318. *Nitrogen-containing Carbohydrate Derivatives. Part VI.* Synthesis and Reactions of some 3-Amino-3-deoxyaldohexoses and their Derivatives.*

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3-Amino-3-deoxy-D-talose and D-galactose hydrochlorides and methyl 3-acetamido-3-deoxy-α-D-mannoside have been synthesised by ring inversion in derivatives of methyl 3-amino-3-deoxy-α-D-glucoside. The removal of various *N*-blocking groups from 3-amino-3-deoxy-hexose derivatives has been investigated.

Reduction of methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-α-D-glucoside (I) provides a ready route to derivatives of methyl 3-amino-3-deoxy-α-D-glucoside.[1] This intermediate has recently been used in the synthesis of desosamine hydrochloride (3,4,6-trideoxy-3-dimethylamino-D-*xylo*-hexose hydrochloride).[2] This paper describes the conversion of derivatives of 3-amino-3-deoxy-D-glucose into other 3-amino-hexoses, and some of their chemistry.

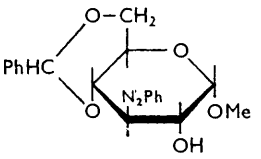
The preparation [1] of the phenylazo-glucoside (I) has been studied further, and it has now been shown that the crude product is contaminated with some unchanged starting compound. The preparation has now been carried out in aqueous pyridine and in aqueous *NN*-dimethylformamide, both methods having the advantage of using less bulk of solution than the aqueous method.[1,3] The crude mixture from reduction of the phenylazo-glucoside (I) has been treated with 1-chloro-2,4-dinitrobenzene in ethanol and the product chromatographed on alumina. The only (2,4-dinitrophenyl)amino-hexoside isolated was the 3-amino-glucoside derivative (III), in 78% yield. Also eluted from the column were 2,4-dinitrodiphenylamine (from the aniline also produced in the reaction) and 2,4-dinitrophenetole (from reaction with the solvent).

When this work was started 3-amino-3-deoxy-D-talose was unknown, and the only route to 3-amino-3-deoxy-D-galactose was that of Kuhn and Baschang,[4] so interconversions

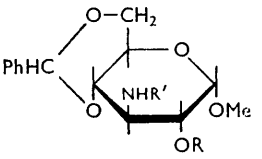
* Part V, Chittenden and Guthrie, *J.*, 1964, 1045.

[1] Guthrie and Johnson, *J.*, 1961, 4166.
[2] Richardson, *Proc. Chem. Soc.*, 1963, 131.
[3] Chittenden and Guthrie, *J.*, 1963, 3658.
[4] Kuhn and Baschang, *Annalen*, 1960, **636**, 164.

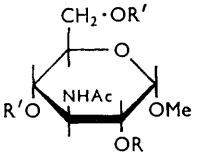
of derivatives of methyl 3-acetamido-3-deoxy-α-D-glucoside were undertaken. However, while these syntheses were in progress, and subsequently, Baer *et al.*[5,6] reported more convenient methods, using Fischer nitromethane cyclisations, which provide the best route to these compounds.



(I)



(II) R = R′ = H
(III) R = H, R′ = $C_6H_3(NO_2)_2$
(IV) R = H, R′ = Ac
(V) R = R′ = Ac
(VI) R = $MeSO_2$, R′ = Ac
(VII) R = H, R′ = Bz
(VIII) R = $MeSO_2$, R′ = Bz
(IX) R = H, R′ = CH_2Ph
(X) R = H, R′ = CO·O·CH_2Ph



(XI) R = R′ = H
(XII) R = R′ = $MeSO_2$
(XIII) R = Ac, R′ = H
(XIV) R = Ac, R′ = $MeSO_2$

Selective *N*-acetylation of the 3-amino-glucoside (II) may be carried out by adding acetic anhydride to the ethanolic reduction mixture without isolation of the parent amino-glucoside. Mild hydrolysis of the 3-acetamido-compound (IV) with 50% aqueous acetic acid gave methyl 3-acetamido-3-deoxy-α-D-glucoside (XI) (previously prepared [7] by *N*-acetylation of methyl 3-amino-3-deoxy-α-D-glucoside, a degradation product from the antibiotic, kanamycin). With methanesulphonyl chloride in pyridine this gave the 2,4,6-tri-*O*-methanesulphonyl derivative (XII). Solvolysis of this compound (XII) for 64 hours by Baker's method caused inversion to occur at positions 2 and 4. The resulting brown syrup was acetylated, and chromatographed on alumina; the peracetylated amino-glycoside was acetolysed, de-*O*-acetylated, and then hydrolysed with dilute hydrochloric acid, to give crystals, in 22% yield, which had the same physical properties as those described by Baer [5] for 3-amino-3-deoxy-D-talose hydrochloride. No investigation was carried out on the comparative ease of removal of the two methanesulphonyloxy-groups (but see below).

Mild acid hydrolysis of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside 2-acetate (V) gave methyl 3-acetamido-3-deoxy-α-D-glucoside 2-acetate (XIII), which was converted into the 4,6-di-*O*-methanesulphonyl compound (XIV). Richardson [2] has independently described these syntheses. The di-*O*-methanesulphonyl derivative (XIV) was solvolysed to cause inversion at position 4. The syrupy product was acetylated, chromatographed on alumina, acetolysed, and de-*O*-acetylated, to give a syrup which had the same chromatographic characteristics [5] as 3-acetamido-3-deoxy-D-galactose. Hydrolysis with dilute hydrochloric acid gave another syrup which had the same chromatographic mobility [5] and optical rotation as 3-amino-3-deoxy-D-galactose hydrochloride. Paper chromatography showed that the reaction was complete after about 6 hours. Taken in conjunction with the longer time (64 hr.) necessary for inversion at C-2 and C-4, this result suggests that the 4-*O*-methanesulphonyl group is more labile than that on C-2, in agreement with Richardson and McLauchlan's findings [8] but not with those of Baker and Schaub.[9]

Reaction of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (IV) with methanesulphonyl chloride in pyridine gave the 2-*O*-methanesulphonyl derivative (VI) which underwent solvolysis to give crystalline methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-mannoside in good yield by inversion at C-2. The product was characterised

[5] Baer, *J. Amer. Chem. Soc.*, 1962, **84**, 83.
[6] Baer and Kienzle, *Canad. J. Chem.*, 1963, **41**, 1606.
[7] Ogawa, Ito, Kondo, and Inoue, *Bull. Agric. Chem. Soc. Japan*, 1959, **23**, 289.
[8] Richardson and McLauchlan, *J.*, 1962, 2499.
[9] Baker and Schaub, *J. Org. Chem.*, 1954, **19**, 646.

by removal of the benzylidene group to give the known [10,11] methyl 3-acetamido-3-deoxy-α-D-mannoside. Our product had $[\alpha]_D$ +43·5° (in water), which supports Richardson's value [10] of +44° and not that of Saltza and his co-workers [11] of +17°. Repetition of the solvolysis under anhydrous conditions gave the de-methanesulphonylated glucoside (IV) (no inversion), in keeping with the findings of Winstein *et al.*[12] but contrary to the attempted anhydrous solvolysis of methyl 3-acetamido-3,6-dideoxy-2-*O*-methanesulphonyl-α-L-galactoside.[8]

The disadvantage of the synthesis of amino-sugar derivatives by solvolysis reactions of the type described above is that the product is always an acetamido-compound. Acid hydrolysis of the *N*-acetyl group removes other blocking groups, such as acetal groups and glycosidic methyl groups, which may be needed in subsequent synthetic steps. Alkaline hydrolysis has not generally been used, presumably because of reports of the stability of the *N*-acetyl group under these conditions.[13] Baker and his co-workers [14] used aqueous barium hydroxide for the hydrolysis when position 1 was blocked, though the yields were in general not good, and it is stated that a *cis*-hydroxyl group adjacent to the acetamido-function is necessary. We have examined the removal of *N*-acetyl and *N*-benzoyl groups by various methods. As expected, the benzamido-group functioned as did the acetamido-group in the solvolyses. Methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (II) was treated with benzoic anhydride in ethanol to give the *N*-benzoyl derivative (VII), which was converted into the 2-*O*-methanesulphonyl derivative (VIII); this was solvolysed to methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-mannoside in excellent yield. The product was characterised by comparison with the compound produced by *N*-benzoylation of methyl 3-amino-3-deoxy-α-D-mannoside followed by condensation with benzaldehyde.

Reaction of methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (VII) with lithium aluminium hydride in tetrahydrofuran, or in di-n-butyl ether–diethyl ether, gave the 3-benzylamino-compound (IX). However, the corresponding 3-benzamido-mannoside under the same conditions, or even in diglyme [di-(2-methoxyethyl) ether] at 90°, gave unchanged starting compound. Attempted hydrogenolysis of the benzylamino-glucoside (IX) with platinised charcoal or with Raney nickel was not successful; although this is a fairly general method for removing *N*-benzyl groups,[15–19] there are reports of unsuccessful hydrogenolyses.[19,20]

Since this route to the free amino-group was not successful, the reaction of *N*-acetyl groups with aqueous alkali was investigated. It was found that hydrolysis could be effected easily and cleanly and in good yield by boiling with N-aqueous sodium hydroxide. This method has been applied to a number of examples (see Experimental section). This hydrolysis has also been reported by Richardson.[2] Cleavage of the corresponding *N*-benzoyl derivatives did not occur.

Derivatives with other *N*-blocking groups used in the 2-amino-sugar series have been prepared, and the removal of the blocking group demonstrated. Methyl 4,6-*O*-benzylidene-3-deoxy-3-(2,4-dinitrophenylamino)-α-D-glucoside (III) has been hydrolysed in good yield by the ion-exchange resin method of Lloyd and Stacey,[21] although the reaction was much

[10] Richardson, *J.*, 1962, 373.
[11] Saltza, Reid, Dutcher, and Wintersteiner, *J. Amer. Chem. Soc.*, 1961, **83**, 2785.
[12] Winstein, Goodman, and Boschan, *J. Amer. Chem. Soc.*, 1950, **72**, 2311.
[13] Kent and Whitehouse, " Biochemistry of the Amino-sugars," Butterworths, London, 1959, p. 232.
[14] Baker *et al.*, *J. Amer. Chem. Soc.*, 1955, **77**, 1, 5911; 1960, **82**, 205, 209; *J. Org. Chem.*, 1954, **19**, 1786.
[15] Shapiro, Flowers, and Hecht, *J. Org. Chem.*, 1957, **22**, 461.
[16] Gadekar, Frederick, Semb, and Vaughan, *J. Org. Chem.*, 1961, **26**, 468.
[17] Vaughan and Blodinger, *J. Amer. Chem. Soc.*, 1955, **77**, 5757.
[18] Hunt and McHal, *J.*, 1957, 2073.
[19] Birkofer, *Ber.*, 1942, **75**, 429.
[20] Jones, *J. Amer. Chem. Soc.*, 1949, **71**, 383.
[21] Lloyd and Stacey, *Tetrahedron*, 1960, **9**, 116.

slower than those reported. Methyl 4,6-*O*-benzylidene-3-benzyloxycarbonyl-3-deoxy-α-D-glucoside (X) has been synthesised by the usual method; catalytic hydrogenation regenerated the parent amino-glucoside (II) in good yield.

Several other derivatives of methyl 3-amino-3-deoxy-α-D-glucoside and -mannoside, generally benzoyl compounds, have been prepared for characterisation purposes.

Experimental

Alumina was of type " H," 100—200 mesh, supplied by Peter Spence Ltd. The identity of compounds was proved where possible by mixed m. p.s and infrared spectrometry. Optical rotations are for chloroform solutions unless otherwise stated. Paper chromatography was on Whatman No. 1 paper with either (A) propan-2-ol–water (1 : 1), or (B) the Fischer–Dörfel system [22] as eluents. Location reagents were either (X) ninhydrin or (Y) aniline hydrogen phthalate.

7(*or* 9)-*Butoxy*-9(*or* 7)-*hydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-*e*]-[1,4]-*dioxepan*.—Periodate-oxidised methyl 4,6-*O*-benzylidene-α-D-glucoside [23] (2·0 g.) was boiled under reflux with butan-1-ol (50 ml.) until solution was complete (*ca.* 15 min.). The solution was concentrated to about 20 ml. and stored overnight at 0°. The solid (1·1 g., 55%), needles, had m. p. 136—138°, $[\alpha]_D^{20}$ +39° (3 min.) ⟶ +44° (2·5 hr. const.) (*c* 0·72 in pyridine) (Found: C, 60·9; H, 7·2. $C_{18}H_{26}O_7$ requires C, 61·0; H, 7·4%). Recrystallisation from water yielded starting material, m. p. 154—156°.

Methyl 4,6-O-*Benzylidene*-3-*deoxy*-3-*phenylazo*-α-D-*glucoside* (I).—Recrystallisation of the crude product [1,23] (10·0 g.) from butan-1-ol, without ether extraction, yielded yellow needles of the phenylazo-sugar. On standing, the mother-liquors precipitated 7(or 9)-butoxy-9(or 7)-hydroxy-6α-methoxy-2-phenyl-*trans*-*m*-dioxano[5,4-*e*]-[1,4]-dioxepan (0·7 g.), m. p. 136—138°.

Periodate-oxidised methyl 4,6-*O*-benzylidene-α-D-glucoside (5·0 g.) was dissolved in pyridine–water (10 : 1; 100 ml.), phenylhydrazine (5 ml.) was added, and the mixture was kept at room temperature for 24 hr. Pouring it into ice–water (1·5 l.) gave a pale yellow sticky solid (4·3 g.), m. p. 136—141°. Crystallisation from propan-1-ol gave the 3-phenylazo-glucoside (3·7 g., 64%), m. p. 180—181°, $[\alpha]_D^{21}$ +8·4° (*c* 1·02).

Repetition of the above experiment, but using *NN*-dimethylformamide–water (5 : 1), gave the crude solid (65%), m. p. 148—155°, purified as above.

Chromatography of the Products of Catalytic Reduction of the Phenylazo-glucoside (I.).—The products of the reduction of recrystallised methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-α-D-glucoside (m. p. 182—183°) [1] were concentrated to give a white solid (1·8 g.) which was treated with 1-chloro-2,4-dinitrobenzene (2·4 g.) and sodium acetate (4·0 g.) in ethanol (40 ml.). The solution was boiled under reflux for 1 hr. and poured into water (200 ml.). The mixture was extracted with chloroform, and the extract was concentrated to about 10 ml., and applied to an alumina column (4 × 45 cm.). Elution with benzene developed a pale yellow band (a) leading a broad yellow band (b). These were not separable, and so an intermediate fraction (c) was collected. Fraction (a) was concentrated to a pale yellow solid, identified as 1-chloro-2,4-dinitrobenzene (1·52 g.), m. p. 52—54° (lit.,[24] 51°). Fraction (b) gave a pale yellow-red solid (0·52 g.), m. p. 102—106°. Recrystallisation from glacial acetic acid gave 2,4-dinitrodiphenylamine (0·42 g.), m. p. 155—156° (lit.,[24] 156°). Fraction (c) yielded 2,4-dinitrodiphenylamine (0·03 g.), m. p. 155—157°. Further elution with benzene–chloroform (7 : 1) developed a third yellow band (d) which yielded 2,4-dinitrophenetole (0·12 g.), m. p. 84—86° (lit.,[24] 87°). A fourth band (e), developed with benzene–chloroform (1 : 1), yielded a yellow oil; after 1 week, crystals formed. Separation of the oil and repeated evaporation from ethanol yielded further crystals, to give a total of 1·7 g. (78%) of methyl 4,6-*O*-benzylidene-3-(2,4-dinitrophenylamino)-3-deoxy-α-D-glucoside (III), m. p. 188—189° (lit.,[1] 188—190°). Continued elution yielded no further products.

Methyl 3-*Acetamido*-3-*deoxy*-α-D-*glucoside* 2-*Acetate* (XIII).—Methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside 2-acetate (V) (18 g.) was heated at 100° with 50% aqueous acetic acid (900 ml.) for 30 min. The solution was concentrated to 100 ml. and the acetic acid removed by co-distillation with water and finally with ethanol. Evaporation to dryness yielded

[22] Fischer and Dörfel, *Z. physiol. Chem.*, 1955, **301**, 224.
[23] Guthrie and Honeyman, *J.*, 1959, 2441.
[24] Vogel, " Practical Organic Chemistry," 3rd edn., Longmans, London, 1956.

a white meringue-like solid (13·1 g., 92%), which was recrystallised with difficulty from butan-1-ol–light petroleum, to give the *product* (7·8 g., 58%), m. p. 172—173°, $[\alpha]_D^{20}$ +120° (*c* 1·44) (Found: C, 47·7; H, 7·0. $C_{11}H_{19}NO_7$ requires C, 47·6; H, 6·9%).

Condensation of the product (0·5 g.) with benzaldehyde (5 ml.) by shaking for 24 hr. in the presence of anhydrous zinc chloride (0·5 g.) and then pouring into ice–water (100 ml.) gave a colourless syrup, which was extracted with chloroform (75 ml.). The extract was washed with 10% sodium hydrogen sulphite solution, sodium hydrogen carbonate solution, and water, and dried. Evaporation of the extract gave a solid (0·7 g.) which gave the original benzylidene-acetamido-glucoside (V) (0·4 g.), m. p. 273—276° (from ethanol).

Methyl 3-*Acetamido*-3-*deoxy*-α-D-*glucoside* 2-*Acetate* 4,6-*Dimethanesulphonate* (XIV).—To methyl 3-acetamido-3-deoxy-α-D-glucoside 2-acetate (10·0 g.) in pyridine (100 ml.) at 0° was added methanesulphonyl chloride (8 ml.), also at 0°. The solution was stored at 0° for 24 hr. The excess of methanesulphonyl chloride was destroyed with a small amount of water, the reaction mixture poured into ice–water (*ca.* 1 l.), and the whole extracted with chloroform (7 × 100 ml.). The extracts were combined and washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and dried. Evaporation yielded a solid (9·3 g.), m. p. 152—156°, which gave (from ethanol) needles of the *product* (7·0 g., 45%), m. p. 174—175°, $[\alpha]_D^{20}$ +102° (*c* 0·64) (Found: C, 36·4; H, 5·3. $C_{13}H_{23}NO_{11}S_2$ requires C, 36·0; H, 5·4%).

Methyl 3-*Acetamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* 2-*Methanesulphonate* (VI).—Methanesulphonyl chloride (6·4 ml.) was added to a solution of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (6·4 g.) in pyridine (200 ml.) at 0°. The mixture was kept at 0° for 2 hr. and then allowed to reach room temperature. After 24 hr. it was worked up as described previously. The chloroform extracts were concentrated to give a pale yellow solid which was recrystallised from ethyl acetate–light petroleum, to give white needles of the *product* (5·5 g., 69%), m. p. 221—222°, $[\alpha]_D^{20}$ +42·6° [*c* 0·495 in $CHCl_3$–DMF (1 : 1)] (Found: C, 50·7; H, 5·8. $C_{17}H_{23}NO_8S$ requires C, 50·8; H, 5·8%).

Methyl 3-*Acetamido*-3-*deoxy*-α-D-*glucoside* 2,4,6-*Trimethanesulphonate* (XII).—A suspension of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (3 g.) [1] in 50% aqueous acetic acid (150 ml.) was heated at 100° for 45 min. The acetic acid was removed by co-distillation with water and finally ethanol. Evaporation yielded a white amorphous solid (2·2 g.). Recrystallisation gave methyl 3-acetamido-3-deoxy-α-D-glucoside (XI) (1·5 g., 83%), m. p. 176—178° (lit.,[7] 176—178°).

This product (1·9 g.), in pyridine (25 ml.), was treated with methanesulphonyl chloride (2·0 ml.) in pyridine at 0°. After 24 hr. the solution was worked up in the usual manner. The chloroform extract, on evaporation, yielded a white solid. Two recrystallisations from ethanol gave the *product* (55%), m. p. 161—162°, $[\alpha]_D^{20}$ +83° (*c* 0·31) (Found: C, 31·1; H, 5·0. $C_{12}H_{23}NO_{12}S_3$ requires C, 30·9; H, 5·0%).

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* (VII).—Benzoic anhydride (1·6 g.) was added slowly with stirring to methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (2·0 g.) in methanol (40 ml.). After 2 min. the solution solidified and, on adding it to water, yielded a white solid (2·0 g.) which was collected and dried. Recrystallisation from dimethylformamide (DMF)–water gave the *product* (1·8 g., 66%), m. p. 303—304°, $[\alpha]_D^{20}$ +25·5° (*c* 0·99 in DMF) (Found: C, 65·1; H, 6·1. $C_{21}H_{23}NO_6$ requires C, 65·4; H, 6·0%).

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* 2-*Methanesulphonate* (VIII).—Methanesulphonyl chloride (1 ml.) was added to methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (1 g.) in pyridine (130 ml.) at 0°. The solution was set aside for 2 hr. at 0°, allowed to come to room temperature, and after 24 hr. it was poured into ice–water; the white solid (0·75 g.) produced was collected. Chloroform extraction of the aqueous solution and evaporation yielded a further amount of solid (0·1 g.). Recrystallisation from chloroform–light petroleum and then from dimethylformamide from water yielded the *product* (0·65 g., 55%), m. p. 232—234°, $[\alpha]_D^{20}$ +17·7° (*c* 0·9 in pyridine) (Found: C, 57·2; H, 5·6. $C_{20}H_{25}NO_8S$ requires C, 57·0; H, 5·4%).

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* 2-*Benzoate*.—Methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (0·3 g.) was suspended in pyridine (20 ml.), and to the stirred suspension at 0° was added a solution of benzoyl chloride in pyridine until the faint colour became permanent. The suspension was stirred for a further 30 min. and the excess of benzoyl chloride decomposed with water. On pouring into ice–water (150 ml.) a white precipitate was formed which, on drying, yielded a solid (0·34 g.). Recrystallisation

from ethanol gave needles of the *product* (0·29 g., 76%), m. p. 258—259·5°, $[\alpha]_D^{20}$ +98·1° (*c* 0·43) (Found: C, 68·5; H, 5·7. $C_{28}H_{27}NO_7$ requires C, 68·7; H, 5·6%).

Methyl 3-*Benzamido*-3-*deoxy*-α-D-*glucoside*.—A suspension of methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (0·7 g.) in 40% aqueous acetic acid (30 ml.) was heated under reflux until solution was complete (*ca.* 45 min.). The solution was worked up in the usual manner to give a white solid. Recrystallisation from a small volume of ethanol yielded needles of the *product* (0·29 g., 64%), m. p. 236·5—238°, $[\alpha]_D^{20}$ +139° (*c* 0·88 in ethanol) (Found: C, 56·4; H, 6·4. $C_{14}H_{19}NO_6$ requires C, 56·6; H, 6·4%).

Methyl 3-*Benzamido*-3-*deoxy*-α-D-*glucoside* 2,4,6-*Tribenzoate*.—Methyl 3-benzamido-3-deoxy-α-D-glucoside (0·26 g.) was treated with benzoyl chloride as above, and after 45 min. the solution was poured into water to give a pale yellow oil. The solution was extracted with chloroform (3 × 15 ml.), and evaporation of the extract yielded a white solid. The solid was suspended in saturated sodium hydrogen carbonate solution, filtered, and washed with a small volume of ether, to give a white solid (0·41 g.). Recrystallisation from aqueous ethanol gave needles of the *product* (0·38 g., 70%), m. p. 190·5—192°, $[\alpha]_D^{20}$ +150° (*c* 0·4) (Found: C, 69·0; H, 5·1. $C_{35}H_{31}NO_9$ requires C, 69·0; H, 5·1%).

A solution of the perbenzoylated glucoside (0·2 g.) in methanol (20 ml.) was treated with ammonia (*d* 0·88; 20 ml.); the solution was set aside for 2 days, and evaporated to give a white solid (0·09 g.). Recrystallisation from ethanol yielded needles (0·08 g., 83%), m. p. 236—238°, identified as methyl 3-benzamido-3-deoxy-α-D-glucoside.

Methyl 3-*Benzylamino*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* (IX).—To a suspension of lithium aluminium hydride (0·5 g.) in ether (150 ml.) boiling under reflux, was added methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (1·3 g.) in di-n-butyl ether (150 ml.). After the addition was complete the flask was attached to a Claisen head and solvent distilled off until the solution temperature reached 85°. The solution was then heated under reflux, with stirring, for 24 hr. The excess of lithium aluminium hydride was decomposed with water, and the solution evaporated to give a white solid, which was extracted by heating under reflux with chloroform (150 ml.) for 3 hr. After cooling, the solution was filtered and the filtrate evaporated to give a solid (0·8 g.). Recrystallisation from ethanol yielded the *product* (0·6 g., 47%), m. p. 200·5—202°, $[\alpha]_D^{20}$ +102·5° (*c* 0·5) (Found: C, 68·1; H, 7·0; N, 3·3. $C_{21}H_{25}NO_5$ requires C, 67·9; H, 6·8; N, 3·7%).

Reaction under similar conditions, using tetrahydrofuran as solvent, yielded the product (54%), m. p. 199—201°, $[\alpha]_D^{20}$ +102° (*c* 0·45).

Attempted Hydrogenolysis of Methyl 3-*Benzylamino*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside*.—A solution of the glucoside (0·2 g.) in ethanol–water (19 : 1) (25 ml.) containing 5% platinised charcoal (*ca.* 5 mg.) was shaken under hydrogen (1 atm.) at room temperature for 5 hr. The solution was filtered and the filtrate evaporated, to give starting material (0·17 g.).

Hydrogenolysis using Raney nickel under hydrogen (5 atm.) at room temperature was also unsuccessful, resulting in the recovery of starting material (85%).

Reaction of Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*mannoside with Lithium Aluminium Hydride*.—To a suspension of lithium aluminium hydride (0·6 g.) in freshly distilled diglyme (120 ml.) was added the title compound (0·2 g.) in diglyme (50 ml.). The suspension was heated at 90° under nitrogen for 24 hr. Working up as described for the glucoside yielded, after recrystallisation, starting material (0·15 g.).

Methyl 3-*Benzamido*-3-*deoxy*-α-D-*mannoside* 2,4,6,-*Tribenzoate*.—Methyl 3-amino-3-deoxy-α-D-mannoside hydrochloride (0·26 g.) (see below) was benzoylated with benzoyl chloride as described above; concentration of the chloroform extract yielded a white solid which could not be recrystallised from common solvents; however, extraction with light petroleum yielded the *product* (0·4 g.), m. p. 94—95°, $[\alpha]_D^{20}$ −62·5° (*c* 0·86) (Found: C, 68·9; H, 5·1. $C_{35}H_{31}NO_9$ requires C, 69·0; H, 5·1%).

Methyl 3-*Benzamido*-3-*deoxy*-α-D-*mannoside*.—Methyl 3-benzamido-3-deoxy-α-D-mannoside 2,4,6-tribenzoate (1 g.) was dissolved in methanol (20 ml.), and to the solution was added ammonia (*d* 0·88; 20 ml.). After 2 days the solution was evaporated to give a syrup; recrystallisation from ethyl acetate–light petroleum yielded a white hygroscopic solid, which was thoroughly dried and shaken with benzaldehyde (0·7 ml.) and zinc chloride (0·5 g.) for 24 hr. The mixture was then set aside at 0° for 12 hr., and working up according to the usul procedure yielded a solid. Recrystallisation from ethyl acetate–light petroleum gave methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-mannoside (0·4 g.), m. p. 173—175°.

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*mannoside* 2-*Benzoate*.—Methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-mannoside (0·4 g.) (see below) was benzoylated as previously described, and concentration of the chloroform extract yielded a white solid (0·34 g.). Recrystallisation from ethanol gave fine needles of the *product* (0·3 g., 60%), m. p. 198·5—200°, $[\alpha]_D^{20}$ −153° (*c* 1·02) (Found: C, 68·3; H, 5·6. $C_{28}H_{27}NO_7$ requires C, 68·7; H, 5·6%).

Solvolyses.—(*a*) *Methyl* 3-*acetamido*-3-*deoxy*-α-D-*glucoside* 2-*acetate* 4,6-*dimethanesulphonate*. A solution of the title compound (5·9 g.) and sodium acetate (5·9 g.), in 2-methoxyethanol (95 ml.) and water (5 ml.), was boiled under reflux for 8 hr. The solution was concentrated to a syrup, which was extracted with hot acetone (60 ml.), filtered, and concentrated to give a syrup. Paper chromatography in system (A) gave a single spot R_F 0·80, developed with spray (X).

The syrup was acetylated using pyridine–acetic anhydride. The reaction mixture was poured into water, and the whole extracted with chloroform. The extract was then chromatographed on alumina. The chromatogram was monitored polarimetrically and chloroform–benzene (5 : 1) developed a band of optically active material. Fractions (50 ml.) were collected, and fractions 21—25 showed activity, while further elution developed no other optically active bands. Fractions 21—25 were combined and concentrated to give a pale yellow syrup of the peracetylated amino-glycoside. Concentration of the non-active fractions yielded no further compounds. The peracetylated amino-glycoside was converted into the peracetylated amino-sugar by dissolving it at 0° in acetic anhydride (10 ml.) containing sulphuric acid (0·2 ml.). After 20 hr. at room temperature, the mixture was worked up according to standard procedure. The peracetylated amino-sugar obtained (0·35 g.) could not be crystallised. It was de-*O*-acetylated after 24 hr. at 0° in methanol containing sodium methoxide (0·03 g.). After dilution with methanol, the solution was de-ionised with Amberlite IR-120(H), concentrated to a small volume, and the acetamido-sugar was precipitated as an oil by addition of an excess of ethyl acetate. Paper chromatography using system (B) showed a single spot, developed with spray (Y), having R_F 0·95 and R_{gm} 1·49 (Baer [5] reported R_{gm} 1·49 for 3-acetamido-3-deoxy-D-galactose).

The oil was hydrolysed in N-hydrochloric acid at 100° for 90 min. The hydrolysate was treated with acid-washed charcoal, filtered, and repeatedly evaporated from water, to yield a syrup which when chromatographed on paper, using system (B) spray (X), gave a single spot having R_F 0·51 and R_{gm} 0·86, $[\alpha]_D^{20}$ +104° (2 min.) ⟶ +80·0° (2 hr.) (in water). {The following data are reported for 3-amino-3-deoxy-D-galactose hydrochloride. Baer: R_{gm} 0·86 [5] and 0·90, and $[\alpha]_D^{23}$ +109° ⟶ +82·0° (2 hr.); [6] Kuhn: [4] $[\alpha]_D^{20}$ +115° (2 min.) ⟶ +89° (2 hr.).}

(*b*) *Methyl* 3-*acetamido*-3-*deoxy*-α-D-*glucoside* 2,4,6-*trimethanesulphonate*. Treatment of the title compound (0·8 g.) as in (*a*) for 64 hr., and with working up as described above, yielded, on concentration of the acetone extract, a brown syrup (0·65 g.). The syrup was acetylated using pyridine–acetic anhydride, the mixture was poured into water (300 ml.), and the whole extracted with chloroform (4 × 50 ml.). After concentration, the extract was chromatographed on alumina. The chromatogram was monitored polarimetrically, and elution with benzene–chloroform (1 : 1) developed a band of optically active material. Fractions (10 ml.) were collected, and fractions 51—57 showed activity, further elution developed no optically active bands. Fractions 51—57 were combined and concentrated, to give a pale yellow syrup of the peracetylated glycoside. Concentration of the non-active fractions yielded no further compounds. The peracetylated amino-glycoside (0·25 g.) was converted into the peracetylated amino-sugar using acetic anhydride and concentrated sulphuric acid, and then de-*O*-acetylated as described above, to give the acetamido-sugar (0·14 g.). This was hydrolysed in N-hydrochloric acid (10 ml.) at 100° for 90 min. The hydrolysate was treated with acid-washed charcoal and evaporated to a yellow syrup which, after being kept in an unevacuated desiccator over potassium hydroxide for 24 hr., crystallised in flat plates (86 mg.). Recrystallisation from aqueous acetic acid yielded 3-amino-3-deoxy-α-D-talose hydrochloride (80 mg.), m. p. 160—161°. Paper chromatography using system (B) and spray (Y) showed a single spot of R_{gm} 1·14 initially yellow-brown turning violet after several hours. (Baer [5] reports, m. p. 160—161°, and R_{gm} 1·15, yellow-brown spot turning violet.)

(*c*) *Methyl* 3-*acetamido*-4,6-*benzylidene*-3-*deoxy*-α-D-*glucoside* 2-*methanesulphonate*. Treatment of the title compound (1 g.) as in (*a*) for 72 hr., and working up as described, yielded, on concentration of the acetone extract, a white solid. Recrystallisation from ethyl acetate–light petroleum or ethanol gave needles of *methyl* 3-*acetamido*-4,6-*O*-*benzylidene*-3-*deoxy*-α-D-*mannoside* (0·65 g., 80%), m. p. 169—171°, $[\alpha]_D^{20}$ +105° (*c* 0·42) (Found: C, 59·1; H, 6·3. $C_{16}H_{21}NO_6$ requires C, 59·4; H, 6·6%).

The product (1 g.) was dissolved in 50% aqueous acetic acid (50 ml.) and the solution heated under reflux for 30 min. at 100°. The solution was evaporated, with repeated addition of water and finally ethanol, to give a white solid which, on recrystallisation from ethanol, yielded methyl 3-acetamido-3-deoxy-α-D-mannoside (0·62 g., 85%), m. p. 241·5—243·5°, $[\alpha]_D^{20}$ +43·5° (*c* 1·68 in water). Richardson [10] reported m. p. 241—243°, $[\alpha]_D^{20}$ +44° (*c* 1·66 in water); Saltza *et al.*[11] reported m. p. 242·5—243·5°, $[\alpha]_D^{23}$ +17° (in water).

Solvolysis of the title compound, as described above but using anhydrous 2-methoxyethanol, yielded methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside.

(*d*) *Methyl* 3-*benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* 2-*methanesulphonate*. Treatment of the title compound (0·75 g.) as in (*a*) for 72 hr. yielded, on concentration of the acetone extract, a white solid (0·5 g.) which was recrystallised from diglyme–water and then from ethyl acetate–light petroleum to give *methyl* 3-*benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*mannoside* (0·4 g., 65%), m. p. 173·5—175°, $[\alpha]_D^{20}$ −60° (*c* 0·5 in DMF) (Found: C, 65·4; H, 6·0. $C_{21}H_{23}NO_6$ requires C, 65·4; H, 6·0%).

Alkaline hydrolyses.—(*a*) *Methyl* 3-*acetamido*-4.6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside*. The acetamido-glucoside (0·8 g.) was suspended in N-aqueous sodium hydroxide (30 ml.) and the suspension was cooled and filtered from unchanged starting material (0·1 g.). The filtrate was extracted with chloroform (3 × 25 ml.) and the solution, on evaporation, gave a white solid. Recrystallisation from chloroform–light petroleum yielded methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (66%), m. p. 182—183°.

(*b*) *Methyl* 3-*acetamido*-4,6,-O-*benzylidene*-3-*deoxy*-α-D-*mannoside*. The acetamido-mannoside (0·9 g.) was treated as above with N-aqueous sodium hydroxide. After 16 hr., solution was complete and, on cooling, white needles (0·38 g.), were precipitated, m. p. 170—172°. The filtrate was extracted as above, and evaporation yielded a white solid (0·32 g.), m. p. 170—171°. Recrystallisation from water yielded long white needles of *methyl* 3-*amino*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*mannoside* (68%), m. p. 172—173°, $[\alpha]_D^{20}$ +55·5° (*c* 0·69) (Found: C, 59·7; H, 6·7. $C_{14}H_{19}NO_5$ requires C, 59·8; H, 6·8%).

(*c*) *Methyl* 3-*acetamido*-3-*deoxy*-α-D-*glucoside*. The acetamido-sugar (0·4 g.) was treated as described above with N-aqueous sodium hydroxide overnight. The solution was evaporated, extracted with hot methanol, and filtered. The filtrate, which showed a positive ninhydrin test, was evaporated to give a pale yellow hygroscopic solid, which was treated with benzoyl chloride; working up by the usual procedure yielded needles of methyl 3-benzamido-3-deoxy-α-D-glucoside 2,4,6-tribenzoate (54%), m. p. 189·5—192°.

(*d*) *Methyl* 3-*acetamido*-3-*deoxy*-α-D-*mannoside*. Treatment of the acetamido-sugar (0·29 g.), as previously described, for 16 hr., and evaporation yielded a white solid which was extracted with ethanol and filtered. The filtrate, which gave a positive ninhydrin test, was concentrated to about 3 ml., and addition of hydrochloric acid gave a solid. Recrystallisation from water–ethanol gave methyl 3-amino-3-deoxy-α-D-mannoside hydrochloride (70%), decomposing at 220°, $[\alpha]_D^{20}$ +59° (*c* 1·5 in water). Richardson [10] reports: decomposition at 210—240°, $[\alpha]_D^{20}$ +60° (*c* 2 in water).

(*e*) *Methyl* 3-*benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside*. The benzamido-sugar (0·13 g.) was treated as described with N-aqueous sodium hydroxide. After 5 days, solution was still incomplete and, on working up, unchanged starting material (0·11 g.), m. p. 302—304°, was recovered.

(*f*) *Methyl* 3-*benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*mannoside*. Treatment of the benzamido-sugar (0·12 g.) as described, after 5 days, yielded starting material (0·11 g.), m. p. 173—175°.

Hydrolysis of Methyl 4,6-O-*Benzylidene*-3-(2,4-*dinitrophenylamino*)-3-*deoxy*-α-D-*glucoside*.—The title compound (0·1 g.) was dissolved in aqueous acetone (2 : 1 acetone–water; 18 ml.) and to the solution was added De-Acidite FF resin (6 g.). The mixture was shaken for 16 hr.; the supernantant liquor had then become almost colourless. The solution was filtered and evaporated, to give a pale yellow solid. Recrystallisation from chloroform–light petroleum yielded a white solid (0·04 g., 58%), m. p. 183—184° (subl. and decomp.), identified as methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside.

Methyl 3-N-*Benzyloxycarbonylamino*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside*.—To a solution of methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (0·9 g.) in water (150 ml.) was added sodium hydrogen carbonate (0·5 g.). The solution was stirred, and benzyl chloroformate (0·6 g.) was added dropwise during 15 min.; it was filtered, to give a white solid (0·9 g.). Two

recrystallisations from chloroform–light petroleum gave needles of the *product* (0·7 g., 53%), m. p. 243·5—244°, $[\alpha]_D^{20}$ +74·7° (*c* 0·4) (Found: C, 63·1; H, 6·2. $C_{22}H_{25}NO_7$ requires C, 63·6; H, 6·1%).

To a solution of the benzyloxycarbonylamino-derivative (1·0 g.) in ethanol (50 ml.) was added palladised charcoal (*ca.* 3 mg.). The system was shaken under hydrogen 1 atm. until uptake ceased. The suspension was filtered, and the filtrate evaporated to give a white solid (0·5 g.). Recrystallisation from chloroform–light petroleum gave methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (0·45 g., 66%), m. p. 182—183°.

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