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SYNTHESIS OF 2-ACETAMIDO-2,6-DIDEOXY-D-GLUCOSE (*N*-ACETYL-D-QUINOVOSAMINE), 2-ACETAMIDO-2,6-DIDEOXY-D-GALACTOSE (*N*-ACETYL-D-FUCOSAMINE), AND 2,4-DIACETAMIDO-2,4,6-TRIDEOXY-D-GLUCOSE FROM 2-ACETAMIDO-2-DEOXY-D-GLUCOSE*

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ABSTRACT

Monotosylation of benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**2**) followed by displacement of the tosyloxy group by iodine and hydrogenation, gave benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-glucopyranoside (**12**), which was catalytically hydrogenolyzed into the known *N*-acetyl-D-quinovosamine (**6**) Inversion of configuration at C-4 of **12** was achieved by its conversion into a 4-*O*-sulfonyl derivative, followed by displacement of the sulfonyloxy group by sodium benzoate, and debenzoylation to give benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-galactopyranoside (**9**), from which the known *N*-acetyl-D-fucosamine (**7**) was obtained by catalytic hydrogenolysis Treatment of the 4-*O*-methylsulfonyl derivative of **9** with sodium azide, followed by hydrogenation, acetylation, and catalytic hydrogenolysis, afforded 2,4-diacetamido-2,4,6-trideoxy-D-glucose (**18**), which was identical with the 2,4-diacetamido-2,4,6-trideoxyhexose obtained from *Bacillus licheniformis* ATCC 9945

INTRODUCTION

For some years our laboratory has been interested in the chemistry of naturally occurring[3–7] and synthetic[8–9] 2-amino-2,6-dideoxy- and 2,4-diamino-2,4,6-trideoxyhexoses and of their derivatives Recently, we have shown[5] that the diacetamidotrideoxy sugar from *Bacillus licheniformis* ATCC 9945 (formerly classified as *Bacillus subtilis*[4 6]) possesses the structure of 2,4-diacetamido-2,4,6-trideoxy-D-glucose Therefore, we undertook the synthesis of this compound, using as starting material benzyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**1**) obtained from the readily available 2-acetamido-2-deoxy-D-glucose In the course of this work, we also synthesized naturally occurring 2-acetamido-2,6-dideoxy-D-glucose

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(*N*-acetyl-D-quinovosamine) and 2-acetamido-2,6-dideoxy-D-galactose (*N*-acetyl-D-fucosamine) Although similar syntheses of these 2-acetamido-2,6-dideoxy sugars have been described[7 10 11], this is the first synthesis of 2,4-diacetamido-2,4,6-trideoxy-D-glucose

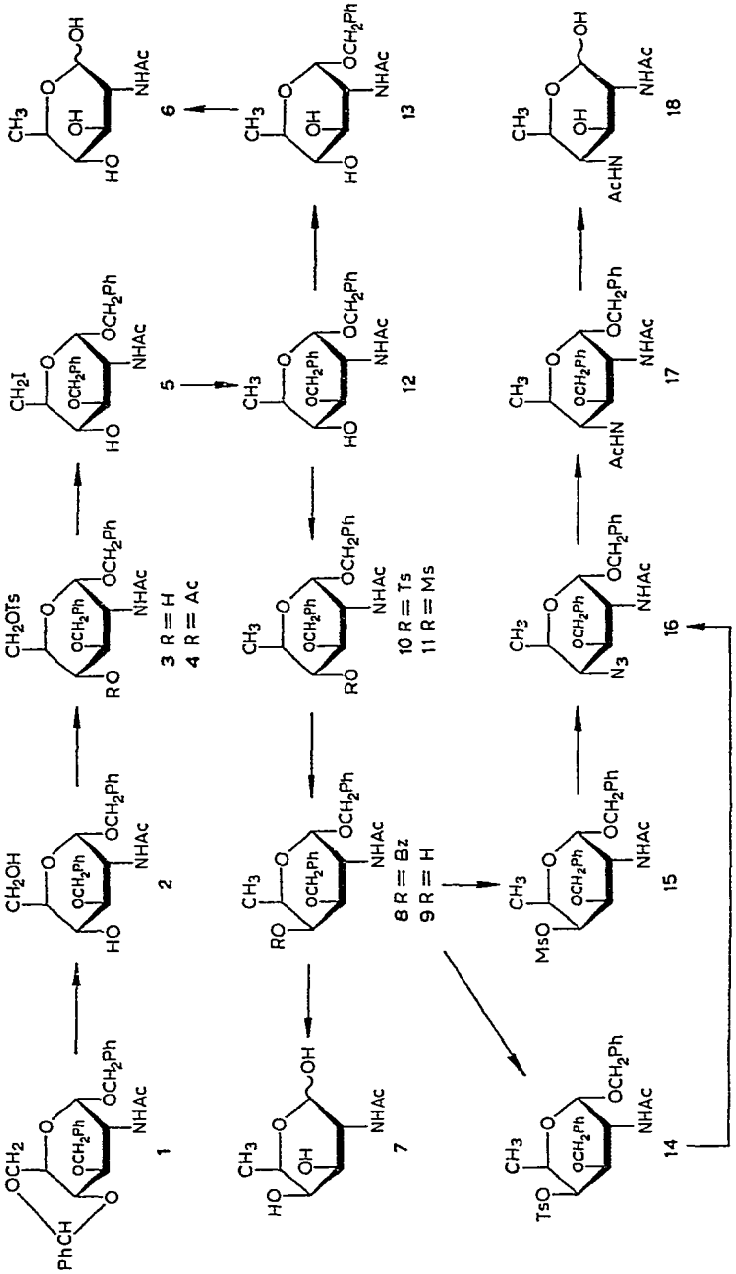
RESULTS AND DISCUSSION

Gross and Jeanloz[12] reported a three-step synthesis of benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside from 2-acetamido-2-deoxy-D-glucose In the present work, this benzylidene derivative was deacylated and benzylated in one step, giving the 3-*O*-benzyl derivative (**1**) For routine work, **1** could be prepared directly from 2-acetamido-2-deoxy-D-glucose without isolation of benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside For this purpose, the starting material was treated with acidic benzyl alcohol, and the crystalline mixture of the two anomeric benzyl glycosides was treated successively with benzaldehyde and benzyl chloride to give benzyl 2-acetamido-4,6-*O*-benzylidene-3-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside The α-D anomer, which was the major product, was isolated by fractional crystallization

The choice of the benzyl group as aglycon was dictated by our previous findings[4 8] that acid treatment of 2,4-diacetamido-2,4,6-trideoxyhexoses causes extensive degradation Destruction of 4-amino sugars under acidic conditions has also been observed by others[13–16]

Mild acidic treatment of **1** afforded benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**2**), which was selectively tosylated in 77% yield to give benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-6-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (**3**), characterized as its 4-acetate (**4**) Treatment of **3** with sodium iodide in *N*,*N*-dimethylformamide at 120°, followed by reduction of the resulting iodide **5** with Raney nickel or with hydrogen at atmospheric pressure, afforded benzyl 2-acetamido-3-*O*-benzyl-2, 6-dideoxy-α-D-glucopyranoside (**12**) in an overall yield of 65% from **3** Catalytic hydrogenolysis of **12** at 1 atm for 24 h gave in 66% yield benzyl 2-acetamido-2,6-dideoxy-α-D-glucopyranoside (**13**), whereas similar hydrogenolysis of **12** for 3 days at 4 5 atm gave known 2-acetamido-2,6-dideoxy-D-glucose (*N*-acetyl-D-quinovosamine) (**6**), which had physical constants identical with the reported values[10,17]

Initially we planned to introduce the amino group at C-4 in **12** by oxidation to the 4-keto derivative, followed by treatment with hydroxylamine to give the oxime and subsequent reduction However, repeated attempts to oxidize **12** with mild reagents, such as ruthenium tetraoxide[18], or dimethyl sulfoxide in the presence of phosphorus pentaoxide[19], or acetic anhydride[20], were not successful Comparable difficulties were encountered by Ali and Richardson[21] in their attempts to oxidize at C-4 in a similar hexopyranoside system Therefore, the configuration at C-4 in **12** was first inverted to yield the *galacto* derivative **8**, and the amino group at C-4 was introduced *via* the corresponding azide, leading back to the *gluco* configuration Such a sequence of reactions was used, for example, for the introduction of the amino


1
2
3 R = H
4 R = Ac
5
6
7
8 R = Bz
9 R = H
10 R = Ts
11 R = Ms
12
13
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group of *N*-methyl-*N*-acetylholosamine[22] [2,4,6-trideoxy-3-*O*-methyl-4-(*N*-methylacetamido)hexose], a derivative of the amino sugar constituent of the cardiac glycosides holantosine A and B and of mitiphyline While our work was being completed, the same procedure was used for the synthesis of 2,4-diacetamido-2,4-dideoxy-D-glucose[23]

Treatment of **12**, with *p*-toluenesulfonyl chloride gave, in 51% yield, benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-*p*-tolylsufonyl-α-D-glucopyranoside (**10**) which was treated with sodium benzoate in *N*,*N*-dimethylformamide to give in 48% yield, benzyl 2-acetamido-4-*O*-benzoyl-3-*O*-benzyl-2,6-dideoxy-α-D-galactopyranoside (**8**) The magnitude of the $J_{4\ 5}$ value (1 0 Hz) in the n m r spectrum of **8** was consistent with the assigned structure Higher yields of **8** from **12** were obtained when the methylsulfonyl group was used instead of the *p*-tolylsulfonyl group Thus, the mesyl derivative **11** was obtained from **12** in 76% yield, and displacement of the mesyloxy group in the latter compound gave **8** in 56% yield

Catalytic debenzoylation of **8** afforded benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-galactopyranoside (**9**) in high yield The known[6 7] 2-acetamido-2,6-dideoxy-D-galactose (*N*-acetyl-D-fucosamine) (**7**) was obtained directly from **9** by catalytic hydrogenolysis at 4 5 atm for 3 days, providing further evidence for the structure of **9**

Tosylation of **9** led to benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside (**14**), which was treated with sodium azide in *N*,*N*-dimethylformamide to give benzyl 2-acetamido-4-azido-3-*O*-benzyl-2,4,6-trideoxy-α-D-glucopyranoside (**16**) The high value (9 0 Hz) of $J_{4\ 5}$ in the n m r spectrum of **16** is in agreement with the *gluco C1* configuration Compound **16** could, however, be prepared more readily *via* the 4-mesyloxy compound **15** which was obtained by treatment of **9** with methanesulfonyl chloride, displacement of the mesyloxy group of **15** was achieved by sodium azide in hexamethylphosphoric triamide Reduction of **16** with hydrogen in the presence of palladium-on-charcoal (10%) catalyst at atmospheric pressure, followed by acetylation, gave benzyl 2,4-diacetamido-3-*O*-benzyl-2,4,6-trideoxy-α-D-glucopyranoside (**17**) in 46% yield Hydrogenolysis of **17** with the same catalyst for 3 days at 4 5 atm gave the desired 2,4-diacetamido-2,4,6-trideoxy-D-glucose (**18**) in 50% yield Compound **18** was identical with the 2,4-diacetamido-2,4,6-trideoxyhexose obtained from the polysaccharide of *B lichenifoi mis* The comparison was based on i r , optical rotation, m p , paper chromatography in three solvent systems, t l c in two solvent systems, and X-ray powder diffraction (Fig 1) All compounds were obtained in crystalline form

Fig 1 X-Ray powder diffraction patterns of synthetic (I) and natural (II) 2,4-diacetamido-2,4,6-trideoxy-D-glucose, taken on a Guinier powder camera

EXPERIMENTAL

Melting points were measured in capillary tubes on a Buchi apparatus and were corrected, except where otherwise stated Optical rotations were determined with a Bendix ETL-NPL polarimeter N m r spectra were recorded with Varian A-60, Varian HA-100, or Bruker 90-MHz instruments, with tetramethylsilane as internal standard and chloroform-*d* as solvent I r spectra were recorded with a Perkin–Elmer 237 spectrometer Thin-layer chromatography was performed on silica gel plates (Riedel de Haen AG, Sedze, Hanover, Germany) Chromatograms were sprayed with 0 5% aqueous solution of Rhodamine BDH, followed by heating, or alternatively with dilute sulfuric acid Unless otherwise stated, silica gel "Davison" grade 950, 60–200 mesh was used for column chromatography Evaporation was performed under reduced pressure with the bath temperature kept below 45° Light petroleum refers to the fraction boiling at 40–60°

*Benzyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranoside* (**1**) — *A* Benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[12] (15 g) was dissolved in *N,N*-dimethylformamide (50 ml) Benzyl chloride (75 ml) was added, followed by ground potassium hydroxide[24] (40 g) The mixture was stirred vigorously while the temperature was raised* to 130° and then kept at this level for 3 h Ice–water was slowly added to the cooled, stirred mixture, and the viscous material that separated was collected and well washed with water A solution of the product in chloroform was washed with water, dried with sodium sulfate, and concentrated Crystallization of the residue from chloroform–hexane afforded **1** (14 6 g, 88%), m p 254–257° This product was sufficiently pure for the next step Recrystallization from benzene yielded material having m p 266°, $[\alpha]_D^{24}$ +132° (*c* 0 6, chloroform)

Anal Calc for $C_{29}H_{31}NO_6$ C, 71 1, H, 6 4, N 2 9 Found C, 71 0, H, 6 2, N, 3 0

B A solution of 2-acetamido-2-deoxy-D-glucose (93 g) in benzyl alcohol (1 3 l) containing gaseous hydrochloric acid (2%, w/w), was stirred and heated for 1 5 h at 70° The solution was then neutralized with lead carbonate, filtered through Celite, and hexane (1 l) was added After 3 h at room temperature more hexane (200 ml) was added and the mixture was kept overnight at 4° The microcrystalline product (94 g) was collected and dried for 5 h at 100° It was treated with benzaldehyde (1 4 l) and fused zinc chloride (85 g) overnight at room temperature The solution was slowly poured into ice–water (4 l) with efficient stirring The precipitate was collected by filtration, washed successively with water, cold ethyl alcohol, and ether, and dried *in vacuo* for 5 h at 80° to yield an amorphous product (98 g), m p 258–263°, $[\alpha]_D^{24}$ +105° (*c* 0 6, pyridine), lit[12] $[\alpha]_D^{26}$ +114° for benzyl 2-acetamido-4,6-*O*-benzylidene-α-D-glucopyranoside and −89° for the β-anomer A solution of the amorphous

*Great care should be taken at this stage, since a vigorous exothermic reaction usually occurs near 110° and efficient, external cooling with ice is then necessary Because of this reaction, it is recommended not to carry out benzylation of quantities of starting material larger than 50 g

product (49 g) in *N,N*-dimethylformamide (150 ml) and benzyl chloride (225 ml) was stirred in the presence of ground potassium hydroxide[24] (120 g) The temperature was raised carefully to 130° (see preceding footnote) and kept at this temperature for 3 h The product was precipitated with hexane, and crystallized from chloroform–hexane to give **1** (42 g, 40% based on 2-acetamido-2-deoxy-D-glucose), m p 255–260°, $[\alpha]_D^{24}$ +125° (*c* 1 0, chloroform) For preparative purposes, method *B* was routinely used, because it is more convenient and faster than method *A*

*Benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**2**) — A suspension of **1** (6 5 g) in acetone (250 ml) containing concentrated hydrochloric acid (2 5 ml) was boiled gently for 4 h The solution was neutralized with lead carbonate, filtered, and evaporated The residue was crystallized from acetone (20 ml) to give 4 14 g (78 5%), m p 175° Recrystallization from acetone afforded pure **2**, m p 176–176 5°, $[\alpha]_D^{27}$ +157° (*c* 0 55, ethanol)

Anal Calc for $C_{22}H_{27}NO_6$ C, 65 8, H, 6 8, N, 3 5 Found C, 65 8, H, 6 9, N, 3 7

*Benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-6-*O*-p-tolylsulfonyl-α-*D*-glucopyranoside* (**3**) — A solution of **2** (4 7 g) in dry pyridine (50 ml) was cooled at −40° and *p*-toluenesulfonyl chloride (2 49 g, 1 1 mol proportion) in pyridine (10 ml) was added dropwise during 1 h, with continuous stirring The mixture was allowed to reach room temperature and stirring was continued onvernight Ice was then added, the mixture was extracted with chloroform, and the extract was washed with cold, aqueous sodium hydrogen carbonate and water It was dried (sodium sulfate) and the pyridine was azeotropically distilled from a toluene–alcohol mixture The syrupy residue was dissolved in acetone (50 ml) and hexane was added to turbidity After 1 day at room temperature, the precipitate (**2**, 0 48 g) was removed by filtration The filtrate, which showed one major spot on t l c (R_F 0 65, ethyl acetate), was evaporated to dryness The crude material (5 7 g) was purified by column chromatography on silica gel (280 g), pre-equilibrated with ethyl acetate–hexane (7 3, v/v) Elution with the same solvent mixture afforded **3** (4 5 g, 77%), which crystallized after being kept for several weeks in benzene–light petroleum, m p 130 5–131°, $[\alpha]_D^{25}$ +120° (*c* 0 9, chloroform)

Anal Calc for $C_{29}H_{33}NO_8S$ C, 62 7, H, 6 0, N, 2 5, S, 5 8 Found C, 62 8, H, 6 0, N, 2 2, S, 5 5

*Benzyl 2-acetamido-4-*O*-acetyl-3-*O*-benzyl-2-deoxy-6-*O*-p-tolylsulfonyl-α-*D*-glucopyranoside* (**4**) — To a solution of **3** (4 4 g) in pyridine (20 ml) was added acetic anhydride (6 ml) and the solution was kept at room temperature overnight Ice and solid sodium hydrogen carbonate were added and the mixture was extracted with chloroform The extract was washed with water, dried (sodium sulfate), and evaporated to give a solid, which was crystallized from benzene–light petroleum (4 2 g, 91%), m p 152 5°, $[\alpha]_D^{27}$ +108° (*c* 0 42, chloroform); n m r data (100 MHz) τ 2 1–3 2 (m, 14 H, aromatic), 4 53 (d, *J* 9 0 Hz, 1 H, NH) 4 9–6 5 (m, 11 H), 7 58 (s, 3 H, Ph–CH_3), 8 04 (s, 3 H, OAc), and 8 20 (s, 3 H, NAc)

Anal Calc for $C_{31}H_{35}NO_9S$ C, 62 3, H, 5 9; N, 2 3, S, 5 3 Found C, 62 5, H, 6 0, N, 2 2, S, 5 1

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-6-iodo-α-D-glucopyranoside (**5**) — A solution of **3** (0 9 g) in *N,N*-dimethylformamide (10 ml) was heated in the presence of potassium iodide (0 9 g) at 120° for 1 h The cooled mixture was filtered and evaporated The residue was extracted with chloroform and crystalline **5** (0 65 g, 80%) was obtained by addition of light petroleum to the extract, m p 174°, $[\alpha]_D^{25}$ +97° (*c* 0 38, chloroform) It was homogeneous on t l c (R_F 0 15, 5 4 v/v, ethyl acetate–hexane)

Anal Calc for $C_{22}H_{26}INO_5$ C, 51 7, H, 5 1, I, 24 0, N, 2 7 Found C, 51 8, H, 5 1, I, 23 9, N, 2 5

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-α-D-glucopyranoside (**12**) — *A*. A solution of **5** (0 34 g) in ethyl alcohol (5 ml) was boiled gently under reflux in the presence of 1 ml of a suspension of Raney Nickel, the reaction was monitored by t l c (5 4, v/v, ethyl acetate–hexane) After 20 min, conversion into **12** (R_F 0 20) had occurred to an extent of ~40% After 1 h, the starting material had disappeared The reaction mixture was cooled and filtered through Celite Crystallization of the residue from chloroform–light petroleum gave **12** (0 215 g, 84%), m p 160°, $[\alpha]_D^{24}$ +118° (*c* 0 43, chloroform)

Anal Calc for $C_{22}H_{27}NO_5$ C, 68 5, H, 7 1, N, 3 6 Found C, 68 5, H, 7 0, N, 3 6

B To a solution of **5** (0 5 g) in methanol (20 ml), triethylamine (0 5 ml) and 10% palladium-on-charcoal (100 mg) were added, and hydrogen was passed through the suspension for 1 h The catalyst was filtered off, and the filtrate was evaporated to give a residue, which was chromatographed on silica gel (30 g, Merck 7734) Elution with 5 1 v/v, chloroform–acetone gave a crystalline material, which was recrystallized from chloroform–light petroleum to give pure **12** (0 3 g, 80%), m p 160–161°

Benzyl 2-acetamido-2,6-dideoxy-α-D-glucopyranoside (**13**) — A solution of **12** (0 2 g) in ethyl alcohol (20 ml) containing a catalytic amount of 10% palladium-on-charcoal was hydrogenated at 1 atm for 24 h After filtration through Celite, the solution was evaporated and the residue was crystallized from ethanol–petroleum ether to give **13** (101 mg, 66%), m p 195–197° (decomp), $[\alpha]_D^{26}$ +184° (*c* 0 62, water)

Anal Calc for $C_{15}H_{21}NO_5$. C, 61 6, H, 7 1, N, 4 7 Found C, 61 4, H, 7 2, N, 4 9

2-Acetamido-2,6-dideoxy-D-glucose (**6**) — A solution of **12** (0 5 g) in methanol (20 ml) was hydrogenated catalytically in the presence of 10% palladium-on-charcoal (50 mg) at 4 5 atm for 24 h at room temperature Water (10 ml) and more catalyst (50 mg) were added and the hydrogenation was continued for an additional 48 h After filtration and evaporation of the mixture, a solid product (0 165 g, 62%) was obtained, having m p 200–204° Recrystallization from ethanol–light petroleum afforded pure **6**, m p 209–210°, $[\alpha]_D^{25}$ +13 6° (at equilibrium, *c* 0 8, water), lit [10] m p 210–211°, $[\alpha]_D^{24}$ +15 8° (*c* 0 98, water); values for the L-isomer are[11] m p 201–204°, $[\alpha]_D^{24}$ −14° (*c* 1 0, water)

Anal Calc for $C_8H_{15}NO_5$ C, 46 8, H, 7 4, N, 6 8 Found C, 47 0, H, 7 1, N, 6 8.

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-4-O-p-tolylsulfonyl-α-D-glucopyranoside (**10**). — To a solution of **12** (0 6 g) in anhydrous pyridine was added *p*-toluenesulfonyl chloride (0 6 g, 2 mol proportion) and the mixture was kept for 40 h at room temperature Ice was added and the mixture was extracted with chloroform The extract was washed with cold, aqueous sodium hydrogen carbonate and water, dried (sodium sulfate), and evaporated Crystallization of the residue from ethanol–light petroleum yielded **10** (0 43 g, 51%) m p 153°, $[\alpha]_D^{25}$ +96° (*c* 0 40, chloroform), t l c. (5 2, v/v, ethyl acetate–light petroleum) R_F 0 72, n m r data (60 MHz) τ 2 1–3 1 (m, 14 H, aromatic), 4 7–6 4 (m, 10 H), 7 71 (s, 3 H, Ph–CH_3), 8 36 (s, 3 H, NAc), and 8 70 (d, $J_{5\ 6}$ 6 5 Hz, 3 H, CH_3–5)

Anal Calc for $C_{29}H_{33}NO_7S$ C, 64 5, H, 6 2, N, 2 6, S, 5 9 Found· C, 64 2, H, 6 0, N, 2 5, S, 6 2

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-4-O-methylsulfonyl-α-D-glucopyranoside (**11**) — To an ice-cooled solution of **12** (0 3 g) in pyridine (5 ml) methanesulfonyl chloride (0 3 ml) was added, and the mixture was stirred for 1 h in an ice-bath and for an additional 2 h at room temperature Ice was added and the mixture was extracted with chloroform The extract was washed with water and evaporated to yield a solid, which was crystallized from chloroform–light petroleum to give **11** (0 275, 76%), m p 209–210° (decomp), $[\alpha]_D^{24}$ +124° (*c* 1 0, chloroform)

Anal Calc for $C_{23}H_{29}NO_7S$ C, 59 6, H, 6 3, N, 3 0, S, 6 9 Found C, 59 7, H, 6 4, N, 2 8, S, 6 6

Benzyl 2-acetamido-4-O-benzoyl-3-O-benzyl-2,6-dideoxy-α-D-galactopyranoside (**8**) — *A* A solution of **10** (1 7 g) in *N*,*N*-dimethylformamide (25 ml) was heated for 22 h at 156° in the presence of sodium benzoate (2 g), and then treated as described for **4** A solution of the resulting product in chloroform was evaporated in the presence of Celite The dried paste was added to the top of a column of silica gel (300 g) Elution with 2 3, v/v, ethyl acetate–hexane gave **8**, which was crystallized from ethyl acetate–hexane to give 740 mg (48%), m p 147–148°, $[\alpha]_D^{23}$ +195° (*c* 0 7, chloroform), n m r data (100 MHz) τ 1 8–3 0 (m, 15 H, aromatic), 4 3–4 8 (m, 2 H), 4 91 (d, $J_{1,2}$ 3 0 Hz, H-1), 5 1–5 7 (m, 5 H), 5 89 (m, $J_{4,5}$ 1 0, $J_{5\ 6}$ 6 5 Hz, H-5), 6 25 (d, $J_{2\ 3}$ 10 5 Hz, H-2 or H-3), 8 13 (s, 3 H, NAc), and 8 82 (d, 3 H, CH_3–5), irradiation at the frequency of CH_3–5 caused the collapse of the H-5 multiplet into a singlet

Anal Calc for $C_{29}H_{31}NO_6$ C, 71 1, H, 6 4, N, 2 9 Found C, 70 9, H, 6 5, N, 3 0

B A suspension of **11** (0 28 g) and sodium benzoate (0 3 g) in *N*,*N*-dimethylformamide (5 ml) was heated for 20 h at 160° To the cooled mixture water was added, and the crystalline material was filtered off and dried The product obtained (0 17 g, 58%) was identical with **8** described under (*A*)

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-α-D-galactopyranoside (**9**) — Catalytic debenzoylation of **8** (0 58 g) was performed at room temperature with M methanolic sodium methoxide (1 ml) in methanol (15 ml) The solution was neutralized with Amberlite IRC-50 (H^+) resin and evaporated Crystallization of the residue from ethyl acetate–hexane gave **9** (377 mg, 83%), m p 180–181°, $[\alpha]_D^{25}$

+172° (*c* 0 41, chloroform), t l c (1 1, v/v, ethyl acetate–light petroleum) R_F 0 06.

Anal Calc for $C_{22}H_{27}NO_5$ C, 68 5, H, 7 1, N, 3 6. Found C, 68 6, H, 7.0; N, 3 3

*2-Acetamido-2,6-dideoxy-*D*-galactose* (**7**) — A solution of **9** (100 mg) in ethyl alcohol (10 ml) was hydrogenated in the presence of a catalytic amount of 10% palladium-on-charcoal at 4 5 atm for 72 h After filtration, the solution was cooled and the crystalline product obtained was recrystallized from ethyl alcohol to give **7** (21 mg, 39%), m p 194–196° (decomp), $[\alpha]_D^{24}$ +89° (at equilibrium, *c* 0 55, water), lit [7] m p 196–197° (decomp), $[\alpha]_D^{23}$ +92° (*c* 2 0, water), the values for the L isomer are[25] m p 197–198°, $[\alpha]_D^{26}$ −82° (*c* 1 46, water)

Anal Calc for $C_8H_{15}NO_5$ C, 46 8, H, 7 4, N, 6 8 Found C, 47 1, H, 7 2, N, 6 8

*Benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-*p*-tolylsulfonyl-α-*D*-galactopyranoside* (**14**) — A solution of **9** (0 4 g) in anhydrous pyridine (5 ml) was treated at room temperature for 40 h with *p*-toluenesulfonyl chloride (0 285 g) The reaction mixture was treated as described for **3** The resulting solid was recrystallized from ethyl acetate–hexane to give **14** (216 mg, 40%), m p 158–161°, $[\alpha]_D^{26}$ +211° (*c* 0 62, chloroform), n m r. data (100 MHz) τ 2 1–3 1 (m, 14 H, aromatic), 4 75 (d, *J* 8 5 Hz, NH), 4 90 (d, $J_{1\ 2}$ 3 0 Hz, H-1), 5 08 (d, $J_{3\ 4}$ 3 0 Hz, $J_{4,5}$ 1 0 Hz, H-4), 5 55 (dd, *J* 13 Hz, benzylic CH_2), 5 58 (q, $J_{2,3}$ 11 0 Hz, $J_{3,4}$ 3 0 Hz, H-3), 5 98 (m, $J_{5,6}$ 6 0 Hz, H-5), 6 38 (q, H-2), 7 69 (s, 3 H, Ph–CH_3), 8 18 (s, 3 H, NAc), and 8 71 (d, 3 H, CH_3–5), irradiation at the frequency of (CH_3–5) caused the collapse of the H-5 multiplet into a singlet, irradiation at the frequency of H-5 changed the CH_3–5 doublet into a singlet, irradiation at the frequency of H-2 transformed H-1 into a singlet, and irradiation at the frequency of H-1 caused the collapse of the H-2 quartet into a doublet ($J_{2,3}$ 11 Hz)

Anal Calc for $C_{29}H_{33}NO_7S$ C, 64 5, H, 6 2, N, 2 6, S, 5 9 Found C, 64 4, H, 6 0, N, 2 8; S, 6 0

*Benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-methylsulfonyl-α-*D*-galactopyranoside* (**15**) — Compound **9** (130 mg) was treated with methanesulfonyl chloride in pyridine as described for the preparation of **11** The crystalline material obtained after evaporation was recrystallized from chloroform–light petroleum to give **15** (110 mg, 72%), m p 201–202°, $[\alpha]_D^{24}$ +163° (*c* 1 0, chloroform)

Anal Calc for $C_{23}H_{29}NO_7S$ C, 59 6, H, 6 3, N, 3 0, S, 6 9 Found C, 59 3, H, 7 1, N, 3 2, S, 6 7

*Benzyl 2-acetamido-4-azido-3-*O*-benzyl-2,4,6-trideoxy-α-*D*-glucopyranoside* (**16**) — *A* A solution of **14** (0 237 g) in *N*,*N*-dimethylformamide (2 ml) was heated for 16 h at 150° under nitrogen in the presence of sodium azide (0 30 g) The cooled mixture was extracted with chloroform and the extract was washed with water, dried (sodium sulfate), and evaporated The resulting solid (180 mg) contained one main component (t l c in 5 3, v/v, ethyl acetate–hexane R_F 0 85) Crystallization from ethyl acetate–light petroleum gave **16** (135 mg, 75%), m p 169–170°, $[\alpha]_D^{27}$ +128° (*c* 0 7, chloroform), n m r data (100 MHz) τ 2 7 (m, 10 aromatic H), 4 58 (d, *J* 9 0 Hz,

NH), 5.1–5 9 (m, 6 H), 6 2–6.95 (m, 3 H) including 6 38 (m, $J_{4,5}$ 9 0 Hz, $J_{5,6}$ 6 0 Hz, H-5), 8 23 (s, 3 H, NAc), and 8 71 (d, 3 H, CH_3–5), irradiation at the frequency of CH_3–5 caused the collapse of the H-5 signal into a doublet (J 9.0 Hz); and irradiation at the frequency of H-5 changed the CH_3-5 doublet into a singlet.

Anal Calc for $C_{22}H_{26}N_4O_4$· C, 64 4; H, 6 4; N, 13 7 Found· C, 64 4; H, 6 2; N, 13.8.

B A solution of **15** (0 47 g) in hexamethylphosphoric triamide was heated for 20 h at 135° in the presence of sodium azide (0 5 g) Water was added to the cooled mixture and the crystalline material was filtered off and dried to give **16** (0.37 g, 88%), m p 165–166° Recrystallization from chloroform–light petroleum afforded a compound (0 25 g, 60%) having m p 170–171°, $[\alpha]_D^{25}$ +128° (*c* 1 0, chloroform)

*Benzyl 2,4-diacetamido-3-*O*-benzyl-2,4,6-trideoxy-α-*D*-glucopyranoside* (**17**) — A solution of **16** (65 mg) in methanol (20 ml) was hydrogenated at atmospheric pressure in the presence of 10% palladium-on-charcoal (20 mg) for 3 h The catalyst was filtered off, and the filtrate was evaporated to give a solid Acetic anhydride (0 1 ml) and pyridine (2 ml) were added and the solution was kept overnight at room temperature Evaporation of the solution and recrystallization of the residue from acetone–ether gave **17** (34 mg, 46%), m p 244–245°, $[\alpha]_D^{22}$ +106° (*c* 1 0, chloroform)

Anal Calc for $C_{24}H_{30}N_2O_5$. C, 67 6; H, 7.0, N, 6 6 Found C, 67.4, H, 7 0, N, 6 6

*2,4-Diacetamido-2,4,6-trideoxy-*D*-glucose* (**18**) — A solution of **17** (80 mg) in methanol (20 ml) was hydrogenolyzed in the presence of 10% palladium-on-charcoal (20 mg) at 4 5 atm for 24 h Water (10 ml) and more catalyst (20 mg) were added to the suspension, and the hydrogenolysis was continued for an additional 24 h Water and catalyst were added again after 48 h, and the reaction was continued for an additional 24 h The catalyst was removed and the filtrate evaporated. The crystalline residue was recrystallized from ethanol–light petroleum to give **18** (27 mg, 60%), m p 263–265° (decomp , not corrected, measured on Fisher-Johns apparatus), $[\alpha]_D^{24}$ +76° (after 5 min) → +63° (after 2 5 h, *c* 0 5, 1 1, v/v, ethanol–water), lit.[4] m p. 262–264° (decomp), $[\alpha]_D^{24}$ +67° (1 1 ethanol–water, equil)

Compound **18** was identical with the natural product[4] in its migration on t l c (R_F 0 15 in 9 1, v/v, acetone–ethanol and 0 12 in 4 1, v/v benzene–methanol), and on paper chromatograms (R_{Glc} 2.46 in 4 1 1, v/v, butanol–ethanol–water, 2.89 in 25 6·25, v/v, butanol–acetic acid–water, and 1 90 in 6 3 2, v/v, butanol–pyridine–water), spots were revealed by the silver nitrate reagent[4] The natural and synthetic (**18**) compounds had identical i r spectra[4] and X-ray powder diffraction patterns (Fig. 1).

Anal Calc for $C_{10}H_{18}N_2O_5$· C, 48 8; H, 7 4, N, 11.4 Found: C, 48 8; H, 7 5; N, 11.0.

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