476. 3-*Amino*-3,6-*dideoxy-derivatives of* L-*Glucose,* L-*Galactose, and* L-*Talose.*[1]

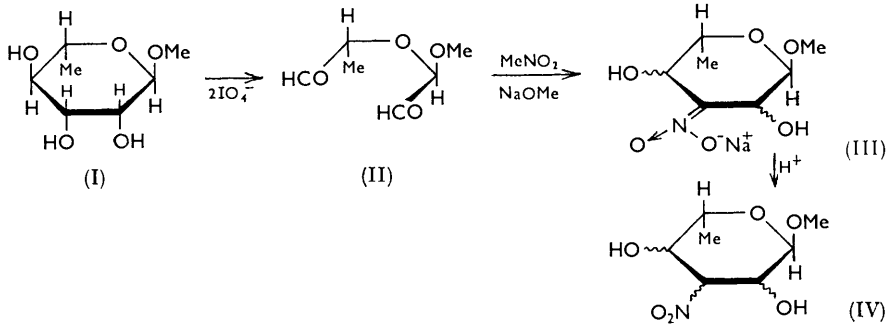
By A. C. Richardson and (in part) K. A. McLauchlan.

The preparation of methyl 3-amino-3,6-dideoxy-α-L-glucoside from methyl α-L-rhamnoside *via* the Fischer nitromethane cyclisation is described. The stereochemistry of the product was determined by comparisons of its molecular rotation and by proton resonance spectroscopy. Reaction of methyl 3-acetamido-3,6-dideoxy-2,4-di-*O*-methanesulphonyl-α-L-glucoside with sodium acetate afforded, *via* an oxazolinium intermediate, methyl 3-acetamido-3,6-dideoxy-2-*O*-methanesulphonyl-α-L-galactoside, and then methyl 3-acetamido-3,6-dideoxy-α-L-taloside. This confirmed the stereochemistry of the glucoside. Acid hydrolysis of the corresponding glycosides afforded 3-amino-3,6-dideoxy-L-glucose and -L-talose, two new amino-sugars. The proton resonance spectra of some acetamido-sugars have been studied.

Recent work on the macrolide antibiotics has led to the isolation of a number of basic sugars related to 3-amino-3,6-dideoxyhexoses.[2] The synthesis of one of these sugars, mycosamine (3-amino-3,6-dideoxy-D-mannose), was accomplished from methyl 3-amino-3-deoxy-α-D-mannoside [3] and, as a result of this present work, the stereochemistry of

[1] Preliminary communication: Richardson, *Proc. Chem. Soc.*, 1961, 255.
[2] Foster and Horton, *Adv. Carbohydrate Chem.*, 1959, **14**, 231.
[3] Saltza, Reid, Dutcher, and Wintersteiner, *J. Amer. Chem. Soc.*, 1961, **83**, 2785.

mycaminose (3,6-dideoxy-3-dimethylamino-β-D-glucose), a component of magnamycin, leucomycin, and spiromycin, has been elucidated by synthesis.[4] The classical syntheses of 3-amino-3,6-dideoxyhexoses (cf. Huber *et al.*[5] and Saltza *et al.*[3]), which are potential intermediates in the synthesis of the other basic sugars isolated from the macrolide antibiotics, are tedious and give low yields. The novel synthesis of amino-sugars by cyclisation of certain dialdehydes with nitromethane, has been useful for the preparation of



reasonably large quantities of 3-amino-sugars.[6-8] The synthesis of 3-amino-3,6-dideoxyhexoses from a 6-deoxyhexopyranoside by this method is now reported.

Oxidation of the readily obtainable methyl α-L-rhamnoside[9] (I) with sodium metaperiodate afforded the dialdehyde (II), which was condensed directly with nitromethane to give a mixture of 3-*aci*-nitro-salts (III), and treatment of this mixture with a cation-exchange resin afforded a syrupy mixture of 3-nitropyranosides (IV). Hydrogenation yielded a mixture of amines, from which one was obtained crystalline in 25—31% yield (based on the rhamnoside). This amine was subsequently shown to be methyl 3-amino-3,6-dideoxy-α-L-glucoside (V). By similar reactions methyl 6-deoxy-α-D-glucoside afforded the D-enantiomorph of (V).[4] No other crystalline compound was obtained from the mother-liquors.

In general, replacement of a hydroxyl by an amino-group in pyranoside derivatives does not substantially affect the molecular rotations.[7,10,11] For comparison of the $[M]_D$ of a methyl α-L-hexoside with that of a methyl 6-deoxy-α-L-hexoside, a correction factor of +3000° must be applied to the former owing to the asymmetrical rotation of the 5,6-exocyclic bond, which does not contribute to the rotation of the 6-deoxy-glycosides;[12] this correction factor has been applied in the values quoted in Table 1 and in subsequent comparisons. When the $[M]_D$ of the amino-glycoside (V) (−25,700°) was compared with those of the methyl α-L-hexopyranosides (many calculated from the D-form) the *manno-*, *gulo-*, *allo-*, *ido-*, and *talo*-configurations were excluded by the low negative rotations (*ca.* −12,000° to −18,000°) associated with these configurations. The *altro-* and *manno*-isomers were also excluded since derivatives with these configurations are known and did not correspond to any of these new derivatives.[3,5] The L-*galacto*-configuration was unlikely since it gave rise to high negative rotations (*ca.* −32,000° to −35,000°), but the molecular rotations of derivatives of compound (V) compared well with those of methyl α-L-glucopyranoside derivatives (Table 1) and consequently the *gluco*-configuration was indicated.

[4] Richardson, *Proc. Chem. Soc.*, 1961, 430; *J.*, in the press.
[5] Huber, Schier, and Druey, *Helv. Chim. Acta*, 1959, **42**, 2447.
[6] Baer and Fischer, *J. Amer. Chem. Soc.*, 1959, **81**, 5184; 1960, **82**, 3709; Baer, *Chem. Ber.*, 1960 **93**, 2865, *J. Amer. Chem. Soc.*, 1962, **84**, 83.
[7] Richardson and Fischer, *J. Amer. Chem. Soc.*, 1961, **83**, 1132.
[8] Richardson, *J.*, 1962, 373.
[9] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1946, **68**, 628.
[10] van Tamelen, Dyer, Carter, Pierce, and Daniels, *J. Amer. Chem. Soc.*, 1956, **78**, 4817.
[11] Ogawa, Ito, Kondo, and Inoue, *Bull. Agric. Chem. Soc. Japan*, 1959, **23**, 289.
[12] Whiffen, *Chem. and Ind.*, 1956, 964; Brewster, *J. Amer. Chem. Soc.*, 1959, **81**, 5483.

TABLE 1.

Comparison of the molecular rotations of derivatives of compound (V) with those of methyl α-L-glucopyranoside derivatives.

Compound	$[M]_D$*
Me α-L-glucoside [a]	−27,900° (H_2O) †
Me 6-deoxy-α-L-glucoside [b]	−27,100° (H_2O)
Me 3-amino-3-deoxy-α-L-glucoside [c, 11]	−24,900° (H_2O) †
Me 2-amino-2-deoxy-α-L-glucoside [d]	−26,100° (H_2O) †
3-Amino-3,6-dideoxy-glycoside (V)	−25,700° (H_2O)
Me 2-acetamido-2-deoxy-α-L-glucoside [e]	−27,800° (H_2O) †
Me 3-acetamido-3-deoxy-α-L-glucoside [11]	−34,200° (H_2O) †
3-Acetamido-3,6-dideoxy-glycoside (VIII)	−31,000° (H_2O)
Me 2-acetamido-2-deoxy-α-L-glucoside 3,4,6-triacetate [e]	−37,000° ($CHCl_3$)
Me 3-acetamido-3-deoxy-α-L-glucoside 2,4,6-triacetate	−38,900° ($CHCl_3$)
Triacetyl derivative of (V)	−38,800° ($CHCl_3$)

* Most of these values are obtained from those quoted for the D-enantiomorphs.

† A correction factor of +3,000° has been applied to these values.

[a] Fischer, *Ber.*, 1893, **26**, 2400. [b] Helferich, Klein, and Schafer, *Ber.*, 1926, **59**, 79. [c] Peat and Wiggins, *J.*, 1938, 1813. [d] Neuberger and Rivers, *J.*, 1939, 12. [e] Kuhn, Zilliken, and Gauhe, *Chem. Ber.*, 1953, **86**, 466. [f] Cron, Evans, Palermiti, Whitehead, Hooper, Chu, and Lemieux, *J. Amer. Chem. Soc.*, 1958, **80**, 4741.

Acidic hydrolysis of the amino-glucoside (V) gave 3-amino-3,6-dideoxy-L-glucose hydrochloride (VI) which did not crystallise. Acetylation of this salt yielded isomeric tetra-acetyl derivatives (VII and X), readily separable by fractional crystallisation. The anomeric configurations of each were assigned from their molecular rotations, the most negative being the α-isomer.[13] This assignment was supported by the proton magnetic resonance spectra of these derivatives, which also afforded unequivocal proof of the *gluco*-configuration (see below).

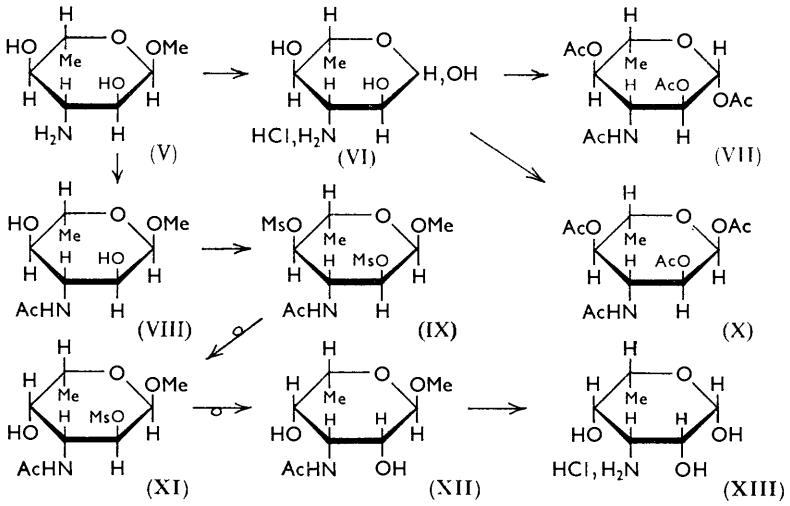
The inversion of methanesulphonyloxy-groups situated *trans* to a vicinal acetamido-substituent *via* oxazolinium intermediates has received much attention in preparative carbohydrate chemistry [14] and has helped to establish the stereochemistry of some 3-amino-1,6-anhydro-3-deoxy-β-D-hexoses.[7] Under the conditions used the displacement of a *cis*-methanesulphonyloxy-group is very slow. In order to confirm that the substituents at positions 2, 3, and 4 in the 3-amino-3,6-dideoxyglycoside (V) are in an all-*trans*-relation this inversion reaction has been applied. The amino-glucoside (V) was converted into methyl 3-acetamido-3,6-dideoxy-α-L-glucoside (VIII) through the triacetyl derivative as well as by selective *N*-acetylation with acetic anhydride in ethanol. The acetamido-derivative was then converted into a di-*O*-methanesulphonate (IX) which, when heated with sodium acetate in 95% 2-methoxyethanol for 48 hr. gave a 60% yield of a sulphur-free compound isomeric with (VIII), indicating that both sulphonyloxy-substituents had been *trans* to the acetamido-function. Such a result is consistent with either the *gluco*- or the *ido*-configuration. However, the $[M]_D$ of methyl 3-acetamido-3-deoxy-α-L-idopyranoside [14b] is −14,300°, which is widely different from that (−31,000°) of our corresponding derivative (VIII), affording further proof of the *gluco*-configuration. The product of the inversion-reaction is thus methyl 3-acetamido-3,6-dideoxy-α-L-taloside (XII) which was further characterised by formation of its di-*O*-acetate. Acidic hydrolysis of the taloside (XII) yielded a new crystalline amino-sugar, 3-amino-3,6-dideoxy-α-L-talose hydrochloride (XIII).

When the inversion-reaction was carried out for 2½ hr., a 77% yield of a mono-*O*-methanesulphonate was obtained. After 24 hr., a mixture of the galactoside (XI) and taloside (XII) was obtained. The greater lability of one of the sulphonyloxy-groups was shown by the rapid release of acid from disulphonate (IX) in boiling water. Baker and

[13] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66.

[14] (*a*) Baker and Schaub, *J. Org. Chem.*, 1954, **19**, 646; Jeanloz, Glazer, and Jeanloz, *ibid.*, 1961, **26**, 532; (*b*) Jeanloz and Jeanloz, *ibid.*, p. 537.

Schaub [14] have also reported that one sulphonyloxy-group in methyl 3-acetamido-3-deoxy-2,4-di-*O*-methanesulphonyl-β-L-xyloside undergoes rapid displacement under mild conditions, and the second much less readily. Although no structural evidence was presented, it was suggested that the group at position 2 was the more reactive. This is contrary to our results.



The monosulphonate would be a mannoside or a galactoside according to whether displacement occurs at position 2 or at position 4. Derivatives of methyl α-L-mannoside are characterised by their low negative rotations (*ca.* −11,000° to −18,000°), those of methyl α-L-galactoside have very high negative rotations (*ca.* −35,000° to −48,000°). The monosulphonate had $[M]_D$ −47,100°, and was converted into a di-*O*-methanesulphonate having $[M]_D$ −46,600°, which compared well with the $[M]_D$'s of the acetates of methyl α-L-galactoside [15] and methyl 6-deoxy-α-L-galactoside [16] (−48,200° and −45,900°, respectively, calculated from values for the D-enantiomorphs) but was widely different from those of the acetates of methyl α-L-mannoside [17] and methyl 6-deoxy-α-L-mannoside [18] (−17,800° and −16,100°, respectively, the former calculated from the value for the D-enantiomorph). It is thus evident that the monosulphonate must be the L-*galacto*-isomer (XI). Attempts to remove, without inversion, the remaining sulphonyloxy-group from compound (XI) with Raney nickel failed (cf. ref. 19). Winstein *et al.*[20] have reported that tosyl groups *trans* to a vicinal benzamido-substitutent can be solvolysed without inversion with sodium acetate in anhydrous acetic acid. From the reaction of compound (XI) under these conditions methyl 3-acetamido-3,6-dideoxy-α-L-galactoside could not be isolated; instead a small yield of the " inverted-product " (XII) was obtained. Even when acetic anhydride was used in place of acetic acid only the product (XII) was isolated (as its di-*O*-acetate). An alternative route to 3-amino-3,6-dideoxy-L-galactose is now under investigation.

The smaller reactivity of the 2-methanesulphonyloxy-group is probably due to its deactivation by the weakly electron-attracting acetal group at position 1, which causes an electron deficiency at position 2. Such an inductive effect would be expected to hinder

[15] Dale and Hudson, *J. Amer. Chem. Soc.*, 1930, **52**, 2534.
[16] Minsaas, *Rec. Trav. chim.*, 1937, **56**, 623.
[17] Dale, *J. Amer. Chem. Soc.*, 1924, **46**, 1048.
[18] Fischer, Bergmann, and Rabe, *Ber.*, 1920, **53**, 2362.
[19] Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013; Kenner and Murray, *J.*, 1949, S178.
[20] Winstein, Goodman, and Boschan, *J. Amer. Chem. Soc.*, 1950, **72**, 2311.

the elimination of the methanesulphonate anion. In support of this it is well known that the 2-hydroxyl group of methyl α-D-glucoside is more acidic than those at other positions, owing probably to the same effect.[21]

From a study of the nuclear magnetic resonance spectra of some aldopyranose acetates, Lemieux *et al.*[22] showed that the protons of acetoxy- and methoxy-substituents attached to a pyranose ring gave sharp absorption peaks, the chemical shifts being, in most cases, characteristic of steric environment. The signal from an axial acetoxy-group was observed at a lower field than that of the equatorial group. Also, the anomeric ring proton, $H_{(1)}$, gave rise to a characteristic low-field doublet, the splitting of which was dependent on the relative configurations of the ring protons at positions 1 and 2: if both $H_{(1)}$ and $H_{(2)}$ were axial the observed splitting was about 8 c.p.s., whilst if one or both was equatorial this was reduced to 3·5 c.p.s.

TABLE 2.

	τ-Values						
Compound	OAc *ax*	OAc *eq*	OMe *ax*	NAc *eq*	Me *eq*	$H_{(1)}$	$H_{(1)}$ Doublet splitting (c.p.s.)
XIV		7·91 7·93	6·58	8·10	8·81		
XV	7·82	7·92 7·96		8·09	8·79	3·78	3·7
VII		7·91 *		8·09	8·76	4·24	8·1
XVI	7·82 †		6·64	8·07	8·84		
XVII	7·84	7·94	6·61	8·08	8·80		
XVIII	7·81 7 84	7·91		8·06	8·78		

* Three coincident resonances. † Two coincident resonances.

This method unequivocally established the stereochemistry of the acetyl derivatives discussed above. The spectra are, in general, complex and full analysis has not been attempted since the stereochemistry of these acetates could be determined completely from the resonance peaks of the acetyl-protons and $H_{(1)}$. The position of these peaks and, where known, the splitting observed in the doublet due to $H_{(1)}$, are recorded in Table 2, together with those due to the acetamido-, methoxyl, and *C*-methyl groups. Only in those compounds containing a 1-acetoxy-group was the low-field doublet due to $H_{(1)}$ observed. The sample of tetra-acetylmycosamine (XVIII) was available in too small a quantity for resonances due to single protons to be seen clearly and so the $H_{(1)}$ doublet was not observed.

The spectrum of methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-L-glucoside (XIV) showed five resonances due to CH_3 groups, two of which were almost coincident (τ 7·91, 7·93) and resulted from acetoxy-groups, which were thus shown to be of identical steric disposition. The resonance resulting from the 5-methyl group was easily recognised since it was split into a doublet by coupling with $H_{(5)}$. The methoxyl and acetamido-resonances were recognised by their chemical shifts.

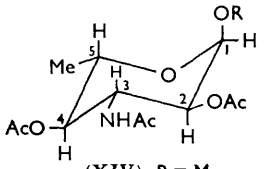
Replacement of the glycosidic methoxyl group by acetoxyl, as in (XV), introduced a third acetoxy-group and the spectrum of the α-tetra-acetyl derivative (XV) showed the presence of two almost identical acetoxyl groups (τ 7·92, 7·96) and a non-identical one at lower field (τ 7·82). The low-field signal can be ascribed to an axial 1-acetoxyl group, thus assigning the resonance positions of equatorial and axial acetoxy-groups and the stereochemistry of these two acetates. This assignment implies an *ax-eq*-arrangement of $H_{(1)}$ and $H_{(2)}$ in (XV) which is supported by the splitting observed in the $H_{(1)}$ doublet (3·7 c.p.s.). The spectrum of the β-tetra-acetyl derivative (VII) showed all acetoxy-groups to be equatorial. In this case the $H_{(1)}$, $H_{(2)}$ coupling produced a splitting of

[21] Wolfrom and Taraboulsi, *J. Amer. Chem. Soc.*, 1953, **75**, 5350; Dutton and Yates, *Canad. J. Chem.*, 1958, **36**, 550.

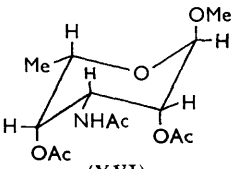
[22] Lemieux, Kullnig, Bernstein, and Schneider, *J. Amer. Chem. Soc.*, 1958, **80**, 6098.

8·1 c.p.s. in the $H_{(1)}$ doublet, in good agreement with that expected for an *ax-ax*-arrangement. These results are in accord with those of Lemieux *et al.*[22] and show without doubt that these derivatives (VII, XIV, XV) possess the *gluco*-configuration.

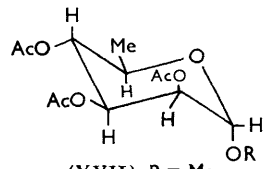
The spectrum of methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-L-taloside indicated that it existed exclusively in the 1C conformation (XVI) with both acetoxyl substituents axial. This result is interesting inasmuch as this conformation contains a 1,3-diaxial interaction between two acetoxyl groups which could be relieved by changing to an alternative conformation. It is not clear why this compound should prefer a seemingly less favourable conformation.



(XIV) R = Me
(XV) R = Ac



(XVI)



(XVII) R = Me
(XVIII) R = Ac

Finally, in Table 2 are included some spectral results for methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-D-mannoside (XVII) and 3-acetamido-1,2,4-tri-*O*-acetyl-3,6-dideoxy-α-D-mannose (XVIII). These derivatives were obtained from mycosamine (3-amino-3,6-dideoxy-D-mannose). The values agree with those for similar groups in the foregoing examples. The constancy of the τ-values of equatorial *C*-methyl, equatorial acetamido- and axial methoxyl groups suggests that these, as well as acetoxyl groups, may be characterised by proton resonance spectroscopy. Further work is required to confirm that these values are dependent upon the precise stereochemistry of the molecule.

Experimental

Evaporations were done *in vacuo*. Optical rotations were determined at 20°. Paper chromatography was by the descending method at room temperature on Whatman No. 1 filter paper with (i) butan-1-ol–ethanol–water (40 : 11 : 19 v/v) or (ii) butan-1-ol–pyridine–water (10 : 3 : 3 v/v) as mobile phase. Compounds were detected by either 1% w/v ninhydrin in butan-1-ol (amino-derivatives) or 3% w/v *p*-anisidine hydrochloride in butan-1-ol (reducing sugars). Molecular weights, where quoted, were determined by potentiometric titration, as were pK_a's.

Methyl 3-Amino-3,6-dideoxy-α-L-glucoside (V).—A stirred solution of methyl α-L-rhamnopyranoside [9] (25 g.) in water (250 ml.) was treated portionwise with sodium metaperiodate (60 g.), ice being added to keep the temperature at 20—30°. After 1 hr. sodium hydrogen carbonate (11·5 g.) was cautiously added and the solution poured into ethanol (750 ml.). The precipitated salts were filtered off and the filtrate was concentrated to a syrup which was extracted with ethanol (250 and 120 ml.). After being kept overnight in the refrigerator, the combined extracts were again filtered and treated with nitromethane (20 ml.), followed by a solution prepared from sodium (4 g.) and methanol (300 ml.). After 40 min. at room temperature the solution was neutralised by the addition of Amberlite 1R-120(H^+) resin (*ca.* 250 g.), then filtered and concentrated. The resulting syrup was extracted with ether (*ca.* 200 ml.), a small amount of insoluble material removed by filtration through Hyflo Supercel, and the extract evaporated to a golden-red syrup. This syrup was hydrogenated in methanol (200 ml.) with Raney nickel T4 catalyst [23] (*ca.* 10 g.) at an initial pressure of 3 atm. After *ca.* ½ hr. the reduction was complete. The catalyst was removed and washed with methanol, and the filtrate concentrated to a crystalline residue. Ethyl acetate (100 ml.) was added and the mixture heated under reflux for 5 min. Complete dissolution did not take place and, after being kept in the refrigerator overnight, the mixture was filtered. The slightly coloured crystals weighed 7·8 g. (31%) and had m. p. 175—176°. Recrystallisation from ethanol afforded pure *methyl 3-amino-3,6-dideoxy-α-L-glucoside*, m. p. 177—178°, $[\alpha]_D$ −145° (*c* 1·9 in H_2O), pK_a 8·35. It moved as a discrete spot on paper chromatograms, having R_F 0·54 (solvent i) (Found:

[23] Nishimura, *Bull. Chem. Soc. Japan*, 1959, **32**, 61.

C, 47·45; H, 8·45; N, 7·8%; *M*, 178. $C_7H_{15}NO_4$ requires C, 47·45; H, 8·45; N, 7·9%; *M*, 177).

Paper chromatography showed the mother-liquor to contain several ninhydrin-positive compounds. The following attempts to obtain a further crystalline isomer failed: (1) Acetylation with pyridine–acetic anhydride. (2) *N*-Acetylation with acetic anhydride in ethanol (see below). (3) Di-*N*-methylation with formic acid–formaldehyde.[4] (4) Reaction of the mixture of *N*-acetates with methanesulphonyl chloride in pyridine.

Methyl 2,4-*Di*-O-*acetyl*-3-*amino*-3,6-*dideoxy*-α-L-*glucoside Hydrochloride.*—The amino-glucoside (1 g.) in warm acetic acid (4 ml.) was treated with acetyl chloride (2 ml.), then heated under reflux until the product crystallised (*ca.* 1—2 min.). The mixture was then cooled, diluted with ether (15 ml.), and filtered. The *di-O-acetate* (1·64 g., 97%) had m. p. 238—241° (decomp.), $[\alpha]_D$ −127° (*c* 1·37; MeOH), pK_a 6·55. Recrystallised from methanol–ether, it had the same m. p. (Found: C, 44·2; H, 6·55; N, 4·7; Cl, 11·7%; *M*, 280. $C_{11}H_{20}ClNO_6$ requires C, 44·35; H, 6·75; N, 4·7; Cl, 11·95%; *M*, 298).

Methyl 3-*Acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-α-L-*glucoside.*—Methyl 3-amino-3,6-dideoxy-α-L-glucoside (10 g.) was treated with pyridine (50 ml.) and acetic anhydride (100 ml.). After a mildly exothermic reaction the mixture was kept at room temperature for 18 hr., then decomposed by ice. Evaporation to dryness afforded a crystalline residue. Recrystallisation from ethanol–ether–light petroleum (b. p. 40—60°) gave the *triacetyl derivative* as needles (13·8 g., 81%), m. p. 194—197°, $[\alpha]_D$ −128° (*c* 1·94 in $CHCl_3$) (Found: C, 51·75; H, 6·8; N, 4·5. $C_{13}H_{21}NO_7$ requires C, 51·45; H, 7·0; N, 4·6%).

Methyl 3-*Acetamido*-3,6-*dideoxy*-α-L-*glucoside* (VIII).—(1) Methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-L-glucoside (10·9 g.) was dissolved in methanol (100 ml.) and concentrated ammonia (*d* 0·88; 100 ml.) added. After storage at room temperature for 18 hr., the solution was evaporated. Recrystallisation of the residue from acetone and then from ethanol–ether gave *methyl* 3-*acetamido*-3,6-*dideoxy*-α-L-*glucoside* (6·68 g., 86%), m. p. 223—224°, $[\alpha]_D$ −145° (*c* 1·08 in H_2O) (Found: C, 49·0; H, 7·55; N, 6·0. $C_9H_{17}NO_5$ requires C, 49·3; H, 7·8; N, 6·4%).

(2) Methyl 3-amino-3,6-dideoxy-α-L-glucoside (5·8 g.) was dissolved in hot ethanol (65 ml.), then cooled to about 50°, and acetic anhydride (7 ml.) was added. After 5 sec. the solution gave a negative ninhydrin test, indicating that *N*-acetylation was complete. Addition of ether (50 ml.) followed by light petroleum (b. p. 40—60°) (125 ml.) caused crystallisation of the *N*-acetate (6·2 g., 86%), m. p. 223—225°, $[\alpha]_D$ −144° (*c* 2·75 in H_2O), identical with the above product (mixed m. p. and infrared spectra).

Methyl 3-*Acetamido*-3,6-*dideoxy*-2,4-*di*-O-*methanesulphonyl*-α-L-*glucoside* (IX).—A suspension of methyl 3-acetamido-3,6-dideoxy-α-L-glucoside (6·15 g.) in pyridine (30 ml.) was treated with methanesulphonyl chloride (7 ml.). The resulting solution was cooled initially in ice–water, then kept at −10° overnight. Addition of a little ice–water decomposed the excess of acid chloride, and subsequent concentration yielded a syrup which crystallised on addition of water. Recrystallisation from ethanol gave the *di*-O-*methanesulphonate* as needles (7·4 g., 71%), m. p. 164°, $[\alpha]_D$ −100° (*c* 2·03 in MeOH) (Found: C, 35·2; H, 5·5; N, 3·4; S, 17·1. $C_{11}H_{21}NO_9S_2$ requires C, 35·2; H, 5·15; N, 3·7; S, 17·05%).

When a solution of the disulphonate in water was boiled a rapid decrease in pH took place owing to released methanesulphonic acid. Prolonged boiling caused complete decomposition.

Treatment of Methyl 3-*Acetamido*-3,6-*dideoxy*-2,4-*di*-O-*methanesulphonyl*-α-L-*glucoside with Sodium Acetate in* 95% 2-*Methoxyethanol.*—(1) The disulphonate (2 g.) was heated under reflux with 95% 2-methoxyethanol (40 ml.) containing sodium acetate (4 g.) for 2½ hr. The mixture was then concentrated, the residue extracted with acetone (2 × 100 ml.), and the combined extracts were evaporated to a crystalline solid. Recrystallisation from ethanol–ether–light petroleum (b. p. 40—60°) gave *methyl* 3-*acetamido*-3,6-*dideoxy*-2-O-*methanesulphonyl*-α-L-*galactoside* (1·22 g., 77%), m. p. 191—192°, $[\alpha]_D$ −140° (*c* 1·27 in MeOH). The m. p. of this compound varied with the rate of heating; at a fast rate it was *ca.* 195—196° (Found: C, 40·7; H, 6·5; N, 4·8; S, 10·7. $C_{10}H_{19}NO_7S$ requires C, 40·4; H, 6·45; N, 4·7; S, 10·8%).

(2) The disulphonate (3 g.) was heated under reflux with 95% 2-methoxyethanol (60 ml.) containing sodium acetate (6 g.) for 44 hr. The mixture was then evaporated and the residue extracted with acetone in a Soxhlet apparatus for 4 hr. Concentration of the extract to a small volume afforded *methyl* 3-*acetamido*-3,6-*dideoxy*-α-L-*taloside* (1·05 g., 60%). Recrystallisation from ethanol and then from ethanol–light petroleum (b. p. 40—60°) gave 0·85 g. of the pure

glycoside, m. p. 195—196°, $[\alpha]_D$ −104° (*c* 3·16 in H_2O) (Found: C, 49·5; H, 8·0; N, 6·2. $C_9H_{17}NO_5$ requires C, 49·3; H, 7·8; N, 6·4%).

When the time of the reaction was decreased to 18 hr. a 38% yield of the monosulphonate (XI) was obtained together with a 32% yield of the taloside (XII)

Methyl 3-*Acetamido*-3,6-*dideoxy*-2,4-*di*-O-*methanesulphonyl*-α-L-*galactoside*.—A mixture of methyl 3-acetamido-3,6-dideoxy-2-*O*-methanesulphonyl-α-L-galactoside (0·13 g.), pyridine (2 ml.), and methanesulphonyl chloride (0·06 ml.) was kept at −10° for 6 hr. Dilution with water (*ca.* 15 ml.) and concentration gave crystals of the *disulphonate* (82 mg., 50%), $[\alpha]_D$ −124° (*c* 0·55 in $CHCl_3$). Recrystallised from chloroform–light petroleum (b. p. 40—60°) this had m. p. 199° (decomp.) (Found: C, 35·6; H, 5·2; N, 3·7. $C_{11}H_{21}NO_9S_2$ requires C, 35·2; H, 5·15; N, 3·4%).

Methyl 3-*Acetamido*-2,4-*di*-O-*acetyl*-3,6-*dideoxy*-α-L-*taloside*.—Methyl 3-acetamido-3,6-dideoxy-α-L-taloside (134 mg.) was acetylated as described for the glucoside. The *triacetyl derivative*, recrystallised from benzene–light petroleum (b. p. 40—60°), had $[\alpha]_D$ −72° (*c* 4·3 in $CHCl_3$) (151 mg., 80%). Recrystallised from acetone–ether–light petroleum (b. p. 40—60°) it had m. p. 166—167° (Found: C, 51·6; H, 7·0; N, 4·6. $C_{13}H_{21}NO_7$ requires C, 51·45; H, 7·0; N, 4·6%).

3-*Amino*-3,6-*dideoxy*-α-L-*talose hydrochloride* (XIII).—Methyl 3-acetamido-3,6-dideoxy-α-L-taloside (0·32 g.) was heated at 95—100° with N-hydrochloric acid for 12 hr., and the solution then concentrated. The crystalline residue was triturated with ethanol and filtered. The product, 3-*amino*-3,6-*dideoxy*-α-L-*talose hydrochloride* (90 mg., 32%), decomposed without melting at 168—170° and had $[\alpha]_D$ −41° (1½ min.) ⟶ −30° (3 min.) ⟶ −25° (1½ hr.) ⟶ −26° (24 hr.) (*c* 1·07 in H_2O). Addition of ether to the mother-liquors precipitated an amorphous material which rapidly crystallised. Filtration afforded a further 93 mg. (33%) of the sugar, which when recrystallised from methanol–acetone decomposed at 170°. It had pK_a 8·25 (Found: C, 36·2; H, 7·05; N, 6·9%; *M*, 198. $C_6H_{14}ClNO_4$ requires C, 36·15; H, 7·05; N, 7·0%; *M*, 199·5).

3-*Amino*-3,6-*dideoxy*-L-*glucose Hydrochloride* (VI).—Methyl 3-amino-3,6-dideoxy-α-L-glucoside (1 g.) was heated in 4N-hydrochloric acid for 3¼ hr., then concentrated to a syrup, which was repeatedly dissolved in water and re-concentrated to remove traces of acid. The syrup was finally dried *in vacuo* over phosphoric oxide and sodium hydroxide. The *amino-sugar* (1·05 g., 95%) (Found: C, 35·6; H, 7·2; N, 7·3. $C_6H_{14}ClNO_4$ requires C, 36·1; H, 7·1; N, 7·05%) was a hygroscopic syrup, $[\alpha]_D$ −46° (*c* 5·25 in H_2O). On paper chromatograms it was detected with both ninhydrin and *p*-anisidine sprays, R_F 0·16 (solvent i), R_F 0·14 (solvent ii). A small amount of streaking was observed on the chromatograms.

The amino-sugar appeared to be unstable since after a month it had darkened, a considerable amount of streaking was observed on paper chromatograms, and $[\alpha]_D$ had decreased to −57° (*c* 2·8 in H_2O).

Acetylation of 3-*Amino*-3,6-*dideoxy*-D-*glucose Hydrochloride*.—The syrupy amino-sugar (1·2 g.) was dissolved in pyridine (15 ml.) and acetic anhydride (15 ml.) and left at room temperature for 2 hr. Concentration afforded crystals. Recrystallisation from ethanol gave 3-*acetamido*-1,2,4-*tri*-O-*acetyl*-3,6-*dideoxy*-β-L-*glucose* (0·74 g., 31%), m. p. 228—229°, $[\alpha]_D$ −22·5° (*c* 1·2 in $CHCl_3$). Recrystallised from ethanol–ether it had m. p. 232—234° (Found: C, 50·8; H, 6·4; N, 4·2. $C_{14}H_{21}NO_8$ requires C, 50·7; H, 6·55; N, 4·2%).

The ethanolic mother-liquors were concentrated to a syrup, which crystallised on the addition of a little water. Recrystallisation from water afforded 3-*acetamido*-1,2,4-*tri*-O-*acetyl*-3,6-*dideoxy*-α-L-*glucose* (0·23 g., 10%), which, after recrystallisation from ethanol–ether–light petroleum (b. p. 40—60°), had m. p. 194—195°, $[\alpha]_D$ −111° (*c* 1·1 in $CHCl_3$) (Found: C, 50·6; H, 6·4; N, 4·05. $C_{14}H_{21}NO_8$ requires C, 50·7; H, 6·55; N, 4·2%).

Proton Magnetic Resonance Spectra.—Spectra were obtained at 60 mc./sec. on a Varian V4300 spectrometer for, when possible, ~5% solutions in chloroform. Tetramethylsilane was used as an internal reference and calibration was by the side-band technique.

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Department of Organic Chemistry, The University, Bristol.
Basic Physics Division, National Physical Laboratory,
Teddington, Middlesex. [*Received, December* 21*st*, 1961.]