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Note

An improved synthesis of D-perosamine and some derivatives

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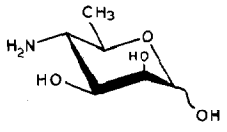
The family of 4-amino-4,6-dideoxy-D-hexoses, first discovered in antibiotics and in bacterial cell-wall[1–3], now includes at least seven configurationally distinct representatives[4–6]. Interest in the biological significance of these unstable monosaccharides and their naturally occurring derivatives has prompted much work on their chemistry[7–9]. One such sugar, 4-amino-4,6-dideoxy-D-mannose (D-perosamine, **1**), is also found *N*-formylated in α-(1→2)-glycosidic linkage as the



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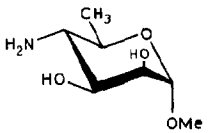

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principal structural component of O-antigenic polysaccharides in several Gram-negative organisms. Foremost among these are the pathogens *Vibrio cholera*[10], *Yersinia enterocolitica*[11], and *Brucella abortus*[12], which respectively cause cholera and acute gastroenteritis in man, and brucellosis in cattle. These findings not only establish a molecular basis for extensive cross-serological reactions documented in earlier studies, but also suggest an approach to the design of artificial vaccines and specific diagnostic reagents to combat these afflictions.

As part of our program to develop a new, totally synthetic, brucellosis vaccine, we now report an improved route to methyl α-D-perosinamide (**2**), culminating in the first total synthesis of D-perosamine hydrochloride (**1**·HCl). Our approach permits the attachment of various *N*-acyl substituents, and allows regiochemical differentiation for D-perosamine, of the hydroxyl groups required for the assembly of derived oligosaccharides.

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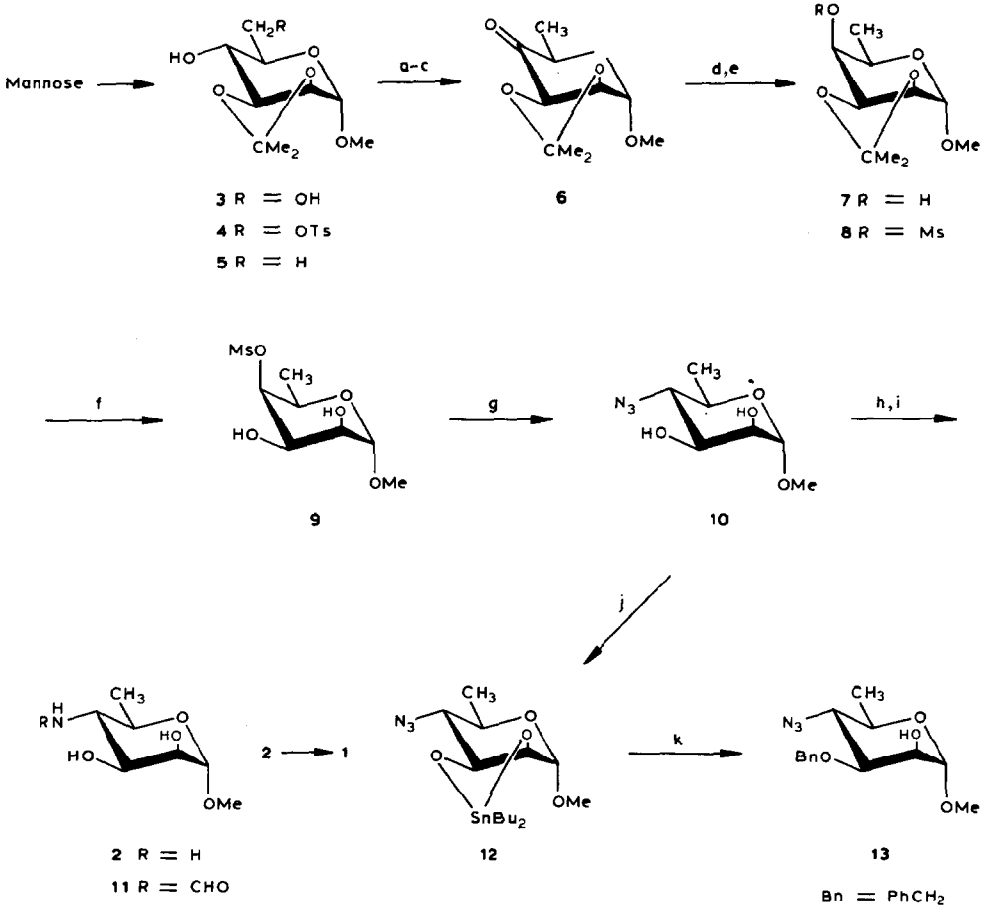
DISCUSSION

Previous routes to compound **2** used readily available monosaccharides as starting materials, but introduced the nitrogen substituent onto C-4 in unacceptably low yield. In the synthesis of L-**2** from L-rhamnose by Brimacombe *et al.*[8], methyl 6-deoxy-2,3-*O*-isopropylidene-4-*O*-(methylsulfonyl)-α-L-talopyranoside (the enantiomer of **8**) underwent replacement, by reaction with NaN_3, in only 14% yield. The synthesis by Stevens *et al.*[6b] of the natural enantiomer **2** from D-mannose relied on NaN_3 opening of methyl 3,4-anhydro-2-*O*-benzoyl-6-deoxy-α-D-talopyranoside (not shown), which afforded the desired 4-azido-4,6-dideoxy-α-D-manno-



Scheme 1. Synthesis of D-perosamine (**1**) and some derivatives. [key: (reagents, time, temperature, and yield) (a) TsCl, Et_3N, 24 h, 25°, 96%; (b) $LiAlH_4$, ether, 6 h, 30°, 100%; (c) oxalyl chloride, dimethyl sulfoxide, Et_3N, 1 h, −55 to 23°, 95%; (d) $NaBH_4$, 3.5:1 ethanol–water, 15 min, 25°, 98%; (e) MsCl, Et_3N, CH_2Cl_2, 2 h, 25°, 70%; (f) methanol–HCl, 5 h, 25° 100%; (g) NaN_3, dimethyl sulfoxide, 6 h, 100°, 93%; (h) H_2, Pd/C, methanol, 1.5 h, 25° 85%; (i) 2:1 ethyl formate–ethanol, 24 h, 85°, 91%; (j) Bu_2SnO, methanol 1 h, reflux; and (k) neat benzyl bromide, 10 h, 100°, 95%.]

pyranoside (**10**) in 20–43% yield[6b]. Our own synthetic sequence, depicted in Scheme 1, also utilizes D-mannose as the starting material, and it shares some features of both of the earlier routes. However, an improved process for amination of C-4, achieved in >90% yield, now makes possible the preparation of D-**2** in multigram quantities.

6-Tosylate **4** was prepared from methyl 2,3-*O*-isopropylidene-α-D-mannopyranoside[13] **3**, and converted into the known[6a] crystalline mesylate **8** by modification of the Stevens synthesis[6a]. Thus, **4** was reduced with $LiAlH_4$ to the known[4c] deoxy sugar **5** in high overall yield. Oxidation of **5** by the method of Swern *et al.*[14] with oxalyl chloride in Me_2SO furnished the 6-deoxyhexosid-4-ulose **6** in 95% yield. Reduction of **6** with sodium borohydride gave **7** as reported[6a,8] (98%), which was then converted into **8** (70%). In fact, **8** was virtually immune to nucleophilic attack by azide under a variety of conditions tested; however by the simple expedient of first removing the adjacent isopropylidene protecting group, the resultant mesylate **9** underwent normal replacement, with NaN_3 in Me_2SO at 100°, to afford azide **10** in 72% yield.

Compound **10** proved to be an extremely versatile intermediate for the synthesis of D-perosamine and its derivatives. Hydrogenation gave methyl α-D-perosaminide (**2**), which was readily formylated to give **11**, which is the repeating structural unit[12] in the *B. abortus* O-polysaccharide. Although earlier workers[6b] were unsuccessful in hydrolyzing **2** to its parent sugar, we found that treatment of this methyl glycoside with anhydrous HF followed by dilute aqueous HCl readily produced **1**·HCl *via* the intermediate glycosyl fluoride[9] (not shown).

To construct short α-(1→2)-linked oligomers of *N*-formylperosamine[15], the 3-hydroxyl group in **10** was selectively protected by using the elegant method of David *et al.*[16]. Benzylation of the stannylene derivative **12** furnished **13** in 95% overall yield from **10**.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover Unimelt apparatus and are uncorrected. Thin-layer chromatography was conducted on Merck precoated plates of silica gel 60F-254. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Infrared spectra were recorded with a Perkin–Elmer 681 spectrophotometer and are calibrated to polystyrene. ^{1}H-N.m.r. spectra were recorded at 300 MHz with a Bruker WM-300 spectrometer. Samples dissolved in $CDCl_3$ used $CHCl_3$ as the internal standard, and samples in D_2O or Me_2SO-d_6 used the HOD peak as internal reference. Chemical-ionization mass spectrometry (c.i.m.s.) using a computerized AEI-MS 902 instrument was performed with isobutane as the reagent gas.

Methyl 2,3-O-isopropylidene-6-O-p-tolylsulfonyl-α-D-mannopyranoside (**4**). — Diol **3** (17 g, 73 mmol)[13] was dissolved in CH_2Cl_2 (150 mL) under argon at 25° in a flame-dried, round-bottomed flask fitted with a magnetic stirring bar. Triethyl-

amine (13.1 mL, 94 mmol) was added, followed by solid TsCl (18 g, 94 mmol) in one portion. The resulting solution was stirred for 24 h at 25°. CH_2Cl_2 (250 mL) was added, and the solution was successively washed with saturated $NaHCO_3$ (5 × 100 mL) and H_2O (3 × 100 mL), dried ($MgSO_4$), and evaporated to a syrup. Chromatography on silica gel (hexane, and then 1:1 hexane–ethyl acetate) afforded tosylate **4** as a viscous oil (27 g, 96%); $[\alpha]_D$ +12.3° (*c* 2.75, CH_2Cl_2): R_F 0.36 in 1:1 hexane–EtOAc; ν_{max}^{film} 3450, 3060, 2940, 1740, 1600, 1450, 1360, 1245, 1220, 1190, 1175, 1090, and 960 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.79, 7.33 (4 H, tosyl), 4.82 (s, 1 H, H-1), 4.32–4.24 (m, 2 H, H-6,6'), 4.11–4.06 (m, 2 H, H-2,3), 3.72 (ddd, 1 H, *J* 3.7, 3.9, and 9.5 Hz, H-5), 3.60 (dd, 1 H, *J* 4.9, 9.5 Hz, H-4), 3.33 (s, 3 H, OCH_3), 2.43 (s, 3 H, tosyl-CH_3), and 1.46, 1.31 (2 s, each 3 H, CH_3); c.i.m.s. *m/z* 389 (M + 1, 2%) and 357 (M + 1 − H_2O, 100%).

Anal. Calc. for $C_{17}H_{24}O_8S$: C, 52.58; H, 6.19; S, 8.25. Found: C, 52.45; H, 6.31; S, 8.25.

*Methyl 6-deoxy-2,3-*O*-isopropylidene-α-*D*-mannopyranoside* (**5**). — A solution of tosylate **4** (27 g, 51 mmol) in Et_2O (500 mL) under argon in a flame-dried, three-necked flask fitted with a reflux condenser, thermometer, and magnetic stirring bar was cooled to 0° and $LiAlH_4$ (2.9 g, 77 mmol) was slowly added, with stirring. After 15 min, the ice bath was removed and the mixture allowed to warm to room temperature, but kept below 30°. After 6 h, the mixture was recooled in ice, and the reaction quenched with saturated aqueous oxalic acid (10 mL). The mixture was warmed to room temperature, stirred for 15 min, and then filtered. The solids were washed with fresh ether, and the filtrate and washings were combined, dried ($MgSO_4$), and evaporated. Chromatography on SiO_2 gel with 3:2 hexane–EtOAc afforded **5** (11 g, 100%) as a colorless syrup; $[\alpha]_D$ +16.4° (*c* 1.4, MeOH), lit.[4] $[\alpha]_D^{27}$ +15.2°; R_F 0.42 (1:1 hexane–EtOAc); ν_{max}^{film} 3460, 2940, 2910, 1455, 1385, 1340, 1240, 1220, 1170, 1140, and 1090 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.82 (bs, 1 H, H-1), 4.10 (d, 1 H, *J* 5.9 Hz, H-2), 4.04 (dd, 1 H, *J* 5.9, 6.9 Hz, H-3), 3.62 (dq, 1 H, *J* 6.3, 9 Hz, H-5), 3.37 (ddd, 1 H, *J* 4.5, 6.9, 9 Hz, H-4), 3.36 (s, 3 H, OCH_3), 1.51, 1.33 (2 s, each 3 H, CH_3), and 1.28 (d, 3 H, *J* 6.3 Hz, CH_3); c.i.m.s. *m/z* 219 (M + 1, 27%) and 187 (M + 1 − CH_3OH, 100%).

*Methyl 6-deoxy-2,3-*O*-isopropylidene-α-*D*-lyxo-hexopyranosid-4-ulose*[14] (**6**). — A solution of oxalyl chloride (5 mL, 55 mmol) in CH_2Cl_2 (125 mL) in a flame-dried vessel containing a magnetic stirring bar under argon was cooled to −55°. To it was added Me_2SO (8.5 mL, 110 mmol) in CH_2Cl_2 (25 mL) *via* a tube, and the solution stirred for 5 min at −55°. Alcohol **5** (11 g, 50.5 mmol) in CH_2Cl_2 (50 mL) was introduced *via* a tube, and the resultant, cloudy solution maintained for 0.5 h at −55°. Triethylamine (35 mL, 250 mmol) was added, and the mixture was warm allowed to room temperature during ~1 h. After quenching with H_2O (250 mL), the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 150 mL). The extracts were combined, successively washed with saturated brine (3 × 100 mL) and saturated $NaHCO_3$ (3 × 150 mL), dried ($MgSO_4$), and evaporated *in vacuo*, to afford **6** (10.3 g, 95%); $[\alpha]_D$ +100° (*c* 1.0, EtOH), lit.[9] $[\alpha]_D$ −105° for

the L enantiomer; R_F 0.7 in 1:1 hexane–EtOAc; ν_{max}^{film} 2940, 1745, 1450, 1385, 1375, 1225, 1160, 1135, 1090, and 1050 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.82 (s, 2 H, H-1), 4.42 (d, 1 H, *J* 6.7 Hz, H-2), 4.39 (d, 1 H, *J* 6.7 Hz, H-3), 4.22 (q, 1 H, *J* 6.8 Hz, H-5), 3.44 (s, 3 H, OCH_3), 1.46, 1.38 (d, 3 H, *J* 6.8 Hz, CH_3), and 1.34 (br. s, 6 H, 2 CH_3); c.i.m.s. *m/z* 219 (M + 1, 47%), and 127 (M + 1 − CH_3OH and Me_2CO, 100%).

*Methyl 6-deoxy-2,3-*O*-isopropylidene-α-*D*-talopyranoside* (**7**). — To a solution of **6** (12.3 g, 57 mmol) in 7:2 EtOH–H_2O (180 mL) at 0° was added $NaBH_4$ (1.5 g, 39.6 mmol). After stirring for 15 min at 0° and 15 min at 25°, the reaction was quenched with acetone (10 mL), and the mixture evaporated under diminished pressure at 50° to a syrup which was dissolved in CH_2Cl_2 (500 mL), and the solution washed successively with saturated $NaHCO_3$ (3 × 150 mL) and H_2O (3 × 150 mL), and dried ($MgSO_4$). Chromatography on silica gel in 7:3 hexane–EtOAc afforded **7** as a syrup (12.1 g, 98%); $[\alpha]_D$ +48.9° (*c* 1.3, MeOH); lit.[8] $[\alpha]_D$ −49° for the L enantiomer; R_F 0.44 in 1:1 hexane–EtOAc; ν_{max}^{film} 3520, 2940, 1450, 1380, 1370, 1255, 1215, 1150, 1080, and 1050 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.91 (s, 1 H, H-1), 4.18 (dd, 1 H, *J* 5.1, 6.2 Hz, H-3), 4.01 (d, 1 H, *J* 6.2 Hz, H-2), 3.81 (q, 1 H, *J* 6.6 Hz, H-5), 3.54 (dd, 1 H, *J* 5.5, 6.4 Hz, H-4), 3.38 (s, 3 H, OCH_3), 1.57, 1.36 (2 s, each 3 H, 2 CH_3), and 1.31 (d, 3 H, *J* 6.6 Hz, CH_3); c.i.m.s. *m/z* 219 (M + 1, 5%) and 187 (M + 1 − CH_3OH, 100%).

*Methyl 6-deoxy-2,3-*O*-isopropylidene-4-*O*-(methylsulfonyl)-α-*D*-talopyranoside* (**8**). — To a solution of **7** (12 g, 55 mmol) in CH_2Cl_2 (165 mL) at 0° were added triethylamine (15.3 mL, 110 mmol) and methanesulfonyl chloride (8.5 mL, 110 mmol). After stirring for 10 min at 0° and for 2 h at 25°, the reaction was quenched with saturated $NaHCO_3$ (10 mL), and the mixture stirred for 0.5 h. Dichloromethane (300 mL) was added, and the aqueous phase was separated. The organic phase was successively washed with saturated $NaHCO_3$ (3 × 100 mL), saturated $CuSO_4$ solution (4 × 100 mL), and H_2O (3 × 100 mL), dried ($MgSO_4$), and evaporated, to afford 14.2 g of impure mesylate which crystallized from 1:4 ethanol–hexane, to give 11.4 g (70%) of pure **8**; m.p. 115–117°, lit.[6a] m.p. 116–117.5°, $[\alpha]_D$ +19.0° (*c* 0.8, MeOH), lit.[6a] $[\alpha]_D$ −20.2°; R_F 0.37 in 1:1 EtOAc–hexane; ν_{max}^{film} 2950, 1465, 1350, 1250, 1215, 1180, 1160, 1145, 1090, and 1040 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): 4.86 (br. s, 1 H, *J* 1.1 Hz, H-1), 4.62 (dd, 1 H, *J* 1.1, 6.5 Hz, H-2), 4.36 (dd, 1 H, *J* 5.6, 6.5 Hz, H-3), 4.04 (dd, 1 H, *J* 2.1, 5.6 Hz, H-4), 3.95 (dq, 1 H, *J* 2.1, 6.7 Hz, H-5), 3.38 (s, 3 H, OCH_3), 3.07 (s, 3 H, mesyl-CH_3), 1.58, 1.34 (2 s, each 3 H, CH_3), and 1.35 (d, 3 H, *J* 6.7 Hz, CH_3); c.i.m.s. *m/z* 297 (M + 1, 63%) and 265 (M + 1 − CH_3OH, 100%).

*Methyl 6-deoxy-4-*O*-(methylsulfonyl)-α-*D*-talopyranoside* (**9**). — To a solution of **8** (13.5 g, 45.6 mmol) in anhydrous MeOH (500 mL) was added saturated, methanolic HCl (10 mL), and the mixture was stirred for 5 h at 25°, and evaporated under diminished pressure at 20°, to afford crystalline **9** (11.7 g, 100%). A portion was recrystallized from 1:1 ether–pentane; m.p. 102–104°, $[\alpha]_D$ −95.7° (*c* 1.0, MeOH); R_F 0.18 in 2:1 EtOAc–hexane; ν_{max}^{KBr} 3500, 2940, 1340, 1170, 1130, 1100,

1065, and 1020 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.77 (d, 1 H, *J* 1.8 Hz, H-1), 4.76 (dd, 1 H, *J* 1, 3.7 Hz, H-4), 4.00 (dq, 1 H, *J* 1, 6.6 Hz, H-5), 3.94 (ddd, 1 H, *J* 3.7, 3.7, 8.5 Hz, H-3), 3.71 (ddd, 1 H, *J* 1.8, 3.7, 11.1 Hz, H-2), 3.37 (s, 3 H, OCH_3), 3.16 (s, 3 H, mesyl-CH_3), and 1.33 (d, 3 H, *J* 6.6 Hz, CH_3); c.i.m.s. *m/z* 257 (M + 1, 23%), 239 (M + 1 − H_2O, 58%), and 225 (M + 1 − H_2O and CH_3OH, 100%).

Anal. Calc. for $C_8H_{16}O_7S$: C, 37.50; H, 6.25; S, 12.50. Found: C, 37.69; H, 6.44; S, 12.50.

*Methyl 4-azido-4,6-dideoxy-α-*D*-mannopyranoside* (**10**). — Mesylate **9** (15 g, 59 mmol) was stirred with NaN_3 (20 g, 295 mmol) in Me_2SO (150 mL) for 6 h at 100°. Most of the solvent was removed by distillation at 90°/67 Pa. The residue was suspended in CH_2Cl_2 (500 mL), and the suspension filtered through a pad of Celite. The filtrate was evaporated in a rotary evaporator to a final volume of 15 mL. Chromatography on a column of silica gel eluted with 3:2 hexane–EtOAc afforded crystalline **10** (8.6 g, 72%). A portion was recrystallized from hexane, to give needles; m.p. 83–84°, lit.[6b] m.p. 81.5–82.5°, $[\alpha]_D$ +131.8° (*c* 1.0, MeOH), lit.[6b] $[\alpha]_D$ +126.9°; R_F 0.45 in 2:1 EtOAc–hexane; ν_{max}^{KBr} 3860–3240, 2940, 2120 (N_3), 1465, 1370, 1290, 1265, 1200, 1140, 1100, 1070, and 1040 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.66 (d, 1 H, *J* 1.4 Hz, H-1), 3.89 (ddd, 1 H, *J* 1.4, 3.3, 4.4 Hz, H-2), 3.81 (ddd, 1 H, *J* 3.3, 6.6, 9.8 Hz, H-3), 3.55 (dq, 1 H, *J* 6.3, 10.5 Hz, H-5), 3.33 (s, 3 H, OCH_3), 3.26 (dd, 1 H, *J* 9.8, 10.5 Hz, H-4), and 1.33 (d, 3 H, *J* 6.3 Hz, CH_3); c.i.m.s. *m/z* 204 (M + 1, 5%) and 172 (M + 1 − CH_3OH, 100%).

*Methyl 4-amino-4,6-dideoxy-α-*D*-mannopyranoside* (**2**). — To a solution of **10** (1.22 g, 6 mmol) in MeOH (100 mL) was added 10% Pd-on-C (200 mg). Hydrogen was bubbled through an E-frit-tipped glass tube into the stirred solution for 1.5 h at 25°. The catalyst was filtered off through Celite, and the filtrate was evaporated *in vacuo*, to afford a solid which was recrystallized from 1:3 ethanol–ether, to give **2** as prisms (0.9 g, 85%); m.p. 150–152°, lit.[6b] m.p. 152–153°, $[\alpha]_D$ +83.2° (*c* 1.0, MeOH), lit.[6b] $[\alpha]_D$ +82.5°; R_F 0.73 in 7:4:1 $CHCl_3$–MeOH–33% NH_4OH; ν_{max}^{Nujol} 3500, 3340, 2740, 1450, 1400, 1380, 1355, 1240, 1120, 1100, and 1085 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 4.54 (br. s, 1 H, *J* 1.4 Hz, H-1), 3.68 (dd, 1 H, *J* 1.4, 3.3 Hz, H-2), 3.45 (dq, 1 H, *J* 6.3, 10 Hz, H-5), 3.41 (dd, 1 H, *J* 3.3, 9.9 Hz, H-3), 3.22 (s, 3 H, OCH_3), 2.56 (dd, 1 H, *J* 9.9, 10 Hz, H-4), and 1.11 (d, 3 H, *J* 6.3 Hz, CH_3); c.i.m.s. *m/z* 178 (M + 1, 88%) and 146 (M + 1 − CH_3OH, 100%).

D-(−)-*Perosamine* (**1**). — In a 29.6-mL (1-oz.) polypropylene bottle fitted with a screw cap and a Teflon-coated, magnetic stirring bar was placed 200 mg (1.13 mmol) of compound **2**. The apparatus was cooled to −78°, and anhydrous HF (5 mL) was rapidly transferred into it *via* a polypropylene syringe fitted with a teflon needle. The bottle was capped, warmed to room temperature, and the mixture stirred for 1.5 h, after which time, the HF was removed under a stream of argon. The resulting, pale-yellow gum was stored at 13.3 Pa for 12 h, whereupon it solidified. The solid was dissolved in distilled water (100 mL), the solution treated with Norit (50 mg), the suspension filtered through a pad of Celite, and the filtrate lypophilized. The crude α-glycosyl fluoride was ground to a fine powder, trans-

ferred to a 100-mL, round-bottomed flask fitted with a stirring bar, dissolved in water (30 mL), and the pH adjusted to 1 with M HCl (~5 mL). The solution was stirred for 24 h at room temperature, diluted to 100 mL with water, and lyophilized, to afford pure D-(−)-perosamine hydrochloride (220 mg, 98%) as an amorphous mixture of anomers; $[\alpha]_D^{23}$ −23° (*c* 1.3, H_2O), lit.[3] $[\alpha]_D^{23}$ −20° (*c* 1.3, H_2O); β anomer: ^{1}H-n.m.r. (D_2O): δ 4.74 (d, 1 H, *J* 1 Hz, H-1), 4.02 (dq, 1 H, *J* 6.4, 10.4 Hz, H-5), 3.86 (dd, 1 H, *J* 3.3, 10.4 Hz, H-3), 3.78 (dd, 1 H, *J* 1.7, 3.3 Hz, H-2), 3.01 (t, 1 H, *J* 10.4 Hz, H-4), and 1.18 (d, 3 H, *J* 6.4 Hz, CH_3); α anomer: δ 5.01 (d, 1 H, *J* 1.7 Hz, H-1), 3.82 (dd, 1 H, *J* 3.2 Hz, H-2), 3.68 (dd, 1 H, *J* 3.2, 10.2 Hz, H-3), 3.57 (dq, 1 H, *J* 6.3, 10.2 Hz, H-5), 2.92 (t, 1 H, *J* 10.2 Hz, H-4), and 1.21 (d, 3 H, *J* 6.3 Hz, CH_3); c.i.m.s. *m/z* 164 (M + 1, 6%), 146 (M + 1 − H_2O, 12%), and 112 (100%).

Methyl 4,6-dideoxy-4-formamido-α-D-mannopyranoside (**11**). — A solution of compound **2** (200 mg, 1.13 mmol) in EtOH (4 mL) was diluted with ethyl formate (12 mL), refluxed for 24 h at 85°, cooled, and evaporated under diminished pressure. Chromatography on silica gel, using 9:1 $CHCl_3$–MeOH, followed by recrystallization from 1:8 ethanol–ether, gave **11** (210 mg, 91%); m.p. 173–174°, $[\alpha]_D$ +82.7° (*c* 1.0, MeOH); R_F 0.36 in 9:1 $CHCl_3$–MeOH; ν_{max}^{KBr} 3420, 3320, 2940, 2760, 1670, 1535, 1450, 1405, 1390, 1320, 1300, and 1130 cm^{-1}; ^{1}H-n.m.r. (Me_2SO-d_6) revealed two rotational isomers; major: δ 8.06 (s, 1 H, CHO), 7.85 (d, 1 H, *J* 11.3 Hz, NH), 4.47 (br. s, 1 H, H-1), 3.74 (q, 1 H, *J* 10 Hz, H-4), 3.60–3.45 (m, 3 H, H-2,3,5), 3.23 (s, 3 H, OCH_3), 1.04 (d, 3 H, *J* 6.2 Hz, CH_3); minor: δ 7.85 (d, 1 H, *J* 11.3 Hz, CHO), 7.48 (dd, 1 H, *J* 9.2, 11.3 Hz, NH), 4.47 (br. s, 1 H, H-1), 3.60–3.45 (m, 3 H, H-2,3,5), 3.30 (s, 3 H, OCH_3), 3.07 (q, 1 H, *J* 10 Hz, H-4), and 1.09 (d, 3 H, *J* 6.2 Hz, CH_3); c.i.m.s. *m/z* 206 (M + 1, 37%), 174 (M + 1 − CH_3OH, 100%), and 156 (M + 1 − CH_3OH and H_2O, 100%).

Anal. Calc. for $C_8H_{15}NO_5$: C, 46.83; H, 7.32; N, 6.83. Found: C, 46.87; H, 7.55; N, 6.71.

Methyl 4-azido-3-O-benzyl-4,6-dideoxy-α-D-mannopyranoside (**13**). — To a solution of compound **10** (203 mg, 1 mmol) in anhydrous MeOH (25 mL) was added dibutyltin oxide (249 mg, 1 mmol). The stirred suspension became a clear solution after boiling for 1 h under reflux. The solvent was evaporated under diminished pressure, and the crude stannylene compound **12** was dried under high vacuum for 2 h. The residue was dissolved in benzyl bromide (2 mL), and the clear solution was stirred for 10 h at 100°. Solvent was removed, *via* Kugelrohr, at 1.07 to 1.33 kPa, and the crude material was chromatographed twice on silica gel using 3:2 hexane–EtOAc, to afford **13** (277 mg, 95%) as a colorless syrup, $[\alpha]_D$ +134° (*c* 1.0, MeOH); ν_{max}^{film} 3460, 2940, 2110 (N_3), 1500, 1455, 1380, 1370, 1285, 1130, 1100, and 1065 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.40–7.26 (m, 5 H, benzyl), 4.67, 4.65 (AB q, 2 H, *J* 11.4 Hz, $PhCH_2$), 4.69 (d, 1 H, *J* 1.6 Hz, H-1), 3.96 (ddd, 1 H, *J* 1.6, 1.9, 3.2 Hz, H-2), 3.69 (dd, 1 H, *J* 3.2, 9.6 Hz, H-3), 3.50 (dq, 1 H, *J* 4.1, 6.1 Hz, H-5), 3.38 (dd, 1 H, *J* 4.1, 9.6 Hz, H-4), 3.33 (s, 3 H, OCH_3), and 1.31 (d, 3 H, *J* 6.1 Hz, CH_3); c.i.m.s. *m/z* 266 (M + 1 − N_2, 27%), 234 (M + 1 − N_2 and CH_3OH, 48%), and 222 (100%).

Anal. Calc. for $C_{14}H_{19}N_3O_4$: C, 57.34; H, 6.48; N, 14.33. Found: C, 57.38; H, 6.66; N, 14.67.

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