623. *The Synthesis of Amino-sugars from Glycopyranosiduloses*

By P. M. Collins and W. G. Overend

A route to amino-sugars from partially protected glycopyranosides by sequential oxidation to the corresponding glycopyranosidulose, oximation, reduction of the oxime, and removal of protecting groups has been evaluated. In this way successful syntheses of L-ribosamine and 6-deoxy-L-talosamine (pneumosamine) have been effected. The steric course of the reduction stage is discussed. An intermediate addition compound, formed in the oximation, under mild conditions, of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose, has been isolated and its structure determined. The behaviour of glycopyranosiduloses in protic solvents has been examined and the results are discussed in the light of current ideas about the behaviour of ketones in similar solvents.

Although the well-known method for the preparation of amines from ketones has been used in cyclitol chemistry for the conversion of inososes into inosamines [1] it has not found much application in carbohydrate chemistry for the preparation of amino-sugars. In 1959 Lindberg and Theander [2] prepared two methyl 3-amino-3-deoxy-β-D-glycopyranosides with the *gluco*- and *allo*-configuration from methyl β-D-*ribo*-hexopyranosid-3-ulose oxime but without isolation of the intermediate labile oxime, and after the preliminary publication [3] of our work, Brimacombe and Cook [4] reported the preparation of L-rhamnosamine from methyl 6-deoxy-α-L-*arabino*-hexopyranosidulose. In the past, few oxo-sugars of this class have been available owing to the lack of satisfactory methods for their preparation and this has precluded a full investigation of their conversion into derivatives of amino-sugars. This obstacle has now been overcome [5] and glycopyranosiduloses are readily obtained. As a result we have examined this route to amino-sugars in more detail and, as the following examples illustrate, it seems that the sequence is both general and useful for obtaining amino-sugars.

Treatment of methyl 2,3-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (I) [6] with hydroxylamine hydrochloride and sodium hydroxide at 60° for 6 hr. gave the oxime (II) in high yield. Reduction of the oxime with either lithium aluminium hydride or hydrogen

[1] L. Anderson and H. A. Lardy, *J. Amer. Chem. Soc.*, 1950, **72**, 3141; L. Anderson, H. A. Lardy, and H. Straube-Rieke, *ibid.*, 1953, **75**, 694; E. L. May and E. Mosettig, *J. Org. Chem.*, 1949, **14**, 1137; H. E. Carter, R. K. Clark, B. Lytle, and G. E. McCasland, *J. Biol. Chem.*, 1948, **175**, 683.

[2] B. Lindberg and O. Theander, *Acta Chem. Scand.*, 1959, **13**, 1226.

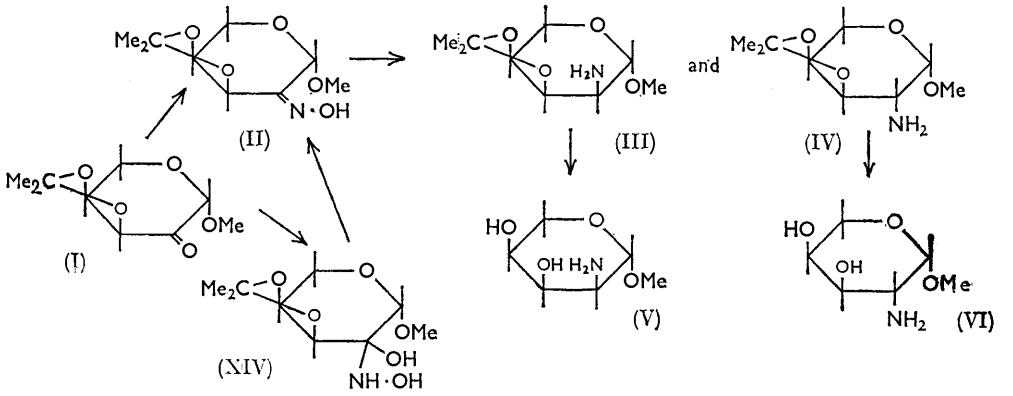
[3] P. M. Collins and W. G. Overend, *Chem. and Ind.*, 1963, 375.

[4] J. S. Brimacombe and M. C. Cook, *Chem. and Ind.*, 1963, 1281; *J.*, 1964, 2663.

[5] See O. Theander, *Adv. Carbohydrate Chem.*, 1962, **17**, 223; K. Heyns and H. Paulsen, *ibid.*, p. 169; W. G. Overend, *Chem. and Ind.*, 1963, 342; P. J. Beynon, P. M. Collins, and W. G. Overend, *Proc. Chem. Soc.*, 1964, 342.

[6] J. S. Burton, W. G. Overend, and N. R. Williams, *Chem. and Ind.*, 1961, 175; *J.*, 1965, 3433.

and Adams catalyst yielded a mixture of methyl 2-amino-2-deoxy-3,4-*O*-isopropylidene-β-L-pentosides, (III) and (IV). However, ammonium chloride was the only product identified when sodium amalgam was the reducing agent. Treatment of the mixture with salicylaldehyde afforded the known methyl 2-deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-L-riboside.[7] Mild acid hydrolysis of the mixture (III) and (IV) afforded a mixture



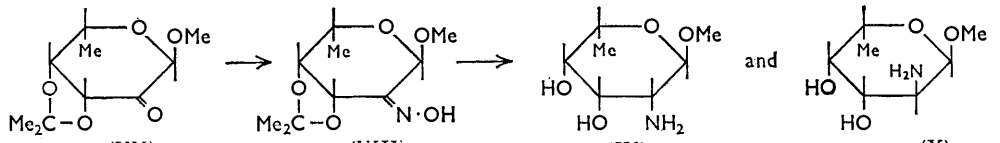
of epimeric amino-glycosides (V) and (VI). Paper-chromatographic analysis revealed that the epimers were present in the approximate ratio of 9 : 1 for both methods of reduction. Both reducing agents led to the *ribo*-isomer as the major component. By fractional crystallisation of the hydrolysate of the product from the lithium aluminium hydride reduction of the oxime (II) the major component, methyl 2-amino-2-deoxy-β-L-ribopyranoside hydrochloride (V, HCl), was isolated. A small amount of a less pure, but chromatographically homogeneous, isomer was obtained which after hydrolysis was indistinguishable chromatographically from D-arabinosamine hydrochloride. Presumably this amorphous material was methyl 2-amino-2-deoxy-β-L-arabinopyranoside (VI) hydrochloride. Acetylation of the mixture (III) and (IV) followed by acid hydrolysis gave a mixture of two amino-sugar hydrochlorides with mobilities on paper chromatograms identical with those obtained with the hydrochlorides of D-arabinosamine and D-ribosamine.[8] From the mixture, pure L-ribosamine hydrochloride was isolated.

An attempt was also made to obtain amino-glycosides by reduction of the hydrazone prepared from compound (I). Catalytic hydrogenation resulted in incomplete reduction but lithium aluminium hydride gave 40% of amino-glycosides. Chromatography of the deacetonated mixture indicated that the isomer distribution was similar to that obtained by reduction of the oxime (II).

When the oxime (VIII) of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosidulose (VII)[3] was reduced with lithium aluminium hydride and subsequently hydrolysed it gave a mixture of amino-glycosides (IX) and (X) isolated as their hydrochlorides. The components were present in the approximate ratio of 4 : 1. Fractional crystallisation afforded a pure sample of the major component and a small, less pure sample of the minor constituent. The same pure amino-glycoside hydrochloride could be isolated from the mixture resulting from the catalytic reduction of the oxime (VIII) and subsequent partial hydrolysis. It was the hydrochloride of methyl 2-amino-2,6-dideoxy-α-L-talopyranoside (IX) which could be converted into 2-amino-2,6-dideoxy-L-talose (6-deoxy-L-talosamine) hydrochloride.[9] In 1961 Barker *et al.*[10] described the isolation of two

[7] M. L. Wolfrom, F. Shafizadeh, and R. K. Armstrong, *J. Amer. Chem. Soc.*, 1958, **80**, 4885.
[8] See R. Kuhn and G. Baschang, *Annalen*, 1959, **628**, 193.
[9] See J. S. Brimacombe and M. J. How, *Chem. and Ind.*, 1962, 1382; *J.*, 1962, 5037 for constants of the D-isomer.
[10] S. A. Barker, J. S. Brimacombe, M. J. How, M. Stacey, and J. M. Williams, *Nature*, 1961, **189**, 303.

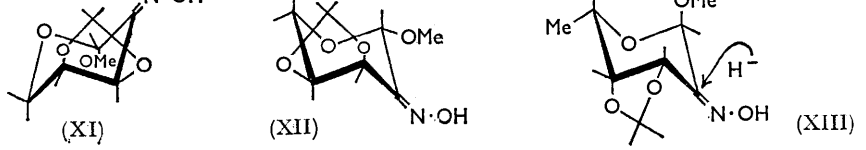
amino-sugars from a hydrolysate of type V *Pneumococcus* capsular polysaccharide. These were identified as 2-amino-2,6-dideoxy-L-talose(pneumosamine) and 2-amino-2,6-dideoxy-L-galactose (L-fucosamine) [amino-sugar (X)]. Neither amino-sugar had been found previously in Nature and the former was hitherto unknown. Our product had physical



(VII) (VIII) (IX) (X)

constants which agreed with those reported for pneumosamine hydrochloride and so the reactions outlined above constitute a synthesis of this naturally-occurring amino-sugar.

The steric course of reductions of oximes is less well documented than is the case for ketones. Indications are that they are similar [1,2] and our results support this. An oxime and the endocyclic ketone from which it is derived would have similar stereochemistry and in hydrogenations their approach to the catalyst surface should be the same (see Collins and Overend [11] for a discussion of this point). Consequently, the amino-group formed on reduction of the oxime will be axially disposed (as is the hydroxyl group formed by hydrogenation of the ketone) [12] when the ring conformation of the product is the same as that of the parent oxime (or ketone). Hence, the formation predominantly of an amino-glycoside with the L-*talo*-configuration on catalytic reduction of the oxime (VIII) is explicable on the same basis as the formation of a 6-deoxy-L-taloside by reduction of compound (VII).[3,11] As the chair conformations (XI) and (XII) of the oxime (II) have similar stabilities it is difficult to predict which conformer undergoes reduction, although a product with the L-*ribo*-configuration would indicate (XI) as the form being reduced. In the lithium aluminium hydride reduction of the oxime (VIII) to give a product with the L-*talo*-configuration, the reagent must attack the oxime as in (XIII) to give an axial amino-group since attack from the other side of the molecule is rendered unfavourable by the β-axial grouping at C-4. Again this is analogous to the formation of a 6-deoxy-L-talo-



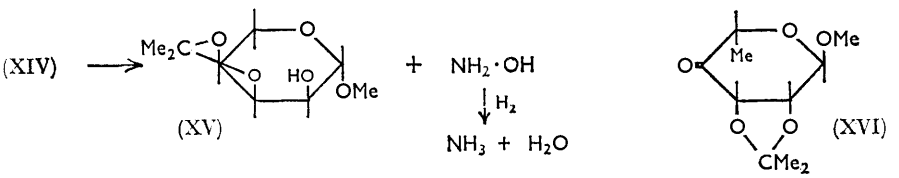
(XI) (XII) (XIII)

side by similar reduction of the glycopyranosidulose (VII).[3] In conformation (XI) hydride attack at the trigonal carbon atom must be from below if the product is to have the L-*ribo*-configuration. Attack from above is less favourable owing to the axial grouping at C-4. The metal hydride reduction of the parent substance (I) follows the same steric course.[13] However, owing to the doubts about the stabilities of the conformations of compounds (I) and (II) caution must be exercised in explanations of the steric course of their reactions and here attention is directed to the fact that metal hydride reduction of glycopyranosiduloses and their oxime derivatives follows the same steric pathway.

When the oximation of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (I) was carried out under mild conditions (room temperature, 1 hr.) a crystalline product (A), which differed from the oxime (II), was isolable. This substance, which had an elemental analysis consistent with a monohydrated oxime, was only moderately stable and after four days' storage under laboratory conditions its infrared (i.r.) spectrum indicated complete

[11] P. M. Collins and W. G. Overend, *J.*, 1965, 1912.
[12] D. H. R. Barton, *J.*, 1953, 1027.
[13] N. R. Williams, personal communication.

dehydration. When heated under reflux in ethanolic or aqueous solution for 30 min. it afforded pure oxime. Catalytic hydrogenation of compound (A) was very rapid, in contrast with the behaviour of the oxime. The hydrogen uptake was 1·7 mol. equiv. and the products were ammonia (0·6 mol. equiv.) and a nitrogen-free carbohydrate fragment which was shown to be methyl 3,4-*O*-isopropylidene-β-L-riboside (XV) by (i) paper-chromatographic and ionophoretic analysis of an acid hydrolysate which showed the presence of ribose but not of arabinose: the pyranosidulose (I) and its oxime (II) when similarly treated gave no identifiable pentoses; and (ii) isolation of the 2-*O*-tosyl derivative which was identical (mixed m. p., $[\alpha]_D$, i.r. spectrum) with a compound prepared by sequential catalytic reduction and tosylation of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (I). This reduction is known to give a product with the *ribo*-configuration. These observations support the view that compound (A) is the tetrahedral addition product with structure (XIV). It is considered that its reduction follows the scheme:



It was demonstrated that under similar conditions of catalytic hydrogenation hydroxylamine (1 mol. equiv.) decomposes in less than 10 min. There is a rapid uptake of hydrogen (*ca.* 0·5 mol. equiv.) and the production of ammonia (*ca.* 0·5 mol. equiv.). The apparent discrepancy in the stoicheiometry of the reactions with compound (A) and with hydroxylamine might be due to decomposition of hydroxylamine into nitrogen and water, which is known to occur in the presence of catalysts.[14]

Additional support for structure (XIV) is given by the nuclear magnetic resonance (n.m.r.) spectrum of compound (A). It demonstrates the presence in the molecule of eight protons besides those in the isopropylidene residue and the aglycone. Of these eight protons the three which occur at lowest field are readily exchanged for deuterium; they are present as a one-proton unresolved broad peak (δ 6·8—7·3 p.p.m.) and a two-proton unresolved broad peak (δ 4·8—5·6 p.p.m.) as might be expected for the group, HO·CR_2·NHOH. On the other hand, the spectrum of the oxime (II) reveals only six protons in the molecule in addition to those in the methyl groups. One of the protons at very low field (δ 11·6 p.p.m.) is exchanged for deuterium. This is characteristic of the C:N·OH group.

The configuration at C-2 in structure (XIV) cannot be defined. If addition to the carbonyl group in compound (I) follows the usual stereochemical course it would be expected that the product would have the *ribo*-configuration (with reference to the hydroxyl groups at C-2, C-3, and C-4. However, as compound (A) has been shown to give methyl 3,4-*O*-isopropylidene-β-L-riboside (XV) on treatment with hydrogen this would imply that the –NH·OH group is cleaved without inversion at C-2, but there is no evidence about the course of this reaction.

The unusual isolation of compound (A) was probably favoured by (i) the ease with which the trigonal carbon atom of some pyranosiduloses forms tetrahedral addition compounds (see below), and (ii) the basic conditions used for the oximation. It is noteworthy that Jencks and his co-worker [15] have shown by kinetic studies that addition products are intermediates in anil formation. Under acid conditions addition is rate-determining whereas under neutral or basic conditions dehydration becomes rate-controlling. Claims have also been made for the isolation of these intermediates in the case of aldehydes.

[14] J. W. Mellor, "Comprehensive Treaties on Inorganic and Theoretical Chemistry," Longmans, Green & Co., New York, 1928, vol. VIII, p. 287.

[15] W. P. Jencks, *J. Amer. Chem. Soc.*, 1959, **81**, 475; 1958, **80**, 4581; B. M. Anderson and W. P. Jencks, *ibid.*, 1960, **82**, 1773; see also W. P. Jencks in *Progr. Phys. Org. Chem.*, 1964, **2**, 71.

Although an intermediate was neither isolated nor sought in the oximation of the hexopyranosidulose (VII), in other experiments it was found that compounds (I) and (VII) behave similarly in protic solvents. Both exhibit mutarotation in ethanol (see Table 2). There is a decrease in intensity of the carbonyl absorption for solutions of the pyranosiduloses in methanol, ethanol, or aqueous dioxan (see Table 3). Paper chromatography of the alcoholic and aqueous solutions revealed the presence of another product in addition to the initial pyranosiduloses (see Table 4), and if [1-^{14}C]ethanol was used as solvent for compound (I) it was found that the new product was radioactive (see Table 5). In each case, an equilibrium was involved because removal of the solvent by rapid evaporation led to the recovery of the initial material only. The pyranosiduloses (I) and (VII) showed none of the above changes when in solution in carbon tetrachloride, nor did compound (I) in dimethyl sulphoxide. The observations do not support a keto–enol equilibrium but are consistent with changes leading to hemi-ketals, ketals, and *gem*-diols, and are in line with what has been noted [16,17] with other ketones in acidified ethanol in which hemi-ketal formation occurs. The dissociation constants for hemi-ketal decomposition with cyclohexanone and compounds (I) and (VII) are shown in Table 1 and indicate an increase in the stability of the ethyl hemi-acetal and *gem*-diol derived from either compounds (I) or (VII) compared with those from cyclohexanone. The amount of the *gem*-diol formed from cyclohexanone was too low to be measured.

TABLE 1

Dissociation constants for hemi-ketal decomposition

Compound	MeOH	EtOH	H_2O
Cyclohexane [17]	1·7	89	Too large to measure
(I)	3·0	7·4	1·5 *
(VII)	—	—	1·1 *

* 40% Aqueous dioxan.

Acetone is similar to cyclohexanone in that it forms a measurable concentration of hemiacetal [16] but not of *gem*-diol although its formation has been established by isotopic exchange.[18] 1,3-Dichloroacetone in water, however, was found [19] to be hydrated without the addition of a catalyst, and fluoral,[20] chloral, and other ketones and aldehydes [21] with electron-withdrawing groups on the α-carbon atom yield stable hydrates. Hence, it seems probable that the ease of formation and stability of the hemi-ketals and *gem*-diols formed in solutions of compounds (I) and (VII) is due (at least partly) to the presence of electron-withdrawing substituents at C-1 and C-3. This conclusion is supported by the stability of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (XVI) in ethanol and aqueous dioxan (see Tables 2 and 3). This compound has one electron-withdrawing and one electron-donating substituent at the α-carbon atoms (C-3 and C-5) and this arrangement of substituents is sufficient to stabilise the molecule so that in ethanol it shows no change in optical rotation during 24 hr. Likewise, in 40% dioxan it shows constant ultraviolet spectral characteristics.

EXPERIMENTAL

Unless otherwise stated paper chromatograms were developed by downward irrigation. The following systems were employed: (A) Whatman No. 1 paper and the organic phase of one of the mixtures (i) ethyl acetate–propan-1-ol–water (5 : 3 : 2) (all proportions are by volume), (ii) ethanol–butan-1-ol–water (1 : 4 : 5), or (iii) butan-1-ol–pyridine–water (6 : 2 : 5). (B) Whatman No. 1 paper impregnated with barium chloride [22] and the organic phase of solvent (iii);

[16] M. L. Bender and J. M. Jones, *J. Amer. Chem. Soc.*, 1960, **82**, 6322.
[17] O. H. Wheeler, *J. Amer. Chem. Soc.*, 1957, **79**, 4191; O. H. Wheeler and J. L. Mateos, *Analyt. Chem.*, 1957, **29**, 538.
[18] M. Cohn and H. C. Urey, *J. Amer. Chem. Soc.*, 1938, **60**, 679.
[19] R. P. Bell, and M. B. Jensen, *Proc. Roy. Soc.*, 1961, *A*, **261**, 38.
[20] D. E. McGreer, R. Stewart, and M. M. Mocek, *Canad. J. Chem.*, 1963, **41**, 1024.
[21] J. Hine. " Physical Organic Chemistry," McGraw-Hill, New York, 1962, 249.
[22] R. Heyworth, H. R. Perkins, and P. G. Walker, *Nature*, 1961, **190**, 261.

with this system the separation of amino-sugars and their glycosides with the *ribo*- and *arabino*-configurations was possible; ninhydrin spray was used for detection. (C) Whatman No. 1 paper impregnated with dimethyl sulphoxide was developed with di-isopropyl ether according to Wickberg's method.[23] Borate buffer (0·1N) was used in the ionophoresis experiments. Infrared spectra were measured in the solid phase in potassium bromide discs. Optical rotations refer to aqueous solutions unless otherwise specified. N.m.r. spectra were determined with a Varian A-60 spectrometer with hexadeuterodimethyl sulphoxide as solvent. Chemical shifts are reported in p.p.m. from tetramethylsilane.

Methyl 3,4-O-*Isopropylidene*-β-L-erythro-*pentopyranosidulose Oxime*.—The pentopyranosidulose [6] (5 g.) was added to a solution of hydroxylamine hydrochloride (2·5 g.) in 0·5N-sodium hydroxide (70 ml.). After being maintained at 60° for 6 hr. the solution was evaporated to dryness under reduced pressure and the residue was extracted with warm ether (3 × 70 ml.). The filtered extract was evaporated to a gum which crystallised (5·1 g., 95%). Recrystallisation was difficult and an amorphous solid was produced by slow evaporation of a solution in diethyl ether–light petroleum (b. p. 40—60°). The *oxime* had m. p. 105—107°, $[\alpha]_D^{20}$ +182° (*c* 1·0 in EtOH) (Found: C, 49·8; H, 7·0; N, 6·1. $C_9H_{15}NO_5$ requires C, 49·8; H, 6·9; N, 6·5%).

When the oximation was carried out at room temperature for 1 hr. a different compound was formed. After recrystallisation from di-isopropyl ether it had m. p. 93—95°, $[\alpha]_D^{20}$ +125° (*c* 0·5 in EtOH). Apparently it was the *addition compound* (A) (Found: C, 46·6; H, 7·5; N, 5·9. $C_9H_{17}NO_6$ requires C, 46·0; H, 7·2; N, 6·0%). Compound (A) (0·2 g.) in water (12 ml.) was heated at 60° for 3 hr. After evaporation the residue was recrystallised twice from isopropyl ether–light petroleum (b. p. 40—60°) to give the oxime, m. p. 99—101°, $[\alpha]_D$ +189° (*c* 1·0 in EtOH). Its infrared spectrum was identical with that obtained from the compound prepared as described above.

Methyl 3,4-O-*Isopropylidene*-β-L-erythro-*pentopyranosidulose Hydrazone*.—The pentopyranosidulose (1·8 g.) in ethanol (18 ml.) was heated under reflux for 1·25 hr. with triethylamine (5·4 ml.) and 64% hydrazine (7·2 ml.).[24] The solution was evaporated to a syrup which distilled as a yellow oil (b. p. 97—100°/10^{-2} mm.) which partially crystallised on storage at 0°, $[\alpha]_D^{21}$ +382° (*c* 0·5 in $CHCl_3$) (Found: C, 50·0; H, 7·4; N, 12·6. $C_9H_{16}N_2O_4$ requires C, 50·0; H, 7·4; N, 12·95%).

Reductions of Methyl 3,4-O-*Isopropylidene*-β-L-erythro-*pentopyranosidulose Oxime*.—(*a*) The oxime (1·9 g.) in ethanol (60 ml.) was added to prereduced Adams catalyst (1 g.). The mixture was shaken in a slight overpressure of hydrogen until uptake ceased (usually 48 hr.). [The reaction could be followed by potentiometric titration with hydrochloric acid and was shown to go to 98% completion.] The filtered solution was evaporated. Distillation of the residue (1·75 g.) gave a colourless oil, b. p. 80—100°/10^{-4} mm., $\nu_{max.}$ 3350 $cm.^{-1}$ (NH_2), R_F 0·5 (chromatography in system C and spraying with 0·1% Chlorophenol Red in ethanol to reveal basic components). A portion (0·5 g.) of the distillate in water (0·4 ml.) was added to salicylaldehyde (0·3 ml.) in ethanol (1·0 ml.) (see Wolfrom *et al.*[7]) and the bright yellow solution was heated at 60° for 1 hr. Evaporation afforded a gum which solidified and was recrystallised from ethanol. Bright yellow needles (0·11 g.) of methyl 2-deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-L-riboside were obtained, m. p. 115—116°, $[\alpha]_D^{20}$ +108° (*c* 0·3 in $CHCl_3$) (Found: C, 63·1; H, 7·1; N, 4·0. Calc. for $C_{16}H_{21}NO_5$: C, 62·5; H, 6·8; N, 4·6%). Wolfrom *et al.*[7] report m. p. 118—120°, $[\alpha]_D^{22}$ +112° (*c* 2·4 in $CHCl_3$).

(*b*) The oxime (3 g.) in dry ether (60 ml.) was treated with a suspension of lithium aluminium hydride (1·2 g.) in dry ether (30 ml.) at the reflux temperature for 20 hr. with stirring. The mixture was cooled, ethyl acetate (5 ml.) was added dropwise, followed by ethanol–water (4 : 1) (6 ml.). The flocculent precipitate was separated by centrifugation and washed with ethanol (3 × 40 ml.). Evaporation under reduced pressure of the combined centrifugate and ethanolic washings yielded a gum, which was dissolved in dry di-isopropyl ether and the insoluble material removed by filtration. Evaporation of the filtrate gave a gum (2·6 g.). The paper-chromatographic behaviour of this product in system C was identical with that of the material obtained from the catalytic reduction. Product (3·3 g.) from the lithium aluminium hydride reduction, in ethanol (25 ml.) and 0·5N-hydrochloric acid (60 ml.), was heated under reflux for 1 hr. The solution was evaporated under reduced pressure at room temperature and recrystallisation of

[23] B. Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[24] D. H. R. Barton, R. E. O'Brien, and S. Sternhill, *J.*, 1962, 470.

the residue from water–ethanol yielded methyl 2-amino-2-deoxy-β-L-ribopyranoside hydrochloride (1·58 g., 49%) as white crystals, m. p. 186—187°, $[\alpha]_D^{20}$ +94° (*c* 0·2), R_F 0·4 in system B (Found: C, 35·8; H, 7·3; Cl, 17·4; N, 7·0. Calc. for $C_6H_{14}ClNO_4$: C, 36·1; H, 7·1; Cl, 17·8; N, 7·0%). Wolfrom *et al.*[7] report m. p. 171—180°, $[\alpha]_D^{20}$ +92·7°. The mother-liquors contained two components, R_F 0·4 and 0·3 in system B. Separation of the mother-liquors in 100 mg. batches on eight sheets of Whatman No. 3 paper with system B afforded 80 mg. of amorphous but chromatographically homogeneous material which, after hydrolysis, had paper-chromatographic behaviour akin to D-arabinosamine hydrochloride.

When the gummy reduction product (1·4 g.) was acetylated [Ac_2O (15 ml.)–C_5H_5N (25 ml.), 60°, 12 hr.] and then hydrolysed with 4N-hydrochloric acid (50 ml.) at 100° for 1 hr. it afforded a hydrolysate which contained two components, R_F 0·20 (weak spot) and 0·24 (major component) (solvent system B) (cf. D-arabinosamine hydrochloride 0·20, D-ribosamine hydrochloride 0·24). Evaporation of the hydrolysate left a gum which was crystallised from acetone–methanol (1 : 1) and the solid was recrystallised from 20 ml. of methanol to which acetone (120 ml.) was added. L-Ribosamine hydrochloride (0·2 g.), m. p. 153—154°, $[\alpha]_{5461}^{20}$ −11·2° (90 sec.) ⟶ +7·8° (13 min.) (constant) (*c* 0·4), $[\alpha]_D^{20}$ +5·6 (5 hr.) (*c* 1·9), R_F 0·24 (solvent system B) (Found: C, 32·0; H, 6·35; N, 7·8. Calc. for $C_5H_{12}ClNO_4$: C, 32·35; H, 6·5; N, 7·55%) was obtained as white crystals which reduced Fehling's solution and gave a positive Elson–Morgan test. The infrared spectrum of the compound was identical with that of an authentic specimen of D-ribosamine hydrochloride synthesised by Kuhn and Baschang [8] who report m. p. 153—154°, $[\alpha]_D^{20}$ −5·8°: Wolfrom *et al.*[7] give m. p. 142—148°, $[\alpha]_D^{20}$ +6·7° for the L-form.

(*c*) The oxime (1 g.) in water–ethanol (30—40 ml.) was treated with sodium amalgam (5%, 30 g.) for 1 hr. with rapid stirring. The base was neutralised and the following procedures were adopted in attempts to isolate the product: (i) the solution was adjusted to pH 8—9 and extracted with either ethyl acetate, chloroform, or ether; (ii) the solution was evaporated to dryness and the residue extracted with ethanol; (iii) the residue obtained in (ii) was acetylated and then extracted with chloroform; (iv) the reaction mixture was passed through a charcoal–Celite column. In no case was any amino-sugar derivative obtained; when the reaction was conducted in basic solution (pH 7·5—8·5) ammonium chloride (60%) was obtained.

Hydrogenation of Compound (A).—Compound (A) (1 g.) in ethanol (40 ml.) consumed 1·7 mol. equiv. of hydrogen at the rate of 10 ml. $min.^{-1}$ when shaken in a slight overpressure of the gas in the presence of Adams catalyst. The solution (strong smell of ammonia) was distilled at 1 mm. and the basic ethanolic distillate, collected in a trap at −80°, was titrated to pH 5 with 0·1N-hydrochloric acid (27 ml.) and then evaporated to a white solid (0·15 g.) which was shown to be ammonium chloride. A portion of the residue from the distillation was hydrolysed (2N-HCl, 100°, 2 hr.) and was shown by paper-chromatographic and ionophoretic analysis to contain ribose but not arabinose:

	R_F			
Substance	A(i)	A(ii)	A(iii)	*M*
Hydrolysate	0·47	0·23	0·37	0·78
D-Ribose	0·47	0·24	0·37	0·76
L-Arabinose	0·34	0·15	0·25	0·90

The remainder of the residue (0·6 g.) in pyridine (10 ml.) with toluene-*p*-sulphonyl chloride (0·5 g.) for 4 days at 35° gave *methyl* 3,4-O-*isopropylidene*-2-O-*tosyl*-β-L-*riboside* (0·18 g.), m. p. 142—143° [from ethanol–light petroleum (b. p. 40—60°)], $[\alpha]_D^{20}$ +107° (*c* 1·7 in $CHCl_3$) (Found: C, 53·5; H, 6·2; S, 8·9. $C_{16}H_{22}O_7S$ requires C, 53·6; H, 6·2; S, 8·9%).

Methyl 3,4-O-*Isopropylidene*-2-O-*tosyl*-β-L-*riboside*.—Methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (0·3 g.) in ethanol (20 ml.) was hydrogenated in the usual way over Adams catalyst. Evaporation of the solution gave a gum (0·3 g.); its infrared spectrum showed strong hydroxyl absorption but none due to a carbonyl group. The gum afforded a crystalline tosylate, m. p. 143—144°, $[\alpha]_D$ +102° (in $CHCl_3$), +107° (in EtOH). Of the two possible products from this reaction sequence only that with the L-*arabino*-configuration has been definitely characterised [25] {m. p. 136°, $[\alpha]_D^{20}$ +181·3° (in $CHCl_3$)} and in admixture with our tosylate it had m. p. 109—113°. Barker and Spoors [26] have prepared a methyl 3,4-*O*-isopropylidene-2-*O*-tosyl-D-riboside of undefined anomeric configuration which has m. p. 143°, $[\alpha]_D$ −113° (in EtOH). It seems that this compound is the D-isomer of our product. Paper-chromatographic analysis

[25] J. Honeyman, *J.*, 1946, 990.
[26] G. R. Barker and J. Spoors, *J.*, 1956, 2656.

of the hydrolysate of the gum obtained from hydrogenation of the pentopyranosidulose showed that it was rich in ribose [13] thereby providing further support to the allocation of the *ribo*-configuration to the tosylate described above.

Methyl 6-Deoxy-3,4-O-isopropylidene-α-L-lyxo-hexopyranosidulose Oxime.—The pyranosidulose (1 g.) [11] was oximated by the procedure described above (0·5 g. hydroxylamine hydrochloride and 70 ml. 0·5N-sodium hydroxide). A gum (1 g.) was obtained, a portion of which was distilled, b. p. 100—110°/10^{-3} mm., $[\alpha]_D^{20}$ −127° (*c* 0·9 in CCl_4) (Found: C, 51·4; H, 7·4; N, 5·6. $C_{10}H_{17}NO_5$ requires C, 51·9; H, 7·4; N, 6·1%). The *oxime* partly crystallised on storage at 0°.

Methyl 2-Amino-2,6-dideoxy-α-L-talopyranoside Hydrochloride.—Methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosidulose oxime (1 g.) in ethanol (30 g.) was hydrogenated in the presence of Adams catalyst according to the usual procedure. After 40 hr. the catalyst was filtered off and the filtrate titrated to pH 3 with N-hydrochloric acid. The titration corresponded to a yield of 58% amine and so the solution was rehydrogenated with fresh catalyst for 24 hr. when the titration corresponded to 77% yield. After dilution with 0·1N-hydrochloric acid (10 ml.) and heating at 100° for 1 hr. the solution was evaporated to small bulk and ethanol was added to give two crops of crystals (0·34 g., and 0·1 g.). The *hydrochloride* had m. p. 265° (decomp.) (darkens at 237°), $[\alpha]_D^{20}$ −82° (*c* 1·0) (Found: C, 39·45; H, 7·4; N, 6·7. $C_7H_{16}ClNO_4$ requires C, 39·3; H, 7·55; N, 6·6%).

Alternatively, the oxime (0·9 g.) was reduced with lithium aluminium hydride (0·5 g.) as described for the oxime of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose. The gummy product was hydrolysed with 0·5N-hydrochloric acid (20 ml.) in ethanol (7 ml.) at 100° for 1 hr. The product was worked up in the usual way and gave two crops (0·4 g., 44%) of the aminotaloside hydrochloride, m. p. 265° (decomp.) (darkens at 237°), chromatographically homogeneous R_F 0·58 (solvent system B). Further crystallisation of the mother-liquors afforded another two crops of crystals (0·09 g.), $[\alpha]_D^{20}$ −138° (*c* 0·5), R_F (system B) 0·55 (~10%) and 0·40 (~90%). Chromatography of this product (40 mg.) on resin (ZeoKarb 225, H^+-form, 100—200 mesh) afforded on elution with 0·3—0·4N-hydrochloric acid a discoloured solid (26 mg.), $[\alpha]_D^{20}$ −154° (*c* 0·3), R_F (system B) 0·40 (chromatographically homogeneous), which was presumably methyl 2-amino-2-deoxy-α-L-fucopyranoside hydrochloride.

6-Deoxy-L-talosamine Hydrochloride.—Methyl 2-amino-2,6-dideoxy-α-L-talopyranoside hydrochloride (0·34 g.) in 5N-hydrochloric acid (10 ml.) was heated at 100° for 2 hr. The residue from evaporation of the yellow solution was crystallised from ethanol–acetone and recrystallised. The hydrochloride (72 mg.) had m. p. 163—164°, $[\alpha]_D^{21}$ +9° (equilib.) (*c* 2·3) (Found: C, 36·0; H, 6·9; N, 6·6. Calc. for $C_6H_{14}ClNO_4$: C, 36·1; H, 7·1; N, 7·0%). It reduced Fehling's solution and gave a positive Elson–Morgan test. 6-Deoxy-L-talosamine hydrochloride isolated from natural sources [10] has m. p. 162—163°, $[\alpha]_D$ +10·4° (equilib.) (*c* 2·3) and the synthetic D-sugar [9] has m. p. 162—164°, $[\alpha]_D$ −10° (*c* 1·7).

The Behaviour of Glycopyranosiduloses in Solution.—(*a*) *Mutarotation.* The optical rotations of solutions of the glycopyranosiduloses were measured in a 1 dm. polarimeter tube which was not fitted with a thermostat. Results are shown in Table 2.

(*b*) *Ultraviolet absorption spectra.* The change in the ultraviolet carbonyl absorption was determined with a Unicam S.P. 700 spectrophotometer with the cells thermostat-controlled at 25·5°. The rate of which equilibrium was reached for alcoholic solutions was very sensitive to the presence of small quantities of water and so rate constants are not quoted for these solutions; however, they are given for aqueous dioxan solutions. Equilibrium was established in less than 1 hr. in 99·9% methanol, but in 99·9% ethanol it took many hours.

(*c*) *Product analysis.* An equilibrated ethanolic solution of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose was evaporated rapidly. Crystallisation of the oily product gave only the initial material. Paper-chromatographic analysis of other solutions was carried

TABLE 2

Specific rotations of methyl *O*-isopropylideneglycopyranosiduloses

Compound	Time (min.) 1	50	200	∞	Solvent	%
(I)	148	133	130	—	MeOH	99·9
	170	166	158	148	EtOH	95
(VII)	−107	−90	—	—	EtOH	95
(XVI)	107	No change after 24 hr.			EtOH	95

TABLE 3

Initial and final carbonyl absorbances of glycopyranosiduloses

Glycopyranosidulose	$\lambda_{max.}$ (mμ)	log I/I_0 Initial	log I/I_0 Final	10^3k (sec.$^{-1}$)	Solvent (%)
(I)	310	0·73	0·221	—	EtOH (95)
		0·78	0·190	3·6	Dioxan (40)
		0·63 *	0·07	—	MeOH (99)
(VII)	315	0·59	0·112	3·0	Dioxan (40)
(XVI)	280	No change during 24 hr.			Dioxan (40)

* Calculated from ε in ethanol.

out with system C, the products being located with an ammoniacal silver nitrate spray. Results are shown in Table 4.

TABLE 4

Paper chromatography of glycopyranosidulose solutions

(R_F values in system C)

Glycopyranosidulose	Et_2O	40% Dioxan	99% EtOH
(I)	0·44	0·44, 0·05	0·44, 0·64
(VII)	0·70	0·70, 0·10	0·70, 0·90

(*d*) *Tracer analysis.* Methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (50 mg.) in [1-^{14}C]ethanol (0·2 ml., 14 μc./mmole) was examined by paper chromatography with system C. The products were located by spraying side strips, and then the central strip of the chromatogram was scanned for β-activity with a Geiger–Müller counter. Results are given in Table 5.

TABLE 5

Count of ^{14}C-β-emission of a chromatogram of a solution of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose in [1-^{14}C]ethanol

R_F at position of count	1·0	0·64	0·44
Average count for 100 sec.	30	270	45

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