REACTIONS OF 1,5-DIKETONES

XVI.* CYCLOHEMIACETALS FROM δ-BICYCLANONES

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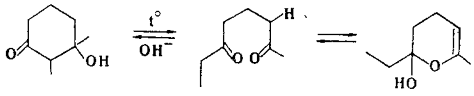
Two-ring 1,5-diketones of the benzylidenedicyclohexanone type are capable of existing in equilibrium with 4a-hydroxy-1,2,3,4,4a,5,6,7,8,9a-decahydroxanthenes, the position of which depends on the structure of the 1,5-diketone.

1,5-Diketones (A), which have an active methylene group in the 6 position relative to the carbonyl group, are converted to cycloketols (B) under the influence of bases [2]. The reverse transformation of the cycloketols to 1,5-diketones was also observed when they were heated [3] and in a number of reactions [4, 5]. The other possibility of cycloisomerization of 1,5-diketones – conversion to hydroxydihydropyrans (C) – was first observed for benzylidenebenzaldicyclohexanone [6]. In the crystalline form it exists as the stable cyclohemiacetal, but equilibrium A⇌C is established in solution, as confirmed by the ability of this compound to react with hydroxylamine to give a dioxime [7]. We later observed the same equilibrium in the case of benzylidenedicyclohexanone [8].



B A C

We examined the effect of substituent R in the linear group of a 1,5-diketone connecting two rings on its conversion to a cyclohemiacetal. For this, we obtained 1,5-diketones Ia-d, for which we used thermal decyclization of 8-R-tricyclo$[7.3.1.0^{2,7}]$tridecan-2-ol-13-ones (IIIa-d†). When IIIa-c are melted, mixtures of diketones Ia-c and hydroxydecahydroxanthenes IIa-c, respectively, are obtained. We were able to separate the mixtures of Ia, b-IIa, b by fractional crystallization. Compound IIc was isolated from the melt of ketol IIIc.

The IR spectra of crystalline substances Ia, b contain a band at 1710 cm^{-1} (C=O), whereas the absorption bands of a hydroxyl group and a double bond are absent. However, the absorption of a carbonyl group is absent in the spectra of IIa-c, whereas there are bands at 3400 and 3300 (OH) and 1620 cm^{-1} (C=C). The IR spectra of solutions of Ia, b and IIa, b correspond to mixtures of 1,5-diketones and hydroxydecahydroxanthenes. The IR spectra of solutions of Ia, b and IIc contain bands at 3600 (OH), 1710 (C=O), and 1620 cm^{-1} (C=C). The IR spectra of freshly prepared solutions of Ib and IIb are close to the spectra of the starting crystalline samples, but after 70 h they become identical and correspond to a mixture of both tautomeric forms.

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*See [1] for communication XV.

† These compounds were obtained by condensation of cyclohexanone with the appropriate aldehydes via the scheme of the diketone condensation [9]. Ketol IIIb has not been previously described; its structure follows from the method used to synthesize it and is confirmed by the IR spectrum, which contains bands at 3400 (OH) and 1710 cm^{-1} (C=O), and also by its ability to give a monosemicarbazone.

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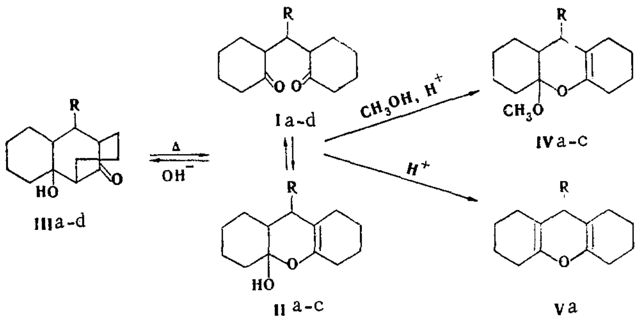
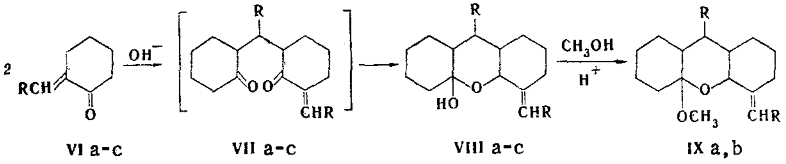


a R=C$_6$H$_5$; b R=p-CH$_3$OC$_6$H$_4$; c R=α-furyl; d R=H

The action of a methanol solution of HCl on a 1,5-diketones Ia-c, hydroxydecahydroxanthenes IIa-c, or mixtures of them gives methoxy derivatives IVa-c in the same yields.* The structure of methoxy derivatives IVa-c is confirmed by their IR spectra, in which there are bands at 2840 and 1110 cm^{-1} (CH$_3$O), whereas absorption of hydroxyl and carbonyl groups is absent. Compound IVb gives two singlets (two CH$_3$O groups, 6H) at 3.2-3.5 ppm in its PMR spectrum, whereas the PMR spectrum of IVc contains one singlet (one CH$_3$O group, 3H). Compounds Ia and IIa are dehydrated to octahydroxanthene Va under the influence of p-toluenesulfonic acid in benzene [8]. The reactions enumerated above correspond to the cyclic form of the compounds under consideration.

On the other hand, I and IIa, I and IIb, and IIc are converted by the action of alcoholic alkali to the corresponding bridged ketols IIIa-c via the scheme typical for 1,5-diketones. Dioximes were also obtained for I and IIa and I and IIb.

We determined the positions of the equilibria in solution (Ia$\rightleftharpoons$IIa and Ic$\rightleftharpoons$IIc) by means of the PMR spectra. The spectrum of a solution of an equilibrium mixture of Ia and IIa contains signals in the form of a doublet (J=7 Hz) at 3.60 ppm, which correspond to form IIa, and of a triplet (J=8.5 Hz) at 3.96 ppm, which corresponds to form Ia, The ratio of the areas of these signals, which is equal to the ratio of IIa to Ia, is 1:4 [8]. The ratio of form IIc to Ic with respect to the doublet (J=7 Hz) at 3.70 ppm and the triplet (J=7.5 Hz) at 4.03 ppm is 1:9. Thus the equilibrium in solutions of these compounds is shifted to favor the diketone, which is the only product that is formed when ketol IIId is melted. The IR spectrum of the melt of this ketol contained only carbonyl absorption (1705 cm^{-1}), and absorption of a hydroxyl group and of a double bond is absent. The action of a methanol solution of HCl on diketone Id brought about aldol-crotonic condensation to give ketol IIId and its dehydration product, whereas acetal Vd was not formed.



The introduction of an arylidene group into the 5 position of the hydroxydecahydroxanthene molecule increases its stability. Compound VIIIa in solution and in the crystalline state gives an IR spectrum in which carbonyl absorption is absent [5]. A similar pattern is also observed in the IR spectra of the dimers of 2-(p-methoxybenzylidene)cyclohexanone (VIb) and 2-furfurylidenecyclohexanone (VIc): carbonyl absorption is absent in them, but there are bands of a hydroxyl group (3480 cm^{-1}) and of a double bond (1640 cm^{-1}). This makes it possible to assign hydroxyhydroxanthene formulas VIIb and VIIc, respectively, to the dimers rather than 1,5-diketone formulas VIIb, c. Compound VIIIb is converted to 4a-methoxy-9-(p-methoxyphenyl)-5-benzylidene-1,2,3,4,4a,5,6,7,8,9a-decahydroxanthene (IXb) under the influence of a methanol solution of HCl.

The addition of 2-benzylidenecyclohexanone VIa to 2,6-dibenzylidenecyclohexanone X leads (apparently through a step involving the formation of 1,5-diketone XI) to XII. The structure of this compound is confirmed by its IR spectrum, in which a band is present at 3400 cm^{-1} (OH), whereas absorption at 1700 cm^{-1} (C=O) is absent, and also by methylation to 4a-methoxy-9-phenyl-4,5-dibenzylidene-1,2,3,4,4a,5,6,7,8,9a-decahydroxanthene (XIII) and dehydration to octahydroxanthene XIV. We obtained diketone XVI by re-

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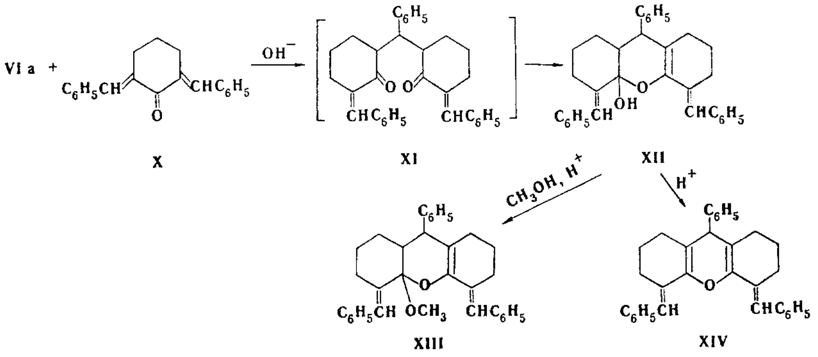
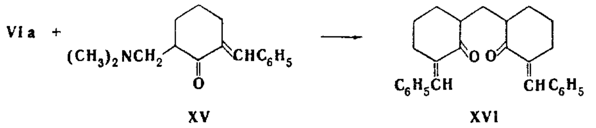
*See also [8].





action of ketone VIa with the hydrochloride of Mannich base XV. This compound forms a dioxime but is not methylated in methanol containing HCl and is not dehydrated by the action of p-toluenesulfonic acid in benzene. The IR spectra of the solid substance and solutions of it contain a band at 1680 cm^{-1} (conjugated carbonyl group), whereas absorption at 3200-3500 cm^{-1} is absent.

On comparing the facts presented above, one may conclude that the presence of a group (phenyl, substituted phenyl, furyl) attached to the methane carbon atom linking the two rings in the 1,5-diketone molecule promotes isomerization of the latter to a hydroxydecahydroxanthene. If the molecule additionally contains an arylidene group conjugated with the carbonyl group, the cyclization goes to completion. However, if there is no substituent attached to the methane carbon atom linking the two rings, cyclization is not observed even when there is an arylidene group in the ring.

EXPERIMENTAL

The IR spectra of mineral oil suspensions and 0.15 M solutions of the compounds in $CHCl_3$ were recorded with a UR-20 spectrometer. The PMR spectra of 0.5 M solutions of the compounds in deuterochloroform were recorded with a ZKR-60 spectrometer at 25°. The chemical shifts are given on the δ scale.

8-(p-Methoxyphenyl)tricyclo[7.3.1.$0^{2,7}$]tridecan-2-ol-13 (IIIb). A total of 40 ml of 1 N alcoholic KOH was added at 80° to 490 g (5 mole) of cyclohexanone, after which a solution of 68 g (0.5 mole) of p-methoxybenzaldehyde in 50 ml of ethanol was added with stirring in the course of 2.5 h. The solution was then heated for another 4 h, after which it was cooled, and the resulting precipitate was removed by filtration to give 113 g of IIIb. Information on this and the other substances is presented in Table 1.

Fusion of Ketols IIIa-d. A weighed sample of the ketol was melted in an argon atmosphere and maintained at 190-200° for 40-70 min. The cooled melt was then triturated with a fivefold volume of ether. The ether-insoluble material was the starting ketol (~ 15-20% of the starting quantity, identified by a mixed-melting-point determination with an authentic sample). On more prolonged heating, the amount of recovered starting ketol did not change. The ether solution was evaporated, and the residue (~ 80% of the starting mass) was triturated in warm petroleum ether. The petroleum ether extract was cooled to precipitate crystalline benzylidenedicyclohexanone (Ia) (from ketol IIIa) or p-methoxybenzylidenedicyclohexanone (Ib) (from ketol IIIb), which was separated and further purified by recrystallization from petroleum ether or alcohol. The filtrate obtained after separation of the 1,5-diketone was vacuum evaporated, and the residue was triturated with alcohol. The alcohol-insoluble solid was IIa (from ketol IIIa), 9-(p-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,9a-decahydro-4a-xanthenol IIb (from ketol IIIb), or 9-(α-furyl)-1,2,3,4,4a,5,6,7,-8,9a-decahydro-4a-xanthenol (from ketol IIIc). This solid was separated by filtration and further purified by recrystallization from alcohol. The filtrate was evaporated, and the residue (judging from thin-layer chromatography and the IR spectrum) was found to be a mixture of 1,5-diketone I and hydroxydecahydroxanthene II. The yields of Ib, IIb, and IIc in Table 1 are based on the pure desmotropes.

9-(p-Methoxyphenyl)-5-(p-methoxybenzylidene)-1,2,3,4,4a,5,6,7,8,9a-decahydro-4a-xanthenol (VIIIb). A total of 5 ml of 40% KOH solution was added with stirring to a solution of 7 g (0.03 mole) of 2-(p-methoxybenzylidene)cyclohexanone in 30 ml of ethanol, and after 24 h, 5.7 g of VIIIb was removed from the mixture by filtration. Another 1.2 g of VIIIb precipitated from the filtrate on standing.

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, deg C[a]	Empirical formula	Found, %		Calc., %		Yield, %
			C	H	C	H	
Ib[b]	107—109	$C_{20}H_{26}O_3$	76,1	8,3	76,4	8,3	38
IIb[c]	121—122	$C_{20}H_{26}O_3$	75,6	8,5	76,4	8,3	8
IIc[d]	154—155	$C_{17}H_{22}O_3$	74,1	8,5	74,4	8,0	14
III[b]	229—230	$C_{20}H_{26}O_3$	76,2	9,1	76,4	9,1	72
IVb	145—146	$C_{21}H_{28}O_3$	76,6	8,6	76,8	8,6	90
IVc	92—93	$C_{18}H_{24}O_3$	74,6	8,3	75,0	8,4	81
VIIIb	187—188	$C_{28}H_{32}O_4$	78,0	7,3	77,8	7,4	98
IXb	138,5—139,5	$C_{29}H_{34}O_4$	77,9	7,8	78,0	7,6	87
XII	140—142	$C_{33}H_{32}O_2$	85,8	7,6	86,1	6,9	87
XIII	96—97	$C_{34}H_{34}O_2$	86,8	7,6	86,1	7,2	92
XIV	164—166	$C_{33}H_{33}O$	89,8	6,9	89,5	6,8	58
XVI[e]	119—120	$C_{27}H_{28}O_2$	84,5	7,6	84,4	7,3	71

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[a] Compound IIIb was recrystallized from dioxane, VIIIb was recrystallized from benzene, and the remaining compounds were recrystallized from alcohol.

[b] The dioxime had mp 236-237° (dec., from dioxane). Found: N 7.9%. $C_{20}H_{28}N_2O_3$. Calculated: N 8.1%.

[c] The dioxime had mp 198-200° (dec., from alcohol). Found: N 9.0%. $C_{17}H_{24}N_2O_3$. Calculated: N 9.2%.

[d] The semicarbazone had mp 214-215° (dec., from aqueous dioxane). Found: N 11.3%. $C_{21}H_{29}N_3O_3$. Calculated: N 11.3%.

[e] The dioxime had mp 187-189° (dec., alcohol-dioxane). Found: N 6.4%. $C_{27}H_{32}N_2O_2$. Calculated: N 6.7%.

9-Phenyl-4,5-dibenzylidene-1,2,3,4,4a,5,6,7,8,9a-decahydro-4a-xanthenol (XII). A solution of 5.6 g of 2-benzylidenecyclohexanone in 15 ml of ethanol and 5 ml of 10% alcohol KOH was added to a suspension of 8.2 g of dibenzylidenecyclohexanone in 200 ml of ether, after which the mixture was stirred for 2 h and then allowed to stand at room temperature for 24 h. Ether (170 ml) was removed by distillation, the residue was shaken with 100 ml of water, and the resulting crystalline precipitate was removed by filtration and dried.

2-Dimethylaminomethyl-6-benzylidenecyclohexanone (XV) Hydrochloride. A mixture of 18.6 g (0.1 mole) of 2-benzylidenecyclohexanone, 3 g (0.1 mole) of paraformaldehyde, and 8 g (0.1 mole) of dimethylamine hydrochloride in 40 ml of ethanol acidified with a few drops of concentrated HCl was refluxed for 5 h, after which it was cooled, and the resulting precipitate was removed by filtration to give 24 g (88%) of XV with mp 152-152.5° (from alcohol-ether). Found: C 68.2; H 8.1; N 5.3%. $C_{16}H_{22}ClNO$. Calculated: C 68.7; H 7.9; N 5.0%. IR spectrum (mineral oil): 2400-2600 (ammonium band), 1680 (C=O), and 1620 cm^{-1} (C=C).

Bis(6-benzylidene-2-cyclohexanonyl)methane (XVI). Solutions of 3.7 g (0.02 mole) of benzylidenecyclohexanone in 20 ml of ethanol, 5.6 g (0.02 mole) of XV in 30 ml of ethanol, and 8 ml of 6 N aqueous sodium hydroxide were mixed, and the mixture was stirred for 17 h, cooled with ice, and acidified to pH 5 with concentrated HCl. The resulting precipitate was removed by filtration, washed with water, and dried to give 5.5 g of XVI.

Action of a Methanol Solution of HCl on Ia-d, IIa-c, VIIIb and XII. A 2.5-mmole sample of the compound under investigation was stirred with 15 ml of 0.25% HCl solution in absolute methanol at room temperature for 1-36 h. The course of the reaction was followed by means of TLC, and the reaction was carried out until the spot of the starting substance vanished on the chromatogram. The reaction product crystallized out from the solution and was removed by filtration and purified by recrystallization.

In the experiment with diketone Id, the precipitate obtained by the action of a methanol solution of HCl (exposure for 7 months) was found to be ketol IIId (19% yield, identified by a mixed-melting-point determination with an authentic sample). The filtrate remaining after separation of ketol IIId was poured into water, and the mixture was neutralized and extracted with ether. The residue remaining after removal of the ether by distillation was chromatographed on activity II Al_2O_3. Cyclohexanone eluted tricyclo[7.3.1.0^{2,7}]tridec-2(7)-en-13-one (14% yield, identified by means of comparison of the thin-layer chromatograms and IR spectra of the product and an authentic sample), whereas cyclohexane-ether (10:1) eluted the starting diketone (9%), and chloroform eluted ketol IIId (16%).

9-Phenyl-4,5-dibenzylidene-1,2,3,4,5,6,7,8-octahydroxanthene (XIV). A mixture of 2.1 g of XII, 40 ml of absolute benzene, and 50 mg of p-toluene-sulfonic acid was refluxed in a flask equipped with a Dean-Stark trap until water liberation ceased. The mixture was then washed with sodium bicarbonate solution and water, and the benzene layer was dried. The benzene was removed by evaporation, and the residue was recrystallized from dioxane-alcohol.

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