495. *Some Ring-opening Reactions of 2,3-Epimino-derivatives of Pyranosides*

By D. H. Buss, L. Hough, and A. C. Richardson

Ring-opening reactions of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside and -D-mannopyranoside have been investigated. The acid-catalysed reactions were stereospecific because epimine ring-opening preceded removal of the benzylidene residue and, using halogen acids in acetone, led to a novel series of acetamidohalogeno-derivatives. Similar reactions of the corresponding *N*-2,4-dinitrophenyl derivatives were not stereospecific because, it is believed, the benzylidene group was removed first.

The catalytic hydrogenation of the 2,3-epiminopyranosides using Raney nickel caused cleavage of the epimino-ring without removal of the benzylidene group. In each case the reduction was stereoselective and led to mixtures of two isomeric amino-dideoxy-compounds, in which the product of *trans*-diaxial ring-opening predominated.

The 2,3-epimino-derivatives of hexopyranosides so far prepared [1-5] have 4,6-*O*-benzylidene blocking groups present. Attempts to remove these residues without disruption of the epimino-ring have been unsuccessful: for example, catalytic hydrogenation of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (I) at room temperature and pressure in the presence of palladium–charcoal or Adams catalyst gave only starting material, whilst treatment with hot 50% aqueous acetic acid gave at least five products on a thin-layer chromatogram. Mineral acids were found to act more specfically, so that the *N*-acetyl-*allo*-epimine (I), when treated with dilute sulphuric acid in acetone, afforded mainly one product which was chromatographically identical with methyl 3-acetamido-3-deoxy-α-D-altropyranoside. The stereospecificity of the reaction suggested that the epimino-ring was more labile towards acid than the benzylidene residue, since had the latter been hydrolysed initially, the ring-opening, by analogy with epoxides, would have led to a greater proportion of methyl 2-acetamido-2-deoxy-α-D-glucopyranoside which was detected in trace amounts only.

The action of hydrochloric acid and of hydriodic acid in acetone was different inasmuch

[1] J. E. Christensen and L. Goodman, *J. Amer. Chem. Soc.*, 1960, **82**, 4738; L. Goodman and J. E. Christensen, *ibid.*, 1961, **83**, 3823.
[2] R. D. Guthrie and D. Murphy, *J.*, 1963, 5288.
[3] D. H. Buss, L. Hough, and A. C. Richardson, *J.*, 1963, 5295.
[4] W. Meyer zu Reckendorf, *Chem. Ber.*, 1964, **97**, 325.
[5] B. R. Baker and T. Neilson, *J. Org. Chem.*, 1964, **29**, 1047, 1051, 1057, 1063.

as the major product in each case contained a halogen substituent, undoubtedly arising from nucleophilic attack on the 2,3-epimine by halide. This behaviour parallels that of the epoxides. These reactions have been more fully investigated because the resulting acetamido-halogeno-derivatives may be of application in cancer chemotherapy, due to their relationship to the "nitrogen mustards." When methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (I) in dilute acetone solution was treated with 1 mol. of either hydrochloric acid at room temperature or hydriodic acid at −25°, one acetamido-halogeno-derivative resulted in each case, without loss of the benzylidene residue. Owing to the existence of only one half-chair conformation of the pyranose ring (Ia) the direction of ring-opening was predicted, on the basis of the Fürst–Plattner rule, to give the 2,3-*trans*-diaxial D-*altro*-configuration (IIa; X = Cl or I). Hassner and Heathcock [6] have shown that epimine rings fused to six-membered carbocyclic rings undergo stereospecific cleavage with acetic acid, hydrochloric acid, and hydriodic acid to give *trans*-diaxial products. On the other hand, Meyer zu Reckendorf [4] has shown that the base-catalysed ring-opening of methyl 2,3-benzoylepimino-4,6-*O*-benzylidene-2,3-dideoxy-β-D-allopyranoside with sodium azide, potassium acetate, or potassium thiolacetate affords products of the *trans*-diequatorial D-*gluco*-configuration. In view of these anomalous results, further evidence for our configurational assignments was necessary. When the above 2-iodo-derivative (II; X = I) was heated under reflux with ethanolic sodium ethoxide for 5 minutes a ready cyclisation occurred to give the *allo*-2,3-epimine (XIII) in excellent yield. The same epimine was produced from the 2-chloro-analogue (II; X = Cl), although cyclisation was less rapid. In each case no other product was detectable by thin-layer chromatography. Past work has shown that epimine formation requires a *trans*-diaxial arrangement of the participating and the departing groups; [1-3,5] and that a *trans*-diequatorial configuration gives rise to the corresponding oxazoline as the major product,[7] with only traces of epimine.[4] Consequently, the two halogeno-derivatives must have the 2,3-*trans*-diaxial D-*altro*-configuration (IIa; X = Cl or I). Since completion of this work Dr. R. D. Guthrie has communicated to us that the azide ring-opening reactions of the *allo*- and *manno*-epimines and their *N*-substituted derivatives occur *trans*-diaxially except in the case of the *N*-benzoyl-*allo*-epimine, which gives what is probably the diequatorial product. This anomalous result is in agreement with those of Meyer zu Reckendorf.[4]

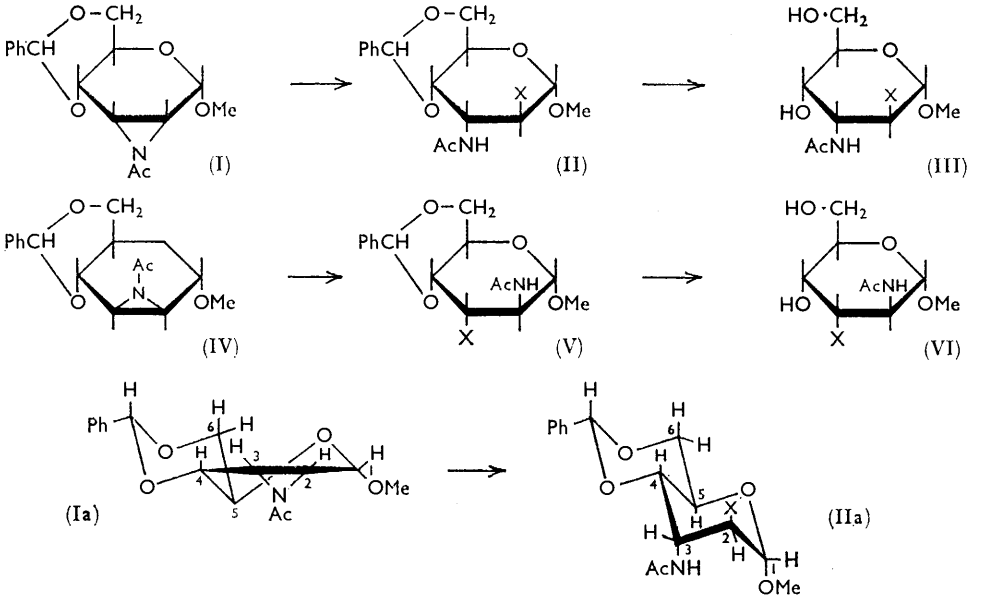
When a dilute acetone solution of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (IV) was similarly treated with 1 mol. of hydrochloric acid at room temperatures, a complex mixture of products was formed. Similar results were obtained with hydriodic acid but on one occasion methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside was isolated in 17% yield as a result of the water present in the mixture, indicative of *trans*-diaxial ring-opening. A simpler reaction ensued at −25° and the crystalline methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-iodo-α-D-altropyranoside (V; X = I) was obtained in 75% yield.

On heating an acetone solution of the *N*-acetyl-*allo*-epimine (I) with an excess of hydrochloric acid, cleavage of the epimine ring was followed by hydrolysis of the benzylidene residue, giving a 61% yield of methyl 3-acetamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (III; X = Cl). The action of an excess of hydriodic acid in acetone on the same acetylepimine (I), either under reflux or at room temperature, always led to several products. However, when the reaction was peformed at −25°, only the 4,6-*O*-benzylidene derivative (II; X = I) resulted, which, on heating, again gave several products. Isolation of the intermediate (II; X = I) followed by hydrolysis with boiling aqueous acetic acid afforded the required methyl 3-acetamido-2,3-dideoxy-2-iodo-α-D-altropyranoside (III; X = I) in high overall yield. That the configuration of the 2-chloro- (III; X = Cl) and the

[6] A. Hassner and C. Heathcock, *Tetrahedron Letters*, 1963, 393.

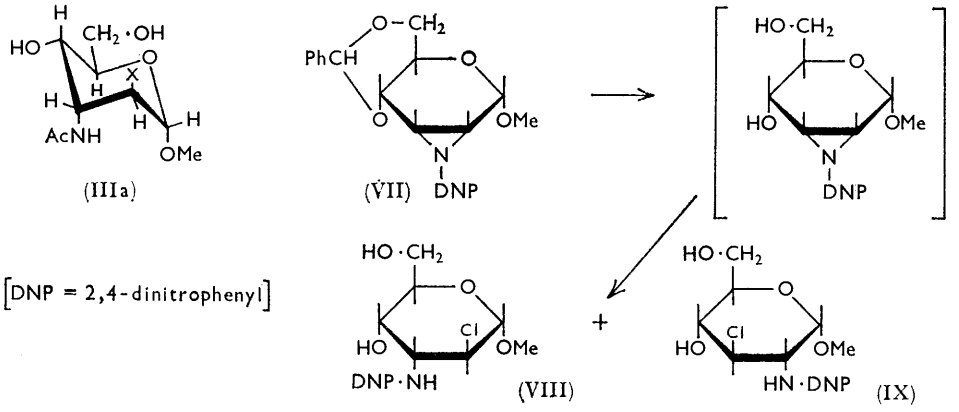
[7] W. Meyer zu Reckendorf and W. A. Bonner, *Proc. Chem. Soc.*, 1961, 429; *Chem. Ber.*, 1962, **95**, 996, 1917; *Tetrahedron*, 1963, **19**, 1721.

2-iodo-derivatives (III; X = I) were the same, namely D-*altro*, was shown by their catalytic reduction to the same product, namely methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside (III; X = H). Attempts to prepare methyl 2,3-dideoxy-2,3-epimino-α-D-allopyranoside by treatment of either (III; X = Cl) or (III; X = I) with sodium ethoxide were unsuccessful, presumably because the pyranose ring does not remain



in the unfavourable chair conformation with three large axial substituents (IIIa), once the locking influence of the benzylidene residue has been removed.

Treatment of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-manno-pyranoside (IV) with an excess of either hydrochloric acid or hydriodic acid afforded



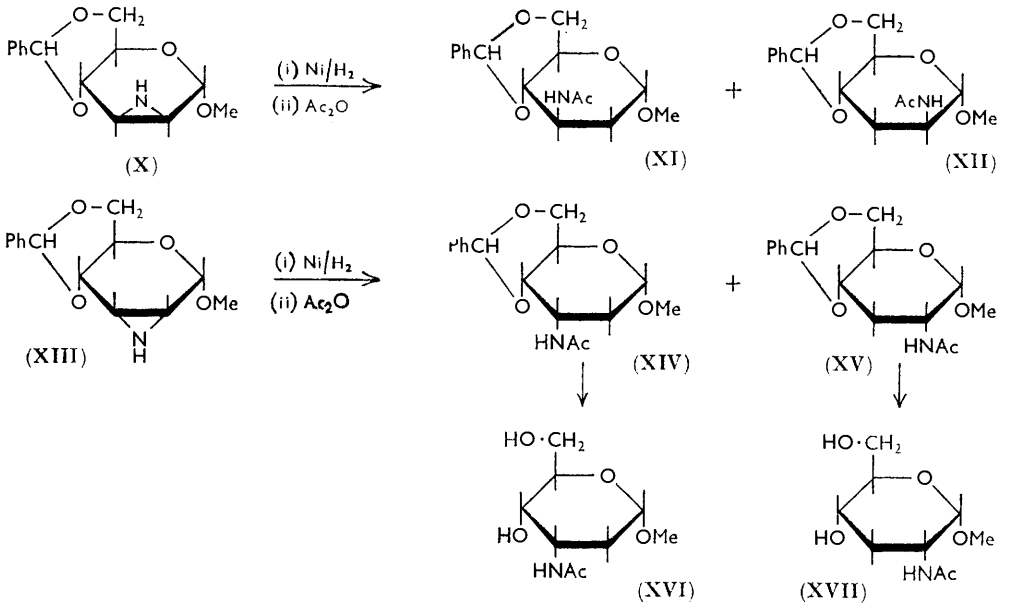
several products; in each case, however, the major product was isolated by preparative thin-layer chromatography. From their infrared spectra and elemental analyses, these were assigned the structures (VI; X = Cl) and (VI; X = I), respectively.

The action of 1 mol. or an excess, of aqueous hydrogen fluoride in acetone on either acetylepimine (I) or (IV) gave a complex mixture from which no pure product was isolated.

N-Substitution with the 2,4-dinitrophenyl (DNP) group in an attempt to stabilise

the epimine ring towards acids was only partly successful. Treatment of the DNP-derivative of the *allo*-isomer (VII) with an excess of hydrochloric acid afforded a mixture of two isomeric chloro-2',4'-dinitrophenylamino-pyranosides (VIII) and (IX), which were separated chromatographically. Although the lack of stereospecificity suggested that the benzylidene ring had been hydrolysed prior to attack upon the epimine ring, attempted selective removal of the *O*-benzylidene substituents was unsuccessful.

Catalytic hydrogenations of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (XIII) and the D-*manno*-analogue (X) using Raney nickel-T4 catalyst at normal temperatures and pressures was non-stereospecific and yielded two products, but in each case diaxial opening predominated. The D-*manno*-epimine (X), which was more easily reduced than its *N*-acetyl derivative (IV), afforded a mixture of two dideoxy-amines (*ca.* 3 : 1 as shown by nuclear magnetic resonance spectroscopy) separable by fractional crystallisation after *N*-acetylation. The major component was identified as methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*arabino*-hexopyranoside (XII) by comparison with an authentic sample.[8] The minor component must therefore be the 3-acetamido-2,3-dideoxy-D-*arabino*-hexopyranoside (XI). The 2,3-epimino-*allo*-derivative (XIII) yielded, on hydrogenation followed by *N*-acetylation, two isomeric syrupy acetamido-derivatives, (XIV) and (XV), which were isolated by thin-layer chromatography in the ratio 4 : 1. The two isomers were distinguished by hydrolysis of the *O*-benzylidene residues with dilute acetic acid, when the major component (XIV) afforded methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside (XVI), previously prepared by reduction of the 2-chloro- (III; X = Cl) and 2-iodo-derivatives (III; X = I). The minor product is therefore methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*ribo*-hexopyranoside (XV).



Experimental

Concentrations were carried out under reduced pressure. M. p.s were determined on a Kofler hot-stage apparatus. Optical rotations were either measured manually in a 5 cm. tube at 20° ± 1° or with an ETL–NPL Automatic Polarimeter Type 143A at 29°, for chloroform solutions unless otherwise stated. Thin-layer chromatography was used exclusively and was

[8] L. Goodman and J. E. Christensen, *J. Org. Chem.*, 1963, **28**, 158.

performed at room temperature on silica gel G (Merck). The separated materials were detected by spraying the dried chromatogram with a 5% v/v solution of sulphuric acid in ethanol and heating at 110—115° for *ca.* 10 min. Preparative separations were effected on thin-layer chromatograms (20 cm. × 20 cm. × 0·25 mm.) of silica gel and the separated components detected as yellow bands by exposure of the plate to iodine vapour in a sealed container. The portion containing the required component was removed and the carbohydrate extracted with a suitable solvent. All products, unless otherwise stated, gave a single spot on chromatograms and their infrared spectra were compatible with the structures assigned. Light petroleum (b. p. 60—80°) was used throughout. Hydrogenations were performed at room temperature and atmospheric pressure, using T4 Raney nickel [9] as the catalyst.

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-(2,4-*dinitrophenylepimino*)-α-D-*mannopyranoside*.—To a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside [3] (X) (320 mg.) in ethanol (20 ml.) was added a solution of sodium hydrogen carbonate (200 mg.) in water (5 ml.), and 2,4-dinitrofluorobenzene (225 mg.). The mixture was shaken at room temperature for 1½ hr., and then taken to dryness. The residue was fractionated between chloroform and water and the organic layer concentrated to a syrup which crystallised on the addition of ethanol. Recrystallisation from ethanol containing a little chloroform afforded the 2,4-*dinitrophenyl derivative* as primrose needles, which slowly darkened on exposure to light (340 mg., 64%), m. p. 179—181° (Found: C, 55·8; H, 4·4. $C_{20}H_{19}N_3O_8$ requires C, 55·9; H, 4·5%).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-(2,4-*dinitrophenylepimino*)-α-D-*allopyranoside* (VII).—To a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside [3] (XIII) (1·10 g.) in ethanol (60 ml.) was added a solution of sodium hydrogen carbonate (0·72 g.) in water (20 ml.), and 2,4-dinitrofluorobenzene (800 mg.). The mixture was shaken at room temperature for 21 hr. and then treated as above, affording the 2,4-*dinitrophenyl derivative* (VII) as pale yellow plates, which also slowly darkened on exposure to light (1·38 g., 77%), m. p. 198—200° (Found: C, 55·75; H, 4·75%).

Methyl 2-*Acetamido*-3-*chloro*-2,3-*dideoxy*-α-D-*altropyranoside* (VI; X = Cl).—Methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside [3] (90 mg.) was dissolved in acetone (6 ml.), treated with concentrated hydrochloric acid (0·15 ml.), and the mixture heated under reflux for 12 min. The acidic solution was treated with an excess of sodium hydrogen carbonate, filtered, and the solid washed with acetone. The combined filtrates were concentrated to a residue from which benzaldehyde was removed by co-concentration with water. Chromatography (chloroform–methanol, 4 : 1, v/v) indicated the presence of at least five components, the major one of which was separated on two plates using the same solvent, to give a syrup which crystallised on the addition of hot ethyl acetate. The *chloro-derivative* (34 mg., 44%) had m. p. 143—144°, $[\alpha]_D^{29}$ +79° (*c* 0·3) (Found: C, 42·3; H, 6·2; Cl, 13·3; N, 5·5. $C_9H_{19}ClNO_5$ requires C, 42·6; H, 6·3; Cl, 14·0; N, 5·5%).

Methyl 2-*Acetamido*-4,6-O-*benzylidene*-2,3-*dideoxy*-3-*iodo*-α-D-*altropyranoside* (V; X = I).—To a cooled solution (acetone–solid carbon dioxide) of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (IV) (240 mg.) in acetone (25 ml.) was added a 0·733N-solution of hydriodic acid in acetone (10·65 ml.). The mixture was kept at −25° for 30 min., then treated with basic lead carbonate. The solid was filtered off, washed with acetone, and the combined filtrates were concentrated into a syrup. A solution of this syrup in chloroform (10 ml.) was washed with aqueous sodium thiosulphate (1 × 5 ml.) and water (2 × 10 ml.), and concentrated to a crystalline residue. Recrystallisation from acetone afforded needles (59 mg.) which were shown to be starting material by chromatography and mixed m. p. Concentration of the mother-liquors gave the *iodo-derivative*, which recrystallised from ethyl acetate–light petroleum as needles (192 mg., 75%) m. p. 150—152° (decomp.), $[\alpha]_D^{29}$ +68° (*c* 0·6) (Found: C, 44·4; H, 4·6; I, 29·5. $C_{16}H_{20}INO_5$ requires C, 44·35; H, 4·6; I, 29·3%).

When this experiment was performed at room temperature and the solution treated with silver carbonate or Amberlite 1R-45 resin, the resultant syrup was shown by chromatography to contain at least seven components, one of which crystallised (17%) from acetone–light petroleum. Two recrystallisations from ethanol–light petroleum gave needles, m. p. 186—190°, which were shown by mixed m. p., chromatography, and infrared spectroscopy to be methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside.

Methyl 2-*Acetamido*-2,3-*dideoxy*-3-*iodo*-α-D-*altropyranoside* (VI; X = I).—Hydriodic acid

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

(0·1 ml.; constant-boiling mixture) was added to a solution of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (IV) (53 mg.) in acetone (4 ml.) and the mixture kept at room temperature for 2½ hr. The acid solution was neutralised with an excess of basic lead carbonate and, after removal of the solids, was concentrated to a syrup which was freed from benzaldehyde by repeated addition of water and re-concentration. Chromatography (chloroform–methanol, 4 : 1, v/v) indicated the presence of at least ten components. Separation on one plate, using the same solvent mixture, afforded the predominant component as a syrup which crystallised on the addition of acetone. The *iodo-derivative* (30 mg., 50%) was recrystallised from acetone–ether–light petroleum as needles, m. p. 138—139°, $[\alpha]_D^{29}$ −11° (*c* 0·4 in H_2O) (Found: C, 31·2; H, 5·0; I, 36·7. $C_9H_{16}INO_5$ requires C, 31·3; H, 4·7; I, 36·8%).

Methyl 3-*Acetamido*-4,6-O-*benzylidene*-2-*chloro*-2,3-*dideoxy*-α-D-*altropyranoside* (II; X = Cl).—Concentrated hydrochloric acid (0·053 ml.) was added to a solution of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside [3] (I) (194 mg.) in acetone (10 ml.) and the mixture was kept at room temperature for 3 hr. The neutral solution was concentrated to a syrup which was freed from benzaldehyde as before. Chromatography (chloroform–ether, 1 : 1, v/v) indicated that, in addition to the major component, there was a small amount of material on the starting line; this was removed on a column of silica gel (Hopkin and Williams) using chloroform–ether (1 : 1, v/v) as eluent. The resultant chromatographically pure pale-orange *chloro-compound* (166 mg., 77%) had $[\alpha]_D^{29}$ +17° (*c* 1·4) (Found: Cl, 11·8; N, 3·8. $C_{16}H_{20}ClNO_5$ requires Cl, 10·4; N, 4·1%).

Methyl 3-*Acetamido*-2-*chloro*-2,3-*dideoxy*-α-D-*altropyranoside* (III; X = Cl).—Concentrated hydrochloric acid (0·3 ml.) was added to a solution of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (I) (580 mg.) in acetone (30 ml.) and the mixture heated under reflux for 5 min. The solution was treated with an excess of sodium hydrogen carbonate, filtered, and the solid washed with acetone. The combined filtrates were concentrated to a syrup which was freed from benzaldehyde in the usual manner. The residue crystallised on the addition of chloroform and was recrystallised from ethyl acetate affording the *chloro-derivative* as needles (290 mg., 61%), m. p. 136—138°, $[\alpha]_D^{20}$ +3·5° (*c* 1·0) (Found: C, 42·7; H, 6·2; Cl, 14·35; N, 5·4. $C_9H_{16}ClNO_5$ requires C, 42·6; H, 6·35; Cl, 14·0; N, 5·5%).

Methyl 3-*Acetamido*-4,6-O-*benzylidene*-2,3-*dideoxy*-2-*iodo*-α-D-*altropyranoside* (II; X = I).—To a cooled solution (methylated spirit–solid carbon dioxide) of methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (I) (570 mg.) in acetone (75 ml.) was added hydriodic acid (0·25 ml.; constant-boiling mixture), and the mixture was kept at −25° for 20 min. The solution was neutralised with basic lead carbonate, filtered, and concentrated to a syrup. Chloroform and light petroleum were added, the solution filtered, and the filtrate taken to dryness. Ether was added, the insoluble material centrifuged off, and the liquors concentrated to a chromatographically pure pale yellow *syrup* (680 mg., 83%), $[\alpha]_D^{29}$ −14° (*c* 1·1) (Found: I, 28·5; N, 3·3. $C_{16}H_{20}INO_5$ requires I, 29·3; N, 3·2%).

Methyl 3-*Acetamido*-2,3-*dideoxy*-3-*iodo*-α-D-*altropyranoside* (III; X = I).—To methyl 3-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-2-iodo-α-D-altropyranoside (II) [prepared as above from 260 mg. of the acetylepimino-derivative (I)] was added 50% v/v aqueous acetic acid (5 ml.) and the mixture heated under reflux for 1 min. Concentration afforded a residue which crystallised after being freed from benzaldehyde in the usual manner. Recrystallisation from ethanol afforded the *iodo-derivative* as needles (260 mg., 89% overall), m. p. 154—155° (decomp.), $[\alpha]_D^{29}$ +8·5° (*c* 0·4 in H_2O) (Found: C, 31·2; H, 4·7; I, 35·9; N, 4·0. $C_9H_{19}INO_5$ requires C, 31·3; H, 4·7; I, 36·8; N, 4·1%).

Action of an Excess of Hydrochloric Acid on Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-(2,4-*dinitrophenylepimino*)-α-D-*allopyranoside* (VII).—A solution of the 2,4-dinitrophenyl derivative (VII) (100 mg.) in acetone (7·5 ml.) was treated with concentrated hydrochloric acid (0·25 ml.) and the mixture heated under reflux for 10 min. The excess of acid was neutralised with sodium hydrogen carbonate, and the solid filtered off and washed with acetone. The combined filtrates were concentrated to a syrup which was co-concentrated with water to remove the benzaldehyde, giving a crystalline residue (68 mg., 77%). Chromatography (ether) showed there to be two yellow components (VIII) and (IX), which were separated with difficulty on two plates (chloroform–ether, 1 : 1, v/v). The faster-moving component, obtained as yellow *needles*, had m. p. 224—226° (Found: C, 40·0; H, 4·5; Cl, 8·9; N, 10·7. $C_{13}H_{16}ClN_3O_8,H_2O$ requires C, 39·5; H, 4·6; Cl, 9·0; N, 10·7%). The *slower-moving component* had m. p. 188—191° (Found: Cl, 9·2; N, 10·9. $C_{13}H_{16}ClN_3O_8$ requires Cl, 9·4; N, 11·1%).

Action of Sodium Ethoxide.—(*a*) *Methyl* 3-*acetamido*-4,6-O-*benzylidene*-2-*chloro*-2,3-*dideoxy*-α-D-*altropyranoside* (II; X = Cl). The chloro-derivative (77 mg.), dissolved in ethanol (1 ml.), was treated with 0·27N-ethanolic sodium ethoxide (3·4 ml.) and the mixture heated under reflux for 7½ hr. Thin-layer chromatography indicated the presence of one product. Concentration gave a residue which was fractionated between chloroform and water. The organic layer, after drying, was concentrated into a syrup which crystallised spontaneously. Recrystallisation from ethyl acetate–light petroleum gave needles of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (XIII) (53 mg., 89%), which melted partly from 143—145° and partly from 151—155°. A further recrystallisation from the same solvent pair gave only the higher-melting form, m. p. 152—154°. The epimine was conclusively identified by its infrared spectrum and by chromatography.

(*b*) *Methyl* 3-*acetamido*-4,6-O-*benzylidene*-2,3-*dideoxy*-2-*iodo*-α-D-*altropyranoside* (II; X = I). To a solution of the iodo-derivative (78 mg.) in ethanol (1 ml.) was added 0·27N-ethanolic sodium ethoxide (1·35 ml.) and the mixture was heated under reflux for 20 min. Examination of the mixture by thin-layer chromatography showed that the epimine was the only product formed and that the reaction was complete within 5 min. Concentration, fractionation of the residue between chloroform and water, and concentration of the organic layer gave a crystalline residue which was recrystallised from ethyl acetate–light petroleum as needles of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (XIII) (42 mg., 89%), m. p. 150—152°.

Methyl 3-*Acetamido*-2,3-*dideoxy*-α-D-ribo-*hexopyranoside* (XVI).—To a solution of methyl 3-acetamido-2,3-dideoxy-2-iodo-α-D-altropyranoside (III; X = I) (100 mg.) in ethanol (0·28 ml.) was added a 5% w/v solution of sodium hydroxide in ethanol (0·28 ml.) and Raney nickel, and the suspension was shaken in an atmosphere of hydrogen for 48 hr. The catalyst was filtered off, washed with ethanol, and the combined filtrates concentrated to a crystalline residue. Recrystallisation from ethanol–ether yielded needles (64 mg.), m. p. 101—104°, which contained sodium iodide. De-ionisation on a mixed-bed resin [Amberlite IR-4B (OH^-) and IR-120(H^+)] afforded the 2-*deoxy-compound* as a syrup (36 mg., 57%), $[\alpha]_D^{20}$ +84° (*c* 0·5 in H_2O) (Found: C, 48·8; H, 8·3. $C_9H_{17}NO_5$ requires C, 49·3; H, 7·8%).

When this experiment was repeated on methyl 3-acetamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (III; X = Cl), a syrup (91%) was produced, which was shown by infrared spectroscopy and chromatography to be identical with methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside prepared as above.

Raney Nickel Hydrogenation of Methyl 4,6-O-*benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*manno*-*pyranoside* (X).—Raney nickel (*ca.* 3 g.) was added to a solution of the epimine (820 mg.) in ethanol (110 ml.) and the suspension was shaken in an atmosphere of hydrogen for 19 hr. The catalyst was filtered off, washed well with ethanol, and the alkaline filtrate concentrated to a syrup (780 mg., 94%), $[\alpha]_D^{29}$ +64·5° (*c* 1·2) (Found: C, 63·6; H, 7·2. $C_{14}H_{19}NO_4$ requires C, 63·4; H, 7·2%). The proton magnetic resonance spectrum showed two methoxyl peaks (τ 6·60 and 6·63; relative intensities *ca.* 3 : 1), due to the presence of the two isomeric methyl glycosides.

Treatment of a portion of the syrup with an excess of acetic anhydride in ethanol at room temperature for 15 min., followed by concentration, afforded a residue which on solution in a little ethanol yielded crystals of *methyl* 3-*acetamido*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-arabino-*hexopyranoside* (XI) which sublimed from 240—245°, $[\alpha]_D^{29}$ +53° (*c* 0·3) (Found: C, 62·2; H, 6·9. $C_{16}H_{21}NO_5$ requires C, 62·5; H, 6·9%). Evaporation of the mother-liquors gave crystals, which on two recrystallisations from ethyl acetate–ether–light petroleum afforded the predominant *N*-acetyl derivative as needles, m. p. 171—173·5°, $[\alpha]_D^{20}$ +63° (*c* 0·65) (Found: C, 62·2; H, 6·8. Calc. for $C_{16}H_{21}NO_5$: C, 62·5; H, 6·9%). The m. p. was undepressed on admixture with an authentic sample of methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*arabino*-hexopyranoside (XII). Goodman and Christensen [8] reported m. p. 169—171°.

Raney Nickel Hydrogenation of Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*allopyranoside* (XIII).—A mixture of Raney nickel (*ca.* 3 g.) and the *allo*-epimine (1·15 g.) in ethanol (120 ml.) was hydrogenated as above for 120 hr. The resulting syrup was shown by thin-layer chromatography to contain two components and virtually no starting material. The amines could not easily be separated chromatographically, so a portion was dissolved in ethanol and treated with acetic anhydride for 1 hr. at room temperature. Concentration afforded a syrup (195 mg.) which contained two isomeric *N*-acetates (XIV) and (XV), which were separated on five plates using chloroform–methanol (4 : 1, v/v) as solvent and isolated as syrups. The

faster-moving component (150 mg.) having $[\alpha]_D^{20}$ +56° (*c* 1·3) (Found: N, 4·2. $C_{16}H_{21}NO_5$ requires N, 4·6%) and the *slower-moving* (44 mg.) having $[\alpha]_D^{20}$ +80° (*c* 0·2) (Found: N, 4·4%).

Treatment of each with boiling 50% v/v aqueous acetic acid for 5 min. gave products, which moved as single spots on chromatograms. On thin-layer chromatograms that from the faster-moving component was indistinguishable from methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranoside (XVI) prepared above, and had an identical infrared spectrum.

When methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (IV) was hydrogenated in the same way for 50 hr. in a 50% v/v ethanol–dioxan mixture, crystallisation of the product from ethanol gave a 67% recovery of starting material. The residue was indistinguishable on thin-layer chromatograms from methyl 3-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*arabino*-hexopyranoside (XI).

Similarly methyl 2,3-acetylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (I) afforded, on hydrogenation for 30 hr., a 79% recovery of starting material and a residue which, on chromatography behaved like methyl 3-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*ribo*-hexopyranoside (XIV).

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