1023. *The Synthesis of Desosamine Hydrochloride.**

By A. C. Richardson.

By use of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside as starting material, 3,4,6-trideoxy-3-dimethylamino-D-*xylo*-hexose hydrochloride has been synthesised; it is identical with the naturally occurring sugar desosamine hydrochloride.

Desosamine is the basic nitrogen-containing component of the macrolide antibiotics erythromycin,[1] narbomycin,[2] picromycin,[3] methymycin,[4] oleandomycin,[5] etc., and was shown by degradation[1] to be a 3,4,6-trideoxy-3-dimethylaminohexose. The D-*xylo*

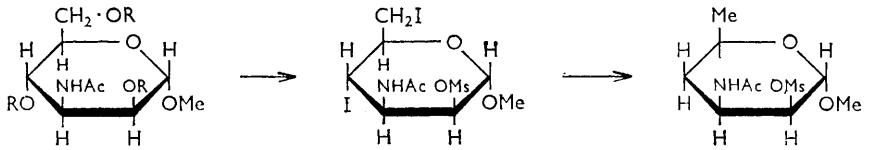
* Preliminary communication, *Proc. Chem. Soc.*, 1963, 131.

[1] Flynn, Sigal, Wiley, and Gerzon, *J. Amer. Chem. Soc.*, 1954, **76**, 3121.
[2] Corbaz *et al.*, *Helv. Chim. Acta*, 1955, **38**, 935.
[3] Brockmann, König, and Oster, *Chem. Ber.*, 1954, **87**, 856.
[4] Djerassi, Bowers, Hodges, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 1733.
[5] Els, Celmer, and Murai, *J. Amer. Chem. Soc.*, 1958, **80**, 3777.

configuration, as in (XIV), of the monosaccharide was deduced from n.m.r. spectra of desosamine and its derivatives,[6,7] and by chemical degradation.[8] The synthesis described herein unequivocally confirms this configuration.

The major difficulty in the synthesis was the creation of the 4-deoxy-grouping adjacent to the 3-dimethylamino-function. Helferich and Gnüchtel [9] found that 1,2,3,6-tetra-*O*-acetyl-4-*O*-methanesulphonyl-D-glucopyranose underwent a replacement reaction with iodide in acetone, to give, in fair yield, what was described as a 4-deoxy-4-iodo-derivative, a suitable precursor of a 4-deoxy-derivative. This result appears to be contrary to the rule [10] which states that only sulphonyloxy-substituents located at primary positions can be replaced directly by iodide. This exception was probably a result of participation of the vicinal 3-acetoxy-substituent (cf. ref. 11) to give a 3- or 4-iodo-derivative. Although later work in these laboratories [12] has thrown doubt on the validity of this original surmise (see below), it seemed likely that neighbouring acylamido-groups would participate much more readily than acyloxy-substituents in the elimination of sulphonyloxy-groups [13] to give intermediary oxazolinium cations which would undergo stereospecific nucleophilic attack to give the *trans*-product, *e.g.*, (XV) ⟶ (XVIII).

The first approach to the synthesis of desosamine, although not fully successful, established that a 3-amino-3,4,6-trideoxy-pyranoside could be synthesised in this way. Methyl 3-acetamido-3-deoxy-α-D-mannopyranoside (I) [14] was converted into the 2,4,6-trimethanesulphonate (II) which, when heated under reflux with sodium iodide in anhydrous ethyl



(I: R = H) (III) (IV)
(II: R = Ms = SO_2·Me)

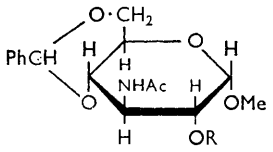
methyl ketone, rapidly lost two of its sulphonyloxy-groups, as was shown by the precipitation of 2 mol. of the sodium methanesulphonate–sodium iodide complex * (4NaOMs,NaI),[15] and a di-iodo-derivative (III) was isolated in *ca.* 60% yield. The remaining sulphonyloxy-substituent was not replaced even after prolonged reaction; it was concluded that this was situated at position 2 and resisted replacement because of the absence of a neighbouring *trans* participating group, so the product was thus assigned the 4,6-di-iodo-mannoside structure (III); it was reductively dehalogenated with hydrogen–Raney nickel to give the corresponding 4,6-dideoxy-derivative (IV) in good yield. It was envisaged that the 2-sulphonyloxy-group could be replaced by benzoate with inversion of configuration by the sodium benzoate–dimethylformamide reagent [16] to give a 4,6-dideoxy-derivative with the

* In the past, it has been incorrectly assumed (see Tipson [10]) that the salt precipitated during the reaction of a methanesulphonate with sodium iodide in an organic solvent is sodium methanesulphonate, and it is now apparent that where the weight of this salt has been used as a measure of the extent of reaction the results require recalculation and possibly revaluation.

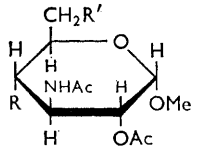
[6] Hofheinz and Grisebach, *Tetrahedron Letters*, 1962, 377.
[7] Woo, Dion, Durham, and Mosher, *Tetrahedron Letters*, 1962, 735.
[8] Bolton, Foster, Stacey, and Webber, *J.*, 1961, 4831; *Chem. and Ind.*, 1962, 1945.
[9] Helferich and Gnüchtel, *Ber.*, 1938, **71**, 1712.
[10] Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 366; Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 192.
[11] Winstein, Grunwald, Buckler, and Hanson, *J. Amer. Chem. Soc.*, 1948, **70**, 816.
[12] Hill, Hough, and Richardson, *Proc. Chem. Soc.*, 1963, 346.
[13] Winstein, Goodman, and Boschan, *J. Amer. Chem. Soc.*, 1950, **72**, 2311; McCasland, Carter, and Clark, *ibid.*, 1949, **71**, 637.
[14] Richardson, *J.*, 1962, 373.
[15] Collmann, *Annalen*, 1868, **148**, 101.
[16] Reist, Goodman, and Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 5775; Reist, Spencer, and Baker, *J. Org. Chem.*, 1959, **24**, 1618.

required *xylo* configuration. However, treatment of (IV) with sodium benzoate in boiling dimethylformamide did not cause replacement of the substituent, as shown by the infrared spectrum of the syrupy product, which contained absorptions due to sulphonate but not to benzoate ester groups. Furthermore, the low specific rotation (+17°) was not consistent with the high values (>135°) reported for 4-deoxy-α-D-*xylo*-hexopyranosides.[17] Baker and Haines [18] reported that the successful use of this reagent in carbohydrate chemistry requires precise conditions of conformation and reactivity, which are obviously absent in (IV).

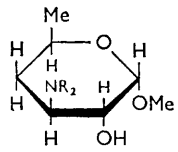
This difficult inversion reaction was circumvented by use of a starting material with the required configuration at C-2. Guthrie and Johnson [19] described a convenient preparation of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside (V) from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside. Acetylation of (V) with a mixture of hot acetic anhydride, pyridine, and dimethylformamide gave the 2-*O*-acetate (VI) in high yield. Removal of the benzylidene residue by brief treatment with hot 50% aqueous acetic acid gave methyl 3-acetamido-2-*O*-acetyl-3-deoxy-α-D-glucopyranoside (VII) in 95% yield. Reaction of this with methanesulphonyl chloride in pyridine afforded the 4,6-dimethanesulphonate (VIII).



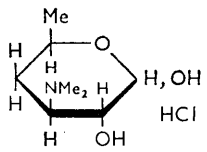
(V: R = H)
(VI: R = Ac)



(VII: R = R' = OH)
(VIII: R = R' = OMs)
(IX: R = OMs, R' = I)
(X: R = R' = I)
(XI: R = R' = H)



(XII: R = H)
(XIII: R = Me)



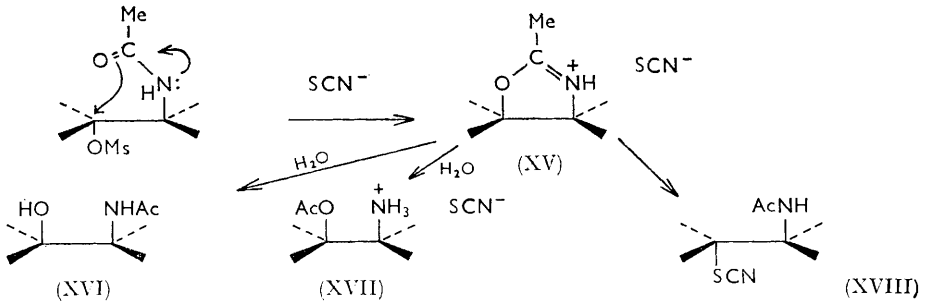
(XIV)

Introduction of the 4,6-dideoxy-grouping into the molecule was investigated through the replacement reactions of (VIII) with both sodium iodide and potassium thiocyanate. With the latter the reaction was conducted in dimethylformamide at *ca.* 150°, when the loss of both sulphonyloxy-groups occurred within 2 hours as shown by the precipitation of 2 mol. of potassium methanesulphonate. However, the amorphous product isolated from the mixture did not possess the expected properties of the 4,6-dithiocyanate derivative. It was almost completely soluble in water, and when the aqueous solution was extracted with chloroform only a small amount (<10% yield) of the product dissolved in the organic phase. The water-soluble product (81% yield) showed two absorption bands in its infrared spectrum which were attributable to thiocyanate. One (*ca.* 2050 cm.$^{-1}$) was very intense and characteristic of inorganic thiocyanate. The other (*ca.* 2150 cm.$^{-1}$) was rather weak and more in keeping with a covalent thiocyanate; it was probably due to the group at C-6. Absorption at *ca.* 3350 cm.$^{-1}$ was also present which was attributable to a hydroxyl or amino-group, or both. The chloroform-soluble material possessed only one, weak thiocyanate absorption (*ca.* 2150 cm.$^{-1}$). These results could be interpreted if the acetamido-group were participating to give an intermediary oxazolinium thiocyanate (XV) which either was failing to rearrange to the covalent thiocyanate (XVIII) or was being hydrolysed to give either the *cis*-acetamido-alcohol (XVI) (cf. ref. 13) or the *cis*-amino-*O*-acetate as the thiocyanate salt (XVII) (cf. ref. 20). Similar results were obtained [21] when methyl 3-acetamido-3,6-dideoxy-2-*O*-methanesulphonyl-α-L-galactopyranoside was treated with thiocyanate in dimethylformamide; the amorphous material had an intense

[17] Hedgley, Overend, and Rennie, *J.*, 1963, 4701.
[18] Baker and Haines, *J. Org. Chem.*, 1963, **28**, 438.
[19] Guthrie and Johnson, *J.*, 1961, 4166.
[20] Meyer zu Reckendorf and Bonner, *Chem. Ber.*, 1962, **95**, 1917.
[21] Ollis, Richardson, and Russell, unpublished results.

thiocyanate absorption band and ultimately partially crystallised, giving the *cis*-acetamido-alcohol, namely, methyl 3-acetamido-3,6-dideoxy-α-L-talopyranoside.

Whereas the use of thiocyanate was not encouraging, the action of sodium iodide on the dimethanesulphonate (VIII) in ethyl methyl ketone first produced a monoiodo-derivative (IX) which was slowly transformed into the di-iodo-derivative (X) by prolonging the reaction time to *ca.* 50 hours. During the reaction approximately 2 mol. of the sodium methanesulphonate–sodium iodide complex were precipitated and addition of water to the reaction mixture afforded the crystalline di-iodo-derivative (X) in 40% yield. By varying the



reaction time above 50 hours the yield remained virtually constant, compound (X) being the only water-insoluble product in the mixture. Attempted isolation of further material from the aqueous mother-liquors resulted in the formation of tars, and it appeared that, as in the case of the thiocyanate reaction, ionic material had been formed in addition to the covalent di-iodo-compound, which suggests the implication of the acetamido-group in the reactions. Consequently, the di-iodo-derivative is assigned the *gluco* configuration. Verification of this by n.m.r. has not been possible since both di-iodo-derivatives, (III) and (X), are not sufficiently soluble in chloroform, carbon tetrachloride, benzene, etc.

The participation of the 3-acetamido-function is in contrast to the behaviour of a similarly placed acyloxy-substituent. It has been observed [18,22] that, in the carbohydrate field, neighbouring carboxylic ester groups do not participate in the elimination reactions of sulphonyloxy-groups in the way that acylamido-substituents do. In agreement with this we [12] found that methyl 4,6-di-*O*-methanesulphonyl-α-D-glucopyranoside 2,3-dibenzoate and 2,3-diacetate undergo replacement at the 4- and 6-positions by an S_N2 process with benzoate, azide, and thiocyanate in dimethylformamide, to give derivatives with the D-*galacto* configuration, which precludes participation from position 3. It is considered as unlikely that the two di-iodo-derivatives, (III) and (X), could have arisen by a similar S_N2 process since dimethylformamide appears to be an essential prerequisite for these bimolecular replacements,[23] whereas both (III) and (X) were formed smoothly in the lower-boiling ethyl methyl ketone.

Fortunately, any uncertainty about the configuration of the 4-iodo-group did not affect the synthesis at hand since the next step was the reductive removal of the iodo-substituents with Raney nickel–hydrogen, which destroys the asymmetry at C-4. The resulting diacetyl-dideoxy-derivative (XI) underwent both *O*- and *N*-acetyl fission in hot sodium hydroxide to give methyl 3-amino-3,4,6-trideoxy-α-D-*xylo*-hexopyranoside (XII) in high yield. When this amine was *N*-methylated with the formic acid–formaldehyde reagent (cf. ref. 24) methyl 3,4,6-trideoxy-3-dimethylamino-α-D-*xylo*-hexopyranoside (XIII) was formed as an oil having an infrared spectrum almost identical with that of the mixture of glycosides formed by treatment of desosamine hydrochloride with methanolic hydrogen chloride.[1] Hydrolysis of the synthetic glycoside (XIII) presented a number of difficulties

[22] Jeanloz and Jeanloz, *J. Amer. Chem. Soc.*, 1958, **80**, 5692.
[23] Reist, Spencer, Baker, and Goodman, *Chem. and Ind.*, 1962, 1794.
[24] Richardson, *J.*, 1962, 2758.

in the isolation of the crystalline sugar from the hydrolysate. Natural desosamine hydrochloride is isolated in *ca.* 50% yield from erythromycin after hydrolysis with 6N-hydrochloric acid.[1] When (XIII) was similarly hydrolysed and the solution concentrated to dryness no crystalline material could be isolated, even after seeding, although chromatography indicated that desosamine hydrochloride was the main product. Similar non-crystalline products were obtained when desosamine hydrochloride and methyl αβ-desosaminide were likewise treated with 6N-hydrochloric acid, suggesting that the sugar might be undergoing decomposition and that the decomposition products were preventing the crystallisation of the highly crystalline hydrochloride. A procedure was then developed to reduce these impurities to a minimum by chloroform extraction of neutral material from the hydrolysate followed by isolation of the monosaccharide by way of its free base. In this way the crystalline sugar hydrochloride (XIV) was readily obtained in 23% yield; it was identical with desosamine hydrochloride, and was further characterised by conversion into desosamine hydrochloride di-*O*-acetate.[1]

This synthesis concludes the structure of desosamine and is its first sterospecific synthesis, although two non-sterospecific syntheses of DL-desosamine had been described.[25]

Experimental

Evaporations were performed *in vacuo*. Ethyl methyl ketone used for iodide replacements was purified by boiling with sodium iodide for *ca.* ½ hr. and redistilling; it was stored in the dark over calcium sulphate. The sodium iodide used in the replacement reactions was rigorously dried (P_2O_5). Optical rotations were determined at *ca.* 20°. Light petroleum had b. p. 40—60°.

Methyl 3-*Acetamido*-3-*deoxy*-2,4,6-*tri*-O-*methanesulphonyl*-α-D-*mannopyranoside* (II).—A suspension of methyl 3-acetamido-3-deoxy-α-D-mannopyranoside [14] (I) (2·5 g.) in pyridine (20 ml.) was treated with methanesulphonyl chloride (3 ml.) and the solution stored in an ice-box for 18 hr. The addition of ice–water afforded crystals (3·72 g., 82%) which were filtered off and washed with water, ethanol, and ether. The *trisulphonate* formed needles, m. p. 165—166° (from aqueous acetone), $[\alpha]_D$ +39° (*c* 0·8 in acetone–dimethylformamide, 2 : 1 v/v), which were sparingly soluble in chloroform (Found: C, 30·5; H, 5·1; N, 2·9; S, 19·6. $C_{12}H_{23}NO_{12}S_3$ requires C, 30·7; H, 4·9; N, 3·0; S, 20·5%).

Methyl 3-*Acetamido*-3,4,6-*trideoxy*-4,6-*di-iodo*-2-O-*methanesulphonyl*-α-D-*mannopyranoside* (III).—The trisulphonate (524 mg.) was heated under reflux in ethyl methyl ketone (10 ml.) with sodium iodide (530 mg.) and a small piece of pumice stone. Within a few minutes the sodium methanesulphonate–sodium iodide [15] complex started to separate as plates, and after 28 hr. the complex was filtered off (320 mg., 1·84 mol.) and washed well with acetone (Found: I^-, 20·6% by iodate titration. Calc. for $NaI,4MeSO_3Na$: I^-, 20·4%). The combined filtrate and washings were then concentrated to a frothy syrup which was fractionated between chloroform and dilute aqueous sodium thiosulphate solution. The colourless organic layer was washed with water, dried (Na_2SO_4), and concentrated to a crystalline residue. Recrystallisation from ethanol afforded the *di-iodo-derivative* (341 mg., 57%), m. p. 200° (decomp.), $[\alpha]_D$ +28° (*c* 1 in $CHCl_3$) (Found: C, 22·4; H, 3·0; I, 47·5; N, 2·6; S, 5·7. $C_{10}H_{17}I_2NO_6S$ requires C, 22·5; H, 3·2; I, 47·5; N, 2·6; S, 6·0%).

Methyl 3-*Acetamido*-3,4,6-*trideoxy*-2-O-*methanesulphonyl*-α-D-lyxo-*hexopyranoside* (IV).—The di-iodo-derivative (III) (560 mg.) was dissolved in warm ethanol and hydrogenated at 4 atm. and room temperature for 16 hr. using Raney nickel. Filtration and concentration gave a syrup which readily crystallised on the addition of ethanol. The *dideoxy-derivative* (235 mg., 80%) had m. p. 161—163° (from ethanol–light petroleum), $[\alpha]_D$ +27° (*c* 0·5 in $CHCl_3$) (Found: C, 42·5; H, 6·9; N, 4·8; S, 11·3. $C_{10}H_{19}NO_6S$ requires C, 42·7; H, 6·8; N, 5·0; S, 11·4%).

Treatment of Methyl 3-*Acetamido*-3,4,6-*trideoxy*-2-O-*methanesulphonyl*-α-D-lyxo-*hexopyranoside* (IV) *with Sodium Benzoate in Dimethylformamide*.—A mixture of the 2-*O*-methanesulphonate (97 mg.), sodium benzoate (115 mg.), and dimethylformamide (3 ml.) was heated under reflux for 24 hr. The mixture, which remained heterogeneous, was diluted with acetone, filtered, and concentrated. The resulting brown syrup was decolourised with charcoal in

[25] Korte, Bilow, and Heinz, *Tetrahedron*, 1962, **18**, 657; Newman, *Chem. and Ind.*, 1963, 372; *J. Org. Chem.*, 1964, **29**, 1461.

methanol to give a pale yellow syrup (62 mg.), $[\alpha]_D$ +17° (*c* 0·6 in $CHCl_3$). Infrared spectroscopy indicated the presence of sulphonate groups and the absence of carboxylic ester groups. The syrupy product ultimately crystallised to give the starting product (10 mg.). When the reaction time was increased beyond 24 hr. no evidence of the replacement of the methanesulphonyloxy-group was obtained.

Methyl 3-*Acetamido*-2-O-*acetyl*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucopyranoside* (VI).—A suspension of methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside (V) (13·5 g.) [19] in a mixture of acetic anhydride (75 ml.), pyridine (75 ml.), and dimethylformamide (7·5 ml.) was heated under reflux for a few minutes until dissolution was complete. Upon cooling, long needles of the product crystallised. After keeping at room temperature overnight the reaction mixture was decomposed by the addition of ice–water, and the diacetyl derivative (14·1 g., 92%) was filtered off and washed with ethanol and ether, m. p. 274—279° with sublimation (lit.,[19] 274—276°) (Found: C, 59·0; H, 6·2; N, 4·1. Calc. for $C_{18}H_{23}NO_7$: C, 59·2; H, 6·3; N, 3·8%).

Methyl 3-*Acetamido*-2-O-*acetyl*-3-*deoxy*-α-D-*glucopyranoside* (VIII).—A suspension of the 4,6-*O*-benzylidene derivative (VI) (1·75 g.) in 50% aqueous acetic acid (20 ml.) was heated for a few minutes under reflux until all the solid had dissolved. The solution was kept at room temperature for 2 hr. and concentrated to a syrup, which crystallised with ease. Recrystallisation from ethanol–ether–light petroleum afforded the *product* (1·26 g., 95%), m. p. 175—177°, $[\alpha]_D$ +118° (*c* 0·5 in $CHCl_3$) (lit.,[26] m. p. 172—173°, $[\alpha]_D$ +120°) (Found: C, 47·6; H, 6·9; N, 5·0. $C_{11}H_{19}NO_7$ requires C, 47·6; N, 6·9; N, 5·1%).

Methyl 3-*Acetamido*-2-O-*acetyl*-3-*deoxy*-4,6-*di*-O-*methanesulphonyl*-α-D-*glucopyranoside* (VIII).—Methyl 3-acetamido-2-*O*-acetyl-3-deoxy-α-D-glucopyranoside (5·3 g.) was dissolved in dry pyridine (32 ml.), and methanesulphonyl chloride (6 ml.) added with cooling. The solution, after 2 hr. at room temperature, was decomposed with ice–water. In most cases the product partially crystallised from the solution, but since this usually only constituted less than half the expected yield it was more convenient to evaporate the whole mixture to dryness rather than to filter it. The crystalline residue thus obtained was shaken vigorously with ethanol, and the suspension kept at 0° overnight. Filtration gave the *di*-O-*methanesulphonate* (6·9 g., 84%), m. p. 174—175°, $[\alpha]_D$ +100° (*c* 0·8 in $CHCl_3$) (Guthrie and Mutter,[26] obtained m. p. 174—175°, $[\alpha]_D$ +102°), m. p. 176—177° (from ethanol) (Found: C, 35·9; H, 5·2; N, 3·3; S, 14·6. $C_{13}H_{23}NO_{11}S_2$ requires C, 36·0; H, 5·4; N, 3·2; S, 14·8%.)

Methyl 3-*Acetamido*-2-O-*acetyl*-3,4,6-*trideoxy*-4,6-*di*-*iodo*-α-D-*glucopyranoside* (X).—A mixture of the disulphonate (VIII) (4·5 g.) and sodium iodide (9 g.) was rigorously dried *in vacuo* and then dissolved in hot dry ethyl methyl ketone (200 ml.). The solution was heated under reflux for 50 hr., and the precipitated sodium methanesulphonate–sodium iodide complex filtered off (2·8 g., 1·7 mol.). The filtrate was concentrated and the residue dissolved in a minimum of acetone. Upon the addition of water the *di-iodo-derivative* (2·07 g., 40%) crystallised, m. p. 233—234° (decomp.) (changing from short needles to long needles in the region 150—200°), $[\alpha]_D$ +51° (*c* 1 in $CHCl_3$) (Found: C, 26·5; H, 3·5; I, 50·6; N, 2·8. $C_{11}H_{17}I_2NO_5$ requires C, 26·6; H, 3·5; I, 51·0; N, 2·8%). When the reaction time was prolonged up to *ca.* 130 hr. the yield was unaffected.

Methyl 3-*Acetamido*-2-O-*acetyl*-3,4,6-*trideoxy*-α-D-xylo-*hexopyranoside* (XI).—The di-iodo-derivative (1·97 g.) was dissolved in hot ethanol (*ca.* 250 ml.) and hydrogenated at *ca.* 4 atm. and 60° over Raney nickel. After 3½ hr. the catalyst was filtered off and the filtrate concentrated to a syrup which was extracted with chloroform and, after removal of a little insoluble material, the extract was evaporated to dryness. The resulting syrup was fractionated between water (100 ml.) and chloroform (10 ml.). The organic layer was further extracted with water (4 × 100 ml.) and the combined aqueous extracts concentrated to a colourless syrup which rapidly crystallised. Recrystallisation from ether afforded the *product* (424 mg., 43%), m. p. 127—129°, $[\alpha]_D$ +107° (*c* 1·7 in $CHCl_3$). A second less-pure crop (77 mg., 8%) was obtained from the ethereal mother liquors, m. p. 110—115°, with an infrared spectrum identical with that of the first crop (Found: C, 53·5; H, 7·4; N, 5·7. $C_{11}H_{19}NO_5$ requires C, 53·9; H, 7·75; N, 5·7%).

Methyl 3-*Amino*-3,4,6-*trideoxy*-α-D-xylo-*hexopyranoside* (XII).—The diacetyl-dideoxy-derivative (210 mg.) was dissolved in N-sodium hydroxide and heated under reflux for 19 hr. The solution was extracted continuously with chloroform for 4½ hr.; evaporation of the chloroform yielded a highly crystalline residue which was recrystallised from ether to give the *product*

[26] Guthrie and Mutter, *J.*, 1964, 1614.

(99 mg., 72%). A further 8 mg. (6%) was obtained from the mother-liquors by sublimation. The amine had an unreliable m. p. in the range 120—130°, after undergoing a very characteristic change from small ill-defined crystals to large refracting rectangular plates in the range 70—120°. A small sample, sublimed for analysis had m. p. 110—120°, after a similar change in crystalline form (Found: C, 52·4; H, 9·2; N, 8·7. $C_7H_{15}NO_3$ requires C, 52·2; H, 9·3; N, 8·7%).

Methyl 3,4,6-*Trideoxy*-3-*dimethylamino*-α-D-xylo-*hexopyranoside* (XIII).—Methyl 3-amino-3,4,6-trideoxy-α-D-*xylo*-hexopyranoside (110 mg.) was dissolved in a mixture of 98—100% formic acid (1 ml.) and *ca.* 40% aqueous formaldehyde (1 ml.), and the solution heated under reflux for 17 min. after which time the evolution of carbon dioxide had ceased. The mixture was concentrated to a white solid which contained mostly polymeric products of formaldehyde. When this was dissolved in hot ethanol and reconcentrated a pale yellow syrup was obtained, which was dissolved in 2N-sodium hydroxide (*ca.* 5 ml.) and extracted continuously with chloroform for 4 hr. Concentration of the extract afforded a mobile oil which was distilled at *ca.* 80—85° (bath)/1 mm., to give the *dimethylamino-glycoside* (100 mg., 78%) as a colourless liquid, $[\alpha]_D$ +140° (*c* 1·7 in H_2O) (Found: C, 56·2; H, 9·9; N, 7·2. $C_9H_{19}NO_3$ requires C, 57·1; H, 10·0; N, 7·4%).

The infrared spectrum of a sample of methyl αβ-desosaminide, prepared [1] from desosamine was almost identical with that of the above, but the rotation was different (84° ± 2).

3,4,6-*Trideoxy*-3-*dimethylamino*-D-xylo-*hexose* (*Desosamine*) *Hydrochloride* (XIV).—A solution of the oily glycoside (XIII) (*ca.* 110 mg.) in 6N-hydrochloric acid (3 ml.) was heated under reflux for 2 hr., the pH adjusted to *ca.* 5—6 with sodium hydrogen carbonate, the solution extracted continuously with chloroform for 18 hr., and the extract discarded. The aqueous phase was adjusted to pH 9·8 with 0·1N-sodium hydroxide, and the solution extracted continuously with chloroform for 5 hr. Concentration of the extract afforded a golden coloured syrup, presumably the free base of the sugar. This syrup was taken up in ether, and a small amount of insoluble material filtered off. After concentration of the ethereal solution the resulting syrup was dissolved in water (*ca.* 2 ml.) and the slightly cloudy solution carefully adjusted to pH 3 with 0·01N-hydrochloric acid. Evaporation of this solution afforded a syrup which readily crystallised upon the addition of a little 90% ethanol. Recrystallisation from a mixture of this solvent and acetone yielded the *product* (28 mg., 23%), m. p. 182°, $[\alpha]_D$ +48 ± 2° (*c* 1 in H_2O). It was identical with desosamine (mixed m. p., infrared spectrum, and rate of movement on paper chromatograms). Flynn *et al.*[1] report m. p. 182—183° for desosamine hydrochloride, and m. p.s as high as 189—191° have been given.[2-4] The specific rotation in water has been recorded as +49·5, +51, and +50·5°.

When authentic desosamine hydrochloride was subjected to the conditions used for the hydrolysis of (XIII) and worked up in the same manner, the sugar could only be recovered crystalline in 25% yield, which is consistent with the 23% yield obtained for synthetic desosamine.

Synthetic desosamine hydrochloride (6 mg.) was heated with a mixture of acetic anhydride (0·1 ml.) and pyridine (0·1 ml.) until solution was achieved. After keeping at room temperature for ½ hr., ether was added until turbidity occurred, and scratching caused crystallisation of 1,2-di-*O*-acetyl-3,4,6-trideoxy-3-dimethylamino-β-D-*xylo*-hexopyranose hydrochloride (4 mg., *ca.* 50%), m. p. 186—190° (lit.,[1] m. p. 194—195°, but there was insufficient of the di-*O*-acetate for recrystallisation). The infrared spectrum of the synthetic sample was identical with that of the di-*O*-acetate derived from the natural sugar.

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