## 203. *The Disulphones derived by Oxidation of the Diethyl Dithioacetals of* D-*Galactose,* D-*Mannose, and* D-*Glucose with Peroxypropionic Acid, and their Conversion into Aldopentoses.*[1]

By L. Hough and T. J. Taylor.

Oxidation of D-galactose and D-glucose diethyl dithioacetals with aqueous peroxypropionic acid at room temperature yielded, respectively, D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-α-D-lyxopyranosylmethane) (IV; R = H) and the corresponding D-*manno*-compound (X; R = H). In a similar oxidation of D-mannose diethyl dithioacetal, two compounds were isolated, namely, 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (XIII; R = H) and D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (X; R = H) which was identical with that prepared from D-glucose diethyl dithioacetal. Each disulphone was cleaved by dilute aqueous ammonia to give, in high yield, an aldopentose and diethylsulphonylmethane. The periodate oxidation of these disulphones is discussed.

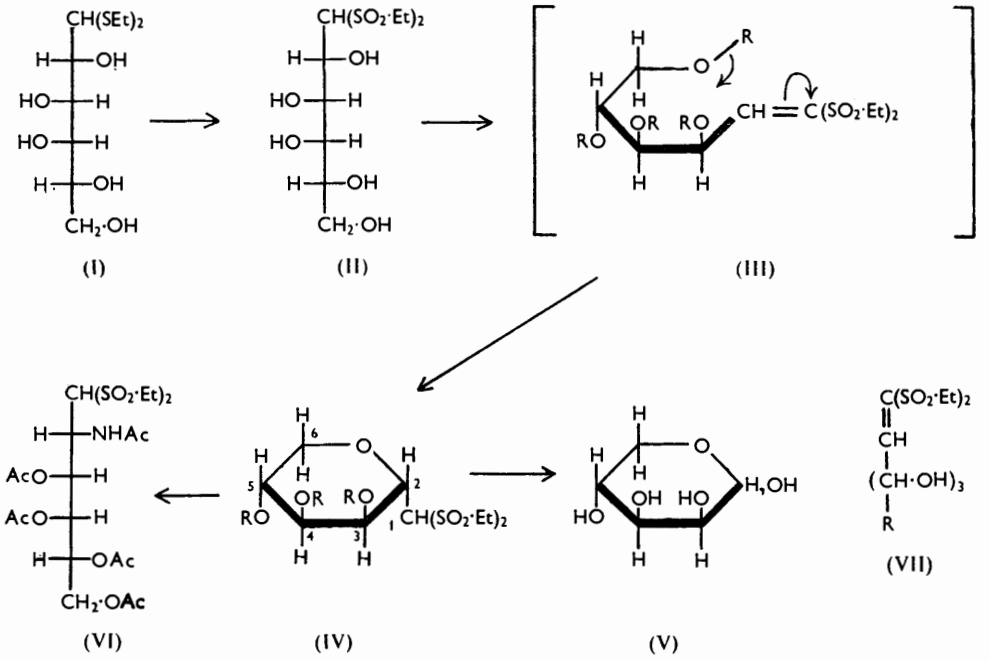
Oxidation of D-aldopentose diethyl dithioacetals with aqueous peroxypropionic acid at room temperature has afforded only unsaturated acyclic disulphones, namely, 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes [2] (*e.g.*, VII; R = H). Similar oxidation of L-rhamnose diethyl dithioacetal gave 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (VII; R = Me) and, in addition, predominantly 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane.[3] The unsaturated acyclic disulphones are analogous to those obtained when fully acetylated aldohexose diethyl dithioacetals are oxidised with monoperoxyphthalic acid in ether.[4] In contrast, oxidations of D-galactose, D-glucose, and D-mannose diethyl dithioacetals with aqueous peroxypropionic acid at room temperature have given cyclic disulphones and not, as expected, the isomeric unsaturated acyclic

[1] For preliminary communications see Hough and Taylor, *Chem. and Ind.*, 1954, (*a*) 575, (*b*) 1018.
[2] *Idem*, *J.*, 1955, 1212.
[3] *Idem*, *J.*, 1955, 3544.
[4] McDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087.

compounds although the latter are probably formed in the reaction as precursors of the cyclic modifications.

Oxidation of D-galactose diethyl dithioacetal (I) with aqueous peroxypropionic acid at room temperature yielded on concentration of the reaction mixture a highly crystalline disulphone. Although this product gave correct analyses for the expected acyclic tetrahydroxyhex-1-ene (III; R = H), it gave only a pale yellow colour in dry pyridine, even after 24 hours, whereas compounds containing the 1 : 1-diethylsulphonylalk-1-ene grouping show a typical magenta or cherry-red coloration.[2,3] Unlike the mildly acidic, unsaturated acyclic disulphones, derived from D-xylose and L-rhamnose diethyl dithioacetals,[2,3] this compound (IV; R = H) was neutral in aqueous solution and could not be hydrogenated in the presence of Raney nickel. Further, acetylation of the crystalline disulphone by a variety of methods gave only a triacetate (IV; R = Ac) and not D-*lyxo*-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonyl-hex-1-ene (III; R = Ac) which was prepared by McDonald and Fischer[4] by oxidising penta-*O*-acetyl-D-galactose diethyl dithioacetal with monoperoxyphthalic acid. Similarly, benzoylation gave only a tribenzoate (IV; R = Bz). It is noteworthy that 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (VII; R = Me) can be fully acetylated.

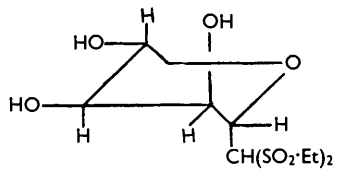
The inability to form a dihydro-derivative and lack of acidity and of coloration with dry pyridine suggest that there is no unsaturated linkage within the molecule, whilst the formation of only tri-*O*-substituted derivatives suggests that the product is cyclic as the result of engagement of a hydroxyl group in the probable intermediate (III; R = H) in intramolecular bonding. The observations that L-rhamnose and aldopentose diethyl dithioacetals afforded unsaturated disulphones, and not cyclic derivatives, on oxidation clearly indicate that the 6-hydroxyl group of the intermediate (III; R = H) is involved in ring closure. Examination of a molecular model (Catalin Ltd.) of the unsaturated



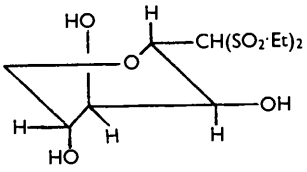

acyclic disulphone (III) showed that the formation of a 2 : 6-epoxy (pyranosyl) ring was possible by attack of the cationoid $C_{(2)}$ on the terminal primary hydroxyl group, thus giving the cyclic disulphone (IV; R = H). Similarly, molecular models of the hex-1-ene derivative (VII; R = Me) and the pent-1-ene derivatives (*e.g.*, VII; R = H) revealed

that owing to restricted rotation about the $C_{(2)}$–$C_{(3)}$ bond the hydroxylated carbon chains were too short to allow ring closure in this way to give the 2 : 5-epoxy (furanosyl) ring. Periodate oxidation gave further evidence in favour of a pyranosyl structure (IV; R = H) for this disulphone (see below). Application of Hudson's isorotation rules to the cyclic disulphone (IV; R = H) ($[M]_D$ + 6308°) and its tri-*O*-acetyl derivative ($[M]_D$ — 10,030°) considered as D-lyxopyranosyl derivatives, and with methyl α- and β-D-lyxopyranoside and their triacetates used to determine values of *B* (—5730° and —11,520° respectively), gave positive values for *A* (+12,038° and +1490° respectively), suggesting an α-configuration for the diethylsulphonylmethyl group. The large difference in the molecular rotations of the cyclic disulphones (IV; R = H and Ac) is perhaps attributable to interaction of one or both of the sulphonyl groups with the neighbouring acetyl groups. This behaviour parallels that of *o*-nitrophenyl β-D-glucoside which has $[M]_D$ —26,500° whereas the tetra-*O*-acetyl derivative [5] has $[M]_D$ + 21,100°. Conformational analysis of D-lyxopyranoside leads to the prediction that it can exist in either the C1 or 1C conformation [6] but that, if D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-α-D-lyxopyranosylmethane) had the C1 conformation (IV*a*), there would be a bulky group in the axial position at the anomeric carbon atom : if, in this conformation the diethylsulphonylmethyl group were in the β-position, there would be a Δ2 condition. Thus the 1C conformation (IV*b*) is preferred since the bulky diethylsulphonylmethyl group is equatorial and there are only two hydroxyl groups in axial positions.

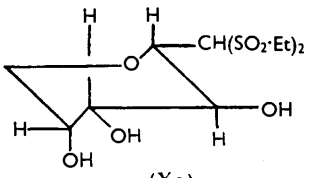
The cyclic disulphone (IV; R = H) was cleaved by an excess of dilute aqueous ammonia (pH 10—11) to give D-lyxose (V) in high yield and diethylsulphonylmethane. The rate of reaction was much slower (6—7 days) than with 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes (*e.g.*, VII; R = H) and the orange-red colour which developed in the latter reaction was not encountered.[2,3] This slower rate is probably due to a diminution of cationoid activity at $C_{(2)}$ as the result of theformation of the 2 : 6-epoxy (pyranosyl) ring. Two obvious routes for the degradative reaction can be considered. Cleavage of the cyclic disulphone (IV; R = H) could proceed by isomerisation to the unsaturated acyclic compound (III; R = H) followed by a relatively slow addition of the elements of water across the double bond in the latter, to give a saturated pentahydroxy-derivative which would rapidly disproportionate into D-lyxose (V) and diethylsulphonylmethane.[2,7]



(IVa)



(IVb)



(Xa)

Alternatively, cleavage could occur directly by a hydroxyl-ion attack at the cationoid $C_{(2)}$ of the 2 : 6-epoxy (pyranosyl) ring with a resultant elimination of diethylsulphonylmethane. Since the solution remained colourless during the reaction with ammonia, thus suggesting that the unsaturated acyclic compound (III; R = H) was absent, the second mechanism is favoured. Furthermore, the reaction of the triacetate (IV; R = Ac) with ammonia (*d* 0·88) in methanol agrees with the latter route and also supports the evidence for the cyclic structure assigned to the crystalline disulphone (IV; R = H). In this reaction a preponderance of lyxose was detected on paper chromatograms together with a small amount of a faster-moving material which was separated and then acetylated to give a 2-acetamido-D-*lyxo*-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhexane (*e.g.*, VI). There can have been but little, if any, of the unsaturated acyclic compound (III; R = Ac) present in this reaction mixture as this would be expected to give in high yield the 2-acetamido-derivative by the addition of the elements of ammonia across the double bond, followed by

[5] Pigman, *J. Res. Nat. Bur. Stand.*, 1944, **33**, 129.
[6] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.
[7] Bourne and Stephens, *J.*, 1954, 4009.

an *O*- to *N*-acyl migration, which would prevent subsequent disproportionation of the molecule.[2,4,7] Thus the 2-acetamido-compound (VI) probably originated from a direct nucleophilic attack by ammonia at $C_{(2)}$ of the cyclic disulphone with inversion of configuration at this carbon atom and concurrent fission of the ring. If an *O*- to *N*-acyl migration ensued, the stable 2-acetamido-compound would result, whereas in the absence of such a migration the 2-amino-intermediate would be expected to disproportionate into D-lyxose and diethylsulphonylmethane. Consequently, slow amination relative to deacetylation would lead to a high yield of D-lyxose. Alternatively, lyxose could arise by direct reaction with hydroxyl ions as described above.

Zinner and Falk [8] have prepared 1 : 1-diethylsulphonyl-D-*galacto*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (II) from D-galactose diethyl dithioacetal using 30% hydrogen peroxide and ammonium molybdate at 0° for oxidation, but these workers have not reported the isolation of the cyclic disulphone (IV; R = H). In our hands, attempted recrystallisation from aqueous ethanol of the D-*galacto*-compound (II) prepared by this method resulted in complete conversion into the cyclic compound (IV; R = H), thus suggesting that it (II) is the primary intermediate in the formation of this derivative. 1 : 1-Diethylsulphonyl-D-*galacto*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (II) was extremely sensitive to mild alkali. On paper chromatograms, with butan-1-ol–pyridine–water as mobile phase, instantaneous cleavage occurred and only lyxose could be detected. Details of the preparation of 1 : 1-di-*n*-butylsulphonyl-D-*lyxo*-3 : 4 : 5 : 6-tetrahydroxyhex-1-ene and the corresponding di*iso*butylsulphonyl compound have also been reported [8] but, as no proof of the structure was given, a cyclic modification of these compounds must be considered.

D-Glucose diethyl dithioacetal (VIII) was also oxidised with aqueous peroxypropionic acid at room temperature, giving a syrup (A) which has been shown to be D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (diethylsulphonyl-α-D-arabopyranosylmethane) (X; R = H) (see below).

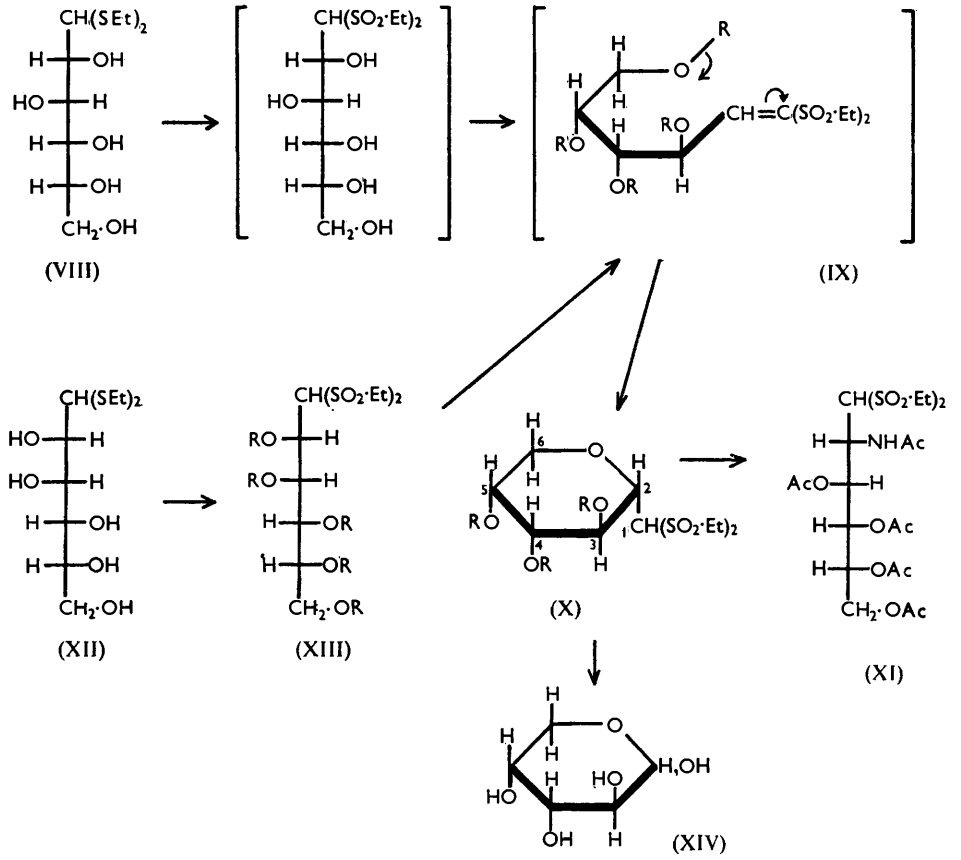
Oxidation of D-mannose diethyl dithioacetal (XII) under the same conditions gave two disulphones, crystalline 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (XIII; R = H) (58%) and a syrup (B) identified as D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (X; R = H) (38%). This reaction was first described by McDonald and Fischer,[9] who obtained an uncharacterised mixture of disulphones and proposed the structure (XIII; R = H) for one component. The formation of a penta-*O*-acetate (XIII; R = Ac) and periodate oxidation (see below) of the disulphone (XIII; R = H) have now proved that their supposition was correct. Zinner and Falk [8] also report the preparation of this pentahydroxyhexane derivative (XIII; R = H) by oxidation of D-mannose diethyl dithioacetal with 30% hydrogen peroxide and ammonium molybdate at 0°, but they quote m. p. 167° whilst we [1b] originally reported m. p. 119°. Re-examination of the melting point of this compound has shown considerable variation with the rate of heating and with the method used for the determination, perhaps owing to the extreme sensitivity to alkali. The *X*-ray powder photograph of a specimen prepared by Zinner and Falk's method [8] was identical with that of our material (XIII; R = H).

The syrupy disulphones, (A) and (B), derived from the oxidations of D-glucose and D-mannose diethyl dithioacetals respectively were identical as they had the same specific rotations and the same rates of movement on paper chromatograms, and *X*-ray powder photographs of the derived tribenzoates (X; R = Bz) were indistinguishable.

Like D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (IV; R = H), but unlike the unsaturated acyclic disulphones (*e.g.*, VII), the syrups (A) and (B) gave only very pale yellow colours with dry pyridine even after prolonged storage, and they could not be hydrogenated in the presence of Raney nickel. Acetylation gave a crystalline triacetate (X; R = Ac) and not the known D-*arabo*-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhex-1-ene (IX; R = Ac).[4] This evidence considered together with the fact that L-rhamnose and pentose diethyl dithioacetals do not yield cyclic disulphones suggests that the syrups (A) and (B) are D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-2 : 4 : 5-trihydroxyhexane (X; R = H). Assignment of the D-*manno*-2 : 6-epoxy (α-D-arabopyranosyl) configuration follows from

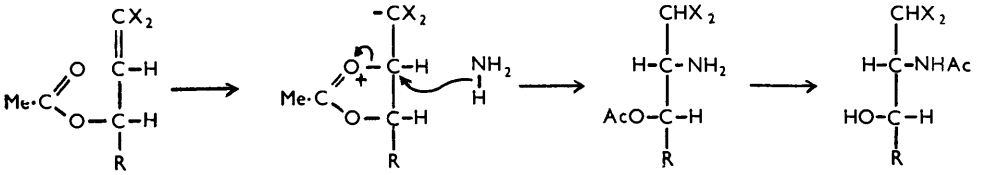
[8] Zinner and Falk, *Chem. Ber.*, 1955, **88**, 566.
[9] McDonald and Fischer, *Biochim. Biophys. Acta*, 1953, **12**, 503.

the application of Hudson's rules of isorotation to the cyclic disulphone (X; R = H) ($[M]_D$ +2092°), with methyl α- and β-D-arabopyranosides ($[M]_D$ — 2840°, —40,300° respectively) to determine the value of *B* (—21,570°), thus giving a positive value for *A* (+23,662°). Conformational analysis is in agreement with this configuration, as the pyranosyl modification in the 1C chair form (X*a*) with the bulky diethylsulphonylmethyl group in the equatorial position would be predicted to be the most stable stereoisomer.




Reaction of the triacetate (X; R = Ac) with ammonia (*d* 0·88) in methanol was analogous to the behaviour of the triacetate (IV; R = Ac), already mentioned. Paper chromatography indicated the presence of largely arabinose together with a small amount of faster-moving material which was isolated and then acetylated to give the known D-*gluco*-2-acetamido-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhexane (XI).[4] This product (XI) would be expected from a nucleophilic attack by ammonia at $C_{(2)}$ of the triacetate (X; R = Ac) with inversion and simultaneous opening of the α-D-arabopyranosyl ring, whereas the β-isomer would lead to the formation of the corresponding D-*manno*-2-2-acetamido-derivative. By the same reasoning, the aforementioned 2-acetamido-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhexane (VI) is predicted to have the D-*galacto*-configuration. MacDonald and Fischer[4] observed that the acyclic D-*arabo*-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhex-1-ene (IX; R = Ac) reacted stereospecifically with ammonia to give a product which on acetylation afforded only the D-*gluco*-2-acetamido-derivative (XI). Such stereospecificity would be the consequence of participation of the neighbouring 3-acetoxy-group with the formation of a cyclic ion which could react with ammonia as indicated on p. 975 to give only the D-*gluco*-configuration. In the

case of the cyclic disulphones (IV; X; R = Ac), such a process is considered to be unlikely for the reasons previously mentioned. Reaction of D-*threo*-3 : 4 : 5-tri-*O*-acetyl-1 : 1-diethylsulphonylpent-1-ene with ammonia resembled that of the above tetra-*O*-acetylhex-1-enes (III; IX; R = Ac) and led to the isolation,[2] in high yield, of a crystalline 2-acetamido-compound to which the D-*xylo*-configuration is tentatively assigned from consideration of the neighbouring group participation theory.




(X = ·$SO_2$·Et)

The syrupy disulphone (X; R = H) was readily obtained from 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (XIII; R = H) by warming it in water, dilute mineral acid, or ethanol for *ca.* 1 min. Zinner and Falk [8] were unable to recrystallise the pentahydroxyhexane (XIII; R = H) owing to its conversion into a compound (m. p. 135°) designated 1 : 1-diethylsulphonyl-D-*arabo*-3 : 4 : 5 : 6-tetrahydroxyhex-1-ene, but without structural proof. The same compound (m. p. 135°) was also prepared by oxidation of D-mannose diethyl dithioacetal in water with 30% hydrogen peroxide. Our syrupy disulphone (X; R = H) failed to crystallise even after several months, but recrystallisation of the pentahydroxyhexane (XIII; R = H) was effected from ethanol containing Cellosolve (2-ethoxyethanol).

The syrupy disulphone (X; R = H) was cleaved by an excess of dilute aqueous ammonia (pH 10—11) to give D-arabinose (XIV) in high yield and diethylsulphonylmethane. As with the cyclic disulphone (IV; R = H), the reaction was appreciably slower than that observed with 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes (*e.g.*, VII; R = H), and no orange-red colour developed.[2,3] In contrast, 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (XIII; R = H) was extremely sensitive to mild alkali, as were 1 : 1-diethylsulphonyl-D-*galacto*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (II) already mentioned and the corresponding 6-deoxy-L-*manno*-compound.[3] Paper chromatography with butan-1-ol–pyridine–water as mobile phase caused instantaneous cleavage and only arabinose was detected, whilst the use of either the acidic or the neutral mobile phase gave streaks, presumably because of conversion into the syrupy disulphone (X; R = H) during chromatography. Conversion of the syrupy disulphone (X; R = H) into D-arabinose (XIV) and diethylsulphonylmethane was also effected by prolonged heating at 95—100°, but the degradation ceased before completion owing to the formation of unknown acidic products.

1 : 1-Diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (XIII; R = H) was oxidised with unbuffered sodium metaperiodate at room temperature in the dark, the expected consumption of 4 mol. of the reagent being obtained with subsequent liberation of 4 equiv. of acid [*i.e.*, 3 mol. of formic acid and 1 mol. of diethylsulphonylacetaldehyde (XVIII) which titrates as a monobasic acid [2]]. Reaction was complete in 1 hr. (see Fig. 1) and is thus analogous to the oxidation of 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane with sodium metaperiodate.[3] Similarly 1 : 1-diethylsulphonyl-D-*galacto*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane (II) consumed in 1 hr. approximately 4 mol. of sodium metaperiodate. Comparison of these oxidations of acyclic polyhydroxyhexanes (*e.g.*, XIII; R = H) with that of acyclic 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypent-1-ene (VII; R = H) is of interest. Under unbuffered conditions, the latter showed a fairly rapid consumption of 2 mol. of periodate (1 hr.) followed by a slow overoxidation, a further mol. being consumed (complete in 24 hr.). The slow consumption of the third

mol. of the reagent is probably due to a slow addition of the elements of water across the double bond in the intermediary αβ-unsaturated aldehyde (XVI) to give 1 : 1-diethylsulphonyl-2-hydroxypropionaldehyde (XVII), followed by oxidation in the normal manner to give a second mol. of formic acid and 1 mol. of diethylsulphonylacetaldehyde (XVIII).[2] Thus the same end products are obtained from the oxidation of both saturated and unsaturated acyclic disulphones, but the overall reaction is much slower in the latter cases. Oxidation of 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypent-1-ene (VI; R = H) at pH 3·56 was slightly quicker (2 mol. of reagent consumed in 35 min.), but the general form of the curve was the same.

Periodate oxidation of D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (IV; R = H) under unbuffered conditions showed a fairly rapid consumption of

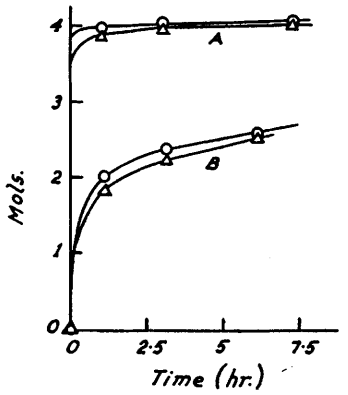
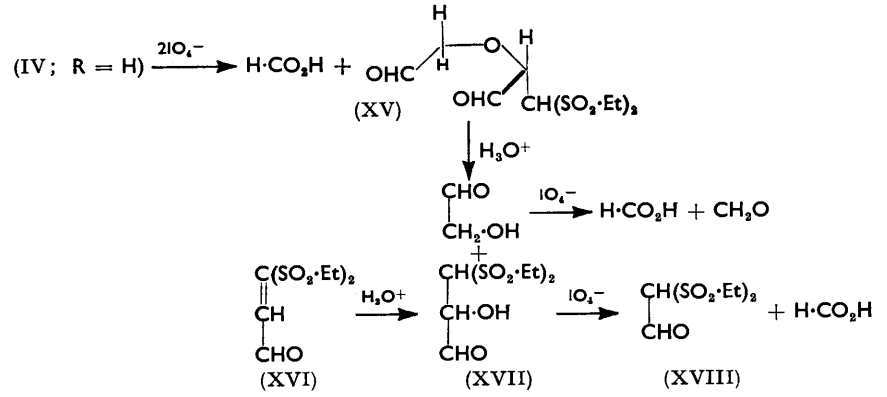



FIG. 1. *Oxidation of* (*A*) 1 : 1-*diethylsulphonyl*-D-manno-2 : 3 : 4 : 5 : 6-*pentahydroxyhexane* (XIII; R = H) *and* (*B*) 1 : 1-*diethylsulphonyl*-D-threo-3 : 4 : 5-*trihydroxypent*-1-*ene* (VII; R = H) *with sodium metaperiodate, without buffer.*

○ *Reagent consumed.* △ *Acid liberated.*

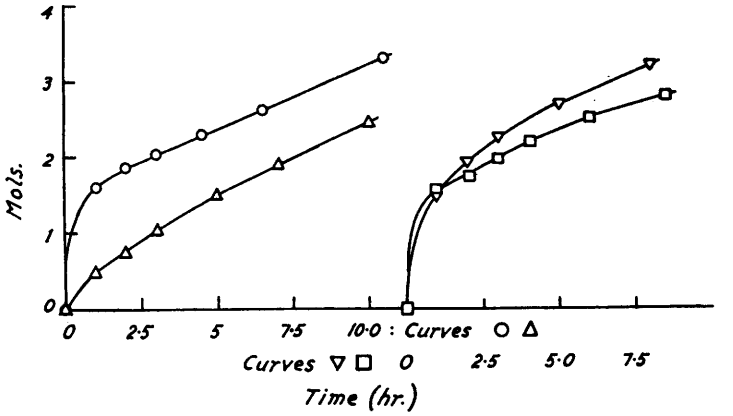
2 mol. of the reagent (2·25 hr.) which was followed by a slower consumption of another 2 mol. (complete in 24 hr.; see Fig. 2). Acid was liberated at a fairly steady rate; at the point where 2 mol. of periodate had been consumed, only 0·98 equiv. of acid had been obtained, but this figure rose to 3·6 equiv. after 24 hr. Thus the rate of liberation of acid during the second stage of the reaction was almost 1·5 times the rate of consumption of periodate. These results indicate that in the first stage the cyclic disulphone (IV; R = H) was oxidised by 2 mol. of periodate to give 1 mol. of formic acid and 1 mol. of the dialdehyde (XV) which was then hydrolysed to give 1 mol. each of glycolaldehyde and 1 : 1-diethylsulphonyl-2-hydroxypropionaldehyde (XVII). Both products would then in the second




stage consume 1 mol. of periodate with the formation from glycollaldehyde of 1 mol. each of formic acid and formaldehyde, and from 1 : 1-diethylsulphonyl-2-hydroxypropionaldehyde (XVII) 1 mol. each of formic acid and diethylsulphonylacetaldehyde (XVIII). Unsuccessful attempts were made to find a pH at which the dialdehyde (XV) would be

stable and so cause oxidation to cease after 2 mol. of periodate had been consumed. At pH 3·56 (see Fig. 2) and lower, the oxidation proceeded as in the unbuffered reaction, whilst at pH 4·6 it was impossible to distinguish between the initial and the second stage. No experiments were carried out at pH > 7 owing to the sensitivity of the cyclic disulphone (IV; R = H) to mild alkali.

FIG. 2. *Oxidation of* D-talo-2 : 6-*epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane* (IV; R = H) *with sodium metaperiodate.*




*Reagent consumed*: ○, *without buffer*; □ *at* pH 3·56; ▽ *at* pH 4·6. △ *Acid liberated, without buffer.*

## EXPERIMENTAL

Evaporations were under reduced pressure. Paper chromatography was performed by the descending method at room temperature on Whatman No. 1 filter paper with butan-1-ol–ethanol–water (40 : 11 : 19 v/v), butan-1-ol–pyridine–water (10 : 3 : 3 v/v) or ethyl acetate–acetic acid–water (9 : 2 : 2 v/v) as mobile phase and ammoniacal silver nitrate for the detection of the polyhydroxy-compounds. M. p.s of the disulphones were determined on a Kofler micro-heating stage. Figures quoted for acetyl content have been corrected in order to allow for the extra acid that arises from the sulphone groups during the determination. The " acetyl " contents of the parent unacetylated disulphones were determined, adjusted for molecular weight, and then subtracted from the values obtained for the corresponding acetylated derivatives.

D-talo-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane* (IV; R = H).—Aqueous peroxypropionic acid (150% of theory for 4 mol. based on propionic anhydride) [2] was carefully added to a solution of D-galactose diethyl dithioacetal (2·9 g.) in dioxan (20 ml.). The mixture was kept at room temperature for 10 min., then cooled in ice for 1—2 hr. Subsequent concentration yielded white crystals which were dried at 60°/0·05 mm. to remove traces of peroxypropionic acid. Recrystallisation from methanol gave needles (3·1 g., 92%) of D-talo-2 : 6-*epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane*, m. p. 193—195°, $[\alpha]_D$ +3·1° (*c*, 1·88 in MeOH), +19·0° (*c*, 2·17 in $H_2O$), $R_F$ 0·70 (Found: C, 36·4; H, 6·0; S, 19·5. $C_{10}H_{20}O_8S_2$ requires C, 36·2; H, 6·0; S, 19·3%).

D-*Lyxose* (V).—D-*talo*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (1 g.) was shaken in dilute aqueous ammonia (20 ml.; pH 10—11) at room temperature. The mixture remained colourless and paper chromatography indicated that reaction was complete in 7 days. After filtering, the solution was deionised with Amberlite IR-120 (H) and IR-4B (OH) resins and then extracted continually with chloroform for 12 hr. to remove diethylsulphonylmethane. Concentration yielded a pale yellow syrup of D-lyxose (0·42 g., 93%), which co-chromatographed with an authentic specimen in all solvents, and had $[\alpha]_D$ −13·2° (equil.; *c*, 3·80 in $H_2O$).

D-Lyxose was converted into D-*threo*pentose phenylosazone, m. p. 153—155° not raised on repeated recrystallisation from benzene. Most m. p.s quoted for this compound are in the region of 165°, but Ehrenstein [10] gives m. p. 153—155° (Found: C, 62·0; H, 6·1; N, 17·4. Calc. for $C_{17}H_{20}O_3N_4$: C, 61·9; H, 6·1; N, 17·1%).

[10] Ehrenstein, *Helv. Chim. Acta*, 1926, **9**, 332.

D-talo-3 : 4 : 5-*Tri*-O-*benzoyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane* (IV; R = Bz).—D-*talo*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (0·52 g.) in dry pyridine (3 ml.) was treated with benzoyl chloride (0·8 g.), set aside at room temperature for 14 hr., then poured into ice-water; an oil separated and this was extracted with chloroform (100 ml.; 2 × 50 ml.). The extracts were washed with 20% hydrochloric acid, 10% sodium hydrogen carbonate solution, and water, and then dried ($Na_2SO_4$). Concentration gave a brown syrup (0·61 g.) which was decolorised in the cold in methanol at room temperature. Reconcentration gave a pale brown sludge, which was triturated with a small volume of methanol to a powder. This was filtered off, washed with ether, and dried. The *tribenzoate* crystallised from methanol in plates, m. p. 197—198° (Found: C, 57·7; H, 5·0. $C_{31}H_{32}O_{11}S_2$ requires C, 57·7; H, 5·0%).

D-talo-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane* (IV; R = Ac).—A solution of D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (0·25 g.) in acetic anhydride (5 ml.) containing concentrated sulphuric acid (1 drop) was heated at 95—100° for ½ hr., then poured into ice-water; an oily *triacetate* separated which crystallised on stirring. Recrystallisation from ethanol gave rectangular plates (0·15 g., 51%), m. p. 187—188°, $[\alpha]_D$ −21·9° (*c*, 3·23 in $CHCl_3$) [Found: C, 41·7; H, 5·8; Ac, 27·4% (corr.; D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane gave acid equivalent to 15·95 acetyl); *M*, 451 (Menzies and Wright's method [11]). $C_{16}H_{26}O_{11}S_2$ requires C, 41·9; H, 5·7; Ac, 28·1%; *M*, 458].

The same product was obtained when D-*talo*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane was treated with acetic anhydride in the presence of anhydrous zinc chloride at 95—100° for 1 hr. (see below) or in pyridine at room temperature for 24 hr.

*Treatment of* D-talo-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane with Ammonia.*—The acetylated disulphone (0·1 g.), dissolved in a mixture of ammonia (2 ml.; *d*, 0·88) and methanol (2 ml.), was kept at room temperature. After 24 hr., paper chromatography indicated the presence of considerable quantities of D-lyxose, together with a small amount of material ($R_F$ 0·67) which stained with ammoniacal silver nitrate but gave no colour with *p*-anisidine hydrochloride spray. No D-*talo*-2 : 6-epoxy-1 :1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane ($R_F$ 0·70) was detected. Subsequent concentration gave a pale yellow syrup which was separated into its components on sheets of Whatman No. 1 filter paper with the neutral solvent as mobile phase. The material ($R_F$ 0·67) was extracted from the appropriate sections of the filter paper with cold methanol, and the extracts were concentrated to a pale yellow syrup. This was acetylated with acetic anhydride containing a trace of sulphuric acid at 95—100° as above and a syrup was isolated which crystallised in several days. Recrystallisation from ethanol gave prisms (14 mg.; m. p. 188—189°), which contained nitrogen, of D-galacto-2-*acetamido*-3 : 4 : 5 : 6-*tetra*-O-*acetyl*-1 : 1-*diethylsulphonylhexane* (VI) (Found: C, 42·3; H, 5·7. $C_{20}H_{33}O_{13}NS_2$ requires C, 42·8; H, 5·9%).

*Oxidation of* D-*Mannose Diethyl Dithioacetal with Peroxypropionic Acid.*—D-Mannose diethyl dithioacetal (2·4 g.) was oxidised as for D-galactose diethyl dithioacetal. Partial concentration yielded white crystals which were removed by filtering. Complete concentration of the filtrate then gave a syrup (B) from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration.

The crystalline product (1·6 g., 52%) was recrystallised from ethanol containing 20% (v/v) of 2-ethoxyethan-1-ol, giving needles of 1 : 1-*diethylsulphonyl*-D-manno-2 : 3 : 4 : 5 : 6-*pentahydroxyhexane* (XIII; R = H) ($C_{10}H_{22}O_9S_2$ requires C, 34·3; H, 6·3. Found: C, 34·3; H, 6·4%). The pentahydroxyhexane (XIII; R = H) was readily (*ca.* 1 min.) converted into the syrup (B) in warm water, dilute mineral acid, ethanol, or methanol. It could not be detected on paper chromatograms; with the basic solvent as mobile phase instantaneous cleavage of the molecule occurred and only the spot characteristic of arabinose was detected, whilst with the acid solvent a streak was obtained presumably due to conversion into the syrupy product during chromatography.

The syrup (B), D-manno-2 : 6-*epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane* (X; R = H) (1·1 g., 38%), which was extremely hygroscopic, set to a hard glass on drying (room temp.; 0·05 mm.). It had $[\alpha]_D$ −11·5° (*c*, 8·1 in MeOH), $[\alpha]_D$ +6·3° (*c*, 1·0 in $H_2O$), $R_F$ 0·57 (Found: C, 35·6; H, 6·0. $C_{10}H_{20}O_8S_2$ requires C, 36·1; H, 6·0%).

D-*Arabinose* (XIV).—D-*manno*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (1 g.) was cleaved with dilute aqueous ammonia (pH 10—11) as for the preparation of D-lyxose. Reaction was complete in 4—5 days and the product (0·40 g., 88%), after recrystallisation from ethanol, had m. p. and mixed m. p. 158—159°, $[\alpha]_D$ −106° (equil.; *c*, 0·93 in $H_2O$).

[11] Menzies and Wright, *J. Amer. Chem. Soc.*, 1921, **23**, 2309, 2314.

On prolonged heating in water at 95—100°, D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane was partially converted into D-arabinose, but as the reaction proceeded the pH fell to 3—4 and reaction stopped.

D-manno-2 : 3 : 4 : 5 : 6-*Penta*-O-*acetyl*-1 : 1-*diethylsulphonylhexane* (XIII; R = Ac).—The pentahydroxyhexane (X; R = H) (0·18 g.) was heated with acetic anhydride (3 ml.) containing concentrated sulphuric acid (1 drop) at 95—100° for ½ hr. Oily acetylated material, which separated when the mixture was poured into ice-water, 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 then gave a pale yellow syrup (0·17 g., 60%) which crystallised overnight. Recrystallised from a minimum of ethanol, the *penta-acetate* had m. p. 147—150° [Found: C, 42·5; H, 5·7; S, 10·5; Ac, 37·9 (corr.; 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane gave acid equivalent to 7·13% acetyl). $C_{20}H_{32}O_{14}S_2$ requires C, 42·8; H, 5·7; S, 11·4; Ac, 38·4%].

D-manno-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane* (X; R = Ac).—The syrup (B) (X; R = H) (0·50 g.), obtained from the oxidation of D-mannose diethyl dithioacetal, was heated with acetic anhydride (4 ml.) and anhydrous zinc chloride (0·1 g.) at 95—100° for 1 hr. The product was worked up as above and concentration of the chloroform extracts gave a pale yellow syrup (0·49 g., 70%) of the *tri*-O-*acetyl compound* which crystallised in 4—5 months. It was drained on a tile and washed with benzene and a little ether, then having m. p. 125—127° [Found: C, 41·6; H, 5·7; S, 14·7; Ac, 26·7 (corr.). $C_{16}H_{26}O_{11}S_2$ requires C, 41·9; H, 5·7; S, 14·0; Ac, 28·1%].

*Treatment of* D-manno-3 : 4 : 5-*Tri*-O-*acetyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane with Ammonia.*—A solution of D-*manno*-3 : 4 : 5-tri-*O*-acetyl-2 : 6-epoxy-1 : 1-diethylsulphonylhexane (0·32 g.) in methanol (6 ml.) and ammonia (*d* 0·88; 6 ml.) was kept at room temperature for 24 hr., after which paper chromatography indicated the presence of large amounts of arabinose and a small amount of faster-running material. The latter material gave no colour with the *p*-anisidine hydrochloride spray or with ninhydrin, but was shown by ammoniacal silver nitrate and gave a green colour with the Elson–Morgan reagent.[12] The solution was concentrated to a syrup which was separated into its components on sheets of Whatman No. 1 filter paper with the acid solvent as mobile phase. The faster-moving material was eluted from the appropriate sections of the filter paper with warm methanol, and the extracts were concentrated to a syrup. This was acetylated with acetic anhydride containing a trace of sulphuric acid at 95—100° as above, and a syrup was isolated which was triturated with ether to a powder. Crystallisation from ether gave crystals (21 mg.) of D-*gluco*-2-acetamido-3 : 4 : 5 : 6-tetra-*O*-acetyl-1 : 1-diethylsulphonylhexane [4] (XI), m. p. and mixed m. p. 178—179° (Found: C, 43·0; H, 5·7; N, 2·5. Calc. for $C_{20}H_{33}O_{13}S_2N$: C, 42·8; H, 5·9; N, 2·5%).

D-manno-2 : 6-*Epoxy*-1 : 1-*diethylsulphonyl*-3 : 4 : 5-*trihydroxyhexane* (X; R = H) *from* D-*Glucose Diethyl Dithioacetal.*—D-Glucose diethyl dithioacetal (0·67 g.) was oxidised as for D-galactose diethyl dithioacetal. Concentration of the mixture gave a hygroscopic syrup (A) (0·72 g., 93%) which was freed from traces of peroxypropionic acid by repeated dissolution in methanol and reconcentration. The syrup set on prolonged drying (room temp.; 0·05 mm.) to a hard glass, $[\alpha]_D$ −13·1° (*c*, 4·4 in MeOH), $R_F$ 0·57, co-chromatographing with the syrup obtained on oxidation of D-mannose diethyl dithioacetal.

D-manno-3 : 4 : 5-*Tri*-O-*benzoyl*-2 : 6-*epoxy*-1 : 1-*diethylsulphonylhexane* (X; R = Bz).—D-*manno*-2 : 6-Epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (0·25 g.) (syrup B) was benzoylated as for the corresponding D-*talo*-compound (IV; R = H), and a pale brown syrup (0·36 g.) was isolated which was triturated to a fine powder with methanol–ether. Crystallised from methanol–ether the *tri*-O-*benzoyl derivative* (X; R = Bz) had m. p. 87—90° (Found: C, 57·4; H, 5·0. $C_{31}H_{32}O_{11}S_2$ requires C, 57·7; H, 5·0%).

Benzoylation of a sample of D-*manno*-2 : 6-epoxy-1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxyhexane (syrup A) gave the same tri-*O*-benzoyl derivative (X; R = Bz) with m. p. 87—91°, mixed m. p. 86—91°, *X*-ray powder photographs of the two compounds being identical (Found: C, 57·9; H, 5·0%).

*Periodate Oxidation of the Diethylsulphones derived from* D-*Galactose,* D-*Mannose, and* D-*Glucose.*—(i) *Uptake.* A mixture of *ca.* 0·3M-sodium metaperiodate, acetate buffer (25 ml.), and disulphone (60—90 mg., weighed accurately) was made up to 100 ml. and stored in an amber bottle in the dark. A control containing none of the disulphone was worked concurrently. At intervals, the periodate uptake was estimated [13] by transferring samples (10 ml. each) from the

[12] Partridge, *Biochem. J.*, 1948, **42**, 238.
[13] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.

oxidation mixture and control, into a mixture of phosphate buffer (pH 7·0; 30 ml.) and 20% potassium iodide solution (5 ml.), then titrating the liberated iodine with 0·01N-sodium thiosulphate (starch indicator).

(ii) *Total acidity.* Solutions of the oxidation mixture and control were prepared as above, but without the acetate buffer. Acid was determined [14] by taking samples (10 ml. each) from the oxidation mixture and control, adding ethylene glycol (2 ml.) to each, and after 5 min. (to ensure complete destruction of the excess of periodate), titrating with 0·01N-sodium hydroxide (methyl-red, screened with methylene-blue). Results are given in the Figs.

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[14] Halsall, Hirst, and Jones, *J.*, 1947, 1427.