

Supporting Information

Assessment of partially deoxygenated deoxynojirimycin derivatives as glucosylceramide synthase inhibitors

Richard J. B. H. N. van den Berg,^a Tom Wennekes,^a Amar Ghisaidoobe,^a Wilma E. Donker-Koopman,^b Anneke Strijland,^b Rolf G. Boot,^b Gijs A. van der Marel,^a Johannes M.F.G. Aerts^b, Herman S. Overkleeft^a

^aGorlaeus Laboratories, Leiden Institute of Chemistry, Leiden University, Leiden, The Netherlands

^bDepartment of Medical Biochemistry, Academic Medical Center, Amsterdam, The Netherlands

j.m.aerts@amc.uva.nl

h.s.overkleeft@chem.leidenuniv.nl

Contents

Biological assays	S2
General Methods	S2
Full characterization of the synthesized compounds	S5

Enzyme Assays: The enzyme assays used for determining the inhibition of activity of glucosylceramide synthase (GCS),[1] glucocerebrosidase (GBA1),[2] β -glucosidase 2 (GBA2),[3] sucrase, lactase and maltase[4] were carried out as described previously.

The enzyme assays are robust and reproducible: for example, the inter-assay coefficient of variation for IC₅₀ values of AMP-DNM (compound **2** in manuscript) determined in five independent assays over a period of four years were 18%, 29%, 14%, 17%, 25%, and 17% for GBA1, GBA2, sucrase, lactase, maltase and glucosylceramide synthase, respectively.

In Vitro Enzyme assays:

The IC₅₀-values were determined by variation of iminosugar concentrations.

The enzymes were pre-incubated with the iminosugar for 30 minutes on ice and then the assays were started by adding the substrate-mix.

The incubation temperature was 37 °C. The reaction was stopped by addition of 0.3M glycine/NaOH buffer, pH=10.6.

The amount of liberated 4-MU was determined with a Perkin Elmer LS2 fluorimeter at 366 nm ex. and 445 nm em.

Glucocerebrosidase (GBA1) activity was measured using recombinant enzyme, Cerezyme (Genzyme, Boston, USA), and 4-methylumbelliferyl-B-glucoside (Sigma) as substrate.

The activity (input = 2.5 ng) was determined with 3 mM 4-MU-B-glucoside in the presence of 0.25% (w/v) sodium taurocholate and 0.1% v/v TritonX-100 in Mac Ilvain buffer and 0.1% BSA (0.1M citrate and 0.2M phosphate), pH= 5.2.

Non-lysosomal Glucosylceramidase (GBA2) activity in membrane suspension, was determined with 3 mM 4-MU-B-glucoside in Mac Ilvain buffer and 0.1% BSA (0.1M citrate and 0.2M phosphate) pH=5.8. Input is 16 mg membrane suspension (gaucher spleen), pre-incubated for 30 min. on ice with 5 mM conduritol B epoxide (CBE from Sigma).

Lactase, maltase and sucrase activities were determined with homogenates of mouse intestine input is 70 μ g protein by measuring liberated glucose from the corresponding disaccharides. The final concentrations of the substrates were 100, 25 and 25 mM respectively. The used procedures are in detail described by Andersson U.; Butters, T.B.; Dwek, R.A.; Platt, F.M. N-Butyldeoxygalactonojirimycin: a more selective inhibitor of glycosphingolipid biosynthesis than N-butyldeoxynojirimycin, in vitro and in vivo. *Biochem. Pharmacol.* **2000**, *59*, 821-829.

In Situ Enzyme Assay:

IC₅₀-values of iminosugar compounds for glucosylceramide synthase (GCS) in living RAW cells with C6NBD_Ceramide as substrate. All compounds were tested at a range of different concentrations, from DMSO stock solutions (DMSO concentration not above 0.001 μ M).

The lipid substrate is complexed to fatty acid free bovine serum albumin at a 1:1 molar ratio. The confluent cells were washed with HBSS.

3 ml / flask rpmi without FCS, with 20 mM Hepes is added to the cells and pre-incubated for 1 hour with 300 μ M CBE. Then a preincubation with the compounds for 15 minutes in RPMI without FCS + 300 nM CBE. After the preincubations 5 nmol C6-NBDCER/BSA complex is added and the cells are incubated at 37 °C in CO₂ incubator for 1 hour.

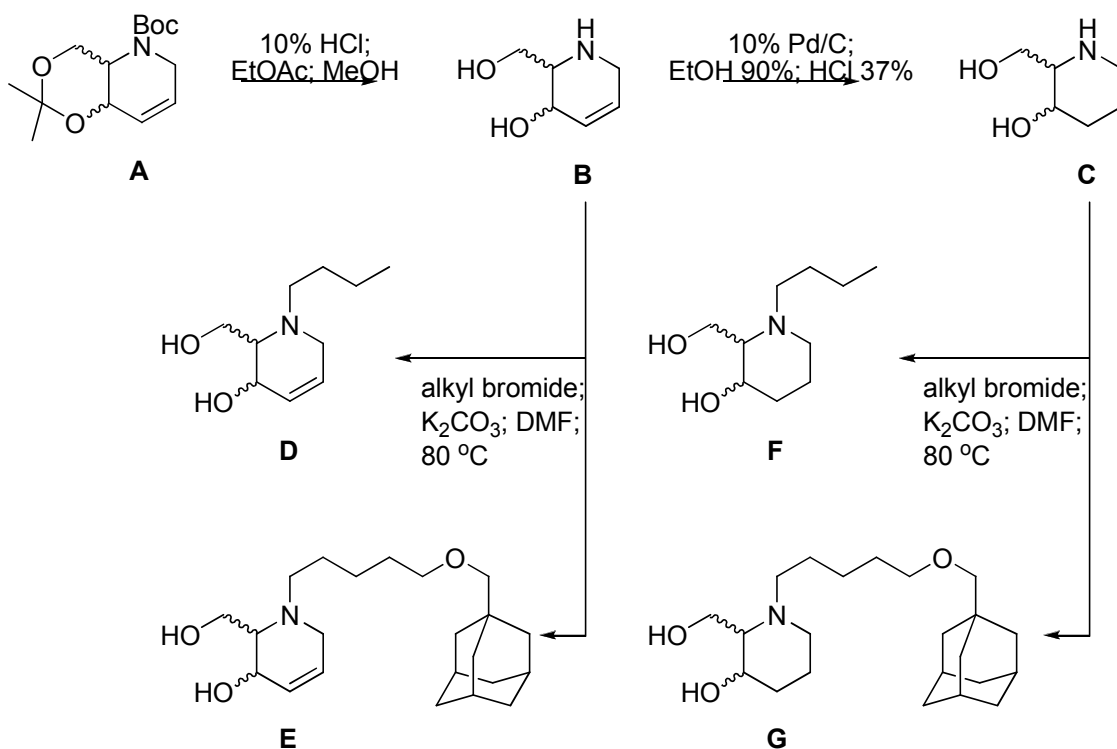
The cells are washed very well (at least 5 times) and harvest by scraping the cells in HBSS. The lipids were extracted and the C6-NBD lipids were separated by thin-layer chromatography. The lipids are quantified with (Thyphoon) a fluorescence scanner.

General chemical synthetic procedures

Dioxanylpiperidene buildingblock **A** and fagomine isomers **I** were prepared as described by Takahata et al.[5,6,7]

Reactions were monitored by TLC analysis using silica gel coated plates (0.2 mm thickness) and detection by spraying with a solution of KMnO_4 (g/L) K_2CO_3 (g/L) followed by charring. Column chromatography was performed on silica gel (40-63 μm). NMR spectra were recorded on a 500-125 MHz or a 400-100 MHz spectrometer. Chemical shifts are given in ppm (δ) relative to tetramethylsilane as internal standard. Coupling constants (J) are given in Hz. All ^{13}C spectra are proton decoupled. For LC/MS analysis a HPLC-system (detection simultaneously at 213 nm, 254 nm and evaporative light detection) equipped with an analytical C-18 column (4.6 mmD x 250 mmL, 5 μ particle size) in combination with buffers A: H_2O , B: acetonitrile, C: 1.0% aqueous trifluoroacetic acid and coupled with an electrospray interface (ESI) was used. For RP-HPLC purifications, an automated HPLC system equipped with a semi-preparative C_{18} column (5 μm C_{18} , 10 $\text{\AA}$, 150 x 21.2 mm) was used. The applied buffers were A: H_2O + trifluoroacetic acid (1% mM) and B: MeCN. High resolution mass spectra were recorded by direct injection (2 μL of a 2 μM solution in water/acetonitrile; 50/50; v/v and 0.1% formic acid) on a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 250 $^\circ\text{C}$) with resolution $R = 60000$ at m/z 400 (mass range $m/z = 150$ -2000) and dioctylphthalate ($m/z = 391.28428$) as a lock mass. The high resolution mass spectrometer was calibrated prior to measurements with a calibration mixture (Thermo Finnigan).

General synthetic scheme for the N-alkylated pyridin and piperidin preparation



General procedure for the deprotection of 2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**B**).

A (1.10 mmol) was dissolved in a mixture of MeOH (4 mL) and 10% HCl in EtOAc (4 mL). After 2 h TLC analysis indicated the complete conversion of starting material into a polar compound. The volatiles were removed and the residue purified by silica gel column chromatography. Elution was performed with $\text{Et}_2\text{O}/\text{EtOH}/\text{NH}_4\text{OH}$ (6:3:1) affording colorless oil.

General procedure for the synthesis of 2-(hydroxymethyl)piperidin-3-ol (**C**).

To a solution of **B** (~1.1 mmol) in EtOH (90%; 10 mL) were added HCl (37%, 15 μ L) and Pd/C (~30 mg). After stirring the mixture for 16 h under an atmosphere of hydrogen the mixture was filtrated and the volatiles evaporated. The residue was purified by silica gel column chromatography. Elution was performed with Et₂O/EtOH/NH₄OH (6:3:1) affording colorless oil.

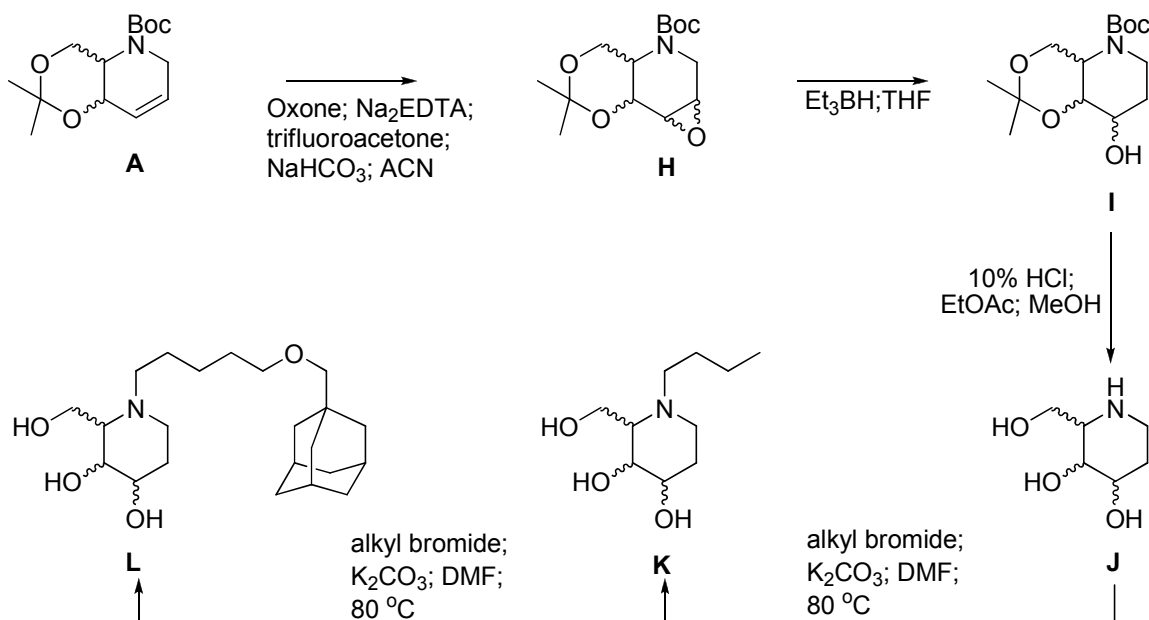
General procedure for the synthesis of 1-butyl-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**D**) and 1-butyl-2-(hydroxymethyl)piperidin-3-ol (**F**).

To a solution of **B** or **C** (0.20 mmol) in DMF (0.5 mL) were added butylbromide (0.30 mmol) in DMF (0.5 mL) and K₂CO₃ (0.60 mmol). After 16 h stirring at 80°C, the mixture was filtrated and the volatiles removed. The residue was purified by silica gel column chromatography. Elution was performed with MeOH/EtOAc/NH₄OH (0:100:0 $\rightarrow$ 30:70:0.03) affording colorless oil.

General procedure for the synthesis of 1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**E**) and 1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)piperidin-3-ol (**G**).

To a solution of **B** or **C** (0.20 mmol) in DMF (0.5 mL) were added adamantanemethanol pentylbromide (0.27 mmol) in DMF (0.5 mL) and K₂CO₃ (0.60 mmol). After 16 h stirring at 80°C, the mixture was filtrated and the volatiles removed. The residue was purified by silica gel column chromatography. Elution was performed with MeOH/EtOAc/NH₄OH (0:100:0 $\rightarrow$ 20:80:0.03) affording colorless oil.

General synthetic scheme for the N-alkylated triolpiperidin preparation - K - L



*General procedure for the synthesis of pyridin substituted compounds (**K**, **L**):*

epoxidation step:

To a cooled (0 °C) solution of **A** (5.0 mmol) in CH₃CN (18.5 mL) were added Na₂EDTA (0.4 mM, 12.0 mL) and trifluoroacetone (2.5 mL). A mixture of NaHCO₃ (1.5 g) and Oxone (7.5 g) was added over a period of 30 min. After stirring for another 30 minutes water was added and the mixture was extracted with DCM. The organic layer was washed with brine, dried with Na₂SO₄ and evaporated. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 95:5 $\rightarrow$ 80:20).

reduction step:

To a cooled (0 °C) solution of **H** (1.0 mmol) in THF (2 mL) was added lithium triethylborohydride (2.0 mL, 2.0 mmol). After TLC analysis showed completed consumption of starting material, ice

were added. The mixture was concentrated, the residue dissolved in DCM (20 mL) and washed with water (5 mL). DCM layer was dried (Na_2SO_4), filtrated and evaporated. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 95:5 $\rightarrow$ 80:20).

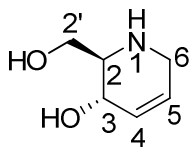
deprotection step:

I (1.0 mmol) was dissolved in a mixture of MeOH (4 mL) and 10% HCl in EtOAc (4 mL). After 2 h TLC analysis indicated the complete conversion of starting material into a polar compound. The volatiles were removed and the residue purified by silica gel column chromatography. Elution was performed with $\text{Et}_2\text{O}/\text{EtOH}/\text{NH}_4\text{OH}$ (6:3:1) affording colorless oil.

General procedure for the synthesis of 1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**K**). To a solution of **J** (0.20 mmol) in DMF (0.5 mL) were added butylbromide (0.30 mmol) in DMF (0.5 mL) and K_2CO_3 (0.60 mmol). After 16 h stirring at 80°C , the mixture was filtrated and the volatiles removed. The residue was purified by silica gel column chromatography. Elution was performed with MeOH/EtOAc/ NH_4OH (0:100:0 $\rightarrow$ 30:70:0.03) affording colorless oil.

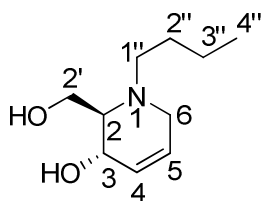
General procedure for the synthesis of 1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-3,4-diol (**L**).

To a solution of **J** (0.20 mmol) in DMF (0.5 mL) were added adamantanemethanol pentylbromide (0.27 mmol) in DMF (0.5 mL) and K_2CO_3 (0.60 mmol). After 16 h stirring at 80°C , the mixture was filtrated and the volatiles removed. The residue was purified by silica gel column chromatography. Elution was performed with MeOH/EtOAc/ NH_4OH (0:100:0 $\rightarrow$ 20:80:0.03) affording colorless oil.



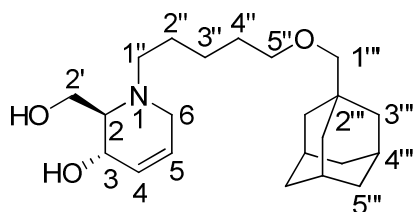
(2*R*,3*S*)-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**4**)

^1H NMR (300 MHz; D_2O) δ : 3.09 (ddd, 1H, H-2, $J_{2,2'a} = 6.4$ Hz, $J_{2,2'b} = 3.5$ Hz, $J_{2,3} = 8.0$ Hz), 3.51 – 3.57 (m, 1H, H-6a), 3.61 – 3.69 (m, 1H, H-6b), 3.75 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.4$ Hz, $J_{2'a,2} = 6.4$ Hz), 3.92 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.4$ Hz, $J_{2'b,2} = 3.5$ Hz), 4.27 (dd, 1H, H-3, $J_{2,3} = 8.1$ Hz, $J_{3,4} = 2.8$ Hz), 5.85 – 5.93 (m, 2H, H-4, H-5). ^{13}C NMR (75 MHz; D_2O) δ : 42.4 (C-6), 59.5 (C-2), 59.6 (C-2'), 63.0 (C-3), 124.6 (C-5), 129.0 (C-4). LC/MS analysis: Rt 0.95 min (linear gradient 0-20% B), ES (ESI): $m/z = 130.0$ [$\text{M} + \text{H}$] $^+$, 259.0 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{12}\text{NO}_2$ 130.08626, found 130.08585. IR ν_{max} (thin film)/ cm^{-1} : 3305, 1635, 1434, 1201, 1139, 1064, 1045, 1012. $\alpha_D = 17.8^\circ$ ($c = 0.80$ MeOH).



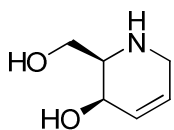
(2*R*,3*S*)-1-butyl-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**5**).

^1H NMR (400 MHz; CDCl_3) δ : 0.94 (t, 3H, H_3 -4''), 1.34 (m, 2H, H_2 -3''), 1.53 (m, 2H, H_2 -2''), 2.77 (m, 2H, H_2 -1''), 2.92 (ddd, 1H, H-2, $J_{2,3} = 4.4$ Hz, $J_{2,2'a} = 6.0$ Hz, $J_{2,2'b} = 5.6$ Hz), 3.11 (br. s, 2H, OH), 3.21 (s, 2H, H_2 -6), 3.67 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.2$ Hz, $J_{2'a,2} = 6.0$ Hz), 3.84 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.2$ Hz, $J_{2'a,2} = 5.6$ Hz), 4.12 (br. s, 1H, H-3), 5.80 – 5.83 (m, 1H, H-5), 5.87 (m, 1H H-4). ^{13}C NMR (100 MHz; CDCl_3) δ : 13.9 (C-4''), 20.3 (C-3''), 29.1 (C-2''), 48.2 (C-6), 53.3 (C-1''), 58.4 (C-2'), 64.4 (C-3), 64.6 (C-2), 127.1, 127.3 (C-4, C-5). LC/MS analysis: Rt 3.29 min (linear gradient 0-50% B), ES (ESI): $m/z = 186.0$ [$\text{M} + \text{H}$] $^+$, 371.2 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{20}\text{NO}_2$ 186.14886, found 186.14875. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2879, 1670, 1432, 1184, 1134, 1066, 1014. $\alpha_D = 7.8^\circ$ ($c = 0.90$ MeOH).



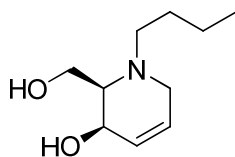
(2*R*,3*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**6**).

^1H NMR (400 MHz; CDCl_3) δ : 1.35 – 1.40 (m, 2H, $\text{H}_{2-3''}$), 1.52 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.55 (m, 4H, $\text{H}_{2-2''}$, $\text{H}_{2-4''}$), 1.63 – 1.72 (m, 6H, $3 \times \text{H}_{2-3''}$), 1.95 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.70 – 2.78 (m, 2H, $\text{H}_{2-1''}$), 2.89 (m, 3H, H-2, $2 \times \text{OH}$), 2.95 (s, 2H, $\text{H}_{2-1''}$), 3.18 (br. s, 2H, H_{2-6}), 3.37 (t, 2H, $\text{H}_{2-5''}$, $J = 6.4$ Hz), 3.65 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.2$ Hz, $J_{2'a,2} = 6.4$ Hz), 3.81 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.2$ Hz, $J_{2,2'b} = 5.6$ Hz), 4.09 (br s., 1H, H-3), 5.80 – 5.83 (m, 1H, H-5), 5.85 – 5.90 (m, 1H, H-4). ^{13}C NMR (100 MHz; CDCl_3) δ : 23.8 (C-3'), 27.0 (C-2'), 28.2 (C-4'), 29.4 (C-4'), 34.0 (C-2'), 37.2 (C-3'), 39.7 (C-5'), 48.3 (C-6), 53.5 (C-1'), 58.5 (C-2'), 64.6, 64.7 (C-2, C-3), 71.4 (C-5'), 81.9 (C-1'), 127.2 (C-4), 127.5 (C-5). LC/MS analysis: Rt 9.61 min (linear gradient 0-50% B), ES (ESI): $m/z = 363.8$ [$\text{M} + \text{H}$] $^+$, 727.7 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{38}\text{NO}_3$ 364.28462, found 364.28468. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2902, 2848, 1672, 1448, 1182, 1139, 1093. $\alpha_D = 7.3^\circ$ ($c = 1.32$ MeOH).



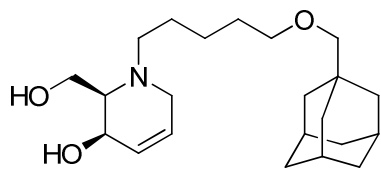
(2*R*,3*R*)-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**7**)

^1H NMR (200 MHz; D_2O) δ : 2.85 (ddd, 1H, H-2, $J_{2,2'a} = 7.3$ Hz, $J_{2,2'b} = 6.2$ Hz, $J_{2,3} = 2.9$ Hz), 3.16 – 3.40 (m, 2H, H_{2-6}), 3.60 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.3$ Hz, $J_{2'a,2} = 7.3$ Hz), 3.70 (dd, 1H, H-2b, $J_{2'a,2'b} = 11.3$ Hz, $J_{2'b,2} = 6.2$ Hz), 4.06 (dd, 1H, H-3, $J_{2,3} = 2.9$ Hz, $J_{3,4} = 4.0$ Hz), 5.85 – 6.04 (m, 2H, H-4, H-5). ^{13}C NMR (50 MHz; D_2O) δ : 44.4 (C-6), 58.3 (C-2), 62.1 (C-2'), 62.6 (C-3), 126.8 (C-5), 131.5 (C-4). LC/MS analysis: Rt 0.95 min (linear gradient 0-20% B), ES (ESI): $m/z = 130.0$ [$\text{M} + \text{H}$] $^+$, 259.1 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{12}\text{NO}_2$ 130.08626, found 130.08582. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2852, 1670, 1434, 1184, 1132, 1058, 1006. $\alpha_D = -48.2^\circ$ ($c = 0.78$ MeOH).



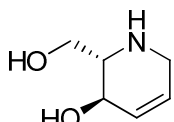
(2*R*,3*R*)-1-butyl-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**8**)

^1H NMR (600 MHz; CDCl_3) δ : 0.93 (t, 3H, $\text{H}_{3-4''}$, $J = 7.8$ Hz), 1.29 – 1.36 (m, 2H, $\text{H}_{2-3''}$), 1.46 – 1.53 (m, 2H, $\text{H}_{2-2''}$), 2.52 – 2.57 (m, 1H, H-1'a), 2.71 (dd, 1H, H-2, $J_{2,2'a} = 3.6$ Hz, $J_{2,2'b} = 6.0$ Hz), 2.78 – 2.82 (m, 1H, H-1'b), 2.94 (d, 1H, H-6a, $J = 17.4$ Hz), 3.28 (d, 1H, H-6b, $J = 17.4$ Hz), 3.43 (br. s, 2H, OH), 3.88 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.4$ Hz, $J_{2'a,2} = 4.2$ Hz), 3.93 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.4$ Hz, $J_{2,2'b} = 6.6$ Hz), 4.31 (s, 1H, H-3), 5.82 – 5.86 (m, 1H, H-4, H-5). ^{13}C NMR (150 MHz; CDCl_3) δ : 13.9 (C-4'), 20.5 (C-3'), 28.2 (C-2'), 50.0 (C-6), 52.6 (C-1'), 60.4 (C-2'), 61.7 (C-2), 67.2 (C-3), 127.2, 128.1 (C-4, C-5). LC/MS analysis: Rt 3.35 min (linear gradient 0-50% B), ES (ESI): $m/z = 186.0$ [$\text{M} + \text{H}$] $^+$, 371.2 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{20}\text{NO}_2$ 186.14886, found 186.14880. IR ν_{max} (thin film)/ cm^{-1} : 3300, 1672, 1419, 1199, 1134, 1066. $\alpha_D = -27.1^\circ$ ($c = 0.42$ MeOH).



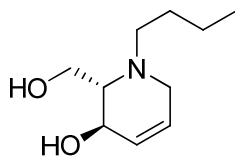
(2*R*,3*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**9**)

^1H NMR (600 MHz; CDCl_3) δ : 1.34 – 1.52 (m, 2H, $\text{H}_2\text{-3''}$), 1.54 (s, 6H, $3 \times \text{H}_2\text{-5''}$), 1.54 – 1.58 (m, 4H, $\text{H}_2\text{-2''}$, $\text{H}_2\text{-4''}$), 1.63 – 1.72 (m, 6H, $3 \times \text{H}_2\text{-3''}$), 1.95 (br. s, 3H, $3 \times \text{H-4''}$), 2.53 – 2.57 (m, 1H, H-1''a), 2.70 (ddd, 1H, H-2 , $J_{2,3} = 3.8$ Hz, $J_{2,2'a} = 3.8$ Hz, $J_{2,2'b} = 6.5$ Hz), 2.78 – 2.83 (m, 1H, H-1''b), 2.93 (d, 1H, H-6a , $J = 17.2$ Hz), 2.95 (s, 2H, $\text{H}_2\text{-1''}$), 3.22 (br. s, 2H, $2 \times \text{OH}$), 3.29 (d, 1H, H-6b , $J = 17.2$ Hz), 3.37 (t, 2H, $\text{H}_2\text{-5''}$, $J = 6.4$ Hz), 3.88 (dd, 1H, H-2'a , $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 4.0$ Hz), 3.93 (dd, 1H, H-2'b , $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 6.2$ Hz), 4.31 (br s., 1H, H-3), 5.81 – 5.87 (m, 2H, H-4 , H-5). ^{13}C NMR (150 MHz; CDCl_3) δ : 24.0 (C-3''), 26.0 (C-2''), 28.2 (C-4''), 29.4 (C-4''), 34.0 (C-2'''), 37.1 (C-3'''), 39.7 (C-5'''), 50.0 (C-6), 52.8 (C-1''), 60.5 (C-2'), 61.7 (C-2), 67.3 (C-3), 71.4 (C-5''), 81.9 (C-1''), 127.2 (C-4), 128.1 (C-5). LC/MS analysis: Rt 9.92 min (linear gradient 0-50% B), ES (ESI): $m/z = 364.3$ [$\text{M} + \text{H}$] $^+$, 727.6 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{38}\text{NO}_3$ 364.28462, found 364.28467. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2900, 2848, 1670, 1201, 1136. $\alpha_D = -0.6^\circ$ ($c = 0.34$ MeOH).



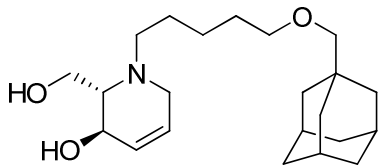
(2*S*,3*R*)-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**10**)

^1H -NMR (400 MHz; D_2O) δ : 3.16 (m, 1H, H-2 , $J_{2,2'a} = 6.4$ Hz, $J_{2,2'b} = 3.2$ Hz, $J_{2,3} = 8.0$ Hz), 3.59 – 3.64 (m, 1H, H-6a), 3.68 – 3.74 (m, 1H, H-6b), 3.82 (dd, 1H, H-2'a , $J_{2'a,2'b} = 12.4$ Hz, $J_{2'a,2} = 6.4$ Hz), 3.98 (dd, 1H, H-2'b , $J_{2'a,2'b} = 12.4$ Hz, $J_{2'b,2} = 3.2$ Hz), 4.33 (dd, 1H, H-3 , $J_{3,4} = 2.8$ Hz, $J_{2,3} = 8.0$ Hz), 5.94 (s, 2H, H-4 , H-5). ^{13}C -NMR (100 MHz; D_2O) δ : 42.4 (C-6), 59.5 (C-2'), 59.6 (C-2), 62.9 (C-3), 124.5 (C-5), 129.1 (C-4). LC/MS analysis: Rt 0.94 min (linear gradient 0-20% B), ES (ESI): $m/z = 130.0$ [$\text{M} + \text{H}$] $^+$, 259.1 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{12}\text{NO}_2$ 130.08626, found 130.08672. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2902, 2848, 1654, 1456, 1091, 1037, 108. $\alpha_D = -37.0^\circ$ ($c = 0.40$ MeOH).



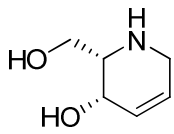
(2*S*,3*R*)-1-butyl-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**11**)

^1H NMR (100 MHz; CDCl_3) δ : 0.92 (t, 3H, $\text{H}_3\text{-4''}$, $J = 7.2$ Hz), 1.28 – 1.40 (m, 2H, $\text{H}_2\text{-3''}$), 1.42 – 1.55 (m, 2H, $\text{H}_2\text{-2''}$), 2.35 (br. s, 2H, OH), 2.64 – 2.73 (m, 2H, $\text{H}_2\text{-1''}$), 2.87 (ddd, 1H, H-2 , $J_{2,3} = 4.1$ Hz, $J_{2,2'a} = 6.4$ Hz, $J_{2,2'b} = 5.7$ Hz), 3.15 (br. s, 2H, $\text{H}_2\text{-6}$), 3.64 (dd, 1H, H-2'a , $J_{2'a,2'b} = 10.9$ Hz, $J_{2'a,2} = 6.4$ Hz), 3.81 (dd, 1H, H-2'b , $J_{2'a,2'b} = 10.9$ Hz, $J_{2'a,2} = 5.7$ Hz), 4.07 (br. s, 1H, H-3), 5.79 – 5.86 (m, 2H, H-4 , H-5). ^{13}C NMR (75 MHz; CDCl_3) δ : 14.0 (C-4''), 20.4 (C-3''), 29.6 (C-2''), 48.2 (C-6), 53.4 (C-1''), 58.7 (C-2'), 64.6 (C-3), 64.8 (C-2), 127.1 (C-5), 128.1 (C-4). LC/MS analysis: Rt 3.39 min (linear gradient 0-50% B), ES (ESI): $m/z = 186.0$ [$\text{M} + \text{H}$] $^+$, 371.1 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{20}\text{NO}_2$ 186.14886, found 186.14853. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2925, 2868, 1635, 1456, 1145, 1051, 1006, 912. $\alpha_D = 10.0^\circ$ ($c = 0.06$ MeOH).



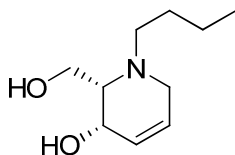
(2*S*,3*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**12**).

¹H NMR (300 MHz; CDCl₃) δ: 1.31 – 1.42 (m, 2H, H₂-3''), 1.52 (s, 6H, 3 × H₂-5'''), 1.52 – 1.59 (m, 4H, H₂-2'', H₂-4''), 1.62 – 1.73 (m, 6H, 3 × H₂-3'''), 1.95 (br. s, 3H, 3 × H-4'''), 2.30 (br. s, 2H, 2 × OH), 2.64 – 2.79 (m, 2H, H₂-1''), 2.89 (ddd, 1H, H-2, *J*_{2,3} = 4.0 Hz, *J*_{2,2'a} = 6.0 Hz, *J*_{2,2'b} = 5.9 Hz), 2.95 (s, 2H, H₂-1'''), 3.16 (br. s, 2H, H₂-6), 3.37 (t, 2H, H₂-5'', *J* = 6.4 Hz), 3.65 (dd, 1H, H-2'a, *J*_{2'a,2'b} = 10.9 Hz, *J*_{2,2'a} = 6.3 Hz), 3.82 (dd, 1H, H-2'b, *J*_{2'a,2'b} = 10.9 Hz, *J*_{2,2'b} = 5.8 Hz), 4.06 (br s., 1H, H-3), 5.79 – 5.83 (m, 1H, H-5), 5.84 – 5.90 (m, 1H, H-4). ¹³C NMR (75 MHz; CDCl₃) δ: 23.8 (C-3''), 27.3 (C-2''), 28.2 (C-4''), 29.4 (C-4''), 34.0 (C-2'''), 37.2 (C-3'''), 39.7 (C-5'''), 48.2 (C-6), 53.6 (C-1''), 58.7 (C-2'), 64.7, 64.8 (C-2, C-3), 71.4 (C-5''), 81.9 (C-1'''), 127.1 (C-4), 128.0 (C-5). LC/MS analysis: Rt 9.85 min (linear gradient 0-50% B), ES (ESI): *m/z* = 364.2 [M + H]⁺, 727.7 [2M + H]⁺. HRMS: [M + H] calculated for C₂₂H₃₈N₁O₃ 364.28462, found 364.28469. IR (neat, cm⁻¹): 2900, 2846, 2358, 2341, 1448, 1157, 1109, 1056, 1006, 912. α_D = 5.0° (c = 0.04 MeOH).



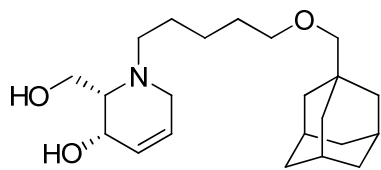
(2*S*,3*S*)-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**13**)

¹H NMR (300 MHz; D₂O) δ: 3.38 (ddd, 1H, H-2, *J*_{2,2'a} = 8.6 Hz, *J*_{2,2'b} = 4.8 Hz, *J*_{2,3} = 3.1 Hz), 3.70 – 3.73 (m, 2H, H₂-6), 3.81 (dd, 1H, H-2'a, *J*_{2'a,2'b} = 12.1 Hz, *J*_{2'a,2} = 8.6 Hz), 3.94 (dd, 1H, H-2'b, *J*_{2'a,2'b} = 12.1 Hz, *J*_{2'b,2} = 4.8 Hz), 4.35 (t, 1H, H-3, *J* = 2.9 Hz), 5.97 – 6.02 (m, 1H, H-5), 6.06 – 6.11 (m, 1H, H-4). ¹³C NMR (75 MHz; D₂O) δ: 43.2 (C-6), 59.1 (C-2), 59.9 (C-2'), 60.8 (C-3), 125.1 (C-5), 127.3 (C-4). LC/MS analysis: Rt 0.95 min (linear gradient 0-20% B), ES (ESI): *m/z* = 130.0 [M + H]⁺, 259.0 [2M + H]⁺. HR-MS [QTOF, MH⁺] *m/z* calculated for C₆H₁₂NO₂ 130.08626, found 130.08612. IR ν_{max}(thin film)/ cm⁻¹: 3300, 2852, 1670, 1419, 1190, 1139, 1083, 1049, 1006. α_D = 83.0° (c = 0.54 MeOH).



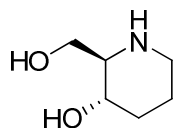
(2*S*,3*S*)-1-butyl-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**14**).

¹H NMR (300 MHz; CDCl₃) δ: 0.93 (t, 3H, H₃-4'', *J* = 7.25 Hz), 1.25 – 1.39 (m, 2H, H₂-3''), 1.41 – 1.55 (m, 2H, H₂-2''), 2.48 – 2.57 (m, 1H, H-1'a), 2.79 (ddd, 1H, H-2, *J*_{2,3} = 2.0 Hz, *J*_{2,2'a} = 3.8 Hz, *J*_{2,2'b} = 7.7 Hz), 2.75 – 2.84 (m, 1H, H-1'b), 2.90 (d, 1H, H-6a, *J* = 16.5 Hz), 3.12 (br. s, 2H, OH), 3.27 (d, 1H, H-6b, *J* = 16.5 Hz), 3.87 (dd, 1H, H-2'a, *J*_{2,2'a} = 4.1 Hz, *J*_{2'a,2'b} = 11.5 Hz), 4.94 (dd, 1H, H-2'b, *J*_{2,2'b} = 6.1 Hz, *J*_{2'a,2'b} = 11.5 Hz), 4.30 (br. s, 1H, H-3), 5.80 – 5.88 (m, 2H, H-4, H-5). ¹³C NMR (75 MHz; CDCl₃) δ: 14.7 (C-4''), 21.3 (C-3''), 29.2 (C-2''), 50.8 (C-6), 53.5 (C-1''), 61.3 (C-2'), 62.6 (C-2), 68.1 (C-3), 128.0 (C-5), 129.2 (C-4). LC/MS analysis: Rt 3.21 min (linear gradient 0-50% B), ES (ESI): *m/z* = 186.0 [M + H]⁺, 371.0 [2M + H]⁺. HR-MS [QTOF, MH⁺] *m/z* calculated for C₁₀H₂₀NO₂ 186.14886, found 186.14861. IR ν_{max}(thin film)/ cm⁻¹: 3332, 2929, 1652, 1458, 1186, 1132, 1074, 1008. α_D = 8.5° (c = 0.03 MeOH).



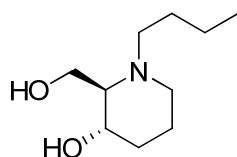
(2*S*,3*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)-1,2,3,6-tetrahydropyridin-3-ol (**15**).

^1H NMR (400 MHz; CDCl_3) δ : 1.32 – 1.42 (m, 2H, $\text{H}_{2-3''}$), 1.53 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.54 – 1.59 (m, 4H, $\text{H}_{2-2''}$, $\text{H}_{2-4''}$), 1.63 – 1.73 (m, 6H, $3 \times \text{H}_{2-3''}$), 1.95 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.55 – 2.62 (m, 1H, $\text{H}_{1''\text{a}}$), 2.72 (ddd, 1H, H_{-2} , $J_{2,3} = 3.8$ Hz, $J_{2,2'\text{a}} = 3.8$ Hz, $J_{2,2'\text{b}} = 5.9$ Hz), 2.81 – 2.88 (m, 1H, $\text{H}_{1''\text{b}}$), 2.95 (s, 2H, $\text{H}_{2-1''}$), 2.96 (d, 1H, $\text{H}_{6\text{a}}$, $J = 17.1$ Hz), 3.32 (d, 1H, $\text{H}_{6\text{b}}$, $J = 17.1$ Hz), 3.37 (t, 2H, $\text{H}_{2-5''}$, $J = 6.4$ Hz), 3.39 (br. s, 2H, $2 \times \text{OH}$), 3.90 (dd, 1H, $\text{H}_{-2'\text{a}}$, $J_{2'\text{a},2'\text{b}} = 10.4$ Hz, $J_{2,2'\text{a}} = 4.0$ Hz), 3.95 (dd, 1H, $\text{H}_{-2'\text{b}}$, $J_{2'\text{a},2'\text{b}} = 10.4$ Hz, $J_{2,2'\text{b}} = 6.0$ Hz), 4.31 (br s., 1H, H_{-3}), 5.81 – 5.89 (m, 2H, H_{-4} , H_{-5}). ^{13}C NMR (100 MHz; CDCl_3) δ : 24.0 ($\text{C}_{-3''}$), 25.8 ($\text{C}_{-2''}$), 28.2 ($\text{C}_{-4''}$), 29.4 ($\text{C}_{-4''}$), 34.0 ($\text{C}_{-2''}$), 37.2 ($\text{C}_{-3''}$), 39.7 ($\text{C}_{-5''}$), 50.0 (C_{-6}), 52.8 ($\text{C}_{-1''}$), 60.5 ($\text{C}_{-2'}$), 61.8 (C_{-2}), 67.3 (C_{-3}), 71.4 ($\text{C}_{-5''}$), 81.9 ($\text{C}_{-1''}$), 127.3 (C_{-4}), 127.8 (C_{-5}). LC/MS analysis: Rt 9.90 min (linear gradient 0-50% B), ES (ESI): $m/z = 364.2$ [$\text{M} + \text{H}$] $^+$, 727.6 [$2\text{M} + \text{H}$] $^+$. HRMS: [$\text{M} + \text{H}$] calculated for $\text{C}_{22}\text{H}_{38}\text{N}_1\text{O}_3$ 364.28462, found 364.28486. IR ν_{max} (thin film)/ cm^{-1} : 2902, 2848, 1670, 1201, 1137. $\alpha_{\text{D}} = 26.7^\circ$ ($c = 0.18$ MeOH).



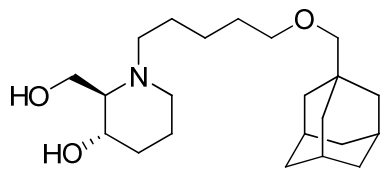
(2*R*,3*S*)-2-(hydroxymethyl)piperidin-3-ol (**16**)

^1H -NMR (300 MHz; D_2O) δ : 1.55 – 1.64 (m, 1H, $\text{H}_{4\text{a}}$), 1.74 – 1.81 (m, 1H, $\text{H}_{5\text{a}}$), 1.99 - 2.06 (m, 1H, $\text{H}_{5\text{b}}$), 2.19 – 2.14 (m, 1H, $\text{H}_{4\text{b}}$), 2.99 (dd, 1H, $\text{H}_{6\text{a}}$, $J_{6\text{a},6\text{b}} = 12.6$ Hz, $J_{5,6\text{a}} = 3.5$ Hz), 3.08 (ddd, 1H, H_{-2} , $J_{2,2'\text{a}} = 5.9$ Hz, $J_{2,2'\text{b}} = 3.5$ Hz, $J_{2,3} = 12.3$ Hz), 3.41 (dt, 1H, $\text{H}_{6\text{b}}$, $J_{6\text{a},6\text{b}} = 12.7$ Hz, $J_{5,6\text{b}} = 2.8$ Hz), 3.80 (ddd, 1H, H_{-3} , $J_{2,3} = 10.3$ Hz, $J_{3,4\text{a}} = 10.3$ Hz, $J_{3,4\text{b}} = 4.4$ Hz), 3.88 (dd, 1H, $\text{H}_{-2'\text{a}}$, $J_{2'\text{a},2'\text{b}} = 12.6$ Hz, $J_{2'\text{a},2} = 5.9$ Hz), 3.97 (dd, 1H, $\text{H}_{-2'\text{b}}$, $J_{2'\text{a},2'\text{b}} = 12.6$ Hz, $J_{2'\text{b},2} = 3.5$ Hz). ^{13}C -NMR (75 MHz; D_2O) δ : 21.0 (C_{-5}), 31.1 (C_{-4}), 44.2 (C_{-6}), 58.7 ($\text{C}_{-2'}$), 62.3 (C_{-2}), 65.3 (C_{-3}). LC/MS analysis: Rt 0.82 min (linear gradient 0-20% B), ES (ESI): $m/z = 132.0$ [$\text{M} + \text{H}$] $^+$, 263.1 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_2$ 132.10191, found 132.10184. IR ν_{max} (thin film)/ cm^{-1} : 3365, 2925, 2856, 1201, 1145, 1083, 1058, 1031. $\alpha_{\text{D}} = 6.1^\circ$ ($c = 1.94$ MeOH).



(2*R*,3*S*)-1-butyl-2-(hydroxymethyl)piperidin-3-ol (**17**)

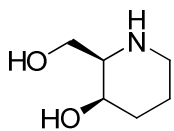
^1H NMR (400 MHz; CDCl_3) δ : 0.94 (t, 3H, $\text{H}_{3-4''}$, $J = 6.4$ Hz), 1.32 (m, 2H, $\text{H}_{2-3''}$), 1.42 (m, 1H, $\text{H}_{4\text{a}}$), 1.50 (m, 2H, $\text{H}_{2-2''}$), 1.61 (m, 1H, $\text{H}_{5\text{a}}$), 1.75 (m, 1H, $\text{H}_{5\text{b}}$), 2.01 (m, 1H, $\text{H}_{4\text{b}}$), 2.31 (ddd, 1H, H_{-2} , $J_{2,3} = 8.0$ Hz, $J_{2,2'\text{a}} = 3.6$ Hz, $J_{2,2'\text{b}} = 2.8$ Hz), 2.37 (ddd, 1H, $\text{H}_{6\text{a}}$, $J_{6\text{a},6\text{b}} = 11.6$ Hz, $J_{6\text{a},5\text{a}} = 8.4$ Hz, $J_{6\text{a},5\text{b}} = 3.0$ Hz), 2.55 – 2.63 (m, 1H, $\text{H}_{-1''\text{a}}$), 2.80 - 2.87 (m, 1H, $\text{H}_{-1''\text{b}}$), 2.98 (ddd, 1H, $\text{H}_{6\text{b}}$, $J_{6\text{a},6\text{b}} = 11.6$ Hz, $J_{2\text{a},6\text{b}} = 3.6$ Hz, $J_{2\text{b},6\text{b}} = 3.2$ Hz), 3.42 (br. s, 2H OH), 3.78 (m, 1H, H_{-3} , $J = 4.4$ Hz), 3.80 (dd, $\text{H}_{-2'\text{a}}$, $J_{2'\text{a},2'\text{b}} = 11.6$ Hz, $J_{2,2'\text{a}} = 3.8$ Hz), 4.00 (dd, 1H, $\text{H}_{-2'\text{b}}$, $J_{2'\text{a},2'\text{b}} = 11.6$ Hz, $J_{2,2'\text{b}} = 2.4$ Hz). ^{13}C NMR (100 MHz; CDCl_3) δ : 13.9 ($\text{C}_{-4''}$), 20.4 ($\text{C}_{-3''}$), 21.8 (C_{-5}), 27.2 ($\text{C}_{-2''}$), 32.2 (C_{-4}), 51.0 (C_{-6}), 53.0 ($\text{C}_{-1''}$), 57.9 ($\text{C}_{-2'}$), 67.0 (C_{-3}), 67.3 (C_{-2}). LC/MS analysis: Rt 3.38 min (linear gradient 0-50% B), ES (ESI): $m/z = 188.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_2$ 188.16451, found 188.16446. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2964, 2879, 1674, 1423, 1201, 1186, 1134, 1060. $\alpha_{\text{D}} = 2.7^\circ$ ($c = 0.30$ MeOH).



(2*R*,3*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

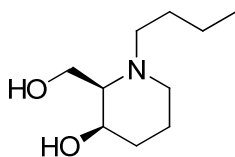
(hydroxymethyl)piperidin-3-ol (**18**)

^1H NMR (300 MHz; CDCl_3) δ : 1.31 – 1.45 (m, 3H, H-4a, H₂-3''), 1.52 (br. s, 6H, 3 $\times$ H₂-5''), 1.54 – 1.77 (m, 12H, H₂-5, H₂-2'', H₂-4'', 3 $\times$ H₂-3'''), 1.95 (br. s, 3H, 3 $\times$ H-4'''), 2.01 (m, 1H, H-4b), 2.30 – 2.35 (ddd, 1H, H-2, $J_{2,3} = 9.3$ Hz, $J_{2,2'a} = 4.4$ Hz, $J_{2,2'b} = 2.2$ Hz), 2.41 (dd, 1H, H-6a, $J_{6a,6b} = J_{6a,5a} = 10.9$ Hz, $J_{6a,5b} = 3.1$ Hz), 2.57 – 2.66 (m, 1H, H-1''a), 2.79 – 2.89 (m, 1H, H-1''b), 2.94 (s, 2H, H₂-1'''), 2.95 – 3.01 (m, 1H, H-6b), 3.37 (t, 2H, H₂-5'', $J = 6.4$ Hz), 3.47 (br. s, 2H, 2 $\times$ OH), 3.73 – 3.78 (m, 1H, H-3), 3.80 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.8$ Hz, $J_{2'a} = 4.1$ Hz), 4.01 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 2.2$ Hz). ^{13}C NMR (75 MHz; CDCl_3) δ : 21.8 (C-5), 23.9 (C-3''), 24.8 (C-2''), 28.2 (C-4'''), 29.3 (C-4''), 32.2 (C-4), 34.0 (C-2''), 37.2 (C-3'''), 39.7 (C-5'''), 51.0 (C-6), 53.2 (C-1''), 57.8 (C-2'), 66.9 (C-3), 67.4 (C-2), 71.3 (C-5''), 81.9 (C-1'''). LC/MS analysis: Rt 9.68 min (linear gradient 0-50% B), ES (ESI): $m/z = 366.1$ [$\text{M} + \text{H}$] $^+$, 731.7 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_3$ 366.30027, found 366.30034. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2900, 2848, 1670, 1450, 1137, 1083, 1058, 991. $\alpha_D = 1.4^\circ$ ($c = 0.56$ MeOH).



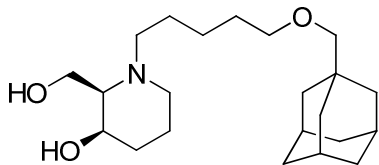
(2*R*,3*R*)-2-(hydroxymethyl)piperidin-3-ol (**19**)

^1H NMR (400 MHz; D_2O) δ : 1.46 - 1.50 (m, 1H, H-5a), 1.62 – 1.76 (m, 2H, H-4a, H-5b), 1.83 – 1.86 (m, 1H, H-4b), 2.60 (ddd, 1H, $J_{6a,6b} = 12.4$ Hz, $J_{6a,5a} = 11.6$, $J_{6a,5b} = 3.2$ Hz), 2.77 (ddd, 1H, H-2, $J_{2,3} = 1.6$ Hz, $J_{2,2'a} = 7.4$, $J_{2,2'b} = 6.8$ Hz), 2.99 (dt, 1H, H-6b, $J_{6a,6b} = 12.8$ Hz), 3.58 (dd, 1H, H-2'a, $J_{2,2'a} = 7.4$ Hz, $J_{2'a,2'b} = 11.2$ Hz), 3.62 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.2$ Hz, $J_{2,2'b} = 6.8$ Hz), 3.94 (d, 1H, H-3, $J_{4,5} = 2.0$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 20.2 (C-5), 30.7 (C-4), 45.0 (C-6), 60.0 (C-2), 62.5 (C-2'), 65.5 (C-3). LC/MS analysis: Rt 1.03 min (linear gradient 0-20% B), ES (ESI): $m/z = 132.0$ [$\text{M} + \text{H}$] $^+$, 263.0 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_2$ 132.10191, found 132.10180. IR ν_{max} (thin film)/ cm^{-1} : 3300, 1670, 1436, 1186, 1134, 1047, 993. $\alpha_D = 3.1^\circ$ ($c = 0.52$ MeOH).



(2*R*,3*R*)-1-butyl-2-(hydroxymethyl)piperidin-3-ol (**20**)

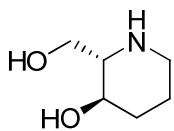
^1H NMR (600 MHz; CDCl_3) δ : 0.94 (t, 3H, H₃-4'', $J = 6.4$ Hz), 1.23 – 1.36 (m, 2H, H₂-3''), 1.43 – 1.49 (m, 2H, H₂-2''), 1.52 – 1.55 (m, 2H, H-4a, H-5a), 1.79 - 1.83 (m, 2H, H-4b, H-5b), 2.28 (ddd, 1H, H-6a, $J_{6a,6b} = 13.2$ Hz, $J_{6a,5a} = 9.0$ Hz, $J_{6a,5b} = 2.4$ Hz), 2.43 (br. s, 1H, H-2), 2.49 – 2.53 (m, 1H, H-1''a), 2.69 - 2.73 (m, 1H, H-1''b), 2.86 (ddd, 1H, H-6b, $J_{6a,6b} = 12.0$ Hz, $J_{2a,6b} = 4.8$ Hz, $J_{2b,6b} = 3.6$ Hz), 3.14 (br. s, 2H, 2 $\times$ OH), 3.80 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.4$ Hz, $J_{2,2'a} = 3.6$ Hz), 3.93 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.4$ Hz, $J_{2,2'b} = 6.0$ Hz), 4.04 (br. s, 1H, H-3). ^{13}C NMR (150 MHz; CDCl_3) δ : 14.0 (C-4''), 20.3 (C-5), 20.5 (C-3''), 27.4 (C-2''), 30.9 (C-4), 50.8 (C-6), 52.9 (C-1''), 61.5 (C-2'), 63.8 (C-2), 69.0 (C-3). LC/MS analysis: Rt 3.58 min (linear gradient 0-50% B), ES (ESI): $m/z = 188.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_2$ 188.16451, found 188.16456. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2879, 1672, 1419, 1182, 1134, 1068. $\alpha_D = -5.7^\circ$ ($c = 0.28$ MeOH).



(2*R*,3*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

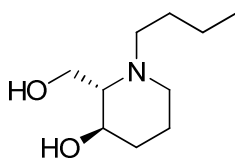
(hydroxymethyl)piperidin-3-ol (**21**)

^1H NMR (600 MHz; CDCl_3) δ : 1.28 – 1.38 (m, 2H, $\text{H}_2\text{-3}''$), 1.49 – 1.59 (m, 6H, H-4a, H-5a, $\text{H}_2\text{-2}''$, $\text{H}_2\text{-4}''$), 1.52 (br. s, 6H, $3 \times \text{H}_2\text{-5}'''$), 1.63 – 1.72 (m, 6H, $3 \times \text{H}_2\text{-3}'''$), 1.79 – 1.88 (m, 2H, H-4b, H-5b), 1.95 (br. s, 3H, $3 \times \text{H-4}'''$), 2.29 – 2.35 (m, 1H, H-6a), 2.42 (br. s, 1H, H-2), 2.50 – 2.55 (m, 1H, H-1''a), 2.70 – 2.75 (m, 1H, H-1''b), 2.86 – 2.88 (m, 1H, H-6b), 2.95 (s, 2H, $\text{H}_2\text{-1}''$), 3.12 (br. s, 2H, $2 \times \text{OH}$), 3.37 (t, 2H, $\text{H}_2\text{-5}''$, $J = 6.4$ Hz), 3.81 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 3.7$ Hz), 3.93 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 5.5$ Hz), 4.04 (br. s., 1H, H-3). ^{13}C NMR (150 MHz; CDCl_3) δ : 20.2 (C-5), 24.0 (C-3''), 25.1 (C-2''), 28.2 (C-4'''), 29.4 (C-4''), 30.9 (C-4), 34.0 (C-2''), 37.1 (C-3'''), 39.7 (C-5'''), 50.9 (C-6), 53.1 (C-1''), 61.5 (C-2'), 63.8 (C-2), 69.0 (C-3), 71.4 (C-5''), 81.8 (C-1'''). LC/MS analysis: Rt 9.88 min (linear gradient 0-50% B), ES (ESI): $m/z = 365.9$ [$\text{M} + \text{H}$] $^+$, 731.8 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_3$ 366.30027, found 366.30036. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2900, 2848, 1672, 1450, 1180, 1136, 1058, 964. $\alpha_D = -3.5^\circ$ ($c = 0.34$ MeOH).



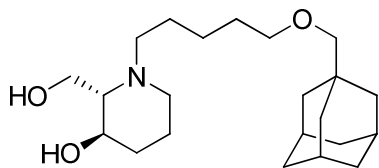
(2*S*,3*R*)-2-(hydroxymethyl)piperidin-3-ol (**22**)

^1H -NMR (400 MHz; D_2O) δ : 1.50 – 1.60 (m, 1H, H-4a), 1.68 – 1.80 (m, 1H, H-5a), 1.97 - 2.03 (m, 1H, H-5b), 2.11 – 2.16 (m, 1H, H-4b), 2.96 (dd, 1H, H-6a, $J_{6a,6b} = 12.4$ Hz, $J_{5,6a} = 3.2$ Hz), 3.05 (ddd, 1H, H-2, $J_{2,2'a} = 6.0$ Hz, $J_{2,2'b} = 3.6$ Hz, $J_{2,3} = 9.6$ Hz), 3.37 (dt, 1H, H-6b, $J_{6a,6b} = 12.8$ Hz), 3.78 (ddd, 1H, H-3, $J_{2,3} = 10.4$ Hz, $J_{3,4a} = 10.4$ Hz, $J_{3,4b} = 4.4$ Hz), 3.86 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.8$ Hz, $J_{2'a,2} = 6.4$ Hz), 3.95 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.8$ Hz, $J_{2'b,2} = 3.6$ Hz). ^{13}C -NMR (100 MHz; D_2O) δ : 20.3 (C-5), 30.3 (C-4), 43.4 (C-6), 57.9 (C-2'), 61.5 (C-2), 64.5 (C-3). LC/MS analysis: Rt 0.87 min (linear gradient 0-20% B), ES (ESI): $m/z = 132.0$ [$\text{M} + \text{H}$] $^+$, 263.1 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_2$ 132.10187, found 132.10191. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2966, 2800, 1670, 1436, 1201, 1136, 1080, 1055, 1022. $\alpha_D = -14.2^\circ$ ($c = 0.66$ MeOH).



(2*S*,3*R*)-1-butyl-2-(hydroxymethyl)piperidin-3-ol (**23**)

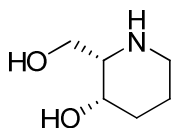
^1H NMR (400 MHz; CDCl_3) δ : 0.94 (t, 3H, $\text{H}_3\text{-4}''$, $J = 6.4$ Hz), 1.30 (m, 2H, $\text{H}_2\text{-3}''$), 1.34 – 1.38 (m, 1H, H-4a), 1.40 - 1.53 (m, 2H, $\text{H}_2\text{-2}''$), 1.53 - 1.62 (m, 1H, H-5a), 1.68 - 1.76 (m, 1H, H-5b), 1.96 - 2.01 (m, 1H, H-4b), 2.23 (ddd, 1H, H-2, $J_{2,3} = 8.0$ Hz, $J_{2,2'a} = 4.0$ Hz, $J_{2,2'b} = 2.4$ Hz), 2.30 (ddd, 1H, H-6a, $J_{6a,6b} = 11.2$ Hz, $J_{6a,5a} = 11.2$ Hz, $J_{6a,5b} = 3.2$ Hz), 2.46 – 2.53 (m, 1H, H-1''a), 2.73 - 2.81 (m, 3H, H-1''b, $2 \times \text{OH}$), 2.91 (ddd, 1H, H-6b, $J_{6a,6b} = 11.6$ Hz, $J_{2a,6b} = 3.6$ Hz, $J_{2b,6b} = 3.6$ Hz), 3.74 (ddd, 1H, H-3, $J_{2,3} = 8.0$ Hz, $J_{3,4a} = 6.4$ Hz, $J_{3,4b} = 4.4$ Hz), 3.79 (dd, H-2'a, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 4.0$ Hz), 3.96 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 2.4$ Hz). ^{13}C NMR (100 MHz; CDCl_3) δ : 13.9 (C-4''), 20.5 (C-3''), 22.1 (C-5), 27.7 (C-2''), 32.4 (C-4), 50.8 (C-6), 53.1 (C-1''), 58.3 (C-2'), 67.2 (C-3), 67.5 (C-2). LC/MS analysis: Rt 3.35 min (linear gradient 0-50% B), ES (ESI): $m/z = 188.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_2$ 188.16451, found 188.16424. IR ν_{max} (thin film)/ cm^{-1} : 3307, 2935, 2871, 1652, 1458, 1120, 1068, 1028, 986, 912. $\alpha_D = 13.3^\circ$ ($c = 0.06$ MeOH).



(2*S*,3*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

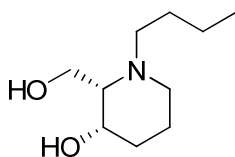
(hydroxymethyl)piperidin-3-ol (**24**)

^1H NMR (400 MHz; CDCl_3) δ : 1.29 – 1.42 (m, 3H, H-4a, H₂-3''), 1.52 (br. s, 6H, 3 $\times$ H₂-5'''), 1.54 – 1.77 (m, 12H, H₂-5, H₂-2'', H₂-4'', 3 $\times$ H₂-3'''), 1.95 (br. s, 3H, 3 $\times$ H-4'''), 2.00 (m, 1H, H-4b), 2.26 (ddd, 1H, H-2, $J_{2,3} = 7.5$ Hz, $J_{2,2'a} = 4.2$ Hz, $J_{2,2'b} = 2.5$ Hz), 2.32 (dd, 1H, H-6a, $J_{6a,6b} = 11.4$ Hz, $J_{6a,5a} = 7.9$ Hz, $J_{6a,5b} = 3.2$ Hz), 2.50 – 2.57 (m, 1H, H-1''a), 2.75 – 2.83 (m, 1H, H-1''b), 2.93 (ddd, 1H, H-6b, $J_{6a,6b} = 11.4$ Hz, $J_{6b,5a} = J_{6a,5b} = 3.4$ Hz), 2.95 (s, 2H, H₂-1'''), 3.37 (t, 2H, H₂-5''. $J = 6.4$ Hz), 3.75 (m, 1H, H-3), 3.78 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.5$ Hz, $J_{2,2'a} = 4.3$ Hz), 3.98 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.5$ Hz, $J_{2,2'b} = 2.3$ Hz). ^{13}C NMR (100 MHz; CDCl_3) δ : 22.0 (C-5), 24.0 (C-3''), 25.3 (C-2''), 28.2 (C-4'''), 29.4 (C-4''), 32.3 (C-4), 34.0 (C-2''), 37.2 (C-3'''), 39.7 (C-5'''), 50.9 (C-6), 53.3 (C-1'''), 58.2 (C-2'), 67.3 (C-3), 67.4 (C-2), 71.3 (C-5''), 81.9 (C-1''). LC/MS analysis: Rt 9.89 min (linear gradient 0-50% B), ES (ESI): $m/z = 366.2$ [$\text{M} + \text{H}$] $^+$, 731.8 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_3$ 366.30027, found 366.30031. IR ν_{max} (thin film)/ cm^{-1} : 2900, 2846, 1652, 1448, 1110, 1095, 1076, 1033, 989, 912. $\alpha_D = 10.0^\circ$ ($c = 0.08$ MeOH).



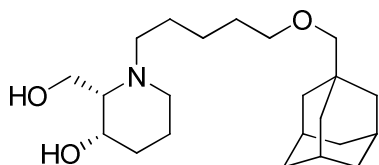
(2*S*,3*S*)-2-(hydroxymethyl)piperidin-3-ol (**25**)

^1H NMR (400 MHz; D_2O) δ : 1.65 – 2.01 (m, 4H, H₂-4, H₂-5), 2.98 (dd, 1H, $J_{6a,6b} = 12.0$ Hz, $J_{6a,5a} = 12.5$), 3.24 (br. s, 1H, H-2), 3.37 (d, 1H, H-6b, $J_{6a,6b} = 10.8$ Hz), 3.70 (dd, 1H, H-2'a, $J_{2,2'a} = 8.8$ Hz, $J_{2'a,2'b} = 12.1$ Hz), 3.79 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.2$ Hz, $J_{2,2'b} = 4.4$ Hz), 4.11 (br. s, 1H, H-3). ^{13}C NMR (75 MHz; D_2O) δ : 17.1 (C-5), 29.1 (C-4), 44.9 (C-6), 60.6 (C-2'), 61.1 (C-2), 63.4 (C-3). LC/MS analysis: Rt 0.80 min (linear gradient 0-20% B), ES (ESI): $m/z = 132.0$ [$\text{M} + \text{H}$] $^+$, 263.0 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_2$ 132.10191, found 132.10166. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2958, 2848, 1635, 1205, 1139, 1045, 1010. $\alpha_D = -2.0^\circ$ ($c = 2.0$ MeOH).



(2*S*,3*S*)-1-butyl-2-(hydroxymethyl)piperidin-3-ol (**26**)

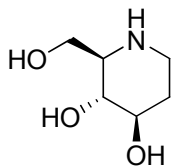
^1H NMR (400 MHz; CDCl_3) δ : 0.92 (t, 3H, H₃-4'', $J = 6.4$ Hz), 1.25 – 1.38 (m, 2H, H₂-3''), 1.43 – 1.52 (m, 2H, H₂-2''), 1.54 – 1.58 (m, 2H, H-4a, H-5a), 1.78 – 1.87 (m, 2H, H-4b, H-5b), 2.31 (ddd, 1H, H-6a, $J_{6a,6b} = 12.0$ Hz, $J_{6a,5a} = 9.8$, $J_{6a,5b} = 3.2$ Hz), 2.45 (br. s, 1H, H-2), 2.49 – 2.56 (m, 1H, H-1''a), 2.70 – 2.77 (m, 1H, H-1''b), 2.88 (ddd, 1H, H-6b, $J_{6a,6b} = 12.0$ Hz, $J_{6b,5a} = 3.6$, $J_{6b,5b} = 3.4$ Hz), 3.23 (br. s, 2H, OH), 3.81 (dd, H-2'a, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 3.6$ Hz), 3.94 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 5.6$ Hz), 4.04 (br. s, 1H, H-3). ^{13}C NMR (100 MHz; CDCl_3) δ : 14.0 (C-4''), 20.2 (C-5), 20.5 (C-3''), 27.3 (C-2''), 30.9 (C-4), 50.9 (C-6), 52.9 (C-1''), 61.5 (C-2'), 63.9 (C-2), 68.9 (C-3). LC/MS analysis: Rt 3.48 min (linear gradient 0-50% B), ES (ESI): $m/z = 188.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_2$ 188.16451, found 188.16424. IR ν_{max} (thin film)/ cm^{-1} : 3300, 2879, 1670, 1419, 1182, 1134, 1066. $\alpha_D = 12.5^\circ$ ($c = 0.32$ MeOH).



(2S,3S)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

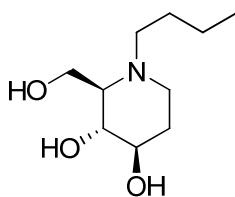
(hydroxymethyl)piperidin-3-ol (**27**)

^1H NMR (400 MHz; CDCl_3) δ : 1.25 – 1.39 (m, 2H, $\text{H}_{2-3''}$), 1.46 – 1.60 (m, 6H, H-4a, H-5a, $\text{H}_{2-2''}$, $\text{H}_{2-4''}$), 1.52 (br. s, 6H, $3 \times \text{H}_{2-5''}$), 1.63 – 1.72 (m, 6H, $3 \times \text{H}_{2-3''}$), 1.78 – 1.88 (m, 2H, H-4b, H-5b), 1.95 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.29 – 2.35 (m, 1H, H-6a), 2.47 (br. s, 1H, H-2), 2.52 – 2.59 (m, 1H, H-1''a), 2.71 – 2.79 (m, 1H, H-1''b), 2.87 – 2.92 (m, 1H, H-6b), 2.95 (s, 2H, $\text{H}_{2-1''}$), 3.37 (t, 2H, $\text{H}_{2-5''}$, $J = 6.4$ Hz), 3.54 (br. s, 2H, $2 \times \text{OH}$), 3.81 (dd, 1H, H-2'a, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 3.8$ Hz), 3.94 (dd, 1H, H-2'b, $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 5.5$ Hz), 4.06 (br. s., 1H, H-3). ^{13}C NMR (100 MHz; CDCl_3) δ : 20.1 (C-5), 24.0 (C-3''), 25.0 (C-2''), 28.2 (C-4''), 29.4 (C-4''), 30.8 (C-4), 34.0 (C-2''), 37.2 (C-3''), 39.7 (C-5''), 50.9 (C-6), 53.1 (C-1''), 61.4 (C-2'), 63.9 (C-2), 68.8 (C-3), 71.4 (C-5''), 81.9 (C-1''). LC/MS analysis: Rt 10.00 min (linear gradient 0-50% B), ES (ESI): $m/z = 366.0$ [$\text{M} + \text{H}$] $^+$, 731.8 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_3$ 366.30027, found 366.30017. IR ν_{max} (thin film)/ cm^{-1} : 2902, 2848, 1670, 1201, 1136. $\alpha_D = 16.7^\circ$ ($c = 0.12$ MeOH).



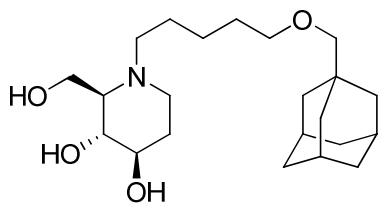
(2R,3S,4R)-2-(hydroxymethyl)piperidin-3,4-diol (**28**)

^1H NMR (500 MHz; D_2O) δ : 1.66 (m, 1H, H-5a, $J = 4.5$ Hz, $J = 11.5$ Hz, $J = 13.6$ Hz), 2.16 (m, 1H, H-5b, $J = 2.7$ Hz, $J = 5.1$ Hz, $J = 13.6$ Hz), 2.94 (ddd, 1H, H-2, $J_{2,3} = 9.5$ Hz, $J_{2,2'a} = 5.5$ Hz, $J_{2,2'b} = 3.1$ Hz), 2.97 (m, 1H, H-6a, $J = 13.5$ Hz, $J = 3.0$ Hz), 3.32 (ddd, 1H, H-6b, $J = 13.1$ Hz, $J = 4.5$ Hz, $J = 2.4$ Hz), 3.43 (t, 1H, H-3, $J_{2,3} = J_{3,4} = 9.5$ Hz), 3.68 (ddd, 1H, H-4, $J_{3,4} = 9.5$ Hz, $J_{4,5a} = 11.5$ Hz, $J_{4,5b} = 5.0$ Hz), 3.82 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.3$ Hz, $J_{2,2'a} = 5.9$ Hz), 3.93 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.3$ Hz, $J_{2,2'b} = 3.1$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 30.1 (C-5), 42.2 (C-6), 59.2 (C-2'), 60.5 (C-2), 71.0 (C-3), 71.5 (C-4). ES (ESI): $m/z = 148.1$ [$\text{M} + \text{H}$] $^+$, 295.0 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09659. IR ν_{max} (thin film)/ cm^{-1} : 3278, 2947, 1633, 1261, 1066, 1038, 1006. $\alpha_D = 12.2^\circ$ ($c = 0.33$ MeOH).



(2R,3S,4R)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**29**)

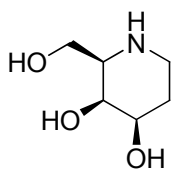
^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_{3-4''}$, $J = 7.5$ Hz), 1.37 – 1.46 (m, 2H, $\text{H}_{2-3''}$), 1.70 – 1.94 (m, 3H, H-5a, $\text{H}_{2-2''}$), 2.25 (m, 1H, H-5b, $J = 2.8$ Hz, $J = 5.3$ Hz, $J = 14.4$ Hz), 3.12 (dd, 1H, H-2, $J_{2,3} = 10.3$ Hz, $J_{2,2'a} = 2.8$ Hz), 3.18 (ddd, 1H, H-1''a, $J = 5.3$ Hz, $J = 12.4$ Hz, $J = 12.5$ Hz), 3.27 (dt, 1H, H-6a, $J = 13.4$ Hz, $J = 3.2$ Hz), 3.36 (ddd, 1H, H-1''b, $J = 5.2$ Hz, $J = 11.9$ Hz, $J = 12.9$ Hz), 3.59 (ddd, 1H, H-6b, $J = 12.9$ Hz, $J = 4.1$ Hz, $J = 2.9$ Hz), 3.63 (dd, 1H, H-3, $J_{2,3} = 10.2$ Hz, $J_{3,4} = 9.4$ Hz), 3.75 (ddd, 1H, H-4, $J_{3,4} = 9.2$ Hz, $J_{4,5a} = 11.5$ Hz, $J_{4,5b} = 4.9$ Hz), 4.00 (dd, 1H, H-2'a, $J_{2'a,2'b} = 13.4$ Hz, $J_{2,2'a} = 3.0$ Hz), 4.13 (d, 1H, H-2'b, $J_{2'a,2'b} = 13.4$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.5 (C-2''), 28.3 (C-5), 49.6 (C-6), 52.9 (C-1''), 53.7 (C-2'), 65.5 (C-2), 69.3 (C-3), 70.3 (C-4). ES (ESI): $m/z = 204.3$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15944. IR ν_{max} (thin film)/ cm^{-1} : 3331, 2937, 2866, 1676, 1453, 1058. $\alpha_D = -23.3^\circ$ ($c = 0.3$ MeOH).



(2*R*,3*S*,4*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

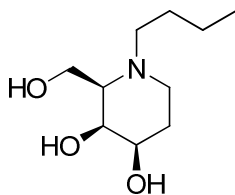
(hydroxymethyl)piperidin-3,4-diol (**30**)

^1H NMR (500 MHz; D_2O) δ : 1.43 – 1.46 (m, 2H, $\text{H}_{2-3''}$), 1.54 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.62 – 1.67 (m, 10H, $\text{H}_{2-3''}$, $\text{H}_{2-4''}$, $\text{H}_{2-2''}$), 1.73 – 1.84 (m, 1H, H_{5a}), 1.97 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.25 (br. d, 1H, H_{5b}), 3.10 (s, 2H, $\text{H}_{2-1''}$), 3.15 (br. d, 1H, $\text{H}_{-1''a}$), 3.19 (ddd, 1H, H_{-2} , $J = 4.5$ Hz, $J = 5.0$ Hz, $J = 12.5$ Hz), 3.25 (ddd, 1H, H_{6a} , $J = 2.5$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.36 (ddd, 1H, $\text{H}_{-1''a}$, $J = 4.5$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.51 (t, 2H, $\text{H}_{2-5''}$, $J = 6.5$ Hz), 3.58 (br. d, 1H, H_{6b} , $J = 12.5$ Hz), 3.63 (dd, 1H, H_{-3} , $J = 9.3$ Hz, $J = 10.1$ Hz), 3.74 (ddd, 1H, H_{-4} , $J = 4.7$ Hz, $J = 9.1$ Hz, $J = 11.3$ Hz), 3.97 (dd, 1H, $\text{H}_{-2'a}$, $J = 2.9$ Hz, $J = 13.1$ Hz), 4.14 (d, 1H, $\text{H}_{-2'b}$, $J = 13.1$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 22.3 (C-2''), 22.7 (C-3''), 28.0 (C-5), 28.0 (C-4''), 28.3 (C-4''), 33.6 (C-2''), 36.8, 39.3 (C-3'', C-5''), 49.7 (C-6), 52.9 (C-1''), 53.8 (C-2'), 65.6 (C-2), 69.2 (C-3), 70.2 (C-4), 71.3 (C-5''), 81.8 (C-1''). ES (ESI): $m/z = 382.6$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{10}\text{NO}_4$ 382.29519, found 382.29532. IR ν_{max} (thin film)/ cm^{-1} : 3365, 2902, 2848, 1639, 1450, 1088. $\alpha_D = -19.2^\circ$ ($c = 0.04$ MeOH).



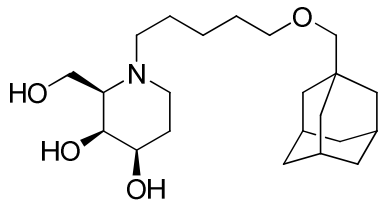
(2*R*,3*R*,4*R*)-2-(hydroxymethyl)piperidin-3,4-diol (**31**)

^1H NMR (500 MHz; D_2O) δ : 1.98 – 2.11 (m, 2H, H_{2-5}), 3.16 (ddd, 1H, H_{6a} , $J_{6a,6b} = J_{5a6a} = 13.2$ Hz, $J_{5b,6a} = 4.0$ Hz), 3.44 (ddd, 1H, H_{-2} , $J_{2,2'a} = 8.6$ Hz, $J_{2,2'b} = 4.9$ Hz, $J_{2,3} = 1.3$ Hz), 3.55 (ddd, 1H, H_{6b} , $J_{6a,6b} = 13.1$ Hz, $J_{5a,6b} = 6.7$ Hz, $J_{5b,6b} = 2.3$ Hz), 3.90 (dd, 1H, $\text{H}_{-2'a}$, $J_{2'a,2'b} = 12.1$ Hz, $J_{2,2'a} = 8.7$ Hz), 3.95 (dd, 1H, $\text{H}_{-2'b}$, $J_{2'a,2'b} = 12.1$ Hz, $J_{2,2'b} = 4.9$ Hz), 4.17 (t 1H, H_{-3} , $J_{2,3} = J_{3,4} = 1.3$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 24.4 (C-5), 42.6 (C-6), 59.8 (C-2'), 60.2 (C-2), 66.2 (C-3), 67.7 (C-4). ES (ESI): $m/z = 148.2$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{13}\text{NO}_3$ 148.09682, found 148.09675. IR ν_{max} (thin film)/ cm^{-1} : 3285, 2922, 1654, 1397, 1145, 1104, 1046, 1020, 991. $\alpha_D = 18.7^\circ$ ($c = 1.36$ MeOH).



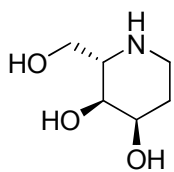
(2*R*,3*R*,4*R*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**32**)

^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_{3-4''}$, $J = 7.0$ Hz), 1.32 – 1.43 (m, 2H, $\text{H}_{2-3''}$), 1.66 – 1.78 (m, 2H, $\text{H}_{2-2''}$), 1.98 (br. d, 1H, H_{5a} , $J = 13.5$ Hz), 2.08 – 2.17 (m, 1H, H_{5b}), 3.16 – 3.23 (m, 2H, $\text{H}_{-1''}$, H_{6a}), 3.31 (ddd, 1H, $\text{H}_{-1''b}$, $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.40 (m, 1H, H_{-2}), 3.51 – 3.55 (m, 1H, H_{6b}), 3.89 – 3.92 (m, 1H, H_{-4}), 4.02 (d, 2H, $\text{H}_{2-2'}$, $J = 4.5$ Hz), 4.23 (s, 1H, H_{-3}). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.4 (C-2''), 24.4 (C-5), 49.5 (C-6), 52.1 (C-1''), 59.4 (C-2'), 63.7 (C-2), 67.3 (C-4), 69.0 (C-3). ES (ESI): $m/z = 204.2$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15950. IR ν_{max} (thin film)/ cm^{-1} : 3359, 2941, 2931, 1653, 1415, 1195, 1113, 1019. $\alpha_D = -16.6^\circ$ ($c = 0.01$ MeOH).



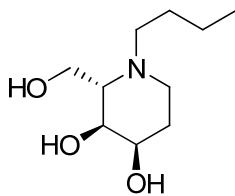
(2*R*,3*R*,4*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)piperidin-3,4-diol (**33**)

^1H NMR (500 MHz; D_2O) δ : 1.43 – 1.45 (m, 2H, $\text{H}_{2-3''}$), 1.53 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.64 – 1.85 (m, 10H, $\text{H}_{2-4''}$, $\text{H}_{2-3''}$, $\text{H}_{2-2''}$), 1.96 (br. s, 4H, $3 \times \text{H}_{4''}$, H-5a), 2.08 – 2.16 (m, 1H, H-5b), 3.11 (s, 2H, $\text{H}_{2-1''}$), 3.19 – 3.23 (m, 2H, H-1''a, H-6a), 3.28 – 3.35 (m, 1H, H-1''b), 3.41 (s, 1H, H-2), 3.51 – 3.54 (m, 3H, $\text{H}_{2-5''}$, H-6b), 3.90 (br. d, 1H, H-4, $J = 11.0$ Hz), 4.02 (br. s, 2H, $\text{H}_{2-2'}$), 4.23 (br. s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 22.7 (C-2''), 22.9 (C-3''), 24.7 (C-5), 27.9 (C-4''), 28.0 (C-4''), 33.6 (C-2''), 36.6, 39.2 (C-3'', C-5''), 50.1 (C-6), 52.9 (C-1''), 59.8 (C-2'), 63.9 (C-2), 67.3 (C-4), 69.3 (C-3), 71.2 (C-5''), 81.7 (C-1''). ES (ESI): $m/z = 382.4$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29534. IR ν_{max} (thin film)/ cm^{-1} : 3365, 2903, 1674, 1435, 1202, 1133. $\alpha_{\text{D}} = -4.5^\circ$ ($c = 0.09$ MeOH).



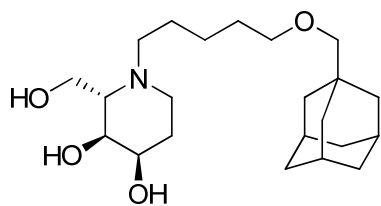
(2*S*,3*R*,4*R*)-2-(hydroxymethyl)piperidin-3,4-diol (**34**)

^1H NMR (400 MHz; D_2O) δ : 1.95 – 2.02 (m, 1H, H-5a), 2.09 (ddd, 1H, H-5b, $J_{5a,5b} = 12.4$ Hz, $J_{5a,6a} = 5.6$ Hz, $J_{5a,6b} = 2.8$ Hz), 3.24 – 3.31 (m, 2H, H_{2-6}), 3.43 (ddd, 1H, H-2, $J_{2,3} = 10.0$ Hz, $J_{2,2'a} = 5.5$ Hz, $J_{2,2'b} = 3.5$ Hz), 3.85 (dd, 1H, H-3, $J_{2,3} = 10.5$ Hz, $J_{3,4} = 3.0$ Hz), 3.90 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.5$ Hz, $J_{2'a} = 5.5$ Hz), 3.95 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.5$ Hz, $J_{2,2'b} = 3.5$ Hz), 4.19 (ddd, 1H, H-4, $J_{3,4} = 2.7$ Hz, $J_{4,5a} = 4.7$ Hz, $J_{4,5b} = 2.7$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 27.2 (C-5), 38.3 (C-6), 55.8 (C-2), 58.0 (C-2'), 65.6 (C-4), 66.4 (C-3). ES (ESI): $m/z = 148.1$ [$\text{M} + \text{H}$] $^+$, 295.0 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09665. IR ν_{max} (thin film)/ cm^{-1} : 3318, 2953, 1600, 1429, 1260, 1067, 1008, 987, 944. $\alpha_{\text{D}} = -87.7^\circ$ ($c = 0.13$ MeOH).



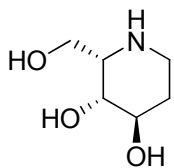
(2*S*,3*R*,4*R*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**35**)

^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_{3-4''}$, $J = 6.5$ Hz), 1.38 – 1.48 (m, 2H, $\text{H}_{2-3''}$), 1.68 – 1.84 (m, 2H, $\text{H}_{2-2''}$), 1.98 – 2.12 (m, 2H, H_{2-5}), 3.21 (ddd, 1H, H-1''a, $J = 5.5$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.34 – 3.41 (m, 4H, H-1''b, H-2, H_{2-6}), 3.92 (dd, 1H, H-3, $J = 2.5$ Hz, $J = 10.0$ Hz), 4.03 (dd, 1H, H-2'a, $J = 3.0$ Hz, $J = 13.5$ Hz), 4.09 (dd, 1H, H-2'b, $J = 1.0$ Hz, $J = 13.5$ Hz), 4.20 (d, 1H, H-4, $J = 3.0$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.6 (C-2''), 27.0 (C-5), 45.9 (C-6), 53.0 (C-1''), 53.7 (C-2'), 61.2 (C-2), 65.2 (C-4), 65.9 (C-3). ES (ESI): $m/z = 204.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15941. IR ν_{max} (thin film)/ cm^{-1} : 3365, 2957, 1075. $\alpha_{\text{D}} = 1.9^\circ$ ($c = 0.21$ MeOH).

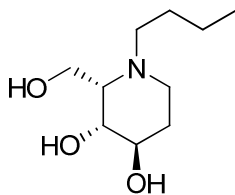


(2*S*,3*R*,4*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)piperidin-3,4-diol (**36**)

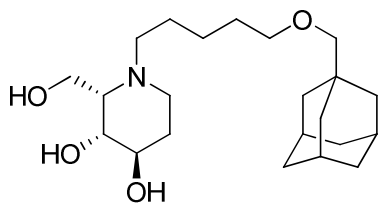
^1H NMR (500 MHz; D_2O) δ : 1.41 – 1.48 (m, 2H, $\text{H}_2\text{-3''}$), 1.54 (s, 6H, $3 \times \text{H}_2\text{-5''}$), 1.63 – 1.85 (m, 10H, $\text{H}_2\text{-4''}$, $\text{H}_2\text{-3''}$, $\text{H}_2\text{-2''}$), 1.96 (br. s, 3H, $3 \times \text{H-4''}$), 2.02 – 2.11 (m, 2H, $\text{H}_2\text{-5}$), 3.11 (s, 2H, $\text{H}_2\text{-1''}$), 3.22 (ddd, 1H, H-1''a , $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 12.5$ Hz), 3.33 – 3.38 (m, 4H, H-1''b , H-2 , $\text{H}_2\text{-6}$), 3.52 (t, 2H, $\text{H}_2\text{-5''}$, $J = 6.0$ Hz), 3.92 (dd, 1H, H-3 , $J = 2.5$ Hz, $J = 10.5$ Hz), 4.01 (d, 1H, H-2'a , $J = 11.0$ Hz), 4.09 (d, 1H, H-2'b , $J = 13.0$ Hz), 4.20 (d, 1H, H-4 , $J = 2.0$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 22.3 (C-2''), 22.7 (C-3''), 27.0 (C-5), 27.9 (C-4''), 28.0 (C-4''), 33.6 (C-2''), 36.7, 39.2 (C-3'', C-5''), 46.0 (C-1''), 53.0 (C-6), 53.8 (C-2'), 61.2 (C-2), 65.1 (C-4), 65.9 (C-3), 71.2 (C-5''), 81.8 (C-1''). ES (ESI): $m/z = 382.6$ [$\text{M} + \text{H}$] $^+$, 763.6 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29523. IR ν_{max} (thin film)/ cm^{-1} : 3423, 2900, 2847, 1067. $\alpha_{\text{D}} = 2.5^\circ$ ($c = 0.33$ MeOH).



(2*S*,3*S*,4*R*)-2-(hydroxymethyl)piperidin-3,4-diol (**37**)
 ^1H NMR (400 MHz; D_2O) δ : 1.65 (ddd, 1H, H-5a , $J_{5a,5b} = 14.8$ Hz, $J_{5a,6a} = 7.6$ Hz, $J_{5a,6b} = 3.6$ Hz), 1.98 – 2.06 (m, 1H, H-5b), 2.91 – 2.98 (m, 2H, $\text{H}_2\text{-6}$), 3.21 (ddd, 1H, H-2 , $J_{2,3} = 2.4$ Hz, $J_{2,2'a} = 7.6$ Hz, $J_{2,2'b} = 6.0$ Hz), 3.69 (dd, 1H, H-2'a , $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'a} = 7.6$ Hz), 3.73 (dd, 1H, H-2'b , $J_{2'a,2'b} = 11.6$ Hz, $J_{2,2'b} = 6.0$ Hz), 3.77 (dd, 1H, H-3 , $J_{3,4} = 4.8$ Hz, $J_{2,3} = 2.4$ Hz), 3.94 (dd, 1H, H-4 , $J_{3,4} = 4.8$ Hz, $J_{4,5} = 7.8$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 27.4 (C-5), 39.5 (C-6), 56.3 (C-2), 61.3 (C-2'), 67.7 (C-4), 68.7 (C-3). ES (ESI): $m/z = 148.1$ [$\text{M} + \text{H}$] $^+$, 295.3 [$2\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09642. IR ν_{max} (thin film)/ cm^{-1} : 3337, 2930, 1651, 1456, 1430, 1183, 1078, 1042, 982. $\alpha_{\text{D}} = -11.6$ ($c = 0.94$, H_2O).

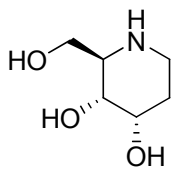


(2*S*,3*S*,4*R*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**38**)
 ^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{C}_3\text{-4''}$, $J = 6.5$ Hz), 1.40 – 1.45 (m, 2H, $\text{H}_2\text{-3''}$), 1.67 – 1.81 (m, 2H, $\text{H}_2\text{-2''}$), 1.89 (dd, 1H, H-5a , $J = 3.6$ Hz, $J = 15.2$ Hz), 2.27 – 2.34 (m, 1H, H-5b , $J = 14.0$ Hz, $J = 3.2$ Hz, $J = 6.4$ Hz, $J = 2.8$ Hz), 3.22 (ddd, 1H, H-1''a , $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.30 (ddd, 1H, H-1''b , $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.37 – 3.38 (m, 2H, $\text{H}_2\text{-6}$), 3.58 (br. s, 1H, H-2), 3.91 – 4.02 (m, 2H, H-4 , H-2'a), 4.05 (dd, 1H, H-2'b , $J = 4.5$ Hz, $J = 13.0$ Hz), 4.09 (br. s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.0 (C-2''), 24.4 (C-5), 46.5 (C-6), 53.2 (C-1''), 59.3 (C-2'), 60.2 (C-2), 64.9 (C-4), 69.5 (C-3). ES (ESI): $m/z = 203.6$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15868. IR ν_{max} (thin film)/ cm^{-1} : 3359, 2930, 1653, 1398, 1148, 1016. $\alpha_{\text{D}} = 1.0^\circ$ ($c = 0.03$ MeOH).



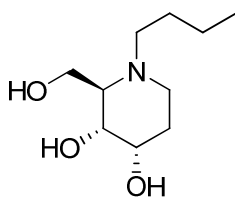
(2*S*,3*S*,4*R*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)piperidin-3,4-diol (**39**)

^1H NMR (500 MHz; D_2O) δ : 1.43 – 1.47 (m, 2H, $\text{H}_2\text{-3''}$), 1.54 (s, 6H, $3 \times \text{H}_2\text{-5''}$), 1.63 – 1.90 (m, 11H, $\text{H}_2\text{-4''}$, $\text{H}_2\text{-3''}$, $\text{H}_2\text{-2''}$, H-5a), 1.96 (br. s, 3H, $3 \times \text{H-4''}$), 2.28 – 2.34 (m, 1H, H-5b), 3.10 (s, 2H, $\text{H}_2\text{-1''}$), 3.21 – 3.47 (m, 4H, $\text{H}_2\text{-1''}$, $\text{H}_2\text{-6}$), 3.52 (t, 2H, $\text{H}_2\text{-5''}$, $J = 6.5$ Hz), 3.58 (br. s, 1H, H-2), 3.98 – 4.06 (m, 3H, H-4, $\text{H}_2\text{-2'}$), 4.12 (br. s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 21.8 (C-2''), 22.8 (C-3''), 24.4 (C-5), 27.9 (C-4''), 28.0 (C-4''), 33.6 (C-2''), 36.7, 39.3 (C-3'', C-5''), 46.6 (C-6), 53.2 (C-1''), 59.6 (C-2'), 60.2 (C-2), 64.8 (C-4), 69.5 (C-3), 71.3 (C-5''), 81.7 (C-1''). ES (ESI): $m/z = 382.2$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29483. IR ν_{max} (thin film)/ cm^{-1} : 3337, 2947, 1675, 1421, 1203, 1016. $\alpha_{\text{D}} = 6.0^\circ$ ($c = 0.36$ MeOH).



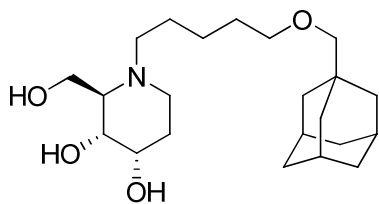
(2*R*,3*S*,4*S*)-2-(hydroxymethyl)piperidin-3,4-diol (**40**)

^1H NMR (400 MHz; D_2O) δ : 1.90 – 1.99 (m, 1H, H-5a), 2.05 (ddd, 1H, H-5b, $J_{5a,5b} = 15.2$ Hz, $J_{5a,6a} = 6.8$ Hz, $J_{5a,6b} = 3.2$ Hz), 3.17 – 3.24 (m, 2H, $\text{H}_2\text{-6}$), 3.37 (ddd, 1H, H-2, $J_{2,3} = 10.4$ Hz, $J_{2,2'a} = 5.6$ Hz, $J_{2,2'b} = 3.2$ Hz), 3.80 (dd, 1H, H-3, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 2.8$ Hz), 3.85 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.8$ Hz, $J_{2,2'a} = 5.6$ Hz), 3.92 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.8$ Hz, $J_{2,2'b} = 3.2$ Hz), 4.07 (ddd, 1H, H-4, $J_{3,4} = 2.4$ Hz, $J_{4,5a} = 3.6$ Hz, $J_{4,5b} = 2.8$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 27.8 (C-5), 38.6 (C-6), 56.1 (C-2), 58.6 (C-2'), 66.1 (C-4), 66.9 (C-3). ES (ESI): $m/z = 148.2$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09657. IR ν_{max} (thin film)/ cm^{-1} : 3331, 2947, 2808, 1615, 1428, 1340, 1270, 1197, 1066, 987, 944. $\alpha_{\text{D}} = 48.0^\circ$ ($c = 1.17$ MeOH).



(2*R*,3*S*,4*S*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**41**)

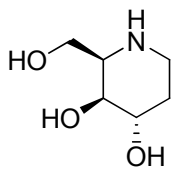
^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_3\text{-4''}$, $J = 7.0$ Hz), 1.38 – 1.46 (m, 2H, $\text{H}_2\text{-3''}$), 1.68 – 1.81 (m, 2H, $\text{H}_2\text{-2''}$), 1.99 – 2.10 (m, 2H, $\text{H}_2\text{-5}$), 3.21 (ddd, 1H, H-1'a, $J = 5.5$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.34 – 3.41 (m, 4H, H-1'b, H-2, $\text{H}_2\text{-6}$), 3.92 (dd, 1H, H-3, $J = 3.0$ Hz, $J = 10.5$ Hz), 4.01 (dd, 1H, H-2'a, $J = 3.0$ Hz, $J = 6.0$ Hz), 4.09 (dd, 1H, H-2'b, $J = 1.0$ Hz, $J = 13.0$ Hz), 4.19 (d, 1H, H-4, $J = 3.0$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.6 (C-2''), 27.0 (C-5), 45.9 (C-6), 53.0 (C-1''), 53.7 (C-2'), 61.2 (C-2), 65.2 (C-4), 65.9 (C-3). ES (ESI): $m/z = 203.9$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15940. IR ν_{max} (thin film)/ cm^{-1} : 3331, 2959, 2872, 1652, 1385, 1200, 1066. $\alpha_{\text{D}} = 2.5^\circ$ ($c = 0.4$ MeOH).



(2*R*,3*S*,4*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

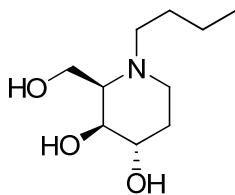
(hydroxymethyl)piperidin-3,4-diol (**42**)

^1H NMR (500 MHz; D_2O) δ : 1.42 – 1.46 (m, 2H, $\text{H}_2\text{-3''}$), 1.54 (s, 6H, $3 \times \text{H}_2\text{-5''}$), 1.62 – 1.81 (m, 10H, $\text{H}_2\text{-4''}$, $\text{H}_2\text{-3''}$, $\text{H}_2\text{-2''}$), 1.97 (br. s, 3H, $3 \times \text{H-4''}$), 2.03 – 2.10 (m, 2H, $\text{H}_2\text{-5}$), 3.07 (s, 2H, $\text{H}_2\text{-1''}$), 3.21 (ddd, 1H, H-1''a , $J = 5.5$ Hz, $J = 12.0$ Hz, $J = 12.5$ Hz), 3.31 – 3.36 (m, 4H, H-1''b , H-2 , $\text{H}_2\text{-6}$), 3.48 (t, 2H, $\text{H}_2\text{-5''}$, $J = 6.0$ Hz), 3.92 (dd, 1H, H-3 , $J = 2.5$ Hz, $J = 10.5$ Hz), 3.98 (dd, 1H, H-2'a , $J = 2.5$ Hz, $J = 13.0$ Hz), 4.09 (d, 1H, H-2'b , $J = 13.0$ Hz), 4.19 (d, 1H, H-4 , $J = 2.5$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 22.4 (C-2''), 22.8 (C-3''), 27.0 (C-5), 28.1 (C-4''), 28.2 (C-4''), 33.8 (C-2''), 36.9, 39.4 (C-3'', C-5''), 53.0 (C-1''), 53.9 (C-2'), 61.3 (C-2), 65.1 (C-4), 65.9 (C-3), 71.4 (C-5''), 81.8 (C-1''). ES (ESI): $m/z = 381.9$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29520. IR ν_{max} (thin film)/ cm^{-1} : 3331, 2901, 2847, 1450, 1111, 1075. $\alpha_{\text{D}} = -0.3^\circ$ ($c = 0.6$ MeOH).



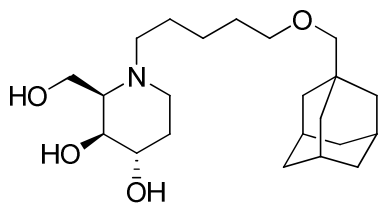
(2*R*,3*R*,4*S*)-2-(hydroxymethyl)piperidin-3,4-diol (**43**)

^1H NMR (400 MHz; D_2O) δ : 1.88 (ddd, 1H, H-5a , $J_{5a,5b} = 15.2$ Hz, $J_{5a,6a} = 5.6$ Hz, $J_{5a,6b} = 2.4$ Hz), 2.21 - 2.29 (m, 1H, H-5b), 3.26 - 3.34 (m, 2H, $\text{H}_2\text{-6}$), 3.58 (ddd, 1H, H-2 , $J_{2,3} = 2.0$ Hz, $J_{2,2'a} = 8.4$ Hz, $J_{2,2'b} = 5.2$ Hz), 3.85 (dd, 1H, H-2'a , $J_{2'a,2'b} = 12.2$ Hz, $J_{2,2'a} = 8.6$ Hz), 3.90 (dd, 1H, H-2'b , $J_{2'a,2'b} = 12.2$ Hz, $J_{2,2'b} = 3.9$ Hz), 3.98 (dt, 1H, H-3 , $J_{3,4} = 4.3$ Hz, $J_{2,3} = 1.2$ Hz), 4.07 (dd, 1H, H-4 , $J_{3,4} = 3.0$ Hz, $J_{4,5} = 6.8$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 24.2 (C-5), 39.3 (C-6), 56.2 (C-2), 60.0 (C-2'), 65.4 (C-4), 66.4 (C-3). ES (ESI): $m/z = 148.2$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09666. IR ν_{max} (thin film)/ cm^{-1} : 3315, 3046, 2831, 1616, 1412, 1273, 1212, 1080, 1081, 1044. $\alpha_{\text{D}} = 10.2^\circ$ ($c = 1.04$ MeOH).



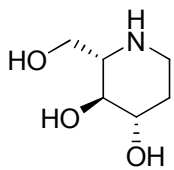
(2*R*,3*R*,4*S*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**44**)

^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_3\text{-4''}$, $J = 7.5$ Hz), 1.36 – 1.44 (m, 2H, $\text{H}_2\text{-3''}$), 1.68 - 1.82 (m, 2H, $\text{H}_2\text{-2''}$), 1.88 (dd, 1H, H-5a , $J = 2.5$ Hz, $J = 15.0$ Hz), 2.30 (m, 1H, H-5b), 3.22 (ddd, 1H, H-1''a , $J = 5.5$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.30 (ddd, 1H, H-1''b , $J = 5.0$ Hz, $J = 11.5$ Hz, $J = 13.5$ Hz), 3.36 – 3.38 (m, 2H, $\text{H}_2\text{-6}$), 3.58 (br. s, 1H, H-2), 3.96 (br. s, 1H, H-4), 3.99 (dd, 1H, H-2'a , $J = 4.0$ Hz, $J = 13.0$ Hz), 4.04 (dd, 1H, H-2'b , $J = 5.0$ Hz, $J = 13.0$ Hz), 4.11 (br s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.1 (C-2''), 24.4 (C-5), 46.5 (C-6), 51.2 (C-1''), 59.3 (C-2'), 60.2 (C-2), 64.9 (C-4), 69.5 (C-3). ES (ESI): $m/z = 204.0$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15944. IR ν_{max} (thin film)/ cm^{-1} : 3355, 2965, 1652, 1436, 1264, 1067, 1017. $\alpha_{\text{D}} = -3.4^\circ$ ($c = 0.5$ MeOH).

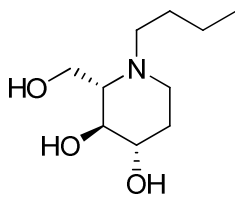


(2*R*,3*R*,4*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-(hydroxymethyl)piperidin-3,4-diol (**45**)

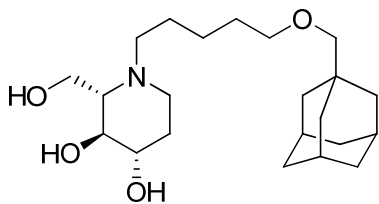
^1H NMR (500 MHz; D_2O) δ : 1.43 – 1.45 (m, 2H, $\text{H}_{2-3''}$), 1.55 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.63 – 1.89 (m, 11H, $\text{H}_{2-4''}$, $\text{H}_{2-3''}$, $\text{H}_{2-2''}$, H-5a), 1.96 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.32 (m, 1H, H-5b), 3.07 (s, 2H, $\text{H}_{2-1''}$), 3.19 – 3.43 (m, 4H, $\text{H}_{2-1''}$, H_{2-6}), 3.49 (t, 2H, $\text{H}_{2-5''}$, $J = 6.5$ Hz), 3.55 (br. s, 1H, H-2), 3.98 – 4.05 (m, 3H, H-4, $\text{H}_{2-2'}$), 4.09 (br. s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 21.8 (C-2''), 22.9 (C-3''), 24.5 (C-5), 28.2 (C-4''), 28.3 (C-4''), 33.8 (C-2''), 36.9, 39.4 (C-3'', C-5''), 53.6 (C-6), 53.2 (C-1''), 59.6 (C-2'), 60.4 (C-2), 64.7 (C-4), 69.5 (C-3), 71.4 (C-5''), 81.8 (C-1''). ES (ESI): $m/z = 381.9$ $[\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 383.29854, found 383.29852. IR ν_{max} (thin film)/ cm^{-1} : 3355, 2901, 2854, 1652, 1373, 1261, 1079. $\alpha_{\text{D}} = -4.5^\circ$ ($c = 0.01$ MeOH).



(2*S*,3*R*,4*S*)-2-(hydroxymethyl)piperidin-3,4-diol (**46**)
 ^1H NMR (300 MHz; D_2O) δ : 1.75 (m, 1H, H-5a), 2.24 (br. d, 1H, H-5b, $J = 13.4$ Hz), 3.08 – 3.17 (m, 2H, H-2, H-6a), 3.45 – 3.58 (m, 2H, H-3, H-6b), 3.75 (brs, 1H, H-4), 3.87 – 3.98 (m, 2H, H-2'a, H-2'b). ^{13}C NMR (75 MHz; D_2O) δ : 29.5 (C-5), 42.8 (C-6), 58.6 (C-2'), 61.0 (C-2), 70.5 (C-3), 71.4 (C-4). ES (ESI): $m/z = 148.1$ $[\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{14}\text{NO}_3$ 148.09682, found 148.09673. IR ν_{max} (thin film)/ cm^{-1} : 3370, 2936, 1645, 1203, 1075, 1017. $\alpha_{\text{D}} = -14.9^\circ$ ($c = 0.23$ MeOH).



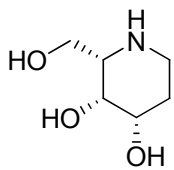
(2*S*,3*R*,4*S*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**47**)
 ^1H NMR (500 MHz; D_2O) δ : 0.95 (t, 3H, $\text{H}_{3-4''}$, $J = 7.4$ Hz), 1.34 – 1.46 (m, 2H, $\text{H}_{2-3''}$), 1.64 – 1.82 (m, 3H, H-5a, $\text{H}_{2-2''}$), 2.24 (m, 1H, H-5b, $J = 2.8$ Hz, $J = 5.3$ Hz, $J = 14.4$ Hz), 3.12 (dd, 1H, H-2, $J_{2,3} = 10.3$ Hz, $J_{2,2'a} = 1.7$ Hz), 3.17 (ddd, 1H, H-1''a, $J = 5.2$ Hz, $J = 11.7$ Hz, $J = 13.2$ Hz), 3.24 (dt, 1H, H-6a, $J = 3.0$ Hz, $J = 13.2$), 3.36 (ddd, 1H, H-1''b, $J = 5.2$ Hz, $J = 11.8$ Hz, $J = 13.3$ Hz), 3.58 (ddd, 1H, H-6b, $J = 2.7$ Hz, $J = 4.3$ Hz, $J = 13.0$ Hz), 3.63 (dd, 1H, H-3, $J_{2,3} = 10.2$ Hz, $J_{3,4} = 9.4$ Hz), 3.73 (ddd, 1H, H-4, $J_{3,4} = 9.2$ Hz, $J_{4,5a} = 11.5$ Hz, $J_{4,5b} = 4.9$ Hz), 3.99 (dd, 1H, H-2'a, $J_{2'a,2'b} = 13.4$ Hz, $J_{2,2'a} = 3.0$ Hz), 4.14 (dd, 1H, H-2'b, $J_{2'a,2'b} = 13.4$ Hz, $J_{2,2'b} = 1.0$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.5 (C-2''), 28.3 (C-5), 49.6 (C-6), 52.9 (C-1''), 53.7 (C-2'), 65.5 (C-2), 69.3 (C-3), 70.3 (C-4). ES (ESI): $m/z = 204.2$ $[\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15951. IR ν_{max} (thin film)/ cm^{-1} : 3330, 2941, 2837, 1653, 1457, 1203, 1116. $\alpha_{\text{D}} = 3.6^\circ$ ($c = 0.06$ MeOH).



(2*S*,3*R*,4*S*)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

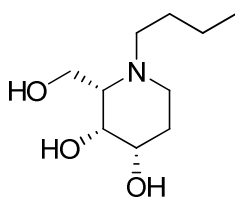
(hydroxymethyl)piperidin-3,4-diol (**48**)

^1H NMR (500 MHz; D_2O) δ : 1.41 – 1.48 (m, 2H, $\text{H}_{2-3''}$), 1.53 (s, 6H, $3 \times \text{H}_{2-5''}$), 1.62 – 1.85 (m, 11H, $\text{H}_{2-3''}$, $\text{H}_{2-4''}$, $\text{H}_{2-2''}$, H-5a), 1.93 (br. s, 3H, $3 \times \text{H}_{4''}$), 2.24 (br. d, 1H, H-5b), 3.10 (s, 2H, $\text{H}_{2-1''}$), 3.13 – 3.27 (m, 3H, H-2, H-1''a, H-6a), 3.36 (ddd, 1H, H-1''b, $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 13.0$ Hz), 3.52 (t, 2H, $\text{H}_{2-5''}$, $J = 6.5$ Hz), 3.58 (br. d, 1H, H-6b, $J = 12.5$ Hz), 3.64 (dd, 1H, H-3, $J = 9.5$ Hz, $J = 10.0$ Hz), 3.75 (ddd, 1H, H-4, $J = 5.0$ Hz, $J = 9.0$ Hz, $J = 11.5$ Hz), 3.98 (dd, 1H, H-2'a, $J = 2.0$ Hz, $J = 13.0$ Hz), 4.14 (d, 1H, H-2'b, $J = 13.5$ Hz). ^{13}C NMR (125 MHz; D_2O) δ : 22.3 (C-2''), 22.7 (C-3''), 27.9 (C-5), 28.0 (C-4''), 28.3 (C-4''), 33.6 (C-2''), 36.7, 39.2 (C-3'', C-5''), 49.7 (C-6), 52.9 (C-1''), 53.7 (C-2'), 65.6 (C-2), 69.3 (C-3), 70.3 (C-4), 71.2 (C-5''), 81.8 (C-1''). ES (ESI): m/z = 382.4 $[\text{M} + \text{H}]^+$, 763.2 $[2\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29538. IR ν_{max} (thin film)/ cm^{-1} : 3325, 2902, 1671, 1201, 1134. $\alpha_{\text{D}} = 1.3^\circ$ ($c = 0.16$ MeOH).



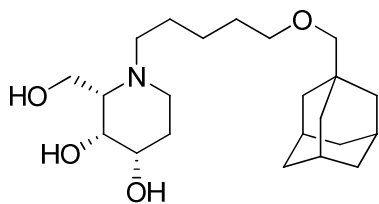
(2*S*,3*S*,4*S*)-2-(hydroxymethyl)piperidin-3,4-diol (**49**)

^1H NMR (400 MHz; D_2O) δ : 1.93 – 2.01 (m, 2H, H_{2-5}), 3.02 (ddd, 1H, H-6a, $J_{6a,6b} = J_{5a,6a} = 13.2$ Hz, $J_{5b,6a} = 4.0$ Hz), 3.29 (ddd, 1H, H-2, $J_{2,2'a} = 8.4$ Hz, $J_{2,2'b} = 5.2$ Hz, $J_{2,3} = 1.2$ Hz), 3.41 (ddd, 1H, H-6b, $J_{6a,6b} = 13.2$ Hz, $J_{5a,6b} = 4.4$ Hz, $J_{5b,6b} = 2.4$ Hz), 3.78 (dd, 1H, H-2'a, $J_{2'a,2'b} = 12.4$ Hz, $J_{2,2'a} = 8.8$ Hz), 3.85 (dd, 1H, H-2'b, $J_{2'a,2'b} = 12.4$ Hz, $J_{2,2'b} = 5.2$ Hz), 4.03 (t 1H, H-3, $J_{2,3} = J_{3,4} = 1.2$ Hz). ^{13}C NMR (100 MHz; D_2O) δ : 24.5 (C-5), 42.6 (C-6), 59.9 (C-2'), 60.4 (C-2), 66.2 (C-3), 67.8 (C-4). ES (ESI): m/z = 148.4 $[\text{M} + \text{H}]^+$, 295.3 $[\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_6\text{H}_{13}\text{NO}_3$ 148.09682, found 148.09675. IR ν_{max} (thin film)/ cm^{-1} : 3301, 2953, 2843, 1615, 1417, 1302, 1142, 1106, 1046, 996. $\alpha_{\text{D}} = -58.8^\circ$ ($c = 0.96$ MeOH).



(2*S*,3*S*,4*S*)-1-butyl-2-(hydroxymethyl)piperidin-3,4-diol (**50**)

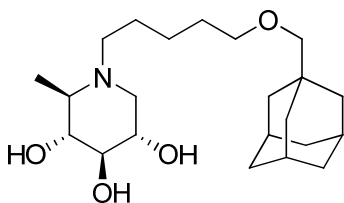
^1H NMR (500 MHz; D_2O) δ : 0.96 (t, 3H, $\text{H}_{3-4''}$, $J = 7.0$ Hz), 1.30 – 1.45 (m, 2H, $\text{H}_{2-3''}$), 1.65 – 1.78 (m, 2H, $\text{H}_{2-2''}$), 1.98 (dd, 1H, H-5a, $J = 3.0$ Hz, $J = 14.0$ Hz), 2.09 – 2.17 (m, 1H, H-5b), 3.16 – 3.23 (m, 2H, H-1'', H-6a), 3.30 (ddd, 1H, H-1''b, $J = 5.5$ Hz, $J = 12.0$ Hz, $J = 12.5$ Hz), 3.41 (m, 1H, H-2), 3.51 – 3.60 (m, 1H, H-6b), 3.89 – 3.92 (m, 1H, H-4), 4.02 (d, 2H, $\text{H}_{2-2'}$, $J = 4.5$ Hz), 4.23 (s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 12.8 (C-4''), 19.4 (C-3''), 24.0 (C-2''), 24.7 (C-5), 50.0 (C-6), 52.8 (C-1''), 59.7 (C-2'), 63.8 (C-2), 67.3 (C-4), 69.3 (C-3). ES (ESI): m/z = 204.2 $[\text{M} + \text{H}]^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{10}\text{H}_{22}\text{NO}_3$ 204.15942, found 204.15951. IR ν_{max} (thin film)/ cm^{-1} : 3330, 2947, 2837, 1653, 1457, 1203, 1113, 1019. $\alpha_{\text{D}} = 0.0^\circ$ ($c = 0.03$ MeOH).



(2S,3S,4S)-1-[5-(adamantan-1-yl-methoxy)pentyl]-2-

(hydroxymethyl)piperidin-3,4-diol (**51**)

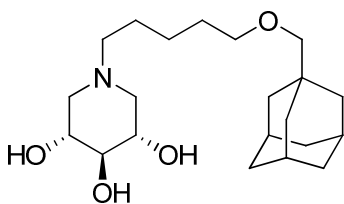
^1H NMR (500 MHz; D_2O) δ : 1.41 – 1.44 (m, 2H, $\text{H}_2\text{-3}''$), 1.54 (s, 6H, $3 \times \text{H}_2\text{-5}''$), 1.60 – 1.83 (m, 10H, $\text{H}_2\text{-4}''$, $\text{H}_2\text{-3}''$, $\text{H}_2\text{-2}''$), 1.96 (br. s, 4H, $3 \times \text{H-4}''$, H-5a), 2.07 – 2.18 (m, 1H, H-5b), 3.06 (s, 2H, $\text{H}_2\text{-1}''$), 3.15 – 3.20 (m, 2H, H-1''a, H-6a), 3.29 (ddd, 1H, H-1''b, $J = 5.0$ Hz, $J = 12.0$ Hz, $J = 12.5$ Hz), 3.38 (s, 1H, H-2), 3.46 – 3.58 (m, 3H, $\text{H}_2\text{-5}''$, H-6b), 3.89 (br. d, 1H, H-4, $J = 11.0$ Hz), 4.00 (d, 2H, $\text{H}_2\text{-2}'$, $J = 4.0$ Hz), 4.22 (s, 1H, H-3). ^{13}C NMR (125 MHz; D_2O) δ : 21.9 (C-2''), 22.8 (C-3''), 24.8 (C-5), 28.1 (C-4''), 28.2 (C-4'), 33.7 (C-2''), 36.9, 39.4 (C-3'', C-5''), 50.1 (C-6), 52.9 (C-1''), 59.9 (C-2'), 64.2 (C-2), 67.3 (C-4), 69.3 (C-3), 71.4 (C-5''), 81.8 (C-1''). ES (ESI): $m/z = 382.4$ [$\text{M} + \text{H}$] $^+$. HR-MS [QTOF, MH^+] m/z calculated for $\text{C}_{22}\text{H}_{40}\text{NO}_4$ 382.29519, found 382.29540. IR ν_{max} (thin film)/ cm^{-1} : 3325, 2903, 2843, 1676, 1433, 1203, 1133. $\alpha_{\text{D}} = -20.3^\circ$ ($c = 0.27$ MeOH).



N-[5-(Adamantan-1-yl-methoxy)-pentyl]-1,6-dideoxynojirimycin

(**52**).

^1H NMR (400 MHz, $\text{CDCl}_3/\text{MeOD}$, 1/1) δ : 3.69 – 3.62 (m, 1H, H-2), 3.38 (t, $J = 6.3$ Hz, 2H, $\text{CH}_2\text{-5}$ pentyl), 3.25 (dd, $J = 8.8$ Hz, 1H, H-3), 3.19 – 3.11 (m, 2H, H-1a, H-4), 2.95 (s, 2H, $\text{OCH}_2\text{-Ada}$), 2.94 – 2.84 (m, 1H, CHH-1 pentyl), 2.80 – 2.67 (m, 1H, CHH-1 pentyl), 2.55 – 2.47 (m, 1H, H-5), 2.44 (dd, $J = 11.2$ Hz, 1H, H-1b), 1.93 (s, 3H, $3 \times \text{CH Ada}$), 1.75 – 1.54 (m, 10H, $3 \times \text{CH}_2 \text{ Ada}$, $\text{CH}_2\text{-2}$, $\text{CH}_2\text{-4}$ pentyl), 1.52 (d, $J = 2.2$ Hz, 6H, $3 \times \text{CH}_2 \text{ Ada}$), 1.42 – 1.33 (m, 2H, $\text{CH}_2\text{-3}$ pentyl), 1.30 (d, $J = 6.2$ Hz, 3H, $\text{CH}_3\text{-6}$). ^{13}C NMR (100 MHz, $\text{CDCl}_3/\text{MeOD}$, 1/1) δ : 13.7 ($\text{CH}_3\text{-6}$), 22.7 (CH_2 pentyl), 23.4 (CH_2 pentyl), 27.8 (CH Ada), 28.7 (CH_2 pentyl), 33.5 (Cq Ada), 36.7 ($\text{CH}_2 \text{ Ada}$), 39.2 ($\text{CH}_2 \text{ Ada}$), 52.3 ($\text{CH}_2\text{-1}$ pentyl), 54.8 (C-1), 60.3 (C-5), 70.8 ($\text{CH}_2\text{-5}$ pentyl), 77.5, 73.8, 67.9 (C-2, C-3, C-4), 81.5 ($\text{OCH}_2\text{-Ada}$). HRMS: found 382.2961 [$\text{M} + \text{H}$] $^+$, calculated for [$\text{C}_{22}\text{H}_{39}\text{NO}_4 + \text{H}$] $^+$ 381.2957.



N-[5-(Adamantan-1-yl-methoxy)-pentyl]-1,5-dideoxy-1,5-imino-

D-xylitol (53). ^1H NMR (400 MHz, $\text{CDCl}_3/\text{MeOD}$; 1/1; 40 $^\circ\text{C}$) δ 3.72 (dd, $J = 3.9$ Hz, 10.9 Hz, 1H), 3.52 (dd, $J = 7.8$ Hz, 10.9 Hz, 1H), 3.52 – 3.41 (m, 1H), 3.37 (t, $J = 6.3$ Hz, 2H, $\text{CH}_2\text{-5}$ pentyl), 3.20 (dd, $J = 7.7$ Hz, 1H, H-3), 3.06 – 2.99 (m, 1H), 2.98 – 2.91 (m, 3H, $\text{OCH}_2\text{-Ada}$, CH), 2.66 – 2.52 (m, 2H), 2.36 – 2.27 (m, 1H), 1.93 (s, 3H, $3 \times \text{CH Ada}$), 1.76 – 1.37 (m, 18H, $6 \times \text{CH}_2 \text{ Ada}$, $3 \times \text{CH}_2$ pentyl). MS (ESI): found 368.2 [$\text{M} + \text{H}$] $^+$, calculated for [$\text{C}_{21}\text{H}_{37}\text{NO}_4 + \text{H}$] $^+$ 368.3.

References

(1) van Weely S.; van Leeuwen, M. B.; Jansen, I. D. C.; de Bruijn, M. A. C.; Brouwer-Kelder, E. M.; Schram, A. W.; Sa Miranda, M. C.; Barranger, J. A.; Petersen, E. M.; Goldblatt, J.; Stotz,

- H.; Schwarzmann, G.; Sandhoff, K.; Svennerholm, L.; Erikson, A.; Tager, J. M.; Aerts, J. M. F. G.. Clinical phenotype of Gaucher disease in relation to properties of mutant glucocerebrosidase in cultured fibroblasts. *Biochim. Biophys. Acta.* **1991**, *1096*, 301-311.
- (2) Aerts, J. M.; Donker-Koopman, W. E.; van der Vliet, M.K.; Jonsson, L. M.; Ginns, E.I.; Murray, G. J.; Barranger, J. A.; Tager, J. M.; Schram, A. W. The occurrence of two immunologically distinguishable beta-glucocerebrosidases in human spleen. *Eur. J. Biochem.* **1985**, *150*, 565-574.
- (3) van Weely, S.; Brandsma, M.; Strijland, A.; Tager, J. M.; Aerts, J. M. Demonstration of the existence of a second, non-lysosomal glucocerebrosidase that is not deficient in Gaucher disease. *Biochim. Biophys. Acta.* **1993**, *1181*, 55-62.
- (4) Wennekes, T.; Meijer, A. J.; Groen, A. K.; Boot, R. G.; Groener, J. E.; van Eijk, M.; Ottenhoff, R.; Bijl, N.; Ghauharali, K.; Song, H.; O'Shea, T. J.; Liu, H.; Yew, N.; Copeland, D.; van den Berg, R. J. B. H. N.; van der Marel, G. A.; Overkleeft, H. S.; Aerts, J. M. F. G. Dual-action lipophilic iminosugar improves glycemic control in obese rodents by reduction of visceral glycosphingolipids and buffering of carbohydrate assimilation. *J. Med. Chem.* **2010**, *53*, 689-698.
- (5) Takahata, H.; Banba, Y.; Ouchi, H.; Nemoto, H.; Kato, A.; Adachi, I. Asymmetric synthesis of the four possible fagomine isomers. *J. Org. Chem.* **2003**, *68*, 3603-3607.
- (6) Takahata, H.; Banba, Y.; Ouchi, H.; Nemoto, H. Concise and highly stereocontrolled synthesis of 1-deoxygalactonojirimycin and its congeners using dioxanylpiperidine, a promising chiral building block. *Org. Lett.* **2003**, *5*, 2527-2529.
- (7) Takahata, H.; Banba, Y.; Sasatani, M.; Nemoto, H.; Kato, A.; Adachi, I. Asymmetric synthesis of 1-deoxynojirimycin and its congeners from a common chiral building block. *Tetrahedron* **2004**, *60*, 8199-8205.