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SOME FURTHER RING-OPENING REACTIONS OF METHYL 4,6-*O*-BENZYLIDENE-2,3-DIDEOXY-2,3-EPIMINO-α-D-ALLOPYRANOSIDE AND ITS DERIVATIVES

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ABSTRACT

Modifications have been made to the preparation of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside from derivatives of 2-amino-2-deoxy-D-glucose, which permit it to be prepared in high yield and on a large scale Further, ring-opening reactions of the epimine and its *N*-substituted derivatives have been studied with halide ion under neutral and acidic conditions It has been found that anomalous, diequatorial ring-opening occurs when the free epimine is treated with ammonium halides (except the fluoride) in *N*,*N*-dimethylformamide, but, with its *N*-substituted derivatives, diaxial ring-opening predominates, although diequatorial ring-opening is significant in many cases Under acidic conditions, the free epimine undergoes hydrolysis of the benzylidene group, without rupture of the epimine ring, but its *N*-substituted derivatives undergo predominant, diaxial ring-opening before hydrolysis of the benzylidene group

Ring-opening reactions of the *N*-methanesulphonyl and *N*-acetyl derivatives with azide occur *trans*-diaxially and *trans*-diequatorially, respectively

INTRODUCTION

Ring-opening reactions of carbohydrate epoxides have been widely studied[1], whereas those of the recently accessible[2-10] nitrogen-analogues, the epimines, have not With azide as the nucleophile, the results obtained showed that ring-opening is not always analogous to that observed in the case of epoxides, which affords predominantly *trans*-diaxial[3] products For example, whereas the *allo*-epimine **7** and its *N*-tosyl and *N*-2,4-dinitrophenyl derivatives (**11**) undergo *trans*-diaxial ring-opening, the *N*-benzoyl derivative **9** gave the *trans*-diequatorial *gluco*-stereoisomer[11] The corresponding

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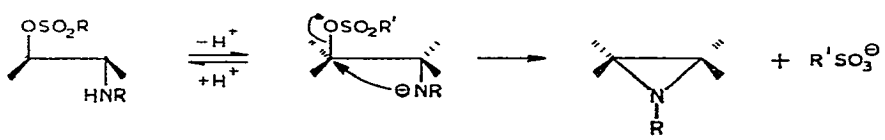
manno-epimine and its *N*-tosyl derivative underwent ring-opening to give *trans*-diaxial products, but the *N*-benzoyl derivative rearranged mainly to the oxazoline, although some of the *trans*-diaxial product was obtained Similar, anomalous ring-openings occur[12] with the *N*-benzoyl-*allo*-epimine in the β-D-glycoside series, in this case, *trans*-diequatorial ring-opening occurred with thiolacetate, azide, and even hydroxide (from basic alumina)

The above reactions were carried out under neutral or slightly basic conditions *N*-Acylepimines are extremely sensitive towards acid[13], and, with hydrogen halides, they underwent rapid opening to give *trans*-diaxial halo-amines in good yields The three-membered ring was so acid-sensitive that it was possible to effect ring opening without hydrolysis of the benzylidene substituent These studies have now been extended by a study of the *allo*-epimine **7**.

DISCUSSION

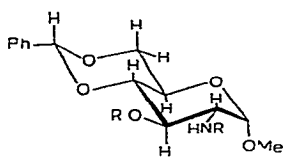
Various methods[2-4,5] available for the preparation of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (**7**) are unsuitable for large-scale work One method[4] utilized the elimination of a sulphonyloxy group situated *trans* to a vicinal benzamido substituent; consequently, the readily available methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-glucopyranoside (**1**) should be a convenient precursor for the epimine However, previous results showed that the reduction of compound **1** with lithium aluminium hydride was unsatisfactory, and treatment with ethanolic sodium ethoxide, to give the epimine, was complicated by competing hydrolysis of the sulphonic ester to give alcohol **2** We reasoned that a larger sulphonate group at C-3 and a bulky alkoxide anion would hinder the approach of the base, and hence prevent competing hydrolysis. Accordingly, the 3-toluene-*p*-sulphonate **3** was converted almost quantitatively into the epimine **7** by sodium isopropoxide Lithium aluminium hydride was much less convenient and only gave a 60% yield of the epimine Furthermore, since higher temperatures might favour the chair-to-boat conformational change (**1**→**6**), a probable prerequisite of epimine formation[9], the action of sodium hydroxide on the compound **1** in the higher boiling solvent 2-methoxyethanol was examined and found to give the epimine **7** in 90–95% yield The latter reaction is the method of choice, and the epimine **7** can now be regarded as a useful and readily obtainable synthetic intermediate

Base-catalysed epimine formation from α,β-*trans*-acylamido-sulphonyloxy systems probably requires a *trans*-coplanar arrangement of participating substituents and the formation of the powerfully nucleophilic anion of the acylamido group

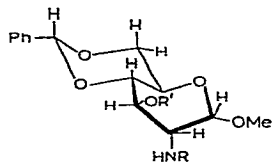


Thus, under mildly basic conditions, which would not favour anion formation, predominant attack by the carbonyl oxygen-atom occurs to give the oxazoline, and

thence the *cis*-acylamido alcohol[14]. Consequently, the rate of formation of the epimine must be related to the pK_a of the amide, and, since acylamide derivatives are considerably weaker acids than are sulphonamide derivatives[15], *N*-sulphonyl derivatives (*e g*, **5**) should be converted more readily into epimines than the corresponding *N*-acyl derivatives and, furthermore, competing oxazoline formation would be excluded This approach has been used successfully in the furanoside series[8] and has now been applied to the preparation of the *N*-mesyl-*allo*-epimine **10** from methyl



1 R = Bz R' = Ms
2 R = Bz R = H
3 R = Bz R = Ts
4 R = R = H
5 R = R = Ms



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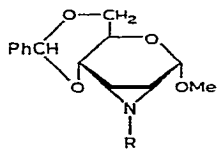
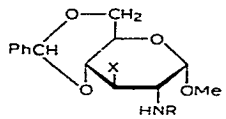
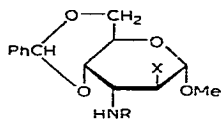


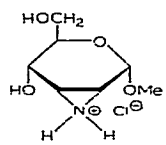
7 R = H
8 R = Ac
9 R = Bz
10 R = Ms
11 R = DNP



12 R = H X = Cl
13 R = Ac X = Cl
14 R = Bz X = Cl
15 R = DNP X = Cl
16 R = H, X = Br
17 R = Ac, X = Br
18 R = H X = I
19 R = Ac, X = I
20 R = Bz X = N_3
21 R = Ac, X = N_3



22 R = H X = Cl
23 R = Ac, X = Cl
24 R = Bz X = Cl
25 R = DNP, X = Cl
26 R = Ac X = I
27 R = H, X = N_3
28 R = Ms X = N_3



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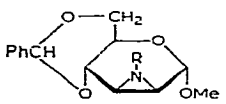

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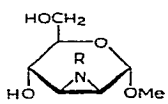
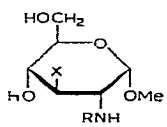
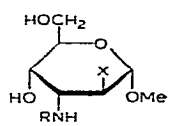
31 R = Ac



32 R = H
33 R = Ac



34 R = H, X = Cl
35 R = Ac X = Cl
36 R = Bz X = Cl
37 R = Ac, X = Br
38 R = Ac X = I



39 R = H, X = Cl
40 R = Ac X = I
41 R = Bz, X = Cl
42 R = Ac, X = Cl

2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**4**). The latter amine was obtained from the readily available *N*-benzoyl derivative **2** by hydrolysis with sodium hydroxide in 95% 2-methoxyethanol, *N*-benzoyl groups are not usually removed by aqueous sodium hydroxide[16], conditions which are effective for the removal of *N*-acetyl groups[16 17] The amino-alcohol **4** gave the di-*N*,*O*-mesyl derivative **5**, in high yield, which was converted into the *N*-mesyl-*allo*-epimine **10** by the action of sodium acetate in boiling 95% 2-methoxyethanol This is probably the most reliable route for epimine synthesis, but the removal of the alkali-stable *N*-mesyl group presents difficulties

The acetylepimino ring is very labile towards acid[13], and the two *N*-acetyl epimines **8** and **31** undergo ring-opening with hydrogen halides to give diaxial acetamido-halo derivatives (*e g*, **23**) before hydrolysis of the benzylidene substituent Consequently, selective removal of the benzylidene group from these derivatives was not possible However, the free epimines **7** and **30** are less prone to ring-opening than are their *N*-acyl derivatives, so that the benzylidene blocking groups can thereby be selectively removed. Thus, the *allo*-epimine **7**, upon treatment with hydrochloric acid in acetone, gave a 70% yield of methyl 2,3-dideoxy-2,3-epimino-α-D-allopyranoside hydrochloride (**29**) The *manno*-epimine **32** was similarly prepared from compound **30** Intermediates that crystallised from the reaction mixtures were shown to be the respective hydrochlorides of the starting epimines **7** and **30**, since, with alkali, they could be reconverted into the epimines Despite the fact that the epimines are very weak bases[18], these salts were stable over periods of several months The stability of the epimine salts to ring-opening was surprising, since the presence of a positive charge on nitrogen should weaken the C-N bond

The ring-opening reactions of the *allo*-epimine and its *N*-substituted derivatives, under essentially neutral conditions with ammonium halides in *N*,*N*-dimethylformamide, were then studied as an alternative route to halo-amino-pyranosides, under comparable conditions, the *allo*-epimine **7** is susceptible to *trans*-diaxial ring-opening by azide[11] With ammonium chloride, the *allo*-epimine **7** gave a 40% yield of a chloro-amine, which had not been encountered previously, although the ring-opening reactions with sodium azide have always been carried out in the presence of ammonium chloride, which acts as a buffer, presumably because azide is a much better nucleophile than chloride The chloroamine gave a crystalline *N*-acetyl derivative, which was different from the syrupy acetamido-chloro-altropyranoside[13] **23** Furthermore, when the *N*-acetyl-*allo*-epimine **8** was treated with hydrochloric acid in acetone[13], the syrupy altropyranoside **23** was the major product (80%), but a minor (3%), isomeric product was also isolated and was identical with the product obtained from the "ammonium chloride reaction" Provided that *trans*-opening of the epimine ring occurs, the new chloro-amine must be the 2-amino-3-chloro-glucoside **12** Acid hydrolysis of compound **12** gave methyl 2-amino-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**34**), the molecular rotation of which (+32 6°) was similar to that (+30 8°) of methyl 2-acetamido-2-deoxy-α-D-glucopyranoside[19], but different from that (+21 6°) of the corresponding allopyranoside[20] Unequivocal support for the *gluco*-stereochemistry was provided by n m r spectroscopy (see below)

The *allo*-epimine **7** also reacted with ammonium bromide and iodide to give 52 and 54%, respectively, of the corresponding halo-derivatives The *N*-acetyl derivative of the iodo-amine was different from the syrupy 3-acetamido-2-iodo-altropyranoside **26**, obtained[13] by the action of hydriodic acid on the acetylepimine **8** Hence, the new iodo-derivative was the glucopyranoside **18** Removal of the benzylidene group from the *N*-acetyl derivative **19** gave methyl 2-acetamido-2,3-dideoxy-3-iodo-α-D-glucopyranoside (**38**), which again was different from the 3-acetamido-2-iodo-altropyranoside (**40**) previously described[13] The bromo derivative was also considered

to be the glucopyranoside **16**, since, after *N*-acetylation and removal of the benzylidene group, the molecular rotation of the product (+28 3°) was in close agreement with that (+28 6°) of the corresponding iodo-derivative and compared favourably with the value (+30 8°) reported[19] for methyl 2-acetamido-2-deoxy-α-D-glucopyranoside

The structures of the three halo-amines were proved beyond doubt by their n m r spectra The three products exhibited very similar n m r. spectra (Table I), suggesting that they were all configurationally identical In all three spectra, the H-1 resonances were low-field doublets at τ 5 3 (J 3 5 Hz), which suggested an *ax-eq* (*cis*)-arrangement of H-1 and H-2 An *eq-eq* (*trans*)-relationship, as found in α-D-mannopyranosides and α-D-altropyranosides, gives rise to a smaller (0 6–1 7 Hz)[21] coupling constant The highest field resonance due to a single proton was observed at τ *ca* 7 0 in all three spectra as a quartet (J 3 5 and 10 0 Hz), the splittings of which suggested it to be H-2 In the case of the chloro- and bromo-derivatives, **12** and **16**, this was confirmed by irradiation at the frequency of H-1, when the quartet collapsed to a doublet with a splitting of 10 Hz (Fig 1) The large coupling constant of H-2 and

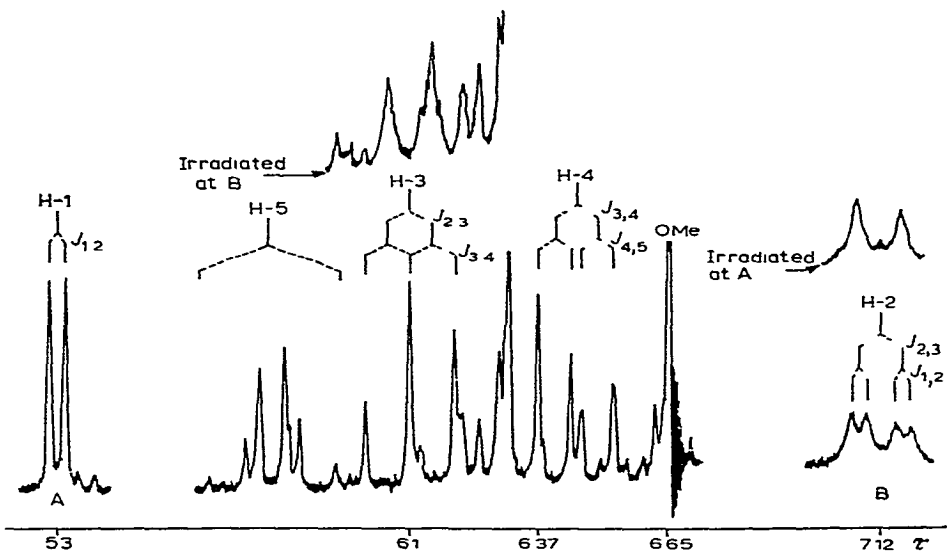


Fig 1 The low-field portion of the 100 MHz n m r spectrum of **12** showing the results of decoupling experiments

H-3 clearly indicates that these protons possess a *trans*-diaxial relationship[22], thereby establishing the *gluco*-stereochemistry of these products The assignment of all other ring-proton resonances was possible for the chloro derivative (Fig 1) The triplet at τ 6 1 (J 10 Hz) collapsed into a doublet when the H-2 quartet was irradiated, showing it to be due to H-3, and consequently a quartet (J 10 and 7 3 Hz) at τ 6 46 was assigned to H-4 The observed first-order coupling constants are clearly in accord with the *C1* conformation of the D-glucopyranose ring The H-5 resonance was observed at τ 5 8 as an octet with an increase in intensity of the limbs towards the centre of the multiplet The general structure of this multiplet was reminiscent of the

AB part of an ABX system, but integration showed it to be due to a single proton A similar resonance was observed in the bromo and iodo derivatives, but, in these cases, it was partly overlapped with other resonances

TABLE I

CHEMICAL SHIFTS (τ VALUES) AND FIRST-ORDER COUPLING CONSTANTS (Hz) AT 100 MHz

Compound	Chloro-amine (12)	Bromo-amine (16)	Iodo-amine (18)
H-1	5 3 d[a]	5 3 d	5 32 d
H-2	7 12 q	7 02 q	6 94 q
H-3	6 10 t	5 96 t	5 86 t
H-4	6 46 q	—	—
H-5	5 80 cm	5 77 cm	5 78 cm
H-6	—	—	—
OMe	6 65 s	6 64 s	6 62 s
NH_2	8 40 s	8 38 s	8 40 s
$J_{1,2}$	3 5	3 5	3 5
$J_{2,3}$	10 0	10 1	10 0
$J_{3,4}$	10 0	10 0	10 0
$J_{4,5}$	7 3	—	—

[a]s = singlet, d = doublet, t = triplet, q = quartet, cm = complex multiplet

Previous results[11,12] on the ring-opening of the α- and β-anomers of derivatives of the D-*allo*-epimine (**7** for the α-anomer) suggested that the *N*-benzoyl derivatives were alone in being anomalous by virtue of diequatorial ring-opening Our results obtained with the free epimine were therefore of some note, because they constitute the first examples of diequatorial ring-opening of the epimine **7**. We have therefore investigated the action of ammonium chloride on the *N*-substituted *allo*-epimines in order to assess whether the anomaly was a function of the reagent or of the substrate, and find that the *N*-benzoyl, *N*-acetyl, and, *N*-2,4-dinitrophenyl derivatives (**9**, **8**, and **11**) each gives mixtures of the *gluco*- and *altro*-isomers, in which the latter preponderated Thus, the *N*-benzoylepimine **9** gave a mixture of two chloro derivatives, the minor component (15%) of which was shown to be the *gluco*-isomer by comparison with the *N*-benzoyl derivative **14** derived from the amino-chloro-glucoside **12** The syrupy, major product (35%), isolated after chromatography, was identical with the chloro derivative formed by the action of hydrochloric acid on the *N*-benzoylepimine **9**. It was best characterised by acid hydrolysis to give crystalline methyl 3-benzamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (**41**), which could be synthesised from the known[13] methyl 3-acetamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (**42**) by acid hydrolysis followed by *N*-benzoylation

The action of ammonium chloride on the *N*-acetylepimine **8** gave mainly (42%) the known altropyranoside **23**, together with a small proportion of the glucopyranoside **13** Likewise, the *N*-2,4-dinitrophenyl derivative **11** afforded mainly the altropyranoside **25**, but the overall recovery of products was only 40%. Hence,

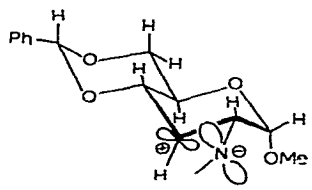
it appears that the pattern by which ammonium halides react with the *allo*-epimine and its derivatives is quite different from that for a mixture of sodium azide and ammonium chloride, where the azide anion is the predominant nucleophile

The above results suggest that the reported[11] failure to characterise a product when the *N*-acetylepimine **8** was heated under reflux with a mixture of sodium azide and ammonium chloride in *N*,*N*-dimethylformamide for 3 h may well have been due to ready de-*N*-acetylation under basic conditions We have now found that, with a shorter reaction time (5–20 min), the *N*-acetylepimine **8** undergoes *trans*-diequatorial ring-opening to give methyl 2-acetamido-3-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside **21**, but that extensive de-*N*-acetylation of the epimine also occurs Since the free epimine is less reactive towards azide than is the *N*-acetyl derivative, the epimine **7** was obtained as a side product. The *gluco*-configuration of the azido-pyranoside was shown by its synthesis[23] from methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-allopyranoside by replacement with sodium azide in *N*,*N*-dimethylformamide. The preparation of the 3-azide **21** from the *N*-acetylepimine **8** was not satisfactory, because the yields of 20–30% could not be maintained on a larger scale

The *N*-mesylepimine underwent reaction with sodium azide–ammonium chloride in *N*,*N*-dimethylformamide to give a crystalline azide identical with that obtained by mesylation of the known[11] methyl 3-amino-2-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-altropyranoside (**27**), hence, normal *trans*-diaxial ring-opening had occurred Surprisingly, the same azide was obtained by the action of sodium azide on methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-2-methanesulphonamido-α-D-glucopyranoside (**5**) This observation can be explained by initial ring closure of compound **5** to the *N*-mesylepimine **10**, followed by *trans*-diaxial ring-opening This further illustrates the ease with which the sulphonamido-sulphonate system undergoes cyclisation to the epimine

The pattern of ring-opening of the *allo*-epimine and its derivatives is confusing and unpredictable, and it is hard to account for the results An S_N2 process would favour the 2,3-*trans*-diaxial arrangement, whereas the products arising from an S_N1 mechanism would be governed by the relative stabilities of the two possible carbonium ions, and 2,3-*cis*, as well as 2,3-*trans*, products might be expected The tentatively suggested[11], diequatorial ring-opening of the *N*-benzoylepimine by prior isomerisation to the oxazoline [namely, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3,2-(2-phenyl-1-oxa-3-azaprop-2-eno)-α-D-allopyranoside], followed by ring-opening by azide at C-3 to give the glucopyranoside, is not valid, since the oxazoline derivative, which can be easily prepared from compound **1** by the action of alkali, is quite stable towards azide in boiling *N*,*N*-dimethylformamide, Dr Guthrie has informed us that he has reached the same conclusion. An S_N1 reaction would involve initial heterolysis of a C–N bond to give a carbonium ion at either C-2 or C-3, whichever is the more favourable. There are two factors which would favour heterolysis of the C-3–N bond. Firstly, the electron-withdrawing effect of the anomeric acetal group would have a destabilising effect upon a positive charge situated at C-2, but not at C-3 Secondly,

cleavage of the C-3–N bond would give the C-3 carbonium ion **43** having the negatively charged nitrogen in an equatorial position Molecular models show that, if both charged centres were in a state of sp^2-hybridisation, the unoccupied *p*-orbital at C-3 and the occupied *p*-orbital on nitrogen could become parallel and that this could result in a certain amount of delocalisation by $p\pi$ overlap This overlap would be enhanced if deformation of the C-2–N bond occurred to allow C-3 and the nitrogen atom to become closer This transition state could be envisaged as an intramolecular



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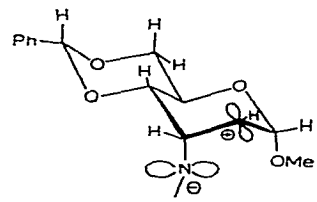

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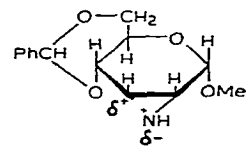

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ion-pair **45**, which would explain why the *trans* and not the *cis* product is obtained If cleavage of the C-2–N bond occurred to give the C-2 carbonium ion **44**, molecular models suggest that no $p\pi$ overlap could occur, although some $p\sigma$ overlap might be possible Stabilisation of carbonium ions by orbital overlap with a β-π system has been previously proposed[24] for the homoallylic system

The foregoing discussion merely explains how these *trans*-diequatorial products may arise, but does not explain why ring-opening is S_N2 in some cases and S_N1 in others Obviously, it would be dangerous to attempt an explanation of this duality of mechanism from our qualitative results

No "anomalous" diequatorial ring-openings have been observed for the corresponding *manno*-epimine **30** This is, perhaps, not surprising, since it would require the formation of the C-2 carbonium ion, which, as previously stated, would be destabilised by the adjacent, electron-withdrawing acetal group

EXPERIMENTAL

All evaporations were effected under diminished pressure, optical rotations were determined for chloroform solutions, unless otherwise stated, and melting points were determined on a Kofler micro-heating stage and are uncorrected Thin-layer chromatography was performed on either Silica Gel G (Merck) or Whatman Chromedia SG 41, and components were located as brown-black spots by spraying with 10% sulphuric acid in ethanol and heating above 120° Silica gel (Hopkins and Williams, or Davison) was utilised for column chromatography

Methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-O-tosyl-α-D-glucopyranoside (**3**). — A solution of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[9] (**2**) (50 g) in pyridine (700 ml) was treated with toluene-*p*-sulphonyl chloride (75 g) and stored for 4 days at room temperature, when t l c (chloroform–ether, 1 1) indicated that reaction was almost complete The reaction mixture was

poured into ice–water, and the crystalline precipitate was recrystallised from ethanol containing a little chloroform to give the product (52 4 g, 75%), m p 179–184° (decomp) A further recrystallisation from ethanol gave material having m p. 193–195° (decomp), $[\alpha]_D$ +30° (Found C, 62 1; H, 5 4, N, 2 6 $C_{28}H_{29}NO_8S$ calc C, 62 3, H, 5 4, N, 2 6%)

Methyl 2-amino-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**4**). — A solution of the amide **2** (10 g) in 95% 2-methoxyethanol (100 ml) containing sodium hydroxide (8 g) was heated under reflux for 4 h, and was then cooled, diluted with water, and extracted three times with chloroform The combined extracts were washed with water, dried ($MgSO_4$), and evaporated Recrystallisation of the residue from ethanol gave needles (4 8 g, 62%), m p 175°, $[\alpha]_D$ +112 5° (*c* 1 0) (Found C, 60 0, H, 6 9, N, 5.1 $C_{14}H_{19}NO_5$ calc C, 59 8, H, 6 8, N, 5 0%)

Starting material was recovered when the preparation was repeated by using 2-methoxyethanol without added water

Methyl 4,6-O-benzylidene-2-deoxy-2-methanesulphonamido-3-O-methanesulphonyl-α-D-glucopyranoside (**5**) — Methanesulphonyl chloride (0 9 ml) was added dropwise to a solution of 0 5 g of the amine **4** in pyridine (4 ml), and the reaction mixture was kept overnight at 4° Addition of ice–water to the mixture gave a crystalline product which was recrystallised from ethanol to give compound **5** as needles (0 62 g, 68%), m p 207 5–208 5°, $[\alpha]_D$ +47° (*c* 1 0) (Found C, 44 1, H, 5 7, N, 3 2, S, 14 2 $C_{16}H_{23}NO_9S_2$ calc C, 43 9, H, 5 5, N, 3 2, S, 14 6%)

Methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (**7**) — (*a*) The sulphonate **3** (10 g) was added to a solution of sodium (1 5 g) in isopropyl alcohol (1 litre) at room temperature The solution was heated under reflux on a water bath for 1 h, during which time sodium toluene-*p*-sulphonate was precipitated After filtration, the solution was evaporated to dryness, and the residue was partitioned between water and chloroform The aqueous layer was extracted with a further portion of chloroform, and the combined chloroform solutions were washed twice with water, dried (Na_2SO_4), and evaporated to a chromatographically pure syrup which rapidly crystallised (crude yield, 4 4 g, 90%) Recrystallisation from ethyl acetate–light petroleum gave the epimine **7** as needles, m p 154–157° (after crystal transitions at 125 and 143°), $[\alpha]_D$ +148° (*c* 0 4) It was identical (mixed m p , i r spectrum, and chromatography) with authentic material[4]

(*b*) The sulphonate **3** (0 2 g) was dissolved in tetrahydrofuran (10 ml) and treated slowly with lithium aluminium hydride (0 2 g) The mixture was kept for 24 h at room temperature and processed, as described previously[9], to give epimine **7** (52 mg, 60%), m p 151–152°

(*c*) Methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-glucopyranoside[9] (**1**, 60 g) was dissolved in a solution of sodium hydroxide (32 g) in 95% aqueous 2-methoxyethanol (600 ml), and the solution was heated under reflux for 2 h It was then diluted with water and extracted with chloroform (3 × 200 ml) The chloroform extract, after drying ($MgSO_4$), was evaporated, and the residue was recrystallised from ethyl acetate–light petroleum to give the epimine **7** as needles

(31 g, 92%), m p. 141–145°, $[\alpha]_D$ +147° (*c* 1.0) The product was identical with the lower-melting form of the epimine obtained by Buss *et al*[4], who reported m p 143–145°, $[\alpha]_D$ +147°.

Methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-(methanesulphonylepimino)-α-D-allopyranoside (**10**) — (*a*) To a solution of 0 1 g of the 3-*O*-mesyl-2-sulphonamido-glucoside **5** in 95% aqueous 2-methoxyethanol (2 ml) was added sodium acetate (0 1 g), and the mixture was heated under reflux for 1 h Addition of water then gave a crystalline product (65 mg, 80%) which was recrystallised from ethanol to give the methanesulphonylepimine **10**, m p 161–163°, $[\alpha]_D$ +121° (*c* 1 0) (Found C, 52 5, H, 5 9; N, 4 1, S, 9 2 $C_{15}H_{19}NO_6S$ calc C, 52 6, H, 5 6, N, 4 1, S, 9 4%)

(*b*) The epimine **7** (0 1 g) was methanesulphonylated, in the usual way, to give, after recrystallisation from ethanol, the *N*-mesyl derivative **10** (0 1 g, 90%), m p 161 5–162 5°, $[\alpha]_D$ +121° (*c* 1 0)

Ring-opening reactions of methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside (**7**) *and its derivatives with ammonium halides* — (*a*) *The action of ammonium chloride on the epimine* To a solution of epimine **7** (1 g) in *N*,*N*-dimethylformamide (50 ml) was added ammonium chloride (0 4 g), and the mixture was heated under reflux for 1 h The solution was evaporated to dryness, and a solution of the residue in methanol was passed through a column of Amberlite IRA-400 (OH^- form) resin The eluate was evaporated to dryness, and the residue was recrystallised from isopropyl alcohol to yield methyl 2-amino-4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**12**), (0 5 g, 40%), m p 155–162°. Two recrystallisations from ethanol–light petroleum yielded a sample having m p 162° (very slow heating), $[\alpha]_D$ +42° (*c* 1 3) More-rapid heating caused partial melting at 155°, with a slow crystal transition to a form melting at 162° Extremely slow heating above 150° allowed the transition to occur without melting, to give a sharp m p of 162° (Found C, 55 9, H, 5 9, Cl, 12 0, N, 4 7 $C_{14}H_{18}ClNO_4$ calc C, 56 1, H, 6 0, Cl, 11.8, N, 4 7%)

N-Acetylation of the chloro-amine **12** (30 mg) in ethanol (0 4 ml) with acetic anhydride (0 04 ml) gave methyl 2-acetamido-4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**13**) (from ethanol) (80%), subl 293°, $[\alpha]_D$ +6° (*c* 0.4) (Found C, 56 3, H, 6 0, Cl, 10 6, N, 4 1 $C_{16}H_{20}ClNO_5$ calc C, 56 2, H, 5 85, Cl, 10 4, N, 4 1%)

Similarly the *N*-benzoylepimine **14** was prepared in 70% yield and had m p 273–274° (from ethanol), $[\alpha]_D$ +36° (*c* 0 5) (Found C, 62 4, H 5 5, Cl, 8.7, N, 3 6 $C_{21}H_{22}ClNO_5$ calc C, 62 5, H, 5 45, Cl, 8 8, N, 3 5%)

The *N*-2,4-dinitrophenyl derivative **15**, prepared in the usual way[13], had m p 301–302° (from chloroform–ethanol), $[\alpha]_D$ −69° (*c* 0 4) (Found C, 51 4, H, 4 5, N, 9 0 $C_{20}H_{20}ClN_3O_8$ calc C, 51 6, H, 4 3, N, 9 0%)

(*b*) *The action of ammonium bromide on the epimine* A solution of 1 g of the epimine **7** in *N*,*N*-dimethylformamide (10 ml) was heated for 20 min at 130° with ammonium bromide The addition of water to the reaction mixture gave a crystalline solid (0 7 g, 52%), recrystallisation of which from ethanol–light petroleum gave

methyl 2-amino-4,6-*O*-benzylidene-3-bromo-2,3-dideoxy-α-D-glucopyranoside (**16**) as needles, m p. 150–150 5°, $[\alpha]_D$ +15° (*c* 0 74) (Found C, 49 0; H, 5.4; N, 4 1. $C_{14}H_{18}BrNO_4$ calc . C, 48.9, H, 5 2, N, 4 1%)

The *N*-acetyl derivative **17**, obtained as above, was recrystallised from *N*,*N*-dimethylformamide, and decomposed at *ca.* 275° without melting; $[\alpha]_D$ +31° (*c* 0 5, *N*,*N*-dimethylformamide) (Found C, 49 8, H, 5 3, N, 3.6 $C_{16}H_{20}BrNO_5$ calc · C, 49 9, H, 5 2, N, 3 6%)

(*c*) *The action of ammonium iodide on the epimine* The epimine **7** (1 g) was treated, as above, with ammonium iodide The product separated out as a gel that solidified when filtered Recrystallisation from ethanol gave methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-iodo-α-D-glucopyranoside (**18**) (0 8 g, 54%), m p 138–140°, $[\alpha]_D$ −20° (*c* 0 5) (Found C, 43 4, H, 4 4, N, 3 5 $C_{14}H_{18}INO_4$ calc C, 43 0, H, 4 6; N, 3 6%)

The *N*-acetyl derivative **19**, obtained in the usual way, had m p 271° (decomp) (from chloroform), $[\alpha]_D$ +4° (*c* 0 36, *N*,*N*-dimethylformamide) (Found C, 44 1, H, 4 7, N, 3 2 $C_{16}H_{20}INO_5$ calc · C, 44 4, H, 4 6, N, 3 2%)

(*d*) *The action of ammonium chloride on the* N-*acetylepimine* **8** To a solution of methyl 2,3-(acetylepimino)-4,6-*O*-benzylidene-2,3-dideoxy-α-D-allopyranoside (**8**) (0 5 g) in *N*,*N*-dimethylformamide (50 ml) was added ammonium chloride (0 2 g), and the mixture was heated under reflux for 2 h The solution was evaporated to dryness, and the syrupy residue was partitioned between water and chloroform The aqueous layer was extracted with a second portion of chloroform, and the combined organic layers were washed twice with water and dried (Na_2SO_4) T l c (chloroform–ether, 1 1) indicated the presence of one predominant, fast-moving component, a small proportion of a slightly slower moving component, and two further components near the starting line The mixture was chromatographed on a column of silica gel with chloroform–ether (1·1) as eluant, and the two fast-moving components were isolated

The major component, obtained as a syrup (0 236 g, 42%), was shown to be methyl 3-acetamido-4,6-*O*-benzylidene-2-chloro-2,3-dideoxy-α-D-altropyranoside (**23**) by comparison with an authentic sample[13], and was characterised as follows A solution of the syrup in acetone (15 ml) and conc hydrochloric acid (0 2 ml) was heated under reflux for 5 min Excess of solid sodium hydrogen carbonate was added, and the solution was filtered, and evaporated to an impure, yellow syrup which could not be crystallised The main component was obtained pure after chromatography on a column of silica gel, and was crystallised from ethyl acetate Recrystallisation from ethyl acetate yielded methyl 3-acetamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (**42**) (18 mg), m p 135–137°, lit [13], m p 136–138°

The second component, isolated in small yield from the column, was recrystallised from isopropyl alcohol to give methyl 2-acetamido-4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**13**) identical (i r spectrum and sublimation temp) with the samples prepared from the chloro-amine **12** (see above), and by the action of hydrochloric acid in acetone on the *N*-acetylepimine **8** (see below)

(*e*) *Action of ammonium chloride on the* N-*benzoylepimine* **9** To a solution of the *N*-benzoylepimine (0 5 g) in *N*,*N*-dimethylformamide (50 ml) was added ammonium chloride (0 2 g), and the mixture was heated under reflux for 1 h and processed as described for the *N*-acetylepimine above T l c (chloroform) showed the presence of two fast-moving components, coincident with compounds **24** and **14**, respectively Evaporation of the chloroform solution, with recrystallisation of the residue from ethanol–ether, yielded methyl 2-benzamido-4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**14**) (85 mg), m p 273–274°, identical (i r. spectrum and mixed m p) with the product prepared above from compound **12**

The mother liquors were subjected to column chromatography to yield methyl 3-benzamido-4,6-*O*-benzylidene-2-chloro-2,3-dideoxy-α-D-altropyranoside (**24**) as a syrup (190 mg), $[\alpha]_D$ +68° (*c* 0 7) (Found C, 60 7, H, 5 5, N, 3 5 $C_{21}H_{22}ClNO_5$ calc C, 62 5, H, 5 5, N, 3 6%)

(*f*) *Action of ammonium chloride on the* (*2,4-dinitrophenyl*)*epimine* (**11**) To a solution of compound **11** (100 mg) in *N*,*N*-dimethylformamide (5 ml) was added ammonium chloride (50 mg), and the mixture was heated under reflux for 1 5 h T l c (ether–light petroleum, 1 1) indicated the presence of two products, one being on the starting line The solution was evaporated (to *ca* half volume) and poured into water After storage for 1 h at *ca* 4°, the precipitate was separated by centrifugation, washed with water, and then shaken with a 2 1 mixture of acetone–ethanol (10 ml) T l c indicated that the extract contained largely the fast-moving component, and the solid residue consisted largely of the compound which failed to move during t l c

The solid residue was recrystallised from chloroform–ethanol to yield methyl 4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-2-(2,4-dinitrophenylamino)-α-D-glucopyranoside (**15**) (12 mg, 11%), m p 300–302°, $[\alpha]_D$ −69° (*c* 0 4), identical (i r spectrum and mixed m p) with the product derived from compound **12**

The extract was evaporated to dryness, and the residue was recrystallised from isopropyl alcohol to yield methyl 4,6-*O*-benzylidene-2-chloro-2,3-dideoxy-3-(2,4-dinitrophenylamino)-α-D-altropyranoside (**25**) (31 mg, 29%), slightly contaminated with the above isomer. A pure sample was obtained by extraction with ethanol, giving granular crystals m p 190–193°, $[\alpha]_D$ −35° (*c* 0 5) (Found C, 51 7, H, 4 5, N, 8 9 $C_{20}H_{20}ClN_3O_8$ calc C, 51 6, H, 4 3, N, 9 0%)

The action of hydrochloric acid on (*a*) *methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-*α*-D-mannopyranoside* (**30**) — (*i*) A solution of the epimine (0 57 g) in acetone (20 ml) was cooled in an acetone–solid CO_2 bath, and 4N hydrochloric acid (1 ml) was added The mixture was then allowed to warm up to room temperature, when fine needles of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside hydrochloride (0 4 g, 62%) separated, m p 153–165° (decomp) (Found C, 56 5, H, 6 3, Cl, 11 5; N, 4 6 $C_{14}H_{18}ClNO_4$ calc C, 56 1, H, 6 0, Cl, 11 8, N, 4 7%). The hydrochloride was very soluble in water, giving an acidic solution, but was not very soluble in ethanol from which it could, with care, be recrystallised It was indefinitely stable in the dry, crystalline state, but was unstable in solution Acetylation of

the hydrochloride, in the usual way, gave a quantitative yield of the *N*-acetylepimine **31**, and treatment with aqueous alkali gave the free epimine **30**

(*ii*) The epimine (14 g) was dissolved in acetone (250 ml), and conc hydrochloric acid (10 ml) was added The hydrochloride was precipitated initially, but, on being shaken vigorously for 15 min, this was transformed into an oil, and t l c (chloroform–methanol, 4 ·1) indicated the presence of a single product The reaction mixture was diluted with water to dissolve the oily product, sodium hydrogen carbonate (15 g) was then added cautiously in small portions, and the solution was extracted once with ether to remove benzaldehyde and evaporated to dryness The residue was extracted with hot ethyl acetate (3 × 200 ml), and the combined extracts were concentrated to *ca* 125 ml, when scratching induced crystallisation The product, methyl 2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (**32**), was usually obtained, initially, as an unstable hydrate, m p 115–117°, ν_{max} *ca* 1650 cm^{-1} When the product was kept at room temperature for several days or dried *in vacuo* for 2 h at 100°, it gave the anhydrous product (6 4 g, 68%), m p 150–153°, $[\alpha]_D$ +107° (*c* 1, water) (Found· C, 47 9, H, 7 35, N, 7 95 $C_7H_{13}NO_4$ calc C, 47 9, H, 7 4, N, 8 0%)

The *N*-acetylepimine **33**, m p 124–125°, $[\alpha]_D$ +68° (*c* 1 2, water), was prepared, by the action of acetic anhydride in ethanol, in 94% yield (Found C, 49 6, H, 6 95, N, 6 35 $C_9H_{15}NO_5$ calc. C, 49 7, H, 6 9, N, 6 45%)

(*b*) *Methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside* (**7**) — (*i*) The epimine (3 5 g) in acetone (60 ml) was treated with conc hydrochloric acid (2 5 ml), and the mixture was shaken for 30 min at room temperature The crystalline product was filtered off and washed with acetone, to give methyl 2,3-dideoxy-2,3-epimino-α-D-allopyranoside hydrochloride (**29**) (2 24 g, 80%), m p 118–122°, $[\alpha]_D$ +134° (*c* 2, water) Recrystallisation from methanol–ether gave the hydrochloride, m p 120–122° (Found C, 39 9, H, 6 7, N, 6 7 $C_7H_{14}ClNO_4$ calc C, 39 7, H, 6 6, N, 6 6%) The hydrochloride was stable in the crystalline state for several months, but underwent a slow transformation into a crisp, amorphous solid

(*ii*) When a cooled solution of the epimine (50 mg) in acetone (0 5 ml) was treated with one equivalent of hydrochloric acid in acetone (0 16 ml), methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-α-D-allopyranoside hydrochloride crystallised immediately (46 mg, 81%), m p 108–112°, $[\alpha]_D$ +137° (*c* 1, water) (Found C, 55 9, H, 6 2, Cl, 11 8, N, 4 7 $C_{14}H_{18}ClNO_4$ calc C, 56 1, H, 6 1, Cl, 11 8, N, 4 7%)

(*c*) *Methyl 2,3-(acetylepimino)-4,6-O-benzylidene-2,3-dideoxy-α-D-allopyranoside*[13] (**8**) — To a solution of the *N*-acetylepimine **8** (5 g) in acetone (250 ml), conc hydrochloric acid (1 36 ml, 1 equiv) was added After 3 h at room temperature, the solution was evaporated to a syrup, which was co-concentrated with water and partitioned between water and chloroform T l c (chloroform–ether, 1 1) indicated the presence of a very small amount of a slower moving product, in addition to the expected chloro-amide **23** Elution from a column of silica gel, with chloroform–ether (1 1), yielded the syrupy, faster-moving product (4 5 g, 80%) shown by its i r spectrum to be methyl 3-acetamido-4,6-*O*-benzylidene-2-chloro-2,3-dideoxy-α-D-altropyranoside[13] (**23**) and by conversion[13] into the crystalline methyl 3-acetamido-

2-chloro-2,3-dideoxy-α-D-altropyranoside (**42**) (see above) Distillation afforded an analytical sample (Found C, 56 2, H, 5.8, N, 3.9. $C_{16}H_{20}ClNO_5$ calc.· C, 56 2, H, 5 85, N, 4 1%)

The minor product (0 156 g, 3%) was methyl 2-acetamido-4,6-*O*-benzylidene-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**13**), which sublimed at 293°, and had $[\alpha]_D$ +6° (*c* 0 4) The infrared spectrum was identical with that of the *N*-acetyl derivative of the chloro-amine **12** described above

(*d*) *Methyl 2,3-(benzoylepimino)-4,6-O-benzylidene-2,3-dideoxy-α-D-allopyranoside* (**9**) — (*i*) Conc hydrochloric acid (0 454 ml) was dissolved in acetone (10 ml), and 1 ml (1 equiv) of this solution was added to a solution of the *N*-benzoylepimine **9** (200 mg) in acetone (9 ml) T.l c (chloroform–ether, 1 1) indicated that reaction had ceased after *ca* 2 h, the solution then contained a little starting material, together with one fast- and one slow-moving component After 3 h, the solution was evaporated, and co-concentrated with water The residue was fractionated on a column of silica gel, with chloroform–ether (1 1) as eluant, to give the faster-moving, syrupy chloroamide **24**, which was dissolved in acetone (1 5 ml) to which conc hydrochloric acid (0 1 ml) was then added After 30 min, the solution was neutralised (Ag_2CO_3), and evaporated to a syrup Benzaldehyde was removed by co-concentration with water, followed by co-concentration with ethanol The resulting syrup crystallised spontaneously to yield methyl 3-benzamido-2-chloro-2,3-dideoxy-α-D-altropyranoside (**41**) (7 mg), m p 154–157° Recrystallisation from ethanol–light petroleum gave a sample identical (mixed m p and i r spectrum) with (*i*) the slower moving component isolated from the column by elution with acetone, (*ii*) the product obtained below from the action of an excess of hydrochloric acid on the *N*-benzoylepimine **9** and (*iii*) the product obtained from the corresponding *N*-acetyl derivative **42** by deacetylation, followed by *N*-benzoylation

(*ii*) To a solution of the *N*-benzoylepimine **9** (1 g) in acetone (40 ml), an excess of conc hydrochloric acid (0 6 ml) was added, and the solution was heated under reflux for 10 min An excess of solid sodium hydrogen carbonate was added, and the solution was filtered and evaporated to a crystalline residue The solid was extracted with chloroform, and the extract was evaporated to a residue (0 47 g, 55%) that was recrystallised from ethanol–light petroleum to yield methyl 3-benzamido-2-chloro-2,3-dideoxy-α-D-altropyranoside as needles, m p 159–160°, $[\alpha]_D$ +22° (*c* 0 4) (Found C, 53 3, H, 5 75, Cl, 10 8, N, 4 3 $C_{14}H_{18}ClNO_5$ calc C, 53 2, H, 5 7, Cl, 11 25, N, 4 4%)

Methyl 3-amino-2-chloro-2,3-dideoxy-α-D-altropyranoside (**39**) *and its N-benzoyl derivative* (**41**) — Methyl 3-acetamido-2-chloro-2,3-dideoxy-α-D-altropyranoside[13] (**42**) (1 g) was heated for 1 h at 100° with N hydrochloric acid (2 ml) The solution was evaporated to a syrup which was co-concentrated twice with ethanol The resulting syrup crystallised on the addition of isopropyl alcohol, yielding compound **39** hydrochloride (0 58 g, 60%), m p 185–190° (decomp) Recrystallisation from isopropyl alcohol–light petroleum gave granular crystals, m p 192–194° (decomp.),

$[\alpha]_D$ +72° (*c* 0 8, water) (Found C, 34 1, H, 6 0, Cl, 28 4, N, 5 7 $C_7H_{15}Cl_2NO_4$ calc C,33 9, H, 6.0, Cl, 28 6; N, 5 6%)

A solution of the above hydrochloride (100 mg) in water was passed through a column of Amberlite IRA-400 (OH^- form) and evaporated Recrystallisation of the residue from isopropyl alcohol gave the free amine **39** (64 mg, 75%), m p 128–130°, $[\alpha]_D$ +87° (*c* 0 5, water) A further recrystallisation gave an analytical sample, m p 132–134° (Found C, 39 7; H, 6 9; N, 6 55 $C_7H_{14}ClNO_4$ calc C, 39.7; H, 6 6, N, 6 6%)

To a solution of the free amine (20 mg) in ethanol (1 ml), benzoic anhydride (25 mg) was added After 1 h at room temperature, the solution was evaporated to a syrup which was partitioned between water (5 ml) and ether (5 ml) The organic layer was extracted with a further portion of water, and the combined aqueous layers were washed with ether Evaporation of the aqueous solution, with recrystallisation of the residue from ethanol–light petroleum, yielded the chloro-amide **41** (14 mg, 47%), m p 158–160°, identical (i r spectrum and mixed m.p) with samples prepared above.

Acid hydrolysis of 4,6-O-benzylidene derivatives — (*a*) Compound **12** (500 mg) was dissolved in a mixture of acetone (10 ml) and chloroform (10 ml) Conc hydrochloric acid (1 ml) was added, and the mixture was shaken for 30 min , when the crystals that had formed were converted into an oil The mixture was evaporated to a syrup, and benzaldehyde was removed by co-concentration with water A solution of the resulting syrup in methanol was passed through a column of Amberlite IRA-400 (OH^- form) and evaporated Recrystallisation of the residue from ethyl acetate gave methyl 2-amino-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**34**) (200 mg, 57%), m p 127–128°, $[\alpha]_D$ +156° (*c* 1, water) (Found C, 39 5, H, 6 6, N, 6 8 $C_7H_{14}ClNO_4$ calc C, 39 7, H, 6 7, N, 6 6%)

(*b*) Compound **14** (0 1 g) was dissolved in a 1 1 mixture of chloroform and acetone (15 ml), and conc hydrochloric acid (0 4 ml) was added The mixture was shaken for 2 h at room temperature (an oil was initially deposited, but later crystallised) and then cooled in the refrigerator to give methyl 2-benzamido-3-chloro-2,3-dideoxy-α-D-glucopyranoside (**36**) (39 mg) The mother liquors were evaporated to dryness, and co-concentrated with water to remove benzaldehyde The residue was recrystallised from ethanol–light petroleum, giving a second crop (16 mg, total yield, 55 mg, 70%), m p 245–246° (decomp), $[\alpha]_D$ +136° (*c* 0,6 methanol) (Found C, 53 2, H, 5 9, Cl, 11 1, N, 4 6 $C_{14}H_{18}ClNO_5$ calc C, 53 2, H, 5 7, Cl, 11 25; N, 4 4%)

(*c*) A suspension of compound **17** (0 6 g) in a 1% solution of hydrogen chloride in methanol (25 ml) was stirred until a clear solution was obtained (*ca* 1 h) The neutralised ($PbCO_3$) mixture was evaporated to give methyl 2-acetamido-3-bromo-2,3-dideoxy-α-D-glucopyranoside (**37**), which, after recrystallisation from ethanol–light petroleum, gave needles (0 35 g, 76%), m p 185–186°, $[\alpha]_D$ +95° (*c* 0 5, water) (Found C, 36 4, H, 5 5; N, 4 5 $C_9H_{16}BrNO_5$ calc C, 36 2, H, 5 4, N, 4 7%)

(*d*) Compound **19** (0 6 g) was hydrolysed as in (*c*) to give (from ethanol–light

petroleum) methyl 2-acetamido-2,3-dideoxy-3-iodo-α-D-glucopyranoside (**38**) (0 4 g, 84%), m p 189°, $[\alpha]_D$ +83° (*c* 0 55, water) (Found C, 31 0, H, 4 6, N, 3 9 $C_9H_{16}INO_5$ calc C, 31 3, H, 4.6; N, 4 1%)

Methyl 2-azido-4,6-O-benzylidene-2,3-dideoxy-3-methanesulphonamido-α-D-altropyranoside (**28**) — (*a*) A solution of the 3-methanesulphonate **5** (80 mg) in *N,N*-dimethylformamide (1 ml) was heated under reflux with sodium azide (80 mg) for 10 min. Addition of water to the hot reaction mixture gave a brown solid, recrystallisation of which from ethanol gave white needles (60 mg, 65%), m p 147–150°, $[\alpha]_D$ +54.3° (*c* 1 0) (Found· C, 47 0, H, 5 2, N, 14 7, S, 8 6 $C_{16}H_{20}N_4O_6S$ calc C, 46 9, H, 5 2, N, 14.6; S, 8.6%)

(*b*) The methanesulphonylepimine **10** (80 mg) was treated with sodium azide (80 mg) and ammonium chloride (5 mg) in *N,N*-dimethylformamide, as above The product (60 mg, 65%), m p 147–150°, was identical with the product from (*a*) (i r spectra and mixed m p)

(*c*) Methyl 3-amino-2-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-altropyranoside[11] (**27**) (100 mg) was methanesulphonylated in the usual way to give compound **28** as needles (70 mg, 56%), m p 147–149°, identical with the product obtained in (*a*) and (*b*) above

The ring-opening of methyl 2,3-(acetylepimino)-4,6-O-benzylidene-2,3-dideoxy-α-D-allopyranoside (**8**) *with azide* — A solution of compound **8** (1 g) was heated under reflux with sodium azide (0 8 g) and ammonium chloride (0 4 g) in *N,N*-dimethylformamide (10 ml) for 5 min Addition of water to the hot solution caused the slow crystallisation of methyl 2-acetamido-3-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside (**21**) (0 35 g, 31%) Recrystallisation from ethanol gave needles, m p 255–256 5°, $[\alpha]_D$ +36° (*c* 1 0) (Found C, 54 85, H, 5 8, N, 16 25 $C_{16}H_{20}N_4O_5$ calc C, 55 2, H, 5 75, N, 16 1%) The identity of the azide was confirmed by comparison with a sample prepared by the action of sodium azide in *N,N*-dimethylformamide on methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-mesyl-α-D-allopyranoside[23]

After removal of the azide, the mother liquors were extracted with chloroform (2 × 30 ml), and the dried ($MgSO_4$) extracts were evaporated to dryness to give a syrup which crystallised from ethanol to give the *allo*-epimine[4] (**7**) (0 1 g, 12%), identified by comparison with an authentic sample[4]

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