

of the oxygen atom. Therefore, sodium oxalate shows much less solubility in glycols than sodium acetate or benzoate (Tables VI and VII). Sodium hyposulfite, $(\text{SO}_2\text{Na})_2$, being a salt of a dibasic acid, shows fair solubility but less than other similar compounds.

Acknowledgment.—The author gratefully acknowledges his indebtedness to Prof. James W. McBain for his interest and advice.

Summary

Any mixture consisting of two solvents, one of the glycolic type (called G-solvent) and the other any organic solvent which can dissolve hydrocarbons, *e. g.*, higher alcohols, chlorinated hydrocarbons, etc. (called H-solvent), has been found to have better solvent power for soaps than any of the pure solvents alone. Extensive study of the solvent property of various G-H mixtures has been made.

The glycol forms hydrogen bonds with the $-\text{COO}^-$ end of the soap, and the alkyl group of the soap is dissolved by the H-solvent, and thus the mixture is more effective than the individual solvents. The cause of the hydrogen-bonding power of glycol in comparison with alcohols is ascribed to the effect of the interaction of one electronegative group on another, making the hydroxylic hydrogen atom of glycols more positive than it would otherwise be. The long known soap-dissolving power of phenols, cresols, methyl alcohol, etc., is also explained from this viewpoint.

It has also been shown that inorganic salts having the group XOO^- , where X is any non-metallic element, *e. g.*, nitrites, hypophosphites, etc., have very high solubility in glycols owing to this glycolic interaction.

RECEIVED OCTOBER 19, 1946

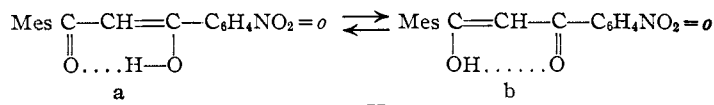
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HOWARD UNIVERSITY]

A Study of the Direction of Enolization of Mesityl-*o*-nitrobenzoylmethane and Mesityl-*p*-nitrobenzoylmethane

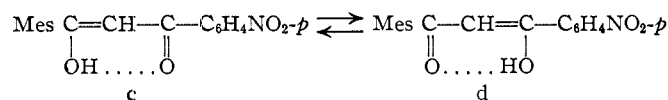
BY R. PERCY BARNES, GLADYS ESTELLE PINKNEY¹ AND WILLIAM A. DACOSTA¹

In continuation of the study of the direction of enolization of β -diketones,² we have made mesityl-*o*-nitrobenzoylmethane and mesityl-*p*-nitrobenzoylmethane and after carrying out certain reactions on related compounds conclude that their enolic modifications are (VII) and (VII'), respectively. These substances are 100% enolic in methanol solution.

First *o*-nitrobenzaldehyde and *p*-nitrobenzaldehyde were condensed separately with acetomesitylene to give the chalcones (I) and (I'), which were brominated to the dibromides (III) and (III').

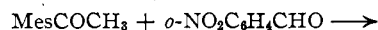


VII



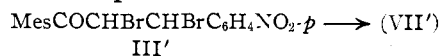
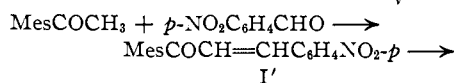
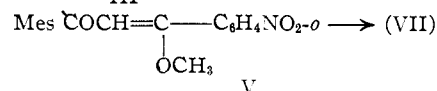
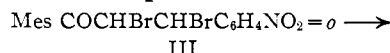
VII'

The dibromide (III) was converted by treatment with alcoholic potassium hydroxide to the methyl ether (V), which upon hydrolysis gave rise to the enol (VII). Dibromide (III') upon treatment with alcoholic potassium hydroxide went directly to the enol (VII').

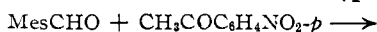
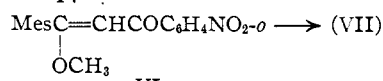
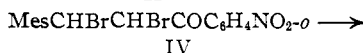
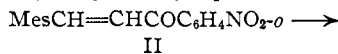
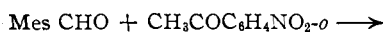


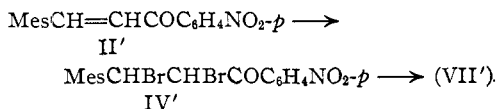
(1) In partial fulfillment of the requirements for the Master's Degree.

(2) R. Percy Barnes and Jonathan L. Snead, THIS JOURNAL, 67, 138 (1945).



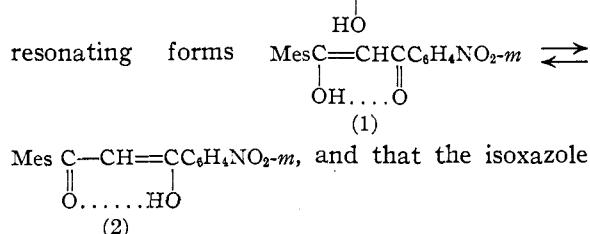
Secondly, *o*-nitroacetophenone and *p*-nitroacetophenone were condensed separately with 2,4,6-trimethylbenzaldehyde to give the chalcones (II) and (II'), which in turn were brominated to (IV) and (IV'). Dibromide (IV) was treated as was its isomer (III), producing the methyl ether (VI), which was also hydrolyzed to the enol (VII). Dibromide (IV') upon treatment with alcoholic potassium hydroxide went directly to enol (VII').





The enol (VII) on prolonged treatment with hydroxylamine hydrochloride was only partially converted into the isoxazole (VIII), the unreacted material being recovered as enol. It is our contention that since the resonating enols (VIIa) and (VIIb) may be expected to be rapidly interconvertible, the effect of the *o*-nitro group is to shift the equilibrium far toward (VIIa) with simultaneous activation of the carbonyl group adjacent to the mesityl nucleus to such an extent that the reaction rate of (VIIa) is the controlling factor in isoxazole formation. Thus the enol (VII) reacts as (VIIa). This activating effect, we believe, is in accordance with the findings on quinoxaline formation from benzils with highly hindered carbonyls.³

In the light of the behavior of enol (VII) and also because of more recent findings (to be reported subsequently), we are compelled to report that the representation of the enolic modifications of mesityl-*m*-nitrobenzoylmethane must be changed from $\text{MesCOCH}=\text{CC}_6\text{H}_4\text{NO}_2\text{-}m$ to the



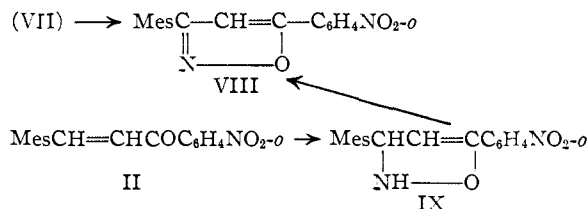
is formed by 1,2-addition of hydroxylamine to the carbonyl of (1) and *not* through the diketone form as represented.⁴

In the case of (VII') the effect of the *p*-nitro group² is such as to cause (VII'c) to preponderate and to enhance its reaction rate over that of (VII'd) since the isoxazole (XI') is the sole product of the complete conversion of the enol. Hence the enol (VII') reacts as (VII'c).

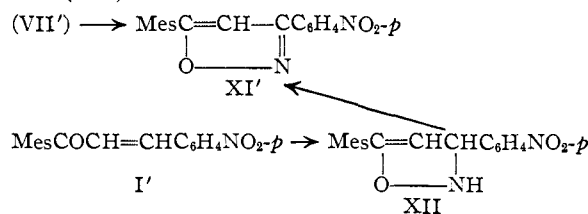
We determine the structure of the isoxazoles by comparing them with materials obtained from oxidation of the isoxazolines prepared from the chalcones. The basis for this is the fact that Blatt⁵ has found that chalcone oximes are not converted to isoxazolines under the same conditions that chalcones produce isoxazolines, but that the chalcone oximes are recovered unchanged. Thus isoxazoline formation does not proceed by 1,2-addition to the carbonyl. The other feasible course of the reaction is 1,4-addition.

The chalcone (II) was converted to the isoxazoline (IX) and this in turn was oxidized to the

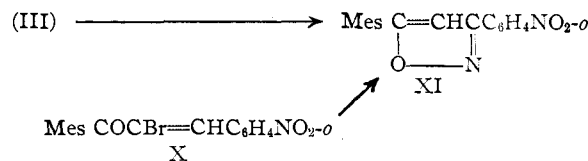
isoxazole (VIII). The isomeric chalcone (I) could not be converted to an isoxazoline.



The chalcone (II') did not yield an isoxazoline, but chalcone (I') was converted to the isoxazoline (XII), which was in turn converted into the isoxazole (XI').



Both the dibromide (III) and the α -bromo-*o*-nitrobenzalacetomesitylene (X) upon treatment with alkaline hydroxylamine yielded the isoxazole (XI).



Experimental

The chalcones I, I', II and II' and their dibromides III, III', IV and IV' were prepared according to standard procedures.^{6,7} It was found, however, that (I) could be obtained in larger yield of purer crude product as follows: To a solution of 2 g. of *o*-nitrobenzaldiacetate (1 mole) in 25 cc. of methanol was added 1.3 g. of acetomesitylene (1 mole) and 1.4 g. of potassium hydroxide (3 moles) in 10 cc. of water. The solution was pale yellow and transparent. On warming to 40°, the solution became cloudy, and after one hour an oil separated. Upon gentle cooling and shaking crystallization occurred. The material was filtered, washed and dried. It weighed 2.2 g. Recrystallization from methanol yielded a material melting sharply at 92°.

TABLE I

Compound	M. p., °C.	Color	Anal. Calcd. for C ₁₈ H ₁₇ NO ₂ : C, 73.2; H, 5.8
I	92	Pale yellow	Found: C, 73.1; H, 6.0
I'	121	Pale yellow	Found: C, 72.9; H, 5.7
II	81-82	Buff	Found: C, 73.0; H, 5.6
II'	109-110	Tan	Found: C, 73.4; H, 6.1
			C ₁₈ H ₁₇ Br ₂ NO ₂ : C, 47.5; H, 3.7
III	124-125	Colorless	Found: C, 47.4; H, 3.7
III'	149-150	Colorless	Found: C, 47.6; H, 3.6
IV	130-133	Colorless	Found: C, 47.3; H, 3.6
IV'	161	Colorless	Found: C, 47.3; H, 4.0

(6) E. P. Kohler and H. M. Chadwell, "Org. Syn." Coll. Vol. 1, 78 (1941).

(7) C. F. H. Allen, R. D. Abell and J. B. Normington, *ibid.*, 205 (1941).

(3) Reynold C. Fuson and Quentin F. Soper, *J. Org. Chem.*, **9**, 193 (1944).

(4) R. Percy Barnes and Alfred S. Spriggs, *THIS JOURNAL*, **67**, 134 (1945).

(5) A. H. Blatt, *ibid.*, **58**, 1133 (1931).

The Methyl Ether of 1-*o*-Nitrophenyl-3-mesityl-propenone-3-*ol*-1 (V).—To a refluxing solution containing 10 g. of the dibromide (III) in 100 cc. of methanol was added slowly a solution of 2.8 g. potassium hydroxide in 9 cc. of methanol. The yellow solution turned dark green upon the addition of potassium hydroxide. Gradually the solution became deep yellow. There was violent bumping. Refluxing was continued for one hour. The solution was then chilled, and with chilling and stirring was acidified with 10 cc. of dilute hydrochloric acid. Pale yellow crystals began to form. The mixture was chilled for an hour, filtered, and the precipitate washed with cold water. The pale yellow solid was recrystallized from methanol yielding 4.2 g. of yellow crystals melting at 92°.

Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 70.1; H, 5.8. Found: C, 70.2; H, 5.85.

The Methyl Ether of 1-Mesityl-3-*o*-nitrophenyl-propenone-3-*ol*-1 (VI).—To a refluxing solution of 0.5 g. of dibromide (IV) in 16 cc. of methanol was added 0.14 g. of potassium hydroxide in 1 cc. of methanol. The solution became deep yellow and refluxing was continued for three hours. The solution was chilled for an hour. A precipitate was formed. It was filtered and washed with cold water. The light yellow powdery material was recrystallized from methanol, yielding 0.2 g. of white crystals melting at 138°.

Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 70.1; H, 5.8. Found: C, 69.9; H, 5.9.

Preparation of Enol (VII). A. From Methyl Ether (V).—To a refluxing solution of 4.2 g. of methyl ether dissolved in 50 cc. of methanol was added dilute hydrochloric acid until the solution was slightly acidic. The solution was refluxed for fifteen minutes. On cooling, yellow crystals separated. The substance was filtered and dried. The yellow solid was recrystallized from ethanol and 3 g. of bright yellow crystals, melting at 150°, was obtained. These crystals gave a deep red coloration with alcoholic ferric chloride.

B. From Methyl Ether (VI).—To a solution of 0.1 g. of methyl ether in 1 cc. of methanol were added a few drops of hydrochloric acid. The solution was refluxed for nine hours. The reaction mixture was chilled and yellow crystals were obtained which gave a color with alcoholic ferric chloride and which melted and mix-melted with the enol obtained from methyl ether (V) at 150°.

Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 69.4; H, 5.5. Found: C, 69.3; H, 5.5.

This substance is 100% enolic in alcoholic solution by Kurt Meyer titration.

Preparation of the Enol (VII'). A. From Dibromide (III').—To a 10-g. sample of the dibromide was added 31 cc. of methanol. The solution was refluxed and 2.8 g. of potassium hydroxide in 17 cc. of methanol was added slowly. The mixture was colorless until over half the potassium hydroxide had been added, when it became orange red. Refluxing was continued for one hour. The solution was then chilled, and, with chilling and stirring, was acidified with dilute hydrochloric acid. A light tan oil separated. It was then left to chill overnight. The next day a light tan solid had separated along with a light tan oil. The crystals were separated from the oil by decantation and washed with water to dissolve potassium bromide. The oil was washed with water and dissolved in methanol, and the solution on gradual cooling gave light tan crystals which were filtered and combined with the previous amount obtained. These crystals gave a positive ferric chloride test. It yielded 3 g. of a material melting at 104–105°.

B. From Dibromide (IV').—To a 0.4-g. sample of dibromide (IV') was added 60 cc. of methanol, the solution refluxed gently, and to it added 0.2 g. of potassium hydroxide in 8 cc. of methanol. When over half of the potassium hydroxide solution had been added the mixture became light red, then finally dark red. It was then refluxed for one hour. Upon chilling and acidifying with dilute hydrochloric acid a light tan solid separated. It was filtered, washed and dried. The melting point was 104–105°. It mix-melted with enol from dibromide (III')

with no depression. A positive ferric chloride test was observed.

Anal. Calcd. for $C_{19}H_{17}NO_4$: C, 69.4; H, 5.5. Found: C, 69.2; H, 5.7.

This substance is 100% enolic by Kurt Meyer titration.

Preparation of the Isoxazole (VIII).—To a hot solution of 0.8 g. of enol (VII) in 30 cc. of ethanol was added 1 g. of hydroxylamine hydrochloride in 2 cc. of water. The mixture was refluxed for forty hours. On cooling, a yellow solid separated which melted at 115–138°. This solid gave a red color with alcoholic ferric chloride. By successive recrystallizations several fractions were obtained. Some colorless crystals melting at 114–115° and which gave no color with alcoholic ferric chloride were obtained.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.1; H, 5.2. Found: C, 69.9; H, 5.4.

Preparation of Isoxazoline (IX).—To a solution of 6 g. of chalcone (II) in 180 cc. of butanol was added 5 g. of hydroxylamine hydrochloride in 5 cc. of water. To this solution was added 5 g. of potassium hydroxide in 6 cc. of water. The mixture turned red-brown. The solution was refluxed for one hour. Upon cooling, potassium chloride separated. The mother liquors were evaporated almost to dryness on the hot plate. The residue was dissolved in the least amount of methanol and bone-blackened. Yellow crystals weighing 2 g. melting at 119–120° were obtained.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 69.7; H, 5.8. Found: C, 69.6; H, 5.6.

Preparation of Isoxazole (VIII) from the Isoxazoline.—To a solution containing 0.4 g. of isoxazoline in 25 cc. of acetic acid was added 0.2 g. of red chromic oxide. The solution turned green. It was heated on the steam-bath at 80° for one half hour with occasional stirring. The solution was cooled and poured into 500 cc. of cold water. The aqueous mixture was extracted with ether, washed with sodium bicarbonate and dried over anhydrous sodium sulfate. On evaporation a solid was obtained which upon recrystallization from methanol yielded cream-colored crystals melting at 114–115°. A mixture of this substance and that from the enol melted sharply at 115°.

Anal. Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.1; H, 5.2. Found: C, 70.0; H, 5.1.

Preparation of the Monobromide (X).—A solution of 6 g. of dibromide (III), 6 g. of freshly fused potassium acetate and 50 cc. of glacial acetic acid was refluxed for three hours on a hot-plate. The mixture was cooled and poured into 500 cc. of cold water. Pale yellow crystals were formed which were recrystallized from methanol. The product weighed 3 g. and melted at 124°.

Anal. Calcd. for $C_{18}H_{17}BrNO_3$: C, 57.8; H, 4.3. Found: C, 58.0; H, 4.1.

Preparation of the Isoxazole (XI). A. From the Dibromide (III).—To a suspension of 5 g. of dibromide in 100 cc. of hot ethanol was added 2.5 g. of hydroxylamine hydrochloride in 5 cc. of water. The mixture was boiled five minutes on the steam-bath, then while still hot 5 g. of potassium hydroxide in 5 cc. of water was added slowly. On the addition of the alkali the solution turned dark green, then deep red. The solution was allowed to stand five minutes and the potassium bromide which separated was filtered. Then the filtrate was chilled and diluted to cloudiness with water. The solution was allowed to stand overnight in the ice-box. A light yellow solid separated. It was filtered, washed and dried. The product weighed 1 g. and melted at 124°.

B. From the Monobromide (X).—To a hot solution of 1 g. of the monobromide in ethanol was added 1 g. of hydroxylamine hydrochloride in 1 cc. of water. Then 1 g. of potassium hydroxide in 1 cc. of water was added slowly. The solution turned green, then dark red and was refluxed for forty-five minutes. The mixture was chilled and diluted to cloudiness with water. A light yellow solid formed which was filtered, washed and dried. It was recrystallized from methanol. The product weighed 0.3 g. and melted at 124°. It mix-melted with the above substances with no depression.

Anal. Calcd. for $C_{13}H_{16}N_2O_3$: C, 70.1; H, 5.2. Found: C, 70.4; H, 5.6.

Preparation of the Isoxazole (XI') from Enol (VII').—To a hot solution of 1 g. of enol in 35 cc. of methanol was added 0.6 g. of hydroxylamine hydrochloride in 5 cc. of water. The mixture was refluxed for three hours. On cooling, a colorless solid separated. This solid was filtered, washed and recrystallized from methanol. It gave 0.7 g. of a material melting at 141° . A negative ferric chloride test was observed.

Preparation of the Isoxazole (XI') by Acid Treatment of the Isoxazoline (XII).—A solution containing 0.5 g. of the isoxazoline in 20 cc. of methanol was acidified with 5 cc. of dilute hydrochloric acid. This solution was refluxed for one hour. On cooling, very light colored crystals began falling out. The solid was filtered and recrystallized from methanol, yielding 0.2 g. of material melting at 141° . On mix-melting with the isoxazole from the enol no depression was found.

Anal. Calcd. for $C_{13}H_{16}N_2O_3$: C, 70.1; H, 5.2. Found: C, 70.3; H, 5.3.

Preparation of the Isoxazoline (XII).—To a solution containing 6 g. of the α,β -unsaturated ketone (I') in 140 cc. of methanol was added 5 g. of hydroxylamine hydro-

chloride in 5 cc. of water and 4 g. of potassium hydroxide in 20 cc. of water. The potassium hydroxide solution was added slowly. The mixture turned a reddish brown. It was refluxed for two hours. Upon cooling potassium chloride fell out, but was not filtered. The mixture was then poured into 500 cc. of cold water and allowed to stand overnight. The next day light tan crystals were found to have settled out. They were filtered and recrystallized from methanol, yielding 2.2 g. of a material melting at $177-178^\circ$.

Anal. Calcd. for $C_{13}H_{16}N_2O_3$: C, 69.7; H, 5.9. Found: C, 69.3; H, 5.8.

Summary

The β -diketones mesityl-*o*-nitrobenzoylmethane (VII) and mesityl-*p*-nitrobenzoylmethane (VII') have been prepared. Chemical evidence indicates that they react preponderantly as 1-*o*-nitrophenyl-3-mesitylpropeneone-3-ol-1 (VIIa) and 1-mesityl-3-*p*-nitrophenylpropeneone-3-ol-1 (VII'c), respectively, in isoxazole formation.

WASHINGTON, D. C.

RECEIVED MAY 1, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HOWARD UNIVERSITY]

A Study of the Direction of Enolization of *p*-Methoxybenzoylmesitylmethane

BY R. PERCY BARNES AND GEORGE W. REED¹

It has long been known that the di-ortho substituents in the mesityl nucleus offer spatial interference to reactions of 1,2-addition to an adjacent carbonyl. More recently, however, it has been shown that the presence of certain groups in the mesityl nucleus or the phenyl group of benzils serves to activate the hindered carbonyl to the extent that such substances undergo quinoxaline formation.² It has also been reported that the presence of a nitro group in the para position of the phenyl ring of benzoylmesitylmethane serves to enhance the activity of the hindered carbonyl, so much so that enolization occurs toward the mesityl nucleus.³

The purpose of this investigation was to determine the effect of the *p*-methoxy group on the direction of enolization of *p*-methoxybenzoylmesitylmethane.

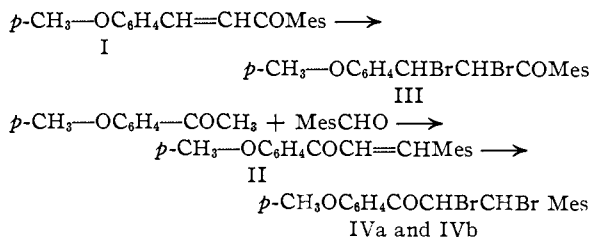
Thus we prepared chalcone (II) and converted it and its isomer, *p*-methoxybenzalacetomesitylene⁴ (I), into their dibromides (III) and (IVa) and (IVb). The dibromides (IVa) and (IVb) derived from the chalcone (II) melted at 105 and 152° , respectively, and behaved alike chemically.

(1) In partial fulfillment of the requirements for the Master's Degree.

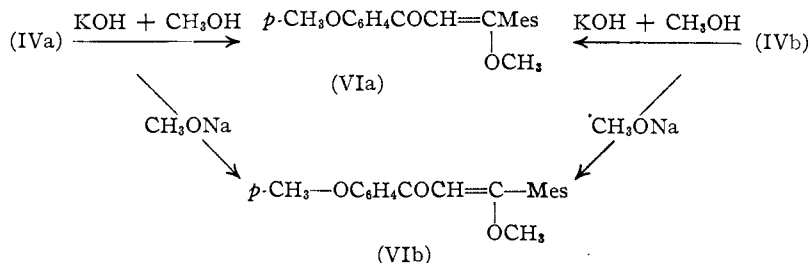
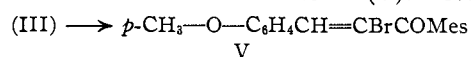
(2) Reynold C. Fuson and Quentin F. Soper, *J. Org. Chem.*, **9**, 193 (1944).

(3) R. Percy Barnes, Gladys Estelle Pinkney and William A. DaCosta, *THIS JOURNAL*, **69**, 3129 (1947).

(4) R. Percy Barnes and Harold Delaney, *ibid.*, **65**, 2155 (1943).



The dibromide (III) was easily converted into the α -bromo-unsaturated ketone (V). Neither



(III) nor (V) gave rise to a stable methyl ether. On the other hand, neither of the isomeric dibromides (IVa) and (IVb) yielded a monobromide. Dibromides (IVa) and (IVb) under one set of conditions yield (VIa); under a different set of conditions they yield (VIb).

Both the dibromide (III) and the monobromide (V) upon treatment with methyl alcoholic potassium hydroxide gave the enol (VII). The methyl ether (VIa) was hydrolyzed with difficulty to the