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SYNTHESIS OF SORBISTIN ANALOGUES*

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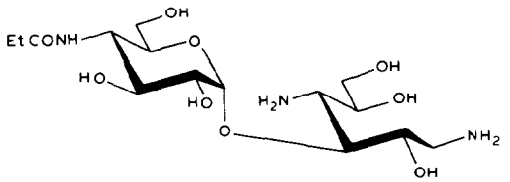
ABSTRACT

D-Galactose was converted into the glycosylating agents 4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-D-glucopyranosyl chloride (**11**) and the methyl β-D-thiopyranoside **19**. Condensation of **11** with 2,5-diazido-1,6-di-*O*-benzoyl-2,5-dideoxy-L-iditol in the presence of mercury salts gave 24% of 2,5-diazido-3-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-D-glucopyranosyl)-1,6-di-*O*-benzoyl-2,5-dideoxy-L-iditol. Methyl trifluoromethanesulfonate-promoted glycosylation of 1,3-diazido-2-*O*-benzyl-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol with **19** in the presence of 2,6-di-*tert*-butyl-4-methylpyridine gave 1,3-diazido-4-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-D-glucopyranosyl)-2-*O*-benzyl-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol (**42**), whereas, in the absence of base, migration of the *O*-isopropylidene group occurred, affording 1,3-diazido-6-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-D-glucopyranosyl)-2-*O*-benzyl-1,3-dideoxy-4,5-*O*-isopropylidene-D-gulitol in addition to **42**.

INTRODUCTION

In order to study the structure–activity relationship in the sorbistin antibiotics[2–5], the synthesis of analogues, containing the same glycosyl part (4-deoxy-4-propionamido-D-glucose) as Sorbistin-A_1 (**1**), but differing in the aglycon, was



1 Sorbistin A_1

*Part II. For Part I, see ref. 1.

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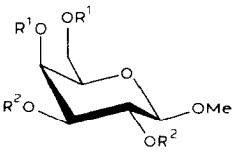
undertaken. For this purpose, 1,4- and 1,5-diaminohexitols were synthesised[1], but their partially protected derivatives contained two free hydroxyl groups, yielding multicomponent mixtures in the coupling reactions. To overcome this problem, protected monohydroxy diazidohexitols as aglycons were synthesised.

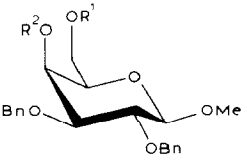
RESULTS AND DISCUSSION

Synthesis of the glycosyl donor. — The glycosyl chloride **11** has been synthesised[6] in eleven steps from methyl α-D-galactopyranoside *via* its 4,6-*O*-benzylidene derivative. Most of the intermediates were syrups which had to be purified by column chromatography. A seven-step route, starting from methyl β-D-galactopyranoside[7,8] (**2**), has now been developed which leads, *via* crystalline intermediates, to the 1-acetate **9**, the precursor of **11**.

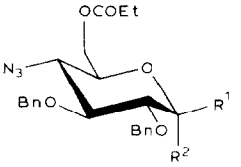
Treatment of **2** with 2-methoxypropene in *N,N*-dimethylformamide in the presence of toluene-*p*-sulfonic acid afforded the 4,6-acetal **3** (55%), which was obtained previously, together with the 3,4-acetal, only as a by-product (10%) when acetone–$CuSO_4$ was used as reagent[9]. Treatment of **3** with benzyl chloride in the presence of potassium hydroxide gave **4** (75%), the *O*-isopropylidene group of which was removed with aqueous acetic acid to give 92% of the diol **5**[8–10]. Reaction of **5** with 1 equiv. of propionic anhydride in pyridine afforded the 6-propionate **6**, the 4-mesylate (**7**) of which was converted by azide in *N,N*-dimethylformamide into the 4-azidoglucose derivative **8** (84%).



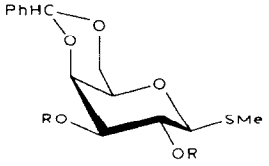
2 $R^1 = R^2 = H$
3 $2R^1 = CMe_2, R^2 = H$
4 $2R^1 = CMe_2, R^2 = Bn$



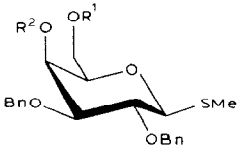
5 $R^1 = R^2 = H$
6 $R^1 = COEt, R^2 = H$
7 $R^1 = COEt, R^2 = Ms$



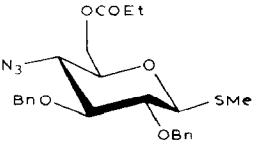
8 $R^1 = OMe, R^2 = H$
9 $R^1 = H, R^2 = OAc$
10 $R^1 = H, R^2 = OMe$
11 $R^1 = H, R^2 = Cl$



12 R = H
13 R = Bn



14 $R^1 = R^2 = H$
15 $R^1 = COEt, R^2 = H$
16 $R^1 = R^2 = COEt$
17 $R^1 = COEt, R^2 = Ts$
18 $R^1 = COEt, R^2 = Ms$



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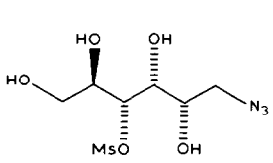
The $J_{1,2}$ value (11 Hz) indicated **8** to be β; the optical rotation (+94°), however, was higher than that (+87°) recorded[6] for the α-anomer **10**. The α-anomer **10** was synthesised[6] and, when **8** and **10** were treated with acetic anhydride in the presence of sulfuric acid, the same 1-acetate **9** was obtained. Thus, **8** and **10** must be anomers and represent another exception[11] to Hudson's rule[12], which is generally valid for simple glycosides.

Treatment of the 1-acetate **9** with dichloromethyl methyl ether then gave **11**.

The glycosyl chloride **11** proved to be inadequate for the coupling reaction with shielded hydroxyl groups (see below) and a more reactive agent was synthesised as follows. Methyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside[13] (**12**) was converted into its 2,3-di-*O*-benzyl derivative **13**, the benzylidene group of which was hydrolysed by aqueous acetic acid to give the diol **14**. Partial acylation of **14** afforded 14% of the diester **16** and 70% of the 6-propionate **15**, both of which were crystalline.

The 4-tosylate (**17**) and 4-mesylate (**18**) of **15** were converted by azide in *N,N*-dimethylformamide into the 4-azido-D-*gluco* derivative **19**.

Synthesis of the aglycon. — 1-Azido-1-deoxy-4-*O*-mesyl-D-glucitol (**20**), easily obtainable from D-glucitol in four steps[1], was reacted with acetone in the presence of toluene-*p*-sulfonic acid to give the 5,6-*O*-isopropylidene derivative **21**, treatment of which with methanolic sodium methoxide afforded the 3,4-anhydro-D-galactitol derivative **22**. Cleavage of the oxirane ring in **22** by sodium azide–ammonium chloride afforded a mixture of the 1,4- (**25**) and 1,3-diazido (**31**) derivatives, the ratio (1:4) of which was determined by g.l.c. after acetylation (→**27** + **33**). The structure of these isomers was established as follows. The syrupy mixture of **25** + **31** was converted with 2-methoxypropene in the presence of toluene-*p*-sulfonic acid



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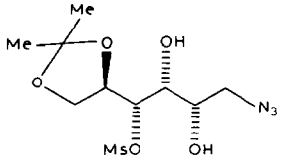

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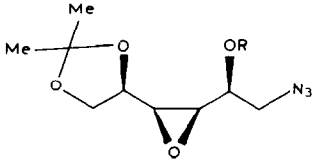
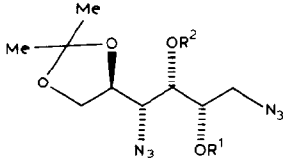
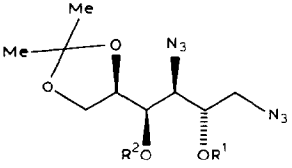


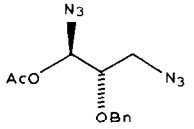
22 R = H
23 R = Ac
24 R = Bn



25 $R^1 = R^2 = H$
26 R^1 = Ac, R^2 = H
27 $R^1 = R^2$ = Ac
28 R^1 = Bn, R^2 = H
29 R^1 = Bn, R^2 = Ac
30 $R^1 + R^2 = CMe_2$



31 $R^1 = R^2 = H$
32 R^1 = Ac, R^2 = H
33 $R^1 = R^2$ = Ac
34 R^1 = Bn, R^2 = H
35 R^1 = Bn, R^2 = Ac
36 $R^1 + R^2 = CMe_2$



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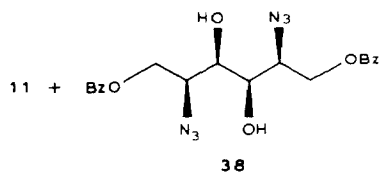
into a mixture (**30** + **36**) of the di-*O*-isopropylidene derivatives which could be separated by column chromatography. The ^{13}C resonances[14] for CMe_2 of the major component (**36**) revealed a dioxolane (109.5 p.p.m.) and a dioxane ring (101.7 p.p.m.), whereas the minor component (**30**) contained two dioxolane rings (110.2 and 109.7 p.p.m.).

For the synthesis of sorbistin analogues, a diazidohexitol aglycon carrying only one free hydroxyl group is the most suitable; therefore, the hydroxyl group of the oxirane **22** was acetylated (→**23**). In order to avoid deacetylation of **23** during cleavage of the oxirane ring, the reaction with sodium azide–ammonium chloride was carried out in the presence of acetic acid[1]. Even so, some deacetylation occurred to give the acetylated (**26** + **32**; 55%) and deacetylated diazides (**25** + **31**; 29%). These mixtures could not be resolved, and they were analysed by g.l.c. after acetylation. The resulting diacetates (**27** + **33**) were identical with those obtained by acetylation of the mixture **25** + **31** (obtained by treatment of **22** with sodium azide), but their relative proportions were inverted (7:3). Thus, the presence of the 2-*O*-acetyl group in **23** inhibits the attack of the azide on C-3, and the 1,4-diazido-D-glucitol derivative **26** is the main product.

In order to investigate the influence of the neighbouring group on the direction of attack of the azide on the oxirane ring, **22** was converted into its 2-*O*-benzyl derivative **24**, the oxirane ring of which was cleaved by sodium azide–ammonium chloride, yielding a 1:3 mixture of the 1,4- (**28**) and 1,3-diazide (**34**) derivatives. After acetylation, the major isomer **35** could be isolated by crystallisation from the mixture (**29** + **35**) of monoacetates. The 1,3-diazido structure was proved by n.m.r. spectroscopy and by application of the sequence hydrolysis of the *O*-isopropylidene group, periodate oxidation, borohydride reduction, and acetylation, which gave the tetritol derivative **37** (the 1,4-diazido isomer **29** should give a pentitol derivative).

Coupling reactions. — The coupling reaction of **11** with 2,5-diazido-1,6-di-*O*-benzoyl-2,5-dideoxy-L-iditol[15] (**38**), having two equivalent hydroxyl groups, using mercuric bromide and mercuric oxide as catalyst in the presence of molecular sieves (5Å), proceeded slowly at room temperature; even at the boiling temperature of the solvent, 40 h were needed to complete the reaction. According to the n.m.r. data, only the α-anomer **39** was formed (δ 4.85, bs, H-1′) and 24% was isolated after column chromatography. Zemplén deacetylation of **39** (→**40**) and then hydrogenation over Pd/C gave the target glycoside isolated as the hydrochloride **41**.



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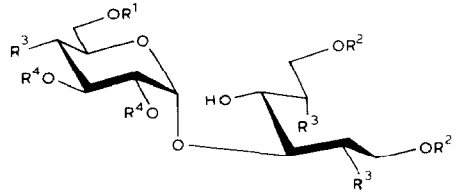
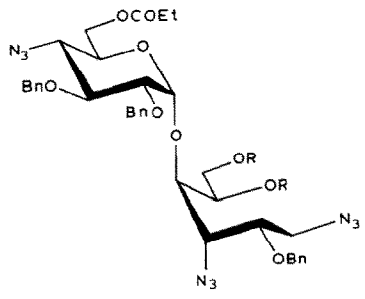


39 R^1 = COEt, R^2 = Bz, R^3 = N_3, R^4 = Bn
40 R^1 = R^2 = H, R^3 = N_3, R^4 = Bn
41 R^1 = R^2 = R^4 = H, R^3 = NH_2 · HCl

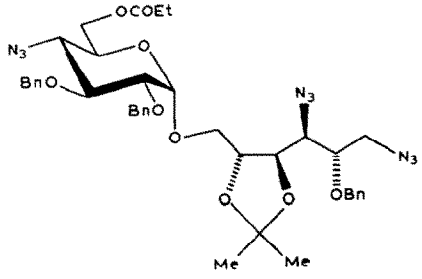
Under similar coupling conditions, **11** did not react with **34** (obtained on Zemplén deacetylation of the crystalline **35**) in which the hydroxyl group is flanked by an azido group and a dioxolane ring. Increasing the reactivity of the hydroxyl group by tributyl stannylation, as used for the synthesis of sorbistin[6], proved to be unsatisfactory. Therefore, the methyl thioglycoside **19** was used as the glycosylating agent.

Glycosylation of **34** with **19** in dichloromethane, promoted by either methyl trifluoromethanesulfonate[16] or dimethyl(methylthio)sulfonium trifluoromethanesulfonate[17,18], proceeded readily but gave a mixture of components with similar chromatographic mobilities, and only 20–30% of the required α-glucosylated compound **42** could be isolated pure. That the interglycosidic linkage in **42** was α was supported by the chemical shift (97.7 p.p.m.) of the resonance of C-1′ and the optical rotation. The ^{13}C-n.m.r. spectrum of the partially fractionated mixture revealed a β-linked compound ($\delta_{C\text{-}1'}$ 103.5) and another, α-linked compound ($\delta_{C\text{-}1'}$ 97.5).

When the glycosylation reaction was performed in ether, a condition which favours the formation of 1,2-*cis*-glycosides[19], the yield of **42** was increased to 55%; the other α-linked compound could also be isolated pure. Although, according to the ^{13}C-n.m.r. spectrum, the latter compound contained a dioxolane-type isopropylidene group[14] [δ 109.9 for $C(CH_3)_2$ and δ 27.0 and 26.6 for $C(CH_3)_2$], the C-6 signal (68.6 p.p.m.) was shifted considerably downfield compared to those of **34** (66.0 p.p.m.) or **42** (65.5 p.p.m.). It was deduced that, during glycosylation, partial migration of the isopropylidene group occurred with subsequent glycosylation at O-6, affording **44**.



42 2R = CMe_2
43 R = H



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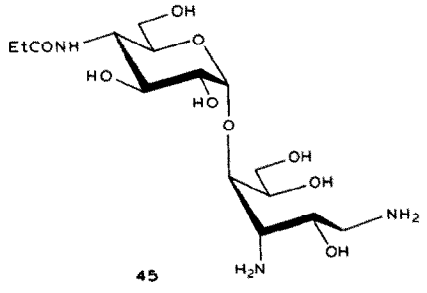

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When the glycosylation of **34** by **19** in ether was performed in the presence of 2,6-di-*tert*-butyl-4-methylpyridine, **44** was not formed and 90% of **42** was obtained.

Removal of the isopropylidene group from **42** with aqueous acetic acid gave **43**, catalytic hydrogenation (Pd/C) of which afforded the sorbistin analogue **45**.

EXPERIMENTAL

General methods. — Organic solutions were dried with Na_2SO_4 and concentrated under diminished pressure. Optical rotations were determined on 1% solutions in chloroform if not stated otherwise. T.l.c. was performed on Kieselgel G with ethyl acetate (*A*), ethyl acetate–carbon tetrachloride mixtures (*B*, 1:1; *C*, 1:3; *D*, 1:5; and *E*, 1:9), ethyl acetate–dichloromethane mixtures (*F*, 1:4; *G*, 1:9; *H*, 1:49; and *I*, 1:99), and ethyl acetate–toluene mixtures (*J*, 1:4; *K*, 1:9; and *L*, 1:19), with detection using 1:1 0.1M potassium permanganate–M sulfuric acid at 105°. N.m.r. spectra were recorded with Varian EM 390 (90 MHz) and Bruker AC 250 (250 MHz) spectrometers, respectively, on solutions in $CDCl_3$ (internal Me_4Si) if not stated otherwise. The light petroleum used had b.p. 60–80°.

Methyl 4,6-O-isopropylidene-β-D-galactopyranoside (**3**). — To a solution of **2** (33 g, prepared *via* 2,3,4,6-tetra-*O*-acetyl-D-galactosyl bromide[7,8]) in *N,N*-dimethylformamide (100 mL) at −10° were added 2-methoxypropene (23 mL) and toluene-*p*-sulfonic acid (0.1 g). The mixture was neutralised after 2 h with solid sodium hydrogencarbonate, filtered, and concentrated. The solid residue was filtered with ether and crystallised from ethyl acetate (300 mL) at 0°. Dilution of the mother liquor with light petroleum gave a second crop (total yield, 22 g, 55.3%), m.p. 155–157°, $[\alpha]_D$ −20° (water), R_F 0.2 (solvent *A*); lit.[9] m.p. 155–157°, $[\alpha]_D$ −12° (water).

Methyl 2,3-di-O-benzyl-4,6-O-isopropylidene-β-D-galactopyranoside (**4**). — To a stirred solution of **3** (20 g) in *N,N*-dimethylformamide (400 mL) were added powdered potassium hydroxide (40 g) and benzyl chloride (40 mL) simultaneously at 30–35° during 1 h. Stirring was continued for 1 h at this temperature, the mixture was then filtered and concentrated, and the residue partitioned between ether and water. The organic solution was washed with water, dried, and concentrated. Column chromatography (solvent *C*) of the residue gave, after recrystallisation from ether–light petroleum, **4** (26.6 g, 75.5%), m.p. 104–106°, $[\alpha]_D$ −7°, R_F 0.4 (solvent *C*). ^{1}H-N.m.r. data: δ 7.5–7.1 (m, 10 H, 2 Ph), 4.9 (d, 1 H, *J* 11 Hz, H-1), and 3.5 (s, 3 H, MeO).

Anal. Calc. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.49; H, 7.47.

Methyl 2,3-di-O-benzyl-β-D-galactopyranoside (**5**). — A solution of **4** (15 g) in aqueous 75% acetic acid (200 mL) was heated for 30 min at ~100°, then cooled, diluted with water, and extracted with chloroform. The extract was washed with water, aqueous 5% sodium hydrogencarbonate, and water, dried, and concentrated. The residue gave, after recrystallisation from ether–light petroleum, **5** (12.5 g, 92.3%), m.p. 70–72°, $[\alpha]_D$ +8°, R_F 0.2 (solvent *B*). ^{1}H-N.m.r. data: δ 7.4–7.1

(m, 10 H, 2 Ph), 4.85 (d, 1 H, *J* 11 Hz, H-1), and 3.5 (s, 3 H, MeO); lit.[10] m.p. 70–72°, $[\alpha]_D$ +10.6°.

*Methyl 2,3-di-*O*-benzyl-6-*O*-propionyl-β-*D*-galactopyranoside* (**6**). — To a stirred solution of **5** (11.2 g) in pyridine (40 mL) was added propionic anhydride (4 mL) at +5°. The solution was kept overnight at room temperature, then poured into water, and the precipitate was collected and recrystallised from ethyl acetate to give **6** (9.5 g, 74%), m.p. 116–118°, $[\alpha]_D$ +4°, R_F 0.8 (solvent *B*). ^{1}H-N.m.r. data: δ 7.45–7.2 (m, 10 H, 2 Ph), 4.9 (d, 1 H, *J* 11 Hz, H-1), 3.6 (s, 3 H, MeO), 2.4 (q, 2 H, *J* 8 Hz, CH_3CH_2CO), and 1.2 (t, 3 H, *J* 8 Hz, CH_3CH_2CO).

Anal. Calc. for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 66.87; H, 7.12.

*Methyl 2,3-di-*O*-benzyl-4-*O*-methanesulfonyl-6-*O*-propionyl-β-*D*-galactopyranoside* (**7**). — To a stirred solution of **6** (25.8 g) in pyridine (40 mL) was added mesyl chloride (6 mL) at a rate to keep the temperature at 30–32°. The mixture was stirred for 4 h at this temperature, then poured onto ice. The precipitate was collected and recrystallised from ethanol to give **7** (29.4 g, 96.3%), m.p. 84–86°, $[\alpha]_D$ +27°, R_F 0.5 (solvent *C*). ^{1}H-N.m.r. data: δ 7.4–7.15 (m, 10 H, 2 Ph), 5.1 (bs, 1 H, H-4), 3.5 (s, 3 H, MeO), 2.9 (s, 3 H, MsO), 2.35 (q, 2 H, CH_3CH_2CO), and 1.15 (t, 3 H, CH_3CH_2CO).

Anal. Calc. for $C_{25}H_{32}O_9S$: C, 59.04; H, 6.34; S, 6.31. Found: C, 59.01; H, 6.52; S, 6.20.

*Methyl 4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-β-*D*-glucopyranoside* (**8**). — To a solution of **7** (28 g) in *N,N*-dimethylformamide (300 mL) was added sodium azide (5 g), and the mixture was stirred for 2 h at 120–125° and then concentrated. The residue was partitioned between ether and water, and the organic solution was washed with water, dried, and concentrated. Recrystallisation of the residue from methanol gave **8** (21 g, 84%), m.p. 67–69°, $[\alpha]_D$ +94°, R_F 0.75 (solvent *D*). ^{1}H-N.m.r. data: δ 7.4–7.15 (m, 10 H, 2 Ph), 4.85 (d, 1 H, *J* 11 Hz, H-1), 4.8–4.65 (m, 2 H, H-2,3), 3.45 (s, 3 H, MeO), 2.35 (q, 2 H, CH_3CH_2CO), and 1.15 (t, 3 H, CH_3CH_2CO).

Anal. Calc. for $C_{24}H_{29}N_3O_6$: C, 63.28; H, 6.42; N, 9.23. Found: C, 63.11; H, 6.48; N, 9.15.

*1-*O*-Acetyl-4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-*D*-glucopyranose* (**9**). — A solution of **8** (20 g) in acetic anhydride (200 mL) containing conc. sulfuric acid (2 mL) was kept for 1 h at room temperature, then poured onto a mixture of ice (2 L) and sodium hydrogencarbonate (250 g). The solution was extracted with chloroform (3 × 200 mL), and the combined extracts were washed with aqueous 5% sodium hydrogencarbonate and water, dried, and concentrated. Column chromatography (solvent *C*) of the residue gave **9** (15.8 g, 74.5%), isolated as a syrup, $[\alpha]_D$ +112°, R_F 0.7 (solvent *C*). The ^{1}H-n.m.r. spectrum was identical with that reported[6].

Compound **9** (1.6 g, 75.5%) was obtained when **10**[6] (2 g) was submitted to the procedure described above.

*4-Azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-*D*-glucopyranosyl chloride*

(**11**). — A solution of **9** (4.8 g) in dichloromethyl methyl ether (20 mL) was boiled in the presence of freshly fused zinc chloride (0.1 g) for 20 h, then concentrated. Column chromatography (solvent *E*) of the residue gave **11** (3.8 g, 83%), isolated as a pale-yellow syrup, $[\alpha]_D$ +144°, R_F 0.6 (solvent *E*); lit.[6] $[\alpha]_D$ +147.5°. ^{1}H-N.m.r. data: δ 6.3 (d, 1 H, *J* 4 Hz, H-1), 3.72 (dd, 1 H, *J* 11 and 4 Hz, H-2), 2.49 (q, 2 H, CH_3CH_2CO), and 1.17 (t, 3 H, CH_3CH_2CO).

*Methyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-*D*-galactopyranoside* (**13**). — To a solution of **12**[13] (2.98 g) in dry *N*,*N*-dimethylformamide (25 mL) was added sodium hydride (0.96 g). The mixture was cooled to 0°, benzyl bromide (3.56 mL) was added dropwise, and the mixture was stirred for 3 h at room temperature. Excess of reagent was decomposed by the addition of methanol, the mixture was concentrated, and the residue was partitioned between dichloromethane and water. After drying and concentration of the organic layer, the residue was recrystallised twice from ethyl acetate–hexane to give **13** (3.87 g, 81%), m.p. 153–154°, $[\alpha]_D$ +21°, R_F 0.4 (solvent *F*). ^{13}C-N.m.r. data: δ 101.2 (Ph*C*), 84.3 (C-1), 81.1 (C-3), 76.2 (C-2), 75.4 (PhCH_2), 73.7 (C-4), 71.5 (PhCH_2), 69.6 (C-5), 69.2 (C-6), and 11.4 (CH_3S).

Anal. Calc. for $C_{28}H_{30}O_5S$: C, 70.27; H, 6.32. Found: C, 70.18; H, 6.43.

*Methyl 2,3-di-O-benzyl-1-thio-β-*D*-galactopyranoside* (**14**). — A solution of **13** (3 g) in aqueous 60% acetic acid (20 mL) was boiled under reflux for 30 min, then concentrated, and toluene was evaporated from the residue which crystallised on storage. Recrystallisation from ethyl acetate–hexane gave **14** (2.25 g, 92%), m.p. 77–78°, $[\alpha]_D$ +1.5°, $[\alpha]_{365}$ +13°, R_F 0.1 (solvent *F*). ^{13}C-N.m.r. data: δ 85.4 (C-1), 82.3 (C-3), 77.9, 77.2 (C-2,5), 75.5 and 72.1 (PhCH_2), 67.3 (C-4), 62.4 (C-6), 12.6 (CH_3S).

Anal. Calc. for $C_{21}H_{26}O_5S$: C, 64.59; H, 6.71. Found: C, 64.54; H, 6.77.

Methyl 2,3-di-O-benzyl-6-O-propionyl- (**15**) *and -4,6-di-O-propionyl-1-thio-β-*D*-galactopyranoside* (**16**). — A solution of **14** (2 g) in dry pyridine (10 mL) was treated at 0° with propionic anhydride (0.79 mL). The mixture was kept for 8 h at 0°, then for 1 day at room temperature. Water was added followed by dichloromethane, and the organic layer was processed in the usual way. Column chromatography (solvent *G*) of the product gave, first, **16** (0.366 g, 14%), m.p. 83–84° (from ethyl acetate–hexane), $[\alpha]_D$ +24°, R_F 0.9 (solvent *G*). ^{13}C-N.m.r. data: δ 85.5 (C-1), 80.8 (C-3), 77.1 (C-2), 75.6 (PhCH_2), 74.4 (C-5), 71.8 (PhCH_2), 66.3 (C-4), 61.9 (C-6), 27.4, 27.2 (2 CH_3CH_2CO), 12.5 (CH_3S), 9.1, and 8.9 (2 CH_3CH_2CO).

Anal. Calc. for $C_{27}H_{34}O_7S$: C, 64.52; H, 6.82. Found: C, 64.67; H, 6.96.

Eluted second was **15** (1.596 g, 70%), m.p. 104–105° (from ethyl acetate–hexane), $[\alpha]_D$ +7°, R_F 0.6 (solvent *G*). ^{13}C-N.m.r. data: δ 85.2 (C-1), 82.2 (C-3), 77.2 (C-2), 75.7 (C-5), 75.5 and 72.3 (2 PhCH_2), 66.7 (C-4), 63.1 (C-6), 27.4 (CH_3CH_2CO), 12.4 (CH_3S), and 9.0 (CH_3CH_2CO).

Anal. Calc. for $C_{24}H_{30}O_6S$: C, 64.54; H, 6.77. Found: C, 64.41; H, 6.70.

*Methyl 2,3-di-O-benzyl-6-O-propionyl-1-thio-4-O-tosyl-β-*D*-galactopyranoside* (**17**). — To a solution of **15** (1.339 g) in dry pyridine (10 mL) was added tosyl

chloride (0.76 g) at room temperature. After 1 day, 4-dimethylaminopyridine (10 mg) and more tosyl chloride (0.76 g) were added and the mixture was kept for 4 days at 60°. Water was added followed by dichloromethane, and the organic layer was processed in the usual way. Column chromatography (solvent *K*) of the product gave **17** (1.539 g, 85%) which crystallised on storage. After recrystallisation from ethyl acetate–hexane, **17** had m.p. 73–74°, $[\alpha]_D$ +46°, R_F 0.4 (solvent *K*). ^{13}C-N.m.r. data: δ 85.7 (C-1), 80.5 (C-3), 76.6 (C-2), 75.6 (Ph*C*H$_2$), 75.1, 74.4 (C-4,5), 72.4 (Ph*C*H$_2$), 62.2 (C-6), 27.3 (*C*H$_3$*C*H$_2$CO), 21.5 (Ts Me), 12.5 (MeS), and 8.9 (*C*H$_3$*C*H$_2$CO).

Anal. Calc. for $C_{31}H_{36}O_8S_2$: C, 61.98; H, 6.04. Found: C, 61.76; H, 6.17.

*Methyl 2,3-di-*O*-benzyl-4-*O*-methanesulfonyl-6-*O*-propionyl-1-thio-β-*D*-galactopyranoside* (**18**). — To a stirred solution of **15** (12.7 g) in pyridine (50 mL) was added mesyl chloride (2.7 mL) at 0°. The mixture was kept for 20 h at room temperature to give, after the usual processing and recrystallisation from ether–hexane, **18** (13.6 g, 91%), m.p. 62–64°, $[\alpha]_D$ +25°, R_F 0.5 (solvent *D*). ^{1}H-N.m.r. data: δ 7.45 (m, 10 H, 2 Ph), 5.2 (bs, 1 H, H-4), 3.0 (s, 3 H, Ms), 2.4 (q, 2 H, CH$_3$C*H*$_2$CO), 2.2 (s, 3 H, MeS), and 1.15 (t, 3 H, C*H*$_3$CH$_2$CO).

Anal. Calc. for $C_{25}H_{32}O_8S_2$: C, 57.22; H, 6.1; S, 12.22. Found: C, 57.12; H, 6.25; S, 12.06.

*Methyl 4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-1-thio-β-*D*-glucopyranoside* (**19**). — (*a*) A stirred mixture of **17** (1.2 g), sodium azide (0.4 g), and *N,N*-dimethylformamide (15 mL) was kept for 7 h at 100°, then concentrated, the residue was partitioned between dichloromethane and water, and the organic layer was concentrated. Column chromatography (solvent *H*) of the residue and recrystallisation of the product (0.88 g, 93%) from ethyl acetate–hexane gave **19**, m.p. 77–78°, $[\alpha]_D$ +82.5°, R_F 0.6 (solvent *D*), 0.3 (solvent *L*). ^{13}C-N.m.r. data: δ 85.4, 84.5, 81.0 (C-1,2,3), 76.1 (C-5), 75.6 and 75.3 (2 Ph*C*H$_2$), 63.3 (C-6), 62.4 (C-4), 27.3 (CH$_3$*C*H$_2$CO), 12.7 (MeS), and 9.0 (*C*H$_3$*C*H$_2$CO).

(*b*) A mixture of **18** (13 g), sodium azide (2.5 g), and *N,N*-dimethylformamide (130 mL) was kept for 6 h at 120° and then processed as in (*a*) to give crystalline **19** (9.7 g, 83%).

Anal. Calc. for $C_{24}H_{29}N_3O_5S$: C, 61.13; H, 6.20; N, 8.91; S, 6.80. Found: C, 60.83; H, 6.32; N, 8.75; S, 6.82.

*1-Azido-1-deoxy-5,6-*O*-isopropylidene-4-*O*-methanesulfonyl-*D*-glucitol* (**21**). — A solution of **20**[1] (14 g) and toluene-*p*-sulfonic acid (1 g) in acetone (150 mL) was stirred for 1 h at room temperature, then neutralised with solid sodium hydrogencarbonate, filtered, and concentrated. The semi-solid residue was treated with ether to give **21** (9.3 g, 58.2%), m.p. 88–90°, $[\alpha]_D$ +26°, R_F 0.4 (solvent *B*). ^{1}H-N.m.r. data: δ 4.75 (t, 1 H, *J* 4 Hz, H-4), 3.72 (t, 1 H, *J* 4 Hz, H-3), 3.43 (d, 2 H, *J* 6 Hz, H-6,6′), 3.05 (s, 3 H, Ms), and 1.40 and 1.32 (2 s, 6 H, CMe$_2$).

Anal. Calc. for $C_{10}H_{19}N_3O_7S$: C, 36.91; H, 5.88; N, 12.91; S, 9.85. Found: C, 36.98; H, 6.02; N, 12.74; S, 9.63.

*3,4-Anhydro-1-azido-1-deoxy-5,6-*O*-isoproylidene-*D*-galactitol* (**22**). — To a

solution of **21** (5 g) in chloroform (20 mL) and methanol (10 mL) was added methanolic 4M sodium methoxide (4 mL) at room temperature. After 30 min, the mixture was diluted with chloroform, washed with water, dried, and concentrated to give **22** (3.5 g, 98%) as a colourless syrup, $[\alpha]_D$ −30°, R_F 0.6 (solvent *B*). ^{1}H-N.m.r. data: δ 4.3–3.8 (m, 4 H, H-2,3,4,5), 3.45 (d, 2 H, *J* 6 Hz, H-6,6'), 3.12 (m, 2 H, H-1,1'), and 1.50 and 1.35 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_9H_{15}N_3O_4$: C, 47.15; H, 6.59; N, 18.33. Found: C, 47.03; H, 6.72; N, 18.16.

*2-O-Acetyl-3,4-anhydro-1-azido-1-deoxy-5,6-O-isopropylidene-*D*-galactitol* (**23**). — A solution of **22** (2.3 g) in pyridine (5 mL) and acetic anhydride (3 mL) gave, after the usual processing, **23** (2.3 g, 85%) as a syrup, $[\alpha]_D$ −4°, R_F 0.55 (solvent *D*). ^{1}H-N.m.r. data: δ 5.18 (m, 1 H, H-2), 3.48 (dd, 2 H, *J* 6 and 2 Hz, H-6,6'), 3.10 (m, 2 H, H-1,1'), 2.14 (s, 3 H, AcO), and 1.45 and 1.35 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{11}H_{17}N_3O_5$: C, 48.70; H, 6.31; N, 15.49. Found: C, 48.58; H, 6.44; N, 15.27.

*3,4-Anhydro-1-azido-1-deoxy-2-O-benzyl-5,6-O-isopropylidene-*D*-galactitol* (**24**). — Sodium hydride (55% suspension in oil, 1 g) was treated with methyl sulfoxide (25 mL), a solution of **22** (2.3 g) in methyl sulfoxide (10 mL) was added, and the mixture was stirred until foaming ceased. Benzyl chloride (2.5 mL) was added at +10° and, after stirring for 30 min at room temperature, the mixture was diluted with water and extracted with ether, and the extract was dried and concentrated. Column chromatography (solvent *E*) of the residue gave **24** (2.3 g, 72%), isolated as a syrup, $[\alpha]_D$ −5°, R_F 0.7 (solvent *D*). ^{1}H-N.m.r. data: δ 7.3 (s, 5 H, Ph), 4.7 (q, 2 H, *J* 10 Hz, $PhCH_2$), 4.2–3.15 (m, 6 H, H-1,1',2,3,4,5), 3.0 (m, 2 H, H-6,6'), and 1.40 and 1.32 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{10}H_{21}N_3O_4$: C, 60.17; H, 6.6; N, 13.15. Found: C, 60.01; H, 6.72; N, 13.00.

Cleavage of the 3,4-oxirane-ring in **22–24** *with sodium azide.* — (*a*) A solution of **22** (2 g), sodium azide (1.3 g), and ammonium chloride (1.1 g) in Methyl Cellosolve (20 mL) was boiled under reflux for 2 h, then concentrated. The residue was partitioned between water and chloroform, and the organic solution was washed with water, dried, and concentrated to give a syrup (2.1 g, 88%), $[\alpha]_D$ −24°, R_F 0.6 (solvent *B*), containing 1,4-diazido-1,4-dideoxy-5,6-*O*-isopropylidene-D-glucitol (**25**) and 1,3-diazido-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol (**31**). ^{1}H-N.m.r. data: δ 4.4–3.1 (m, 10 H), and 1.40 and 1.48 (2 s, 6 H, CMe_2).

Treatment of the above syrup with pyridine (10 mL) and acetic anhydride (5 mL) gave, after the usual processing, a syrup (2.5 g, 91%), $[\alpha]_D$ −24°, R_F 0.6 (solvent *D*), which, according to g.l.c., contained 2,3-di-*O*-acetyl-1,4-diazido-1,4-dideoxy-5,6-*O*-isopropylidene-D-glucitol (**27**) and 2,4-di-*O*-acetyl-1,3-diazido-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol (**33**) in the ratio 1:4. ^{1}H-N.m.r. data (250 MHz) for **27**: δ 5.38 (dd, *J* 5 and 3.5 Hz) and 5.27 (m) (H-2,3), 2.14 and 2.13 (2 s, 6 H, 2 AcO), and 1.46 and 1.33 (2 s, 6 H, CMe_2); for **33**: 5.18 (dd, *J* 5 and 3.5 Hz)

and 5.03 (m) (H-2,4), 2.11 (s, 6 H, 2 AcO), and 1.47 and 1.37 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{11}H_{18}N_6O_5$: C, 42.04; H, 5.78; N, 26.75. Found: C, 42.15; H, 5.88; N, 26.55.

(*b*) A solution of **23** (5.5 g) and sodium azide (2.6 g) in Methyl Cellosolve (50 mL) and acetic acid (4.8 mL) was heated for 1 h, at ~100°. T.l.c. then showed **23** (R_F 0.5, solvent *C*) to have reacted. The solution was concentrated, the residue was partitioned between chloroform and water, the organic solution was washed with water, dried, and concentrated, and the residue was submitted to column chromatography (solvent *C*).

The fractions containing the component having R_F 0.4 were concentrated to give a syrup (3.3 g, 55%) containing (t.l.c.) 2-*O*-acetyl-1,4-diazido-1,4-dideoxy-5,6-*O*-isopropylidene-D-glucitol (**26**) and 2-*O*-acetyl-1,3-diazido-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol (**32**) in the ratio 7:3. ^{1}H-N.m.r. data: δ 5.25–5.0 (m, H-2), 2.18 (minor) and 2.16 (major, Ac), and 1.45 and 1.35 (2 s, CMe_2).

Anal. Calc. for $C_{11}H_{18}N_6O_5$: C, 42.04; H, 5.78; N, 26.75. Found: C, 41.88; H, 6.00; N, 26.55.

The fractions containing the component having R_F 0.35 were concentrated to give a syrup, containing (g.l.c.) the dihydroxy derivatives **25** and **31** in the ratio 7.5:2.5.

(*c*) A solution of **24** (5.2 g), sodium azide (2.6 g), and ammonium chloride (2.1 g) in Dimethyl Cellosolve (50 mL) was boiled for 24 h and then processed as in (*a*) to give a syrup (4 g) which was treated with pyridine (10 mL) and acetic anhydride (8 mL). The product was subjected to column chromatography (solvent *E*). The fractions containing the component having R_F 0.5 were concentrated to give a syrup (4 g) containing (g.l.c.) 3-*O*-acetyl-1,4-diazido-2-*O*-benzyl-1,4-dideoxy-5,6-*O*-isopropylidene-D-glucitol (**29**) and 4-*O*-acetyl-1,3-diazido-2-*O*-benzyl-1,3-dideoxy-5,6-*O*-isopropylidene-D-gulitol (**35**) in the ratio 1:3. Crystallisation of this mixture from hexane gave **35** (2.7 g, 42.6%), m.p. 55–58°, $[\alpha]_D$ −20°. N.m.r. data (250 MHz): ^{1}H, δ 7.35 (m, 5 H, Ph), 5.25 (t, 1 H, *J* 4.5 Hz, H-4), 4.62 (q, 2 H, *J* 10 Hz, PhCH_2), 4.3 (m, 1 H, H-5), 4.1–3.4 (m, 6 H, H-1,1′,2,3,6,6′), 2.12 (s, 3 H, AcO), and 1.45 and 1.33 (2 s, 6 H, CMe_2); ^{13}C, δ 110.0 (CMe_2), 77.2 (C-2), 75.0 (C-5), 72.8 (PhCH_2), 71.4 (C-4), 65.6 (C-6), 62.3 (C-3), 50.9 (C-1), 26.0 and 25.2 [$C(CH_3)_2$], and 20.5 ($COCH_3$).

Anal. Calc. for $C_{18}H_{24}N_6O_5$: C, 53.45; H, 5.98; N, 20.78. Found: C, 53.51; H, 6.04; N, 20.75.

*1,3-Diazido-2-*O*-benzyl-1,3-dideoxy-5,6-*O*-isopropylidene-*D*-gulitol* (**34**). — A solution of **35** (2.022 g) in methanol (20 mL) was treated with sodium methoxide overnight at room temperature. The usual processing then afforded **34** (1.78 g, 98%), as a colourless syrup, $[\alpha]_D$ −32.5°, R_F 0.5 (solvent *C*). ^{13}C-N.m.r. data: δ 109.8 (CMe_2), 77.0, 76.8 (C-2,5), 73.0 (PhCH_2), 69.9 (C-4), 66.0 (C-6), 63.9 (C-3), 51.3 (C-1), 26.4 and 25.2 [$C(CH_3)_2$].

Anal. Calc. for $C_{16}H_{22}N_6O_4$: C, 53.03; H, 6.12. Found: C, 53.37; H, 5.99.

*1,4-Diazido-1,4-dideoxy-2,3:5,6-di-*O*-isopropylidene-*D*-glucitol* (**30**) *and 1,3-*

diazido-1,3-dideoxy-2,4:5,6-di-O-isopropylidene-D-gulitol (**36**). — To a solution of the syrupy mixture (1.6 g) of **25** and **31**, from (*a*) above, in 1,4-dioxane (10 mL) were added 2-methoxypropene (5 mL) and toluene-*p*-sulfonic acid (0.1 g) at room temperature. After 30 min, the solution was neutralised with sodium hydrogencarbonate and then concentrated. Column chromatography (solvent *B*) of the syrupy residue gave, first, **30** (0.3 g, 17%), $[\alpha]_D$ −76°, R_F 0.6. N.m.r. data (250 MHz): ^{1}H, δ 4.35–3.95 (m, 5 H), 3.65–3.5 (dd, 1 H, *J* 4 and 13 Hz), 3.45–3.3 (m, 2 H), and 1.43 and 1.36 (2 s, 9 and 3 H, 2 CMe_2); ^{13}C, δ 110.2 and 109.7 (2 CMe_2), 78.2, 76.2, 75.2, 62.5 (C-2,3,4,5), 66.7 (C-6), 51.6 (C-1), 26.8, 26.5, 26.3 and 25.0 [2 $C(CH_3)_2$].

Eluted second was **36** (1.2 g, 65%), $[\alpha]_D$ +28°, R_F 0.5. N.m.r. data (250 MHz): ^{1}H, δ 4.45–4.3 (m, 1 H), 4.25–4.1 (dd, 1 H, *J* 7 and 8.5 Hz), 4.0–3.85 (m, 2 H), 3.8–3.7 (dd, 1 H, *J* 6 and 8.5 Hz), 3.55–3.25 (m, 3 H), and 1.47, 1.45, 1.41 and 1.39 (4 s, 2 CMe_2); ^{13}C, δ 109.5 and 101.7 (2 CMe_2), 74.5, 72.0, 70.8, 60.5 (C-2,3,4,5), 65.1 (C-6), 52.0 (C-1), and 26.3, 24.7, 23.4 and 23.2 [2 $C(CH_3)_2$].

Anal. Calc. for $C_{12}H_{20}N_6O_4$: C, 46.14; H, 6.45; N, 26.91. Found for **30**: C, 46.02; H, 6.33; N, 26.55. Found for **36**: C, 45.95; H, 6.55; N, 26.70.

4-O-Acetyl-1,3-diazido-2-O-benzyl-1,3-dideoxy-D-erythritol (**37**). — A solution of **35** (0.404 g) in aqueous 60% acetic acid (20 mL) was kept for 30 min at 100°, then concentrated, and toluene was evaporated from the residue which was treated with methanolic sodium methoxide at room temperature. A solution of the syrupy product in ethanol (5 mL) and water (10 mL) was treated with sodium metaperiodate (0.855 g) overnight at 4°. The excess of metaperiodate was decomposed with glycerol (0.5 mL), sodium borohydride (0.757 g) was added, and, after 1 h, acetic acid. The mixture was extracted with dichloromethane, the extract was washed with water and concentrated, and the syrupy residue was treated with acetic anhydride (1 mL) in pyridine (5 mL) overnight. Column chromatography (solvent *L*) of the product gave **37** (0.194 g, 63.8%) as an oil, $[\alpha]_D$ −14°, R_F 0.4 (solvent *L*). ^{13}C-N.m.r. data: δ 77.0 (C-2), 73.4 ($PhCH_2$), 63.6 (C-4), 60.8 (C-3), 50.9 (C-1), and 20.6 ($COCH_3$).

Anal. Calc. for $C_{13}H_{16}N_6O_3$: C, 51.31; H, 5.30. Found: C, 51.04; H, 5.35.

2,5-Diazido-3-O-(4-azido-2,3-di-O-benzyl-6-O-propionyl-α-D-glucopyranosyl)-1,6-di-O-benzoyl-2,5-dideoxy-L-iditol (**39**). — To a solution of **38**[15] (3.4 g) in dichloromethane (150 mL) were added mercuric oxide (0.9 g), mercuric bromide (5.4 g), and molecular sieves (5 Å, 10 g), and the slurry was stirred for 1 h at room temperature. A solution of **11** (2 g) in dichloromethane (10 mL) was added, stirring was continued for 20 h at room temperature, and the mixture was then boiled under reflux for 40 h. The cooled slurry was filtered, washed with aqueous 5% potassium iodide and water, dried, and concentrated. Column chromatography (solvent *E*) of the residue gave **39** (1.4 g, 24%), isolated as a syrup, $[\alpha]_D$ +30°, R_F 0.35. N.m.r. data (250 MHz, COSY 45°): ^{1}H, δ 8.2–7.9 (m, 4 H, aromatic), 7.7–7.4 (m, 16 H, aromatic), 5.0–4.7 (m, 4 H, 2 $PhCH_2$), 4.8 (d, 1 H, *J* 3.5 Hz, H-1′), 3.9 (2 t, 2 H, *J* 9.7 and 9.9 Hz, H-3′,5′), 3.6 (dd, 1 H, *J* 3.5 and 9.7 Hz, H-2′), 3.45 (t,

1 H, *J* 9.9 Hz, H-4'), 2.32 (q, 2 H, *J* 7 Hz, CH_3CH_2CO), and 1.1 (t, 3 H, *J* 7 Hz, CH_3CH_2CO); ^{13}C, δ 137.3, 136.1, 133.5, 133.4, 129.8, 129.7, 129.4, 129.1, 129.0, 128.8, 128.6, 128.5, 128.3, and 128.2 (aromatic C), 102.0 (C-1'), 79.9 and 79.7 (C-3',5'), 79.0 (C-2'), 76.0 and 74.9 (2 $PhCH_2$), 64.5, 63.9 and 63.2 (C-1,6,6'), 62.1 (C-4'), 27.2 (CH_3CH_2CO), 9.0 (CH_3CH_2CO), and 84.4, 71.6, 59.4 and 59.3 (C-2,3,4,5).

Anal. Calc. for $C_{43}H_{45}N_9O_{11}$: C, 59.81; H, 5.25; N, 14.59. Found: C, 59.55; H, 5.30; N, 14.42.

*2,5-Diazido-3-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-α-*D*-glucopyranosyl)-2,5-dideoxy-*L*-iditol* (**40**). — To a solution of **39** (1 g) in methanol (10 mL) was added methanolic M sodium methoxide (0.2 mL) at 40°. After 30 min, the solution was neutralised with solid carbon dioxide and then concentrated. Column chromatography (solvent *E*) of the residue gave **40** (0.45 g, 65%), isolated as a syrup, $[\alpha]_D$ +85°, R_F 0.25 (solvent *E*). N.m.r. data (250 MHz): ^1H, δ 7.45–7.2 (m, 10 H, 2 Ph), 4.9 (d, 1 H, *J* 3 Hz, H-1'), 3.6 (dd, 1 H, *J* 3 and 10 Hz, H-2'), 3.4 (t, 1 H, *J* 10 Hz, H-4'), 5.0–4.65 (m, 4 H, 2 $PhCH_2$), and 4.2–3.2 (m, 15 H); ^{13}C, δ 137.3, 136.0, 128.8, 128.6, 128.5, 128.1, and 128.0 (aromatic C), 101.4 (C-1'), 75.7 and 74.9 (2 $PhCH_2$), 83.6, 79.8, 79.2, 73.3, 71.8, 63.3, 62.0, 61.8, 60.75, and 60.7.

Anal. Calc. for $C_{26}H_{33}N_9O_8$: C, 52.08; H, 5.55; N, 21.03. Found: C, 51.80; H, 5.73; N, 20.78.

*2,5-Diamino-3-*O*-(4-amino-4-deoxy-α-*D*-glucopyranosyl)-2,5-dideoxy-*L*-iditol* (**41**). — A solution of **40** (0.3 g) in ethanol (10 mL) was hydrogenated in the presence of 10% Pd/C (1 g) for 4 h at room temperature, then filtered, acidified to Methyl Red with M hydrochloric acid, and freeze-dried to give **41**·3 HCl (0.2 g, 91%), m.p. 100–102°, $[\alpha]_D$ +36° (*c* 0.5, water), R_F 0.8 (ethanol–conc. ammonia, 1:1). N.m.r. data (250 MHz, D_2O): ^1H, δ 5.33 (d, 1 H, *J* 4 Hz, H-1'), 4.3–3.2 (m, 15 H); ^{13}C, δ 102.0 (C-1'), 82.2, 71.6, 70.8, 69.0, 67.6, 60.9, 60.0, 59.2, 55.5, 55.2, and 52.5.

Anal. Calc. for $C_{12}H_{27}N_3O_8 \cdot 3$ HCl: C, 31.97; H, 6.71; N, 9.32; Cl, 23.60. Found: C, 31.88; H, 6.92; N, 9.15; Cl, 23.15.

*1,3-Diazido-4-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-*D*-glucopyranosyl)-2-*O*-benzyl-1,3-dideoxy-5,6-*O*-isopropylidene-*D*-gulitol* (**42**) *and 1,3-diazido-6-*O*-(4-azido-2,3-di-*O*-benzyl-4-deoxy-6-*O*-propionyl-α-*D*-glucopyranosyl)-2-*O*-benzyl-1,3-dideoxy-4,5-*O*-isopropylidene-*D*-gulitol* (**44**). — (*a*) A mixture of **34** (1 g), **19** (1.952 g), 2,6-di-*tert*-butyl-4-methylpyridine (1.129 g), and 4 Å molecular sieves (4 g) was stirred in dry ether (30 mL) under argon for 1 h at room temperature, and then methyl trifluoromethanesulfonate (1.21 mL) was injected. After 3 h, more **19** (0.65 g), 2,6-di-*tert*-butyl-4-methylpyridine (0.4 g), and methyl trifluoromethanesulfonate (0.4 mL) were added and stirring was continued for 1 h. The mixture was neutralised with triethylamine, diluted with dichloromethane, filtered through Celite, washed with M sulfuric acid, saturated aqueous sodium hydrogencarbonate, and water, dried, and concentrated. Column chromatography (solvent *I*) of the residue afforded syrupy **42** (1.952 g, 90%), $[\alpha]_D$ +88°, R_F 0.55 (solvent

H). ^{13}C-N.m.r. data: δ 109.7 (CMe_2), 97.7 (C-1'), 80.2, 79.1, 77.8, 77.1, 76.6 (C-2,4,5,2',3'), 75.6, 73.3, 72.5 (3 PhCH_2), 69.2 (C-5'), 65.5 (C-6), 63.1 (C-6'), 62.5, 62.2 (C-3,4'), 50.8 (C-1), 27.3 (CH_3CH_2CO), 26.3, 25.3 [$C(CH_3)_2$], and 9.0 (CH_3CH_2CO).

(*b*) Compound **34** (0.724 g) was treated with **19** (1.178 g) and methyl trifluoromethanesulfonate (1.1 mL) in dry ether (20 mL) as in (*a*), but in the absence of 2,6-di-*tert*-butyl-4-methylpyridine. Column chromatography (solvent *H*) of the product gave, first, **42** (0.788 g, 50%), followed by a mixture (0.484 g) of **42** and **44**. Rechromatography of the mixture afforded **42** (0.074 g; total yield: 0.862 g, 55%), **44** (0.078 g, 5%), and a mixture (0.298 g) of **42** and **44**. Compound **44** was a syrup, $[\alpha]_D$ +70°, R_F 0.48 (solvent *H*). ^{13}C-N.m.r. data: δ 100.9 (CMe_2), 97.5 (C-1'), 79.8, 79.8, 78.8, 77.8, 75.0 (C-2,4,5,2',3'), 75.7, 73.3, 73.3 (3 PhCH_2), 68.6 (C-6), 68.3 (C-5'), 63.0 (C-6'), 62.1, 60.6 (C-3,4'), 51.9 (C-1), 27.3 (CH_3CH_2CO), 27.0, 26.6 [$C(CH_3)_2$], and 9.0 (CH_3CH_2CO).

Anal. Calc. for $C_{39}H_{47}N_9O_9$: C, 59.61; H, 6.03. Found for **42**: C, 59.85; H, 6.21. Found for **44**: C, 59.48; H, 6.23.

*1,3-Diazido-4-O-(4-azido-2,3-di-O-benzyl-4-deoxy-6-O-propionyl-α-*D*-glucopyranosyl)-2-O-benzyl-1,3-dideoxy-*D*-gulitol* (**43**). — A solution of **44** (0.856 g) in aqueous 60% acetic acid (20 mL) was boiled under reflux for 30 min and then concentrated, and toluene was evaporated from the residue. Column chromatography (solvent *G*) then gave **44** (0.732 g, 90%), isolated as a syrup, $[\alpha]_D$ +39°, R_F 0.45 (solvent *G*). ^{13}C-N.m.r. data: δ 100.6 (C-1'), 83.8, 79.8, 79.6, 76.5 (C-2,4,2',3'), 75.8, 74.5 and 71.8 (3 PhCH_2), 72.4 (C-5), 69.4 (C-5'), 63.0, 62.7 (C-6,6'), 62.4, 61.3 (C-3,4'), 50.4 (C-1), 27.3 (CH_3CH_2CO), and 9.0 (CH_3CH_2CO).

Anal. Calc. for $C_{36}H_{43}N_9O_9$: C, 57.98; H, 5.81. Found: C, 57.71; H, 5.74.

*1,3-Diamino-1,3-dideoxy-4-O-(4-deoxy-4-propionamido-α-*D*-glucopyranosyl)-*D*-gulitol* (**45**). — A solution of **43** (0.5 g) in ethanol (30 mL) was hydrogenated over 10% Pd/C (0.5 g) at 1 atms. for 4 h. 0.1M Hydrochloric acid (13.5 mL) was added and the hydrogenation was continued overnight. The mixture was filtered, then concentrated. Column chromatography (methanol–conc. ammonia, 7:3) of the residue gave **45** (0.218 g, 82%), as an amorphous solid, $[\alpha]_D$ +43° (*c* 2, water), R_F 0.5 (methanol–conc. ammonia, 7:3), which was converted into its amorphous dihydrochloride, $[\alpha]_D$ +58° (*c* 1.1, water). ^{13}C-N.m.r. data (D_2O): δ 178.7 (CH_3CH_2CO), 99.3 (C-1'), 73.3, 72.3, 72.2, 71.3, 70.1, 65.8 (C-2,4,5,2',3',5'), 61.5 and 61.4 (C-6,6'), 54.5 and 51.8 (C-3,4'), 41.8 (C-1), 29.7 (CH_3CH_2CO), and 9.9 (CH_3CH_2CO).

Anal. Calc. for $C_{15}H_{31}N_3O_9 \cdot 2$ HCl: C, 38.30; H, 7.07. Found: C, 38.11; H, 7.13.

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