Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting information

Mechanochemical synthesis of (4S)-N-alkyl-4,5-bis-sulfooxypentanamide via a one-pot sequential aminolysis-sulfation reaction of (S)-γ-hydroxymethyl-γ-butyrolactone (2H-HBO)

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1- General information

All experiments were carried out in a commercial planetary ball mill Pulverisette 7 Premium 7 Line (Fritsch, Germany), equipped with two jars (20 mL) containing each 80 balls of 5 mm of diameter, the material of these bowls is zirconium oxide or stainless steel. All chemicals were purchased from Merck or Acros suppliers and used without further purification. The (*S*)-γ-hydroxymethyl-γ-butyrolactone (2H-HBO) (**1**) was furnished by the URD ABI (Pomacle). Reactions were monitored using Macherey-Nagel TLC Silica gel 60 F254 or Silica gel C18 F254. Products were revealed by charring with cerium molybdate reagent. High-resolution electrospray mass spectrometry (ESI-HRMS) was operated on a Synapt G2-Si Q-TOF high resolution hybrid Mass Spectrometer provided with an electrospray (ESI) ionization source (Waters, Manchester, UK). Data acquisition and processing were performed with MassLynx software (V4.2, Waters). NMR analysis were performed on a spectrometer Bruker operating at 400 MHz for ^{1}H and 100 MHz ^{13}C. NMR samples of (4*S*)-*N*-alkyl-4.5-dihydroxypentanamides **2a-f** were prepared in CD_3OD, DMSO-*d6* or pydidine-*d5*, their sulfated derivatives **4e-f** were dissolved in D_2O. Infrared spectra were obtained using a Fourrier-transform infrared (FT-IR) spectrometer (IRaffinity-1S, Shimadzu) and ATR method (MIRacle 10, shimadzu). Optical rotations were measured by an Anton Paar MCP 100 polarimeter at 20 or 25 °C with MeOH or H_2O as solvent (concentration c given as g.100 mL^{-1}). Melting points were determined using a Stuart SMP10. Critical Micelle Concentration (CMC) of the selected molecules were determined with a TC1 tensiometer (Lauda Scientific) using the Du Noüy ring method.

2- Procedure of aminolysis of (*S*)-γ-hydroxymethyl-γ-butyrolactone 1 (2H-HBO) for synthesis of derivatives 2a-f and 2g-j

2H-HBO (**1**) (1 eq.) and primary alkylamine (1 eq.) or secondary amine (1-4 eq.) were added in a stainless steel or zirconia jar (20 mL) containing 80 stainless steel or zirconia balls (diameter = 5 mm) respectively. The jar was flushed with argon and placed in a planetary ball-milling (P7PL) and shaken at 400 rpm in reverse mode for a number of cycles of 5 min (1 min pause between each cycle) depending of the alkylamine (See Table 1 and 2). The reaction was then stopped and the resulting reaction mixture was collected in a minimum of ethanol.

For derivatives **2a-c**, and **2g-j** (See Table 2), silica was added and then ethanol was evaporated. The crude product was then purified by flash chromatography (solid deposit) using a gradient EtOAc/MeOH (100:0 to 75:25) as eluent. The corresponding (4*S*)-*N*-alkyl-4,5-dihydroxypentanamide was afforded after evaporation of the solvents under reduced pressure as white solid.

For derivative **2d-f**, the crude product was purified by recrystallization in ethanol. The corresponding (4*S*)-*N*-alkyl-4,5-dihydroxypentanamide was afforded after evaporation of the solvents under reduced pressure as white solid.

3- Procedure for sulfatation of (4*S*)-*N*-alkyl-4,5-dihydroxypentanamide derivatives 2b and 2e

Crude (4*R*) *N*-alkyl-4,5-dihydroxypentanamide **2b** or **2e** (1 eq.) beforehand synthesized, sulfur trioxide pyridine complex (97 %, 3-8 eq.) and anhydrous AcOEt (LAG, η = 0.6 µL/mg) or NaCl (120 %wt) were added in a zirconia jar (20 mL) containing 80 zirconia balls (diameter = 5 mm) (see Table 3). The jar, flushed with argon, was placed in the P7PL and shaken at 400 or 500 rpm in reverse mode for a number of cycles of 5 minutes (1 min pause between each cycle), optimized for each product (see Table 3). The reaction was then quenched with $NaHCO_3$ (8 eq.) by grinding in reverse mode for 3 cycles of 3 min (400 rpm, 1 min pause between each cycle). The crude product (**3b/4b** or **3e/4e**) was directly analyzed by NMR (D_2O).

4- Procedure for synthesis of (4*S*)-*N*-alkyl-4,5-bis-sulfooxypentanamide 4b-e in solvent media

Amide derivatives **2b-e** were prepared by dissolving alkylamine (1.05 eq) in 2-propanol (C≈0.1 mM) and added to 2H-HBO (1 eq.) in a round-bottomed flask. The mixture was stirred at 50 °C until TLC showed complete conversion (≈48 h for compounds **2b** and **2c**) or 24h (compounds **2d** and **2e**). Recrystallization in a minimum of solvent (25% of 2-propanol in acetonitrile for **2b**, 2-propanol for **2c**, Ethanol for **2d** and **2e**) afford pure amide derivatives in 83, 71, 77 and 74% yield respectively for **2b**, **2c**, **2d**, **2e**.

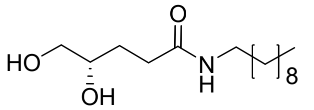
Sulfated products **4b-e** were prepared by adding Sulfur trioxide pyridine complex (2 eq. per OH group) in dry pyridine (C≈0.1 mM) at RT until TLC showed complete conversion (≈48 h). MeOH (10 eq.) was added and the reaction was stirred 30 min at RT. Sodium hydrogenocarbonate (8 eq.) was then added. Solvents were removed under reduce pressure and the crude product was purified by reverse flash chromatography (C18, 80 g) using H_2O/MeOH (95:5 to 0:1) as eluent. The products were obtained after evaporation of the solvents under reduced pressure in 60, 59, 71, 73% yield for **4b**, **4c**, **4d**, **4e**, respectively.

5- Procedure for one-pot sequential synthesis of (4*S*) *N*-alkyl-4,5-bis-sulfooxypentanamide 4b-e

2H-HBO (**1**) (1 eq.) and alkylamine (1 eq.) were added in a zirconia jar (20 mL) containing 80 zirconia balls (diameter = 5 mm).The jar, flushed with argon, was placed in the P7PL and shaken at 400 in reverse mode for 8, 10, or 11 cycles of 5 min (1 min pause between each cycle) depending of the alkylamine (See Table 3). TLC revealed complete conversion of 2H-HBO. Sulfur trioxide pyridine complex (97%, 4 eq.) and anhydrous AcOEt (LAG, η = 0.6 µL/mg) were added. The jar was flushed with argon and shaken at 400 or 500 rpm in reverse mode for 16 cycles of 5 minutes (1 min pause between each cycle). The reaction was then quenched with $NaHCO_3$ (8 eq.) by grinding in reverse mode for 3 cycles of 3 min (400 rpm, 1 min pause between each cycle). The reaction was then stopped and the resulting reaction mixture was collected in minimum of water. Water was evaporated and the crude product was purified by reverse flash chromatography (C18, 80 g) using H_2O/MeOH (95:5 to 0:1) as eluent. The product was afforded as a white solid after evaporation of the solvents under reduced pressure.

6- Physical datas of compounds

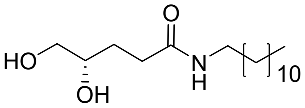
(4*S*)-*N*-decyl-4,5-dihydroxypentanamide 2a



White solid (265.2 mg, 75%). R_f = 0.42 (EtOAc/MeOH 9:1); mp = 96 °C; $[\alpha]^{20}$ = - 9,0 ° (C = 0.1 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3294, 2922, 2848, 1631, 1543-1415 cm^{-1}

^1H NMR (400 MHz, CD_3OD) δ (ppm) 3.57 (m, 1H, H_4), 3.50 – 3.42 (m, 2H, H_{5a},H_{5b}), 3.15 (t, *J* = 7.1 Hz, 2H, CH_2), 2.39 – 2.23 (m, 2H, H_{2a},H_{2b}), 1.83 (m, 1H, H_{3a}), 1.63 (m, 1H, H_{3b}), 1.55-1.44 (m, 2H, CH_2), 1.38-1.24 (m, 14H, 7 CH_2), 0.90 (t, *J* = 6.6 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, CD_3OD) δ (ppm) 176.0 (C_1), 72.7 (C_4), 67.1 (C_5), 40.5 (CH_2), 33.3 (C_2), [33.1, 30.7, 30.7] (3 CH_2), 30.6 (C_3), [30.5, 30.4, 30.4, 28.0, 23.8] (5 CH_2), 14.4 (CH_3). HRMS (ESI): *m/z* calculated for $C_{15}H_{31}NNaO_3$ 296.2202, found 296.2200 $[M+Na]^+$

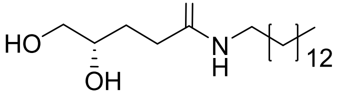
(4*S*)-*N*-dodecyl-4,5-dihydroxypentanamide 2b



White solid (241.8 mg, 76%). R_f = 0.42 (EtOAc/MeOH 9:1); mp = 102 °C; $[\alpha]^{20}$ = - 7.8 ° (C = 0.5 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3299, 2918, 2847, 1632, 1542-1416 cm^{-1}

^1H NMR (400 MHz, CD_3OD) δ(ppm) 3.57 (m, 1H, H_4), 3.50 – 3.42 (m, 2H, H_{5a}, H_{5b}), 3.15 (t, *J* = 7.1 Hz, 2H, CH_2), 2.39 – 2.23 (m, 2H, H_{2a}, H_{2b}), 1.83 (m, 1H, H_{3a}), 1.62 (m, 1H, H_{3b}), 1.54-1.44 (m, 2H, CH_2), 1.40-1.23 (m, 18H, 9 CH_2), 0.90 (t, *J* = 6.8 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, CD_3OD) δ(ppm) 176.0 (C_1), 72.7 (C_4), 67.1 (C_5), 40.5 (CH_2), 33.3 (C_2), [33.1, 30.8, 30.8, 30.7, 30.7] (5 CH_2), 30.6 (C_3), [30.5, 30.4, 30.4, 28.0, 23.7] (5 CH_2), 14.4 (CH_3). HRMS (ESI): *m/z* calculated for $C_{17}H_{36}NO_3$ 302.2695, found 302.2691 $[M+H]^+$

(4*S*)-*N*-tetradecyl-4,5-dihydroxypentanamide 2c

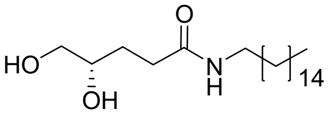


White solid (179.1 mg, 66%). R_f = 0.44 (EtOAc/MeOH 9:1); mp = 104 °C; $[\propto]^{20}$ = - 2.0 ° (C = 0.05 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3301, 2918, 2847, 1633, 1540-1417 cm^{-1}

^1H NMR (400 MHz, CD_3OD) δ(ppm) 3.57(m, 1H, H_4), 3.50 – 3.42 (m, 2H, H_{5a}, H_{5b}), 3.15 (t, *J* = 7.1 Hz, 2H,CH_2), 2.39 – 2.23 (m, 2H, H_{2a}, H_{2b}), 1.83 (m, 1H, H_{3a}), 1.62 (m, 1H, H_{3b}), 1.53-1.44 (m, 2H,CH_2), 1.40-1.23 (m, 22H, 11 CH_2), 0.90 (t, *J* = 6.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, CD_3OD) δ(ppm) 176.0 (C_1), 72.7 (C_4), 67.1 (C_5), 40.5 (CH_2), 33.3 (C_2), [33.1, 30.8, 30.8, 30.8, 30.7, 30.7, 30.7] (7 CH_2), 30.5 (C_3), [30.5, 30.4, 30.4, 28.0, 23.7] (5 CH_2), 14.4 (CH_3). HRMS (ESI): *m/z* calculated for $C_{19}H_{40}NO_3$ 330.3008, found 330.3014 $[M+H]^+$

(4*S*)-*N*-hexadecyl-4,5-dihydroxypentanamide 2d

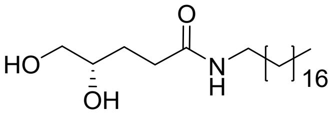


White solid (244.9 mg, 72%). R_f = 0.45 (EtOAc/MeOH 9:1); mp = 108 °C; $[\propto]^{20}$ = - 24.0 ° (C = 0.1 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3296, 2918, 2847, 1632, 1542-1416 cm^{-1}

^1H NMR (400 MHz, DMSO-d_6) δ(ppm) 7.71 (t, *J* = 5.6 Hz, 1H, NH), 4.48 (d, *J* = 4.8 Hz, 1H, OH_4), 4.43 (t, *J* = 5.7 Hz, 1H, OH_5), 3.36 (m, 1H, H_4), 3.29 -3.18 (m, 2H, H_{5a}, H_{5b}), 3.00 (q, *J* = 6.5 Hz, 2H, CH_2), 2.17 (m, 1H, H_{2a}), 2.07 (m, 1H, H_{2b}), 1.67 (m, 1H, H_{3a}), 1.43 (m, 1H, H_{3b}), 1.46-1.33 (m, 2H, CH_2), 1.32-1.17 (m, 26H, 13 CH_2), 0.85 (t, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, DMSO-d_6) δ(ppm) 172.2 (C_1), 70.8 (C_4), 65.7 (C_5), 38.4 (CH_2), 31.8 (C_2), 31.3 (1 CH_2), 29.5 (C_3), [29.1, 29.0, 29.00, 28.8, 28.7, 26.4, 22.1] (13 CH_2), 13.9 (CH_3). HRMS (ESI): *m/z* calculated for $C_{21}H_{44}NO_3$ 358.3321, found 358.3311 $[M+H]^+$

(4*S*)-*N*-octadecyl-4,5-dihydroxypentanamide 2e

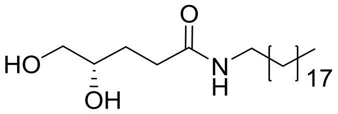


White solid (277.4 mg, 71%). R_f = 0.49 (EtOAc/MeOH 9:1); mp = 110 °C; $[\propto]^{20}$ = - 16.0 ° (C = 0.05 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3299, 2917, 2847, 1632, 1542-1464 cm^{-1}

^1H NMR (400 MHz, Pyridine-d_5) δ(ppm) 8.48 (m, 1H, NH), 6.28 (s, 2H, 2 OH), 4.23 (m, 1, H, H_4), 4.03 – 3.99 (m, 2H, H_{5a}, H_{5b}), 3.50 (q, *J* = 6.7 Hz, 2H, CH_2), 2.87 – 2.78 (m, 2H, H_{2a}, H_{2b}), 2.44 (m, 1H, H_{3a}), 2.26 (m, 1H, H_{3b}), 1.62 (q, *J* = 7.3 Hz, 2H, CH_2), 1.43-1.17 (m, 30H, 15 CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Pyridine-d_5) δ(ppm) 174.0 (C_1), 72.9 (C_4), 67.8 (C_5), 40.3 (CH_2), 33.8 (C_2), 32.6 (1 CH_2), 31.1 (C_3), [30.7, 30.5, 30.4, 30.4, 30.4, 30.4, 30.1, 30.1, 27.9, 23.4] (15 CH_2), 14.7 (CH_3). HRMS (ESI): *m/z* calculated for $C_{23}H_{48}NO_3$ 386.3634, found 386.3644 $[M+H]^+$

(4*S*)-*N*-nonadecyl-4,5-dihydroxypentanamide 2f

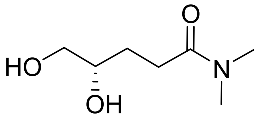


White solid (264.3 mg, 62%). R_f = 0.50 (EtOAc/MeOH 9:1); mp = 112 °C; $[\propto]^{20}$ = - 36.0 ° (C = 0.05 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3255, 2918, 2850, 1662, 1564-1429 cm^{-1}

^1H NMR (400 MHz, Pyridine-d_5) δ(ppm) 8.48 (m, 1H, NH), 6.28 (s, 1H, OH), 6.22 (s, 1H, OH), 4.23 (m, 1H, H_4), 4.03 – 3.99 (m, 2H, H_{5a}, H_{5b}), 3.50 (q, *J* = 6.7 Hz, 2H, CH_2), 2.89 – 2.76 (m, 2H, H_{2a}, H_{2b}), 2.43 (m, 1H, H_{3a}), 2.25 (m, 1H, H_{3b}), 1.62 (q, J = 7.2 Hz, 2H, CH_2), 1.39-1.21 (m, 30H, 16 CH_2), 0.88 (t, *J* = 6.7 Hz, 3H, CH_3).

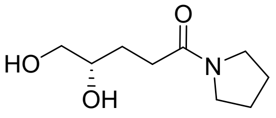
^{13}C NMR (101 MHz, Pyridine-d_5) δ(ppm) 174.1 (C_1), 72.9 (C_4), 67.8 (C_5), 40.2 (CH_2), 33.7 (C_2), 32.6 (1 CH_2), 31.1 (C_3), [30.7, 30.5, 30.4, 30.4, 30.4, 30.4, 30.1, 30.1, 27.9, 23.4] (16 CH_2), 14.7 (CH_3). HRMS (ESI): *m/z* calculated for $C_{24}H_{49}NNaO_3$ 422.3610, found 422.3607 $[M+Na]^+$

(4S)-*N*-dimethyl-4,5-dihydroxypentanamide 2g



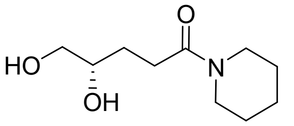
Viscous liquid (111.2 mg, 77%). R_f = 0.32 (EtOAc/MeOH 8:2); $[\propto]^{25}$ = - 10.0 ° (C = 0.1 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3421, 2937, 1732, 1624, 1506-1406, 1269 cm^{-1}
^{1}H NMR (400 MHz, CD_3OD) δ (ppm) 3.60 (m, 1H, H_4), 3.51 – 3.43 (m, 2H, H_{5a}, H_{5b}), 3.08 (s, 3H, CH_3), 2.93 (s, 3H, CH_3), 2.59 – 2.44 (m, 2H, H_{2a}, H_{2b}), 1.89 – 1.80 (m, 1H, H_{3a}), 1.62 (m, 1H, H_{3b}). ^{13}C NMR (101 MHz, CD_3OD) δ (ppm) 175.6 (C_1), 72.6 (C_4), 67.2 (C_5), 37.8 (CH_3), 35.8 (CH_3), 30.3 (C_2), 29.8 (C_3). HRMS (ESI): *m/z* calculated for $C_7H_{15}NNaO_3$ 184.0950, found 184.0956 $[M+Na]^+$

(4S)-*N*-pyrrolidinyl-4,5-dihydroxypentanamide 2i



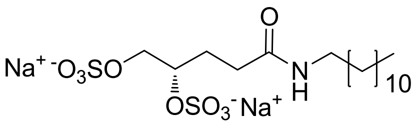
Viscous liquid (151.6 mg, 70%). R_f = 0.45 (EtOAc/MeOH 8:2); $[\propto]^{25}$ = - 19.0 ° (C = 0.1 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3387, 2877, 1712, 1620, 1454, 1226, 1064 cm^{-1}
^{1}H NMR (600 MHz, CD_3OD) δ (ppm) 3.60 (m, 1H, H_4), 3.55 - 3.49 (m, 2H, $H_{1'a}$, $H_{1'b}$), 3.48 - 3.44 (m, 2H, H_{5a}, H_{5b}), 3.41 (t, *J* = 6.9 Hz, 2H, $H_{4'a}$ and $H_{4'b}$), 2.54 - 2.40 (m, 2H, H_{2a}, H_{2b}), 2.02 - 1.95 (m, 2H, $H_{2'a}$, $H_{2'b}$), 1.92 – 1.82 (m, 3H, $H_{3'a}$, $H_{3'b}$, H_{3a}), 1.64 (m, 1H, H_{3b}). ^{13}C NMR (151 MHz, CD_3OD) δ (ppm) 174.1 (C_1), 72.6 (C_4), 67.2 (C_5), 48.0 ($C_{1'}$), 46.9 ($C_{4'}$), 31.6 (C_2), 29.6 (C_3), 26.9 ($C_{2'}$), 25.4 ($C_{3'}$). HRMS (ESI): *m/z* calculated for $C_9H_{17}NNaO_3$ 210.1106, found 210.1116 $[M+Na]^+$

(4S)-*N*-piperidinyl-4,5-dihydroxypentanamide 2j



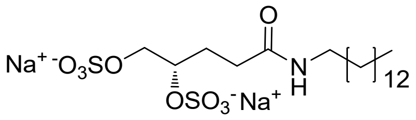
Viscous liquid (86.9 mg, 45%). R_f = 0.47 (EtOAc/MeOH 8:2); $[\propto]^{25}$ = - 22.0 ° (C = 0.1 g/100 mL, MeOH), IR ATR ν_{max} (cm^{-1}) = 3358, 2937, 2856, 1712, 1614, 1442, 1269, 1066 cm^{-1}
^{1}H NMR (400 MHz, CD_3OD) δ (ppm) 3.60 (m, 1H, H_4), 3.55 - 3.50 (m, 4H, $2H_{1'}$ $2H_{5'}$), 3.47 – 3.46 (m, 2H, H_{5a}, H_{5b}), 2.59 – 2.43 (m, 2H, H_{2a}, H_{2b}), 1.84 (m, 1H, H_{3a}), 1.68 (m, 2H, $2H_{3'}$), 1.63 – 1.56 (m, 3H, H_{3b}, $2H_{4'}$), 1.53 (m, 2H, $2H_{2'}$). ^{13}C NMR (101 MHz, CD_3OD) δ (ppm) 173.7 (C_1), 72.6 (C_4), 67.2 (C_5), 48.0 ($C_{1'}$), 44.0 ($C_{5'}$), 30.3 (C_2), 30.1 (C_3), 27.6 ($C_{2'}$), 26.8 ($C_{4'}$), 25.5 ($C_{3'}$). HRMS (ESI): *m/z* calculated for $C_{10}H_{19}NNaO_3$ 224.1263, found 224.1268 $[M+Na]^+$

(4*S*)-*N*-dodecyl-4,5-bis(sulfooxy)pentanamide, bis sodium salt 4b



White solid (718.4 mg, 77%). R_f = 0.43 (EtOAc/MeOH 7:3); $[\propto]^{20}$ = - 15.4 ° (C = 0.5 g/100 mL, H_2O), IR ATR ν_{max} (cm^{-1}) = 2923, 1644-1464, 1227 cm^{-1}
^{1}H NMR (400 MHz, D_2O) δ(ppm) 4.58 (m, 1H, H_4), 4.29 (dd, *J* = 10.9, 4.1 Hz, 1H, H_{5a}), 4.19 (dd, *J* = 10.9, 4.1 Hz, 1H, H_{5b}), 3.20 (t, *J* = 7.1 Hz, 2H, CH_2), 2.48 – 2.35 (m, 2H, H_{2a}, H_{2b}), 2.06 – 2.01 (m, 2H, H_{3a}, H_{3b}), 1.58-1.49 (m, 2H, CH_2), 1.39-1.272 (m, 18H, 9 CH_2), 0.91 (t, *J* = 6.9 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, D_2O) δ(ppm) 175.3 (C_1), 76.6 (C_4), 68.6 (C_5), 39.4 (CH_2), 31.5 (C_2), [31.2, 28.8, 28.8, 28.6, 28.6, 28.5, 28.3, 28.1] (8 CH_2), 27.1 (C_3), [25.9, 22.1] (2 CH_2), 13.4 (CH_3). HRMS (ESI): *m/z* calculated for $C_{17}H_{33}NNa_3O_9S_2$ 528.1290, found 528.1281 $[M+Na]^+$

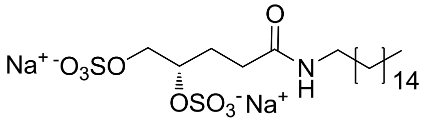
(4*S*)-*N*-tetradecyl-4,5-bis(sulfooxy)pentanamide, bis sodium salt 4c



White solid (323.6 mg, 62%). R_f = 0.40 (EtOAc/MeOH 7:3); $[\propto]^{20}$ = - 13.0 ° (C = 0.1 g/100 mL, H_2O), IR ATR ν_{max} (cm^{-1}) = 2918, 2850, 1647, 1552, 1228, 1074-1045 cm^{-1}

^1H NMR (400 MHz, D_2O) δ(ppm) 4.59 (m, 1H, H_4), 4.29 (dd, *J* = 11.0, 3.9 Hz, 1H, H_{5a}), 4.18 (dd, *J* = 10.9, 4.2 Hz, 1H, H_{5b}), 3.19 (m, 2H, CH_2), 2.47–2.35 (m, 2H, H_{2a}, H_{2b}), 2.05–2.00 (m, 2H, $H_{3a,}$ H_{3b}), 1.58-1.46 (m, 2H, CH_2), 1.41-1.22 (m, 22H, 11 CH_2), 0.91 (t, *J* = 6.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, D_2O) δ(ppm) 174.7 (C_1), 76.8 (C_4), 68.9 (C_5), 39.7 (CH_2), 31.9 (1 CH_2), 31.6 (C_2), [29.8, 29.7, 29.7, 29.6, 29.4, 29.3, 28.8] (9 CH_2), 27.2 (C_3), [26.9, 22.6] (2 CH_2), 13.9 (CH_3). HRMS (ESI): *m/z* calculated for $C_{19}H_{37}NNa_3O_9S_2$ 556.1603, found 556.1611 $[M+Na]^+$

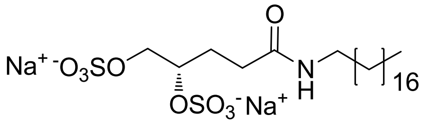
(4*S*)-*N*-hexadecyl-4,5-bis(sulfooxy)pentanamide, bis sodium salt 4d



White solid (346.9 mg, 79%). R_f = 0.23 (EtOAc/MeOH 8:2); $[\propto]^{20}$ = - 8.0 ° (C = 0.1 g/100 mL, H_2O), IR ATR ν_{max} (cm^{-1}) = 2916, 1653, 1548, 1465, 1228, 1074 cm^{-1}

^1H NMR (400 MHz, D_2O) δ(ppm) δ (ppm) 4.60 (m, 1H, H_4), 4.30 (dd, *J* = 11.0, 3.8 Hz, 1H, H_{5a}), 4.18 (dd, *J* = 11.0, 4.3 Hz, 1H, H_{5b}), 3.26–3.15 (m, 2H, CH_2), 2.47–2.35 (m, 2H, H_{2a}, H_{2b}), 2.03 (q, *J* = 7.4 Hz, 2H, H_{3a}, H_{3b}), 1.59-1.50 (m, 2H, CH_2), 1.40-1.25 (m, 26 H, 13 CH_2), 0.91 (t, *J* = 6.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, D_2O) δ(ppm) 174.6 (C_1), 76.9 (C_4), 68.9 (C_5), 39.7 (CH_2), 32.0 (1 CH_2), 31.6 (C_2), [30.0, 29.8, 29.8, 29.8, 29.5, 29.4] (10 CH_2), 28.9 (CH_2), 27.2 (C_3), [27.0, 22.7] (2 CH_2), 13.9 (CH_3). HRMS (ESI): *m/z* calculated for $C_{21}H_{41}NNa_3O_9S_2$ 584.1916, found 584.1898 $[M+Na]^+$

(4*S*)-*N*-octadecyl-4,5-bis(sulfooxy)pentanamide, bis sodium salt 4e



White solid (445.6 mg, 79%). Rf = 0.36 (EtOAc/MeOH 8:2); $[\propto]^{20}$ = - 7.0 ° (C = 0.1 g/100 mL, H_2O), IR ATR ν_{max} (cm^{-1}) = 2916, 2849, 1651, 1558, 1471, 1233, 1072 cm^{-1}

^1H NMR (400 MHz, D_2O) δ(ppm) δ (ppm) 4.61 (m, 1H, H_4), 4.31 (dd, *J* = 11.0, 3.8 Hz, 1H, H_{5a}), 4.18 (dd, *J* = 11.0, 4.3 Hz, 1H, H_{5b}), 3.21 – 3.17 (m, 2H, CH_2), 2.48–2.36 (m, 2H, H_{2a} et H_{2b}), 2.03 (q, *J* = 7.4 Hz, 2H, H_{3a}, H_{3b}), 1.59-1.50 (m, 2H, CH_2), 1.44-1.25 (s, 30H, 15 CH_2), 0.91 (t, *J* = 6.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, D_2O) δ(ppm) 174.6 (C_1), 76.9 (C_4), 68.9 (C_5), 39.7(CH_2), 32.0 (1 CH_2), 31.6 (C_2), [30.0, 30.0, 29.9, 29.9, 29.5, 29.5, 28.9] (13 CH_2), 27.2 (C_3), [27.0, 22.7] (2 CH_2), 13.9 (CH_3). HRMS (ESI): *m/z* calculated for $C_{23}H_{45}NNa_3O_9S_2$ 612.2229, found 612.2250[M +Na]$^+$

7- Green chemistry metrics.

To estimate the environmental impact of the one-pot tow-step procedure mechanosynthesis in solventless conditions, we calculated some green metrics as described in *ACS Sustainable Chem. Eng.,* **2019**, 7, 19235−19245.

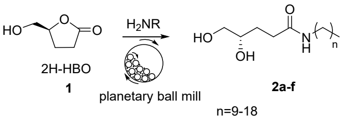
E-factor = [total mass of raw materials minus the total mass of product]/ mass of product

PMI = Σ(mass of stoichiometric reactants)/[mass of product]

RME = mass of product /Σ(mass of stoichiometric reactants) × 100

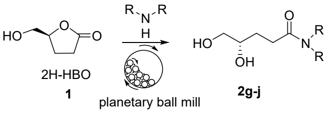
AE = [MW of product] ÷ Σ(MW of stoichiometric reactants) × 100

Table 1 Mechano-aminolysis of 2H-HBO (**1**) with primary amines-Calcul of green metrics



Entry	**RNH$_2$**	**MM g.mol^{-1}**	**mass RNH$_2$**	**mass 2H-HBO 1 MM 116.12**	**Yield %**	**MM g.mol^{-1}**	**Mass 2a-f**	**E Factor Ideal value = 0**	**AE Ideal value = 100%**	**PMI Ideal value = 1**	**RME Ideal value = 100%**
1	$C_{10}H_{21}NH_2$	157.30	204 mg	150 mg	75% **2a**	273.42	265 mg	**0.33**	**100%**	**1.33**	**74%**
2	$C_{12}H_{25}NH_2$	185.35	196 mg	123 mg	76% **2b**	301.47	242 mg	**0.32**	**100%**	**1.32**	**75%**
3	$C_{14}H_{29}NH_2$	213.41	177 mg	96 mg	66% **2c**	329.53	179 mg	**0.52**	**100%**	**1.52**	**65%**
4	$C_{16}H_{33}NH_2$	241.46	232 mg	111 mg	72% **2d**	357.58	245 mg	**0.40**	**100%**	**1.40**	**71%**
5	$C_{18}H_{37}NH_2$	269.51	273 mg	117 mg	71% **2e**	385.63	277 mg	**0.41**	**100%**	**1.41**	**71%**
6	$C_{19}H_{39}NH_2$	283.535	300 mg	123 mg	62% **2f**	399.66	264 mg	**0.60**	**100%**	**1.60**	**62%**

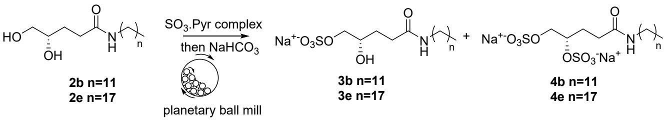
Table 2 Mechano-aminolysis of 2H-HBO (**1**) with secondary amines



Entry	Alkylamine[a] /eq.	rpm / Time(min)[b]	Product	Conversion [%][c]	Yield [%][d]
1	$(CH_3)_2NH$ /1	400 / 71	**2g**	68	NI
2	$(CH_3)_2NH$ /1.5	400 / 71	**2g**	79	NI
3	$(CH_3)_2NH$ /4	400/ 71	**2g**	>97	77
4	$(C_2H_5)_2NH$ /1	400/ 71			
		then 500 / 23	**2h**	0	-
5	pyrrolidine /1	400/ 71	**2i**	88	70
6	piperidine/1	400/ 143	**2j**	73	38
7	piperidine/2	400/ 71	**2j**	91	52

[a] 2H-HBO (1 eq.) and alkylamine (1-4 eq.) in a zirconia jar (20 mL) equipped with 80 zirconia balls of 5 mm diameter were grinded during x cycles in inverse mode in a planetary ball mill. [b] Corresponding to 4, 12 or 24 cycles of 5 min, each cycle is followed by a pause time of 1 min. [c] Corresponding to 4, 12 or 24 cycles of 5 min, each cycle is followed by a pause time of 1 min. [d] Estimated by ^1H NMR (H-4 ratio between **1** and **2**). *E* Isolated by flash chromatography. NI : Not Isolated

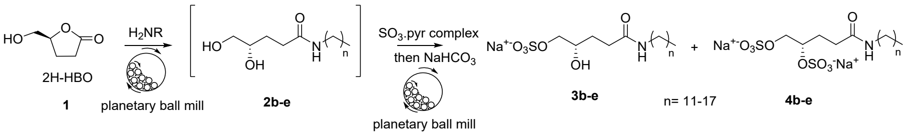
Table 3 Optimization of sulfation reaction in solventless conditions with compound **2b-e**



Entry	Alkylamide[a] (3/4)	SO_3.Pyr	rpm/Time(min)[b]	Auxiliary[c] (eq./OH)	Conversion [%][e]
1	**2b**	4	400 / 59	-	78 (5:95)
2	**2b**	4	400 / 59	NaCl	>97 **4b**
3	**2b**	4	400 / 59	EtOAc[d]	>97 (3:97)
4	**2b**	4	400 / 95	NaCl	>97 **4b**
5	**2b**	1.5	400 / 95	NaCl	83 (7:93)
6	**2e**	2	400 / 95	-	71 (27:73)
7	**2e**	2	500 / 95	-	>97 **4e**
8	**2e**	2	200 / 95	-	47 (28:72)
9	**2e**	1	200 / 95	-	41 (29 :71)
10	**2e**	0.5	200 / 95	-	23 (83 :17)

[a] *N*-Alkyl-amide (1 eq.) and SO_3.Pyr complex were grinded in a zirconia jar (20 mL) equipped with 80 zirconia balls of 5 mm diameter in a P7PL Fritsch ball mill. [b] Corresponding to 7, 10 or 16 cycles of 5 min, each cycle is followed by a pause time of 1 min. [c] The amount of NaCl (120%) is calculated comparatively to the total amount of powder. LAG is defined by η = liquid quantity (μL) / solid reactants mass (mg). [d] $\eta = 2$. [e] Estimated by ^{1}H NMR.

Table 4 One-pot sequential mechanosynthesis of compounds **4b-e –** Calcul of green metrics



Entry	RNH_2	MM	m RNH_2	m 1 MM 116.12	EtOAc LAG MM 88.11 d 0.9	SO_3.Pyr 97% 4eq. MM 159.16	Yield %	$NaHCO_3$ 8 eq MM 84.01	MM	m 4b-e	E Factor Ideal value = 0	AE Ideal value = 100 %	PMI Ideal value = 1	RME Ideal value = 100%
5	$C_{12}H_{25}NH_2$	185.35	341 mg	214 mg	0.89 mL / 801 mg 4.891 eq.	1180 mg 4.02 eq.	77% **4b**	1240 mg 8 eq.	505.55	718 mg	**1.62**	**79.87%**	**2.62**	**38%**
6	$C_{14}H_{29}NH_2$	213.41	209 mg	114 mg	0.57 mL / 513 mg 5.93 eq.	621 mg 3.97 eq.	62% **4c**	655 mg 7.95 eq.	533.60	324 mg	**1.72**	**80.75%**	**2.71**	**37%**
7	$C_{16}H_{33}NH_2$	241.46	189 mg	91 mg	0.47 mL / 423 mg 6.12 eq.	497 mg 3.98 eq.	79% **4d**	524 mg 8 eq.	561.66	347 mg	**1.95**	**81.53%**	**2.95**	**34%**
9	$C_{18}H_{37}NH_2$	269.51	257 mg	111 mg	0.59 mL / 531 mg 6.3 eq.	608 mg 3.99 eq.	79% **4e**	640 mg 8 eq.	589.71	446 mg	**1.58**	**82.25 %**	**3.05**	**33%**

Solvent conditions

Aminolysis (step 1)

RNH$_2$	**MM**	**m RNH$_2$** **1.05 eq.**	**m 1** **MM 116.12**	**Isopropanol** **MM 60.01** **d 0.786**	**Yield %**	**MM**	**m 2a-f**	**E Factor** **Ideal value = 0**	**AE** **Ideal value = 100%**	**PMI** **Ideal value = 1**	**RME** **Ideal value = 100%**
$C_{12}H_{25}NH_2$	185.35	638 mg 1 eq.	400 mg	6.9 ml 5.42 g 26.2 eq.	83% **2b**	301.47	860 mg	**6.5**	**100%**	**7.5**	**13.3 %**
$C_{14}H_{29}NH_2$	213.41	734 mg 1eq.	400 mg	6.9 ml 5.4 g 26,2 eq.	71% **2c**	329.53	807 mg	**7.1**	**100%**	**8.1**	**12.3%**
$C_{16}H_{33}NH_2$	241.46	654 mg 1.05 eq	300 mg	5.2 ml 4.1 g 26.3 eq.	77% **2d**	357.58	719 mg	**6**	**100%**	**7**	**14,2%**
$C_{18}H_{37}NH_2$	269.51	488 mg 1.05 eq.	200 mg	3.5 ml 2.75 g 25.3 eq.	74% **2e**	385.63	495 mg	**5.94**	**100%**	**6.94**	**14.4%**

Sulfatation (step 2)

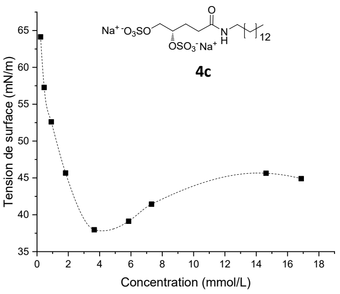
Entry	**Amide**	**MM** **g.mol^{-1}**	**Mass amide** **mg**	**Pyridine** **V mL** **Mass g** **MM 79.1**	**SO$_3$.Pyr 97%** **4eq.** **MM 159.16**	**NaHCO$_3$** **8 eq** **MM 84.01**	**MM** **4b-e**	**Yield** **%**	**Mass** **4b-e** **mg**	**E Factor** **Ideal value = 0**	**AE** **Ideal value = 100 %**	**PMI** **Ideal value = 1**	**RME** **Ideal value = 100%**
5	**2b**	301.47	769	12.0 mL 11.80 g	1.627 g	1.706 g	505.55	60	779 **4b**	**19.4**	**81%**	**20.4**	**4.9%**
6	**2c**	329.53	605	11.0 mL 10.80 g	1.170 g	1.30 g	533.60	59	578 **4c**	**23**	**81.9%**	**24**	**4.16%**
7	**2d**	357.58	545	9.0 mL 8.84 g	970 mg	1.02 g	561.66	71	606 **4e**	**17.8**	**82.6**	**18.8**	**5.3%**
9	**2e**	385.63	553	14.0 mL 13.75 g	913 mg	903 mg	589.71	73	615 **4f**	**25.2**	**83.3**	**26.2**	**3.8%**

These metric values are been calculated without considering the work-up step.

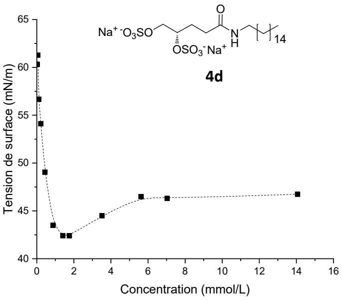
8- Procedure for CMC determination

CMC determination were realized on a selection of disulfated molecules with potential surfactant properties. First, surfactant solutions at different concentrations were prepared by dissolving a known quantity of synthetized molecule in ultrapure water. The three studied molecules were easily soluble at room temperature. Each solution was then put in a crystallizer. After standing for 30 min (corresponding to the time required to reach the equilibrium surface tension), the surface tension was measured with a TC1 tensiometer (Lauda Scientific) using the Du Noüy ring method. The temperature of surface tension measurement was so maintained at 25±1 °C and all measurements were repeated three times. The surface tension measurements at high concentration were limited due to the available quantity of the surfactants. A concentration-surface tension curve was then obtained and the CMC was determined at the minimum of the break point.

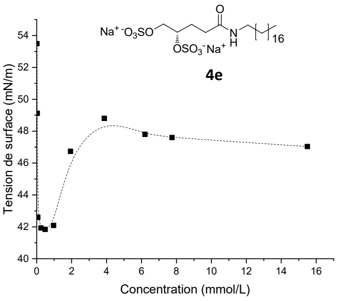
The following curves were obtained. Each point corresponds to the average of three measurements.



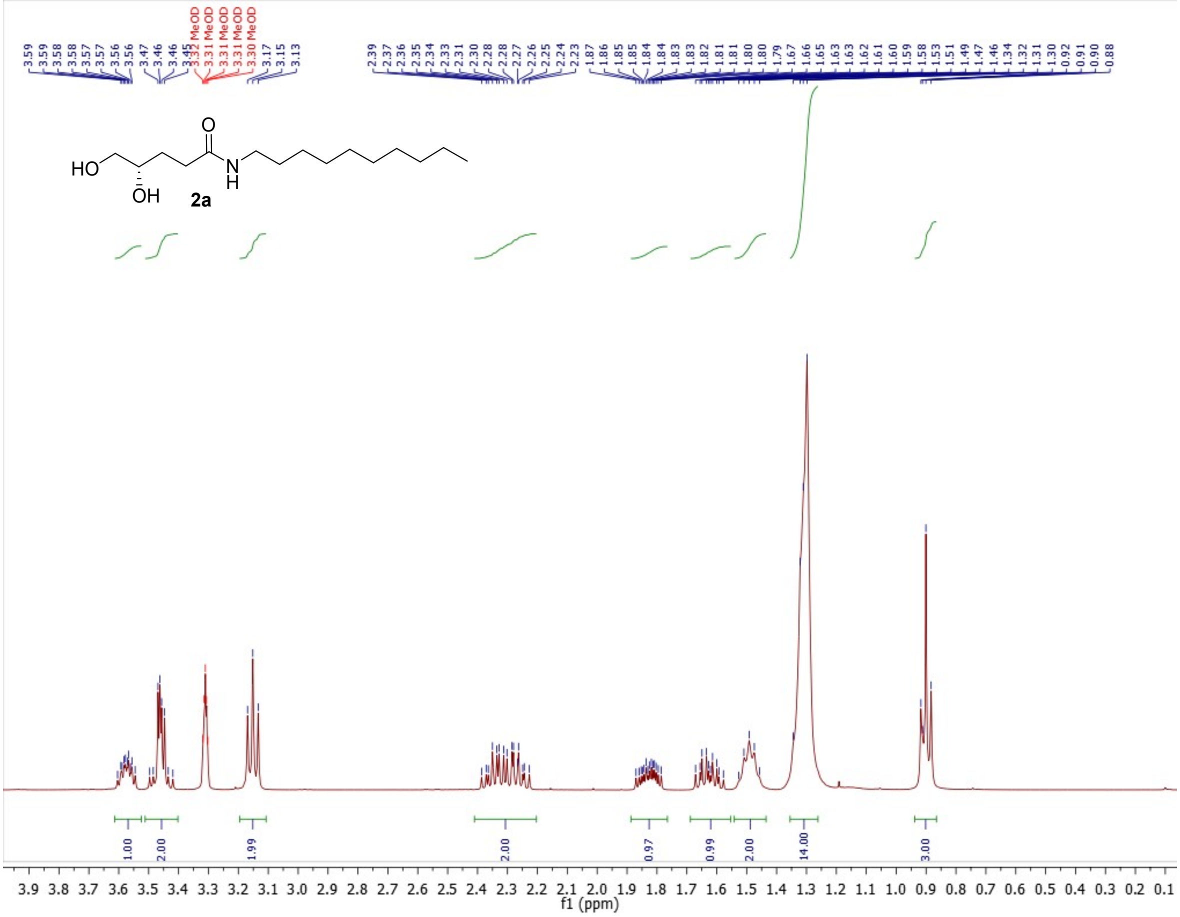
CMC= 4.0 ± 0.5 mmol.L^{-1}



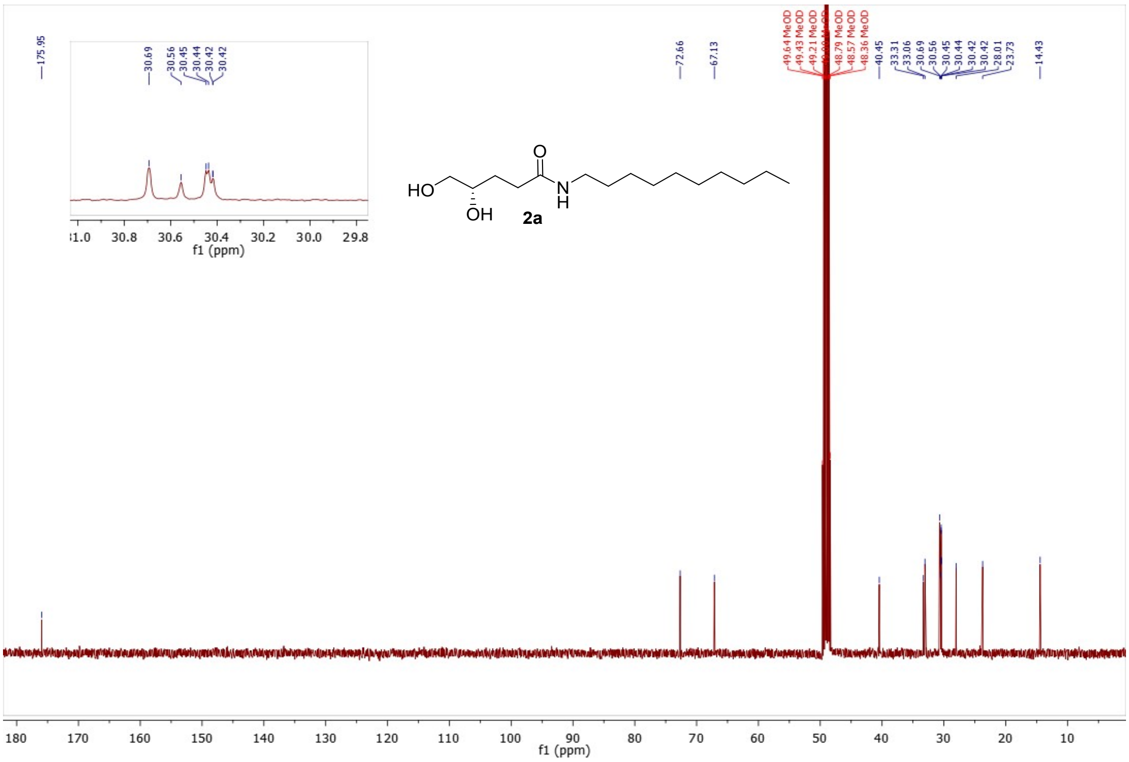
CMC= 1.4 ± 0.2 mmol.L^{-1}



CMC= 0.6 ± 0.06 mmol.L^{-1}



8- NMR Spectra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48.79 MeOD
48.57 MeOD
48.36 MeOD
40.45
33.31
33.06
30.69
30.56
30.45
30.44
30.42
30.42
28.01
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14.43
HO
OH
O
N
H
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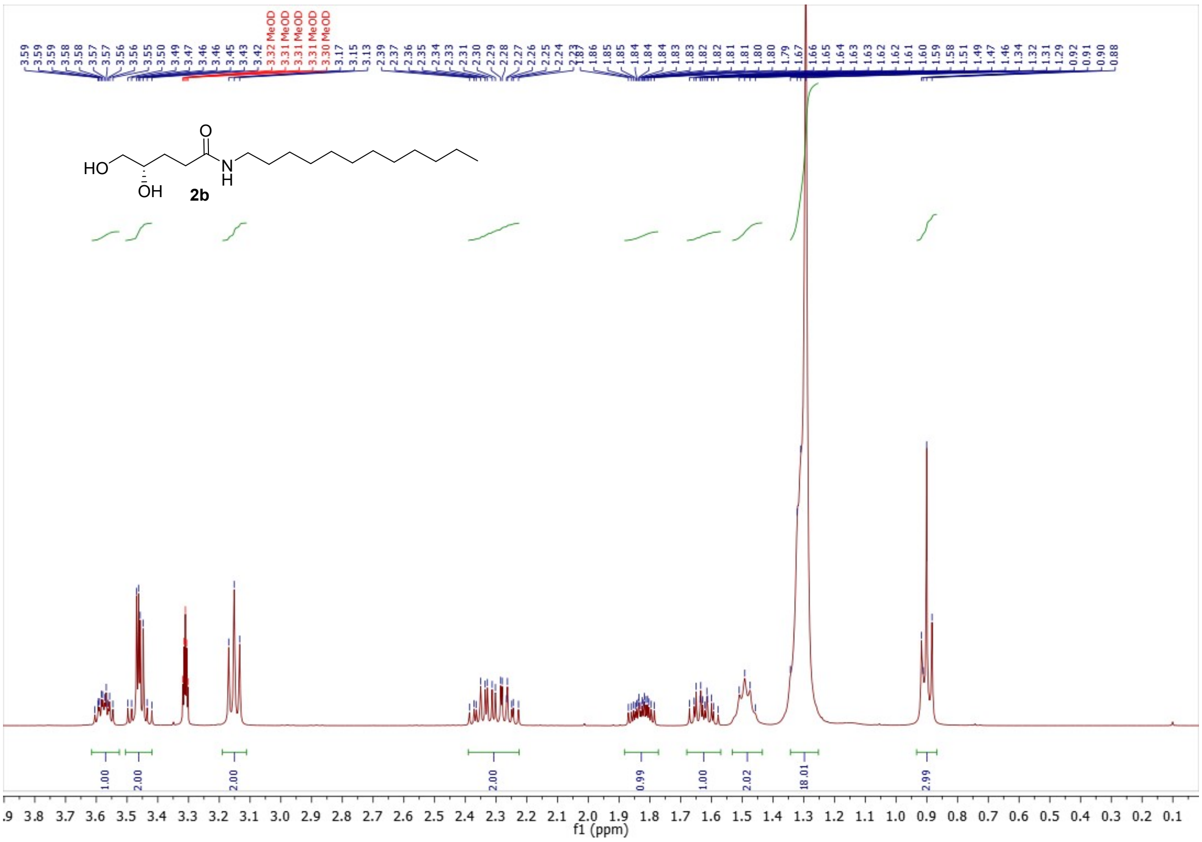
f1 (ppm)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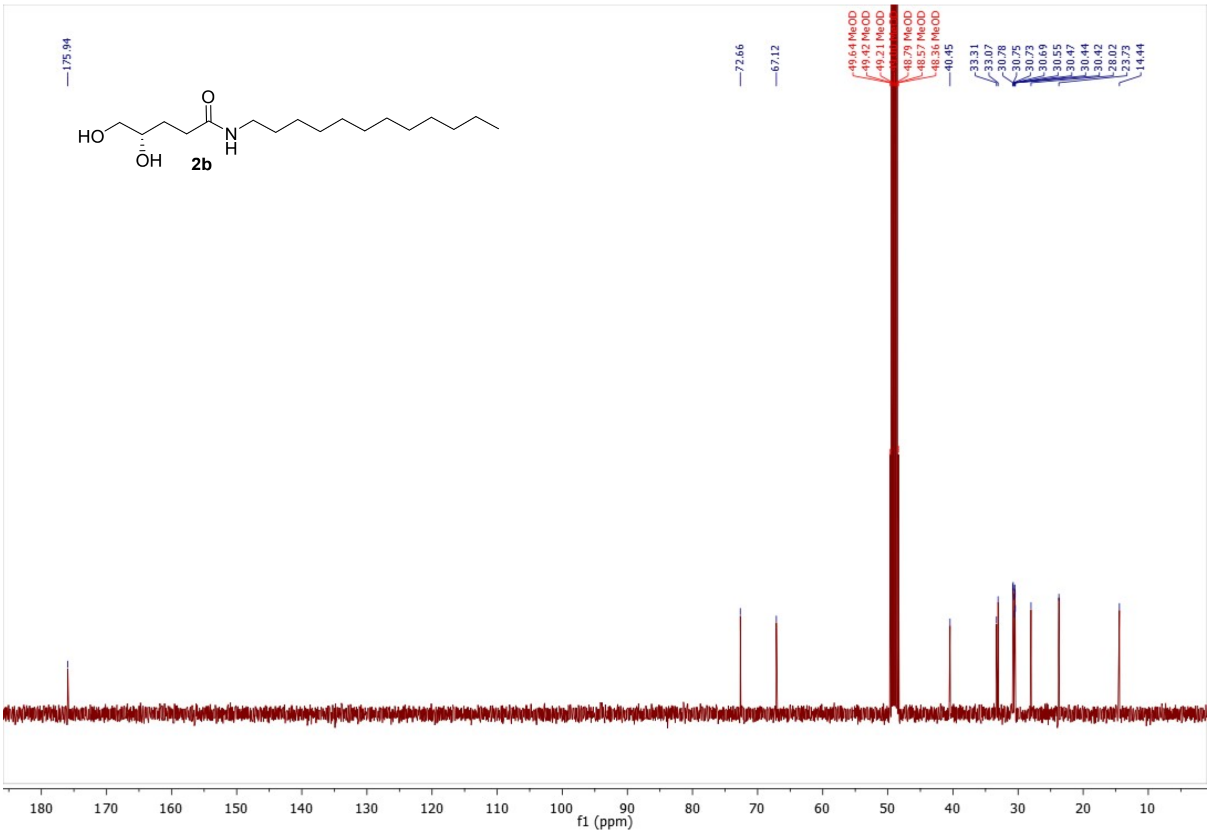
0.1
f1 (ppm)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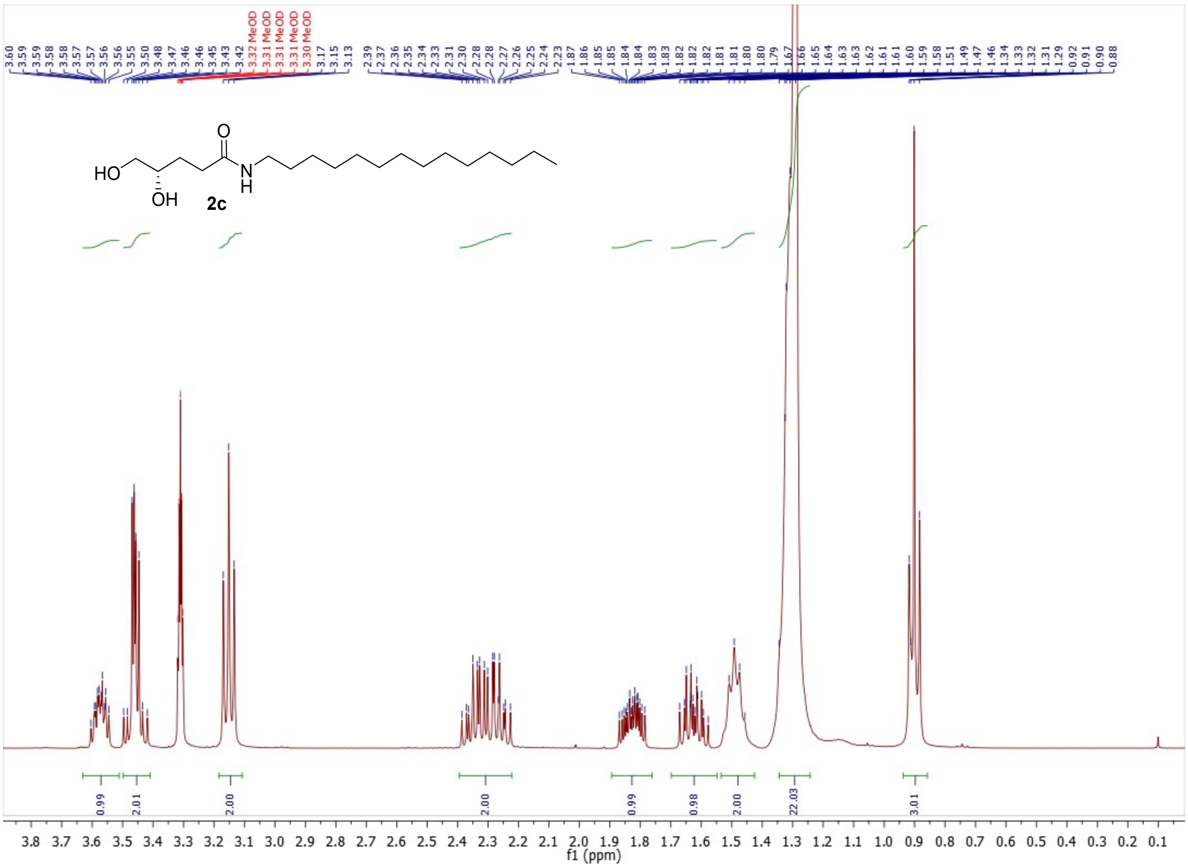
f1 (ppm)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H
OH
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2.00
2.00
0.99
0.98
2.00
22.03
3.01
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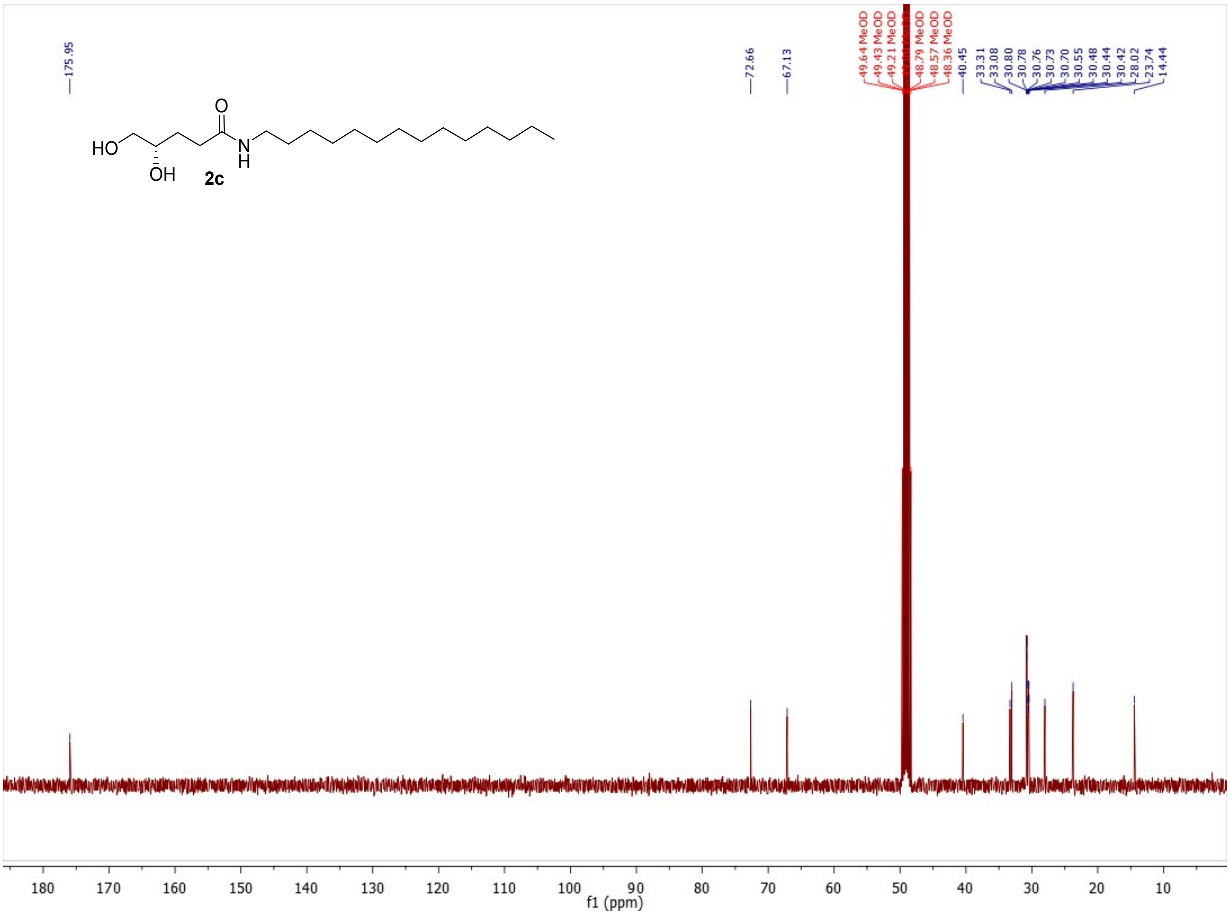
f1 (ppm)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67.13
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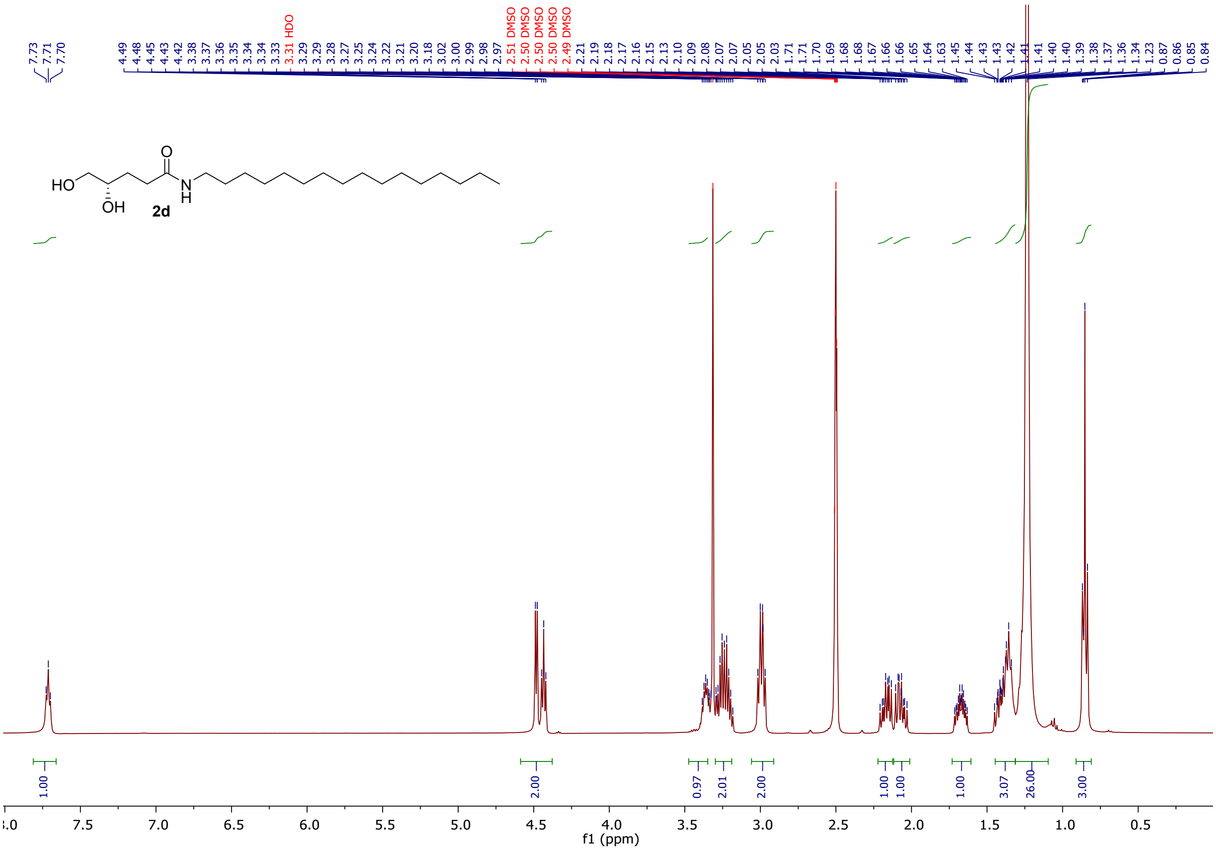
HO
O
N
H
OH
2c
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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3.37
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3.34
3.34
3.33
3.31 HDO
3.29
3.29
3.28
3.27
3.25
3.24
3.22
3.21
3.20
3.18
3.02
3.00
2.99
2.98
2.97
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
2.21
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2.13
2.10
2.09
2.08
2.07
2.07
2.05
2.05
2.03
1.71
1.71
1.70
1.69
1.68
1.68
1.67
1.66
1.66
1.65
1.64
1.63
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1.41
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OH
O
N
H
2d
1.00
2.00
0.97
2.01
2.00
1.00
1.00
1.00
3.07
26.00
3.00
8.0
7.5
7.0
6.5
6.0
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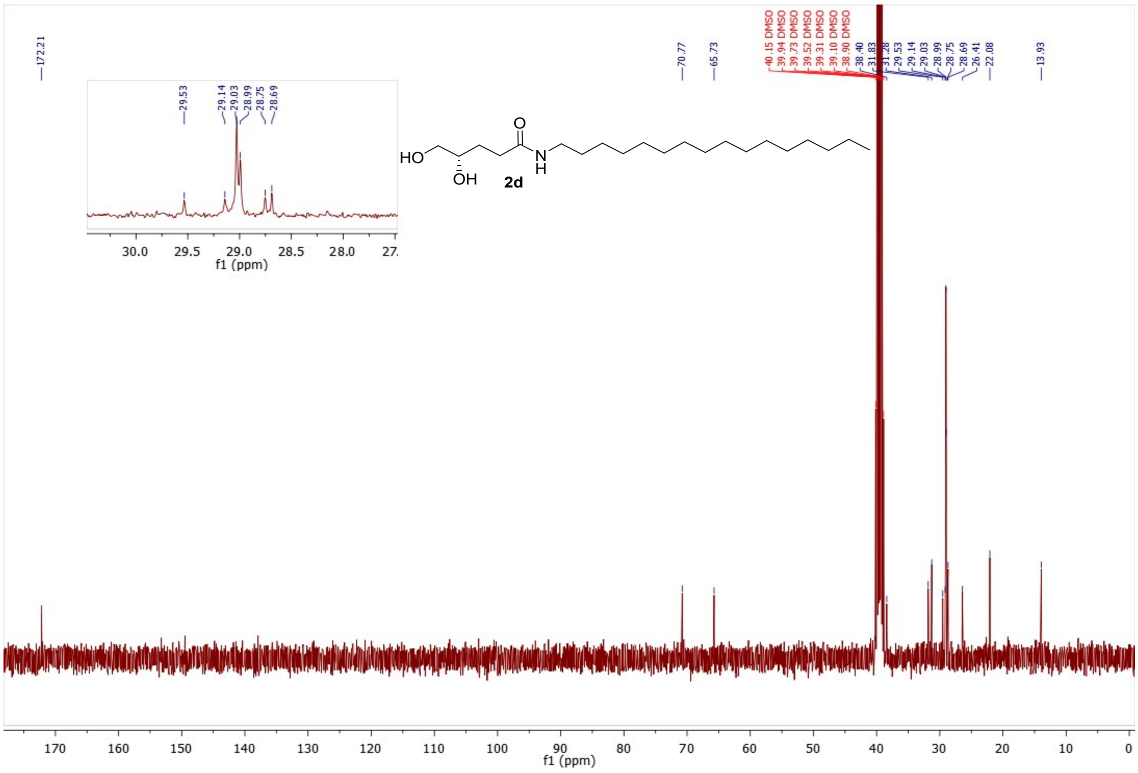
f1 (ppm)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39.94 DMSO
39.73 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
38.90 DMSO
38.40
31.83
31.28
29.53
29.14
29.03
28.99
28.75
28.69
26.41
22.08
13.93
29.53
29.14
29.03
28.99
28.75
28.69
30.0
29.5
29.0
28.5
28.0
27.
f1 (ppm)
HO
OH
O
N
H
2d
170
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140
130
120
110
100
90
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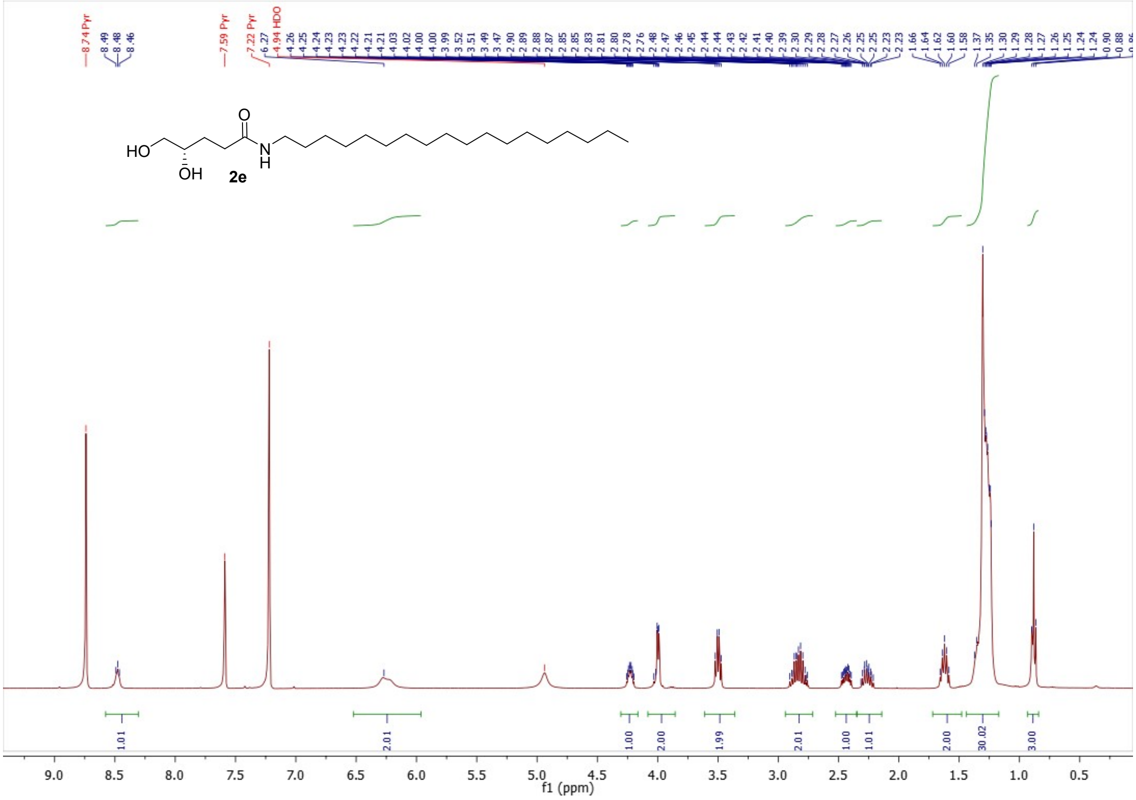
50
40
30
20
10
0
f1 (ppm)



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7.59 Pyr
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6.27
4.94 HDO
4.26
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4.24
4.23
4.23
4.22
4.21
4.21
4.03
4.02
4.00
4.00
3.99
3.52
3.51
3.49
3.47
2.90
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2.87
2.85
2.85
2.83
2.81
2.80
2.78
2.76
2.48
2.47
2.46
2.45
2.44
2.44
2.43
2.42
2.41
2.40
2.39
2.30
2.29
2.28
2.27
2.26
2.25
2.25
2.23
2.23
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1.60
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1.29
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1.27
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1.24
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0.88
HO
OH
O
N
H
2e
1.01
2.01
1.00
2.00
1.99
2.01
1.00
1.01
2.00
30.02
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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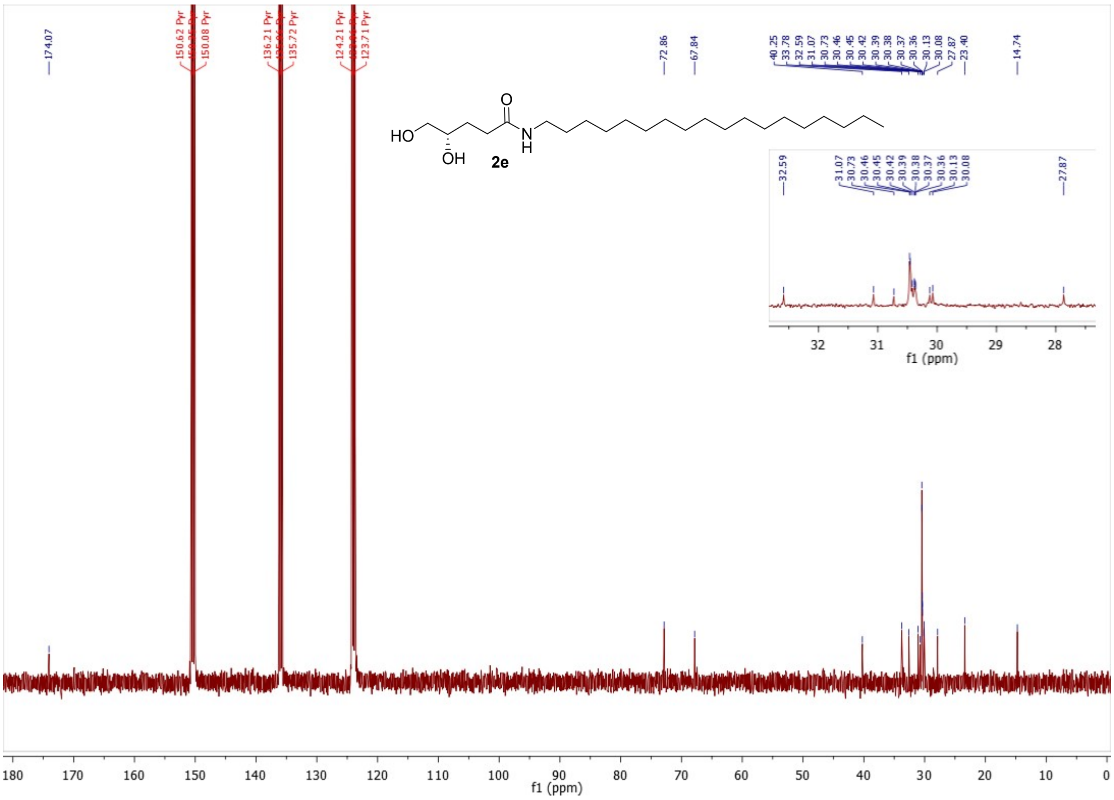

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150.08 Pyr
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135.72 Pyr
124.21 Pyr
123.71 Pyr
72.86
67.84
40.25
33.78
32.59
31.07
30.73
30.46
30.45
30.42
30.39
30.38
30.37
30.36
30.13
30.08
27.87
23.40
14.74
HO
OH
O
N
H
2e
32.59
31.07
30.73
30.46
30.45
30.42
30.39
30.38
30.37
30.36
30.13
30.08
27.87
32
31
30
29
28
f1 (ppm)
180
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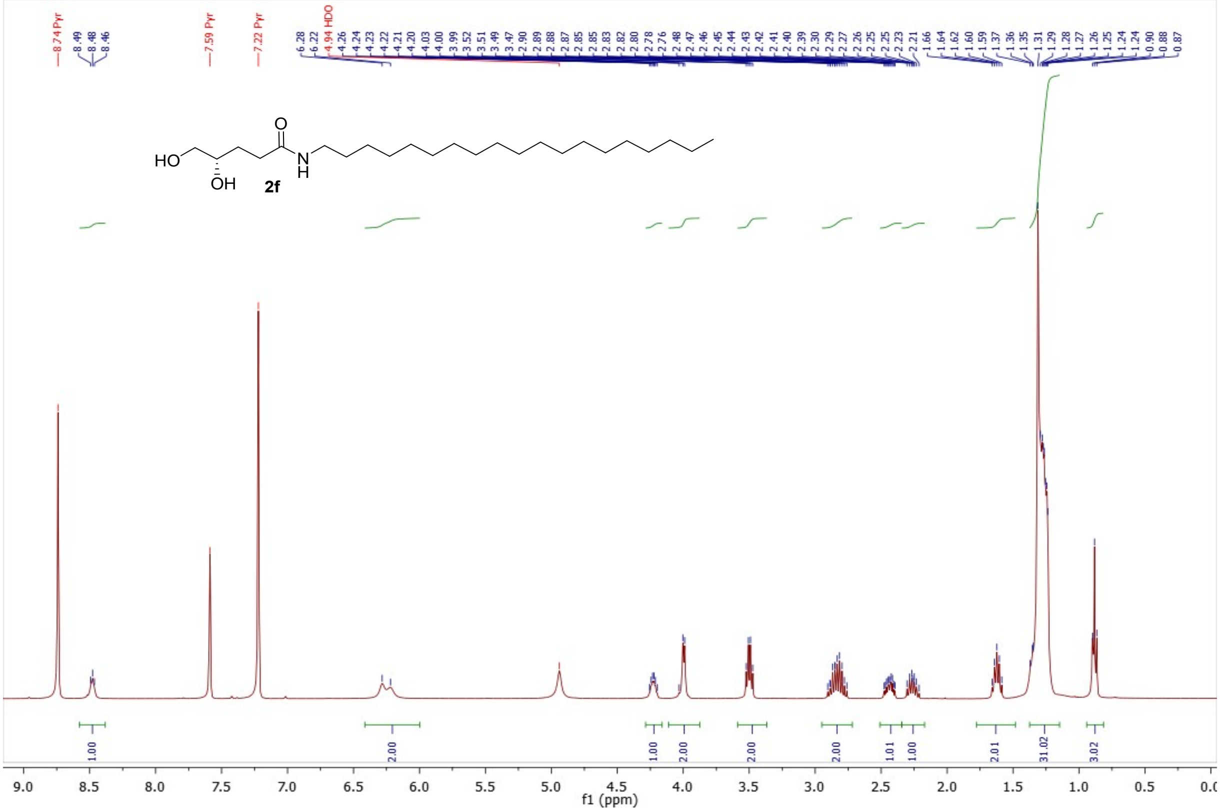
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.74 Pyr
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8.48
8.46
7.59 Pyr
7.22 Pyr
6.28
6.22
4.94 HDO
4.26
4.24
4.23
4.22
4.21
4.20
4.03
4.00
3.99
3.52
3.51
3.49
3.47
2.90
2.89
2.88
2.87
2.85
2.85
2.83
2.82
2.80
2.78
2.76
2.48
2.47
2.46
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.30
2.29
2.27
2.26
2.25
2.25
2.23
2.21
1.66
1.64
1.62
1.60
1.59
1.37
1.36
1.35
1.31
1.29
1.28
1.27
1.26
1.25
1.24
1.24
0.90
0.88
0.87
O
HO
N
H
OH
2f
1.00
2.00
1.00
2.00
2.00
2.00
1.01
1.00
2.01
31.02
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
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2.5
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1.0
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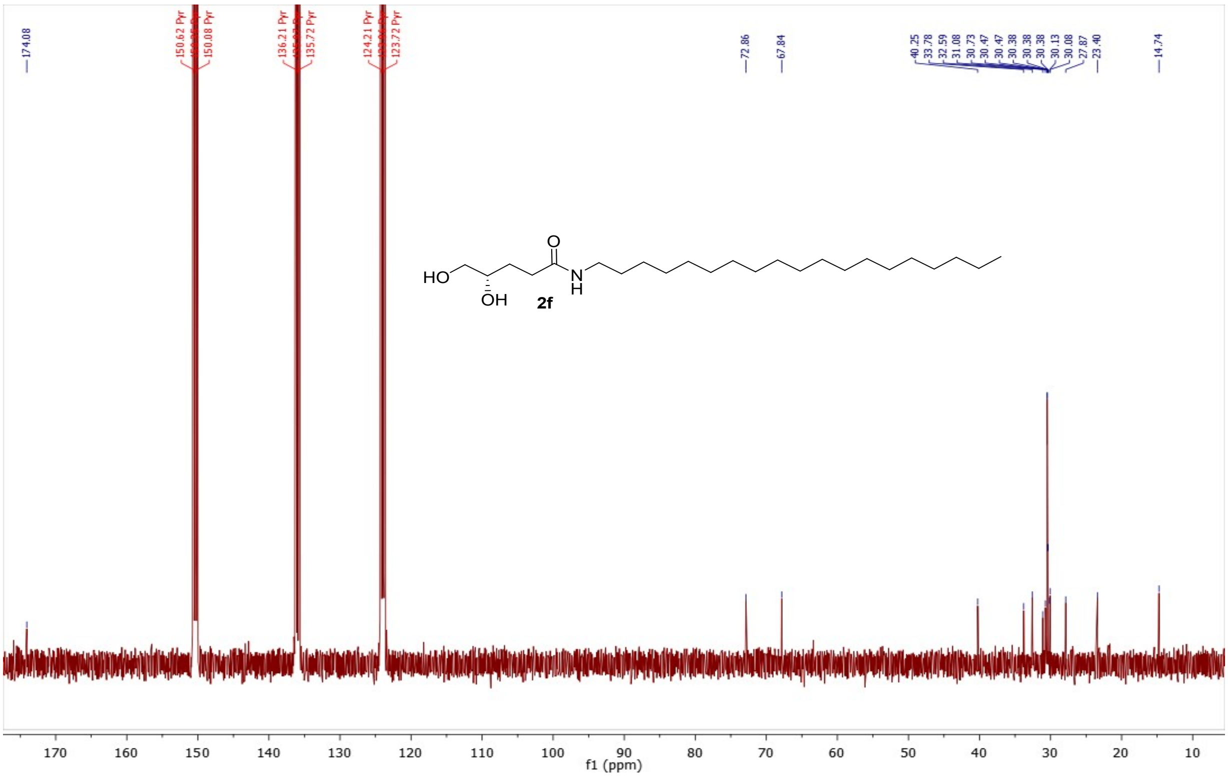
0.0
f1 (ppm)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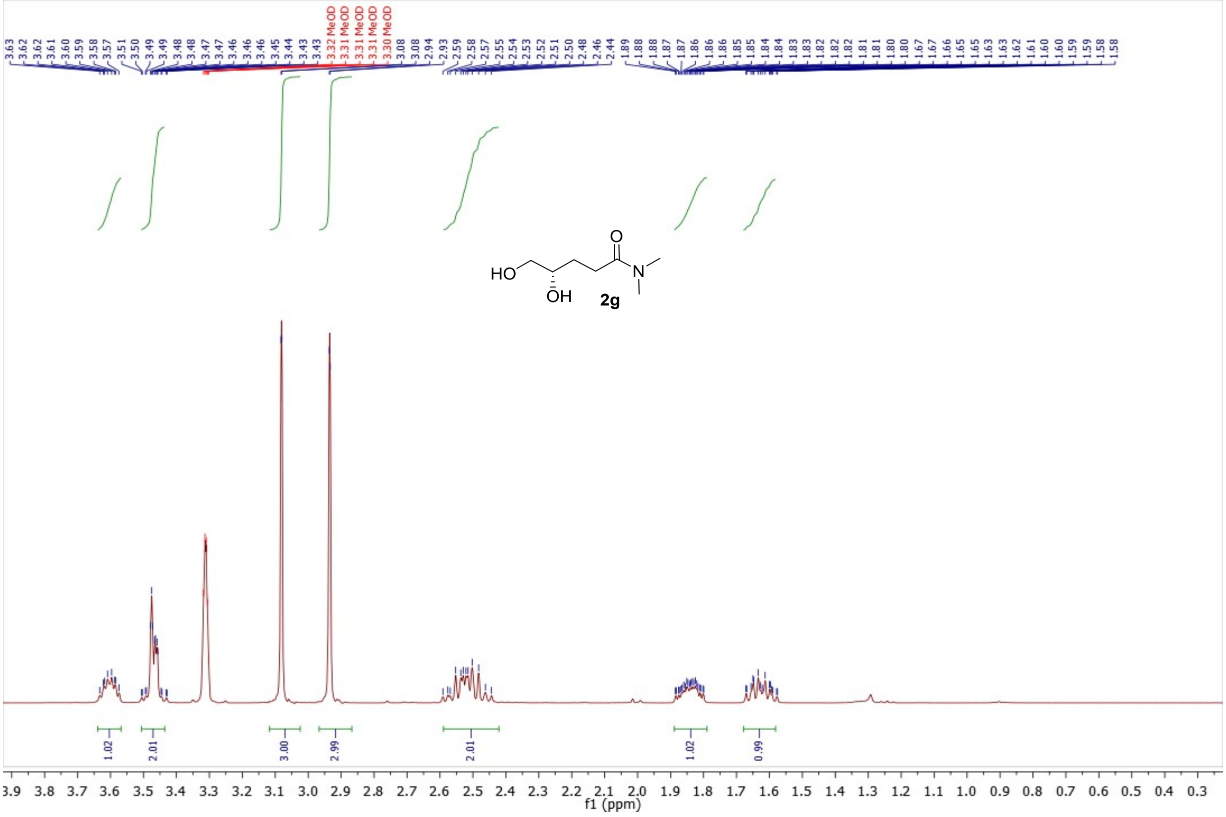
150.08 Pyr
136.21 Pyr
135.72 Pyr
124.21 Pyr
123.72 Pyr
72.86
67.84
40.25
33.78
32.59
31.08
30.73
30.47
30.47
30.38
30.38
30.38
30.13
30.08
27.87
23.40
14.74
O
HO
N
H
OH
2f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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3.48
3.47
3.47
3.46
3.46
3.46
3.45
3.44
3.43
3.43
3.32 MeOD
3.31 MeOD
3.31 MeOD
3.31 MeOD
3.30 MeOD
3.08
3.08
2.94
2.93
2.59
2.58
2.57
2.55
2.54
2.53
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2.51
2.50
2.48
2.46
2.44
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1.88
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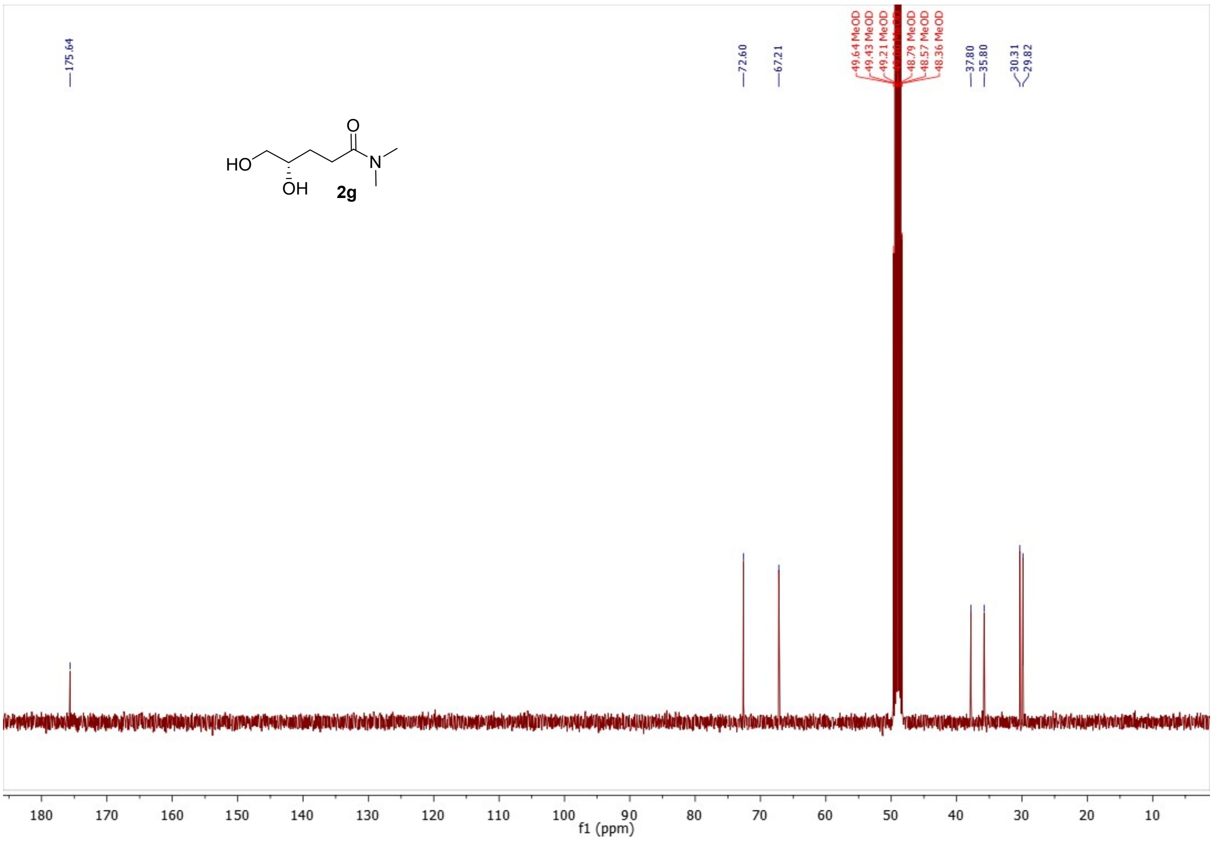
1.82
1.82
1.81
1.81
1.80
1.80
1.67
1.67
1.66
1.65
1.65
1.63
1.63
1.62
1.61
1.60
1.60
1.59
1.59
1.58
1.58
HO
OH
O
N
2g
1.02
2.01
3.00
2.99
2.01
1.02
0.99
3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3
f1 (ppm)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67.21
49.64 MeOD
49.43 MeOD
49.21 MeOD
48.79 MeOD
48.57 MeOD
48.36 MeOD
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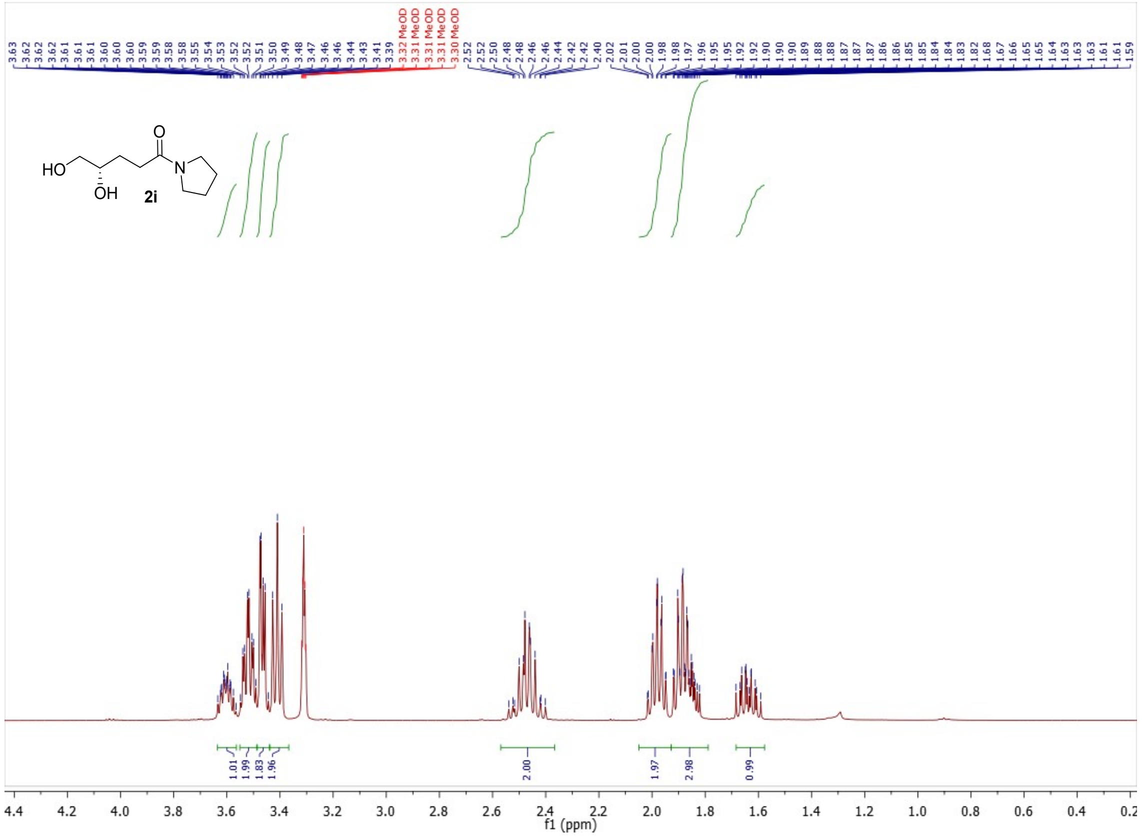
29.82
HO
OH
O
N
2g
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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3.48
3.47
3.46
3.46
3.44
3.43
3.41
3.39
3.32 MeOD
3.31 MeOD
3.31 MeOD
3.30 MeOD
2.52
2.52
2.50
2.48
2.48
2.46
2.46
2.44
2.42
2.42
2.40
2.02
2.01
2.00
2.00
1.98
1.98
1.97
1.96
1.95
1.95
1.92
1.92
1.90
1.90
1.90
1.89
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1.88
1.87
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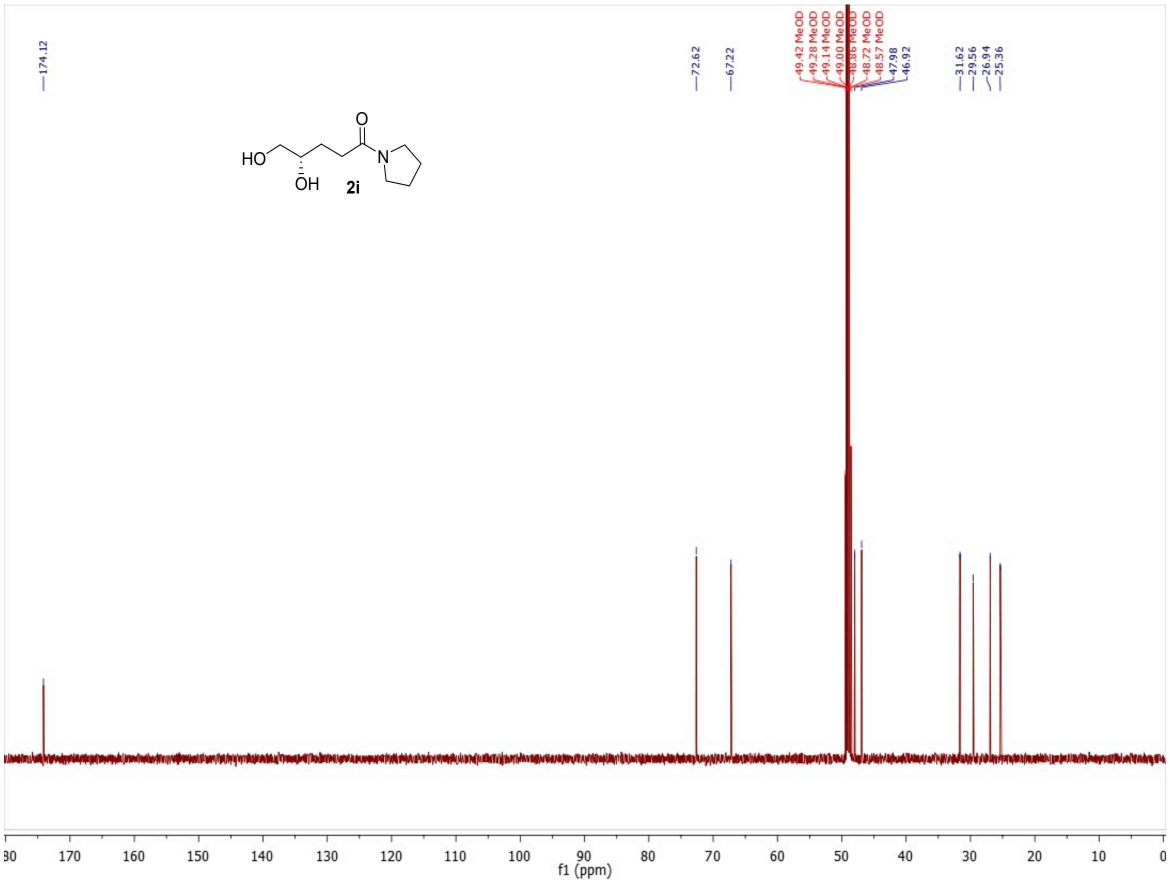
1.61
1.59
HO
OH
O
N
2i
1.01
1.99
1.83
1.96
2.00
1.97
2.98
0.99
4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2
f1 (ppm)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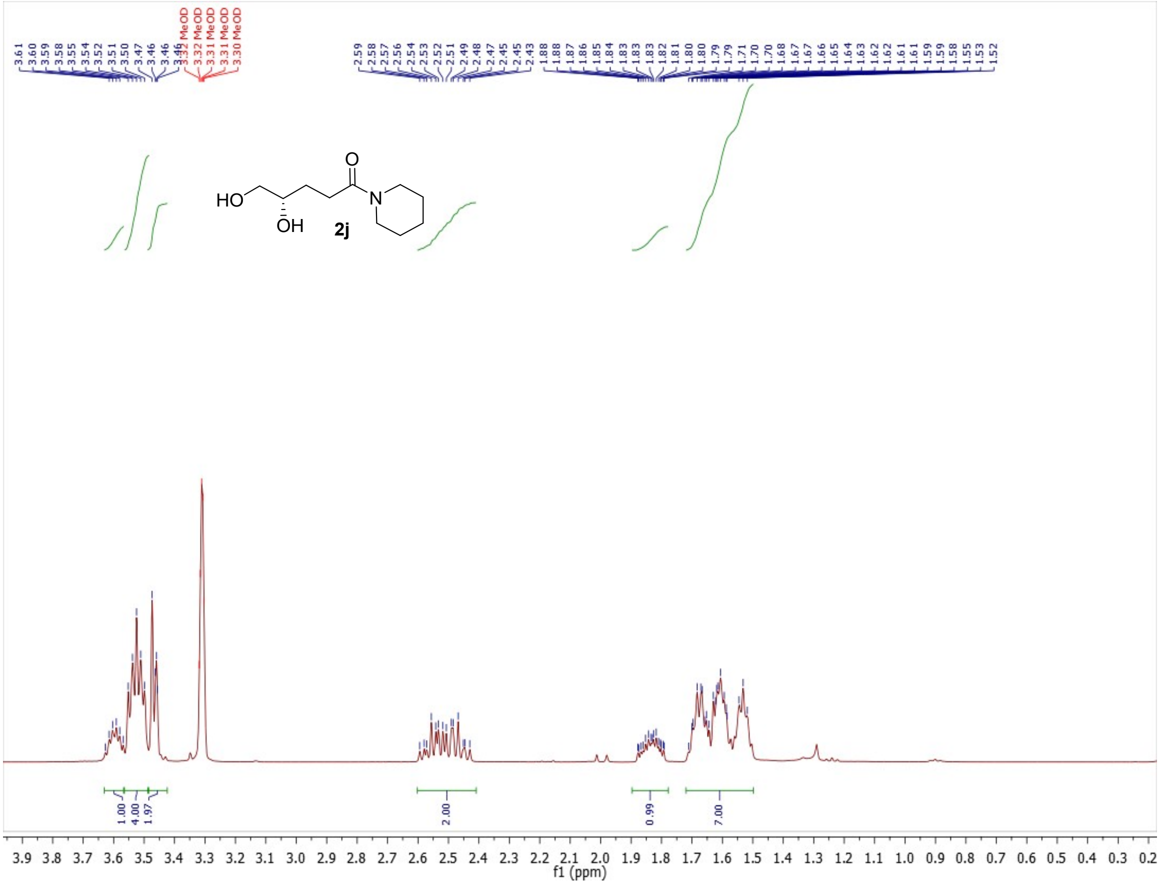
48.86 MeOD
48.72 MeOD
48.57 MeOD
47.98
46.92
31.62
29.56
26.94
25.36
HO
OH
O
N
2i
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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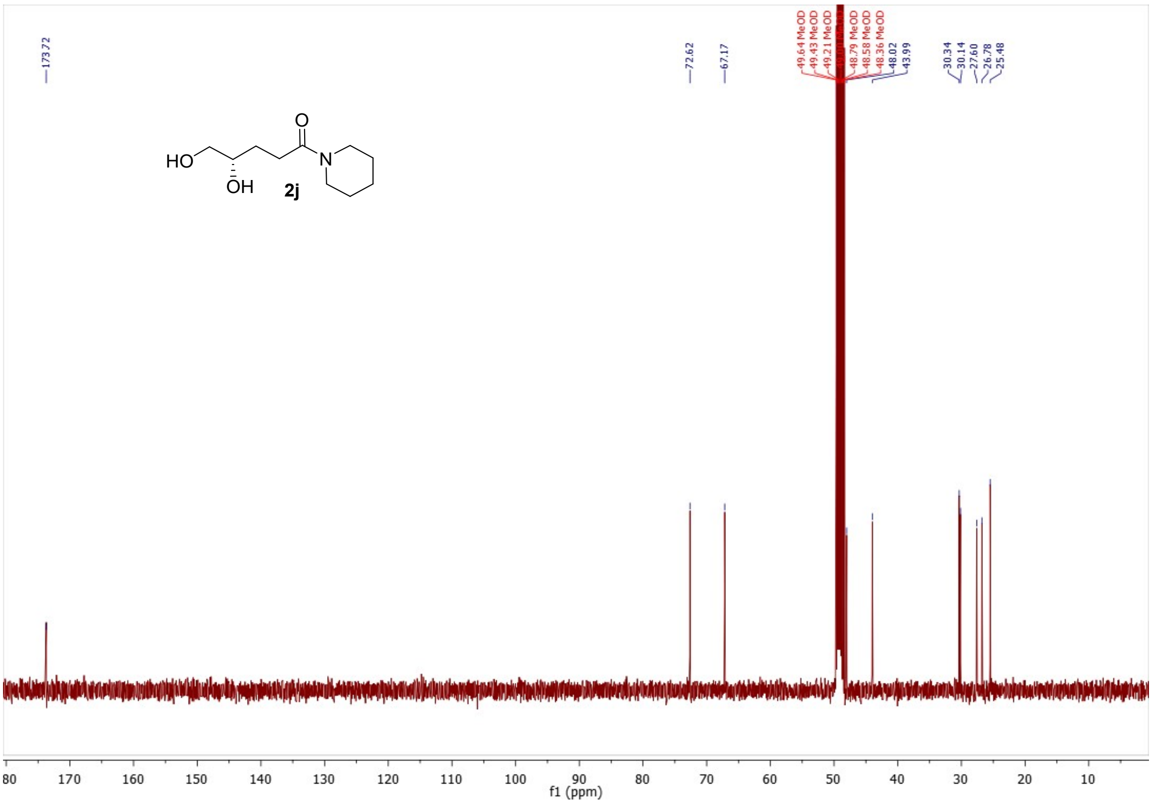
3.32 MeOD 3.32 MeOD 3.31 MeOD 3.31 MeOD 3.30 MeOD
2.59 2.58 2.57 2.56 2.54 2.53 2.52 2.51 2.49 2.48 2.47 2.45 2.45 2.43
1.88 1.88 1.87 1.86 1.85 1.84 1.83 1.83 1.82 1.81 1.80 1.80 1.79 1.79 1.71 1.70 1.68 1.67 1.67 1.66 1.65 1.64 1.63 1.62 1.62 1.61 1.61 1.59 1.59 1.58 1.55 1.53 1.52
HO
OH
O
N
2j
1.00
4.00
1.97
2.00
0.99
7.00
3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2
f1 (ppm)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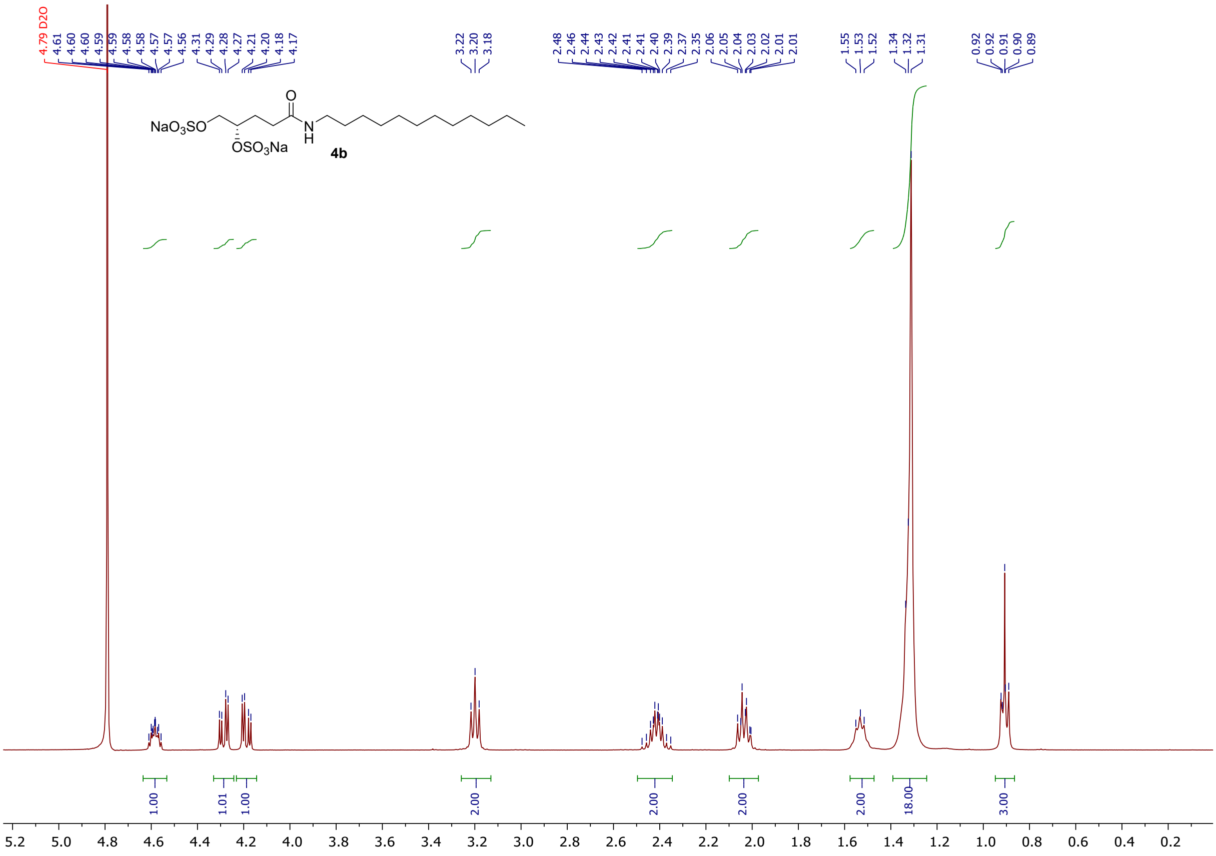
48.02
43.99
30.34 30.14 27.60 26.78 25.48
HO
OH
O
N
2j
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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4.57
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4.29
4.28
4.27
4.21
4.20
4.18
4.17
3.22
3.20
3.18
2.48
2.46
2.44
2.43
2.42
2.41
2.41
2.40
2.39
2.37
2.35
2.06
2.05
2.04
2.03
2.02
2.01
2.01
1.55
1.53
1.52
1.34
1.32
1.31
0.92
0.92
0.91
0.90
0.89
NaO3SO
O
N
H
OSO3Na
4b
1.00
1.01
1.00
2.00
2.00
2.00
2.00
18.00
3.00
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
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1.8
1.6
1.4
1.2
1.0
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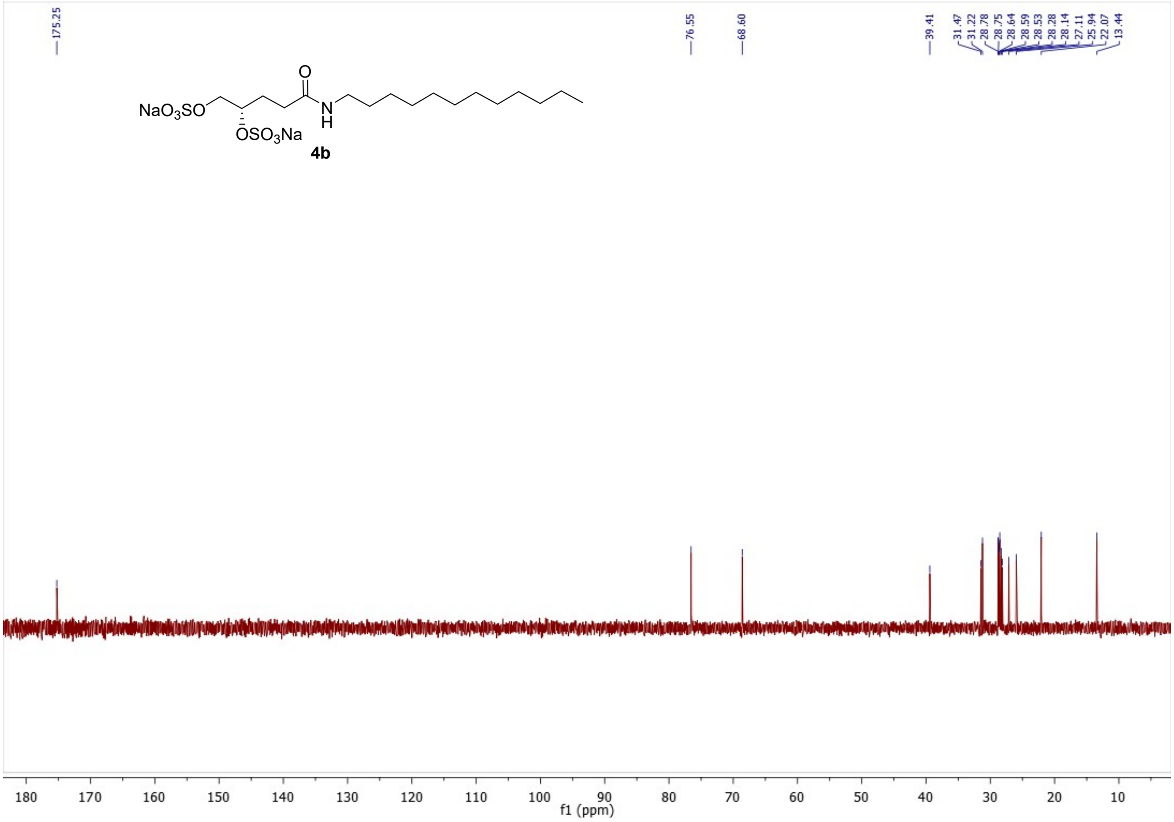
0.4
0.2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28.28
28.14
27.11
25.94
22.07
13.44
NaO3SO
O
N
H
OSO3Na
4b
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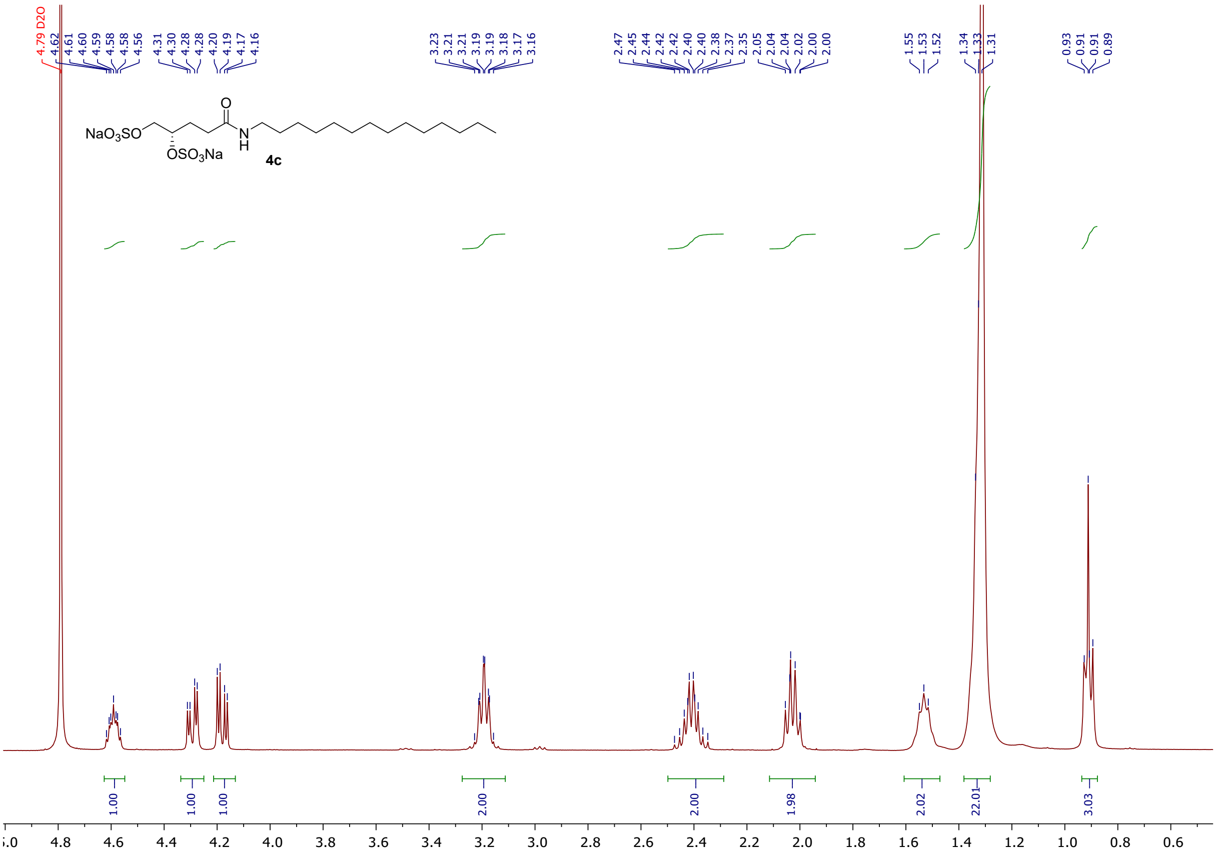
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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3.18
3.17
3.16
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2.45
2.44
2.42
2.42
2.40
2.40
2.38
2.37
2.35
2.05
2.04
2.04
2.02
2.00
2.00
1.55
1.53
1.52
1.34
1.33
1.31
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0.91
0.91
0.89
NaO3SO
O
N
H
OSO3Na
4c
1.00
1.00
1.00
2.00
2.00
1.98
2.02
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3.03
.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
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2.6
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2.2
2.0
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1.6
1.4
1.2
1.0
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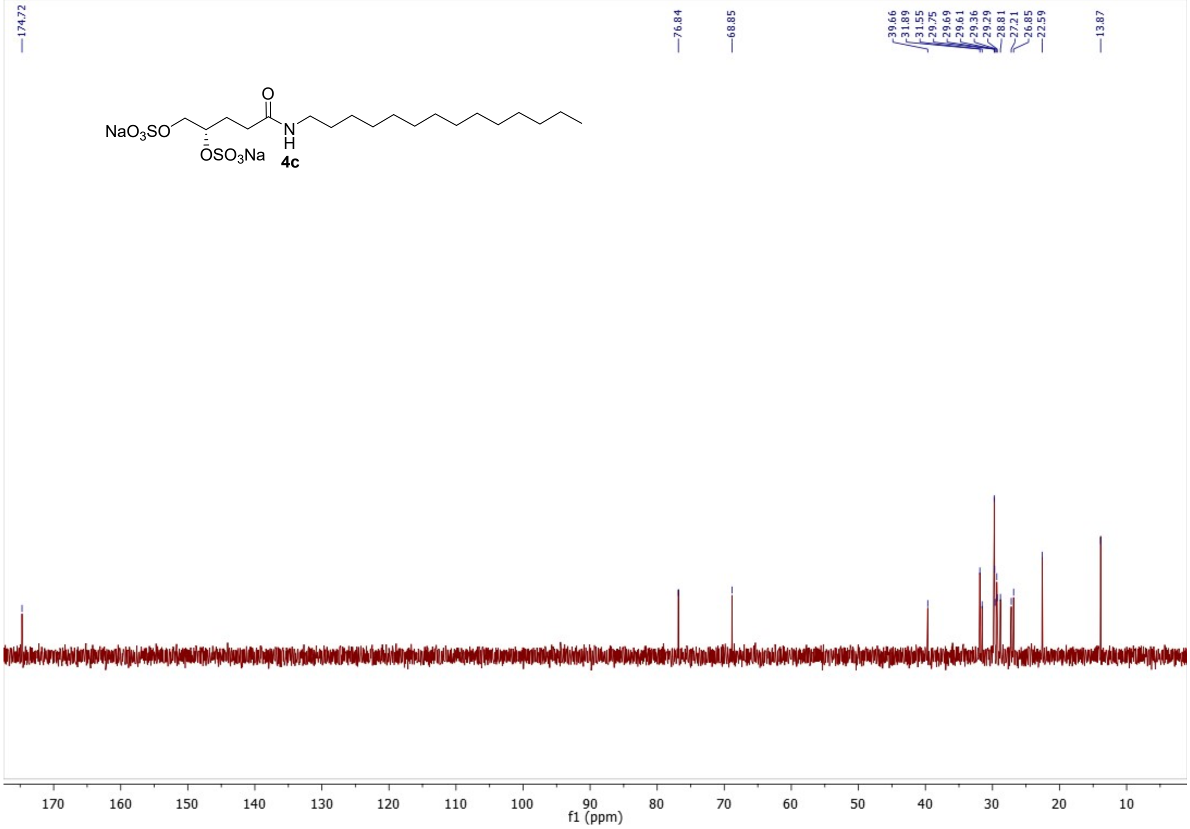
0.6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29.36
29.29
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27.21
26.85
22.59
13.87
NaO3SO
O
N
H
OSO3Na
4c
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140
130
120
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100
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80
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60
50
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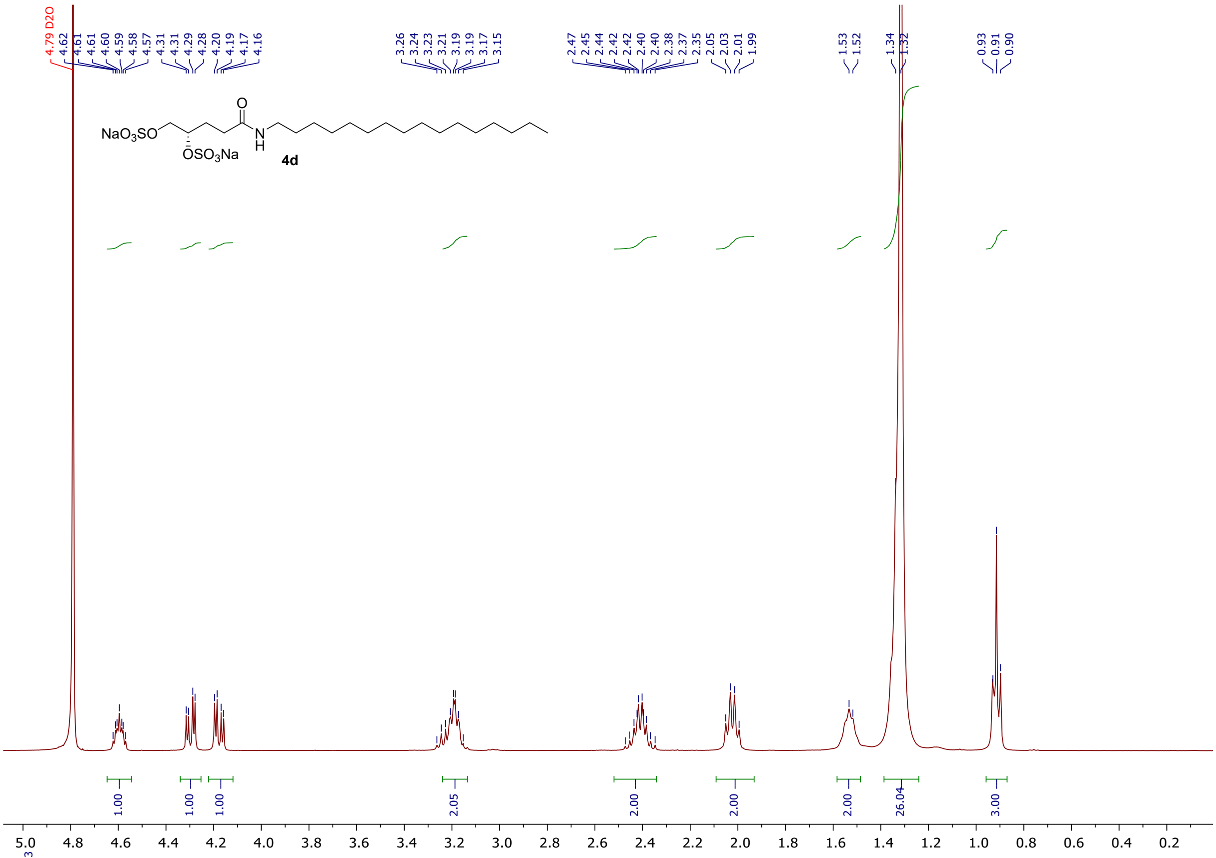
30
20
10
f1 (ppm)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4.60
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4.19
4.17
4.16
3.26
3.24
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2.45
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2.38
2.37
2.35
2.05
2.03
2.01
1.99
1.53
1.52
1.34
1.32
0.93
0.91
0.90
NaO3SO
OSO3Na
O
N
H
4d
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1.00
1.00
2.05
2.00
2.00
2.00
26.04
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4.6
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4.0
3.8
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2.6
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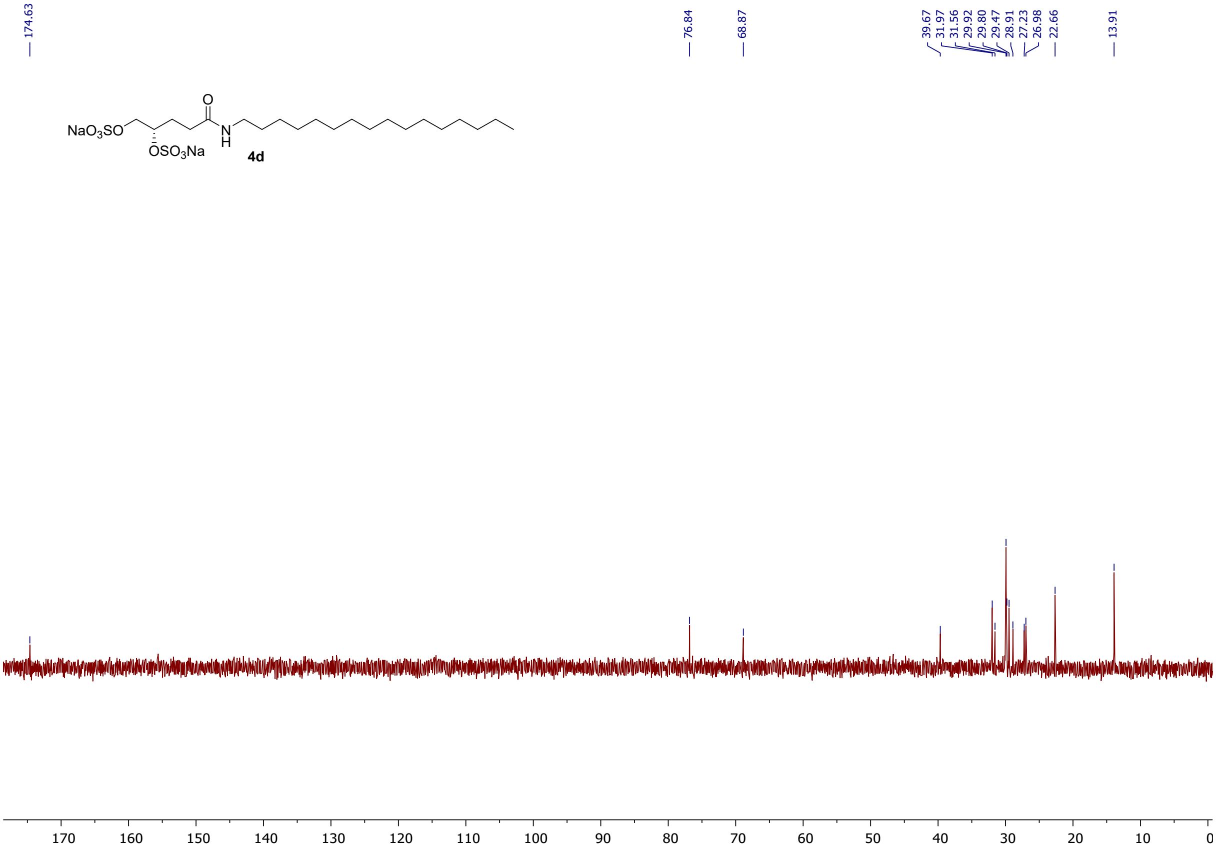
0.4
0.2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28.91
27.23
26.98
22.66
13.91
NaO3SO
OSO3Na
O
N
H
4d
170
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70
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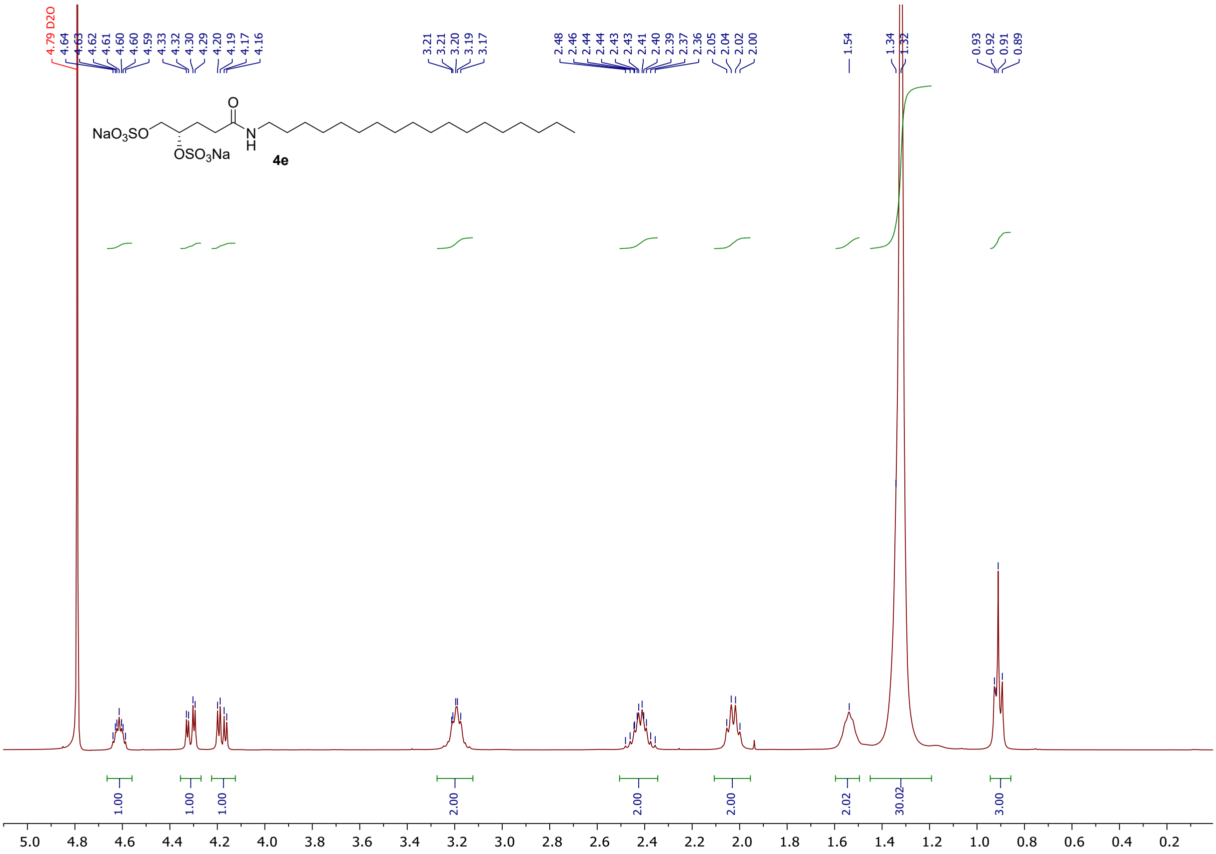
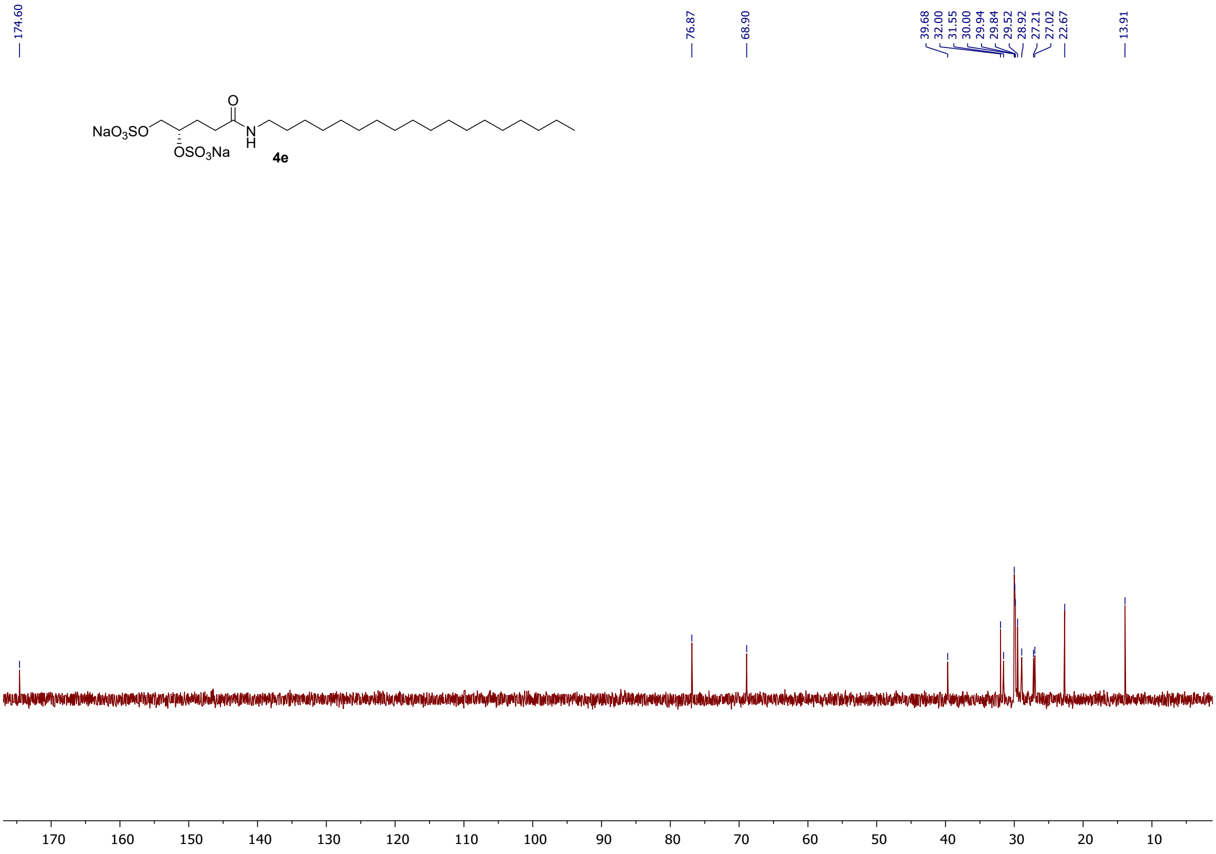
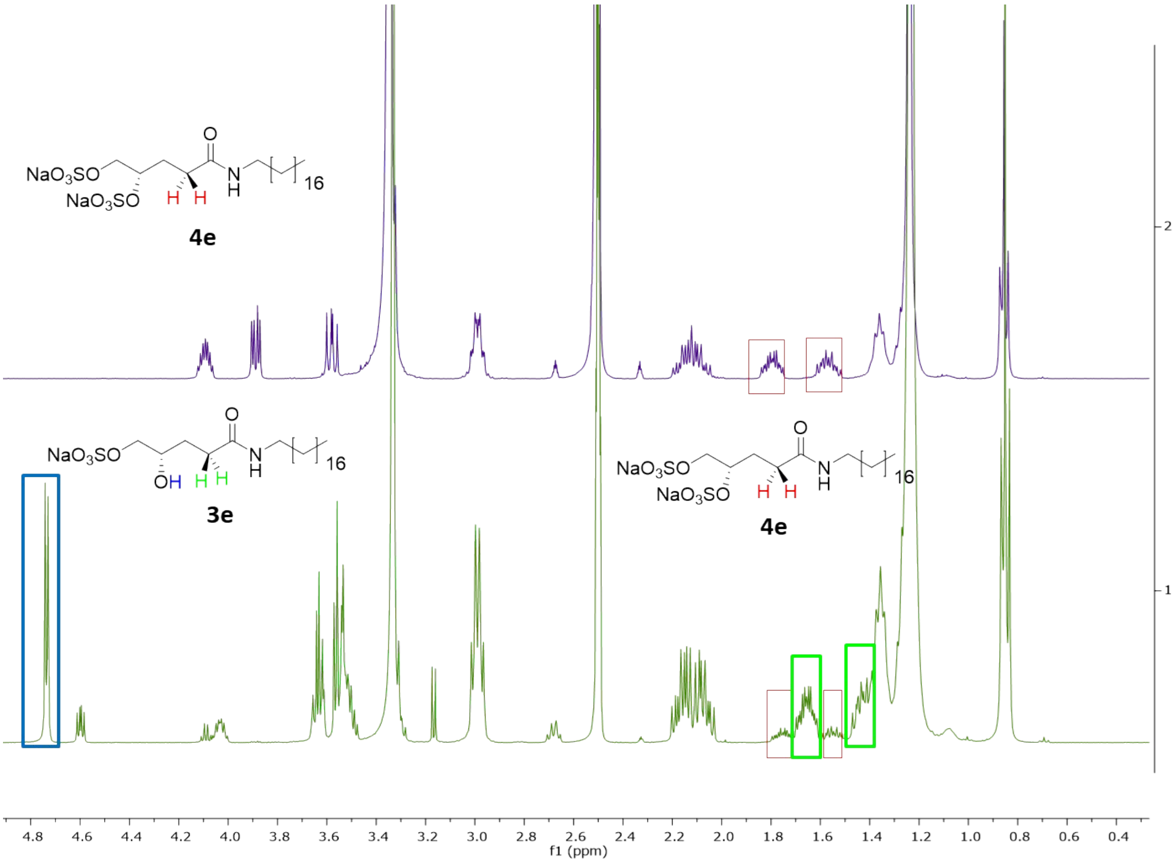
20
10
0

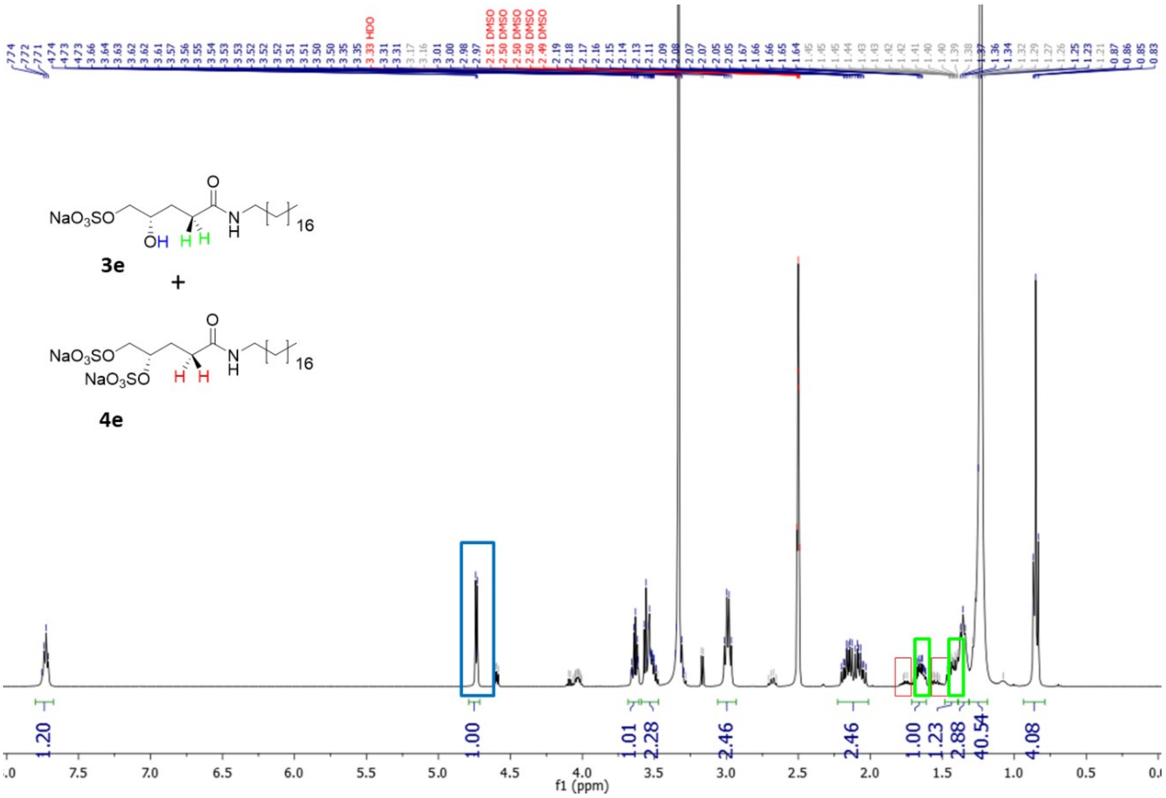




NMR spectra of pure disulfated compound 4e and mixture of mono-and disulfated compounds 3e and 4e



NaO3SO
NaO3SO
16
4e
3e
OH
2
1
f1 (ppm)



3e
+
4e
HDO
DMSO
1.20
1.00
1.01
2.28
2.46
2.46
1.00
1.23
2.88
40.54
4.08
f1 (ppm)