[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

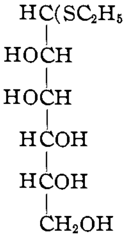
The Disulfones Derived from the Dithioacetals of Certain Hexoses[1]

BY R. BARKER[2] AND D. L. MACDONALD[2]

RECEIVED OCTOBER 5, 1959

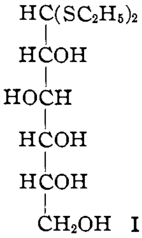
The diethyl dithioacetals of D-glucose, D-mannose and D-galactose are oxidized, under appropriate conditions, to the corresponding 1-deoxy-1,1-bis-(ethylsulfonyl)-hexitols, which on acetylation give the 1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexenes. The unacetylated derivatives are very rapidly degraded in dilute aqueous ammonium hydroxide solution to bis-(ethylsulfonyl)-methane and a pentose. On treatment with dilute acetic acid they are converted into 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-hexitols and these latter compounds are similarly but much more slowly degraded by dilute ammonium hydroxide.

The discovery of the oxidation of aldohexose diethyl dithioacetals by organic peracids to the corresponding disulfone derivatives and their subsequent degradation with dilute alkalies[3,4] to yield the next lower aldose and bis-(ethylsulfonyl)-methane has stimulated considerable interest in these reactions.[5,6] However, these reactions are not always simple, the structure of the disulfone obtained depending on the conditions employed for the oxidation. The current paper is a reinvestigation of several earlier researches in the field.



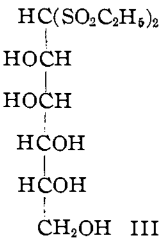
$$\begin{array}{c} HC(SC_2H_5)_2 \\ | \\ HOCH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ CH_2OH \end{array}$$

I



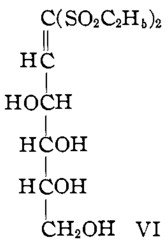
$$\begin{array}{c} HC(SC_2H_5)_2 \\ | \\ HCOH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ CH_2OH \end{array}$$

II



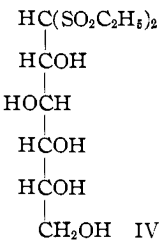
$$\begin{array}{c} HC(SO_2C_2H_5)_2 \\ | \\ HOCH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ CH_2OH \end{array}$$

III



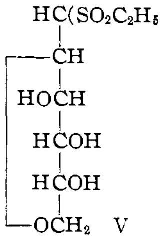
$$\begin{array}{c} C(SO_2C_2H_5)_2 \\ \| \\ HC \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ CH_2OH \end{array}$$

VI



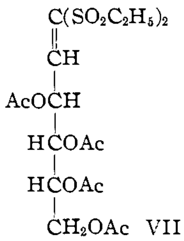
$$\begin{array}{c} HC(SO_2C_2H_5)_2 \\ | \\ HCOH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ CH_2OH \end{array}$$

IV



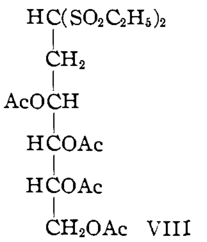
$$\begin{array}{c} HC(SO_2C_2H_5)_2 \\ | \\ CH \\ | \\ HOCH \\ | \\ HCOH \\ | \\ HCOH \\ | \\ OCH_2 \end{array}$$

V



$$\begin{array}{c} C(SO_2C_2H_5)_2 \\ \| \\ CH \\ | \\ AcOCH \\ | \\ HCOAc \\ | \\ HCOAc \\ | \\ CH_2OAc \end{array}$$

VII



$$\begin{array}{c} HC(SO_2C_2H_5)_2 \\ | \\ CH_2 \\ | \\ AcOCH \\ | \\ HCOAc \\ | \\ HCOAc \\ | \\ CH_2OAc \end{array}$$

VIII

Hough and Taylor[5] reported that the oxidation of D-mannose diethyl dithioacetal (I) with aqueous peroxypropionic acid yielded both crystalline 1-deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (III) and its sirupy anhydride, 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (V), whereas D-glucose diethyl dithioacetal (II) yielded only the same D-mannitol anhydride (V). Zinner and Falk[6] found that D-mannose diethyl dithioacetal (I) when oxidized by peroxypropionic acid or by hydrogen peroxide containing ammonium molybdate yielded the pentahydroxy disulfone III, whereas oxidation with hydrogen peroxide alone produced a derivative proposed to be 1,1-bis-(ethylsulfonyl)-D-*arabino*-3,4,5,6-tetrahydroxy-1-hexene (VI) on the basis of its ability to decolorize bromine water and permanganate. Unfortunately, these authors[6] did not report any structural studies on these derivatives, or any sulfur analyses.

We now find that when a solution of D-mannose diethyl dithioacetal (I) in hot dioxane is treated with a slight excess of peroxypropionic acid, the solution becomes superheated and on cooling a disulfone derivative crystallizes out as fine needles, m.p. 195–198°, in yields of 90–95%. This derivative is identical with that reported previously by MacDonald and Fischer[4] who obtained it in similar yield by carrying out the oxidation at a slightly lower temperature. As mentioned by these authors and confirmed in this report, paper chromatography of this compound in butanol–acetic acid–water suggests that the crystalline material is a mixture of two components of R_f 0.41 and 0.63. However, experiments described below lead to the conclusion that the material is actually homogeneous and that the second component is formed during the preparation of the solution from which samples are withdrawn for chromatography. The crystalline material can be recrystallized only with difficulty, the majority of it being readily converted to a sirupy product of R_f 0.63. Analyses of the recrystallized material indicate that it is a pentahydroxy compound III; it rapidly consumes 4 moles of periodate and yields 3 moles of formic acid and 1 mole of formaldehyde. It is very rapidly degraded by dilute aqueous ammonium hydroxide to give bis-(ethylsulfonyl)-methane and D-arabinose. Compound III is therefore similar to that described by Hough and Taylor[5]; its melting point, 195–198°, is considerably higher than the 119° which they first reported[7] but they later stated that the melting point depended on the rate of heating.[5] They did not report any rotation value for their compound.

Hough and Taylor[5] stated that acetylation of their disulfone III resulted in the formation of a penta-*O*-acetyl derivative. Acetylation of our

---

[1] This work was supported in part by a grant from the National Science Foundation, and represents part of the Ph.D. Thesis of Robert Barker, submitted to the Graduate Division, University of California, January, 1958.

[2] National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md.

[3] D. L. MacDonald and H. O. L. Fischer, THIS JOURNAL, **74**, 2087 (1952).

[4] D. L. MacDonald and H. O. L. Fischer, *Biochim. et Biophys. Acta*, **12**, 203 (1953).

[5] L. Hough and T. J. Taylor, *J. Chem. Soc.*, 970 (1956).

[6] H. Zinner and K.-H. Falk, *Chem. Ber.*, **88** 566 (1955).

[7] L. Hough and T. J. Taylor, *Chemistry & Industry*, 575 (1954).

disulfone III by their procedure yielded only a tetraacetate that was identified by melting point, mixed melting point and infrared spectrum as the previously described[3] D-*arabino*-3,4,5,6-tetraacetoxy-1,1-bis-(ethylsulfonyl)-1-hexene (VII).[8] The crude acetate contained traces of material difficult to remove by recrystallization. However, both the crude and purified materials could be reduced in excellent yield to the known[3] D-*arabino*-3,4,5,6-tetraacetoxy-1,1-bis-(ethylsulfonyl)-hexane (VIII), and the virtual superimposability of their infrared spectra provided further evidence that the double bond was not introduced during the process of recrystallization. The unsaturated acetate VII showed a characteristic double bond absorption at 6.2 μ, and gave a cherry-red color in dry pyridine and a black precipitate with osmium tetroxide, reactions characteristic of unsaturated disulfones.[3,9,10] Prior to acetylation the disulfone III showed no absorption at 6.2 μ, it could not be reduced catalytically and it gave no color reactions with osmium tetroxide or with pyridine.

Zinner and Falk[6] obtained a crystalline pentahydroxy disulfone derivative of m.p. 167° from D-mannose diethyl dithioacetal by oxidation with peroxypropionic acid or with hydrogen peroxide containing ammonium molybdate. They reported that attempted recrystallization of this compound converted it into an unsaturated disulfone VI, m.p. 135°; the latter was also obtained by oxidation of the dithioacetal with 20% aqueous hydrogen peroxide. In our hands, all attempts to prepare this unsaturated derivative have been unsuccessful. The saturated disulfone III of R_f 0.4, is readily converted, by brief heating in dilute aqueous acetic acid, into a sirup (V) having R_f 0.63, which has not crystallized in four years. This sirup rapidly consumes 2 moles of periodate with the liberation of 1 molar equivalent of formic acid, and it forms a crystalline triacetate on acetylation by a variety of methods. We agree with the conclusions of Hough and Taylor[5] that this sirup is 2,6-anhydro-1,1-bis-(ethylsulfonyl)-D-mannitol (V). In contrast to the behavior of the pentahydroxy disulfone III, this anhydro derivative is only slowly degraded by dilute aqueous ammonium hydroxide to bis-(ethylsulfonyl)-methane and D-arabinose.

With respect to D-glucose diethyl dithioacetal (II), we find, as did Hough and Taylor,[5] that oxidation with peroxypropionic acid in hot dioxane yields, on removal of solvent, a sirup with R_f 0.63 (V) identical with that obtained by treatment of 1-deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (III) with dilute aqueous acetic acid. However, when the oxidation is carried out in hot isopropyl alcohol solution, a crystalline material with m.p. 170–175° is obtained in a yield of about 80%. This crystalline material rapidly consumes 4 moles of periodate, with the formation of 3 moles of formic acid and 1 mole of formaldehyde. It is rapidly degraded by dilute aqueous ammonium hydroxide to D-arabinose, and readily converted by dilute acetic acid to the sirup V. Acetylation gave D-*arabino*-3,4,5,6-tetraacetoxy-1,1,bis-(ethylsulfonyl)-1-hexene (VII). The parent unacetylated compound with m.p. 170–175° could not be reduced by Adams catalyst whereas the acetate readily took up 1 mole of hydrogen to give D-*arabino*-3,4,5,6-tetraacetoxy-1,1-bis-(ethylsulfonyl)-hexane (VIII) in good yield. These properties, coupled with the analyses on the compound, lead to the conclusion that this material is 1-deoxy-1,1-bis-(ethylsulfonyl)-D-glucitol (IV).

In experiments on the oxidation of D-galactose diethyl dithioacetal (IX), Hough and Taylor[5] reported that oxidation with peroxypropionic acid produced crystalline 2,6-anhydro-1,1-bis-(ethylsulfonyl)-D-talitol (X). Using hydrogen peroxide and ammonium molybdate, Zinner and Falk[6] obtained a crystalline disulfone to which they assigned the structure XI. They reported that their compound was readily recrystallized from aqueous alcohol without change and that a crystalline pentaacetate and tetrabenzoate could be prepared. Hough and Taylor[5] prepared this compound by the published method,[6] and reported that it consumed 4 moles of periodate. They mentioned the ready degradation of the material by mild alkali to D-lyxose, but stated that recrystallization resulted in complete conversion to the anhydride X.

In the present work, we find that oxidation of D-galactose diethyl dithioacetal (IX) in boiling dioxane solution with peroxypropionic acid gives an excellent yield of a crystalline disulfone which is only slowly degraded by dilute aqueous ammonium hydroxide. The physical constants of this material, as well as those of its triacetate and tribenzoate, are in agreement with the values obtained by Hough and Taylor[5,11] for 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol (X). When the oxidation is carried out in dioxane solution at a lower temperature, the crystalline product consists of a mixture of two components, one identical with that obtained above. The second component however, is extremely sensitive to dilute aqueous ammonium hydroxide, being converted rapidly to D-lyxose. When the reaction is carried out at −10° in dimethylformamide, a crystalline product, m.p. 151–152°, is obtained, which is very unstable in dilute ammonium hydroxide solution. The material crystallizes in reasonably pure form in yields of 80%, but all attempts to recrystallize it resulted in its conversion to the anhydro compound X. The material rapidly consumes 4 moles of periodate, releasing 3 moles of formic acid and 1 mole of formaldehyde. It gives no color with dry pyridine, and acetylation yields the known[3] D-*lyxo*-1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-

---

[8] Hough and Taylor (ref. 5) carried out acetyl determinations in an unspecified manner, and corrected for the extra acid derived from the sulfone groups. In our hands, no such correction was necessary. Determination of the "acetyl" content of the unacetylated sulfone by the method of Kunz and Hudson, THIS JOURNAL, **48**, 1978 (1926), showed that no correction was required, and with the acetylated compounds this method gave results which were in good agreement with those obtained by other methods; E. P. Clark, *Ind. Eng. Chem., Anal. Ed.*, **9**, 539 (1937); A. Elek and R. A. Harte, *ibid.*, **8**, 267 (1936). Consumption of base could be observed only when the parent unacetylated disulfone was heated in basic solution, and this consumption was found to vary with small changes in the conditions employed.

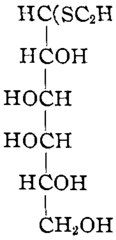
[9] L. Hough and T. J. Taylor, *J. Chem. Soc.*, 1212 (1955).

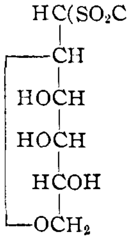
[10] L. Hough and T. J. Taylor, *ibid.*, 3544 (1955).

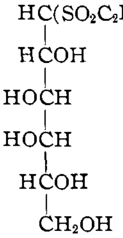
[11] L. Hough and T. J. Taylor, *Chemistry & Industry*, 1018 (1954).

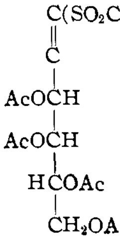
1-hexene (XII). Thus the compound appears to be 1-deoxy-1,1-bis-(ethylsulfonyl)-D-galactitol (XI).

The physical constants (m.p. 151–152°, [α]D −17° in 5% aqueous acetic acid) of our compound differ considerably from those reported by Zinner and Falk[6] (m.p. 197°, [α]D −1.5° in water) for the compound to which they assign structure XI. A careful comparison of the two preparations was desirable, and during the course of the present work, several attempts were made to prepare compound XI by the published procedure.[6] Apparently the conditions for the oxidation are rather critical, for the only product obtained was identical in all respects with the anhydro compound X.


IX


X


XI


XII

Experimental[12]

Peroxypropionic Acid.[13]—Propionic anhydride (252 ml.) was mixed with 210 ml. of 30% hydrogen peroxide and the mixture chilled to −10° in an ice-salt-bath; 84 ml. of concentrated sulfuric acid was added dropwise to the rapidly stirred mixture and the temperature maintained at −10°. When the addition of acid was complete a further 210 ml. of cold hydrogen peroxide was added and the mixture allowed to stand at room temperature for 8–16 hours. At this time the mixture was distilled at 25–30° and 15 mm. pressure. The distillate (350–500 ml.) contained no hydrogen peroxide as determined by permanganate titration and was at least 3–4 molar with respect to peracid.[14]

1-Deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (III).—D-Mannose diethyl dithioacetal (2.0 g.) was dissolved by warming in 40 ml. of dioxane and the solution brought to boiling. A 15% excess over the theory for 4 moles of peroxypropionic acid was added rapidly, causing superheating. The reaction was immediately cooled under the cold water tap. At a temperature of 40° crystals began to form and at room temperature the mixture had become semi-solid. The crop was filtered off, washed thoroughly with cold dioxane and ether and then air-dried. The yield was 2.3 g. (94%) of material, m.p. 185–190°. Recrystallization from absolute ethanol yielded 1.0 g., m.p. 195–198°, $[\alpha]^{23}D$ +7.0° (c 0.5, water). The compound showed no absorption at 6.2 μ.

Anal. Calcd. for $C_{10}H_{22}O_9S_2$ (350.4): C, 34.28; H, 6.28; S, 18.30. Found: C, 34.28; H, 6.40; S, 18.35.

1-Deoxy-1,1-bis-(ethylsulfonyl)-D-glucitol (IV).—D-Glucose diethyl dithioacetal (2.0 g.) was dissolved in 40 ml. of boiling isopropyl alcohol and a 10% excess of peroxypropionic acid was added rapidly. A vigorous exothermic reaction occurred and the reaction was shaken for a half-hour at which time crystallization started. After standing one hour a crop of crystals was removed by filtration, washed well with ether and air-dried. The yield was 1.33 g. (55%), m.p. 170°. A second crop of crystals (0.7 g. 29%) was obtained from the mother liquors on storage at 4°. The two crops were combined and recrystallized from hot propyl alcohol giving 1.2 g., m.p. 170–175° with decomposition, $[\alpha]^{27}D$ +22.0° (c 0.5, 5% aqueous acetic acid). No absorption in the region of 6.2 μ was observed.

Anal. Calcd. for $C_{10}H_{22}O_9S_2$ (350.4): C, 34.28; H, 6.28; S, 18.30. Found: C, 34.45; H, 6.22; S, 18.60.

D-*arabino*-1,1-Bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexene (VII).—A. 1-Deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (0.5 g.) was treated with 4 ml. of acetic anhydride containing one drop of concentrated sulfuric acid at 100°. The material rapidly dissolved and the solution became bright blue. After 10 minutes the reaction was cooled in ice and chipped ice was added to destroy the excess acetic anhydride. After a further 10 minutes 20 ml. of ice-water was added. A gummy precipitate formed which crystallized on trituration. Filtration followed by solution in 10 ml. of hot isopropyl alcohol and slow cooling gave plate-like crystals, yield 0.6 g. (84%), m.p. 155–156°. Four further recrystallizations from the same solvent yielded 0.35 g. (49%), m.p. 159–160°, undepressed by mixture with an authentic sample of D-*arabino*-1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexene.[3]

Anal. Calcd. for $C_{18}H_{28}O_{12}S_2$(500.5): C, 43.19; H, 5.64; S, 12.81; CH_3CO, 34.4. Found: C, 43.00; H, 5.57; S, 12.50; CH_3CO, 34.3.

B. 1-Deoxy-1,1-bis-(ethylsulfonyl)-D-glucitol (0.5 g.) was acetylated in the same manner. The crude product weighed 0.7 g. (98%) and melted at 115–125°. Four recrystallizations from isopropyl alcohol gave 0.37 g. (52%), m.p. 159–160°, mixed with authentic material m.p. 159–160°. The infrared spectra of the two compounds were identical, and showed characteristic absorption at 6.2 μ, as did the crude, unrecrystallized material.

Anal. Calcd. for $C_{18}H_{28}O_{12}S_2$ (500.5): C, 43.19; H, 5.64; S, 12.81; CH_3CO, 34.4. Found: C, 42.99; H, 5.70; S, 12.39; CH_3CO, 35.6.

D-*arabino*-1,1-Bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxyhexane[3] (VIII).—D-*arabino*-1,1-Bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexene (415 mg., 0.83 mmole) was shaken in ethanol with 190 mg. of prereduced platinum oxide in an atmosphere of hydrogen at 23° and 794 mm. A rapid uptake of hydrogen occurred which reached 0.82 mmole in 40 minutes and was unchanged after another hour. The catalyst was removed by filtration and the solution concentrated to give 400 mg. of a colorless sirup. This was dissolved in isopropyl ether and seeded with authentic D-*arabino*-1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxyhexane.[3] Refrigeration yielded 0.33 g. (80%) of crystals, m.p. 102–104°, mixed with an authentic sample of m.p. 102–104°.

The crude material with m.p. 155–156°, obtained from the acetylation of 1-deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol, could be reduced in a similar fashion to give a comparable yield of D-*arabino*-1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxyhexane.

The unacetylated derivatives III and IV in 5% aqueous acetic acid showed no hydrogen uptake during 24 hours. Chromatography indicated that the starting material was recovered largely unaltered. A small part had been converted to the cyclic derivative V as shown by its relative resistance to degradation by dilute aqueous ammonia.

2,6-Anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (V).—A. 1-Deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (2.0 g.) was heated in 20 ml. of 5% aqueous acetic acid for 10 minutes on a steam-bath. The solvent was then removed at 60° and the resulting sirup dried at room temperature and 0.1 mm. pressure overnight. This sirup which could not be crystallized showed $[\alpha]^{20}D$ −14.0° (c 4.2, methanol). Hough and Taylor[5] report [α]D −13.1° (c 4.4, methanol).

Anal. Calcd. for $C_{10}H_{20}O_8S_2$ (332.4): C, 36.20; H, 6.06; S, 19.30. Found: C, 36.06; H, 5.88; S, 19.08.

B. 1-Deoxy-1,1-bis-(ethylsulfonyl)-D-glucitol (1 g as treated in 10 ml. of 5% aqueous acetic acid as under A. The product was identical with that obtained above, and had $[\alpha]^{20}D$ −13.5° (c 4.6, methanol).

---

[12] Microanalyses were carried out by the Microchemical Laboratory, University of California, and by Dr. A. Elek, Los Angeles, Calif. Unless otherwise stated the solvents were reagent grade used without further purification. All evaporations were carried out under reduced pressure. Melting points were determined in capillaries with Anschütz thermometers.

[13] J. d'Ans and W. Frey, *Ber.*, **45**, 1845 (1912).

[14] H. Böhme, *Org. Syntheses*, **20** 70 (1940).

2,6-Anhydro-1,1-bis-(ethylsulfonyl)-D-mannitol Triacetate.—1-Deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (0.5 g.) was converted to the sirupy anhydro compound as described above. After thorough drying, 4 ml. of acetic anhydride and one drop of concd. sulfuric acid were added and the mixture heated at 100°. After 20 minutes the reaction was cooled in ice and chipped ice was added, followed by water. A gummy precipitate formed which did not crystallize. The aqueous mixture was extracted 3 times with 25-ml. portions of chloroform and the pooled chloroform extracts washed with 50 ml. each of ice-cold saturated aqueous sodium bicarbonate and water and then dried over sodium sulfate. Concentration of the solution gave a yellow sirup which was dissolved in hot isopropyl alcohol. Crystallization took place after cooling to room temperature and standing overnight; yield 0.4 g. (61%), m.p. 124–125°. Three recrystallizations from the same solvent gave 0.27 g. (41%), m.p. 126–127°, $[\alpha]^{25}\text{D}$ −18.0° (*c* 1.6, chloroform). Hough and Taylor[5] report m.p. 125–127°.

Anal. Calcd. for $C_{16}H_{26}O_{11}S_2$ (458.5): C, 42.00; H, 5.73; S, 14.00; CH_3CO, 28.2. Found: C, 41.96; H, 5.65; S, 13.88; CH_3CO, 28.1.

Acetylation of 0.5 g. of the sirup in pyridine–acetic anhydride gave after recrystallization 0.31 g. (47%) of the same product, m.p. 126–127°.

D-Arabinose.—A. 1-Deoxy-1,1-bis-(ethylsulfonyl)-D-mannitol (1.0 g.) was treated with 10 ml. of 0.28% aqueous ammonia. The compound dissolved rapidly and bis-(ethylsulfonyl)-methane which crystallized from the reaction mixture was removed by filtration after 30 minutes. The filtrate was extracted four times with 10-ml. portions of chloroform and the aqueous layer concentrated to dryness. Addition of methanol and crystallization at 4° yielded 0.37 g. (86%) of D-arabinose, $[\alpha]^{22}\text{D}$ −102° at equilibrium (*c* 3.5, water).

The precipitate which had been filtered from the reaction weighed 0.45 g. (78%) and had m.p. 101–102°, undepressed when mixed with authentic bis-(ethylsulfonyl)-methane.

B. Treatment of 1-deoxy-1,1-bis-(ethylsulfonyl)-D-glucitol (1.0 g.) in a similar fashion gave 0.34 g. (78%) of D-arabinose and 0.47 g. (81%) of bis-(ethylsulfonyl)-methane.

C. 2,6-Anhydro-1,1-bis-(ethylsulfonyl)-D-mannitol (1.0 g.) was treated with 10 ml. of 0.28% aqueous ammonia and left at room temperature. After five days the reaction was worked up as under A. The yield of D-arabinose was 0.30 g. (66%) and of bis-(ethylsulfonyl)-methane 0.41 g. (68%).

1-Deoxy-1,1-bis-(ethylsulfonyl)-D-galactitol (XI).—D-Galactose diethyl dithioacetal (2 g.) was dissolved in 20 ml. of N,N-dimethylformamide and chilled to −20° in a Dry Ice-bath. The solution was stirred vigorously and a 20% excess of peroxypropionic acid was added over a period of an hour, care being taken that the temperature did not rise above −10°. After the addition of oxidant had been completed the reaction was placed at −10° for 48 hours. At this time a crop of crystals was filtered off and washed with 2 volumes of cold ether; yield 0.75 g. (32%). This product contains, essentially, only material which is rapidly degraded by dilute ammonia. In some instances, traces of unoxidized mercaptal could be detected chromatographically. After thorough drying *in vacuo* over magnesium perchlorate and sodium hydroxide it melted at 151–152°, $[\alpha]^{22}\text{D}$ −17.0° (*c* 1.5, 5% aqueous acetic acid).

Anal. Calcd. for $C_{10}H_{22}O_9S_2$ (350.4): C, 34.28; H, 6.28; S, 18.30. Found: C, 34.57; H, 6.39; S, 18.64.

A second crop of material was obtained by placing the combined mother liquors and the ether washings at −10° for 48 hours, yield 1.3 g. (55%), m.p. 149–150°. This crop contained a slight amount of the cyclic derivative X, as revealed by its relative resistance to degradation by dilute ammonium hydroxide.

Attempts to recrystallize this compound were largely unsuccessful and resulted in conversion of the material to 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol (X).

D-*lyxo*-1,1-Bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexene (XII).—A sample of 1-deoxy-1,1-bis-(ethylsulfonyl)-D-galactitol (0.5 g.) was treated with 4 ml. of acetic anhydride and one drop of concentrated sulfuric acid at 100° for 20 minutes. The material dissolved rapidly and the reaction mixture soon became bright blue turning to brown. The reaction was cooled in ice and chipped ice was added to destroy the excess acetic anhydride. An oil separated on the addition of water. The water was decanted and the oil dissolved with warming in isopropyl alcohol. Crystals were obtained on slow cooling in a water-bath with occasional scratching; yield 0.6 g. (80%), m.p. 106–108°. Three further recrystallizations from isopropyl alcohol yielded 0.35 g. (47%) of material, m.p. 118–119°, $[\alpha]^{22}\text{D}$ +20.0° (*c* 1.0, chloroform). A mixed melting point with an authentic sample of D-*lyxo*-1,1-bis-(ethylsulfonyl)-3,4,5,6-tetraacetoxy-1-hexene (XII) was 119–120°. The compounds have identical infrared spectra.

Anal. Calcd. for $C_{18}H_{28}O_{12}S_2$ (500.5): C, 43.19; H, 5.64; S, 12.81; CH_3CO, 34.4. Found: C, 43.09; H, 5.51; S, 12.59; CH_3CO, 33.5.

2,6-Anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol (X).—D-Galactose diethyl dithioacetal (2 g.) was dissolved with heating in 40 ml. of dioxane. The solution was brought to boiling and peroxypropionic acid (15% in excess of the required 4 moles) was added rapidly. The solution became superheated (105°). After swirling for 5 to 10 minutes, crystals began to form and at a temperature of 40–50° the reaction became semi-solid. When the reaction had cooled to room temperature the product was filtered off, washed five times with cold dioxane, several times with ether and air-dried giving 2.4 g. of material, m.p. 160–175°. Two recrystallizations from ethanol yielded 2.0 g. (86%) of needles, m.p. 202–202.5° and $[\alpha]^{22}\text{D}$ +4.7° (*c* 1.3, methanol), and +14.7° (*c* 2.17, water). Hough and Taylor[5] report m.p. 193–195° and $[\alpha]\text{D}$ +3.1° (*c* 1.99, methanol) and +19.0° (*c* 2.17, water).

Anal. Calcd. for $C_{10}H_{20}O_8S_2$ (332.4): C, 36.20; H, 6.06; S, 19.30. Found: C, 36.21; H, 6.05; S, 19.19.

2,6-Anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol Triacetate.—Treatment of 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol with acetic anhydride–sulfuric acid, acetic anhydride–perchloric acid, acetic anhydride–pyridine or with isopropenyl acetate–sulfuric acid resulted in the formation of a triacetate in yields of 85–90%. Three or four recrystallizations from isopropyl alcohol gave 45–55% yields of triacetate, m.p. 188–189° and $[\alpha]^{22}\text{D}$ −12.0° (*c* 2.66, methanol), $[\alpha]^{25}\text{D}$ −27.0° (*c* 1.6, chloroform). Hough and Taylor[5] report m.p. 187–188° and $[\alpha]\text{D}$ −21.9° (*c* 3.23, chloroform).

Anal. Calcd. for $C_{16}H_{26}O_{11}S_2$ (458.5): C, 42.00; H, 5.73; S, 14.00; CH_3CO, 28.2. Found: C, 42.19; H, 5.87; S, 13.97; CH_3CO, 27.7.

2,6-Anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol Tribenzoate.—Treatment of 2,6-anhydro-1-deoxy-1,1-bis-(ethylsulfonyl)-D-talitol with benzoyl chloride and pyridine in the usual manner, followed by four recrystallizations from ethanol yielded 77% of purified material, m.p. 201°, $[\alpha]^{20}\text{D}$ −19.0° (*c* 3.32, pyridine). Hough and Taylor[5] report m.p. 197–198°.

Anal. Calcd. for $C_{31}H_{32}O_{11}S_2$ (644.7): C, 57.73; H, 5.00; S, 9.96. Found: C, 57.70; H, 5.12; S, 10.17.

D-Lyxose.—A. One gram of 1-deoxy-1,1-bis-(ethylsulfonyl)-D-galactitol was treated with 5 ml. of 0.28% ammonium hydroxide. The compound dissolved immediately and bis-(ethylsulfonyl)-methane precipitated from the mixture. After 30 minutes this was removed by filtration (0.49 g., 82%) and after recrystallization from methanol it showed m.p. 102–103° undepressed on admixture with an authentic sample. The filtrate, which contained only D-lyxose as shown by chromatography, was extracted four times with chloroform and the aqueous layer concentrated. The sirup obtained was dissolved in methanol and seeded with D-lyxose. After two days at 4° a crop of crystals was removed, yield 0.36 g. (80%), $[\alpha]^{20}\text{D}$ −13.0° at equilibrium (*c* 4.0, water).

B. 2,6-Anhydro-1,1-bis-(ethylsulfonyl)-D-talitol (0.5 g.) was slurried in 5 ml. of water containing one drop of concentrated aqueous ammonia. Chromatography of aliquots indicated that the reaction was complete after six days. After 7 days the solution was extracted four times with 10-ml. portions of chloroform to remove bis-(ethylsulfonyl)-methane. The aqueous layer was concentrated and the residue was dried *in vacuo* at 40° overnight. The yield of D-lyxose, crystallized from methanol as above, was 0.19 g. (85%), $[\alpha]^{22}\text{D}$ −13.0° at equilibrium (*c* 2.0, water).

The chloroform extracts were dried (sodium sulfate) and concentrated and the resulting crystals taken up in a minimal amount of hot water. Cooling gave 0.2 g. (70%) of bis-(ethylsulfonyl)-methane, m.p. 101–103°, undepressed by admixture with an authentic sample.

Periodate Oxidations.—All oxidations were carried out in unbuffered 0.08 *M* sodium metaperiodate in the dark. Samples of 200–300 mg. (accurately weighed) were used and in all cases approximately 8 moles of oxidant per mole of compound was used in a total volume of 100 ml. Consumption of oxidant was followed[15] by adding 1-ml. samples withdrawn at intervals to 5 ml. of 0.066 *M* phosphate buffer *p*H 7.4–7.5 containing 1 ml. of 20% aqueous potassium iodide. Iodine liberated was titrated after 10 minutes with 0.01 *N* sodium arsenite. At intervals the consumption of oxidant was also checked by adding a 1-ml. aliquot of the reaction to 10 ml. of 2 *N* sulfuric acid containing 1 ml. of 20% aqueous potassium iodide and titrating the iodine liberated with 0.1 *N* thiosulfate. In all cases the possibility of iodine consumption by the products of the reaction was checked by adding 5 ml. of 0.1 *N* iodine to an aliquot of the reaction mixture and titrating with 0.1 *N* thiosulfate after 10 minutes.

Volatile acid was determined on 5-ml. samples of the reaction mixture. Two ml. of ethylene glycol and 2 ml. of concentrated sulfuric acid were added and the sample steam distilled until 50-ml. aliquots of the distillate required only one drop of 0.005 *N* sodium hydroxide to give a pink color with phenolphthalein.

Formaldehyde was determined by adding 50 ml. of the reaction mixture to 100 ml. of a 0.4% aqueous solution of dimedon (5,5-dimethyl-1,3-cyclohexanedione) and adjusting the *p*H to 6.5 with 3 *N* sodium hydroxide. The precipitate was removed by filtration, washed with water and air-dried and then recrystallized from methanol. Melting points were compared with a sample prepared from formaldehyde. The results obtained with the various materials expressed as moles per mole of compound were

Compound	IO_4^- consumed			HCOOH produced		HCHO produced	
	1 hr.	24 hr.	96 hr.	1 hr.	96 hr.	1 hr.	96 hr.
III	3.97	4.06	4.10	3.03	2.94	0.87	0.94
IV	3.84	4.14	4.08	2.76	2.87	0.96	.89
XI	4.09	4.16	4.80	3.10	3.19	1.04	.98
V	2.01	3.92	4.15	0.96	3.03	0.0	.86
X	1.95	4.01	4.06	0.92	2.98	0.1	.78

Paper chromatography was carried out by the descending method at room temperature using Whatman #1 paper with butanol–acetic acid–water (4:1:5 v./v.) as the solvent. Ammoniacal silver nitrate or periodate–benzidine[16] were used to detect polyhydroxy compounds. The R_f's of the various materials were: III, 0.41; IV, 0.42; XI, 0.42; V, 0.63; X, 0.67. The 1-deoxy-1,1-bis-(ethylsulfonyl)-hexitols III and IV invariably showed two components on chromatography, but it is probable that the materials are actually homogeneous and that the second component was formed during the preparation of the solution from which samples were withdrawn for chromatography. For instance, a sample of III was dissolved in 5% aqueous acetic acid by cautious warming and this solution was spotted on the paper. The developed chromatogram showed two spots, R_f 0.41 and 0.63; no streaking was observed, indicating that little or no interconversion had occurred during chromatography. If a sample of III is prepared for chromatography by heating at 100° for one minute in a dilute acetic acid solution, only the faster moving component is found. Chromatography of a second sample, prepared by first heating in dilute acetic acid and then making the solution slightly basic with ammonia shows that the component with R_f 0.63 is relatively stable to basic conditions; a reaction time of 4 to 5 days is required before this component is completely degraded to D-arabinose. Chromatography of a sample prepared by suspending III in dilute aqueous ammonia and acidifying after 5 minutes shows that in this time, the crystalline material is completely degraded to D-arabinose.

1-Deoxy-1,1-bis-(ethylsulfonyl)-D-galactitol could be dissolved in dilute acetic acid in the cold, and showed but one component on chromatography. However, it showed a behavior similar to that of the other hexitol derivatives when treated as above.

BERKELEY 4, CALIF.

---

[15] G. D. Greville and D. H. Northcote, *J. Chem. Soc.*, 1945 (1952).

[16] M. Viscontini, D. Hoch and P. Karrer, *Helv. Chim. Acta*, **38**, 642 (1955).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

Some Oxidation and Reduction Products of 2,4-*O*-Ethylidene-D-erythrose[1]

BY R. BARKER[2] AND D. L. MACDONALD[2]

RECEIVED OCTOBER 19, 1959

Certain improvements in the synthesis of 4,6-*O*-ethylidene-D-glucose are described, and the compound has been used as a convenient starting material for the preparation of D-erythronolactone and some erythritol derivatives.

Recently, there has been considerable interest in D-erythrose and its oxidation and reduction products, particularly with reference to their use as intermediates in the synthesis of other sugars and their conversion to various phosphate esters. For instance 2,4-*O*-ethylidene-D-erythrose has been used as an intermediate in the preparation of D-erythrose 4-phosphate[3] and D-erythritol 4-phosphate.[4] It has also been used as a starting material for the preparation of certain glycosides of D-erythrose,[5] a diethylidene octose,[6] and certain labeled pentoses.[7] D-Erythronolactone has recently been used as an intermediate in the preparation of D-ribulose derivatives,[8] and for the preparation of certain phosphates of D-erythronic acid.[9]

A suitable starting material for all of the above syntheses is 4,6-*O*-ethylidene-D-glucose, the preparation of which has been described.[10,11] However, the procedure of Hockett, Collins and Scattergood gives a product which is difficult to purify to constant melting point. This difficulty, which results from the presence of ammonium sulfate in the product, has been overcome and the improved procedure is described below. The periodate oxidation of 4,6-*O*-ethylidene-D-glucose to form 2,4-*O*-ethylidene-D-erythrose using sodium bicarbonate to

---

[1] This work was supported in part by a grant from the Eli Lilly Research Grants Committee, and is in part abstracted from the Ph.D. Thesis of Robert Barker, submitted to the Graduate Division, University of California, January, 1958.

[2] National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md.

[3] C. E. Ballou, H. O. L. Fischer and D. L. MacDonald, THIS JOURNAL, **77**, 5967 (1955).

[4] D. L. MacDonald, H. O. L. Fischer and C. E. Ballou, *ibid.*, **78**, 3720 (1956).

[5] C. E. Ballou, Abstr. Am. Chem. Soc., 134th Meeting, Chicago, Ill., 1958, p. 9-D.

[6] R. Schaffer, THIS JOURNAL, **81**, 2838 (1959).

[7] H. L. Frush and H. S. Isbell, *J. Research Natl. Bur. Standards*, **51**, 307 (1953).

[8] D. L. MacDonald, J. D. Crum and R. Barker, THIS JOURNAL, **80**, 3379 (1958).

[9] R. Barker and F. Wold, manuscript in preparation.

[10] B. Helferich and H. Appel, *Ber.*, **64**, 1841 (1931).

[11] R. C. Hockett, D. V. Collins and A. Scattergood, THIS JOURNAL, **73**, 599 (1951).