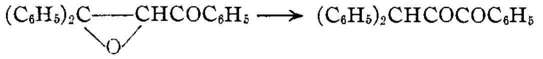
[Contribution from the Converse Memorial Laboratory of Harvard University]

The Tautomerism of Alpha Diketones. II. Benzhydryl Phenyl Diketone

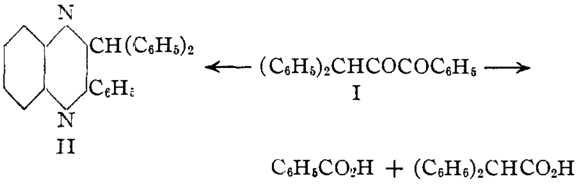
By E. P. Kohler and N. Weiner

In the first paper of this series[1] it was shown that benzyl phenyl diketone differs from the isomeric beta diketone not only in the extent to which it is enolized under various conditions but also with respect to the manner in which it is acylated and alkylated. In order to study the effect of an additional phenyl group we have prepared the corresponding benzhydryl compound by rearranging benzoyl diphenyl ethylene oxide with bases



$$(C_6H_5)_2C\overset{O}{—}CHCOC_6H_5 \longrightarrow (C_6H_5)_2CHCOCOC_6H_5$$

That the additional phenyl group has little if any effect on the reactions which involve both of the carbonyl groups, is shown by the ease with which the new diketone reacts with ortho phenylene diamine to form a quinoxaline derivative, and the rapidity with which it is oxidized to benzoic and diphenyl acetic acids by alkaline hydrogen peroxide



$$\underset{\text{II}}{} \longleftarrow \underset{\text{I}}{(C_6H_5)_2CHCOCOC_6H_5} \longrightarrow C_6H_5CO_2H + (C_6H_6)_2CHCO_2H$$

The additional phenyl group, however, has a marked effect on the enolization. Unlike the less highly phenylated compound the diketone does not form a copper derivative and does not develop color in an alcoholic solution of ferric chloride. It not only gives a negative result when titrated with bromine by the Kurt Meyer method but also resists bromination under all conditions. It therefore is completely ketonic, the additional phenyl group depressing the enolization as effectively as it does that of the isomeric phenyl dibenzoyl methane.

In strong aqueous alkalies the solid yellow diketone slowly turns red without dissolving. Its red solutions in alcoholic alkalies and in sodium alcoholate doubtless contain enolates but it is difficult to isolate them because in these alkaline solutions the diketone undergoes the benzilic rearrangement with the utmost ease—the counterpart of the ease with which phenyl dibenzoylmethane is cleaved to benzoic acid and desoxybenzoin

$$(C_6H_5)_2CHCOCOC_6H_5 + H_2O \longrightarrow \underset{\text{III}}{(C_6H_5)_2CHC(C_6H_5)OHCOOH}$$

Although these alkaline solutions are exceedingly unstable they were used successfully for methylating the diketone not only with dimethyl sulfate but also with methyl iodide. In each case but one product was obtained and a methoxyl determination showed that this is an O-methyl derivative. The diketone also was readily benzoylated, both by means of the Schotten–Baumann reaction and with benzoyl chloride in pyridine. Here likewise the result is a single compound—the O-benzoate. In respect to alkylation and acylation, therefore, benzhydryl phenyl diketone differs wholly not only from all beta diketones but also from all alpha keto esters that have been described.

$$\underset{\text{IV}}{(C_6H_5)_2C{=}C(OCH_3)COC_6H_5} \longleftarrow (C_6H_5)_2CHCOCOC_6H_5 \longrightarrow \underset{\text{V}}{(C_6H_5)_2{=}C(OCOC_6H_5)COC_6H_5}$$

Since the diketone is not enolized, both carbonyl groups are available for interaction with ketone reagents, but the two groups would not be expected to react with equal ease. Some reactions with agents of this type involve but one of the carbonyl groups and give rise to a single product. In these cases, doubtless, the outcome does not depend upon the relative activity of the groups but upon the relative stability of the two possible products. Thus the diketone is very easily reduced, both catalytically and with zinc and acid, and all methods of reduction give a single product

$$(C_6H_5)_2CHCOCOC_6H_5 + 2H \longrightarrow \underset{\text{VI}}{(C_6H_5)_2CHCOCHOHC_6H_5}$$

Here only the carbonyl group adjacent to phenyl appears to be affected but since it is known that the system $R^1COCHOHR^2 \rightleftharpoons R^1CHOHCOR^2$ is mobile both in acid and in basic media, the formation of a single product indicates only that the two possible carbinols differ greatly in stability, and the structure of the product shows which of the two is the more stable.

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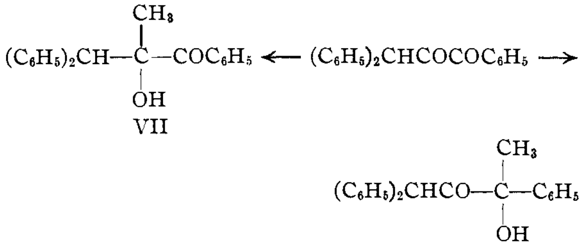
(1) Kohler and Barnes, This Journal, **54**, 211 (1932).

Similarly, the diketone reacts very readily with hydroxylamine acetate and at least 91% of the product consists of a single monoxime. The structure of this oxime could not be established with certainty, but whatever its structure, it doubtless represents merely the form most stable under the conditions of the experiment, because oxime formation is reversible at every step.

In reactions with organic magnesium compounds, however, the situation is different because the Grignard reaction is not reversible. This reaction, accordingly, gave rise to isomeric products—as, for example, in the case of methylmagnesium iodide, the two isomeric ketols VII and VIII



$$(C_6H_5)_2CH\text{—}\underset{OH}{\overset{CH_3}{C}}\text{—}COC_6H_5 \longleftarrow (C_6H_5)_2CHCOCOC_6H_5 \longrightarrow (C_6H_5)_2CHCO\text{—}\underset{OH}{\overset{CH_3}{C}}\text{—}C_6H_5$$

VII

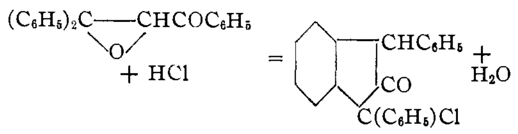
VIII

Owing to the formation of secondary products, the isolation of the ketols involved considerable losses but it was possible to estimate the relative amounts with sufficient accuracy to show that they vary greatly with the nature of the magnesium compound. Thus with methylmagnesium iodide, less than 50% of the product is formed by addition to the carbonyl adjacent to the benzhydryl group (VII) while with phenylmagnesium bromide more than 75% of it is due to this mode of addition.

As will be seen from the foregoing account the most conspicuous peculiarity of benzhydryl phenyl diketone is its behavior on alkylation and acylation. The significance of this behavior will be discussed in a later paper dealing with similar substances.

Experimental Part

Benzhydryl phenyl diketone cannot be prepared by the method that was used successfully for obtaining benzyl phenyl diketone, namely, by rearranging an isomeric oxido ketone with hydrogen chloride. When this method was applied to benzoyl diphenyl ethylene oxide, water was eliminated and the result was a compound which contained very active chlorine but no active hydrogen, and which was oxidized to ortho dibenzoyl benzene. The product is therefore an indane derivative and the reaction is represented by the equation



XIII

Since it was impossible to rearrange the oxido ketone with acids it was necessary to resort to bases. Here also considerable difficulty was encountered due to the reluctance of the diketone to crystallize and the ease with which it undergoes the benzilic acid rearrangement. But once crystals were available for inoculation the diketone could be prepared without much trouble by operating in a boiling solution, limiting the quantity of base and acidifying promptly. The procedure was as follows.

A solution of 3 g. of sodium in methyl alcohol was added to 30 g. of the oxido ketone dissolved in the smallest possible quantity of boiling ethyl alcohol. As soon as the vigorous reaction subsided the red solution was acidified (10 g. of sulfuric acid diluted to 50 cc.), then diluted to one liter with cracked ice, and extracted with ether. The extract was dried with sodium sulfate and evaporated as completely as possible in order to remove all of the alcohol. The residual yellow oil was crystallized by dissolving it in twice its volume of absolute ether, chilling the solution to −15–20°, and then diluting it to incipient cloudiness with low-boiling petroleum ether and inoculating it. Under these conditions the diketone crystallized rapidly in long flat needles resembling benzil both in form and color and melting at 49–50°. The yield was 22–25 g. or 73–84%.

Anal. Calcd. for $C_{21}H_{26}O_2$: C, 84.0; H, 5.3. Found: C, 83.9; H, 5.4.

Oxidation.—To a solution of 3 g. of the diketone in 25 cc. of methyl alcohol were added first 1.7 g. of 30% hydrogen peroxide, and then 0.6 g. of sodium hydroxide dissolved in 5 cc. of water. A vigorous reaction followed the addition of the base and the red color of the solution disappeared. By suitable manipulations the colorless solution yielded 2.0 g. of diphenylacetic acid and 1.2 g. of benzoic acid.

Condensation with *o*-Phenylenediamine, Benzhydryl Phenyl Quinoxaline. II.—A solution of 4.0 g. of the diketone and 2.4 g. of ortho phenylene diamine hydrochloride in 40 cc. of alcohol was boiled for an hour, then allowed to cool. It deposited 4.65 g. of a solid which after recrystallization from alcohol melted at 198–199°.

Anal. Calcd. for $C_{27}H_{20}N_2$: C, 87.1; H, 5.4. Found: C, 87.2; H, 5.6.

Reaction with Bases, α,β,β-Triphenyl Lactic Acid. III.—The benzilic acid rearrangement product of the diketone is most readily obtained directly from the oxido ketone. Thus when 10 g. of the ketone was added to 60 cc. of a saturated solution of potassium hydroxide in methyl alcohol, the mixture rapidly passed through the color changes of yellow, orange and deep red, then gradually became colorless and solidified. The resulting potassium salt was dissolved in 600 cc. of hot water, the solution was filtered to remove a small quantity of insoluble material, then acidified. After recrystallization from acetone and petroleum ether the acid melted, with brisk decomposition, at 243–245°. The yield was 10 g.

Anal. Calcd. for $C_{21}H_{18}O_3$: C, 79.3; H, 5.7. Found: C, 79.2; H, 5.4.

The brisk decomposition at the melting point represents loss of water and results in the formation of triphenyl acrylic acid. Thus 1.03 g. of the acid heated to 240–260° in a metal bath lost 0.13 g. instead of 0.11 g. calculated and left an acid which melted at 208–212°.

The methyl ester of triphenyl lactic acid, prepared by means of the silver salt, crystallized in acicular prisms and melted at 186°.

Anal. Calcd. for $C_{22}H_{20}O_3$: C, 79.5; H, 6.0. Found: C, 79.4; H, 6.1.

Methylation of the Diketone, α-Methoxy β-Phenyl Benzalacetophenone. IV.—A solution of 0.27 g. of sodium hydroxide in 30 cc. of water was added slowly to a solution of 2.0 g. of the diketone in 20 cc. of methyl alcohol. The solution turned red but remained clear. The red solution was shaken with 3 g. of dimethyl sulfate until the red color disappeared. It deposited 1.83 g. of yellow solid melting before recrystallization at 98–104° and after recrystallization from methyl alcohol at 103–104°. An additional 0.1 g. of the same product was obtained from the acid filtrate making a total yield of 94%.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.1; H, 5.7; OCH_3, 9.9. Found: C, 83.9; H, 5.8; OCH_3, 10.2.

Methylation with methyl iodide at the ordinary temperature is too slow to be feasible because much of the diketone undergoes the benzilic acid rearrangement. Higher temperatures are more favorable for methylation but even at these temperatures the diketone, in part, is rearranged into triphenyl lactic acid which is then methylated. The best results were obtained as follows. A solution of 0.33 g. of sodium hydroxide was added a drop at a time through a reflux condenser to a boiling solution of 2 g. of the diketone and 3 g. of methyl iodide in 10 cc. of methyl alcohol. Each drop of base produced a red color and no more base was added until this color had changed back to yellow. When all of the diketone had disappeared the solution was neutralized and diluted with water. It deposited a yellow oil which later solidified. On treatment with ether a part of the product dissolved, leaving 0.35 g. of a colorless solid which was identified as the methyl ester of triphenyl lactic acid. The ethereal solution and the ethereal extract of aqueous alcoholic solution yielded 1.43 g. of the same methoxyl compound that had been obtained with dimethyl sulfate.

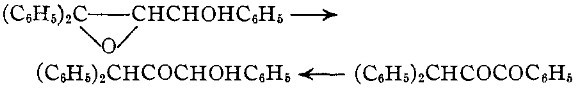
Benzoylation. Benzoate of α-Hydroxy-β-phenyl Benzalacetophenone. V.—Benzoylation in pyridine by the usual procedure gave a product which after recrystallization from acetone and petroleum ether melted at 161°. The yield was 93.5%. The same product was obtained when the sodium derivative was benzoylated in the following manner. A solution of 0.5 g. of sodium hydroxide in 5 cc. of water was added to a solution of 2 g. of the diketone in dioxane. To the resulting red solution a solution of 1.5 g. of benzoyl chloride in 10 cc. of dioxane was added slowly with vigorous shaking until the color disappeared. The solution was then mixed with ether and washed with water until free from dioxane. The ethereal solution yielded 2.15 g. of the benzoate and 0.4 g. of a yellow oil composed mainly of unchanged diketone.

Anal. Calcd. for $C_{28}H_{20}O_3$: C, 83.2; H, 5.0. Found: C, 83.1; H, 5.2.

The benzoate is not hydrolyzed by acids and it is not reduced by hydrogen and Adams' catalyst. Bases convert it into the same products that would be obtained by similar treatment of the diketone and hydroxylamine acetate transforms it into the same oxime that is formed from the diketone.

Reduction: 1,3,3-Triphenyl-1-hydroxy Propanone (VI).—When a solution of 2 g. of the ketone in 3 cc. of ethyl acetate was shaken with hydrogen in the presence of Adams' catalyst, the gas was absorbed rapidly until one mole had disappeared, whereupon absorption stopped abruptly. The solution contained but one substance, melting at 125–126° when crude and at 128° after recrystallization from acetone–petroleum ether. Catalytic reduction in acetic anhydride was less rapid, but it likewise gave only the product melting at 1280. Reduction in an alkaline medium was not feasible, owing to the ease with which the diketone is rearranged, but reduction with zinc and acid occurred readily; it likewise gave but the one product.

The reduction product proved to be identical with a substance which had been obtained previously from an oxido alcohol.[2] The formation in these diverse ways leaves no doubt as to its structure



$$(C_6H_5)_2C\text{——}CHCHOHC_6H_5 \longrightarrow$$

$$(C_6H_5)_2CHCOCHOHC_6H_5 \longleftarrow (C_6H_5)_2CHCOCOC_6H_5$$

The reduction product could not be rearranged into an isomeric ketol by boiling with acids or with bases. In an alkaline solution it forms an oxime which melts at 159°.

Anal. Calcd. for $C_{21}H_{19}O_2N$: C, 79.5; H, 6.0. Found: C, 79.5; H, 6.3.

Oxime of the Diketone.—When the diketone was treated in the usual manner with hydroxylamine acetate it formed a single monoxime—a substance which crystallized from ether–petroleum ether in nodules of fine needles and which melted at 135–136°.

Anal. Calcd. for $C_{21}H_{17}O_2N$: C, 80.0; H, 5.4. Found: C, 79.7; H, 5.7.

The oxime forms a copper derivative with cupric acetate and it develops a deep red color in alcoholic solutions of ferric chloride. It therefore belongs to the class of α-oximes[3]—the oximes in which the hydroxyl group is *trans* with respect to an RCO group.

II. The Reaction with Organic Magnesium Compounds

When the diketone is added to excess of standardized methylmagnesium iodide[4] it consumes

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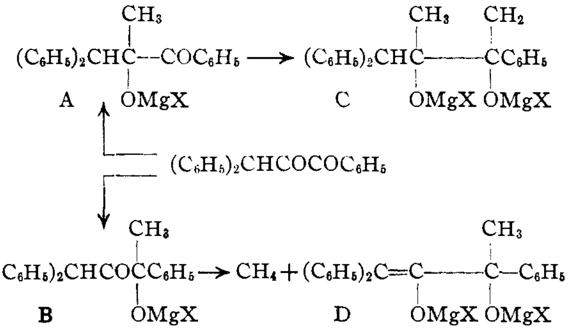
[2] Kohler, Richtmyer and Hester, This Journal, **53**, 216 (1931).

[3] Taylor and Marks, *J. Chem. Soc.*, 2302 (1930); 2018 (1931).

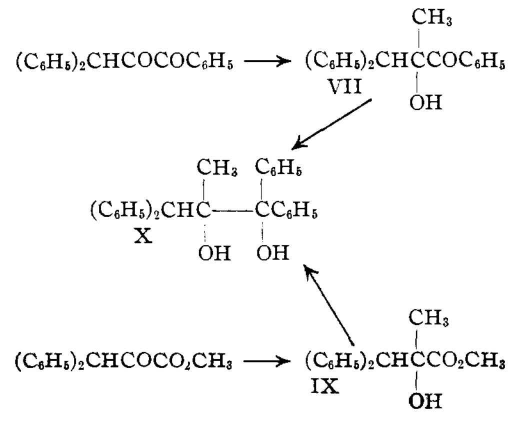
[4] This Journal, **53**, 205 (1931).

almost exactly two moles of reagent and liberates 0.47 mole of methane. These values show that it inaugurates the series of reactions which are represented as follows

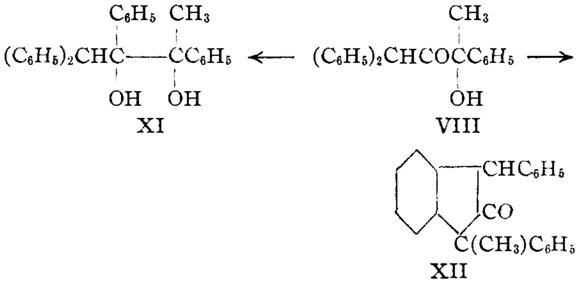


Independent experiments showed that while the magnesium derivative B is largely enolized by a second molecule of the reagent, it also in small part combines; it is therefore formed in a somewhat larger proportion than is indicated by the gas evolved.

As the chart shows, it is not possible to secure the ketol VII—corresponding to A—by operating in this manner. This ketol can however be obtained by adding one equivalent of the reagent to a solution of the ketone. It was identified with a substance which had been obtained previously in an entirely different series of reactions and which had been represented by formula VII.[5] Its melting point seems unduly high for a substance of this type but we have verified the formula by relating the ketol to known substances by means of a series of reactions which can be represented as follows



The isomeric ketol VIII corresponding to B and D can be obtained by operating in the usual manner. When it is treated with phenylmagnesium bromide, a part of it is converted into the magnesium derivative D but a part of it also combines with the reagent and forms the magnesium derivative of a glycol that is isomeric with X. Hydrogen iodide converts it into an indane derivative



1,3,3-Triphenyl-2-methyl-2-hydroxy Propanone-1, VII.—A solution of methylmagnesium iodide made from 0.9 g. of magnesium was added to a solution of 10 g. of the diketone in 50 cc. of ether. The product was 9.5 g. of an oil that was free from diketone. A solution of 4.5 g. of this oil in 20 cc. of methyl alcohol was shaken for a minute with 10 cc. of 20% methyl alcoholic hydroxide, then acidified and diluted with water. From the aqueous alcoholic solution ether extracted 2.5 g. of a substance which crystallized in needles and melted at 178°. This substance was identified as the ketol by comparison with an authentic sample.[5] The melting point given in the earlier paper is 188°. A repetition of the experiment showed that this is an error; the melting point is 178°.

1,3,3-Triphenyl-1-methyl-1-hydroxy Propanone-2, VIII.—An ethereal solution of 10 g. of the diketone was added to a solution of methylmagnesium iodide containing 2 g. of magnesium. An orange solid separated but redissolved immediately. The mixture was stirred for several hours to complete the precipitation of a magnesium compound which separated slowly. This solid magnesium compound yielded a solid product while the solution yielded only oils. The solid crystallized from ether–petroleum ether in needles melting at 72–73°.

Anal. Calcd. for $C_{22}H_{20}O_2$: C, 83.5; H, 6.3. Found: C, 83.5; H, 6.5.

1,3-Diphenyl-1-methylindanone-2, XII.—With reduction in view, the ketone (VIII) was heated for an hour and a half with excess of hydriodic acid but instead of being reduced it was condensed to an indane derivative. After recrystallization from acetone, the product melted with decomposition at about 185°.

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.6; H, 6.0. Found: C, 88.4; H, 6.3.

1,2,3,3 - Tetraphenyl - 1 - methylpropanediol - 1,2, XI.—A solution of 2 g. of the same ketol (VIII) was added to a solution of phenylmagnesium bromide made from 2 g. of magnesium. The solution was boiled for six hours before it was decomposed with acid in the usual manner. It yielded 0.5 g. of fine needles which after recrystallization from ether–petroleum ether melted at 184°.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 85.3; H, 6.6. Found: C, 84.8; H, 6.6.

1,1,3,3-Tetraphenyl-2-methylpropanediol-1,2, X.—A solution of 5 g. of the oil obtained by adding methylmagne-

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[5] Kohler, *Am. Chem. J.*, **36**, 536 (1906).