[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

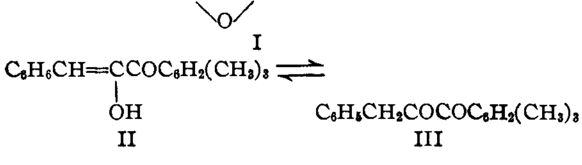
Steric Hindrance in Alpha Diketones: Mesitylbenzylglyoxal

BY R. P. BARNES

In 1934 Kohler and Barnes[2] showed that phenylbenzylglyoxal differs from the isomeric beta diketone both in the extent to which it is enolized under various conditions and in the manner in which it is acylated and alkylated. In the second paper of this series Kohler and Weiner[3] studied the effect of the introduction of a second phenyl group into phenylbenzylglyoxal. They showed that the additional phenyl group has little if any effect on reactions which involve both of the carbonyl groups, but completely represses the enolization.

In this article there are presented the results of a study of the behavior of a third alpha diketone, mesitylbenzylglyoxal (II). This compound was chosen in order to study the effect of steric hindrance in such an alpha diketone, and to that end the extent of its enolization and its behavior toward alkylating, acylating and certain carbonyl reagents was determined. Other carbonyl reactions of mesitylbenzylglyoxal are still under investigation.

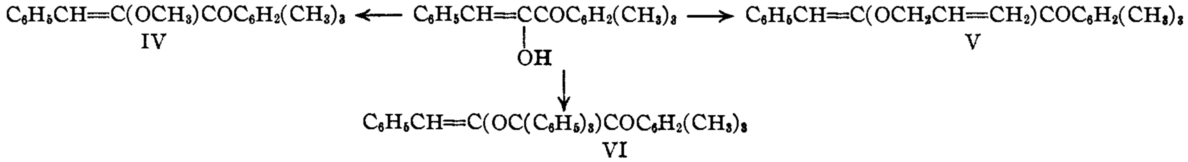
Mesitylbenzylglyoxal was prepared by oxidizing benzalacetomesitylene with sodium peroxide and isomerizing the resulting oxido ketone with alkali



$$C_6H_5CH{=}CHCOC_6H_2(CH_3)_3 \longrightarrow \underset{\text{I}}{C_6H_5\overset{}{CH}{-}\!\!{-}CHCOC_6H_2(CH_3)_3}\ (\text{—O— bridge}) \longrightarrow$$

$$\underset{\text{II}}{C_6H_5CH{=}\underset{\displaystyle OH}{\underset{|}{C}}COC_6H_2(CH_3)_3} \rightleftharpoons \underset{\text{III}}{C_6H_5CH_2COCOC_6H_2(CH_3)_3}$$

Mesitylbenzylglyoxal is 100% enolic in the solid state, but partially ketonizes in the melt and in solution. It is cleaved quantitatively to phenylacetic and trimethylbenzoic acids by sodium peroxide, a reaction which, according to Weitz and Scheffer,[4] is specific for alpha diketones. Alkaline solutions of mesitylbenzylglyoxal, alkylated with either methyl iodide or dimethyl sulfate, yield 100% O-methyl ether as indicated by methoxyl determinations. Similarly allyl bromide and triphenylchlormethane in acetone solution lead to the allyl and trityl ether, respectively. The allyl ether does not rearrange to the isomeric C-compound upon distillation *in vacuo.* The fact that the methyl and allyl ethers distil unchanged does not strengthen Hantzsch's hypothesis[5] that alkylation results in O-alkylates which subsequently rearrange to C-isomers. The formation of trityl ethers of enols although not new, is not a very common reaction.[6]

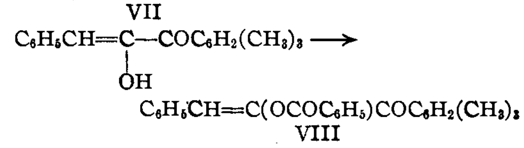


$$\underset{\text{IV}}{C_6H_5CH{=}C(OCH_3)COC_6H_2(CH_3)_3} \longleftarrow C_6H_5CH{=}\underset{\displaystyle OH}{\underset{|}{C}}COC_6H_2(CH_3)_3 \longrightarrow \underset{\text{V}}{C_6H_5CH{=}C(OCH_2CH{=}CH_2)COC_6H_2(CH_3)_3}$$

$$\downarrow$$

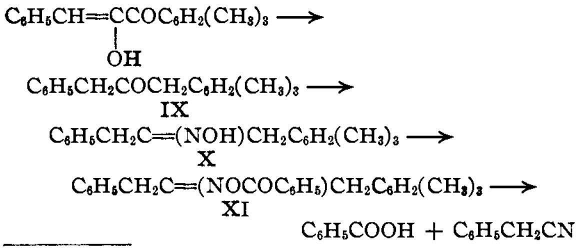
$$\underset{\text{VI}}{C_6H_5CH{=}C(OC(C_6H_5)_3)COC_6H_2(CH_3)_3}$$

In acylation mesitylbenzylglyoxal resembles phenylbenzylglyoxal and benzhydryl diketone in that only O-acylation products are formed.



$$\underset{\text{VII}}{C_6H_5CH{=}C(OCOCH_3)COC_6H_2(CH_3)_3} \longleftarrow C_6H_5CH{=}\underset{\displaystyle OH}{\underset{|}{C}}{-}COC_6H_2(CH_3)_3 \longrightarrow \underset{\text{VIII}}{C_6H_5CH{=}C(OCOC_6H_5)COC_6H_2(CH_3)_3}$$

The diketone is not reduced catalytically, but treatment with tin and acids produces a mono ketone which is presumably formed by way of the benzoin. This ketone forms an oxime and an oxime benzoate. Pyrolysis of the oxime benzoate gives a mixture from which benzoic acid and benzyl cyanide are isolated.



$$C_6H_5CH{=}\underset{\displaystyle OH}{\underset{|}{C}}COC_6H_2(CH_3)_3 \longrightarrow \underset{\text{IX}}{C_6H_5CH_2COCH_2C_6H_2(CH_3)_3} \longrightarrow \underset{\text{X}}{C_6H_5CH_2C{=}(NOH)CH_2C_6H_2(CH_3)_3} \longrightarrow \underset{\text{XI}}{C_6H_5CH_2C{=}(NOCOC_6H_5)CH_2C_6H_2(CH_3)_3} \longrightarrow C_6H_5COOH + C_6H_5CH_2CN$$

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(1) This work was begun in the Converse Memorial Laboratory of Harvard University as a supplement to the paper reported by Kohler and Barnes, Reference 2.

(2) Kohler and Barnes, THIS JOURNAL, **56**, 211 (1934).

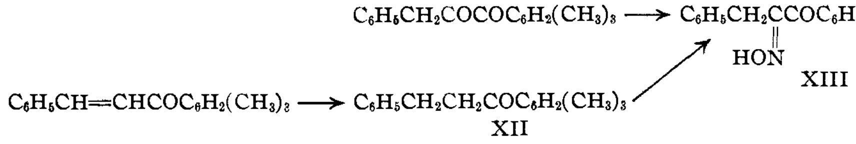
(3) Kohler and Weiner, *ibid.*, **56**, 434 (1934).

(4) Weitz and Scheffer, *Ber.*, **54**, 2327 (1921).

(5) Hantzsch, *Z. anorg. allgem. Chem.*, **209**, 213 (1932).

(6) P. Karrer, G. Schwarzenbach and K. Schöpp, *Helv. Chim Acta*, **16**, 302 (1933).

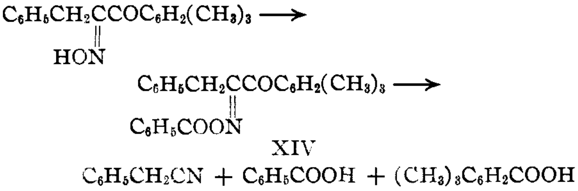
That the mesityl group offers steric hindrance to reactions involving both carbonyl groups is evidenced by the fact that mesitylbenzylglyoxal does not form a quinoxaline with *o*-phenylenediamine under any conditions. However, it forms an α-oxime. The constitution of the oxime rests upon the fact that oximation of the catalytically reduced benzalacetomesitylene with a nitrite yields the same product.



$$C_6H_5CH_2COCOC_6H_2(CH_3)_3 \longrightarrow C_6H_5CH_2\underset{\displaystyle HON}{\underset{\|}{C}}COC_6H_2(CH_3)_3 \quad \text{XIII}$$

$$C_6H_5CH{=}CHCOC_6H_2(CH_3)_3 \longrightarrow \underset{\text{XII}}{C_6H_5CH_2CH_2COC_6H_2(CH_3)_3} \nearrow$$

The configuration of this oxime[7] is established by the fact that it forms a benzoate which, although insoluble in 5% sodium hydroxide, decomposes upon heating yielding benzyl cyanide and presumably a mixed anhydride which yields benzoic and trimethylbenzoic acids



$$C_6H_5CH_2\underset{\displaystyle HON}{\underset{\|}{C}}COC_6H_2(CH_3)_3 \longrightarrow$$

$$\underset{\text{XIV}}{C_6H_5CH_2\underset{\displaystyle C_6H_5COON}{\underset{\|}{C}}COC_6H_2(CH_3)_3} \longrightarrow$$

$$C_6H_5CH_2CN + C_6H_5COOH + (CH_3)_3C_6H_2COOH$$

Mesitylbenzylglyoxal likewise gives rise to a semicarbazone

$$C_6H_5CH_2C{=}(NNHCONH_2)COC_6H_2(CH_3)_3$$
XV

Experimental Part

Preparation of α-Phenyl-β-mesitoylethylene Oxide (I).—To a mechanically stirred solution of 173.5 g. of benzalacetomesitylene in 2000 cc. of alcohol was added 72 cc. of 6 *N* sodium hydroxide. Over a period of ten minutes, 144 cc. of 30% hydrogen peroxide was added in 25-cc. portions. Immediately upon addition of the hydrogen peroxide the yellow color began to fade. Vigorous stirring was continued for half an hour after the addition of the hydrogen peroxide, after which a colorless oil settled out. This oil could not be crystallized. It was extracted with ether, washed with dilute hydrochloric acid and with water, dried over calcium chloride and distilled. During these operations the colorless oil became yellow, and there was obtained 147 g. boiling at 195° (8 mm.). This was an 80% yield. Indirect titrations with bromine indicated 10% enol.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.7. Found: C, 81.2; H, 6.7.

Isomerization of the Oxido Ketone to Mesitylbenzylglyoxal (II).—A solution of 48 g. of the oxido ketone in 100 cc. of alcohol was boiled for ten minutes with a concentrated aqueous solution of 27.6 g. of sodium hydroxide. The solution turned cherry red. It was then cooled, extracted with ether and acidified with cold dilute hydrochloric acid. Upon evaporation of the ether there resulted a quantitative yield of brownish-yellow crystals, which upon crystallization from methyl alcohol were colorless and melted at 100°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.7. Found: C, 80.9; H, 6.8.

Mesitylbenzylglyoxal in alcoholic solution gives a deep cherry-red color with ferric chloride. When added to a standard solution of methylmagnesium iodide, it consumes 1.97 moles of the reagent and liberates 1.02 moles of gas. It therefore contains one carbonyl group and one active hydrogen.

Tautomerism.—The amount of enol was determined by titration with bromine by the indirect method.[8] The pure solid enol was 100% enol. All equilibria were effected in an atmosphere of dry oxygen-free nitrogen. The values were: 91% at 111°; 78% at 220°; 69% in the distillate and 91% in the residue after distillation from soft glass into a Pyrex condenser and receiver. Thus the vapor pressure of the keto form is greater than that of the enol form. The enol content for approximately 0.037 *N* solutions was: 90% in methyl alcohol; 91% in ethyl alcohol; 84% in chloroform; 82% in benzene; 81% in petroleum ether. The enol content of these different solutions does not seem to be very significant. These values only roughly parallel those for phenylbenzylglyoxal.

Oxidation.—To a methyl alcoholic solution of 1 g. of mesitylbenzylglyoxal was added an excess of 15% hydrogen peroxide. The solution was made alkaline with sodium hydroxide and warmed on the water-bath until the yellow color disappeared. It was cooled and extracted with ether. The ethereal extract contained no unchanged material. The aqueous layer on acidification yielded a mixture of phenylacetic and trimethylbenzoic acids.

Methylation: Methyl Ether of α-Hydroxybenzalacetomesitylene (IV).—Methylation was effected (1) by adding dropwise and with vigorous shaking 20% aqueous potassium hydroxide to an aqueous suspension of 10 g. of enol and twice the calculated quantity of dimethyl sulfate until permanent alkalinity was established; (2) by adding dropwise a 10% solution of sodium methylate to a boiling methyl alcoholic solution of 10 g. of enol and excess of methyl iodide, and refluxing until acid. Each method gave a practically quantitative yield of 10 g. of pale yellow oil boiling at 157° (2 mm.), which formed very pale yellow crystals, melting at 75°. This substance gives no color with alcoholic ferric chloride.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.1; OCH_3, 11.1. Found: C, 81.1; H, 7.0; OCH_3, 11.3.

Allylation: Allyl Ether of α-Hydroxybenzalaceto mesitylene (V).—To a solution of 10 g. of enol in 50 cc. of

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[7] A. H. Blatt and R. P. Barnes, This Journal, **56**, 1148 (1934).

[8] The method of sampling and equilibrating was the same as that reported by Kohler and Barnes, This Journal, **56**, 211 (1934).

acetone was added 4.6 g. of allyl bromide and 10 g. of anhydrous potassium carbonate. The solution was refluxed for two hours. The solid was filtered off and thoroughly washed with acetone. The acetone was distilled off leaving 10 g. of a deep yellow oil, which was crystallized from methyl alcohol in very deep yellow crystals, melting at 55°.

Anal. Calcd. for $C_{21}H_{22}O_2$: C, 82.4; H, 7.2. Found: C, 82.4; H, 7.1.

The allyl ether of α-hydroxybenzalacetomesitylene gives no color reaction with alcoholic ferric chloride. It distils unchanged at 230° (30 mm.). Heating with mineral acids regenerates the enol. It also reduces permanganate.

Reaction with Triphenylchloromethane: Trityl Ether of α-Hydroxybenzalacetomesitylene (VI).—A solution of 10 g. of enol and 10.5 g. of triphenylchloromethane in 75 cc. of acetone was refluxed for two hours with 10 g. of anhydrous potassium carbonate. The solid was filtered off and the acetone distilled. The residue was taken up in ether and washed with water. Upon evaporation, 5 g. of a yellow solid was deposited. Crystallization from acetone gave a product melting at 195–198°.

Anal. Calcd. for $C_{36}H_{32}O_2$: C, 87.4; H, 6.3. Found: C, 88.0; H, 6.8.

The trityl ether of α-hydroxybenzalacetomesitylene is very sparingly soluble in alcohol and produces no color with ferric chloride. It reduces permanganate and upon heating with mineral acids is hydrolyzed to the enol.

Acetylation: Acetate of α-Hydroxybenzalacetomesitylene (VII).—A solution of 5 g. of mesitylbenzylglyoxal in 20 g. of acetic anhydride and one drop of concentrated sulfuric acid was refluxed for two hours. The excess acid was distilled off. Cold water was added to the residue and it was extracted with ether, washed with sodium bicarbonate solution and with water. It was finally dried and concentrated. A yield of 5.9 g. of colorless crystals melting at 109° was obtained. The product gives no color test with ferric chloride, but is easily hydrolyzed with mineral acids.

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.9; H, 6.5. Found: C, 77.6; H, 6.7.

The Schotten–Baumann Reaction: Benzoate of α-Hydroxybenzalacetomesitylene (VIII).—To a solution of 5 g. of the enol in 40 cc. of ether was added an excess of 10% sodium hydroxide. Into this alkaline solution, with shaking, was slowly dribbled 2.6 g. of benzoyl chloride. The mixture was warmed for a few minutes. The ethereal solution was washed with water, dried and distilled at 208° (2 mm.). The yield was 7.4 g. of pale yellow oil. The oil was crystallized from dilute alcohol yielding a colorless solid, melting at 81°. Its alcoholic solution gives no color with ferric chloride and is easily hydrolyzed with acids.

Anal. Calcd. for $C_{25}H_{22}O_3$: C, 81.1; H, 5.9. Found: C, 81.1; H, 6.1.

Reduction: 1-Mesityl-3-phenylpropanone-2 (IX).—Every attempt at catalytic hydrogenation failed. To 5 g. of the enol dissolved in 50 cc. of acetic acid was added 20 g. of twenty-mesh tin, a crystal of copper sulfate, and 50 cc. of concentrated hydrochloric acid. The mixture was refluxed for nine hours and poured into boiling water. A colorless oil separated which upon cooling solidified. Crystallization from alcohol gave slightly pinkish needles, melting at 72°. The yield was 74%.

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.7; H, 7.9. Found: C, 85.5; H, 8.0.

The Oxime (X).—A solution of 5 g. of 1-mesityl-3-phenyl-propanone-2 in 100 cc. of alcohol was heated with an aqueous solution of 2.6 g. of hydroxylamine hydrochloride and 3 g. of anhydrous sodium acetate. The resulting solution was cooled and diluted with water. It yielded 4.8 g. of a colorless crystalline product. On crystallization from dilute alcohol it melted at 85°. The yield was 90%.

Anal. Calcd. for $C_{18}H_{21}ON$: C, 80.0; H, 7.8. Found: C, 80.5; H, 7.9.

The Oxime Benzoate (XI).—A chilled solution of 5.3 g. of the oxime in 10 cc. of pyridine was added to a chilled mixture of 4.3 g. of benzoyl chloride and 20 cc. of pyridine, and allowed to stand for four hours. The reaction mixture was decomposed by pouring into ice and hydrochloric acid. It was extracted with ether, washed with water, dried over calcium chloride and concentrated. Addition of petroleum ether caused an almost quantitative precipitation of a colorless crystalline product. Upon crystallization from alcohol it melted at 86°. A mixed melting point with the parent oxime was about 70°.

Anal. Calcd. for $C_{25}H_{25}O_2N$: C, 80.8; H, 6.7. Found: C, 80.5; H, 6.8.

The oxime benzoate of 1-mesityl-3-phenylpropanone-2 decomposes violently above its melting point. When 1 g. of this substance was decomposed in this fashion, the red oily residue taken up in ether and washed with sodium carbonate solution, the aqueous solution upon acidification yielded benzoic acid. The ethereal solution was washed with water, dried and distilled. Benzyl cyanide was obtained and identified as benzalbenzyl cyanide. The red residue left from the distillation was indefinite.

The Oxime (XII).—All attempts to obtain the quinoxaline or the dioxime were unsuccessful. The monoxime, however, was easily obtained when 2 g. of the alpha diketone was dissolved in the smallest amount of warm alcohol and warmed with an aqueous solution of 2 g. of hydroxylamine hydrochloride and 2 g. of anhydrous sodium acetate. The solution was diluted with water and a quantitative yield of the crude oxime was precipitated. Upon crystallization from dilute alcohol, very pale yellow needles, melting at 88°, were obtained.

Anal. Calcd. for $C_{18}H_{19}O_2N$: C, 76.9; H, 6.8. Found: C, 76.9; H, 6.7.

Reduction of Benzalacetomesitylene: Benzylacetomesitylene (XIII).—When a solution of 25 g. of benzalacetomesitylene in 200 cc. of alcohol was shaken with hydrogen in the presence of 0.3 g. of Adams catalyst, hydrogen was gradually taken up. Reduction was complete in six hours when one mole of hydrogen had been absorbed and the color had faded. Distillation at 163–165° (3 mm.) gave a quantitative yield of pale yellow oil which could not be crystallized.

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.7; H, 7.9. Found: C, 85.5; H, 8.0.

Oximination of Benzylacetomesitylene (XII).—To a solution of 4.6 g. of sodium in 100 cc. of methyl alcohol was added 23.5 g. of amyl nitrite. Slowly and with shaking 25 g. of benzylacetomesitylene was added to the solution. It was tightly stoppered and allowed to stand in the refrigerator for several days. No solid separated out. The solution was poured into water and extracted with ether. The ether was evaporated off and the oil crystallized from dilute alcohol. There resulted 25 g. of a pale yellow solid, whose melting point and mixed melting point with the oxime of mesityl benzyl glyoxal was 87°.

The Oxime Benzoate (XIV).—A chilled solution of 5.62 g. of the oxime in 10 cc. of pyridine was added to a chilled mixture of 4.3 g. of benzoyl chloride and 25 cc. of pyridine and allowed to stand at room temperature for four hours. The reaction mixture was decomposed by pouring into ice and hydrochloric acid. It was extracted with ether, washed with water, dried over calcium chloride and concentrated. Addition of petroleum ether caused an almost quantitative precipitation of a colorless crystalline product.

Anal. Calcd. for $C_{25}H_{23}O_3N$: C, 77.9; H, 6.0. Found: C, 77.6; H, 6.0.

The oxime benzoate of mesitylbenzylglyoxal melts at 95°; insoluble in 5% sodium hydroxide. When 1 g. of the substance is heated above its melting point it decomposes violently, turning reddish-brown. The decomposition products are taken up in ether, and washed with sodium carbonate solution. The alkaline solution yields benzoic and trimethylbenzoic acids, separated by sublimation and identified by their melting points and mixed melting points. The ethereal solution yields benzyl cyanide, identified as benzalbenzyl cyanide.

The Semicarbazone (XV).—A solution of 3 g. of the alpha diketone in 25 cc. of alcohol was warmed with an aqueous solution of 3 g. of semicarbazide hydrochloride and 3 g. of anhydrous sodium acetate. Upon dilution with water there was precipitated a pale yellow solid, which after crystallization from alcohol melted at 227°.

Anal. Calcd. for $C_{19}H_{21}O_2N_3$: C, 70.6; H, 6.5. Found: C, 70.2; H, 6.6.

Summary

The results of the study of mesitylbenzylglyoxal show that di-ortho substituents in the mesityl group offer steric hindrance to all addition reactions to the carbonyl groups except in the case of reduction.

The di-ortho substituents seem to stabilize the enol and do not hinder addition to oxygen of the carbonyl groups.

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The Preparation of Substituted *o*-Aroylbenzoic Acids in the Identification of Aromatic Hydrocarbons[1]

BY H. W. UNDERWOOD, JR., AND WILLIAM L. WALSH

At present there exists no satisfactory general method for the identification of aromatic hydrocarbons. Nitration and oxidation to quinones, while satisfactory procedures in certain cases, do not constitute methods applicable to all compounds of this class. Likewise, oxidation of side chains is not only limited in scope, but difficult to carry out on a small scale and valueless in distinguishing aromatic hydrocarbons containing different groups in the side chain such as methyl, ethyl, propyl, etc.

The present method has been applied, with minor modifications in individual cases, to a large number of aromatic hydrocarbons. It consists in the formation of crystalline acids which, for more positive identification, may be titrated and in certain cases dehydrated to the corresponding substituted anthraquinones. The melting points of the derivatives are for the most part scattered over a wide range, thereby facilitating identification. In the case of ethylbenzene, *m*- and *p*-xylenes (b. p. 136, 139, 138°, respectively) the melting points of the *o*-aroylbenzoic acids resulting from their condensation with phthalic anhydride lie too close together to make identification positive (m. p. 122, 126, 132°, respectively). Accordingly, tetrachlorophthalic anhydride has been substituted for phthalic anhydride, yielding *o*-aroyltetrachlorobenzoic acids (m. p. 173, 224, 246°, respectively) which possess the additional advantages of increased molecular weight and superior crystallizing properties.

A summary of the results is given in Table I, in which A represents the aromatic hydrocarbon used; B, the procedure described in the experimental part for the preparation of the derivative; C, the melting point of the corresponding *o*-aroylbenzoic acid; D and E, the theoretical and actual neutralization equivalents of each acid; F, the percentage by volume of alcohol in the dilute

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[1] Due to the death of Professor Underwood the present paper has been prepared by the junior author.