706. *The Disulphones derived by Oxidation of* 2-*Amino*-2-*deoxy*-D-*glucose Diethyl Dithioacetal Hydrochloride and its* N-*Acetyl Derivative with Peroxypropionic Acid.*

By L. Hough and Mahmoud I. Taha.

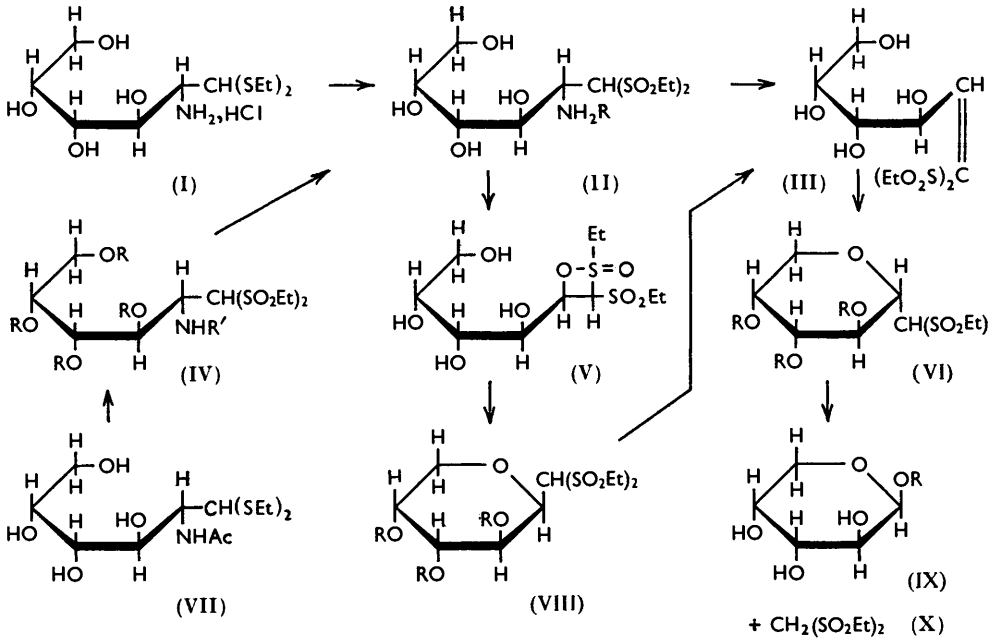
When 2-amino-2-deoxy-D-glucose diethyl dithioacetal was oxidised to the disulphone with peroxypropionic acid at −10°, ammonium chloride was eliminated and cyclisation occurred to give D-*manno*-2 : 6-epoxy-1 : 2-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-α-D-arabopyranosylmethane). In a similar oxidation of 2-acetamido-2-deoxy-D-glucose diethyl dithioacetal, de-*N*-acetylation occurred with the formation of D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate. Treatment of this with aqueous ammonia yielded initially a mixture of D-*gluco*- and D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane and D-arabinose, and finally only D-arabinose. Displacement of the diethylsulphonylmethyl group from D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane with sodium methoxide gave methyl β-D-arabopyranoside. The mechanisms of these reactions are discussed.

Aldohexose diethyl dithioacetals are converted by aqueous peroxy-acids [1,2,3] or by hydrogen peroxide containing a little ammonium molybdate,[1,3] into either 1 : 1-diethylsulphonyl-2 : 3 : 4 : 5 : 6-pentahydroxyhexanes or 2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexanes (*e.g.*, VI; R = H), or a mixture of the two. It was of interest, therefore, to study similar oxidations of 2-amino-2-deoxy-D-glucose diethyl dithioacetal hydrochloride (I) and its *N*-acetyl derivative (VII) in order to assess the influence of an amino- or acetamido-function on the activated centre at $C_{(2)}$ of the disulphone.

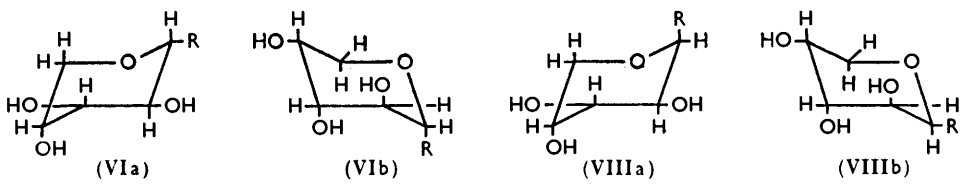
Oxidation of 2-amino-2-deoxy-D-glucose diethyl dithioacetal hydrochloride [4] (I) with aqueous peroxypropionic acid at −10° yielded ammonium chloride and a syrup, $[\alpha]_D$ +10°. On paper chromatograms the syrup was indistinguishable from D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane ($[\alpha]_D$ +6·3°) (VI; R = H) derived from the oxidation of D-glucose diethyl dithioacetal and of D-mannose diethyl dithioacetal,[3] and the structure was confirmed by comparison of the crystalline triacetates (VI; R = Ac). The syrup gave a pale yellow colour in dry pyridine, in contrast to the typical magenta or cherry-red colour given by 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes.[2] In an excess of dilute aqueous ammonia (pH 10—11), the syrupy disulphone (VI; R = H) was

[1] Zinner and Falk, *Chem. Ber.*, 1955, **88**, 566.
[2] Hough and Taylor, *J.*, 1955, 1212, 3544.
[3] *Idem*, *J.*, 1956, 970.
[4] Whitehouse, Kent, and Posternak, *J.*, 1954, 2315.

cleaved to give D-arabinose (IX; R = H) in high yield and diethylsulphonylmethane (X). In the formation of the cyclic disulphone (VI; R = H), deamination probably took place after the formation of D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane hydrochloride (II; R = HCl) since the analogous 1 : 1-diethylsulphonyl-2 : 3 : 4 : 5 : 6-pentahydroxyhexanes and their penta-*O*-acetyl derivatives readily lose



the elements of water [3] and of acetic acid [5] respectively. The process would be facilitated by the presence of the positive charge on the nitrogen atom and would lead to the formation of the D-*arabo*-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhex-1-ene (III). However, this unsaturated disulphone (III) would cyclise to the 2 : 6-epoxypyranosyl structure (VI; R = H) by the attack of the cationoid $C_{(2)}$ on the terminal primary hydroxyl group.[3] Of the two possible stereoisomeric forms, namely D-*manno*- (VI; R = H) and D-*gluco*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VIII; R = H), only the former was isolated and conformational considerations favour the formation of this configuration. Thus, when the bulky diethylsulphonylmethyl group is assumed to be equatorial, non-bonded interactions would be least in the D-*manno*-stereoisomer (VI; R = H) since



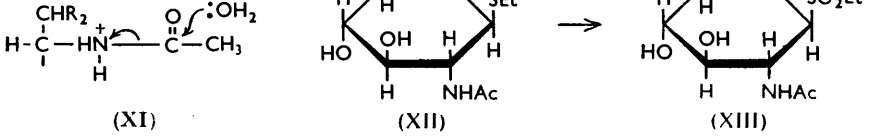
the pyranosyl modification in the 1C chair form [VIa; R = $CH(SO_2Et)_2$] has only one hydroxyl group in an axial position, whereas the D-*gluco*-stereoisomer (VIII; R = H) in the C1 chair form [VIIIb; R = $CH(SO_2Et)_2$] has two axial hydroxyl groups and Δ2 condition.

When 2-acetamido-2-deoxy-D-glucose diethyl dithioacetal [6] (VII) was treated with

[5] MacDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087.
[6] Hough and Taha, *J.*, 1956, 2042.

aqueous peroxypropionic acid at −10° a highly crystalline disulphone was obtained. Analysis and molecular-weight estimation [7] of the product indicated that the compound had the molecular formula $C_{13}H_{29}O_{11}NS_2$; *N*-acetyl was absent, which was supported by the formation of a pink colour with ninhydrin on paper chromatograms. These facts, considered together with its highly crystalline nature and neutrality in aqueous solution, suggested that the product was a salt of an organic acid with an amine. On acetylation the disulphone afforded the known [5] crystalline D-*gluco*-2-acetamido-3 : 4 : 5 : 6-tetra-acetoxy-1 : 1-diethylsulphonylhexane (IV; R = R′ = Ac), proving that the disulphone was a derivative of D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxy-hexane ($C_{10}H_{23}O_8NS_2$) (IV; R = R′ = H). These results indicated that the unknown disulphone was the peroxypropionic acid ($C_3H_6O_3$) salt of D-*gluco*-2-amino-1 : 1-diethyl-sulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane (II; R = Et·CO_3H) which was confirmed by its liberating iodine from acidified iodide solution. Clearly the peroxypropionate of the amino-disulphone (II; R = Et·CO_3H) was formed during the oxidation as a result of rapid hydrolysis of the *N*-acetyl group. Acid hydrolysis of amides is normally slow,[8] the rate-determining step being the hydration of the acetyl group of the conjugate acid (XI) which in this case, however, is facilitated by the strongly electrophilic diethylsulphonyl-methyl group. In contrast, 2-acetamido-2-deoxy-β-D-glucopyranosylthioethane [6] (XII) yielded on oxidation under the same conditions, the corresponding sulphone (XIII), no de-*N*-acetylation having occurred.

The poor ionic character of peroxypropionic acid compared with hydrochloric acid appears to be responsible for the stability of the amino-disulphone (II; R = Et·CO_3H) under conditions which resulted in the elimination of ammonium chloride from D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane hydrochloride (II; R = HCl). These views gain some support from the fact that, in an attempt to isolate the *N*-acetyl derivative (IV; R = H, R′ = Ac), the peroxypropionate (II; R = Et·CO_3H) was treated with acetic anhydride in the presence of silver acetate [9] in methanol; on removal of silver ions by the addition of hydrochloric acid, the acetylated product was deaminated, ammonium chloride and D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VI; R = H) being formed.

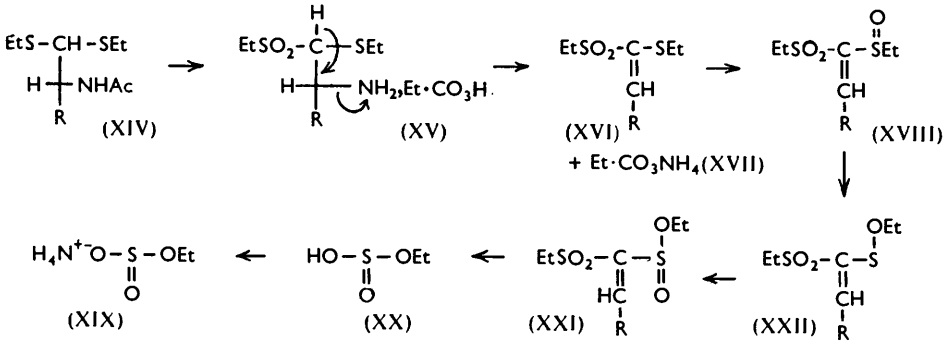


(XI) (XII) (XIII)

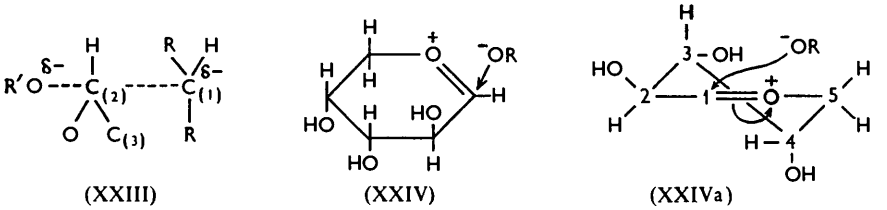
When 2-acetamido-2-deoxy-D-glucose diethyl dithioacetal (VII) was treated with aqueous peroxypropionic acid *at room temperature* an exothermic reaction ensued from which ammonium ethyl sulphite [10] (XIX) was isolated in 87% yield. A possible route for the formation of this compound under these conditions is as follows. If oxidation of the dithioacetal (XIV; R = D-*arabo*tetrahydroxybutyl) to the monosulphone [11] was accompanied by de-*N*-acetylation as appears likely from the above experiments, yielding 2-amino-2-deoxy-1-ethylsulphonyl-1-ethylthio-D-glucose peroxypropionate (XV), then, by analogy with a β-amino-acid, the peroxypropionate would be deaminated easily under acid conditions to give ammonium peroxypropionate (XVII) and the unsaturated mono-sulphone (XVI). Further oxidation of the latter (XVI) would yield initially the 1-sulphone

[7] Menzies and Wright, *J. Amer. Chem. Soc.*, 1921, **23**, 2309, 2314.
[8] Meloche and Laidler, *ibid.*, 1951, **73**, 1712; de Roo and Bruylants, *Bull. Soc. chim. belges*, 1954, **63**, 140.
[9] White, *J.*, 1940, 428.
[10] Divers and Ogawa, *J.*, 1899, **75**, 534.
[11] Bourne and Stephens, *Ann. Rev. Biochem.*, 1956, **25**, 79.

1-sulphoxide derivative (XVIII) in which the ethyl group of the sulphoxide is in an allylic position with respect to the ethylenic group and would, therefore, be expected to migrate under the influence of acids, as a positively charged radical to the sulphoxide oxygen, giving the sulphide (XXII). The sulphur atom would then be oxidised further giving the αβ-unsaturated ester (XXI) which on acid hydrolysis would yield ethyl hydrogen sulphite (XX); this would replace peroxypropionic acid in its ammonium salt (XVII) to form ammonium ethyl sulphite (XIX).



D-*gluco*-2-Amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate (II; R = Et·CO_3H) was treated with dilute aqueous ammonia (pH 10—11) to give D-arabinose (IX; R = H) in high yield and diethylsulphonylmethane (X). Examination on paper chromatograms indicated that degradation to D-arabinose (IX; R = H) was complete after 5—6 days and that during the reaction at least two intermediates were produced. In order to isolate these intermediates, D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate (II; R = Et·CO_3H) was allowed to react with dilute aqueous ammonia (pH 10—11) for 24 hr. at room temperature and the mixture was then chromatographed on a column of cellulose :[12] three products were obtained, namely, D-arabinose (18%), D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VI; R = H) (38%), and an unknown syrupy disulphone, $C_{10}H_{20}O_8S_2$ (34%), isomeric with the preceding compound. In dilute aqueous ammonia the unknown compound gave initially a mixture of the D-*manno*-2 : 6-epoxy-



disulphone (VI; R = H) and D-arabinose, but after 6—7 days only D-arabinose was obtained. Paper chromatography with butan-1-ol–pyridine–water as mobile phase caused partial transformation of the unknown compound into D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VI; R = H), showing the lability of the former to base. The unknown disulphone gave only a pale yellow colour in dry pyridine, even after 24 hr., and in aqueous solution was neutral, which suggested [3] that there was no unsaturated linkage within the molecule. The formation of a tri-*O*-acetyl derivative (VIII; R = Ac) indicated the presence of a ring structure involving one of the hydroxyl groups. Periodate oxidation suggested a pyranosyl structure, since the compound consumed two mols. of the

[12] Hough, Jones, and Wadman, *J.*, 1949, 2511; 1950, 1702.

oxidant with the simultaneous liberation of one mol. of acid, thus providing evidence for three free hydroxyl groups attached to contiguous carbon atoms. These facts, considered together with its isomerisation in dilute alkaline solutions to D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VI; R = H), suggested that the unknown disulphone was probably D-*gluco*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-β-D-arabopyranosylmethane) (VIII; R = H). However, application of Hudson's isorotation rules [13] to the cyclic disulphone ($[M]_D$ +1660°) considered as a D-arabopyranosyl derivative, and to methyl α- and β-D-arabopyranoside [14] ($[M]_D$ −2840° and −40,300° respectively) to determine the value of *B* (−21,570°), gave a positive value for *A* (+23,230°), which is contrary to the assignment of the β-configuration to the diethylsulphonylmethyl group. Conformational analysis and experimental evidence,[15] however, lead to the prediction that D-arabopyranoside exists in the 1C (VIa and VIIIa) rather than the C1 (VIb and VIIIb) chair form. In the case of the cyclic disulphone (VIII; R = H), however, where R is a diethylsulphonylmethyl group and is in the β-position, it is unlikely that the compound exists in the 1C conformation [VIIIa; R = $CH(SO_2Et)_2$] since the bulky diethylsulphonylmethyl group would be in an axial position and, therefore, the C1 conformation [VIIIb; R = $CH(SO_2Et)_2$] is favoured. Thus we conclude that methyl D-arabopyranosides and D-*gluco*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VIII; R = H) do not exist in the same conformation, but in the 1C and the C1 chair form respectively, which perhaps accounts for the invalidity of the application of Hudson's rules of isorotation to the latter compound if considered as a D-arabopyranosyl derivative. Similar explanations have been suggested [16,17] for the exceptional character of the rotations of anomeric derivatives having the pyranose ring structure in the mannose, fructose, and sorbose series. The disulphone (VIII; R = H) was obviously formed as a result of deamination of D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane (IV; R = R′ = H) under the influence of base. Under acidic conditions, elimination of the amino-group from D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane salt (II; R = HCl) gave the D-*manno*-2 : 6-epoxy-cyclic disulphone (VI; R = H) as the sole product and deamination probably proceeded by a S_N1 type of mechanism facilitated by the cationoid character of the nitrogen atom. The different behaviour in base can, however, be accounted for by the dissociation from $C_{(2)}$ of the amino-group, which is not cationoid in this case, as a result of participation by one of the neighbouring ethylsulphonyl groups at $C_{(1)}$ with formation of the cyclic intermediate (V). Subsequent cyclisation will proceed with retention of configuration at $C_{(2)}$ since attack by the hydroxyl group attached to $C_{(6)}$ to form the 2 : 6-epoxy-cyclic disulphone could only take place at the side to which the amino-group was attached and would lead only to the D-*gluco*-configuration.

The transformation of the D-*gluco*-2 : 6-epoxy-disulphone (VIII; R = H) under mild alkaline conditions to the D-*manno*-isomer (VI; R = H) accounts for the formation of the latter compound in the reaction between D-*gluco*-2-amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate (II; R = Et·CO_3H) and dilute aqueous ammonia and presumably proceeded *via* the unsaturated acyclic disulphone (III) by β-elimination and addition. The opening of the pyranose ring under basic conditions would be facilitated by the tendency of the hydrogen atom at $C_{(1)}$ to ionise as a result of the electron-attracting effect of the diethylsulphonyl groups. Subsequent recyclisation would undoubtedly be in favour of the formation of the D-*manno*-2 : 6-epoxy- (VI; R = H) rather than the D-*gluco*-isomer (VIII; R = H) since the former has the least number of non-bonded interactions. Paper chromatography revealed that in dilute aqueous ammonia the transformation of

[13] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66.
[14] *Idem, ibid.*, 1925, **47**, 265.
[15] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.
[16] Hudson, *J. Amer. Chem. Soc.*, 1926, **48**, 1424; 1939, **61**, 2972.
[17] Pacsu, *ibid.*, 1939, **61**, 2669.

D-*gluco*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (VIII; R = H) into the D-*manno*-isomer was fast (less than 24 hr.) compared with the formation of D-arabinose which required 6—7 days to be complete; after 5 hr. no arabinose was present, but much of the D-*gluco*-disulphone (VIII; R = H) was converted into the D-*manno*-isomer (VI; R = H). These observations, and the fact that the D-*manno*-isomer (VI; R = H) was not transformed in dilute aqueous ammonia into the D-*gluco*-isomer (VIII; R = H) but was degraded directly to D-arabinose, suggested that the degradation of the D-*gluco*-2 : 6-epoxy-disulphone (VIII; R = H) proceeded *via* the D-*manno*-isomer (VI; R = H).

Previous results [3] suggested that cleavage of the cyclic disulphone (VI; R = H) occurs directly by a hydroxyl-ion attack at the cationoid $C_{(2)}$ of the 2 : 6-epoxy(pyranosyl)-ring with a resultant elimination of diethylsulphonylmethane (X) rather than *via* the saturated disulphone $\{HO{\cdot}H_2C{\cdot}[CH(OH)]_4{\cdot}CH(SO_2Et)_2\}$ by addition of the elements of water across the double bond in (III). Further support for the former mechanism was obtained by reaction of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-α-D-arabopyranosylmethane) (VI; R = H) with sodium methoxide in methanol from which crystalline methyl β-D-arabopyranoside was obtained in 33% yield; paper chromatography indicated the presence of starting material (VI; R = H) and the absence of 1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxy-2-methoxyhexane $\{HO{\cdot}H_2C{\cdot}[CH(OH)]_3{\cdot}CH(OMe){\cdot}CH(SO_2Et)_2\}$ and other isomers of methyl arabinosides. The formation of this arabopyranoside (IX; R = Me) confirms the assignment of the pyranose structure to the cyclic sulphone. Since the reaction occurred with complete inversion to give the β-methyl compound (IX; R = Me), the bimolecular mechanism is favoured, although the S_N1 mechanism cannot be overlooked in view of the recent investigations of the *O*-acylglycosyl halides. A bimolecular displacement reaction (S_N2) would involve a transition state (XXIII) where $C_{(1)}$, $C_{(2)}$, and the attacking hydroxyl (or methoxyl) ion are collinear, and where $C_{(3)}$, $C_{(2)}$, the 2-hydrogen atom, and the oxygen atom of the epoxy-ring are coplanar. During this transition, the 3- and the 4-hydroxyl group are brought further apart where they are *trans*-diequatorial in the case of the D-*manno*-configuration (VIa), but nearer in the case of *trans*-diaxial hydroxyls in the D-*gluco*-isomer (VIIIb), and therefore the formation of the intermediate is more favoured in the case of the cyclic D-*manno*-disulphone (VI; R = H). Similar considerations also apply to an S_N1 mechanism involving participation of the ring-oxygen atom with elimination of the diethylsulphonylmethyl group to form the oxonium ion (XXIV). Formation of D-arabinose (IX; R = H) or methyl D-arabopyranoside [*e.g.*, (IX; R = Me)] would be a result of attack at the anomeric carbon atom by a hydroxyl or methoxyl ion respectively, and conformational considerations indicate that the most likely route would be through the half-chair form (XXIVa). Attack by the hydroxyl or methoxyl ion could then occur either from above the plane of the ring, giving the β-isomer in which two functional groups would be equatorial and two would be axial (VIIIa), or from beneath to give the α-isomer; but the latter process is less likely since it would lead to a conformation in which three substituent groups are axial (VIb).

Experimental

Paper chromatography was carried out at 22° on Whatman No. 1 filter paper by the descending method with (i) butan-1-ol–ethanol–water (40 : 11 : 19 v/v), (ii) butan-1-ol–pyridine–water (10 : 3 : 3 v/v), or (iii) ethyl acetate–acetic acid–water (9 : 2 : 2 v/v) as mobile phase. The separated substances were detected with (*a*) a *ca.* 4% solution of silver nitrate containing excess of ammonia, (*b*) a solution of *p*-anisidine hydrochloride [12] in butan-1-ol–ethanol–water, or (*c*) a solution of *ca.* 1% ninhydrin in butan-1-ol. Solutions were evaporated under reduced pressure. Optical rotations are at *ca.* 20°.

2-*Amino*-2-*deoxy*-D-*glucose Diethyl Dithioacetal Hydrochloride*.—2-Amino-2-deoxy-D-glucose hydrochloride (15 g.) was shaken overnight with fuming hydrochloric acid (50 ml.; saturated at 0°) and ethanethiol (25 g.). The solution was diluted with ethanol (250 ml.), then neutralised

with lead carbonate, and the insoluble lead salts were filtered off and washed with ethanol (200 ml.). Concentration of the combined filtrate and washings yielded a colourless syrup (17 g.) which slowly crystallised. Recrystallisation from ethanol–ether gave needles with m. p. 79—80°, $[\alpha]_D$ −16·0° (*c* 2·5 in H_2O), R_F 0·67 [solvent (iii)] (Found : C, 37·1; H, 7·6; N, 4·1; S, 18·6; Cl, 9·8. Calc. for $C_{10}H_{24}O_4NS_2Cl$: C, 37·4; H, 7·5; N, 4·4; S, 19·9; Cl, 11·1%). Whitehouse, Kent, and Posternak [4] record m. p. 75—76°, $[\alpha]_D$ −18·5° in H_2O. Treatment of 2-amino-2-deoxy-D-glucose hydrochloride with ethanethiol and hydrochloric acid (*d* 1·18) for *ca.* 2 months resulted in a 100% recovery of the starting material (see ref. 18).

Peroxypropionic Acid Oxidation of 2-Amino-2-deoxy-D-glucose Diethyl Dithioacetal Hydrochloride.—The diethyl dithioacetal (5·0 g.) in methanol (50 ml.) was cooled to −10° in acetone–solid carbon dioxide, and an excess of cold aqueous peroxypropionic acid (150% of theory for 4 mols., based on propionic anhydride) [2] was added with shaking. The solution was then set aside at room temperature for 1 hr. During subsequent concentration, ammonium chloride (*ca.* 0·9 g.) separated and was filtered off. Further concentration of the filtrate then gave a brown syrup from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration. The syrup was decolorised (charcoal) in hot methanol. Evaporation of the solution yielded a colourless syrup (*ca.* 4·0 g.) of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane which had $[\alpha]_D$ +10° (*c* 3·8 in H_2O), R_F 0·69 [solvent (iii)] (Found : C, 35·8; H, 6·3. Calc. for $C_{10}H_{20}O_8S_2$: C, 36·1; H, 6·0%). Hough and Taylor [3] record $[\alpha]_D$ +6·3° in H_2O.

D-manno-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane.*—A solution of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (0·5 g.) in acetic anhydride (5 ml.) containing sulphuric acid (1 drop) was heated at 95—100° for ½ hr., then poured into ice-water; an oily triacetate separated which was extracted into chloroform (2 × 30 ml.), and the extracts were washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Concentration of the chloroform solution than gave a pale yellow syrup (0·46 g.) which crystallised overnight. Recrystallised from methanol–ether, the triacetate had m. p. 128° not depressed on admixture with authentic D-*manno*-3 : 4 : 5-tri-*O*-acetyl-2 : 6-epoxy-1 : 1-diethylsulphonylhexane, $[\alpha]_D$ −7·0° (*c* 3·6 in MeOH) [Found : C, 41·7; H, 5·6; S, 13·3; Ac, 26·95 (corrected [2,3]). Calc. for $C_{16}H_{26}O_{11}S_2$: C, 41·9; H, 5·7; S, 14·0; Ac, 28·1%]. Hough and Taylor [3] record m. p. 125—127°.

Treatment of D-manno-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane with Ammonia.*—The disulphone (1·0 g.) was shaken with dilute aqueous ammonia (20 ml.; pH 10—11) at room temperature. The mixture became pale brown and paper chromatography indicated that reaction was complete in 4—5 days. During this time crystals separated : they (*ca.* 0·4 g.) were filtered off, washed with water, and after recrystallisation from methanol had m. p. 102°, not depressed on admixture with authentic diethylsulphonylmethane. The combined filtrate and washings were concentrated, yielding a brownish syrup (*ca.* 0·5 g.) which was decolorised (charcoal) in hot methanol. Evaporation of this solution yielded a pale yellow syrup which crystallised gradually. Recrystallisation from methanol afforded D-arabinose, m. p. and mixed m. p. 158—159°, $[\alpha]_D$ −100° (equil.; *c* 2·3 in H_2O), R_F 0·13 [solvent (iii)].

Treatment of D-manno-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane with Sodium Methoxide.*—Sodium (*ca.* 0·1 g.) was added to the sulphone (0·3 g.) in methanol (10 ml.) at 0°, and the solution stored in the ice-box for 5 days. Amberlite IR-120 (H) ion-exchange resin (*ca.* 5 g.) was added and the mixture was shaken for 2 hr. The resin was filtered off and washed 5 times with methanol, and the combined filtrate and washings were concentrated, yielding a colourless syrup which when examined on paper chromatograms with spray (*a*) was observed to contain, besides unchanged starting material, a component with R_F 0·41 (solvent iii) indistinguishable from methyl β-arabopyranoside. On storage crystalline methyl β-D-arabopyranoside (0·045 g.) separated and was filtered off and washed several times with acetone. It had m. p. 168°, $[\alpha]_D$ −222° (*c* 1·45 in H_2O), R_F 0·41 (solvent iii). Hudson [14] records m. p. 169°, $[\alpha]_D$ +245·5° in H_2O, for the L-isomer.

Peroxypropionic Acid Oxidation of 2-Acetamido-2-deoxy-D-glucose Diethyl Dithioacetal.—2-Acetamido-2-deoxy-D-glucose diethyl dithioacetal (10 g.) in methanol (50 ml.) was oxidised as for 2-amino-2-deoxy-D-glucose diethyl dithioacetal hydrochloride, but at −10°, giving crystalline D-gluco-2-*amino*-1 : 1-*diethylsulphonyl*-3 : 4 : 5 : 6-*tetrahydroxyhexane peroxypropionate* (*ca.* 10 g.) which after two recrystallisations from methanol–ether had m. p. 88—90°,

[18] Wolfrom and Anno, *J. Amer. Chem. Soc.*, 1952, **74**, 6150.

$[\alpha]_D$ +10° (*c* 2·03 in H_2O), R_F 0·57 [solvent (iii)] (Found: C, 35·4; H, 6·8; S, 14·3; N, 3·3%; *M*, 430.[7] $C_{13}H_{29}O_{11}NS_2$ requires C, 35·6; H, 6·7; S, 14·6; N, 3·2%; *M*, 439). The compound oxidised acidic iodide solutions with the liberation of iodine.

Oxidation of 2-acetamido-2-deoxy-D-glucose diethyl dithioacetal (0·6 g.) with aqueous peroxypropionic acid *at room temperature* yielded a crystalline compound (*ca.* 0·2 g.), m. p. 204°, which was identified as ammonium ethyl sulphite [10] according to the following evidence; it sublimed unchanged when heated gradually; with warm aqueous sodium hydroxide, it liberated ammonia and with warm dilute hydrochloric acid liberated sulphur dioxide; a white precipitate, which dissolved in concentrated hydrochloric acid, was obtained when treated with barium chloride solution; it was extremely hygroscopic and unstable in the presence of water (Found: C, 19·0; H, 7·2; N, 10·9; S, 25·4. Calc. for $C_2H_9O_3NS$: C, 18·9; H, 7·1; N, 11·0; S, 25·1%).

D-gluco-2-*Acetamido*-3 : 4 : 5 : 6-*tri*-O-*acetyl*-1 : 1-*diethylsulphonylhexane*.—D-*gluco*-2-Amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate (0·1 g.) in dry pyridine (2 ml.) was treated with acetic anhydride (2 ml.) as above, yielding the acetate as crystals (0·12 g.) which after recrystallisation from ether had m. p. and mixed m. p. 178°, $[\alpha]_D$ +15° (*c* 3·6 in $CHCl_3$) (Found: C, 42·8; H, 5·8; N, 2·5; S, 10·9; Ac, 37·9. Calc. for $C_{20}H_{33}O_{13}NS_2$: C, 42·8; H, 5·9; N, 2·5; S, 11·4; Ac, 38·5%). McDonald and Fischer [5] record m. p. 176·5—178°, $[\alpha]_D$ +13·5° (in $CHCl_3$).

Reaction of D-gluco-2-*Amino*-1 : 1-*diethylsulphonyl*-3 : 4 : 5 : 6-*tetrahydroxyhexane Peroxypropionate with Dilute Aqueous Ammonia and Separation of the Products*.—The disulphone (7 g.) was treated with dilute aqueous ammonia (100 ml.; pH 10—11) at room temperature, gradually becoming pale yellow. After 24 hr., the solution was concentrated to a pale yellow syrup (*ca.* 5·0 g.) which when examined on paper chromatograms with spray (*a*) was observed to contain at least three products [R_F 0·13, 0·69, 0·86; solvent (iii)]. The syrup was fractionated on a cellulose column, with benzene–ethanol (10 : 1 v/v) as mobile phase. Three fractions were obtained. Fraction 1 gave syrupy D-gluco-2 : 6-*epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane* (*ca.* 1·8 g.), $[\alpha]_D$ +5·0° (*c* 3·4 in H_2O), R_F 0·86 [solvent (iii)] (Found: C, 36·3; H, 6·2. $C_{10}H_{20}O_8S_2$ requires C, 36·1; H, 6·0%). Fraction 2 gave syrupy D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (*ca.* 2·0 g.) with $[\alpha]_D$ +10·0° (*c* 2·3 in H_2O), R_F 0·69 [solvent (iii)]. Fraction 3 gave crystalline D-arabinose (*ca.* 0·4 g.) which after recrystallisation from methanol had m. p. and mixed m. p. 158°, $[\alpha]_D$ −108° (*c* 2·0 in H_2O), R_F 0·13 [solvent (iii)].

D-gluco-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane*.—A solution of D-*gluco*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (fraction 1) (0·5 g.) in acetic anhydride (5 ml.) containing sulphuric acid (1 drop) was heated at 95—100° for ½ hr., then poured into ice-water. The *triacetate* was extracted into chloroform (2 × 20 ml.), and the extracts were washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Concentration of the chloroform solution gave a colourless syrup (0·4 g.), $[\alpha]_D$ +13·3° (*c* 3·0 in MeOH) (Found: C, 42·0; H, 5·5. $C_{16}H_{26}O_{11}S_2$ requires C, 41·9; H, 5·7%).

D-manno-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane*.—D-*manno*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (fraction 2) (0·5 g.) was acetylated as for the D-*gluco*-isomer, yielding crystals (0·45 g.) which after two recrystallisations from methanol–ether had m. p. and mixed m. p. 128°, $[\alpha]_D$ −7·0° (*c* 2·5 in MeOH).

D-*Arabinose from* D-gluco-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane*.—The disulphone (0·5 g.) was kept in dilute aqueous ammonia (10 ml.; pH 10—11) at room temperature for 7 days. Crystals separated, which (*ca.* 0·2 g.) were filtered off, washed with water, and after recrystallisation from methanol had m. p. 102°, not depressed on admixture with authentic diethylsulphonylmethane. The combined filtrate and washings were concentrated, yielding a syrup (*ca.* 0·2 g.) which crystallised. Recrystallisation from methanol gave D-arabinose with m. p. and mixed m. p. 159°, $[\alpha]_D$ −106° (equil.; *c* 3·6 in H_2O), R_F 0·13 [solvent (iii)].

Transformation of D-gluco-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane into the* D-manno-*Isomer*.—The D-*gluco*-disulphone (0·5 g.) was kept in dilute aqueous ammonia (10 ml.; pH 10—11) at room temperature for 24 hr. The solution was concentrated to a pale yellow syrup which consisted mainly of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane [R_F 0·69 (solvent iii)] with a little of D-arabinose [R_F 0·13 (solvent iii)] as revealed by paper chromatography. The two components were separated by chromatography on filter paper (18·25″ × 22·5″) with solvent (iii), and the D-*manno*-disulphone was extracted from the appropriate part of the chromatogram with hot methanol. The methanol extract

was concentrated to a colourless syrup (*ca.* 0·2 g.) with $[\alpha]_D$ +8·5° (*c* 2·4 in H_2O), R_F 0·69 [solvent (iii)].

D-*manno*-3 : 4 : 5-Tri-*O*-acetyl-2 : 6-epoxy-1 : 1-diethylsulphonylhexane (*ca.* 0·1 g.) was obtained from the triol (0·1 g.) as above and after recrystallisation from acetone–light petroleum (b. p. 40—60°) had m. p. and mixed m. p. 128°, $[\alpha]_D$ −7·2° (*c* 4·0 in MeOH).

2-*Acetamido*-2-*deoxy*-β-D-*glucopyranosylsulphonylethane*.—2-Acetamido-2-deoxy-β-D-glucopyranosylthioethane [6] (1·0 g.) in methanol (20 ml.) was oxidised with peroxypropionic acid (150% of theory for 2 mols., based on propionic anhydride) at −10° as above, giving crystals of the *sulphone* (*ca.* 1·2 g.) which after recrystallisation from methanol–ether had m. p. 172°, $[\alpha]_D$ +42° (*c* 2·4 in H_2O) (Found : C, 40·5; H, 6·6; S, 9·33; N, 4·7; Ac, 14·0. $C_{10}H_{19}O_7NS$ requires C, 40·4; H, 6·4; S, 10·8; N, 4·7; Ac, 14·5%).

Treatment of 2-acetamido-2-deoxy-β-D-glucopyranosylsulphonylethane with dilute aqueous ammonia for 10 days resulted in a 100% recovery of the starting material. The compound was also stable to dilute hydrochloric acid.

Attempted Synthesis of D-gluco-2-*Acetamido*-1 : 1-*diethylsulphonyl*-3 : 4 : 5 : 6-*tetrahydroxyhexane*.—D-*gluco*-2-Amino-1 : 1-diethylsulphonyl-3 : 4 : 5 : 6-tetrahydroxyhexane peroxypropionate (1·0 g.), silver acetate (0·4 g.), and acetic anhydride (1·0 g.) in methanol [9] (20 ml.) were shaken for 3 hr. at room temperature in the dark, then refluxed for 5 min. and filtered hot, and the residue washed with hot water (10 ml.). The combined filtrate and washings were acidified with one drop of concentrated hydrochloric acid and after 2 hr. at room temperature the silver chloride was filtered off. During subsequent concentration ammonium chloride (*ca.* 0·1 g.) separated and was filtered off. Further concentration of the filtrate gave a colourless syrup (0·5 g.) of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane with R_F 0·69 [solvent (iii)]. Acetylation of this syrup (0·1 g.) gave the triacetate (*ca.* 0·1 g.) which after recrystallisation from methanol–ether had m. p. and mixed m. p. 128°.

Periodate Oxidation.—D-*manno*- and D-*gluco*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexanes were oxidised with sodium metaperiodate at room temperature and the oxidant uptake and acid liberated were determined.[6] The results were as follows :

Compounds		½ hr.	1 hr.	2 hr.	3 hr.	4 hr.	6 hr.	9 hr.
D-*manno*-Disulphone	Uptake *	0·66	1·26	1·33	1·60	1·76	1·93	2·05
	Acid	0·22	0·30	0·40	0·66	0·88	0·95	1·0
D-*gluco*-Disulphone	Uptake	0·0	0·40	0·60	0·79	2·0	2·0	2·05
	Acid	0·0	0·2	0·25	0·3	1·0	1·0	1·0

* Moles/mole of compound oxidised.

We thank Drs. W. D. Ollis and J. F. W. McOmie for helpful discussions.

THE UNIVERSITY, BRISTOL. [*Received, March 11th*. 1957.]