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Electronic supplementary information for:

Selective Golgi α-mannosidase inhibitors: *N*-alkyl substituted pyrrolidines with a basic functional group

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Content:

1. Synthesis

General methods

TLC was performed on aluminum sheets pre-coated with silica gel 60 F254 (Merck). Visualization was achieved by immersing the plates into a 10% solution of phosphomolybdic acid (PMA) in ethanol followed by heating the plate. Flash column chromatography was carried out on silica gel 60 (0.040–0.060 mm, Merck) with distilled solvents (hexanes, ethyl acetate, chloroform, methanol). All commercially available reagents and anhydrous solvents were used as received. 7-Bromoheptanenitrile was purchased from Fluorochem. All reactions containing sensitive reagents were carried out under a nitrogen atmosphere. Melting points were determined using a Boetius PHMK 05 microscope. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C with the Bruker AVANCE III HD 400 and Bruker AVANCE III HDX 600 spectrometers. Chemical shifts are given in ppm (δ) relative to the residual signal of appropriate deuterated solvent used ($CDCl_3$, CD_3OD). The ultrasonic bath USC-300TH was used for sonication. Optical rotations were determined on a Jasco P-2000 polarimeter at 20 °C. High-resolution mass spectra were recorded with an Orbitrap Elite (Thermo Scientific) mass spectrometer with ESI ionization in positive mode.

General method for *N*-alkylation (Method A)

The protected iminolyxitol **1** (0.45 mmol, 1 eq) was dissolved in DMF (3 mL), K_2CO_3 (2 eq) and corresponding bromide (1.1. eq) were added. The mixture was stirred at 40 °C for 16 h. The mixture was poured into EtOAc/H_2O (30 mL, 1:1, v/v). The organic phase was separated, washed with water (2 × 20 mL). The organic extract was dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (hexane/EtOAc 40:1 → 10:1).

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-octyl-L-lyxitol (2)

The *N*-alkylation of **1** (259 mg, 0.90 mmol) with 1-bromooctane (191 mg, 0.99 mmol) carried out according to the general procedure (Method A) afforded **2** as a yellow oil (359 mg, 99%), $[\alpha]_D$ + 47.7 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.1, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.1, 5.3 Hz, 1H, H-5'), 3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.90 (dt, *J* = 11.7, 8.2 Hz, 1H, CH_2-N), 2.21 (dd, *J* = 10.3, 5.3 Hz, 1H, H-4), 2.05–1.97 (m, 2H, H-1', CH_2-N), 1.48 (s, 3H, CH_3, ^{i}Pr), 1.47–1.39 (m, 2H, CH_2) 1.30 (s, 3H, CH_3, ^{i}Pr), 1.26 (br s, 8H, 4× CH_2), 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.92–0.85 (m, 5H, CH_2, CH_3), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 32.0 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.6 (CH_3, ^{i}Pr), 22.8 (CH_2), 18.5 (^{t}Bu), 14.3 (CH_3), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z*: calcd for $[C_{22}H_{45}NO_3Si]H^+$: 400.3242, found: 400.3241.

5-*O*-*tert*-Butyldimethylsilyl-*N*-decyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (3)

The *N*-alkylation of **1** (259 mg, 0.90 mmol) with 1-bromodecane (219 mg, 0.99 mmol) carried out according to the general procedure (Method A) afforded **3** as a yellow oil (293 mg, 76%), $[\alpha]_D$ + 39.3 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.94–2.85 (m, 1H, CH_2-N), 2.21 (dd, *J* = 10.4, 5.5 Hz, 1H, H-4), 2.04–1.96 (m, 2H, H-1', CH_2-N), 1.48 (s, 3H, CH_3, ^{i}Pr), 1.47–1.40 (m, 2H, CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.26 (br s, 14H, 7× CH_2), 0.90 (s, 9H, 3× CH_3, ^{t}Bu), 0.88 (s, 3H, CH_3), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 32.1 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 28.1 (CH_2), 27.7 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.6 (CH_3, ^{i}Pr), 22.8 (CH_2), 18.5 (^{t}Bu), 14.3 (CH_3), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z*: calcd for $[C_{24}H_{49}NO_3Si]H^+$: 428.3554, found: 428.3554.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-*N*-dodecyl-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (4)

The *N*-alkylation of **1** (125mg, 0.44 mmol) with 1-bromododecane (119 mg, 0.48 mmol) carried out according to the general procedure (Method A) to afforded **4** as a yellow oil (170 mg, 86%), $[\alpha]_D$ + 39.4 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.1, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.1, 5.3 Hz, 1H, H-5'), 3.20 (d, *J* = 11.0 Hz, 1H, H-1), 2.90 (dt, *J* = 11.7, 8.2 Hz, 1H, CH_2-N), 2.21 (dd, *J* = 10.3, 5.3 Hz, 1H, H-4), 2.05–1.96 (m, 2H, H-1', CH_2-N), 1.48 (s, 3H, CH_3, ^{i}Pr), 1.47–1.39 (m, 2H, CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.25 (br s, 18H, 9× CH_2), 0.90 (s, 9H, 3× CH_3, ^{t}Bu), 0.89–0.86 (m, 3H, CH_3), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.9 (C-3), 78.2 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 32.1 (CH_2), 29.8 (4× CH_2), 29.7 (CH_2), 29.5 (CH_2), 28.1 (CH_2), 27.7 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.6 (CH_3, ^{i}Pr), 22.9 (CH_2), 18.5 (^{t}Bu), 14.3 (CH_3), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z*: calcd for $[C_{26}H_{53}NO_3Si]H^+$: 456.3868, found: 428.3870.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-tetradecyl-L-lyxitol (5)
The *N*-alkylation of **1** (261 mg, 0.91 mmol) with 1-bromotetradecane (277 mg, 1.00 mmol) carried out according to the general procedure (Method A) afforded **5** as a yellow oil (170 mg, 86%), $[\alpha]_D$ + 29.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.94–2.85 (m, 1H, CH_2-N), 2.21 (dd, *J* = 10.4, 5.5 Hz, 1H, H-4), 2.05–1.96 (m, 2H, H-1', CH_2-N), 1.48 (s, 3H, CH_3, ^{i}Pr), 1.47–1.36 (m, 2H, CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.25 (br s, 22H, 11× CH_2), 0.90 (s, 9H, 3× CH_3, ^{t}Bu), 0.89–0.86 (m, 3H, CH_3), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 32.1 (CH_2), 29.9 (2× CH_2), 29.8 (2× CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 28.1 (CH_2), 27.7 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.6 (CH_3, ^{i}Pr), 22.9 (CH_2), 18.5 (^{t}Bu), 14.3 (CH_3), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z*: calcd for $[C_{28}H_{57}NO_3Si]H^+$: 484.4181, found: 484.4182.

General method for deprotection (Method B)
The solution of protected iminolyxitol in MeOH (3.5 mL per 0.1 mmol of iminolyxitol) was cooled to 0 °C and 6M HCl (1.75 mL, HCl/MeOH 1:2, v/v) was added. After 15 min, the ice-water bath was removed and the stirring was continued overnight at rt. The reaction mixture was neutralized with $NaHCO_3$, salts were removed by filtration, and the solvent was evaporated. The crude product was purified by column chromatography ($CHCl_3$/MeOH/NH_3 1:0:0 → 10:1:0 → 7:1:0.1, v/v/v).

1,4-Dideoxy-1,4-imino-*N*-octyl-L-lyxitol (6)
Deprotection of **2** (359 mg, 0.90 mmol) according to the general procedure (Method B) afforded **6** as an orange oil (132 mg, 60%), $[\alpha]_D$ + 53.7 (*c* 0.25, CH_3OH). ^{1}H NMR (600 MHz, CD_3OD): δ 4.22 (dd, *J* = 6.5, 5.0 Hz, 1H, H-3), 4.15 (td, *J* = 5.3, 3.8 Hz, 1H, H-2), 3.79 (dd, *J* = 11.2, 5.6 Hz, 1H, H-5), 3.69 (dd, *J* = 11.3, 4.4 Hz, 1H, H-5'), 3.07 (dd, *J* = 10.8, 3.6 Hz, 1H, H-1), 2.84 (dt, *J* = 11.9, 8.2 Hz, 1H, CH_2-N), 2.78 (dd, *J* = 10.8, 5.6 Hz, 1H, H-4), 2.63 (dd, *J* = 10.8, 5.7 Hz, 1H, H-1'), 2.43 (dt, *J* = 12.0, 7.6 Hz, 1H, CH_2-N), 1.52 (dd, *J* = 15.3, 7.1 Hz, 2H, CH_2), 1.38–1.31 (m, 10H, 5× CH_2), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (151 MHz, CD_3OD): δ 72.9 (C-3), 71.2 (C-2), 70.1 (C-4), 60.4 (C-5), 58.6 (C-1), 57.4 (CH_2-N), 33.0 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 23.7 (CH_2), 14.4 (CH_3). HRMS (ESI-MS): *m/z*: calcd for $[C_{13}H_{27}NO_3]H^+$: 246.2064, found: 246.2064.

***N*-Decyl-1,4-dideoxy-1,4-imino-L-lyxitol (7)**
Deprotection of **3** (293 mg, 0.67 mmol) according to the general procedure (Method B) afforded **7** as an orange oil (126 mg, 67%), $[\alpha]_D$ + 59.4 (*c* 0.25, CH_3OH). ^{1}H NMR (600 MHz, CD_3OD): δ 4.24 (dd, *J* = 6.6, 5.1 Hz, 1H, H-3), 4.15 (td, *J* = 5.4, 3.5 Hz, 1H, H-2), 3.80 (dd, *J* = 11.1, 5.8 Hz, 1H, H-5), 3.68 (dd, *J* = 11.1, 3.9 Hz, 1H, H-5'), 3.05 (dd, *J* = 10.7, 3.4 Hz, 1H, H-1), 2.78 (dt, *J* = 11.8, 8.2 Hz, 1H, CH_2-N), 2.71 (dd, *J* = 10.0, 5.9 Hz, 1H, H-4), 2.57 (dd, *J* = 10.7, 5.7 Hz, 1H, H-1'), 2.38 (dt, *J* = 12.0, 7.5 Hz, 1H, CH_2-N), 1.53 (dd, *J* = 15.2, 7.1 Hz, 2H, CH_2), 1.37–1.31 (m, 14H, 7× CH_2), 0.93 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (151 MHz, CD_3OD): δ 73.4 (C-3), 71.5 (C-2), 68.9 (C-4), 60.9 (C-5), 59.4 (C-1), 57.1 (CH_2-N), 33.1 (CH_2), 30.7 (2× CH_2), 30.7 (CH_2), 30.5 (CH_2), 29.0 (CH_2), 28.6 (CH_2), 23.7 (CH_2), 14.4 (CH_3). HRMS (ESI-MS): *m/z*: calcd for $[C_{15}H_{31}NO_3]H^+$: 274.2377, found: 274.2376.

1,4-Dideoxy-*N*-dodecyl-1,4-imino-L-lyxitol (8)
Deprotection of **4** (170 mg, 0.37 mmol) according to the general procedure (Method B) afforded **8** as an orange oil (81 mg, 73%), $[\alpha]_D$ + 39.1 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.24 (dd, *J* = 6.5, 5.1 Hz, 1H, H-3), 4.15 (td, *J* = 5.4, 3.6 Hz, 1H, H-2), 3.80 (dd, *J* = 11.2, 5.7 Hz, 1H, H-5), 3.69 (dd, *J* = 11.2, 4.1 Hz, 1H, H-5'), 3.06 (dd, *J* = 10.7, 3.5 Hz, 1H, H-1), 2.81 (dt, *J* = 11.8, 8.2 Hz, 1H, CH_2-N), 2.75 (dd, *J* = 10.4, 5.9 Hz, 1H, H-4), 2.60 (dd, *J* = 10.7, 5.7 Hz, 1H, H-1'), 2.41 (dt, *J* = 12.0, 7.6 Hz, 1H, CH_2-N), 1.53 (dd, *J* = 14.8, 7.0 Hz, 2H, CH_2), 1.31 (br s, 18H, 9× CH_2), 0.91 (t, *J* = 6.8 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, CD_3OD): δ 73.3 (C-3), 71.4 (C-2), 69.1 (C-4), 60.8 (C-5), 59.3 (C-1), 57.1 (CH_2-N), 33.1 (CH_2), 30.7 (4× CH_2), 30.6 (CH_2), 30.5 (CH_2), 28.8 (CH_2), 28.5 (CH_2), 23.7 (CH_2), 14.4 (CH_3). HRMS (ESI-MS): *m/z*: calcd for $[C_{17}H_{35}NO_3]H^+$: 302.2690, found: 302.2692.

1,4-Dideoxy-1,4-imino-*N*-tetradecyl-L-lyxitol (9)
Deprotection of **5** (413 mg, 0.85 mmol) according to the general procedure (Method B) afforded **9** as an orange oil (198 mg, 70%), $[\alpha]_D$ - 10.7 (*c* 0.20, CH_3OH). ^{1}H NMR (600 MHz, CD_3OD) δ 4.27 (dd, *J* = 6.3, 4.9 Hz, 1H, H-3), 4.21 (dd, *J* = 9.5, 4.9 Hz, 1H, H-2), 3.85 (dd, *J* = 11.4, 5.4 Hz, 1H, H-5), 3.76 (dd, *J* = 11.4, 5.0 Hz, 1H, H-5'), 3.16 (dd, *J* = 10.9, 3.5 Hz, 1H, H-1), 2.99–2.90 (m, 2H, CH_2-N, H-4), 2.76 (dd, *J* = 9.3, 5.0 Hz, 1H, H-1'), 2.56 (dd, *J* = 16.7, 8.5 Hz, 1H, CH_2-N), 1.58 (dd, *J* = 14.9, 7.2 Hz, 2H, CH_2), 1.37–1.29 (m, 22H, 11× CH_2), 0.92 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (151 MHz, CD_3OD): δ 73.0 (C-3), 71.3 (C-2), 69.7 (C-4), 60.6 (C-5),

58.9 (C-1), 57.3 (CH_2-N), 49.9 (CH_2), 33.1 (CH_2), 30.8 (4× CH_2), 30.7 (2× CH_2), 30.5 (CH_2), 30.5 (CH_2), 28.4 (CH_2), 23.7 (CH_2), 14.4 (CH_3). HRMS (ESI-MS): *m/z*: calcd for $[C_{19}H_{40}NO_3]H^+$: 330.3003, found: 330.3004.

General procedure for preparation of amide (Method C)
To a solution of corresponding acid (2 mmol, 1 eq) in toluene (5 mL), DMF (0.16 eq) and $SOCl_2$ (1 eq) were added. The reaction mixture was stirred at 80 °C for 1 hour. The mixture was cooled to 0 °C and poured to cold ammonia solution (25%, 25 mL). After stirring for 30 min, the precipitate was collected, washed with water (50 mL), hexol (50 mL) and dried under vacuum.

8-Bromooctanamide (13)[1]
8-Bromooctanoic acid **10** (0.5 g, 2.24 mmol) was transformed to amide **13** according to the general procedure (Method C). White solid (0.427 g, 86%), mp 101–102 °C, ref[1] mp 99–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.59 (s, 1H, $CONH_2$), 5.44 (s, 1H, $CONH_2$), 3.40 (t, *J* = 6.8 Hz, 2H, CH_2-Br), 2.23–2.20 (m, 2H, C*H*$_2$-$CONH_2$), 1.88–1.79 (m, 2H, CH_2), 1.67–1.61 (m, 2H, CH_2), 1.46–1.32 (m, 4H, 2× CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.6 ($CONH_2$), 35.9 (*C*H_2-$CONH_2$), 34.0 (CH_2-Br), 32.8 (CH_2), 29.1 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 25.5 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_8H_{16}BrNO]H^+$: 222.0488, found: 222.0491.

9-Bromononanamide (14)[2]
9-Bromononanoic acid **11** (0.5 g, 2.11 mmol) was transformed to amide **14** according to the general procedure (Method C). White solid (0.410 g, 82%), mp 83–85 °C, ref[2] mp 84–86 °C. ^{1}H NMR (400 MHz, CD_3OD): δ 3.47 (t, *J* = 6.8 Hz, 2H, CH_2-Br), 2.26–2.20 (m, 2H, C*H*$_2$-$CONH_2$), 1.92–1.83 (m, 2H, CH_2), 1.70–1.59 (m, 2H, CH_2), 1.52–1.43 (m, 2H, CH_2), 1.38 (br s, 6H, 3× CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_9H_{18}BrNO]H^+$: 236.0645, found: 236.0652.

10-Bromodecanamide (15)[1]
10-Bromodecanoic acid **12** (0.5 g, 1.99 mmol) was transformed to amide **15** according to the general procedure (Method C). White solid (0.490 g, 98%), mp 108–110 °C, ref[1] mp 106–108 °C. ^{1}H NMR (400 MHz, CD_3OD): δ 3.46 (t, *J* = 6.8 Hz, 2H, CH_2-Br), 2.28–2.18 (m, 2H, C*H*$_2$-$CONH_2$), 1.91–1.82 (m, 2H, CH_2), 1.67–1.61 (m, 2H, CH_2), 1.53–1.42 (m, 2H, CH_2), 1.37 (br s, 8H, 4× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 179.3 ($CONH_2$), 36.5 (*C*H_2-$CONH_2$), 34.4 (CH_2-Br), 34.0 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 26.9 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{10}H_{20}BrNO]H^+$: 250.0801, found: 250.0806.

General procedure for preparation of nitriles (Method D)
Triflic anhydride (1.1 eq) was added to a stirred solution (ice-cooled) of the corresponding amide (5 mmol, 1 eq) and Et_3N (2 eq) in dry DCM (5 mL) at such rate that the temperature was kept below 5 °C. The reaction mixture was allowed to warm to rt and stirred for 2 h. The reaction mixture was poured into water (5 mL). The resulting mixture was extracted with DCM (2× 10 mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4), filtered and the solvent was removed. The crude product was purified by column chromatography (hexane/EtOAc 40:1 → 20:1).

8-Bromooctanitrile (17)[3]
The dehydration of amide **13** (107 mg, 4.82 mmol) carried out according to the general procedure (Method D) gave nitrile **17** (85 mg, 87%), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 (t, *J* = 6.7 Hz, 2H, CH_2-Br), 2.34 (t, *J* = 7.1 Hz, 2H, CH_2-CN), 1.91–1.82 (m, 2H, CH_2), 1.72–1.62 (m, 2H, CH_2), 1.51–1.41 (m, 4H, 2× CH_2), 1.41–1.31 (m, 2H, CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_8H_{14}BrN]H^+$: 204.0382, found: 204.0382.

9-Bromononanitrile (18)[3]
The dehydration of amide **14** (140 mg, 5.93 mmol) carried out according to the general procedure (Method D) gave nitrile **18** (120 mg, 93%), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 (t, *J* = 6.8 Hz, 2H, CH_2-Br), 2.34 (t, *J* = 7.1 Hz, 2H, CH_2-CN), 1.90–1.81 (m, 2H, CH_2), 1.66 (dt, *J* = 19.8, 7.2 Hz, 2H, CH_2), 1.48–1.40 (m, 4H, 2× CH_2), 1.39–1.32 (m, 4H, 2× CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_9H_{16}BrN]H^+$: 218.0539, found: 218.0537.

10-Bromodecanitrile (19)[4]
The dehydration of amide **15** (152 mg, 6.08 mmol) carried out according to the general procedure (Method D) gave nitrile **19** (113 mg, 80%), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 (t, *J* = 6.8 Hz, 2H, CH_2-Br), 2.34 (t, *J* = 7.1 Hz, 2H, CH_2-CN), 1.90–1.81 (m, 2H, CH_2), 1.66 (dt, *J* = 19.8, 7.2 Hz, 2H, CH_2), 1.49–1.40 (m, 4H, 2× CH_2), 1.32 (br s, 6H, 3× CH_2).

5-*O*-*tert*-Butyldimethylsilyl-*N*-(6-cyanohexyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (20)
The *N*-alkylation of **1** (200 mg, 0.70 mmol) with nitrile **16** (115 µL, 0.08 mmol) carried out according to the general procedure (Method A) afforded **20** as a colorless oil (222 mg, 80%), $[\alpha]_D$ + 67.5 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 4.61–4.55 (m, 2H, H-3, H-2), 3.91 (dd, *J* = 10.2, 6.0 Hz, 1H, H-5), 3.74–3.70 (m, 1H, H-5'), 3.18 (d, *J* = 10.9 Hz, 1H, H-1), 2.91 (dt, *J* = 12.0, 8.0 Hz, 1H, CH_2-N), 2.32 (t, *J* = 7.2 Hz, 2H, CH_2-CN), 2.21 (dd, *J* = 10.0, 5.6 Hz, 1H, H-4), 2.04–2.00 (m, 1H, CH_2-N), 1.98 (dd, *J* = 10.8, 4.3 Hz, 1H, H-1'), 1.69–1.64 (m, 2H, CH_2), 1.46 (s, 3H, CH_3, ^{i}Pr), 1.45–1.27 (m, 6H, 3× CH_2) 1.29 (s, 3H, CH_3, ^{i}Pr), 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.06 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 119.9 (CN), 111.0 (^{i}Pr), 80.8 (C-3), 78.1 (C-2), 70.3 (C-4), 62.1 (C-5), 60.1 (C-1), 54.3 (CH_2-N), 31.0 (CH_2), 28.7 (CH_2), 27.8 (CH_2), 26.8 (CH_2), 26.3 (CH_3 ^{i}Pr), 26.0 (3× CH_3, ^{t}Bu), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu), 17.2 (CH_2), -5.3 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{21}H_{40}N_2O_3Si]H^+$: 397.2881, found: 397.2883.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(7-cyanoheptyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (21)
The *N*-alkylation of **1** (109 mg, 0.40 mmol) with nitrile **17** (85 mg, 0.04 mmol) carried out according to the general procedure (Method A) afforded **21** as a colorless oil (127 mg, 82%), $[\alpha]_D$ + 58.7 (*c* 0.25, $CHCl_3$) ^1H NMR (400 MHz, $CDCl_3$): δ 4.62–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.1 Hz, 1H, H-5), 3.73 (dd, *J* = 10.2, 5.5 Hz, 1H, H-5'), 3.20 (d, *J* = 11.0 Hz, 1H, H-1), 2.96–2.87 (m, 1H, CH_2-N), 2.33 (t, *J* = 7.2, 2H, CH_2-CN), 2.22 (dd, *J* = 10.1, 5.6 Hz, 1H, H-4), 2.03–1.97 (m, 2H, CH_2-N, H-1'), 1.68–1.60 (m, 2H, CH_2), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.40 (m, 4H, 2× CH_2), 1.36–1.25 (m, 4H, 2× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 119.9 (CN), 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.3 (C-4), 62.1 (C-5), 60.1 (C-1), 54.5 (CH_2-N), 28.8 (2× CH_2), 27.9 (CH_2), 27.3 (CH_2), 26.3 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.5 (CH_3, ^{i}Pr), 25.5 (CH_2), 18.4 (^{t}Bu), 17.3 (CH_2), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{22}H_{42}N_2O_3Si]H^+$: 411.3037, found: 411.3041.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(8-cyanooctyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (22)
The *N*-alkylation of **1** (134 mg, 0.47 mmol) with nitrile **18** (112 mg, 0.05 mmol) carried out according to the general procedure (Method A) afforded **22** as a colorless oil (157 mg, 79%), $[\alpha]_D$ + 50.3 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.2 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.20 (d, *J* = 11.0 Hz, 1H, H-1), 2.95–2.86 (m, 1H, CH_2-N), 2.32 (t, *J* = 7.1 Hz, 2H, CH_2-CN), 2.21 (dd, *J* = 10.2, 5.6 Hz, 1H, H-4), 2.02–1.96 (m, 2H, CH_2-N, H-1'), 1.68–1.60 (m, 2H, CH_2), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.39 (m, 4H, 2× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.31–1.25 (m, 6H, 3× CH_2) 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 120.0 (CN), 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.6 (CH_2-N), 29.3 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.0 (CH_2), 27.5 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu), 17.7 (CH_2), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{23}H_{44}N_2O_3Si]H^+$: 425.3194, found: 425.3200.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(9-cyanononyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (23)
The *N*-alkylation of **1** (126 mg, 0.44 mmol) with nitrile **19** (112 mg, 0.05 mmol) carried out according to the general procedure (Method A) afforded **23** as a colorless oil (148 mg, 77%), $[\alpha]_D$ + 38.5 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.2 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.20 (d, *J* = 11.0 Hz, 1H, H-1), 2.95–2.86 (m, 1H, CH_2-N), 2.33 (t, *J* = 7.1 Hz, 2H, CH_2-CN), 2.21 (dd, *J* = 10.2, 5.6 Hz, 1H, H-4), 2.02–1.96 (m, 2H, CH_2-N, H-1'), 1.68–1.60 (m, 2H, CH_2), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.39 (m, 4H, 2× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.31–1.25 (m, 8H, 4× CH_2), 0.90 (s, 9H, 3× CH_3, ^{t}Bu), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 120.0 (CN), 111.0 (^{i}Pr), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.6 (CH_2-N), 29.5 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.0 (CH_2), 27.6 (CH_2), 26.4 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.6 (CH_2), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu), 17.3 (CH_2), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{24}H_{46}N_2O_3Si]H^+$: 439.3350, found: 439.3342.

General procedure for preparation of amidines (Method E)
The corresponding nitrile (0.05 mmol, 1 eq) was dissolved in dry ether (9 mL) and LiHMDS (7.5 eq) was added. The mixture was sonicated for 2 h at rt under a nitrogen atmosphere. The solvent was evaporated. The residue was stirred with water (15 mL) for 30 min and extracted with DCM (3 × 10 mL), washed with brine (30 mL), dried (Na_2SO_4), filtered and concentrated. Deprotection of the crude products **24**-**27** following the procedure described in Method F provided the target amidines as hydrochlorides.

1,4-Dideoxy-*N*-heptanamidinyl-1,4-imino-L-lyxitol hydrochloride (28)
The reaction was carried out according to the general procedure (Method E) with nitrile **20** (200 mg, 0.05 mmol) to afford **28** as a brown amorphous solid (104 mg, 70%), $[\alpha]_D$ + 19.5 (*c* 0.25, CH_3OH). ^1H NMR (400 MHz, CD_3OD): δ 4.43–4.36 (m, 2H, H-2, H-3), 4.07–4.96 (m, 2H, H-5, H-5'), 3.67–3.60 (m, 1H, H-4), 3.53–3.46 (m,

2H, CH_2-N, H-1), 3.38–3.33 (m, 1H, H-1'), 3.20–3.05 (m, 1H, CH_2-N), 1.77–1.29 (m, 10H, 5× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 162.8 (C, amidine), 72.2 (C-2), 72.0 (C-4), 70.8 (C-3), 59.7 (C-5), 57.9 (CH_2-N), 57.6 (C-1), 30.4 (CH_2), 30.0 (2× CH_2), 27.6 (CH_2), 26.1 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{12}H_{25}N_3O_3]H^+$: 260.1969, found: 260.1963.

1,4-Dideoxy-1,4-imino-*N*-octanamidinyl-L-lyxitol hydrochloride (29)
The reaction was carried out according to the general procedure (Method E) with nitrile **21** (226 mg, 0.06 mmol) to afford amidine **29** as a brown amorphous solid (153 mg, 92%), $[\alpha]_D$ + 19.6 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.45–4.35 (m, 2H, H-2, H-3), 4.08–3.96 (m, 2H, H-5, H-5'), 3.67–3.61 (m, 1H, H-4), 3.53–3.47 (m, 2H, CH_2-N, H-1), 3.39–3.33 (m, 1H, H-1'), 3.19–3.08 (m, 1H, CH_2-N), 1.84–1.28 (m, 12H, 6× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 162.8 (C, amidine), 72.2 (C-2), 72.0 (C-4), 70.8 (C-3), 59.7 (C-5), 58.0 (CH_2-N), 57.6 (C-1), 30.2 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 27.4 (CH_2), 26.0 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{13}H_{27}N_3O_3]H^+$: 274.2125, found: 274.2124.

1,4-Dideoxy-1,4-imino-*N*-nonanamidinyl-L-lyxitol hydrochloride (30)
The reaction was carried out according to the general procedure (Method E) with **22** (100 mg, 0.02 mmol) to afford amidine **30** as a brown amorphous solid (67 mg, 89%), $[\alpha]_D$ + 12.1 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.45–4.36 (m, 2H, H-2, H-3), 4.07–3.96 (m, 2H, H-5, H-5'), 3.66–3.58 (m, 1H, H-4), 3.56–3.43 (m, 2H, CH_2-N, H-1), 3.42–3.33 (m, 1H, H-1'), 3.20–3.08 (m, 1H, CH_2-N), 1.87–1.28 (m, 14H, 7× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 162.8 (C, amidine), 72.2 (C-2), 72.0 (C-4), 70.7 (C-3), 59.6 (C-5), 58.0 (CH_2-N), 57.6 (C-1), 30.0 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (2× CH_2), 27.5 (CH_2), 26.0 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{14}H_{29}N_3O_3]H^+$: 288.2282, found: 288.2282.

***N*-Decanamidinyl-1,4-dideoxy-1,4-imino-L-lyxitol hydrochloride (31)**
The reaction was carried out according to the general procedure (Method E) with **23** (140 mg, 0.03 mmol) to afford amidine **31** as a brown amorphous solid (97 mg, 90%), $[\alpha]_D$ + 18.0 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.46–4.37 (m, 2H, H-2, H-3), 4.07–3.98 (m, 2H, H-5, H-5'), 3.68–3.60 (m, 1H, H-4), 3.53–3.46 (m, 2H, CH_2-N, H-1), 3.36 (dd, *J* = 10.4, 4.3 Hz, 1H, H-1'), 3.20–3.09 (m, 1H, CH_2-N), 1.83–1.27 (m, 16H, 8× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 162.8 (C, amidine), 72.1 (C-2), 72.0 (C-4), 70.7 (C-3), 59.6 (C-5), 58.1 (CH_2-N), 57.6 (C-1), 30.4 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 30.1 (CH_2), 30.0 (2× CH_2), 27.6 (CH_2), 26.1 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{15}H_{31}N_3O_3]H^+$: 302.2438, found: 302.2434.

General procedure for nitrile reduction (Method F)
Lithium triethylborohydride (10 eq, 1.7M in THF) was added dropwise to a solution of the corresponding nitrile (0.3 mmol, 1 eq) in THF (3 mL) at 0 °C. The resulting mixture was sonicated at 0–5 °C (ice cooled) for 45 min (TLC: EtOAc/MeOH/NH_3 20:1:0.1, v/v/v). The mixture was slowly poured into cold water (20 mL), and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography ($CHCl_3$/MeOH 1:0 → 10:1).

***N*-(7-Aminoheptyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (32)**
Nitrile **20** (68 mg, 0.17 mmol) was transformed to amine **32** according to the general procedure (Method F). The crude product was used in the next step without further purification. HRMS (ESI-MS): *m/z* calcd for $[C_{21}H_{44}N_2O_3Si]H^+$: 401.3194, found: 401.3200.

***N*-(8-Aminooctyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (33)**
Reduction of nitrile **21** (109 mg, 0.27 mmol) according to the general procedure (Method F) afforded the amine **33** as a colorless oil (68 mg, 63%), $[\alpha]_D$ + 62.4 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (br s, 2H, NH_2), 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.92–2.85 (m, 1H, CH_2-N), 2.85–2.79 (m, 2H, C*H*$_2$-NH_2), 2.23 (dd, *J* = 10.2, 5.6 Hz, 1H, H-4), 2.05–1.97 (m, 2H, CH_2-N, H-1'), 1.67–1.58 (m, 2H, CH_2), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.38 (m, 2H, CH_2), 1.37–1.20 (m, 8H, 4× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.8 (C-3), 78.1 (C-2), 70.4 (C-4), 61.9 (C-5), 60.0 (C-1), 54.7 (CH_2-N), 40.2 (CH_2-NH_2), 29.5 (CH_2), 29.3(CH_2), 29.2 (CH_2), 27.9 (CH_2), 27.6 (CH_2), 26.7 (CH_2), 26.3 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{22}H_{46}N_2O_3Si]H^+$: 415.3350, found: 415.3373.

***N*-(8-Aminononyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (34)**
Reduction of nitrile **22** (157 mg, 0.37 mmol) according to the general procedure (Method F) afforded the amine **34** as a colorless oil (104 mg, 66%), $[\alpha]_D$ + 55.7 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.98 (br s, 2H, NH_2), 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'),

3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.94–2.85 (m, 1H, CH_2-N), 2.84–2.79 (m, 2H, C*H*$_2$-NH_2), 2.22 (dd, *J* = 10.3, 5.6 Hz, 1H, H-4), 2.03–1.97 (m, 2H, CH_2-N, H-1'), 1.64–1.59 (m, 2H, CH_2), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.39 (m, 2H, CH_2), 1.35–1.24 (m, 10H, 5× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 0.89 (s, 9H, 3× CH_3, ^{t}Bu), 0.07 (s, 6H, 2× CH_3-Si).^{13}C NMR (101 MHz, $CDCl_3$): δ 111.0 (^{i}Pr), 80.8 (C-3), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 40.4 (CH_2-NH_2), 29.7 (CH_2), 29.6 (2× CH_2), 29.59 (CH_2), 29.3 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 26.8 (CH_2), 26.3 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{23}H_{48}N_2O_3Si]H^+$: 429.3507, found: 429.3510.

General procedure for preparation of protected guanidines (Method G)
The amine (0.15 mmol, 1 eq) was dissolved in mixture of THF/DMF (4.5 mL, 2:1, v/v) and *N*,*N*′-bis(*tert*-butoxycarbonyl)-1*H*-pyrazole-1-carboxamidine (1.1 eq) was added. The mixture was sonicated at 40–45 °C for 1 h. The solvent was evaporated, the residue was diluted with water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (hexane/EtOAc 40:1 → 10:1).

5-*O*-*tert*-Butyldimethylsilyl-*N*-(7-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)heptyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (35)
Guanidine **35** was prepared from amine **32** (58 mg, 0.15 mmol) according to the general procedure (Method G). Yellowish oil (51 mg, 55%), $[\alpha]_D$ + 25.3 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.49 (br s, 1H, NH-Boc), 8.29 (s, 1H, NH), 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.75 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.39 (td, *J* = 7.2, 5.3 Hz, 2H, C*H*$_2$-NH), 3.22 (d, *J* = 11.0 Hz, 1H, H-1), 2.99–2.85 (m, 1H, CH_2-N), 2.24 (dd, *J* = 10.2, 5.5 Hz, 1H, H-4), 2.06–1.99 (m, 2H, H-1', CH_2-N), 1.56–1.53 (m, 2H, CH_2), 1.50 (s, 9H, 3× CH_3, Boc), 1.49 (s, 9H, 3× CH_3, Boc), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.47–1.39 (m, 2H, CH_2), 1.29 (s, 3H, CH_3, ^{i}Pr), 1.35–1.27 (m, 6H, 3× CH_2), 0.89 (s, 9H, 3× CH_3, ^{t}Bu-Si), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.8 (C, guanidine), 156.3 (C=O), 153.5 (C=O), 111.0 (^{i}Pr), 83.1 (^{t}Bu, Boc), 80.8 (C-3), 79.3 (^{t}Bu, Boc), 78.0 (C-2), 70.3 (C-4), 61.9 (C-5), 59.9 (C-1), 54.6 (CH_2-N), 41.1 (CH_2-NH), 29.3 (CH_2), 29.1 (CH_2), 28.5 (3× CH_3, Boc), 28.2 (3× CH_3, Boc), 27.7 (CH_2), 27.5 (CH_2), 27.0 (CH_2), 26.2 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu-Si), 25.4 (CH_3, ^{i}Pr), 18.4 (^{t}Bu-Si), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{32}H_{62}N_4O_7Si]H^+$: 643.4461, found: 643.4463.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(8-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)octyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (36)
Guanidine **36** was prepared from amine **33** (103 mg, 0.25 mmol) according to the general procedure (Method G). Yellowish oil (72 mg, 44%), $[\alpha]_D$ + 54.6 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.39 (td, *J* = 7.2, 5.3 Hz, 2H, C*H*$_2$-NH), 3.20 (d, *J* = 11.0 Hz, 1H, H-1), 2.90 (dt, *J* = 11.9, 7.8 Hz, 1H, CH_2-N), 2.21 (dd, *J* = 10.3, 5.6 Hz, 1H, H-4), 2.05–1.98 (m, 2H, H-1', CH_2-N), 1.57–1.54 (m, 2H, CH_2), 1.50 (s, 9H, 3× CH_3, Boc), 1.49 (s, 9H, 3× CH_3, Boc), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.38 (m, 2H, CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.36–1.20 (m, 8H, 4× CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 0.89 (s, 9H, 3× C*H*$_3$, ^{t}Bu-Si), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.8 (C, guanidine), 156.3 (C=O), 153.5 (C=O), 111.0 (^{i}Pr), 83.1 (^{t}Bu, Boc), 80.9 (C-3), 79.3 (^{t}Bu, Boc), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 41.2 (CH_2-NH), 29.9 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 28.5 (3× CH_3, Boc), 28.2 (3× CH_3, Boc), 28.0 (CH_2), 27.6 (CH_2), 27.0 (CH_2), 26.3 (CH_3, ^{i}Pr), 26.1 (3× CH_3, ^{t}Bu-Si), 25.6 (CH_3, ^{i}Pr), 18.4 (^{t}Bu-Si), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{33}H_{64}N_4O_7Si]H^+$: 657.4617, found: 657.4621.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(9-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)nonyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-L-lyxitol (37)
Guanidine **37** was prepared from amine **34** (35 mg, 0.08 mmol) according to general procedure (Method G). Yellowish oil (39 mg, 74%), $[\alpha]_D$ + 35.5 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63–4.55 (m, 2H, H-3, H-2), 3.92 (dd, *J* = 10.2, 6.3 Hz, 1H, H-5), 3.74 (dd, *J* = 10.2, 5.4 Hz, 1H, H-5'), 3.39 (td, *J* = 7.2, 5.3 Hz, 2H, C*H*$_2$-NH), 3.21 (d, *J* = 11.0 Hz, 1H, H-1), 2.94–2.85 (m, 1H, C*H*$_2$-N), 2.22 (dd, *J* = 10.3, 5.6 Hz, 1H, H-4), 2.05–1.97 (m, 1H, 2H, H-1', CH_2-N), 1.57–1.53 (m, 2H, CH_2), 1.50 (s, 9H, 3× CH_3, Boc), 1.49 (s, 9H, 3× CH_3, Boc), 1.47 (s, 3H, CH_3, ^{i}Pr), 1.46–1.38 (m, 2H, CH_2), 1.30 (s, 3H, CH_3, ^{i}Pr), 1.35–1.22 (m, 10H, 5× CH_2), 0.89 (s, 9H, 3× CH_3, ^{t}Bu-Si), 0.07 (s, 6H, 2× CH_3-Si). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.8 (C, guanidine), 156.3 (C=O), 153.5 (C=O), 111.0 (^{i}Pr), 83.1 (^{t}Bu, Boc), 80.9 (C-3), 79.3 (^{t}Bu, Boc), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (CH_2-N), 41.2 (CH_2-NH), 29.9 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.5 (3× CH_3, Boc), 28.2 (3× CH_3, Boc), 28.0 (CH_2), 27.7 (CH_2), 27.0 (CH_2), 26.3 (CH_3, ^{i}Pr), 26.1 (3× *C*H$_3$, ^{t}Bu-Si), 25.5 (CH_3, ^{i}Pr), 18.4 (^{t}Bu-Si), -5.2 (2× CH_3-Si). HRMS (ESI-MS): *m/z* calcd for $[C_{34}H_{66}N_4O_7Si]H^+$: 671.4774, found: 671.4781.

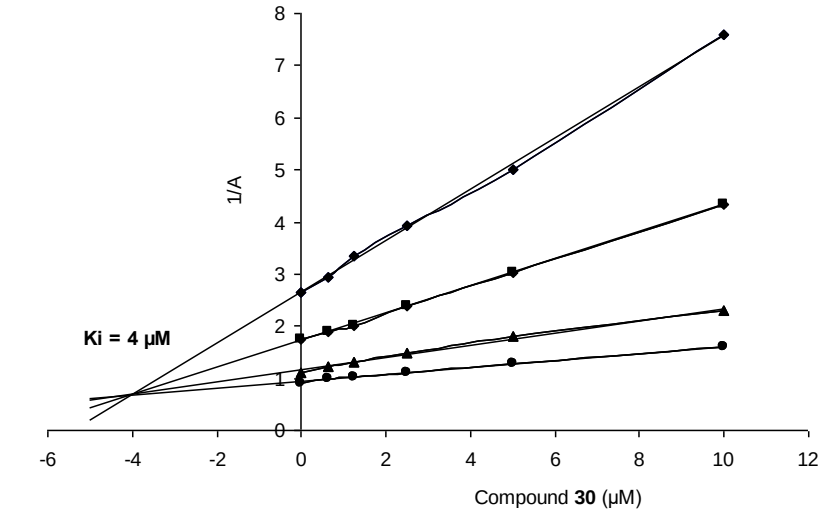
General method for deprotection (Method H)
The solution of protected iminolyxitol in MeOH (3.5 mL per 0.1 mmol of iminolyxitol) was cooled to 0 °C and 6M HCl (1.75 mL, HCl/MeOH 1:2, v/v) was added dropwise. After 15 min, the ice-water bath was removed and the stirring was continued at rt for 16h. The solvent was evaporated, the residue was redissolved in water (15 mL) and extracted with DCM (3 × 10 mL). After lyophilisation of the water layer, the target iminolyxitol was obtained as hydrochloride.

1,4-Dideoxy-*N*-(7-guanidinoheptyl)-1,4-imino-L-lyxitol hydrochloride (38)
Guanidine **35** (51 mg, 0.01 mmol) was deprotected according to the general procedure (Method H) to afford **38** as a brown amorphous solid (25 mg, 99%), $[\alpha]_D$ + 34.5 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.41 (dd, *J* = 9.6, 5.2 Hz, 1H, H-2), 4.39–4.35 (m, 1H, H-3), 4.01 (dd, *J* = 6.1, 3.7 Hz, 2H, H-5, H-5'), 3.66–3.60 (m, 1H, H-4), 3.52–3.44 (m, 2H, CH_2-N, H-1), 3.36 (dd, *J* = 11.9, 5.8 Hz, 1H, H-1'), 3.18 (t, *J* = 7.0 Hz, 2H, C*H*$_2$-NH), 3.13 (dd, *J* = 10.8, 6.6 Hz, 1H, CH_2-N), 1.79–1.73 (m, 2H, CH_2), 1.64–1.57 (m, 2H, CH_2), 1.42 (br s, 6H, 3× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 158.6 (C, guanidine), 72.2 (C-3), 72.0 (C-4), 70.8 (C-2), 59.7 (C-5), 58.0 (CH_2-N), 57.6 (C-1), 42.4 (CH_2-NH), 29.7 (2× CH_2), 27.5 (CH_2), 27.4 (CH_2), 26.0 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{13}H_{28}N_4O_3]H^+$: 289.2234, found: 289.2236.

1,4-Dideoxy-*N*-(8-guanidinooctyl)-1,4-imino-L-lyxitol hydrochloride (39)
Guanidine **36** (69 mg, 0.01 mmol) was deprotected according to the general procedure (Method H) to afford **39** as a brown amorphous solid (35 mg, 99%), $[\alpha]_D$ + 19.9 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.42 (dd, *J* = 9.7, 5.4 Hz, 1H, H-2), 4.40–4.36 (m, 1H, H-3), 4.07–3.96 (m, 2H, H-5, H-5'), 3.67–3.61 (m, 1H, H-4), 3.52–3.46 (m, 2H, CH_2-N, H-1), 3.36 (dd, *J* = 11.9, 5.8 Hz, 1H, H-1'), 3.18 (t, *J* = 7.0 Hz, 2H, C*H*$_2$-NH), 3.15–3.10 (m, 1H, CH_2-N), 1.81–1.71 (m, 2H, CH_2), 1.63–1.54 (m, 2H, CH_2), 1.39 (br s, 8H, 4× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 158.6 (C, guanidine), 72.1 (C-3), 72.0 (C-4), 70.7 (C-2), 59.6 (C-5), 58.0 (CH_2-N), 57.6 (C-1), 42.5 (CH_2-NH), 30.0 (2× CH_2), 29.8 (CH_2), 27.5 (2× CH_2), 26.1 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{14}H_{30}N_4O_3]H^+$: 303.2391, found: 303.2394.

1,4-Dideoxy-*N*-(9-guanidinononyl)-1,4-imino-L-lyxitol hydrochloride (40)
Guanidine **37** (66 mg, 0.01 mmol) was deprotected according to the general procedure (Method H) to afford **40** as a brown amorphous solid (34 mg, 99%), $[\alpha]_D$ + 13.5 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.39 (dd, *J* = 9.7, 5.2 Hz, 1H, H-2), 4.37–4.33 (m, 1H, H-3), 4.04–3.94 (m, 2H, H-5, H-5'), 3.61 (dd, *J* = 12.5, 5.3 Hz, 1H, H-4), 3.49–3.41 (m, 2H, CH_2-N, H-1), 3.33 (dd, *J* = 11.9, 5.8 Hz, 1H, H-1'), 3.15 (t, *J* = 7.0 Hz, 2H, C*H*$_2$-NH), 3.12–3.07 (m, 1H, CH_2-N), 1.75–1.65 (m, 2H, CH_2), 1.60–1.51 (m, 2H, CH_2), 1.35 (br s, 10H, 5× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 158.6 (C, guanidine), 72.1 (C-3), 72.0 (C-4), 70.7 (C-2), 59.6 (C-5), 58.1 (CH_2-N), 57.6 (C-1), 42.5 (CH_2-NH), 30.3 (2× CH_2), 30.1 (2× CH_2), 30.0 (2× CH_2), 29.8 (2× CH_2), 27.6 (2× CH_2), 26.1 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{15}H_{32}N_4O_3]H^+$: 317.2547, found: 317.2551.

***N*-(8-Aminooctyl)-1,4-dideoxy-1,4-imino-L-lyxitol hydrochloride (41)**
Deprotection of **33** (95 mg, 0.02 mmol) according to the general procedure (Method H) afforded **41** as a brown amorphous solid (63 mg, 91%), $[\alpha]_D$ + 18.0 (*c* 0.25, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.37 (dd, *J* = 9.7, 5.4 Hz, 1H, H-2), 4.34–4.30 (m, 1H, H-3), 4.01–3.91 (m, 2H, H-5, H-5'), 3.60–3.56 (m, 1H, H-4), 3.47–3.39 (m, 2H, CH_2-N, H-1), 3.30 (dd, *J* = 11.9, 5.8 Hz, 1H, H-1'), 3.13–3.06 (m, 1H, CH_2-N'), 2.90–2.84 (m, 2H, C*H*$_2$-NH_2), 1.75–1.67 (m, 2H, CH_2), 1.66–1.58 (m, 2H, CH_2), 1.36 (br s, 8H, 4× CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 72.2 (C-3), 72.0 (C-4), 70.7 (C-2), 59.7 (C-5), 58.0 (CH_2-N), 57.6 (C-1), 40.7 (CH_2-NH_2), 29.9 (CH_2), 29.9 (CH_2), 28.5 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 26.1 (CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{13}H_{28}N_2O_2]H^+$: 261.2173, found: 261.2173.



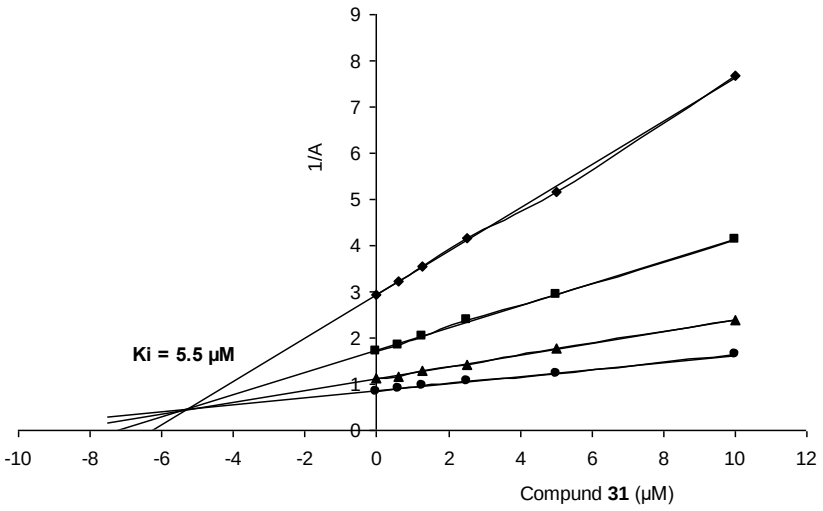


Figure S1. Dixon plots of the inhibition of Golgi α-mannosidase GMIIb by the compounds and **30** and **31** in the presence of different substrate (*p*NP-Man) concentration: 0.5 mM (♦), 1 mM (■), 2 mM (▲), 4 mM (●).

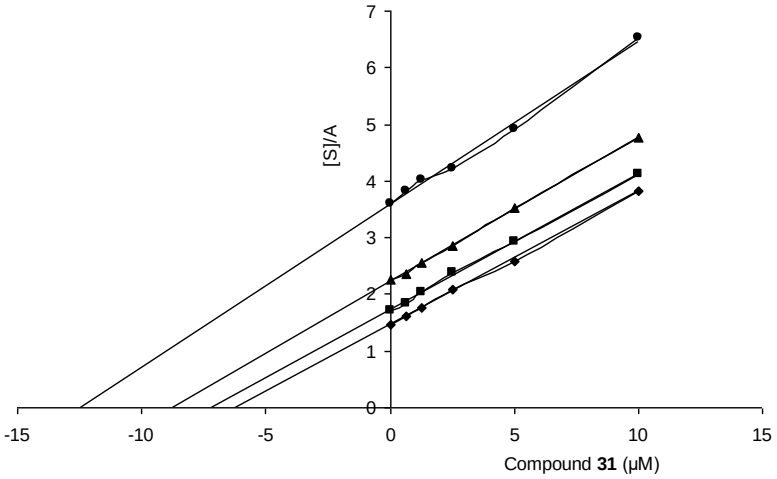


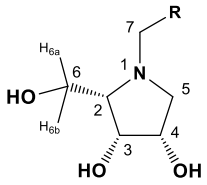
Figure S2. Cornish-Bowden plot[5] of the inhibition of Golgi α-mannosidase GMIIb by the compound **31** in the presence of different substrate (*p*NP-Man) concentration: 0.5 mM (♦), 1 mM (■), 2 mM (▲), 4 mM (●).

Table S1. Selectivity indices of *N*-alkyl substituted 1,4-dideoxy-1,4-imino-L-lyxitols calculated for α-mannosidases (GMIIb, LManII).

Compound	**6**	**7**	**8**	**9**	**28**	**29**	**30**	**31**	**38**	**39**	**40**	**41**	**44**	**46**
Selectivity index[a]	75	194	351	n.d.[b]	258	350	850	390	196	271	215	70	>113[c]	>238[d]

[a] SI = [IC_{20}(LManII)/IC_{20}(GMIIb)]. The ratio means a concentration of the inhibitor causing 20% inhibition of the enzymatic reaction. IC_{20} was used to be able to calculate selectivity indices as all compounds inhibited the reaction with LManII to the level below 50 % even at 4 mM concentration.
[b] inhibition of LManII in the presence of the compound **9** was lower than 20% even at 4 mM concentration.
[c] SI = [IC_{50}(LManII)/IC_{50}(GMIIb)] calculated from IC_{50} measured by Šesták et al.[6]
[d] SI = [IC_{50}(LManII)/IC_{50}(GMIIb)] calculated from IC_{50} measured by Klunda et al.[7]

Table S2. Selected geometrical parameters, interatomic distances d (in Å), bond angles φ (in °) and dihedral angles ϕ (in °), for the neutral forms of **8**, **30**, **43 - 47** calculated at the ωB97xD/6-311+G(2d,p) level of theory with the SMD solvent model (conformations below 6% of population are not shown).



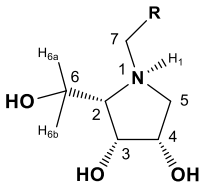
Geometrical parameters	8			30	43				
	E_3	^5E	^5E	E_3	E_4	E_3	E_4	^5E	^5E
d(N_1-C_2)	1.472	1.471	1.467	1.473	1.473	1.481	1.471	1.469	1.468
d(C_2-C_3)	1.525	1.559	1.556	1.553	1.555	1.530	1.554	1.559	1.558
d(C_3-C_4)	1.529	1.540	1.546	1.530	1.531	1.529	1.531	1.537	1.537
d(C_4-C_5)	1.535	1.513	1.510	1.518	1.516	1.529	1.518	1.511	1.511
d(C_5-N_1)	1.469	1.461	1.459	1.469	1.465	1.470	1.463	1.460	1.460
d(C_2-C_6)	1.527	1.522	1.520	1.531	1.532	1.529	1.529	1.524	1.524
d(N_1-C_7)	1.456	1.455	1.454	1.457	1.454	1.461	1.452	1.453	1.453
φ(N_1-C_2-C_3)	105.0	104.8	105.1	104.8	104.5	105.9	105.0	104.6	104.6
φ(C_2-C_3-C_4)	102.1	104.3	105.0	104.1	104.0	102.6	104.1	104.0	104.0
φ(C_3-C_4-C_5)	103.3	101.8	102.0	101.1	101.1	102.2	101.3	101.7	101.7
φ(C_4-C_5-N_1)	106.0	102.4	102.0	105.5	104.3	105.8	104.2	101.5	101.5
φ(N_1-C_2-C_6)	109.2	110.3	109.3	109.0	109.4	110.0	108.5	110.5	110.5
φ(C_2-N_1-C_7)	113.9	113.8	113.5	115.7	115.8	113.8	115.1	114.2	114.2
φ(C_5-N_1-C_2)	109.0	106.4	106.9	109.1	109.3	108.6	109.4	106.8	106.8
ϕ(N_1-C_2-C_3-C_4)	35.5	-2.6	-1.55	-23.4	-20.8	29.9	-19.6	-4.6	-4.6
ϕ(C_2-C_3-C_4-C_5)	-36.8	27.7	21.8	36.9	37.1	-38.1	36.1	30.1	30.1
ϕ(C_3-C_4-C_5-N_1)	25.2	-43.4	-37.8	-37.6	-40.2	33.2	-39.8	-45.0	-45.0
ϕ(C_6-C_2-N_1-C_7)	86.5	84.0	85.4	108.4	102.3	99.5	99.9	86.4	86.4
ϕ(C_2-N_1-C_7-R)	-161.4	-169.4	-169.5	-64.8	-65.7	-66.6	-165.6	-167.9	-167.9
ϕ(C_4-C_5-N_1-C_7)	126.2	170.1	166.7	153.8	159.4	113.1	159.9	170.9	170.9
ϕ(H_3-C_3-O_3-H($O)_3$)	122.4	-164.7	159.4	-148.1	-149.7	131.6	-149.0	-147.7	-128.3
ϕ(H_4-C_4-O_4-H($O)_4$)	160.3	-160.8	74.0	176.3	175.4	159.2	174.8	-159.0	-160.6
ϕ(H_{6a}-C_6-O_6-H($O)_6$)	79.1	73.9	81.4	72.3	69.5	71.7	69.1	60.9	175.0
ϕ(O_6-C_6-C_2-N_1)	46.4	48.7	57.6	40.5	40.1	45.4	42.2	-177.6	57.6

Geometrical parameters	44					45	46
	E_4	E_3	E_4	E_3	^5E	E_4	E_4
d(N_1-C_2)	1.473	1.474	1.471	1.481	1.469	1.474	1.473
d(C_2-C_3)	1.556	1.526	1.554	1.530	1.559	1.555	1.556
d(C_3-C_4)	1.531	1.530	1.531	1.530	1.537	1.531	1.531
d(C_4-C_5)	1.516	1.533	1.518	1.530	1.511	1.516	1.516
d(C_5-N_1)	1.464	1.469	1.463	1.470	1.460	1.465	1.464
d(C_2-C_6)	1.532	1.526	1.529	1.529	1.524	1.531	1.532
d(N_1-C_7)	1.454	1.457	1.452	1.461	1.454	1.454	1.454
φ(N_1-C_2-C_3)	104.5	105.2	104.7	105.8	104.6	104.5	104.5
φ(C_2-C_3-C_4)	104.0	102.2	104.1	102.6	104.0	104.0	104.0
φ(C_3-C_4-C_5)	101.1	103.1	101.3	102.2	101.7	101.1	101.0
φ(C_4-C_5-N_1)	104.3	105.9	104.1	105.8	101.6	104.4	104.3
φ(N_1-C_2-C_6)	109.4	109.8	108.4	110.1	110.7	109.4	109.4
φ(C_2-N_1-C_7)	115.8	113.5	115.1	113.9	114.3	115.6	115.8
φ(C_5-N_1-C_2)	109.3	109.1	109.4	108.5	106.7	109.3	109.3
ϕ(N_1-C_2-C_3-C_4)	-20.7	34.5	-19.3	30.2	-4.3	-21.0	-20.8
ϕ(C_2-C_3-C_4-C_5)	37.1	-37.3	36.0	-38.2	29.9	37.1	37.1
ϕ(C_3-C_4-C_5-N_1)	-40.4	27.1	-40.0	33.0	-44.9	-40.1	-40.3

$\phi(C_6\text{-}C_2\text{-}N_1\text{-}C_7)$	102.1	89.0	99.4	99.1	86.2	103.0	102.0
$\phi(C_2\text{-}N_1\text{-}C_7\text{-}R)$	-65.2	-164.6	-165.6	-65.9	-169.2	-65.3	-64.8
$\phi(C_4\text{-}C_5\text{-}N_1\text{-}C_7)$	159.6	123.0	160.5	113.4	171.0	158.7	159.7
$\phi(H_3\text{-}C_3\text{-}O_3\text{-}H(O)_3)$	-149.5	123.2	-149.2	131.0	-147.7	-149.5	-149.6
$\phi(H_4\text{-}C_4\text{-}O_4\text{-}H(O)_4)$	175.5	160.5	174.8	159.4	-159.0	175.1	175.4
$\phi(H_{6a}\text{-}C_6\text{-}O_6\text{-}H(O)_6)$	69.5	76.7	69.7	75.9	60.9	70.8	69.8
$\phi(O_6\text{-}C_6\text{-}C_2\text{-}N_1)$	40.0	47.7	42.1	45.4	-178.0	40.9	39.9

Geometrical parameters	**47**		
	E_3	E_3	^5E
$d(N_1\text{-}C_2)$	1.474	1.482	1.469
$d(C_2\text{-}C_3)$	1.527	1.531	1.554
$d(C_3\text{-}C_4)$	1.529	1.528	1.553
$d(C_4\text{-}C_5)$	1.534	1.529	1.512
$d(C_5\text{-}N_1)$	1.470	1.471	1.459
$d(C_2\text{-}C_6)$	1.531	1.534	1.531
$d(N_1\text{-}C_7)$	1.456	1.462	1.453
$\varphi(N_1\text{-}C_2\text{-}C_3)$	104.8	105.6	103.8
$\varphi(C_2\text{-}C_3\text{-}C_4)$	101.8	102.1	108.9
$\varphi(C_3\text{-}C_4\text{-}C_5)$	103.0	102.0	102.7
$\varphi(C_4\text{-}C_5\text{-}N_1)$	105.8	105.8	101.5
$\varphi(N_1\text{-}C_2\text{-}C_6)$	109.6	110.5	115.0
$\varphi(C_2\text{-}N_1\text{-}C_7)$	113.4	113.8	114.4
$\varphi(C_5\text{-}N_1\text{-}C_2)$	108.9	108.3	103.6
$\phi(N_1\text{-}C_2\text{-}C_3\text{-}C_4)$	36.2	32.2	13.0
$\phi(C_2\text{-}C_3\text{-}C_4\text{-}C_5)$	38.4	-39.7	16.6
$\phi(C_3\text{-}C_4\text{-}C_5\text{-}N_1)$	27.0	33.6	-40.6
$\phi(C_6\text{-}C_2\text{-}N_1\text{-}C_7)$	86.6	96.9	69.1
$\phi(C_2\text{-}N_1\text{-}C_7\text{-}R)$	-165.8	-67.3	-175.3
$\phi(C_4\text{-}C_5\text{-}N_1\text{-}C_7)$	123.6	113.3	175.1
$\phi(H_3\text{-}C_3\text{-}O_3\text{-}H(O)_3)$	117.8	124.1	-127.4
$\phi(H_4\text{-}C_4\text{-}O_4\text{-}H(O)_4)$	162.3	161.8	-160.1
$\phi(H_{6a}\text{-}C_6\text{-}O_6\text{-}H(O)_6)$	70.4	68.2	173.9
$\phi(O_6\text{-}C_6\text{-}C_2\text{-}N_1)$	50.7	50.0	60.8

Table S3. Selected geometrical parameters, interatomic distances d (in Å), bond angles φ (in °) and dihedral angles ϕ (in °), for the protonated forms of **8**, **30**, **43** and **45** calculated at the ωB97xD/6-311+G(2d,p) level of theory with the SMD solvent model.



Geometrical parameters	8		30	43		45
	E_4	^4E	^4E	E_4	E_4	^4E
d(N_1-C_2)	1.529	1.517	1.532	1.515	1.516	1.521
d(C_2-C_3)	1.522	1.553	1.524	1.552	1.553	1.523
d(C_3-C_4)	1.525	1.536	1.526	1.538	1.538	1.531
d(C_4-C_5)	1.526	1.506	1.524	1.510	1.510	1.529
d(C_5-N_1)	1.497	1.505	1.496	1.500	1.500	1.499
d(C_2-C_6)	1.520	1.533	1.520	1.529	1.529	1.520
d(N_1-C_7)	1.497	1.494	1.503	1.492	1.497	1.506
d(N_1-H_1)	1.040	1.041	1.041	1.037	1.037	1.041
φ(N_1-C_2-C_3)	104.9	104.2	105.7	104.9	105.3	105.7
φ(C_2-C_3-C_4)	104.6	104.4	102.6	104.6	102.5	102.9
φ(C_3-C_4-C_5)	102.4	101.8	102.6	102.4	102.5	102.5
φ(C_4-C_5-N_1)	104.5	105.2	104.1	104.4	105.0	103.8
φ(N_1-C_2-C_6)	111.1	112.6	111.9	111.0	112.4	112.0
φ(C_2-N_1-C_7)	113.4	115.4	111.3	112.9	113.9	110.2
φ(C_5-N_1-C_2)	107.6	107.9	107.0	107.7	107.4	106.8
φ(C_2-N_1-H_1)	108.1	108.5	109.1	108.9	108.2	109.6
φ(C_7-N_1-H_1)	106.0	105.8	107.1	107.0	106.0	108.2
ϕ(N_1-C_2-C_3-C_4)	-18.6	-24.7	28.6	-18.5	32.5	26.1
ϕ(C_2-C_3-C_4-C_5)	35.9	39.0	-41.8	35.9	-41.6	-41.1
ϕ(C_3-C_4-C_5-N_1)	-39.9	-38.6	39.3	-39.8	35.3	40.7
ϕ(C_6-C_2-N_1-C_7)	103.6	114.6	104.8	103.8	90.7	108.1
ϕ(C_2-N_1-C_7-R)	-173.6	-70.3	-168.3	-174.8	64.8	-179.6
ϕ(C_4-C_5-N_1-C_7)	155.7	151.1	101.9	155.1	113.2	97.8
ϕ(H_3-C_3-O_3-H(O_3)	-150.0	-153.0	-78.1	-149.9	105.7	-78.3
ϕ(H_4-C_4-O_4-H(O_4)	-151.5	-146.9	-52.1	-151.3	163.7	-52.3
ϕ(H_{6a}-C_6-O_6-H(O_6)	-146.6	-150.5	-151.0	-146.1	43.4	-149.2
ϕ(O_6-C_6-C_2-N_1)	-46.5	-49.5	-57.4	-46.5	70.6	-57.4
ϕ(H_2-C_2- N_1-H_1)	-134.3	-126.8	-132.5	-141.9	-134.3	-124.2

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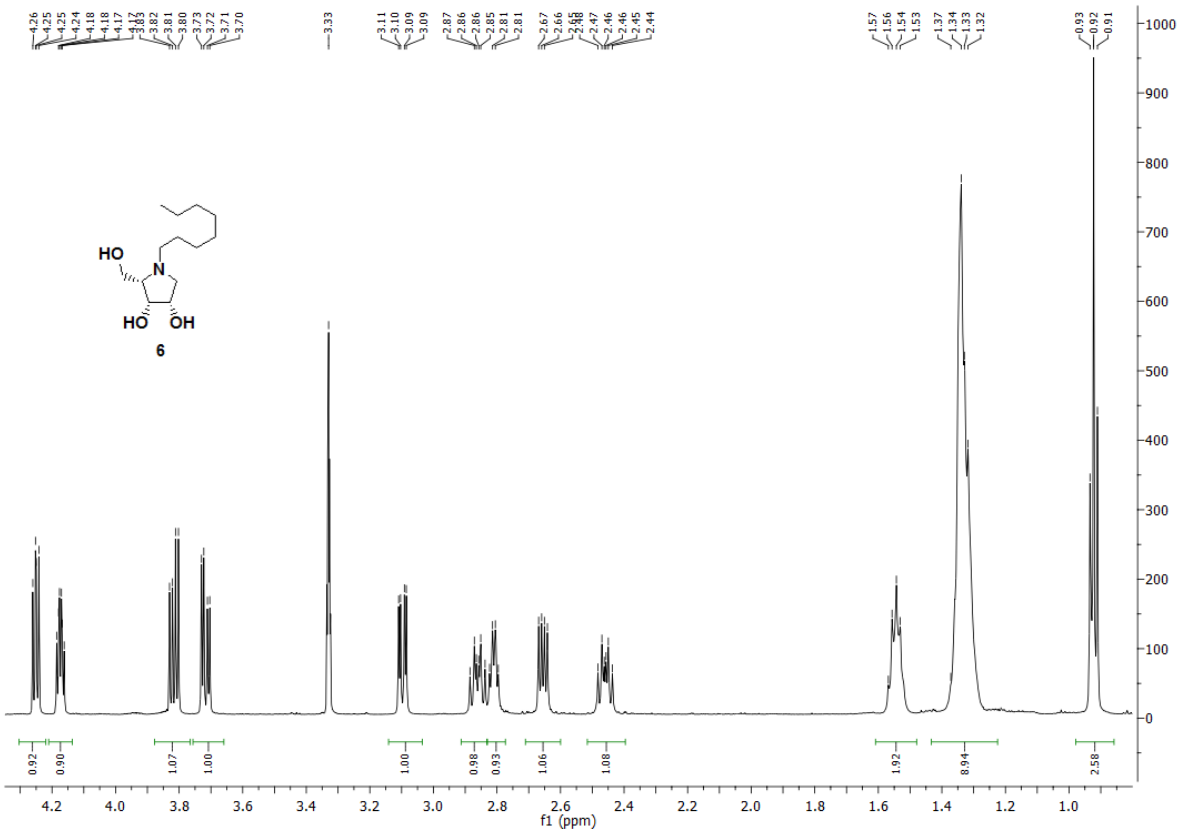
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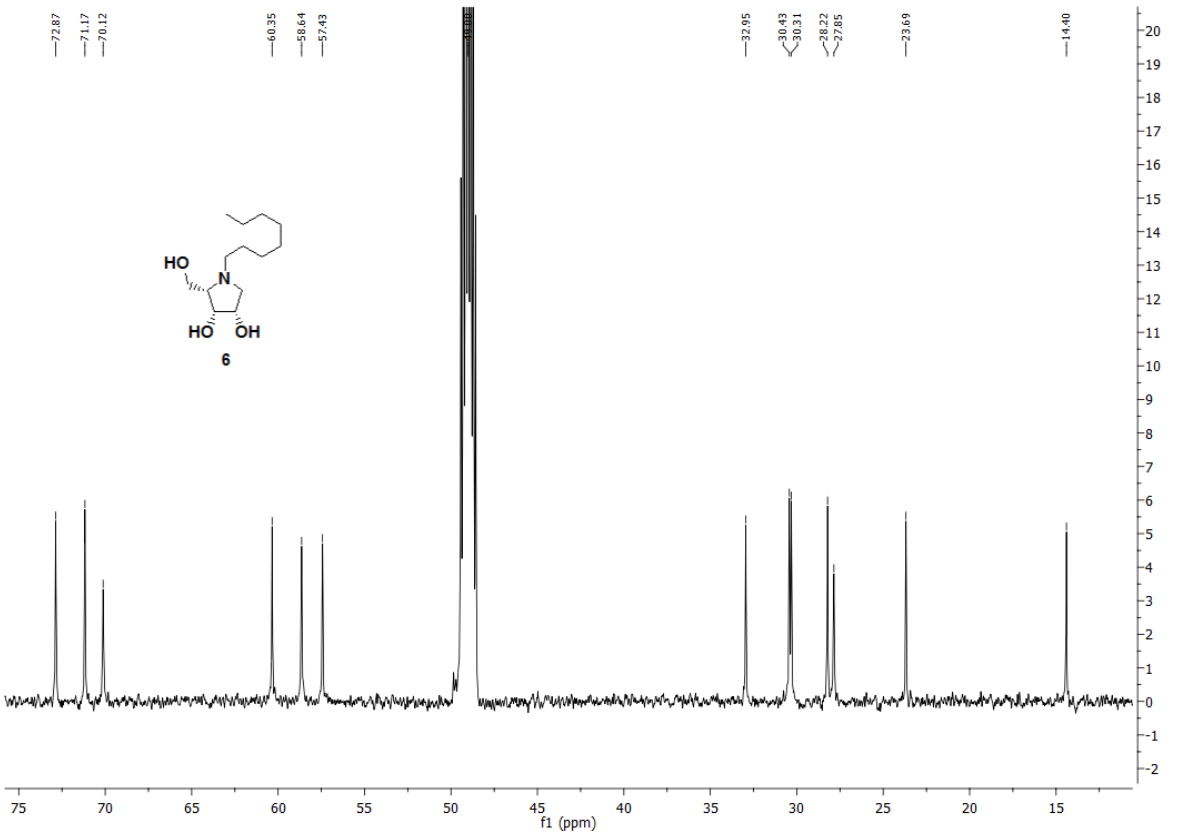
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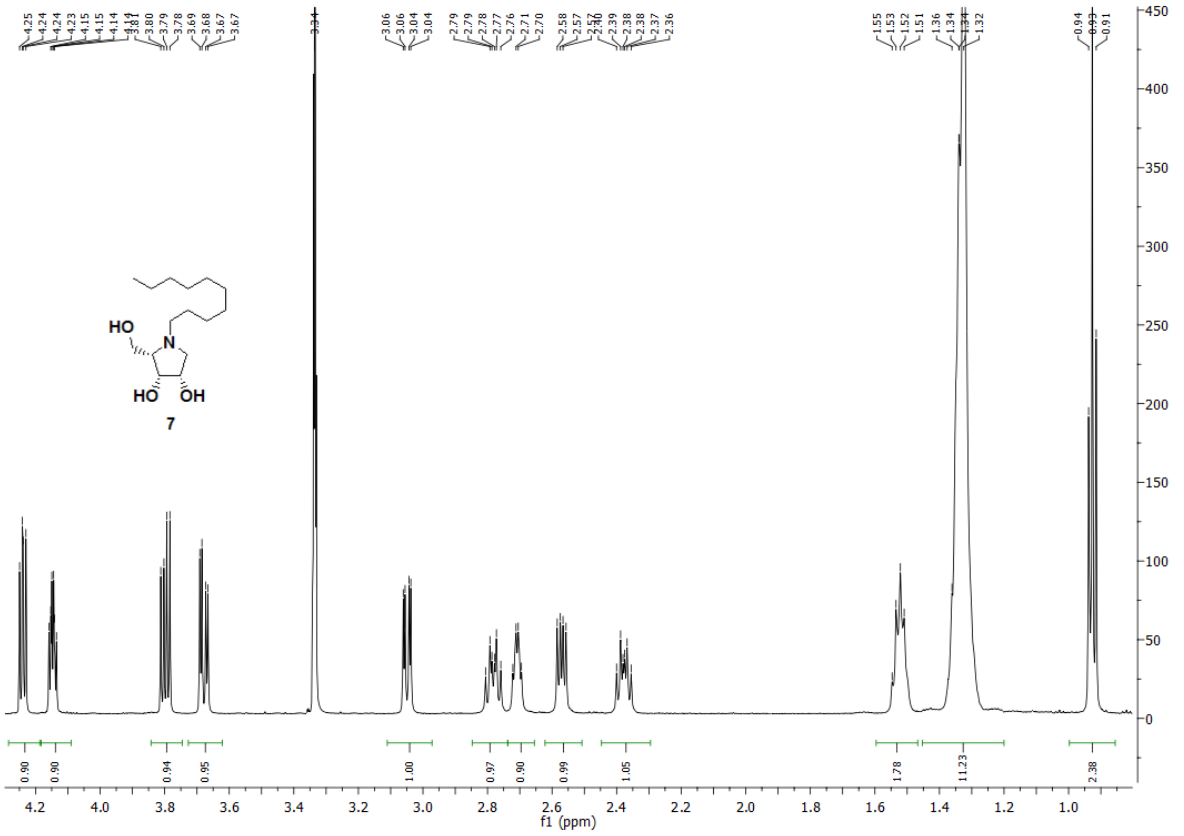
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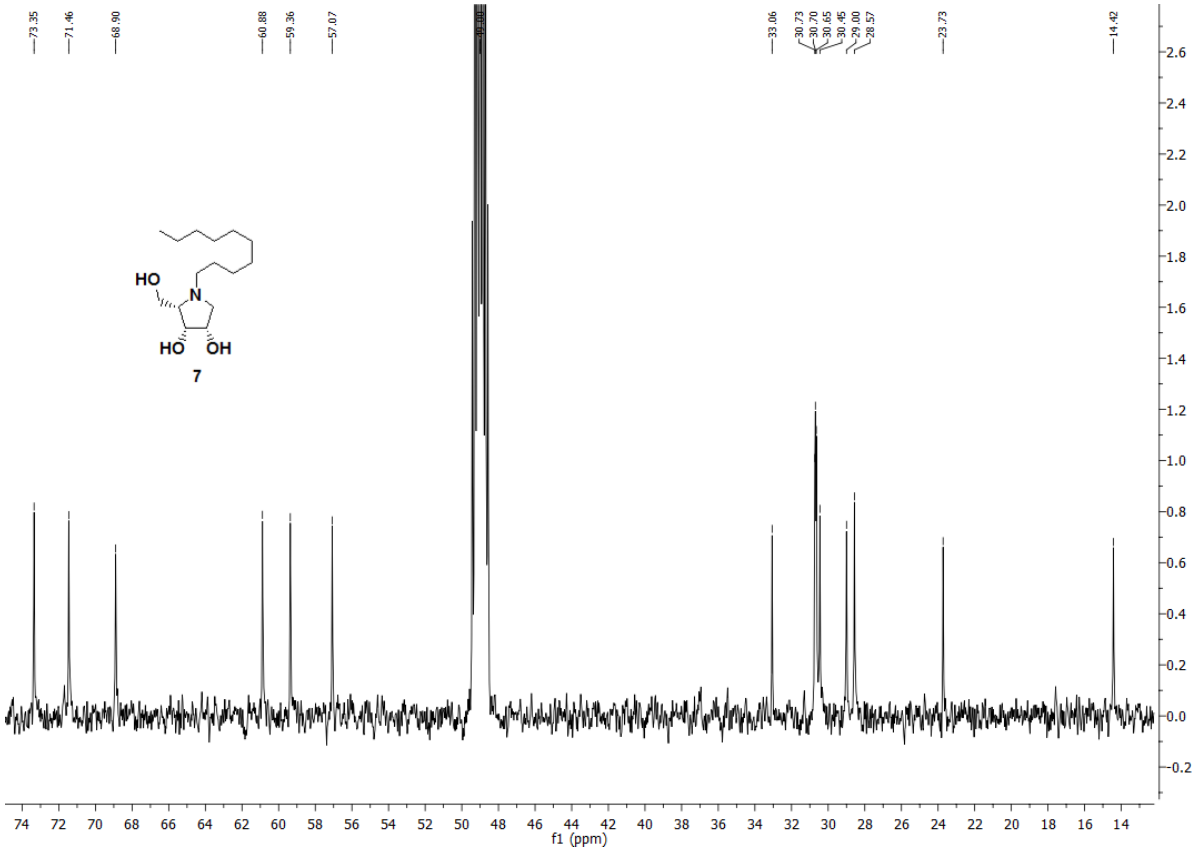
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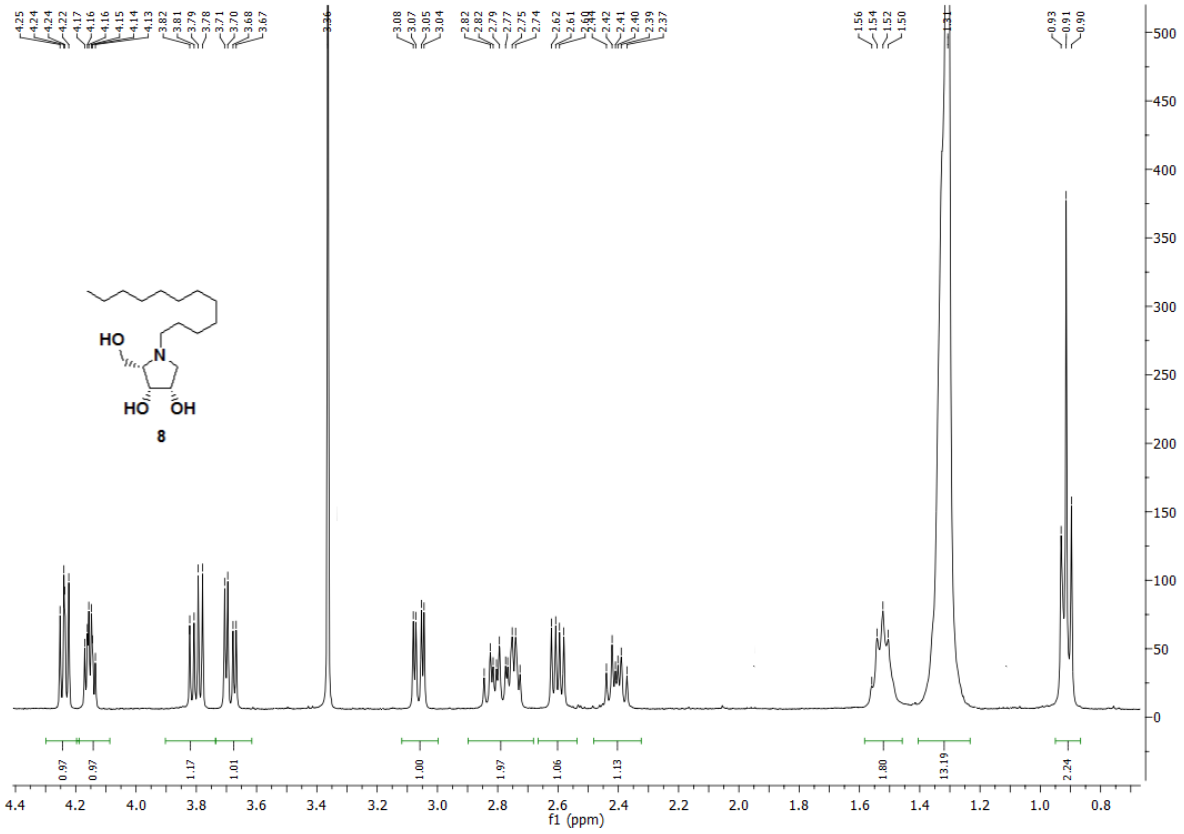
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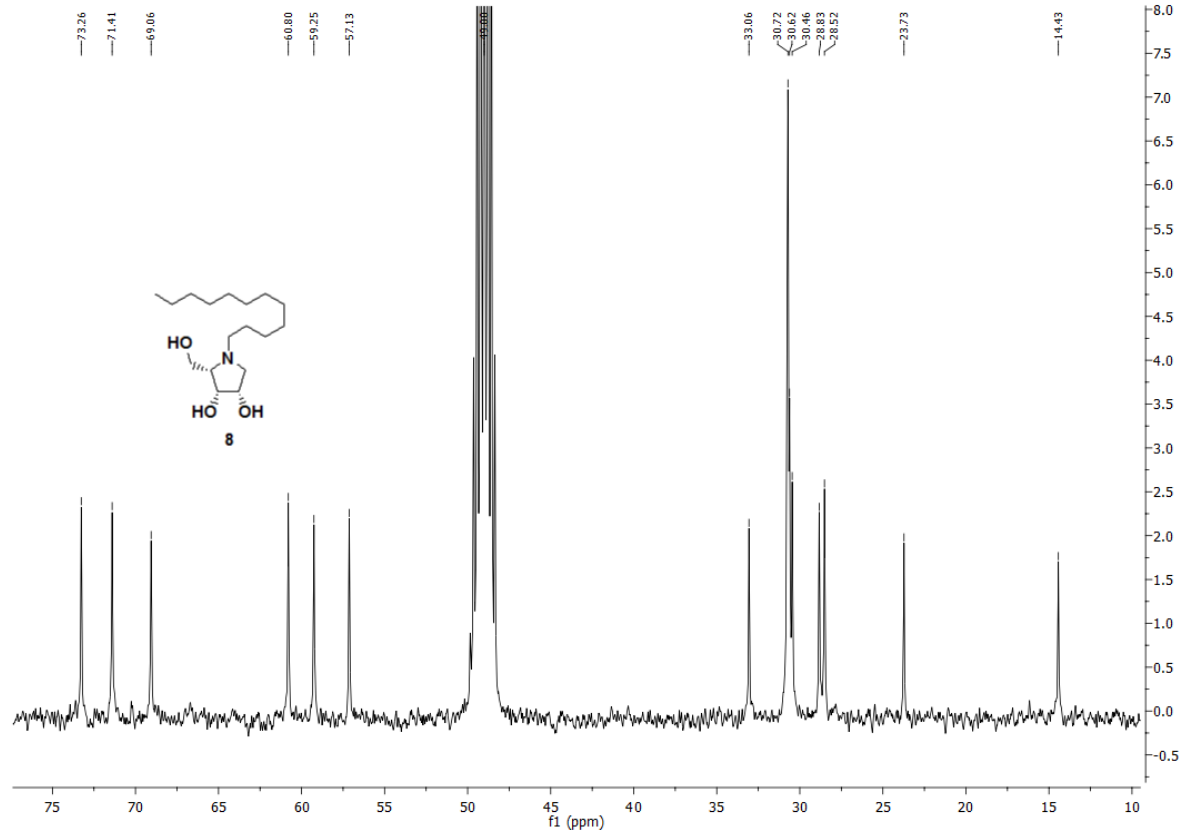
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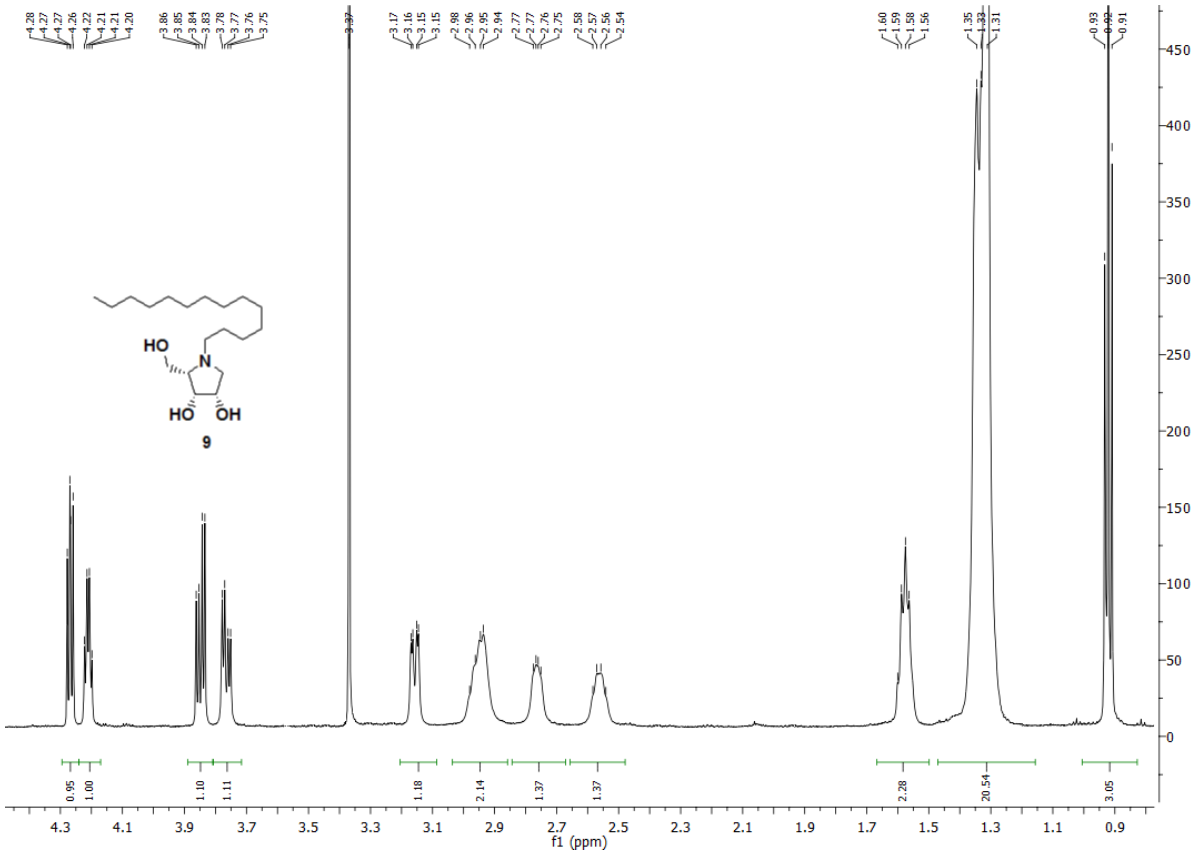
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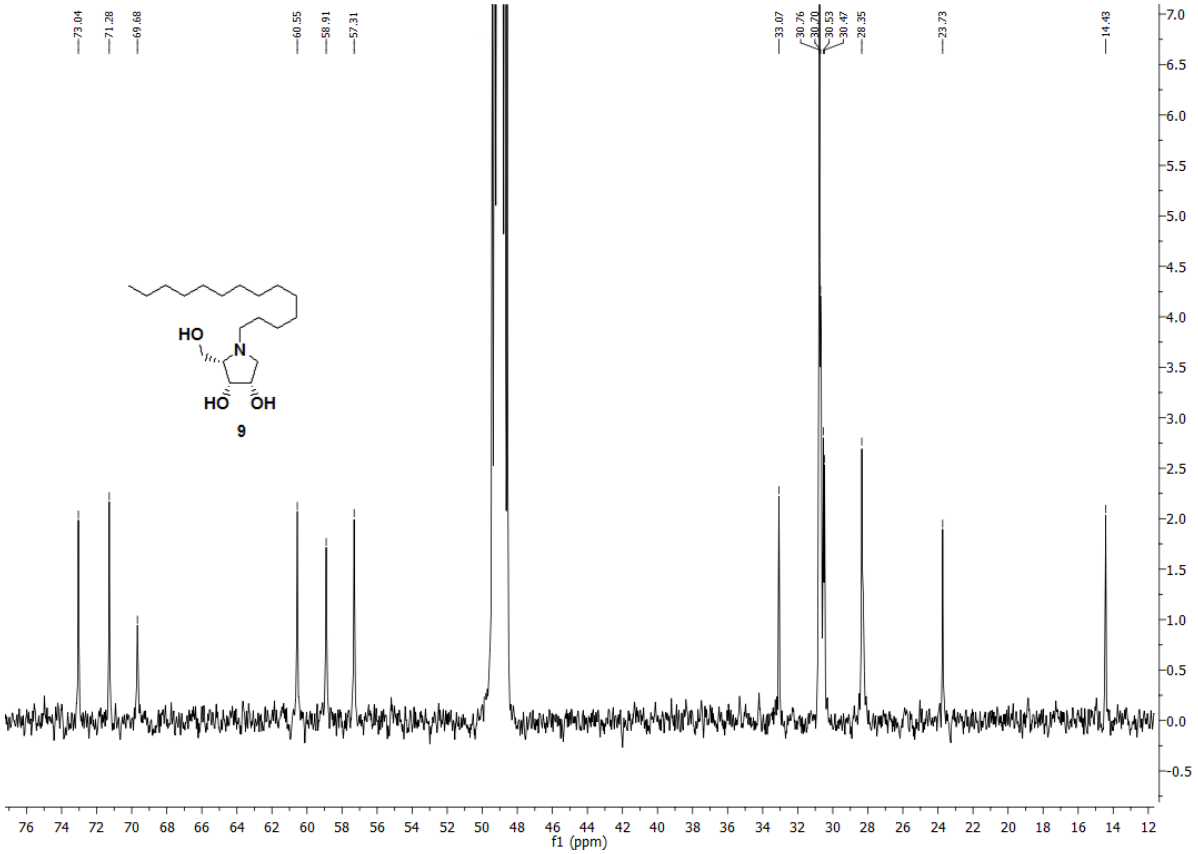
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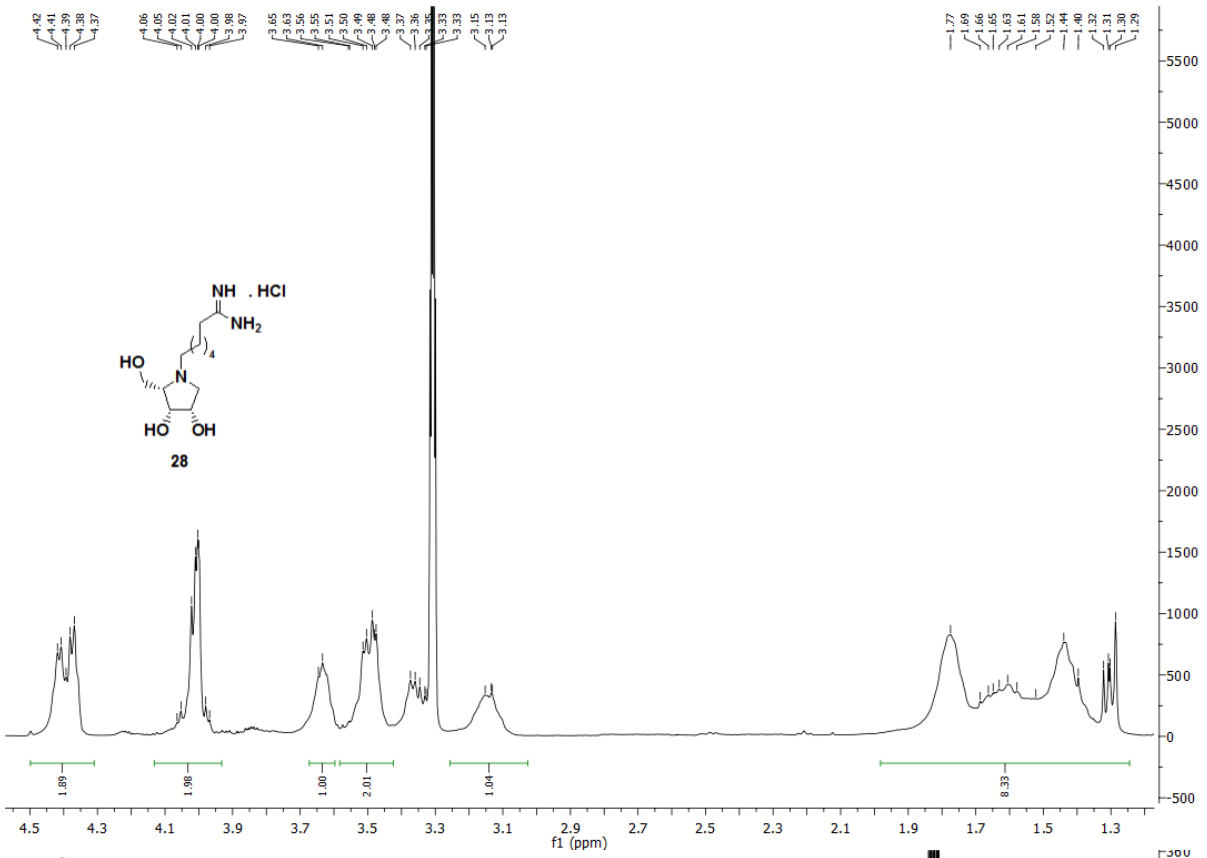
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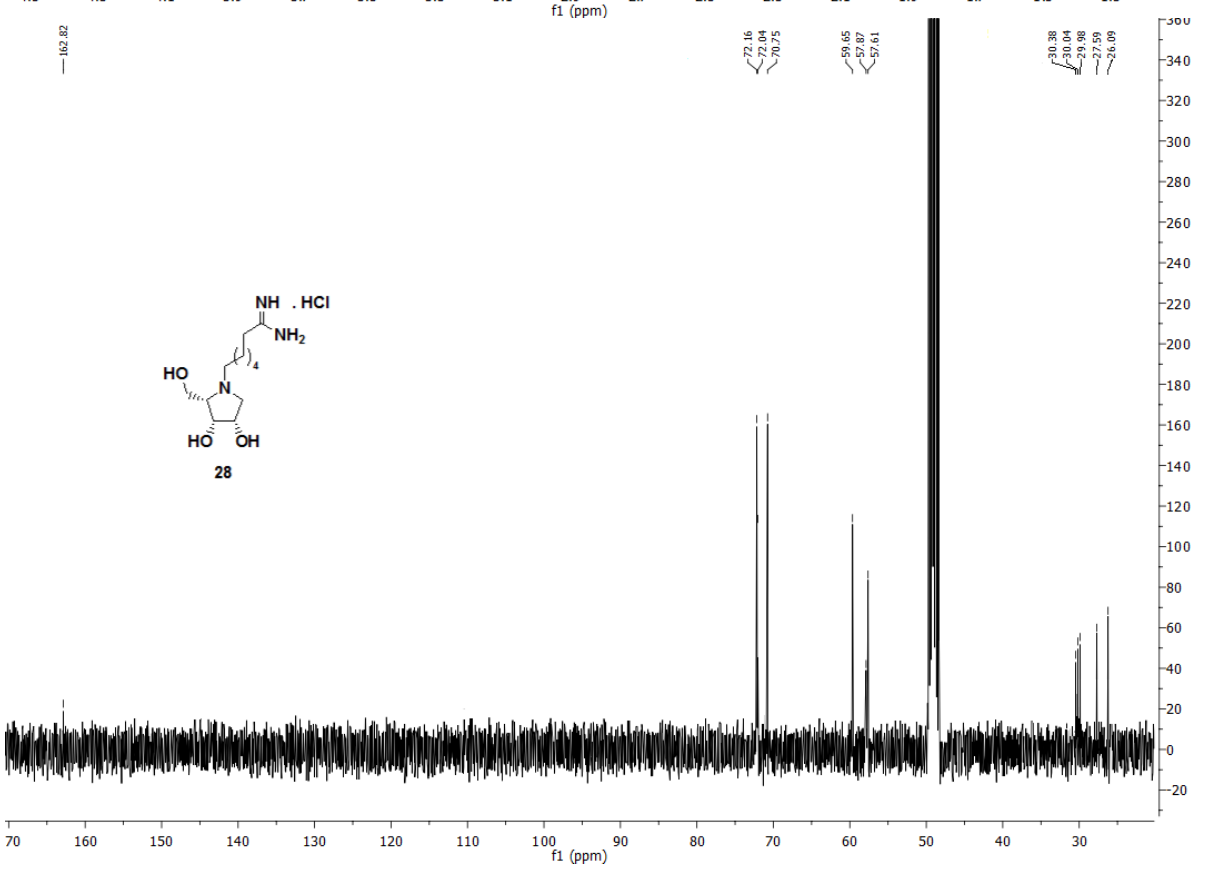
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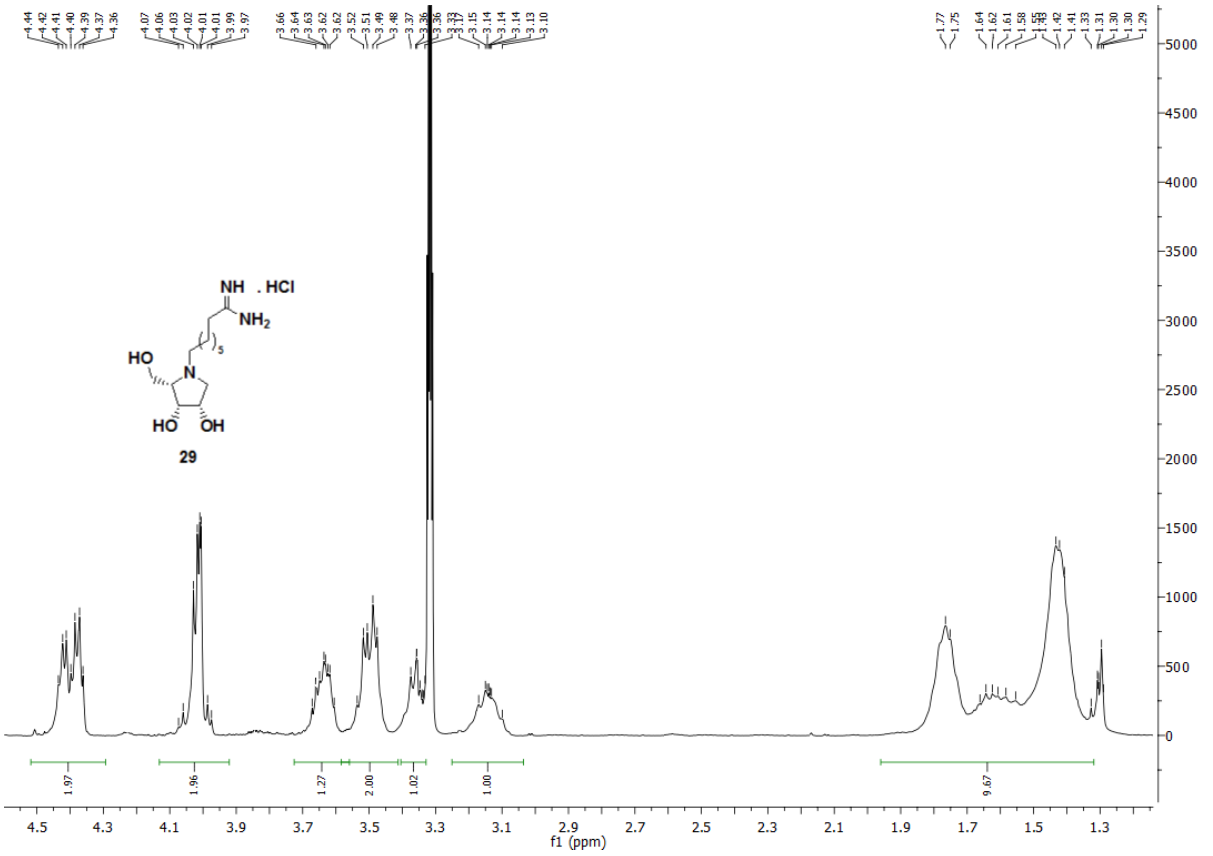
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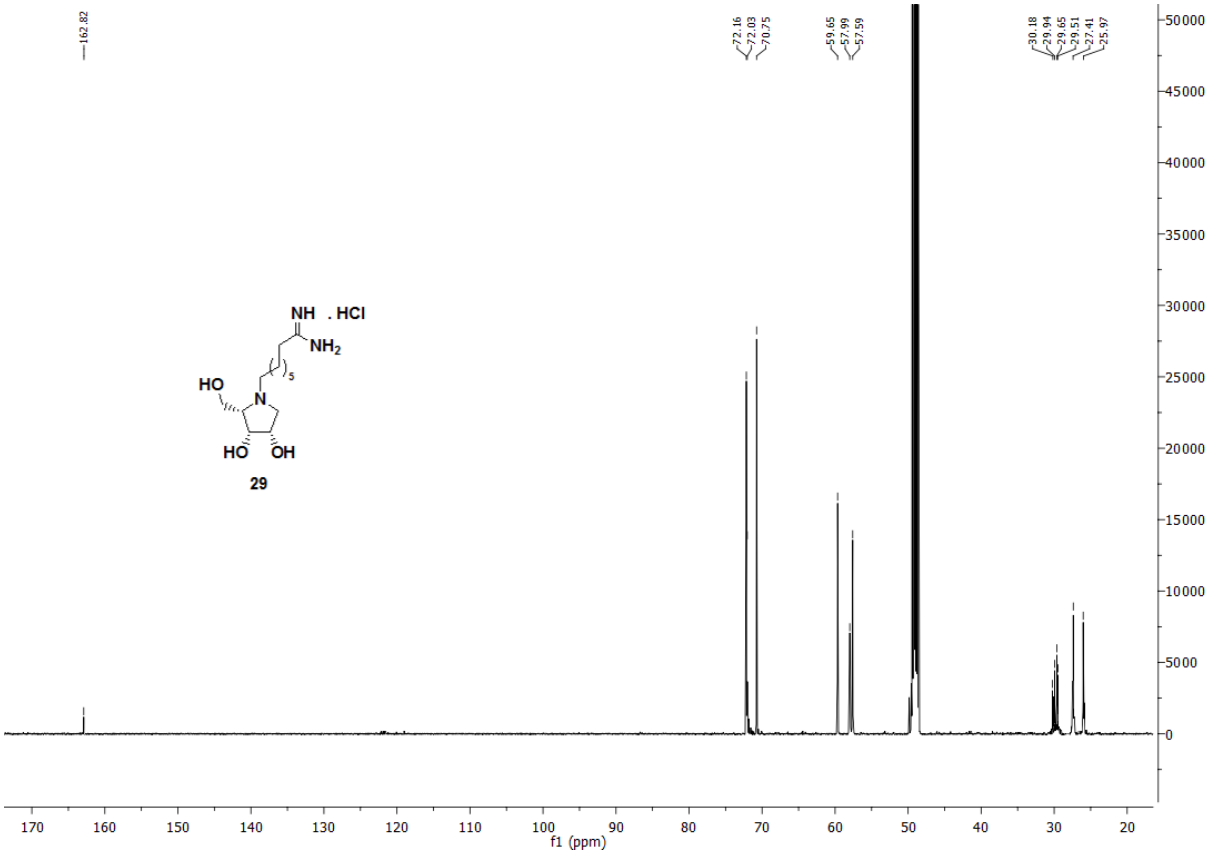
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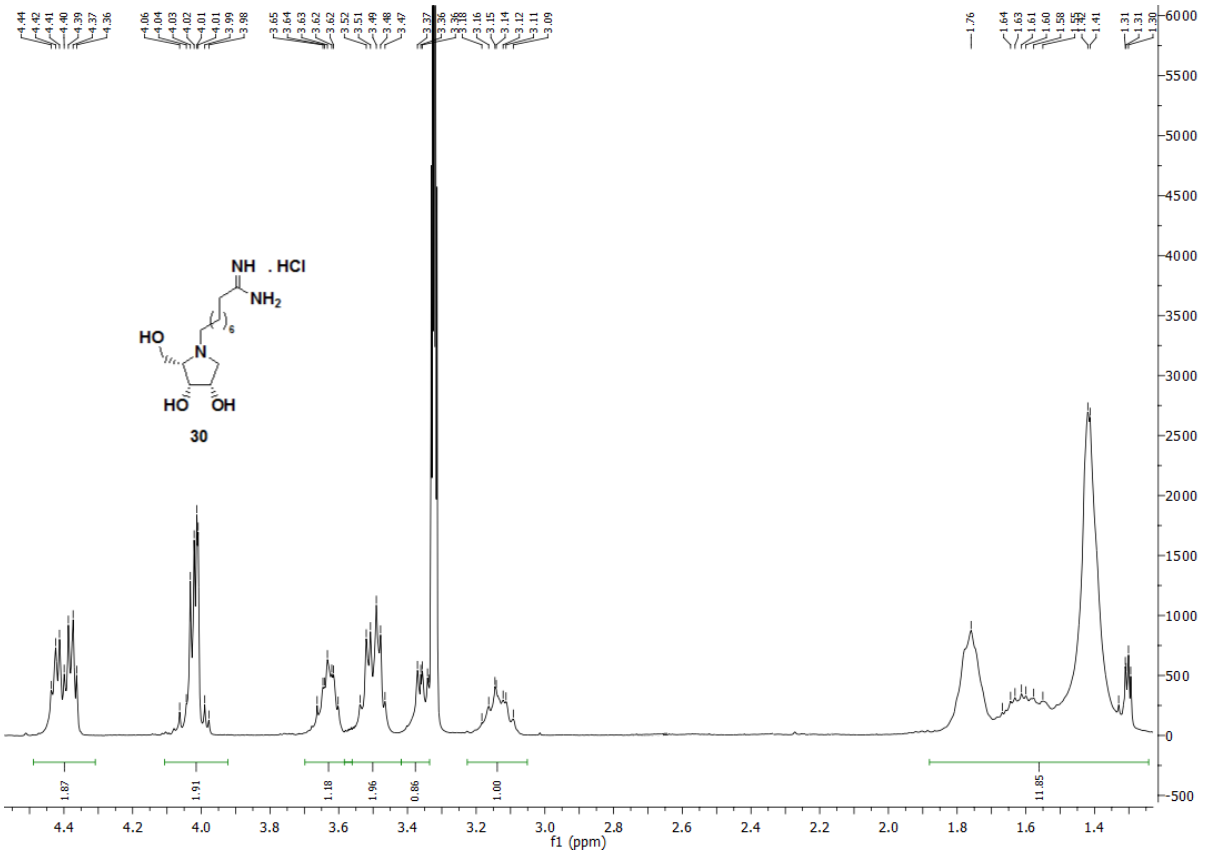
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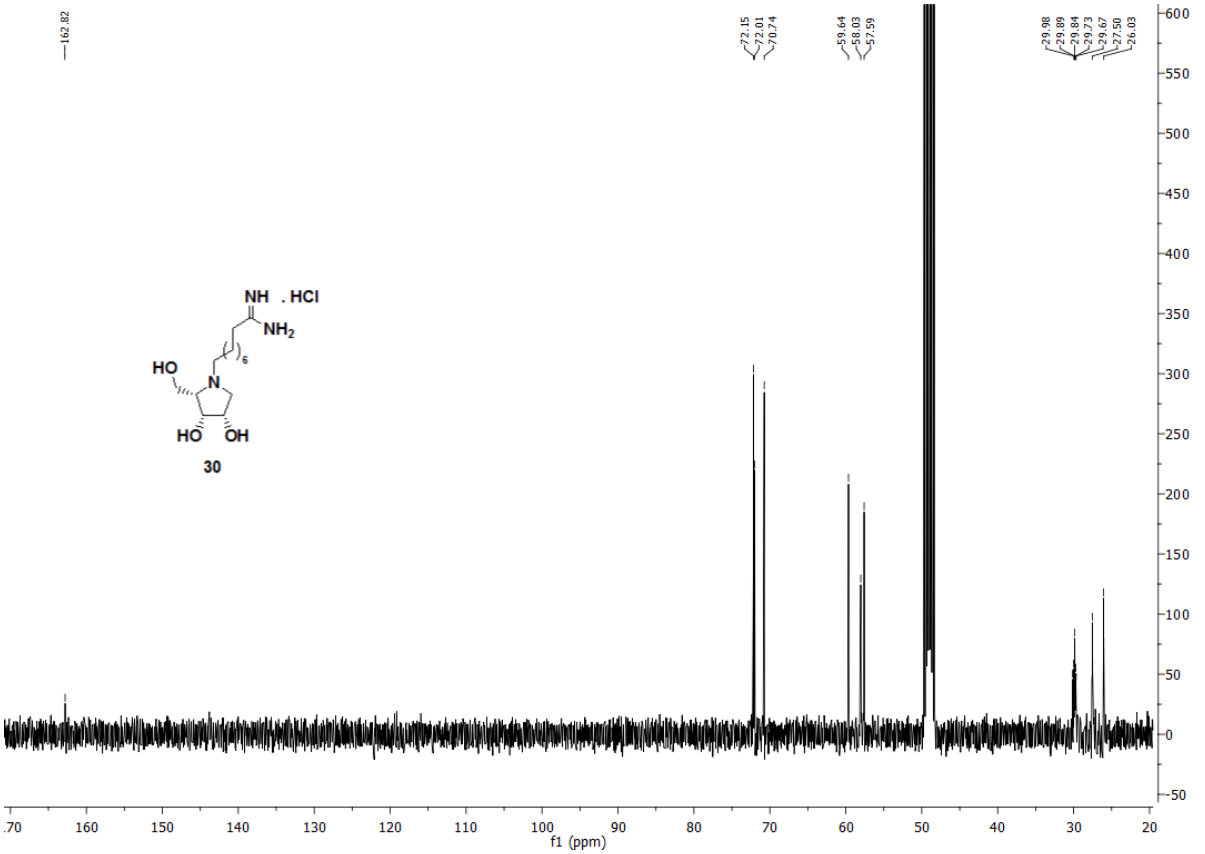
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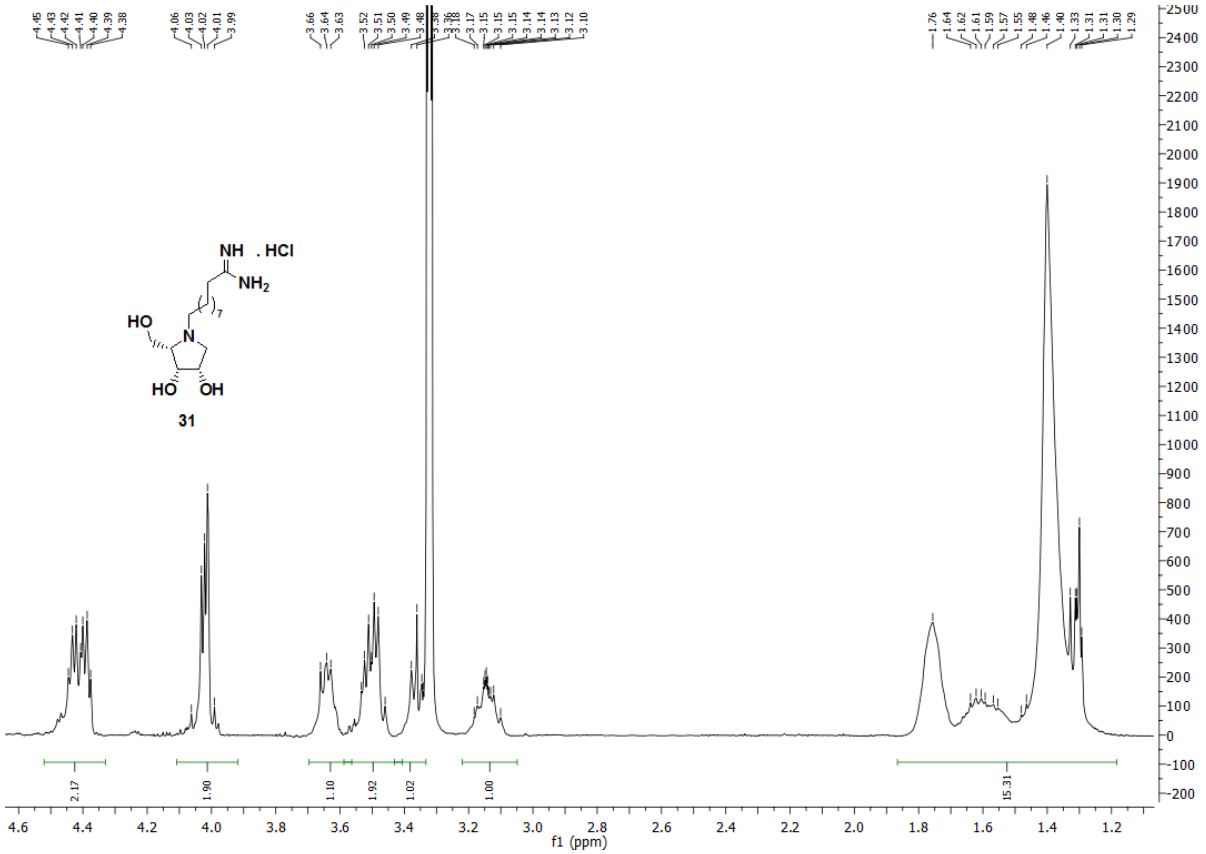
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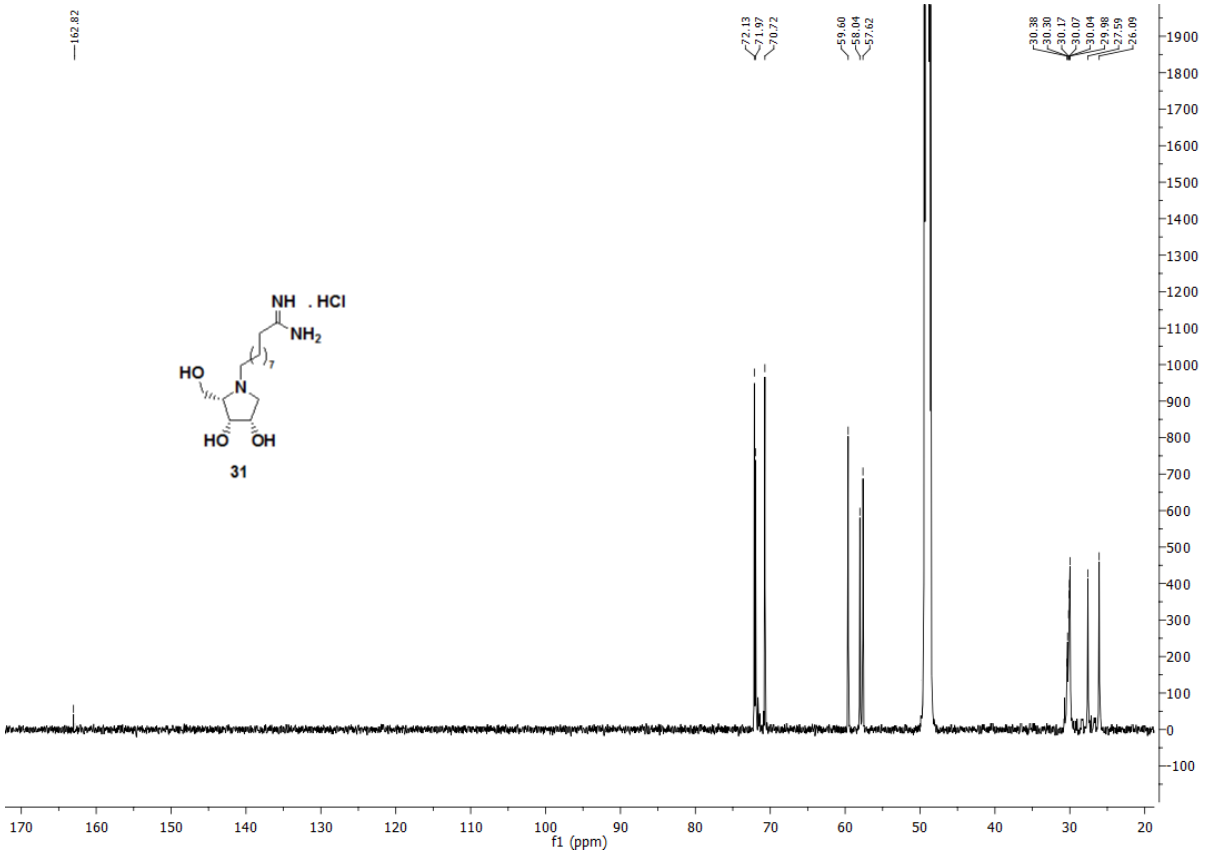
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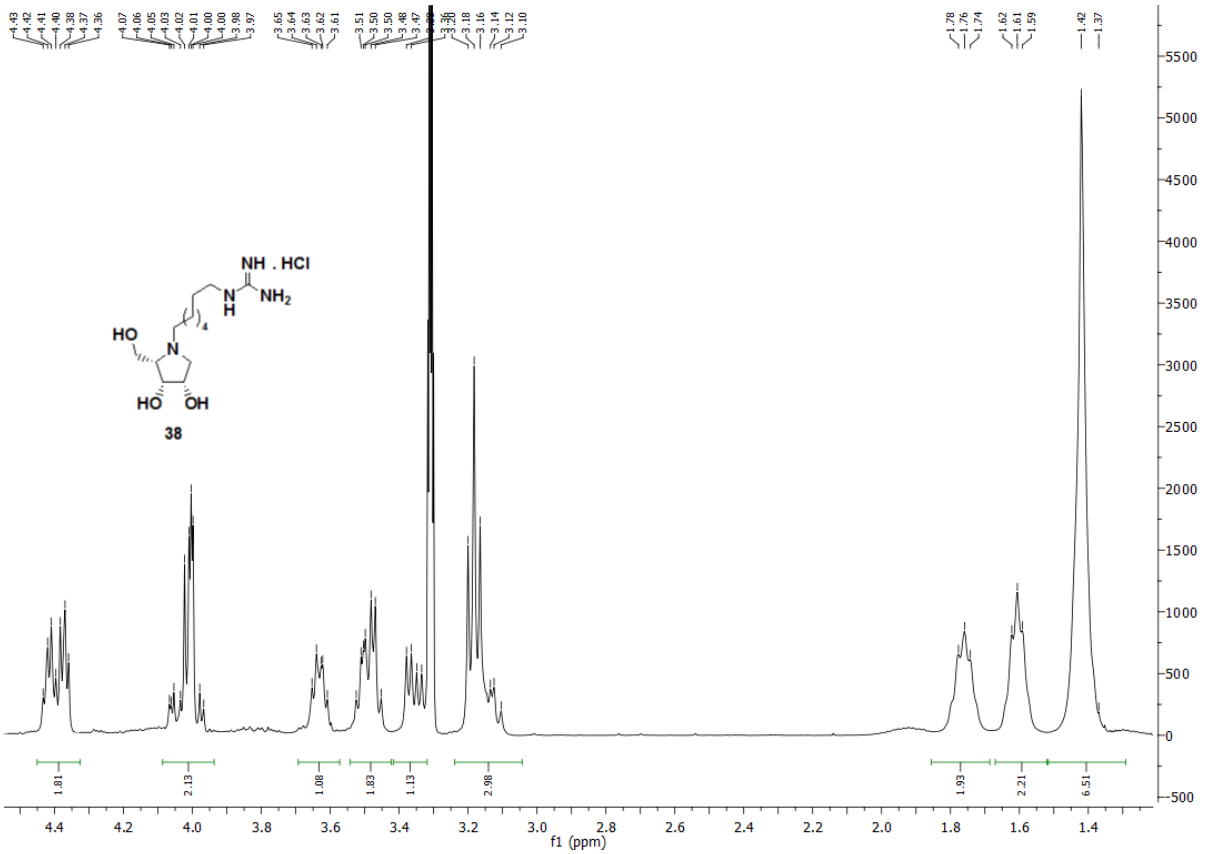
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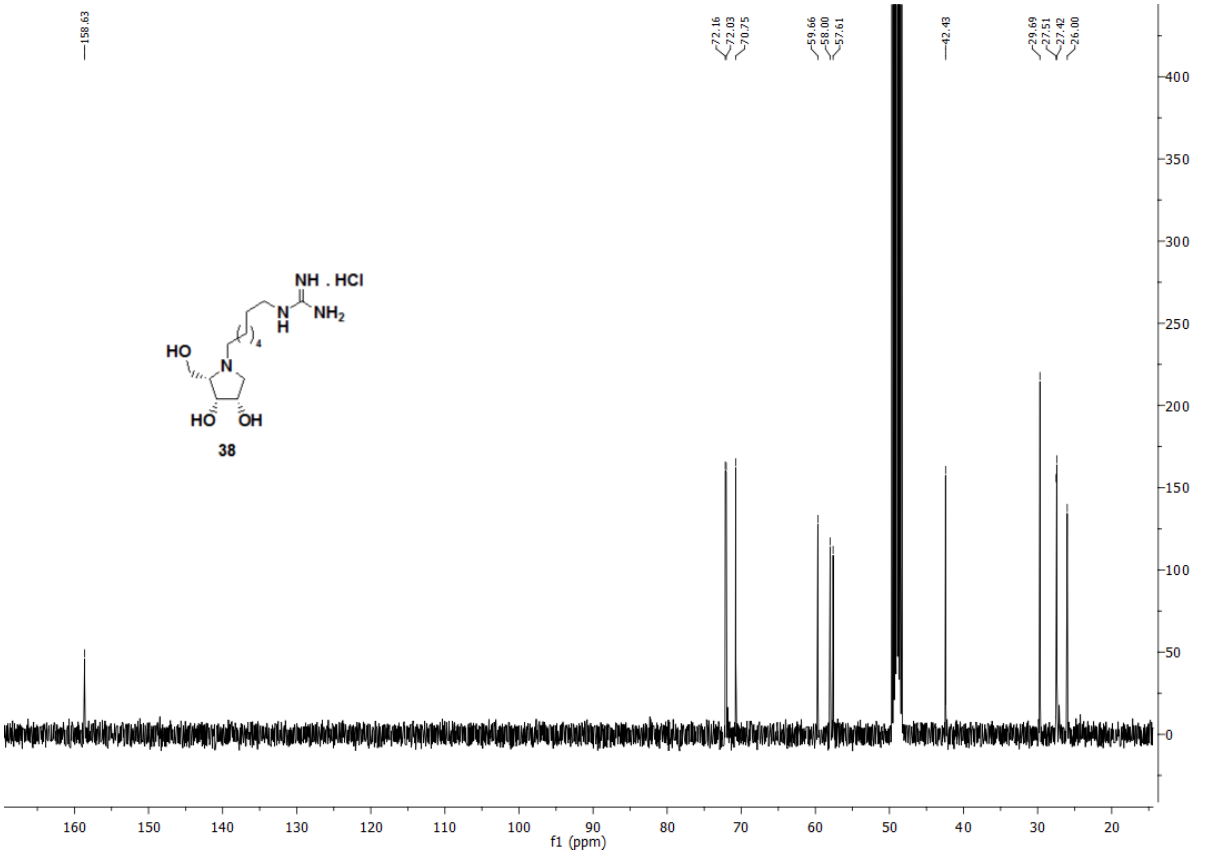
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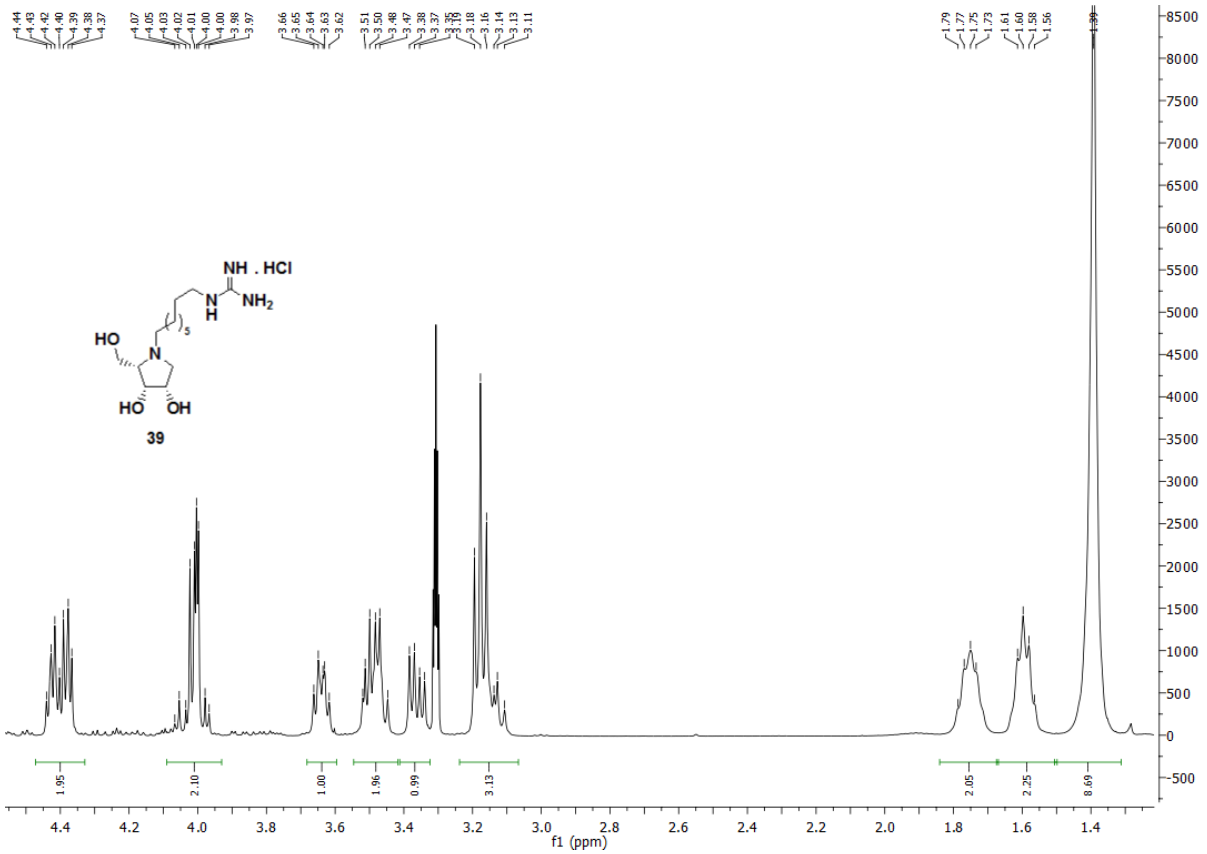
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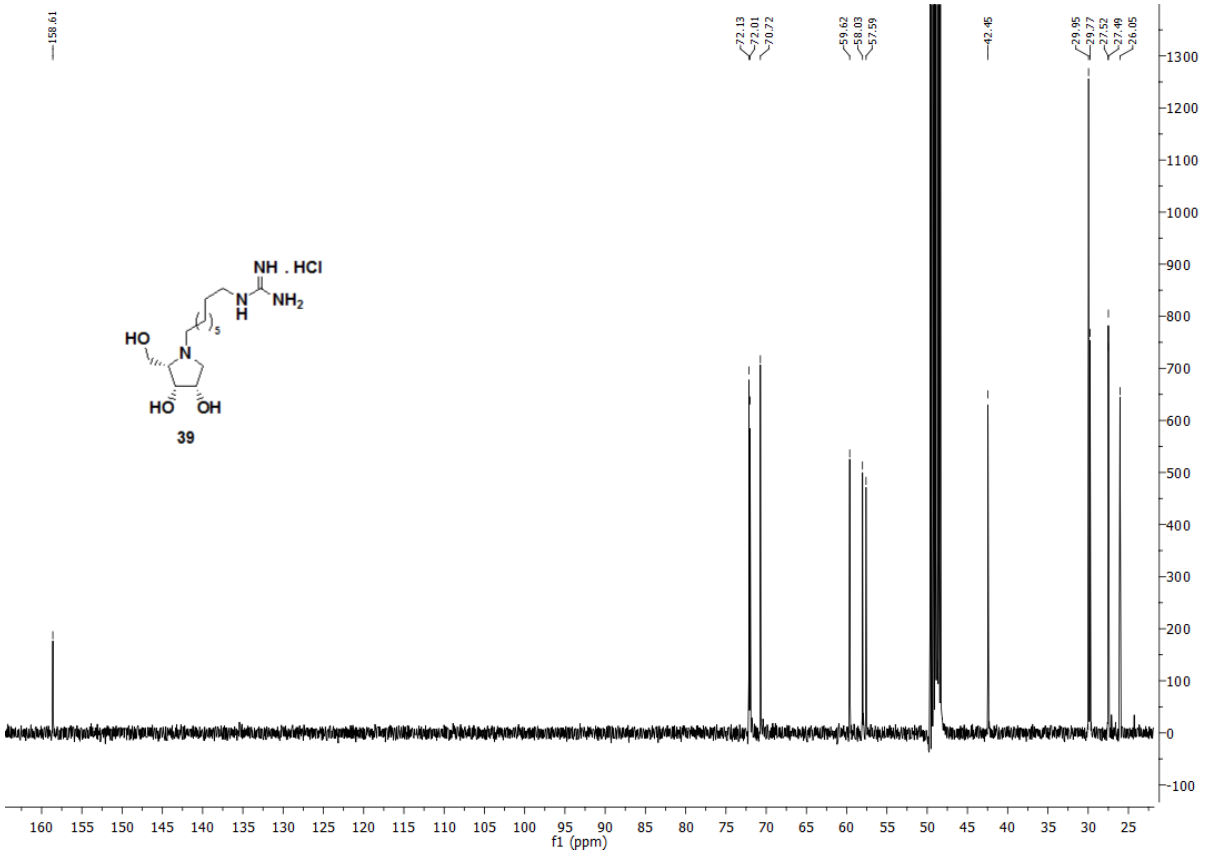
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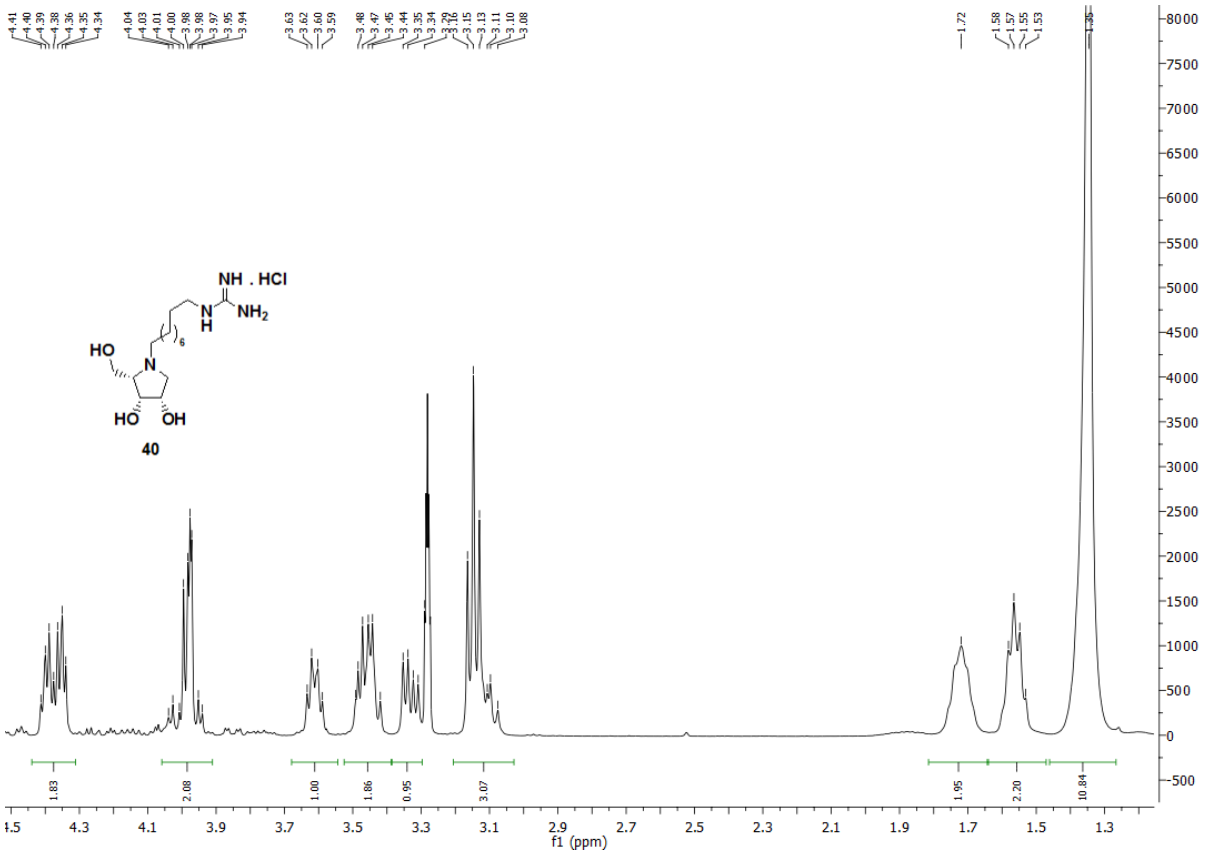
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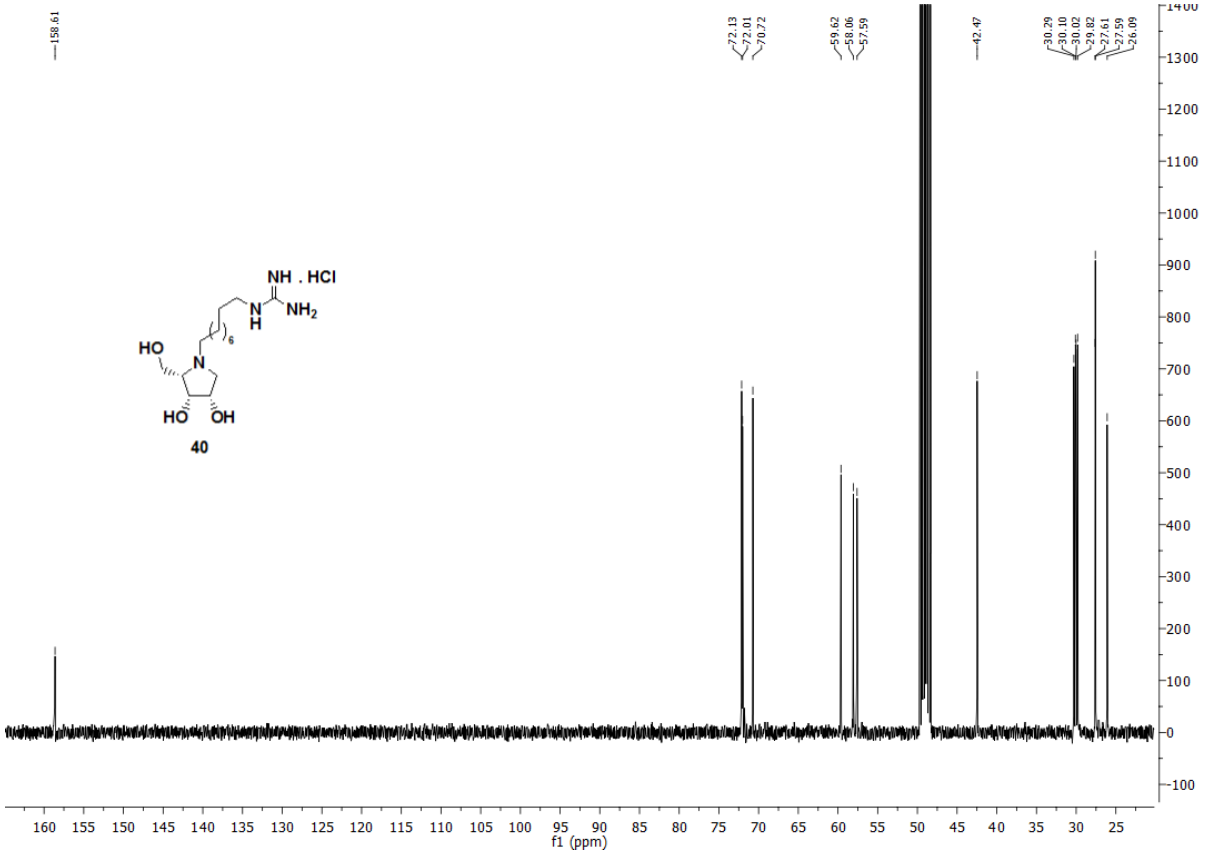
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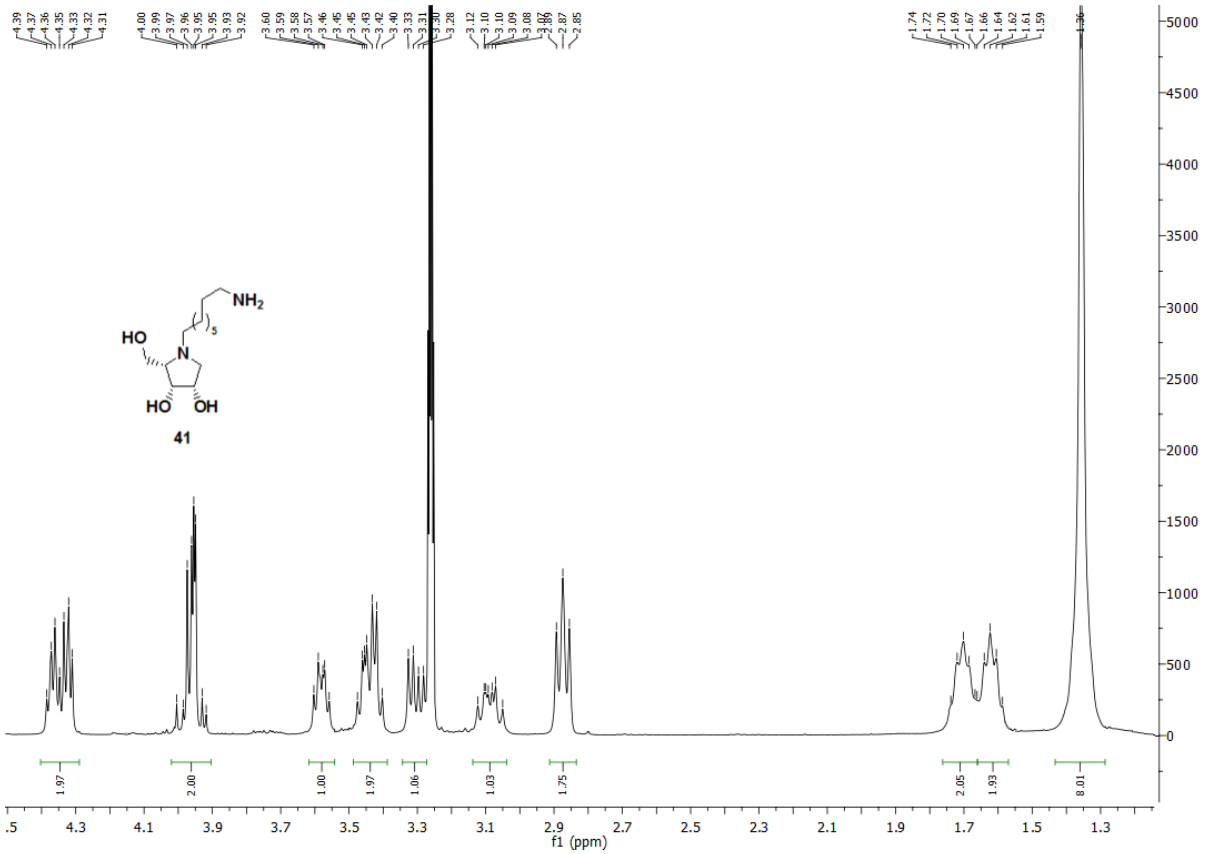
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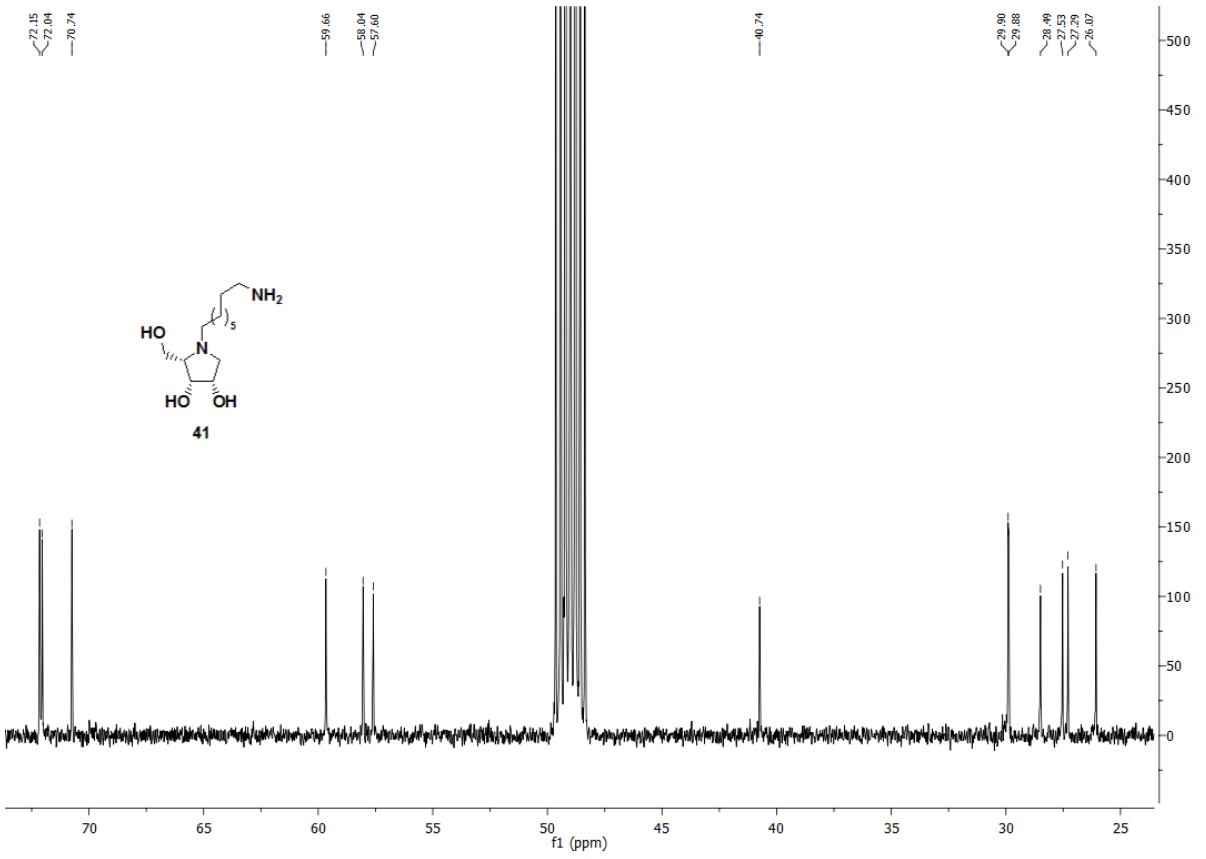
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