# REACTIONS OF BENZOFURAZAN OXIDE

# WITH

# SOME 1,3-DIKETONES

By

MUHAMMAD UTHMAN MAHMUD TAHA

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# REACTIONS OF BENZOFURAZAN OXIDE WITH SOME 1,3-DIKETONES

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MUHAMMAD UTHMAN MAHMUD TAHA

Approved:

Professor Makhloof J. Haddadin _____
Advisor and Chairman

Professor Costas H. Issidorides _____
Member

Professor Souheil E. Saheb _____
Member

Professor Landry T. Slade _____
Member

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## ABSTRACT

The reaction, in diethylamine or triethylamine, of benzofurazan oxide (5) with benzoylacetone (9), p-methoxybenzoylacetone (10), p-bromobenzoylacetone (11), p-methylbenzoylacetone (12), and p-nitrobenzoylacetone (13) resulted in the formation, in fair to good yield, of 2-methyl-3-benzoylquinoxaline-di-N-oxide (20), 2-methyl-3-p-methoxybenzoylquinoxaline-di-N-oxide (21), 2-methyl-3-p-bromobenzoylquinoxaline-di-N-oxide (22), 2-methyl-3-p-methylbenzoylquinoxaline-di-N-oxide (23), and 2-methyl-3-p- nitrobenzoylquinoxaline-di-N-oxide (24) respectively. In every case, the isolated quinoxaline-di-N-oxide was the sole product.

Substitution on the aromatic ring does not seem to be a major factor in the control of the nature of the product.

The above reaction is a simple method for the synthesis of 2,3-disubstituted quinoxaline-di-N-oxides which are difficult to obtain by other methods.

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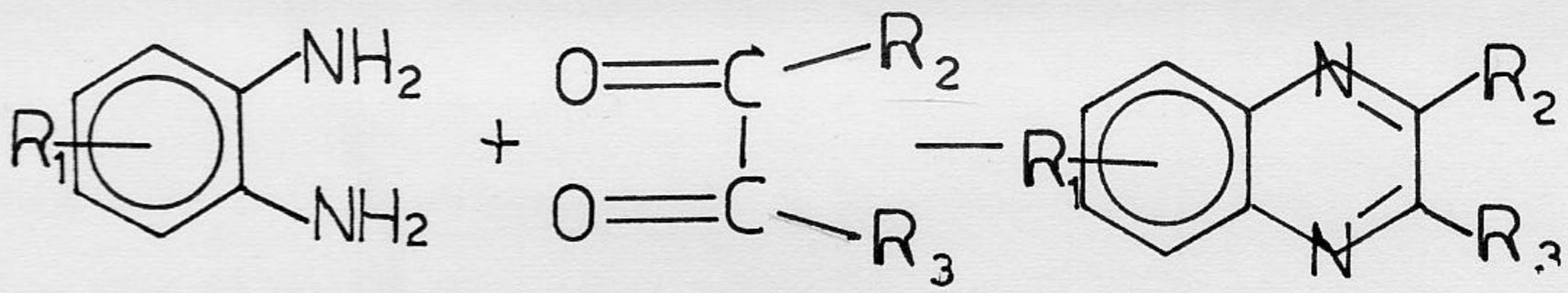
# INTRODUCTION

Recent interest in quinoxaline-di-N-oxides has been centred around their promising activity as anti-bacterial agents.[1] Although some of these compounds are effective against amoebic infections in some experimental animals[1], their use for human beings has not been successful so far. The availability of a variety of quinoxaline-di-N-oxides, through easy methods of synthesis, would allow further screening of such compounds for therapeutic purposes.

The classical method for the preparation of quinoxaline-di-N-oxides (4) consists of treatment of quinoxalines (3) with hydrogen peroxide in acetic acid.[2] Quinoxalines (3), in turn, are synthesized from the condensation of 1,2-dicarbonyl compounds (2) with o-amino anilines (1).[3]

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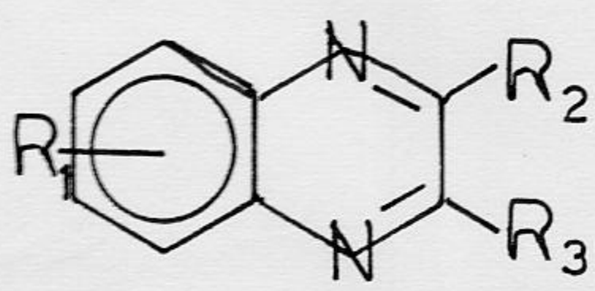


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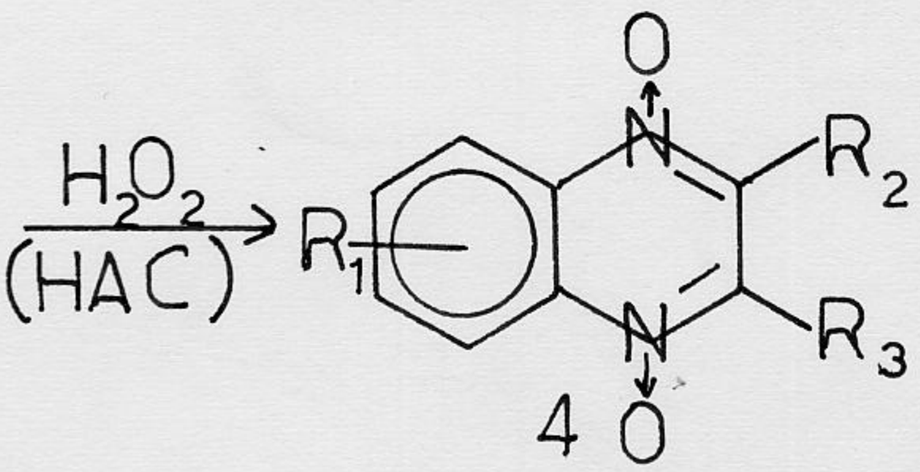


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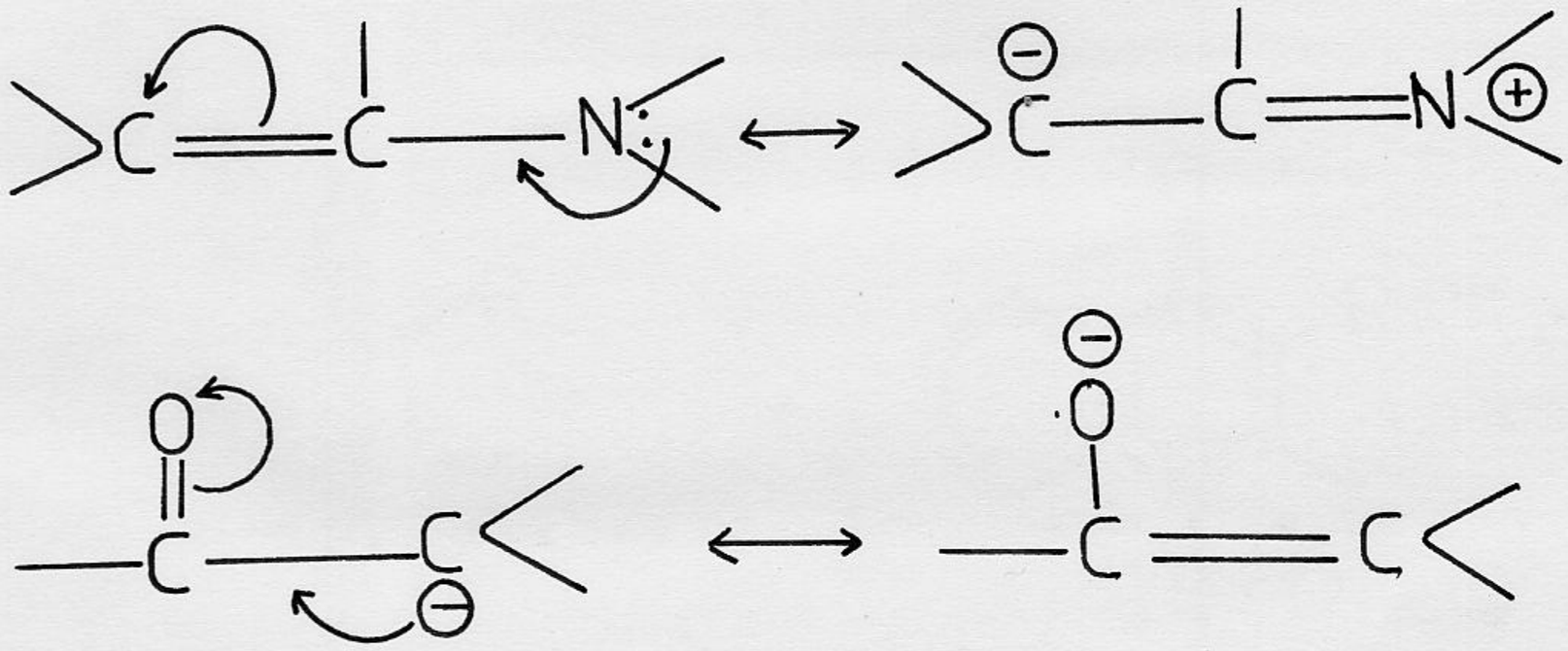
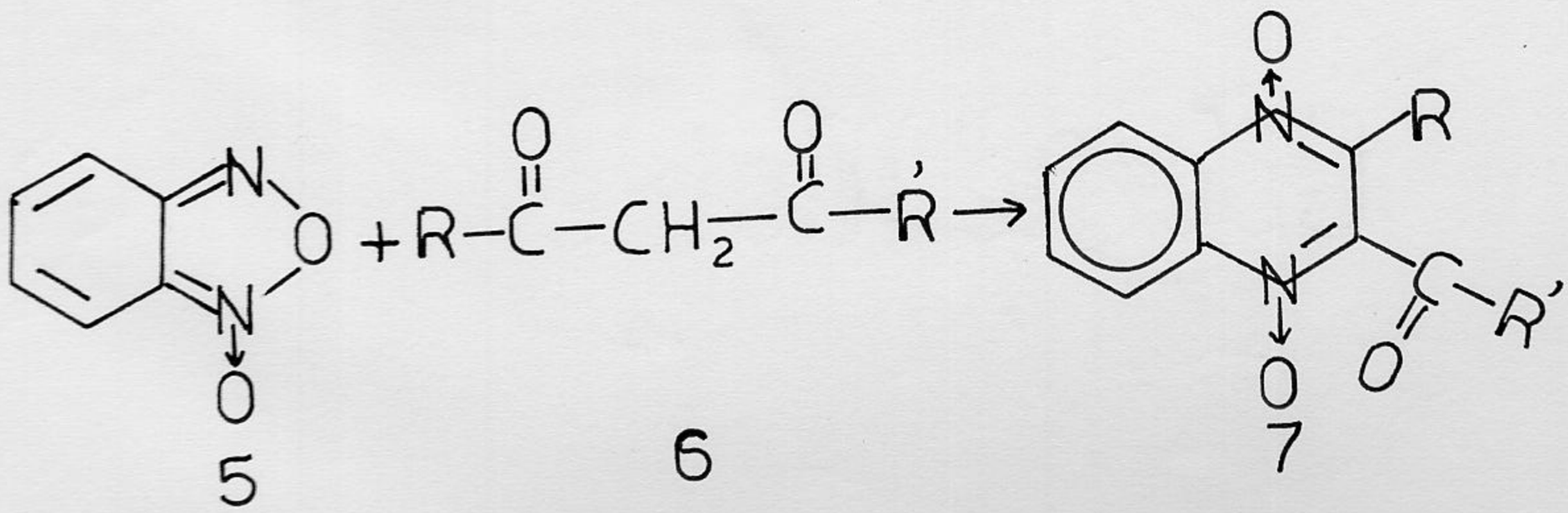
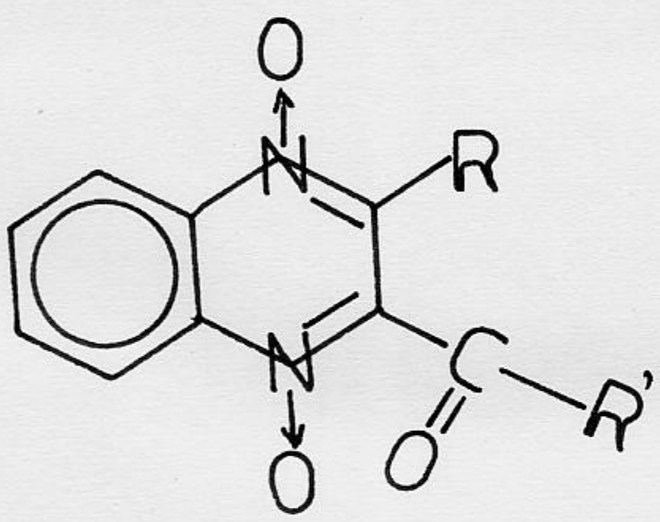
A new route for the synthesis of quinoxaline-di-N-oxides from benzofurazan oxide and enamines was reported by Haddadin and Issidorides in 1965.[4] The electronic similarity between enamines and enolate anions led these investigators to devise another method



for the synthesis of quinoxaline-di-N-oxides from benzofurazan oxide (5) and 1,3-diketones (6) or B-keto esters.[5] Symmetrical 1,3-diketones (acetylacetone; R = R' = $CH_3$, and dibenzoylmethane; R = R' = Q) in triethylamine were used.



In the above reactions, the equivalence of the substituents in the 1,3-diketones (6, R = R') rules out the formation of more than one quinoxaline-di-N-oxide. On the other hand, if R is different from R' in diketone 6 the reaction might lead to one or a mixture of the two products (7, 8).



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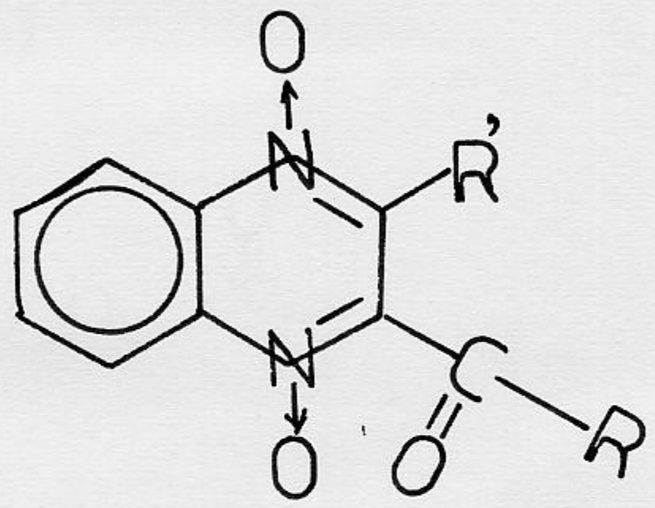

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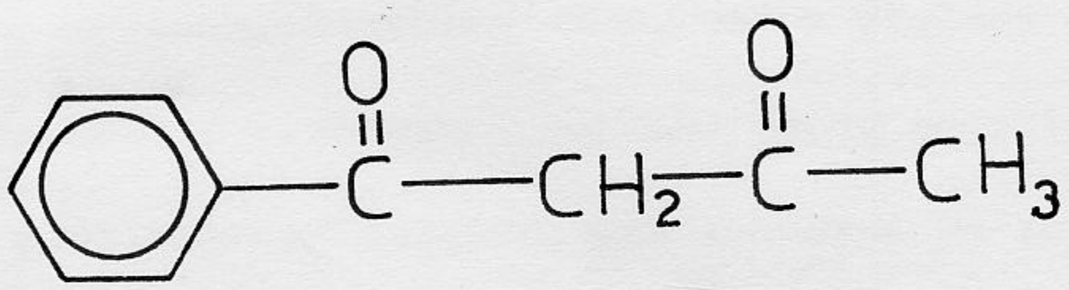
Purpose of the Work

The purpose of this work was to study the behavior of unsymmetrical 1,3-diketones with benzofurazan oxide, and to investigate the factors that control the nature ofproduct(s). Furthermore, the scope of the reaction ofbenzofurazan oxide with 1,3-diketones would be tested.

## DISCUSSION OF RESULTS

The reaction of benzofurazan oxide (5) with the following aroylacetones was studied:



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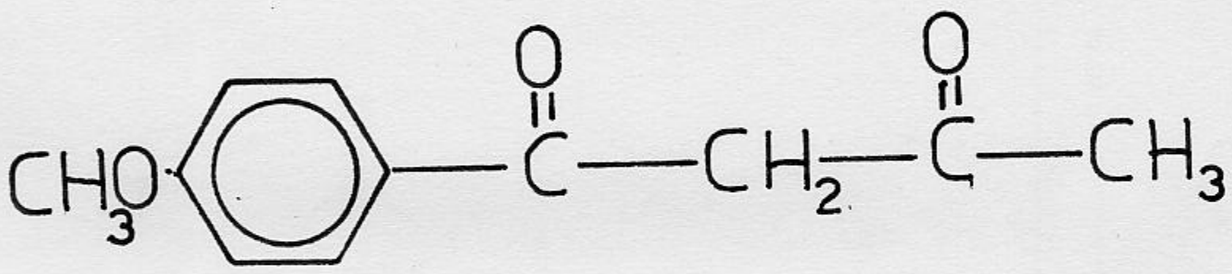

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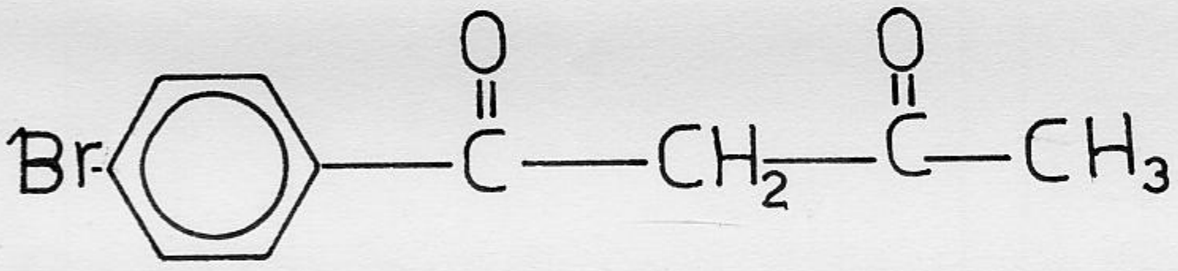
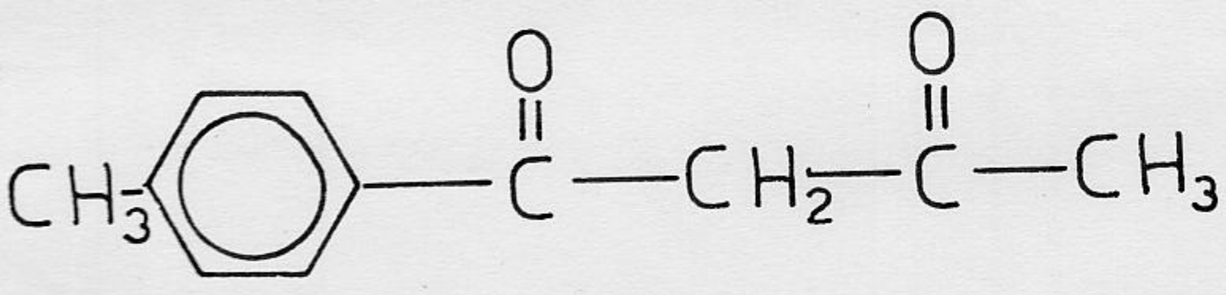
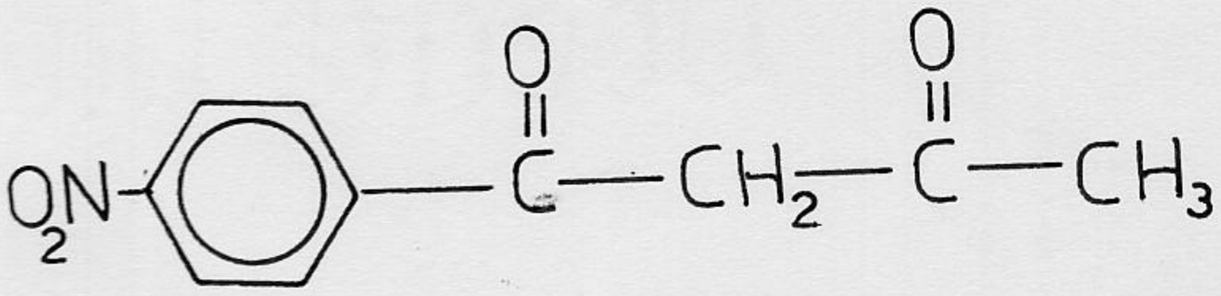
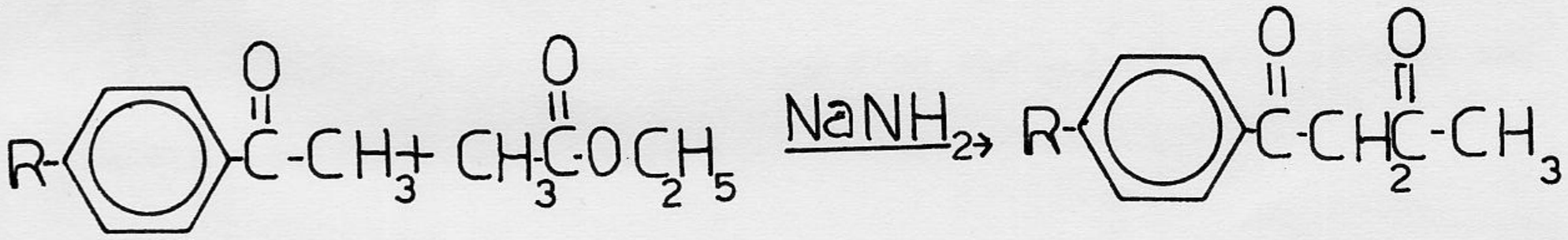






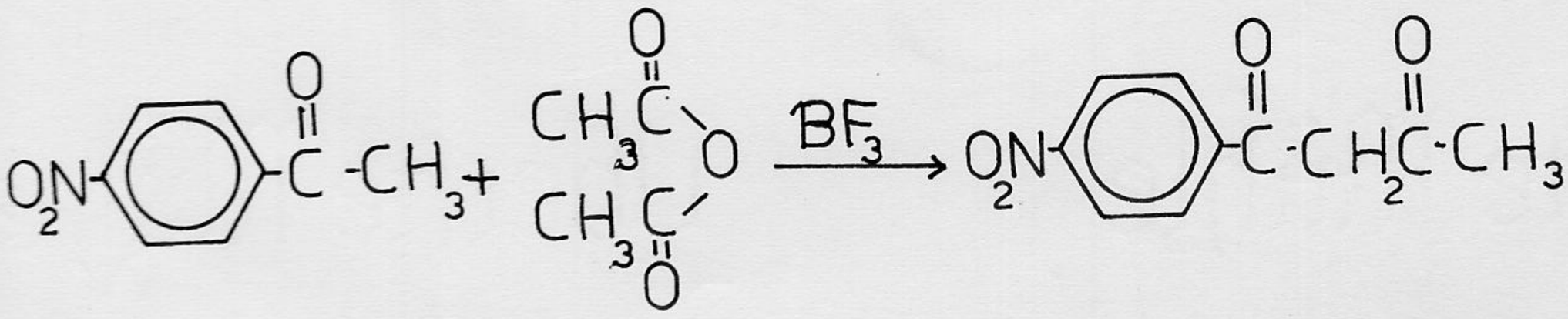
The above ketones were chosen as representative of unsymmetrical 1,3-diketones for the proposed investigation.

The preparation of p-methoxybenzoylacetone[6], p-bromobenzoylacetone[7,6], and p-methylbenzoylacetone[7] involved a Claisen condensation of the appropriate ketone with ethyl acetate using sodamide as a base. The synthesis of p-nitrobenzoylacetone was achieved by acylation of



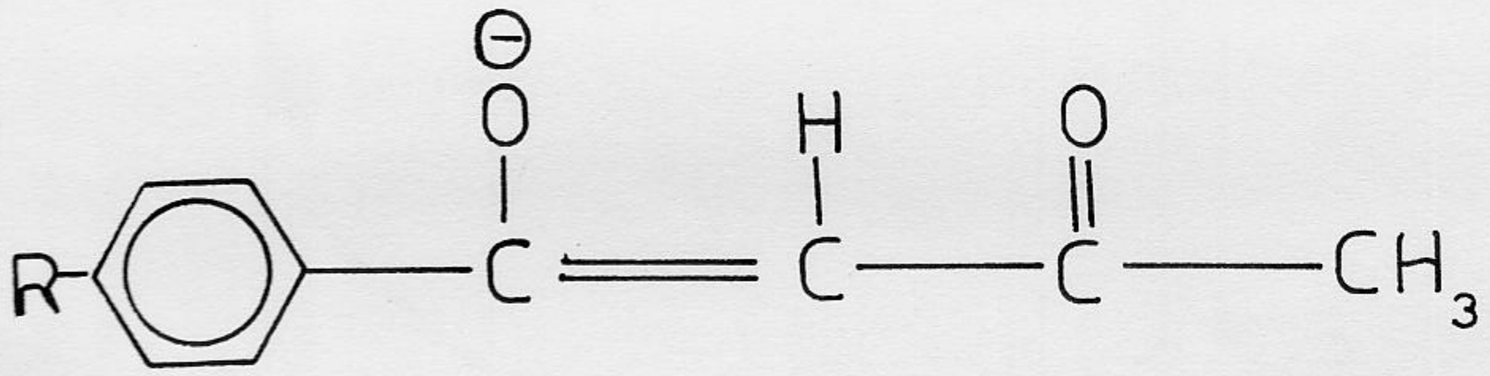
R = $CH_3O$, Br, $CH_3$

p-nitroacetophenone with acetic anhydride and borontrifluoride.[8]



The procedure for the preparation of quinoxaline-di-N-oxides consisted in dissolving the specific 1,3-diketone and benzofurazan oxide in warm triethylamine or diethylamine and allowing the solution to stand at room temperature. It was observed that the formation of quinoxaline-di-N-oxides from 1,3-diketones and benzofurazan oxide was faster in diethylamine than in triethylamine with no noticeable difference in the overall yield.

The difference in rate of the reaction is probably due to the fact that diethylamine is more basic than triethylamine and, therefore, a better reagent to abstract a proton from the 1,3-diketone to form the reactive enolate anion 14 or/and from intermediate 15.



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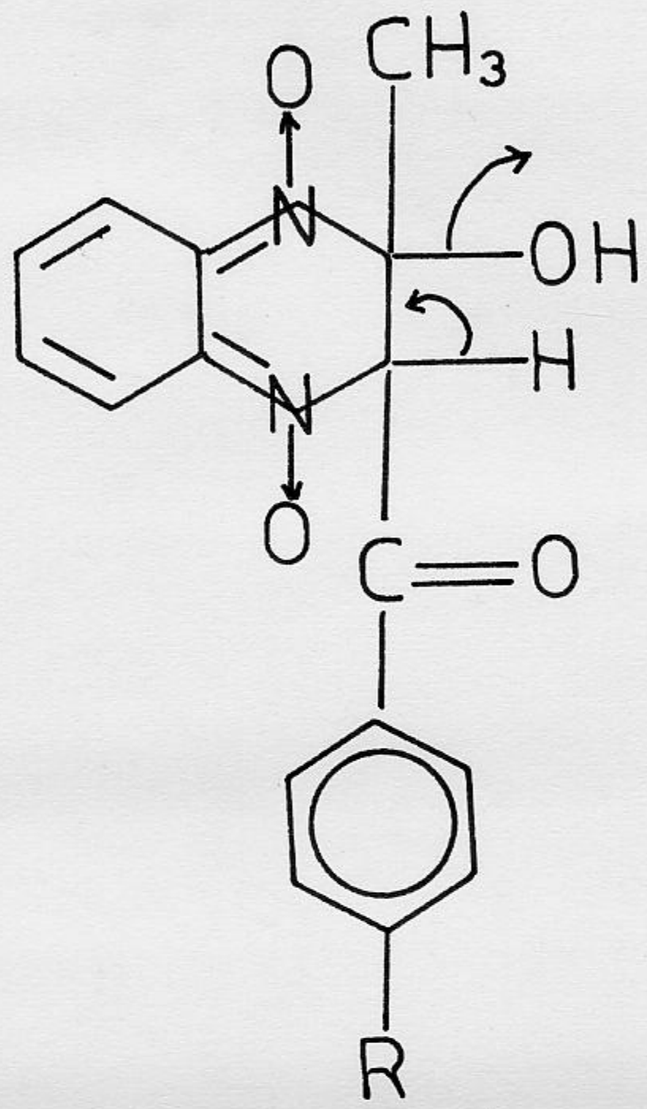


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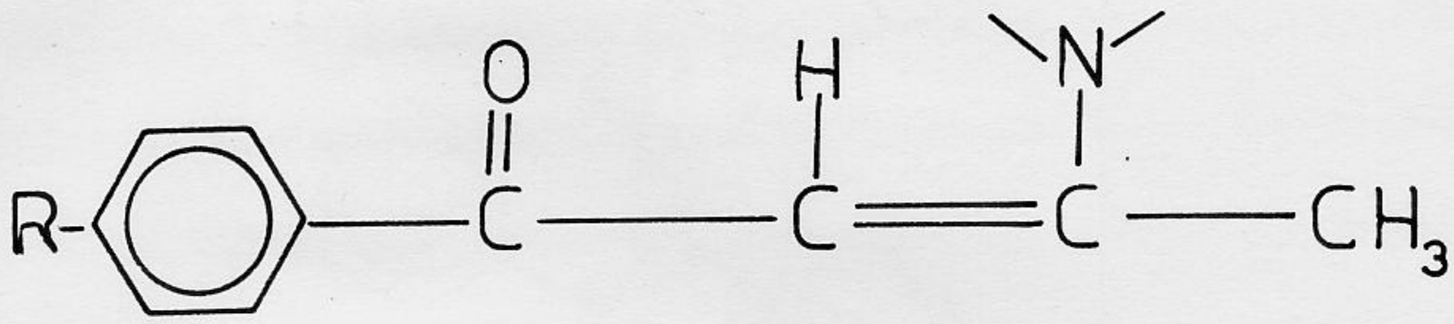
It is also conceivable that the reaction in diethylamine proceeds via an enamine which results from the reaction between diethylamine and the 1,3-diketone, and it is expected that such an enamine, due to steric effects, would have structure 16 rather than structure 18, and consequently give rise to quinoxaline-di-N-oxide 17. Since there is



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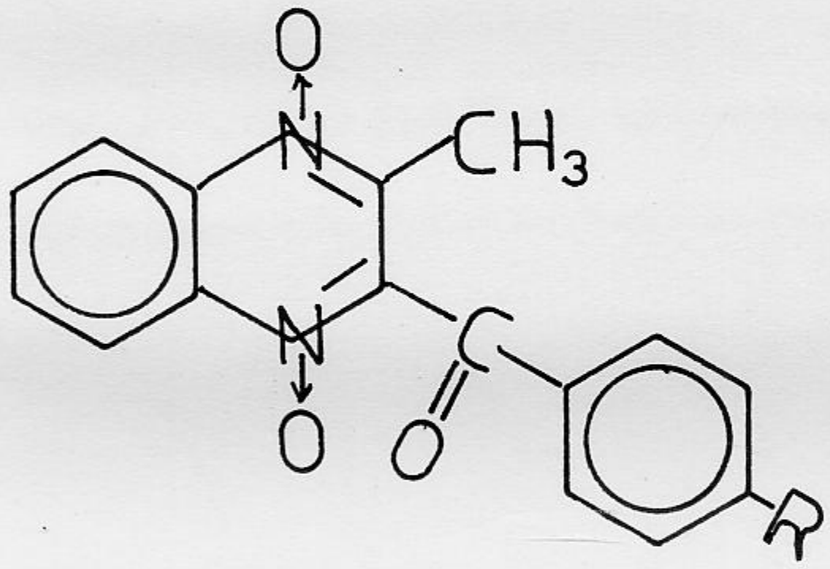

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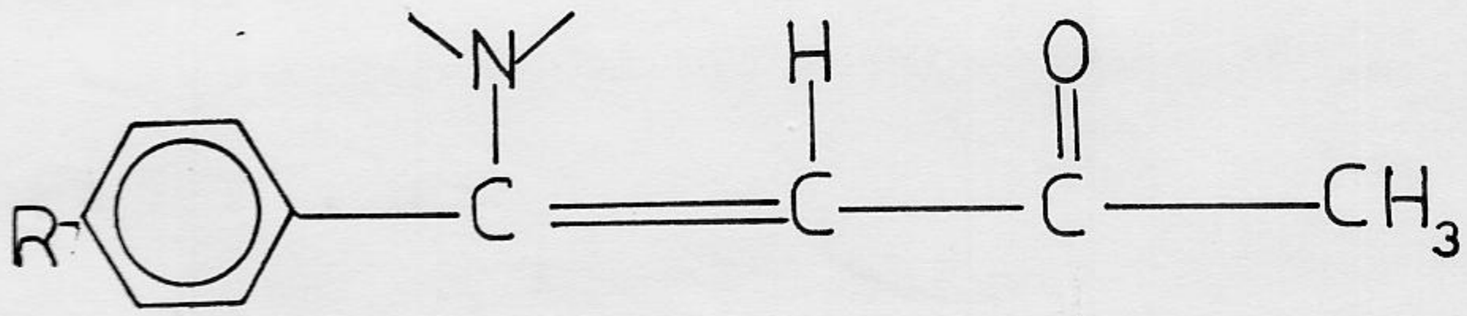

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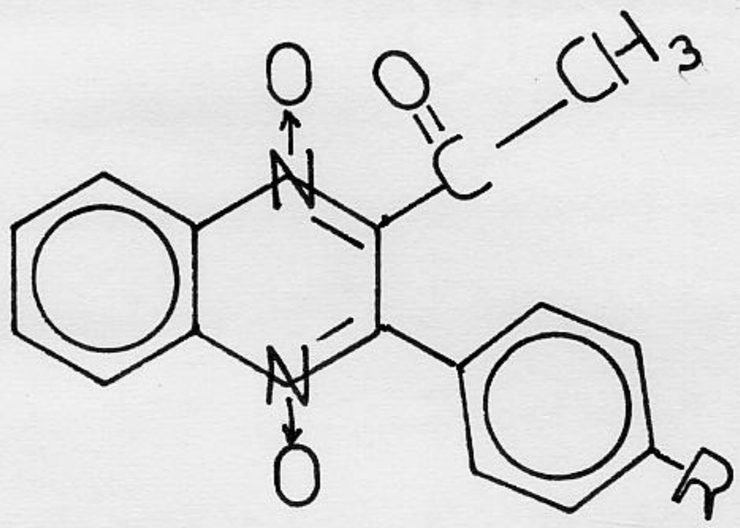
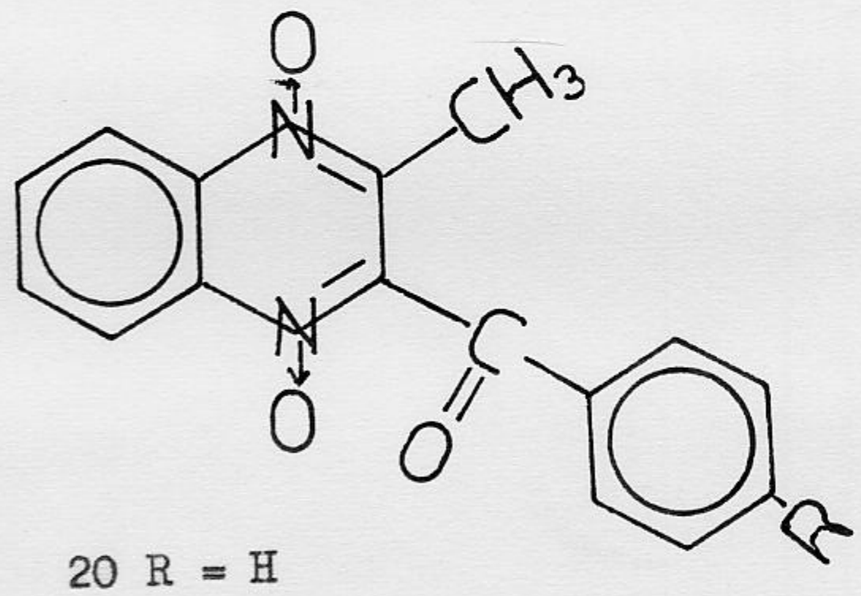
no evidence for the formation of quinoxaline-di-N-oxide of type 19,



19

the intermediacy of enamine 18 lacks concrete support, yet cannot be ruled out.

The structural evidence for 2-methyl-3-benzoylquinoxaline-di-N-oxide (20), 2-methyl-3-p-methoxybenzoylquinoxaline-di-N-oxide (21),



20 R = H

21 R = $OCH_3$

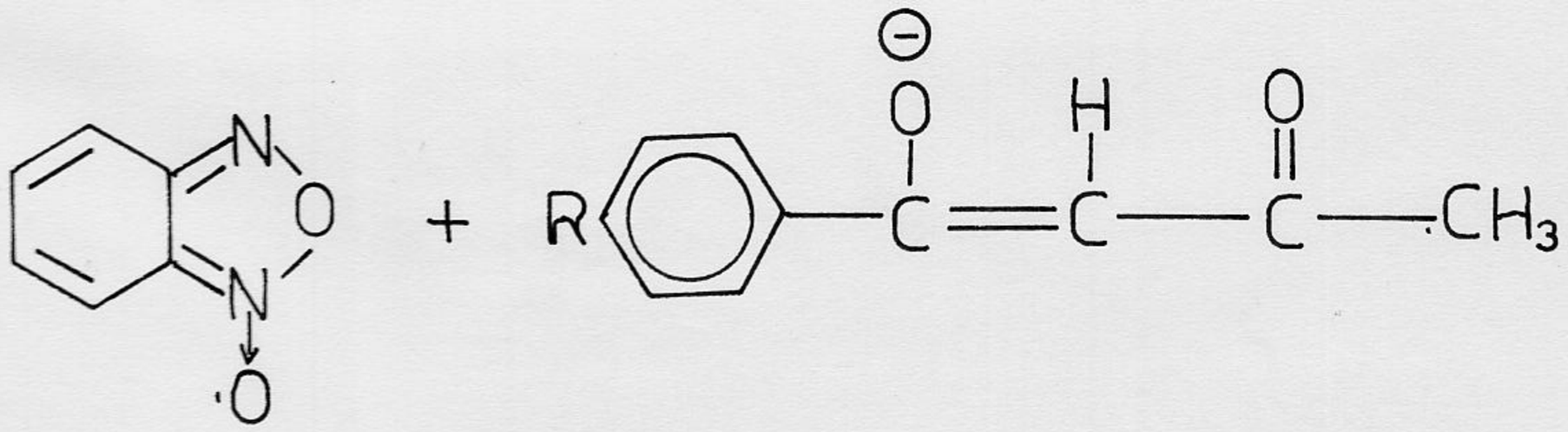
22 R = Br

23 R = $CH_3$

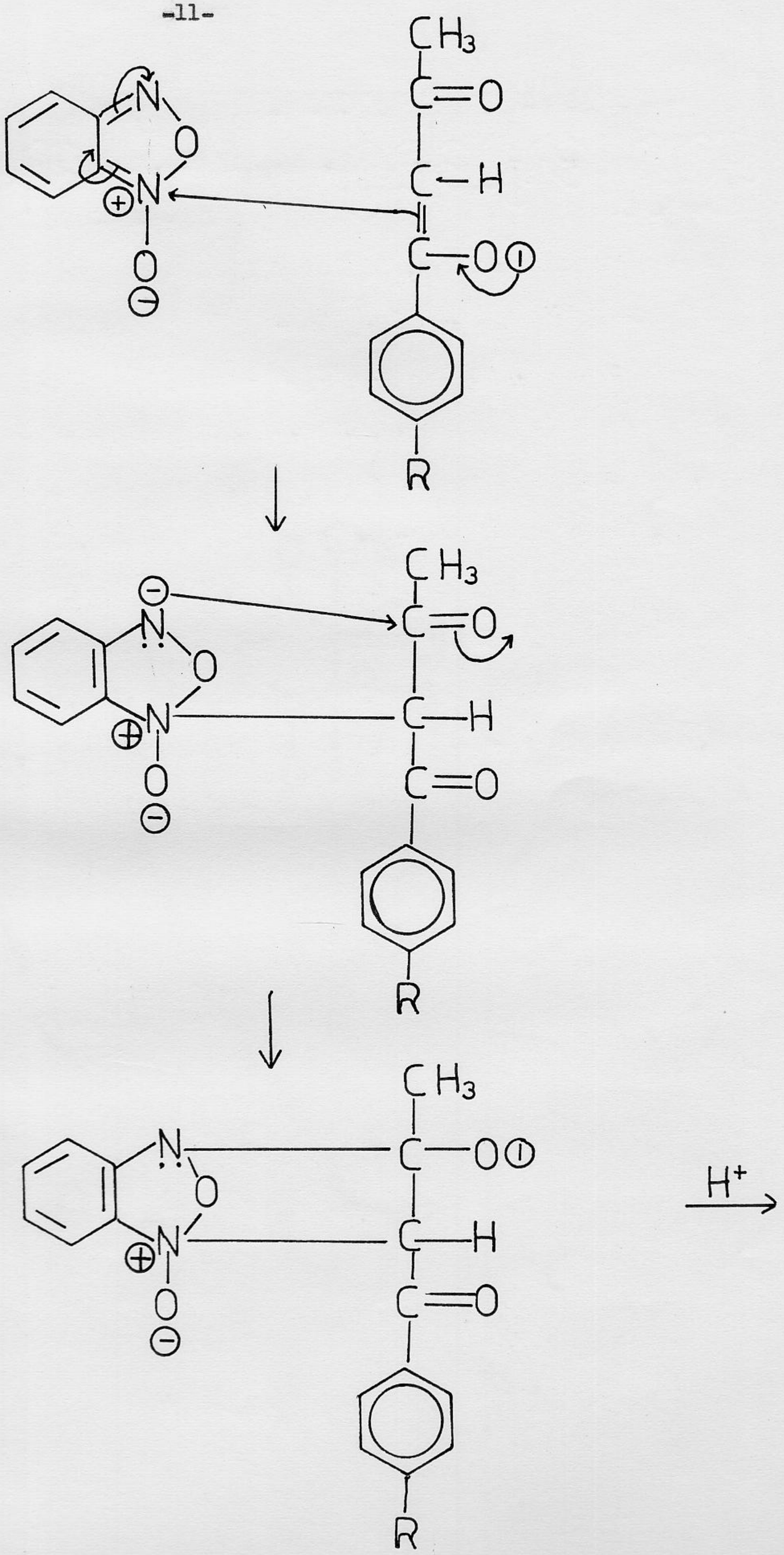
24 R = $NO_2$

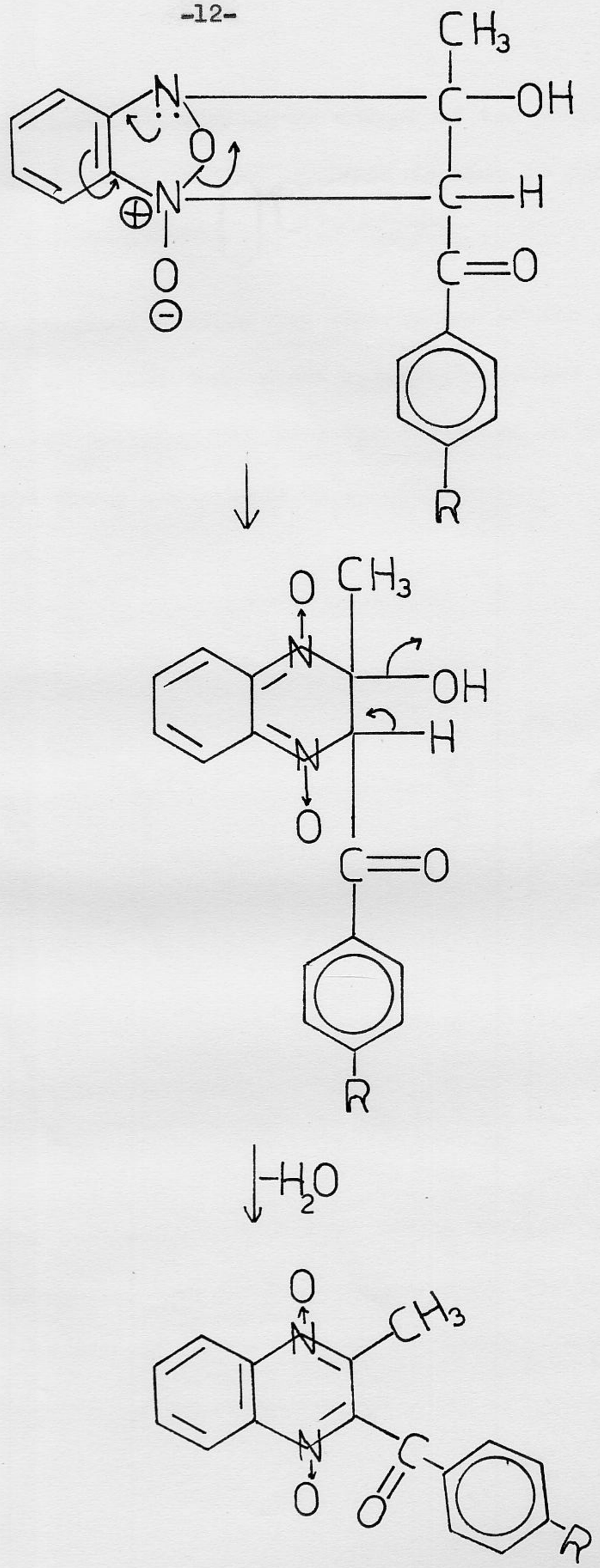
2-methyl-3-p-bromobenzoylquinoxaline-di-N-oxide (22), 2-methyl-3-p-methylbenzoylquinoxaline-di-N-oxide (23), and 2-methyl-3-p-nitrobenzoylquinoxaline-di-N-oxide (24) is based on the following: These products gave correct elemental analysis. Their infrared spectra displayed bands at 1320-1330 $Cm^{-1}$ (N-oxide), 1665-1683 $Cm^{-1}$ (conjugated carbonyl), and 763-780 $Cm^{-1}$ (ortho-substituted phenyl). Cleavage of these quinoxaline-di-N-oxides (20, 21, 22, 23, and 24) with methanolic potassium hydroxide, and subsequent acidification gave benzoic acid, p-methoxybenzoic acid, p-bromobenzoic acid, p-methylbenzoic acid, and p-nitrobenzoic acid respectively. The other hydrolysis products were not identified due to extensive decomposition as evidenced by a succession of colors. It is known that aliphatic substituted quinoxaline-di-N-oxides at position 2 or/and 3 are unstable in base.[2] The formation of quinoxaline-di-N-oxides possessing structure 19, if at all, was not detected.

A postulated mechanism for the reaction of benzofurazan oxide with aroylacetone is shown below:



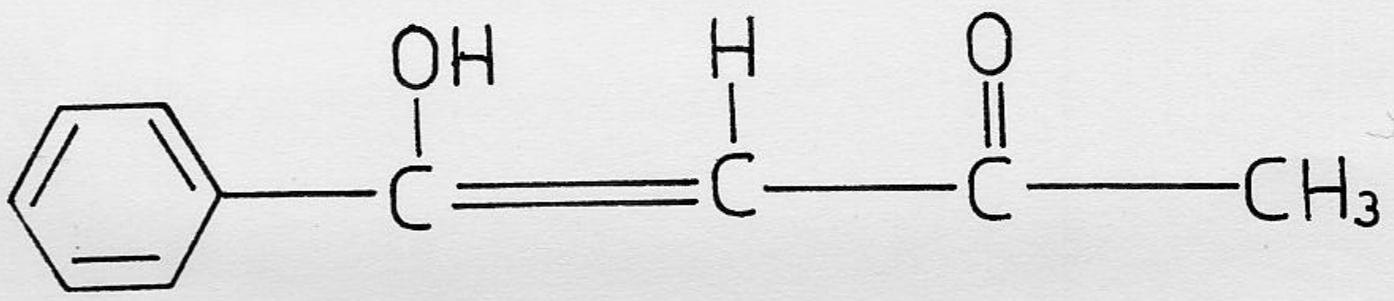
R = H , $CH_3O$ , Br , $CH_3$ , $NO_2$


CH3
C=O
C-H
C-O⊖
R
H+


CH3
OH
H
C=O
R
O
N
O
⊕
⊖
-H2O

Another mechanism involving an attack of the enolate anion on benzofurazan oxide in a Michael addition fashion is equally satisfactory.[9]

Lowe and Ferguson[10] studied the enolization of the aroylacetones (structures 9-13) and found that these 1,3-diketones are over 90% enolic in a nonpolar solvent, and that the direction of enolization is towards the phenyl group (structure 25).

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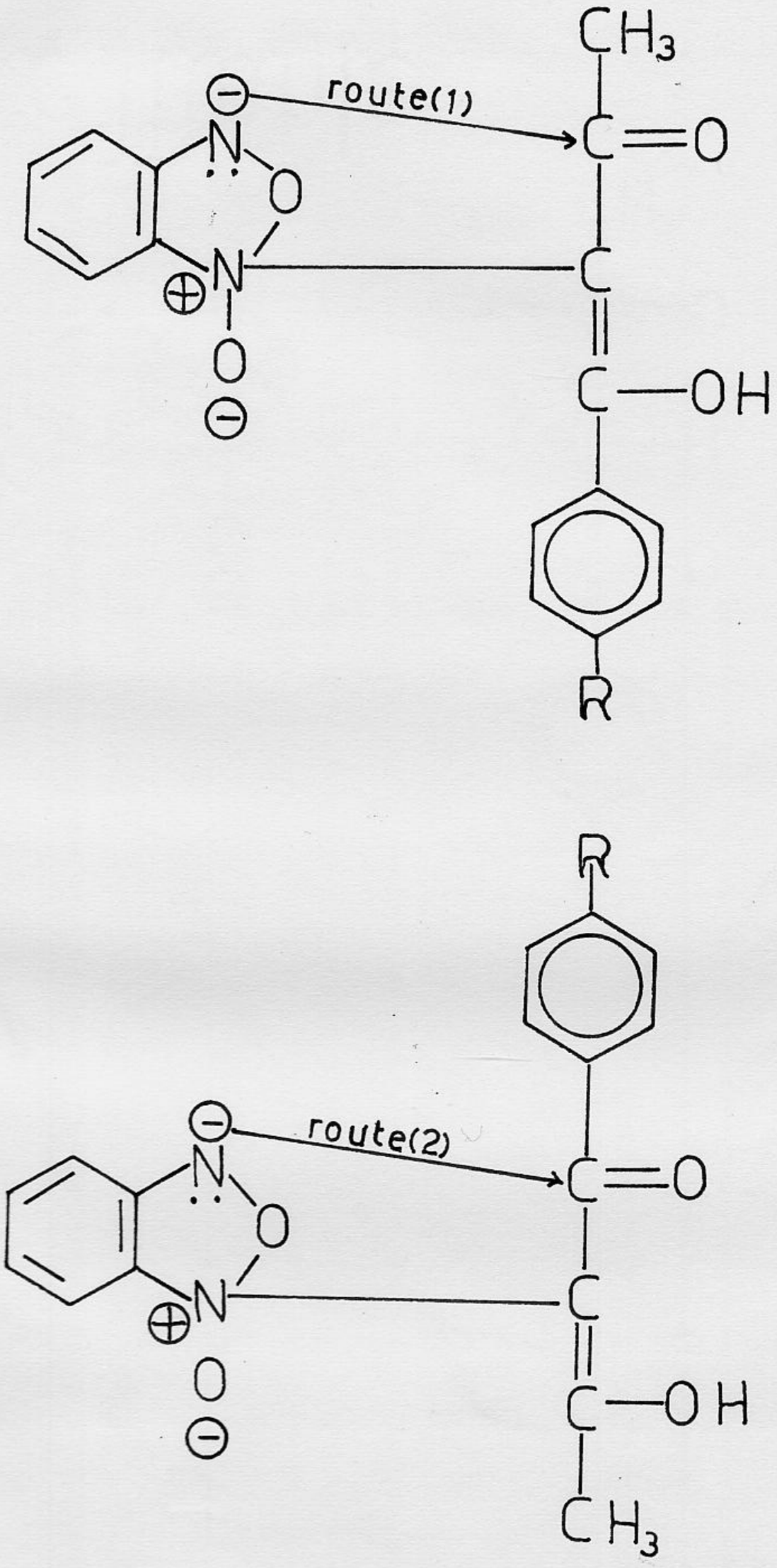
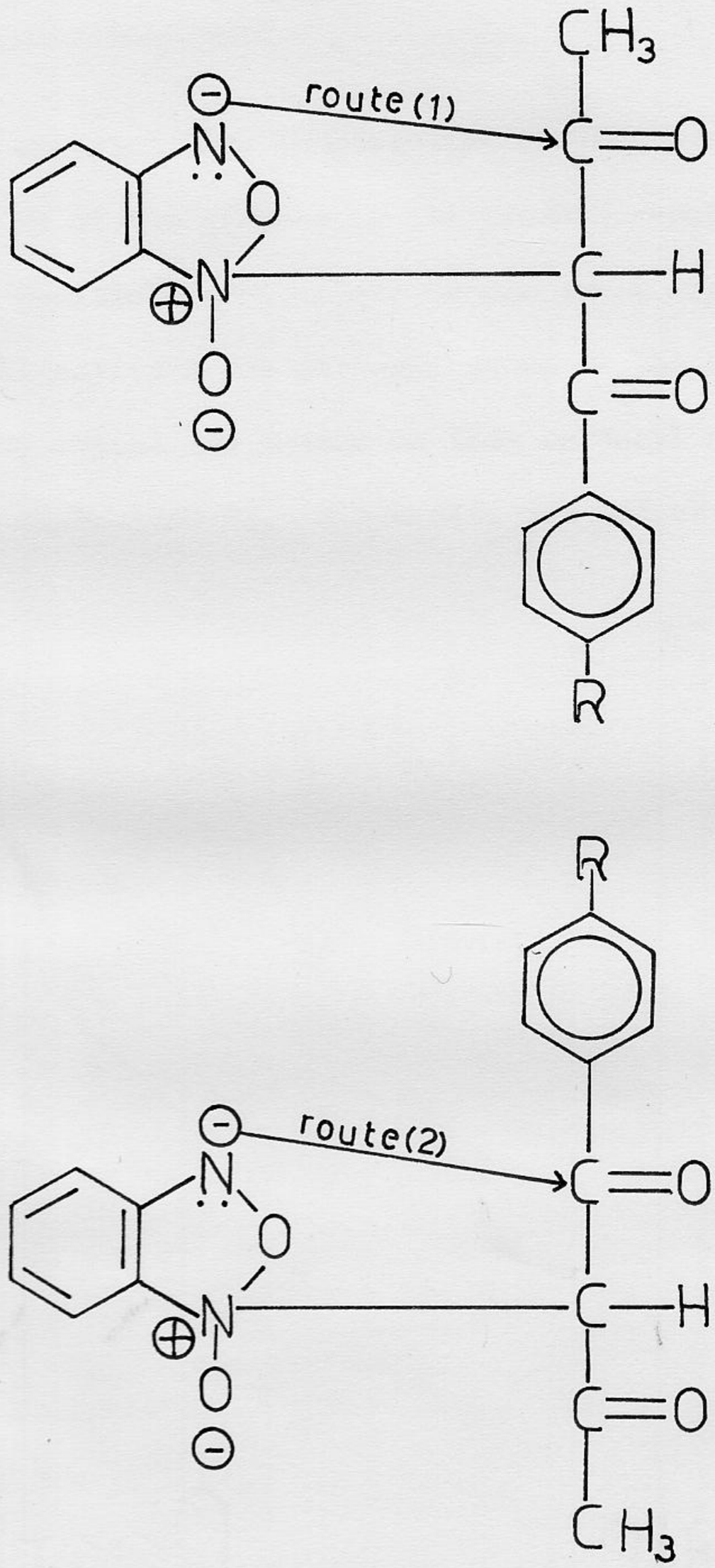
Is the direction of enolization one of the factors that controls the nature of products when benzofurazan oxide reacts with aroylacetones? In scheme I the attack of the carbanion can be through route (1) or route (2). Since the system shown in scheme I is similar to enol 25, the enolization is assumed to be towards the phenyl group and so route (1) is favoured in which the attack is on the free carbonyl




SCHEME I

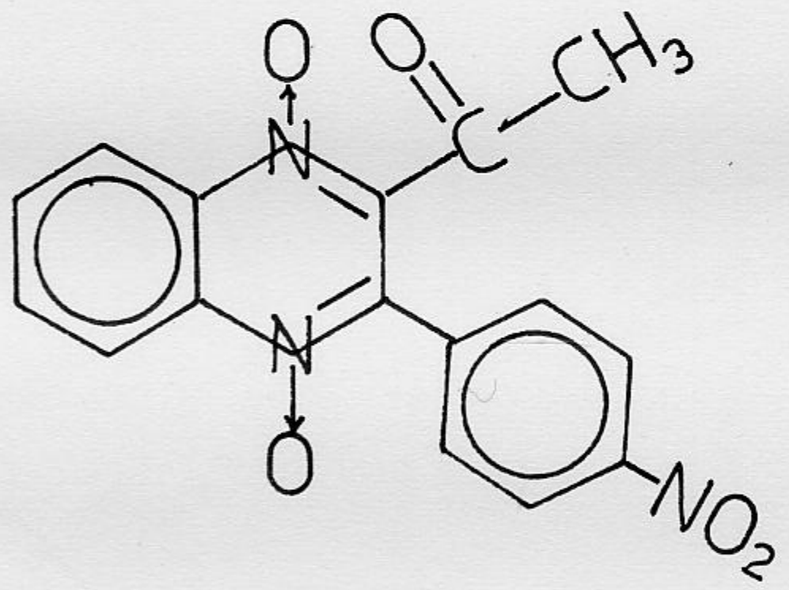
group. On the other hand, for steric reasons route (1) is also favoured as shown in scheme II.




SCHEME II

Since the two effects are in the same direction, it is difficult to decide which is more important in determining the nature of products. It might be that one factor is more important than the other or both factors are equally important.

It was expected that substitution on the phenyl ring might effect the nature of the product in the present reaction, especially in the case of p-nitrobenzoylacetone as one would expect that the nitro group will activate the carbonyl group on the aromatic ring, and therefore, would orient the attack on that carbonyl group and result in quinoxaline-di-N-oxide 26. Since this was not observed, it is



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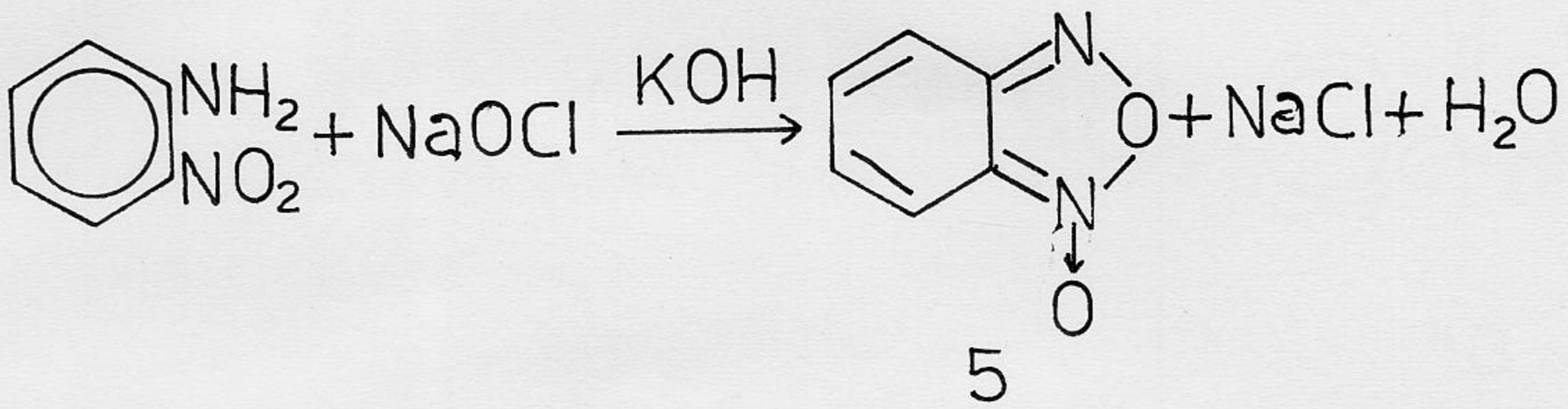
evident that substitution on the aromatic ring is not a major factor in the control of the nature of the product.

It is clear that the reaction of benzofurazan oxide with aroylacetones results in the formation of predominantly one quinoxaline-di-N-oxide and constitutes a simple method for the synthesis of such not so easily accessible compounds.

## EXPERIMENTAL*

### Preparation of Benzofurazan Oxide (5).[11]




5

Potassium hydroxide (42g, 0.64 mole) was dissolved in 95% ethanol (500 ml) with warming. o-Nitroaniline (80g, 0.58 mole) was dissolved in the warm solution and the latter was cooled to 0° in an ice bath. Commercial sodium hypochlorite (Clorox) (1200 ml) was added slowly to the stirred solution during 20 minutes with the temperature kept below 10°. On addition of sodium hypochlorite, the red solution turned deep red which, upon stirring, faded into yellow. The flocculent yellow precipitate was collected, washed with water and dried in air. The crude product, after recrystallization from a mixture of 95% ethanol (45 ml) and water (15 ml), yielded yellow benzofurazan oxide, 67.5g (80%), m.p. 72-73° (lit.[11] 72-73°).

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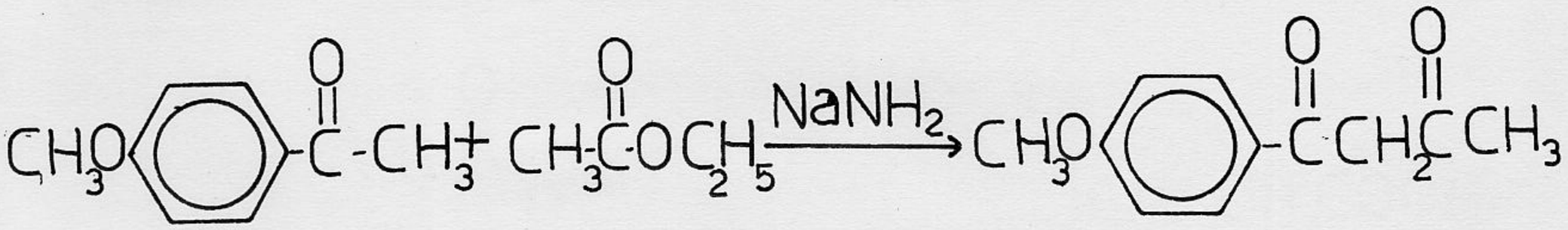
* Melting points are uncorrected. Infrared spectra were taken in nujol using Perkin-Elmer infrared spectrophotometer Model 257. Elemental analyses were performed by F. Pascher, Bonn, Germany.

Preparation of 1,3-Diketones

1. p-Methoxybenzoylacetone (10).[6]



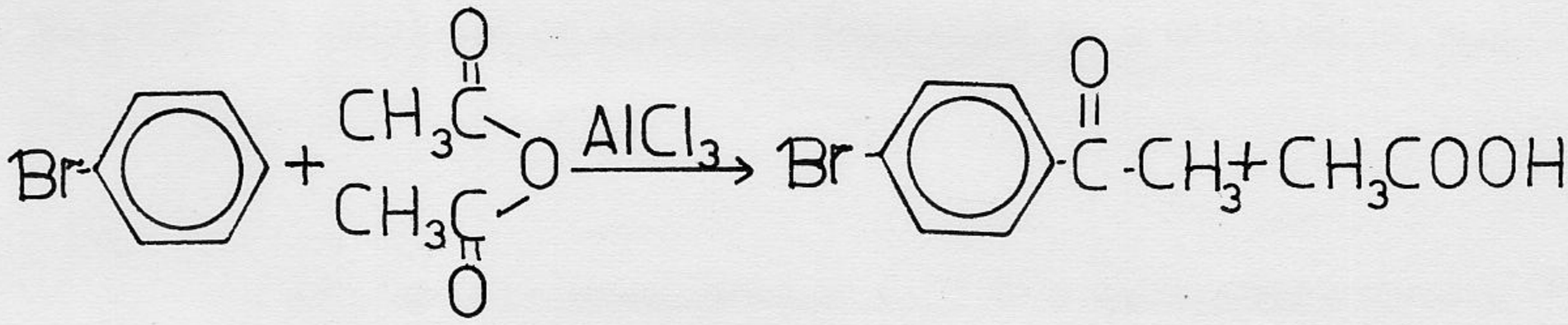

10

Finely powdered sodium amide (4g, 0.1 mole) was added to a mixture of p-acetylanisole (15g, 0.1 mole) and ethyl acetate (22g, 0.25 mole) in dry ether (70 ml). A vigorous reaction ensued, and the mixture was shaken occasionally. After 35 minutes the reaction slowed down and a large mass of solid was formed. The mixture was gently warmed in a water bath for 25 minutes, and the sodium salt of the 1,3-diketone was dissolved in the required amount of water. The aqueous layer was acidified with acetic acid. p-Methoxybenzoylacetone precipitated and was collected by suction filtration. Yield: 5.5g, m.p. 55-56° (lit.[6] 55-56°).

Infrared: 1605, 1260, 1171, 1020, 840, and 777 $Cm^{-1}$.

2. p-Bromobenzoylacetone (11)

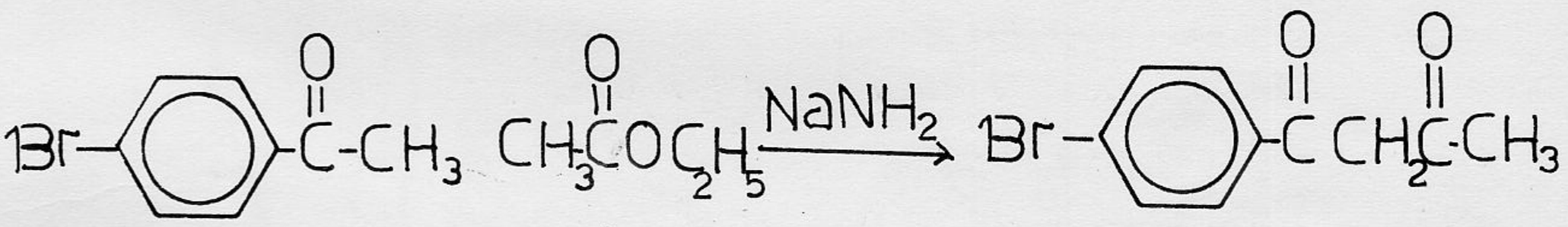
(a) p-Bromoacetophenone from p-Bromobenzene.[12]




Dry bromobenzene (78.5g, 52.5 ml), dry carbon disulphide (200 ml), and finely-powdered anhydrous aluminium chloride (150g) were placed in a 1-litre three-necked flask. The flask was equipped with a sealed mechanical stirrer, a separatory funnel protected by calcium chloride guard tube, and a reflux condenser connected to a gas absorption device. The mixture was stirred and was gently refluxed while distilled acetic anhydride (51g, 47.5 ml) was added during 1½ hours. Gentle reflux was maintained for another 1½ hours. After most of the carbon disulphide was distilled off, the mixture was allowed to cool and then poured into a mixture of crushed ice (500g) and concentrated hydrochloric acid (300 ml). The decomposed product was extracted with 150 ml and 100 ml portions of ether. The combined ethereal extracts were washed twice with water, once with 10% sodium

hydroxide solution, and finally twice with water. The ethereal solution was dried with anhydrous magnesium sulfate. Evaporation of the solvent left a liquid that was distilled at reduced pressure. The product, p-bromoacetophenone, distilled at 140°/18 mmHg (lit.[12] b.p. 130°/15 mmHg) and on cooling crystallized to a white solid, m.p. 49-50° (lit.[12] 50°). The yield was 29.5g.

(b) <u>p-Bromobenzoylacetone (11) from p-Bromoacetophenone</u>[7,6]




11

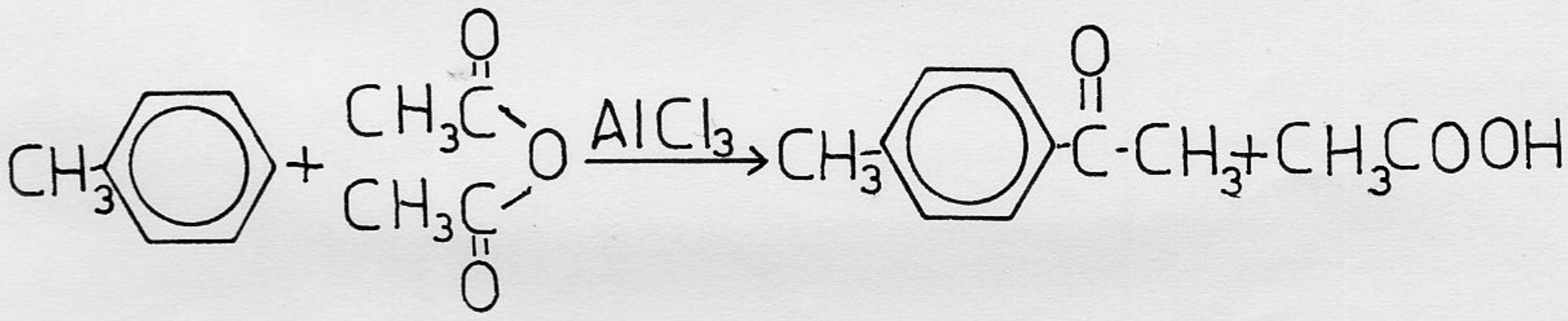
Sodamide (4g, 0.1 mole) and dry ether (40 ml) were placed in a 500-ml three-necked round-bottomed flask equipped with a sealed mechanical stirrer, a separatory funnel and a reflux condenser both carrying calcium chloride guard tubes. A solution of p-bromoacetophenone (10.1g, 0.5 mole) in dry ether (40 ml) was added to the stirred suspension of sodium amide over a period of 10 minutes. Ethyl acetate (8.8g, 0.1 mole) in dry ether (20 ml) was introduced during few minutes. When the vigorous reaction slowed down (1½ hours), the mixture was

refluxed for 20 minutes. The gelatinous precipitate was collected, washed with ether, dried in air, and then dissolved in water. Acidification of the aqueous solution with glacial acetic acid yielded p-bromobenzoylacetone which was washed thoroughly with water and dried. Yield: 4.7g, m.p. 90-91° (lit.[13] 92.5°).

Infrared: 1588, 1277, 1075, 1010, 842, and 782 $Cm^{-1}$.

3. p-Methylbenzoylacetone (12).

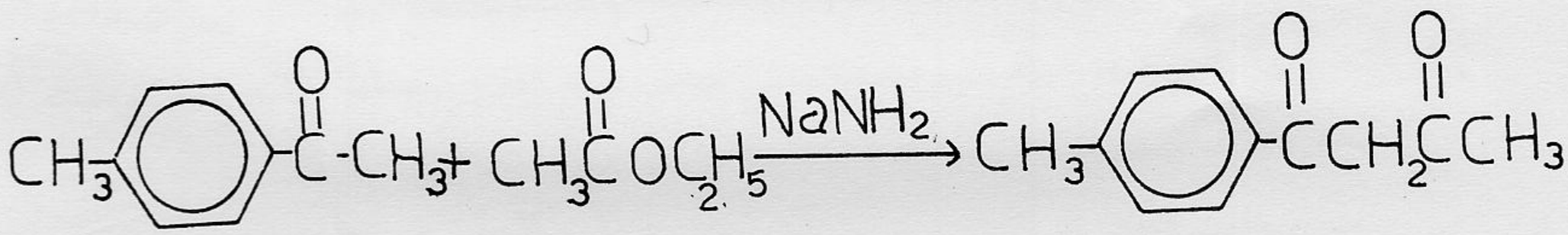
(a) p-Methylacetophenone from Toluene.[14]




Finely powdered anhydrous aluminium chloride (150g) and sodium-dried toluene (253 ml) were placed in a 1-litre three-necked flask. The flask was equipped with a sealed mechanical stirrer, a separatory funnel protected by calcium chloride guard tube and a reflux condenser connected to a gas absorption device. To the stirred mixture distilled acetic anhydride (51g, 47.5 ml) was added dropwise during 25 minutes.

The mixture was refluxed until practically there was no evolution of gas. The mixture was allowed to cool to room temperature and then poured into a mixture of crushed ice (300g) and concentrated hydrochloric acid (300ml). The toluene layer was washed with water followed by 10% sodium hydroxide solution, and water. After removal of the solvent, the residue was distilled under reduced pressure. The yield of p-methylacetophenone was 50g, b.p. 107°/8 mmHg (lit.[14] 93- 94°/7 mmHg).

(b) <u>p-Methylbenzoylacetone (12) from p-Methylacetophenone.</u>[7]




12

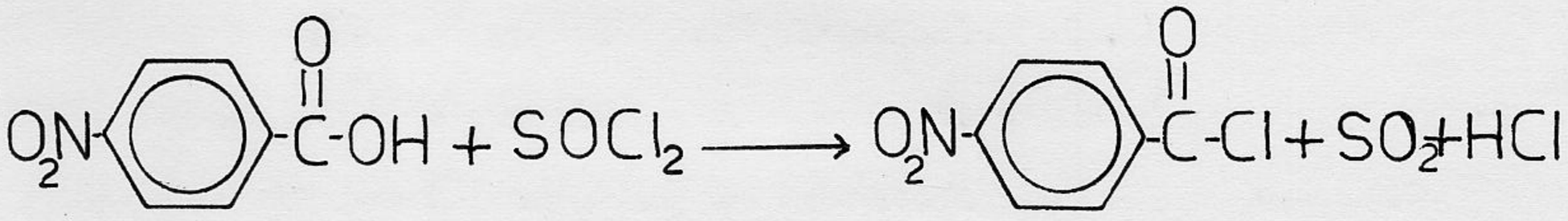
Sodamide (24g, 0.6 mole) and dry ether (50 ml) were placed in a 500-ml three-necked round- bottomed flask equipped with a sealed mechanical stirrer, a separatory funnel and a reflux condenser both carrying calcium chloride guard tubes. A solution of p-methylacetophenone (40.2g, 0.3 mole) in dry ether (50 ml) was added to the stirred suspension of sodium amide over a period of 10 minutes. After

2 minutes the mixture began to thicken and ethyl acetate (52.8g, 0.6 mole) in dry ether (50 ml) was introduced during 5 minutes. A bulky precipitate was formed. The mixture was refluxed for 40 minutes to complete the reaction, and then was poured into water (300 ml). The solution was acidified with dilute hydrochloric acid, and extracted with ether. After evaporation of the solvent, the residue was dissolved in an equal volume of methanol. Copper acetate (40g) in water (350 ml) was heated to boiling and then filtered into the methanolic solution and the mixture was allowed to cool to room temperature. The copper salt was filtered through a Büchner funnel and sucked dry in air. After the solid was thoroughly washed with ligroin (b.p. 30-75°) and dried, the pale green solid was acidified with 10% sulfuric acid (800 ml) and extracted with ether (700 ml, three portions). The solvent (ether) was evaporated after the solution had been dried over anhydrous sodium sulfate. The residue was distilled under reduced pressure and the product, p-methylbenzoylacetone, was collected at 185°/approx. 9 mmHg (lit.[13] b.p. 126-132°/6 mmHg), 23.4g.

Infrared: 1600 (broad band), 1275, 1182, 1118, 1078, 850, 830, and 775 $Cm^{-1}$.

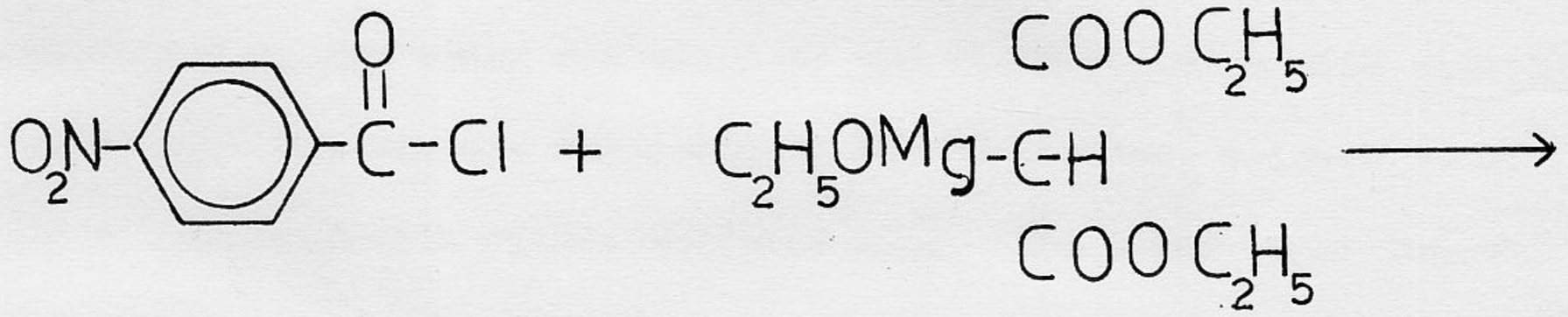
4. p-Nitrobenzoylacetone (13).

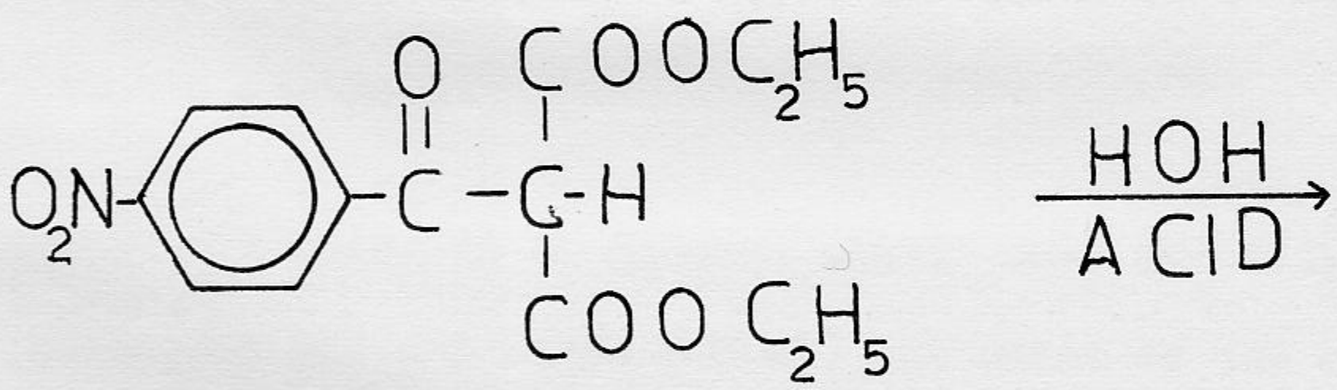
(a) p-Nitrobenzoyl Chloride from p-Nitrobenzoic Acid.[15]



p-Nitrobenzoic acid (300g) was placed in a 2-liter round bottomed flask with a reflux condenser. Excess thionyl chloride with little dimethylformamide was added, and the mixture was refluxed for 1 hour. After removal of the excess thionyl chloride the residue was distilled under reduced pressure. p-Nitrobenzoyl chloride distilled at 125°/2 mmHg (lit.[16] 197°/73 mmHg or 155°/20 mmHg) and, on cooling, solidified to a yellow crystalline solid m.p. 71° (lit.[16] 71°). The yield was 300 g.

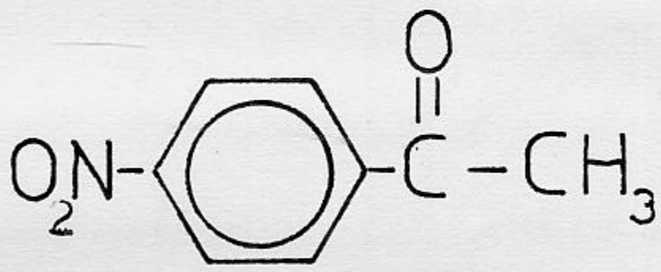
(b) <u>p-Nitroacetophenone (13) from p-Nitrobenzoyl Chloride</u>.[17]







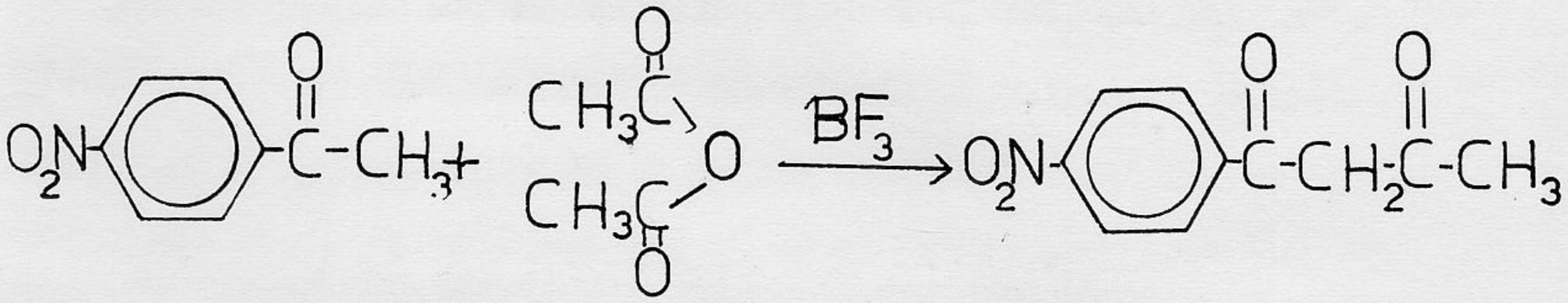



Magnesium (5.35g, 0.22 mole) was placed in a 500-ml three-necked flask equipped with a sealed mechanical stirrer, dropping funnel and a reflux condenser. both carrying calcium chloride guard tubes. After the addition of absolute ethanol (5 ml) and carbon tetrachloride (0.5 ml) the reaction started immediately. After few minutes dry ether

(70 ml) was added carefully. The flask was placed in a water bath, and a solution of diethylmalonate (35.2g, 0.22 mole) in absolute ethanol (20 ml) and dry ether (25 ml) was added at such a rate that rapid refluxing was maintained. The mixture was refluxed until the magnesium dissolved (4 hours). p-Nitrobenzoyl chloride (37.1g, 0.20 mole) dissolved in dry ether was added to the clear solution with vigorous stirring. The mixture was refluxed for 30 minutes, allowed to cool and then acidified with dilute sulfuric acid. The ether layer together with ether extracts of the aqueous layer was washed with water and the solvent was evaporated to leave a residue of crude diethyl-p-nitrobenzoyl malonate.

A solution of glacial acetic acid (60 ml), concentrated sulfuric acid (7.5 ml) and water (40 ml) was added to the crude diethyl p-nitrobenzoylmalonate and the mixture was refluxed until decarboxylation was complete (6 hours). The mixture, after being chilled in an ice bath, was extracted several times with ether. The ethereal solution was washed with water, dried with anhydrous sodium sulfate, then with Drierite. The solvent was evaporated and the residue was recrystallized from ligroin (b.p. 66-75°). The yield of yellow crystals of p-nitroacetophenone was 15.2g, m.p. 80-81° (lit.[18] 80-81°).

(c) <u>p-Nitrobenzoylacetone (13) from p-Nitroacetophenone.</u>[8]



13

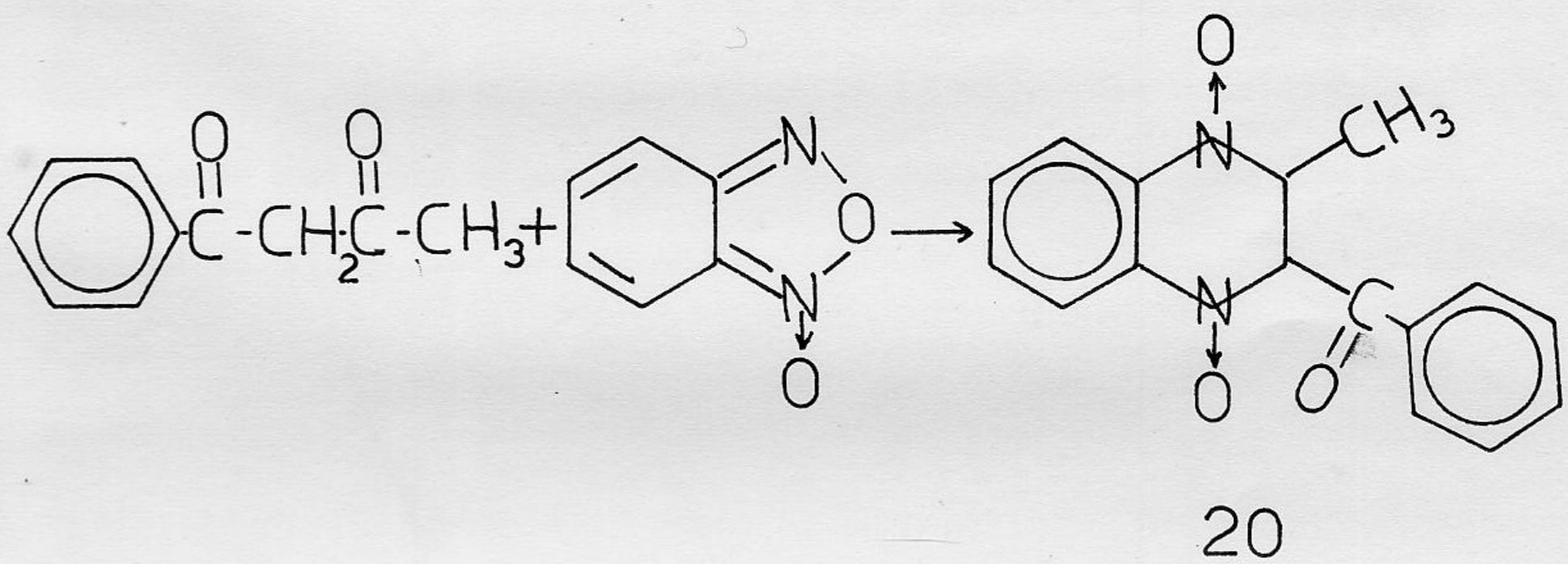
p-Nitroacetophenone (14.9g, 0.09 mole) dissolved in acetic anhydride (63 ml, 0.63 mole) was placed in a 250-ml three-necked flask equipped with a mechanical stirrer, an inlet tube fitted 1 cm. above the surface of the liquid, and a calcium chloride guard tube. The stirred mixture was saturated (as indicated by the abundant evolution of white fumes) with boron trifluoride at 0-10° for two hours. To the mixture was added 13% sodium acetate (630 ml) and the resulting mixture was refluxed for twenty minutes. The mixture was chilled in an ice-bath and the precipitate was filtered, washed thoroughly with water, crushed and dissolved in cold 2% sodium hydroxide (270 ml). The resulting solution was shaken with ether, and the ethereal solution was extracted with portions of 2% sodium hydroxide until it gave negative enol test. The combined alkaline extracts were filtered, chilled, and acidified with 10% sulfuric acid. The solid was collected

by suction filtration. Recrystallization from 95% ethanol gave yellow crystals of p-nitrobenzoylacetone. Yield 9g, m.p. 112-113° (lit.[8] 111.4 - 112.6°).

Infrared: 1600 (broad band), 865, 785, 755, and 705 $Cm^{-1}$.

Preparation of Quinoxaline-Di-N-Oxides

1. 2-Methyl-3-benzoylquinoxaline-di-N-oxide (20).



20

(a) Reaction in Triethylamine

A warm solution of benzofurazan oxide (6.8g, 0.05 mole) in triethylamine (25 ml) was mixed with a warm solution of benzoylacetone (8.1g, 0.05 mole) in triethylamine (25 ml). The resulting solution was allowed to stand at room temperature. A solid appeared in 10

minutes which after 16 hours was thinned with triethylamine, collected by suction filtration and washed with methanol (yield: 4.7g). The filtrate and washings were allowed to sland for two days. The filtrate gave a second crop (2.9g) and a third crop (1.6g) on long standing. Similarly, the washings gave an additional total of 1.1g of product. The total yield was 10.3g (74%).

(b) Reaction in Diethylamine

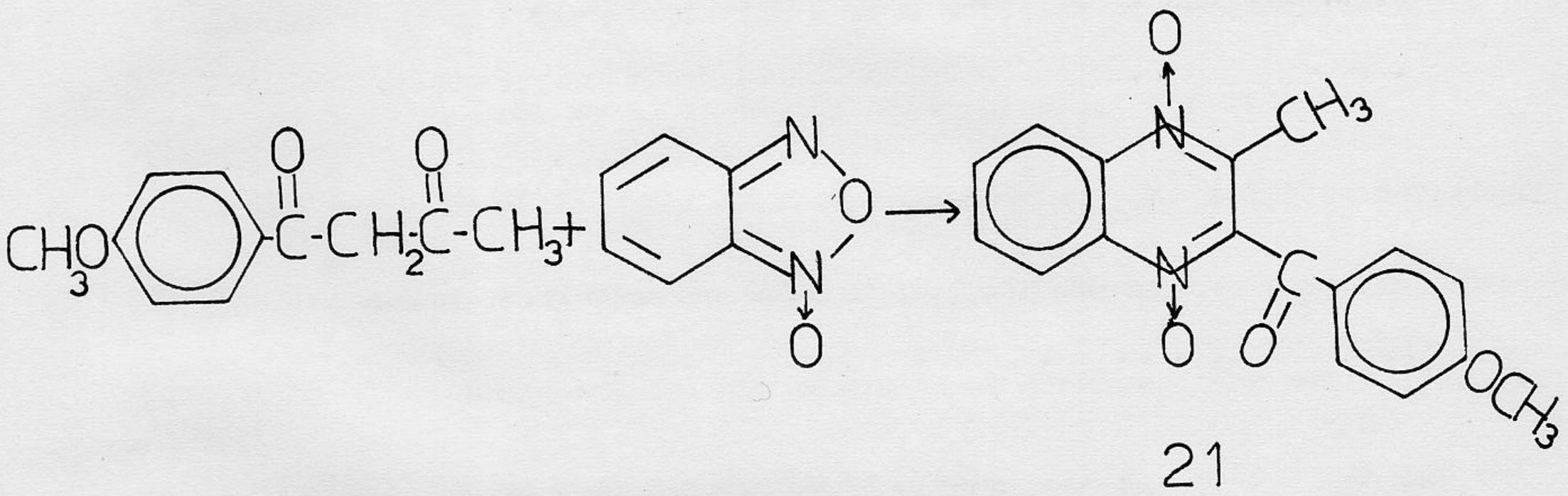
A warm solution of benzoylacetone (0.81g, 0.005 mole) in diethylamine (5 ml) was mixed with a warm solution of benzofurazan oxide (0.68, .005 mole) in diethylamine (3 ml). The resulting solution was warmed and allowed to stand at room temperature. The solution changed to a deep red colour with a rise in temperature. In one minute a yellow precipitate was formed which increased quickly. The precipitate was collected and washed with diethylamine. (Yield: 0.98g). After one day of standing at room temperature, the mother liquor gave a second crop (0.04g). The total yield was 1.02g (70%).

Recrystallization of the crude 2-methyl-3-benzoylquinoxaline-di-N-oxide (20) from methanol gave yellow needle shaped crystals melting at 223-224° (d).

Infrared: 1672, 1597, 1328, 1250, 1075, 953, 812, 763, 718, and 652 $Cm^{-1}$.

Elemental Analysis Calculated for $C_{16}H_{12}O_3N_2$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.55; H, 4.30; N, 10.09.

## 2. 2-Methyl-3-p-Methoxybenzoyl-Quinoxaline-di-N-Oxide (21)



21

### (a) Reaction in Triethylamine

A warm solution of benzofurazan oxide (6.8g, 0.05 mole) in triethylamine (25 ml) was mixed with a warm solution of p-methoxybenzoyl-acetone (9.6g, 0.05 mole) in triethylamine (25 ml). The resulting solution was warmed for two minutes on a hot plate and allowed to stand at room temperature. In four minutes a yellow precipitate appeared which increased with time. The precipitate was collected after 4 days and washed with methanol (yield: 9.6g). On long standing the mother liquor gave (1.4g) and the washings gave (0.6g). The total yield was 11.6g (75%).

(b) Reaction in Diethylamine

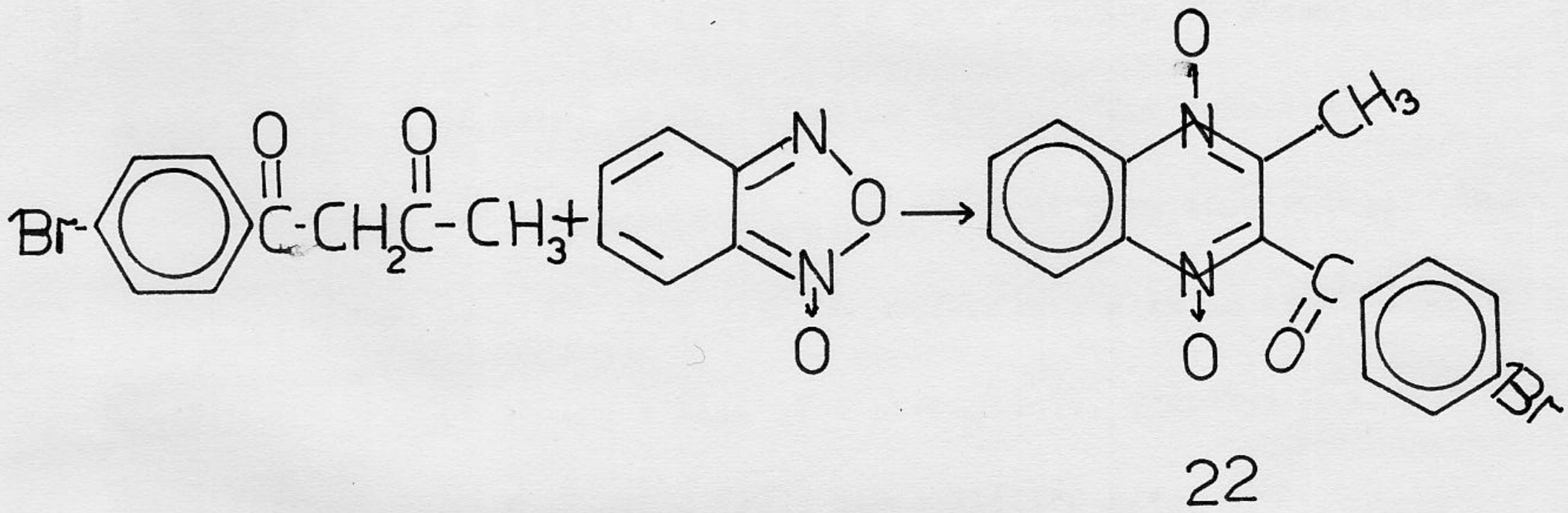
A warm solution of benzofurazan oxide (1.36g, 0.01 mole) in diethylamine (5 ml) was mixed with a warm solution of p-methoxybenzoylacetone (1.90 g, 0.01 mole) in diethylamine (5 ml). The resulting solution was allowed to stand at room temperature. The solution developed a deep red colour with rise in temperature. In one minute a precipitate developed which increased quickly after three minutes. The solid was collected and washed with diethylamine (yield: 2.22g). After one day the mother liquor gave a second crop (0.18g). The total yield was 2.40g (77.5%).

Recrystallization of the crude p-methoxybenzoylquinoxaline-di-N-oxide (21) from methanol gave yellow needle shaped crystals that melted at 217° (d).

Infrared: 1665, 1590, 1330, 1250, 1075, 945, 818, and 780 $Cm^{-1}$.

Elemental Analysis calculated for $C_{17}H_{14}O_4N_2$; C, 65.80; H, 4.55; N, 9.03. Found: C, 65.93; H, 4.53; N, 9.22.

3. 2-Methyl-3-p-Bromobenzoyl-Quinoxaline-di-N-Oxide (22)



22

(a) Reaction in Triethylamine

A warm solution of p-bromobenzoylacetone (2.41g, 0.01 mole) in triethylamine (6 ml) was mixed with a warm solution of benzofurazan oxide (1.36g, 0.01 mole) in triethylamine (4 ml). The resulting solution was warmed and allowed to stand at room temperature. In two minutes a precipitate appeared and after two days the yellow precipitate was collected and washed with methanol (yield: 2.55g). On long standing the mother liquor gave 0.05g. The total yield was 2.60g (72.5%).

(b) Reaction in Diethylamine

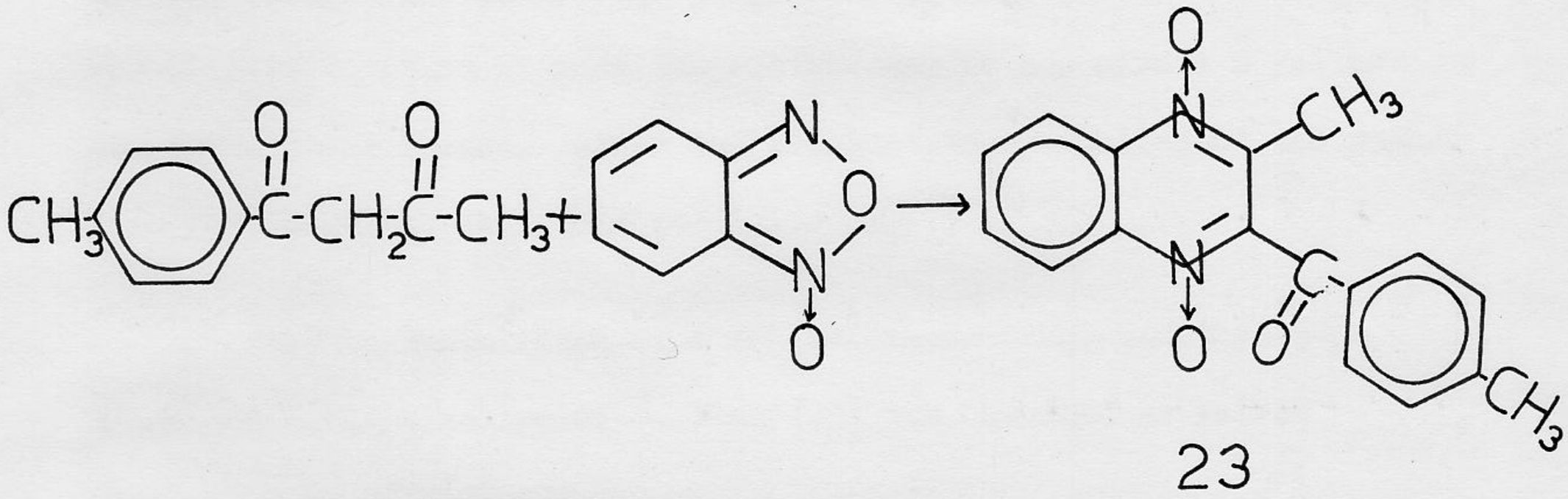
A warm solution of p-bromobenzoylacetone (2.41, 0.01 mole) in diethylamine (6 ml) was mixed with a warm solution of benzofurazan oxide (1.36g, 0.01 mole) in diethylamine (4 ml). The resulting solution was warmed and then allowed to stand at room temperature. The solution became deep red with rise in temperature with an instantaneous precipitation of a yellow solid. The precipitate, 2-methyl-3-p-bromo-benzoylquinoxaline-di-N-oxide (22), was collected after two days (2.45g). On long standing the mother liquor gave 0.03 g. The total yield was 2.48g (69.8%).

The product (22) was recrystallized from methanol to yield yellow needle shaped crystals that melted at 224-225° (d).

Infrared: 1672, 1585, 1330, 1251, 1065, 948, 810, and 775 $Cm^{-1}$.

Elemental Analysis Calculated for $C_{16}H_{11}O_3N_2Br$: C, 53.50; H, 3.09; N, 7.80; Br, 22.25. Found: C, 53.59; H, 3.12; N, 7.81; Br, 22.10.

4. <u>2-Methyl-3-p-Methylbenzoyl-Quinoxaline-di-N-Oxide (23)</u>



23

(a) <u>Reaction in Triethylamine</u>

A warm solution of benzofurazan oxide (0.68g, 0.005 mole) in triethylamine (4 ml) was mixed with a warm solution of p-methyl-benzoylacetone (0.88g, 0.005 mole) in triethylamine (2 ml). The resulting solution was heated to boiling and allowed to stand at room temperature for 24 hours. The yellow precipitate was collected and washed with methanol (yield: 0.42g). On long standing the mother liquor gave an additional 0.75g while the washings gave 0.03g. The total yield was 1.20g (81.8%).

(b) Reaction in Diethylamine.

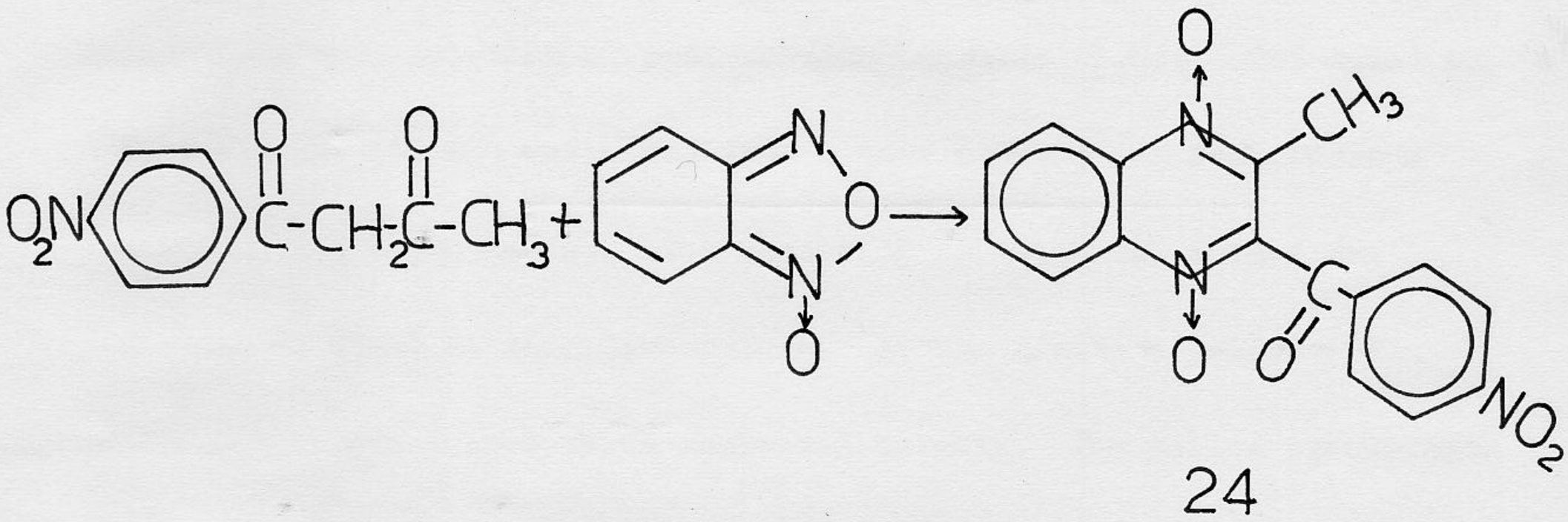
A warm solution of benzofurazan oxide (2.72, 0.02 mole) in diethylamine (5 ml) was mixed with a warm solution of p-methylbenzoylacetone (3.52, 0.02 mole) in diethylamine (5 ml). The warm solution was allowed to stand at room temperature and in one minute a yellow precipitate was formed. After the precipitate was collected and washed with diethylamine, the yield was 4.10g (70%).

When recrystallized from chloroform-methanol, 2-methyl-3-p-methylbenzoylquinoxaline-di-N-oxide (23) was obtained as yellow crystals m.p. 223 (d).

Infrared: 1665, 1602, 1330, 1248, 1183, 1072, 945, 825, and 767 $Cm^{-1}$.

Elemental Analysis Calculated for $C_{17}H_{14}O_3N_2$: C, 69.37; H, 4.80; N, 9.52. Found: C, 69,42; H, 4.76; N, 9.46.

5. <u>2-Methyl-3-p-Nitrobenzoylquinoxaline-di-N-Oxide (24)</u>.



24

(a) <u>Reaction in Triethylamine</u>

A warm solution of benzofurazan oxide (0.68g, 0.005 mole) in triethylamine (5 ml) was mixed with a warm solution of p-nitrobenzoylacetone (1.04g, 0.005 mole) in triethylamine (50 ml). The resulting solution was warmed and allowed to stand at room temperature. A precipitate appeared in ten minutes and increased gradually. After 24 hours, the yellow solid was collected by suction filtration and washed with triethylamine (yield: 0.46g). After another 24 hours the filtrate gave a second crop (0.19g). A third crop (0.20g) was

collected after 48 hours. The total yield was 0.85g (52.3%).

(b) Reaction in Diethylamine.

A warm solution of p-nitrobenzoylacetone (1.04g, .005 mole) in diethylamine (50 ml) was mixed with a warm solution of benzofurazan oxide (0.68g, 0.005 mole). The resulting solution was warmed and allowed to stand at room temperature. In one minute a yellow precipitate was formed which increased quickly. The yellow precipitate was collected and washed with diethylamine (yield: 0.42g). The filtrate gave a second crop (0.35g) after 7 hours and a third crop (0.11g) after 17 hours. The total yield was 0.88g (54.2%).

Recrystallization of the crude 2-methyl-3-p-nitrobenzoyl-quinoxaline-di-N-oxide (24) from methanol gave yellow needle shaped crystals melting at 217-218° (d).

Infrared: 1683, 1600, 1525, 1320, 1240, 1072, 945, 808, 773, and 722 $Cm^{-1}$.

Elemental Analysis Calculated for $C_{16}H_{11}O_5N_3$: C, 59.08; H, 3.41; N, 12.92. Found: C,58.90 ; H,3.47 ; N,13.02 .

Cleavage of Quinoxaline-di-N-Oxides.

The specific quinoxaline-di-N-oxide (0.9-0.7g) was placed in a 100-ml round bottomed flask with a reflux condenser. To the solid was added 5% methanolic potassium hydroxide (50 ml) and the solution was refluxed for 15-25 minutes. Successive change of colours from yellow to deep green to greenish blue was observed. The solution was cooled, acidified with hydrochloric acid and diluted with water in cases where salts precipitated. The acidic solution was extracted with ether, and after treating the ethereal solution with charcoal and evaporation of the ether, an acid (0.3 - 0.2g) was obtained, the identity of which was established by mixture melting point, and superimposable infrared spectra with authentic sample.

| QUINOXALINE-DI-N-OXIDE | ACID |
|---|---|
| 2-Methyl-3-benzoylquinoxaline-di-N-oxide (20). | Benzoic acid |
| 2-Methyl-3-p-methoxybenzoylquinoxaline-di-N-oxide (21) | p-Methoxybenzoic acid |
| 2-Methyl-3-p-bromobenzoylquinoxaline-di-N-oxide (22) | p-bromobenzoic acid |
| 2-Methyl-3-p-methylbenzoylquinoxaline-di-N-oxide (23) | p-methylbenzoic acid |
| 2-Methyl-3-p-nitrobenzoylquinoxaline-di-N-oxide (24) | p-nitrobenzoic acid |

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