[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

O-Methylene and Other Derivatives of D-Arabitol (Synonym, D-Lyxitol), 1-Deoxy-D-arabitol and 1-Deoxy-D-lyxitol[1]

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RECEIVED JUNE 11, 1954

The reaction of aqueous formaldehyde upon D-arabitol in the presence of concentrated hydrochloric acid has led to the isolation of 1,3-*O*-methylene-D-arabitol, 1,3:2,4-di-*O*-methylene-D-arabitol, and what is presumably bis-(1,3:2,4-di-*O*-methylene-5-D-arabityloxy)-methane. Evidence in proof of these formulations has been presented and the bearing of the results upon the rules for predicting favored ring structures in the *O*-methylene acetals of polyhydric alcohols has been discussed. Many new derivatives of 1,3-*O*-methylene-, 2,4-*O*-methylene-, 1,3:2,4-di-*O*-methylene-, 1-deoxy-, 5-deoxy-, 1,3-*O*-benzylidene- and 2,3-*O*-benzylidene-D-arabitol have been described.

The condensation of xylitol (a *meso* form) with formaldehyde has been described in an earlier publication from this Laboratory by Hann, Ness and Hudson.[2] They proved conclusively that the product, which was isolated in 91% yield, was 2,4:3,5-di-*O*-methylene-D,L-xylitol; because of the symmetry of the xylitol molecule, however, the name 1,3:2,4-di-*O*-methylene-D,L-xylitol[3] can be applied equally well. Ribitol, which is the other *meso* pentitol, also condenses with formaldehyde to a di-*O*-methylene derivative. That compound, first described by Schulz and Tollens,[4] was proved by Hann and Hudson[5] to be 1,3:2,4-di-*O*-methylene-D,L-ribitol (synonym, 2,4:3,5-di-*O*-methylene-D,L-ribitol). Thus, both xylitol and ribitol condense with formaldehyde to yield positionally identical di-*O*-methylene derivatives. The methylenation of ribitol, in contrast to that of xylitol, afforded only 18% of the di-*O*-methylene compound under the experimental conditions used by Hann and Hudson[5]; the principal product, isolated in 63% yield, was a mono-*O*-methylene compound whose structure they proved to be 2,4-*O*-methyleneribitol (a *meso* form).

In order to complete the study of the *O*-methylene derivatives of the pentitols, it became necessary to examine the behavior of formaldehyde toward one of the optically active arabitols (since D-arabitol = D-lyxitol and L-arabitol = L-lyxitol). To this end, D-arabitol was condensed with 37% aqueous formaldehyde in the presence of concentrated hydrochloric acid.[6] When the reaction was carried out at room temperature, the product that usually was isolated agreed in composition and molecular weight with that of a bis-(di-*O*-methylene-D-arabityloxy)-methane (m.p. 138–139°, $[\alpha]^{20}D$ +38.5° in water). This compound appears to have been formed by the condensation of two molecules of a di-*O*-methylene-D-arabitol, each through its free hydroxyl group, with an additional molecule of formaldehyde; a similar product had been encountered earlier during the preparation of 1,3:2,4-di-*O*-methylene-L-epirhamnitol.[7] For reasons that will become apparent later in this discussion, attempts to obtain intermediate degradation products were unsuccessful and nothing further can be said regarding the detailed structure of the bis compound. Condensations at +5° yielded as high as 49% of a di-*O*-methylene-D-arabitol (m.p. 124–125°, $[\alpha]^{20}D$ +32.4° in water). Later, in a large-scale condensation carried out at 0°, in addition to the di-*O*-methylene compound there was isolated also a very small amount of a mono-*O*-methylene-D-arabitol (m.p. 86–87°, $[\alpha]^{20}D$ −19.9° in water).

The determination of structure of the mono-*O*-methylene compound was accomplished without any serious difficulty. It was oxidized readily by periodate, with the consumption of one molecular equivalent of oxidant and the liberation of one molecular equivalent of formaldehyde. Thus, one of the primary hydroxyl groups and the adjoining secondary hydroxyl group must be free, and the structure is limited accordingly to that of a 1,3-, 2,3-, 3,4- or 3,5-*O*-methylene-D-arabitol. Because D-arabitol is known to condense with benzaldehyde to form a 1,3-*O*-benzylidene derivative,[8] it might be expected that our mono-*O*-methylene derivative would be the analogous 1,3-*O*-methylene-D-arabitol (I). This hypothesis was confirmed by the following sequence of reactions. Tosylation of I yielded the 1,3-*O*-methylene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (II); its *O*-methylene group was cleaved by acetolysis and although neither the expected acetylated intermediate nor the 2,4,5-tri-*O*-tosyl compound obtained by a subsequent deacetylation would crystallize, the final sirup could be converted to the crystalline 1,3-*O*-benzylidene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (III); and this *O*-benzylidene compound was shown to be identi-

(1) Presented in part before the Division of Carbohydrate Chemistry at the Kansas City Meeting of the American Chemical Society, March 31, 1954. For the preceding paper in this series, see E. Zissis and N. K. Richtmyer, THIS JOURNAL, **75**, 129 (1953).

(2) R. M. Hann, A. T. Ness and C. S. Hudson, *ibid.*, **66**, 670 (1944); see also R. M. Hann, N. K. Richtmyer, H. W. Diehl and C. S. Hudson, *ibid.*, **72**, 561 (1950), for additional derivatives and related compounds.

(3) The optically active 1,3:2,4-di-*O*-methylene-D-xylitol (synonym, 2,4:3,5-di-*O*-methylene-L-xylitol) also is known. It was prepared indirectly from 1,3:2,4-di-*O*-methylene-D-glucitol by A. T. Ness, R. M. Hann and C. S. Hudson [THIS JOURNAL, **66**, 665 (1944)], and some of its derivatives were described later by those same authors [*ibid.*, **75**, 132 (1953)].

(4) M. Schulz and B. Tollens, *Ann.*, **289**, 20 (1896).

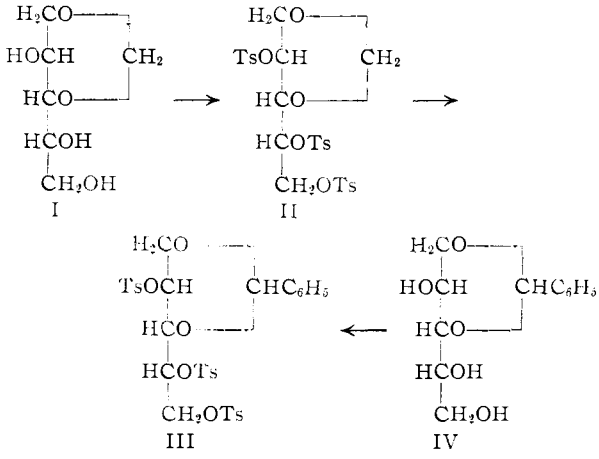
(5) R. M. Hann and C. S. Hudson, THIS JOURNAL, **66**, 1906 (1944).

(6) The experimental attack on this problem was begun in this Laboratory in 1944 by Dr. Raymond M. Hann. The first crystalline material was obtained only after one of the sirupy condensation mixtures had been kept in a desiccator for 4 years. Dr. Hann, with the assistance of Mr. Harry W. Diehl, then returned to the problem and succeeded in isolating and characterizing the first two condensation products, the first tosyl compound, and the first iodo compound that are described and marked with this footnote number in the Experimental section. Upon the death of Dr. Hann on April 30, 1949, the research was discontinued for several years before it was again resumed by the present authors.

(7) N. K. Richtmyer, L. C. Stewart and C. S. Hudson, THIS JOURNAL, **72**, 4934 (1950). In the Experimental section of that paper, page 4936, the 1,3:2,4-di-*O*-methylene-L-epirhamnitol was designated incorrectly as the 2,4:3,5-dimethylene derivative; *cf. ibid.*, **74**, 6313 (1952).

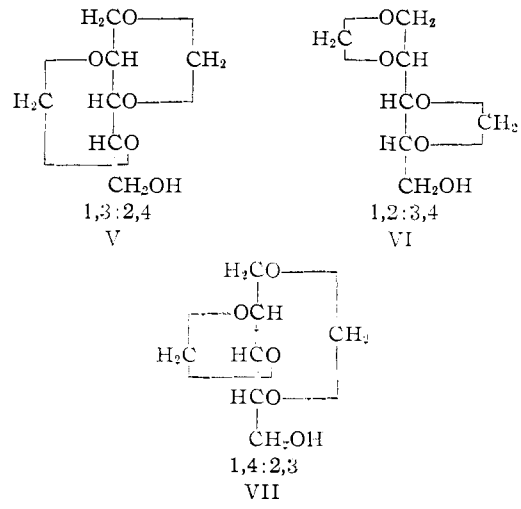
(8) W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **65**, 1663 (1943).

cal with the substance obtained by the direct tosylation of some of the 1,3-*O*-benzylidene-D-arabitol (IV) remaining from the earlier work of Haskins, Hann and Hudson[8] in this Laboratory.



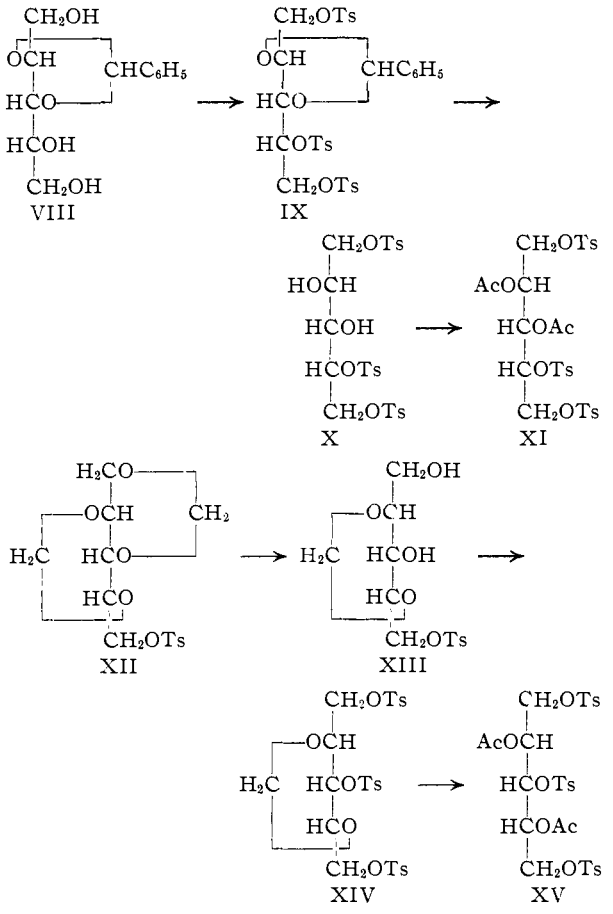
Determination of the structure of the di-*O*-methylene-D-arabitol began with its conversion to an *O*-tosyl derivative, reaction of the latter with sodium iodide, and reduction of the resulting iodo compound to a deoxydi-*O*-methylene-D-arabitol that was found to have a *C*-methyl group. Since there must have been one free primary hydroxyl group, the two *O*-methylene groups must therefore be located either at the 1,2,3,4- or the 2,3,4,5-positions on the D-arabitol chain. To distinguish between these two possibilities we prepared 1-deoxy-D-arabitol, recently described by Bollenback and Underkofler,[9] but attempts to condense it with formaldehyde in the presence of concentrated hydrochloric acid failed to produce any crystalline material. The 5-deoxy-D-arabitol (= 1-deoxy-D-lyxitol) was then prepared by reductive desulfurization with Raney nickel of the known D-lyxose diethyl mercaptal; methylenation of this 5-deoxy-D-arabitol afforded an 81% yield of the same deoxydi-*O*-methylene compound that had already been prepared from the di-*O*-methylene-D-arabitol whose structure we were attempting to elucidate. Therefore, the *O*-methylene groups in the di-*O*-methylene and the deoxydi-*O*-methylene compounds must be distributed among the 1,2,3,4- rather than the 2,3,4,5-positions of D-arabitol, and the possible formulas for the original di-*O*-methylene compound have been reduced to three, namely, V, VI and VII.

By analogy with xylitol and ribitol we might expect that a 1,3:2,4 combination of *O*-methylene groups (V) would have been introduced also into the D-arabitol molecule and that the procedure of limited acetolysis would cleave the 1,3-*O*-methylene group without seriously affecting the 2,4-*O*-methylene group. Our experiments, however, indicated that in the acetolysis of the 1,2,3,4-di-*O*-methylene-D-arabitol the two groups were attacked at nearly the same rate, so that no intermediate product or any derivative thereof could ever be isolated. With the 5-*O*-tosyl derivative of the di-*O*-methylene-D-arabitol, on the other hand, we were sometimes successful in obtaining, by acetolysis and subsequent deacetylation, small yields of a crystalline mono-*O*-methylene-5-*O*-tosyl derivative. The latter compound was not oxidizable by periodate, so that, with the 5-position of the D-arabitol molecule already occupied by a tosyl group, the product could be only the 1,3-, the 2,3- or the 2,4-*O*-methylene derivative. Since it cannot be either the 1,2- or the 3,4-*O*-methylene-5-*O*-tosyl-D-arabitol (both of which should be oxidizable by periodate), the parent compound could not have been the 1,2:3,4-di-*O*-methylene-D-arabitol and formula VI is thereby eliminated from further consideration.



Upon complete tosylation of the mono-*O*-methylene-5-*O*-tosyl-D-arabitol, an *O*-methylene-tri-*O*-tosyl-D-arabitol (m.p. 68–73°, $[\alpha]^{20}D$ +31.8° in chloroform) was obtained that was quite different from the 1,3-*O*-methylene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (II, m.p. 135–136°, $[\alpha]^{20}D$ −13.9°) whose structure had already been established. Hence, the *O*-methylene group in the mono-*O*-methylene-5-*O*-tosyl compound cannot be in the 1,3-position but can be only in the 2,3- or 2,4-position. To decide between these two possibilities we made use of some of the 2,3-*O*-benzylidene-D-arabitol (VIII) remaining from the earlier researches of Haskins, Hann and Hudson.[8] Its tosylation gave an amorphous 2,3-*O*-benzylidene-1,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (**IX**); removal of the *O*-benzylidene group by acid hydrolysis furnished the crystalline 1,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (**X**); and acetylation then yielded the crystalline 2,3-di-*O*-acetyl-1,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (**XI**, m.p. 83–84°). From our own *O*-methylene-tri-*O*-tosyl-D-arabitol (m.p. 68–73°), following an acetolysis experiment, we were fortunate to isolate a small amount of a different di-*O*-acetyl-tri-*O*-tosyl-D-arabitol (m.p. 138–140°). The last-named compound, since it cannot be the 2,3-di-*O*-acetyl derivative, must be the 2,4-di-*O*-acetyl derivative, and the *O*-methylene compound from which it was derived must have been 2,4-*O*-methylene-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (**XIV**). The original di-*O*-methylene compound, therefore, can only have been the 1,3:2,4-di-*O*-methylene-D-arabitol (V). This last sequence of reactions is shown in formulas XII to XV.

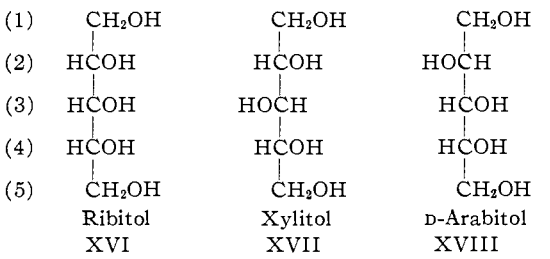
(9) C. N. Bollenback and L. A. Underkofler, THIS JOURNAL, **72**, 741 (1950).



Although this proof of structure of our original product as 1,3:2,4-di-*O*-methylene-D-arabitol (V) has been derived in part through a process of elimination rather than by a complete direct proof, we feel that the reasoning and conclusions are sound. Strong supporting evidence is available also from a comparison of the tri-*O*-tosyl compounds represented by formulas II and XIV. The former—authentic 1,3-*O*-methylene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (II)—reacted with sodium iodide to eliminate sodium *p*-toluenesulfonate, but no iodo compound could be isolated; apparently the contiguous primary and secondary sulfonyloxy groups at C_4 and C_5 had also been eliminated, which is in accord with the experience of Tipson and Cretcher[10] in similar cases. The latter—believed to be 2,4-*O*-methylene-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XIV)—formed both a mono- and a diiodo compound, just as we should expect from a substance of that structure. If, on the other hand, a 2,3-*O*-methylene group were present, then the corresponding tri-*O*-tosyl derivative would have had contiguous sulfonyloxy groups at C_4 and C_5 and its reaction with sodium iodide, like that of II, would be expected to be accompanied by deep-seated destruction. That a diiodo compound could be obtained even at 115° is, to us, convincing evidence of the 1,3,5-tri-*O*-tosyl arrangement and consequently of the 2,4-*O*-methylene group in the key compound XIV.

(10) R. S. Tipson and L. H. Cretcher, *J. Org. Chem.*, **8**, 95 (1943); see also R. S. Tipson, in *Advances in Carbohydrate Chem.*, **8**, 201 (1953).

We are now in a position to summarize the reactions of the three pentitols with formaldehyde and to see whether the new results with D-arabitol are in accord with the generalizations that have been elaborated by Hann and Hudson[11] and extended later by Barker and Bourne.[12] The rules for the preferential synthesis of acetals from polyhydric alcohols state that the first preference is for a βC-ring and the second preference is for a β-ring.[13] From ribitol (XVI), a high yield of the 2,4-*O*-methylene derivative (with a βC-ring) has been obtained,[5] and both ribitol and xylitol (XVII) formed the favored 1,3:2,4-di-*O*-methylene derivatives[5,2] (each with a βC- and a β-ring). D-Arabitol



(XVIII), by contrast, offers no possibility for the formation of a βC-ring but the second preference—for a β-ring—was realized first in the isolation of 1,3-*O*-benzylidene-D-arabitol[8] in 84% yield. Methylenation has now produced the analogous 1,3-*O*-methylene-D-arabitol (although in very small amount) and also a di-*O*-methylene derivative that contains a 1,3-*O*-methylene structure. Although the asymmetry of the D-arabitol molecule is such that either a 1,3- or a 3,5-ring might be expected, only the 1,3-ring has so far been noted.

If we assume that the 1,3-*O*-methylene ring is formed first, what positions should we then expect the second *O*-methylene group to enter? The three possibilities are the 2,4(βT)-, the 2,5(γ)- and the 4,5(α)-positions. Although the rare γT-ring is formed in the production of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol[14] and of the closely related 6-deoxy-1,3:2,5-di-*O*-methylene-L-mannitol,[15] no γ-ring has yet been observed and it must occupy a lowly position in the order of preference. Of the other two choices (a βT- or an α-ring), Hann and Hudson[11] stated that the βT-relationship is "unfavorable" and that a primary and a secondary alcohol group in α-position may form an acetal if the one in β-position is not available. They concluded that arabitol would not be expected to form a 2,4-acetal, but rather a 1,3- or 3,5-monoacetal; and that a diacetal of arabitol (1,3:4,5 or 1,2:3,5) appears to be capable of formation. Thus, their pre-

(11) R. M. Hann and C. S. Hudson, THIS JOURNAL, **66**, 1909 (1944); see also A. T. Ness, R. M. Hann and C. S. Hudson, *ibid.*, **70**, 765 (1948).

(12) S. A. Barker and E. J. Bourne, *J. Chem. Soc.*, 905 (1952); and especially their review in *Advances in Carbohydrate Chem.*, **7**, 137 (1952).

(13) In the code devised by Barker and Bourne, the Greek letters signify the relative positions of the two hydroxyl groups engaged in the cyclization, and C and T indicate whether these groups are disposed *cis* or *trans* in the usual Fischer projection formula; C and T are required only when both hydroxyl groups are secondary.

(14) A. T. Ness, R. M. Hann and C. S. Hudson, THIS JOURNAL, **65**, 2215 (1943).

(15) W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **67**, 1800 (1945).

diction of a monoacetal structure was correct but that of a diacetal structure was not.

Barker and Bourne[12] have stated that the third preference (after βC- and β-rings) is for an α-, αT-, βT-, or γT-ring. Later, in an explanation of the preferential formation of certain rings in acetals of the polyhydric alcohols, Barker, Bourne and Whiffen[16] indicated that probably the α-ring is preferred to the three others in that group. Thus, their prediction for a diacetal of D-arabitol would be the same as that of Hann and Hudson,[11] which our experimental results have not verified. However, if we assume that the 1,3-*O*-methylene ring is formed first, in accord with the rules, then the influence of that preformed ring, as Barker, Bourne and Whiffen have discussed, may influence the order of preferential entrance of an α-, αT-, βT-, or γT-ring. Whereas βT-rings are not uncommon, we have in 1,3:2,4-di-*O*-methylene-D-arabitol, to the best of our knowledge, the first example of the formation of a βT-ring by the methylenation of a polyhydric alcohol containing a free primary hydroxyl group. As a corollary, it appears that our reaction is the first example in which, after the much-preferred βC- and β-positions had been filled, the choice lay between an α- and a βT-ring. From this one case we may conclude that, in such methylenations, formation of a βT-ring takes precedence not only over an αT- or a γT-ring[12] but also over an α-ring.[16a]

A final word may be added in regard to the limited acetolysis of *O*-methylene acetals. Hann, Wolfe and Hudson[17] found that acetolysis of 2,4:3,5-di-*O*-methylene-D-glucitol at 0° for 30 minutes cleaves the 3,5(βT)-ring while leaving the 2,4-(βC)-ring intact and they obtained a 79% yield of crystalline acetylated product. The easy rupture of the 2,4(βT)-ring in our di-*O*-methylene-D-arabitol is thus in accord with the earlier precedent; it offers an explanation of our failure to obtain a partially degraded acetolysis product from the 1,3:2,4-di-*O*-methylene-D-arabitol and the rareness with which we obtained a methylene-monotosyl derivative from 1,3:2,4-di-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol. Our failure to obtain either an intermediate acetolysis or hydrolysis product from the bis compound also is consistent with its indicated formulation as bis-(1,3:2,4-di-*O*-methylene-5-D-arabityloxy)-methane.

Experimental

The 1,3:2,4-Di-*O*-methylene- and the 2,4-*O*-Methylene-D-arabitol Series

The Condensation of D-Arabitol with Formaldehyde to Bis-(di-*O*-methylene-D-arabityloxy)-methane.[6]—Although two of the first three condensations of D-arabitol with formaldehyde in the presence of concentrated hydrochloric acid at room temperature yielded small amounts of the di-*O*-methylene-D-arabitol, subsequent runs at room temperature produced the bis compound as the only crystalline product. In a typical experiment, a mixture of 25 g. of D-arabitol, 25 ml. of 37% aqueous formaldehyde and 25 ml. of concentrated hydrochloric acid in a crystallizing dish was placed in a desiccator containing beakers of concentrated sulfuric acid, granular calcium chloride and stick sodium hydroxide. The desiccator was evacuated with a water-pump and kept at 20° for 2 weeks. The resulting moderately thick sirup was stirred with 10 ml. of absolute ethanol and the desiccator evacuated and left for several days. After the repeated addition of absolute ethanol, reconcentration to a sirup and inoculation with di-*O*-methylene-D-arabitol had failed to produce crystalline material even after several months, 25 ml. of aqueous formaldehyde and 25 ml. of concentrated hydrochloric acid were added and the solution was concentrated in a desiccator as before. About a month later a spontaneous crystallization began in the sirup and this process was encouraged by adding ethanol, stirring, and reconcentrating. After another week the product was filtered, washed with ethanol and dried at room temperature. In two similar experiments the yields were 12.5 g. of crude product melting at 132–135° and 14.2 g. melting at 125–130°, respectively. Three recrystallizations from 95% ethanol sufficed to bring the m.p. to a constant value of 138–139°. The rotation of the prismatic needles was $[\alpha]^{20}D$ +38.5° in water (*c* 0.9).

Anal. Calcd. for $C_{15}H_{24}O_{10}$: C, 49.44; H, 6.64; mol. wt., 364. Found: C, 49.69, 49.61; H, 6.48, 6.63; mol. wt. (Rast), 353.

Attempts to effect a partial degradation of the bis compound and thus gain some information on its finer structure were unsuccessful; neither hydrolysis to constant rotation with concentrated hydrochloric acid at 20° nor acetolysis for varying short lengths of time at 0° yielded any crystalline product.

The Condensation of D-Arabitol with Formaldehyde to 1,3:2,4-Di-*O*-methylene-D-arabitol (2,4:3,5-Di-*O*-methylene-D-lyxitol) (V).[6]—A fairly successful preparation of the di-*O*-methylene compound was recorded as follows. A mixture of 25 g. of D-arabitol, 25 ml. of 37% aqueous formaldehyde and 25 ml. of concentrated hydrochloric acid was stirred for about 5 minutes at 20°. The solution was placed in an unevacuated desiccator containing beakers of granular calcium chloride, concentrated sulfuric acid, and stick sodium hydroxide, and the desiccator was stored in a refrigerator at +5° for 1 month. The desiccator was evacuated and returned to the refrigerator for another 2 weeks; the thickening sirup was stirred every 2 or 3 days during this period. The resulting thick sirup was stirred with a small amount of absolute ethanol, inoculated with crystals of the dimethylene compound, and the desiccator again evacuated and refrigerated for another week. The magma was filtered and the solid was washed with ethanol to yield 7.5 g. of crude product, m.p. 115–117°. The filtrate was concentrated to a thick sirup *in vacuo;* to this was added 25 ml. each of aqueous formaldehyde and concentrated hydrochloric acid; and the mixture, placed in the unevacuated desiccator containing fresh drying agents, was refrigerated for 2 weeks. The desiccator was then evacuated and refrigerated for another 2 weeks; absolute ethanol was added to the sirup and after several days at +5° the new magma was filtered; 10 g. of crude product melting at 112–118° was obtained. An additional 2.1 g., with m.p. 100–110°, was recovered by concentration of the mother liquor. One recrystallization of the total crude product from absolute ethanol furnished 14.1 g. (49%), as prismatic needles, of 1,3:2,4-di-*O*-methylene-D-arabitol (V). The m.p., 124–125°, was unchanged by further recrystallizations, and the value $[\alpha]^{20}D$ +32.4° in water (*c* 1) was observed for the purified compound.

Anal. Calcd. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.93; H, 6.84.

Acetolysis of the di-*O*-methylene compound, although carried out many times and under a variety of conditions, failed to produce any crystalline intermediate acetoxymethyl-acetyl-monomethylene derivative; deacetylation of the resulting sirups and subsequent acetylation, benzoylation or tosylation were equally unsuccessful in producing a crystalline derivative. When the acetolysis of one 10-g. sample in a mixture of 70 ml. of acetic anhydride, 30 ml. of glacial

(16) S. A. Barker, E. J. Bourne and D. H. Whiffen, *J. Chem. Soc.*, 3865 (1952).

(16a) FOOTNOTE ADDED AUGUST 10, 1954.—In the May 29, 1954, issue of *Chemistry & Industry*, a copy of which has just become available to us, J. A. Mills (page 633) stated that "nearly all known stable cyclic acetals of sugars and sugar alcohols conform to patterns predictable by methods of conformational analysis already familiar in the alicyclic field. In some cases the analysis may permit a definite prediction of structure, whereas the impirical rules do not." Mills then predicted that methylenation of arabitol would afford the 1,3:2,4-diacetal rather than the 2,4:3,5-diacetal; this prediction is now confirmed by our experimental results.

(17) R. M. Hann, J. K. Wolfe and C. S. Hudson, THIS JOURNAL, **66**, 1898 (1944).

acetic acid, and 2 ml. of concentrated sulfuric acid was allowed to proceed for 30 minutes in an ice-bath, followed by isolation of the sirupy product, deacetylation, and deionization, about 3 g. of D-arabitol was isolated. The cleavage of both *O*-methylene groups under these relatively mild conditions appears to be in marked contrast to the acetolysis of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol, which, after 5 days at 20°, according to Hann, Wolfe and Hudson,[18] gave a yield of only 14% of crystalline D-mannitol hexaacetate.

Transformation of 1,3:2,4-Di-*O*-methylene-D-arabitol (V) to the Bis-(di-*O*-methylene-D-arabityloxy)-methane.—A mixture of 2.5 g. of the dimethylene-D-arabitol, 7 ml. of aqueous formaldehyde and 5 ml. of concentrated hydrochloric acid was allowed to stand at room temperature for 2 weeks in an evacuated desiccator containing the usual drying agents. The 0.8 g. of crystalline material that could be separated by filtration was found to be a mixture of the starting compound with about 0.4 g. of the bis compound; the latter was isolated readily by fractional crystallization from absolute ethanol.

5-*O*-Acetyl-1,3:2,4-di-*O*-methylene-D-arabitol.—A mixture of 2 g. of 1,3:2,4-di-*O*-methylene-D-arabitol (V), 12 ml. of acetic anhydride and 0.5 g. of fused sodium acetate was heated on the steam-bath for 1.5 hours, and then poured onto cracked ice. After standing overnight in the refrigerator, the acetic acid solution was neutralized with solid sodium bicarbonate and the acetyl derivative recovered by extraction with chloroform. The extract was washed, dried, and concentrated to a sirup that crystallized readily on the addition of *n*-pentane. Recrystallization from a mixture of chloroform and *n*-pentane yielded 1.7 g. (69%) of product that upon further recrystallization melted at 68–70°. The clusters of thick needles showed $[\alpha]^{20}D$ +11.9° in chloroform (*c* 1).

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.47; CH_3CO, 19.7. Found: C, 49.51; H, 6.61; CH_3CO, 20.0.

5-*O*-Chloroacetyl-1,3:2,4-di-*O*-methylene-D-arabitol.—In an attempt to obtain a chlorine-substituted acetolysis product that might be crystalline, 2.5 g. of powdered di-*O*-methylene-D-arabitol (V) was added to a cold solution of 25 g. of chloroacetic anhydride and 1.5 ml. of concentrated sulfuric acid in 50 ml. of glacial acetic acid. The reaction mixture was shaken for 15 minutes in an ice-bath, poured onto ice, and the chloroform-soluble material isolated in the usual manner. The resulting sirup, which weighed only 0.4 g., was dissolved in aqueous ethanol and upon standing for several days in the refrigerator deposited about 0.1 g. of stout prisms. Two recrystallizations from chloroform and *n*-pentane yielded a product with m.p. 69–70°. The small yield and the analytical data indicate that chloroacetylation of a small amount of the di-*O*-methylene-D-arabitol had occurred, with little or no chloroacetolysis taking place under the conditions of the experiment.

Anal. Calcd. for $C_9H_{13}ClO_6$: C, 42.78; H, 5.18; Cl, 14.04. Found: C, 42.78; H, 5.42; Cl, 14.19.

1,3:2,4-Di-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol (XII).[6]—A solution of 5 g. of 1,3:2,4-di-*O*-methylene-D-arabitol (V) and 8 g. of *p*-toluenesulfonyl chloride in 25 ml. of dry pyridine was allowed to stand overnight at room temperature. When the mixture was poured onto cracked ice, the tosyl derivative crystallized immediately and in nearly the theoretical amount. Recrystallization of the dried product from 95% ethanol gave flat, elongated prisms with m.p. 131–132°[19] and $[\alpha]^{20}D$ +15.6° in chloroform (*c* 1).

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49; S, 9.70. Found: C, 51.11; H, 5.65; S, 9.42.

(18) Reference 17; see also R. Allerton and H. G. Fletcher, Jr., THIS JOURNAL, **76**, 1756 (1954).

(19) In Dr. Hann's original preparation of this tosyl compound he recorded in his notebook a melting point of 98–99°, not only for the crude crystalline material but also for the products that had been recrystallized both once and twice from 95% ethanol: values of $[\alpha]^{20}D$ +15.6° and +15.4°, respectively, were observed for the recrystallized products; and analytical data were in good agreement with the theory. However, a second preparation, carried out 3 weeks later by Mr. Harry W. Diehl in this Laboratory, produced only the higher-melting form reported here. An inspection of the original sample by Dr. Hann showed that it had changed and it then melted also at 131–132°. In our own experiments we have not encountered this apparently metastable, lower-melting modification of 1,3:2,4-di-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol.

5-Deoxy-5-iodo-1,3:2,4-di-*O*-methylene-D-arabitol.[6]—A mixture of 9.5 g. of the dimethylenetosyl-D-arabitol (XII), 9.5 g. of dry sodium iodide and 150 ml. of ethyl methyl ketone was refluxed for 5 hours, cooled, and the separated sodium *p*-toluenesulfonate removed by filtration (theory 5.58 g., found 5.65 g.). The filtrate was concentrated to a crystalline mass that was filtered, washed thoroughly with cold water, and dried. The iodo compound weighed 7.7 g. (94%). After several recrystallizations from 95% ethanol the needle-like crystals melted at 147–149° and showed $[\alpha]^{20}D$ +6.6° in chloroform (*c* 1.2).

Anal. Calcd. for $C_7H_{11}IO_4$: C, 29.39; H, 3.88; I, 44.36. Found: C, 29.37, 29.46; H, 3.94, 4.09; I, 44.71, 44.78.

Conversion of 5-Deoxy-5-iodo-1,3:2,4-di-*O*-methylene-D-arabitol to 5-Deoxy-1,3:2,4-di-*O*-methylene-D-arabitol (1-Deoxy-2,4:3,5-di-*O*-methylene-D-lyxitol).—Ten grams of the iodo compound in a mixture of 600 ml. of methanol and 5.4 ml. of diethylamine was hydrogenated at room temperature and atmospheric pressure in the presence of 10 g. of Raney nickel catalyst. The reaction was complete within 1.5 hours with the absorption of 900 ml. of hydrogen (theory 840 ml.). After removal of the nickel by filtration, the solution was concentrated *in vacuo* to a thin sirup. Extraction of the sirup several times with boiling *n*-pentane and extraction of the further-concentrated sirup with *n*-hexane yielded a total of 2.8 g. (50%) of crystalline product. The deoxy compound was recrystallized from *n*-hexane, forming shiny needles with m.p. 77–79° and $[\alpha]^{20}D$ +31.2° in water (*c* 1). The m.p. was not depressed when this deoxy compound was mixed with authentic 1-deoxy-2,4:3,5-di-*O*-methylene-D-lyxitol prepared as described later in this paper.

Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55; CH_3 (to C), 9.38. Found: C, 52.76; H, 7.74; CH_3 (to C), 9.14.

Acetolysis of 1,3:2,4-Di-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol (XII) and the Isolation of 2,4-*O*-Methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol (XIII).—Five grams of the 1,3:2,4-dimethylene-5-tosyl-D-arabitol was dissolved in 25 ml. of an ice-cold mixture prepared by adding 2 ml. of concentrated sulfuric acid to 70 ml. of acetic anhydride and 30 ml. of glacial acetic acid. The mixture was shaken for 30 minutes in an ice-bath and then poured onto cracked ice. The sirup that formed did not crystallize when left overnight in the refrigerator and so, after neutralization of the acids with bicarbonate, it was extracted with chloroform and the solution washed, dried, and concentrated. The sirup, expected to contain principally 3-*O*-acetoxymethyl-1-*O*-acetyl-2,4-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol, weighed 7 g. Because it showed no inclination to crystallize, the sirupy product was deacetylated by dissolving it in 75 ml. of acetone, adding 50 ml. of *N* aqueous sodium hydroxide, and allowing the mixture to stand for 5 hours at 20°. The reaction mixture was neutralized with *N* sulfuric acid, decolorized with a little activated carbon, and concentrated in a stream of air. Needles soon began to separate and the filtered and dried product weighed 2.5 g. (52% based on the original dimethylenetosyl derivative). The 2,4-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol (XIII) was recrystallized twice from hot water and then from 30% ethanol; the resulting needles melted at 110–111° and showed $[\alpha]^{20}D$ +31.3° in chloroform (*c* 1). The compound was not oxidized by sodium periodate in aqueous solution.

Anal. Calcd. for $C_{13}H_{18}O_7S$: C, 49.05; H, 5.70; S, 10.07. Found: C, 49.12; H, 5.87; S, 10.05.

2,4-*O*-Methylene-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XIV).—A solution of 1.8 g. of the 2,4-*O*-methylene-5-*O*-*p*-tolylsulfonyl-D-arabitol (XIII) and 4.5 g. of *p*-toluenesulfonyl chloride in 15 ml. of dried pyridine was left overnight at room temperature. The reaction mixture was poured onto cracked ice and the precipitated gum extracted with chloroform. The extract was washed with ice-cold dilute sulfuric acid, aqueous sodium bicarbonate and water, dried with sodium sulfate, and concentrated to a small volume. Upon the addition of *n*-pentane and standing overnight in the refrigerator, the solution deposited 3.4 g. (90%) of clusters of prisms. Several recrystallizations from mixtures of chloroform and *n*-pentane furnished a product with m.p. 68–73°, $[\alpha]^{20}D$ +31.8° in chloroform (*c* 1.2), and a composition that included one-third of a molecule of chloroform of crystallization. Attempts to recrystallize the compound from other solvents were unsuccessful unless a few drops of chloroform were added.

Anal. Calcd. for $C_{27}H_{30}O_{11}S_3 \cdot {}^1/_3CHCl_3$: C, 49.25; H, 4.59; $CHCl_3$, 5.97. Found (air-dried product): C, 49.04; H, 4.61; $CHCl_3$ (by loss in weight, 2 hours at 80° *in vacuo*), 6.10. Calcd. for $C_{27}H_{30}O_{11}S_3$: C, 51.74; H, 4.83; S, 15.35. Found (product dried 2 hours at 80° *in vacuo*): C, 51.93; H, 5.06; S, 15.31.

1(or 5)-Deoxy-1(or 5)-iodo-2,4-*O*-methylene-3,5(or 1,3)-di-*O*-*p*-tolylsulfonyl-D-arabitol.—A mixture of 0.517 g. of the crystalline methylenetritosyl-D-arabitol (XIV) and 1 g. of dry sodium iodide in 15 ml. of ethyl methyl ketone was boiled gently for 5 hours. The precipitated, filtered, and dried sodium *p*-toluenesulfonate weighed 0.194 g. (calcd. for replacement of 1 tosyloxy group, 0.151 g.). The solvent was removed in a current of air, and the resulting mass of crystals diluted with water and filtered. The 0.43 g. of product was recrystallized from hot 95% ethanol, from a mixture of chloroform and *n*-pentane, and finally from aqueous acetone; the resulting needles melted at 141–143° and their composition agreed with that of a monoiodo compound.

Anal. Calcd. for $C_{20}H_{23}IO_8S_2$: C, 41.24; H, 3.98; I, 21.79; S, 11.01. Found: C, 41.42; H, 4.27; I, 21.62; S, 11.22.

1,5-Dideoxy-1,5-diiodo-2,4-*O*-methylene-3-*O*-*p*-tolylsulfonyl-D-arabitol.—When 1.2 g. of the crystalline methylenetritosyl-D-arabitol (XIV) was heated with 2 g. of dry sodium iodide in 20 ml. of 2,5-hexanedione for 5 hours at 115°, the reaction mixture became dark and deposited 0.86 g. of sodium *p*-toluenesulfonate (calcd. for replacement of 2 tosyloxy groups, 0.70 g.). The filtered solution was concentrated to a small volume, diluted with water, and chilled, whereupon the product crystallized in fine needles. Upon recrystallization from aqueous acetone the compound weighed 0.5 g.; after two further recrystallizations from 95% ethanol, the diiodo derivative melted at 109–111°.

Anal. Calcd. for $C_{13}H_{16}I_2O_5S$: C, 29.01; H, 3.00; I, 47.17; S, 5.96. Found: C, 29.16; H, 3.18; I, 46.93; S, 5.67.

Acetolysis of 2,4-*O*-Methylene-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XIV) and Isolation of a Dianhydro-*O*-*p*-tolylsulfonylpentitol.—In the first experiment, 0.2 g. of the methylene tritosyl compound was dissolved at 20° in 20 ml. of a mixture of 70 ml. of acetic anhydride and 30 ml. of glacial acetic acid and the rotation determined to be $[\alpha]^{20}D$ +32°. The addition of 5 drops of concentrated sulfuric acid caused a drop in rotation, with values (calcd. as starting product) of $[\alpha]^{20}D$ +17° being reached after 6 hours and +13° (constant) within 3 days. The solution was poured onto ice and worked up in the customary way, but only a sirup could be obtained.

In the second experiment, 0.6 g. of compound was acetolyzed similarly, yielding 0.58 g. of a colorless sirup. This was dissolved in 14 ml. of acetone and 5 ml. of water; 2 ml. of *N* aqueous sodium hydroxide was added (calcd. for removal of 1 acetyl and 1 acetoxymethyl group from the expected intermediate compound: 1.6 ml. of *N* alkali) but after 1 hour at 20° the solution no longer contained excess alkali, and an additional 2 ml. was added. At the end of 5 hours, titration of the solution with *N* sulfuric acid indicated the consumption of 3.35 ml. of alkali (4 molecular equivalents) in the reaction. Partial evaporation of the aqueous acetone solution resulted in the crystallization of a product that was filtered and washed with water; wt. 0.1 g. Three recrystallizations from aqueous ethanol and one from chloroform–pentane yielded flat prisms melting at 101–102°. The analysis of the compound and the amount of alkali consumed in its formation indicated that it is undoubtedly a dianhydro-monotosyl-pentitol of completely unknown structure and configuration.

Anal. Calcd. for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22; S, 11.86. Found: C, 53.51; H, 5.22; S, 11.20.

Acetolysis of 2,4-*O*-Methylene-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XIV) and Isolation of 2,4-Di-*O*-acetyl-1,3,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XV).—In still a third acetolysis, 1.4 g. of compound in a mixture of 98 ml. of acetic anhydride, 42 ml. of glacial acetic acid and 2 ml. of concentrated sulfuric acid was left overnight at 20°. The rotation had become constant at $[\alpha]^{20}D$ +12.1° (calcd. as starting compound). The reaction mixture was poured onto ice and the product isolated in the usual manner as a sirup that weighed 1.1 g. The sirup was dissolved in 60 ml. of methanolic hydrogen chloride and the solution left overnight at 20° to effect deacetylation; no detectable change in rotation was observed. The mixture was diluted with a small amount of ice and the solvents removed in a current of air. The resulting sirup began to crystallize spontaneously when its solution, in a mixture of chloroform and pentane, was allowed to evaporate very slowly at room temperature. The crystalline material was freed from adhering sirup by several recrystallizations from chloroform-pentane and from absolute ethanol, to yield finally about 0.2 g. of prisms melting at 138–140°. The expected deacetylation by the methanolic hydrogen chloride appears to have been incomplete, for the product had the composition of a diacetyltritosyl derivative.

Anal. Calcd. for $C_{30}H_{34}O_{13}S_3$: C, 51.56; H, 4.90; S, 13.76. Found: C, 51.36, 51.36, 51.79; H, 4.85, 4.94, 5.19; S, 13.83, 13.98.

The 1,3-*O*-Methylene-D-arabitol Series

1,3-*O*-Methylene-D-arabitol (3,5-*O*-Methylene-D-lyxitol) (I).—In a large-scale condensation, a mixture of 115 g. of D-arabitol and 115 ml. each of 37% aqueous formaldehyde and concentrated hydrochloric acid was kept at 0° for 1 week, and then concentrated to a thick sirup in an evacuated desiccator at 0° during the course of the succeeding 6 months. The first crop of crystals weighed 6.3 g. and consisted principally of 1,3:2,4-di-*O*-methylene-D-arabitol. The mother liquor was concentrated to a thick sirup that was dissolved in absolute ethanol and the solution, cooled to 0°, diluted to incipient cloudiness with *n*-pentane. After a few days at 0° the solution began to deposit a new crop of crystals; these were filtered and washed at 0° with cold absolute ethanol. The somewhat sticky product could be recrystallized from a small amount of absolute ethanol by chilling to 0°. The 1.8 g. thus obtained was recrystallized twice more, yielding clusters of needles with m.p. 86–87° and $[\alpha]^{20}D$ −19.9° in water (*c* 1). Analyses showed the compound to be a monomethylene-D-arabitol.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.09; H, 7.43.

The reaction of this 1,3-*O*-methylene-D-arabitol (I) with sodium metaperiodate consumed 1 molecular equivalent of oxidant, identical values of 1.05 being found at the end of 1 and 18 hours at 20°. No formic acid was liberated. The determination of formaldehyde according to Reeves,[20] with 1,3-*O*-benzylidene-D-arabitol[8] as the control, indicated the formation of one molecular equivalent of that aldehyde.

The mother liquor from the first filtration of the monomethylene derivative, by suitable manipulation, yielded an additional 13.5 g. of crystalline material. This, however, was a mixture from which could be separated 2.7 g. of the pure monomethylene compound plus a considerable amount of unchanged D-arabitol. The mother liquor from the 13.5 g. was condensed with formaldehyde and hydrochloric acid for 1 week at room temperature to give, in several fractions, 23.3 g. of mixed dimethylene-D-arabitol and bis-(dimethylene-D-arabityloxy)-methane.

It is thus evident that under the conditions now existing in this Laboratory, the condensation of D-arabitol with formaldehyde leads invariably to a complex mixture of products. In spite of many variations in procedure, substitution of trioxymethylene or trioxane for aqueous formaldehyde, and use of sulfuric or phosphoric acid for concentrated hydrochloric acid, no improvement could be effected.

1,3-*O*-Methylene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (II).—Tosylation of 0.5 g. of 1,3-*O*-methylene-D-arabitol (I) with 100% excess of *p*-toluenesulfonyl chloride in pyridine for 3 days at 20° produced 1.65 g. of once-recrystallized tritosyl derivative. Two further recrystallizations from a mixture of chloroform and *n*-pentane gave needles with m.p. 135–136° and $[\alpha]^{20}D$ −13.9° (*c* 0.8) in chloroform.

Anal. Calcd. for $C_{27}H_{30}O_{11}S_3$: C, 51.74; H, 4.83; S, 15.35. Found: C, 51.79; H, 4.75; S, 15.65.

When a similar tosylation was carried out for only 20 hours at room temperature, a small amount of a ditosyl derivative, probably 1,3-*O*-methylene-4,5-di-*O*-*p*-tolylsulfonyl-D-arabitol, was also isolated. It was recrystallized from chloroform–pentane, absolute ethanol, and again from chloroform–pentane. The clusters of prisms melted at 161–163° dec.

(20) R. E. Reeves, THIS JOURNAL, **63**, 1476 (1941).

Anal. Calcd. for $C_{20}H_{24}O_9S_2$: C, 50.83; H, 5.12; S, 13.57. Found: C, 50.38; H, 5.14; S, 13.32.

When 0.3 g. of the tritosyl derivative was refluxed for 5 hours with sodium iodide in ethyl methyl ketone, 1 molecular equivalent of sodium *p*-toluenesulfonate was recovered but the filtrate yielded only unchanged tritosyl derivative and a water-soluble residue.

Transformation of 1,3-*O*-Methylene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (II) to 1,3-*O*-Benzylidene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (III).—The rotation of a solution of 0.35 g. of the 1,3-methylenetritosyl derivative in a mixture of 28 ml. of acetic anhydride, 12 ml. of glacial acetic acid, and 10 drops of concentrated sulfuric acid changed overnight at 20° from $[\alpha]^{20}D$ −12.4° to +21.9° (calcd. as starting product), with no further change being noted in 4 more days. The solution was poured onto ice and the product extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate and then water, dried with sodium sulfate, and concentrated to 0.4 g. of a colorless sirup that failed to crystallize within 10 days. The sirupy product was deacetylated by allowing its solution in methanolic hydrogen chloride to stand for 4 days at 20°; during that time the observed rotation had fallen to about half the original value. The reaction mixture was concentrated in a stream of air to 0.4 g. of sirup that did not crystallize. Accordingly, its solution in 10 ml. of absolute ethanol was cooled in an ice-bath and to it were added 3 ml. each of benzaldehyde and concentrated hydrochloric acid. The homogeneous solution was placed in the refrigerator; a few oily droplets were observed after 1 day, and these crystallized during the next 3 days. The product was filtered, washed with 95% ethanol, and dried to yield about 100 mg. with m.p. 120–125°. Recrystallization from 95% ethanol and then from chloroform-pentane afforded needles with m.p. 123–125° and $[\alpha]^{20}D$ −17.7° in chloroform (*c* 0.12, *l* 4). These data, together with a mixed m.p. of 124–126°, identified the substance as 1,3-*O*-benzylidene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (III) (m.p. 124–126°, $[\alpha]^{20}D$ −18.1°), whose preparation through tosylation of the known 1,3-*O*-benzylidene-D-arabitol (IV) is described elsewhere in this paper.

The 1-Deoxy-D-arabitol and 1-Deoxy-D-lyxitol Series

1-Deoxy-D-arabitol (5-Deoxy-D-lyxitol).—The reductive desulfurization of D-arabinose diethyl mercaptal[21] with Raney nickel gave 1-deoxy-D-arabitol in 65% yield (average) after one recrystallization from 95% ethanol. Because the substance has only a very small rotation in water it was purified until its rotation in 5% aqueous ammonium molybdate became constant. Thus, after three recrystallizations from 5 parts of hot methanol by the addition of 5 parts of ether, our 1-deoxy-D-arabitol melted at 129–131° and showed $[\alpha]^{20}D$ +0.7° in water (*c* 10, *l* 4), −31.4° in 5% aqueous ammonium molybdate (*c* 0.40), and +16.9° in the acidified molybdate solution (*c* 0.41).[22] The product has been reported previously by Bollenback and Underkofler,[9] who obtained it by the reductive desulfurization of tetra-*O*-acetyl-D-arabinose diethyl mercaptal to tetra-*O*-acetyl-1-deoxy-D-arabitol and subsequent deacetylation of that crystalline substance. They reported m.p. 131–132° and $[\alpha]^{23}D$ +2.46° in water (*c* 1.02), with m.p. 129–131° and $[\alpha]^{30}D$ −1.46° in water (*c* 1.02) for the antipodal L-form.

The attempted condensation of 1-deoxy-D-arabitol with benzaldehyde and concentrated hydrochloric acid at 0° overnight yielded a very small amount of a new compound. The product, recrystallized from chloroform-pentane as elongated prisms, melted at 136–138° and had the composition of a monobenzylidene-1-deoxy-D-arabitol (*Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.21; H, 7.19). The condensation of D-arabitol under somewhat more drastic conditions is known to yield the 1,3-*O*-benzylidene-D-arabitol[8]; a 2,3-*O*-benzylidene-D-arabitol also has been described[8]; 5-deoxy-D-arabitol (1-deoxy-D-lyxitol) forms a dibenzylidene derivative readily (see below); however, the position of the benzylidene residue in the compound derived from 1-deoxy-D-arabitol has not been determined for lack of material.

The attempted condensation of 1-deoxy-D-arabitol with 37% aqueous formaldehyde and concentrated hydrochloric acid was unsuccessful; the reaction was tried for 1 week at room temperature, 3 hours at 50°, and overnight at 60°, with subsequent concentration *in vacuo* to a sirup, but in no case could crystals be secured.

2,3,4,5-Tetra-*O*-benzoyl-1-deoxy-D-arabitol.—The benzoylation of 1 g. of 1-deoxy-D-arabitol with 4 ml. of benzoyl chloride and 15 ml. of pyridine in the usual manner afforded a nearly quantitative yield of the tetrabenzoate. The product was recrystallized twice from absolute ethanol; the resulting clusters of prisms melted at 135–137° and showed $[\alpha]^{20}D$ +41.6° in chloroform (*c* 1).

Anal. Calcd. for $C_{33}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.43; H, 5.23.

1-Deoxy-D-lyxitol (5-Deoxy-D-arabitol).—Starting material for this substance was the known D-lyxose diethyl mercaptal first described by Wolfrom and Moody.[23] As an alternative to their procedure using concentrated hydrochloric acid we substituted fused zinc chloride as the condensing agent exactly as described earlier for D-xylose diethyl mercaptal.[24] The yield was about 60%. The product, after three recrystallizations from absolute ethanol, melted at 102–103° and showed $[\alpha]^{20}D$ +42.1° in water (*c* 4) in good agreement with the previously reported m.p. 103–104° and $[\alpha]^{24}D$ +41° in water (*c* 5).[23]

The reductive desulfurization of D-lyxose diethyl mercaptal with Raney nickel in the usual manner yielded 1-deoxy-D-lyxitol as a sirup that could not be crystallized even after purification through its crystalline tetraacetate.

2,3,4,5-Tetra-*O*-acetyl-1-deoxy-D-lyxitol.—Acetylation of the crude sirupy 1-deoxy-D-lyxitol with acetic anhydride and fused sodium acetate on the steam-bath furnished the tetraacetate in 67% yield. The product was recrystallized twice from chloroform by the addition of pentane; the clusters of radiating prisms melted at 58–59° and showed $[\alpha]^{20}D$ +46.1° in chloroform (*c* 1).

Anal. Calcd. for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63; CH_3CO, 56.6. Found: C, 51.06; H, 6.46; CH_3CO, 56.8.

2,3,4,5-Tetra-*O*-benzoyl-1-deoxy-D-lyxitol.—To 1 g. of sirupy 1-deoxy-D-lyxitol (regenerated from its tetraacetate) in 10 ml. of pyridine was added 4 ml. of benzoyl chloride. Some heat was evolved, and the mixture was heated further on the steam-bath for 10 minutes to complete the reaction. Decomposition of the solution with cracked ice and isolation of the benzoate in the usual manner yielded 3.6 g. (89%) of crystalline product. After two recrystallizations from 95% ethanol the needle clusters of the tetrabenzoate melted at 106–107° and showed $[\alpha]^{20}D$ +12.0° in chloroform (*c* 1).

Anal. Calcd. for $C_{33}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.51; H, 5.16.

2,3,4,5-Di-*O*-benzylidene-1-deoxy-D-lyxitol.—Into an ice-cold solution of 1 g. of sirupy 1-deoxy-D-lyxitol in 3 ml. of concentrated hydrochloric acid was stirred 3 ml. of benzaldehyde. The mixture set to a mass of crystals within 2 hours; these were broken up with a stirring rod and left for an additional hour at 0°. The product was filtered, washed well with cold 5% aqueous sodium hydroxide and water, and dried to yield 1.5 g. (65%) of benzylidene derivative. Several recrystallizations from ethanol produced clusters of fine needles of the dibenzylidene-1-deoxy-D-lyxitol with m.p. 143–146° and $[\alpha]^{20}D$ −45.2° in chloroform (*c* 1.3).

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.13; H, 6.64.

1-Deoxy-2,4:3,5-di-*O*-methylene-D-lyxitol (5-Deoxy-1,3:2,4-di-*O*-methylene-D-arabitol).—A mixture of 2 g. of sirupy 1-deoxy-D-lyxitol (regenerated from its tetraacetate), 5 ml. of concentrated hydrochloric acid and 4 ml. of 37% aqueous formaldehyde was heated in a stoppered flask for 1 hour at 50° and then concentrated in an evacuated desiccator containing solid potassium hydroxide. The resulting thin sirup crystallized readily when cooled in an ice-bath. The product, filtered with the aid of *n*-hexane, weighed 1.9 g. (81%). Three recrystallizations from *n*-hexane furnished shiny needles that melted at 77–79° and showed $[\alpha]^{20}D$ +31.5° in water (*c* 1). The melting point was not depressed when this dimethylene compound was mixed with the dimethylene compound prepared from 1,3:2,4-di-*O*-methylene-D-arabitol (IV) through conversion of its free CH_2OH group to a CH_3 group.

(21) M. L. Wolfrom, D. I. Weisblat, W. H. Zophy and S. W. Waisbrot, THIS JOURNAL, **63**, 201 (1941).

(22) N. K. Richtmyer and C. S. Hudson, *ibid.*, **73**, 2249 (1951).

(23) M. L. Wolfrom and F. B. Moody, *ibid.*, **62**, 3465 (1940).

(24) E. Zissis and N. K. Richtmyer, *ibid.*, **75**, 129 (1953).

The 1,3- and the 2,3-*O*-Benzylidene-D-arabitol Series

1,3-*O*-Benzylidene-2,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (III).—To 0.5 g. of 1,3-*O*-benzylidene-D-arabitol (IV)[6] in 7 ml. of dry pyridine was added 10 g. (25 molecular equivalents) of powdered *p*-toluenesulfonyl chloride, and the mixture allowed to stand at room temperature for 5 days. When the mixture was poured onto cracked ice, a gum resulted; this was washed with water by decantation, and then dissolved in hot 95% ethanol. As the solution cooled, a sirup was deposited; this was dissolved in a large amount of hot ethanol, and its solution, kept overnight in the refrigerator, deposited 0.3 g. of crystalline material with m.p. 110–120°. Two recrystallizations from ethanol and one from chloroform–pentane yielded needles with m.p. 124–126° and $[\alpha]^{20}D$ −18.1° in chloroform (*c* 0.2).

Anal. Calcd. for $C_{33}H_{34}O_{11}S_3$: C, 56.39; H, 4.88; S, 13.69. Found: C, 56.53; H, 5.10; S, 13.76, 13.40.

1,3-*O*-Benzylidene-4,5-di-*O*-*p*-tolylsulfonyl-D-arabitol.—A reaction mixture of 3 g. of 1,3-*O*-benzylidene-D-arabitol (IV)[8] and 14 g. (6 molecular equivalents) of *p*-toluenesulfonyl chloride in 15 ml. of dry pyridine was kept at room temperature for 3 days and then poured onto cracked ice. The product crystallized readily, and after being filtered, washed with water and then a small amount of ethanol, and dried overnight in the air, it weighed 8 g. Two recrystallizations from 95% ethanol afforded 5.7 g. with m.p. 58–73°. A recrystallization from chloroform–pentane raised the melting point to 123–133° (the lower-melting product may have contained a dimorphic or solvated modification), and two additional recrystallizations in the same manner yielded needles with m.p. 135–136° and $[\alpha]^{20}D$ −17.8° in chloroform (*c* 1). Allocation of the two tosyl groups to the C_4- and C_5-positions in this compound is based only on general rules of substitution and not on any direct evidence.

Anal. Calcd. for $C_{26}H_{28}O_9S_2$: C, 56.92; H, 5.14; S, 11.69. Found: C, 57.13, 57.17; H, 5.04, 5.01; S, 11.80.

The mother liquors from the recrystallizations of the ditosyl compound, upon concentration and fractional crystallization from chloroform–pentane, finally yielded 33 mg. of the tritosyl compound, with m.p. 124–125° and mixed m.p. 124–126°.

2-*O*-Acetyl-1,3-*O*-benzylidene-4,5-di-*O*-*p*-tolylsulfonyl-D-arabitol.—Although the introduction of a third tosyl group into the 1,3-benzylideneditosyl compound was accomplished only with great difficulty, acetylation with acetic anhydride and pyridine proceeded readily at room temperature overnight. A 93% yield of product was thus obtained; after recrystallization first from 95% ethanol and then from chloroform–pentane the needle-like acetate melted at about 145° dec. and showed $[\alpha]^{20}D$ −46.7° in chloroform (*c* 0.3). The same product was obtained by acetylation with acetic anhydride and fused sodium acetate.

Anal. Calcd. for $C_{28}H_{30}O_{10}S_2$: C, 56.93; H, 5.12; S, 10.86. Found: C, 57.09; H, 5.32; S, 11.13.

2,4-Di-*O*-acetyl-1,3-*O*-benzylidene-5-*O*-*p*-tolylsulfonyl-D-arabitol.—To a solution of 2.10 g. of 1,3-*O*-benzylidene-D-arabitol in 15 ml. of dry pyridine, cooled to 0° and stirred vigorously, was added 1.67 g. (1 molecular equivalent) of recrystallized *p*-toluenesulfonyl chloride in 10 ml. of pyridine. After the solution had remained an additional hour at 0° and then 1 hour at room temperature, 10 ml. of acetic anhydride was added and the reaction mixture left overnight. The sirup that resulted when the mixture was poured onto ice was extracted with chloroform and the extract washed, dried, and concentrated in the usual manner. Crystallization began when the sirup was mixed with a small amount of absolute ethanol. Accordingly, the sirup was dissolved in hot ethanol and diluted with *n*-pentane; the solution, kept overnight in the refrigerator, deposited 2.8 g. of clusters of needles melting at 115–125°. By a series of fractional crystallizations from methanol, from acetone–water, and from chloroform–pentane, there could be separated a small amount of compound that melted at about 145° dec. and was identified by analysis and mixed melting point as the 2-*O*-acetyl-1,3-*O*-benzylidene-4,5-di-*O*-*p*-tolylsulfonyl-D-arabitol described immediately above. The main portion of the reaction product was the desired 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-5-*O*-*p*-tolylsulfonyl-D-arabitol: fine needles from aqueous acetone, with m.p. 128–130° and $[\alpha]^{20}D$ −18.8° in chloroform (*c* 1.7).

Anal. Calcd. for $C_{23}H_{26}O_9S$: C, 57.73; H, 5.48; S, 6.70. Found: C, 57.81; H, 5.70; S, 6.78.

Tosylation of 2,3-*O*-Benzylidene-D-arabitol (VIII) and Isolation of 1,4,5-Tri-*O*-*p*-tolylsulfonyl-D-arabitol (X).—The reaction of 1.3 g. of 2,3-*O*-benzylidene-D-arabitol[8] in dry pyridine with double the theoretical amount of *p*-toluenesulfonyl chloride for 24 hours resulted in the formation of a hard gum (presumed to contain 2,3-*O*-benzylidene-1,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (IX)) that could not be crystallized. After 2 weeks, 1.4 g. of this product was heated in 25 ml. of 95% ethanol with 8 ml. of concentrated sulfuric acid for 4 hours on the steam-bath; benzaldehyde was liberated. The mixture was poured on ice, and the resulting gum crystallized readily when rubbed with 95% ethanol to yield 0.55 g. of material. The tritosyl compound was recrystallized twice from 95% ethanol and once from chloroform–pentane to form needles with m.p. 125–126° and $[\alpha]^{20}D$ +26.8° in chloroform (*c* 0.9).

Anal. Calcd. for $C_{26}H_{30}O_{11}S_3$: C, 50.80; H, 4.92; S, 15.65. Found: C, 50.94; H, 5.11; S, 15.45.

2,3-Di-*O*-acetyl-1,4,5-tri-*O*-*p*-tolylsulfonyl-D-arabitol (XI).—Acetylation of the preceding 1,4,5-tritosyl compound with acetic anhydride and pyridine in the usual manner yielded a sirup that crystallized readily when rubbed with absolute ethanol. The yield was 75%. Three recrystallizations from chloroform–pentane produced flat prisms melting at 83–84°.

Anal. Calcd. for $C_{30}H_{34}O_{13}S_3$: C, 51.56; H, 4.90; S, 13.76. Found: C, 51.55; H, 4.90; S, 13.56.

Acknowledgment.—The authors wish to thank Mr. Harry W. Diehl for contributing his original preparations of the dimethylene and the bis compounds for use in these researches; Mr. Edward W. Tracy for preparing and desulfurizing the D-arabinose and D-lyxose diethyl mercaptals; and Dr. William C. Alford and his associates of the Institutes' microanalytical laboratory for carrying out the microanalyses.

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