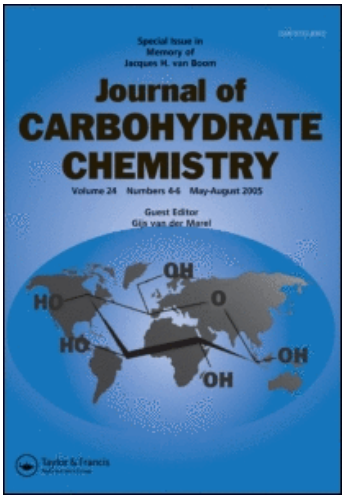

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A NEW STEREOSPECIFIC SYNTHESIS OF 1,2,4-TRIDEOXY-1,4-IMINO-D-*erythro*-PENTITOL

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ABSTRACT

1,2,4-Trideoxy-1,4-imino-D-*erythro*-pentitol [(2*R*,3*S*)-3-hydroxy-2-hydroxymethylpyrrolidine] (**4**) was synthesised from 2,5-di-*O*-tosyl-D-ribono-1,4-lactone in 42 % overall yield. The key steps were deoxygenation at C-2 and a stereospecific inversion of the configuration at C-4. Compound **4** inhibited α-D-glucosidase (K_i = 25 μM) and β-D-glucosidase (K_i = 80 μM).

INTRODUCTION

Five-membered iminosugars (1,4-dideoxy-1,4-iminoalditols) **1** are potent inhibitors of glycosidases. Recently, the immucillins, 1-*C*-substituted iminoribitols (**2**, **3**, Y = OH), have been shown to be very potent inhibitors of purine nucleoside phosphorylase (PNP).[1] In studies of structure-activity relationships, the 2′-deoxy analogues **2** and **3** (Y = H) have been synthesised by deoxygenation of the parent compounds **2** and **3** (Y = OH).[2]

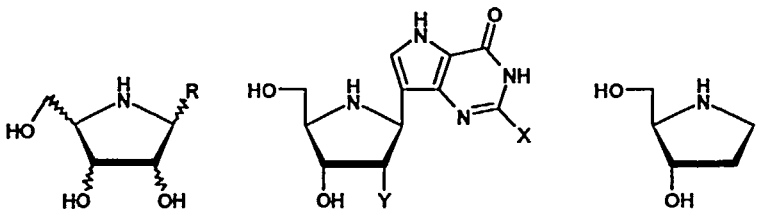


Figure 1

1,2,4-Trideoxy-1,4-imino-D-*erythro*-pentitol (**4**), the iminosugar residue in the 2'-deoxyimmucillins (**2**, **3**, Y = H), is a natural product which has been isolated from the seeds of the legume *Castanospermum australe*.[3] Recent interest in **4** has centered on its incorporation into DNA oligonucleotide analogues (Figure 2). These analogues have been evaluated as inhibitors of *N*-glycosylases,[4] and their interactions with complementary DNA and RNA have been examined.[5]

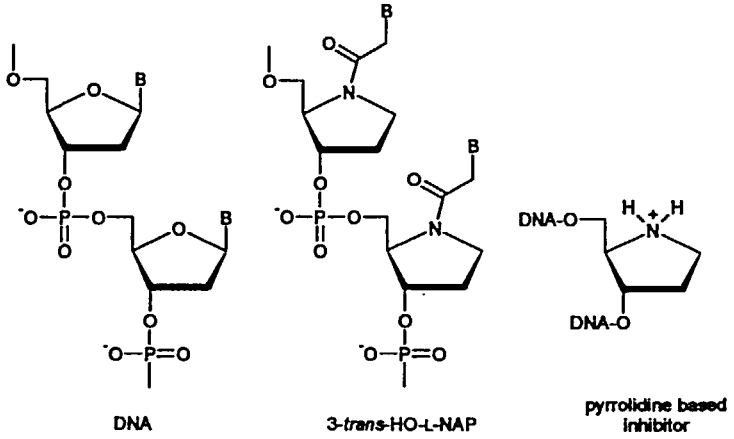


Figure 2

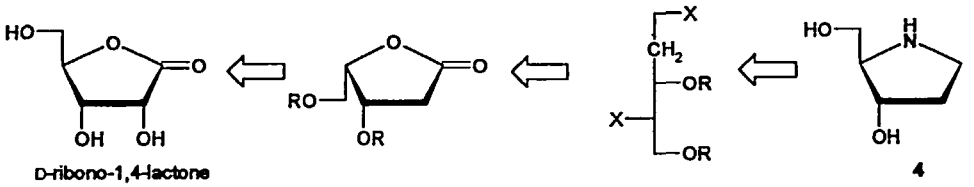
Although several syntheses of 1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol (**4**) have been reported[4,5,6,7,8] none of them are entirely satisfactory. The two most direct syntheses both use D-serine derivatives as starting materials. The more recent one consists of 8 steps from (*R*)-Garner aldehyde (D-serine derivative) and features a chromium(II) chloride-mediated coupling reaction of (*R*)-Garner aldehyde with allyl bromide to give the corresponding homoallylic alcohol.[6] The coupling proceeds with moderate diastereoselectivity forming the required alcohol and an isomer in a 6:4 ratio. After sepa-

ration, the diastereomerically pure homoallylic alcohol is transformed into **4** in an overall yield of 21 % from (*R*)-Garner aldehyde.

The other method [5] was originally reported by Rapoport.[9] It involves 6 steps from D-serine and proceeds by way of *N*-(phenylsulfonyl)-D-serine to **4** in an overall yield of 13 %. The two steps that cause the low yield are (i) coupling of the serine derivative with vinylmagnesium bromide which proceeds in 50 % average yields, and (ii) the lack of diastereoselectivity in the final reduction step, which necessitates separation of **4** from its C-3 isomer (5:2 ratio).

Our continuing interest in developing efficient syntheses of iminosugars,[10] together with an interest in the application of **4** as the core structure in DNA analogues[4,5] (Figure 2), led us to develop a stereospecific synthesis of **4** based on a chiral pool starting material. Access to the 2-deoxy-iminoribitol **4** in a suitably protected form would also be of interest, since it might enable a more direct approach to the 2′-deoxyimmucillins (**2**, **3**, Y = H).

Our approach uses D-ribono-1,4-lactone as the starting material, and involves as the key steps deoxygenation at C-2, stereospecific inversion of the configuration at C-4, reduction of the lactone moiety and activation of the hydroxy groups for ring closure with an amine to form the pyrrolidine **4** (Scheme 1).



Scheme 1

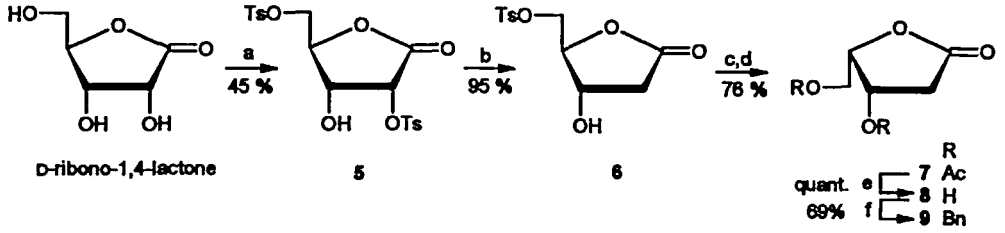
Retrosynthetic analysis of **4**

RESULTS AND DISCUSSION

Selective deoxygenation at C-2 in aldonolactones is easily performed by sequential treatment of either a 2-bromo-2-deoxy- or a 2-tosyloxylactone with hydrazine followed by bromine.[11] Thus, 2,5-di-*O*-tosyl-D-ribono-1,4-lactone (**5**) was the starting material of choice, since it is readily available in 45 % yield as a shelf-stable crystalline solid by selective ditosylation of D-ribono-1,4-lactone.[12] Deoxygenation of **5** gave the 2-deoxylactone **6** in 95 % yield.[13]

Previously we have shown that 5-*O*-mesyl-2,3-di-*O*-isopropylidene-D-ribono-1,4-lactone, by treatment with aqueous base followed by acidification to pH 3, was transformed into the 2,3-di-*O*-isopropylidene-L-lyxono-1,4-lactone.[11,14] Thus a stereoselective inversion at C-4 had taken place. The reaction proceeded by formation of a 4,5-epoxide of an open-chain carboxylate derivative, then intramolecular attack by the carboxylate anion opens the epoxide at C-4 with inversion of the configuration. Using this concept, the 5-*O*-tosylated 2-deoxylactone **6** gave the 2-deoxylactone **8** with the L-*threo*-configuration by treatment with strong base (Scheme 2). In order to remove the salts, the crude product was acetylated under standard conditions to give 3,5-di-*O*-acetyl-2-deoxy-L-*threo*-pentono-1,4-lactone (**7**).

Following the synthetic strategy (Scheme 1), stable protecting groups at C-3 and C-5 were required, and **7** was thus deacetylated and then benzylated. Deacetylation was performed using hydrochloric acid in methanol, benzylation was affected using benzyl trichloroacetimidate[15] in dioxane under slightly acidic conditions,[16] since standard basic conditions would lead to isomerisation and elimination reactions. These steps gave 3,5-di-*O*-benzyl-2-deoxy-L-*threo*-pentono-1,4-lactone (**9**) in 69 % yield after chromatography, which was necessary in order to remove trichloroacetamide. The *threo*-configuration was further established since ^1H and ^{13}C NMR data were different from those published for the *erythro*-isomer.[16] Thus, $J_{3,4}$ was 5.9 Hz for compound **9** while $J_{3,4}$ was reported to be 2 Hz for the *erythro*-isomer.



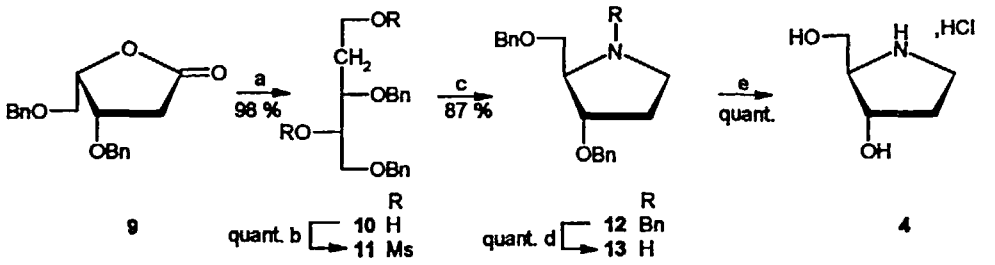
Scheme 2

a) 2.3 eq TsCl, pyridine/acetone, 0 °C; b) 3 eq 80 % aq hydrazine, Br_2, dioxane, 0 °C-rt; c) i: 3 eq KOH, H_2O, ii: conc HCl; d) Ac_2O, cat $HClO_4$, rt; e) 2 vol % AcCl in MeOH, rt; f) 5 eq benzyl trichloroacetimidate, CF_3SO_3H (pH 3), dioxane, rt.

Reduction of the benzylated lactone **9** using $LiAlH_4$ in THF (Scheme 3) gave the corresponding diol **10** (98 %) which was converted directly to the dimesylate **11** in quan-

titative yield. The mesylation was performed by slow addition of **10** to the solution of MsCl in pyridine to avoid possible intramolecular ring closure of the intermediate monomesylates. Cyclisation of the dimesylate **11** with benzylamine in DMF gave the protected pyrrolidine **12** in 87 % yield. Selective *N*-debenzylation could be performed by hydrogenation of **12** in MeOH in the presence of catalytic amounts of $Pd(OH)_2$ and 25 % aq NH_3 to give **13** in quantitative yield.

Finally, complete debenzylation of **12** by hydrogenation in the presence of 10 % palladium on charcoal gave the natural product 1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol (**4**).



Scheme 3

a) $LiAlH_4$, THF, 0 °C - rt; b) 3 eq MsCl, pyridine; c) $BnNH_2$, DMF, 50-60 °C; d) 10 % $Pd(OH)_2$, H_2, cat 25 % aq NH_3, MeOH, rt; e) 10 % Pd/C, H_2, cat HCl, EtOH, rt.

1,2,4-Trideoxy-1,4-imino-D-*erythro*-pentitol (**4**) was evaluated as an inhibitor of a set of commercially available glycosidases. It showed activity towards α- and β-glucosidases, only. The α-glucosidase (yeast) was inhibited with a K_i of 25 μM and β-glucosidase (almonds) with a K_i of 80 μM. Compared to the two 1,4-dideoxy-1,4-imino-pentitols having a hydroxy group at C-2, the inhibition was in the same range for α-glucosidase as for the D-*ribo*-isomer (K_i of 23 μM)[17] while the 1,4-dideoxy-1,4-imino-D-arabinitol showed an IC_{50} of 0.18 μM.[18] The 2-deoxy-1,4-iminopentitol **4** was a stronger inhibitor of the β-glucosidase than the D-*arabino*-analogue which had an IC_{50} value of 200 μM.[18]

CONCLUSION

In this paper, the first stereospecific synthesis of 1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol (**4**) has been described. From the readily available 2,5-di-*O*-tosyl-D-

ribono-1,4-lactone, compound **4** was obtained in 42 % overall yield. All the reactions were easily performed on a multi-gram scale, which makes this route an attractive alternative to the existing methods.

Further work on the applications of 1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol is in progress.

EXPERIMENTAL

General methods. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz, referenced to the solvent peak ($CDCl_3$: δ 7.27 for ^{1}H, 77.4 for ^{13}C; D_2O: δ 4.63 for ^{1}H) or dioxane (δ = 67.4 for ^{13}C) as internal standard. NMR spectra were assigned using HH and CH correlated spectra. Specific rotations were measured on a Perkin-Elmer 241 polarimeter. TLC was performed on Merck 60 F254 precoated plates. Flash column chromatography was performed with silica gel 60 (Merck, 40-63 μm). All solvents were distilled before use. All evaporations were performed in vacuo below 40 °C.

Inhibition analysis. α-D-Glucosidase from Bakers yeast, β-D-glucosidase from almonds, α-D-galactosidase from green coffee beans, β-D-galactosidase from *Eschericia coli*, α-D-mannosidase from jack bean, β-D-mannosidase from snail and α-L-fucosidase from bovine kidney were purchased from Sigma. K_i determination were run at 25 °C for the α-glycosidases and at 35 °C for the β-glycosidases using the corresponding *p*-nitrophenyl α- or β-glycosides at various concentrations, ranging from 3×10^{-3} to 7×10^{-4} M at pH 6.8 (0.12 M phosphate buffer). For the inhibition studies, inhibitors were incorporated in the buffer to give a final concentration of 2×10^{-5} M. Enzymes were incorporated in the buffer to give a final concentration of 0.2 units/mL. Dissociation constants for inhibition were calculated from a Hanes-plot ([*S*]/*v* against [*S*]) from the rates of substrate hydrolysis in the absence and presence of inhibitor.

2-Deoxy-5-*O*-tosyl-D-*erythro*-pentono-1,4-lactone (6). Ditosyl lactone **5**[12] (10.0 g, 21.9 mmol) was dissolved in dioxane (100 mL) and cooled to 0 °C. NH_2NH_2 (80 % aq 6.4 mL) was added and stirring was continued for 30 min at rt. After cooling to 0 °C, Br_2 (ca 8 mL) was added dropwise until N_2 evolution ceased. The reaction mixture was concentrated. The residue was dissolved in H_2O (50 mL), neutralised with sat $NaHCO_3$ and

extracted with $CHCl_3$ (4 × 40 mL). The extract was dried ($NaSO_4$) and concentrated to give **6** as a colourless crystalline residue (6.0 g, 95 %); mp 53-55 °C, $[\alpha]_D^{20}$ +32.1° (*c* 3.2, CH_2Cl_2). Lit[19]: mp 55-57 °C, $[\alpha]_D^{20}$ +39.6 ° (*c* 5.3, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.45 (3H, s, CH_3), 2.51 (1H, dd, *J* = 18.0, 3.0, H-2), 2.87 (1H, dd, *J* = 18.0, 7.0, H-2'), 3.23 (1H, br. s, OH), 4.18 (1H, dd, *J* = 11.0, 3.0, H-5), 4.26 (1H, dd, *J* = 11.0, 3.0, H-5'), 4.55 (2H, m, H-3, H-4), 7.47 (2H, arom. H), 7.75 (2H, arom. H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.3 (CH_3), 37.3 (C-2), 67.9, 68.1 (C-3, C-5), 84.0 (C-4), 127.5, 129.9, 131.3, 145.4 (arom. C), 175.2 (C-1).

3,5-Di-*O*-acetyl-2-deoxy-L-*threo*-pentono-1,4-lactone (7). Tosyl lactone **6** (10.57 g, 36.9 mmol) was dissolved in H_2O (200 mL) containing KOH (6.2 g, 110.8 mmol) and stirred overnight at rt. The reaction mixture was acidified with conc HCl to pH 1, concentrated and co-concentrated with toluene to a yellow residue of 2-deoxy-L-*threo*-pentono-1,4-lactone (**8**) mixed with salts. The crude product was acetylated using Ac_2O (120 mL) and 5 drops of $HClO_4$ for 3 h at rt. The reaction was quenched with ice (200 mL), stirred for 1.5 h and extracted with CH_2Cl_2 (3 × 100 mL). The organic phase was washed with H_2O (3 × 100 mL), sat $NaHCO_3$ (100 mL), dried ($NaSO_4$), filtered and concentrated to a yellow oil of sufficient purity for further reaction (6.07 g, 76 % from **6**). An analytical sample (colourless oil) was obtained by column chromatography (EtOAc/pentane 2:1, R_f = 0.33); $[\alpha]_D^{25}$ –33.8° (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.08 (3H, s, CH_3), 2.12 (3H, s, CH_3), 2.64 (1H, dd, *J* = 18.3, 2.3, H-2), 2.93 (1H, dd, *J* = 18.3, 6.6, H-2'), 4.32 (1H, dd, *J* = 11.5, 2.0, H-5), 4.37 (1H, d, *J* = 11.5, H-5'), 4.79 (1H, m, H-4), 5.56 (1H, ddd, *J* = 6.6, 4.9, 2.3, H-3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.0 (CH_3), 36.3 (C-2), 61.8 (C-5), 69.8 (C-3), 82.4 (C-4), 170.2, 170.7 (C=O), 173.5 (C-1).

Anal. Calcd for $C_9H_{12}O_6$ (216.19): C, 50.00; H 5.59. Found: C, 49.70; H, 5.48.

2-Deoxy-L-*threo*-pentono-1,4-lactone (8). The lactone **7** (5.13 g, 23.7 mmol) was dissolved in 2 vol % AcCl in MeOH (150 mL) and stirred overnight at rt. The solution was concentrated and co-concentrated with toluene to give **8** as colourless oil in quantitative yield. ^1H NMR (D_2O, 300 MHz): δ 2.45 (1H, dd, *J* = 18.0, 1.5, H-2), 2.94 (1H, dd, *J* = 18.0, 6.0, H-2'), 3.80 (2H, m, H-5, H-5'), 4.56 (2H, m, H-3, H-4). ^{13}C NMR (D_2O, 75 MHz): δ 39.1 (C-2), 60.1 (C-5), 68.2 (C-3), 86.1 (C-4), 179.9 (C-1).

3,5-Di-*O*-benzyl-2-deoxy-L-*threo*-pentono-1,4-lactone (9). Lactone **8** (3.39 g, 17 mmol) was dissolved in anhydrous dioxane (80 mL) under argon. Benzyl-2,2,2-trichloroacetimidate[15,16] (22.0 mL, 119 mmol) and CF_3SO_3H (0.4 mL, pH 2.5-3) were added, and the solution was stirred at rt overnight. The solution was concentrated, and the residue was partitioned between H_2O (100 mL) and CH_2Cl_2 (100 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases were washed with water, dried ($NaSO_4$) and concentrated to a crystalline residue, which was dissolved in CH_2Cl_2 (50 mL) and pentane (50 mL) and cooled to 0 °C to crystallise the trichloroacetimidate. Filtration, washing of the residue with CH_2Cl_2/pentane 1:1 followed by concentration of the combined filtrates gave a residue (25 g), which was further purified by column chromatography (d = 6 cm, h = 18 cm, EtOAc/pentane 1:2, R_f = 0.24). This gave **9** as an oil (3.64 g, 69 % yield). Further chromatography afforded an analytical sample; $[\alpha]_{436\,nm}^{27}$ –2.0 °, $[\alpha]_{365\,nm}^{27}$ –7.0 ° (*c* 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.61 (1H, dd, *J* = 17.3, 5.9, H-2), 2.70 (1H, dd, *J* = 17.3, 2.9, H-2'), 3.84 (1H, dd, *J* = 10.7, 5.1, H-5), 3.87 (1H, dd, *J* = 10.7, 5.1, H-5'), 4.31 (1H, ddd, *J* = 5.9, 5.1, 2.9, H-3), 4.43, 4.54, 4.57, 4.59 (4H, 4 × d, *J* = 12.0, C$\underline{H}_2$Ph), 4.61 (1H, q, *J* = 5.1, H-4), 7.22-7.36 (10H, arom. H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 35.9 (C-2), 68.1 (C-5), 72.1, 74.1 (2 × $\underline{C}H_2$Ph), 74.9 (C-3), 82.3 (C-4), 128.0-138.2 (arom. C), 175.1 (C-1).

Anal. Calcd for $C_{19}H_{20}O_4$ (312.36): C, 73.06; H, 6.45. Found: C, 72.97; H, 6.38.

3,5-Di-*O*-benzyl-2-deoxy-L-*threo*-pentitol (10). The dibenzyloxylactone **9** (0.60 g, 1.92 mmol) was dissolved in THF (15 mL, anal grade) and cooled to 0 °C. $LiAlH_4$ (300 mg, 7.9 mmol) was added in one portion and stirring was continued at 0 °C for 15 min and at rt for 1 h. The reaction was quenched by adding H_2O (300 µL), 15 % aq NaOH (300 µL) and H_2O (900 µL), successively. The mixture was filtered through celite, and the residue washed with EtOAc (3 × 30 mL). Concentration afforded **10** as colourless oil (0.61 g, 98 % yield). Column chromatography (EtOAc, R_f = 0.43) afforded an analytical sample. $[\alpha]_D^{24}$ +3.50° (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.81 (1H, m, H-2), 1.93 (1H, m, H-2'), 3.56 (1H, dd, *J* = 10.0, 1.5, H-5), 3.59 (1H, d, *J* = 10.0, H-5'), 3.72, 3.77 (3H, m, H-1, H-1', H-4), 3.91 (1H, m, H-3), 4.54 (2H, 2 × d, *J* = 12.0, C$\underline{H}_2$Ph), 4.56 (1H, d, *J* = 11.5, CH_2Ph), 4.63 (1H, d, *J* = 11.5, C$\underline{H}_2$Ph), 7.20-7.40 (10H, arom. H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 33.7 (C-2), 59.7 (C-1), 71.5 (CH_2), 72.3 (C-3), 73.1 (CH_2), 73.9 (CH_2), 77.4 (C-4), 126.5-138.4 (arom. C).

Anal. Calcd for $C_{19}H_{24}O_4$ (316.40): C, 72.13; H, 7.65. Found: C, 71.81; H, 7.44.

3,5-Di-*O*-benzyl-2-deoxy-1,4-di-*O*-mesyl-L-*threo*-pentitol (11). To a solution of MsCl (2.20 mL, 28.44 mmol) in pyridine (75 mL) was added dropwise the diol **10** (2.99 g, 9.48 mmol) in pyridine (36 mL) during 30 min at 0 °C. Stirring was continued at 0 °C for 50 min and at rt for further 40 min. After concentration the residue was dissolved in CH_2Cl_2 (100 mL), washed with H_2O (3 × 50 mL), dried ($MgSO_4$), filtered and concentrated to give a light yellow oil in quantitative yield. The crude product **11** was sufficiently pure for further synthesis. Purification by column chromatography (EtOAc/pentane 1:1, R_f = 0.42) afforded an analytical sample **11** as a colourless oil; $[\alpha]_D^{25}$ –27.4° (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.91 (1H, m, H-2), 2.08 (1H, m, H-2'), 2.93 (3H, Ms), 3.01 (3H, Ms), 3.73 (2H, dd, *J* = 10.5, 5.0, H-5, H-5'), 3.89 (1H, m, H-3), 4.30 (2H, m, H-1, H-1'), 4.52 (2H, 2 × d, *J* = 11.7, C$\underline{H}_2$Ph), 4.61 (2H, 2 × d, *J* = 11.3, C$\underline{H}_2$Ph), 4.86 (1H, q, *J* = 5.0, H-4), 7.23-7.40 (10H, arom. H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.4 (C-2), 37.8, 38.9 (2 × CH_3), 66.4 (C-1), 68.9 (C-5), 73.7, 74.0 (2 × $\underline{C}H_2$Ph), 74.6 (C-3), 81.8 (C-4), 128.3-137.7 (arom. C).

Anal. Calcd for $C_{21}H_{28}O_8S_2$ (472.57): C, 53.37, H, 5.97, S, 13.57. Found: C, 53.94; H, 6.25; S, 13.33.

***N*-Benzyl-3,5-di-*O*-benzyl-1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol (12).** To dimesylate **11** (0.57 g, 1.21 mmol) in anhydrous DMF (10 mL) was added $BnNH_2$ (6 mL). The solution was stirred at 50-60 °C for 16 h. Concentration afforded an oil, which was purified by column chromatography (EtOAc/pentane 1:3, R_f = 0.34) to give a colourless oil (0.39 g, 87 %); $[\alpha]_D^{25}$ –23.3° (*c* 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.85 (2H, m, H-2, H-2'), 2.55 (1H, dd, *J* = 17.8, 8.6, H-1), 2.88 (2H, m, H-1', H-4), 3.35 (1H, dd, *J* = 9.8, 6.8, H-5), 3.45 (1H, dd, *J* = 9.8, 4.7, H-5'), 3.54 (1H, d, *J* = 13.0, NC$\underline{H}_2$Ph), 3.93 (1H, m, H-3), 4.04 (1H, d, *J* = 13.0, NC$\underline{H}_2$Ph), 4.50, 4.51 (4H, OC$\underline{H}_2$Ph), 7.2-7.4 (15H, arom. H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.0 (C-2), 52.7 (C-1), 60.2 (NCH_2Ph), 70.3 (C-4), 70.9 (OCH_2Ph), 72.0 (C-5), 73.7 (OCH_2Ph), 82.4 (C-3), 126.5-139.9 (arom. C).

Anal. Calcd for $C_{26}H_{29}O_2N$ (387.52): C, 80.59; H, 7.54; N, 3.61. Found: C, 80.59; H, 7.58; N, 3.59.

3,5-Di-*O*-benzyl-1,2,4-trideoxy-1,4-imino-D-*erythro*-pentitol (13). The *N*-benzylamine **12** (2.65 g, 7.06 mmol) was dissolved in MeOH (70 mL) and 25 % aq NH_3 (0.7 mL) and 10 % $Pd(OH)_2$ (280 mg) were added. The mixture was hydrogenated at rt

and 1 atm for 2 days. The solution was filtered through celite, the residue washed with MeOH and the combined filtrate concentrated to give **13** as a colourless oil in quantitative yield (sufficiently pure for further synthesis). Purification by column chromatography (EtOAc/ MeOH 9:1, 1 vol % NEt_3) afforded an analytical sample of amine **13**; $[\alpha]_D^{25}$ +11.7° (*c* 0.8, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.85 (1H, s, NH), 1.88 (2H, m, H-2, H-2'), 3.02 (2H, m, H-1, H-1'), 3.31 (1H, dt, *J* = 5.5, 3.8, H-4), 3.47 (2H, 2 × dd, *J* = 10.7, 5.5, H-5, H-5'), 3.91 (1H, ddd, *J* = 5.6, 3.8, 3.8, H-3), 7.2-7.4 (10H, arom. H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.3 (C-2), 44.2 (C-1), 63.0 (C-4), 70.1 ($\underline{C}H_2Ph$), 70.4 (C-5), 72.2 ($\underline{C}H_2Ph$), 80.3 (C-3), 126.5-137.4 (arom. C).

Anal. Calcd for $C_{19}H_{23}O_2N$ (297.40): C, 76.74; H, 7.79; N, 4.71. Found: C, 76.87; H, 7.68; N, 4.42.

1,2,4-Trideoxy-1,4-imino-D-*erythro*-pentitol (4). Amine **13** (110 mg, 0.39 mmol) was dissolved in EtOH (5 mL) and Pd/C (50 mg) and 3 drops of conc HCl were added. The mixture was hydrogenated at rt and 1 atm for 24 hours. The solution was filtered through celite, the residue washed with EtOH and the combined filtrate concentrated to give the hydrochloride salt of **4** as oil in quantitative yield; $[\alpha]_D^{25}$ +46.2° (*c* 0.49, H_2O) (ref[3]: $[\alpha]_D^{20}$ +46.5 (H_2O)). ^1H NMR (D_2O, 500 MHz): δ 1.99 (1H, dddd, *J* = 17.1, 7.3, 5.9, 3.8, H-2), 2.22 (1H, dddd, *J* = 17.1, 8.5, 8.5, 5.9, H-2'), 3.42 (2H, m, H-1, H-1'), 3.56 (1H, dt, *J* = 7.3, 4.3, H-4), 3.68 (1H, dd, *J* = 12.4, 7.3, H-5), 3.86 (1H, dd, *J* = 12.4, 4.3, H-5'), 4.33 (1H, dt, *J* = 5.9, 4.3). ^{13}C NMR (D_2O, 75 MHz): δ 32.7 (C-2), 44.6 (C-1), 59.2 (C-4), 67.9 (C-5), 71.6 (C-3). The NMR data were in accordance with literature data.[20]

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