sorbitol. This fact is a proof that the diacetal, known previously only as 2,3,4,5-dimethylene-D-sorbitol,[2] is 2,4:3,5-dimethylene-D-sorbitol. It also indicates that in the D-sorbitol methylene acetals the acetal linkage which is formed through the secondary hydroxyl group at position 3 is more stable to acetolysis than that at position 5, an inference which allows assignment of the structure of 1,6-dibenzoyl-3-acetoxymethyl-5-acetyl-2,4-methylene-D-sorbitol to the acetolysis product of 1,6-dibenzoyl-2,4:3,5-dimethylene-D-sorbitol.

The 2,4:3,5-dimethylene-D-sorbitol has been converted to 1,6-didesoxy-2,4:3,5-dimethylene-D-sorbitol by known reactions.

BETHESDA, MARYLAND RECEIVED AUGUST 19, 1944

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Selective Exchange of Tosyloxy for Iodo Groups in Certain Cyclic Acetals of 1,6-Ditosyl-D-sorbitol. 2,4:3,5-Dimethylene-D-epirhamnitol

BY A. T. NESS, RAYMOND M. HANN AND C. S. HUDSON

In 1932 Oldham and Rutherford[1] heated methyl 2,3-diacetyl-4,6-ditosyl-β-D-glucoside and methyl 2,3,4,6-tetratosyl-β-D-glucoside with sodium iodide in acetone solution at 100° for two hours. They found that under these experimental conditions the tosyloxy group ($(p)\mathrm{CH_3C_6H_4SO_2O}$— = TsO—) which was attached to the primary carbon atom at position 6 was *the only one to be replaced by iodine*, according to the equation $\mathrm{H_2\overset{|}{C}—OSO_2C_6H_4CH_3}(p) + \mathrm{NaI} = \mathrm{H_2\overset{|}{C}—I} + \mathrm{NaOSO_2C_6H_4CH_3}(p)$. Although the discoverers of the selectivity of this reaction proposed it, cautiously and specifically, as "a method for the identification and estimation of the 6-hydroxyl group in glucose," it has subsequently been designated under the name of the "Oldham–Rutherford rule" as offering the possibility of distinguishing primary from secondary hydroxyl groups in the carbohydrate series. The extent of its applicability can of course only be determined by experiments on various types of carbohydrate derivatives. It has been pointed out,[2] for instance, that the presence of tosyl groups on both a primary and an adjacent secondary hydroxyl group, as in 5,6-ditosyl-1,3:2,4-dibenzylidene-D-sorbitol and certain completely tosylated polyhydroxy alcohols (tetratosyl erythritol and tritosyl glycerol), can lead to the formation of an unsaturated compound rather than the iodo derivative. Such types of structure were not present in the substances which Oldham and Rutherford studied. Recently, in connection with studies on the acetals of the sugar alcohols, we have encountered an interesting two-stage variation of the reaction, which appears to be based on the influence of the D-sorbitol configuration; the present communication reports the anomalous results which were obtained when several 1,6-ditosylated derivatives of D-sorbitol were subjected to iodination under the usual conditions of the Oldham–Rutherford technique.

Further study of the recently described 2,4-methylene-D-sorbitol[3] has shown that, upon tosylation in pyridine solution with about two molecular equivalents of *p*-toluenesulfonyl chloride, it yields the expected 1,6-ditosyl-2,4-methylene-D-sorbitol (I). Attempts to convert this ditosyl derivative to a 1,6-didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol (III) by heating it at 100° for two hours in an acetone solution with sodium iodide (the usual conditions employed by Oldham and Rutherford[1]) resulted in the formation of a product (m. p. 195–196°; $[\alpha]^{20}\mathrm{D}$ −13.4° in acetone), the analysis of which indicated that it is a desoxy-iodo-tosyl-2,4-methylene-D-sorbitol.[4] Confirmation of this composition was obtained when it was found that this product as well as the 1,6-ditosyl-2,4-methylene-D-sorbitol (I) could be partially converted to the 1,6-didesoxy-1,6-dihalogenated acetal (III) by extending the reaction period to five hours. As pointed out by Oldham and Rutherford, such prolongation of the time of heating may lead to side reactions of undetermined nature; in the present experiments some free iodine was formed and the yield of 1,6-didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol was low, namely, 19% from the ditosylate (I) and 31% from the desoxy-iodo-tosyl-2,4-methylene-D-sorbitol. In reviewing the factors which might be responsible for this low yield, the possibility of anhydro formation was considered and it was recalled that 2,3,7-tritosyl-D-gluco-D-*gulo*-heptosan $<1,5>\beta<1,6>$ upon being heated in acetonylacetone solution with sodium iodide, formed 2,3-ditosyl-4,7-anhydro-D-gluco-D-*gulo*-heptosan $<1,5>\beta<1,6>$,[5] while similar treatment of its 4-

---

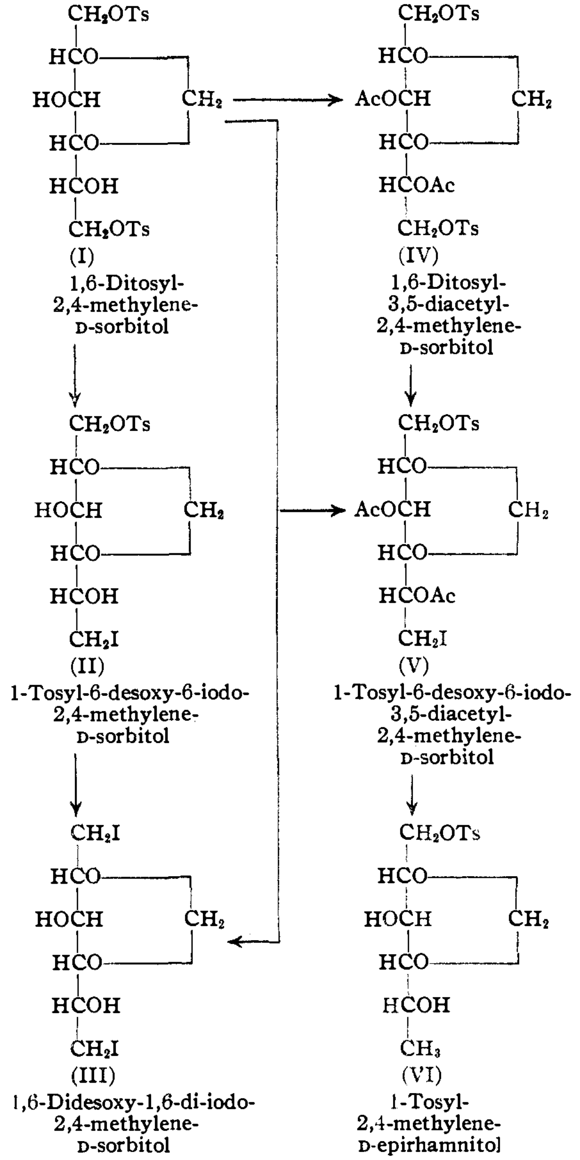
(1) Oldham and Rutherford, THIS JOURNAL, **54**, 366 (1932).

(2) Tipson and Cretcher, *J. Org. Chem.*, **8**, 95 (1943); Hann, Ness and Hudson, THIS JOURNAL, **66**, 73 (1944).

(3) Ness, Hann and Hudson, *ibid.*, **66**, 665 (1944).

(4) A similar partial iodination has been observed by Dr. John K. Wolfe of this Laboratory. 1,6-Ditosyl-2,4:3,5-dibenzylidene-D-sorbitol (m. p. 123–124°; $[\alpha]^{20}\mathrm{D}$ +7.8° in chloroform) yielded a desoxy-iodo-tosyl-2,4:3,5-dibenzylidene-D-sorbitol melting at 143–144° and rotating $[\alpha]^{20}\mathrm{D}$ +17.3° in chloroform, when subjected to iodination by the usual Oldham–Rutherford procedure. The definitive structure of this desoxy-iodo-tosyl-dibenzylidene-D-sorbitol is under investigation.

(5) Montgomery, Richtmyer and Hudson, THIS JOURNAL, **65**, 1848 (1943).


(I) 1,6-Ditosyl-2,4-methylene-D-sorbitol

(IV) 1,6-Ditosyl-3,5-diacetyl-2,4-methylene-D-sorbitol

(II) 1-Tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol

(V) 1-Tosyl-6-desoxy-6-iodo-3,5-diacetyl-2,4-methylene-D-sorbitol

(III) 1,6-Didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol

(VI) 1-Tosyl-2,4-methylene-D-epirhamnitol

acetyl derivative yielded 83% of the corresponding 7-iodohydrin, because the blocking of the secondary hydroxyl at position four by the acetyl group prevented the formation of the 4,7-anhydro ring. The experimental findings in this case suggested that the substitution of halogen might be expected to proceed more readily in 1,6-ditosyl-3,5-diacetyl-2,4-methylene-D-sorbitol (IV) than in 1,6-ditosyl-2,4-methylene-D-sorbitol (I). This surmise proved to be correct insofar as the production of undesirable by-products was concerned, but the main product, which was formed in a yield of about 80%, was not a di-iodinated compound, but a desoxy-iodo-tosyl-3,5-diacetyl-2,4-methylene-D-sorbitol (m. p. 134–135°; $[\alpha]^{20}D$ −31.5° in chloroform). Although a determination of the position of the iodo group in this diacetate was not possible at this stage of the research, evidence that it occupied the same relative position, one or six, as it did in the previously mentioned desoxy-iodo-tosyl-2,4-methylene-D-sorbitol, (m. p. 195–196°) was readily obtained since the acetylation of the latter compound gave a quantitative yield of the same diacetate. While it is well known that the reaction conditions necessary to effect substitution of the tosyloxy group attached to a primary hydroxyl group may vary with the structure of the tosylated compound,[6] the uniform behavior of the D-sorbitol derivatives in giving good yields of a single relatively pure monohalogenated derivative rather than a mixture suggested that the configuration of D-sorbitol is particularly favorable to halogenation of only one of the two tosylated primary hydroxyl groups. In seeking an answer to the question as to whether the iodination had occurred at position one or six, the desoxy-iodo-tosyl-3,5-diacetyl-2,4-methylene-D-sorbitol was reduced with hydrogen and Raney nickel in an alcoholic solution containing slightly over three molecular equivalents of alkali; the monotosyl-desoxy-2,4-methylene-hexitol which was formed is limited in structure to 1-tosyl-3,5-methylene-L-gulomethylitol or 1-tosyl-2,4-methylene-D-epirhamnitol (VI). A definitive proof that it possesses the latter structure was readily obtained; it was found that the preferential monotosylation of the recently described 2,4-methylene-D-epirhamnitol (XI)[7] yields a crystalline tosyl derivative which is identical with the above monotosyl-desoxy-2,4-methylene-hexitol; the compound is therefore 1-tosyl-2,4-methylene-D-epirhamnitol (VI) and its immediate precursor is the 3,5-diacetate (V) of 1-tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol (II).

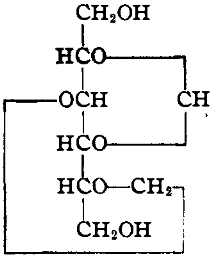
Further evidence that the iodination of a 1,6-ditosylated-D-sorbitol derivative occurs more readily at position six was obtained through a study of the 1,6-ditosyl-2,4:3,5-dimethylene-D-sorbitol (VIII) which is obtained from the 2,4:3,5-dimethylene-D-sorbitol (VII) that is described in the accompanying communication. This 1,6-ditosylate, upon iodination in accordance with the Oldham–Rutherford conditions, yields a desoxy-iodo-tosyl-2,4:3,5-dimethylene-D-sorbitol

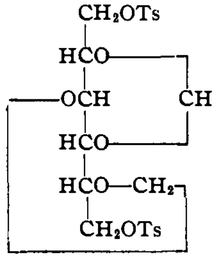
---

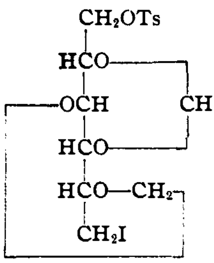
[6] Freudenberg and Raschig [*Ber.*, **60**, 1634 (1927)] found that a reaction period of thirty-six hours at 125° apparently was necessary to convert 6-tosyl-di-isopropylidene-D-galactose to the corresponding 6-iodohydrin. Levene and Raymond [*J. Biol. Chem.*, **102**, 317 (1933)] have shown that replacement of the tosyloxy group in 5-tosylated derivatives of 1,2-isopropylidene-xylose is not complete after heating six hours at 100°. The stability of the tosyloxy group in 1,4-ditosyl-2,3-isopropylidene-D-xylulose and in 1-tosyl-β-diacetone-D-fructose to replacement by iodine has been ascribed by Levene and Raymond [*J. Biol. Chem.*, **120**, 609 (1937)] to the influence of the adjacent keto group. Evidence supporting this inference has been obtained in the case of two other ketoses: Müller and Reichstein [*Helv. Chim. Acta*, **21**, 263 (1938)] have shown that only the 6-tosyloxy group of 1,6-ditosyl-2,3-isopropylidene-L-sorbose is replaced by iodine when the compound is heated with sodium iodide and acetone for twenty-four hours at 100°, and Morgan and Reichstein [*ibid.*, **21**, 1028 (1938)] have obtained similar results with 1,6-ditosyl-2,3-isopropylidene-D-fructose; replacement of the 1-tosyloxy group of these ketals could be effected by heating the solutions at 125–130° from thirty-six to forty-eight hours.

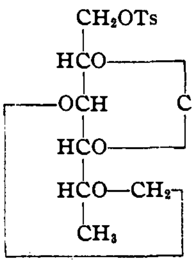
[7] Ness, Hann and Hudson, THIS JOURNAL, **66**, 1235 (1944).

which is reducible to a desoxy-tosyl-2,4:3,5-dimethylene-D-sorbitol; this diacetal is identical with the compound that is formed by the condensation of 1-tosyl-2,4-methylene-D-epirhamnitol (VI) and formaldehyde, and it is therefore 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol (X) and the halogenated diacetal from which it was formed must be 1-tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol (IX).

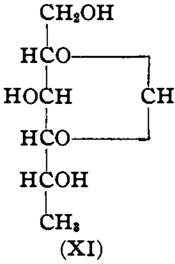

(VII)
2,4:3,5-Dimethylene-D-sorbitol

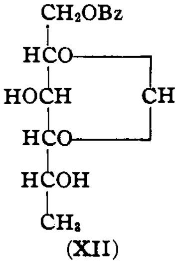

(VIII)
1,6-Ditosyl-2,4:3,5-dimethylene-D-sorbitol

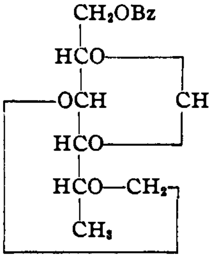

(IX)
1-Tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol

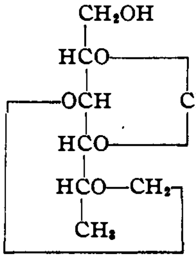

(X)
1-Tosyl-2,4:3,5-dimethylene-D-epirhamnitol

The ease of formation of derivatives of D-epirhamnitol by the reduction of these readily obtainable 6-desoxy-6-iodo compounds of D-sorbitol offers a ready source for these previously difficultly accessible substances. The isolation of 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol (X) as one of the products in the research is of particular importance since its reductive detosylation forms the new 2,4:3,5-dimethylene-D-epirhamnitol (XIV), an isomer of the recently discovered 1,3:2,4-dimethylene-D-epirhamnitol.[7] A confirmation of the structure assigned to the new diacetal was obtained as follows: the known 2,4-methylene-D-epirhamnitol (XI) was preferentially monobenzoylated at position one to yield 1-benzoyl-2,4-methylene-D-epirhamnitol (XII); this acetal was condensed with formaldehyde and the reaction product, 1-benzoyl-2,4:3,5-dimethylene-D-epirhamnitol (XIII) proved to be identical with the compound formed by the benzoylation of 2,4:3,5-dimethylene-D-epirhamnitol (XIV).


(XI)
2,4-Methylene-D-epirhamnitol


(XII)
1-Benzoyl-2,4-methylene-D-epirhamnitol


(XIII)
1-Benzoyl-2,4:3,5-dimethylene-D-epirhamnitol


(XIV)
2,4:3,5-Dimethylene-D-epirhamnitol

We express our appreciation to Mr. Harry W. Diehl for assistance in the preparation of some of the acetal derivatives.

Experimental

1,6-Ditosyl-2,4-methylene-D-sorbitol (I).—To an ice-cold solution of 1.0 g. of 2,4-methylene-D-sorbitol[8] in 10 cc. of pyridine, 2.0 g. of *p*-toluenesulfonyl chloride was added and the solution was allowed to stand at room temperature (25°) for four hours. The crystalline precipitate (1.8 g.; 69%), which deposited upon pouring the reaction mixture into 400 cc. of water, was recrystallized from 15 parts of alcohol as tufts of needles which melted at 129–130°; a chloroform solution (*c*, 1.03) of the substance showed no detectable rotation, but in pyridine (*c*, 0.99) it rotated $[\alpha]^{20}\text{D}$ −5.1°; it is soluble in acetone, ethyl acetate and dioxane and nearly insoluble in water.

Anal. Calcd. for $C_{21}H_{26}O_{10}S_2$: C, 50.19; H, 5.22; S, 12.76. Found: C, 50.14; H, 5.20; S, 12.63.

1-Tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol (II).—A solution of 1.0 g. of 1,6-ditosyl-2,4-methylene-D-sorbitol and 1.0 g. of sodium iodide in 50 cc. of acetone was heated in a pressure bottle at 100° for two hours. The precipitated sodium *p*-toluenesulfonate (0.40 g.; 0.38 g. is one molecular equivalent) was separated by filtration and the acetone was evaporated from the filtrate by an air current; the residue was extracted with 50 cc. of cold water and the insoluble reaction product (0.8 g.; m. p. 184–186°; 89%) was recrystallized twice from 40 parts of alcohol and gave 0.5 g. (56%) of 1-tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol which formed fine needles melting at 195–196° (decomposition) and rotating $[\alpha]^{20}\text{D}$ −13.4° in acetone (*c*, 1.18). The compound is readily soluble in cold pyridine and acetone and in warm alcohol, and nearly insoluble in cold alcohol, chloroform and water. Upon acetylation in pyridine solution by acetic anhydride the acetal gave a quantitative yield of an acetate which is identical with 1-tosyl-6-desoxy-6-iodo-3,5-diacetyl-2,4-methylene-D-sorbitol that is described later in the experimental section; since the latter substance, as will be shown, can be converted to an epirhamnitol derivative (VI) it is evident that the tosyl-desoxy-iodo-methylene-D-sorbitol from which it is derived must have its tosyl and iodo groups present at positions 1 and 6, respectively.

Anal. Calcd. for $C_{14}H_{19}O_7SI$: C, 36.69; H, 4.18; S, 7.00; I, 27.70. Found: C, 36.82; H, 4.27; S, 6.87; I, 27.59.

1,6-Didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol (III) from **1-Tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol**

(II).—A solution of 1.4 g. of 1-tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol and 1.4 g. of sodium iodide in 60 cc. of acetone was heated in a pressure bottle at 100° for five hours; the cooled mixture was filtered to separate the crystalline sodium tosylate (0.3 g.; 50%) and the filtrate, which was colored red by free iodine, was concentrated to dryness by an air current; the crystalline residue was extracted with a dilute aqueous solution of sodium thiosulfate and the insoluble portion (0.8 g.; 62%) upon recrystallization from 50 parts of acetone gave 0.4 g. (31%) of pure 1,6-didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol. The compound crystallized as fine needles which showed a rotation $[\alpha]^{20}\mathrm{D}$ −16.0° in pyridine (*c*, 0.98); upon heating in a capillary tube the compound decomposed with liberation of free iodine; the decomposition point of the pure compound, varying from 208–212°, depended on the rate of heating; the substance is nearly insoluble in cold acetone, chloroform and alcohol, but can be recrystallized from hot acetone or a 1:1 alcohol–dioxane mixture.

Anal. Calcd. for $C_7H_{12}O_4I_2$: C, 20.31; H, 2.92; I, 61.31. Found: C, 20.41; H, 2.87; I, 61.06.

1,6-Didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol (III) from 1,6-Ditosyl-2,4-methylene-D-sorbitol (I).—A solution of 2.0 g. of 1,6-ditosyl-2,4-methylene-D-sorbitol and 2.0 g. of sodium iodide in 50 cc. of acetone was heated in a pressure bottle at 100° for five hours; the precipitated sodium *p*-toluenesulfonate (1.3 g.; 87%) was separated by filtration and the filtrate was concentrated to dryness by an air current. The crystalline residue, which contained free iodine, was extracted with 50 cc. of water containing 2.0 g. of sodium thiosulfate and the insoluble portion (1.0 g.; m. p. 192–193°; 62%), which doubtless contained unchanged 1-tosyl-6-desoxy-6-iodo-2,4-methylene-D-sorbitol, was recrystallized from 25 parts of 1:1 alcohol–dioxane; the yield of pure 1,6-didesoxy-1,6-di-iodo-2,4-methylene-D-sorbitol was 0.3 g. (19%).

1,6-Ditosyl-3,5-diacetyl-2,4-methylene-D-sorbitol (IV).—A solution of 5.0 g. of 1,6-ditosyl-2,4-methylene-D-sorbitol (I) in a mixture of 25 cc. of pyridine and 25 cc. of acetic anhydride was allowed to stand for forty-eight hours at 25° and then poured into 800 cc. of ice-cold water; the gummy precipitate which deposited gradually crystallized and upon recrystallization from 15 parts of alcohol it formed needles which melted at 130–131° and rotated $[\alpha]^{20}\mathrm{D}$ −4.8° in chloroform (*c*, 1.02). The compound is readily soluble in acetone, ethyl acetate, benzene and pyridine, and nearly insoluble in water.

Anal. Calcd. for $C_{25}H_{30}O_{12}S_2$: C, 51.18; H, 5.16; S, 10.93. Found: C, 51.26; H, 5.19; S, 10.82.

1-Tosyl-6-desoxy-6-iodo-3,5-diacetyl-2,4-methylene-D-sorbitol (V).—A solution of 1.0 g. of 1,6-ditosyl-3,5-diacetyl-2,4-methylene-D-sorbitol (IV) and 1.0 g. of sodium iodide in 25 cc. of acetone was heated in a pressure bottle at 100° for two hours; the acetone was evaporated by an air current and the sirupy residue crystallized upon the addition of water. The crude product (0.7 g.; 78%) was recrystallized from 12 parts of alcohol as needles which melted at 134–135° and rotated $[\alpha]^{20}\mathrm{D}$ +31.5° in chloroform (*c*, 0.96); the substance is readily soluble in acetone, ethyl acetate and pyridine, and nearly insoluble in water. A slightly better yield (84%) of product was obtained by heating equal amounts of the 1,6-ditosyl-3,5-diacetyl-2,4-methylene-D-sorbitol and sodium iodide with 8 parts of acetonyl acetone at 80° for five hours.

Anal. Calcd. for $C_{18}H_{23}O_9SI$: C, 39.86; H, 4.27; S, 5.91; I, 23.40. Found: C, 39.99; H, 4.12; S, 5.94; I, 23.28.

1-Tosyl-6-desoxy-2,4-methylene-D-sorbitol (VI) from 1-Tosyl-6-desoxy-6-iodo-3,5-diacetyl-2,4-methylene-D-sorbitol (V).—A solution of 1.0 g. of 1-tosyl-6-desoxy-6-iodo-3,5-diacetyl-2,4-methylene-D-sorbitol in a mixture of 50 cc. of alcohol and 6.1 cc. of *N* sodium hydroxide (3.3 molecular equivalents) was agitated with hydrogen and Raney nickel under slight positive pressure; in one hundred five minutes, 76 cc. of hydrogen (measured at 26° and 754 mm.) was taken up; since the expected consumption under these conditions was 45.6 cc. it seemed probable that some side reaction (formation of an anhydro or unsaturated derivative) of undetermined nature occurred simultaneously with the reduction. The catalyst was removed by filtration and the filtrate was extracted with chloroform; the extract was concentrated *in vacuo* to dryness and the crystalline residue so obtained was recrystallized from 15 parts of alcohol. The yield was 0.17 g. (28%) of 1-tosyl-6-desoxy-2,4-methylene-D-sorbitol (VI) which melted at 147–148° and rotated $[\alpha]^{20}\mathrm{D}$ −3.7° in chloroform (*c*, 0.84); the compound did not depress the melting point of authentic 1-tosyl-2,4-methylene-D-epirhamnitol obtained by the tosylation of 2,4-methylene-D-epirhamnitol as described in the following paragraph.

1-Tosyl-2,4-methylene-D-epirhamnitol (VI) from 2,4-Methylene-D-epirhamnitol (XI).—A solution of 2.4 g. (1.1 molecular equivalents) of *p*-toluenesulfonyl chloride in 10 cc. of pyridine was added dropwise to a vigorously stirred ice-cold solution of 2.0 g. of 2,4-methylene-D-epirhamnitol[7] in 15 cc. of pyridine. The reaction mixture was allowed to stand at 25° for four hours and then poured into 500 cc. of ice water and held at 5° for eighteen hours. The precipitated reaction product (2.9 g.; 78%) was recrystallized from 10 parts of 70% alcohol; it formed prismatic needles which melted at 147–148° and rotated $[\alpha]^{20}\mathrm{D}$ −3.8° in chloroform (*c*, 0.82). The compound is readily soluble in pyridine, acetone and ethyl acetate, and nearly insoluble in water.

Anal. Calcd. for $C_{14}H_{20}O_7S$: C, 50.59; H, 6.07; S, 9.65. Found: C, 50.68; H, 6.09; S, 9.56.

1-Tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol (IX) from 1,6-Ditosyl-2,4:3,5-dimethylene-D-sorbitol (VIII).—A solution of 2.0 g. of 1,6-ditosyl-2,4:3,5-dimethylene-D-sorbitol (VIII)[8] and 2.0 g. (3.4 molecular equivalents) of sodium iodide in 25 cc. of acetone was heated in a pressure bottle at 100° for two hours. The cooled reaction mixture, which contained crystalline sodium *p*-toluenesulfonate, was poured into cold water and the precipitated product (1.8 g.; quantitative) was recrystallized from 25 parts of alcohol. It formed glistening plates which melted at 128–129° and rotated $[\alpha]^{20}\mathrm{D}$ −8.5° in chloroform (*c*, 0.91). Analysis showed it to be a tosyl-desoxy-iodo-dimethylene-D-sorbitol. Proof that it is 1-tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol was obtained by its reduction as described later, to a 1-tosyl-6-desoxy-2,4:3,5-dimethylene-D-sorbitol which is identical with the 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol that is formed by the condensation of 1-tosyl-2,4-methylene-D-epirhamnitol (VI) and formaldehyde.

Anal. Calcd. for $C_{15}H_{19}O_7SI$: C, 38.31; H, 4.07; S, 6.82; I, 26.99. Found: C, 38.49; H, 4.17; S, 6.77; I, 27.14.

1,6-Didesoxy-1,6-di-iodo-2,4:3,5-dimethylene-D-sorbitol from 1-Tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol.—A mixture of 4.0 g. of 1-tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol, 3.8 g. (3 molecular equivalents) of sodium iodide and 40 cc. of acetic anhydride was refluxed for two hours. The cooled reaction mixture was poured into ice water and the suspension was agitated by an air current; as the conversion of the anhydride to acetic acid progressed the didesoxy-di-iodo-dimethylene-D-sorbitol crystallized. The yield was 3.3 g. (92%). The compound was recrystallized from 20 parts of alcohol in the form of needles which melted at 151–152° and rotated $[\alpha]^{20}\mathrm{D}$ +17.0° in chloroform (*c*, 1.23); it is readily soluble in ethyl acetate, acetone, pyridine and hot methyl and ethyl alcohols, sparingly soluble in cold methyl and ethyl alcohols and nearly insoluble in water.

Anal. Calcd. for $C_8H_{12}O_4I_2$: C, 22.55; H, 2.84; I, 59.58. Found: C, 22.72; H, 2.92; I, 59.62.

1-Tosyl-2,4:3,5-dimethylene-D-epirhamnitol (X) from 1-Tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol (IX).—To a solution of 2.0 g. of 1-tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol (IX) in 225 cc. of methyl alcohol, 2.0 g. of Raney nickel and 0.4 g. of potas-

---

[8] Hann, Wolfe and Hudson, This Journal, 66, 1898 (1944).

sium hydroxide was added and the mixture was agitated in a glass bottle under a slight positive pressure of hydrogen. In one hour about 100 cc. of hydrogen (calculated, 95.3 cc. S. T. P.) was taken up and no further absorption occurred in an additional thirty minutes. The catalyst was separated by filtration and the filtrate was saturated with carbon dioxide and then concentrated *in vacuo* to dryness; the dry residue was extracted with 15 cc. of hot alcohol and the extract upon dilution with 10 cc. of water deposited 0.45 g. (31%) of needles which melted at 120–121° and rotated $[\alpha]^{20}\mathrm{D}$ +5.3° in chloroform (*c*, 0.81). A mixed melting point with authentic 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol (m. p. 120–121°; $[\alpha]^{20}\mathrm{D}$ +5.0° in chloroform) prepared by the condensation of formaldehyde with 1-tosyl-2,4-methylene-D-epirhamnitol, as described in the following paragraph, showed no depression. Our first preparation of this compound (April, 1942) by the reduction of 1-tosyl-6-desoxy-6-iodo-dimethylene-D-sorbitol gave a melting point of 88–89° and analyses agreeing with 1-tosyl-6-desoxy-dimethylene-D-sorbitol. In April, 1944, the melting point of this sample of the compound was found to be 120–121° and reanalysis confirmed its composition. The form melting at 88–89° is evidently an unstable dimorph.

Anal. Calcd. for $C_{15}H_{20}O_7S$: C, 52.31; H, 5.85; S, 9.31. Found: C, 52.35; H, 5.91; S, 9.09.

1-Tosyl-2,4:3,5-dimethylene-D-epirhamnitol (X) from 1-Tosyl-2,4-methylene-D-epirhamnitol (VI).—A solution of 1.0 g. of 1-tosyl-2,4-methylene-D-epirhamnitol in a mixture of 3 cc. of dioxane and 2 cc. of 37% aqueous formaldehyde solution was cooled to 0° and saturated with dry gaseous hydrochloric acid. The reaction mixture was held at 5° for twenty-four hours and then poured into 200 cc. of ice-cold water; the gummy precipitate did not crystallize and accordingly the suspension was extracted with three 50-cc. portions of chloroform; the extract was washed with 5% sodium bicarbonate solution and water and concentrated *in vacuo* to a sirupy residue (1.1 g.) which was crystallized from 15 cc. of methanol. The yield was 0.7 g. (70%) of 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol, identical with the 1-tosyl-6-desoxy-2,4:3,5-dimethylene-D-sorbitol obtained by the reduction of 1-tosyl-6-desoxy-6-iodo-2,4:3,5-dimethylene-D-sorbitol in alkaline solution by hydrogen and Raney nickel.

2,4:3,5-Dimethylene-D-epirhamnitol (XIV) from 1-Tosyl-2,4:3,5-dimethylene-D-epirhamnitol (X).—A solution of 2.0 g. of 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol in 150 cc. of 80% methyl alcohol was gently shaken with 50 g. of 2.5% sodium amalgam for eighteen hours at 25°. Following separation of the mercury, the solution was nearly neutralized to phenolphthalein by *N* hydrochloric acid and it was then saturated with carbon dioxide and concentrated *in vacuo* to dryness. The dry crystalline residue was extracted with chloroform and, upon evaporation, the extract deposited 1.1 g. (quantitative) of needles melting at 126–128°. One recrystallization from 10 parts of a 1:4 alcohol-benzene mixture yielded 0.7 g. (64%) of pure 2,4:3,5-dimethylene-D-epirhamnitol melting at 127–128° and rotating $[\alpha]^{20}\mathrm{D}$ +30.0° in chloroform (*c*, 1.13) and +40.2° in water (*c*, 1.36). The compound is readily soluble in alcohol, water, acetone and ethyl acetate, and nearly insoluble in benzene and petroleum ether.

Anal. Calcd. for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.48; H, 7.47.

1-Benzoyl-2,4-methylene-D-epirhamnitol (XII) from 2,4-Methylene-D-epirhamnitol (XI).—A solution of 2.0 g. of 2,4-methylene-D-epirhamnitol in 30 cc. of pyridine was cooled to 0° and 1.3 cc. of benzoyl chloride (one molecular equivalent) was added dropwise, with shaking; after being allowed to stand for three hours at 25° the mixture was poured into 300 cc. of ice-cold water and the aqueous solution was extracted with three 50-cc. portions of chloroform; the washed extract was concentrated *in vacuo* to dryness and the crystalline residue was recrystallized from 5 parts of alcohol. The 1-benzoyl-2,4-methylene-D-epirhamnitol, which crystallized in the form of cottony needles, melted at 140–141° and rotated $[\alpha]^{20}\mathrm{D}$ +12.0° in chloroform (*c*, 1.35); the yield was 1.4 g. (44%).

Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43; C_6H_5-CO, 37.2. Found: C, 59.62; H, 6.34; C_6H_5CO, 37.1.

1-Benzoyl-2,4:3,5-dimethylene-D-epirhamnitol (XIII) from 1-Benzoyl-2,4-methylene-D-epirhamnitol (XII).—An ice-cold solution of 0.6 g. of 1-benzoyl-2,4-methylene-D-epirhamnitol (XII) in a mixture of 5 cc. of dioxane and 2 cc. of an aqueous 37% formaldehyde solution was saturated with dry gaseous hydrochloric acid and the reaction mixture was allowed to stand at 5° for forty hours; the solution was then poured into 200 cc. of ice-cold water and the acid was just neutralized to phenolphthalein by the addition of *N* sodium hydroxide; the sirup which precipitated soon crystallized and the reaction product (0.4 g.; m. p. 115–117°; 67%) was recrystallized from 8 parts of alcohol and gave 0.3 g. (50%) of 1-benzoyl-2,4:3,5-dimethylene-D-epirhamnitol. The substance crystallizes in the form of narrow elongated plates which melt at 117–118° and rotate $[\alpha]^{20}\mathrm{D}$ +29.6° in chloroform (*c*, 1.12); it is soluble in acetone, ethyl acetate and pyridine and nearly insoluble in water. A mixed melting point with 1-benzoyl-2,4:3,5-dimethylene-D-epirhamnitol, m. p. 117–118°, prepared by the benzoylation of 2,4:3,5-dimethylene-D-epirhamnitol (XIV), showed no depression.

Anal. Calcd. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.16; C_6H_5CO, 35.7. Found: C, 61.32; H, 6.28; C_6H_5CO, 35.4.

1-Benzoyl-2,4:3,5-dimethylene-D-epirhamnitol (XIII) from 2,4:3,5-Dimethylene-D-epirhamnitol (XIV).—To a stirred ice-cold solution of 0.5 g. of 2,4:3,5-dimethylene-D-epirhamnitol (XIV) in 10 cc. of pyridine 1.0 cc. (3.3 molecular equivalents) of benzoyl chloride was added dropwise and the solution was allowed to stand at 25° for forty hours; the precipitate (0.8 g.; quantitative) which formed on pouring the mixture into 100 cc. of ice-cold water was separated by filtration and recrystallized from 7 parts of alcohol; the yield of recrystallized product was 0.4 g. (50%). The compound melted at 117–118° and a mixed melting point determination with the 1-benzoyl-2,4:3,5-dimethylene-D-epirhamnitol, prepared from 1-benzoyl-2,4-methylene-D-epirhamnitol (XII) and formaldehyde, showed no depression of this value.

Summary

It has been shown that the 2,4-methylene, 2,4-methylene-3,5-diacetyl and the 2,4:3,5-dimethylene-acetals of 1,6-ditosyl-D-sorbitol form tosyl-desoxy-iodo acetals when they are heated with sodium iodide in acetone solution at 100° for two hours.

The substitution of iodine has been shown to occur at position six since the catalytic reductions of the tosyl-desoxy-halogenated D-sorbitol acetals yield 1-tosyl methylene acetals of D-epirhamnitol.

A new diacetal of D-epirhamnitol, namely, 2,4:3,5-dimethylene-D-epirhamnitol, has been prepared by the reductive detosylation of 1-tosyl-2,4:3,5-dimethylene-D-epirhamnitol.

BETHESDA, MARYLAND RECEIVED AUGUST 19, 1944