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A NOVEL ROUTE TO 1,4-ANHYDRO DERIVATIVES OF β-D-GALACTOPYRANOSE*

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ABSTRACT

Treatment of 1-*O*-acetyl-4-*O*-mesyl derivatives of α-D-glucopyranose with sodium azide in *N,N*-dimethylformamide gave 1,4-anhydro derivatives of β-D-galactopyranose and not the expected 4-azides. 1,4-Anhydro-6-azido-2,3-di-*O*-benzoyl-6-deoxy-β-D-galactopyranose was converted into the corresponding 6-bromide, using hydrogen bromide in glacial acetic acid. Similar treatment of 6-azido- and 4,6-diazido-hexoses leads to rapid and specific substitution of the 6-azide by bromide in each case.

INTRODUCTION

The synthesis of 1,4-anhydrohexoses by treatment of 4- and 5-sulphonic esters with base or nucleophiles has been reported on several occasions[1–4]. The configuration of the resulting products has sometimes been in doubt[2,5]. Brimacombe *et al.*[3] concluded that, in general, such reactions occur via intramolecular displacement of the 4-*O*-sulphonyl group, accompanied by inversion of configuration at C-4, whilst noting that nucleophilic reactions of rhamnopyranoside 4-sulphonates occur via an unusual ring contraction involving cleavage of the C-5–O-5 bond[6,7], a mechanism which might also operate in the formation of 1,4-anhydro sugars. Here, we report in full[8] on the formation of 1,4-derivatives of β-D-galactose during attempts to carry out nucleophilic substitution with azide on 1-*O*-acetyl-4-*O*-mesyl derivatives of α-D-glucopyranose. The direct conversion of 6-azidohexoses into the corresponding 6-bromides, using hydrogen bromide in glacial acetic acid, has also been studied.

RESULTS AND DISCUSION

Nucleophilic substitution of the 1-*O*-acetyl-4,6-di-*O*-mesyl derivative **2** with azide, followed by conversion into the 1-bromide **4** and subsequent phosphoryla-

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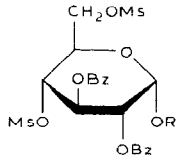
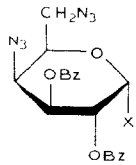
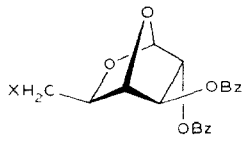
tion, was considered as a possible route to 4,6-diamino derivatives of galactose 1-phosphate[9]. However, treatment of **2** with sodium azide in hexamethylphosphoric triamide gave a crystalline azide **5** (49%), the spectral data of which were not in accord with the expected structure **3**. I.r. and ^{1}H-n.m.r. spectra indicated the presence of azide and benzoate (× 2) substituents, and the absence of mesyl, acetyl, and hydroxyl groups. When the azide **5** reacted with hydrogen bromide in glacial acetic acid, immediate effervescence was noted and another crystalline derivative **6** was isolated in good yield (70%). The i.r. and ^{1}H-n.m.r. spectra of **6** were similar to those of **5** apart from the absence of an azide absorption band. The mass spectrum of **6** showed a base peak at *m/z* 339 ($M^+ - 94$), resulting from loss of CH_2Br, suggesting that **5** and **6** could be 1,4-anhydropyranoses (1,5-anhydrofuranoses). Inspection of the ^{1}H-n.m.r. spectrum of the azide **5** supported this conclusion. The anomeric bridgehead proton appeared as a narrow doublet at δ 6.03 ($J_{1,2}$ 2.5 Hz), comparable with that of 1,4-anhydrides having an *exo* proton at C-2, such as 1,4-anhydro-6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranose[4], although less than that observed[10] for bicyclo[2.2.2]heptane derivatives (3.2–6.0 Hz). It is noteworthy that the coupling of *endo* protons with vicinal bridgehead protons is normally zero[3,10]. A triplet at δ 4.1 was assigned to H-5. Spin decoupling of this signal caused the H-6 signal to collapse to a singlet, leaving the remainder of the spectrum unaffected, suggesting $J_{4,5}$ ~0 Hz in agreement with a dihedral angle of ~90° in the proposed structure (**5**). The observed long-range coupling ($J_{2,4}$ 1.5 Hz) was also in accord with the strained 1,4-anhydride (**5**)[11,12]. In the broadly similar spectrum of the derived bromide **6**, a $J_{4,5}$ value of 2.5 Hz was observed, the signal for H-5 appearing as a septet.



1 R = Me
2 R = Ac



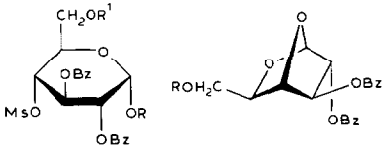
3 X = OAc
4 X = Br



5 X = N_3
6 X = Br

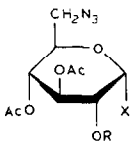
In order to avoid any possibility of mechanistic involvement by the concurrent azide substitution at C-6 in the formation of the anhydro ring, the 1-*O*-acetyl derivatives **8** and **10** were prepared by treatment of methyl 2,3-di-*O*-benzoyl-4,6-di-*O*-mesyl-α-D-glucopyranoside (**1**) with sodium benzoate and sodium acetate in butanone, respectively, to give the 6-acyl derivatives **7** and **9**, followed by acetolysis. Treatment of **8** with sodium azide in hexamethylphosphoric triamide gave the 1,4-anhydro tribenzoate **11**, and similar treatment of **10** gave the corresponding 6-*O*-acetyl-1,4-anhydro-2,3-di-*O*-benzoyl derivative **12**. The ^{1}H-n.m.r. spectra were totally in accord with the 1,4-anhydro structure, a long-range coupling ($J_{2,4}$ 1.5 Hz) being observed in each case.

The 1,4-anhydro ring of **11** and **12** was unexpectedly resistant to acid-catalysed hydrolysis; thus, treatment of the 6-acetate **12** with 3% HCl in boiling acetone gave the corresponding 6-hydroxy derivative **13**. However, *O*-deacetylation of **12** followed by treatment with aqueous HCl gave D-galactose, whilst de-esterification followed by treatment with concentrated nitric acid gave galactaric (mucic) acid, confirming the *galacto* configuration of the 1,4-anhydrides.

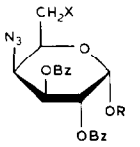


7 R = Me, R^1 = Bz
8 R = Ac, R^1 = Bz
9 R = Me, R^1 = Ac
10 R = Ac, R^1 = Ac

11 R = Bz
12 R = Ac
13 R = H



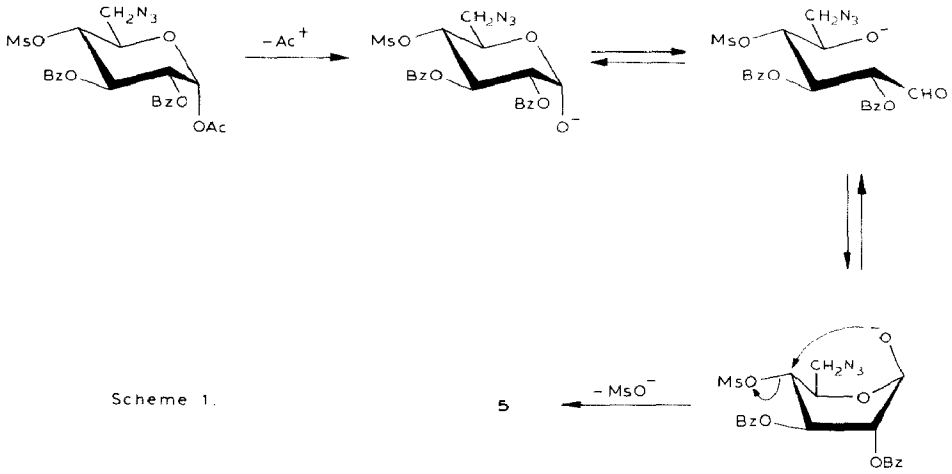
14 R = Ac, X = OAc
15 R = Ts, X = OAc
16 R = Ac, X = Br
17 R = Ts, X = Br



18 R = Me, X = N_3
19 R = Me, X = Br
20 R = Ac, X = Br

Originally, we proposed a ring-contraction mechanism to account for the differing behaviour of the 1-acetate **2** towards azide, compared with the corresponding methyl glycoside **1**, where the expected nucleophilic displacements at C-4 and C-6 occur smoothly[13]. Similar mechanisms had been proposed[14] for similar reactions of pyranoside 4-sulphonates in which direct displacement is inhibited by the presence of an axial substituent at C-2. However, this mechanism has been shown to be unlikely by the work of Brimacombe *et al.*[15], who showed that 1-*O*-acetyl-6-deoxy-2,3-*O*-isopropylidene-4-*O*-mesyl-α-L-mannopyranose and the epimeric L-talopyranose-4-sulphonate each gave a 1,4-anhydride with inversion of configuration at C-4 when treated with sodium azide in *N,N*-dimethylformamide. Attack by azide anion leads to *O*-deacetylation, followed by anomerisation of the resulting anion, and subsequent elimination of the mesyloxy anion from C-4 to give the 1,4-anhydro-β-D-galactopyranose (Scheme 1)[16]. Conclusive support for the Brimacombe mechanism has been provided by the work of Dessinges *et al.*[16], who were able to show by ^{17}O- and ^{18}O-induced isotopic shifts in the ^{13}C-n.m.r. spectrum of **5** that the bridging 1,4-oxygen was derived from the anomeric oxygen, and not from O-5 of **2**. It is interesting to note that treatment of 1,2,3,6-tetra-*O*-benzoyl-4-*O*-mesyl-α-D-glucopyranose with sodium azide in dimethyl sulphoxide gave[17] the 1,4-anhydro tribenzoate **11**, whereas similar treatment of 1,2,3-tri-*O*-benzoyl-4-*O*-mesyl-β-L-arabinopyranose gave the corresponding 4-azidoxylopyranose[17].

The general applicability of the nucleophilic replacement reaction of the azide group by bromide was tested using the 6-azides **14** and **15**. In each case, treatment with hydrogen bromide in glacial acetic acid was accompanied by vigorous effervescence to give the 1,6-dibromides **16** and **17** in good yield. Similar treatment of the diazidoglycoside **18** for only 2 min gave the 4-azido-6-bromo derivative **19** in 64% yield, thereby providing a convenient route to derivatives of 4-amino-4,6-dideoxy-D-galactose. Initial protonation of the azide group followed



Scheme 1.

5

by displacement of HN_3 with bromide ion is the most probable mechanism; no other reaction products were detected, suggesting a simple mechanism of this type. The i.r. spectrum of the gas evolved in the above experiments showed strong absorption bands at 2130 and 2160 cm^{-1} characteristic of the azide group. The gaseous product resulting from similar treatment of sodium azide displayed an identical spectrum.

Acetolysis of **19** gave the corresponding 1-acetate **20**, but subsequent treatment with hydrogen bromide in glacial acetic acid resulted in slow decomposition, presumably due to loss of the 4-azido group. Acetolysis of the 4,6-diazido-galactoside **18** provided an alternative route to the corresponding 4,6-diazido 1-acetate **3**, thus avoiding the formation of a 1,4-anhydride.

Thus, replacement of a primary azide group with bromide is possible, even in the presence of a secondary azide group, provided short reaction times (~2 min) are employed. Prolonged exposure of 4-azidohexoses to hydrogen bromide in glacial acetic acid results in slow decomposition.

EXPERIMENTAL

Solutions were concentrated under reduced pressure below 40°. Melting points were measured on a Kofler hot-stage and are uncorrected. ^{1}H-N.m.r. spectra were recorded with a Varian HA-100 spectrometer on solutions in $CDCl_3$ unless otherwise stated. First-order coupling constants were measured to ±0.2 Hz. I.r. spectra were recorded with a Perkin–Elmer 681 spectrophotometer. Optical rotations were measured on 1% solutions in chloroform, using a Perkin–Elmer 141 polarimeter at 20 ±2°. T.l.c. was performed on Kieselgel G (Merck), with detection by charring with ethanolic sulphuric acid. Light petroleum (b.p. 40–60°) was used throughout.

*1,4-Anhydro-6-azido-2,3-di-*O*-benzoyl-β-*D*-galactopyranose* (**5**). — The 4,6-

dimesylate[9] **2** (3 g) and sodium azide (2 g) were heated in hexamethylphosphoric triamide (3 mL) for 3 h at 80°. The mixture was cooled and poured into ice–water (50 mL), the precipitate was collected, and a solution in dichloromethane (15 mL) was dried ($MgSO_4$) and concentrated to dryness, to give a syrup that crystallised on the addition of ethanol to give **5** (1.0 g, 49%), m.p. 118–120°, $[\alpha]_D$ +239° (Found: C, 61.1; H, 4.5; N, 10.1. $C_{20}H_{17}N_3O_6$ calc.: C, 60.8; H, 4.3; N, 10.6%). ^{1}H-N.m.r. data (100 MHz, C_5D_5N): δ 6.03 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 5.28 (d, 1 H, $J_{2,3}$ 1.5, $J_{3,4}$ 0.0 Hz, H-3), 5.21 (m, 1 H, $J_{2,4}$ 1.5 Hz, H-2), 4.84 (d, 1 H, $J_{4,5}$ 0.0 Hz, H-4), 4.10 (t, 1 H, J_5 6 Hz, H-5), 3.24 (d, 2 H, H-6,6′).

*Reaction of 1,4-anhydro-6-azido-2,3-di-*O*-benzoyl-6-deoxy-β-*D*-galactopyranose* (**5**) *with hydrogen bromide.* — To a solution of **5** (0.4 g) in dichloromethane (5 mL) at 0° was added 45% hydrogen bromide in glacial acetic acid (5 mL) dropwise. Immediate effervescence occurred. After 5 min, the solution was diluted with dichloromethane (10 mL), washed successively with ice–water, saturated, aq. sodium hydrogencarbonate (2 × 20 mL), and ice–water, dried ($MgSO_4$), filtered, and concentrated at 10°. The syrupy residue crystallised on the addition of ethanol, and recrystallisation from ethanol gave 1,4-anhydro-2,3-di-*O*-benzoyl-6-bromo-6-deoxy-β-D-galactopyranose (**6**; 0.3 g, 70%), m.p. 117–119°, $[\alpha]_D$ +58° (Found: C, 54.9; H, 3.8. $C_{20}H_{17}BrO_6$ calc.: C, 55.4; H, 3.9%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.14 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.55 (s, 1 H, $J_{2,3} = J_{3,4}$ = 0.0 Hz, H-3), 4.93 (dd, 1 H, $J_{2,4}$ 1.6 Hz, H-2), 5.00 (d, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 4.41 (ddd, 1 H, $J_{5,6}$ 8.6, $J_{5,6'}$ 6.0 Hz, H-5), 3.79 (dd, 1 H, $J_{6,6'}$ 10.0 Hz, H-6), 3.57 (dd, 1 H, H-6′). Mass spectrum: *m/z* 353 [0.35%, (M^+ − Br)].

*1,4-Anhydro-2,3,6-tri-*O*-benzoyl-α-*D*-glucopyranose* (**11**). — 1-*O*-acetyl-2,3,6-tri-*O*-benzoyl-4-*O*-mesyl-α-D-glucopyranose[9] (**8**, 1 g) and sodium azide (0.5 g) were heated in hexamethylphosphoric triamide (2 mL) for 2 h at 80°. The mixture was cooled and poured into water (20 mL), and the precipitate was collected and recrystallised twice from ethanol to give **11** (0.4 g, 52%), m.p. 136–138°, $[\alpha]_D$ +117° (Found: C, 69.0; H, 4.85. $C_{27}H_{22}O_8$ calc.: C, 68.4; H, 4.65%). ^{1}H-N.m.r. data (100 MHz, C_5D_5N): δ 6.27 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 5.53 (d, 1 H, $J_{2,3}$ 1.5, $J_{3,4}$ 0.0 Hz, H-3), 5.42 (m, 1 H, $J_{2,4}$ 1.5 Hz, H-2), 4.93 (d, 1 H, $J_{4,5}$ 0.0 Hz, H-4), 4.50 (s, 3 H, H-5,6,6′).

*Methyl 6-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-mesyl-α-*D*-glucopyranoside* (**9**). — Methyl 2,3-di-*O*-benzoyl-4,6-di-*O*-mesyl-α-D-glucopyranoside[13] (**1**, 20 g) and anhydrous sodium acetate (12 g) were heated at 80° in hexamethylphosphoric triamide (10 mL) for 3 h. The cooled mixture was poured into ice–water (200 mL), and the resulting white precipitate was collected, washed with water, and recrystallised from ethanol to give **9** (17 g, 84%), m.p. 191–192°, $[\alpha]_D$ +136° (Found: C, 55.5; H, 5.0. $C_{24}H_{26}O_{11}S$ calc.: C, 55.2; H, 5.0%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.54 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 6.06 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H-3), 5.41 (dd, 1 H, H-2), 5.13 (t, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 4.30 (m, 1 H, H-5), 5.60 (m, 2 H, H-6,6′).

*1,6-Di-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-mesyl-α-*D*-glucopyranose* (**10**). — The

6-acetate **9** (5 g) was stirred with 4% conc. sulphuric acid in acetic anhydride (25 mL) for 24 h at 20° and the mixture was poured into ice–water (3 L) with stirring. The resulting white precipitate was collected, washed with water, and crystallised from methanol. Recrystallisation of the crude product (4 g, 76%) gave **10**, m.p. 196–199°, $[\alpha]_D$ +128.5° (Found: C, 54.5; H, 4.9. $C_{25}H_{26}O_{12}S$ calc.: C, 54.5; H, 4.7%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.54 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 6.06 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H-3), 5.41 (dd, 1 H, H-2), 5.13 (t, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 4.40 (m, 2 H, H-6,6'), 4.30 (m, 1 H, H-5).

*6-O-Acetyl-1,4-anhydro-2,3-di-O-benzoyl-β-*D*-galactopyranose* (**12**). — The 1,6-diacetate **10** (2 g) and sodium azide (0.5 g) were heated for 1 h at 90° in hexamethylphosphoric triamide (3 mL). The cooled mixture was poured into water (50 mL), the precipitate was collected, and a solution in dichloromethane (20 mL) was filtered and concentrated to afford a syrup that crystallised on the addition of ethanol. Recrystallisation from ethanol gave **12** (1 g, 67%), m.p. 124.5–126°, $[\alpha]_D$ +214° (Found: C, 64.1; H, 5.1. $C_{22}H_{20}O_8$ calc.: C, 64.1; H, 4.9%). ^{1}H-N.m.r. data (100 MHz, C_5D_5N): δ 6.00 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 5.27 (d, 1 H, $J_{2,3}$ 1.5, $J_{3,4}$ 0.0 Hz, H-3), 5.22 (m, 1 H, $J_{2,4}$ 1.5 Hz, H-2), 4.93 (d, 1 H, $J_{4,5}$ 0.0 Hz, H-4), 4.10 (m, 3 H, H-5,6,6').

Reaction of **12** *with dilute HCl.* — A solution of **12** (0.13 g) in 3% HCl in acetone (5 mL) was heated for 5 h under reflux, then neutralised with sodium hydrogencarbonate, filtered, and concentrated to give a syrup that crystallised on the addition of di-isopropyl ether. Recrystallisation from chloroform–light petroleum gave 1,4-anhydro-2,3-di-*O*-benzoyl-β-D-galactopyranose (**13**; 0.09 g, 80%), m.p. 132–135°, $[\alpha]_D$ +235° (Found: C, 67.8; H, 5.1. $C_{20}H_{18}O_6$ calc.: C, 67.8; H, 5.1%). ^{1}H-N.m.r. data (100 MHz, C_5D_5N): δ 5.97 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 5.26 (m, 2 H, H-2,3), 4.83 (d, 1 H, $J_{3,4} = J_{4,5}$ = 0, $J_{2,4}$ 1.5 Hz, H-4), 4.03 (t, 1 H, $J_{5,6} = J_{5,6'}$ = 5.5 Hz, H-5), 3.64 (d, 2 H, H-6,6').

Reactions that confirm the D-galacto *configuration of the 1,4-anhydro series.* — (*a*) To a solution of **12** (1 g) in the minimum of dichloromethane was added methanolic 7.5% sodium methoxide (10 mL). After 12 h, the solution was deionised with Dowex 50-X2 (H^+) resin, filtered, and concentrated to a white syrup which, after exhaustive extraction with light petroleum, gave a clear, chromatographically homogeneous syrup, $[\alpha]_D$ +48°. Treatment of the syrup with aqueous 20% HCl under reflux for 30 min gave a reducing sugar indistinguishable from D-galactose (p.c.; pyridine–ethyl acetate–acetic acid–water, 5:5:1:3; tank solvent: pyridine–ethyl acetate–water, 11:40:6).

(*b*) When the de-esterified syrup, prepared from **12** (0.5 g) as in (*a*), was treated with conc. nitric acid at 0° for 24 h, a crystalline solid was formed. Decantation of the acid, followed by washing by repeated decantation with ethanol, gave a product (0.3 g, 77%), m.p. 210–214°, which was indistinguishable from authentic galactaric acid.

*1,3,4-Tri-O-acetyl-6-azido-6-deoxy-2-O-tosyl-α-*D*-glucopyranose* (**15**). — 1,3,4-Tri-*O*-acetyl-2,6-di-*O*-tosyl-α-D-glucopyranose[17] (5 g) and sodium azide (3 g)

were heated at 80° in *N,N*-dimethylformamide for 3 h. The cooled mixture was poured into ice–water, and the precipitate was collected and recrystallised from ethanol to give **15** (2.7 g, 68%), m.p. 106.5–108°, $[\alpha]_D$ +100° (Found: C, 47.0; H, 4.8; N, 8.3. $C_{19}H_{23}N_3O_{10}S$ calc.: C, 47.0; H, 4.7; N, 8.7%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.26 (d, 1 H, $J_{1,2}$ 3.8, H-1), 5.63 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.7 Hz, H-3), 5.04 (t, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.62 (dd, 1 H, H-2), 4.00 (ddd, 1 H, $J_{5,6}$ 3.2, $J_{5,6'}$ 4.8 Hz, H-5), 3.41 (dd, 1 H, $J_{6,6'}$ 13.4 Hz, H-6), 3.24 (dd, 1 H, H-6').

*Reaction of 1,2,3,4-tetra-*O*-acetyl-6-azido-6-deoxy-α-*D*-glucopyranose* (**14**) *with hydrogen bromide.* — 45% Hydrogen bromide in glacial acetic acid (5 mL) was added dropwise to a solution of **14**[18] (1 g) in dichloromethane (5 mL) at 0°. Immediate effervescence occurred and a yellow precipitate was formed. After 1 h at 20°, the mixture was diluted with dichloromethane (20 mL), washed successively with ice–water (2 × 30 mL), saturated aq. sodium hydrogencarbonate (2 × 30 mL), and ice–water (30 mL), dried ($MgSO_4$), and concentrated to a syrup that crystallised on the addition of ether. Recrystallisation from chloroform–ether afforded 2,3,4-tri-*O*-acetyl-6-bromo-6-deoxy-α-D-glucopyranosyl bromide (**16**; 0.8 g, 64%), m.p. 160–175° (sublimes), $[\alpha]_D$ +196°; lit.[19] 160–180° (sublimes), $[\alpha]_D$ +189°. ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.62 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.54 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.9 Hz, H-3), 5.24 (t, 1 H, $J_{4,5}$ 9.9 Hz, H-4), 4.82 (dd, 1 H, H-2), 4.82 (m, 1 H, $J_{5,6}$ 3.2, $J_{5,6'}$ 4.7 Hz, H-5), 3.76 (dd, 1 H, $J_{6,6'}$ 11.9 Hz, H-6), 3.40 (dd, 1 H, H-6').

Reaction of **15** *with hydrogen bromide.* — Using the procedure described above, **15** (2.4 g) in dichloromethane (12 mL) was treated with 45% hydrogen bromide in glacial acid for 12 h. Recrystallisation of the product from chloroform–light petroleum gave 3,4-di-*O*-acetyl-6-bromo-6-deoxy-2-*O*-tosyl-α-D-glucopyranosyl bromide (**17**; 1.9 g, 68%), m.p. 155–157°, $[\alpha]_D$ +163° (Found: C, 37.2; H, 3.7. $C_{17}H_{20}Br_2O_8S$ calc.: C, 37.5; H, 3.7%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.45 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.48 (t, 1 H, $J_{2,3}$ 9.4, $J_{3,4}$ 9.4 Hz, H-3), 5.11 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.51 (dd, 1 H, H-2), 4.30 (m, 1 H, $J_{5,6}$ 3.0, $J_{5,6'}$ 4.5 Hz, H-5), 3.55 (dd, 1 H, $J_{6,6'}$ 12.0 Hz, H-6), 3.39 (dd, 1 H, H-6').

*Reaction of methyl 4,6-diazido-2,3-di-*O*-benzoyl-4,6-dideoxy-α-*D*-galactopyranoside* (**18**) *with hydrogen bromide.* — Using the procedure described above, **18**[13] (1 g) in dichloromethane (5 mL) was treated with 45% hydrogen bromide in glacial acetic acid (5 mL) for 2 min. Concentration afforded a clear syrup, which crystallised on the addition of ethanol (10 mL) to give methyl 4-azido-2,3-di-*O*-benzoyl-6-bromo-4,6-dideoxy-α-D-galactopyranoside (**19**; 0.7 g, 64%), m.p. 121–124°, $[\alpha]_D$ +37° (Found: C, 51.0; H, 4.0; N, 8.0. $C_{21}H_{20}BrN_3O_6$ calc.: C, 51.4; H, 4.1; N, 8.5%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 5.91 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.6 Hz, H-3), 5.53 (dd, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 5.12 (d, 1 H, H-1), 4.45 (dd, 1 H, $J_{4,5}$ 1.7 Hz, H-4), 4.22 (m, 1 H, $J_{5,6}$ 7.0 Hz, H-5), 3.50 (m, 2 H, H-6,6').

*1-*O*-Acetyl-4-azido-2,3-di-*O*-benzoyl-6-bromo-4,6-dideoxy-α-*D*-galactopyranose* (**20**). — The 6-bromogalactoside **19** (2 g) was stirred with 4% conc. sulphuric acid in acetic anhydride (10 mL) for 20 h at 20° and the mixture was then poured

into ice–water (40 mL) with stirring. The white precipitate was collected, washed exhaustively with water, and recrystallised from ethanol to give **20** (1.7 g, 80%), m.p. 134.5–137°, $[\alpha]_D$ +18° (Found: C, 50.9; H, 3.9; N, 7.9. $C_{22}H_{20}BrN_3O_7$ calc.: C, 51.0; H, 3.85; N, 8.1%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.50 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 5.94 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.2 Hz, H-3), 5.86 (dd, 1 H, H-2), 5.62 (dd, 1 H, $J_{4,5}$ 1.7 Hz, H-4), 4.33 (m, 1 H, H-5), 3.49 (m, 2 H, H-6,6′).

1-O-Acetyl-4,6-diazido-2,3-di-O-benzoyl-4,6-dideoxy-α-D-galactopyranose (**3**). — The diazidogalactoside[13] **18** (5 g) was stirred with 4% conc. sulphuric acid in acetic anhydride (25 mL) for 2 h at 5° and the mixture was then poured into ice–water (200 mL) with stirring. The white precipitate formed during 1 h was collected and washed exhaustively with water. Recrystallisation from ethanol gave **3** (3.5 g, 66%), m.p. 144–148°, $[\alpha]_D$ +35° (Found: C, 55.0; H, 4.2. $C_{22}H_{20}N_6O_7$ calc.: C, 55.0; H, 4.2%). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 6.54 (d, 1 H, $J_{1,2}$ 3.1 Hz, H-1), 5.94 (dd, 1 H, $J_{2,3}$ 10.7, $J_{3,4}$ 3.0 Hz, H-3), 5.88 (dd, 1 H, H-2), 4.30 (m, 2 H, H-4,5), 3.64 (dd, 1 H, $J_{5,6}$ 6.5, $J_{6,6'}$ 12.0 Hz, 1 H, H-6), 3.42 (dd, 1 H, $J_{5,6'}$ 6.5 Hz, H-6′).

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