Author: Rijssel, Erwin Roelof van
Title: Stereoelectronic and conformational effects in carbohydrate derived oxocarbenium, iminium and ammonium ions
Issue Date: 2015-01-14

Chapter 5

A library of lipophilic iminosugars based on all eight stereoisomeric pentofuranosyl iminosugars

5.1 Introduction

Iminosugars are carbohydrates in which the endocyclic oxygen is replaced by nitrogen. They can act as inhibitors for glycosidases and glycosyl transferases owing to their structural similarity with the putative transition states of the corresponding enzymatic transformations.[1-7] Furanosyl based iminosugars are attractive as potential inhibitors for furanose processing enzymes, because furanose containing oligosaccharides are not produced in humans or other mammals but do play important roles in microbial organisms.[8-10] In addition they can serve as interesting lead compounds to develop inhibitors for pyranose processing enzymes, because their three-dimensional structures can effectively mimic the pyranosyl oxocarbenium ions.[7,11] For example, 1,4-dideoxy-1,4-imino-D-arabinitol is known to be a powerful inhibitor of a range of α-glucosidases.[1,4,11-15]

Eight different stereoisomers are possible in the pentofuranose iminosugar family. Different strategies towards the synthesis of each of the eight iminosugars have been developed, the first one being reported in 1968 to access 1,4-dideoxy-1,4-imino-L-xylitol.[16] Although new approaches are still regularly being published to synthesize these iminosugars, most of these studies comprise the synthesis of only a single or a limited number of the eight diastereomers.[12-13,17-23] To effectively generate a library of furanosyl iminosugars, encompassing all stereoisomers, a general route of synthesis to access them all is desirable. In this Chapter a general strategy is described to access all eight stereoisomeric furanosyl iminosugars. These have been used to generate a library of functionalized iminosugars in which the iminosugar amines are alkylated with 7 different alkyl chains to produce a library of 64 furanosyl iminosugars. The choice of alkyl chains has been made based on the successful iminosugar therapeutic agents that are currently on the market, that is Zavesca (Miglustat, *N*-butyl 1-deoxynojirimycin)[14] and Glyset (Miglitol, *N*-hydroxyethyl 1-deoxynojirimycin),[14] as well as the library of alkylated pyranosyl iminosugars that has been compiled in-house.[24-26] The different alkyl chains are depicted in Figure 5.1, alongside the panel of different iminosugar stereoisomers.

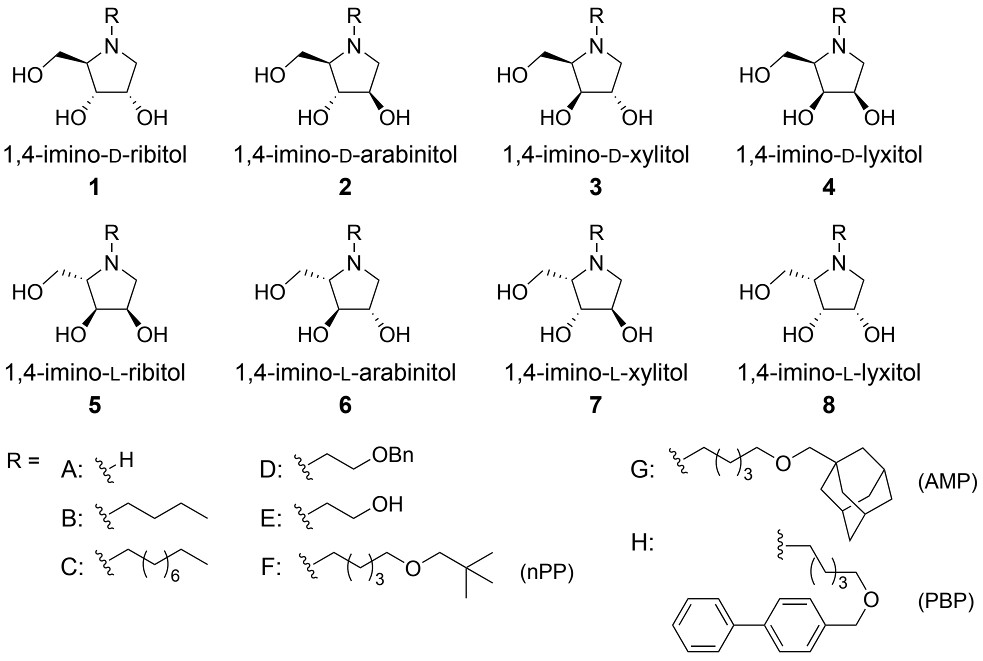


Figure 5.1 Target furanose iminosugars.

5.2 Results and discussion

Most of the published approaches for the synthesis of iminosugars are based on either a double reductive amination strategy or on a nucleophilic substitution of one or both of the hydroxyl groups with a nitrogen nucleophile such as azide or benzylamine.[12] To access all eight furanose iminosugars, the synthetic strategy that is retrosynthetically outlined in Figure 5.2 was selected. In this strategy a double nucleophilic S_N2 displacement of the C1- and C4-hydroxyls with benzylamine is used. To this end the C1- and C4 hydroxyls of otherwise perbenzylated pentitols were transformed into good leaving groups. Because the S_N2 substitutions lead to inversion of stereochemistry at C4, the use of D-furanosyl starting compounds lead to products having the L-configuration and vice versa. All D-pentoses as well as L-arabinose and L-xylose are commercially available at reasonable cost and can therefore be used as starting material. The remaining two, L-ribose and L-lyxose, are too expensive and therefore a double inversion strategy was devised in which the D-sugars are used as starting materials. In this approach the C1- and C4-hydroxyls are first displaced by iodine to give the 1,4-di-iodo-L-pentoses that are then subjected to the second double displacement with benzylamine to give the protected D-iminosugars.

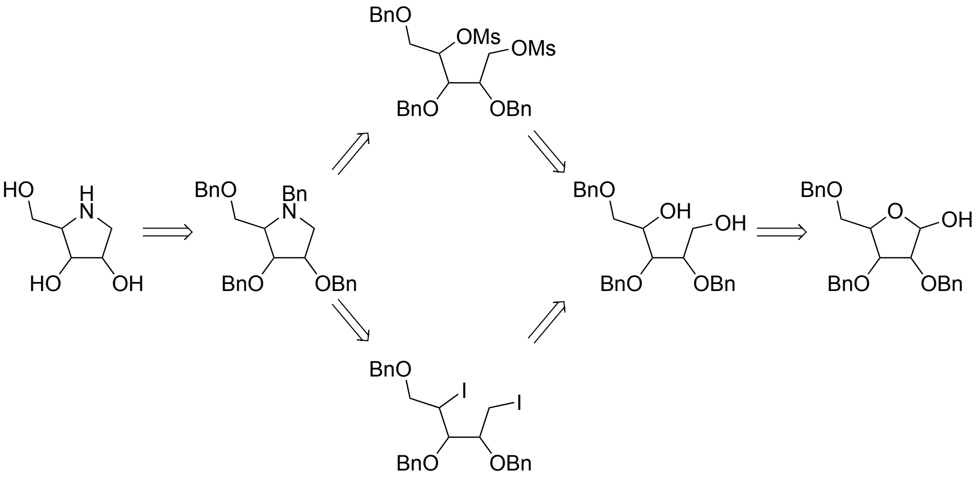
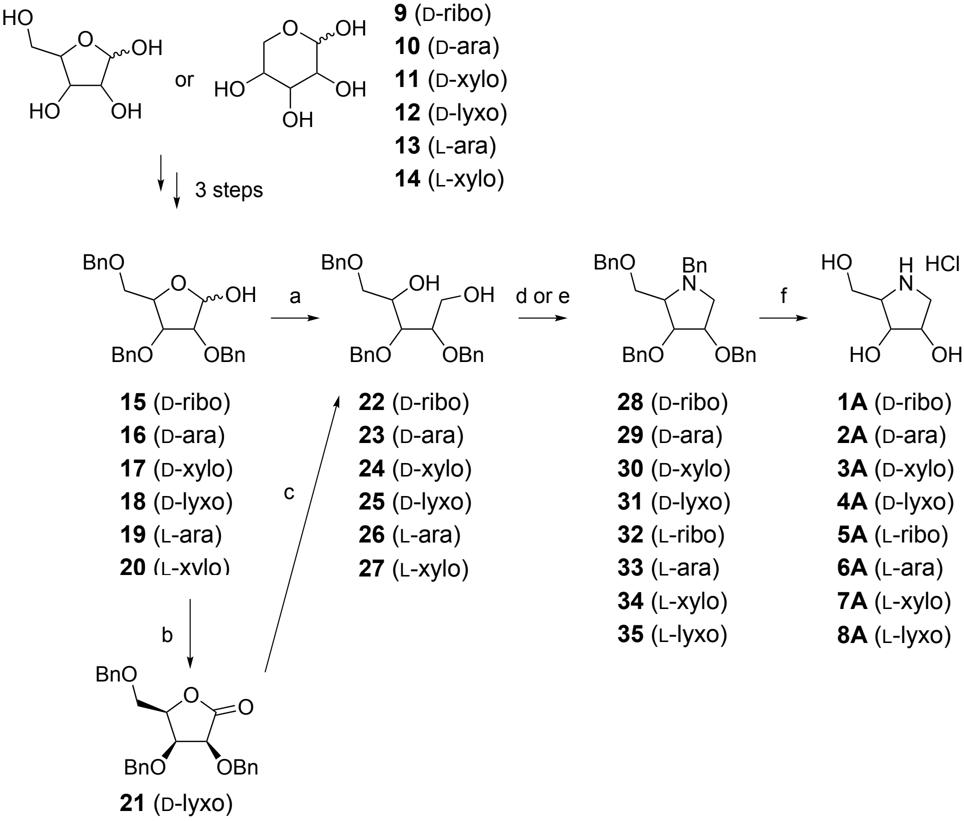


Figure 5.2 Retrosynthetic analysis of the target iminosugars based on a double displacement strategy.

The syntheses of the eight stereoisomeric iminosugars **1**-**8** is depicted in Scheme 5.1, starting from the six commercially available furanoses, D-ribose (**9**), D-arabinose (**10**), D-xylose (**11**), D-lyxose (**12**), L-arabinose (**13**) and L-xylose (**14**). These were transformed, *via* a three step reaction sequence entailing: 1) a kinetic Fischer methylation to give the methyl furanosides; 2) complete benzylation of the remaining alcohols and 3) the acid catalyzed hydrolysis of the methyl acetal, into the lactols **15**-**20**.[27-30] Because it proved to be difficult to purify the D-lyxo-furanoside from its pyranosyl counterpart at this stage, the lactol (**18**) was oxidized to provide the crystalline furanolactone (**21**) that was obtained in an overall yield of 64% over 4 steps. The five tri-*O*-benzylated pentofuranoses (**15**-**17**, **19**, **20**) were reduced using sodium borohydride to give the corresponding diols (**22-24**,**26**-**27**) with yields ranging from 92 to 98%. For the reduction of D-lyxonolactone **21** a stronger reducing agent was required, and therefore lithium aluminum hydride was employed to deliver lyxitol **25**. All six diols were di-mesylated using mesyl chloride in pyridine, after which a double displacement with benzylamine led to the fully protected iminosugars **29, 30, 32**-**35** (in 46% - 92% yield). The remaining two protected iminosugars were synthesized using the double inversion protocol. Therefore 2,3,5-tri-*O*-benzyl D-ribitol (**22**) and D-lyxitol (**25**) were subjected to a Garegg-Samuelson reaction using iodine, triphenylphosphine and imidazole.[31] Because tetrahydrofuran side products are readily formed in this reaction (generated from activation of the primary alcohol and subsequent ring closure by nucleophilic displacement of the secondary alcohol), it proved to be challenging to optimize these reactions. The best conditions were found in stirring the reaction mixture at low temperature (-30 °C to -20 °C) for a prolonged period of time (± 4 days) to allow for the formation of the bis(triphenylphosphonium oxides). Next the mixtures were concentrated, taken up in toluene and brought to reflux temperature to effect the displacement with iodine resulting in the 1,4-di-iodo L-pentitols. The di-iodides were then subjected to benzylamine at 55 °C to generate the perbenzylated iminofuranoses having the D-ribose (**28**) and D-lyxose (**31**) configuration in 69% and 55% yield over the last two steps, respectively. Global deprotection of the perbenzylated iminosugars was accomplished by subjection of the eight protected iminosugars to a 4.5-5 bar hydrogen overpressure in the presence of palladium on carbon in a slightly acidic medium to deliver all the unprotected iminosugars as hydrochloride salt (**1A**-**8A**) in very high to quantitative yields.

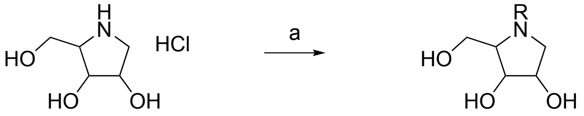
Scheme 5.1 Synthesis of the iminofuranoses (**1A**-**8A**, see Figure 5.1 for stereochemistry).



Reagents and conditions: (a) $NaBH_4$, EtOH, **22** (from **15**): 97%, **23** (from **16**): 98%, **24** (from **17**): 97%, **26** (from **19**): 85%, **27** (from **20**): 92%; (b) Ac_2O, DMSO; (c) $LiAlH_4$, THF, 0 °C, **25** (from **21**): 89%; (d) i) PPh_3, I_2, imidazole, DCM, -30 °C to -20 °C, ii) toluene, Δ; iii) $BnNH_2$, 55 °C, **28** (from **22**): 69% over 2 steps, **31** (from **25**): 55% over 2 steps; (e) i) MsCl, pyridine, 0 °C; ii) $BnNH_2$, 55 °C, **29** (from **27**): 84% over 2 steps, **30** (from **26**): 92% over 2 steps, **32** (from **25**): 88% over 2 steps, **33** (from **24**): 71% over 2 steps, **34** (from **23**): 46% over 2 steps, **35** (from **22**): 70% over 2 steps. (f) H_2, Pd/C, HCl, EtOH, H_2O, **1A** (from **28**): 99%, **2A** (from **29**): quant., **3A** (from **30**): quant., **4A** (from **31**): 98%, **5A** (from **32**): quant., **6A** (from **33**): quant., **7A** (from **34**): quant., **8A** (from **35**): quant.

Next, the introduction of the various alkyl chains was undertaken. Initially the alkylation was attempted using K_2CO_3 as base in combination with the relevant alkyl bromides in DMF, conditions previously reported for the alkylation of a large variety of pyranosyl iminosugars.[25-26] Unfortunately the use of these reagents led to the concomitant formation of carbamate and cyclic carbonate side products. Formation of these byproducts can be explained by attack of the carbonate anion on the alkylating agent to give a dialkyl carbonate, which can be substituted by the iminosugar amine to give a stable carbamate, or be used to form a cyclic carbonate by the *cis*-diol systems in de ribo and lyxo configured iminosugars. To circumvent the formation of these side products, the base was changed to *N*,*N*-diisopropylethylamine (DiPEA), which indeed led to clean alkylation reactions. Table 5.1 summarizes the yields for all the alkylation reactions, ranging from 5% to 59%. The variation in yields for these reactions can in part be accounted for by losses during the column chromatography purification step that was required to remove ammonium salt byproducts. The last of the substituents, the hydroxyethyl group, was generated by debenzylation of the benzyloxyethyl substituent. All these debenzylations proceeded quantitatively to yield the *N*-hydroxyethyl iminofuranoses as hydrochloride salts.

Table 5.1 *N*-alkylation of the iminofuranoses.



R =	D-ribo	D-ara	D-xylo	D-lyxo	L-ribo	L-ara	L-xylo	L-lyxo
Butyl[a]	**1B** 35%	**2B** 13%	**3B** 27%	**4B** 14%	**5B** 12%	**6B** 45%	**7B** 5%	**8B** 7%
Nonyl[a]	**1C** 44%	**2C** 47%	**3C** 43%	**4C** 29%	**5C** 59%	**6C** 46%	**7C** 36%	**8C** 29%
EtOBn[a]	**1D** 32%	**2D** 26%	**3D** 25%	**4D** 16%	**5D** 27%	**6D** 25%	**7D** 26%	**8D** 16%
EtOH[b]	**1E** 31%	**2E** 25%	**3E** 11%	**4E** 13%	**5E** 25%	**6E** 22%	**7E** 23%	**8E** 15%
nPP[a]	**1F** 44%	**2F** 26%	**3F** 31%	**4F** 22%	**5F** 27%	**6F** 45%	**7F** 36%	**8F** 21%
AMP[a]	**1G** 33%	**2G** 37%	**3G** 36%	**4G** 12%	**5G** 36%	**6G** 36%	**7G** 40%	**8G** 9%
PBP[a]	**1H** 41%	**2H** 34%	**3H** 36%	**4H** 16%	**5H** 25%	**6H** 25%	**7H** 38%	**8H** 15%

Reagents and conditions: (a) R-Br, DiPEA, DMF, 60 °C. (b) Alkylated derivatives **1D**-**8D** were treated with: H_2, Pd/C, HCl, EtOH, H_2O (yield over 2 steps).

5.3 Conclusion

The synthesis of all eight stereoisomeric pentofuranosyl iminosugars has been described, using a double displacement strategy of suitably functionalized alditols. A library consisting of 64 compounds was constructed by alkylation of the eight diastereomers, to give a collection of lipophilic iminosugars that have the potential to inhibit glycolipid processing enzymes. Using the free energy surface scanning method outlined in Chapter 2 and 3, the conformational preferences of the iminosugars can be mapped and the outcome of these studies will be valuable in the interpretation of results emanating from enzyme inhibition studies using the here described iminosugar library.

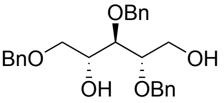
Experimental section

General. All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. Reactions were performed at room temperature unless stated otherwise and were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ (10 g/L) in 10% sulfuric acid (aq.) or a solution of $KMnO_4$ (20 g/L) and K_2CO_3 (10 g/L) in H_2O followed by charring at ~150 °C. Flash column chromatography was performed on silica gel (40-63µm). ^1H and ^{13}C spectra were recorded on a Bruker AV 600 or AV 400 in $CDCl_3$ or CD_3OD. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^1H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments.

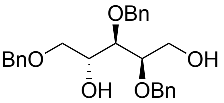
General procedure A: Pd/C catalyzed hydrogenolysis: The perbenzylated iminosugar (7.5 mmol – 8 mmol) was dissolved in a mixture of 2M HCl (aq.) / EtOH (0.05 M, 3/1, v/v) and transferred to a Parr high pressure hydrogenation flask. The atmosphere was exchanged to argon after which a catalytic amount of palladium on carbon (~0.1 eq, 10 wt. % on carbon) was added. The flask was put under reduced pressure and ventilated with hydrogen gas. This procedure was repeated twice after which the pressure was adjusted to 4.5-5 bar hydrogen overpressure. The reaction was allowed to react for 24 hours while mechanically shaken and the pressure being maintained at the value initially set. The mixture was filtered over a glass microfiber filter, followed by rinsing the filter with EtOH. The mixture was concentrated under reduced pressure followed by several coevaporation steps with EtOH and MeOH to yield the deprotected iminosugar as hydrochloride salt.

General procedure B: base catalyzed alkylation: The unprotected iminosugar (0.50 mmol) as hydrochloride salt was dissolved in DMF (0.2 M, 2.5 ml) after which alkyl bromide (1.5 eq, 0.75 mmol) and *N*,*N*-diisopropylethylamine (3 eq, 260 µl, 1.5 mmol) were added. The reaction mixture was stirred overnight at 70 °C after which the reaction mixture was concentrated. The crude product was purified by silica gel column chromatography and subsequently by preparative reversed phase HPLC purification (solvent A: H_2O + 0.1% TFA, solvent B: ACN) yielding the compound as TFA salt. When DiPEA TFA salt was present as impurity, the compound was neutralized with NH_4OH (aq., 1 eq) and purified by reversed phase column chromatography (H_2O/MeOH) yielding the product as free base.

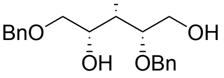
General procedure C: small scale Pd/C catalyzed hydrogenolysis: The ethyloxybenzyl iminosugar (0.07 mmol – 0.18 mmol) was dissolved in a mixture of 0.25M HCl (aq.) / EtOH (0.01 M, 12/1, v/v) and transferred to a Parr high pressure hydrogenation flask. The atmosphere was exchanged to argon after which a catalytic amount of palladium on carbon (~0.1 eq, 10 wt. % on carbon) was added. The flask was put under reduced pressure and ventilated with hydrogen gas. This procedure was repeated twice after which the pressure was adjusted to 4.5-5 bar hydrogen overpressure. The reaction was allowed to react for 4 hours-overnight while mechanically shaken and the pressure being maintained at the value initially set. The mixture was filtered over a glass microfiber filter, followed by rinsing the filter with EtOH. The mixture was concentrated under reduced pressure followed by several coevaporation steps with EtOH and MeOH to yield the deprotected iminosugar as hydrochloride salt.



2,3,5-Tri-*O*-benzyl-D-ribitol (22). 2,3,5-Tri-*O*-benzyl-D-ribofuranose (**15**, 25 g, 60 mmol) was dissolved in EtOH (600 ml) and cooled to 0 °C. Sodium borohydride (5.3 g, 139 mmol) was added and the reaction stirred at room temperature for 3 hours. The pH of the reaction mixture was adjusted to pH 4-5 with acetic acid and the mixture concentrated. The residue was taken up in EtOAc and washed with 1 M HCl (aq.), $NaHCO_3$ (sat. aq.), and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (30-60% EtOAc/pentane) yielding the title compound (25 g, 58 mmol, 97 % yield). R_f = 0.45 (50/50 EtOAc/pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.13 (m, 15H, C*H*$_{Ar}$ Bn), 4.72 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.51 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.47 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.05 – 3.95 (m, 1H, C-4), 3.89 – 3.72 (m, 4H, C-1, C-2, C-3), 3.60 (dd, *J* = 9.8, 3.7 Hz, 1H, C-5a), 3.56 (dd, *J* = 9.7, 5.9 Hz, 1H, C-5b), 2.91 (s, 1H, O*H*-4), 2.54 (s, 1H, O*H*-1). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 138.1, 137.9 (*C*$_q$ Bn), 128.6, 128.5, 128.5, 128.1, 128.0, 128.0, 127.9 (*C*H$_{Ar}$ Bn), 79.5, 79.4 (*C*-2, *C*-3), 74.1, 73.5, 72.1 (3x*C*H$_2$ Bn), 71.1 (*C*-5), 70.7 (*C*-4), 61.1 (*C*-1). $[\alpha]^{20}_D$ = 18.1° (c = 1, $CHCl_3$). IR (neat): 602, 694, 733, 806, 520, 849, 908, 1026, 1067, 1088, 1207, 1273, 1314, 1329, 1360, 1395, 1452, 1497, 1719, 2866, 3030, 3063, 3348. HR-MS: $[M+H^+]$ Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21622.



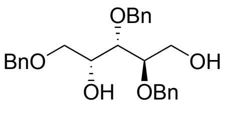
2,3,5-Tri-*O*-benzyl-D-arabinitol (23). 2,3,5-Tri-*O*-benzyl-D-arabinofuranose (**16**, 17 g, 41 mmol) was dissolved in ethanol (410 ml) and cooled to 0 °C. Sodium borohydride (3.6 g, 95 mmol) was added and the reaction stirred for 5 hours at room temperature. The pH of the reaction mixture was adjusted to pH 4-5 with acetic acid and the mixture concentrated. The residue was taken up in EtOAc and washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (20-70% EtOAc/pentane) yielding the title compound (17 g, 41 mmol, 98 % yield). R_f = 0.7 (50/50 EtOAc/pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 15H, C*H*$_{Ar}$ Bn), 4.64 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.54 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.51 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.04 – 3.98 (m, 1H, C-4), 3.83 – 3.67 (m, 4H, C-1, C-2. C-3), 3.68 – 3.59 (m, 2H, C-5), 2.67 (s, 2H, 2xO*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 137.9, 137.9 (*C*$_q$ Bn), 128.6, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9 (*C*H$_{Ar}$ Bn), 79.5 (*C*-2), 78.4 (*C*-3), 73.8, 73.6, 72.9 (3x*C*H$_2$ Bn), 71.1 (*C*-5), 70.6 (*C*-4), 61.5 (*C*-1). $[\alpha]^{20}_D$ = 4.6° (c = 1, $CHCl_3$). IR (neat): 602, 696, 733, 806, 820, 851, 880, 910, 1001, 1026, 1069, 1086, 1207, 1271, 1315, 1350, 1396, 1452, 1497, 1705, 1717, 2866, 2920, 3030, 3063, 3445. HR-MS: $[M+H^+]$ Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21637.



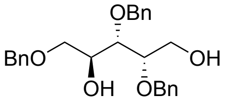
2,3,5-Tri-*O*-benzyl-D-xylitol (24). 2,3,5-Tri-*O*-benzyl-D-xylofuranose (**17**, 23 g, 54 mmol) was dissolved in ethanol (550 ml), put under an argon atmosphere and cooled to 0 °C. Sodium borohydride (4.7 g, 123 mmol) was added and the reaction stirred at room temperature for 4 hours. The pH of the reaction was adjusted to pH 4-5 by addition of acetic acid and the resulting mixture was concentrated. The residue was taken up in EtOAc and washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The product was purified by flash chromatography (25-60% EtOAc/pentane) yielding the title compound (22 g, 52 mmol, 97% yield). R_f = 0.65 (50/50 EtOAc/pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 13H, C*H*$_{Ar}$ Bn), 7.24 – 7.21 (m, 2H, C*H*$_{Ar}$ Bn), 4.65 (d, *J* = 11.4 Hz, 1H, C*H*H

Bn-3), 4.61 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-2), 4.57 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-2), 4.51 – 4.46 (m, 2H, C*H*H Bn-3, CH*H* Bn-5), 4.42 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-5), 4.07 – 4.01 (m, 1H, C-4), 3.81 – 3.73 (m, 2H, C-1), 3.73 – 3.63 (m, 2H, C-2, C-3), 3.50 (dd, *J* = 9.4, 6.4 Hz, 1H, C-5a), 3.41 (dd, *J* = 9.4, 6.2 Hz, 1H, C-5b), 3.02 (s, 1H, O*H*-4), 2.86 (s, 1H, O*H*-1). ^{13}C NMR (101 MHz, CDCl$_3$) δ 138.1, 138.0, 137.9 (*C*$_q$ Bn), 128.5, 128.5, 128.5, 128.4, 128.0, 128.0, 127.9, 127.8 (*C*H$_{Ar}$ Bn), 78.7 (*C*-2), 77.3 (*C*-3), 74.2 (*C*H$_2$ Bn-3), 73.3 (*C*H$_2$ Bn-5), 72.4 (*C*H$_2$ Bn-2), 71.3 (*C*-5), 68.6 (*C*-4), 60.6 (*C*-1). $[\alpha]^{20}_{D}$ = -9.7° (c = 1, CHCl$_3$). IR (neat): 694, 716, 733, 822, 881, 903, 918, 980, 1018, 1024, 1057, 1084, 1096, 1206, 1248, 1279, 1294, 1366, 1385, 1400, 1452, 1497, 1578, 1726, 2471, 2542, 2716, 2866, 3028, 3343. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21633.

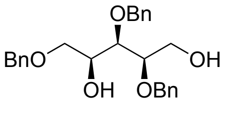
2,3,5-Tri-*O*-benzyl-D-lyxitol (25). 2,3,5-Tri-*O*-benzyl-D-lyxono-1,4-lactone (**21**, 12 g, 28 mmol) in THF (120 ml) was slowly added to a solution of lithium aluminum hydride (2.6 g, 68 mmol) in THF (120 ml) at 0 °C. The reaction mixture was stirred for 1.5 hour at 0 °C, after which the reaction was quenched with EtOAc. Sodium potassium tartrate (sat. aq.) was slowly added and the mixture was stirred for 30 minutes before ethyl acetate was added and the layers separated. The organic layer was washed with NaHCO$_3$ (sat. aq.) and brine before being dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (50% EtOAc/pentane) yielding the title compound (11 g, 25 mmol, 89 % yield). *R*$_f$ = 0.6 (50/50 EtOAc/pentane). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 – 7.24 (m, 15H, C*H*$_{Ar}$ Bn), 4.73 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.61 (s, 2H, C*H*$_2$ Bn), 4.52 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.51 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.46 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.00 (td, *J* = 6.1, 2.1 Hz, 1H, C-4), 3.90 – 3.82 (m, 1H, C-1a), 3.79 (dd, *J* = 6.4, 2.1 Hz, 1H, C-3), 3.76 – 3.71 (m, 1H, C-1b), 3.71 – 3.68 (m, 1H, C-2), 3.53 (dd, *J* = 9.4, 6.1 Hz, 1H, C-5a), 3.46 (dd, *J* = 9.5, 6.1 Hz, 1H, C-5b), 2.49 (s, 2H, O*H*-1, O*H*-4). ^{13}C NMR (101 MHz, CDCl$_3$) δ 138.0, 137.9, 137.9 (*C*$_q$ Bn), 128.6, 128.5, 128.3, 128.0, 128.0, 128.0, 127.9 (*C*H$_{Ar}$ Bn), 79.6 (*C*-2), 77.1 (*C*-3), 74.4, 73.5, 72.5 (3x*C*H$_2$ Bn), 71.3 (*C*-5), 69.8 (*C*-4), 60.6 (*C*-1). $[\alpha]^{20}_{D}$ = -18.9° (c = 1, CHCl$_3$). IR (neat): 602, 646, 694, 733, 820, 851, 868, 910, 959, 1026, 1049, 1090, 1207, 1246, 1265, 1308, 1327, 1362, 1395, 1454, 1497, 2864, 2920, 3030, 3061. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21629.



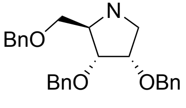
2,3,5-Tri-*O*-benzyl-L-arabinitol (26). Synthesized as in Chapter 4.



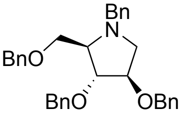
2,3,5-Tri-*O*-benzyl-L-xylitol (27). 2,3,5-Tri-*O*-benzyl-L-xylofuranose (**20**, 12g, 28 mmol) was dissolved in ethanol (285 ml), cooled to 0 °C and sodium borohydride (2.5 g, 65 mmol) added. The reaction was stirred for 5 hours at room temperature after which the pH of the reaction mixture was adjusted to pH 4-5 with acetic acid and the mixture concentrated. The residue was taken up in EtOAc and washed with 1M HCl (aq.), NaHCO$_3$ (sat. aq.) and brine. The solution was dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (70% EtOAc/pentane) yielding the title compound (11 g, 26 mmol, 92 % yield). $[\alpha]^{20}_{D}$ = 10.6° (c = 1, CHCl$_3$). Analytical data was the same as for its enantiomer (**24**).



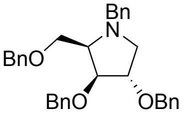
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-ribitol (28). 2,3,5-Tri-*O*-benzyl-D-ribitol (**22**, 7.6 g, 18 mmol), triphenylphosphine (11 g, 41 mmol) and imidazole (3.7 g, 54 mmol) were coevaporated thrice with dry toluene before being dissolved in DCM (180 ml) and cooled to -30 °C. Iodine (11 g, 43 mmol) was slowly added and the reaction mixture stirred for 2 days at -30 °C, then 1 day at -20 °C. The solution was concentrated under reduced pressure, dry



toluene (180 ml) added and the mixture refluxed for 2 hours. The reaction mixture was diluted with Et_2O, washed with $Na_2S_2O_3$ (sat. aq.) and brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was coevaporated with Et_2O to remove residual toluene and then dissolved in Et_2O after which it was filtered to remove most of the Ph_3PO. The crude 1,4-Dideoxy-1,4-diiodo-2,3,5-tri-*O*-benzyl-L-lyxitol (18 mmol) was dissolved in benzylamine (59 ml, 540 mmol) and stirred for 2 days at 55 °C. The mixture was diluted with EtOAc, washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (15-22.5% Et_2O/pentane) yielding the title compound (6.1 g, 12 mmol, 69% yield over 2 steps). R_f = 0.55 (40/60 Et_2O/pentane). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 20H, CH_{Ar} Bn), 4.64 (d, *J* = 12.2 Hz, 1H, C*H*H-Bn-3), 4.59 (d, *J* = 12.2 Hz, 1H, CH*H* Bn-3), 4.52 – 4.42 (m, 4H, 2xCH*H* Bn-2, 2xCH*H* Bn-5), 3.99 (d, *J* = 12.9 Hz, 1H, CH*H* *N*-Bn), 3.90 (dt, *J* = 7.9, 5.5 Hz, 1H, C-2), 3.85 (dd, *J* = 5.1, 3.6 Hz, 1H, C-3), 3.58 (d, *J* = 13.0 Hz, 1H, C*H*H *N*-Bn), 3.39 (dd, *J* = 9.9, 4.6 Hz, 1H, C-5a), 3.32 (dd, *J* = 9.9, 6.2 Hz, 1H, C-5b), 3.11 (dd, *J* = 9.0, 5.7 Hz, 1H, C-1a), 3.05 (dt, *J* = 6.1, 4.3 Hz, 1H, C-4), 2.68 (dd, *J* = 8.8, 8.3 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2 (C_q *N*-Bn), 138.6, 138.4, 138.4 (C_q *O*-Bn), 129.0, 128.4, 128.4, 128.3, 128.2, 127.7, 127.7, 127.6, 127.6, 127.6, 127.1 (CH_{Ar} Bn), 79.0 (*C*-3), 76.5 (*C*-2), 73.4, 71.6 (CH_2 Bn-2, CH_2 Bn-5), 71.4 (CH_2 Bn-3), 71.1 (*C*-5), 68.2 (*C*-4), 60.2 (CH_2 *N*-Bn), 55.9 (*C*-1). $[\alpha]^{20}_D$ = -32.9° (c = 1, $CHCl_3$). IR (neat): 602, 694, 731, 820, 845, 908, 1026, 1051, 1072, 1092, 1207, 1258, 1310, 1321, 1364, 1452, 1495, 2799, 2857, 3028, 3061. HR-MS: $[M+H^+]$ Calculated for $C_{33}H_{35}NO_3$: 494.26897; found: 494.26796.

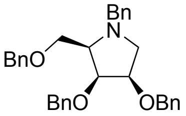


1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-arabinitol (29). 2,3,5-Tri-*O*-benzyl-L-xylitol (**27**, 11 g, 25 mmol) was dissolved in pyridine (52 ml), cooled to 0 °C and methanesulfonyl chloride (9.7 ml, 124 mmol) added. The reaction mixture was stirred at this temperature after which the reaction was quenched with H_2O and diluted with EtOAc. The suspension was washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$ and concentrated. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-L-xylitol (14 g, 25 mmol) was dissolved in benzylamine (81 ml, 750 mmol) and stirred at 55 °C overnight after which the reaction mixture was allowed to cool to room temperature and subsequently diluted with EtOAc. The mixture was washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine before being dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10-15% Et_2O/pentane) yielding the title pyrrolidine (11 g, 21 mmol, 84 % yield over 2 steps). R_f = 0.9 (10/90 acetone/toluene). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.19 (m, 20H, CH_{Ar} Bn), 4.52 (s, 2H, CH_2 Bn-5), 4.50 (s, 2H, CH_2 Bn-3), 4.45 (d, *J* = 12.2 Hz, 1H, C*H*H Bn-2), 4.37 (d, *J* = 12.2 Hz, 1H, CH*H* Bn-2), 4.14 (d, *J* = 13.3 Hz, 1H, C*H*H *N*-Bn), 3.93 – 3.86 (m, 2H, C-2, C-3), 3.60 (d, *J* = 5.7 Hz, 2H, C-5), 3.49 (d, *J* = 13.8 Hz, 1H, CH*H* *N*-Bn), 3.04 (d, *J* = 10.7 Hz, 1H, C-1a), 2.86 (q, *J* = 5.3 Hz, 1H, C-4), 2.56 (dd, *J* = 10.7, 5.1 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.5, 138.3, 138.3 (C_q Bn), 129.1, 128.5, 128.3, 127.9, 127.8, 127.7, 127.7, 127.6, 127.0 (CH_{Ar} Bn), 86.0 (*C*-3), 81.6 (*C*-2), 73.3 (CH_2 Bn-5), 71.5 (CH_2 Bn-3), 71.4 (*C*-5), 71.0 (CH_2 Bn-2), 68.5 (*C*-4), 59.2 (CH_2 *N*-Bn), 57.1 (*C*-1). $[\alpha]^{20}_D$ = -40.0° (c = 1, $CHCl_3$). IR (neat): 602, 694, 731, 820, 845, 908, 951, 1026, 1074, 1092, 1153, 1206, 1258, 1333, 1366, 1452, 1495, 2797, 2857, 2891, 3028, 3061. HR-MS: $[M+H^+]$ Calculated for $C_{33}H_{35}NO_3$: 494.26897; found: 494.26795.

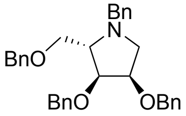


1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-xylitol (30). 2,3,5-Tri-O-benzyl-l-arabinitol (**26**, 10 g, 24 mmol) was dissolved in pyridine (50 ml), cooled to 0 °C and methanesulfonyl chloride (9.2 ml, 118 mmol) added. The mixture was stirred at this temperature for 5 hours. The reaction was quenched with H_2O and the mixture taken up in a mixture of EtOAc and 1M HCl (aq.), washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-L-arabinitol (13.7 g, 23.7 mmol) was dissolved in benzylamine (78 ml, 710 mmol) and stirred at 55 °C overnight. The reaction mixture was diluted with EtOAc and washed with 1M HCl (aq.), Na_2CO_3 (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10-17.5% Et2O/pentane) yielding the title pyrrolidine (11 g, 22 mmol, 92 % yield over 2 steps). *R*$_f$ = 0.7 (40/60 Et$_2$O/pentane). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41 – 7.24 (m, 20H, C*H*$_{\text{Ar}}$ Bn), 4.66 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-3), 4.61 (d, *J* = 12.1 Hz, 1H, CH*H* Bn-3), 4.59 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-5), 4.55 (d, *J* = 12.0 Hz, 1H, CH*H* Bn-5), 4.46 (s, 2H, C*H*$_2$ Bn-2), 4.16 (d, *J* = 13.3 Hz, 1H, C*H*H *N*-Bn), 4.11 (dd, *J* = 6.2, 2.9 Hz, 1H, C-3), 4.04 (td, *J* = 5.9, 3.0 Hz, 1H, C-2), 3.90 (dd, *J* = 9.6, 6.0 Hz, 1H, C-5a), 3.70 (dd, *J* = 9.6, 5.2 Hz, 1H, C-5b), 3.52 (d, *J* = 13.3 Hz, 1H, CH*H* *N*-Bn), 3.31 (dd, *J* = 10.2, 6.3 Hz, 1H, C-1a), 3.18 (q, *J* = 5.8 Hz, 1H, C-4), 2.36 (dd, *J* = 10.2, 5.5 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, CDCl$_3$) δ 139.1, 138.6, 138.5, 138.3 (*C*$_q$ Bn), 129.1, 128.5, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.7, 127.6, 127.0 (*C*H$_{\text{Ar}}$ Bn), 83.6 (*C*-3), 82.2 (*C*-2), 73.6 (*C*H$_2$ Bn-5), 72.2 (*C*H$_2$ Bn-3), 71.5 (*C*H$_2$ Bn-2), 69.6 (*C*-5), 65.4 (*C*-4), 59.5 (*C*H$_2$ N-Bn), 57.3 (*C*-1). [α]$^{20}_{\text{D}}$ = -35.5° (c = 1, CHCl$_3$). IR (neat): 602, 694, 731, 820, 845, 908, 966, 1003, 1026, 1072, 1088, 1206, 1246, 1308, 1344, 1364, 1452, 1495, 2799, 2859, 2911, 3028, 3061. HR-MS: [M+H$^+$] Calculated for C$_{33}$H$_{35}$NO$_3$: 494.26897; found: 494.26807.

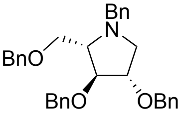
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-lyxitol (31). 2,3,5-Tri-*O*-benzyl-D-lyxitol (**25**, 5.3 g, 13 mmol), triphenylphosphine (7.5 g, 28.8 mmol) and imidazole (2.6 g, 38 mmol) were coevaporated thrice with dry toluene before being dissolved in DCM (125 ml) and cooled to -30 °C. Iodine (7.6 g, 30 mmol) was slowly added and the reaction mixture stirred for 3 days at -35 °C, then 1 day at -25 °C. The solution was concentrated under reduced pressure, dry toluene (125 ml) added and the mixture refluxed for 2 hours. The reaction mixture was diluted with Et$_2$O, washed with Na$_2$S$_2$O$_3$ (sat. aq.) and brine, dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was coevaporated with Et$_2$O to remove residual toluene and then dissolved in Et$_2$O after which it was filtered to remove most of the Ph$_3$PO. The crude 1,4-Dideoxy-1,4-diiodo-2,3,5-tri-*O*-benzyl-L-ribitol (12.5 mmol) was dissolved in benzylamine (41 ml, 375 mmol) and stirred for 2 days at 55 °C. The mixture was diluted with EtOAc, washed with 1M HCl (aq.), NaHCO$_3$ (sat. aq.) and brine, dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (12.5-15% Et$_2$O/pentane) yielding the title compound (3.4 g, 6.8 mmol, 55% over 2 steps). *R*$_f$ = 0.55 (40/60 Et$_2$O/pentane). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 – 7.14 (m, 20H, C*H*$_{\text{Ar}}$ Bn), 4.74 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-3), 4.61 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-3), 4.54 (d, *J* = 12.4 Hz, 1H, C*H*H Bn-2), 4.52 (d, *J* = 12.3 Hz, 1H, C*H*H Bn-2), 4.50 (s, 2H, C*H*H Bn-5), 4.07 (t, *J* = 5.3 Hz, 1H, C-3), 4.05 (d, *J* = 13.7 Hz, 1H, C*H*H *N*-Bn), 3.95 (dt, *J* = 6.1, 5.0 Hz, 1H, C-2), 3.91 (dd, *J* = 9.4, 6.1 Hz, 1H, C-5a), 3.68 (dd, *J* = 9.4, 6.0 Hz, 1H, C-5b), 3.59 (d, *J* = 13.6 Hz, 1H, CH*H* *N*-Bn), 3.17 (q, *J* = 6.0 Hz, 1H, C-4), 3.07 (dd, *J* = 10.7, 4.9 Hz, 1H, C-1a), 2.56 (dd, *J* = 10.7, 6.1 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, CDCl$_3$) δ 139.4 (*C*$_q$ *N*-Bn), 138.8, 138.7, 138.6 (*C*$_q$ *O*-Bn), 128.9, 128.4, 128.4, 128.3, 128.3, 127.8, 127.8, 127.6, 127.5, 126.9 (*C*H$_{\text{Ar}}$ Bn), 78.8 (*C*-3), 77.4 (*C*-2), 73.5 (*C*H$_2$ Bn-5), 73.0 (*C*H$_2$ Bn-3), 71.7 (*C*H$_2$ Bn-2), 70.7 (*C*-5), 64.4 (*C*-4), 59.8 (*C*H$_2$ *N*-Bn), 54.9 (*C*-1). [α]$^{20}_{\text{D}}$ = -36.0° (c = 1, CHCl$_3$). IR (neat): 602, 617, 636, 694, 731, 808, 820, 847, 907, 953, 1026, 1061, 1090, 1142, 1207, 1256, 1281, 1308, 1344, 1364, 1398, 1452, 1495, 2793, 2862, 2913, 3028, 3061. HR-MS: [M+H$^+$] Calculated for C$_{33}$H$_{35}$NO$_3$: 494.26897; found: 494.26804.



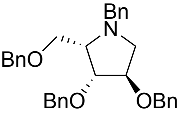
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-ribitol (32). 2,3,5-Tri-*O*-benzyl-D-lyxitol (**25**, 4.7 g, 11 mmol) was dissolved in pyridine (24 ml), cooled to 0 °C and methanesulfonyl chloride (4.4 ml, 56 mmol) added. The mixture was stirred at this temperature for 5 hours. The reaction was quenched with H$_2$O and the mixture taken up in a mixture of EtOAc and 1M HCl (aq.), washed with 1M HCl (aq.), NaHCO$_3$ (sat. aq.) and brine. The solution was dried over anhydrous MgSO$_4$, filtered and concentrated. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-D-ribitol (6.2 g, 11 mmol) was dissolved in benzylamine (35 ml, 323 mmol) and stirred overnight at 55 °C. The reaction mixture was diluted with EtOAc and washed with 1M HCl (aq.), Na$_2$CO$_3$ (sat. aq.) and brine. The solution was dried over anhydrous MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10-20% Et$_2$O/pentane) yielding the title pyrrolidine (4.7 g, 9.5 mmol, 88 % yield over 2 steps). [α]$^{20}_{\text{D}}$ = 30.7° (c = 1, CHCl$_3$). Analytical data was the same as for its enantiomer (**28**).



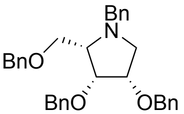
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-arabinitol (33). 2,3,5-Tri-*O*-benzyl-D-xylitol (**24**, 10 g, 24 mmol) was dissolved in pyridine (50 ml), cooled to 0 °C and methanesulfonyl chloride (9.2 ml, 118 mmol) added. The mixture was stirred at this temperature for 4 hours. The reaction was quenched with H_2O and the mixture taken up in a mixture of EtOAc and 1M HCl (aq.), washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-D-xylitol (13 g, 22 mmol) was dissolved in benzylamine (71 ml, 650 mmol) and stirred overnight at 55 °C. The reaction mixture was diluted with EtOAc and washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10-15% Et_2O/pentane) yielding the title pyrrolidine (7.6 g, 15 mmol, 71% yield over 2 steps). $[\alpha]^{20}_{D}$ = 38.0° (c = 1, $CHCl_3$). Analytical data was the same as for its enantiomer (**29**).



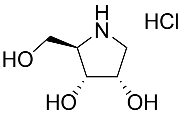
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-xylitol (34). 2,3,5-Tri-*O*-benzyl-D-arabinitol (**23**, 10 g, 24 mmol) was dissolved in pyridine (50 ml), cooled to 0 °C and methanesulfonyl chloride (9.2 ml, 118 mmol) added. The reaction mixture was stirred at this temperature for 5 hours after which the reaction was quenched with H_2O and diluted with EtOAc. The suspension was washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$ and concentrated. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-D-arabinitol (12.9 g, 22.3 mmol) was dissolved in benzylamine (73 ml, 670 mmol) and stirred at 55 °C overnight after which the reaction mixture was allowed to cool to room temperature and subsequently diluted with EtOAc. The mixture was washed with 1M HCl (aq.), Na_2CO_3 (sat. aq.) and brine before being dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (2-3% EtOAc/toluene) yielding the title pyrrolidine (5.0 g, 10 mmol, 46 % yield over 2 steps). $[\alpha]^{20}_{D}$ = 34.1° (c = 1, $CHCl_3$). Analytical data was the same as for its enantiomer (**30**).



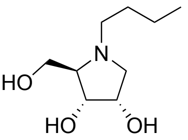
1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-lyxitol (35). 2,3,5-Tri-*O*-benzyl-D-ribitol (**22**, 6.3 g, 15 mmol) was dissolved in pyridine (32 ml), cooled to 0 °C and methanesulfonyl chloride (5.8 ml, 75 mmol) added. The reaction mixture was stirred at this temperature for 2.5 hours after which the reaction was quenched with H_2O and diluted with EtOAc. The suspension was washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$ and concentrated. The crude 1,4-Di-*O*-methanesulfonyl-2,3,5-tri-*O*-benzyl-D-ribitol (8.5 g, 15 mmol) was dissolved in benzylamine (49 ml, 450 mmol) and stirred at 55 °C for 2 days after which the reaction mixture was allowed to cool to room temperature and subsequently diluted with EtOAc. The mixture was washed with 1M HCl (aq.), Na_2CO_3 (sat. aq.) and brine before being dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (12.5-20% Et_2O/pentane) yielding the title pyrrolidine (5.2 g, 11 mmol, 70 % yield over 2 steps). $[\alpha]^{20}_{D}$ = 34.9° (c = 1, $CHCl_3$). Analytical data was the same as for its enantiomer (**31**).



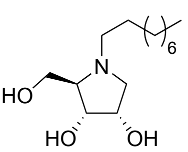
1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (1A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-ribitol (**28**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.4 g, 7.9 mmol, 99%). ^1H NMR (600 MHz, MeOD) δ 4.26 (td, *J* = 4.0, 1.9 Hz, 1H, C-2), 4.13 (dd, *J* = 8.3, 4.0 Hz, 1H, C-3), 3.91 (dd, *J* = 12.0, 3.3 Hz, 1H, C-5a), 3.78 (dd, *J* = 12.0, 5.9 Hz, 1H, C-5b), 3.54 (ddd, *J* = 8.8, 5.9, 3.3 Hz, 1H, C-4), 3.39 (dd, *J* = 12.4, 4.0 Hz, 1H, C-1a), 3.26 (dd, *J* = 12.5, 2.0 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 72.9 (*C*-3), 71.1 (*C*-2), 63.9 (*C*-4), 59.4 (*C*-5), 51.1 (*C*-1). $[\alpha]^{20}_{D}$ = 51.6° (c = 1, MeOH). IR (neat): 754, 922, 967, 980, 1003, 1034, 1051, 1098, 1132, 1192, 1233, 1323, 1385, 1418, 1449, 2475, 2538, 2596, 2695, 2716, 2747, 2849, 2895, 2938, 3256, 3289, 3345, 3383. HR-MS: $[M+H^+]$ Calculated for $C_5H_{11}NO_3$: 134.08117; found: 134.08173.



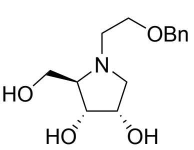
1,4-Dideoxy-1,4-butylimino-D-ribitol (1B). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-17.5% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (33 mg, 0.17 mmol, 35%). ^{1}H NMR (600 MHz, MeOD) δ 4.06 (q, *J* = 5.8 Hz, 1H, C-2), 3.88 (t, *J* = 5.1 Hz, 1H, C-3), 3.62 (dd, *J* = 11.5, 5.0 Hz, 1H, C-5a), 3.60 (dd, *J* = 11.6, 4.5 Hz, 1H, C-5b), 3.29 (dd, *J* = 10.1, 6.0 Hz, 1H, C-1a), 2.92 – 2.87 (m, 1H, N-C*H*H butyl), 2.68 (q, *J* = 4.7 Hz, 1H, C-4), 2.56 – 2.45 (m, 2H, C-1a, N-CH*H* butyl), 1.56 – 1.45 (m, 2H, N-CH$_2$C*H*$_2$ butyl), 1.41 – 1.28 (m, 2H, C*H*$_2$CH$_3$ butyl), 0.95 (t, *J* = 7.4 Hz, 3H, C*H*$_3$ butyl). ^{13}C NMR (151 MHz, MeOD) δ 73.9 (*C*-3), 72.9 (*C*-4), 70.9 (*C*-2), 62.3 (*C*-5), 58.9 (*C*-1), 57.2 (N-C*H*$_2$ butyl), 30.9 (N-CH$_2$C*H*$_2$ butyl), 21.6 (*C*H$_2$CH$_3$ butyl), 14.3 (*C*H$_3$ butyl). [α]$^{20}_{D}$ = -33.9° (c = 0.7, MeOH). HR-MS: [M+H$^+$] Calculated for $C_9H_{19}NO_3$: 190.14377; found: 190.14488.



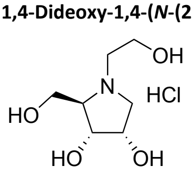
1,4-Dideoxy-1,4-nonylimino-D-ribitol (1C). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (26.5-29% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (57 mg, 0.22 mmol, 44%). ^{1}H NMR (600 MHz, MeOD) δ 4.09 – 4.02 (m, 1H, C-2), 3.88 (t, *J* = 5.1 Hz, 1H, C-3), 3.60 (d, *J* = 5.0 Hz, 2H, C-5), 3.27 (dd, *J* = 9.8, 5.8 Hz, 1H, C-1a), 2.86 (ddd, *J* = 11.8, 9.9, 6.9 Hz, 1H, N-C*H*H nonyl), 2.65 (q, *J* = 4.7 Hz, 1H, C-4), 2.52 – 2.42 (m, 2H, C-1a, N-CH*H*), 1.58 – 1.44 (m, 2H, N-CH$_2$CH$_2$ nonyl), 1.39 – 1.22 (m, 12H, 6xC*H*$_2$ nonyl), 0.90 (t, *J* = 7.1 Hz, 3H, C*H*$_3$ nonyl). ^{13}C NMR (151 MHz, MeOD) δ 74.0 (*C*-3), 72.8 (*C*-4), 70.9 (*C*-2), 62.5 (*C*-5), 59.0 (*C*-1), 57.4 (N-*C*H$_2$ nonyl), 33.0, 30.7, 30.6, 30.4 (4x*C*H$_2$ nonyl), 28.9 (N-CH$_2$*C*H$_2$ nonyl), 28.5, 23.7 (2x*C*H$_2$ nonyl), 14.5 (*C*H$_3$ nonyl). [α]$^{20}_{D}$ = -34.5° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22259.



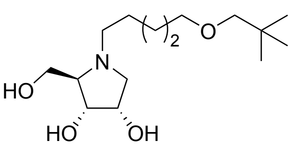
1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-ribitol (1D). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification (12.5-16% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (42 mg, 0.16 mmol, 32%). ^{1}H NMR (600 MHz, MeOD) δ 7.38 – 7.32 (m, 4H, 2x *o*-C*H*$_{Ar}$ Bn, 2x *m*-C*H*$_{Ar}$ Bn), 7.30 – 7.25 (m, 1H, *p*-C*H*$_{Ar}$ Bn), 4.53 (s, 2H, C*H*$_2$ Bn), 4.05 (q, *J* = 5.7 Hz, 1H, C-2), 3.89 (t, *J* = 5.2 Hz, 1H, C-3), 3.68 – 3.54 (m, 4H, C-5, N-CH$_2$C*H*$_2$ ethyl), 3.34 – 3.32 (m, 1H, C-1a), 3.15 (ddd, *J* = 12.3, 6.9, 4.9 Hz, 1H, N-C*H*H ethyl), 2.80 – 2.73 (m, 2H, C-4, N-C*H*H ethyl), 2.62 (dd, *J* = 9.9, 6.4 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 139.3 (*C*$_q$ Bn), 129.4, 129.0 (*o*-*C*H$_{Ar}$ Bn, *m*-*C*H$_{Ar}$ Bn), 128.8 (*p*-*C*H$_{Ar}$ Bn), 74.1 (*C*H$_2$ Bn), 73.8 (*C*-3), 72.7 (*C*-4), 71.1 (*C*-2), 69.3 (N-CH$_2$*C*H$_2$), 62.0 (*C*-5), 59.6 (*C*-1), 56.4 (N-*C*H$_2$). [α]$^{20}_{D}$ = -18.8° (c = 0.8, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{21}NO_4$: 268.15433; found: 268.15586.



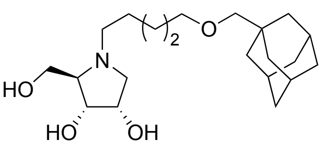
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-D-ribitol hydrochloride (1E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-ribitol (**1D**, 15 mg, 0.06 mmol) was subjected to *General procedure C* yielding the title compound (12 mg, 0.06 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.31 – 4.23 (m, 1H, C-2), 4.15 – 4.09 (m, 1H, C-3), 4.02 (dd, *J* = 12.3, 3.2 Hz, 1H, C-5a), 3.94 – 3.83 (m, 3H, C-5b, N-CH$_2$C*H*$_2$ ethyl), 3.79 (dd, *J* = 12.5, 3.8 Hz, 1H, C-1b), 3.68 – 3.59 (m, 2H, C-4, N-C*H*H ethyl), 3.40 (d, *J* = 10.3 Hz, 2H, C-1a, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 72.8 (*C*-4), 72.6 (*C*-3), 70.5 (*C*-2), 61.3 (N-*C*H$_2$ ethyl), 59.7 (*C*-1), 58.6 (*C*-5), 57.5 (N-CH$_2$*C*H$_2$ ethyl). [α]$^{20}_{D}$ = 16.6° (c = 0.7, MeOH). HR-MS: [M+H$^+$] Calculated for $C_7H_{15}NO_4$: 178.10738; found: 178.10762.



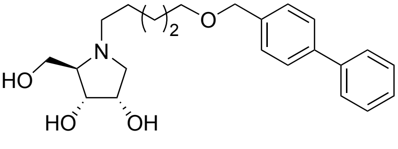
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-D-ribitol (1F). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (21-25% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (64 mg, 0.22 mmol, 44%). ^{1}H NMR (600 MHz, MeOD) δ 4.05 (q, *J* = 5.8 Hz, 1H, C-2), 3.88 (t, *J* = 5.1 Hz, 1H, C-3), 3.61 (dd, *J* = 11.5, 5.0 Hz, 1H, C-5a), 3.59 (dd, *J* = 11.6, 4.4 Hz, 1H, C-5b), 3.42 (t, *J* = 6.4 Hz, 2H, O-C*H*$_2$ pentyl), 3.28 (dd, *J* = 9.8, 5.8 Hz, 1H, C-1a), 3.06 (s, 2H, OC*H*$_2$ neopentyl), 2.91 – 2.84 (m, 1H, N-C*H*H pentyl), 2.65 (q, *J* = 4.6 Hz, 1H, C-4), 2.52 – 2.44 (m, 2H, C-1b, N-C*H*H pentyl), 1.65 – 1.48 (m, 4H, N-CH$_2$C*H*$_2$ pentyl, O-CH$_2$C*H*$_2$ pentyl), 1.46 – 1.32 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl), 0.90 (s, 9H, 3xC*H*$_3$ neopentyl). ^{13}C NMR (151 MHz, MeOD) δ 82.4 (O-*C*H$_2$ neopentyl), 74.0 (*C*-3), 72.8 (*C*-4), 72.3 (O-*C*H$_2$ pentyl), 70.9 (*C*-2), 62.4 (*C*-5), 58.9 (*C*-1), 57.3(N-*C*H$_2$ pentyl), 32.9 (*C*$_q$ neopentyl), 30.5 (O-CH$_2$*C*H$_2$ pentyl), 28.7 (N-CH$_2$*C*H$_2$ pentyl), 27.2 (3x*C*H$_3$ neopentyl), 25.1 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_D$ = -31,7° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{15}H_{31}NO_4$: 290.23258; found: 290.23279.

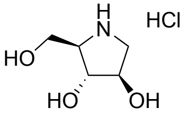


1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-D-ribitol (1G). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (33-37% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (60 mg, 0.16 mmol, 33%). ^{1}H NMR (600 MHz, MeOD) δ 4.04 (q, *J* = 5.8 Hz, 1H, C-2), 3.86 (t, *J* = 5.0 Hz, 1H, C-3), 3.59 (d, *J* = 4.8 Hz, 2H, C-5), 3.39 (t, *J* = 6.4 Hz, 2H, O-C*H*$_2$ pentyl), 3.26 (dd, *J* = 9.6, 5.9 Hz, 1H, C-1a), 2.97 (s, 2H, O-C*H*$_2$ adamantanemethyl), 2.90 – 2.79 (m, 1H, N-C*H*H pentyl), 2.61 (q, *J* = 4.7 Hz, 1H, C-4), 2.51 – 2.39 (m, 2H, C-1b, N-C*H*H pentyl), 1.95 (s, 3H, 3xC*H* adamantanemethyl), 1.80 – 1.65 (m, 6H, 3xC$_q$C*H*$_2$ adamantanemethyl), 1.64 – 1.46 (m, 10H, N-CH$_2$C*H*$_2$ pentyl, O-CH$_2$C*H*$_2$ pentyl, 3xCHC*H*$_2$ adamantanemethyl), 1.46 – 1.27 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 83.0 (O-*C*H$_2$ adamantanemethyl), 74.0 (*C*-3), 72.9 (*C*-4), 72.4 (O-*C*H$_2$ pentyl), 70.9 (*C*-2), 62.6 (*C*-5), 59.0 (*C*-1), 57.2 (N-*C*H$_2$ pentyl), 40.8 (3xC$_q$C*H*$_2$ adamantanemethyl), 38.3 (3xCHC*H*$_2$ adamantanemethyl), 35.1 (*C*$_q$ adamantanemethyl), 30.5 (O-CH$_2$*C*H$_2$ pentyl), 29.7 (3x*C*H adamantanemethyl), 28.8 (N-CH$_2$*C*H$_2$ pentyl), 25.2 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_D$ = -23.4° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 368.27954; found: 368.27952.

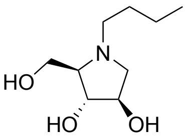


1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-D-ribitol (1H). 1,4-Dideoxy-1,4-imino-D-ribitol hydrochloride (**1A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (32.5-37% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (79 mg, 0.21 mmol, 41%). ^{1}H NMR (600 MHz, MeOD) δ 7.62 – 7.54 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.44 – 7.37 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.31 (t, *J* = 7.4 Hz, 1H, *p*-C*H*$_{Ar}$ Ph), 4.51 (s, 2H, O-C*H*$_2$ phenylbenzyl), 4.04 (q, *J* = 5.8 Hz, 1H, C-2), 3.87 (t, *J* = 5.1 Hz, 1H, C-3), 3.58 (d, *J* = 4.8 Hz, 2H, C-5), 3.49 (t, *J* = 6.5 Hz, 2H, O-C*H*$_2$ pentyl), 3.25 (dd, *J* = 9.7, 5.9 Hz, 1H, C-1a), 2.88 – 2.79 (m, 1H, N-C*H*H pentyl), 2.61 (q, *J* = 4.6 Hz, 1H, C-4), 2.49 – 2.39 (m, 2H, C-1b, N-C*H*H pentyl), 1.68 – 1.57 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.56 – 1.47 (m, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.46 – 1.32 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.0, 141.7, 138.9 (3x*C*$_q$ Ph), 129.8, 129.3 (4x*C*H$_{Ar}$ Ph), 128.3 (*p*-*C*H$_{Ar}$ Ph), 127.9 127.9 (4x*C*H$_{Ar}$ Ph), 74.0 (*C*-3), 73.5 (O-*C*H$_2$ phenylbenzyl), 72.8 (*C*-4), 71.2 (O-*C*H$_2$ pentyl), 70.9 (*C*-2), 62.6 (*C*-5), 58.9 (*C*-1), 57.1 (N-*C*H$_2$ pentyl), 30.6 (O-CH$_2$*C*H$_2$ pentyl), 28.7 (N-CH$_2$*C*H$_2$ pentyl), 25.1 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_D$ = -31.2° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23266.

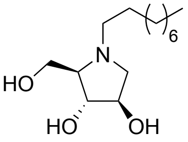




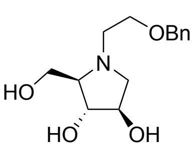
1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (2A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-arabinitol (**29**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.4 g, 8.0 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.22 – 4.18 (m, 1H, C-2), 3.98 (s, 1H, C-3), 3.90 (dd, *J* = 11.6, 4.7 Hz, 1H, C-5a), 3.80 (dd, *J* = 11.6, 9.3 Hz, 1H, C-5b), 3.52 (ddd, *J* = 9.0, 4.5, 2.7 Hz, 1H, C-4), 3.47 (dd, *J* = 12.0, 4.0 Hz, 1H, C-1a), 3.29 (d, *J* = 12.0 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 77.4 (*C*-2), 76.1 (*C*-3), 69.8 (*C*-4), 60.9 (*C*-5), 51.9 (*C*-1). $[\alpha]^{20}_{D}$ = 36.4° (c = 1, MeOH). IR (neat): 606, 714, 764, 823, 918, 966, 1003, 1038, 1074, 1109, 1167, 1215, 1260, 1298, 1360, 1375, 1396, 1449, 1576, 2488, 2745, 2762, 2833, 2887, 2941, 2959, 2968, 3022, 3277, 3372, 3416. HR-MS: $[M+H^+]$ Calculated for $C_5H_{11}NO_3$: 134.08117; found: 134.08169.



1,4-Dideoxy-1,4-butylimino-D-arabinitol (2B). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (12 mg, 0.06 mmol, 13%). ^{1}H NMR (600 MHz, MeOD) δ 4.07 – 4.02 (m, 1H, C-2), 3.94 – 3.89 (m, 1H, C-3), 3.79 (dd, *J* = 11.5, 5.2 Hz, 1H, C-5a), 3.77 (dd, *J* = 11.5, 6.1 Hz, 1H, C-5b), 3.27 (d, *J* = 11.0 Hz, 1H, C-1a), 3.14 – 3.07 (m, 1H, N-C*H*H butyl), 3.00 (dd, *J* = 11.1, 4.6 Hz, 1H, C-1b), 2.89 – 2.83 (m, 1H, C-4), 2.71 – 2.64 (m, 1H, N-C*H*H butyl), 1.64 – 1.56 (m, 2H, N-CH_2CH_2 butyl), 1.43 – 1.32 (m, 2H, CH_2CH_3 butyl), 0.96 (t, *J* = 7.4 Hz, 3H, CH_3 butyl). ^{13}C NMR (151 MHz, MeOD) δ 79.4 (*C*-3), 76.7 (*C*-2), 76.3 (*C*-4), 61.8 (*C*-5), 60.5 (*C*-1), 57.5 (N-CH_2 butyl), 30.0 (N-CH_2CH_2 butyl), 21.4 (CH_2CH_3 butyl), 14.2 (CH_3 butyl). $[\alpha]^{20}_{D}$ = -23.3° (c = 0.2, MeOH). HR-MS: $[M+H^+]$ Calculated for $C_9H_{19}NO_3$: 190.14377; found: 190.14470.

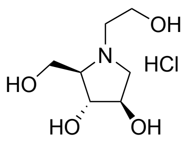


1,4-Dideoxy-1,4-nonylimino-D-arabinitol (2C). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (25-42% A/B in 8.5 minutes) and reversed phase column chromatography yielded the title compound (61 mg, 0.23 mmol, 47%). ^{1}H NMR (600 MHz, MeOD) δ 4.09 – 4.01 (m, 1H, C-2), 3.94 – 3.91 (m, 1H, C-3), 3.78 (d, *J* = 5.7 Hz, 2H, C-5), 3.28 (d, *J* = 11.0 Hz, 1H, C-1a), 3.14 – 3.06 (m, 1H, N-C*H*H nonyl), 3.00 (dd, *J* = 11.0, 4.7 Hz, 1H, C-1b), 2.89 – 2.85 (m, 1H, C-4), 2.71 – 2.65 (m, 1H, N-C*H*H nonyl), 1.66 – 1.57 (m, 2H, N-CH_2CH_2 nonyl), 1.39 – 1.24 (m, 12H, 6xCH_2 nonyl), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3 nonyl). ^{13}C NMR (151 MHz, MeOD) δ 79.4 (*C*-3), 76.6 (*C*-2), 76.3 (*C*-4), 61.8 (*C*-5), 60.5 (*C*-1), 57.7 (N-CH_2 nonyl), 33.0, 30.6, 30.5, 30.4, 28.2 (5xCH_2 nonyl), 27.8 (N-CH_2CH_2 nonyl), 23.7 (CH_2nonyl), 14.5 (CH_3 nonyl). $[\alpha]^{20}_{D}$ = -18.9° (c = 1, MeOH). HR-MS: $[M+H^+]$ Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22228.

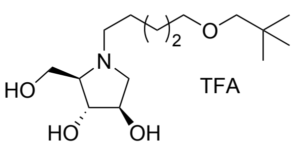


1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-arabinitol (2D). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (11-20% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (35 mg, 0.13 mmol, 26%). ^{1}H NMR (600 MHz, MeOD) δ 7.38 – 7.31 (m, 4H, 2x *o*-CH_{Ar} Bn, 2x *m*-CH_{Ar} Bn), 7.30 – 7.25 (m, 1H, *p*-CH_{Ar} Bn), 4.53 (s, 2H, CH_2 Bn), 3.95 – 3.92 (m, 1H, C-2), 3.91 – 3.87 (m, 1H, C-3), 3.70 (dd, *J* = 11.4, 4.5 Hz, 1H, C-5a), 3.66 – 3.61 (m, 2H, C-5b, N-CH_2C*H*H ethyl), 3.60 (dd, *J* = 10.2, 5.3 Hz, 1H, N-CH_2C*H*H ethyl), 3.14 – 3.10 (m, 1H, N-C*H*H ethyl), 3.09 (d, *J* = 9.4 Hz, 1H, C-1a), 2.78 (dd, *J* = 10.5, 5.4 Hz, 1H, C-1b), 2.62 (dt, *J* = 13.1, 5.1 Hz, 1H, N-C*H*H ethyl), 2.53 (q, *J* = 4.4 Hz, 1H, C-4). ^{13}C NMR (151 MHz, MeOD) δ 139.5 (C_q Bn), 129.4, 129.0 (*o*-CH_{Ar} Bn, *m*-CH_{Ar} Bn), 128.7 (*p*-CH_{Ar} *p*-Bn), 80.4 (*C*-3), 77.4 (*C*-2), 74.4 (*C*-4), 74.2 (CH_2 Bn), 69.8 (N-CH_2CH_2 ethyl), 62.2 (*C*-5), 61.1 (*C*-1), 55.5 (N-CH_2 ethyl). $[\alpha]^{20}_{D}$ = -22.6° (c = 0.7, MeOH). HR-MS: $[M+H^+]$ Calculated for $C_{14}H_{21}NO_4$: 268.15433; found: 268.15420.

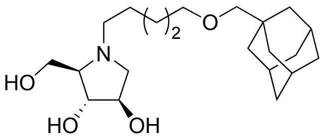
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-D-arabinitol hydrochloride (2E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-arabinitol (**2D**, 47 mg, 0.18 mmol) was subjected to *General procedure C* yielding the title compound (39 mg, 0.18 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.22 (s, 1H, C-2), 3.99 (s, 1H, C-3), 3.96 (d, *J* = 6.6 Hz, 2H, C-5), 3.95 – 3.86 (m, 2H, N-CH$_2$C*H*$_2$ ethyl), 3.72 (d, *J* = 12.1 Hz, 1H, C-1a), 3.66 – 3.54 (m, 3H, C-1b, C-4, N-C*H*H ethyl), 3.35 (s, 1H, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 78.3 (*C*-4), 77.6 (*C*-3), 75.7 (*C*-2), 61.5 (*C*-1), 60.6 (*C*-5), 60.4 (N-*C*H$_2$ ethyl), 57.9 N-CH$_2$*C*H$_2$ ethyl). [α]$^{20}_{D}$ = 5.9° (c = 0.8, MeOH). HR-MS: [M+H$^+$] Calculated for $C_7H_{15}NO_4$: 178.10738; found: 178.10816.



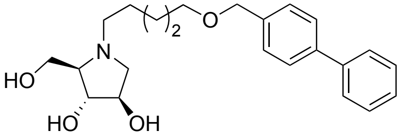
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-D-arabinitol trifluoroacetatic acid (2F). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc) and HPLC purification (21-26% A/B in 10 minutes) yielded the title compound (53 mg, 0.13 mmol, 26%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 – 4.16 (m, 1H, C-2), 3.95 (s, 1H, C-3), 3.94 – 3.89 (m, 2H, C-5), 3.60 (d, *J* = 11.8 Hz, 1H, C-1a), 3.49 – 3.40 (m, 5H, C-1b, C-4, N-C*H*H pentyl, O-C*H*$_2$ pentyl), 3.19 – 3.11 (m, 1H, N-C*H*H pentyl), 3.07 (s, 2H, O-C*H*$_2$ neopentyl), 1.85 – 1.73 (m, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.68 – 1.58 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$), 1.51 – 1.40 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 0.90 (s, 9H, 3xC*H*$_3$ neopentyl). ^{13}C NMR (151 MHz, MeOD) δ 82.5 (O-*C*H$_2$ neopentyl), 78.6 (O-*C*H$_2$ pentyl), 77.7 (*C*-4), 75.7 (*C*-3), 72.0 (*C*-2), 60.9 (*C*-5), 60.6 (*C*-1), 58.9 (N-*C*H$_2$ pentyl), 32.9 (*C*$_q$ neopentyl), 30.2 (O-CH$_2$*C*H$_2$ pentyl), 27.1 (3x*C*H$_3$ neopentyl), 26.1 (N-CH$_2$*C*H$_2$ pentyl), 24.5 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). [α]$^{20}_{D}$ = -1.2° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{15}H_{31}NO_4$: 290.23258; found: 290.23312.



1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-D-arabinitol (2G). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (25-58% A/B in 9.5 minutes) and reversed phase column chromatography yielded the title compound (68 mg, 0.19 mmol, 37%). ^{1}H NMR (600 MHz, MeOD) δ 4.03 – 3.96 (m, 1H, C-2), 3.94 – 3.89 (m, 1H, C-3), 3.74 (dd, *J* = 11.5, 5.1 Hz, 1H, C-5a), 3.71 (dd, *J* = 11.4, 5.3 Hz, 1H, C-5b), 3.39 (t, *J* = 6.4 Hz, 2H, O-C*H*$_2$ pentyl), 3.16 (d, *J* = 10.7 Hz, 1H, C-1a), 3.02 – 2.93 (m, 3H, N-C*H*H pentyl, O-C*H*$_2$ adamantanemethyl), 2.84 (dd, *J* = 10.8, 4.9 Hz, 1H, C-1b), 2.66 (q, *J* = 4.7 Hz, 1H, C-4), 2.56 – 2.48 (m, 1H, N-C*H*H pentyl), 1.95 (s, 3H, 3xC*H* adamantanemethyl), 1.80 – 1.65 (m, 6H, 3xC$_q$C*H*$_2$ adamantanemethyl), 1.63 – 1.53 (m, 10H, N-CH$_2$C*H*$_2$ pentyl, O-CH$_2$C*H*$_2$ pentyl, 3xCHC*H*$_2$ adamantanemethyl), 1.46 – 1.33 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$). ^{13}C NMR (151 MHz, MeOD) δ 83.0 (O-*C*H$_2$ adamantanemethyl), 80.0 (*C*-3), 76.9 (*C*-2), 75.4 (*C*-4), 72.4 (O-*C*H$_2$ pentyl), 62.1 (*C*-5), 60.5 (*C*-1), 57.2 (N-*C*H$_2$ pentyl), 40.8 (3xC$_q$*C*H$_2$ adamantanemethyl), 38.3 (3xCH*C*H$_2$ adamantanemethyl), 35.1 (*C*$_q$ adamantanemethyl), 30.5 (O-CH$_2$*C*H$_2$ pentyl), 29.7 (3x*C*H adamantanemethyl), 28.2 (N-CH$_2$*C*H$_2$ pentyl), 25.1 (N-(CH$_2$)$_2$*C*H$_2$). [α]$^{20}_{D}$ = -22.8° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 368.27954; found: 368.27953.

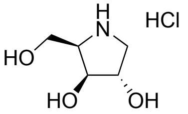


1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-D-arabinitol (2H). 1,4-Dideoxy-1,4-imino-D-arabinitol hydrochloride (**2A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (32-37% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (65 mg, 0.17 mmol, 34%). ^{1}H NMR (600 MHz, MeOD) δ 7.62 – 7.55 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.44 – 7.37 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.34 – 7.28 (m, 1H, *p*-C*H*$_{Ar}$ Ph), 4.51 (s, 2H, O-C*H*$_2$ phenylbenzyl), 3.96 – 3.92 (m, 1H, C-2),

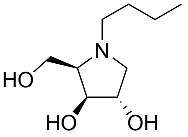


3.92 – 3.89 (m, 1H, C-3), 3.68 (dd, *J* = 11.2, 4.9 Hz, 1H, C-5a), 3.64 (dd, *J* = 11.2, 4.2 Hz, 1H, C-5b), 3.50 (t, *J* = 6.5 Hz, 2H, O-C*H*$_2$ pentyl), 3.01 (d, *J* = 10.4 Hz, 1H, C-1a), 2.86 – 2.78 (m, 1H, N-C*H*H pentyl), 2.63 (dd, *J* = 10.4, 5.3 Hz, 1H, C-1b), 2.42 (q, *J* = 4.4 Hz, 1H, C-4), 2.35 – 2.28 (m, 1H, N-C*H*H pentyl), 1.67 – 1.58 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.56 – 1.47 (m, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.47 – 1.32 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.1, 141.7, 138.9 (3x*C*$_q$ Ph), 129.8, 129.3 (4x*C*H$_{Ar}$ Ph), 128.3 (*p*-*C*H$_{Ar}$ Ph), 127.9, 127.9 (4x*C*H$_{Ar}$ Ph), 80.8 (*C*-3), 77.3 (*C*-2), 74.4 (*C*-4), 73.5 (O-*C*H$_2$ phenylbenzyl), 71.3 (O-*C*H$_2$ pentyl), 62.5 (*C*-5), 60.5 (*C*-1), 56.6 (N-*C*H$_2$ pentyl), 30.6 (O-CH$_2$*C*H$_2$ pentyl), 28.9 (N-CH$_2$*C*H$_2$ pentyl), 25.2 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). [α]$^{20}_{D}$ = -29.6° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23263.

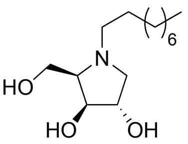
1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (3A) 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-xylitol (**30**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.4 g, 8.0 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.25 (dd, *J* = 4.0, 1.5 Hz, 1H, C-2), 4.16 (dd, *J* = 3.3, 1.5 Hz, 1H, C-3), 3.96 (dd, *J* = 11.7, 4.5 Hz, 1H, C-5a), 3.87 (dd, *J* = 11.7, 9.1 Hz, 1H, C-5b), 3.80 (ddd, *J* = 9.1, 4.5, 3.2 Hz, 1H, C-4), 3.56 (dd, *J* = 12.3, 4.1 Hz, 1H, C-1a), 3.16 (d, *J* = 12.3 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 76.1 (*C*-2), 75.8 (*C*-3), 65.1 (*C*-4), 59.0 (*C*-5), 52.0 (*C*-1). [α]$^{20}_{D}$ = 13.3° (c = 1, MeOH). IR (neat): 608, 718, 773, 822, 901, 918, 972, 1016, 1034, 1055, 1082, 1098, 1204, 1246, 1281, 1294, 1366, 1385, 1402, 1454, 1578, 2295, 2351, 2399, 2469, 2540, 2650, 2714, 2805, 2955, 3026, 3341. HR-MS: [M+H$^+$] Calculated for $C_5H_{11}NO_3$: 134.08117; found: 134.08186.



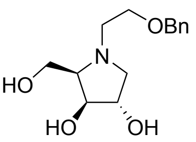
1,4-Dideoxy-1,4-butylimino-D-xylitol (3B). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (15-17.5% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (25 mg, 0.13 mmol, 27%). ^{1}H NMR (600 MHz, MeOD) δ 4.08 – 3.97 (m, 2H, C-2, C-3), 3.80 (dd, *J* = 11.1, 6.7 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.1, 4.4 Hz, 1H, C-5b), 3.38 (dd, *J* = 10.5, 5.4 Hz, 1H, C-1a), 2.86 – 2.79 (m, 1H, N-C*H*H ethyl), 2.78 – 2.74 (m, 1H, C-4), 2.38 – 2.32 (m, 1H, N-C*H*H butyl), 2.24 (dd, *J* = 10.4, 5.2 Hz, 1H, C-1b), 1.52 – 1.44 (m, 2H, N-CH$_2$C*H*$_2$ butyl), 1.41 – 1.27 (m, 2H, C*H*$_2$CH$_3$ butyl), 0.94 (t, *J* = 7.4 Hz, 3H, C*H*$_3$ butyl). ^{13}C NMR (151 MHz, MeOD) δ 79.0 (*C*-3), 77.4 (*C*-2), 69.0 (*C*-4), 61.0 (*C*-5), 59.9 (*C*-1), 57.1 (N-*C*H$_2$ butyl), 31.2 (N-CH$_2$*C*H$_2$ butyl), 21.7 (*C*H$_2$CH$_3$ butyl), 14.4 (*C*H$_3$ butyl). [α]$^{20}_{D}$ = -62.8° (c = 0.5, MeOH). HR-MS: [M+H$^+$] Calculated for $C_9H_{19}NO_3$: 190.14377; found: 190.14421.



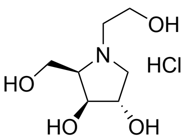
1,4-Dideoxy-1,4-nonylimino-D-xylitol (3C). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography, HPLC purification (27-31% A/B in 8.5 minutes) and reversed phase column chromatography yielded the title compound (56 mg, 0.22 mmol, 43%). ^{1}H NMR (600 MHz, MeOD) δ 4.07 – 3.98 (m, 2H, C-2, C-3), 3.80 (dd, *J* = 11.1, 6.7 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.1, 4.4 Hz, 1H, C-5b), 3.38 (dd, *J* = 10.5, 5.4 Hz, 1H, C-1a), 2.84 – 2.79 (m, 1H, N-C*H*H nonyl), 2.79 – 2.75 (m, 1H, C-4), 2.39 – 2.29 (m, 1H, N-C*H*H nonyl), 2.24 (dd, *J* = 10.4, 5.2 Hz, 1H, C-1b), 1.54 – 1.46 (m, 2H, N-CH$_2$C*H*$_2$ nonyl), 1.37 – 1.23 (m, 12H, 6xC*H*$_2$ nonyl), 0.90 (t, *J* = 7.1 Hz, 3H, C*H*$_3$ nonyl). ^{13}C NMR (151 MHz, MeOD) δ 79.0 (*C*-3), 77.4 (*C*-2), 69.0 (*C*-4), 61.0 (*C*-5), 59.8 (*C*-1), 57.4 (N-*C*H$_2$ nonyl), 33.1, 30.7, 30.7, 30.4 (4x*C*H$_2$ nonyl), 29.0 (N-CH$_2$*C*H$_2$ nonyl), 28.6, 23.7 (2x*C*H$_2$ nonyl), 14.5 (*C*H$_3$ nonyl). [α]$^{20}_{D}$ = -51.7° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22193.



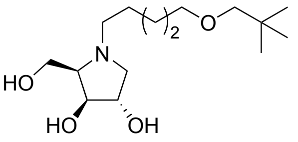
1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-xylitol (3D). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography, HPLC purification (13.5-17% A/B in 9.5 minutes) and reversed phase column chromatography yielded the title compound (34 mg, 0.13 mmol, 25%). ^{1}H NMR (600 MHz, MeOD) δ 7.38 – 7.31 (m, 4H, *o*-C*H*$_{Ar}$ Bn, *m*-C*H*$_{Ar}$ Bn), 7.30 – 7.25 (m, 1H, *p*-CH$_{Ar}$ Bn), 4.52 (s, 2H, C*H*$_2$ Bn), 4.04 – 3.98 (m, 2H, C-2, C-3), 3.79 (dd, *J* = 11.3, 6.1 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.3, 4.6 Hz, 1H, C-5b), 3.64 – 3.56 (m, 2H, N-CH$_2$C*H*$_2$ ethyl), 3.41 (dd, *J* = 10.5, 5.6 Hz, 1H, C-1a), 3.11 – 3.04 (m, 1H, N-C*H*H ethyl), 2.85 (q, *J* = 5.7 Hz, 1H, C-4), 2.69 – 2.61 (m, 1H, N-C*H*H ethyl), 2.35 (dd, *J* = 10.4, 5.2 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 139.5 (*C*$_q$ Bn), 129.4, 128.9 (*o*-*C*H$_{Ar}$ Bn, *m*-*C*H$_{Ar}$ Bn), 128.7 (*p*-*C*H$_{Ar}$ Bn), 79.0 (*C*-3), 77.5 (*C*-2), 74.1 (O-*C*H$_2$ Bn), 69.9 (N-CH$_2$*C*H$_2$ ethyl), 68.8 (*C*-4), 61.2 (*C*-5), 60.4 (*C*-1), 56.1 (N-CH$_2$*C*H$_2$). $[\alpha]^{20}_D$ = -30° (c = 0.7, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{21}NO_4$: 268.15433; found: 268.15469.



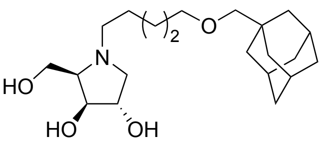
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-D-xylitol hydrochloride (3E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-xylitol (**3D**, 15 mg, 0.06 mmol) was subjected to *General procedure C* yielding the title compound (12 mg, 0.06 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.26 – 4.21 (m, 2H, C-2, C-3), 4.08 – 4.01 (m, 2H, C-5), 3.94 – 3.82 (m, 4H, C-1a, C-4, N-CH$_2$C*H*$_2$ ethyl), 3.77 – 3.68 (m, 1H, N-C*H*H ethyl), 3.47 (d, *J* = 12.6 Hz, 1H, C-1b), 3.39 – 3.34 (m, 1H, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 76.6, 75.9 (*C*-2, *C*-3), 73.7 (*C*-4), 61.9 (N-*C*H$_2$ ethyl), 60.9 (*C*-1), 58.9 (*C*-5), 58.1 (N-CH$_2$*C*H$_2$). $[\alpha]^{20}_D$ = -16.7° (c = 0.2, MeOH). HR-MS: [M+H$^+$] Calculated for $C_7H_{15}NO_4$: 178.10738; found: 178.10800.



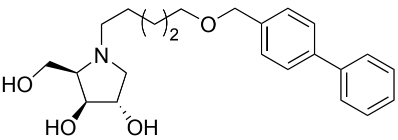
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-D-xylitol (3F). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography, HPLC purification (22-26% A/B in 9 minutes) and reversed phase column chromatography yielded the title compound (46 mg, 0.16 mmol, 31%). ^{1}H NMR (600 MHz, MeOD) δ 4.06 – 3.99 (m, 2H, C-2, C-3), 3.80 (dd, *J* = 11.1, 6.7 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.2, 4.4 Hz, 1H, C-5b), 3.42 (t, *J* = 6.4 Hz, 2H, O-C*H*$_2$ pentyl), 3.38 (dd, *J* = 10.4, 5.4 Hz, 1H, C-1a), 3.06 (s, 2H, O-C*H*$_2$ neopentyl), 2.85 – 2.79 (m, 1H, N-C*H*H pentyl), 2.79 – 2.76 (m, 1H, C-4), 2.40 – 2.33 (m, 1H, N-C*H*H pentyl), 2.25 (dd, *J* = 10.4, 5.1 Hz, 1H, C-1b), 1.62 – 1.56 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.56 – 1.47 (m, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.44 – 1.32 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl), 0.90 (s, 9H, 3xC*H*$_3$ neopentyl). ^{13}C NMR (151 MHz, MeOD) δ 82.4 (O-C*H*$_2$ neopentyl), 79.0 (*C*-3), 77.4 (*C*-2), 72.4 (O-*C*H$_2$ pentyl), 69.0 (*C*-4), 61.0 (*C*-5), 59.8 (*C*-1), 57.3 (N-*C*H$_2$ pentyl), 32.9 (*C*$_q$ neopentyl), 30.6 (O-CH$_2$*C*H$_2$ pentyl), 28.8 (N-CH$_2$*C*H$_2$ pentyl), 27.2 (3x*C*H$_3$ neopentyl), 25.3 (N-(CH$_2$)$_2$CH$_2$ pentyl). $[\alpha]^{20}_D$ = -48.9° (c = 0.9, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{15}H_{31}NO_4$: 290.23258; found: 290.23295.



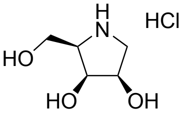
1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-D-xylitol (3G). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography, HPLC purification (33-38% A/B in 9.5 minutes) and reversed phase column chromatography yielded the title compound (66 mg, 0.18 mmol, 36%). ^{1}H NMR (600 MHz, MeOD) δ 4.09 – 3.99 (m, 2H, C-2, C-3), 3.81 (dd, *J* = 11.1, 6.7 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.2, 4.4 Hz, 1H, C-5b), 3.41 – 3.36 (m, 3H, C-1a, O-C*H*$_2$ pentyl), 2.97 (s, 2H, O-C*H*$_2$ adamantanemethyl), 2.87 – 2.81 (m, 1H, N-C*H*H pentyl), 2.81 – 2.76 (m, 1H, C-4), 2.40 – 2.34 (m, 1H, N-C*H*H pentyl), 2.26 (dd, *J* = 10.4, 5.0 Hz, 1H, C-1b), 1.95 (s, 3H, C*H* adamantanemethyl), 1.80 – 1.64 (m, 6H, 3xC$_q$C*H*$_2$ adamantanemethyl), 1.62 – 1.48 (m, 10H, N-CH$_2$C*H*$_2$ pentyl, O-CH$_2$C*H*$_2$ pentyl, 3xCHC*H*$_2$ adamantanemethyl), 1.42 – 1.31 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151



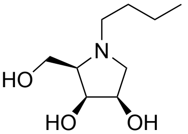
MHz, MeOD) δ 83.0 (O-*C*H$_2$ adamantanemethyl), 79.0 (*C*-3), 77.4 (*C*-2), 72.5 (O-*C*H$_2$ pentyl), 69.0 (*C*-4), 61.0 (*C*-5), 59.8 (*C*-1), 57.3 (N-*C*H$_2$ pentyl), 40.8 (3xC$_q$*C*H$_2$ adamantanemethyl), 38.3 (3xCH*C*H$_2$ adamantanemethyl), 35.1 (*C*$_q$ adamantanemethyl), 30.6 (O-CH$_2$*C*H$_2$ pentyl), 29.7 (3x*C*H adamantanemethyl), 28.8 (N-CH$_2$*C*H$_2$ pentyl), 25.3 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_{D}$ = -37.2° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 368.27954; found: 368.27963.



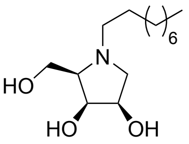
1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-D-xylitol (3H). 1,4-Dideoxy-1,4-imino-D-xylitol hydrochloride (**3A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography, HPLC purification (32-40% A/B in 9 minutes) and reversed phase column chromatography yielded the title compound (69 mg, 0.18 mmol, 36%). ^{1}H NMR (600 MHz, MeOD) δ 7.62 – 7.56 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.44 – 7.37 (m, 4H, 4xC*H*$_{Ar}$ Ph), 7.31 (t, *J* = 7.4 Hz, 1H, *p*-C*H*$_{Ar}$ Ph), 4.51 (s, 2H, O-C*H*$_2$ phenylbenzyl), 4.08 – 4.01 (m, 2H, C-2, C-3), 3.81 (dd, *J* = 11.2, 6.6 Hz, 1H, C-5a), 3.68 (dd, *J* = 11.2, 4.5 Hz, 1H, C-5b), 3.49 (t, *J* = 6.5 Hz, 2H, O-C*H*$_2$ pentyl), 3.39 (dd, *J* = 10.5, 5.4 Hz, 1H, C-1a), 2.89 – 2.77 (m, 2H, C-4, N-C*H*H pentyl), 2.42 – 2.34 (m, 1H, N-C*H*H pentyl), 2.28 (dd, *J* = 10.5, 5.0 Hz, 1H, C-1b), 1.62 (p, *J* = 7.5, 7.0 Hz, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.52 (p, *J* = 7.7 Hz, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.44 – 1.32 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.0, 141.7, 138.9 (3x*C*$_q$ Ph), 129.8, 129.3 (4x*C*H$_{Ar}$ Ph), 128.3 (*p*-*C*H$_{Ar}$ Ph), 127.9, 127.9 (4x*C*H$_{Ar}$ Ph), 78.9 (*C*-3), 77.3 (*C*-2), 73.5 (O-*C*H$_2$ phenylbenzyl), 71.2 (O-*C*H$_2$ pentyl), 69.1 (*C*-4), 60.9 (*C*-5), 59.8 (*C*-1), 57.3 (N-*C*H$_2$ pentyl), 30.6 (O-CH$_2$*C*H$_2$ pentyl), 28.7 (N-CH$_2$*C*H$_2$ pentyl), 25.2 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_{D}$ = -48.1° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23253.



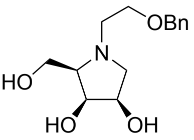
1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (4A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-D-lyxitol (**31**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.3 g, 7.8 mmol, 98%). ^{1}H NMR (600 MHz, MeOD) δ 4.40 (td, *J* = 7.3, 4.0 Hz, 1H, C-2), 4.21 (t, *J* = 4.0 Hz, 1H, C-3), 3.94 (dd, *J* = 11.8, 4.6 Hz, 1H, C-5a), 3.89 (dd, *J* = 11.8, 8.9 Hz, 1H, C-5b), 3.64 (dt, *J* = 8.8, 4.4 Hz, 1H, C-4), 3.42 (dd, *J* = 11.7, 7.3 Hz, 1H, C-1a), 3.14 (dd, *J* = 11.7, 7.3 Hz, 1H, C-1b). ^{13}C NMR (151 MHz, MeOD) δ 71.8 (*C*-2), 71.3 (*C*-3), 64.5 (*C*-4), 59.3 (*C*-5), 48.5 (*C*-1). $[\alpha]^{20}_{D}$ = 23.4° (c = 1, MeOH). IR (neat): 61, 667, 899, 920, 982, 1040, 1115, 1202, 1269, 1287, 1350, 1412, 1460, 1601, 2480, 2583, 2666, 2716, 2733, 2783, 2891, 2930, 2976, 3221, 3404. HR-MS: [M+H$^+$] Calculated for $C_5H_{11}NO_3$: 134.08117; found: 134.08122.



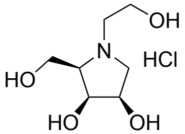
1,4-Dideoxy-1,4-butylimino-D-lyxitol (4B). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (15-17.5% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (14 mg, 0.07 mmol, 14%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 (dd, *J* = 6.6, 5.2 Hz, 1H, C-3), 4.12 (td, *J* = 5.4, 3.5 Hz, 1H, C-2), 3.77 (dd, *J* = 11.1, 5.9 Hz, 1H, C-5a), 3.64 (dd, *J* = 11.1, 3.8 Hz, 1H, C-5b), 3.01 (dd, *J* = 10.7, 3.4 Hz, 1H, C-1a), 2.78 – 2.71 (m, 1H, N-C*H*H butyl), 2.69 – 2.64 (m, 1H, C-4), 2.53 (dd, *J* = 10.7, 5.7 Hz, 1H, C-1b), 2.37 – 2.30 (m, 1H, N-C*H*H butyl), 1.48 (p, *J* = 7.8 Hz, 2H, N-CH$_2$C*H*$_2$ butyl), 1.40 – 1.27 (m, 2H, C*H*$_2$CH$_3$ butyl), 0.94 (t, *J* = 7.4 Hz, 3H, C*H*$_3$ butyl). ^{13}C NMR (151 MHz, MeOD) δ 73.3 (*C*-3), 71.4 (*C*-2), 68.8 (*C*-4), 60.9 (*C*-5), 59.4 (*C*-1), 56.8 (N-*C*H$_2$ butyl), 31.2 (N-CH$_2$*C*H$_2$ butyl), 21.7 (*C*H$_2$CH$_3$ butyl), 14.4 (*C*H$_3$ butyl). $[\alpha]^{20}_{D}$ = -74.3° (c = 0.3, MeOH). HR-MS: [M+H$^+$] Calculated for $C_9H_{19}NO_3$: 190.14377; found: 190.14341.



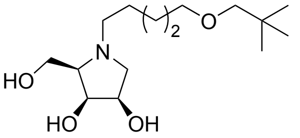
1,4-Dideoxy-1,4-nonylimino-D-lyxitol (4C). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (25-30% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (37 mg, 0.14 mmol, 29%). ^{1}H NMR (600 MHz, MeOD) δ 4.22 (dd, *J* = 6.5, 5.2 Hz, 1H, C-3), 4.13 (td, *J* = 5.4, 3.7 Hz, 1H, C-2), 3.78 (dd, *J* = 11.1, 5.8 Hz, 1H, C-5a), 3.65 (dd, *J* = 11.1, 4.0 Hz, 1H, C-5b), 3.03 (dd, *J* = 10.7, 3.5 Hz, 1H, C-1a), 2.76 (dt, *J* = 11.9, 8.1 Hz, 1H, N-C*H*H nonyl), 2.71 – 2.66 (m, 1H, C-4), 2.55 (dd, *J* = 10.7, 5.7 Hz, 1H, C-1b), 2.35 (dt, *J* = 11.9, 7.5 Hz, 1H, N-C*H*H nonyl), 1.56 – 1.40 (m, 2H, N-CH$_2$C*H*$_2$ nonyl), 1.38 – 1.21 (m, 12H, 6xC*H*$_2$ nonyl), 0.90 (t, *J* = 7.0 Hz, 3H, C*H*$_3$ nonyl). ^{13}C NMR (151 MHz, MeOD) δ 73.3 (*C*-3), 71.4 (*C*-2), 68.9 (*C*-4), 60.9 (*C*-5), 59.3 (*C*-1), 57.1 (N-*C*H$_2$ nonyl), 33.1, 30.7, 30.7, 30.4 (4x*C*H$_2$ nonyl), 29.0 (N-CH$_2$*C*H$_2$ nonyl), 28.6, 23.7 (2x*C*H$_2$ nonyl), 14.5 (*C*H$_3$ nonyl). [α]$^{20}_{D}$ = -54.6° (c = 0.7, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22193.



1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-lyxitol (4D). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification (12-16% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (22 mg, 0.08 mmol, 16%). ^{1}H NMR (600 MHz, MeOD) δ 7.38 – 7.31 (m, 4H, *o*-C*H*$_{Ar}$ Ph, *m*-C*H*$_{Ar}$ Ph), 7.31 – 7.25 (m, 1H, *p*-C*H*$_{Ar}$ Ph), 4.53 (s, 2H, O-C*H*$_2$ Bn), 4.21 (dd, *J* = 6.7, 5.0 Hz, 1H, C-3), 4.14 – 4.09 (m, 1H, C-2), 3.76 (dd, *J* = 11.3, 5.2 Hz, 1H, C-5a), 3.67 (dd, *J* = 11.3, 4.2 Hz, 1H, C-5b), 3.66 – 3.58 (m, 2H, N-CH$_2$C*H*$_2$ ethyl), 3.11 – 3.03 (m, 2H, C-1a, N-C*H*H ethyl), 2.87 – 2.81 (m, 1H, C-4), 2.74 – 2.67 (m, 2H, C-1b, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 139.5 (*C*$_q$ Bn), 129.4, 129.0 (2x *o*-*C*H$_{Ar}$ Bn, 2x *m*-*C*H$_{Ar}$ Bn), 128.7 (*p*-*C*H$_{Ar}$ Bn), 74.2 (O-*C*H$_2$ Bn), 73.3 (*C*-3), 71.6 (*C*-2), 69.6 (N-CH$_2$*C*H$_2$ ethyl), 68.8 (*C*-4), 60.8 (*C*-5), 59.7 (*C*-1), 55.9 (N-*C*H$_2$ ethyl). [α]$^{20}_{D}$ = -25.9° (c = 0.4, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{21}NO_4$: 268.15433; found: 268.15462.



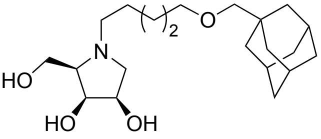
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-D-lyxitol hydrochloride (4E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-D-lyxitol (**4D**, 18 mg, 0.07 mmol) was subjected to *General procedure C* yielding the title compound (16 mg, 0.07 mmol, quant.). ^{1}H NMR (600 MHz, MeOD) δ 4.45 – 4.41 (m, 1H, C-2), 4.41 – 4.36 (m, 1H, C-3), 4.05 (dd, *J* = 12.4, 7.6 Hz, 1H, C-5a), 4.00 (dd, *J* = 12.4, 4.3 Hz, 1H, C-5b), 3.93 – 3.84 (m, 2H, N-CH$_2$C*H*$_2$ ethyl), 3.76 – 3.71 (m, 1H, C-4), 3.68 – 3.62 (m, 1H, N-C*H*H ethyl), 3.59 (dd, *J* = 12.0, 5.2 Hz, 1H, C-1a), 3.50 (dd, *J* = 12.0, 5.7 Hz, 1H, C-1b), 3.33 – 3.28 (m, 1H, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 72.0 (*C*-4), 71.9 (*C*-3), 70.7 (*C*-2), 59.4 (N-*C*H$_2$ ethyl), 59.3 (*C*-5), 58.3 (*C*-1), 57.7 (N-CH$_2$*C*H$_2$ ethyl). [α]$^{20}_{D}$ = -9.4° (c = 0.3, MeOH). HR-MS: [M+H$^+$] Calculated for $C_7H_{15}NO_4$: 178.10738; found: 178.10777.



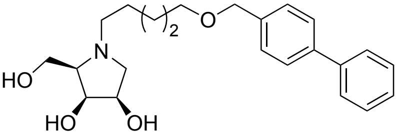
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-D-lyxitol (4F). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification (21-24% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (33 mg, 0.11 mmol, 22%). ^{1}H NMR (600 MHz, MeOD) δ 4.22 (dd, *J* = 6.5, 5.2 Hz, 1H, C-3), 4.13 (td, *J* = 5.4, 3.6 Hz, 1H, C-2), 3.78 (dd, *J* = 11.1, 5.8 Hz, 1H, C-5a), 3.66 (dd, *J* = 11.1, 4.0 Hz, 1H, C-5b), 3.42 (t, *J* = 6.4 Hz, 2H, O-C*H*$_2$ pentyl), 3.06 (s, 2H, O-C*H*$_2$ neopentyl), 3.03 (dd, *J* = 10.7, 3.4 Hz, 1H, C-1a), 2.81 – 2.75 (m, 1H, N-C*H*H pentyl), 2.73 – 2.67 (m, 1H, C-4), 2.56 (dd, *J* = 10.7, 5.7 Hz, 1H, C-1b), 2.40 – 2.34 (m, 1H, N-C*H*H pentyl), 1.59 (p, *J* = 6.9 Hz, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.53 (p, *J* = 8.0 Hz, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.45 – 1.30 (m, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl), 0.90 (s, 9H, 3xC*H*$_3$ neopentyl). ^{13}C NMR (151 MHz, MeOD) δ 82.4 (O-*C*H$_2$ neopentyl), 73.3 (*C*-3), 72.4 (O-*C*H$_2$ pentyl), 71.4 (*C*-2), 68.9 (*C*-4), 60.8 (*C*-5), 59.3 (*C*-1), 57.1 (N-*C*H$_2$ pentyl), 32.9

(C_q neopentyl), 30.6 (O-CH_2CH_2 pentyl), 28.8 (N-CH_2CH_2 pentyl), 27.2 (3xCH_3 neopentyl), 25.2 (N-$(CH_2)_2CH_2$ pentyl). $[\alpha]^{20}_D$ = -47.6° (c = 0.7, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{15}H_{31}NO_4$: 290.23258; found: 290.23286.

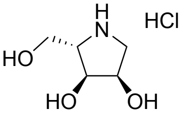
1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-D-lyxitol (4G). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification (32-37% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (22 mg, 0.06 mmol, 12%). ^{1}H NMR (600 MHz, MeOD) δ 4.23 (dd, *J* = 6.4, 5.1 Hz, 1H, C-3), 4.16 – 4.12 (m, 1H, C-2), 3.79 (dd, *J* = 11.2, 5.7 Hz, 1H, C-5a), 3.69 (dd, *J* = 11.2, 4.2 Hz, 1H, C-5b), 3.39 (t, *J* = 6.4 Hz, 2H, O-CH_2 pentyl), 3.06 (dd, *J* = 10.7, 3.5 Hz, 1H, C-1a), 2.97 (s, 2H, O-CH_2 neopentyl), 2.87 – 2.78 (m, 1H, N-CHH pentyl), 2.79 – 2.73 (m, 1H, C-4), 2.62 (dd, *J* = 10.7, 5.7 Hz, 1H, C-1b), 2.46 – 2.38 (m, 1H, N-CHH pentyl), 1.97 – 1.92 (m, 3H, 3xC*H* adamantanemethyl), 1.79 – 1.65 (m, 6H, 3x$CHCH_2$ adamantanemethyl), 1.63 – 1.49 (m, 10H, 3xC_qCH_2 adamantanemethyl, O-CH_2CH_2 pentyl, N-CH_2CH_2 pentyl), 1.44 – 1.28 (m, 2H, N-$(CH_2)_2CH_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 83.1 (O-CH_2 adamantanemethyl), 73.2 (*C*-3), 72.5 (O-CH_2 pentyl), 71.4 (*C*-2), 69.1 (*C*-4), 60.8 (*C*-5), 59.2 (*C*-1), 57.1 (N-CH_2 pentyl), 40.8 (3xC_qCH_2 adamantanemethyl), 38.3 (3x$CHCH_2$ adamantanemethyl), 35.2 (C_q adamantanemethyl), 30.5 (O-CH_2CH_2 pentyl), 29.8 (3x*C*H adamantanemethyl), 28.6 (N-CH_2CH_2 pentyl), 25.2 (N-$(CH_2)_2CH_2$ pentyl). $[\alpha]^{20}_D$ = -32.3° (c = 0.4, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 368.27954; found: 368.27956.

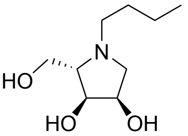


1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-D-lyxitol (4H). 1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (**4A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification (31-38% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (32 mg, 0.08 mmol, 16%). ^{1}H NMR (600 MHz, MeOD) δ 7.65 – 7.56 (m, 4H, 4xCH_{Ar} Ph), 7.44 – 7.38 (m, 4H, 4xCH_{Ar} Ph), 7.35 – 7.29 (m, 1H, *p*-CH_{Ar} Ph), 4.53 (s, 2H, O-CH_2 phenylbenzyl), 4.24 (dd, *J* = 6.2, 4.9 Hz, 1H, C-3), 4.21 – 4.15 (m, 1H, C-2), 3.83 (dd, *J* = 11.5, 5.3 Hz, 1H, C-5a), 3.76 (dd, *J* = 11.5, 5.2 Hz, 1H, C-5b), 3.52 (t, *J* = 6.4 Hz, 2H, O-CH_2 pentyl), 3.14 (dd, *J* = 11.0, 3.8 Hz, 1H, C-1a), 3.01 – 2.88 (m, 2H, C-4, N-CHH pentyl), 2.74 (dd, *J* = 10.5, 5.5 Hz, 1H, C-1b), 2.60 – 2.50 (m, 1H, N-CHH pentyl), 1.64 (p, *J* = 6.9 Hz, 2H, O-CH_2CH_2 pentyl), 1.61 – 1.53 (m, 3H, N-CH_2CH_2 pentyl), 1.47 – 1.36 (m, 2H, N-$(CH_2)_2CH_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.1, 141.8, 138.9 (3xC_q Ph), 129.9, 129.4 (4xCH_{Ar} Ph), 128.3 (*p*-CH_{Ar} Ph), 127.9, 127.9 (CH_{Ar} Ph), 73.5 (O-CH_2 phenylbenzyl), 72.9 (*C*-3), 71.2 (*C*-2), 71.2 (O-CH_2 pentyl), 69.7 (*C*-4), 60.5 (*C*-5), 58.7 (*C*-1), 57.2 (N-CH_2 pentyl), 30.4 (O-CH_2CH_2 pentyl), 27.9 (N-CH_2CH_2 pentyl), 25.0 (N-$(CH_2)_2CH_2$ pentyl). $[\alpha]^{20}_D$ = -25° (c = 0.6, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23260.

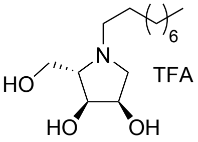


1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (5A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-ribitol (**32**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.4 g, 7.8 mmol, quant.). $[\alpha]^{20}_D$ = -61.2° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**1A**).

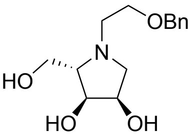




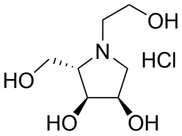
1,4-Dideoxy-1,4-butylimino-L-ribitol (5B). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (12 mg, 0.06 mmol, 12%). $[\alpha]^{20}_{D}$ = 14.2° (c = 0.2, MeOH). Analytical data was the same as for its enantiomer (**1B**).



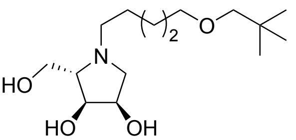
1,4-Dideoxy-1,4-nonylimino-L-ribitol trifluoroacetic acid (5C). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc) and HPLC purification (25-42% A/B in 8.5 minutes) yielded the title compound (111 mg, 0.30 mmol, 59%). ^{1}H NMR (600 MHz, MeOD) δ 4.27 – 4.23 (m, 1H, C-2), 4.08 (dd, *J* = 7.8, 4.2 Hz, 1H, C-3), 3.96 (dd, *J* = 12.3, 3.3 Hz, 1H, C-5a), 3.82 (dd, *J* = 12.3, 5.3 Hz, 1H, C-5b), 3.68 (dd, *J* = 12.6, 4.6 Hz, 1H, C-1a), 3.51 – 3.48 (m, 1H, C-4), 3.48 – 3.42 (m, 1H, N-C*H*H nonyl), 3.25 (dd, *J* = 12.6, 3.2 Hz, 1H, C-1b), 3.23 – 3.16 (m, 1H, N-C*H*H nonyl), 1.78 – 1.69 (m, 2H, N-CH_2CH_2 nonyl), 1.41 – 1.26 (m, 12H, 6xCH_2 nonyl), 0.90 (t, *J* = 7.1 Hz, 3H, CH_3 nonyl). ^{13}C NMR (151 MHz, MeOD) δ 72.7 (*C*-4), 72.7 (*C*-3), 70.5 (*C*-2), 59.5 (N-CH_2 nonyl), 59.0 (*C*-1), 58.7 (*C*-5), 33.0, 30.5, 30.3, 30.2, 27.5 (5xCH_2 nonyl), 26.3 (N-CH_2CH_2 nonyl), 23.7 (CH_2 nonyl), 14.4 (CH_3 nonyl). $[\alpha]^{20}_{D}$ = -1.6° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22229.



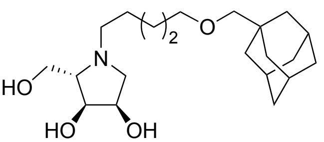
1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-ribitol (5D). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification (12-15% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (36 mg, 0.14 mmol, 27%). $[\alpha]^{20}_{D}$ = 16.7° (c = 0.7, MeOH). Analytical data was the same as for its enantiomer (**1D**).



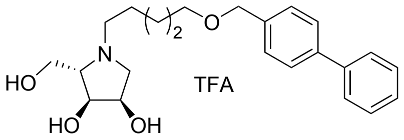
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-L-ribitol hydrochloride (5E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-ribitol (**5D**, 33 mg, 0.12 mmol) was subjected to *General procedure C* yielding the title compound (30 mg, 0.12 mmol, quant.). $[\alpha]^{20}_{D}$ = -16.3° (c = 0.6, MeOH). Analytical data was the same as for its enantiomer (**1E**).



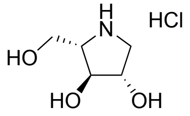
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-L-ribitol (5F). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification (21-25% A/B in 9.5 minutes) and reversed phase column chromatography yielded the title compound (39 mg, 0.14 mmol, 27%). $[\alpha]^{20}_{D}$ = 21.3° (c = 0.8, MeOH). Analytical data was the same as for its enantiomer (**1F**).



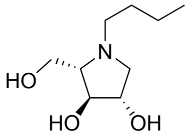
1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-L-ribitol (5G). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc), HPLC purification (25-57% A/B in 9 minutes) and reversed phase column chromatography yielded the title compound (67 mg, 0.18 mmol, 36%). $[\alpha]^{20}_{D}$ = 18° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**1G**).



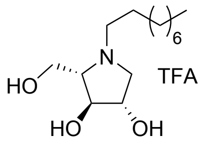
1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-L-ribitol trifluoroacetic acid (5H). 1,4-Dideoxy-1,4-imino-L-ribitol hydrochloride (**5A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc) and HPLC purification (31-37% A/B in 10 minutes) yielded the title compound (62 mg, 0.12 mmol, 25%). ^{1}H NMR (600 MHz, MeOD) δ 7.63 – 7.58 (m, 4H, 4xCH_{Ar} Ph), 7.45 – 7.39 (m, 4H, 4xCH_{Ar} Ph), 7.33 (t, *J* = 7.4 Hz, 1H, *p*-CH_{Ar} Ph), 4.53 (s, 2H, O-CH_2 phenylbenzyl), 4.25 – 4.21 (m, 1H, C-2), 4.10 – 4.05 (m, 1H, C-3), 3.94 (dd, *J* = 12.3, 3.1 Hz, 1H, C-5a), 3.81 (dd, *J* = 12.3, 5.2 Hz, 1H, C-5b), 3.66 (dd, *J* = 12.2, 3.6 Hz, 1H, C-1a), 3.54 (t, *J* = 6.2 Hz, 2H, O-CH_2 pentyl), 3.46 (dd, *J* = 20.4, 9.3 Hz, 2H, C-4, N-C*H*H pentyl), 3.27 – 3.13 (m, 2H, C-1b, N-C*H*H pentyl), 1.76 (p, *J* = 8.0 Hz, 2H, O-CH$_2$CH_2 pentyl), 1.70 – 1.64 (m, 2H, N-CH$_2$CH_2 pentyl), 1.48 (p, *J* = 7.3, 6.6 Hz, 2H, N-(CH$_2$)$_2$CH_2 pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.0, 141.8, 138.8 (3xC_q Ph), 129.9, 129.4 (4x*C*H$_{Ar}$ Ph), 128.4 (*p*-*C*H$_{Ar}$ Ph), 127.9, 127.9 (4x*C*H$_{Ar}$ Ph), 73.6 (O-*C*H$_2$ phenylbenzyl), 72.7 (*C*-4), 72.7 (*C*-3), 70.9 (O-*C*H$_2$ pentyl), 70.4 (*C*-2), 59.3 (N-*C*H$_2$ pentyl), 59.0 (*C*-1), 58.6 (*C*-5), 30.1 (O-CH$_2$*C*H$_2$ pentyl), 26.0 (N-CH$_2$*C*H$_2$ pentyl), 24.4 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_{D}$ = -1° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23269.



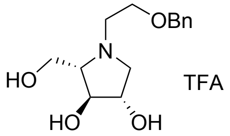
1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (6A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-arabinitol (**33**, 3.7 g, 7.5 mmol) was subjected to *General procedure A* yielding the title compound (1.3 g, 7.5 mmol, quant.). $[\alpha]^{20}_{D}$ = -38.9° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**2A**).



1,4-Dideoxy-1,4-butylimino-L-arabinitol (6B). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (43 mg, 0.23 mmol, 45%). $[\alpha]^{20}_{D}$ = 10.1° (c = 0.9, MeOH). Analytical data was the same as for its enantiomer (**2B**).

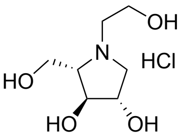


1,4-Dideoxy-1,4-nonylimino-L-arabinitol trifluoroacetic acid (6C). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (0-15% MeOH/EtOAc) and HPLC purification (25-43% A/B in 9 minutes) yielded the title compound (85 mg, 0.23 mmol, 46%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 – 4.17 (m, 1H, C-2), 3.96 – 3.94 (m, 1H, C-3), 3.94 – 3.89 (m, 2H, C-5), 3.59 (d, *J* = 11.8 Hz, 1H, C-1a), 3.48 – 3.38 (m, 3H, C-1b, C-4, N-C*H*H nonyl), 3.17 – 3.09 (m, 1H, N-C*H*H nonyl), 1.81 – 1.70 (m, 2H, N-CH$_2$CH_2 nonyl), 1.41 – 1.24 (m, 12H, 6xCH_2 nonyl), 0.90 (t, *J* = 7.1 Hz, 3H, CH_3 nonyl). ^{13}C NMR (151 MHz, MeOD) δ 78.6 (*C*-4), 77.7 (*C*-3), 75.8 (*C*-2), 60.9 (*C*-5), 60.6 (*C*-1), 58.9 (N-*C*H$_2$ nonyl), 33.0, 30.5, 30.3, 30.2, 27.7 (5x*C*H$_2$ nonyl), 26.3 (N-CH$_2$*C*H$_2$ nonyl), 23.7 (*C*H$_2$ nonyl), 14.4 (*C*H$_3$ nonyl). $[\alpha]^{20}_{D}$ = 0° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22206.

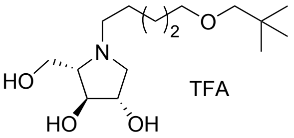


1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-arabinitol trifluoroacetic acid (6D). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (0-15% MeOH/EtOAc) and HPLC purification (15-23% A/B in 8 minutes) yielded the title compound (49 mg, 0.13 mmol, 25%). ^{1}H NMR (600 MHz, MeOD) δ 7.40 – 7.34 (m, 4H, 2x *o*-CH_{Ar} Bn, 2x *m*-CH_{Ar} Bn), 7.33 – 7.29 (m, 1H, *p*-C*H*$_{\text{Ar}}$ Bn), 4.58 (s, 2H, O-C*H*$_2$ Bn), 4.20 – 4.16 (m, 1H, C-2), 3.97 – 3.95 (m, 1H, C-3), 3.95 – 3.91 (m, 2H, C-5), 3.85 (ddd, *J* = 10.3, 7.3, 2.9 Hz, 1H, N-CH$_2$C*H*H ethyl), 3.79 (ddd, *J* = 11.6, 6.2, 2.9 Hz, 1H, N-CH$_2$C*H*H ethyl), 3.73 (ddd, *J* = 13.4, 6.1, 2.8 Hz, 1H, N-C*H*H ethyl), 3.64 (d, *J* = 12.0 Hz, 1H, C-1a), 3.59 – 3.52 (m, 2H, C-1b, C-4), 3.45 (ddd, *J* = 13.4, 7.3, 2.7 Hz, 1H, N-C*H*H ethyl). ^{13}C NMR (151 MHz, MeOD) δ 138.7 (*C*$_{\text{q}}$ Bn), 129.5, 129.2 (2x *o*-*C*H$_{\text{Ar}}$ Bn, 2x *m*-*C*H$_{\text{Ar}}$ Bn), 129.0 (*p*-*C*H$_{\text{Ar}}$ Bn), 78.5 (*C*-4), 77.6 (*C*-3), 75.8 (*C*-2), 74.3 (O-*C*H$_2$ Bn), 65.8 (N-CH$_2$*C*H$_2$ ethyl), 61.6 (*C*-1), 60.7 (*C*-5), 58.0 (N-*C*H$_2$ ethyl). $[\alpha]^{20}_{D}$ = -10.5° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{14}H_{21}NO_4$: 268.15433; found: 268.15417.

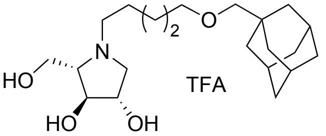
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-L-arabinitol hydrochloride (6E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-arabinitol trifluoroacetic acid (**6D**, 29 mg, 0.11 mmol) was subjected to *General procedure C* yielding the title compound (25 mg, 0.11 mmol, quant.). $[\alpha]^{20}_{D}$ = -10.9° (c = 0.5, MeOH). Analytical data was the same as for its enantiomer (**2E**).

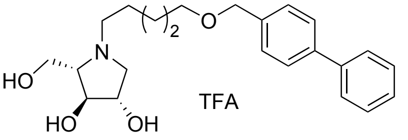


1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-L-arabinitol trifluoroacetic acid (6F). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography and HPLC purification (21-26% A/B in 9.5 minutes) yielded the title compound (92 mg, 0.23 mmol, 45%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 – 4.17 (m, 1H, C-2), 3.96 – 3.94 (m, 1H, C-3), 3.94 – 3.89 (m, 2H, C-5), 3.59 (d, *J* = 11.8 Hz, 1H, C-1a), 3.50 – 3.39 (m, 5H, C-1b, C-4, O-C*H*$_2$ pentyl, N-C*H*H pentyl), 3.19 – 3.11 (m, 1H, N-C*H*H pentyl), 3.07 (s, 2H, O-C*H*$_2$ neopentyl), 1.82 – 1.75 (m, 2H, N-CH$_2$C*H*$_2$ pentyl), 1.67 – 1.60 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.46 (p, *J* = 7.7 Hz, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl), 0.90 (s, 9H, 3xC*H*$_3$ neopentyl). ^{13}C NMR (151 MHz, MeOD) δ 82.5 (O-*C*H$_2$ neopentyl), 78.6 (*C*-4), 77.7 (*C*-3), 75.8 (*C*-2), 72.0 (O-*C*H$_2$ pentyl), 60.9 (*C*-5), 60.6 (*C*-1), 58.9 (N-*C*H$_2$ pentyl), 32.9 (*C*$_{\text{q}}$ neopentyl), 30.2 (O-CH$_2$*C*H$_2$ pentyl), 27.1 (3x*C*H$_3$ neopentyl), 26.2 (N-CH$_2$*C*H$_2$ pentyl), 24.6 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_{D}$ = 0.2° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{15}H_{31}NO_4$: 290.23258; found: 290.23270.

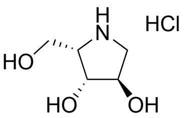


1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-L-arabinitol trifluoroacetic acid (6G). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc) and HPLC purification (25-60% A/B in 10 minutes) yielded the title compound (87 mg, 0.18 mmol, 36%). ^{1}H NMR (600 MHz, MeOD) δ 4.22 – 4.17 (m, 1H, C-2), 3.95 (s, 1H, C-3), 3.94 – 3.89 (m, 2H, C-5), 3.59 (d, *J* = 11.7 Hz, 1H, C-1a), 3.49 – 3.42 (m, 3H, C-1b, C-4, N-C*H*H pentyl), 3.40 (t, *J* = 6.2 Hz, 2H, O-C*H*$_2$ pentyl), 3.18 – 3.12 (m, 1H, N-C*H*H pentyl), 2.98 (s, 2H, O-C*H*$_2$ adamantanemethyl), 1.98 – 1.91 (m, 3H, 3xC*H* adamantanemethyl), 1.82 – 1.65 (m, 8H, N-CH$_2$C*H*$_2$ pentyl, 3xCHC*H*$_2$ adamantanemethyl), 1.65 – 1.59 (m, 2H, O-CH$_2$C*H*$_2$ pentyl), 1.58 – 1.54 (m, 6H, 3xC$_{\text{q}}$C*H*$_2$ adamantanemethyl), 1.45 (p, *J* = 7.6 Hz, 2H, N-(CH$_2$)$_2$C*H*$_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 83.1 (O-*C*H$_2$ adamantanemethyl), 78.6 (*C*-4), 77.7 (*C*-3), 75.8 (*C*-2), 72.0 (O-*C*H$_2$ pentyl), 60.9 (*C*-5), 60.6 (*C*-1), 58.9 (N-*C*H$_2$ pentyl), 40.8 (3xC$_{\text{q}}$*C*H$_2$ adamantanemethyl), 38.3 (3xCH*C*H$_2$ adamantanemethyl), 35.1 (*C*$_{\text{q}}$ adamantanemethyl), 30.1 (O-CH$_2$*C*H$_2$ pentyl), 29.7 (3x*C*H adamantanemethyl), 26.1 (N-CH$_2$*C*H$_2$ pentyl), 24.6 (N-(CH$_2$)$_2$*C*H$_2$ pentyl). $[\alpha]^{20}_{D}$ = 0.6° (c = 1, MeOH). HR-MS: [M+H$^+$] Calculated for $C_{21}H_{37}NO_4$: 368.27954; found: 368.27965.

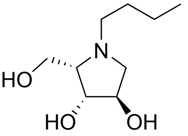




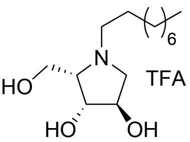
1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-L-arabinitol trifluoroacetic acid (6H). 1,4-Dideoxy-1,4-imino-L-arabinitol hydrochloride (**6A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-15% MeOH/EtOAc) and HPLC purification (28-48% A/B in 9 minutes) yielded the title compound (63 mg, 0.13 mmol, 25%). ^{1}H NMR (600 MHz, MeOD) δ 7.63 – 7.58 (m, 4H, 4xCH_{Ar} Ph), 7.45 – 7.40 (m, 4H, CH_{Ar} Ph), 7.33 (t, *J* = 7.4 Hz, 1H, *p*-CH_{Ar} Ph), 4.54 (s, 2H, O-CH_2 phenylbenzyl), 4.16 (s, 1H, C-2), 3.94 (s, 1H, C-3), 3.93 – 3.88 (m, 2H, C-5), 3.58 – 3.52 (m, 3H, C-1a, O-CH_2 pentyl), 3.49 – 3.43 (m, 1H, N-C*H*H pentyl), 3.43 – 3.38 (m, 2H, C-1b, C-4), 3.17 – 3.10 (m, 1H, N-CH*H* pentyl), 1.82 – 1.74 (m, 2H, N-CH_2CH_2 pentyl), 1.72 – 1.63 (m, 2H, O-CH_2CH_2 pentyl), 1.47 (p, *J* = 7.7 Hz, 2H, N-$(CH_2)_2CH_2$ pentyl). ^{13}C NMR (151 MHz, MeOD) δ 142.0, 141.8, 138.9 (3xC_q Ph), 129.9, 129.4 (4xCH_{Ar} Ph), 128.4 (*p*-CH_{Ar} Ph), 127.9, 127.9 (4xCH_{Ar} Ph), 78.6 (*C*-4), 77.7 (*C*-3), 75.7 (*C*-2), 73.6 (O-CH_2 phenylbenzyl), 70.9 (O-CH_2 pentyl), 60.9 (*C*-5), 60.6 (*C*-1), 58.8 (N-CH_2 pentyl), 30.1 (O-CH_2CH_2 pentyl), 26.1 (N-CH_2CH_2 pentyl), 24.5 (N-$(CH_2)_2CH_2$ pentyl). $[\alpha]^{20}_D$ = 0.2° (c = 1, MeOH). HR-MS: [$M+H^+$] Calculated for $C_{21}H_{37}NO_4$: 386.23258; found: 368.23271.



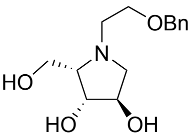
1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (7A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-xylitol (**34**, 3.95 g, 8 mmol) was subjected to *General procedure A* yielding the title compound (1.44 g, 8.0 mmol, quant.). $[\alpha]^{20}_D$ = -17.8° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**3A**).



1,4-dideoxy-1,4-butylimino-L-xylitol (7B). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-17.5% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (5 mg, 0.03 mmol, 5%). $[\alpha]^{20}_D$ = 80° (c = 0.1, MeOH). Analytical data was the same as for its enantiomer (**3B**).

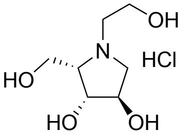


1,4-Dideoxy-1,4-nonylimino-L-xylitol trifluoroacetic acid (7C). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc) and HPLC purification (25-43% A/B in 9 minutes) yielded the title compound (68 mg, 0.18 mmol, 36%). ^{1}H NMR (600 MHz, MeOD) δ 4.23 – 4.18 (m, 2H, C-2, C-3), 4.06 – 3.99 (m, 2H, C-5), 3.84 (dd, *J* = 12.6, 3.8 Hz, 1H, C-1a), 3.76 (td, *J* = 6.9, 3.3 Hz, 1H, C-4), 3.60 – 3.53 (m, 1H, N-C*H*H pentyl), 3.22 (d, *J* = 12.6 Hz, 1H, C-1b), 3.19 – 3.10 (m, 1H, N-CH*H* pentyl), 1.81 – 1.70 (m, 2H, N-CH_2CH_2 pentyl), 1.42 – 1.26 (m, 12H, 6xCH_2 pentyl), 0.90 (t, *J* = 7.1 Hz, 3H, CH_3 pentyl). ^{13}C NMR (151 MHz, MeOD) δ 76.8 (*C*-3), 75.6 (*C*-2), 73.2 (*C*-4), 60.3 (*C*-1), 59.7 (N-CH_2 pentyl), 59.1 (*C*-5), 33.0, 30.4, 30.3, 30.2, 27.6 (5xCH_2 pentyl), 26.5 (N-CH_2CH_2 pentyl), 23.7 (CH_2 pentyl), 14.4 (CH_3 pentyl). $[\alpha]^{20}_D$ = 22.4° (c = 1, MeOH). HR-MS: [$M+H^+$] Calculated for $C_{14}H_{29}NO_3$: 260.22202; found: 260.22217.

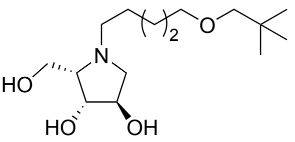


1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-xylitol (7D). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (11.5-20% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (34 mg, 0.13 mmol, 26%). $[\alpha]^{20}_D$ = 12.1° (c = 0.7, MeOH). Analytical data was the same as for its enantiomer (**3D**).

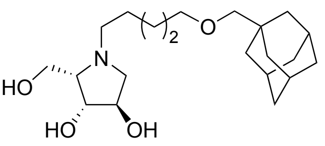
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-L-xylitol hydrochloride (7E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-xylitol (**7D**, 31 mg, 0.12 mmol) was subjected to *General procedure C* yielding the title compound (27 mg, 0.12 mmol, quant.). $[\alpha]^{20}_{D}$ = 13.2° (c = 0.5, MeOH). Analytical data was the same as for its enantiomer (**3E**).



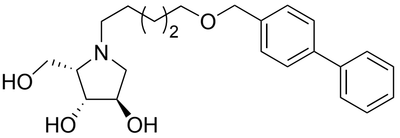
1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-L-xylitol (7F). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-15% MeOH/EtOAc), HPLC purification (22-26% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (52 mg, 0.18 mmol, 36%). $[\alpha]^{20}_{D}$ = 26.7° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**3F**).



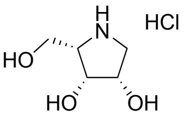
1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-L-xylitol (7G). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (25-60% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (73 mg, 0.20 mmol, 40%). $[\alpha]^{20}_{D}$ = 25.7° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**3G**).



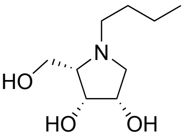
1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-L-xylitol (7H). 1,4-Dideoxy-1,4-imino-L-xylitol hydrochloride (**7A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (10-12.5% MeOH/EtOAc), HPLC purification (32-39% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (72 mg, 0.19 mmol, 38%). $[\alpha]^{20}_{D}$ = 16.5° (c = 1, MeOH). Analytical data was the same as for its enantiomer (**3H**).

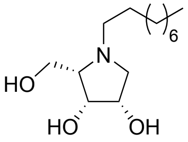


1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (8A). 1,4-Dideoxy-1,4-benzylimino-2,3,5-tri-*O*-benzyl-L-lyxitol (**35**, 4.0 g, 8.0 mmol) was subjected to *General procedure A* yielding the title compound (1.37 g, 8.0 mmol, quant.). $[\alpha]^{20}_{D}$ = -28.5° (c = 0.9, MeOH). Analytical data was the same as for its enantiomer (**4A**).

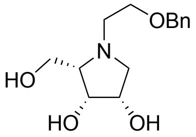


1,4-Dideoxy-1,4-butylimino-L-lyxitol (8B). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 1-bromobutane (103 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-17.5% MeOH/EtOAc), HPLC purification and reversed phase column chromatography yielded the title compound (7 mg, 0.04 mmol, 7%). $[\alpha]^{20}_{D}$ = 54.3° (c = 0.1, MeOH). Analytical data was the same as for its enantiomer (**4B**).

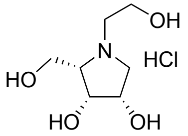




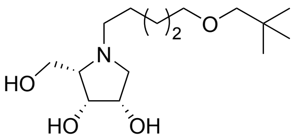
1,4-Dideoxy-1,4-nonylimino-L-lyxitol (8C). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 1-bromononane (155 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-17.5% MeOH/EtOAc), HPLC purification (25-30% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (38 mg, 0.15 mmol, 29%). $[\alpha]^{20}_{D}$ = 50.3° (c = 0.8, MeOH). Analytical data was the same as for its enantiomer (**4C**).



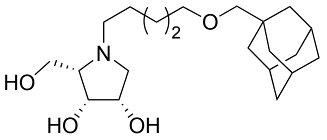
1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-lyxitol (8D). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 2-bromo(benzyloxy)ethane (161 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (12.5-17.5% MeOH/EtOAc), HPLC purification (12-16% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (21 mg, 0.08 mmol, 16%). $[\alpha]^{20}_{D}$ = 24.8° (c = 0.4, MeOH). Analytical data was the same as for its enantiomer (**4D**).



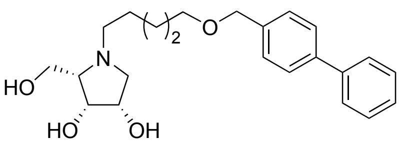
1,4-Dideoxy-1,4-(*N*-(2-hydroxyethyl))imino-L-lyxitol hydrochloride (8E). 1,4-Dideoxy-1,4-(*N*-(2-benzyloxyethyl))imino-L-lyxitol (**8D**, 21 mg, 0.08 mmol) was subjected to *General procedure C* yielding the title compound (17 mg, 0.08 mmol, quant.). $[\alpha]^{20}_{D}$ = 6.5° (c = 0.3, MeOH). Analytical data was the same as for its enantiomer (**4E**).



1,4-Dideoxy-1,4-(*N*-(5-neopentoxypentyl))imino-L-lyxitol (8F). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-neopentyloxypentane (178 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (15-17.5% MeOH/EtOAc), HPLC purification (21-24% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (30 mg, 0.10 mmol, 21%). $[\alpha]^{20}_{D}$ = 45° (c = 0.6, MeOH). Analytical data was the same as for its enantiomer (**4F**).



1,4-Dideoxy-1,4-(*N*-(5-(adamantane-1-yl-methoxy)pentyl))imino-L-lyxitol (8G). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(adamantane-1-yl-methoxy)pentane (236 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (15-17.5% MeOH/EtOAc), HPLC purification (34-40% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (17 mg, 0.05 mmol, 10%). $[\alpha]^{20}_{D}$ = 28.2° (c = 0.3, MeOH). Analytical data was the same as for its enantiomer (**4G**).



1,4-Dideoxy-1,4-(*N*-(5-(*p*-phenylbenzyloxy)pentyl))imino-L-lyxitol (8H). 1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (**8A**, 85 mg, 0.50 mmol) was alkylated with 5-bromo-1-(*p*-phenylbenzyloxy)pentane (250 mg, 0.75 mmol) in *General procedure B*. Silica gel column chromatography (15-17.5% MeOH/EtOAc), HPLC purification (31-38% A/B in 10 minutes) and reversed phase column chromatography yielded the title compound (29 mg, 0.08 mmol, 15%). $[\alpha]^{20}_{D}$ = 55.2° (c = 0.6, MeOH). Analytical data was the same as for its enantiomer (**4H**).

References and notes

[1] Fleet, G. W. J.; Nicholas, S. J.; Smith, P. W.; Evans, S. V.; Fellows, L. E.; Nash, R. J. *Tetrahedron Lett.* **1985**, *26*, 3127-3130, 10.1016/s0040-4039(00)98636-2.

[2] Liu, K. K. C.; Kajimoto, T.; Chen, L. R.; Zhong, Z. Y.; Ichikawa, Y.; Wong, C. H. *J. Org. Chem.* **1991**, *56*, 6280-6289, 10.1021/jo00022a013.

[3] Winchester, B.; Aldaher, S.; Carpenter, N. C.; Dibello, I. C.; Choi, S. S.; Fairbanks, A. J.; Fleet, G. W. J. *Biochem. J.* **1993**, *290*, 743-749.

[4] Kato, A.; Adachi, I.; Miyauchi, M.; Ikeda, K.; Komae, T.; Kizu, H.; Kameda, Y.; Watson, A. A.; Nash, R. J.; Wormald, M. R.; Fleet, G. W. J.; Asano, N. *Carbohydr. Res.* **1999**, *316*, 95-103, 10.1016/s0008-6215(99)00043-9.

[5] Takebayashi, M.; Hiranuma, S.; Kanie, Y.; Kajimoto, T.; Kanie, O.; Wong, C. H. *J. Org. Chem.* **1999**, *64*, 5280-5291, 10.1021/jo9902446.

[6] Saotome, C.; Kanie, Y.; Kanie, O.; Wong, C. H. *Bioorg. Med. Chem.* **2000**, *8*, 2249-2261, 10.1016/s0968-0896(00)00170-x.

[7] Saotome, C.; Wong, C. H.; Kanie, O. *Chem. Biol.* **2001**, *8*, 1061-1070, 10.1016/s1074-5521(01)00074-6.

[8] Pedersen, L. L.; Turco, S. J. *Cell. Mol. Life Sci.* **2003**, *60*, 259-266, 10.1007/s000180300021.

[9] Chlubnova, I.; Legentil, L.; Dureau, R.; Pennec, A.; Almendros, M.; Daniellou, R.; Nugier-Chauvin, C.; Ferrieres, V. *Carbohydr. Res.* **2012**, *356*, 44-61, 10.1016/j.carres.2012.04.002.

[10] Taha, H. A.; Richards, M. R.; Lowary, T. L. *Chem. Rev.* **2013**, *113*, 1851-1876, 10.1021/cr300249c.

[11] da Cruz, F. P.; Newberry, S.; Jenkinson, S. F.; Wormald, M. R.; Butters, T. D.; Alonzi, D. S.; Nakagawa, S.; Becq, F.; Norez, C.; Nash, R. J.; Kato, A.; Fleet, G. W. J. *Tetrahedron Lett.* **2011**, *52*, 219-223, 10.1015/j.tetlet.2010.10.173.

[12] Bouillon, M. E.; Pyne, S. G. *Tetrahedron Lett.* **2014**, *55*, 475-478, 10.1016/j.tetlet2013.11.068.

[13] Suzuki, K.; Nakahara, T.; Kanie, O. *Curr. Top. Med. Chem.* **2009**, *9*, 34-57, 10.2174/156802609787354315.

[14] Jenkinson, S. F.; Best, D.; Saville, A. W.; Mui, J.; Martinez, R. F.; Nakagawa, S.; Kunimatsu, T.; Alonzi, D. S.; Butters, T. D.; Norez, C.; Becq, F.; Bleriot, Y.; Wilson, F. X.; Weymouth-Wilson, A. C.; Kato, A.; Fleet, G. W. J. *J. Org. Chem.* **2013**, *78*, 7380-7397, 10.1021/jo4005487.

[15] Minami, Y.; Kurlyarna, C.; Ikeda, K.; Kato, A.; Takebayashi, K.; Adachi, I.; Fleet, G. W. J.; Kettawan, A.; Karnoto, T.; Asano, N. *Bioorg. Med. Chem.* **2008**, *16*, 2734-2740, 10.1016/j.bmc.2008.01.032.

[16] Paulsen, H.; Bruning, J.; Propp, K.; Heyns, K. *Tetrahedron Lett.* **1968**, 999-&, 10.1016/s0040-4039(01)98844-6.

[17] Dangerfield, E. M.; Gulab, S. A.; Plunkett, C. H.; Timmer, M. S. M.; Stocker, B. L. *Carbohydr. Res.* **2010**, *345*, 1360-1365, 10.1016/j.carres.2010.03.016.

[18] Kim, J. Y.; Mu, Y.; Jin, X.; Park, S. H.; Pham, V. T.; Song, D. K.; Lee, K. Y.; Ham, W. H. *Tetrahedron* **2011**, *67*, 9426-9432, 10.1016/j.tet.2011.09.084.

[19] Wang, G. N.; Yang, L.; Zhang, L. H.; Ye, X. S. *J. Org. Chem.* **2011**, *76*, 2001-2009, 10.1021/jo1020322.

[20] Choi, H. G.; Park, D. S.; Lee, W. K.; Sim, T. *Tetrahedron Lett.* **2013**, *54*, 5775-5777, 10.1016/j.tetlet.2013.08.040.

[21] Stocker, B. L.; Jongkees, S. A. K.; Win-Mason, A. L.; Dangerfield, E. M.; Withers, S. G.; Timmer, M. S. M. *Carbohydr. Res.* **2013**, *367*, 29-32, 10.1016/j.carres.2012.11.011.

[22] Ansari, A. A.; Vankar, Y. D. *RSC Adv.* **2014**, *4*, 12555-12567, 10.1039/c3ra47555g.

[23] Chirke, S. S.; Rajender, A.; Rao, B. V. *Tetrahedron* **2014**, *70*, 103-109, 10.1016/j.tet.2013.11.004.

[24] Wennekes, T.; van den Berg, R. J. B. H. N.; Donker, W.; van der Marel, G. A.; Donker, W.; van der Marel, G. A.; Strijland, A.; Aerts, J. M. F. G.; Overkleeft, H. S. *J. Org. Chem.* **2007**, *72*, 1088-1097, 10.1021/jo061280p.

[25] Ghisaidoobe, A.; Bikker, P.; de Bruijn, A. C. J.; Godschalk, F. D.; Rogaar, E.; Guijt, M. C.; Hagens, P.; Halma, J. M.; van't Hart, S. M.; Luitjens, S. B.; van Rixel, V. H. S.; Wijzenbroek, M.; Zweegers, T.; Donker-Koopman, W. E.; Strijland, A.; Boot, R.; van der Marel, G.; Overkleeft, H. S.; Aerts, J. M. F. G.; van den Berg, R. J. B. H. N. *ACS Med. Chem. Lett.* **2011**, *2*, 119-123, 10.1021/ml100192b.

[26] Ghisaidoobe, A. T.; van den Berg, R. J. B. H. N.; Butt, S. S.; Strijland, A.; Donker-Koopman, W. E.; Scheij, S.; van den Nieuwendijk, A. M. C. H.; Koomen, G.-J.; van Loevezijn, A.; Leemhuis, M.; Wennekes, T.; van der Stelt, M.; van der Marel, G. A.; van Boeckel, C. A. A.; Aerts, J. M. F. G.; Overkleeft, H. S. *J. Med. Chem.* **2014**, 10.1021/jm501181z.

[27] Ayers, B.; Long, H.; Sim, E.; Smellie, I. A.; Wilkinson, B. L.; Fairbanks, A. J. *Carbohydr. Res.* **2009**, *344*, 739-746, 10.1016/j.carres.2009.02.006.

[28] Behr, J. B.; Guillerm, G. *Tetrahedron Asymm.* **2002**, *13*, 111-113, 10.1016/s0957-4166(02)00081-2.

[29] Postema, M. H. D.; Calimente, D.; Liu, L.; Behrmann, T. L. *J. Org. Chem.* **2000**, *65*, 6061-6068, 10.1021/jo0005159.

[30] Wennekes, T.; Bonger, K. M.; Vogel, K.; van den Berg, R. J. B. H. N.; Strijland, A.; Donker-Koopman, W. E.; Aerts, J. M. F. G.; van der Marel, G. A.; Overkleeft, H. S. *Eur. J. Org. Chem.* **2012**, 6420-6454, 10.1002/ejoc.201200923.

[31] Guo, L. N.; Liu, Y. H.; Wan, Y.; Wang, P. G.; Zhao, W. *Tetrahedron Lett.* **2013**, *54*, 2579-2582, 10.1016/j.tetlet.2013.02.115.