1 : 1-*Diethylsulphonyl Derivatives of* L-*Rhamnose and Their Conversion into* 5-*Deoxy*-L-*arabinose.*

By L. HOUGH and T. J. TAYLOR.

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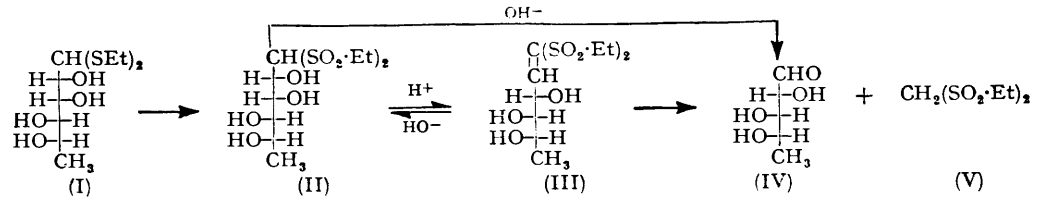
Oxidation of L-rhamnose diethyl dithioacetal (I) with peroxypropionic acid gave a mixture of 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II) and 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III). Both were cleaved by dilute aqueous ammonia to give 5-deoxy-L-arabinose (IV) and diethylsulphonylmethane (V).

ALDOPENTOSE DIETHYL DITHIOACETALS are converted into 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes on oxidation with aqueous peroxypropionic acid (Hough and Taylor, *J.*, 1955, 1212), whereas under the same conditions D-mannose diethyl dithioacetal yields

two products, diethylsulphonyl-D-*arabo*pyranosylmethane and 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane, the latter crystallising from the reaction mixture (McDonald and Fischer, *Biochim. Biophys. Acta.*, 1953, **12**, 203; Hough and Taylor, *Chem. and Ind.*, 1954, 575, 1018). On the other hand, D-galactose and D-glucose diethyl dithioacetals yield only diethylsulphonylpentopyranosylmethanes (Hough and Taylor, *loc. cit.*, p. 1018) which are probably formed from the corresponding hex-1-ene derivatives by ring closure as a result of attack at the cationoid $C_{(2)}$ atom by the terminal primary hydroxyl group. The pent-1-ene derivatives do not cyclise because the carbon chain is not of sufficient length to allow an attack at $C_{(2)}$ (as revealed by molecular models). Thus it was of interest to examine the oxidation of L-rhamnose (6-deoxy-L-mannose) diethyl dithioacetal, since by analogy with D-mannose diethyl dithioacetal it might be expected to yield two acyclic derivatives, a 2 : 3 : 4 : 5-tetrahydroxyhexane (as II) and a 3 : 4 : 5-trihydroxyhex-1-ene (as III), cyclisation of the latter being prevented by the absence of a primary hydroxyl group at $C_{(6)}$.



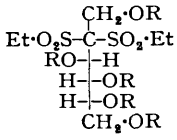
As expected, L-rhamnose diethyl dithioacetal (I) was oxidised by aqueous peroxypropionic acid at room temperature to a mixture of 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II; 49%) and 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III; 17%). In the same conditions diethyl dithioacetals of aldoheptoses having the *manno*-configuration also yield acyclic diethylsulphonyl compounds of the saturated type (details to be published). Compounds having this configuration appear to be relatively stable and their isolation is facilitated by their sparing solubility in aqueous solutions. In warm solutions of mineral acid they are converted into the appropriate unsaturated (*e.g.* II ⟶ III) or cyclic derivatives.

The tetrahydroxyhexane (II), which formed a highly crystalline tetra-acetate, was rapidly cleaved by dilute aqueous ammonia to give 5-deoxy-L-arabinose (IV) in good yield and diethylsulphonylmethane (V). Although the classical methods for the descent of the aldose series have been used for the preparation of 5-deoxy-L-arabinose (*e.g.* Fischer, *Ber.*, 1896, **29**, 1381; Ruff and Kohn, *Ber.*, 1902, **35**, 2362; Deulofeu, *J.*, 1930, 2602), the method described herein is undoubtedly more convenient. 5-Deoxy-L-arabinose yielded a highly crystalline benzoylhydrazone. Disproportionation of (II) was also brought about by shaking an aqueous suspension with Amberlite IR-4B (hydroxy-form) resin, but yields of the 5-deoxypentose were low owing to combination of either the sugar or some intermediate with the resin (cf. Hough and Taylor, 1955, *loc. cit.*). Some indication of the instability of the tetrahydroxyhexane (II) in mildly alkaline systems is illustrated by the fact that paper chromatography with a basic solvent caused instantaneous cleavage, and only 5-deoxy-L-arabinose was detected; by using a neutral solvent a streak was obtained owing to degradation during chromatography. The tetrahydroxyhexane (II) could be detected on paper chromatograms when ethyl acetate–acetic acid–water was used as mobile phase. This marked sensitivity of (II) and other saturated acyclic aldose derivatives of this type towards mild base, as compared with the unsaturated derivatives (see later), would also be expected from the diethylsulphonyl derivatives of ketoses (*e.g.* VI; R = H), since they cannot form unsaturated derivatives.

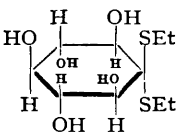
McDonald and Fischer (American Chemical Society Meeting, New York, Sept., 1954) have shown that oxidation of 2 : 2-diethylthio-D-*arabo*-1 : 3 : 4 : 5 : 6-pentahydroxyhexane (D-fructose diethyl dithioacetol) with peroxypropionic acid gave only D-erythrose, none of the intermediate disulphone (VI; R = H) being isolated. However, oxidation of D-*arabo*-1 : 3 : 4 : 5 : 6-penta-*O*-acetyl-2 : 2-diethylthiohexane with peroxyphthalic acid

yielded the corresponding disulphone (VI; R = Ac) which was cleaved with hydrazine to give D-erythrose and diethylsulphonylmethane (McDonald and Fischer, *loc. cit.*) and with methanolic ammonia to give D-erythrose bisacetamide and 1 : 1 : 3 : 3-tetraethylsulphonylpropane [formed by condensation of one molecule of formaldehyde from $C_{(1)}$ of the original hexane derivative with two molecules of diethylsulphonylmethane (Bourne and Stephens, *J.*, 1954, 4009)]. McDonald and Fischer (*loc. cit.*) have also shown that (VII), the diethyl dithioacetol derived from *myo*inosose-2, could be oxidised by peroxypropionic acid to the corresponding diethylsulphonyl compound, which on treatment with a trace of ammonia disproportionated into *xylo*trihydroxyglutaraldehyde and diethylsulphonylmethane.

(VI)



(VII)



The other 1 : 1-diethylsulphonyl compound (III) derived from L-rhamnose formed a crystalline triacetate; the presence of a double bond was indicated by its colour reaction with dry pyridine (McDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087) and by the formation of a dihydro-derivative on catalytic hydrogenation under mild conditions. The dihydro-derivative moved more slowly than the parent hex-1-ene derivative (III) on paper chromatograms and was clearly distinguishable from it. Compared with the hexane derivative (II), the hex-1-ene (III) was slowly cleaved by dilute aqueous ammonia (complete in 30 hr.) to give 5-deoxy-L-arabinose (IV), in high yield, and diethylsulphonylmethane. The difference in reaction rate is probably due to a relatively slow addition of the elements of water to the double bond in (III) to give a saturated compound [*e.g.* (II)], which then rapidly disproportionates into the 5-deoxypentose and diethylsulphonylmethane, and the reaction is thus analogous to a reverse aldol condensation (cf. Bourne and Stephens, *loc. cit.*). As in the case of the 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes, the degradation was accompanied by the production of an intense orange-red colour (Hough and Taylor, *loc. cit.*, 1955). This colour reaction was not observed when the tetrahydroxyhexane derivative (II) was cleaved with ammonia, and appears to be characteristic of the αβ-unsaturated disulphones. However, the formation of the colour and of acidic products (Hough and Taylor, *loc. cit.*, 1955) suggests that a side reaction also involving base (cf. colour reaction with pyridine) is operative, since dilute sodium hydroxide solution on (III) causes a similar orange-yellow coloration. It is also noteworthy that aqueous solutions of diethylsulphonyl derivatives of this unsaturated type are weakly acid, whilst those of the saturated acyclic and cyclic types are neutral. Diethylsulphonylmethane is also neutral, but triethylsulphonylmethane is a strong acid (Doering and Levy, *J. Amer. Chem. Soc.*, 1955, **77**, 509).

Oxidation of the tetrahydroxyhexane (II) with sodium metaperiodate at room temperature gave in 2 hr. the expected consumption of 3 mol. of the reagent with subsequent liberation of 3 equiv. of acid, *i.e.*, 2 mol. of formic acid and 1 mol. of diethylsulphonylacetaldehyde. Under the same conditions, the trihydroxyhex-1-ene (III) showed a rapid consumption of 2 mol. of reagent (3 hr.), followed by a slow overoxidation, and thus is analogous to the oxidation of 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypent-1-ene with sodium metaperiodate (cf. Hough and Taylor, *loc. cit.*, 1955).

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–pyridine–water (10 : 3 : 3 v/v), butan-1-ol–ethanol–water (40 : 11 : 19 v/v), or ethyl acetate–acetic acid–water (9 : 2 : 2 v/v) as mobile phase, ammoniacal silver nitrate being used for the detection of the polyhydroxy-compounds. R_f values are approximate. M. p.s of the disulphones were determined on a Kofler micro-heating stage. Values given for acetyl have been

corrected, to allow for the extra acid that arises in the determination from the sulphone groups. The " acetyl " contents of the parent unacetylated disulphones were determined, and the values adjusted for molecular weight, and then subtracted from those obtained for the corresponding acetylated derivatives.

Peroxypropionic Acid Oxidation of L-*Rhamnose Diethyl Dithioacetal.*—L-Rhamnose diethyl dithioacetal (5·4 g.) in dioxan (15 ml.) was treated with aqueous peroxypropionic acid (150% of theory for 4 mol., based on propionic anhydride; Hough and Taylor, *loc. cit.*, 1955) at room temperature. After 10 min., the mixture was cooled in ice for 1 hr. On concentration of the mixture, needles of 1 : 1-*diethylsulphonyl*-L-manno-2 : 3 : 4 : 5-*tetrahydroxyhexane* (II) (3·3 g.; 49%) separated. Crystallised from ethanol, they had m. p. 178—180°, $[\alpha]_D$ +7·4° (*c*, 4·06 in MeOH) (Found: C, 36·2; H, 6·6. $C_{10}H_{22}O_8S_2$ requires C, 35·9; H, 6·6%). This compound (R_f 0·72) could be detected on paper chromatograms only when the acid solvent was used; under these conditions no deoxypentose was detected. The neutral solvent caused degradation during chromatography and a streak was obtained. With the basic solvent, only 5-deoxy-L-arabinose (R_f 0·56) could be detected.

Evaporation of the mother liquor gave a syrup from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration. The residue was dissolved in a minimum quantity of ethanol, the solution cooled, and ether added; more of the derivative (II) (0·4 g.; m. p. 176—178°) was then obtained. On the paper chromatogram, with the basic solvent, it gave the spot (R_f 0·56) due to 5-deoxy-L-arabinose and a trace (R_f 0·81). The syrup (1·5 g.), from the ethanol–ether mother liquors, was boiled with ether, and the resulting solution cooled. Light petroleum (b. p. 40—60°) was added until the solution was opalescent and after some time and at 0°, small rosettes of 1 : 1-*diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhex*-1-*ene* (III) (1·1 g.; 17%) were deposited. Recrystallised in a similar manner they had m. p. 105—107°, $[\alpha]_D$ −40·2° (*c*, 4·87 in MeOH), R_f 0·81 (Found: C, 37·8; H, 6·3. $C_{10}H_{22}O_7S_2$ requires C, 38·0; H, 6·3%). A 0·01M-aqueous solution of this compound had pH 3·2 at room temperature.

5-*Deoxy*-L-*arabinose.*—(i) 1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II) (1·13 g.) was dissolved in dilute aqueous ammonia (10 ml.; pH 9—10), and within a few minutes diethylsulphonylmethane (m. p. 101—103°) separated. The mixture, which remained colourless, was kept at room temperature for 16 hr., diethylsulphonylmethane was filtered off, and the filtrate was de-ionised with Amberlite IR-120 and IR-4B resins and then extracted continuously with chloroform for 6 hr. to remove any residual diethylsulphonylmethane. Subsequent concentration gave a pale yellow syrup of 5-deoxy-L-arabinose (0·33 g.; 73%), $[\alpha]_D$ −6·9° (*c*, 2·16 in H_2O). Ruff and Kohn (*loc. cit.*) record $[\alpha]_D$ −5·1°. On paper chromatograms 5-deoxy-L-arabinose gave a yellow spot (R_f 0·56) with the *p*-anisidine hydrochloride spray.

(ii) 1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (1 g.) in water (10 ml.) was shaken with Amberlite IR-4B resin (hydroxyl form; 2 g.) for 6 hr. The resin was filtered off and washed by shaking it with water (2 × 50 ml.) for 1—2 hr., and then the combined filtrates were extracted continuously with chloroform for 6 hr. Further washings did not contain 5-deoxy-L-arabinose. Concentration then gave a pale yellow syrup of the 5-deoxypentose (0·09 g.; 22%). More (0·19 g.; 48%) of the chromatographically pure aldose was obtained by shaking the resin with 0·5N-sulphuric acid (150 ml.) for 2 hr., and then with water (2 × 50 ml.) for 1 hr. After neutralisation ($BaCO_3$) and filtration, the liquors were extracted continuously with chloroform for 6 hr. and then evaporated.

(iii) 1 : 1-Diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (122 mg.) was dissolved in dilute aqueous ammonia (5 ml.; pH 9—10), and immediately the solution became yellow and rapidly darkened to orange-red. Paper chromatography indicated that reaction was complete in 30 hr. The 5-deoxypentose (34 mg.; 66%) was isolated as in (i).

The 5-deoxypentose was converted into 5-deoxy-L-*erythro*pentose phenylosazone which had m. p. 172—174° not depressed on admixture with an authentic specimen (Gorin, Hough, and Jones, *J.*, 1953, 2140) [Found by Barry, McCormick, and Mitchell's method (*J.*, 1955, 222): *M*, 317. Calc. for $C_{17}H_{20}O_2N_4$: *M*, 312]. 5-Deoxy-L-arabinose gave a highly crystalline *benzoylhydrazone* when refluxed with benzoylhydrazine (1 mol.) for 1 hr. in a minimum of 98% ethanol. Recrystallisation from 98% ethanol gave small plates, m. p. 192—193° (decomp.) (Found: C, 57·0; H, 6·3. $C_{12}H_{16}O_4N_2$ requires C, 57·1; H, 6·3%).

L-manno-2 : 3 : 4 : 5-*Tetra*-O-*acetyl*-1 : 1-*diethylsulphonylhexane.*—1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (0·30 g.) was heated at 95—100° with acetic anhydride (5 ml.) and concentrated sulphuric acid (1 drop) for ½ hr., and the mixture then poured into ice-water. An oil separated which was extracted with chloroform (2 × 50 ml.), and the extract

washed with sodium carbonate solution and then with water and dried ($MgSO_4$). Subsequent concentration gave a pale yellow syrup (0·31 g.; 70%) which crystallised spontaneously. Recrystallised from ether–light petroleum (b. p. 40—60°), the *tetra-acetate* had m. p. 95—98° [Found : C, 43·1; H, 5·9; S, 13·1; Ac, 32·8 (corr.). $C_{18}H_{30}O_{12}S_2$ requires C, 43·0; H, 6·0; S, 12·8; Ac, 34·2%]. The tetrahydroxyhexane (II) gave acid equivalent to 10·6% acetyl.

L-arabo-3 : 4 : 5-*Tri*-O-*acetyl*-1 : 1-*diethylsulphonylhex*-1-*ene*.—1 : 1-Diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (0·21 g.) was acetylated as above, giving a pale yellow syrup (0·23 g.; 81%) which had crystallised after 3—4 weeks. After being dried on a porous tile and carefully washed with benzene–light petroleum, the *triacetate* had m. p 115—116° [Found : C, 43·0; H, 5·7; S, 15·4; Ac, 26·8 (corr.). $C_{16}H_{26}O_{10}S_2$ requires C, 43·3; H, 5·9; S, 14·5; Ac, 29·2%]. The trihydroxyhex-1-ene (III) gave acid equivalent to 15·4% acetyl.

1 : 1-*Diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhexane*.—A solution of 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III) (0·16 g.) in 95% ethanol (20 ml.) was hydrogenated at 5 atm. for 4—5 hr. in the presence of Raney nickel (2 g.; approx. 3 months old). The pressure and time required for complete reduction of these unsaturated disulphones appear to depend on the age of the Raney nickel [cf. the formation of 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypentane from the corresponding pent-1-ene (Hough and Taylor, *loc. cit.*, 1955)]. The catalyst was filtered off and the filtrate concentrated. Recrystallisation of the residue from ethanol gave fine *needles* (0·076 g.), m. p. 147°, $[\alpha]_D$ −12·6° (*c*, 0·99 in MeOH), R_f 0·75 (Found : C, 37·9; H, 7·0. $C_{10}H_{22}O_7S_2$ requires C, 37·7; H, 6·9%).

Periodate Oxidation of 1 : 1-*Diethylsulphonyl*-L-manno-2 : 3 : 4 : 5-*tetrahydroxyhexane* (II) *and* 1 : 1-*Diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhex*-1-*ene* (III).—(i) *Uptake*. A mixture of *ca.* 0·3M-sodium periodate solution (4 ml.), acetate buffer (pH 3·56; 25 ml.), and disulphone (50—60 mg. accurately weighed) was made up to 100 ml. with water and stored in an amber bottle in the dark. A blank containing none of the disulphone was worked concurrently. At intervals, the periodate uptake was estimated by transferring samples (10 ml.) from the oxidation mixture and the blank, into a mixture of phosphate buffer (pH 7·0; 30 ml.) and 20% potassium iodide solution (5 ml.), then titrating the iodine liberated with 0·01N-sodium thiosulphate solution, starch being used as indicator. This method is superior to that involving titration in acid, in that at pH 7 only the periodate reacts with iodide, and is reduced to iodate. Thus, any iodate which may have reacted during the oxidation is not inadvertently estimated as periodate (cf. Neumüller and Vasseur, *Arkiv. Kemi.*, 1953, **5**, 235).

(ii) *Total acidity*. Solutions of the oxidation mixture and the blank were prepared as above, but the acetate buffer omitted. Acid was determined (Halsall, Hirst, and Jones, *J.*, 1947, 1427) by taking samples (10 ml.) from the oxidation mixture and the blank, adding ethylene glycol (2 ml.) to each, and after a delay of 5 min. to ensure complete destruction of excess of

Time	$NaIO_4$ uptake, mol.		Total acid, equiv.	
hr.	hexane (II)	hex-1-ene (III)	hexane (II)	hex-1-ene (III)
1	2·88	1·26	2·82	1·09
2	2·93	1·73	2·82	1·44
3	2·98	1·98	—	1·67
4	—	2·12	2·82	1·83
6	3·02	2·26	—	1·98
11	—	2·42	—	—
22	—	2·56	—	2·32

periodate, titrating with 0·01N-sodium hydroxide solution, methyl red (screened with methylene blue) being used as indicator. Results are given in the Table.

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