Supporting Information

Highly Efficient Preparation of Selectively Isotope Cluster-Labeled Long Chain Fatty Acids via Two Consecutive C_{sp^3}- C_{sp^3} Cross Coupling Reactions

Sébastien Lethu, Shigeru Matsuoka* and Michio Murata*

JST ERATO, Lipid Active Structure Project and Project Research Center for Fundamental Sciences, Osaka University, Machikaneyama 1-1, Toyonaka, Osaka 560-0043, Japan.

matsuokas11@chem.sci.osaka-u.ac.jp, murata@chem.sci.osaka-u.ac.jp

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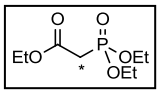
I. General Considerations

Unless otherwise indicated, all reactions were carried out with magnetic stirring in oven-dried glassware under argon atmosphere. Commercially available reagents were purchased from common suppliers and used without further purification. [2-^{13}C]-bromoacetic acid (99% ^{13}C) was purchased from Cambridge Isotope Laboratories Inc., USA. The dehydrated solvents dichloromethane (CH_2Cl_2), tetrahydrofuran (THF) and toluene were purchased from Kanto Chemical Co. Inc. and were used without further dehydration. N,N'-dimethylformamide (DMF) was stored over 4Å molecular sieves under argon. Analytical thin-layer chromatographies were carried out on Merck precoated silica gel $60F_{254}$ aluminium sheets and revealed with UV 254 nm and anisaldehyde or phosphomolybdic acid. Flash chromatographies were performed with Biotage prepacked columns using a Biotage Isolera One purification system. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECS 400 (400 MHz) spectrometer. Chemical shifts (δ) are given in parts per million (ppm) relative to the solvent residual peak of $CDCl_3$ (7.26 ppm for ^{1}H, 77.16 ppm for ^{13}C). Splitting patterns are indicated as followed: s, singlet; d, doublet; t, triplet; q, quartet; qi, quintuplet; m, multiplet; b, broad and combinations thereof. Coupling constants *J* are reported in hertz (Hz). IR spectra were realized on JASCO FT/IR-6100. Mass spectra were obtained on Thermo Scientific LTQ Orbitrap XL. Melting points were measured on Büchi M-565 and are uncorrected.

II. Experimental procedures for the synthesis of the common synthons 10 and 11

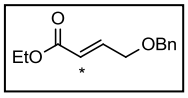
Ethyl [2-^{13}C]-2-(diethylphosphono)acetate **2**



To [2-^{13}C]-bromoacetic acid (3.91 g, 28.0 mmol) was added oxalyl chloride (2.64 mL, 30.8 mmol) and the mixture was warmed at 40 °C for 20 h before cooling down to 0 °C. Dry ethanol (2.45 mL, 42.0 mmol) was then slowly added at 0 °C and the resulting mixture was stirred at room temperature for 1 h. The mixture was cooled to 0 °C, quenched with water and extracted with Et_2O (x3). The combined organic layers were washed with saturated $NaHCO_3$, saturated NH_4Cl and brine, dried over $MgSO_4$ and filtered. Careful evaporation under reduced pressure afforded the ethyl [2-^{13}C]-bromoacetate **1** as a colorless liquid that was used without further purification. To ethyl [2-^{13}C]-bromoacetate **1** was added triethylphosphite (5.19 mL, 30.0 mmol) and the mixture was stirred at 135 °C for 18 h. After cooling down to room temperature, the crude product was purified by chromatography on silica gel (gradient hexane/EtOAc 5/5 to 0/10) to provide the desired phosphonate **2** (5.65 g, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.17 (m, 6H), 2.95 (dd, 2H, $^1J_{C\text{-}H}$ = 129.9 Hz and $^2J_{P\text{-}H}$ = 21.6 Hz), 1.34 (t, 6H, $^3J_{H\text{-}H}$ = 7.1 Hz), 1.27 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9 (dd, $^1J_{C\text{-}C}$ = 59.0 Hz and $^2J_{C\text{-}P}$ = 6.2 Hz), 62.7 (d, $^2J_{C\text{-}P}$ = 6.7 Hz), 61.6, 34.4 (d, $^1J_{C\text{-}P}$ = 134.2 Hz), 16.3 (d, $^3J_{C\text{-}P}$ = 6.7 Hz), 14.1 ppm. IR (neat): ν = 2982, 2937, 2908, 1733, 1255, 1115, 1049, 1017, 961, 780, 608 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_7{}^{13}CH_{17}O_5PNa$ $[M+Na]^+$ 248.0739, found 248.0741.

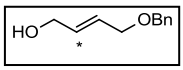
^{1}H NMR consistent with the litterature[1]

Ethyl [2-^{13}C]-4-(benzyloxy)but-2-enoate **3**



To a suspension of sodium hydride (60% in oil, 480.0 mg, 12.0 mmol) in THF (10 mL) at 0 °C was slowly added a solution of phosphonoacetate **2** (2.25 g, 10.0 mmol) in THF (10 mL). After stirring 15 min at 0 °C, the mixture was cooled to -78 °C and a solution of α-benzyloxyacetaldehyde (2.25 g, 15.0 mmol) in THF (20 mL) was slowly added to the resulting slurry. The mixture was stirred at -78 °C for 1 h, quenched with saturated NH_4Cl and extracted with EtOAc (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford olefin **3** (1.94 g, 88%) as a colorless oil in a separable mixture E/Z 98/2. ***Isomer E:*** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.27 (m, 5H), 6.99 (dtd, 1H, $^3J_{H\text{-}H}$ = 15.7 Hz, $^3J_{H\text{-}H}$ = 4.3 Hz, $^2J_{C\text{-}H}$ = 3.1 Hz), 6.14 (ddt, 1H, $^1J_{C\text{-}H}$ = 164.4 Hz, $^3J_{H\text{-}H}$ = 15.7 Hz, $^4J_{H\text{-}H}$ = 2.0 Hz), 4.57 (s, 2H), 4.25-4.16 (m, 4H), 1.29 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4 (d, $^1J_{C\text{-}C}$ = 74.8 Hz), 144.3 (d, $^1J_{C\text{-}C}$ = 71.9 Hz), 137.8, 128.6, 127.9, 127.7, 121.5, 72.9, 68.7, 60.5, 14.4 ppm. IR (neat): ν = 3066, 3031, 2981, 2939, 2904, 2852, 1714, 1294, 1262, 1174, 1116, 1095, 1037, 1028, 964, 736, 697 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{12}{}^{13}CH_{16}O_3Na$ [M+Na]$^+$ 244.1025, found 244.1034. ***Isomer Z:*** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.27 (m, 5H), 6.43 (dt, 1H, $^3J_{H\text{-}H}$ = 11.7 Hz, $^4J_{H\text{-}H}$ = 4.9 Hz), 5.82 (ddt, 1H, $^1J_{C\text{-}H}$ = 164.8 Hz, $^3J_{H\text{-}H}$ = 11.7 Hz, $^4J_{H\text{-}H}$ = 2.3 Hz), 4.65 (m, 2H), 4.56 (s, 2H), 4.16 (q, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz), 1.28 (t, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2 (d, $^1J_{C\text{-}C}$ = 73.8 Hz), 148.3 (d, $^1J_{C\text{-}C}$ = 70.0 Hz), 138.1, 128.6, 128.0, 127.9, 119.7, 73.0, 68.6, 60.4, 14.4 ppm. IR (neat): ν = 3063, 3031, 2980, 2939, 2904, 2861, 1712, 1382, 1219, 1185, 1093, 1056, 1028, 805, 735, 697 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{12}{}^{13}CH_{16}O_3Na$ [M+Na]$^+$ 244.1025, found 244.1037.

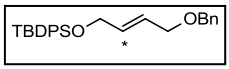
(*E*)-[2-^{13}C]-4-(benzyloxy)but-2-en-1-ol **4**



To a solution of ester **(*E*)-3** (1.92 g, 8.68 mmol) in CH_2Cl_2 (30 mL) at -78 °C was added DIBAL-H (1M in hexane, 19.1 mL, 19.1 mmol). The mixture was stirred at -78 °C for 30 min and at 0 °C for 15 min. Excess of DIBAL-H was neutralized by careful addition of few drops of MeOH at 0 °C. A saturated Rochelle's salt aqueous solution was added at 0 °C and the mixture was then vigorously stirred at room temperature for 4 h. Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 5/5) to afford alcohol **4** (1.44 g, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.25 (m, 5H), 5.91 (ddtt, 1H, $^1J_{C\text{-}H}$ = 155.2 Hz, $^3J_{H\text{-}H}$ = 15.6 Hz, $^3J_{H\text{-}H}$ = 5.4 Hz, $^4J_{H\text{-}H}$ = 1.4 Hz), 5.90-5.79 (m, 1H), 4.53 (s, 2H), 4.14 (m, 2H), 4.04 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 132.4, 128.5, 127.8 (d, $^1J_{C\text{-}C}$ = 71.9 Hz), 127.9, 127.8, 72.4, 70.2, 63.0 (d, $^1J_{C\text{-}C}$ = 46.0 Hz) ppm. IR (neat): ν = 3373, 3062, 3030, 2921, 2852, 1453, 1359, 1087, 1061, 1000, 966, 735, 696 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{10}{}^{13}CH_{14}O_2Na$ [M+Na]$^+$ 202.0920, found 202.0930.

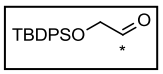
Analyses consistent with the litterature[2]

(*E*)-[2-^{13}C]-((4-(benzyloxy)but-2-en-1-yl)oxy)(tert-butyl)diphenylsilane **5**



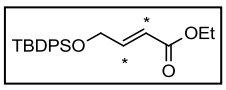
To a solution of alcohol **4** (1.28 g, 7.15 mmol) in DMF (25 mL) were added imidazole (1.07 g, 15.73 mmol) and TBDPSCl (2.76 mL, 10.73 mmol). The mixture was stirred at room temperature for 3 h, quenched with water (40 mL) and extracted with Et_2O (x3). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to furnish compound **5** (2.97 g, 100%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72-7.67 (m, 4H), 7.46-7.26 (m, 11H), 5.97-5.86 (m, 1H), 5.85 (ddtt, 1H, $^1J_{C\text{-}H}$ = 155.1 Hz, $^3J_{H\text{-}H}$ = 15.4 Hz, $^3J_{H\text{-}H}$ = 4.5 Hz, $^4J_{H\text{-}H}$ = 1.3 Hz), 4.53 (s, 2H), 4.24 (m, 2H), 4.05 (m, 2H), 1.08 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 135.7, 133.8, 132.3, 129.8, 128.5, 127.9, 127.8, 127.7, 126.3 (d, $^1J_{C\text{-}C}$ = 72.9 Hz), 72.1, 70.4, 63.9 (d, $^1J_{C\text{-}C}$ = 47.9 Hz), 27.0, 19.4 ppm. IR (neat): ν = 3070, 3030, 2957, 2930, 2891, 2855, 1428, 1105, 967, 823, 736, 698, 613 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{26}{}^{13}CH_{32}O_2SiNa$ $[M+Na]^+$ 440.2097, found 440.2128.

[1-^{13}C]-2-((tert-butyldiphenylsilyl)oxy)acetaldehyde **6**



A solution of olefin **5** (2.71 g, 6.5 mmol) in CH_2Cl_2 (40 mL) was cooled to -78 °C and ozone was bubbled through until it turned blue. Argon was then bubbled through until the mixture turned colorless. Triphenylphosphine (6.82 g, 26.0 mmol) was added at -78 °C and the reaction was allowed to warm to room temperature and stirred for 3 h before concentration under reduced pressure. The residue was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 95/5 to 6/4) to give aldehyde **6** (1.61 g, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.73 (dt, 1H, $^1J_{C\text{-}H}$ = 175.3 Hz, $^3J_{H\text{-}H}$ = 0.8 Hz), 7.69-7.64 (m, 4H), 7.49-7.37 (m, 6H), 4.22 (dd, 2H, $^2J_{C\text{-}H}$ = 4.1 Hz, $^3J_{H\text{-}H}$ = 0.8 Hz), 1.11 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.8, 135.7, 132.7, 130.2, 128.1, 70.1 (d, $^1J_{C\text{-}C}$ = 44.1 Hz), 26.9, 19.4 ppm. IR (neat): ν = 3072, 3050, 2959, 2931, 2890, 2858, 1697, 1472, 1428, 1111, 1105, 887, 823, 740, 699, 608 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{17}{}^{13}CH_{22}O_2SiNa$ $[M+Na]^+$ 322.1315, found 322.1330.

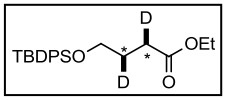
Ethyl [2,3-$^{13}C_2$]-4-((tert-butyldiphenylsilyl)oxy)but-2-enoate **7**



To a suspension of sodium hydride (60% in oil, 0.22 g, 5.5 mmol) in THF (5 mL) at 0 °C was added a solution of the phosphonoacetate **2** (1.35 g, 6.0 mmol) in THF (5 mL). After stirring 15 min at 0 °C, the mixture was cooled down to -78 °C and a solution of aldehyde **6** (1.50 g, 5.0 mmol) in THF (10 mL) was then added to the resulting slurry. The mixture was stirred at -78 °C for 1 h, quenched with saturated NH_4Cl and extracted with EtOAc (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford olefin **7** (1.60 g, 86%) as a colorless oil in a separable mixture E/Z 98/2. ***Isomer E:*** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.63 (m, 4H), 7.47-7.36 (m, 6H), 6.98 (dddd, 1H, $^1J_{C\text{-}H}$ = 156.2 Hz, $^3J_{H\text{-}H}$ = 15.4 Hz, $^3J_{H\text{-}H}$ = $^2J_{C\text{-}H}$ = 3.2 Hz), 6.27 (ddtd, 1H, $^1J_{C\text{-}H}$ = 165.1 Hz, $^3J_{H\text{-}H}$ = 15.4 Hz, $^4J_{H\text{-}H}$ = $^2J_{C\text{-}H}$ = 2.1 Hz), 4.35 (m, 2H), 4.22 (q, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz), 1.32 (t, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz), 1.08 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9 (d, $^1J_{C\text{-}C}$ = 74.8 Hz), 147.0 (d, $^1J_{C\text{-}C}$ = 72.9 Hz), 135.6, 133.2, 130.0, 128.0, 119.8 (d, $^1J_{C\text{-}C}$ = 72.9 Hz), 63.0 (d, $^1J_{C\text{-}C}$ = 46.0 Hz), 60.5, 26.9, 19.4, 14.5 ppm. IR (neat): ν = 3071, 3049, 2958, 2931, 2895, 2857, 1716, 1282, 1265, 1159, 1111, 1035, 944, 823, 740, 700, 614 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{20}{}^{13}C_2H_{28}O_3SiNa$ $[M+Na]^+$

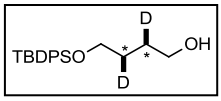
393.1767, found 393.1781. ***Isomer Z:*** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70-7.64 (m, 4H), 7.47-7.33 (m, 6H), 6.47 (ddt, 1H, $^{1}J_{C\text{-}H}$ = 157.6 Hz, $^{3}J_{H\text{-}H}$ = 11.7 Hz, $^{3}J_{H\text{-}H}$ = 4.7 Hz), 5.70 (ddtd, 1H, $^{1}J_{C\text{-}H}$ = 164.5 Hz, $^{3}J_{H\text{-}H}$ = 11.7 Hz, $^{4}J_{H\text{-}H}$ = 2.5 Hz, $^{2}J_{C\text{-}H}$ = 0.7 Hz), 4.83 (m, 2H), 4.06 (q, 2H, $^{3}J_{H\text{-}H}$ = 7.2 Hz), 1.19 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.2 Hz), 1.07 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (d, $^{1}J_{C\text{-}C}$ = 73.8 Hz), 151.6 (d, $^{1}J_{C\text{-}C}$ = 69.0 Hz), 135.7, 133.6, 129.8, 127.9, 118.3 (d, $^{1}J_{C\text{-}C}$ = 69.0 Hz), 62.8 (d, $^{1}J_{C\text{-}C}$ = 46.0 Hz), 60.2, 27.0, 19.3, 14.3 ppm IR (neat): ν = 3071, 3050, 2958, 2931, 2894, 2857, 1714, 1184, 1106, 1082, 1031, 821, 801, 740, 699, 612 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{20}{}^{13}C_2H_{28}O_3SiNa$ $[M+Na]^{+}$ 393.1767, found 393.1772.

Ethyl [2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butanoate **8**



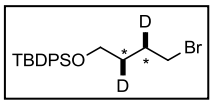
To a solution of olefin **(*E*)-7** (1.30 g, 3.5 mmol) in toluene (12 mL) was added Wilkinson's catalyst (0.32 g, 0.35 mmol). Deuterium was bubbled through the solution for 1 min and the mixture was stirred at room temperature for 16 h under deuterium atmosphere before concentration. The crude residue was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford ester **8** (1.28 g, 98%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.64 (m, 4H), 7.47-7.35 (m, 6H), 4.12 (q, 2H, $^{3}J_{H\text{-}H}$ = 7.2 Hz), 3.69 (m, 2H), 2.43 (dm, 1H, $^{1}J_{C\text{-}H}$ = 127.9 Hz), 1.87 (dm, 1H, $^{1}J_{C\text{-}H}$ = 127.9 Hz), 1.25 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.2 Hz), 1.06 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8 (d, $^{1}J_{C\text{-}C}$ = 57.5 Hz), 135.7, 133.9, 129.7, 127.8, 63.0 (d, $^{1}J_{C\text{-}C}$ = 39.3 Hz), 60.4, 30.7 (dt, $^{1}J_{C\text{-}C}$ = 35.4 Hz, $^{1}J_{C\text{-}D}$ = 19.2 Hz), 27.5 (dt, $^{1}J_{C\text{-}C}$ = 35.4 Hz, $^{1}J_{C\text{-}D}$ = 19.2 Hz), 27.0, 19.4, 14.4 ppm. IR (neat): ν = 3072, 3051, 2958, 2930, 2894, 2858, 1732, 1428, 1240, 1182, 1110, 1085, 1043, 822, 740 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{20}{}^{13}C_2H_{28}D_2O_3SiNa$ $[M+Na]^{+}$ 397.2049, found 397.2054.

[2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butan-1-ol **9**



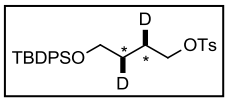
To a solution of ester **8** (1.12 g, 3.0 mmol) in CH_2Cl_2 (20 mL) at -78 °C was added DIBAL-H (1M in hexane, 6.6 mL, 6.6 mmol). The mixture was stirred at -78 °C for 30 min and at 0 °C for 15 min. Excess of DIBAL-H was neutralized by careful addition of few drops of MeOH at 0 °C. A saturated Rochelle's salt aqueous solution was added at 0 °C and the mixture was then vigorously stirred at room temperature for 3 h. Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 6/4) to afford alcohol **9** (0.98 g, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70-7.65 (m, 4H), 7.47-7.36 (m, 6H), 3.73-3.63 (m, 4H), 1.93 (bs, 1H), 1.64 (dm, 2H, $^{1}J_{C\text{-}H}$ = 130.7 Hz), 1.06 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 133.8, 129.8, 127.8, 64.1 (d, $^{1}J_{C\text{-}C}$ = 38.3 Hz), 62.9 (d, $^{1}J_{C\text{-}C}$ = 38.3 Hz), 29.6 (dt, $^{1}J_{C\text{-}C}$ = 35.5 Hz, $^{1}J_{C\text{-}D}$ = 18.2 Hz), 28.9 (dt, $^{1}J_{C\text{-}C}$ = 35.5 Hz, $^{1}J_{C\text{-}D}$ = 18.2 Hz), 27.0, 19.3 ppm. IR (neat): ν = 3349, 3071, 3050, 2957, 2929, 2891, 2857, 1472, 1428, 1106, 1084, 1046, 1007, 998, 822, 739 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{18}{}^{13}C_2H_{27}D_2O_2Si$ $[M+H]^{+}$ 333.2124, found 333.2143.

[2,3-$^{13}C_2$-2,3-D_2]-(4-bromobutoxy)(tert-butyl)diphenylsilane **10**



To a solution of alcohol **9** (116.4 mg, 0.35 mmol) in THF (1.5 mL) were added triphenylphosphine (183.6 mg, 0.7 mmol) and carbon tetrabromide (232.1 mg, 0.7 mmol). The mixture was stirred at room temperature for 2 h, filtrated on a pad of Celite, washed with THF and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 95/5) to afford the common synthon **10** (132.6 mg, 96%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (m, 4H), 7.46-7.36 (m, 6H), 3.69 (m, 2H), 3.41 (m, 2H), 1.96 (dm, 1H, $^1J_{C\text{-}H}$ = 119.8 Hz), 1.66 (dm, 1H, $^1J_{C\text{-}H}$ = 119.8 Hz), 1.05 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 134.0, 129.8, 127.8, 63.0 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 33.9 (d, $^1J_{C\text{-}C}$ = 34.5 Hz), 30.7 (dt, $^1J_{C\text{-}CD}$ = 34.5 Hz, $^1J_{C\text{-}C}$ = 19.2 Hz), 29.1 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 27.0, 19.4 ppm. IR (neat): ν = 3070, 3050, 2958, 2929, 2895, 2857, 1427, 1109, 1083, 822, 739, 699, 611 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{18}{}^{13}C_2H_{25}D_2{}^{79}BrOSiNa$ $[M+Na]^+$ 417.1099, found 417.1102.

[2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butyl 4-methylbenzenesulfonate **11**



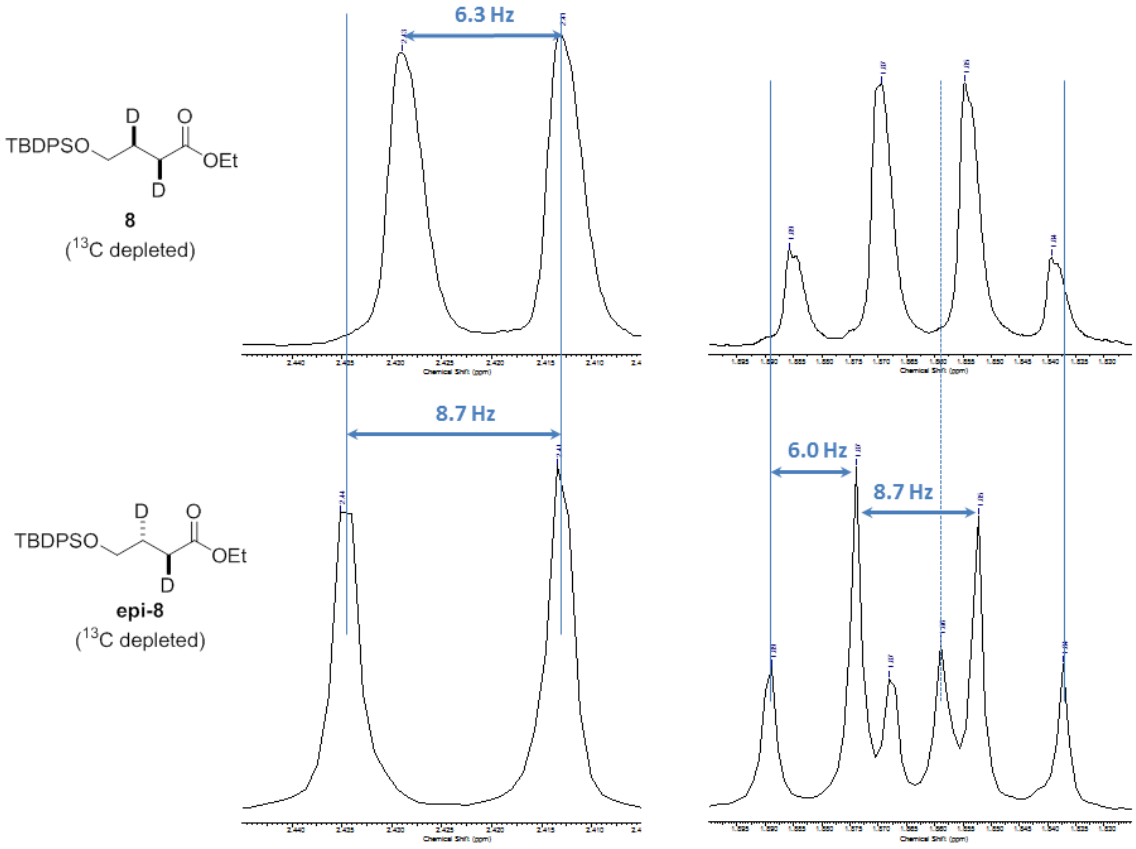
To a solution of alcohol **9** (0.84 g, 2.54 mmol) in CH_2Cl_2 (10 mL) at 0 °C were added triethylamine (0.85 mL, 6.08 mmol), tosyl chloride (0.73 g, 3.80 mmol) and DMAP (0.15 g, 1.27 mmol). The mixture was stirred at room temperature for 2 h, diluted with EtOAc (20 mL), washed with 1M HCl, saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 7/3) to afford the common synthon **11** (1.16 g, 94%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (m, 2H), 7.61 (m, 4H), 7.46-7.34 (m, 6H), 7.32 (m, 2H), 4.04 (m, 2H), 3.59 (m, 2H), 2.43 (s, 3H), 1.74 (dm, 1H, $^1J_{C\text{-}H}$ = 128.4 Hz), 1.53 (dm, 1H, $^1J_{C\text{-}H}$ = 125.8 Hz), 1.01 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 135.7, 133.9, 133.4, 130.0, 129.8, 128.0, 127.8, 70.7 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 63.0 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 28.0 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 27.0, 25.3 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 21.8, 19.3 ppm. IR (neat): ν = 3071, 3050, 2957, 2930, 2890, 2857, 1472, 1428, 1361, 1175, 1112, 815, 740, 699, 688, 665, 607 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{25}{}^{13}C_2H_{32}D_2O_4SSiNa$ $[M+Na]^+$ 509.2032, found 509.2037.

III. Determination of the *syn*-enantioselectivity of compound 8

Evaluation of the selectivity of the deuteration from compound **7** to compound **8** was realized according to the works of Whitesides and coworkers who pioneered the determination of the relative configurations at CHD-CHD centers of aliphatic acyclic chains by using ^{1}H-NMR with ^{2}H-decoupling.[3]

However, with our isotope cluster-labeled moiety, differences between erythro and threo compounds couldn't be seen because ^{13}C broadened the pattern in ^{1}H-NMR. To overcome such issue, we used non-^{13}C-labeled version of **8**, synthesized as described above. The erythro compound **epi-8** was synthesized as previously, using this time the *Z*-olefin as substrate.

Figure: Comparison of ^{2}H-decoupled ^{1}H-NMR signals



^{1}H-NMR spectra were recorded at 400 MHz with ^{2}H-decoupling at 61.4 MHz, using the solvent residual peak of $CDCl_3$ (7.26 ppm) as the reference. The H_a-H_b coupling constants are measured from the H_a doublet.

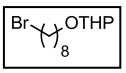
Vertical lines were superimposed for comparison of the peaks. Comparison of H_a doublet and H_b doublet of triplets clearly shows that no diastereomer is formed during the deuteration process from the *E*-olefin. Moreover, the two coupling constants found are consistent with the ones described by Whitesides: $^{3}J_{H\text{-}H}$ = 6.3 Hz for the threo deuterated ester, analogue of compound **8** and $^{3}J_{H\text{-}H}$ = 8.7 Hz for the erythro one. With the latest, we can also determine that $^{3}J_{H\text{-}H}$ coupling constant between H_b and CH_2 is 6.0 Hz. That coupling constant, very close to the one found between H_a and H_b in the threo compound, explains why the patterns are broader for the threo than for the erythro.

IV. General methods for the synthesis of labeled stearic acids

1) Synthesis of starting materials for the preparation of Grignard reagents

Protection by THP

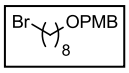
2-((8-bromooctyl)oxy)tetrahydro-2H-pyran



To a solution of 8-bromo-1-octanol (2.09 g, 10.0 mmol) in CH_2Cl_2 (20 mL) were added *p*-toluenesulfonic acid (95.1 mg, 0.5 mmol) and 3,4-dihydro-*2H*-pyran (1.27 mL, 15.0 mmol). The mixture was stirred for 3 h, quenched with saturated $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford THP-protected compound (2.54 g, 87%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.56 (m, 1H), 3.86 (m, 1H), 3.72 (m, 1H), 3.49 (m, 1H), 3.42-3.33 (m, 3H), 1.84 (m, 3H), 1.70 (m, 1H), 1.63-1.47 (m, 6H), 1.46-1.26 (m, 8H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 99.0, 67.7, 62.5, 34.1, 32.9, 30.9, 29.8, 29.4, 28.8, 28.2, 26.2, 25.6, 19.8 ppm. IR (neat): ν = 2930, 2854, 1200, 1134, 1119, 1077, 1066, 1031, 1022, 986, 905, 869, 815 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{13}H_{25}{}^{79}BrO_2Na$ $[M+Na]^+$ 315.0930, found 315.0933.

Protection by PMB

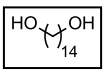
1-(((8-bromooctyl)oxy)methyl)-4-methoxybenzene



To a suspension of sodium hydride (60% in oil, 440.0 mg, 11.0 mmol) in THF (20 mL) at 0 °C was added *p*-methoxybenzyl alcohol (1.38 g, 10.0 mmol). The mixture was stirred at 0 °C for 1 h and 1,8-dibromooctane was added (3.70 mL, 20.0 mmol). The mixture was allowed to warm to room temperature and stirred for 20 h. The reaction was quenched with saturated NH_4Cl and extracted with EtOAc (x3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford PMB-protected compound (1.58 g, 48%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (m, 2H), 6.88 (m, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.43 (t, 2H, $^3J_{H\text{-}H}$ = 6.6 Hz), 3.40 (t, 2H, $^3J_{H\text{-}H}$ = 6.8 Hz), 1.84 (qi, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz), 1.59 (qi, 2H, $^3J_{H\text{-}H}$ = 6.9 Hz), 1.47-1.26 (m, 8H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 130.9, 129.4, 113.9, 72.6, 70.2, 55.4, 34.2, 32.9, 29.8, 29.4, 28.8, 28.2, 26.2 ppm. IR (neat): ν = 2999, 2930, 2853, 2791, 1612, 1511, 1464, 1302, 1244, 1172, 1095, 1035, 820 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{16}H_{25}{}^{79}BrO_2Na$ $[M+Na]^+$ 351.0930, found 351.0934.

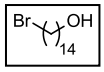
Formation of benzyl-protected bromoalcan-1-ol

1,14-Tetradecanediol



To a solution of methyltetradecanedioate (4.30 g, 15.0 mmol) in CH_2Cl_2 (75 mL) at -78 °C was added DIBAL-H (1M in hexane, 75.0 mL, 75.0 mmol). The mixture was stirred at -78 °C for 30 min and at 0 °C for 15 min. Excess of DIBAL-H was neutralized by careful addition of few drops of MeOH at 0 °C. A saturated Rochelle's salt aqueous solution (25 mL) was added at 0 °C and the mixture was then vigorously stirred at room temperature for 3 h. Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (x5). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude white solid obtained (3.36 g, 97%) was found to be the pure diol and was used in the next step without further purification. Mp = 88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (d, 4H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.56 (qi, 4H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.41-1.19 (m, 22H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 29.72, 29.70, 29.6, 25.9 ppm. IR (neat): ν = 3410, 3347, 2919, 2889, 2848, 1461, 1356, 1060, 1051, 1017, 972, 728, 608 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{14}H_{30}O_2Na$ $[M+Na]^+$ 253.2138, found 253.2137.

14-Bromotetradecan-1-ol

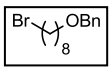


To a suspension of 1,14-tetradecanediol (3.26 g, 14.1 mmol) in cyclohexane (30 mL) was added HBr (1.59 mL, 14.1 mmol). The mixture was warmed to reflux and stirred for 70 h before extraction with hexane (x3) and EtOAc (x2). The combined organic layers were washed with saturated $NaHCO_3$ (x3) and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 7/3) to afford 14-bromotetradecan-1-ol (2.29 g, 55%) as a white solid. Mp = 45.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (d, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 3.40 (d, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.85 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.56 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.41-1.19 (m, 21Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 29.72, 29.70, 29.6, 25.9 ppm. IR (neat): ν = 3276, 2916, 2848, 1472, 1462, 1071, 1060, 1043, 1035, 1023, 1005, 993, 731, 719, 650 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{14}H_{29}{}^{79}BrONa$ $[M+Na]^+$ 315.1294, found 315.1315.

Protection by benzyl

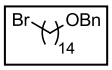
In a typical procedure, to a solution of the appropriate bromo alcohol (10 mmol) in THF (20 mL) were added benzyl bromide (2.66 g, 15 mmol) and then sodium hydride (60% in oil, 0.8 g, 20 mmol). The mixture was stirred for 18 h before careful quench with saturated $NaHCO_3$. The mixture was diluted with water and extracted with Et_2O (x3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford the desired benzyl-protected alcohols.

(((8-bromooctyl)oxy)methyl)benzene



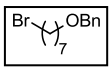
Colorless oil (2.72 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.26 (m, 5H), 4.50 (s, 2H), 3.47 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 3.40 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.85 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.62 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 1.48-1.26 (m, 8H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 128.5, 127.8, 127.6, 73.0, 70.6, 34.2, 32.9, 29.9, 29.4, 28.8, 28.3, 26.2 ppm. IR (neat): ν = 3088, 3064, 3030, 2930, 2854, 2790, 1453, 1362, 1099, 1028, 733, 696 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{15}H_{23}{}^{79}$BrONa $[M+Na]^{+}$ 321.0825, found 321.0842.

(((14-bromotetradecyl)oxy)methyl)benzene



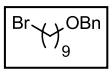
White solid (3.67 g, 86%). Mp = 32.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.25 (m, 5H), 4.50 (s, 2H), 3.46 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 3.41 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.85 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.61 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 1.49-1.21 (m, 20H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 34.2, 33.0, 29.9, 29.73, 29.68, 29.63, 29.58, 28.9, 28.3, 26.3 ppm. IR (neat): ν = 3052, 3030, 2920, 2850, 2796, 1498, 1467, 1455, 1367, 1205, 1125, 1106, 1088, 1076, 1029, 1017, 992, 737, 729, 724, 697, 639 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{21}H_{35}{}^{79}$BrONa $[M+Na]^{+}$ 405.1764, found 405.1788.

(((7-bromoheptyl)oxy)methyl)benzene



Colorless oil (2.49 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.26 (m, 5H), 4.51 (s, 2H), 3.47 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 3.40 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.86 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.63 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 1.49-1.28 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 128.5, 127.8, 127.6, 73.0, 70.5, 34.1, 32.9, 29.8, 28.7, 28.2, 26.2 ppm. IR (neat): ν = 3088, 3065, 3030, 2932, 2855, 2790, 1453, 1362, 1253, 1099, 1075, 1028, 733, 696 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{14}H_{21}{}^{79}$BrONa $[M+Na]^{+}$ 307.0668, found 307.0673.

(((9-bromononyl)oxy)methyl)benzene



Colorless oil (2.71 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.26 (m, 5H), 4.51 (s, 2H), 3.47 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 3.41 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.85 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 1.62 (qi, 2H, $^{3}J_{H\text{-}H}$ = 6.7 Hz), 1.49-1.28 (m, 10H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 128.5, 127.7, 127.6, 73.0, 70.6, 34.2, 33.0, 29.9, 29.5, 28.8, 28.3, 26.3 ppm. IR (neat): ν = 3088, 3065, 3030, 2927, 2853, 2793, 1453, 1362, 1099, 1028, 733, 696 cm^{-1}. HRMS (ESI^{+}, MeOH) calcd for $C_{16}H_{25}{}^{79}$BrONa $[M+Na]^{+}$ 335.0981, found 335.1004.

2) General Methods

- Formation of Grignard reagents

To a suspension of magnesium turnings (1.5 equiv) in THF (0.5 mL/mmol of substrate) containing a small iodine crystal were added few drops of the appropriate brominated compound (1 equiv) in THF (0.5 mL/mmol of substrate). The mixture was heated until the reaction started, then the brominated compound was added drop by drop to maintain a non-assisted gentle reflux. After complete addition of the starting material, the mixture was heated under reflux for 1 h. The solution of Grignard reagent was cooled down and titrated prior to use.[4]

- C_{sp3}-C_{sp3} coupling

To a 0.5M solution of **10** or **11** (1 equiv) in THF at 0 °C under argon atmosphere, were added $CuCl_2$ (0.05 equiv), phenylmethylacetylene (0.2 equiv) and the appropriate Grignard reagent (2 equiv). The mixture was stirred at room temperature for 1 h, cooled down to 0 °C and quenched by 1M HCl. After addition of saturated NH_4Cl at 0 °C, the solution was extracted with Et_2O (x3) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford the desired compounds **13** and **27a-c**.

In some cases *i.e.* for intermediates of compounds **16** and **17** as well as compounds **18** and **24a-c**, the pure couplings products couldn't be provided due to contamination by the hydrolyzed products from the Grignard reagents. Thus, they were only partially purified under the same conditions described above and then used impure in the TBDPS-deprotection step.

- Deprotection of TBDPS

To a 0.2M solution of the appropriate TBDPS-protected alcohol (1 equiv) in THF was added TBAF (1M in THF, 1.5 equiv) and the mixture was stirred at room temperature for 2 h before quenching with saturated NH_4Cl. The solution was extracted with EtOAc (x3) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 7/3) to afford the hydroxyl compounds **14**, **16**, **17**, **19** and **25a-c**.

- Tosylation

To a 0.2M solution of the appropriate hydroxyl (1 equiv) in CH_2Cl_2 at 0 °C were added triethylamine (2.4 equiv), dimethylaminopyridine (0.5 equiv) and tosyl chloride (1.5 equiv). The mixture was allowed to warm to room temperature and stirred for 2 h before dilution by EtOAc. The organic layer was washed with HCl 1M, saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtrated and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 8/2) to afford the tosylated compounds **20** and **26a-c**.

- Deprotection of Bn

To a 0.05M solution of the appropriate labeled benzyl-protected stearyl alcohol (1 equiv) in CH_2Cl_2 at -78 °C was added boron trichloride (2 equiv, 1M in CH_2Cl_2). The reaction mixture was allowed to warm to room temperature, stirred for 2 h, quenched with MeOH and diluted with water. The organic layer was washed with water, dried over $MgSO_4$, filtrated and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 7/3) to afford the stearyl alcohols **22** and **28a-c**.

- Jones'oxidation

Preparation of the Jones' reagent: CrO_3 (1.0 g, 10.0 mmol) was dissolved in water (3 mL) upon which was added H_2SO_4 (1 mL) at 0 °C.

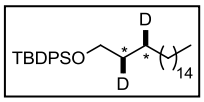
To a 0.05M solution of the appropriate labeled stearyl alcohol (1 equiv) in acetone was added the Jones' reagent (1 mL/mmol of substrate) and the mixture was vigorously stirred at room temperature for 10 min. Isopropanol was added until the orange color disappeared and only a blue suspension remained. HCl 1M was then added to dissolve the blue-green solid and the mixture was extracted with

EtOAc (x3). Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 5/5) to afford the desired labeled stearic acids **15**, **23** and **29a-c**.

3) Analyses of the labeled compounds

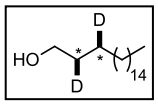
2,3-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-tert-butyl(octadecyloxy)diphenylsilane **13**



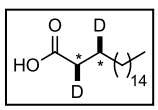
Following the C_{sp3}-C_{sp3} coupling method with compound **11** (243.4 mg, 0.50 mmol), the desired compound **13** was obtained as a colorless oil (250.9 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70-7.64 (m, 4H), 7.33-7.45 (m, 6H), 3.65 (m, 2H), 1.73-1.10 (m, 30H), 1.05 (s, 9H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 134.4, 129.6, 127.7, 64.1 (d, $^1J_{C\text{-}C}$ = 39.3 Hz), 32.3 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.9, 29.8, 29.5, 29.4 (d, $^1J_{C\text{-}C}$ = 34.5 Hz), 27.0, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 22.9, 19.4, 14.3 ppm. IR (neat): ν = 3070, 3050, 2957, 2922, 2852, 1464, 1427, 1111, 1085, 823, 739, 700, 611 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{32}{}^{13}C_2H_{55}D_2OSi$ $[M+H]^+$ 513.4366, found 513.4395.

[2,3-$^{13}C_2$-2,3-D_2]-stearyl alcohol **14**



Following the TBDPS-deprotection method with compound **13** (236.7 mg, 0.46 mmol), the desired alcohol **14** was obtained as a white solid (116.1 mg, 92%). Mp = 58.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63 (m, 2H), 1.73-1.07 (m, 31H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.2 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.84, 29.77, 29.73. 29.51, 29.46 (d, $^1J_{C\text{-}C}$ = 34.5 Hz), 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 22.8, 14.3 ppm. IR (neat): ν = 3319, 3234, 2964, 2955, 2915, 2848, 1472, 1462, 1064, 1052, 1044, 729, 720 cm^{-1}. HRMS (ESI$^+$, MeOH + HCOONa) calcd for $C_{16}{}^{13}C_2H_{36}D_2ONa$ $[M+Na]^+$ 297.3008, found 297.3008.

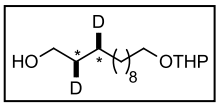
[2,3-$^{13}C_2$-2,3-D_2]-stearic acid **15**



Following the Jones' oxidation method with alcohol **14** (68.6 mg, 0.25 mmol), the desired labeled stearic acid **15** was obtained as a white solid (52.3 mg, 73%). Mp = 69.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (dm, 1H, $^1J_{C\text{-}H}$ = 127.7 Hz), 1.83-1.05 (m, 28H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.8 (d, $^1J_{C\text{-}C}$ = 55.6 Hz), 33.7 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 32.1, 29.85, 29.74, 29.59 (d, $^3J_{C\text{-}C}$ = 3.7 Hz), 29.52, 29.37 (d, $^2J_{C\text{-}C}$ = 3.7 Hz), 29.08 (d, $^1J_{C\text{-}C}$ = 35.5 Hz), 24.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 22.9, 14.3 ppm. IR (neat): ν = 2963, 2954, 2914, 2847, 1695, 1471, 1463, 1339, 1308, 1255, 1239, 1228, 944, 729, 719 cm^{-1}. HRMS (ESI$^-$, MeOH) calcd for $C_{16}{}^{13}C_2H_{33}D_2O_2$ $[M-H]^-$ 287.2835, found 287.2822.

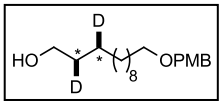
With different protecting groups

[2,3-$^{13}C_2$-2,3-D_2]- 12-((tetrahydro-*2H*-pyran-2-yl)oxy)dodecan-1-ol **16**



Following the C_{sp3}-C_{sp3} coupling and TBDPS-deprotection methods with common synthon **11** (243.4 mg, 0.50 mmol), the desired compound **16** was obtained as a colorless oil (62.5 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.57 (m, 1H), 3.87 (m, 1H), 3.72 (dt, 1H, $^3J_{H\text{-}H}$ = 9.6 Hz and $^3J_{H\text{-}H}$ = 6.9 Hz), 3.62 (m, 2H), 3.49 (m, 1H), 3.38 (dt, 1H, $^3J_{H\text{-}H}$ = 9.6 Hz and $^3J_{H\text{-}H}$ = 6.7 Hz), 1.82 (m, 1H), 1.76-1.07 (m, 24H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 99.0, 67.9, 63.1 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 62.5, 32.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 30.9, 29.9, 29.7, 29.6, 29.4 (d, $^1J_{C\text{-}C}$ = 35.1 Hz), 26.4, 25.7, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 19.9 ppm. IR (neat): ν = 3393, 2921, 2852, 1137, 1120, 1077, 1022, 987 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{15}{}^{13}C_2H_{32}D_2O_3Na$ $[M+Na]^+$ 313.2593, found 313.2594.

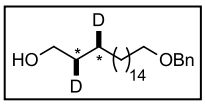
[2,3-$^{13}C_2$-2,3-D_2]- 12-((4-methoxybenzyl)oxy)dodecan-1-ol **17**



Following the C_{sp3}-C_{sp3} coupling and TBDPS-deprotection methods with common synthon **11** (243.4 mg, 0.50 mmol), the desired compound **16** was obtained as a white solid (151.6 mg, 93%). Mp = 56.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, 2H, $^3J_{H\text{-}H}$ = 8.6 Hz), 6.88 (d, 2H, $^3J_{H\text{-}H}$ = 8.6 Hz), 4.43 (s, 2H), 3.80 (s, 3H), 3.63 (m, 2H), 3.43 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.59 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.74-1.07 (m, 17H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 131.0, 129.4, 113.9, 72.7, 70.4, 63.2 (d, $^1J_{C\text{-}C}$ = 36.4 Hz), 55.4, 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.9, 29.7, 29.6, 29.5 (d, $^1J_{C\text{-}C}$ = 34.5 Hz), 26.4, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz) ppm. IR (neat): ν = 3410, 3314, 2916, 2879, 2848, 2793, 1615, 1516, 1465, 1304, 1252, 1176, 1171, 1100, 1058, 1047, 1030, 1011, 976, 822, 815, 808, 725 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{18}{}^{13}C_2H_{32}D_2O_3Na$ $[M+Na]^+$ 349.2593, found 349.2594.

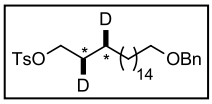
16,17-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-18-(benzyloxy)octadecan-1-ol **19**



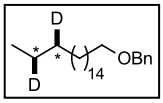
Following the C_{sp3}-C_{sp3} coupling and TBDPS-deprotection methods with compound **11** (243.4 mg, 0.50 mmol), the desired compound **19** was obtained as a white solid (170.5 mg, 90%). Mp = 60.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.24 (m, 5H), 4.50 (s, 2H), 3.63 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.74-1.10 (m, 29H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 63.2 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.92, 29.82, 29.76, 29.64, 29.5 (d, $^1J_{C\text{-}C}$ = 35.6 Hz), 26.4, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz) ppm. IR (neat): ν = 3429, 3364, 2916, 2879, 2847, 2794, 1469, 1118, 736, 721, 695 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{43}D_2O_2$ $[M+H]^+$ 381.3607, found 381.3611.

[2,3-$^{13}C_2$-2,3-D_2]-18-(benzyloxy)octadecyl 4-methylbenzenesulfonate **20**



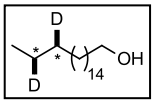
Following the tosylation method with compound **19** (114.0 mg, 0.30 mmol), the desired compound **20** was obtained as a white solid (153.0 mg, 96%). Mp = 68.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, 2H, $^3J_{H\text{-}H}$ = 8.3 Hz), 7.38-7.24 (m, 7H), 4.50 (s, 2H), 4.01 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 2.45 (s, 3H), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.81-1.04 (m, 28H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 138.9, 133.4, 129.9, 128.5, 128.0, 127.8, 127.6, 73.0, 70.8 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 70.7, 29.9, 29.83, 29.76, 29.65, 29.52 (d, $^2J_{C\text{-}C}$ = 3.8 Hz), 29.1, 28.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 26.4, 25.0 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 21.8 ppm. IR (neat): ν = 3029, 2918, 2849, 1470, 1361, 1169, 1105, 1095, 936, 837, 811, 733, 699, 666 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{30}{}^{13}C_2H_{49}D_2O_4S$ $[M+H]^+$ 535.3695, found 535.3703.

[16,17-$^{13}C_2$-16,17-D_2]-((octadecyloxy)methyl)benzene **21**



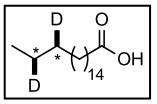
To a solution of lithium aluminium hydride (26.2 mg, 0.69 mmol) in THF (3 mL) at 0 °C was added compound **20** (123.0 mg, 0.23 mmol) in THF (2 mL). The mixture was allowed to warm to room temperature and was then warmed to reflux for 1 h before cooling down to 0 °C. Water and HCl 1M were added until the precipitate disappeared and the mixture was extracted by EtOAc (x3). Combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by prepacked chromatography on silica gel (gradient hexane/EtOAc 10/0 to 9/1) to afford **21** (80.7 mg, 96%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.24 (m, 5H), 4.50 (s, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.62 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.47-1.01 (m, 28H), 0.87 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 31.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.93, 29.85, 29.76, 29.65, 29.4 (d, $^1J_{C\text{-}C}$ = 35.5 Hz), 26.4, 22.3 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 14.1 (d, $^1J_{C\text{-}C}$ = 34.5 Hz) ppm. IR (neat): ν = 3064, 3042, 3029, 2965, 2954, 2915, 2847, 2793, 1471, 1463, 1454, 1362, 1101, 748, 729, 720, 698, 615 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{42}D_2ONa$ $[M+Na]^+$ 387.3477, found 387.3490.

[16,17-$^{13}C_2$-16,17-D_2]-stearyl alcohol **22**



Following the TBDPS-deprotection method with compound **21** (62.0 mg, 0.17 mmol), the desired compound **22** was obtained as a white solid (45.8 mg, 98%). Mp = 59.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.57 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.47-1.01 (m, 29H), 0.88 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 31.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.85, 29.77, 29.59, 29.37 (d, $^1J_{C\text{-}C}$ = 34.5 Hz), 25.9, 22.3 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 14.1 (d, $^1J_{C\text{-}C}$ = 34.5 Hz) ppm. IR (neat): ν = 3319, 3234, 2964, 2955, 2915, 2848, 1472, 1462, 1064, 1052, 1044, 729, 720 cm^{-1}. HRMS (ESI$^+$, MeOH + HCOONa) calcd for $C_{16}{}^{13}C_2H_{36}D_2ONa$ $[M+Na]^+$ 297.3008, found 297.3006.

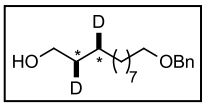
[16,17-$^{13}C_2$-16,17-D_2]-stearic acid **23**



Following the Jones' oxidation method with compound **22** (35.7 mg, 0.13 mmol), the desired compound **23** was obtained as a white solid (29.9 mg, 80%). Mp = 68.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (t, 2H, $^3J_{H\text{-}H}$ = 7.5 Hz), 1.63 (qi, 2H, $^3J_{H\text{-}H}$ = 7.5 Hz), 1.46-1.01 (m, 26H), 0.87 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.8, 34.1, 31.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.84, 29.74, 29.58, 29.39, 29.38 (d, $^1J_{C\text{-}C}$ = 33.8 Hz), 29.2, 24.8, 22.3 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 14.1 (d, $^1J_{C\text{-}C}$ = 34.5 Hz) ppm. IR (neat): ν = 2963, 2954, 2914, 2871, 2848, 1699, 1472, 1463, 1295, 940, 729, 720 cm^{-1}. HRMS (ESI$^-$, MeOH) calcd for $C_{16}{}^{13}C_2H_{33}D_2O_2$ $[M-H]^-$ 287.2835, found 287.2822.

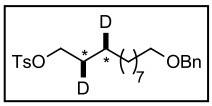
9,10-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-11-(benzyloxy)dodecan-1-ol **25a**



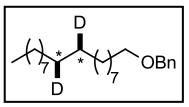
Following the C_{sp3}-C_{sp3} coupling and TBDPS-deprotection methods with common synthon **11** (243.4 mg, 0.50 mmol), the desired compound **25a** was obtained as a pale yellow oil (129.9 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.24 (m, 5H), 4.50 (s, 2H), 3.63 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.73-1.10 (m, 15H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 63.2 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.9, 29.70, 29.68, 29.64, 29.61, 29.26, 26.3, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz) ppm. IR (neat): ν = 3353, 3065, 3030, 2921, 2852, 2792, 1454, 1362, 1098, 1043, 1028, 733, 696 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{16}{}^{13}C_2H_{28}D_2O_2Na$ $[M+Na]^+$ 305.2331, found 305.2332.

[2,3-$^{13}C_2$-2,3-D_2]-11-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26a**



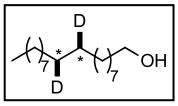
Following the tosylation method with compound **25a** (113.0 mg, 0.40 mmol), the desired compound **26a** was obtained as a colorless oil (158.7 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, 2H, $^3J_{H\text{-}H}$ = 8.2 Hz), 7.38-7.24 (m, 7H), 4.50 (s, 2H), 4.01 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 2.45 (s, 3H), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.78-1.04 (m, 14H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 138.9, 133.4, 129.9, 128.5, 128.0, 127.8, 127.6, 73.0, 70.8 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 70.7, 29.9, 29.66, 29.61, 29.54, 29.50, 29.46, 29.1, 28.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 26.3, 25.0 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 21.8 ppm. IR (neat): ν = 3063, 3033, 2924, 2853, 2793, 1359, 1188, 1175, 1097, 958, 814, 736, 697, 663 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{34}D_2O_4SNa$ $[M+Na]^+$ 459.2419, found 459.2421.

[9,10-$^{13}C_2$-9,10-D_2]-((octadecyloxy)methyl)benzene **27a**



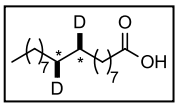
Following the C_{sp3}-C_{sp3} coupling method with compound **26a** (131.0 mg, 0.30 mmol), the desired compound **27a** was obtained as a colorless oil (109.1 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.24 (m, 5H), 4.50 (s, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.45-1.02 (m, 28H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 32.1, 29.9, 29.82, 29.77, 29.65, 29.60, 29.32 (m), 28.9, 26.4, 22.9, 14.3 ppm. IR (neat): ν = 3065, 3029, 2920, 2852, 2789, 1454, 1361, 1101, 1028, 731, 696 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{42}D_2ONa$ $[M+Na]^+$ 387.3477, found 387.3480.

[9,10-$^{13}C_2$-9,10-D_2]-stearyl alcohol **28a**



Following the TBDPS-deprotection method with compound **27a** (91.2 mg, 0.25 mmol), the desired alcohol **28a** was obtained as a white solid (66.2 mg, 96%). Mp = 58.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.56 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.48-1.01 (m, 29H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.6 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 32.1, 29.81, 29.77, 29.64, 29.59, 29.3 (m), 28.9, 25.9, 22.9, 14.3 ppm. IR (neat): ν = 3326, 3235, 2965, 2955, 2915, 2870, 2848, 1470, 1463, 1062, 729, 721 cm^{-1}. HRMS (ESI$^+$, MeOH + HCOONa) calcd for $C_{16}{}^{13}C_2H_{36}D_2ONa$ $[M+Na]^+$ 297.3008, found 297.3004.

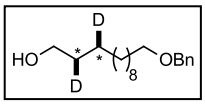
[9,10-$^{13}C_2$-9,10-D_2]-stearic acid **29a**



Following the Jones' oxidation method with alcohol **28a** (41.2 mg, 0.15 mmol), the desired labeled stearic acid **29a** was obtained as a white solid (37.0 mg, 85%). Mp = 69.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (t, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.63 (qi, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.47-1.01 (m, 26H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.2, 34.0, 32.1, 29.82, 29.73, 29.61, 29.3 (m), 28.9, 24.8, 22.9, 14.3 ppm. IR (neat): ν = 2954, 2913, 2869, 2848, 1700, 1471, 1463, 1430, 1310, 1298, 1282, 1228, 940, 728, 721 cm^{-1}. HRMS (ESI$^-$, MeOH) calcd for $C_{16}{}^{13}C_2H_{33}D_2O_2$ $[M\text{-}H]^-$ 287.2835, found 287.2814.

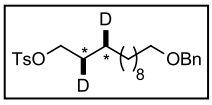
10,11-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-12-(benzyloxy)dodecan-1-ol **25b**



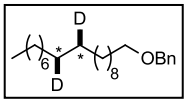
Following the C_{sp^3}-C_{sp^3} coupling and TBDPS-deprotection methods with common synthon **11** (243.4 mg, 0.50 mmol), the desired compound **25b** was obtained as a white solid (142.4 mg, 96%). Mp = 33.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.24 (m, 5H), 4.50 (s, 2H), 3.63 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.74-1.10 (m, 17H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 63.2 (d, $^1J_{C\text{-}C}$ = 36.4 Hz), 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.9, 29.7, 29.6, 29.4 (d, $^1J_{C\text{-}C}$ = 36.3 Hz), 26.3, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz) ppm. IR (neat): ν = 3418, 3360, 3347, 3064, 3035, 2918, 2911, 2880, 2848, 2794, 1466, 1454, 1367, 1347, 1116, 1091, 1057, 1048, 1039, 1027, 1013, 980, 733, 725, 696 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{17}{}^{13}C_2H_{30}D_2O_2Na$ $[M+Na]^+$ 319.2487, found 319.2491.

[2,3-$^{13}C_2$-2,3-D_2]-12-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26b**



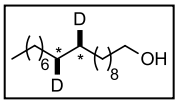
Following the tosylation method with compound **25b** (103.8 mg, 0.35 mmol), the desired compound **26b** was obtained as a colorless oil (139.7 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, 2H, $^3J_{H\text{-}H}$ = 8.3 Hz), 7.38-7.24 (m, 7H), 4.50 (s, 2H), 4.01 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 2.45 (s, 3H), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.78-1.04 (m, 16H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 138.9, 133.4, 129.9, 128.5, 128.0, 127.8, 127.6, 73.0, 70.8 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 70.7, 29.9, 29.70, 29.66, 29.61, 29.49 (d, $^2J_{C\text{-}C}$ = 3.8 Hz), 29.1, 28.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 26.3, 25.0 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 21.8 ppm. IR (neat): ν = 3065, 3030, 2924, 2852, 1360, 1188, 1175, 1097, 959, 814, 734, 697, 663 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{24}{}^{13}C_2H_{37}D_2O_4S$ $[M+H]^+$ 451.2756, found 451.2784.

[10,11-$^{13}C_2$-10,11-D_2]-((octadecyloxy)methyl)benzene **27b**



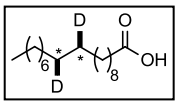
Following the C_{sp^3}-C_{sp^3} coupling method with compound **26b** (126.3 mg, 0.28 mmol), the desired compound **27b** was obtained as a colorless oil (99.9 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.24 (m, 5H), 4.50 (s, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.62 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.45-1.02 (m, 28H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 32.1, 29.9, 29.80, 29.76, 29.65, 29.32 (m), 28.9, 26.4, 22.9, 14.3 ppm. IR (neat): ν = 3065, 3042, 3030, 2965, 2955, 2915, 2869, 2848, 2793, 1471, 1463, 1454, 1367, 1359, 1101, 1026, 1009, 748, 729, 721, 698, 615 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{42}D_2ONa$ $[M+Na]^+$ 387.3477, found 387.3500.

[10,11-$^{13}C_2$-10,11-D_2]-stearyl alcohol **28b**



Following the TBDPS-deprotection method with compound **27b** (80.2 mg, 0.22 mmol), the desired alcohol **28b** was obtained as a white solid (57.9 mg, 96%). Mp = 58.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.56 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.44-1.01 (m, 29H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.6 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 32.1, 29.82, 29.80, 29.76, 29.64, 29.59, 29.3 (m), 28.9, 25.9, 22.9, 14.3 ppm. IR (neat): ν = 3323, 3236, 3225, 2965, 2955, 2915, 2870, 2848, 1471, 1463, 1063, 729, 721 cm^{-1}. HRMS (ESI$^+$, MeOH + HCOONa) calcd for $C_{16}{}^{13}C_2H_{36}D_2ONa$ $[M+Na]^+$ 297.3008, found 297.3006.

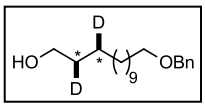
[10,11-$^{13}C_2$-10,11-D_2]-stearic acid **29b**



Following the Jones' oxidation method with alcohol **28b** (41.2 mg, 0.15 mmol), the desired labeled stearic acid **29b** was obtained as a white solid (36.6 mg, 85%). Mp = 69.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (t, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.63 (qi, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.46-1.01 (m, 26H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.1, 34.2, 32.1, 29.82, 29.75, 29.58, 29.3 (m), 28.9, 24.8, 22.9, 14.3 ppm. IR (neat): ν = 2954, 2913, 2869, 2848, 1699, 1471, 1463, 1298, 942, 728, 721 cm^{-1}. HRMS (ESI$^-$, MeOH) calcd for $C_{16}{}^{13}C_2H_{33}D_2O_2$ $[M-H]^-$ 287.2835, found 287.2821.

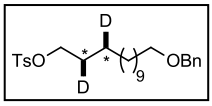
11,12-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-13-(benzyloxy)dodecan-1-ol **25c**



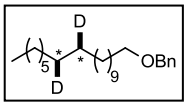
Following the C_{sp^3}-C_{sp^3} coupling and TBDPS-deprotection methods with common synthon **11** (243.4 mg, 0.50 mmol), the desired compound **25c** was obtained as a white solid (151.7 mg, 98%). Mp = 35.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.24 (m, 5H), 4.50 (s, 2H), 3.63 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.74-1.10 (m, 19H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 63.2 (d, $^1J_{C\text{-}C}$ = 37.4 Hz), 32.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 29.9, 29.7, 29.6, 29.5 (d, $^1J_{C\text{-}C}$ = 36.0 Hz), 26.3, 25.4 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz) ppm. IR (neat): ν = 3357, 3279, 3065, 3030, 2915, 2888, 2872, 2848, 2793, 1471, 1463, 1454, 1363, 1102, 1079, 1043, 1026, 1004, 991, 979, 978, 873, 748, 730, 698, 615 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{18}{}^{13}C_2H_{32}D_2O_2Na$ $[M+Na]^+$ 333.2644, found 333.2646.

[2,3-$^{13}C_2$-2,3-D_2]-13-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26c**



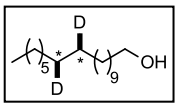
Following the tosylation method with compound **25c** (124.2 mg, 0.40 mmol), the desired compound **26c** was obtained as a colorless oil (162.7 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, 2H, $^3J_{H\text{-}H}$ = 8.4 Hz), 7.38-7.24 (m, 7H), 4.50 (s, 2H), 4.01 (m, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 2.45 (s, 3H), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.80-1.04 (m, 18H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 138.9, 133.4, 129.9, 128.5, 128.0, 127.8, 127.6, 73.0, 70.8 (d, $^1J_{C\text{-}C}$ = 38.3 Hz), 70.7, 29.93, 29.73, 29.72, 29.65, 29.64, 29.61, 29.49 (d, $^1J_{C\text{-}C}$ = 3.8 Hz), 29.11, 28.96, 28.5 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 26.3, 25.0 (dt, $^1J_{C\text{-}C}$ = 34.5 Hz, $^1J_{C\text{-}D}$ = 19.2 Hz), 21.8 ppm. IR (neat): ν = 3026, 2988, 2940, 2919, 2851, 2798, 1467, 1354, 1175, 1126, 1113, 1095, 1027, 954, 937, 833, 814, 794, 732, 722, 695, 663 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{25}{}^{13}C_2H_{38}D_2O_4SNa$ $[M+Na]^+$ 487.2732, found 487.2734.

[11,12-$^{13}C_2$-11,12-D_2]-((octadecyloxy)methyl)benzene **27c**



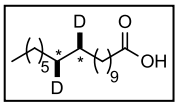
Following the C_{sp3}-C_{sp3} coupling method with compound **26c** (139.4 mg, 0.30 mmol), the desired compound **27c** was obtained as a colorless oil (109.2 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.24 (m, 5H), 4.50 (s, 2H), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.61 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.47-1.01 (m, 28H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 128.5, 127.8, 127.6, 73.0, 70.7, 32.1, 29.9, 29.83, 29.77, 29.65, 29.61, 29.32 (m), 28.9, 26.4, 22.9, 14.3 ppm. IR (neat): ν = 3026, 2986, 2919, 2851, 2798, 1467, 1454, 1355, 1176, 1113, 1096, 1073, 1028, 954, 937, 833, 815, 794, 732, 722, 695, 664 cm^{-1}. HRMS (ESI$^+$, MeOH) calcd for $C_{23}{}^{13}C_2H_{42}D_2ONa$ $[M+Na]^+$ 387.3477, found 387.3479.

[11,12-$^{13}C_2$-11,12-D_2]-stearyl alcohol **28c**



Following the TBDPS-deprotection method with compound **27c** (91.2 mg, 0.25 mmol), the desired alcohol **28c** was obtained as a white solid (63.5 mg, 93%). Mp = 58.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64 (t, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.57 (qi, 2H, $^3J_{H\text{-}H}$ = 6.7 Hz), 1.50-1.01 (m, 29H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.6 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.3, 33.0, 32.1, 29.82, 29.76, 29.64, 29.59, 29.3 (m), 29.06, 28.9, 25.9, 22.9, 14.3 ppm. IR (neat): ν = 3322, 3235, 2965, 2955, 2915, 2870, 2848, 1471, 1463, 1062, 729, 721 cm^{-1}. HRMS (ESI$^+$, MeOH + HCOONa) calcd for $C_{16}{}^{13}C_2H_{36}D_2ONa$ $[M+Na]^+$ 297.3008, found 297.3008.

[11,12-$^{13}C_2$-11,12-D_2]-stearic acid **29c**



Following the Jones' oxidation method with alcohol **28c** (41.2 mg, 0.15 mmol), the desired labeled stearic acid **29c** was obtained as a white solid (35.2 mg, 81%). Mp = 69.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (t, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.63 (qi, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz), 1.47-1.01 (m, 26H), 0.88 (t, 3H, $^3J_{H\text{-}H}$ = 6.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3, 34.0, 32.1, 29.77, 29.74, 29.63, 29.58, 29.3 (m), 28.9, 24.8, 22.8, 14.3 ppm. IR (neat): ν = 2954, 2913, 2870, 2847, 1699, 1471, 1430, 1310, 1296, 941, 720 cm^{-1}. HRMS (ESI$^-$, MeOH) calcd for $C_{16}{}^{13}C_2H_{33}D_2O_2$ $[M-H]^-$ 287.2835, found 287.2813.

V. References

[1] Uesato, S.; Kobayashi, K.; Inouye, H. *Chem. Pharm. Bull.* **1982**, *30*, 927.

[2] Hayes, M. P.; Hatala, P. J.; Sherer, B. A.; Tong, X.; Zanatta, N.; Borer, P. N.; Kallmerten, J. *Tetrahedron* **2001**, *57*, 1515.

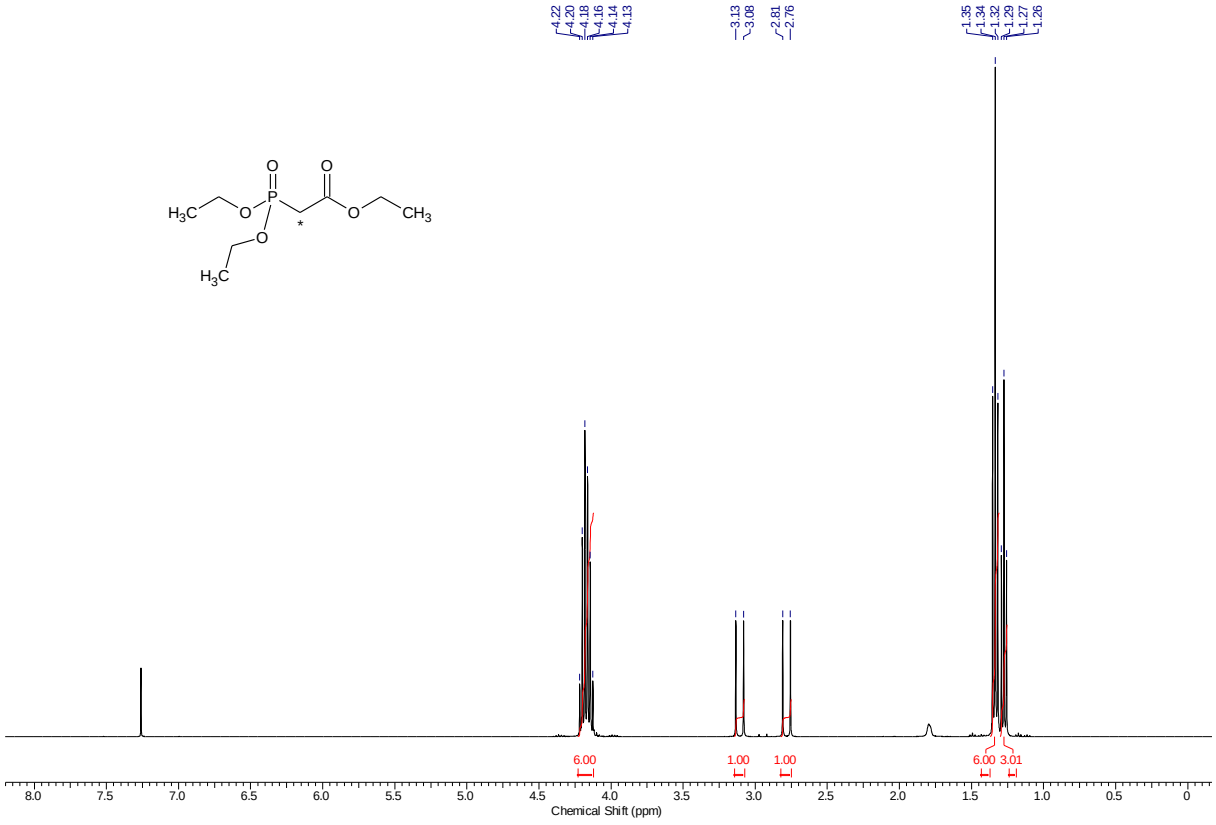
[3] Bock, P. L.; Boschetto, D. M.; Rasmussen, J. R. Demers, J. P.; Whitesides, G .M. *J. Am. Chem. Soc.* **1974**, *96*, 2814.

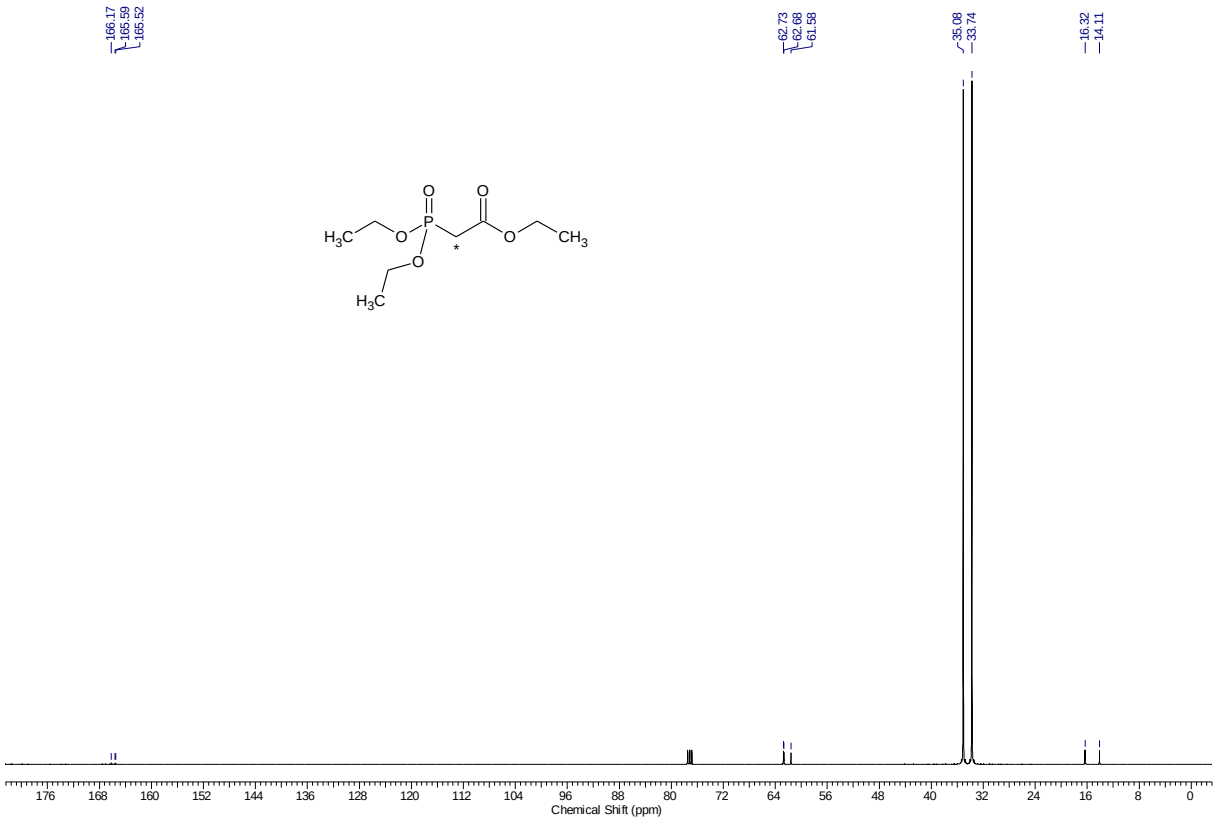
[4] Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.

VI. NMR spectra of labeled compounds

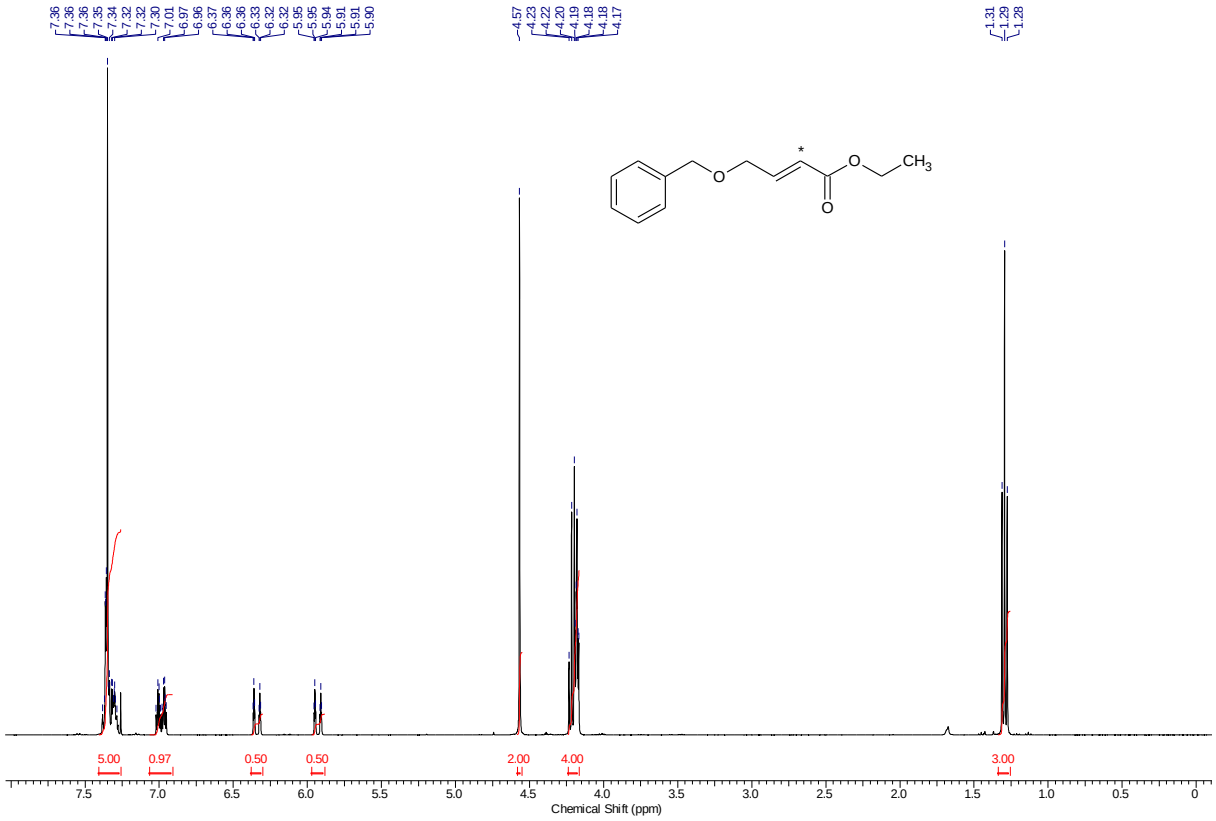
Synthesis of the common synthons 10 and 11

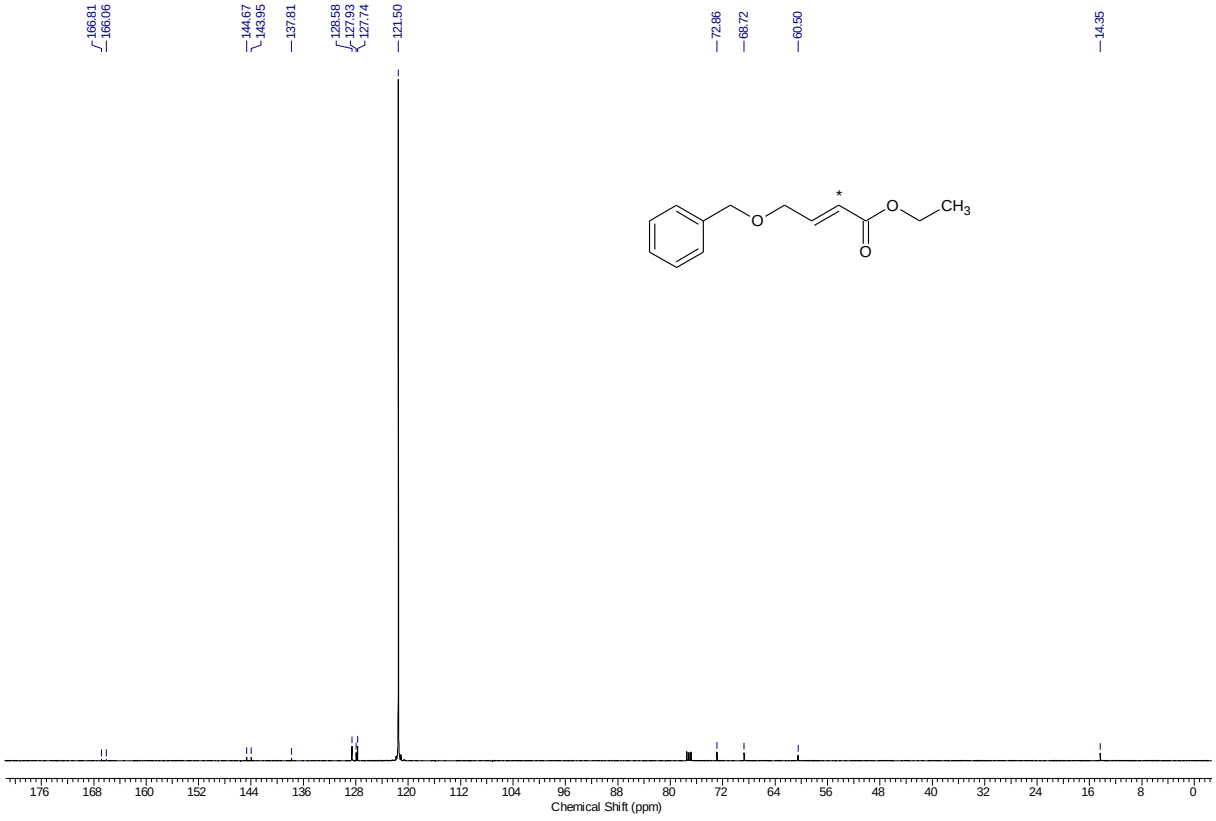
Ethyl [2-^{13}C]-2-(diethylphosphono)acetate **2**



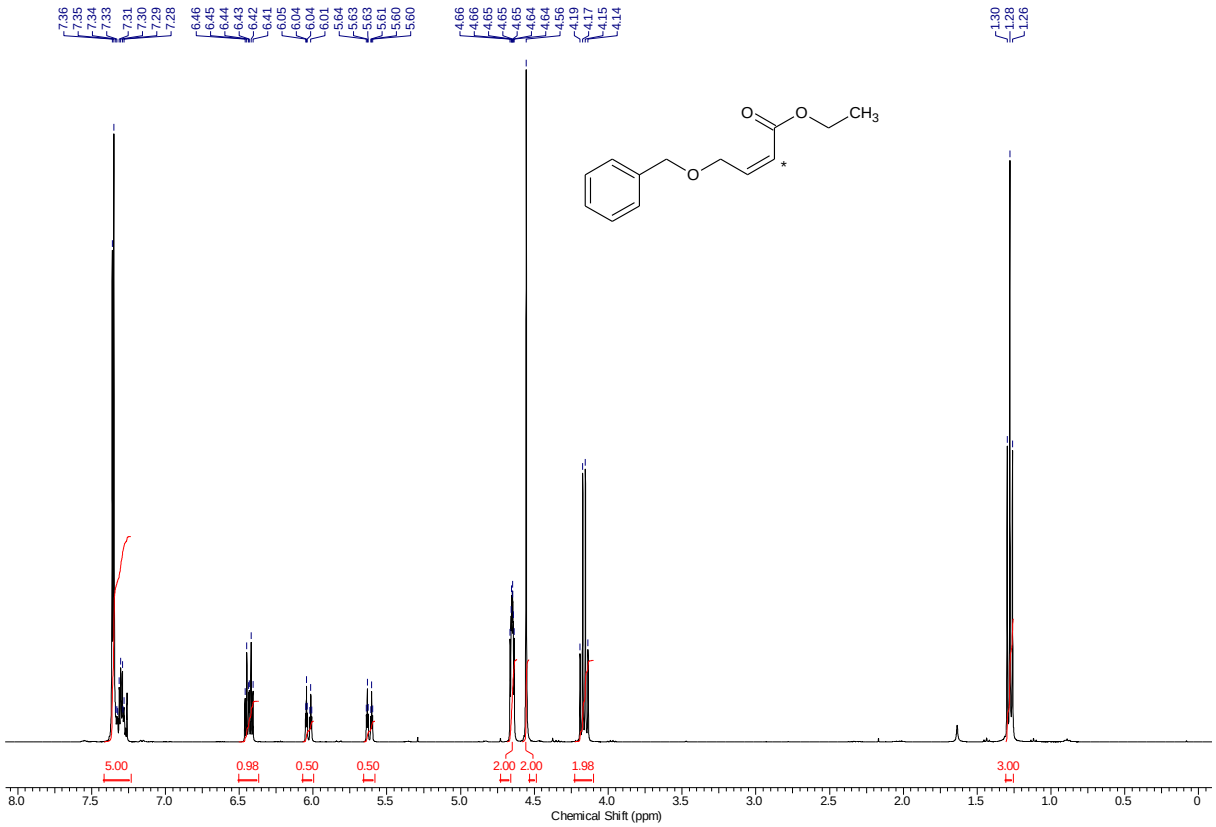


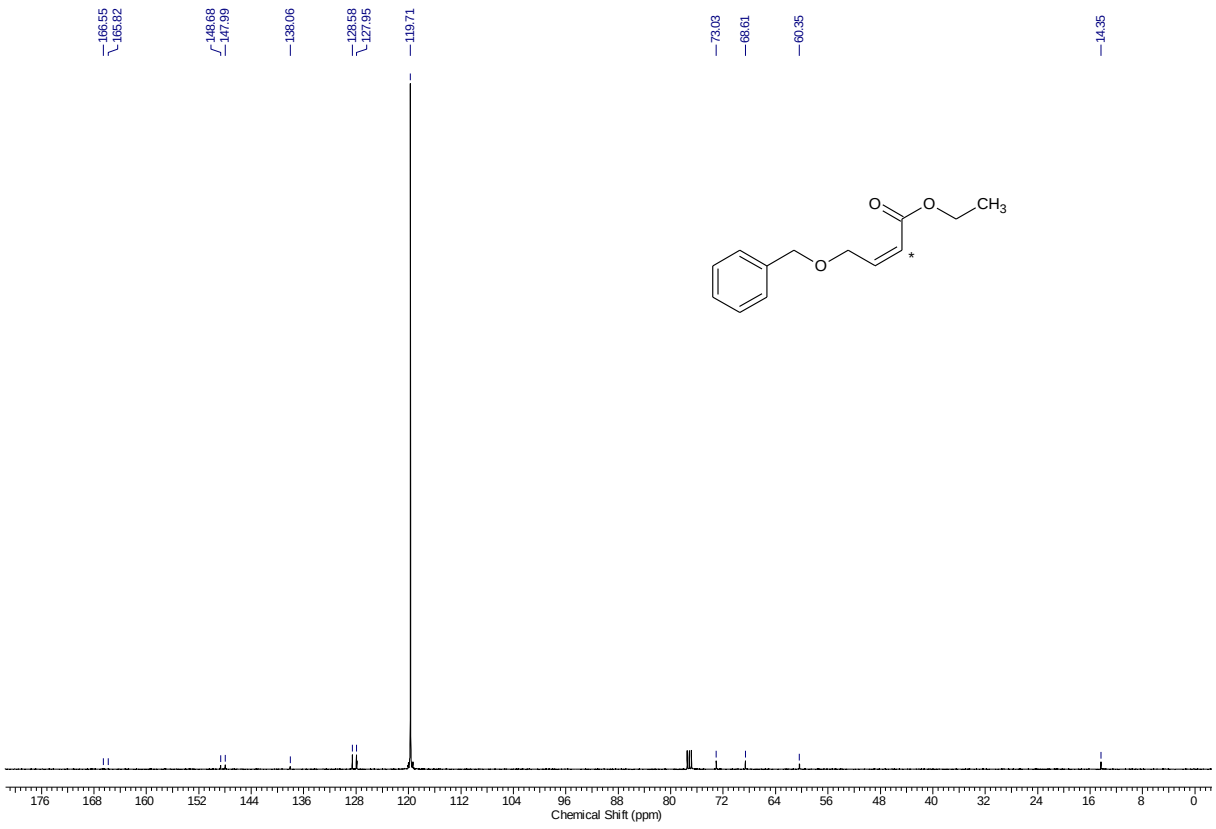
Ethyl [2-^{13}C]-4-(benzyloxy)but-2-enoate **(*E*)-3**



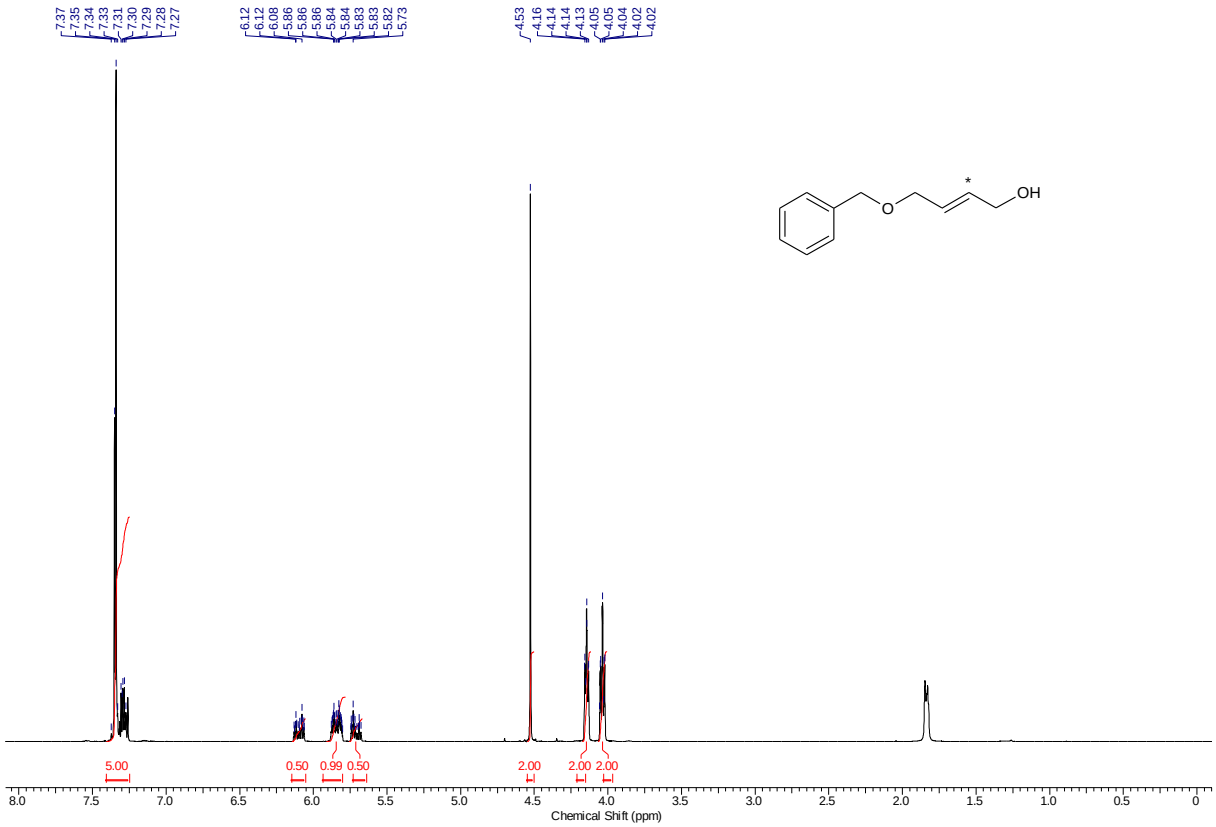


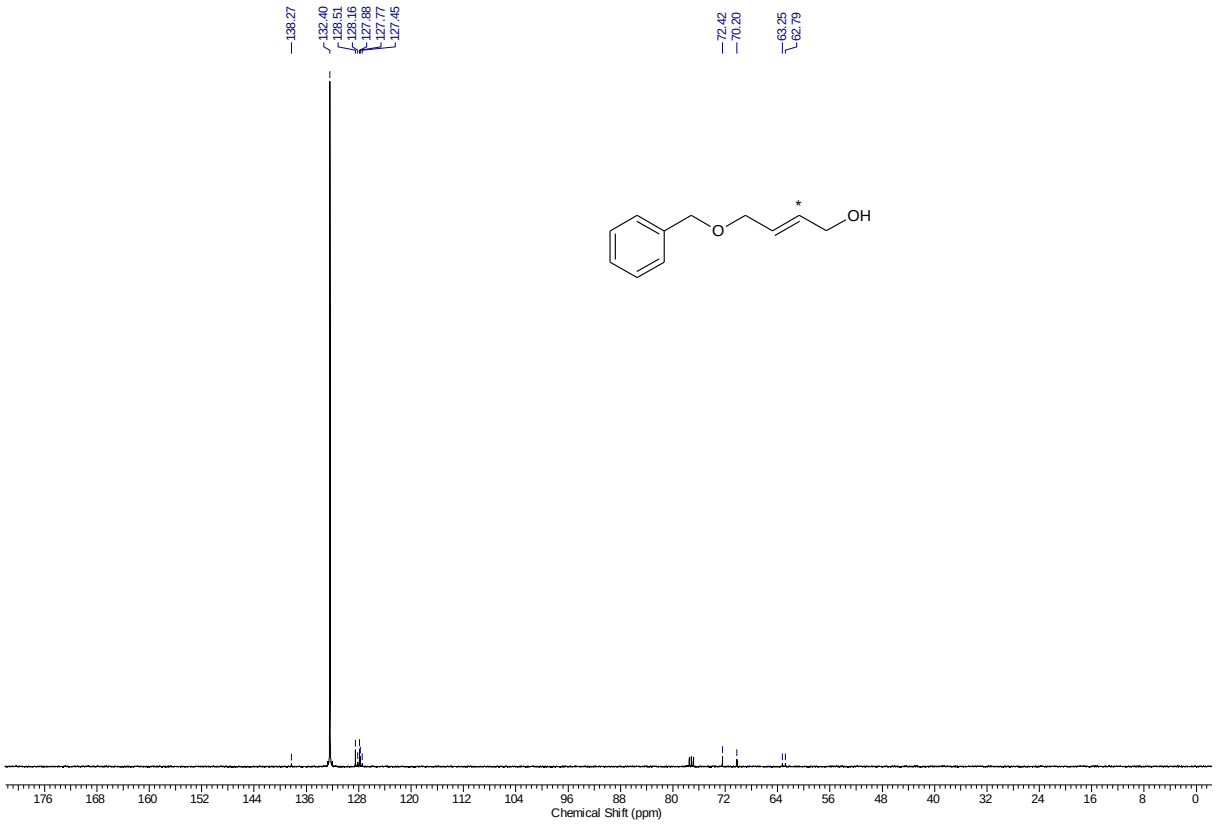
Ethyl [2-^{13}C]-4-(benzyloxy)but-2-enoate **(*Z*)-3**



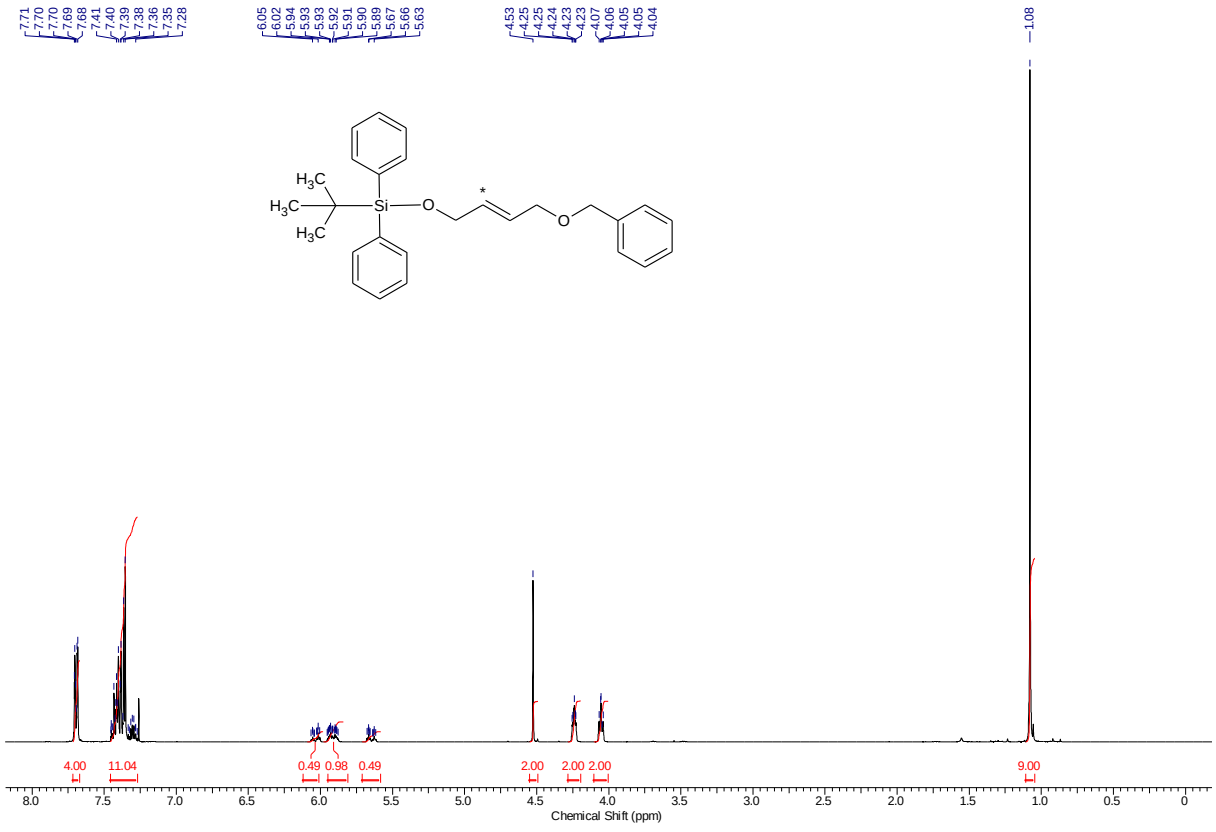


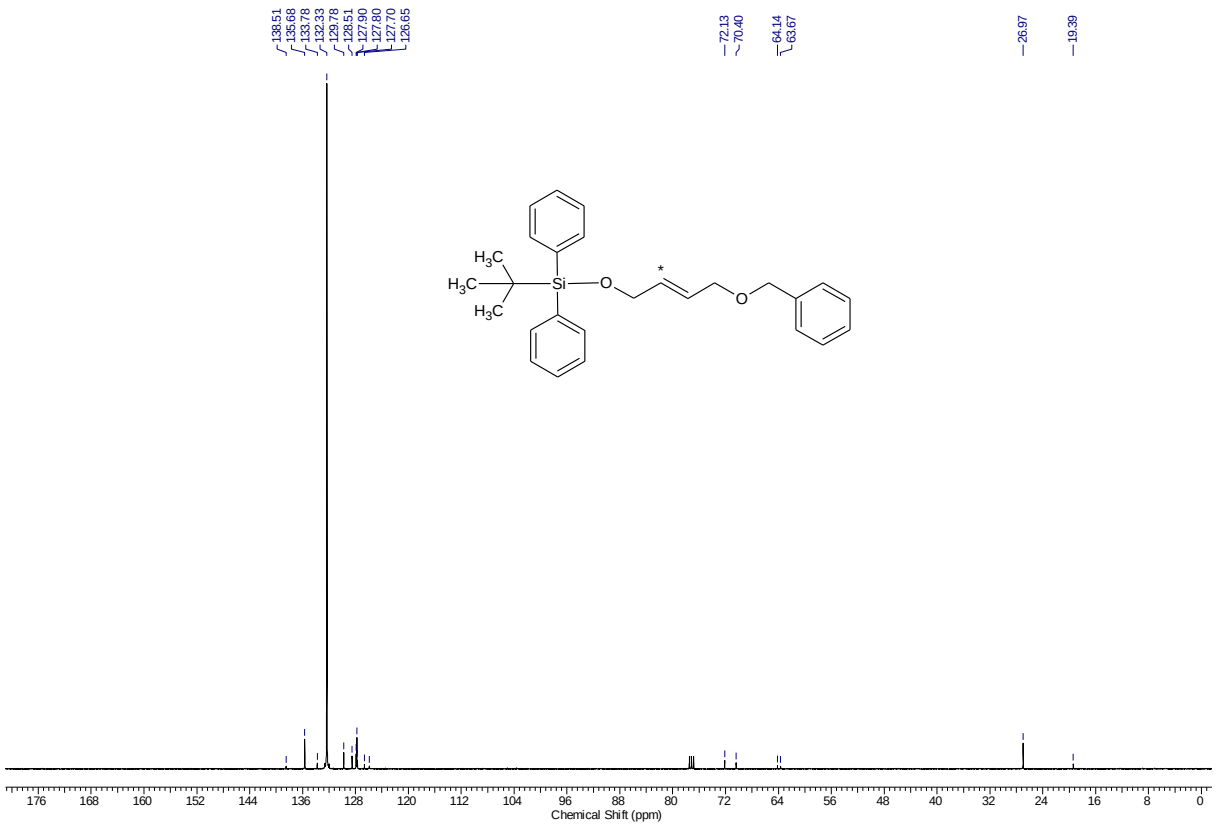
(E)-[2-^{13}C]-4-(benzyloxy)but-2-en-1-ol **4**



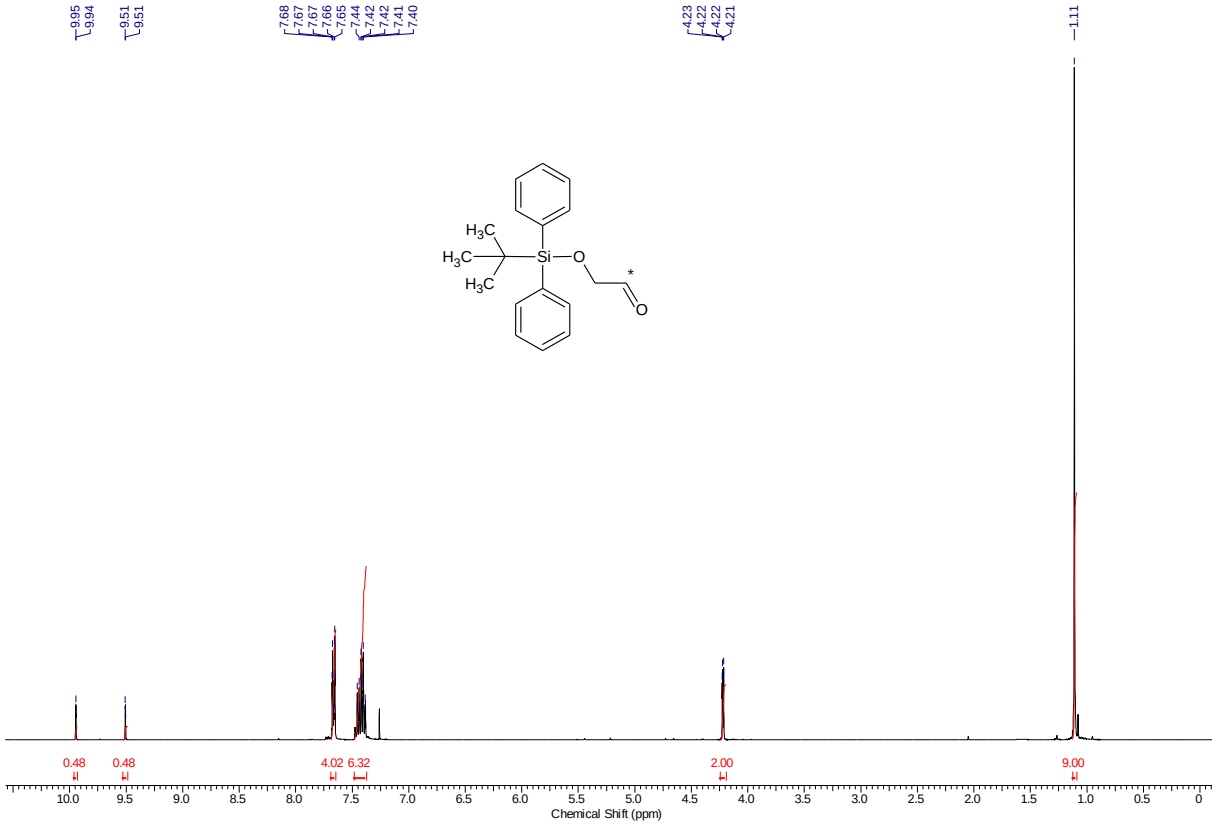


(E)-[2-^{13}C]-((4-(benzyloxy)but-2-en-1-yl)oxy)(tert-butyl)diphenylsilane **5**

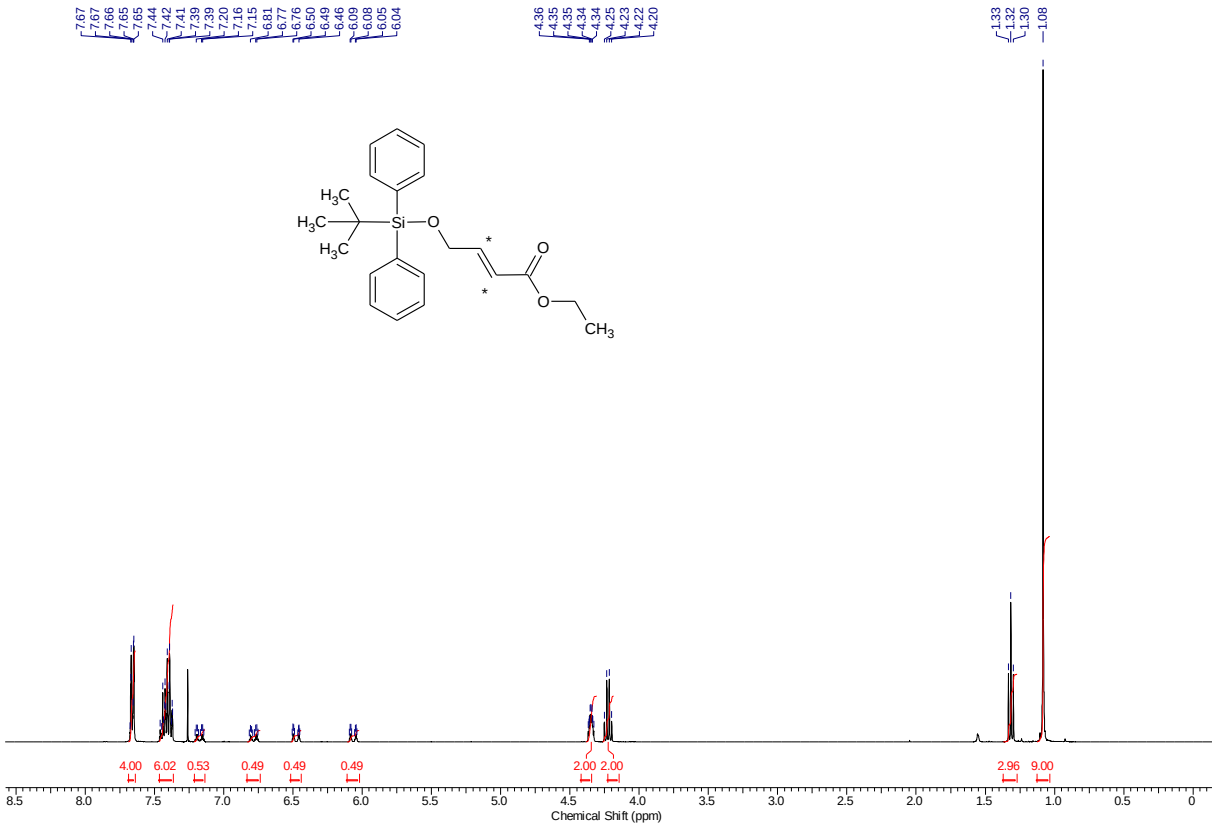


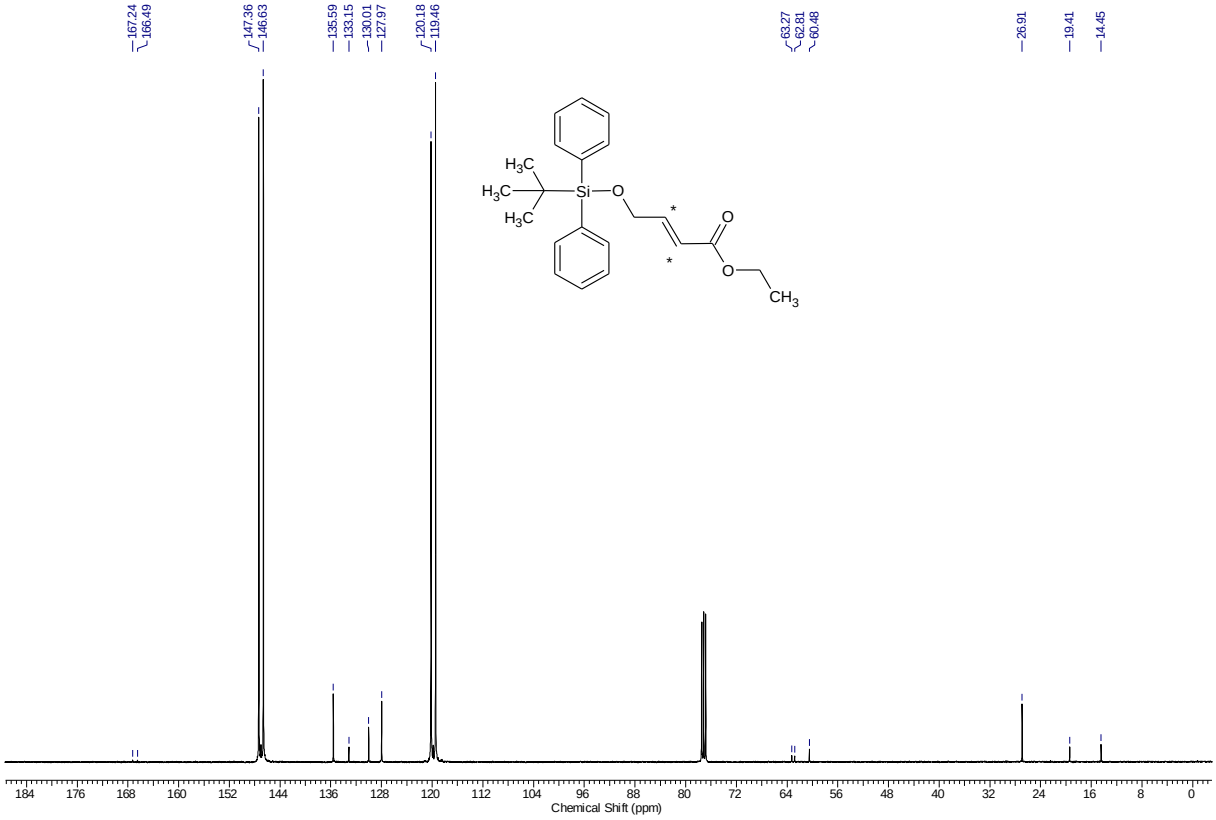


[1-^{13}C]-2-((tert-butyldiphenylsilyl)oxy)acetaldehyde **6**

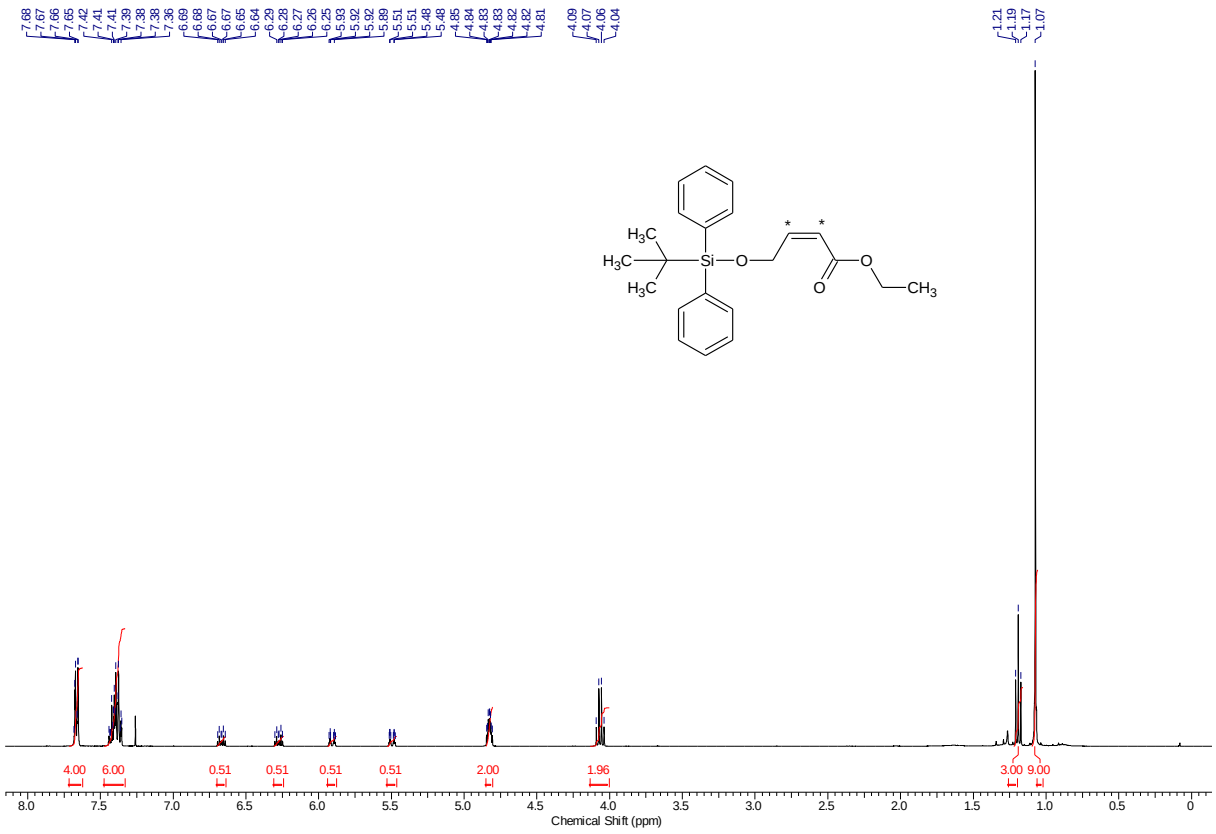


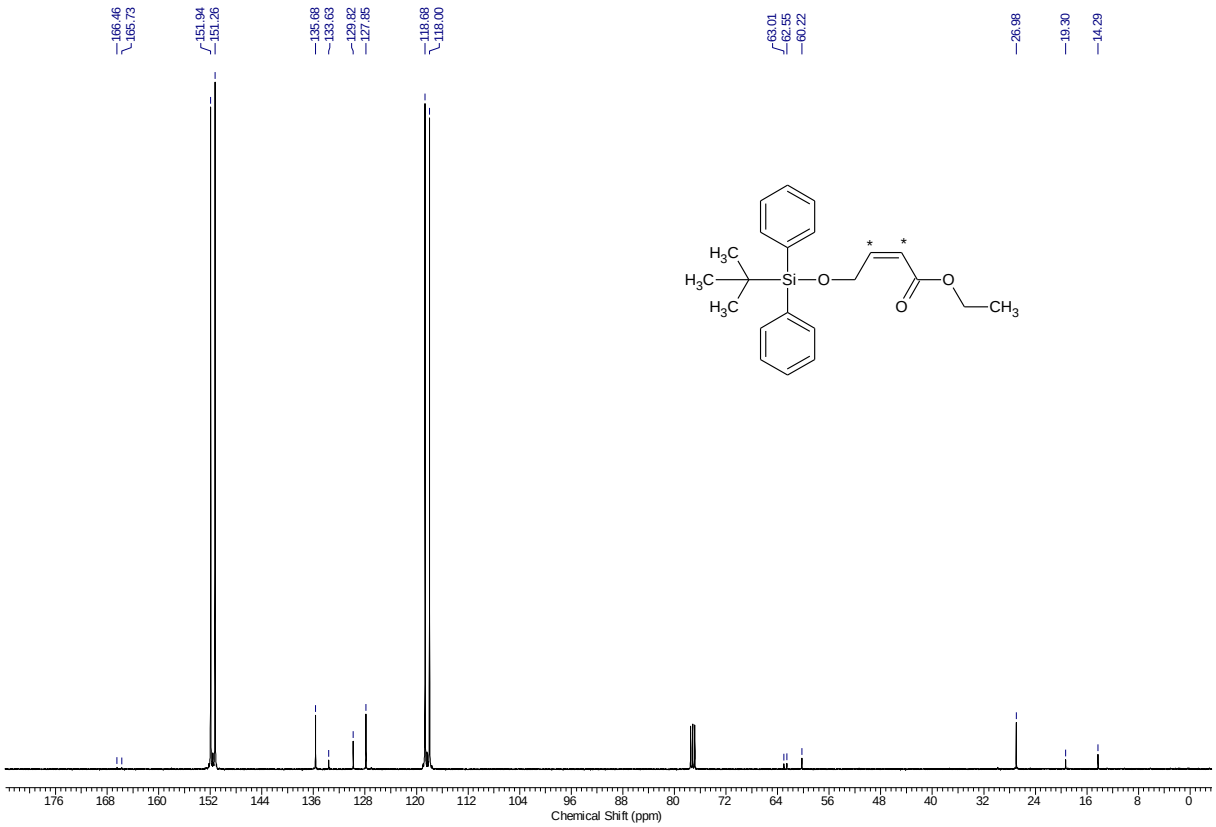
Ethyl [2,3-$^{13}C_2$]-4-((tert-butyldiphenylsilyl)oxy)but-2-enoate **(*E*)-7**



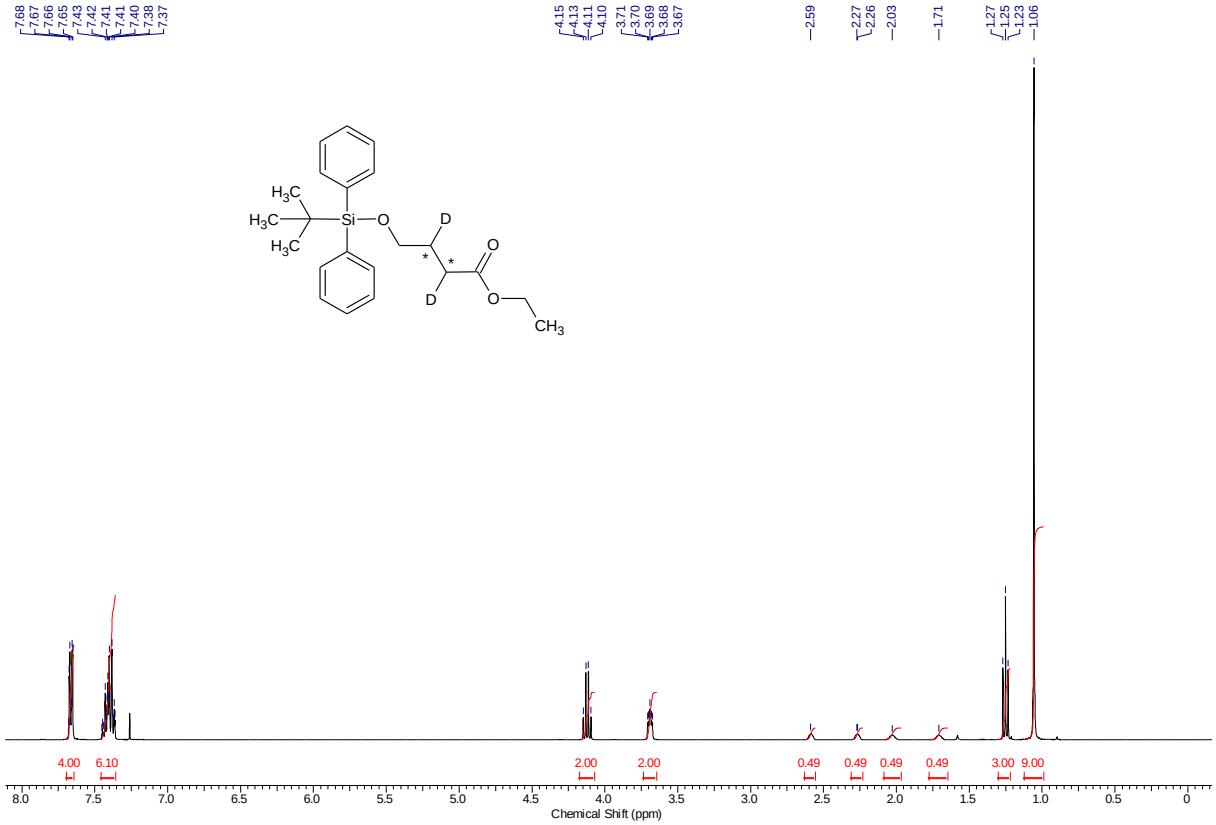


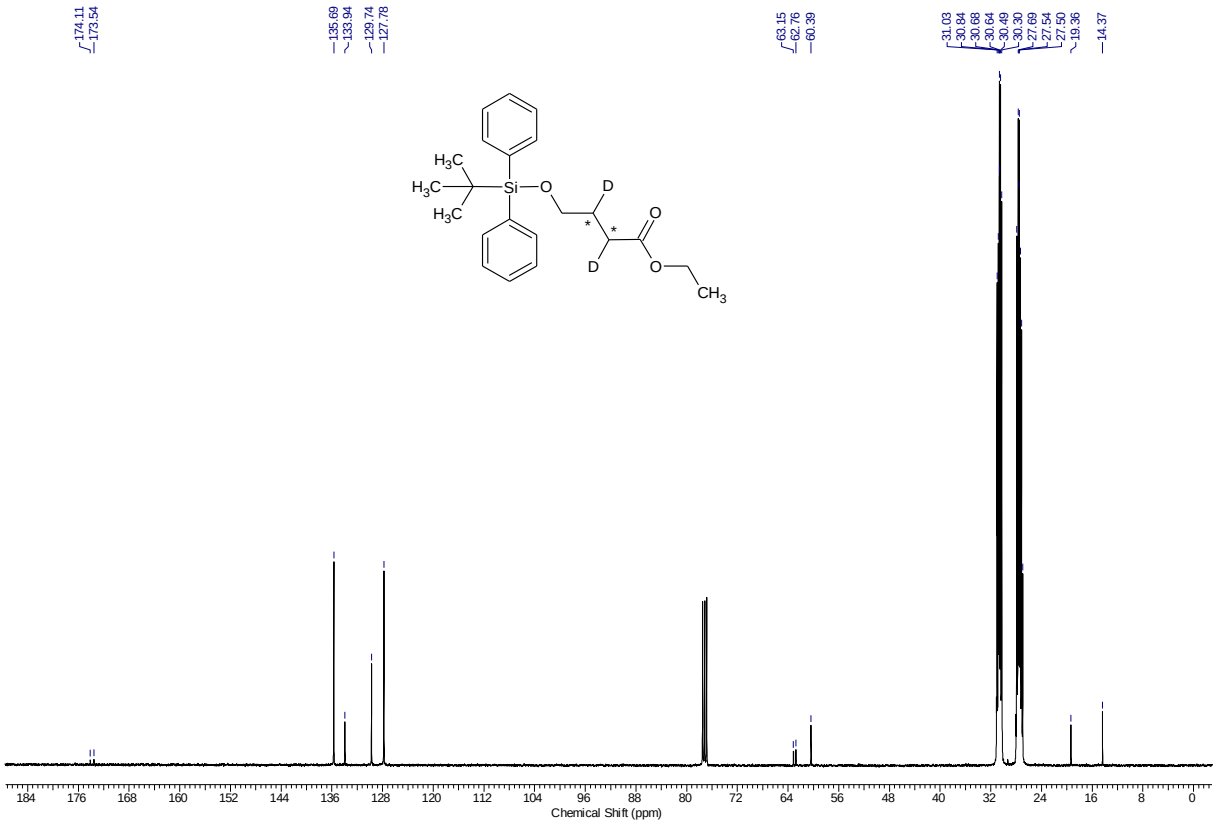
Ethyl [2,3-$^{13}C_2$]-4-((tert-butyldiphenylsilyl)oxy)but-2-enoate **(*Z*)-7**



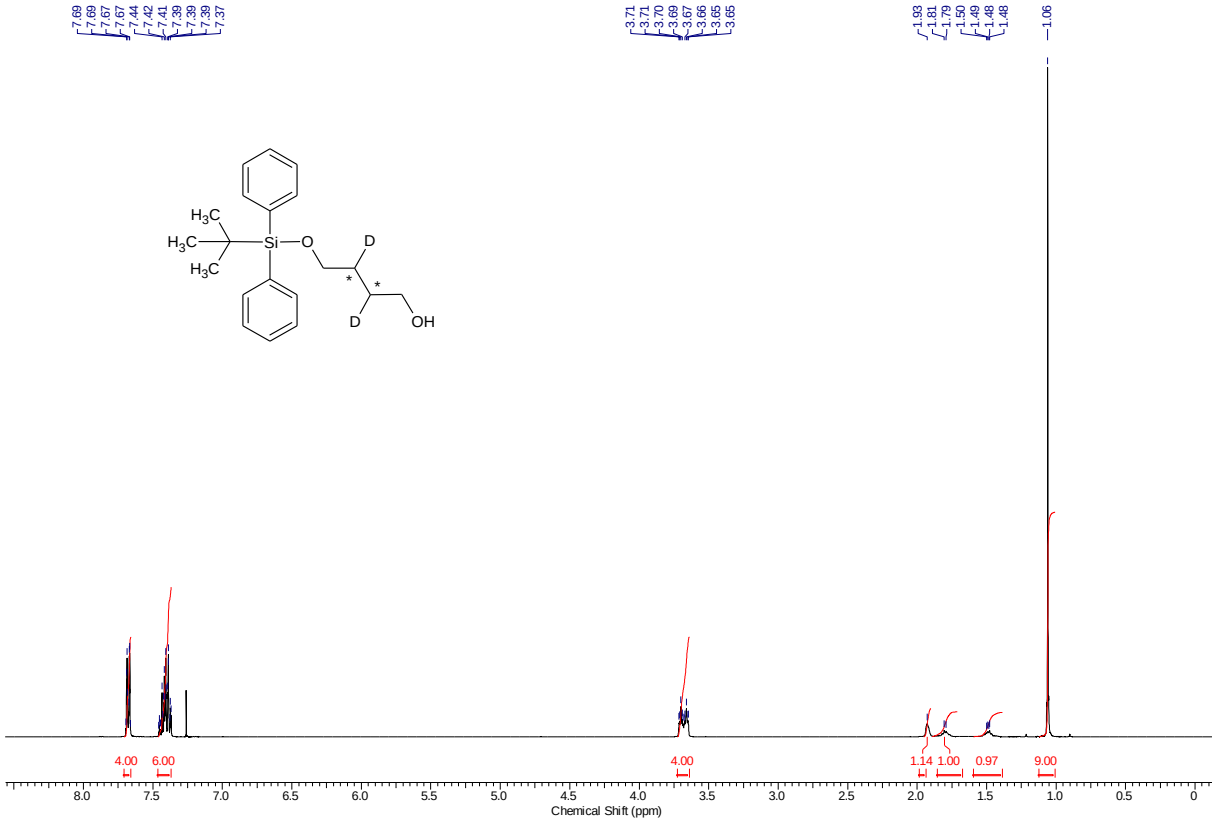


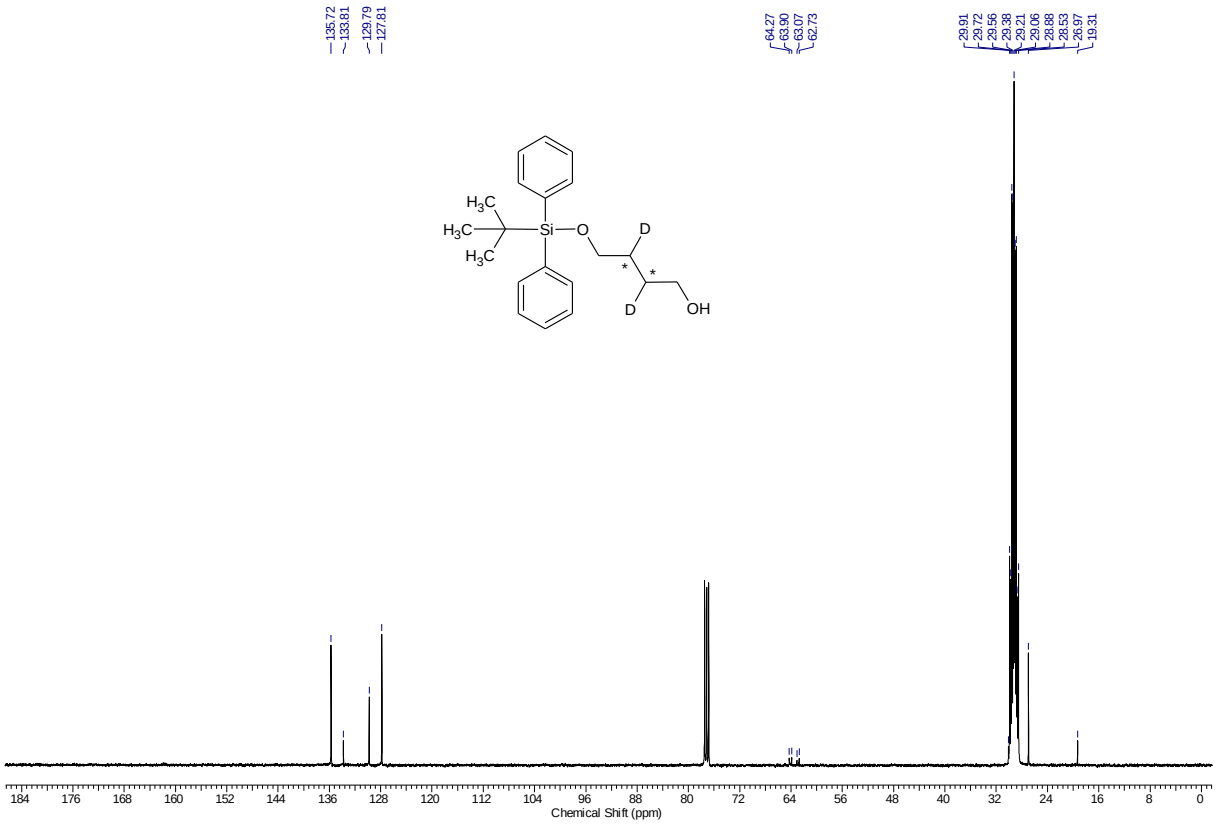
Ethyl [2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butanoate **8**



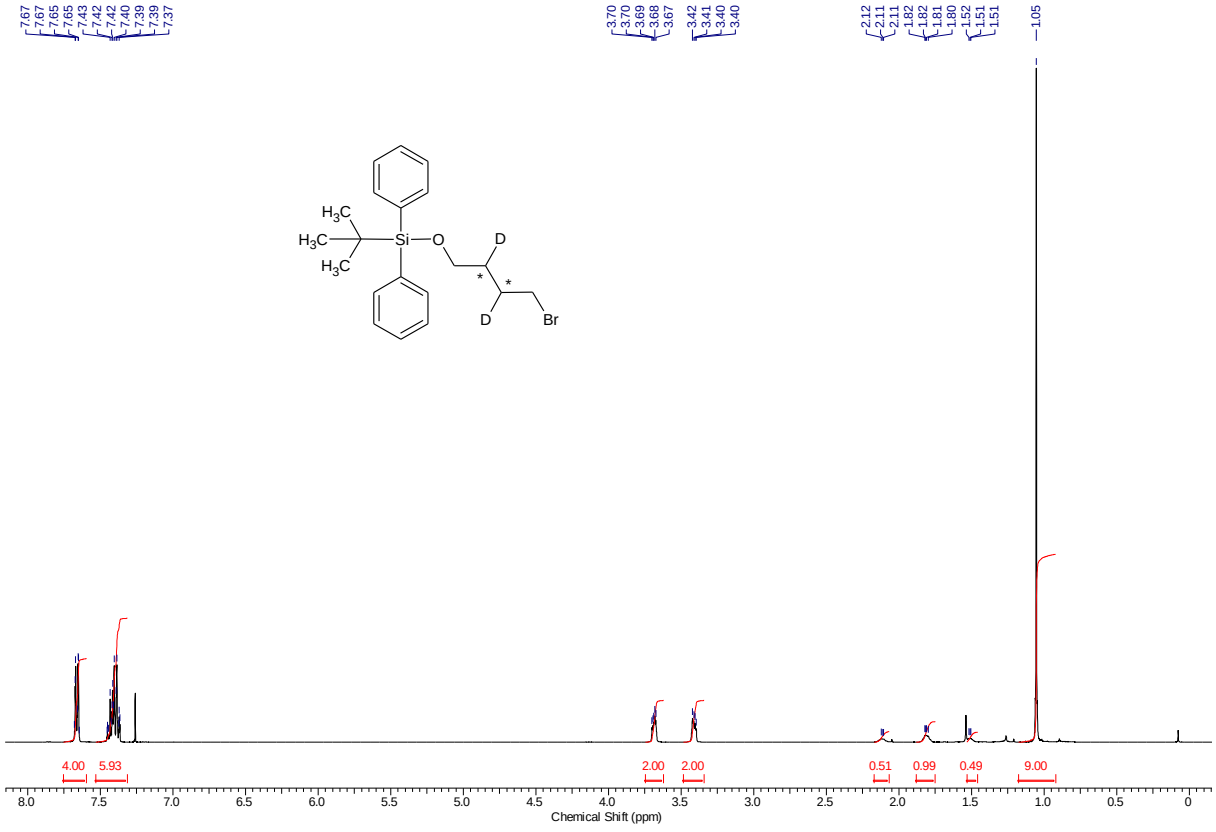


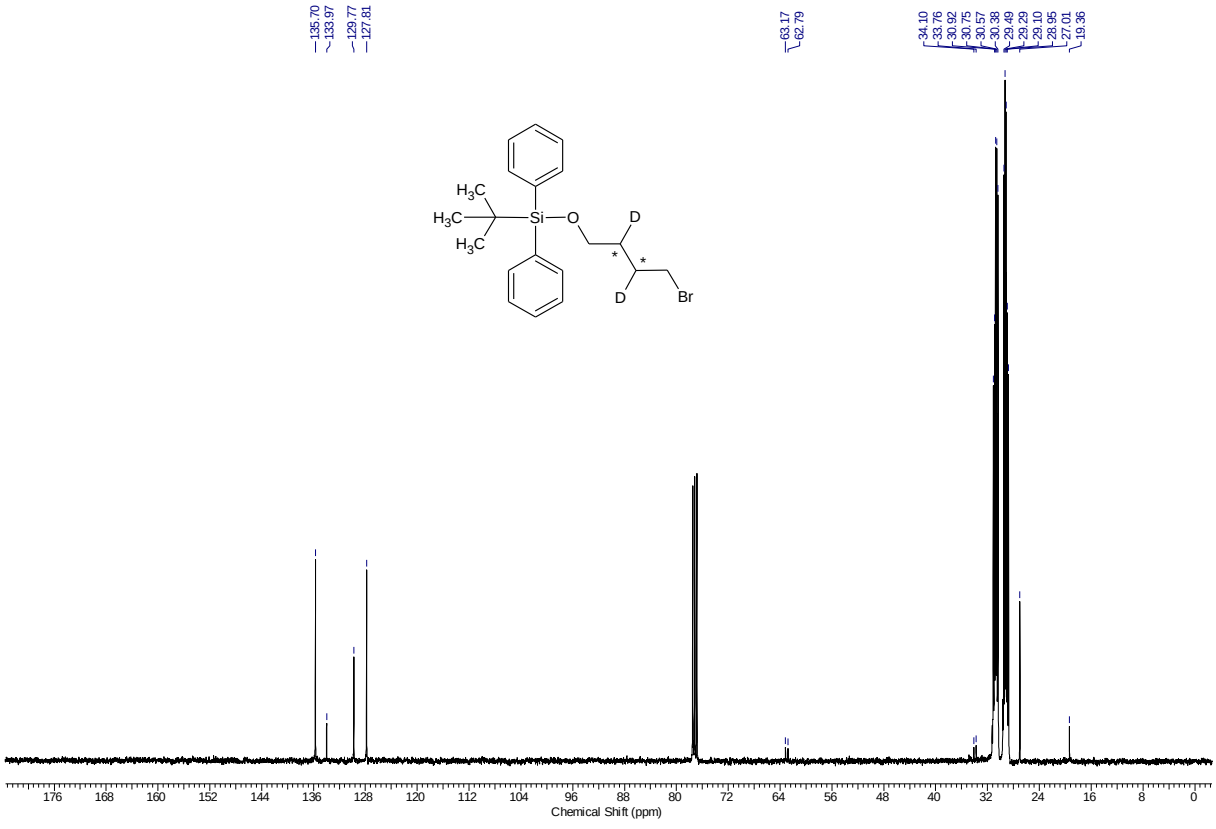
[2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butan-1-ol **9**



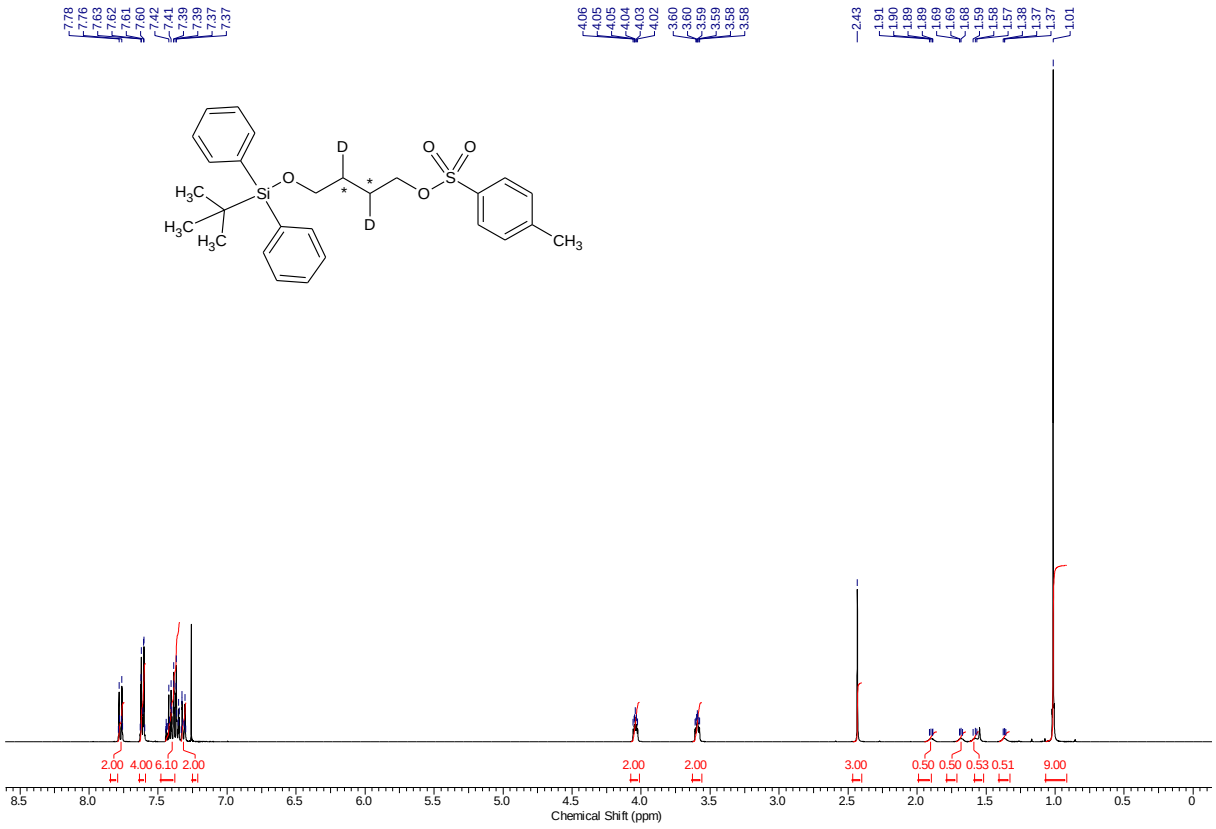


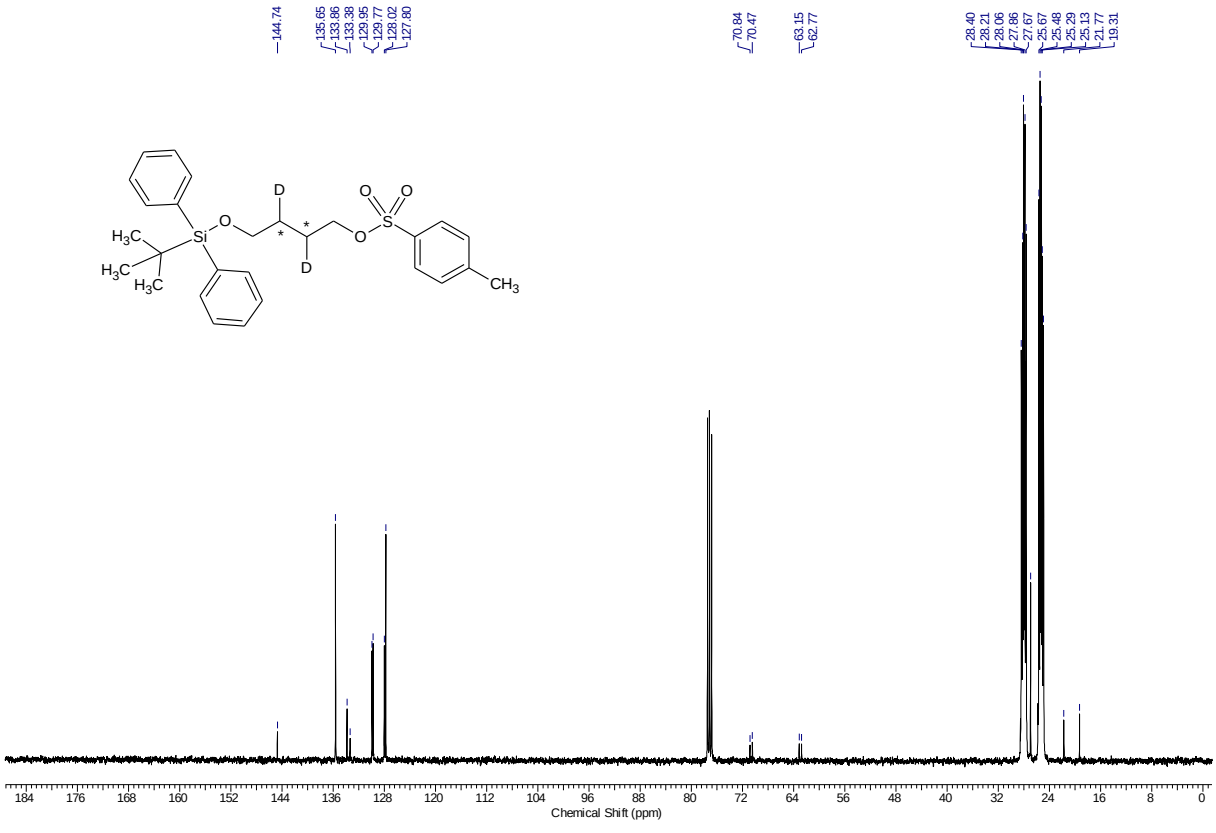
[2,3-$^{13}C_2$-2,3-D_2]-(4-bromobutoxy)(tert-butyl)diphenylsilane **10**





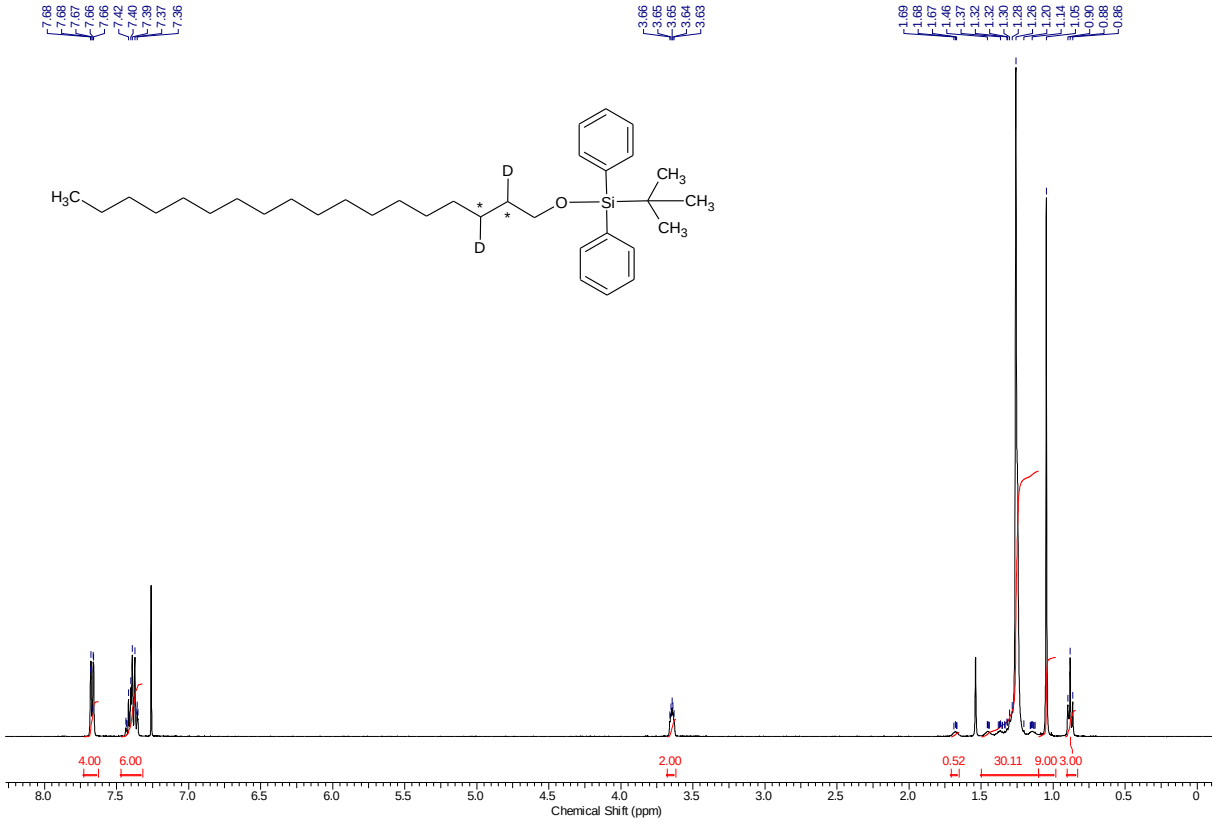
[2,3-$^{13}C_2$-2,3-D_2]-4-((tert-butyldiphenylsilyl)oxy)butyl 4-methylbenzenesulfonate **11**

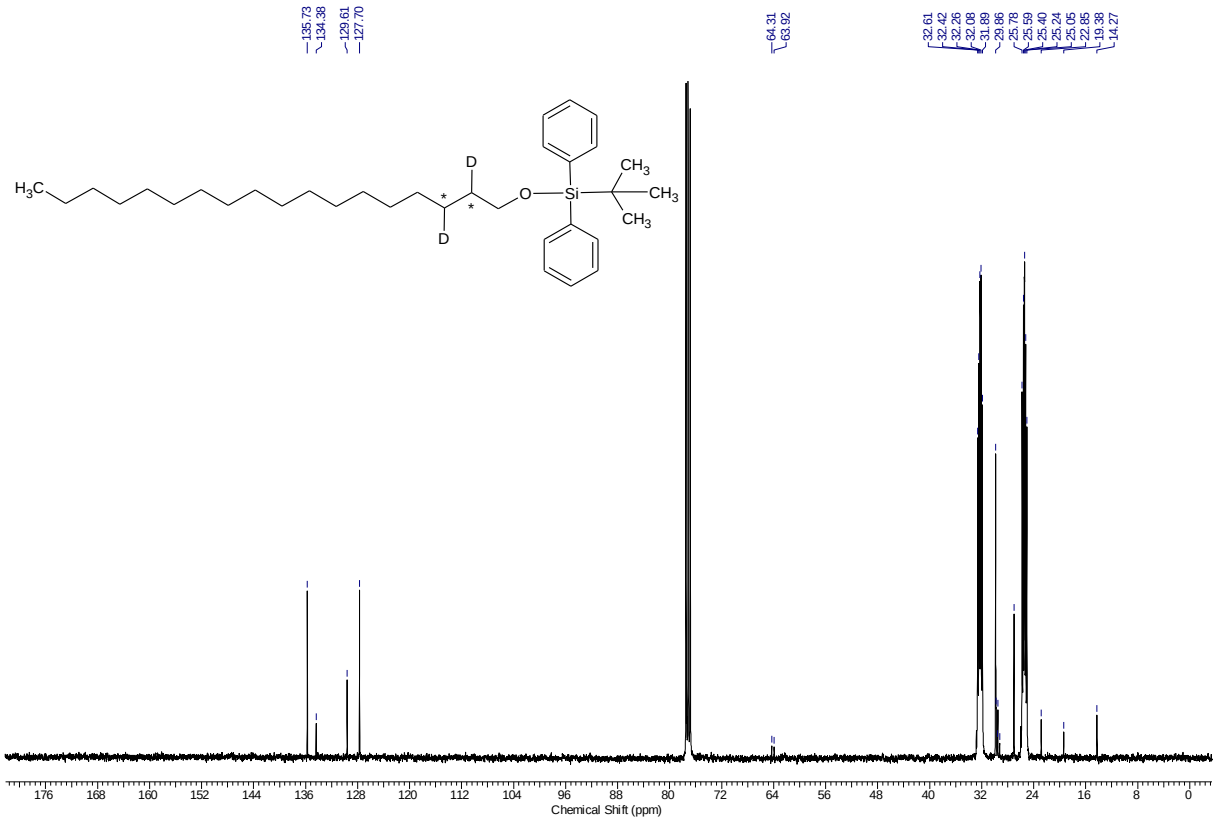




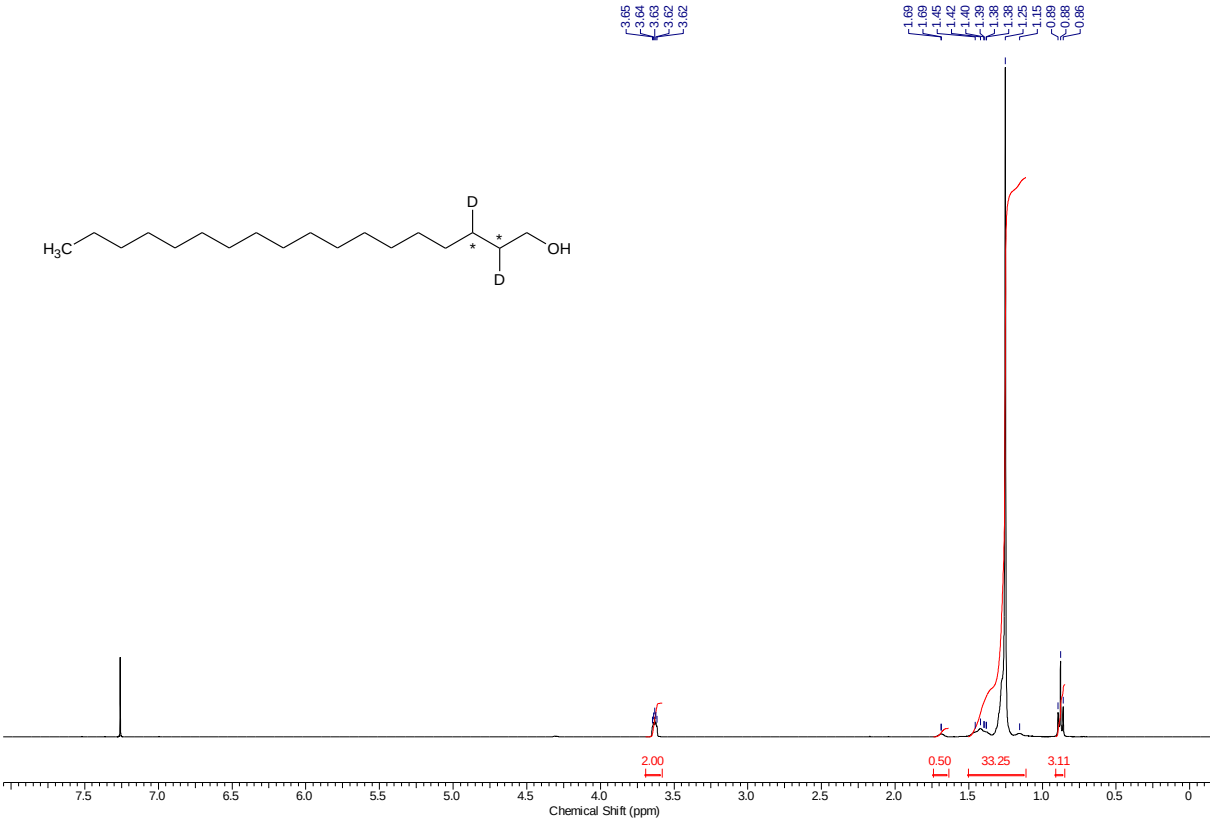
2,3-labeled positions

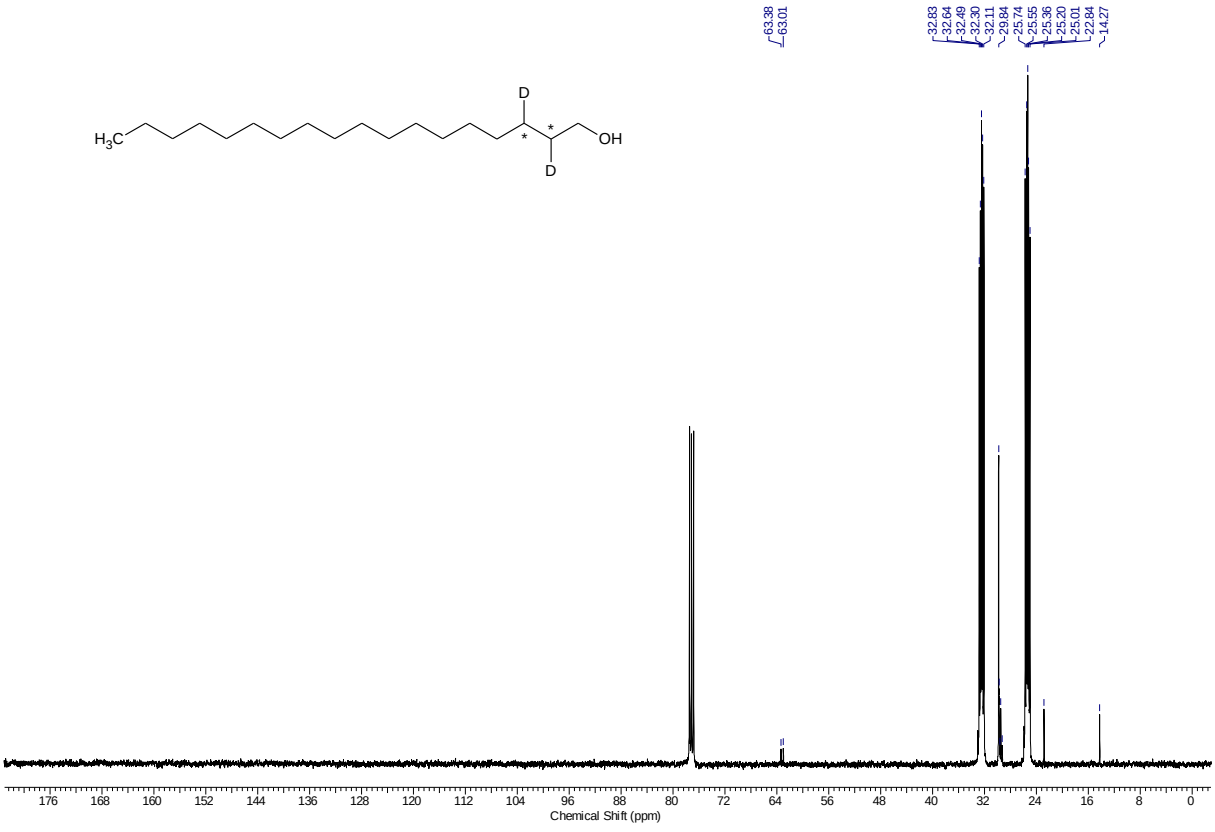
[2,3-$^{13}C_2$-2,3-D_2]-tert-butyl(octadecyloxy)diphenylsilane **13**



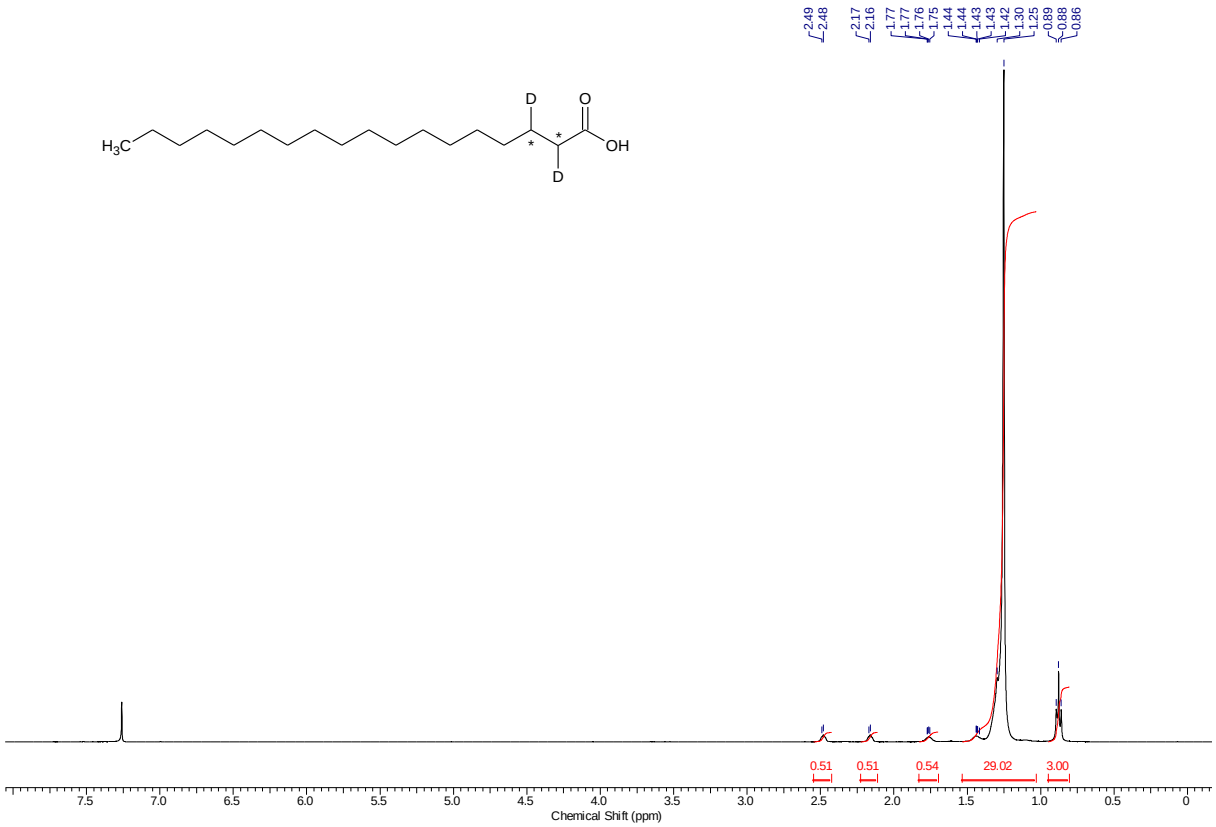


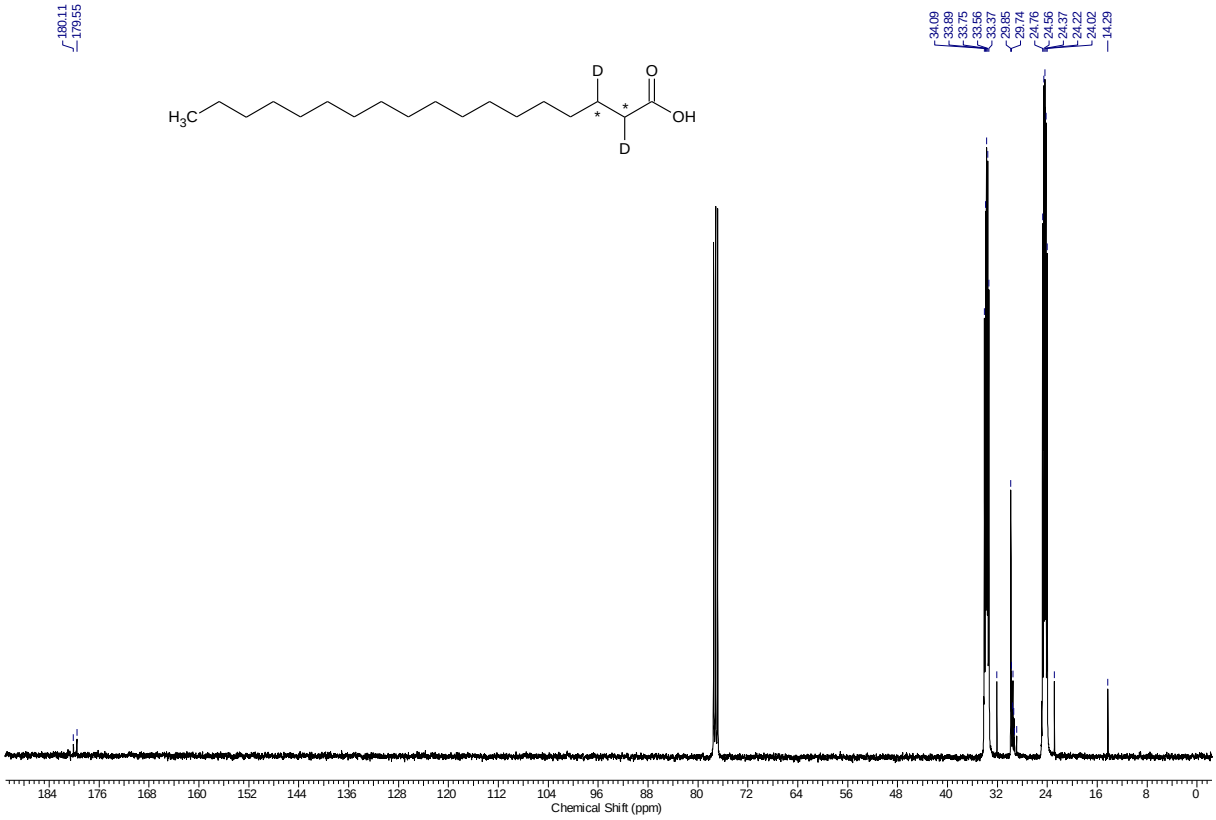
[2,3-$^{13}C_2$-2,3-D_2]-stearyl alcohol **14**





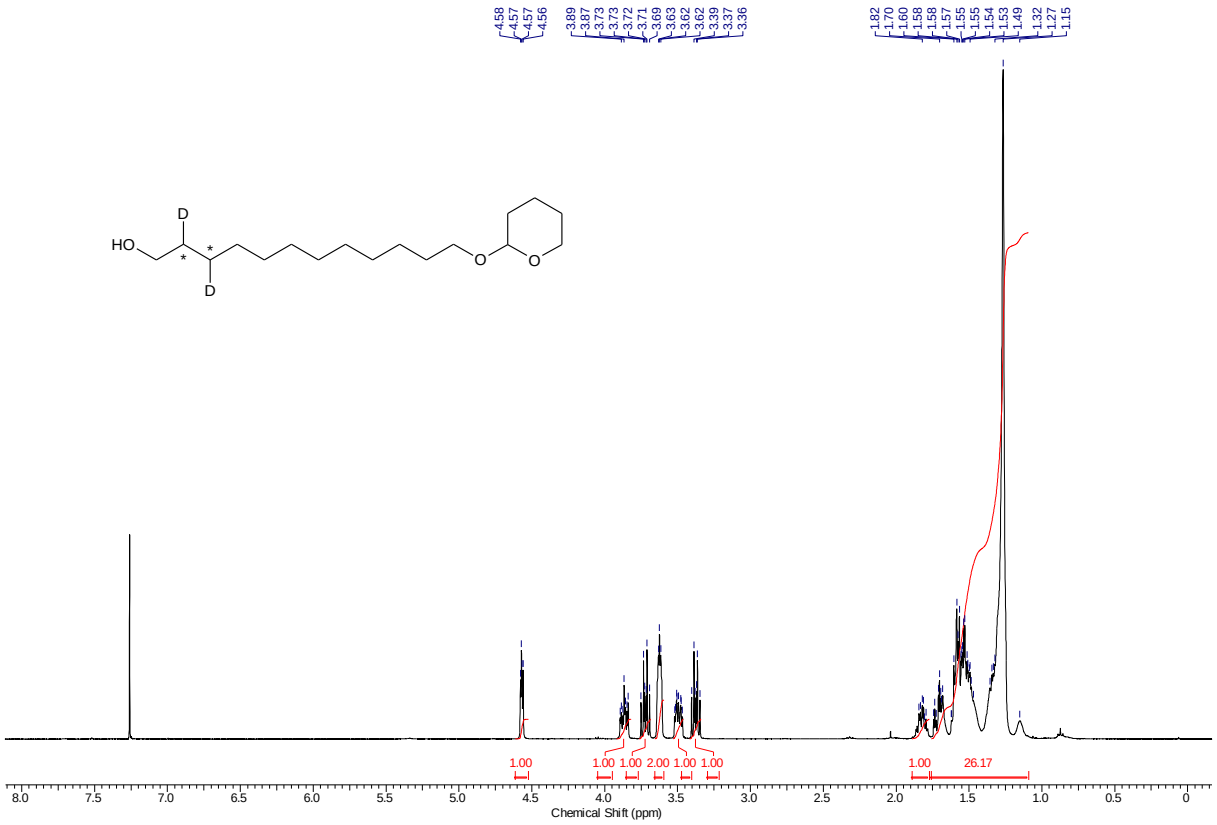
[2,3-$^{13}C_2$-2,3-D_2]-stearic acid **15**

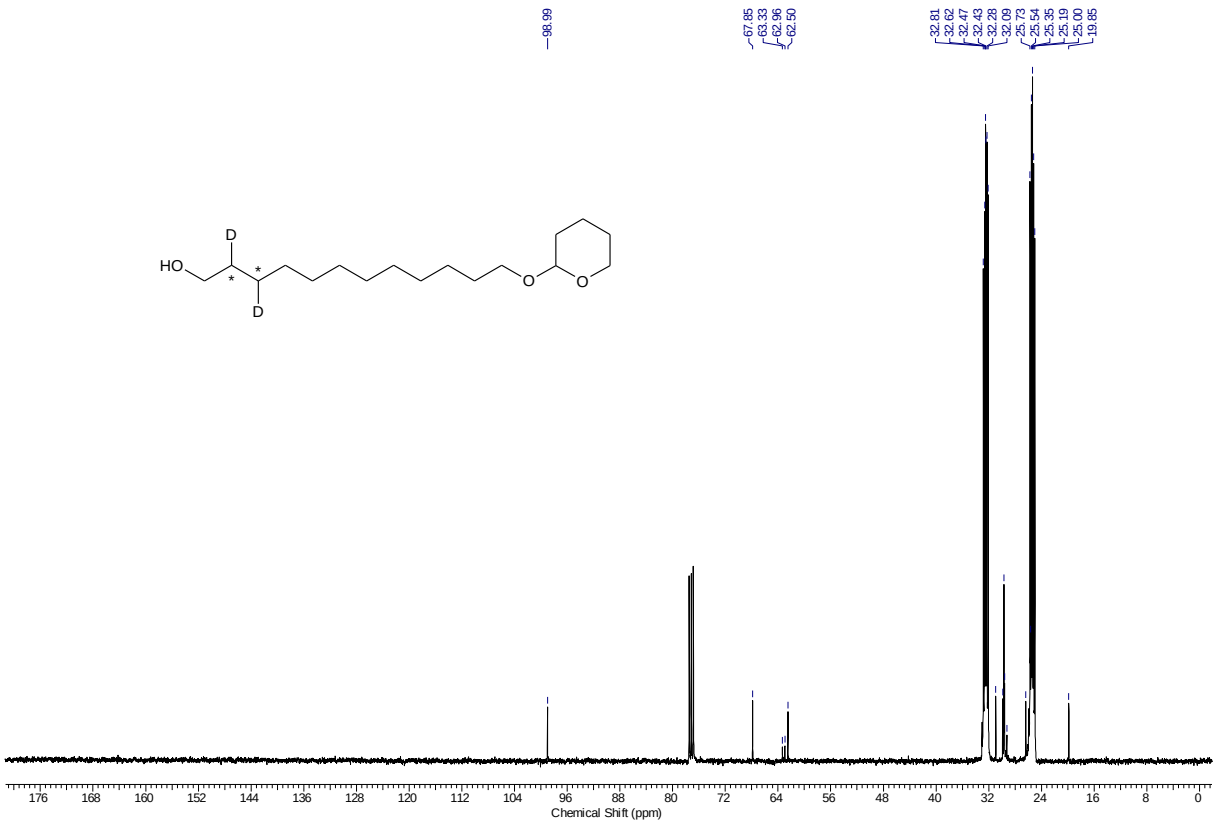




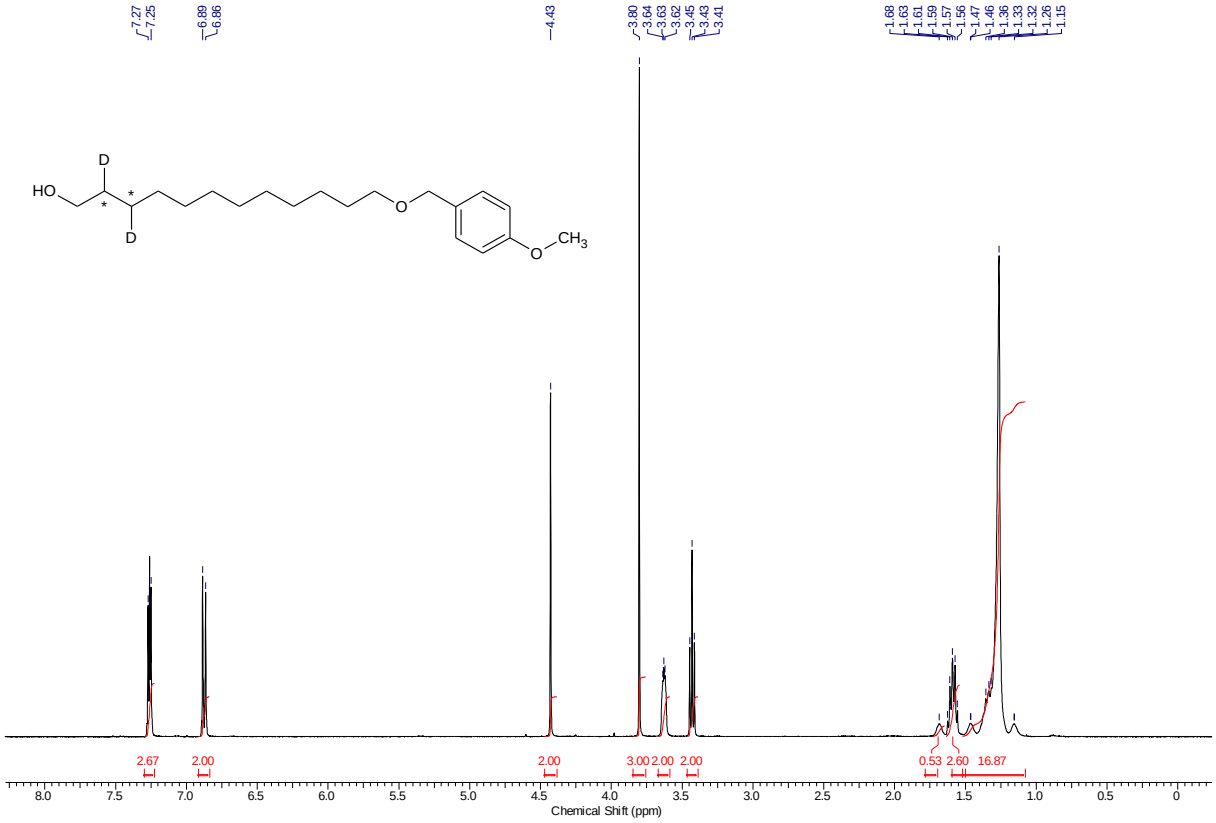
With different protecting groups

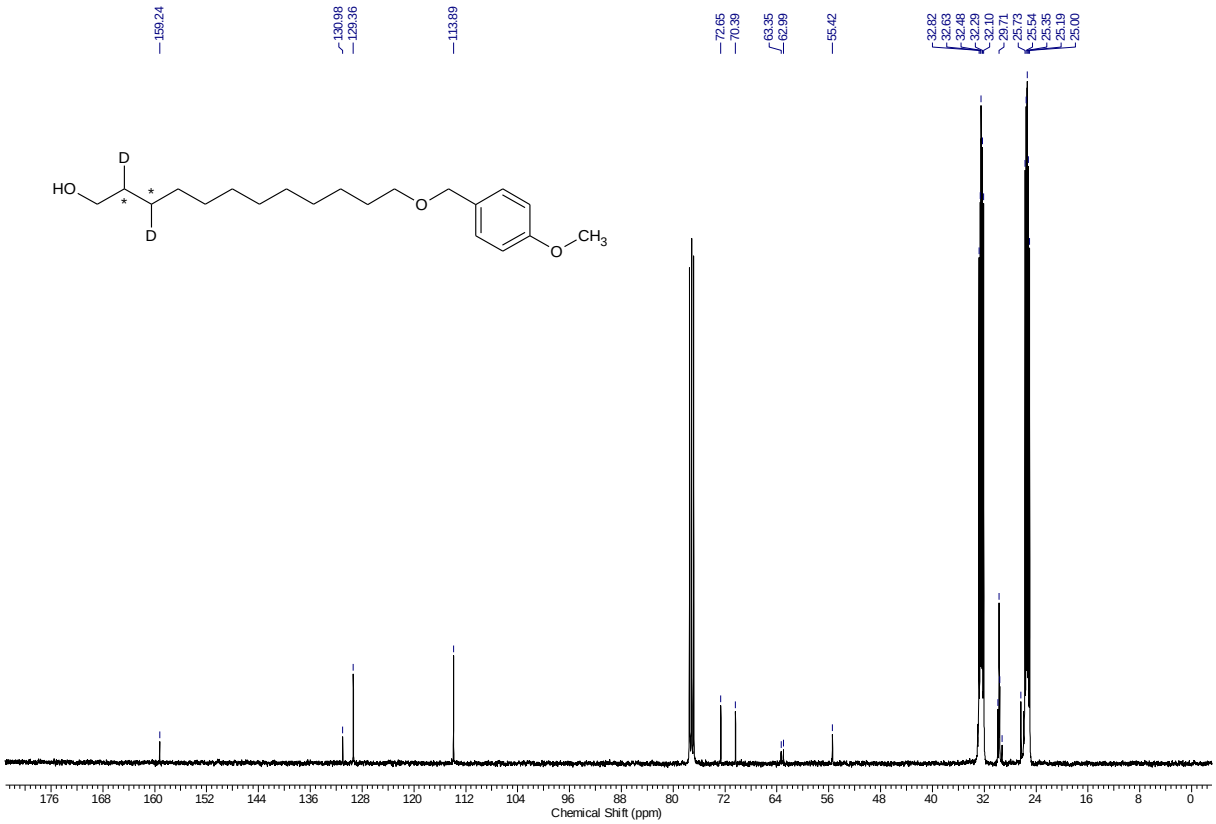
[2,3-$^{13}C_2$-2,3-D_2]- 12-((tetrahydro-*2H*-pyran-2-yl)oxy)dodecan-1-ol **16**





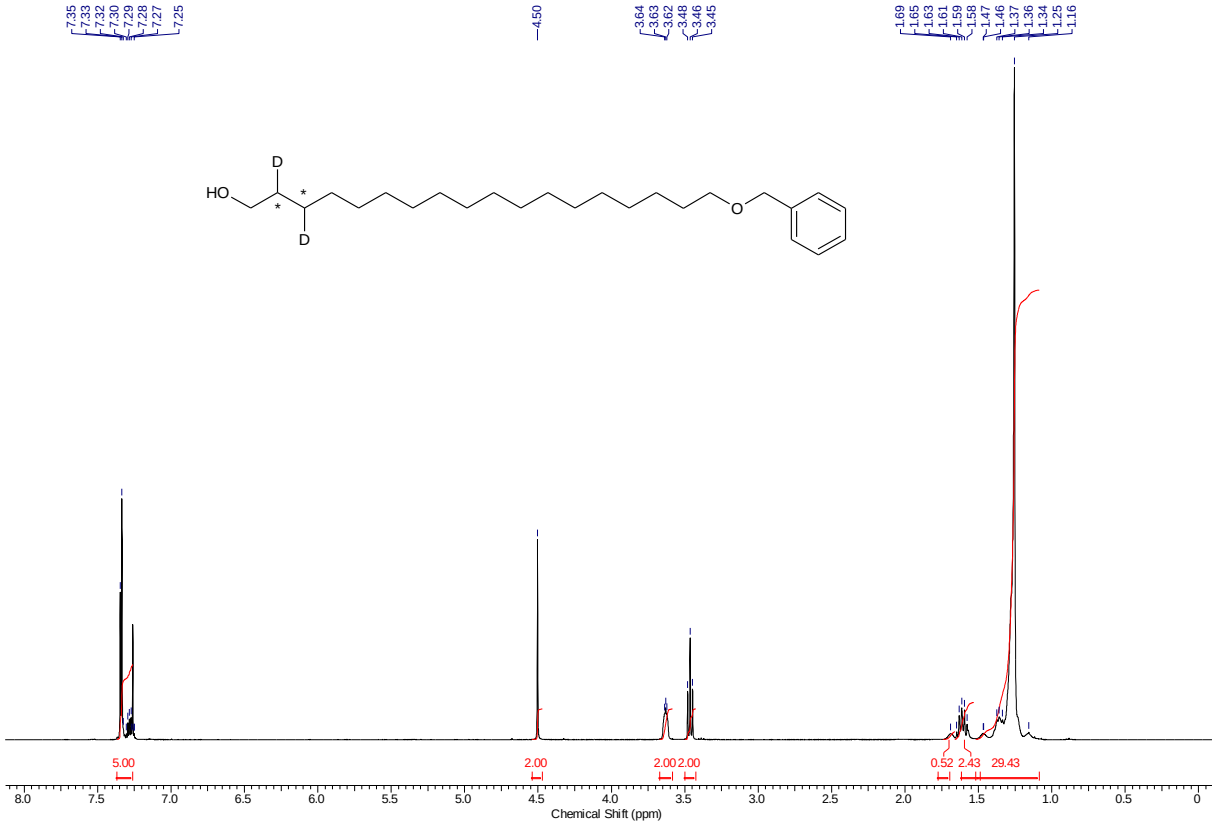
[2,3-$^{13}C_2$-2,3-D_2]- 12-((4-methoxybenzyl)oxy)dodecan-1-ol **17**

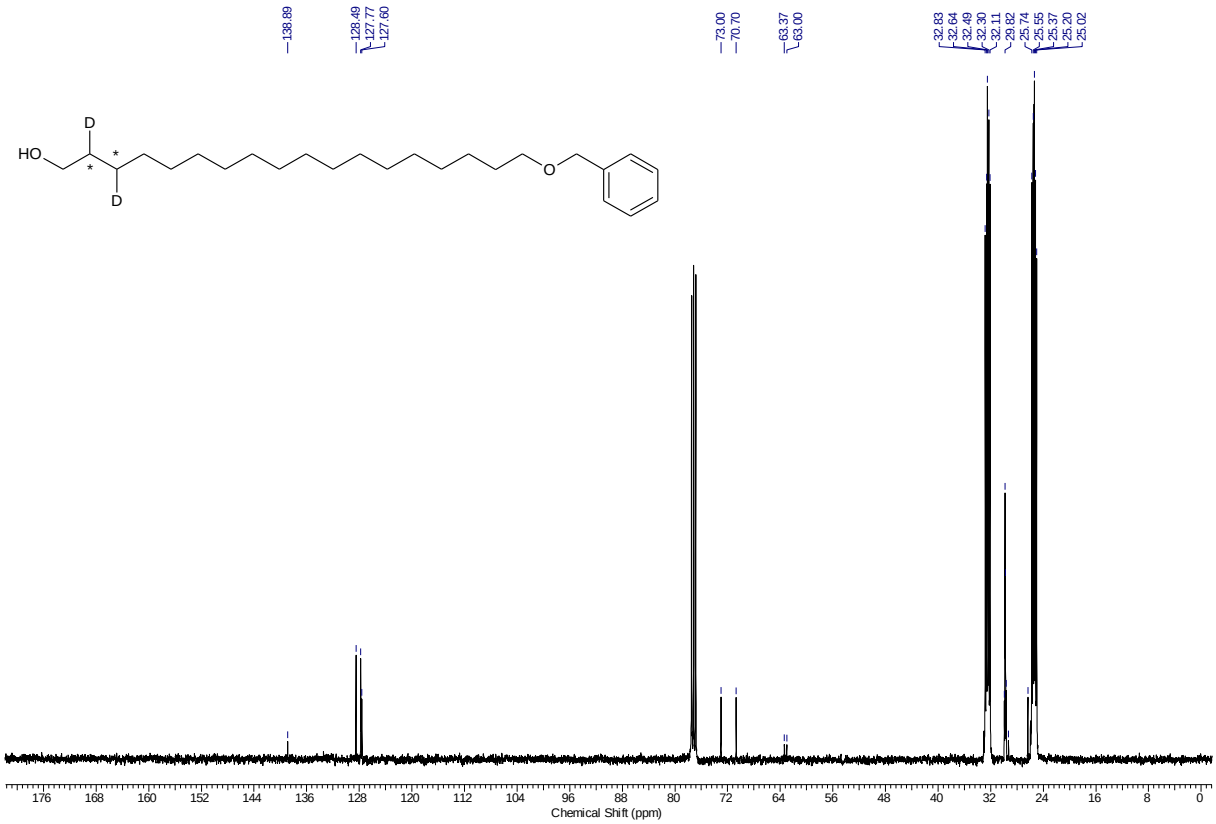




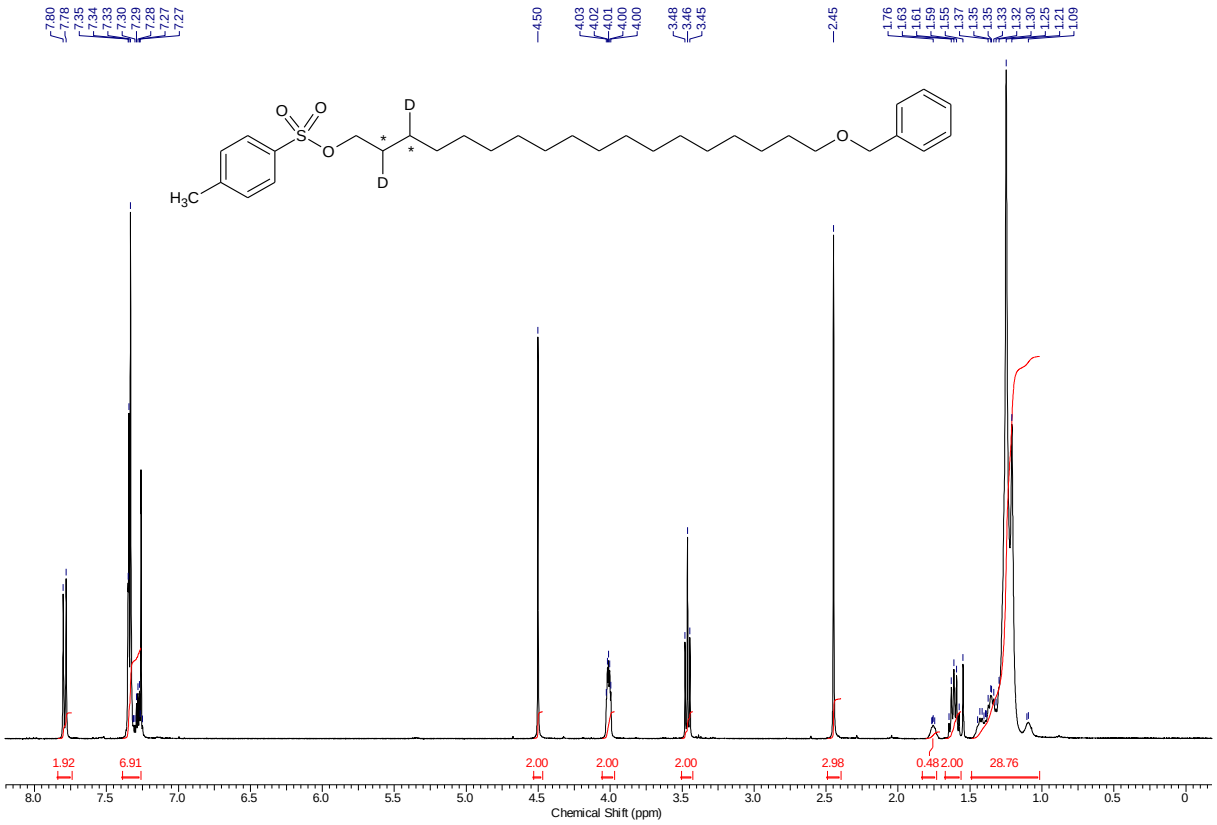
16,17-labeled positions

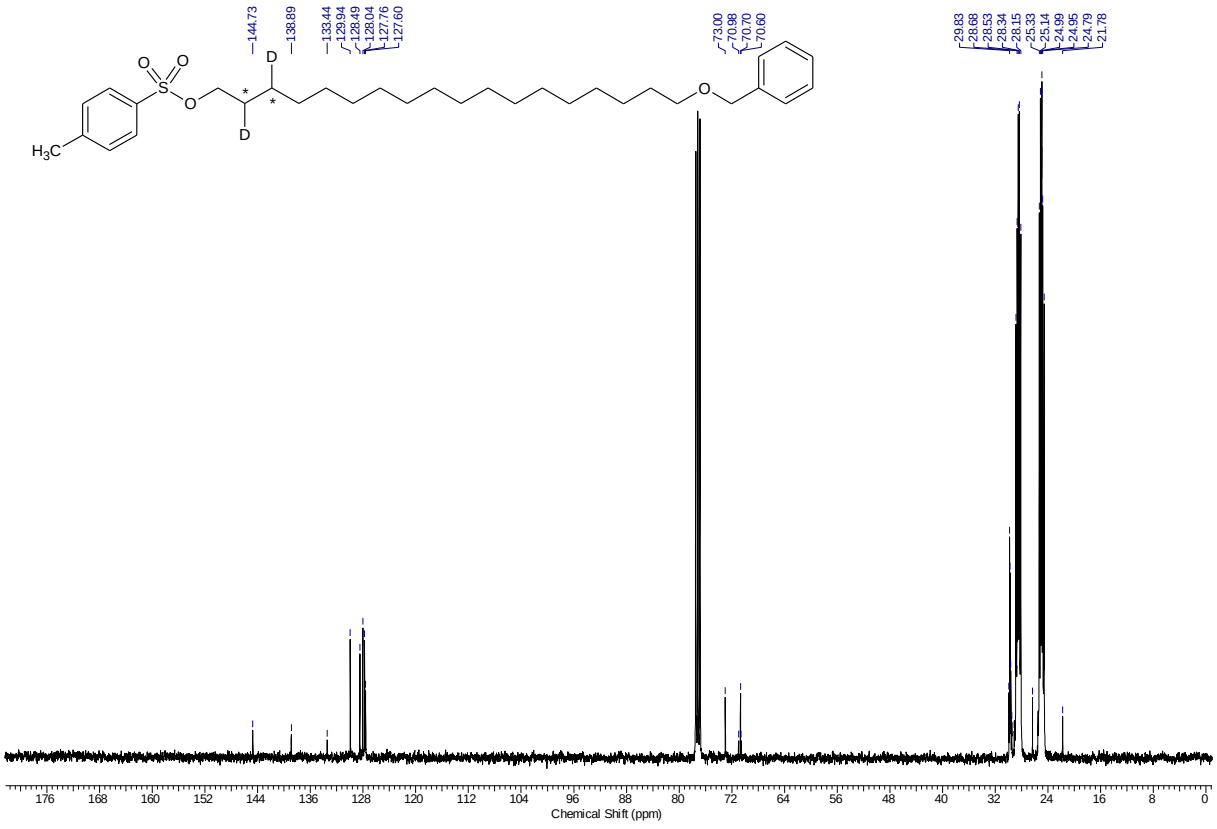
[2,3-$^{13}C_2$-2,3-D_2]-18-(benzyloxy)octadecan-1-ol **19**



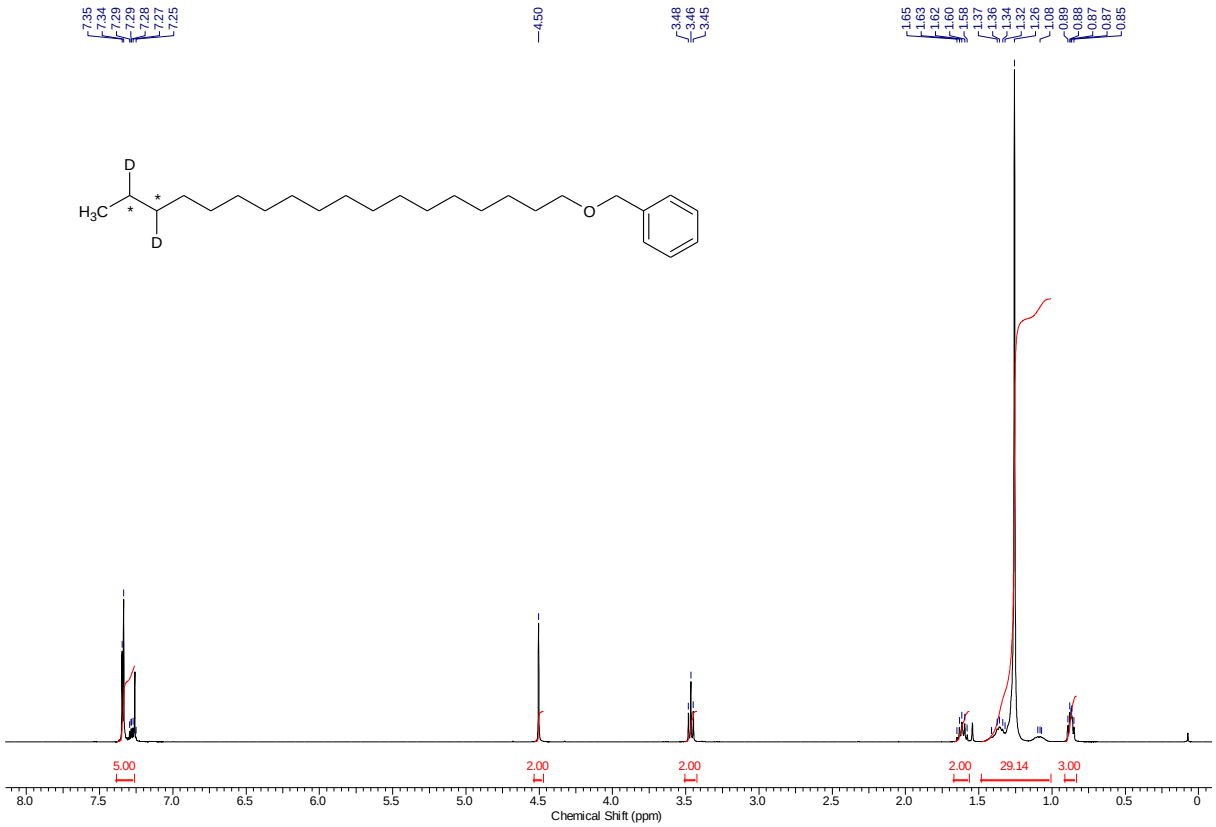


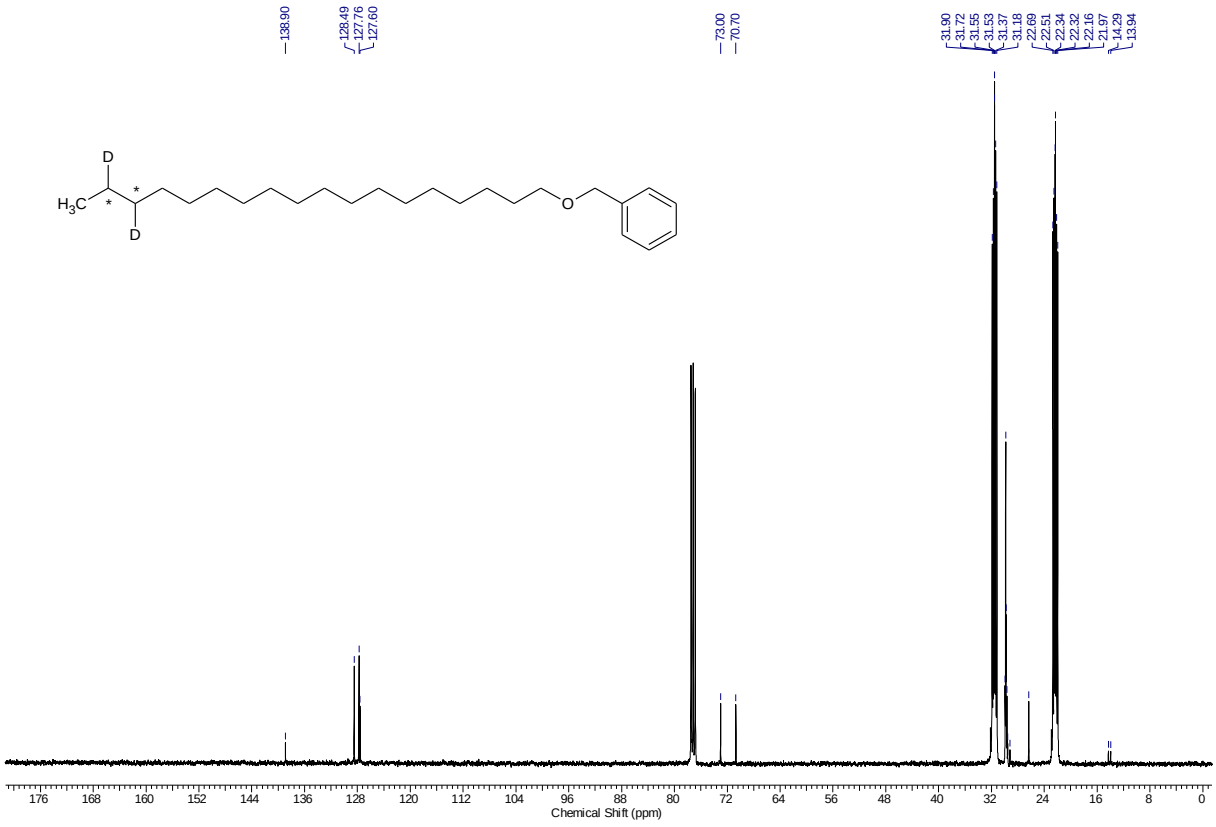
[2,3-$^{13}C_2$-2,3-D_2]-18-(benzyloxy)octadecyl 4-methylbenzenesulfonate **20**



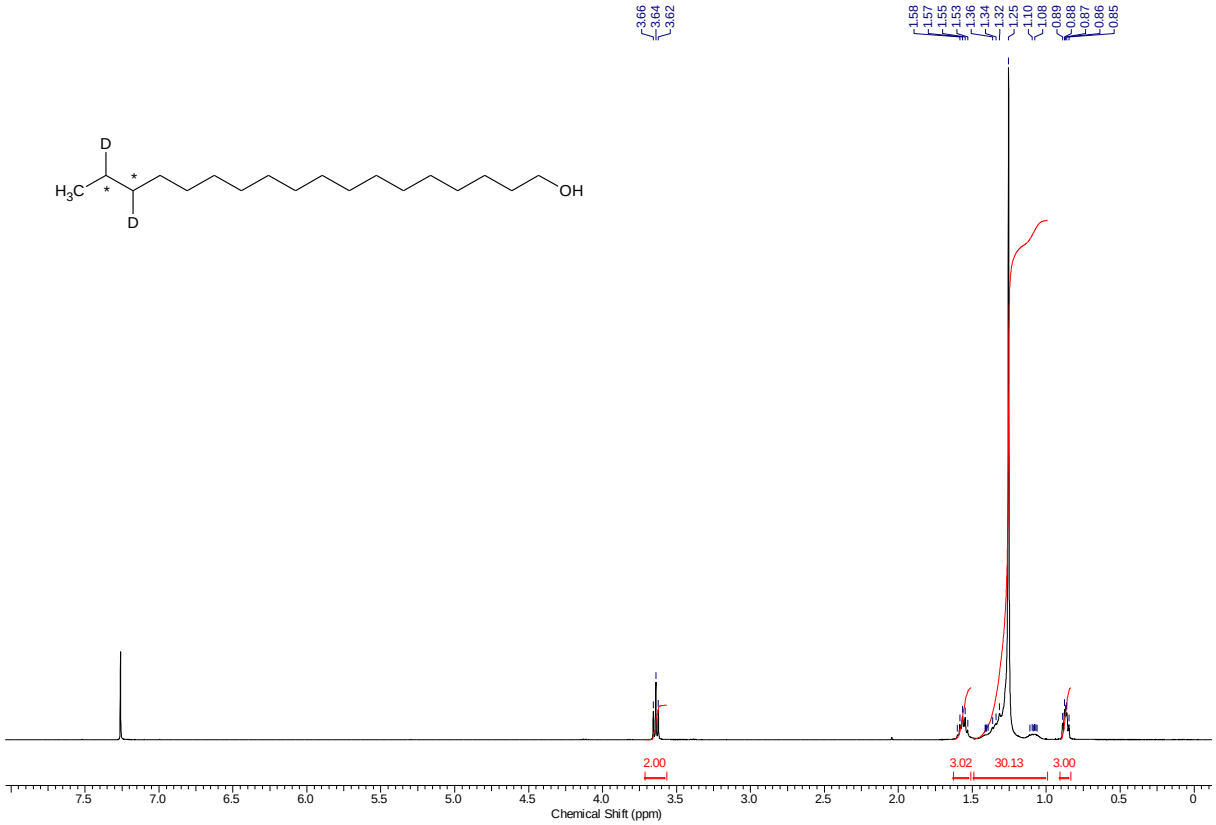


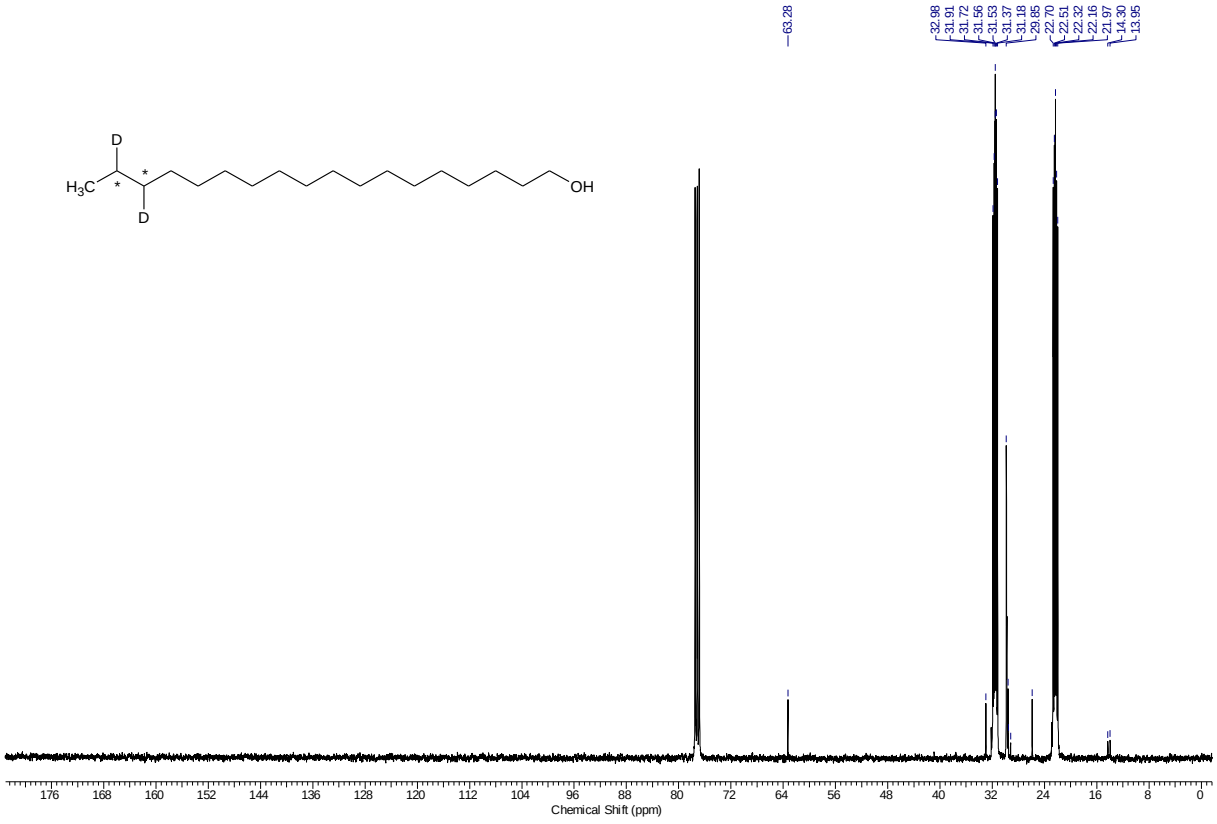
[16,17-$^{13}C_2$-16,17-D_2]-((octadecyloxy)methyl)benzene **21**



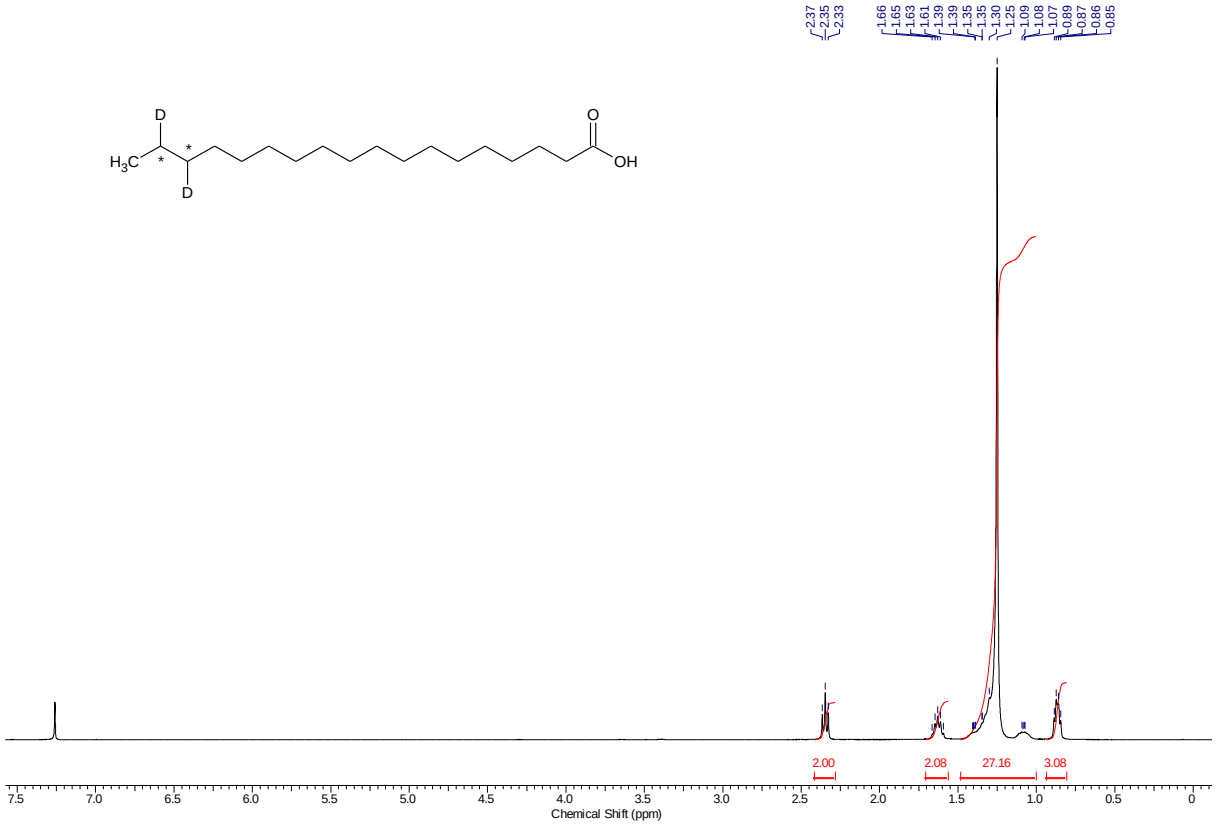


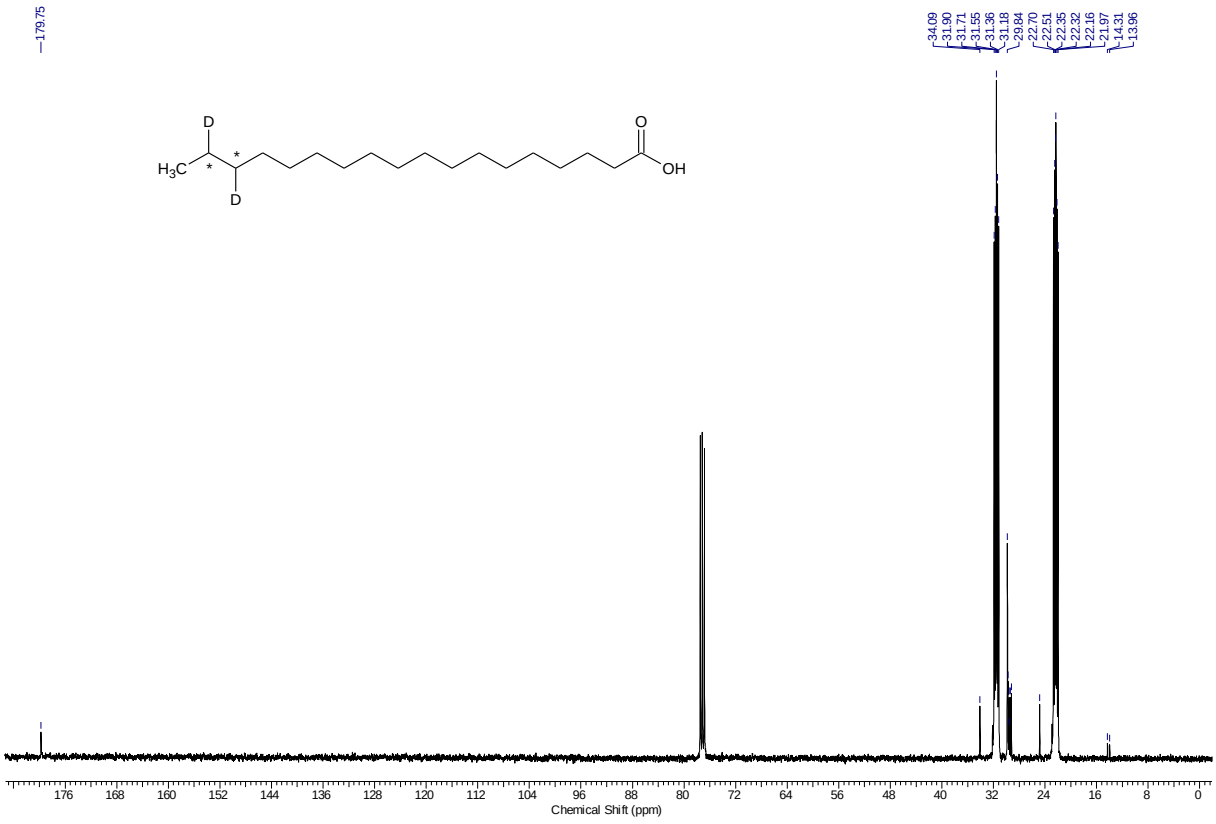
[16,17-$^{13}C_2$-16,17-D_2]-stearyl alcohol **22**





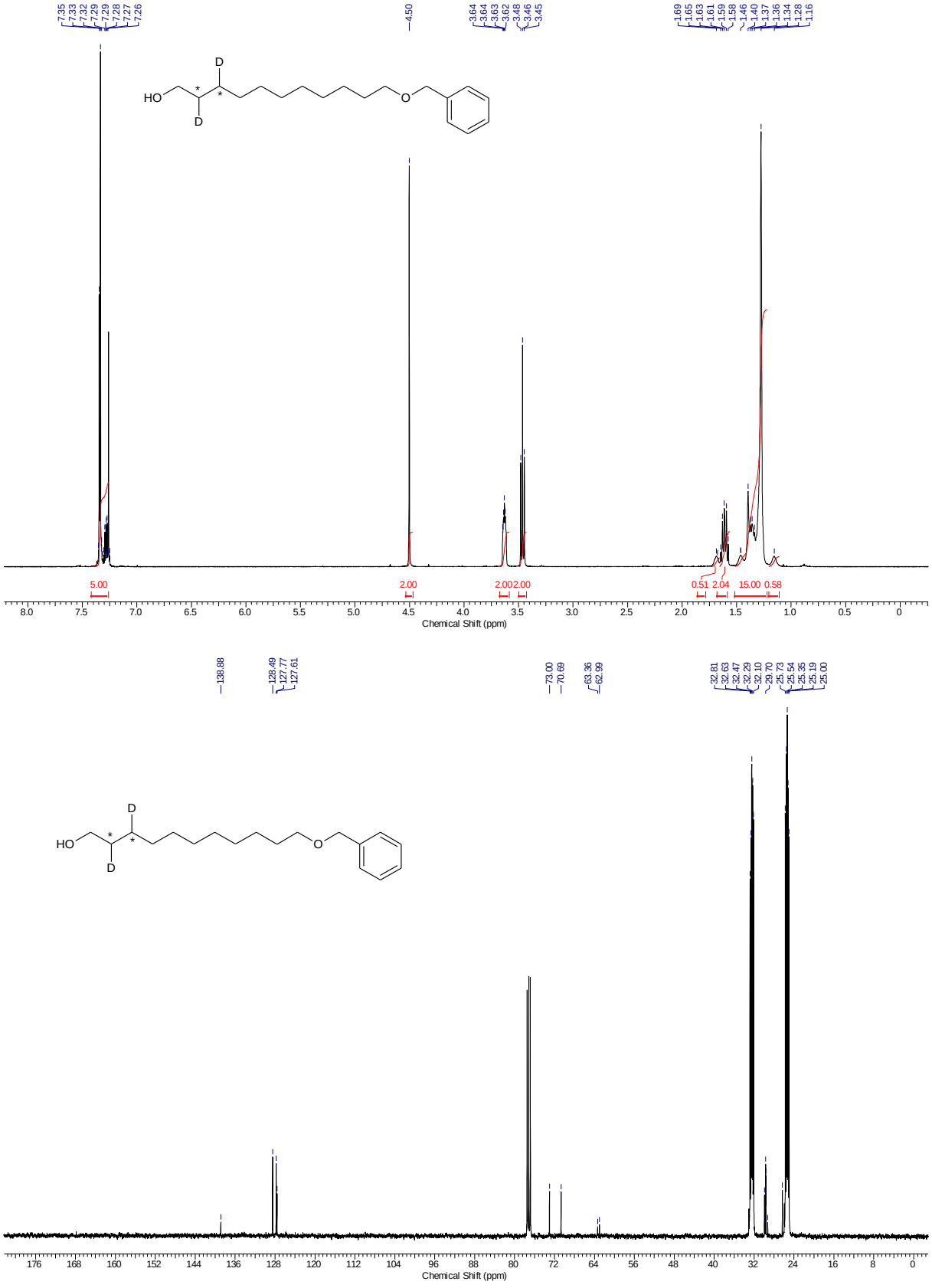
[16,17-$^{13}C_2$-16,17-D_2]-stearic acid **23**



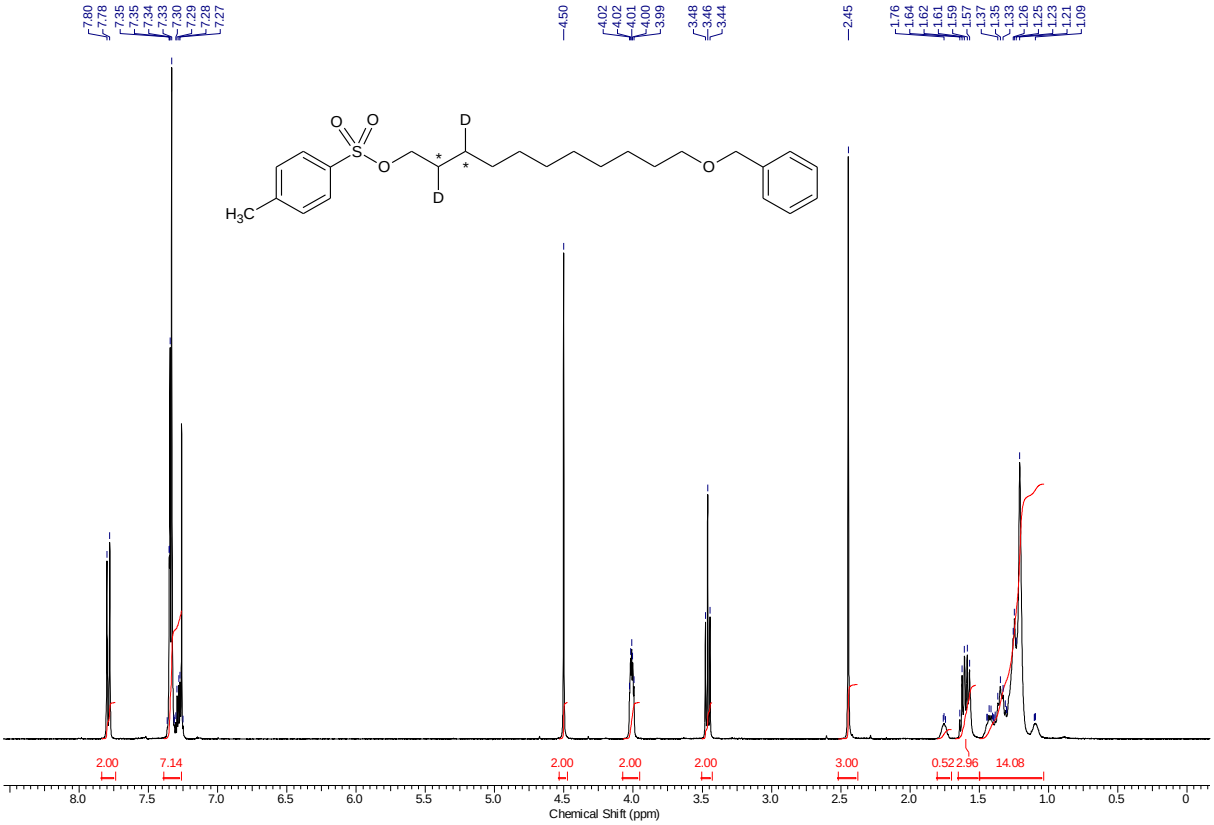


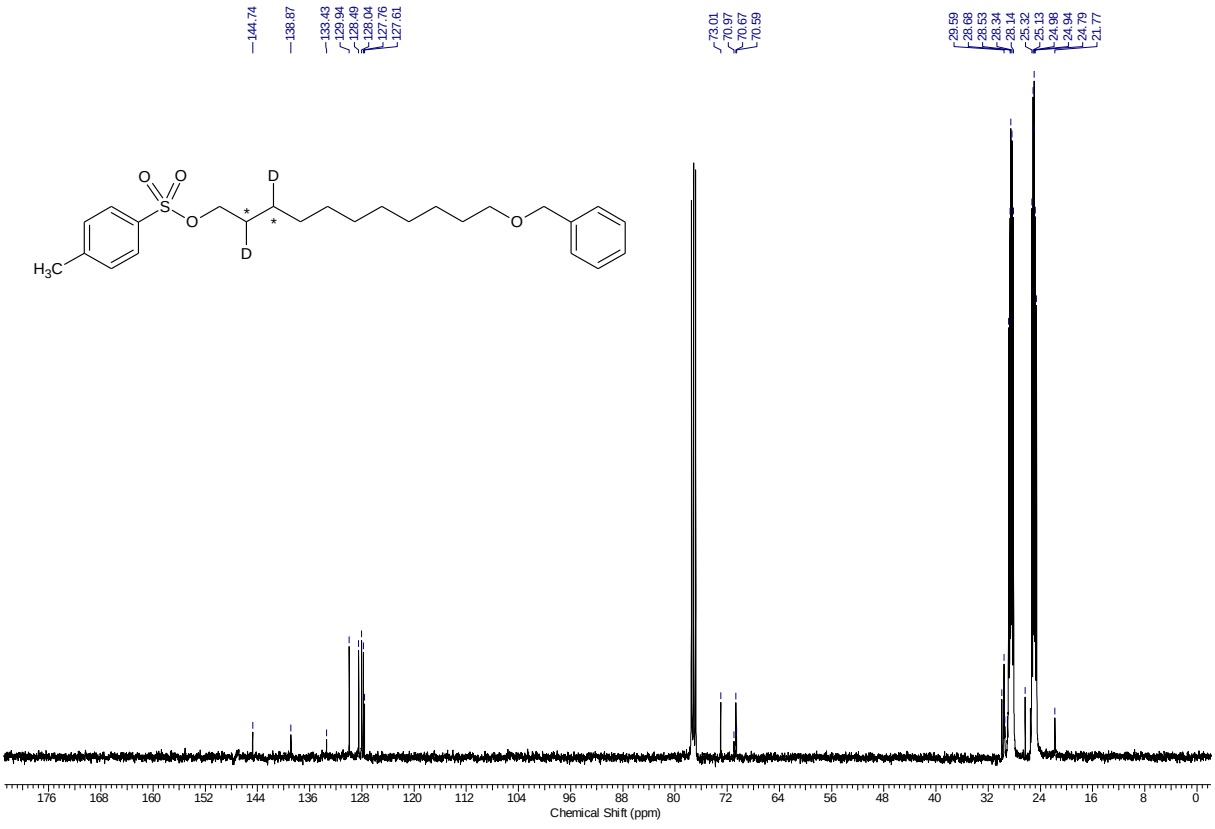
9,10-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-11-(benzyloxy)dodecan-1-ol **25a**

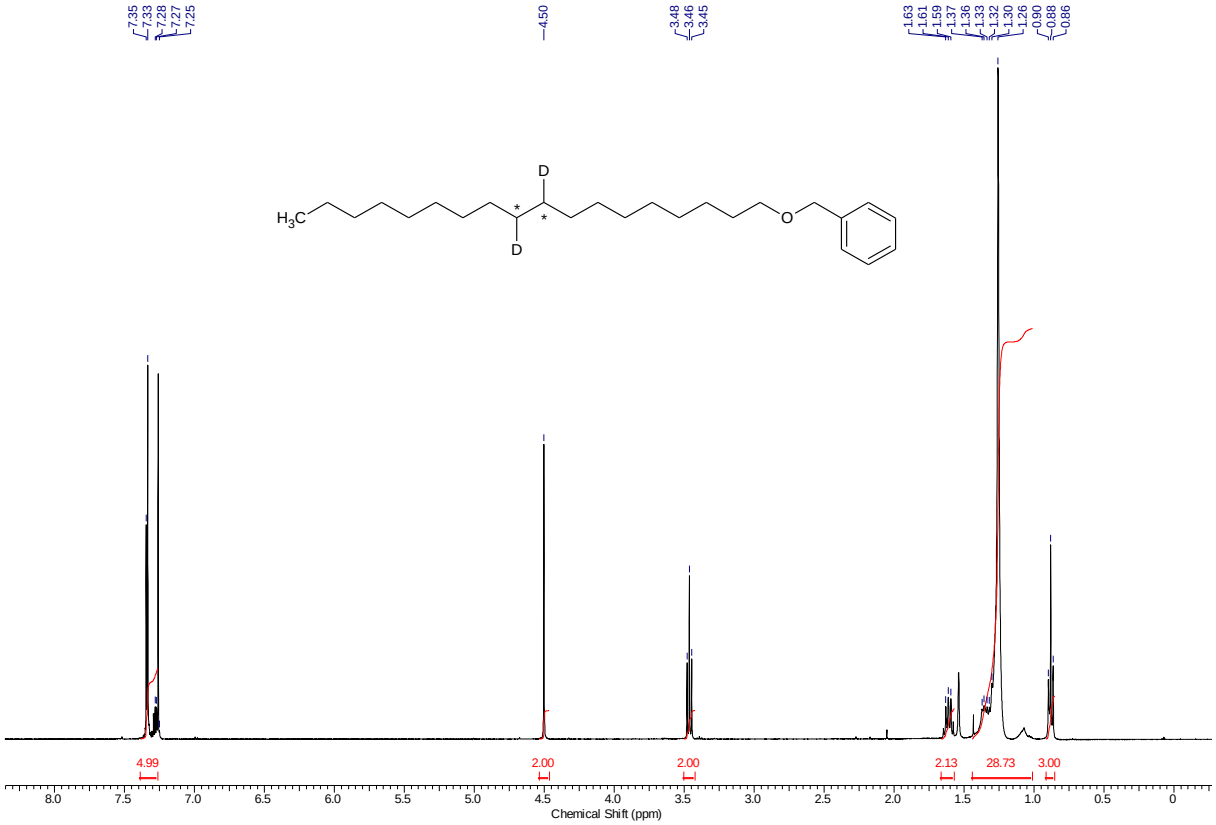


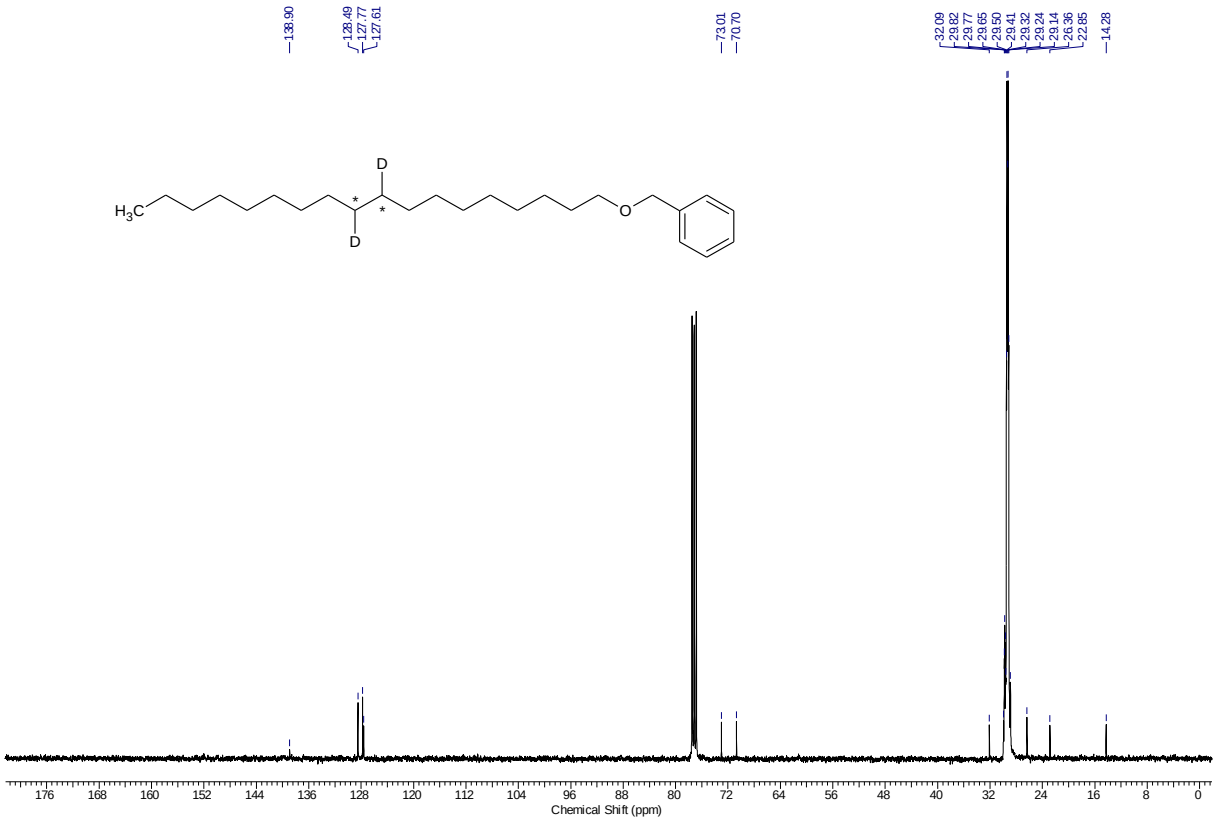
[2,3-$^{13}C_2$-2,3-D_2]-11-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26a**



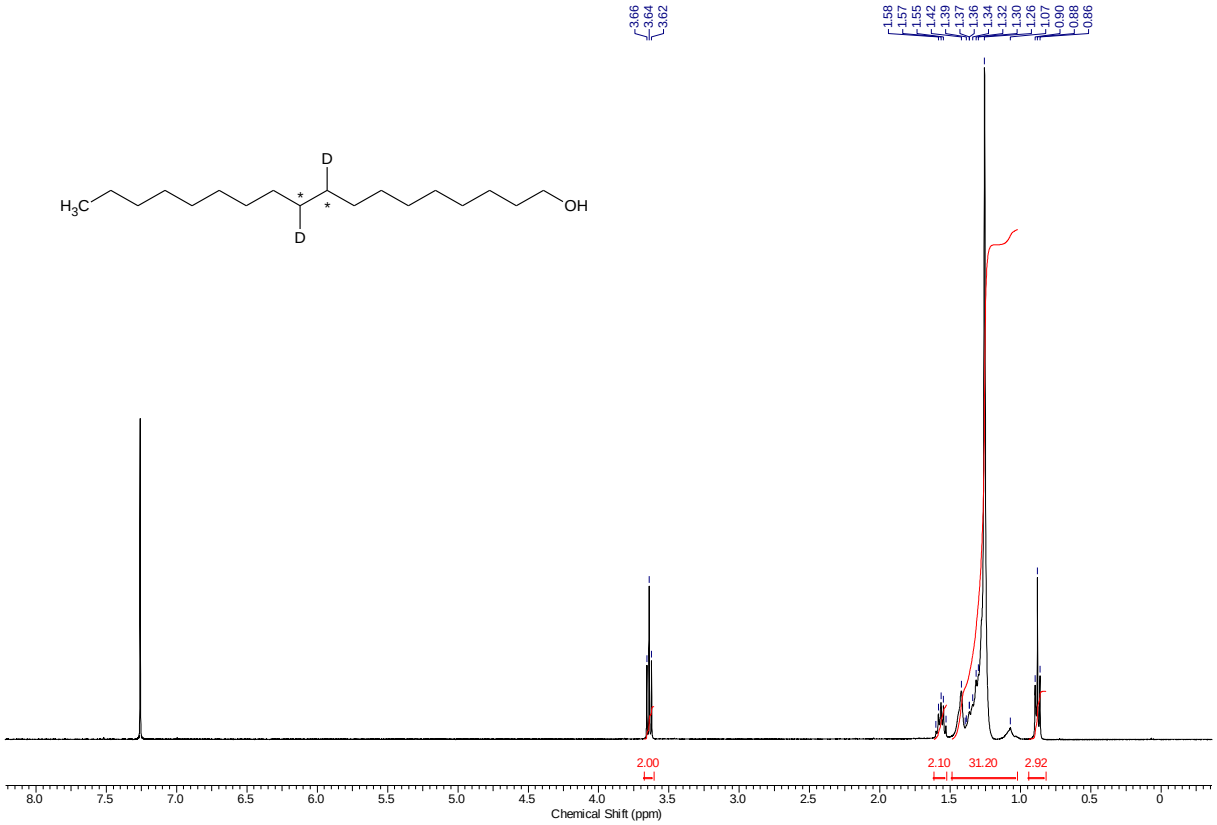


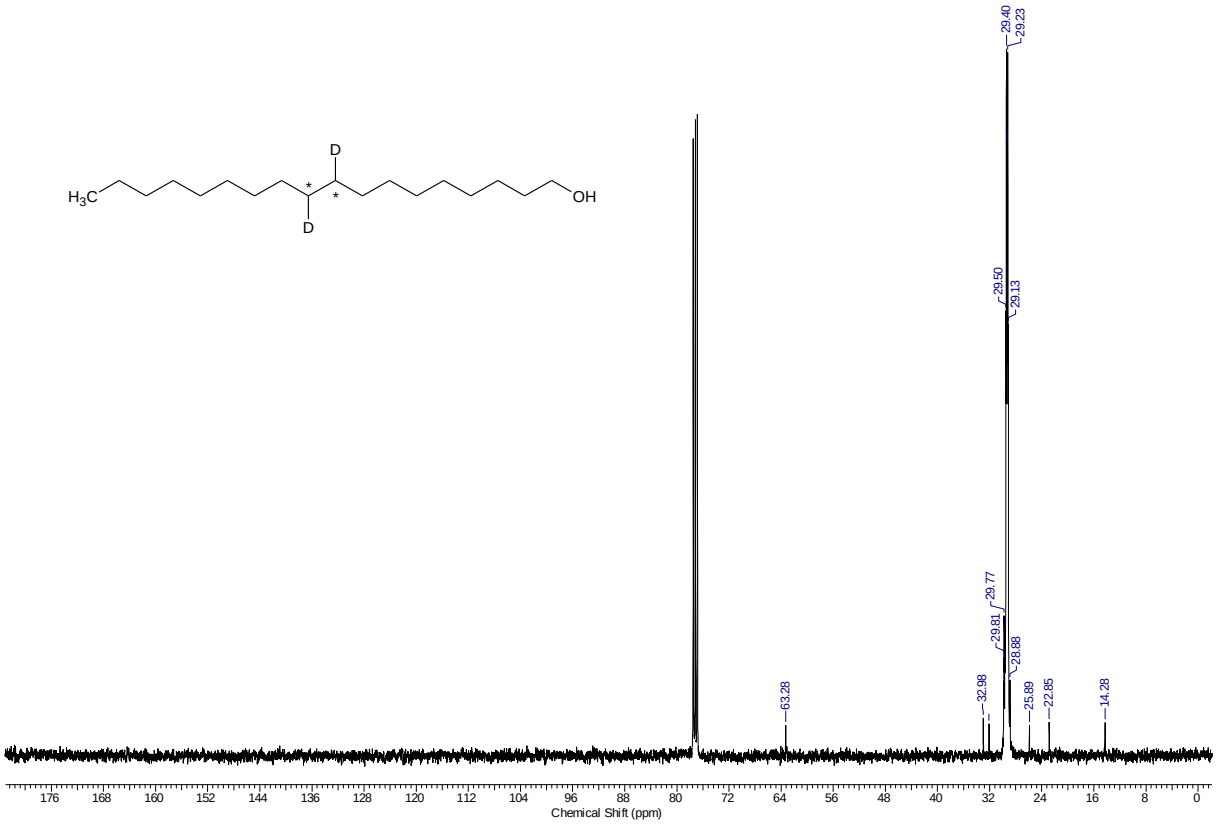
[9,10-$^{13}C_2$-9,10-D_2]-((octadecyloxy)methyl)benzene **27a**



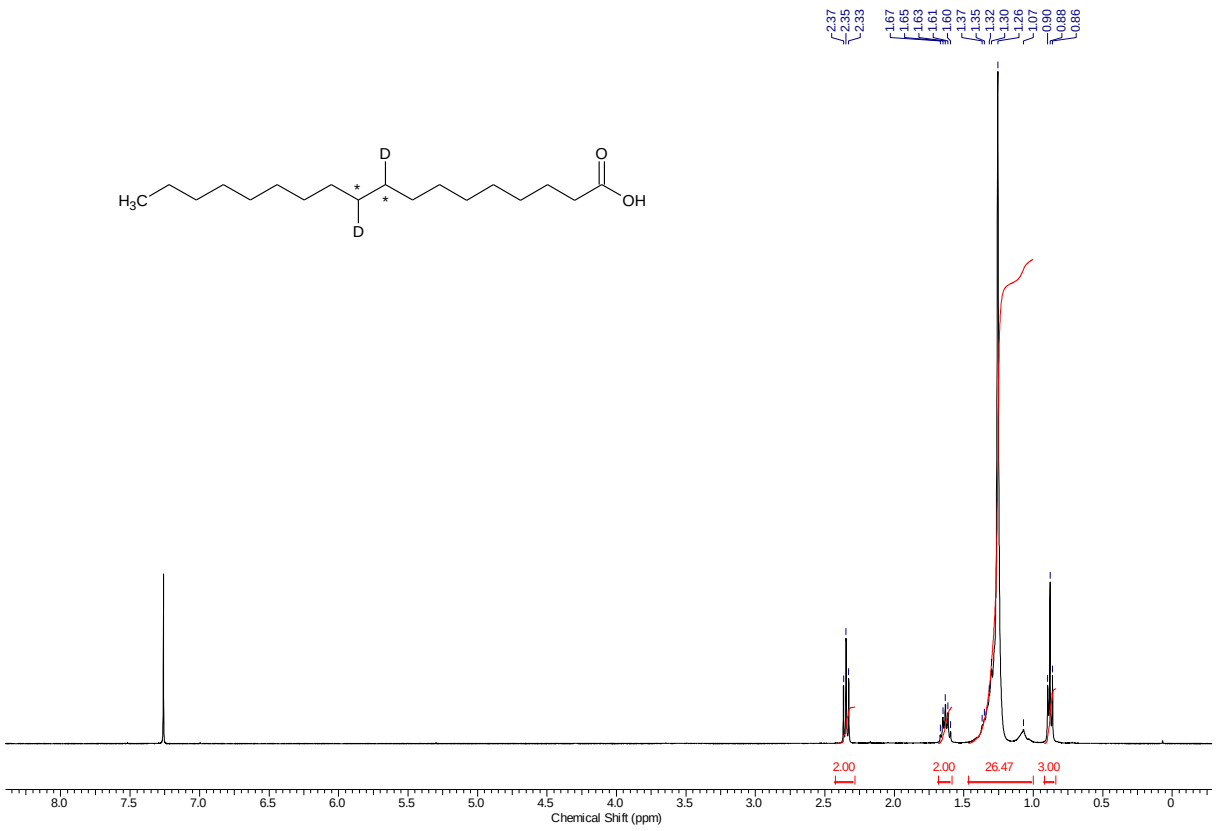


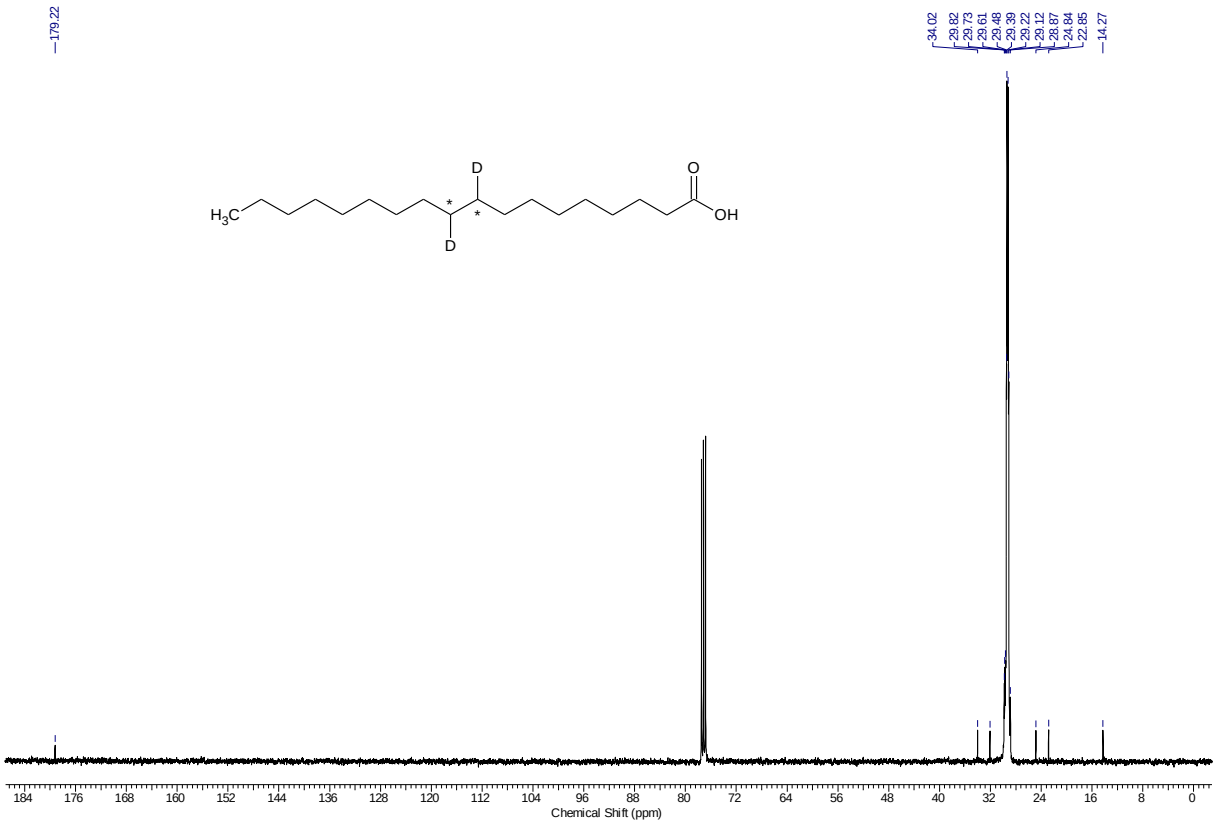
[9,10-$^{13}C_2$-9,10-D_2]-stearyl alcohol **28a**





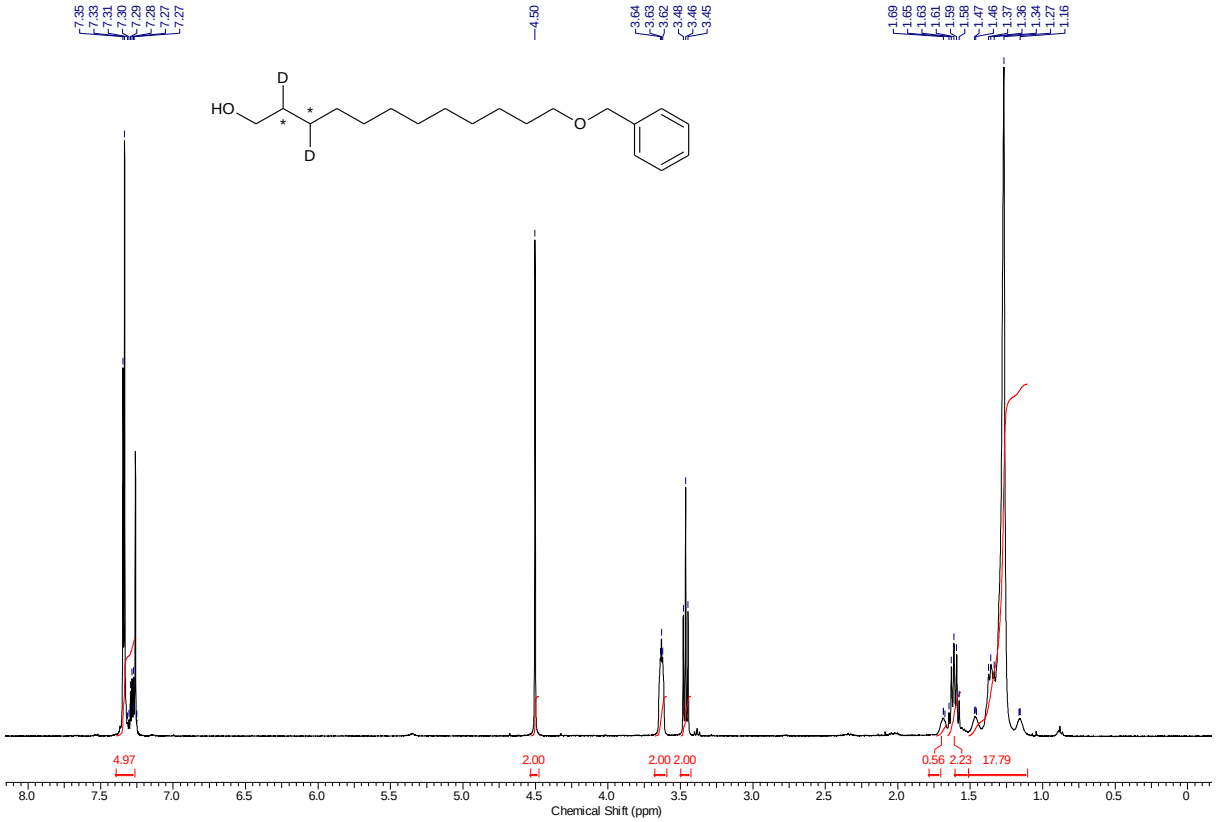
[9,10-$^{13}C_2$-9,10-D_2]-stearic acid **29a**

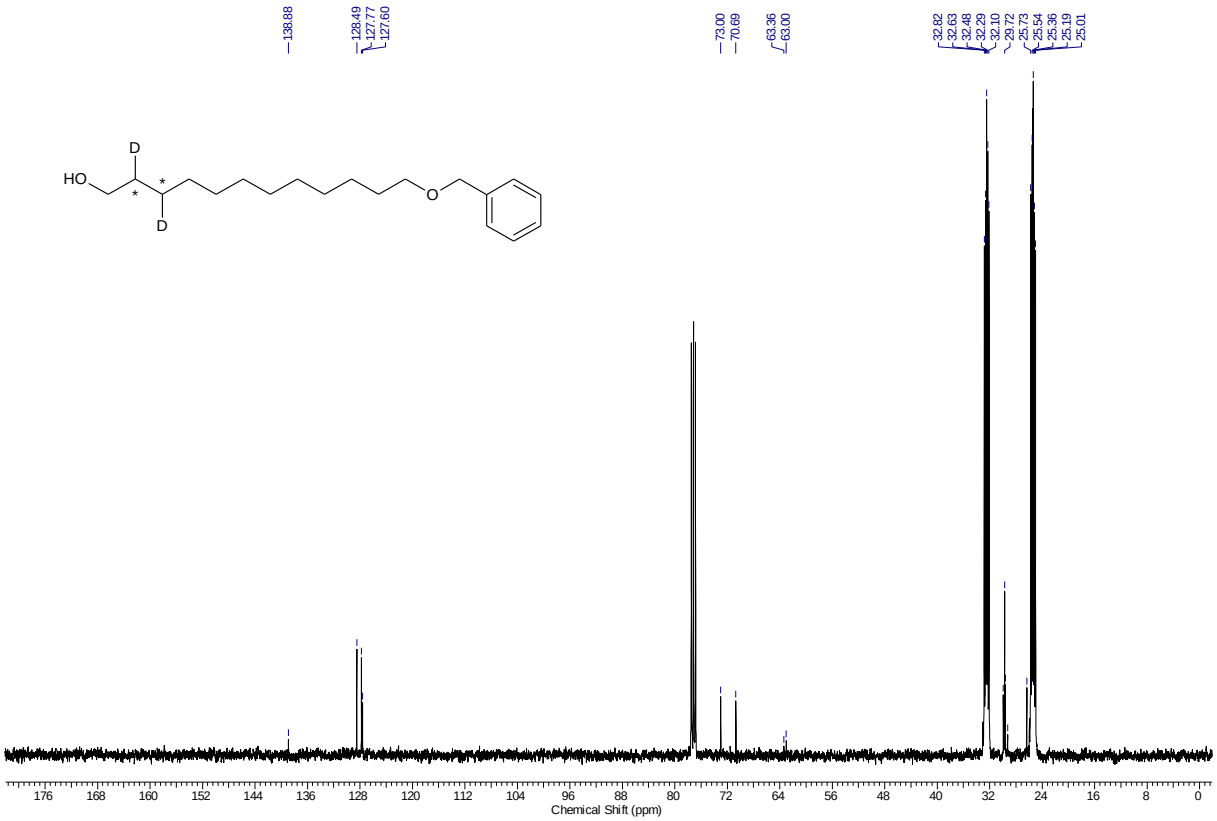




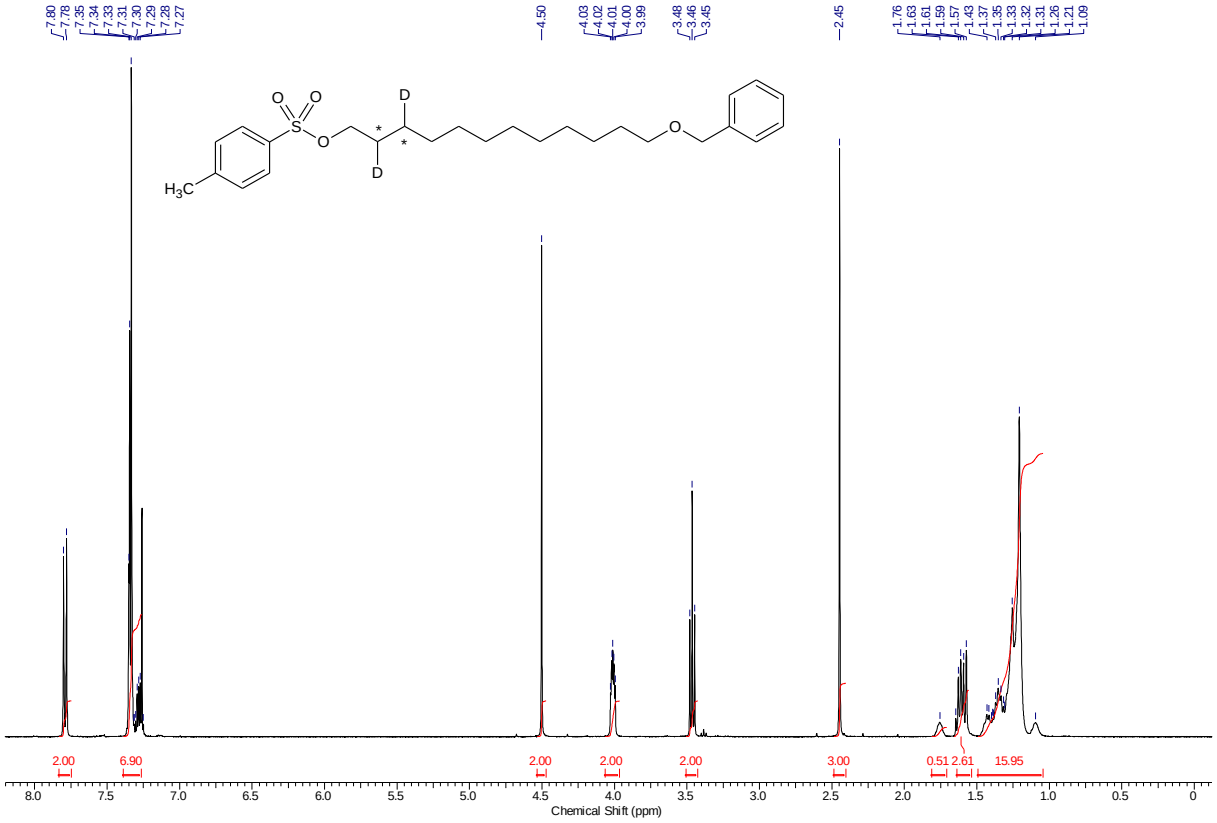
10,11-labeled positions

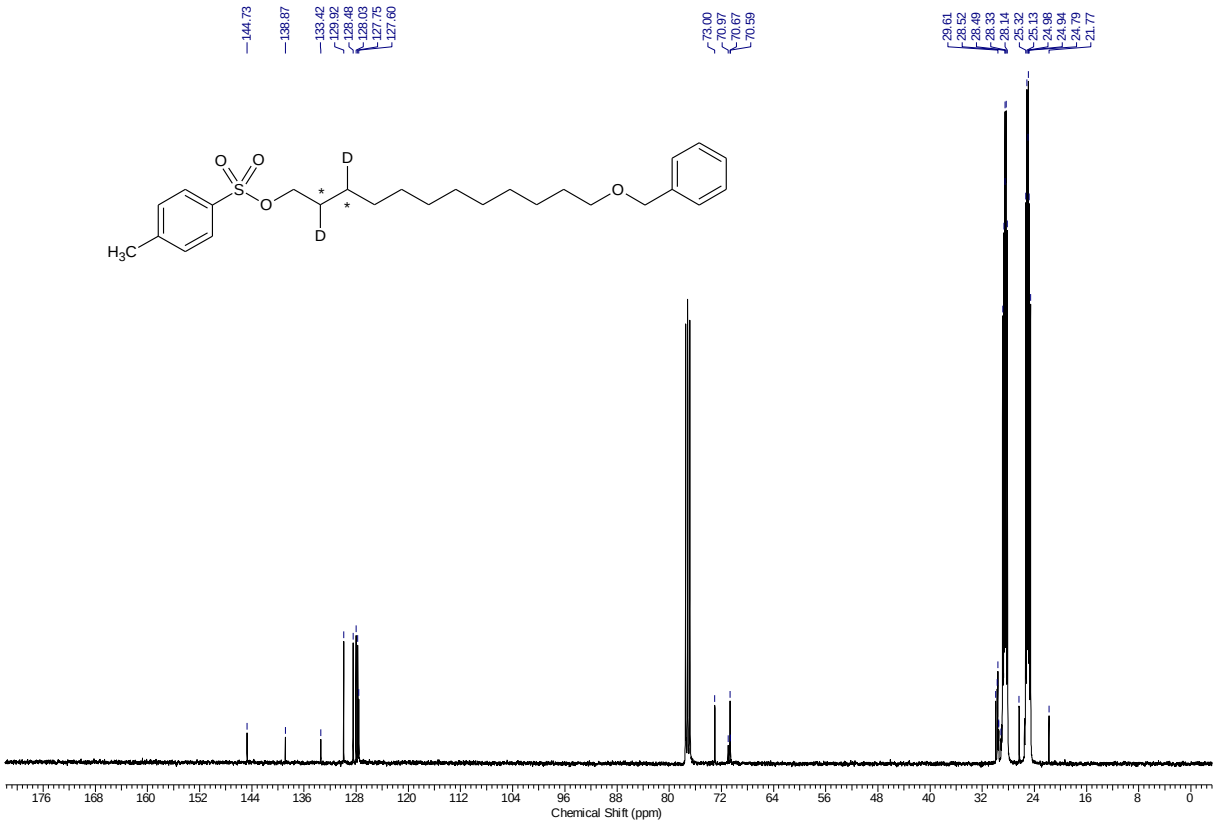
[2,3-$^{13}C_2$-2,3-D_2]-12-(benzyloxy)dodecan-1-ol **25b**



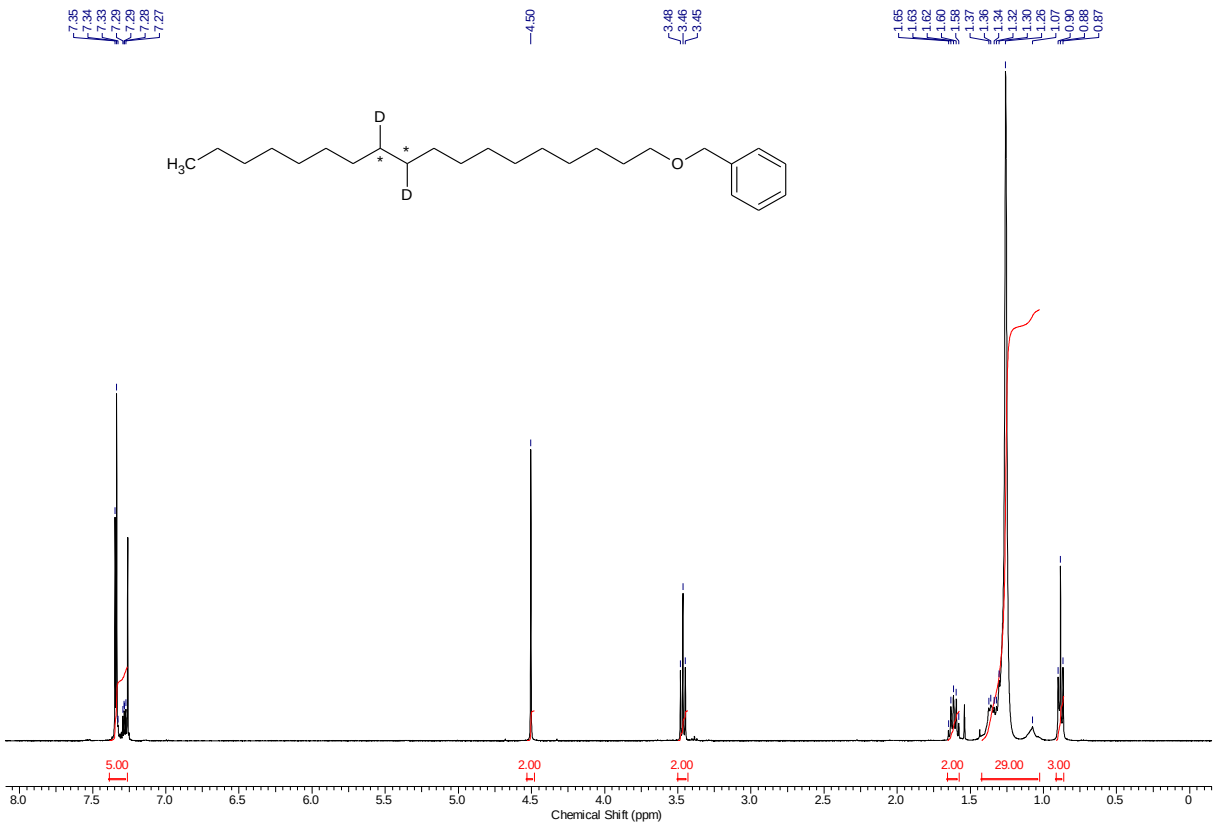


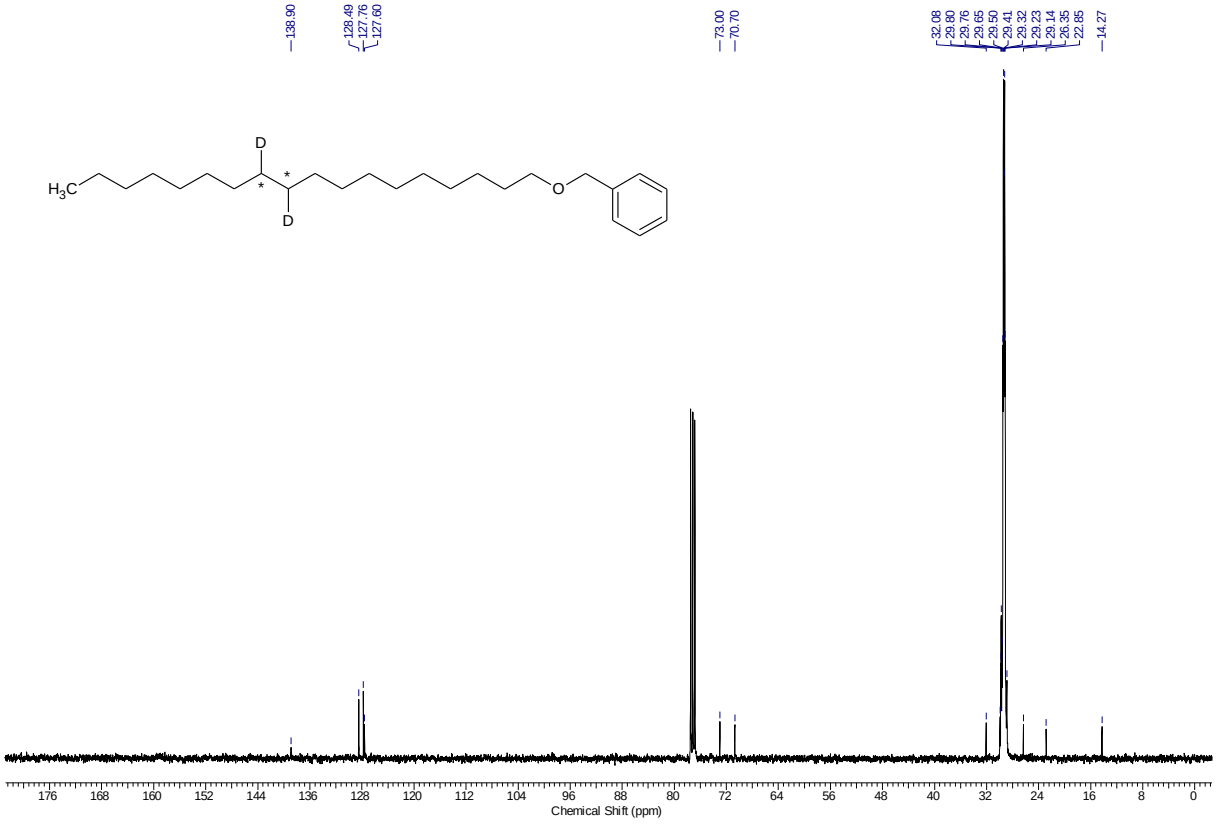
[2,3-$^{13}C_2$-2,3-D_2]-12-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26b**



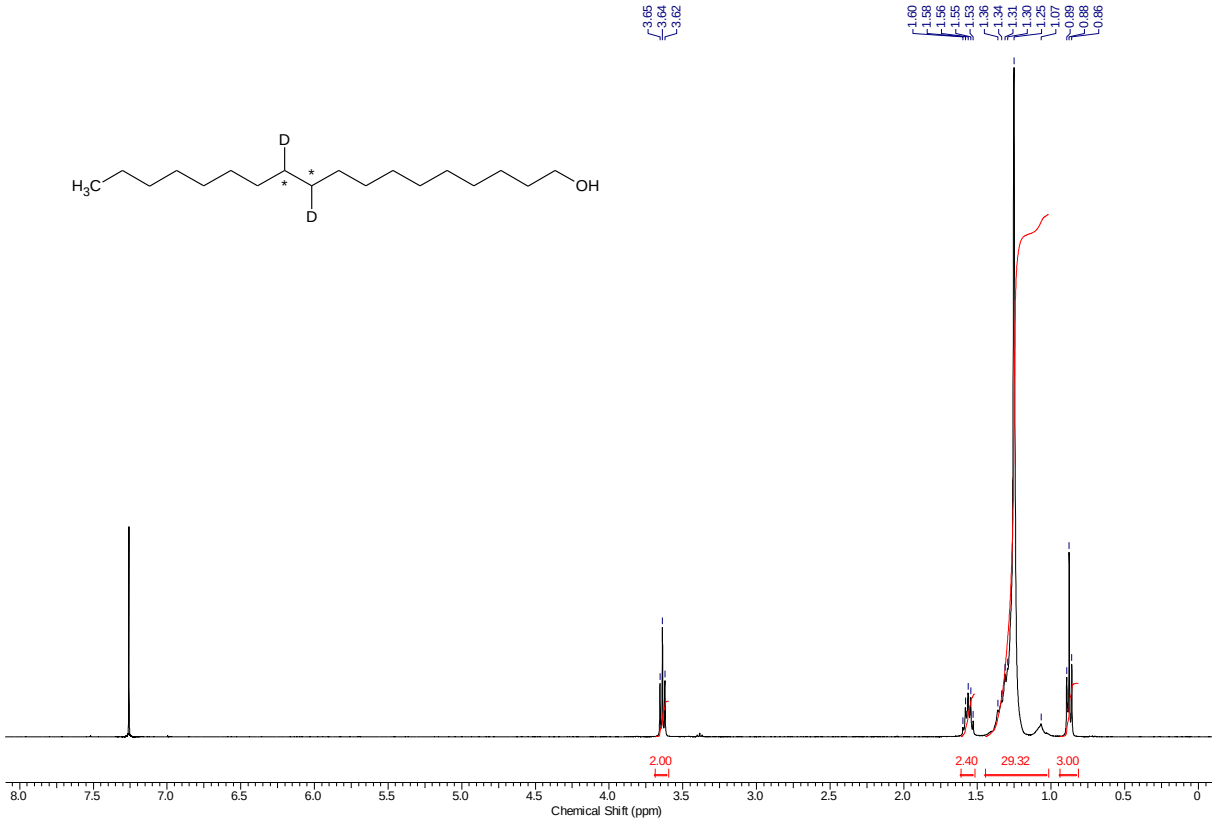


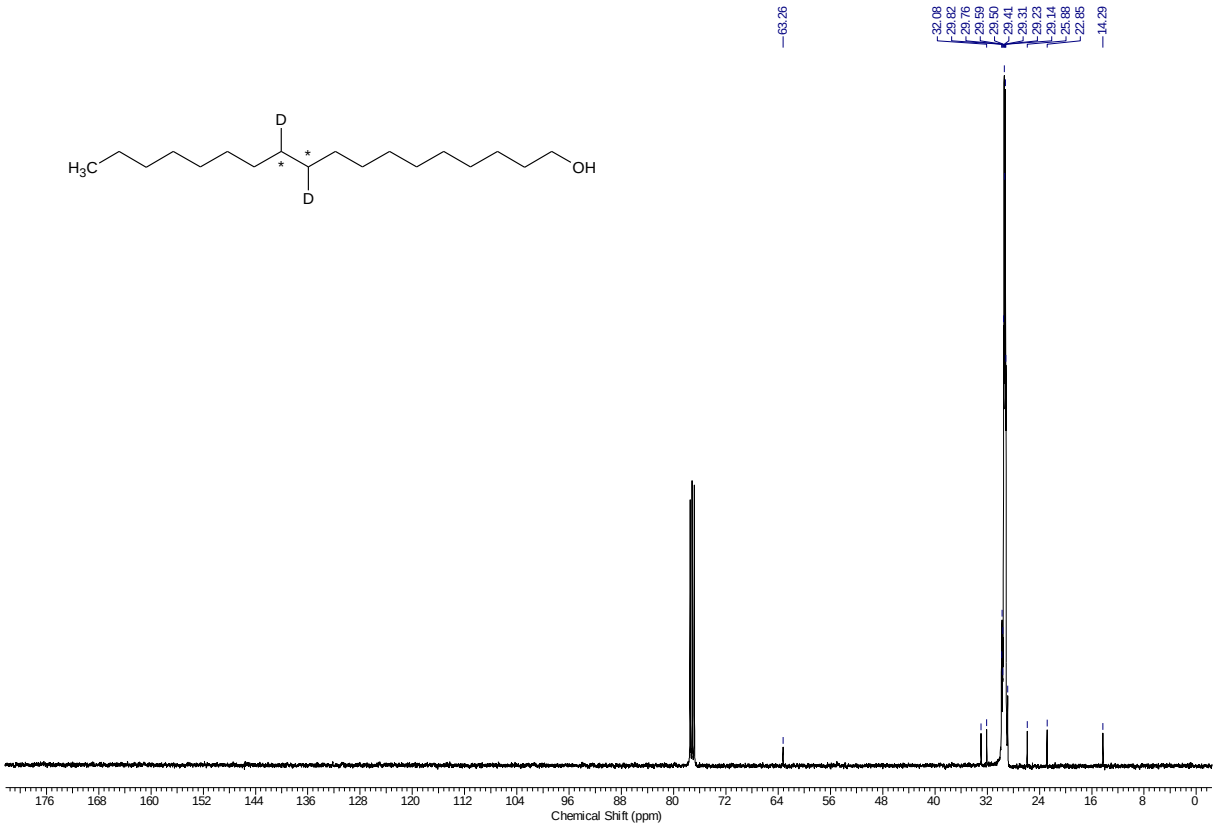
[10,11-$^{13}C_2$-10,11-D_2]-((octadecyloxy)methyl)benzene **27b**



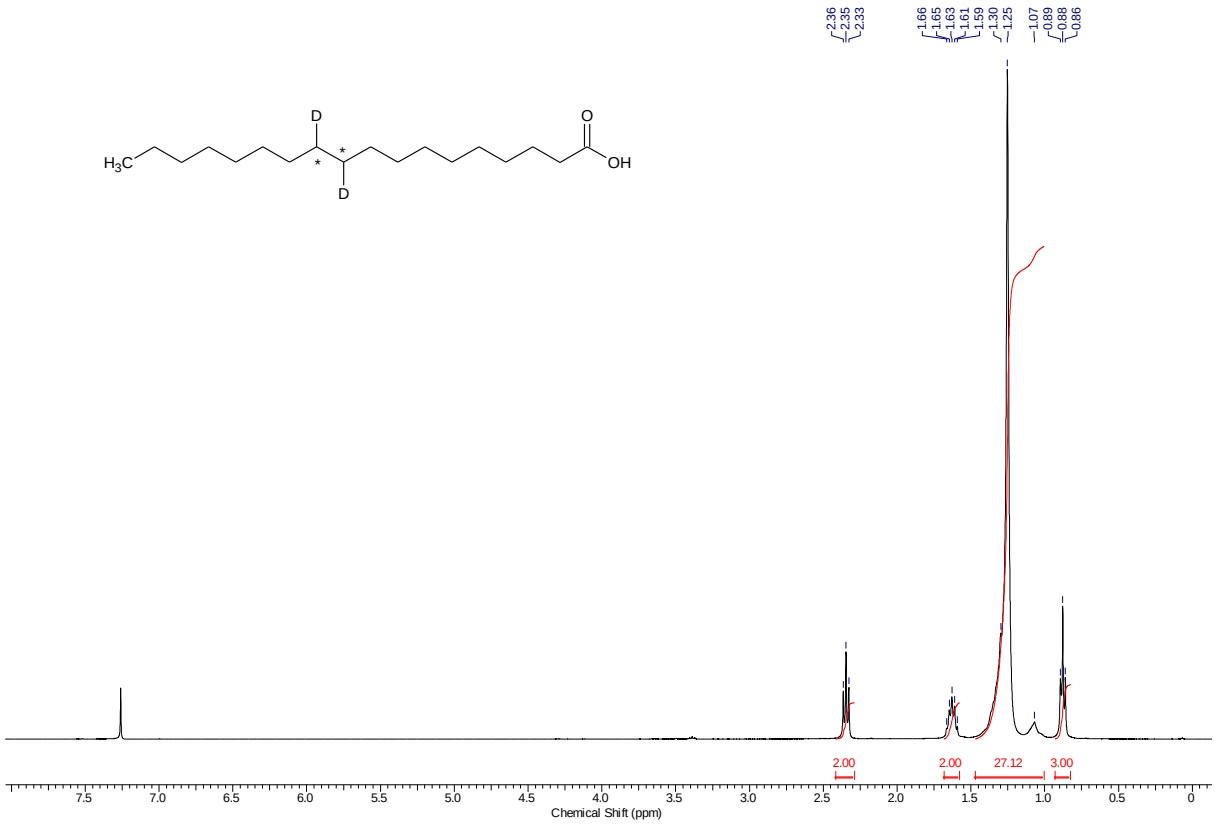


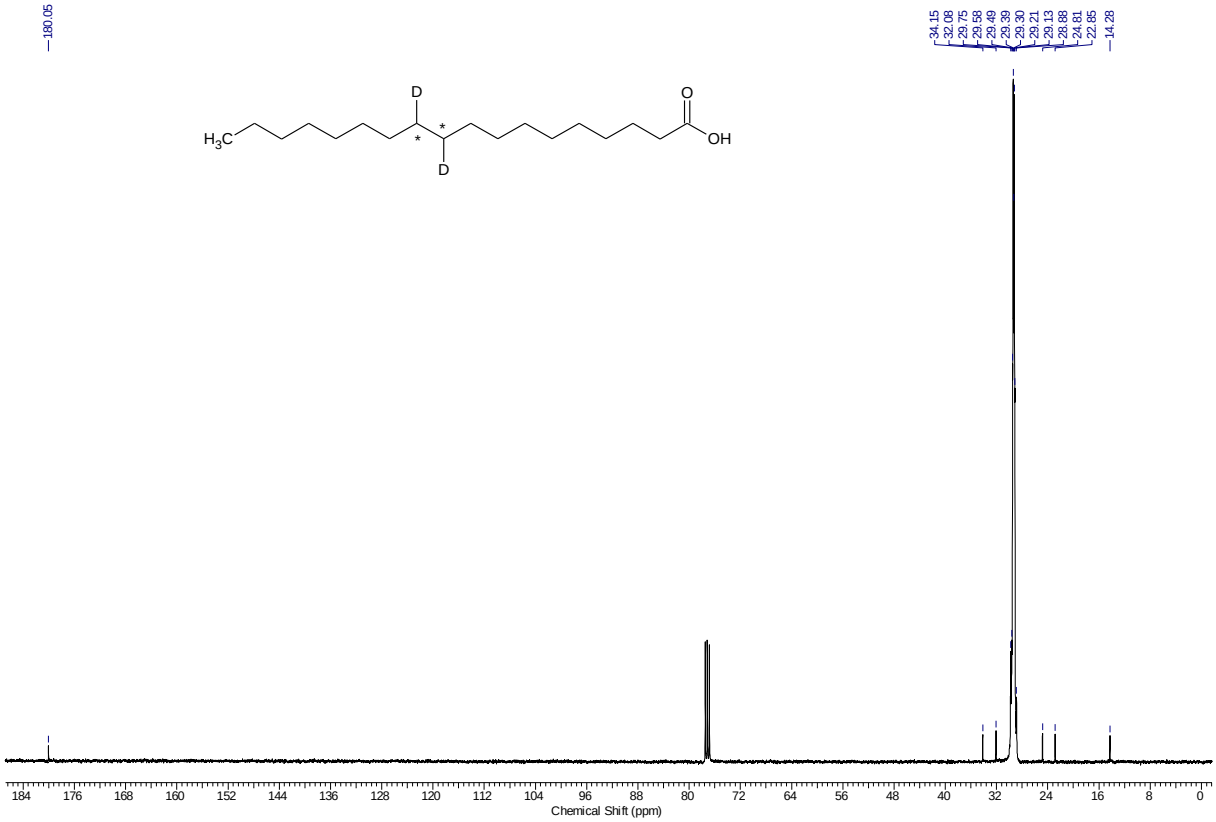
[10,11-$^{13}C_2$-10,11-D_2]-stearyl alcohol **28b**





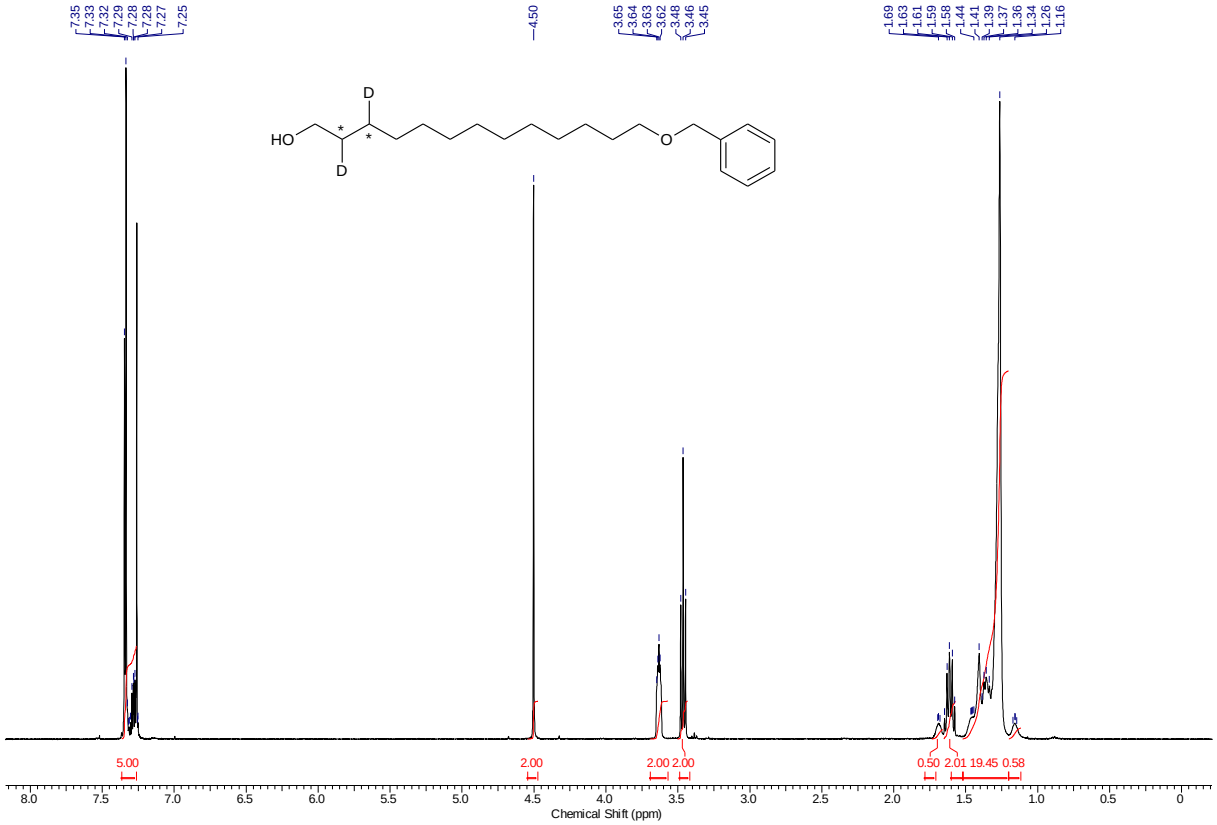
[10,11-$^{13}C_2$-10,11-D_2]-stearic acid **29b**

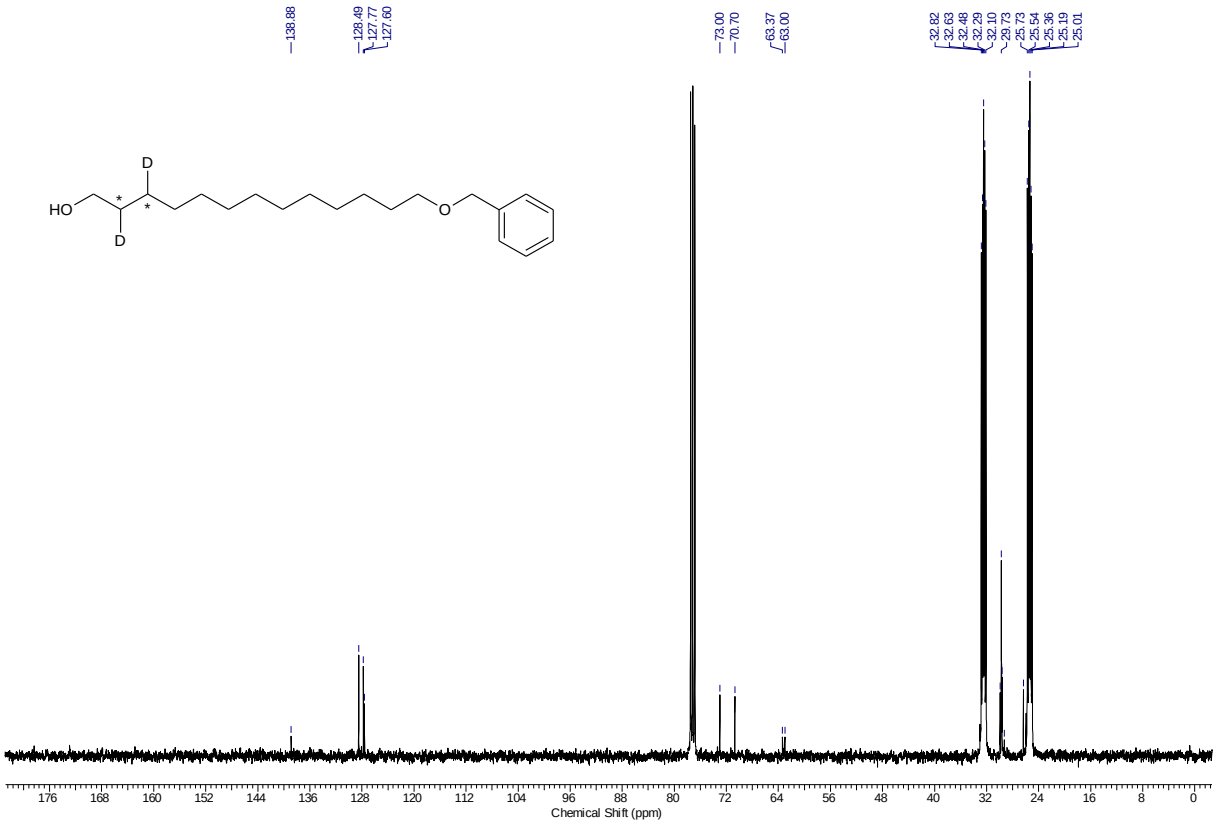




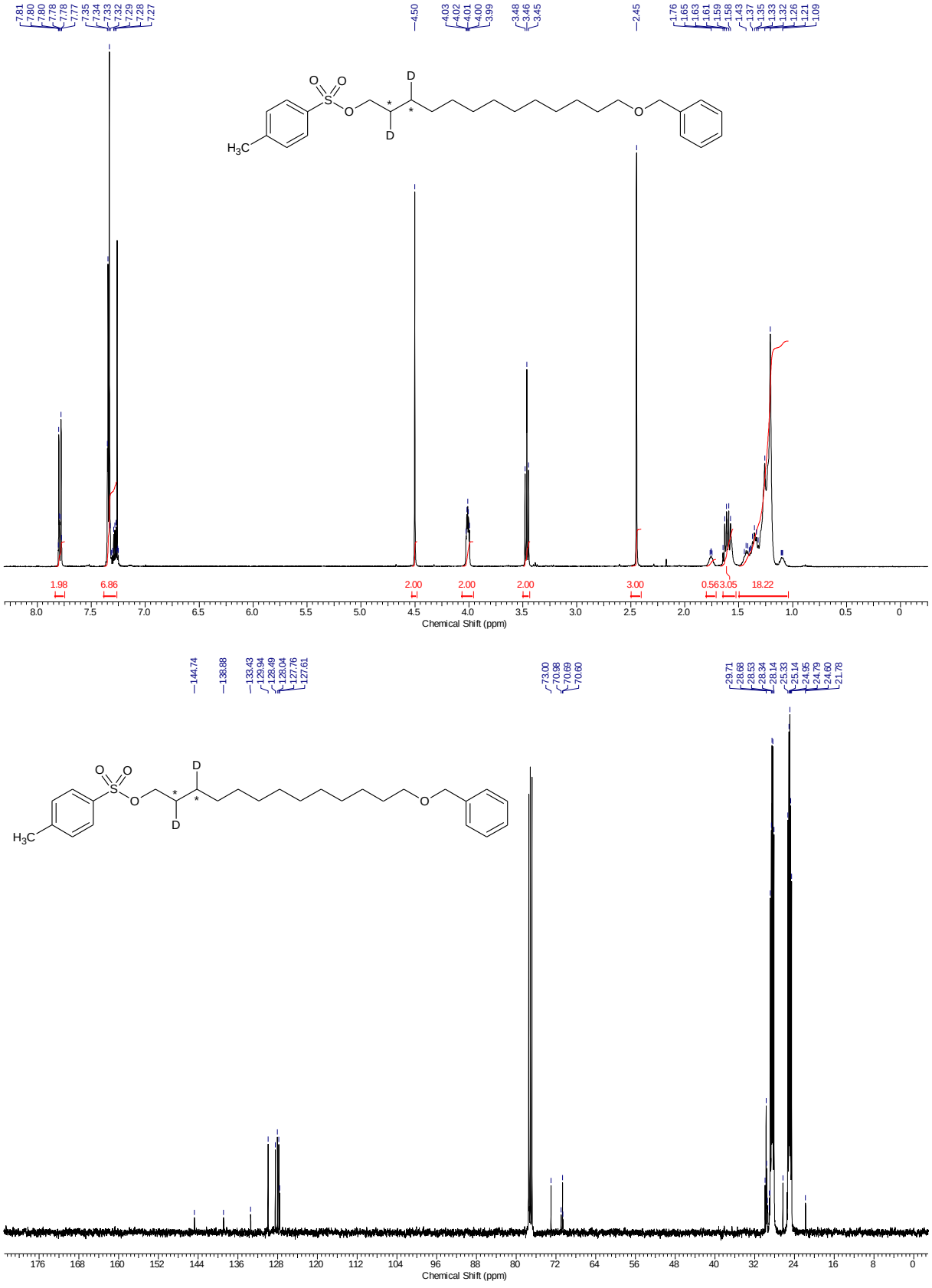
11,12-labeled positions

[2,3-$^{13}C_2$-2,3-D_2]-13-(benzyloxy)dodecan-1-ol **25c**

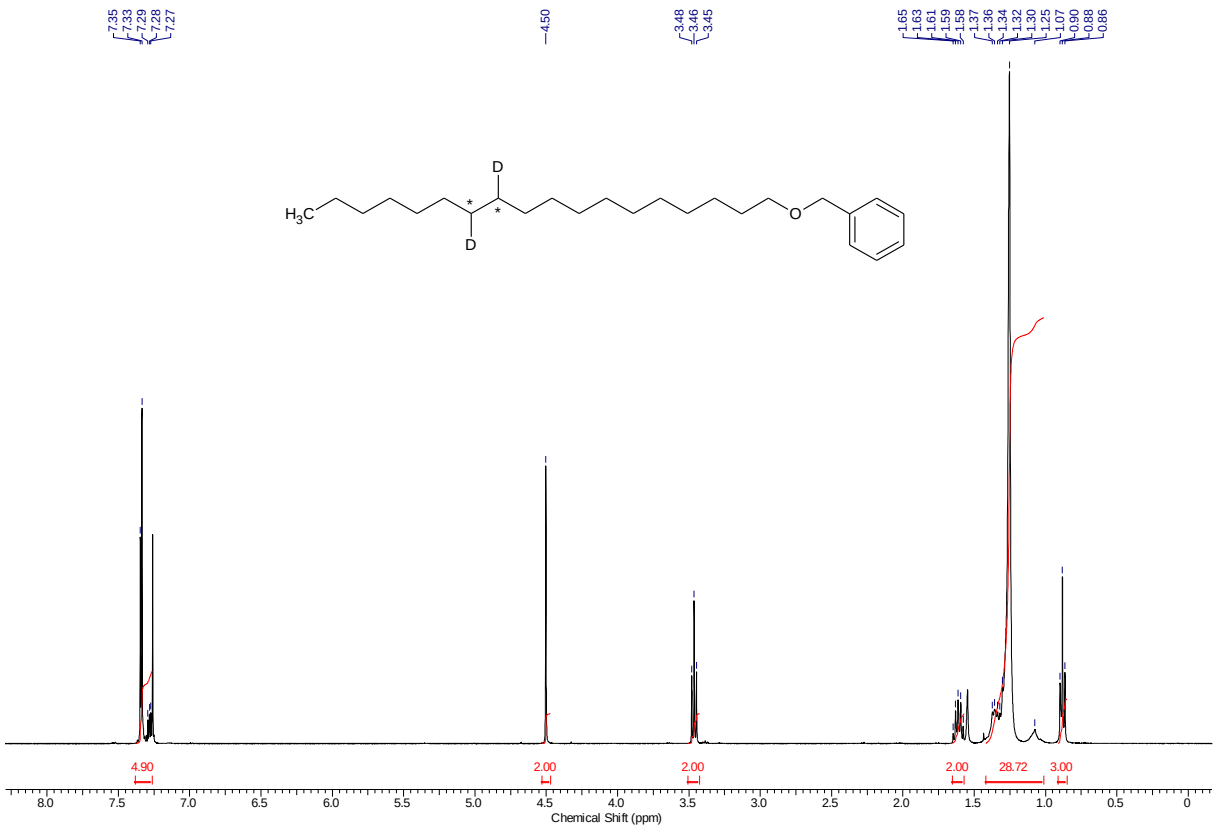


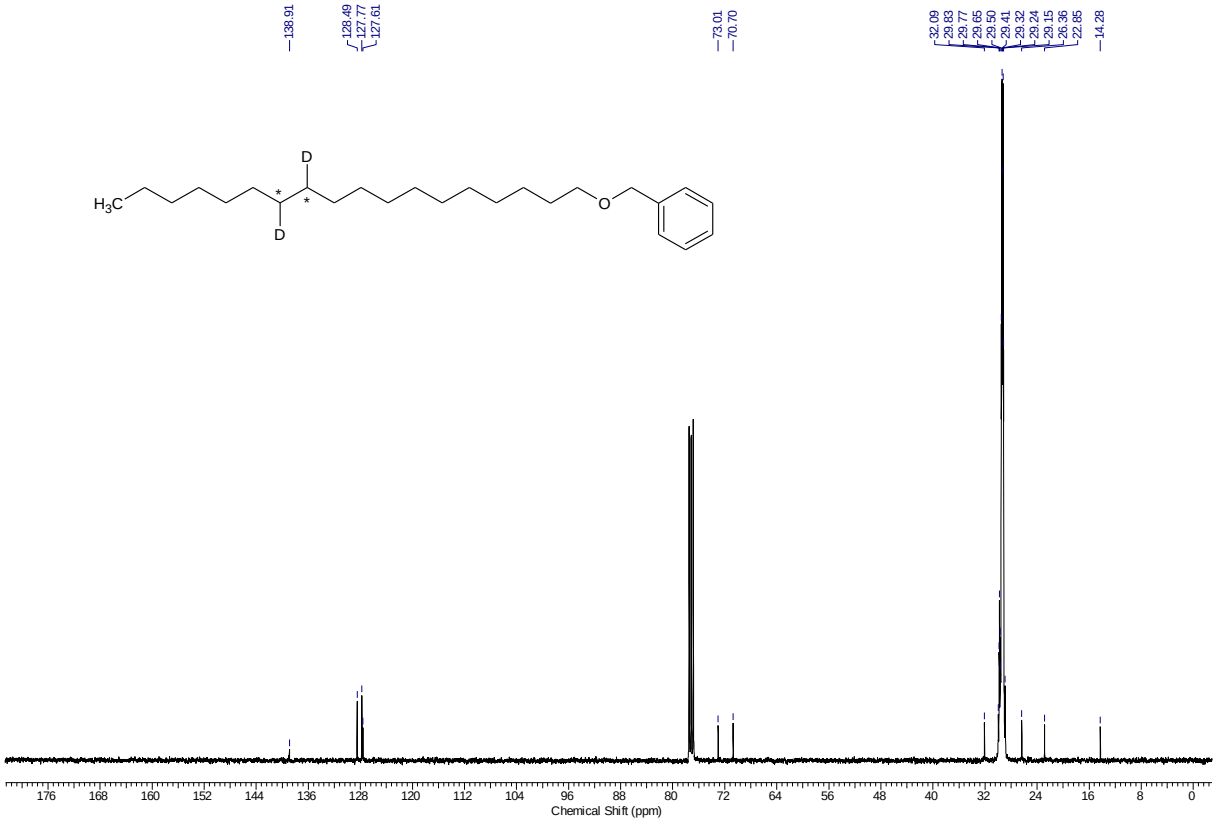


[2,3-$^{13}C_2$-2,3-D_2]-13-(benzyloxy)dodecyl 4-methylbenzenesulfonate **26c**

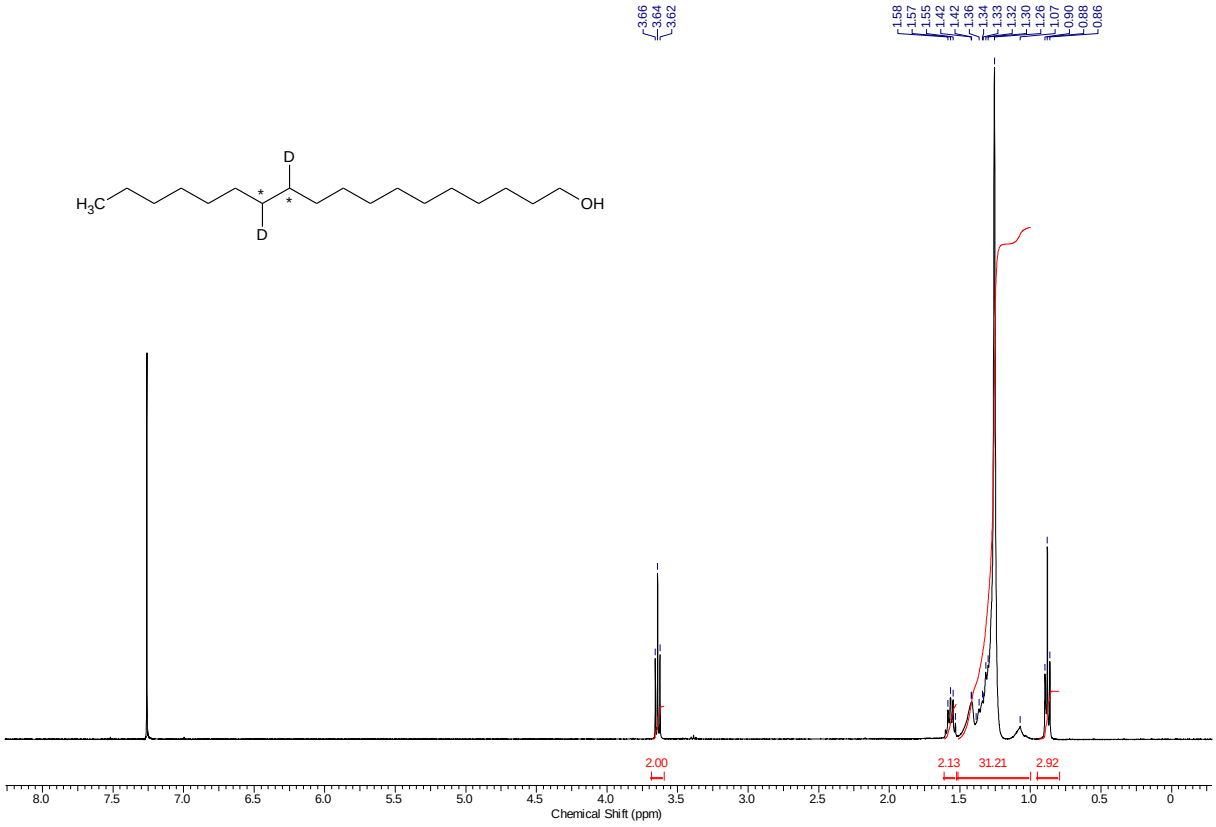


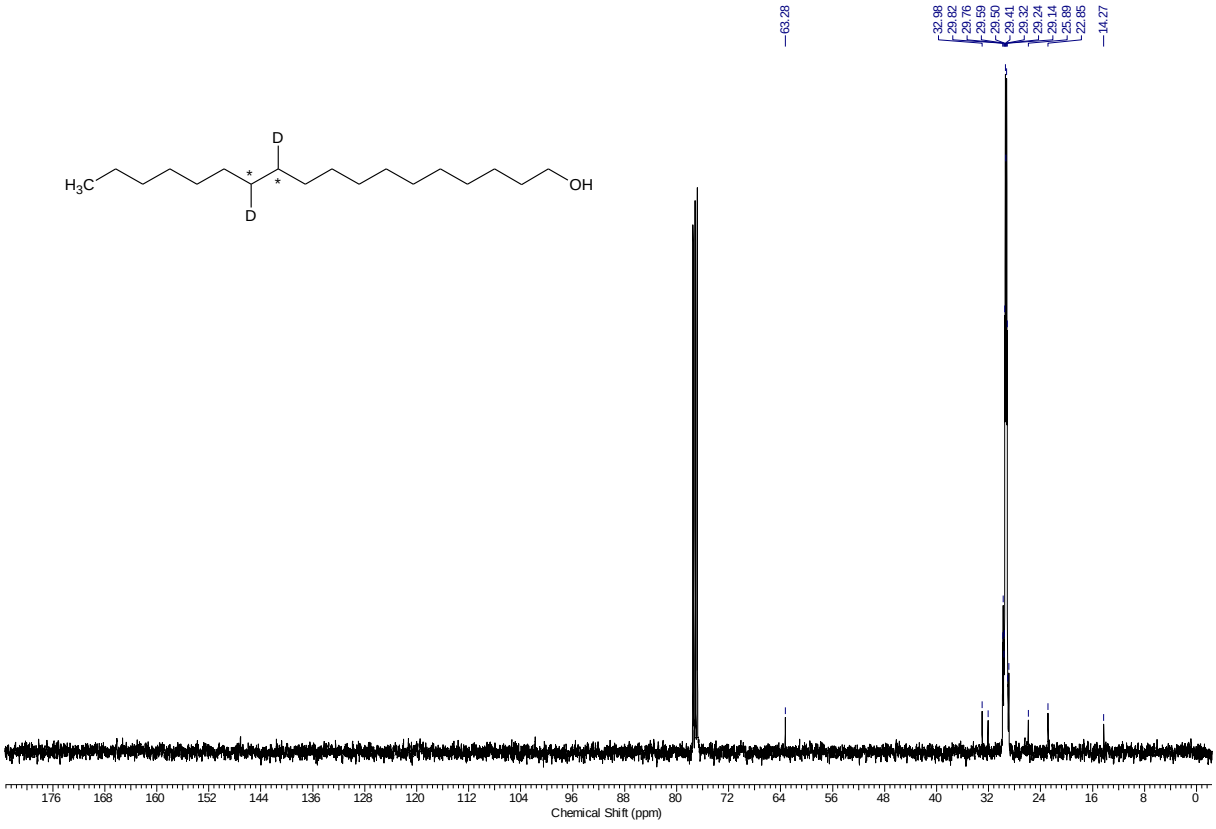
[11,12-$^{13}C_2$-11,12-D_2]-((octadecyloxy)methyl)benzene **27c**





[11,12-$^{13}C_2$-11,12-D_2]-stearyl alcohol **28c**





[11,12-$^{13}C_2$-11,12-D_2]-stearic acid **29c**