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SYNTHESIS OF 2-AMINO-2-DEOXY- AND 3-AMINO-3-DEOXY-α-D-MANNOPYRANOSYL α-D-MANNOPYRANOSIDE BY SEQUENTIAL OSMYLATIONS OF A DIENIC DISACCHARIDE

HANS H. BAER AND LISA SIEMSEN

Ottawa-Carleton Institute for Research and Graduate Studies in Chemistry, Department of Chemistry, University of Ottawa, Ottawa, Ontario K1N 9B4 (Canada)

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ABSTRACT

Partial oxyamination of 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside with chloramine-T and osmium tetraoxide gave 4,6-di-*O*-acetyl-2-deoxy-2-(*p*-toluenesulfonamido)-α-D-mannopyranosyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside and its 3-deoxy-3-(*p*-toluenesulfonamido) regioisomer, each in 18–19% isolated yield. Osmium tetraoxide-catalyzed *cis*-hydroxylation of the remaining alkenic residue in these products led in high yields to the corresponding triols having the α-D-*manno*,α-D-*manno* configuration. These were *N*-desulfonylated (and simultaneously *O*-deacetylated) by the action of sodium in liquid ammonia to furnish 2-amino-2-deoxy-α-D-mannopyranosyl α-D-mannopyranoside and 3-amino-3-deoxy-α-D-mannopyranosyl α-D-mannopyranoside as new, trehalose-type amino sugars.

INTRODUCTION

We have recently described[1] the preparation of 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1**) and its osmium tetraoxide-catalyzed *cis*-oxyamination with chloramine-T, which furnished the 2,2′-, 2,3′-, and 3,3′-diamino derivatives of α-D-mannopyranosyl α-D-mannopyranoside. A small proportion (10%) of monoaminated, unsaturated material resulting from incomplete reaction of **1** was usually present in the crude product, and separated from it by column chromatography but not examined more closely. Assuming that this material consisted of the 2-*p*-toluenesulfonamido disaccharide **2** and (or) its regioisomer **5**, we decided to characterize it more fully and to utilize it, if possible, for the preparation of the hitherto unknown 2-, or 3-monoamino, or both derivatives of α-D-mannopyranosyl α-D-mannopyranoside. The parent disaccharide has recently attracted attention as a substitute for α,α-trehalose in the synthesis of cord factor analogs[2] that may serve as probes in the field of mycobacterial biochemistry. Furthermore, the isomeric

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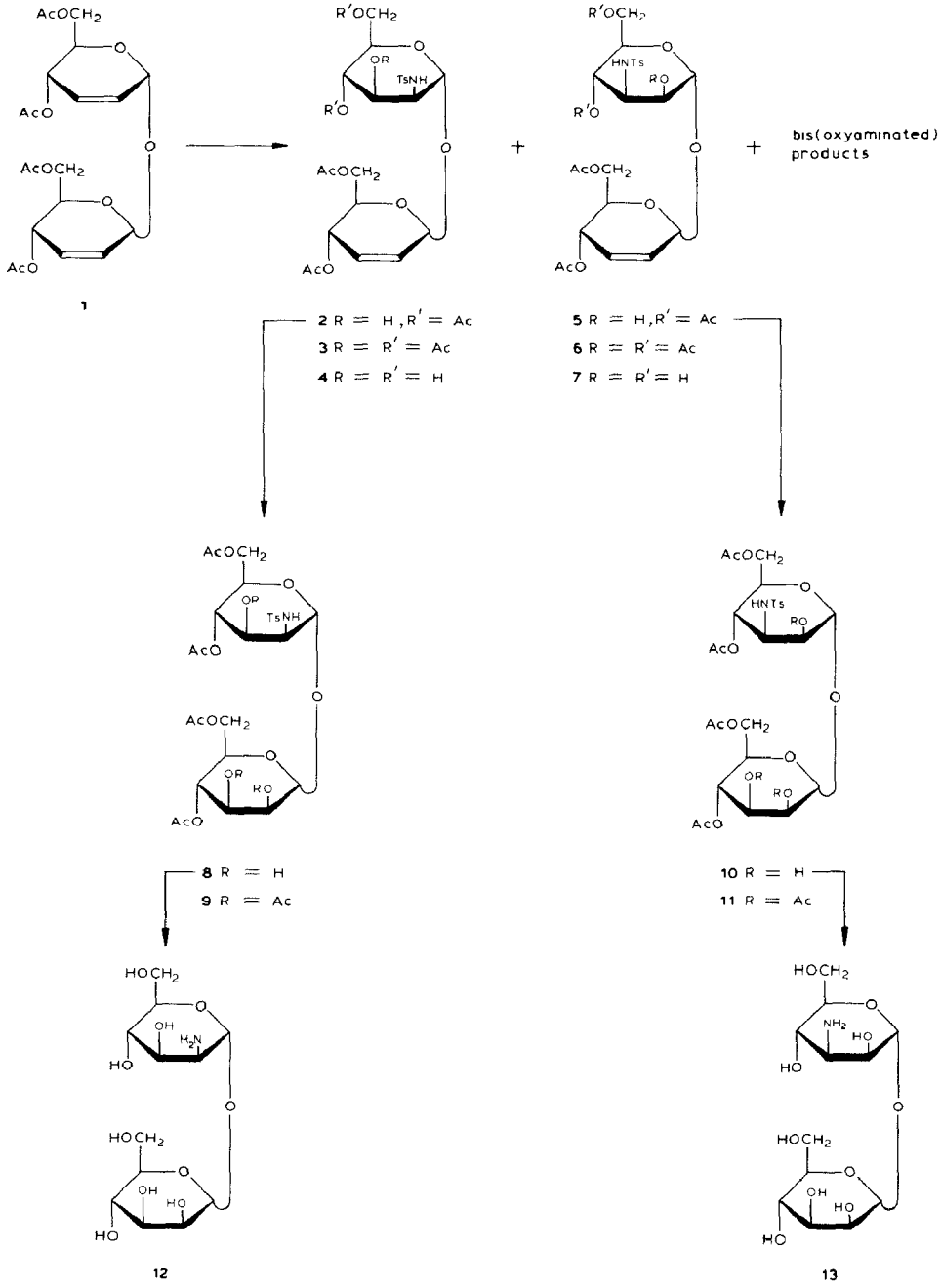
AcOCH2
AcO
R'OCH2
OR
TsNH
R'O
HNTs
RO
+
bis(oxyaminated) products
1
2 R = H, R' = Ac
3 R = R' = Ac
4 R = R' = H
5 R = H, R' = Ac
6 R = R' = Ac
7 R = R' = H
OP
8 R = H
9 R = Ac
10 R = H
11 R = Ac
HOCH2
OH
H2N
HO
NH2
12
13

amino sugars 2-amino-2-deoxy-α-D-glucopyranosyl α-D-glucopyranoside (trehalosamine)[3], 2-amino-2-deoxy-α-D-glucopyranosyl α-D-mannopyranoside[4], and 3-amino-3-deoxy-α-D-glucopyranosyl α-D-glucopyranoside[5,6], which occur as actinomycetal metabolites, have been reported to show antibiotic activity. In view of these observations, it appeared worthwhile to make the title disaccharides **12** and **13** available by synthesis, for eventual study of their biological potentialities.

RESULTS AND DISCUSSION

At the outset, several attempts were made to modify the conditions of oxyamination of **1** with the aim of increasing the proportion of isolable, monooxyaminated products. This was only moderately successful inasmuch as the use of one molar equivalent of chloramine-T invariably gave mixtures of unreacted **1** (fast-moving in t.l.c.), the three slow-moving, bis(oxyaminated) compounds previously[1] obtained, and the partially unsaturated derivatives now desired. Nevertheless, these could be readily separated by chromatography, and the derivatives **2** and **5** having intermediate mobilities (R_F 0.6 and 0.5) and arising in combined yields of 36–42% could each be isolated pure in nearly equal proportions (18–19%). For characterization by physical and spectroscopic data, the two products were converted into the pentaacetates **3** and **6**, both crystalline. Further characterization was provided by saponification of a mixture of **2** and **5**, followed by separation of the crystalline, *O*-deacetylated compounds **4** and **7**.

The enosides **2** and **5** were *cis*-hydroxylated under osmium tetraoxide catalysis in the presence of either *N*-methylmorpholine-*N*-oxide[7] or trimethylamine-*N*-oxide[8]. The former procedure furnished the partially acetylated tosylamido disaccharides **8** and **10** in 85–90% yields, but the reactions required 8 days at 50° for completion, whereas the latter procedure gave **8** and **10** in yields of 86 and 76%, respectively, after reaction times of 1–2 days at 40°. Both compounds were characterized by their ^{1}H-n.m.r. spectra and those of their peracetylated derivatives **9** and **11**.

N-Desulfonylation with concomitant *O*-deacetylation of **8** and **10** was performed by treatment with sodium in liquid ammonia, as described[1] for their bis(tosylamido) analogs, to give the amino disaccharides **12** and **13** as amorphous powders in yields of 68 and 83%, respectively. The product from the second sequence gave i.r. and ^{1}H-n.m.r. spectra identical with those of **13** concurrently synthesized[9] by an independent, stereospecific route. For additional confirmation, a sample of the latter amine was converted into its fully *O*-acetylated *N*-tosyl derivative, which proved identical with **11** from the present synthesis. Since osmylation is controlled by steric approach and occurs in six-membered cyclic systems exclusively on the face of the olefinic double bond opposite to that of preexisting allylic substituents[10], *i.e.*, from the less hindered side, it was concluded that **2** and the succeeding derivatives, including **12**, must have the same configurations as, and hence be 2-aminated regioisomers of, **5** and its derived products.

EXPERIMENTAL

General methods. — General preparative, chromatographic, and instrumental methods were the same as those previously described[1]. Unless otherwise stated, the following solvent combinations (v/v) were used for t.l.c. and in column chromatography: (*A*) 1:2 ethyl acetate–hexane, (*B*) the same solvents, but 1:1.5, (*C*) the same, but 1:1, (*D*) the same, but 1.5:1, (*E*) the same, but 4:1, (*F*) 1:4 methanol–chloroform, and (*G*) 6:3:1 methanol–chloroform-conc., aqueous NH_3. Specific rotations were measured at ~25°. The ^{1}H-n.m.r. data refer to 300-MHz spectra recorded with reference to the chloroform lock signal (δ 7.23), unless otherwise indicated (Varian XL 300 instrument).

Partial oxyamination of **1**. *4,6-Di-O-acetyl-2-deoxy-2-(p-toluenesulfonamido)-α-D-mannopyranosyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside* (**2**) *and 4,6-di-O-acetyl-3-deoxy-3-(p-toluenesulfonamido)-α-D-mannopyranosyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside* (**5**), *and their peracetyl derivatives* **3** *and* **6**. — To a solution of diene[1] **1** (4.42 g, 10 mmol) in *tert*-butyl alcohol (175 mL) at 50° was added freshly prepared chloramine-T trihydrate (2.82 g, 10 mmol) followed by $AgNO_3$ (6.5 g), and the mixture was stirred for 30 min. An 80mM solution of OsO_4 in alkene-free hexane (3 mL) was then added, and stirring was continued at 40° for 19 h. The t.l.c. (solvent *D*) then showed remnant **1** (R_F 0.7) and u.v.-reactive spots having R_F 0.4, 0.3, and 0.1–0.2. Heating of the mixture for a further 3 h did not change this pattern. Processing with $NaHSO_3$, and isolation of the organic material as described for the full oxyamination[1] gave a mixture of syrupy compounds. Fractionation by l.c. (Waters Associates PrepPak–500/Silica column, with solvent *B* as the eluant) produced unchanged **1** (1.02 g, 23% recovery), **2** (1.0 g, 16%), **5** (1.26 g, 20%), and mixtures of bis(oxyaminated) products (1.80 g, 22%), in that order.

A similar experiment using **1** (5.45 g), chloramine-T trihydrate (3.50 g), $AgNO_3$ (8.0 g), and catalyst solution (3.7 mL) gave **1** (1.45 g, 26.6%), **2** (1.45 g, 18.7%), **5** (1.50 g, 19.3%), and a mixed fraction of **2** and **5** (0.30 g, 3.9%) after product separation by medium-pressure chromatography on silica gel (solvent *C*). Isolation of the slow-moving, bis(oxyaminated) products was dispensed with.

Compounds **2** (R_F 0.4) and **5** (R_F 0.3) were obtained as colorless, dry foams that would not crystallize.

^{1}H-N.m.r. data for **2** ($CDCl_3$): δ 7.76 and 7.29 (AB-q, arom.), 5.92 (dnm, $J_{2',3'}$ 10, $J_{3',4'}$ ~2, $J_{1',3'}$ ~ −1 Hz, H-3'), 5.70 (ddd, $J_{2',3'}$ 10, $J_{1',2'}$ 3, $J_{2',4'}$ −2 Hz, H-2'), 5.28 (dnq, $J_{3',4'} \approx J_{1',4'} \approx -J_{2',4'} \approx 2$ Hz, $J_{4',5'}$ 9.5 Hz, H-4'), 5.21 (d, $J_{2,NH}$ 8.5 Hz, NH-2), 5.17 (nm, H-1'), 4.97 (d, $J_{1,2}$ 1.6 Hz, H-1), 4.82 (t, $J_{3,4} = J_{4,5} = 10$ Hz, H-4), 4.15 (two overlapping dd, *J* 5.5 and 12.5 Hz, H-6$_A$,6$'_A$), 4.1–3.8 (m, 5 H, H-6$_B$,6$'_B$,5,5',3), 3.69 (ddd, $J_{1,2}$ 1.6, $J_{2,3}$ 4.5, $J_{2,NH}$ 8.5 Hz, H-2), 2.39 (s, 3 H, *Ph*-Me), 2.09, 2.07, 2.06, and 2.04 (s, 4 × 3 H, OAc).

^{1}H-N.m.r. data for **5** ($CDCl_3$): δ 7.73 and 7.28 (AB-q, arom.), 5.97 (dnm, $J_{2',3'}$ 10.5, $J_{3',4'}$ ~2, $J_{1',3'}$ ~ −1 Hz, H-3'), 5.77 (ddd, $J_{2',3'}$ 10.5, $J_{1',2'}$ 3, $J_{2',4'}$ −2 Hz,

H-2′), 5.31 (dnq, $J_{3',4'} \approx J_{1',4'} \approx -J_{2',4'} \approx 2$ Hz, $J_{4',5'} \sim 10$ Hz, H-4′), 5.27 (nm, H-1′), 5.24 (d, $J_{3,NH}$ 8.5 Hz, NH-3), 5.16 (d, $J_{1,2}$ 1.6 Hz, H-1), 4.96 (t, $J_{3,4} = J_{4,5} =$ 10 Hz, H-4), 4.19 (two overlapping dd, $J \sim 5$–6 and 13 Hz, H-6_A,$6'_A$), 4.10–3.85 (m, 4 H, H-6_B,$6'_B$,5,5′), 3.82 (m, 2 H, H-2,3), 2.39 (s, 3 H, Ph-CH_3), 2.11, 2.03, 2.01 (s, 3 × 3 H, OAc), and 1.69 (s, 3 H, AcO-4, strongly shielded by TsNH-3).

A sample of **2** (1.0 g) was acetylated (acetic anhydride–pyridine) at 0° overnight, giving after customary work-up the peracetyl derivative **3** (0.80 g, 75%) as a white, slightly impure (t.l.c.) material that was purified on a silica gel column (solvent *C*) and subsequently crystallized from ethanol. The crystals contained ethanol of crystallization (~1/3 mol, by n.m.r.), m.p. 71–73°, $[\alpha]_D^{25}$ +63.2° (*c* 0.6, chloroform); *m/z* (c.i., ether): 672 ($M^+ + 1$); ^{1}H-n.m.r. ($CDCl_3$; assignments aided by HOMCOR method): δ 7.72 and 7.27 (AB-q, arom.), 5.92 (dnm, $J_{2',3'}$ 10.5, $J_{3',4'}$ ~2, $J_{1',3'} \sim -1$ Hz, H-3′), 5.71 (dt, $J_{2',3'}$ 10.5, $J_{1',2'} \approx -J_{2',4'} \approx 2.4$ Hz, H-2′), 5.30 (dnm, $J_{4',5'}$ 9.4 Hz, H-4′), 5.18 (d, $J_{2,NH}$ 8.8 Hz, NH-2), 5.16 (nm, H-1′), 5.13 (dd, $J_{2,3}$ 4.2, $J_{3,4}$ 10 Hz, H-3), 5.08 (t, $J_{3,4} = J_{4,5} = 10$ Hz, H-4), 5.01 (d, $J_{1,2}$ 1.6 Hz, H-1), 4.22–4.15 (m, 2 H, H-6_A,$6'_A$), 4.02–3.87 (m, 4 H, H-6_B,$6'_B$,5,5′), 3.84 (ddd, $J_{2,NH}$ 8.8, $J_{1,2}$ 1.6, $J_{2,3}$ 4.2 Hz, H-2), 2.36 (s, 3 H, Ph-CH_3), 2.07, 2.06, 2.04, 1.96 (s, 4 × 3 H, OAc), and 1.71 (s, 3 H, AcO-3, shielded by TsNH-2).

Anal. Calc. for $C_{29}H_{37}NO_{15}S$ (671.7): C, 51.86; H, 5.55; N, 2.09. Found: C, 51.76; H, 5.80; N, 2.05 (for ethanol-free sample).

A sample of **5** (620 mg) was acetylated like **2**. The crude **6** (660 mg, 100%) appeared homogeneous in t.l.c. but could be crystallized, from ethanol, only after passage through a small silica gel column (with solvent *A*). It then contained ethanol of crystallization, m.p. 64–66°, $[\alpha]_D^{25}$ +60.1° (*c* 0.8, chloroform); *m/z* (c.i., ether): 672 ($M^+ + 1$); ^{1}H-n.m.r. ($CDCl_3$; assignments aided by HOMCOR method): δ 7.68 and 7.27 (AB-q, arom.), 5.96 (dnm, $J_{2',3'}$ 10.3, $J_{3',4'}$ ~2, $J_{1',3'} \sim -1$ Hz, H-3′), 5.76 (ddd, $J_{2',3'}$ 10.3, $J_{1',2'}$ 2.8, $J_{2',4'}$ −2.0 Hz, H-2′), 5.28 (dnm, $J_{4',5'}$ 9.7, $J_{3',4'}$ 2, $J_{1',4'}$ ~1.5, $J_{2',4'}$ −2 Hz, H-4′), 5.22 (nm, H-1′), 5.16 (d, $J_{1,2}$ 1.6 Hz, H-1), 4.97 (d, $J_{3,NH}$ 9.5 Hz, NH-3), 4.96 (t, $J_{3,4} = J_{4,5} = 10.3$ Hz, H-4), 4.60 (dd, $J_{1,2}$ 1.65, $J_{2,3}$ 3.35 Hz, H-2), 4.22–4.15 (m, 2 H, H-6_A,$6'_A$), 4.10–3.90 (m, 4 H, H-6_B,$6'_B$,5,5′), 3.91 (td, $J_{2,3}$ 3.4, $J_{3,4} \approx J_{3,NH} \approx 10$ Hz, H-3), 2.37 (s, 3 H, Ph-CH_3), 2.09, 2.05, 2.02, 2.00 (s, 4 × 3 H, OAc), and 1.77 (s, 3 H, AcO-4, shielded by TsNH-3).

Anal. Calc. for $C_{29}H_{37}NO_{15}S$ (671.7): C, 51.86; H, 5.55; N, 2.09. Found: C, 51.70; H, 5.79; N, 2.05 (for ethanol-free sample).

*2-Deoxy-2-(*p*-toluenesulfonamido)-* (**4**) *and 3-deoxy-3-(*p*-toluenesulfonamido)-α-*D*-mannopyranosyl 2,3-dideoxy-α-*D*-*erythro*-hex-2-enopyranosides* (**7**). — In order to determine whether the oxyamination products might be separable without recourse to chromatography if they were first deacetylated, and also to provide additional characterization, a mixture (2.33 g) containing comparable proportions of **2** and **5** was saponified by the Zemplén method with sodium methoxide (336 mg) in methanol (100 mL). After 15 min, t.l.c. (solvent *F*) indicated the complete replacement of the fast-moving starting material (R_F 0.85) by slow-moving products (R_F 0.35), and after de-ionization with methanol-washed Amberlite IR-120 (H^+)

cation-exchange resin followed by evaporation of the solution, a white foam (**4** and **7**) was obtained in quantitative yield (1.70 g). Traces of fast-moving impurities were readily removed by column chromatography using ethyl acetate as the eluant, but direct crystallization could not be induced, and chromatographic separation of **4** and **7** proved exceedingly difficult owing to their similar mobilities. Nevertheless, fractions enriched in either component were eventually obtained, and from such fractions were obtained samples of pure **4** and **7** by fractional crystallization from combinations of acetone (or ethanol) and ether (or ethyl acetate).

The marginally more-mobile component (in t.l.c. with solvent *E*) was obtained as crystals, m.p. 176–177°, sparingly soluble in cold water or acetone, and proved to be **4**; $[\alpha]_D^{25}$ +103° (*c* 0.5, water), +44° (*c* 0.25, acetone); ^{1}H-n.m.r. [($^2H_6$)acetone-Me_4Si]: δ 7.81 and 7.38 (AB-q, arom.), 5.96 (dd, $J_{2',3'}$ 10.3, $J_{1',3'}$ −1.2 Hz, with $J_{3',4'}$ close to zero, H-3'), 5.69 (dt, $J_{2',3'}$ 10.3, $J_{1',2'} \approx -J_{2',4'} \approx 2.2$ Hz, H-2'), 5.20 (nm, 2 H, H-1,1'), 4.13 (m, reduced to dd after D_2O exchange, $J_{2',4'} \sim -2$, $J_{4',5'}$ 10 Hz, H-4'), 3.83 (dd, *J* 4.5 and 9 Hz, H-3), 3.75–3.55 (m, 7 H, unresolved), 3.44 (dd, $J_{1,2}$ 1.5, $J_{2,3}$ 4.6 Hz, H-2), and 2.42 (s, 3 H, Ph-CH_3). Signals removable by D_2O exchange occurred at δ 4.2, 4.0, and 2.9.

Anal. Calc. for $C_{19}H_{27}NO_{10}S$ (461.5): C, 49.95; H, 5.90; S, 6.95. Found: C, 49.55; H, 5.87; S, 6.73.

To prove that the foregoing product did in fact originate from **2**, a sample was peracetylated (acetic anhydride–pyridine) and, then, gave a 300-MHz, ^{1}H-n.m.r. spectrum identical with that of **3** (and clearly different from that of **6**), except that the 8.8-Hz doublet for NH-2 was shifted upfield by 0.25 p.p.m., possibly due to a concentration effect.

The other component (**7**) was obtained as a crystalline hemi-hydrate, m.p. 134–135°, with slight sintering at 115–120°; $[\alpha]_D^{25}$ +58° (*c* 0.4, water), +52° (*c* 0.4, acetone); ^{1}H-n.m.r. [($^2H_6$)acetone-Me_4Si]: δ 7.83 and 7.39 (AB-q, arom.), 6.00 (dnm, $J_{2',3'}$ 10 Hz, H-3'), 5.75 (ddd, H-2'), 5.26 (nm, H-1'), 5.07 (d, $J_{1,2}$ 2 Hz, H-1), 4.07 (m, H-4'), 3.8–3.5 (m, 8 H, unresolved), 3.47 (nm, H-2), and 2.42 (s, 3 H, PhCH_3). Signals removable by D_2O exchange were present at δ 4.3, 3.9, and 2.9.

Anal. Calc. for $C_{19}H_{27}NO_{10}S \cdot 0.5\ H_2O$ (470.5): C, 48.50; H, 6.00; S, 6.81. Found: C, 48.57; H, 5.82; S, 6.71.

A sample of **7** was peracetylated (acetic anhydride–pyridine) and then gave a 300-MHz ^{1}H-n.m.r. spectrum completely superposable on that of **6**, except that in this case, too, the doublet for N–H ($J_{3,NH}$ 9.5 Hz) was shifted upfield by 0.2 p.p.m.

*4,6-Di-*O*-acetyl-2-deoxy-2-(*p*-toluenesulfonamido)-α-*D*-mannopyranosyl 4,6-di-*O*-acetyl-α-*D*-mannopyranoside* (**8**). — *(A) By use of* N*-methylmorpholine-*N*-oxide.* To a solution of **2** (200 mg, 0.32 mmol) in *tert*-butyl alcohol (5 mL) and water (1 mL) was added *N*-methylmorpholine-*N*-oxide (90 mg, 0.77 mmol) and OsO_4 (~30 μmol; 0.4 mL of a 80mM stock solution). The mixture was kept at 50° for 8 days, during which period compound **2**, R_F 0.6, was slowly but almost completely converted into **8**, R_F 0.2 (t.l.c., solvent *E*). The mixture was stirred for 1 h with added $NaHSO_3$ (0.5 mL, saturated aqueous solution), and evaporated to near

dryness. The residue was partitioned between ethyl acetate and water, and the aqueous layer was exhaustively extracted with ethyl acetate. The combined organic phases were dried ($MgSO_4$), and evaporated, to give **8** as a colorless, dry foam (180 mg, 85%) which failed to crystallize from any of several solvents tried.

*(B) By use of trimethylamine-*N*-oxide.* A solution of **2** (900 mg) in *tert*-butyl alcohol (20 mL) and water (2 mL), containing trimethylamine-*N*-oxide dihydrate (400 mg) and 80mM OsO_4 solution (0.2 mL), was maintained at 40° for 20 h, after which the reaction appeared complete (t.l.c., solvent *E*). Processing as under *A*, and passage of the crude product through a column of silica gel (20 g) by means of ethyl acetate yielded **8** as a dry foam (815 mg, 86%), $[\alpha]_D^{25}$ +41.8° (*c* 1.8, chloroform); ^{1}H-n.m.r. ($CDCl_3$): substituent resonances at δ 7.72 and 7.30 (AB-q, arom.), 2.39 (s, 3 H, PhCH_3), 2.14, 2.12, 2.08, and 2.06 (s, 4 × 3 H, OAc); analysis of the ring proton signals was unprofitable because of crowding.

Anal. Calc. for $C_{27}H_{37}NO_{16}S \cdot H_2O$ (681.7): C, 47.57; H, 5.77. Found: C, 47.63; H, 5.74.

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-(*p*-toluenesulfonamido)-α-*D*-mannopyranosyl 2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranoside* (**9**). — A solution of **8** (170 mg) in acetic anhydride (3 mL) and pyridine (3 mL) was stored overnight at 0°. Complete conversion into fast-moving **9** was indicated by t.l.c. The solution was coevaporated with excess toluene (6 times), and ethyl acetate followed by carbon tetrachloride was then added and evaporated from the residue which was finally obtained as a colorless, dry foam (180 mg), $[\alpha]_D^{25}$ +47° (*c* 1.1, chloroform); attempted crystallization was unsuccessful; ^{1}H-n.m.r. ($CDCl_3$): δ 7.74 and 7.30 (AB-q, arom.), 5.17 (dd, $J_{1',2'}$ 2, $J_{2',3'}$ 3.5 Hz, H-2'), 5.28 and 5.1–5.0 (2- and 4-proton multiplets, not first order; H-1,1',3,3',4,4'), 4.89 (d, $J_{2,NH}$ 8.3 Hz, NH-2), 4.19 (2 dd, 2 H, *J* 5 and 13 Hz for each, H-6_A,$6'_A$), 4.00 (2 dd, 2 H, *J* 2 and 13 Hz for each, H-6_B,$6'_B$), 3.85 (m, 3 H, H-2,5,5'), 2.39 (s, 3 H, PhCH_3), 2.12, 2.08, 2.05, 2.045, 1.99, 1.97 (s, 6 × 3 H, OAc), and 1.65 (s, 3 H, AcO-3).

Anal. Calc. for $C_{33}H_{43}NO_{19}S$ (789.7): C, 50.19; H, 5.49; S, 4.06. Found: C, 50.06; H, 5.40; S, 3.91.

*4,6-Di-*O*-acetyl-3-deoxy-3-(*p*-toluenesulfonamido)-α-*D*-mannopyranosyl 4,6-di-*O*-acetyl-α-*D*-mannopyranoside* (**10**). — *(A) By use of* N*-methylmorpholine-*N*-oxide.* Performed exactly as described for **2** (see *A*), the hydroxylation of **5** (200 mg) gave **10** as a chromatographically homogeneous solid (190 mg, 90%). Crystallized from ethanol, it retained 0.5 mol of solvent (n.m.r.), m.p. 108–112°, $[\alpha]_D^{25}$ +49° (*c* 0.45, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.73 and 7.32 (AB-q, arom.), 5.31 (d, $J_{3,NH}$ 8.5 Hz, NH-3), 5.18 (d, *J* 1.0 Hz, H-1 or -1'), 5.09 (d, *J* 1.5 Hz, H-1' or -1), 5.04 (t, $J_{3',4'} = J_{4',5'}$ = 9.7 Hz, H-4'), 4.96 (t, $J_{3,4} = J_{4,5}$ = 10.25 Hz, H-4), 4.30 (dd, *J* 4.85 and 12.2 Hz, H-6_A or -$6'_A$), 4.20 (dd, *J* 4.75 and 12.3 Hz, H-$6'_A$ or -6_A), 4.07 (dd, *J* 2.4 and 12 Hz, H-6_B or -$6'_B$), 3.98 (dd, *J* 2.2 and 12.2 Hz, H-$6'_B$ or -6_B), 3.95–3.70 (m, 5 H, poorly resolved, H-2,2',3',5,5'), 3.62 (~septet, dd after D_2O exchange, $J_{2,3}$ 3.2, $J_{3,NH}$ 8.5, $J_{3,4}$ 10.3 Hz, H-3), 2.41 (s, 3 H, PhCH_3), 2.17, 2.06, 2.03 (s, 3 × 3 H, OAc), and 1.69 (s, 3 H, AcO-4).

Anal. Calc. for $C_{27}H_{37}NO_{16}S$ (663.6): C, 48.86; H, 5.62; B, 4.83. Found: C, 48.75; H, 5.67; N, 4.62 (for ethanol-free sample).

(B) By use of trimethyl-N-oxide. Performed exactly as described for **2** (see *B*), but with a reaction-time of 2 days, the hydroxylation of **5** (900 mg) gave a slightly impure, crude product (1.00 g) which crystallized in part from ethanol (to give 425 mg of pure **10**). Purification of the mother liquor by chromatography with ethyl acetate as the eluant gave an additional 300 mg of pure **10**, for a total yield of 76%.

2,4,6-Tri-O-acetyl-3-deoxy-3-(p-toluenesulfonamido)-α-D-mannopyranosyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (**11**). — A sample of **10** (100 mg) was acetylated as described for **8**. The white, solid product (115 mg, 98%) showed only traces of impurities in t.l.c. (solvent *C*). Crystallization from 10:1 ethanol–water gave pure **11** (80 mg, 67%), m.p. 200–202°, $[\alpha]_D^{25}$ +37.5° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.75 and 7.37 (AB-q, arom.), 5.30 (m, 2 H, H-3′,4′), 5.20 (dd, $J_{1',2'}$ 1.6, $J_{2',3'}$ 3 Hz, H-2′), 5.11 (d, $J_{1,2}$ 1.2 Hz, H-1), 5.06 (d, $J_{1',2'}$ 1.5 Hz, H-1′), 4.95 (t, $J_{3,4} = J_{4,5}$ = 10.3 Hz, H-4), 4.88 (d, $J_{3,NH}$ 9 Hz, NH-3), 4.53 (dd, $J_{1,2}$ 1.2, $J_{2,3}$ 3.3 Hz, H-2), 4.21 and 4.17 (2 dd, *J* ~5 and 12.5 for each, H-6_A,$6'_A$), 4.09 and 4.01 (2 dd, *J* 2.2 and 12.5 for each, H-6_B,$6'_B$), 3.87 (m, 2 H, H-5,5′), 3.80 (ddd, *J* 3.4, 9.5, and 10.5 Hz, H-3), 2.41 (s, 3 H, PhCH_3), 2.14, 2.12, 2.09, 2.06, 2.04, 2.01 (s, 6 × 3 H, OAc), and 1.79 (s, 3 H, AcO-4).

Anal. Calc. for $C_{33}H_{43}NO_{19}S$ (789.7): C, 50.19; H, 5.49; S, 4.06. Found: C, 50.44; H, 5.65; S, 4.13.

A sample of the amino sugar **13** originating from an independent synthesis[9] was subjected to sequential *N*-tosylation and *O*-acetylation, and the 300-MHz, ^{1}H-n.m.r. spectrum of the product was superposable on that of **11**. Dr. B. Radatus is thanked for this contribution.

2-Amino-2-deoxy-α-D-mannopyranosyl α-D-mannopyranoside (**12**). — Compound **8** (800 mg) was dissolved in liquid NH_3 (~50 mL) at −40 to −50° (bath temperature), and Na (400 mg) was introduced in small pieces, with efficient magnetic stirring, in the course of 5–10 min. When the dark-blue color faded, it was restored by addition of further Na (400 mg), and the reaction was allowed to proceed for a total of 45 min. It was quenched by stirring the mixture for 0.5 h with NH_4Cl (1.20 g), introduced portionwise, and NH_3 was left to evaporate from the white mass, first in a stream of N_2 at ambient temperature and pressure, and then on a rotary evaporator at 30° to remove last traces. The dry powder so obtained was partially dissolved in methanol (50 mL), the insoluble part was filtered off over Celite and washed with methanol, and the filtrate was diluted with water (30 mL). The solution was treated with a weak-acid, cation-exchange resin followed by a strong-base, anion-exchange resin, each being washed well with methanol–water after filtration. This sequential treatment with the two types of resin was repeated twice with the respective filtrates, and finally the solution was evaporated to near-dryness and the residue taken up in a small volume of water for a last treatment with resins. The weak-acid resin batches were combined and eluted twice with 15%,

aqueous NH_3 (200 mL). Evaporation of the ammonical eluate gave a light-brown, dry foam. An aqueous solution of the foam was decolorized and clarified by activated charcoal and Celite, and evaporated, and trituration of the moist residue with 2-propanol gave **12** (280 mg, 68%) as an off-white powder; the product was moderately soluble in methanol but insoluble in ethanol, $[\alpha]_D^{25}$ +43° (*c* 0.4, water); R_F 0.2 (t.l.c., solvent *G*); ^{1}H-n.m.r. (D_2O, lock signal δ 4.63): δ 4.93 and 4.91 (narrow signals, H-1,1′), 3.05 (nm at highest field, W_H ~6 Hz, H-2), 3.8–3.4 (unresolved signals for the remaining protons).

The peracetyl derivative, obtained from **12** with acetic anhydride–pyridine, showed the following ^{1}H-n.m.r. data ($CDCl_3$): δ 5.67 (d, $J_{2,NH}$ 8.6 Hz, NH-2), 5.30 (m, 3 H, containing the H-3′,4′ signals, not first-order, and a dd for H-3, with $J_{2,3}$ 4.6, $J_{3,4}$ 9.8 Hz), 5.23 (dd, splittings 1.7 and 3.2 Hz, H-2′), 5.10 (~t, total width 20.8 Hz, consistent with *J* 9.8 and 11 Hz, H-4), 5.09 (very narrow m, 2 H, H-1,1′), 4.60 (ddd, $J_{1,2}$ 1.2, $J_{2,3}$ 4.6, $J_{2,NH}$ 8.6 Hz, H-2), 4.26 (septet, 2 H, H-6_A,$6'_A$), 4.10–3.95 (m, 4 H, H-5,5′,6_B,$6'_B$), 2.14, 2.065, 2.06, 2.055, 2.04, 2.35, 1.985, and 1.98 (s, 8 × 3 H, OAc).

To a sample of **12** (5 mg) in water (0.5 mL) was added acetic anhydride (1 drop), followed after 15 min by M H_2SO_4 (0.5 mL), and the solution was heated in a steam bath for 30 min, cooled, neutralized with $Ba(OH)_2$ solution to pH 6, and freed from the precipitate by centrifugation. The supernatant was heated with Na_2CO_2 (15 mg) for 5 min at 98° and gave a purple color with 1.3% *p*-dimethylaminobenzaldehyde in 1:1 ethanol–conc. HCl (Morgan–Elson test for 2-acetamido-2-deoxyaldoses)[11].

The hydrochloride of **12** was obtained as a white powder by careful acidification of a methanolic suspension of **12** with ethereal HCl at 0°, and evaporation of the resultant solution, with some added ethanol; $[\alpha]_D^{25}$ +39.8° (*c* 0.5, water).

Anal. Calc. for $C_{12}H_{24}ClNO_{10}$ (377.8): C, 38.15; H, 6.40; Cl, 9.38. Found: C, 38.03; H, 6.27; Cl, 9.00.

*3-Amino-3-deoxy-α-*D*-mannopyranosyl α-*D*-mannopyranoside* (**13**). — Compound **10** (700 mg) was treated with Na in liquid NH_3, and the reaction product was isolated, exactly as described for **8**. The free amino sugar **13** was obtained as a dry, off-white powder (300 mg, 83%), $[\alpha]_D^{25}$ +66° (*c* 0.6, water), identical with independently-prepared[9] **13** ($[\alpha]_D$ +67.5°) according to the i.r. and n.m.r. spectra, and t.l.c. (R_F 0.15, solvent *G*); ^{1}H-n.m.r. (D_2O, δ 4.63 lock signal): δ 4.96 (d, $J_{1',2'}$ 2 Hz, H-1′), 4.91 (d, $J_{1,2}$ 1.7 Hz, H-1), 3.81 (dd, $J_{2',3'}$ 3.4 Hz, H-2′), 3.70 (dd, $J_{2,3}$ 3.2 Hz, H-2), 3.26 (t, *J* 10 Hz, H-4 or -4′), and 2.75 (dd, $J_{3,4}$ 10 Hz, H-3); the remaining ring protons gave unresolved multiplets at 3.7–3.6 and 3.6–3.5 Hz (3 and 5 H, respectively). The analytical sample was obtained in crystalline form by trituration with ethanol and, on drying *in vacuo*, it stubbornly retained ~0.25 mol/mol of that solvent, as revealed by the n.m.r. spectrum.

Anal. Calc. for $C_{12}H_{23}NO_{10}$ (341.3): C, 42.22; H, 6.79; N, 4.10. Calc. for $C_{12}H_{23}NO_{10} \cdot 0.25\ C_2H_6O$: C, 42.55; H, 7.00; N, 3.97. Found: C, 42.33; H, 7.05; N, 3.76.

The Morgan–Elson reaction, performed as described for **12** after *N*-acetylation and hydrolysis of **13**, was negative.

The peracetyl derivative of **13**, obtained with acetic anhydride–pyridine, gave a 300-MHz, ^{1}H-n.m.r. spectrum ($CDCl_3$) that was identical in every respect with the spectrum reported[9] for an independently-prepared specimen. The chemical shifts of the acetyl signals are listed for comparison: δ 2.12, 2.11, 2.04, 2.04, 2.02, 2.01, 1.95, and 1.89.

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