THE CHEMISTRY OF FLUORENE AND ITS DERIVATIVES[1]

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Received July 16, 1937

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[1] This paper is based on a thesis submitted by George Rieveschl, Jr., to the Faculty of the College of Liberal Arts of the University of Cincinnati in partial fulfillment of the requirements for the B. A. degree with High Honors in Chemistry, June, 1937.

The thesis was awarded the Henry Hochstetter Prize on nomination by the Cincinnati Section of the American Chemical Society for the best senior thesis in Chemistry or Chemical Engineering.

I. INTRODUCTION

The hydrocarbon fluorene has been known for seventy years, yet the amount of investigation that has been devoted to it is small in comparison with that devoted to other hydrocarbons such as anthracene or phenanthrene. In the case of fluorene there has been no sudden stimulus to intense research such as the celebrated alizarin synthesis gave to the study of anthracene. The chemistry of phenanthrene is at this moment undergoing the same phenomenal development, because the chemistry of such biologically significant compounds as sex hormones, carcinogenic substances, and the sterols is basically the chemistry of phenanthrene. Although investigation in the fluorene field has progressed at a relatively slow rate, the result has been a significant amount of literature which is indeed both varied and substantial.

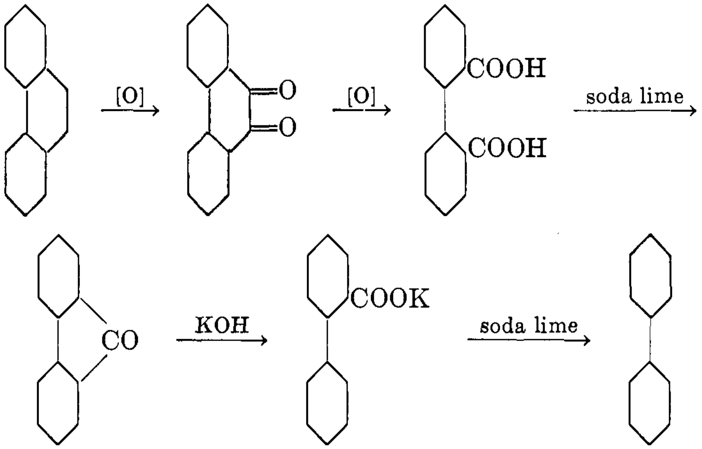
As far as we have been able to determine A. E. Everest's (91) book, published in 1927, contains the only general survey of the chemistry of fluorene. In view of the important developments which have occurred in the last ten years we have attempted to present here a comprehensive and critical discussion of the present knowledge of fluorene and its compounds. Some emphasis has been placed upon general methods of synthesis and cases of practical applicability. In addition, we have endeavored to make suggestions for future research.

II. THE DISCOVERY OF FLUORENE AND THE ELUCIDATION OF ITS STRUCTURE

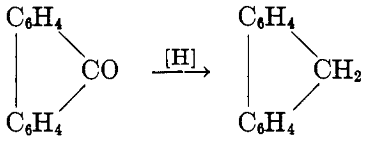
The chemistry of fluorene begins at a comparatively early date in the history of organic chemistry. During his memorable researches on the pyrogenetic hydrocarbons at the Collège de France in 1867, Marcellin Berthelot (29) isolated a new substance from the fraction of crude anthracene oil boiling between 300° and 310°C. He recrystallized the vividly fluorescent material from boiling alcohol and obtained white fluorescent laminae, which melted at 113°C. Berthelot was so impressed by the beautiful fluorescence, more pronounced than that of anthracene, that he gave the substance the name "Fluorène." He also identified fluorene as a product from the decomposition of retene. He described its odor as being "insipid, sweetish, and at the same time distressing to breathe." Berthelot established the difference between fluorene and all other hydrocarbons known at that time by an examination of the physical properties and an elementary analysis, the results of which he reported as follows: carbon, 93.5–94.0 per cent; hydrogen, 6.2–6.5 per cent.[2]

The discovery of phenanthrene in 1872 by Fittig and Ostermayer (102) and independently in the same year by Graebe (125) played an important part in the prompt elucidation of the constitution of fluorene.

Fittig and Ostermayer (103) in their investigation of phenanthrene carried out the degradation shown below, leading to the known biphenyl.



The compound resulting from the action of soda lime on the then unknown diphenic acid was rightly interpreted as being biphenylene ketone. Later they also obtained biphenylene ketone from phenanthraquinone by treatment with aqueous potassium hydroxide; they reported a melting point of 83.5–84.0°C. Fittig (99) distilled the biphenylene ketone with zinc dust and found that it was reduced to a substance crystallizing in white plates and melting at 113–114°C. He regarded this compound as biphenylenemethane, as shown below.



$$\left.\begin{array}{l}C_6H_4\\ |\\ C_6H_4\end{array}\right\rangle CO \xrightarrow{[H]} \left.\begin{array}{l}C_6H_4\\ |\\ C_6H_4\end{array}\right\rangle CH_2$$

Graebe (126), using the biphenylene ketone of Fittig, carried out the reduction with red phosphorus and hydriodic acid and obtained the same hydrocarbon.

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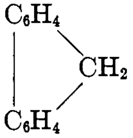
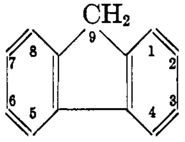
[2] A calculation of carbon and hydrogen from the formula $C_{13}H_{10}$ gives 93.9 per cent carbon and 6.1 per cent hydrogen.

Barbier (13), who had intensively investigated fluorene, observed that the compound obtained by the oxidation of fluorene with potassium dichromate and sulfuric acid was identical with the biphenylene ketone of Fittig and Ostermayer. Later Barbier (15) improved Berthelot's method of isolation of fluorene from coal tar and succeeded in obtaining large quantities of it. His analyses showed that it could be represented by the formula $C_{13}H_{10}$. He regarded fluorene as "biphenyl in which two atoms of hydrogen are replaced by an equal volume of methylene," for on treating fluorene with red-hot lime he obtained biphenyl. It can be easily seen from the work of Barbier that he was relatively certain of the structure of fluorene.

In 1878 Fittig and Schmitz (104) reported that the biphenylenemethane previously obtained by Fittig from biphenylene ketone was identical with fluorene obtained by Berthelot and Barbier. They prepared the picrate and the dibromo derivative from their own biphenylenemethane and found that these compounds were identical with those prepared by Barbier from fluorene isolated from coal tar. The structural formula could then be represented with certainty as[3]



or



Barbier in his experiments purified fluorene by preparing the picrate and then adding ammonia. The resulting fluorene melted at 113°C. and possessed the beautiful violet fluorescence which so impressed Berthelot. However, in 1883 Hodgkinson and Matthews (143) showed that the fluorescence was due to the presence of some impurity which was removed by recrystallization from glacial acetic acid or by sublimation over potassium carbonate. The fluorescence is thought to be due to the presence of rubene derivatives.

III. FLUORENE AND FLUORENONE

Fluorene when pure is a dazzling white substance crystallizing in flakes from alcohol. It is fairly soluble in hot alcohol, more so in acetic acid, carbon disulfide, ether, and benzene, and insoluble in water. DeCarli (65) determined the solubility of fluorene in liquid sulfur dioxide (24 g. per 100 g. of sulfur dioxide) and also in liquid ammonia, in which it was practically insoluble. Glacial acetic acid (143) was found to be one of the best solvents for fluorene and its derivatives.

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[3] The system of numbering shown has been adopted internationally.

Various investigators have reported slightly different melting points for fluorene. Mortimer and Murphy (211), after careful purification, gave the melting point as 114.2°C. By recrystallization from hot glacial acetic acid we have obtained samples which consistently melt at 113–114°C. Carnelly (38) reported an isomeric form of fluorene melting at 118°C. The boiling point is 298°C. (211). Mortimer and Murphy have also determined the vapor pressure at various temperatures (table 1). The density of fluorene, $d_{4^\circ}^{17.9^\circ}$, is 0.91648 (43).

Vanscheidt (322) described a colorimetric test for hydrocarbons containing the group $(C{=}C)_2CH_2$, such as exists in cyclopentadiene, indene, and fluorene. These compounds in pyridine or acetone give colored solutions with alcoholic potassium hydroxide. The reaction is evidently not due to the active methylene hydrogen in these compounds, for other closely related compounds such as diphenylmethane and triphenylmethane do not give the reaction.

TABLE 1

Vapor pressure of fluorene

TEMPERATURE	VAPOR PRESSURE	TEMPERATURE	VAPOR PRESSURE
°C.	*mm.*	*°C.*	*mm.*
150	11.9	230	155.0
160	17.4	240	202.0
170	24.9	250	259.0
180	34.8	260	332.0
190	48.1	270	419.0
200	65.4	280	527.0
210	88.6	290	656.0
220	120.4	300	808.0

The isolation of fluorene from coal-tar fractions in which it is present to the extent of 1.6 per cent is, at the present time, effected through the formation of a potassium derivative at a high temperature (300°C.). Separation is easily accomplished, and subsequent treatment with water regenerates fluorene (113, 327, 330). Sodamide has also been used in this separation (184, 331).

A number of molecular addition products with fluorene have been reported. They are summarized in table 2.

McEwen (195) has recently studied the behavior of fluorene and some of its derivatives as an example of an extremely weak acid. Fluorene after exposure to ultraviolet light from a quartz-mercury lamp shows phosphorescence followed by a photochemical effect (161).

Fluorenone, the oxidation product of fluorene, is a beautiful yellow crystalline material[4] melting at 83–84°C. and boiling at 341°C. (152). In preparing fluorenone by the method of Huntress, Herschberg, and Cliff (using sodium dichromate in acetic acid) we have obtained it in rhombic crystals over 3 cm. in length. The solubility of fluorenone has been determined in various solvents (table 3).

TABLE 2

Molecular addition products of fluorene

REAGENT	RATIO OF MOLES OF FLUORENE TO MOLES OF REAGENT	MELTING POINT	COLOR AND FORM
		°C.	
Picric acid (104)	1:1	80–82	Red needles
2,4-Dinitrochlorobenzene (35)	1:1	39 (approx.)	Straw yellow
Picramide (88)	1:1	127.5	Yellowish brown
Tetryl (89)	1:1	77.5 (decomp.)	
Trinitro-*m*-cresol (63)	1:1	109 (explodes at 421)	Deep yellow
3,5-Dinitro-*p*-hydroxybenzoic acid (210)	1:2	218–221 (closed tube)	Yellow powder
1,3,6,8-Tetranitronaphthalene (222)	1:2	154–155	Brownish needles
s-Trinitrobenzene (177, 306)	2:3	105	Golden yellow plates
Trimesic acid trichloride (23)	1:1	75–77	Yellow
3,5-Dinitrobenzonitrile (23)	1:2	128–130	Yellow
2,7-Chlorophenanthraquinone (140)			
1,2,3,4,5,6,7-Heptachloroanthraquinone (140)			Deeply colored melts
1-Nitroanthraquinone (140)			

TABLE 3

Solubility of fluorenone

SOLVENT	GRAMS PER GRAM OF SOLVENT AT 22°C.
Alcohol (95 per cent)	0.075
Carbon tetrachloride	0.19
Ether	0.31
Benzene	0.68

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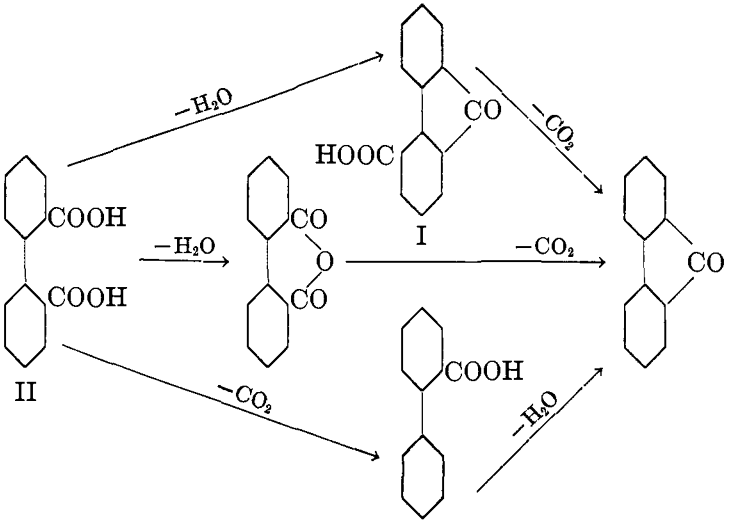
[4] Kerp (Ber. **29**, 228 (1896)) reported a pseudo form, melting at 85°C. and forming dark red crystals. Although Stobbe (Ber. **44**, 1481 (1911)) has confirmed this observation, it would seem to require further investigation.

Postovski and Lugovkin (234) have shown that fluorene on oxidation with selenium oxide gives only 5 per cent of fluorenone. Under the same conditions diphenylmethane gives 87 per cent of benzophenone, indicating the greater resistance of fluorene to oxidation owing to the linking of benzene rings. Courtot (53) used solutions of potassium permanganate at room temperature to oxidize fluorene and derivatives to the corresponding fluorenones; the yields were mostly quantitative. Usually the oxidation is carried out with sodium dichromate and acetic acid. This method is suitable for large-scale laboratory production of fluorenone (152).

Huntress, Herschberg, and Cliff (152) also studied the conversion of diphenic acid to fluorenone. As seen by the equations, the transformation may take place in three ways.[5] At 360°C. the conversion was rapid and quantitative. No conclusion as to the mechanism of the reaction could be drawn, because under the same conditions both fluorenone-4-carboxylic acid (I) and diphenic acid (II) gave the same result. These authors recommend their method for the preparation of fluorenone of high purity.



Fluorenone combines with one molecule of perchloric acid to form an oxonium perchlorate of the formula $C_{13}H_8OHClO_4$ (144). This formation of a perchlorate has been suggested as a method for the isolation and identification of ketones, especially in the case of those compounds which fail to yield picrates. Other addition products such as fluorenone zinc chloride (243), fluorenone nitrate (198, 244, 261b), and fluorenone mercuric chloride (4, 198) have been prepared.

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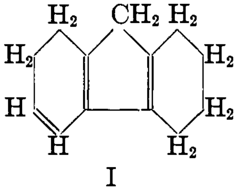
[5] Huntress, Herschberg, and Cliff overlooked the previous preparation by Graebe and Mensching (Ber. **13**, 1302 (1880)) of fluorenone from diphenic anhydride by heating.

IV. REDUCTION PRODUCTS OF FLUORENE

Several distinct reduction products of fluorene are known. Guye (135) has reported an octahydrofluorene, $C_{13}H_{18}$, which he obtained along with the decahydrofluorene, $C_{13}H_{20}$, by heating fluorene with phosphorus and hydriodic acid in a sealed tube. Liebermann and Spiegel (185), who used the same method, obtained the perhydro compound, $C_{13}H_{22}$. Decahydrofluorene was also prepared by Schmidt and Mezger (266) with phosphorus and iodine. More careful work by Ipatieff (156) has shown that decahydrofluorene was the chief product of the hydrogenation of fluorene at 290°C. under 120 atm. pressure, and on further treatment with hydrogen at 285°C., under a higher pressure, perhydrofluorene was obtained. Nickel oxide was used as the catalyst.

Sadikov and Michailov (252), in a more recent investigation, studied the hydrogenation of fluorene under pressure in the presence of various catalysts. Osmium proved to be superior to nickel oxide, giving a 78 per cent yield of the decahydro compound and a 22 per cent yield of the perhydro compound. The addition of small amounts of the oxides of cerium and thorium to the osmium catalyst increased the yield of perhydrofluorene to 93 per cent and 100 per cent, respectively. Although nickel oxide by itself proved to be somewhat inefficient, the presence of 1 per cent of cerium oxide brought about a 98.2 per cent yield of perhydrofluorene. The addition of 1 per cent of thorium oxide to the nickel oxide catalyst was surprisingly inefficient; in fact, all of the fluorene was recovered unchanged.

From a "fat" French coal found in the Loire region, Pictet and Ramseyer (229) obtained hexahydrofluorene, $C_{13}H_{16}$, by extraction with benzene. At red heat it was dehydrogenated to fluorene. The fact that hydrogen was given off at high temperatures led these authors to state that this property may be common to other hydrogenated hydrocarbons, thus accounting for the presence of aromatic hydrocarbons in coal tar and hydrogen in coal gas as a result of distillation at ordinary pressure. The following two formulas were proposed:



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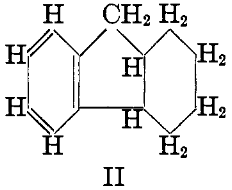
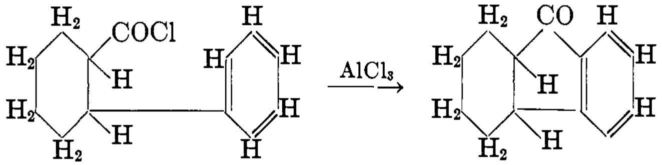


II

An investigation of the dehydration of benzylcyclohexanols by Cook and Hewett (48) led to the synthesis of 1,2,3,4,10,11-hexahydrofluorenone.

2-Phenylhexahydrobenzoyl chloride was treated with aluminum chloride in carbon disulfide at 0°C. Ring closure took place as shown in the following equation:



Reduction with amalgamated zinc and hydrochloric acid gave 1,2,3,4,10,11-hexahydrofluorene (Pictet's formula II). Cook and Hewett reported it to boil at 127°C. at 15 mm. pressure, while Pictet and Ramseyer gave 110–120°C. at 10 mm. pressure. Whether the two products were identical or were structural isomers (I and II) cannot be stated with certainty.

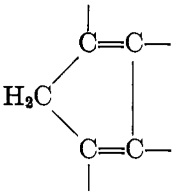
9-Aminohexahydrofluorene was obtained catalytically in two forms from fluorenone oxime (213). The hydrochloride of the α-form melted at 236°C. and the hydrochloride of the β-form at 306°C. The α-form proved to be racemic, resolution being effected with active tartaric acid.

Lebeau and Picon (184) have reported a 9-methyltetrahydrofluorene.

V. GENERAL METHODS OF SYNTHESIS OF DERIVATIVES OF FLUORENE AND FLUORENONE

The synthesis of fluorene and fluorenone derivatives may be considered in two general divisions: first, synthesis by direct substitution in the fluorene molecule itself; second, synthesis through indirect methods from appropriate intermediate compounds.

Fluorene is particularly interesting, owing to the presence of a methylene group which is activated by two pairs of doubly linked carbon atoms. This



has been shown by Thiele (308) to be an excellent illustration of the polar influence of the ethylenic double bond.[6] Examination of the structures of cyclopentadiene (I), indene (II), and fluorene (III) shows that fluorene may

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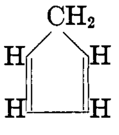
[6] Goss and Ingold (J. Chem. Soc. **1928**, 1268) have given an explanation of the reactivity of the methylene group in terms of the electron theory.

be considered as dibenzocyclopentadiene and indene as benzocyclopentadiene.



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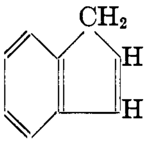

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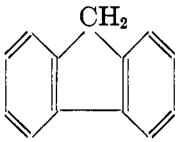
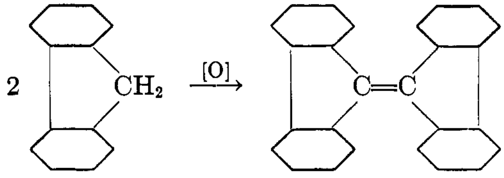
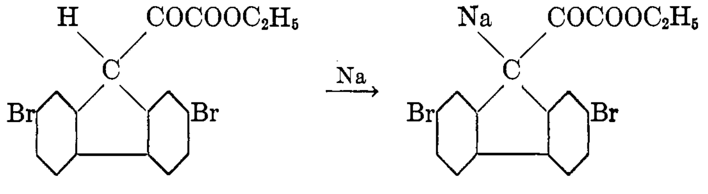


III

Thiele and Henle (311, cf. 310) found that the reactivity of the methylene group in these compounds was in the order cyclopentadiene > indene> fluorene. This was formulated on the basis that the activity of the methylene group decreases as the ethylene groupings of the five-atom ring are rendered inactive by benzene nuclei. The reactivity in fluorene was evidenced by the formation of sodium and potassium derivatives as well as condensations with the carbonyl group (to be considered later). If fluorene in the vapor state is passed over heated lead oxide the red hydrocarbon dibiphenyleneëthylene is obtained, showing the reactivity of the hydrogen atoms in the 9-position (70).



Sieglitz (283) found that, owing to the activity of the 9-hydrogen atom in ethyl 2,7-dibromofluorene-9-oxalate, it could be substituted by sodium and could thus yield a number of derivatives.



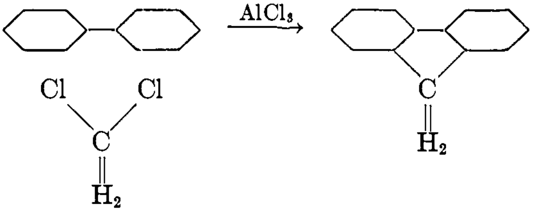
Courtot and Geoffroy (55) found in attempts to introduce hydroxyl groups that alkali fusion of sulfonated fluorenes oxidized the methylene group to give substituted biphenylcarboxylic acids. Fluorenone behaved in a similar manner. Other derivatives also show this transformation and it may be considered a general chemical property of fluorene compounds. This greatly restricts the versatility of these substances.

The study of substituted fluorenones on fusion with alkali has been extended to 1,4-dimethylfluorenone (255).

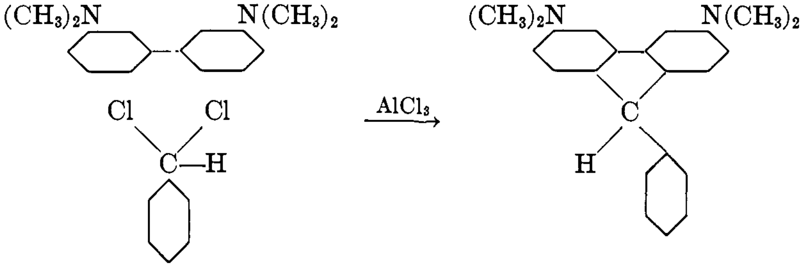
Substitution in the two benzene nuclei of the molecule seems to proceed upon a rather definite plan. Courtot (55), in his extensive investigations of fluorene, showed that chlorine, bromine, nitric acid, and sulfuric acid react in the 2-position. Further substitution leads to 2,7-compounds (250) in all but a few cases. Very little is known of the orientation of trisubstituted derivatives. As a rule, it may be said that present knowledge permits the preparation only of derivatives involving the 2-,7-,and 9-positions by direct substitution. There are a few exceptions such as 2,5-dinitrofluorene, 2,3-diacetylfluorene, and 2-amino-3-nitrofluorene, which have been prepared by direct substitution, and further research might well show others.

Syntheses through indirect methods are numerous and up to the present time have yielded primarily substituted fluorenones; however, there are some cases in which the fluorene derivative has been obtained.

P. Adam (1) at an early date showed that biphenyl and methylene dichloride in the Friedel-Crafts reaction yielded fluorene. The reaction indicated very well the structure of fluorene and its close relationship to biphenyl.

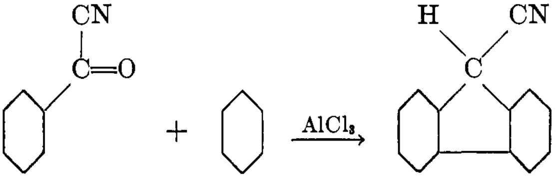


Dutt (78) was probably the first investigator to attempt an extension of this method. By the reaction of 3,3′-tetramethyldiaminobiphenyl and benzal chloride with aluminum chloride in carbon disulfide he obtained 3,6-tetramethyldiamino-9-phenylfluorene.

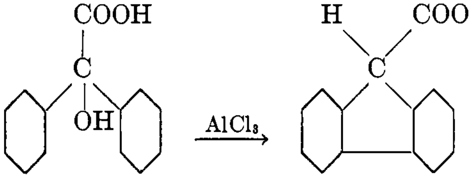


It seems to us that a more intensive investigation into the general applicability of this method would be profitable.

Delacre (69) described the action of ethyl trichloroacetate on benzene in the presence of aluminum chloride to give fluorene-9-carboxylic acid and recommended this method as a general one for the synthesis of fluorene derivatives. As far as we have been able to determine, however, no further investigation has been made. Vörlander (324) obtained 9-cyanofluorene by condensing benzoyl cyanide with benzene in the presence of aluminum chloride, and later (325) prepared fluorene-9-carboxylic acid directly by using benzilic acid in place of benzoyl cyanide (reaction II). When the benzene was replaced with toluene a methyl-substituted fluorene was formed in reaction I.

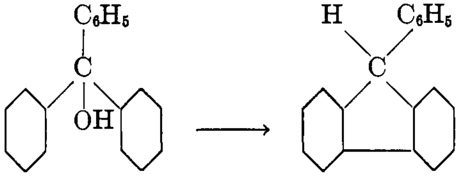


(I)



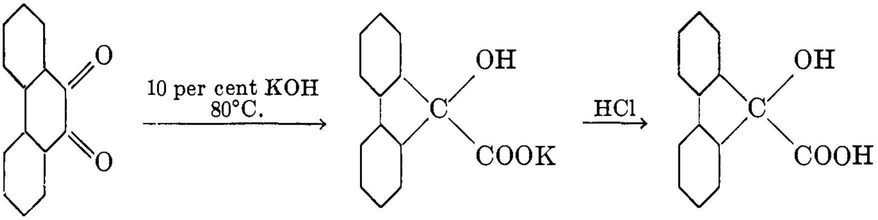
(II)

Kliegl (162) has shown that a similar dehydration to give ring closure occurs on the distillation of triphenylcarbinol with crystalline phosphoric acid to give 9-phenylfluorene.

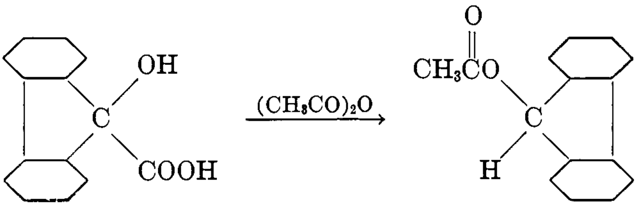


Indirect syntheses yielding substituted fluorenones are more common and have been investigated with some thoroughness in relation to their applicability as general methods. Miller and Bachman (200) have given an excellent critical review of these methods.

The conversion of phenanthraquinone derivatives into derivatives of fluorenone has proved to be one of the most reliable methods. Phenanthraquinone, bearing a structural similarity to open chain α-diketones, undergoes with ease the benzilic acid rearrangement. The product is 9-hydroxyfluorene-9-carboxylic acid or biphenyleneglycolic acid (109, 166, 261a). The latter compound, an α-hydroxy acid, should readily oxidize to fluorenone.

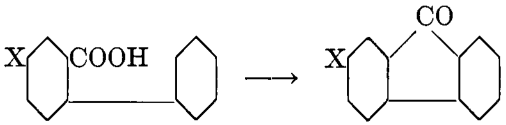


This oxidation was found to occur readily, boiling with water or alkalies in the presence of air being sufficient to bring it about. When 9-hydroxyfluorene-9-carboxylic acid was boiled with acetic anhydride in an atmosphere of hydrogen, 9-fluorylacetate (9-acetoxyfluorene) was formed with the evolution of carbon dioxide (261). Hydrolysis of the latter compound yielded 9-hydroxyfluorene, which could be reduced to fluorene or oxidized to fluorenone. The passage from phenanthraquinone directly to fluorenone was easily accomplished with alkaline permanganate (5).

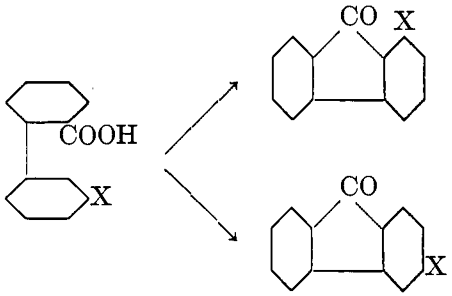


Schmidt and Bauer (261), using appropriate derivatives of phenanthraquinone, carried out a number of these syntheses. Such compounds as 4,5-dinitrofluorenone, 4-nitro-9-hydroxyfluorene-9-carboxylic acid, and 2-bromo-7-nitrofluorenone were prepared. The nature of the substituents in the phenanthraquinone molecule had a definite effect upon the ease with which the rearrangement took place. Phenanthraquinone itself with 10 per cent potassium hydroxide required a temperature of 80°C. The mononitro derivatives required a temperature of 50–65°C., while with the dinitro compounds the transformation took place at only 15°C. The effect is similar with bromo derivatives, but not to such a marked extent. This method is limited by the fact that many of the desired phenanthraquinones are yet unknown, so the advancement of the chemistry of fluorene by this means depends on the development of phenanthrene chemistry. The rapid expansion of this field, however, in the past ten years is encouraging to investigators interested in fluorene compounds. No investigation has yet been made using the newer knowledge of phenanthraquinone derivatives as a means of preparing new fluorenones.

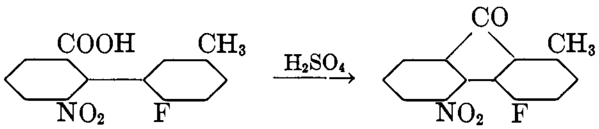
The dehydration of *o*-carboxybiphenyl derivatives constitutes another method which is of value because of the high yields. The ring closure is



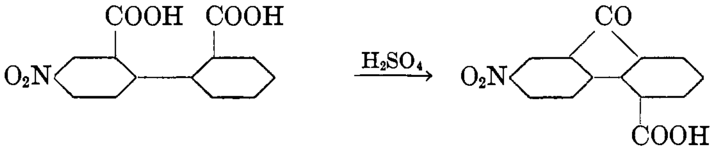
usually effected with concentrated sulfuric acid. A distinct disadvantage is encountered in this method if the substitutent in the second ring is in the meta position, as on ring closure two compounds are possible.



No complications are involved, however, if the substituents are in the first ring or in the ortho and para positions of the second ring. As an example of this reaction, Stoughton and Adams (303) treated 2-nitro-6-carboxy-2′-fluoro-5′-methylbiphenyl with concentrated sulfuric acid and obtained a quantitative yield of 1-methyl-4-fluoro-5-nitrofluorenone.

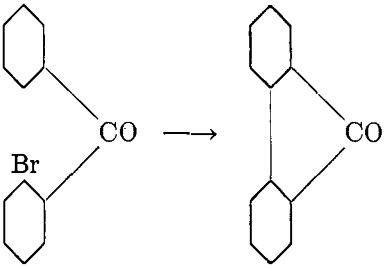


When substituted diphenic acids were used, a substituted carboxyfluorenone was obtained. Moore and Huntress (206a) have prepared 7-nitrofluorenone-4-carboxylic acid from 4-nitrodiphenic acid.



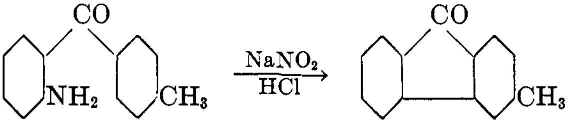
Similarly Fieser (97) prepared 1,6-dimethoxyfluorenone-4-carboxylic acid from 5,5′-dimethoxydiphenic acid.

Fluorenones may also be synthesized from *o*-halogen benzophenone derivatives.

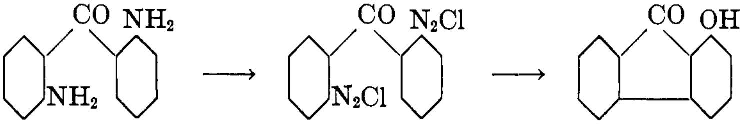


Montagne (203, 204) employed this method in the synthesis of several monobromo and dibromo derivatives of fluorenone. As Miller and Bachman (200) have pointed out, the method possesses disadvantages in that the yields are small, the intermediate compounds difficult to prepare, and rearrangement is possible because of the high temperature required to effect the elimination of halogen acid.

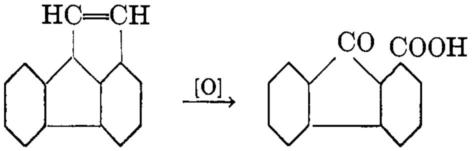
A method, somewhat similar to the preceding one, which has given satisfactory results consisted of the successive diazotization and internal coupling of derivatives of *o*-aminobenzophenone. Ullmann and Mallett (316) prepared 3-methylfluorenone by the action of nitrous acid on *o*-aminophenyl *p*-tolyl ketone.



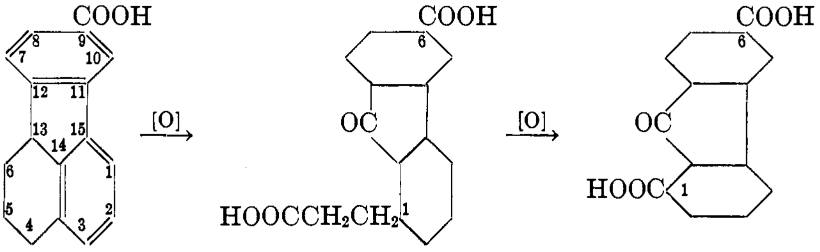
Staedel (290) has given a similar synthesis of 1-hydroxyfluorenone from *o*,*o*′-diaminobenzophenone.



The hydrocarbon fluoranthene offers another road to the synthesis of fluorenone derivatives. Fittig and Gebhard (100) and Fittig and Liepmann (101) showed very early that the oxidation of fluoranthene with chromic acid yielded fluorenone-1-carboxylic acid along with some fluoranthenequinone.



Fieser and Seligman (98) in their work on carcinogenic compounds involving the cholanthrene nucleus have confirmed this result. It is only recently that the extension of this method has been investigated (34a). For example, by oxidizing 4,5,6,13-tetrahydrofluoranthene-9-carboxylic acid (obtained by reducing fluoranthene-9-carboxylic acid with sodium amalgam), 6-carboxyfluorenone-1, β-propanoic acid was obtained, which could in turn be further oxidized to fluorenone-1,6-dicarboxylic acid.



This method presents the same problem encountered with phenanthrene. The chemistry of fluoranthene is still a relatively unexplored field and subsequent development will have a definite effect upon the advancement of fluorene chemistry.

VI. DERIVATIVES[7] OF THE TYPE $(C_6H_4)_2C{=}N$—

Fluorenone is similar in structure to benzophenone, as both contain the carbonyl group situated between two aromatic nuclei. Consequently fluorenone undergoes all the characteristic reactions of an aromatic ketone. It forms an oxime readily and condenses easily with hydrazine derivatives to give hydrazones. A number of these characteristic ketone derivatives are summarized in table 4.

---

[7] The classification of the following compounds is based on the structure of the fluorene molecule. Compounds involving the 9-carbon atom (the methylene group) are described under several structural types (sections VI, VII, and VIII), and compounds involving substitution in the nucleus are classified according to the nature of the substituent. Compounds which fall under both heads will be treated as belonging to the second group. This arrangement should aid in the logical presentation of the subject matter and afford a better view of the chemical properties of fluorene derivatives.

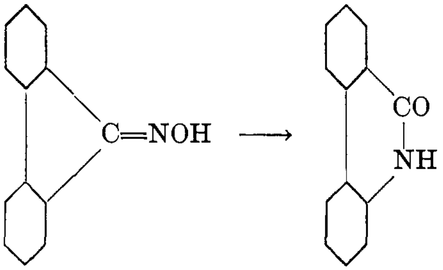
Schmidt and Soll (268) have shown that substitution of the oxygen in the carbonyl group by the oxime group results in a weakening of the coloring power, that is, >C=O is a more powerful chromophore than >C=NOH. Substitution of the oxime hydrogen has some effect on the color, but the effect is less marked.

TABLE 4

Derivatives of fluorenone

COMPOUND	MELTING POINT	COLOR AND FORM
	°C.	
Fluorenone oxime (268)	193–194	Light yellow needles
Fluorenone oxime (sodium salt) (268)	Decomposes	Pale yellow
Fluorenone oxime (potassium salt) (268, 344)	Decomposes	Pale yellow
Acetylfluorenone oxime (268)	79	Light yellow
Fluorenone oxime benzoate (268)	179	Pale yellow
Fluorenone oxime methyl ether (268)	145.6	Reddish yellow
Fluorenone phenylhydrazone (120)	151–151.5	Yellow needles
Fluorenone *p*-nitrophenylhydrazone (271, 232)	269 (decomposes)	Orange-yellow needles
Fluorenone hydrazone (336)	149	Light yellow plates
Fluorenone benzoylhydrazone (246)	171	Yellow needles
Fluorenone phenylsemicarbazone (295)	222	

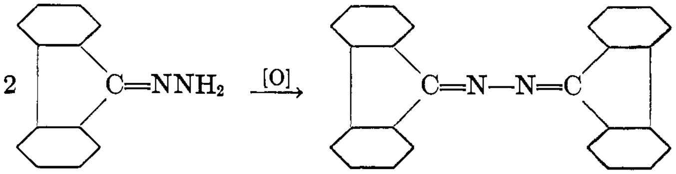
Fluorenone oxime also undergoes the Beckmann transformation on heating with zinc chloride. Pictet and Gonset (228) reported a 30 per cent yield of phenanthridone using this method.



Phenanthridone has also been prepared by Graebe and Schectakow (128) by treating 4-aminofluorenone with dilute potassium hydroxide. Moore and Huntress (206) extended both of these reactions by using substituted fluorenones.

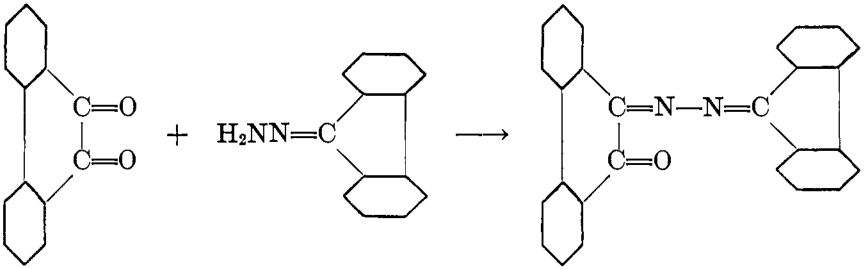
Fluorenone hydrazone takes part in many reactions. Curtius and Kof (60) treated fluorenone hydrazone in absolute alcohol with sodium amalgam and obtained di-9-fluorylamine (cf. 34), $[(C_6H_4)_2CH]_2NH$, in yellow needles melting at 167°C.

Fluorenone ketazine, $(C_6H_4)_2C{=}N{-}N{=}C(C_6H_4)_2$, was prepared by the oxidation of fluorenone hydrazone with quinone or iodine in alcohol. It formed dark red needles with a blue luster, m.p. 259°C. (336).

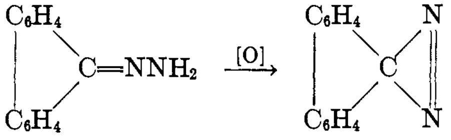


Curtius and Kof (60) have also prepared it either by heating fluorenone hydrazone with fluorenone or by heating fluorenone with hydrazine hydrate.

Other ketazines derived from fluorenone hydrazone have been prepared. Benzalfluorenone ketazine, $(C_6H_4)_2C{=}N{-}N{=}CHC_6H_5$ was prepared by boiling together benzaldehyde and fluorenone hydrazone in alcohol (296). Gerhardt (112) has shown that aromatic keto-hydrazones react with ortho-quinones to yield ketazines of the type $R_2C{=}N{-}N{=}R{=}O$. For example, with phenanthraquinone a 45 per cent yield of phenanthraquino-fluorenone ketazine, crystallizing in deep brownish needles, was obtained.



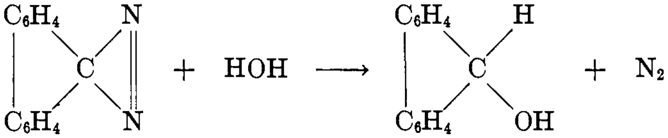
Biphenylenediazomethane (9-diazofluorene) has been obtained by shaking fluorenone hydrazone in benzene with yellow mercuric oxide for 48 hr. (296), and by passing carbon dioxide-free air through a solution of the hydrazone in the presence of sodium (294).



Bennett and Noyes (21) prepared 2-amino-9-diazofluorene from the hydrazone by oxidation in air, using mercury acetamide in an alcoholic solution containing a minute amount of sodium ethylate.

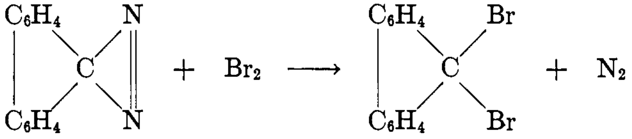
9-Diazofluorene crystallizes in red needles melting at 94–95°C. It is converted into dibiphenyleneëthylene (bifluorylidene), $(C_6H_4)_2C{=}C(C_6H_4)_2$, by carbon dioxide, iodine, hydrogen bromide, and ammonium sulfide (296).

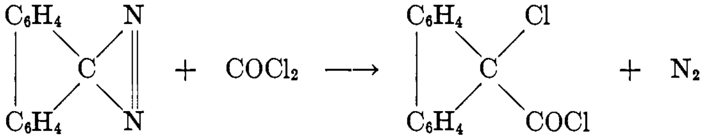
Staudinger and Gaule (294) have synthesized other derivatives from 9-diazofluorene. On standing with slightly acidified alcohol, 9-fluorenol, $(C_6H_4)_2CHOH$, was formed.



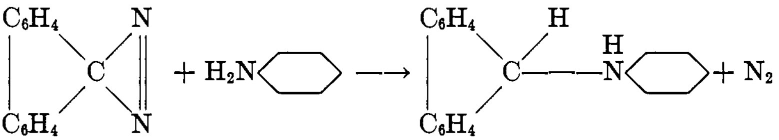
When hydrogen chloride was passed into a solution of 9-diazofluorene a good yield of 9-chlorofluorene was obtained.

9,9-Dichlorofluorene was formed when thionyl chloride was substituted for hydrogen chloride. Bromine in carbon disulfide reacted to give 9,9-dibromofluorene, and with phosgene the product was 9-chlorofluorene-9-carbonyl chloride.



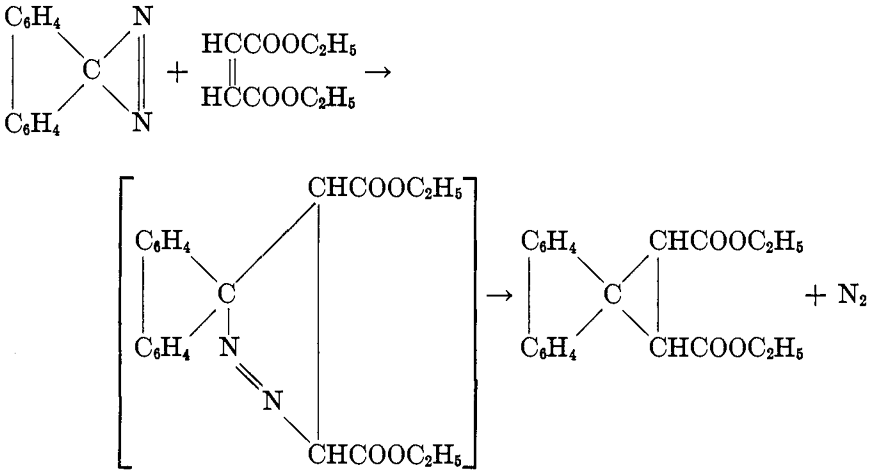


If heated with aniline, 9-fluorylphenylamine (9-fluorylaniline) resulted.



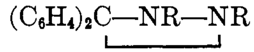
9,9-Dinitrofluorene, which decomposed on standing, was prepared by passing nitrogen dioxide into a solution of 9-diazofluorene (335, 141). These reactions are important, for they provide a ready means of synthesis of fluorene derivatives with substituents in the 9-position.

It is well known that derivatives of ethylene react with diazomethane to yield rings of three carbon atoms. Staudinger and Gaule found that 9-diazofluorene behaved similarly. Using diethyl fumarate in ether, they obtained diethyl biphenylenecyclopropane-2,3-dicarboxylate.



Ethyl cinnamate gave ethyl 1-biphenylene-2-phenylcyclopropane-3-carboxylate.

The same authors (294), having in mind this principle of ring formation, proposed an ingenious scheme for the preparation of isomeric diazo compounds and hydrazones and made attempts to carry it out experimentally. They reasoned that since ethylene derivatives gave rings with three carbon atoms, azo compounds might be expected to form rings containing one carbon and two nitrogen atoms. Compounds of the type,

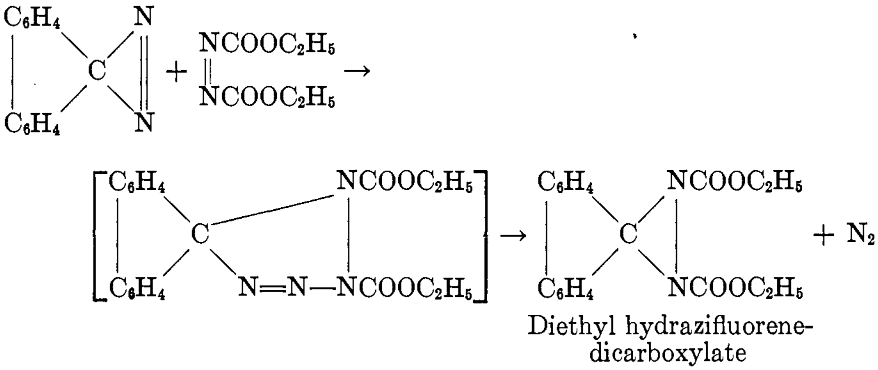


$$(C_6H_4)_2C\text{—}NR\text{—}NR$$

would thus be formed with 9-diazofluorene, and by choosing R so that it could be substituted by hydrogen a hydrazi compound of the type

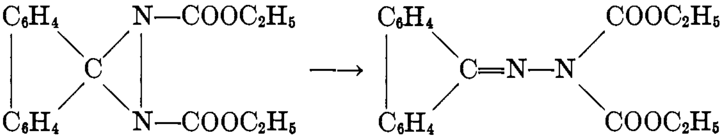
$$(C_6H_4)_2CNH\text{—}NH$$

would be obtained. This compound would be isomeric with fluorenone hydrazone, $(C_6H_4)_2C{=}N\text{—}NH_2$. The hydrazi compound on oxidation should yield a diazo compound different from 9-diazofluorene if the ordinary diazo compounds do not have the ring structure formulated by Curtius. They were successful in preparing a hydrazi compound by the following reaction.

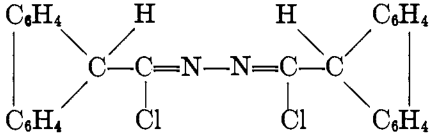


Diethyl hydrazifluorenedicarboxylate

Further experiment failed, for it was found that the hydrazi compound rearranged to give diethyl fluorenone hydrazonedicarboxylate.



Stollé, Münzel, and Wolf (301) studied a series of compounds similar to those just discussed. Biphenyleneacethydrazide, $(C_6H_4)_2CHCONHNH_2$, was prepared from hydrazine hydrate and ethyl fluorene-9-carboxylate. Further treatment of this compound (biphenyleneacethydrazide) with another mole of the ester yielded *sym*-dibiphenyleneacethydrazide, $(C_6H_4)_2CHCONHNHOCHC(C_6H_4)_2$, which with phosphorus pentachloride



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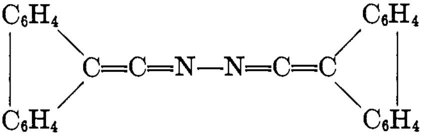
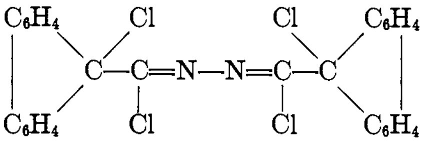


Dibiphenylenesuccinonitrile

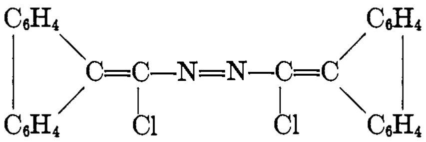
II

gave dibiphenyleneacethydrazide chloride (I). By splitting out hydrochloric acid a compound was formed to which the unusual structure shown in formula II was assigned. It was stable and melted at 242°C. If the two hydrogen atoms in compound I attached to the 9-carbon atoms were substituted by chlorine and then removed by shaking with mercury, introduction of another double bond was attained, causing a shift of bonds in relation to the nitrogen atoms, thus:



Dibiphenylenechloroacethydrazide chloride

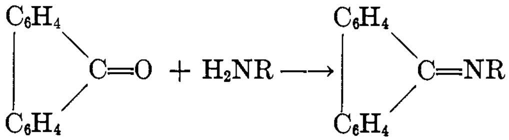
III



Dibiphenylenechlorovinyldiimide

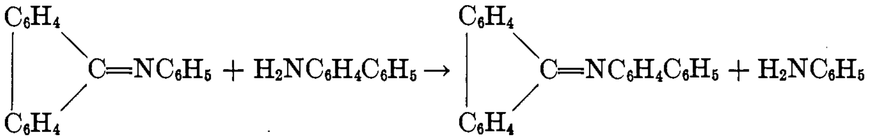
IV

Many derivatives of the type $(C_6H_4)_2C{=}NR$ have been described. Reddelien (242, cf. 230) carefully investigated the condensation of aromatic ketones with amines. Zinc chloride was found to have a catalytic effect upon the condensation.



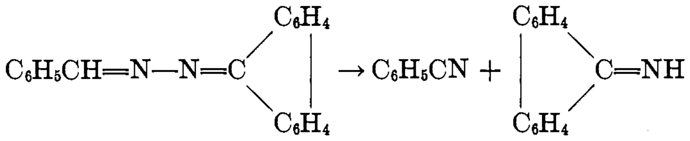
Using this method he prepared the following series of derivatives: fluorenoneanil, $(C_6H_4)_2C{=}NC_6H_5$; fluorylidene-*p*-toluidine, $(C_6H_4)_2C{=}NC_6H_4CH_3$; fluorylidene-*p*-hydroxyaniline, $(C_6H_4)_2C{=}NC_6H_4OH$; difluorylidene-*p*-diaminobenzene, $C_6H_4[N{=}C(C_6H_4)_2]_2$.

Reddelien (245) prepared other derivatives by taking advantage of displacement reactions which occur when fluorenoneanil is treated with an excess of another amine. For example, fluorenoneanil on heating with *p*-aminobiphenyl gave fluorylidene-*p*-aminobiphenyl and the theoretical amount of aniline.



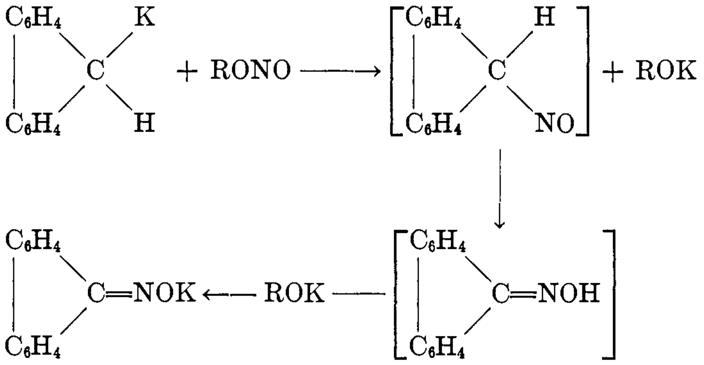
Fluorenoneanil reacted with *p*-aminobenzoic acid, methylamine, and ammonia to give fluorenoneanil-*p*-carboxylic acid, methyl-9-iminofluorene, and iminofluorene, respectively.

Iminofluorene $(C_6H_4)_2C{=}NH$ was prepared by Kliegl (163, cf. 114) by the reduction of fluorenone oxime with tin and hydrochloric acid, and it may be considered the first product of the reduction of fluorenone oxime. Pinck and Hilbert (230) prepared the imine in excellent yields from fluorenone and liquid ammonia. Boiling with water regenerated fluorenone. Iminofluorene was also formed by the thermal decomposition of benzalfluorenone ketazine (146).

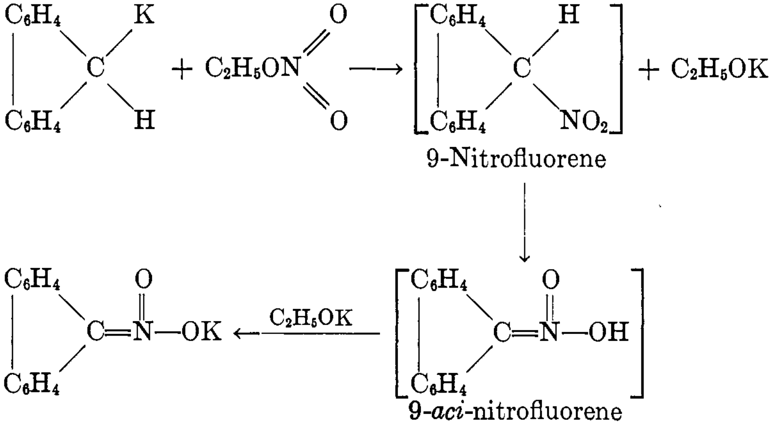


Degiorgi (68) reported the synthesis of fluorenoneaminoguanidine by the condensation of aminoguanidine and fluorenone.

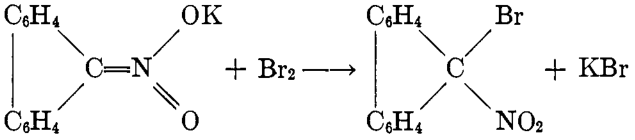
Thiele and Henle (311) in their studies of the characteristic reactions of the methylene group stated that fluorene did not react with amyl nitrite in the presence of sodium ethylate; however, when potassium ethylate was used fluorene condensed easily with alkyl nitrites to give potassium fluorenone oxime (344). The reaction probably takes place in the following manner:



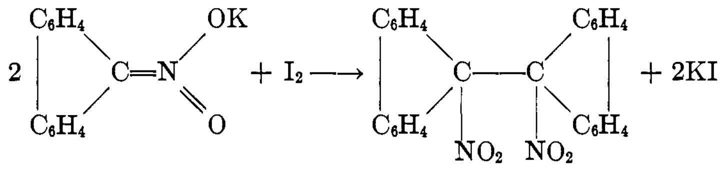
With ethyl nitrate and potassium ethylate Wislicenus and Waldmüller (344, cf. 232) obtained potassium 9-*aci*-nitrofluorene.



It gave an intense dark green color with ferric chloride. Neutralization with acid gave 9-*aci*-nitrofluorene, which in contact with ethyl alcohol was transformed into 9-nitrofluorene. Heat converted both forms into fluorenone. The potassium salt of the *aci*-form reacted with bromine to give 9-bromo-9-nitrofluorene.

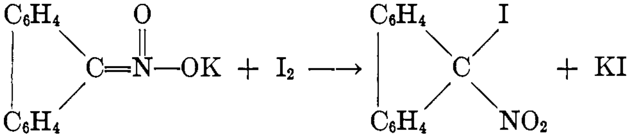


Nenitzescu (216, 217) investigated the action of iodine and other reagents upon potassium 9-*aci*-nitrofluorene. Unlike bromine and chlorine, iodine was found to cause the formation of a dimeric compound.

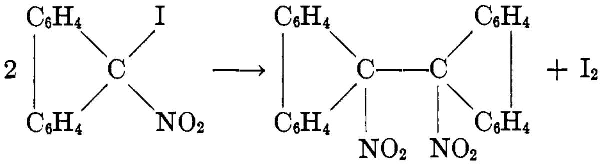


9,9′-Dinitrodifluoryl

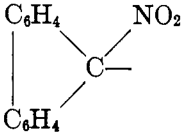
The latter compound was also obtained by the electrolysis of potassium 9-*aci*-nitrofluorene. If, however, the reaction with iodine was carried out at 0°C. the product was 9-iodo-9-nitrofluorene.



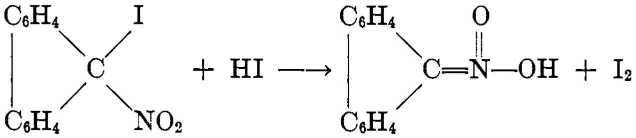
Heating 9-iodo-9-nitrofluorene for a few minutes in acetic acid also gave the dimeric dinitro compound.



The intermediate formation of the free radical, 9-nitrofluoryl, was postu-



lated. From this the mechanism of the reaction of iodine on potassium 9-*aci*-nitrofluorene was clear. Hydriodic acid reacted with 9-iodo-9-nitrofluorene to yield 9-*aci*-nitrofluorene.

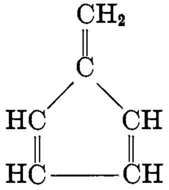


The same compound was obtained if hydriodic acid was replaced by sodium bisulfite.

The reaction between the salts of 9-*aci*-nitrofluorene and alkyl halides gave the ester, which was transformed by heat into 9-fluorenone oxime and an aldehyde.

VII. DERIVATIVES OF THE TYPE $(C_6H_4)_2C{=}C{=}$

Employing Thiele's theoretical compound, fulvene (I), we may consider



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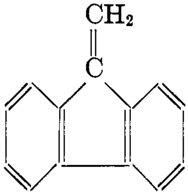
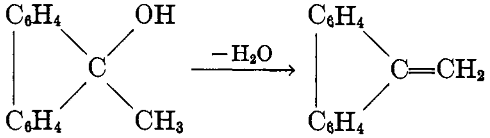


II

compounds of this type as derivatives of dibenzofulvene (II). This basic compound, dibenzofulvene or 9-methylenefluorene, has been prepared, but it was quite unstable. Ferrer (95, 334) obtained it by distilling 9-methyl-9-hydroxyfluorene with aluminum phosphate *in vacuo*.



The compound was not isolated at this point, but was brominated to dibromobiphenyleneëthylene. When the dibromo compound was refluxed in alcoholic solution with zinc in daylight a polymer was obtained which may have been tribiphenylenecyclohexane. When the debromination was carried out in the dark, however, 9-methylenefluorene was obtained as crystals, melting at 53°C., which were stable for several hours.

Sieglitz and Jassoy (286, cf. 193) set out to prepare 9-methylenefluorene in the manner shown below.

$$(C_6H_4)_2CHCH_2NHCOOC_2H_5 \rightarrow$$

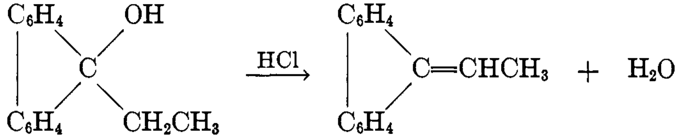
Fluoryl-9-methylurethan

$$(C_6H_4)_2CHCH_2NH_2 \xrightarrow[\text{degradation}]{\text{Hofmann}} (C_6H_4)_2C{=}CH_2$$

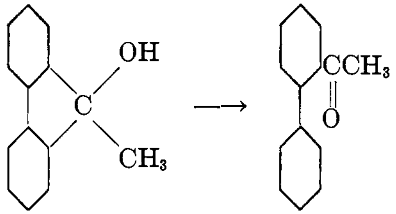
On distillation of the urethan with calcium oxide *in vacuo* and in an atmosphere of hydrogen they found to their surprise that an appreciable amount of 9-methylenefluorene was formed directly. They reported the melting point as 46–48°C. The same polymer found by Ferrer was also encountered.

$$(C_6H_4)_2CHCH_2NHCOOC_2H_5 \rightarrow (C_6H_4)_2C{=}CH_2 + C_2H_5NH_2 + CO_2$$

9-Hydroxy-9-ethylfluorene was dehydrated by means of hydrogen chloride, giving 9-ethylidenefluorene (64).

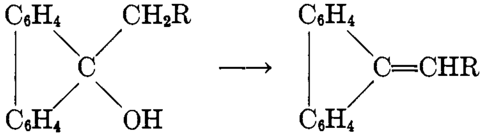


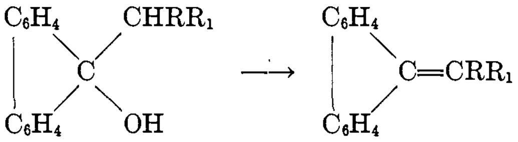
It was unstable and oxidized spontaneously in air to form an oxide which exploded at 100°C. Endeavoring to prepare 9-methylenefluorene by the same method from 9-methylfluorenol, Daufresne (64) found that rearrangement instead of dehydration took place, giving rise to an isomer of greater stability. He represented the reaction as follows:



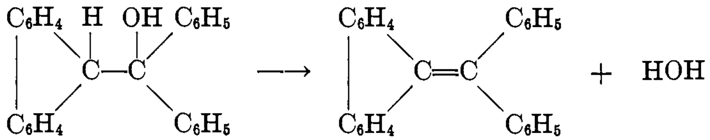
This view is probably erroneous, for he also stated that the compound did not react with hydroxylamine or semicarbazide.

The generality of this method for preparing alkyl or aromatic derivatives of 9-methylenefluorene by the dehydration of substituted fluorenols has not been investigated. The following equations represent the possibilities, where R and R_1 may be aliphatic or aromatic.

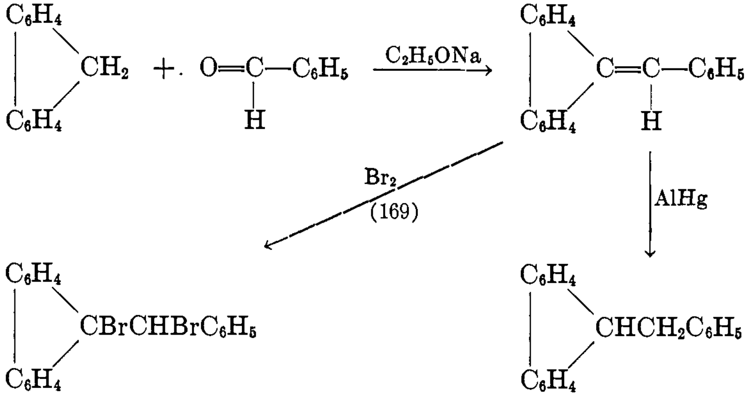




Courtot (52, 131), however, studied the dehydration of carbinols, which are isomeric with the compounds shown above, to give derivatives of 9-methylenefluorene. These compounds are of the type $(C_6H_4)_2CHC(OH)R_1R_2$, and are prepared by the action of ketones and aldehydes on 9-fluorylmagnesium bromide. For instance, 9-fluoryldiphenylcarbinol was dehydrated quantitatively to 1,1-diphenyl-2,2-biphenyleneëthylene (158) by passing hydrogen chloride into the boiling methyl alcohol solution.



Mono-aromatic derivatives, of the type $(C_6H_4)_2C{=}CHR$, have been more easily obtained by the condensation of aromatic aldehydes with fluorene, using sodium methylate or ethylate as the condensing agent (311). Bromine added normally to these compounds to give the dibromo derivatives. Reduction of the double bond was effected with aluminum amalgam. Thiele and Henle (309, 311) prepared numerous compounds in this way. For example, 9-benzylidenefluorene was prepared from benzaldehyde and fluorene. The condensation, bromination, and reduction are shown in the following equations.



Furfural, cinnamaldehyde, and anisaldehyde reacted similarly. Sieglitz (282) extended the series, using more complex aldehydes, and investigated the characteristic halochromism of the compounds in concentrated sulfuric acid. Table 5 summarizes his results. It is interesting to note the distinct change of halochromism encountered with the isomeric chlorobenzaldehydes.

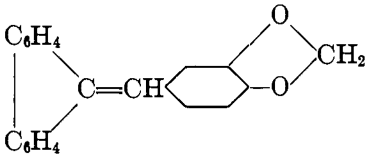
DeFazi (66) carried out this condensation with piperonal (3,4-methylenedioxybenzaldehyde) and 4-dimethylaminobenzaldehyde. Together with the expected 3,4-methylenedioxybenzylidenefluorene and 4-dimethylaminobenzylidenefluorene he obtained more deeply colored compounds which he assumed to be isomers. Bergmann (24) encountered similar deeply colored compounds on condensing benzaldehyde, *p*-methoxybenzaldehyde, and α-naphthaldehyde with fluorene and proved them to be the vinylene homologs. Reasoning by analogy Bergmann (24) thought it likely that DeFazi's compounds embodied a similar relationship. He proved by synthesis that this was the case. DeFazi's two compounds from piperonal were then 3,4-methylenedioxybenzylidenefluorene (I) and 3,4-methylenedioxycinnamylidenefluorene (II). The formation of II is probably due to the intermediate production of acetaldehyde from sodium ethylate (236, 258).

TABLE 5

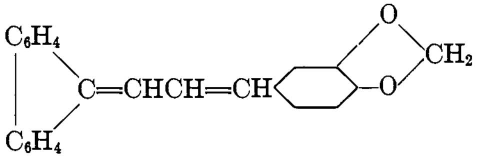
Halochromism in concentrated sulfuric acid

COMPOUND	COLOR	MELTING POINT	HALOCHROMISM
		°C.	
9,9′-Isophthalaldifluorene	Yellow	178–179	Deep green
9,9′-Terephthalaldifluorene	Yellow	209–210	Olive-green
9-*p*-Bromobenzylidenefluorene	Yellow	144	Green blue
9-*m*-Bromobenzylidenefluorene	Yellow	92–93	Deep green
9-*m*-Iodobenzylidenefluorene	Yellow	103	Deep green
9-*o*-Chlorobenzylidenefluorene*	Yellow	176	Dark brown
9-*m*-Chlorobenzylidenefluorene	Light yellow	90.5	Deep green
9-*p*-Chlorobenzylidenefluorene	Faint yellow	149.5	Deep blue

* Only obtained in a 15 per cent yield.

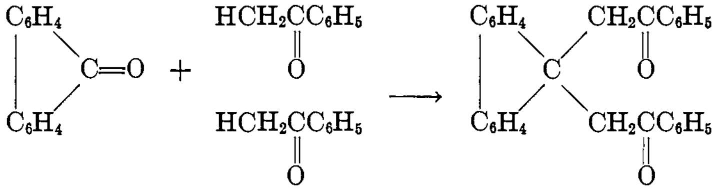


I

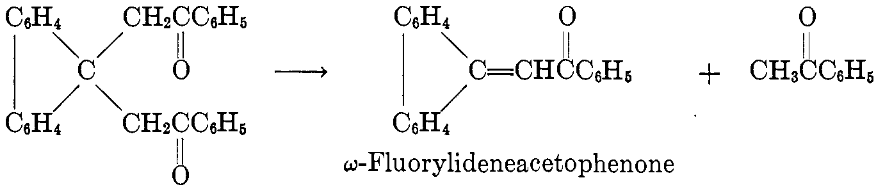


II

Dufraisse and Carvalho (76) condensed fluorenone and acetophenone in ether, using sodamide as the condensing agent, to obtain 9,9-diphenacylfluorene.

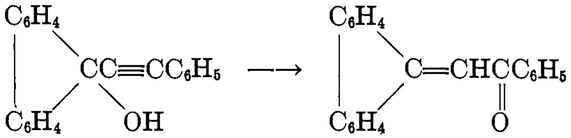


On pyrolysis at 230°C. 9,9-diphenacylfluorene decomposed into ω-fluorylideneacetophenone (299) and acetophenone.

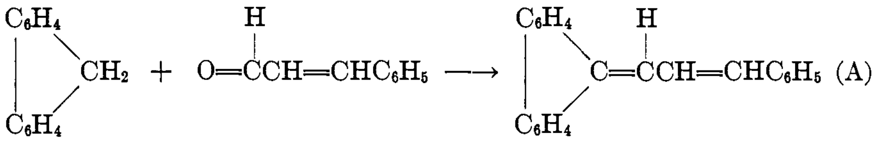


ω-Fluorylideneacetophenone

ω-Fluorylideneacetophenone was also prepared using hydrogen chloride instead of sodamide. These same authors, in attempts to prepare rubene derivatives of fluorene, synthesized phenylethynylfluorenol from fluorenone and phenylacetylene (77). Isomerization took place readily giving the same ω-fluorylideneacetophenone.



Kuhn and Winterstein (182) prepared a series of biphenylene analogs by condensing fluorene and appropriate aldehydes, as shown in the following equations:



1-Biphenylene-4-phenylbutadiene-1,3[8]

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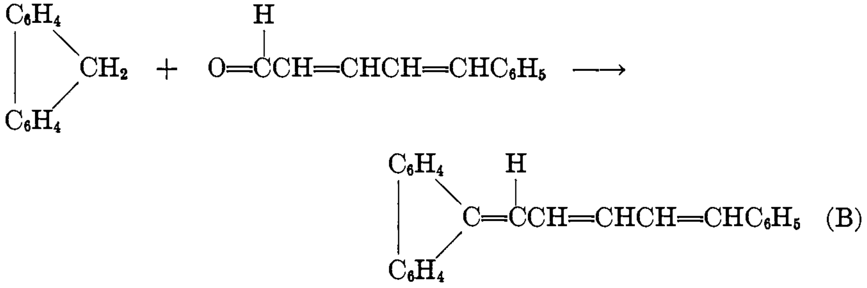
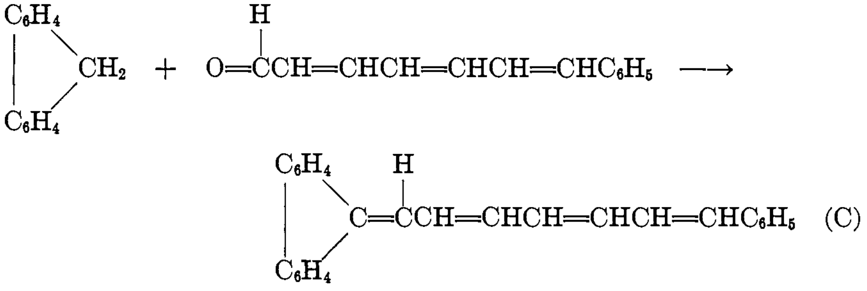
[8] On reduction with aluminum amalgam this compound gave 9-fluoryl-1-benzyl-2-ethylene; with sodium amalgam, 1-biphenylene-4-phenylbutene; and catalytically with hydrogen, 9-fluoryl-1-phenyl-3-propane.



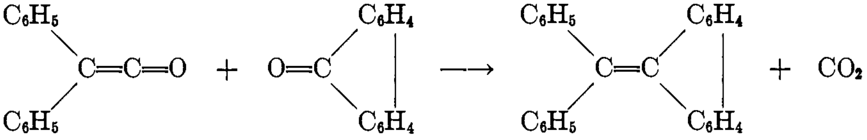
1-Biphenylene-6-phenylhexatriene-1,3,5



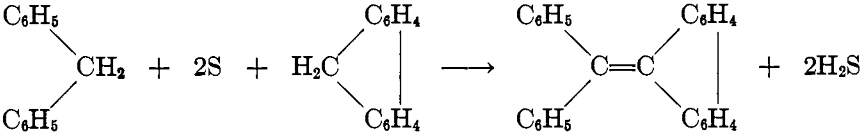
1-Biphenylene-8-phenyloctatetraene-1,3,5,7

The yield in reaction A was 63 per cent, but in reactions B and C it dropped to 11 per cent and 5 per cent, respectively.

Two novel reactions led to the production of 1,1-diphenyl-2,2-biphenyleneëthylene (see page 313). Staudinger and Gaule (293) obtained it from diphenylketene and fluorenone.

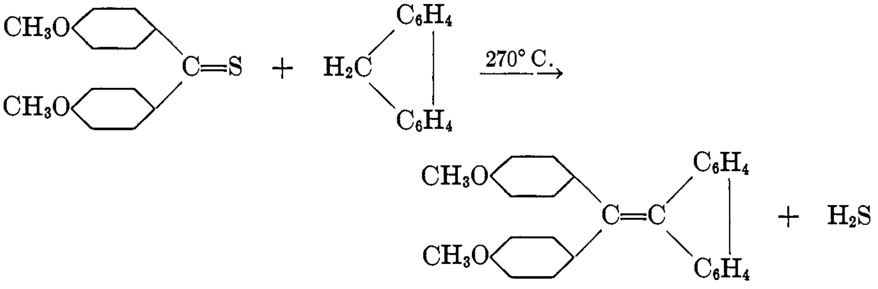


Szperl and Wierusj (307) reported it as the main product when a mixture of diphenylmethane and fluorene was heated with sulfur until hydrogen sulfide ceased to be evolved.



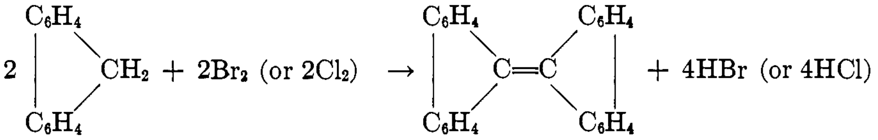
It crystallized from acetone in needles containing one molecule of acetone of crystallization, which it lost on exposure to air. The by-products of the reaction were the dimers, both saturated and unsaturated, of fluorene and diphenylmethane.

Schönberg (274) refined the method of Szperl by using a thiobenzophenone instead of free sulfur.

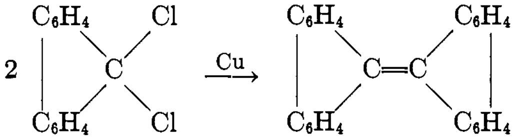


p,*p*′-Dimethoxydiphenyl-9-methylenefluorene

The unsaturated dimolecular compound of fluorene, dibiphenylene-ethylene or bifluorylidene, $(C_6H_4)_2C{=}C(C_6H_4)_2$, is formed with ease, owing to the reactivity of the hydrogen atoms in the 9-position. De la Harpe and van Dorpe (70) first described its preparation. Mantz (192) found that the action of chlorine or bromine at high temperatures resulted in its formation.



Schmidt and Wagner (271, cf. 289) obtained it in very good yields by treating 9,9-dichlorofluorene with copper powder in benzene solution.



Bifluorylidene is one of the few colored hydrocarbons; it is deep red and melts at 187–188°C. (cf. page 296).

VIII. DERIVATIVES OF THE TYPE $(C_6H_4)_2C<$

Derivatives of fluorene in which either one or both of the hydrogen atoms of the 9-carbon atom are replaced by various substituents are well known.

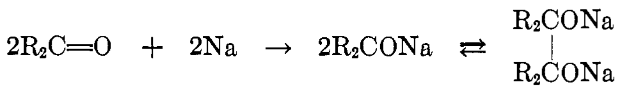
A. Hydroxy compounds. 9-Fluorenols

The reduction of fluorenone to fluorenol (9-hydroxyfluorene) and to the corresponding pinacol has been studied in some detail. 9-Fluorenol was first obtained by Barbier (14) from fluorenone, using sodium amalgam in alcoholic solution. Werner and Grob (332) used zinc dust and potassium hydroxide and zinc dust and ammonia. Aluminum amalgam in alcohol

$$(C_6H_4)_2CO \xrightarrow{[H]} (C_6H_4)_2CHOH$$

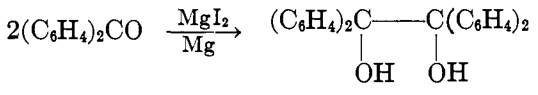
seems to be the most satisfactory reducing agent, giving a quantitative yield (47).

Bachmann (9) reported that when the reduction was carried out in ether solution with the theoretical amount of sodium, fluorenopinacol was obtained in a 95 per cent yield after hydrolysis with dilute acid. An excess of sodium seemed to favor the formation of fluorenol, for with a 30 per cent excess of sodium, 75 per cent of the pinacol and 25 per cent of fluorenol was formed. It is evident from his work that "the sodium derivatives of ketones, the so-called metal ketyls, are not, therefore, monomolecular free radicals but sodium pinacolates or equilibrium mixtures of sodium-ketyl and sodium pinacolate in which the equilibrium is nearly entirely in favor of the sodium pinacolate."



$$2R_2C{=}O + 2Na \rightarrow 2R_2CONa \rightleftarrows \begin{array}{c} R_2CONa \\ | \\ R_2CONa \end{array}$$

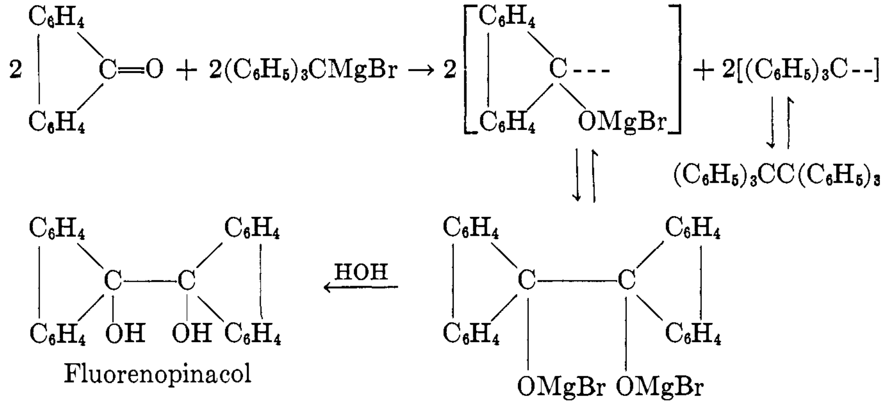
Gomberg and Bachmann (121), in their experiments with the reducing action of mixtures of magnesium iodide (or bromide) and magnesium on aromatic ketones, also obtained the pinacol, this time in a 99 per cent yield.



$$2(C_6H_4)_2CO \xrightarrow[Mg]{MgI_2} \begin{array}{ccc} (C_6H_4)_2C & \text{——} & C(C_6H_4)_2 \\ | & & | \\ OH & & OH \end{array}$$

It is important to note that fluorenone, fluorenol, and fluorenopinacol tended to form very definite complexes with each other. Gomberg and Bachmann obtained a tan-colored complex, m.p. 123–124°C., consisting of 1 mole of fluorenopinacol and 1 mole of fluorenone. Bachmann found another complex of fluorenol and fluorenopinacol, m.p. 151°C. It was crystalline and the proportions were equimolar.

Bachmann (8) also carried out the reduction of fluorenone with triphenylmethylmagnesium bromide.

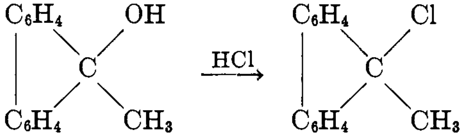


Fluorenopinacol

The presence of the free radicals was postulated on the basis of definite color changes which the solution underwent during the reaction. The yield of the pinacol was 80 per cent.

Meerwein (196) prepared the methyl and ethyl analogs and rearranged them to the pinacolones, 9,9-methylacetylfluorene, etc. The reduction of fluorenone with zinc and acetyl chloride gave a pinacolone, 9,9-biphenylenephenanthrone, directly (28, 121, 129, 163, 168). It may also be prepared in the usual way.

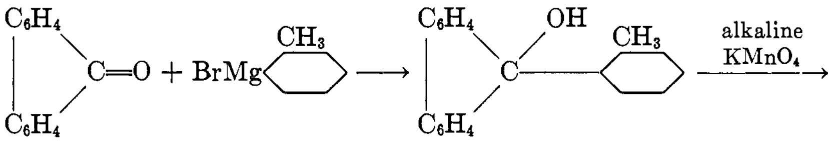
Fluorenone reacts normally with Grignard reagents and constitutes the principal method of preparing substituted fluorenols (cf. page 333). Methylmagnesium iodide (or bromide) and fluorenone gave 9-methyl-9-fluorenol (95, 333, 334). The substituted fluorenols on treatment with halogen acids were converted easily to the halogen compound; thus, methylfluorenol in ether with hydrogen chloride yielded 9-methyl-9-chlorofluorene (compare Daufresne (64)).



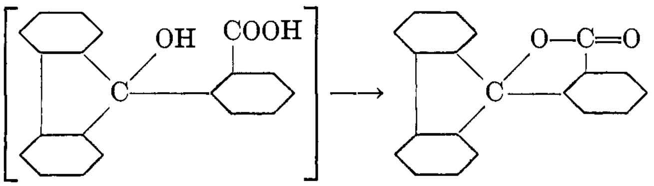
More complex fluorenols have been synthesized by the same method. Ullmann and von Wurstemberger (317) prepared 9-phenylfluorenol from phenylmagnesium bromide and fluorenone. Schniepp and Marvel (273) extended this particular type of synthesis by employing *p*-alkylphenylmagnesium halides. The following were synthesized: 9-*p*-ethylphenylfluorenol, 9-*p*-*n*-propylphenylfluorenol, and 9-*p*-tolylfluorenol (cf. 176). The chloro compounds were prepared by treating the crude fluorenols with hydrochloric acid and calcium chloride. The chlorine atom was especially reactive, as evidenced by the formation of alkyl ethers by merely heating with the proper alcohol. The chloro compounds on heating in benzene with copper bronze in an atmosphere of hydrogen gave the corresponding di-*p*-alkylphenyldibiphenyleneëthanes.

Bergmann and Schuchardt (28) similarly prepared 9-*p*-anisylfluorenol and 9-*p*-anisyl-9-chlorofluorene (cf. 323).

Weiss and Knapp (329) prepared a 9-substituted fluorenol which was eventually transformed into a lactone.

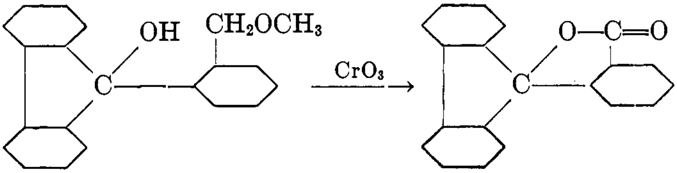


9-*o*-Tolyl-9-hydroxy-fluorene

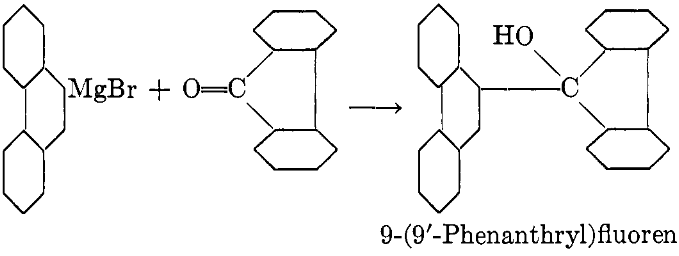


o-Biphenylenephthalide

Koelsch (171) obtained the same *o*-biphenylenephthalide by the oxidation of 9-(*o*-α-ethoxytolyl)fluorenol, prepared from *o*-(α-ethoxytolyl)magnesium bromide and fluorenone.

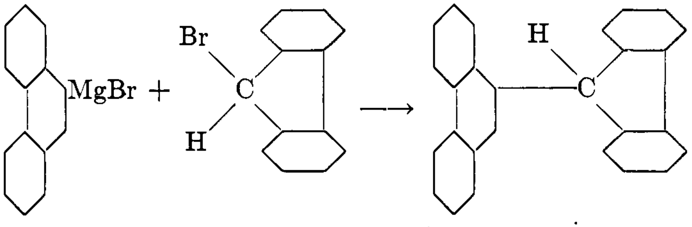


A fluorenol in which the phenanthrene nucleus is substituted in the 9-position has been prepared by Bachmann (10). This fluorenol on reduc-



9-(9′-Phenanthryl)fluorenol

tion with hydriodic acid[9] gave a quantitative yield of 9-(9′-phenanthryl)-fluorene, which was also prepared by the modified Grignard synthesis shown below.



9-(9′-Phenanthryl)fluorene

There are numerous other examples of synthesis from fluorenone and Grignard reagents (51, 130), and in all cases the reaction seems to go quite well.

Schmidt and Mezger (265) reported the existence of 9,9-dihydroxy-fluorene, m.p. 94°C. It resulted from the hydrolysis of the so-called α-form of 9-acetoxyfluorene (9-fluoryl acetate) which melted at 69–70°C. The β-form of this compound was said to melt at 208–209°C., but it was obtained in such small amounts that its hydrolysis could not be investigated. It is probable that the two compounds were $(C_6H_4)_2CHOCOCH_3$ and $(C_6H_4)_2C(OH)COCH_3$ and not stereoisomeric forms.

No confirmation of the existence of 9,9-dihydroxyfluorene has ever been made. Reactions that might be expected to give the dihydroxy compound produce fluorenone (289).

B. Halogen compounds

9-Chloro-, 9,9-dichloro-, 9-bromo-, and 9,9-dibromo-fluorene (see pages 305–320) have been prepared. Two iodine derivatives, 9-iodofluorene (181, 321) and 9-iodo-9-nitrofluorene (see page 311), are also known. It is probable that other iodo derivatives could be prepared under anhydrous conditions (238).

9-Chlorofluorene is reported to be best prepared by the action of phosphorus pentachloride on fluorenol (57, 163, 166, 294, 332). Thionyl chloride also was found to be a very efficient reagent for the preparation of 9-chlorofluorene from the fluorenol (153).

Probably the treatment of fluorenol in acetic acid solution with dry hydrogen chloride, with or without zinc chloride, is equally effective (57).

9,9-Dichlorofluorene was first prepared by Ida Smedley (289) by the action of phosphorus pentachloride on fluorenone. It formed large color-

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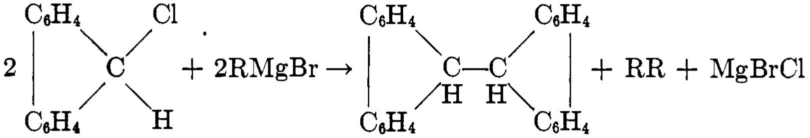
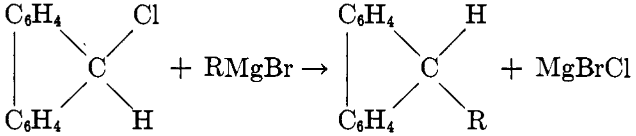
[9] Hydriodic acid is one of the best reducing agents for accomplishing the transition from fluorenols to fluorenes. See Vanscheidt (J. Russ. Phys. Chem. Soc. **58**, 139 (1926); Chem. Abstracts **21**, 581 (1927)).

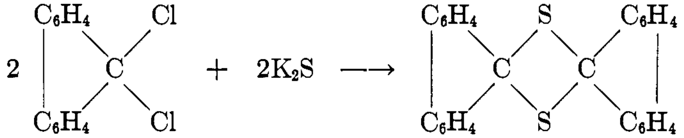
less prisms melting at 103°C. Schmidt and Wagner (271, cf. 294) gave the melting point as 99°C. The dichloride proved to be a very reactive substance. Warming with hydroxylamine or phenylhydrazine gave fluorenone oxime and fluorenone phenylhydrazone, respectively. Treatment with alcoholic potassium hydroxide yielded 9,9-diethoxyfluorene; with phenol 9,9-diphenoxyfluorene was obtained.

Miller and Bachman (199) investigated the value of 9-chlorofluorene for synthetic purposes. It was found to undergo two types of reactions with alkyl magnesium halides.


(I)

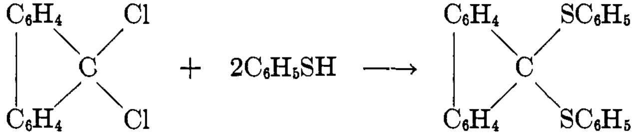

(II)

Several sulfur compounds of fluorene have been prepared from fluorenone dichloride. Ida Smedley (289) prepared thiofluorenone from potassium sulfide and the dichloride. It was an intense red in color. Bergman and



Hervey maintained that Smedley's compound was a disulfide (26).

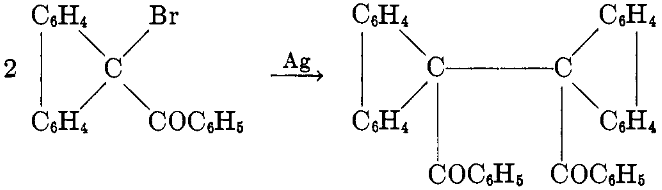
On heating phenyl mercaptan for a long period with 9,9-dichlorofluorene in benzene solution 9,9-diphenylmercaptofluorene was formed. Other reactions of this type have also been studied (25, 30, 191, 197, 275, 276, 277, 278).



9-Bromofluorene has been prepared in good yields by the action of hydrogen bromide on fluorenol (2, 154, 292).

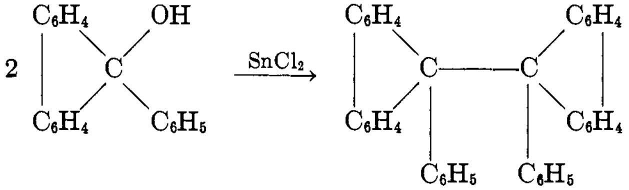
Fluorene derivatives in which one of the hydrogen atoms on the 9-carbon atom is replaced by an alkyl or aromatic radical and the other hydrogen atom by chlorine or bromine may be synthesized easily by the action of the Grignard reagent on fluorenone followed by treatment with the phosphorus or hydrogen halide (231, 259). Hydriodic acid reduces the hydroxyl group and $(C_6H_4)_2CHR$ is obtained.

These halogen compounds serve as the starting point for the synthesis of symmetrically substituted ethanes involving the fluorene molecule (see page 320). The ethanes are very easily oxidized, usually on exposure to air, to give peroxides. Several cases of the formation of free radicals have added to the interest of these compounds. For example, 9-bromo-9-benzoylfluorene on treatment with silver powder gave dibenzoylbifluoryl.



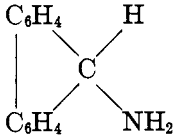
The hot colored solutions of this compound did not obey Beer's law. This led to the assumption of the presence of the free radical, benzoylfluoryl (115).

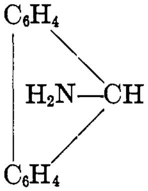
Compounds of the type $[(C_6H_4)_2ArC—]_2$ have been prepared by Gomberg and Cone (122) and have been shown by Schlenk, Herzenstein, and Weickel (260) to form free radicals. Schniepp and Marvel (273) investigated di-*p*-alkylphenylbiphenyleneëthanes and the effect of the *p*-alkyl group on the dissociation of the ethane (cf. 122, 259, 260). All the compounds readily formed peroxides. The reduction of 9-substituted fluorenols with stannous chloride constitutes another method of preparing these dimolecular compounds. For example, on boiling an acetic acid solution of 9-phenylfluorenol for 15 min. with stannous chloride a good yield of 1,1-diphenyl-2,2-dibiphenyleneëthane was obtained (323).



C. *9-Aminofluorene and derivatives*

The intensive investigation of 9-aminofluorene was largely due to the isomerism attributed to it by Schmidt and Stützel (270). Previously Wegerhoff (328) had reported that it melted between 50° and 60°C. Kerp (159) gave a melting point of 161°C., but the compound melting at this temperature was shown by Kuhn and Jacob (180) to be the acetate. Schmidt and Stützel prepared the amine by reduction of fluorenone oxime with zinc and acetic acid. They reported that the principal product was the α-form, which melted at 53–55°C. A β-form, which melted at 123°C., was also isolated. The latter form was converted into the α-form by boiling in solvents. The two modifications, however, yielded identical derivatives, with the exception of the phenylcarbamide derivative. They prepared the symmetrical thiourea, the hydrochloride, and the acetyl compound. Schmidt and Stützel supposed this to be a case of *cis–trans* isomerism. This would, however, require a folded ring type of stereoisomerism (see section XVIII).

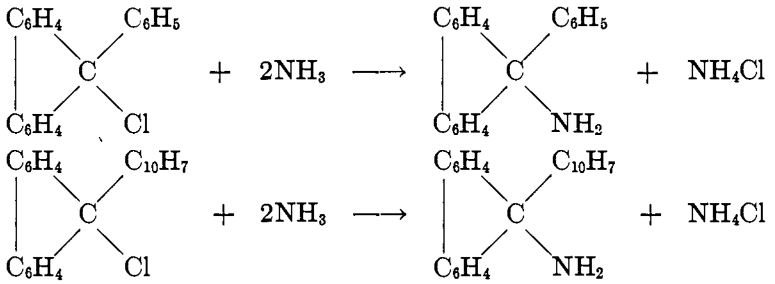




Kuhn and Jacob (179), in their reinvestigation of the reduction, claimed to have isolated the α-form but not the β-form; however, they reported a γ-form that melted at 64°C. Kliegl, Wünsch, and Weigele (165) stated emphatically that only one 9-aminofluorene exists. Ingold and Wilson (155) have recently improved the preparation of 9-aminofluorene from fluorenone oxime by reduction with zinc. 9-Aminofluorene, by this method, was obtained as needles from ligroin, melting at 62–63°C. We have carried out this preparation several times with excellent results, and think that no doubt most of the conflicting results in the investigation of this compound have been due to its relative instability in air and its tendency to absorb carbon dioxide. It is probable that the β-form was the carbonate.

Ingold and Wilson (155) have shown that 9-aminofluorene reacts with ketones in the usual way to give Schiff bases. Using acetophenone and fluorenone as ketones, they obtained α-phenylethylidene-9-aminofluorene, $(C_6H_4)_2CHN{=}C(CH_3)C_6H_5$, and fluorylidene-9-aminofluorene, $(C_6H_4)_2CHN{=}C(C_6H_4)_2$.

The reactivity of fluorenes with halogen substituted in the 9-position would lead us to expect an easy preparation of 9-aminofluorene by treatment with anhydrous ammonia. Courtot and Peticolas (56), using 9-chlorofluorene and liquid ammonia, obtained only traces of the primary amine, together with the secondary amine and dibiphenyleneëthylene. It seems to us that this reaction is influenced by the labile nature of the hydrogen in the 9-position, because when this hydrogen was replaced by a relatively large group, such as phenyl or naphthyl, the compound reacted normally with ammonia to give the 9-substituted primary amine. Thus Pinck and Hilbert (231) readily prepared 9-phenyl-9-aminofluorene and 9-α-naphthyl-9-aminofluorene by this reaction. The secondary amine could be

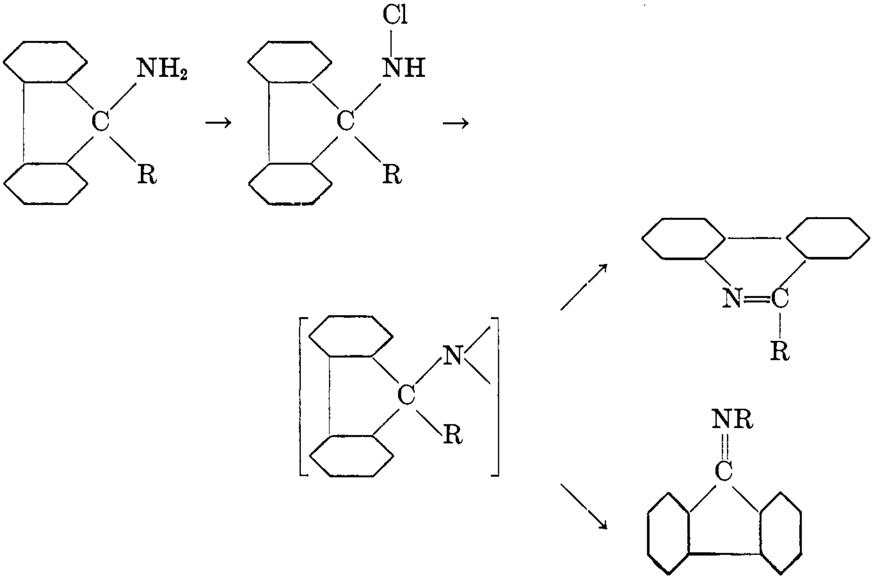


formed by using an excess of ammonia in a steel bomb at 180°C. A result similar to Courtot's was experienced in attempting to prepare 9-methyl-9-aminofluorene from 9-methyl-9-bromofluorene and ammonia. Dibiphenyleneëthylene, the secondary amine, and the primary amine were the products of the reaction.

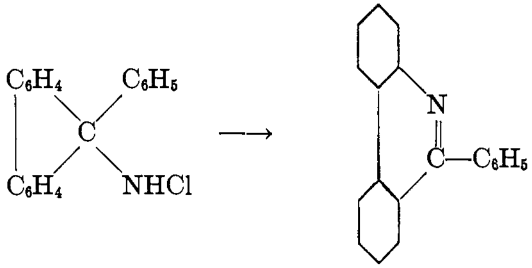
The character of the group attached to nitrogen also seems to have an important effect upon the course of the reaction. If aromatic or aliphatic primary amines were used the reaction took place smoothly. Courtot and Peticolas (cf. 242 and 154) in this way prepared *N*-phenyl-9-aminofluorene (fluorylaniline), *N*-*p*-tolyl-9-aminofluorene, and *N*-α-naphthyl-9-aminofluorene. (Cf. page 304 for di-9-fluorylamine $[(C_6H_4)_2CH]_2NH$.)

Compounds of the type $(C_6H_4)_2CHNHR$ may also be prepared by the reduction of *N*-substituted ketimines of fluorenone.

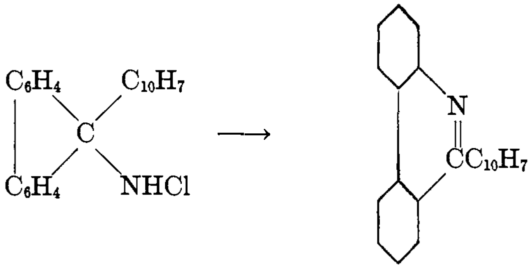
Recently Pinck and Hilbert (231) have published the results of an investigation into the application of the Stieglitz rearrangement (233). In an *N*-substituted 9-aminofluorene, stabilization can be attained by undergoing two types of rearrangement.



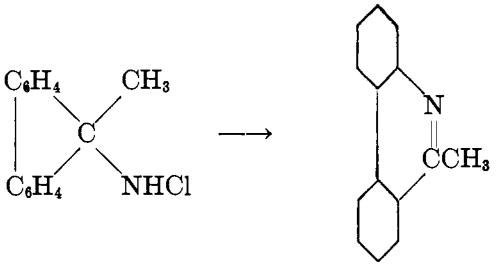
Two products are then theoretically possible, either a phenanthridine derivative or an imine. Pinck and Hilbert reasoned that the strained condition of the cyclopentadiene ring should favor the opening of the ring with subsequent reformation to give the phenanthridine type. This was found to be true. The monochloroamines[10] of 9-phenyl-9-aminofluorene, 9-α-naphthyl-9-aminofluorene, and 9-methyl-9-aminofluorene were prepared by treating alcoholic solutions of the amines with hypochlorous acid. Their rearrangement was accomplished in an anhydrous pyridine[11] solution of the chloroamine with excess dry sodium methylate.



9-Phenylphenanthridine



9-α-Naphthylphenanthridine



9-Methylphenanthridine

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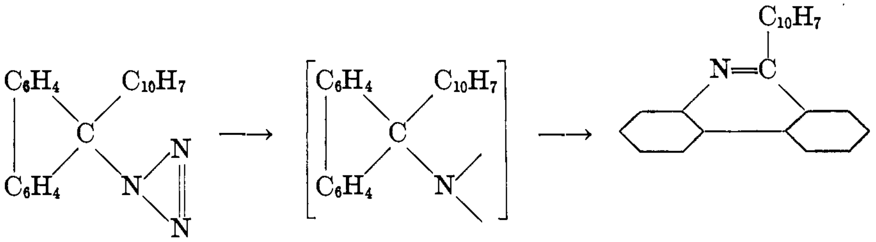
[10] The dichloroamine was obtained by passing an excess of chlorine into an alcoholic solution of 9-phenyl-9-aminofluorene. It is remarkably stable.

[11] The purpose of the pyridine was to catalyze the removal of hydrogen chloride. Color changes during the reaction indicated an intermediate compound, possibly of the free radical type.

Similarly 9-α-naphthylphenanthridine was also prepared by the thermal decomposition of 9-α-naphthyl-9-fluoreneazide (231).



In none of these reactions was any imino derivative formed. It was concluded that the strained condition of the five-membered ring instead of the relative electronegativeness of the substituents of the tertiary carbon atom was probably the factor controlling the rearrangement of the intermediate compound.

In 1930 Nakamura (214) reported that the hydrochloride of 9-aminofluorene showed a very definite local anesthetic action when applied to the tongue. The hydrochlorides of the three amino compounds prepared by Pinck and Hilbert (231) also possess this property. We have confirmed Nakamura's experience with 9-aminofluorene. We have also prepared 2-benzoyl-9-aminofluorene and find that although the local anesthetic action of its hydrochloride is slower to take effect it is more intense and prolonged.

D. Fluorene-9-carboxylic acids

Fluorene-9-carboxylic acid (biphenyleneacetic acid) has been obtained in a variety of ways (50, 69, 109, 324, 325). Several of the indirect methods have already been described. The most direct method of preparation is, of course, the reaction between 9-sodium fluorene and carbon dioxide. Schlenk and Bergmann (257) prepared the sodium compound by treating fluorene with the sodium derivative of triphenylmethane. These authors reported two forms of the acid, the α-form melting at 222°C. and the β-form melting at 232°C. Kliegl (164) repeated the work and obtained only one compound which melted at 221–223°C. with slight evolution of gas. Characteristic derivatives have been prepared by Stollé and Wolf (302) and Wislicenus and Ruthing (343). Fluorene-9-carbonyl chloride was obtained from the acid by the action of thionyl chloride.[12] It formed unstable crystals which were hydrolyzed by water with extraordinary ease.

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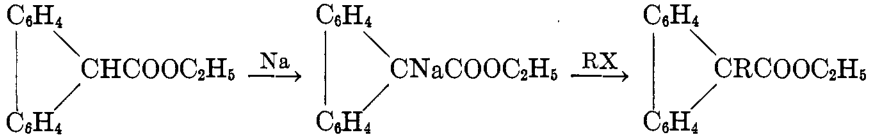
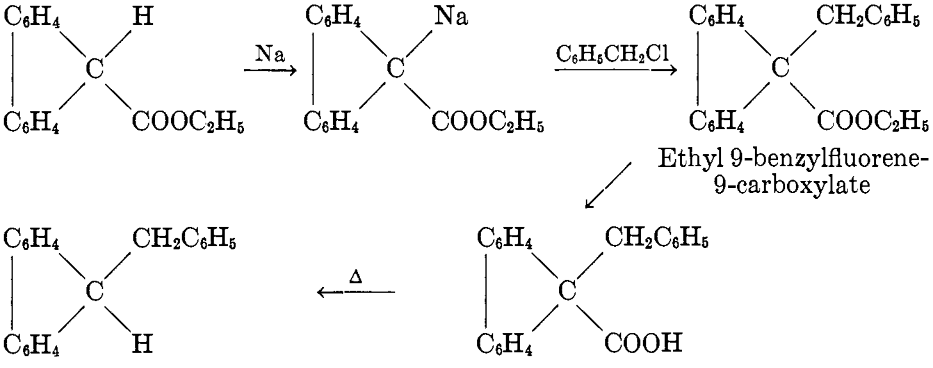
[12] If 2 parts of thionyl chloride are used, dibiphenylenesuccinyl dichloride, $(C_6H_4)_2C(COCl)C(COCl)(C_6H_4)_2$, is formed. Further heating (200 hr.) with an excess of thionyl chloride gives 9-chlorofluorene-9-carbonyl chloride, $(C_6H_4)_2Cl$-$(COCl)$.

The anilide was formed from either the chloride or the ethyl ester by action with aniline at 150°C.; it was a white crystalline powder, melting at 255°C. The amide, $(C_6H_4)_2CHCONH_2$, prepared from the chloride and ammonia, crystallized in needles, melting at 251°C. Adickes (2) reported the preparation of the ethyl ester in 90 per cent yields.

Wislicenus and Mocker (340, cf. 292) found that ethyl fluorene-9-carboxylate itself formed a sodium or potassium derivative which reacted easily with organic halides. The metal derivative was very sensitive to atmospheric oxygen and the reaction was carried out in an atmosphere of hydrogen. The substituted esters were saponified by boiling with potassium hydroxide, but care was needed, since carbon dioxide was split out on long boiling. The free acids, $(C_6H_4)_2CRCOOH$, also lost carbon dioxide on heating to about 250°C. Since all these reactions proceed smoothly and fluorene-9-carboxylic acid is easily obtained, this method constitutes a very convenient one for the synthesis of 9-substituted derivatives of fluorene. For example, 9-benzylfluorene was synthesized in the following way:





Ethyl 9-benzylfluorene-9-carboxylate

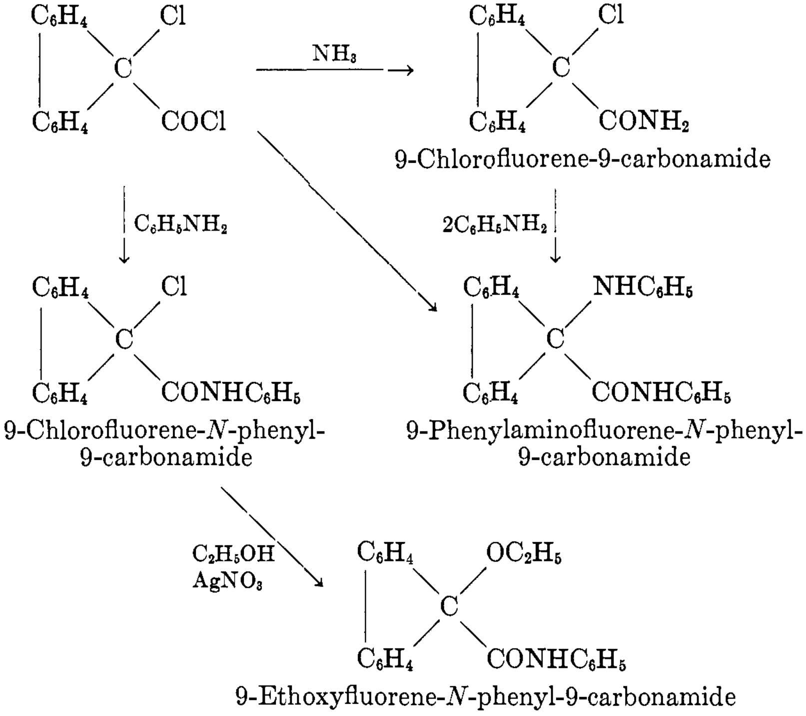
9-Benzylfluorene

9-Benzylfluorene-9-carboxylic acid

Wislicenus and Mocker (340) prepared a number of similar derivatives, as did Ruhemann (248).

Perhaps the best known 9-derivative of fluorene-9-carboxylic acid is 9-hydroxyfluorene-9-carboxylic acid, $(C_6H_4)_2C(OH)COOH$, usually called biphenyleneglycolic acid. As stated before, it is easily obtained from phenanthraquinone by heating with aqueous alkali. Klinger (166) prepared it in 94 per cent yields by heating 1 part of phenanthraquinone with 10 parts of 20 per cent sodium hydroxide for 3 hr. at 70–80°C. The esters were prepared by the use of hydrogen chloride with the proper alcohol. The hydroxyl radical was easily replaced, for even a small excess of hyrogen chloride in the esterification gave rise to the 9-chloroester. The methyl hydroxy ester melts at 159°C. and the ethyl ester at 92°C. (109).

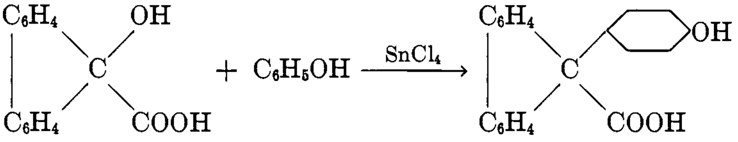
Phosphorus pentachloride reacted with biphenyleneglycolic acid to give 9-chlorofluorene-9-carbonyl chloride, $(C_6H_4)_2CClCOCl$, in good yields. Klinger (166, 167) prepared several derivatives of this compound, as shown below.



The analogous bromine compound (9-bromofluorene-9-carbonyl bromide) was prepared by heating biphenyleneglycolic acid with phosphorus tribromide; it reacted similarly to the chloro compound.

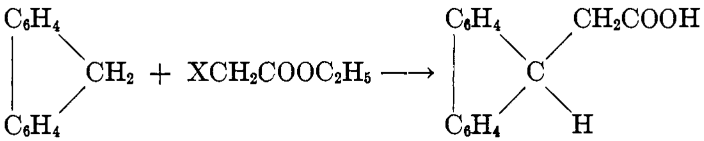
Bistrzycki and von Weber (31) studied the condensation of phenols and phenyl ethers with biphenyleneglycolic acid, using concentrated sulfuric acid or stannic chloride as the condensing agent. For example, 9-*p*-

hydroxyphenylfluorene-9-carboxylic acid was prepared by boiling biphenyleneglycolic acid and phenol in benzene solution containing some



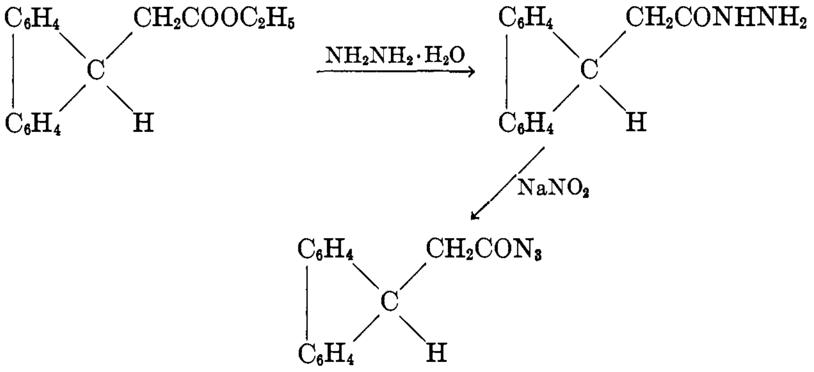
stannic chloride. Some of the *o*-hydroxylactone was also formed, showing that condensation took place to a small extent in the ortho position. On heating or boiling in aqueous sodium carbonate solution this and other similar compounds lost carbon dioxide to give 9-fluorene derivatives.

Fluorene-9-acetic acid, $(C_6H_4)_2CHCH_2COOH$, is closely related to 9-hydroxyfluorene-9-carboxylic acid and may be considered here. It was most simply prepared by heating a monohalogenoacetic ester with fluorene at a relatively high temperature in the presence of alkali (347).



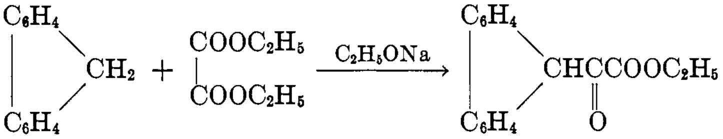
Other methods have also been reported (193, 339, 340). Zimmerman and Wilcoxon (349), in their recent experiments on the effect of various compounds upon the growth of plants, found that fluorene-9-acetic acid had some effect in producing root initiation.

Sieglitz and Jassoy (285) prepared fluorene-9-acethydrazide by boiling ethyl fluorene-9-acetate with hydrazine hydrate. The acid azide was obtained in quantitative yields by treating the hydrazide in acetic acid with sodium nitrite.

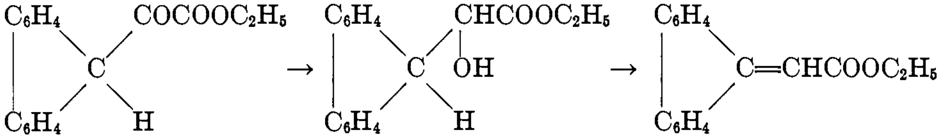


E. 9-Fluoryloxalic ester and 9-formylfluorene

In 1900 Wislicenus (337) described the condensation of ethyl oxalate with fluorene in the presence of sodium ethylate to give ethyl 9-fluoryloxalate.



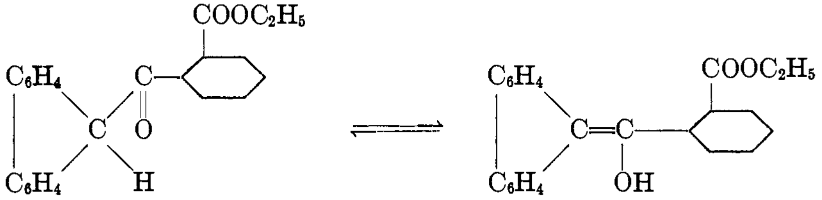
It formed intensely yellow needles. On hydrolysis it gave the acid, $(C_6H_4)_2CHCOCOOH$ (338). Reduction (283, 285, 346) with aluminum amalgam in alcoholic sodium hydroxide gave some ethyl fluorene-9-hydroxyacetate, but dehydration took place largely, giving ethyl 9-fluorylideneacetate (ethyl dibenzofulvenecarboxylate).



This was not unexpected, in view of Courtot's results with compounds of this same type. Reduction with zinc amalgam in dilute hydrochloric acid, however, gave an 80 per cent yield of ethyl fluorene-9-hydroxyacetate (346). Catalytic hydrogenation gave the same result (181).

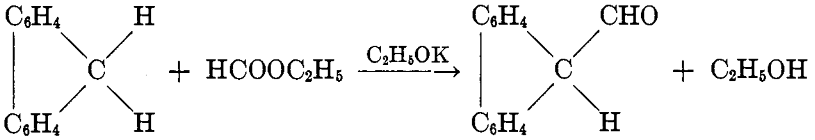
Later Kuhn and Levy (181) repeated Wislicenus' condensation and were struck by the similarity of the color of ethyl 9-fluoryloxalate to that of the yellow fluorylideneacetic acid (dibenzofulvenecarboxylic acid), $(C_6H_4)_2C{=}CHCOOH$, just mentioned. Reasoning on the basis of the color relationship they were led to propose that 9-fluoryloxalic ester might have the enolic structure of α-hydroxy-β-biphenyleneacrylic ester, $(C_6H_4)_2C{=}C(OH)COOC_2H_5$. A thorough investigation supported this view, that is, that 9-fluoryloxalic ester was completely enolized in the crystalline state. The ketonic form predominated in acetic acid solution, as shown by the diminution of the yellow color and by titrations with bromine. If alkali was added to an alcoholic solution of the ester the yellow color deepened. The following tautomerism probably exists.

Wislicenus and Neber (341) had previously shown that a tautomerism of exactly the same type existed in the case of ethyl fluorenephthaloylate.



The two tautomers were capable of isolation and were interconvertible.

Wislicenus and Waldmüller (345, cf. 338) also carried out the condensation of fluorene and ethyl formate, using potassium ethylate as the

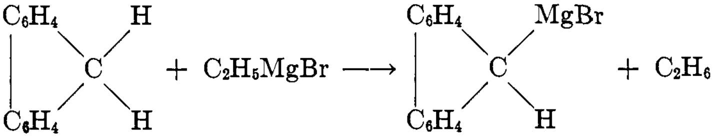


condensing agent, to give 9-formylfluorene (9-fluorylaldehyde). It formed derivatives which were characteristic of the carbonyl group (oxime, phenylhydrazone), but it also formed a derivative with phenyl isocyanate, a reagent for the hydroxyl group (342). Keto-enol tautomerism was probably present here also.

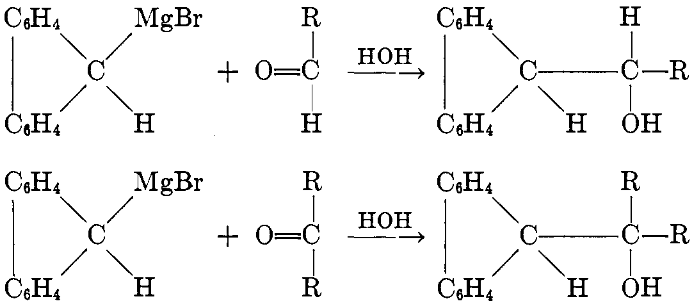
These cases of tautomerism are due to the lability of the hydrogen atom in the 9-position. We may well expect tautomerism in all compounds with a carbonyl group adjacent to the 9-carbon atom.

F. Magnesium derivatives of fluorene

Grignard and Courtot (131) first prepared 9-fluorylmagnesium bromide by heating fluorene in toluene with ethylmagnesium bromide at 135°C.

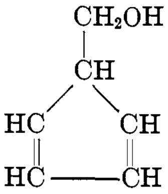


It had all the usual properties of a Grignard reagent and reacted with aldehydes and ketones to give carbinols containing fluorene as a substituent.



As previously mentioned, these carbinols are very easily dehydrated, giving derivatives of 9-methylenefluorene. For example, fluorenone reacted with the fluorylmagnesium bromide, giving an 80 per cent yield of 9-fluoryl-9-fluorenol, $(C_6H_4)_2CHC(OH)(C_6H_4)_2$, which on treating with hydrogen chloride in a boiling acetic acid solution was dehydrated to dibiphenyleneëthylene, $(C_6H_4)_2C{=}C(C_6H_4)_2$.

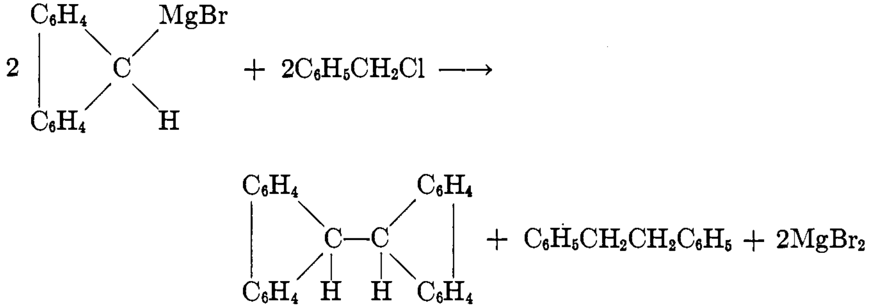
Courtot (51, 130) later extended these reactions of fluorylmagnesium bromide, using various aldehydes and ketones. He named the carbinols as derivatives of fulvanol, the alcohol of Thiele's theoretical fulvene.



Fulvanol

Thus 9-fluorylcarbinol, $(C_6H_4)_2CHCH_2OH$, was termed dibenzofulvanol. A large number of such derivatives and their dehydration products were prepared.

Quite recently Miller and Bachman (199) have studied the Grignard reagent of fluorene. They were unable to duplicate Courtot's (50) preparation of fluorylmagnesium bromide in good yields. By measuring the amount of ethane evolved the reaction was estimated to proceed to only 32 per cent of completion. When the Grignard reagent was heated with benzyl chloride the following somewhat unusual double coupling reaction occurred.

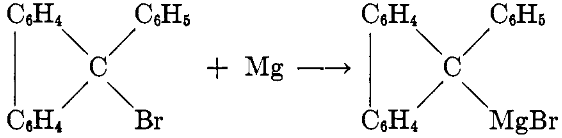


No trace of 9-benzylfluorene was found. Acetyl chloride, on the other hand, reacted normally to give 9-acetylfluorene in good yields.

Miller and Bachman's failure to obtain the Grignard reagent in good yields is not in accord with the results of Zerewitinoff (348), who treated fluorene in pyridine solution with methylmagnesium iodide at 85°C. and obtained 1.04 moles of methane. It is possible that the pyridine catalyzed the reaction. Miller and Bachman used xylene as the solvent, and Courtot used toluene.

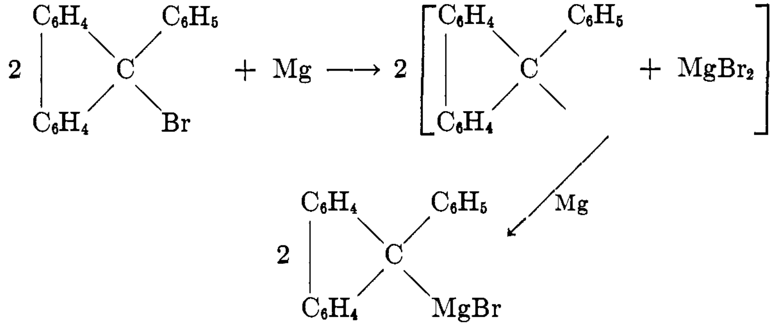
Miller and Bachman also investigated the use of fluoryl lithium, which had been prepared earlier by Schlenk and Bergmann (257) from ethyl lithium and fluorene, and described an improved preparation (199) of this compound.[13] It reacted easily with alkyl bromides or chlorides to give 9-alkylfluorene.

The formation of the Grignard reagent of 9-bromo-9-phenylfluorene has been shown to take place in an illuminating manner (7). If 1 gram-atom of magnesium reacted with 1 mole of 9-bromo-9-phenylfluorene the Grignard reagent was formed normally.



If, however, only 0.5 gram-atom of magnesium reacted, the free radical, 9-phenylfluoryl (phenylbiphenylenemethyl), and magnesium bromide were present at the end of the reaction. On adding an additional 0.5 gram-atom of magnesium to the reaction mixture the free radical was converted to the Grignard reagent.

[13] Miller and Bachman regarded the lithium compound as far more useful than the Grignard reagent in this type of synthesis. It is interesting to note that they were unable to obtain sodium fluorene under usual laboratory conditions (cf. 157).

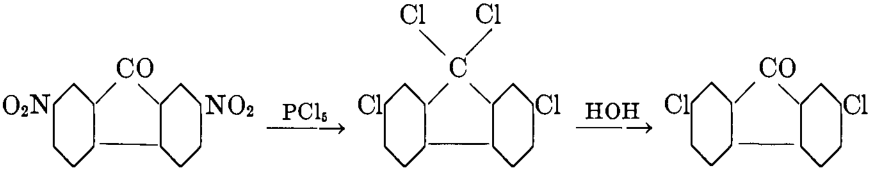


This Grignard reagent was isolated in a crystalline form and analyzed. It reacted normally with carbon dioxide and with water.

IX. NUCLEAR HALOGEN DERIVATIVES

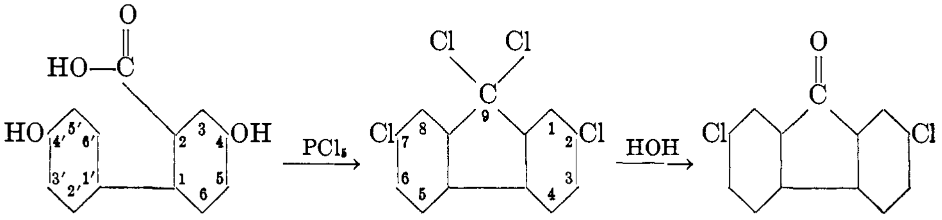
A. Chloro compounds

The first definite work on the chlorination of fluorene was done by Hodgkinson and Matthews (143). The chlorination was carried out in dry chloroform and gave a dichlorofluorene which they reported as 2,7-dichlorofluorene, m.p. 128°C. Oxidation converted it into 2,7-dichlorofluorenone, m.p. 158°C. Schmidt and Wagner (272) obtained a dichlorofluorenone by the action of phosphorus pentachloride on 2,7-dinitrofluorenone, followed by boiling the product formed with water.



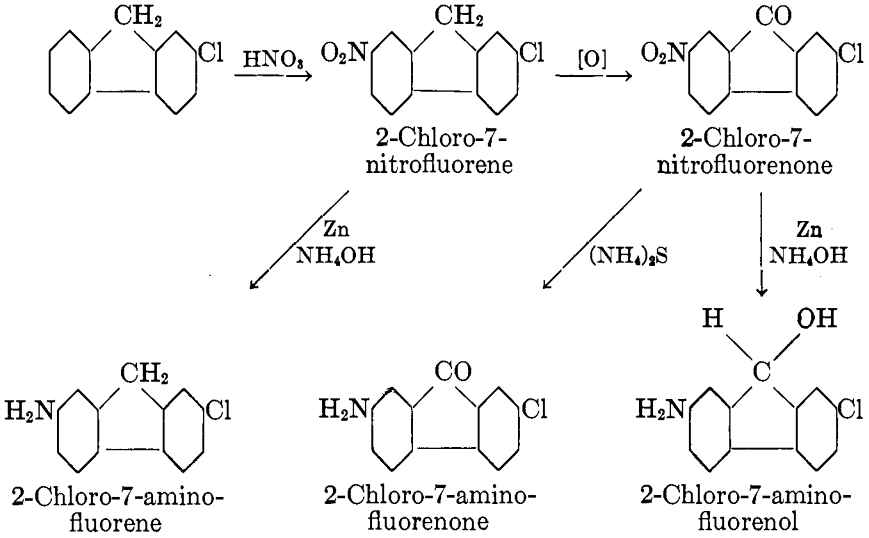
Their compound, m.p. 188°C., was interpreted as being 2,7-dichlorofluorenone. Sieglitz and Schatzkes (287, cf. 120, 32) later showed that Hodgkinson and Matthews' 2,7-dichlorofluorenone was contaminated with 2,7-dichlorofluorene.

Schmidt, Retzlaff, and Haid (267) prepared 2,7-dichlorofluorenone indirectly, thus proving that the chlorine atoms were in the 2- and the 7-positions.



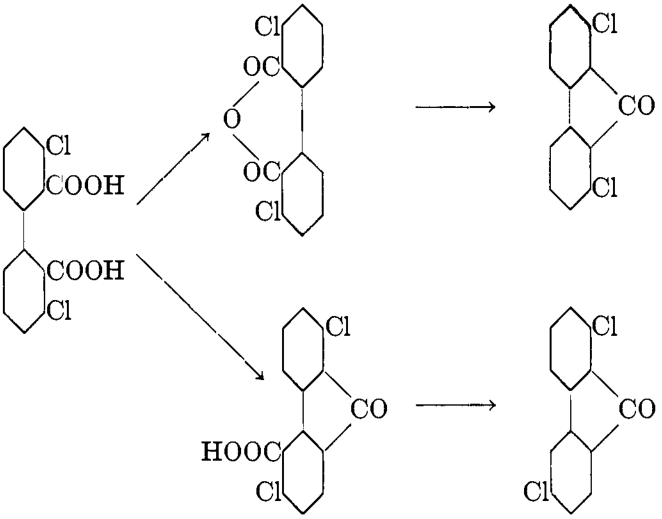
4,4′-Dihydroxybiphenyl-2-carboxylic acid (55)

Courtot and Vignati (58) found that chlorination of fluorene in chloroform at 0–5°C. gave a mixture of the 2-chloro and 2,7-dichloro compounds which was very difficult to separate. Buffle (36), however, stated that 2-chlorofluorene may be obtained in a good yield by chlorinating fluorene in benzene solution at 80°C., using iodine or antimony pentachloride as a catalyst. The preparation of 2-chlorofluorene from 2-aminofluorene by the Sandmeyer reaction was reported by Courtot and Vignati and by Chanussot (40) at about the same time. Oxidation with chromic acid gave 2-chlorofluorenone. Courtot and Vignati (58) reduced the latter compound with zinc and ammonia and obtained 2-chlorofluorenol. 2,7-Dichlorofluorene behaved similarly. These authors also carried out the following reactions:

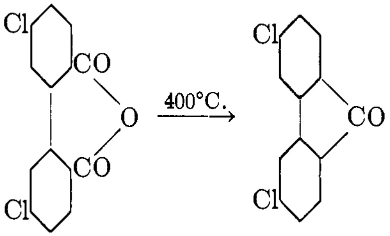


2,7-Dichlorofluorene exhibited a greater reactivity of the methylene group than fluorene itself. Condensation with aromatic aldehydes took place with ease in the presence of a small amount of sodium ethylate (cf. page 313). Many compounds of this type have been prepared by Sieglitz and Schatzkes (287). Some of them were reduced with aluminum amalgam to the corresponding saturated compounds.

Huntress and Cliff (150) succeeded in preparing a number of dichlorofluorenones from various dichlorodiphenic acids and their anhydrides. 1,8-Dichlorofluorenone resulted in quantitative yields from the action of heat on 3,3′-dichlorodiphenic anhydride; however, when 3,3′-dichlorodiphenic acid was heated the product was 1,6-dichlorofluorenone-5-carboxylic acid, from which 1,6-dichlorofluorenone could be obtained by further heating.

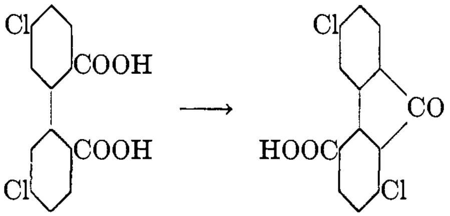


3,6-Dichlorofluorenone was obtained by the pyrolysis of 5,5′-dichlorodiphenic anhydride.

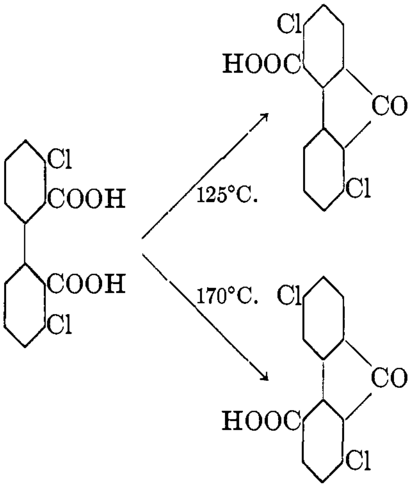


Huntress, Cliff, and Atkinson (151) extended the study of 3,3′-dichlorodiphenic acid and investigated the action of concentrated sulfuric acid upon it. At 125°C. the expected 1,6-dichlorofluorenone-5-carboxylic acid was obtained, but when the temperature was raised to 170°C. a dichlorofluorenonecarboxylic acid was obtained which was different from 1,6-dichlorofluorenone-5-carboxylic acid. In other words, "two isomeric monobasic acids are prepared at different temperatures by the same procedure from the same starting material, when the conventional theory will account for only one." They termed the isomer formed at 170°C. "Acid X." The most curious fact of all is that both isomers had exactly the same melting point (242.5°C.), but the melting point of a mixture of equal parts was approximately 200°C. and their acid chlorides melted at different temperatures. Two other interesting facts were noted. On redissolving 1,6-dichlorofluorenone-5-carboxylic acid in sulfuric acid and heating at 170°C., "Acid X" was formed in a 67 per cent yield. The carboxyl group of "Acid X" was removed and the product was found to be 1,6-dichlorofluorenone, showing "that during the isomerization to 'Acid X' both the fluorenone nucleus and the relative position of the two halogen atoms in it are preserved."

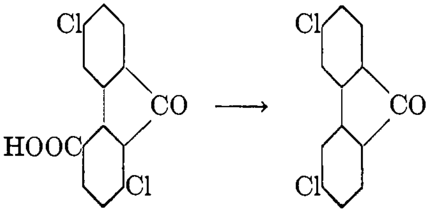
Three years later Huntress and Atkinson (148) were able to establish the constitution of "Acid X" as that of 1,6-dichlorofluorenone-4-carboxylic acid. The acid proved to be identical with the compound obtained by the action of concentrated sulfuric acid on 5,5′-dichlorodiphenic acid. The reaction giving the isomeric acid was thus shown to involve the migration of the halogens. This emphasizes the danger in the use of high temperatures in the synthesis of fluorenones.



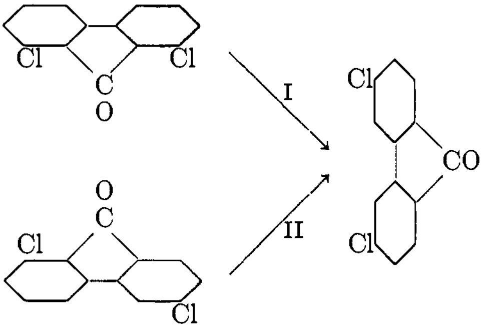
"Acid X"



On attempting to decarboxylate 1,6-dichlorofluorenone-4-carboxylic acid by heating in sulfuric acid it was noted that 3,6-dichlorofluorenone was formed.



Further experiments showed that both 1,8-dichlorofluorenone and 1,6-dichlorofluorenone rearranged to 3,6-dichlorofluorenone on heating in sulfuric acid at 185–200°C.



These rearrangements are unusual, for in rearrangement II the one chlorine atom migrated to a position meta to its original position, and in rearrangement I both chlorine atoms did so. Rearrangements involving meta transpositions are rare, and it seems curious that Huntress and Atkinson did not point this out. It is also noteworthy that the position taken is para to the carbonyl group and meta to the phenyl.

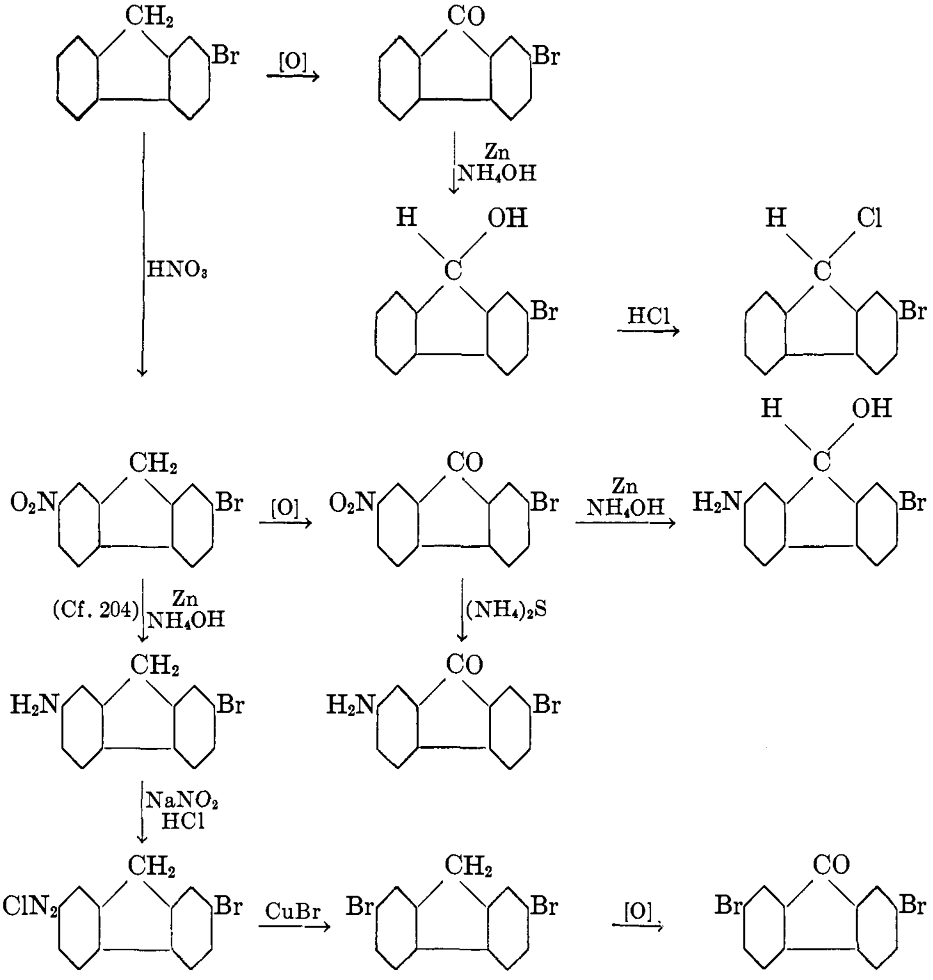
More highly chlorinated compounds, whose orientation is unknown, have been recorded. Holm (145) prepared a trichlorofluorene, m.p. 147°C., by chlorinating fluorene in carbon disulfide. Hodgkinson and Matthews (143) described a "pentachlorofluorenedichloride," $C_{13}H_3Cl_7$, which they obtained in an impure state by chlorinating fluorene in carbon tetrachloride in the presence of iodine. On attempting to carry out an alkali fusion of this compound they encountered serious explosions. Alcoholic potash reacted to give a compound containing fewer chlorine atoms.

B. Bromo compounds

The bromination of fluorene results in the formation of 2-bromofluorene and 2,7-dibromofluorene (12, 15, 46, 143, 145, 282, 313). A synthetic proof of the position of the bromine atom was embodied in the preparation of the corresponding bromofluorenones from the proper phenanthraquinone derivatives (261). Courtot and Vignati (59) prepared 2-bromofluorene from 2-aminofluorene by the Sandmeyer reaction. These authors showed also that bromine entered the same positions when fluorenone is brominated, and also that the bromine atom in 2-bromofluorene may be replaced by an amino group by reaction with ammonia in the presence of copper salts.

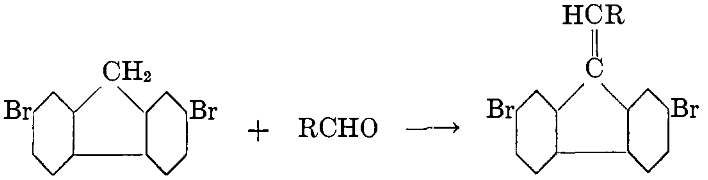
The mixture of 2-bromofluorene and 2,7-dibromofluorene obtained in the bromination proved very difficult to separate (175). Courtot obtained a good separation only after ten recrystallizations from 90 per cent alcohol. Clarkson and Gomberg (46) and Miller and Bachman (199), however, obtained a very good separation by distillation *in vacuo*.

Courtot and Vignati (59) have carried out numerous reactions with 2-bromofluorene, as shown by the following equations:

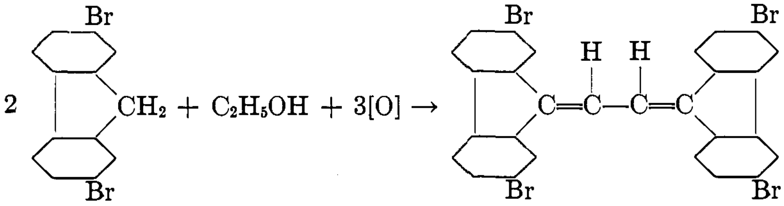


(Cf. 53 and 86)

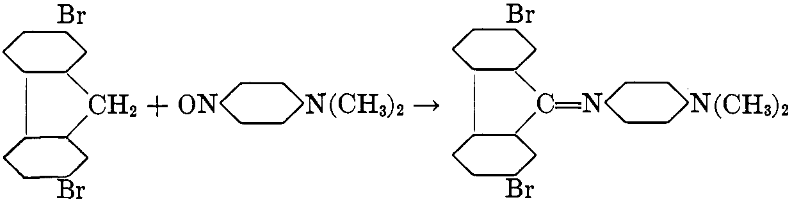
The introduction of the two bromine atoms into the nucleus also enhanced the reactivity of the methylene group. Sieglitz (282b, cf. 182) prepared an impressive list of derivatives by condensing aromatic aldehydes with 2,7-dibromofluorene in alcoholic solution in the presence of sodium ethylate.



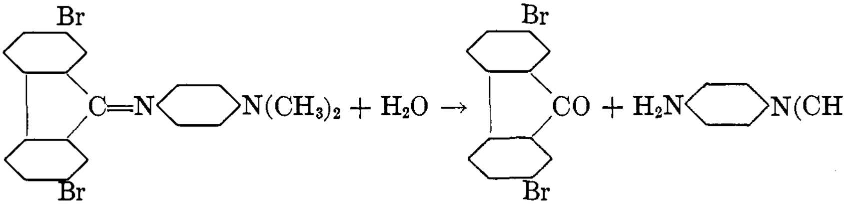
As a by-product of each preparation Sieglitz obtained a small amount of *sym*-tetrabromobiphenylenebutadiene. Stahrfoss (291) showed that it was formed according to the following equation:



Novelli (219) prepared several azomethines by condensing nitroso compounds with 2,7-dibromofluorene, for example, by condensing *p*-nitrosodimethylaniline with 2,7-dibromofluorene in the presence of sodium ethylate.



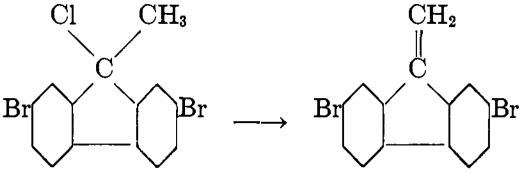
The various azomethines were highly colored and were very sensitive to acids, hydrolysis taking place readily. The yield of 2,7-dibromofluorenone



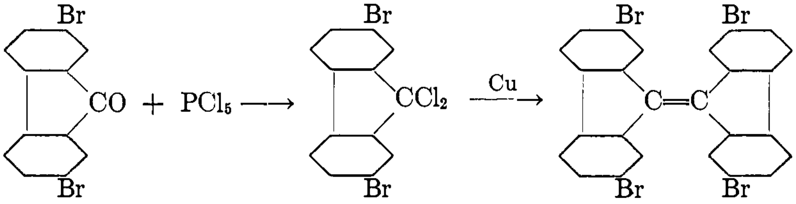
was nearly quantitative, and Novelli recommended this procedure as being more satisfactory than the usual dichromate oxidation.

Sieglitz (283) found that 2,7-dibromofluorene, like fluorene, condensed with ethyl oxalate but with more ease, to give ethyl 2,7-dibromo-9-fluoryloxalate. He then carried out some syntheses with this compound analogous to those previously described.

The enhanced reactivity of groups in the 9-position of 2,7-dibromofluorene is apparent in that 9-methyl-9-chloro-2,7-dibromofluorene may lose hydrogen chloride to give 9-methylene-2,7-dibromofluorene (286).



Schmidt and Wagner (272) synthesized various dimeric compounds from 2,7-dibromofluorenone and 2-bromofluorenone in the following manner:



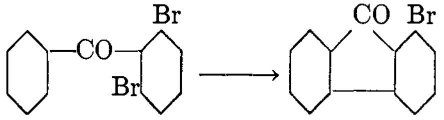
2,7-Dibromofluorenone

2,7-Dibromo-9,9-dichlorofluorene

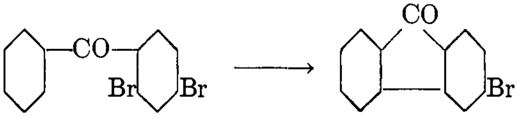
2,2′,7,7′-Tetrabromodibiphenyleneëthylene

The dibiphenyleneëthylene derivative could be reduced catalytically to the corresponding ethane. Chlorine and bromine also added readily to the double bond.

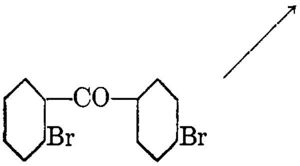
Other bromo compounds in addition to the 2- and the 2,7-derivatives have been prepared. Montagne and Charante (203, 204) synthesized bromofluorenones from bromobenzophenones by boiling them in alcohol for several days.



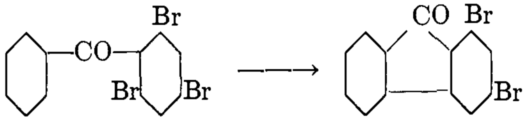
1-Bromofluorenone



3-Bromofluorenone



These reactions are impracticable as methods of preparation, as the yields are very small. Montagne (203) prepared 1,3-dibromofluorenone in a similar way from 2,4,6-tribromobenzophenone. Heating at a temperature of 400°C. for several days was necessary.



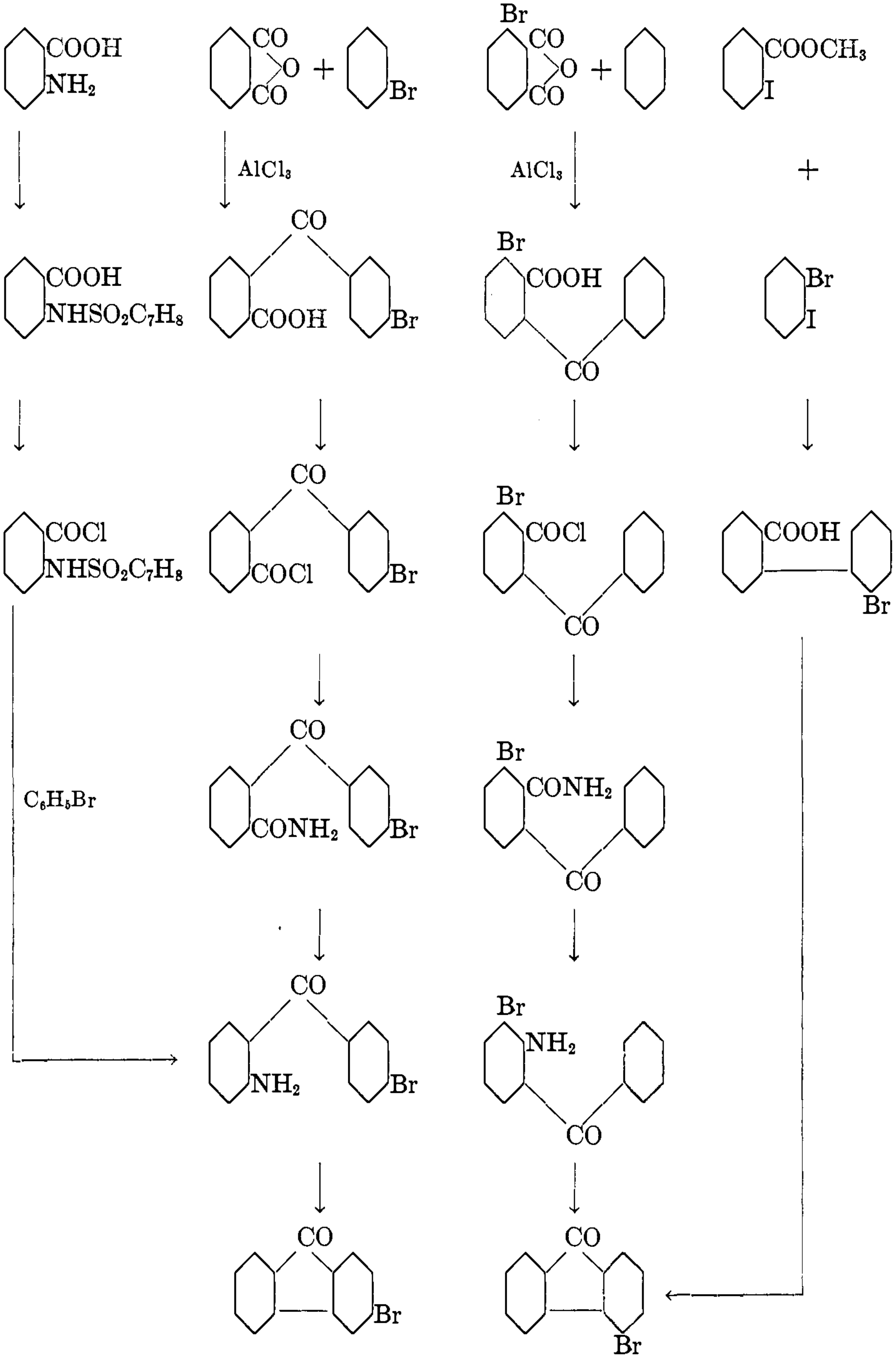
1,3-Dibromofluorenone

The bromine atoms in 1,3-dibromofluorenone are very labile, for on reduction with sodium amalgam only fluorenol is obtained.

Miller and Bachman (200) recently described nuclear syntheses for 3- and 4-bromofluorenones which were suitable for preparative purposes, since they did not require such difficultly obtainable intermediates as was the case with Montagne's method; moreover, the yields were reported to be fairly good despite the number of steps involved. (See formulae on page 344.) Miller and Bachman pointed out that by the application of these methods dibromofluorenones which are yet unknown can be synthesized. The yield of 3-bromofluorenone from phthalic anhydride was 55 per cent and from anthranilic acid 21 per cent. 4-Bromofluorenone was obtained in a 14 per cent yield from methyl-*o*-iodobenzoate and in a 25 per cent yield from bromophthalic anhydride. The last two intermediates were rather difficult to obtain and the syntheses are not so generally applicable. Miller and Bachman found, however, that 4-bromofluorene, which yielded the fluorenone on oxidation, could be obtained in good yields by another method which will be discussed later.

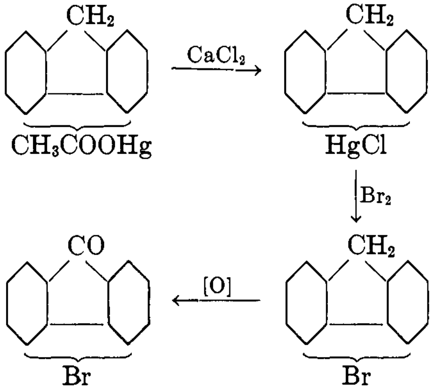
Reduction of the two bromofluorenones (3- and 4-) with zinc dust gave the corresponding fluorenols in excellent yields. The fluorenols could then be reduced to the fluorenes with amalgamated zinc and hydrochloric acid. The lability of the bromine atom in the 3-position noticed by Montagne was also found by Miller and Bachman, for 3-bromofluorenol on reduction with hydriodic acid and phosphorus gave only fluorene. These authors stated that this lability was remarkable "in view of the equally great stability of the bromine atom in the 2-position." Experiments showed that 2-bromofluorene did not yield a Grignard reagent (199) and also that it was only about 50 to 75 per cent as reactive as bromobenzene, as shown by its behavior with potassium phenolate and sodium acetate (186). Miller and Bachman stated that the contrast between the 2-bromo- and the 3-bromo-fluorenes is reminiscent of the somewhat similar contrast in stability offered by the 1-bromo- and the 2-bromo-naphthalenes.

Miller and Bachman also determined the positions in which fluorene mercurates (201). Knowing the properties of all the four possible mono-



3-Bromofluorenone 4-Bromofluorenone

bromofluorenones they could easily determine the position in which mercuration took place by the following scheme:



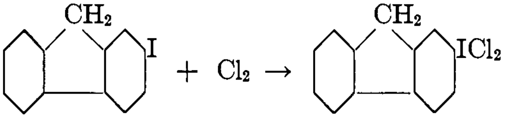
Applying this method they found that fluorene in the presence of acetic acid mercurated in the 4-position, but in the absence of solvents some of the 3-isomer was formed. Fluorene-4-mercuric acetate, when treated with alcoholic calcium chloride, gave fluorene-4-mercurichloride which on subsequent bromination yielded 4-bromofluorene, thus providing a simple synthesis for this isomer. 3-Bromofluorene was obtained in a similar manner from fluorene-3-mercuriacetate. Neither of the two mercury compounds prepared by Miller and Bachman corresponded to the mercury compound reported by Goswami and Das Gupta (123), who used the same method of mercuration.

More highly brominated fluorene compounds have been reported, but their constitution is unknown. A tribromofluorene and a tetrabromofluorene have been described by Barbier (15). Schmidt and Bauer (261) obtained a tribromofluorene which on oxidation yielded a tribromofluorenone identical with the compound prepared by brominating 2,7-dibromofluorenone. The position of the third bromine atom is doubtful. Eckert and Langecker (87) brominated 2-aminofluorene and obtained tribromo-2-aminofluorene. On oxidation and removal of the amino group a tribromofluorenone was obtained. They also brominated some 2-methoxy compounds.

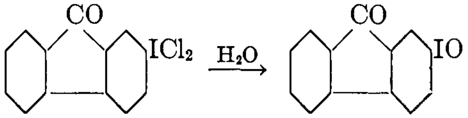
C. Iodo and fluoro compounds

Work upon iodine-substituted compounds is still in the preliminary stages, as only the 2-iodofluorene is known. Chanussot (39) and Courtot (53) have prepared 2-iodofluorene from the diazo compound. Oxidation with dichromate and acetic acid gave 2-iodofluorenone.

Chanussot (41) carried out reactions with 2-iodofluorene and 2-iodofluorenone analogous to those undergone by iodobenzene. Fluorene-2-iodo dichloride was prepared in quantitative yields by passing chlorine into a chloroform solution of 2-iodofluorene.



The dichloride decomposed at 70–75°C. to a white substance which was probably 2-iodo-7-chlorofluorene. 2-Iodofluorenone formed a similar dichloride. On shaking fluorenone-2-iodo dichloride with pyridine and water good yields of 2-iodosofluorenone were obtained.



Fluorene-2-iodo dichloride reacted similarly, giving 2-iodosofluorene. Both 2-iodofluorene and 2-iodofluorenone were oxidized by hypochlorous acid to the corresponding iodoxycompounds which exploded violently on heating.

Bergmann, Hoffman, and Winter (27) prepared 2-fluorofluorene and 2-fluorofluorenone from the amines by the diazo reaction, using fluoroboric acid. 2-Fluorofluorenone reacted with phosphorus pentachloride to give 9,9-dichloro-2-fluorofluorene, which could be used to synthesize the usual dimeric compounds.

The only other known fluoro compound was prepared by Stoughton and Adams (303) from 2-nitro-6-carboxy-2′-fluoro-5′-methylbiphenyl (see page 300).

As can be seen, much remains to be done on the iodine and fluorine derivatives.

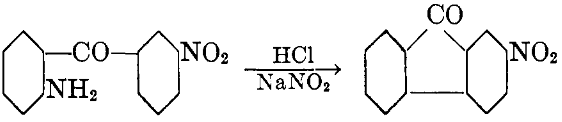
X. NITRO AND AMINO COMPOUNDS

A. Mononitro and monoamino compounds

The nitration of fluorene has received considerable attention from a number of investigators. During the course of their researches many conflicting statements have been made. At the present time, however, the structures of the majority of the compounds are known with reasonable certainty.

The first product formed on the nitration of fluorene or fluorenone proved to be the 2-nitro compound (15, 27, 71, 111, 205, 209, 261, 280, 304).

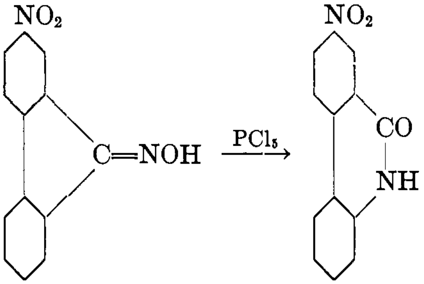
A convenient preparation of 2-nitrofluorene has been described by Kuhn (221) and is based on the procedure of Diels (71). 2-Nitrofluorene crystallized from hot glacial acetic acid in light yellow prisms, m.p. 157°C. Oxidation with chromic acid or permanganate gave 2-nitrofluorenone, m.p. 217–218°C. Ullmann and Mallett (316) prepared it indirectly by diazotizing 2-amino-3-nitrobenzophenone.



Gerhardt (111) prepared the hydrazone, which on long boiling in alcohol gave 2-nitrofluorenone ketazine.

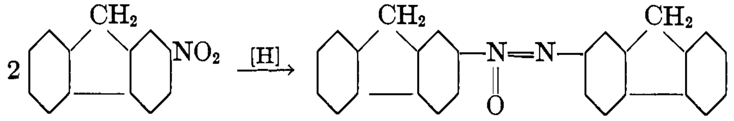
2-Nitrofluorene, like fluorene, will condense with aromatic aldehydes. Loevenich and Loeser (187) carried out a long series of these condensations, using sodium ethylate as the condensing agent. Candea and Macovski (37) extended this work, using piperidine as the condensing agent.

Moore and Huntress (206) prepared 2-nitrofluorenone-5-carboxylic acid by the action of concentrated sulfuric acid on 4-nitrodiphenic acid. It was a pure yellow substance. By means of the Hofmann reaction 5-amino-2-nitrofluorenone, deep scarlet in color, was prepared. The same authors showed that the oxime of 2-nitrofluorenone underwent a normal Beckmann rearrangement and gave a 90 per cent yield of 7-nitrophenanthridone (206). This was, therefore, the *syn*-form.



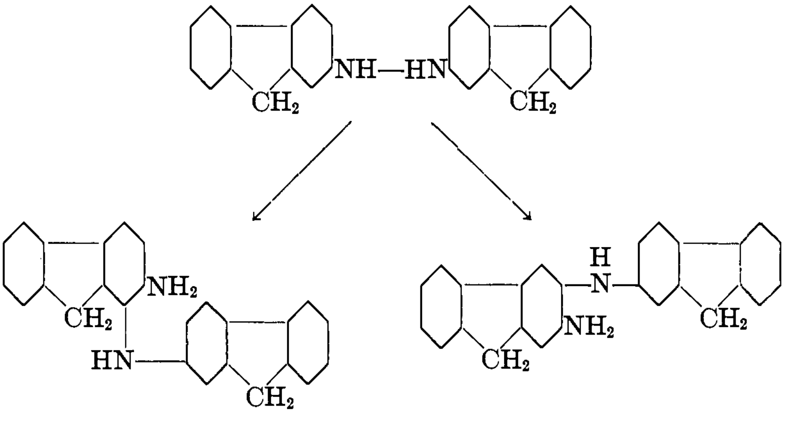
There is a possibility of two stereoisomeric forms of 2-nitrofluorenone oxime. The oxime was prepared by Moore and Huntress from fluorenone, hydroxylamine hydrochloride, and alcohol (representing an acid solution) and had a melting point of 262.5–263°C. Langecker (183, cf. 149) prepared the oxime in the same way, but used in addition barium carbonate (i.e., a neutral solution), and found the melting point to be 249°C. This may well be the *anti*-form.

Cislak, Eastman, and Senior (44) investigated the reduction of 2-nitrofluorene using Diels' method (zinc, dilute alcohol, and calcium chloride), but employed only one-tenth the usual amount of zinc. The product of



this reaction was reported to be 2,2′-azoxybisfluorene, m.p. 279°C. This compound was characterized by its almost complete insolubility in ordinary organic solvents; by virtue of this insolubility it escaped further reduction, as shown by attempts to reduce a suspension of it in alcohol with zinc and acetic acid. An attempt was made to oxidize it to the corresponding fluorenone, using dichromate and acetic acid, but even prolonged boiling caused no oxidation. This is very unusual in view of the fact that all other fluorene compounds are oxidized to the corresponding fluorenones under these conditions.

The compound was found, however, to be soluble in phenol, in which it was reduced with zinc and hydrochloric acid. The main product was 2-aminofluorene, but in addition a small amount of another substance was formed. It was proved that the substance was not 2,2′-hydrazobisfluorene or 2,2′-azobisfluorene. They concluded that the hydrazo compound was formed during reduction and then had undergone a rearrangement of the *o*-semidine type. The following two compounds were then possible.



2-Amino-1,2′-difluorylamine 2′-Amino-2,3′-difluorylamine

There is no evidence as to which was the correct formula, but an investigation of the compounds formed on acetylation showed that it was either one or the other. Cislak, Eastman, and Senior made the statement that

2-nitrofluorene when boiled with ammonium sulfide was not reduced to the amino compound, while 2-nitrofluorenone under the same conditions was easily reduced to 2-aminofluorenone. Courtot and Vignati reported the reduction of 2-chloro-7-nitrofluorene to the corresponding amine by ammonium sulfide as previously stated.

The complete reduction of 2-nitrofluorene gave 2-aminofluorene, which crystallized in straw-colored needles melting at 127°C. It was first prepared by Strasburger (304) from 4-aminodiphenic acid. Diels (71) used zinc dust and calcium chloride with dilute alcohol to reduce 2-nitrofluorene, while Austin (6) employed stannous chloride in acid solution. Bennett and Noyes (22) have reported excellent yields of 2-aminofluorene, using catalytic reduction with hydrogen and platinum oxide. Diels (71) prepared a number of derivatives (cf. 21) of 2-aminofluorene, such as 2-fluorenediazonium chloride, which crystallized out as small yellow crystals and was stable in warm water, but on boiling decomposed to 2-hydroxyfluorene. The hydrazine was prepared from the diazo compound by reduction with sodium bisulfite.

A quinoline derivative was prepared by Diels and Staehlin (73) from 2-aminofluorene. Later Loevenich and Loeser (188) and I. Kh. Fel'dman (93) extended this work.

Ray and Rieveschl have prepared 2-isocyanofluorene from 2-aminofluorene and phosgene; it reacted instantly with amines and alcohols to give ureas and urethans of fluorene (241).

The reduction of 2-nitrofluorenone to 2-aminofluorenone has usually been accomplished with ammonium sulfide (21, 22, 71, 111); other reducing agents also reduce the carbonyl group in the 9-position. 2-Aminofluorenone is a deep red compound melting at 163°C. The diazo compound is unusually stable and may be crystallized from warm water. It decomposes, when dry, at 128°C. Diazo compounds of both 2-fluorene and 2-fluorenone react normally in the Sandmeyer reaction (53).

Several other mononitro derivatives involving other than the 2-position are known. 1-Nitrofluorenone is at present unknown; however, 1-aminofluorenone was prepared by Goldschmiedt (117) from fluorenone-1-carbonamide by the Hofmann reaction. It is interesting to note that only a very few 1-substituted fluorenones or fluorenes have been prepared, despite the fact that as early as 1902 Goldschmiedt provided the basis for the synthesis of a great number of such derivatives.

Eckert and Langecker (87) prepared 3-nitrofluorenone by the deamination of 2-amino-3-nitrofluorenone (the preparation of which will be discussed later). They converted their supposed 3-nitrofluorenone to the amine and thence to the known 3-hydroxyfluorene, thus proving its structure. They gave the melting point of 3-nitrofluorenone as 210°C. This agrees with the value reported by Schmidt and Soll (269), who obtained it from 3-nitrophenanthraquinone by the benzilic acid rearrangement followed by oxidation. The latter authors prepared the oxime by heating the ketone and hydroxylamine hydrochloride together in alcoholic solution. They obtained a compound, melting at 240°C., which analyzed correctly for nitrogen.

Bardout (16) prepared 3-nitrofluorenone, both by Eckert and Langecker's method and by a modified method, and reported it as melting at 232°C. (239°C., corr.). He converted it to the known 3-hydroxyfluorenone (90) and to the methoxyfluorenone (314). The bromo derivative was reported as melting at 165.5°C. (corr.). Miller and Bachman (200) gave a melting point of 162°C., apparently uncorrected. Bardout's oxime melted at 217°C. (221°C., corr.). Bardout failed to find any trace of a possible isomer.

Two Japanese investigators, Hayashi and Nakayama (138), have confirmed Bardout's preparation of 3-nitrofluorene, but did not oxidize it to the fluorenone. They reduced it to 3-aminofluorene, m.p. 151.5–152°C., by means of stannous chloride.

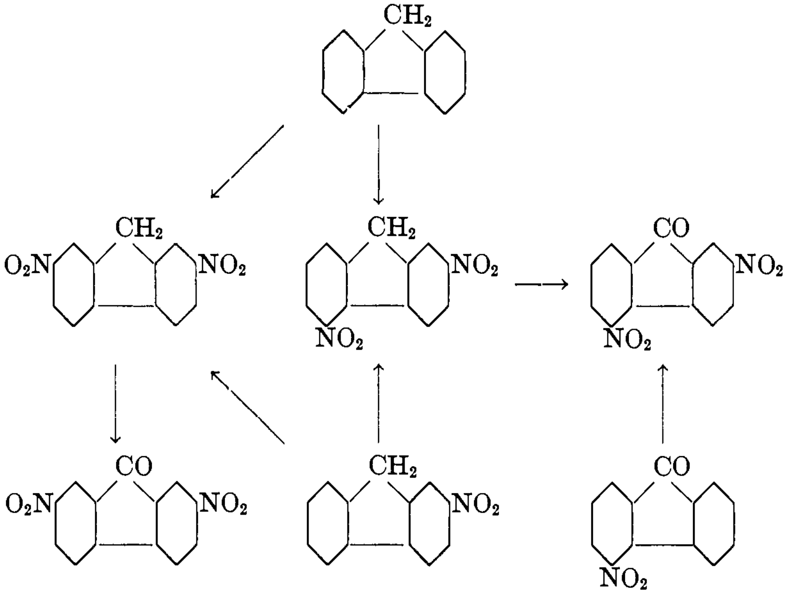
No decision can be made between the two conflicting values, but it is unusual for an oxime to melt lower than the ketone.

Schmidt and Bauer (261a) obtained 4-nitrofluorenone from 4-nitrophenanthraquinone in the usual manner. Courtot (53, cf. 209) later improved the preparation of 4-nitrophenanthraquinone. He gave the melting point of 4-nitrofluorenone as 135°C. Reduction with ammonium sulfide yielded 4-aminofluorenone, and with zinc and acid, 4-aminofluorenol.

2-Bromo-9-nitrofluorene was used by Thurston and Shriner (313) in an attempt to establish the asymmetry of the *aci*-nitro link. A small but definite rotation was reported for the unpurified potassium salt. 2-Bromofluorene reacted with *d*-2-octyl nitrate in the presence of potassium ethylate (cf. page 309) to give the salt of 2-bromo-9-*aci*-nitrofluorene.

B. Dinitro and diamino compounds

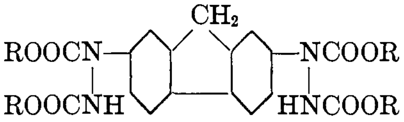
This phase of the chemistry of fluorene has been investigated with some thoroughness, affording varied results. It has been generally agreed that mononitration of fluorene gives 2-nitrofluorene in good yields. When nitration was carried beyond the mononitro stage, 2,5-dinitrofluorene (209), melting at 207°C., and 2,7-dinitrofluorene, which decomposes at 295–300°C., were obtained. The latter isomer was formed in a 66 per cent yield (3) and the former in a 22 per cent yield (45, 53). A similar result was obtained when 2-nitrofluorene was nitrated, 2,5- and 2,7-dinitrofluorenes being the products. Anantakrishnan and Hughes carefully checked these results. Oxidation of the two isomers yielded 2,5-dinitrofluorenone, m.p. 241°C., and 2,7-dinitrofluorenone, m.p. 292°C. Gallas (110) condensed 2,7-dinitrofluorenone and 2,7-dinitrofluorene in the presence of zinc chloride to obtain 2,7,2′,7′-tetranitrodibiphenylene-ethylene, which could be reduced to the corresponding tetraamino compound. Morgan and Thomason (209) established the constitution of 2,5-dinitrofluorenone by nitrating 4-nitrofluorenone (positions 4 and 5 are identical in monosubstituted compounds). The following equations represent these reactions:



Morgan and Thomason made the statement that the second nitro group is directed by the phenylene radical, thus entering the second ring in the ortho and para positions (positions 5 and 7).

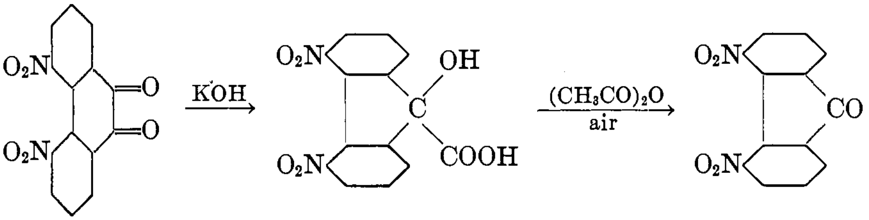
The dinitro compounds just described may be reduced to the corresponding diamino compounds. 2,7-Diaminofluorene is the best known diamine. Schultz (279) had established its structure by showing that it was formed in the distillation of 4,4′-diaminodiphenic acid with lime (72). It crystallized in needles, m.p. 165°C., which were nearly colorless, but darkened on standing a short time. Its use in analytical chemistry will be discussed later. 2,5-Diaminofluorene is a pinkish white substance melting at 175°C. (209). Solutions of it give an olive-green color with ferric chloride.

Stollé and Adam (300) reported a unique method for the preparation of 2,7-diaminofluorene. They added azodicarboxylic esters to fluorene. On reduction with hydriodic acid these gave 2,7-diaminofluorene.

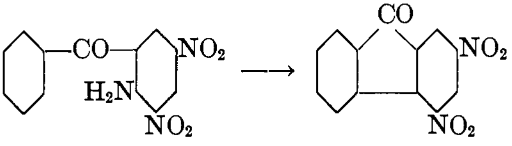


Courtot (53, cf. 267, 280) studied the reduction of 2,5- and 2,7-dinitrofluorenones. Reduction with zinc and ammonium hydroxide gave the diaminofluorenols, while ammonium sulfide affected only the nitro groups, giving the diaminofluorenones. Courtot remarked that the colored derivatives of aminofluorenols were more intensely colored than the corresponding derivatives of aminofluorenones; for example, 2,5-diaminofluorenone was brownish red, while 2,5-diaminofluorenol was deep red.

4,5-Dinitrofluorenone has been prepared by Schmidt and Bauer (261a) from 4,5-dinitrophenanthraquinone. It crystallized in yellow needles which did not melt at 350°C. No study of the reduction of this compound has been reported.



Ullmann and Broido (315) prepared 2,4-dinitrofluorenone indirectly by diazotizing 2-amino-3,5-dinitrobenzophenone with sodium nitrite in concentrated sulfuric acid. It formed yellow needles which melted at 197°C.



Wislicenus and Weitemeyer (346b) showed that nitration of ethyl fluorene-9-glyoxalate in acetic acid gave a 90 per cent yield of 2,9-dinitrofluorene. Heating this compound above its melting point resulted in the formation of 2-nitrofluorenone. The same dinitro compound was obtained by the action of nitric acid on 9-nitrofluorene or ethyl 2-nitrofluorene-9-glyoxalate. Bennett and Noyes (22) obtained the corresponding diamine

(2,9-diaminofluorene) by reducing 2-aminofluorenone hydrazone with zinc and acid. All attempts to condense 2-nitrofluorene with ethyl nitrate to give 2-nitro-9-*aci*-nitrofluorene failed (346b). It also refused to condense with esters of formic acid.

Rose (247) has carried out nitration experiments with 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.

Schmidt and Stützel (270b), and later Kuhn and Jacob (179), investigated the nitration of 9-acetylaminofluorene. The first group of investigators characterized the dinitrofluorenone which they obtained as 1,8-dinitrofluorenone, on the basis of the products of oxidation. Kuhn and Jacob apparently confirmed these results.

Langecker (183) in 1931, seeking to prepare 1- or 1,8-substituted products of fluorenone, reinvestigated the nitration of 9-acetylaminofluorene. He found the main product of the nitration to be 2-nitrofluorenone. Huntress and Cliff (149) then undertook a critical examination of the work of Schmidt and Stützel. A recalculation of the analytical data given by Schmidt and Stützel for 1,8-dinitrofluorenone showed that the nitrogen content of the compound was not 10.40 per cent, but really only 8.08 per cent. The value is 6.22 per cent for a mononitrofluorenone and 10.36 per cent for a dinitrofluorenone. Schmidt and Stützel reported that on oxidation *o*-nitrobenzoic acid was obtained. Huntress and Cliff pointed out the proximity of the melting points of *o*- and *m*-nitrobenzoic acids. Even though *o*-nitrobenzoic acid were obtained, it would only account for the position of one of the nitro groups. Using the exact conditions of Schmidt and Stützel in four separate experiments, these authors obtained 70 per cent yields of 2-nitrofluorenone. Carrying the nitration further they obtained 2,7-dinitrofluorenone and a new dinitrofluorenone, m.p. 213–214°C., which was neither 2,4- nor 2,5-dinitrofluorenone. It is thus seen that the question is still unsettled.

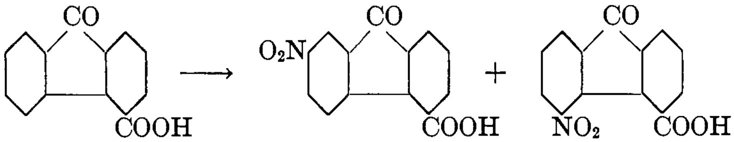
Anantakrishnan and Hughes (3) recently studied the nitration of 9-bromofluorene. Mild treatment with nitric acid in acetic anhydride resulted in the formation of 9-bromo-2-nitrofluorene, m.p. 145°C. This compound was identical with the compound formed by the bromination of 2-nitrofluorene (175). Two products were obtained by using a stronger nitrating mixture; they were separable by fractional crystallization from acetone. These two compounds were identified as 9-bromo-2,7-dinitrofluorene, m.p. 255°C., and 9-bromo-2,5-dinitrofluorene, m.p. 199°C., by oxidation to the corresponding dinitrofluorenones, the bromine atom being removed during the oxidation. A similar result was obtained by nitrating 9-bromo-2-nitrofluorene. From the several cases just described it seems that substituents in the 9-position have no effect upon the position taken by the entering nitro group; in other words, the same positions are involved whether fluorene itself or a 9-substituted derivative is nitrated.

Diels, Schill, and Tolson (72), continuing their work on the nitration of fluorene, investigated the action of nitric acid on 2-acetylaminofluorene. A mixture of two mononitro compounds was obtained. Saponification yielded two aminonitrofluorenes which were widely different in basicity. The more basic one was found to be 2-amino-7-nitrofluorene, as shown by reduction to the known 2,7-diaminofluorene. The less basic compound was reported as 2-amino-1-nitrofluorene. Twenty-six years later Eckert and Langecker (87) showed that this compound was really 2-amino-3-nitrofluorene. The position of the nitro group was determined by first oxidizing the nitration products to the corresponding nitroacetylaminofluorenones and then hydrolyzing. 2-Amino-7-nitrofluorenone (45, 138) was removed by extraction with hydrochloric acid. The residue, 2-amino-3-nitrofluorenone, on deamination yielded the known 3-nitrofluorenone, which was in turn reduced to the known 3-aminofluorenone and then through the diazo compound to 3-hydroxyfluorenone. (See page 355.) 2-Amino-3-nitrofluorenone on reduction with sodium sulfide gave 2,3-diaminofluorenone, which showed characteristic reactions of an orthodiamine.

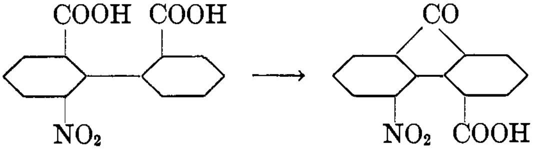
Eckert and Langecker (87) also investigated the nitration of other derivatives of fluorene involving the 2-position. 2-Acetylaminofluorenone gave results analogous to 2-acetylaminofluorene. 2-Aminofluorenone, however, gave only 2-amino-7-nitrofluorenone.

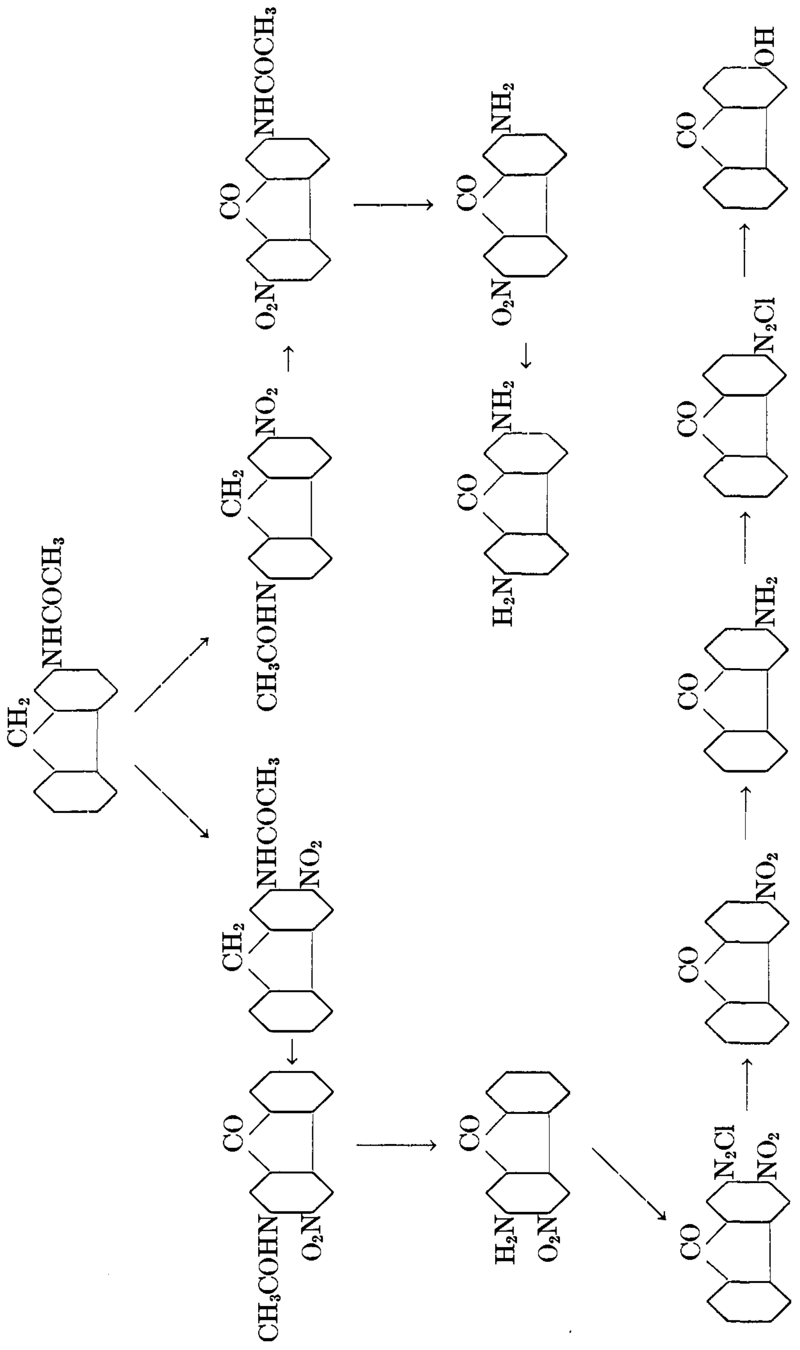
Ruiz (249) nitrated 2-methoxyfluorene, using Eckert and Langecker's method, to 2-methoxy-3-nitrofluorene. His experiments on the nitration of 2-hydroxyfluorene gave uncertain results; the nitro group, however, was shown to be in the same ring as the hydroxyl group.

The nitration of fluorenone-4-carboxylic acid resulted in approximately equal amounts of 7-nitrofluorenone-4-carboxylic acid (2-nitrofluorenone-5-carboxylic acid) and 5-nitrofluorenone-4-carboxylic acid (206).

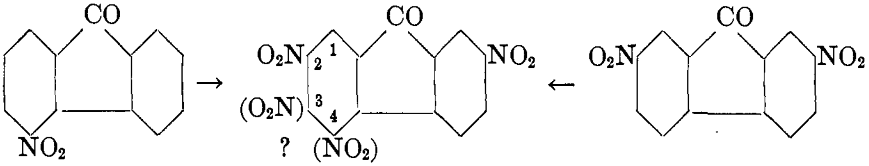


The latter compound may be prepared by heating 6-nitrodiphenic acid with concentrated sulfuric acid (19, 206).



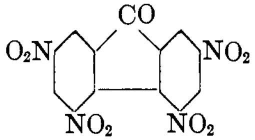

CH2
NHCOCH3
CH3COHN
NO2
O2N
CO
NH2
H2N
N2Cl
OH

The question of the orientation of any trinitro compounds is still unsettled. Schmidt (261b, 267) and his coworkers reported the preparation of 2,6,7-(or 2,3,7-)trinitrofluorenone by boiling fluorenone with fuming nitric acid. The constitution of the nitro compound was based on the fact that oxidation gave 3,4-dinitrobenzoic acid and that it could be prepared by further nitration of 2,7-dinitrofluorenone. The entrance of the third nitro group into a position ortho to another nitro group is definitely unusual. Also, if the phenylene radical is the directing factor, as stated by Morgan and Thomason, the nitro group would not enter the position assigned to it by Schmidt. The literature revealed that Bell (18) had reported the formation of 2,4,7-trinitrofluorenone, which is identical with Schmidt's compound, by the nitration of 4-nitrofluorenone with concentrated nitric acid. It is seen then that the position of one nitro group (3-) in Schmidt's compound is incorrect on the assumption that no migration of the nitro group took place during the reaction. The formation of the 2,4,7-trinitro compound seems more plausible, in view of the fact that dinitration of fluorene or fluorenone involves the 5-position (positions 4 and 5 being equal).



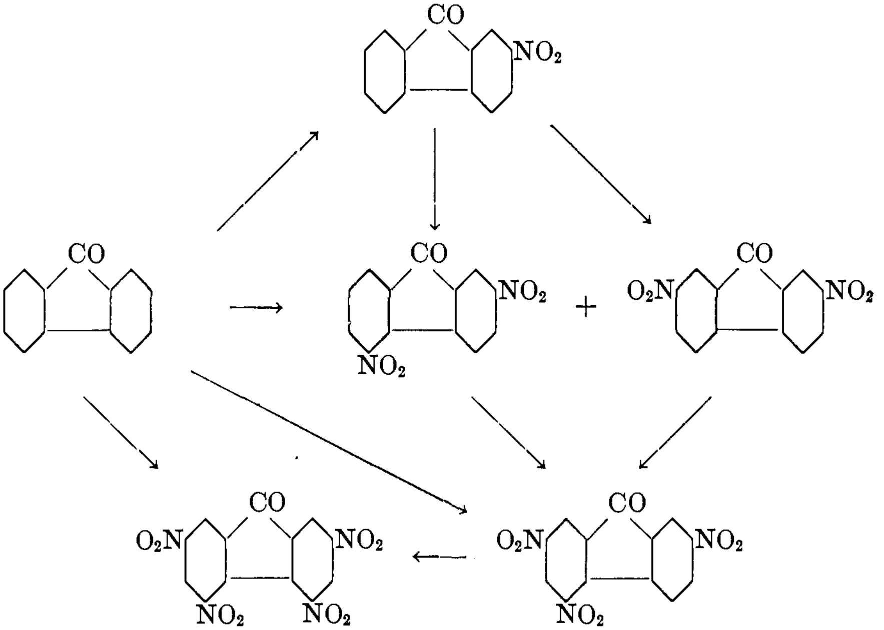
(Bell) (Schmidt)

Schmidt reported that on boiling fluorenone with concentrated sulfuric acid and red fuming nitric acid 2,3,6,7-tetranitrofluorenone was obtained. It seems more reasonable to us that this compound should prove to be 2,4,5,7-tetranitrofluorenone, for on the introduction of the fourth nitro group into 2,4,7-trinitrofluorenone the 5-position represents the only remaining position which is meta to another nitro group and also ortho to the phenylene radical (the para position being filled).



The validity of Schmidt's results could be easily checked by the dinitration of the known 4,5-dinitrofluorenone. If a compound were obtained identical with Schmidt's 2,3,6,7-tetranitrofluorenone, it would be evident that the positions 3 and 6 are in error.

The following is a tentative scheme for the nitration of fluorenone:



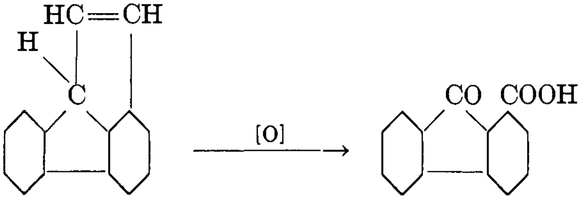
Courtot (53) made a preliminary attempt to determine the orientation of such trisubstituted compounds as X-nitrofluorene-2,7-disulfonic acid and X-nitro-2,7-dibromofluorene, which were prepared by nitrating the respective disubstituted fluorene compounds.

XI. CARBOXYLIC ACIDS

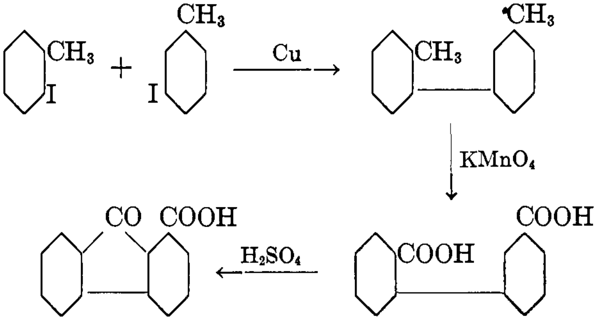
Fluorene-2-carboxylic acid was first prepared by Fortner (107) by the hydrolysis of 2-cyanofluorene, which he obtained from 2-aminofluorene by the Sandmeyer reaction. The silver salt was a white insoluble compound and the methyl ester melted at 120°C. It underwent all the characteristic reactions of an aromatic carboxylic acid. The preparation of fluorene-1-carboxylic acid by Fieser and Seligman (98) in an 84 per cent yield from fluorenone-1-carboxylic acid, using sodium amalgam as the reducing agent, was significant in that it afforded a method of preparing other fluorenecarboxylic acids from the better known fluorenonecarboxylic acids.

Owing to the fact that oxidation is a common method for the preparation of carboxylic acids and that the indirect syntheses also usually lead to fluorenones rather than to fluorenes, we may naturally expect more to be known of the fluorenone acids. All four possible monocarboxylic acids of fluorenone are, therefore, known.

Fluorenone-1-carboxylic acid was prepared easily by the oxidation of fluoranthene with chromic acid (98, 100b, 101, 117, 136). This is the best method of preparation; the yield was approximately 50 per cent (98).



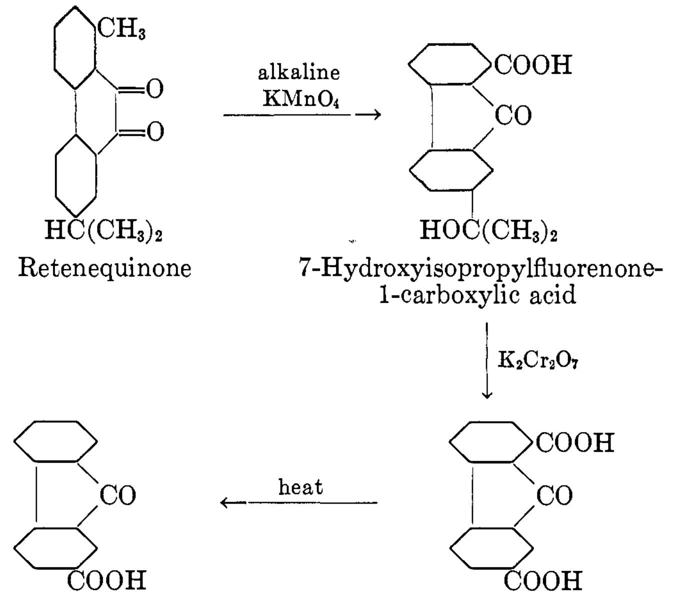
Mayer and Freitag (194, cf. 284) synthesized it in the following way:



(Cf. 170)

Syntheses of this type are impractical in most cases for preparative purposes, but they are of considerable theoretical importance.

Fluorenone-2-carboxylic acid can be obtained by the oxidation of fluorene-2-carboxylic acid with chromic acid (107), but a more convenient method has been described by Dziewonski and Schnayder (84, cf. 178). 2-Fluoryl methyl ketone, prepared by the action of acetyl chloride on fluorene in the presence of aluminum chloride, on oxidation gave fluorenone-2-carboxylic acid. Hinkel, Ayling, and Beynon (142) prepared it by the oxidation of 2-fluorenealdehyde, which they obtained in 75 per cent yield as a result of one operation on fluorene. The acid was first reported by Bamberger and Hooker (11, cf. 189), who obtained it as a product of the action of heat upon the 1,7-dicarboxylic acid prepared by the oxidation of retenequinone. The following equations illustrate the various products of oxidation:



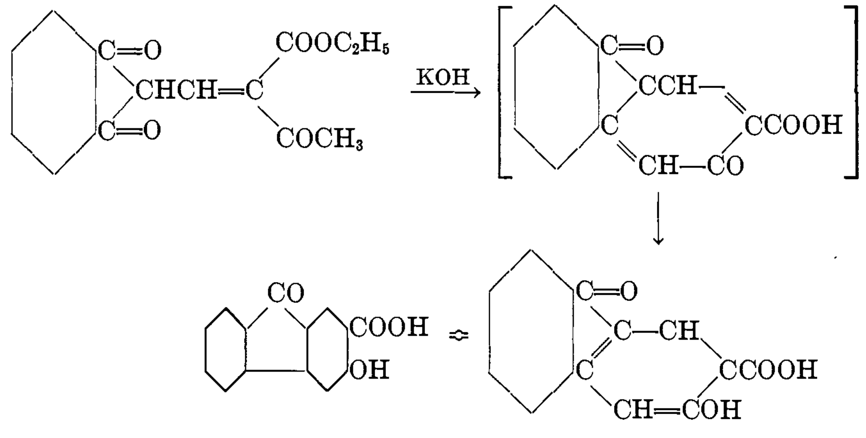
Retenequinone

7-Hydroxyisopropylfluorenone-1-carboxylic acid

Fluorenone-1,7-dicarboxylic acid

Fluorenone-2-carboxylic acid

Errera and La Spada (90) synthesized the 3-hydroxy derivative of fluorenone-2-carboxylic acid by heating ethyl indandionemethenylacetoacetate with an aqueous solution of potassium hydroxide. The reaction probably took place in the following manner.



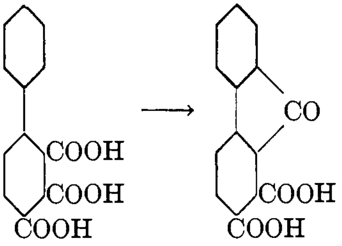
Heating the acid to its melting point (279°C.) caused carbon dioxide to split off, giving 3-hydroxyfluorenone, m.p. 228°C.

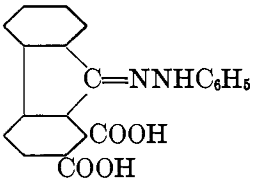
Fluorenone-3-carboxylic acid was prepared by heating 2,3′-diphenic acid with sulfuric acid (287). The reaction was shown to be correct, for the same acid was obtained by oxidizing 3-methylfluorenone with potassium permanganate. It was a yellow crystalline substance, melting at 285°C.

Fluorenone-4-carboxylic acid was the product of the reaction of various reagents upon diphenic acid or diphenic anhydride. It crystallized in yellow needles, melting at 227°C. In its preparation Graebe and Aubin (127) used concentrated sulfuric acid, phosphorus oxychloride, or zinc chloride, while Pick (227) and Gotz (124) used aluminum chloride in benzene or toluene solution. Underwood and Kochman (319) used stannic chloride. Huntress, Herschberg, and Cliff (152) showed that heat caused its conversion to fluorenone.

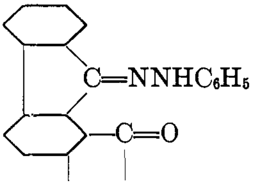
Besides the fluorenone-1,7-dicarboxylic acid already mentioned, several other dicarboxylic acids have been prepared. Von Braun, Manz, and Kratz (34a) have shown that fluoranthene-9-carboxylic acid on oxidation with chromic acid gave a mixture of fluorenone-1,6- and -1,7-dicarboxylic acids; however, if the fluoranthene nucleus were first partially reduced and then oxidized, fluorenone-1,6-dicarboxylic acid was obtained, as shown on page 302.

Fluoranthene-3-carboxylic acid was oxidized to fluorenone-1,2-dicarboxylic acid, which readily formed an anhydride melting at 318–320°C. This same acid has been prepared recently by Charrier and Ghigi (42) by the action of concentrated sulfuric acid on biphenyl-2,3,4-tricarboxylic acid. They gave the melting point of the acid as 330°C. and of the anhydride as 315–320°C., which checked with von Braun's work. Heat caused the loss of carbon dioxide to give fluorenone-2-carboxylic acid. On attempting to prepare the phenylhydrazone of fluorenone-1,2-dicarboxylic acid they obtained two compounds which were formulated as follows:



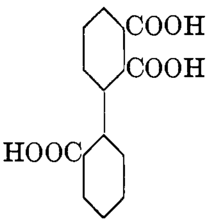


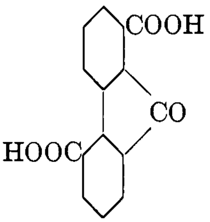
Simple phenylhydrazone



Anilinoimidophenylhydrazone

Fluorenone-1,5-dicarboxylic acid was prepared in a similar manner, using biphenyl-2,3,2′-tricarboxylic acid.

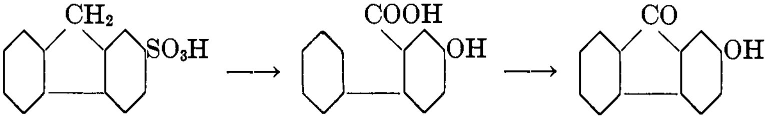




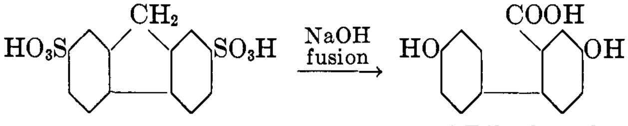
Boiling with quinoline and copper powder caused the removal of the carboxyl group in the 5-position, giving fluorenone-1-carboxylic acid (cf. page 300).

XII. SULFONIC ACIDS

The action of sulfuric acid on fluorene led to substitution in the 2-position and further treatment gave rise to fluorene-2,7-disulfonic acid. Sulfonation in acetic anhydride resulted in an almost quantitative yield of fluorene-2-sulfonic acid (15, 326). Fluorenone-2-sulfonic acid was formed on oxidation. Courtot and Geoffroy (55, 54, cf. 143) used chlorosulfonic acid. These same authors proved by fusion with alkali that the sulfonic acid group entered the 2-position. This treatment opened the five-membered ring. Sulfuric acid, however, reconverted the product to 2-hydroxyfluorenone.



Fluorene-2,7-disulfonic acid was obtained by heating fluorene and concentrated sulfuric acid at about 95°C. (267). Schmidt, who carried out an alkali fusion of this compound, interpreted the compound obtained as 2,7,9,9-tetrahydroxyfluorene; however, Courtot and Geoffroy showed later that the true reaction was as follows:



4,4′-Dihydroxybiphenyl-2-carboxylic acid

Heating the latter compound with zinc chloride gave 2,7-dihydroxyfluorenone; phosphorus pentachloride converted it into 2,7,9,9-tetrachlorofluorene.

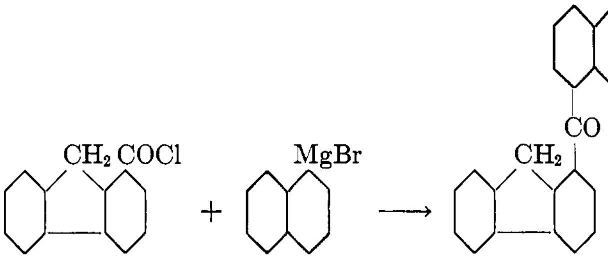
Both fluorene-2-sulfonic acid and fluorene-2,7-disulfonic acid yielded the usual derivatives of an aromatic sulfonic acid; however, as pointed out, alkali fusion did not give the hydroxy compound directly.

Courtot (53) has shown that 2-nitrofluorene when sulfonated gave 2-nitrofluorene-7-sulfonic acid in quantitative yields. 2-Aminofluorene-7-sulfonic acid was obtained on reduction with stannous chloride. The sodium salt of the latter compound gave a remarkably stable diazo compound. Courtot prepared a trisulfonic acid by treating fluorene-2,7-disulfonic acid with oleum, but he was unable to determine the position of the third sulfonic acid group. Solutions of the potassium salt of this compound exhibited in alkaline solution an intense green color which changed to red on acidification.

XIII. KETONES

The majority of fluorene ketones which are known have been prepared by the Friedel–Crafts reaction. Again the 2- and 7-positions were taken up by the entering keto group; however, there is one example of a fluorene-2,3-diketone being formed along with the normal 2,7-isomer. Ketones involving other positions may be synthesized from the acid chloride of the appropriate fluorenecarboxylic acid or fluorenonecarboxylic acid. For example, Gotz (124) synthesized 4-benzoylfluorenone from fluorenone-4-carbonyl chloride and benzene in the presence of aluminum chloride.

Fieser (98) has described another method, using a Grignard reagent and the carbonyl chloride. In this way he synthesized 1-α-naphthoylfluorene in a 56 per cent yield from fluorene-1-carbonyl chloride and α-naphthylmagnesium bromide. This method, of course, cannot be used with fluorenones.

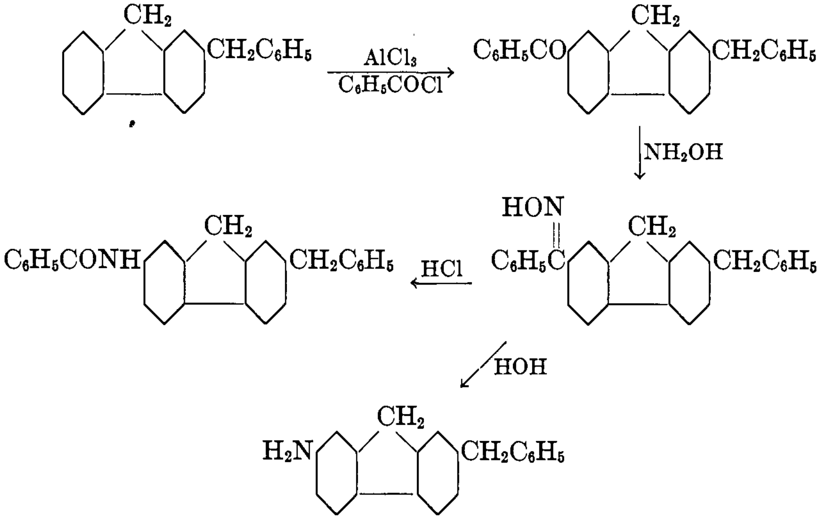


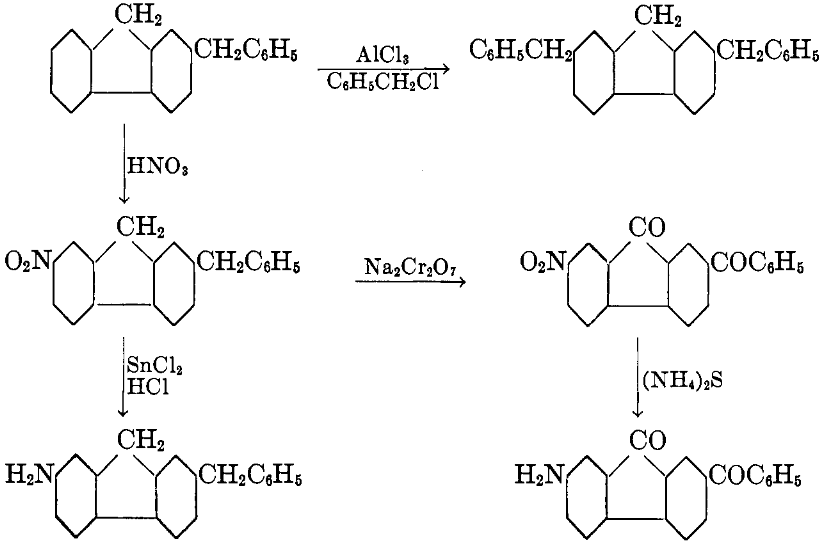
2-Benzoylfluorene (phenyl 2-fluoryl ketone) was prepared by Fortner in 1902 (106, cf. 94) by the action of benzoyl chloride on fluorene in the presence of aluminum chloride in carbon disulfide solution. Perrier's method produces a purer product (238); in 1903 he called attention to his paper presented in 1892 before the Acadêmie des Sciences, Paris, in which he described the preparation of this compound and its oxime (224). Perrier first allowed the benzoyl chloride to react with aluminum chloride and then added the fluorene. The product was insoluble in carbon disulfide and so could be washed free of tar before hydrolysis. Fortner showed that the benzoyl group entered the 2-position by synthesizing 2-benzoylfluorene from 2-aminofluorene. Reduction with zinc dust gave 2-benzylfluorene, a compound previously reported by Goldschmiedt (116), who obtained it from fluorene and benzyl chloride in the presence of zinc dust. Sodium dichromate and acetic acid oxidized 2-benzoylfluorene to 2-benzoylfluorenone.

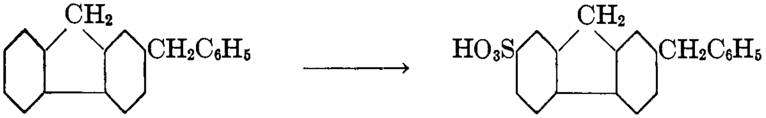
These compounds have been investigated quite recently by Dziewonski and coworkers. 2,7-Dibenzoylfluorene was prepared from 2-benzoylfluorene by the Friedel-Crafts reaction with heat (82). In proving the constitution of 2,7-dibenzoylfluorene and other similar compounds, Dziewonski made use of the Beckmann rearrangement of the oximes to give derivatives of the known amino compounds. Thus 2,7-dibenzoylfluorene dioxime underwent rearrangement to 2,7-dibenzoylaminofluorene. The latter may be prepared by benzoylating 2,7-diaminofluorene or the benzoyl derivative may be hydrolyzed to 2,7-diaminofluorene (79).

Dziewonski and Reicher (83) also studied the preparation of 2-benzylfluorene by the Friedel-Crafts reaction.

A summary of some of the other reactions carried out by Dziewonski and others is given below.





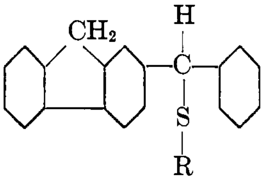


The amino compounds were diazotized and coupled in the standard way with various naphthalene derivatives to give highly colored compounds.

Ray and Pelletier (223) prepared the oxime of 2-benzoylfluorene and reduced it to the amine with sodium amalgam.

Ray and Harrold (137) reduced 2-benzoylfluorene to phenyl-2-fluorylcarbinol. This carbinol was converted into the chloride and the bromide; the iodide was obtained by the reaction of the bromide with methyl iodide (238).

These halides reacted with mercaptans to give a number of sulfides of the general formula I. Alcohols also reacted with these halides to give



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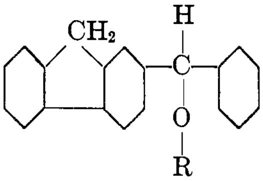


II

the corresponding ethers (II).

Ray and Palinchak (240) have prepared 2-benzoyl-9-nitrofluorene and are trying to resolve it by combining it with an optically active substance. The results so far have been unusual.

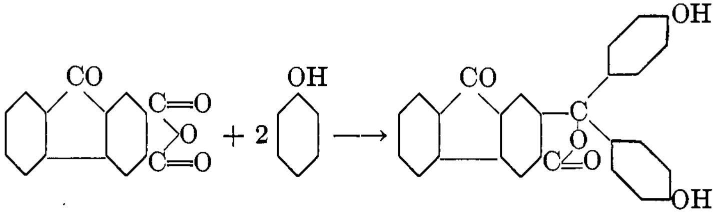
Dziewonski and Schweiger (85) prepared 2-propionylfluorene and 2,7-dipropionylfluorene by the interaction of propionyl chloride, fluorene, and aluminum chloride in carbon disulfide. The constitution of these compounds was established from the oximes, as described previously. 2-Propionylfluorene on oxidation with sodium dichromate and acetic acid gave a mixture of 2-propionylfluorenone and fluorenone-2-carboxylic acid.

The investigation of Dziewonski and Schnayder (84) on the condensation of acetyl chloride with fluorene in the Friedel–Crafts reaction gave results analogous to those obtained with other acid chlorides. 2-Acetylfluorene and 2,7-diacetylfluorene were formed and their constitution established from the oximes.

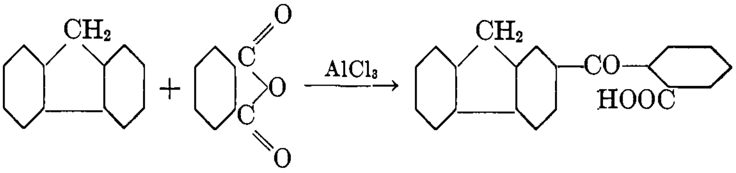
In addition, oxidation of 2-acetylfluorene gave fluorenone-2-carboxylic acid, while vigorous oxidation of 2,7-diacetylfluorene with an excess of sodium dichromate and acetic acid gave fluorenone-2,7-dicarboxylic acid (81).

Dziewonski and Kleszcz (80) investigated the same condensation more carefully, particularly with reference to the temperature at which the reaction was carried out. They found that at 5–10°C. 2-acetylfluorene was the main product; however, at 20–25°C. a mixture of 2,7-diacetylfluorene and an isomeric diacetylfluorene was obtained. When the reaction was carried out at the boiling point of the solvent (carbon disulfide) the isomeric diketone was the main product. The dioxime of the isomer was prepared and on rearrangement yielded a diacetyldiaminofluorene which was easily hydrolyzed to a diaminofluorene. Dziewonski and Kleszcz characterized the isomer as 1,2-diacetylfluorene, because the diaminofluorene that they obtained was identical with the 1,2-diaminofluorene of Diels, Schill, and Tolson (72). Dziewonski and Kleszcz were apparently unaware that Eckert and Langecker (87) had shown in 1928 that Diels' 1,2-diaminofluorene was really 2,3-diaminofluorene. It is then evident that the compound is actually 2,3-diacetylfluorene instead of 1,2-diacetylfluorene; however, it is still incorrectly reported in the literature as 1,2-diacetylfluorene.

2,3-Diacetylfluorene on vigorous oxidation should yield the unknown fluorenone-2,3-dicarboxylic acid. This acid represents the fluorene analog of phthalic acid and should undergo the many interesting reactions of phthalic acid and phthalic anhydride. For example, the anhydride of fluorenone-2,3-dicarboxylic acid should give with phenol and zinc chloride the fluorene analog of phenolphthalein.

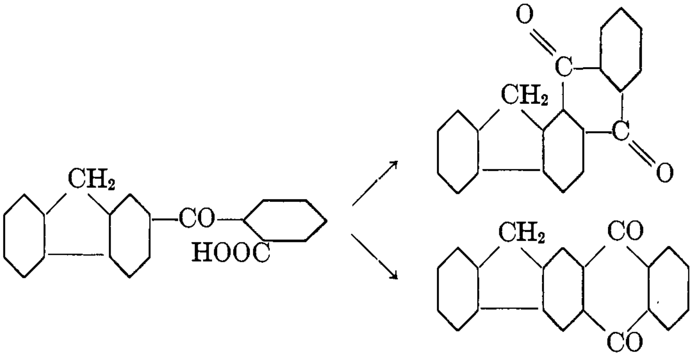


2-Fluoroyl-*o*-benzoic acid has been prepared by the Friedel–Crafts reaction from fluorene and phthalic anhydride (61, 119).



Goldschmiedt and Lipschitz (118, 119) reported two isomeric methyl esters of 2-fluoroyl-*o*-benzoic acid, one melting at 200–202°C. and the other at 126–128°C. They prepared the latter ester without isolation of the intermediate acid chloride; it is possible that the high melting compound was due to the unreacted acid.

When the ethyl ester was heated at 230°C. with potassium hydrogen sulfate, or when the acid alone (61) was heated to 300–320°C., phthalylfluorene was formed; in the latter case the yield was 100 per cent. The ring closure may take place in either the 1- or the 3-position.



Ring closure was shown to take place in the 3-position (17, 215). Koelsch (172) also found the 3-position more reactive than the 1-position, when he studied the cyclization of 2-fluorene-γ-butyric acid.[14] He showed that

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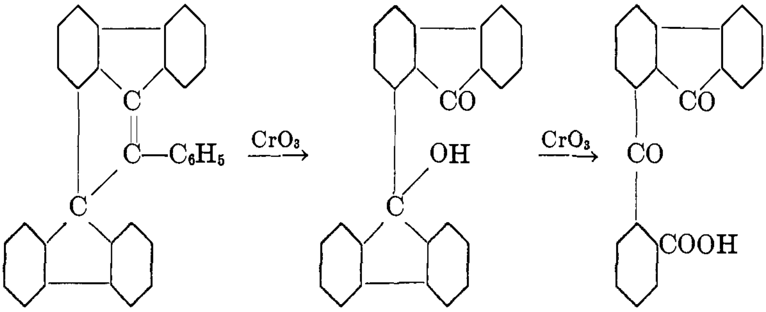
[14] This compound was prepared by condensing succinic anhydride with fluorene in the presence of aluminum chloride and reducing the carbonyl group with zinc amalgam.

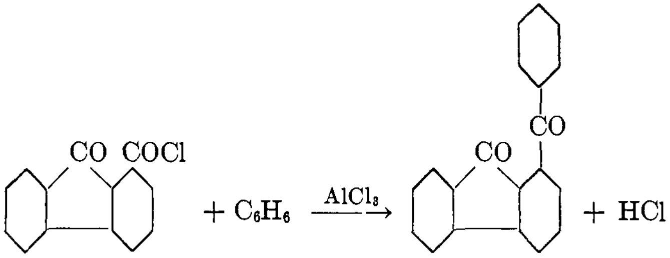
the 3-position was involved in the ring closure by reducing the ketotetrahydrobenzofluorene to a tetrahydrobenzofluorene which was dehydrogenated with sulfur to 2,3-benzofluorene. Oxidation gave the known 2,3-benzofluorenone (312). Many similar compounds have been prepared (10, 33, 96, 173, 190, 226, 253, 321).

2-Fluoroyl-*o*-benzoic acid may be oxidized to the corresponding fluorenone with chromic acid (62, 119). Ray (237) has carried out the reduction of the ketone to the carbinol with zinc and potassium hydroxide. This carbinol should be resolvable, and Ray and Liszniewska (239) have obtained slight indications of its resolution. The ketone group also has been completely reduced to methylene (17, 215).

1-Fluorenonoyl-*o*-benzoic acid [*o*-(fluorenone-1-carbonyl)benzoic acid] was prepared by Koelsch (170) by the degradation of 1-biphenylene-2-phenyl-3,4-phenyleneindene.

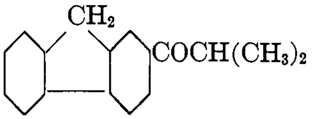


Decarboxylation with cupric carbonate gave 1-benzoylfluorenone. The reaction was checked by a synthesis of the latter compound from fluorenone-1-carboxylic acid.

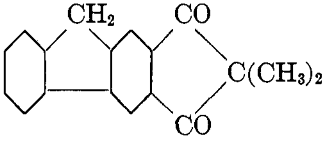


1-Fluorenonoyl-*o*-benzoic acid was found to exist in two interconvertible forms, one yellow and the other orange. By proper crystallization from acetic acid either form could be obtained.

Freund, Fleischer, and Stemmer (108) attempted to prepare fluorene indandiones by condensing dimethylmalonyl chloride with fluorene. Three crystalline compounds were separated from the reaction mixture, one of which was identified as a fluorene isopropyl ketone.



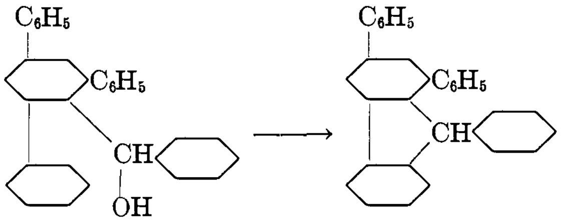
The other two compounds analyzed correctly for fluorenedimethylindandiones, but the authors were unable to determine their structure. One of them probably was 2,3-fluorenedimethylindandione.



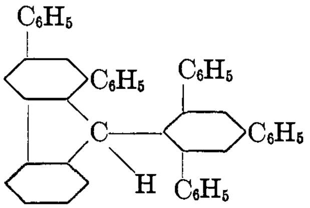
XIV. FLUORENE DERIVATIVES FROM HIGHLY PHENYLATED COMPOUNDS. SPIRO COMPOUNDS

During the last ten years there has been an increasing number of investigations of compounds containing many aromatic rings. Attempts to prepare derivatives of these compounds, especially when carbinols were converted to halides, frequently brought about a transformation to fluorene derivatives which seemed to represent a more stable system.

Kohler and Blanchard (174) described several examples. Triphenylbenzohydrol was transformed into 1,3,9-triphenylfluorene when it was treated with a halogen acid.

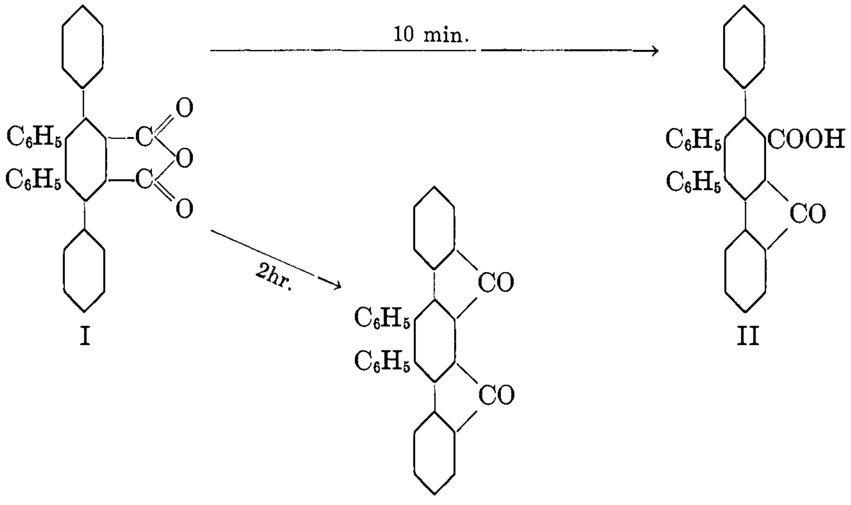


Similarly hexaphenylbenzohydrol gave 1,3-diphenyl-9-triphenylphenylfluorene.



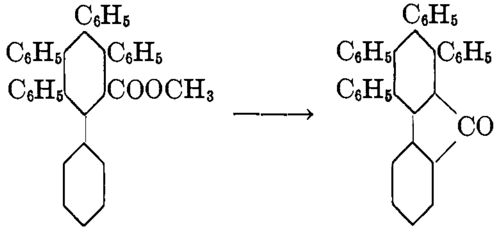
On attempting to prepare the acid chloride of triphenylbenzoic acid, they obtained 1,3-diphenylfluorenone. The latter compound when treated with phenylmagnesium bromide gave 1,3,9-triphenylfluorenol.

Dilthey, Thewalt, and Trösken (74) synthesized several unusual fluorene compounds from polyphenylbenzenes. On heating tetraphenylphthalic anhydride (I) in benzene in the presence of aluminum chloride for 10 min. a reaction occurred which gave 2,3,4-triphenylfluorenone-1-carboxylic acid (II). When the mixture was boiled for 2 hr. they obtained a compound which they called diphenyldifluorenone (III).

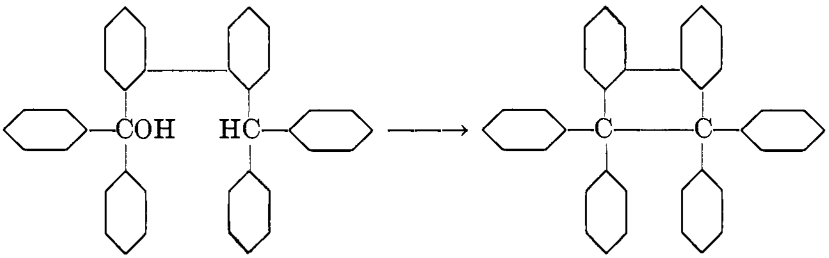


I II III

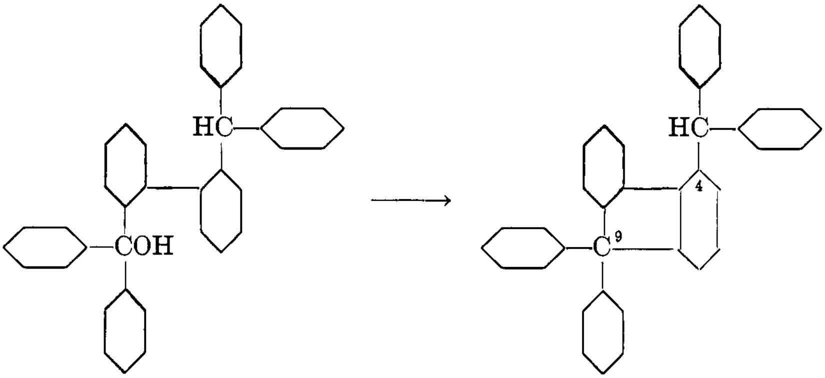
1,2,3,4-Tetraphenylfluorenone was prepared by heating the methyl ester of pentaphenylbenzoic acid in benzene solution with either aluminum chloride or phosphorus oxychloride.



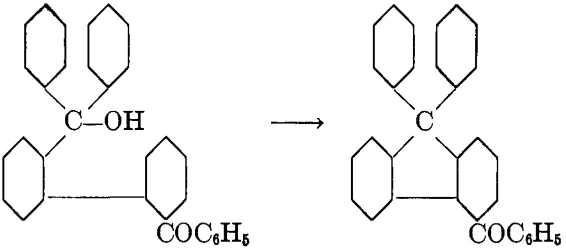
Sergeev (281) in his investigations of polyphenyl derivatives of *o*,*o*′-ditolyl attempted to carry out the following synthesis:

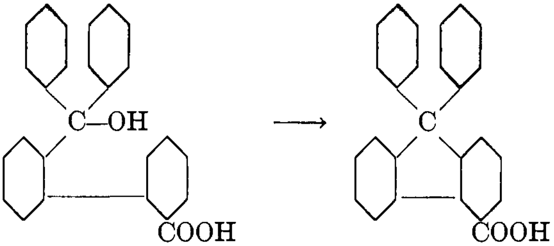


However, all attempts to split off water resulted in 100 per cent yields of 4-benzohydryl-9,9-diphenylfluorene.



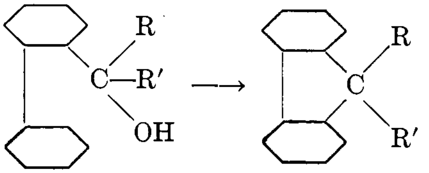
Two other instances of this type of transformation were encountered by Sergeev, as shown in the following equations:





The first reaction took place under the influence of acidic reagents; the second resulted when he attempted to replace the hydroxyl group with halogen.

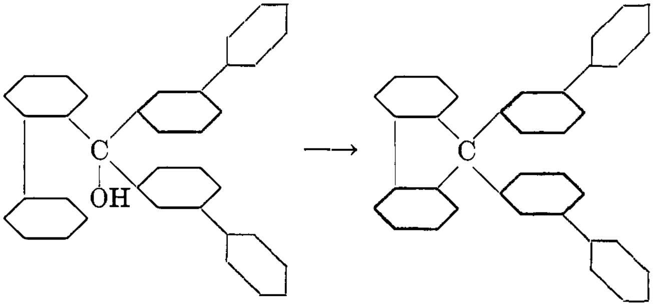
This type of ring closure to form fluorene derivatives seems always to occur in carbinols in which one valency is linked to an aromatic ring, which in turn has another phenyl group ortho to the carbinol group. In other words, we may expect fluorene compounds from carbinols of the following type.[15]



There is additional experimental evidence to justify this statement. Ullmann and von Wurstemberger (318) obtained 9,9-diphenylfluorene by heating crude 2-phenyltriphenylcarbinol with sulfuric acid (R and R′ = Ph). Khotinsky and Patzewitch (160) obtained the same results, using acetic acid to bring about the ring closure. A synthesis of 9-phenylfluorene in quantitative yields from *o*-phenylbenzohydrol has been described by Koelsch (173). Boiling the carbinol in acetic acid containing a little sulfuric acid caused ring closure.

Clarkson and Gomberg (46) succeeded in preparing 2-phenyltriphenylcarbinol in the pure crystalline state, but repeated attempts to prepare the chloride always resulted in the formation of 9,9-diphenylfluorene. Further investigation concerning the conditions under which ring closure took place showed that even very mild treatment was sufficient.

9,9-Di(3-biphenyl)fluorene was formed from 2,3′,3″-triphenyltriphenylcarbinol when a small amount of acid was added.



Clarkson and Gomberg then prepared 9-(2-biphenyl)-9-fluorenol, expecting a greater stability and consequent successful preparation of the chloride. The fluorenol was unchanged by recrystallization from acetic

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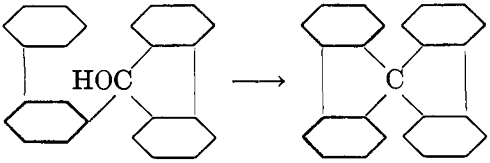
[15] If the linkage between the two phenyl radicals contained a carbon atom or an oxygen atom, ring closure should give rise to anthracene derivatives or xanthenes, respectively.

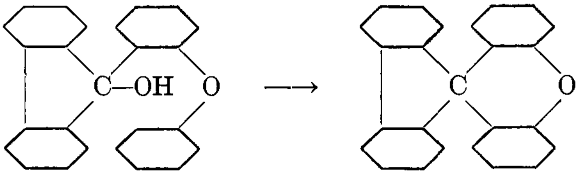
acid, but on the addition of *one drop* of hydrochloric acid ring closure took place. It can be seen that by this ring closure a compound is formed in



I

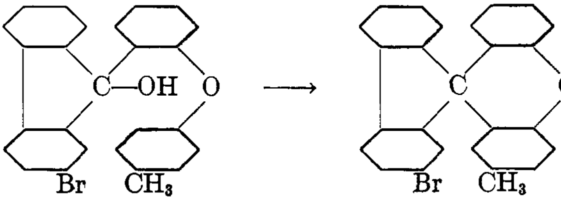
which one carbon atom is common to two rings. Compounds of this type are called spiro compounds, or, more simply, spirans. 9,9-Spirobifluorene (I) is unusual in that it is the simplest representative compound possible in which all four valencies of the spiro carbon atom are linked to purely aromatic groups.

Clarkson and Gomberg by this method prepared a series of interesting spirans, some of which are shown in the following equations.



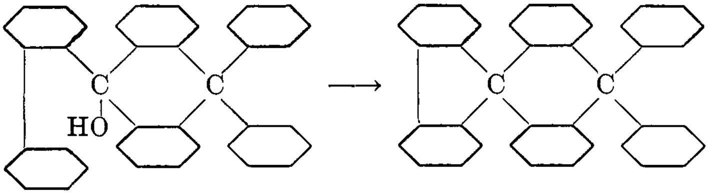
9-(2-Phenoxyphenyl)-
9-fluorenol

Spiro-9-fluorene-9′-
xanthene



9-(2-Phenyl-*p*-tolyl ether)-
2-bromo-9-fluorenol

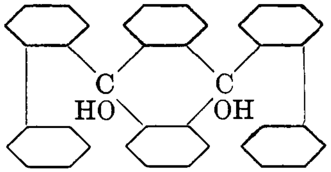
Spiro-9-(2-bromofluorene)-
9′-(2′-methylxanthene)



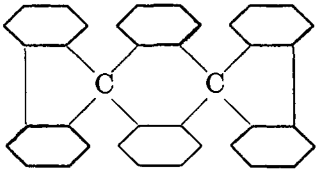
9-(2-Biphenyl)-10,10-di-
phenyl-9,10-dihydro-
9-anthranol

Spiro-9-fluorene-9′-(10,10-
diphenyl)-9,10-dihydro-
anthracene

The next logical step was the preparation of a dispiro compound involving the closure of two rings. It was accomplished as shown in the following equation:



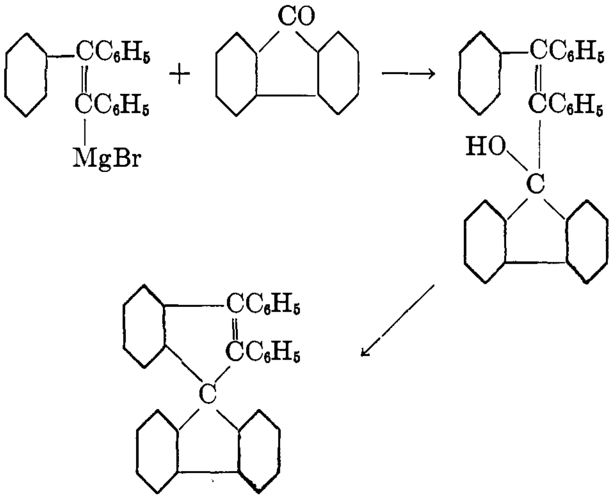
9,10-Di(2-biphenyl)anthraquinol



Dispiro-9,9′-difluorene-(9,10-dihydroanthracene)

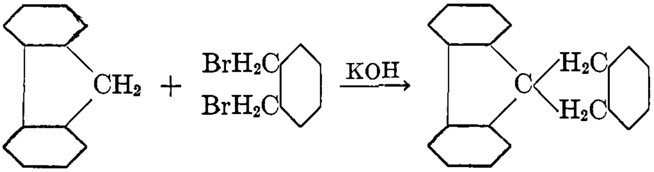
In all these reactions the ring closure was effected by seeming catalytic action of mild dehydrating agents. The yields in most cases were quantitative. All the complex spirans were nicely crystalline, colorless, and very insoluble in the usual organic reagents.

Koelsch (169) reported a spiro compound which he obtained similarly. α-Diphenylene-β,γ,γ-triphenylallyl alcohol, obtained from triphenylvinylmagnesium bromide and fluorenone, on treatment with an acidic reagent formed 1-biphenylene-2,3-diphenylindene.



1-Biphenylene-2,3-diphenylindene

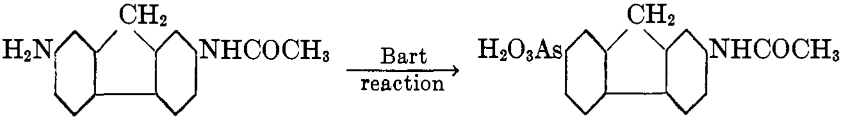
A spiro compound has been prepared directly from fluorene. Fluorene and *o*-xylylene dibromide heated in the presence of potassium hydroxide gave xylylenefluorene (92).



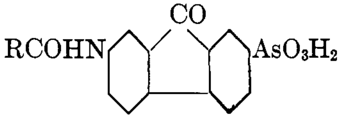
XV. ARSENIC AND PHOSPHORUS COMPOUNDS OF FLUORENE[16]

Arsenic compounds of fluorene have been prepared by two groups of investigators, Cislak and Hamilton in America and Morgan and Stewart in England. Cislak and Hamilton, however, were the first to publish their results. The investigations of Morgan and Stewart were more thorough.

Cislak and Hamilton (45), in an attempt to find new arsenicals which might be of value in chemotherapy, prepared 2-arsonofluorene, 2-arsonofluorenone, and 2-acetylamino-7-arsonofluorene. The following equation illustrates the preparation of the latter derivative.



Morgan and Stewart (207) found that "trypanocidal potency is manifested when an arsenic radical was introduced into fluorenone in conjunction with an amino group." Compounds of the following types were prepared and their therapeutic value determined.



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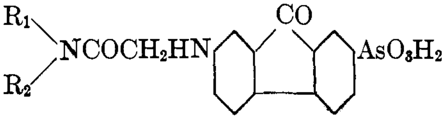
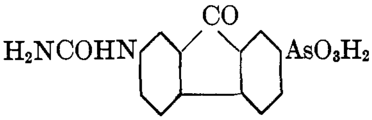


II



III

The sodium salt of 7-acetylaminofluorenone-2-arsonic acid (type I) was found to be the most efficacious, having an M.L.D.[17] of 15 and an M.C.D. of 10. The conclusion from the work was "that a curative power is mani-

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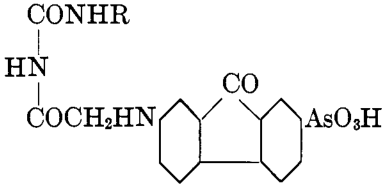
[16] For mercury compounds see page 343.

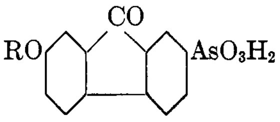
[17] M.L.D. and M.C.D. are the minimum lethal dose and the minimum curative dose, respectively, in milligrams per 20 g. of mouse.

fested when R equals H, reaches a maximum when R is CH_3, and then decreases rapidly until it disappears when R is C_6H_5. Derivatives of type II have little therapeutic value." 7-Carbamidofluorenone-2-arsonic acid (III) had an M.L.D. of 30 and an M.C.D. of 15.

Morgan and Stewart (208) continued their work and investigated the trypanocidal action of compounds in which the length of the side chain had been increased to form ureides (IV). These compounds were of little value.



IV



V

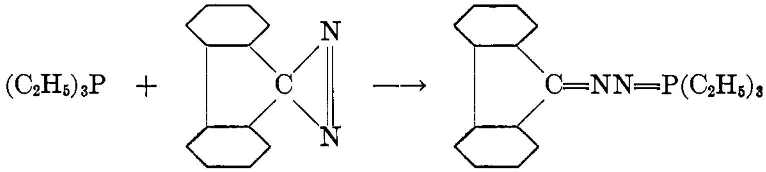
A compound of type V, 7-carbamylmethoxyfluorenone-2-arsonic acid (R being CH_2CONH_2), however, was very effective, having an M.L.D. of 30 and an M.C.D. of 10.

Using 7-aminofluorenol-2-arsonic acid as a starting material they prepared a number of derivatives. One compound of the fluorenol type, 7-glycineamidofluorenol-2-arsonic acid, was curative in doses which did not exceed one-half the minimum lethal dose.

If we regard the 2,7-positions to be in an extended para relationship we find that Benda's observation (20), "that all but a few of the corresponding trypanocidal drugs have nitrogen in para combination with the arsenic," is applicable.

Whether or not these compounds will be of value in the treatment of sleeping sickness cannot be said, but the results obtained thus far seem to indicate a very good beginning.

Phosphorus compounds of the phosphazine type have been prepared by Staudinger and Meyer (297, 298) from diazofluorene and phosphine derivatives. The following equation illustrates their formation:



Triphenylphosphinefluorenoneazine and phenyldiethylphosphinefluorenoneazine were also prepared. On heating, all decomposed with the evolution of nitrogen.

XVI. FLUORENE DYES

Although a large number of fluorene dyes have been prepared, no commercial use of them has apparently yet been made. Sircar and Bhattacharyya (288) have synthesized tetrazo derivatives of 2,7-diaminofluorenone by coupling with various intermediates. Dyes similar to those obtained from benzidine were naturally expected. Table 6 gives the intermediate and the color of the tetrazo compound. All these dyes except Nos. 5, 6, and 12 were substantive to cotton. These same authors also prepared a series of azo dyes from 2-aminofluorenone (288).

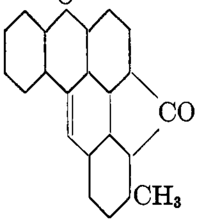
Novelli (220) prepared the bisazo derivative of 2,3,6-naphtholdisulfonic acid and 2,7-diaminofluorene. The sodium salt (4 Na) was a dark violet substance and dyed wool and silk directly. The sodium salt (6 Na) was red and a direct dye for cotton. Other dyes were prepared using H- and K-acids. The study of possible trypanocidal action of these compounds was to be undertaken.

TABLE 6

Fluorene dyes

NO.	INTERMEDIATE	COLOR
1	Phenol	Deep brown
2	*m*-Cresol	Dark brown
3	*o*-Hydroxybenzoic acid	Deep brown
4	β-Naphthol	Deep brown
5	2-Hydroxy-3-naphthoic acid	Brownish violet
6	1-Aminonaphthalene-4-sulfonic acid	Deep reddish brown
7	2,3,6-Naphtholdisulfonic acid	Reddish violet
8	2,6,8-Naphtholdisulfonic acid	Deep brown
9	1-Aminonaphthalene-5-sulfonic acid	Deep brown
10	1-Hydroxy-8-aminonaphthalene-3,6-disulfonic acid	Deep brown
11	1,8-Dihydroxynaphthalene-3,6-disulfonic acid	Bluish violet
12	Dimethylaniline	Deep brown

Sachs and Öholm (251) prepared a vat dye from fluorene and 1,2-naphthoquinone-4-sulfonic acid which gave a variety of mordanted colors. Schaarschmidt and Herzenberg (256) prepared several vat dyes of fluorene which were similar in structure to those of anthraquinone and phenanthraquinone. For example, methylphenanthroanthraquinonefluorenone



was a brown vat dye. Anthraquinone-2,1-fluorenone (254) was an intense red vat dye.

Mukherjee and Dutt (212) condensed aromatic amines and hydroxy compounds with fluorenone to give dibiphenylenexanthenes which were similar in properties to phthalein dyes.

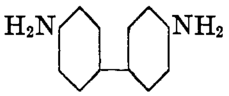
The dyes derived from 2,7-diaminofluorene and 2,7-diaminofluorenone seem to have possibilities in industry, but the present cost of these amines is quite high. Fluorene, nevertheless, is readily available in commercial quantities when the industrial world requires it.

XVII. FLUORENE AND 2,7-DIAMINOFLUORENE IN ANALYTICAL CHEMISTRY

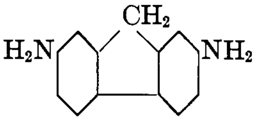
Ditz (75) was the first to report an analytical use for fluorene. He noticed that on the addition of a weak solution of formaldehyde to a solution of fluorene in concentrated sulfuric acid a blue color was formed. Attempts to estimate formaldehyde in milk by this method were unsuccessful, because the test was not sufficiently sensitive for minute amounts of formaldehyde.

Guglialmelli and Delmon (132) studied the color reactions produced by fluorene and concentrated sulfuric acid with various carbohydrates. The test was carried out by adding sulfuric acid to a mixture of 0.5 cc. of an alcoholic solution or suspension of the carbohydrate and 2 to 3 drops of a 2 per cent solution of fluorene in alcohol. Under these conditions carbohydrates which produce furfural when treated with sulfuric acid gave an intense color varying from red to indigo-violet. The colors obtained with glucose, sucrose, α-methylglucoside, and especially with arabinose were very characteristic, and the test may be used for the differentiation of these sugars. DeFazi (67) later extended this test for detecting traces of various aldehydes.

It is evident from the formulas that 2,7-diaminofluorene is very similar in structure to benzidine. Pregl (235) considered it more effective than benzidine in spot tests.



Benzidine



2,7-Diaminofluorene

Guglialmelli and Ruiz (134) found that 2,7-diaminofluorene hydrochloride may replace benzidine in the precipitation of soluble salts of sulfuric, tungstic, molybdic, and chromic acids. It also precipitates meta- and para-tungstates; this is an appreciable advantage over benzidine, since a part of tungstic acid in acid media is converted into meta-, para- and poly-tungstates, which are more or less soluble and would escape precipitation by benzidine. A quantitative procedure for tungsten has been described by these authors. It was also reported that ferro- and ferricyanides and very slight traces of chlorine in water could be detected by this reagent. Nino and Calvet (218) worked out a method for the quantitative determination of zinc, using the diamine as the precipitating agent.

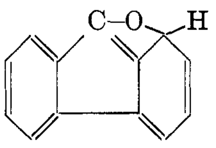
Further studies of the analytical use of 2,7-diaminofluorene were carried out by Schmidt and his coworkers. Schmidt and Hinderer (263, cf. 105) used it to detect small amounts of zinc, cadmium, and copper. 2,7-Diaminofluorene is claimed to possess distinct advantages over benzidine in the detection of peroxidases and persulfates (262, 264). Potassium persulfate can be detected with certainty in dilutions of 1:1,000,000. Since 2,7-diaminofluorene hydrochloride is very sensitive to peroxidases, it may be used to detect blood and to differentiate between boiled and fresh milk. One drop of blood in 50,000 cc. of water gives a distinct blue color; benzidine gives no color at all at this concentration. Schmidt and Hinderer also showed that $0.0_{6}17$ g. of chlorine per cubic centimeter of water could be detected with 2,7-diaminofluorene, whereas with benzidine, chlorine can be detected with certainty only in about three times this concentration. 2,7-Diaminofluorene hydrochloride possessed the distinct advantage of being easily soluble in water. The isomer, 2,5-diaminofluorene, was also investigated.

XVIII. STEREOCHEMISTRY OF FLUORENE

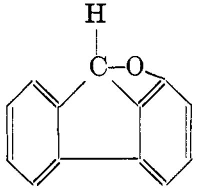
In the course of our description of the chemistry of fluorene we have commented on the claims of various investigators that they had isolated isomers whose existence was not accounted for by the conventional planar formula for the molecule.

Carnelly (38, cf. section III) reported that he had isolated an isomeric form of fluorene itself. This has never been confirmed. The tendency for fluorene to form complexes with other compounds probably explains his results.

Kerp (cf. page 292) reported a red isomeric form of fluorenone to which he assigned the formula



or



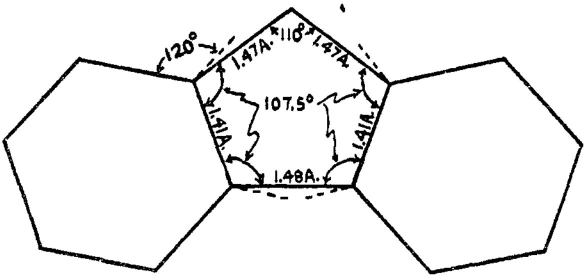
Although Stobbe apparently confirmed the existence of this red isomer, it would seem profitable to reinvestigate it in the light of present knowledge.

The existence of isomeric 9-amino compounds (cf. section VIII C) has not been substantiated by recent exhaustive investigations. Of the two 9-carboxylic acids of Schlenk and Bergmann (cf. section VIII D) the lower melting form probably resulted from imperfect crystals, according to the recent work of Jeanes and Adams (157). These authors found that slow crystallization gave harder and brighter crystals which melted at 232°C. with slight decomposition. Rapid crystallization gave the lower melting (226°C.) form.

Pfeiffer and Lübbe (225) showed that Schlenk and Bergmann's supposed isomeric 9-benzoylfluorene was in reality 9,9-dibenzoylfluorene.

But even though the existence of all cases of stereoisomerides so far reported has been rendered doubtful, the question is by no means disposed of.

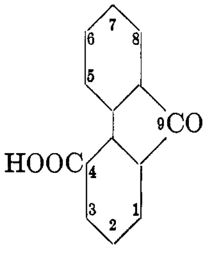
From a consideration of valency angles and interatomic distances a model is produced that would result in considerable strain if a planar formula is assumed (231).



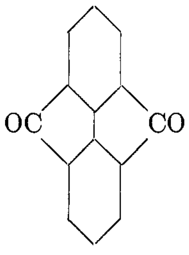
The evidence obtained in x-ray examinations of fluorene might be expected to distinguish between planar and non-planar formulas. But here again the results are open to various interpretations. Stuart (305) has interpreted the data of Hengstenberg and Mark (139) as evidence for the planar configuration. Dipole moments reported by Hughes, Lefevre, and Lefevre (147) also seem to support this view. Cook and Iball (49) do not agree with these views and maintain that their data are best satisfied by a non-planar formula with each benzene ring inclined 20° to the five-membered ring and 40° to each other. They do not go so far as to postulate isomers, since they suggest that "it may be that the molecule possesses sufficient elasticity to undergo oscillation between two non-planar forms."

The tendency of the five-membered fluorene ring to expand during the Stieglitz rearrangement has been described (cf. page 327). This seems to be evidence of considerable strain, which would imply a planar configuration. In section XIV, however, the formation of spirofluorene compounds seems to represent a more stable ring system. This would imply little strain in the fluorene molecule.

Miller, Parker, and Tomlinson (202) point out that fluorenone-4-carboxylic acid (I) does not undergo further condensation to a compound of the type II.



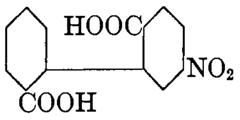
I



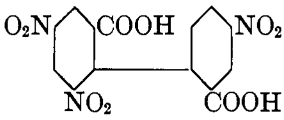
II

This they advance as evidence for the non-planar formula. It seems to us, on the contrary, to indicate that the bond joining the benzene rings is bent, *increasing* the distance between the 4- and 5-positions, which is to be expected if the compound has a planar formula.

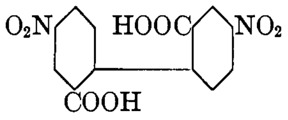
Somewhat more convincing is the work of Bell and Robinson (19). They found that although 5-nitrodiphenic acid (III) gave a fluorenone on heating with sulfuric acid, 4,4′,6′-trinitrodiphenic acid (IV) did not.



III



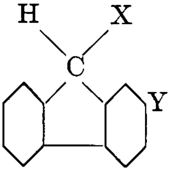
IV



V

Now, by resolution into its optical antipodes, it has been shown that the two benzene rings of IV are not coplanar. The failure of this compound to form a fluorenone would seem to suggest that fluorenone requires coplanar rings. Any reasoning, however, that is built on the failure of a compound to react is fraught with uncertainty. The explanation might well be that the right conditions were not used. Especially is this the case here, because Underwood and Kochmann (320) have also reported that 4,4′-dinitrodiphenic acid (V) does not give a fluorenone. If this is correct it points to a possible electrochemical effect rather than to steric hindrance.

Of course the resolution of a monosubstituted fluorene compound would be conclusive evidence for the non-planar form. But even such expected antipodes as



have resisted all efforts at resolution (22). This failure of the diastereoisomeric salts to separate, even in what should be classical cases, makes the possibility of resolving non-planar forms remote.

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