

CONDENSATIONS OF ALDEHYDES AND KETONES  
BY USE OF POTASSIUM CYANIDE

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By

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## ACKNOWLEDGMENT

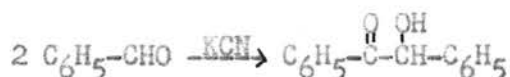
The author sincerely wishes to express his indebtedness to Dr. Ernest M. Hodnett for his interest and help which made this work possible.

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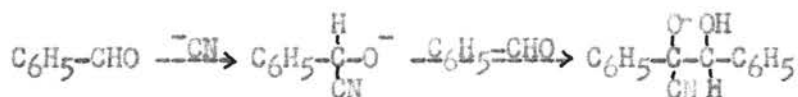
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## INTRODUCTION

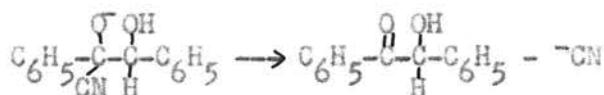
The benzoin condensation occurs when an aromatic aldehyde is treated with sodium cyanide or potassium cyanide, usually in aqueous ethanolic solution.



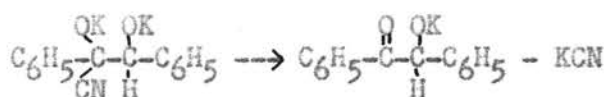
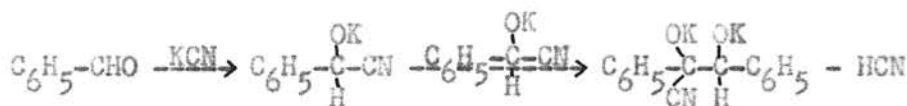
Lapworth (1) proposed an ionic mechanism which consists of two successive aldol additions



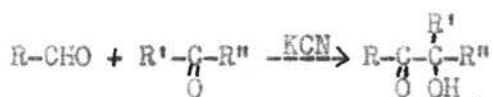
Mandelonitrile anion



Morton and Stevens (7) found that the benzoin condensation also takes place in anhydrous petroleum ether. This led to the postulation of a non-ionic mechanism.



The purpose of this investigation was to condense aldehydes with ketones in the following manner to produce substituted benzoin:



As a means of studying the problem, benzaldehyde and various ketones were caused to react under conditions that give benzoin when only aldehydes are used.

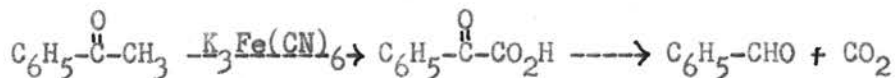
## HISTORY

No reference to condensations of aldehydes and ketones in the presence of cyanides was found in the literature.

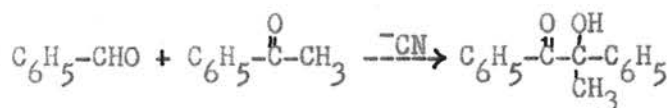
Buchka and Irish (3) in attempting to oxidize acetophenone to phenylglyoxalic acid by use of potassium ferricyanide obtained along with some benzoic acid, a white solid which gave upon analysis the empirical formula  $C_{16}H_{15}O_2N$ . Since the reaction was carried out in the presence of potassium hydroxide, they postulated the following reaction:



Under the influence of alkaline potassium ferricyanide, acetophenone would be oxidized to phenylglyoxalic acid, and the latter subsequently decarboxylated to benzaldehyde.



The benzaldehyde formed in the process could react with the acetophenone in the presence of cyanide ions to form a C-methylated benzoin, which could then form a cyanohydrin.



The latter formula corresponds to  $C_{16}H_{15}O_2N$ .



## PRELIMINARY DISCUSSION

Since acetophenone has a structure somewhat like that of benzaldehyde and has fewer  $\alpha$ -hydrogen atoms than most aliphatic ketones, it was chosen as the first ketone to condense with benzaldehyde. It was planned to treat mixtures of acetophenone and benzaldehyde with potassium cyanide in water-alcohol solutions.

Since it was possible that the reactive  $\alpha$ -hydrogen atoms of acetophenone would cause the reactions to proceed in the aldol manner, a condensation of benzaldehyde with benzophenone, which has no  $\alpha$ -hydrogen atoms, was planned.

4-Dimethylaminobenzaldehyde always acts as a hydrogen donor when it forms unsymmetrical benzoin (1). It was hoped that this fact would prevent the aldol condensation of this aldehyde and a ketone. For this reason a condensation with 4-dimethylaminobenzaldehyde and acetophenone was tried.

If the benzoin condensation in anhydrous petroleum ether proceeds by the non-ionic mechanism proposed, the formation of the substituted benzoin might be favored. This type of reaction between benzaldehyde and acetophenone was attempted in an anhydrous petroleum solvent.

## EXPERIMENTAL PROCEDURE

A. Condensation of Acetophenone and Benzaldehyde.

Thirty grams (0.25 mole) of acetophenone, 10 g. (0.15 mole) of potassium cyanide, 100 ml. of ethyl alcohol, and 25 ml. of water were placed in a 500-ml. three-neck flask fitted with a reflux condenser, dropping funnel, and thermometer. The mixture was heated to boiling on a water bath. Twenty-six and one-half grams (0.25 mole) of benzaldehyde was added through the dropping funnel at such a rate that all the benzaldehyde was added in fifteen minutes.\*

Soon after the addition of the aldehyde the solution went through the successive color changes of yellow, orange, and red. Shortly thereafter a white solid began to form on the walls of the flask. The reaction was stopped when the mixture began to bump.

The mixture was cooled by means of an ice bath and then acidified with 25 ml. of acetic acid. Upon acidification the solution turned from a red to yellow color and a red oil settled to the bottom of the flask. The mixture was filtered on a Buchner funnel. Twelve and one-half grams of a white solid (I) was obtained, which upon recrystallization from glacial acetic acid melted at 255-6° C.\*\* The yield was 30% of the theoretical (based on acetophenone).

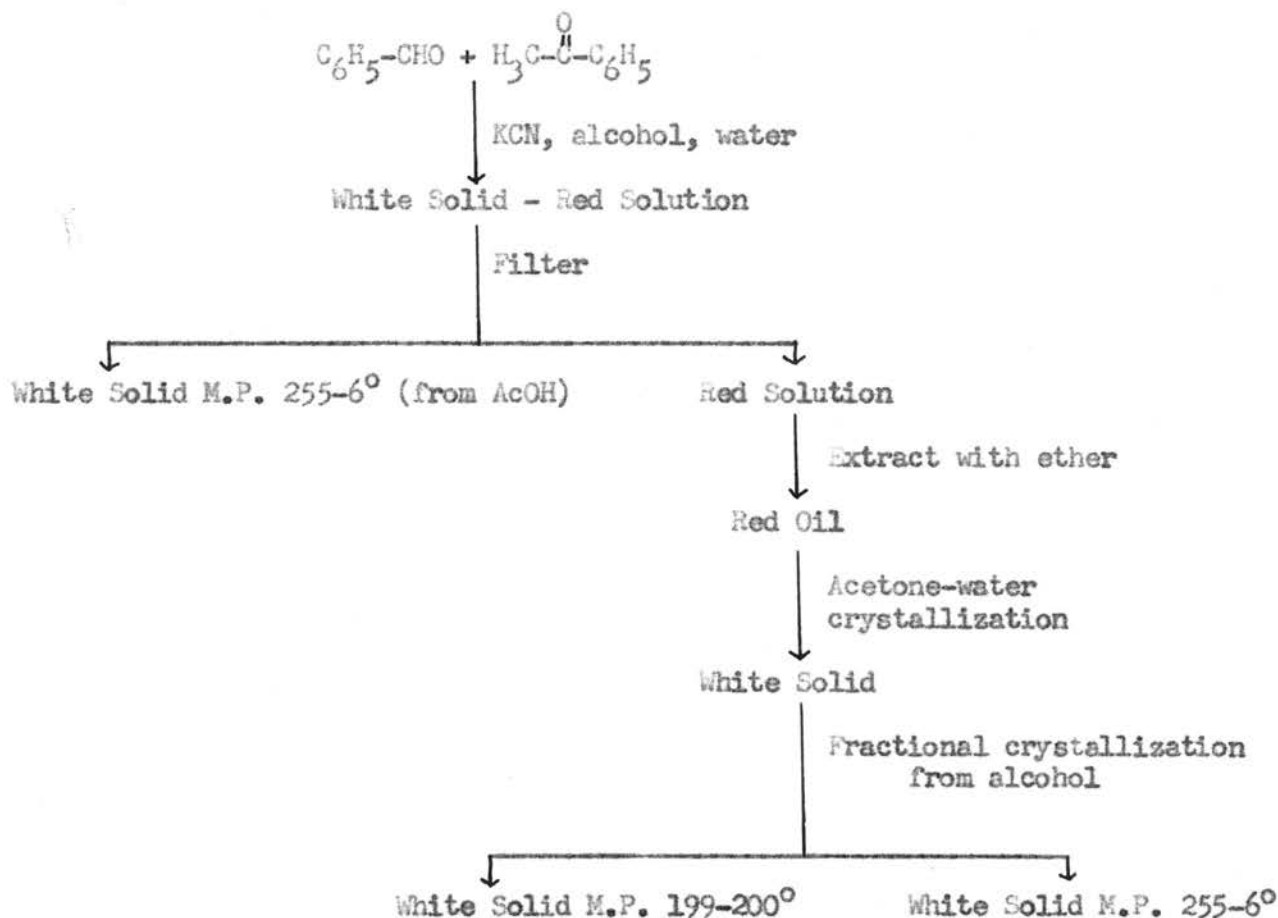
The resulting solution was extracted with three 100-ml. portions of ether. The ether extracts were dried over anhydrous calcium chloride and the ether was then removed by distillation. Twenty-five grams of a red oil remained.

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\* It was found that the rate of addition did not affect the type of product formed or the yield.

\*\* The melting point was the same if the acidification was omitted.

By use of acetone-water mixtures a white solid was obtained by crystallization from the oil. By fractional crystallization of this solid from alcohol two white solid products were obtained. One melted at  $255-6^{\circ}$  and the other at  $199-200^{\circ}$  uncorrected. These two solids were obtained in such small amounts that further characterization was not possible.



In order to show that the potassium cyanide was acting only as a catalyst and not forming an addition compound the amount of potassium cyanide used was varied from 0.038 to 0.25 mole. The other conditions of the reaction were held constant. Results are shown in Table I. The amount of product is essentially the same for the first three runs and decreases markedly only on the last run.

Table I

Amount of Solid (I) Formed by Heating 0.25 Moles of Benzaldehyde  
and 0.25 Moles of Acetophenone for 20 Minutes at 78° with  
Varying Amounts of Potassium Cyanide

Run No.	Potassium Cyanide (moles)	Solid (I) (g.)
1	0.25	12.0
2	0.15	12.5
3*	0.175	11.5
4*	0.038	3.5

#### B. Determination of Structure of Solid (I).

When solid (I) was tested for nitrogen by the sodium-fusion method a positive test was obtained. Upon recrystallization of solid (I) from glacial acetic acid however the nitrogenous products disappeared. A Kjeldahl determination of nitrogen gave 1-2% with the unpurified product.

Molecular-weight determinations were tried by the Rast method. They failed at first to give reproducible results as the amounts of unknown used were based on the supposition that the molecular weight was between 200 and 300. When the larger ratios of unknown and camphor were used (corresponding to a molality of 0.3 to 0.5), the result was 495. The molecular weight of dibenzaltriacetophenone is 524.

The purified product gave a red precipitate with 2,4-dinitrophenylhydrazine, indicating the presence of the carbonyl group.

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\* On runs 3 and 4 the oil obtained was yellow and not red as in runs 1 and 2.

Since it is known that benzaldehyde and acetophenone condense in basic solution to form chalcone, it was thought the latter might be an intermediate in the formation of the solid (I). Accordingly some chalcone was prepared, and then condensed with acetophenone in the presence of potassium cyanide. The product obtained was a white amorphous powder melting at  $254-5^{\circ}$  C. A mixture of the latter with the benzaldehyde-acetophenone condensation product melted at the same temperature.

#### Preparation of Chalcone (4)

Fifteen grams (0.125 mole) of acetophenone, 10 g. (25 mole) of sodium hydroxide, 150 ml. of alcohol, and 50 ml. of water were placed in a three-neck flask fitted with a stirrer, and supported in a beaker so as to permit cooling with cracked ice. Thirteen and one-half grams (0.12 mole) of benzaldehyde was then added. The temperature of the reaction was not allowed to exceed  $30^{\circ}$  C. nor to go below  $15^{\circ}$  C. The reaction was allowed to proceed for three hours. Stirring was stopped and a yellow oil settled to the bottom of the flask. With the addition of 20 ml. of water and stirring the oil changed to yellow lumps. The mixture was filtered on a Buchner funnel and washed with water until the washings were neutral to litmus. After drying in air the crude product weighed 24.1 g. (97% yield). Upon recrystallization from alcohol, 21 g. of pure chalcone (melting at  $55.5-57.5^{\circ}$  C. uncorrected) was obtained. Literature values for chalcone are: melting point,  $55-57^{\circ}$  C.; yield, 84%.

#### Preparation of Dibenzaltriacetophenone from Chalcone

Fifteen grams (0.125 mole) of acetophenone, 10 g. (0.15 mole) of potassium cyanide, 150 ml. of alcohol, and 5 g. of water were placed in a

three-neck flask fitted with a reflux condenser, and heated on a water bath. After heating had begun, 20.2 g. (0.099 mole) of chalcone was added. Shortly after the solution began to reflux, the solution turned first yellow, then orange and finally red. Shortly thereafter a white substance began to form on the walls of the flask. The reaction was stopped after 20 minutes of refluxing. The reaction mixture was cooled by means of an ice bath, acidified by adding 25 ml. of acetic acid, and filtered. Sixteen grams of a white amorphous powder was obtained which after recrystallization from glacial acetic acid gave a melting point of  $254.5^{\circ}$  C. uncorrected (yield 64%).

### C. Other Condensations.

#### Reaction of 4-Dimethylaminobenzaldehyde and Acetophenone

Thirty grams (0.25 mole) of acetophenone, 6 g. (0.09 mole) of potassium cyanide and 200 ml. of ethyl alcohol were heated in a three-neck flask, fitted with a reflux condenser. Soon after heating was started 37 g. (0.25 mole) of 4-dimethylaminobenzaldehyde was added and the solution was allowed to reflux for one hour at  $78^{\circ}$  C. The solution was then cooled by means of an ice bath and was acidified with 25 ml. of acetic acid. The solution was extracted with three 100-ml. portions of ether, the ether extracts were dried over anhydrous calcium chloride, and the ether removed by distillation. After removal of the ether a red oil remained. By heating the oil in ethyl alcohol/water mixtures and scratching the sides of the beaker, 10.5 g. of a yellow-orange precipitate was obtained. Its melting point was  $110-112^{\circ}$  uncorrected. The literature values (2) for 4-dimethylaminochalcone are: melting point,  $113-114^{\circ}$  (corrected); yield, 16%.

## Reaction of Benzaldehyde and Benzophenone

Eighteen and two-tenths grams (0.1 mole) of benzophenone, 5 g. (0.076 mole) of potassium cyanide, 100 ml. of ethyl alcohol, and 5 ml. of water were placed in a three-neck flask fitted with a reflux condenser, and the mixture was heated on a water bath. Ten and six-tenths grams (0.1 mole) of benzaldehyde was then added. Soon after the addition of benzaldehyde the solution turned yellow to light orange. The reaction was allowed to proceed for one hour at  $80^{\circ}$  C. The reaction was stopped and cooled by an ice bath. Eighteen grams of a white solid was obtained by filtration.

By means of fractional recrystallization from alcohol-water mixtures, 4.2 g. of benzoin, melting at  $136^{\circ}$  C. uncorrected, and 11 g. of benzophenone, melting at  $48-49^{\circ}$  C. uncorrected, were recovered.

## Reaction of Benzaldehyde and Acetophenone in Anhydrous Petroleum Solvent.

Five and three-tenths grams (0.05 mole) of benzaldehyde, 6.05 g. (0.05 mole) of acetophenone, and 5 g. of potassium cyanide (0.076 mole) were placed in a 50-ml. Erlenmeyer flask containing 40 ml. of anhydrous Skellysolve. Air was excluded from the flask by blowing in natural gas. The flask was then fitted with a glass stopper and sealed with collodion.

The flask was shaken intermittently during a period of seven days. However, none of the methylated benzoin nor any benzoin itself was found.

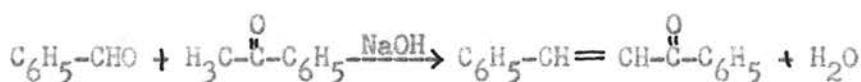
## DISCUSSION

When benzaldehyde reacted with acetophenone, in the presence of potassium cyanide, the product was found to be the higher-melting isomer (melting point,  $254^{\circ}$ ) of dibenzaltriacetophenone when the reaction mixture was heated on a water bath. Some of the lower-melting isomer was obtained from the solution by use of acetone-water mixtures.

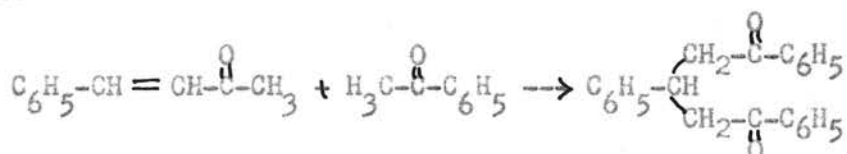
Kostanecki and Rossbach (5) have investigated the reaction of acetophenone and benzaldehyde in the presence of sodium hydroxide, and obtained as the end products two isomers of dibenzaltriacetophenone one melting at  $199^{\circ}$  C. and the other at  $256^{\circ}$  C. When the reaction was carried out at room temperature the  $199^{\circ}$  isomer was obtained and at a higher temperature, the  $256^{\circ}$  isomer.

Apparently potassium cyanide is basic enough to catalyze the same aldol-type of reaction between benzaldehyde and acetophenone as sodium hydroxide.

Kostanecki and Rossbach suggested that the reaction first proceeds through the formation of chalcone by an aldol condensation between acetophenone and benzaldehyde:

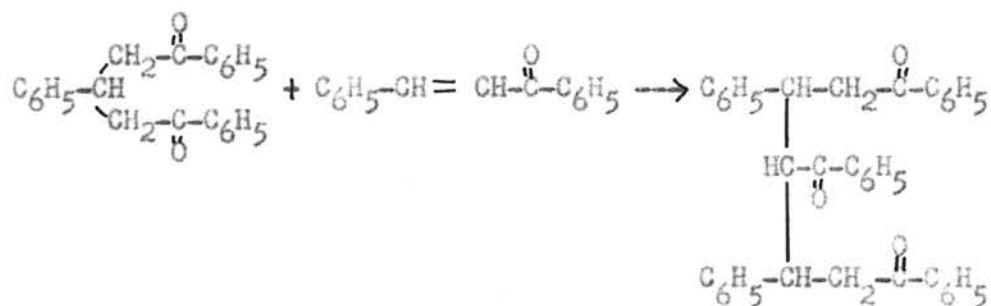


Chalcone can then add another molecule of acetophenone to form benzaldiacetophenone:

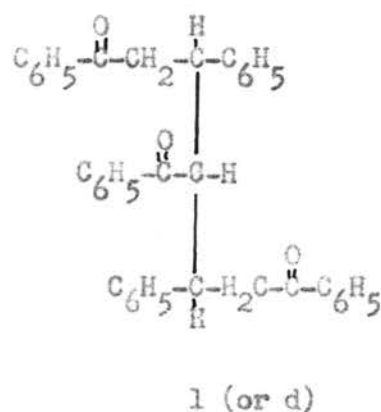
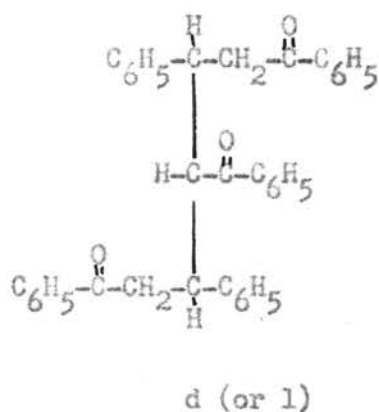
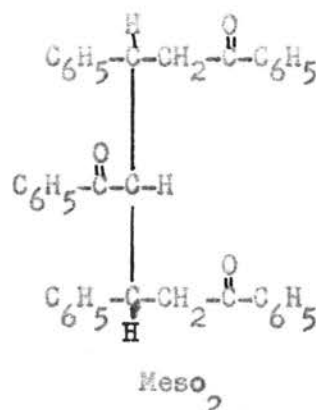
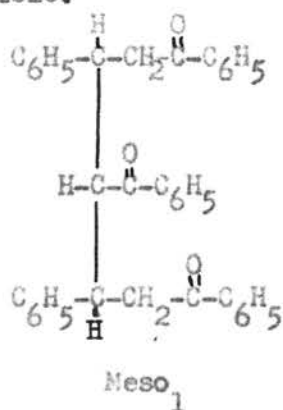


which can then add to another molecule of chalcone to form dibenzaltriacetophenone:

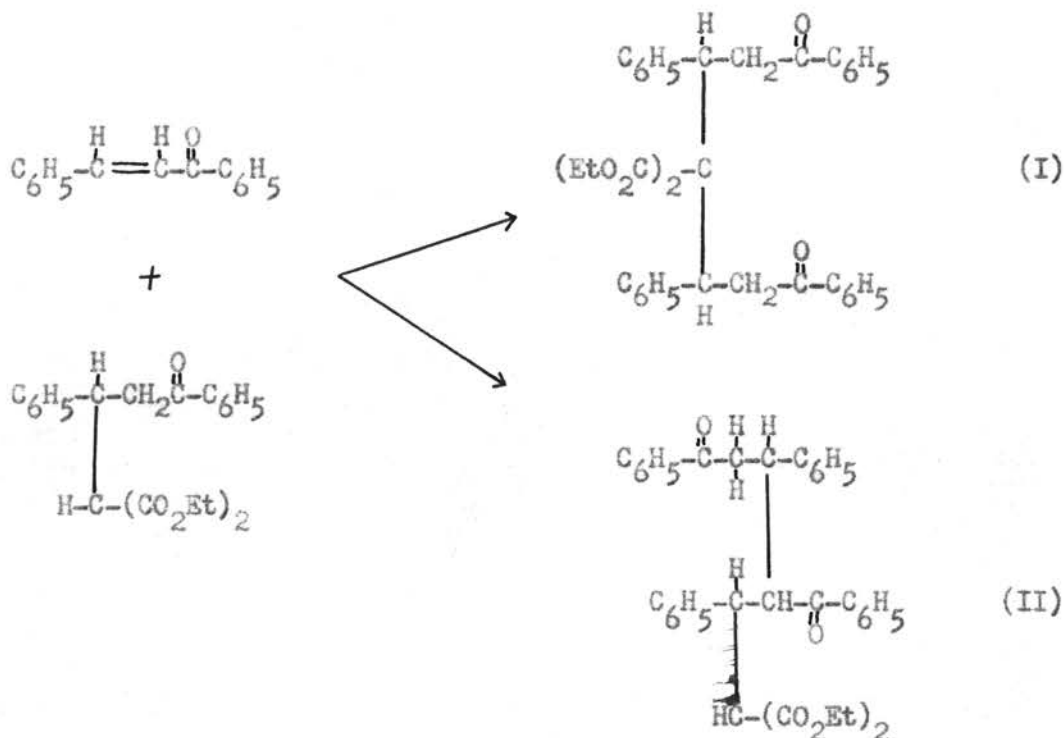




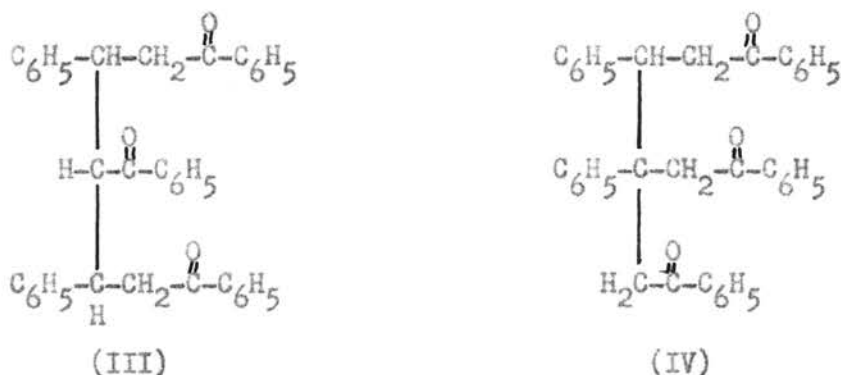
It is interesting that two isomers may be formed. Since dibenzaltriacetophenone has two identical asymmetric carbon atoms, a d, an l, and two meso forms are possible.



Michael (6) found that ethyl  $\alpha$ -carbethoxy- $\beta$ -phenyl- $\gamma$ -benzoylbutyrate adds to chalcone to produce (I) and (II)



If this idea were applied to the addition of benzaldiacetophenone to chalcone then the two isomers (III) and (IV) would be expected.



Since (IV) is less symmetrical it would be the lower-melting isomer.

Even though 4-dimethylaminobenzaldehyde never acts as a hydrogen acceptor when it undergoes a benzoin condensation, in the presence of cyanide ion it accepted the  $\alpha$ -hydrogen atom of acetophenone to form 4-dimethylaminochalcone.

In view of the above results and the fact that no products were obtained from the attempted condensation of benzaldehyde with benzophenone or the

attempted condensation of benzaldehyde and acetophenone in anhydrous petroleum solvent, it is concluded that the preparation of alkylated or arylated benzoin from ketones is not feasible. Because of either the reactive  $\alpha$ -hydrogen atoms or the inertness of the ketone, a benzoin-type condensation appears not to occur.

## SUMMARY

1. A benzoin-type condensation using benzaldehyde and acetophenone was attempted. It was found that because of the reactive  $\alpha$ -hydrogen atoms of acetophenone the reactions proceeded in the aldol manner with the formation of two isomers of dibenzaltriacetophenone, one melting at  $199^{\circ}$  C. and the other at  $256^{\circ}$  C. uncorrected.

2. A condensation with 4-dimethylaminobenzaldehyde was tried which resulted in the formation of 4-dimethylaminochalcone.

3. An attempt to prevent the reaction from proceeding in the aldol manner by using benzophenone resulted only in the production of benzoin from the benzaldehyde.

4. It was thought that if the reaction were tried in a non-ionizing solvent an aldol condensation might be prevented. No evidence of reaction was obtained, however, when the reaction was tried in an anhydrous petroleum solvent.

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## BIOGRAPHY

William Warren Ross was born December 20, 1925 in Chicago, Illinois. He attended Downers' Grove Community High School in Downers' Grove, Illinois, graduating in June, 1943.

Shortly thereafter he enrolled at North Central College, Naperville, Illinois. Before completing his freshman year he was inducted for service with the U. S. Navy.

After serving two years with the Navy Mr. Ross was discharged in May, 1946. He then enrolled at the University of Dubuque, Dubuque, Iowa and remained there for one year. He then re-enrolled at North Central College. During two summer semesters he was employed by Universal Oil Products Company, Riverside, Illinois.

He and Betty Ann Maxted were married in September, 1949.

Mr. Ross received the Bachelor of Arts degree from North Central College in June, 1949, and entered the Graduate School of Oklahoma A. and M. College in September, 1949.

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By Use of Potassium Cyanide

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THESIS ADVISER: Ernest M. Hodnett

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