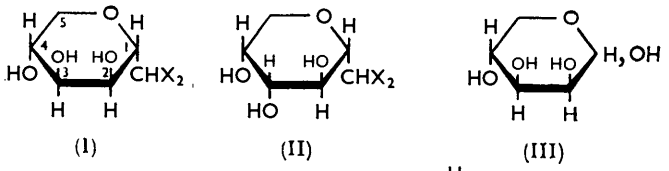
192. *Conformational and Electronic Factors influencing the Nucleophilic Degradation of Diethylsulphonylglycopyranosylmethane Derivatives.*[1]

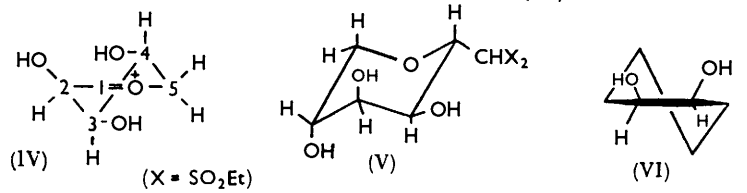
By L. Hough and A. C. Richardson.

Diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane failed to undergo cleavage with dilute aqueous ammonia, whereas diethylsulphonyl-(3,4-*O*-isopropylidene-α-D-arabinopyranosyl)methane was split, under the same conditions, into diethylsulphonylmethane and 3,4-*O*-isopropylidene-D-arabinose. These facts have been interpreted by the use of conformational analysis and support the suggested nucleophilic mechanism for the cleavage of diethylsulphonylglycopyranosylmethane derivatives with base, involving an intermediate oxonium cation. The methylation of diethylsulphonylglycopyranosylmethane derivatives resulted in the formation 1,1-diethylsulphonyl-1-glycopyranosylethane derivatives, which were not degraded by alkali, due to the inductive effect of the newly introduced methyl group. The diethylsulphones of hydroxy-, acetoxy-, and methoxy-acetone have been used as model compounds for studying the latter effect. The periodate oxidation of the cyclic disulphones is also discussed.

The oxidation of D-galactose and D-glucose diethyl dithioacetals with aqueous peroxypropionic acid resulted in the formation of diethylsulphonyl-α-D-lyxopyranosylmethane (I) and the D-arabino-isomer (II), respectively.[2] These cyclic derivatives were degraded by dilute aqueous ammonia into diethylsulphonyl methane and the aldopentose (*e.g.*, III) and past evidence has indicated that this degradation proceeded by a nucleophilic displacement.[2,3] In the preceding paper we have studied the alkaline hydrolysis of diethylsulphonyl-α-D-lyxopyranosylmethane (I) and found the rate-determining step to be the dissociation of the $C_{(\alpha)}$–$C_{(1)}$ bond.* The participation of a lone pair of electrons on the ring oxygen atom was essential for reaction and undoubtedly resulted in the formation of an oxonium cation, from which D-lyxose (III) was formed by the rapid attack of a hydroxyl ion. It has been shown that the 2-hydroxyl group does not participate in this reaction.[3b]



(I) (II) (III)



(IV) (X = SO_2Et) (V) (VI)

The intermediate oxonium cation, owing to the endocyclic double bond, exists in the half-chair conformation (IV),[3,4] analogous to that of cyclohexene,[5] in which $C_{(2)}$, $C_{(1)}$, ring O, and $C_{(5)}$ are coplanar. Consequently, the dissociation of the $C_{(\alpha)}$–$C_{(1)}$ bond will be influenced by the ease with which the original chair conformation of the pyranoside ring

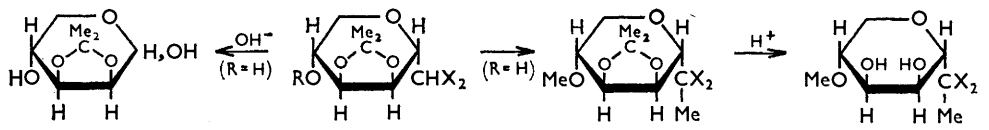
* For a note on nomenclature see reference 1.

[1] For preliminary communication see Hough and Richardson, *Proc. Chem. Soc.*, 1959, 193.
[2] Hough and Taylor, *J.*, 1956, 970.
[3] (*a*) Hough and Taha, *J.*, 1957, 3564; (*b*) Hough and Richardson, *J.*, 1961, 5561.
[4] Newth and Phillips, *J.*, 1958, 130.
[5] Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21.

(V) is converted into the half-chair (IV). For the unsubstituted cyclic disulphones, the energy of such a conformational change would be more than compensated for by the steric relief resulting from the departure of the bulky diethylsulphonylmethyl group. However, substitution of the hydroxyl groups, especially by cyclic acetal formation, would in some cases hinder this conformational change and thus impede the reaction.

The fusion of a five-membered isopropylidene ring to a six-membered pyranose ring should hold the latter in a half-chair conformation. This postulate is based upon the known specificity of the reaction of acetone with *cis*-hydroxyl groups on adjacent carbon atoms which leads to a general flattening of the ring.[6,7] Both *cis*- and *trans*-diols in a pyranose chair conformation have the same O–O distance (2·86 Å), which is too large to be spanned by a single carbon atom. For the *trans*-isomer, however, this distance cannot be reduced without greatly increasing non-bonded interactions and strain, whereas the distance in the *cis*-isomer can be readily decreased by rotating the carbon atoms, to which the hydroxyl groups are attached, about their connecting bond. There is reason to suppose that little energy is required for this process.[6] Such a conformational change in the formation of a mono-*O*-isopropylidene derivative gives rise to a structure more closely approaching a half-chair (VI) than a chair in which the two hydroxyl groups are truly *cis* and four contiguous carbon atoms are coplanar. Molecular models (Courtauld) have also served to support this postulate. Further support for the half-chair has been provided by Foster,[8] who used this conformation to explain the large difference in mobilities of methyl α- and β-lyxopyranosides during electrophoresis in borate buffer.

Formation of mono-*O*-isopropylidene derivatives of the two cyclic disulphones (I and II) was readily accomplished in acetone containing anhydrous copper sulphate and a trace of sulphuric acid. The highly crystalline D-*lyxo*-isomer (I) afforded crystalline



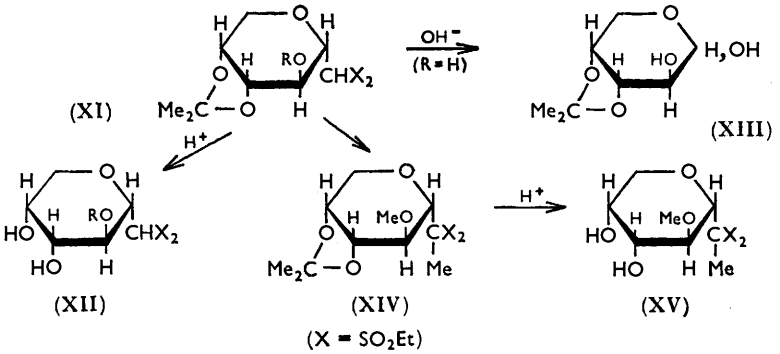
(VIII) (VII) (IX) (X)

diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (VII; R = H), which readily formed a crystalline mono-*O*-acetate (VII; R = Ac). In contrast, the D-*arabino*-isomer yielded syrupy diethylsulphonyl-(3,4-*O*-isopropylidene-α-D-arabinopyranosyl)-methane (XI; R = H) from which a non-crystalline mono-*O*-acetate (XI; R = Ac) was formed. However, traces of acetic acid caused slow hydrolysis of the isopropylidene group, and crystalline (2-*O*-acetyl-α-D-arabinopyranosyl)diethylsulphonylmethane (XII; R = Ac) was isolated. Treatment of this disulphone with aqueous ammonia yielded D-arabinose as the sole reducing sugar, and thus showed the absence of the isopropylidene group. The structure of the acetate was confirmed by periodate oxidation during which one mole of periodate were reduced in about 4 hr., followed by slow over-oxidation.

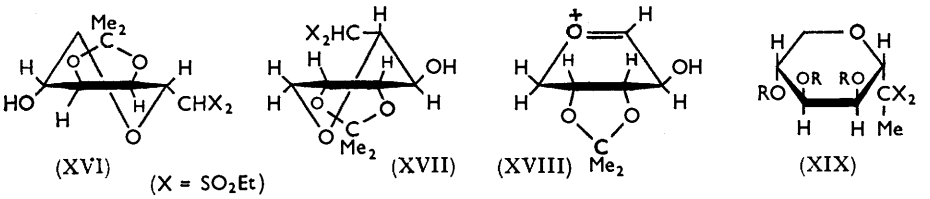
When diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (VII; R = H) was dissolved in dilute aqueous ammonia, the cleavage, characteristic of other diethylsulphonylpyranosylmethane derivatives, did not occur, and the isopropylidene derivative was recovered, even after several weeks. The formation of the intermediate oxonium ion, necessary for cleavage to take place, would require the coplanarity of $C_{(5)}$, ring O, $C_{(1)}$, and $C_{(2)}$ (as in IV). Since the isopropylidene ring is already holding $C_{(1)}$, $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$ in one plane, the pyranoside half-chair (XVI) would have to become completely planar for reaction to occur. This would cause considerable steric and angular

[6] Angyal and McDonald, *J.*, 1952, 686.
[7] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 21.
[8] Foster, *J.*, 1957, 4214.

strain, thus making the formation of the intermediate oxonium cation improbable under the mild conditions employed. The cleavage of the cyclic disulphones is enhanced [9] by a higher pH and it was subsequently found that the isopropylidene derivative was very slowly cleaved by 3N-sodium hydroxide, the reaction being complete in 6 weeks, to give



diethylsulphonylmethane and 2,3-*O*-isopropylidene-D-lyxose (VIII). This sugar was also produced when concentrated ammonia solution (*d* 0·88) was used. Stereochemical implications similar to the above have been put forward in order to explain the extraordinary lack of reactivity of halogen substituents located at brideghead positions in bicyclic compounds.[10]



In contrast, diethylsulphonyl-(3,4-*O*-isopropylidene-α-D-arabinopyranosyl)methane (XI; R = H) was readily split by dilute aqueous ammonia into diethylsulphonylmethane and 3,4-*O*-isopropylidene-D-arabinose (XIII), the physical constants of which were in agreement with those of the L-isomer.[11] The structure of this pentose was confirmed by periodate oxidation under unbuffered conditions; it then reduced one mole of periodate, and did not release either formic acid or formaldehyde, to give the formyl ester of 2,3-isopropylidene-D-erythrose. The conformation of diethylsulphonyl-(3,4-*O*-isopropylidene-α-D-arabinopyranosyl)methane (XI; R = H) would be the half-chair (XVII) in which $C_{(2)}$, $C_{(3)}$, $C_{(4)}$, and $C_{(5)}$ are coplanar. As before, the formation of the intermediate oxonium cation would require $C_{(5)}$, ring O, $C_{(1)}$, and $C_{(2)}$ to become coplanar. Both these steric requirements could be met if the pyranoside ring adopted the half, or partially flattened, boat conformation (XVIII), thus enabling cleavage to take place. Raphael and Stenlake [12] have described the half-boat conformation as a possible conformation of cyclohexene. Thus, the behaviour of the two mono-*O*-isopropylidene derivatives of the cyclic disulphones with base provides good evidence for the intermediary oxonium cation.

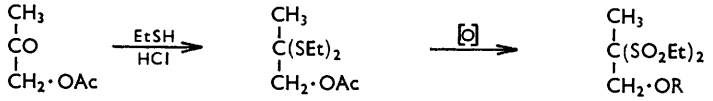
Diethylsulphonylglycopyranosylmethane derivatives behave as very weak acids, owing to activation of the $C_{(\alpha)}$-hydrogen by the adjacent disulphone groups and by the ring

[9] Hough and Richardson, preceding paper.
[10] Bethell and Gold, *Quart. Rev.*, 1958, **12**, 173.
[11] Jones, Kent, and Stacey, *J.*, 1947, 1341.
[12] Raphael and Stenlake, *Chem. and Ind.*, 1953, 1286.

oxygen atom.[13] On account of this property, these derivatives on methylation with silver oxide and methyl iodide underwent not only *O*-methylation but also $C_{(\alpha)}$-methylation, and 1,1-diethylsulphonyl-1-glycopyranosylethane derivatives were produced. Thus, methylation of diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (VII; R = H) afforded 1,1-diethylsulphonyl-1-(2,3-*O*-isopropylidene-4-*O*-methyl-α-D-lyxopyranosyl)ethane (IX) and similarly the D-*arabino*-isopropylidene derivative (XI; R = H) afforded 1,1-diethylsulphonyl-1-(3,4-*O*-isopropylidene-2-*O*-methyl-α-D-arabinopyranosyl)-ethane (XIV). Acid hydrolysis of both ethanes afforded the corresponding diols (X and XV, respectively). From a similar methylation of the tri-*O*-acetate of the D-*lyxo*-cyclic disulphone (I), 1,1-diethylsulphonyl-1-(2,3,4-tri-*O*-acetyl-α-D-lyxopyranosyl)ethane (XIX; R = Ac) was formed which yielded the corresponding triol upon de-*O*-acetylation. Methylation of diethylsulphonylmethane did not take place so readily, because of the absence of an ethereal oxygen atom adjacent to the diethylsulphonylmethyl group, and resulted in a mixture of starting material and 1,1-diethylsulphonylethane; no di-*C*-methylated product was isolated. Unlike the mildly acidic diethylsulphonylglycopyranosylmethanes, the ethane analogues were neutral and were stable in both aqueous ammonia and sodium hydroxide solution at room temperature.

The formation of an intermediate oxonium cation from the cyclic disulphones is dependent not only on the necessary conformational change of the pyranosyl ring but also on electronic factors affecting the cleavage of the $C_{(\alpha)}$–$C_{(1)}$ bond. The rupture of this linkage depends upon the ability of the bonding electrons to break away in the direction of $C_{(\alpha)}$. Such a process would be facilitated if $C_{(\alpha)}$ were cationoid in character but not if it were anionoid. The ionisation of the $C_{(\alpha)}$-hydrogen atom under the influence of alkali would cause $C_{(\alpha)}$ to become anionoid, thus it is unlikely that the ionised species of the cyclic disulphones play any part in their degradation. However, in the case of the non-ionised species, the electrophilic sulphone groups would exert an electron-attracting inductive effect ($-I$) on $C_{(\alpha)}$, thus making it cationoid and facilitating the cleavage of the bond. A $C_{(\alpha)}$-methyl group would exert an opposite effect ($+I$), which would tend to neutralise the inductive effect on the sulphone groups and hence inhibit cleavage, thus accounting for the failure of the $C_{(\alpha)}$-methyl disulphones to undergo cleavage with base. The additive inductive effect of an extra methyl group at the site of nucleophilic reaction in chloromethyl methyl ether caused a considerable (>100) increase in the unimolecular rate constant.[14]

In order to ascertain that the stability of 1,1-diethylsulphonyl-1-glycopyranosyl-ethane derivatives was not due to steric factors, 2,2-diethylsulphonyl-1-methoxypropane (XXII; R = Me) was prepared by a modification of the method of Dietrich, Johannessohn, Rabald, and Peris.[15]

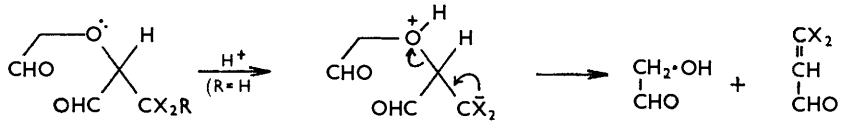


(XX) (XXI) (XXII)

The bisethylthio-compound (XXI), prepared from the ketone (XX), was conveniently oxidised with aqueous peroxypropionic acid but the resulting *O*-acetate could not be de-*O*-acetylated by the usual basic reagents because of its sensitivity towards alkali, which caused cleavage into 1,1-diethylsulphonylethane, formaldehyde, and acetic acid. The de-*O*-acetylation was readily accomplished by dilute hydrochloric acid. The successful methylation of the hydroxy-disulphone (XXII; R = H) with silver oxide and methyl ioxide was achieved only under strictly anhydrous conditions at room temperature,

[13] Coxon, Hough, and Richardson, unpublished results.
[14] Ballinger, de la Mare, Kohnstam, and Prestt, *J.*, 1955, 3641.
[15] Dietrich, Johannessohn, Rabald, and Peris, U.S.P. 2,309,937 (*Chem. Abs.*, 1943, **37**, 4206).

otherwise degradation of the disulphone occurred and 1,1-diethylsulphonylethane was formed. The methoxy derivative (XXII; R = Me) was unaffected by aqueous ammonia, a fact which discounted any steric reason for the stability of the glycopyranosylethanes and supported the theory based on the inductive effect of the methyl group.



(XXIII) (XXIV) (X = SO_2·Et) (XXV)

The periodate oxidation of 1,1-diethylsulphonyl-1-α-D-lyxopyranosylethane (XIX; R = H) did not show any significant over-oxidation in contrast to its methane analogue; [2] thus oxidation ceased after the reduction of two moles of oxidant and the release of one mole of formic acid. Hough and Taylor [2] found that diethylsulphonyl-α-D-lyxopyranosylmethane (I; R = H) rapidly reduced two moles of periodate with the liberation of one mole of formic acid, which was consistent with the formation of the dialdehyde (XXIII; R = H). However, this was followed by a slower reaction involving a further two moles of periodate due to the breakdown of the dialdehyde and another two moles of formic acid were liberated.

The results of periodate oxidation reveal that the presence of the $C_{(\alpha)}$-hydrogen atom causes hydrolysis of the dialdehyde and subsequent over-oxidation. Since this hydrogen atom is acidic,[13] the over-oxidation results can be accounted for by the irreversible disproportionation of the zwitterion (XXIV) into glycollaldehyde and the unsaturated disulphone (XXV), and their subsequent oxidation.

The stability of the dialdehyde (XXIII; R = Me) to oxidation by periodate thus permits the ring size of disulphonylglycopyranosylmethanes and similar derivatives to be determined unambiguously by *C*-methylation before oxidation with periodate. Furthermore, since $C_{(1)}$ is the only remaining asymmetric centre in the dialdehyde, its optical rotation can be used as a means of determination of the anomeric configuration, as in the case of methyl pentapyranosides.[16]

Experimental

The uptake of sodium metaperiodate was estimated by the thiosulphate method.[17] Liberated formic acid was determined by addition of ethylene glycol (1 ml.) to a portion (10 ml.), followed 3 min. later by titration with 0·01N-sodium hydroxide, Methyl Red, screened with Methylene Blue, being used as indicator. Formaldehyde was determined by the chromotropic acid method of O'Dea and Gibbons.[18] All other pertinent data concerning chromatography, etc., are given in the preceding paper.

Diethylsulphonyl-(2,3-O-isopropylidene-α-D-lyxopyranosyl)methane (VII; R = H).—A solution of diethylsulphonyl-α-D-lyxopyranosylmethane (17 g.) in dry acetone (350 ml.), containing anhydrous copper sulphate (35 g.) and concentrated sulphuric acid (5 drops), was shaken for 18 hr. The acid was then neutralised with ammonia solution (*d* 0·88; 1 ml.), and the solution was filtered and concentrated. The residue crystallised from ethanol as cubes (15·9 g.; 83%) of *diethylsulphonyl-(2,3-O-isopropylidene-α-D-lyxopyranosyl)methane*, m. p. 138—139°, $[\alpha]_D$ +29·1° (*c* 3·6 in methanol) (Found: C, 41·9; H, 6·5; S, 16·9. $C_{13}H_{24}O_8S_2$ requires C, 41·9; H, 6·5; S, 17·2%). More (1 g.; 5%) isopropylidene derivative was obtained by addition of light petroleum (b. p. 60—80°) to the ethanolic mother liquors.

Solutions of the isopropylidene derivative in varying concentration of ammonia solution (<2N) were examined on paper chromatograms, but no reducing sugar was detected, even after prolonged storage, and unchanged material was recovered in each case. In concentrated

[16] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994.
[17] Neumüller and Vasseur, *Arkiv Kemi*, 1953, **5**, 235.
[18] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

ammonia solution (*d* 0·88), however, some degradation occurred and 2,3-*O*-isopropylidene-D-lyxose was detected on paper chromatograms [R_{Rh} 2·0 (solvent ii)].

2,3-O-*Isopropylidene*-D-*lyxose* (VIII).—A solution of diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (1·44 g.) in 3N-sodium hydroxide (5 ml.) was stored at 25° in a ½ dm. polarimeter tube. The optical rotation (α) was measured at intervals:

Time (hr.)	0	17	94	112	142	168	262	310	510	700	850	1200
α°	5·2	5·1	4·2	4·1	3·9	3·72	3·1	28	2·1	1·7	1·5	1·4

After 50 days, the solution was extracted continuously with chloroform, and the chloroform solution was dried and concentrated. The crystalline residue was then extracted with ether (40 ml.), and the insoluble diethylsulphonylmethane (0·39 g.) filtered off; it had m. p. and mixed m. p. 101—102°. The filtrate was concentrated, and the residue (1·01 g.) dissolved in water. The aqueous solution was then extracted with benzene (3 × 25 ml.), and concentrated to a colourless syrup (0·47 g.). Chromatography indicated the presence of D-lyxose and a fast-moving reducing sugar [R_{Rh} 1·8 (solvent ii) and 2·12 (solvent i)]. The syrup partially crystallised, and the crystals were drained onto a tile. Recrystallisation from ether afforded 2,3-O-*isopropylidene*-D-*lyxose*, m. p. 72—75° (Found: C, 49·8; H, 7·3. $C_8H_{14}O_5$ requires C, 50·6; H, 7·4%).

(4-O-*Acetyl*-2,3-O-*isopropylidene*-α-D-*lyxopyranosyl*)*diethylsulphonylmethane* (VII; R = Ac).—Diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (1·0 g.) was mixed with pyridine (7 ml.) and acetic anhydride (7 ml.), and the resulting solution kept at room temperature for 20 hr. The solution was then poured into ice–water and extracted with chloroform. After being washed with water several times and dried ($MgSO_4$), the chloroform solution was concentrated to a syrup which rapidly crystallised. Recrystallisation from ethanol afforded (4-O-*acetyl*-2,3-O-*isopropylidene*-α-D-*lyxopyranosyl*)*diethylsulphonylmethane* (0·68 g.; 61%), which had m. p. 99—101°, $[\alpha]_D$ +27° (*c* 1·0 in methanol) (Found: C, 43·6; H, 6·1; S, 14·2. $C_{15}H_{26}O_9S_2$ requires C, 43·5; H, 6·3; S, 15·4%).

1,1-*Diethylsulphonyl*-1-(2,3-O-*isopropylidene*-4-O-*methyl*-α-D-*lyxopyranosyl*)*ethane* (IX).—Diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane (3·0 g.) in chloroform (10 ml.) was mixed with methyl iodide (30 ml.) and anhydrous calcium sulphate (5 g.). The mixture was heated under reflux for 24 hr., silver oxide (11 g.) being added in small portions during the first 3 hr. The reaction mixture was filtered and concentrated to a syrup which was crystallised thrice from methanol, giving 1,1-*diethylsulphonyl*-1-(2,3-O-*isopropylidene*-4-O-*methyl*-α-D-*lyxopyranosyl*)*ethane* (0·68 g.) as cubes, m. p. 111—112°, $[\alpha]_D$ +22·4° (*c* 1·45 in methanol) (Found: C, 44·9; H, 7·5; OMe, 7·7. $C_{15}H_{28}O_8S_2$ requires C, 45·0; H, 7·0; OMe, 7·8%).

1,1-*Diethylsulphonyl*-1-(4-O-*methyl*-α-D-*lyxopyranosyl*)*ethane* (X).—A solution of the above 4-*O*-methyl derivative (0·88 g.) in ethanol (25 ml.)–2N-hydrochloric acid (10 ml.) was heated under reflux for 1½ hr. After neutralisation with lead carbonate the hydrolysate was concentrated to a syrup, which was dissolved in acetone and filtered. Subsequent concentration afforded a syrup which slowly crystallised. Recrystallisation from water yielded needles of 1,1-*diethylsulphonyl*-1-(4-O-*methyl*-α-D-*lyxopyranosyl*)*ethane*, m. p. 157—158°, $[\alpha]_D$ +0·9° (*c* 1·62 in methanol), R_{Rh} 2·12 (solvent ii) and 2·36 (solvent i) (Found: C, 40·1; H, 7·1; OMe, 9·0. $C_{12}H_{24}O_8S_2$ requires C, 40·0; H, 6·7; OMe, 8·6%).

On dissolution of this compound in aqueous ammonia, no reducing sugar could be detected, even after several days, and starting material was recovered.

Diethylsulphonyl-(3,4-O-*isopropylidene*-α-D-*arabinopyranosyl*)*methane* (XI; R = H).—α-D-Arabinopyranosyldiethylsulphonylmethane (4 g.) was condensed with acetone as described for the D-*lyxo*-isomer. The syrupy product contained two components, one of which [R_F 0·61 (solvent ii)] co-chromatographed with the starting material. The other [R_F 0·79 (solvent ii)] reacted with ammoniacal silver nitrate only after the paper chromatogram had been sprayed with glacial acetic acid and heated. Water (100 ml.)–chloroform (100 ml.) was added to the syrup, and the mixture shaken until solution was complete. The chloroform layer was separated, washed with water, and dried ($MgSO_4$); concentration afforded the 3,4-*O*-isopropylidene derivative as a syrup (2·37 g.), $[\alpha]_D$ −36·6° (*c* 2·15 in methanol), R_F 0·83 (solvent ii).

The Acetylation of Diethylsulphonyl-(3,4-O-*isopropylidene*-α-D-*arabinopyranosyl*)*methane.*—A solution of the 3,4-*O*-isopropylidene derivative (1·39 g.) in pyridine (10 ml.) and acetic

anhydride (10 ml.) was kept at room temperature overnight and then poured into ice–water. The acetate was extracted with chloroform (2 × 25 ml.), and the chloroform solution washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and finally with water. After being dried (Na_2SO_4), the solution was concentrated to a syrup, which crystallised after 6 weeks. Recrystallisation from ethanol afforded (2-O-*acetyl*-α-D-*arabinopyranosyl*)*diethylsulphonylmethane* (0·64 g.), m. p. 163—165°, $[\alpha]_D$ −20·7° (*c* 1·12 in methanol) (Found: C, 38·4; H, 5·6; S, 15·7. $C_{12}H_{22}O_9S_2$ requires C, 38·6; H, 5·9; S, 17·1%); ν 3550 and 1750 cm.$^{-1}$, indicating hydroxyl and ester groups, respectively.

Dissolution of the mono-*O*-acetate in dilute aqueous ammonia caused degradation, and diethylsulphonylmethane (m. p. 101—102°) gradually crystallised; arabinose was the only reducing sugar detected on paper chromatograms.

The mono-*O*-acetate (0·045 g.) was treated with 0·005M-sodium metaperiodate (100 ml.), the following results being obtained:

Time (hr.)	1	3	5	24	72
Uptake (moles of periodate per mole of disulphone)	0·24	0·66	1·21	2·35	3·06

Treatment of Diethylsulphonyl-(3,4-O-*isopropylidene*-α-D-*lyxopyranosyl*)*methane with Aqueous Ammonia.*—The 3,4-*O*-isopropylidene derivative (3·0 g.) was dissolved in 50% aqueous methanol (20 ml.), and ammonia (0·5 ml.; *d* 0·88) added. The reaction was followed by paper chromatography and one reducing sugar [R_F 0·65 (solvent i) and 0·70 (solvent ii)] was detected. After 15 days, by which time only a small amount of starting material could be detected, diethylsulphonylmethane was filtered off, the filtrate concentrated, and the residue extracted with ether. The ethereal extract was concentrated and benzene then added to give a gel which, upon filtration, crystallised spontaneously. Several recrystallisations from ether yielded fine needles (0·1 g.) of 3,4-*O*-isopropylidene-D-arabinose hemihydrate, m. p. 76—78°, $[\alpha]_D$ −110° (*c* 1·03 in water) (Found: C, 48·5; H, 7·5. Calc. for $C_8H_{14}O_5,\frac{1}{2}H_2O$: C, 48·5; H, 7·6%). The compound slowly decomposed. Jones, Kent, and Stacey [11] report m. p. 78°, $[\alpha]_D$ +111° for the L-isomer.

The sugar (0·0326 g.) was oxidised with 0·002M-sodium metaperiodate (100 ml.) and the following results obtained:

Time (hr.)	1	2	4	6	24
Uptake (moles of periodate per mole of carbohydrate)	0·87	0·93	0·95	0·95	0·97

Neither formaldehyde nor formic acid was detected after 24 hr.

1,1-*Diethylsulphonyl*-1-(3,4-O-*isopropylidene*-2-O-*methyl*-α-D-*arabinopyranosyl*)*ethane.*—Diethylsulphonyl-(3,4-*O*-isopropylidene-α-D-arabinopyranosyl)methane (7 g.) in acetone (25 ml.) was mixed with methyl iodide (100 ml.) and silver oxide (15 g.). The mixture was heated under reflux for 1 hr., more silver oxide (15 g.) then added, and heating continued for a further 5 hr. Filtration and subsequent concentration yielded a residue, which, when recrystallised from methanol, yielded plates (1·15 g.) of 1,1-*diethylsulphonyl*-1-(3,4-O-*isopropylidene*-2-O-*methyl*-α-D-*arabinopyranosyl*)*ethane*, m. p. 175—183°, $[\alpha]_D$ −8·1° (*c* 1·18 in methanol) (Found: C, 44·7; H, 7·1; OMe, 8·4. $C_{15}H_{28}O_5S_2$ requires C, 45·0; H, 7·1; OMe, 7·8%).

1,1-*Diethylsulphonyl*-1-(2-O-*methyl*-α-D-*arabinopyranosyl*)*ethane* (XV).—The isopropylidene derivative (0·4 g.) was heated at 95—100° with 0·02N-hydrochloric acid (10 ml.) for 1 hr. Solution was then complete, and neutralisation with silver carbonate followed by filtration and concentration yielded a syrup which, in the presence of a little ethanol, slowly crystallised. The crystals were drained on a porous tile and washed with acetone. Recrystallisation from ethyl acetate–ether afforded 1,1-*diethylsulphonyl*-1-(2-O-*methyl*-α-D-*arabinopyranosyl*)*ethane monohydrate* as cubes (0·05 g.), m. p. 85—91°, $[\alpha]_D$ +0·4° (*c* 3·79 in methanol), R_{Rh} 2·3 (solvent i) and 1·92 (solvent ii) (Found: C, 38·1; H, 7·1; S, 15·6; OMe, 8·3; H_2O, 4·9. $C_{12}H_{24}O_8S_2,H_2O$ requires C, 38·1; H, 6·9; S, 16·9; OMe, 8·2; H_2O, 4·7%). When dried at 60°/12 mm., the disulphone gave the anhydrous compound, m. p. 121—122°. The disulphone rapidly reduced 1·1 moles of sodium metaperiodate, after which no further reaction took place. It was unaffected by aqueous ammonia, as indicated by paper chromatography.

Diethylsulphonyl-(2,3,4-*tri*-O-*acetyl*-α-D-*lyxopyranosyl*)*methane.*[2]—A mixture of diethylsulphonyl-α-D-lyxopyranosylmethane (10 g.), acetic anhydride (100 ml.), and concentrated hydrochloric acid (2 drops) was heated at 95—100° for ½ hr. The solution was cooled and poured

into vigorously stirred ice–water. The crystals were recrystallised from ethanol, giving the tri-*O*-acetate as plates (12 g.; 88%), m. p. 187—189°, $[\alpha]_D$ −22° (*c* 2·1 in chloroform).

1,1-*Diethylsulphonyl*-1-(2,3,4-*tri*-O-*acetyl*-α-D-*lyxopyranosyl*)*ethane* (XIX; R = Ac).—A mixture of diethylsulphonyl-(2,3,4-tri-O-acetyl-α-D-lyxopyranosyl)methane (14·25 g.), acetone (25 ml.), methyl iodide (125 ml.), silver oxide (50 g.), and anhydrous powdered calcium sulphate (20 g.) was heated under reflux for 5 hr. Insoluble material was then filtered off, and concentration gave crystals which, on recrystallisation from ethanol, yielded 1,1-*diethylsulphonyl*-1-(2,3,4-*tri*-O-*acetyl*-α-D-*lyxopyranosyl*)*ethane* (12·0 g.; 82%), m. p. 167°, $[\alpha]_D$ −27·4° (*c* 0·8 in chloroform) (Found: C, 42·4; H, 5·6; S, 13·8; Ac, 22·5. $C_{17}H_{28}O_{11}S_2$ requires C, 43·1; H, 5·9; S, 13·6; Ac, 27·3%).

1,1-*Diethylsulphonyl*-1-α-D-*lyxopyranosylethane* (XIX; R = H).—The tri-*O*-acetate (7·36 g.) was suspended in methanol (100 ml.), N-sodium methoxide (4 ml.) added, and the mixture shaken until solution was complete. After 5 min. at room temperature the solution was de-ionised with Amberlite IR-120 (H) resin. Filtration and concentration yielded a syrup; addition of ethyl acetate caused spontaneous crystallisation. Recrystallisation from ethyl acetate yielded needles of 1,1-*diethylsulphonyl*-1-α-D-*lyxopyranosylethane*, m. p. 176—178°, $[\alpha]_D$ −3·1° (*c* 2·77 in methanol), R_F 0·69 (solvent i) and 0·71 (solvent ii) (Found: C, 38·4; H, 6·6; S, 18·3. $C_{11}H_{22}O_8S_2$ requires C, 38·2; H, 6·4; S, 18·5%).

The disulphone was unaffected by aqueous ammonia or sodium hydroxide solution, as indicated by paper chromatography.

Some preparations of this compound contained a little of the methane analogue, which was removed by treatment of the impure material with aqueous ammonia for 7 days. The purified ethane derivative was recovered from the solution by continuous extraction with chloroform, and recrystallised from chloroform–light petroleum.

The disulphone (0·17 g.) was treated with 0·03M-sodium metaperiodate (100 ml.) and the following results were obtained:

Time (hr.)	½	1½	2½	5	24
Uptake (moles per mole of disulphone)	1·69	1·87	1·95	1·98	2·05
Acid	0·65	0·89	0·87	1·01	1·05

C-*Methylation of Diethylsulphonylmethane*.—Diethylsulphonylmethane (2 g.) was methylated as for diethylsulphonyl-(2,3-*O*-isopropylidene-α-D-lyxopyranosyl)methane. This afforded impure white crystals (1·27 g.), m. p. 55—65°. A small portion (0·18 g.) was purified on alumina (32 × 0·9 cm.; 100/200 mesh). Elution with ether (100 ml.) yielded 1,1-diethylsulphonylethane which was sublimed and then crystallised from ethanol, forming needles (0·1 g.), m. p. and mixed m. p. 74—75° (Found: C, 34·1; H, 6·6. Calc. for $C_6H_{14}O_4S_2$: C, 33·7; H, 6·5%). Further elution of the column with benzene afforded a small quantity of diethylsulphonylmethane, m. p. and mixed m. p. 101—102°.

2,2-*Diethylthiopropyl Acetate* (XXI).—Acetoxyacetone [19] (11·6 g.) was added dropwise to a stirred mixture of ethanethiol (25 ml.) and concentrated hydrochloric acid (20 ml.) at 0°. Stirring was continued for a further hour and the solution then allowed to rise slowly to room temperature. The mixture was then diluted with water (50 ml.) and extracted with ether (200 ml.), and the ethereal layer washed with water and dried (K_2CO_3). Concentration afforded a pale yellow oil, which was distilled at 130—145°/12 mm. to give 2,2-diethylthiopropyl acetate as a pale yellow liquid (17·9 g.; 81%).

2,2-*Diethylsulphonylpropyl Acetate* (XXII; R = Ac).—To a stirred solution of the diethylthiopropyl acetate (5·4 g.) in ethanol (100 ml.) at −10° was slowly added an excess of aqueous peroxypropionic acid. After 1 hr. at 0°, the solution was concentrated. Crystallisation from ethanol afforded needles (5·8 g.; 84%) of 2,2-diethylsulphonylpropyl acetate, m. p. 106—107° (Found: C, 38·0; H, 5·9; S, 21·7; Ac, 19·1. Calc. for $C_9H_{18}O_6S_2$: C, 37·8; H, 6·3; S, 22·4; Ac, 15·1%).

A solution of this acetate (0·15 g.) in a minimum of acetone was treated with dilute aqueous ammonia. After 1 hr., concentration afforded 1,1-diethylsulphonylethane which was recrystallised from ethanol; it (0·062 g.; 75%) had m. p. and mixed m. p. 74—75°. This experiment was repeated on a smaller scale, but in the absence of acetone. Quantitative estimation showed that, after ½ hr., 1·04 moles of formaldehyde per mole of disulphone had been released.

2,2-*Diethylsulphonylpropanol* (XXII; R = H).[15]—A solution of 2,2-diethylsulphonylpropyl

[19] Perkin, *J.*, 1891, **59**, 786.

acetate (8·6 g.) in acetone (20 ml.) and 2N-hydrochloric acid (20 ml.) was heated under reflux for 3½ hr. and then kept overnight at room temperature. The solution was diluted with water (50 ml.) and extracted with chloroform (4 × 50 ml.). The combined extracts were washed with water, dried ($MgSO_4$), and concentrated. Crystallisation from ether–light petroleum (b. p. 60—80°) yielded 2,2-diethylsulphonylpropanol (6 g.; 82%), m. p. 62—64° (Found: C, 34·7; H, 6·6; S, 26·0. Calc. for $C_7H_{16}O_5S_2$: C, 34·4; H, 6·7; S, 26·3%).

2,2-*Diethylsulphonyl*-1-*methoxypropane* (XXII; R = Me).—2,2-Diethylsulphonylpropanol (2 g.) was shaken for 2 hr. with methyl iodide (30 ml.) and powdered anhydrous calcium sulphate (5 g.) in a stoppered flask. Silver oxide (3 g.) was then added in small portions during 3 hr. Vigorous shaking was continued for a further 18 hr., and the insoluble material was then filtered off and the filtrate concentrated to a syrup which rapidly crystallised. Recrystallisation from 30% ethanol and then from ether afforded prisms (0·63 g.; 30%) of 2,2-*diethylsulphonyl*-1-*methoxypropane*, m. p. 95—97° (Found: C, 37·3; H, 7·2; OMe, 12·6. $C_8H_{18}O_5S_2$ requires C, 37·2; H, 7·0; OMe, 12·0%).

In a preparation from which the drying agent was omitted, 1,1-diethylsulphonylethane was obtained in 35% yield.

No formaldehyde could be detected in a solution of the methoxy-derivative in aqueous ammonia after 2 months, and the compound was recovered (m. p. and mixed m. p. 95—97°).

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