1010. *The Preparation of 2,3-Epimino-derivatives of Pyranosides.**

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

Methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside has been prepared by the action of lithium aluminium hydride on methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl-α-D-altropyranoside and its 2-acetamido-analogue. Treatment of these methanesulphonates with ethanolic sodium ethoxide caused elimination of the sulphonyloxy-group by participation of the neighbouring acylamino-substituent in two competitive ways. Participation by the amide-nitrogen gave the acyl epimino-derivative and was followed by deacylation to the aforementioned epimino-sugar, whereas participation by the amide-carbonyl group afforded the corresponding oxazoline. In both cases stereochemical inversion occurred at position 3.

Analogous derivatives of the α-D-allopyranoside were prepared by similar methods, although oxazolines were not encountered in the cyclisations with base, presumably owing to steric factors.

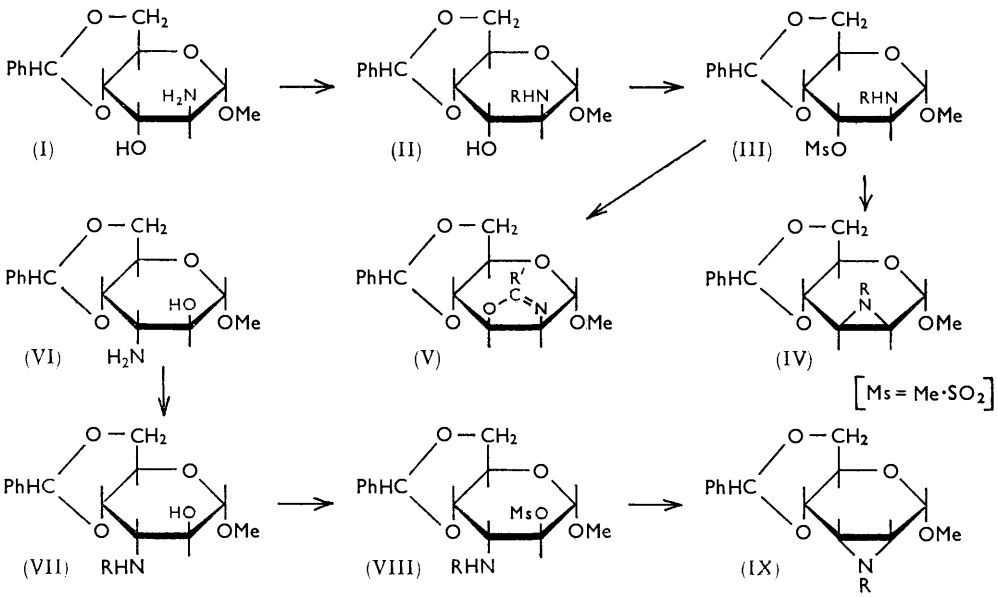
Epimino-derivatives of carbohydrates have been little studied; by analogy with the epoxides they might well undergo ring-opening, which would provide a novel route to difficultly accessible amino-sugars of biochemical interest. Further, they would behave as alkylating agents *in vivo* and are consequently of interest in cancer chemotherapy. Christensen and Goodman [1] have described, in a preliminary publication, the synthesis of one such epimine, namely, methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (IX; R = H), by the action of base on methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-methanesulphonyl-3-[(methylthio)thiocarbamido]-α-D-altropyranoside (VIII; R = MeS·CS·), followed by removal of the *N*-substituent.

Recently one of us (A. C. R.) observed that treatment of methyl 3-benzamido-3,6-dideoxy-2,4-di-*O*-methanesulphonyl-α-L-glucopyranoside with lithium aluminium hydride failed to yield the expected methyl 3-benzylamino-3,6-dideoxy-α-L-glucopyranoside. Instead there was isolated a 40% yield of a weakly basic (pK_a 5·5) crystalline material ($C_7H_{13}NO_3$), which was probably an epimino-pyranoside formed by the elimination of a methanesulphonyloxy-group by the rearward participation of the amide-nitrogen atom. The action of lithium aluminium hydride upon methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl-α-D-altropyranoside (III; R = Bz) and the 3-benzamido-2-*O*-methanesulphonyl isomer (VIII; R = Bz) has now been examined. These esters were prepared in excellent yields from the 2- and 3-aminoaltrosides (I and VI, respectively) by treatment with benzoic anhydride in ethanol to give the corresponding *N*-benzoyl derivatives (II and VII; R = Bz) which were then methanesulphonylated. On treatment with lithium aluminium hydride each benzamido-sulphonate gave isomeric crystalline products in *ca.* 60% yield, shown to be very weak secondary amines by the N–H stretching absorptions at *ca.* 3300 cm.$^{-1}$ which disappeared after *N*-acylation with either benzoic or acetic anhydride. On this evidence and elemental analysis, the products must be the 2,3-epimino-pyranosides, presumably resulting from elimination of the methanesulphonyloxy-group by rearward attack of the amide-nitrogen atom with inversion of configuration, to form an aziridine ring, followed by deacylation. Thus, the 3-*O*-methanesulphonate (III; R = Bz) gave methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (IV; R = H), and the 2-*O*-methanesulphonate afforded the corresponding α-D-allopyranoside (IX; R = H). The latter aziridine was remarkable inasmuch as it was isolated in at least three polymorphic forms, whose infrared spectra

* Preliminary communication: Guthrie, Murphy, Buss, Hough, and Richardson, *Proc. Chem. Soc.* 1963, 84, where these compounds were named as aziridino-derivatives.

[1] Christensen and Goodman, *J. Amer. Chem. Soc.*, 1960, **82**, 4738.

were identical in chloroform solution but different in Nujol mulls; two of these forms were reported by Christensen and Goodman.[1] Although the *manno*-analogue was usually isolated with $[\alpha]_D$ *ca.* +105°, in one case we isolated a product with $[\alpha]_D$ +16·5°, and Guthrie and Murphy [2] obtained one with $[\alpha]_D$ +23°, but the preparations of the lower-rotating form could not be duplicated. However, both forms afforded identical *N*-acetyl derivatives, which is consistent with the observations of Guthrie and Murphy [2] who have prepared both the *allo*- and the *manno*-epimine (IV and IX; R = H) in an independent but concurrent investigation. Further, the *allo*-epimine (IX; R = H) was also isolated as two



differently rotating forms ($[\alpha]_D$ +52°, *ca.* +143°). Attempts to repeat the preparation of the lower-rotating form gave in all cases the higher-rotating isomer. Unfortunately the lower-rotating forms were used in subsequent experiments before this behaviour was fully appreciated as a result of an exchange of information with Dr. R. D. Guthrie, and consequently no further physical measurements have been carried out on them. It is clear that the optical rotations of these compounds cannot be regarded as reliable, since we are unable to account for this anomalous behaviour. It is noteworthy that the optical rotations of the corresponding D-*manno*-[3] and D-*allo*-epoxides [4] (+107° and +140°, respectively) showed a marked similarity to the consistent values obtained for the analogous epimines (+105° and +143°). The physical constants of the derived *N*-acetyl- and *N*-benzoyl-epimines were reliable and consistent, and hence more suitable for characterisation.

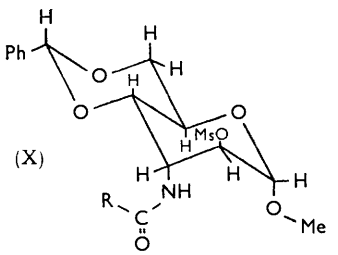
Taguchi and Kojima [5] have studied the action of hot ethanolic sodium ethoxide on DL-*trans*- and DL-*cis*-2-benzamidocyclohexyl toluene-*p*-sulphonate and only in the case of the *trans*-isomer was the sulphonyloxy-group eliminated by participation of the neighbouring benzamido-substituent. Two competitive participation mechanisms were, however, involved; in one the amide-carbonyl group gave a five-membered (oxazoline) ring, and the other involving participation by the amide-nitrogen atom to form an aziridine ring (debenzoylation then occurring). The ratio of oxazoline to epimine formation was *ca.* 1 : 4. In similar conditions reaction of the carbohydrate benzamido-sulphonates

[2] Guthrie and Murphy, preceding paper.
[3] Robertson and Griffith, *J.*, 1935, 1193.
[4] Young and Elderfield, *J. Org. Chem.*, 1942, **7**, 241.
[5] Taguchi and Kojima, *J. Amer. Chem. Soc.*, 1959, **81**, 4316.

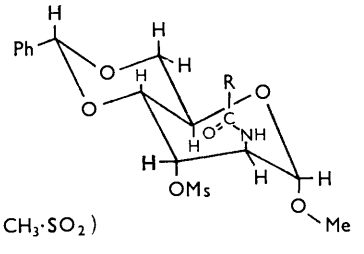
(III and VIII; R = Bz) was usually complete in 5—10 minutes, as revealed by thin-layer chromatography. The 2-benzamidoaltroside (III; R = Bz) afforded the *manno*-epimine (IV; R = H) and the oxazoline derivative (V; R′ = Ph) which were readily separated since the former only was soluble in dilute aqueous alkali. The structure of the oxazoline was shown by the absence of N–H stretching absorption and the presence of a N=C absorption at *ca.* 1650 cm.$^{-1}$ in the infrared spectrum, and by stability of the compound towards alkali and instability towards acid, which is known to cause opening of oxazoline rings. As in the case of the cyclohexane derivative, epimine formation predominated, since the *manno*-epimine (IV; R = H) and the corresponding oxazoline (V; R′ = Ph) were obtained in 56% and 25% yield, respectively. Bonner and Meyer zu Reckendorf [6] have also observed 52% of oxazoline formation when methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl-α-D-glucopyranoside was treated under conditions similar to the above, although they did not detect the *allo*-epimine (IX; R = H).

Unlike normal amides, the benzoylepimine (IV; R = Bz) and analogous derivatives underwent very rapid hydrolysis in hot ethanolic sodium ethoxide as revealed by thin-layer chromatography. When the cyclisation was carried out at room temperature the benzoylepimine was isolated in 38% yield, and clearly the acylepimines are intermediates in the formation of the free imines. Treatment of the 2-acetamido-3-*O*-methanesulphonate (III; R = Ac) with hot ethanolic sodium ethoxide afforded, as before, a mixture of the *manno*-epimine (IV; R = H) and the oxazoline (V; R′ = Me), but at room temperature only unchanged starting material was recovered.

In contrast to the above, treatment of the 3-acylamino-2-*O*-methanesulphonates (VIII; R = Bz and Ac) with hot sodium ethoxide afforded only the *allo*-epimine (IX; R = H). The absence of oxazolines in these cyclisations can be explained by the unfavourable 1,3-diaxial interaction between the 3-acylamino- and the 1-methoxyl groups in the C1 conformation (X), presumably necessary for aziridine ring formation, resulting in



(X)



(XI)

(Ms = $CH_3 \cdot SO_2$)

hindrance of the *N*-acyl to free rotation. Consequently the carbonyl group cannot attain a suitable position behind the departing 2-methanesulphonyloxy-group for neighbouring-group participation, and exclusive attack by nitrogen occurs leading to epimine formation This hindrance to carbonyl attack is absent in the C1 conformation of the 2-acylamino-3-*O*-sulphonates (XI), which affords both epimine and oxazoline.

In contrast to epoxides these epimines are remarkably resistant to ring opening since they withstood prolonged treatment with lithium aluminium hydride and ethanolic sodium ethoxide. Guthrie and Murphy,[2] however, report that ring opening is effected by azide, to give the *trans*-diaxial azido-amine.

Experimental

Concentrations were carried out under reduced pressure. M. p.s were determined on a Kofler microscope stage. Optical rotations were determined for chloroform solutions in a 5 cm. tube at 20° ± 1°. Thin-layer chromatography was performed at room temperature on silica gel (Merck) with, as mobile phase, either (i) chloroform–ether (1 : 1 v/v) or (ii) ether. The

[6] Bonner and Meyer zu Reckendorf, *Chem. Ber.*, 1962, **95**, 1917.

separated materials were detected by spraying the dried chromatogram with a 5% v/v solution of sulphuric acid in ethanol and heating at 115° for *ca.* 10—15 min. Light petroleum (b. p. 60—80°) was used throughout. Unless otherwise stated, all products gave a single spot on chromatograms and their infrared spectra were in accord with the structures assigned.

Methyl 2-Benzamido-4,6-O-benzylidene-2-deoxy-α-D-altropyranoside (II; R = Bz).—Benzoic anhydride (3·7 g.) was added to a suspension of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside [7] (I) (4·15 g.) in warm ethanol (105 ml.), and the resulting solution was kept at room temperature for 20 min. Concentration afforded a syrup, which crystallised on the addition of light petroleum. The N-*benzoyl derivative* (5·2 g., 91%) was collected and recrystallised twice from ethanol–light petroleum, giving needles, m. p. 162—164°, $[\alpha]_D$ −1° (*c* 1·0) (Found: C, 65·2; H, 6·0. $C_{21}H_{23}NO_6$ requires C, 65·4; H, 6·0%).

Methyl 2-Benzamido-4,6-O-benzylidene-2-deoxy-3-O-methanesulphonyl-α-D-altropyranoside (III; R = Bz).—Methanesulphonyl chloride (0·45 ml.) was added to a solution of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (2·1 g.) in pyridine (7 ml.), and the resulting pale orange solution kept at 4° for 16 hr. The excess of methanesulphonyl chloride was decomposed by the addition of a little water, and concentration afforded a gel. A solution of this in chloroform (35 ml.) was washed with water (3 × 25 ml.), dried ($CaSO_4$), and concentrated to a syrup which crystallised on the addition of ethanol. After addition of light petroleum, the *sulphonate* (1·8 g., 74%) was filtered off and recrystallised from ethanol–light petroleum to give needles, m. p. 147—148° (decomp.), $[\alpha]_D$ −11° (*c* 2·3) (Found: C, 57·3; H, 5·6. $C_{22}H_{25}NO_8S$ requires C, 57·0; H, 5·4%).

Methyl 2-Acetamido-4,6-O-benzylidene-2-deoxy-3-O-methanesulphonyl-α-D-altropyranoside (III; R = Ac).—Methanesulphonyl chloride (0·12 ml.) was added to a solution of methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside [8] (II; R = Ac) (0·39 g.) in pyridine (2 ml.), and the solution was kept at room temperature for 16 hr. The excess of methanesulphonyl chloride was decomposed with a little water, and concentration afforded a syrup. A solution of this in chloroform (10 ml.) was washed with water (2 × 10 ml.), dried ($CaSO_4$), and concentrated to a syrup which crystallised on addition of ethanol. Recrystallisation from ethanol–light petroleum afforded the *sulphonate* as plates (0·36 g., 75%), m. p. 142—145°, $[\alpha]_D$ +64° (*c* 0·7) (Found: C, 51·1; H, 5·8. $C_{17}H_{23}NO_8S$ requires C, 50·9; H, 5·8%).

Methyl 4,6-O-Benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (IV; R = H).—Lithium aluminium hydride (0·5 g.) was slowly added to a solution of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl-α-D-altropyranoside (0·6 g.) in tetrahydrofuran (30 ml.), after which the mixture was heated under reflux for 4 hr. After cooling, the excess of lithium aluminium hydride was decomposed by the addition of an aqueous solution of Rochelle salt (33% w/v), and the clear supernatant solution was decanted off. The residue was thoroughly washed with chloroform, and the combined extracts and supernatant solution were filtered and concentrated to a crystalline residue. Recrystallisation from ethanol–light petroleum gave the *epimine* (0·2 g., 60%). A further recrystallisation from ethyl acetate–light petroleum gave needles, m. p. 145—146°, $[\alpha]_D$ +105° (*c* 1·0) (Found: C, 64·3; H, 6·4; N, 5·3. $C_{14}H_{17}NO_4$ requires C, 63·9; H, 6·6; N, 5·3%). Guthrie and Murphy [2] report m. p. 145—146° and $[\alpha]_D$ +105°. In one preparation, which could not be repeated, the epimine had $[\alpha]_D$ +16·5° (*c* 1·1).

When the above experiment was repeated with reaction times of 35 min. and 44 hr., the epimine was produced in 60% and 64% yield, respectively. In another experiment, the lithium aluminium hydride was added to a cooled solution (acetone–carbon dioxide) of the sulphonate (III; R = Bz) in tetrahydrofuran, then allowed to react at room temperature for 45 min.; the epimine (IV; R = H) was obtained in 66% yield.

A similar experiment, with methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl α-D-altropyranoside (III; R = Ac) (78 mg.) and a reaction time of 11 hr. gave the same epimine in 20% yield.

Action of Sodium Ethoxide on Methyl 2-Benzamido-4,6-O-benzylidene-2-deoxy-3-O-methanesulphonyl-α-D-altropyranoside (III; R = Bz).—(*a*) To a solution of the benzamido-derivative (250 mg.) in warm ethanol (10 ml.) was added a solution of sodium (15·5 mg.) in ethanol (2·5 ml.). The solution was kept at room temperature for 45 min., then water was added and the crystals

[7] Robertson, Myers, and Tetlow, *Nature*, 1938, **142**, 1076.
[8] Foster, Stacey, and Vardheim, *Acta Chem. Scand.*, 1958, **12**, 1605.

were filtered off. Recrystallisation from ethanol yielded needles (75 mg., 38%), m. p. 165—167°, shown to be methyl 2,3-benzoylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-manno-pyranoside (see below) by mixed m. p. and infrared spectra.

(*b*) The 2-benzamido-derivative (750 mg.) was heated under reflux with 0·27N-ethanolic sodium ethoxide (15 ml.) for 30 min. Chromatography indicated that the reaction was usually complete within 10 min. and that two components were formed with R_F 0·14 and 0·82 (solvent i), the slower spot being coincident on co-chromatography with the epimine (IV; R = H). The sodium methanesulphonate which had separated during the reaction was dissolved by addition of a little water; addition of more water precipitated needles (150 mg., 25%) of the oxazoline, *methyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-3,2-(2-*phenyl*-1-*oxa*-3-*azaprop*-2-*eno*)-α-D-*mannopyranoside* (V; R′ = Ph), m. p. 150—151°, $[\alpha]_D$ −67° ± 3° (*c* 1·84). In another preparation, a second isomorphic form was encountered, having m. p. 147—148°. Both forms had different infrared spectra in Nujol mulls, but the same in chloroform solution (Found: C, 68·3; H, 5·8; N, 3·9. $C_{21}H_{21}NO_5$ requires C, 68·7; H, 5·7; N, 3·8%).

The aqueous-ethanolic mother-liquors were concentrated to dryness after the removal of the oxazoline, and fractionated between water and chloroform. The organic layer was washed once with water, dried (Na_2SO_4), and concentrated to a syrup which readily crystallised in the presence of ethyl acetate. Two recrystallisations from ethyl acetate–light petroleum afforded 240 mg. (56%) of slightly impure *manno*-epimine (IV; R = H), m. p. 138—142°, as suggested by thin-layer chromatography. It was contaminated with a trace of a faster-moving component (R_F 0·45, solvent ii) which was not removed by repeated recrystallisation from the same solvent pair. Nevertheless, the product had an infrared spectrum identical with that of the *manno*-epimine.

Action of Sodium Ethoxide on Methyl 2-*Acetamido*-4,6-O-*benzylidene*-2-*deoxy*-3-O-*methanesulphonyl*-α-D-*altropyranoside* (III; R = Ac).—The 2-acetamido-derivative (252 mg.) was heated under reflux with 0·14N-ethanolic sodium ethoxide (10 ml.) for 40 min. and then taken to dryness. The residue was fractionated between water and chloroform, and the organic layer dried (Na_2SO_4) and evaporated to a crystalline residue *A* (*ca.* 130 mg.). Chromatography indicated the presence of two components with R_F's 0·14 and 0·30 (solvent i). Separation of these components from a portion of *A* was achieved on a column of silica gel using ether as eluent. The faster component was recrystallised from light petroleum, to give the methyl-oxazoline, *methyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-3,2-(2-*methyl*-1-*oxa*-3-*azaprop*-2-*eno*)-α-D-*manno-pyranoside* (V; R′ = Me), m. p. 141°, having a characteristic absorption band at 1650 cm.$^{-1}$ (Found: C, 62·7; H, 6·1. $C_{16}H_{19}NO_5$ requires C, 62·9; H, 6·2%). The slower component, recrystallised from ethyl acetate–light petroleum (b. p. 40—60°), had m. p. 141—143°, $[\alpha]_D$ +102° (*c* 0·45), and its infrared spectrum was identical with that of the epimine. The *N*-acetyl derivative of this epimine was isolated in 40% overall yield from the mixture *A* by treating a solution in a minimum of ethanol with an excess of acetic anhydride.

Methyl 2,3-*acetylepimino*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-*mannopyranoside* (IV; R = Ac).—Acetic anhydride (2·5 ml.) was added to a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (0·95 g.) in pyridine (10 ml.). The solution was kept at room temperature for 30 min., then concentrated to a crystalline residue. Recrystallisation from ethanol–light petroleum gave needles of the N-*acetyl derivative* (0·97 g., 88%), m. p. 211—212°, $[\alpha]_D$ +45° (*c* 1·2) (Found: C, 63·2; H, 6·1. $C_{16}H_{19}NO_5$ requires C, 63·0; H, 6·3%). Guthrie and Murphy [2] find m. p. 205—206° and $[\alpha]_D$ +49·3°.

Acetylation was more readily achieved by treating an ethanolic solution of the epimine with acetic anhydride; the acetylepimine crystallised in high yield.

Treatment of the acetylepimine with lithium aluminium hydride as above for (III; R = Ac) gave the epimine (IV; R = H).

Methyl 2,3-*Benzoylepimino*-4,6-O-*benzylidene*-2,3-*dideoxy*-α-D-*mannopyranoside* (IV; R = Bz).—Benzoic anhydride (0·85 g.) was added to a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (0·75 g.) in pyridine (10 ml.). The solution was kept at room temperature for 1 hr. and concentrated to a crystalline residue. Recrystallisation from ethanol–light petroleum gave the N-*benzoyl derivative* (0·88 g., 84%), m. p. 166—168°, $[\alpha]_D$ +1·5° (*c* 2·4) (Found: C, 68·9; H, 5·9; N, 4·0. $C_{21}H_{21}NO_5$ requires C, 68·6; H, 5·8; N, 3·8%). Guthrie and Murphy [2] report m. p. 165—166° and $[\alpha]_D$ +5·8°.

Treatment of the benzoylepimine with lithium aluminium hydride for 2 hr. gave the parent epimine (IV; R = H).

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*altropyranoside* (VII; R = Bz).—Benzoic anhydride (0·9 g.) was added to a solution of methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside [7] (VI) (1·0 g.) in ethanol (50 ml.) and kept at room temperature for 1 hr. Concentration afforded a syrup, which after extraction with boiling light petroleum (40 ml.) crystallised on addition of ethanol. Filtration gave the N-*benzoyl derivative* (0·9 g., 67%) which was recrystallised from ethanol–light petroleum as prisms, m. p. 155—156°, $[\alpha]_D$ +92° (*c* 1·1) (Found: C, 65·7; H, 5·9. $C_{21}H_{23}NO_6$ requires C, 65·4; H, 6·0%).

Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-2-O-*methanesulphonyl*-α-D-*altropyranoside* (VIII; R = Bz).—Methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside (0·56 g.) was methanesulphonylated as described above for (III; R = Bz). The *sulphonate* (0·59 g., 87%), when crystallised from acetone–light petroleum and then recrystallised from the same solvent pair, had m. p. 91—96°, $[\alpha]_D$ +4° (*c* 2). The product (R_F 0·25) was contaminated by traces of an unidentified compound (R_F 0·10), as revealed by chromatography (solvent ii), which could not be removed by repeated recrystallisation or by chromatography on silica gel (Found: C, 57·45; H, 6·2. $C_{22}H_{25}NO_8S$ requires C, 57·0; H, 5·45%).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-2,3-*epimino*-α-D-*allopyranoside* (IX; R = H).—Lithium aluminium hydride (0·25 g.) was added to a solution of methyl 3-benzamido-4,6-*O*-benzylidene-3-deoxy-2-*O*-methanesulphonyl-α-D-altropyranoside (0·32 g.) in tetrahydrofuran (15 ml.) and heated under reflux for 3 hr. The mixture was processed as described above for compound (IV; R = H), giving a syrup which crystallised on addition of ethanol. Recrystallisation from ethyl acetate–light petroleum gave the epimine as needles (0·096 g., 53%), m. p. 150—154°, $[\alpha]_D$ +143° (*c*, 0·66) (Found: C, 63·6; H, 6·4. Calc. for $C_{14}H_{17}NO_4$: C, 63·9; H, 6·6%). Guthrie and Murphy [2] find m. p. 152—153° and $[\alpha]_D$ +150°, and Christensen and Goodman [1] reported two forms, m. p.s 153—154° and 143—145°.

In the initial preparation the epimine had m. p. 151—154° and $[\alpha]_D$ +52° (*c* 1·15), but in all subsequent experiments the higher-rotating form was isolated.

Action of Sodium Ethoxide on Methyl 3-*Benzamido*-4,6-O-*benzylidene*-3-*deoxy*-2-O-*methanesulphonyl*-α-D-*altropyranoside* (VIII; R = Bz).—(*a*) To a solution of the benzamido-compound (100 mg.) in ethanol was added a solution from sodium (6·2 mg.) in ethanol (1 ml.), and the solution was made up to 10 ml. with ethanol. After 1½ hr. the solution was concentrated, and the crystalline residue fractionated between chloroform and water. The chloroform solution was concentrated to a syrup which crystallised on addition of ethanol; recrystallisation from ethanol–light petroleum yielded needles (23 mg., 29%), m. p. 188—189°, shown to be methyl 2,3-benzoylepimino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside by mixed m. p. and infrared spectra.

(*b*) The 3-benzamido-derivative (505 mg.) was heated under reflux with 0·27N-ethanolic sodium ethoxide for 30 min., and sufficient water then added to dissolve the precipitated sodium methanesulphonate. Chromatography indicated that only the epimine had been formed. The aqueous-ethanolic solution was evaporated to dryness and the residue fractionated between chloroform and water. After washing and drying (Na_2SO_4) of the chloroform layer, evaporation afforded a residue which recrystallised from ethyl acetate–light petroleum to give an isomorph (207 mg., 72%) of the *allo*-epimine (IX; R = H) as long needles, m. p. 143—144°, $[\alpha]_D$ +151° (*c* 0·3). Recrystallisation from the same solvent mixture did not change the m. p. When this isomorph was melted and immediately recrystallised from ethyl acetate–light petroleum, another isomorph was isolated, having m. p. 154—155°, $[\alpha]_D$ +142° (*c* 1·0), which on further recrystallisation gave the previous form, m. p. 142—143°. In chloroform solutions the two isomorphs had infrared spectra identical with that of the sample previously prepared by the lithium aluminium hydride method, but all three had different spectra in Nujol mulls. The three isomorphs were indistinguishable on thin-layer chromatograms.

Action of Sodium Ethoxide on Methyl 3-*Acetamido*-4,6-O-*benzylidene*-3-*deoxy*-2-O-*methanesulphonyl*-α-D-*altropyranoside* (VIII; R = Ac).—To a solution of the acetamido-compound [9] (4·66 g.), m. p. 170—172°, in ethanol (60 ml.) was added a solution from sodium (0·56 g.) in ethanol (90 ml.), and the mixture was heated under reflux for 20 min. Thin-layer chromatography (solvent i) indicated that the acetylepimine (IX; R = Ac) was formed within a few minutes, followed by the epimine, and that after 20 min. starting material and the intermediary *N*-acetyl derivative had completely disappeared. Water (100 ml.) was added, and most of the

[9] Baker and Schaub, *J. Org. Chem.*, 1954, **19**, 646.

ethanol removed by evaporation under reduced pressure. Filtration gave methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (1·62 g., 53%), m. p. 145—151°, $[\alpha]_D$ +148° (*c* 0·7). The filtrate was extracted with chloroform (3 × 100 ml.), the combined extracts were washed with water (1 × 100 ml.) and concentrated to a crystalline residue, $[\alpha]_D$ +137° (*c* 1·0). Recrystallisation from ethyl acetate–light petroleum gave needles of the same epimine (1·07 g., 35%), m. p. 139—143°.

Methyl 2,3-Acetylepimino-4,6-O-benzylidene-2,3-dideoxy-α-D-allopyranoside (IX; R = Ac).—(*a*) Acetic anhydride (0·5 ml.) was added to a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (50 mg.) in ethanol (1 ml.) and kept at room temperature for 45 min. Concentration afforded a residue which, recrystallised from ethanol–light petroleum, gave the N-*acetyl derivative* (52 mg., 90%), m. p. 184—185°, $[\alpha]_D$ +147° (*c* 0·2) (Found: C, 63·1; H, 6·3. $C_{16}H_{19}NO_5$ requires C, 63·0; H, 6·3%). Guthrie and Murphy [2] report m. p. 187—188° and $[\alpha]_D$ +149°.

(*b*) The *allo*-epimine (1·45 g.) in ethanol (20 ml.) was treated with acetic anhydride (3·6 ml.). Crystallisation of the *N*-acetyl derivative commenced immediately. It was filtered off and washed with light petroleum to give 1·51 g. (90%) of material, m. p. 184—185°. A further crop (0·15 g., 9%) was obtained by concentration of the mother-liquors.

Methyl 2,3-Benzoylepimino-4,6-O-benzylidene-2,3-dideoxy-α-D-allopyranoside (IX; R = Bz).—Benzoyl chloride (0·1 ml.) was added to a solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (80 mg.) in pyridine (1 ml.) and kept at room temperature for 30 min. Water and ethanol were added, and filtration gave the *N*-benzoyl derivative (84 mg., 75%). Two recrystallisations from ethanol gave needles, m. p. 190—191°, $[\alpha]_D$ +112° (*c* 0·33) (Found: C, 68·8; H, 5·5. Calc. for $C_{21}H_{21}NO_5$: C, 68·6; H, 5·8%). Guthrie and Murphy [2] find m. p. 194—195° and $[\alpha]_D$ +108°; Christensen and Goodman reported m. p. 195—198°.

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Department of Organic Chemistry,
The University, Bristol.

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