

hol it was obtained in colorless elongated six-sided plates which melted at 119–120° (cor.); yield 1.9 g. (86%).

Anal. Calcd. for $C_{24}H_{20}O_8$: C, 72.07; H, 5.34; C_6H_5CO , 37.1. Found: C, 72.21; H, 5.28; C_6H_5CO , 37.0.

1,6-Dibenzoyl-2,3,4,5-tetraacetyl-dulcitol from 1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol.—The solution of 0.7 g. of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol in 25 cc. of a rearranging solution (prepared by adding 2 cc. of concentrated sulfuric acid dropwise to an ice-cold mixture of 70 cc. of acetic anhydride and 30 cc. of acetic acid) was complete in fifteen minutes at 20°. Shortly thereafter spontaneous crystallization of characteristic quadrilateral plates of 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol occurred. After standing overnight at 20° the reaction mixture was filtered and the separated tetraacetate (0.6 g.; 86%) recrystallized from 10 parts of glacial acetic acid. The substance melted at 224–225° (cor.) and a mixed melting point with authentic 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol⁸ gave the same value.

2,3,4,5-Dibenzylidene-dulcitol from 1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol.—A solution of 20 g. of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol in 25 cc. of chloroform was cooled in an ice-bath and 5 cc. of 0.1 *N* sodium methylate solution added. The mixture was allowed to stand at 5° for twenty hours, and after addition of 5 cc. of 0.1 *N* sulfuric acid, the solvent was removed by concentration *in vacuo*, and the dry residue extracted with 20 cc. of warm alcohol. The dibenzylidene-dulcitol, which separated from the extract as it cooled, was recrystallized from 7 parts of 95% alcohol or 25 parts of 50% alcohol and obtained in approximately rectangular plates which melted at 149–150° (cor.); yield 1.1 g. or 85%.

Anal. Calcd. for $C_{20}H_{22}O_8$: C, 67.02; H, 6.19. Found: C, 67.08; H, 6.29.

1,6-Diacetyl-2,3,4,5-dibenzylidene-dulcitol.—(1) A solution of 0.2 g. of 2,3,4,5-dibenzylidene-dulcitol in a mixture of 2 cc. of pyridine and 2 cc. of acetic anhydride was allowed to stand at room temperature. After two hours,

spontaneous crystallization of clusters of prisms occurred from the solution and after twenty hours they were filtered off and recrystallized from 50 parts of alcohol by addition of 8 parts of dioxane; yield 0.25 g. (quantitative). The substance melts at 168–169° (cor.). A mixed melting point determination with 1,6-diacetyl-dulcitol,³ which melts at almost the same temperature, 167–168° (cor.), gave a melting point range of 161–165° (cor.). (2) A rapid stream of dry hydrochloric acid gas was passed through a suspension of 1.8 g. of 1,6-diacetyl-dulcitol³ in 3 cc. of benzaldehyde for three minutes. Complete solution occurred during the first minute and was followed by an immediate separation of crystalline material. After standing overnight, the pasty mass was triturated with 5 cc. of ether, and the solid reaction product separated by filtration. Recrystallized from a mixture of alcohol and dioxane, the pure compound melted at 168–169° (cor.) and a mixed melting point determination with 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol prepared by acetylation of 2,3,4,5-dibenzylidene-dulcitol, as described in the preceding paragraph, showed a melting point of 168–170° (cor.); yield 2.5 g. (83%).

Anal. Calcd. for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92; CH_3CO , 19.5. Found: C, 65.18; H, 5.99; CH_3CO , 19.4.

Summary

The dibenzoate of a new dibenzylidene-dulcitol has been prepared from 1,6-dibenzoyl-dulcitol and benzaldehyde. The dibenzoate is converted to the known 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol by an acid acetylating mixture. The diacetate of the diacetal is identical with 1,6-diacetyl-dibenzylidene-dulcitol prepared from 1,6-diacetyl-dulcitol and benzaldehyde. These facts establish the structure of the diacetal as 2,3,4,5-dibenzylidene-dulcitol.

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

A Second 2,3,4,5-Dibenzylidene-dulcitol

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In a recent communication¹ we described a 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol [m. p. 119–120° (cor.)] which was obtained from 1,6-dibenzoyl-dulcitol and benzaldehyde by the condensing action of gaseous hydrochloric acid. It has now been observed that the substitution of fused zinc chloride as a condensing agent in the reaction yields not only this derivative of melting point 119–120°, but in addition an isomer which melts at 147–148° (cor.). It will be shown that both of the isomers are 1,6-dibenzoyl-2,3,4,5-

dibenzylidene-dulcitol. For purposes of clarity, the previously described isomer (m. p. 119–120°) will be designated provisionally as the stable isomer (or I) and the newly discovered isomer (m. p. 147–148°), which can be converted into the stable isomer (I), will be designated the unstable isomer (or II). The yield of the unstable isomer (II) was markedly affected by the character of the zinc chloride employed and by the temperature at which the condensation was conducted. As described in the experimental part, a commercial fused zinc chloride of reagent quality was su-

(1) Haskins, Hann and Hudson, *THIS JOURNAL*, **64**, 136 (1942).

perior in condensing action and in production of the unstable isomer (II) to the same zinc chloride which had been re-fused alone or in contact with dry hydrochloric acid gas. The effect of temperature was also quite marked; condensations conducted at room temperature (23–25°) yielded 67% of the unstable isomer (II) and 17% of the stable isomer (I), but at 60° a 71% yield of the latter compound was obtained and none of the unstable isomer (II) could be isolated. The failure to obtain the unstable isomer (II) at the more elevated temperature suggested that it was converted into the stable isomer (I) under the experimental conditions employed. A test, performed by allowing the pure crystalline unstable isomer (II) to stand at 60° for twenty-four hours in the presence of benzaldehyde and fused zinc chloride, gave a quantitative transformation to the stable isomer (I). This conversion under such mild experimental conditions would seem to exclude acyl migration of the benzoyl groups as a factor in the isomerism. Additional evidence supporting the conclusion that acyl migration had not occurred was attained when it was found that the unstable isomer (II), upon treatment with an acid acetylating mixture, was converted to the known 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol.² Since it has already been shown¹ that the stable isomer (I) is also converted to 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol under the same conditions, it seems evident that the isomerism is to be ascribed to the position or stereo structure of the two benzylidene groups. In the general case of a 1,6-dibenzoyl-dibenzylidene-dulcitol there are three possible position isomers [(2,3:4,5), (2,4:3,5), (2,5:3,4)] and each of the benzylidene residues contains an asymmetric carbon atom. Because of this complexity it is possible at the present time to designate the structure only as 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol. Since the isomers cannot now be identified by structural or stereo differences we shall, as previously mentioned, provisionally name the stable isomer (I) (m. p. 119–120°) and compounds derived from it, as members of series I, and the unstable isomer (II) (m. p. 147–148°) and its derivatives as members of series II. The unstable isomer (II), upon debenzoylation, yields a new 2,3,4,5-dibenzylidene-dulcitol II (m. p. 173–174°). The latter substance, upon treatment with appropriate reagents, yields a series of disubstituted derivatives (summarized

in Table I) differing in melting point and solubility from similar derivatives of the previously known¹ 2,3,4,5-dibenzylidene-dulcitol I (m. p. 149–150°). As would be expected, neither the

TABLE I
COMPARISON OF MELTING POINTS OF DERIVATIVES OF
2,3,4,5-DIBENZYLIDENE-DULCITOLS I AND II

Derivative	Dibenzylidene- dulcitol Series I	Dibenzylidene- dulcitol Series II
	M. p. (cor.), °C.	M. p. (cor.), °C.
Parent dibenzylidene-dulcitol	149–150°	173–174°
1,6-Dibenzoyl-	119–120	147–148
1,6-Diacetyl-	169–170	167–168
1,6-Ditosyl-	167–168	175–176
1,6-Ditrityl-	184–186	240–242
1,6-Diiodo-	127–128	162–163

parent compounds nor their derivatives exhibit optical activity. The 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol II was converted to 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol I by allowing it to stand with benzaldehyde and fused zinc chloride at 60° for twenty-four hours, and the diacetyl derivative thus obtained yielded 2,3,4,5-dibenzylidene-dulcitol I upon deacetylation. The ready conversion of the diacetals to ditrityl derivatives, and to ditosyl derivatives which were convertible to diiodo compounds upon treatment with sodium iodide and acetic anhydride, constitutes additional supporting evidence that the parent diacetals contain two free primary hydroxyl groups, and supports the previous conclusion that no acyl migration of benzoyl groups has occurred in the course of the synthesis of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II.

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

1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol I from 1,6-Dibenzoyl-dulcitol, Benzaldehyde and Zinc Chloride at 60°.—A mixture of 3 g. of 1,6-dibenzoyl-dulcitol, 3 g. of powdered fused zinc chloride and 12 cc. of benzaldehyde was heated at 60° for twenty-four hours. The homogeneous liquid reaction mixture was treated with 10 cc. of alcohol and upon cooling the solution it deposited 3.1 g. (71%) of the previously described 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol¹ I, which melted at 119–120° (cor.) and showed no depression in melting point upon admixture with an authentic sample prepared by the hydrochloric acid method.

1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II from 1,6-Dibenzoyl-dulcitol, Benzaldehyde and Zinc Chloride at 20°.—The solution of a suspension of 2.5 g. of 1,6-di-

(2) Hann, Maclay and Hudson, *THIS JOURNAL*, **61**, 2432 (1939).

benzoyl-dulcitol and 2.5 g. of powdered zinc chloride in 10 cc. of benzaldehyde was complete after vigorous agitation for one hour at room temperature. Shortly thereafter crystals formed in the reaction mixture and gradually increased in amount to form a pasty mass. After eighteen hours, the crystals were separated by filtration and washed successively with water, alcohol and petroleum ether. The yield was 2.4 g. (67%). The compound was recrystallized from a mixture of 30 parts of alcohol and 10 parts of dioxane and obtained in colorless needles which melted at 147–148° (cor.).

Anal. Calcd. for $C_{34}H_{30}O_8$: C, 72.07; H, 5.34; C_6H_5CO , 37.1. Found: C, 72.19; H, 5.40; C_6H_5CO , 37.0.

The benzaldehyde mother liquor and washings, after being cooled to 5° for twenty-four hours, deposited 0.6 g. (17%) of the stable isomer (I). In two parallel experiments, the zinc chloride was re-fused directly and also in contact with a current of dry hydrochloric acid gas. In each of these experiments, 1.6 g. of unchanged 1,6-dibenzoyl-dulcitol was recovered and 1.2 g. (92% based on the 1,6-dibenzoyl-dulcitol which had reacted) of the stable isomer (I) was obtained, but none of the unstable isomer (II) could be isolated.

1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol I from 1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II, Benzaldehyde and Zinc Chloride at 60°.—A mixture of 0.5 g. of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II (m. p. 147–148°), 0.5 g. of powdered fused zinc chloride and 2 cc. of benzaldehyde was heated at 60° for twenty-four hours. The solution of the reaction mixture in 5 cc. of warm alcohol deposited 0.45 g. (90%) of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol I as it cooled. From a parallel experiment with 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol I, benzaldehyde and zinc chloride the benzoylated diacetal was recovered unchanged in quantitative yield.

1,6-Dibenzoyl-2,3,4,5-tetraacetyl-dulcitol from 1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II.—A solution of 0.5 g. of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II in 25 cc. of a rearranging solution (prepared by adding 2 cc. of concentrated sulfuric acid dropwise to an ice-cold mixture of 70 cc. of acetic anhydride and 30 cc. of glacial acetic acid) was allowed to stand at 20°. After fifteen minutes characteristic quadrilateral plates of 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol began to deposit in the solution and after eighteen hours they were removed by filtration and washed with ether. The yield was 0.5 g. (quantitative). After one recrystallization from ten parts of acetic acid the compound melted at 224–225° (cor.) and a mixed melting point with authentic 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol² showed no melting point depression.

2,3,4,5-Dibenzylidene-dulcitol II from 1,6-Dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II.—A solution of 2 g. of 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol II in 25 cc. of chloroform was cooled in an ice-bath and 5 cc. of 0.1 *N* sodium methylate solution was added. The mixture was allowed to stand at 5° for eighteen hours and, after addition of 5 cc. of 0.1 *N* sulfuric acid, the solvent was removed and the dry residue extracted with 40 cc. of boiling absolute alcohol. The diacetal, which deposited from the alcoholic solution as it cooled, was recrystallized from 30 parts of alcohol and formed clusters of prisms. The yield

of the pure compound, which melted at 173–174° (cor.), was 0.9 g. (69%).

Anal. Calcd. for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 66.97; H, 6.15.

1,6-Diacetyl-2,3,4,5-dibenzylidene-dulcitol II.—A solution of 0.6 g. of 2,3,4,5-dibenzylidene-dulcitol II in a mixture of 2 cc. of acetic anhydride and 2 cc. of pyridine, upon standing for a short time, deposited crystals of the 1,6-diacetyl derivative. After standing for twenty-four hours, the reaction mixture was poured over crushed ice and the precipitate removed by filtration and recrystallized from a mixture of 40 parts of alcohol and 10 parts of dioxane. The pure substance formed elongated prisms which melted at 167–168° (cor.). A mixed melting point determination with 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol I, which has nearly the same melting point, namely, 168–169° (cor.), gave the depressed value of 162–164° (cor.).

Anal. Calcd. for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92; CH_3CO , 19.5. Found: C, 65.03; H, 6.01; CH_3CO , 19.3.

1,6-Diacetyl-2,3,4,5-dibenzylidene-dulcitol I from 1,6-Diacetyl-2,3,4,5-dibenzylidene-dulcitol II.—A mixture of 0.7 g. of 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol II, 0.7 g. of powdered fused zinc chloride and 3 cc. of benzaldehyde was allowed to stand at 60° for twenty-four hours. The reaction mixture was dissolved in 10 cc. of warm alcohol and upon cooling, 0.7 g. of material melting at 164–166° (cor.) was deposited from the solution. The crude product apparently still contained a small amount of unchanged 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol II, but it consisted principally of 1,6-diacetyl-2,3,4,5-dibenzylidene-dulcitol I because upon deacetylation with sodium methylate in the usual manner it gave a yield of 0.5 g. (88%) of 2,3,4,5-dibenzylidene-dulcitol I.

1,6-Ditriptyl-2,3,4,5-dibenzylidene-dulcitol II.—To a cold solution of 1.7 g. of triphenylmethyl chloride in 10 cc. of pyridine, 1.0 g. of finely powdered 2,3,4,5-dibenzylidene-dulcitol II was added. Solution of the diacetal occurred readily and after two hours a crystalline deposit of the ditriptyl derivative formed. After seventy-two hours the reaction mixture was poured over crushed ice and the precipitate separated by filtration. The crude product, which was contaminated with triphenylcarbinol, was extracted with hot alcohol and the insoluble residue was recrystallized from 25 parts of dioxane in the form of needles which melted at 240–242° (cor.).

Anal. Calcd. for $C_{68}H_{60}O_6$: C, 82.63; H, 5.98. Found: C, 82.70; H, 6.18.

1,6-Ditosyl-2,3,4,5-dibenzylidene-dulcitol II.—This derivative was obtained in a yield of 91% by the action of tosyl chloride in pyridine solution upon 2,3,4,5-dibenzylidene-dulcitol II. It was recrystallized from 7 parts of dioxane and obtained in fine needles melting at 175–176° (cor.).

Anal. Calcd. for $C_{34}H_{34}O_{10}S_2$: C, 61.24; H, 5.14; S, 9.62. Found: C, 61.43; H, 5.16; S, 9.57.

1,6-Diiodo-2,3,4,5-dibenzylidene-dulcitol II.—A solution of 0.6 g. of 1,6-ditosyl-2,3,4,5-dibenzylidene-dulcitol II and 0.6 g. of sodium iodide in 15 cc. of acetic anhydride was refluxed for one hour. The sodium salt of *p*-toluenesulfonic acid deposited in the solution as the reaction pro-

gressed. The cooled reaction mixture was poured over crushed ice and the precipitated diiodo-diacetal removed by filtration and recrystallized from 80 parts of absolute alcohol. The compound crystallized in quadrilateral plates which melted with decomposition at 162–163° (cor.). The yield was 0.5 g. (quantitative).

Anal. Calcd. for $C_{20}H_{20}O_4I_2$: C, 41.54; H, 3.49. Found: C, 41.42; H, 3.67.

Disubstituted Derivatives of 2,3,4,5-Dibenzylidene-dulcitol I.—These compounds were prepared in the same manner as the isomeric compounds of 2,3,4,5-dibenzylidene-dulcitol II. (a) The 1,6-ditrityl-2,3,4,5-dibenzylidene-dulcitol I deposited from its solution in 5 parts of dioxane in the form of fine needles which melted at 184–186° (cor.).

Anal. Calcd. for $C_{38}H_{30}O_8$: C, 82.63; H, 5.98. Found: C, 82.76; H, 6.02.

(b) 1,6-Ditosyl-2,3,4,5-dibenzylidene-dulcitol I was obtained in a yield of 91% in the form of fine needles. It was recrystallized from 5 parts of dioxane and melted when pure at 167–168° (cor.).

Anal. Calcd. for $C_{34}H_{34}O_{10}S_2$: C, 61.24; H, 5.14. Found: C, 61.40; H, 5.14.

(c) 1,6-Diiodo-2,3,4,5-dibenzylidene-dulcitol I formed in elongated prisms upon cooling its solution in 70 parts of absolute alcohol. It melted at 127–128° (cor.). The yield was quantitative.

Anal. Calcd. for $C_{20}H_{20}O_4I_2$: C, 41.54; H, 3.49. Found: C, 41.56; H, 3.49.

Summary

The condensation of 1,6-dibenzoyl-dulcitol and benzaldehyde by fused zinc chloride at 60° yielded the 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol of melting point 119–120° (cor.) previously obtained when gaseous hydrochloric acid was employed as a condensing agent; it is now designated the stable isomer (I). When the condensation through zinc chloride was conducted at 20° an isomeric 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol melting at 147–148° (cor.) was obtained. The latter isomer, because of its ease of conversion into the stable isomer (I) of melting point 119–120° (cor.), will be designated the unstable isomer (II). Both compounds yield 1,6-dibenzoyl-2,3,4,5-tetraacetyl-dulcitol upon treatment with an acid acetylating mixture, hence their isomerism is due to position or stereo-isomerism of the benzylidene groups. The compounds upon debenzoylation yield two different 2,3,4,5-dibenzylidene-dulcitol, from which two corresponding series of disubstituted derivatives differing in melting point and other physical properties may be obtained.

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[CONTRIBUTION FROM THE ANIMAL CHEMISTRY AND NUTRITION SUBSECTION OF IOWA STATE COLLEGE]

The Preparation of $\Delta^{6,8(14)}$ -, $\Delta^{7,9(11)}$ -, $\Delta^{7,14}$ - and $\Delta^{8,14}$ -Cholestadienes¹

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The preparation of various cholestane derivatives possessing di-unsaturation in rings B and C or rings B and D was made possible by the recent preparation² of Δ^8 - and $\Delta^{8(14)}$ -cholestenes which possess mono-unsaturation in ring C. Thus, $\Delta^{6,8(14)}$ -, $\Delta^{7,9(11)}$ -, $\Delta^{7,14}$ - and $\Delta^{8(14)}$ -cholestadienes were prepared from Δ^8 - and $\Delta^{8(14)}$ -cholestenes by various methods. The methods of preparation and the specific rotations of these cholestadienes were compared with those of known analogous steroid derivatives possessing di-unsaturation in rings B and C or rings B and D. The double bonds are located in ring A or B or rings A and B in the hitherto known cholestadienes which are $\Delta^{2,4}$ -cholestadiene ($\Delta^{2,4}$ -coprostadiene), $\Delta^{3,5}$ -cholestadiene, $\Delta^{4,6}$ -cholestadiene (referred to as "7-dehydrocholestene isomer")³ and $\Delta^{5,7}$ -cholesta-

diene (referred to as 7-dehydrocholestene).⁴

$\Delta^{6,8(14)}$ -cholestadiene (I) was prepared by the alcoholic hydrochloric acid dehydration of Δ^8 -cholesten-7-ol (II) which was obtained by the aluminum isopropoxide reduction of Δ^8 -cholesten-7-one (III).² The double bond probably rearranges from the 8- to the 8(14)-position during the treatment with alcoholic hydrochloric acid. The structure of $\Delta^{6,8(14)}$ -cholestadiene (I) is supported by its method of preparation, its non-formation of a maleic anhydride addition product and its absorption spectrum maximum at about 245 μ . Only one steroid derivative is known to contain a $\Delta^{6,8(14)}$ -unsaturated structure and this compound, $\Delta^{6,8(14)}$ -cholestadiene-3,9-diol ($[\alpha]_D -19.7^\circ$), was prepared by the action of perbenzoic acid on $\Delta^{6,8}$ -cholestadiene-3-ol.⁵ The structure of cholestadieneol-3C is not known,⁵ al-

(1) Journal Paper No. J915 of the Iowa Agricultural Experiment Station, Project No. 506.

(2) Eck and Hollingsworth, *This Journal*, **63**, 2986 (1941).

(3) Eck and Hollingsworth, *ibid.*, **63**, 107 (1941).

(4) Dimroth and Trautmann, *Ber.*, **69B**, 669 (1936).

(5) Windaus, Linsert and Eckhardt, *Ann.*, **534**, 22 (1938).