

A STUDY OF QUANTUM MECHANICS

A THESIS

Submitted in partial fulfillment  
of the requirements for the Degree of  
Master of Science in Chemistry

by

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## A STUDY OF QUINOLINE COMPOUNDS

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Date Approved by Chairman

Feb. 17, 1944

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## CHAPTER I

### INTRODUCTION

H. K. Porter<sup>1</sup>, working in this laboratory, observed that the product obtained from the condensation of malonamide and isatin in a concentrated ammonium hydroxide solution was different from that reported in the literature by Lindwall and Hill<sup>2</sup>, who used an anhydrous alcoholic ammonia solution as the reaction solvent. This product from malonamide and isatin suggested an interesting source of new quinoline compounds, and seemed worthy of further investigation. This thesis reports the work done in an attempt to identify the products obtained from the malonamide-isatin condensation.

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<sup>1</sup>Porter, Georgia School of Technology, Master's Thesis (1942)

<sup>2</sup>Lindwall and Hill, J. Am. Chem. Soc., 57, 735-7 (1935)

CHAPTER II

EXPLANATION

## CHAPTER II

## EXPERIMENTAL

The Preparation of the Malonamide-Isatin Product

(XVIII)

The malonamide-isatin condensation product was prepared according to the method described by Porter<sup>1</sup>.

Twenty-nine and four-tenths grams (0.2 mol.) of isatin and 20.4 g. (0.2 mol.) malonamide were dissolved in 500 ml. of concentrated ammonium hydroxide solution. In approximately thirty minutes a yellow precipitate began settling out. After forty-eight hours the solid was filtered and washed alternately with water and ethyl alcohol. The dried product weighed 34.0 g.

The compound has no definite melting point but sublimes when heated to approximately 300 degrees C.

The observed nitrogen percentage was 15.62.

Five grams of the original product was recrystallized from glacial acetic acid, and a light yellow solid was obtained. The percent nitrogen (15.42) checked the result obtained before recrystallization.

Neither the original condensation product (XVIII) nor the material obtained from glacial acetic acid would couple with

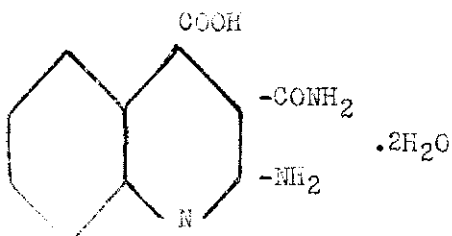
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<sup>1</sup>Porter, Georgia School of Technology, Master's Thesis, (1942)

beta-naphthol after treatment with sodium hypobromite<sup>2</sup>.

A small amount of the original compound (XVIII) was dissolved in cold concentrated sulfuric acid, and on dilution with water a bright yellow substance precipitated out. This solid was filtered, washed free of acid and dried in a vacuum desiccator. The nitrogen percentage found was 15.50.

One possible formula for the malonamide-isatin condensation product (XVIII) is shown below:



This compound has a nitrogen percentage of 15.73.

After partial dehydration, the product from acetic acid gave per cent C (52.37) and H (4.34) which agrees fairly well with the theoretical percentages C (52.90); H (4.45) for the above compound with one molecule of water of crystallization.

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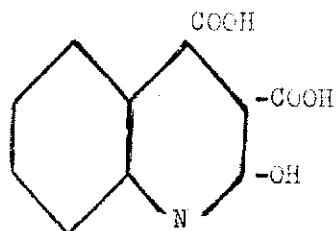
<sup>2</sup>The fact that the compound did not couple with beta-naphthol may be explained by the formation of the stable azimine.

Product Obtained from the Action of Potassium  
Hydroxide on the Malonamide-Isatin Product (XVIII)

Twenty grams of the original malonamide-isatin product (XVIII) was dissolved in 350 ml. of 33 per cent aqueous potassium hydroxide and the resulting solution was heated under reflux on a steam bath for fifteen hours. The reaction mixture was diluted to a volume of 600 ml. with water, boiled with Nuchar and filtered. The filtrate was cooled and made barely acid with acetic acid. The white solid which separated out was filtered, washed with cold water, and dried in a vacuum desiccator. The crude product weighed 18 grams. The compound was recrystallized from water. The acid has a melting point above 350 degrees C.

A nitrogen analysis indicated five molecules of water of crystallization. Three molecules of water are lost by heating the compound in an oven at 100 degrees C. for twelve hours.

The white product when recrystallized from propionic anhydride gives a bright yellow substance. The nitrogen percentage of the compound from propionic anhydride was found to be 6.08. This compares favorably with the calculated percentage of 6.01 for the following structure.

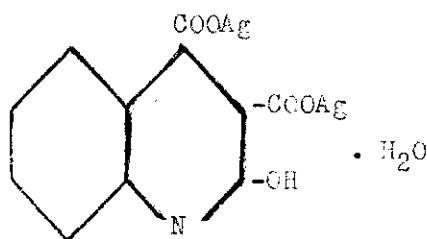


The yellow compound when dissolved in a base and precipitated by the addition of an acid gives a white product which resembles the original material before recrystallization from propionic anhydride.

Preparation of the Silver Salt of the Acid (XXII) Obtained from  
Potassium Hydroxide Hydrolysis of (XVIII)

Five grams of the white solid obtained by the hydrolysis of (XVIII) was dissolved in an excess of concentrated ammonium hydroxide, and the excess ammonia removed by heating. A little more than the calculated amount of silver nitrate solution was then added, and a light yellow product precipitated out. After heating for an hour, the silver salt was filtered, washed several times with distilled water and dried in an oven at 100 degrees C. for ten hours.

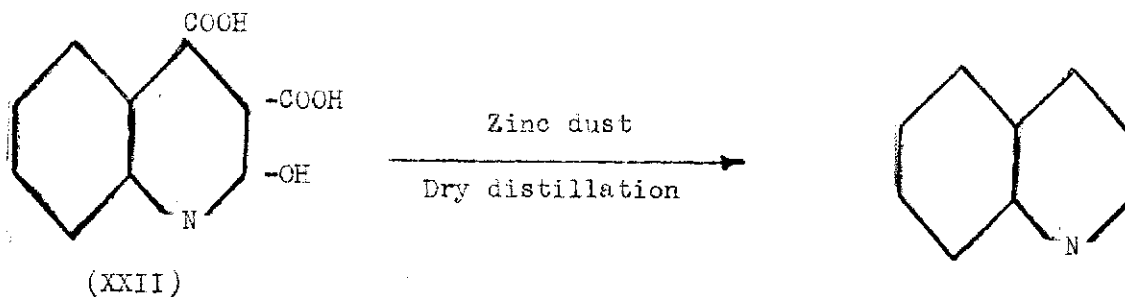
The percentage of silver observed was 46.73. This compares favorably with the calculated percentage of 46.50 for the following structure.



The Preparation of Quinoline from (XXII)

Approximately 2 grams of the acid (XXII) was mixed thoroughly with zinc dust and dry distilled under reduced pressure. The brown liquid which distilled over was dissolved in ethyl alcohol, and the picrate formed by the usual method. The yellow product was filtered, washed with water, and recrystallized from ethyl alcohol. The picrate had a melting point of 202 degrees C. (corr.). A mixture composed of equal amounts of the above picrate and a known picrate of quinoline gave a melting point of 201.6 degrees C. (corr.).

A probable reaction mechanism is shown below:



Reaction of (XVIII) with Hydrochloric Acid

Twenty grams of the original malonamide-isatin product (XVIII) was dissolved in 300 ml. of concentrated hydrochloric acid. The resulting solution was heated on a steam bath for four hours. After approximately thirty minutes of refluxing a bright yellow substance began precipitating out. The reaction mixture was diluted with water to a volume of 700 ml., and the yellow solid obtained by filtration. After washing with cold water and drying in a vacuum desiccator over calcium chloride, the crude product weighed 19.0 grams.

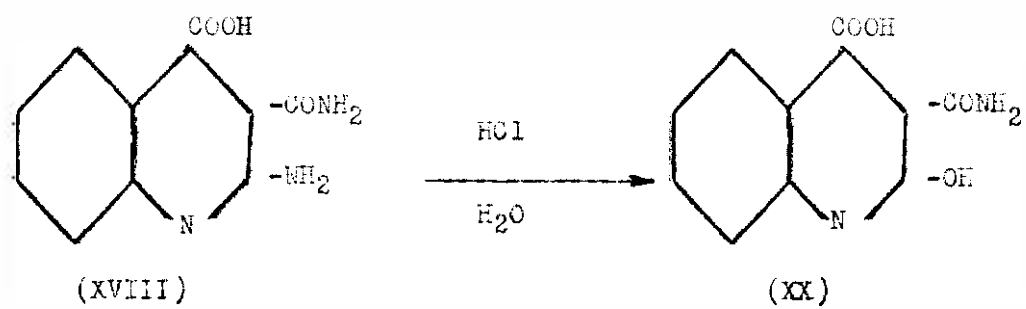
The compound when recrystallized from water has no definite melting point, but sublimes when heated above 300 degrees C. The nitrogen percentage observed (9.75) indicates three molecules of water of crystallization. After recrystallization from propionic anhydride the per cent nitrogen observed was 12.00. The percent C (57.40) and H (3.21) agree fairly well with the theoretical percentage (N; 12.06; C: 56.47; H: 3.47) for 2-hydroxy-3-amido-4-quinoline carboxylic acid.

The acid dissolves in 5 per cent aqueous sodium bicarbonate, giving a colorless solution.

An attempted neutral equivalent determination proved futile because of the apparent hydrolysis of the substance.

An attempt to obtain quinoline from (XX) by dry distillation with zinc dust failed.

A possible reaction mechanism is as follows:



Reaction of (XX) with Sodium Hypobromite

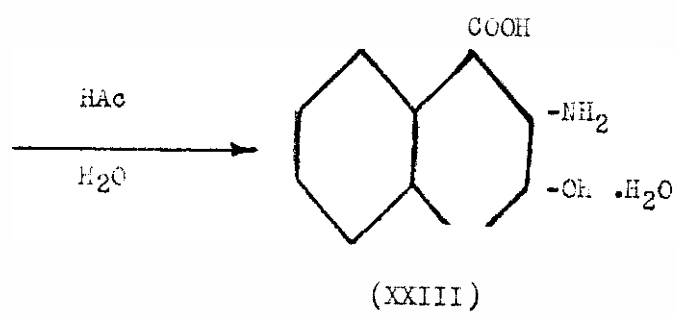
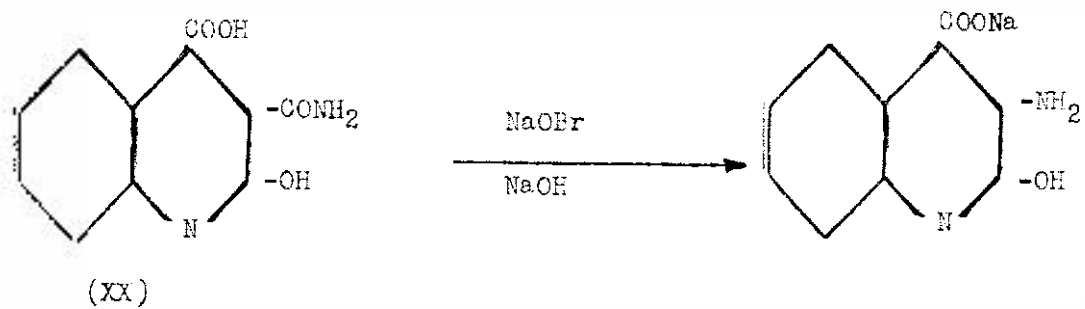
Thirty-six grams of sodium hydroxide was dissolved in 750 ml. of water, the resulting solution cooled and 14 grams of bromine added with stirring. Fourteen grams of the compound from hydrochloric acid (XX) was dissolved in this cold solution, and the mixture heated on a water bath for two hours. The solution was treated with Nuchar and neutralized with dilute acetic acid. The light yellow solid separating out was filtered and washed several times with cold water. The dried product weighed 8 grams. The compound was further purified by dissolving in potassium hydroxide solution, treating with Nuchar, and precipitating with dilute acetic acid.

The substance has no definite melting point, but decomposes when heated to 245 degrees C. (corr.).

The percentage composition from analysis was H: 4.00; C: 55.14; N: 12.76 agreeing fairly well with the theoretical percentages (C: 54.01; H: 4.50; N: 12.65).

A neutralization equivalent gave a value of 227. The theoretical neutralization equivalent, with one molecule of water of crystallization, is 222.1.

The proposed reaction is as follows:



Diazotization of (XXIII) and Coupling with beta-Naphthol

The method used was that described by Coghill<sup>3</sup>.

Two grams of the product (XXIII) obtained from the sodium hypobromite reaction was dissolved in 50 ml. of 5 per cent sodium carbonate solution, containing 1 gram of sodium nitrite. The mixture was cooled to 0 degrees C. in an ice bath and ten ml. of (1:1) sulfuric acid solution was added, with stirring. A bright red color appeared upon the addition of the acid. The diazo compound was then added to 100 ml. of a cold solution containing 8 grams of sodium hydroxide and 1.3 grams of beta-naphthol. The mixture was then made slightly acid with dilute sulfuric acid, and the dark red crystals separating out were recrystallized from an alcoholic-water solution and dried in a vacuum desiccator over phosphorous pentoxide.

Approximately 60 milligrams of the purified product was obtained.

The compound has no definite melting point, but begins to decompose at 150 degrees C.

A nitrogen analysis on the above product was low, probably due to compounds produced by side reactions.

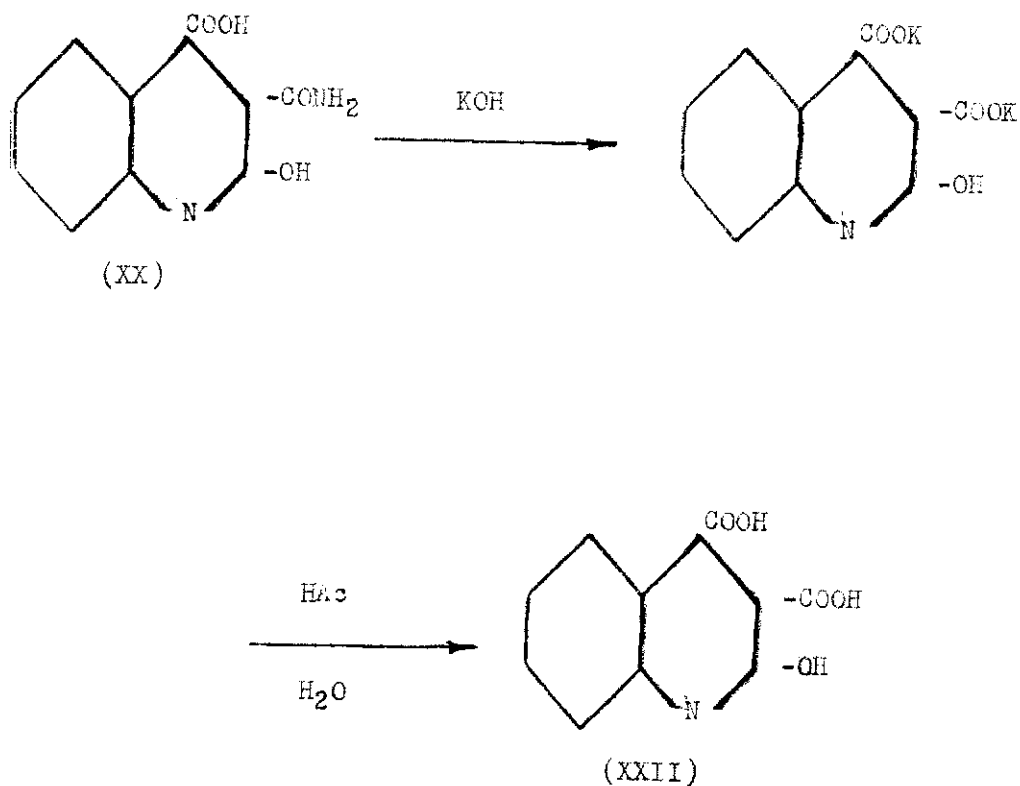
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<sup>3</sup>Coghill and Sturtevant, Organic Compounds, McGraw-Hill Co., New York, N. Y. (1936) p 113

Hydrolysis of (XX) with Potassium Hydroxide

The above compound was hydrolyzed by refluxing with 33 per cent potassium hydroxide solution for eight hours. A light yellow product was obtained. This acid gave a neutral equivalent of 136, and was shown to be identical with compound (XXII) obtained from treating the original malonamide-isatin product (XVIII) with potassium hydroxide.

A possible reaction mechanism is shown below.



Preparation of p-Benzylphenoxyacetone



The sodium salt of p-benzylphenol was prepared by reacting equivalent amounts of metallic sodium and p-benzylphenol in a benzene solution. An equivalent amount of chloroacetone was added, and when the reaction was complete the benzene was removed by distillation. The p-benzylphenoxyacetone was distilled under reduced pressure. The product when recrystallized from an alcoholic-water solution was a light tan color and had a melting point of 80 degrees C. (corr.).

Equivalent amounts of p-benzylphenoxyacetone and isatin were dissolved in a 33 per cent potassium hydroxide solution, and the resulting mixture was heated under reflux for twenty-four hours. None of the desired product, 3-benzylphenoxy-4-quinoline-carboxylic acid, was obtained.

FIGURE I

Derivatives of Original Product (XVIII)

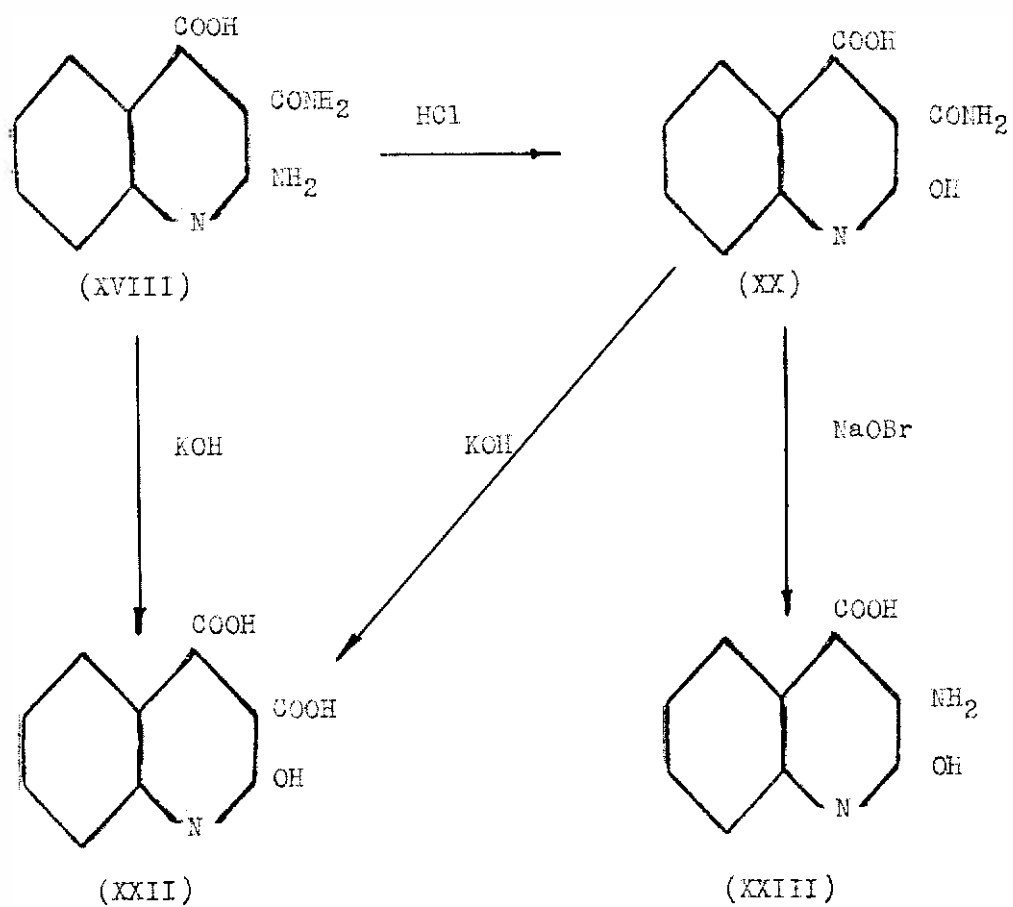


FIGURE II

## Derivatives of Compound (XXII)

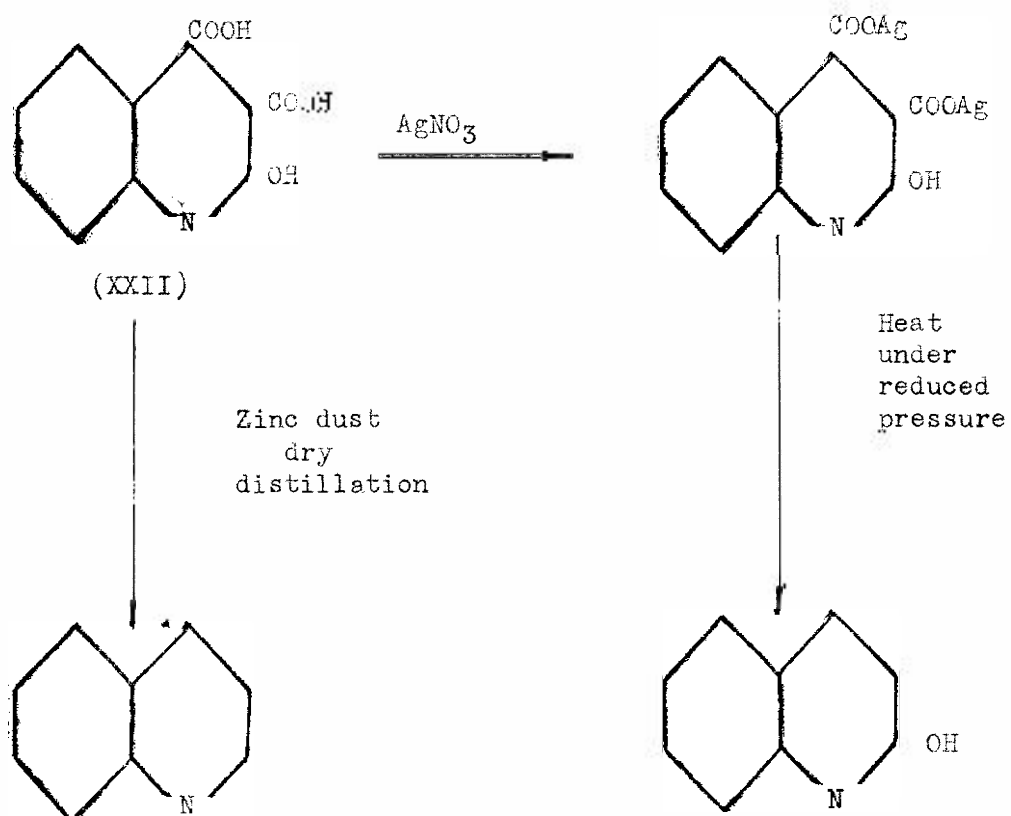
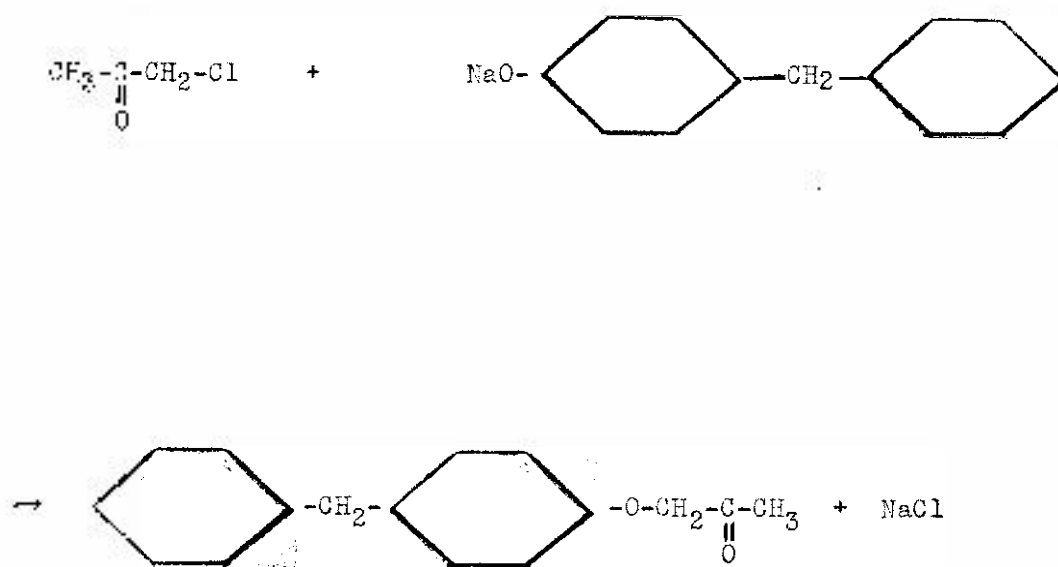


FIGURE III

The Preparation of p-Benzylphenoxyacetone



CHAPTER III

DISCUSSION OF RESULTS

## CHAPTER III

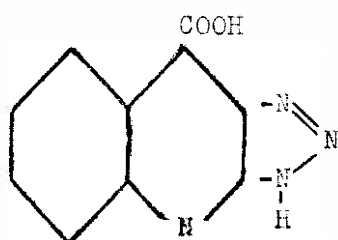
## DISCUSSION OF RESULTS

An attempt has been made to identify the products obtained from the condensation of malonamide and isatin in a concentrated ammonium hydroxide solution as the reaction solvent. No claim is made that the structures of these compounds have been proven conclusively. Product (XXII) is believed to be a 2-hydroxy-3, 4-quinoline-dicarboxylic acid because both carbostyryl and quinoline were obtained from it thus indicating the presence of the quinoline ring as well as a hydroxyl group in the 2 position. The silver salt checked fairly well for two carboxylic groups. The other analytical data and observed reactions are in accord with this structure.

The product from hydrochloric acid (XX) is thought to be 2-hydroxy-3-amido-4-quinoline carboxylic acid because on treating with 33 per cent potassium hydroxide it gives a compound whose properties are identical with those of (XXII). Substance (XX) when treated with sodium hypobromite gives compound (XXIII) which gives a test for a primary amine. The analytical data and observed reactions of (XXIII) are in accord with those of 2-hydroxy-3-amino-4-quinoline carboxylic acid.

The original malonamide-isatin condensation product (XVIII) is believed to be 2-amino-3-amido-4-quinoline carboxylic acid, because of the analytical data and observed reactions of this substance. Compound

(XXII), a dicarboxylic acid, is obtained by treating (XVIII) with potassium hydroxide; product (XX), 2-hydroxy-3-amido-4-quinoline carboxylic acid, is produced by reacting (XVIII) with concentrated hydrochloric acid for several hours. The failure of (XVIII) to couple with beta-naphthol after treatment with sodium hypobromite may be explained by the tendency of o-diamines to form the very stable azimine type compound shown below:



The formation of the azimine ring would prevent coupling with beta-naphthol.

CHAPTER IV

SUMMARY

## CHAPTER IV

## SUMMARY

The following compounds have been prepared and their chemical properties studied: 2-amino-3-amido-4-quinoline carboxylic acid, 2-hydroxy-3-amido-4-quinoline carboxylic acid, 2-hydroxy-3-amino-4-quinoline carboxylic acid, 2-hydroxy-3, 4-quinoline dicarboxylic acid, the disilver salt of 2-hydroxy-3, 4-quinoline carboxylic acid, and p-benzylphenoxyacetone.

BIBLIOGRAPHY

## BIBLIOGRAPHY

Aeschlimann, Journal of the Chemical Society; 128; 2902  
(1926)

Coghill and Sturtevant, Organic Compound, McGraw-Hill Co.  
p 113 (1936)

Lindwall and Hill, Journal of the American Chemical Society;  
57: 735-7 (1935)

Lindwall and Znike, Journal of the American Chemical Society;  
58: 49-50 (1936)

Porter, Georgia School of Technology, Master's Thesis  
(1942)