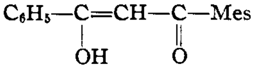
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HOWARD UNIVERSITY]

A Study on the Direction of Enolization of *p*-Bromodibenzoylmethane

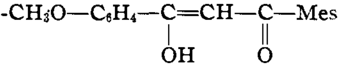
BY R. PERCY BARNES AND LOUIS B. DODSON[1]

In 1940, Barnes, Pierce, and Cochrane[2] reported on the properties of the enolic modification of benzoylmesitoylmethane and found that the mesityl nucleus had a directing influence upon enolization to such an extent that only one stable enolic modification existed from two series of reactions, namely



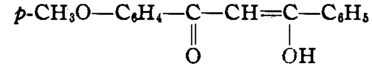
$$C_6H_5{-}\underset{\substack{|\\ OH}}{C}{=}CH{-}\underset{\substack{\|\\ O}}{C}{-}Mes$$

Later, Barnes and Cochrane[3] reported two parallel series of reactions that gave rise to the single enolic modification of *o*-methoxybenzoylmesitoylmethane



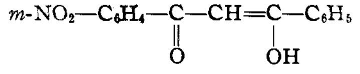
$$o\text{-}CH_3O{-}C_6H_4{-}\underset{\substack{|\\ OH}}{C}{=}CH{-}\underset{\substack{\|\\ O}}{C}{-}Mes$$

Continuing the investigation of the direction of enolization in β-diketones, Barnes and Brandon[4] studied the properties of *p*-methoxydibenzoylmethane and showed that its enolic modification reacts as 1-phenyl-3-*p*-methoxyphenylpropene-one-3-ol-1



$$p\text{-}CH_3O{-}C_6H_4{-}\underset{\substack{\|\\ O}}{C}{-}CH{=}\underset{\substack{|\\ OH}}{C}{-}C_6H_5$$

Soon afterwards, Barnes and Dodson[5] found that *m*-nitrodibenzoylmethane reacts toward hydroxylamine, hydrazine and phenylhydrazine as 1-phenyl-3-*m*-nitrophenyl-propene-one-3-ol-1



$$m\text{-}NO_2{-}C_6H_4{-}\underset{\substack{\|\\ O}}{C}{-}CH{=}\underset{\substack{|\\ OH}}{C}{-}C_6H_5$$

The purpose of this investigation was to study the direction of enolization of *p*-bromodibenzoylmethane.

To this end the isomeric *p*-bromochalcones (I) and (II) were obtained[6,7] in order to prepare their corresponding isoxazolines. The isoxazoline reaction was carried out according to Blatt.[8] The isoxazoline (VII) obtained from benzal-*p*-bromoacetophenone (I) was found to be identical with that obtained by Blatt and Stone.[9] However, these authors name the compound 3-*p*-bromophenyl-5-phenylisoxazoline, since on oxidation it yields 3-*p*-bromophenyl-5-phenylisoxazole. The structure of the isoxazole was shown by its synthesis from the dibromide of benzal-*p*-bromoacetophenone. As the result of this evidence Blatt and Auwers and Seyfried[10] interpret the isoxazoline formation as going by some mechanism other than by 1,4-addition.

We believe that the 1,4-addition of hydroxylamine to the unsaturated ketone is logical in view of the isoxazole (IX) arising out of the dibromide and the monobromide of benzal-*p*-bromoacetophenone (I), and that the isoxazoline (VII) should be named 3-phenyl-5-*p*-bromophenylisoxazoline.

In connection with the mechanism of the isoxazoline formation, it should be noted that the chance of an oxime being formed as an intermediate in the reaction is ruled out, as Blatt[8] has shown.

The isoxazoline (VII) was oxidized according to Blatt's procedure.[8] The isoxazole (IX) obtained exhibited the same melting point as the compound Blatt names 3-*p*-bromo-phenyl-5-phenylisoxazole.

When the dibromide (III) and the monobromide (V) of benzal-*p*-bromo-acetophenone reacted with hydroxylamine hydrochloride and potassium hydroxide, an isoxazole was obtained which melted and mix-melted with the one obtained from the isoxazoline (VII) at 178–179°. Therefore the compounds (III), (V) and (VII) yield the same isoxazole, 3-phenyl-5-*p*-bromophenylisoxazole (IX).

The behavior of the dibromide (III) at first seems contradictory to the 1,2-addition we would expect to occur under normal conditions. However, the reaction with the monobromide (V) in the same medium seems to indicate that it is an intermediate in the dibromide reaction.

In working with the other series of reactions (Series B) involving *p*-bromobenzalacetophenone (II), we encountered similar results found with the isomeric chalcone. An isoxazoline, 3-*p*-bromophenyl-5-phenylisoxazoline (VIII) was formed and it in turn was oxidized to 3-*p*-bromophenyl-5-phenylisoxazole (X). The isoxazoline reaction is again interpreted as 1,4-addition. The dibromide (IV) and monobromide (VI) yield the same isoxazole (X) when reacting with hydroxylamine hydrochloride in alkaline solution. Identification of the isoxazoles was made by mix-melting points.

The melting points of the isoxazoles from the parallel series of reactions present an interesting picture. They melted approximately at the same temperature, IX, 178–179°; X, 179–180°. The depression of the melting point was slight but definite when (IX) and (X) were mix-melted. The mixture melted at 174–175°. This is in keep-

---

[1] In partial fulfillment of the requirements for the Master's Degree; presented before the Organic Section of the American Chemical Society Meeting held in New York, September 11 to 15, 1944.

[2] Barnes, Pierce and Cochrane, THIS JOURNAL, **62**, 1084 (1940).

[3] Barnes and Cochrane, *ibid.*, **64**, 2262 (1942).

[4] Barnes and Brandon, *ibid.*, **65**, 1070 (1943).

[5] Barnes and Dodson, *ibid.*, **65**, 1585 (1943).

[6] Weygand, *Ann.*, **459**, 118 (1927).

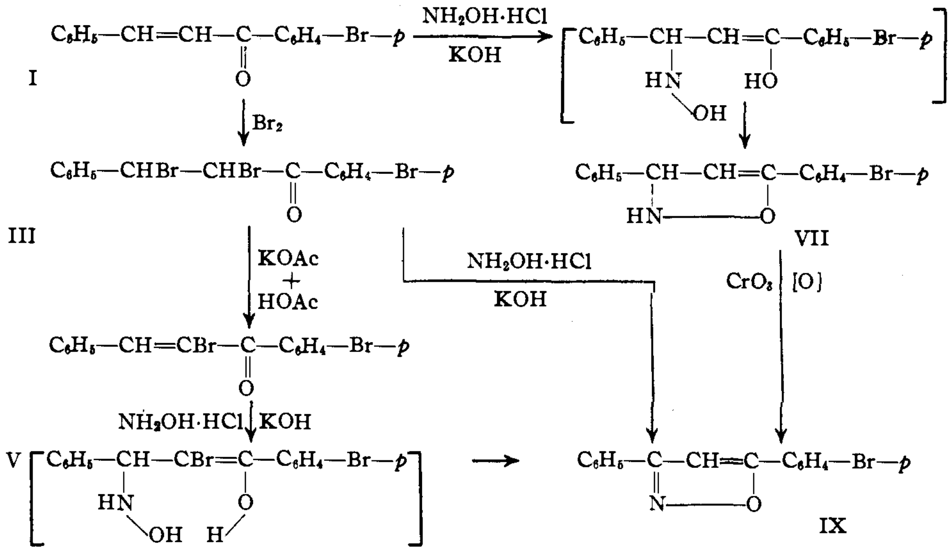
[7] Dilthey, *J. prakt. Chem.*, **101**, 202 (1921).

[8] Blatt, THIS JOURNAL, **53**, 1140 (1931).

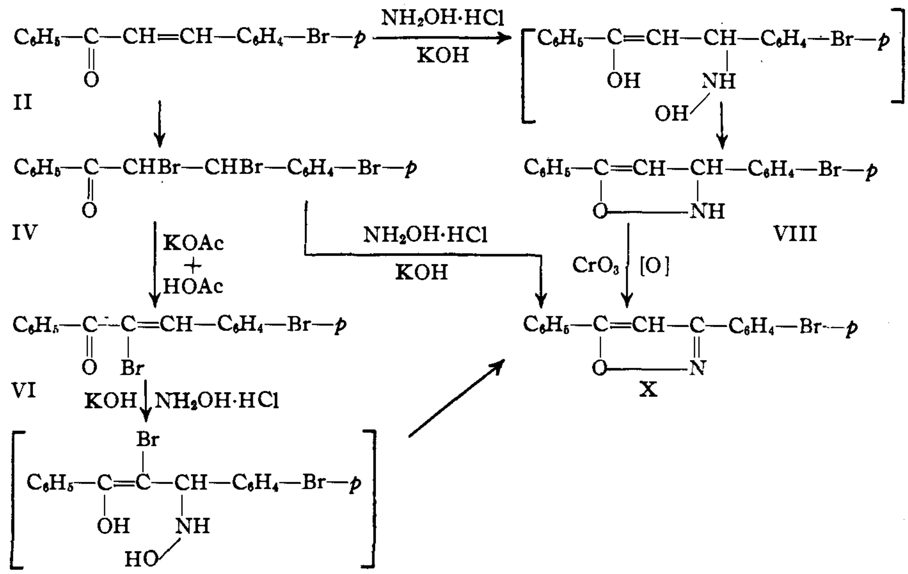
[9] Blatt and Stone, *ibid.*, **53**, 4139 (1931).

[10] Auwers and Seyfried, *Ann.*, **484**, 187 (1930).

SERIES A



SERIES B

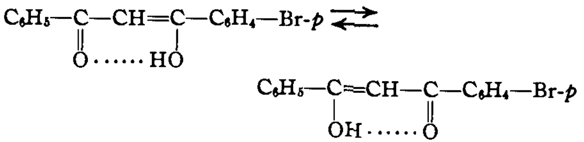


ing with the statement by Adams and Johnson:[11] "Certain mixtures of organic substances, particularly of homologs and of isomers, possess rather sharp melting points which remain practically constant after repeated crystallizations from a solvent."

Having obtained the two different isoxazoles from the parallel series of reactions involving the isomeric *p*-bromochalcones, we set out to consider the direction of enolization of *p*-bromodibenzoylmethane as exhibited by its formation of the isoxazole with hydroxylamine hydrochloride. An interesting result was observed.

The melting point of the product from the enol (XI) was found to be 174–175° after crystallization, and it did not mix-melt sharply with either isoxazole, (IX) or (X). On the other hand, the melting point of the product from the enol was the same as that of the mixture of isoxazole, (IX) and (X).

The conclusion is that a mixture of the two isoxazoles was formed from the enol and that both enolic forms of the diketone were present in the solution. The mechanism is represented as follows:



XI

$$C_6H_5\text{—}\underset{\underset{O\cdots\cdots HO}{\|\qquad|}}{C\text{—}CH{=}C}\text{—}C_6H_4\text{—}Br\text{-}p \rightleftarrows C_6H_5\text{—}\underset{\underset{OH\cdots\cdots O}{|\qquad\|}}{C{=}CH\text{—}C}\text{—}C_6H_4\text{—}Br\text{-}p$$

When the isoxazole formation involving the enol was carried out in alkaline solution, similar

---

[11] Adams and Johnson, "Elementary Laboratory Experiments in Organic Chemistry," The Macmillan Co., New York, 1940, p. 12.

results were obtained. The product obtained in alkaline medium, mix-melted unchanged with that obtained in acid medium.

The importance of considering the medium in proposing a structure is shown again in the work done on *m*-nitrodibenzoylmethane. Bodforss[12] assigned a structure to the enol as the result of alkaline oxidation cleavage opposite to the one proposed by Barnes and Dodson[5] who worked in acidic medium.

However, in spite of the uncertainty of the mechanism of the hydroxylamine reaction with α,β-unsaturated ketones, their derivatives, and β-diketones, conclusive proof has been shown that according to its behavior toward hydroxylamine in acidic or basic media, *p*-bromodibenzoylmethane exists as both enolic modifications.

Experimental

Isoxazole of *p*-Bromodibenzoylmethane.—A solution of 5.0 g. of the enol in 75 cc. of boiling methanol was treated with 2 g. of hydroxylamine hydrochloride in 5 cc. of water. The solution was refluxed for three hours, during which time the isoxazole separated as colorless crystals. The solution was cooled and filtered. The yield was 4.3 g. The melting point after recrystallization from methanol was 174–175°.

A solution of 2.5 g. of the enol in 40 cc. of boiling methanol was treated with 1 g. of hydroxylamine hydrochloride in 5 cc. of water, followed by 2 g. of potassium hydroxide in 5 cc. of water. The solution was alkaline to litmus paper. A yield of 0.6 g. was obtained after three hours of refluxing. The product melted and mix-melted with the above described material at 174–175°. This substance melted and mix-melted identically with a 50–50 mixture of (IX) and (X).

3-*p*-Bromophenyl-5-phenylisoxazoline (VIII).—The isoxazoline was prepared from *p*-bromobenzalacetophenone according to Blatt's method.[8] The yield was 6.2 g. and after recrystallizing from methanol the melting point was 130.5–131°.

Anal. Calcd. for $C_{15}H_{12}BrNO$: C, 59.6; H, 3.9. Found: C, 59.2; H, 3.5.

3-Phenyl-5-*p*-bromophenylisoxazole (IX).—A solution of 3.4 g. of the monobromide (V) in 75 cc. of boiling methanol was treated with 1.37 g. of hydroxylamine hydrochloride in 2.5 cc. of water, followed by 3.33 g. of potassium hydroxide in 5 cc. of water. The reaction proceeds like that of the dibromide. On recrystallization from ethanol, the product melted and mix-melted at 178–179° with the other two isoxazoles obtained from (III) and (VII).

3-*p*-Bromophenyl-5-phenylisoxazole (X). A. From the Isoxazoline of *p*-Bromobenzalacetophenone.—The isoxazoline was oxidized according to the procedure described by Blatt.[8] The melting point of the isoxazole was 179–180°.

B. From the Monobromide of *p*-Bromobenzalacetophenone.—The monobromide in 75 cc. of methanol was treated as usual with 1.75 g. of hydroxylamine hydrochloride in 2.5 cc. of water and 4.25 g. of potassium hydroxide in 5 cc. of water. The isoxazole obtained melted and mix-melted with that described above at 179–181°.

Anal. Calcd. for $C_{15}H_{10}BrNO$: C, 60.0; H, 3.3. Found: C, 59.7; H, 3.5.

Summary

Herein, we have shown that according to its behavior toward hydroxylamine in acidic or basic media, *p*-bromodibenzoylmethane exists as both enolic modifications.

Washington, D. C. Received June 28, 1944

---

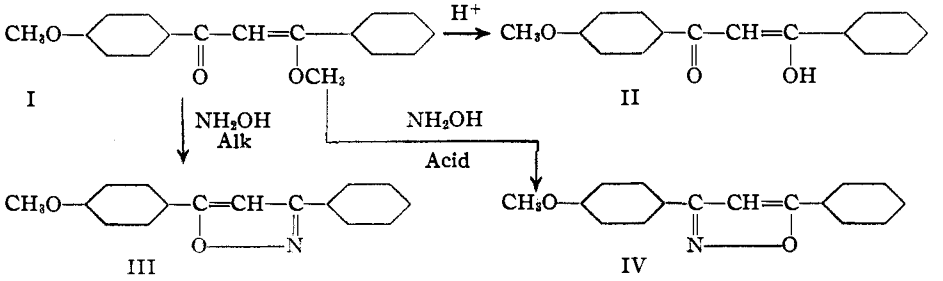
[12] Bodforss, *Ber.*, **49**, 2795 (1916).

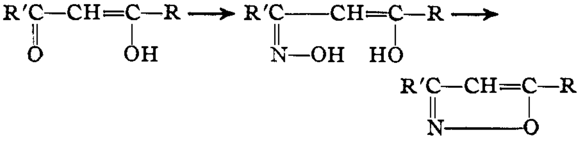
[Contribution from the Department of Chemistry, Howard University]

A Study of the Direction of Enolization of Mesitoyl-*m*-nitrobenzoylmethane

By R. Percy Barnes and Alfred S. Spriggs[1]

It has been shown[2,3,4] that isoxazole formation from enolic modifications of β-diketones is an important method for determining enolic structure. In this connection, it is interesting to note another fact regarding isoxazole formation. The conclusions of these last investigations, based on isoxazole formation, are valid only if we consider oxime formation by 1,2-addition to the carbonyl as an intermediate process, according to the general scheme





$$R'\underset{\underset{O}{\|}}{C}-CH=\underset{\underset{OH}{|}}{C}-R \longrightarrow R'\underset{\underset{N-OH}{\|}}{C}-CH=\underset{\underset{HO}{|}}{C}-R \longrightarrow R'\underset{\underset{N\text{———}}{\|}}{C}-CH=\underset{\underset{O}{|}}{C}-R$$

---

[1] In partial fulfillment of the requirements for the Master's Degree.

[2] Barnes and Brandon, This Journal, **65**, 1070 (1943).

[3] Barnes and Dodson, *ibid.*, **65**, 1585 (1943).

[4] Barnes and Dodson, *ibid.*, **67**, 132 (1945).