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FURANOID DISULPHONE DERIVATIVES

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ABSTRACT

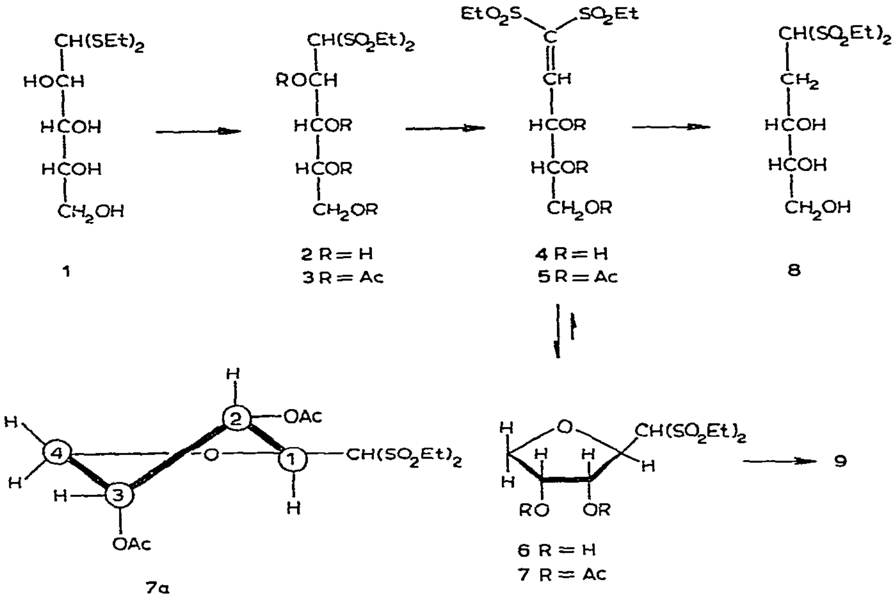
Oxidation of D-arabinose diethyl dithioacetal (**1**) with peroxypropionic acid yielded the acyclic disulphone **2** which on treatment with dilute acetic acid gave a furanoid derivative, β-D-erythrofuranosylbis(ethylsulphonyl)methane (**6**), and not 1,1-bis(ethylsulphonyl)-D-*erythro*-3,4,5-trihydroxypent-1-ene (**4**) as previously reported[1]. In solution, the cyclic sulphone exists in equilibrium with a small proportion of the acyclic pent-1-ene **4**, as indicated by n.m.r. spectroscopy and by catalytic hydrogenation to the acyclic pentane derivative **8**. Oxidation of D-xylose diethyl dithioacetal also gave a furanoid derivative.

INTRODUCTION

Oxidation of D-arabinose diethyl dithioacetal (**1**) in *p*-dioxane with peroxypropionic acid was observed to occur with concomitant loss of the elements of water to give a disulphone which was assigned an acyclic structure[1], namely, 1,1-bis(ethylsulphonyl)-D-*erythro*-3,4,5-trihydroxypent-1-ene (**4**). The presence of the double bond was indicated by hydrogenation which gave 1,1-bis(ethylsulphonyl)-D-*erythro*-3,4,5-trihydroxypentane (**8**). The disulphone obtained from D-xylose diethyl dithioacetal by oxidation–dehydration was also assigned an acyclic structure, as were a variety of similar derivatives prepared by Zinner and Falk[2]. Closer examination of the oxidation of these diethyl dithioacetals has now revealed that they behave similarly to hexose derivatives[3], giving, initially, pent-1-ene derivatives which undergo cyclisation to form furanoid derivatives.

RESULTS AND DISCUSSION

Oxidation of D-arabinose diethyl dithioacetal (**1**) with peroxypropionic acid in *p*-dioxane at 0° gave a product, $C_9H_{20}O_8S_2$, which crystallised from the reaction mixture during the first hour; no absorption due to ethylenic stretching was detected in the i.r. spectrum, and this is consistent with the 1,1-bis(ethylsulphonyl)-D-*arabino*-2,3,4,5-tetrahydroxypentane (**2**) structure. The mother liquors were shown by t.l.c. to contain both the pentane derivative **2** and a compound previously supposed[1] to be the



pent-1-ene 4 (R = H). The pentane derivative 2 was not described by the previous workers[1], but the melting points of both pentane and "pent-1-ene" diethylsulphonyl derivatives have been found to vary over the range 110–130°. The pentane derivative 2 (R = H) was readily converted into the "pent-1-ene" by heating in dilute acetic acid for 2 h. Alternatively, when the oxidation of the dithioacetal **1** was conducted in methanol rather than in *p*-dioxane, t.l.c. indicated that, after 1 h, the major product was the pentane derivative 2 and, after 24 h, only the "pent-1-ene" was present. At no stage did crystalline material separate out of the reaction mixture.

The n.m.r. spectrum of the "pent-1-ene" in pyridine solution showed one low-field signal due to the ethylenic hydrogen atom, as in 4, and also a low-field singlet and a doublet each integrating for one hydrogen atom These signals could be accounted for H-2, H-α*, or H-β in the furanoid form 6. The weakly acidic hydrogen[4] on C-α or C-β undergoes exchange with the solvent and hence appears as a broad singlet (τ' 4.7). The signal due to H-1 appeared as a doublet (τ' 4.2) by coupling to H-2. These signals resembled those[4] of bis(ethylsuphonyl)-(2,3,4-tri-*O*-acetyl-β-D-ribopyranosyl)methane in triethylamine–water–chloroform-*d* solution, where H-1 appeared as a sharp doublet (τ 5.17) and H-β as a broad singlet (τ 5.42). A small doublet (τ' 4.1) suggested the presence of a small proportion (*ca.* 20%) of the acyclic pent-1-ene derivative 4. The i.r. spectrum of the cyclic disulphone 6 was identical with that of the product described previously[1].

Acetylation of the sulphone 6 gave a crystalline furanoid diacetate 7. The

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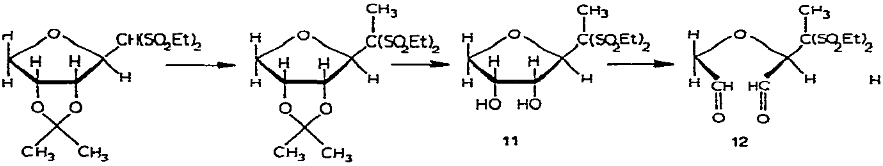
*The methane carbon atom and its hydrogen substituent are designated as either C-α and H-α or C-β and H-β, respectively, according to whether the glycosyl group to which this carbon atom is attached has the α- or the β-D anomeric configuration[4].

syrupy products isolated previously[1,2] were thought to be triacetates, but the sulphones were obtained by oxidation of the dithioacetals in *p*-dioxane (see above); consequently, the products were probably mixtures of the furanoid diacetate (**7**) and the acyclic triacetate (**5**), the latter arising during the acetylation of **2** *via* **3**. The n.m.r. spectrum of (3,4-di-*O*-acetyl-β-D-erythrofuranosyl)-bis(ethylsulphonyl)methane (**7**) showed the presence of two acetate groups (τ 7.95 and 8.2) and suggested the twist (T_3^2) conformation **7a**, since the signals due to H-β (3.9), H-1 (4.75), H-2 (3.65), H-3 (4.3), H-4a (5.5), and H-4e (5.9) showed the following coupling constants: $J_{1,2}$ 7.5, $J_{2,3}$ 5.0, $J_{3,4a}$ 4.5, and $J_{3,4e}$ 3.0 Hz. Application of the Karplus equation[5] ($J = J_0 \cos^2 \varphi - 0.28$; where $J_0 = 8.5$ for $0° \leqslant \varphi \leqslant 90°$ and 9.5 for $90° \leqslant \varphi \leqslant 180°$) gave approximate dihedral angles of $\varphi_{1,2}$ 150°, $\varphi_{2,3}$ 42°, $\varphi_{3,4a}$ 46°, and $\varphi_{3,4e}$ 55°, in accord with the β-D configuration at the anomeric C-1.

Periodate oxidation of the furanoid sulphone **6** led to extensive oxidation due to the presence of the acidic hydrogen H-β as shown previously[1,3], and to prevent[3] this over-oxidation, the C-methylation of the diacetate **7** to give **11** (R = Ac) was attempted, but a mixture resulted. However, the sulphone **6** formed a crystalline 3,4-*O*-isopropylidene derivative (**9**) which, on methylation, gave 1,1-bis(ethylsulphonyl)-1-(3,4-*O*-isopropylidene-D-erythrofuranosyl)ethane (**10**). Hydrolysis of the latter afforded the required *C*-methyl derivative **11** which consumed only one mole of oxidant when treated with an excess of sodium metaperiodate. The oxidation product **12** had $[\alpha]_D$ −45° [*cf.* +43.5° for the product of oxidation of 1,1-bis(ethylsulphonyl)-1-(α-D-lyxopyranosyl)ethane[3] (**13**)]. The 2,4-dinitrophenylhydrazones of the oxidation products from **11** and **13** showed identical i.r. spectra. Hence, the furanoid disulphone has the β-D-configuration, namely the structure β-D-erythrofuranosyl-bis(ethylsulphonyl)methane (**6**).



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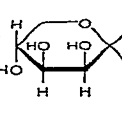

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Catalytic hydrogenation of the furanoid sulphone **6** in ethanol gave the acyclic dihydro derivative[1], 1,1-bis(ethylsulphonyl)-D-*erythro*-3,4,5-trihydroxypentane (**8**), in 55% yield, in accord with n.m.r. evidence which suggested that the furanoid form **6** exists in equilibrium in solution with a small proportion of the acyclic "pent-1-ene".

Oxidation of D-xylose diethyl dithioacetal in *p*-dioxane gave 1,1-bis(ethylsulphonyl)-D-*xylo*-2,3,4,5-tetrahydroxypentane which on heating in very dilute acid underwent dehydration and cyclisation, affording bis(ethylsulphonyl)-D-threofuranosylmethane. Acetylation gave a syrupy acetate whose n.m.r. spectrum revealed the presence of two acetoxyl groups (τ 7.85 and 7.9), thus suggesting the furanoid structure, but the complex resonances of the ring protons suggested that it may be a mixture of the α- and β-anomers.

EXPERIMENTAL

General. — All solutions were concentrated under reduced pressure. Optical rotations were determined at 25 ±2°. Melting points were determined on a Kofler micro-heating stage. T.l.c. was carried out with Kieselgel G (Merck); the separated materials were detected on the plates by either exposure to iodine vapour or by spraying with a 5% solution of conc. sulphuric acid in ethanol and then heating at *ca.* 120°. Oxidations of dithioacetals with aqueous peroxypropionic acid[6] were carried out as described previously[1] with an excess of the oxidant (150% of theory for 4 mol.).

1,1-Bis(ethylsulphonyl)-D-arabino-*2,3,4,5-tetrahydroxypentane* (**2**). — To a suspension of D-arabinose diethyl dithioacetal (5 g) in *p*-dioxane (20 ml) cooled in an ice-bath, an excess of aqueous peroxypropionic acid[6] was slowly added. The resultant solution was left for 1.5 h at 0°. During this period, crystals separated out from the reaction mixture and were collected. Recrystallisation from methanol–ether afforded compound **2** (3.7 g; 62%), m.p. variable, $[\alpha]_D$ +2° (*c* 2.06, methanol) (Found: C, 33.5; H, 6.25; S, 19.9. $C_9H_{20}O_8S_2$ calc.; C, 33.7; H, 6.25; S, 20.0).

The mother liquors contained both **2** and **6** (t.l.c.).

β-D-*Erythrofuranosyl-1,1-bis(ethylsulphonyl)methane* (**6**). — To a suspension of D-arabinose diethyl dithioacetal (486 mg) in methanol (3 ml), cooled in an ice-bath, an excess of aqueous peroxypropionic acid was slowly added. The resultant solution was left to stand at room temperature for 24 h. Subsequent concentration, with addition of methanol to remove the last traces of acid, yielded a syrup, which crystallised from methanol. Recrystallisation from the minimum of methanol afforded compound **6** (360 mg; 62%), m.p. variable, $[\alpha]_D$ −66° (*c* 1.15, methanol) (Found: C, 35.55; H, 5.9; S, 21.1. $C_9H_{18}O_7S_2$ calc.; C, 35.75; H, 5.95; S, 21.2).

Compound **6** was formed in quantitative yield when 1,1-diethylsulphonyl-D-*arabino*-2,3,4,6-tetrahydroxypentane (**2**) was heated in dilute acetic acid for 2 h at 95°.

(3,4-Di-O-acetyl-β-D-*erythrofuranosyl)-1,1-bis(ethylsulphonyl)methane* (**7**). — A mixture of **6** (1.10 g), acetic anhydride (20 ml), and conc. sulphuric acid (2 drops) was heated at 95–100° for 0.5 h. The solution was cooled, poured into ice–water, and extracted with chloroform, and the chloroform layer was washed with aqueous sodium carbonate and then water. Subsequent concentration yielded a syrup, which crystallised from ethanol. Recrystallisation from ethanol afforded the diacetate **7** (1.10 g; 78%), m.p. 111–3°, $[\alpha]_D$ +1° (*c* 2.56, chloroform) (Found: C, 40.5; H, 5.7; S, 16.5. $C_{13}H_{22}O_9S_2$ calc.; C, 40.4; H, 5.7; S, 16.6).

1,1-Bis(ethylsulphonyl)-(3,4-O-isopropylidene-β-D-*erythrofuranosyl)methane* (**9**). — Compound **6** (4.9 g) was shaken with dry acetone (125 ml), anhydrous cupric sulphate (10 g), and conc. sulphuric acid (2 drops) for 24 h. After neutralisation with conc. ammonium hydroxide solution (*d*, 0.88), the mixture was filtered. Concentration of the filtrate yielded a syrup which crystallised from ethanol–water. Recrystallisation from ethanol–water afforded the isopropylidene derivative **9** (4.2 g; 75%), m.p. 88–90°,

$[\alpha]_D$ −73° (*c* 1.52, chloroform) (Found: C, 42.2; H, 6.4; S, 18.6. $C_{12}H_{22}O_7S_2$ calc.; C, 42.1; H, 6.4; S, 18.7).

1,1-Bis(ethylsulphonyl)-1-(3,4-O-isopropylidene-β-D-erythrofuranosyl)ethane (**10**). — A mixture of the isopropylidene derivative **9** (2.1 g), active silver oxide[7] (10 g), methyl iodide (6 ml), and acetone (12 ml) was boiled under reflux for 2 h. Methyl iodide (6 ml) and acetone (6 ml) were then added, and the refluuxing was continued. After a further 3 h, the mixture was filtered. Concentration of the filtrate yielded a syrup which crystallised on standing. Recrystallisation from methanol–water afforded the *C*-methyl derivative **10** (1.53 g; 73%), m.p. 82–4°, $[\alpha]_D$ −47° (*c* 0.86, chloroform) (Found: C, 43.6; H, 6.75; S, 18.15. $C_{13}H_{24}O_7S_2$ calc.: C, 43.8; H, 6.75; S, 18.0).

1-(β-D-Erythrofuranosyl)-1,1-bis(ethylsulphonyl)ethane (**11**). — The *C*-methyl derivative **10** (1.47 g) was heated under reflux in a mixture of 2M hydrochloric acid (4 ml) and methanol (50 ml) for 4 h. After neutralisation with silver carbonate, the mixture was filtered. Concentration of the filtrate yielded a syrup, which crystallised on standing, affording the diol **11** (886 mg; 68%), m.p. variable, $[\alpha]_D$ −43° (*c* 2.08, methanol) (Found: C, 37.85; H, 6.4; S, 20.1. $C_{10}H_{20}O_7S_2$ calc.: C, 37.95; H, 6.3; S, 20.25).

Oxidation of the disulphone **11** *with sodium metaperiodate*. — (*a*) The disulphone (27.3 mg) was oxidised in the usual manner[3,4], with 83mM aqueous sodium metaperiodate under unbuffered conditions, and the consumption of oxidant was determined; uptake (moles/mole) 0.98 (0.25 h), 0.98 (0.5 h), and 0.98 (1 h).

(*b*) The sulphone (207 mg) was oxidised with a mixture of 0.3M aqueous sodium metaperiodate (5 ml) and 2M hydrochloric acid (5 ml). After 0.5 h, the optical rotation was constant, corresponding to $[\alpha]_D$ −45° for the dialdehyde. Continuous extraction of the reaction mixture with chloroform afforded, after concentration of the extract, the dialdehyde **12** as a syrup which formed a 2,4-dinitrophenylhydrazone. The i.r. spectrum of this derivative was identical with that of the 2,4-dinitrophenylhydrazone of the dialdehyde obtained[3] by periodate oxidation of 1,1-bis(ethylsulphonyl)-α-D-lyxopyranosylethane (**13**).

*1,1-Bis(ethylsulphonyl)-*D-erythro*-3,4,5-trihydroxypentane* (**8**). — The furanoid sulphone **6** (502 mg) was hydrogenated at 48 lb/in^2 at room temperature in ethanol (*ca.* 100 ml) with T-4 Raney nickel[8] as catalyst. After 24 h, the mixture was filtered and concentrated. The product was purified by fractionation on a column of silica gel with ethyl acetate as eluent. Concentration of the required fractions yielded a syrup, which crystallised on standing. Recrystallisation from ethyl acetate afforded compound **8** (297 mg; 58%), m.p. 101–3°, $[\alpha]_D$ −34° (*c* 1.06, acetone) (Found: C, 35.66; H, 6.6. $C_9H_{20}O_7S_2$ calc.: C, 35.5; H, 6.6).

*1,1-Bis(ethylsulphonyl)-*D-xylo*-2,3,4,5-tetrahydroxypentane*. — To a suspension of D-xylose diethyl dithioacetal (1.9 g) in *p*-dioxane (80 ml), cooled in an ice-bath, an excess of aqueous peroxypropionic acid was slowly added. The resultant solution was left for 1.5 h at 0°, and the crystals that had separated out from the reaction mixture were then collected. Recrystallisation from methanol afforded the tetrahydroxy derivative (9.5 g; 40%), m.p. variable, $[\alpha]_D$ +15° (*c* 2.15, water) (Found: C, 33.65, H, 6.1; S, 19.7. $C_9H_{20}O_8S_2$ calc.: C, 33.7; H, 6.25; S, 20.0).

*1,1-Bis(ethylsulphonyl)-*D*-threofuranosylmethane.* — 1,1-Bis(ethylsulphonyl-D-*xylo*-2,3,4,5-tetrahydroxypentane (2.01 g) was heated at 95–100° in a mixture of water (15 ml) and glacial acetic acid (4 drops) for 2 h. The solution was then left at room temperature for 3 h and concentrated to yield a syrup, which crystallised on storage, affording the *threo* derivative (1.9 g; 100%), m.p. variable, $[\alpha]_D$ +14° (*c* 1.58, methanol). The i.r. spectrum was identical with that for the product obtained by Hough and Taylor[1].

*(3,4-Di-*O*-acetyl-*D*-threofuranosyl)-1,1-bis(ethylsulphonyl)methane.* — A mixture of 1,1-bis(ethylsulphonyl)-D-threofuranosylmethane (136 mg), acetic anhydride (4 ml), and conc. sulphuric acid (2 drops) was heated for 0.5 h at 95–100°. The solution was cooled, poured into ice–water, and extracted with chloroform. The extract was washed with aqueous sodium hydrogen carbonate and then water. Subsequent concentration yielded the syrupy diacetate (104 mg; 60%), $[\alpha]_D$ −6° (*c* 2.08, chloroform) (Found: C, 40.25; H, 5.6; S, 16.4. $C_{13}H_{22}O_9S_2$ calc.: C, 40.4; H, 5.7; S, 16.6).

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REFERENCES

1 L. Hough and T. J. Taylor, *Chem. Ind.* (London), (1954) 575; *J. Chem. Soc.*, (1955) 1212.
2 H. Zinner and K. H. Falk, *Ber.*. 89 (1956) 2451.
3 L. Hough and A. C. Richardson, *J. Chem. Soc.*, (1962) 1019, 1024.
4 B. Coxon and L. Hough, *Carbohyd. Res.*, 8 (1968) 379.
5 M. Karplus, *J. Chem. Phys.*, 30 (1959) 11; L. Hough and A. C. Richardson, in S. Coffey (Ed.), *Rodd's Chemistry of Carbon Compounds*, Vol. 1F, Elsevier, London, 1967, p. 139.
6 J. d'Ans and W. Frey, *Ber.*, 45 (1912) 1845.
7 B. Helferich and W. Klein *Ann*, 450 (1926) 219.
8 N. Nishimura, *Bull. Chem. Soc. Japan*, 32 (1959) 61.