UNIVERSITY OF CINCINNATI

May 21 1943

I hereby recommend that the thesis prepared under my supervision by Sister Mary Rose Stockston

entitled Synthesis of 7-Nitrofluorenone-2-Carboxylic Acid

be accepted as fulfilling this part of the requirements for the degree of Doctor of Philosophy.

Approved by:

Francis E. Ray

Hoke S. Greene

Form 668—G. S. and Ed.—1M—7-37

SYNTHESIS OF 7-NITROFLUORENONE-2-CARBOXYLIC ACID

A dissertation submitted to the

Graduate School
Of the University of Cincinnati

in partial fulfillment of the
requirements for the degree
of

DOCTOR OF PHILOSOPHY

1943

by

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B.S. of Ed. Teachers College Athenaeum of Ohio 1937

M.A. University of Cincinnati 1942

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ACKNOWLEDGEMENT

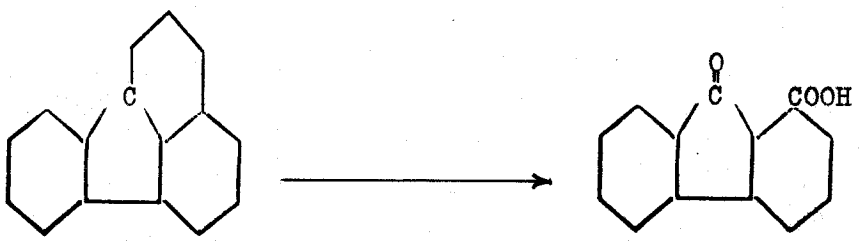
The many helpful suggestions and generous encouragement given by Dr. Francis Earl Ray are greatly appreciated.

I

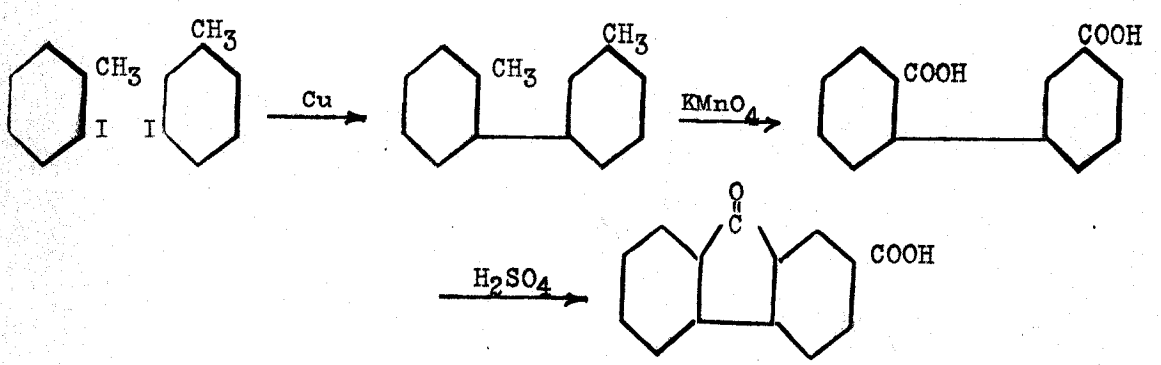
HISTORICAL DEVELOPMENT

A. Fluorene-monocarboxylic Acids

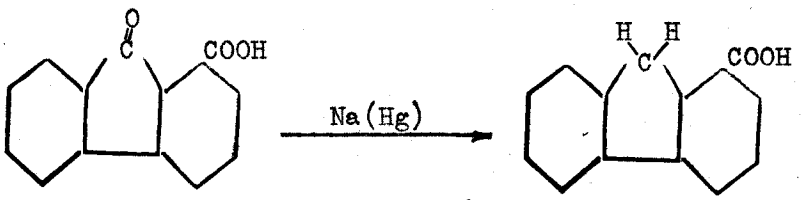
1. The fluorene carboxylic acids have been known since 1878 when the first one, fluorenone-1-carboxylic acid, was prepared by Fittig and Gebhard (1) by the oxidation of fluoranthene with chromic acid.



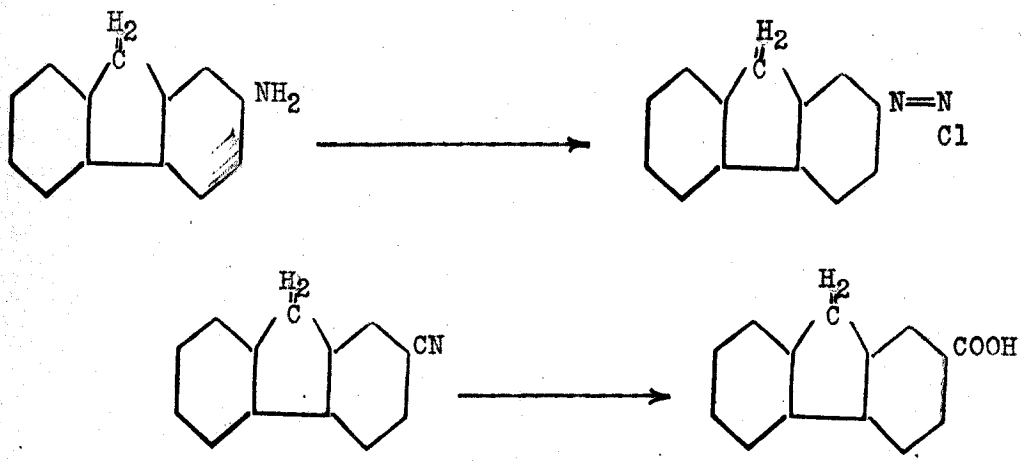
This method has been used with various modifications until in 1935, Fieser and Seligman (2) obtained a yield of approximately fifty per cent of fluorenone-1-carboxylic acid. Mayer and Freitag (3) prepared fluorenone-1-carboxylic acid in the following manner which although impractical for preparative purposes is of considerable theoretical importance in proving its structure.



2. Fluorene-1-carboxylic acid was prepared in an eighty-four per cent yield from fluorenone-1-carboxylic acid, by Fieser and Seligman (2), using sodium amalgam as a reducing agent.

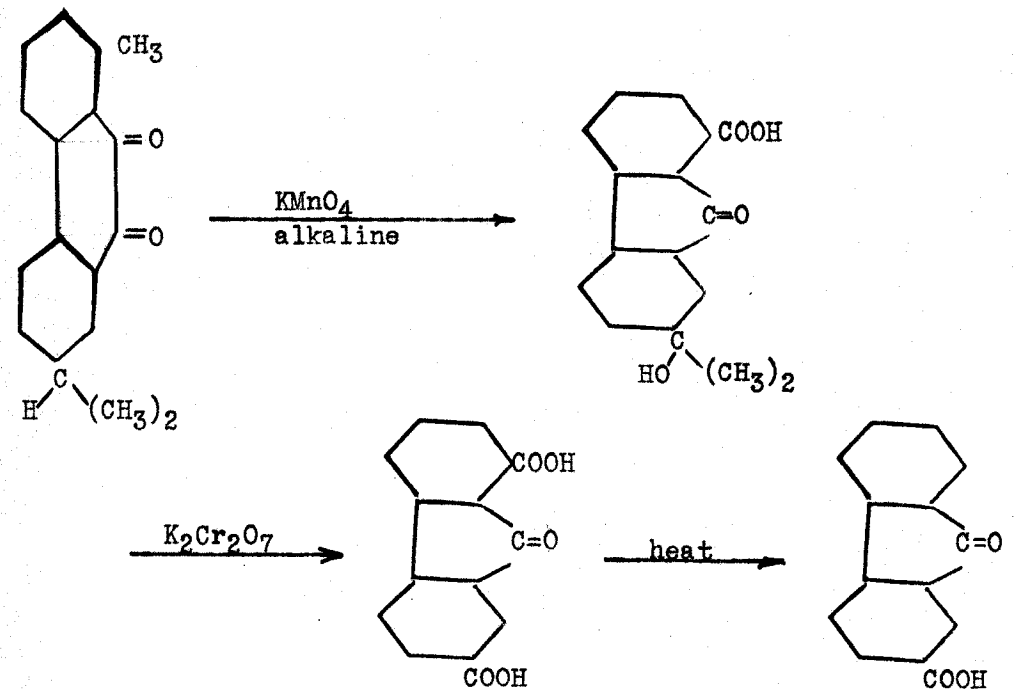


3. In 1904, Fortner (4) first prepared fluorene-2-carboxylic acid. This was accomplished by the hydrolysis of 2-cyanofluorene, which was obtained from 2-aminofluorene by the Sandmeyer reaction.



4. He oxidized the fluorene-2-carboxylic acid with chromic acid to fluorenone-2-carboxylic acid. (4)

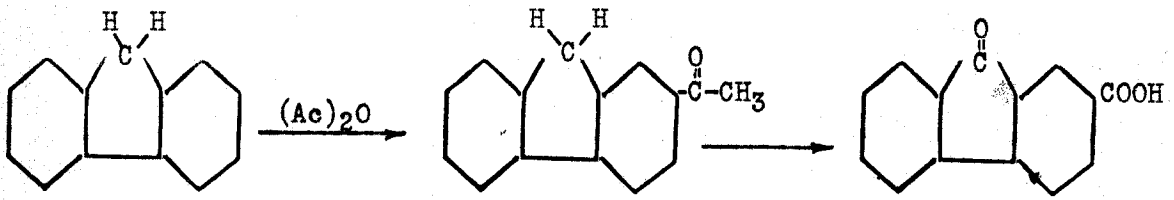
This latter acid was first reported by Bamberger and Hooker (5) who obtained it by heating 1,7-dicarboxylic acid, prepared by the oxidation of retenequinone.



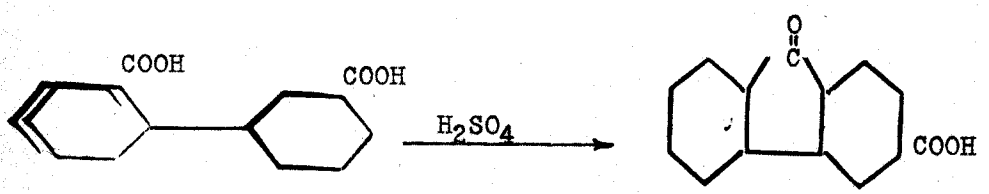
Dziewonski and Schnayder (6), however, have prepared fluorenone-2-carboxylic acid by a more convenient method; i. e. the oxidation of 2-fluorylmethylketone which they prepared by the action of acetyl chloride on fluorene in the presence of aluminum chloride. The yield of fluorenone-2-carboxylic acid was very low.

Rieveschl (7) prepared this acid from 2-acetylfluorene which he obtained in a quantitative yield by using acetic anhydride, instead of acetyl chloride, a slight excess of crude fluorene and a higher tempera-

ture than did Dziewonski and Schnayder. By using this method, Rieveschl was able to prepare the fluorenone-2-carboxylic acid in an over-all yield of from fifty-eight per cent to sixty-two per cent. This is a very good yield when one considers that crude fluorene is used and that two steps are involved in the synthesis. Furthermore the reagents are cheap and the reaction can be carried out in large quantities.



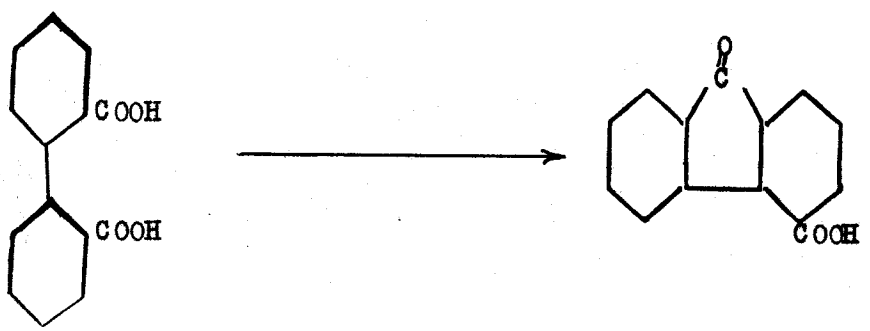
5. Fluorenone-3-carboxylic acid was prepared in 1921 by Sieglitz and Schatzkes (8) by heating 2,3'-diphenic acid with sulfuric acid.



These investigators proved the structure by comparing it with fluorenone-3-carboxylic acid obtained by the oxidation of 3-methylfluorenone with potassium permanganate. The acid was a yellow crystalline substance melting at 285°.

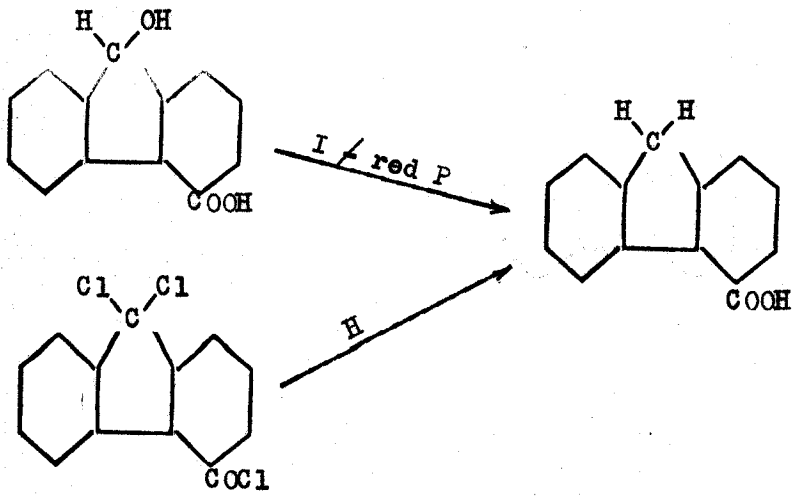
6. Fluorene-3-carboxylic acid has not as yet been reported in the literature.

7. Fluorenone-4-carboxylic acid, crystallizing in yellow needles and melting at 227°, was prepared by the reaction of various reagents upon diphenic acid or diphenic anhydride. Graebe and Aubin (9); Stobbe and Seydel (10); and Bischoff and Adkins (11) found that cyclization occurred very rapidly with concentrated sulfuric acid. Underwood and Kochmann (12) heated diphenic acid with stannic or zinc chloride for seven hours, while Pick (13) and Gotz (14) used aluminum chloride in benzene or toluene solution to obtain ring closure. Moore and Huntress (15) adopted Graebe and Aubin's procedure and reported an eighty-six per cent yield of the acid. Rieveschl (7) found that by careful regulation of the conditions of the reaction and by using certain precautions in isolating the acid, he obtained a yield of pure fluorenone-4-carboxylic acid of ninety-six per cent.

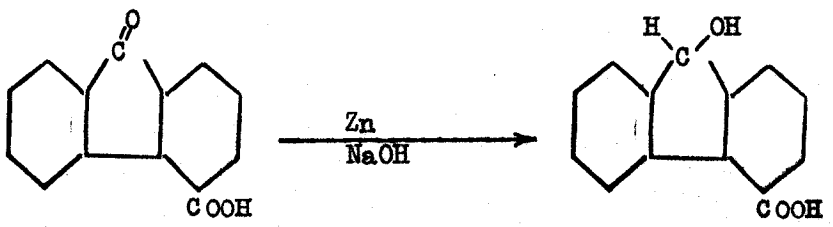


8. Fluorene-4-carboxylic acid was prepared by Bachmann and Sheehan (16) by the reduction of fluorenol-4-carboxylic acid with iodine and red phosphorus. On recrystallization from benzene, fine colorless needles melting at 191° - 191.8° were obtained. Graebe and Aubin (17) reduced the acid

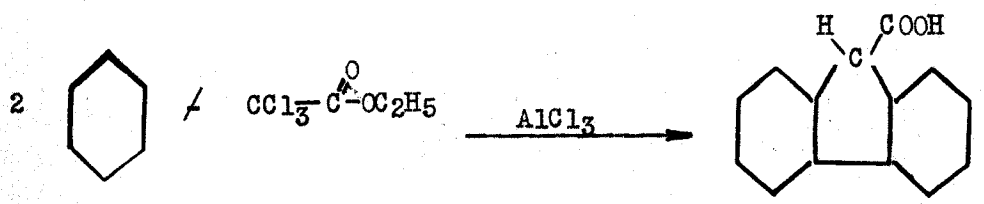
chloride of 9,9-dichloro-4-fluorenecarboxylic acid resulting in a compound melting at 175° which they considered to be fluorene-4-carboxylic acid. The methyl ester of the fluorene-4-carboxylic acid of Bachmann and Sheehan melted at 63.5° - 64.5° while that of Graebe and Aubin melted at 64°.



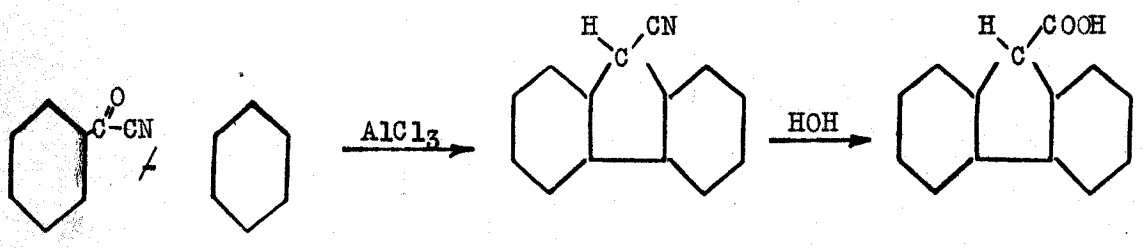
9. Bachmann and Sheehan (16), using powdered zinc and sodium hydroxide as reducing agents, obtained fluorenol-4-carboxylic acid from fluorenone-4-carboxylic acid. After several recrystallizations from benzene, this acid melted at 202° - 203°.



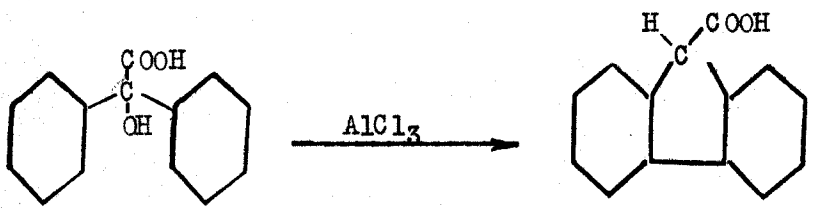
10. Delacre (18) by means of the Friedel-Craft reaction obtained fluorene-9-carboxylic acid from ethyl trichloracetate and benzene.



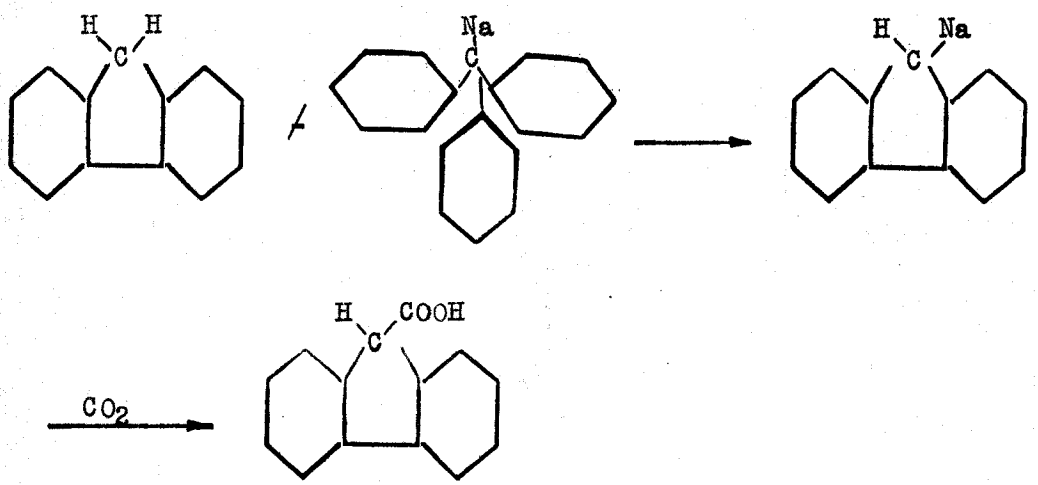
Vorlander (19) condensed benzoyl cyanide with benzene in the presence of aluminum chloride, obtaining 9-cyanofluorene, which on hydrolysis gave fluorene-9-carboxylic acid.



Several years later he and Pritzche (20) prepared fluorene-9-carboxylic acid directly by using benzilic acid in place of benzoyl cyanide.



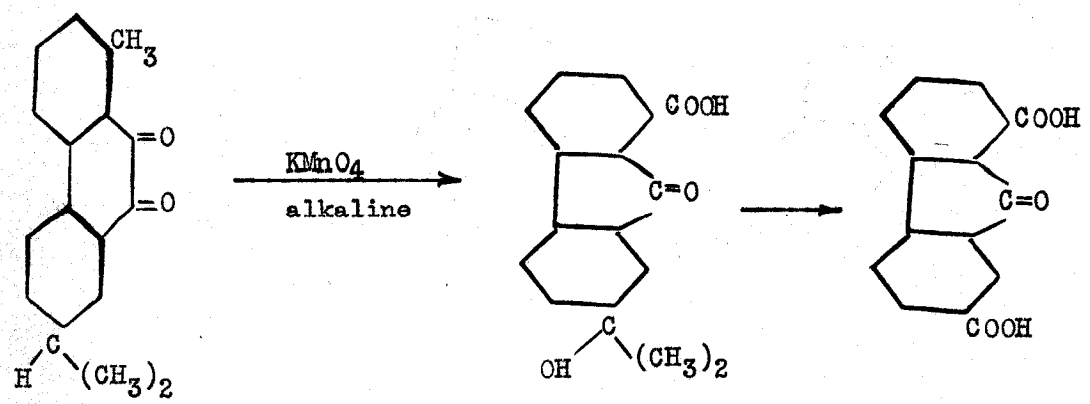
The most direct method for the preparation of fluorene-9-carboxylic acid, however, is that of Schlenk and Bergman (21), by the reaction between 9-sodiumfluorene and carbon dioxide. The sodiumfluorene was prepared by treating fluorene with the sodium derivative of triphenylmethane.



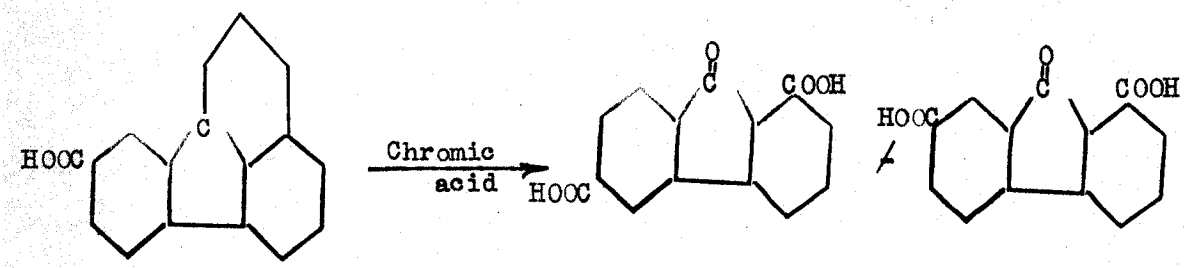
These authors reported two forms of the acid, the α-form melting at 222° and the β-form melting at 232°. Kliegl (22) repeated their work and obtained one compound melting at 221° - 223° with slight evolution of gas.

B. Fluorene-dicarboxylic Acids

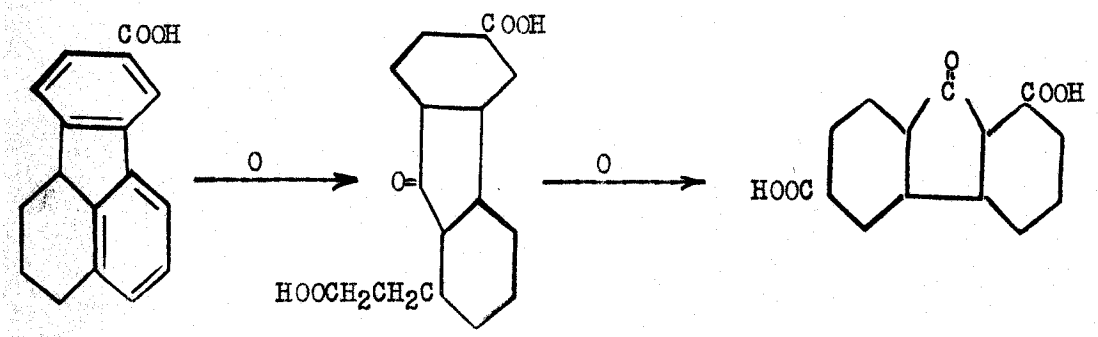
1. Of the dicarboxylic acids of fluorene, the first to be prepared was fluorenone-1,7-dicarboxylic acid. This was prepared in 1885 by Bamberger and Hooker (5) by the oxidation of retenequinone:



2. Von Braun, Manz, and Kratz (23) on the oxidation of fluoranthene-9-carboxylic acid with chromic acid found a mixture of fluorenone-1,6- and -1,7-dicarboxylic acids.

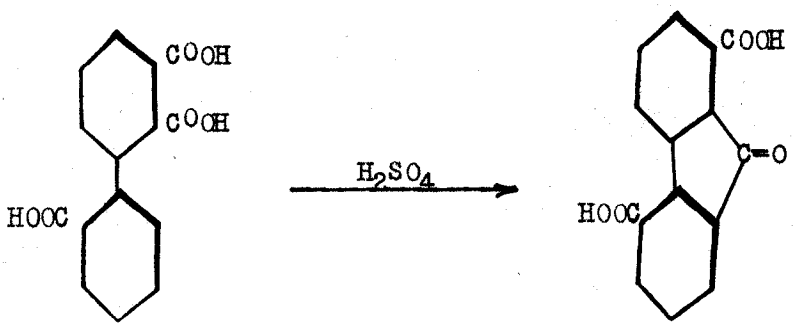


However, if the fluoranthene nucleus were first partially reduced and then oxidized, fluorenone-1,6-dicarboxylic acid alone was obtained.



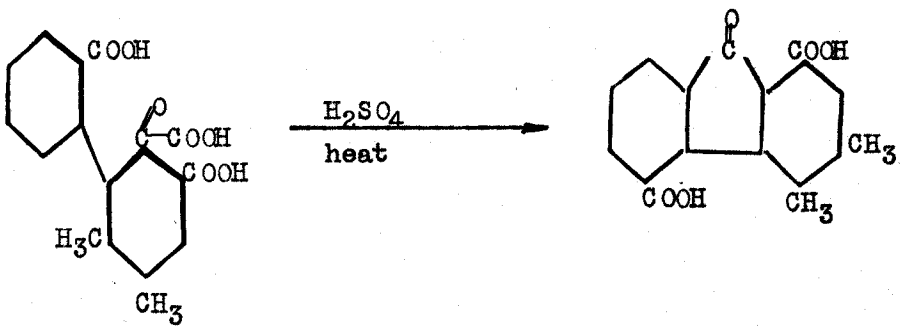
3. Fluoranthene-3-carboxylic acid was oxidized to fluorenone-1,2-dicarboxylic acid, which readily formed an anhydride melting at 318° - 320°. This same acid was prepared by Charrier and Ghigi (24) by the action of concentrated sulfuric acid on biphenyl-2,3,4-tricarboxylic acid. Their acid melted at 330° and the anhydride at 315° - 320°. Heat caused the loss of carbon dioxide to give fluorenone-2-carboxylic acid.

4. Fluorenone-1,5-dicarboxylic acid was prepared similarly, using biphenyl-2,3,2'-tricarboxylic acid.

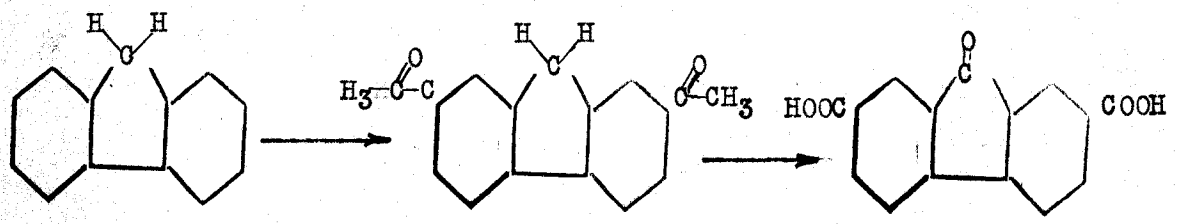


Boiling with quinoline and copper powder caused the removal of the carboxyl group in the 5-position, leaving fluorenone-1-carboxylic acid.

5. Fluorene,1-5-dicarboxylic acid has never been reported; however, Ghigi (25) prepared 3,4-dimethylfluorene-1,5-dicarboxylic acid by heating 2,3-dimethyldiphenyl-5,2'-dicarboxylic-6-glyoxalic acid with concentrated sulfuric acid.



6. Fluorenone-2,7-dicarboxylic acid was first obtained by Dziewonski and Schnayder (26) from the oxidation of 2,7-diacetylfluorene. Their yield was very low. Rindsberg (27) modified the method of Dziewonski and Schnayder by using only a slight excess of acetyl chloride in the preparation of the diacetyl derivative and by performing the oxidation with a strong solution of anhydrous sodium dichromate in acetic acid.



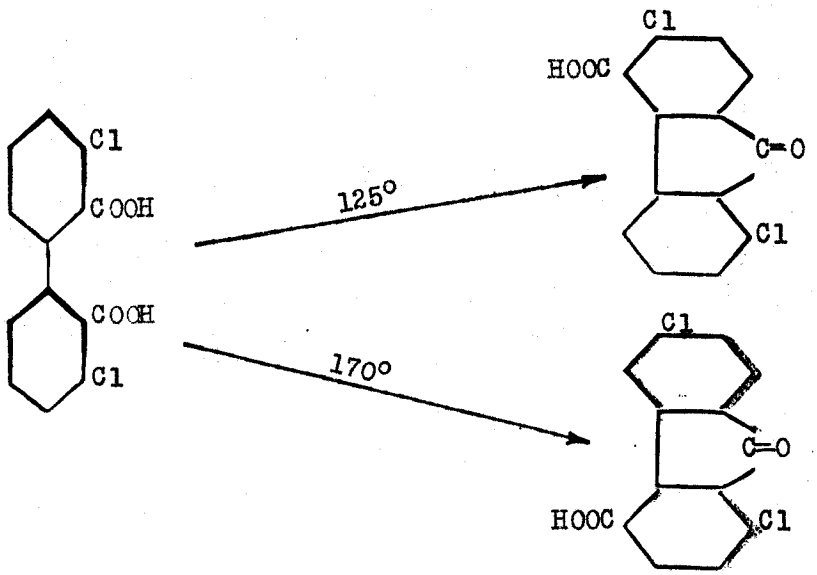
7. Sheldrick and Wyler (28) have secured a British patent on a method for preparing fluorene-2,7-dicarboxylic acid. N-alkyl-n-phenyl-amides of fluorene-2-mono- and -2,7-dicarboxylic acids were prepared by treating fluorene with alkylphenylcarbamyl halides in the presence of aluminum chloride. Fluorene-2-mono- and -2,7-dicarboxylic acids were then prepared by hydrolyzing the above products with either aqueous sulfuric acid or alcoholic potassium hydroxide.

8. Dziewonski and Kleszcz (29) have prepared 2,3-diacetylfluorene but up to the present time this has not been oxidized to fluorenone-2,3-dicarboxylic acid.

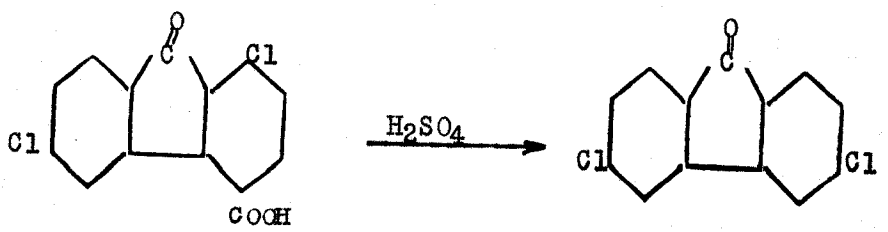
C. Dichlorofluorenonecarboxylic Acids

1. Huntress, Cliff, and Atkinson (30) investigated the action of concentrated sulfuric acid on 3,3'-dichloro-diphenic acid. At 125° the expected 1,6-dichlorofluorenone-5-carboxylic acid was obtained, but when the temperature was raised to 170° a dichlorofluorenone-carboxylic acid was obtained which was different from 1,6-dichlorofluorenone-5-carboxylic acid. In other words, two isomeric monobasic acids were obtained at different temperatures. They termed the isomer formed at 170° "Acid X".

2. Three years later Huntress and Atkinson (31) were able to establish the constitution of "Acid X" as that of 1,6-dichlorofluorenone-4-carboxylic acid. The acid proved to be identical with that obtained by the action of concentrated sulfuric acid on 5,5'-dichlorodiphenic acid. On attempting to decarboxylate 1,6-dichlorofluorenone-4-carboxylic acid



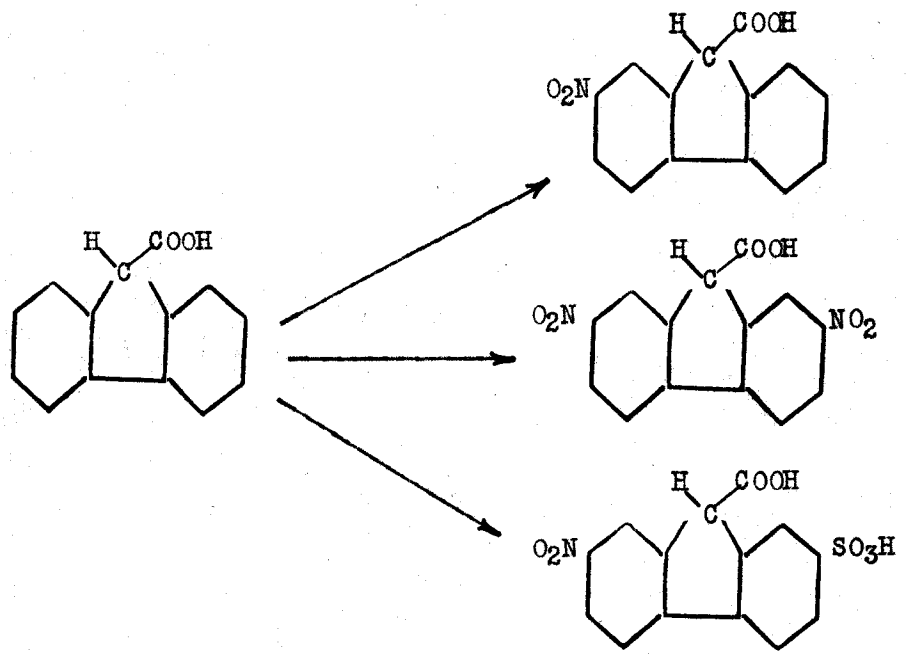
by heating in sulfuric acid it also was noted by these authors that 3,6-dichlorofluorenone was formed. This emphasizes the danger in the use of



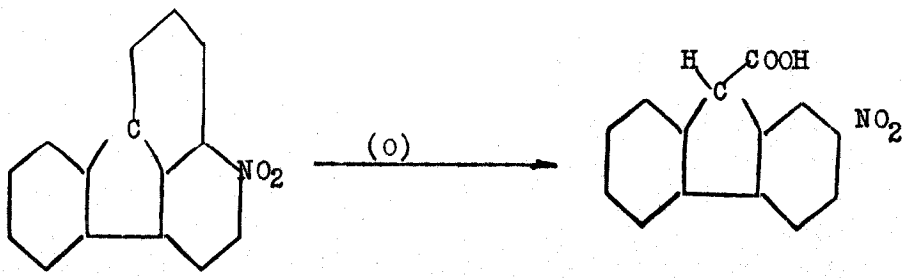
high temperatures in the synthesis of fluorenones.

D. Nitrofluorene-carboxylic Acids

1. Rose (32) nitrated fluorene-9-carboxylic acid. He obtained 2-nitrofluorene-9-carboxylic acid, 2,7-dinitrofluorene-9-carboxylic acid, and 2-nitro-7-sulfofluorene-9-carboxylic acid.

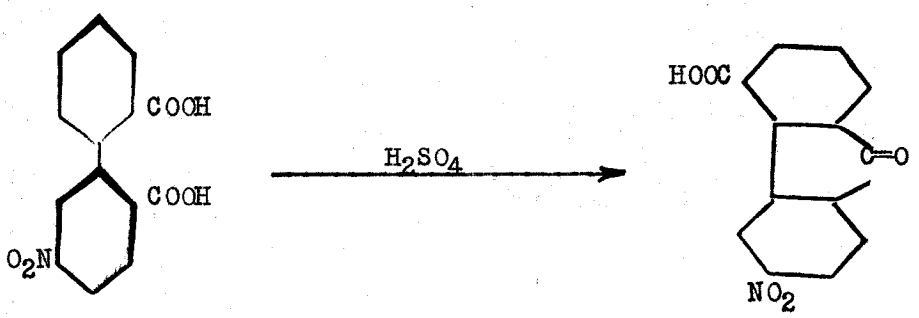


2. 2-Nitrofluorene-1-carboxylic acid was prepared by von Braun and Manz (33) by the oxidation of 4-nitrofluoranthene with chromic anhydride. The purified acid was in the form of yellow needles melting at 223° - 225°.

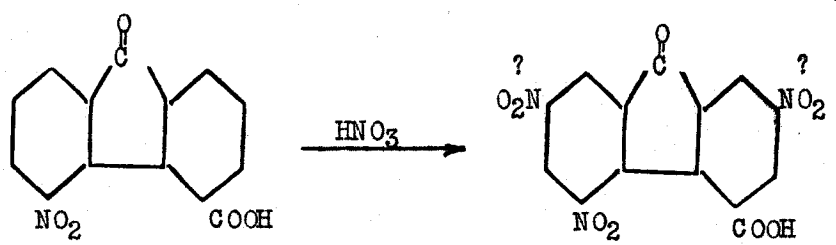


3. Bell and Briggs (34) attempted to prepare 2,7-dinitrofluorenone-4-carboxylic acid by heating 4,4'-dinitrodiphenic anhydride with aluminum chloride but after decomposition of the reaction mass with hydrochloric acid the only isolable product was 4,4'-dinitrodiphenic acid.

4. Bell and Robinson (35) treated 5-nitrodiphenic acid with sulfuric acid and probably obtained 6-nitrofluorenone-4-carboxylic acid which melted at 282° after recrystallization from acetic anhydride. These same

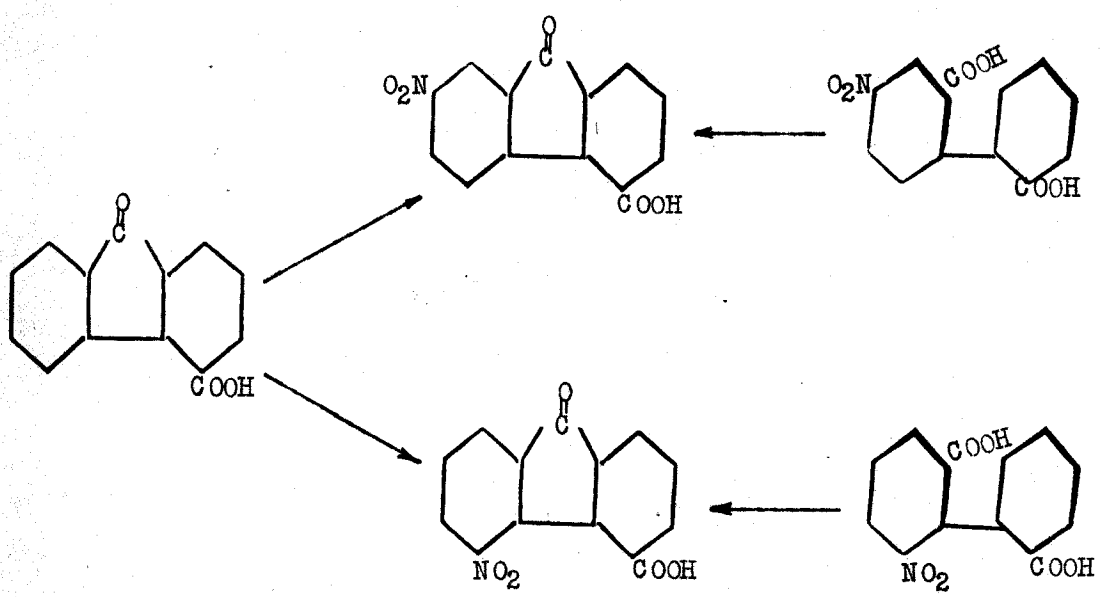


investigators nitrated 5-nitrofluorenone-4-carboxylic acid. The resultant product on crystallizing from aqueous alcohol formed glistening, pale yellow plates, melting at 254° - 255° which they believed to be 2,5,7-trinitrofluorenone-4-carboxylic acid, but no proof was given.



5. The nitration of fluorenone-4-carboxylic acid resulted in approximately equal amounts of 7-nitrofluorenone-4-carboxylic acid and 5-nitro-

fluorenone-4-carboxylic acid (3). The 7-nitrofluorenone-4-carboxylic acid which melted at 262° - 262.5° was identified by comparing it with a sample of the same acid made by the condensation of 4-nitrodiphenic acid with concentrated sulfuric acid. In a similar manner the 5-nitrofluorenone-4-carboxylic acid, melting at 238° - 239°, was compared with a sample made by condensing 6-nitrodiphenic acid with sulfuric acid.



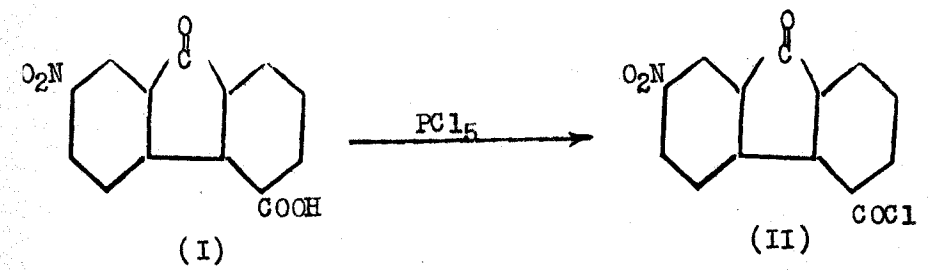
E. Derivatives of 7-Nitrofluorenone-4-carboxylic Acid (I)

1. The acid chloride of 7-nitrofluorenone-4-carboxylic acid (II) was prepared in almost quantitative yield by refluxing the acid with phosphorus pentachloride using toluene as a solvent. The pure acid chloride was crystallized from anhydrous benzene in the form of fine, yellow needles melting at 203.5° - 204°.

2. 7-Nitrofluorenone-4-carboxylic Acid Amide (III). On treating a suspension of 7-nitrofluorenone-4-carboxylic acid chloride in benzene with a stream of dry ammonia gas, the amide of 7-nitrofluorenone-4-carboxylic acid was formed. This crystallized from glacial acetic acid in bright yellow microscopic needles melting at 263.5° - 264°.

3. 7-Nitro-4-aminofluorenone (IV). Difficulties which caused very low yields were encountered in the form of troublesome by-products when an attempt was made to convert the amide of 7-nitrofluorenone-4-carboxylic acid to 7-nitro-4-amino-fluorenone by means of the Hofmann reaction. The nitroaminoketone recrystallized from pyridine in the form of deep scarlet micro needles melting at 293°.

4. 7-Nitro-4-acetylaminofluorenone (V). The monoacetyl derivative of 7-nitro-4-aminofluorenone proved interesting in that the color changed from deep scarlet micro needles for the amine to brilliant yellow spangles for the acetyl derivative. This compound on recrystallization from a solution of glacial acetic acid and acetic anhydride melted at 307° - 308° (36).



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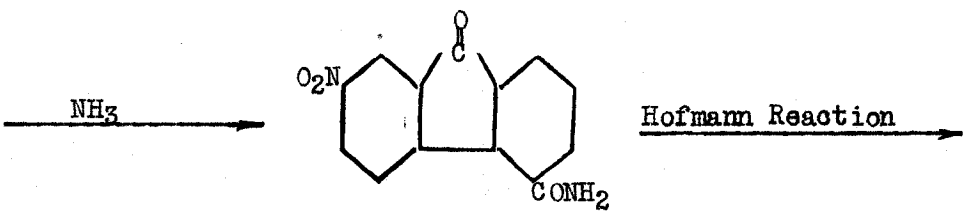
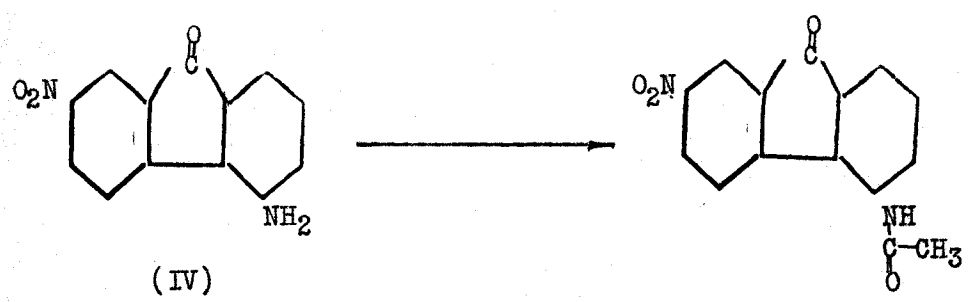


(III)



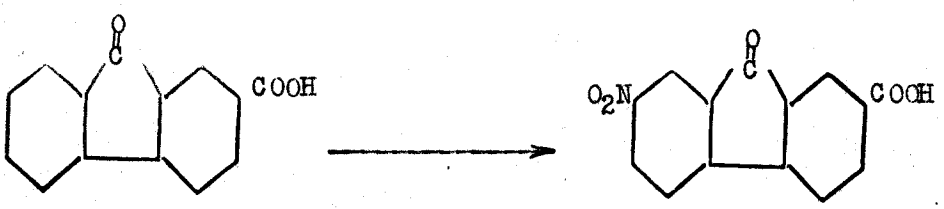
(IV) (V)

II

PROCEDURE AND DISCUSSION

A. Introduction

It will thus be seen that 7-nitrofluorenone-2-carboxylic acid is unknown. From the known orientation of the fluorene molecule it seemed probable that the direct nitration of fluorenone-2-carboxylic acid would result in substitution in the 7-position. Francis (37) in 1941, using two moles of sodium nitrate to each mole of fluorenone-2-carboxylic acid in a concentrated sulfuric acid solution obtained a yellow product which melted above 300° . It was the purpose of this investigation to determine the position of the nitro group.

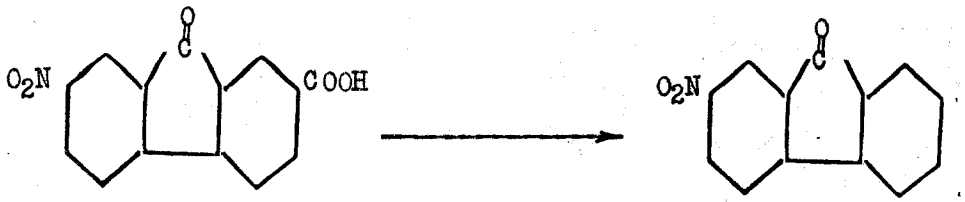


After many attempts, he finally obtained the acid chloride by fusing his nitrofluorenone-2-carboxylic acid with phosphorus pentachloride and distilling off the phosphorusoxychloride and excess phosphorus pentachloride under reduced pressure.

B. Attempted Decarboxylation of Nitrofluorenone-2-carboxylic Acid

The most logical course to pursue in order to determine the position of the nitro group would be to attempt to decarboxylate the nitro-

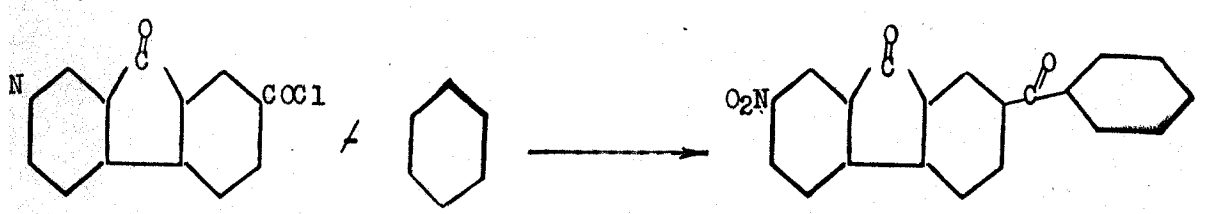
fluorenone-2-carboxylic acid. The decarboxylated product should be 2-nitrofluorenone (the 2- and 7-positions are identical) which is well-



known and could be easily identified. All attempts at decarboxylation led to decomposition products and in some cases actual explosions. If there were but one nitro group present, the explosion would be difficult to explain. (Later our nitrofluorenone-2-carboxylic acid was shown to be a complex consisting of one mole mononitro- and one mole dinitrofluorenone-2-carboxylic acid.)

C. Attempts to Prepare 7-Nitro-2-benzoylfluorenone

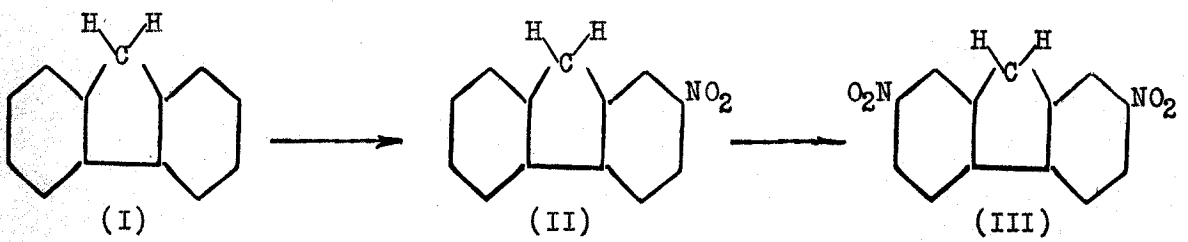
Since decarboxylation failed, an attempt to prove the position of the nitro group by preparing a derivative of the acid with a known compound was made. Dziewonski (38) had prepared 7-nitro-2-benzoylfluorenone. We had the acid chloride of our nitrofluorenone-2-carboxylic acid, which, if it would react with benzene by the Friedel-Craft reaction should give a nitro-2-benzoylfluorenone that could then be compared with an authentic



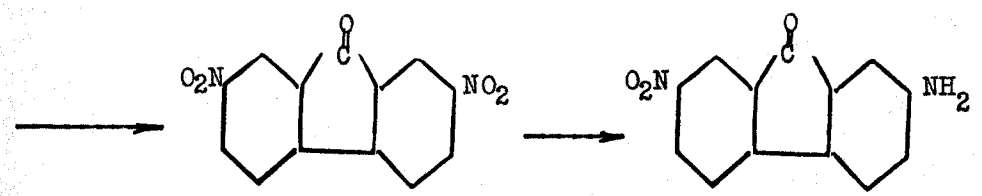
sample of the 7-nitro-2-benzoylfluorenone of Dziewonski. A number of attempts using various Friedel-Craft catalysts resulted in the recovery of unreacted acid chloride of nitrofluorenone-2-carboxylic acid.

D. Preparation of 7-Nitrofluorenone-2-carboxylic Acid

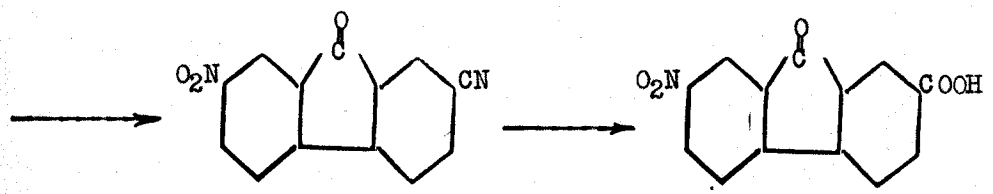
It was then decided to synthesize 7-nitrofluorenone-2-carboxylic acid (VII) from fluorene (I) by the following series of reactions, and compare this compound with our nitrofluorenone-2-carboxylic acid.



(I) (II) (III)



(IV) (V)



(VI) (VII)

We first prepared 2-nitrofluorene (II) from fluorene by the method given in Organic Synthesis (39). 2,7-Dinitrofluorene (III) was then prepared from 2-nitrofluorene by the method of Francis (37). The literature gives three different melting points for 2,7-dinitrofluorene: Morgan and Thomason (40) give the melting point as vigorous decomposition at 269°; Anantakrishnan and Hughes (41) state that their compound melted with vigorous decomposition at 295° - 300°; and Courtot (42) obtained a melting point of 334° after he had recrystallized his compound from nitrobenzene. Each time we prepared 2,7-dinitrofluorene, our product consistently melted at 269° in agreement with the melting point given by Morgan and Thomason. Repeated recrystallizations from acetic anhydride of a small sample, however, gave long, almost colorless, glistening needles melting sharply at 299°. This melting point is in agreement with that given by Anantakrishnan and Hughes (41).

Crude 2,7-dinitrofluorene was oxidized to 2,7-dinitrofluorenone (IV) with sodium dichromate, using a mixture of glacial acetic acid and acetic anhydride as a solvent. The product melted over a range 240° - 270° which was not in accordance with the melting point given by Anantakrishnan and Hughes (41). By fractional extraction we succeeded in separating our supposed 2,7-dinitrofluorenone into almost equal parts of 2,5-dinitrofluorenone melting at 239° and 2,7-dinitrofluorenone melting at 293°. When, however, our crude 2,7-dinitrofluorenone was completely dissolved in glacial acetic acid, the crystalline product which precipitated on cooling melted at 268°. From this it is evident that the separation of the 2,5- and 2,7-dinitro-isomers can best be accomplished by fractional extraction.

The reduction of the pure 2,7-dinitrofluorenone to 2-amino-7-nitrofluorenone (V) with ammonium sulfide resulted after two recrystallizations from monochlorbenzene in beautiful glistening black needles which melted at 281°- 282°. Eckert and Langecker (43) report a melting point of about 279° for 2-amino-7-nitrofluorenone.

2-Amino-7-nitrofluorenone was converted to the nitrile by the Sandmeyer reaction. It was difficult to extract the 2-cyano-7-nitrofluorenone from the reaction mixture. The final sublimation product was orange needles melting at 245° - 247°.

2-Cyano-7-nitrofluorenone (VI) was refluxed with a solution of five per cent potassium hydroxide in which the nitrile gradually dissolved, giving a red solution. The evolution of ammonia showed that hydrolysis was taking place. The refluxing continued for thirty-four hours. The 7-nitrofluorenone-2-carboxylic acid (VII) was precipitated from the alkaline solution with hydrochloric acid, and on sublimation gave an orange product melting at 210° - 213°.

E. Preparation of 2-Amino-?-nitrofluorenone

This indicated that 7-nitrofluorenone-2-carboxylic acid which melted at 210° - 213° was not the same compound as our nitrofluorenone-2-carboxylic acid which melted above 300°. As a further check, however, we decided to convert the amide of our nitrofluorenone-2-carboxylic acid to the amine by the Hofmann reaction and compare our resultant product with an authentic sample of 2-amino-7-nitrofluorenone.

The amide of nitrofluorenone-2-carboxylic acid was prepared by allowing dry ammonia gas to bubble into a solution of the acid chloride of nitrofluorenone-2-carboxylic acid. The amide on recrystallization from xylene melted at 322° - 324°. An analysis showed that this was a complex composed of equimolar amounts of the amide of nitro- and dinitrofluorenone-2-carboxylic acid. We hoped, however, that the Hofmann reaction would separate the complex into its components, but this did not happen, since the amine formed by the reaction, which melted sharply at 321°, analyzed for a complex of equimolar amounts of aminofluorenone and amino-nitrofluorenone. This is further proof that the nitro group of the nitrofluorenone-2-carboxylic acid prepared by the direct nitration of fluorenone-2-carboxylic acid is not in the 7-position as was originally supposed, because the melting point of an authentic sample of 2-amino-7-nitrofluorenone melts at 281° while the one made by the Hofmann reaction melts at 321 , and, too, the analysis of the amine made by the Hofmann reaction does not check with the theoretical analysis.

F. Preparation of (_)-Chlorofluorenone

As the nitrofluorenone-2-carboxylic acid was not 7-nitrofluorenone-2-carboxylic acid as we had supposed, we attempted to find out, if possible, the position of the nitro group by other means. This we proposed doing by reducing the nitro group of our acid and replacing the resultant amino group with a chlorine atom by the Sandmeyer reaction. The 1-, 2-, and 3-chlorofluorenones are known. The chlorofluorenone prepared from our acid, if the analysis checked with the theoretical,

could be compared with authentic samples of the three known chlorofluorenones. If it were not identical with one of the three known compounds, it would then be 4-chlorofluorenone.

Our crude nitrofluorenone-2-carboxylic acid was reduced with ammonium sulfide. A red crystalline product which gave positive tests for an amine and an acid but which did not melt, resulted. A nitrogen analysis showed this to be a mixture of an aminofluorenone-2-carboxylic acid and an amino-nitrofluorenone-2-carboxylic acid. As this mixture could not be separated the chloro derivative was prepared by the Sandmeyer reaction. On sublimation this gave beautiful pale yellow needles which melted at 296°, and was easily decarboxylated to a chlorofluorenone by adding copper carbonate to the fused acid. The decarboxylated product after two sublimations under reduced pressure melted at 146° - 147.5°. The carbon analysis of both these chloro-products indicated that they were complexes of equimolar chloro- and a chloro-nitrofluorenone-2-carboxylic acid and chloro- and a chloro-nitrofluorenone respectively.

The bromofluorenone-2-carboxylic acid was prepared in a manner similar to that by which the chlorofluorenone-2-carboxylic acid was prepared. A product consisting of pale yellow needles melting at 310° resulted. This was easily decarboxylated, giving a product melting at 165°. The yields of both these products were too small to permit analyses to be made.

G. Complex Compounds in the Fluorene Series

All of our analyses indicated that the derivatives of our nitrated fluorenone-2-carboxylic acid were complexes consisting of equimolar amounts of a mononitro- and a dinitro-compound. This phenomenon was at first difficult to understand. A search of the literature, however, showed that a number of instances occur where two different fluorene derivatives form a complex made up of equimolar amounts of the two which are difficult to separate.

In 1883, Hodgkinson and Matthews (44) reported the preparation of a dichlorofluorene melting at 128°. Sieglitz and Schatzkes (45) in 1921, found, on conversion to the dichlorofluorenone, that two compounds melting at 168° and 182° were obtained. This was confirmed by Courtot (46) in 1930, who at that time succeeded in separating this supposed dichlorofluorene into a monochlorofluorene and a dichlorofluorene by nitrating the complex. The monochlorofluorene was nitrated while the dichlorofluorene remained unchanged.

Gomberg and Bachmann (47) found on reducing fluorenone, that fluorenopinacol forms a molecular complex with fluorenone. When a mixture of colorless pinacol and yellow ketone was dissolved in a small amount of hot alcohol and the solution allowed to cool, large tan-colored crystals of the double compound crystallized from the solution, melting at 123°-124°. By treating the complex with sulfuric acid, the pinacol part of the complex was transformed to the pinacolone, the fluorenone remained unchanged by this procedure. The fluorenone was easily separ-

ated from the rather insoluble pinacolone by means of hot alcohol. The complex was thus found to contain one molecule of pinacol to one molecule of fluorenone.

Bachmann (48) reacted fluorenone with excess sodium which was hydrolyzed after thirteen days of shaking. When the crude product was recrystallized from alcohol two kinds of crystals were obtained; one was the known pinacol, the other was unknown and melted at 151°. This latter compound was found to be a complex produced by combination of fluorenol and fluorenopinacol. The proportions of each constituent in the complex were determined by treating the compound with a solution of sodium ethylate; under these conditions the pinacol was converted to a mixture of fluorenone and fluorenol. The mixture of ketone and hydrol was separated by recrystallization from benzene, from which the fluorenol crystallizes with benzene of crystallization. The weights of fluorenone and fluorenol obtained by this method indicated that the complex consists of one mole of pinacol to one mole of fluorenol. This result was confirmed by recrystallizing mixtures of different proportions of pinacol and fluorenol from benzene. From the mixture of two parts by weight (one mole) of pinacol to one part (one mole) of fluorenol, only the complex melting at 151° was obtained; the other proportions gave mixtures of the complex and one of the components.

Schlenk and Herzenstein (49) formed a complex between fluorenone and biphenylfluorenylcarbinol which crystallized from ligroin in beautiful, light yellow crystals melting at 123°. This complex also was very difficult to separate into its components. These investigators were

unable to determine the constitution of their complex because the analysis alone gave insufficient data to permit the elucidation of the structure.

Then, too, we succeeded in separating our supposed 2,7-dinitrofluorenone made from the 2,7-dinitrofluorene melting at 269° in agreement with the melting point reported for 2,7-dinitrofluorene by Morgan and Thomason (40) into equimolar amounts of 2,7- and 2,5-dinitrofluorenone, which proves that the supposed 2,7-dinitrofluorene reported by Morgan and Thomason is a complex of 2,5- and 2,7-dinitrofluorene.

III

EXPERIMENTAL

A. Purification of Fluorene

Two hundred grams of crude fluorene with 500 cc. glacial acetic acid and 30 g. charcoal (Darco) were boiled for 30 minutes under reflux in a liter, round bottom flask. This was then filtered through a hot water funnel into a liter erlenmeyer flask. It was allowed to stand for an hour and was then filtered. It was washed with two 100 cc. portions of alcohol. The yield was 150 g. The purified fluorene was white crystals melting at 113°.

B. Preparation of 2-Acetylfluorene

Eighty grams (0.48 mole) fluorene was placed in a three-neck, one-liter, round bottom flask equipped with a dropping funnel, mercury-sealed mechanical stirrer, and a reflux condenser connected to a hydrogen chloride trap. The fluorene was dissolved with stirring in 350 cc. dry carbon disulfide. To this solution was added 113 g. (0.85 mole) pure aluminum chloride and the mixture was stirred thoroughly until it became homogeneous. A dark red color developed. In the dropping funnel was placed 37.8 cc. (0.41 mole) pure, redistilled acetic anhydride. About 1 cc. of this was added drop by drop, until the reaction started. The further addition of acetic anhydride was adjusted to such a rate that the heat of reaction kept the carbon disulfide in gentle reflux. The addition required about 50 minutes. After the addition of about half the acetic anhydride a heavy precipitate of the addition product formed

which made stirring very difficult; however, stirring and refluxing on a water bath was continued for one hour. The heavy dark green mass was filtered on a large Buchner funnel and sucked as dry as possible. The product was removed from the funnel, placed in a beaker, just covered with carbon disulfide, stirred mechanically for 10 minutes and filtered again. The residue was then washed twice with 50 cc. portions of carbon disulfide. After all the carbon disulfide had been removed the addition product was hydrolyzed by adding it in portions to a stirred mixture of 800 cc. water and 30 cc. concentrated hydrochloric acid. Each portion was allowed to hydrolyze before adding more. The crude 2-acetylfluorene was filtered and washed several times with water. It weighed 108 g. and melted between 110° - 115°. The impure tan compound was purified by recrystallizing twice from alcohol, using Darco to remove the color. The melting point then was 132° which is the same as that given in the literature (50).

C. Preparation of Fluorenone-2-carboxylic Acid

The entire yield of 2-acetylfluorene (108 g.) was placed in a 5-liter round bottom flask equipped with a reflux condenser, a mechanical stirrer, and a cylinder to facilitate the addition of dichromate. Then 650 cc. glacial acetic acid was added and the acetylfluorene dissolved with heating. Four hundred fifty grams commercial sodium dichromate, ground to a coarse powder, was added in small portions to the hot acetic acid solution of 2-acetylfluorene. The reaction was very vigorous at first which indicated the oxidation of the methylene group, but it soon

moderated and the dichromate was then added at a faster rate, requiring about 45 minutes for complete addition. A dropping funnel was then fitted in the glass cylinder and 200 cc. acetic anhydride was dropped in over the course of 90 minutes, refluxing being continued all the while. The mixture was refluxed for 6 hours more. The hot contents of the flask were poured into about $2\frac{1}{2}$ gallons of hot water contained in a 4-gallon crock, stirred for 15 minutes and was filtered on a large Buchner funnel. All the chromium salts were washed out with water containing a little sulfuric acid, to prevent hydrolysis. The wet filter cake, including the paper, was transferred to a beaker containing 700 cc. of a five per cent solution of potassium hydroxide. The mixture was stirred mechanically, heated to 80° and filtered hot. The alkali insoluble material was washed with a little hot dilute potassium hydroxide. The filtrate was placed in a beaker, stirred with 15 g. Darco for 20 minutes and again filtered and refiltered to remove all the carbon. The solution of the potassium salt was heated with vigorous stirring to 70° and hydrochloric acid (1:1) was added drop by drop from a dropping funnel. The fluorenone-2-carboxylic acid was thrown down as a thick yellow mass. A slight excess of hydrochloric acid was added and the precipitate allowed to digest for 10 minutes with stirring. The acid was filtered hot and all the potassium chloride removed by several washings with hot water. After the acid was sucked as dry as possible it was dried in an oven at 150°. It was a bright yellow and weighed 32 g. It was recrystallized from acetic anhydride and melted with partial sublimation at 339° - 341° (copper block), which is the same melting point as that given in the literature (50).

D. Preparation of Nitrofluorenone-2-carboxylic Acid

Nitrofluorenone-2-carboxylic acid was prepared by the method of Francis (37). In a 400 cc. beaker, equipped with a mechanical stirrer and a thermometer, was placed 20 g. (0.089 mole) fluorenone-2-carboxylic acid and 16 g. (0.188 mole) powdered sodium nitrate. To this was added 100 cc. concentrated sulfuric acid, with stirring. The stirred mixture was heated on a sand bath to 54° at which temperature the solid materials dissolved. Heating was continued until a yellow precipitate resulted. The temperature was maintained between 88° - 92° for twenty minutes longer. The reaction mixture was allowed to cool slightly and was then poured into 500 cc. cold water and filtered. The nitrofluorenone-2-carboxylic acid was returned to the beaker and washed several times with water, with mechanical stirring. It was then filtered on a Buchner funnel, sucked free of water and then washed with alcohol and ether. The yield was 22 g. The melting point was 317° (copper block).

E. Attempted Decarboxylation of Nitrofluorenone-2-carboxylic Acid

A number of attempts to decarboxylate the nitrofluorenone-2-carboxylic acid were made, using as catalysts varying amounts of copper powder, copper carbonate, soda lime, and copper chromite in quinoline solution. Decomposition products resulted and in most cases the nitrofluorenone-2-carboxylic acid decomposed with an explosion. It was then decided that the nitro group present in the nucleus aided in the oxidation of the acid especially since ammonia was among the decomposition products recognized.

F. Preparation of Sodium Salt of Nitrofluorenone-2-carboxylic Acid

In a beaker fitted with a mechanical stirrer and a thermometer was placed 3.5 g. nitrofluorenone-2-carboxylic acid, 0.52 g. sodium hydroxide and 300 cc. water. The mixture was heated with stirring, until all dissolved, giving a red solution. This was filtered hot. The filtrate was allowed to cool. Then 75 cc. ninety-five per cent ethyl alcohol was added. The beaker was placed on an ice bath and the sodium salt precipitated with stirring. It was filtered and dried. A greenish yellow powder resulted, amounting to 2.5 g.

G. Attempted Decarboxylation of Sodium Salt of Nitrofluorenone-2-carboxylic Acid

Two and one-half grams of sodium salt of nitrofluorenone-2-carboxylic acid and 0.9 g. soda lime were well mixed and placed in an electrolytic beaker over which was placed an evaporating dish containing ice water. The mixture was heated slowly. Decomposition of the product resulted; it caught fire, the odor of ammonia was detected.

b) Three grams of the above mentioned sodium salt was well mixed in a mortar with 4 g. soda lime. A glass tube about 3/4 inch in diameter and 15 inches long was provided. The mixture was placed in one end of the tube which was then stoppered with glass wool. A stream of nitrogen was sent into the tube to dispel the oxygen present. It was then heated with a yellow flame. The contents in the tube caught fire; ammonia, water, and carbon were among the products recognized. It was then decided that the nitrofluorenone-2-carboxylic acid and its sodium salt

could not be decarboxylated so other methods for proving the structure of the acid had to be devised.

H. Preparation of the Acid Chloride of Nitrofluorenone-2-carboxylic Acid

The acid chloride of the nitrofluorenone-2-carboxylic acid was prepared by the method of Francis (37). Two grams (0.007 mole) of nitrofluorenone-2-carboxylic acid was placed in a short neck, round bottom flask arranged for vacuum distillation and 3 g. (0.014 mole) phosphorous pentachloride was added. The flask was well shaken in order to mix the two ingredients intimately. It was then placed on an oil bath and heated until the mixture began to undergo fusion (near 160°). The temperature was allowed to rise to 170° - 175° and was maintained within this range until complete fusion occurred. Suction was then applied and the phosphorous oxychloride and any excess phosphorous pentachloride distilled off. A dark red viscous liquid remained in the bottom of the flask which hardened on cooling. The flask was arranged for refluxing and the fusion mass was dissolved in 25 cc. dry benzene. A spatula full of Darco was added to the hot solution and the solution was refluxed for five minutes longer. The hot mixture was filtered and the filtrate was collected in a 50 cc. erlenmeyer flask. The orange-yellow solution was cooled and the acid chloride precipitated by the drop-wise addition of petroleum ether. The crystals melting at 157° were collected on a filter and washed with petroleum ether. The yield was about 1 g.

Anal. Calc'd $C_{14}H_6O_4NCl$: Cl, 12.34%
$C_{14}H_5O_6N_2Cl$: Cl, 10.67%
$C_{28}H_{11}O_{10}N_3Cl_2$: Cl, 11.45% Found: Cl, 11.99%, 12.09%

I. Attempted Preparation of Nitro-2-benzoylfluorenone

Since 7-nitro-2-benzoylfluorenone has been prepared by Dziewonski (38) by another method, it was thought that if the acid chloride of nitrofluorenone-2-carboxylic acid would react with benzene by the Friedel-Craft reaction, a comparison of the product formed by this reaction with an authentic sample of Dziewonski's 7-nitro-2-benzoylfluorenone would indicate whether the nitro group of the acid chloride were in the 7-position or not. Several attempts to prepare the nitro-2-benzoylfluorenone ended in failure.

a) One gram of the acid chloride of nitrofluorenone-2-carboxylic acid was dissolved in 25 cc. warm dry benzene and was placed in a dropping funnel. Two grams aluminum chloride was mixed with 25 cc. dry benzene in a small, three-neck round bottom flask equipped with a mechanical stirrer, condenser, and dropping funnel. The acid chloride-benzene solution was added dropwise to the aluminum chloride-benzene mixture. Heat was applied at intervals in order that hydrogen chloride might be continuously evolved. The solution turned red, then darker, and finally a black tarry substance precipitated. The benzene layer was decanted. The tarry material was placed in a beaker. About 150 cc. dilute hydrochloric acid was added and the addition product was broken up by stirring for about forty-five minutes. It was then filtered and washed; a brown powder resulted. This was dissolved in 150 cc. glacial acetic acid and refluxed for twenty minutes. It was filtered hot. The residue was a dark brown powder which melted with decomposition at 152°.

The filtrate was evaporated by distillation to about one-half its original volume. A brown precipitate filtered off. It was evaporated

almost to dryness, a brown substance resulted. These products together with the one mentioned above were impure unreacted acid chloride.

b) One gram acid chloride of nitrofluorenone-2-carboxylic acid was dissolved in 25 cc. warm dry benzene. One-half gram aluminum chloride was mixed with 20 cc. dry benzene in a flask, as mentioned above. The acid chloride solution was dropped into the flask over a period of 45 minutes with constant stirring. A dark tarry substance settled to the bottom of the flask. The flask was heated and the contents refluxed for half an hour on the water bath, until the evolution of hydrogen chloride ceased. The next day this was filtered, and the filtrate was allowed to evaporate. The precipitate which settled out of the filtrate on cooling melted at 155°, it was unreacted acid chloride. The residue was treated as in the above experiment with the same results.

c) In a 150 cc. beaker was mixed 0.5 g. acid chloride of nitrofluorenone-2-carboxylic acid and 0.14 g. aluminum chloride with about 10 cc. dry carbon disulfide. This was well stirred on a steam bath until the carbon disulfide had evaporated, then 2 cc. thiophene free dry benzene was added and the mixture well stirred. A reddish brown gummy product resulted. This was stirred into about 100 cc. dilute hydrochloric acid until it became powdery. It melted over a wide range. It was recrystallized from glacial acetic acid and then did not melt at 317°. It showed positive qualitative tests for nitrogen and chlorine. Hence it was most likely an addition product of the acid and aluminum chloride. According to Dziewonski (38) the 7-nitro-2-benzoylfluorenone melts at 198°.

d) Another method for the preparation of nitro-2-benzoylfluorenone was attempted using as a catalyst mercuric chloride-aluminum addition

product as prepared by Cummings, Hopper, and Wheeler (51). Twelve cubic centimeters of dry benzene and 12 g. mercuric chloride were treated gradually in a flask fitted with a reflux condenser with 0.5 g. aluminum powder, the flask was vigorously shaken during the addition. A green precipitate suddenly appeared. The reaction was continued for about 3/4 hour. An olive green precipitate remained in the flask after the benzene was filtered off. The mercury formed during the reaction (about $1\frac{1}{2}$ g.) was poured off the desired product.

About 1.5 g. of the Friedel-Craft catalyst prepared above was placed in a small three-neck round bottom flask, fitted with a condenser and stirrer. Fifteen cubic centimeters of dry carbon disulfide was added through the condenser; the misture was stirred vigorously while 1 g. acid chloride of nitrofluorenone-2-carboxylic acid was added bit by bit. This was stirred at room temperature for 3 hours. The color changed from olive green to a deep reddish orange. After the 3 hours, it was heated to 45° on a water bath and maintained at this temperature for 2 more hours, until the evolution of hydrogen chloride ceased. The mixture was a deep red orange. It did not change color during the last 2 hours. The contents of the flask was poured into 400 cc. cold water and stirred vigorously for a short time. It was then filtered and washed several times with cold water. A greenish yellow precipitate resulted whose melting point was: loosened at 160°, dark at 200°, red at 230°, did not melt at 280°. The precipitate was stirred with 75 cc. dilute hydrochloric acid, was filtered, and was washed with water. A yellow precipitate resulted, melting as follows: loosened at 160°, red viscous melt at 230°, no further change at 280°.

e) Twelve cubic centimeters of dry benzene and 12 g. mercuric chloride were shaken together in a small flask, 0.5 g. aluminum powder was added in small portions. A green precipitate resulted. This was freed from mercury and about 0.25 g. was placed in a small three-neck, round bottom flask, equipped with a stirrer and condenser. Ten cubic centimeters of carbon disulfide was added to act as a solvent, and 1 g. acid chloride of nitrofluorenone-2-carboxylic acid was added in small portions. The mixture was then stirred for $1\frac{1}{2}$ hours. The solution turned orange in color. It was heated to about 75° for about 2 hours. No reaction on litmus during this time. At the end of the 2 hours, the flask cracked and water from the water bath seeped in, so the reaction was stopped. The contents of the flask were poured into about 50 cc. dilute hydrochloric acid and stirred for 1/2 hour. This was then filtered and dried. The melting point ranged between 165°-180°. On recrystallization from glacial acetic acid, the product did not melt at 300°.

Since the attempts to prepare nitro-2-benzoylfluorenone from the acid chloride of nitro-fluorenone-2-carboxylic acid and benzene with various catalysts were unsuccessful, it was decided that the nitro group in the nucleus of the acid chloride acted as an inhibitor to the success of the Friedel-Craft reaction.

J. Preparation of Methyl Ester of Nitrofluorenone-2-carboxylic Acid

One gram of the acid chloride of nitrofluorenone-2-carboxylic acid was refluxed in 10 cc. dry redistilled methyl alcohol for two hours. Some of the acid chloride went into solution. It was filtered and the

filtrate was allowed to cool. A pale yellow precipitate resulted melting at 179°-180°. On recrystallization from alcohol, the melting point was 181°-182°. An analysis of this compound showed it to be a complex consisting of one mole of methyl ester of nitrofluorenone-2-carboxylic acid and one mole of methyl ester of dinitrofluorenone-2-carboxylic acid.

Anal. Calc'd $C_{15}H_9O_5N$: N, 4.94%
$C_{15}H_8O_7N_2$: N, 8.53%
$C_{30}H_{17}O_{12}N_3$: N, 6.87% Found: N, 7.37%

K. Preparation of 7-Nitrofluorenone-2-carboxylic Acid

It was then decided to synthesize 7-nitrofluorenone-2-carboxylic acid by a method which would leave no doubt as to its structure.

1. Preparation of 2-Nitrofluorene. 2-Nitrofluorene was prepared by the method given in Organic Synthesis (39). Sixty grams (0.36 mole) fluorene was dissolved in 500 cc. warm glacial acetic acid in a liter three-neck round bottom flask fitted with a thermometer, a mechanical stirrer, and a dropping funnel, and supported in a water bath. The temperature was brought up to 50°, and 80 cc. (1.3 mole) concentrated nitric acid was added with stirring in the course of fifteen minutes. During the addition of the nitric acid, the solution became slightly yellow and a small amount of material precipitated. The water bath was slowly brought to a temperature of 60°-65°, the precipitate then dissolved and the color of the solution deepened. Stirring was continued and heat applied continuously until the temperature reached 80°. After 5 minutes the water bath was removed and the mixture which consisted of a semi-solid paste of fine yellow needles was allowed to

cool to room temperature. This took about 2 hours. The product was collected on a Buchner funnel, sucked as dry as possible, and washed with two 25 cc. portions of cold glacial acetic acid containing 0.5 g. potassium acetate. It was then washed five times with water and dried. The 2-nitrofluorene thus obtained melted at 155° and weighed 55 g. Organic Synthesis gives the melting point 155°-156° (39). This procedure was repeated six times, giving a total of 323 g. 2-nitrofluorene.

2. Preparation of 2,7-Dinitrofluorene. 2,7-Dinitrofluorene was prepared from 2-nitrofluorene by the method of Francis (37). In a liter three-neck round bottom flask equipped with a thermometer, mechanical stirrer, and powder funnel was placed a mixture of 300 cc. glacial acetic acid and 300 cc. fuming nitric acid. During an hour's time 60 g. 2-nitrofluorene. At no time during the reaction was the temperature permitted to go above 30°. After the last addition of the nitrofluorene, the mixture was permitted to continue stirring for about 1/2 hour. At the end of this time it was filtered through a sintered glass funnel, washed with glacial acetic acid and with water. When dried it gave a yield of 65 g. melting at 269° which agrees with the melting point given by Morgan and Thomason (40) for their supposed 2,7-dinitrofluorene. Four runs of this reaction were made giving a total yield of 250 g.

A small amount of this, however, on repeated recrystallizations from acetic anhydride, gave long, almost colorless, glistening needles melting at 299°. This melting point is in agreement with that given by Anantakrishnan and Hughes (41) for 2,7-dinitrofluorene namely 295°-300°.

The "2,7-dinitrofluorene" which melted at 269° in agreement with the melting point of Morgan and Thomason was separated on oxidation into equimolar quantities of 2,5-dinitrofluorenone and 2,7-dinitrofluorenone.

3. Preparation of 2,7-Dinitrofluorenone. Crude 2,7-dinitrofluorene was oxidized according to the method of Francis (37). Twelve hundred cubic centimeters of glacial acetic acid and 400 cc. acetic anhydride were mixed in a 500 cc. round bottom short-neck flask equipped with a mechanical stirrer, condenser, and dropping funnel. Twenty-four grams of 2,7-dinitrofluorene was completely dissolved in the mixture with stirring and refluxing. Eighty-four grams of sodium dichromate dissolved in 300 cc. glacial acetic acid was slowly added to the refluxing mixture over a period of 1/2 hour. The reaction became vigorous. The reaction mixture was kept hot and stirring was continued for 2 hours, whence the entire mixture was poured into 3 liters of hot water. It was filtered and washed with water containing a little sulfuric acid until all the chromium salts were removed. The yield was 25 g. It melted over a range 240° - 270°. Six runs of the above preparation were made giving a total yield of 143 g. As the melting point range did not agree with any given in the literature (41), the product was purified further.

4. Separation of 2,5- and 2,7-Dinitrofluorenone. a) About 15 g. of the 2,7-dinitrofluorenone prepared above was partly dissolved in 500 cc. xylene and filtered hot. About 5 g. of a rather dark product crystallized melting from 270°-295°. This was recrystallized about three times from the same solvent, each time the melting point range became less. It was boiled with Darco which removed some of the dark color.

Finally it was dissolved and refluxed in some fresh xylene. Five grams of a yellow product crystallized out which melted sharply at 293°. This agrees with the melting point for 2,7-dinitrofluorenone reported in the literature (41).

The original filtrate was distilled down to about 100 cc. On standing overnight a precipitate was in the distilling flask. This was filtered and recrystallized from 250 cc. xylene. The precipitate on drying melted at 239° and amounted to 5 g. This agrees with the literature's melting point (241°) for 2,5-dinitrofluorenone. (41)

b) Fifty grams of the impure 2,7-dinitrofluorenone was placed in a beaker and 310 cc. acetic anhydride was added. This was allowed to reflux (a large round bottom flask containing cold water was placed over the beaker to act as a condenser) for about 15 minutes; partial solution occurred. The solution was filtered hot. The filtrate was allowed to cool and crystallize. The crystals formed were filtered and dried after which they weighed 20 g. and melted at 220° - 240°. This was an impure product of 2,5-dinitrofluorenone. The original residue was dissolved in 500 cc. acetic anhydride and allowed to reflux after the addition of Darco for fifteen minutes. The solution after filtering off the carbon was a very light yellow. This was set aside to crystallize. After filtering and drying, the product weighed 19 g. and melted at 293°. This was recrystallized from 550 cc. acetic anhydride and refluxed strongly for 10 minutes. It was then set aside to cool slowly. Fine needles with high refractive power precipitated. These were filtered and washed several times with water. Seventeen grams of golden yellow glistening needles melting at 293° - 294° resulted. This separation process was

repeated several times as mentioned above and each time about an equal amount of the 2,5-dinitro and the 2,7-dinitrofluorenone was obtained. Evidently the "2,7-dinitrofluorene" melting at 269° obtained by Morgan and Thomason (40) is a complex made up of equimolar quantities of 2,5-dinitro- and 2,7-dinitrofluorene. This is not unheard of in fluorene chemistry, as is mentioned earlier in the discussion. The 2,7-dinitrofluorenone did not dissolve in hot "cellosolve" nor in hot benzene.

c) Five grams of 2,7-dinitrofluorenone was placed in a beaker and glacial acetic acid was added in amounts of 100 cc. at a time until all dissolved. This happened when 300 cc. acetic acid had been added. It was allowed to reflux for ten minutes and then was set aside to crystallize. Three grams of a product melting at 268° resulted. From this it is evident that in order to secure a separation of the 2,5- and 2,7-dinitro- isomers, fractional extraction must be resorted to.

5. Preparation of 2-Amino-7-nitrofluorenone. Twenty grams of the purified 2,7-dinitrofluorenone, 1200 cc. ninety-five percent alcohol, and 135 cc. concentrated ammonium hydroxide were placed in a 2-liter three-neck round bottom flask equipped with a condenser and mechanical stirrer. The solution was kept below the boiling point most of the time and a stream of hydrogen sulfide was bubbled into the mixture. The mixture turned red, then darker, and finally a precipitate which shone like gilt paint began to appear. The reaction was carried on for $4\frac{1}{2}$ hours. It was then cooled to 20° after having added 167 cc. water. It was filtered and washed with alcohol and water. The residue was a dark brown product weighing 17 g. This was washed in 175 cc. alcohol, filtered and washed twice with 25 cc. alcohol. It was then dried after which it melted at

261° - 266°. About 1/2 g. of this was dissolved in 50 cc. monochlorbenzene. A red solution resulted from which shiny black needles crystallized which melted at 275°. On recrystallization from the same solvent the melting point was 281° - 282°. This is in agreement with the melting point, near 279°, reported by Eckert and Langecker. (43)

6. Preparation of 2-Cyano-7-nitrofluorenone. 2-Cyano-7-nitrofluorenone was prepared by the Sandmeyer reaction, as follows:

a) Preparation of Cuprous Chloride. Cuprous chloride was prepared from 21 g. crystallized copper sulfate and 4.9 g. sodium chloride dissolved in 68 cc. hot water in a round bottom flask. The flask was well-shaken during a period of ten minutes while a solution of sodium sulfite (4.2 g. sodium bisulfite and 2.8 g. sodium hydroxide in 32 cc. water) was slowly added. This was cooled to room temperature and washed several times with water by decantation.

b) Preparation of Cuprous Cyanide. A liter beaker containing 96 cc. water was fitted with a mechanical stirrer. The cuprous chloride was added and to this stirring mixture 13 g. sodium cyanide dissolved in 19 cc. water was added. The cuprous chloride went into solution with the evolution of heat. This was cooled in an ice bath to 0° - 5°.

c) Diazotization of 2-Amino-7-nitrofluorenone. Fourteen grams of 2-amino-7-nitrofluorenone was mixed in a 400 cc. beaker with 17 cc. concentrated hydrochloric acid and enough cracked ice was added from time to time to keep the temperature at 0° - 5°. A solution of 4.2 g. sodium nitrite in 15 cc. water was added through a dropping funnel with stirring over a period of fifteen minutes. The mixture became reddish brown and

thick and pasty, on the addition of more ice and vigorous stirring the viscosity became less. It was tested from time to time with alkaline beta-naphthol and for the end of the reaction with starch-iodide paper. It was neutralized with sodium carbonate.

d) Preparation of Nitrile. To the cold cuprous cyanide solution was added 20 cc. toluene. The diazonium mixture was slowly added over a period of 1/2 hour with continued mechanical stirring. It was stirred for another half hour at the cold temperature. At this time it gave a negative test for diazonium compound with beta-naphthol. It was then allowed to reach room temperature with constant stirring. Over night the color of the mixture changed to dark brown. The next day it was heated to 50° and was stirred at this temperature for 2½ hours. Then it was placed in a water bath and heated under reflux for 7½ hours. The volume swelled and nitrogen was evolved. The crude yield was 19 g. It was a dirt brown powder which did not melt.

7. Purification of 2-Cyano-7-nitrofluorenone. Eleven grams of the impure 2-cyano-7-nitrofluorenone was placed in a Soxhlet extractor and extracted with 100 cc. cellosolve for sixteen hours. The precipitate which settled out in the flask on cooling was recrystallized from alcohol and melted at 200°-205°. The remainder was extracted further from 100 cc. butyl cellosolve for fifteen hours. In all about 2 g. was extracted. This was recrystallized twice from butyl cellosolve and then sublimed. The sublimation product was orange needles melting at 245° - 247°.

Anal. Calc'd $C_{14}H_6O_3N_2$: N, 11.20% Found: N, 11.21%

8. Hydrolysis of 2-Cyano-7-nitrofluorenone. Eight grams of the impure 2-cyano-7-nitrofluorenone was placed in a round bottom flask and refluxed with 150 cc. five per cent potassium hydroxide for twelve hours at which time the evolution of ammonia ceased. It was filtered and the filtrate was boiled in Darco for 10 minutes and was again filtered. The resulting filtrate smelled so strongly of ammonia that it was placed in the flask together with the undissolved nitrile and refluxed for twenty-two hours longer at which time the evolution of ammonia had ceased about one hour before the refluxing was stopped. This was filtered. All the nitrile had dissolved. The filtrate was boiled in Darco and again filtered. This filtrate was a dark red. It was treated with 1:1 hydrochloric acid, whereupon a hard-to-filter red precipitate appeared. This was digested for about 1/2 hour, but this did not seem to aid the filtration. The product was then centrifuged, this was much faster than filtering, and the precipitate was then recrystallized from acetic anhydride. A yellow substance resulted melting at 200° - 205°. On sublimation this yielded an orange colored product melting at 210° - 213°. The yield of the 7-nitrofluorenone-2-carboxylic acid was small.

L. Preparation of Acid Amide of Nitrofluorenone-2-carboxylic Acid

Two grams of acid chloride of nitrofluorenone-2-carboxylic acid was dissolved in 80 cc. hot dry benzene. Dry ammonia was allowed to bubble in for ten minutes whereupon a mustard colored precipitate appeared. The excess ammonia was driven off by heating. The product was then filtered and recrystallized from xylene. It melted at 322° - 324°.

Anal. Calc'd $C_{14}H_8O_4N_2$: N, 10.44%
$C_{14}H_7O_6N_3$: N, 13.41%
$C_{28}H_{15}O_{10}N_5$: N, 12.05% Found: N, 12.41%

M. Preparation of 2-Amino-(_)-nitrofluorenone.

Two grams of nitrofluorenone-2-carboxylic acid amide was mixed in 50 cc. water. One cc. bromine was dissolved in 25 cc. water at 0°. To this was added a solution of 7.5 g. potassium hydroxide in 50 cc. water. A pale yellow solution resulted when the potassium hydroxide dissolved in the bromine water. The temperature was kept at 0° - 5°. The acid amide suspension was added at the same temperature; all went into solution, forming a red solution. This was allowed to stand for several hours after which it was filtered and the filtrate was refluxed for 1½ hours on a water bath. It was then filtered, leaving a black residue. This did not melt. It was dissolved in monochlorbenzene, giving a red solution. It was filtered, as the filtrate cooled brownish red crystals appeared which melted sharply at 321°. This product diazotized, hence it was an amine. This melting point does not conform with that of 2-amino-7-nitrofluorenone which melts at 281° - 282°.

Anal. Calc'd. $C_{13}H_8O_3N_2$: N, 11.66%
$C_{13}H_7O_5N_3$: N, 14.73%
$C_{26}H_{15}O_8N_5$: N, 13.33% Found: N, 13.35%

N. Preparation of Chlorofluorenone

Chlorofluorenone was prepared by the decarboxylation of chlorofluorenone-2-carboxylic acid which was obtained by the Sandmeyer reaction from aminofluorenone-2-carboxylic acid.

1. Preparation of Aminofluorenone-2-carboxylic Acid. Twelve hundred cubic centimeters of ninety-five per cent alcohol was placed in a three-neck flask arranged in a manner similar to the previously reported reduction, 20 g. nitrofluorenone-2-carboxylic acid and 150 cc. concentrated ammonium hydroxide were added whereupon an amber solution appeared. Hydrogen sulfide was bubbled in and heat was applied until a steady reflux began. The entire condenser was white with ammonium polysulfide and some free sulfur. After 2 hours of heating the solution was permitted to reach room temperature with stirring and bubbling in of hydrogen sulfide for another hour. Almost immediately on the introduction of hydrogen sulfide the solution became red, but it took some time before it all went into solution. At the end of the 3-hour reduction period the reaction was stopped. One-hundred seventy cubic centimeters of water was added to the flask and the solution was allowed to reach a temperature of 20° in an ice bath. It was poured into a liter beaker and 250 cc. 1:1 hydrochloric acid was added, whereupon a cherry red suspension appeared, giving an almost white precipitate. This was filtered and on washing with water it turned gray. It weighed $9\frac{1}{2}$ g. It gave a blue flame when heated and gave off sulfur dioxide fumes. Call this precipitate A.

In the filtrate a new precipitate appeared, red and glimmering, like the precipitate in the previously prepared amine. This was filtered and washed with alcohol. It weighed $6\frac{1}{2}$ g. On drying it was tiny red needles which did not melt. Call this precipitate B.

The precipitate A was dissolved in carbon disulfide and filtered, a red precipitate which did not melt was taken off and placed with precipitate B. The filtrate of carbon disulfide on evaporation gave 7 g. sulfur.

The filtrate resulting from precipitate B was evaporated by distillation. A white crystalline material distilled over melting at 119°-124°. This proved to be sulfur. The residue in the distilling flask gave a red precipitate C which did not melt. This weighed 6 g. It was only slightly soluble in alcohol and in nitro-benzene. That which did not dissolve in either of these two solvents, precipitate D, was a brownish red material weighing 4 g. It also did not melt. This proved to be an acid, i. e. it dissolved in sodium hydroxide and reprecipitated on the addition of dilute hydrochloric acid.

Five grams of precipitate B was placed in a refluxing flask with 18 cc. concentrated hydrochloric acid and about 150 cc. water and refluxed for six hours. Then the mixture was steam-distilled, a white substance which proved to be sulfur distilled over. The red precipitate B which did not go into solution with this treatment proved to be an acid. Some of the original precipitate B was tested for completed reduction to the amine; it failed to react with acidic zinc and tin.

2. Purification of Aminofluorenone-2-carboxylic Acid.

a) Purification of Precipitate D. Four grams of precipitate D was placed in an erlenmeyer flask to which was added 1 g. potassium hydroxide in 15 cc. water. Precipitate D went into solution. About 50 cc. more water was added and the solution was boiled in Darco and filtered. The acid was precipitated by the slow addition of 1:1 hydrochloric acid. A brittle, unmelting brownish-red acid resulted which weighed 2½ g. Half of this was boiled several times with alcohol and filtered. The red resulting residue was placed in a vacuum desiccator to dry for analysis.

Anal. Found: N, 8.04% 8.18%

b) Purification of Precipitate B. After the steam distillation, a part of the remaining precipitate B was refluxed several times in alcohol. That which did not dissolve after three attempts and using 800 cc. alcohol was dried in a vacuum desiccator for analysis.

Anal. Found: N, 8.00%

From the analyses it was concluded that the precipitates B and D were the same substance. Calculations showed that the aminofluorenone-2-carboxylic acid is a mixture of an aminofluorenone-2-carboxylic acid and an aminonitrofluorenone-2-carboxylic acid.

Anal. Calc'd $C_{14}H_9O_3N$: N, 5.85%
$C_{14}H_8O_5N_2$: N, 9.85%
$C_{28}H_{17}O_8N_3$: N, 8.03% Found: N, 8.00%, 8.04%, 8.18%

3. Preparation of Hydrochloride of Aminofluorenone-2-Carboxylic Acid. One gram of the steam distilled residue B was dissolved in 500 cc. hydrochloric acid and evaporated to dryness under reduced pressure. After washing several times with absolute alcohol it was brown and did not melt. It was dried in a vacuum desiccator for analysis. It, too, proved to be a mixture of equimolar amounts of the hydrochloride of aminofluorenone-2-carboxylic acid and of aminonitrofluorenone-2-carboxylic acid.

Anal. Calc'd $C_{28}H_{19}O_8N_3Cl_2$: N, 7.01% Found: N, 7.62%

4. Preparation of Chlorofluorenone-2-carboxylic Acid. Chlorofluorenone-2-carboxylic acid was prepared from aminofluorenone-2-carboxylic acid by the Sandmeyer reaction.

a) Preparation of Cuprous Chloride. One and five tenths grams of copper sulfate and 0.4 g. sodium chloride were dissolved in 5 cc. hot water. A solution of 0.3 g. sodium bisulfite and 0.2 g. sodium hydroxide

in 2 cc. water was slowly added to the first solution. Cuprous chloride precipitated. This was washed several times with water by decantation.

b) Preparation of Diazonium Compound. One gram aminofluorenone-2-carboxylic acid was mixed with 3 cc. concentrated hydrochloric acid and 10 cc. water. The temperature was kept at 10° - 15°. To this was added a solution of 0.35 g. sodium nitrite in 10 cc. water, through a dropping funnel. Stirring continued for 10 minutes after the last addition of sodium nitrite. Excess nitrous acid was removed with urea. The mixture was filtered, giving a red solution.

c) Preparation of Chlorofluorenone-2-carboxylic Acid. The cuprous chloride was added to 30 cc. 6 N hydrochloric acid and heated to boiling. All dissolved. The diazonium filtrate was added slowly with stirring. A yellow precipitate resulted. It was kept hot for five minutes in order to coagulate the precipitate and to allow the nitrogen to escape. It was filtered after standing for several hours, washed with water and dried. The chlorofluorenone-2-carboxylic acid melted at 286° - 290°. On sublimation this gave beautiful pale yellow needles melting at 296°.

Anal.	Calc'd	$C_{14}H_7O_3Cl$:	C, 64.90%	H, 2.70%
		$C_{14}H_6O_5Cl\ N$:	C, 55.35%	H, 1.97%
		$C_{28}H_{13}O_8Cl_2N$:	C, 59.78%	H, 2.31%
		Found:	C, 59.33%	H, 2.35%

5. Decarboxylation of Chlorofluorenone-2-carboxylic Acid. A small part of the chlorofluorenone-2-carboxylic acid was placed in a test tube fitted with a cold finger. This was heated to melting and a small bit of copper carbonate was placed on top of the fused compound. Small yellow needles sublimed on the cold finger, melting at 132° - 134°. On resublima-

tion this compound melted at 146° - 147.5°. This compound, too, analyzed as a mixture of equimolar amounts of chlorofluorenone and a chloronitrofluorenone.

Anal.	Calc'd	$C_{13}H_7OCl$:	C, 72.72%	H, 3.43%
		$C_{13}H_6O_3ClN$:	C, 60.11%	H, 2.31%
		$C_{26}H_{13}O_4Cl_2N$:	C, 65.82%	H, 2.74%
		Found:	C, 66.56%	H, 2.18%

O. Preparation of Bromofluorenone

Bromofluorenone was prepared in a manner similar to that by which the chlorofluorenone complex was prepared.

1. Preparation of Bromofluorenone-2-carboxylic Acid. Bromofluorenone-2-carboxylic acid was also prepared by the Sandmeyer reaction.

a) Preparation of Cuprous Bromide. One and one-half grams of copper sulfate and 0.6 g. sodium bromide were placed in a small round bottom flask to which 5 cc. hot water was added. The flask was shaken until all dissolved. To this was added slowly with shaking a solution of 0.3 g. sodium bisulfite and 0.2 g. sodium hydroxide in 2 cc. water. The cuprous bromide was cooled to room temperature and washed by decantation.

b) Preparation of Diazonium Compound. One gram aminofluorenone-2-carboxylic acid was mixed with 5.13 cc. hydrobromic acid (48%) and 10 cc. water, keeping the temperature at 10° - 15°. To this was slowly added a solution of 0.35 g. sodium nitrite in 10 cc. water. Stirring was continued for 10 minutes after the addition of the last of the sodium nitrite solution. Excess nitrous acid was removed with urea. The diazonium compound was filtered, giving a light yellow solution,

c) Preparation of the Bromofluorenone-2-carboxylic Acid. The cuprous bromide was added to 50 cc. forty-eight per cent hydrobromic acid. It all went into a dark solution. This was heated to boiling. The diazonium solution was slowly added through a dropping funnel to the stirred hot solution. A yellow precipitate resulted. This was digested for five minutes until nitrogen was no longer evolved and then allowed to stand for two hours. It was filtered and gave a brown residue. On sublimation, yellow needles melting at 310° resulted. The yield was too small to permit an analysis to be made.

2. Decarboxylation of Bromofluorenone-2-carboxylic Acid. The bromofluorenone-2-carboxylic acid prepared above was decarboxylated with copper carbonate in the same manner as was the chlorofluorenone-2-carboxylic acid. On sublimation yellow needles resulted, melting at 160°-165°. The yield in this case, too, was too small to permit an analysis to be made.

IV

SUMMARY

We have succeeded in synthesizing 7-nitrofluorenone-2-carboxylic acid by reactions that leave no doubt as to its constitution.

Investigation of the product obtained by Francis (37) from the nitration of fluorenone-2-carboxylic acid showed it to be a complex of equimolar amounts of a mononitro- and a dinitrofluorenone-2-carboxylic acid, which persisted as a complex in a number of its derivatives.

The 2,7-dinitrofluorene melting at 269° of Morgan and Thomason (40) has been shown to be a mixture of equimolar amounts of 2,5- and 2,7-dinitrofluorene.

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