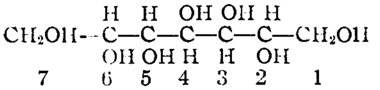
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE][1]

The 1,3:5,7-Dibenzylidene and 1,3:5,7-Dimethylene Acetals of the D-, L- and D,L-Perseitols

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

Dibenzylidene-D-perseitol[2] is of particular interest to the carbohydrate chemist because its original preparation and accurate analysis by Maquenne[3] led to the recognition that D-perseitol (I), discovered in the avocado by Avequin[4] in 1831 and long considered to be an isomer of mannitol, is indeed a heptitol. In the present article proofs are presented for the structure of dibenzylidene-D-perseitol and for that of a corresponding dimethylene-D-perseitol which we have prepared. The structures agree with those expected from perseitol as predicted by the generalizations[5] correlating the configuration of polyhydric alcohols with the structures of the benzylidene and methylene acetals derived from them.



$$\begin{array}{ccccccc} & H & H & OH & OH & H & \\ CH_2OH- & C- & C- & C- & C- & C- & CH_2OH \\ & OH & OH & H & H & OH & \\ 7 & 6 & 5 & 4 & 3 & 2 & 1 \end{array}$$

D-Manno-D-*gala*-heptitol (D-Perseitol)

(I)

Maquenne[3] prepared dibenzylidene-D-perseitol by mixing benzaldehyde and a finely divided suspension of D-perseitol in aqueous-alcoholic solution which had been saturated with gaseous hydrochloric acid, and in his original description of the crystalline diacetal he stated that it softened at 215° but did not show a sharp melting point; in a later article[6] he recorded the softening point as 219° and this value is also given in his book on sugars.[7] Lobry de Bruyn and Alberda van Ekenstein[8] recorded a melting point of 230–235°. In our initial preparation of dibenzylidene-D-perseitol we dissolved the heptitol in 50% sulfuric acid and added benzaldehyde and alcohol; the diacetal which crystallized melted at the much lower temperature of 153–155°; it rotated $[\alpha]^{20}D$ $-58.2°$ in pyridine solution. Upon recrystallization from a pyridine–alcohol mixture the melting point of the compound increased progressively and after three recrystallizations it attained a maximum value of 280 ± 2°[9] but the substance still showed a rotation of $-58.1°$ in pyridine. Next we prepared dibenzylidene-D-perseitol by Maquenne's procedure. In three experiments the products melted initially over ranges of 230–240°, 240–248° and 225–235°; after several recrystallizations from a pyridine–alcohol mixture the melting point reached the maximum value of 280 ± 2° and the specific rotation was $-57.9°$. The fact that recrystallization from pyridine–alcohol of dibenzylidene-D-perseitol, regardless of its method of preparation or its initial melting point, yields a final product melting at 280 ± 2° and rotating about $-58°$ suggests that the products obtained initially by the different procedures of preparation may be mixtures of diastereomers in various proportions. Fischer[10] first called attention to the possibility of the occurrence of diastereomers in cyclic benzylidene acetals, due to different configurations of the acetal carbon atom of the benzylidene group, in his discussion of the formation of the labile and stable forms of what is now known to be 3,5-benzylidene-gluco-*gulo*-heptitol.[11] In the case of dibenzylidene-D-perseitol four diastereomers are theoretically possible. Whether the product melting in a range of 150–155° obtained by the sulfuric acid method and that melting at 280 ± 2° represent two relatively pure diastereomeric forms must await further evidence. As mentioned in the experimental part, these two products yield identical tribenzoyl-dibenzylidene-D-perseitols upon benzoylation in pyridine solution and identical trimethyl-dibenzylidene-D-perseitols upon methylation with thallous hydroxide and methyl iodide; it therefore seems evident that their isomerism is not due to different positions of the acetal linkages, but is to be ascribed to the stereoisomerism of the benzylidene groups. Ordinary crystalline dimorphism seems improbable.[11] An interconversion of the configurations present in the asymmetric carbon atoms of the benzylidene groups is possibly favored by the basic conditions attending the recrystallization, benzoylation and methylation.

Proof of the Structure of 1,3:5,7-Dibenzylidene-D-perseitol.—In initial tests to determine the structure of dibenzylidene-D-perseitol a solution of the diacetal (m. p. 280 ± 2°) in 2-methoxyethanol ("methyl cellosolve") was found to be fully resistant to oxidation by aqueous sodium

---

[1] Presented Sept. 18, 1947, at the New York meeting of the American Chemical Society.

[2] For a review of the reasoning leading to the selection of the D-symbol in naming natural perseitol see Hudson, "Advances in Carbohydrate Chemistry," Vol. I, p. 14, Academic Press, Inc., New York, N. Y., 1945.

[3] Maquenne, *Compt. rend.*, **107**, 583 (1888).

[4] Avequin, *Journal de chimie médicale, de pharmacie et de toxicologie*, [1] **7**, 467 (1831).

[5] Hann and Hudson, THIS JOURNAL, **66**, 1909 (1944).

[6] Maquenne, *Ann. chim. phys.*, [6] **19**, 16 (1890).

[7] L. Maquenne, "Les sucres et leurs principaux dérivés," Carré and Naud, Paris, 1900, p. 183.

[8] Lobry de Bruyn and Alberda van Ekenstein, *Rec. trav. chim.*, **18**, 151 (1899).

[9] The melting points of the higher-melting forms were determined on a Berl and Kullmann copper block and are corrected; melting points below 250° were determined in a Hershberg apparatus with the stem of the calibrated thermometer in the rapidly stirred bath. All the crystalline compounds described in the experimental part were recrystallized to constant melting point and specific rotation $[\alpha]^{20}D$; *c* is the concentration in 100 ml. of solution; the tube length was 4 dm.

[10] E. Fischer, *Ber.*, **27**, 1524 (1894).

[11] Hann, Ness and Hudson, THIS JOURNAL, **68**, 1769 (1946).

metaperiodate; this fact indicates that the structure of the compound does not include an α-glycol grouping. However, this limitation is by no means sufficient for establishing the structure since many conceivable structures conform with it. Additional evidence was sought through methylation studies. Attempts to methylate the dibenzylidene-D-perseitol melting at 153–155° with Purdie's reagents (silver oxide and methyl iodide) were unsuccessful, the diacetal being recovered almost quantitatively as the 280 ± 2° isomer by hot pyridine extraction of the silver oxide residues from the attempted methylation, but the methylation of the higher-melting isomer with Purdie's reagents gave nearly quantitative yields of a sirup showing the correct methoxyl content for a trimethyl-dibenzylidene-perseitol. Crystalline trimethyl-dibenzylidene-D-perseitol (m. p. 121–122°; $[\alpha]^{20}\text{D}$ $-43.5°$ in chloroform) was eventually obtained by methylation with thallous hydroxide and methyl iodide[12] of either the lower or higher melting dibenzylidene-D-perseitol. The hydrolysis of either the sirupy or the crystalline trimethyl-dibenzylidene-D-perseitol gave a crystalline trimethyl-D-perseitol (m. p. 120–121°; $[\alpha]^{20}\text{D}$ $+11.8°$ in water) which is not oxidized by sodium metaperiodate in aqueous solution. This evidence discloses the structure of the trimethyl derivative. Inspection of the formula of D-perseitol (I) shows that to fulfill the condition of absence of an α-glycol grouping in the trimethyl-D-perseitol, one methyl group must be at carbon atoms 1 or 2 and another at carbon atoms 6 or 7; of the four possible combinations of these positions, 1,6-, 1,7- and 2,7 are excluded because no combination of three methylated hydroxyl groups which includes such a pair can fulfill the condition that the trimethyl derivative be free of an α-glycol grouping; in the remaining 2,6-combination the third methyl group can be only at position 4 to exclude such a grouping, and therefore the compound is 2,4,6-trimethyl-D-perseitol. Accordingly, dibenzylidene-D-perseitol is a 1,3,5,7-diacetal and there can be little doubt that it is specifically 1,3:5,7-dibenzylidene-D-perseitol. The trimethyl ether of the diacetal is to be formulated as 2,4,6-trimethyl-1,3:-5,7-dibenzylidene-D-perseitol.

Proof of the Structure of 1,3:5,7-Dimethylene-D-perseitol.—The treatment of D-perseitol with aqueous formaldehyde solution and concentrated hydrochloric acid yielded a crystalline dimethylene-D-perseitol which melted at 251–253° and rotated $[\alpha]^{20}\text{D}$ $-19.3°$ in water. This dimethylene acetal was not oxidized by aqueous sodium metaperiodate, a result which shows that it possesses no α-glycol grouping. It formed a tritosyl ester which did not react when heated with sodium iodide in acetone solution at 100° for two hours, an indication by the Oldham–Rutherford rule that tosyl groups are not attached at carbon atoms 1 or 7, which accordingly must be involved in the acetal linkages. Proof that the hydroxyl groups in the diacetal are secondary and at positions 2, 4 and 6 follows from the fact that methylation of the dimethylene-D-perseitol with thallous hydroxide and methyl iodide gave a crystalline trimethyl-dimethylene-D-perseitol (m. p. 140–141°; $[\alpha]^{20}\text{D}$ $-6.2°$ in water) which was identical with the product resulting from the methylenation of authentic 2,4,6-trimethyl-D-perseitol (obtained through the benzylidene series as described) with aqueous formaldehyde solution and concentrated hydrochloric acid. Accordingly, the acetal linkages in the dimethylene perseitol must be at positions 1, 3, 5 and 7 and there can be little doubt that the substance is specifically 1,3:5,7-dimethylene-D-perseitol. Its tritosyl derivative is to be formulated as 2,4,6-tritosyl-1,3:5,7-dimethylene-D-perseitol and its methyl ether as 2,4,-6-trimethyl-1,3:5,7-dimethylene-D-perseitol.

Does the 1,3:5,7-diacetal structure that is present in the dibenzylidene- and dimethylene-D-perseitols conform with the previously mentioned generalizations regarding cyclic acetal structures of polyhydric alcohols?[5] An inspection of the formula of perseitol (I) shows according to the generalizations that the only pair of secondary hydroxyl groups favored to enter into methylene or benzylidene acetal formation consists of those at positions 3 and 6, which are *gamma* in position and *trans* in configuration. This combination was regarded as favorable to the formation of an acetal of the dioxepane seven-atom ring type when the generalizations were proposed because such an acetal was a prominent feature in the mannitol series. Later, it was also found in the closely similar L-rhamnitol (6-desoxy-L-mannitol) series.[13] Subsequent studies in the iditol[14] and talitol[15] series and the present one in the perseitol series fail to disclose the presence of such a dioxepane acetal although the configurations in each case seem favorable for its occurrence. However, in the iditol, talitol and perseitol configurations there are favorable positions for one or more dioxane six-atom ring acetals which conflict with the dioxepane ring acetal. Thus in perseitol the 1,3-acetal obviously competes with a 3,6-acetal. There is no such competition in the mannitol and rhamnitol series. We would accordingly extend the original generalizations by stating that formation of the dioxepane ring may not occur if competing dioxane-ring acetals are indicated by favorable positions in the configuration. It is readily evident that such competition will always occur in the case of any heptitol.

Using some L-perseitol which had been made by the reduction of D-gala-L-*manno*-heptose, we have prepared the enantiomorphous 1,3:5,7-dibenzylidene-L-perseitol and 1,3:5,7-dimethylene-L-perseitol, following the procedures already described. The L-perseitol behaved precisely like its enantio-

---

[12] The procedure of Fear and Menzies, *J. Chem. Soc.*, 937 (1926).

[13] Haskins, Hann and Hudson, THIS JOURNAL, **67**, 1800 (1945).

[14] Hann and Hudson, *ibid.*, **67**, 602 (1945).

[15] Hann, Haskins and Hudson, *ibid.*, **69**, 624 (1947).

morph and it was especially noted that the indications of lability in the dibenzylidene acetal were duplicated.

A 1,3:5,7-dibenzylidene-D,L-perseitol melting at 271–272° was obtained by one recrystallization of a mixture of equal amounts of the higher-melting (280°) D- and L- forms from pyridine–alcohol solution. In an effort to obtain a D,L-compound from the low-melting (153–155°) D- and L- forms, cold solutions of equal amounts of them in 2-methoxyethanol were mixed and concentrated to crystallization at room temperature by an air current. The product melted at 235–237° and two recrystallizations from the same solvent raised the melting point to 271–272° which did not change on further recrystallization. The optical-crystallographic measurements which Mr. George L. Keenan reports (see Table I) show that the crystals of 1,3:5,7-dibenzylidene-D,L-perseitol (m. p. 271°) represent a true racemate having indices of refraction that are different from those of the crystals of its components.

An aqueous solution of equal amounts of the enantiomorphous dimethylene-perseitols deposited crystals of a dimethylene-D,L-perseitol hemihydrate melting at 236–237° and showing no detectable rotation in aqueous solution. The fact that it is a hydrate indicates that the crystals are a true racemate because the component enantiomorphs crystallize in anhydrous condition. The measurements of Mr. Keenan (see Table I) verify the true racemic character.

We thank Mr. Charles A. Kinser and Mrs. Betty Mount for the microchemical analyses and Mr. George L. Keenan for the optical-crystallographic measurements.

Experimental

1,3:5,7-Dibenzylidene-D-perseitol and Some of its Derivatives

1,3:5,7-Dibenzylidene-D-perseitol.—(A) To a solution of 5.0 g. of D-perseitol in 25 ml. of 50% sulfuric acid 25 ml. of benzaldehyde and 25 ml. of ethanol were added; needle-like crystals appeared in the clear solution in a few minutes. After three hours at 25° the magma was thinned with 100 ml. of ethanol, filtered and the precipitate washed with water and alcohol. The product (8.2 g., 89%) melted at 153–155° and there was no change in its weight or melting point upon digesting it with 200 ml. of hot water for two hours. It was insoluble in usual organic solvents except pyridine and 2-methoxyethanol. Its $[\alpha]^{20}$D value in pyridine (*c*, 0.5) was −58.2°. In four repetitions products were obtained which melted at 152–154°, 153–155°, 151–154° and 150–152°.

Anal. Calcd. for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23. Found: C, 64.74; H, 6.29.

The dibenzylidene-D-perseitol (m. p. 153–155°) was recrystallized by solution in 15 parts of pyridine and the addition of 40 parts of alcohol. The melting point of the once-recrystallized product was 268 ±2°; after a second recrystallization it melted at 277 ±2° and after a third it reached a maximum value of 280 ±2°. Its $[\alpha]^{20}$D value was then −58.1° in pyridine (*c*, 0.9), and its analysis showed that there had been no change in its elementary composition.

(B) The dibenzylidene-D-perseitol was prepared by the procedure of Maquenne.[3] A slurry of suspended D-perseitol, prepared by adding 5 ml. of ethanol to a solution of 2.5 g. of the heptitol in 5 ml. of hot water, was cooled to 0° and saturated with dry hydrochloric acid gas; 5 ml. of benzaldehyde was added and the mixture agitated until solution was complete. Small needles soon separated and the magma which formed on allowing the reaction mixture to stand at 25° for three hours was thinned with 100 ml. of ethanol and the crystalline product was separated by filtration, washed with water and alcohol and dried. The yield was 3.9 g. (83%). The compound, which melted at 230–240°, was recrystallized by solution in 12 parts of pyridine and the addition of 20 parts of alcohol and it formed small needles which melted at 280 ±2° and rotated −57.9° in pyridine (*c*, 0.9). A mixed melting point determination with the dibenzylidene-D-perseitol (m. p. 280 ±2°) prepared by the pyridine–alcohol recrystallization of dibenzylidene-D-perseitol (m. p. 153–155°) showed no depression. A second preparation of the dibenzylidene-D-perseitol by Maquenne's method gave a yield of 97% of a product which melted at 240–248°. A quantitative yield of diacetal showing a melting point of 225–235° was deposited from a homogeneous solution of 2.0 g. of D-perseitol, 10 ml. of concentrated hydrochloric acid, 5 ml. of benzaldehyde and 5 ml. of ethanol which was allowed to stand at 5° for four hours. The melting point of these products was raised to 280 ±2° by recrystallization from pyridine–alcohol mixtures.

Stability of 1,3:5,7-Dibenzylidene-D-perseitol against Oxidation by Sodium Metaperiodate.—To a solution of 0.1086 g. of 1,3:5,7-dibenzylidene-D-perseitol (m. p. 280 ±2°) in 90 ml. of 2-methoxyethanol 3.0 ml. (5.73 molecular equivalents) of aqueous 0.534 *M* sodium metaperiodate solution was added and the volume was adjusted to 100 ml. at 25° with 2-methoxyethanol. Analysis of 10-ml. aliquots at the expiration of one, six and forty-eight hours showed that no oxidant had been consumed, indicating that dibenzylidene-D-perseitol has no pair of contiguous hydroxyl groups in its structure.

2,4,6-Tribenzoyl-1,3:5,7-dibenzylidene-D-perseitol.—To an ice-cold solution of 2.0 g. of 1,3:5,7-dibenzylidene-D-perseitol (m. p. 280 ±2°) in 20 ml. of pyridine, 3.0 ml. (50% excess) of benzoyl chloride was added dropwise. The reaction mixture was allowed to stand three days at room temperature (22–25°) and then poured into 500 g. of crushed ice. The gummy precipitate which formed was washed with water and upon trituration with 50 ml. of ethanol it yielded 3.2 g. (90%) of a crystalline product which melted at 181–182°. The compound was recrystallized from 100 parts of ethanol as long prismatic rods which melted at 181–182° and showed an $[\alpha]^{20}$D value +76.8° in chloroform (*c*, 0.85). It is soluble in pyridine, acetone, benzene and hot ethanol and nearly insoluble in water, cold ethanol and methanol, and hexane. Benzoylation of the dibenzylidene-perseitol (m. p. 153–155°) under the same conditions gave the same tribenzoate in a yield of 90%. This result is in agreement with the conclusion that these two dibenzylidene-D-perseitols are not ring-position isomers.

Anal. Calcd. for $C_{42}H_{36}O_{10}$: C, 71.99; H, 5.18; C_6H_5CO, 45.0. Found: C, 71.95; H, 5.19; C_6H_5CO, 44.7.

2,4,6-Trimethyl-1,3:5,7-dibenzylidene-D-perseitol.—Repeated attempts to obtain a trimethyl derivative of the 1,3:5,7-dibenzylidene-D-perseitol (m. p. 280 ±2°) by methylation of the diacetal with silver oxide and methyl iodide (Purdie's reagents) gave nearly quantitative yields of a stiff brown sirup which showed a methoxyl content of 21.82% (theory 21.63%). A crystalline 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol was obtained by the thallous hydroxide and methyl iodide procedure in the following manner. A suspension of 2.0 g. of 1,3:5,7-dibenzylidene-D-perseitol (m. p. 280 ±2°) in 20 ml. of acetone and 40 ml. (4.5 molecular equivalents) of 0.584 *N* thallous hydroxide solution was concentrated *in vacuo* to dryness and further dried by reconcentration with absolute alcohol. The dry residue was refluxed for eighteen hours with 40 ml. of methyl iodide and 10 g. of Drierite, the yellow precipitate was separated by filtration and washed with methyl iodide and the filtrate was evaporated to dryness; it yielded 2.0 g. of a solid melting at 110–130°. This product was dissolved in 20 ml. of acetone and following the addition of 36 ml. (4.0 molecular equivalents) of 0.584 *N* thallous hydroxide the reaction mixture was concentrated as before to a dry solid and refluxed for eighteen hours with 40 ml. of methyl iodide and 10 g. of Drierite; the solids were removed by filtration and the filtrate was concentrated and yielded 1.8 g. of a gummy solid. This product was dissolved in 20 ml. of acetone and the second step repeated as just described. The final filtrate was evaporated and it yielded 1.8 g. of a sirup which was dissolved in 5 parts of warm methanol; as the solution cooled it deposited 0.75 g. of prismatic crystals (m. p. 120–122°) and concentration of the mother liquor gave a further 0.25 g. (m. p. 112–120°) to make the total yield of product 1.0 g. (45%). The compound was recrystallized from 10 parts of methanol and yielded 0.8 g. of pure 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol as rosettes of prisms which melted at 121–122° and showed an $[\alpha]^{20}\mathrm{D}$ value −43.5° in chloroform (*c*, 0.62). It is readily soluble in acetone, chloroform, ether and benzene, moderately soluble in methanol and ethanol, and practically insoluble in water. Methylation of the dibenzylidene-D-perseitol (m. p. 153–155°) by this procedure gave a 45% yield of the same trimethyl derivative.

Anal. Calcd. for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02; OCH_3, 21.6. Found: C, 66.91; H, 7.12; OCH_3, 21.7.

2,4,6-Trimethyl-D-perseitol.—(A) A solution of 5.0 g. of sirupy 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol in a mixture of 30 ml. of ethanol, 20 ml. of water and 2 ml. of concentrated hydrochloric acid was refluxed for six hours and after neutralization with sodium hydroxide the solution was concentrated *in vacuo* to dryness. The sirupy dark residue was extracted with 50 ml. of ethanol, the solution was warmed on the steam-bath with decolorizing carbon, filtered, and the yellow filtrate was concentrated *in vacuo* to dryness; it yielded 3.0 g. (quantitative) of a dark yellow viscous sirup. The sirup was dissolved in 50 ml. of hot acetone and as the solution cooled fine needles (1.0 g., m. p. 119–121°) formed; they were separated by filtration and the filtrate upon concentration to a small volume and dilution with 50 ml. of ether gave a further 1.0 g. of product (m. p. 114–119°) to make the total yield 2.0 g. (67%). The compound was recrystallized from 20 parts of acetone as small needles which melted at 120–121° and showed $[\alpha]^{20}\mathrm{D}$ values of +11.8° in water (*c*, 1.03) and +14.7° (*c*, 0.84) in ethanol. It is readily soluble in methanol and ethanol, moderately soluble in chloroform and acetone, and nearly insoluble in benzene, hexane, ether and isopentane. (B) A solution of 0.5 g. of 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol (m. p. 121–122°) in a mixture of 10 ml. of ethanol, 1.0 ml. of concentrated hydrochloric acid and 9 ml. of water was refluxed for six hours, neutralized with sodium hydroxide and concentrated *in vacuo*. The residue was extracted with 10 ml. of acetone, the filtered extract was concentrated to a volume of 3 ml., seeded and crystallization allowed to progress at 5° for eighteen hours; the yield of needles of 2,4,6-trimethyl-D-perseitol melting at 120–121° and rotating +11.8° in water (*c*, 0.42) was 0.17 g. (54%). The product did not depress the melting point of 2,4,6-trimethyl-D-perseitol prepared from sirupy 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol as just described under (A), but it did depress the melting point of 2,4,6-trimethyl-1,3:5,7-dibenzylidene-D-perseitol (m. p. 121–122°).

Anal. Calcd. for $C_{10}H_{22}O_7$: C, 47.23; H, 8.72; OCH_3, 36.6. Found: C, 46.97; H, 8.70; OCH_3, 36.5.

Stability of 2,4,6-Trimethyl-D-perseitol against Oxidation by Sodium Metaperiodate.—To a solution of 0.1031 g. of 2,4,6-trimethyl-D-perseitol in 30 ml. of water 5.0 ml. (5.92 molecular equivalents) of 0.480 *M* aqueous sodium metaperiodate was added and the volume adjusted to 50 ml. with water. The analysis of 5-ml. aliquots at the expiration of one, two, eighteen and forty-two hours showed no consumption of oxidant. This result indicates the absence of a contiguous pair of hydroxyl groups in trimethyl-D-perseitol, which limits its structure to that of 2,4,6-trimethyl-D-perseitol.

1,3:5,7-Dimethylene-D-perseitol and Some of its Derivatives

1,3:5,7-Dimethylene-D-perseitol.—A solution of 20.0 g. of D-perseitol in a mixture of 20 ml. of concentrated hydrochloric acid and 25 ml. of aqueous 37% formaldehyde solution was evaporated at 25° in a crystallizing dish placed in an evacuated desiccator containing small beakers holding concentrated sulfuric acid and pellets of sodium hydroxide. After five days, the damp solid was triturated with 25 ml. of absolute ethanol and the slurry was evaporated to dryness in the evacuated desiccator. The dry solid was transferred to a Büchner funnel with 100 ml. of cold ethanol, washed and dried. The yield of product, which melted at 230–240°, was 16.8 g. (76%). The compound was recrystallized from 15 parts of 50% ethanol and it formed long needles which melted at 251–253° and showed $[\alpha]^{20}\mathrm{D}$ −19.3° in water (*c*, 1.0). It is soluble in hot water and hot aqueous alcohols but nearly insoluble in chloroform, ether, benzene and cold methanol and ethanol.

Anal. Calcd. for $C_9H_{16}O_7$: C, 45.76; H, 6.83. Found: C, 45.79; H, 6.82.

Stability of 1,3:5,7-Dimethylene-D-perseitol against Oxidation by Sodium Metaperiodate.—To a solution of 0.2410 g. of 1,3:5,7-dimethylene-D-perseitol in 30 ml. of water, 7.10 ml. (4.0 molecular equivalents) of 0.575 *M* sodium metaperiodate solution were added and the volume was adjusted to 50 ml. with water. The analysis of 5-ml. aliquots at the expiration of one, two, eighteen, forty-two and one hundred fifteen hours indicated that no oxidant had been consumed.

Dibenzoyl- and Monobenzoyl-1,3:5,7-dimethylene-D-perseitol.—A solution of 1.5 g. of 1,3:5,7-dimethylene-D-perseitol in 37.5 ml. of pyridine was cooled to 0° and 2.7 ml. (3.6 molecular equivalents) of benzoyl chloride was added dropwise. After standing for forty-eight hours at 25° the reaction mixture was poured into 300 ml. of ice-cold water and the crystalline precipitate (2.4 g., m. p. 175–195°) which formed was recrystallized from 50 parts of ethanol and yielded 1.0 g. (36%) of pure dibenzoyl-1,3:5,7-dimethylene-D-perseitol as long lath-like crystals which melted at 212–214° and showed $[\alpha]^{20}\mathrm{D}$ −30.2° in acetone (*c*, 1.04) and −9.3° in chloroform (*c*, 0.86). The compound is soluble in acetone, chloroform, pyridine, benzene and hot ethanol and nearly insoluble in water, cold ethanol, hexane and ether.

Anal. Calcd. for $C_{23}H_{24}O_9$: C, 62.16; H, 5.44; C_6H_5CO, 47.3. Found: C, 62.19; H, 5.49; C_6H_5CO, 47.5.

The aqueous solution from which the 2.4 g. of reaction product had been separated by filtration was extracted with chloroform and the washed and dried extract was concentrated *in vacuo* to dryness. The crystalline residue was recrystallized from 30 parts of ethanol and gave 0.3 g. (21%) of pure monobenzoyl-1,3:5,7-dimethylene-D-perseitol in the form of small needles which melted at 217–219° and showed $[\alpha]^{20}\mathrm{D}$ +74.3° in acetone (*c*, 0.43) and +31.2° in chloroform (*c*, 0.21). The crystals are readily soluble in pyridine and hot ethanol, slightly soluble in acetone and chloroform and nearly insoluble in water, cold ethanol, benzene, hexane and ether.

Anal. Calcd. for $C_{16}H_{20}O_8$: C, 56.46; H, 5.92; C_6H_5CO, 30.9. Found: C, 56.51; H, 5.97; C_6H_5CO, 31.1.

2,4,6-Tribenzoyl-1,3:5,7-dimethylene-D-perseitol.—To a suspension of 1.5 g. of powdered 1,3:5,7-dimethylene-D-perseitol in 30 ml. of ice-cold pyridine, 4.5 ml. (6 molecular equivalents) of benzoyl chloride was added dropwise and the mixture was agitated gently on a shaking machine at 25° for forty-eight hours. The doughy product which precipitated upon pouring the mixture into ice-cold water was crystallized from 40 ml. of hot ethanol and gave two fractions (2.8 g. melting at 161–162° and 0.5 g. melting at 156–159°) of nearly pure tribenzoyldiacetal. The combined crystalline product (3.3 g., 95%) was recrystallized from 15 parts of ethanol and formed prisms which melted at 161–162° and showed $[\alpha]^{20}D$ +2.6° in acetone (*c*, 0.96) and +14.4° in chloroform (*c*, 1.0). The tribenzoate is readily soluble in acetone, chloroform, pyridine, benzene and ether and nearly insoluble in cold ethanol, water and hexane.

Anal. Calcd. for $C_{30}H_{28}O_{10}$: C, 65.68; H, 5.15; C_6H_5CO, 57.5. Found: C, 65.84; H, 5.22; C_6H_5CO, 57.3.

Ditosyl- and Monotosyl-1,3:5,7-dimethylene-D-perseitol.—Ice-cold solutions of 6.0 g. (3.7 molecular equivalents) of *p*-toluenesulfonyl chloride in 10 ml. of pyridine and 2.0 g. of 1,3:5,7-dimethylene-D-perseitol in 50 ml. of the same solvent were mixed and allowed to stand at 20–25° for two days. The gummy precipitate which formed on pouring the reaction mixture into 300 ml. of ice-cold water gradually crystallized and the crude product (3.0 g., 50%; m. p. 150–160°) was recrystallized from 40 parts of ethanol and yielded 2.5 g. of pure ditosyl-1,3:5,7-dimethylene-D-perseitol in the form of long lath-like crystals which melted at 164–165° and showed $[\alpha]^{20}D$ −2.5° in chloroform (*c*, 0.9) and −8.7° in acetone (*c*, 1.04). The substance is soluble in pyridine, acetone, benzene and chloroform and nearly insoluble in water, cold ethanol, ether and hexane.

Anal. Calcd. for $C_{22}H_{28}O_{11}S_2$: C, 50.72; H, 5.18; S, 11.77. Found: C, 50.72; H, 5.23; S, 11.69.

The mother liquor from which the 3.0 g. of ditosyl-1,3:5,7-dimethylene-D-perseitol had been separated was extracted with 250 ml. of chloroform and the washed and dried extract was concentrated *in vacuo* to dryness. The crystalline residue was twice recrystallized from 10 parts of alcohol and yielded 0.5 g. of pure monotosyl-1,3:5,7-dimethylene-D-perseitol as elongated six-sided plates which melted at 174–175° (decomposition); a chloroform solution (*c*, 0.22) of the compound failed to show optical activity, but in acetone solution (*c*, 0.88) a rotation $[\alpha]^{20}D$ +9.2° was observed. The substance is soluble in acetone, pyridine and hot ethanol, slightly soluble in chloroform and nearly insoluble in water, benzene, hexane and ether.

Anal. Calcd. for $C_{16}H_{22}O_9S$: C, 49.22; H, 5.68; S, 8.21. Found: C, 49.40; H, 5.81; S, 8.10.

2,4,6-Tritosyl-1,3:5,7-dimethylene-D-perseitol.—A solution of 2.0 g. of 1,3:5,7-dimethylene-D-perseitol and 10.0 g. (six molecular equivalents) of *p*-toluenesulfonyl chloride in 30 ml. of pyridine was allowed to stand in the dark at 20–25° for eight weeks and then poured into 800 ml. of ice and water. The product (6.2 g., quantitative; m. p. 160–165°) was recrystallized from 80 parts of ethanol and gave 5.1 g. of pure 2,4,6-tritosyl-1,3:5,7-dimethylene-D-perseitol which melted at 172–173° and rotated $[\alpha]^{20}D$ −4.7° in chloroform (*c*, 0.86) and −5.9° in acetone (*c*, 0.85). The compound is soluble in chloroform, acetone and pyridine and nearly insoluble in water and cold alcohols. The tritosyl derivative did not react with sodium iodide in acetone solution upon heating at 100° for two hours, a result which indicates that tosyl groups are not attached through primary hydroxyl groups.

Anal. Calcd. for $C_{30}H_{34}O_{13}S_3$: C, 51.56; H, 4.90; S, 13.76. Found: C, 51.47; H, 4.91; S, 13.69

2,4,6-Trimethyl-1,3:5,7-dimethylene-D-perseitol by the Methylation of 1,3:5,7-Dimethylene-D-perseitol.—A solution of 4.0 g. of 1,3:5,7-dimethylene-D-perseitol in 110 ml. (3.8 molecular equivalents) of 0.584 *N* aqueous thallous hydroxide[11] was concentrated *in vacuo* to dryness, with the inlet tube carrying a soda lime tube to exclude carbon dioxide, and the residue was dried through concentration *in vacuo* by two evaporations with absolute ethanol. The gray powdery product was refluxed for twenty hours with 10.0 g. of Drierite and 80 ml. of methyl iodide, the solids were separated by filtration and the filtrate was evaporated to dryness; it yielded 3.0 g. of crystalline material melting at 140–170°. This substance was dissolved in 90 ml. of 0.584 *N* thallous hydroxide and the solution concentrated *in vacuo* to dryness as previously described, the crystalline residue was refluxed for twenty-two hours with 10 g. of Drierite and 60 ml. of methyl iodide, the mixture was filtered and the filtrate was evaporated to dryness; it yielded 3.0 g. of product melting at 132–134°. After one more methylation in the same manner there was obtained 2.8 g. of product melting at 138–139°, which was recrystallized from 10 parts of absolute ethanol and yielded 2.1 g. (45%) of pure 2,4,6-trimethyl-1,3:5,7-dimethylene-D-perseitol as needles melting at 140–141° and rotating $[\alpha]^{20}D$ −6.2° in water (*c*, 0.83). A mixed melting point with the compound prepared by the methylenation of 2,4,6-trimethyl-D-perseitol with aqueous 37% formaldehyde solution and concentrated hydrochloric acid, as described in the following paragraph, showed no depression.

2,4,6-Trimethyl-1,3:5,7-dimethylene-D-perseitol by the Methylenation of 2,4,6-Trimethyl-D-perseitol.—A solution of 1.0 g. of 2,4,6-trimethyl-D-perseitol in a mixture of 2.5 ml. of concentrated hydrochloric acid and 2.5 ml. of aqueous 37% formaldehyde solution was allowed to evaporate to dryness in an evacuated desiccator containing small beakers of concentrated sulfuric acid and pellets of sodium hydroxide; after five days the dry solid (1.0 g., 90%; m. p. 138–142°) which resulted was crystallized from 20 parts of ether and yielded 0.8 g. (70%) of pure 2,4,6-trimethyl-1,3:5,7-dimethylene-D-perseitol melting at 140–141° and rotating $[\alpha]^{20}D$ −6.0° in water (*c*, 0.81). The compound is readily soluble in chloroform, acetone, benzene and water, sparingly soluble in ether and nearly insoluble in hexane.

Anal. Calcd. for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97; OCH_3, 33.4. Found: C, 51.81; H, 8.00; OCH_3, 33.5.

Acetals of the L- and D,L-Perseitols

1,3:5,7-Dibenzylidene-L-perseitol.—About seven grams of crystalline L-perseitol was prepared by the reduction of D-gala-L-*manno*-heptose. From one gram of it the 1,3:5,7-dibenzylidene-L-perseitol was prepared as has been described in the case of the D-form, using sulfuric acid as the catalyst. The crystals melted at 153–155° and rotated +57.7° in pyridine. They were then recrystallized by refluxing with fifteen parts of pyridine fifteen minutes and adding thirty parts of ethanol to the hot solution; the product then melted at 280 ± 2° and rotated +57.6° in pyridine. Both enantiomorphs thus show the same behavior, namely, a labile form passing on recrystallization to a stable form.

1,3:5,7-Dibenzylidene-D,L-perseitol.—A mixture of equal amounts of the D- and L-enantiomorphs, each of which melted at 280 ± 2°, was dissolved in ten parts of hot pyridine and crystallized by the addition of 25 parts of ethanol. The fine needle-like crystals appear to be a true racemate according to Mr. Keenan's measurements of their indices of refraction (see table) and this conclusion is supported by our observation that they are much less soluble in pyridine than are those of the components. The racemate melts at 271–272°, a lower temperature than the 280° value shown by its components. The same racemate was likewise prepared from equal amounts of the labile forms of the enantiomorphs (m. p. 153–155°) by dissolving them in one thousand parts of 2-methoxyethanol without heating, followed by evaporation of the solvent at 27° by an air current. The crystalline residue melted at 235–237°; one recrystallization of it from hot 2-methoxyethanol raised this value to 267–268°, and a second increased it to 271–272°. Further recrystallization from either 2-methoxyethanol or the pyridine–ethanol mixture caused no change.

1,3:5,7-Dimethylene-L-perseitol.—The substance was prepared essentially as has been described for its enantiomorph. The recrystallized product melted at 252–254° and showed $[\alpha]^{20}D$ +19.0° in water (*c*, 1.01). Like its enantiomorph it was not oxidized by sodium metaperiodate.

1,3:5,7-Dimethylene-D,L-perseitol.—A solution of equal amounts of the enantiomorphs in fifty parts of hot 80% ethanol deposited fine needle-like crystals which melted at 236–237° and showed no rotation in aqueous solution. The substance is a hemihydrate which becomes anhydrous when heated at 120° *in vacuo* for some hours. The hemihydrate crystals obviously represent a true racemate. The anhydrous material also melts at 236–237°; apparently the water of crystallization leaves the hemihydrate before the substance melts.

Anal. Calcd. for $C_9H_{16}O_7 \cdot {}^1/_2H_2O$: C, 44.08; H, 6.99; H_2O, 3.67. Found: C, 43.90; H, 7.08; H_2O, 3.59.

Calcd. for $C_9H_{16}O_7$ (anhydrous): C, 45.76; H, 6.83. Found: C, 45.91; H, 6.83.

The racemic character of 1,3:5,7-dibenzylidene- and 1,3:5,7-dimethylene-D,L-perseitols was verified by determination of their optical-crystallographic properties by Mr. George L. Keenan. The data for the compounds and their component optically active forms are compiled in Table I.

TABLE I

OPTICAL-CRYSTALLOGRAPHIC PROPERTIES OF THE 1,3:5,7-DIBENZYLIDENE- AND 1,3:5,7-DIMETHYLENE PERSEITOLS

	Dibenzylidene perseitol		Dimethylene perseitol	
	D or L	D,L	D or L	D,L-hemihydrate
$n\alpha$	1.567[a]	1.583[a]	1.515[a]	1.530[a]
$n\beta$	1.615[b]	1.613[b]	1.535[b]	Indeterminate
$n\gamma$	1.625	1.637[b]	1.540[b]	1.530[b]
Elongation	Negative	Negative	Negative	Negative
Extinction	Parallel and inclined	Parallel	Parallel	Parallel and inclined
M. p., °C.	280	271	251	236

[a] Shown lengthwise. [b] Shown crosswise. All the substances crystallize as rods. The refractive indices are for ordinary light at 25° and are ±0.002.

Summary

Proof is presented that dibenzylidene-D-perseitol (dibenzylidene-D-manno-D-*gala*-heptitol) is the 1,3:5,7-dibenzylidene diacetal. Neither it nor the trimethyl-D-perseitol which is obtained by its methylation and hydrolysis is oxidized by sodium periodate and the absence of α-glycol groupings in this related pair of compounds limits the structure of the diacetal to that of 1,3:5,7-dibenzylidene-D-perseitol and that of the derived trimethyl-heptitol to 2,4,6-trimethyl-D-perseitol.

The condensation of D-perseitol with formaldehyde yields a diacetal which must be 1,3:5,7-dimethylene-D-perseitol since its trimethyl derivative is identical with the compound formed by methylenation of 2,4,6-trimethyl-D-perseitol.

The enantiomorphous 1,3:5,7-dibenzylidene- and 1,3:5,7-dimethylene-L-perseitols have been prepared from D-gala-L-*manno*-heptitol and they combine with the D-forms to form true racemate crystals.

BETHESDA, MARYLAND RECEIVED SEPTEMBER 29, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

The Cleavage of Tetraacetyl-β-D-thioglucosides with Bromine in Acetic Acid[1]

BY WILLIAM A. BONNER

Several years ago it was shown[2] that phenyl tetraacylglucosides were brominated quantitatively when treated with excess bromine in glacial acetic acid. That bromination occurred at the *para* position was shown by hydrolysis of the glucoside and isolation of the brominated aglucone, *p*-bromophenol. In this respect the phenyl glycosides, which are cyclic acetals, resemble true phenyl alkyl ethers such as anisole.

It seemed desirable to extend this reaction to the phenyl polyacylthioglycosides, and to determine whether these undergo similar *para*-bromination. Such was anticipated, since aromatic thioethers are known[3] to undergo nuclear halogenation with readiness. In addition, adducts of bromine to the sulfur atom of the thioglycoside were considered likely, since halogens have been shown[4] to add readily to organic sulfides to form what are presumably halo sulfonium halides.

When phenyl tetraacetyl-β-D-thioglucoside in glacial acetic acid was treated with about thirteen equivalents of bromine and permitted to stand at room temperature for several hours, a white, crystalline material was isolated. On recrystallization pure α-D-glucose pentaacetate was obtained. The crude reaction product was not pure α-D-glucose pentaacetate, however, since its specific rotation (88.5 to 91.7°, depending upon reaction conditions) and its melting point (98–103°) were somewhat below those for the pure substance. The presence of small quantities of the β-anomer may explain these low values, as well as the presence of other impurities. The crude material, however, was substantially α-D-glucose pentaacetate, since this was obtained in reasonable purity on one or two recrystallizations. Based on pentaacetate the yield of crude product varied between 75 and 81%, depending upon reaction conditions.

This striking and unexpected reaction which involves cleavage of the acylated thioglucoside and replacement of the sulfur moiety with acetoxy was found to be quite general with respect to the thioaglucone. Both benzyl tetraacetyl-β-D-thioglucoside and ethyl tetraacetyl-β-D-thioglucoside produced α-D-glucose pentaacetate in comparable

---

[1] Presented before the Division of Sugar Chemistry and Technology of the American Chemical Society. New York, September, 1947.

[2] Hurd and Bonner. THIS JOURNAL, **67**, 1764 (1945).

[3] Bourgeois, *Ber.*, **28**, 2321 (1895); Böeseken and Waterman, *Rec. trav. chim.*, **29**, 321 (1910); Bourgeois and Abraham, *ibid.*, **30**, 418 (1911).

[4] Patein. *Bull. soc. chim.*, **50**, 201 (1888); Fries and Vogt, *Ann.*, **381**, 337 (1911); Chelintzev, *J. Russ. Phys.-Chem. Soc.*, **44**, 1885 (1913).