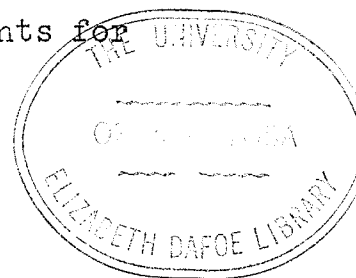


SYNTHESIS OF 3-BROMO-  
6-NITROFLUORENONE

by

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To My Beloved Parents

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## ABSTRACT

A synthesis of 3-bromo-6-nitrofluorenone has been accomplished and the evidence that 2-nitrofluoranthene brominated in the 9-position has been confirmed. The theoretical implications of these results have been discussed. As a result of this work nine new compounds have been prepared, namely, 4-nitro tosyl anthranilic acid, 4-bromo-2-methyl-4'-nitrobenzophenone, 5-bromo-2-(p-nitrobenzoyl) benzoic acid, 5-bromo-2-(p-nitrobenzoyl) benzoyl chloride, 5-bromo-2-(p-nitrobenzoyl) benzamide, 2-amino-4-bromo-4'-nitrobenzophenone, 3-bromo-6-nitrofluorenone, 3-bromo-6-nitrofluorenone oxime, 4-bromo-2-hydroxy-4'-nitrobenzophenone.

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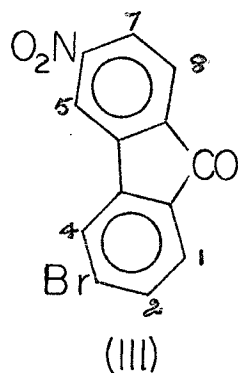
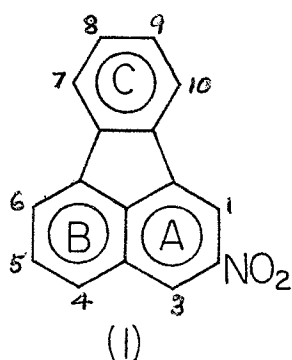
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## INTRODUCTION

In 1965, in these laboratories A. Dolenko (20) studied the bromination of 2-nitrofluoranthene (I). The bromo-2-nitro-derivative thus obtained, on oxidative degradation, gave a compound which on theoretical grounds appeared to be 3-bromo-6-nitrofluorenone (III).



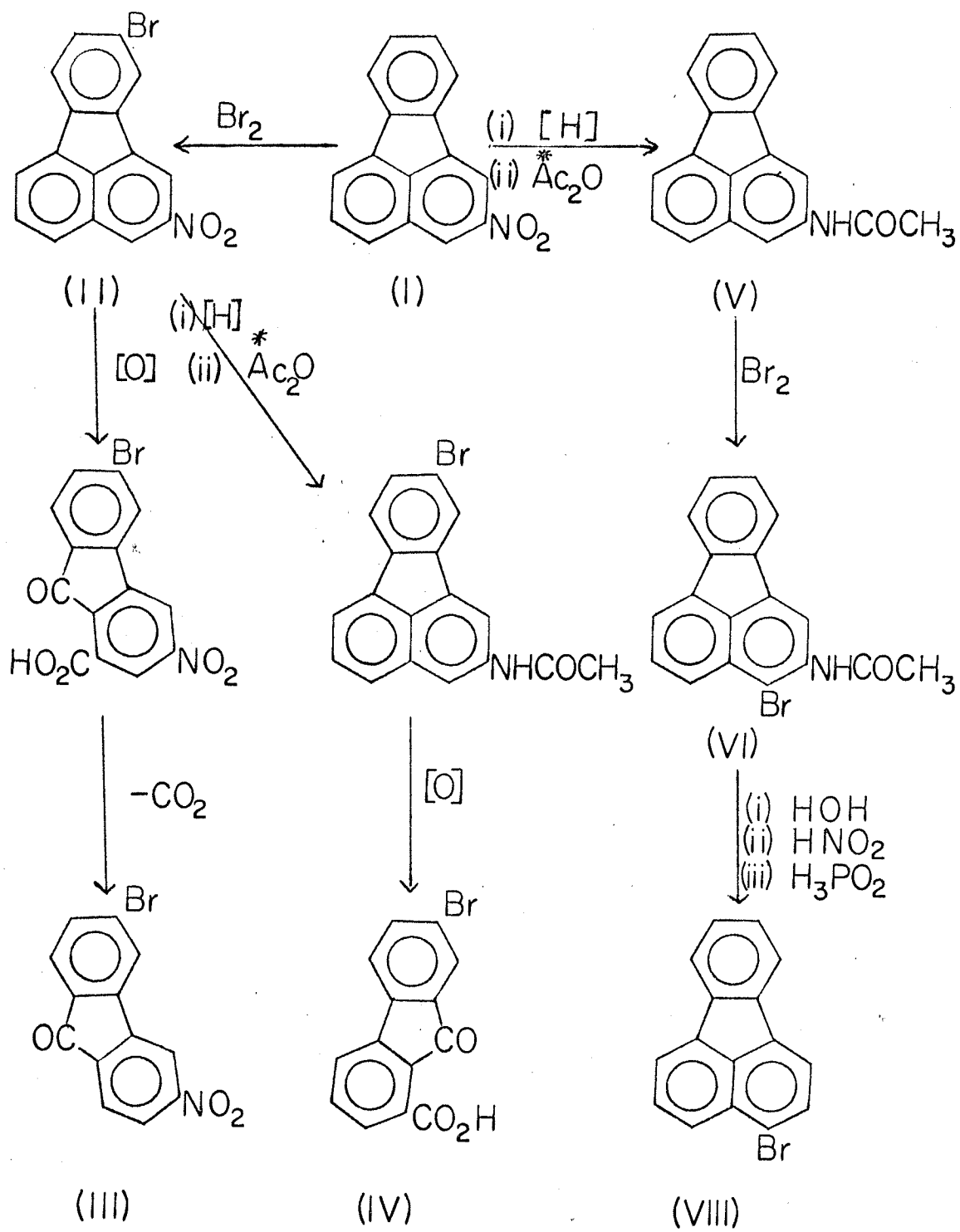
If so, this would establish that the bromination of fluoranthene had occurred in the C-ring and in the 9-position. As 3-bromo-6-nitrofluorenone has not been reported in the literature, it seemed very desirable that its synthesis should be undertaken by a method or methods that would leave no doubt as to its orientation. A comparison could then be done with Dolenko's product. The synthesis of this substance forms the content of this thesis.

In the past few years the preparation and the orientation of disubstituted fluoranthenes has been the subject of careful study in this laboratory and in many other laboratories. This work has revealed some directive properties of the fluoranthene nucleus. The studies on



3-substituted fluoranthenes by Campbell and Keir (13) led to the generalization that a meta-directing group in ring A of fluoranthene would direct a second substituent to the 9-position. Furthermore an ortho-para-directing group in the same ring would direct a second substituent to the 8-position. The work of Kloetzel, King and Menkes (47) necessitated a modification of the above generalization, that a strongly activating group in ring A, should cause further substitution in the same ring. This was later substantiated by the work of Charlesworth and Blackburn (14) who found that 3-amino and 3-acetamidofluoranthenes brominated in the 2-position.

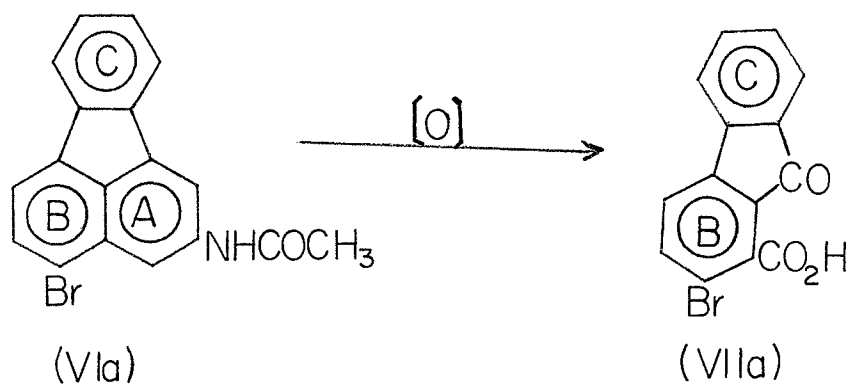
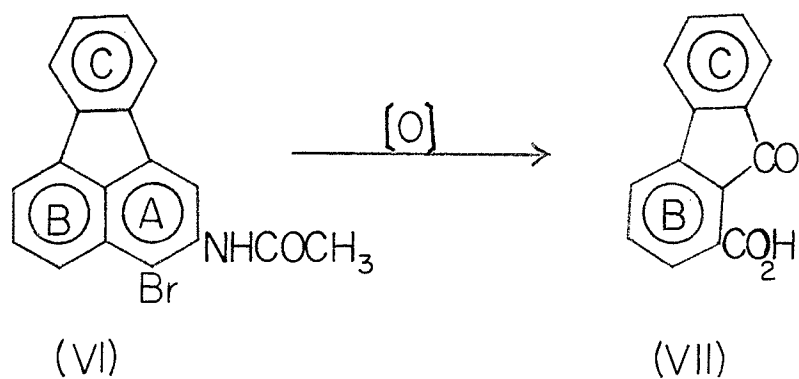
Dolenko (20) extended the study to determine the directive properties of 2-substituted fluoranthenes. The results on the directive effects of nitro (a deactivating and meta-directing) and acetamido (a strongly activating) groups in the 2-position were shown to be in accordance with the above mentioned rules; i.e., 2-nitrofluoranthene brominated in the 9-position as expected from Campbell's generalization, and 2-acetamidofluoranthene ~~was~~ brominated in the 3-position according to Kloetzel's modification. The orientations of bromine in the brominated fluoranthenes were established according to the scheme on page 3. The bromo-fluorenone-carboxylic acid (IV) was shown to be identical with an authentic sample of 7-bromo-fluorenone-1-carboxylic acid, thus showing that bromine was in the 9-position of the fluoranthene. The oxidation of the 9-bromo-



\* Ac<sub>2</sub>O — (CH<sub>3</sub>CO)<sub>2</sub>O

2-nitrofluoranthene (II), followed by the decarboxylation of the oxidation product to the bromo-nitrofluorenone (III) was also carried out with the hope of obtaining an additional evidence. The bromine in the 9-position of the fluoranthene would give 3-bromo-6-nitrofluorenone. The present work has shown the identity of the bromo-nitrofluorenone (III) to 3-bromo-6-nitrofluorenone, thus confirming the evidence that 2-nitrofluoranthene brominated in the 9-position.

The orientation of bromine in the 2-acetamido-bromo-fluoranthene (VI) was established (20) by converting it to the bromofluoranthene (VIII). This bromofluoranthene was shown to be identical with 3-bromofluoranthene, thus indicating that bromine was either in the 3-position or in the 4-position. So far there have been no instances in which a substituent has been shown to enter the B-ring (i.e., 4, 5 and 6-positions). Therefore it was concluded by Dolenko (20) that the bromine was in the 3-position. This conclusion could be confirmed by carrying out an oxidation in the acetamido-bromo-fluoranthene stage. 2-Acetamido-3-bromo-fluoranthene (VI) would give the fluorenone-1-carboxylic acid (VII), because the ring A being electronically rich, would be more susceptible to oxidation than the rings B and C. Whereas 2-acetamido-4-bromofluoranthene (VIa) would give 2-bromo-fluorenone-1-carboxylic acid (VIIa), because again the ring A, being activated by the acetamido group, would be degraded during oxidation.



Time did not permit either Dolenko or the writer to perform this oxidation, but it would seem very desirable that it should be tried by some other worker in the near future.

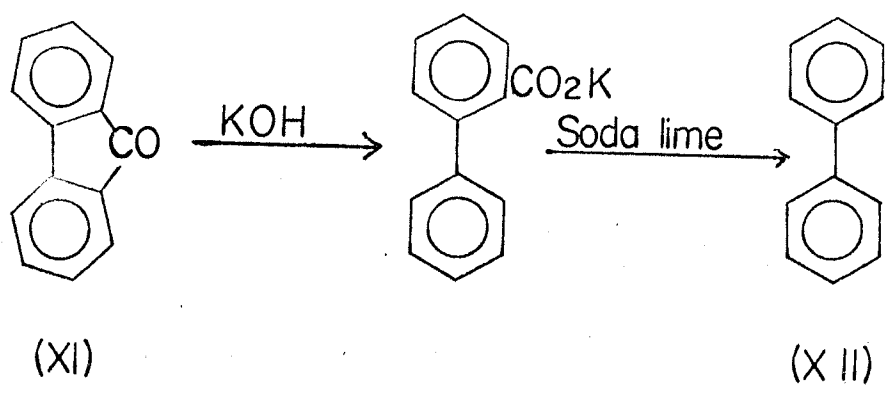
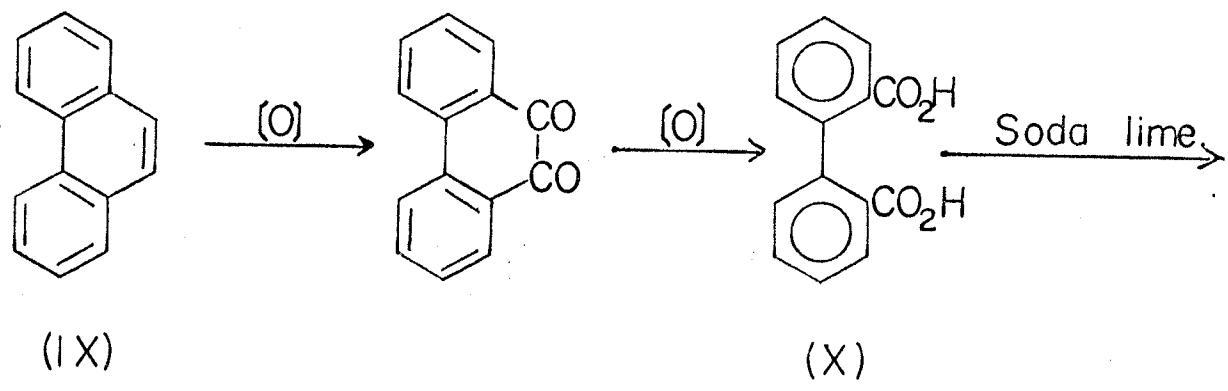
## LITERATURE SURVEY

### (1) The Discovery and the Structure of Fluorene

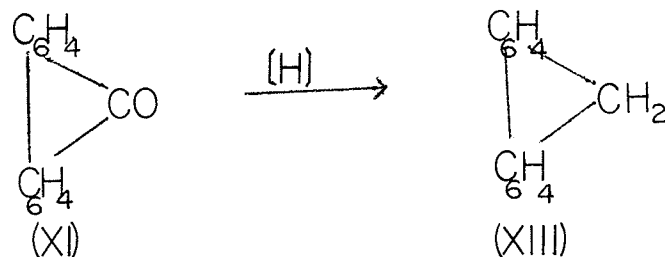
The chemistry of fluorene began at a comparatively early date in the history of organic chemistry. During his memorable researches on the pyrogenetic hydrocarbons, in 1867 Berthelot (9) isolated a new substance from the fraction of crude anthracene oil boiling between 300 and 310°C. This substance on recrystallization from hot ethanol gave a white fluorescent solid melting at 113°C. Because of the fluorescence Berthelot named it as "Fluorene". However, in 1883 Hodgkinson and Mathews (41) 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 discovery of phenanthrene (IX) in 1872 by Fittig and Ostermayer (31) and independently in the same year by Graebe (35), played an important role in the prompt elucidation of the constitution of fluorene. Fittig and Ostermayer (32) carried out the following degradation, leading to the known biphenyl (XII). (See next page for the flow sheet). The compound resulting from the action of soda lime on the then unknown diphenic acid (X) was rightly interpreted as biphenylene ketone (XI)  $\bar{m}.p.$  83.5 - 84°C<sup>7</sup>.

Fittig (27) distilled the biphenylene ketone with zinc dust and found that it was reduced to a white substance melting at 113-114°C. He regarded this compound as

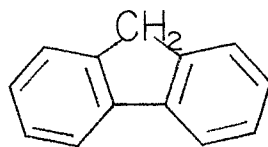


biphenylene methane (XIII).

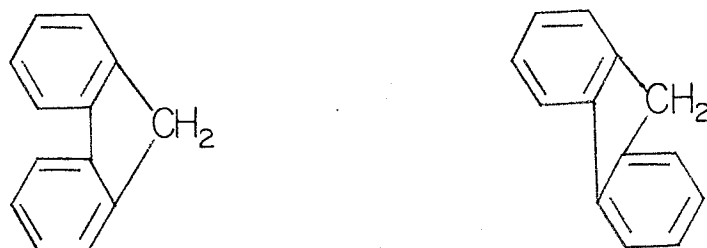


Graebe (36), using the biphenylene ketone of Fittig, carried out the reduction with red phosphorus and hydriodic acid and obtained the same hydrocarbon. Barbier (5) observed that the compound obtained by the oxidation of fluorene with potassium dichromate and sulphuric acid was identical with the biphenylene ketone of Fittig and Ostermayer.

In 1878, Fittig and Schmitz (33) reported that the biphenylene methane previously obtained by Fittig from the biphenylene ketone was identical with fluorene obtained by Berthelot and Barbier. Hence the structural formula of fluorene could be represented as:



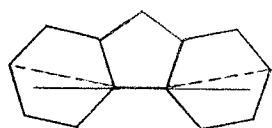
In 1925, Kuhn and Jacob (49) proposed a space formula for fluorene (XIV) based on Kaufler's formula for diphenyl in order to explain their claimed separation of two forms of 9-amino fluorene.



(XIV)

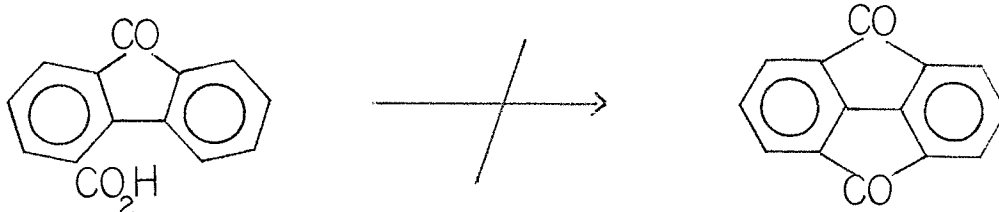
Since then, there has been extensive investigation of the possibility of stereoisomerism of 9-substituted fluorenes. All such attempts have failed or been disproved, so that such extreme forms as pictured in (XIV) seems unlikely if not impossible.

Mills, Palmer and Tomkinson (56) suggested that a strainless configuration for the fluorene molecule could be achieved by the planes of the benzene rings becoming inclined to the 5-membered ring. The stereochemical implications of such a non-planar structure have been widely investigated, with some equivocal results, reviewed by Cook and Iball (17). But the evidence does seem to indicate that the rings are bent away from the coaxial diphenyl bond with a distortion of the valence angles from the benzene rings by  $12^\circ$ , to give (XV) a planar structure as pictured by Pinck and Hilbert (64), where the five membered ring is nearly a regular pentagon.



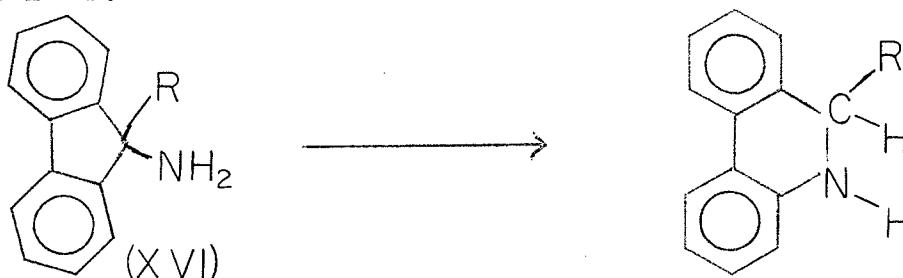
(XV)

This formula is probable from dipole measurements (8), (42) and x-ray studies (39) and is further supported by the failure of fluorenone-4-carboxylic acid to close a fourth ring (56), the distance being too great to be bridged.

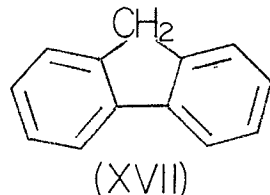




Such a planar configuration as (XV) would be in a state of strain and has been used (64) to account for the ready enlargement of the five-membered ring in the Stieglitz rearrangement of the amines of the type (XVI) to yield phenanthridines.



Mills and Nixon (55) suggested that this internal strain could be relieved at least partially by a preferred arrangement of the double bonds as shown in (XVII).



Evidence favouring this formula is scant but may be found in the ring closures of  $\gamma$ -2-fluorylbutyric acid (48) and of  $\delta$ -(2-fluoryl)-benzoic acid (7) both of which take place into the 3-position. These facts seemed to indicate that the double bond in fluorene is located entirely between positions 2 and 3 as shown in (XVII).

From the above discussion, it is evident that the problem of the bond structure of fluorene is similar to that of naphthalene, anthracene, etc., and like them fluorene should be susceptible to attack by the methods used by Fieser and Lothrop (22), (23), (24), (25) which depend on the Claisen rearrangement of allyl ethers and the diazo coupling

of the hydroxyl derivatives.

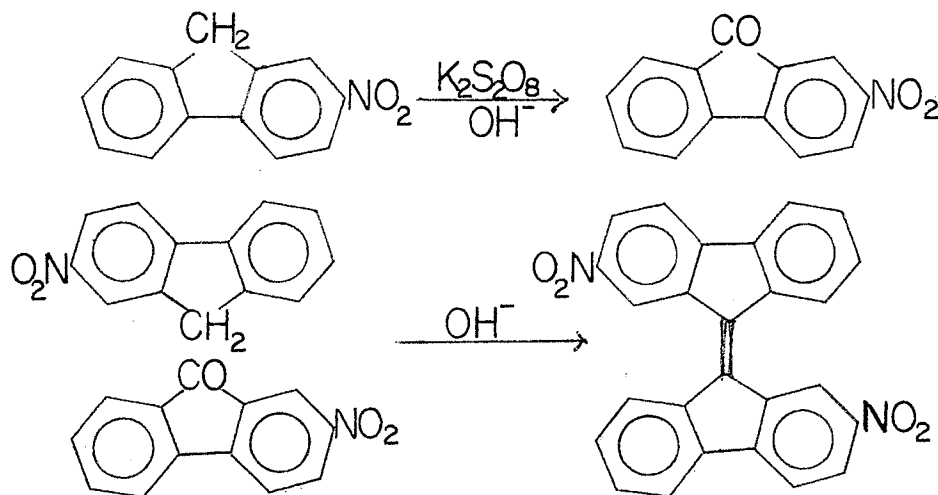
A preliminary investigation (51) of the rearrangement of the allyl ethers of 2-hydroxyfluorene and 3-hydroxyfluorene indicates that the aromatic ring in fluorene is benzoid rather than naphthoid and it is suggested that the special reactivity of positions 2- and 7- may be ascribed to the superior directive properties of the phenyl group.

## (2) Oxidation of Fluorene

Fluorenone, the main oxidation product of fluorene has been obtained in a number of ways.

- (a) Huntress, Herschberg and Cliff (46) used sodium dichromate in acetic acid as the oxidising agent and obtained fluorenone in good yields. This method is suitable for large scale laboratory preparation of fluorenone.
  - (b) Postowski and Lugowkin (65) have shown that fluorene on oxidation with selenium oxide gave only 5% fluorenone.
  - (c) Courtot (18) used solutions of potassium permanganate at room temperature to oxidise fluorene and derivatives to the corresponding fluorenones. The yields were mostly quantitative.
- (3) Gutmann, Butle and Fenton (37) studied the oxidation of fluorene, 2-acetamido fluorene and 2-nitrofluorene by alkaline potassium persulphate solutions. They found that fluorene and 2-acetamido fluorene

were resistant to oxidation whereas 2-nitrofluorene was attacked at the methylene carbon to yield 2-nitrofluorenone and 2,2'-dinitro-9,9'-bifluorenylidene.



Since of the three fluorene derivatives investigated only 2-nitrofluorene which has a strongly electron attracting substituent on the nucleus was attacked, it appears that successful oxidation of fluorene compounds by persulphate depends upon the formation of an anion.

- (e) Wheeler (73) used chromyl chloride as an oxidising agent and obtained fluorenone in 35% yield.
- (f) Sprinzak (71) observed that when a solution of fluorene in pyridine was stirred in an atmosphere of oxygen at room temperature in the presence of a small amount of Triton B, one mole of oxygen per mole of fluorene was absorbed with heat evolution and fluorenone was formed in almost quantitative yield. The reaction was not sensitive to light and started without an induction period.

This high reactivity may be attributed to the presence of appreciable concentration of carbanions recognizable by the colour of their solutions.

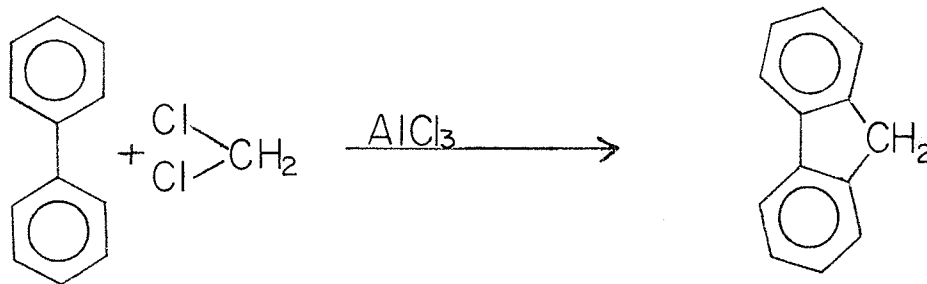
- (g) Recently Ogata, Kotake and Aoki (60) in their investigation of peracetic oxidations of polynuclear aromatic compounds, found that fluorene on oxidation with peracetic acid gave a dihydroxy fluorenone. The positions of the two hydroxyl groups are still uncertain.

### (3) Synthesis of Fluorenones

#### (a) Oxidation of Fluorenes

Fluorenones may be obtained by the oxidation of fluorenes by methods described in the previous section. So the methods of formation of fluorenes could be extended as a synthetic route to fluorenones, by including the oxidation step. Hence the formation of fluorenes is considered first.

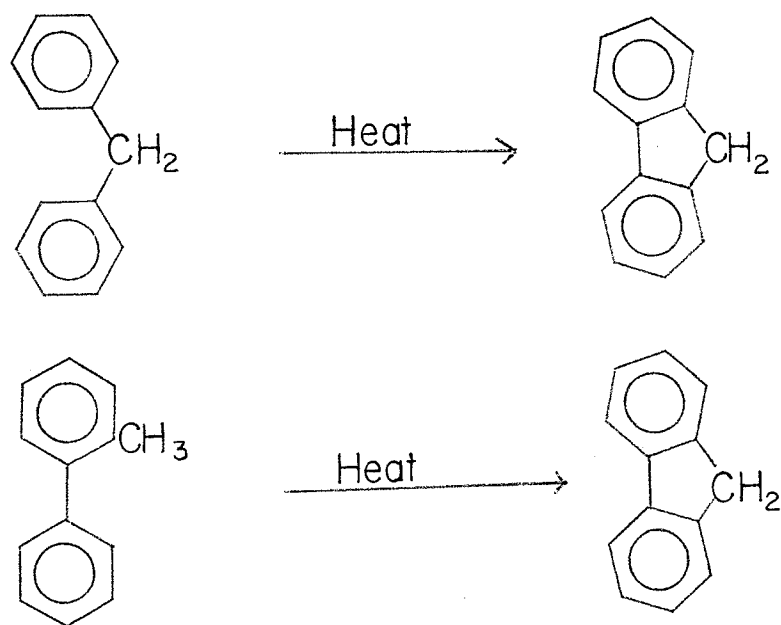
In 1886, Adam (2) showed that biphenyl and methylene dichloride in a Friedel-Crafts reaction yielded fluorene. The reaction indicated very well the structure of fluorene and its close relationship to biphenyl.



The synthesis of new biphenyl derivatives has led to the

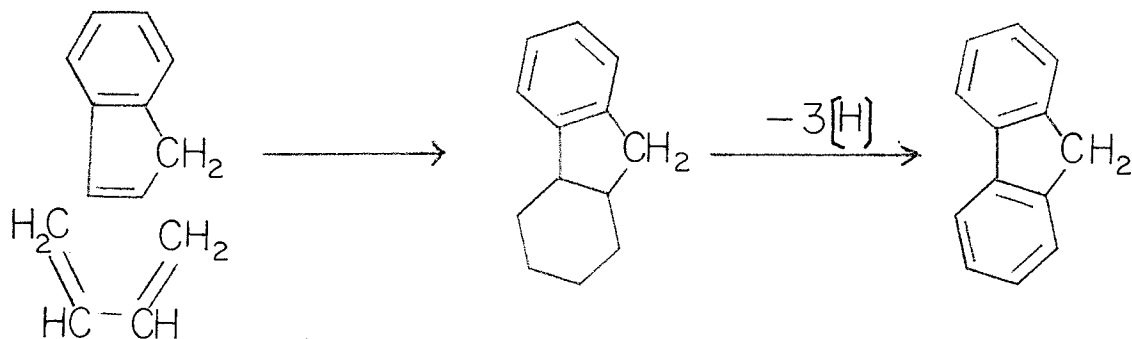
successful preparation of fluorenone and fluorene derivatives with substituents in 3, 4 and 6 positions (63).

Fluorenes are also obtained by the cyclodehydrogenation, usually by heating to a high temperature in the presence of a catalyst, of diphenyl methane and of *o*-methyl biphenyls (61), (62), (63).



Longo and Pirona (50) have made a study of the synthesis of fluorene compounds from biphenyl derivatives and in particular the influence of the positions of substituting groups on the formation of fluorene structures. They were able to prepare 1-methyl fluorene and 1, 6-dimethyl fluorene through the synthesis of some then new biphenyls.

Another synthesis of fluorenes involves a "diene" addition of butadiene to indene to give a tetrahydrofluorene (3) which on dehydrogenation gives fluorene.



A synthesis of limited scope involves the application of Mannich reaction to  $\alpha$ -indane derivatives. Harradence and Lions (38) prepared a few fluorene derivatives by the above method.

#### (b) Direct Substitution

Fluorenones may also be prepared by direct substitution on fluorenone or on fluorene followed by oxidation. Originally this method was used to prepare 2- and 2, 7- substituted fluorenones. But substitution studies on both fluorene and fluorenone indicated that this method may also be used to prepare 3- and 3, 6- substituted fluorenones. It is also worthwhile to note that this method suffers from the marked disadvantage in the separation of the mixture of fluorenones formed. For example, consider the nitration of fluorenone. The various nitration products formed, are as shown in the scheme on the following page. The aforementioned scheme may be used to obtain fluorenones with substituents in 2, 4, 5 and 7 positions. The 3-, and 3, 6- substituted fluorenones have been obtained by a slight variation in the method of

