Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.1; H, 5.2. Found: C, 69.9; H, 5.5.

α-*m*-Nitrophenyl-β-mesitoylethylene Oxide (XIV).—To a hot solution of 2 g. of the unsaturated ketone in 35 cc. of alcohol was added with cooling and rapid stirring 1 g. of superoxol. The solution was made alkaline by the slow addition of saturated aqueous sodium hydroxide (3 g. in 5 cc. of water) and stirring continued for thirty minutes. The solution became yellow and crystals began to form. The solution was diluted with 20 cc. of water and stirred for fifteen more minutes and then chilled. Colorless crystals which separated were filtered, washed and dried. The melting point was 115°.

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.4; H, 5.5. Found: C, 69.2; H, 5.7.

The Enol of Mesityl-*m*-nitrobenzyl Diketone (XV).—To a solution of 15 g. of the oxide in 25 cc. of methanol was added cautiously and with warming a solution of 0.9 g. of sodium hydroxide in 2 cc. of water. The solution was boiled for ten minutes. The resulting deep brown solution was chilled and acidified with dilute hydrochloric acid, yielding 1.3 g. of a colorless solid. The melting point was 144.5–145°. This compound gives a deep brown color with alcoholic ferric chloride solution.

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.4: H, 5.5. Found: C, 69.3; H, 5.7.

Summary

1. The β-diketone, mesitoyl-*m*-nitrobenzoylmethane, has been prepared, and certain chemical evidence, based on oxime, isoxazoline and isoxazole formation, given in support of its direction of enolization.

2. In connection with this work, the isomeric enolic modification of the α-diketone, mesityl-*m*-nitrobenzyldiketone, was made but not studied.

WASHINGTON, D. C. RECEIVED JUNE 28, 1944

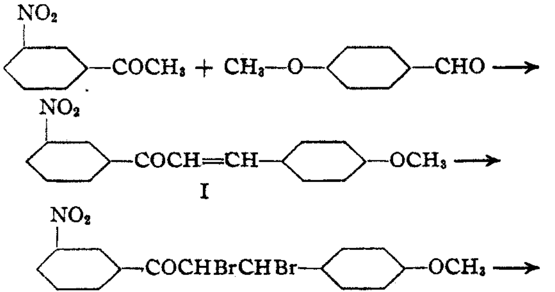
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HOWARD UNIVERSITY]

A Study of the Direction of Enolization of 3-Nitro-4'-methoxydibenzoylmethane[1]

BY R. PERCY BARNES AND JONATHAN L. SNEAD[1]

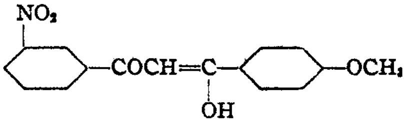
Because of the effect of the *p*-methoxy,[2] the *m*-nitro,[3] the *p*-bromo,[4] the mesityl and *m*-nitro groups[5] on the direction of enolization of β-diketones, and further in view of certain substituent effects on certain desoxybenzoins,[6] we made 3-nitro-4'-methoxydibenzoylmethane to study the combined substituent effect of these groups upon the direction and extent of enolization of this β-diketone.

To this end, we condensed *m*-nitroacetophenone with anisaldehyde, producing the α,β-unsaturated ketone (I). This compound was brominated, yielding the dibromide (II), which was refluxed with sodium methylate. The product of this reaction was acidified with hydrochloric acid, forming the enol (III).



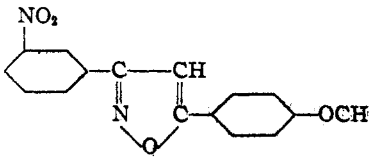
I

II



III

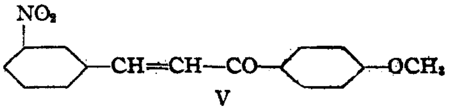
This diketone is essentially 100% enolic in methanol,[7] and upon treatment with hydroxylamine hydrochloride, yields the isoxazole (IV).



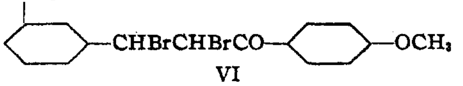
IV

The dibromide (II) upon refluxing with hydroxylamine hydrochloride in aqueous alcoholic solution with subsequent treatment with potassium hydroxide gave rise to the isoxazole (IV).

The α,β-unsaturated ketone (V) was brominated to the dibromide (VI) which was refluxed with sodium methylate, giving a product which when acidified with hydrochloric acid also yielded the enolic modification (III).



V



VI

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[1] In partial fulfillment of the requirements for the degree of Master of Science; presented before the Fall Meeting of the Organic Division of the Washington, D. C., section of the American Chemical Society, October 12, 1944.

[2] Barnes and Brandon, THIS JOURNAL, **65**, 1070 (1943).

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

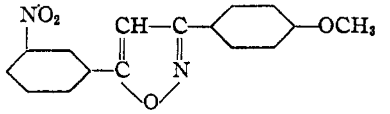
[4] Barnes and Dodson, *ibid.*, **67**, 132 (1945).

[5] Barnes and Spriggs, *ibid.*, **67**, 134 (1945).

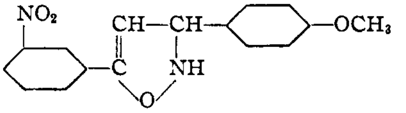
[6] Barnes, Cooper, Tulane and Delaney, *J. Org. Chem.*, **8**, No. 2 1943).

[7] Cooper and Barnes, *Ind. Eng. Chem.*, **10**, 379 (1938).

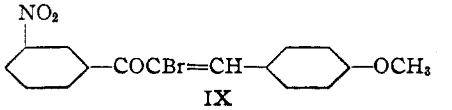
The dibromide (VI) yielded the isoxazole (VII).



VII



VIII



IX

The α-β-unsaturated ketone (I) was refluxed with hydroxylamine hydrochloride in alkaline medium producing the isoxazoline (VIII), which in turn was oxidized to the isoxazole (VII).

The monobromide (IX) was subjected to the same treatment as the dibromides (II) and (VI) with the production of the isoxazole (VII).

Thus it is apparent that the dibromides (II) and (VI) react with hydroxylamine hydrochloride by way of 1,2-addition to the carbonyl group whereas the α,β-unsaturated ketone (I) and the monobromide (IX) react by way of 1,4-addition to the conjugated system.

Assuming therefore that the enolic modification of this β-diketone reacts with hydroxylamine by way of 1,2-addition to the carbonyl group, as β-diketones do in certain instances,[8,9] the enolic modification of 3-nitro-4′-methoxydibenzoylmethane must be (III).

Experimental

p-Methoxybenzal-m-nitroacetophenone (I).—To 20 g. of *m*-nitroacetophenone, partially dissolved in 450 cc. of alcohol, was added with shaking 21 g. of anisaldehyde. Then with constant stirring and chilling 6 g. of sodium hydroxide dissolved in 20 cc. of water, was added. The stirring and chilling were continued for one hour, during which time crystals appeared. The product was filtered, washed, dried and crystallized from alcohol. The reaction yielded 40 g. of solid material, melting at 167–168°.

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.8; H, 4.6. Found: C, 67.3; H, 4.6.

α,β-Dibromo-p-methoxybenzal-m-nitroacetophenone (II).—To a solution of 24 g. of *p*-methoxybenzal-*m*-nitroacetophenone in 375 cc. of chloroform was added dropwise, with constant stirring, a solution of 13.5 g. of bromine in 20 cc. of chloroform. Constant stirring was continued for one hour, after which the solvent was evaporated with air and the residue purified by recrystallization from alcohol. A white solid, weighing 31.2 g. and melting at 102°, was obtained.

Anal. Calcd. for $C_{16}H_{13}Br_2NO_4$: C, 43.4; H, 3.0. Found: C, 42.9; H, 3.2.

1-p-Methoxyphenyl-3-m-nitrophenylpropene-one-3-ol-1 (III): **A. From the Dibromide** (II).—A solution of 20 g. of the dibromide (II) in 150 cc. of methanol was heated gently on a steam-bath. After refluxing had begun, a solution of 6 g. of potassium hydroxide in 50 cc. of methanol was added in small portions. When about half the alkali had been added, the dibromide was completely in solution and the reaction mixture colorless. After all the alkali had been added, the solution became yellow, an indication that the reaction was complete. Then the solution was chilled and acidified with dilute hydrochloric acid (1:2) with stirring. The material obtained was filtered, washed and recrystallized from alcohol. The 6.8 g. of crystals obtained melted at 128–128.5°, and gave a positive enol test with ferric chloride.

B. From the Dibromide (VI).—Partially dissolved in 150 cc. of methanol, 6 g. of dibromide (VI) was heated to refluxing on steam-bath. To this was added 1 g. of potassium hydroxide in 50 cc. of methanol. When the alkali had been added, the dibromide was completely in solution. Then the reaction mixture turned from colorless to yellow, indicating completeness of reaction. The product was recrystallized from alcohol to yield 2.1 g. of a yellow material, melting at 128–129°. These crystals, which gave a positive enol test, mix-melted unchanged with the enol from dibromide (II).

Anal. Calcd. for $C_{16}H_{13}NO_5$: C, 64.2; H, 4.4. Found: C, 63.6; H, 4.4.

This substance is essentially 100% enolic in methanol.[7]

3-m-Nitrophenyl-5-p-methoxyphenylisoxazole (IV): **A. From Enol** (III).—To 5 g. of the enol in 100 cc. of alcohol was added 1.2 g. of hydroxylamine hydrochloride in 100 cc. of water. This solution was refluxed gently for thirty minutes on the steam-bath. On cooling, a light colored solid separated which was recrystallized from alcohol and yielded 3.5 g. of material melting at 175–176°.

B. From the Dibromide (II).—To 5 g. of dibromide in boiling alcohol was added 1 g. of hydroxylamine hydrochloride in 5 cc. of water. While hot, this solution was treated with 4.5 g. of potassium hydroxide in 5 cc. of water. The highly colored solution (dark red) was allowed to stand for ten minutes and then cooled. After filtration, the crystals were washed thoroughly with water to take out the potassium bromide formed. The reaction yielded 0.5 g. of a light colored substance, which melted and mix-melted sharply with that obtained from the enol.

Anal. Calcd. for $C_{16}H_{12}N_2O_4$: C, 64.9; H, 4.1. Found: C, 64.3; H, 4.5.

m-Nitrobenzal-p-methoxyacetophenone (V).—To a solution of 10 g. of *p*-methoxyacetophenone in 175 cc. of alcohol was added with shaking 10 g. of *m*-nitrobenzaldehyde. To this solution was added, with stirring, 2.7 g. of sodium hydroxide in 10 cc. of water. Stirring and chilling were continued for one hour, after which the crystals were filtered and recrystallized from alcohol. The yield was 18 g. of product which melted at 153–154°.

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.8; H, 4.6. Found: C, 67.5; H, 4.8.

α,β-Dibromo-m-nitrobenzal-p-methoxyacetophenone (VI).—To 10 g. of the condensation product, dissolved in 275 cc. of chloroform, was added dropwise with constant stirring 5.7 g. of bromine in 50 cc. of chloroform. After stirring for one hour, the solvent was evaporated and the residue crystallized from alcohol. The yield was 13 g. of product which melted at 165–166°.

Anal. Calcd. for $C_{16}H_{13}Br_2NO_4$: C, 43.4; H, 3.0. Found: C, 43.0; H, 3.1.

3-p-Methoxyphenyl-5-m-nitrophenylisoxazole (VII): **A. From the Dibromide** (VI).—To 5 g. of dibromide in 150 cc. of alcohol was added 1 g. of hydroxylamine hydrochloride in 5 cc. of water. While hot, the reaction mixture was treated with 4.5 g. of potassium hydroxide in 5 cc. of water. The solution became red as potassium bromide separated. After allowing to stand for ten minutes, the reaction mixture was cooled and filtered. Upon recrystallization from alcohol, and thorough washing with water, 2.5 g. of material was obtained which melted at 182–183°.

B. From the Isoxazoline (VIII).—Dissolved in 100 cc. of glacial acetic acid, 2.1 g. of the isoxazoline was heated to 80°. While hot, 1.3 g. of chromic oxide was added to the solution with stirring. The stirring was continued for two hours, after which the reaction mixture was poured

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(8) Weygand and Bauer, *Ann.*, **459**, 127 (1928).

(9) Barnes and Spriggs, This Journal, **67**, 134 (1945).

into 400 cc. of water and chilled. The resulting precipitate was filtered, washed and mixed with an amount of alcohol insufficient for complete solution. The residue was recrystallized from alcohol. The yield was 0.5 g. of product, melting at 181–182°, and mix-melting unchanged with (VII).

C. **From the Monobromide (IX).**—Five grams of the monobromide was dissolved in 150 cc. of boiling alcohol. To this solution was added 1 g. of hydroxylamine hydrochloride in 5 cc. of water, and 4.5 g. of potassium hydroxide in 5 cc. of water. The solution turned red as potassium salts separated. After standing for ten minutes, the reaction mixture was cooled and filtered. After recrystallization from alcohol, the material melted and mix-melted with the products from (A) and (B) at 182°.

Anal. Calcd. for $C_{16}H_{12}N_2O_4$: C, 64.9; H, 4.1. Found: C, 65.3; H, 4.2.

3-*p*-Methoxyphenyl-5-*m*-nitrophenylisoxazoline (VIII).—To 11.3 g. of the α,β-unsaturated ketone (I) in 300 cc. of alcohol was added 4.2 g. of hydroxylamine hydrochloride, in 20 cc. of water, and 8 g. of potassium hydroxide in 20 cc. of water. The reaction mixture, which turned dark, was refluxed for two hours. The solution was allowed to stand overnight and the crystals which separated were washed thoroughly with water to take out the potassium chloride formed. Upon recrystallization, 3.5 g. of material melting at 175–179° was obtained. Another recrystallization from alcohol did not change the melting point range.

Anal. Calcd. for $C_{16}H_{14}N_2O_4$: C, 64.4; H, 4.7. Found: C, 65.0; H, 4.9.

α-Bromo-*p*-methoxybenzal-*m*-nitroacetophenone (IX).—A solution of 10 g. of the dibromide in 150 cc. of glacial acetic acid was refluxed for two hours with 20 g. of freshly fused potassium acetate. The solution became slightly colored. It was cooled and poured into a large volume of water. A dark red oil separated. This oil was dissolved in ether, washed with water, freed of the last traces of acetic acid by shaking with sodium bicarbonate solution, washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* over solid potassium hydroxide. There resulted a viscous, dark red oil which weighed 6.8 g.

Anal. Calcd. for $C_{16}H_{12}BrNO_4$: C, 53.1; H, 4.3. Found: C, 53.0; H, 3.6.

Summary

The authors have prepared 3-nitro-4′-methoxydibenzoylmethane, and have shown that in alcoholic solution it is essentially 100% enolic and behaves as 1-*p*-methoxy-phenyl-3-*m*-nitrophenylpropene-one-3-ol-1 in isoxazole formation, giving rise to 3-*m*-nitrophenyl-5-*p*-methoxyphenylisoxazole (IV).

WASHINGTON, D. C. RECEIVED OCTOBER 2, 1944

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE COLLEGE OF WASHINGTON]

The Bromination of 4-Phenylphenyl Trimethylacetate

BY LEE C. HENSLEY AND STEWART E. HAZLET

In previous studies of the bromination of 4-phenylphenol esters of various acids, the acetyloxy group has been shown to direct an entering bromine atom to an adjacent position in the biphenyl nucleus,[1] but the presence of a larger benzoyloxy[2] or benzenesulfonyloxy group[3] caused bromine to enter the molecules at the remote para position. Similar substitution at the remote end of the biphenyl system was found when the corresponding chloro- and bromoacetates were brominated,[4] although, of necessity, the experimental conditions were modified considerably. In the present report, the trimethylacetyloxy group also has been shown to direct an entering bromine atom to the remote para position under the same experimental conditions as those employed for the haloacetates; difficulties similar to those encountered with the chloro- and bromoacetates were met when acetic acid was used as solvent.

A reason for the selection of the trimethylacetate for study was that in this compound, on the basis of Fisher–Hirshfelder models,[5] effective simple spacial hindering dimensions of the acyloxy group are somewhat comparable to those in the benzoate; *i. e.*, a rather large acyloxy group with a possible screening effect is present. The results of this investigation corroborate the suggestions advanced previously that steric hindrance may function, in part, in determining the orienting influences of the groups present and force bromination to take place in the ring not bearing the acyloxy group. An alternative view, that the strengths of the acids corresponding to the acyloxy groups involved are factors, is eliminated by the present work with 4-phenylphenyl trimethylacetate. The ionization constant of trimethylacetic acid is lower than that of acetic acid which, in turn, is lower than that of benzoic, bromoacetic, chloroacetic or benzenesulfonic acid.[6] This does not parallel the orienting influences of the acyloxy groups; acetyloxy was the only one which permitted substitution in an adjacent position.

Some related compounds have been prepared; descriptions of these are given in the Experimental Part.

Experimental Part

Trimethylacetic Acid.—This material was obtained by the method of Puntambeker and Zoellner[7] from *t*-butyl chloride or bromide, which had been prepared according to the procedure of Norris and Olmsted[8]; of the two, the chloride gave somewhat better yields.

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[1] Hazlet and Kornberg, THIS JOURNAL, **61**, 3037 (1939).

[2] Hazlet, Alliger and Tiede, *ibid.*, **61**, 1447 (1939).

[3] Hazlet, *ibid.*, **59**, 1087 (1937).

[4] (a) Hazlet, Hensley and Jass, *ibid.*, **64**, 2449 (1942); (b) Hensley and Hazlet, *ibid.*, **65**, 987 (1943).

[5] Manufactured and distributed by the Fisher Scientific Co., Pittsburgh, Penna.

[6] "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., 1929, Vol. VI, p. 262 *et seq.*

[7] Gilman and Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 2nd ed., 1941, p. 524.

[8] *Ibid.*, p. 144.