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NOTE

A Practical Approach to Dideoxy-1,4- and 1,5-iminopentitols from Protected Sugar Hemiacetals.

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Abstract

The convenient and straightforward preparation of dideoxy-1,4- and 1,5-iminopentitol derivatives from protected sugar hemiacetals by way of *N*-*tert*-butanesulfinyl glycosylamines and open-chain aminoalditols is reported. The synthetic procedure is a method of choice for the making of these important scaffolds of biological interest.

Keywords

Sugar Hemiacetals; *N*-*tert*-butanesulfinyl glycosylamines; aminoalditols; Dideoxyiminopentitols

1. Introduction

Polyhydroxylated pyrrolidines and piperidines known as 1,4- and 1,5-dideoxyiminosugars have been known as natural products since the discovery of fagomine (1,2-dideoxynojirimycin, Figure 1) and moranoline in the 1970's [1,2]. The name 'moranoline' was later abandoned and 1-deoxynojirimycin (DNJ) preferred. A large diversity of 1-deoxyiminosugars was found *a posteriori* in microorganisms and plants [e.g., DMDP (2,5-dihydroxymethyl-3,4-dihydroxypyrrolidine also known as 2,5-dideoxy-2,5-imino-D-mannitol), Figure 1] [3] and many new structures synthesized [4]. The biological studies on

these compounds revealed their remarkable properties as inhibitors of glycosidases, as well as of other carbohydrate-processing enzymes [5]. When protonated, they mimic charge and shape of the cationic intermediates generated in the glycosidase catalyzed reactions. As such, these sugar analogues have considerable therapeutic potential and three 1,5-dideoxy-1,5-iminohexitol derivatives have now been commercialized as drugs (Figure 1). *N*-[2-hydroxyethyl]-1-deoxynojirimycin (miglitol) to treat diabetes mellitus type 2, *N*-butyl-deoxynojirimycin (miglustat) to act towards type I Gaucher disease and progressive neurologic manifestations of Niemann-Pick disease type C (NP-C) and 1-deoxygalactonojirimycin (migalastat) for the treatment of Fabry disease [6–11].

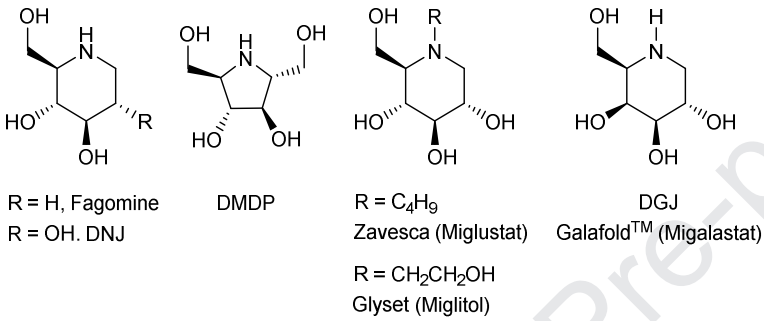


Figure 1. Natural 1-deoxyiminosugars and derivatives used as drugs.

A diversity of synthetic methodologies have been developed to access 1-deoxyiminosugars in the piperidine and pyrrolidine series, most often from sugars as starting materials [12], [13–17]. Such methods include for example, from protected, reducing aldo-furanoses or –pyranoses, double oxidation-double reductive amination sequences [18–20] or reduction, double mesylation and double S_N2 reactions [21]. Also from aldonolactones, formation of an open-chain amide, cyclization by oxidation and reductive amination to generate a lactam and reduction of the carbonyl group [22,23] has proven to be a convenient method. Remarkably, all these synthetic routes appear to be methods of choice although manipulation of the *oxo*-intermediates is commonly quite challenging and double reductive amination protocols give typically moderate overall yields (~ 50%) over long reaction times (48 h). Of relevance to our work is the method of Buchanan and Wrightman who reported the synthesis of a 2,3,5-tri-*O*-benzyliminoxylitol by a three-step procedure via an open chain oxime [24]. The technique consisting in forming a glycosylamine and reacting it with a nucleophile to generate an open-chain aminoalditol has been used mostly with C-nucleophiles to reach eventually 1-C-susbtituted iminoalditol compounds in the pyrrolidine and piperidine series [17]. The *in situ* or stepwise reductive amination of sugar hemiacetals

with amines by way of a glycosylamine, followed by the activation of the free OH group and cyclisation was reported by a few authors [25], [26,27] as an approach to 1-deoxyiminosugars but remained limited to few examples and their generality was not demonstrated. Furthermore, the reaction sequences involved generally long periods of time (usually ≥ 16 h) and/or low temperatures, the iminosugar compounds being obtained in their N-protected form; thus requiring an additional step for deprotection.

As shown in our previous work, *N-tert*-butanesulfinyl glycosylamines are highly efficient aldose imine surrogates and their reactions with organometallic nucleophiles have led to a diversity of 1-C-substituted iminoalditols derivatives [28,29]. On this basis, a short, general and convenient synthetic route to 1-deoxyiminoalditols using hydride as the nucleophile was envisaged (Figure 2).

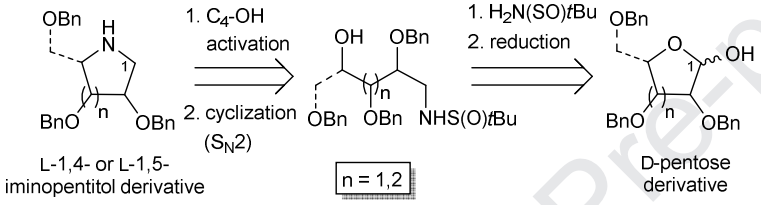


Figure 2. Synthetic plan from protected Hemiacetals.

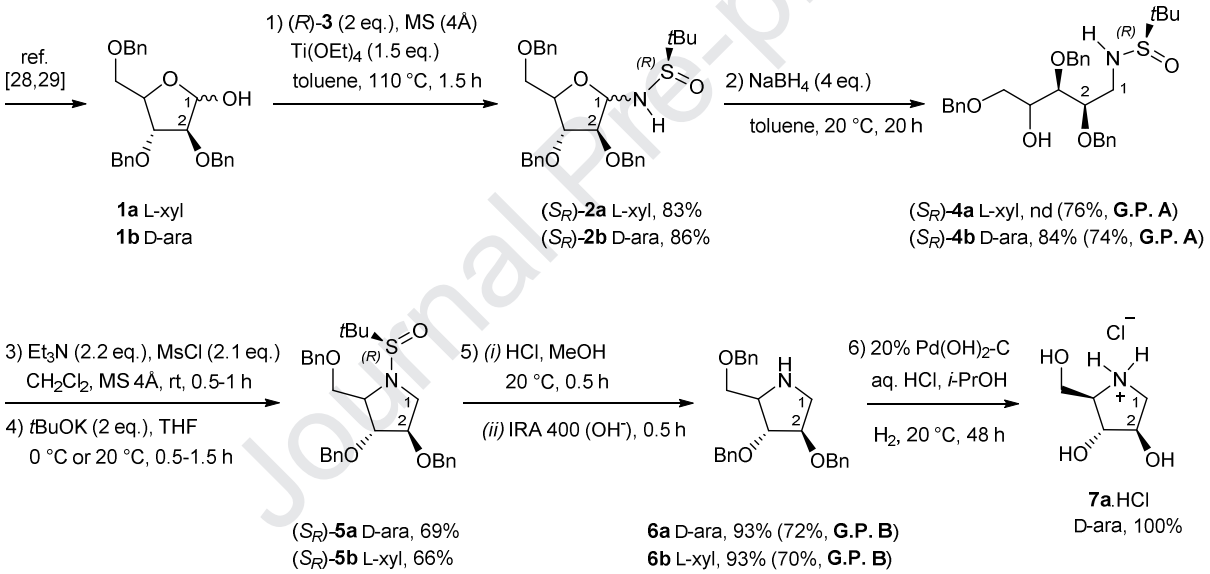
Combined with the cyclisation of the resulting open-chain aminoalditols, the route should lead in very few steps and short reaction times to protected or deprotected cyclic iminopentitols. We report in this note the implementation of the methodology.

2. Results and Discussion

Starting from known tri-*O*-benzyl pentofuranoses (**1a, 1b**), that were respectively obtained from L-xylose and D-arabinose, formation of the sulfinyl glycosylamines of type **2** was executed under conditions improved from the ones we previously described [28,29]. Thus, using $Ti(OEt)_4$ as the promoter and commercial (*R*)-(+)-2-methyl-2-propanesulfinamide ((*R*)-**3**, 2 equiv.) [30] in dry toluene, compounds (S_R)-**2a** (83%) and (S_R)-**2b** (86%) could be isolated in excellent yields after 1.5 h at 110 °C. Addition of $NaBH_4$ (4 equiv.) was then performed in toluene at room temperature (ca. 20 °C) with the D-arabinofuranosylamine (S_R)-**2b** to obtain compound (S_R)-**4b** in good yield (84%, 72% over 2 steps) after a reaction time of 20 h. Alternatively, for the synthetic utility of the proposed study, the glycosylamines were not isolated. Instead, following general procedure A (**G.P. A**), step (1) was carried out, and the crude reaction mixture was directly treated with $NaBH_4$ (4 equiv.) at 110 °C for 1 h to

afford the corresponding iminoalditols ((*S*$_R$)-**4a** and (*S*$_R$)-**4b**) in high yields (e.g., 76 and 74% respectively over the two-step sequence).

Of note, the reaction sequence could also be realized using the (*S*)-(–)-chiral sulfinyl auxiliary. Heating under microwave irradiation (i.e., 110 °C for 1.5 h) could also be achieved in step (1) to form the sulfinyl glycosylamines in comparable yields with that under standard heating. Subsequent reduction at 110 °C for 1 h could then be carried out at the bench, with no improvement of the reaction sequence yield (Scheme 1). Notably, synthesis of the aminoalditol compounds **4** could not be fully accomplished under microwave irradiation as a dramatic yield decrease was observed for the reduction step (e.g., 58% for (S$_R$)-**4b**). The free OH position was next activated as a mesylate, and the crude mesylate treated with *t*-BuOK (0 °C or 20 °C, 0.5-1.5 h) to perform the cyclization, thus giving pyrrolidine derivatives (S$_R$)-**5a** and (S$_R$)-**5b** in moderate yields (66–69%).

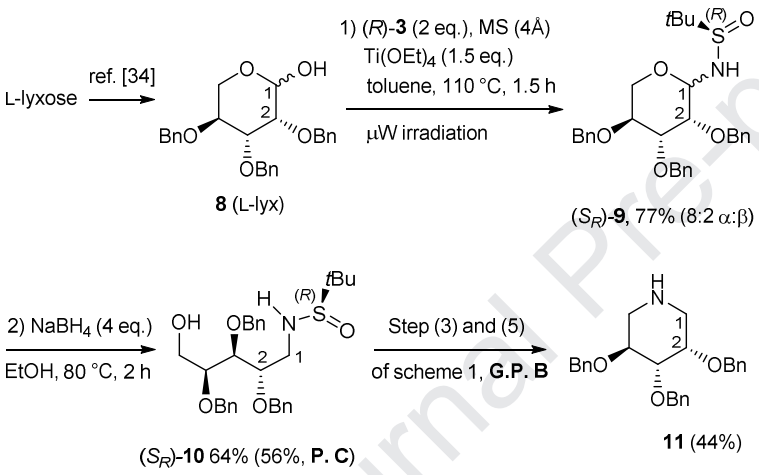


Scheme 1. Reactions of pentofuranose hemiacetals. General Procedure A (**G.P. A**): step (1), then addition of $NaBH_4$ (4 eq.), 110 °C, 1 h (compound **2** not isolated); General Procedure B (**G.P. B**): step (3) and (5) (use of crude **5**).

The sulfinyl group was cleaved by simple treatment with acidic methanol to give **6a** and **6b** in good yield (93%) [28]. Once again, the two reactions could be completed in a single sequence. The sulfinyl group could be cleaved from the intermediate mesylate, which was not isolated and subsequently cyclized upon acidification and neutralisation of the reaction mixture with a basic anion exchange resin (step (3) and (5), general procedure B or **G.P. B**), thus giving directly **6a** and **6b** from (S$_R$)-**4a** and (S$_R$)-**4b** in 72 and 70% yield respectively

[29]. Starting from L-xylofuranose derivative **1a** [31], the sequence gave the O-benzylated 1,4-imino-D-arabinitol **6a**, and from D-arabinofuranose **1b** [32], the corresponding 1,4-imino-L-xylitol derivative **6b** was obtained, both resulting from an inversion of configuration at C-4 upon ring closure. Compound **6a** was then deprotected by hydrogenolysis to afford the known D-DAB **7a** as its hydrochloride salt [22].

The scope of the reactions was then extended and the same sequence was applied to a *tri-O*-benzylated pentopyranose, with the goal of forming a 1,5-dideoxy-1,5-iminopentitol derivative. 3,4,5-Trihydroxypiperidines and their *N*- and *O*-alkylated and arylated synthetic derivatives have been shown exhibiting outstanding array of biological activities and promising potential in the area of antibacterial, anti-inflammatory and antiviral agents [33].



Scheme 2. Reaction of a L-lyxopyranose hemiacetal. Procedure C (**P. C)**: Step (1), then evaporation of the solvent and step (2) carried out.

The known tri-*O*-benzyl-L-lyxopyranose **8** [34] was thus prepared in three steps from L-lyxose. Reaction with Ellman's (*R*)-*tert*-butanesulfinamide [30] was performed at 110 °C to give the desired glycosylamine (S_R)-**9** readily (Scheme 2). The L-lyxopyranosylamine derivative was not soluble in toluene. It could be isolated (77%) and characterized. Importantly, heating under µW irradiation was mandatory to allow formation of (S_R)-**9** in good yield over a short period of time [35]. Afterwards, the toluene was evaporated and the crude compound (S_R)-**9** was reduced to the corresponding aminopentitol derivative (S_R)-**10** (64%) upon addition of $NaBH_4$ (4 equiv.) in EtOH at 80 °C for 2 h (49% over two steps). Step (1) and (2) could obviously be performed without isolation of (S_R)-**9** to give (S_R)-**10** in good overall yield (56%, procedure C (**P. C**)). The open-chain compound was thereafter

cyclized by way of the mesylate under the conditions described for the pyrrolidines (**G.P. B**), thus affording the 1,5-dideoxy-1,5-imino-L-lyxitol **11** in moderate yield (44%).

3. Conclusion

We have reported in this note a brief synthesis of protected or free 1,4-imino or 1,5-iminopentitol derivatives using a sulfinyl glycosylamine as an aldose imine equivalent. Reduction of the latent imine provides an open-chain aminoalditol, which can be readily cyclized by an internal S_N2 process. This method will be applicable to a large diversity of pentose hemiacetals to prepare the corresponding cyclic iminoalditols in moderate to good overall yields in a convenient and straightforward manner. Although the use of a chiral sulfinyl group is required for the proposed study, it is important to note that (*R*)- and (*S*)-2-methyl-2-propanesulfinamides are inexpensive and readily to prepare [30]. Furthermore, the sulfinylamino function has optimal properties to allow implementation of this methodology: stable glycosylamine and open-chain intermediates, favourable reactivity of the latent N-sulfinyl imine, and ready deprotection of the nitrogen atom, thus providing the possibility of post-functionalisation of this endocyclic atom.

4. Experimental section

4.1. General remarks

Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. Toluene (puriss. p.a., ACS reagent, ≥ 99.7% (GC)) and THF (99.9% GC) with 2,6-di-*tert*-butyl-4-methylphenol (250 mg/L) as stabilizer were purified by passage through a column containing activated alumina under nitrogen pressure (Dry Solvent Station GT S100, GlassTechnology, Geneva, CH). Dichloromethane (99.99% GC) was distilled from calcium hydride (CaH_2) and used as solvent in reactions under anhydrous conditions. Methanol (anhydrous, 99.8%) and *N*,*N*-dimethylformamide (anhydrous, 99.8%) were purchased from Sigma-Aldrich. MS 4 Å was activated by drying in an oven at 500 °C (48 h). It was then allowed to reach room temperature (ca. 20 °C) and kept over $CaCl_2$ in a desiccator prior to use. Amberlite® IRA-400 was prepared in its OH^- form by passing 1M KOH until the effluent is free from chloride ions, then washed with distilled H_2O until neutral and MeOH. Microwave activation was performed in sealed vessel, using a Biotage Initiator system. The following setting was used: Normal absorption level, Fixed Hold Time: on, Power: 100 Watt, Hold time: 90 minutes, Temperature: 110 °C. The internal temperature was measured by an IR-sensor. NMR spectra were recorded at 298 K with a Bruker Avance III HD nanobay 400

MHz spectrometer equipped with a BBO probe. The structures of the new compounds were assigned with the aid of 1 D [^{1}H NMR, ^{13}C NMR, Distortionless Enhancement by Polarization Transfer (DEPT)] and 2 D Correlation Spectroscopy [(^{1}H−^{1}H COSY and ^{1}H−^{13}C Heteronuclear Single Quantum Coherence (HSQC)] experiments. ^{1}H NMR (400 MHz) chemical shift values are listed in parts per million (ppm). Tetramethylsilane (TMS) was used as an internal standard, or alternatively, spectra were calibrated using the signals of the corresponding non-deuterated solvent. Data are reported as follows: chemical shift (ppm on the δ scale), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constant *J* (Hz), and integration. ^{13}C NMR (101 MHz) chemical shifts are given in ppm. Spectra were calibrated using the corresponding non-deuterated solvent or TMS as an internal standard. NMR primary data should be processed by MestReNova. High-resolution mass spectra were recorded with a Brucker maXis ESI qTOF ultrahigh-resolution mass spectrometer coupled to a Dionex Ultimate 3000 RSLC system (FR2708, Orléans). MS data were acquired in positive mode and were processed using Data Analysis 4.4 software (Bruker). Infrared spectra were recorded with a Thermo Scientific Nicolet IS10 FTIR spectrometer using diamond ATR golden gate sampling and are reported in wave numbers (cm^{-1}). Specific optical rotations were measured with a JASCO P-2000 digital polarimeter, in a thermostated (20 °C) 1 dm long cell with high-pressure sodium lamp and are reported as follow: [α]DT [solvent, c (g/100 mL)]. Analytical thin-layer chromatography (TLC) was performed with Merck Silica Gel 60 F254 precoated plates. Visualization of the developed chromatogram was performed under ultraviolet light (254 nm) and on staining by immersion in aqueous, acidic ceric ammonium molybdate followed by charring at 150 °C. Flash chromatography was performed in air on Silica Gel 60 (230–400 mesh) with petroleum ether (PE, bp 40–65 °C) and ethyl acetate as eluents, unless otherwise stated. Organic solutions were concentrated under reduced pressure with a Buchi rotary evaporator.

4.2. General procedures

*4.2.1. General procedure for the preparation of 1-N-tert-butanesulfinylamino-1-deoxy-pentitol derivatives of type **4a** and **4b** from protected sugar hemiacetals (**1a**, **1b**) (**G.P. A**).*

A single-necked flask equipped with a reflux condenser and an argon inlet system was charged with related tri-*O*-benzyl-pentofuranose, 4 Å activated molecular sieves (0.4 g per mmol of substrate) and (*S*)- or (*R*)-2-methyl-2-propanesulfinamide (2.0 equiv.). Dry toluene (4 mL per mmol of substrate) was inserted and the mixture was stirred for 5 min at room

temperature (~20 °C). Titanium(IV) ethoxide ($Ti(OEt)_4$, 1.5 equiv.) was then added and the reaction mixture was stirred at 110 °C until no more starting material was observed by TLC (generally, 1.5 h). The content was next allowed to reach 20 °C and $NaBH_4$ (4.0 equiv.) was added. The resulting suspension was stirred at 110 ^oC until no more sulfinyl glycosylamine intermediate remained in the reaction mixture (1 h). The suspension was then allowed to cool down to room temperature and sat. aqueous NaCl was added. The mixture was stirred at 20 °C for 10 min and the precipitate and molecular sieves were filtered through a pad of celite®. The cake was rinsed (EtOAc) and the aqueous layer was discarded. The organic phase was washed (sat. aq. NH_4Cl), dried over $MgSO_4$, filtered through a cotton plug and concentrated *in vacuo*. The crude product was purified through column chromatography (SiO_2, PE:EtOAc) to provide the 1-*N*-*tert*-butanesulfinylamino-1-deoxy-pentitol derivative.

4.2.2. General procedure for the Synthesis of 1,4-Dideoxy-1,4-iminopentitol derivatives of type ***6a*** *and* ***6b*** *and 1,5-Dideoxy-1,5-imino-L-lyxitol* ***11****, from corresponding N-tert-butanesulfinylamino-1-deoxy-pentitols (****G.P. B****).*

To a solution of compound **4** in anhydrous CH_2Cl_2 (0.08 M), under argon atmosphere, were added Et_3N (2.2 equiv.) and MsCl (2.0 equiv.) and the reaction mixture was stirred at room temperature until no more starting material was present (30−60 min). The mixture was then diluted (CH_2Cl_2) and the organic phase was washed with aq. NH_4Cl. The aqueous phase was extracted 3× with CH_2Cl_2 and the combined organic phases were dried over $MgSO_4$. The solvent was evaporated at the evaporator to give the crude mesylated intermediate which was used in the next cyclization step without further purification.

A single-necked flask under argon atmosphere was charged with AcCl (5 equiv., 0.4 M) and dry MeOH and the mixture was stirred at 20 °C for 30 min (solution A). Another flask under argon atmosphere (flask B) was charged with dry MeOH and crude mesylated intermediate (0.4 M), and solution A was added through syringe to flask B. The reaction mixture was stirred for 1 h; Amberlite IRA-400 (OH^- form) ion-exchange resin was then added until pH 8. The mixture was stirred further for 1 h at the same temperature and the suspension was filtered through a cotton plug. The solvents were evaporated under reduced pressure and the residue was purified by chromatography to provide compound **6a**, **6b** or **11** in good yield.

4.3. Synthesis of Compounds ***4-7*** *and* ***9-11****.*

4.3.1. 2,3,5-Tri-O-benzyl-1-[(S_R*)-N-tert-butanesulfinylamino]-1-deoxy-L-xylitol (*S_R*)-****4a****.*

Compound (S_R)-**4a** was synthesized according to **G.P. A**, and isolated as a colorless oil (1.9 g, 76%). R_f 0.2 (SiO_2, PE:EtOAc 1:1) ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.36–7.21 (overlapped, 15 H, H_{Ar}), 4.78–4.38 (overlapped, 6 H, OC*H*$_2$Ph), 4.00–3.87 (overlapped, 2 H, H-4, H-2), 3.70 (dd, *J* = 6.1, 2.2 Hz, 1 H, H-3), 3.60–3.43 (overlapped, 3 H, H-1a, H-5a, N*H*), 3.39 (dd, *J* = 9.3, 6.4 Hz, 1 H, H-5b), 3.27 (dt, *J* = 12.7, 6.2 Hz, 1 H, H-1b), 2.48 (d, *J* = 7.5 Hz, 1 H, O*H*), 1.16 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.0 (C, C_{Ar}), 138.0 (C, C_{Ar}), 137.9 (C, C_{Ar}), 128.5–127.7 (CH, CH_{Ar}), 79.3 (CH, C-2), 77.3 (CH, C-3), 74.3 (CH_2, O*C*H$_2$Ph), 73.3 (CH_2, O*C*H$_2$Ph), 72.8 (CH_2, O*C*H$_2$Ph), 71.3 (CH_2, C-5), 68.9 (CH, C-4), 55.8 (C, *t*Bu), 45.7 (CH_2, C-1), 22.6 (CH_3, *t*Bu) ppm. HRMS (ESI): calcd. for $C_{30}H_{40}NO_5S$ [M+H$^+$] 526.2627; found 526.2621.

*4.3.2. 2,3,5-tri-O-benzyl-(S_R)-N-tert-butanesulfinyl-1,4-dideoxy-1,4-imino-D-arabinitol (S_R)-**5a**.*

To a solution of compound (S_R)-**4a** (200 mg, 0.38 mmol) in anhydrous CH_2Cl_2 (5 mL), under argon atmosphere were added triethylamine (113 µL, 0.84 mmol) and MsCl (59 µL, 0.76 mmol) and the reaction mixture was stirred at room temperature for 1 h. The mixture was diluted by addition of CH_2Cl_2 (20 mL) and the organic solution was washed with saturated aq. NaCl (30 mL). Next, the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL) and combined organic phases were dried over $MgSO_4$ and filtered over a cotton plug. Solvent removal through rotary evaporation gave the crude mesylated intermediate which was used for the cyclisation step without further purification.

To a solution of the just generated mesylated intermediate in anhydrous THF (5 mL) under argon atmosphere was added *t*-BuOK (85 mg, 0.76 mmol) and the reaction mixture was stirred at 20 °C for 30 min. Saturated aq. NH_4Cl (10 mL) was then added and the mixture was extracted with EtOAc (3 × 15 mL). Next, the combined organic phases were washed with saturated aq. NaCl (20 mL), dried over $MgSO_4$, filtered over a cotton plug and concentrated under vacuum. The crude product was purified by flash chromatography (SiO_2, PE : EtOAc 2:1) to give (S_R)-**5a** (132 mg, 69%) as colorless oil. R_f 0.32 (SiO_2, PE:EtOAc 2:1). $[\alpha]_D^{20}$ −9.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.37–7.20 (overlapped, 15 H, H_{Ar}), 4.60 (s, 2 H, OC*H*$_2$Ph), 4.51–4.40 (overlapped, 4 H, OC*H*$_2$Ph), 4.08–3.97 (overlapped, 3 H, H-1a, H-2, H-3), 3.86–3.77 (m, 1 H, H-4), 3.57–3.46 (m, 2 H, H-5), 2.79 (dd, *J* = 10.2, 4.3 Hz, 1 H, H-1b), 1.15 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.2 (C, C_{Ar}), 138.1 (C, C_{Ar}), 137.9 (C, C_{Ar}), 128.5−127.6 (CH, CH_{Ar}), 83.1 (CH, C-2 or C-3), 82.1 (CH, C-3 or C-2), 73.1 (CH_2, OCH_2Ph), 72.1 (CH_2, OCH_2Ph), 71.6 (CH_2, OCH_2Ph), 71.2 (CH_2, C-5),

68.26 (CH, C-4), 57.6 (C, *t*Bu), 44.8 (CH_2, C-1), 23.6 (CH_3, *t*Bu) ppm. IR (neat): 3021 (C−H), 2929 (C−H), 2857 (C−H), 1714, 1451 (C=C), 1064 (C−O), 739 (C−H), 694 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{38}NO_4S$ [M+H^+] 508.2522; found: 508.2519.

4.3.3. 2,3,5-Tri-O-benzyl-1,4-dideoxy-1,4-imino-D-arabinitol ***6a****.*

Compound **6a** was synthesized from imino-L-xylitol (S_R)-**4a** according to **G.P. B**. It was isolated as a colorless oil (110 mg, 72%). R_f 0.45 (SiO_2, CH_2Cl_2:MeOH 15:1). NMR data are consistent with that of the literature [22]. $[\alpha]_D^{20}$ −1.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.31–7.21 (overlapped, 15 H, H_{Ar}), 4.59–4.39 (overlapped, 6 H, OCH_2Ph), 4.05–3.97 (m, 1 H, H-2), 3.87 (dd, *J* = 4.8, 1.9 Hz, 1 H, H-3), 3.61 (dd, *J* = 9.5, 5.1 Hz, 1 H, H-5a), 3.55 (dd, *J* = 9.5, 5.6 Hz, 1 H, H-5b), 3.24 (q, *J* = 4.8 Hz, 1 H, H-4), 3.09 (d, *J* = 3.6 Hz, 2 H, H-1), 2.24 (br s, 1 H, N*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.3 (C, C_{Ar}), 138.2 (C, C_{Ar}), 138.2 (C, C_{Ar}), 128.4–127.6 (CH, CH_{Ar}), 85.8 (CH, C-3), 84.6 (CH, C-2), 73.2 (CH_2, O*C*H_2Ph), 71.9 (CH_2, O*C*H_2Ph), 71.1 (CH_2, O*C*H_2Ph), 70.4 (CH_2, C-5), 64.2 (CH, C-4), 51.1 (CH_2, C-1) ppm. IR (neat): 3034 (C−H), 2917 (C−H), 2863 (C−H), 1739, 1451 (C=C), 1087 (C−O), 736 (C−H), 688 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{30}NO_3$ [M+H^+] 404.2226; found: 404.2218.

Alternatively, it could be prepared by removal of the chiral sulfinyl auxiliary from imino-D-arabinitol **5a**.

In a 2-mL single-necked round-bottomed flask under argon atmosphere was inserted AcCl (17 μL, 0.24 mmol) and dry MeOH (0.5 mL) and the solution was stirred at 20 °C for 30 min (solution A). In parallel, another 2-mL flask under argon atmosphere was charged with imino-D-arabinitol (S_R)-**5a** (30 mg, 0.06 mmol) and solution A was added through syringe. The reaction mixture was stirred for 15 min and neutralized by addition of resin Amberlite IRA-400 (OH^- form) until pH 8. The solution was filtered through a cotton plug and concentrated under vacuum to afford **6a** in good yield (23 mg, 93%).

4.3.4. 1,4-Dideoxy-1,4-imino-D-arabinitol ***7a****.HCl.*

A vigorously stirred suspension of **6a (**70 mg, 0.173 mmol), 20% $Pd(OH)_2$−C (40 mg), and aq. HCl (1 N, 0.6 mmol, 600 μL) in *i*PrOH (5 mL) was degassed under vacuum and saturated with hydrogen (3x). The reaction mixture was stirred at 20 °C for 48 h under hydrogen atmosphere (balloon of H_2). The mixture was filtered over a pad of celite® and the solid residue was rinsed with MeOH. The solvents were evaporated under reduced pressure to

give **7a**.HCl as colorless syrup in quantitative yield (29 mg). Characterization data are consistent with those reported in the literature [22]. $[\alpha]_D^{20}$ +24.5 (*c* 0.47, H_2O); (Lit $[\alpha]_D$ +27.27 (*c* 0.47, D_2O)). ^{1}H NMR (400 MHz, D_2O): δ 4.37–4.31 (m, 1 H, H-2), 4.15–4.06 (m, 1 H, H-3), 3.96 (dd, *J* = 12.2, 4.6 Hz, 1 H, H-5), 3.84 (dd, *J* = 12.2, 8.2 Hz, 1 H, H-5), 3.67–3.54 (overlapped, 2 H, H-4, H-1a), 3.37 (d, *J* = 12.6 Hz, 1 H, H-1b) ppm. ^{13}C NMR (101 MHz, D_2O): δ 75.6 (CH, C-3), 74.2 (CH, C-2), 66.6 (CH, C-4), 58.9 (CH_2, C-5), 50.0 (CH_2, C-1) ppm. HRMS (ESI): calcd. for $C_5H_{12}NO_3$ [M+H$^+$] 134.0817; found: 134.0812.

*4.3.5. 2,3,5-Tri-O-benzyl-1-[(S_R)-N-tert-butanesulfinylamino]-1-deoxy-D-arabinitol (S_R)-**4b**.*

The title compound was synthesized according to **G.P. A** to afford (S_R)-**4b** as yellowish syrup (277 mg, 74%). R_f 0.1 (SiO_2, PE:EtOAc 5:5). $[\alpha]_D^{20}$ –34.5 (*c* 0.78, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.39–7.22 (overlapped, 15H, H_{Ar}), 4.70–4.48 (overlapped, 6 H, 3 × OC*H*$_2$Ph), 4.02–3.94 (br m, 1 H, H-4), 3.92–3.86 (m, 1 H, H-2), 3.71–3.59 (overlapped, 3 H, H-3, H-5a, H-5b), 3.46–3.25 (overlapped, 3 H, H-1a, H-1b, N*H*), 2.92 (br s, 1 H, O*H*), 1.13 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.1 (C, C_{Ar}), 138.0 (C, C_{Ar}), 137.8 (C, C_{Ar}), 128.7–127.9 (CH, CH_{Ar}), 79.4 (CH, C-2), 77.4 (CH, C-3), 73.7 (CH_2, OCH_2Ph), 73.6 (CH_2, OCH_2Ph), 73.3 (CH_2, OCH_2Ph), 71.2 (CH_2, C-5), 70.7 (CH, C-4), 55.9 (C, *t*Bu), 45.6 (CH_2, C-1), 22.7 (CH_3, *t*Bu) ppm. IR (neat): 3309 (O−H), 3062 (C−H), 3030 (C−H), 2865 (C−H), 1454 (C=C), 1068 (C−O), 735 (C−H), 697 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{40}NO_5S$ [M+H$^+$] 526.2622; found 526.2622.

Alternatively, it could be prepared by reduction of the isolated glycosylamine derived from **1b**, compound **2b** [29].

An oven-dried 5-mL single-necked round-bottomed flask was charged with compound (S_R)-**2b** (50 mg, 95 μmol) and flushed with argon. Dry THF (0.5 mL) was inserted (syringe) and $NaBH_4$ (7 mg, 0.19 mol) was added in one portion. The reaction mixture was then allowed to stir at 20 °C for 20 h under argon atmosphere. The mixture was quenched by the addition of aq. NH_4Cl (10 mL), and it was extracted twice with EtOAc (2 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered through a cotton plug and the solvents were evaporated under reduced pressure. The crude product was purified by column chromatography (SiO_2, PE:EtOAc 5:5 to 3:7) to afford D-arabinitol (S_R)-**4b** in good yield (42 mg, 84%).

*4.3.6. 2,3,5-Tri-O-benzyl-(S_R)-N-tert-butanesulfinyl-1,4-dideoxy-1,4-imino-L-xylitol (S_R)-**5b**.*

To a solution of compound (S_R)-**4b** (96 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (3.5 mL), in the presence of 4Å MS, under argon atmosphere were added Et_3N (100 µL, 0.73 mmol) and MsCl (57 µL, 0.73 mmol) and the reaction mixture was stirred at 20 °C for 30 min. The molecular sieves were filtered through Celite®, the cake rinsed with CH_2Cl_2 and the organic solution washed with aq. NH_4Cl (10 mL). Next, the aqueous phase was extracted once with CH_2Cl_2, combined organic phases were dried over $MgSO_4$ and filtered over a cotton plug. Solvent evaporation gave the crude mesylated intermediate which was used in the cyclisation step without further purification.

To a solution of the just generated mesylated intermediate in anhydrous THF (3.5 mL) under argon atmosphere was added *t*-BuOK (40 mg, 0.36 mmol) and the reaction mixture was stirred at 0 °C for 1 h. Extra *t*-BuOK (20 mg, 0.18 mmol) was added and stirring was pursued for another 30 min. Aqueous NH_4Cl (10 mL) was then added and the mixture was extracted twice with EtOAc (2 × 5 mL). The combined organic phases were then washed with saturated aq. NaCl, dried over $MgSO_4$, filtered over a cotton plug and concentrated under vacuum. The crude product was purified by flash chromatography (SiO_2, PE:EtOAc 7:3) to give (S_R)-**5b** (60 mg, 66%) as a pale yellow oil.

R_f 0.4 (SiO_2, PE:EtOAc 7:3). $[\alpha]_D^{20}$ –36.1 (*c* 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.40–7.19 (overlapped, 15 H, H_{Ar}), 4.64–4.42 (overlapped, 6 H, OCH_2Ph), 4.17 (dt, *J* = 6.9, 4.3 Hz, 1 H, H-2), 4.06 (dd, *J* = 6.0, 4.6 Hz, 1 H, H-3), 4.01–3.94 (m, 1 H, H-4), 3.87 (dd, *J* = 11.5, 6.9 Hz, 1 H, H-1a), 3.74 (d, *J* = 4.8 Hz, 2 H, H-5), 3.02 (dd, *J* = 11.5, 3.7 Hz, 1 H, H-1b), 1.16 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.3 (C, C_{Ar}), 138.1 (C, C_{Ar}), 138.1 (C, C_{Ar}), 128.4−127.5 (CH, CH_{Ar}), 83.2 (CH, C-3), 81.5 (CH, C-2), 73.5 (CH_2, OCH_2Ph), 72.5 (CH_2, OCH_2Ph), 71.8 (CH_2, OCH_2Ph), 68.2 (CH_2, C-5), 59.7 (CH, C-4), 57.7 (C, *t*Bu), 51.2 (CH_2, C-1), 23.1 (CH_3, *t*Bu) ppm. IR (neat): ν = 3029 (C−H), 2924 (C−H), 2865 (C−H), 1454 (C=C), 1362, 1074 (C−O), 1028 (C−N), 753 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{38}NO_4S$ [M+H^+] 508.2516; found: 508.2515.

4.3.7. 2,3,5-Tri-O-benzyl-1,4-dideoxy-1,4-imino-L-xylitol ***6b****.*

The titled compound was synthesized from (S_R)-**4b** according to **G.P. B** to afford **6b** as a yellow oil (51 mg, 70 %). R_f 0.4 (SiO_2, CH_2Cl_2:MeOH 9:1). $[\alpha]_D^{20}$ +7.9 (*c* 0.96, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.39–7.20 (overlapped, 15 H, H_{Ar}), 4.60–4.42 (overlapped, 6 H, 3 × OCH_2Ph), 4.05–3.93 (overlapped, 2 H, H-2, H-3), 3.73–3.69 (m, 1 H, H-5a), 3.66–3.58 (m, 1 H, H-5b), 3.49 (dd, *J* = 11.5, 5.5 Hz, 1 H, H-4), 3.35 (dd, *J* = 11.8, 5.6 Hz, 1 H, H-

1a), 2.90 (d, J = 12.0 Hz, 1 H, H-1b), 2.25 (br s, 1 H, N*H*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.5 (C, C_{Ar}), 138.3 (C, C_{Ar}), 138.2 (C, C_{Ar}), 128.5−127.7 (CH, CH_{Ar}), 83.2 (CH, C-2 or C-3), 82.9 (CH, C-3 or C-2), 73.5 (CH_2, OCH_2Ph), 71.9 (CH_2, OCH_2Ph), 71.5 (CH_2, OCH_2Ph), 69.3 (CH_2, C-5), 60.5 (CH, C-4), 50.9 (CH_2, C-1) ppm. IR (neat): 3062 (C−H), 3029 (C−H), 2914 (C−H), 2861 (C−H), 1453 (C=C), 1094 (C−O), 1027 (C−N), 735 (C−H), 697 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{30}NO_3$ [M+H$^+$] 404.2220; found: 404.2220.

Alternatively, compound **6b** could be obtained from imino-L-xylitol **5b**.

In a 10-mL single-necked round-bottomed flask under argon atmosphere was inserted AcCl (37 μL, 0.52 mmol) and dry MeOH (3.0 mL) and the solution was stirred at 20 °C for 30 min (solution A). In parallel, another 10-mL flask under argon atmosphere was charged with imino-L-xylitol (S_R)-**5b** (53 mg, 0.104 mmol) and solution A was added through syringe. The reaction mixture was stirred for 15 min and neutralized by addition of resin Amberlite IRA-400 (OH^- form) until pH 8. The solution was filtered through a cotton plug and concentrated under vacuum to afford **6b** in good yield (39 mg, 93%).

*4.3.8. 2,3,4-tri-O-benzyl-(S_R)-N-tert-butanesulfinyl-α/β-L-lyxopyranosylamine (S_R)-**9**.*

A 5-mL microwave vial under argon atmosphere was charged with 2,3,4-tri-*O*-benzyl-L-lyxopyranose (0.5 g, 1.19 mmol) **8** [34], 4 Å activated molecular sieves (0.5 g), (*R*)-(+)-2-methyl-2-propanesulfinamide (0.288 g, 2.38 mmol) and a microwave magnetic stir bar. Dry toluene (5 mL) was inserted and the mixture was stirred during 10 min at 20 °C. $Ti(OEt)_4$ (0.41 g, 1.78 mmol) was added, the vial was sealed and the reaction mixture was heated at 110 °C for 1.5 h under microwave irradiation. After cooling to room temperature, the cap was removed and the brown solution was diluted (CH_2Cl_2, 50 mL). Brine was added (50 mL) and the mixture was stirred for 5 min. Molecular sieves and the precipitate were filtered over celite and the cake was rinsed with CH_2Cl_2 (3 × 20 mL). The phases were separated and the aqueous phase was extracted twice with CH_2Cl_2 (2 × 20 mL). The combined organic layers were then dried over $MgSO_4$, filtered over a cotton plug and evaporated under reduced pressure. The crude compound product was purified by column chromatography (SiO_2, EtOAc : PE, 1:1) to provide (S_R)-**9** as yellow oil (0.48 g, 77%). Mixture of anomers ca. 8:2, not assigned. R_f 0.38 (SiO_2, EtOAc : PE, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.40–7.19 (overlapped, 15 H, H_{Ar}), 5.64 (br s, 0.7 H, N*H maj.*), 5.05 (br d, J = 7.8 Hz, 0.8 H, H-1 *maj.*), 4.97 (dd, J = 8.0, 5.4 Hz, 0.2 H, H-1 *min.*), 4.70–4.42 (overlapped, 6 H, OC*H*$_2$Ph

maj., OC*H*$_2$Ph *min.*), 4.07 (dd, *J* = 12.8, 2.0 Hz, 0.8 H, H-5b *maj.*), 3.94 (t, *J* = 3.2 Hz, 0.8 H, H-2 *maj.*), 3.90–3.75 (overlapped, 1.6 H, H-2 *min.*, H-5a *min.*, H-5b *min.*, H-3 *maj.*), 3.72–3.65 (m, 0.8 H, H-4 *maj.*), 3.63–3.50 (overlapped, 1.2 H, H-5a *maj.*, H-3 *min.*, H-4 *min.*, N*H* *min.*), 1.18 (s, 1.8 H, *t*Bu *min.*), 1.08 (s, 7.6 H, *t*Bu *maj.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.2 (C, C_{Ar} *min.*), 138.0 (C, C_{Ar} *maj.*), 138.0 (C, C_{Ar} *min.*), 137.9 (C, C_{Ar} *maj.*), 137.8 (C, C_{Ar} *min.*), 137.6 (C, C_{Ar} *maj.*), 128.5 (CH, CH_{Ar} *min.*), 128.5–127.7 (CH, CH_{Ar} *min.*, CH_{Ar} *maj.*), 82.9 (CH, C-1 *maj.*), 82.6 (CH, C-1 *min.*), 77.3 (CH, C-3 *maj.*), 76.2 (CH, C-3 *min.*), 74.8 (CH, C-4 *min.*), 74.7 (CH, C-4 *maj.*), 73.9 (CH_2, OCH_2Ph *maj.*), 73.5 (CH, C-2 *maj.*), 73.4 (CH, C-2 *min.*), 73.0 (CH_2, OCH_2Ph *min.*), 71.7 (CH_2, OCH_2Ph *maj.*), 71.7 (CH_2, OCH_2Ph *maj.*), 71.5 (CH_2, OCH_2Ph *min.*), 71.5 (CH_2, OCH_2Ph *min.*), 64.0 (CH_2, C-5 *min.*), 58.7 (CH_2, C-5 *maj.*), 56.1 (C, *t*Bu *maj.*), 55.9 (C, *t*Bu *min.*), 22.4 (CH_3, *t*Bu *maj.*), 22.4 (CH_3, *t*Bu *min.*) ppm. HRMS (ESI): calcd. for $C_{30}H_{38}NO_5S$ [M+H$^+$] 524.2471; found 524.2465.

*4.3.9. 2,3,4-Tri-O-benzyl-1-(S_R)-N-tert-butanesulfinylamino-1-deoxy-L-lyxitol (S_R)-**10**.*

Procedure C (P. C). A 5-mL microwave vial under argon atmosphere was charged with 2,3,4-Tri-*O*-benzyl-L- lyxopyranose **8** [34] (0.1 g, 0.24 mmol), 4 Å activated molecular sieves (0.2 g), (*R*)-(+)-2-methyl-2-propanesulfinamide (58 mg, 0.48 mmol) and a microwave magnetic stir bar. Dry toluene (2 mL) was inserted and the mixture was stirred during 10 min at 20 °C. $Ti(OEt)_4$ (82 mg, 0.36 mmol) was added, the vial was sealed and the reaction mixture was heated at 110 °C for 1.5 h under microwave irradiation. After cooling to room temperature, the cap was removed and the solvent was evaporated under reduced pressure (septum pierced by a needle).

The crude 2,3,4-tri-*O*-benzyl-(S_R)-*N*-*tert*-butanesulfinyl-α/β-L-lyxopyranosylamine (S_R)-**9** was then dissolved by adding 5 mL of absolute ethanol, the mixture was flushed with argon and $NaBH_4$ (36 mg, 0.95 mmol) was added. The reaction mixture was subsequently heated at 80 °C under argon atmosphere, until no more of the sulfinyl intermediate was observed (2 h). Next, the suspension was allowed to cool down to room temperature and the solvent was evaporated. The residue was dissolved in CH_2Cl_2 (20 mL) and molecular sieves were eliminated by filtration through a cotton plug. The organic phase was washed with sat. aq. NH_4Cl (20 mL) and the aqueous phase was extracted 3× with CH_2Cl_2 (3 × 10 mL). Combined organic layers were dried over $MgSO_4$, filtered over a cotton plug and the solvent was evaporated under reduced pressure. The crude product was purified by column

chromatography (SiO_2, PE : EtOAc 1:2 to 1:3) to afford the titled compound (S_R)-**10** in 56% yield (ca. 71 mg). R_f 0.25 (SiO_2, PE:EtOAc 1:2). $[\alpha]_D^{20}$ −59.4 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.39–7.23 (overlapped, 15 H, H_{Ar}), 4.77–4.49 (overlapped, 6 H, OC*H*$_2$Ph), 3.93–3.86 (dd, *J* = 5.2, 3.8 Hz, 1 H, H-3), 3.85-3.76 (overlapped, 2 H, H-2, H-5a), 3.75–3.63 (overlapped, 3 H, H-4, H-5b, N*H*), 3.52–3.29 (m, 2 H, H-1), 2.45 (t, *J* = 6.1 Hz, 1 H, O*H*), 1.08 (s, 9 H, *t*Bu) ppm. ^{1}H NMR (400 MHz, Benzene-d_6): δ 7.22–7.14 (overlapped, 6 H, H_{Ar}), 7.03–6.92 (overlapped, 9 H, H_{Ar}), 4.58–4.31 (overlapped, 6 H, OC*H*$_2$Ph), 3.94 (t, *J* = 6.3 Hz, 1 H, O*H*), 3.87 (dd, *J* = 5.5, 3.8 Hz, 1 H, H-2), 3.83 (q, *J* = 5.0 Hz, 1 H, , H-3), 3.72–3.62 (m, 2 H, H-5), 3.56 (q, *J* = 4.9 Hz, 1 H, H-4), 3.44–3.30 (m, 2 H, H-1), 0.80 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS) δ 138.1 (C, C_{Ar}), 138.1 (C, C_{Ar}), 137.8 (C, C_{Ar}), 128.6–127.9 (CH, CH_{Ar}) 79.8 (CH), 79.4 (CH), 79.4 (CH), 74.2 (CH_2, O*C*H$_2$Ph), 72.7 (CH_2, O*C*H$_2$Ph), 72.1 (CH_2, O*C*H$_2$Ph), 61.2 (CH_2, C-5), 55.7 (C, *t*Bu), 45.6 (CH_2, C-1), 22.6 (CH_3, *t*Bu) ppm. ^{13}C NMR (101 MHz, Benzene-d_6) δ 139.3 (C, C_{Ar}), 139.2 (C, C_{Ar}), 138.9 (C, C_{Ar}), 128.7–127.8 (CH, CH_{Ar}) 80.8 (CH, C-4), 80.6 (CH, C-2), 79.4 (CH, C-3), 77.8 (CH, $CHCl_3$), 74.7 (CH_2, O*C*H$_2$Ph), 72.9 (CH_2, O*C*H$_2$Ph), 72.1 (CH_2, O*C*H$_2$Ph), 61.5 (CH_2, C-5), 55.6 (C, *t*Bu), 45.7 (CH_2, C-1), 22.7 (CH_3, *t*Bu) ppm. IR (neat): 3392 (O−H), 3031 (C−H), 2930 (C−H), 2876 (C−H), 1707, 1454 (C=C), 1043 (C−O), 736 (C−H), 691 (C−H) cm^{-1}. HRMS (ESI): calcd for $C_{30}H_{40}NO_5S$ [M+H+]: 526.2627; found: 526.2632.

Alternatively, compound (S_R)-**10** could be obtained from the reduction of isolated 2,3,4-tri-*O*-benzyl-(S_R)-*N*-*tert*-butanesulfinyl-α/β-L-lyxopyranosylamine (S_R)-**9**.

An oven-dried 5-mL single-necked round-bottomed flask under argon atmosphere, was charged with compound (S_R)-**9** (90 mg, 0.17 mmol), and absolute ethanol (5 mL). $NaBH_4$ (26 mg, 0.69 mmol) was then added, portionwise, and the reaction mixture was stirred at 80 °C for 2 h. The suspension was allowed to cool down to room temperature and the solvent was removed by rotary evaporation. The crude residue was dissolved in EtOAc (20 mL) and the organic phase was washed with sat. brine (20 mL). Next, the aqueous layer was discarded and the organic phase was dried ($MgSO_4$), filtered over a cotton plug and evaporated under reduced pressure. The crude product was purified by column chromatography (SiO_2, PE:EtOAc 1:2 to 1:3) to provide compound (S_R)-**10** in moderate yield (58 mg, 64%).

4.3.10. 2,3,4-Tri-O-benzyl-1,5-dideoxy-1,5-imino-L-lyxitol ***11***.

Compound **11** was synthesized from amino-L-lyxitol (S_R)-**10** according to **G.P. B**. It was isolated as a colorless syrup (18 mg, 44% over two steps) after purification by

chromatography (SiO_2, CH_2Cl_2:MeOH 100:1 to 30/1). R_f 0.4 (SiO_2, CH_2Cl_2:MeOH 15:1). $[\alpha]_D^{20}$ +33.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.43–7.22 (overlapped, 15 H, H_{Ar}), 4.77–4.53 (overlapped, 6 H, 3 × O*C*H_2Ph), 3.79–3.68 (overlapped, 2 H), 3.61 (br d, *J* = 5.3 Hz, 1 H), 3.13 (br dd, *J* = 13.4, 2.8 Hz, 1 H, H-5a or H-1a), 3.05 (dd, *J* = 13.6, 6.0 Hz, 1 H, H-1a or H-5a), 2.64 (br d, *J* = 13.8 Hz, 1 H, H-1b or H-5b), 2.57 (br dd, *J* = 13.6, 7.3 Hz, 1 H, H-5b or H-1b) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 138.9 (C, C_{Ar}), 138.7 (C, C_{Ar}), 138.7 (C, C_{Ar}), 128.4−127.5 (CH, CH_{Ar}), 79.8 (CH), 76.6 (CH), 74.7 (CH), 72.5 (CH_2, OCH_2Ph), 72.4 (CH_2, OCH_2Ph), 71.4 (CH_2, OCH_2Ph), 47.7 (CH_2, C-5), 46.8 (CH_2, C-1) ppm. IR (neat): 3310 (N−H), 3028 (C−H), 2923 (C−H), 2866 (C−H), 1717, 1448 (C=C), 1097 (C−O), 729 (C−H), 694 (C−H) cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{30}NO_3$ $[M+H^+]$ 404.2226; found: 404.2218.

Notes.

The authors declare no conflicts of interest.

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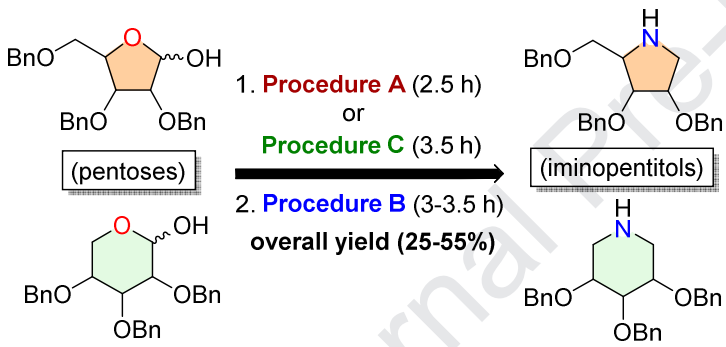
[35] *N-tert*-butanesulfinyl-pentopyranosylamines are much prone to hydrolysis than their furanosyl counterparts. They are typically obtained in moderate yields (ca. 45%) through treatment of protected pentopyranose hemiacetals with compounds of type **3** (2 equiv.), $Ti(OEt)_4$ (1.5 equiv.), MS (4Å) in toluene at 70 °C for 48 h; see ref. [17] and [28,29].

Graphical abstract.



Highlights

- Short, general and convenient method
- Synthesis of dideoxy-1,4- and 1,5-iminopentitols from protected sugar hemiacetals
- Use of a sulfinyl glycosylamine as an aldose imine equivalent
- Moderate to good overall yields (24-55%) obtained through two reaction sequences of 2.5 and 3.5 h

Declaration of interests

☑ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Cyril Nicolas, the 17th of October 2019