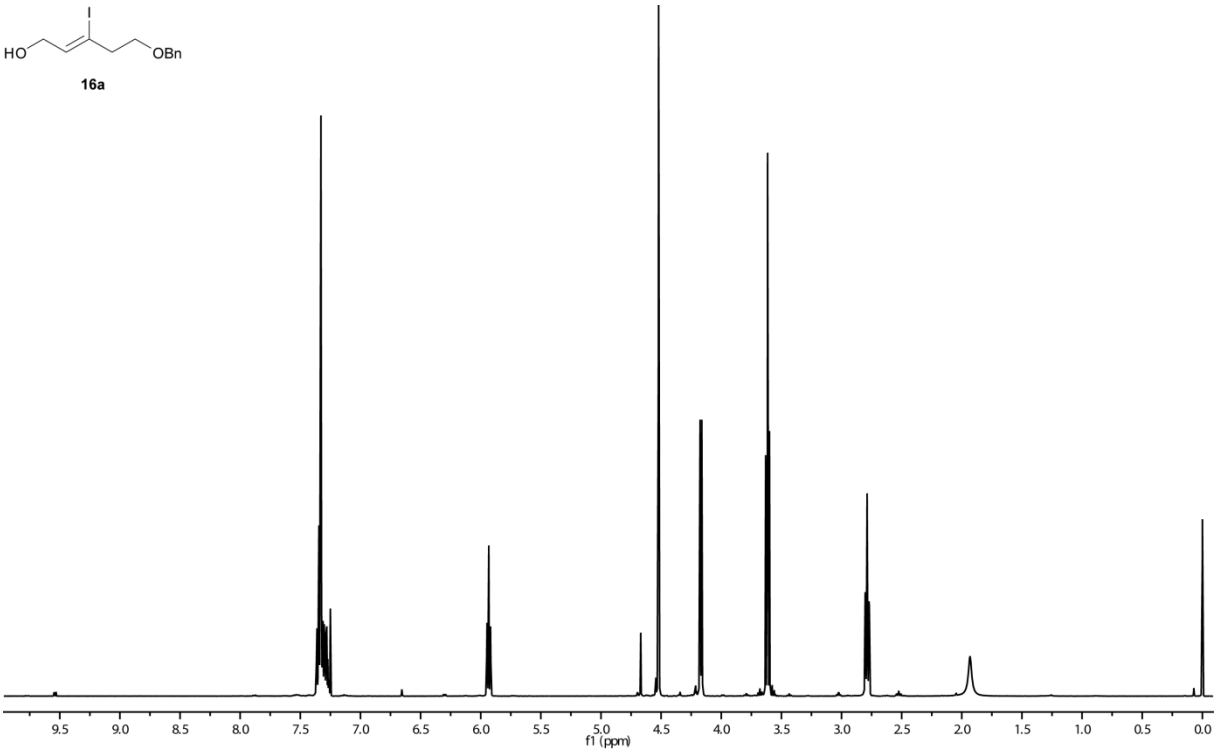


Figure 8 ^{1}H-NMR spectrum of compound **16a**.

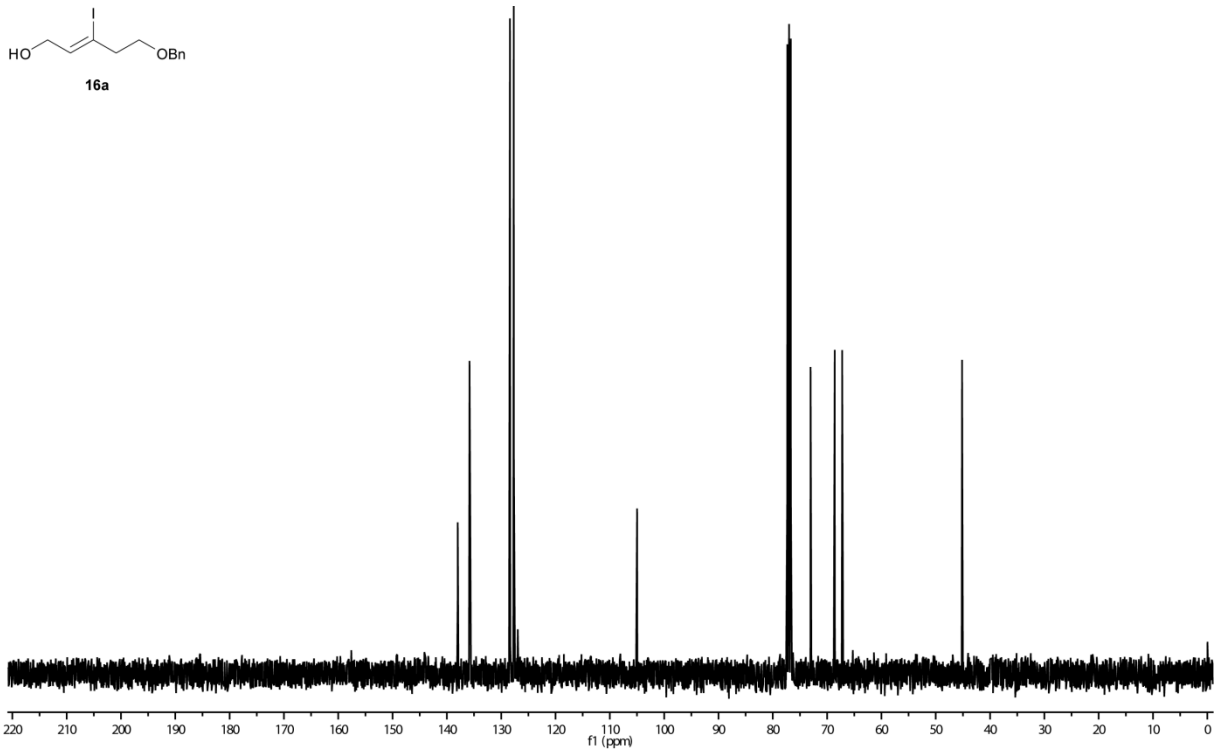


Figure 9 ^{13}C-NMR spectrum of compound **16a**.

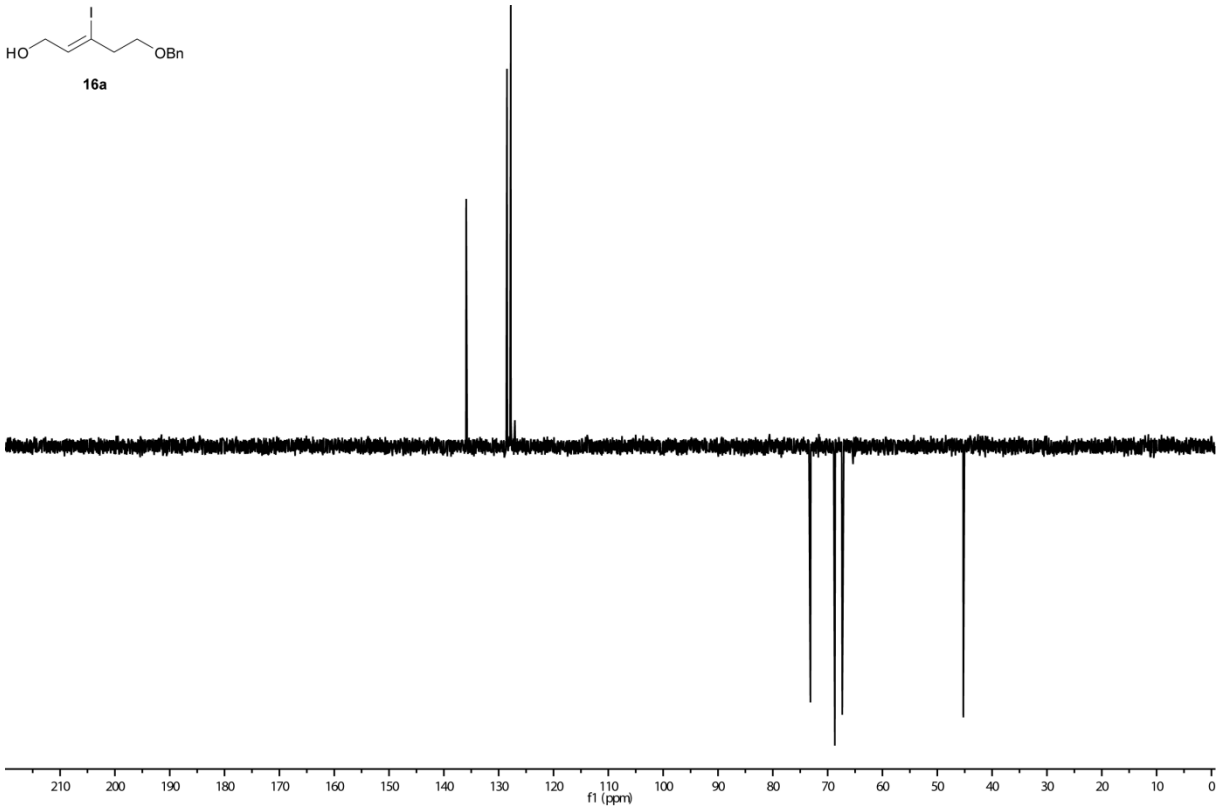


Figure 10 DEPT spectrum of compound **16a**.

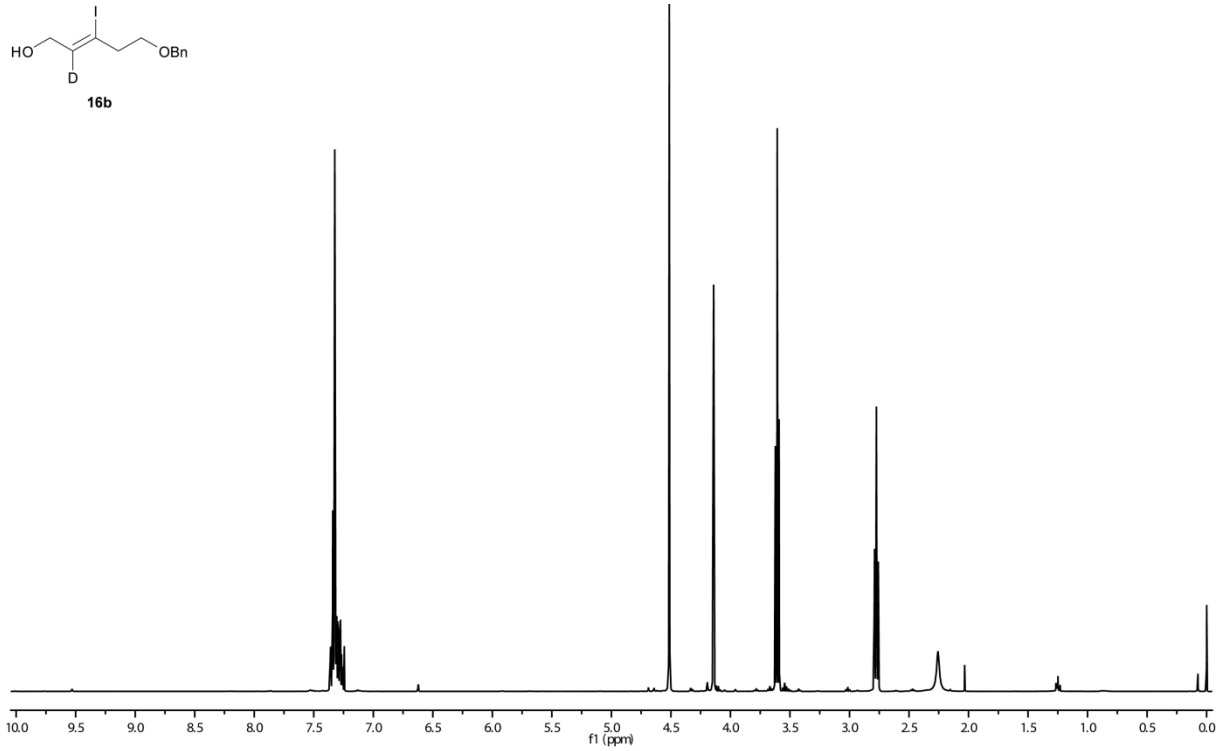


Figure 11 ^{1}H-NMR spectrum of compound **16b**.

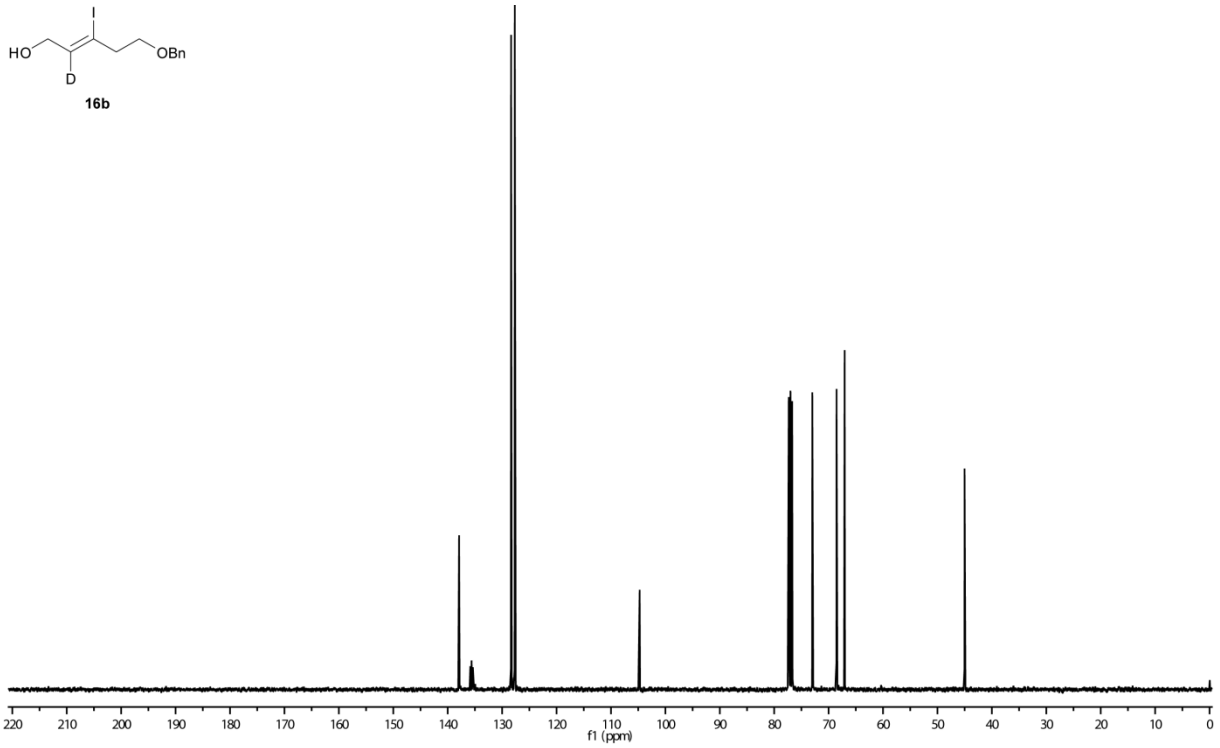


Figure 12 ^{13}C-NMR spectrum of compound **16b**.

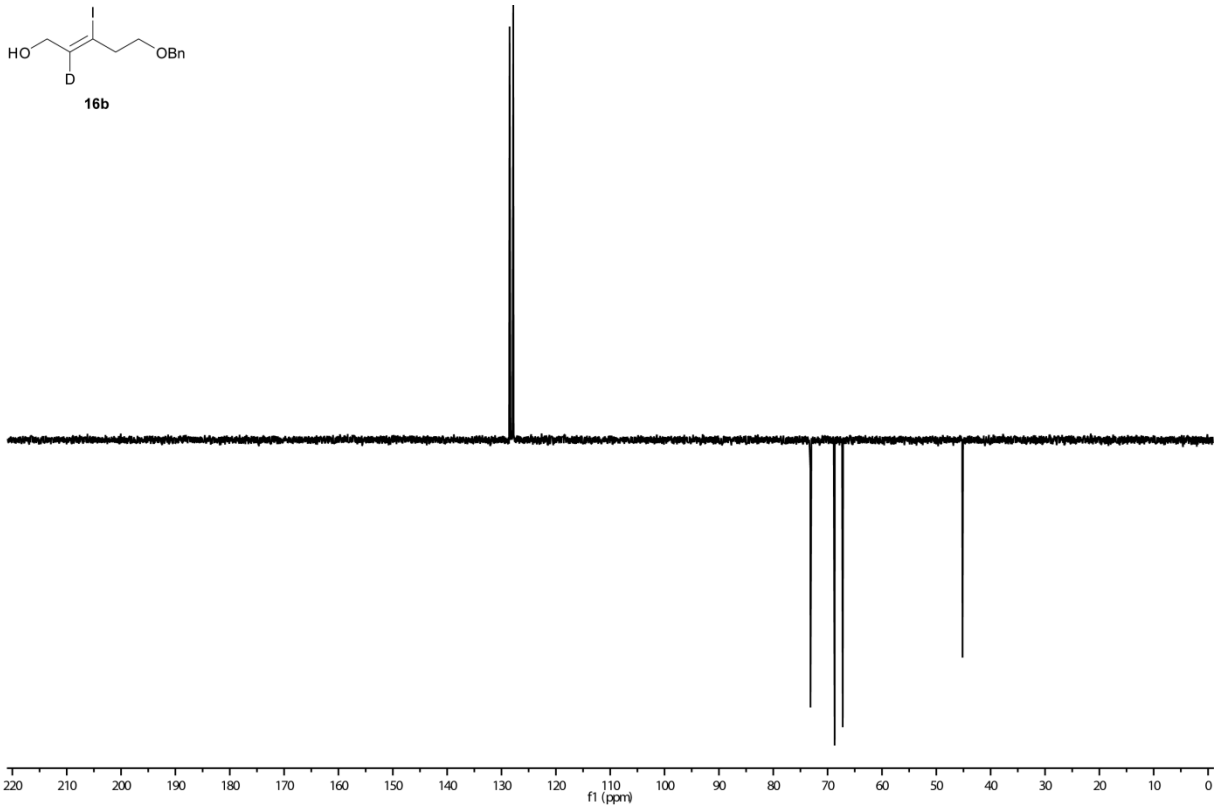


Figure 13 DEPT spectrum of compound **16b**.

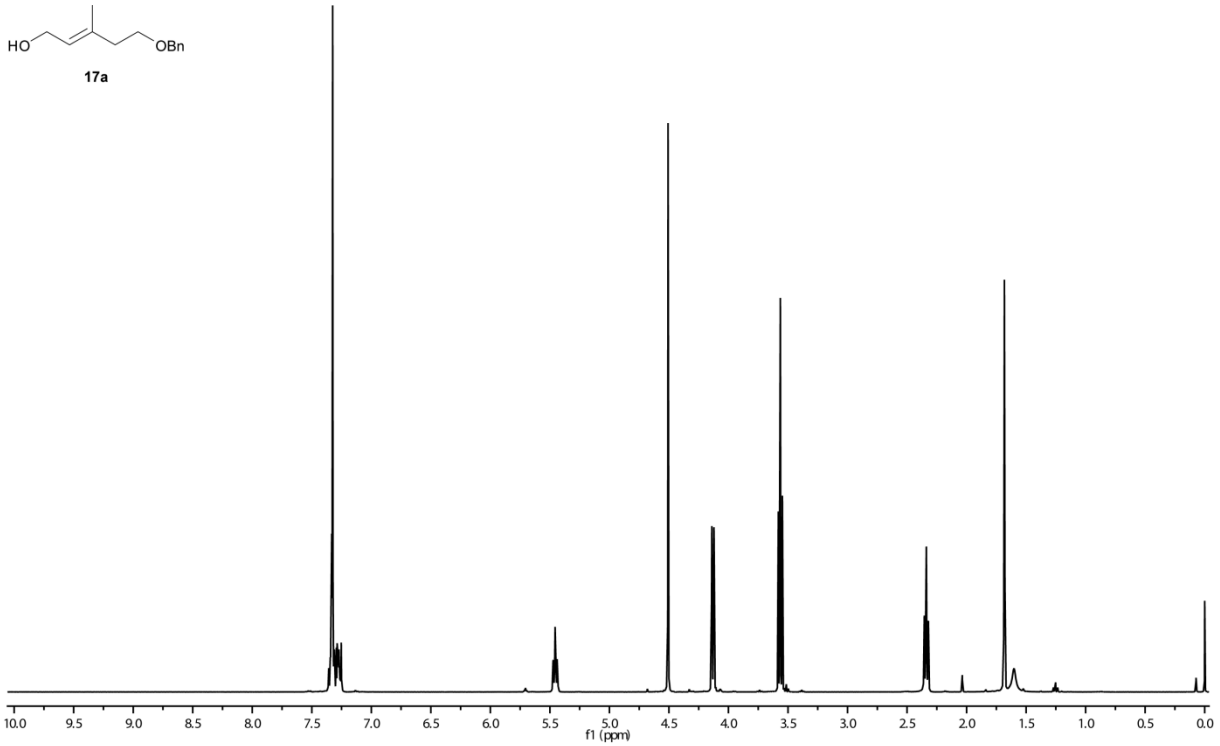


Figure 14 ^{1}H-NMR spectrum of compound **17a**.

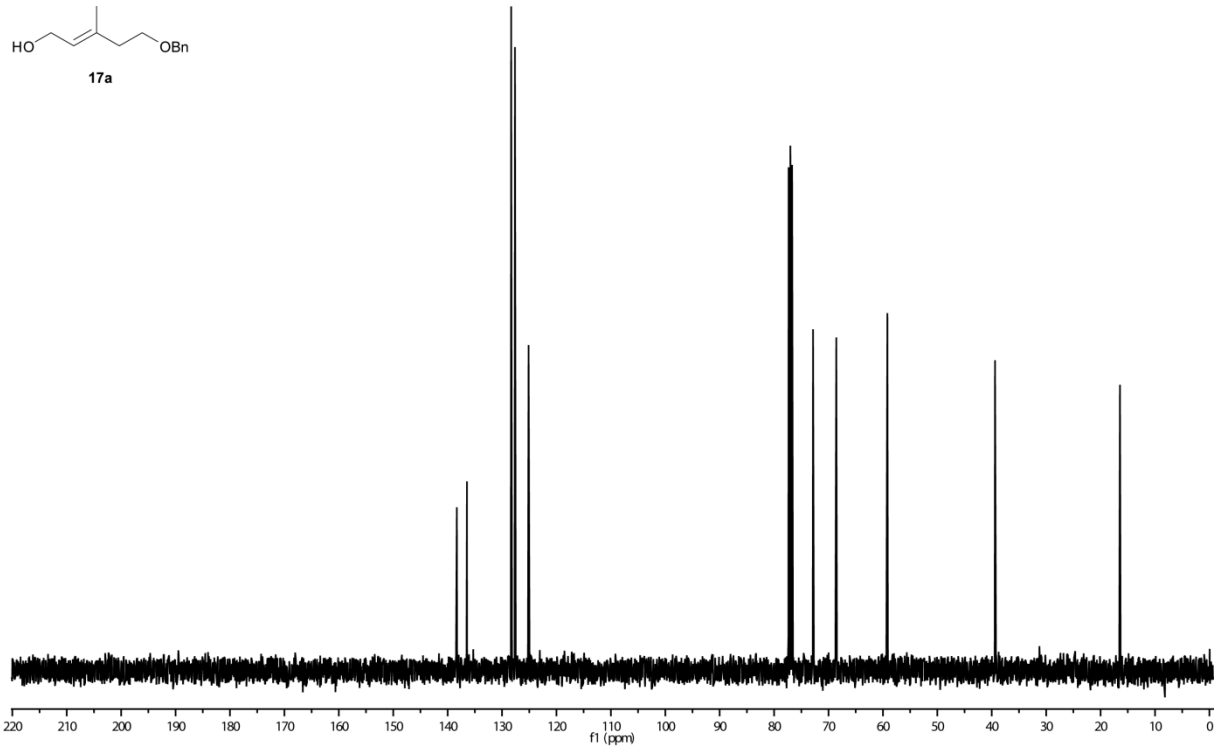


Figure 15 ^{13}C-NMR spectrum of compound **17a**.

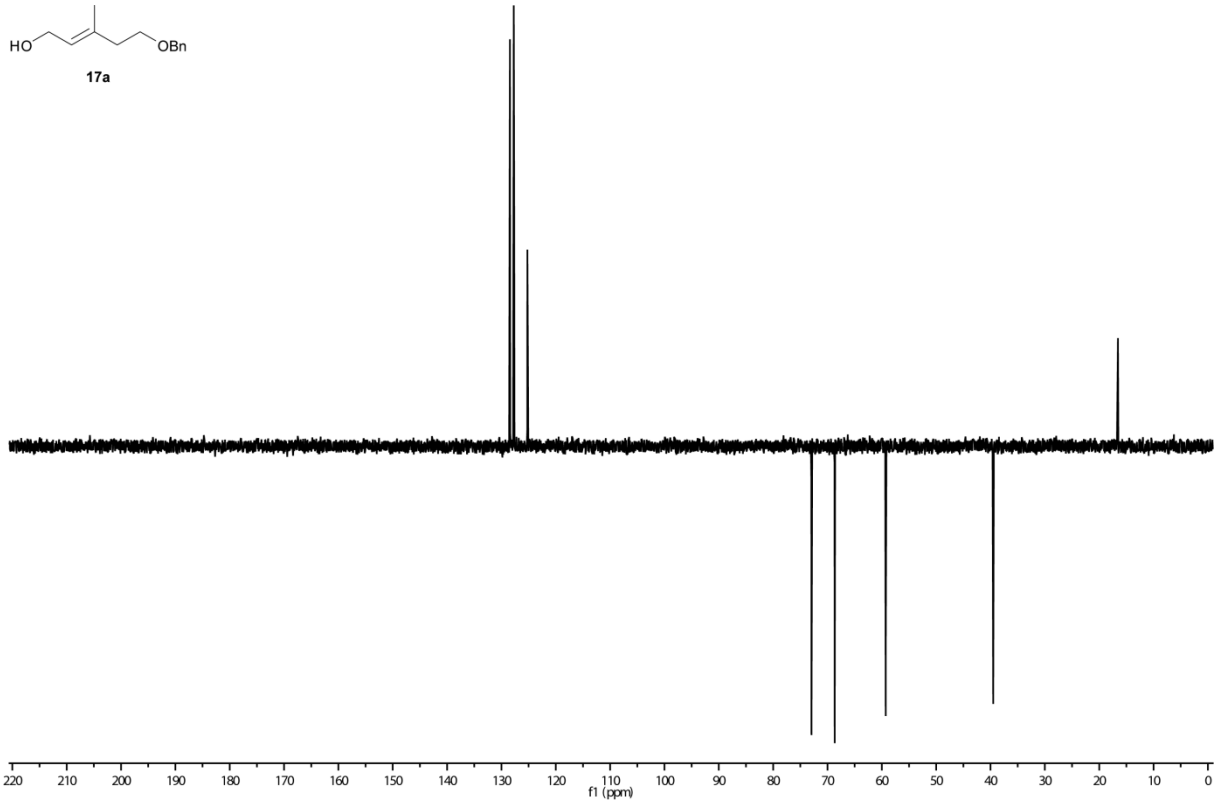


Figure 16 DEPT spectrum of compound **17a**.

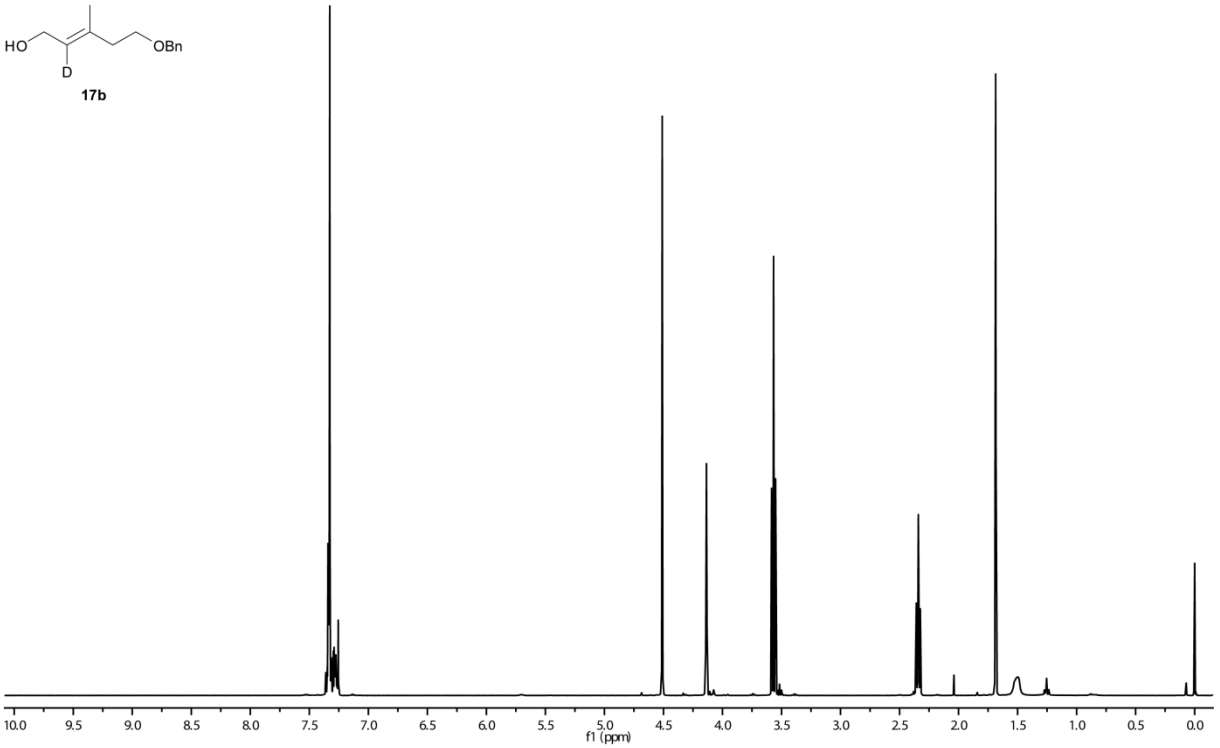


Figure 17 ^{1}H-NMR spectrum of compound **17b**.

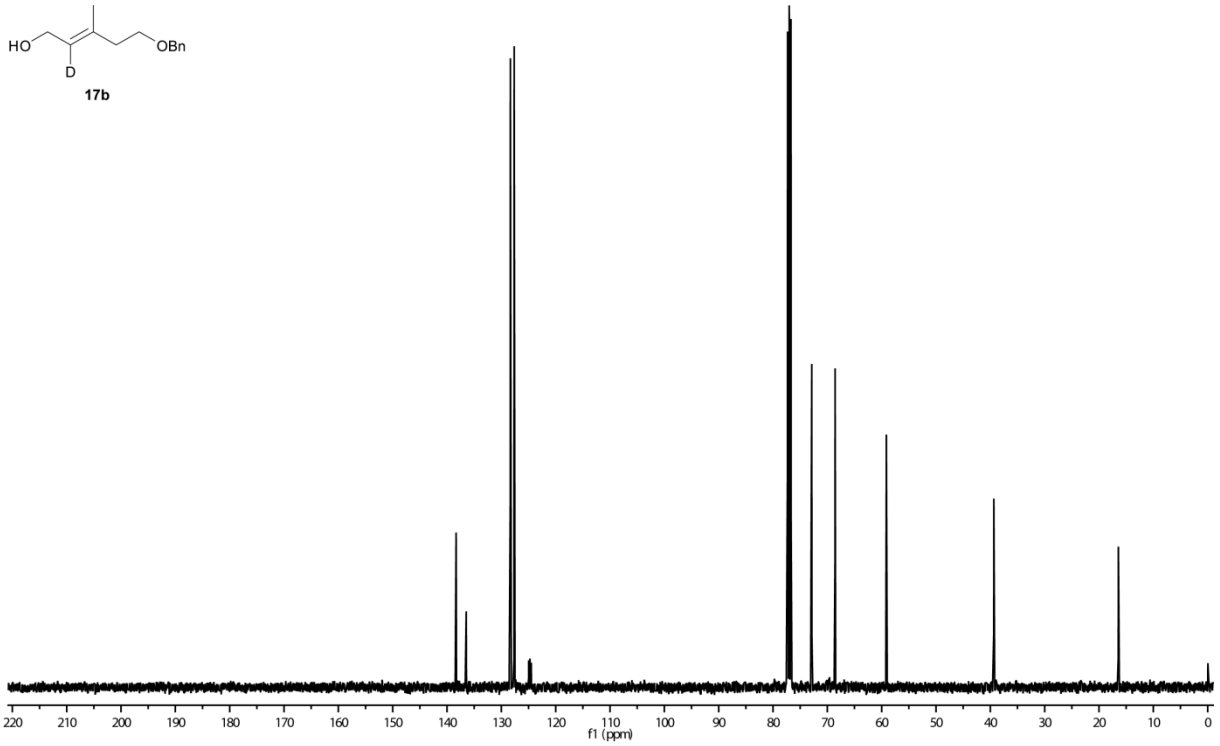


Figure 18 ^{13}C-NMR spectrum of compound **17b**.

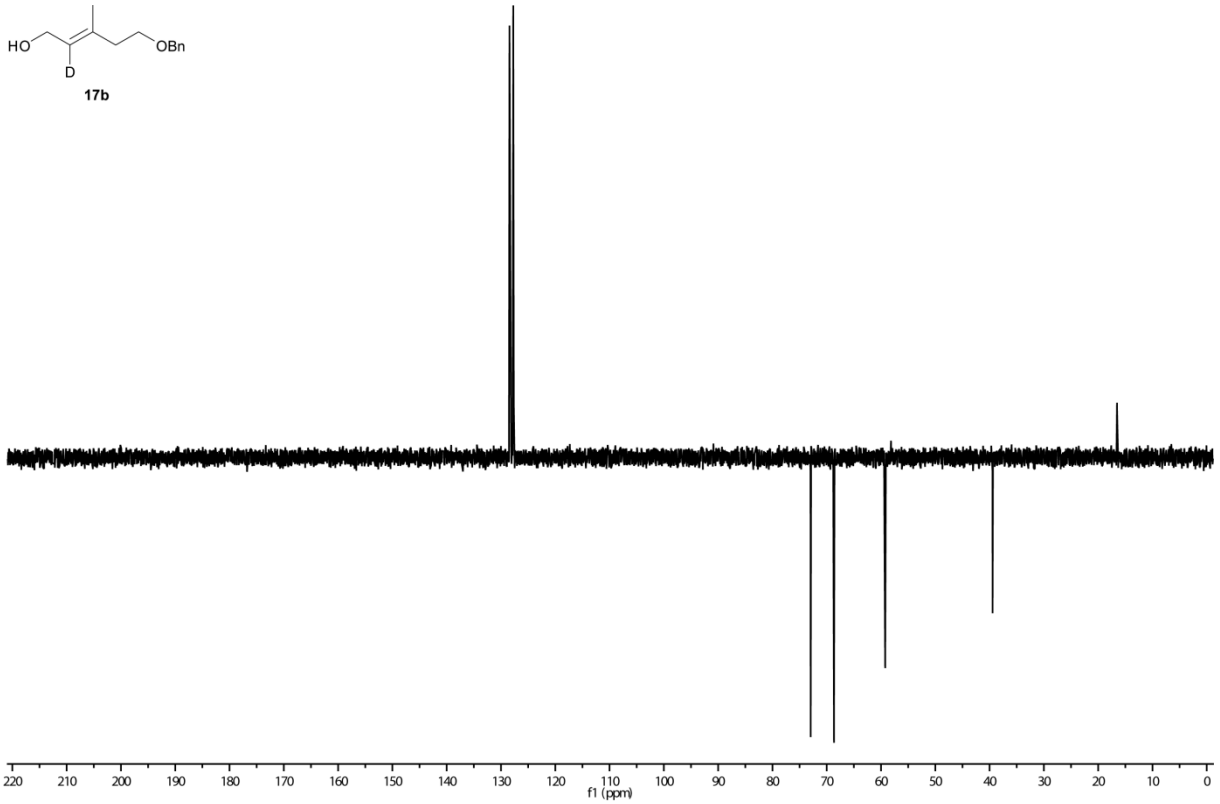


Figure 19 DEPT spectrum of compound **17b**.

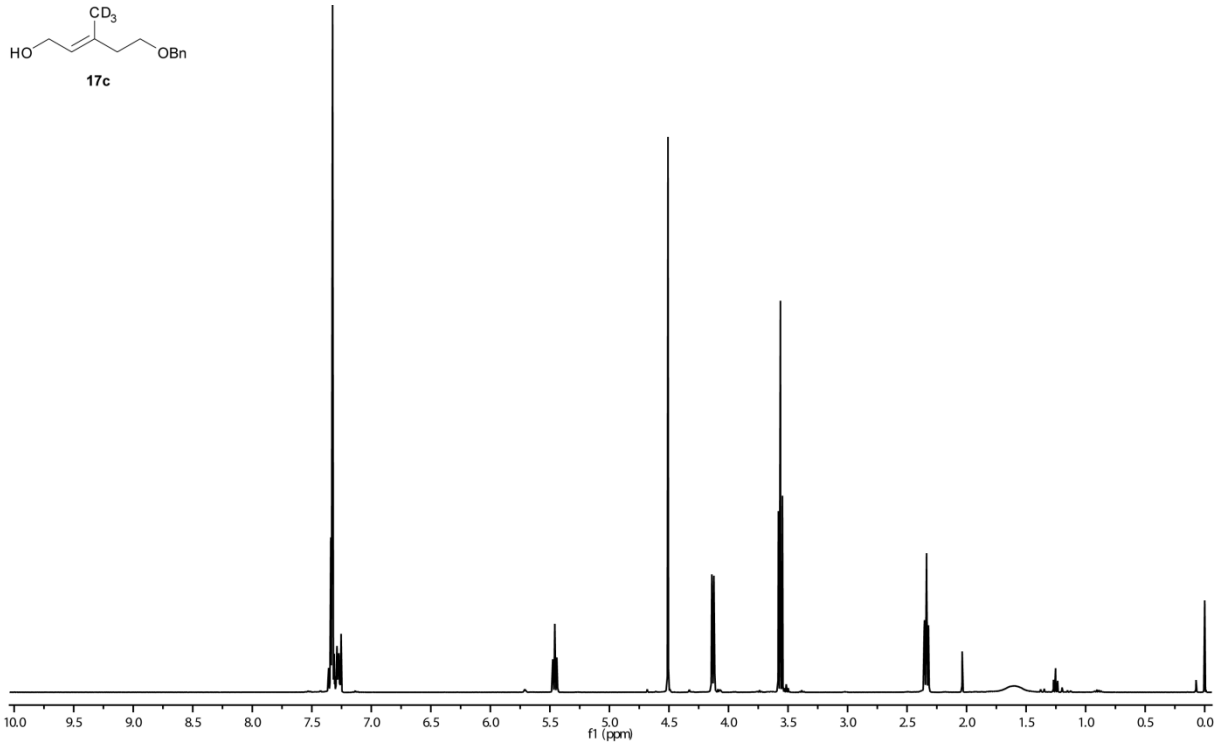


Figure 20 ^{1}H-NMR spectrum of compound **17c**.

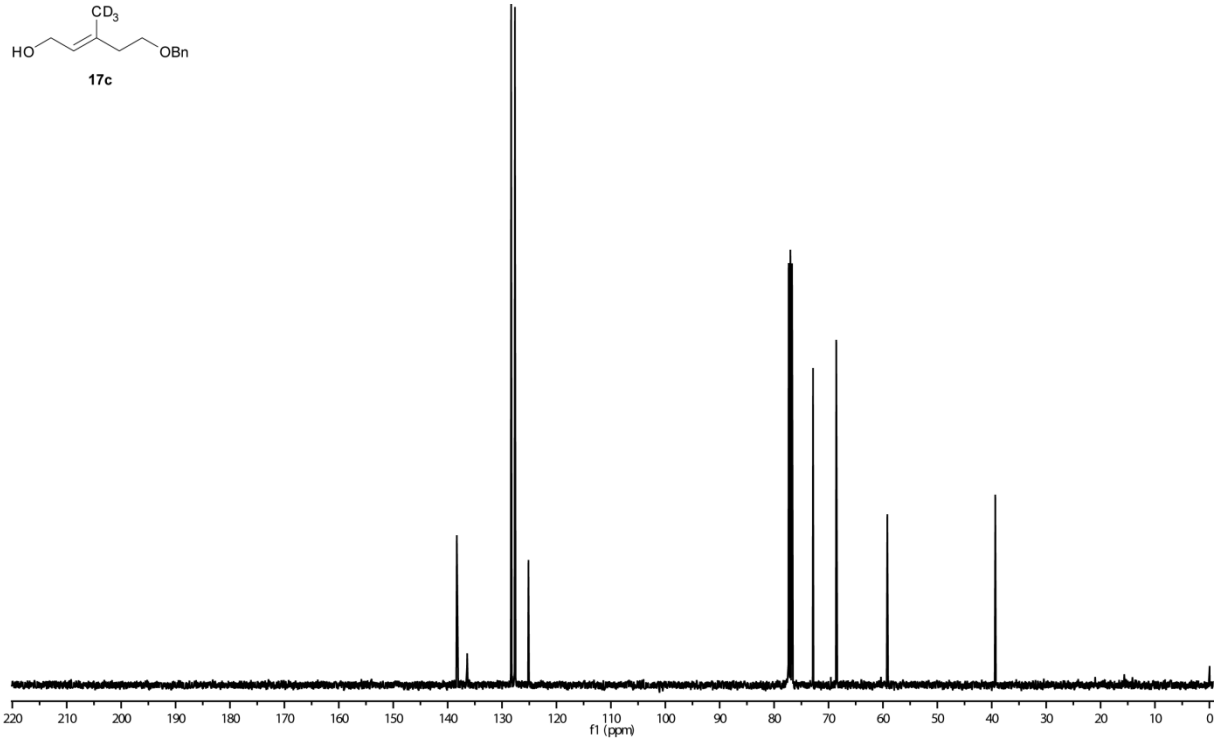


Figure 21 ^{13}C-NMR spectrum of compound **17c**.

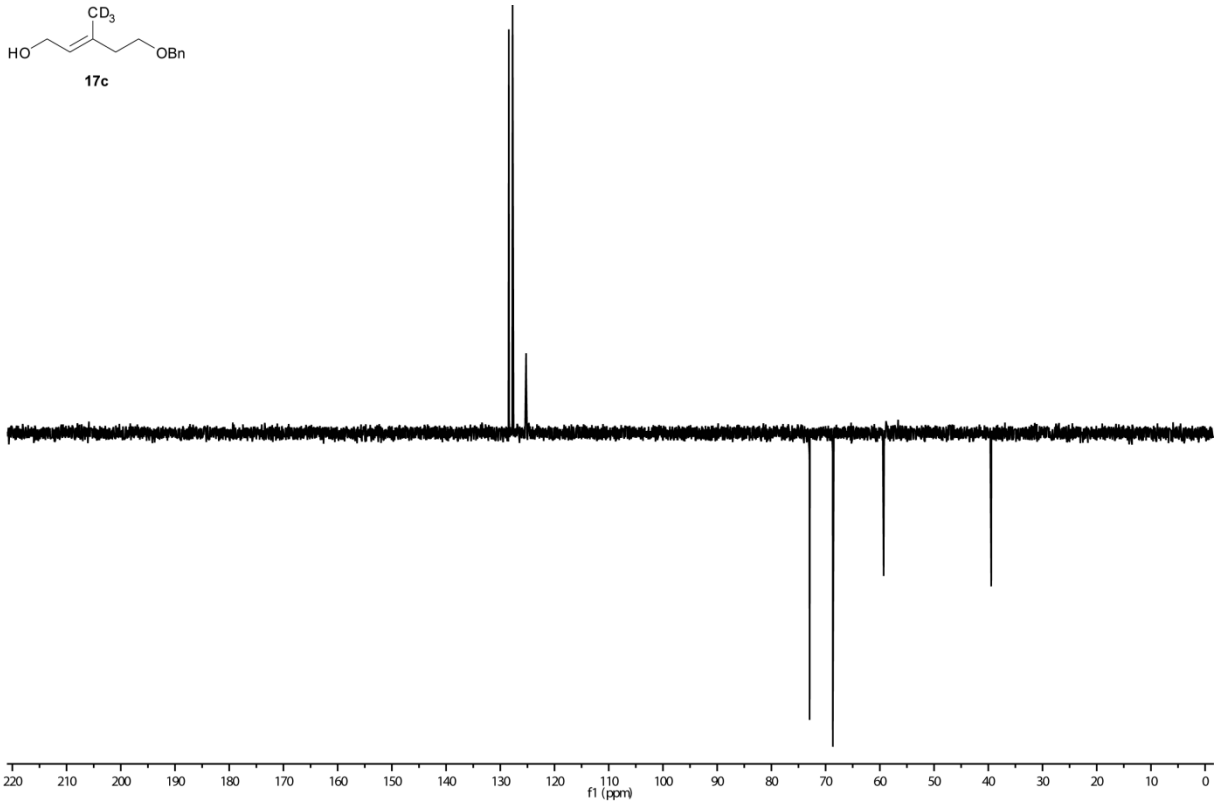


Figure 22 DEPT spectrum of compound **17c**.

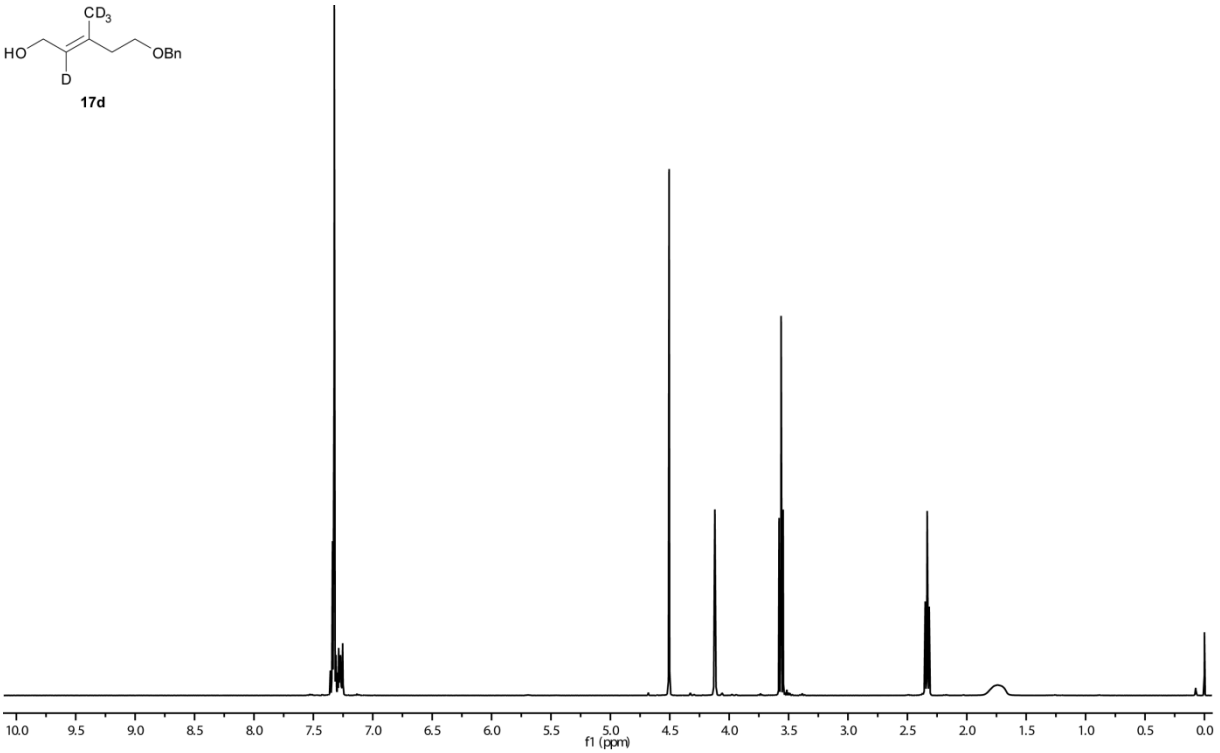


Figure 23 ^{1}H-NMR spectrum of compound **17d**.

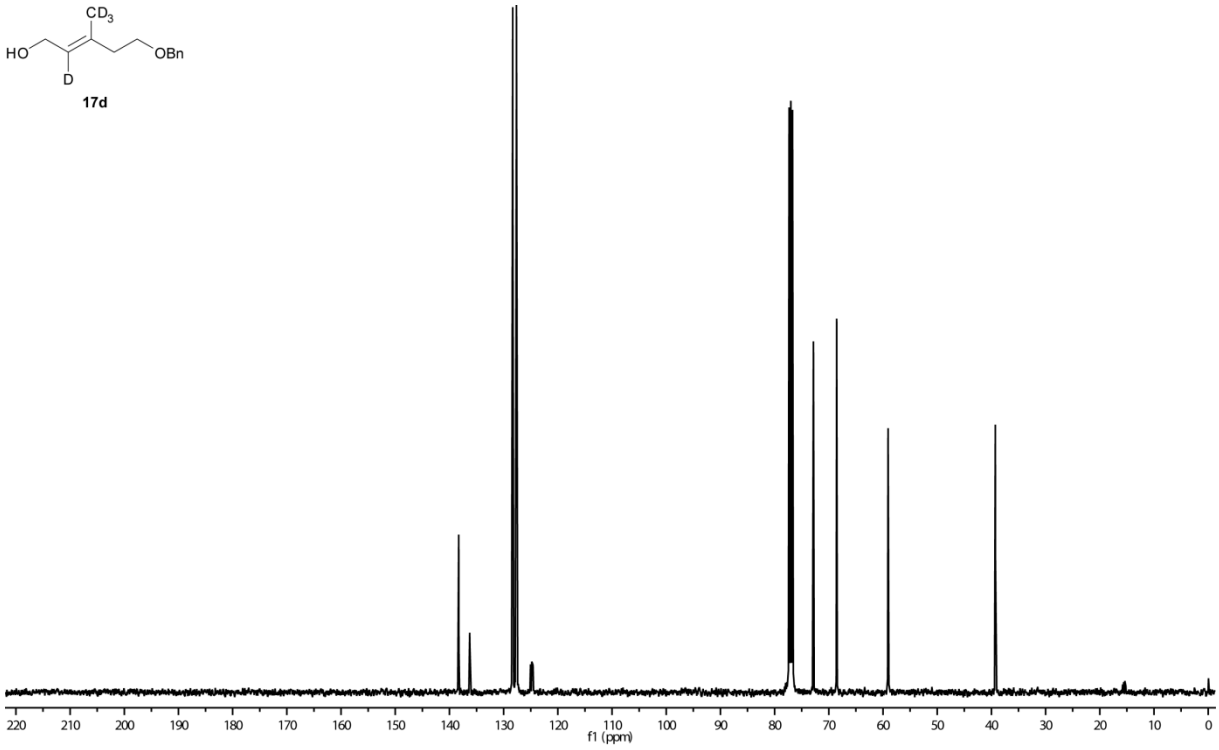


Figure 24 ^{13}C-NMR spectrum of compound **17d**.

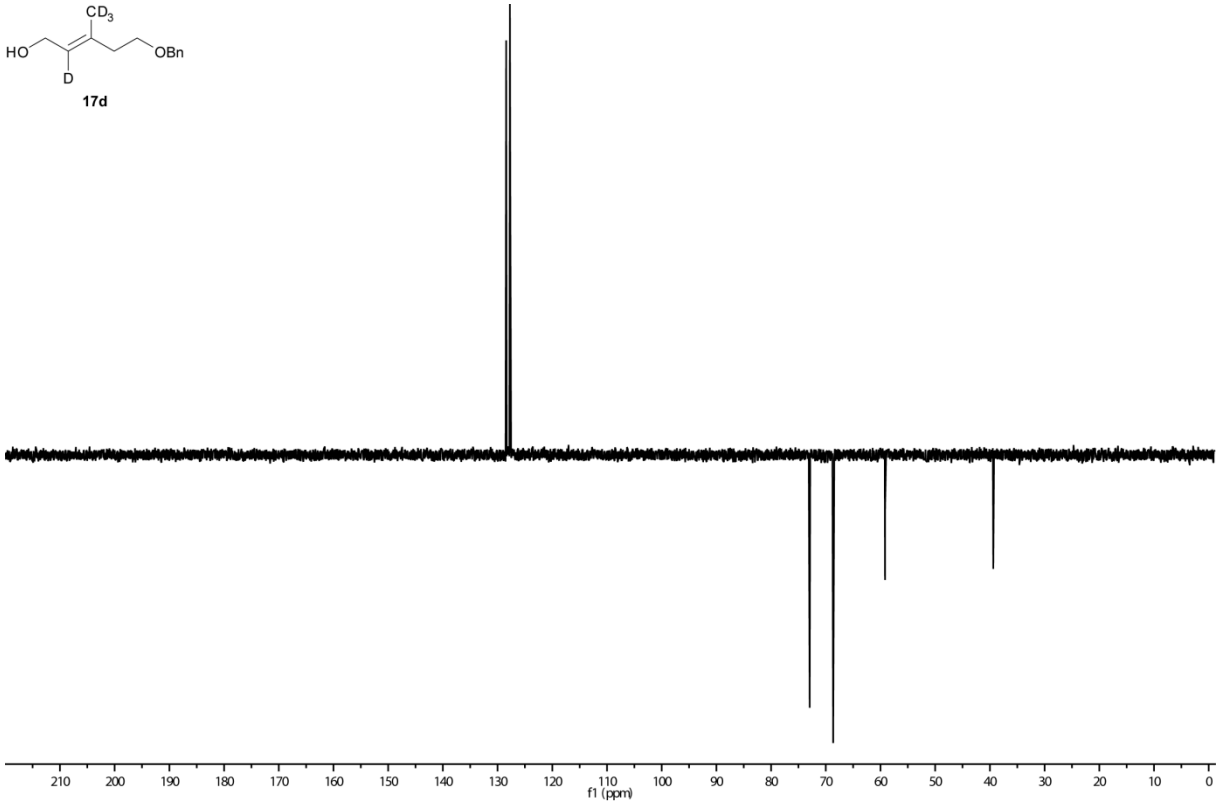


Figure 25 DEPT spectrum of compound **17d**.

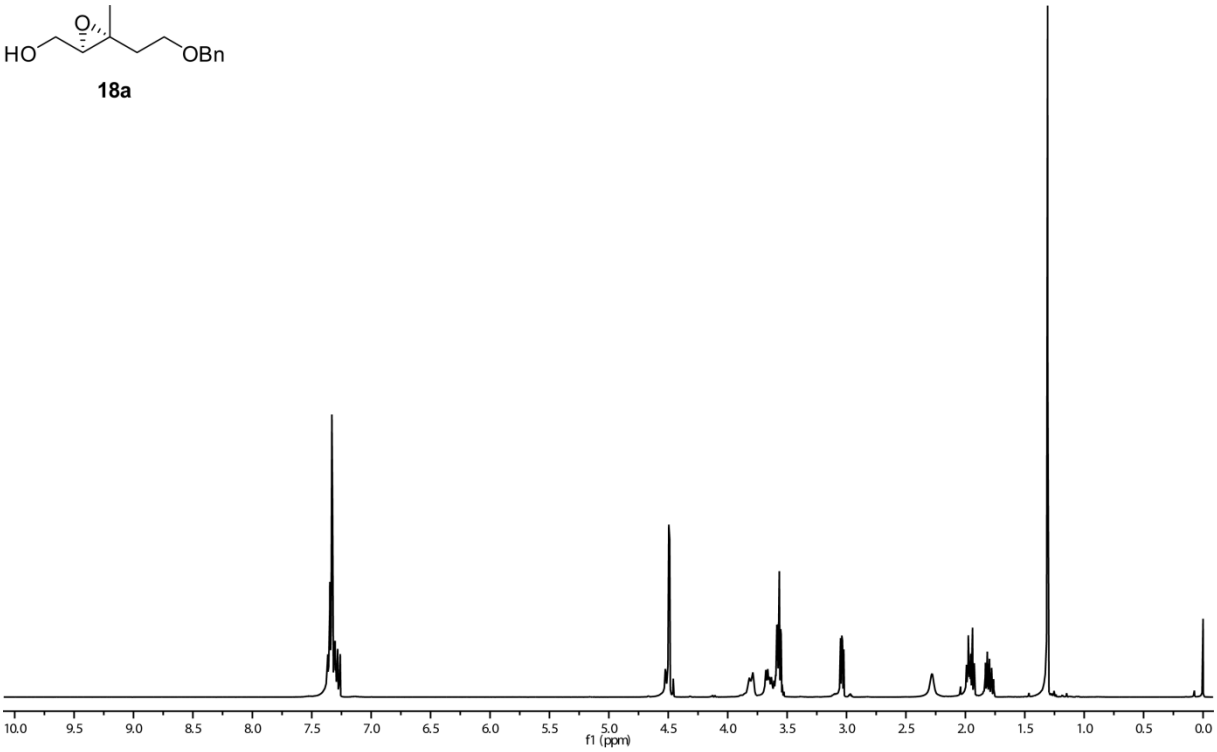


Figure 26 ^{1}H-NMR spectrum of compound **18a**.

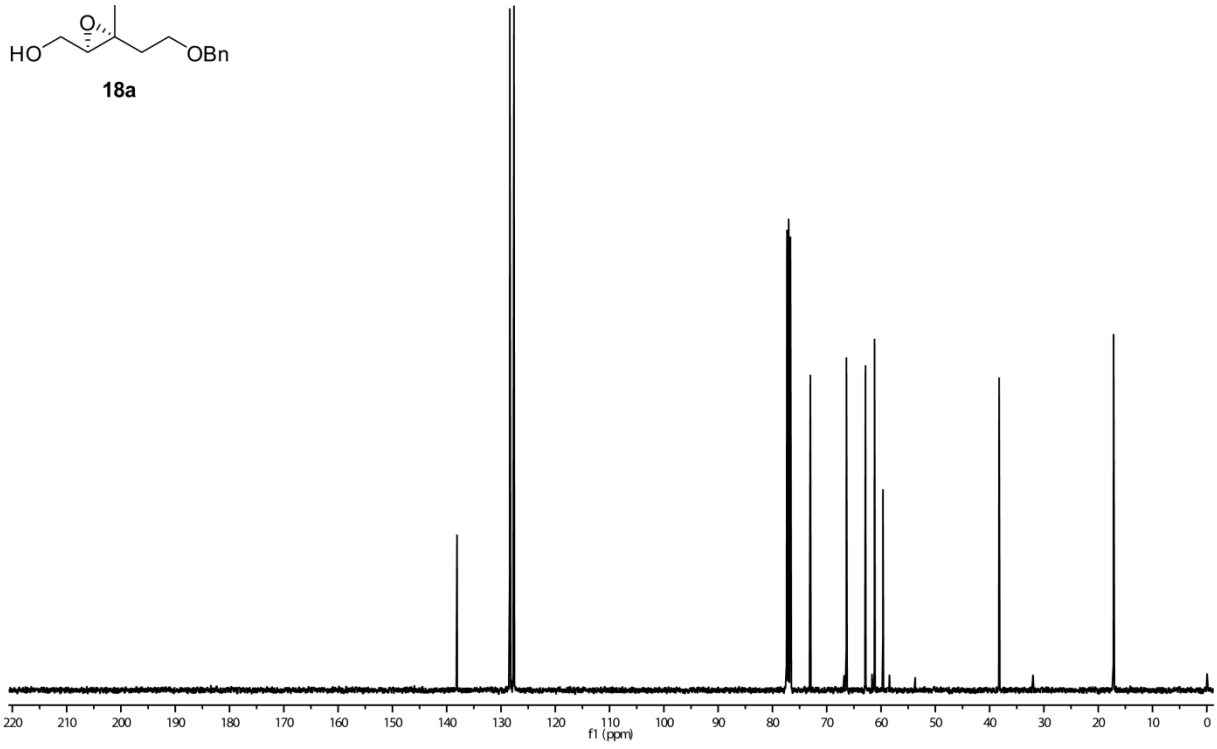


Figure 27 ^{13}C-NMR spectrum of compound **18a**.

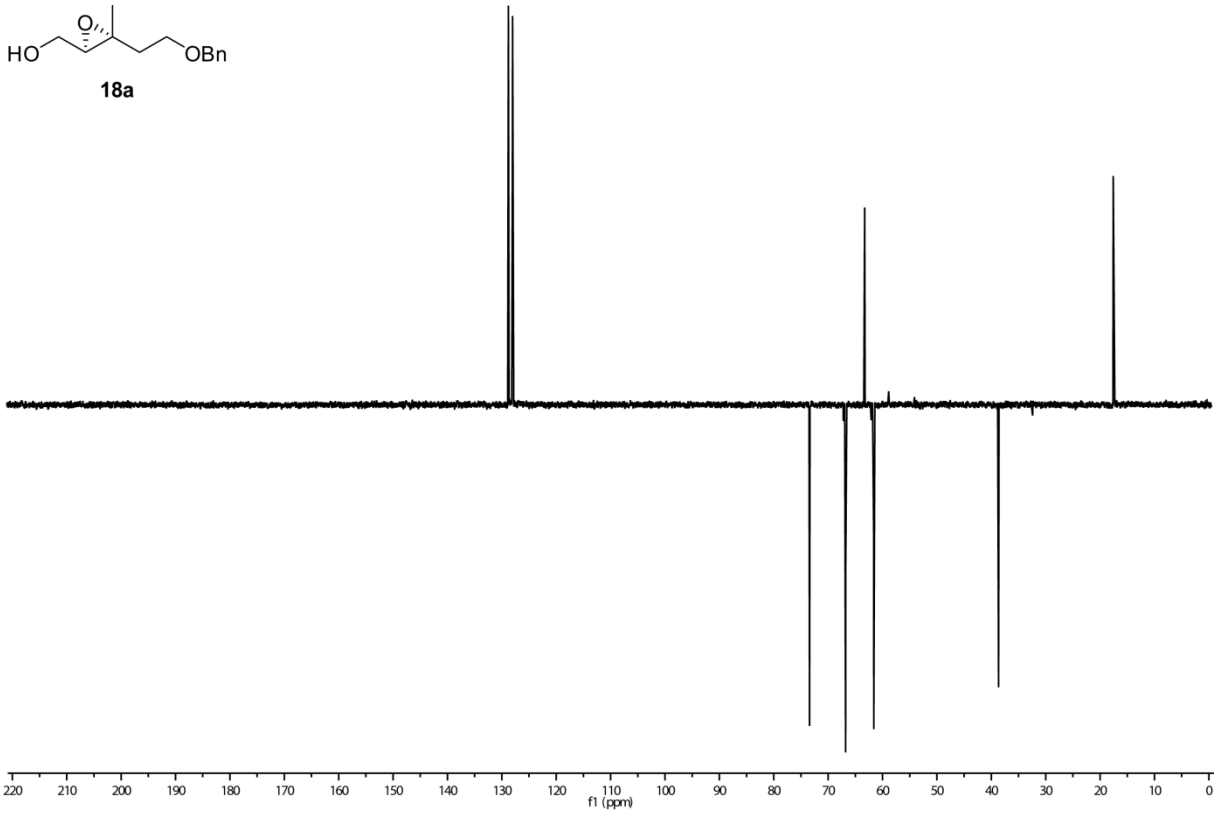


Figure 28 DEPT spectrum of compound **18a**.

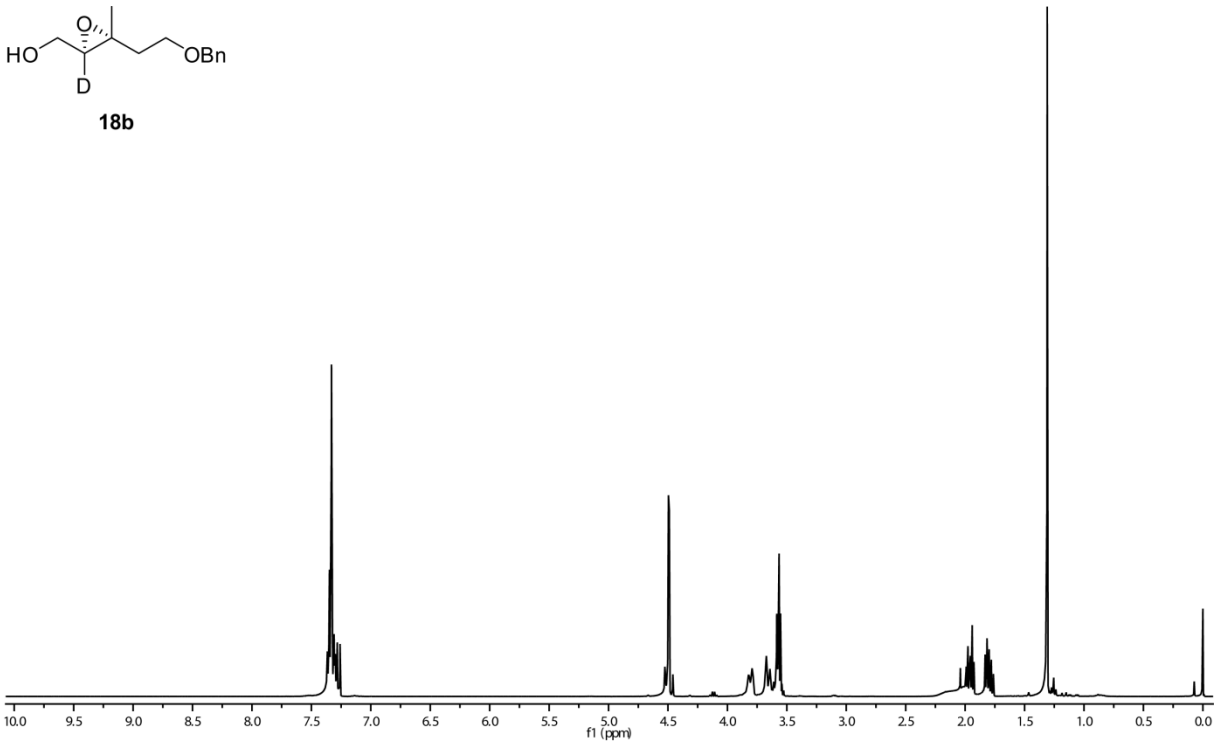


Figure 29 ^{1}H-NMR spectrum of compound **18b**.

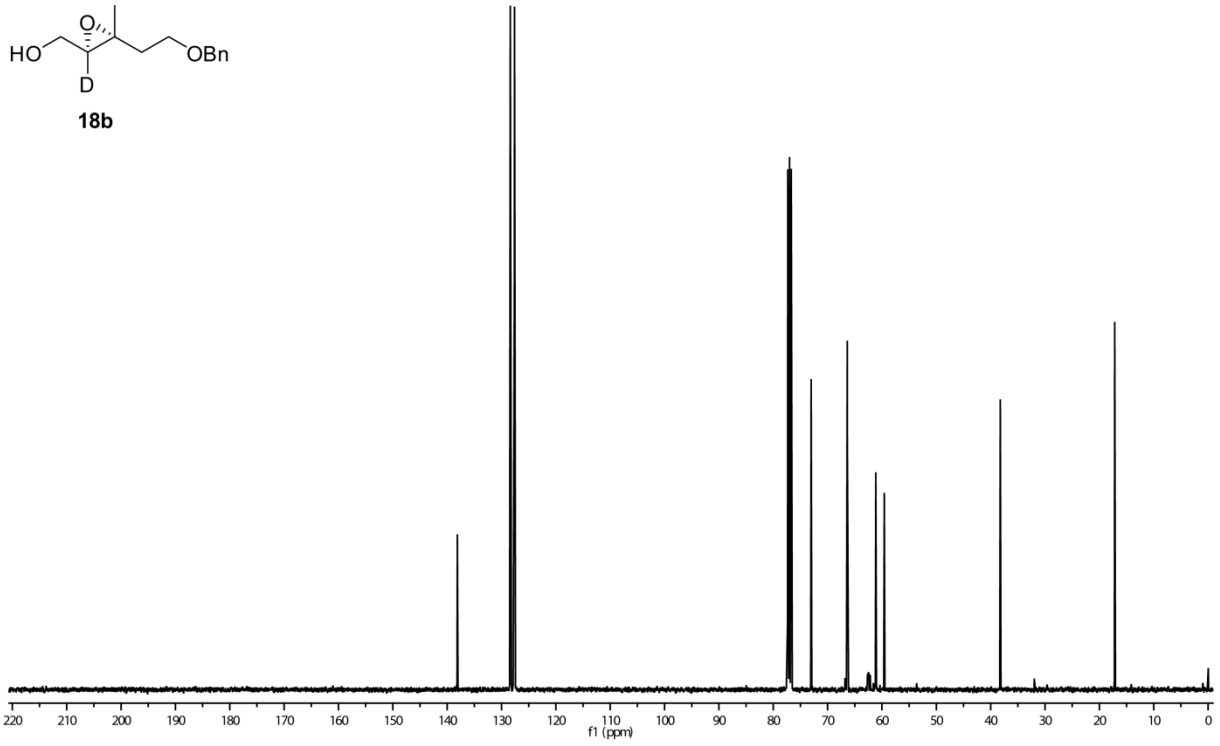


Figure 30 ^{13}C-NMR spectrum of compound **18b**.

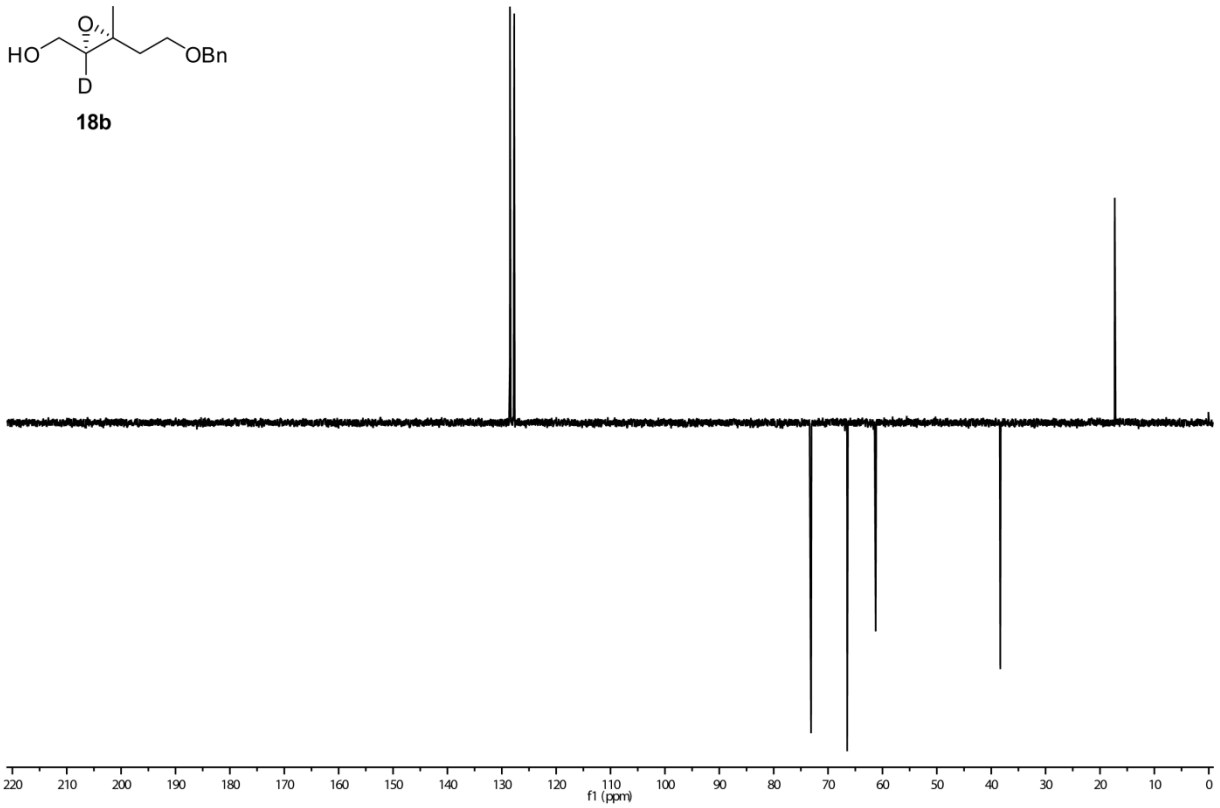


Figure 31 DEPT spectrum of compound **18b**.

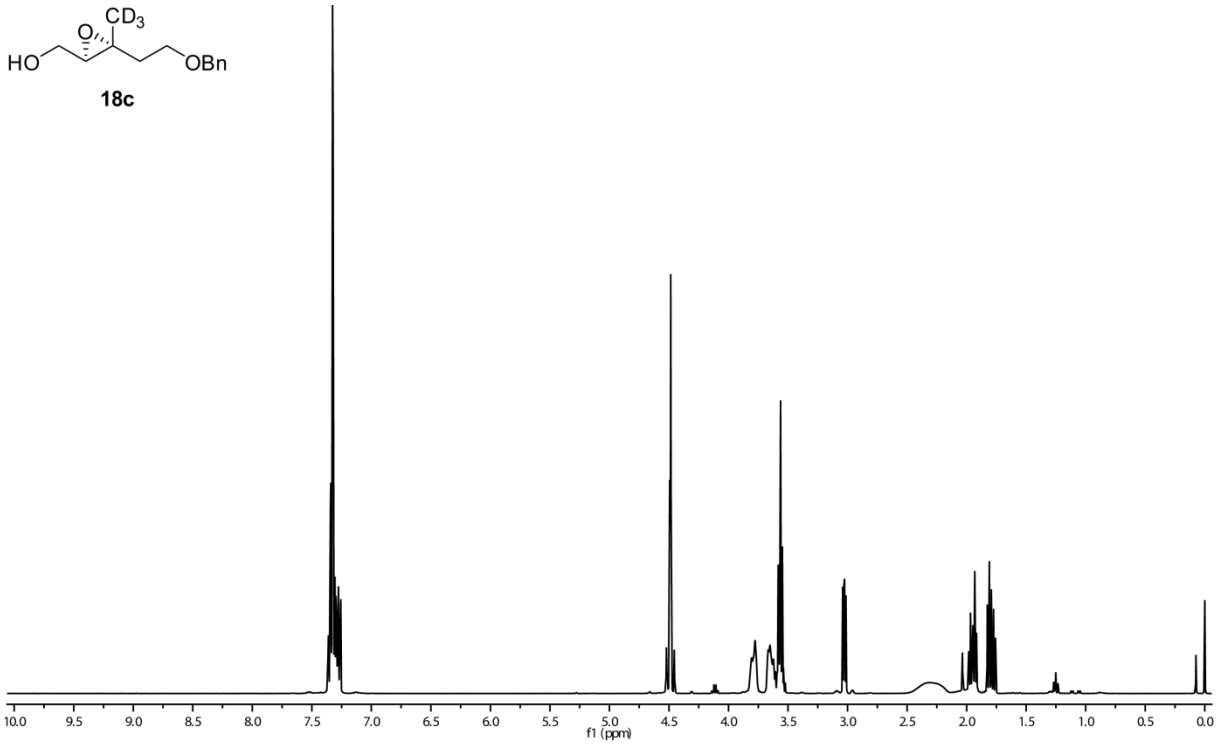


Figure 32 ^{1}H-NMR spectrum of compound **18c**.

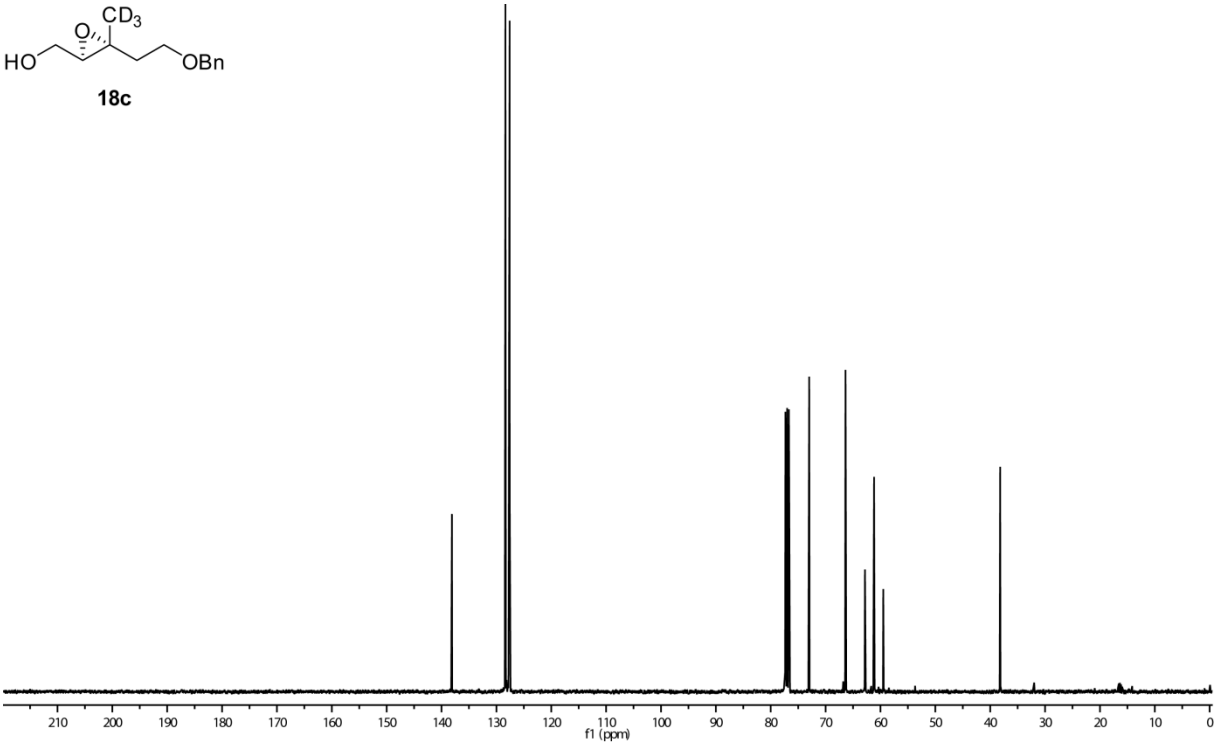


Figure 33 ^{13}C-NMR spectrum of compound **18c**.

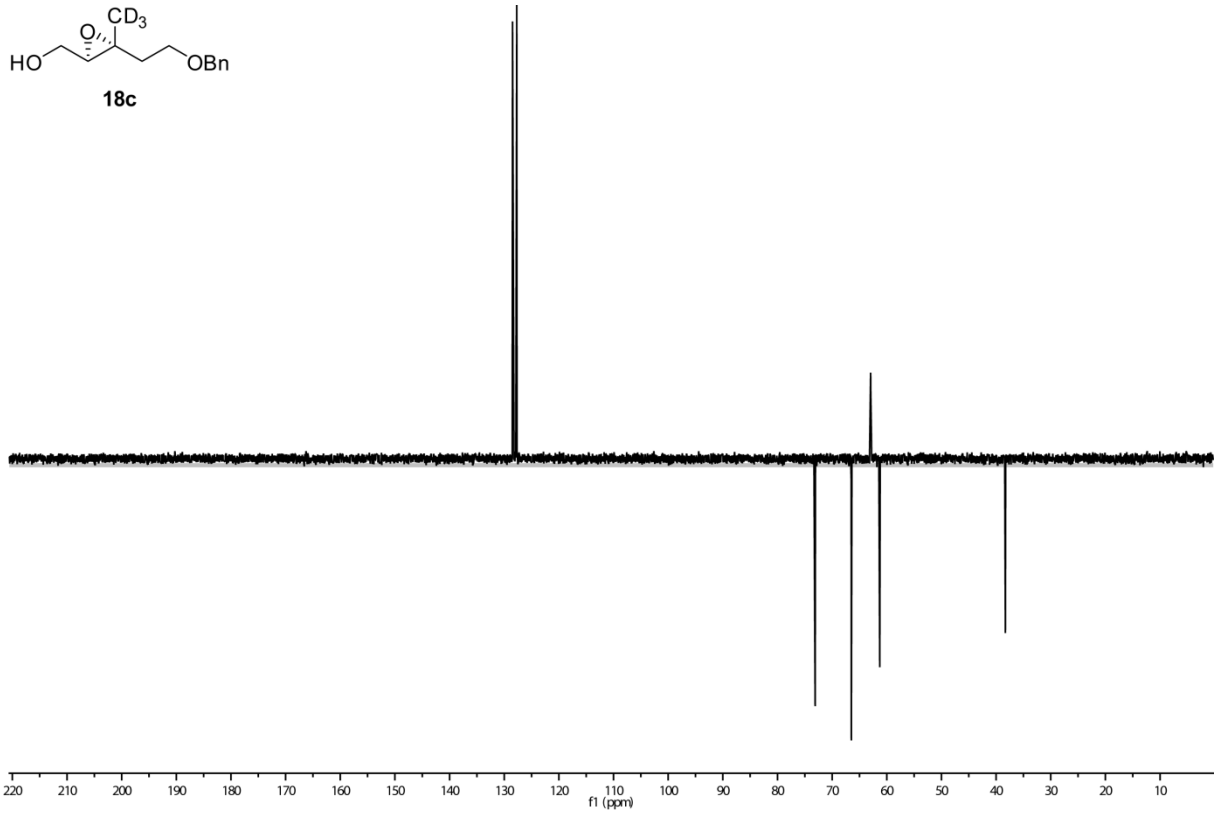


Figure 34 DEPT spectrum of compound **18c**.

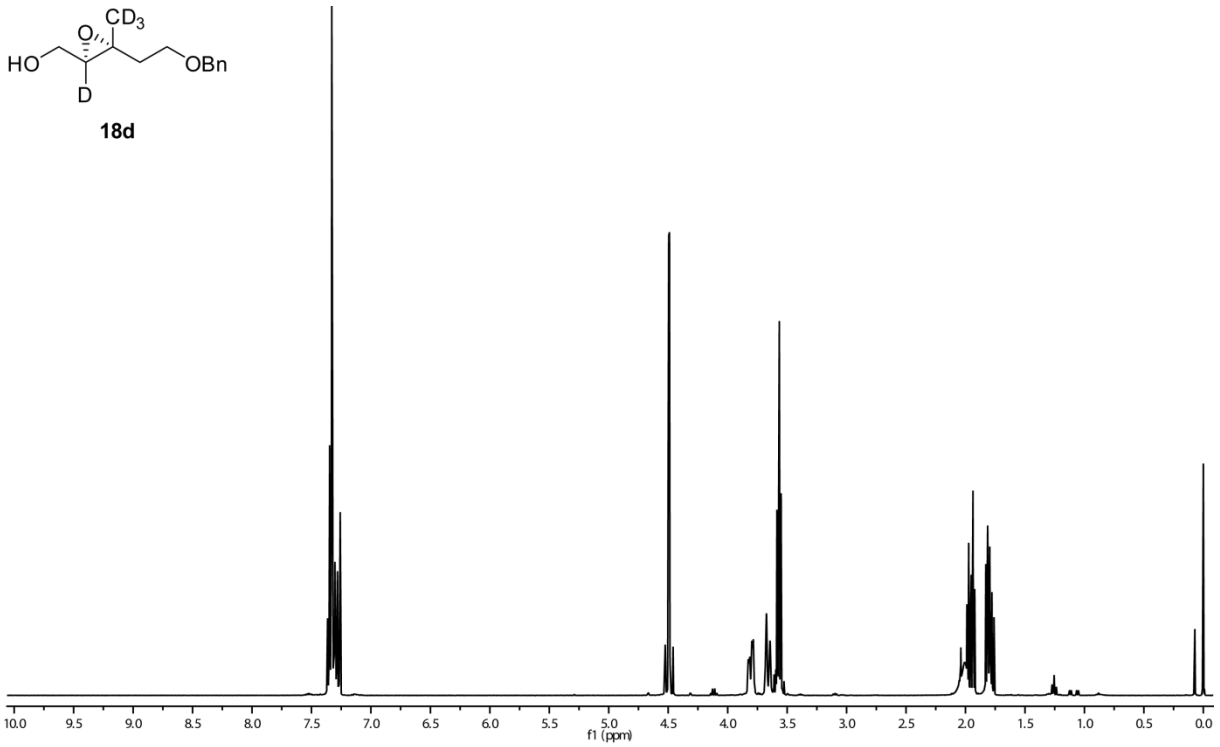


Figure 35 ^{1}H-NMR spectrum of compound **18d**.

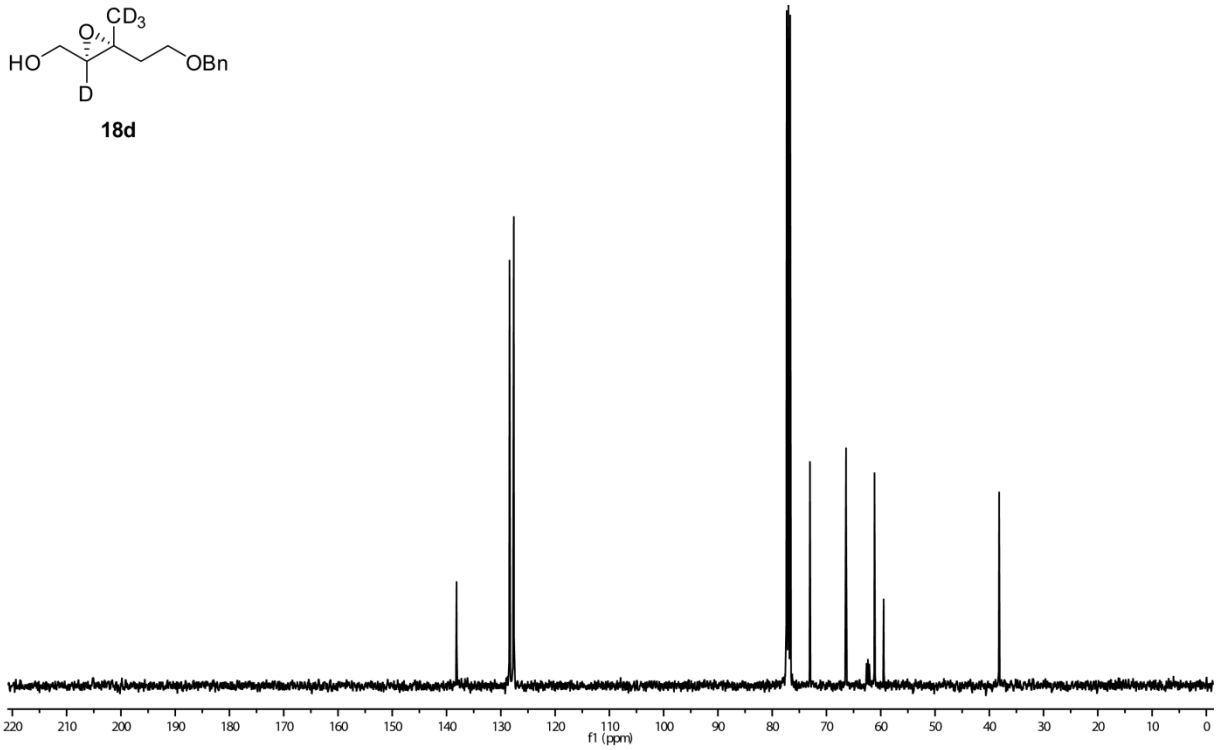


Figure 36 ^{13}C-NMR spectrum of compound **18d**.

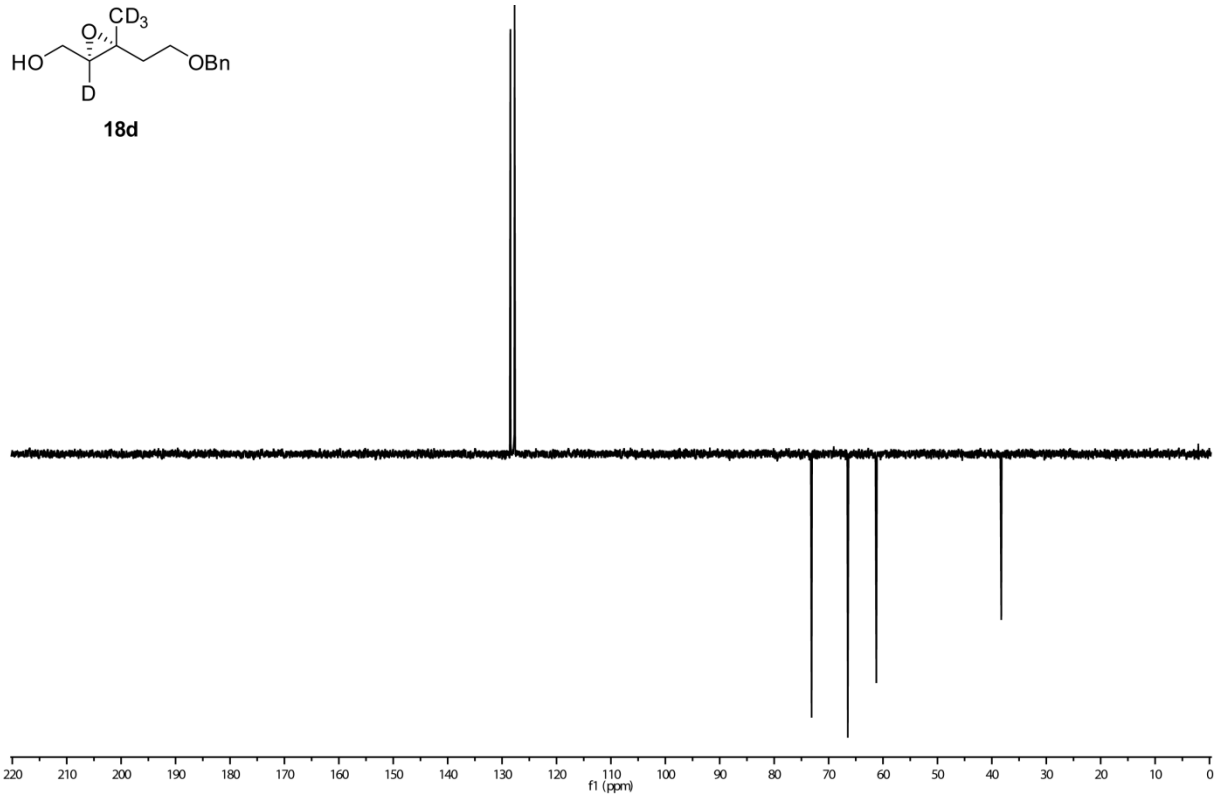


Figure 37 DEPT spectrum of compound **18d**.

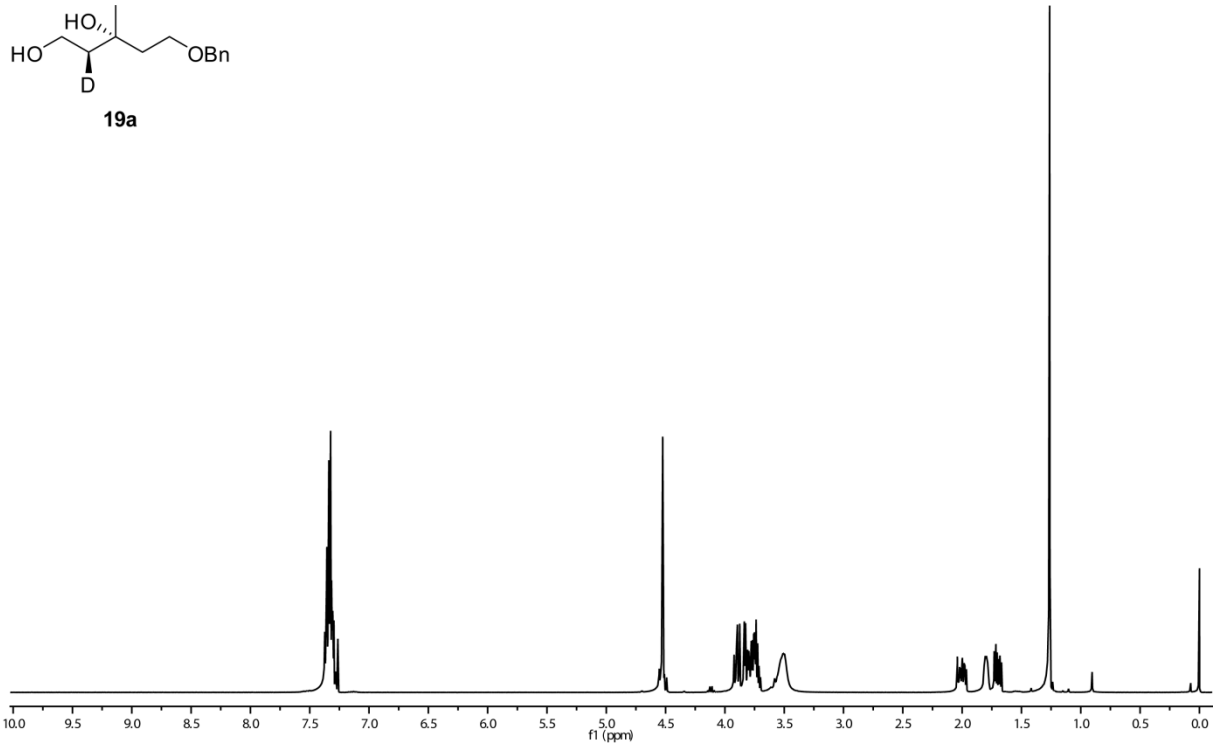


Figure 38 ^{1}H-NMR spectrum of compound **19a**.

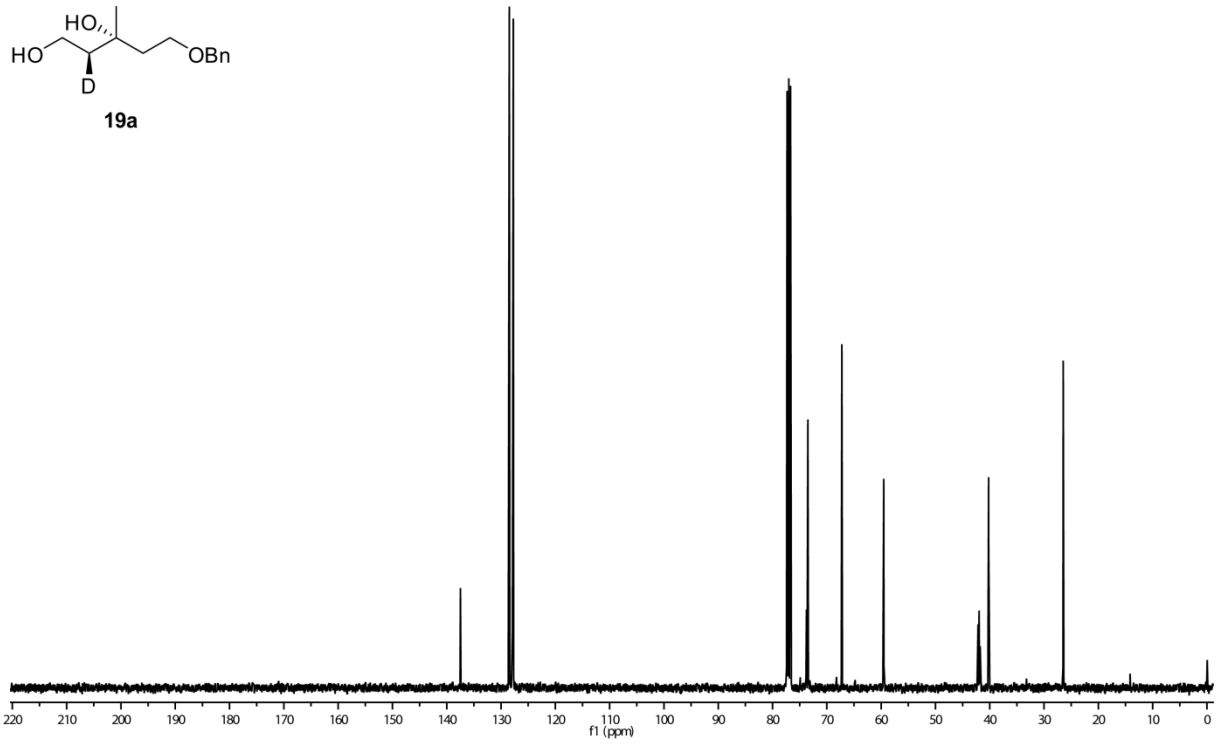


Figure 39 ^{13}C-NMR spectrum of compound **19a**.

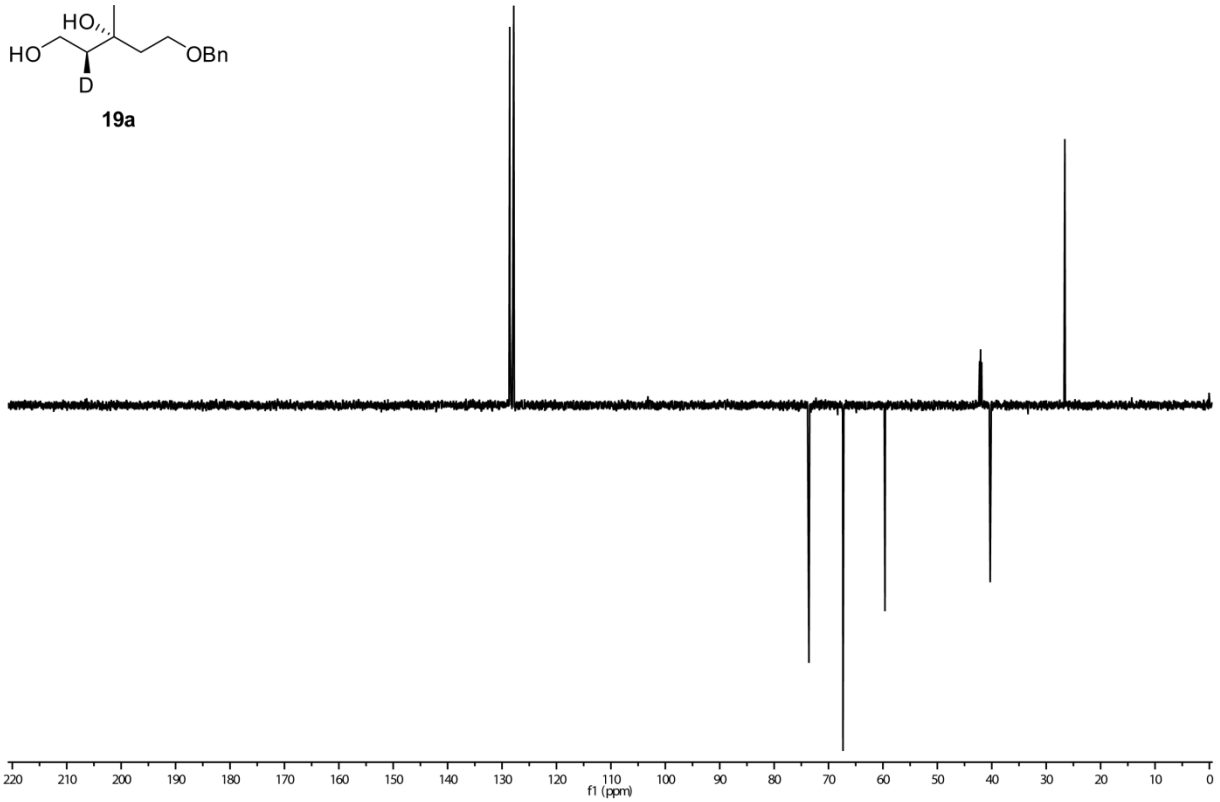


Figure 40 DEPT spectrum of compound **19a**.

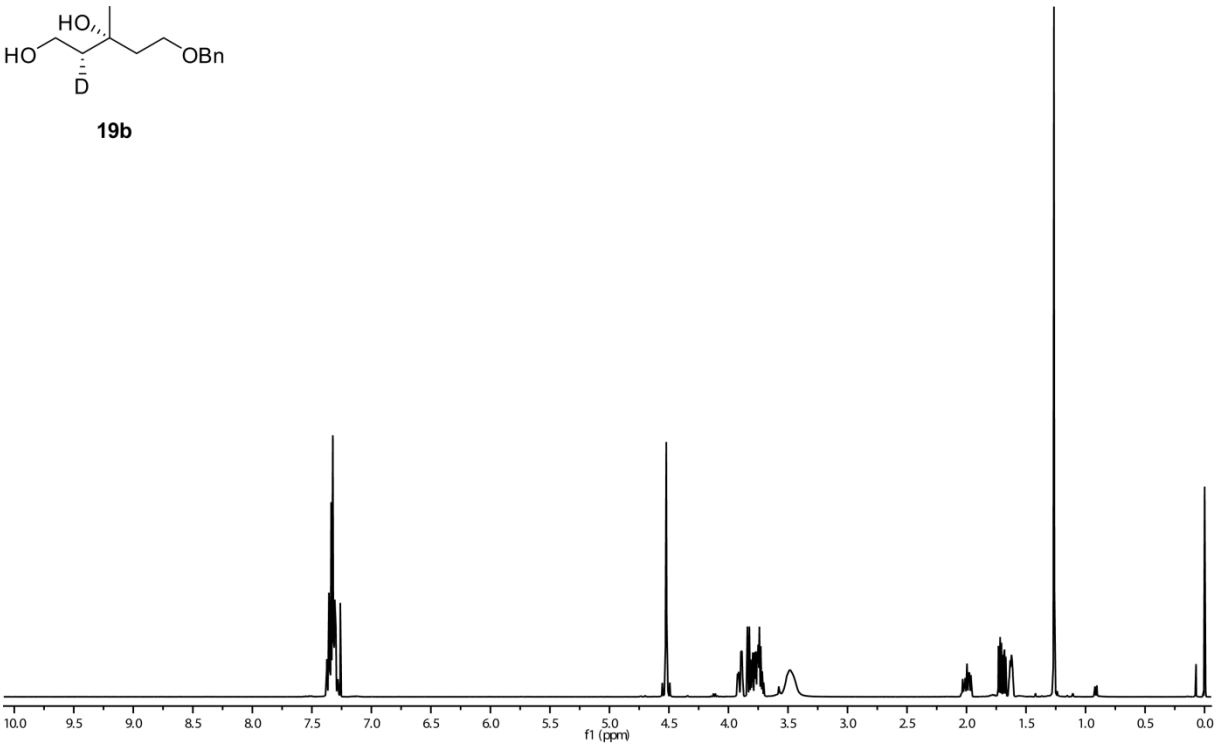


Figure 41 ^{1}H-NMR spectrum of compound **19b**.

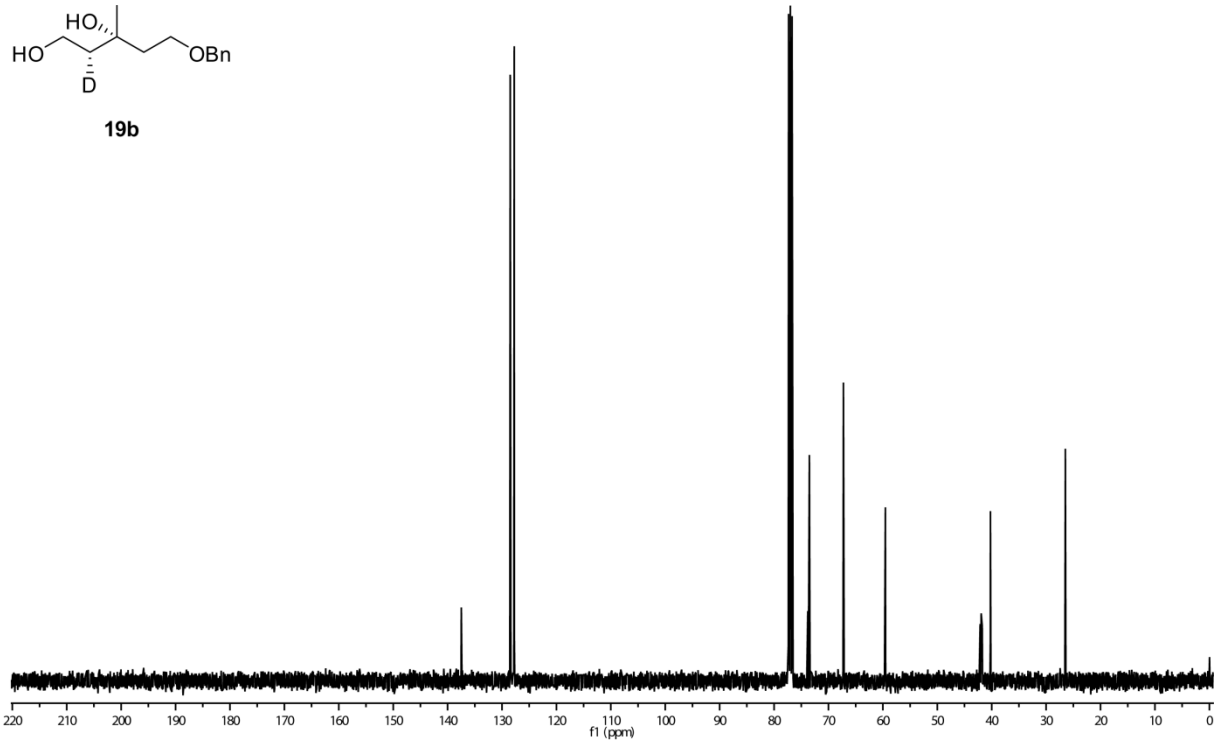


Figure 42 ^{13}C-NMR spectrum of compound **19b**.

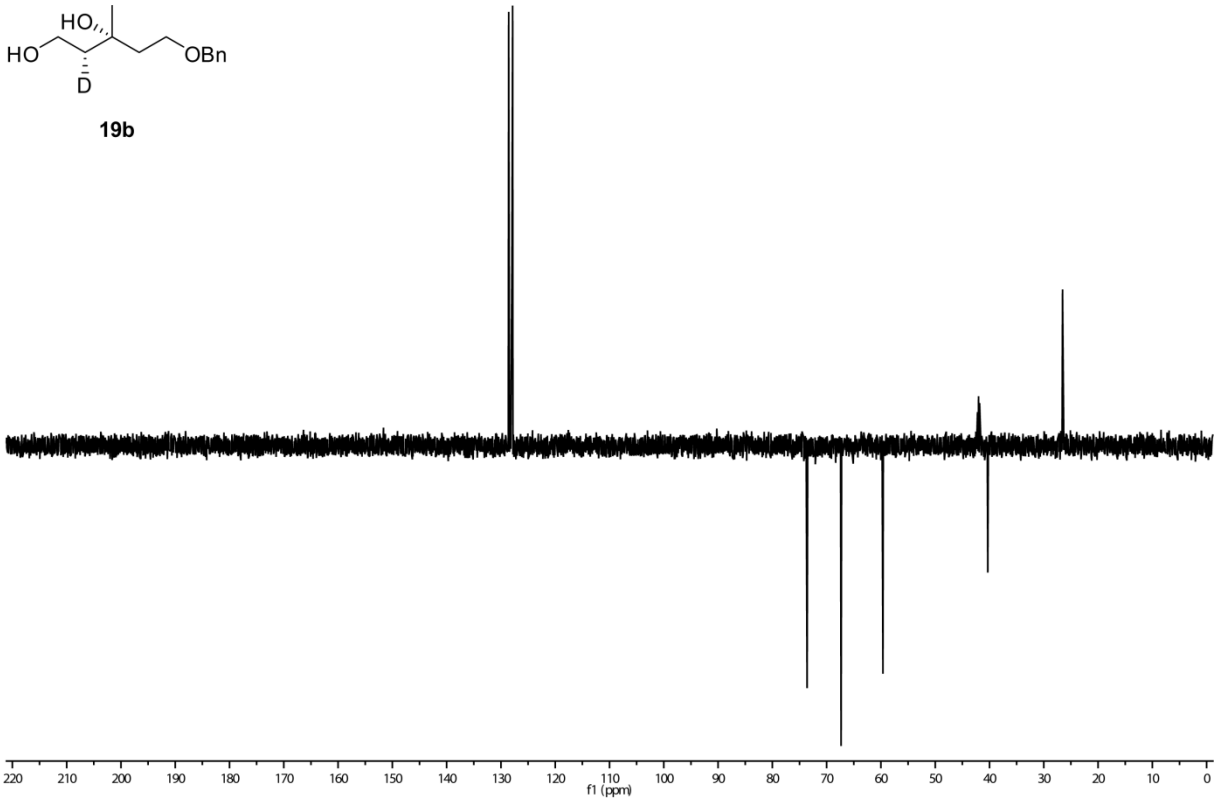


Figure 43 DEPT spectrum of compound **19b**.

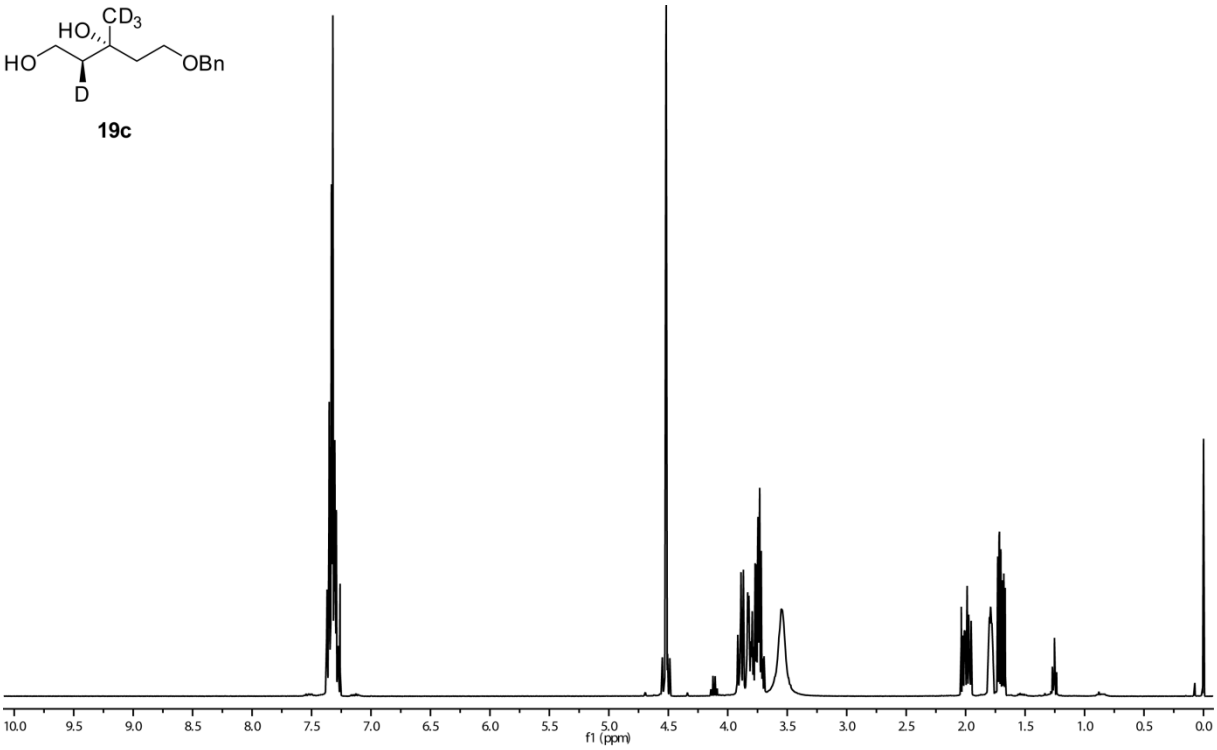


Figure 44 ^{1}H-NMR spectrum of compound **19c**.

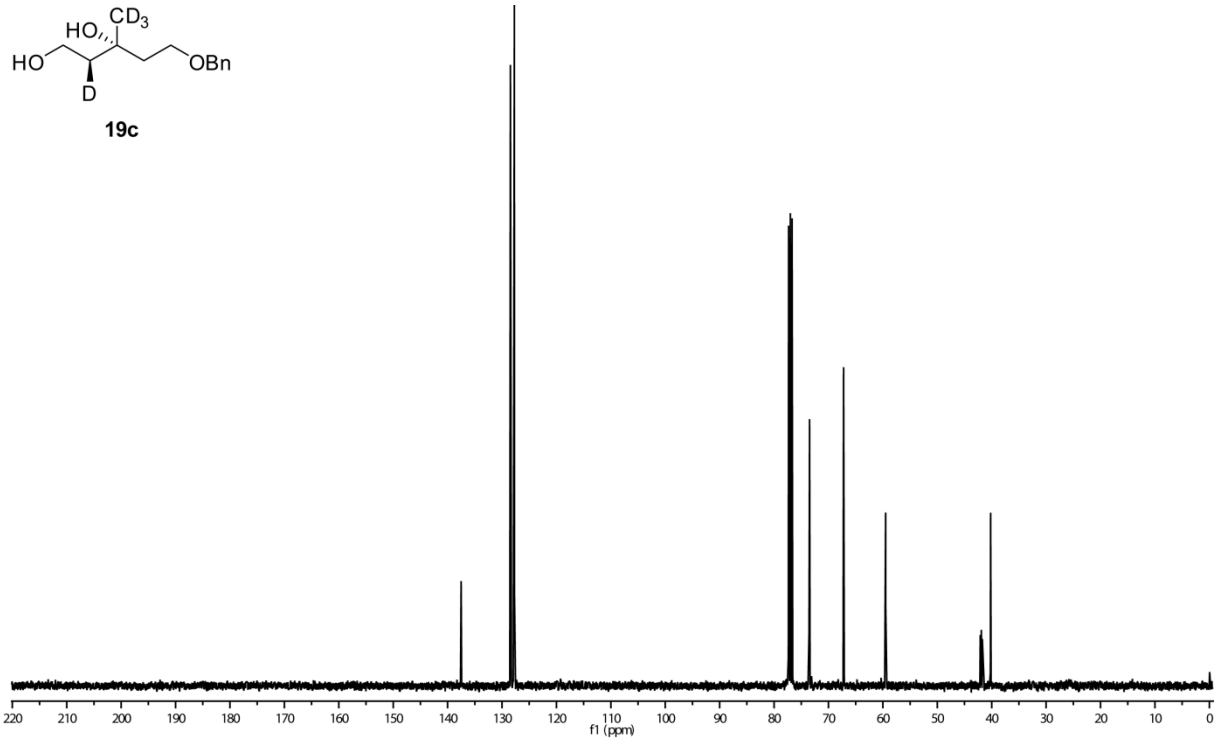


Figure 45 ^{13}C-NMR spectrum of compound **19c**.

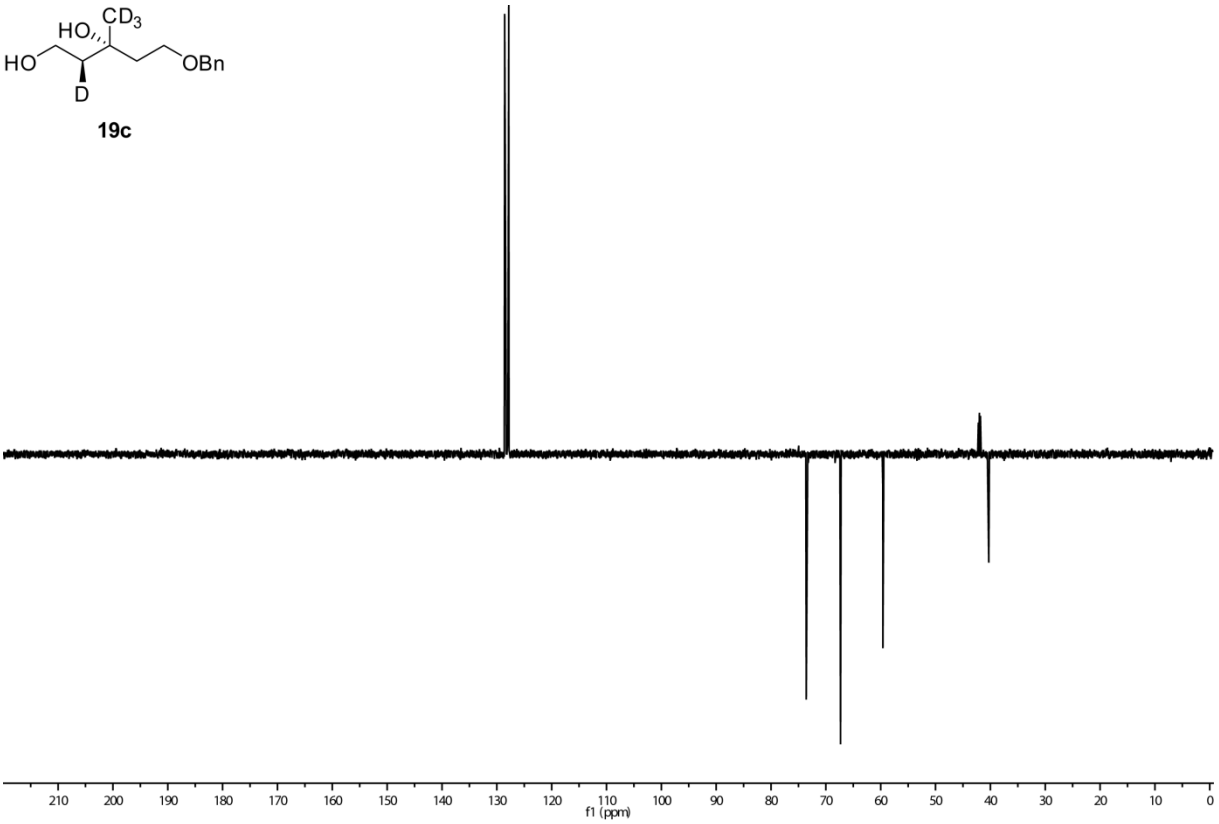


Figure 46 DEPT spectrum of compound **19c**.

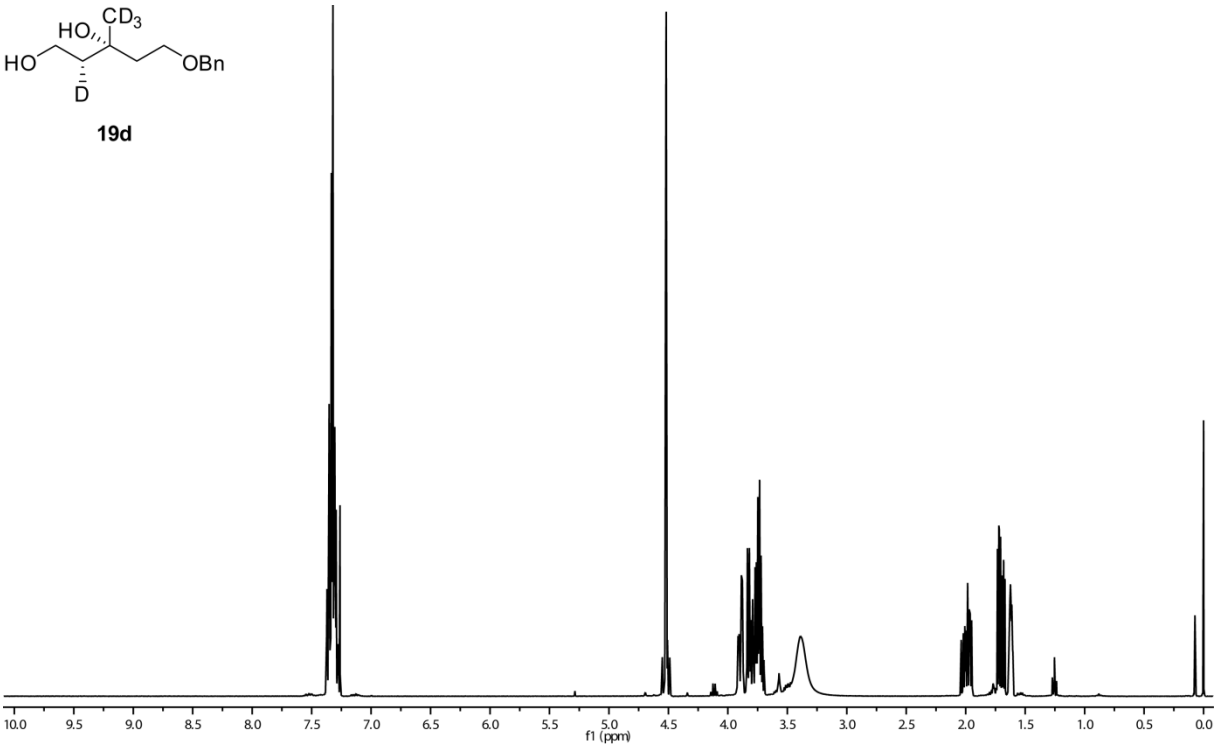


Figure 47 ^{1}H-NMR spectrum of compound **19d**.

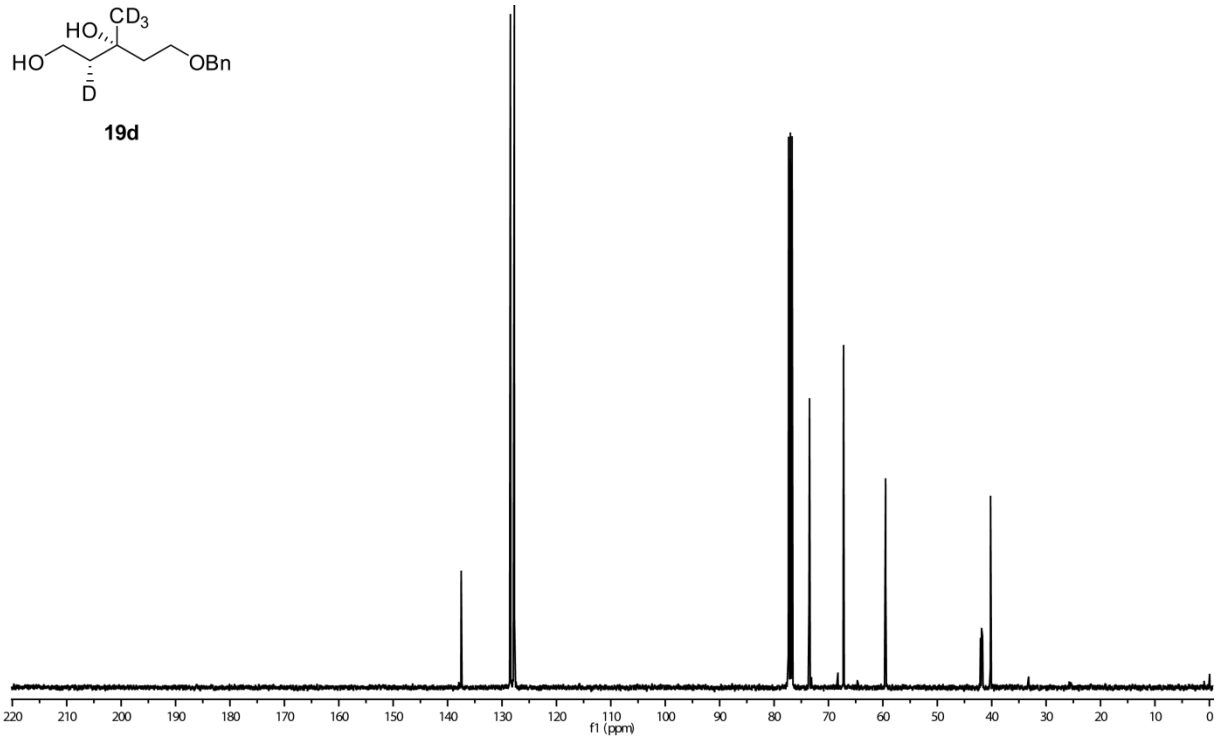


Figure 48 ^{13}C-NMR spectrum of compound **19d**.

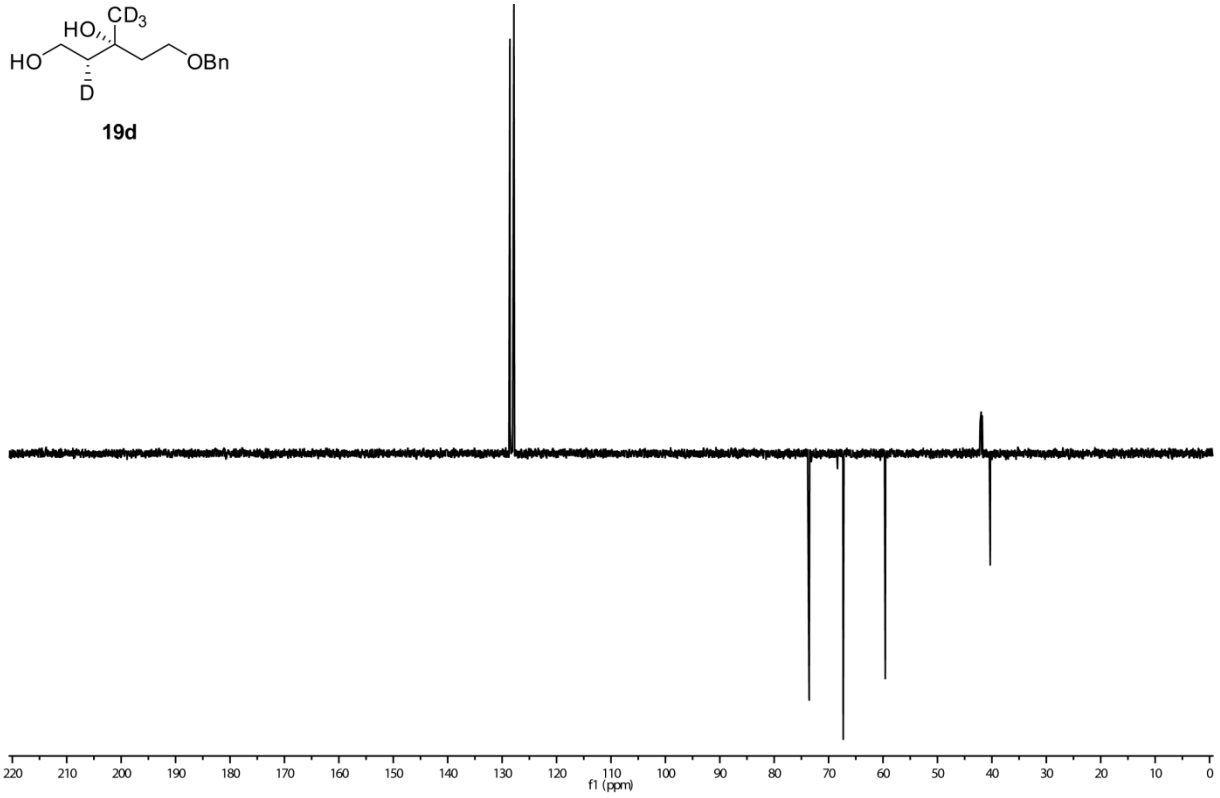


Figure 49 DEPT spectrum of compound **19d**.

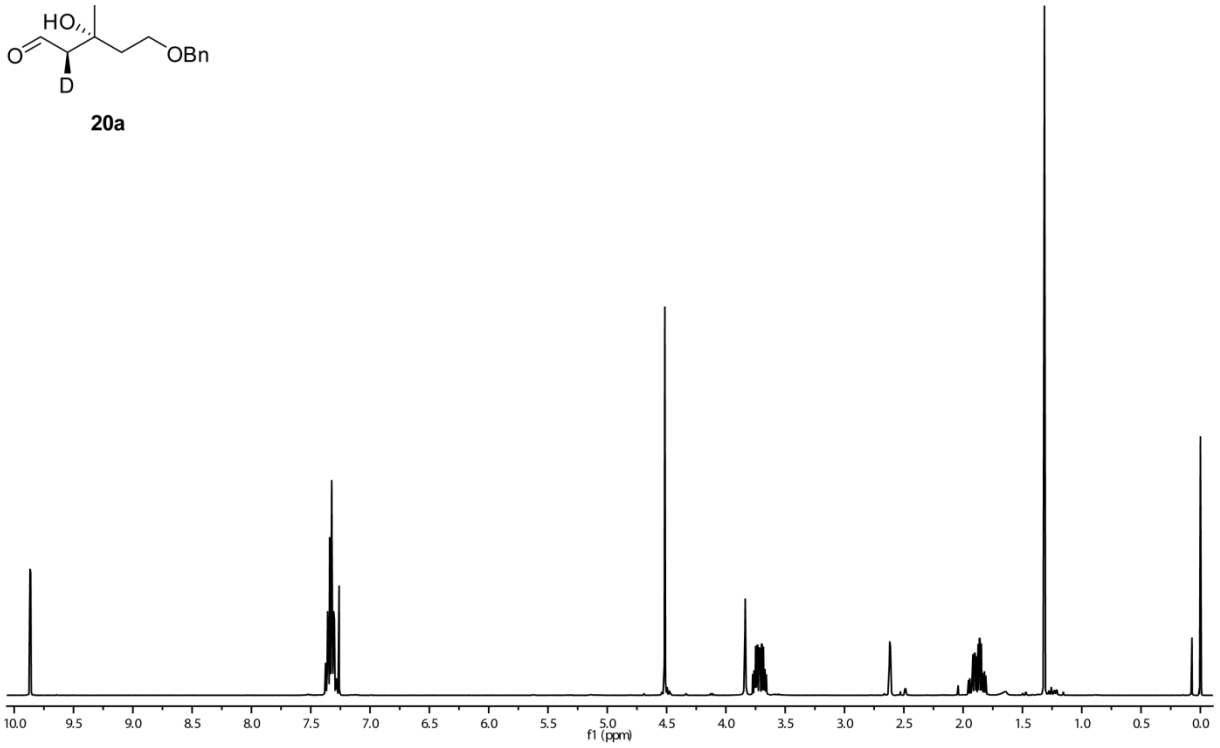


Figure 50 ^{1}H-NMR spectrum of compound **20a**.

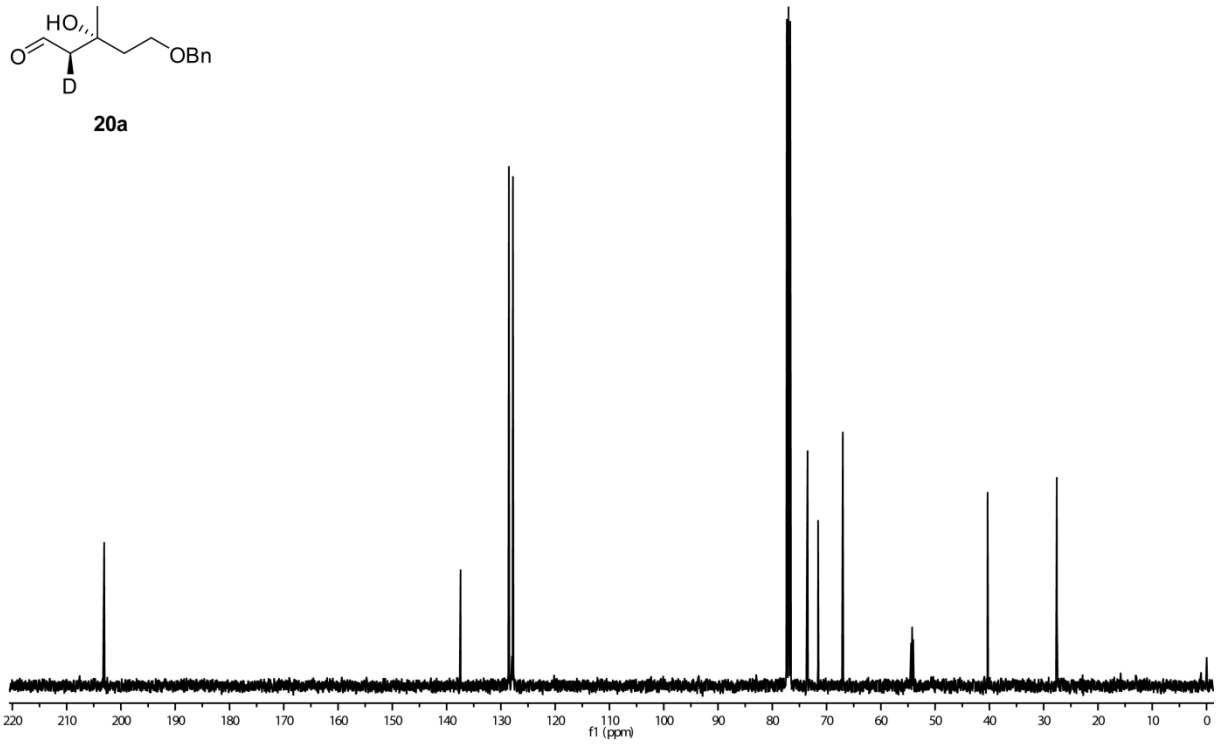
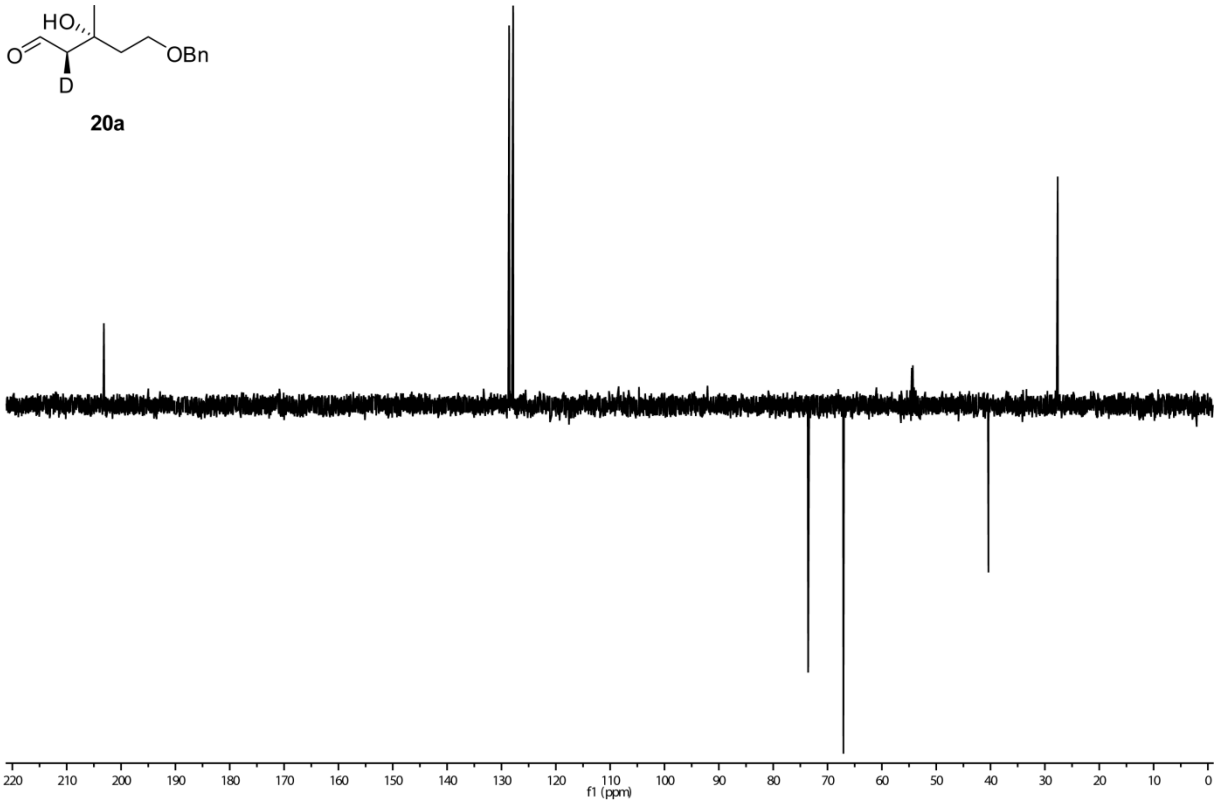
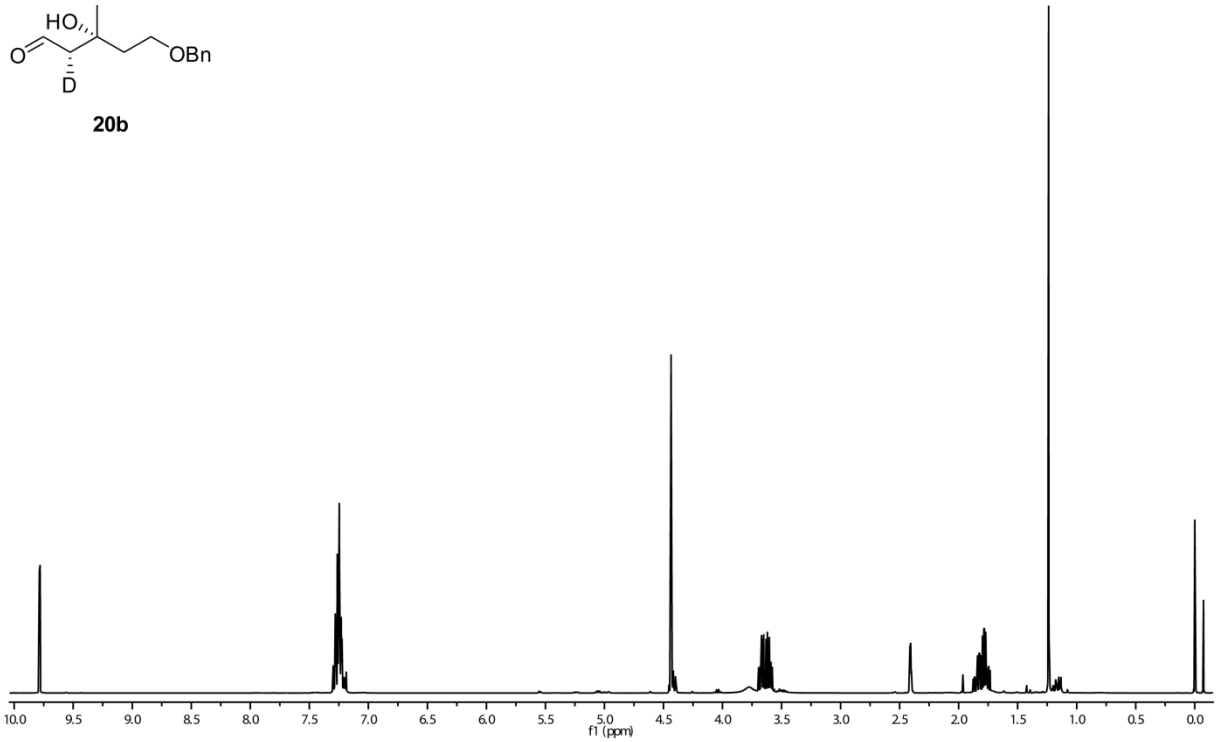


Figure 51 ^{13}C-NMR spectrum of compound **20a**.



20a

Figure 52 DEPT spectrum of compound **20a**.



20b

Figure 53 ^{1}H-NMR spectrum of compound **20b**.

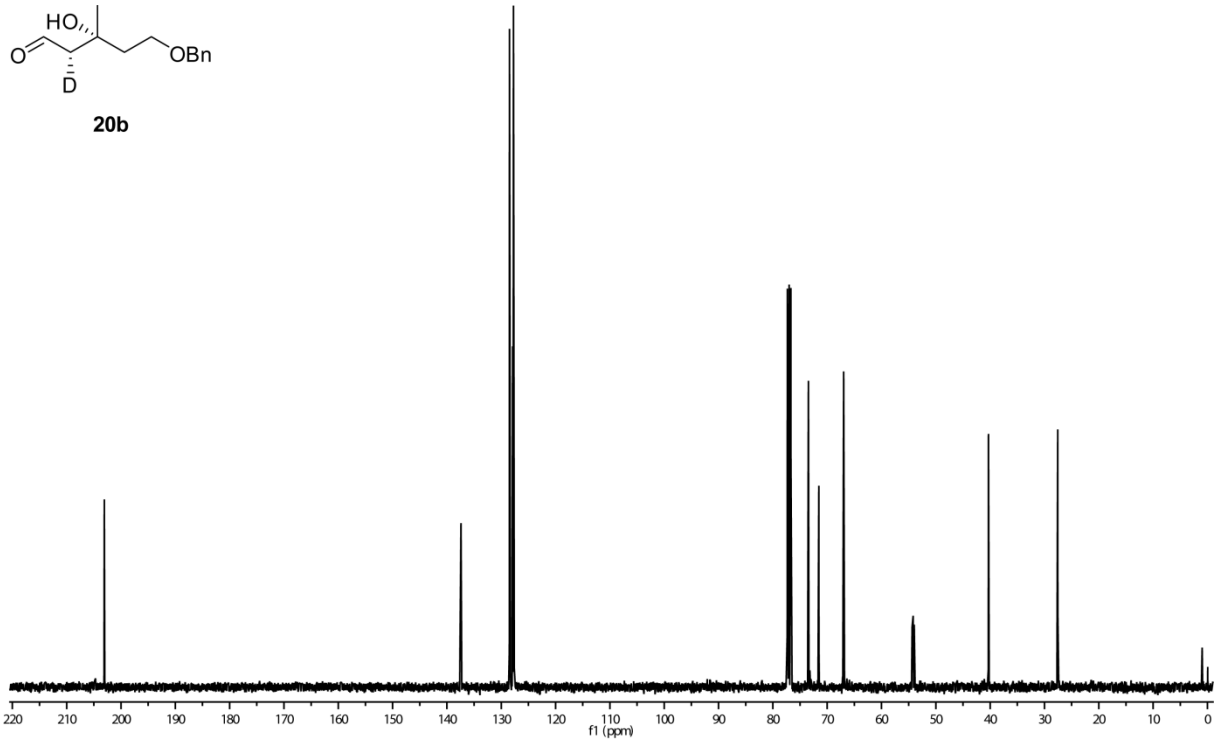


Figure 54 ^{13}C-NMR spectrum of compound **20b**.

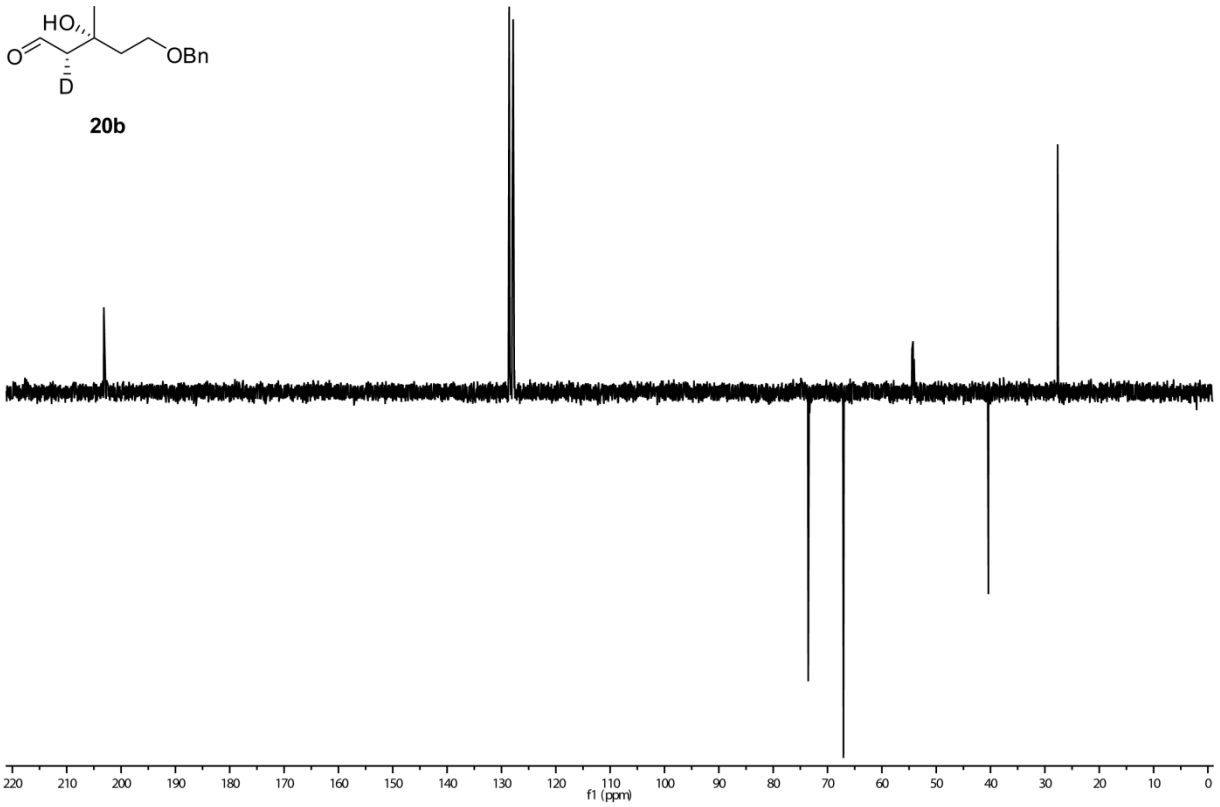


Figure 55 DEPT spectrum of compound **20b**.

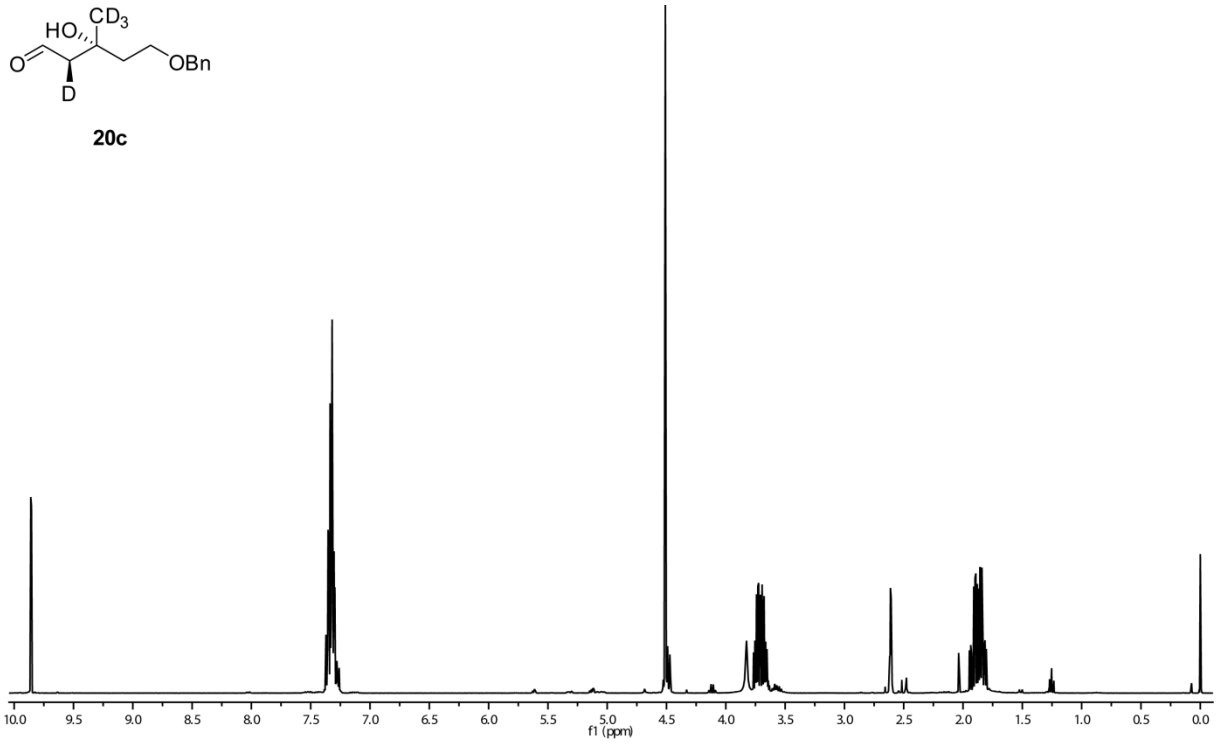


Figure 56 ^{1}H-NMR spectrum of compound **20c**.

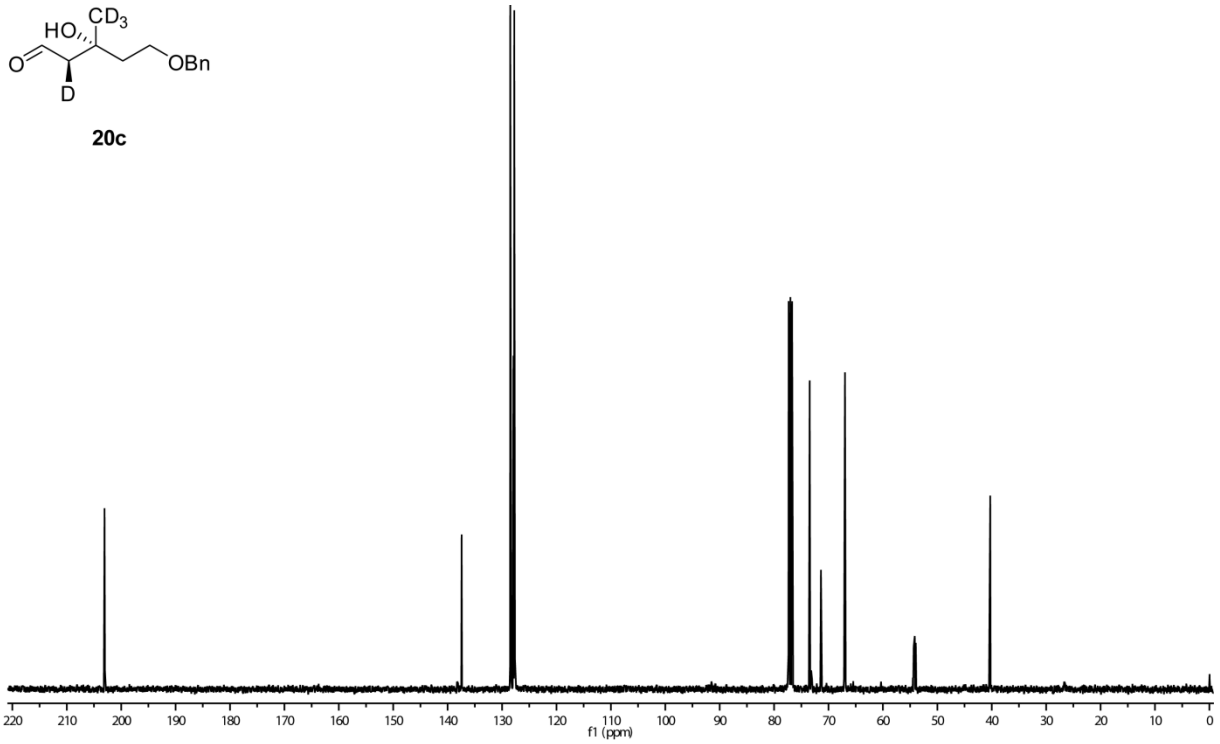


Figure 57 ^{13}C-NMR spectrum of compound **20c**.

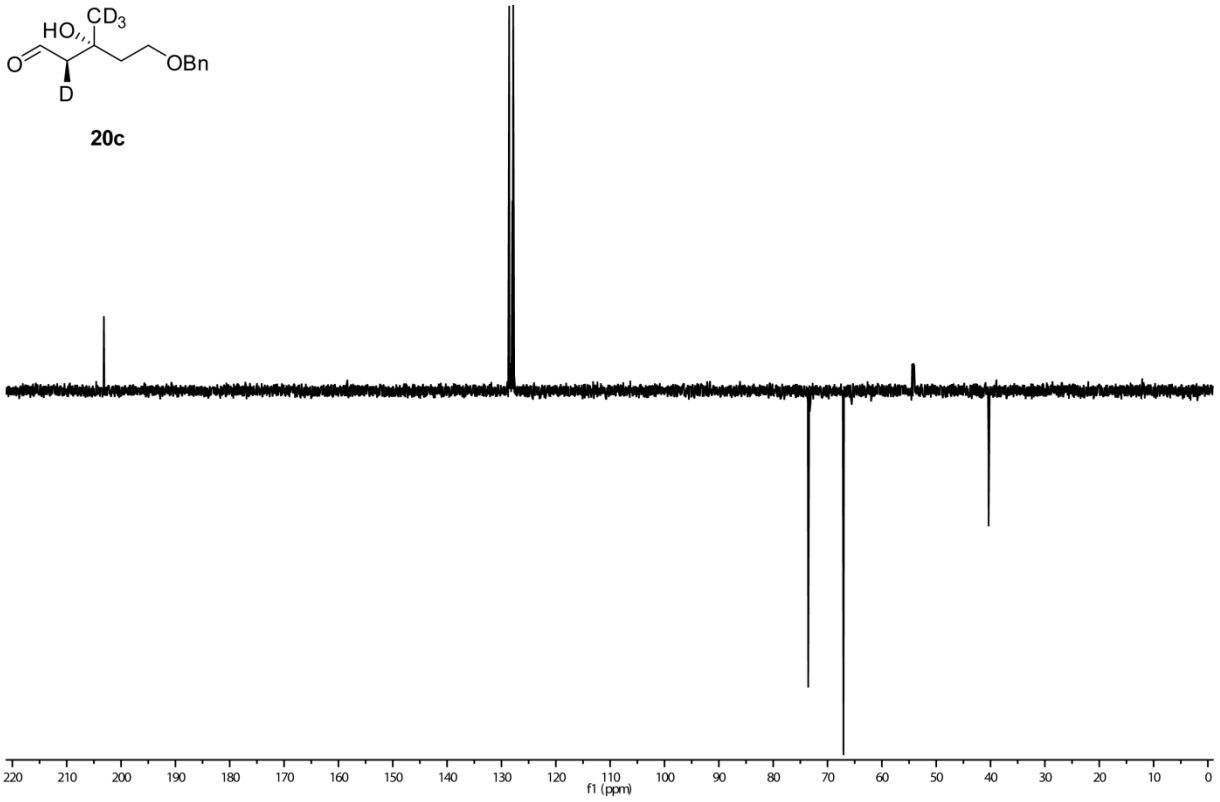


Figure 58 DEPT spectrum of compound **20c**.

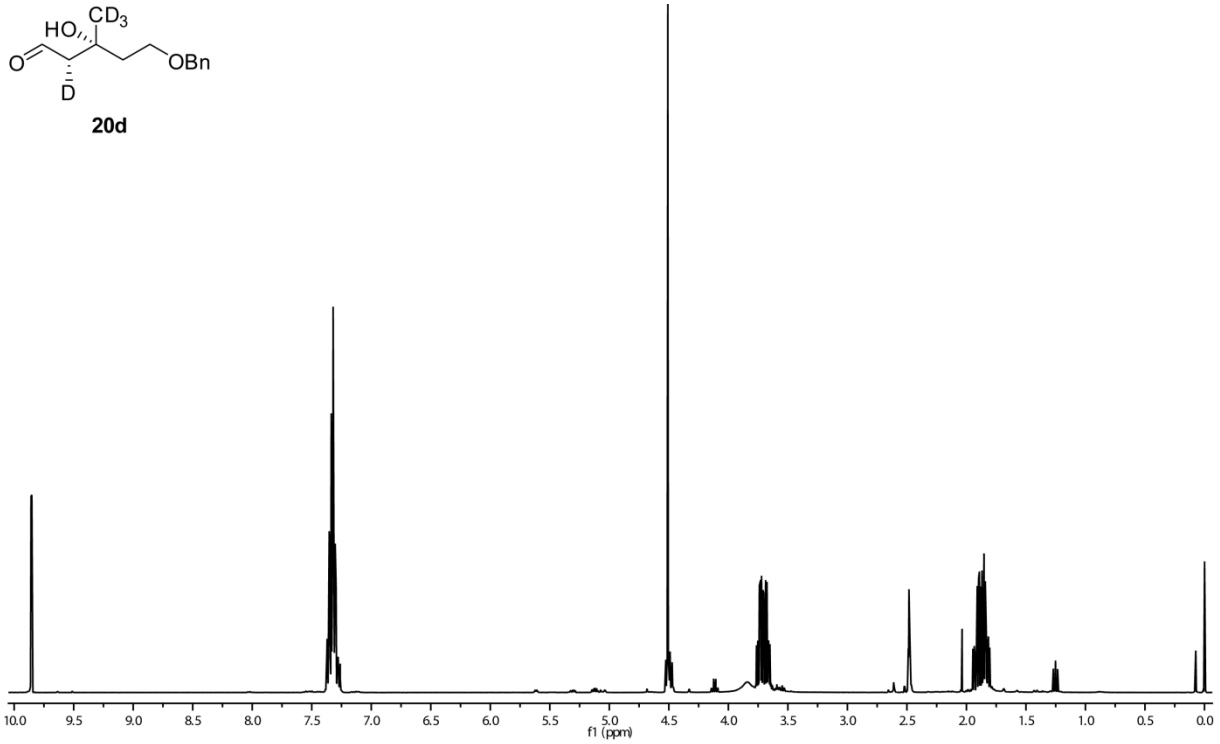


Figure 59 ^{1}H-NMR spectrum of compound **20d**.

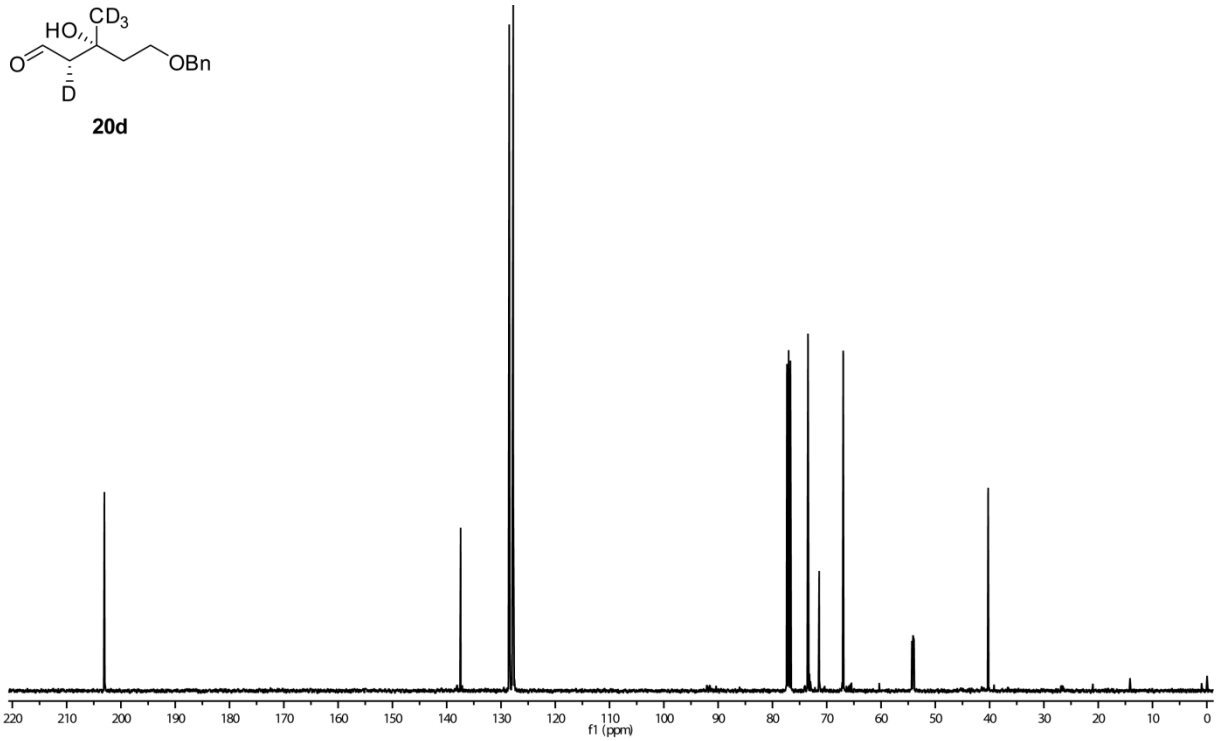


Figure 60 ^{13}C-NMR spectrum of compound **20d**.

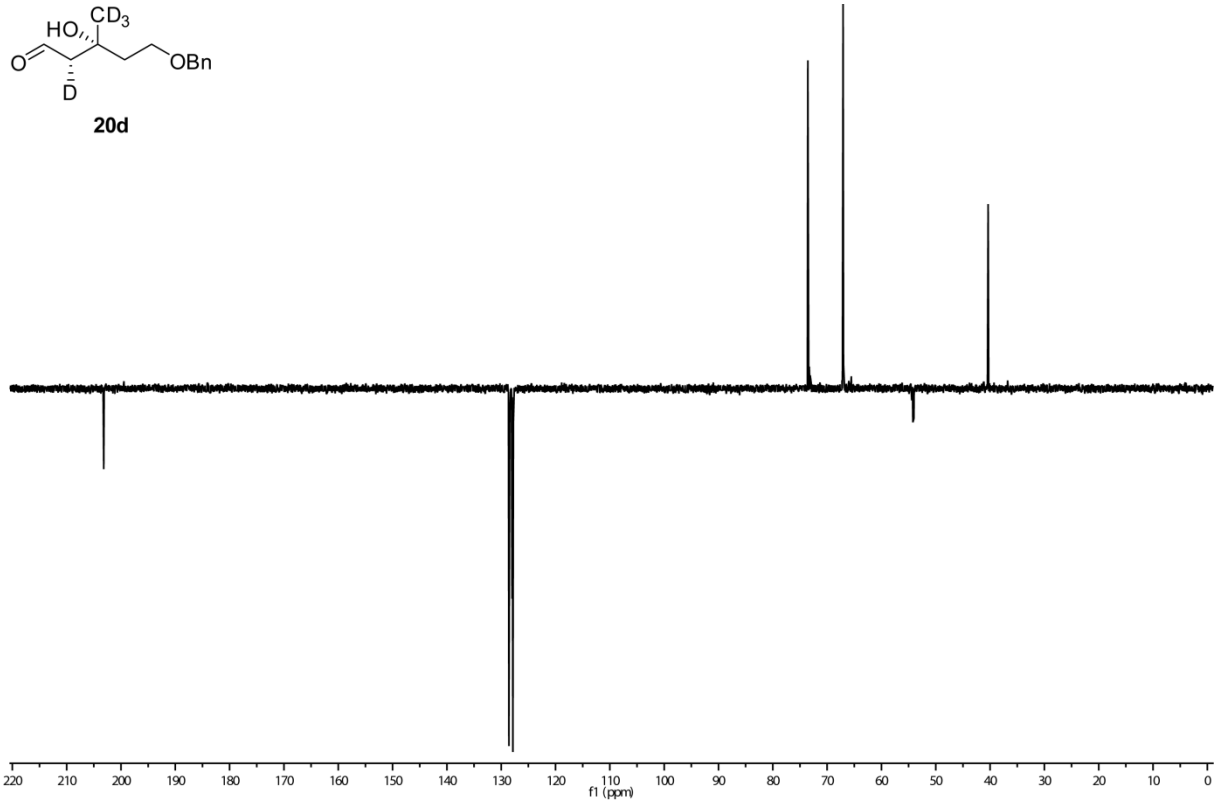


Figure 61 DEPT spectrum of compound **20d**.

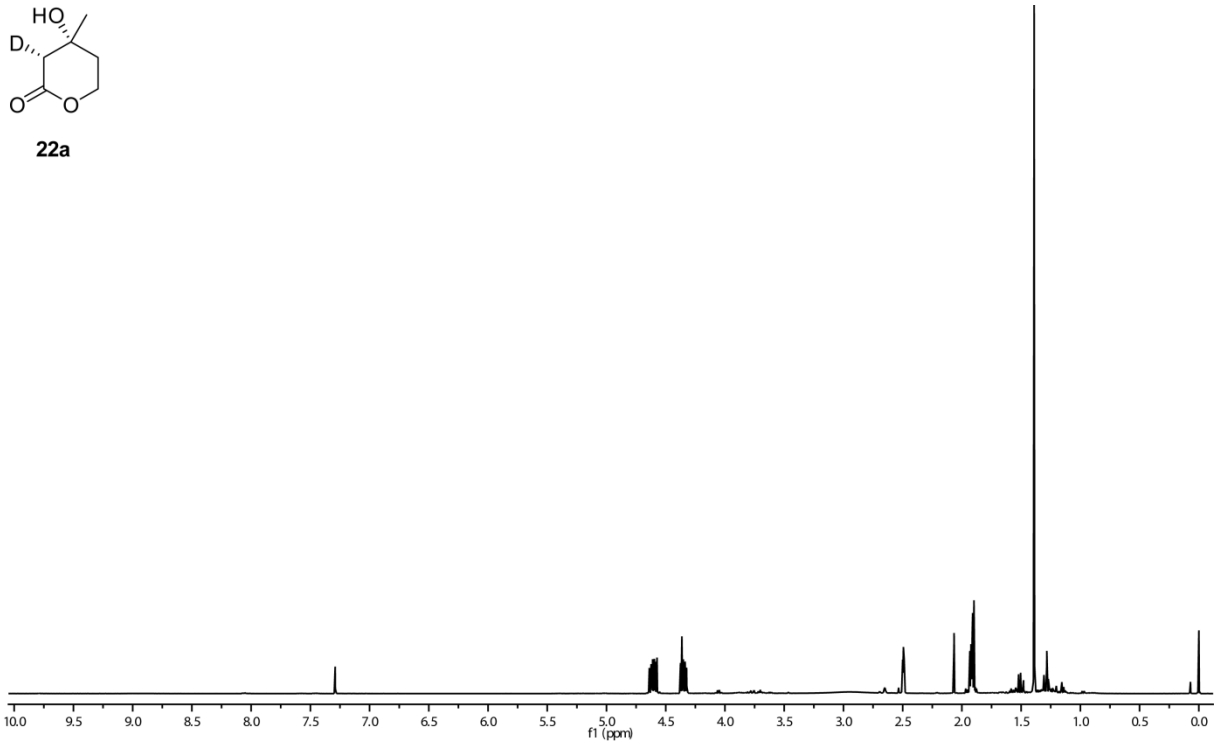


Figure 62 ^{1}H-NMR spectrum of compound **22a**.

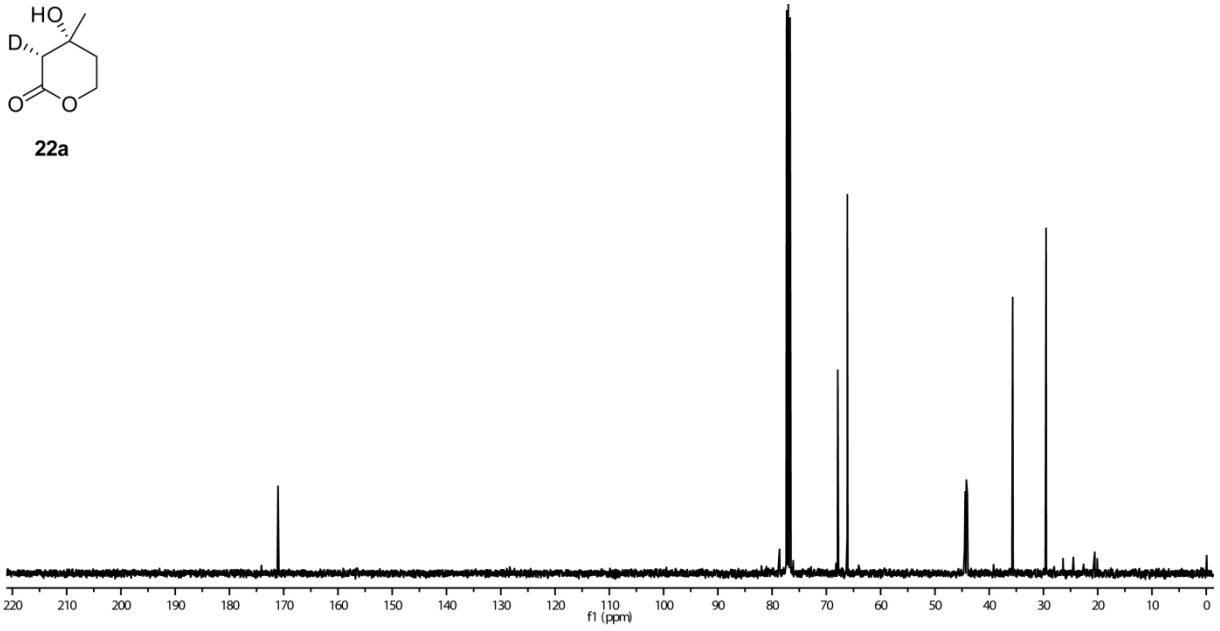


Figure 63 ^{13}C-NMR spectrum of compound **22a**.

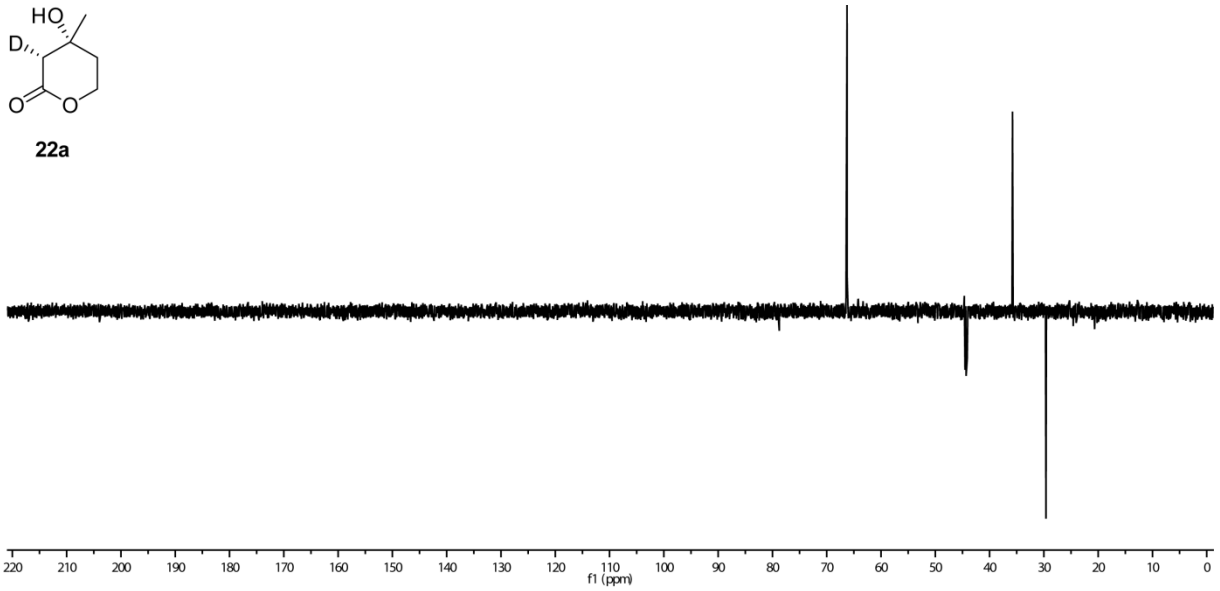


Figure 64 DEPT spectrum of compound **22a**.

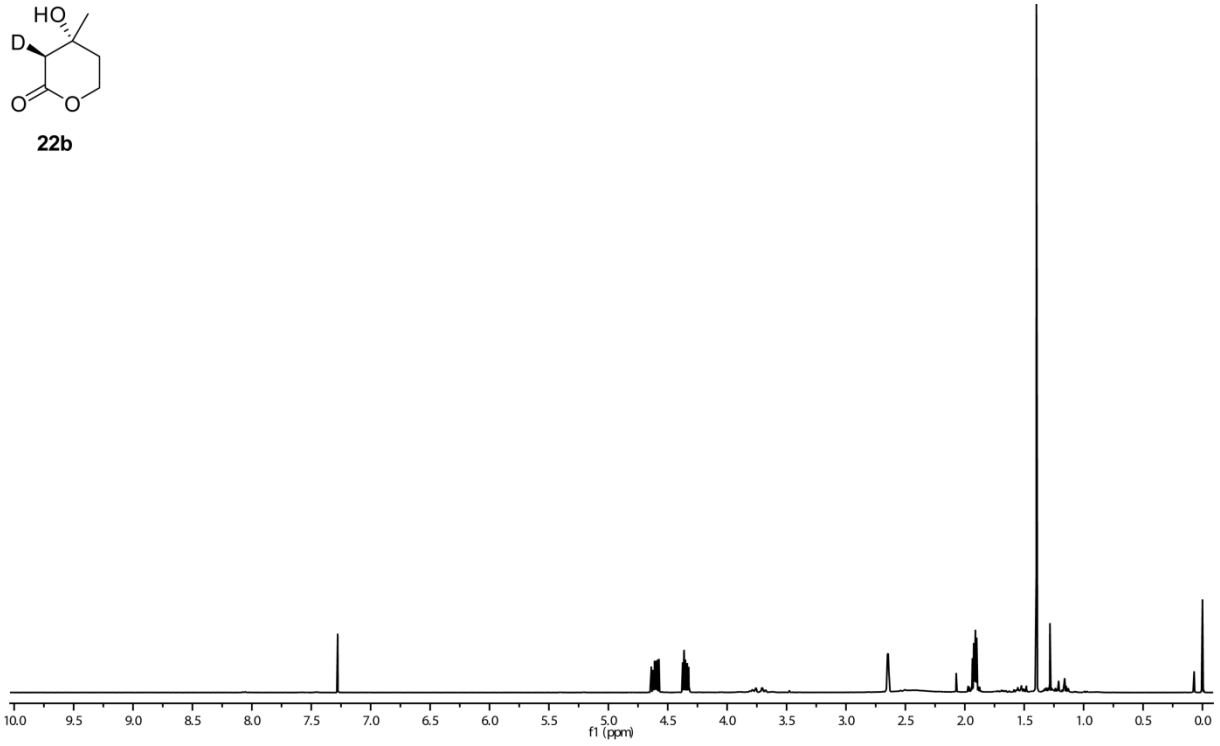


Figure 65 ^{1}H-NMR spectrum of compound **22b**.

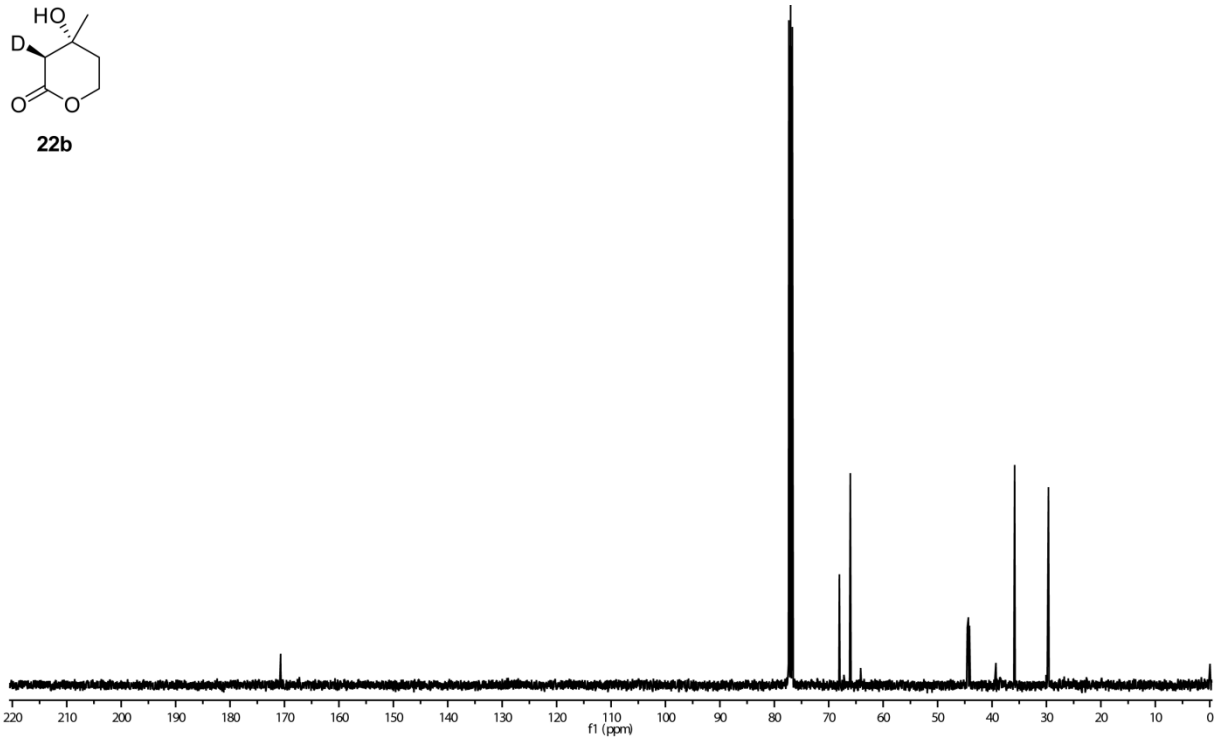


Figure 66 ^{13}C-NMR spectrum of compound **22b**.

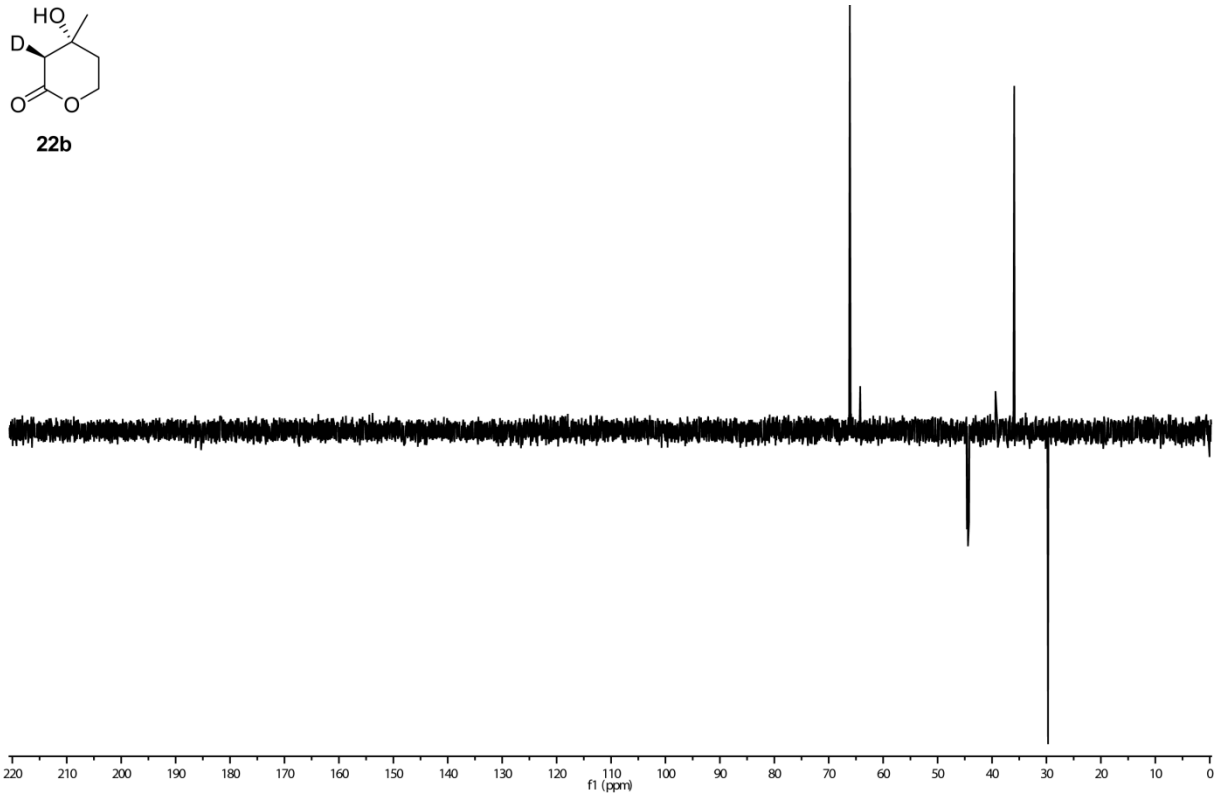


Figure 67 DEPT spectrum of compound **22b**.

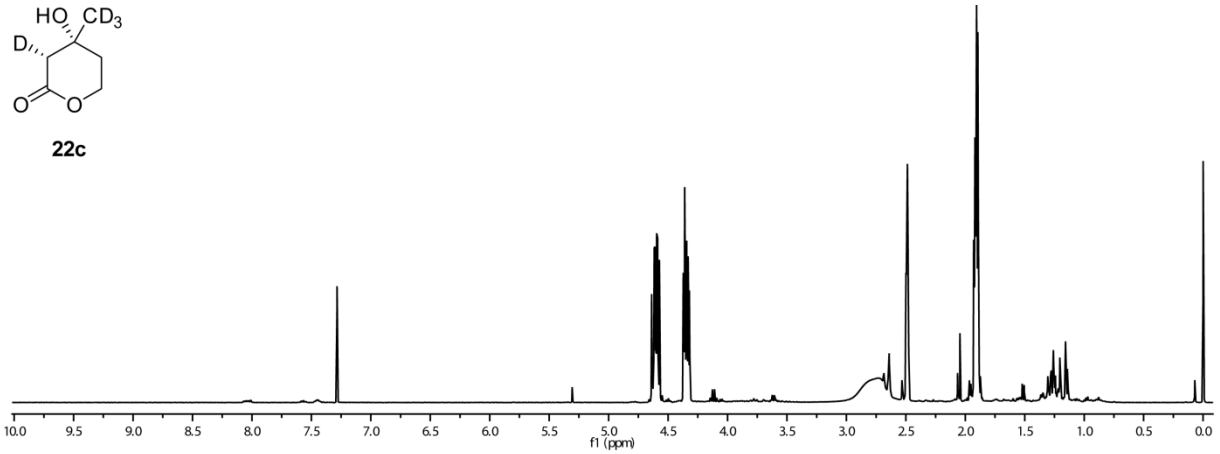


Figure 68 ^{1}H-NMR spectrum of compound **22c**.

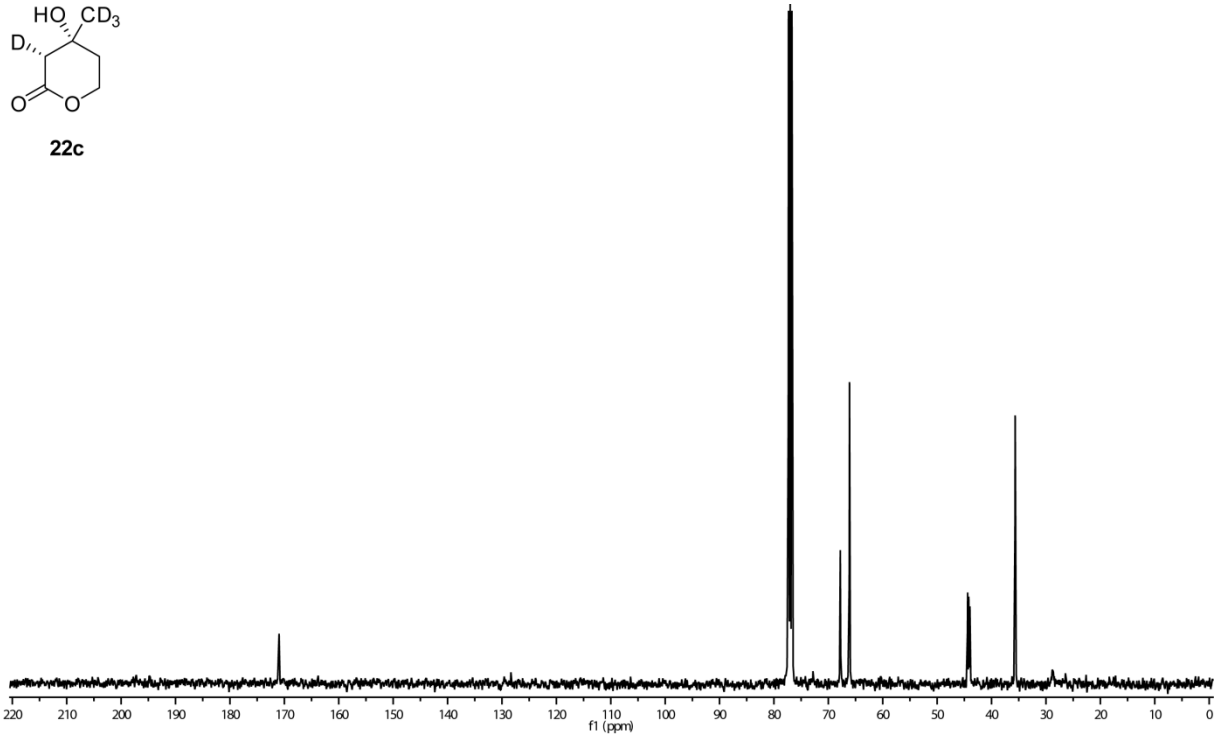


Figure 69 ^{13}C-NMR spectrum of compound **22c**.

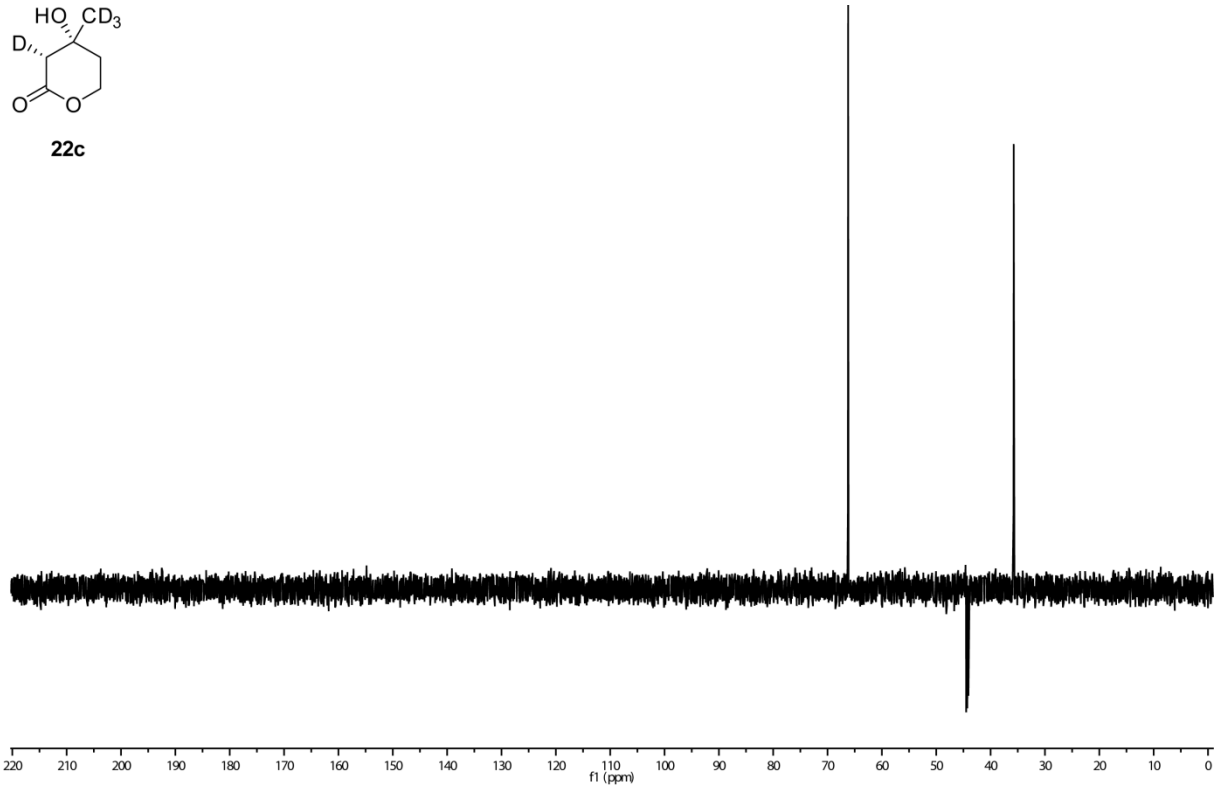


Figure 70 DEPT spectrum of compound **22c**.

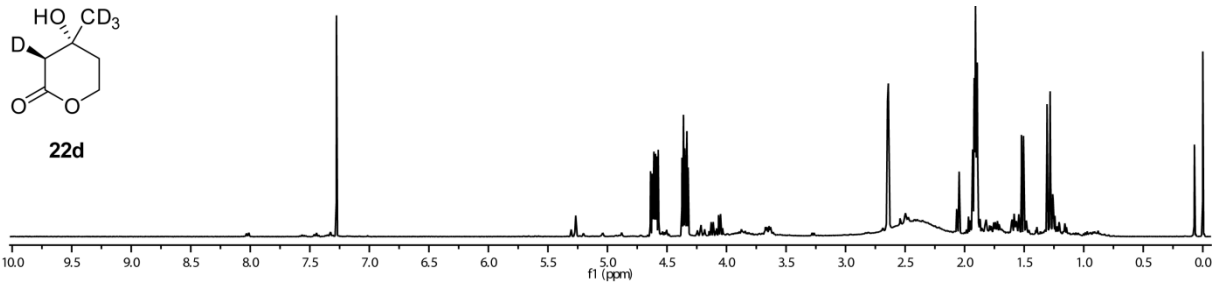


Figure 71 ^{1}H-NMR spectrum of compound **22d**.

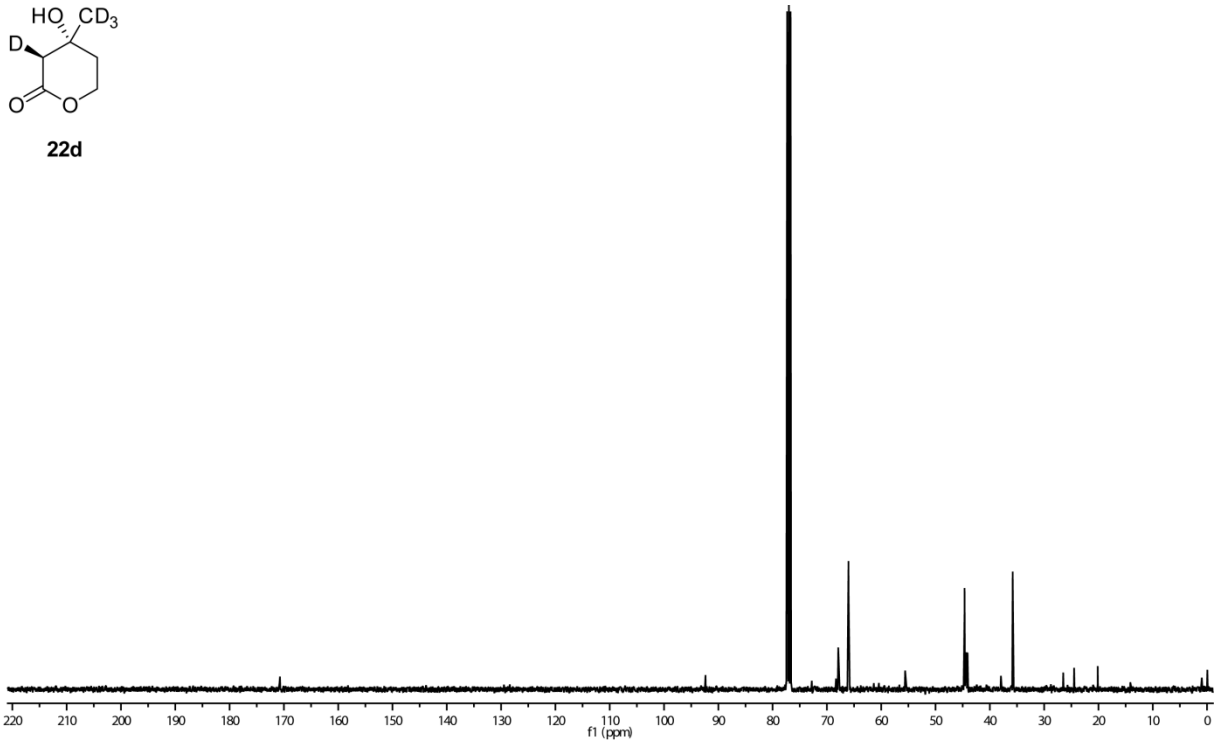


Figure 72 ^{13}C-NMR spectrum of compound **22d**.

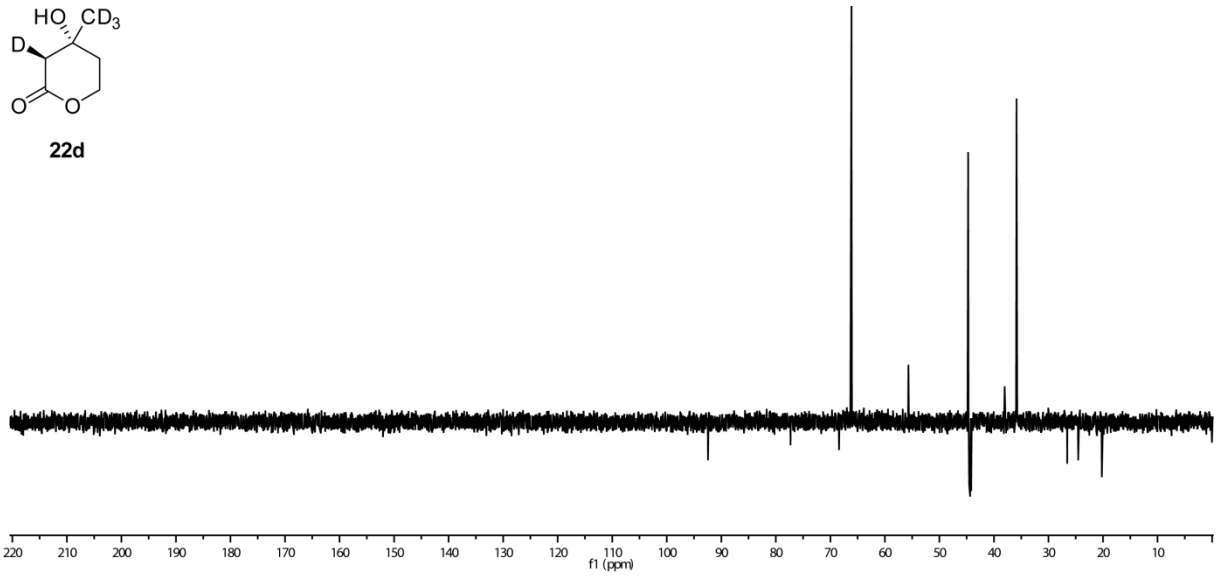


Figure 73 DEPT spectrum of compound **22d**.