1009. *Nitrogen-containing Carbohydrate Derivatives. Part IV.* Some Azido- and Epimino-sugars.*

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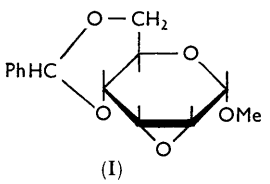
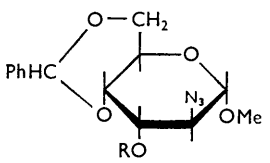
The azide ion has been used to open the epoxide rings in methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside and -mannoside. The resulting azido-glycosides were readily reduced to the corresponding amino-compounds. Some replacements of secondary sulphonate esters by azide ion are discussed. The synthesis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannoside (VII) and -alloside (X) from the appropriate azido-sulphonate derivatives is discussed.

When this work started there were few well-characterised azido-sugar derivatives other than the aldosyl azides.[1] An azido-sugar may be looked on as a blocked amino-sugar from which the free amino-sugar could be obtained by mild reduction. Possible methods for introducing azido-groups into sugars were therefore explored. The azide ion is a powerful nucleophile and routes utilising this property have been used.

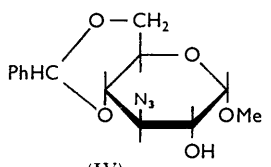


(I)



(II: R = H)

(III: R = Me·SO2)



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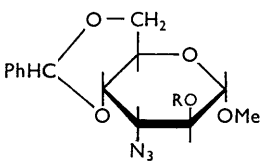
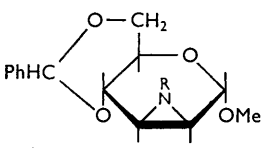


(V: R = H)

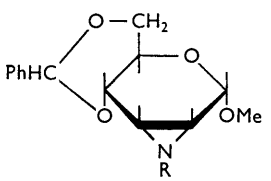
(VI: R = Me·SO2)



(VII: R = H)

(VIII: R = Ac)

(IX: R = Bz)



(X: R = H)

(XI: R = Ac)

(XII: R = Bz)

A widely used method of introducing a nucleophile into a sugar is by opening of an epoxide ring;[2] simple aliphatic azido-alcohols have been made by this method.[3] Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (I) in boiling aqueous 2-methoxyethanol with 5 mol. of sodium azide gave methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside (II) (35%) and methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (IV) (3%). Considerable decomposition occurred during the reaction, presumably caused by the alkali liberated. Addition of ammonium chloride, which removed the hydroxyl ions as they were formed, increased the yield of the 2-azidoaltroside (II) to 75% and of the 3-azidoglucoside (IV) to 5%. The two products were readily separated by chromatography on alumina. The ratio of products formed is in agreement with the ratio of diaxial to diequatorial products obtained from this epoxide (I) and other nucleophiles, *i.e.*, there is predominant diaxial opening.[2] The two azido-sugars were characterised by their ready hydrogenation (Adams catalyst) to the known amino-sugars, both of which had been

* Part III, *J.*, 1963, 3658.

[1] Micheel and Klemer, *Adv. Carbohydrate Chem.*, 1961, **16**, 85.
[2] Newth, *Quart. Rev.*, 1959, **13**, 30.
[3] VanderWerf, Heisler, and McEwen, *J. Amer. Chem. Soc.*, 1954, **76**, 1231.

synthesised by other routes.[4,5] Acid hydrolysis of the benzylidene group in the 2-azido-altroside (II) did not affect the azide group and gave methyl 2-azido-2-deoxy-α-D-altroside.

Reaction of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside with sodium azide in the same way gave only methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-altroside (V) (69%). No trace of the expected methyl 2-azidoglucoside could be found on chromatography of the crude product, though, surprisingly, methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altroside (1%) was isolated. The 3-azidoaltroside (V) was readily hydrogenated to the known [5] 3-amino-compound. Again the reaction with azide yielded the diaxial product.

Hitherto, the method of synthesising the 2- and 3-aminoaltroside derivatives mentioned above has been by the ammonolysis of epoxides in sealed tubes for long times.[4,6] Our two-step reaction is easier to carry out and is probably of general use in the synthesis of other epoxide-derived amino-sugars. The similar synthesis of steroid azido-alcohols has recently been described.[7]

The second possible method of introducing an azido-group into a sugar would be by nucleophilic displacement of a sulphonate ester. Fission of secondary carbohydrate sulphonates by hydrazine is well established: [8,9] for example, Wolfrom and his co-workers have thus synthesised 2-amino-2-deoxy-D- and -L-ribose. The products of such displacements, which need anhydrous hydrazine, are the unstable hydrazino-derivatives which must be immediately hydrogenated to the amino-sugars. Direct ammonolysis of secondary sulphonates has been used similarly,[10] but drastic conditions are necessary. Both displacements occur with inversion.[9]

In view of the disadvantages of the above methods, the use of azide ion in similar reactions has been explored. Carbohydrate primary sulphonates have been replaced by azide,[11] and so, as recently described,[12] have secondary steroid sulphonates. Treatment of 1,2:5,6-di-*O*-isopropylidene-D-glucose 3-toluene-*p*-sulphonate or methyl 4,6-*O*-benzylidene-α-D-glucoside 2,3-ditoluene-*p*-sulphonate with azide ion in *NN*-dimethylformamide gave only unchanged starting compound. The unexpected lack of attack by azide ion on the former compound has been recently discussed.[13] On the assumption that an axial sulphonate group would be displaced more readily because of ease of approach of the nucleophile and removal of steric compression in the product, reaction with methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate was tried. This yielded methyl 2,3-diazido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannoside,[14] which will be discussed in a later publication.

Methyl 4,6-*O*-benzylidene-α-D-glucoside 2-toluene-*p*-sulphonate with sodium azide in boiling 2-methoxyethanol gave methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-altroside (V). This is analogous to the ammonolysis of the same glucoside which gave the corresponding 3-aminoaltroside derivative.[15] Peat and Wiggins [16] showed that this reaction consisted of two stages, the first being the formation of the 2,3-anhydro-mannoside, which is then

[4] Myers, Robertson, and Tetlow, *Nature*, 1938, **142**, 1076.
[5] Guthrie and Johnson, *J.*, 1961, 4166.
[6] Myers and Robertson, *J. Amer. Chem. Soc.*, 1943, **65**, 8.
[7] Ponsold, *Chem. Ber.*, 1962, **95**, 1727.
[8] Freudenberg and Brauns, *Ber.*, 1922, **55**, 3233.
[9] Lemieux and Chu, *J. Amer. Chem. Soc.*, 1958, **80**, 4745; Wolfrom, Shafizadeh, and Armstrong, *ibid.*, 1958, **80**, 4885; Wolfrom, Shafizadeh, Armstrong, and Shen, *ibid.*, 1959, **81**, 3716; Kuhn and Baschang, *Annalen*, 1959, **628**, 193; Roth and Pigman, *J. Org. Chem.*, 1961, **26**, 2455; Coxon and Hough, *J.*, 1961, 1643.
[10] Freudenberg, Burkhart, and Brauns, *Ber.*, 1926, **59**, 714.
[11] Cramer, Otterbach, and Springmann, *Chem. Ber.*, 1959, **92**, 384.
[12] Henbest and Jackson, *J.*, 1962, 954.
[13] Wolfrom, Bernsmann, and Horton, *J. Org. Chem.*, 1962, **27**, 4505.
[14] Guthrie and Murphy, *Chem. and Ind.*, 1962, 1473.
[15] Haworth, Hirst, and Bodycote, *J.*, 1934, 151.
[16] Peat and Wiggins, *J.*, 1938, 1810.

opened by the reagent. A similar sequence probably occurs in the reaction of steroid α-diol monosulphonates with azide.[7]

Since this work was started Baker and his co-workers [17] have reported the displacement of the axial methanesulphonate group from methyl 2,3,6-tri-*O*-benzoyl-α-D-galactoside 4-methanesulphonate with sodium azide in boiling *NN*-dimethylformamide to give the corresponding 4-azido-4-deoxy-D-glucose derivative. Jeanloz and Rapin [18] treated 1,6-anhydro-D-glucose 2,3,4-tritoluene-*p*-sulphonate with sodium azide under the same conditions, obtaining the 2,4-diazido-2,4-dideoxy-D-glucose derivative. In a report of concurrent work, Wolfrom and his co-workers have also discussed the fission of sugar sulphonates by azide and hydrazine.[13]

One group of great potential use in the synthesis of amino-sugar derivatives is the epimino-group; this should lead to ready synthesis of, for example, diamino-sugars, aminomercapto-sugars, and deoxy-sugars bearing amino-groups; epimino-sugars could possibly have a cytostatic action. Christensen and Goodman [19] have described in a preliminary communication the synthesis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-alloside (X) *via* ammonolysis of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside. A more convenient synthesis has now been developed.

Alkylaziridines have been prepared from *trans*-amino-alcohols through the sulphates.[20] Alkaline hydrolysis of the α-amino-sulphate ester gives the aziridine, with inversion at the oxygen-bearing carbon atom. This method should be readily applicable to sugar derivatives containing a *trans*-α-amino-hydroxy-system, through the sulphonate ester, since the latter group will leave in the same way as the sulphate group. The difficulty of this method lies in the synthesis of the *trans*-α-amino-sulphonate since amino-groups are generally more reactive than, or as reactive as, hydroxyl groups towards acylating reagents. This has been overcome by sulphonylation of the azidoaltrosides (II) and (V) and reduction of the azido-group to amino *in situ*. Treatment of methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-methanesulphonate (III) with hydrazine hydrate and Raney nickel in methanol gave crystalline methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannoside (VII). The *N*-acetyl and *N*-benzoyl derivatives were readily prepared by standard methods. All three compounds were identical with those prepared by Dr. L. Hough and his co-workers by a different route during concurrent work.[21] Reaction of the corresponding 3-azido-2-*O*-mesyl compound (VI) under the same conditions gave methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-alloside (X), characterised as above; again all compounds were identical with those prepared by Buss *et al.*[21]

Hydrolysis of the *N*-acetyl- and *N*-benzoyl-epiminomannosides with hot N-aqueous potassium hydroxide to the parent aziridine showed that the latter ring is not easily opened by alkali. The *N*-acetylepimino-alloside was also easily hydrolysed with alkali.

Two values were found for the specific rotation of the *manno*-epimine (VII). Early preparations had $[\alpha]_D$ +23° (in $CHCl_3$) but later syntheses led to products which consistently had $[\alpha]_D$ +105°; it was shown that this was not a concentration effect. Unfortunately only a small amount of the low-rotating isomer was made and no physical measurement other than the melting point was measured; this was the same for both compounds. A similar behaviour has been observed by Buss *et al.*[21] who prepared one sample of $[\alpha]_D$ +16·5°, but all other preparations with $[\alpha]_D$ +105°. Attempts in our laboratories to isolate the low-rotating form a second time failed; these included repeated preparations, recrystallisation from various solvents, and alkaline hydrolysis of the *N*-acetyl derivative (VIII). Although we have isolated only one form of the *allo*-epimine (X), $[\alpha]_D$ +150° (in $CHCl_3$), the Bristol group originally isolated a form with $[\alpha]_D$ +52°, not obtainable from

[17] Reist, Spencer, Baker, and Goodman, *Chem. and Ind.*, 1962, 1794.
[18] Jeanloz and Rapin, Amer. Chem. Soc. Meeting, Sept. 1962, Abs. 4-D.
[19] Christensen and Goodman, *J. Amer. Chem. Soc.*, 1960, **82**, 4738.
[20] Dickey, Ficket, and Lucas, *J. Amer. Chem. Soc.*, 1952, **74**, 994.
[21] Buss, Hough, and Richardson, *J.*, following paper.

later preparations. No explanation is offered for this anomalous behaviour. Goodman and Christensen [19] record two melting points, but no $[\alpha]_D$'s for the *allo*-epimine (X). The two forms of the *manno*-aziridine led to the same *N*-acetyl derivative.

The aziridino-rings of both the *allo*- and *manno*-isomers have been opened with sodium azide in 2-methoxyethanol, to give derivatives of methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-altroside; this work will be described in a future paper.

One unsuccessful attempt at the synthesis of the *manno*-epimine was catalytic hydrogenation of methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate, followed by treatment with sodium methoxide. The first step went as expected to give syrupy methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate, characterised as the known,[22] crystalline 2-acetamido-derivative. Reaction of the amino-compound with sodium methoxide gave a substance (A) (56%) which contained a C_3H_6 unit more than the expected imine (VII). In only one experiment was evidence obtained for formation of the expected imine. A similar unexpected product (B) (72%) was isolated in trying to make the *allo*-epimine (X). Infrared spectra and analysis suggest that substances (A) and (B) are isomeric, presumably with respect to the orientation at positions 2 and 3; no structures are yet proposed for these molecules.

All the azides described above were readily characterised by the strong infrared absorption at about 2120 $cm.^{-1}$, in most cases accompanied by weaker bands at about 2180 and 2200 $cm.^{-1}$.

Experimental

Chromatography was on alumina, type H, 100—200 mesh, supplied by Peter Spence Ltd. Rotations were measured for chloroform solutions unless otherwise stated. Where possible, compounds were identified by mixed m. p. and by infrared spectroscopy; new compounds had infrared spectra consistent with the assigned structures. Adams catalyst was prepared by the method of Adams and Shriner,[23] and Raney nickel by the method of Dominguez *et al.*[24]

Fission by Azide.—(*a*) *Methyl* 2,3-*anhydro*-4,6-O-*benzylidene*-α-D-*alloside*. Sodium azide (3·45 g.) and methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (3·45 g.) in 2-methoxyethanol (40 ml.) and water (5 ml.) were boiled under reflux for 4 hr., then cooled and poured into ice–water (200 ml.). This mixture was extracted with chloroform, and the extract was dried (Na_2SO_4) and evaporated to a thick syrup, which was chromatographed. Elution with benzene followed by recrystallisation from ethanol gave *methyl* 2-*azido*-4,6-O-*benzylidene*-2-*deoxy*-α-D-*altroside* (II) (35%), m. p. 79—80°, $[\alpha]_D^{18}$ +65·0° (*c* 1·0) (Found: C, 54·8; H, 5·4; N, 13·7. $C_{14}H_{17}N_3O_5$ requires C, 54·7; H, 5·6; N, 13·7%). Elution with benzene–chloroform (1 : 1), followed by recrystallisation from ethanol, gave *methyl* 3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside* (IV) (3%), m. p. 161—162°, $[\alpha]_D^{18}$ +143° (*c* 1·0) (Found: C, 54·8; H, 5·5; N, 13·5%).

Repetition of the experiment, but with addition of 2 mol. of ammonium chloride gave a chloroform extract which on evaporation gave a solid product. Recrystallisation from ethanol gave methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside (II) (72%), m. p. 79—80°. Chromatography of the mother-liquor as above gave more 2-azidoaltroside (II) (3%), m. p. 79—80°, and then methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (IV) (5%), m. p. 161—162°.

(*b*) *Methyl* 2,3-*anhydro*-4,6-O-*benzylidene*-α-D-*mannoside*. The anhydromannoside (30 g.), sodium azide (30 g.), and ammonium chloride (12 g.) in 2-methoxyethanol (300 ml.) and water (80 ml.) were boiled under reflux for 4 hr. The solution was evaporated and the residue extracted with chloroform. Evaporation gave a semi-crystalline mass, which was extracted with a little boiling ethanol. Cooling gave large transparent cubes (13·9 g.), m. p. 135—136°. The mother-liquor was evaporated to a brown syrup which was chromatographed. Elution with chloroform followed by recrystallisation of the product from ethanol gave a further crop (9·9 g.), m. p. 135—136° (total yield 23·8 g., 69%). The combined crops were recrystallised from ethanol to give *methyl* 3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altroside* (V), m. p. 135—136°, $[\alpha]_D^{18}$ +37·9° (*c* 1·00) (Found: C, 54·4; H, 5·5. $C_{14}H_{17}N_3O_5$ requires C, 54·7; H, 5·6%).

[22] Foster, Vardheim, and Stacey, *Acta Chem. Scand.*, 1958, **12**, 1605.
[23] Adams and Shiner, *J. Amer. Chem. Soc.*, 1923, **45**, 2171.
[24] Dominguez, Lopez, and Franco, *J. Org. Chem.*, 1961, **26**, 1625.

Elution with ethanol gave methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altroside (1%), m. p. 185—186° (lit.,[6] m. p. 188°).

(*c*) *Methyl* 4,6-O-*benzylidene*-α-D-*glucoside* 2-*toluene*-p-*sulphonate*. The glucoside 2-toluene-*p*-sulphonate (10 g.) in 2-methoxyethanol (100 ml.) was added to sodium azide (10 g.) in water (20 ml.), and the solution boiled under reflux for 24 hr. Hot water was added to turbidity, followed by cooling, to give unchanged starting material (36%), m. p. 148—149°. The mother-liquor was diluted with cold water (200 ml.) and then extracted with chloroform. The extract was washed thoroughly with water and dried (Na_2SO_4). Evaporation gave a syrup which on crystallisation from ethanol gave methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-altroside (V) (17%), m. p. 135—136°. Nothing further could be isolated from the mother-liquors.

(*d*) 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucose* 3-*toluene*-p-*sulphonate*. The 3-toluene-*p*-sulphonate (6 g.) and sodium azide (6 g.) in *NN*-dimethylformamide (100 ml.) and water (20 ml.) were boiled under reflux for 48 hr. The solution was then saturated by addition of hot water. Cooling gave unchanged starting material (90%), m. p. 119—120°.

(*e*) *Methyl* 4,6-O-*benzylidene*-α-D-*glucoside* 2,3-*ditoluene*-p-*sulphonate*. The glucoside di-toluene-*p*-sulphonate (10 g.), in 2-methoxyethanol (100 ml.), and sodium azide (10 g.) in water (5 ml.) were mixed with *NN*-dimethylformamide (20 ml.) and boiled under reflux for 60 hr. The mixture was poured into cold water, and the white syrupy precipitate was collected and washed with water. Crystallisation from ethanol–acetone (1 : 1) gave starting material (87%), m. p. 153—154°. No other substance could be isolated from the mother-liquors.

Reactions of Methyl 2-*Azido*-4,6-O-*benzylidene*-2-*deoxy*-α-D-*altroside*.—(*a*) *Hydrolysis*. The 2-azidoaltroside (II) (4 g.) in 60% acetic acid (50 ml.) was refluxed until all the solid had dissolved (2 hr.). The acetic acid and benzaldehyde were removed by co-distillation with water *in vacuo*, and the solution was then evaporated to give a white solid (3·42 g.). Two recrystallisations from ethanol gave *methyl* 2-*azido*-2-*deoxy*-α-D-*altroside* (40%), m. p. 140—141°, $[\alpha]_D^{20}$ +63·8° (*c* 1·05 in MeOH) (Found: C, 38·5; H, 6·2. $C_7H_{13}N_3O_5$ requires C, 38·4; H, 6·0%).

(*b*) *Methanesulphonylation*. The 2-azidoaltroside (II) (2·5 g.) and methanesulphonyl chloride (1·2 ml.) in pyridine (8 ml.) were mixed at 0° and then kept overnight at room temperature. After hydrolysis of the excess of methanesulphonyl chloride, the solution was poured into ice–water. This mixture was extracted with chloroform, and the extract washed with cold dilute hydrochloric acid and cold water and then dried (Na_2SO_4). Evaporation *in vacuo* gave a yellow glass (3·2 g.). Crystallisation and then recrystallisation from ethanol gave white plates of *methyl* 2-*azido*-4,6-O-*benzylidene*-2-*deoxy*-α-D-*altroside* 3-*methanesulphonate* (III) (1·8 g., 54%), m. p. 152—153°, $[\alpha]_D^{20}$ +39·0° (*c* 1·0) (Found: C, 47·2; H, 5·0. $C_{15}H_{19}N_3O_7S$ requires C, 46·8; H, 5·0%).

(*c*) *Toluene*-p-*sulphonylation*. The 2-azidoaltroside (10 g.) in pyridine (50 ml.) containing toluene-*p*-sulphonyl chloride (20 g.) was left at room temperature for 4 days. After hydrolysis of the excess of toluene-*p*-sulphonyl chloride with a little water the solution was poured into ice–water (200 ml.); the solid product was washed with water and dried at 65°. Recrystallisation from ethanol–acetone (1 : 1) gave *methyl* 2-*azido*-4,6-O-*benzylidene*-2-*deoxy*-α-D-*altroside* 3-*toluene*-p-*sulphonate* (15·0 g.), m. p. 189—190° (decomp.), $[\alpha]_D^{20}$ +56·2° (*c* 1·0) (Found: C, 55·0; H, 4·9. $C_{21}H_{23}N_3O_7S$ requires C, 54·7; H, 5·0%).

(*d*) *Hydrogenation*. The 2-azidoaltroside (0·21 g.) in ethanol (50 ml.) was hydrogenated at 1 atm./30° for 20 min. in the presence of Adams catalyst. There was no net uptake of gas. After removal of the catalyst, the ethanol was evaporated to give a white solid (0·19 g.), m. p. *ca.* 163°. Recrystallisation from ethanol gave methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altroside, m. p. 167—168°, $[\alpha]_D^{18}$ +105° (*c* 1·0) {lit.,[4] m. p. 168°, $[\alpha]_D^{18}$ +104·7° (*c* 1·0)}.

Reactions of Methyl 3-*Azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altroside*.—(*a*) *Hydrogenation*. The 3-azidoaltroside (0·5 g.) in methanol (50 ml.) was hydrogenated at 1 atm. and at room temperature over Adams catalyst (0·1 g.) for 15 hr. The catalyst was removed and the solvent evaporated, to give white crystals (0·52 g.). Two recrystallisations from ethanol gave methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altroside (0·36 g.), m. p. 186—187° (lit.,[6] m. p. 188°).

(*b*) *Acetylation*. The 3-azidoaltroside (5 g.) in pyridine (50 ml.) was treated with acetic anhydride (3 g.) and kept at room temperature for 30 hr. The solution was poured into ice–water (500 ml.), and the precipitate twice recrystallised from ethanol to give *methyl* 3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altroside* 2-*acetate* (4·6 g.), m. p. 122—123°, $[\alpha]_D^{20}$ +20·8° (*c* 1·2) (Found: C, 54·9; H, 5·5. $C_{16}H_{19}N_3O_6$ requires C, 55·0; H, 5·5%).

(*c*) *Methanesulphonylation*. This was carried out as described above for the corresponding

2-azido-derivative. The solid product, on recrystallisation from methanol, gave *methyl* 3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altroside* 2-*methanesulphonate* (VI) (79%), m. p. 130—131°, $[\alpha]_D^{20}$ +9·3° (*c* 1·12) (Found: C, 46·5; H, 4·7. $C_{15}H_{19}N_3O_7S$ requires C, 46·8; H, 5·0%).

(*d*) *Toluene*-p-*sulphonylation*. The 3-azidoaltroside was treated with toluene-*p*-sulphonyl chloride as described for the 2-azido-derivative. The product, on recrystallisation from methanol, gave *methyl* 3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altroside* 2-*toluene*-p-*sulphonate* (96%), m. p. 117—118°, $[\alpha]_D^{18}$ +26·2° (*c* 1·03) (Found: C, 55·1; H, 4·9. $C_{21}H_{23}N_3O_7S$ requires C, 54·7; H, 5·0%).

Reduction of Methyl 3-*Azido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucoside*.—The 3-azidoglucoside (0·2 g.) was hydrogenated as described for the 2-azidoaltroside derivative. The syrupy product was acetylated by pyridine–acetic anhydride to give a white solid (0·13 g.). Recrystallisation from ethanol gave methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside 2-acetate, m. p. 276—278° (lit.,[5] m. p. 275—276°).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*mannoside* (VII).—Methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-methanesulphonate (II) (15 g.) in methanol was treated with hydrazine hydrate (99—100%) (15 g.). Raney nickel (*ca.* 1 g.) was added and the mixture boiled under reflux until decomposition of the hydrazine was complete (~2·5 hr.). Filtration and evaporation gave a white solid, m. p. 110—116°. Recrystallisation from aqueous methanol gave *methyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*mannoside* (VII) (8·5 g., 83%), m. p. 145—146°, $[\alpha]_D^{20}$ +105° (*c* 1) (Found: C, 64·1; H, 6·5. $C_{14}H_{17}NO_4$ requires C, 63·9; H, 6·5; N, 5·3%). Earlier preparations had $[\alpha]_D$ +22·8° (*c* 1·14), m. p. 145—146° (Found: C, 63·8; H, 6·6; N, 5·4%). Buss *et al.*[21] report m. p. 145·5—146·5°, $[\alpha]_D$ +16·5°, for an early sample, though later work gave only samples of $[\alpha]_D$ +105°.

Treatment of the epiminomannoside (VII) with acetic anhydride–pyridine and working up in the usual way gave, after recrystallisation from ethanol, *methyl* 2,3-*acetylepimino*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-*mannoside* (VIII) (85%), m. p. 205—206° (decomp.), $[\alpha]_D^{18}$ +49·3° (*c* 0·69) (Found: C, 62·8; H, 6·3; N, 4·6. $C_{16}H_{19}NO_5$ requires C, 62·9; H, 6·3; N, 4·6%). The same product was obtained from each form of the epiminomannoside. Buss *et al.*[21] report m. p. 211·5—212°, $[\alpha]_D$ +45·5°.

Hydrolysis of the *N*-acetylepiminomannoside (VIII) in boiling N-aqueous potassium hydroxide for 1 hr. gave after cooling, the epiminomannoside (VII) (96%), m. p. 145—146°, $[\alpha]_D$ +105°.

Reaction of the epiminomannoside (VII) with benzoyl chloride–pyridine in the usual way gave, after recrystallisation from ethanol, *methyl* 2,3-*benzoylepimino*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-*mannoside* (IX) (70%), m. p. 165—166°, $[\alpha]_D$ +3·6° (*c* 0·87) (Found: C, 68·8; H, 5·8. $C_{21}H_{21}NO_5$ requires C, 68·7; H, 5·8%). Buss *et al.*[21] report m. p. 166—168°, $[\alpha]_D$ +1·5°.

Hydrolysis of the *N*-benzoylepimine (IX) in boiling aqueous N-potassium hydroxide for 20 hr. gave, on cooling, the epiminomannoside (VII) (80%), m. p. 145—146°.

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*alloside* (X).—Methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-altroside 2-methanesulphonate (VI) (25 g.) in boiling methanol (250 ml.) was treated with hydrazine hydrate (99—100%) (20 g.). Raney nickel (*ca.* 1 g.) was added and the mixture was boiled under reflux until the hydrazine had all decomposed (3 hr.). Filtration and evaporation gave a white solid, m. p. 147—150°. Recrystallisation from aqueous methanol gave methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-alloside (X) (48%), m. p. 152—153°, $[\alpha]_D^{20}$ +150° (*c* 0·8) (Found: C, 64·0; H, 6·3; N, 5·5. Calc. for $C_{14}H_{17}NO_4$: C, 63·9; H, 6·5; N, 5·3%). Christensen and Goodman[19] report m. p. 153—154° and 143—145°, but no $[\alpha]_D$'s. Buss *et al.*[21] report m. p. 151—154°, $[\alpha]_D$ +52° for early preparations, but $[\alpha]_D$ +143—147° for later ones.

Repetition of the above experiment, but with the corresponding 2-toluene-*p*-sulphonate, gave the epiminoalloside (X) (66%), m. p. 152—153°. Treatment of the aqueous-methanolic recrystallisation mother-liquor with acetic anhydride gave a precipitate which yielded, after three recrystallisations from ethanol, the *N*-acetylepiminoalloside (XI) (see below) (30%), m. p. 187—188°. The formation of this aziridine is therefore essentially quantitative.

Acetylation of the epiminoalloside (X) with acetic anhydride in pyridine or in ethanol, gave, after the usual working up and recrystallisation of the product from ethanol, *methyl* 2,3-*acetylepimino*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-*alloside* (XI) (82%), m. p. 187—188°, $[\alpha]_D$ +149° (*c* 0·86) (Found: C, 63·1; H, 6·3. $C_{16}H_{19}NO_5$ requires C, 62·9; H, 6·3%). Buss *et al.*[21] report m. p. 184—185°, $[\alpha]_D$ +147° (*c* 0·20).

The *N*-acetylepimine (1 g.) was boiled under reflux with 1·5N-aqueous potassium hydroxide until all the solid had dissolved (10 min.). The solution was cooled and the crystalline epiminoalloside (75%), m. p. 152—153°, $[\alpha]_D^{22}$ +150° (*c* 0·95), was collected.

Treatment of the epiminoalloside (XI) with benzoyl chloride in pyridine in the usual way gave, after recrystallisation from ethanol, methyl 2,3-benzoylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-alloside (XII) (75%), m. p. 194—195°, $[\alpha]_D^{20}$ +108° (*c* 1·26) (Found: C, 68·7; H, 5·8. Calc. for $C_{21}H_{21}NO_5$: C, 68·7; H, 5·8%). Buss *et al.*[21] report m. p. 190—191°, $[\alpha]_D$ +112°; Christensen and Goodman [19] report 195—198°.

Attempted Preparation of Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*mannoside*.—Methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate (1·5 g.) in methanol (50 ml.) was hydrogenated at 1 atm. over Adams catalyst. After 50 hr. the catalyst was removed and a white foaming syrup was obtained by removal of the solvent *in vacuo*. The syrup could not be completely freed from solvent and hence its weight always exceeded the theoretical. The infrared spectrum of the syrup was consistent with its being methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate. This was confirmed by acetylation (acetic anhydride–pyridine) which gave methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-altroside 3-toluene-*p*-sulphonate (41% based on the azide), m. p. 174—175°, $[\alpha]_D^{18}$ +61° (*c* 1·0 in acetone) {lit.,[22] m. p. 174°, $[\alpha]_D^{18}$ +62° (*c* 1·0 in acetone)}.

A solution of the syrupy 2-aminoaltroside (from 10 g. of azide) in 0·5N-methanolic sodium methoxide (200 ml.) was boiled under reflux for 2 hr. The solution was then poured into ice–water (600 ml.). The white crystalline precipitate was collected and washed with water (500 ml.). Recrystallisation from aqueous methanol gave substance (A) (5·02 g.) as fine white needles, m. p. 106—107°, $[\alpha]_D$ +59·9° (*c* 0·84) [Found: C, 67·3; H, 7·4; N, 4·6%; *M* (Rast), 273. Calc. for $C_{17}H_{23}NO_4$: C, 66·9; H, 7·6; N, 4·6%; *M*, 305].

The syrupy 2-aminoaltroside (from 10 g. of the azide) in (5 : 1) dioxan–water (250 ml.) was treated with potassium hydroxide (7 g.) and boiled under reflux for 2 hr. Pouring into ice–water (1·5 l.) gave a white precipitate, which on two recrystallisations from aqueous ethanol gave substance (A) (4·5 g.), m. p. 105—107°. Extraction of the mother-liquor with chloroform gave a small amount of a syrup, which on treatment with acetic anhydride–pyridine gave methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannoside (VIII) (0·21 g.), m. p. 205—206° (decomp.).

The syrupy 2-aminoaltroside (from 4·5 g. of the azide) in 2-methoxyethanol (50 ml.) was boiled with hydrated sodium acetate (4 g.) for 24 hr. The solution was poured into water (500 ml.), and the precipitate twice recrystallised from aqueous ethanol to give substance (A) (1·19 g.), m. p. 106—107°. No other product could be isolated.

Substance (A) was stable to boiling 1·2N-aqueous potassium hydroxide, to catalytic hydrogenation (Adams catalyst), and to sodium azide in boiling *NN*-dimethylformamide.

Attempted Synthesis of Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*alloside*.—Methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-α-D-altroside 2-toluene-*p*-sulphonate (10 g.) in methanol (200 ml.) was hydrogenated at 1 atm. and at room temperature for 20 hr. with Adams catalyst. The catalyst was removed and the solution evaporated *in vacuo* to give a white foam (11 g.), whose infrared spectrum was that expected for methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altroside 2-toluene-*p*-sulphonate.

A solution of the syrupy 3-aminoaltroside (from 10 g. of azide) in 0·5N-methanolic sodium methoxide (200 ml.) was boiled under reflux for 2 hr., and the solution poured into cold water (200 ml.). The white precipitate was collected and recrystallised from aqueous methanol, to give substance (B) (4·75 g.), m. p. 132—133°, $[\alpha]_D^{20}$ +140° (*c* 1·18) (Found: C, 66·8; H, 7·2%).

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