Chirospecific synthesis of 1,4-dideoxy-1,4-imino-D-arabinitol and 1,4-dideoxy-1,4-imino-L-xylitol *via* one-pot cyclisation

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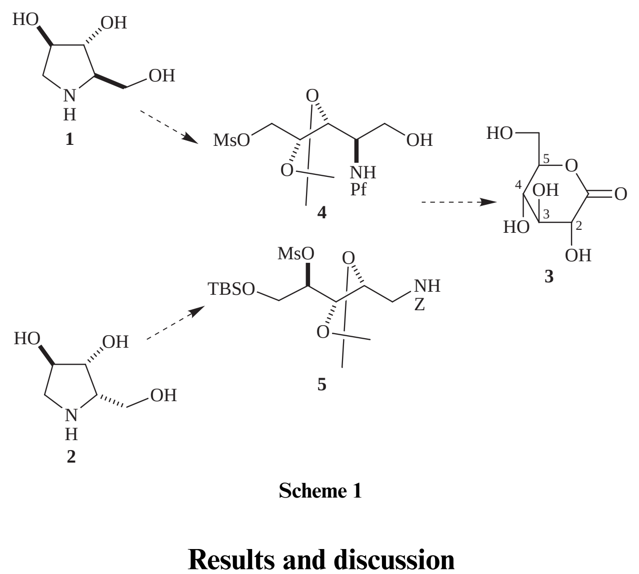
The multi-protected compounds 4 and 5 were treated with 20% iodine in methanol to give 1,4-dideoxy-1,4-imino-D-arabinitol 1 and 1,4-dideoxy-1,4-imino-L-xylitol 2 directly. Iodine was an efficient catalyst for deprotection of *O*-isopropylidene, *O*-(*tert*-butyldimethylsilyl), *N*-(9-phenylfluoren-9-yl) and *N*-benzyloxycarbonyl groups, resulting in intramolecular cyclisation.

1,4-Dideoxy-1,4-iminopentitols have been attracting the interest of synthetic chemists due to their potential biological activities,[1] even though their structures are simple and compact. Among them, 1,4-dideoxy-1,4-imino-D-arabinitol **1**, isolated from *Arachniodes Standishii*[2a] and *Angylocalyx boutiqueanus*,[2b] has been shown to be a good enzyme inhibitor with a broad inhibitory spectrum toward mammalian glycosidases, such as ER a-glucosidase II, Golgi a-mannosidase I and II, intestinal isomaltase, and trehalase.[1b,c] 1,4-Dideoxy-1,4-imino-L-xylitol **2**[3e,f] as the 2-epimer of compound **1** has also proven to be a potential glycosidase inhibitor.[1] Since the first reported[3a,e] synthesis of compounds **1** and **2**, several synthetic strategies[3] have been developed to prepare these valuable compounds economically from both carbohydrate and non-carbohydrate sources. Our objective was to develop a short and efficient route to the preparation of enantiomerically pure compounds **1** and **2**, from the same starting material without any chiral inversion. We also report herein that iodine was an efficient catalyst for the deprotection of both O- and N-protecting groups of compounds **4** and **5**, resulting in intramolecular amination. Our general retrosynthesis of compounds **1** and **2** is outlined in Scheme 1. It begins with the very cheap D-glucono-δ-lactone **3** and proceeds through one-pot cyclisation.



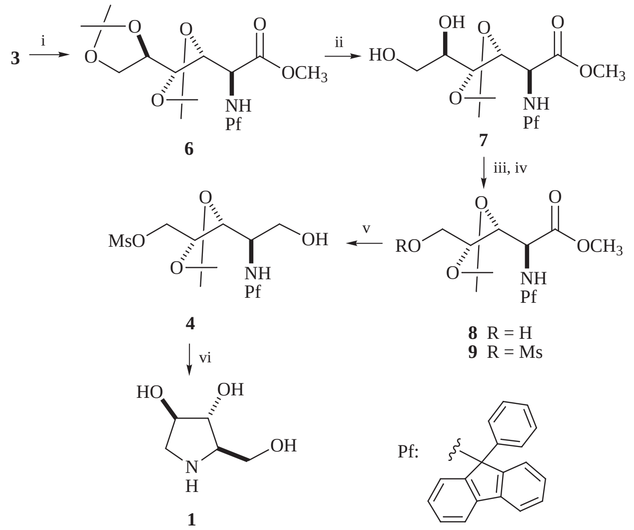
Scheme 1

Results and discussion

As our chiral educt we chose D-glucono-δ-lactone **3** which has three stereocentres as required for C2, C3 and C4 in the target molecules **1** and **2**. The stereochemistry of C2, C3 and C4 in our starting material was used for compound **1**, while that at C3, C4 and C5 was for compound **2** (Scheme 1).

1,4-Dideoxy-1,4-imino-D-arabinitol 1

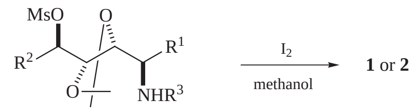
We chose the 9-phenylfluoren-9-yl (Pf) group for protection of the amine since this protecting group has been shown to inhibit deprotonation at the α-position of an α-amino ester.[4] The diisopropylidenemannonate **6** was synthesised in four high yielding steps from D-glucono-δ-lactone **3** as described;[5] the overall yield for this conversion was 75% (Scheme 2). The terminal



Scheme 2 *Reagents and conditions*: i, ref. 5; ii, Dowex 50W-8X, 90% MeOH; iii, $NaIO_4$, $NaBH_4$, MeOH; iv, MsCl, Et_3N, THF; v, ice-cooled $LiAlH_4$ and THF; vi, I_2, MeOH, reflux

isopropylidene group was selectively cleaved by treatment of mannonate **6** with Dowex 50W-X8 resin (H^+-form) in 90% methanol[6] to give the diol **7**. The diol **7** was oxidised in the presence of $NaIO_4$; this was followed by sodium borohydride reduction of the resulting aldehyde which led to the formation of alcohol **8** in quantitative yield. After mesylation of alcohol **8**, the ester group of mesylate **9** was reduced by DIBAL-H at −40 °C to give compound **4** in 87% yield. Compound **4**, protected with *O*-isopropylidene and *N*-9-phenylfluoren-9-yl groups, was refluxed with 20% iodine in methanol for 10 h. To the reaction mixture was added Dowex 50W-8X (H^+-form), the mixture was filtered and the filtrate was washed with methanol, then eluted with 3 M aq. NH_3 to afford target compound **1** (76% yield) without further purification. This step could be achieved through deprotections and intramolecular cyclisation in one-pot simultaneously. It is generally accepted that the *anti* diols protected by an isopropylidene group as in structure **4** are not converted into a five-membered ring because of their steric hindrance, therefore the five-membered ring can only be formed

Table 1 One-pot cyclisation by treatment with iodine in methanol[a]



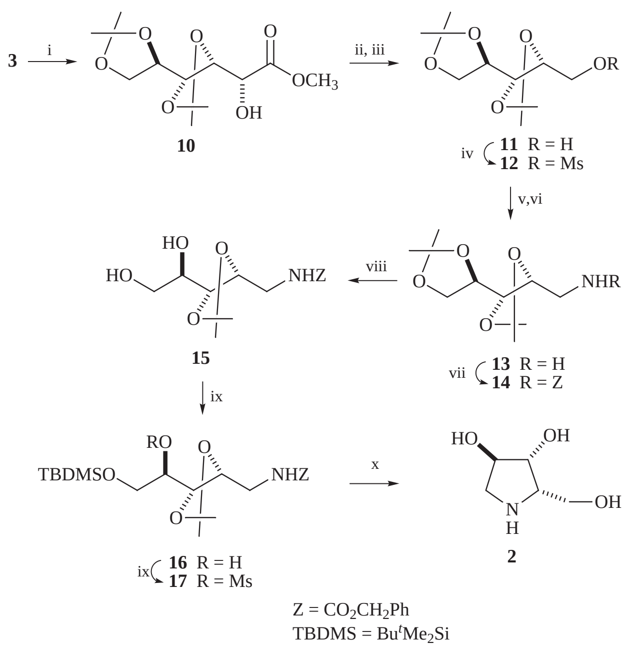
Entry	R^1	R^2	R^3	I_2(w/w %)	Reaction time (t/h)	Product (% yield)[b]
1	H	CH_2OH	Pf[c]	5	60	**1** (65)
2	H	CH_2OH	Pf	10	25	**1** (68)
3	H	CH_2OH	Pf	20	12	**1** (76)
4	H	CH_2OH	Pf	30	7	**1** (73)
5	OTBDMS	H	Z[d]	10	48	**2** (52)
6	OTBDMS	H	Z	20	12	**2** (63)

[a] All reactions were carried out under reflux. [b] Isolated yield. [c] 9-Phenylfluoren-9-yl. [d] Benzyloxycarbonyl.

after a number of tedious steps, such as repeated deprotection–protection, and working up *via* water-soluble polyhydroxylated intermediates. An application of 20% iodine in methanol allowed us to simplify the tedious step including deprotection of O- and N-protecting groups, which led to intramolecular cyclisation directly. As shown in Table 1 iodine was a much more efficient catalyst for deprotection and intramolecular amination.

1,4-Dideoxy-1,4-imino-L-xylitol 2

The gluconate **10** was easily synthesized from lactone **3** as described,[5] and was then reduced with LAH in THF to give the diol in 97% yield without further purification. The diol was oxidised in the presence of $NaIO_4$, and sodium borohydride reduction of the resulting aldehyde led to the formation of alcohol **11** in quantitative yield (Scheme 3). After mesylation of



Scheme 3 *Reagents and conditions*: i, ref. 5; ii, LAH, THF, 0 °C; iii, $NaIO_4$, $NaBH_4$, MeOH; iv, MsCl, Et_3N, THF; v, NaN_3, DMF, rt; vi, H_2, Pd/C, EtOAc; vii, Z-Cl, K_2CO_3, CH_2Cl_2; viii, Dowex 50W-8X, 90% MeOH; ix, TBDMSCl, imidazole, DMF; x, I_2, MeOH, reflux

alcohol **11**, mesylate **12** was treated with NaN_3 in DMF to give the corresponding azide, which was then hydrogenated in the presence of palladium on charcoal. The corresponding amine **13** was protected as its benzyloxycarbonyl (Z) derivative **14** in quantitative yield. By treatment of compound **14** with Dowex 50W-8X, regioselective hydrolysis took place leading to diol **15** in 95% yield. The primary alcohol of diol **15** was protected with TBDMSCl, and the resulting alcohol **16** was allowed to react with MsCl in THF to give multi-protected compound **5** in quantitative yield. By treatment of multi-protected compound **5** with the same procedure for compound **1**, a one-pot cyclisation took place leading to target molecule **2** in 63% yield. The detailed role of iodine is unclear except that iodine in methanol solution may act as a Lewis acid species.[7] In summary we report that iodine was an efficient catalyst for one-pot cyclisation of multi-protected compounds **4** and **5**. This approach will be useful to the preparation of pyrrolidine rings having a *trans*-diol structural unit, including compounds such as alexine, australine and lentiginosine.[8] We have also achieved an efficient and chirospecific synthesis of target molecules **1** and **2**.

Experimental

General

Dowex 50W-X8 was purchased from Sigma Chemical Co. All non-aqueous reactions were carried out under nitrogen. THF was distilled from Na/benzophenone; methanol was distilled from Mg; acetonitrile, 2,2-dimethoxypropane, DMF, and methylene dichloride were distilled from CaH_2. Column chromatography was carried out using 230–400 mesh silica gel. MPs were measured on a Thomas–Hoover capillary apparatus and are uncorrected. Proton and carbon magnetic resonance spectra were measured downfield relative to tetramethyl silane in $CDCl_3$ unless otherwise noted (value in ppm); coupling constants J are reported in hertz; ^1H NMR, ^{13}C NMR and two-dimensional chemical-shift-correlation (2D COSY) experiments were conducted on Bruker AW-500 and ARX-300 spectrometers. Elemental analyses were carried out by the Korea Research Institute of Chemical Technology. Final solutions before evaporation were dried over anhydrous Na_2SO_4.

Methyl 2-deoxy-3,4 : 5,6-di-*O*-isopropylidene-2-[(9-phenylfluoren-9-yl)amino]-D-mannonate 6

This was prepared from D-glucono-δ-lactone as described:[5b] yield, 76%; mp 111–113 °C (lit.,[5b] 113 °C).

Methyl 2-deoxy-3,4-*O*-isopropylidene-2-[(9-phenylfluoren-9-yl)-amino]-D-mannonate 7

To a solution of mannonate **6** (6.2 g, 11.7 mmol) in 90% MeOH (60 cm^3) was added Dowex 50W-8X resin (6 g). The reaction mixture was stirred for 18 h at rt, then was filtered, and the filtrate was evaporated. The crude residue was chromatographed on silica gel [hexane–EtOAc (1 : 1, then 1 : 5)] to give *compound* **7** (5.5 g, 95%) as a solid, mp 68–70 °C; $[a]_D^{20}$ −102 (c 1.42, $CHCl_3$); δ_H 1.07 (3 H, s), 1.25 (3 H, s), 2.59 (1 H, d), 3.25 (3 H, s), 3.48 (1 H, dd), 3.66 (1 H, m), 3.71 (1 H, dd), 3.84 (1 H, dd), 3.91 (1 H, dd), 7.06–7.50 (11 H, m) and 7.73 (2 H, d);

δ_C 26.1, 26.5, 29.6, 52.2, 58.4, 64.2, 72.6, 72.8, 76.7, 80.1, 81.4, 109.8, 120.2, 120.3, 125.4, 125.9, 126.2, 127.5, 127.6, 128.4, 128.7, 128.8, 129.2, 140.6, 141.0, 142.0, 147.1, 147.3 and 174.6 (Found: C, 70.5; H, 6.6; N, 2.6. $C_{29}H_{31}NO_6$ requires C, 71.1; H, 6.4; N, 2.9%).

Methyl 2-deoxy-3,4-*O*-isopropylidene-2-[(9-phenylfluoren-9-yl)-amino]-D-lyxonate 8

To a solution of diol **7** (4.3 g, 8.6 mmol) in EtOH (20 cm^3) was added aq. $NaIO_4$ (2.1 g, 10.3 mmol) in (6.5 cm^3), then the mixture was stirred for 2 h. After the alcohol spot for substrate **7** had disappeared on TLC, to the reaction mixture was added $NaBH_4$ (0.39 g, 10.3 mmol) and the mixture was stirred for another 10 min before being evaporated, then water (20 cm^3) was added and the mixture was extracted with EtOAc (30 cm^3 × 3). The organic phase was washed with brine, dried, and concentrated under reduced pressure. The residue was chromatographed on silica gel [hexane–EtOAc (3 : 1)] to give *compound* **8** (3.9 g, 98%) as a solid, mp 64–66 °C; $[a]_D^{20}$ −150 (*c* 1.16, $CHCl_3$); δ_H 1.09 (3 H, s), 1.28 (3 H, s), 2.63 (1 H, d), 3.23 (3 H, s), 3.35 (1 H, s, OH), 3.76–3.92 (4 H, m) and 7.09–7.73 (13 H, m); δ_C 26.4, 26.8, 51.9, 58.6, 63.8, 72.6, 80.2, 80.3, 109.5, 120.2, 125.5, 125.7, 126.1, 127.4, 127.5, 128.4, 128.5, 128.6, 128.9, 140.4, 141.1, 143.1, 147.9 and 174.7 (Found: C, 72.8; H, 6.5; N. 3.4. $C_{28}H_{29}NO_5$ requires C, 73.2; H, 6.4; N, 3.1%).

Methyl 2-deoxy-3,4-*O*-isopropylidene-5-*O*-methylsulfonyl-2-[(9-phenylfluoren-9-yl)amino]-D-lyxonate 9

To a solution of alcohol **8** (2.8 g, 6.1 mmol) in THF (15 cm^3) were added triethylamine (630 mg, 6.24 mmol) and methanesulfonyl chloride (714 mg, 6.24 mmol). The reaction mixture was stirred for 20 min at rt, then was quenched with saturated aq. $NaHCO_3$ (20 cm^3). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (20 cm^3 × 2). The combined organic phase was washed successively water and brine, dried, and concentrated under reduced pressure. The residue was chromatographed on silica gel [hexane–EtOAc (5 : 1)] to give *compound* **9** (3.2 g, 97%) as a solid, mp 155–158 °C; $[a]_D^{20}$ −204 (*c* 1.00, $CHCl_3$); δ_H 1.10 (3 H, s), 1.31 (3 H, s), 2.62 (1 H, dd), 3.12 (3 H, s), 3.24 (3 H, s), 3.82 (1 H, dd), 4.00 (1 H, m), 4.46 (1 H, dd), 4.77 (1 H, dd) and 7.11–7.74 (13 H, m); δ_C 26.6, 26.8, 37.8, 51.9, 58.8, 70.3, 72.6, 78.0, 78.2, 110.6, 120.2, 120.3, 125.1, 125.9, 126.1, 127.5, 128.3, 128.5, 128.6, 128.8, 140.1, 141.3, 143.4, 147.9, 148.2 and 174.4 (Found: C, 64.4; H, 6.0; N, 2.4. $C_{29}H_{31}NO_7S$ requires C, 64.8; H, 5.8; N, 2.6%).

4-Deoxy-2,3-*O*-isopropylidene-1-*O*-methylsulfonyl-4-[(9-phenylfluoren-9-yl)amino]-D-arabinitol 4

To an ice-cooled solution of $LiAlH_4$ (60 mg, 1.6 mmol) in THF (2 cm^3) was added a solution of mesyl ester **9** (850 mg, 1.6 mmol) in THF (5 cm^3). The reaction mixture was warmed to rt, stirred for 30 min, then quenched by sequential addition of water (60 mm^3), 15% aq. NaOH (60 mm^3), and water (180 mm^3). The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel [CH_2Cl_2–EtOAc (50 : 1)] to give *compound* **4** (709 mg, 87%) as an oil, $[a]_D^{20}$ −48 (*c* 1.10, $CHCl_3$); δ_H 1.21 (3 H, s), 1.32 (3 H, s), 1.96 (1 H, s, OH), 2.22 (1 H, dd), 2.79 (1 H, dd), 3.03 (3 H, s), 3.34 (1 H, d), 3.73 (1 H, dd), 4.00 (1 H, m), 4.21 (1 H, dd), 4.38 (1 H, dd) and 7.19–7.72 (13 H, m); δ_C 26.7, 26.8, 26.9, 37.6, 51.8, 55.1, 60.5, 67.7, 70.2, 72.3, 78.0, 109.6, 115.3, 120.2, 124.6, 125.5, 125.9, 127.5, 128.1, 128.2, 128.4, 128.6, 140.3, 144.4, 149.0 and 150.6 (Found: C, 65.7, H, 6.3; N, 2.6. $C_{28}H_{31}NO_6S$ requires C, 66.0; H, 6.1; N, 2.8%).

1,4-Dideoxy-1,4-imino-D-arabinitol 1 and its hydrochloride salt

A solution of multi-protected compound **4** (260 mg, 0.51 mmol) and iodine (60 mg) in methanol (1.5 cm^3) was refluxed overnight, cooled to rt, and then treated with Dowex 50W-8X (200 mg). The mixture was filtered, and the residue was washed with MeOH (100 cm^3). The remaining residue was eluted with 3 mol dm^3 NH_4OH. The ammoniacal solution was evaporated, then co-evaporated with toluene to give free base **1** (52 mg, 76%) as a sticky oil, $[a]_D^{20}$ +8.1 (*c* 0.98, water) {lit.,[2a] mp 115 °C; $[a]_D^{20}$ +7.8 (*c* 0.46, water)}; δ_H(D_2O) 2.78 (1 H, dd, *J* 12.2 and 5.7), 2.94 (1 H, m), 3.06 (1 H, dd, *J* 12.2 and 5.7), 3.58 (1 H, dd, *J* 11.5 and 4.9), 3.76 (1 H, m) and 4.06 (1 H, m); δ_C 48.9, 59.8, 64.1, 75.1 and 76.7.

To the free base was added conc. HCl. The mixture was evaporated, then co-evaporated with toluene. The crystalline residue was recrystallised from methanol–diethyl ether to afford compound **1** as its hydrochloride salt. ^1H and ^{13}C NMR data were consistent with those reported, mp 113–114 °C; $[a]_D^{20}$ +34.7 (*c* 0.78, water) {lit.,[3a] mp 115 °C; $[a]_D^{20}$ +37.9 (*c* 0.53, water)} (Found: C, 35.0; H, 7.4; N, 8.1. Calc. for $C_5H_{12}ClNO_3$: C, 35.4; H, 7.1; N, 8.3%).

2,3 : 4,5-Di-*O*-isopropylidene-D-arabinitol 11

To an ice-cooled solution of $LiAlH_4$ (758 mg, 20.0 mmol) in THF (3 cm^3) was added a solution of gluconate **10** (5.8 g, 20.0 mmol) in THF (25 cm^3). The reaction mixture was warmed to rt, stirred for 2 h, and quenched by the sequential addition of water (0.76 cm^3), 15% aq. NaOH (0.76 cm^3), and water (2.5 cm^3). The mixture was filtered, and the filtrate was concentrated under reduced pressure to give the corresponding alcohol which was used in the next step without further purification. To a solution of the corresponding alcohol in EtOH (25 cm^3) were added $NaIO_4$ (5.1 g, 24 mmol) and water (10 cm^3), and the mixture was stirred for 2 h. To the reaction mixture was added $NaBH_4$ (453 mg, 12 mmol) and the mixture was stirred for 10 min before being evaporated. The residue was then treated with water (25 cm^3) and extracted with EtOAc (50 cm^3 × 3). The combined organic phase was washed with brine, dried, and concentrated under reduced pressure. The residue was chromatographed on silica gel [hexane–EtOAc (4 : 1)] to give *compound* **11** (4.31 g, 93%) as an oil, $[a]_D^{20}$ −2.1 (*c* 1.0, $CHCl_3$); δ_H 1.28 (3 H, s), 1.32 (3 H, s), 1.33 (3 H, s), 1.35 (3 H, s), 2.58 (1 H, m, OH), 3.63–3.67 (2 H, m), 3.74 (1 H, m), 3.90 (1 H, dd), 3.95 (1 H, m), 4.00 (1 H, m) and 4.09 (1 H, dd); δ_C 24.9, 26.4, 26.6, 26.7, 62.6, 67.6, 76.6, 78.3, 80.6, 109.2 and 109.6 (Found: C, 57.2; H, 8.9. $C_{11}H_{20}O_5$ requires C, 56.9; H, 8.7%).

2,3 : 4,5-Di-*O*-isopropylidene-1-*O*-methylsulfonyl-D-arabinitol 12

To a solution of alcohol **11** (1.1 g, 4.8 mmol) in THF (7 cm^3) were added triethylamine (583 mg, 5.8 mmol) and methanesulfonyl chloride (659 mg, 5.8 mmol) at 0 °C. After stirring of the mixture for 1 h at 0 °C, 5% aq. citric acid (20 cm^3) was added and the mixture was extracted with EtOAc (30 cm^3 × 3). The combined extracts were washed with brine, dried, and evaporated, and the residue was chromatographed on silica gel [hexane–EtOAc (4 : 1)] to give *compound* **12** (1.45 g, 97%) as a solid, mp 110–112 °C; $[a]_D^{20}$ +2.6 (*c* 1.3, MeOH); δ_H 1.27–1.35 (12 H, m), 3.00 (3 H, s), 3.66 (1 H, m), 3.89 (1 H, dd), 3.95 (1 H, m), 4.07–4.11 (2 H, m), 4.24 (1 H, m) and 4.46 (1 H, dd); δ_C 27.4, 29.0, 29.2, 29.3, 40.0, 70.1, 71.5, 79.1, 79.6, 80.6, 112.3 and 112.7 (Found: C, 46.2; H, 7.4. $C_{12}H_{22}O_7S$ requires C, 46.4; H, 7.1%).

1-[(Benzyloxycarbonyl)amino]-1-deoxy-2,3 : 4,5-di-*O*-isopropylidene-D-arabinitol 14

To a solution of mesylate **12** (520 mg, 1.7 mmol) in dried DMF (3 cm^3) was added NaN_3 (78 mg, 5.1 mmol). After stirring of the mixture overnight at 60 °C, water (10 cm^3) was added and the mixture was extracted with EtOAc (20 cm^3 × 3). The combined extracts were washed with brine, dried, and evaporated. A solution of the crude residue in EtOAc (5 cm^3) was hydrogenated over 10% palladium on charcoal (50 mg) at atmospheric pressure for 6 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure. To a solution of the oily residue amine **13** in CH_2Cl_2 (10 cm^3) was added aq. K_2CO_3 (470 mg, 3.4 mmol in 7 cm^3) and the mixture was cooled in an ice-bath. To this stirred mixed-phase solution was added dropwise a solution of benzyl chloroformate (341 mg, 2.0 mmol) in CH_2Cl_2 (5 cm^3), and the mixture was then stirred at rt for 30 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (20 cm^3 × 3). The organic phase was washed successively with water and brine, dried, and concentrated under reduced pressure. The residue was chromatographed on silica gel [hexane–EtOAc (8:1)] to give *compound* **14** (440 mg, 72%) as a solid, $[\alpha]_D^{20}$ −4.6 (*c* 1.0, $CHCl_3$); δ_H 1.26–1.35 (12 H, m), 3.42 (2 H, m), 3.52 (1 H, m), 3.86–3.98 (3 H, m), 4.07 (1 H, m), 5.03 (2 H, m) and 7.27 (5 H, m); δ_C 24.1, 25.6, 25.8, 26.0, 42.1, 65.7, 66.8, 75.8, 76.0, 76.3, 78.0, 78.4, 108.5, 108.9, 127.0, 127.1, 135.6 and 155.3 (Found: C, 62.1; H, 7.8; N, 3.4. $C_{19}H_{27}NO_6$ requires C, 62.5; H, 7.5; N, 3.8%).

1-[(Benzyloxycarbonyl)amino]-1-deoxy-2,3-*O*-isopropylidene-D-arabinitol 15

To a solution of compound **14** (250 mg, 0.68 mmol) in 90% MeOH was added Dowex 50W-X8 resin (200 g). The reaction mixture was stirred for 18 h at rt, then was filtered, and the filtrate was evaporated. The crude residue was chromatographed on silica gel [hexane–EtOAc (1:1, then 1:5)] to give *compound* **15** (211 mg, 95%) as a solid, $[\alpha]_D^{20}$ −17.8 (*c* 1.0, $CHCl_3$); δ_H 1.38 (6 H, m), 3.17 (1 H, s, OH), 3.51 (2 H, m), 3.65–3.70 (3 H, m), 3.80 (1 H, m), 3.90 (1 H, m), 4.10 (1 H, m), 5.11 (2 H, m) and 7.33 (5 H, m); δ_C 27.3, 27.4, 43.3, 64.6, 67.5, 73.4, 77.2, 77.4, 77.7, 79.3, 109.6, 128.5, 128.6, 128.9, 136.6 and 157.6 (Found: C, 58.6; H, 7.8; N, 3.9. $C_{16}H_{23}NO_6$ requires C, 59.1; H, 7.1; N, 4.3%).

1-[(Benzyloxycarbonyl)amino]-5-*O*-(*tert*-butyldimethylsilyl)-1-deoxy-2,3-*O*-isopropylidene-D-arabinitol 16

To a solution of diol **15** (133 mg, 0.41 mmol) in dry DMF (5 cm^3) were added imidazole (31 mg, 0.45 mmol) and TBDMSCl (68 mg, 0.45 mmol) at rt. After stirring of the mixture for 6 h, saturated aq. $NaHCO_3$ (10 cm^3) was added and the mixture was extracted with EtOAc (30 cm^3 × 3). The combined extracts were washed with brine, dried, and evaporated, and the residue was chromatographed on silica gel [hexane–EtOAc (6:1)] to give *compound* **16** (173 mg, 96%) as an oil, $[\alpha]_D^{20}$ −8.5 (*c* 1.0, $CHCl_3$); δ_H 0.00 (6 H, s), 0.82 (9 H, s), 1.28 (6 H, d), 3.39 (1 H, m), 3.47–3.58 (4 H, m), 3.72 (1 H, m), 3.96 (1 H, m), 5.02 (2 H, m) and 7.22 (5 H, m); δ_C −3.1, −3.0, 20.5, 28.1, 29.1, 29.2, 45.3, 66.4, 69.0, 75.2, 79.0, 79.2, 79.4, 79.5, 81.5, 111.2, 128.1, 130.2, 130.7 and 158.8 (Found: C, 59.6; H, 8.9; N, 3.1. $C_{22}H_{37}NO_6Si$ requires C, 60.1; H, 8.5; N, 3.2%).

1-[(Benzyloxycarbonyl)amino]-5-*O*-(*tert*-butyldimethylsilyl)-1-deoxy-2,3-*O*-isopropylidene-4-*O*-methylsulfonyl-D-arabinitol 5

To a solution of alcohol **16** (160 mg, 0.36 mmol) in THF (5 cm^3) were added triethylamine (36 mg, 0.43 mmol) and methanesulfonyl chloride (49 mg, 0.43 mmol) at 0 °C. After stirring of the mixture for 1 h at 0 °C, 5% aq. citric acid (20 cm^3) was added and the mixture was extracted with EtOAc (30 cm^3 × 3). The combined extracts were washed with brine, dried, and evaporated, and the residue was chromatographed on silica gel [hexane–EtOAc (4:1)] to give *compound* **5** (179 g, 96%) as an oil, $[\alpha]_D^{20}$ +11.3 (*c* 1.0, $CHCl_3$); δ_H 0.00 (6 H, s), 0.80 (9 H, s), 1.29 (6 H, s), 3.00 (3 H, s), 3.33 (1 H, m), 3.45 (1 H, m), 3.75 (1 H, dd, *J* 10 and 5) 3.81 (1 H, m), 3.87 (1 H, dd, *J* 10 and 3), 4.11 (1 H, m), 4.59 (1 H, m), 5.00 (2 H, d), 5.09 (1 H, s, NH) and 7.22 (5 H, m); δ_C 18.7, 26.3, 27.2, 27.5, 39.0, 43.4, 53.9, 63.1, 67.2, 75.9, 77.2, 82.4, 110.3, 128.49, 128.52, 128.9, 136.9 and 156.9 (Found: C, 52.8; H, 8.1; N, 2.8. $C_{23}H_{39}NO_8SSi$ requires C, 53.4; H, 7.6; N, 2.7%).

1,4-Dideoxy-1,4-imino-L-xylitol 2 and its hydrochloride salt

A solution of multi-protected compound **5** (180 mg, 0.35 mmol) and iodine (36 mg) in methanol (0.5 cm^3) was refluxed overnight, cooled to rt, and treated with Dowex 50W-8X (110 mg). The mixture was filtered, and then the residue was washed with MeOH (100 cm^3). The remaining residue was eluted with 3 mol dm^3 NH_4OH. The ammoniacal solution was evaporated, then co-evaporated with toluene to give *compound* **2** (29 mg, 63%) as a sticky oil, $\delta_H(D_2O)$ 2.38 (1 H, dd, *J* 12.6 and 1.4), 3.32 (1 H, dd, *J* 12.7 and 5.0), 3.41 (1 H, m), 3.67 (1 H, dd, *J* 11.4 and 7.2), 3.79 (1 H, dd, *J* 11.4 and 6.1), 4.12 (1 H, m) and 4.17 (1 H, m).

To the free base was added conc. HCl. The mixture was evaporated, then co-evaporated with toluene. The crystalline residue was recrystallised from methanol–diethyl ether to afford compound **2** as its hydrochloride salt. ^1H NMR data were consistent with those reported,[3f] mp 121–123 °C; $[\alpha]_D^{20}$ −4.3 (*c* 0.38, water) {lit.,[3e] mp 128–129 °C; $[\alpha]_D^{20}$ −9.9 (*c* 0.71, water)}; $\delta_C(D_2O$; 300 MHz) 52.6, 58.5, 63.9, 76.12 and 76.32 (Found: C, 35.1; H, 7.5; N, 7.9. $C_5H_{12}ClNO_3$ requires C, 35.4; H, 7.1; N, 8.3%).

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