Supporting Information

Design, Synthesis, and Biological Evaluation of *N*-Alkylated Deoxynojirimycin (DNJ) Derivatives for the Treatment of Dengue Virus Infection

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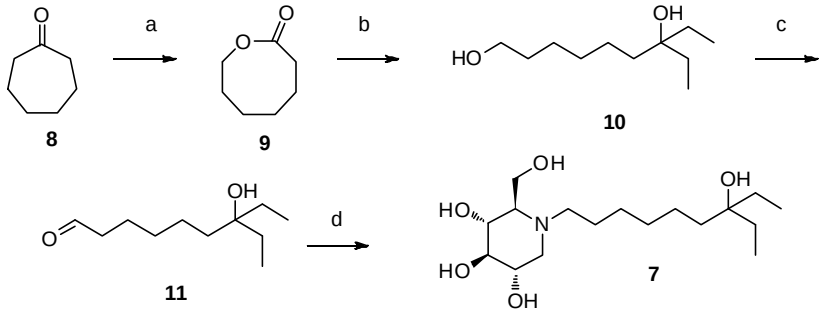
CONTENTS:

1. Synthesis of Compounds 1-5 and 7

General information. ^{1}H NMR spectra were recorded on a 300 MHz INOVA VARIAN spectrometer. Chemical shifts values are given in ppm and referred as the internal standard to TMS (tetramethylsilane). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet and dd, doublet of doublets. The coupling constants (*J*) are reported in Hertz (Hz). Optical rotations were recorded on a JASCO P-2000 Digital Polarimeter. The data was collected at 24 °C in a 10 cm cell in methanol. $[\alpha]_D$ values are given in 10^{-1} deg · cm^2 g^{-1} (concentration *c* is given as g/100 mL). Mass Spectra were obtained on a 1200 Aligent LC-MS spectrometer (ES-API, Positive). Silica gel column chromatography was performed over silica gel 100-200 mesh, and the eluent was a mixture of ethyl acetate and hexanes, or mixture of methanol and ethyl acetate. All the tested compounds possess a purity of at least 95%. Analytical HPLC was run on the Agilent 1100 HPLC instrument, equipped with Agilent, ZORBAX SB-C18 column and UV detection at 210 nm. Eluent system was: A (Water, 0.1% Formic acid) and B (Methanol, 0.1% Formic acid); flow rate = 1 mL/min; Method A: 45%A, 55%B (**3a-3d**, **3i-3m**, **3s-3v**, **4a-4c** and **5c-5e**); Method B: 35%A, 65%B (**3h**, **3n-3r** and **4d-4f**); Method C: 25%A, 75%B (**3e-3g**). For compounds **1a-1c**, **2a-2l**, **5a-5b**, **6** and **7**, the purity was determined based on ^{1}H NMR.

a. Synthesis of (2R,3R,4R,5S)-1-(7-Ethyl-7-hydroxynonyl)-2-(hydroxymethyl) piperidine-3,4,5-triol (7).



(a) *m*CPBA, CH_2Cl_2, rt, 41%; (b) EtMgBr (1 M in THF), THF, Argon, 0 °C, then sat. NH_4Cl (a.q.), 87%; (c) PCC, CH_2Cl_2, rt, 69%; (d) DNJ, HOAc, EtOH; then H_2 (45 psi), 5% Pd/C, EtOH, 61%

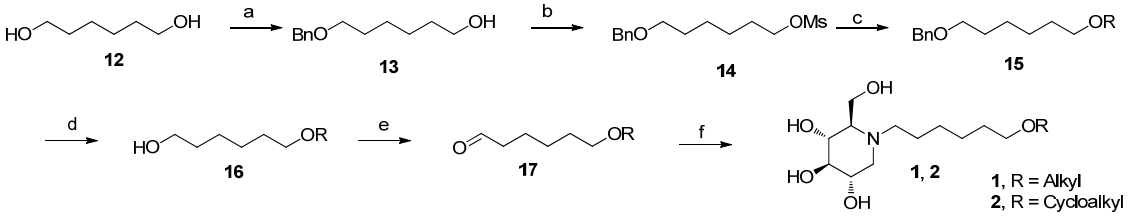
*a.a Preparation of Oxocan-2-one (**9**).* Cycloheptanone (**8**, 5.60g, 50 mmol) in dichoromethane (75 mL) was added dropwise to a solution of *meta*-chloroperoxybenzoic acid (*m*CPBA, 16.80 g, 75 mmol) in dichloromethane (50 mL) at 0 °C. After addition, the reaction mixture was stirred at room temperature in the dark for 5 days. The solid was removed by filtration, and the filtrate was washed with sat. sodium bicarbonate solution (50 mL), followed by brine (50 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated to give a residue, which was slurried in a mixture of ethyl acetate and hexanes (10 : 90). The solid was filtered off and the solvent was evaporated to afford the crude product, which was further purified through silica gel column chromatography (ethyl acetate : hexanes = 10 : 90) to give 2.60 g of pure compound **9** as colorless oil. Yield, 41%.

*a.b. Preparation of 7-Ethylnonane-1,7-diol (**10**).* Oxocan-2-one (**9**, 1.98 g, 15.5 mmol) in tetrahydrofuran (THF, 30 mL) was added dropwise to a solution of ethylmagnesium bromide in THF (1 M, 75.5 mL, 75.5 mmol) at 0 °C under Argon atmosphere. After addition, the reaction mixture was stirred and allowed to warm up to room temperature over 2 hours. The reaction was quenched with cold sat. ammonium chloride solution (50 mL), and then extracted with ethyl acetate (30 mL x 3). The combined organic layer was dried over anhydrous sodium sulfate and concentrated to give the crude product, which was further purified through silica gel column chromatography (ethyl acetate : hexanes = 30 : 70) to afford 2.53 g of pure compound **10** as colorless oil. Yield, 87%.

*a.c. Preparation of 7-Ethyl-7-hydroxynonanal (**11**).* 7-Ethylnonane-1,7-diol (**10**, 3.35 g, 17.8 mmol) in dry dichloromethane (40 mL) was added to a suspension of pyridinium chlorochromate (PCC, 4.60 g, 21.3 mmol) in dry dichloromethane (60 mL). The reaction mixture was stirred at room temperature for 6 hours, and then filtered through a silica gel pad and washed with ethyl acetate (50 mL). The filtrate was concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 20 : 80) to afford 2.30 g of pure compound **11** as colorless oil. Yield, 69%.

*a.d. Synthesis of (2R,3R,4R,5S)-1-(7-Ethyl-7-hydroxynonyl)-2-(hydroxymethyl) piperidine-3,4,5-triol (**7**).* A solution of 1-deoxynojirimycin (DNJ, 653 mg, 4.0 mmol) in acetic acid (8 mL) was stirred at room temperature overnight, and then the solvent was removed under reduced pressure. The resulting residue was treated with 200 proof ethanol (20 mL) and 7-ethyl-7-hydroxynonanal (**11**, 969 mg, 5.2 mmol), followed by acetic acid (0.5 mL). The reaction mixture was stirred at room temperature under Argon atmosphere for another 2 hours. Then, it was transferred to the hydrogenation bottle, followed by addition of 5% Pd/C (160 mg) and 200 proof ethanol (10 mL). The mixture was hydrogenated under 45 psi of H_2 for 24 hours. After the reaction was complete, it was filtered through a silica gel pad. The filtrate was concentrated and purified through silica gel column chromatography (methanol : ethyl acetate = 30 : 70) to afford 0.81 g of pure compound **7** as white solid. Yield, 61%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.85 (d, *J* = 7.2 Hz, 2H, OCH_2), 3.52-3.44 (m, 1H, OCH), 3.36 (t, *J* = 9.3 Hz, 1H, OCH), 3.13 (t, *J* = 9.0 Hz, 1H, OCH), 3.02 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.89-2.79 (m, 1H, NCH), 2.67-2.57 (m, 1H, NCH), 2.27-2.15 (m, 2H, 2 x NCH), 1.52-1.33 (m, 14H), 0.84 (t, *J* = 7.5 Hz, 6H, 2 x CH_3). MS: MH^+ = 334.

b. Synthesis of DNJ Derivatives 1-2.



(a) BnBr, KOH, 18-Crown-6, THF, rt, 55%; (b) $MeSO_2Cl$, Pyr., 0 °C, 97%; (c) ROH, NaH (60%), DMF, 75 °C; (d) H_2 (60psi), 10% Pd/C, EtOH; (e) PCC, CH_2Cl_2, Argon, rt; (f) DNJ, HOAc, EtOH; then H_2 (45psi), 10% Pd/C, EtOH

*b.a. Preparation of 6-(Benzyloxy)hexan-1-ol (**13**).* To a stirring solution of 1,6-hexanediol (**12**, 23.15 g, 196 mmol) and 18-crown-6 (2.15 g, 8 mmol) in THF (200 mL) at 0 °C, was added finely ground potassium hydroxide (10.06 g, 179 mmol), followed by the addition of benzyl bromide (19.4 mL, 163 mmol). The reaction mixture was stirred for 48 hours at room temperature, and then washed with brine

(200 mL). The aqueous layer was extracted with ethyl acetate (100 mL x 2). All the organic layer was combined, dried over anhydrous sodium sulfate and concentrated to give the crude product, which was further purified through silica gel column chromatography (ethyl acetate : hexanes = 20 : 80) to afford 22.42 g of pure compound **13** as colorless oil. Yield was 55%.

*b.b. Preparation of 6-(Benzyloxy)hexyl Methanesulfonate (**14**).* To a stirring solution of 6-(benzyloxy)hexan-1-ol (**13**, 21.42 g, 103 mmol) in pyridine (100 mL) at 0 °C, methanesulfonyl chloride (9.6 mL, 123 mmol) was added dropwise. After addition, the reaction mixture was stirred at 0 °C for 3 hours. Then, the reaction was quenched into ice water (100 mL), and the pH was adjusted to 1~2 with 2 N hydrochloric acid (HCl). The mixture was extracted with dichloromethane (100 mL x 3). The combined organic layer was dried over anhydrous sodium sulfate , concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 10 : 90 to 20 : 80) to afford 28.50 g of pure compound **14** as colorless oil. Yield, 97%.

*b.c. General Procedure for the Preparation of Intermediates **16**.* To a solution of the alcohol **15** (6 mmol) in anhydrous dimethylformamide (DMF, 10 mL) at room temperature, NaH (60%, 480 mg, 12 mmol) was added. The mixture was stirred at room temperature for 90 min and treated with a solution of 6-(benzyloxy)hexyl methanesulfonate (**14**, 1.43 g, 5mmol) in anhydrous DMF (5 mL). The reaction mixture was then heated to 75 °C for 1 hour. After cooling to room temperature, the reaction was quenched with ice/water (50 mL) and extracted with ethyl acetate (30 mL x 3). The combined organic layer was dried over anhydrous sodium sulfate, concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 2 : 98) to afford the pure compound **16**.

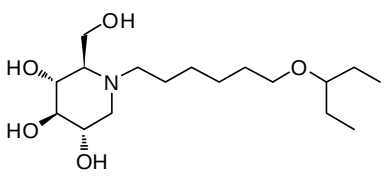
*b.d. General Procedure for the Preparation of Alcohols **17**.* A reaction mixture of the compound **16** (606 mg) and 10% Pd/C (242 mg) in 200 proof ethanol (20 mL) was hydrogenated under 60 psi of H_2 for 24 hours. After the reaction was complete, it was treated with celite (800 mg), and then filtered

through a silica gel pad. The filtrate was concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 5 : 95 to 30 : 70) to afford the pure compound **17**.

*b.e. General Procedure for the Preparation of Aldehydes **18**.* To a stirred suspension of PCC (647 mg, 3 mmol) and silica gel (647 mg) in dry dichloromethane (10 mL), was added a solution of the alcohol **17** (2 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at room temperature under argon atmosphere for 4 hours. Then, it was filtered through a silica gel pad, and washed with ethyl acetate (20 mL). The filtrate was concentrated and then purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 15 : 85) to afford the pure compound **18**.

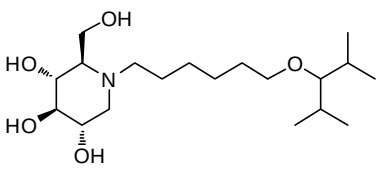
*b.f. General Procedure for the Synthesis of DNJ Derivatives **1-2**.* A solution of DNJ (33 mg, 0.2 mmol) in acetic acid (1 mL) was stirred at room temperature overnight. The solvent was then removed under reduced pressure. The resulting residue was treated with 200 proof ethanol (5 mL) and the aldehyde **18** (0.26 mmol), followed by acetic acid (2 drops as catalyst). The reaction mixture was stirred at room temperature under argon atmosphere for another hour. Then, it was transferred to the hydrogenation bottle, followed by addition of 10% Pd/C (32 mg) and 200 proof ethanol (5 mL). The mixture was hydrogenated under 45 psi of H_2 for 24 hours. After the reaction was complete, it was treated with celite (100 mg), and then filtered through a silica gel pad. The filtrate was concentrated and purified through silica gel column chromatography (methanol : ethyl acetate = 5 : 95 to 20 : 80) to afford the pure compound **1** or **2**.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(pentan-3-yloxy)hexyl)piperidine-3,4,5-triol (1a).



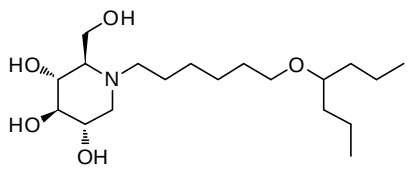
White semi-solid. Yield, 87%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.85 (d, J = 2.4 Hz, 2H, OCH_2), 3.50-3.43 (m, 3H, 3 x OCH), 3.36 (t, J = 9.3 Hz, 1H, OCH), 3.16-3.10 (m, 2H, 2 x OCH), 3.00 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.83-2.80 (m, 1H, NCH), 2.63-2.60 (m, 1H, NCH), 2.24-2.13 (m, 2H, 2 x NCH), 1.59-1.28 (m, 12H, 6 x CH_2), 0.90 (t, J = 7.5 Hz, 6H, 2 x CH_3),. MS: calculated for MH^+ = 334, found 334.

(2R,3R,4R,5S)-1-(6-((2,4-Dimethylpentan-3-yl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (1b).



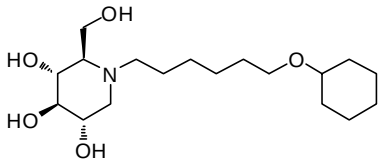
White semi-solid. Yield, 49%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.87 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.55-3.45 (m, 3H, 3 x OCH), 3.38 (t, *J* = 9.6 Hz, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.05 (dd, *J* = 11.4, 4.8 Hz, 1H, NCH), 2.88-2.83 (m, 1H, NCH), 2.71-2.65 (m, 2H, NCH and OCH overlapped), 2.32-2.22 (m, 2H, 2 x NCH), 1.84-1.73 (m, 2H, 2 x CH), 1.60-1.29 (m, 8H, 4 x CH_2), 0.91 (dd, *J* = 6.9, 1.5 Hz, 12H, 2 x $C(CH_3)_2$). MS: calculated for MH^+ = 362, found 362.

(2R,3R,4R,5S)-1-(6-(Heptan-4-yloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (1c).



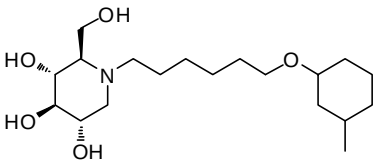
White semi-solid. Yield, 93%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.53-3.34 (m, 4H, 4 x OCH), 3.27-3.25 (m, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.04 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.89-2.81 (m, 1H, NCH), 2.69-2.64 (m, 1H, NCH), 2.30-2.20 (m, 2H, 2 x NCH), 1.58-1.31 (m, 16H, 8 x CH_2), 0.94-0.90 (m, 6H, 2 x CH_3). MS: calculated for MH^+ = 362, found 362.

(2R,3R,4R,5S)-1-(6-(Cyclohexyloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2a).



Off-white semi-solid. Yield, 81%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.52-3.44 (m, 3H, 3 x OCH), 3.36 (t, *J* = 9.3 Hz, 1H, OCH), 3.27-3.24 (m, 1H, OCH), 3.14 (t, *J* = 9.0 Hz, 1H, OCH), 3.02 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.87-2.79 (m, 1H, NCH), 2.67-2.62 (m, 1H, NCH), 2.27-2.16 (m, 2H, 2 x NCH), 1.91-1.23 (m, 18H). MS: calculated for MH^+ = 346, found 346.

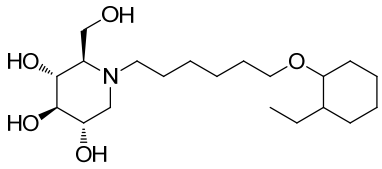
(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-((3-methylcyclohexyl)oxy)hexyl)piperidine-3,4,5-triol (2b).



Colorless semi-solid. Yield, 91%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (s, 2H, OCH_2), 3.57-3.34 (m, 4H, 4 x OCH), 3.26-3.21 (m, 1H, OCH), 3.15 (t,

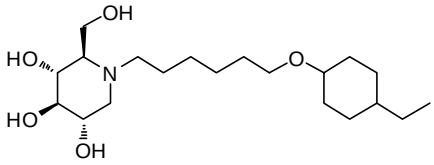
J = 9.3 Hz, 1H, OCH), 3.03 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.90-2.80 (m, 1H, NCH), 2.68-2.59 (m, 1H, NCH), 2.29-2.18 (m, 2H, 2 x NCH), 2.01-0.78 (m, 20H). MS: calculated for MH^+ = 360, found 360.

(2R,3R,4R,5S)-1-(6-((2-Ethylcyclohexyl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2c).



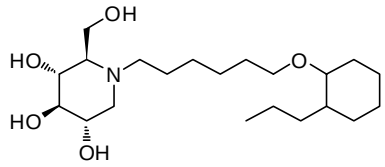
White semi-solid. Yield, 93%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.85 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.54 (m, 4H, 4 x OCH), 3.28-3.25 (m, 1H, OCH), 3.13 (t, *J* = 9.0 Hz, 1H, OCH), 3.01 (dd, *J* = 11.4, 4.8 Hz, 1H, NCH), 2.88-2.78 (m, 1H, NCH), 2.64-2.62 (m, 1H, NCH), 2.26-2.15 (m, 2H, 2 x NCH), 1.94-1.15 (m, 19H), 0.88 (t, *J* = 7.5 Hz, 3H, CH_3). MS: calculated for MH^+ = 374, found 374.

(2R,3R,4R,5S)-1-(6-((4-Ethylcyclohexyl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2d).



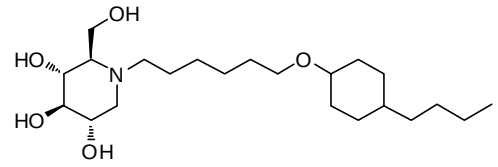
Light-yellow semi-solid. Yield, 61%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.91-3.84 (m, 2H, 2 x OCH), 3.57-3.39 (m, 4H, 4 x OCH), 3.24-3.12 (m, 3H, 2 x OCH and 1 x NCH), 2.99-2.97 (m, 1H, NCH), 2.81-2.79 (m, 1H, NCH), 2.50-2.42 (m, 2H, 2 x NCH), 2.06-1.10 (m, 19H), 0.91-0.86 (m, 3H, CH_3). MS: calculated for MH^+ = 374 , found 374.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-((2-propylcyclohexyl)oxy)hexyl)piperidine-3,4,5-triol (2e).



White semi-solid. Yield, 81%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.63-3.33 (m, 4H, 4 x OCH), 3.28-3.25 (m, 1H, OCH), 3.13 (t, *J* = 9.0 Hz, 1H, OCH), 3.02 (dd, *J* = 11.1, 4.8 Hz, 1H, NCH), 2.87-2.78 (m, 1H, NCH), 2.63-2.57 (m, 1H, NCH), 2.25-2.14 (m, 2H, 2 x NCH), 1.87-0.95 (m, 21H), 0.90 (t, *J* = 7.5 Hz, 3H, CH_3). MS: calculated for MH^+ = 388, found 388.

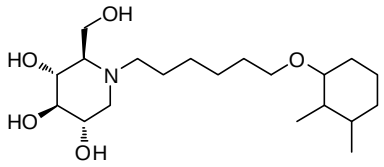
(2R,3R,4R,5S)-1-(6-((4-Butylcyclohexyl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2f).



White semi-solid. Yield, 90%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.87 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.54-3.35 (m, 5H, 5 x OCH), 3.16 (t, *J* = 9.3 Hz, 1H, OCH), 3.06 (dd, *J* = 11.4, 4.8 Hz, 1H,

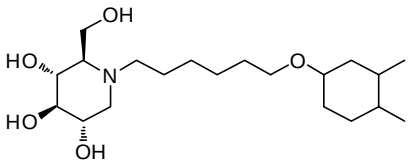
NCH), 2.94-2.84 (m, 1H, NCH), 2.72-2.63 (m, 1H, NCH), 2.34-2.24 (m, 2H, 2 x NCH), 2.04-1.10 (m, 23H), 0.92-0.88 (m, 3H, CH_3). MS: calculated for MH^+ = 402, found 402.

(2R,3R,4R,5S)-1-(6-((2,3-Dimethylcyclohexyl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2g).



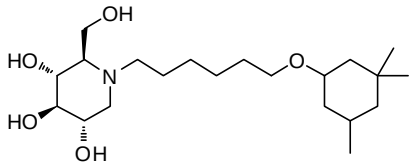
Colorless semi-solid. Yield, 88%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (s, 2H, OCH_2), 3.54-3.44 (m, 2H, 2 x OCH), 3.40-3.35 (m, 2H, 2 x OCH), 3.30-3.11 (m, 2H, 2 x OCH, overlapped with the peaks of CH_3OH), 3.02 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.90-2.80 (m, 1H, NCH), 2.69-2.59 (m, 1H, NCH), 2.28-2.18 (m, 2H, 2 x NCH), 1.76-1.07 (m, 16H), 0.93-0.74 (m, 6H, 2 x CH_3). MS: calculated for MH^+ = 374, found 374.

(2R,3R,4R,5S)-1-(6-((3,4-Dimethylcyclohexyl)oxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2h).



White semi-solid. Yield, 87%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.51-3.40 (m, 3H, 3 x OCH), 3.37 (t, *J* = 9.3 Hz, 1H, OCH), 3.29-3.23 (m, 1H, OCH), 3.14 (t, *J* = 9.3 Hz, 1H, OCH), 3.03 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.86-2.83 (m, 1H, NCH), 2.66-2.63 (m, 1H, NCH), 2.29-2.19 (m, 2H, 2 x NCH), 1.76-1.25 (m, 16H), 0.91-0.82 (m, 6H, 2 x CH_3). MS: calculated for MH^+ = 374, found 374.

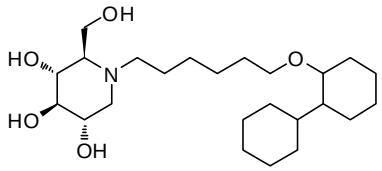
(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-((3,3,5-trimethylcyclohexyl)oxy)hexyl)piperidine-3,4,5-triol (2i).



Light-yellow semi-solid. Yield, 92%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.61-3.34 (m, 5H, 5 x OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.04 (dd, *J* = 11.1, 4.8 Hz, 1H, NCH), 2.91-

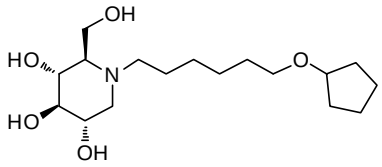
2.81 (m, 1H, NCH), 2.70-2.60 (m, 1H, NCH), 2.31-2.20 (m, 2H, 2 x NCH), 1.87-1.05 (m, 15H), 0.94-0.88 (m, 9H, 3 x CH_3). MS: calculated for MH^+ = 388, found 388.

(2R,3R,4R,5S)-1-(6-([1,1'-Bi(cyclohexan)]-2-yloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2j).



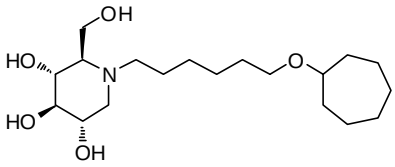
Colorless semi-solid. Yield, 86%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (s, 2H, OCH_2), 3.66-3.61 (m, 1H, OCH), 3.53-3.45 (m, 1H, OCH), 3.38 (t, *J* = 9.3 Hz, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.08-3.01 (m, 2H), 2.87-2.82 (m, 1H, NCH), 2.67-2.65 (m, 1H, NCH), 2.30-2.11 (m, 3H), 1.77-1.01 (m, 28H). MS: calculated for MH^+ = 428, found 428.

(2R,3R,4R,5S)-1-(6-(Cyclopentyloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2k).



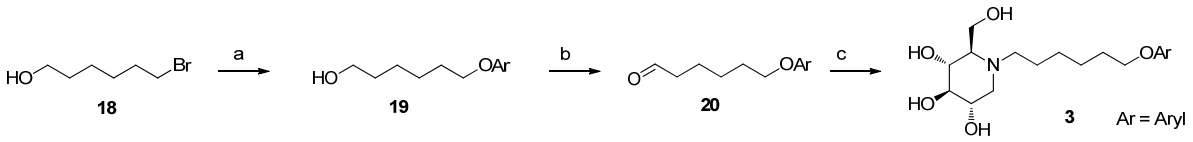
White semi-solid. Yield, 83%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.90-3.86 (m, 3H, 3 x OCH), 3.53-3.35 (m, 4H, 4 x OCH), 3.15 (t, *J* = 9.0 Hz, 1H, OCH), 3.04 (dd, *J* = 11.7, 5.1 Hz, 1H, NCH), 2.90-2.82 (m, 1H, NCH), 2.70-2.63 (m, 1H, NCH), 2.31-2.22 (m, 2H, 2 x NCH), 1.74-1.31 (m, 16H). MS: calculated for MH^+ = 332, found 332.

(2R,3R,4R,5S)-1-(6-(Cycloheptyloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (2l).



White semi-solid. Yield, 93%. $[\alpha]_D$ = - 4 (c = 2.0, methanol). ^{1}H NMR (300 MHz, CD_3OD): δ 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.53-3.34 (m, 5H, 5 x OCH), 3.14 (t, *J* = 9.3 Hz, 1H, OCH), 3.04 (dd, *J* = 11.4, 4.8 Hz, 1H, NCH), 2.89-2.81 (m, 1H, NCH), 2.69-2.64 (m, 1H, NCH), 2.30-2.19 (m, 2H, 2 x NCH), 1.94-1.29 (m, 20H). MS: calculated for MH^+ = 360, found 360.

c. Synthesis of DNJ Derivatives 3.



(a) ArOH, K_2CO_3, DMF, 80 ºC; (b) PCC, CH_2Cl_2, Argon, rt; (c) DNJ, HOAc, EtOH; then H_2 (45psi), 10% Pd/C, EtOH

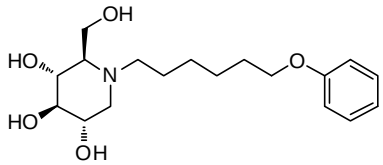
*c.a. General Procedure for the Preparation of Alcohols **21.*** To a stirring solution of the substituted phenol **20** (1.5 mmol) and 6-bromo-1-hexanol (**19**, 0.14 mL, 1 mmol) in DMF (3 mL), was added potassium carbonate (207 mg, 1.5 mmol). The reaction mixture was stirred at 80 ºC for 4 hours. After cooling to room temperature, the reaction was quenched with water (30 mL), and extracted with ethyl acetate (20 mL x 3). The combined organic layer was washed with brine (30 mL), dried over sodium sulfate, and then concentrated under reduced pressure. The resulting residue was purified through silica gel column chromatography (ethyl acetate : hexanes = 5 : 95 to 20 : 80) to afford the pure compound **21**.

*c.b. General Procedure for the Preparation of Aldehydes **22.*** To a stirring suspension of PCC (363 mg, 1.68 mmol) and silica gel (363 mg) in dry dichloromethane (10 mL), was added a solution of the alcohol **21** (1.40 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at room temperature under argon atmosphere for 4 hours. Then, it was filtered through a silica gel pad, and washed with ethyl acetate (20 mL). The filtrate was concentrated and then purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 10 : 90) to afford the pure compound **22**.

*c.c. General Procedure for the Synthesis of DNJ Derivatives **3.*** A solution of DNJ (49 mg, 0.3 mmol) in acetic acid (1 mL) was stirred at room temperature overnight, and then the solvent was removed under reduced pressure. The resulting residue was treated with 200 proof ethanol (5 mL) and the aldehyde **22** (0.39 mmol), followed by acetic acid (2 drops as catalyst). The reaction mixture was stirred at room temperature under argon atmosphere for another hour. Then, it was transferred to the hydrogenation bottle, followed by addition of 10% Pd/C (30 mg) and 200 proof ethanol (5 mL). The mixture was hydrogenated under 45 psi of H_2 for 24 hours. After the reaction was complete, it was treated with celite

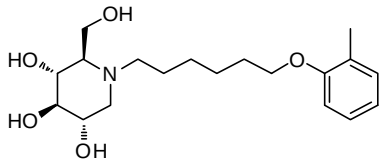
(100 mg), and then filtered through a silica gel pad. The filtrate was concentrated and purified through silica gel column chromatography (methanol : ethyl acetate = 5 : 95 to 20 : 80) to afford the pure compound **3**.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-phenoxyhexyl)piperidine-3,4,5-triol (3a).



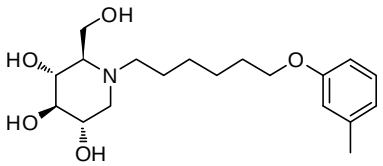
White solid. Yield, 89%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.26-7.21 (m, 2H, CH_{ar}), 6.90-6.85 (m, 3H, CH_{ar}), 3.96 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, J = 2.7 Hz, 2H, OCH_2), 3.51-3.43 (m, 1H, OCH), 3.35 (t, J = 9.3 Hz, 1H, OCH), 3.13 (t, J = 9.3 Hz, 1H, OCH), 3.01 (dd, J = 11.1, 4.8 Hz, 1H, NCH), 2.86-2.79 (m, 1H, NCH), 2.66-2.61 (m, 1H, NCH), 2.24-2.12 (m, 2H, 2 x NCH), 1.82-1.75 (m, 2H, CH_2), 1.57-1.47 (m, 4H, 2 x CH_2), 1.41-1.32 (m, 2H, CH_2). MS: calculated for MH^+ = 340, found 340.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(*o*-tolyloxy)hexyl)piperidine-3,4,5-triol (3b).



White solid. Yield, 35%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.11-7.06 (m, 2H, CH_{ar}), 6.85-6.76 (m, 2H, CH_{ar}), 3.95 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, J = 3.0 Hz, 2H, OCH_2), 3.49-3.42 (m, 1H, OCH), 3.34 (t, J = 9.3 Hz, 1H, OCH), 3.12 (t, J = 9.0 Hz, 1H, OCH), 2.99 (dd, J = 11.1, 4.8 Hz, 1H, NCH), 2.82-2.80 (m, 1H, NCH), 2.62-2.59 (m, 1H, NCH), 2.21-2.09 (m, 5H, 2 x NCH and $ArCH_3$ overlapped), 1.83-1.76 (m, 2H, CH_2), 1.59-1.49 (m, 4H, 2 x CH_2), 1.42-1.34 (m, 2H, CH_2). MS: calculated for MH^+ = 354, found 354.

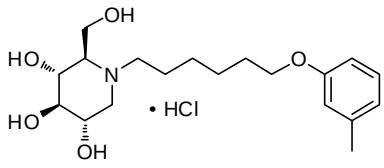
(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(*m*-tolyloxy)hexyl)piperidine-3,4,5-triol (3c).



White semi-solid. Yield, 98%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.13-7.08 (m, 1H, CH_{ar}), 6.73-6.66 (m, 3H, CH_{ar}), 3.94 (t, J = 6.3 Hz, 2H, $ArOCH_2$), 3.86 (d, J = 2.7 Hz, 2H, OCH_2), 3.52-3.44 (m, 1H, OCH), 3.36 (t, J = 9.6 Hz, 1H, OCH), 3.14 (t, J = 9.3 Hz, 1H, OCH), 3.02 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.86-2.80 (m, 1H, NCH), 2.68-2.63 (m, 1H, NCH), 2.28 (s, 3H, $ArCH_3$), 2.27-2.15 (m, 2H, 2 x NCH),

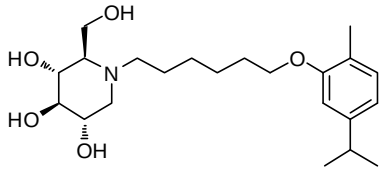
1.79-1.72 (m, 2H, CH_2), 1.57-1.46 (m, 4H, 2 x CH_2), 1.41-1.33 (m, 2H, CH_2). MS: calculated for MH^+ = 354, found 354.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(*m*-tolyloxy)hexyl)piperidine-3,4,5-triol Hydrochloride (3d).



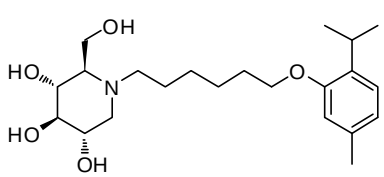
The product was obtained as white semi-solid by the treatment of **3c** with conc. hydrochloric acid. Yield 95%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.14-7.08 (m, 1H, CH_{ar}), 6.73-6.66 (m, 3H, CH_{ar}), 4.12 (d, *J* = 12.3 Hz, 1H), 3.98-3.87 (m, 3H), 3.73-3.56 (m, 2H), 3.48-3.33 (m, 3H), 3.25-3.15 (m, 1H), 3.06-2.95 (m, 2H), 2.28 (s, 3H, $ArCH_3$), 1.83-1.72 (m, 4H, 2 x CH_2), 1.63-1.48 (m, 4H, 2 x CH_2). MS: calculated for MH^+ = 354, found 354.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(5-isopropyl-2-methylphenoxy)hexyl)piperidine-3,4,5-triol (3e).



White semi-solid. Yield, 86%. ^{1}H NMR (300 MHz, CD_3OD): δ 6.98 (d, *J* = 7.8 Hz, 1H, CH_{ar}), 6.71-6.65 (m, 2H, CH_{ar}), 3.96 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, *J* = 3.0 Hz, 2H, OCH_2), 3.51-3.43 (m, 1H, OCH), 3.34 (t, *J* = 9.3 Hz, 1H, OCH), 3.12 (t, *J* = 9.0 Hz, 1H, OCH), 2.99 (dd, *J* = 11.1, 4.8 Hz, 1H, NCH), 2.87-2.77 (m, 2H, NCH and ArCH overlapped), 2.64-2.59 (m, 1H, NCH), 2.21-2.09 (m, 5H, 2 x NCH and $ArCH_3$ overlapped), 1.83-1.76 (m, 2H, CH_2), 1.60-1.49 (m, 4H, 2 x CH_2), 1.42-1.34 (m, 2H, CH_2), 1.21 (d, *J* = 6.9 Hz, 6H, $C(CH_3)_2$). MS: calculated for MH^+ = 396, found 396.

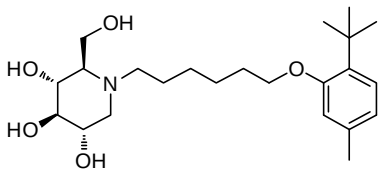
(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(2-isopropyl-5-methylphenoxy)hexyl)piperidine-3,4,5-triol (3f).



White solid. Yield, 95%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.02 (d, *J* = 7.5 Hz, 1H, CH_{ar}), 6.68-6.66 (m, 2H, CH_{ar}), 3.95 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, *J* = 3.3 Hz, 2H, OCH_2), 3.50-3.42 (m, 1H, OCH), 3.34

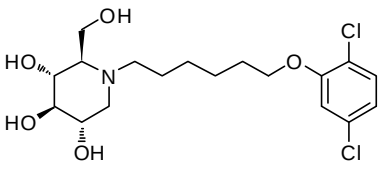
(t, J = 9.0 Hz, 1H, OCH), 3.27-3.20 (m, 1H, ArCH), 3.12 (t, J = 9.0 Hz, 1H, OCH), 2.99 (dd, J = 11.1, 4.5 Hz, 1H, NCH), 2.86-2.76 (m, 1H, NCH), 2.63-2.54 (m, 1H, NCH), 2.27 (s, 3H, $ArCH_3$), 2.20-2.08 (m, 2H, 2 x NCH), 1.85-1.76 (m, 2H, CH_2), 1.60-1.49 (m, 4H, 2 x CH_2), 1.42-1.34 (m, 2H, CH_2), 1.17 (d, J = 6.9 Hz, 6H, $C(CH_3)_2$). MS: calculated for MH^+ = 396, found 396.

(2R,3R,4R,5S)-1-(6-(2-(tert-Butyl)-5-methylphenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3g).



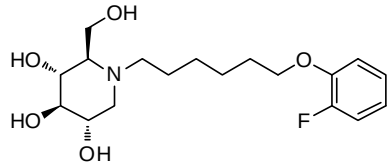
White solid. Yield, 77%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.08 (d, J = 7.8 Hz, 1H, CH_{ar}), 6.71 (s, 1H, CH_{ar}), 6.63 (dd, J = 7.8, 1.2 Hz, 1H, CH_{ar}), 3.97 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, J = 2.4 Hz, 2H, OCH_2), 3.51-3.43 (m, 1H, OCH), 3.35 (t, J = 9.0 Hz, 1H, OCH), 3.13 (t, J = 9.0 Hz, 1H, OCH), 3.01 (dd, J = 11.1, 5.1 Hz, 1H, NCH), 2.86-2.79 (m, 1H, NCH), 2.66-2.56 (m, 1H, NCH), 2.26 (s, 3H, $ArCH_3$), 2.23-2.11 (m, 2H, 2 x NCH), 1.90-1.81 (m, 2H, CH_2), 1.64-1.51 (m, 4H, 2 x CH_2), 1.44-1.36 (m, 2H, CH_2), 1.35 (s, 9H, $C(CH_3)_3$). MS: calculated for MH^+ = 410, found 410.

(2R,3R,4R,5S)-1-(6-(2,5-Dichlorophenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3h).



This compound was synthesized using soudium cyanoborohydride method (See the synthesis of **5a**). White solid. Yield, 90%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.32 (d, J = 8.7 Hz, 1H, CH_{ar}), 7.07 (d, J = 1.8 Hz, 1H, CH_{ar}), 6.91 (dd, J = 8.4, 2.1 Hz, 1H, CH_{ar}), 4.05 (t, J = 6.3 Hz, 2H, $ArOCH_2$), 3.91 (m, 2H, OCH_2), 3.60-3.51 (m, 1H, OCH), 3.45 (t, J = 9.3 Hz, 1H, OCH), 3.25-3.14 (m, 2H, OCH and NCH overlapped), 3.06-2.98 (m, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.52-2.45 (m, 2H, 2 x NCH), 1.89-1.40 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 408, found 408.

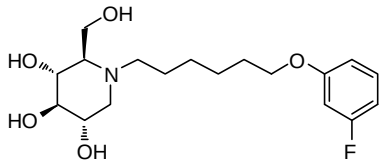
(2R,3R,4R,5S)-1-(6-(2-Fluorophenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3i).



White solid. Yield, 96%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.08-7.02 (m, 3H, CH_{ar}), 6.91-6.83 (m, 1H, CH_{ar}), 4.01 (t, J = 6.6 Hz, 2H, $ArOCH_2$),

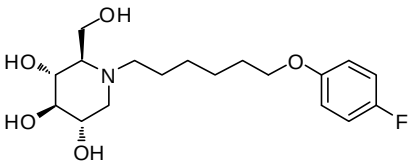
3.86 (d, J = 2.4 Hz, 2H, OCH_2), 3.53-3.45 (m, 1H, OCH), 3.37 (t, J = 9.3 Hz, 1H, OCH), 3.15 (t, J = 9.3 Hz, 1H, OCH), 3.02 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.89-2.79 (m, 1H, NCH), 2.68-2.58 (m, 1H, NCH), 2.27-2.16 (m, 2H, 2 x NCH), 1.83-1.36 (m, 8H, 4 x CH_2). calculated for MS: MH^+ = 358, found 358.

(2R,3R,4R,5S)-1-(6-(3-Fluorophenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3j).



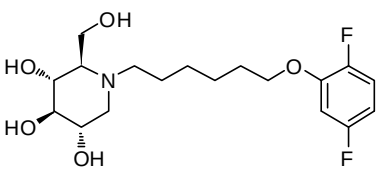
White semi-solid. Yield, 96%. $[\alpha]_D$ = - 6 (c = 1.5, methanol). ^{1}H NMR (300 MHz, CD_3OD): δ 7.23-7.18 (m, 1H, CH_{ar}), 6.71-6.60 (m, 3H, CH_{ar}), 3.94 (t, J = 6.3 Hz, 2H, $ArOCH_2$), 3.85 (s, 2H, OCH_2), 3.52-3.44 (m, 1H, OCH), 3.36 (t, J = 9.3 Hz, 1H, OCH), 3.13 (t, J = 9.3 Hz, 1H, OCH), 3.00 (dd, J = 11.1, 5.1 Hz, 1H, NCH), 2.84-2.77 (m, 1H, NCH), 2.65-2.60 (m, 1H, NCH), 2.23-2.12 (m, 2H, 2 x NCH), 1.79-1.35 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 358, found 358.

(2R,3R,4R,5S)-1-(6-(4-Fluorophenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3k).



White semi-solid. Yield, 96%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.00-6.93 (m, 2H, CH_{ar}), 6.90-6.84 (m, 2H, CH_{ar}), 3.93 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.86 (d, J = 2.7 Hz, 2H, OCH_2), 3.53-3.45 (m, 1H, OCH), 3.37 (t, J = 9.6 Hz, 1H, OCH), 3.14 (t, J = 9.0 Hz, 1H, OCH), 3.02 (dd, J = 11.1, 5.1 Hz, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.68-2.60 (m, 1H, NCH), 2.27-2.16 (m, 2H, 2 x NCH), 1.81-1.33 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 358, found 358.

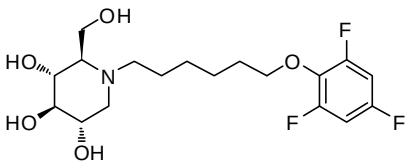
(2R,3R,4R,5S)-1-(6-(2,5-Difluorophenoxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3l).



White semi-solid. Yield, 89%. $[\alpha]_D$ = - 5 (c = 2.1, methanol). ^{1}H NMR (300 MHz, CD_3OD): δ 7.09-7.01 (m, 1H, CH_{ar}), 6.90-6.84 (m, 1H, CH_{ar}), 6.64-6.56 (m, 1H, CH_{ar}), 4.03 (t, J = 6.3 Hz, 2H, $ArOCH_2$), 3.87 (d, J = 2.7 Hz, 2H, OCH_2), 3.53-3.45 (m, 1H, OCH), 3.37 (t, J = 9.3 Hz, 1H, OCH), 3.15 (t, J = 9.3 Hz, 1H, OCH), 3.05 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.93-2.83 (m, 1H, NCH), 2.71-2.61 (m, 1H, NCH),

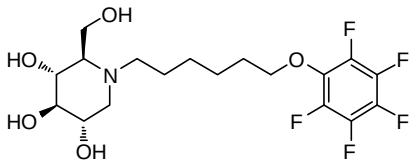
2.31-2.20 (m, 2H, 2 x NCH), 1.86-1.77 (m, 2H, CH_2), 1.62-1.49 (m, 4H, 2 x CH_2), 1.43-1.33 (m, 2H, CH_2). MS: calculated for MH^+ = 376, found 376.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(2,4,6-trifluorophenoxy)hexyl)piperidine-3,4,5-triol (3m).



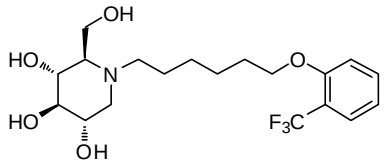
Light-yellow semi-solid. Yield, 71%. ^{1}H NMR (300 MHz, CD_3OD): δ 6.91-6.85 (m, 2H, CH_{ar}), 4.06 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.86 (s, 2H, OCH_2), 3.52-3.44 (m, 1H, OCH), 3.36 (t, *J* = 9.3 Hz, 1H, OCH), 3.13 (t, *J* = 9.0 Hz, 1H, OCH), 3.00 (dd, *J* = 11.1, 5.1 Hz, 1H, NCH), 2.85-2.77 (m, 1H, NCH), 2.65-2.60 (m, 1H, NCH), 2.23-2.12 (m, 2H, 2 x NCH), 1.79-1.32 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 394, found 394.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(perfluorophenoxy)hexyl)piperidine-3,4,5-triol (3n).



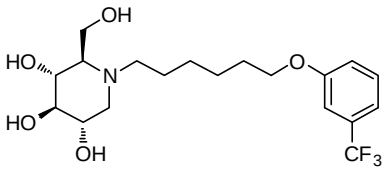
White semi-solid. Yield, 74%. ^{1}H NMR (300 MHz, CD_3OD): δ 4.19 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.87 (d, *J* = 2.4 Hz, 2H, OCH_2), 3.53-3.45 (m, 1H, OCH), 3.37 (t, *J* = 9.6 Hz, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.04 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.90-2.82 (m, 1H, NCH), 2.70-2.63 (m, 1H, NCH), 2.29-2.18 (m, 2H, 2 x NCH), 1.83-1.35 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 430, found 430.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(2-(trifluoromethyl)phenoxy)hexyl)piperidine-3,4,5-triol (3o).



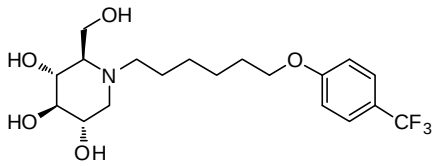
White semi-solid. Yield, 93%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.55 (m, 2H, CH_{ar}), 7.12 (d, *J* = 8.7 Hz, 1H, CH_{ar}), 7.01 (t, *J* = 7.8 Hz, 1H, CH_{ar}), 4.07 (t, *J* = 6.3 Hz, 2H, $ArOCH_2$), 3.88 (s, 2H, OCH_2), 3.56-3.48 (m, 1H, OCH), 3.41 (t, *J* = 9.6 Hz, 1H, OCH), 3.18 (t, *J* = 9.3 Hz, 1H, OCH), 3.09 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.97-2.87 (m, 1H, NCH), 2.76-2.67 (m, 1H, NCH), 2.38-2.29 (m, 2H, 2 x NCH), 1.93-1.38 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 408, found 408.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(3-(trifluoromethyl)phenoxy)hexyl)piperidine-3,4,5-triol (3p).



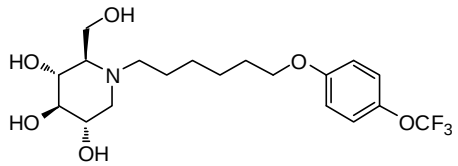
White semi-solid. Yield, 94%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.44 (t, J = 7.8 Hz, 1H, CH_{ar}), 7.21-7.14 (m, 3H, CH_{ar}), 4.02 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.87 (d, J = 2.4 Hz, 2H, OCH_2), 3.54-3.46 (m, 1H, OCH), 3.38 (t, J = 9.3 Hz, 1H, OCH), 3.15 (t, J = 9.3 Hz, 1H, OCH), 3.05 (dd, J = 11.7, 5.1 Hz, 1H, NCH), 2.91-2.83 (m, 1H, NCH), 2.71-2.66 (m, 1H, NCH), 2.30-2.20 (m, 2H, 2 x NCH), 1.86-1.35 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 408, found 408.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(4-(trifluoromethyl)phenoxy)hexyl)piperidine-3,4,5-triol (3q).



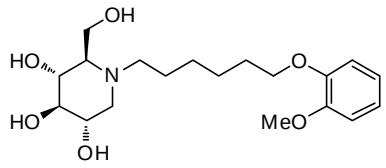
White semi-solid. Yield, 96%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.55 (d, J = 8.4 Hz, 2H, CH_{ar}), 7.04 (d, J = 8.4 Hz, 2H, CH_{ar}), 4.04 (t, J = 6.3 Hz, 2H, $ArOCH_2$), 3.88 (s, 2H, OCH_2), 3.55-3.47 (m, 1H, OCH), 3.39 (t, J = 9.6 Hz, 1H, OCH), 3.16 (t, J = 9.3 Hz, 1H, OCH), 3.07 (dd, J = 11.1, 4.8 Hz, 1H, NCH), 2.91-2.86 (m, 1H, NCH), 2.74-2.69 (m, 1H, NCH), 2.34-2.25 (m, 2H, 2 x NCH), 1.86-1.38 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 408, found 408.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(4-(trifluoromethoxy)phenoxy)hexyl) piperidine-3,4,5-triol (3r).



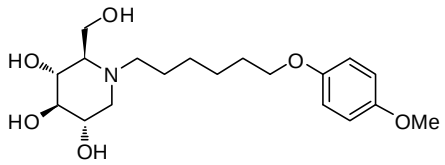
White semi-solid. Yield, 94%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.16 (d, J = 8.4 Hz, 2H, CH_{ar}), 6.98-6.93 (m, 2H, CH_{ar}), 3.98 (t, J = 6.6 Hz, 2H, $ArOCH_2$), 3.87 (d, J = 2.4 Hz, 2H, OCH_2), 3.54-3.46 (m, 1H, OCH), 3.38 (t, J = 9.6 Hz, 1H, OCH), 3.16 (t, J = 9.3 Hz, 1H, OCH), 3.06 (dd, J = 11.4, 4.8 Hz, 1H, NCH), 2.93-2.85 (m, 1H, NCH), 2.73-2.65 (m, 1H, NCH), 2.33-2.24 (m, 2H, 2 x NCH), 1.84-1.35 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 424, found 424.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(2-methoxyphenoxy)hexyl)piperidine-3,4,5-triol (3s).



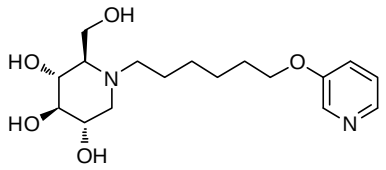
White solid. Yield, 85%. ^{1}H NMR (300 MHz, CD_3OD): δ 6.81 (s, 4H, CH_{ar}), 3.91-3.86 (m, 4H, 2 x OCH_2), 3.72 (s, 3H, OCH_3), 3.53-3.45 (m, 1H, OCH), 3.37 (t, *J* = 9.6 Hz, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.03 (dd, *J* = 11.1, 4.8 Hz, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.68-2.61 (m, 1H, NCH), 2.28-2.18 (m, 2H, 2 x NCH), 1.78-1.31 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 370, found 370.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(4-methoxyphenoxy)hexyl)piperidine-3,4,5-triol (3t).



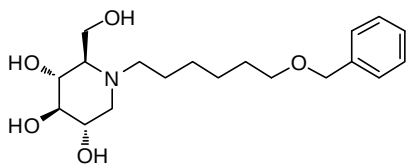
White solid. Yield, 93%. ^{1}H NMR (300 MHz, CD_3OD): δ 6.95-6.85 (m, 4H, CH_{ar}), 3.97 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.85 (t, *J* = 2.4 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 3.51-3.43 (m, 1H, OCH), 3.35 (t, *J* = 9.0 Hz, 1H, OCH), 3.13 (t, *J* = 9.0 Hz, 1H, OCH), 2.99 (dd, *J* = 11.1, 4.8 Hz, 1H, NCH), 2.84-2.76 (m, 1H, NCH), 2.64-2.57 (m, 1H, NCH), 2.22-2.09 (m, 2H, 2 x NCH), 1.83-1.32 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 370, found 370.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(6-(pyridin-3-yloxy)hexyl)piperidine-3,4,5-triol (3u).



Colorless semi-solid. Yield, 47%. ^{1}H NMR (300 MHz, CD_3OD): δ 8.21 (d, *J* = 2.1 Hz, 1H, CH_{ar}), 8.10 (d, *J* = 3.6 Hz, 1H, CH_{ar}), 7.42-7.32 (m, 2H, CH_{ar}), 4.05 (t, *J* = 6.3 Hz, 2H, $ArOCH_2$), 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.53-3.45 (m, 1H, OCH), 3.37 (t, *J* = 9.3 Hz, 1H, OCH), 3.15 (t, *J* = 9.3 Hz, 1H, OCH), 3.03 (dd, *J* = 11.1, 4.5 Hz, 1H, NCH), 2.89-2.82 (m, 1H, NCH), 2.69-2.62 (m, 1H, NCH), 2.28-2.19 (m, 2H, 2 x NCH), 1.86-1.34 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 341, found 341.

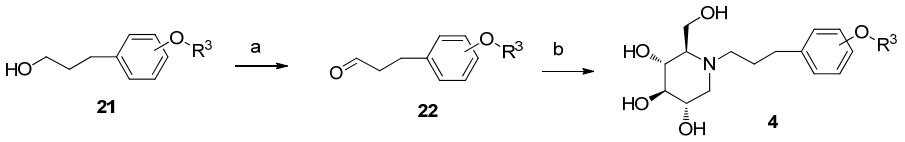
(2R,3R,4R,5S)-1-(6-(Benzyloxy)hexyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (3v).



White semi-solid. Yield, 69%. $[\alpha]_D$ = - 4 (c = 1.5, methanol). ^{1}H NMR (300 MHz, CD_3OD): δ 7.34-7.25 (m, 5H, CH_{ar}), 4.49 (s, 2H, $ArCH_2O$), 3.86 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.53-3.45 (m, 3H, 3 x

OCH), 3.37 (t, J = 9.6 Hz, 1H, OCH), 3.14 (t, J = 9.0 Hz, 1H, OCH), 3.04 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.69-2.64 (m, 1H, NCH), 2.30-2.21 (m, 2H, 2 x NCH), 1.66-1.27 (m, 8H, 4 x CH_2). MS: calculated for MH^+ = 354, found 354.

d. Synthesis of DNJ Derivatives 4.



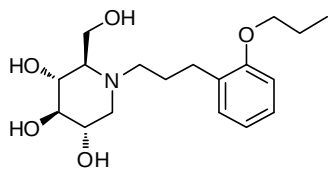
21 22 4

(a) PCC, CH_2Cl_2, Argon, rt; (b) DNJ, HOAc, EtOH; then H_2 (45psi), 10% Pd/C, EtOH

*d.a. General Procedure for the Preparation of Aldehydes **24.*** To a stirring suspension of PCC (647 mg, 3 mmol) and silica gel (647 mg) in dry dichloromethane (10 mL), was added a solution of the alcohol **23** (2 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at room temperature under argon atmosphere for 4 hours. Then, it was filtered through a silica gel pad, and washed with ethyl acetate (20 mL). The filtrate was concentrated and then purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 10 : 90) to afford the pure compound **24**.

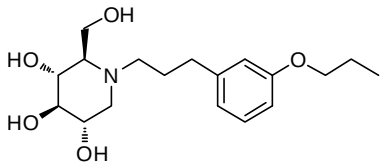
*d.b. General Procedure for the Synthesis of DNJ Derivatives **4.*** A solution of DNJ (33 mg, 0.2 mmol) in acetic acid (1 mL) was stirred at room temperature overnight. The solvent was then removed under reduced pressure. The resulting residue was treated with 200 proof ethanol (5 mL) and the aldehyde **24** (0.26 mmol), followed by acetic acid (2 drops as catalyst). The reaction mixture was stirred at room temperature under argon atmosphere for another hour. Then, it was transferred to the hydrogenation bottle, followed by addition of 10% Pd/C (33 mg) and 200 proof ethanol (5 mL). The mixture was hydrogenated under 45 psi of H_2 for 24 hours. After the reaction was complete, it was treated with celite (100 mg), and then filtered through a silica gel pad. The filtrate was concentrated and purified through silica gel column chromatography (methanol : ethyl acetate = 5 : 95 to 20 : 80) to afford the pure compound **4**.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(3-(2-propoxyphenyl)propyl)piperidine-3,4,5-triol (4a).



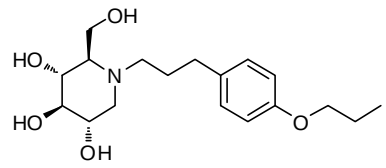
White solid. Yield, 97%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.15-7.10 (m, 2H, CH_{ar}), 6.89-6.80 (m, 2H, CH_{ar}), 3.93 (t, *J* = 6.3 Hz, 2H, $ArOCH_2$), 3.81 (t, *J* = 3.0 Hz, 2H, OCH_2), 3.50-3.42 (m, 1H, OCH), 3.36 (t, *J* = 9.3 Hz, 1H, OCH), 3.11 (t, *J* = 9.3 Hz, 1H, OCH), 2.98 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.73-2.57 (m, 3H, NCH and $ArCH_2$, overlapped), 2.25-2.12 (m, 2H, 2 x NCH), 1.86-1.76 (m, 4H, 2 x CH_2), 1.08 (t, *J* = 7.5 Hz, 3H, CH_3). MS: calculated for MH^+ = 340, found 340.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(3-(3-propoxyphenyl)propyl)piperidine-3,4,5-triol (4b).



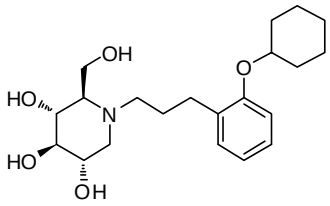
White semi-solid. Yield, 97%. $[\alpha]_D$ = - 6 (c = 1.7, methanol). ^{1}H NMR (300 MHz, CD_3OD): δ 7.18-7.12 (m, 1H, CH_{ar}), 6.77-6.69 (m, 3H, CH_{ar}), 3.90 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.81 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.49-3.43 (m, 1H, OCH), 3.35 (t, *J* = 9.3 Hz, 1H, OCH), 3.13 (t, *J* = 9.3 Hz, 1H, OCH), 2.99 (dd, *J* = 11.4, 5.1 Hz, 1H, NCH), 2.87-2.84 (m, 1H, NCH), 2.67-2.54 (m, 3H, NCH and $ArCH_2$, overlapped), 2.27-2.16 (m, 2H, 2 x NCH), 1.84-1.74 (m, 4H, 2 x CH_2), 1.03 (t, *J* = 7.5 Hz, 3H, CH_3). MS: calculated for MH^+ = 340, found 340.

(2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(3-(4-propoxyphenyl)propyl)piperidine-3,4,5-triol (4c).



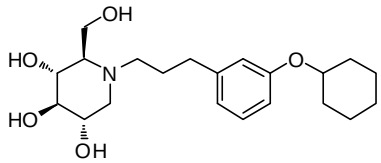
White solid. Yield, 97%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.11-7.06 (m, 2H, CH_{ar}), 6.83-6.78 (m, 2H, CH_{ar}), 3.88 (t, *J* = 6.6 Hz, 2H, $ArOCH_2$), 3.79 (d, *J* = 2.7 Hz, 2H, OCH_2), 3.50-3.42 (m, 1H, OCH), 3.34 (t, *J* = 9.6 Hz, 1H, OCH), 3.12 (t, *J* = 9.3 Hz, 1H, OCH), 2.97 (dd, *J* = 11.4, 4.8 Hz, 1H, NCH), 2.88-2.78 (m, 1H, NCH), 2.67-2.50 (m, 3H, NCH and $ArCH_2$, overlapped), 2.23-2.11 (m, 2H, 2 x NCH), 1.82-1.71 (m, 4H, 2 x CH_2), 1.03 (t, *J* = 7.5 Hz, 3H, CH_3). MS: calculated for MH^+ = 340, found 340.

(2R,3R,4R,5S)-1-(3-(2-(Cyclohexyloxy)phenyl)propyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (4d).



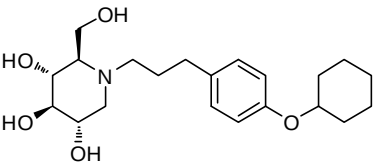
White solid. Yield, 92%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.14-7.08 (m, 2H, CH_{ar}), 6.90-6.78 (m, 2H, CH_{ar}), 4.37-4.31 (m, 1H, ArOCH), 3.88-3.77 (m, 2H, OCH_2), 3.53-3.44 (m, 1H, OCH), 3.39 (t, J = 9.3 Hz, 1H, OCH), 3.14 (t, J = 9.0 Hz, 1H, OCH), 3.02 (dd, J = 11.7, 5.1 Hz, 1H, NCH), 2.92-2.85 (m, 1H, NCH), 2.79-2.71 (m, 1H, NCH), 2.59 (t, J = 7.8 Hz, 2H, $ArCH_2$), 2.33-2.21 (m, 2H, 2 x NCH), 2.01-1.40 (m, 12H, 6 x CH_2). MS: calculated for MH^+ = 380, found 380.

(2R,3R,4R,5S)-1-(3-(3-(Cyclohexyloxy)phenyl)propyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (4e).



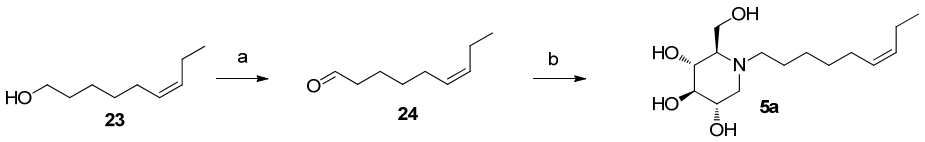
White solid. Yield, 96%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.17-7.12 (m, 1H, CH_{ar}), 6.76-6.71 (m, 3H, CH_{ar}), 4.31-4.25 (m, 1H, ArOCH), 3.81 (s, 1H, OCH_2), 3.51-3.43 (m, 1H, OCH), 3.36 (t, J = 9.6 Hz, 1H, OCH), 3.13 (t, J = 9.0 Hz, 1H, OCH), 3.00 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.92-2.82 (m, 1H, NCH), 2.70-2.53 (m, 3H, NCH and $ArCH_2$, overlapped), 2.28-2.17 (m, 2H, 2 x NCH), 2.01-1.36 (m, 12H, 6 x CH_2). MS: calculated for MH^+ = 380, found 380.

(2R,3R,4R,5S)-1-(3-(4-(Cyclohexyloxy)phenyl)propyl)-2-(hydroxymethyl)piperidine-3,4,5-triol (4f).



White solid. Yield, 95%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.08 (d, J = 8.4 Hz, 2H, CH_{ar}), 6.81 (d, J = 8.4 Hz, 2H, CH_{ar}), 4.26-4.20 (m, 1H, ArOCH), 3.80 (s, 2H, OCH_2), 3.51-3.43 (m, 1H, OCH), 3.36 (t, J = 9.3 Hz, 1H, OCH), 3.13 (t, J = 9.3 Hz, 1H, OCH), 2.99 (dd, J = 11.1, 4.8 Hz, 1H, NCH), 2.90-2.81 (m, 1H, NCH), 2.70-2.58 (m, 1H, NCH), 2.56-2.50 (m, 2H, $ArCH_2$), 2.27-2.16 (m, 2H, 2 x NCH), 2.01-1.29 (m, 12H, 6 x CH_2). MS: calculated for MH^+ = 380, found 380.

e. Synthesis of DNJ Derivative 5a.

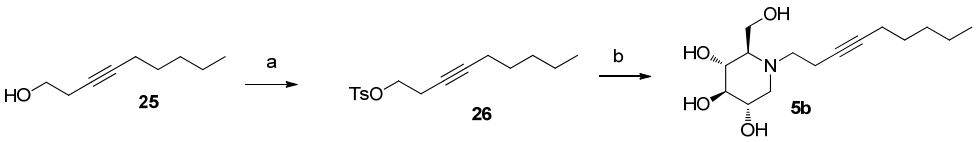


(a) PCC, CH_2Cl_2, Argon, rt, 89%; (b) DNJ, $Na(CN)BH_3$ (1M in THF), HOAc, CH_3OH, Argon, rt, 75%

*e.a. Preparation of (Z)-Non-6-enal (**26**).* To a stirring suspension of PCC (841 mg, 3.9 mmol) and silica gel (841 mg) in dry dichloromethane (20 mL), was added a solution of the alcohol **25** (427 mg, 3 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at room temperature under argon atmosphere for 4 hours. Then, it was filtered through a silica gel pad, and washed with ethyl acetate (20 mL). The filtrate was concentrated and then purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 10 : 90) to afford 375 mg of pure compound **26** as colorless oil. Yiled, 89%.

*e.b. Synthesis of (2R,3R,4R,5S)-2-(Hydroxymethyl)-1-((Z)-non-6-en-1-yl)piperidine-3,4,5-triol (**5a**).* To a solution of DNJ (33 mg, 0.2 mmol) and (Z)-non-6-enal (**26**, 36 mg, 0.26 mmol) in methanol (5 mL), was added acetic acid (24 μL, 0.4 mmol), followed by the addition of sodium cyanoborohydride (1 M in THF, 0.3 mL, 0.3 mmol). The reaction mixture was stirred at room temperature under argon atmosphere for 24 hours. Then, it was quenched with water (5 mL), concentrated and purified through silica gel column chromatography (methanol : ethyl acetate = 5 : 95 to 20 : 80) to afford 43 mg of pure compound **5a** as colorless semi-solid. Yield, 75%. ^{1}H NMR (300 MHz, CD_3OD): δ 5.38-5.29 (m, 2H, 2 x CH=), 3.86 (d, J = 1.8 Hz, 2H, OCH_2), 3.54-3.46 (m, 1H, OCH), 3.38 (t, J = 9.6 Hz, 1H, OCH), 3.16 (t, J = 9.0 Hz, 1H, OCH), 3.04 (dd, J = 11.1, 4.8 Hz, 1H, NCH), 2.88-2.80 (m, 1H, NCH), 2.71-2.64 (m, 1H, NCH), 2.32-2.22 (m, 2H, 2 x NCH), 2.08-1.99 (m, 4H, 2 x CH_2), 1.58-1.26 (m, 6H, 3 x CH_2), 0.95 (t, J = 7.8 Hz, 3H, CH_3). MS: calculated for MH^+ = 288, found 288.

f. Synthesis of DNJ Derivative 5b.

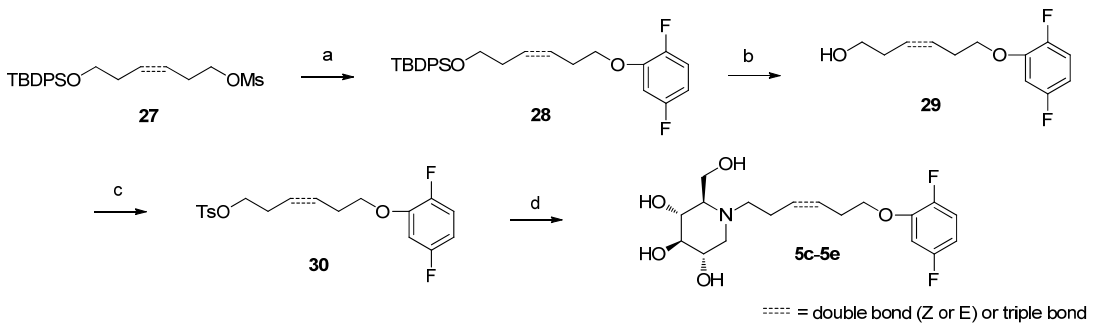


(a) TsCl, Pyr., 0 °C, 66%; (b) DNJ, Na_2CO_3, DMF, 75 °C, 49%

*f.a. Preparation of Non-3-yn-1-yl 4-Methylbenzenesulfonate (**28**).* To a stirring solution of non-3-yn-1-ol (**27**, 421 mg, 3 mmol) in pyridine (6 mL) at 0 °C, was added 4-toluenesulfonyl chloride (686 mg, 3.6 mmol). The reaction mixture was stirred at 0 °C for 3hrs. Then, it was quenched with 2 N HCl, acidified to pH 1~2 at 0 °C, and extracted with ethyl acetate (20 mL x 3). The combined organic layer was washed with brine (20 mL), dried over anhydrous sodium sulfate , concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 10 : 90) to afford 585 mg of pure compound **28** as colorless oil. Yield, 66%.

*f.b. Synthesis of (2R,3R,4R,5S)-2-(Hydroxymethyl)-1-(non-3-yn-1-yl)piperidine-3,4,5-triol (**5b**).* A reaction mixture of non-3-yn-1-yl 4-methylbenzenesulfonate (**28**, 294 mg, 1 mmol), DNJ (49 mg, 0.3 mmol) and sodium carbonate (159 mg, 1.5 mmol) in DMF (3 mL) was stirred at 75 °C in a sealed tube for 24 hours. After cooling to room temperature, the reaction was quenched with water (10 mL), concentrated and slurried in a mixture of methanol and dichloromethane (40 : 60, 10 mL). The solid was filtered off and the filtrate was concentrated to give the crude product, which was purified by preparative TLC plate (methanol : ethyl acetate = 10 : 90) to afford 45 mg of pure compound **5b** as white semi-solid. Yield, 49%. ^{1}H NMR (300 MHz, CD_3OD): δ 3.92-3.81 (m, 2H, OCH_2), 3.49-3.41 (m, 1H, OCH), 3.33 (t, J = 9.0 Hz, 1H, OCH), 3.12 (t, J = 9.0 Hz, 1H, OCH), 3.01-2.81 (m, 3H), 2.35-2.09 (m, 6H), 1.48-1.28 (m, 6H, 3 x CH_2), 0.91 (t, J = 7.2 Hz, 3H, CH_3). MS: calculated for MH^+ = 286, found 286.

g. Synthesis of DNJ Derivatives 5c-5e.



(a) 2,5-difluorophenol, K_2CO_3, DMF, 80 ºC; (b) TBAF (1M in THF), THF, rt; (c) TsCl, Pyr., 0 °C; (d) DNJ, Na_2CO_3, DMF, 75 °C

*g.a. General Procedure for the Preparation of Intermediates **30.*** To a solution of the mesylate **29** (3 mmol) and 2,5-difluorophenol (585 mg, 4.5 mmol) in DMF (10 mL), was added potassium carbonate (622 mg, 4.5 mmol). The reaction mixture was stirred at 80 °C for 1 hour. After cooling to room temperature, it was quenched with water (20 mL) and extracted with ethyl acetate (20 mL x 3). The combined organic layer was washed with brine (20 mL), dried over anhydrous sodium sulfate , concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 5 : 95) to afford the pure compound **30**.

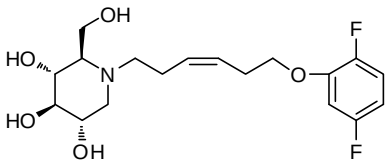
*g.b. General Procedure for the Preparation of Alcohols **31.*** To a stirred solution of the intermediate **30** (2.44 mmol) in THF (20 mL), was added tetra-*n*-butylammonium fluoride (1 M in THF, 12.2 mL, 12.2 mmol). The reaction mixture was stirred at room temperature for 2 hours. Then, it was quenched with water (30 mL) and extracted with ethyl acetate (30 mL x 3). The combined organic layer was washed with brine (30 mL), dried over anhydrous sodium sulfate , concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 10 : 90 to 25 : 75) to afford the pure compound **31**.

*g.c. General Procedure for the Preparation of Tosylates **32.*** To a stirring solution of the alcohol **31** (2.15 mmol) in pyridine (5 mL) at 0 °C, 4-toluenesulfonyl chloride (492 mg, 2.58 mmol was added. The reaction mixture was stirred at 0 °C for 3hrs. Then it was quenched with 2 N HCl, acidified to pH 1~2 at 0 °C, and extracted with ethyl acetate (20 mL x 3). The combined organic layer was washed with brine,

dried over anhydrous sodium sulfate , concentrated and purified through silica gel column chromatography (ethyl acetate : hexanes = 0 : 100 to 10 : 90) to afford the pure compound **32**.

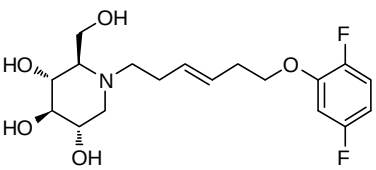
*g.d. General Procedure for the Synthesis of DNJ Derivatives **5c-5e**.* A reaction mixture of the tosylate **32** (126 mg, 0.33 mmol), DNJ (16 mg, 0.1 mmol) and sodium carbonate (53 mg, 0.5 mmol) in DMF (3 mL) was stirred at 75 °C in a sealed tube for 24 hours. After cooling to room temperature, the reaction was quenched with water (10 mL), concentrated and slurried in a mixture of methanol and dichloromethane (40 : 60, 10 mL). The solid was filtered off and the filtrate was concentrated to give the crude product, which was purified by preparative thin layer chromatography (TLC) plate (methanol : ethyl acetate = 10 : 90) to afford the pure compound **5c**-**5e**.

(2R,3R,4R,5S)-1-((Z)-6-(2,5-Difluorophenoxy)hex-3-en-1-yl)-2-(hydroxymethyl)piperidine-3,4,5-triol (5c).



Colorless semi-solid. Yield, 30%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.10-7.01 (m, 1H, CH_{ar}), 6.91-6.85 (m, 1H, CH_{ar}), 6.64-6.58 (m, 1H, CH_{ar}), 5.56-5.48 (m, 2H, 2 x CH=), 4.06-4.01 (m, 2H, $ArOCH_2$), 3.87-3.84 (m, 2H, OCH_2), 3.49-3.42 (m, 1H, OCH), 3.34 (t, J = 7.2 Hz, 1H, OCH), 3.13 (t, J = 9.0 Hz, 1H, OCH), 3.00 (dd, J = 11.4, 5.1 Hz, 1H, NCH), 2.82-2.77 (m, 1H, NCH), 2.69-2.67 (m, 1H, NCH), 2.60-2.54 (m, 2H), 2.34-2.14 (m, 4H). MS: calculated for MH^+ = 374, found 374.

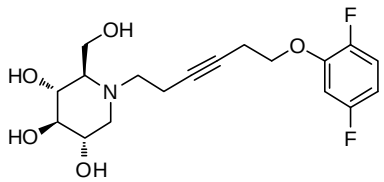
(2R,3R,4R,5S)-1-((E)-6-(2,5-Difluorophenoxy)hex-3-en-1-yl)-2-(hydroxymethyl)piperidine-3,4,5-triol (5d).



Colorless semi-solid. Yield, 6%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.00-6.92 (m, 1H, CH_{ar}), 6.81-6.74 (m, 1H, CH_{ar}), 6.55-6.48 (m, 1H, CH_{ar}), 5.52-5.47 (m, 2H, 2 x CH=), 3.93 (t, J = 6.9 Hz, 2H, $ArOCH_2$), 3.76 (s,

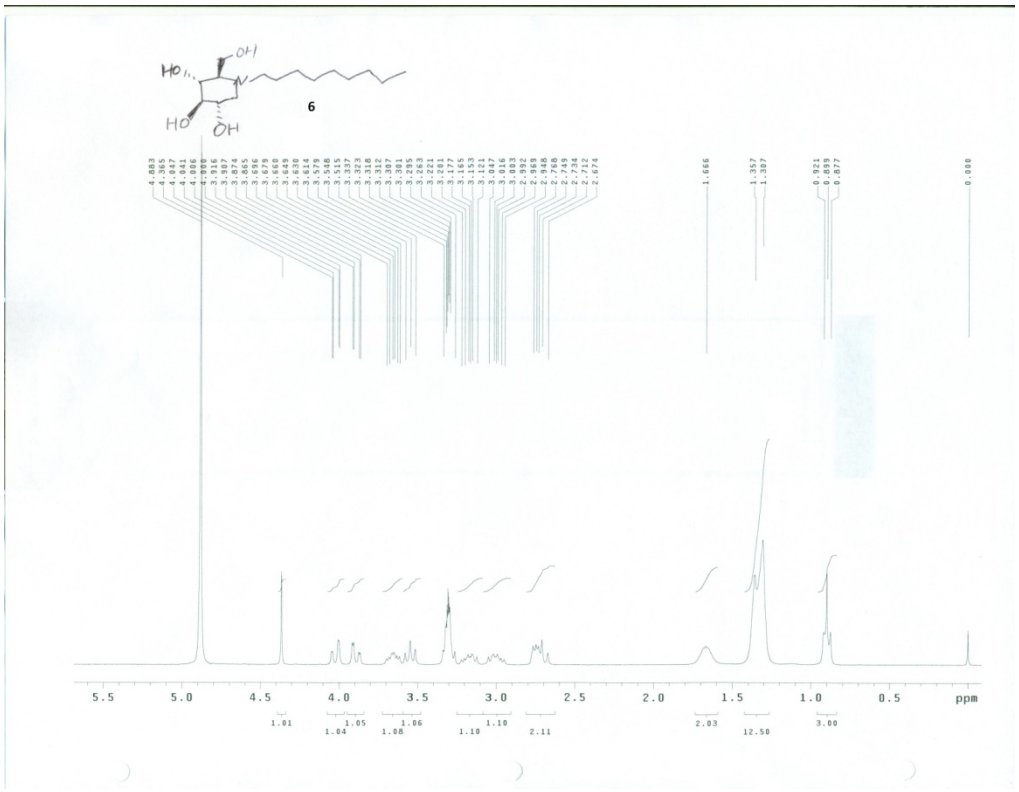
2H, OCH_2), 3.41-3.33 (m, 1H, OCH), 3.25 (t, *J* = 11.2 Hz, 1H, OCH), 3.03 (t, *J* = 9.3 Hz, 1H, OCH), 2.89 (dd, *J* = 11.1, 5.1 Hz, 1H, NCH), 2.77-2.69 (m, 1H, NCH), 2.63-2.53 (m, 1H, NCH), 2.42-2.36 (m, 2H), 2.17-2.04 (m, 4H). MS: calculated for MH^+ = 374, found 374.

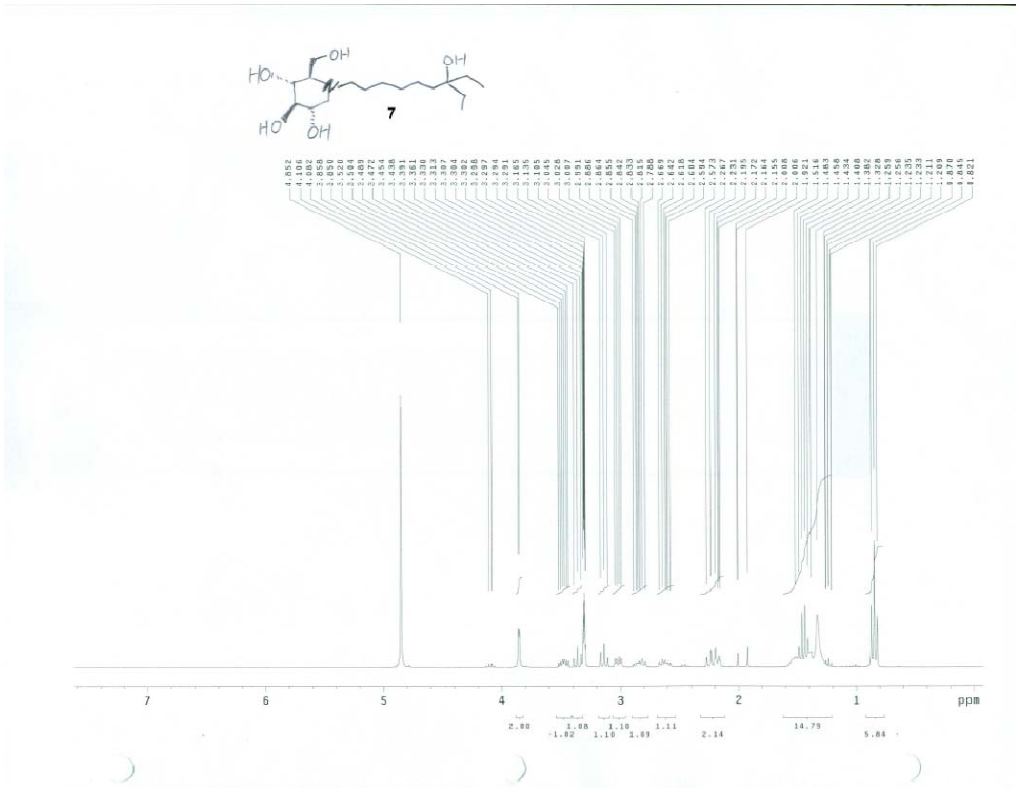
(2R,3R,4R,5S)-1-(6-(2,5-Difluorophenoxy)hex-3-yn-1-yl)-2-(hydroxymethyl)piperidine-3,4,5-triol (5e).

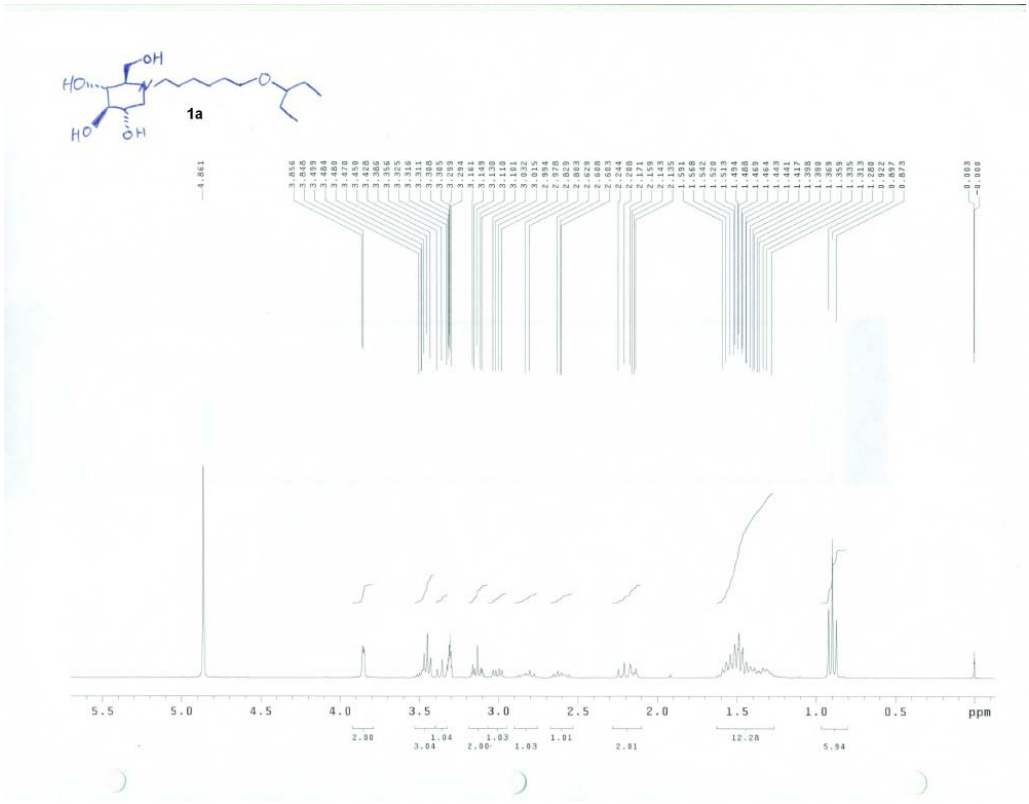


Colorless semi-solid. Yield, 37%. ^{1}H NMR (300 MHz, CD_3OD): δ 7.11-7.03 (m, 1H, CH_{ar}), 6.93-6.87 (m, 1H, CH_{ar}), 6.67-6.61 (m, 1H, CH_{ar}), 4.11-4.07 (m, 2H, $ArOCH_2$), 3.92-3.80 (m, 2H, OCH_2), 3.48-3.40 (m, 1H, OCH), 3.35-3.32 (m, 1H, OCH, overlapped with the peaks of CH_3OH), 3.11 (t, *J* = 9.3 Hz, 1H, OCH), 2.99-2.83 (m, 3H), 2.66-2.60 (m, 2H), 2.37-2.16 (m, 4H). MS: calculated for MH^+ = 372, found 372.

2. NMR Spectra of Compounds 1-7



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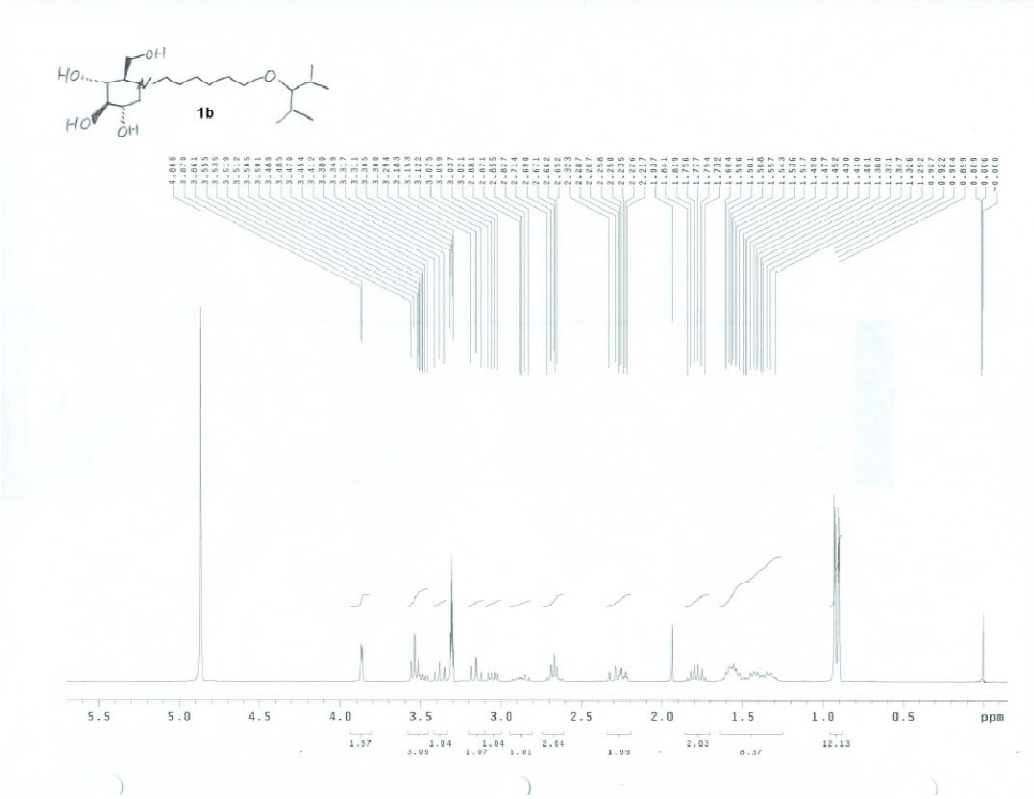
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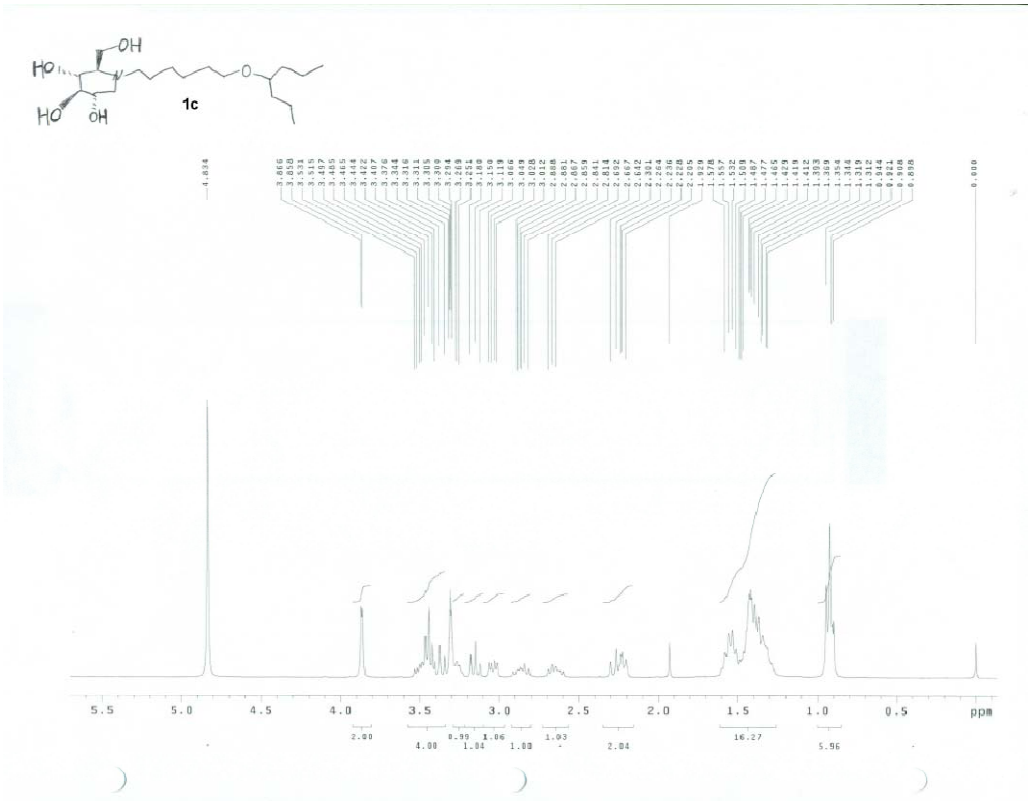
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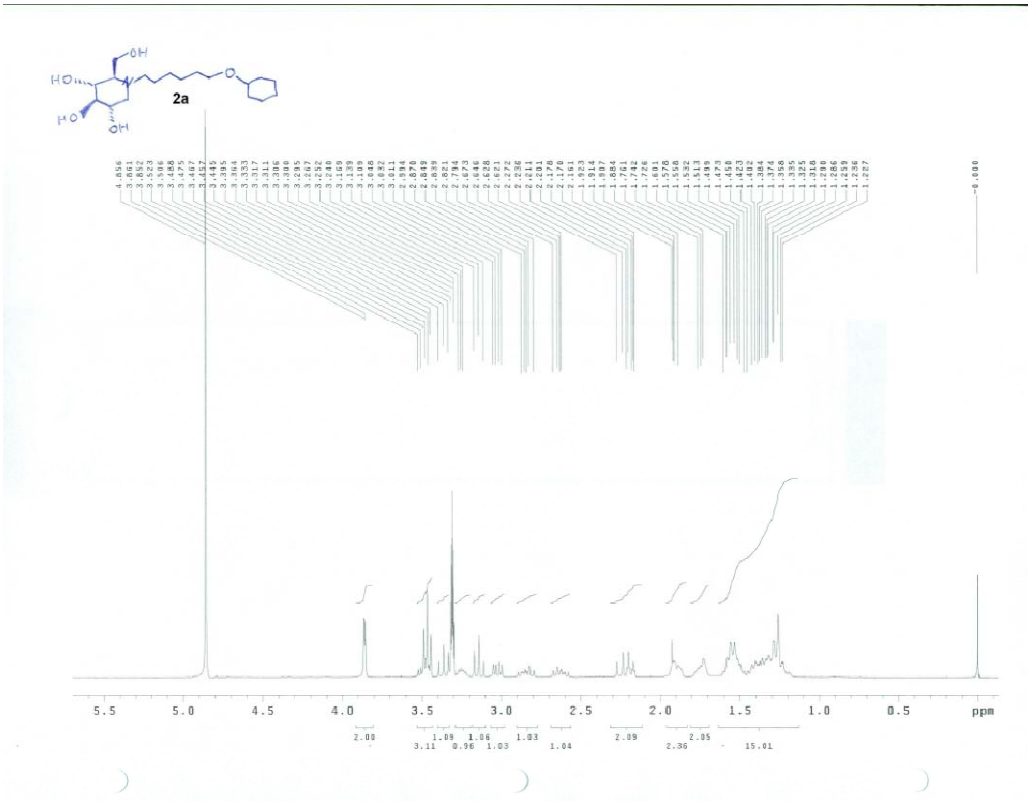
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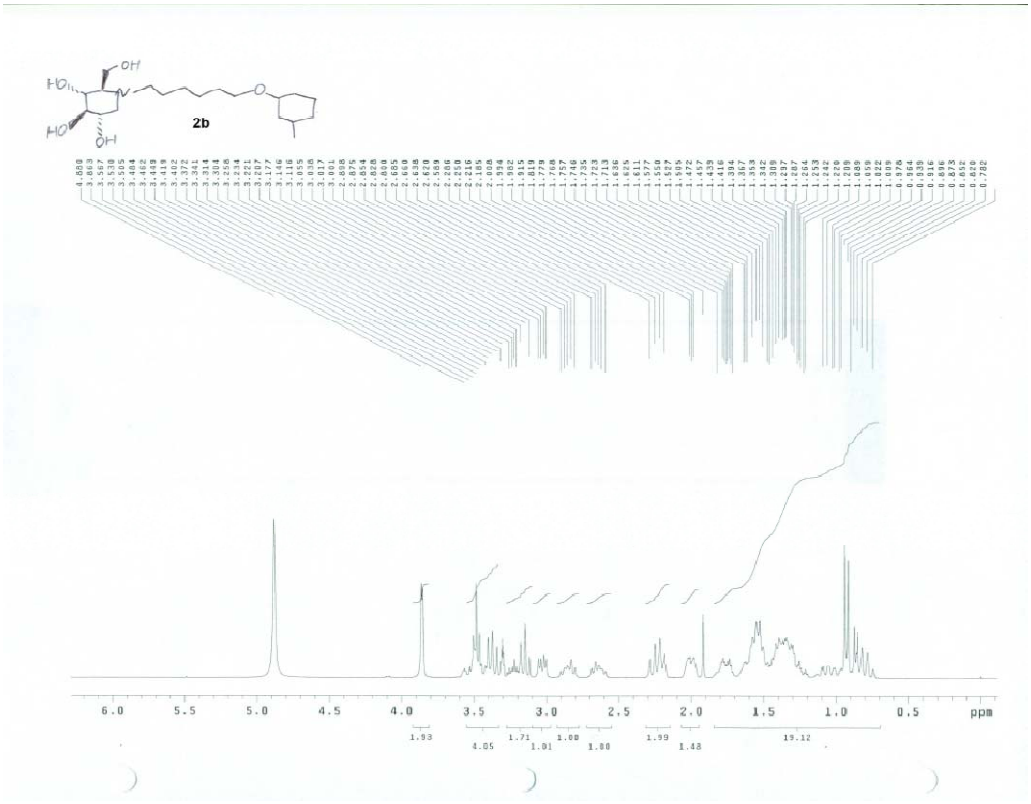
ppm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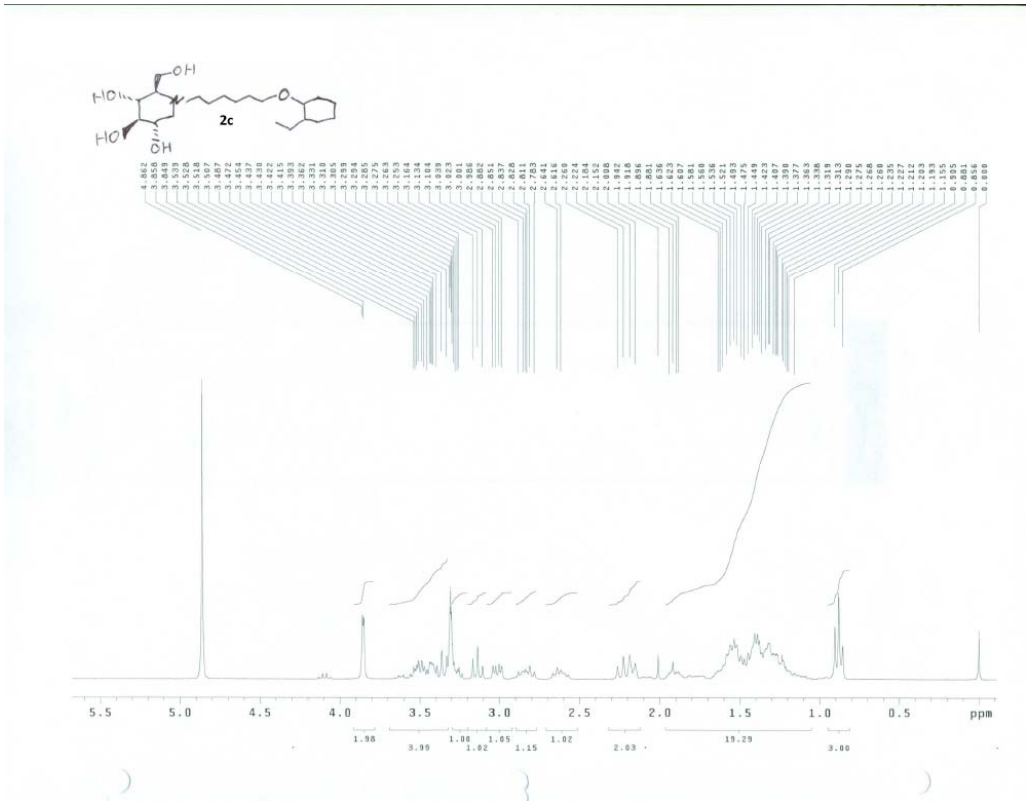
1.99
1.48
19.12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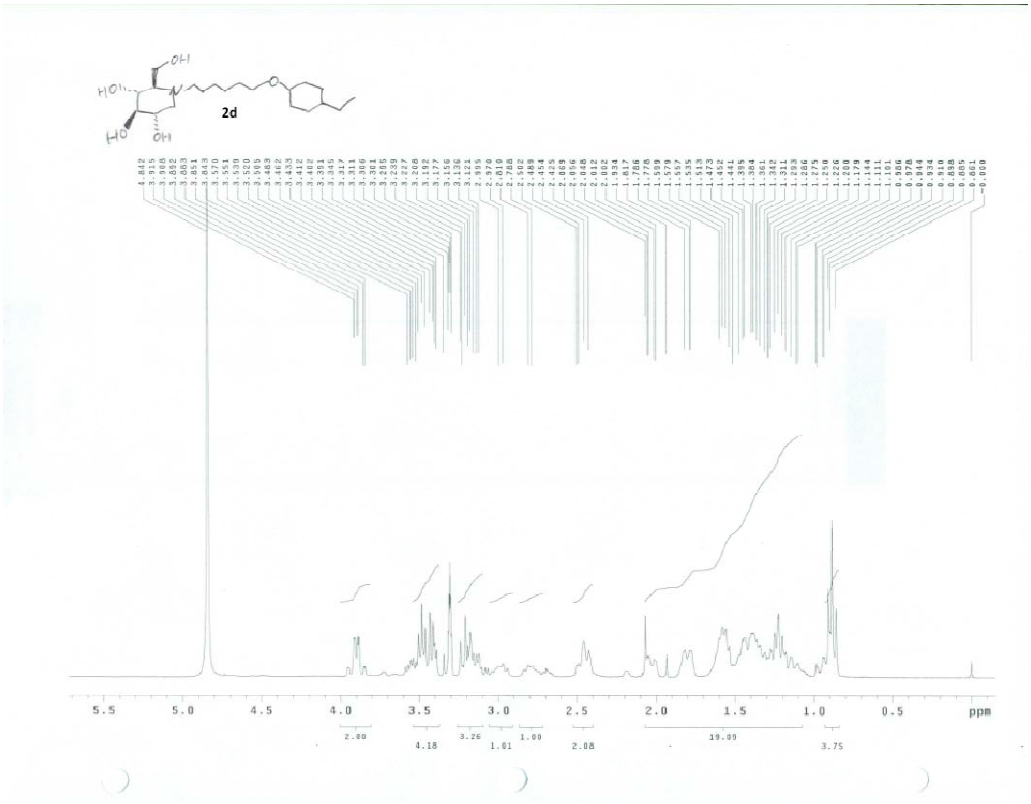
19.29
3.00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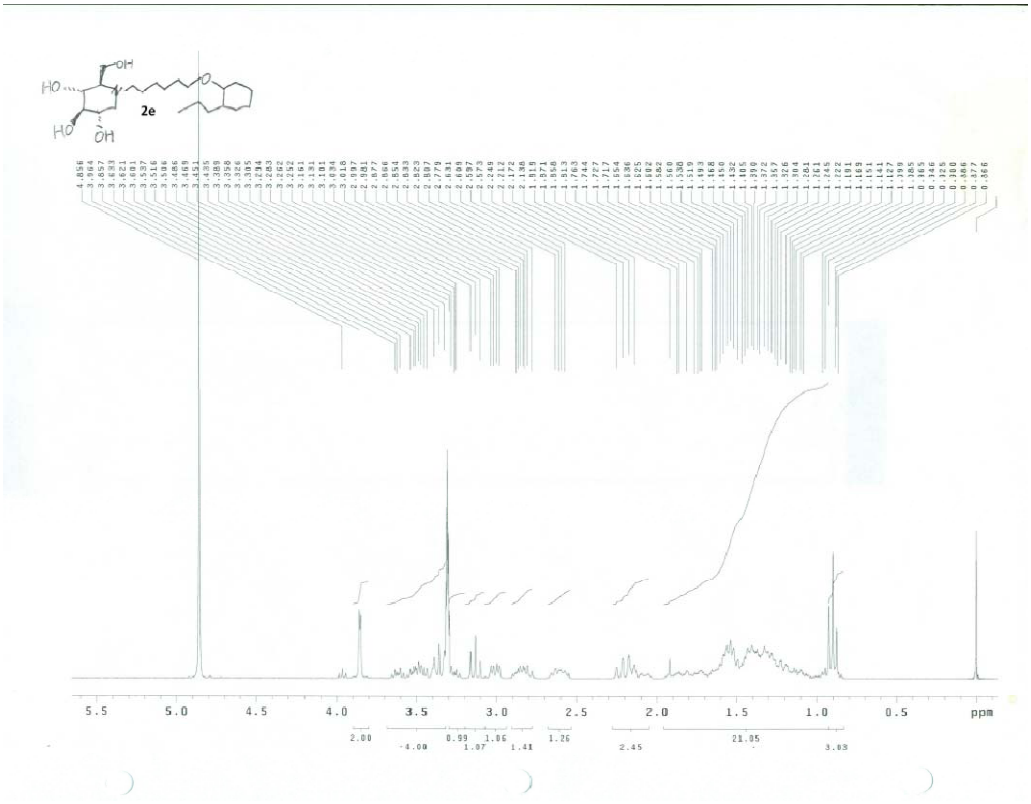
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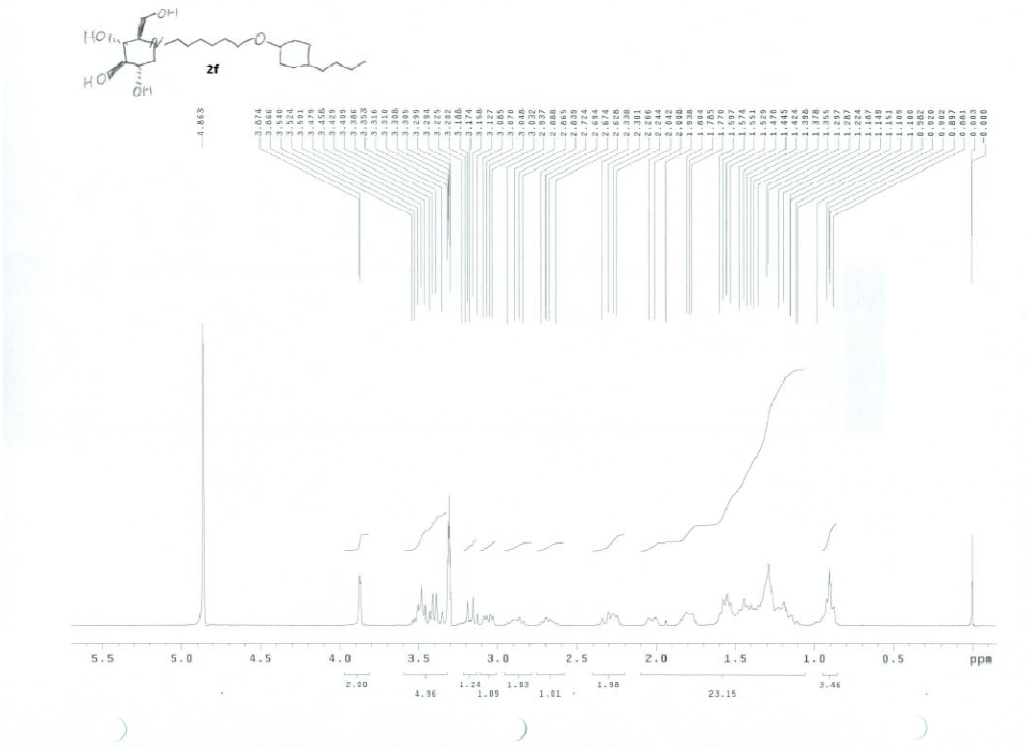
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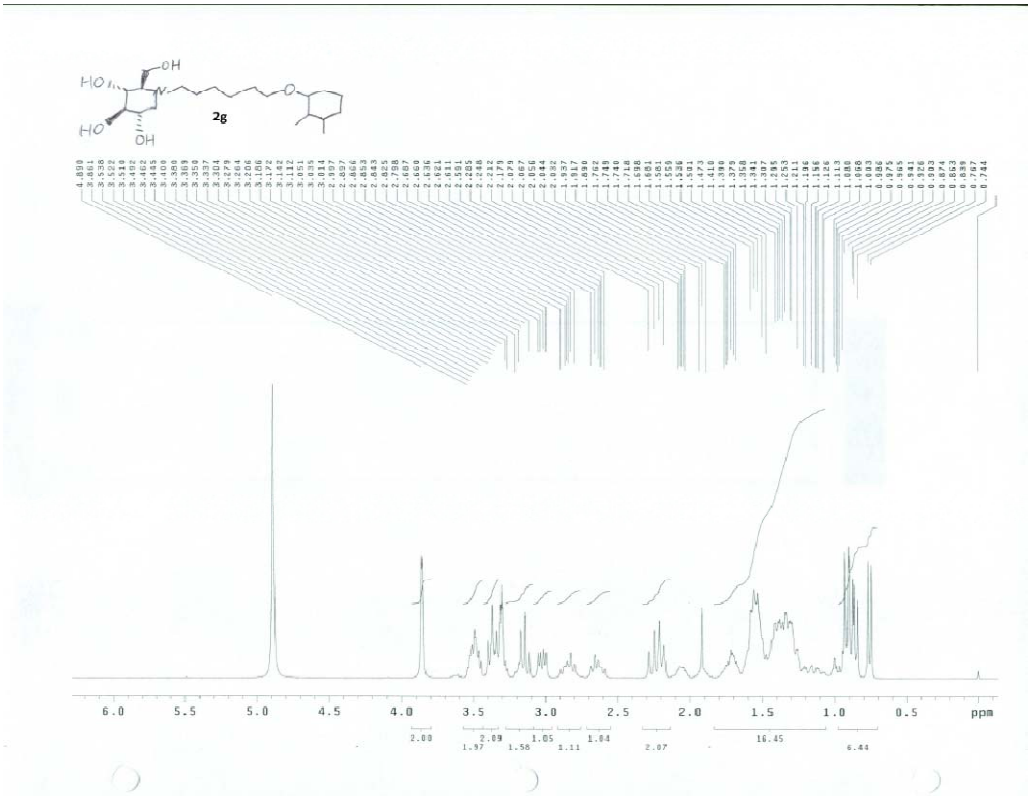
3.46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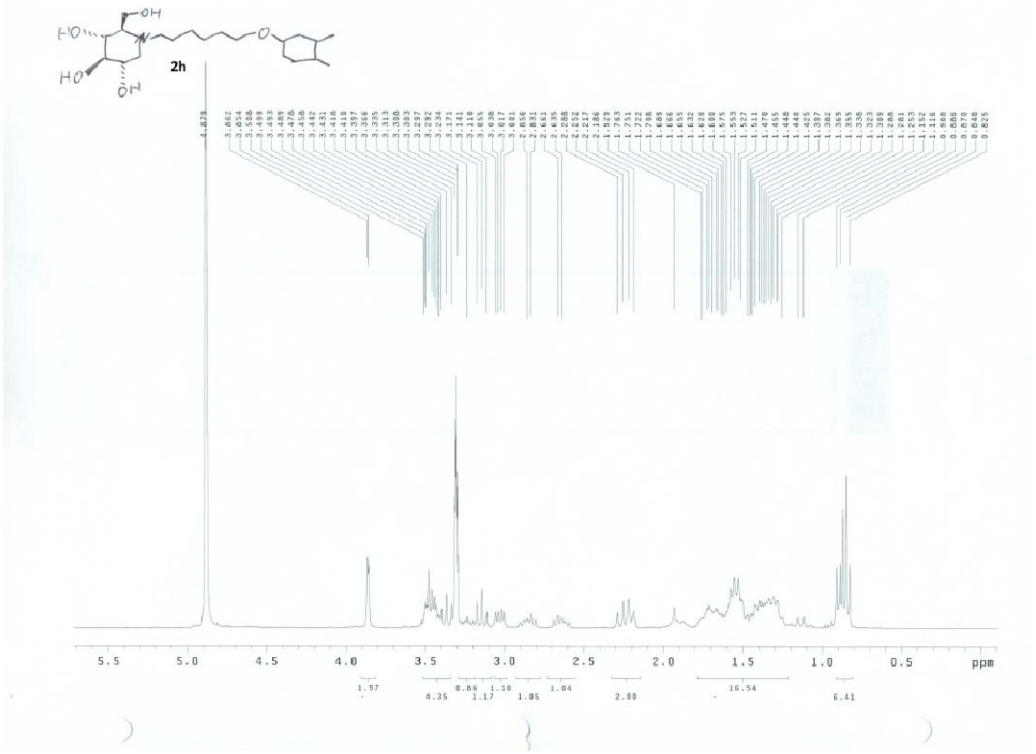
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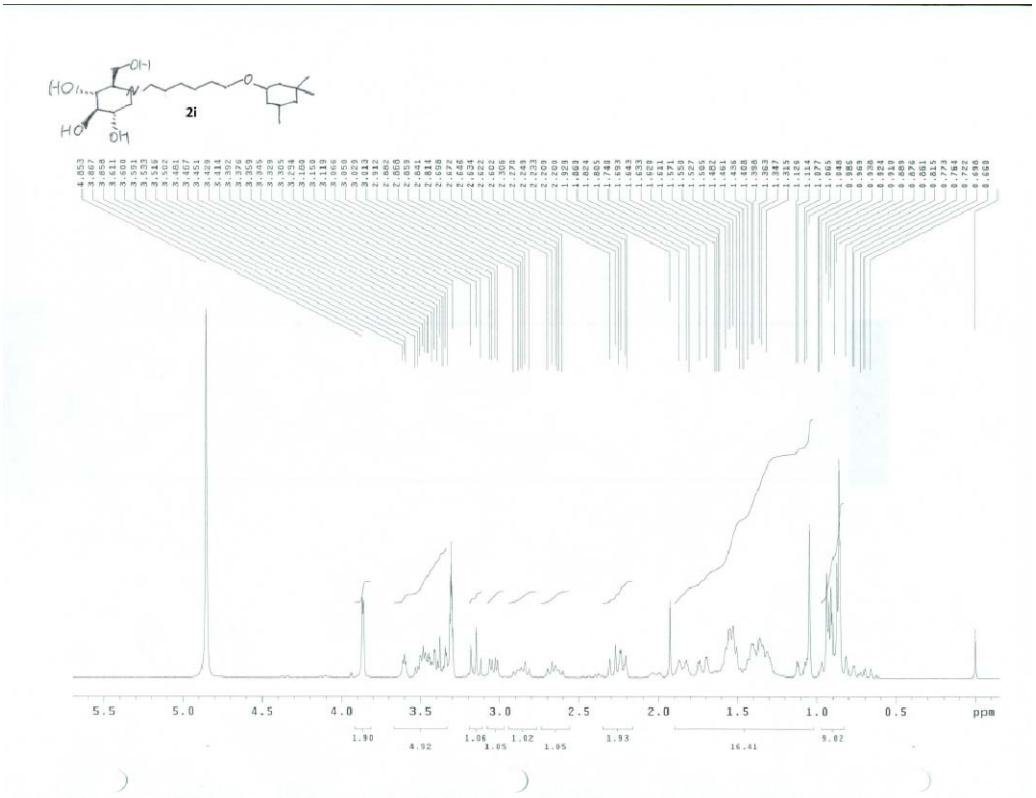
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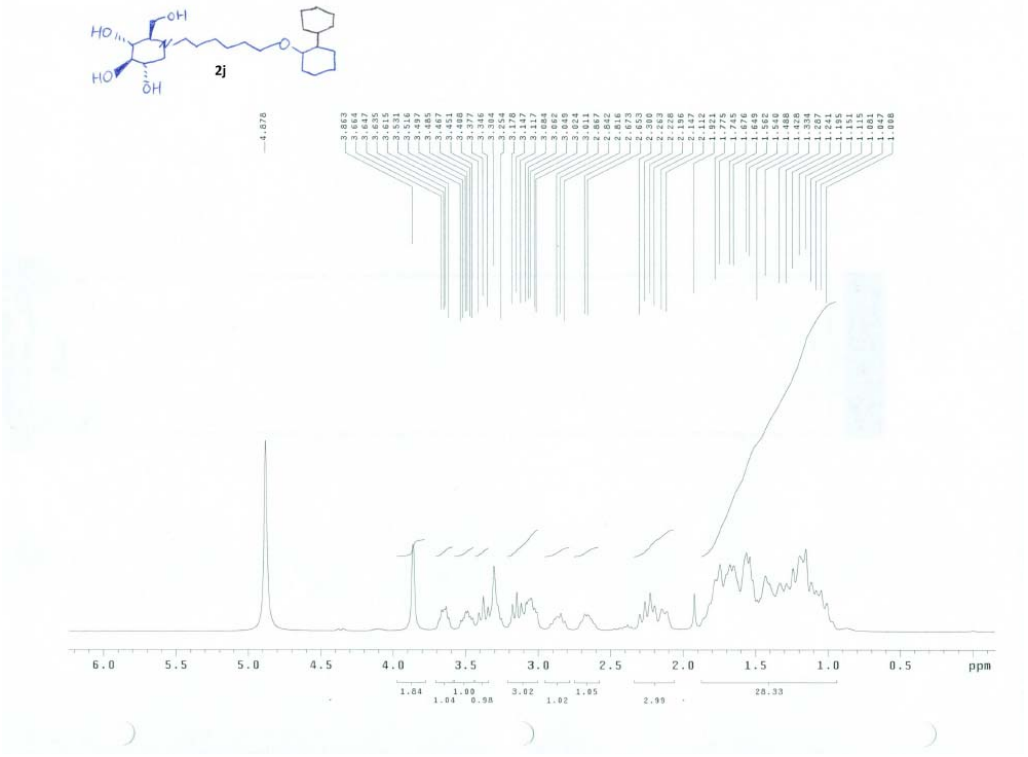
9.02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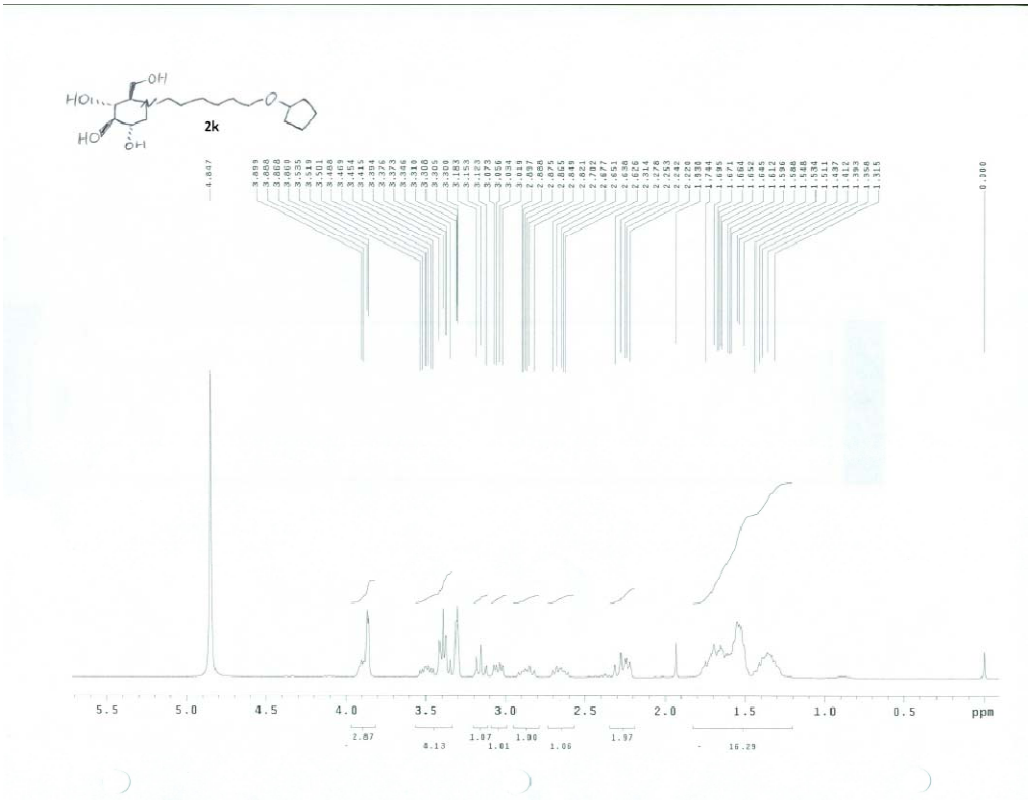
ppm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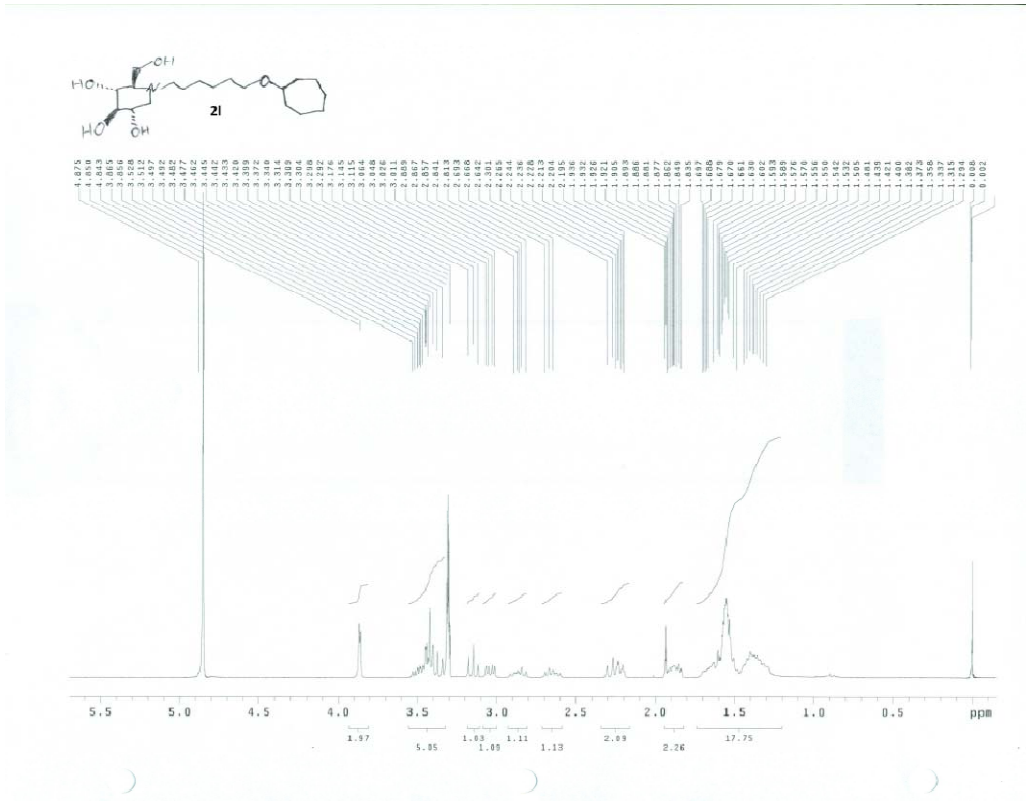
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1.11
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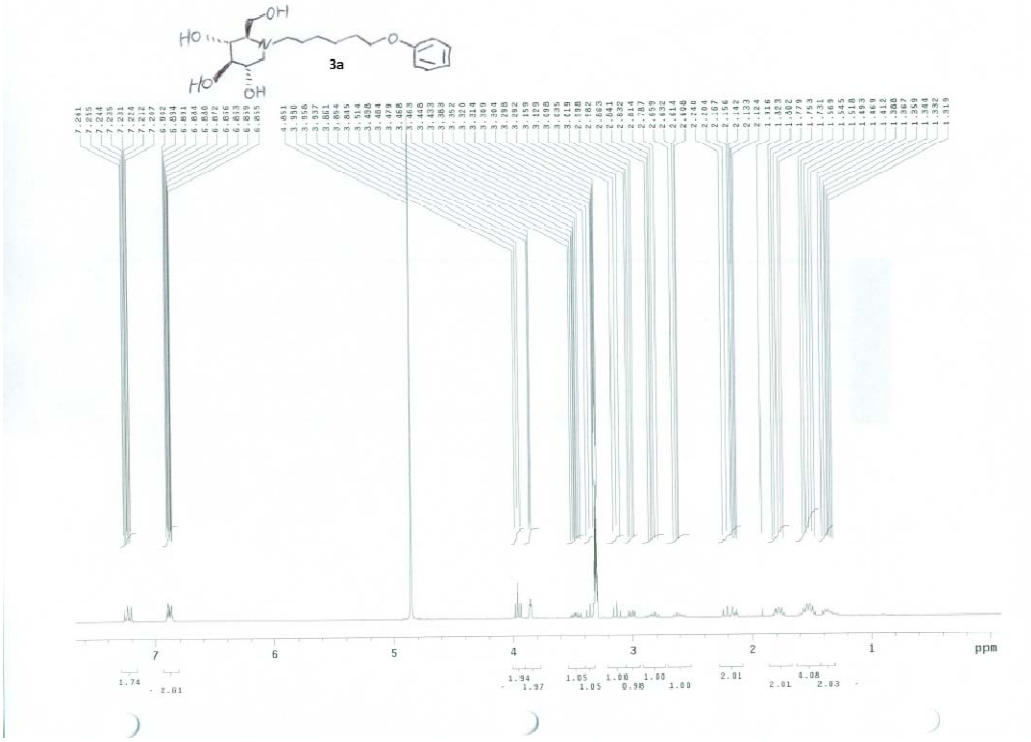
17.75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2
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ppm
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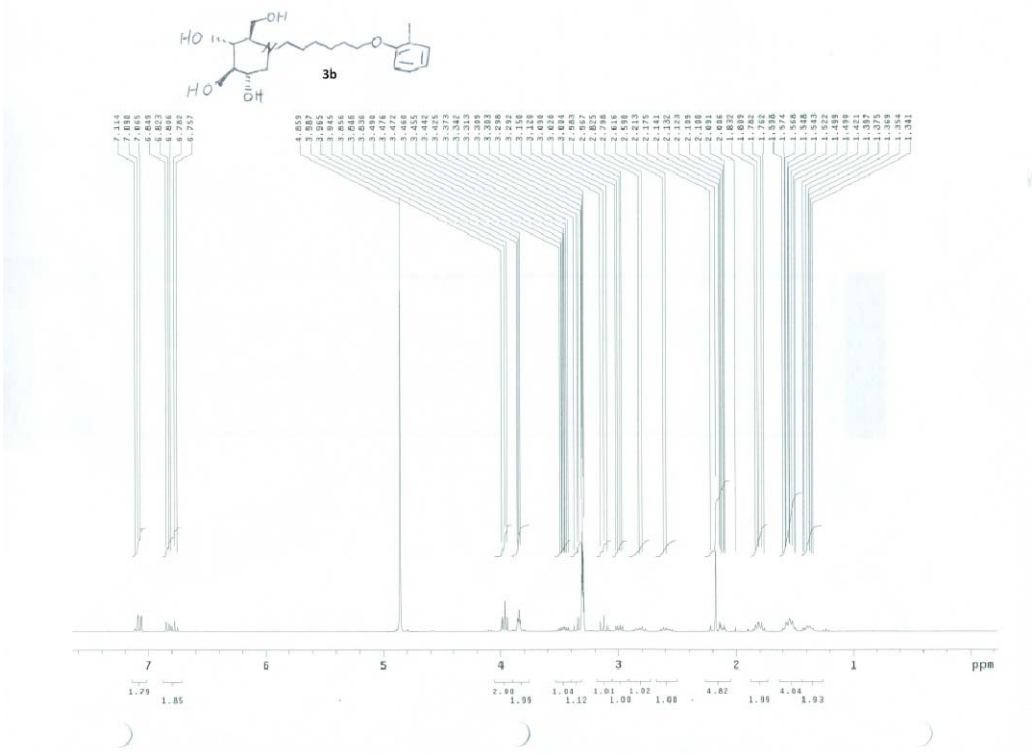
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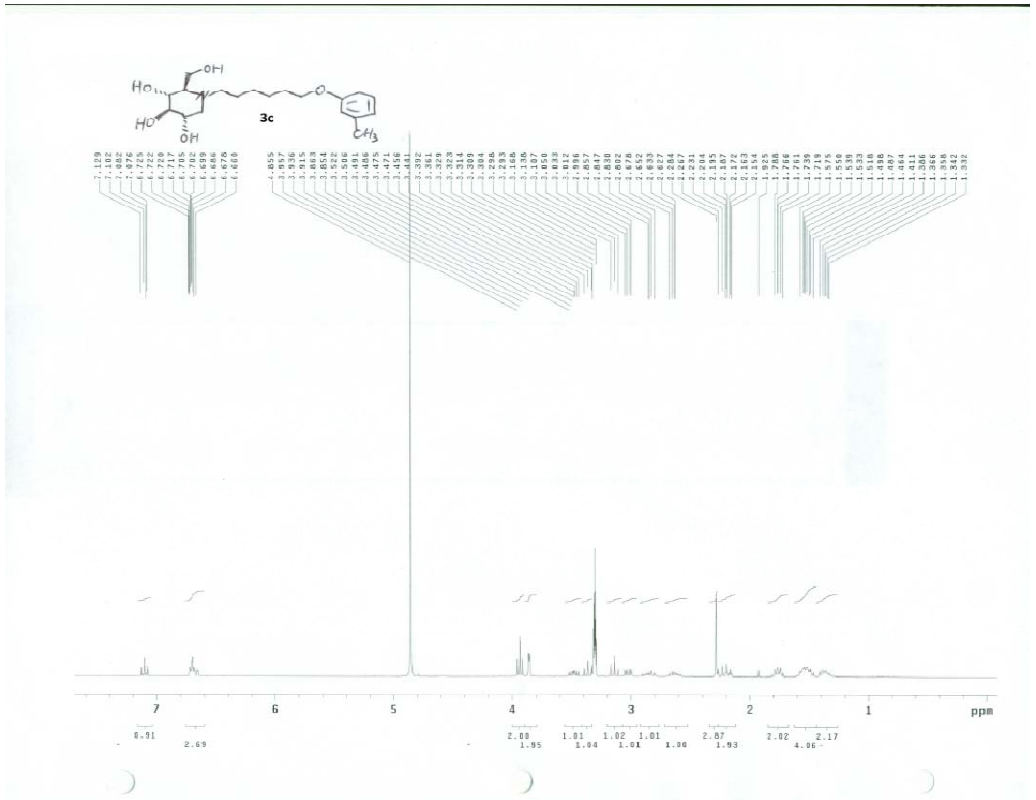
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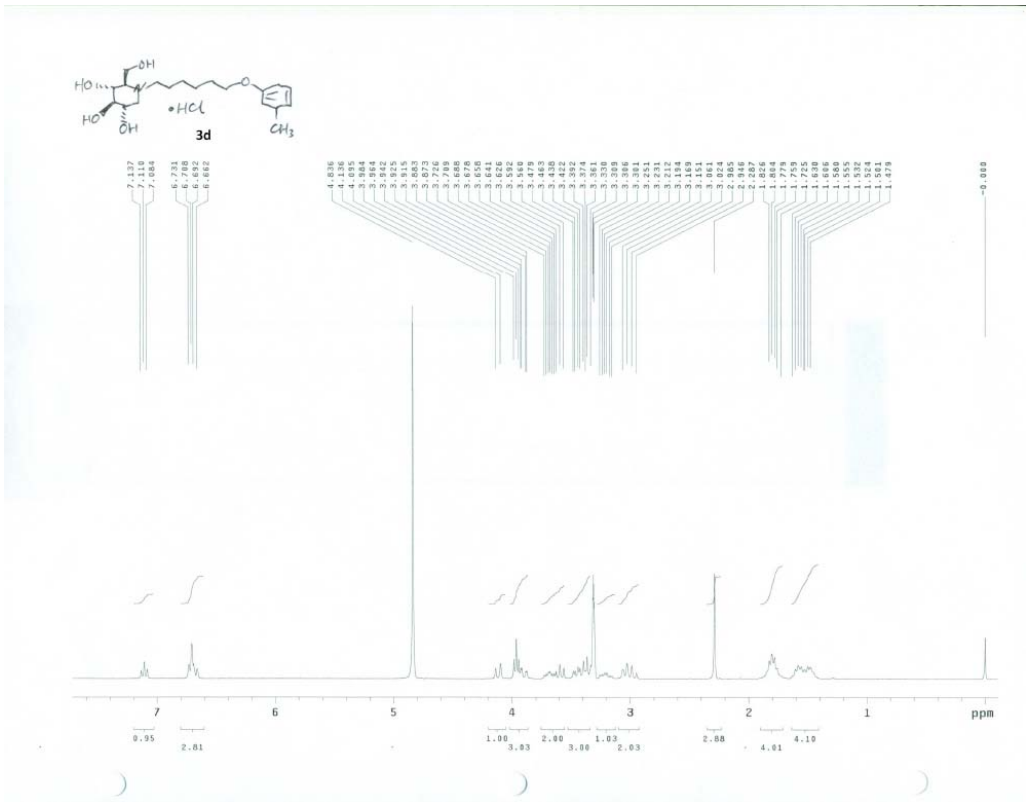
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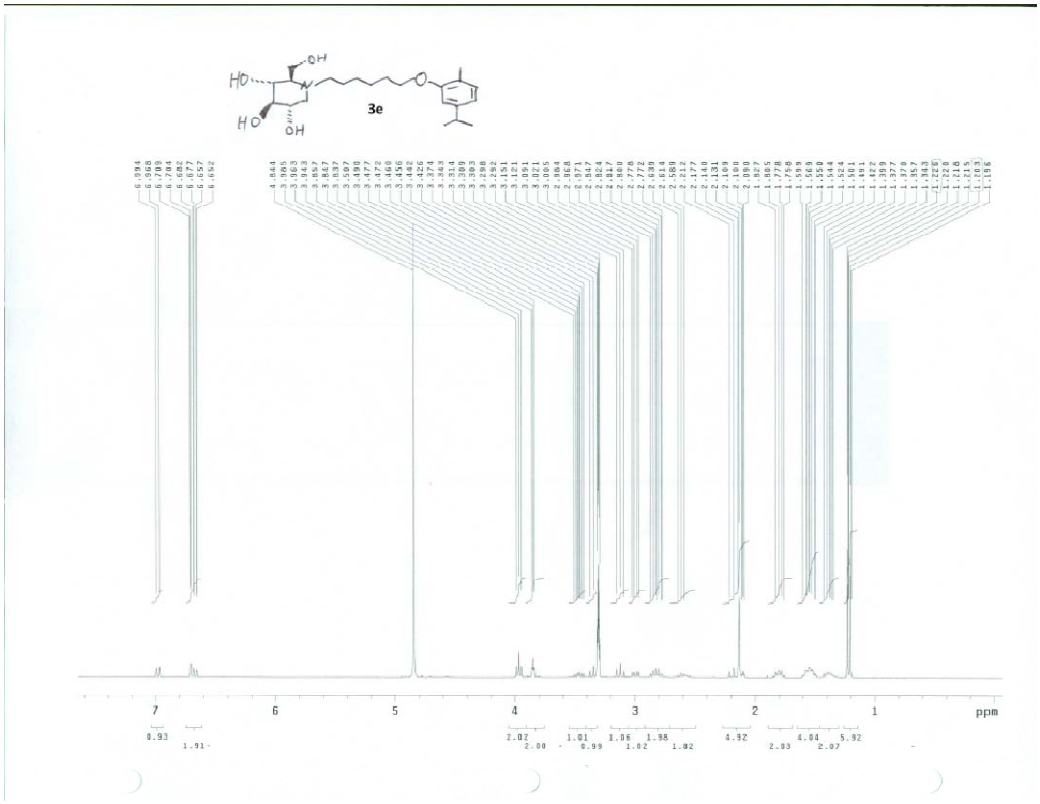
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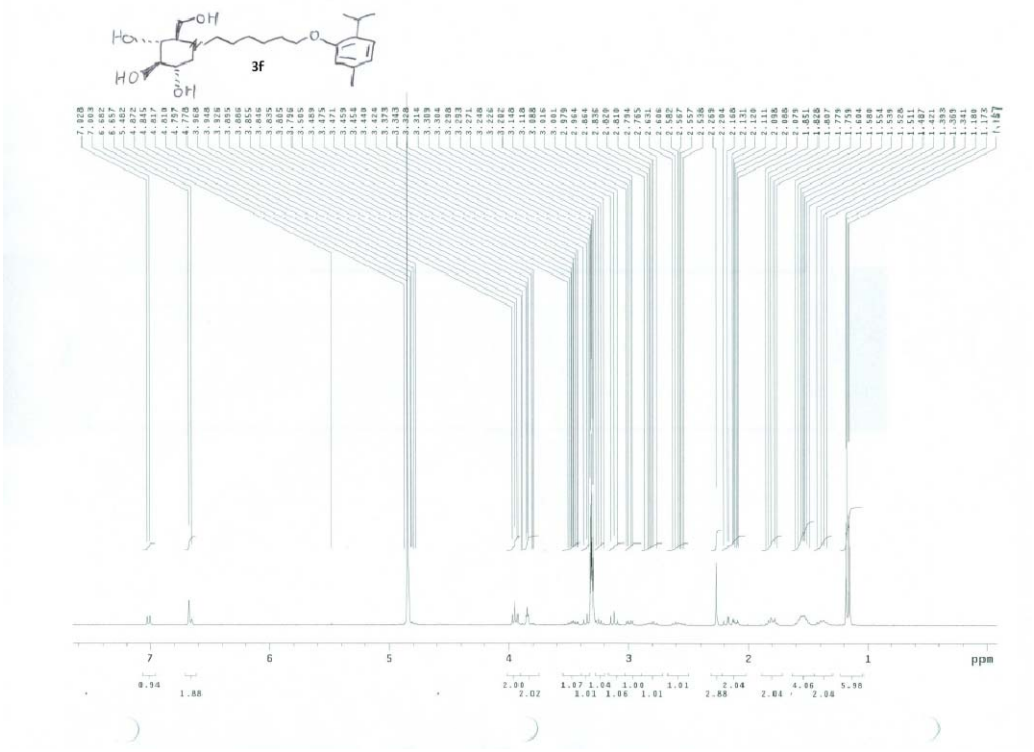
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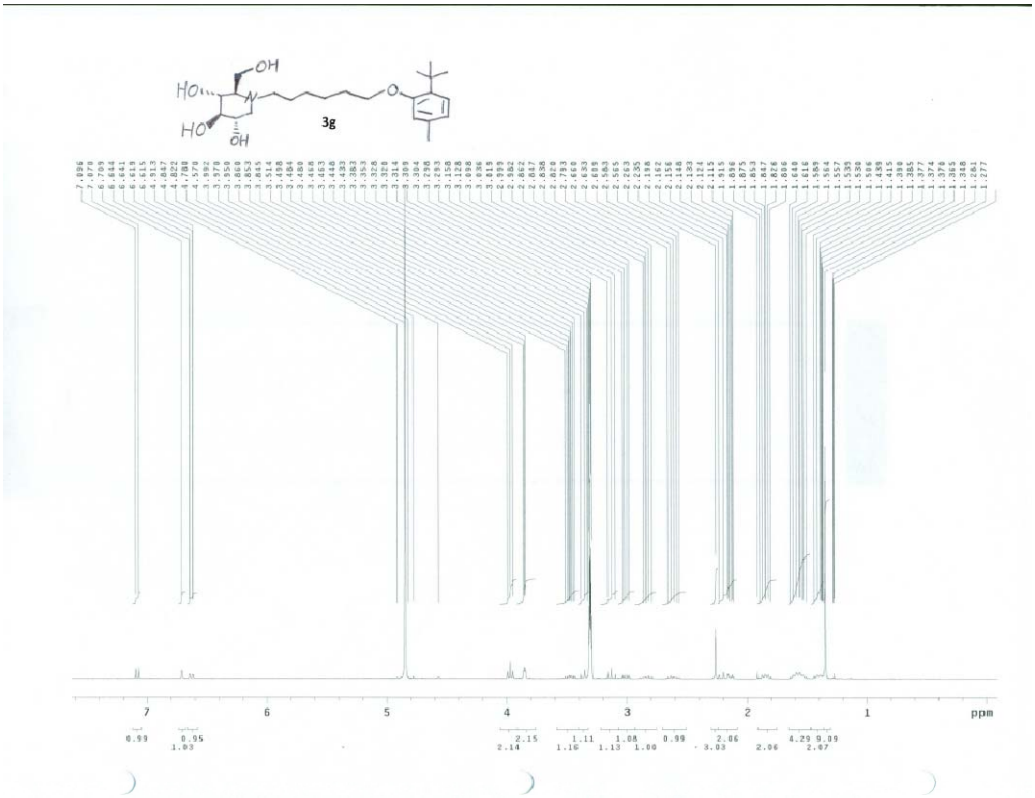
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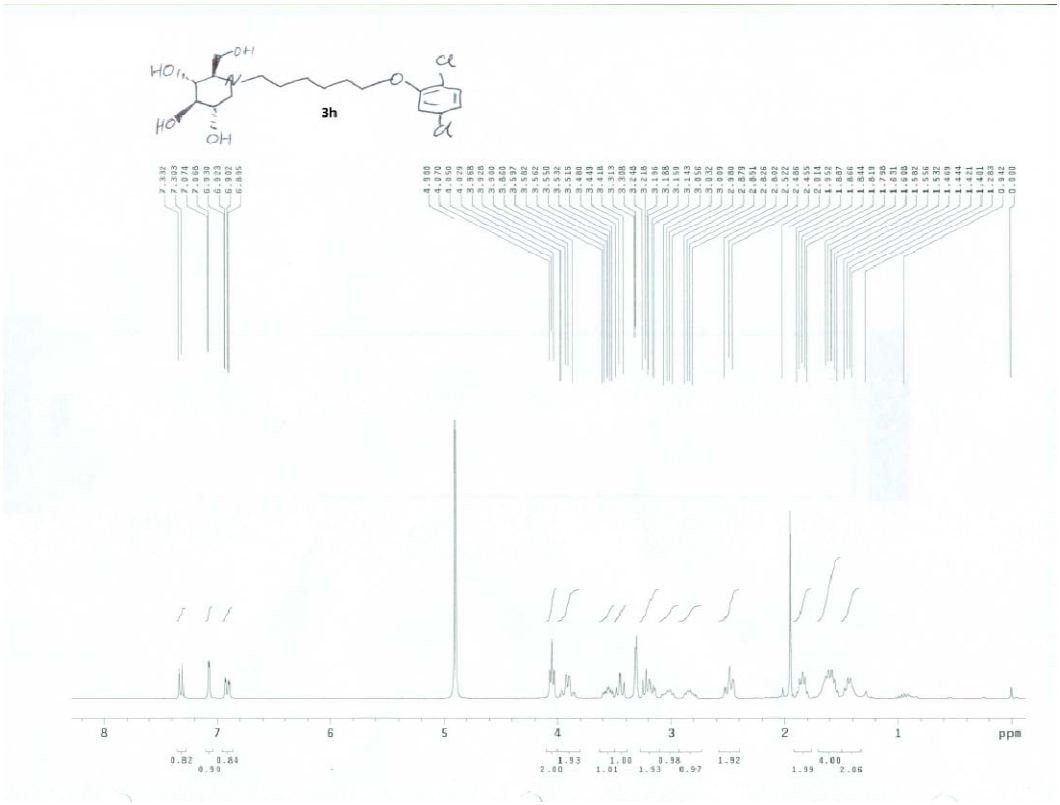
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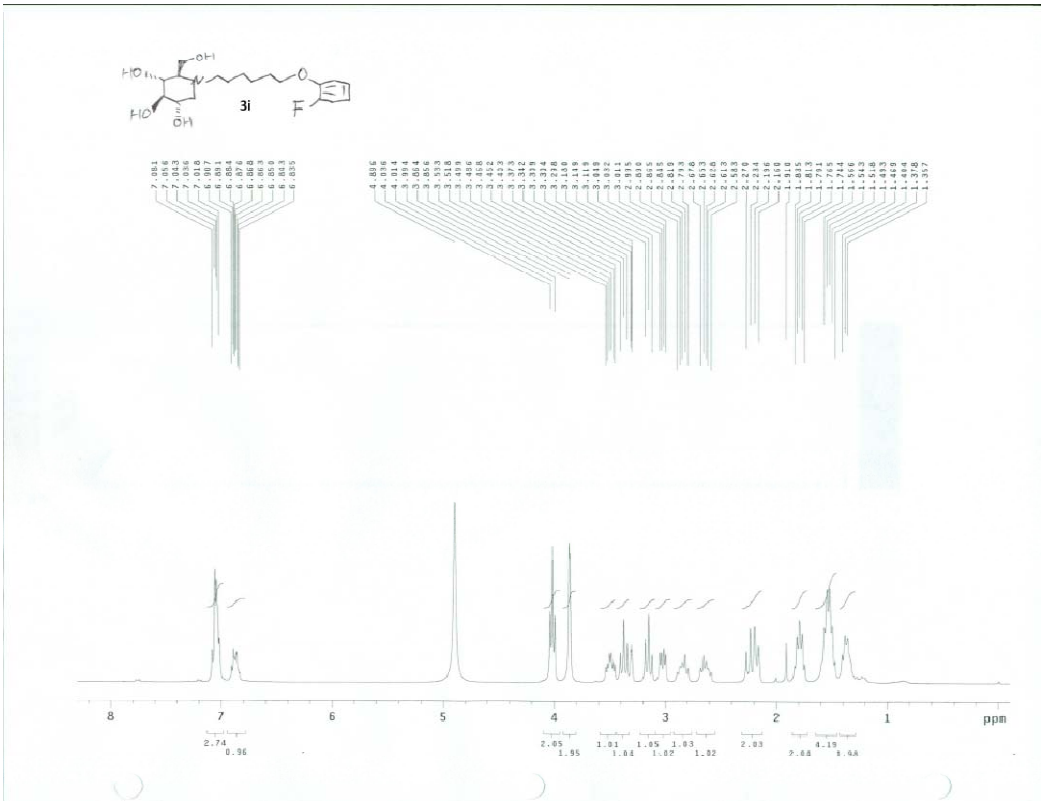
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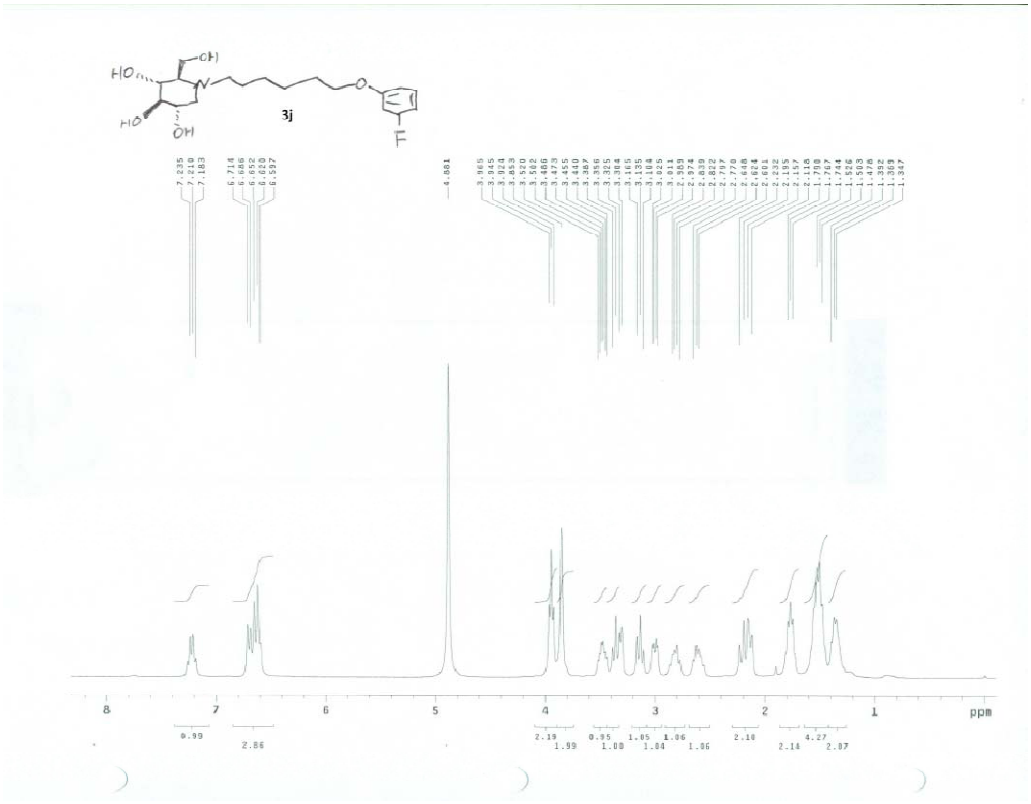
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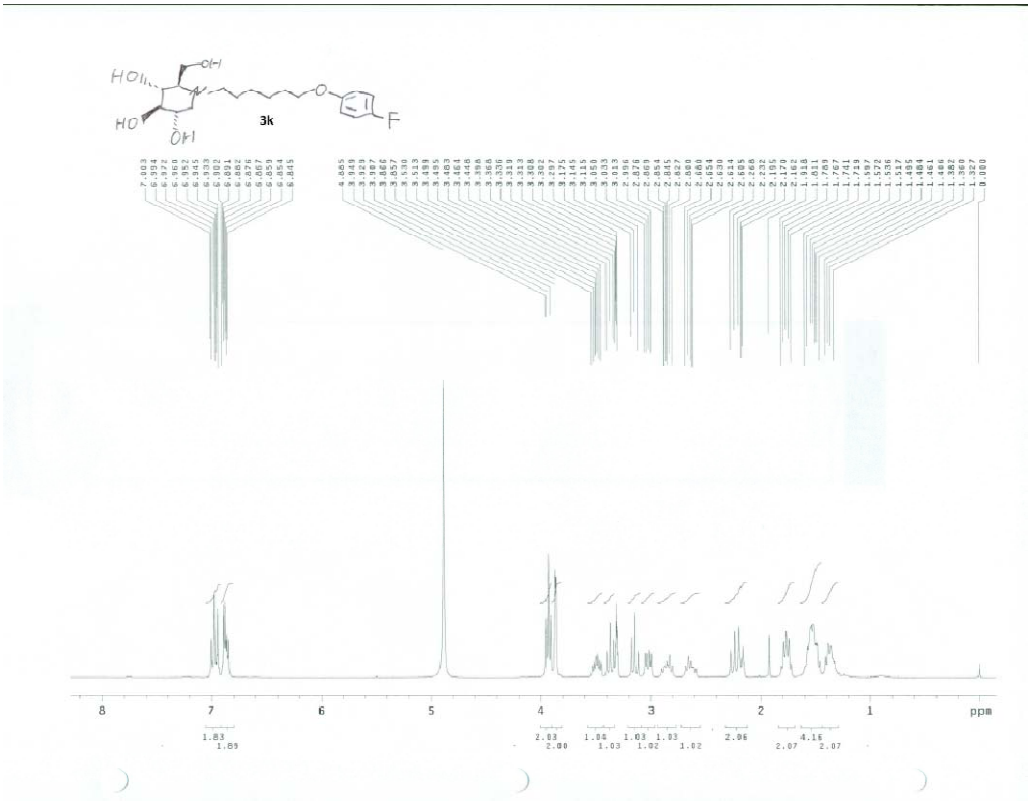
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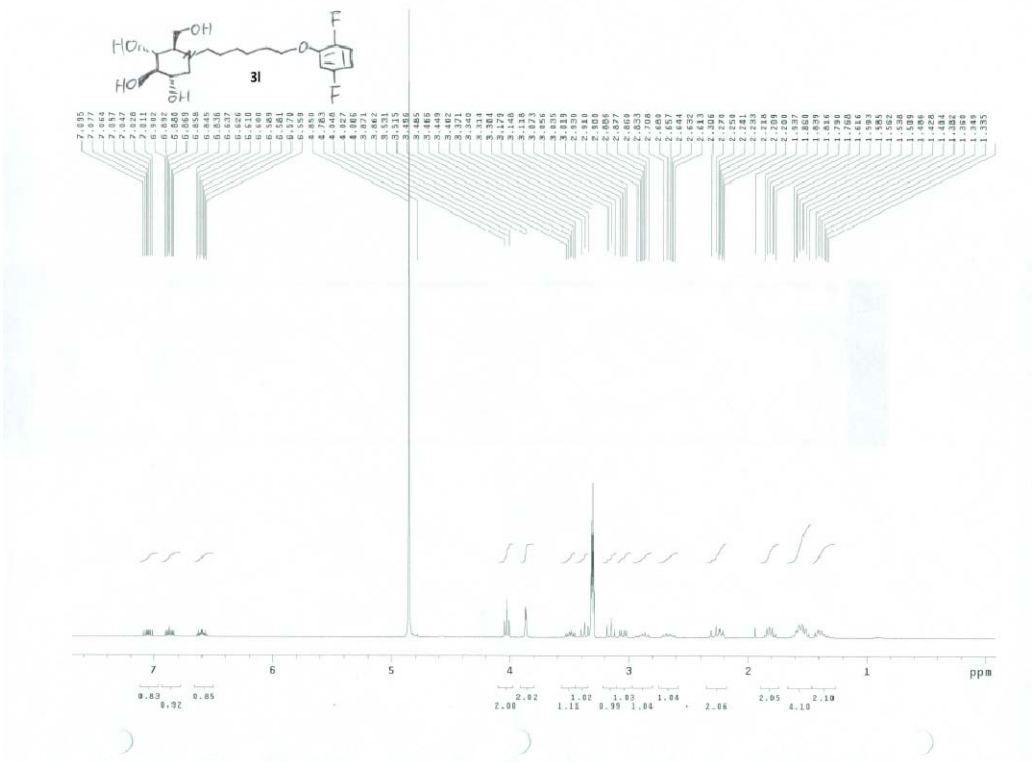
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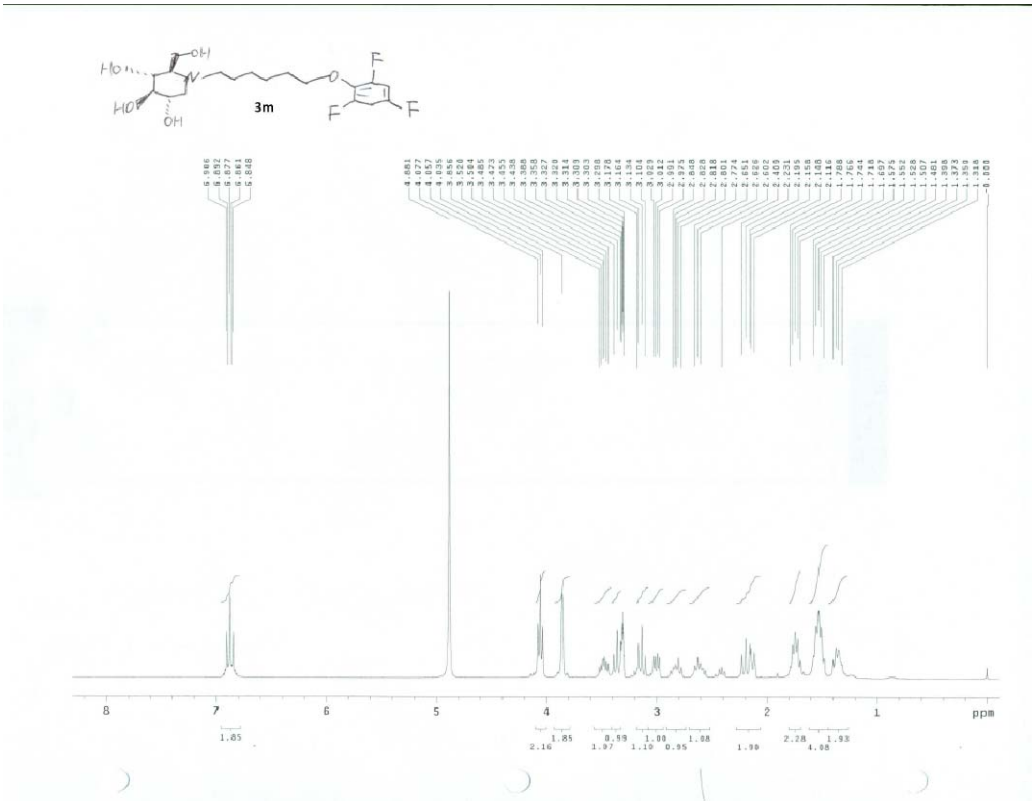
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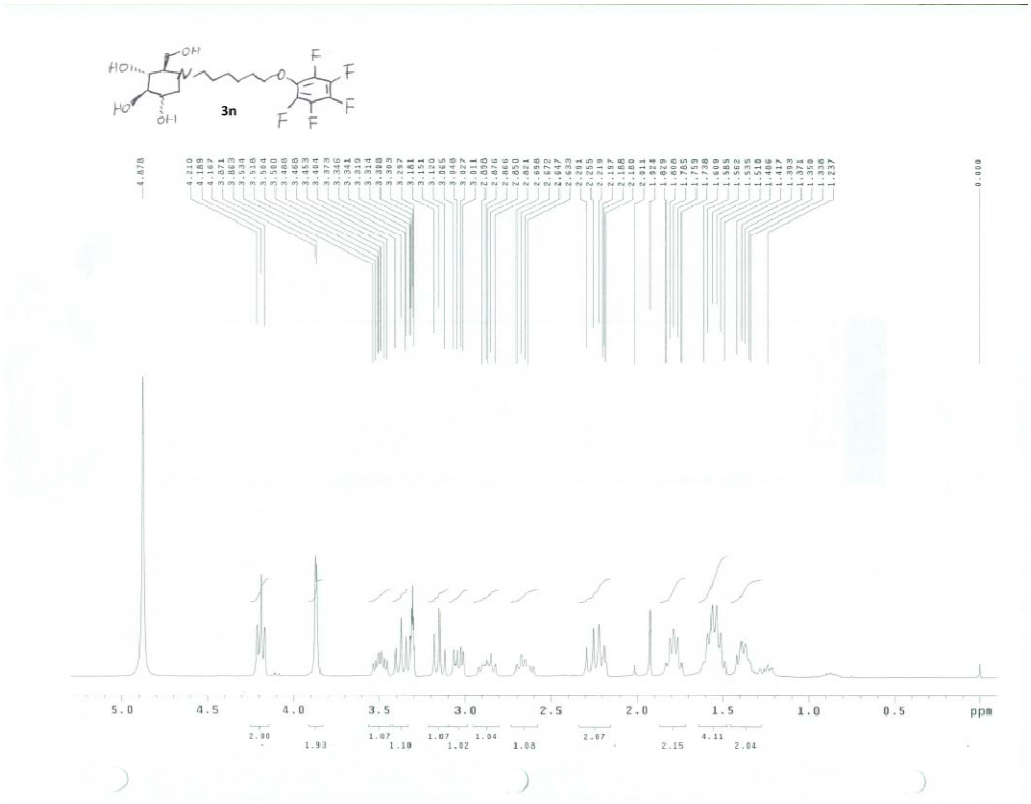
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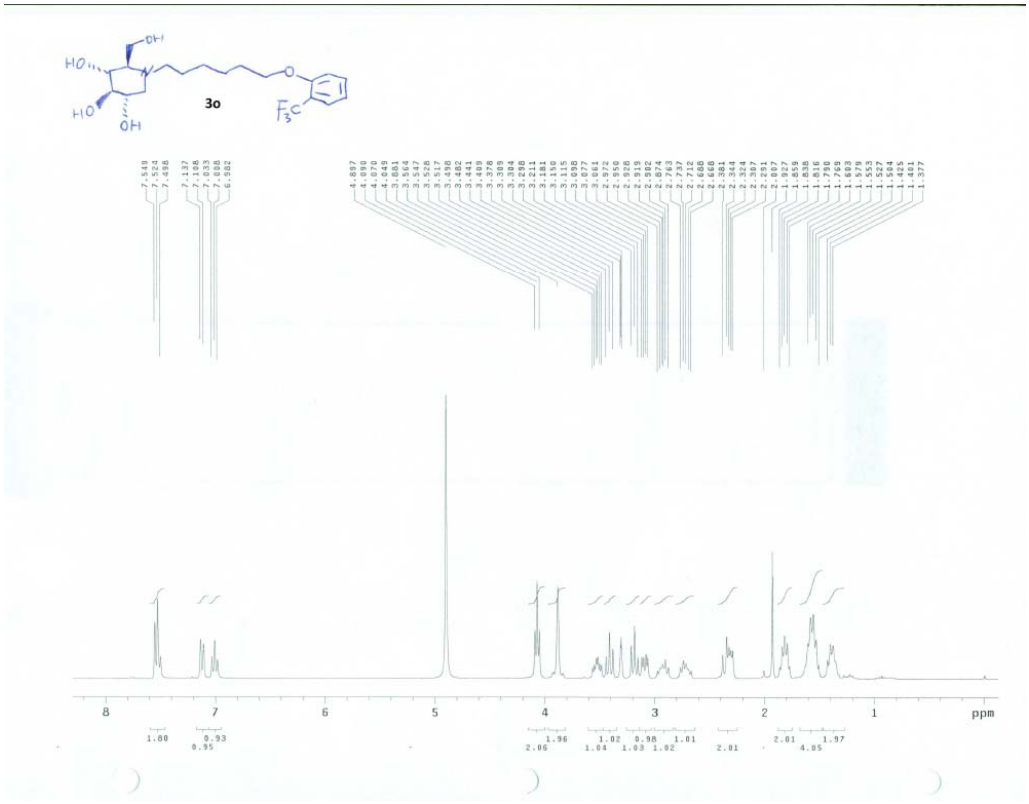
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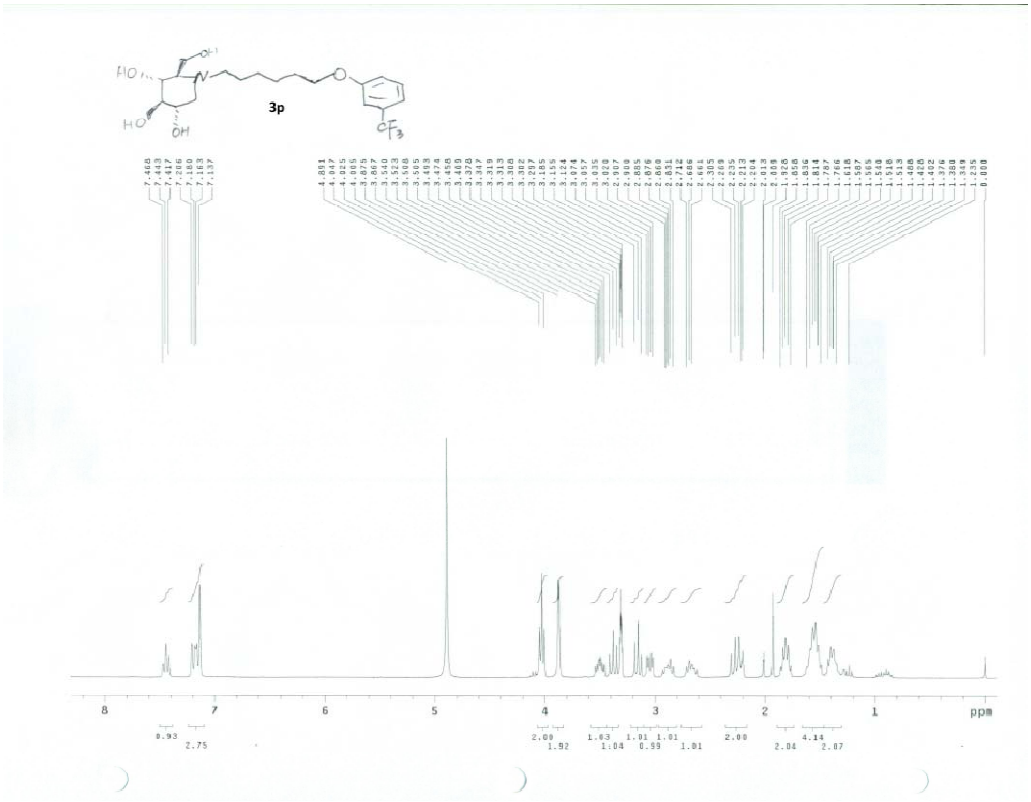
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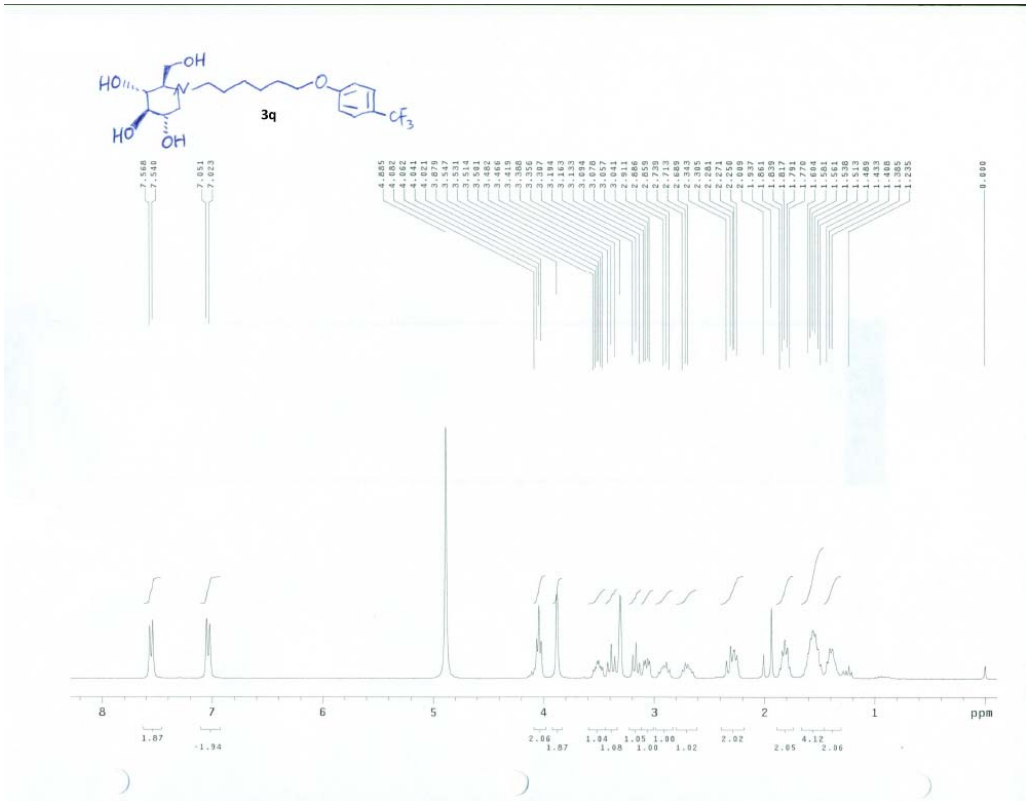
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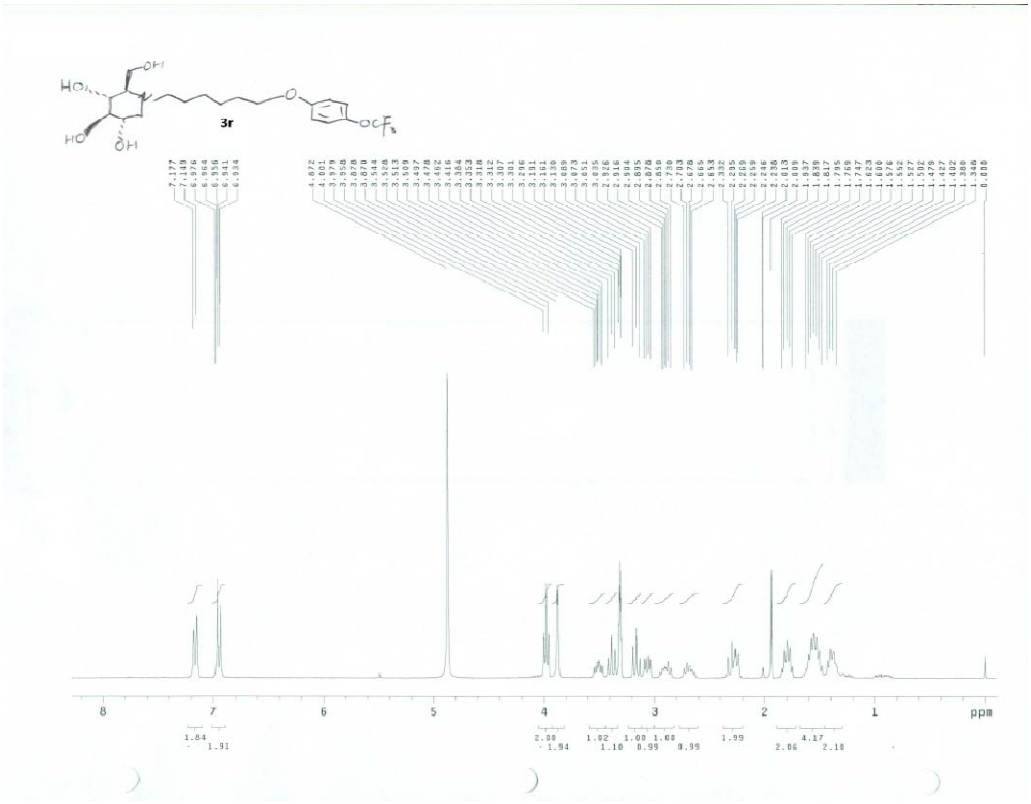
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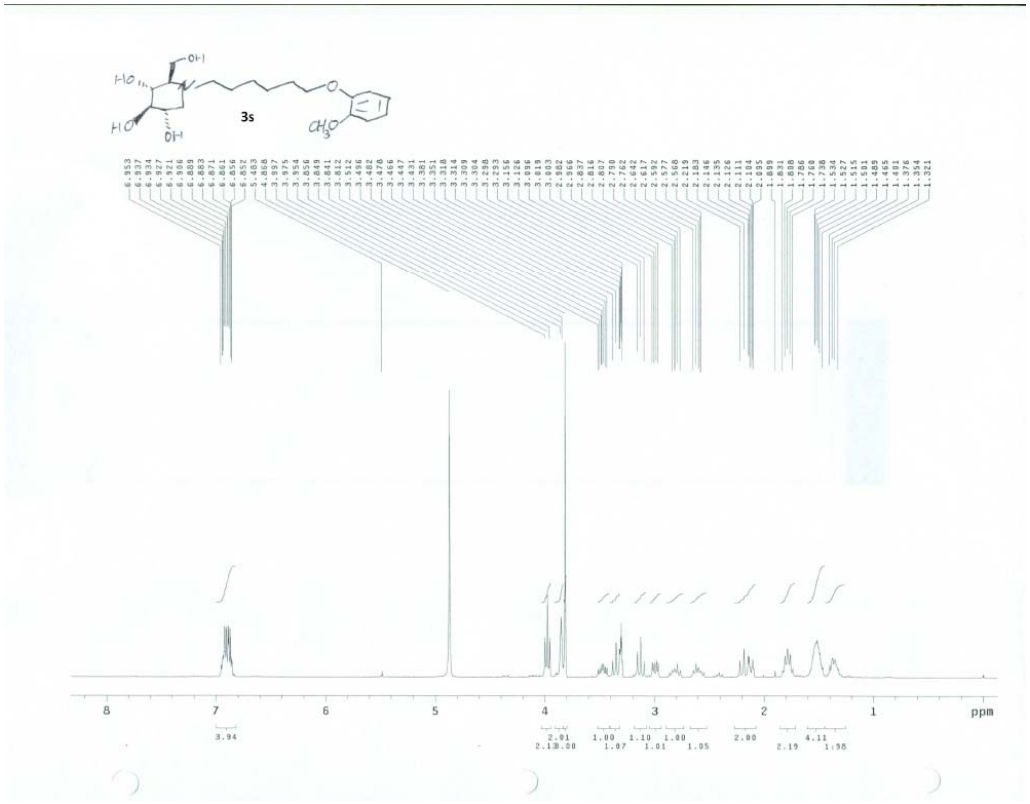
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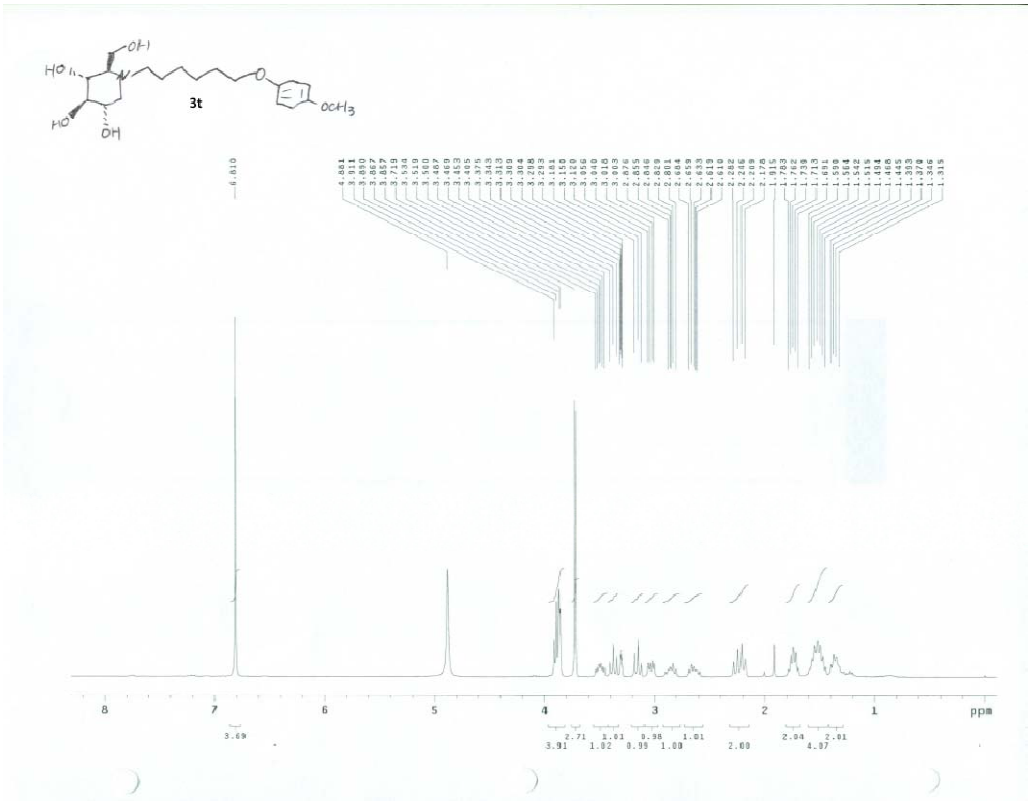
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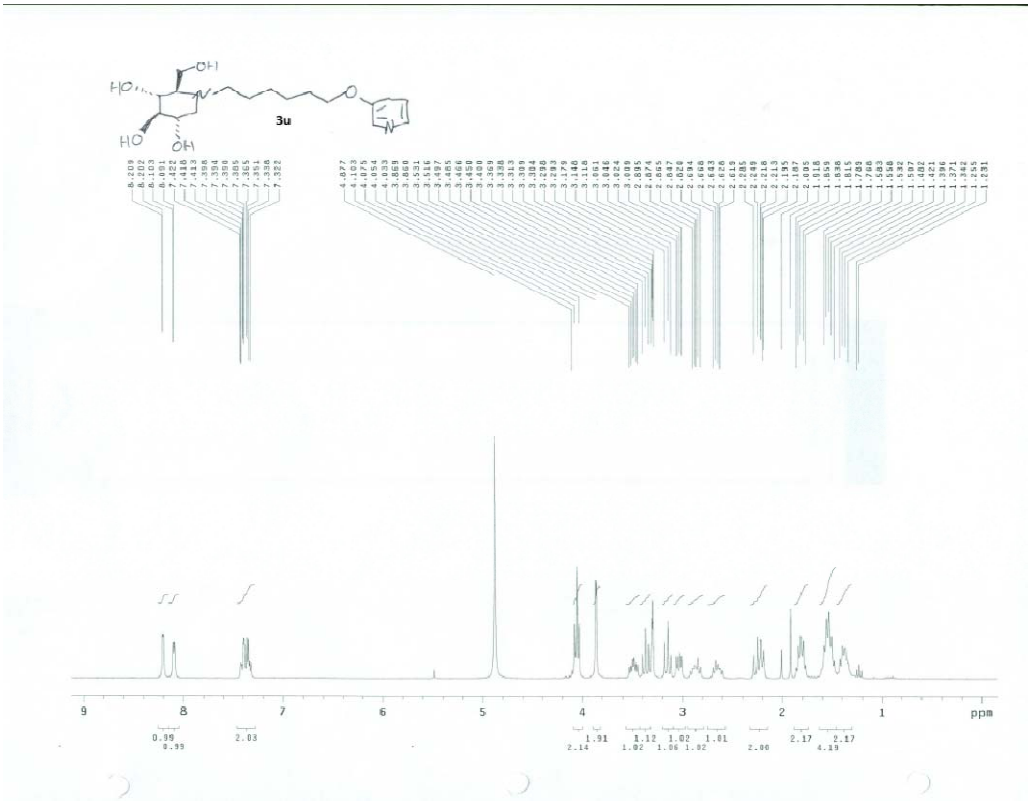
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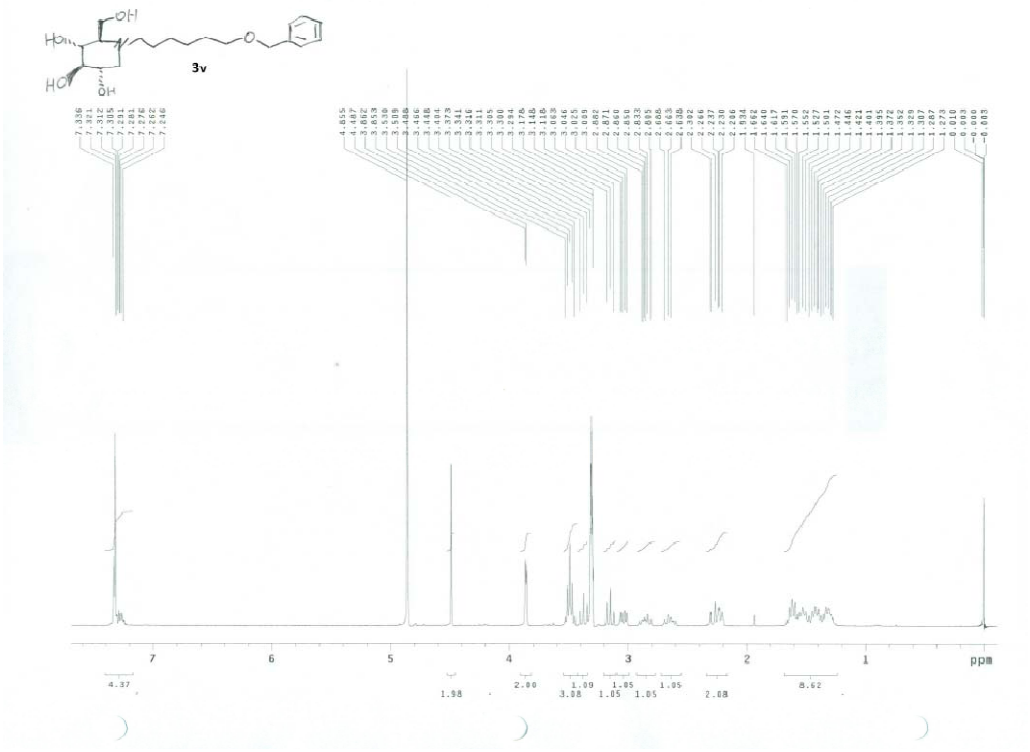
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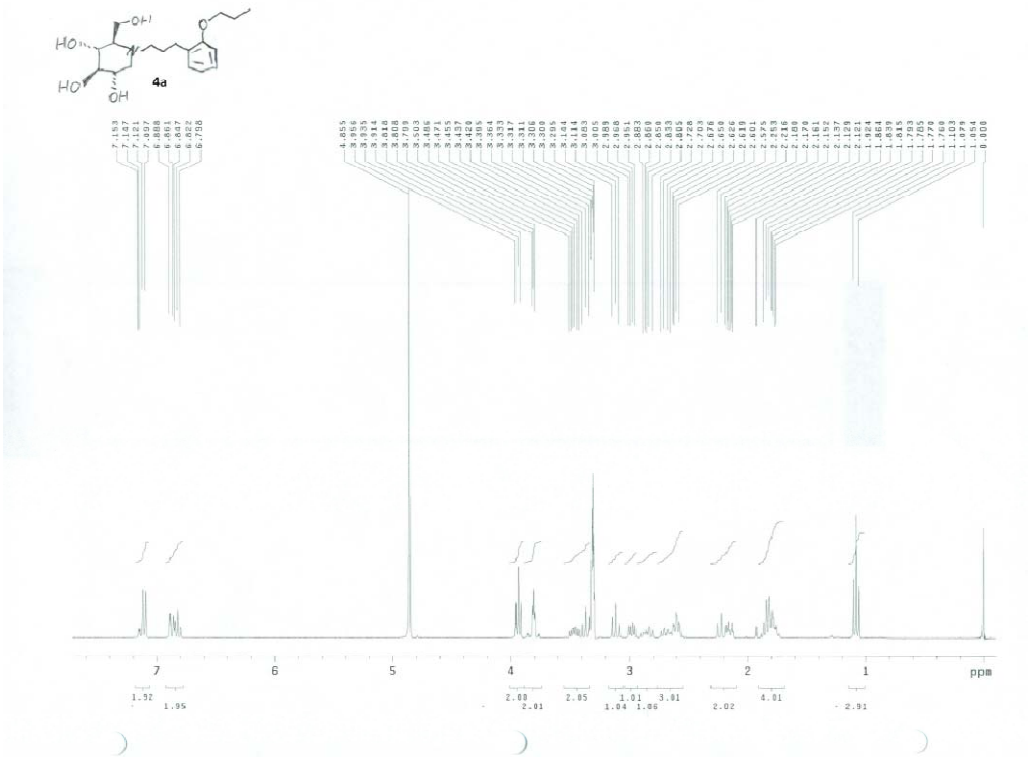
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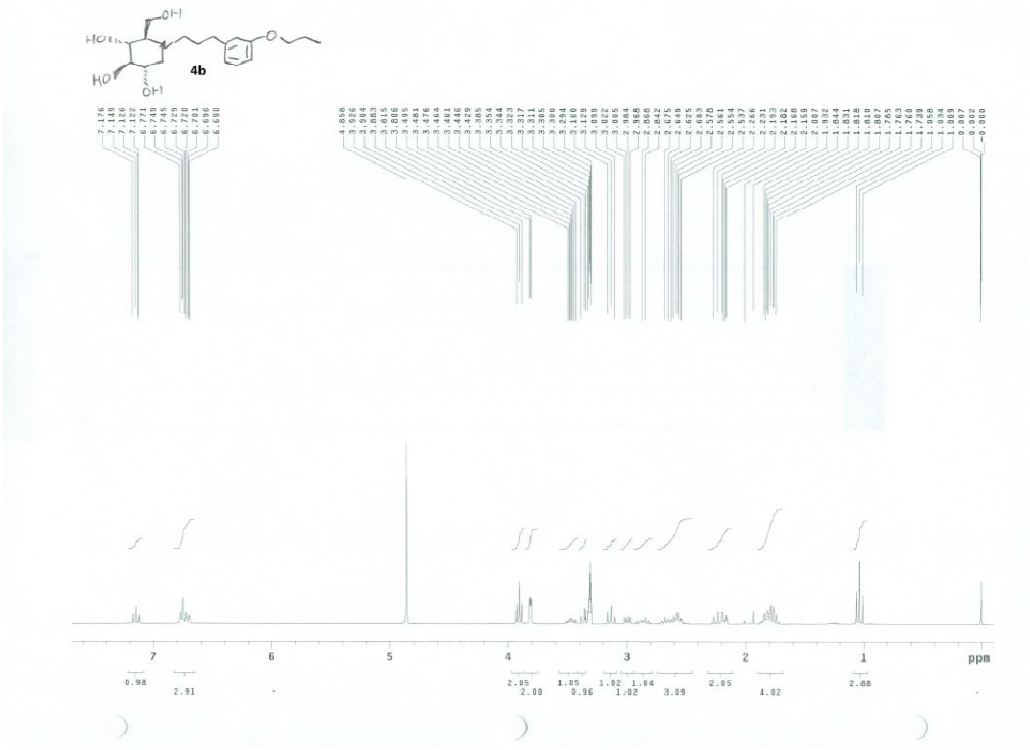
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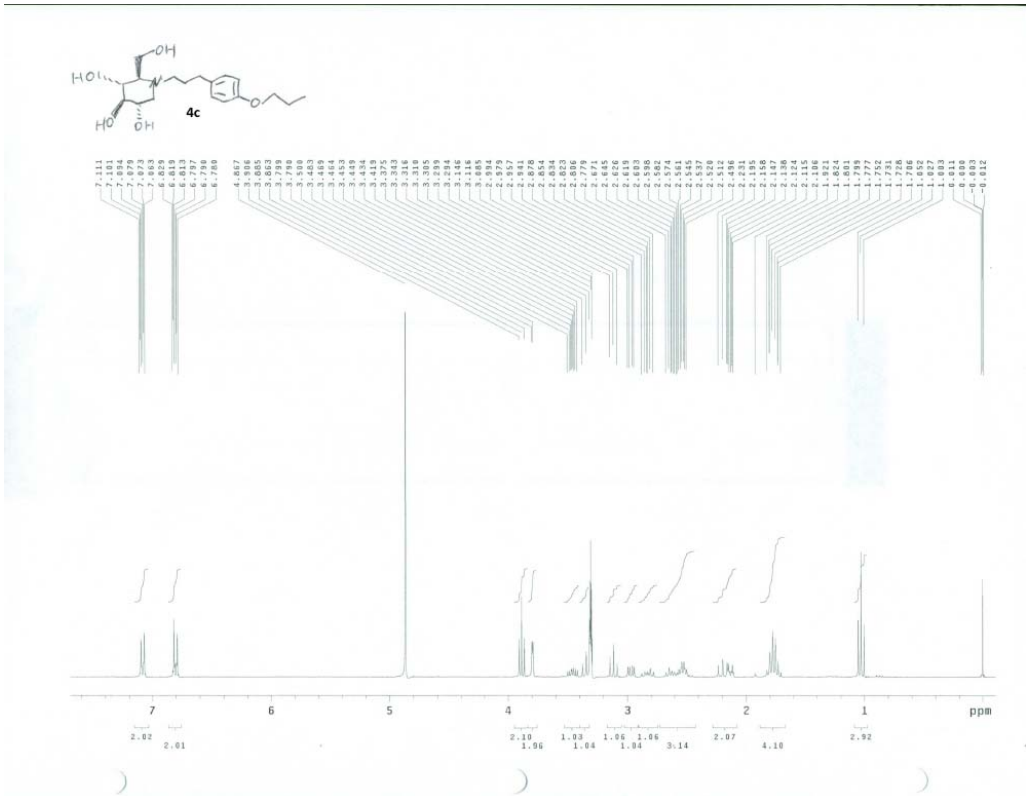
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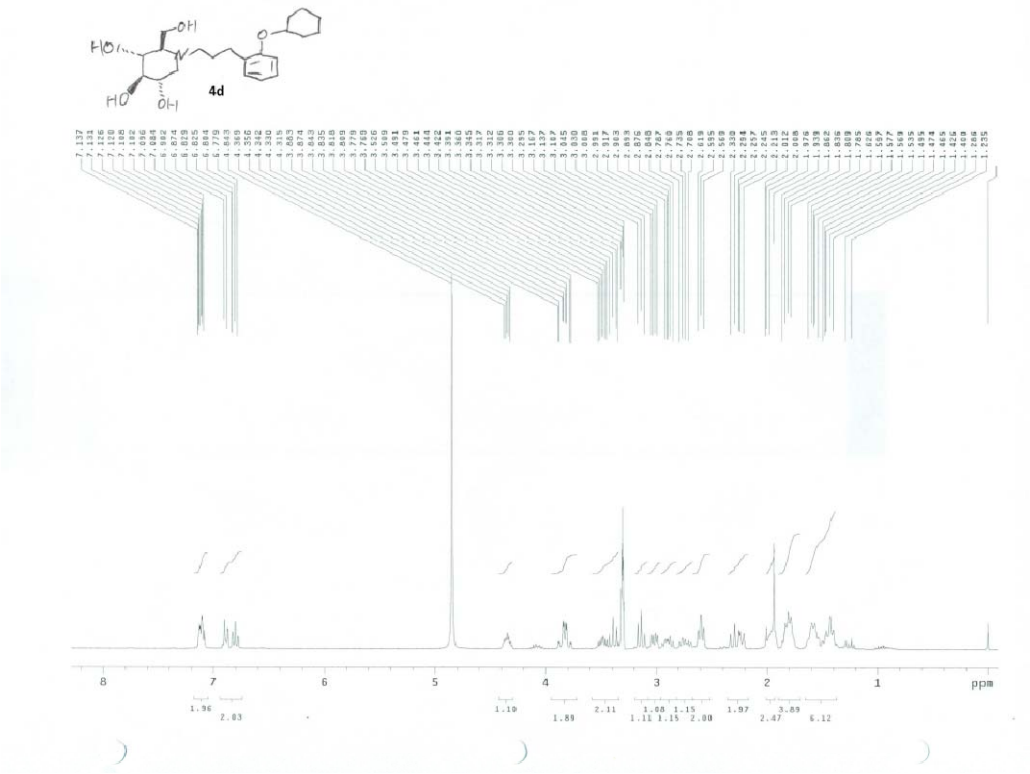
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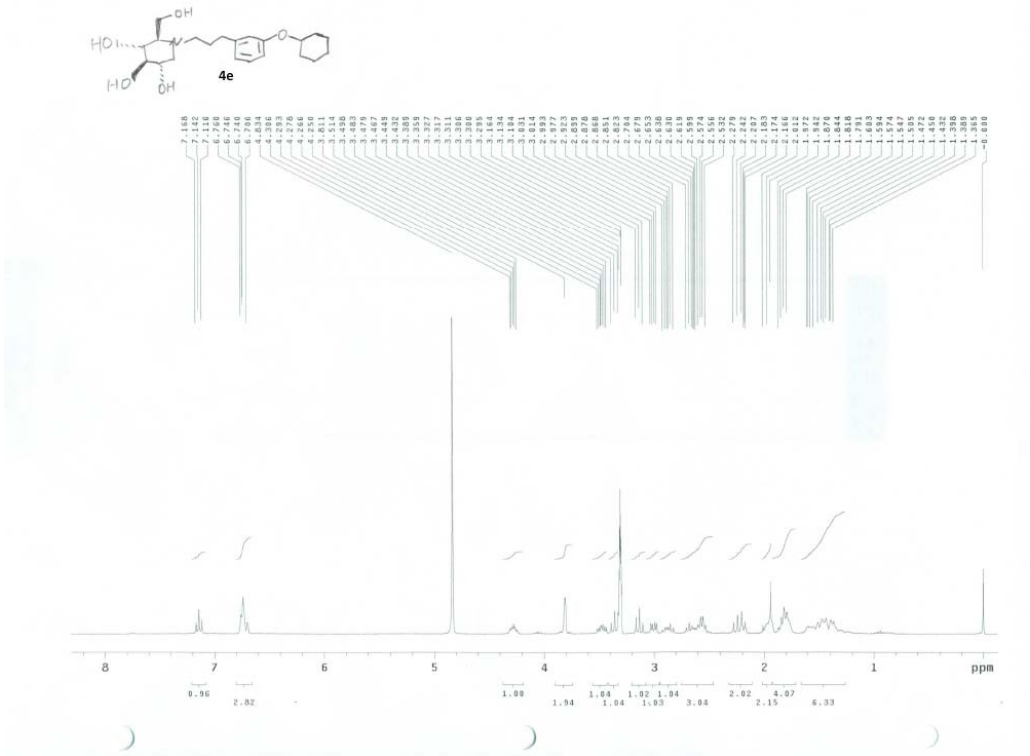
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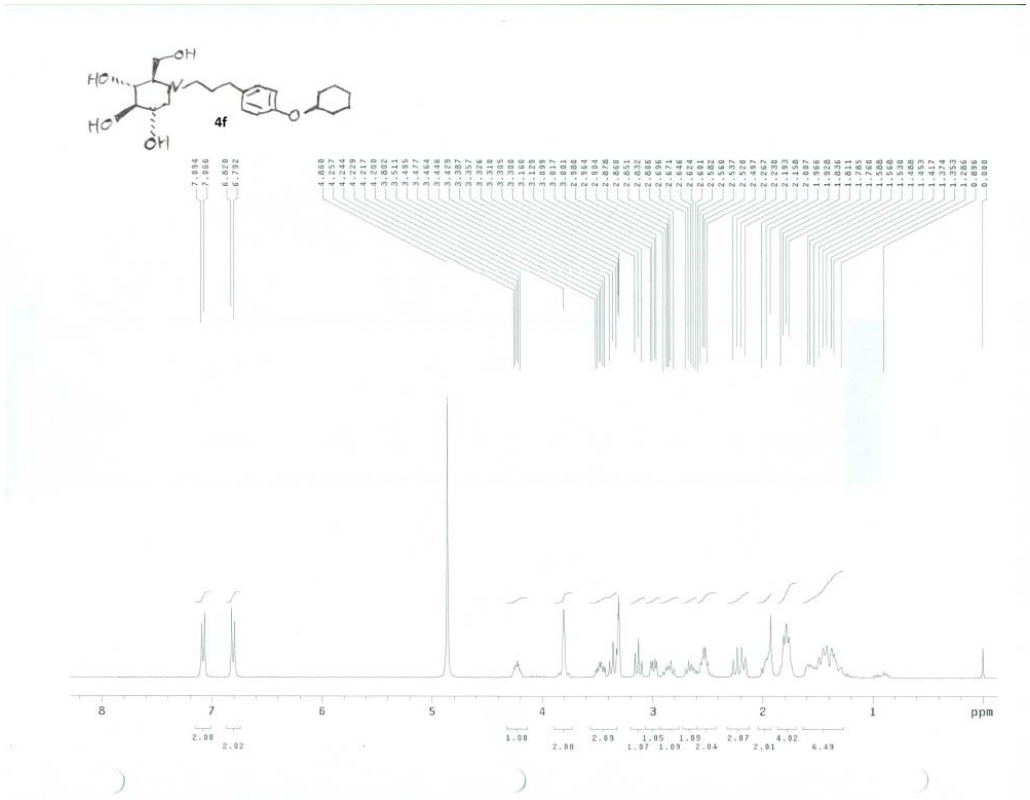
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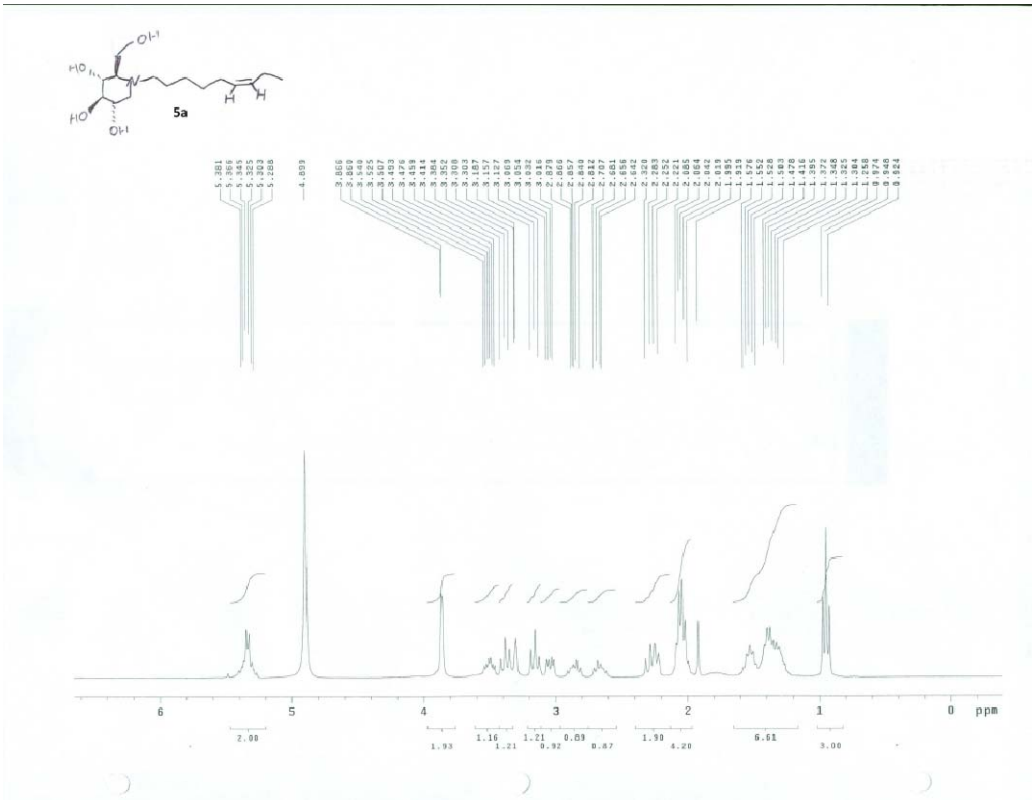
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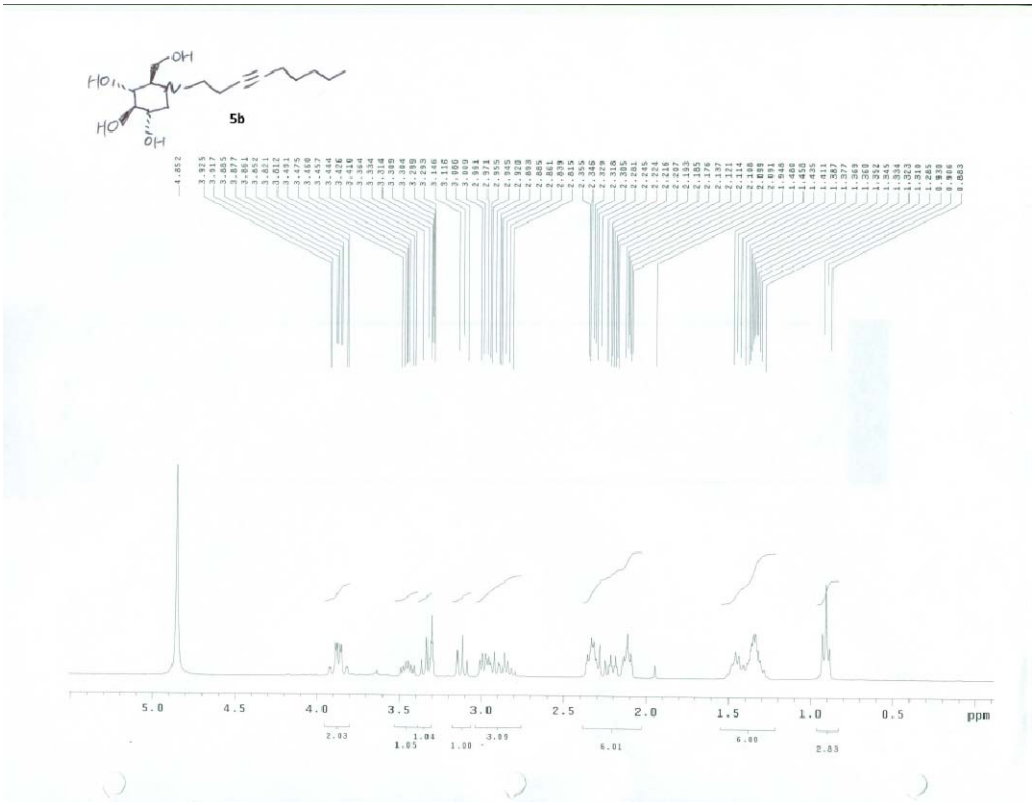
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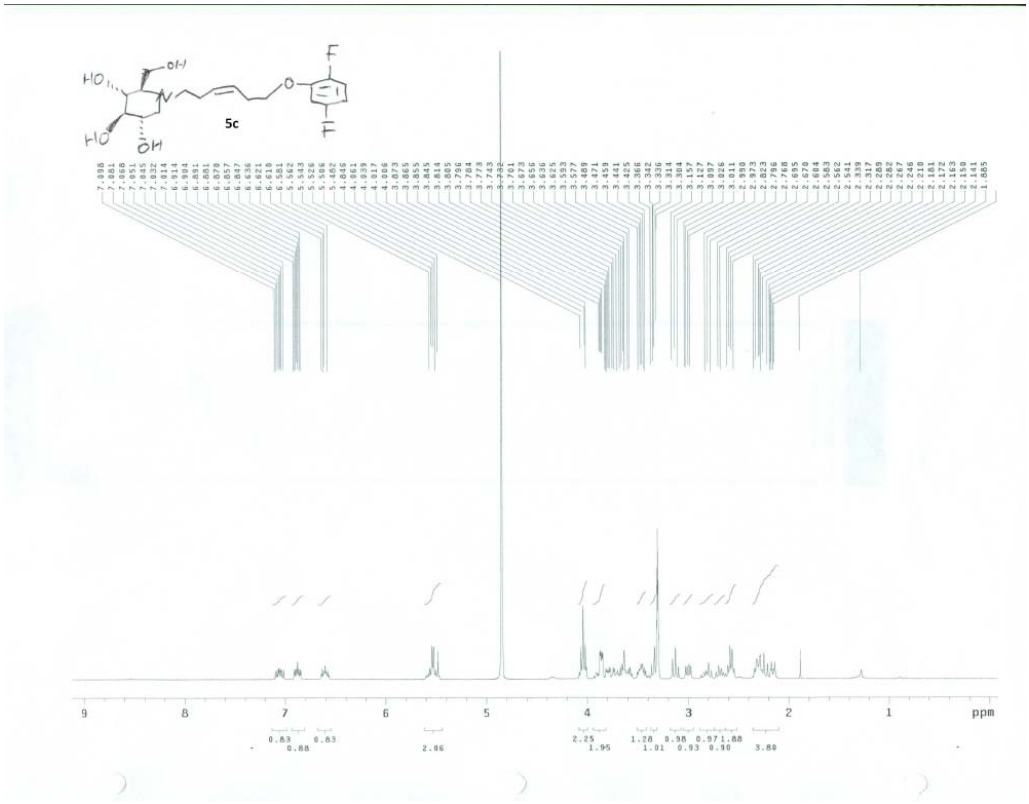
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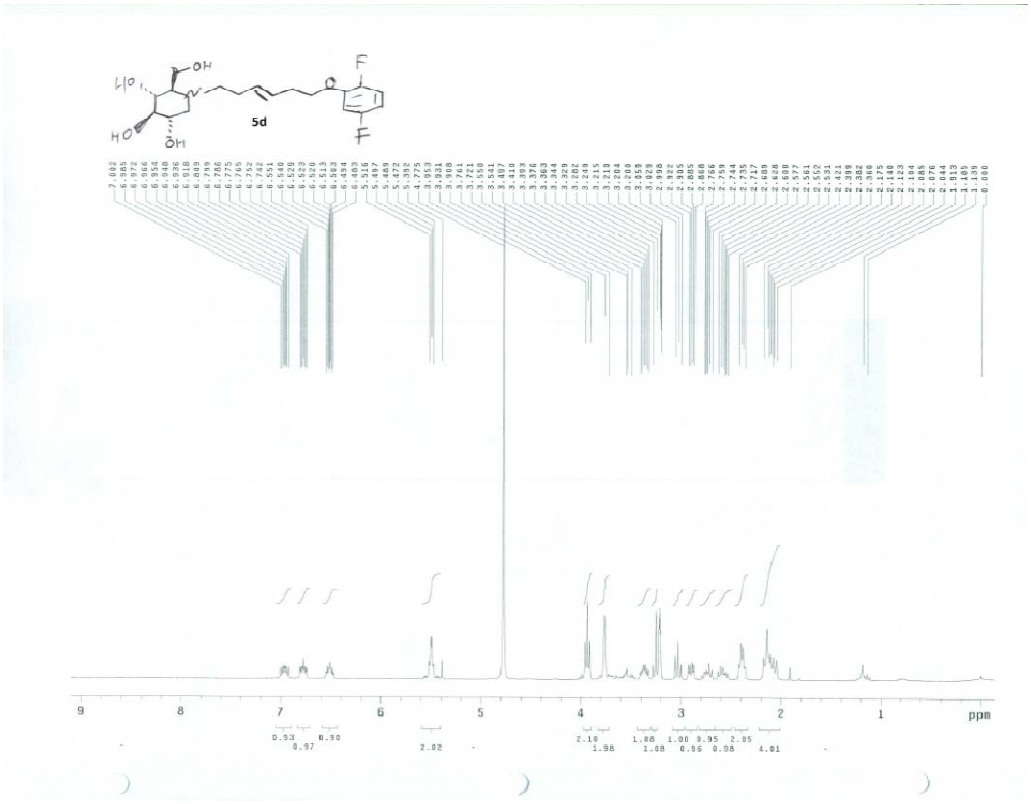
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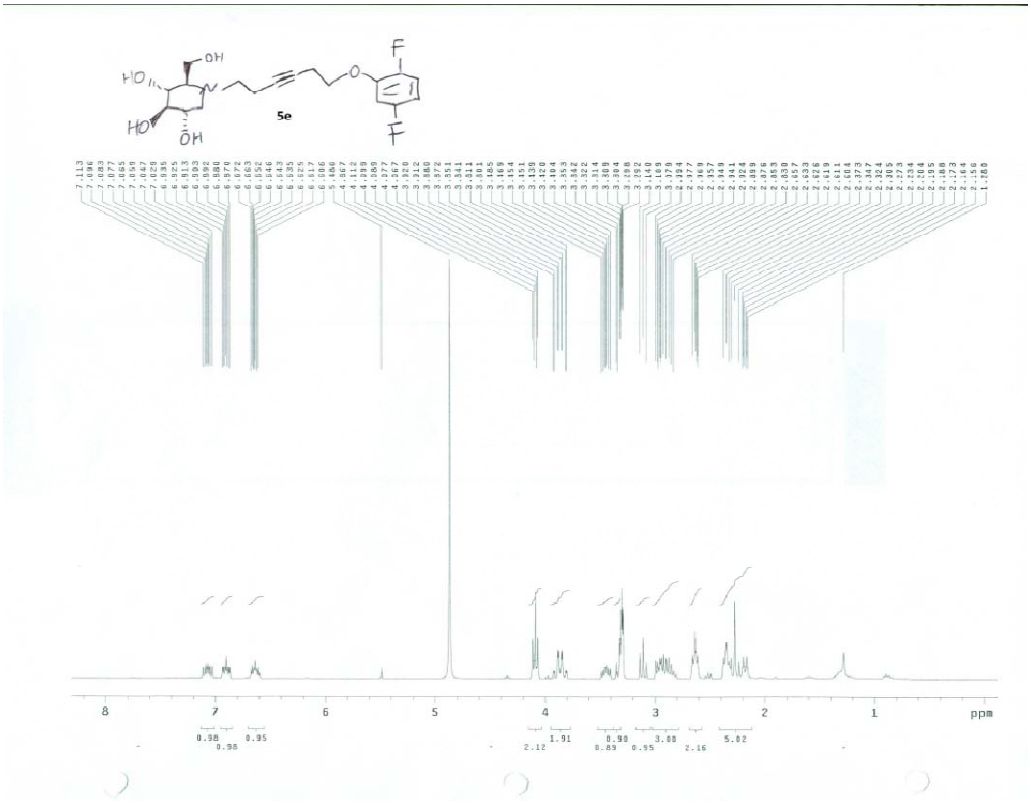
5e
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5
4
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2
1
ppm

3. X-ray Structure and Data of 3l

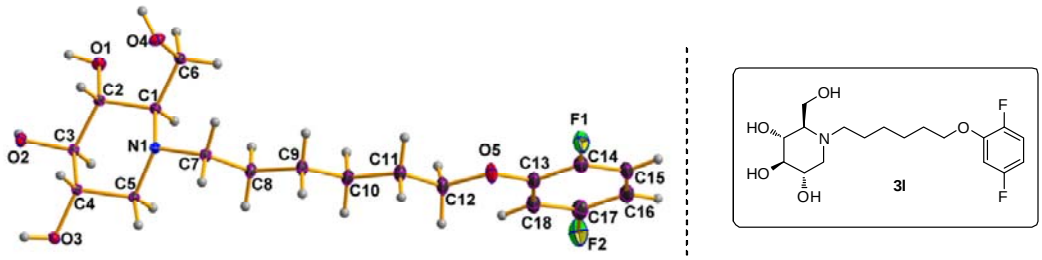

Table 1. Crystal data and structure refinement for 11mxu1h.

Identification code	11mxu1h
Empirical formula	C18 H27 F2 N O5
Formula weight	375.41
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, C2
Unit cell dimensions	a = 13.6384(5) A alpha = 90 deg. b = 7.1514(3) A beta = 101.0480(10) deg. c = 19.5985(8) A gamma = 90 deg.
Volume	1876.09(13) A^3
Z, Calculated density	4, 1.329 Mg/m^3
Absorption coefficient	0.109 mm^-1
F(000)	800
Crystal size	0.56 x 0.54 x 0.24 mm
Theta range for data collection	2.12 to 28.74 deg.
Limiting indices	-18<=h<=18, -9<=k<=9, -26<=l<=26
Reflections collected / unique	17793 / 2611 [R(int) = 0.0218]
Completeness to theta = 28.74	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9744 and 0.9417
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	2611 / 5 / 247
Goodness-of-fit on F^2	1.061
Final R indices [I>2sigma(I)]	R1 = 0.0263, wR2 = 0.0719
R indices (all data)	R1 = 0.0276, wR2 = 0.0729
Largest diff. peak and hole	0.253 and -0.150 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 11mxu1h.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
F(1)	4099(1)	16693(1)	5646(1)	29(1)
F(2)	3961(1)	10318(2)	7119(1)	35(1)
O(1)	5524(1)	4168(1)	1028(1)	13(1)
O(2)	3929(1)	2168(1)	191(1)	12(1)
O(3)	1927(1)	3080(1)	404(1)	12(1)
O(4)	5126(1)	9063(1)	759(1)	14(1)
O(5)	3661(1)	13524(2)	4950(1)	22(1)
N(1)	3383(1)	7254(2)	1083(1)	10(1)
C(1)	4400(1)	6484(2)	1319(1)	10(1)
C(2)	4562(1)	4981(2)	798(1)	10(1)
C(3)	3757(1)	3465(2)	710(1)	10(1)
C(4)	2740(1)	4383(2)	497(1)	9(1)
C(5)	2625(1)	5778(2)	1065(1)	10(1)
C(6)	5204(1)	7999(2)	1386(1)	12(1)
C(7)	3165(1)	8907(2)	1482(1)	11(1)
C(8)	3255(1)	8636(2)	2268(1)	14(1)
C(9)	3190(1)	10502(2)	2636(1)	16(1)
C(10)	3386(1)	10277(2)	3426(1)	17(1)
C(11)	3364(1)	12134(2)	3813(1)	19(1)
C(12)	3517(1)	11764(2)	4588(1)	20(1)
C(13)	3846(1)	13427(2)	5656(1)	19(1)
C(14)	4075(1)	15107(2)	6017(1)	20(1)
C(15)	4261(1)	15191(2)	6734(1)	22(1)
C(16)	4228(1)	13573(2)	7120(1)	24(1)
C(17)	4004(1)	11928(2)	6760(1)	23(1)
C(18)	3813(1)	11802(2)	6038(1)	21(1)

Table 3. Bond lengths [A] and angles [deg] for 11mxu1h.

F(1)-C(14)	1.3500(19)
F(2)-C(17)	1.3558(19)
O(1)-C(2)	1.4270(14)
O(1)-H(1O)	0.832(9)
O(2)-C(3)	1.4291(14)
O(2)-H(2O)	0.833(9)
O(3)-C(4)	1.4329(14)
O(3)-H(3O)	0.833(9)
O(4)-C(6)	1.4325(15)
O(4)-H(4O)	0.843(9)
O(5)-C(13)	1.3583(17)
O(5)-C(12)	1.4400(17)
N(1)-C(5)	1.4728(15)
N(1)-C(7)	1.4789(15)
N(1)-C(1)	1.4813(15)
C(1)-C(2)	1.5273(16)
C(1)-C(6)	1.5293(17)
C(1)-H(1)	0.9500
C(2)-C(3)	1.5286(17)
C(2)-H(2)	0.9500
C(3)-C(4)	1.5189(16)
C(3)-H(3)	0.9500
C(4)-C(5)	1.5255(16)
C(4)-H(4)	0.9500
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(8)	1.5337(17)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.5280(18)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.5271(18)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.533(2)
C(10)-H(10A)	0.9900

C(10)-H(10B)	0.9900
C(11)-C(12)	1.5166(19)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(18)	1.389(2)
C(13)-C(14)	1.399(2)
C(14)-C(15)	1.381(2)
C(15)-C(16)	1.388(2)
C(15)-H(15)	0.9500
C(16)-C(17)	1.376(2)
C(16)-H(16)	0.9500
C(17)-C(18)	1.392(2)
C(18)-H(18)	0.9500

C(2)-O(1)-H(1O)	109.5(13)
C(3)-O(2)-H(2O)	108.9(13)
C(4)-O(3)-H(3O)	106.1(13)
C(6)-O(4)-H(4O)	107.2(14)
C(13)-O(5)-C(12)	115.98(12)
C(5)-N(1)-C(7)	111.96(9)
C(5)-N(1)-C(1)	110.59(10)
C(7)-N(1)-C(1)	113.80(9)
N(1)-C(1)-C(2)	107.45(9)
N(1)-C(1)-C(6)	112.10(10)
C(2)-C(1)-C(6)	111.30(10)
N(1)-C(1)-H(1)	108.6
C(2)-C(1)-H(1)	108.6
C(6)-C(1)-H(1)	108.6
O(1)-C(2)-C(1)	108.47(9)
O(1)-C(2)-C(3)	110.11(10)
C(1)-C(2)-C(3)	112.45(10)
O(1)-C(2)-H(2)	108.6
C(1)-C(2)-H(2)	108.6
C(3)-C(2)-H(2)	108.6
O(2)-C(3)-C(4)	110.55(10)
O(2)-C(3)-C(2)	109.16(9)
C(4)-C(3)-C(2)	108.82(10)
O(2)-C(3)-H(3)	109.4
C(4)-C(3)-H(3)	109.4
C(2)-C(3)-H(3)	109.4
O(3)-C(4)-C(3)	113.43(10)

O(3)-C(4)-C(5)	109.43(9)
C(3)-C(4)-C(5)	107.34(9)
O(3)-C(4)-H(4)	108.8
C(3)-C(4)-H(4)	108.8
C(5)-C(4)-H(4)	108.8
N(1)-C(5)-C(4)	108.46(9)
N(1)-C(5)-H(5A)	110.0
C(4)-C(5)-H(5A)	110.0
N(1)-C(5)-H(5B)	110.0
C(4)-C(5)-H(5B)	110.0
H(5A)-C(5)-H(5B)	108.4
O(4)-C(6)-C(1)	111.64(10)
O(4)-C(6)-H(6A)	109.3
C(1)-C(6)-H(6A)	109.3
O(4)-C(6)-H(6B)	109.3
C(1)-C(6)-H(6B)	109.3
H(6A)-C(6)-H(6B)	108.0
N(1)-C(7)-C(8)	116.42(10)
N(1)-C(7)-H(7A)	108.2
C(8)-C(7)-H(7A)	108.2
N(1)-C(7)-H(7B)	108.2
C(8)-C(7)-H(7B)	108.2
H(7A)-C(7)-H(7B)	107.3
C(9)-C(8)-C(7)	111.29(11)
C(9)-C(8)-H(8A)	109.4
C(7)-C(8)-H(8A)	109.4
C(9)-C(8)-H(8B)	109.4
C(7)-C(8)-H(8B)	109.4
H(8A)-C(8)-H(8B)	108.0
C(10)-C(9)-C(8)	111.81(12)
C(10)-C(9)-H(9A)	109.3
C(8)-C(9)-H(9A)	109.3
C(10)-C(9)-H(9B)	109.3
C(8)-C(9)-H(9B)	109.3
H(9A)-C(9)-H(9B)	107.9
C(9)-C(10)-C(11)	113.22(12)
C(9)-C(10)-H(10A)	108.9
C(11)-C(10)-H(10A)	108.9
C(9)-C(10)-H(10B)	108.9
C(11)-C(10)-H(10B)	108.9
H(10A)-C(10)-H(10B)	107.7
C(12)-C(11)-C(10)	109.46(12)
C(12)-C(11)-H(11A)	109.8

C(10)-C(11)-H(11A)	109.8
C(12)-C(11)-H(11B)	109.8
C(10)-C(11)-H(11B)	109.8
H(11A)-C(11)-H(11B)	108.2
O(5)-C(12)-C(11)	108.69(12)
O(5)-C(12)-H(12A)	110.0
C(11)-C(12)-H(12A)	110.0
O(5)-C(12)-H(12B)	110.0
C(11)-C(12)-H(12B)	110.0
H(12A)-C(12)-H(12B)	108.3
O(5)-C(13)-C(18)	124.98(13)
O(5)-C(13)-C(14)	116.83(14)
C(18)-C(13)-C(14)	118.18(13)
F(1)-C(14)-C(15)	119.47(14)
F(1)-C(14)-C(13)	118.36(12)
C(15)-C(14)-C(13)	122.16(15)
C(14)-C(15)-C(16)	120.00(15)
C(14)-C(15)-H(15)	120.0
C(16)-C(15)-H(15)	120.0
C(17)-C(16)-C(15)	117.42(13)
C(17)-C(16)-H(16)	121.3
C(15)-C(16)-H(16)	121.3
F(2)-C(17)-C(16)	119.20(13)
F(2)-C(17)-C(18)	117.01(14)
C(16)-C(17)-C(18)	123.79(15)
C(13)-C(18)-C(17)	118.44(14)
C(13)-C(18)-H(18)	120.8
C(17)-C(18)-H(18)	120.8

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for 11mxu1h.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
F(1)	40(1)	23(1)	24(1)	-4(1)	6(1)	-6(1)
F(2)	50(1)	30(1)	21(1)	5(1)	-1(1)	2(1)
O(1)	9(1)	14(1)	17(1)	-2(1)	1(1)	3(1)
O(2)	12(1)	9(1)	14(1)	-4(1)	3(1)	2(1)
O(3)	10(1)	11(1)	14(1)	-2(1)	2(1)	-2(1)
O(4)	12(1)	12(1)	18(1)	3(1)	7(1)	1(1)
O(5)	32(1)	21(1)	12(1)	-6(1)	3(1)	-2(1)
N(1)	9(1)	8(1)	11(1)	-1(1)	3(1)	0(1)
C(1)	9(1)	10(1)	9(1)	-1(1)	2(1)	0(1)
C(2)	7(1)	10(1)	11(1)	-1(1)	2(1)	1(1)
C(3)	11(1)	8(1)	11(1)	-1(1)	3(1)	0(1)
C(4)	9(1)	8(1)	12(1)	-1(1)	3(1)	-1(1)
C(5)	10(1)	10(1)	12(1)	-1(1)	3(1)	-1(1)
C(6)	11(1)	12(1)	13(1)	-1(1)	1(1)	-2(1)
C(7)	13(1)	9(1)	12(1)	-2(1)	4(1)	0(1)
C(8)	18(1)	14(1)	12(1)	-2(1)	5(1)	0(1)
C(9)	19(1)	15(1)	14(1)	-5(1)	5(1)	0(1)
C(10)	18(1)	20(1)	15(1)	-6(1)	4(1)	1(1)
C(11)	22(1)	22(1)	14(1)	-6(1)	4(1)	-1(1)
C(12)	23(1)	20(1)	15(1)	-7(1)	2(1)	-1(1)
C(13)	18(1)	24(1)	14(1)	-5(1)	2(1)	0(1)
C(14)	20(1)	23(1)	18(1)	-5(1)	4(1)	-2(1)
C(15)	19(1)	28(1)	19(1)	-10(1)	1(1)	-2(1)
C(16)	20(1)	35(1)	15(1)	-6(1)	0(1)	2(1)
C(17)	24(1)	26(1)	17(1)	1(1)	0(1)	4(1)
C(18)	23(1)	23(1)	17(1)	-5(1)	1(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for 11mxu1h.

	x	y	z	U(eq)
H(1O)	5672(14)	3510(20)	713(8)	20
H(2O)	4272(12)	1280(20)	384(9)	18
H(3O)	1794(13)	2840(30)	-19(5)	17
H(4O)	5649(10)	8860(30)	600(9)	21
H(1)	4431	5913	1760	11
H(2)	4550	5558	360	11
H(3)	3787	2827	1138	12
H(4)	2723	5042	74	11
H(5A)	1948	6333	966	12
H(5B)	2718	5137	1521	12
H(6A)	5137	8847	1774	15
H(6B)	5872	7407	1498	15
H(7A)	2477	9328	1288	14
H(7B)	3624	9926	1407	14
H(8A)	2713	7802	2356	17
H(8B)	3901	8028	2460	17
H(9A)	3686	11381	2508	19
H(9B)	2517	11047	2478	19
H(10A)	4047	9683	3579	21
H(10B)	2875	9430	3553	21
H(11A)	3899	12967	3713	23
H(11B)	2715	12763	3654	23
H(12A)	2926	11114	4700	24
H(12B)	4109	10955	4735	24
H(15)	4413	16356	6963	27
H(16)	4354	13602	7614	28
H(18)	3663	10632	5813	26