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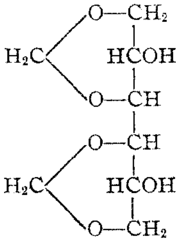
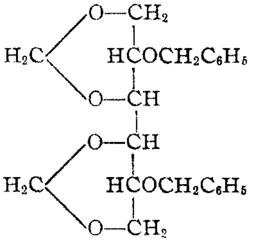
The Structure of Dimethylene Dulcitol (1,3:4,6-Dimethylene-dulcitol)

BY RAYMOND M. HANN, W. T. HASKINS AND C. S. HUDSON

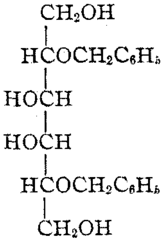
In a recent communication[1] it was established that the dibenzylidene-dulcitol of Emil Fischer[2] is 1,3:4,6-dibenzylidene-dulcitol. In the present paper proof is presented that the dimethylene-dulcitol of Weber and Tollens[3] has an analogous structure; accordingly this hexitol diacetal may now be fully designated as 1,3:4,6-dimethylene-dulcitol, a substance of meso configuration (I).



(I)
1,3:4,6-Dimethylene-dulcitol



(II)
2,5-Dibenzyl-1,3:4,6-dimethylene-dulcitol



(III)
2,5-Dibenzyl-dulcitol

The crystalline dimethylene-dulcitol, which was prepared from dulcitol, formaldehyde and hydrochloric acid in quantitative yield by the procedure of Weber and Tollens, was acetylated, and the diacetate, upon refluxing in toluene solution with solid potassium hydroxide and benzyl chloride,[4] gave a quantitative yield of a crystalline dibenzyl-dimethylene-dulcitol (II). The latter substance was hydrolyzed by alcoholic *N* hydrochloric acid and the resulting dibenzyl-dulcitol was found to be identical with the known crystalline 2,5-dibenzyl-dulcitol (III).[1] The positions of attachment of the methylene residues in the dibenzyl-dimethylene-dulcitol, considering the five- and six-membered rings customarily associated with cyclic acetal formation, are thus limited to 1,3 and 4,6 and dibenzyl-dimethylene-dulcitol is therefore 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol. Confirmation of this fact was obtained by synthesizing 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol from authentic 2,5-dibenzyl-dulcitol[1] and formaldehyde by the condensing action of concentrated hydrochloric acid, the synthetic product proving to be identical with the compound that had been obtained by the benzylation of dimethylene-dulcitol diacetate. It is evident from this series of reactions that the dimethylene-dulcitol of Weber and Tollens is 1,3:4,6-dimethylene-dulcitol. Additional support for this conclusion was obtained when it was ascertained that 1,3:4,6-dimethylene-dulcitol was not oxidized by aqueous per-iodic acid, a fact which confirmed the absence of a glycol grouping in its structure; the diacetal also readily yielded a crystalline ditosyl derivative which, however, could not be converted into an iodo compound by treatment with sodium iodide in acetic anhydride solution; its stability under these circumstances indicated that the tosyl groups in ditosyl-dimethylene-dulcitol were attached to secondary alcohol groups.[1]

We express our appreciation to Dr. A. T. Ness for performing the microchemical analyses in connection with this work, and to the Atlas Powder Company for furnishing a supply of dulcitol.

Experimental

1,3:4,6-Dimethylene-dulcitol.—The solution of 50 g. of dulcitol in a mixture of 100 cc. of formaldehyde solution (37%) and 100 cc. of concentrated hydrochloric acid was completed by slight warming, and the reaction mixture was transferred to a large desiccator containing anhydrous calcium chloride, sodium hydroxide pellets and several small beakers of concentrated sulfuric acid. After seven days the diacetal crystallized spontaneously from the solution and after a further fourteen days the reaction mixture had formed a semi-dry crystalline magma. The mass was broken up and transferred to a Büchner funnel with the aid of 100 cc. of alcohol. The crude yield was 57 g. (quantitative). The compound was recrystallized in a yield of 80% by solution in 10 parts of warm water followed by the addition of 10 parts of alcohol. It deposited from the solution during cooling as glistening well-formed prisms which melted at 249–250° (cor.). Weber and Tollens[3] reported a melting point of 244–245° (uncor.). The compound and its derivatives are optically inactive. The diacetal is fairly stable in hot 0.1 *N* hydrochloric acid solution,

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(1) Haskins, Hann and Hudson, THIS JOURNAL, **64**, 132 (1942).

(2) Fischer, *Ber.*, **27**, 1524 (1894).

(3) Weber and Tollens, *Ann.*, **299**, 318 (1898).

(4) Zemplén, Csürös and Angyal, *Ber.*, **70**, 1848 (1937).

being recovered unchanged after boiling for one-half hour in this medium; it is hydrolyzed to formaldehyde and dulcitol by boiling for one hour with *N* hydrochloric acid.

Anal. Calcd. for $C_8H_{14}O_6$: C, 46.60; H, 6.84. Found: C, 46.60; H, 6.85.

Failure of Per-iodic Acid to Oxidize 1,3:4,6-Dimethylene-dulcitol.—To a solution of 0.2725 g. of 1,3:4,6-dimethylene-dulcitol in 15 cc. of water, 4.6 cc. (2.00 molecular equivalents) of 0.576 *M* per-iodic acid solution was added and the volume was adjusted to 25-cc. with water. Analysis of 5-cc. sub-samples at the expiration of one, twenty-two and one hundred and twenty hours indicated that no oxidation occurred at 20°. The failure of the diacetal to reduce per-iodic acid indicates that there is no glycol grouping present in the compound.

2,5-Dibenzoyl-1,3:4,6-dimethylene-dulcitol.—To a well-stirred ice-cold solution of 6.0 g. of dimethylene-dulcitol in 300 cc. of 20% sodium hydroxide, six 5-cc. portions of benzoyl chloride were added at fifteen minute intervals. The reaction mixture was warmed to 60° to complete the decomposition of the benzoyl chloride, and the insoluble dibenzoate was removed by filtration and dried. The yield was 5.5 g. (45%). The compound may be recrystallized from 100 parts of alcohol and it formed long needles which melted at 233–234° (cor.). Weber and Tollens[3] reported a melting point of 228–231° (uncor.).

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35; C_6H_5CO, 50.7. Found: C, 63.90; H, 5.43; C_6H_5CO, 50.4.

2,5-Diacetyl-1,3:4,6-dimethylene-dulcitol.—A solution of 10.0 g. of dimethylene-dulcitol in a mixture of 100 cc. of pyridine and 100 cc. of acetic anhydride was refluxed for fifteen minutes and, after cooling, poured upon crushed ice. The precipitated 2,5-diacetyl-1,3:4,6-dimethylene-dulcitol (14.1 g., quantitative) was removed by filtration and recrystallized from 250 parts of boiling alcohol, being deposited in thin iridescent plates which melted at 264–265° (cor.). Weber and Tollens[3] recorded a melting point of 258–260° (uncor.).

Anal. Calcd. for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25; CH_3CO 29.7. Found: C, 49.86; H, 6.25; CH_3CO, 29.4.

2,5-Ditosyl-1,3:4,6-dimethylene-dulcitol.—A suspension of 1.0 g. of finely powdered dimethylene-dulcitol in 15 cc. of pyridine was cooled in an ice-bath and 2.8 g. (three molecular equivalents) of *p*-toluenesulfonyl chloride was added. The reaction mixture was allowed to stand at 20° for twenty-four hours and then heated on the steam-bath for two hours and poured upon crushed ice. The ditosylated diacetal, which precipitated in a yield of 1.4 g. (56%), was recrystallized from 350 parts of boiling acetic anhydride, from which it was deposited in the form of needles. Upon melting in a capillary tube the substance darkened at 220° (cor.) and then slowly decomposed to form a black tar. A solution of 0.1 g. of the compound in a mixture of 50 cc. of acetic anhydride and 1.0 g. of sodium iodide was refluxed for one-half hour; on cooling the solution the ditosylated derivative was recovered in quantitative yield, a result which indicated that the tosyl groups were attached to secondary alcoholic groups in the ditosyl-dimethylene-dulcitol molecule.

Anal. Calcd. for $C_{22}H_{26}O_{10}S_2$: C, 51.35; H, 5.09; S, 12.46. Found: C, 51.40; H, 5.24; S, 12.31.

2,5-Dibenzyl-1,3:4,6-dimethylene-dulcitol from 2,5-Diacetyl-1,3:4,6-dimethylene-dulcitol.—A reaction mixture consisting of 2.0 g. of finely powdered 2,5-diacetyl-1,3:4,6-dimethylene-dulcitol, 7.9 cc. of benzyl chloride (ten molecular equivalents), 19.3 g. of powdered potassium hydroxide (fifty molecular equivalents), and 15 cc. of toluene was refluxed in an oil-bath for four hours. The cooled mixture was diluted with 200 cc. of cold water and the precipitate of 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol (2.7 g., quantitative) was separated by filtration and recrystallized from 60 parts of alcohol. The compound was obtained in fine needles which melted at 164° (cor.).

Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.34; H, 6.78.

2,5-Dibenzyl-1,3:4,6-dimethylene-dulcitol from 2,5-Dibenzyl-dulcitol, Formaldehyde and Hydrochloric Acid.—A solution of 0.5 g. of authentic 2,5-dibenzyl-dulcitol[1] in a mixture of 5 cc. of purified dioxane, 2.5 cc. of concentrated hydrochloric acid and 2.5 cc. of 37% formaldehyde was immersed in a boiling water-bath for fifteen minutes, and then diluted with 50 cc. of water. The precipitated 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol (0.3 g., 57%) was separated by filtration and upon recrystallization from 20 cc. of alcohol it was obtained in the form of needles which melted at 164° (cor.). This melting point was not changed upon mixing the substance with 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol obtained by the benzylation of 1,3:4,6-dimethylene-dulcitol.

Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.31; H, 6.76.

Hydrolysis of 2,5-Dibenzyl-1,3:4,6-dimethylene-dulcitol to 2,5-Dibenzyl-dulcitol.—A solution of 0.5 g. of 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol (prepared by the benzylation of 2,5-diacetyl-1,3:4,6-dimethylene-dulcitol) in a mixture of 40 cc. of alcohol, 6 cc. of water and 4 cc. of concentrated hydrochloric acid was placed in a pressure bottle and heated for twelve hours in a boiling water-bath. The cooled reaction mixture was diluted with 50 cc. of water and the precipitate (0.30 g., 64%) which separated was removed by filtration and recrystallized from 70 parts of alcohol. The substance deposited from the alcoholic solution in the form of fine needles which melted at 168–169° (cor.) and this melting point was not depressed upon admixing the compound with authentic 2,5-dibenzyl-dulcitol.[1]

Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.19; H, 7.17.

Summary

The diacetate of the dimethylene-dulcitol of Weber and Tollens has been converted to a dibenzyl-dimethylene-dulcitol which is found to be identical with the 2,5-dibenzyl-1,3:4,6-dimethylene-dulcitol that is obtained when authentic 2,5-dibenzyl-dulcitol is condensed with formaldehyde by the action of concentrated hydrochloric acid. These facts limit the structure of the dimethylene-dulcitol of Weber and Tollens to that of 1,3:4,6-dimethylene-dulcitol.

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