305.5 mμ (ε 10,000)]. It gave a nearly black ferric chloride test and positive Fehling, periodate and silver nitrate tests. The decomposition of the ketone with dilute sulfuric acid was slow at room temperature and could be followed conveniently over a period of three days by loss of optical activity. This relative stability at moderate temperatures gives basis for postulating the split of only one of the oxide groups of the dioxide X at room temperature.

Diosphenolene Reduction. Diosphenol.—The reduction of 0.81 g. of diosphenolene recrystallized three times from ethanol or methanol in 10 ml. of ethanol using prereduced platinum oxide catalyst proceeded rapidly at room temperature. After 1.1 equivalents of hydrogen had been absorbed, the solution was filtered to remove catalyst, and water was added until the filtrate was cloudy. The white needles which appeared in the cold filtrate were separated and dried to constant weight at atmospheric pressure giving 0.25 g. (31%) of diosphenol, m.p. 80–81°. By sublimation from a bath at 80° at atmospheric pressure it was possible to obtain material, m.p. 83–83.5°, which failed to give a melting point depression when mixed with authentic diosphenol. An additional 7% of product, m.p. 63–66°, which was separated from the reaction mixture was presumably a mixture of diosphenol and diosphenolene. The ultraviolet absorption spectrum of the main product showed a single maximum at 274 mμ (ε 9,540) corresponding to authentic diosphenol of comparable purity, $\lambda_{\max}^{\mathrm{EtOH}}$ 272.5 mμ (ε 9,880). Ease of sublimation of the product and color with ferric chloride were identical to authentic diosphenol.

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

Derivatives of D-*gluco*-Dialdohexose

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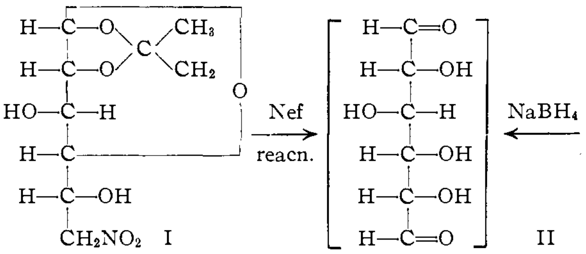
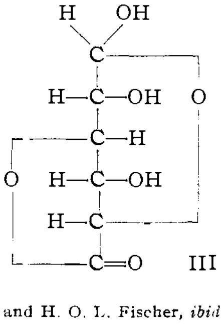
D-*gluco*-Dialdohexose isolated as its tetraethyl bis-mercaptal, has been prepared by the controlled reduction of D-glucuronolactone by means of sodium borohydride. This compound can also be obtained by carrying out a Nef reaction on 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose.

Recently, interest in the dialdohexose type of sugar has been renewed, with the preparation of derivatives of D-*manno*-dialdohexose by oxidation of appropriately substituted derivatives of D-inositol[1] and of derivatives of *galacto*-dialdohexose by catalytic reduction of tetra-O-acetylmucyl dichloride.[2] A number of other substituted dialdoses have been reported in the literature,[1,2] but as yet no derivatives of a dialdose with the D-*gluco* configuration have been described.

Chemically, D-*gluco*-dialdohexose is intermediate between D-glucose and D-glucuronic acid in its state of oxidation. Lindberg and Theander[3] have reported that oxidation of methyl β-D-glucopyranoside with dichromate gave a methyl glycoside of D-*gluco*-dialdohexose in very low yield, but the material was isolated as an impure sirup, and no crystalline derivatives amenable to structure proof were prepared. In a like manner, a derivative of D-*gluco*-dialdohexose may be an intermediate in the enzymatic oxidation of uridine diphosphate glucose to uridine diphosphate glucuronic acid. This enzyme preparation was obtained from a water extract of calf liver acetone powder, and catalyzed the aforementioned oxidation with concomitant reduction of two molar equivalents of diphosphopyridine nucleotide.[4] However, all attempts to demonstrate the expected intermediate dialdose derivatives were unsuccessful. Inasmuch as the D-*gluco*-dialdohexose may possibly have some real biological significance, we have attempted to prepare this compound and this communication deals with the preparation of a derivative of it using two distinctly different approaches, namely, oxidation of a D-glucose derivative and reduction of D-glucuronolactone.

Grosheintz and Fischer[5] prepared a mixture of 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose and 1,2-*O*-isopropylidene-6-deoxy-6-nitro-L-idose from 1,2-*O*-isopropylidene-D-*xylo*-dialdopentose and nitromethane and separated the products by preferential acetonation of the L-idose isomer. By the use of the Nef reaction,[6] the 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose (I) has been converted into D-*gluco*-dialdohexose (II), which was isolated from the aqueous solution as its insoluble crystalline tetraethyl bis-mercaptal in a yield of 47%. This derivative was further characterized as its crystalline tetraacetate.





III

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An alternative route to the preparation of D-*gluco*-dialdohexose derivatives involves the reduction of D-glucuronolactone, using sodium borohydride. This reagent has been used extensively for the reduction of sugars[7] and sugar derivatives and conditions have been described for the preparation of either aldoses or glycitols from the aldonic acid lactones.[7a,7c] This reducing agent has also been employed for the preparation of aldonic acids by reduction of the carbonyl function in salts of D-glucuronic acid,[7c] D-galacturonic acid[7c] and 5-keto-D-gluconic acid (L-sorburonic acid).[8] On the other hand, it has been utilized for the reduction of the carboxylic acid function of various uronic acids; in these reactions, glycosides of the parent hexose were obtained from glycosides of D-galacturonic methyl ester,[7c] D-glucuronic methyl ester[7c,9] and ethyl ester,[9] and L-sorburonic acid methyl ester.[10] In all of these reactions involving reduction of the carboxylic acid function of uronic acids, no report of an attempt to stop the reaction at the aldehyde stage has appeared. As mentioned above, this partial reduction proceeds readily with sugar acid lactones, and if applied successfully to uronic derivatives, it offers an alternative route to the preparation of dialdoses.

In the present work conditions are described for carrying out such a reaction on D-glucuronolactone (III), to produce in rather poor yield (10%) D-*gluco*-dialdohexose isolated as the tetraethyl bismercaptal. Under the experimental conditions employed, a *p*H of about 5 appeared to give the highest yield. When the reduction was carried out at *p*H 4, the yield was slightly poorer, while at a *p*H of 3 or 6, none of the dialdose derivative was obtained. Also, it should be noted that under the conditions given, the yield of dialdose was markedly dependent upon the size of the run; when carried out on a 25- or 100-g. scale, the yield of purified material dropped to 2–3%. In like manner, a few reductions were carried out on 1,2-*O*-isopropylidene-D-glucurone[11] but in no instance was any dialdose bis-mercaptal isolated.

The isolation of the same bis-mercaptal from D-glucuronolactone and from 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose provides further confirmation of the correctness of the assignment of the D-*gluco* configuration to the isopropylidene-nitrodeoxyhexose of m.p. 126–127°.[5]

Experimental[12]

Preparation of D-*gluco*-Dialdohexose Tetraethyl Bis-mercaptal. (a) From 1,2-*O*-Isopropylidene-6-deoxy-6-nitro-D-glucose.—Five grams of 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose[5] was dissolved in 25 ml. of ice-cold 1 *N* sodium hydroxide, and this solution was added dropwise, over a period of 15 minutes, to 25 ml. of concentrated hydrochloric acid. During the addition, the acid was kept in a water-bath at 15–20° and was vigorously stirred. After the addition was complete, the solution was cooled in an ice-bath and saturated with hydrogen chloride gas. Ethanethiol (12.5 ml.) was then added and the mixture swirled while cooling in ice; after 15 minutes the reaction mixture was poured into 400 ml. of ice and water. The product began to crystallize within five minutes and, after three hours at 0°. it was filtered, washed with water and dried *in vacuo* over sodium hydroxide. The crude product (6.1 g.) was recrystallized from 150 ml. of petroleum ether (b.p. 60–70°) and there was obtained 4.05 g. of colorless material, m.p. 79–80°. A second recrystallization from 10 parts of methanol by addition of 10 parts of water gave 3.72 g. (47.5%), m.p. 80–81°, $[\alpha]^{24}\text{D}$ +8.0° (*c* 2, dry acetone).

Anal. Calcd. for $C_{14}H_{30}O_4S_4$ (390.6): C, 43.04; H, 7.74; S, 32.83. Found: C, 43.08; H, 7.72; S, 32.72.

(b) From D-Glucuronolactone.—A solution of D-glucuronolactone (5.00 g.) in water (50 ml.) was cooled in an ice-salt-bath and to the mechanically stirred solution there was added over a period of ten minutes 0.54 g. of sodium borohydride dissolved in 10 ml. of water. During this addition, the temperature of the mixture was maintained between −1 and +4°, and the *p*H, as measured with a Beckman model H2 *p*H meter, was kept between 4.7 and 5.2 by dropwise addition of approximately 0.2 *N* hydrochloric acid. After stirring for a further five minutes, the *p*H of the solution was adjusted to 6 with ammonium hydroxide and the solution was concentrated *in vacuo* (bath temperature 45°). The residue was cooled in ice, and 12 ml. of ethanethiol and 10 ml. of concentrated hydrochloric acid were added. The flask was swirled to dissolve the sirup and then left at room temperature for 30 minutes. The reaction mixture was then diluted with 400 ml. of ice-water, and seeded with the mercaptal obtained above. After standing overnight at 4°, the precipitate was filtered, well washed with water and dried *in vacuo* over sodium hydroxide. The product (1.7 g.) was dissolved in ten parts of hot methanol, an equal volume of warm water was added and the solution was clarified by centrifugation. The material which crystallized from the seeded supernatant solution was dried *in vacuo* over sodium hydroxide and recrystallized from petroleum ether (b.p. 60–70°) to give 1.3 g. of material (11.6%), m.p. 80–81°, undepressed on admixture with material prepared from the 1,2-*O*-isopropylidene-6-deoxy-6-nitro-D-glucose.

Tetra-*O*-acetyl-D-glucodialdohexose Tetraethyl Bis-mercaptal.—The mercaptal (7.41 g.) was acetylated by allowing it to stand overnight with a mixture of dry pyridine (50 ml.) and acetic anhydride (50 ml.). The excess acetic anhydride was decomposed by addition of a little ice, and the solution concentrated *in vacuo*. The sirupy residue was taken up in methylene chloride and washed successively with 1 *N* potassium carbonate, 1 *N* sulfuric acid and water and then dried (sodium sulfate). The solvent was removed at reduced pressure and the remaining sirup taken up in pentane (65 ml.) and seeded.[13] From the solution there crystallized 9.33 g. (88%) of the tetraacetate, m.p. 69.5–70.5°. A second recrystallization from pentane gave pure material, m.p. 70–71°, $[\alpha]^{24}\text{D}$ −13.5° (*c* 2, methanol).

Anal. Calcd. for $C_{22}H_{38}O_8S_4$ (558.8): C, 47.29; H, 6.85; S, 22.95. Found: C, 47.30; H, 6.59; S, 23.21.

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[12] Analyses by Dr. A. Elek, Los Angeles, Calif.

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