[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF CREIGHTON UNIVERSITY]

REACTIONS OF ALDEHYDES OR MONOALDEHYDO ISOPROPYLIDENE DIALDEHYDE SUGARS WITH 5-(*p*-HYDROXY OR *p*-ACETOXYPHENYL)CYCLOHEXANEDIONE-1,3 AND DERIVATIVES

PHILIPPOS E. PAPADAKIS

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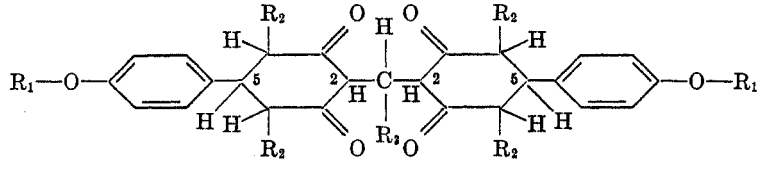
The condensation of cyclic β-diketones with aldehydes has been well studied (1–4) and one such diketone, dimethone (5,5-dimethylcyclohexanedione-1,3), is widely used for the identification of aliphatic and aromatic aldehydes.

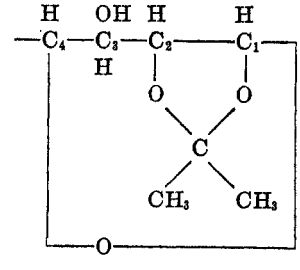
Current interest in the physiological properties of compounds derived from the condensation of cyclic β-diketones with aldehydes has led us to prepare alkylidene and arylidene derivatives Type (I) of two β-diketones, 5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 and 5-(*p*-hydroxyphenyl)cyclohexanedione-1,3, the preparation and properties of which we described several years ago (5). The present paper reports also the preparation of a dialdehyde



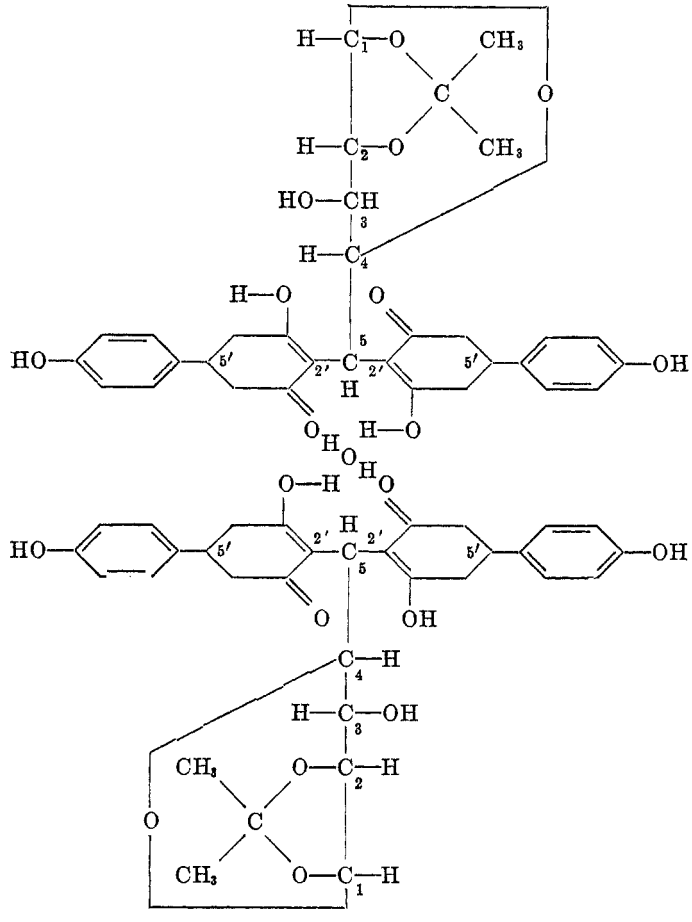
(I)

TABLE I

LEGEND FOR FORMULA I

EXPT. NO.	R_1	R_2	R_3
1	H	H	H
2	CH_3CO	$COOC_2H_5$	H
3	CH_3CO	$COOC_2H_5$	CH_3
4	CH_3CO	$COOC_2H_5$	$CH_3(CH_2)_2$
5	CH_3CO	$COOC_2H_5$	$CH_3(CH_2)_5$
6	CH_3CO	$COOC_2H_5$	$CH_3(CH_2)_8$
7	CH_3CO	$COOC_2H_5$	C_6H_5
8	CH_3CO	$COOC_2H_5$	*p*-OH-*m*-$OCH_3C_6H_3$
9	CH_3CO	$COOC_2H_5$	*p*-OHC_6H_4
10	H	H	

sugar derivative [5,5-Bis-⟨2′,2′-{5′,5′-(*p*-hydroxyphenyl)cyclohexanedione-1′,3′}⟩-1,2-isopropylidene-5-desoxy-D-xylofuranose]$_2$·H_2O Type (II).



II

A general procedure for the preparation of methone derivatives with aliphatic and aromatic aldehydes was described by Horning and Horning (6). Aldehydo sugars react in a similar way with methone to form *bis* derivatives. Hockett and Schaefer (7) prepared aldehydo-2,4,3,5-diethylidene-L-xylodimethone by boiling a water solution of diethylidene-L-xylose and methone.

The method of preparation of the alkylidene and arylidene *bis*-derivatives of the dione (I) is described in the experimental part and the results are summarized in Table II. The sugar derivative was prepared by boiling for five minutes a water solution of 1,2-acetone-D-xylo-trihydroxyglutaric acid dialdehyde (8) and 5-(*p*-hydroxyphenyl)cyclohexanedione-1,3 (5), using a method similar to that of Hockett and Schaefer (7). The product obtained corresponds to a formula

TABLE II

DATA ON ALKYLIDENE, ARYLIDENE, AND CARBOHYDRATE *Bis*-(SUBSTITUTED CYCLOHEXANEDIONE-1,3) DERIVATIVES

EXPT. NO.	M.P., °C.	FORMULA	ANALYSES			
			Calc'd		Found	
			C	H	C	H
1	249	$C_{25}H_{24}O_6$	71.41	5.75	71.09	5.64
2	178	$C_{41}H_{44}O_{16}\cdot H_2O$	60.74	5.67	60.39	5.44
3	175	$(C_{42}H_{46}O_{16})_2\cdot H_2O$	61.84	5.77	61.43	6.08
					61.75	5.24
					62.00	5.66
4	129	$C_{44}H_{50}O_{16}$	63.29	6.03	63.26	6.28
5	83	$C_{47}H_{56}O_{16}$	64.30	6.54	64.23	6.30
		$C_{27}H_{36}O_9$	64.08	7.14		
6	117	$C_{50}H_{62}O_{16}$	65.34	6.80	65.40	6.79
6a	143	$(C_{50}H_{62}O_{16})_2\cdot H_2O$	64.69	6.84	64.94	7.29
7	168	$C_{47}H_{48}O_{16}$	64.96	5.56	64.75	5.66
8	178	$C_{48}H_{50}O_{18}\cdot H_2O$	61.79	5.58	61.35	5.45
		$(C_{48}H_{50}O_{18})_2\cdot H_2O$	62.40	5.52	62.46	5.37
9	183	$C_{47}H_{48}O_{17}\cdot 3H_2O$	60.12	5.76	60.05	5.78
					60.52	5.87
10	169–172	$(C_{32}H_{34}O_{10})_2\cdot H_2O$	65.40	6.00	65.42	6.09
					65.36	6.22
					65.42	6.26

$(C_{32}H_{34}O_{10})_2\cdot H_2O$ and is assumed to have the structure [5,5-Bis-⟨2′,2′-{5′,5′-(*p*-hydroxyphenyl)cyclohexanedione-1′,3′}⟩-1,2-isopropylidene-5-desoxy-D-xylofuranose]$_2\cdot H_2O$, Type (II). It is thought that stabilization of such a structure might be possible through bonding hydrogens, as indicated.

By analogy we may assume that the *bis*-dimethone derivative of the aldehydo-2,4,3,5-diethylidene-L-xylose of Hockett and Schaefer (7) is a hemi-hydrate.

Anal. Calc'd for $(C_{25}H_{36}O_8)_2\cdot H_2O$: C, 63.44; H, 7.87.

Hockett and Schaefer found: C, 63.3, 63.4; H, 8.52, 8.14.

Their calculated values, on the basis of the dimethone $C_{25}H_{36}O_8$ were C, 64.7; H, 7.7. This assumption is supported by the work of Ness and Fletcher (9) who prepared the anhydrous compound, m.p. 233–239° and obtained satisfactory analytical results. (The Hockett and Schaefer compound had m.p. 196–199°.)

The condensation products obtained in the course of the present work are assumed to have the following structures Type (1):

(1) 2,2-Methylene-*bis*-[5-(*p*-hydroxyphenyl)cyclohexanedione-1,3]

(2) 2,2-Methylene-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]

(3) [2,2-Ethylidene-*bis*-{5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3}]$_2\cdot H_2O$

(4) 2,2-Butylidene-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]

(5) 2,2-Heptylidene-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]
(6) 2,2-Decylidene-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]
(7) 2,2-Benzylidene-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]
(8) [2,2-Vanillydene-*bis*-{5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3}]$_2 \cdot H_2O$
(9) 2,2-(*p*-Hydroxybenzylidene)-*bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3]$\cdot 3H_2O$
(10) [5,5-Bis-⟨2′,2′-{5′,5′-(*p*-hydroxyphenyl)cyclohexanedione-1′,3′}⟩-1,2-isopropylidene-5-desoxy-D-xylofuranose]$_2 \cdot H_2O$ (II).

The structures of the compounds (1–10) as specified by the names are tentative. The results of further investigation and the physiological properties of these compounds will be reported in the future. Table II shows the analytical results and melting points of the compounds (1–10).

EXPERIMENTAL

5-(p-Acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 and *5-(p-hydroxyphenyl)cyclohexanedione-1,3* were prepared according to methods described previously (5). The aldehyde derivatives of the diketone type (I), experiments 1–9, were formed by a modified Horning and Horning method (6). In a typical experiment 0.02 mole of 5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3, 0.01 mole of an aldehyde, and a third of a drop of piperidine were dissolved in the least amount of 75% methanol and the solution was refluxed for half an hour. After evaporation of the methanol, cold water and a drop of dilute hydrochloric acid was added. The precipitate formed was filtered off and washed with small amounts of ether. The part that did not dissolve readily in ether was recrystallized from methanol. In cases where syrups were formed, after the evaporation of the methanol, water was added and the mixture was allowed to stand. The material solidified and formed a crust on the inner wall of the container. After several hours the water was decanted and the crust of material was removed, dried, and analyzed. The ether solution contained a yellow amorphous material, which was not analyzed. Details of purification varied depending on the solubilities of the reagents and products in the different solvents.

Compound 10 (assumed structure II) was synthesized by boiling a water solution of 5-(*p*-hydroxyphenyl)cyclohexanedione-1,3 (5) and 1,2-acetone-D-xylotrihydroxyglutaric dialdehyde (8) according to the Hockett and Schaefer method (7). The product melted at 169–172° with decomposition. On further heating there was bubbling, with the envelopes of the bubbles having opaque material which finally became a clear liquid of amber color at 205°.

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SUMMARY

The preparation of 2,2-(alkylidene or arylidene)-*bis*-[5-(*p*-hydroxyphenyl)-cyclohexanedione-1,3] or *bis*-[5-(*p*-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3] (I) has been described.

[5,5-Bis ⟨2′,2′-{5′,5′-(*p*-hydroxyphenyl)cyclohexanedione-1′,3′}⟩-1,2-isopropylidene-5-desoxy-D-xylofuranose]$_2$-monohydrate was synthesized from 5-(*p*-

hydroxyphenyl)cyclohexanedione-1,3 and 1,2-acetone-D-xylotrihydroxyglutaric dialdehyde, using the method of Hockett and Schaefer.

OMAHA, NEBR.

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