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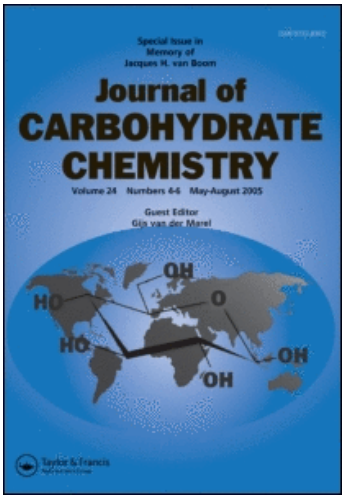

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Hydroxylated Piperidines: Synthesis of 1,5-Alkylimino-1,5-Dideoxy Derivatives of Xylitol, d- and l-Arabinitol, and Ribitol

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HYDROXYLATED PIPERIDINES : SYNTHESIS OF 1,5-ALKYLIMINO-1,5-DIDEOXY DERIVATIVES OF XYLITOL, D- AND L-ARABINITOL, AND RIBITOL

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ABSTRACT

Direct routes are reported for the synthesis of *N*-propyl, *N*-butyl- and *N*-pentyl-1,5-dideoxy-1,5-iminoxylitol (**7a,b,c**), the analogous derivatives (**8a,b,c**, and **9a,b,c**) of 1,5-dideoxy-1,5-imino-D- and -L-arabinitol, and of *N*-propyl-1,5-dideoxy-1,5-iminoribitol (**10**).

INTRODUCTION

The observation that hydroxylated pyrrolidines, piperidines, pyrrolizidines and indolizidines can display powerful and specific inhibitory activity against glycosidases[1] has led to much interest in the synthesis and biological evaluation of such compounds, heightened by the awareness that the inhibition of glycosidases can have potential application in a number of areas of medicinal chemistry, perhaps most notably in the area of anti-HIV chemotherapy.[2]

Amongst the piperidine subgroup, it is well established that deoxynojirimycin (DNJ, **1a**) is an effective inhibitor of glucosidases,[3] including α-glucosidases I and II of glycoprotein processing,[4] and can be used for the purification of α-glucosidase I by affinity chromatography.[5] The *N*-butyl analogue of deoxynojirimycin (butyl-DNJ, **1b**) has attracted particular interest due to its ability to reduce dramatically the cytopathic

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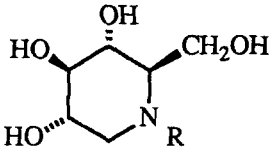
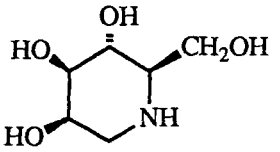
effect of HIV and the yield of infectious viral particles.[2] The epimeric 1,5-dideoxy-1,5-imino-D-mannitol (DMJ, **2**), is an effective mannosidase inhibitor,[6] including activity against α-mannosidase I of glycoprotein processing.[7] Similarly, the D-*galacto*-configured isomer, deoxygalactojirimycin (**3**) is an inhibitor of α-[8] and β-galactosidases.[9]



1a, R = H
1b, R = *n*-C_4H_9



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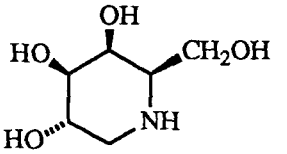
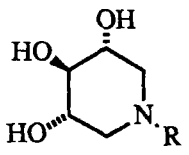
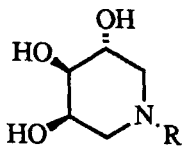


3

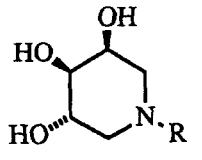
There are reports that the presence of a hydroxymethyl group is not always essential for binding of a glycoside to a glycosidase,[10] and the inhibition of α-L-fucosidase by DMJ (**2**)[11] also supports this contention. Recently, Ganem and coworkers have reported syntheses of the iminopentitols **4, 5** and **6**, truncated analogues of **1a**, **2**, and **3**, respectively, by routes which involved Bernet-Vasella openings of appropriate hexose derivatives, and ring closure after excision of C-6. It was found that **4** inhibited sweet almond β-glucosidase, whilst **5** inhibited jackbean α-mannosidase.[12] We now report an alternative direct route to compounds of this type, which we have employed to prepare the 1,5-dideoxy-1,5-iminopentitols **7a-c**, **8a-c**, and **9a-c**, the structures of which incorporate alkyl chains bridging in length that which seems to be optimal for anti-HIV activity in butyl-DNJ (**1b**). We have also used a similar method to prepare the *N*-alkyl-1,5-dideoxy-1,5-iminoribitol **10**.



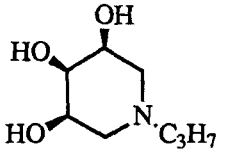
4, R = H



5, R = H



6, R = H



10

7a, R = *n*-C_3H_7
7b, R = *n*-C_4H_9
7c, R = *n*-C_5H_{11}

8a, R = *n*-C_3H_7
8b, R = *n*-C_4H_9
8c, R = *n*-C_5H_{11}

9a, R = *n*-C_3H_7
9b, R = *n*-C_4H_9
9c, R = *n*-C_5H_{11}

RESULTS AND DISCUSSION

The iminoxylitol derivatives **7a-c** could be prepared from xylitol itself, as indicated in Scheme 1. Xylitol was converted into its 2,3,4-tri-*O*-benzyl ether (**11**) in three high-

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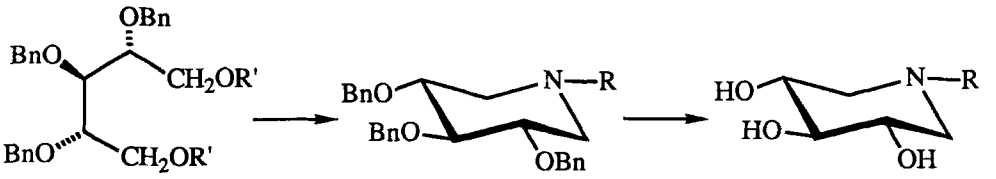
yielding steps, essentially as described by Barker and coworkers.[13] The diol **11** was converted (80%) into its ditosylate **12**,[13] which on warming with the appropriate amine at 40 °C for 2 days gave after chromatography the *N*-alkyl-1,5-dideoxy-1,5-imino-xylitols **13a, 13b** and **13c** in high yield. The structures of these compounds were clear from spectroscopic data, with both ^1H and ^{13}C NMR spectra showing the symmetry of the compounds. Catalytic hydrogenation of each of **13a, 13b,** and **13c** gave *N*-propyl-, *N*-butyl-, and *N*-pentyl-1,5-dideoxy-1,5-iminoxylitol (**7a, 7b** and **7c**), each of which could be isolated as crystalline solids. A similar reaction of **12** with benzylamine gave the *N*-benzyl derivative **13d**, a potential precursor of the parent compound 1,5-dideoxy-1,5-iminoxylitol **4**.[12]



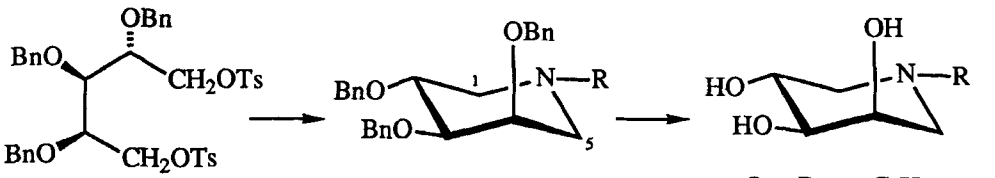
11, R' = H
12, R' = Ts

13a, R = *n*-C_3H_7
13b, R = *n*-C_4H_9
13c, R = *n*-C_5H_{11}
13d, R = Bn

7a, R = *n*-C_3H_7
7b, R = *n*-C_4H_9
7c, R = *n*-C_5H_{11}

Scheme 1

The isomeric series of compounds **8a, b, c** were prepared in an analogous manner (Scheme 2) from 1,5-di-*O*-toluene-*p*-sulfonyl-2,3,4-tri-*O*-benzyl-D-arabinitol (**14**),[13] prepared in four high yielding steps from D-arabinitol. Treatment of **14** with *n*-propylamine, *n*-butylamine and *n*-pentylamine gave the protected iminoalditols **15a, b, c** in isolated yields of ~80%. These could be deprotected to give the series of *N*-alkyl-1,5-dideoxy-1,5-imino-D-arabinols **8a, 8b** and **8c**, related to deoxymannojirimycin. **2**. The



14

15a, R = *n*-C_3H_7
15b, R = *n*-C_4H_9
15c, R = *n*-C_5H_{11}

8a, R = *n*-C_3H_7
8b, R = *n*-C_4H_9
8c, R = *n*-C_5H_{11}

Scheme 2

structures of compounds **15** and **8** were fully supported by spectroscopic data which indicated that they adopted the chair conformation as shown.

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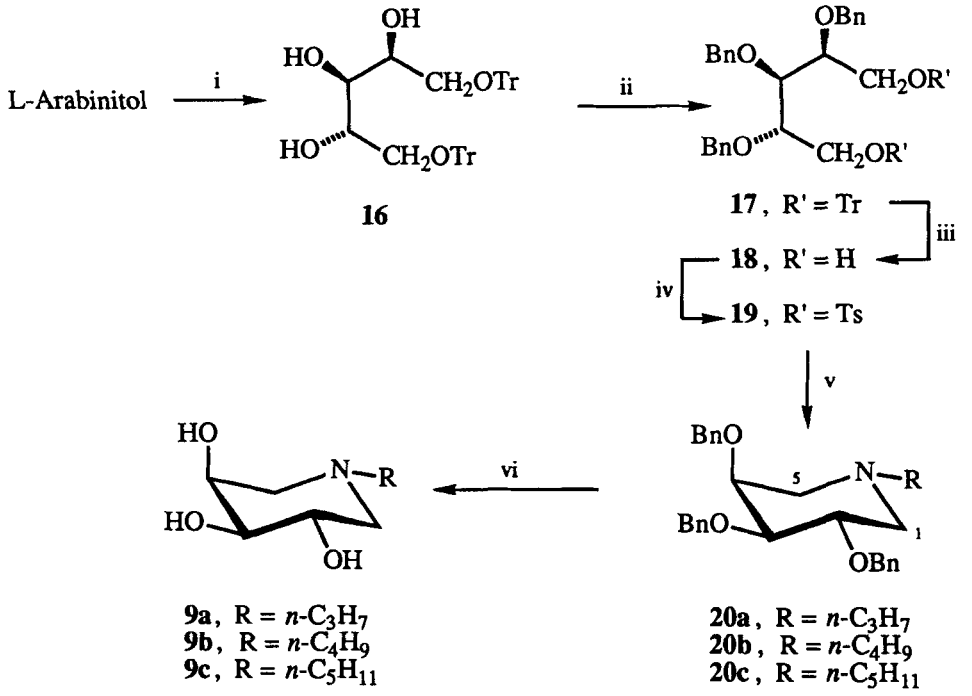
The enantiomeric compounds **9a-c** were prepared similarly from L-arabinitol (Scheme 3), but with the introduction of some modifications to Barker's chemistry in the early stages. Thus L-arabinitol, on treatment with trityl chloride, triethylamine and *p*-dimethylaminopyridine (DMAP) in dimethylformamide (DMF) gave the 1,5-di-*O*-trityl ether **16**, isolated in 75% yield as a crystalline ethanol solvate. This was converted (excess NaH, benzyl bromide, DMF) into the crystalline fully-protected derivative **17** (70%), which was hydrolysed to **18** and converted to ditosylate **19** as described for the enantiomeric series.[13] Ditosylate **19** then gave rise to the piperidines **20a-c** on reaction with the appropriate amines, which were deprotected as before to give triols **9a-c**, which can be regarded as analogues of deoxygalactojirimycin (**3**) lacking the hydroxymethyl group.



Scheme 3: i, TrCl, DMAP, Et_3N, DMF; ii, NaH, BnBr, DMF; iii, dil. HCl, dioxan, Δ; iv, TsCl, C_5H_5N, CH_2Cl_2; v, RNH_2, 40 °C; vi, H_2, Pd/C, HOAc.

We have also carried out one example of a similar sequence commencing from ribitol (Scheme 4). 1,5-Di-*O*-toluene-*p*-sulfonyl-2,3,4-tri-*O*-benzyl-ribitol **21**[13,14] was treated with propylamine to give the piperidine **22** as a low-melting solid, which could be hydrogenated to give the triol **10**.

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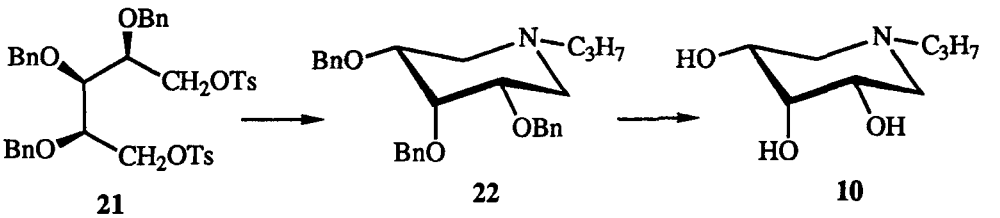

Scheme 4

None of compounds **7a-c, 8a-c, 9a-c** or **10** showed significant activity in the inhibition of replication of HIV-1. Evaluation against glycosidases will be reported elsewhere.

EXPERIMENTAL

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NMR spectra were recorded on a Bruker WP200SY instrument at 200 and 50 MHz for ^1H and ^{13}C spectra, respectively, and using deuteriochloroform as solvent unless otherwise stated. *J* values are given in Hz. Mass spectrometry was performed using updated M.S.9 and VG ZAB-E high resolution instruments. Specific rotations were measured at room temperature using a Bendix-NPL 143D automatic polarimeter (path length 1 cm). Melting points were determined in capilliaries and are uncorrected. Adsorbtion chromatography was carried out using Kieselgel H type 60 (Merck). Light petroleum refers to material of bp 40-60 °C. Organic extracts were dried with anhydrous sodium sulfate.

1,5-Di-*O*-trityl-L-arabinitol (16). A solution of L-arabinitol (4.8 g), trityl chloride (19.35 g), triethylamine (15.5 mL), and DMAP (0.31 g) in DMF (110 mL) was stirred at room temperature for 16 h. The mixture was partitioned between ice-water (200 mL) and dichloromethane (3 x 200 mL). The washed, dried organic layers were concentrated and the residue was chromatographed on silica with light petroleum-diethyl ether (7:1 to 0:1) as eluent. The product fractions were concentrated and the residue crystallized from ethanol to give the di-*O*-trityl ether **16** (14.45 g, 67%) as its ethanol solvate, mp 68-70 °C, $[\alpha]_D$ +5.3° (*c* 1.1, $CHCl_3$); ^1H NMR δ 1.2 (3H, t, *Me*CH_2OH), 2.6-2.8 (3H, 3d, exchangeable, OH), 3.2-3.4 (4H, m, 1-H_2, 5-H_2), 3.60 (1H, dt, *J* 6.7, 1.6, becomes dd, *J* 6.7, 1.6 on D_2O shake, 3-H), 3.72 (2H, q, Me*C*H_2OH), 3.85 (1H, m), 3.95 (1H, m), 7.2-7.5 (30H, m, CPh_3); ^{13}C NMR δ 18.2 and 58.2 (EtOH), 64.9 and 65.8 (C-1, C-5), 69.4, 71.5 and 71.9 (C-2, -3,-4), 86.98 and 87.04 (*C*Ph_3).

Anal. Calcd for $C_{43}H_{40}O_5.C_2H_5OH$: C, 79.14; H, 6.80. Found: C ,79.0; H, 7.0.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-benzyl-L-arabinitol (17). To a stirred solution of ditrityl ether **16** (14.45 g) in DMF) (100 mL) at 0°C was added sodium hydride (50%, 7.5 g) in portions over 20 min, followed by benzyl bromide (9 mL), added over 20 min. After a further 30 min, ethanol was added dropwise to destroy excess NaH, and the mixture was then partitioned between ice-water (200 mL) and ether (3 x 200 mL). The organic extracts were washed with aqueous urea (10%, 200 mL) and water, dried and concentrated. The resultant pale yellow solid was recrystallized from acetone-ethanol (1:1) to give **17** (14.3 g, 74%) as colourless crystals, mp 142-145 °C, $[\alpha]_D$ + 7.4° (*c* 0.9, $CHCl_3$) [Lit.[13] for the enantiomer, mp 146-147 °C, $[\alpha]_D$ - 5.1° (*c* 1.95, toluene)].

2,3,4-Tri-*O*-benzyl-L-arabinitol (18). A solution of the di-*O*-trityl ether **17** (10.7 g) in dioxan (200 mL) and aqueous HCl (0.1 M, 5.4 mL) was heated under reflux for 24 h, cooled, neutralized with aqueous NaOH (1M, 0.54 mL), and concentrated. The residue was co-concentrated with dioxan, and then extracted with dichloromethane (2 x 100 mL). The dried organic extracts were concentrated and the residue was chromatographed on silica eluting firstly with toluene (to remove triphenylmethanol) and then with toluene-ethyl acetate (4:1). Solvent evaporation and recrystallization from ether gave diol **18** (3.36 g, 67%), mp 76-78 °C, $[\alpha]_D$ + 18.0° (*c* 1.3, $CHCl_3$) [Lit.[13] for the enantiomer, mp 76-77 °C, $[\alpha]_D$ -14.6° (*c* 2.9, DMSO)]; ^{1}H NMR δ 2.17 and 2.33 (each 1H, t, exchangeable, OH), 3.65-3.9 (7H, m), 4.4-4.8 (6H, 3 AB dd, OC*H*$_2$Ph), 7.3 (15H, m, OCH$_2$*Ph*); ^{13}C NMR δ 60.7 and 61.3 (C-1, C-5), 71.9, 72.6 and 74.2 (O*C*H$_2$Ph), 78.9, 79.2 and 79.4 (C-2,-3,-4).

1,5-Di-*O*-toluene-*p*-sulfonyl-2,3,4-tri-*O*-benzyl-L-arabinitol (19). The diol **18** (3.36 g) was treated as described for the enantiomer[13] to give ditosylate **19** (4.1 g, 71%), mp 98-100 °C (Lit[13] for D-isomer, mp 97-99 °C); ^{1}H NMR δ 2.38 and 2.40 (each 3H, s, Me), 3.64 (1H, dd, 3-H), 3.7-3.9 (2H, m, 2-,4-H), 4.05-4.6 (10H, m), 7.0-7.3 (19H, m), 7.66 and 7.72 (each 2H, d); ^{13}C NMR δ 21.4 (Ar *Me* x2), 68.9 and 69.4 (C-1, C-5), 72.3, 73.2 and 73.9 (O*C*H$_2$Ph), 76.5, 76.9 and 77.1 (C-2,-3,-4).

General procedure for cyclization to form piperidines. The ditosylate dissolved in excess amine (~ 10 mL per g ditosylate) was kept in a thermostatted water bath at 40 °C for 48 h. The solution was diluted with ethyl acetate, washed with brine and water, dried and concentrated. The residue was chromatographed on neutral alumina, eluting with light petroleum-ether (4:1 to 1:1). The following compounds were prepared by this procedure:

***N*-Propyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-iminoxylitol (13a):** [0.258 g, 86%, from ditosylate **12** (0.49 g) in propylamine (8 mL)], oil; ^{1}H NMR δ 0.9 (3H, t, *J* 7.3, CH_3), 1.47 (2H, m, $CH_3C\mathit{H}_2$), 1.96 (2H, t, *J* 10.7, 1/5-H_{ax}), 2.35 (2H, m, N-C*H*$_2$Et), 3.09 (2H, dd, *J* 11.0, 4.0, 1/5-H_{eq}), 3.45 (1H, t, *J* 8.8, 3-H), 3.60 (2H, dt, 2/4-H), 4.72

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(4H, AB dd, *J* 11.5, OC*H*$_2$Ph), 4.92 (2H, s, OC*H*$_2$Ph), 7.3-7.4 (15H, m); ^{13}C NMR δ 11.7 (Me), 20.1 (CH_2), 56.3 (C-1/5), 59.7 (N-*C*H$_2$Et), 73.0 and 75.3 (O*C*H$_2$Ph), 78.9 (C-2/4), 86.5 (C-3); *m/z* 445 (M^+), 444 (M^+-H), 416 (M^+-Et) [Found : MH^+(ammonia CI) 446.2695. Calcd for $C_{29}H_{36}NO_3$ 446.2693].

***N*-Butyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-iminoxylitol (13b):** [0.31 g, 81%, from ditosylate **12** (0.61 g) in *n*-butylamine (7 mL)] oil; ^{1}H NMR δ 0.9 (3H, t), 1.2-1.5 (4H, m), 2.39 (2H, m, NC*H*$_2$-Pr), other signals as for **13a**; ^{13}C NMR δ 14.0 (Me), 20.6 and 29.1 (CH_2), 57.5 (N-*C*H$_2$-Pr), other signals as for **13a**; *m/z* 459 (M^+), 416 (M^+-C_3H_7) [Found : MH^+ (ammonia CI) 460.2852. Calcd for $C_{30}H_{38}NO_3$ 460.2852].

***N*-Pentyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-iminoxylitol (13c):** [0.33g, 63%, from ditosylate **12** (0.81 g) in *n*-amylamine (8 mL)] oil; ^{1}H NMR δ 0.93 (3H, t), 1.2-1.55 (6H, m), 2.38 (2H, t, N-C*H*$_2$-Bu), other signals as for **13a**;^{13}C NMR δ 14.0 (Me), 22.5, 26.6 and 29.6 (CH_2), 57.9 (N-*C*H$_2$Bu), other signals as for **13a**; *m/z* 473 (M^+), 416 (M^+-C_4H_9) [Found : MH^+ (FAB) 474.3008. Calcd for $C_{31}H_{40}NO_3$ 474.3006].

***N*-Benzyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-iminoxylitol (13d):** [0.14 g, 83%, from **12** (0.20 g) in benzylamine (5 mL)] oil; ^{1}H NMR δ 1.98 (2H, t, *J* 10.6, 1/5-H_{ax}), 3.05 (2H, dd, *J* 10.6, 4.2, 1/5-H_{eq}), 3.43 (1H, t, *J* 8.7, 3-H), 3.53 (2H, s, NC*H*$_2$Ph), 3.61 (2H, dt, 2/4-H), 4.63 (4H, AB dd, *J* 11.6, OC*H*$_2$Ph), 4.88 (2H, s, OC*H*$_2$Ph), 7.2-7.4 (20H, m); ^{13}C NMR δ 56.0 (C-1/5), 62.0 (N-*C*H$_2$Ph), 72.9 and 75.3 (O*C*H$_2$Ph), 78.8 (C-2/4), 86.4 (C-3); *m/z* 492 (M^+-H), 402 (M^+-PhCH_2).

***N*-Propyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-imino-D-arabinitol (15a):** [0.48 g, 82%, from **14** (1 g) and propylamine (12 mL)] oil, $[\alpha]_D$ -22.6° (*c* 0.25, $CHCl_3$);^{1}H NMR δ 0.88 (3H, t, *J* 7.3, Me), 1.51 (2H, m, C*H*$_2$Me), 2.2-2.4 (4H, m, N-C*H*$_2$, 1-H_{ax}, 5-H_{ax}), 2.74 (2H, m, 1-H_{eq}, 5-H_{eq}), 3.51 (1H, dd, *J* 6.6, 2.8, 3-H), 3.82 (2H, m, 2-,4-H), 4.55-4.75 (6H, m, C*H*$_2$Ph), 7.3 (15H, m); ^{13}C NMR δ 11.9 (Me), 19.7 (CH_2), 53.2 and 54.3 (C-1, C-5), 60.2 (N-*C*H$_2$Et) 71.3, 72.1, 72.4 (O*C*H$_2$Ph), 73.8 (C-3), 75.2 (C-2 and C-4); *m/z* 445 (M^+), 416 (M^+-Et) [Found: MH^+(FAB) 446.2695. Calcd for $C_{29}H_{36}NO_3$, 446.2693].

***N*-Butyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-imino-D-arabinitol (15b):** [0.517 g, 79%, from **14** (1 g) and butylamine (12 mL)] oil, $[\alpha]_D$ -20.9° (*c* 2.25, $CHCl_3$);^{1}H NMR δ 0.91 (3H, t, Me), 1.2-1.35 (2H, m), 1.35-1.55 (2H, m), other signals as for **15a**; ^{13}C NMR δ 14.0 (Me), 20.7 and 28.7 (CH_2), 58.0 (N-*C*H$_2$), other signals as for **15a**; *m/z* (FAB) 460 (MH^+), 416 (M^+-Pr) [Found: MH^+ (FAB) 460.2852. Calcd for $C_{30}H_{38}NO_3$ 460.2852].

***N*-Pentyl-2,3,4-tri-*O*- benzyl-1,5-dideoxy-1,5-imino-D-arabinitol (15c):** [0.51 g, 78%, from **14** (1 g) and *n*-amylamine (12 mL)] oil, $[\alpha]_D$ -18.2° (*c* 1.38, $CHCl_3$) ;^{1}H NMR δ 0.90 (3H, t, Me), 1.2-1.4 (4H, m, 2CH_2), 1.4-1.6 (2H, m, CH_2), other signals as

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for **15a**; ^{13}C NMR δ 14.0 (Me), 22.6, 26.3 and 29.8 (CH_2), 58.4 (N-CH_2), other signals as for **15a**; *m/z*. 473 (M^+), 472 (M^+-H), 416 (M^+-C_4H_9) [Found: MH^+ (FAB) 474.3008. Calcd for $C_{31}H_{40}NO_3$ 474.3006].

***N*-Propyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-imino-L-arabinitol (20a)**: [0.43 g, 78%, from **19** (0.91 g) and propylamine (10 mL)] oil, $[\alpha]_D$ +18.1° (*c* 0.86, $CHCl_3$), with spectroscopic data as for **15a** [Found : MH^+ (FAB) 446.2695. Calcd for $C_{29}H_{36}NO_3$ 446.2693].

***N*-Butyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-imino-L-arabinitol (20b)**: [0.113 g, 90%, from **19** (0.20 g) and *n*-butylamine (4 mL)] oil, $[\alpha]_D$ +23.9° (*c* 1.05, $CHCl_3$), with data as for **15b** [Found : MH^+ (FAB) 460.2852. Calcd for $C_{30}H_{38}NO_3$ 460.2852].

***N*-Pentyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-imino-L-arabinitol (20c)**: [0.34 g, 91%, from **19** (0.58 g) in *n*-amylamine (9 mL)] oil, $[\alpha]_D$ +22.8° (*c* 1.2, $CHCl_3$), with spectroscopic data as for **15c** [Found : MH^+ (FAB) 474.3008. Calcd for $C_{31}H_{40}NO_3$ 474.3006].

***N*-Propyl-2,3,4-tri-*O*-benzyl-1,5-dideoxy-1,5-iminoribitol (22)**: [0.19 g, 48%, from **21** (0.65 g) in propylamine (10 mL)], colourless crystals, mp 40-42°C (from ether); ^1H NMR δ 0.87 (3H, t, *J* 7.3, Me), 1.5 (2H, m, CH_2), 2.4 (2H, m, N-CH_2Et), 2.47 (2H, t, *J* 10.5, H-1/5_{ax}), 2.80 (2H, dd, *J* 10.3, 4.5, H-1/5_{eq}), 3.48 (2H, ddd, *J* 10.8, 4.5, 2.3, H-2/4), 4.13 (1H, t, *J*~2, H-4), 4.55 (4H, s, OCH_2Ph), 4.88 (2H, s, OCH_2Ph), 7.2-7.4 (15H, m); ^{13}C NMR δ 11.9 (Me), 20.0 (CH_2), 51.4 (C-1/5), 60.0 (N-CH_2Et), 70.9 and 73.6 (OCH_2Ph), 73.8 (C-3), 76.9 (C-2/4); *m/z* 445 (M^+), 416 (M^+-Et).

Anal. Calcd for $C_{29}H_{35}NO_3$: C, 78.15; H, 7.93; N, 3.14. Found: C, 78.7; H, 8.1; N, 3.2.

General procedure for catalytic hydrogenolysis. The protected amine (~0.5 g) in glacial acetic acid (~30 mL per g substrate) was hydrogenated at 1 atm in the presence of Pd/C (5%, 0.2 g per g substrate). When gas uptake was complete, the mixture was filtered through celite, which was washed with EtOH, and the combined filtrates were concentrated, and then lyophilized once more after addition of water (5 mL). The residue was chromatographed on silica, with ethanol-chloroform- aqueous ammonia (45:45:10) as eluent. The residue after solvent evaporation was crystallised from ethanol-ether. By this procedure were prepared:

***N*-Propyl-1,5-dideoxy-1,5-iminoxylitol (7a)** (77%): mp 125-126 °C; ^1H NMR (D_2O) δ 0.79 (3H, t, Me), 1.42 (2H, m, CH_2), 1.93 (2H, t, *J* 11.1, 1/5-H_{ax}), 2.33 (2H, m, N-CH_2Et), 2.97 (2H, dd, *J* 10.6, 4.8 1/5-H_{eq}), 3.13 (1H, t, *J* 9.2, 3-H), 3.47 (2H, ddd, *J* 10.8, 9.2, 4.8, 2/4-H); ^{13}C NMR (DMSO-d_6) δ 11.7 (Me), 19.7 (CH_2), 58.7 (C-1/5), 59.0 (N-CH_2Et) 70.0 (C-2/4), 79.2 (C-3); *m/z* 176 (MH^+), 146 (M^+-Et).

Anal. Calcd for $C_8H_{17}NO_3$: C, 54.82; H, 9.80; N, 7.99. Found: C, 54.7; H, 9.9; N, 7.8.

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***N*-Butyl-1,5-dideoxy-1,5-iminoxylitol (7b)** (62%): mp 143-144 °C; ^{1}H NMR (D_2O) δ 0.8 (3H, t, Me), 1.1-1.3 (2H, m, CH_2), 1.3-1.45 (2H, m, CH_2), 2.36 (2H, t, NCH_2-Pr), other signals as for **7a**; ^{13}C NMR (DMSO-d_6) δ 13.8 (Me), 20.0, and 28.7 (CH_2), 56.7 (N-CH_2-Pr), others as for **7a**; *m/z* 189 ($M^{+\cdot}$), 146 (M^+-C_3H_7).(Found: M^+, 189.1367. Calcd for $C_9H_{19}NO_3$ 189.1364).

Anal. Calcd for $C_9H_{19}NO_3$: C, 57.10; H, 10.14; N, 7.40. Found: C, 57.4; H, 10.6; N, 7.4.

***N*-Pentyl-1,5-dideoxy-1,5-iminoxylitol (7c)** (60%): mp 153-154 °C;^{1}H NMR (D_2O) δ 0.81 (3H, t, Me), 1.1-1.3 (4H, m, 2xCH_2), 1.35-1.5 (2H, m, CH_2), other signals as for 7a; ^{13}C NMR (DMSO-d_6) δ 13.9 (Me) 22.0, 26.2, and 29.0 (CH_2), 57.0 (N-CH_2Bu), others as for **7a**; *m/z* 203 (M^+), 146 (M^+-C_4H_9) (Found: M^+, 203.1513. Calcd for $C_{10}H_{21}NO_3$ 203.1520).

Anal. Calcd for $C_{10}H_{21}NO_3$: C, 59.07; H, 10.43; N, 6.89. Found: C, 58.5; H, 10.7; N, 6.9.

***N*-Propyl-1,5-dideoxy-1,5-imino-D-arabinitol (8a)** (76%): mp. 93-95 °C, $[\alpha]_D$ -54.0° (*c* 0.5, H_2O); ^{1}H NMR (D_2O) δ 0.81 (3H, t, Me), 1.3-1.5 (2H, m, CH_2), 2.05 (1H, t, *J* 10.1, 1-H_{ax}), 2.2-2.4 (3H, m, 5-H_{ax}, N-CH_2Et), 2.8 (2H, m, 1-H_{eq}, 5-H_{eq}), 3.43 (1H, dd, $J_{3,2}$ 8.5, $J_{3,4}$ 3.3, 3-H), 3.80 (1H, dt, *J* 8.4, 4.2, 2-H), 3.95 (1H, m, 4-H); ^{13}C NMR (DMSO-d_6) δ 11.7 (Me), 19.5 (CH_2), 56.1 and 56.5 (C-1, C-5), 59.3 (NCH_2Et), 67.1 and 68.1 (C-2, C-4), 73.2 (C-3); *m/z* 175 (M^+), 146 (M^+-Et).

Anal. Calcd for $C_8H_{17}NO_3$: C, 54.82; H, 9.80; N, 7.99. Found : C, 54.9; H, 9.9; N, 7.9.

***N*-Butyl-1,5-dideoxy-1,5-imino-D-arabinitol (8b)** (73%): hygroscopic crystals, $[\alpha]_D$ -54.0° (*c* 0.96, EtOH); ^{1}H NMR (D_2O) δ 1.15-1.3 (2H, m), 1.3-1.5 (2H, m), other signals as for **8a**; ^{13}C NMR (DMSO-d_6) δ 13.9 (Me), 20.0 and 28.6 (CH_2), 57.1 (NCH_2Pr), other signals as for **8a**; *m/z* (CI, NH_3) 190 (MH^+), 172 (MH^+-H_2O), 146 (M^+-C_3H_7) (Found : MH^+ 190.1443. Calcd for $C_9H_{20}NO_3$ 190.1443).

***N*-Pentyl-1,5-dideoxy-1,5-imino-D-arabinitol (8c)** (70%): mp 62-65 °C, $[\alpha]_D$ -50.0° (*c*, 0.6, H_2O); ^{1}H NMR (D_2O) δ 1.15-1.3 (4H, m), 1.35-1.5 (2H, m), other signals as for **8a**; ^{13}C NMR (DMSO-d_6) δ 13.8 (Me), 22.0, 26.0 and 29.1 (CH_2), 57.4 (N-CH_2-Bu), other signals as for **8a**; *m/z* 203 (M^+) 188 (M^+-Me), 146 (M^+-C_4H_9).

Anal. Calcd for $C_{10}H_{21}NO_3$: C, 59.07; H, 10.43; N, 6.89.Found: C; 58.5; H, 10.3; N, 6.8.

***N*-Propyl-1,5-dideoxy-1,5-imino-L-arabinitol (9a)** (71%): mp 92-94°C, $[\alpha]_D$ +48.1° (*c* 0.5, H_2O), with spectroscopic data as for the enantiomer **8a.**

Anal. Calcd for $C_8H_{17}NO_3$: C, 54.82; H, 9.80; N, 7.99. Found: C, 54.5; H, 10.2; N, 7.9.

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***N*-Butyl-1,5-dideoxy-1,5-imino-L-arabinitol (9b)** (74%): mp 64-65 °C (hygroscopic), $[\alpha]_D$ +46.3° (*c* 0.48, H_2O), with spectroscopic data as for **8b**.

Anal. Calcd for $C_9H_{19}NO_3$: C, 57.10, H, 10.14; N, 7.40. Found: C, 57.0; H, 10.3; N, 7.3.

***N*-Pentyl-1,5-dideoxy-1,5-imino-L-arabinitol (9c)** (70%): mp 70-71 °C, $[\alpha]_D$ +53.6° (*c* 0.41, H_2O), with spectroscopic data as for **8c**.

Anal. Calcd for $C_{10}H_{21}NO_3$: C, 59.07, H, 10.43; N, 6.89. Found: C, 59.2; H, 10.6; N, 6.8.

***N*-Propyl-1,5-dideoxy-1,5-iminoribitol (10)** (68%), as an oil that could not be crystallized; ^1H NMR (D_2O) δ 0.82 (3H, t, Me), 1.4-1.6 (2H, m, CH_2), 2.4-2.6 (4H, m, 1/5-H_{ax}, NC*H*$_2$Et), 2.82 (2H, dd, *J* 11.5, 4.3, 1/5-H_{eq}), 3.79 (2H, ddd, *J* 9.9, 4.3, 2.7, 2/4-H), 3.87 (1H, t, J 2.7, 3-H); ^{13}C NMR (DMSO-d_6) δ 11.7 (Me), 21.2 (CH_2), 53.5 (C-1/5), 59.1 (NCH_2Et), 67.9 (C-2/4), 70.6 (C-3); *m/z* 175 (M^+), 146 (M^+-Et) [Found : MH^+ (FAB) 176.1287. Calcd for $C_8H_{18}NO_3$ 176.1287].

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