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SYNTHESIS OF SOME DERIVATIVES OF 6-AMINO-1,5-ANHYDRO-6-DEOXY-D-GLUCITOL AND 2-AMINO-1,5-ANHYDRO-2-DEOXY-D-GLUCITOL*†

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ABSTRACT

6-Amino-1,5-anhydro-6-deoxy-D-glucitol (**11**) was prepared from 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) in six steps. Reduction of **1** with tributyltin hydride, followed by deacetylation, monomolar tosylation, and reacetylation, afforded 2,3,4-tri-*O*-acetyl-1,5-anhydro-6-*O*-toluene-*p*-sulfonyl-D-glucitol (**9**). Alternatively, tritylation of 1,5-anhydro-D-glucitol, followed by acetylation, detritylation, and tosylation, gave **9**. Mesylation gave **8**. Treatment of **8** or **9** with azide anion afforded the azide **10**, reduction of which with tributyltin hydride gave **11**, which was mesylated or tosylated, and then deacetylated to give the 6-methanesulfonamido or 6-toluene-*p*-sulfonamido derivative. Similarly, mesylation or tosylation of 3,4,6-tri-*O*-acetyl-2-amino-1,5-anhydro-2-deoxy-D-glucitol (**20**) gave the 2-methanesulfonamido or 2-toluene-*p*-sulfonamido derivatives. Treatment of **11** and **20** with sulfur trioxide–pyridine afforded the sulfoamino derivatives, deacetylation of which gave sugar analogs of cyclamate-like compounds.

INTRODUCTION

In connection with a program for the development of non-cariogenic sweeteners according to the structure–sweetness correlation method of Daniel and Whistler[1], convenient syntheses of sweet 3-deoxy-*erythro*-pentitol[2], 3-*C*-(hydroxymethyl)erythritol, and 3-*C*-methylerythritol have been described[3]. We now report on 1,5-anhydrohexitol derivatives that contain methanesulfonamido, toluene-*p*-sulfonamido, or sulfoamino groups, either at C-6 or C-2, which are analogs of cyclamate.

RESULTS AND DISCUSSION

Reduction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[4] (**1**) by an

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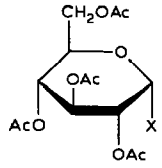
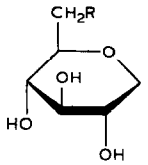
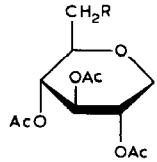
improved sequence of reactions[5] gave 87% of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol (**2**). Deacetylation of **2** and treatment of the product **3** with 1 mol of toluene-*p*-sulfonyl chloride in pyridine afforded 82% of the 6-tosylate **4**, the triacetate (**9**) of which is known[6,7]. Tritylation of **3** gave the 6-*O*-trityl derivative **5**, acetylation of which afforded 68% of known 2,3,4-tri-*O*-acetyl-1,5-anhydro-6-*O*-trityl-D-glucitol[8] (**6**). Hydrolysis of the trityl group in **6** and reaction of the product **7** with methanesulfonyl chloride in pyridine provided 85% of the mesylate **8**. Similarly, treatment of **7** with toluene-*p*-sulfonyl chloride at 25° yielded 77% of **9**.



1 X = Br
2 X = H



3 R = OH
4 R = OTs
5 R = OTr
15 R = NHMs
16 R = NHTs



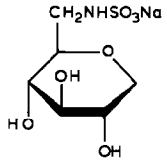
6 R = OTr
7 R = OH
8 R = OMs
9 R = OTs
10 R = N_3
11 R = NH_2
12 R = NHMs
13 R = NHTs
14 R = $NHSO_3Na$

Treatment of the mesylate **8** with sodium azide in boiling, aqueous acetone gave 62% of azide **10**, but only 42% of **10** was obtained from the tosylate **9**. Reduction[9] of the azido function in **10** with tributyltin hydride gave the syrupy amino derivative **11** (52% after purification by flash column chromatography).

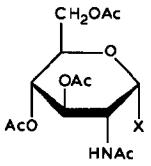
Treatment of **11** with methanesulfonyl chloride in pyridine at 0–5° gave 83% of crystalline 2,3,4-tri-*O*-acetyl-1,5-anhydro-6-deoxy-6-methanesulfonamido-D-glucitol (**12**). Alternatively, treatment of **11** with toluene-*p*-sulfonyl chloride in pyridine at 0–5° gave 56% of the crystalline 6-toluene-*p*-sulfonamido derivative **12**. Deacetylation of **12** and **13** with aqueous methanolic triethylamine afforded >93% of **15** and **16**. Similarly, deacetylation of **14** gave 94% of crystalline 1,5-anhydro-6-deoxy-6-sulfoamino-D-glucitol (**17**).

Sulfation of **11** was accomplished by reaction with *freshly prepared*[10] pyridine–sulfur trioxide followed by conversion into the sodium salt. Deacetylation of **14** with aqueous methanolic triethylamine then gave **17** in good yield.

In the 2-amino-2-deoxy series, the starting material, 3,4,6-tri-*O*-acetyl-2-amino-1,5-anhydro-2-deoxy-D-glucitol[11,12] (**20**), was prepared by the reduction of the corresponding glycosyl chloride[13] **18** followed by selective *N*-deacetylation of the product **19** using triethyloxonium fluoroborate[14]. Compound **20** was obtained in only 51% yield due to difficulties during purification.

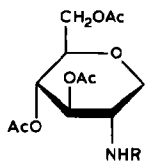


17



18 X = Cl

19 X = H

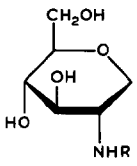


20 R = H

21 R = Ms

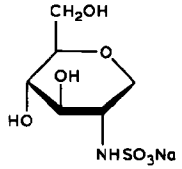
22 R = Ts

23 R = SO_3Na



24 R = Ms

25 R = Ts



26

Treatment of **20** with methanesulfonyl chloride in pyridine at 0–10° gave 61% of the crystalline methanesulfonamido derivative **21**. Similarly, toluene-*p*-sulfonylation of **20** afforded 55% of the crystalline toluene-*p*-sulfonamido derivative **22**.

Sulfation of **20**, as for **11**, afforded **23** in good yield and purity, in contrast to the previous method[15] of sulfation of analogous compounds. Deacetylation of **23** with aqueous methanolic triethylamine gave 71% of **26**. Because the ^{1}H-n.m.r. spectra of unsubstituted 1,5-anhydro-D-hexitols are uninformative, as most of the proton signals coincide, only the ^{1}H- (Tables I and II) and ^{13}C-n.m.r. spectra (Table III) of substituted 1,5-anhydro-D-hexitols are recorded for the assignment of the structures and the determination of conformations.

The ^{13}C-n.m.r. spectra of several 1,5-anhydro-D-hexitols have already been reported[16], and the assignments in Table III are related to those in the literature[16,17] and in agreement with the structural assignments.

Preliminary examination indicated that compounds **15, 17, 24,** and **26** are slightly sweet, but also exhibit a mild bitter after-taste.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical reactions were measured with a Perkin–Elmer Model 141 polarimeter. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with Varian T-60A (^{1}H) and Nicolet NT-200 (^{13}C, 50.3 MHz) spectrometers. Mass spectra were determined for samples that were introduced by direct insertion or from a g.l.c. capillary column of silicone DB5-15N

TABLE I

^{1}H-N.M.R. DATA (δ) FOR THE 1,5-ANHYDROHEXITOL DERIVATIVES[a]

Compound	*H-1* a	e	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*-OAc*	*CH_3*	*-NH or NH_2*	*Aromatic*
4	3.18q	3.73q	4.76sex	4.33q	4.2	——	4.4m (4 H)	—	2.4s		7.18–7.78m (4 H)
5	3.28q	3.66q	4.7m	4.28q	4.0	——	4.6m (4 H)	—	—	—	7.08–8.16m (15 H)
6	3.26q	3.6q	4.86m	4.23q	4.0	——	4.6m (4 H)	1.98s 2.06s 2.12s			7.29–7.96m (15 H)
7	3.26q	3.63q	4.89m	4.2q	4.0	——	4.6m (4 H)	1.96s 2.13s 2.16s	—	—	—
8	3.26q	3.6q	4.86m	4.2q	4.1	——	4.56m (4 H)	1.96s 2.13s 2.19s	2.92s	—	—
9	3.16q	3.6q	4.77 ——	4.36m (2 H)	4.53m	4.39 ——	4.86m (2 H)	1.99s 2.16s 2.19s	2.32s		7.18–7.8m (4 H)
10	3.28q	3.66q	5.13m	4.3m (2 H)	4.39	——	4.79m (4 H)	1.99s 2.13s 2.20s	—	—	—

11	3.33q 3.73q	5.06	4.6m (3 H)	4.3 —— 4.6m (2 H)		1.96s 2.13s 2.19s	—	8.39s	—
12	3.3q 3.8q	5.09	4.36 (2 H)	4.56m	4.6 —— 4.7m (2 H)	1.99s 2.19s 2.22s	3.3s	8.16s	—
13	3.29q 3.76q	5.1	4.4m (2 H)	4.51m	4.59 —— 4.66m (2 H)	1.99s 2.13s 2.16s	2.31s	8.19s	7.16–7.85m (4 H)
14	3.3q 3.8q	4.99	4.39m (2 H)	4.59m	4.6 —— 4.79m (2 H)	1.96s 2.19s 2.21s	—	8.13s	—
20	3.23q 3.66q	5.16m	4.36q	4.59m	4.6 —— 4.86m (2 H)	1.96s 2.16s 2.19s	—	8.0s	—
21	3.16q 3.86q	5.03m	4.38q	4.4 —— 4.96m (4 H)		1.96s 2.12s 2.16s	2.9s	7.96s	—
22	3.19q, 3.79q	4.8m	4.3q	4.48 —— 5.06m (4 H)		1.98s 2.09s	2.43s	7.99s	7.13–8.80m (4 H)
24	3.16q 3.89q	5.09m	4.39q	4.53m	4.6 —— 4.89 (3 H)	—	2.49s	8.19s	—
25	3.23q 3.79q	4.99m	4.29q	4.13 —— 4.49m (4 H)		—	2.41s	8.09s	7.19–7.8m (4 H)

[a]First-order analysis at 200 MHz.

TABLE II

COUPLING CONSTANTS (Hz) OF THE 1,5-ANHYDOHEXITOL DERIVATIVES[a]

Compound	$J_{1e,1a}$	$J_{1e,2}$	$J_{1a,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
4	12	6	10	9	2	—
5	12	—	10.5	9.5	—	—
6	12	—	10	—	—	—
7	12	—	—	10	2	—
8	12	6	—	9.5	—	—
9	12	—	10	—	—	9
10	12.5	6	10	9	—	9
11	12	—	—	—	—	—
12	12.5	—	—	—	—	—
13	12.5	6	—	—	2	9
14	12	6	—	—	2	9
20	12	—	—	—	—	9
21	12.5	—	—	—	—	—
22	12.5	—	—	9	2	—
24	11.5	—	—	9	2	9
25	12.5	—	—	9	2	—

[a]First-order analysis at 200 MHz.

TABLE III

^{13}C-N.M.R. DATA[a] FOR THE 1,5-ANHYDRO-D-GLUCITOL DERIVATIVES

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*-CH$_3$*
4[b]	69.6	70.4	78.6	70.6	81.3	61.9	24.0
5[c]	69.8	70.3	78.4	70.7	81.5	61.8	—
7[d]	69.7	70.1	78.3	70.5	81.3	61.4	—
10[d]	69.7	70.1	78.2	70.4	81.3	61.9	—
11[d]	69.5	70.1	78.2	70.5	81.2	61.8	—
15	69.6	70.2	78.6	70.6	81.3	61.6	38.6
16[b]	69.5	70.4	78.4	70.7	81.3	61.8	21.4
17	69.5	70.3	78.3	70.5	81.2	61.8	—
20[d]	69.8	54.3	78.4	70.7	81.3	61.5	—
24	69.9	54.6	78.4	70.6	81.3	61.5	38.3
25[b]	69.9	54.8	78.6	70.6	81.5	61.5	21.6
26	69.9	54.5	78.4	70.7	81.6	61.6	—

[a]For solutions in $CDCl_3$ (internal Me_4Si). [b]Additional signals for aromatic carbons were observed at δ 130.4, 129.8, 128.4, and 128.0. [c]Additional signals were observed at δ 118.6 (Ph_3C) and 145–126.3 (15 C aromatic). [d]Contains additional data for acetyl groups.

attached by a jet separator to a Finnigan 4000 GC/MS mass spectrometer equipped with an INCOS data system; the ion-source temperature was 250°, the ion-source voltage was 70 eV, and the electron-multiplier voltage was 1500 V. The purity of products was determined by t.l.c. on silica gel GF_{254} (Merck), using *A*, ethyl acetate–dichloromethane–methanol (7:2:1); *B*, chloroform–methanol (8:2); and

detection by charring with sulfuric acid. Column chromatography was performed on Grade 62 silica gel (Davidson, 60–200 mesh), and flash column chromatography[18] on EM 9385 silica gel (240–400 mesh) (Baker Analytical Reagents).

All organic solutions were dried with sodium sulfate and concentrated (generally at <40°) under reduced pressure. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide[4] (**1**), 1,5-anhydro-D-glucitol[5] (**3**), and 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride[13] (**18**) were prepared by literature procedures.

*1,5-Anhydro-6-*O*-toluene-*p*-sulfonyl-*D*-glucitol* (**4**). — To a cooled solution of 1,5-anhydro-D-glucitol (**3**; 5.0 g, 0.03 mmol) in anhydrous pyridine (50 mL) was added tosyl chloride (5.84 g, 0.03 mol), and the solution was stirred at 25° for 24 h. T.l.c. (solvent *B*) then showed complete reaction. The pyridine was evaporated and the residue was subjected to column chromatography (solvent *A*). Fractions containing the product (R_F 0.58) were combined and concentrated to yield **4** (8.2 g, 85%) as a syrup, $[\alpha]_D^{20}$ +52° (*c* 1.6, chloroform).

Anal. Calc. for $C_{13}H_{18}O_7S$: C, 49.04; H, 5.71; S, 10.07. Found: C, 48.96; H, 5.51; S, 10.3.

*1,5-Anhydro-6-*O*-trityl-D-glucitol* (**5**). — To a solution of **3** (4.92 g, 30 mmol) in dry pyridine (50 mL) was added triphenylmethyl chloride (8.9g, 32 mmol). The mixture was stirred for 12 h at 35–45°. T.l.c. (solvent *A*) then showed complete reaction. The pyridine was evaporated and the residue was subjected to column chromatography (solvent *B*). Fractions containing the product (R_F 0.61) were combined, and concentrated to a syrup which was crystallized from ether–hexane to give **5** (9.4 g, 77%), m.p. 168–170°, $[\alpha]_D^{20}$ +20° (*c* 1.5, chloroform).

Anal. Calc. for $C_{25}H_{27}O_5$: C, 73.62; H, 6.68. Found: C, 73.46; H, 6.72.

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-*O*-trityl-D-glucitol* (**6**). — Compound **5** (2.0 g) was treated conventionally with acetic anhydride (6 mL) in dry pyridine (20 mL) for 12 h at room temperature. The product was subjected to column chromatography (solvent *A*). Fractions containing the product (R_F 0.49) were combined and concentrated to give **6** (2.33 g, 89%) as a syrup, which was crystallized twice from ethanol to give material having m.p. 93–95°, $[\alpha]_D^{20}$ +83° (*c* 1.3, chloroform); lit.[8] m.p. 92–93°, $[\alpha]_D$ +82° (*c* 3.4, pyridine).

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-D-glucitol* (**7**). — A solution of **6** (2.59 g, 4 mmol) in aqueous 70% acetic acid (35 mL) was heated for 6 h at 60°, cooled, filtered, and concentrated to a syrup which crystallized from ether–ethyl acetate to give **7** (1.25 g, 92%), m.p. 108–112°, $[\alpha]_D^{20}$ +46° (*c* 1.5, chloroform); lit.[8] m.p. 111–113°, $[\alpha]_D$ +49.9° (*c* 3, chloroform).

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-*O*-methanesulfonyl-D-glucitol* (**8**). — To a solution of **7** (2.9 g, 10 mmol) in dry pyridine (20 mL) was added mesyl chloride (1.26 g, 11 mmol) at 0°, and the mixture was kept for 16 h at 0°. The excess of reagent was decomposed with water, and the mixture was concentrated to a syrup which was extracted with chloroform. The extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried, and concentrated.

Column chromatography (chloroform and then solvent *B*) of the residue yielded **8** (2.68 g, 73%), m.p. 131–133° (from ethanol), $[\alpha]_D^{20}$ +41.5° (*c* 1, chloroform).

Anal. Calc. for $C_{13}H_{20}O_{10}S$: C, 42.38; H, 5.47; S, 8.70. Found: C, 42.22; H, 5.31; S, 8.58.

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-*O*-toluene-*p*-sulfonyl-*D*-glucitol* (**9**). — (*a*) Conventional acetylation of **4** (0.75 g, 2.3 mmol) with acetic anhydride (3 mL) and dry pyridine (5 mL) gave **9** (0.98 g, 94%), m.p. 144–145°, $[\alpha]_D^{20}$ +63° (*c* 1.2, chloroform), R_F 0.68 (solvent *A*); lit.[6,7] m.p. 143.5–144.5°, $[\alpha]_D^{20}$ +62.2° (chloroform).

(*b*) To a solution of **7** (2.9 g, 10 mmol) in dry pyridine (20 mL) was added tosyl chloride (2.92 g, 15 mmol). The reaction was performed as for compound **3**, to give crystalline **9** (3.24 g, 73%).

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-azido-6-deoxy-*D*-glucitol* (**10**). — (*a*) To a stirred solution of **8** (5.09 g, 14.1 mmol) in aqueous acetone (80 mL, 5:3) was added sodium azide (10.0 g, 15.3 mmol). The mixture was boiled under reflux for 72 h and then concentrated, and the residue was extracted with chloroform (5 × 30 mL). The combined extracts were dried and concentrated. Column chromatography (solvent *A*) of the syrupy residue gave fractions containing a product with R_F 0.62. The combined fractions were concentrated and the residue was crystallized from ether–hexane to give **10** (3.1 g, 88%), m.p. 89–91°.

(*b*) A solution of **9** (6.22 g, 14 mmol) and sodium azide (10.0 g, 15.3 mmol) in *N,N*-dimethylformamide (40 mL) was stirred and boiled under reflux for 8 h, then cooled, poured into water, and extracted with ether (10 × 25 mL). The combined extracts were washed with water (10 mL), dried, and concentrated, and the residue was crystallized from ether–hexane to give **10** (1.26 g, 40%), m.p. 89–91°, $[\alpha]_D^{20}$ +8° (*c* 1.6, chloroform), ν_{max}^{KBr} 2090 cm^{-1} (N_3).

Anal. Calc. for $C_{12}H_{17}N_3O_7$: C, 45.71; H, 5.43; N, 13.32. Found: C, 45.57; H, 5.26; N, 13.18.

*2,3,4-Tri-*O*-acetyl-6-amino-1,5-anhydro-6-deoxy-*D*-glucitol* (**11**). — To a solution of **10** (3.1 g, 10 mmol) in dry benzene (60 mL) was added 2,2′-azobis(2-methylpropiononitrile) (0.1 g). To the stirred and boiling solution was added tributyltin hydride (3.5 g, 12 mmol) dropwise during 15 min. The mixture was boiled under reflux under argon for 16 h. The reaction was monitored by t.l.c. (solvent *A*), which showed the formation of a product of R_F 0.53. After 3 h, the solution was concentrated to dryness. Column chromatography (solvent *A*) of the residue gave fractions containing a product of R_F 0.53, which were combined and concentrated to give **11** (1.8 g, 63%) as a syrup, $[\alpha]_D^{20}$ +9° (*c* 1.6, chloroform).

Anal. Calc. for $C_{12}H_{19}NO_7$: C, 49.82; H, 6.61; N, 4.84. Found: C, 49.73; H, 6.44; N, 4.71.

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-deoxy-6-methanesulfonamido-*D*-glucitol* (**12**). — To a stirred solution of **11** (2.89 g, 10 mmol) in dry pyridine (20 mL) was added mesyl chloride (3 mL) at 0°. The mixture was kept for 12 h at 0°. Conventional

work-up and crystallization of the product from ethanol than gave **12** (0.5 g, 82%), m.p. 148–150°, $[\alpha]_D^{20}$ +66° (*c* 1, methanol), R_F 0.56 (solvent *A*).

Anal. Calc. for $C_{13}H_{21}NO_9S$: C, 42.49; H, 5.76; N, 3.81; S, 8.72. Found: C, 42.33; H, 5.84; N, 3.67; S, 8.59.

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-deoxy-6-toluene-*p*-sulfonamido-*D*-glucitol* (**13**). — Compound **11** (2.89 g, 10 mmol) was tosylated as described for **7**, to give **13** (3.04 g, 71%), m.p. 124–126° (dec.), $[\alpha]_D^{20}$ +59° (*c* 1, chloroform), R_F 0.49 (solvent *A*).

Anal. Calc. for $C_{19}H_{25}NO_9S$: C, 51.45; H, 5.68; N, 3.15; S, 7.23. Found: C, 53.02; H, 5.71; N, 2.97; S, 7.11.

*2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-deoxy-6-sulfoamino-*D*-glucitol sodium salt* (**14**). — To a stirred solution of **11** (2.89 g, 10 mmol) in dry pyridine (30 mL) was added freshly prepared pyridine–sulfur trioxide complex (2.2 g, 14 mmol). The mixture was stirred for 24 h at room temperature and then poured into aqueous $NaHCO_3$ (3 g in 100 mL of water). The solution was freeze-dried, the residue was extracted with boiling, aqueous 95% ethanol (3 × 100 mL), and the extracts were filtered hot, combined, and stored at 0°. A solid deposited which was recrystallized from aqueous 95% ethanol to give **14** (2.69 g, 69%), m.p. 208–210° (dec.), $[\alpha]_D^{20}$ +6° (*c* 1, water). Mass spectrum (70 eV): *m/z* 392 (0.8%) (M^+ + 1), 348 (12.1), 332 (5.1), 273 (30.1), 265 (6.1), 230 (3.1), 173 (5.1), 171 (6.5), 111 (20.1), 93 (6.8), 65 (4.5), 61 (18.3).

Anal. Calc. for $C_{12}H_{18}NNaO_{10}S$: C, 36.82; H, 4.63; N, 3.57; S, 8.19. Found: C, 36.71; H, 4.72; N, 3.39; S, 8.03.

*1,5-Anhydro-6-deoxy-6-methanesulfonamido-*D*-glucitol* (**15**). — A solution of **12** (1.84 g, 5 mmol) in triethylamine–water–methanol (1:4:5, 75 mL) was kept for 8 h at room temperature and then concentrated, and the residue was crystallized from methanol to give **15** (1.12 g, 93%), m.p. 128–131° (dec.), $[\alpha]_D^{25}$ +21° (*c* 1, chloroform), R_F 0.39 (solvent *B*).

Anal. Calc. for $C_7H_{15}NO_6S$: C, 34.84; H, 6.26; N, 5.80; S, 13.29. Found: C, 34.66; H, 6.14; N, 5.69; S, 13.13.

*1,5-Anhydro-6-deoxy-6-toluene-*p*-sulfonamido-*D*-glucitol* (**16**). — Compound **13** (1.1 g, 2.5 mmol) was deacetylated as for **12**, to give **16** (0.78 g, 95%) as a syrup, $[\alpha]_D^{25}$ +6° (*c* 1, chloroform), R_F 0.33 (solvent *B*).

Anal. Calc. for $C_{13}H_{19}NO_6S$: C, 49.19; H, 6.03; N, 4.41; S, 10.10. Found: C, 49.14; H, 5.83; N, 4.32; S, 9.94.

*1,5-Anhydro-6-deoxy-6-sulfoamino-*D*-glucitol sodium salt* (**17**). — A solution of **14** (1.95 g, 5 mmol) in triethylamine–water–methanol (1:4:5, 100 mL) was kept for 8 h at room temperature and then concentrated, and the residue was crystallized from ethanol to give **17** (1.41 g, 94%), m.p. 177–179° (dec.), $[\alpha]_D^{20}$ +22° (*c* 1.5, water). Mass spectrum (70 eV): *m/z* 259 (5.1%), 162 (88.4), 157 (9.2), 147 (30.1), 129 (61.1), 111 (10.0), 99 (5.1), 87 (9.1), 80 (5.3), 73 (6.1), 69 (13.1), 65 (7.2).

Anal. Calc. for $C_6H_{21}NNaO_7S$: C, 27.16; H, 4.56; N, 5.28; S, 12.08. Found: C, 27.03; H, 4.28; N, 5.11; S, 11.91.

*2-Acetamido-3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-*D*-glucitol* (**19**). — 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**18**; 3.65 g, 10 mmol) was reduced with tributyltin hydride (3.5 g, 12 mmol) at reflux temperature for 2 h, using benzene as solvent, to give **19** (2.58 g, 78%), m.p. 164–166°, $[\alpha]_D^{20}$ ~0° (*c* 1.1, chloroform), R_F 0.69 (solvent *A*); lit.[11,12] m.p. 165–168°, $[\alpha]_D^{20}$ 0° (*c* 1.1, chloroform).

*3,4,6-Tri-*O*-acetyl-2-amino-1,5-anhydro-2-deoxy-*D*-glucitol* (**20**). — To a stirred solution of **19** (3.3 g, 10 mmol) in the minimum volume of dry dichloromethane was added dropwise a solution of triethyloxonium fluoroborate (2.0 g, 0.5 mmol) in dichloromethane (10 mL) during 5–10 min at 5° under nitrogen. The resulting solution was stirred at room temperature for 3 h and then concentrated, and the crystalline solid was collected and washed rapidly with cold, dry dichloromethane. A solution in 0.01M hydrochloric acid (10 mL) was kept for 15 min at room temperature, neutralized with cold aqueous sodium hydrogencarbonate, and extracted with chloroform (3 × 30 mL). The combined extracts were concentrated, and the residue was crystallized from ethanol to give **20** (2.08 g, 72%), m.p. 160–165° (dec.), $[\alpha]_D^{20}$ +2° (*c* 1.2, chloroform); ν_{max}^{KBr} 3400 cm^{-1} (NH_2). ^{1}H-N.m.r. data: see Tables I and II.

Anal. Calc. for $C_{12}H_{19}NO_7$: C, 49.82; H, 6.61; N, 4.84. Found: C, 49.74; H, 6.57; N, 4.71.

*3,4,6-Tri-*O*-acetyl-2-amino-1,5-anhydro-2-deoxy-2-methanesulfonamido-*D*-glucitol* (**21**). — Compound **20** (1.44 g, 5 mmol) was mesylated as for **17**, to give **21** (1.53 g, 83%), m.p. 144–146° (dec.) (from ethanol), $[\alpha]_D^{20}$ ~0° (*c* 1.5, chloroform), R_F 0.59 (solvent *A*). ^{1}H-N.m.r. data: see Tables I and II.

Anal. Calc. for $C_{13}H_{21}NO_9S$: C, 42.49; H, 5.76; N, 3.81; S, 8.72. Found: C, 42.31; H, 5.81; N, 3.66; S, 8.59.

*3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-toluene-*p*-sulfonamido-*D*-glucitol* (**22**). — Compound **20** (1.44 g, 5 mmol) was tosylated as for **3**, to give **22** (1.5 g, 68%), m.p. 186–188° (dec.) (from ethanol), $[\alpha]_D^{20}$ +2.4° (*c* 1, chloroform), R_F 0.5 (solvent *A*).

Anal. Calc. for $C_{19}H_{25}NO_9S$: C, 51.45; H, 5.68; N, 3.15; S, 7.23. Found: C, 51.23; H, 5.52; N, 2.98; S, 7.17.

*3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-2-sulfoamino-*D*-glucitol sodium salt* (**23**). — Compound **20** (2.89 g, 10 mmol) was sulfated as for **11**, to give **23** (2.46 g, 63%), m.p. 218–220° (dec.) (from ethanol), $[\alpha]_D^{20}$ ~0°, R_F 0.39 (solvent *B*). Mass spectrum (70 eV): *m/z* 392 (0.6%) (M^+ + 1), 348 (7.4), 332 (6.1), 271 (16.1), 265 (5.9), 231 (3.3), 173 (6.8), 171 (8.9), 111 (31.0), 93 (5.6), 65 (4.5), 61 (121).

Anal. Calc. for $C_{12}H_{18}NNaO_{10}S$: C, 36.82; H, 4.63; N, 3.57; S, 8.19. Found: C, 36.69; H, 4.71; N, 3.36; S, 7.99.

*1,5-Anhydro-2-deoxy-2-methanesulfonamido-*D*-glucitol* (**24**). — Compound **21** (1.95 g, 5 mmol) was deacetylated as for **12**, to give **24** (1.26 g, 96%), m.p. 143–146° (from methanol), $[\alpha]_D^{20}$ ~0° (*c* 2.1, methanol), R_F 0.31 (solvent *B*).

Anal. Calc. for $C_{17}H_{15}NO_6$: C, 34.84; H, 6.26; N, 5.80; S, 13.29. Found: C, 34.79; H, 6.38; N, 5.62; S, 12.96.

*1,5-Anhydro-2-deoxy-2-toluene-*p*-sulfonamido-*D*-glucitol* (**25**). — Compound **22** (2.2 g, 5 mmol) was deacetylated as for **12**, to give **25** (1.49 g, 95%), m.p. 168–170° (from methanol), $[\alpha]_D^{20}$ +4° (*c* 1.2, methanol), R_F 0.28 (solvent *B*).

Anal. Calc. for $C_{13}H_{19}NO_6S$: C, 49.19; H, 6.03; N, 4.41; S, 10.10. Found: C, 49.02; H, 5.89; N, 4.29; S, 9.98.

*1,5-Anhydro-2-deoxy-2-sulfoamino-*D*-glucitol sodium salt* (**26**). — Compound **23** (1.95 g, 5 mmol) was deacetylated as for **12**, to give **26** (1.26 g, 96%), m.p. 170–172° (dec.) (from aqueous 95% ethanol), $[\alpha]_D^{20}$ ~0° (*c* 1.2, methanol), R_F 0.19 (solvent *B*). Mass spectrum (70 eV): *m/z* 161 (72%) ($M^+ - 104$), 156 (83), 147 (21.2), 129 (26.1), 111 (17.1), 87 (7.3), 80 (5.1), 69 (10.1), 65 (7.2).

Anal. Calc. for $C_6H_{12}NNaO_7S$: C, 27.16; H, 4.56; N, 5.28; S, 12.08. Found: C, 26.99; H, 4.38; N, 5.12; S, 11.96.

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