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AN APPROACH TO THE SYNTHESIS OF BRANCHED-CHAIN AMINO SUGARS FROM *C*-METHYLENE SUGARS*†

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ABSTRACT

The reaction of 1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose (**4**) with mercuric azide in hot 50% aqueous tetrahydrofuran yielded, after reductive demercuration, 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-glucofuranose (**5**). Partial, acid hydrolysis of **5** afforded the diol **7**, which gave 3-azido-3-deoxy-1,2-*O*-isopropylidene-5,6-di-*O*-methanesulphonyl-3-*C*-methyl-α-D-glucofuranose (**8**) on sulphonylation. On hydrogenation over a platinum catalyst and *N*-acetylation, the dimethanesulphonate **8** furnished 3,6-acetylepimino-3,6-dideoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-3-*C*-methyl-α-D-glucofuranose (**9**), which was also prepared by an analogous sequence of reactions on 3-azido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-3-*C*-methyl-6-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose (**13**). The formation of the *N*-acetylepimine **9** establishes the D-*gluco* configuration for **5**.

1,2-*O*-Isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose (**20**) reacted with mercuric azide in aqueous tetrahydrofuran at ~85° to give 3,6-anhydro-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-glucofuranose (**22**) as a result of intramolecular participation by the C-6 hydroxyl group in the initial intermediate.

INTRODUCTION

Current investigations in our laboratories are aimed at the introduction into sugars of a Me-C-NH_2 branch, such as occurs in the antibiotic sugar vancosamine[3] (3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*lyxo*-hexose; **1**), a component of vancomycin. One of our approaches[4] to this synthetic problem followed traditional lines[5,6], since it was based on the reduction of branched-chain nitro sugars derived from the cyclization of a "dialdehyde" (periodate-oxidized methyl α-L-rhamnopyranoside) with nitroethane. Although this approach provided[4] a synthesis of derivatives of *epi*-vancosamine (3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*arabino*-hexose), considerable

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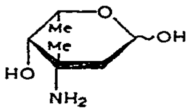
*Dedicated to the memory of Professor Edward J. Bourne.
†Branched-chain Sugars: Part VI[1]. For Part V, see Ref. 2.

difficulties attend the assignment of structures to the various stereoisomers obtained in the nitroethane reaction. It is also disconcerting, from a synthetic viewpoint, to have little or no control over the configurations of the stereoisomers formed in the nitroethane procedure. A method by which a restricted number of stereoisomers is formed would represent a welcome advance in the synthesis of branched-chain amino sugars, particularly if the substrate chosen offered some hope of controlling the stereochemistry of the products.



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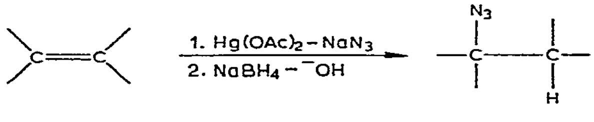
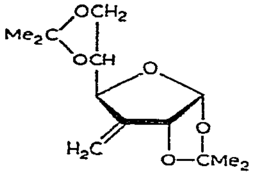


2 3

Heathcock has briefly reported[7] on a method for the synthesis of alkyl azides that fitted most of the criteria sought. Thus, the reaction of an alkene **2** with mercuric azide, generated *in situ* from mercuric acetate and sodium azide (see Experimental), in a two-phase system of 50% aqueous tetrahydrofuran at 50–90° furnishes an organomercury(II) adduct which can be reductively demercurated to give an alkyl azide **3**. The method works well for the synthesis of tertiary or secondary alkyl azides from terminal alkenes or strained cyclic alkenes and is regiospecific (Markovnikov addition). An exploratory investigation of the applicability of Heathcock's procedure to carbohydrates was conducted with 1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose[8] (**4**), since the fused, bicyclic ring-system might be expected to exert some control over the stereochemistry of the addition.

RESULTS AND DISCUSSION

The unsaturated sugar **4** reacted sluggishly with mercuric azide in 50% aqueous tetrahydrofuran at ~90°, and a substantial proportion of the starting material remained (t.l.c.) after 96 h, when the organomercury(II) adduct was reductively demercurated with sodium borohydride in sodium hydroxide solution. The i.r. and n.m.r. spectra (see Experimental for details) of the product (43% yield) showed it to be a 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-hexofuranose. The choice between the D-*gluco* **5** or D-*allo* **6** configuration for the tertiary azide was



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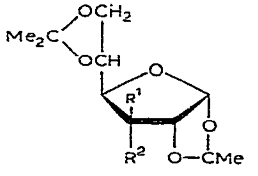
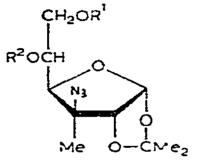


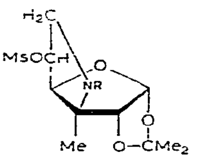
5 $R^1 = N_3$, $R^2 = Me$
6 $R^1 = Me$, $R^2 = N_3$

originally, but erroneously, based [1a] on correlations made with work reported by Bourgeois[9] (see later) during the progress of our investigation. However, the chemical evidence described below is compatible only with the D-*gluco* configuration **5** for this tertiary azide; the correct configuration is assumed in the formulae that follow.

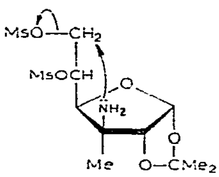
On partial hydrolysis with 70% acetic acid at room temperature, **5** afforded the diol **7**, which was transformed into the dimethanesulphonate **8** in the usual way. Hydrogenation of **8** in methanol over a platinum catalyst and *N*-acetylation of the reduced material furnished 3,6-acetylepimino-3,6-dideoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-3-*C*-methyl-α-D-glucofuranose (**9**). The structure of **9** was indicated by the presence of only *one* methanesulphonyl group (n.m.r. evidence) and from the absence of i.r. absorptions attributable to an NH group, although the presence of an *N*-acetyl group (ν_{max} 1650 cm^{-1}, singlet* at τ 7.96) was revealed by the spectroscopic evidence. It is reasonable to conclude that catalytic reduction of **8** to give the branched-chain amine **10** is followed by intramolecular displacement of the sulphonyloxy group at C-6 to furnish the epimine **11**, which was subsequently isolated as the *N*-acetyl derivative **9**. It was possible to isolate the epimino derivative **11** following catalytic reduction of the mixed disulphonate **13**, prepared by sequential toluene-*p*-sulphonylation and methanesulphonylation of the diol **7**. *N*-Acetylation of **11** afforded **9**. Intramolecular participation involving the C-3 amino group requires that **5** and its progeny possess the D-*gluco* configuration, since the formation of *trans*-fused, five-membered rings, required by the D-*allo* configuration, can be discounted. The diol **7** was also converted into the 6-benzoate **14** and thence into the corresponding 5-methanesulphonate **15**.



7 $R^1 = R^2 = H$
8 $R^1 = R^2 = Ms$
12 $R^1 = Ts, R^2 = H$
13 $R^1 = Ts, R^2 = Ms$
14 $R^1 = Bz, R^2 = H$
15 $R^1 = Bz, R^2 = Ms$



9 R = Ac
11 R = H



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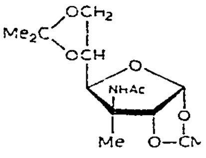

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We have already shown[1] that catalytic reduction and *N*-acetylation of the branched-chain azide **5** affords an acetamido derivative **16** (now correctly assigned) identical with one obtained by Bourgeois[9a] by an alternative route. The preparation of **16** from the sulphonylated cyanohydrin **17** by Bourgeois' procedure can now be

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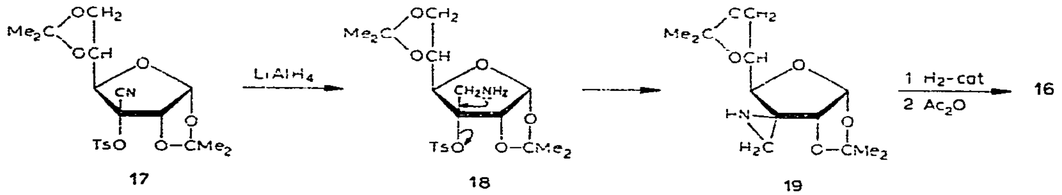
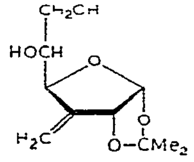
*In the n.m.r. spectra of related *N*-acetylepimines, two sets of signals have been observed for H-1, H-2, and the N-Ac group, due to the presence of two rotamers in solution, arising from hindered internal rotation about the N-Ac bond[10,11]. However, no duplicity in these signals was observed in the n.m.r. spectrum of **9**, even after cooling the sample to −70°.

considered to follow the route **17**→**18**→**19**→**16**. In particular, the formation of the spiro-aziridine **19** from **18** is required to take place with inversion of configuration at the tertiary centre (*cf.* Ref. 9*a*). This stereochemistry should be favoured by a reaction involving participation by a neighbouring group, since the incoming and departing groups are located on opposite faces of the molecule whether the reaction is concerted or not. A number of the compounds described in Bourgeois' communication[9a] must be accorded the D-*gluco* configuration in the light of this evidence*.



17 18 19



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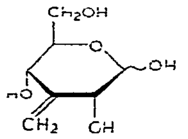

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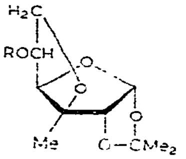

22 R = H
23 R = Ac

The addition of mercuric azide to 1,2-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose (**20**) was also examined with a view to ascertaining the effect of an internal nucleophile on the reaction. The diol **20** was obtained on partial hydrolysis of **4**, which also yielded the completely hydrolysed sugar **21**, presumably as the pyranoide-ring form. The reaction of **20** with mercuric azide, followed by demercuration, furnished a product (~37%) which contained a *C*-methyl group (n.m.r. evidence) but no azido group (i.r. evidence), and which yielded a monoacetate on acetylation. The chemical and spectroscopic evidence are compatible with the structure 3,6-anhydro-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-glucofuranose (**22**); the n.m.r. spectrum of the monoacetate **23** was cleanly first-order and was readily reconciled with the structure proposed.

The mechanism of the reaction of mercuric azide with alkenes would be expected to be similar to that of oxymercurations with mercuric acetate, although the greater nucleophilicity of the azide ion compared to the acetate ion must be borne in mind. In this context, it is interesting to note that a closely related carbohydrate derivative **24** failed to undergo oxymercuration–demercuration[12]. In view of the limited amount of information at our disposal, it is perhaps unrewarding to delve too deeply into the precise mechanism of the addition of mercuric azide to the unsaturated sugars

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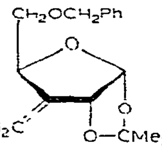
*Dr. Bourgeois has kindly informed us that recent investigations in his laboratory have led to the same conclusion.

4 and **20**. As with oxymercurations, various modes of addition, including molecular *cis*-addition[13] and additions *via* mercurinium ions[7,14] and mercury-substituted carbocations[14], are possible, depending on electronic or steric constraints imposed by the alkene. However, it is notable that the preponderant, if not exclusive, product from the addition of mercuric azide to the unsaturated sugar **4** involves attack of azide ion at the tertiary centre from the less-hindered side of the bicyclic ring-system. There is a good analogy with the oxymercuration of such bicyclic alkenes as **25**, which furnishes the *exo*-alcohol **26** (89%) following demercuration[15], although the initial oxymercuration reaction appears to be much more rapid than that of mercuric azide with **4**. Brown[15] has also noted the preference for *exo* attack by lithium aluminium hydride on the corresponding ketones, and a similar preference is found[16] with the ketone from which **4** was derived. Such information may be helpful in predicting the stereochemistry of the addition of mercuric azide to other unsaturated sugars, particularly when steric constraints have been introduced in the design of a synthesis. The result obtained with the unsaturated sugar **20** demonstrates that suitably located hydroxyl groups are able to complete very effectively with azide ion in the capture of the initial intermediate. While competition by the internal nucleophile clearly militates against a concerted molecular addition of mercuric azide to the unsaturated sugar **20**, it does not distinguish between possible ionic intermediates formed initially.



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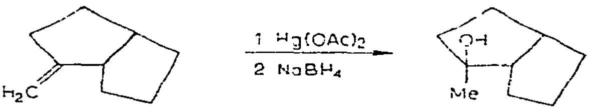
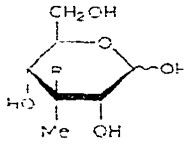
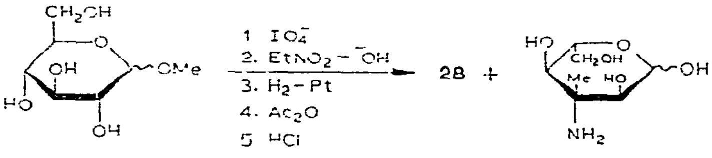


25 26



27 R = N_3
28 R = NH_2



29 L-28

The characterization of the branched-chain azide **5** permitted a chemical solution to a problem of long-standing interest, namely the characterization of the products obtained by base-catalysed condensation of nitroethane with periodate-oxidized methyl α-(or β)-D-glucopyranoside[6,17]. Hydrolysis of **5** with dilute hydrochloric acid gave 3-azido-3-deoxy-3-*C*-methyl-D-glucopyranose (**27**), which afforded 3-amino-3-deoxy-3-*C*-methyl-D-glucopyranose (**28**) [m.p. 155–157° (dec.), $[\alpha]_D$ +18 ±1° (*c* 0.5, water)] following hydrogenation in methanol over a platinum catalyst.

One of the products obtained[17] from methyl α(or β)-D-glucopyranoside (**29**) *via* the nitroethane procedure, by the sequence of reactions shown, possesses physical constants [m.p. 158–160° (dec.), $[\alpha]_D$ +22.4° (*c* 1.02, water)] in close agreement with those of **28**, and can therefore be assigned the D-*gluco* configuration. The other product derived *via* the nitroethane route is the enantiomer L-**28** [m.p. 159–161° (dec.), $[\alpha]_D$ −22° (*c* 1, water)], which presumably arises from a base-catalysed stereomutation of the "dialdehyde" prior to condensation with nitroethane. The foregoing chemical correlation linking the two routes confirms the tentative assignments made for D- and L-**28** and their progenitors on the basis of n.m.r. spectroscopy[6,17].

EXPERIMENTAL

Kieselgel G (Merck) was used for t.l.c., and spots were detected with vanillin–sulphuric acid[18]. I.r. spectra were recorded for Nujol mulls with a Perkin–Elmer Infracord spectrometer, and n.m.r. spectra were measured for solutions in deuteriochloroform (1% of tetramethylsilane as the internal standard) with a Perkin–Elmer R-10 spectrometer. Optical rotations were measured at ambient temperature with a Perkin–Elmer 141 automatic polarimeter. Unless otherwise indicated, light petroleum refers to the fraction having b.p. 40–60°.

Caution: Mercuric azide is explosive, but there is no danger if the instructions given[7] are followed. It is important to add mercuric acetate to the solution of sodium azide in aqueous tetrahydrofuran, and not *vice versa*, when generating mercuric azide *in situ*.

3-Azido-3-deoxy-1,2:5,6-di-O-isopropylidene-3-C-methyl-α-D-glucofuranose (**5**). — A stirred suspension of 1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose[8] (**4**, 2.6 g) in a mixture of tetrahydrofuran (15 ml) and water (15 ml) containing mercuric acetate (3.2 g) and sodium azide (1.95 g) was heated at ~90° for 96 h. The mixture was cooled (~45°) and diluted with 15% sodium hydroxide solution (10 ml), whereafter a solution of sodium borohydride (0.2 g) in 15% sodium hydroxide solution (10 ml) was added. Separation and evaporation of the organic layer afforded a syrupy residue which was chromatographed on silica gel (ether–light petroleum, 1:3) to give the branched-chain azide **5** (1.3 g, 43%), b.p. ~79°/0.4 mmHg, $[\alpha]_D$ −15° (*c* 1.2, chloroform), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 52.4; H, 7.1; N, 14.0. $C_{13}H_{21}N_3O_5$ calc.: C, 52.2; H, 7.0; N, 14.0%). N.m.r. data: τ 4.13 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 5.63 (d, 1 H, H-2); and 8.45, 8.49, 8.60, and 8.65 (4 s, 15 H, intensity ratio 1:1:1:2, C(3)-Me and 2CMe$_2$). Starting material (~40%) was also recovered by the chromatographic procedure.

3-Azido-3-deoxy-1,2-O-isopropylidene-3-C-methyl-α-D-glucofuranose (**7**). — A solution of the diacetal **5** (0.8 g) in 70% acetic acid (24 ml) was set aside at room temperature for 19 h, after which time solid sodium hydrogen carbonate was added to neutralise the acid. Solids were filtered off and the filtrate was concentrated at room temperature. The residue was extracted with ether (4 × 25 ml), and the combined ethereal extracts were concentrated. Chromatography of the residue on silica gel (ether–light petroleum, 1:1) gave the monoacetal **7** (0.63 g, 91%), m.p. 67–68.5° (from cyclohexane), $[\alpha]_D$ −1.5° (*c* 1, chloroform), ν_{max} 3400 (OH) and 2100 cm^{-1} (N_3) (Found: C, 46.5; H, 6.5; N, 16.2. $C_{10}H_{17}N_3O_5$ calc.: C, 46.3; H, 6.6; N, 16.2%). N.m.r. data: τ 4.07 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 5.64 (d, 1 H, H-2); and 8.38, 8.48, and 8.67 (3 s, 9 H, C(3)-Me and CMe_2).

3-Azido-3-deoxy-1,2-O-isopropylidene-5,6-di-O-methanesulphonyl-3-C-methyl-α-D-glucopyranose (**8**). — A cooled (0°) solution of the monoacetal **7** (0.52 g) in pyridine (10 ml) was treated with methanesulphonyl chloride (0.9 g) for 1 h, and the solution was then kept at room temperature overnight. Work-up in the usual way and chromatography on silica gel (elution first with chloroform and then with ether–chloroform, 1:4) gave the dimethanesulphonate **8** (0.5 g, 60%), m.p. 80–82° [from ethanol–light petroleum (b.p. 60–80°)], $[\alpha]_D$ −11° (*c* 1, chloroform), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 34.7; H, 4.8; N, 10.1; S, 15.7. $C_{12}H_{21}N_3O_9S_2$ calc.: C, 34.7; H, 5.1; N, 10.1; S, 15.4%). N.m.r. data: τ 4.07 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 5.47 (d, 1 H, H-2); 6.80 and 6.88 (2 s, 6 H, 2OMs); and 8.38, 8.47, and 8.64 (3 s, 9 H, C(3)-Me and CMe_2).

3,6-Acetylepimino-3,6-dideoxy-1,2-O-isopropylidene-5-O-methanesulphonyl-3-C-methyl-α-D-glucofuranose (**9**). — A solution of the dimethanesulphonate **8** (0.5 g) in methanol (15 ml) containing Adams' catalyst (0.15 g) was shaken overnight at room temperature under a slight overpressure of hydrogen. The catalyst was then filtered off and the solvent was removed. The residue in pyridine (5 ml) was treated with acetic anhydride (1 ml) until no starting material remained (t.l.c.). Chromatography on silica gel (chloroform–ether, 9:1) furnished **9** (0.3 g, 74%), m.p. 45–50° (from carbon tetrachloride–cyclohexane), $[\alpha]_D$ −17.5° (*c* 0.3, chloroform), ν_{max} 1650 cm^{-1} (NAc) (Found: C, 46.6; H, 6.65; N, 3.85; S, 8.9. $C_{13}H_{21}NO_7S$ calc.: C, 46.5; H, 6.3; N, 4.2; S, 9.5%). N.m.r. data: τ 4.14 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.85 (m, 1 H, H-5), 5.48 (d, 1 H, H-2), 6.88 (s, 3 H, OMs), 7.96 (s, 3 H, NAc), and 8.48 and 8.67 (2 s, 9 H, intensity ratio 2:1, C(3)-Me and CMe_2).

3-Azido-3-deoxy-1,2-O-isopropylidene-3-C-methyl-6-O-toluene-p-sulphonyl-α-D-glucofuranose (**12**). — A cooled (0°) solution of the monoacetal **7** (0.52 g) in pyridine (5 ml) was treated with toluene-*p*-sulphonyl chloride (0.38 g) for 1 h, and the solution was then set aside at room temperature until the reaction was complete (t.l.c.). Work-up in the usual way and chromatography on silica gel (chloroform) afforded the monotosylate **12** (0.3 g, 36%), m.p. 100–102° [from ethanol–light petroleum (b.p. 60–80°)], $[\alpha]_D$ +8° (*c* 1, chloroform), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 49.1; H, 5.4; N, 9.9; S, 7.7. $C_{17}H_{23}N_3O_7S$ calc.: C, 49.4; H, 5.6; N, 10.2; S, 7.7%). N.m.r. data: τ ~2.30 (m, 4 H, Ar-*H*); 4.20 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 5.63 (d, 1 H, H-2); 7.53 (s, 3 H, Ar*Me*); and 8.40, 8.52, and 8.68 (3 s, 9 H, C(3)-Me and CMe_2).

3-Azido-3-deoxy-1,2-O-isopropylidene-5-O-methanesulphonyl-3-C-methyl-6-O-toluene-p-sulphonyl-α-D-glucofuranose (**13**). — A solution of the sulphonate **12** (0.25 g) in pyridine (5 ml) was treated with methanesulphonyl chloride (0.2 g) overnight at room temperature. Work-up and chromatography on silica gel (ether–light petroleum, 1:4) gave the disulphonate **13** (0.3 g, ~100%), $[\alpha]_D$ +7° (*c* 1.1, chloroform),

ν_{max} 2100 cm^{-1} (N_3), as a syrup that could not be induced to crystallise. N.m.r. data: τ ~2.30 (m, 4 H, Ar-*H*); 4.17 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 6.87 (s, 3 H, OMs); 7.54 (s, 3 H, Ar*Me*); and 8.41, 8.50, and 8.67 (3 s, 9 H, C(3)-Me and CMe_2).

3,6-Dideoxy-3,6-epimino-1,2-O-isopropylidene-5-O-methanesulphonyl-3-C-methyl-α-D-glucofuranose (**11**). — A solution of the disulphonate **13** (0.25 g) in dry methanol (10 ml) containing Adams' catalyst (0.1 g) was shaken overnight at room temperature under a slight overpressure of hydrogen. The catalyst and solvent were removed, and the residue was treated with a cold, dilute, aqueous solution of sodium hydrogen carbonate. After concentration of the solution to dryness, the residue was extracted with benzene (3 × 20 ml). Evaporation of the combined extracts afforded the epimine **11** (0.14 g, 94%), m.p. 138–139° (from ethanol–cyclohexane), $[\alpha]_D$ +40° (*c* 0.9, chloroform), ν_{max} 3380 (NH) (Found: C, 45.0; H, 6.7; N, 4.5. $C_{11}H_{19}NO_6S$ calc.: C, 45.0; H, 6.5; N, 4.8%). N.m.r. data: τ 3.97 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 6.87 (s, 3 H, OMs), and 8.47 and 8.64 (2 s, 9 H, intensity ratio 1:2, C(3)-Me and CMe_2).

Acetylation of the epimine **11** furnished the *N*-acetylepimine **9** identical (m.p., i.r. and n.m.r. spectra) with that obtained previously.

3-Azido-6-O-benzoyl-3-deoxy-1,2-O-isopropylidene-3-C-methyl-α-D-glucofuranose (**14**). — A solution of the monoacetal **7** (0.33 g) in pyridine (6 ml) was treated with benzoyl chloride (0.18 g) at room temperature for 8 h, after which time the reaction mixture was processed in the usual way. Chromatography on silica gel (ether–light petroleum, 1:3) gave the monobenzoate **14** (0.4 g, 86%), m.p. 85–87° (from light petroleum), $[\alpha]_D$ −4° (*c* 0.9, chloroform); ν_{max} 1730, 1600 (benzoate), and 2100 cm^{-1} (N_3) (Found: C, 56.3; H, 5.9; N, 11.3. $C_{17}H_{21}N_3O_6$ calc.: C, 56.2; H, 5.8; N, 11.6%). N.m.r. data: τ ~2.20 (m, 5 H, OBz); 4.11 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 5.10–6.15 (5 H, H-2, H-4–H-6'); and 8.34, 8.49, and 8.65 (3 s, 9 H, C(3)-Me and CMe_2).

3-Azido-6-O-benzoyl-3-deoxy-1,2-O-isopropylidene-5-O-methanesulphonyl-3-C-methyl-α-D-glucofuranose (**15**). — The monobenzoate **14** (1.3 g) in dry pyridine (20 ml) was treated with methanesulphonyl chloride (0.9 g) at room temperature for 16 h. Work-up and chromatography on silica gel (ether–light petroleum, 1:1) afforded the diester **15** (1.4 g, 89%), m.p. 84–85° (from cyclohexane), $[\alpha]_D$ +2° (*c* 1, chloroform), ν_{max} 1730 (benzoate) and 2100 cm^{-1} (N_3) (Found: C, 49.1; H, 5.3; N, 9.5; S, 7.3. $C_{18}H_{23}N_3O_8S$ calc.: C, 49.0; H, 5.2; N, 9.5; S, 7.25%). N.m.r. data τ ~2.20 (m, 5 H, OBz); 4.03 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 6.91 (s, 3 H, OMs); and 8.34, 8.46, and 8.63 (3 s, 9 H, C(3)-Me and CMe_2).

3-Acetamido-3-deoxy-1,2:5,6-di-O-isopropylidene-3-C-methyl-α-D-glucofuranose (**16**). — A solution of the azido derivative **5** (0.9 g) in dry methanol (40 ml) containing Adams' catalyst (0.2 g) was shaken at room temperature for 24 h under a slight overpressure of hydrogen. After removal of the catalyst and solvent, the residue was treated in pyridine (5 ml) with acetic anhydride (2 ml) until t.l.c. (chloroform–ethyl acetate, 3:1) showed that the acetylation was complete. Work-up in the usual way and chromatography on silica gel (chloroform–ethyl acetate, 3:1) furnished the acetamido derivative **16** (0.7 g, 74%), m.p. 106–108° [from light petroleum (b.p. 60–80°)], $[\alpha]_D$ −19° (*c* 1, chloroform), ν_{max} 1650 and 1540 cm^{-1} (NHAc) (Found:

C, 57.1; H, 7.8; N, 4.3. $C_{15}H_{25}NO_6$ calc.: C, 57.1; H, 7.9; N, 4.4%). N.m.r. data: τ 4.07 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); 4.91 (d, 1 H, H-2); 5.60–6.30 (4 H, H-4–H-6'); 7.99 (s, 3 H, NAc); and 8.44, 8.48, 8.55, 8.63, and 8.68 (5 s, 15 H, C(3)-Me and 2CMe_2). The n.m.r. spectrum was indistinguishable from that of a material prepared by Bourgeois[9a] having m.p. 103.5–105°, $[\alpha]_D$ −19° (chloroform).

*1,2-O-Isopropylidene-3-C-methylene-α-*D-ribo-*hexofuranose* (**20**) and *3-C-methylene-*D-ribo-*hexopyranose* (**21**). — A solution of the diacetal **4** (1.5 g) in 70% acetic acid (20 ml) was set aside at room temperature until t.l.c. (ethyl acetate–light petroleum, 1:2) indicated that no starting material remained. The acid was neutralised with aqueous sodium hydrogen carbonate, and the solvents were removed at room temperature. The residue was extracted with ether (4 × 25 ml), and the combined ethereal extracts were concentrated to dryness. Chromatography of the residue on silica gel (ethyl acetate–light petroleum, 1:2) afforded first the monoacetal **20** (0.8 g, 63%), $[\alpha]_D$ +122° (*c* 1, chloroform); this material solidified on standing, but a suitable solvent for recrystallisation could not be found. Continued elution afforded the *C*-methylenehexose **21** (0.33 g, 32%), m.p. 132–134° [from ethanol–light petroleum (b.p. 60–80°)], $[\alpha]_D$ +62° (*c* 0.5, chloroform), ν_{max} 1650 cm^{-1} (weak, C=C) (Found: C, 47.4; H, 7.0. $C_7H_{12}O_5$ calc.: C, 47.8; H, 6.8%).

An almost quantitative yield of the monoacetal **20** was obtained when the hydrolysis was performed with 50% acetic acid at room temperature.

*3,6-Anhydro-1,2-O-isopropylidene-3-C-methyl-α-*D-*glucofuranose* (**22**). — A stirred solution of the *C*-methylene derivative **20** (0.8 g) in aqueous tetrahydrofuran (16 ml, 1:1 v/v) containing sodium azide (0.9 g) and mercuric acetate (1.46 g) was heated at ~85° for 90 h, whereupon the organomercury adduct was reduced with sodium borohydride as previously described. Chromatography of the final residue on silica gel (ether–light petroleum, 1:1) furnished the anhydro sugar **22** (0.3 g, 37.5%), ν_{max} 3400 cm^{-1} (OH), which after sublimation at 70°/0.05 mmHg had m.p. 64–66°, $[\alpha]_D$ +23° (*c* 1.2, chloroform), ν_{max} 3400 cm^{-1} (OH) (Found: C, 56.2; H, 7.3. $C_{10}H_{16}O_5$ calc.: C, 55.5; H, 7.4%). N.m.r. data: τ 4.13 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.58 (d, 1 H, H-2), and 8.50 and 8.67 (2 s, 9 H, intensity ratio 1:2, C(3)-Me and CMe_2). Starting material (~30%) was also recovered from the column.

*5-O-Acetyl-3,6-anhydro-1,2-O-isopropylidene-3-C-methyl-α-*D-*glucofuranose* (**23**). — Acetylation of the anhydro sugar **22** in the usual way afforded the monoacetate **23** (85%), b.p. 100° (bath)/0.05 mmHg, $[\alpha]_D$ +63° (*c* 0.6, chloroform), ν_{max} 1740 cm^{-1} (acetate) (Found: C, 55.9; H, 7.2. $C_{12}H_{18}O_6$ calc.: C, 55.8; H, 7.0%). N.m.r. data: τ 3.98 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.77 (m, 1 H, $J_{4,5}$ 4 Hz, $J_{5,6} = J_{5,6'} = \sim 9$ Hz, H-5), 5.40 (d, 1 H, H-4), 5.57 (d, 1 H, H-2), 5.77 and 6.27 (2 t, 2 H, J_{gem} ~9 Hz, H-6,6'), 7.87 (s, 3 H, OAc), and 8.47 and 8.61 (2 s, 9 H, intensity ratio 1:2, C(3)-Me and CMe_2).

*3-Azido-3-deoxy-3-C-methyl-*D-*glucopyranose* (**27**). — A solution of the diacetal **5** (0.2 g) in water (~10 ml) was stirred overnight with Amberlite IR-120(H^+) resin at room temperature. Removal of the resin and solvent furnished the free sugar **27** (0.13 g, 89%), m.p. 166–168° (dec.) [from ethanol–light petroleum (b.p. 60–80°)],

$[\alpha]_D$ +51° (c 1, methanol), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 38.6; H, 5.9; N, 19.4. $C_7H_{13}N_3O_5$ calc.: C, 38.4; H, 5.9; N, 19.2%).

*3-Amino-3-deoxy-3-C-methyl-*D*-glucopyranose* (**28**). — A solution of the azido sugar **27** (0.15 g) in dry methanol (10 ml) containing Adams' catalyst (0.1 g) was shaken at room temperature under a slight overpressure of hydrogen for 3 h. Water was added to dissolve any product that had precipitated from solution, and the catalyst and solvents were removed to give the amino sugar **28** (0.1 g, 76%), m.p. 155–157° (dec.; from methanol–benzene), $[\alpha]_D$ $+18 \pm 1°$ (c 0.5, water); lit.[17] m.p. 158–160° (dec.), $[\alpha]_D$ +22.4° (c 1.02, water).

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