Supplementary Information

Chemoenzymatic β-Specific Methylene C(sp^3)–H Deuteration of Carboxylic Acids

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1. General Information

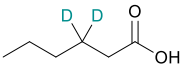
General. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm 230-400 mesh silica gel containing a fluorescent indicator. Visualization was accomplished by exposure to a UV lamp, and/or treatment with a solution of phosphomolybdic acid (PMA) followed by brief heating with heating gun. Most of the products were compatible with standard silica gel chromatography. Column chromatography was performed on silica gel 60N (spherical and neutral, 200-300 mesh) using standard methods.

Structural analysis. NMR spectra were measured on a Bruker Avance-400 spectrometer and chemical shifts (δ) are reported in parts per million (ppm). ^{1}H NMR spectra were recorded at 400 MHz in NMR solvents ($CDCl_3$) and referenced internally to corresponding solvent resonance, and ^{13}C NMR spectra were recorded at 100 MHz, chemical shifts were reported in ppm on the δ scale relative to $CHCl_3$ (δ = 7.26 for ^{1}H NMR, δ = 77.16 for ^{13}C NMR). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). High-resolution mass Spectra (HRMS) were obtained on a WATERS I-Class VION IMS QTof using ESI.

Materials. Commercial reagents were purchased from J&K, Energy, Adamas, Sigma-Aldrich, Aladdin, Alfa Aesar, Acros Organics or TCI and used as received unless otherwise stated.

2. General procedure for one-pot β-Specific methylene C(sp^3)–H deuteration of carboxylic acids

Carboxylic acids (5.0 mmol) and 8-aminoquinoline (6.0 mmol, 1.2 equiv.) were dissolved in toluene (5.0 mL), and then $B(OCH_2CF_3)_3$ (1.5 mmol, 0.3 equiv.) was added to the solution. The mixture was heated to reflux with a Dean-Stark setup for 48 h. After cooling down, to the required volume of solution (0.5 mL) was added acetic anhydride (0.20 mmol, 0.40 equiv.). The reaction mixture was stirred at room temperature for 2 h followed by additions of deuterium oxide (2.0 mL), palladium acetate (0.025 mmol, 5.0 mol%) and pivalic acid (0.50 mmol, 1.0 equiv.). After reaction at 90 ˚C for 24 h, to the cooled mixture were added NovoCor® ADL (2.5 mL) and water (200 mL). The resulting mixture was stirred at 50 ˚C for another 24 h. After cooling down to room temperature, the mixture was filtered through diatomite and extracted with ethyl acetate. The organic phase was concentrated to about 1 mL, then extracted three times with 1.0 M NaOH aq., then 1.0 M HCl aq. was added to acidification until pH = 2, and then the water phase was extracted three times with DCM. The combined organic phases were dried over anhydrous magnesium sulfate and concentrated in vacuo to obtain the deuterated carboxylic acids. The residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether or DCM/MeOH) if necessary. Deuterium incorporation was determined by ^{1}H NMR analysis of the corresponding benzyl ester or methyl ester.

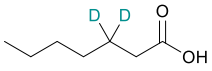


1b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (50 mg, 83% yield, 94% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 2H), 1.27-1.36 (m, 4H), 0.93-0.86 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 33.9, 31.0, 23.7, 22.4-23.7 (m, β-CD_2), 13.9.

HRMS (ESI-) m/z calcd. for $C_6H_9D_2O_2^-$ [M-H]$^-$: 117.0890, found: 117.0889

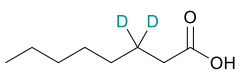


2b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (65 mg, 98% yield, 98% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 2H), 1.25-1.36 (m, 6H), 0.89 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 33.9, 31.4, 28.5, 23.7-24.1 (m, β-CD_2), 22.5, 14.0.

HRMS (ESI-) m/z calcd. for $C_7H_{11}D_2O_2^-$ [M-H]$^-$: 131.1046, found: 131.1044



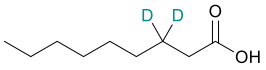
3b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (62 mg, 85% yield, 96% deuterium

incorporation).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 2H), 1.25-1.33 (m, 8H), 0.88 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 180.3, 33.9, 31.7, 28.9, 28.8, 23.8-24.2 (m, β-CD_2), 22.6, 14.1.

HRMS (ESI-) m/z calcd. for $C_8H_{13}D_2O_2^-$ [M-H]$^-$: 145.1203, found: 145.1205

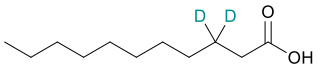


4b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (65 mg, 81% yield, 96% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 2H), 1.22-1.35 (m, 10H), 0.87 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 33.9, 31.8, 29.2, 29.1, 28.9, 23.6-24.2 (m, β-CD_2), 22.7, 14.1.

HRMS (ESI-) m/z calcd. for $C_9H_{15}D_2O_2^-$ [M-H]$^-$: 159.1360, found: 159.1358

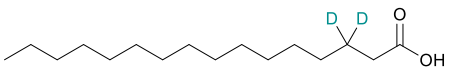


5b: The title compound was prepared on a 0.5 mmol scale and obtained as a colorless solid (46 mg, 49% yield, 97% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 2H), 1.23-1.32 (m, 14H), 0.88 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.5, 33.9, 31.9, 29.5, 29.4, 29.3, 29.2, 28.8, 23.7-24.3 (m, β-CD_2), 22.7, 14.1.

HRMS (ESI-) m/z calcd. for $C_{11}H_{19}D_2O_2^-$ [M-H]$^-$: 187.1673, found: 187.1674

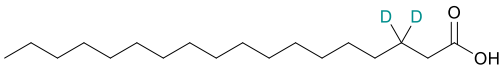


6b: The title compound was prepared on a 0.5 mmol scale and obtained as a white solid (89 mg, 69% yield, 95% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 2H), 1.21-1.31 (m, 24H), 0.88 (t, 3H, J = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.0, 33.8, 31.9, 29.71, 29.70, 29.69, 29.68, 29.66, 29.61, 29.4, 29.3, 29.2, 28.8, 23.5 (m, β-CD_2), 22.7, 14.1.

HRMS (ESI-) m/z calcd. for $C_{16}H_{31}D_2O_2^-$ [M-H]$^-$: 257.2455, found: 257.2455

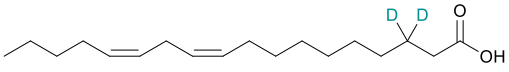


7b: The title compound was prepared on a 0.5 mmol scale and obtained as a white solid (61 mg, 43% yield, 97% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 2H), 1.19-1.34 (m, 28H), 0.87 (t, 3H, J = 6.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 33.9, 31.9, 29.7, 29.69, 29.67, 29.62, 29.4, 29.3, 29.2, 28.8, 23.7-24.1 (m, β-CD_2), 22.7, 14.1.

HRMS (ESI-) m/z calcd. for $C_{18}H_{33}D_2O_2^-$ $[M-H]^-$: 285.2768, found: 285.2754

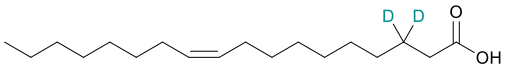


8b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (87 mg, 62% yield, 95% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.28-5.41 (m, 4H), 2.77 (t, 2H, J = 6.4 Hz), 2.33 (s, 2H), 2.01-2.08 (m, 4H), 1.24-1.40 (m, 14H), 0.89 (t, 3H, J = 6.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 130.2, 130.0, 128.0, 127.9, 33.9, 31.5, 29.6, 29.3, 29.12, 29.12, 28.8, 27.22, 27.20, 25.6, 23.5-24.3 (m, β-CD_2), 22.6, 14.1.

HRMS (ESI-) m/z calcd. for $C_{18}H_{29}D_2O_2^-$ $[M-H]^-$: 281.2455, found: 281.2453

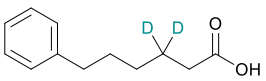


9b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (130 mg, 61% yield, 94% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.30-5.39 (m, 2H), 2.33 (s, 2H), 1.95-2.08 (m, 4H), 1.41-1.18 (m, 20H), 0.88 (t, 3H, J = 6.7 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 130.0, 129.7, 33.9, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.8, 27.24, 27.17, 23.7-24.1 (m, β-CD_2), 22.7, 14.1.

HRMS (ESI-) m/z calcd. for $C_{18}H_{31}D_2O_2^-$ $[M-H]^-$: 283.2612, found: 283.2609

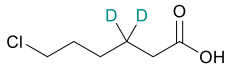


10b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil by flash column chromatography (ethyl acetate/petroleum ether = 1/5, R_f = 0.28) (81 mg, 84% yield, 96% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16-7.25 (m, 2H), 7.03-7.15 (m, 3H), 2.53 (t, 2H, J = 7.7 Hz), 2.27 (s, 2H), 1.50-1.62 (m, 2H), 1.31 (dt, 2H, J = 7.2, 6.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 142.4, 128.4, 128.3, 125.7, 35.7, 31.1, 31.1, 28.7, 28.5, 24.4-24.7 (m, β-CD_2).

HRMS (ESI-) m/z calcd. for $C_{12}H_{13}D_2O_2^-$ [M-H]$^-$:193.1203, found: 193.1201

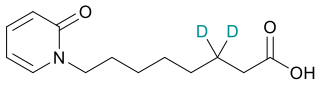


11b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (32 mg, 42% yield, 91% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.53 (t, 2H, *J* = 6.4 Hz), 2.37 (t, 2H, *J* = 6.5 Hz), 1.74-1.84 (m, 2H), 1.45-1.53 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.2, 44.7, 33.7, 32.1, 26.1, 23.2-23.6 (m, *β*-CD_2).

HRMS (ESI-) m/z calcd. for $C_6H_8D_2ClO_2^-$ [M-H]$^-$: 151.0500, found: 151.0498

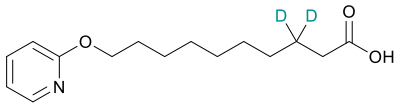


12b: The title compound was prepared on a 0.5 mmol scale and obtained as a white solid by flash column chromatography (DCM/ MeOH = 10: 1, R_f= 0.25) (38 mg, 32% yield, 93% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (m, 2H), 6.57 (d, 1H, *J* = 9.1 Hz), 6.17 (dd, 1H, *J* = 6.8 Hz, 6.8 Hz), 3.88 (t, 2H, *J* = 7.5 Hz), 2.19 (s, 2H), 1.68 (dt, 2H, *J* = 7.1 Hz, 6.8 Hz), 1.39-1.17 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 162.8, 139.5, 137.6, 120.9, 106.3, 49.9, 35.1, 33.8, 29.0, 28.6, 26.2, 24.4-24.8 (m, *β*-CD_2).

HRMS (ESI-) m/z calcd. for $C_{13}H_{16}D_2NO_3^-$ [M-H]$^-$: 238.1418, found: 238.1416

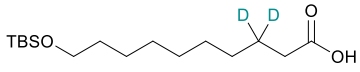


13b: The title compound was prepared on a 0.5 mmol scale and obtained as a colorless solid by flash column chromatography (DCM/ MeOH = 10: 1, R_f= 0.30) (89 mg, 67% yield, 95% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (dd, 1H, *J* = 5.1, 1.9 Hz), 7.60-7.52 (m, 1H), 6.84 (dd, 1H, *J* = 7.0, 5.1 Hz), 6.72 (d, 1H, *J* = 8.3 Hz), 4.26 (t, 2H, *J* = 6.7 Hz), 2.33 (s, 2H), 1.76 (m, 2H), 1.43 (m, 2H), 1.26-1.35 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4, 164.0, 146.8, 138.6, 116.5, 111.0, 66.1, 33.8, 29.29, 29.24, 29.05, 29.03, 28.7, 25.9, 24.6-24.8(m, *β*-CD_2).

HRMS (ESI-) m/z calcd. for $C_{15}H_{20}D_2NO_3^-$ [M-H]$^-$: 266.1730, found: 266.1729

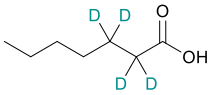


14b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (44 mg, 29% yield, 95% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.59 (t, 2H, J = 6.6 Hz), 2.33 (s, 2H), 1.50 (t, 2H, J = 6.8 Hz), 1.26-1.33 (m, 10H), 0.89 (s, 9H), 0.04 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 63.3, 33.8, 32.8, 29.4, 29.3, 29.1, 28.8, 26.0, 25.6-25.9 (m, β-CD_2), 18.4, -5.2.

HRMS (ESI-) m/z calcd. for $C_{16}H_{31}D_2O_3Si^-$ [M-H]$^-$: 303.2330, found: 303.2329

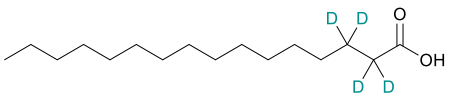


15b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (66 mg, 98% yield, α-96%, β-98% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.35 (m, 6H), 0.88 (t, 3H, J = 6.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 33.2-33.6 (m, α-CD_2), 31.3, 28.4, 23.6-23.9 (m, β-CD_2), 22.4, 14.0.

HRMS (ESI-) m/z calcd. for $C_7H_9D_4O_2^-$ [M-H]$^-$: 133.1172, found: 133.1170



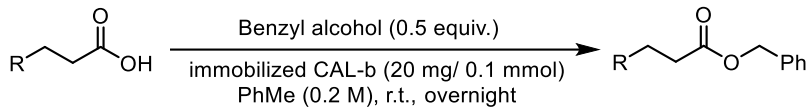
16b: The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (87 mg, 67% yield, α-94%, β-96% deuterium incorporation).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.31 (m, 24H), 0.88 (t, 3H, J = 6.8 Hz).

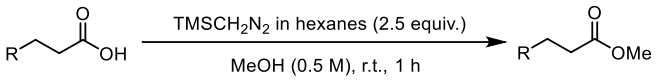
^{13}C NMR (100 MHz, $CDCl_3$): δ 184.2, 37.4-37.7 (m, α-CD_2), 30.9, 28.68, 28.66, 28.64, 28.63, 28.5, 28.4, 28.3, 28.1, 27.7, 25.9, 23.3-23.6 (m, β-CD_2), 21.6, 13.1.

HRMS (ESI-) m/z calcd. for $C_{16}H_{27}D_4O_2^-$ [M-H]$^-$: 259.2580, found: 259.2574

3. Procedure for esterification



The carboxylic acid (0.10 mmol), alcohol (0.50 mmol) and Immobilized *Candida Antarctica* Lipase-B (20 mg) were added to toluene (0.50 mL), and the reaction was stirred at room temperature overnight. After filtration and concentration in vacuum, the corresponding esters were obtained quantitatively. Using the enzyme-catalyzed esterification method developed by us, no dedeuteration products were observed.



The carboxylic acid (0.10 mmol) was dissolved in 0.20 mL of MeOH, (trimethylsilyl)diazomethane (2.5 equiv., 2.0 M in hexanes) was added dropwise until the colorless reaction solution turned to bright yellow. The reaction mixture was stirred for another 30 min, and quenched with acetic acid. The reaction mixture became colorless. After dilution and extraction with ether, the organic layers were collected and dried with $MgSO_4$ and removed the solvent in vacuum. The corresponding methyl esters was obtained without further purification.[1]

4. Procedure for gram scale reaction

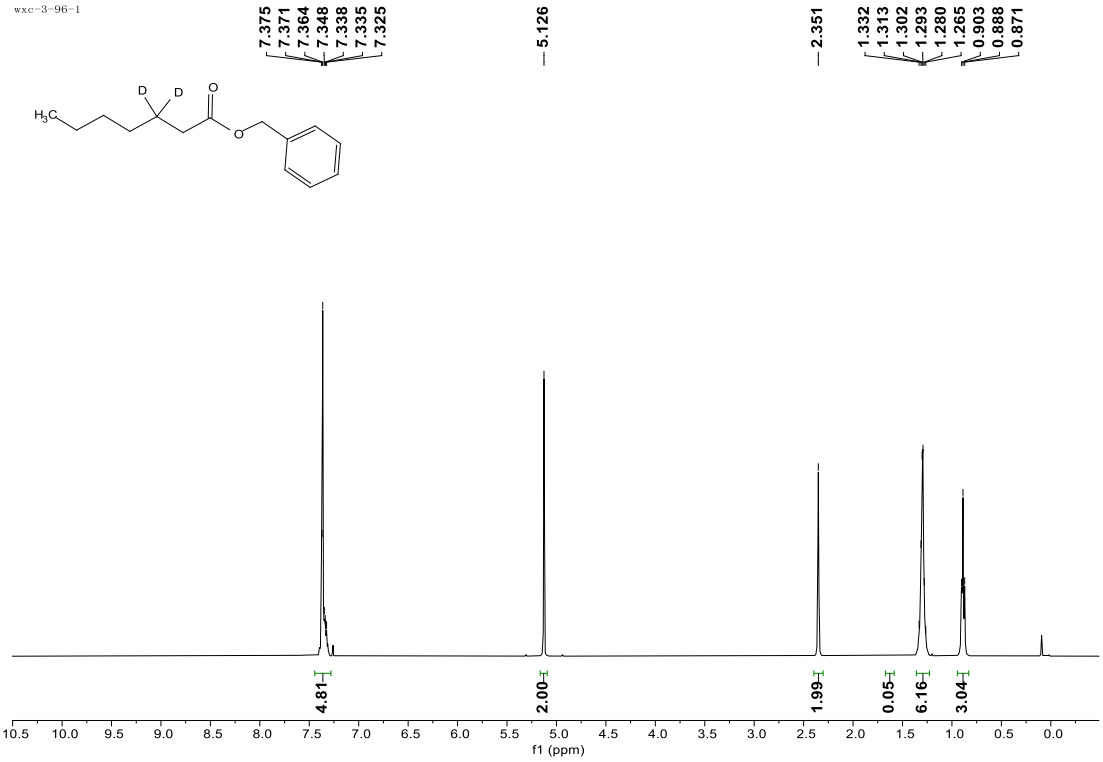
The carboxylic acid (5.0 mmol) and 8-aminoquinoline (6.0 mmol, 1.2 equiv.) were dissolved in 5.0 mL of toluene, and then $B(OCH_2CF_3)_3$ (1.5 mmol, 0.30 equiv.) was added to the solution. The mixture was stirred with a Dean-Stark system for 48 h in air. Then acetic anhydride (2.0 mmol, 0.4 equiv.) was added in the solution. The reaction mixture was stirred at room temperature for 2h, and deuterium oxide (20 mL), palladium acetate (0.25 mmol, 5.0 mol%) and trimethylacetic acid (5.0 mmol, 1.0 equiv.) was added to the solution. The solution was stirred at 90 °C for 24 h in air. Then 2.0 L water and 20 mL NovoCor® ADL was added in the tube. The mixture was stirred at 50 °C for 24 h in air. The mixture was filtered, and the water was concentrated to about 200 mL then extracted three times with ethyl acetate. The organic phase was concentrated to about 10 mL, then extracted three times with 1.0 M NaOH aq., then 1.0 M HCl solution was added to acidification until pH = 2, and then the water phase was extracted three times with DCM. The combined organic phases were dried over anhydrous magnesium sulfate and concentrated in vacuo to obtain the deuterated carboxylic acids.

5. Determination of deuteration rates by NMR spectroscopy

The decrease of the proton signal intensity was measured and compared with the values obtained from non-deuterated starting materials. The corresponding methyl- or benzyl ester of the carboxylic acid was synthesized, and the protons of methyl or benzyl group were used as internal standard to calculate the relative decrease in ^{1}H-signal intensity at the deuteration site.

$$\text{deuteration} = [100 - (\frac{\text{residual integral}}{\text{number of labelling sites}} \times 100)]\%$$

Take product **2b** for example:



After esterification, we use the two proton signals at the benzyl position as an integral of 2 as the internal standard, the deuterated rate is:

$$\text{deuteration} = (100 - \frac{0.05}{2.00} \times 100)\% = 98\%$$

6. General procedure for optimization experiments of amidation reaction, deuteration reaction and hydrolysis reaction.

Amidation reaction

To a 25 mL vial containing a magnetic stirrer were added *n*-octanoic acid (0.72 g, 5.00 mmol), 8-aminoquinoline (0.87 g, 6.00 mmol, 1.20 equiv.) and 5.00 mL of toluene, followed by addition of the selected amount of catalyst in open air. After heating for required reaction time, 1/10 of the reaction mixture was transferred to a vial and then dried under vacuum. To the residue was added 0.5 mL of $CDCl_3$ and 0.5 mmol of dibromomethane in sequence. After complete dissolution, the clear solution was transferred to an NMR tube and the ^1H NMR spectrum was recorded. The peak area of dibromomethane (4.95 ppm) was integrated as 2.00, then the carbonyl α-proton of the amide product was integrated as "*x*". The yield was determined as:

$$\text{yield} = \frac{x}{2} \times 100\%$$

Deuteration reaction

N-(Quinoline-8-yl) octanamide (27.0 mg, 0.1 mmol) and the additives were added to a 10 mL Schlenk tube, and then the selected amount of $Pd(OAc)_2$, D_2O (0.4 mL) and an oven-dried PTFE-coated magnetic stirrer were added to the solution in open air. After heating for the required time, the reaction mixture was extracted 3 times by ethyl acetate. The solvent of the combined organic phases was removed under vacuum, and then 0.5 mL of $CDCl_3$ and 0.1 mmol of dibromomethane were added to the vial in sequence. The resulting solution was transferred to an NMR tube and the ^1H NMR spectrum was recorded. The peak area of dibromomethane (4.95 ppm) was integrated as 2.00, then the carbonyl β-proton of the amide product was integrated as "*y*". The yield was determined as:

$$\text{deuteration} = \frac{2-y}{2} \times 100\%$$

Amide hydrolysis reaction

To a 10 mL vial containing a magnetic stirrer were added *n*-(quinoline-8-yl) octanamide (2.70 mg, 0.01 mmol), lipase, *n*-dodecane (1.70 mg, 0.01 mmol, 1.00 equiv.) and tap water in open air. The resulting mixture was heated for the required reaction time. The yield was determined by GC-FID method using *n*-dodecane as internal standard. After the reaction, the reaction mixture was ultrasonicated for 1 min. A sample of 0.01 mL solution was transferred to a centrifugal tube and 1.0 mL of ethyl acetate was added and centrifuged. Transfer 0.1 mL of supernatant into another centrifuge tube and add 1.0 mL of ethyl acetate for centrifugation. Next, 0.5 mL of supernatant was transferred to a chromatography tube, 1.0 mL ethyl acetate was added, and GC experiment was performed.

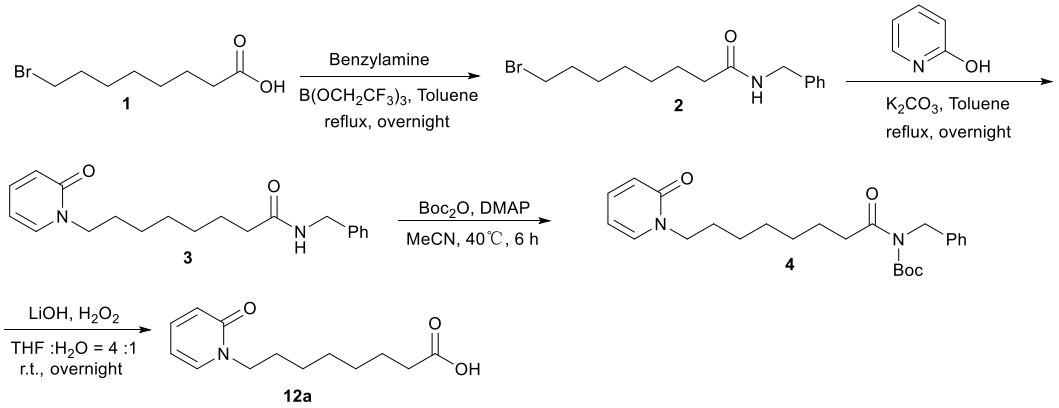
GC-FID analysis: Yields were determined by GC analysis on a Thermo Scientific Trace 1300 system using nitrogen as carrier gas and a TRACE™ TR-1MS GC column (100% dimethylpolysiloxane stationary phase, 30 m × 0.25 mm × 0.25 μm). The following

acquisition parameters were used: Oven program: 50 °C for 1 min, 20 °C/min to 210 °C for 5 min, 10 °C/min to 280 °C for 1 min, 5 °C/min to 320 °C for 1 min; total flow rate: 15 mL/min; injector temperature: 220 °C; detector temperature: 350 °C; splitless injection.

Retention time: *n*-dodecane (8.2 min), octanoic acid (9.3 min), 8-aminoquinoline (15.5 min), *N*-(quinoline-8-yl) octanamide (28.3 min)

7. Synthesis of starting materials

Synthesis of 8-(2-oxopyridin-1(2H)-yl)octanoic acid (12a)



*Synthesis of Compound **2***

1 (2.20 g, 10.0 mmol), benzylamine (0.963 g, 9.00 mmol, 0.900 equiv.) and $B(OCH_2CF_3)_3$ (0.308 g, 1.00 mmol, 10 mol%) was added in 10 mL toluene. The reaction mixture was refluxed overnight. After extraction, washed with 1 M NaOH (aq), dried over anhydrous Na_2SO_4 and concentrated in vacuum, the corresponding product **2** was afforded through silica gel column chromatography (ethyl acetate/hexanes) in 2.44 g (87% yield, m.p. : 83-85 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 5H), 5.87 (s, 1H), 4.42 (d, *J* = 5.7 Hz, 2H), 3.39 (t, *J* = 6.8 Hz, 2H), 2.20 (t, *J* = 7.6 Hz, 2H), 1.83 (p, *J* = 7.0 Hz, 2H), 1.65 (p, *J* = 7.3 Hz, 2H), 1.42 (p, *J* = 6.8 Hz, 2H), 1.28 - 1.36 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 138.3, 128.6, 127.7, 127.4, 43.5, 36.6, 33.9, 32.6, 29.0, 28.4, 27.9, 25.5.

HRMS (ESI+) m/z calcd. for $C_{15}H_{22}NO_2Br$ $[M+H]^-$: 312.0958, found: 312.0957.

*Synthesis of Compound **3***

Compound **2** (2.49 g, 8.00 mmol), 2-hydroxypyridine (0.912 g, 9.60 mmol, 1.20 equiv.) and K_2CO_3 (3.31 g, 24.0 mmol, 3.00 equiv.) were added to toluene (16.0 mL). The reaction mixture was refluxed overnight. The reaction mixture was extracted with DCM three times, and the combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The corresponding product **3** was afforded

through silica gel column chromatography (methanol/dichloromethane) in 1.96 g (75% yield, m.p. : 65-69 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.36 (m, 7H), 6.75 (d, *J* = 17.9 Hz, 1H), 6.45 (d, *J* = 9.1 Hz, 1H), 6.15 (t, *J* = 6.7 Hz, 1H), 4.40 (d, *J* = 5.4 Hz, 2H), 3.85 (d, *J* = 7.0 Hz, 2H), 2.20 (t, *J* = 7.5 Hz, 2H), 1.65 (dp, *J* = 21.8, 7.2 Hz, 4H), 1.25-1.36 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 139.3, 138.7, 128.5, 127.7, 127.2, 49.6, 43.3, 36.3, 29.1, 28.9, 26.8, 26.2, 25.5.

HRMS (ESI+) m/z calcd. for $C_{20}H_{26}N_2O_2$ $[M+H]^-$: 327.2067, found: 327.2064.

*Synthesis of Compound **4***

Compound **3** (1.96 mg, 6.00 mmol), Boc_2O (3.93 g, 18.0 mmol, 3.00 equiv.), DMAP (0.740 g, 0.600 mmol, 0.100 equiv.) were dissolved in MeCN (24.0 mL), and the reaction mixture was stirred at 40 ºC for 6 h. After concentrated in vacuum, the corresponding product **4** was afforded through silica gel column chromatography (methanol/dichloromethane) in 2.38 g (93% yield).

*Synthesis of Compound **12a***

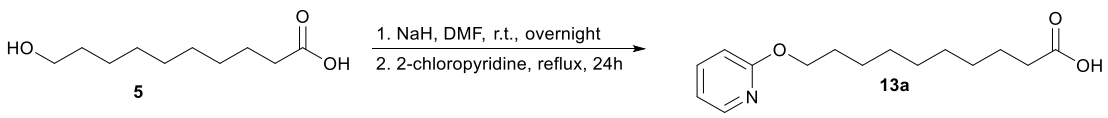
To a solution of compound **4** (2.35 g, 5.50 mmol) in THF/ H_2O (4:1, 110 mL), LiOH (0.360 g, 15.0 mmol, 2.72 equiv.) and H_2O_2 (3.30 mL, 30 % wt in H_2O) was added. The reaction mixture was stirred at room temperature overnight. Upon completion, saturated aqueous Na_2SO_3 solution was added, and the solution was stirred for another 1 h. After acidification with 1 M Hydrochloric acid solution, the reaction mixture was extracted with DCM three times. The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The corresponding product **12a** was afforded through silica gel column chromatography (methanol/dichloromethane) in 1.19 g (91% yield, m.p. : 43-47 ºC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H), 7.36 (t, *J* = 8.1 Hz, 1H), 7.31 (d, *J* = 6.7 Hz, 1H), 6.68 (d, *J* = 9.1 Hz, 1H), 6.24 (t, *J* = 6.8 Hz, 1H), 3.94 (t, *J* = 7.5 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 1.69-1.80 (m, 2H), 1.57-1.68 (m, 2H), 1.29-1.41 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 163.0, 139.8, 137.5, 120.7, 106.8, 50.1, 34.1, 29.1, 28.9, 28.8, 26.3, 24.6.

HRMS (ESI+) m/z calcd. for $C_{13}H_{19}NO_3$ $[M+H]^-$: 238.1438, found: 238.1443

Synthesis of 10-(pyridin-2-yloxy)decanoic acid (13a)



To a solution of compound **5** (2.02 g, 10.0 mmol) in DMF (10.0 mL), NaH (20.0 mmol, 2.00 equiv.) was added, and the reaction mixture was stirred at room temperature

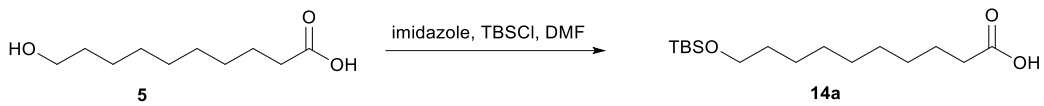
overnight. 2-chloropyridine (1.36 g, 12.0 mmol, 1.20 equiv.) was added, and the reaction mixture was refluxed for 24 h. Upon completion, the solution was quenched by water, and extracted with diethyl ether/hexanes (1:3) three times. The combined extracts were dried over anhydrous Na_2SO_4, and concentrated under vacuum. The corresponding product **13a** was afforded through silica gel column chromatography (ethyl acetate/hexanes) in 2.85 g (78% yield, m.p. : 48-50 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 5.1, 1.9 Hz), 1H, 7.60-7.52 (m, 1H), 6.84 (dd, *J* = 7.0, 5.1 Hz, 1H), 6.72 (d, 1H, *J* = 8.3 Hz), 4.26 (t, *J* = 6.7 Hz, 2H), 2.33 (s, 2H), 1.76 (p, *J* = 6.9 Hz, 2H), 1.63 (t, *J* = 7.3 Hz, 2H), 1.43 (q, *J* = 7.1 Hz, 2H), 1.26-1.35 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 164.0, 146.8, 138.6, 116.5, 111.1, 66.1, 34.1, 29.30, 29.26, 29.1, 29.02, 29.01, 25.9, 24.7.

HRMS (ESI+) m/z calcd. for $C_{15}H_{20}D_2NO_3^-$ $[M+H]^-$: 266.1730, found: 266.1729

Synthesis of 10-OTBS-decanoic acid (14a)

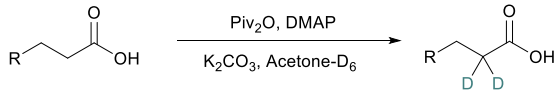


5 **14a**

To a solution of TBSCl (5.25 g, 35.0 mmol, 3.50equiv.) in DMF (20.0 mL), imidazole (6.80 g, 100 mmol, 10.0 equiv.) was added at 0 °C. After stirred at 0 °C for 1 h, compound **5** (2.02 g, 10.0 mmol) dissolved in DMF (5.00 mL) was added and stirred for another 4 h. Upon completion, brine was added to the mixture and extracted with diethyl ether/hexanes (1:3), the combined extracts were dried over Na_2SO_4 and concentrated in vacum. The mixture was solubilized with Methanol (150 mL), THF (80.0 mL). K_2CO_3 (4.50 g) in H_2O (50.0 mL) was added to the solution at 0 °C. The solution was stirred for 1 h, then 150 mL brine was added. The reaction mixture was acidified with 1 M HCl until pH reaches ~3, extracted with diethyl ether : hexanes = 1 : 3 three times, dried over Na_2SO_4, and evaporated. The corresponding product **14a** was afforded through silica gel column chromatography (ethyl acetate/hexane) in 2.82 g (93% yield).

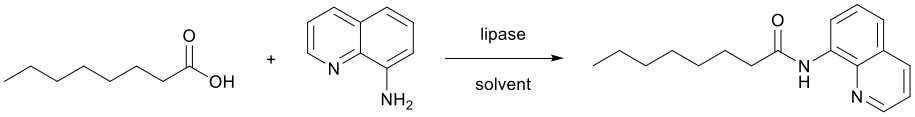
The NMR data was available according to the reported data.[2]

General procedure for Alpha-deuterated caboxylic acid



According to the known literature,[3] we obtained α-deuterated carboxylic acid.

8. Enzymatic synthesis of acyl-quinoline-8-ammonia [a]



Entry	Enzyme	Temp °C	m(E)/ (mg / 0.1 mmol)	Solvent	4Å MS (mg)	Yield (%)
1	ROL	60	20	dioxane	0	trace
2	ROL	80	20	toluene	0	trace
3	rugosa	60	20	dioxane	0	NR
4	rugosa	60	20	toluene	0	NR
5	cala	90	20	toluene	0	trace
6	cala	100	20	toluene	0	trace
7	calb	90	20	PBS buffer	0	trace
8	calb	90	20	acetonitrile	0	21
9	calb	90	20	solventless	0	2
10	calb	90	20	toluene	0	80
11	calb	100	20	toluene	0	47
12	calb	85	40	toluene	0	75
13	calb	90	40	toluene	0	83
14	calb	95	40	toluene	0	84
15	calb	90	40	benzene	0	28
16	calb	90	40	chlorobenzene	0	59
17	calb	90	40	DMF	0	0
18	calb	90	40	dioxane	0	78
19	calb	90	40	MTBE	0	75
20	calb	90	40	Benzotrifluoride	0	83
21	calb	90	40	Diphenyl ether	0	34
22	calb	90	40	tetrahydronaphthalene	0	87

23	calb	95	40	toluene	20	89
24	calb	90	40	tetrahydronapht halene	20	91
25	calb	90	40	tetrahydronapht halene	40	91
26	calb	90	40	tetrahydronapht halene	60	88

[a] 0.10 mmol acid, lipase and 0.12 mmol 8-AQ was added to 0.50 mL solvent. The reaction mixture was stirred for 24 h. Yield was detected by GC.

9. Complete environmental factor comparison of synthesis of α,β-tetradeuterated palmitic acid.

The **complete E-factor** (cEF) contains all material used for the synthesis, which includes all reagents, inorganics, organic solvents and water. The individual contributions to the cEF (reagents, inorganic, organic solvents and water) were calculated by adding up all material from this category and dividing this quantity by the amount of product generated. This calculation method was pioneered by Sheldon and Kaspar *et al.*[4], which considers all materials used as:

$$\mathrm{cEF} = \frac{\sum M\mathrm{reagents} + \sum M\mathrm{auxilliaries} + \sum M\mathrm{solvents} - M\mathrm{product}}{M\mathrm{product}}$$

Synthesis of α,α,β,β-tetradeuterated palmitic acid:

1. Present work:

The palmitic acid (5.0 mmol, 1.28 g), K_2CO_3 (0.07 g), Piv_2O (0.19 g), DMAP (0.06 g), acetone-d_6 (4.0 g), 48 h, 40 °C. The reaction mixture with D_2O (2.75 g) was stirred at room temperature for 1 h. To the reaction mixture was added 1 M HCl aq. (2.0 g, 0.5 g) and extracted with CH_2Cl_2 (42 g), and the solvent was removed under reduced pressure. Evaporation was carried out for the removal of pivalic acid.
The acid and 8-aminoquinoline (0.87 g, 6.0 mmol, 1.2 equiv.) were dissolved in 5.0 mL (4.35 g) of toluene, and then $B(OCH_2CF_3)_3$ (0.46 g, 1.5 mmol, 0.3 equiv.) was added to the solution. The mixture was stirred with a Dean-Stark system for 48 h in air. Then acetic anhydride (2.04 g, 2.0 mmol, 0.4 equiv.) was added to the solution. The reaction mixture was stirred at room temperature for 2 h, and deuterium oxide (20 mL, 22.1 g), palladium acetate (0.25 mmol, 5.0 mol%, 0.06 g) and pivalic acid (5.0 mmol, 1.0 equiv., 0.5 g) were added to the solution. The solution was stirred at 90 °C for 24 h in air. Then 2.0 L (2000.00 g) water and 20 mL NovoCor® ADL was added in the tube. The mixture was stirred at 50 °C for 48 h in air. The mixture was filtered, and the water was

concentrated to about 200 mL then extracted three times with ethyl acetate (300 g). The combined organic phases were concentrated to about 10 mL, then extracted three times with 1.0 M NaOH aq. (15 g water and 0.6 g NaOH). Then1.0 M HCl (20 g water and HCl 1.5 g) solution was used to acidify the combined aqueous phases until pH = 2, and then the mixture was extracted three times with DCM (79.60 g). The combined organic phases were dried over anhydrous magnesium sulfate (1.2 g) and concentrated in vacuo to deliver the deuterated carboxylic acids (**0.86 g**).

cEF=(1.28+0.19+0.06+0.87+0.46+2.04+0.06+0.5+0.5+0.07+0.6+1.5+1.2+4+42+4.35+300+79.60+2.75+2.0+22.1+2000+15+20-0.86)/0.86=6.3+4.5+500+2397.5-1
=**2907.3**
with contributions from reagents (6.3), inorganic (4.5), organic solvents (500) and water (2397.5)

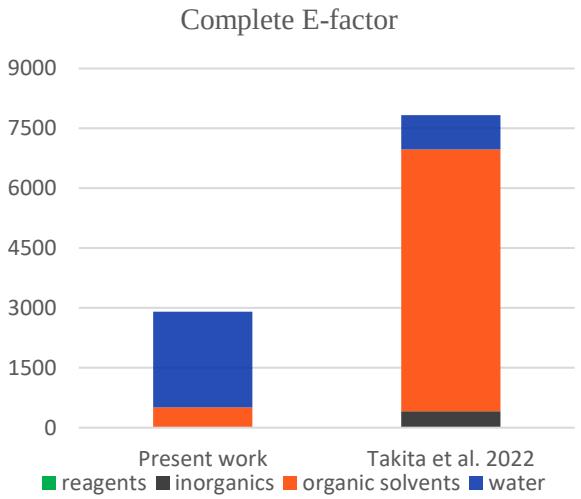
Takita's method (*Angew. Chem. Int. Ed.,* **2022,** *61*, e202202779)

Palmitic acid (1.28 g), 8-aminoquinoline (0.72 g), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide monohydrochloride (WSCD•HCl, 1.25 g), DMAP (0.61 g), and CH_2Cl_2 (70 g) were added to a Schlenk tube under an argon atmosphere at room temperature. After stirring overnight, the reaction was quenched with aqueous NH_4Cl (50 g, 3.6 g) and washed with brine (45 g, 16.2 g). The organic layer was dried over Na_2SO_4(1.2 g), filtered, and evaporated under reduced pressure. The product was purified by silica gel (10 g) flash column chromatography (500 g). Amide, palladium acetate (0.045 g), and cesium pivalate (92 mg) were added to a 10-mL screw-cap tube under air. Toluene (43.6 g) was added to dissolve the amide, and then D_2O (5.5 g) was added to the mixture. The reaction was stirred at 80 °C for 18 h, and the progress was monitored by ESI-MS. The reaction mixture was cooled to room temperature, transferred to a separation funnel, diluted with EtOAc (50 g), and washed with brine (150 g, 54 g). The organic layer was dried over Na_2SO_4 (1.2 g), filtered, and evaporated under reduced pressure. The crude β-deuterated material was roughly purified by silica gel (10 g) flash column chromatography (500 g). This material, potassium carbonate (0.63 g), and methanol-d_1 (18 g) were added to a screw-cap tube under air. The reaction was stirred at 80 °C for 18 h, and the progress was monitored by ESI-MS. The reaction mixture was cooled to room temperature, transferred to a separation funnel, diluted with EtOAc (40 g), and washed with brine (150 g, 54 g). The organic layer was dried over Na_2SO_4 (1.2 g), filtered, and evaporated under reduced pressure. The obtained material was purified by silica gel (10 g) flash column chromatography (500 g) to afford amide-d_4. Amide-d_4, nickel bis(2,2,6,6-tetramethyl-3,5-heptanedionate) (0.4 g), and MeOH-d_1 (CH_3OD, 47 g) were added to a screw cap tube with N_2 purging. The reaction was stirred at 100 °C for 16 h, and the progress was monitored by TLC and ESI-MS. The reaction mixture was transferred to a separation funnel, diluted with EtOAc (100 g), and washed with brine. The organic layer was dried over Na_2SO_4 (1.2 g), filtered, and evaporated under reduced pressure. The crude material was purified by silica gel (10 g) flash column chromatography (500 g) to afford the ester-d_4. The obtained ester-d_4, THF

(28.5 g), and methanol-d_1 (CH_3OD, 13.7 g) were added to a screw-cap tube with N_2 purging. After cooling to 0 °C, NaOD/D_2O solution (40 wt.%, 1.2 g, 0.48 g) was added to the reaction mixture. The mixture was stirred at 0 °C for 5 min and then at room temperature for 2 h. The reaction progress was monitored by TLC. The reaction was quenched with 1 N HCl (10 g, 0.24 g), diluted with diethyl ether (285 g), and separated. The organic layer was dried over Na_2SO_4 (8.0 g), filtered, and evaporated under reduced pressure. The obtained material was purified by flash column chromatography (10 g, 500 g) to afford the corresponding acid-d_4 in 38% yield (0.48 g).

cEF=(1.28+0.72+1.25+0.61+0.045+0.4+3.6+16.2+1.2+10+54+1.2+10+0.63+54+1.2+10+1.2+10+0.48+0.24+8+10+70+500+50+500+18+40+500+47+100+500+28.5+13.7+285+500+45+50+5.5+150+150+1.2+10-0.48)/0.48 = 9+400+6567+858-1 = 7833

with contributions from reagents (9), inorganic (400), organic solvents (6567) and water (858)



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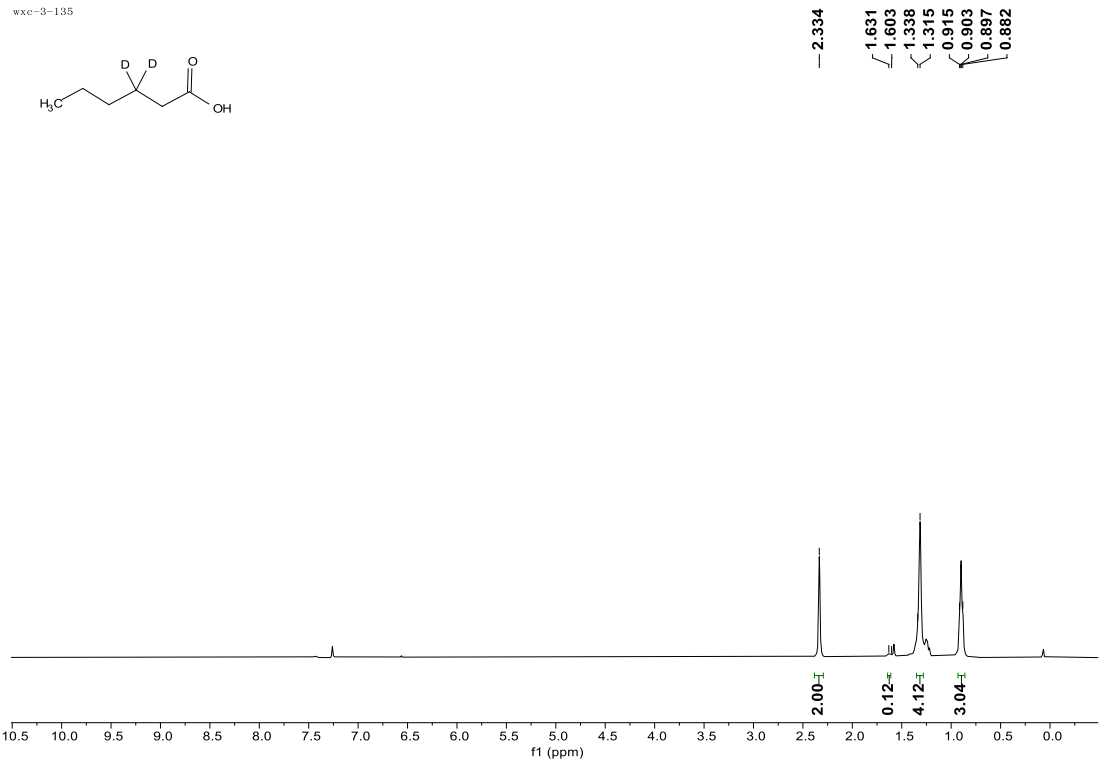
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0.882
2.00
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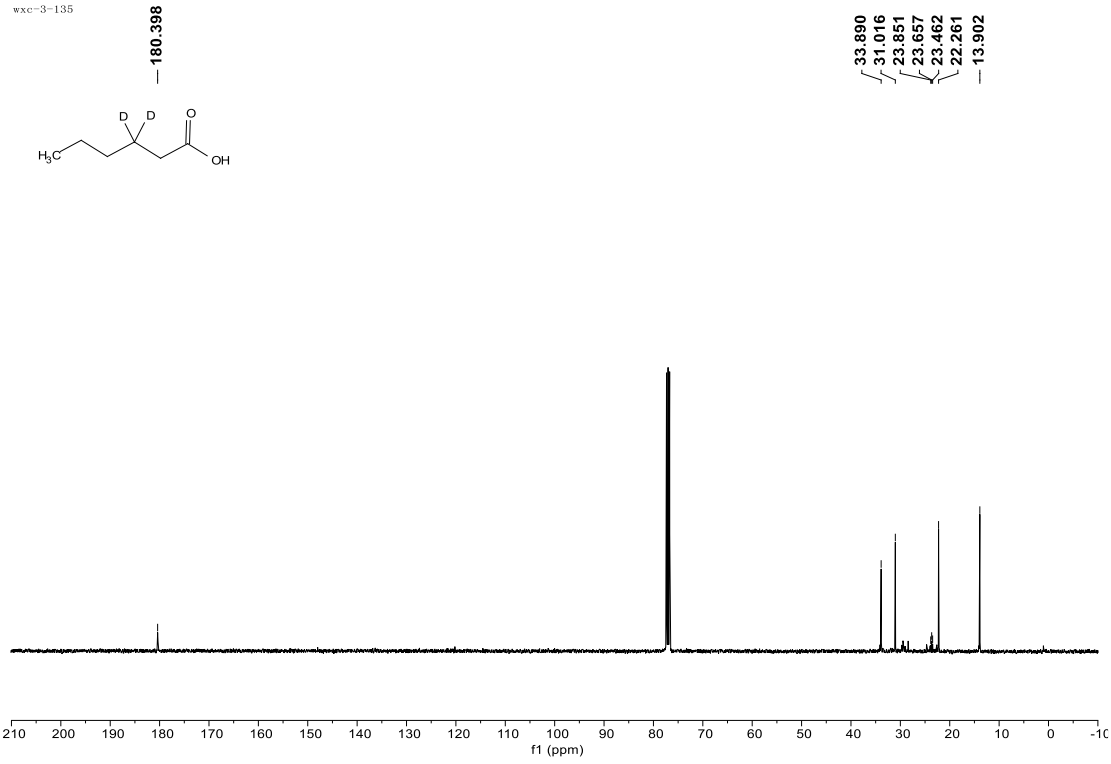
4.12
3.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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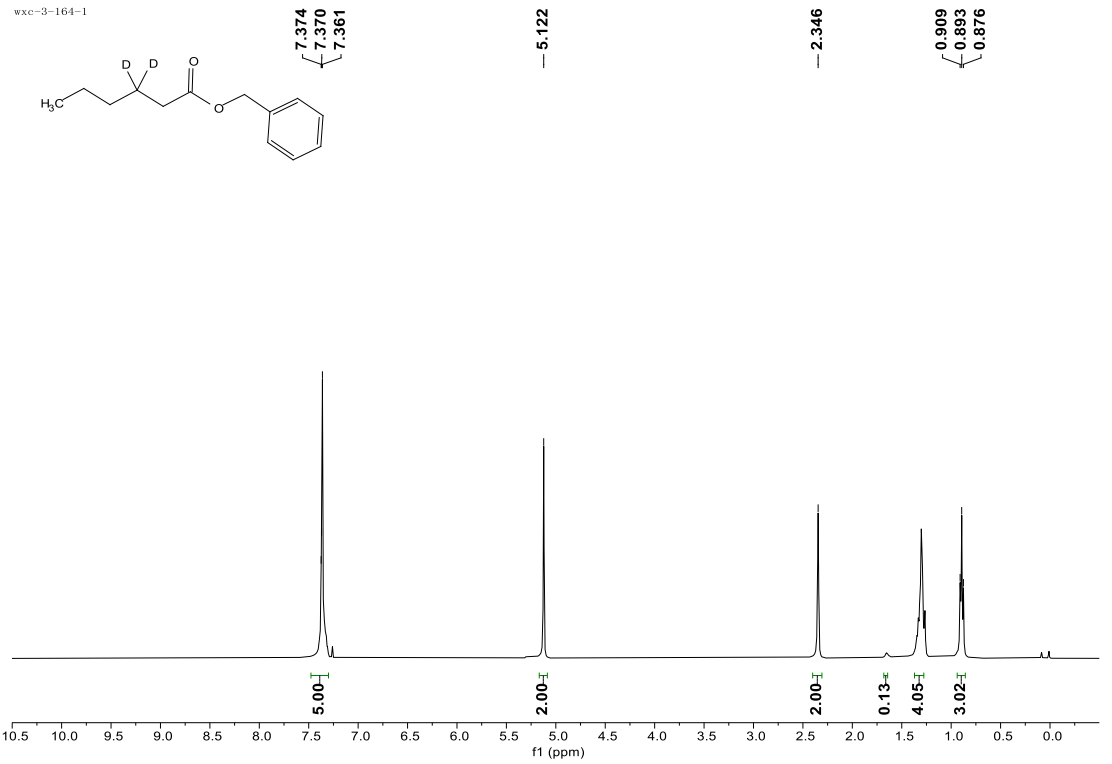
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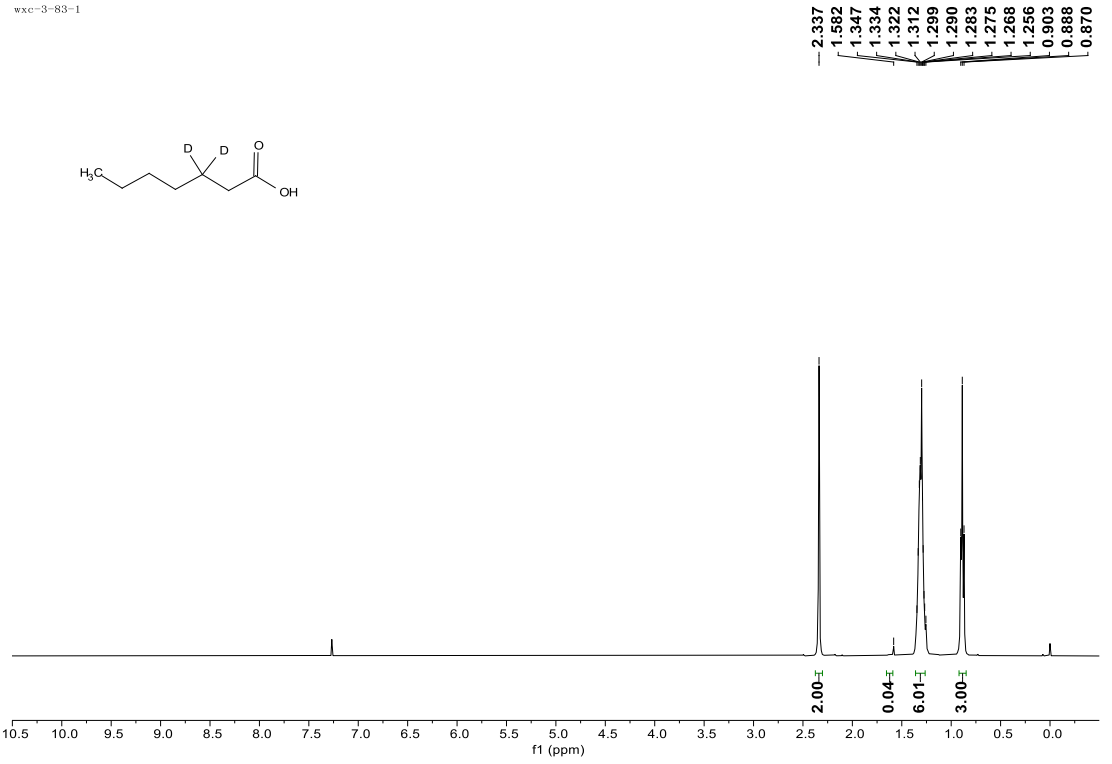
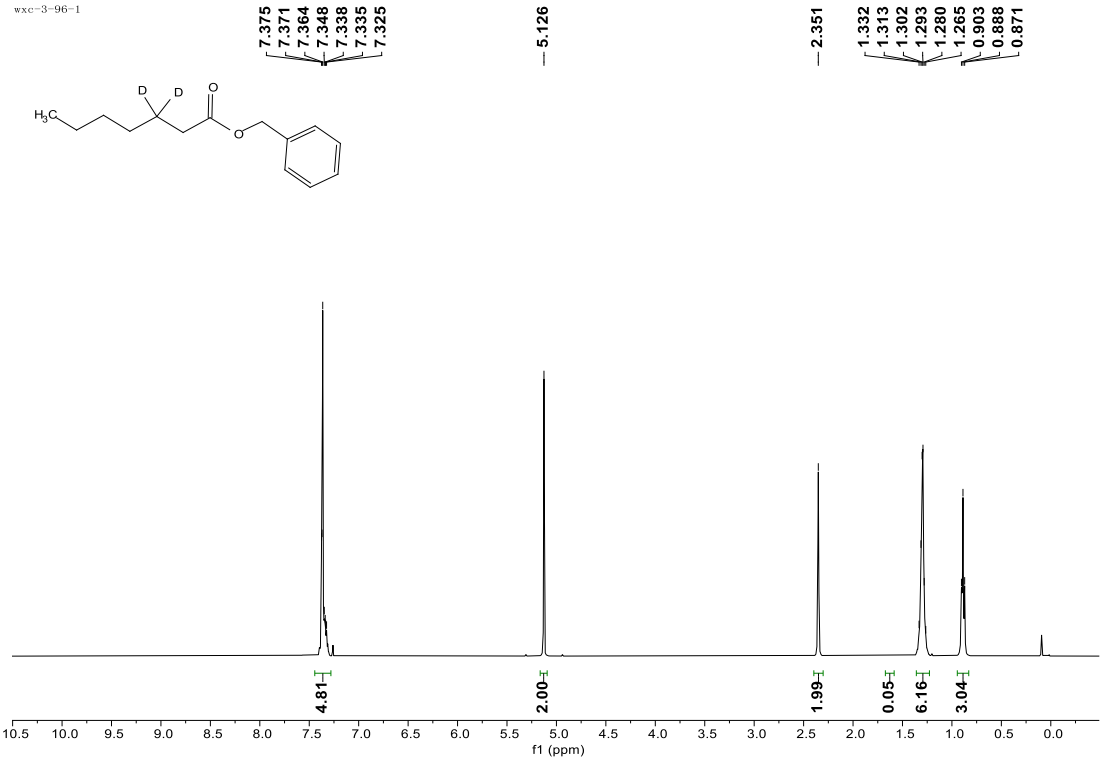
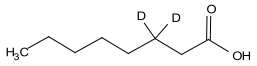
2.00
2.00
0.13
4.05
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

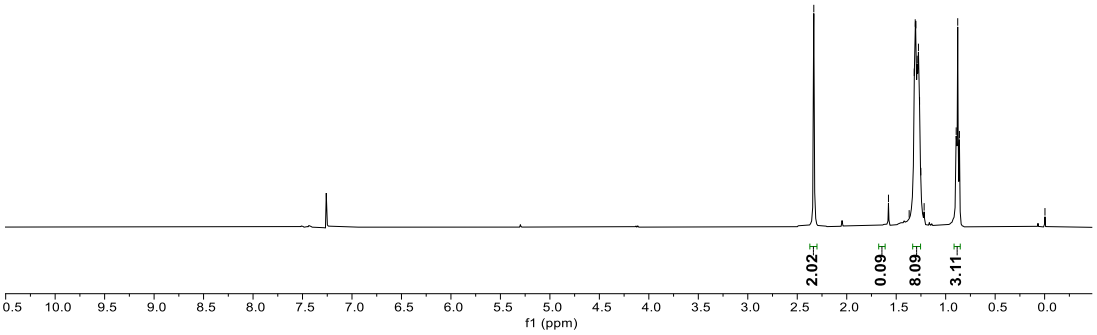

wxc-3-83-1
2.337
1.582
1.347
1.334
1.322
1.312
1.299
1.290
1.283
1.275
1.268
1.256
0.903
0.888
0.870
D
D
O
H3C
OH
2.00
0.04
6.01
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


wxc-3-83-1
180.725
33.977
31.378
28.531
24.301
24.108
23.915
23.720
23.525
22.473
14.009
D
D
O
H3C
OH
f1 (ppm)

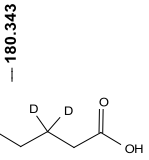

wxc-3-96-1
7.375
7.371
7.364
7.348
7.338
7.335
7.325
5.126
2.351
1.332
1.313
1.302
1.293
1.280
1.265
0.903
0.888
0.871
D
D
O
H3C
O
4.81
2.00
1.99
0.05
6.16
3.04
f1 (ppm)

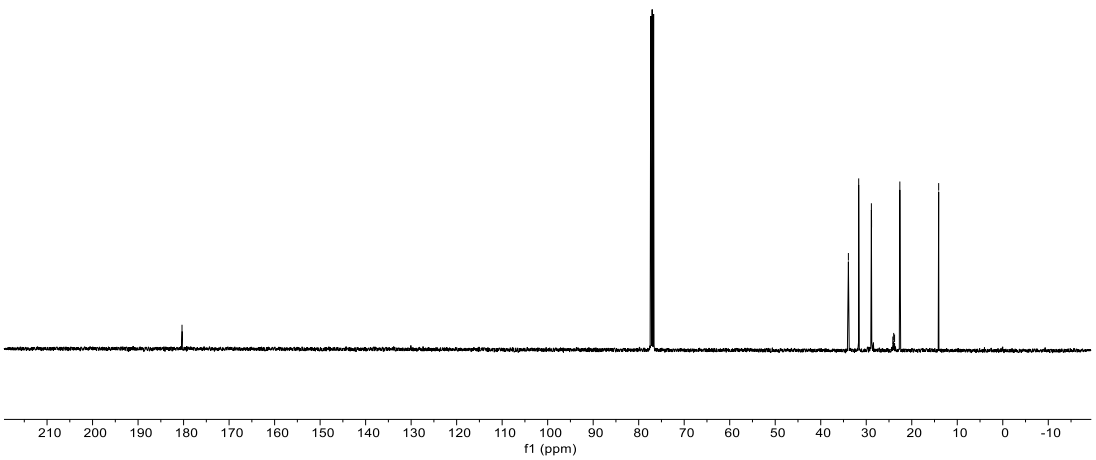
wxc-3-111-1-3



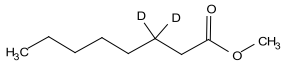


wxc-3-111-2-3

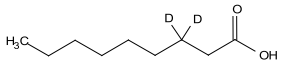


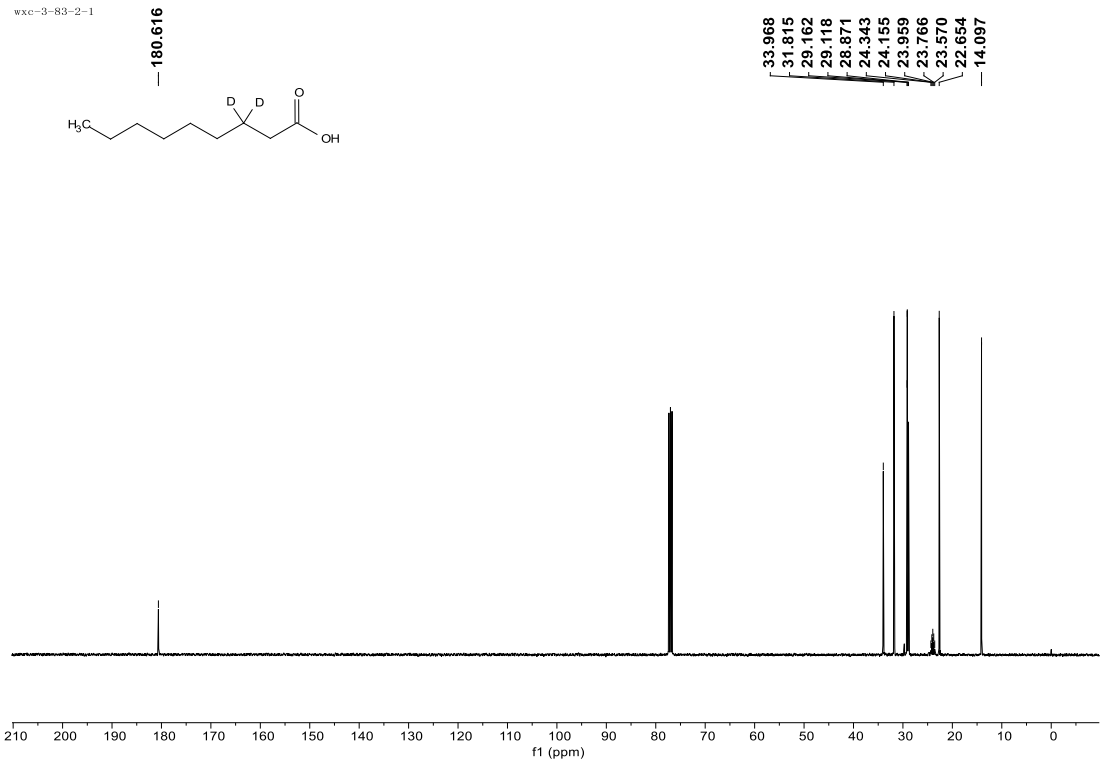


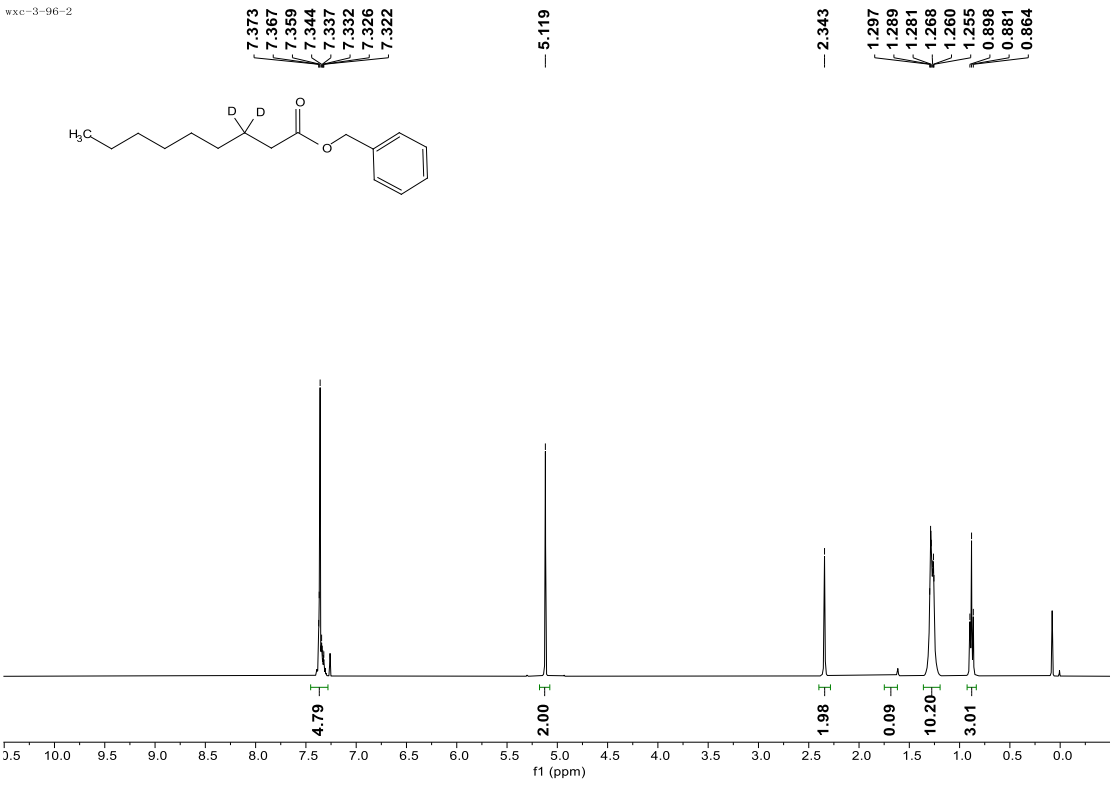
wxc-3-71



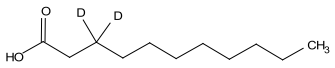
wxc-3-83-2-1



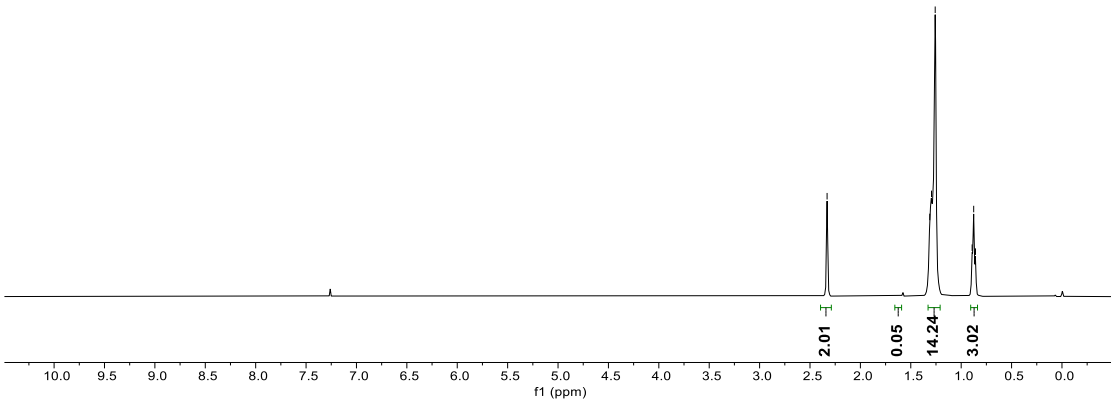

wxc-3-83-2-1
180.616
33.968
31.815
29.162
29.118
28.871
24.343
24.155
23.959
23.766
23.570
22.654
14.097
D
D
O
H3C
OH
f1 (ppm)


wxc-3-96-2
7.373
7.367
7.359
7.344
7.337
7.332
7.326
7.322
5.119
2.343
1.297
1.289
1.281
1.268
1.260
1.255
0.898
0.881
0.864
D
D
O
O
H3C
4.79
2.00
1.98
0.09
10.20
3.01
f1 (ppm)

wxc-3-147



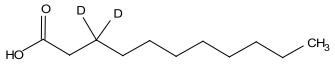
2.330
1.312
1.294
1.258
0.891
0.876
0.858

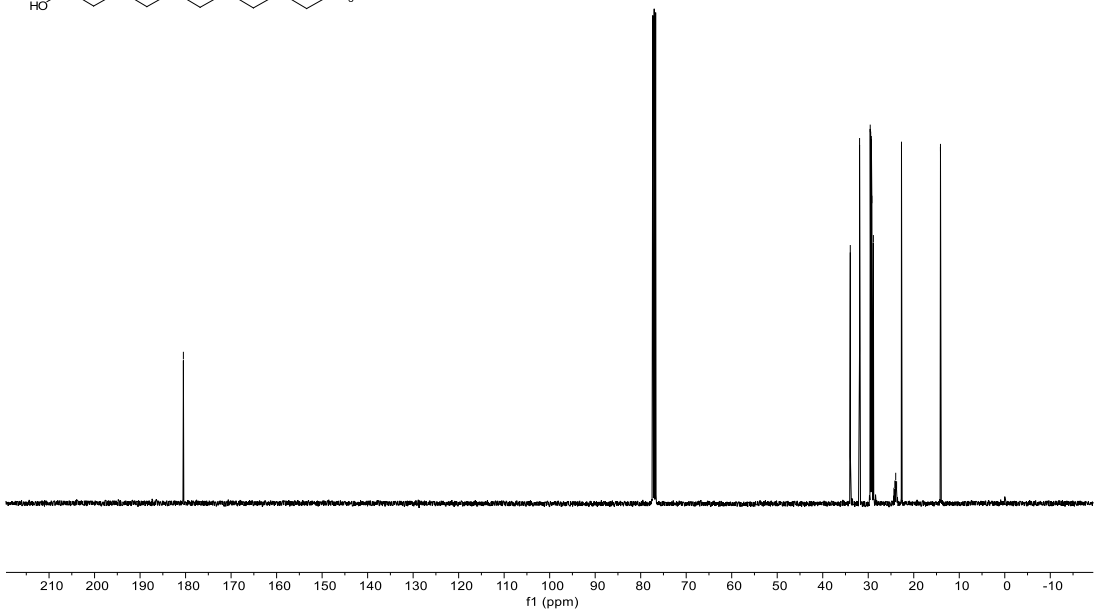


wxc-3-147

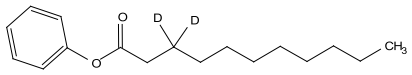
180.481

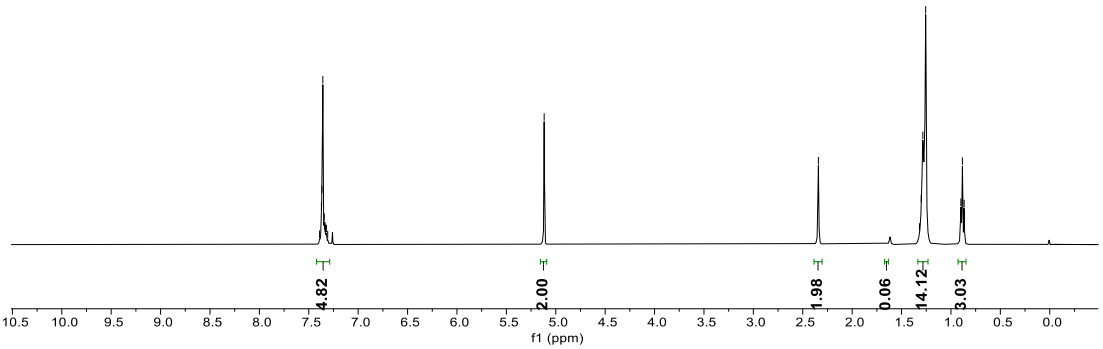
33.945
31.905
29.563
29.457
29.320
29.203
28.871
24.353
24.154
23.964
23.770
22.695
14.128



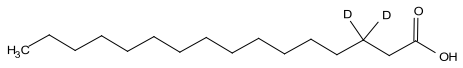


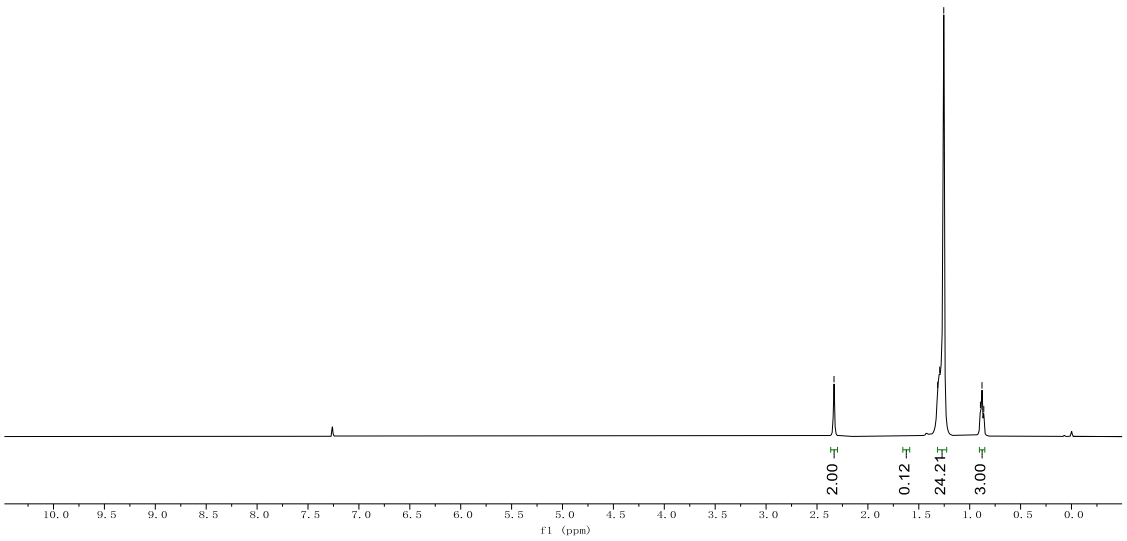
wxc-C11ester

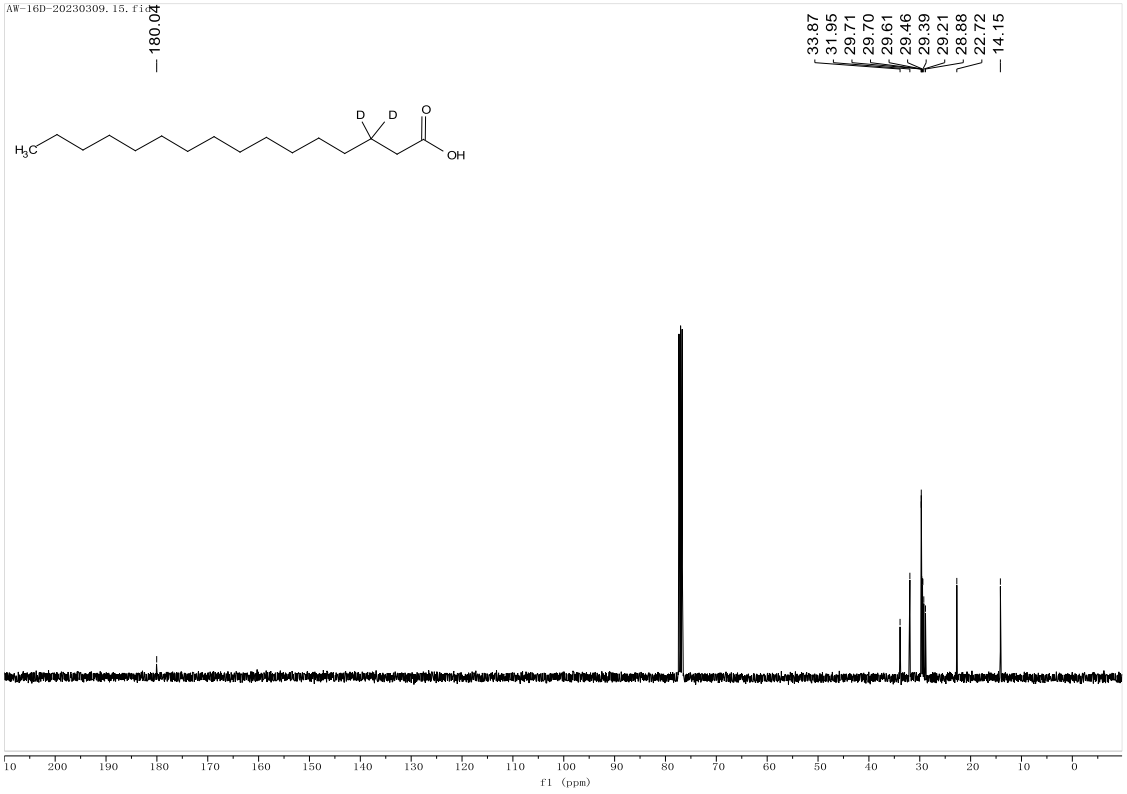


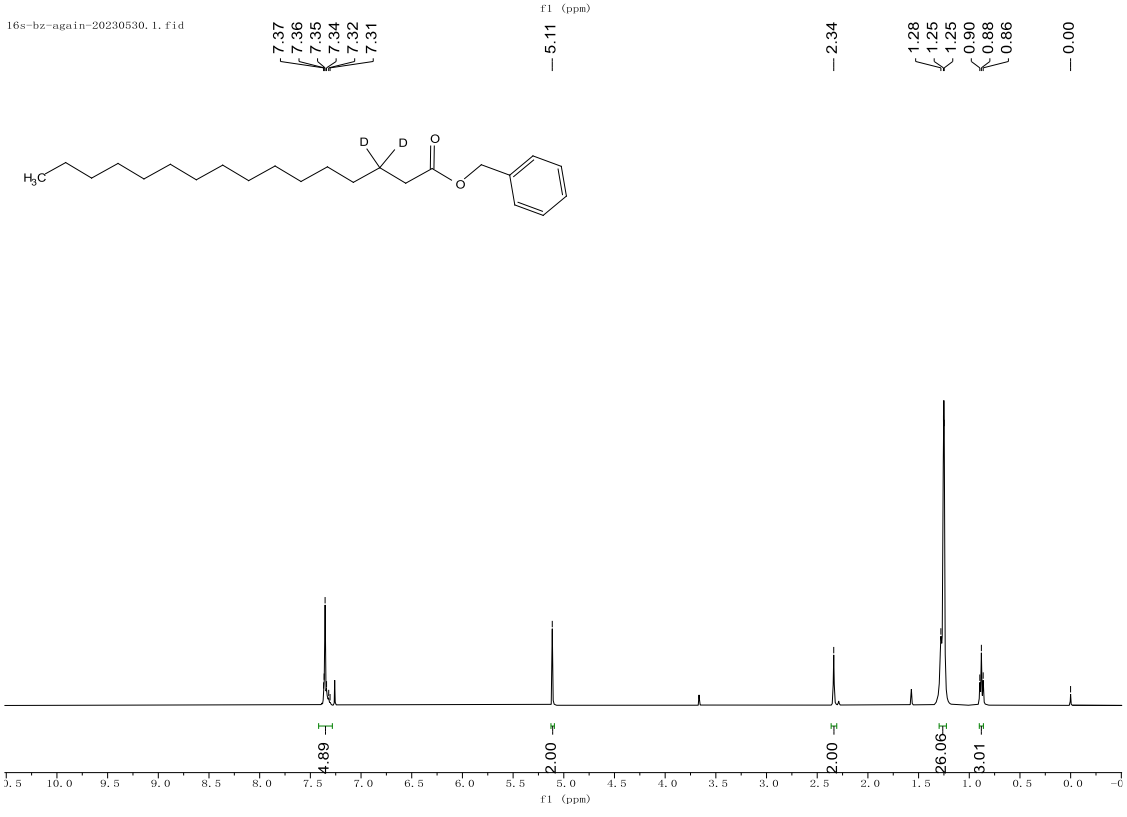


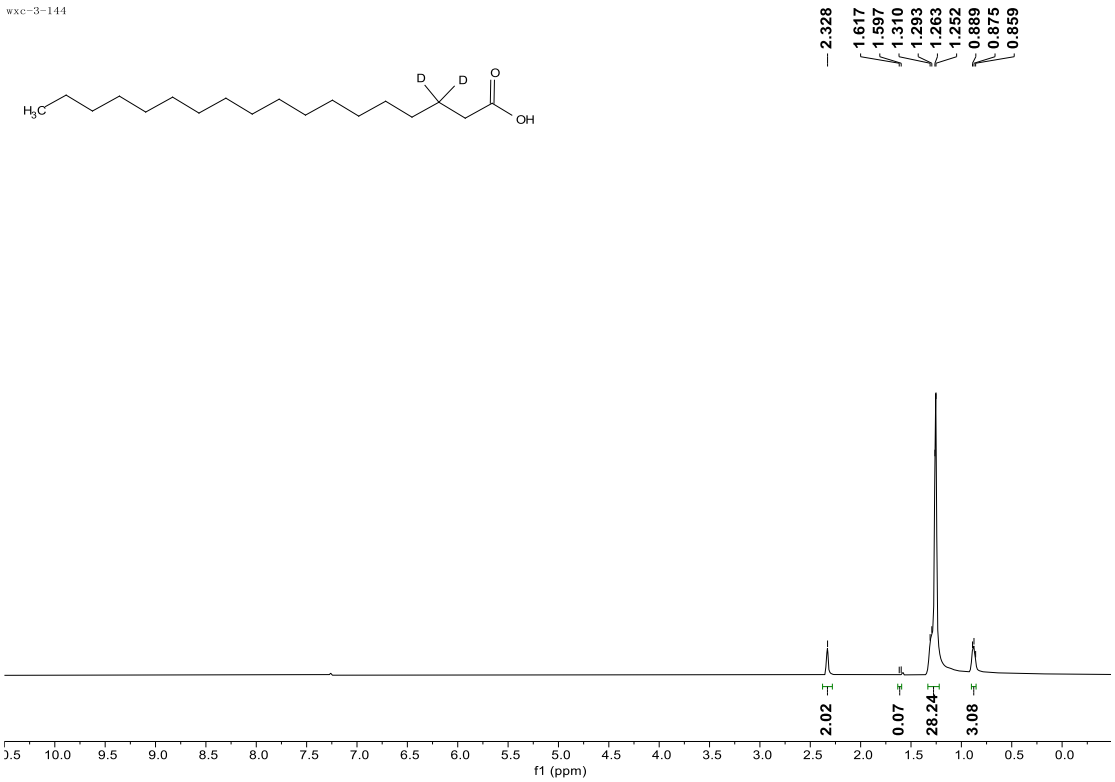
AW-16D-20230309.14.fid

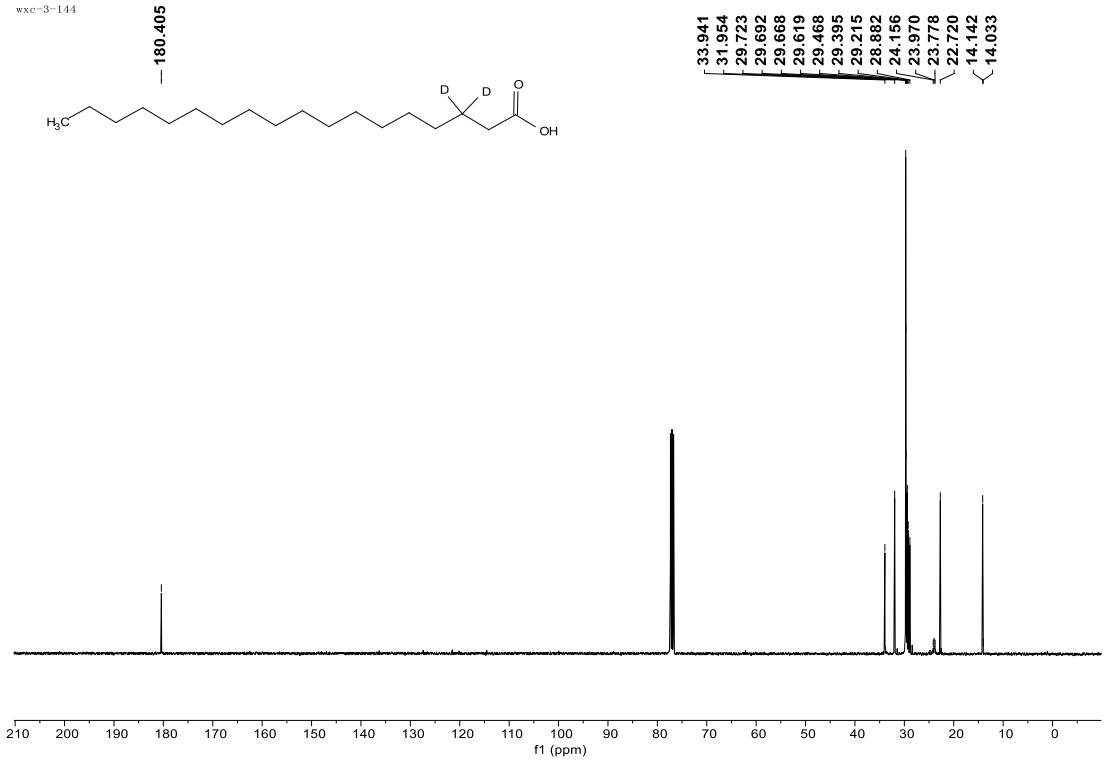


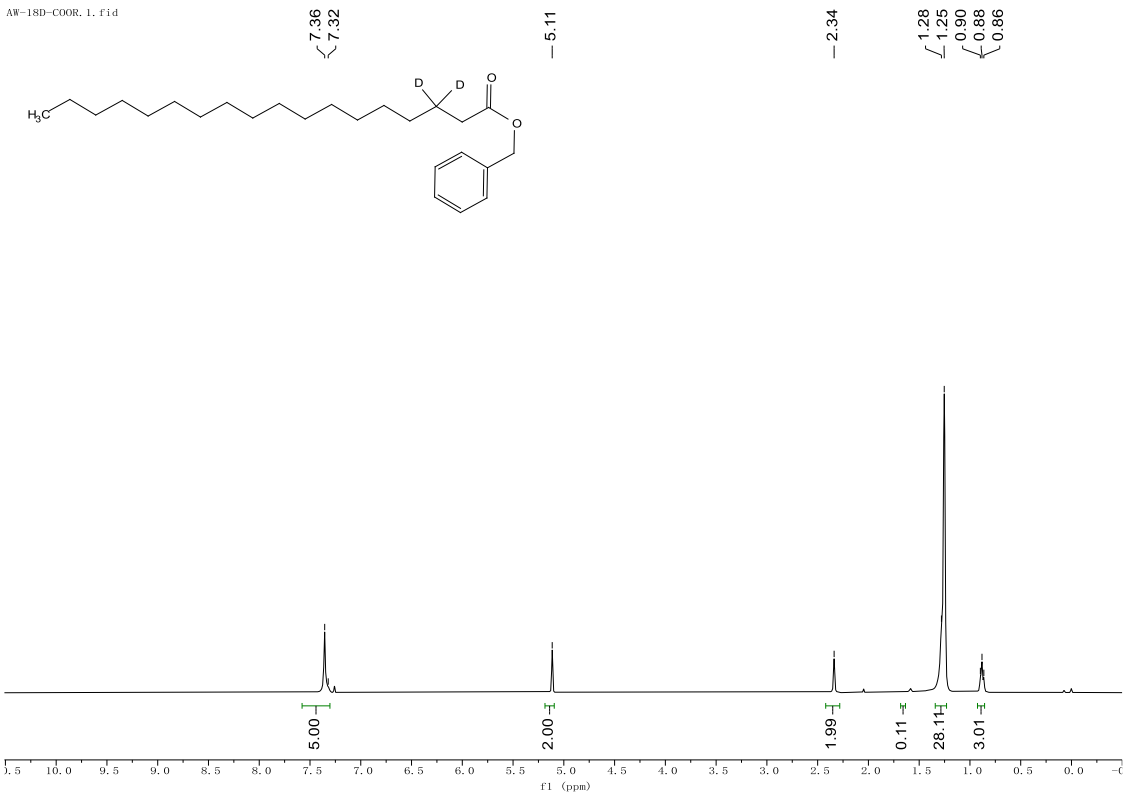


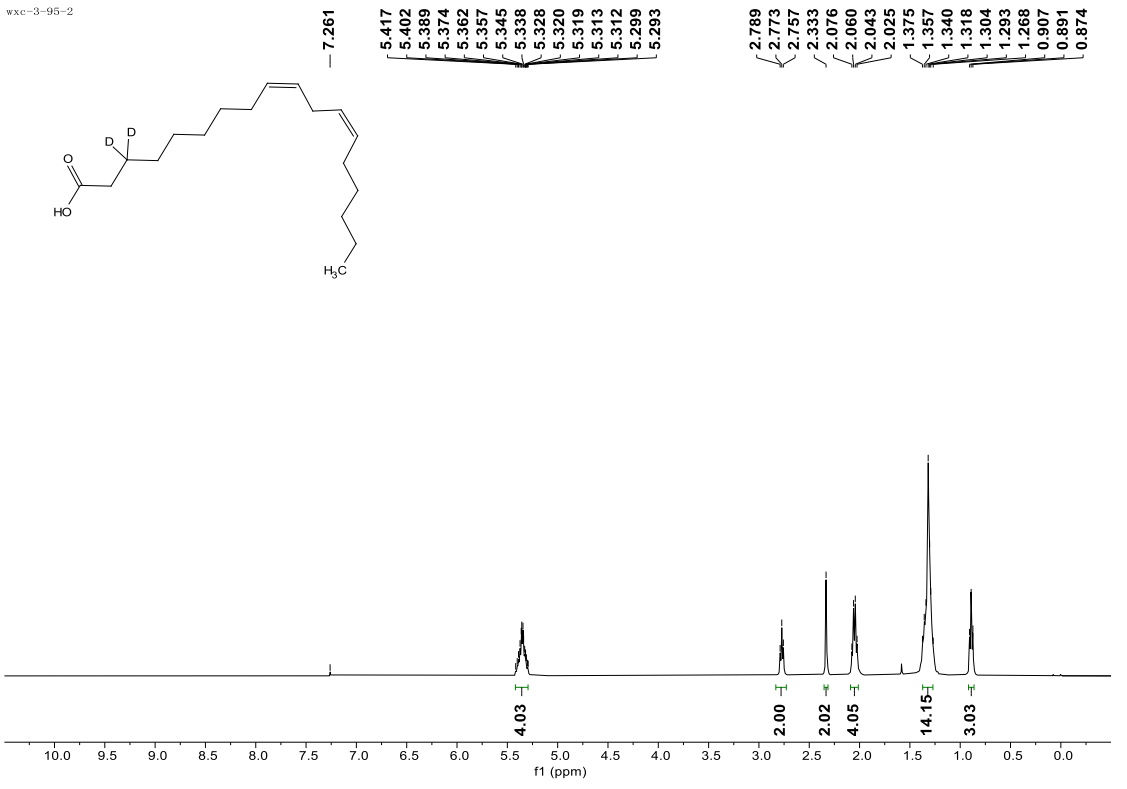

AW-16D-20230309.15.fid
180.04
33.87
31.95
29.71
29.70
29.61
29.46
29.39
29.21
28.88
22.72
14.15
D
D
O
OH
H3C
f1 (ppm)

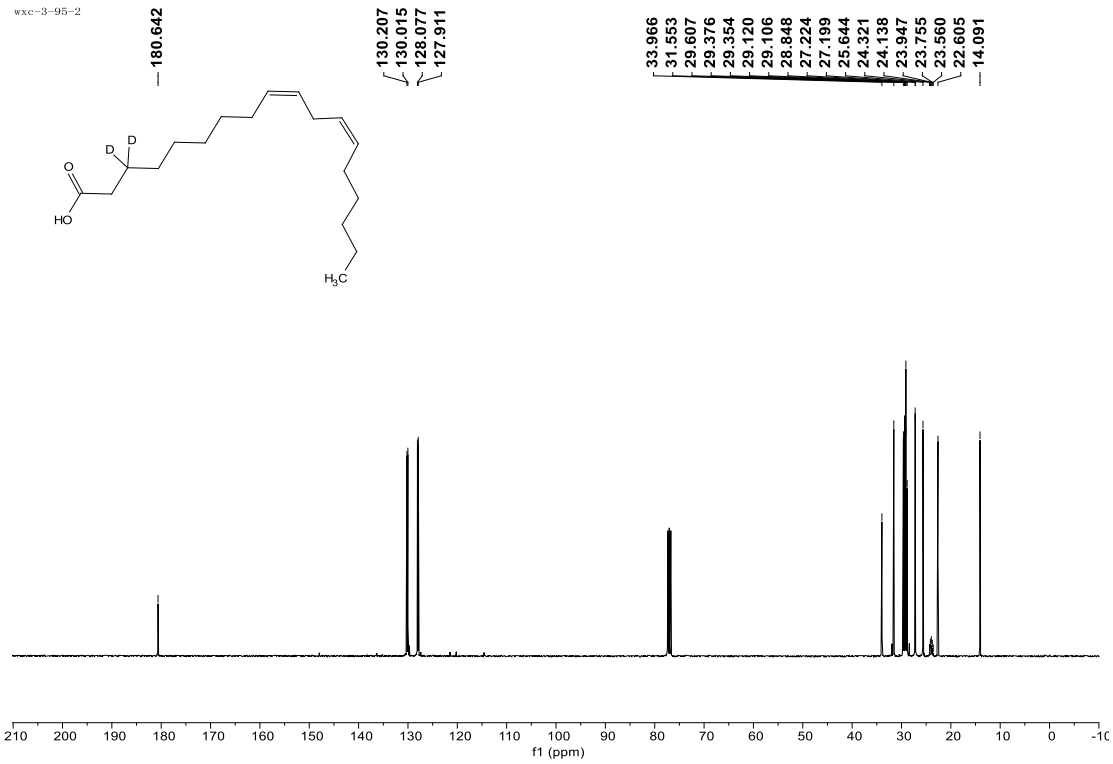

16s-bz-again-20230530.1.fid
7.37
7.36
7.35
7.34
7.32
7.31
5.11
2.34
1.28
1.25
1.25
0.90
0.88
0.86
0.00
D
D
O
O
H3C
4.89
2.00
2.00
26.06
3.01
f1 (ppm)

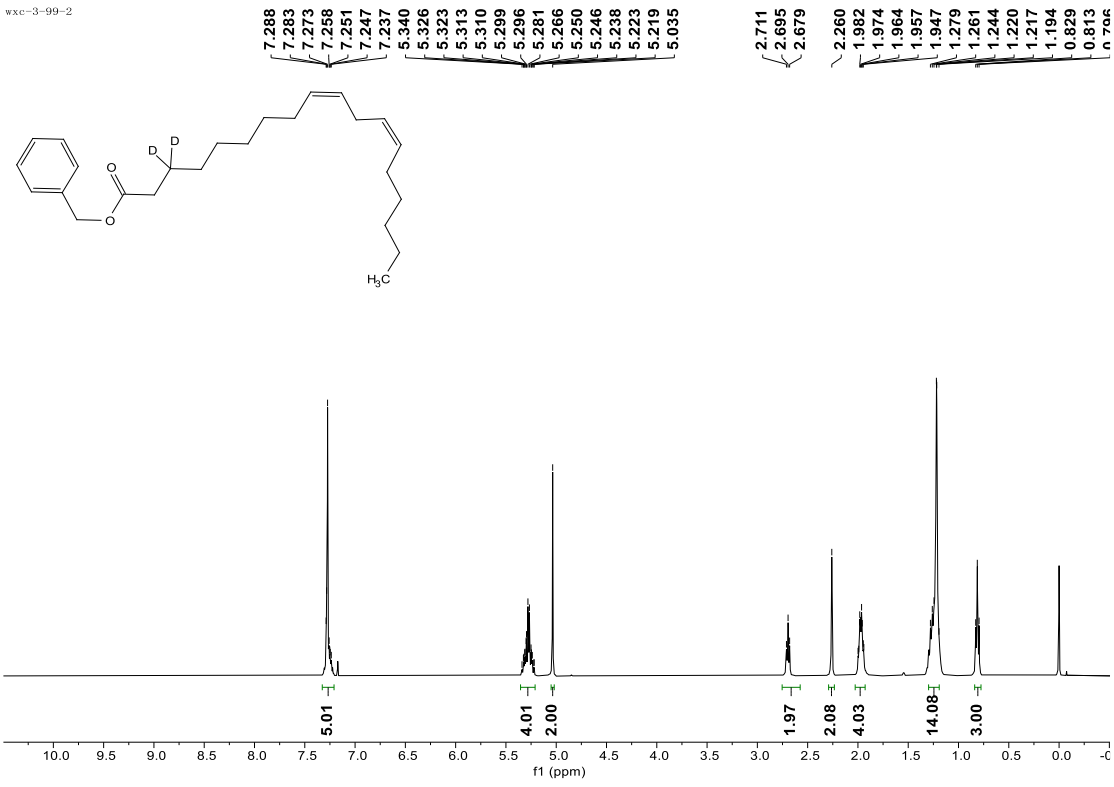

wxc-3-144
2.328
1.617
1.597
1.310
1.293
1.263
1.252
0.889
0.875
0.859
D
D
O
H3C
OH
2.02
0.07
28.24
3.08
f1 (ppm)

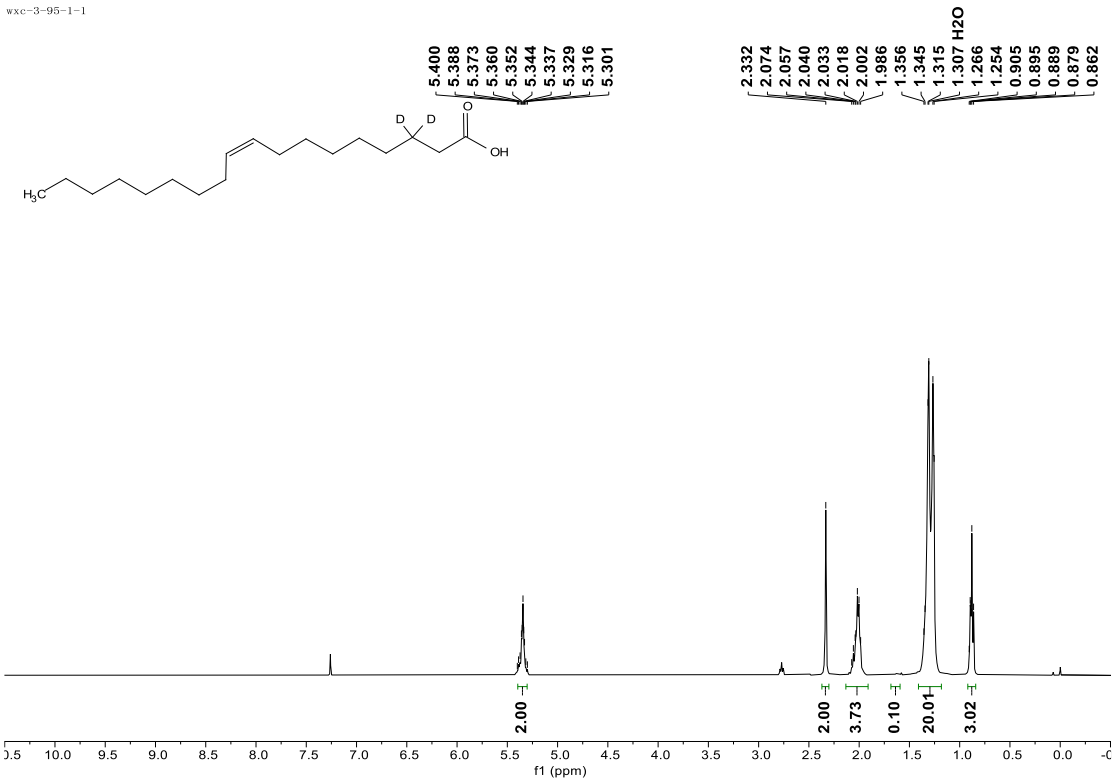

wxc-3-144
180.405
33.941
31.954
29.723
29.692
29.668
29.619
29.468
29.395
29.215
28.882
24.156
23.970
23.778
22.720
14.142
14.033
D
D
O
H3C
OH
f1 (ppm)

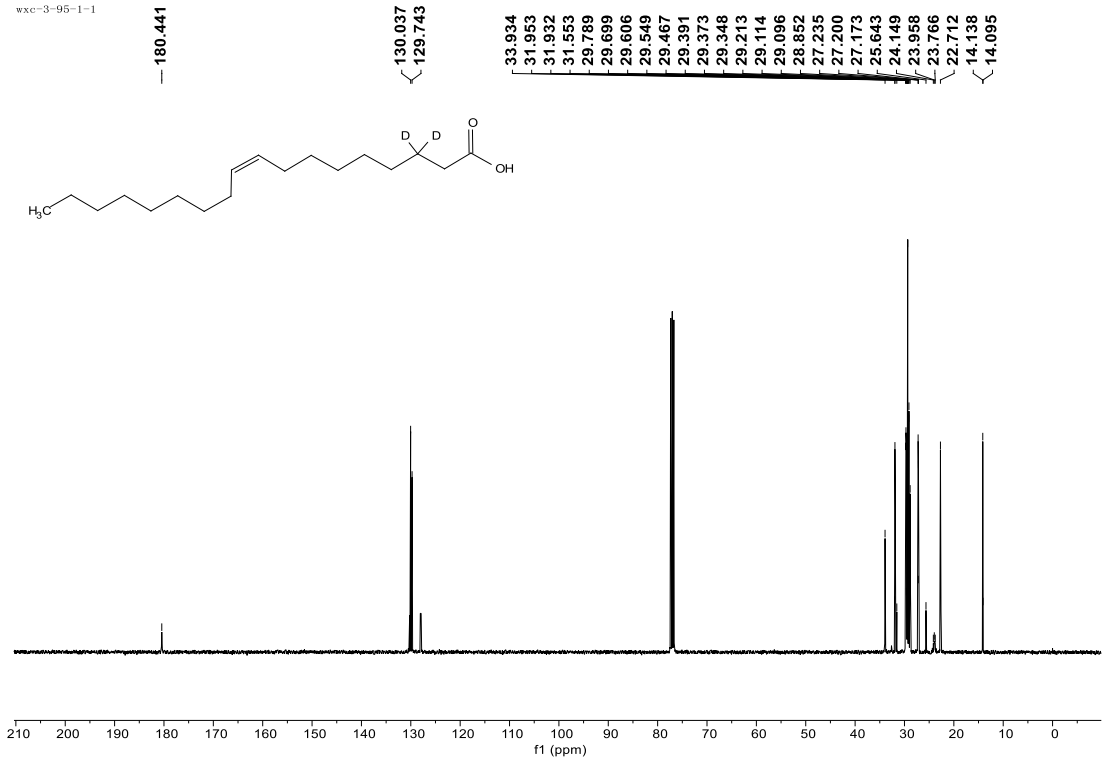

AW-18D-COOR.1.fid
7.36
7.32
5.11
2.34
1.28
1.25
0.90
0.88
0.86
D
D
O
O
H3C
5.00
2.00
1.99
0.11
28.11
3.01
f1 (ppm)

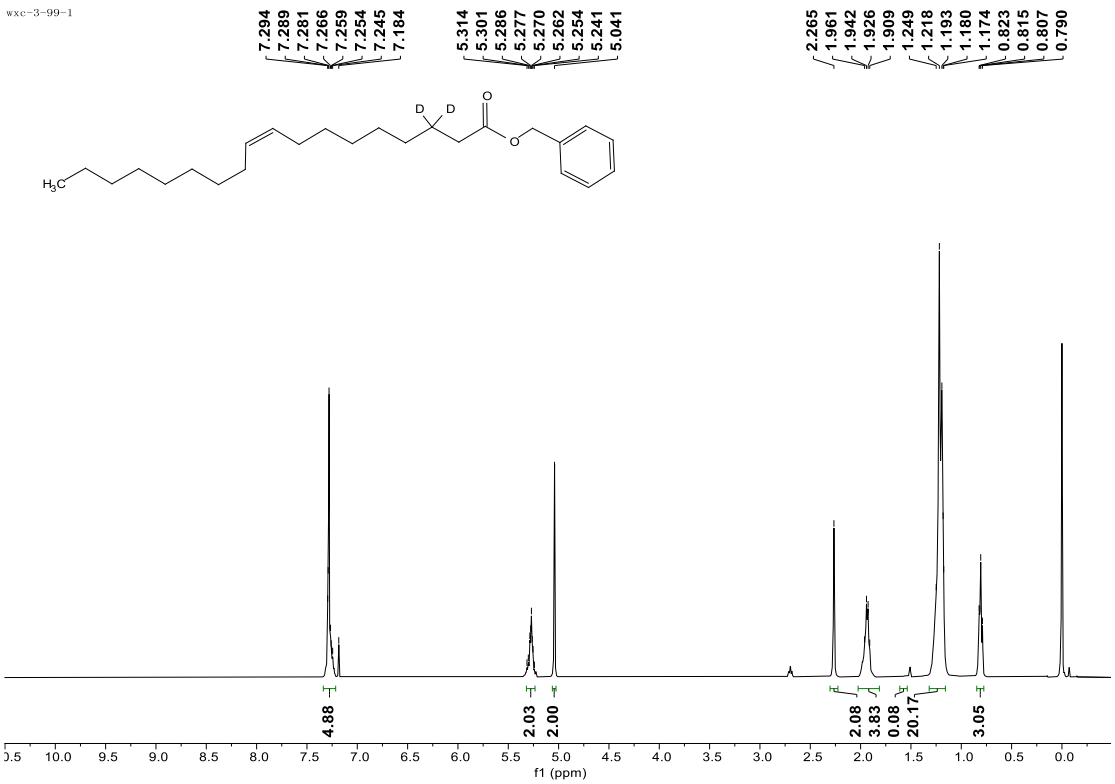

wxc-3-95-2
7.261
5.417
5.402
5.389
5.374
5.362
5.357
5.345
5.338
5.328
5.320
5.319
5.313
5.312
5.299
5.293
2.789
2.773
2.757
2.333
2.076
2.060
2.043
2.025
1.375
1.357
1.340
1.318
1.304
1.293
1.268
0.907
0.891
0.874
D
D
O
HO
H3C
4.03
2.00
2.02
4.05
14.15
3.03
f1 (ppm)

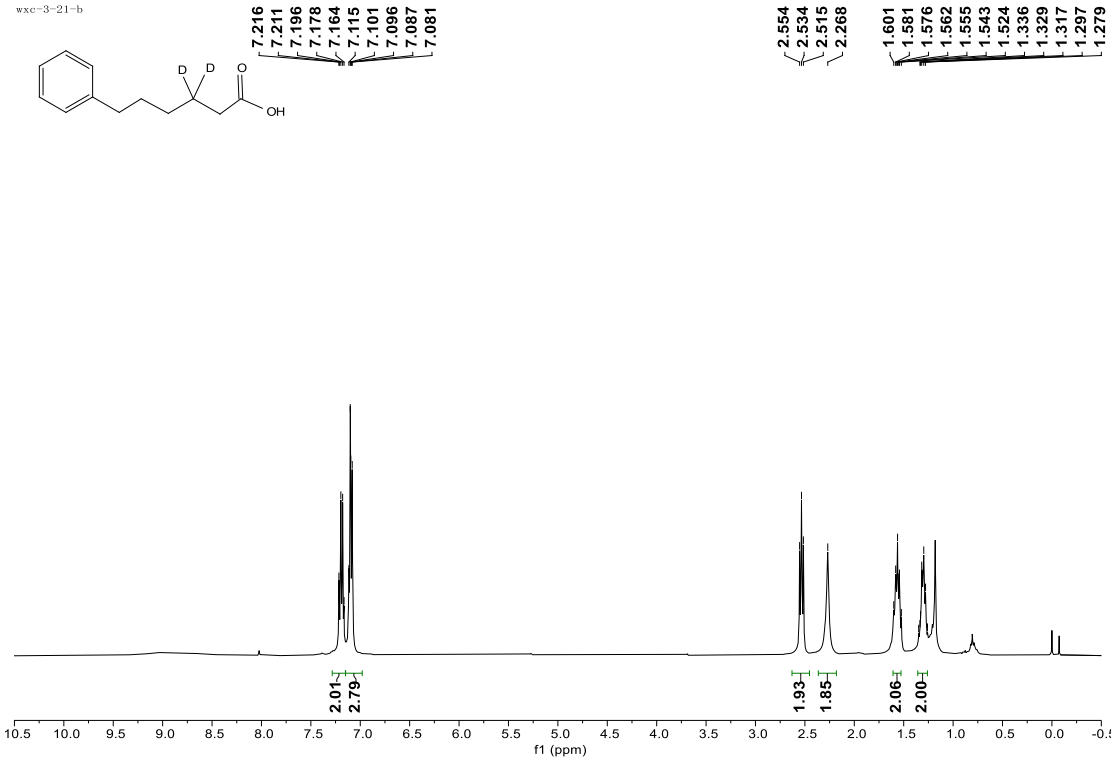

wxc-3-95-2
180.642
130.207
130.015
128.077
127.911
33.966
31.553
29.607
29.376
29.354
29.120
29.106
28.848
27.224
27.199
25.644
24.321
24.138
23.947
23.755
23.560
22.605
14.091
D
D
O
HO
H3C
f1 (ppm)

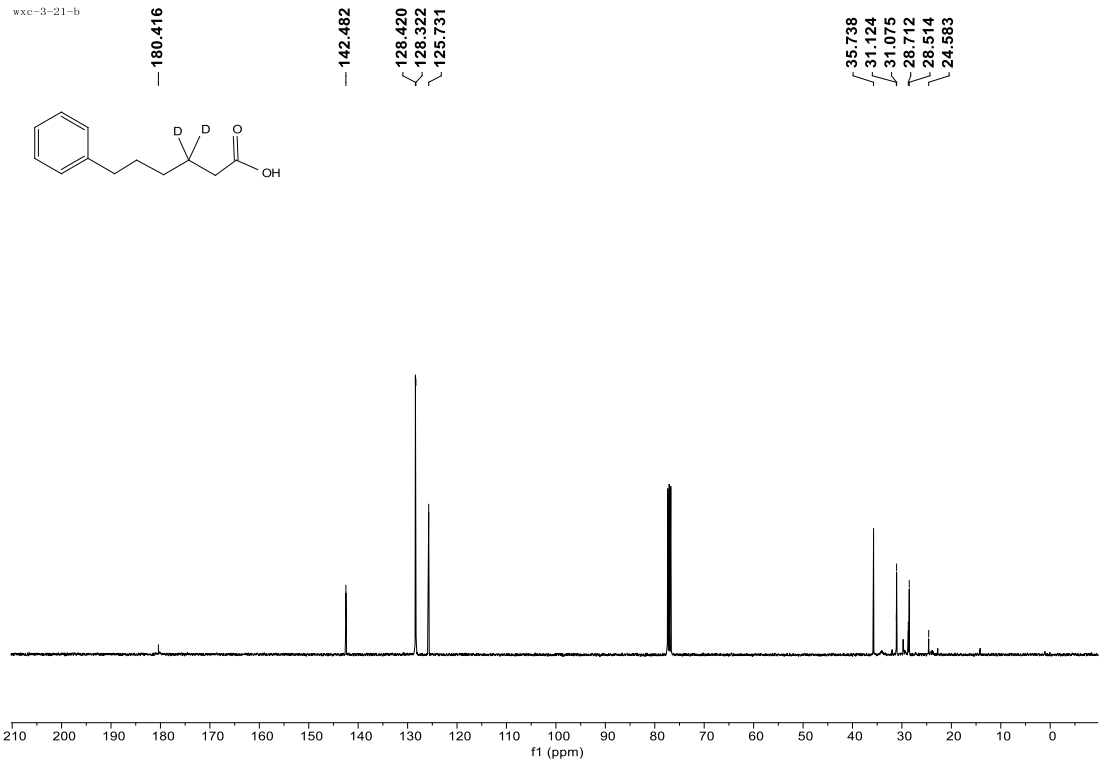

wxc-3-99-2
7.288
7.283
7.273
7.258
7.251
7.247
7.237
5.340
5.326
5.323
5.313
5.310
5.299
5.296
5.281
5.266
5.250
5.246
5.238
5.223
5.219
5.035
2.711
2.695
2.679
2.260
1.982
1.974
1.964
1.957
1.947
1.279
1.261
1.244
1.220
1.217
1.194
0.829
0.813
D
D
O
O
H3C
5.01
4.01
2.00
1.97
2.08
4.03
14.08
3.00
f1 (ppm)

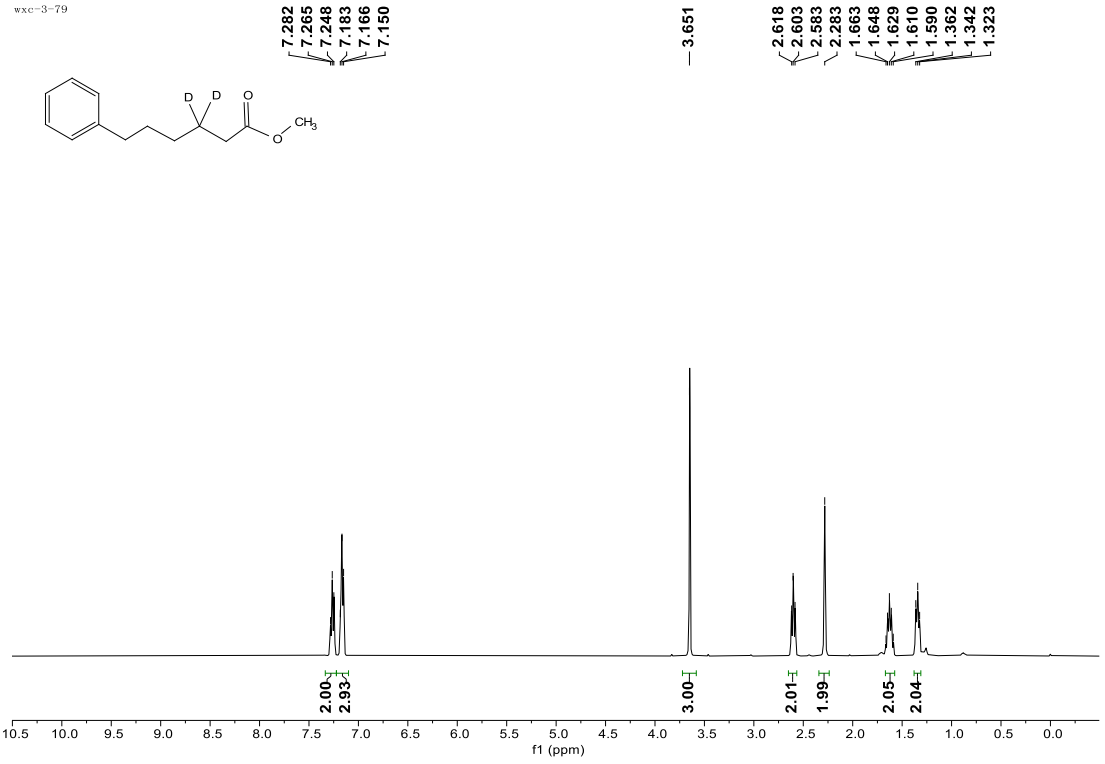

wxc-3-95-1-1
5.400
5.388
5.373
5.360
5.352
5.344
5.337
5.329
5.316
5.301
2.332
2.074
2.057
2.040
2.033
2.018
2.002
1.986
1.356
1.345
1.315
1.307 H2O
1.266
1.254
0.905
0.895
0.889
0.879
0.862
D
D
O
OH
H3C
2.00
2.00
3.73
0.10
20.01
3.02
f1 (ppm)

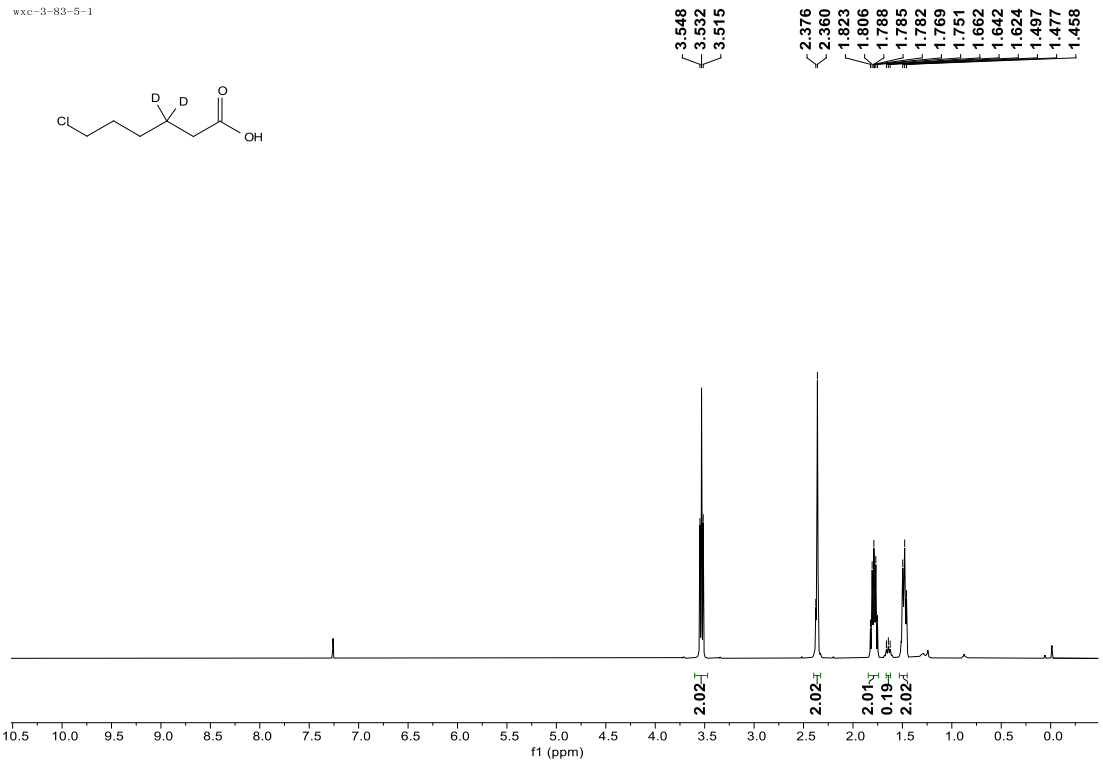

wxc-3-95-1-1
180.441
130.037
129.743
33.934
31.953
31.932
31.553
29.789
29.699
29.606
29.549
29.467
29.391
29.373
29.348
29.213
29.114
29.096
28.852
27.235
27.200
27.173
25.643
24.149
23.958
23.766
22.712
14.138
14.095
D
D
O
OH
H3C
f1 (ppm)

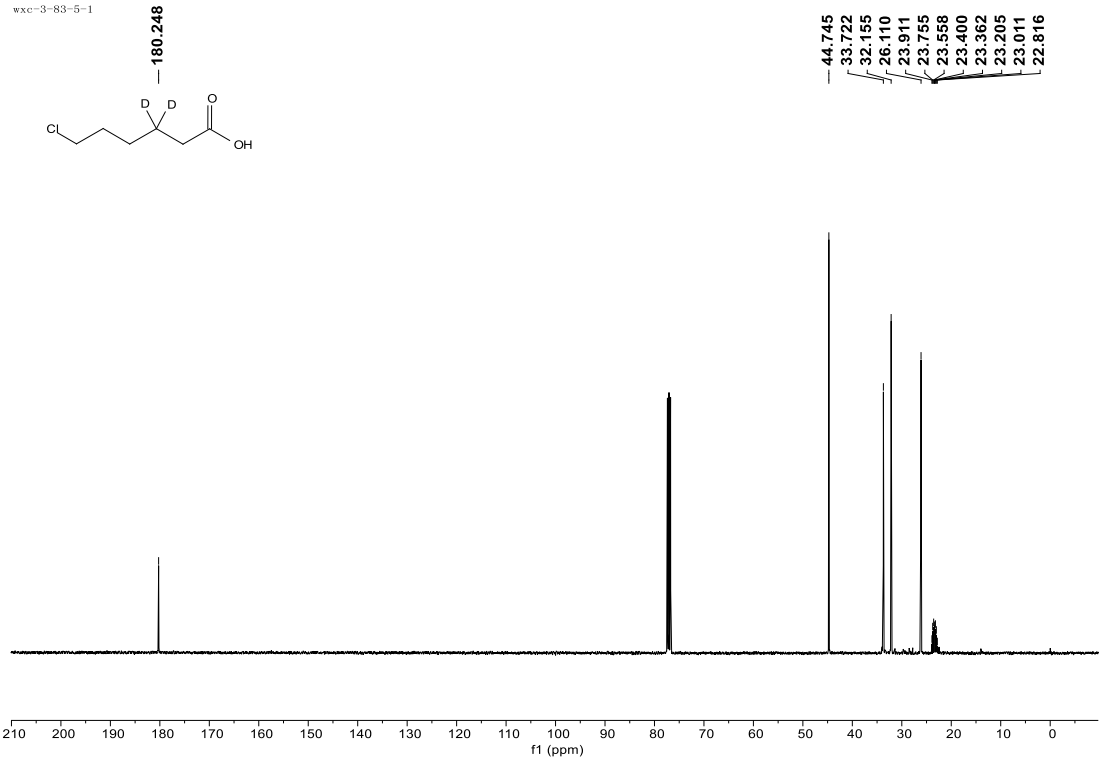

wxc-3-99-1
7.294
7.289
7.281
7.266
7.259
7.254
7.245
7.184
5.314
5.301
5.286
5.277
5.270
5.262
5.254
5.241
5.041
2.265
1.961
1.942
1.926
1.909
1.249
1.218
1.193
1.180
1.174
0.823
0.815
0.807
0.790
D
D
O
O
H3C
4.88
2.03
2.00
2.08
3.83
0.08
20.17
3.05
f1 (ppm)

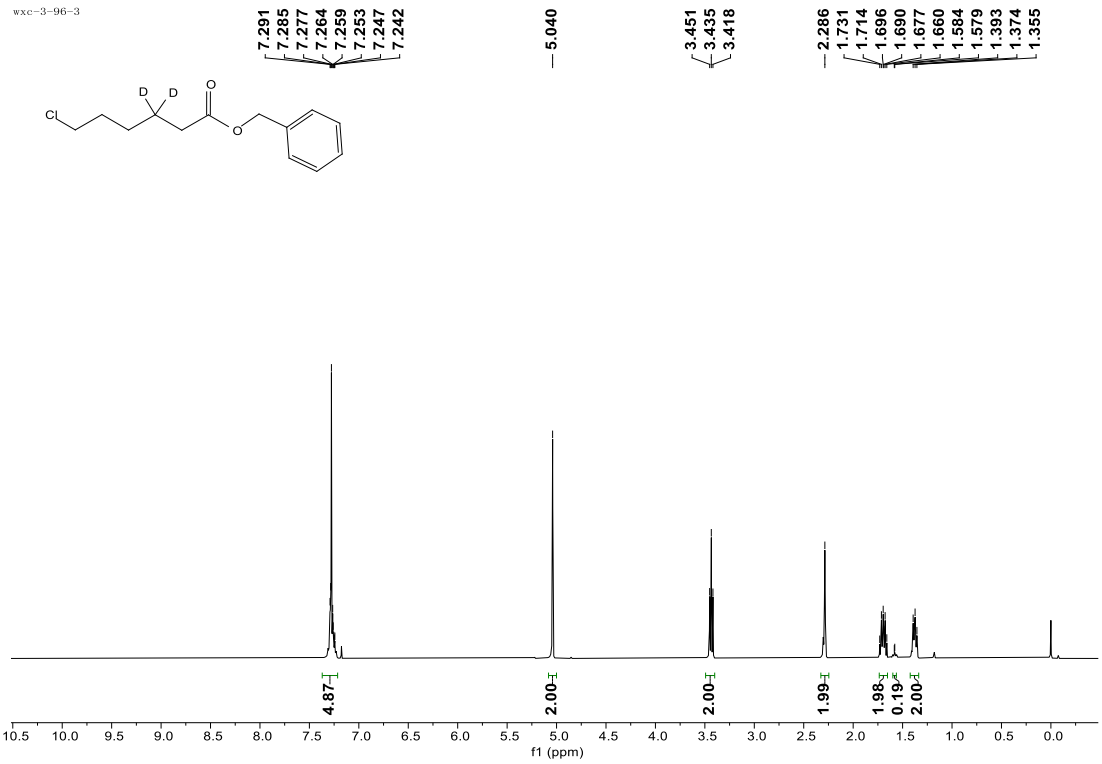

wxc-3-21-b
7.216
7.211
7.196
7.178
7.164
7.115
7.101
7.096
7.087
7.081
2.554
2.534
2.515
2.268
1.601
1.581
1.576
1.562
1.555
1.543
1.524
1.336
1.329
1.317
1.297
1.279
D
D
O
OH
2.01
2.79
1.93
1.85
2.06
2.00
f1 (ppm)

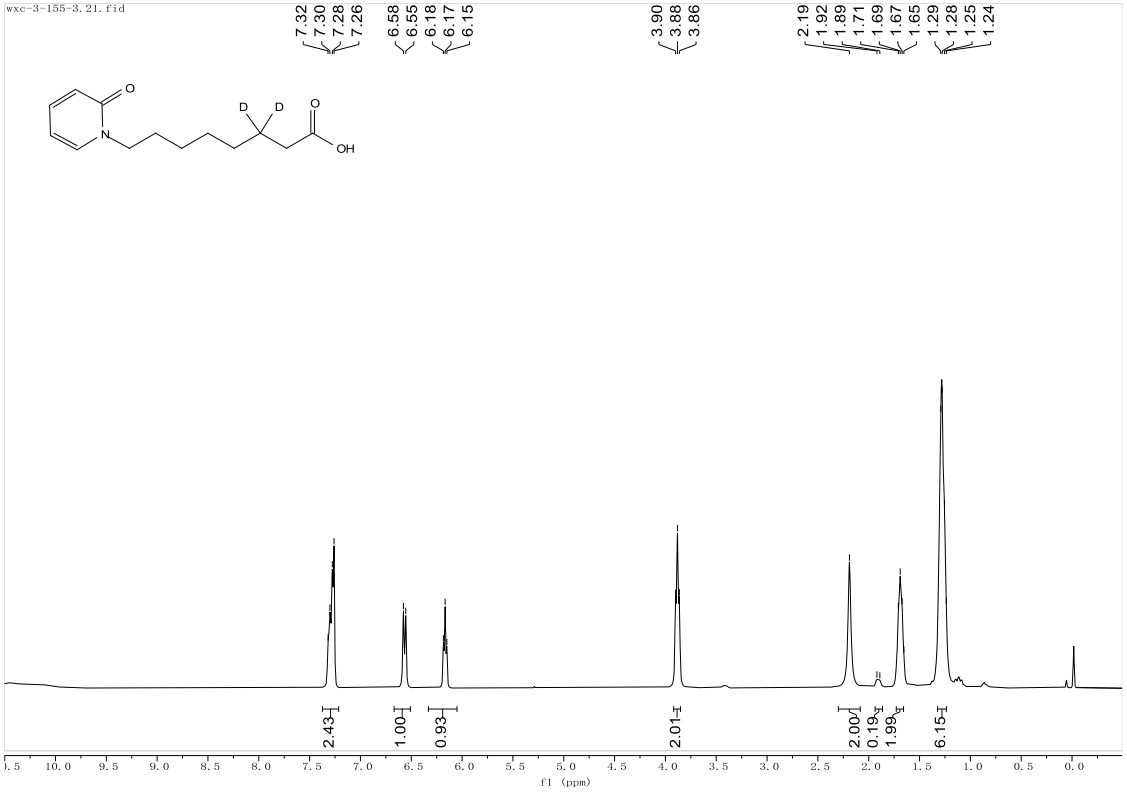

wxc-3-21-b
180.416
142.482
128.420
128.322
125.731
35.738
31.124
31.075
28.712
28.514
24.583
D
D
O
OH
f1 (ppm)


wxc-3-79
7.282
7.265
7.248
7.183
7.166
7.150
3.651
2.618
2.603
2.583
2.283
1.663
1.648
1.629
1.610
1.590
1.362
1.342
1.323
D
D
O
O
CH3
2.00
2.93
3.00
2.01
1.99
2.05
2.04
f1 (ppm)

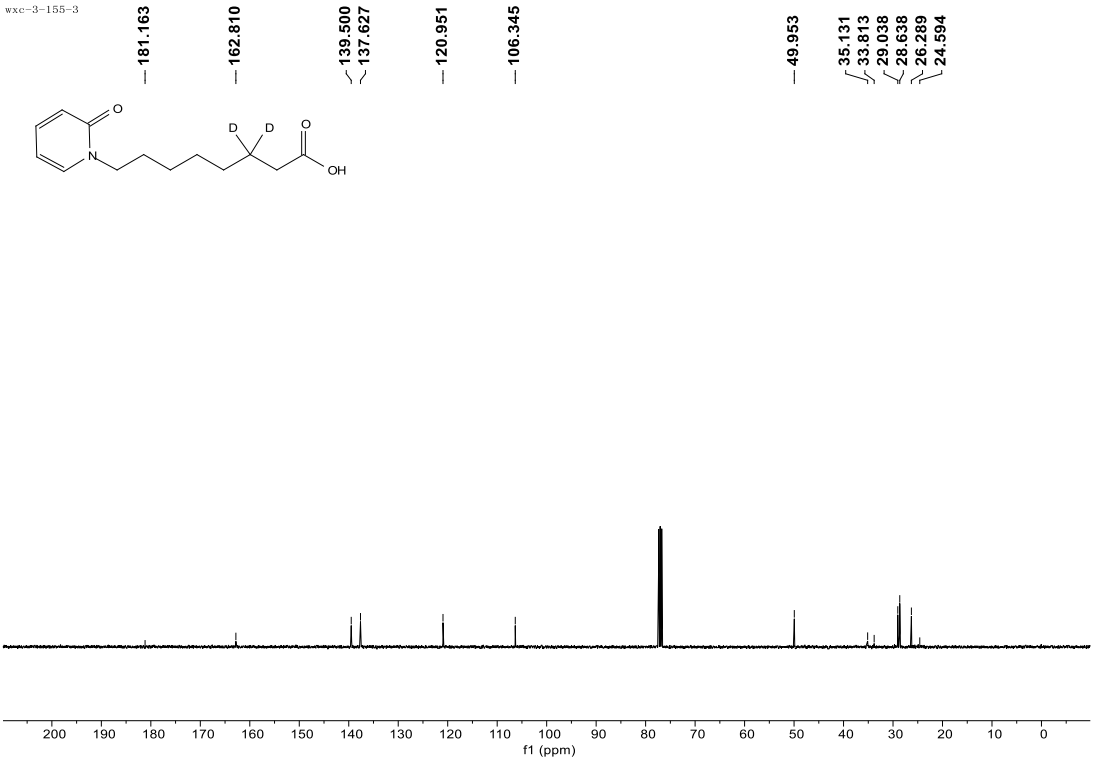

wxc-3-83-5-1
3.548
3.532
3.515
2.376
2.360
1.823
1.806
1.788
1.785
1.782
1.769
1.751
1.662
1.642
1.624
1.497
1.477
1.458
D
D
O
Cl
OH
2.02
2.02
2.01
0.19
2.02
f1 (ppm)


wxc-3-83-5-1
180.248
44.745
33.722
32.155
26.110
23.911
23.755
23.558
23.400
23.362
23.205
23.011
22.816
D
D
O
Cl
OH
f1 (ppm)

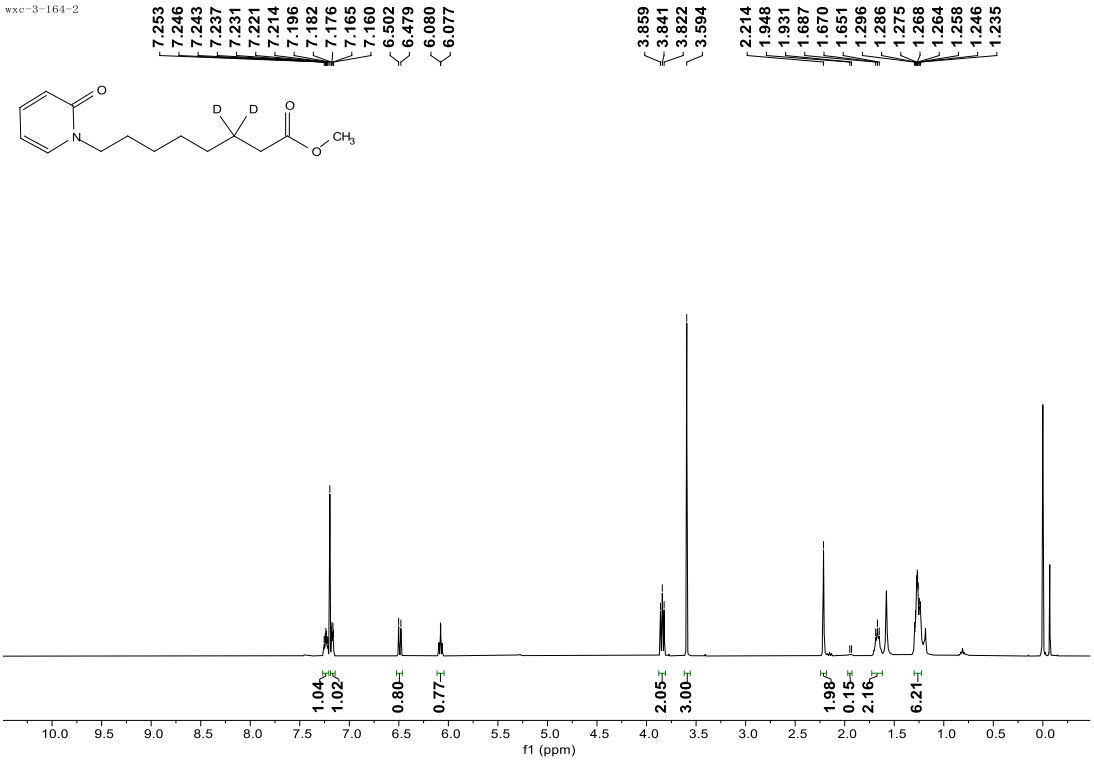

wxc-3-96-3
7.291
7.285
7.277
7.264
7.259
7.253
7.247
7.242
5.040
3.451
3.435
3.418
2.286
1.731
1.714
1.696
1.690
1.677
1.660
1.584
1.579
1.393
1.374
1.355
D
D
O
Cl
O
4.87
2.00
2.00
1.99
1.98
0.19
2.00
f1 (ppm)

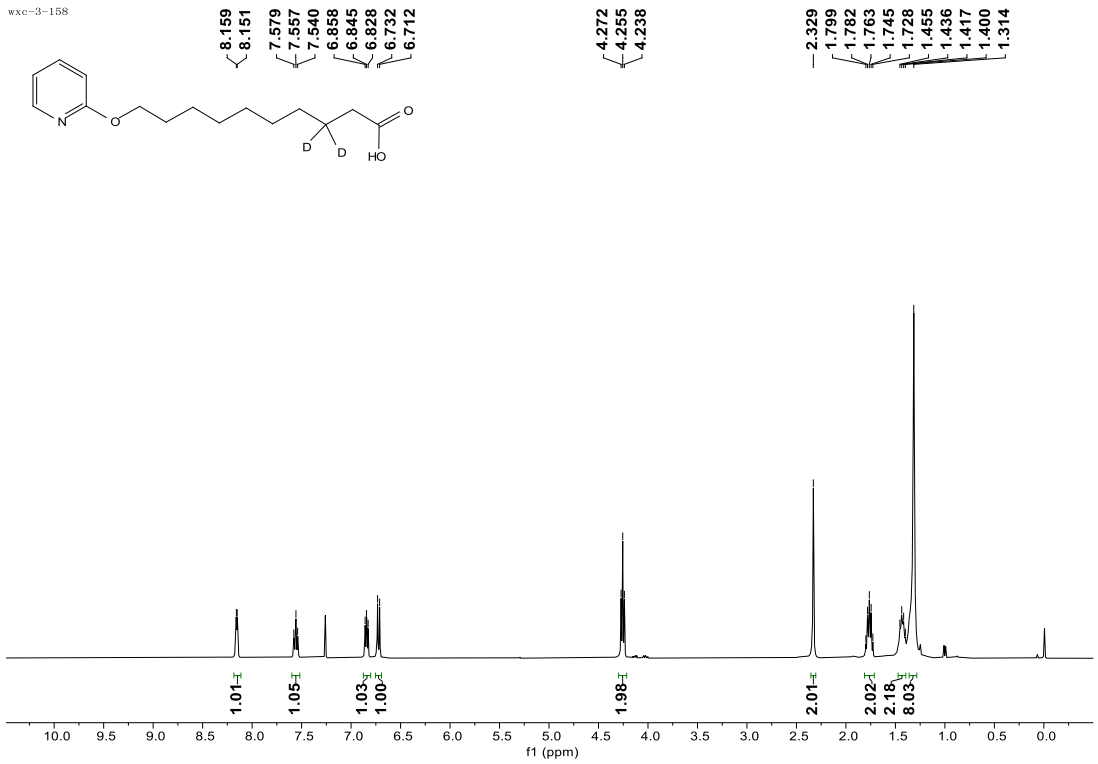

wxc-3-155-3.21.fid
7.32
7.30
7.28
7.26
6.58
6.55
6.18
6.17
6.15
3.90
3.88
3.86
2.19
1.92
1.89
1.71
1.69
1.67
1.65
1.29
1.28
1.25
1.24
O
N
D
D
O
OH
2.43
1.00
0.93
2.01
2.00
0.19
1.99
6.15
f1 (ppm)

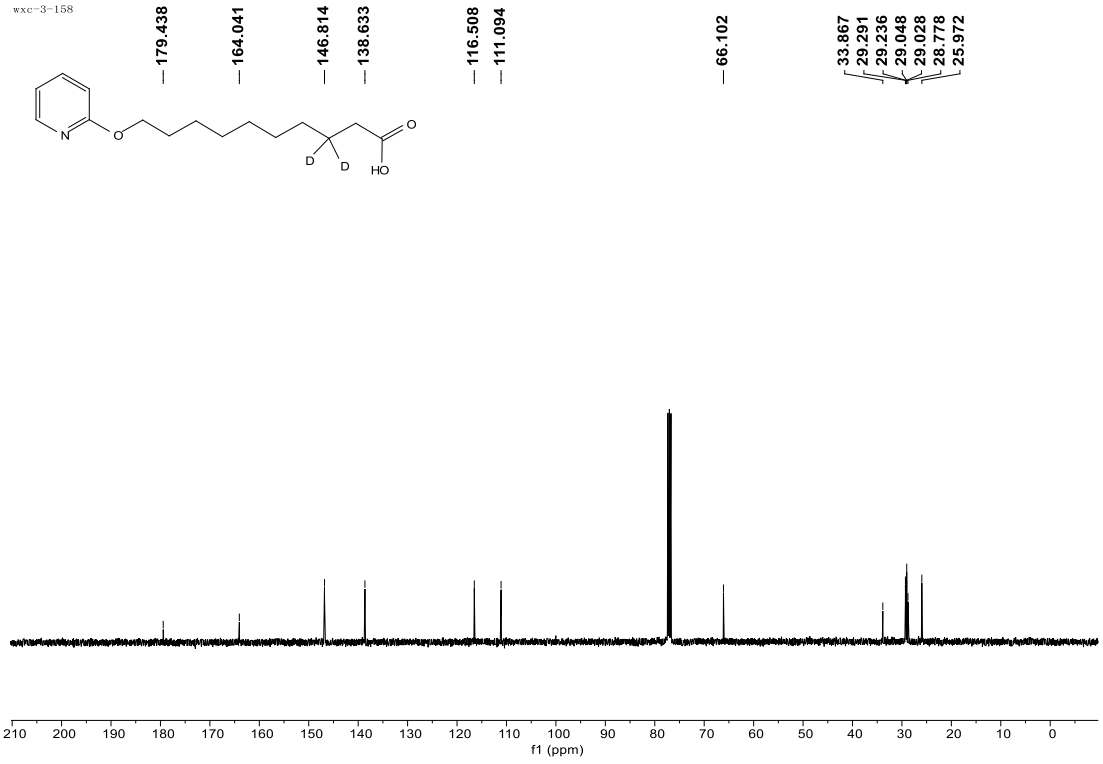
wxc-3-155-3

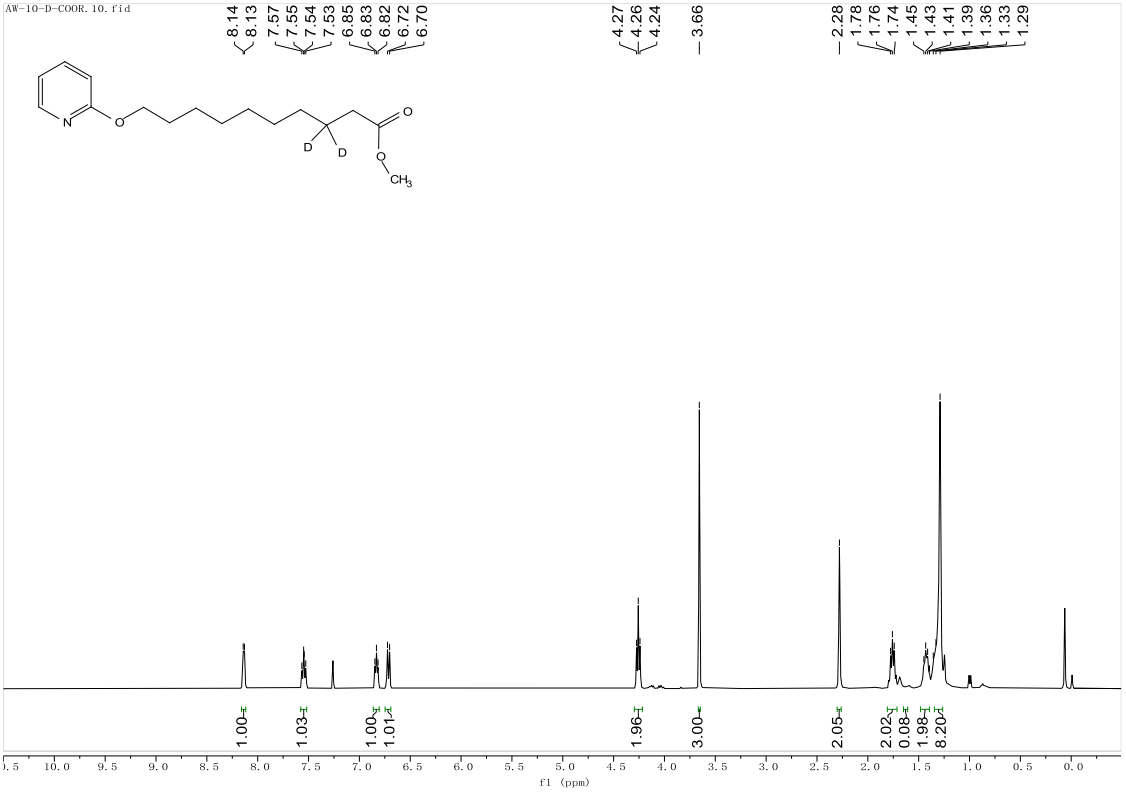


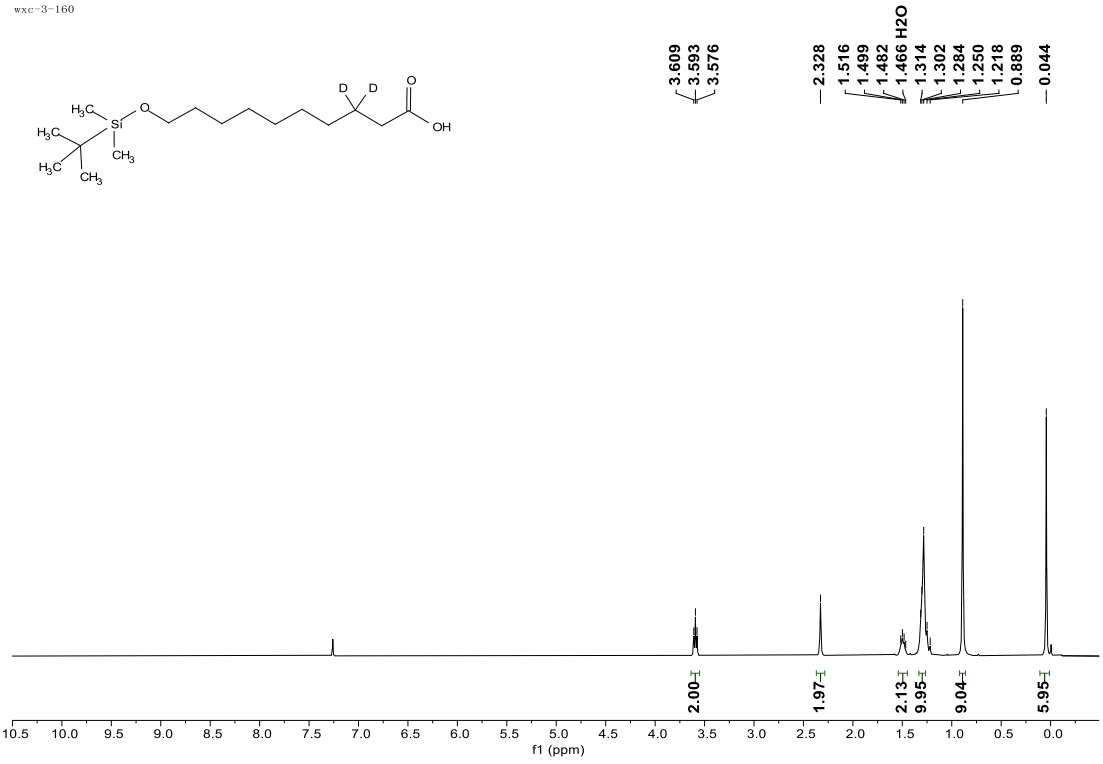
wxc-3-164-2

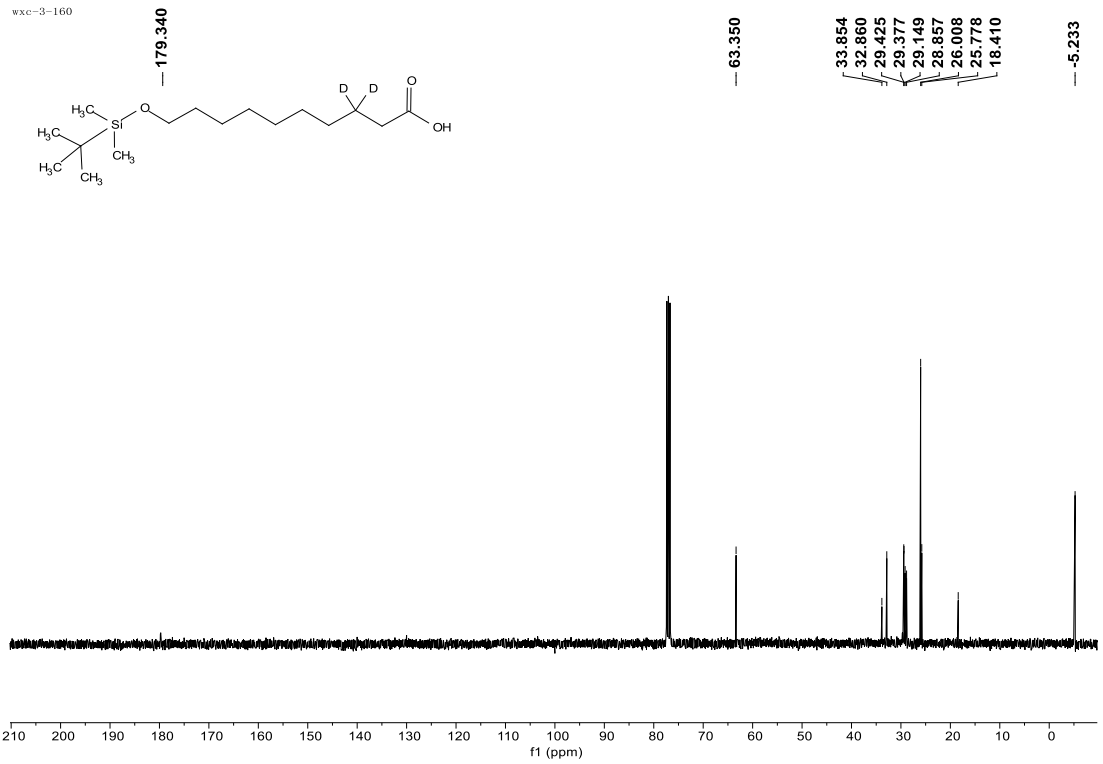


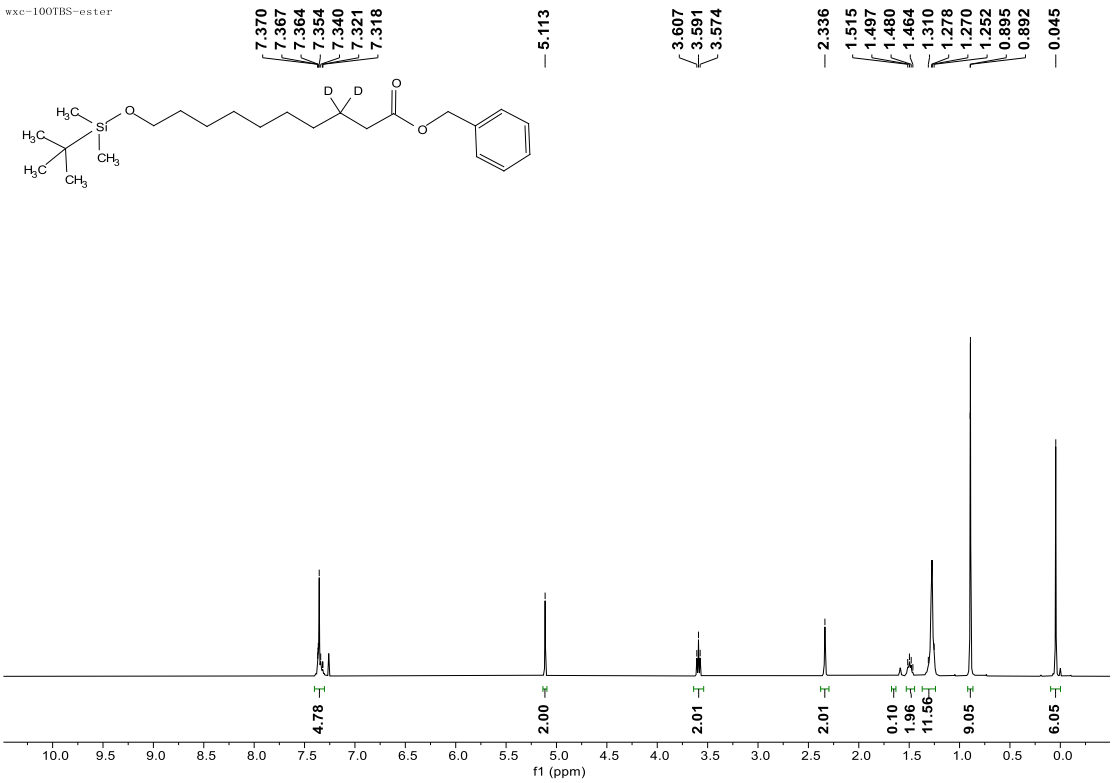

wxc-3-158
8.159
8.151
7.579
7.557
7.540
6.858
6.845
6.828
6.732
6.712
4.272
4.255
4.238
2.329
1.799
1.782
1.763
1.745
1.728
1.455
1.436
1.417
1.400
1.314
N
O
D
D
O
HO
1.01
1.05
1.03
1.00
1.98
2.01
2.02
2.18
8.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


wxc-3-158
179.438
164.041
146.814
138.633
116.508
111.094
66.102
33.867
29.291
29.236
29.048
29.028
28.778
25.972
N
O
D
D
O
HO
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

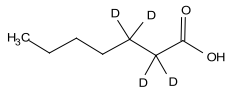

AW-1O-D-COOR.1O.fid
8.14
8.13
7.57
7.55
7.54
7.53
6.85
6.83
6.82
6.72
6.70
4.27
4.26
4.24
3.66
2.28
1.78
1.76
1.74
1.45
1.43
1.41
1.39
1.36
1.33
1.29
N
O
D
D
O
O
CH3
1.00
1.03
1.00
1.01
1.96
3.00
2.05
2.02
0.08
1.98
8.20
f1 (ppm)

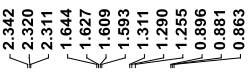

wxc-3-160
3.609
3.593
3.576
2.328
1.516
1.499
1.482
1.466 H2O
1.314
1.302
1.284
1.250
1.218
0.889
0.044
D
D
O
OH
H3C
Si
CH3
H3C
CH3
H3C
2.00
1.97
2.13
9.95
9.04
5.95
f1 (ppm)

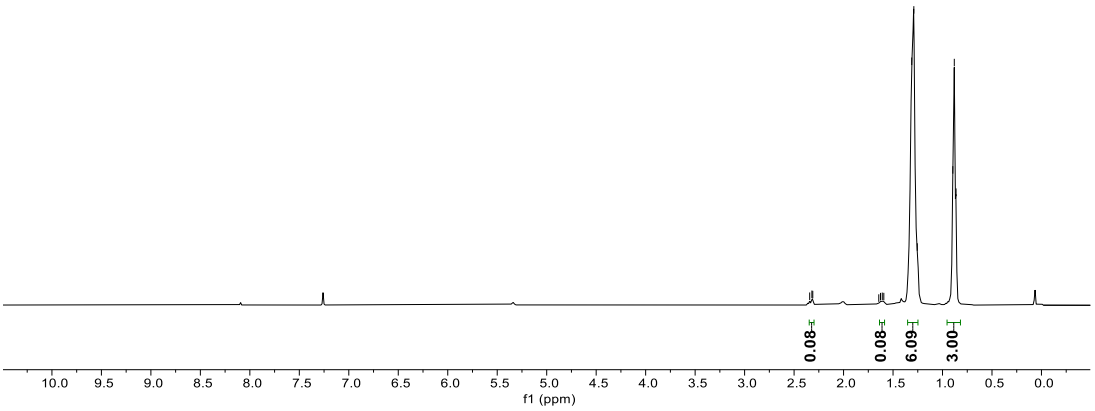

wxc-3-160
179.340
63.350
33.854
32.860
29.425
29.377
29.149
28.857
26.008
25.778
18.410
-5.233
D
D
O
OH
Si
f1 (ppm)


wxc-100TBS-ester
7.370
7.367
7.364
7.354
7.340
7.321
7.318
5.113
3.607
3.591
3.574
2.336
1.515
1.497
1.480
1.464
1.310
1.278
1.270
1.252
0.895
0.892
0.045
D
D
O
Si
4.78
2.00
2.01
2.01
0.10
1.96
11.56
9.05
6.05
f1 (ppm)

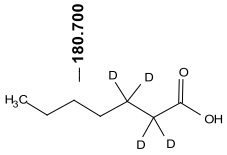
wxc-3-141

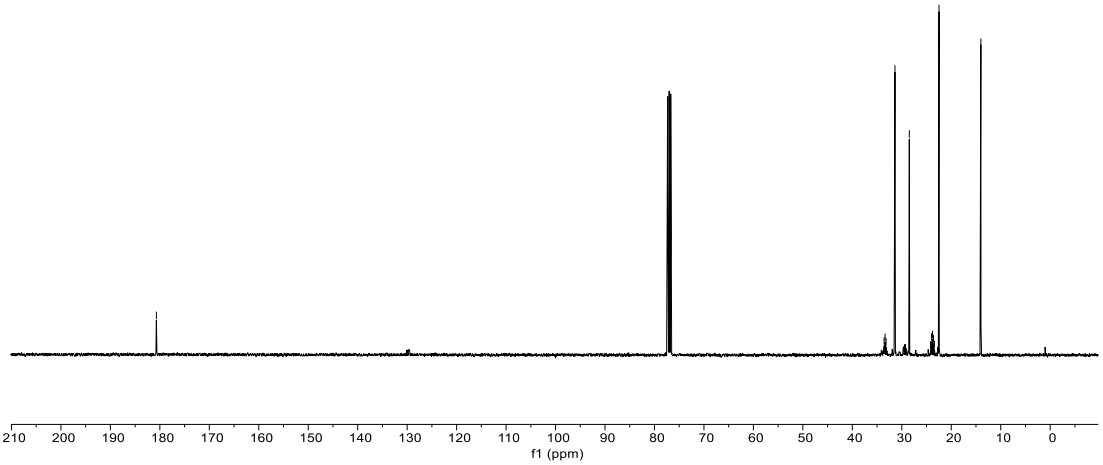




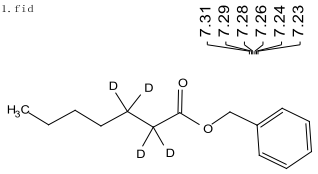


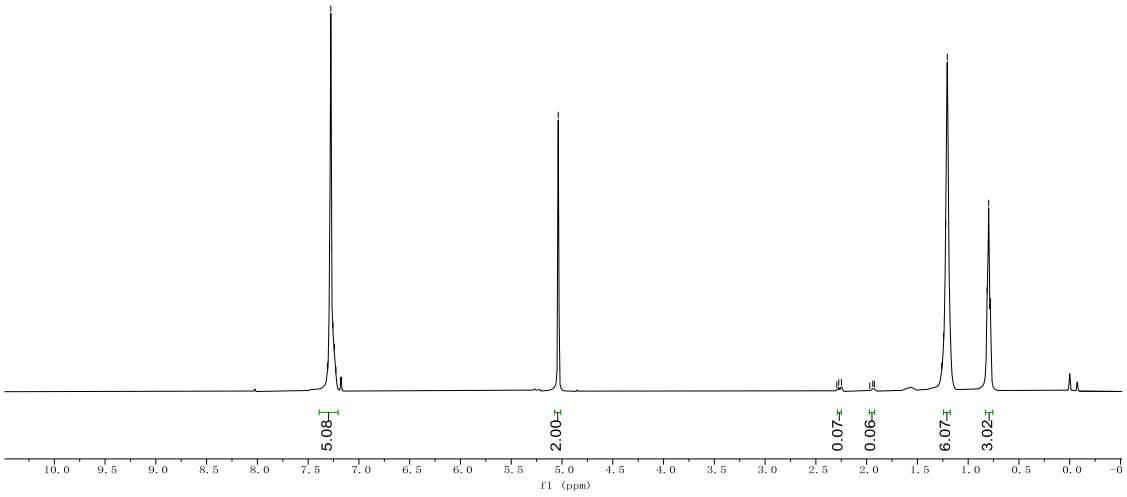
wxc-3-141



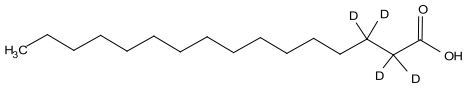


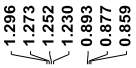
AW-7D-COOR.1.fid

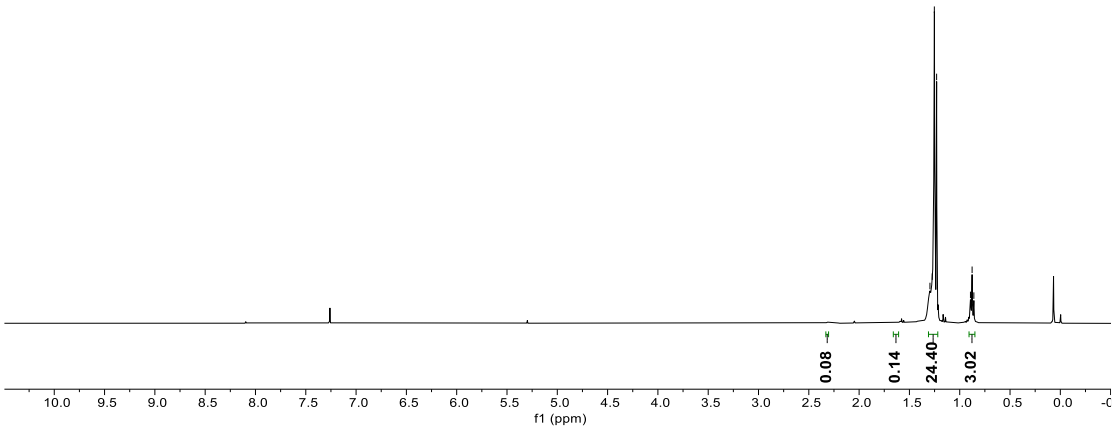




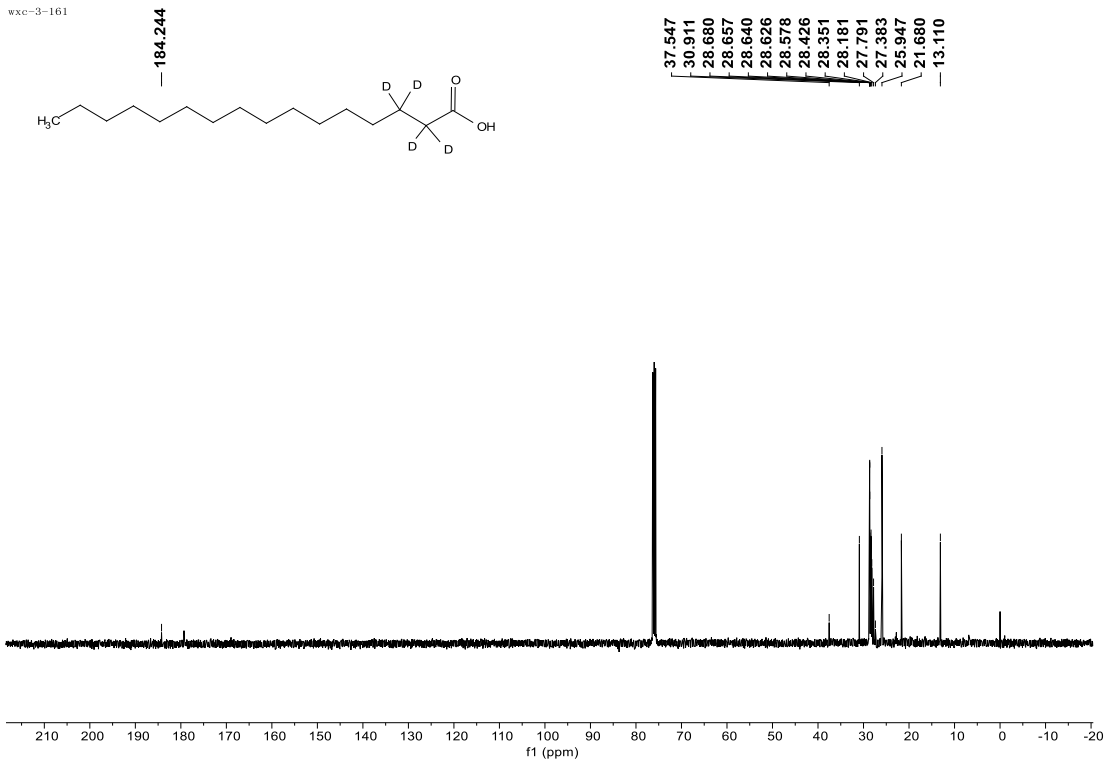
wxc-3-161



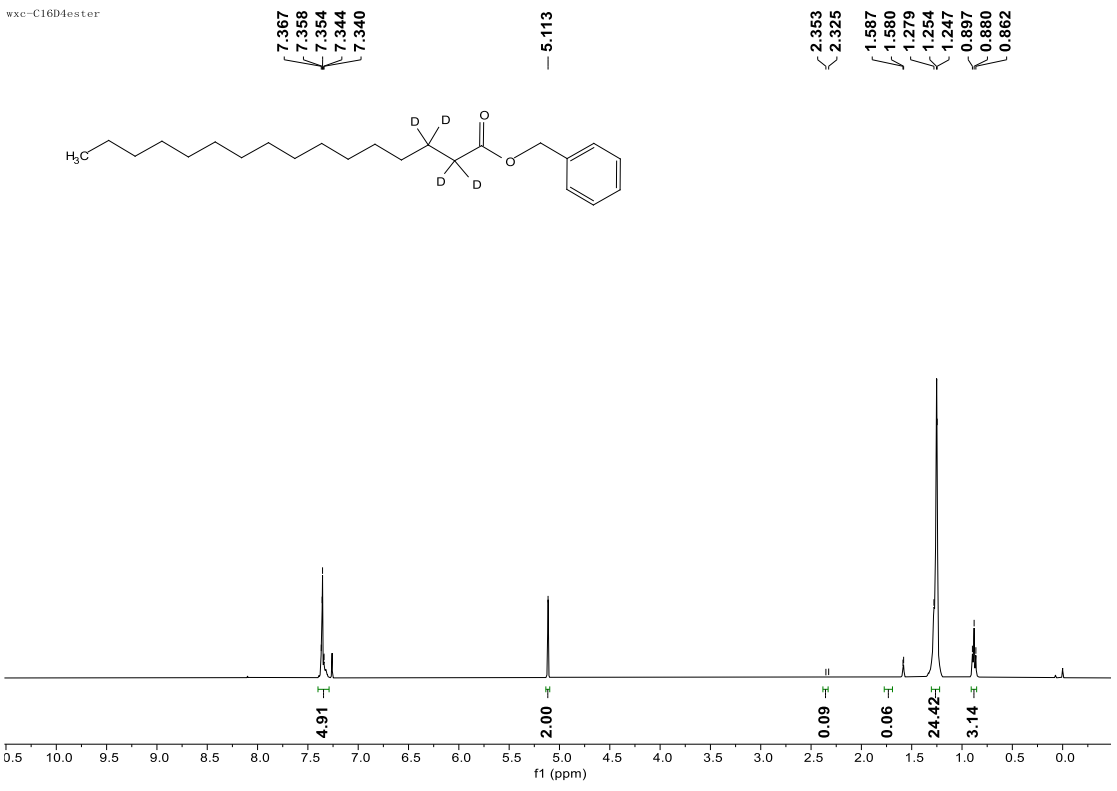


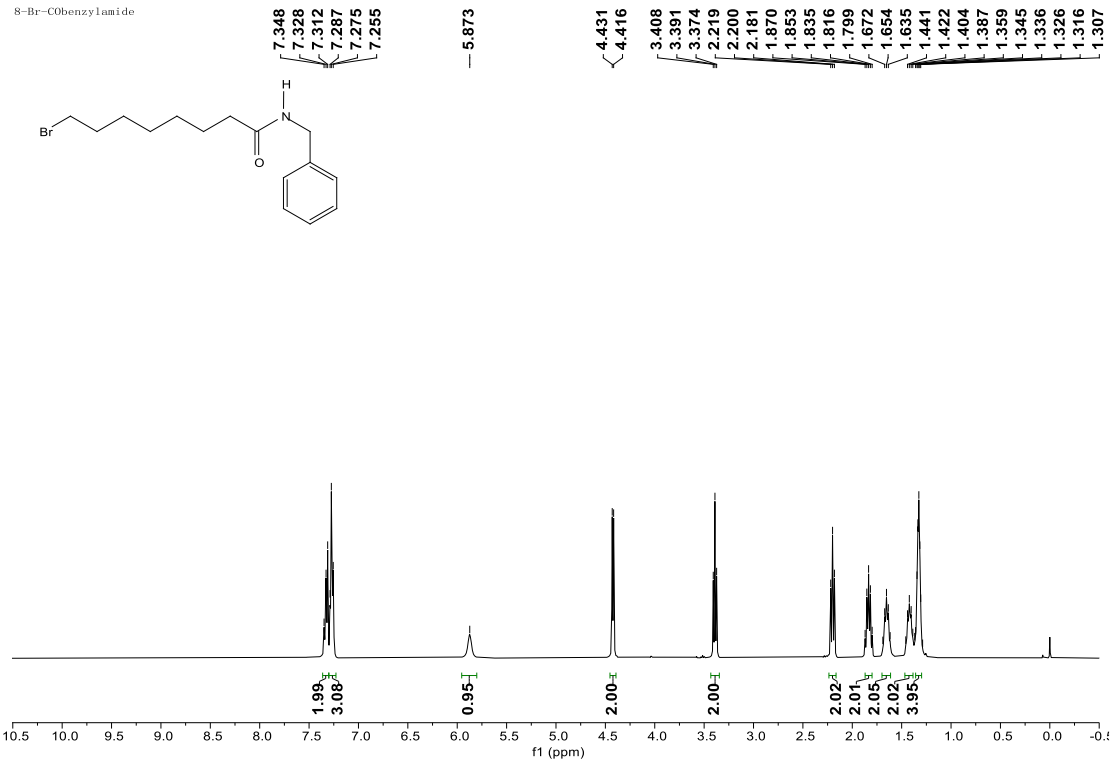


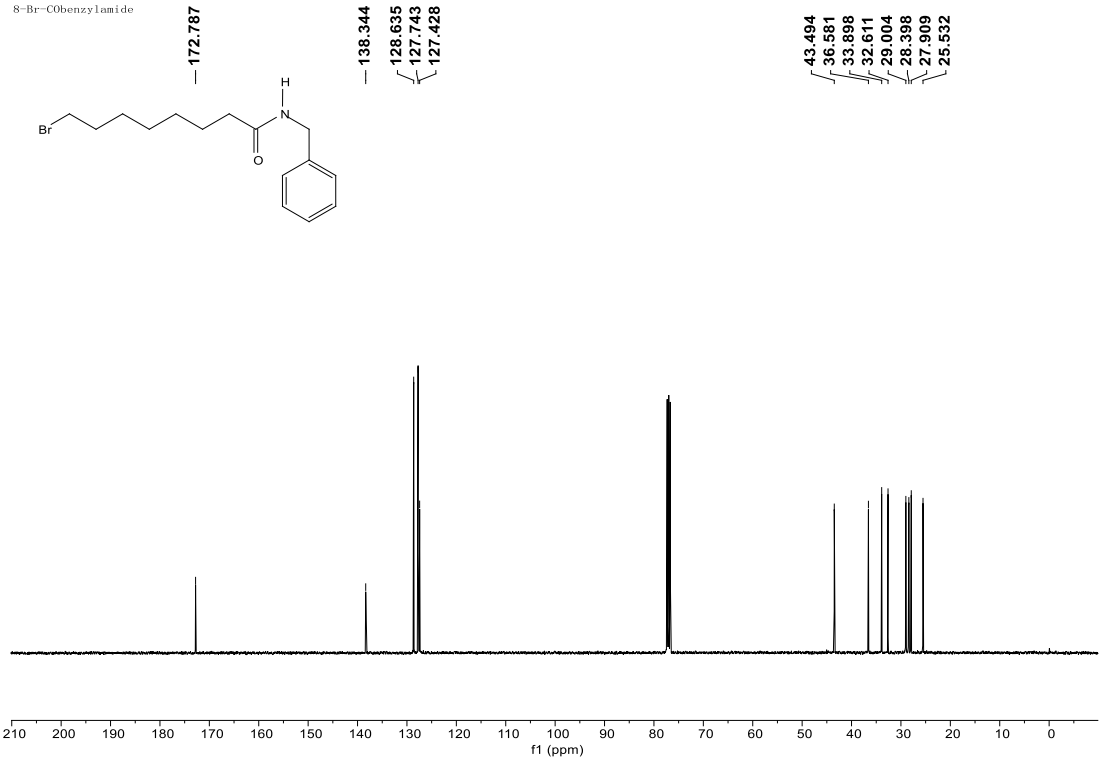
wxc-3-161

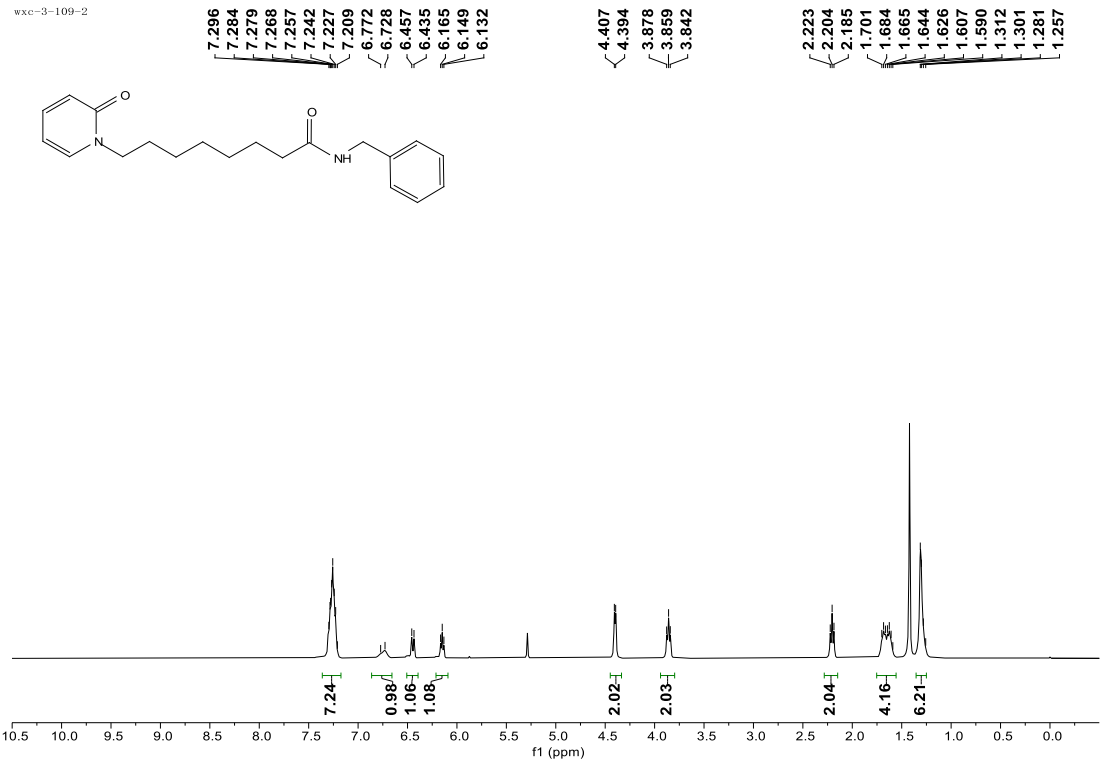


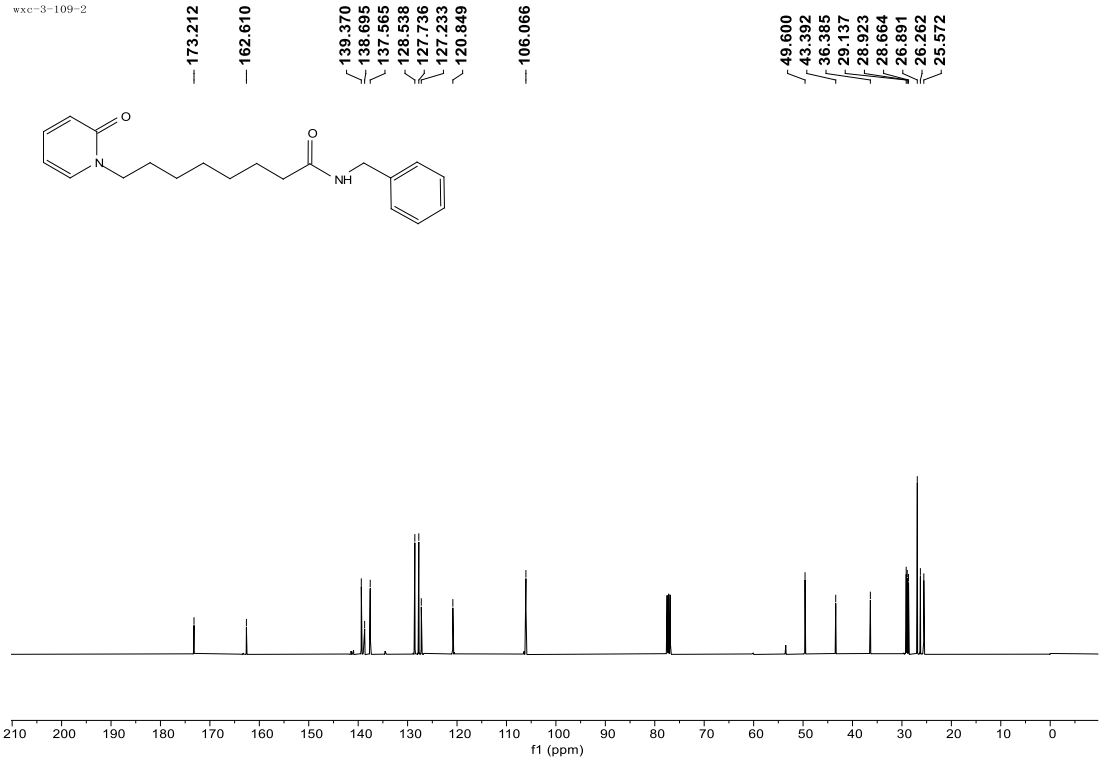
wxc-C16D4ester

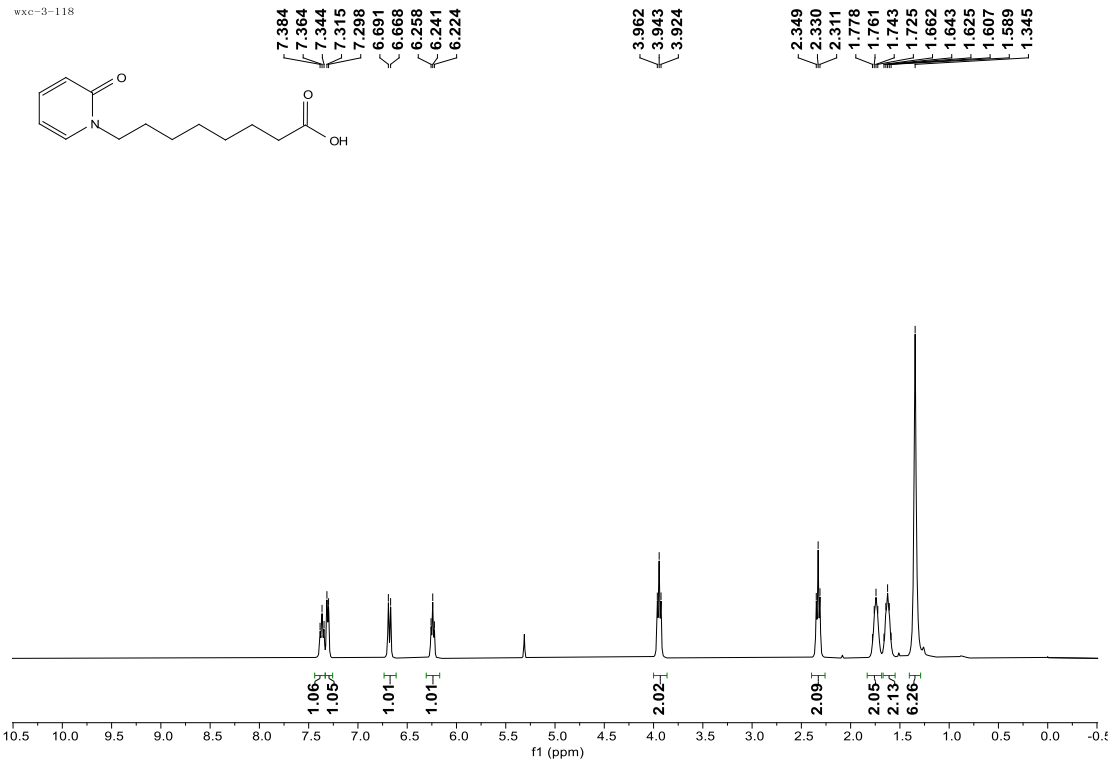


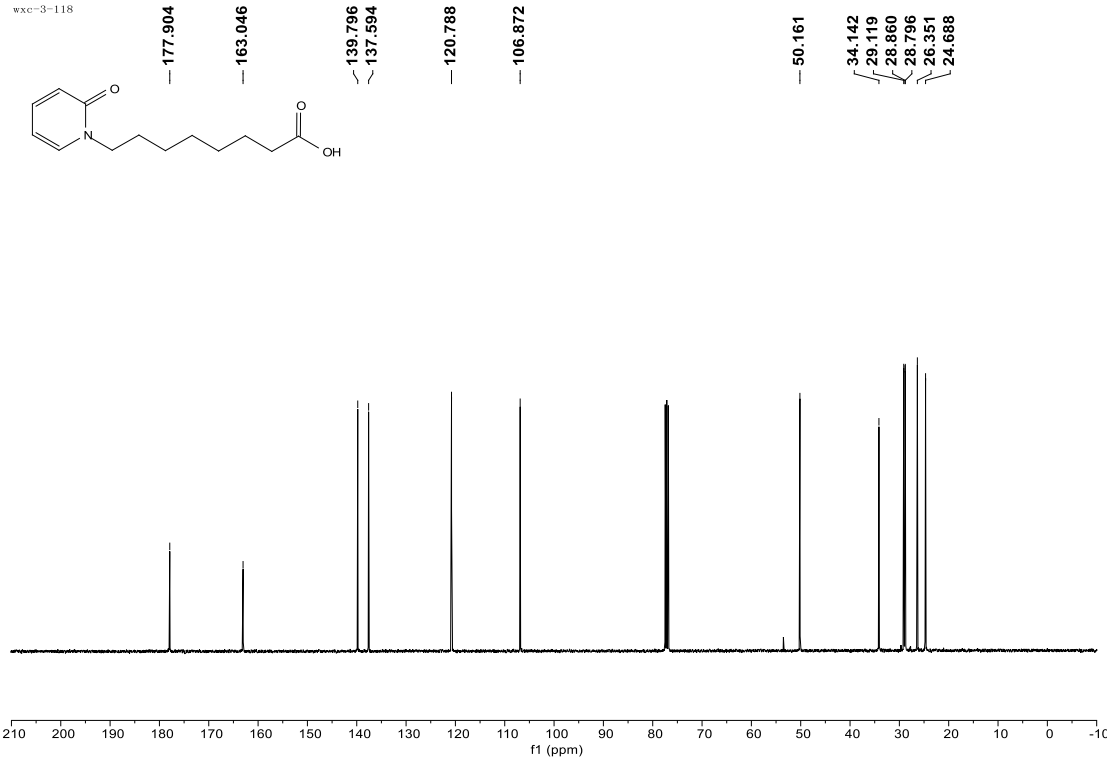

8-Br-CObenzylamide
7.348
7.328
7.312
7.287
7.275
7.255
5.873
4.431
4.416
3.408
3.391
3.374
2.219
2.200
2.181
1.870
1.853
1.835
1.816
1.799
1.672
1.654
1.635
1.441
1.422
1.404
1.387
1.359
1.345
1.336
1.326
1.316
1.307
H
N
Br
O
1.99
3.08
0.95
2.00
2.00
2.02
2.01
2.05
2.02
3.95
f1 (ppm)


8-Br-CObenzylamide
172.787
138.344
128.635
127.743
127.428
43.494
36.581
33.898
32.611
29.004
28.398
27.909
25.532
H
N
Br
O
f1 (ppm)

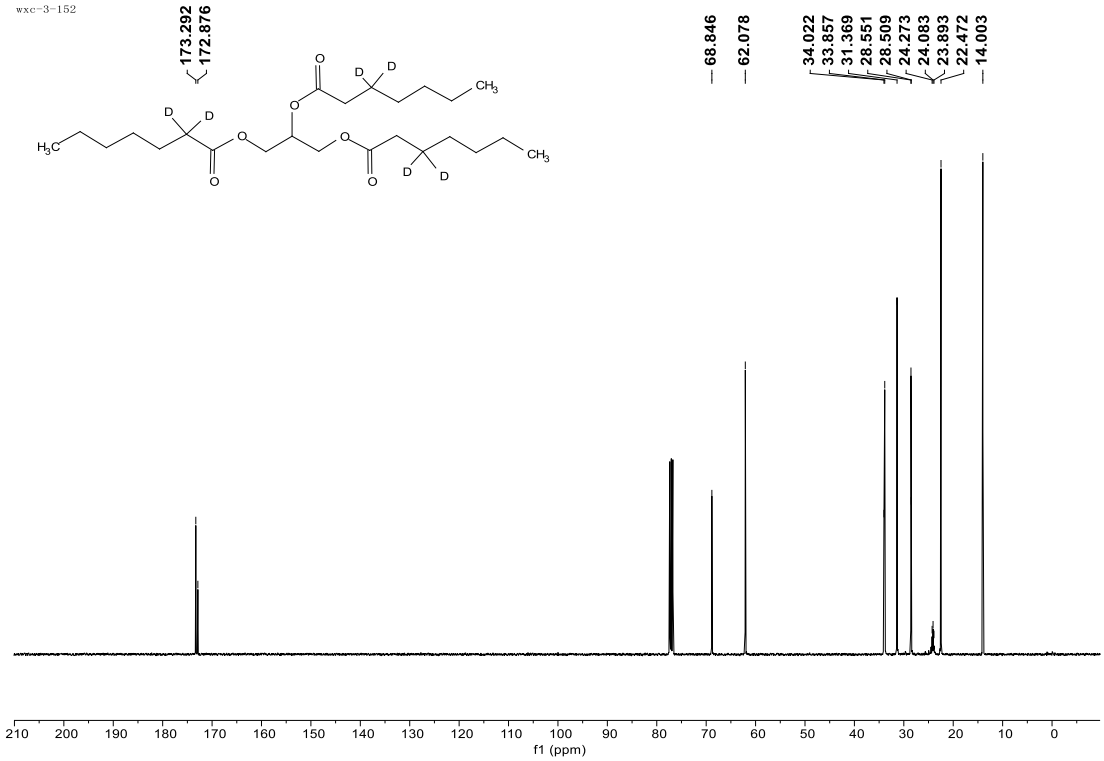

wxc-3-109-2
7.296
7.284
7.279
7.268
7.257
7.242
7.227
7.209
6.772
6.728
6.457
6.435
6.165
6.149
6.132
4.407
4.394
3.878
3.859
3.842
2.223
2.204
2.185
1.701
1.684
1.665
1.644
1.626
1.607
1.590
1.312
1.301
1.281
1.257
O
N
O
NH
7.24
0.98
1.06
1.08
2.02
2.03
2.04
4.16
6.21
f1 (ppm)


wxc-3-109-2
173.212
162.610
139.370
138.695
137.565
128.538
127.736
127.233
120.849
106.066
49.600
43.392
36.385
29.137
28.923
28.664
26.891
26.262
25.572
O
N
O
NH
f1 (ppm)


wxc-3-118
7.384
7.364
7.344
7.315
7.298
6.691
6.668
6.258
6.241
6.224
3.962
3.943
3.924
2.349
2.330
2.311
1.778
1.761
1.743
1.725
1.662
1.643
1.625
1.607
1.589
1.345
O
N
O
OH
1.06
1.05
1.01
1.01
2.02
2.09
2.05
2.13
6.26
f1 (ppm)


wxc-3-118
177.904
163.046
139.796
137.594
120.788
106.872
50.161
34.142
29.119
28.860
28.796
26.351
24.688
O
N
O
OH
f1 (ppm)


wxc-3-152
7.259
5.262
5.250
5.238
5.226
4.296
4.287
4.277
4.258
4.247
4.145
4.138
4.127
4.112
4.107
4.097
2.276
1.292
1.263
0.872
0.857
0.839
1.01
2.08
2.05
6.05
0.18
18.14
9.08
f1 (ppm)


wxc-3-152
173.292
172.876
68.846
62.078
34.022
33.857
31.369
28.551
28.509
24.273
24.083
23.893
22.472
14.003
f1 (ppm)