ABSTRACT OF THESIS

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Degree Ph.D. *Date* August, 1968

Title of Thesis Polycyclic Azacompounds with special reference to the Azafluoranthenes.

1. During the attempted synthesis of 9-fluorenemethylamine, required for a Bischler-Napieralski cyclisation to 2-azafluoranthene, several 9-substituted fluorene derivatives were obtained. 9-Bromofluorene with potassium cyanide gave 9-cyano-9,9′-bifluorene. 9-Carbamoylfluorene with lithium aluminium hydride, 9-cyanofluorene with lithium aluminium hydride-aluminium trichloride, and 9-formylfluorene oxime with thionyl chloride gave 9,9′-dicyano-9,9′-bifluorene. 9-Formylfluorene oxime was obtained as a mixture of α- and β-isomers, of which only the β-form could be obtained pure. Reduction of the oxime mixture with lithium aluminium hydride gave 9-hydroxy-9-fluorenemethylamine. Attempted degradation of 9-fluoreneacetic acid to 9-fluorenemethylamine was unsuccessful.

2. The attempted preparation of 2-azafluoranthene by a cyclisation involving acylation of 1-cyanofluorene with dimethyl oxalate was unsuccessful.

3. Ethyl 1-fluorenemethylurethane could not be cyclised with potassium methoxide to a 2-azafluoranthene.

4. 2-Azafluoranthene was synthesised by a procedure involving ring closure of methyl 9-formylfluorene-1-carboxylate with ammonia. The oxidation and reduction of the base is discussed.

5. Nitration of 2-azafluoranthene gave 9-nitro- and 4,9-dinitro-2-azafluoranthene, and the orientation of the nitro groups in these compounds is discussed.

6. Nitration of 1,2-diazafluoranthene gave a mononitro- and a dinitro-compound.

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POLYCYCLIC AZACOMPOUNDS WITH SPECIAL REFERENCE TO THE AZAFLUORANTHENES

by

James M. Birnie, B.Sc.

Thesis presented for the Degree of Doctor of Philosophy.

University of Edinburgh. August 1968.

TO MY PARENTS

and

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SUMMARY.

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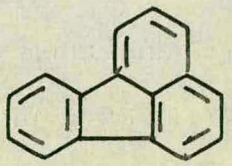
5. Nitration of 2-azafluoranthene gave 9-nitro- and 4,9-dinitro-2-azafluoranthene, and the orientation of the nitro groups in these compounds is discussed.

6. Nitration of 1,2-diazafluoranthene gave a mononitro- and a dinitro-compound.

INTRODUCTION.

MONOAZAFLUORANTHENES

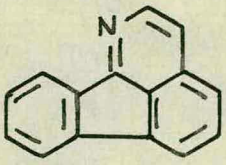
The polycyclic hydrocarbon fluoranthene has been known for over a century, although it was not until 1929 that the German workers Anton and Von Braun[1] established the structure of the molecule as (I), by synthesis from a fluorene derivative.



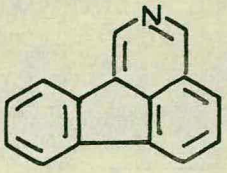
I

Since then various substituted fluoranthenes have been synthesised in which one or more of the hydrogen atoms have been replaced by a suitable functional group. More recently success has been achieved in replacing the carbon atoms of the molecule with a heteroatom. Replacement by nitrogen has led to the series of heterocycles known as the azafluoranthenes.

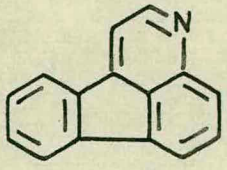
There are five theoretically possible, isomeric monoazafluoranthenes and the possible formulas are listed below (II - VI).



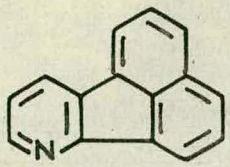
[1-aza-(II) Indeno[1,2,3-i,j] isoquinoline]



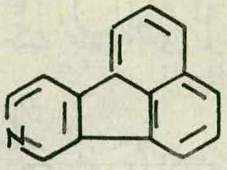
[2-aza-(III) Indeno[1,2,3-de] isoquinoline]



[3-aza-(IV) Indeno[1,2,3-de] quinoline]

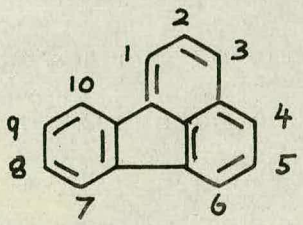


7-aza-(V)
Acenaphtho [1,2-b]
pyridine

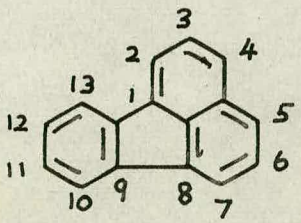


8-aza-(VI)
Acenaphtho[1,2-c]
pyridine

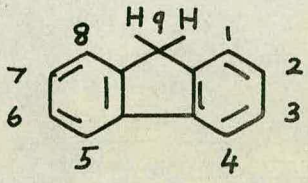
These fluoranthene derivatives have been numbered in the literature in two different styles, A and B, as has the parent fluoranthene molecule



A



B

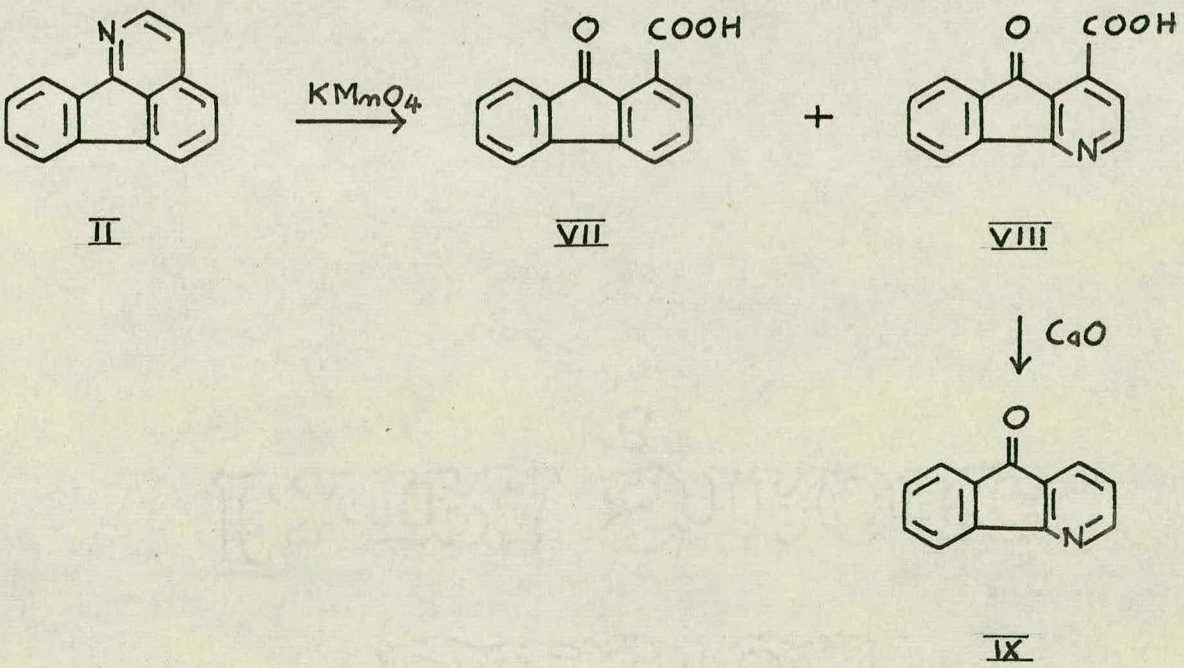


C

The former system is that employed in Chemical Abstracts, and will be used throughout this thesis in numbering the carbon and nitrogen atoms of the azafluoranthenes; the latter was adopted by European Chemists and is in accordance with the Richter system of notation, and was used in the early publications on the azafluoranthenes. The structurally related hydrocarbon fluorene is numbered as in C. Since 1957 Chemical Abstracts has also named the monoazafluoranthenes

in accordance with their relationship to the heterocycles pyridine, quinoline and isoquinoline. This form of nomenclature is shown in brackets below the formula diagrams.

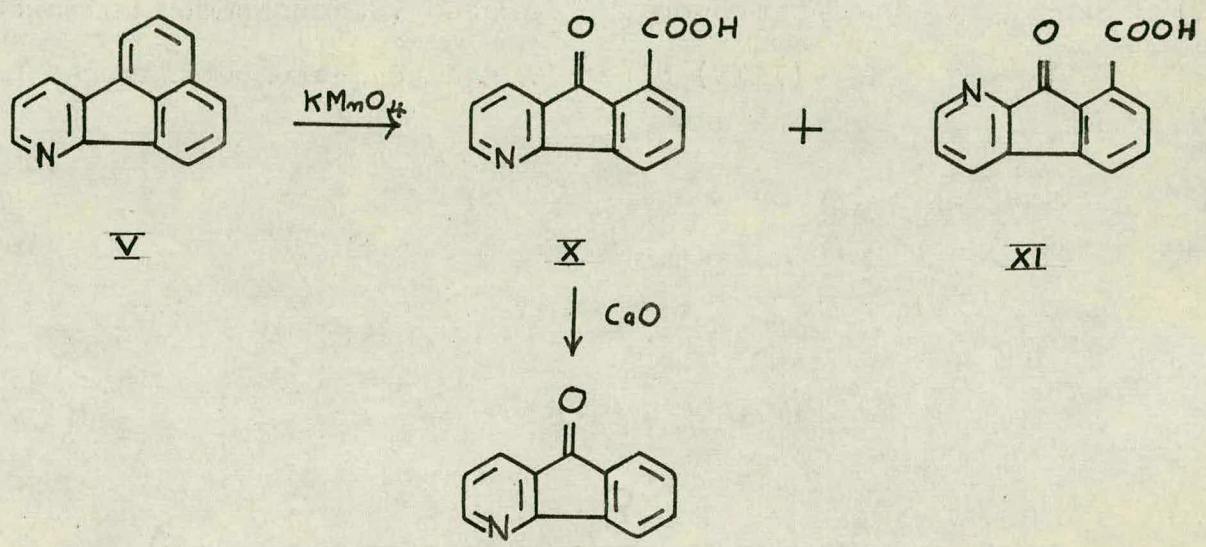
The first azafluoranthene to be isolated was appropriately 1-azafluoranthene, obtained by Kruber[2] in 1949 from the high boiling, fluoranthene-pyrene fraction of coal tar. He established the structure of the heterocycle by oxidative breakdown with potassium permanganate, obtaining fluorenone-1-carboxylic acid (VII) and 4-azafluorenone-1-carboxylic acid (VIII)



II VII VIII IX

Decarboxylation of the latter with lime yielded the known 4-aza-fluorenone (IX).

R. Oberkobusch[3] in 1953 isolated from coal tar 1-azafluoranthene and a new isomer 7-azafluoranthene (V). Oxidation of the latter with permanganate yielded the two isomeric acids 4-azafluorenone-8-carboxylic acid (X) and 1-azafluorenone-8-carboxylic acid (XI).



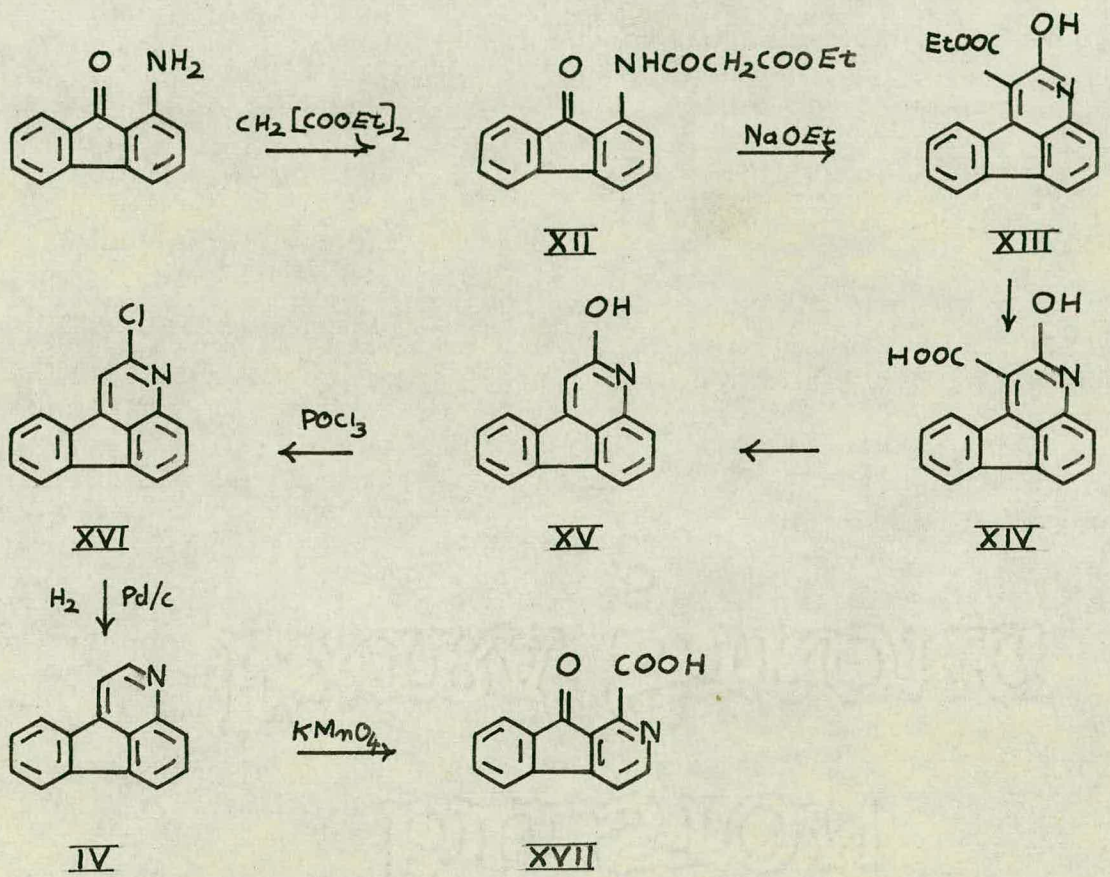
V X XI

IX

Decarboxylation of the former with lime yielded the known 4-azafluorenone (IX).

The 3-azafluoranthene molecule was synthesised independently by Cook and Moffat[4] in 1950 and by Koelsch and Steinhauer[5] in 1953. Both pairs of workers condensed diethylmalonate with 1-aminofluorenone to obtain 1-carboxyacetamidofluorenone (XII), which was then cyclised under the influence of sodium ethoxide in ethanol

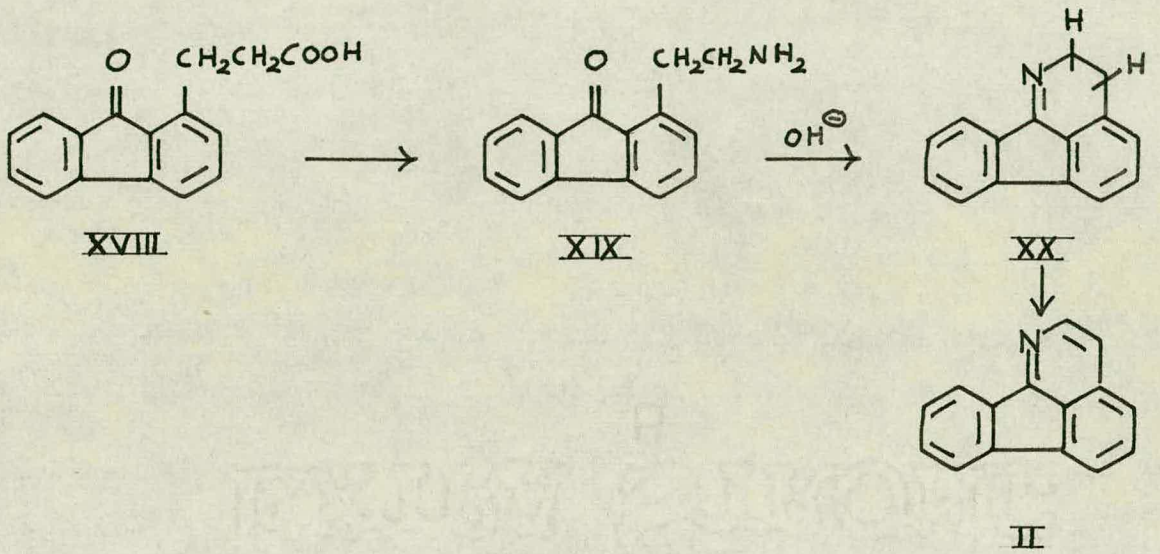
[or nitrobenzene], to the ester (XIII). Hydrolysis of the latter to the acid (XIV), and subsequent decarboxylation yielded 3-azafluoranth-2-ol (XV) which was converted into 2-chloro-3-azafluoranthene (XVI) with phosphorus oxychloride.



Cook and Moffat proceeded as far as the chlorocompound (XVI), with which they condensed ammonia and a variety of amines, while Koelsch and Steinhauer reduced the chlorocompound to the parent 3-azafluoranthene (IV), which they oxidised to 2-azafluorenone-1-carboxylic acid (XVII).

Campbell and Reid[6] synthesised the 1-azafluoranthene isolated from coal tar by Kruber[2]. Application of the Curtius reaction to β-[9-oxo-1-fluorenyl] propionic acid (XVIII) gave the substituted

ethylamine (XIX), which with alkali yielded 2,3-dihydro-1-aza-fluoranthene (XX). This on dehydrogenation with palladised charcoal yielded 1-azafluoranthene (II).

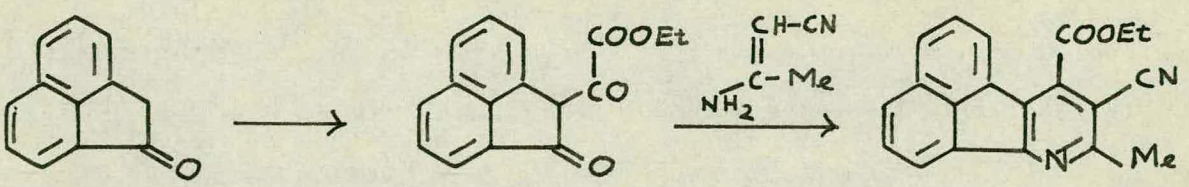


XVIII XIX XX

II

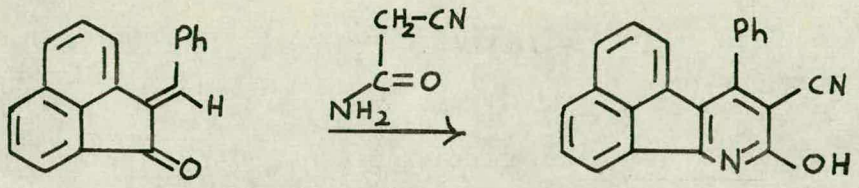
1-Azafluoranthene is a pale yellow compound melting at 91-92°C and not 83°C as stated initially by Kruber[2]. It appears that the latter's sample of the hydrocarbon was contaminated with some 7-isomer.

In 1957, Chatterjea and Prasad[7] prepared derivatives of the 7-azafluoranthene isolated initially by Oberkobusch[3]. Acenaphthenone (XXI) was converted into its glyoxylic ester (XXII), and condensed with 2-aminocrotonitrile in ethanol to yield the 7-azafluoranthene derivative (XXIII).



XXI XXII XXIII

They also condensed benzylidene-acenaphthenone (XXIV) with cyano-acetamide to yield the 7-azafluoranthene derivative (XXV).



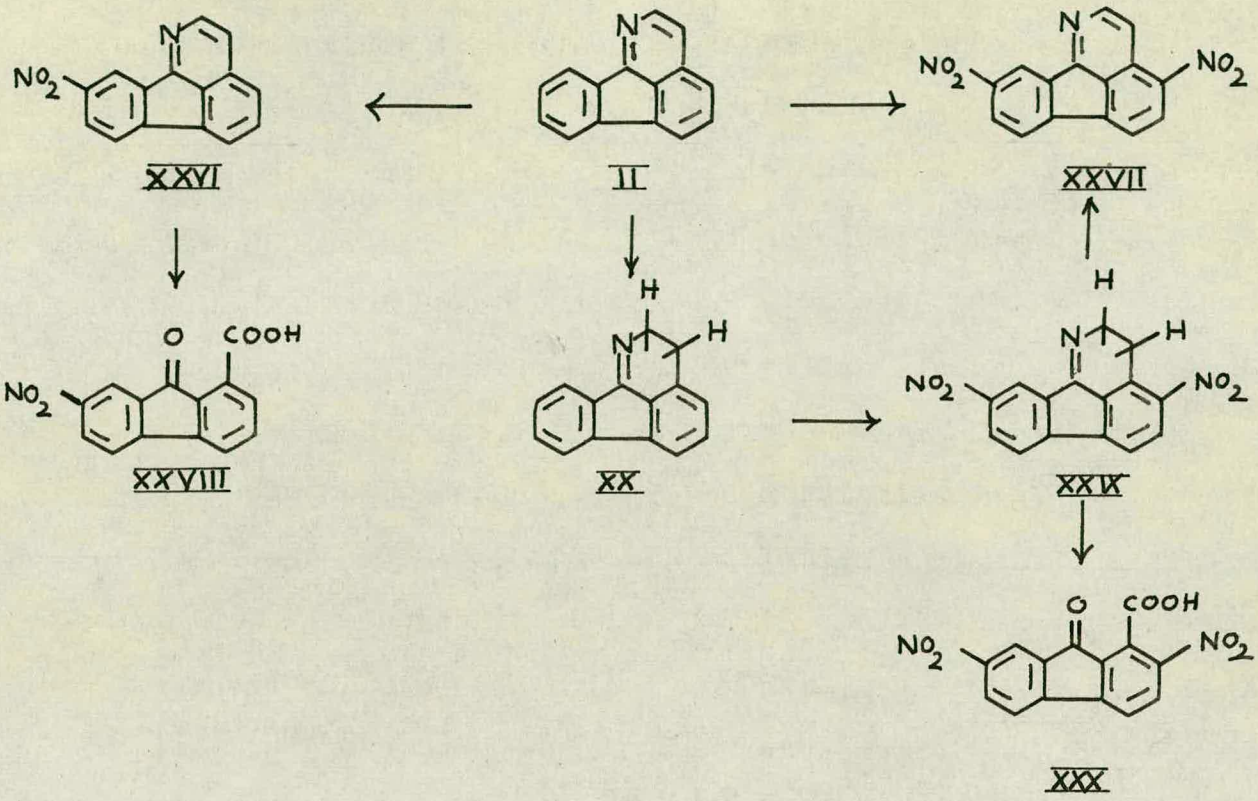
XXIV XXV

At the commencement of the work detailed in this thesis no work had been carried out on the isolation or synthesis of the remaining two monoazafluoranthenes, the 2- and 8-isomers. It was the purpose of this thesis to synthesise 2-azafluoranthene, and investigate the properties of this heterocycle.

The properties of the 1-, 3- and 7-azafluoranthenes have been reasonably well investigated. 1-Azafluoranthene, as has already been mentioned, is a pale yellow compound, mp = 91-92°C; 3-aza-fluoranthene is a yellow compound mp = 102-3°C; and the 7-isomer is a colourless compound mp = 96-97°C.

Campbell and Reid[6] and Koelsch and Steinhauer[5] determined the preferred position of electrophilic attack in the 1- and 3-aza-fluoranthenes respectively, the electrophile in both cases being the nitronium ion. Nitration of 1-azafluoranthene yielded 9-nitro (XXVI) and 4,9-dinitro-1-azafluoranthene (XXVII) under different reaction conditions.

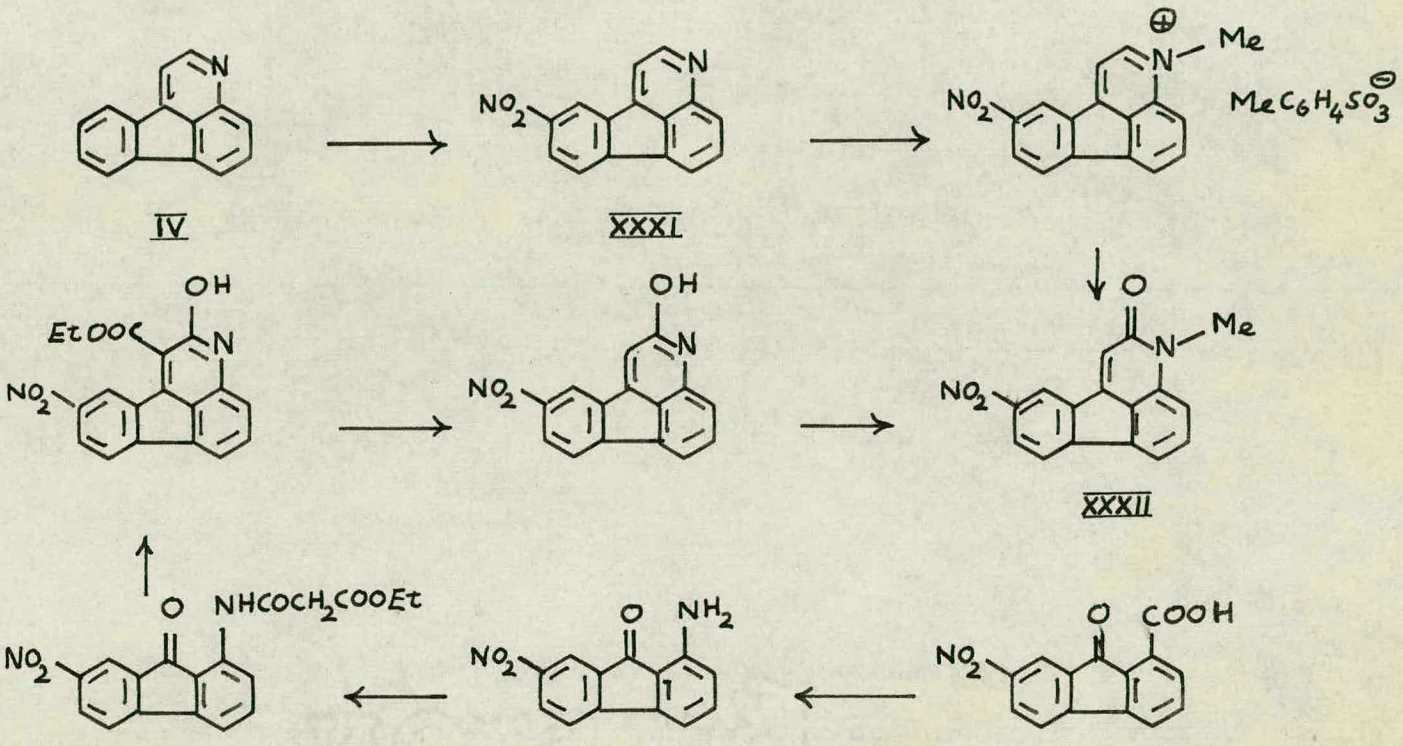
The mononitro-compound was obtained by dissolving 1-azafluoran-thene nitrate in concentrated sulphuric acid and allowing nitration to proceed at room temperature for ninety minutes, and then at 60°C



for twenty minutes. The dinitro-compound was obtained by treatment of a solution of 1-azafluoranthene in concentrated sulphuric acid with one mole of potasium nitrate at room temperature for 20 hours. The constitution of the mononitro-compound followed from oxidation of its methiodide to 7-nitrofluorenone-1-carboxylic acid (XXVIII). The dinitroazafluoranthene was orientated by its preparation by the dehydrogenation of 2,3-dihydro-4,9-dinitro-1-azafluoranthene (XXIX), [obtained by nitration of 2,3-dihydro-1-azafluoranthene (XX)], whose constitution was established by its oxidation to 2,7-dinitro-fluorenone-1-carboxylic acid (XXX).

Mononitration of 3-azafluoranthene under identical conditions as for the 1-aza-isomer, i.e. by dissolving the nitrate in sulphuric

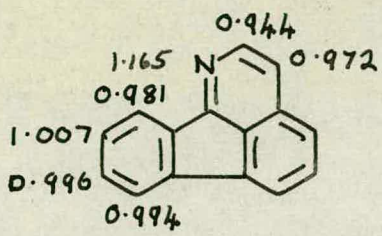
acid, yielded 9-nitro-3-azafluoranthene (XXXI). Orientation of the nitro group was determined by oxidation of the metho-p-toluene-sulphonate of (XXXI) by alkaline permanganate to the corresponding 3-methyl-9-nitro-3-aza-2-fluoranthone (XXXII). The position of the nitro group in this substance was established by synthesis.



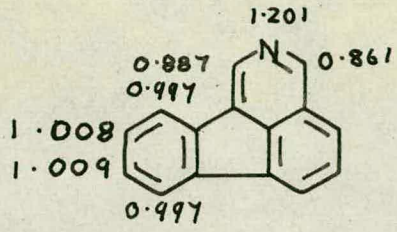
7-Nitrofluorenone-1-carboxylic acid (XXVIII) was converted into 1-amino-7-nitrofluorenone, and a pyridone ring was built on this by the Camps reaction. Decarboxylation and methylation gave a product identical with that obtained from 9-nitro-3-azafluoranthene.

In 1966, Michl and Zahradnik[8] calculated by H.M.O. [Hückel molecular orbital] theory the π-electron densities at the carbon

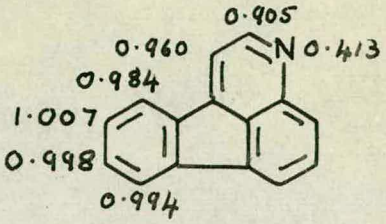
atoms of the azafluoranthenes. These are outlined below:



II



III

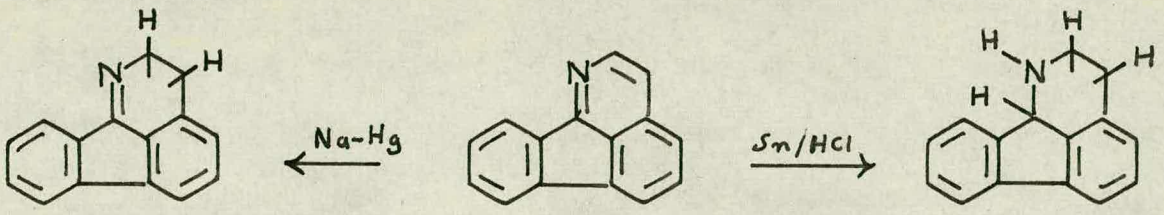


IV

These calculations show that the π-electron density at the 9-carbon atom in both the 1- and 3-azafluoranthenes is greater than the π-electron density at the corresponding 8-carbon atom. As the 1- and 3-azafluoranthese are both nitrated at the 9-position there appears to be a relation between the position of electrophilic attack and the position of highest π-electron density in the un-excited hydrocarbon. On this basis nitration of 2-azafluoranthene should result in the formation of an 8-nitro compound as the π-electron density at the 8-position in this molecule is greater than at the corresponding 9-position. What is more likely, assuming that the position of highest π-electron density in the molecule is indeed the most susceptible to electrophilic attack, is that a mixture of 8- and 9-nitro-compounds will be obtained, as the difference between the π-electron densities at these two positions is very small. It should be emphasised, however, that these quantum mechanical calculations apply to the azafluoranthene nucleus as such, whereas in the nitration of the azafluoranthenes in concentrated sulphuric acid the heterocycle in its protonated form is probably the

principal reacting species. The position of electrophilic attack in the 2-azafluoranthene molecule, as determined by experiment, will be further discussed in the following section.

The effect of reducing agents on the azafluoranthenes has been determined solely for the 1-azafluoranthene isomer. Campbell and Reid[6] failed to reduce this heterocycle with $LiAlH_4$ in ether; they recovered starting material after refluxing for 3 hours. Reduction with 5% sodium amalgam in ethanol gave a 60% yield of 2,3-dihydro-1-azafluoranthene (XX), whilst reduction with tin and hydrochloric acid gave a 40% yield of the tetrahydro-1-azafluoranthene (XXXIII).

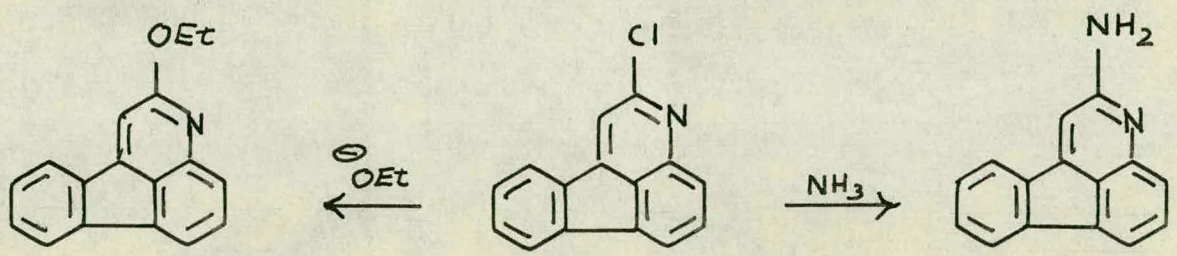


XX II XXXIII

Reduction of 2,3-dihydro-1-azafluoranthene (XX) with tin and hydrochloric acid gave a 50% yield of 10a,1,2,3-tetrahydro-1-azafluoranthene (XXXIII).

As the 1- and 2-azafluoranthenes can be regarded as o-phenylene derivatives of isoquinoline, and the 3-azafluoranthene as an o-phenylene derivative of quinoline, it is to be expected that chloro derivatives such as (XVI), with a chlorine atom adjacent to a nitrogen atom, will be susceptible to ready replacement by nucleophiles.

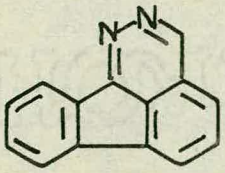
Although no 2-chloro-1-azafluoranthene has been prepared, 2-chloro-3-azafluoranthene has, and it has been shown[4,5] to be readily attacked by nucleophiles such as $-NH_2$, -NHR, and -OR at the 2-position.



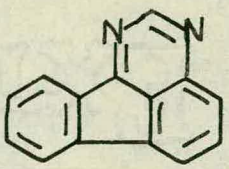
XVI

DIAZAFLUORANTHENES

There are several possible diazafluoranthenes, but the only isomers to be discussed in this thesis are the 1,2- and 1,3-diaza-derivatives, (XXXIV) and (XXXV) respectively.

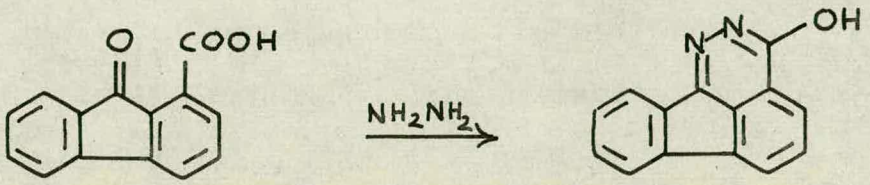


XXXIV



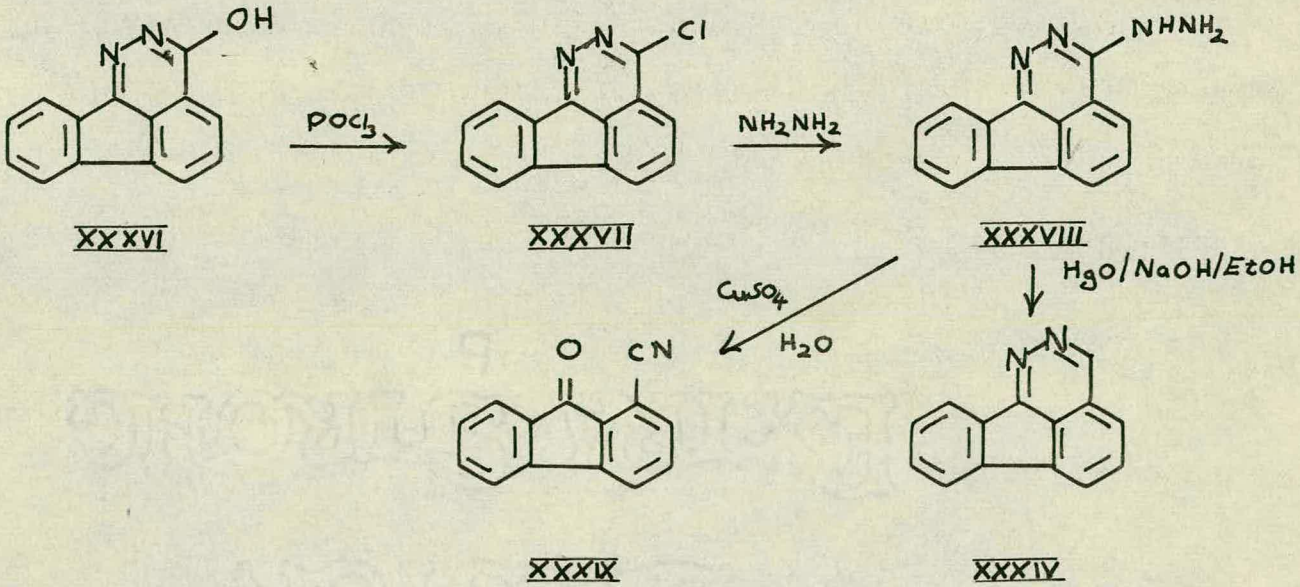
XXXV

The first derivative of 1,2-diazafluoranthene was obtained by Campbell and Stafford[9], by boiling fluorenone-1-carboxylic acid with hydrazine hydrate in dioxan.



VII XXXVI

Dokunikhin and Mihalenko[10,11], converted (XXXVI) into its chloro derivative (XXXVII) with phosphorus oxychloride, and then into the hydrazide (XXXVIII). Oxidation of the latter with alcoholic sodium hydroxide and mercuric oxide gave the parent heterocycle 1,2-diazafluoranthene (XXXIV).

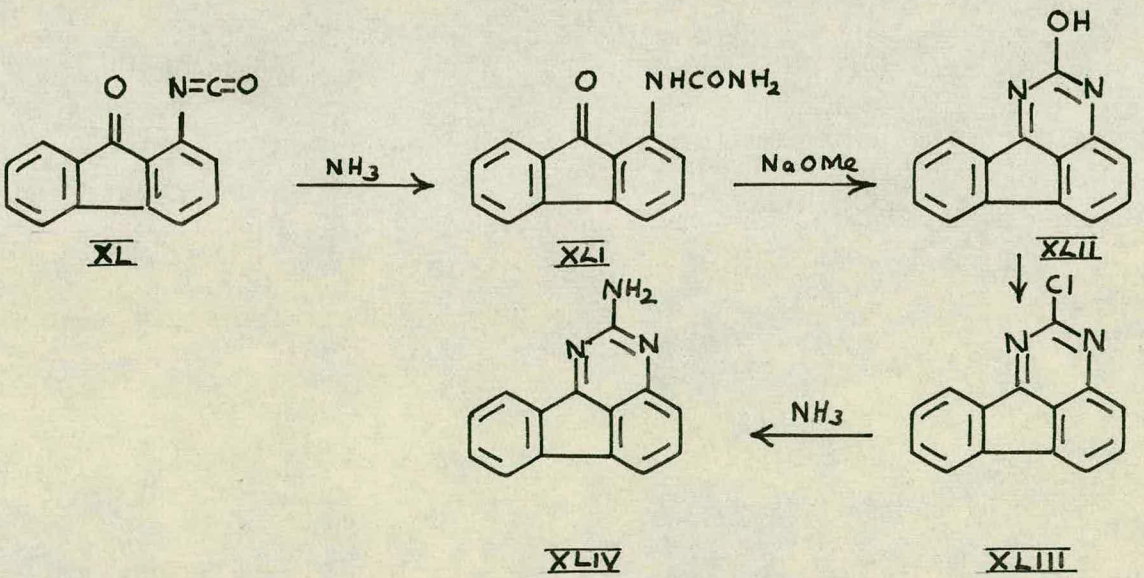


XXXVI XXXVII XXXVIII XXXIX XXXIV

Oxidation of (XXXVIII) with aqueous copper sulphate yielded 1-cyanofluorenone (XXXIX).

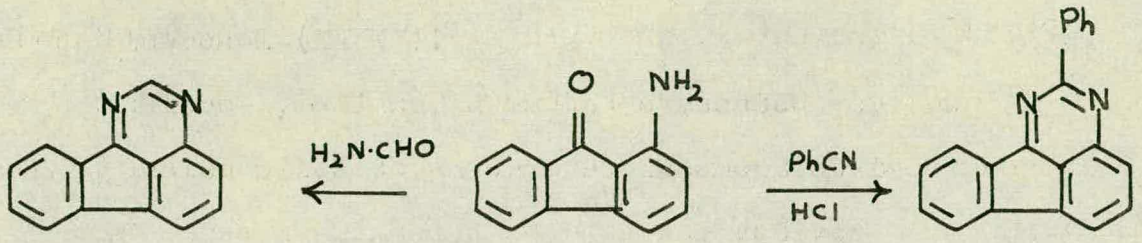
3-Chloro-1,2-diazafluoranthene reacted very readily with various nucleophiles to undergo replacement at the 3-position.

1,3-Diazafluoranthene and its derivatives have been prepared by Cook and Moffat[4]. Reaction between fluorenon-1-yl isocyanate (XL) and anhydrous ammonia gave 1-carbamido-fluorenone (XLI), which was cyclised with sodium methoxide in nitrobenzene to 2-hydroxy-1,3-diazafluoranthene (XLII). The latter was converted into 2-chloro-1,3-diazafluoranthene (XLIII) with phosphorus oxychloride, which yielded the 2-amino derivative (XLIV) by condensation with ammonia.



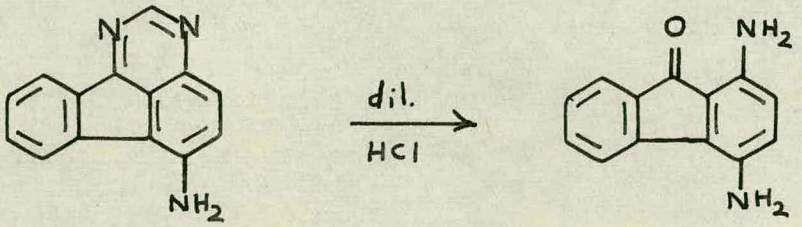
XL XLI XLII XLIII XLIV

Condensation of 1-aminofluorenone with phenyl cyanide in the presence of hydrogen chloride at 190°C gave 2-phenyl-1,3-diazafluoranthene (XLV). The parent hydrocarbon 1,3-diazafluoranthene (XXXV) was formed directly in low yield by interaction of 1-aminofluorenone and boiling formamide.



XXXV XLV

Unlike the other azafluoranthenes, the 1,3-diazafluoranthene nucleus is rapidly cleaved by hot, dilute hydrochloric acid as illustrated by 6-amino-1,3-diazafluoranthene which yields 1,4-diaminofluorenone.

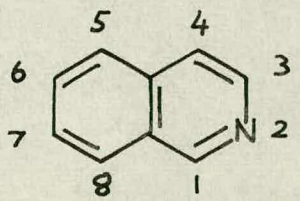


1,3-Diazafluoranthene is a white compound which chars on heating to 230°C; 1,2-diazafluoranthene is a pale yellow compound melting at 123-25°C.

As the principal aim of this thesis was to synthesise 2-azafluoranthene (III) which is a derivative of the simple heterocycle isoquinoline, a short account will be given of the preferred methods used to synthesise this hydrocarbon and its derivatives, with special attention being given to those procedures applicable to the synthesis of 2-azafluoranthene.

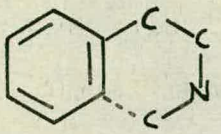
Synthesis of Isoquinolines

The synthesis of isoquinoline and its derivatives (XLVI) may be divided into a number of types, depending upon the point at which the hetero ring is closed.

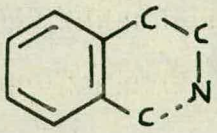


XLVI

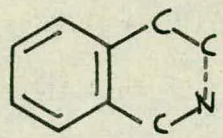
There are five possible ways in which these compounds may be theoretically prepared, giving rise to five type synthesis: namely, ring closure between the benzene nucleus and carbon atom 1 [Type I], between atoms 1 and 2 [Type II], between atoms 2 and 3 [Type III], between carbon atoms 3 and 4 [Type IV], and between carbon atom 4 and the nucleus [Type V]. The dotted line in the following formulas indicates the point at which union is effected.



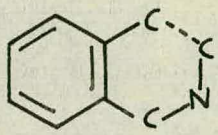
I



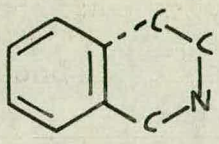
II



III



IV



V

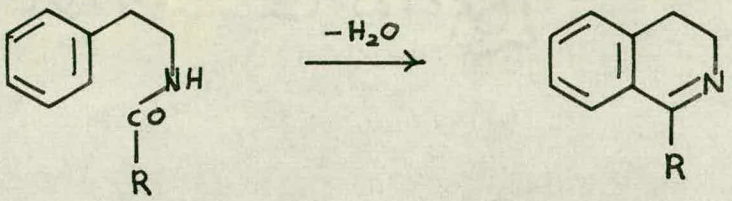
A brief description will be given of the more common and useful examples of each of these five type syntheses.

Type I

The most important class of syntheses involving ring closure between the benzene nucleus and carbon atom 1 are the Bischler-Napieralski, the Pictet-Gams, and the Pictet-Spengler cyclisations, which utilise a β-arylethylamine as the primary starting material. These three reactions have been thoroughly described in a lengthy review by Whalley and Govindachari.[12]

The Bischler-Napieralski reaction consists in the cyclodehydration of β-phenyl ethylamides to 3,4-dihydroisoquinolines (XLVII) by heating to high temperatures with phosphorus pentoxide, phosphorus

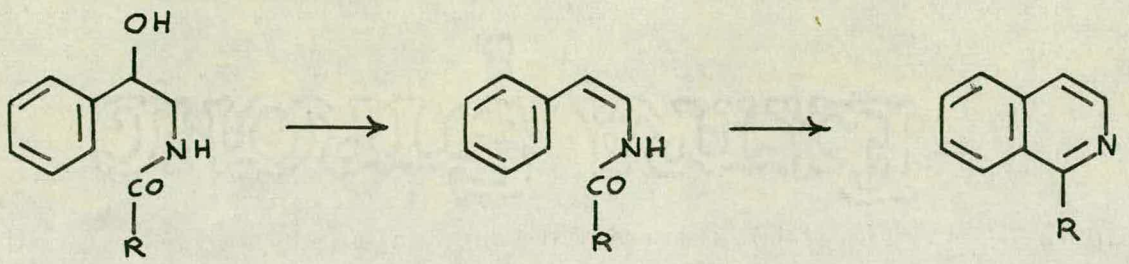
pentachloride or phosphorus oxychloride.[13]



XLVII

The 3,4-dihydroisoquinolines prepared by this procedure are readily converted into the aromatic isoquinoline by chemical oxidation, or by catalytic dehydrogenation. The former procedure is exemplified by the use of iodine and sodium acetate in alcohol, and other oxidising agents such as mercuric acetate or potassium permanganate have also been employed. Dehydrogenation of the dihydro compounds is accomplished with catalysts such as palladium-charcoal, platinum and Raney nickel. In some cases, the direct dehydrogenation of the Bischler-Napieralski product has been found to be less satisfactory than the dehydrogenation of the corresponding tetrahydroisoquinoline.[14]

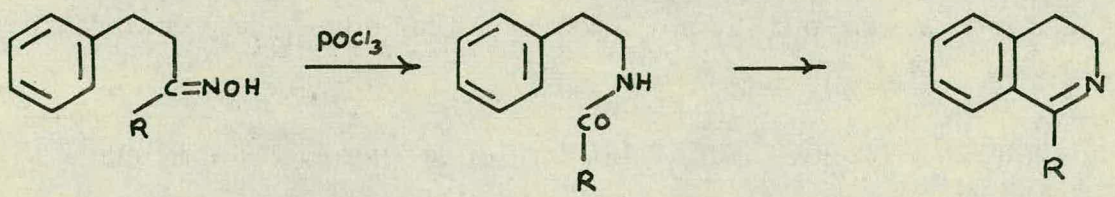
The most important variation in the reaction is that introduced by Pictet and Gams,[15] involving the cyclisation of a β-hydroxy-[or methoxy]-β-phenylethylamide (XLVIII). This procedure yields the isoquinoline directly and eliminates the dehydrogenation necessary when the original Bischler-Napieralski reaction is used.



XLVIII XLIX

Removal of water from the ethylamine side chain to create a double bond has been found to precede cyclisation, the intermediate vinyl-amide (XLIX) being easily isolable in certain reactions.[16]

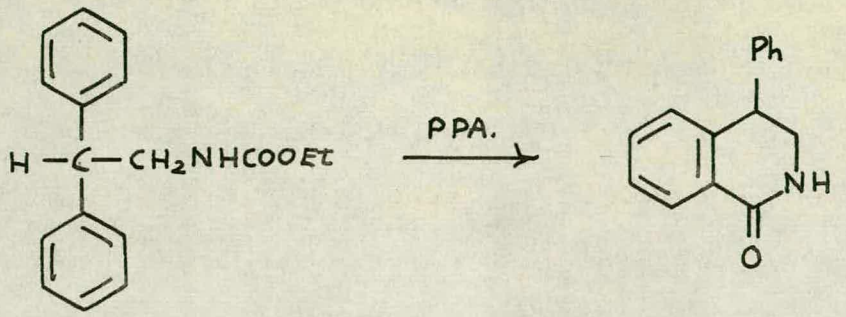
An oxime capable of undergoing a Beckmann rearrangement to an N-acyl-β-phenylethylamine may be used as the initial reactant of the Bischler-Napieralski reaction, the intermediate amide (L) yielding a 3,4-dihydroisoquinoline.[17]



L

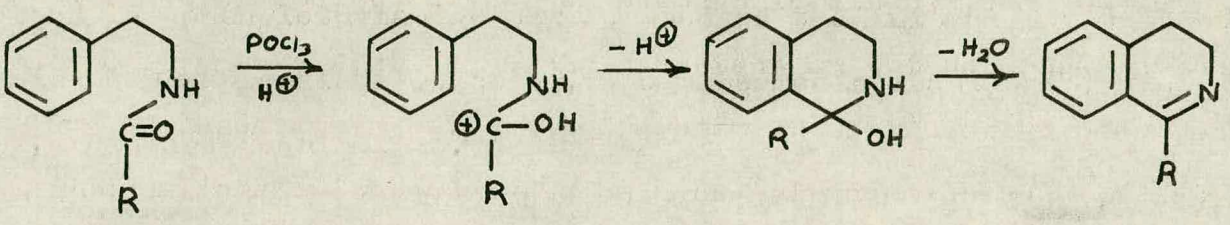
This particular procedure has enjoyed only limited application.

In some cases cyclisation of urethanes and substituted ureas have yielded isoquinoline derivatives having a hydroxyl or an amino function in the 1-position. The urethane (LI) yields 3,4-dihydro-4-phenyl-isocarbostyril (LII) by this procedure.[18]



LI LII

The cyclisation of these β-arylethylamides [and urethanes] appears to be the result of an electrophilic attack[19] upon an aromatic ring by a carbonium ion (LIII).

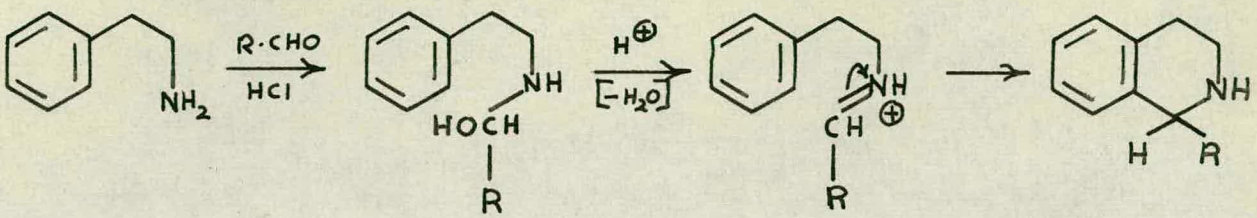


LIII

This reasoning is supported by the evidence that whereas a m-methoxy group facilitates cyclisation, a m-nitro group makes cyclisation almost impossible.

The Pictet-Spengler reaction consists in the condensation of a β-arylethylamine with a carbonyl compound with hydrochloric acid as a catalyst to yield a tetrahydroisoquinoline.

The mechanism is probably an intramolecular type of Mannich reaction involving the protonated form (LIV) of the Schiff base.



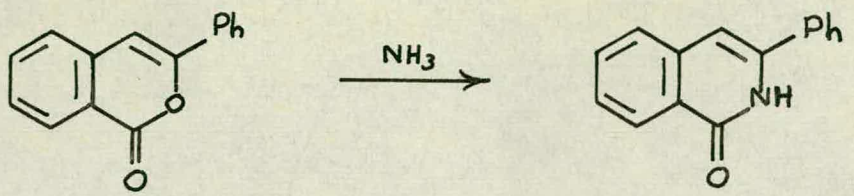
LIV

The reaction succeeds with R = H in (LIV), but is best carried out in this instance with methylal, from which formaldehyde is generated, as the initial reactant.[20] Alkoxy and hydroxy groups meta to the ethylamine side chain facilitate cyclisation, and in fact few phenylethylamines lacking such a group para to the position of closure have been cyclised. For this reason the Pictet-Spengler reaction is not so widely used as the Bischler-Napieralski.

All "Type I" syntheses require a β-arylethylamine as a starting material, and several authors[21] have reviewed the literature on this subject. In the present author's work, the preparation of the required β-arylethylamine as a precursor to the cyclisation to a 2-azafluoranthene proved extremely difficult and will be discussed later.

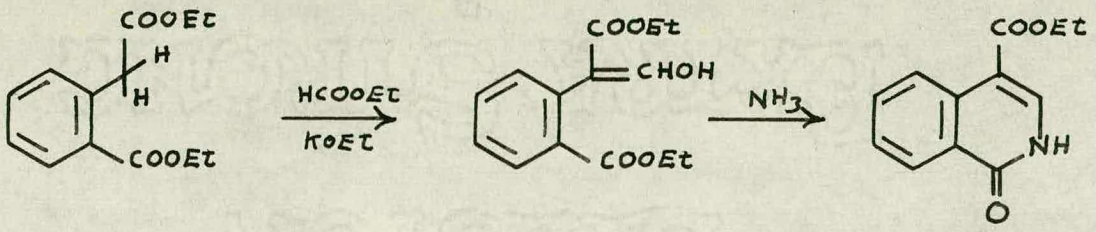
Type II and III syntheses

Gabriel[22] reported the conversion of 3-phenylisocoumarin (LV) to 3-phenylisocarbostyril (LVI) by treatment of the oxygen heterocycle with alcoholic ammonia at 100°C. The reaction of isocoumarins with ammonia and amines is quite general and has been applied to the preparation of many substituted isocarbostyrils.[23]



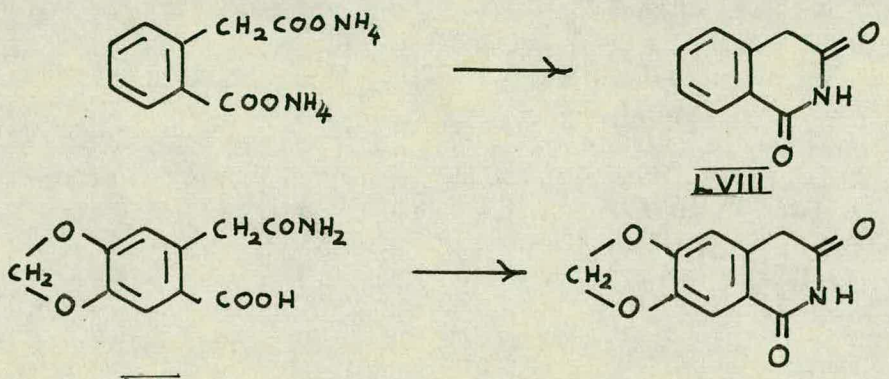
LV LVI

Closely related reactions are known. The hydroxymethylene derivatives of homophthalic esters (LVII) can be transformed directly to the isocarbostyril compounds with aqueous ammonia.[24]



LVII

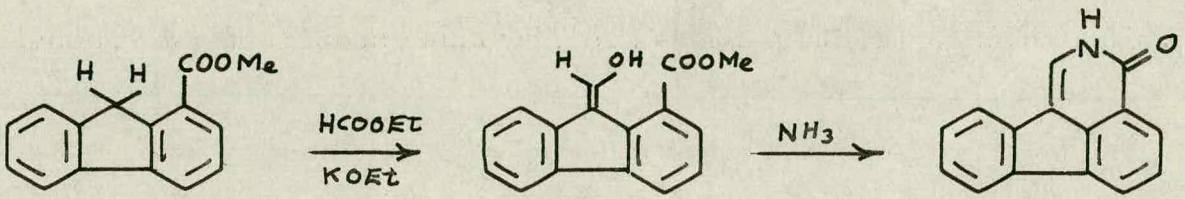
Homophthalimides (LVIII) can be used as a route to isoquinolines. They can be prepared by heating homophthalic acid diammonium salts;[25] by the cyclisation of homophthalamic acids (LIX) by heat;[26] and by treatment of homophthalonitriles with strong acid.[27]



LVIII

LIX

These procedures for the formation of isoquinoline derivatives effect a condensation involving carbon atoms 1 and 3 of the potential heterocycle, and they have consequently been classified as "Type II and III" syntheses. This type of ring closure seems particularly applicable to the synthesis of 2-azafluoranthene, as the starting material fluorene is readily formylated at the 9-methylene group, and a compound such as (LX) seems to be a suitable derivative for cyclisation to an isocarbostyril.

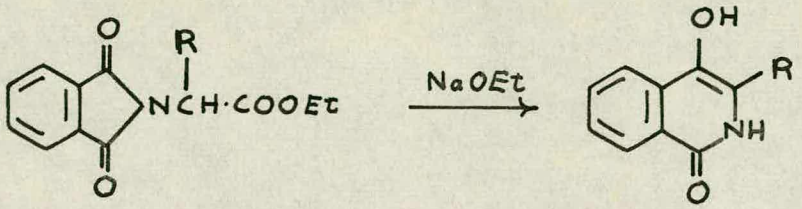


LX

Type IV

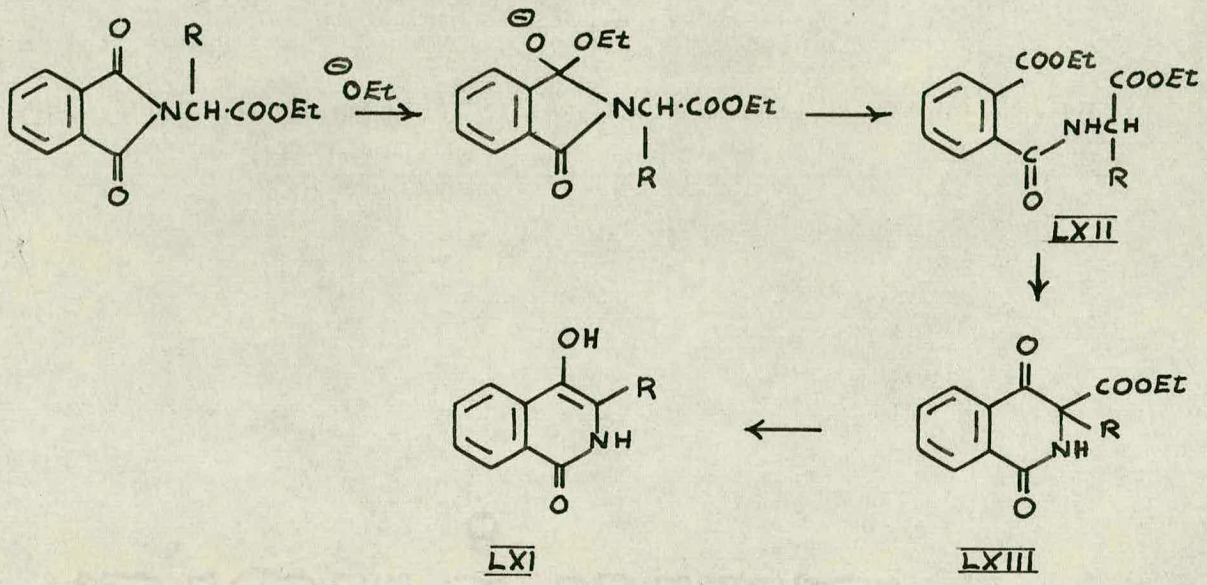
Ring closure between carbon atoms 3 and 4 to yield isoquinolines is restricted to a few examples, all of which involve the condensation of a nuclear carboxyl group with an active hydrogen atom.

Phthalimide, substituted on the nitrogen with an alkyl acetic ester residue, can be rearranged with sodium ethoxide to a 3-alkyl-4-hydroxyisocarbostyril (LXI).[28]

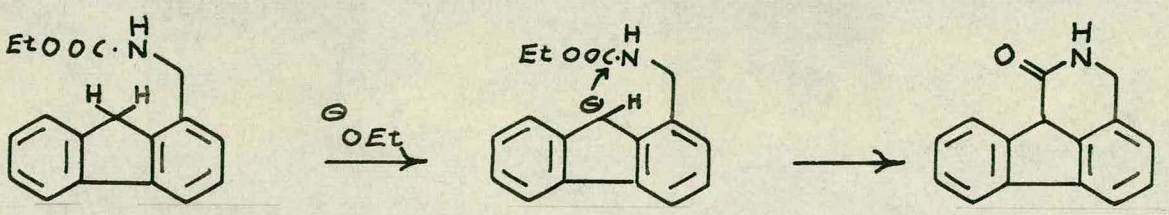


LXI

A possible mechanism for this reaction involves a base-catalysed opening of the imide ring to the diester (LXII), which then undergoes an intramolecular ester condensation to give (LXIII). This undergoes a ketonic cleavage of the β-ketoester system with elimination of the ester group to yield (LXI).[29] An alternative mechanism is that of Hauser.[30]

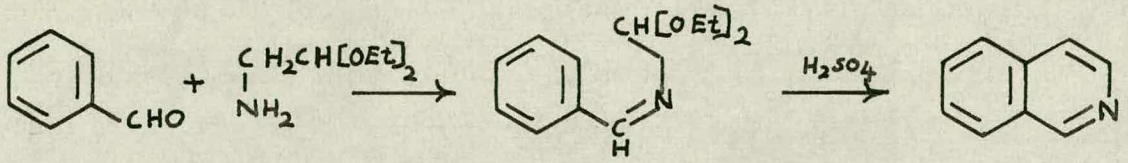


This procedure also seems applicable to syntheses with fluorene as a starting material, as this hydrocarbon readily loses a proton from the 9-methylene group to give a carbanion which will attack the carbonyl of an ester group.



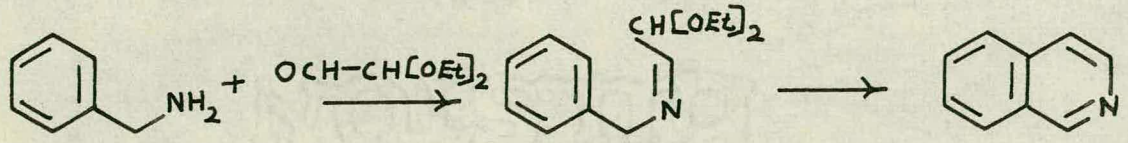
Type V syntheses

Ring closure between carbon atom 4 and the nucleus is usually achieved by the Pomerantz-Fritsch reaction. When benzaldehyde is heated with aminoacetaldehyde diethylacetal (LXIV), benzalaminoacetal (LXV) is formed. Treatment of the Schiff base with strong sulphuric acid produces isoquinoline.[31,32]



LXIV LXV

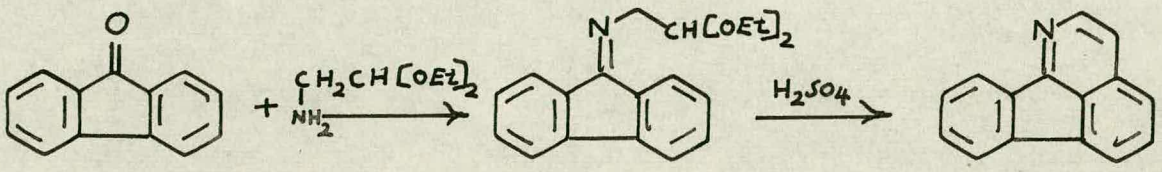
An alternative reaction, first reported by Schlittler and Muller,[33] involves the condensation of a benzylamine with glyoxalsemiacetal (LXVI). Cyclisation of the resulting Schiff base (LXVII) yields isoquinoline.



LXVI LXVII

Cyclisation generally occurs with activating groups such as alkoxyl or hydroxyl in the aromatic ring, otherwise the yields are very poor. Despite this drawback, the Pomerantz-Fritsch synthesis offers the possibility of preparing isoquinolines with substituent groups in positions often difficult to obtain in the more popular Bischler-Napieralski or Pictet-Spengler syntheses.

It is not possible to use this procedure to prepare 2-aza-fluoranthene, because, starting from the 1-carbon atom of fluorene, the required ortho position for cyclisation is not available. However, condensation of fluorenone with aminoacetal to yield the Schiff base (LXVIII) would offer a possible synthesis of 1-azafluoranthene.



LXVIII

OBJECT OF RESEARCH

In the "Introduction" it was indicated that the 2- and 8-azafluoranthenes had still to be isolated. It was the purpose of this research to synthesise 2-azafluoranthene, and to determine the properties of this heterocycle, particularly to find that position in the molecule most susceptible to attack by electrophiles.

Several syntheses were attempted using the hydrocarbon fluorene as a starting material before 2-azafluoranthene was finally obtained, and these yielded some interesting points about the chemistry of 9-substituted fluorene derivatives.

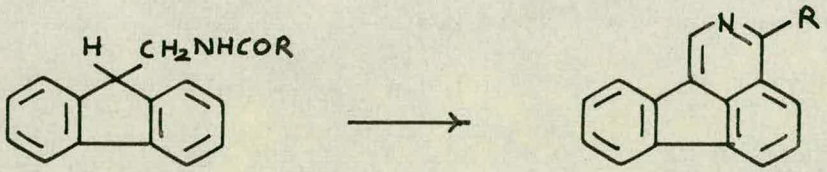
DISCUSSION.

SECTION I.

Attempts to synthesise 2-azafluoranthene from 9-fluorenemethylamine by a Bischler-Napieralski reaction; the preparation of some 9-substituted fluorene compounds.

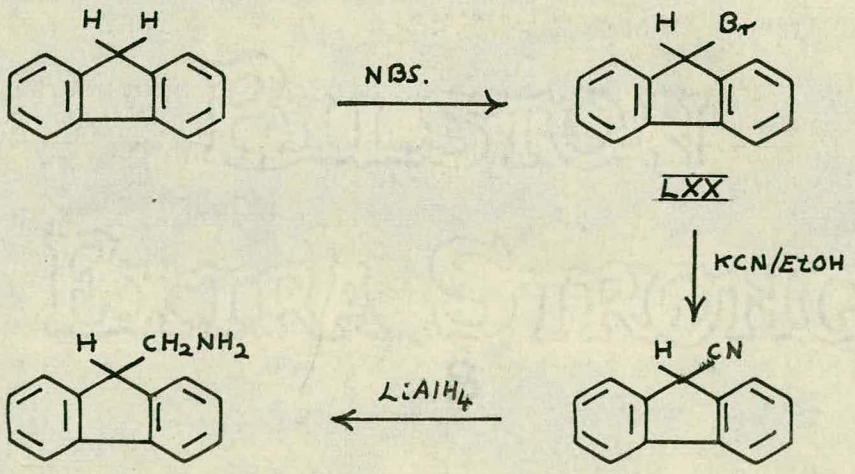
PART I: The unexpected formation of 9-cyano-9,9′-bifluorene and 9,9′-dicyano-9,9′-bifluorene.

It was initially intended to synthesise 2-azafluoranthene by a Bischler-Napieralski cyclisation of the β-phenylethylamide (LXIX).



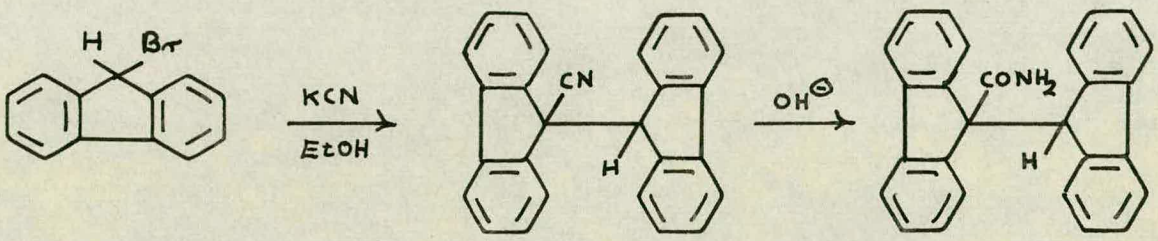
LXIX

An attempt was made to prepare the necessary β-phenylethylamine, 9-fluorenemethylamine (LXXII), by the lithium aluminium hydride reduction of 9-cyanofluorene (LXXI), the nitrile being obtained from the parent hydrocarbon fluorene in the manner shown.



LXXII LXXI LXX

Treatment of fluorene with N-bromosuccinimide afforded 9-bromofluorene (LXX) in excellent yield.[34,35] However, boiling the bromo-compound in aqueous ethanol with potassium cyanide gave 9-cyano-9,9´-bifluorene (LXXIII) instead of the expected 9-cyanofluorene (LXXI).

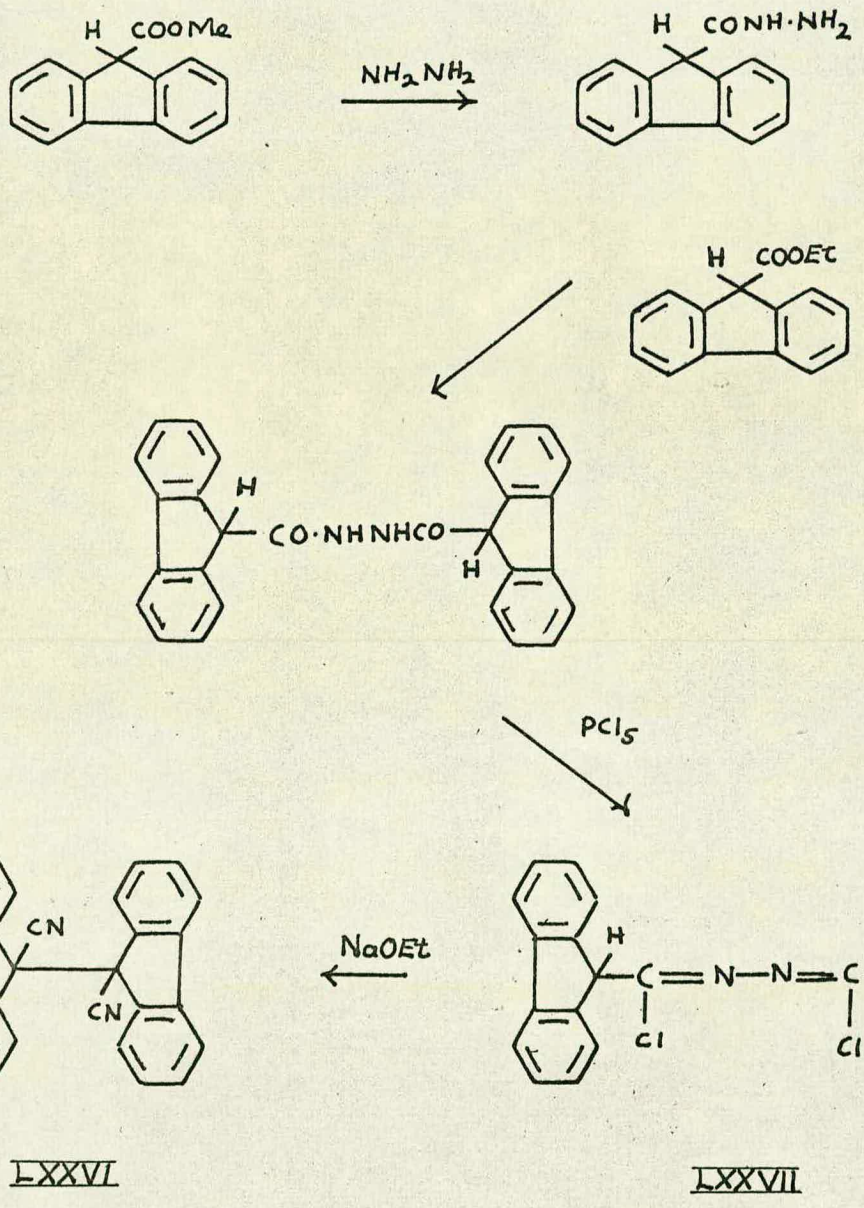


LXX LXXIII LXXIV

Hydrolysis of the bifluorenyl compound (LXXIII) with alkaline hydrogen peroxide afforded [9,9´-bifluorene]-9-carboxamide (LXXIV).

After this work had been completed, Cavalla[36] reported the preparation of the same 9-cyano-9,9´-bifluorene by stirring 9-bromofluorene with excess sodium cyanide in dimethyl sulphoxide. Attempted reduction of the bifluorenyl (LXXIII) with lithium aluminium hydride yielded only 9,9´-bifluorene.

Rapid alkylation of the initially formed 9-cyanofluorene by 9-bromofluorene seems a plausible mechanism for the formation of (LXXIII). Other 9-substituted fluorene derivatives containing weakly acidic hydrogen have been readily alkylated in a similar manner. Ethyl fluorene-9-carboxylate has been alkylated with 9-chlorofluorene in the presence of ammonia,[37] and methyl fluorene-9-carboxylate has been alkylated with 9-bromofluorene in the presence of sodium methoxide.[38] A recent publication[39] indicates that



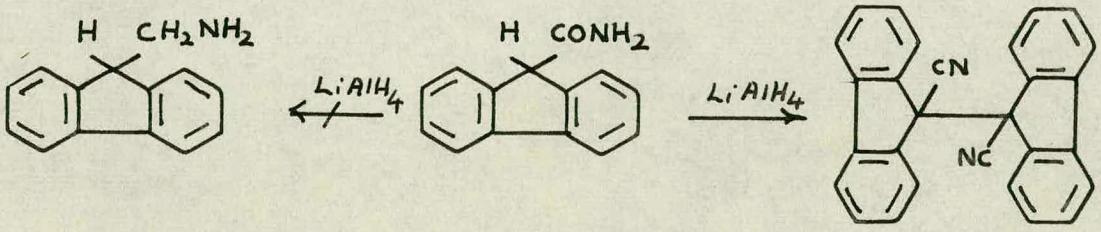
LXXVI

LXXVII

9-cyanofluorene is more acidic than methyl fluorene-9-carboxylate.

The preparation of 9-bromofluorene has been reported many times without much reference being made to the compound's potential as a skin irritant. Cavendish[40] reported a case of severe skin eruption contracted in preparing this bromocompound, and work on the compound was terminated after the present author was similarly afflicted by a widespread dermatitis. E.W. Powell[41] has recently published an excellent communication on the hazards associated with the use of 9-bromofluorene.

Reduction of the readily available 9-carbamoylfluorene (LXXV) with lithium aluminium hydride seemed an alternative method of preparing 9-fluorenemethylamine (LXXII).



LXXII LXXV LXXVI

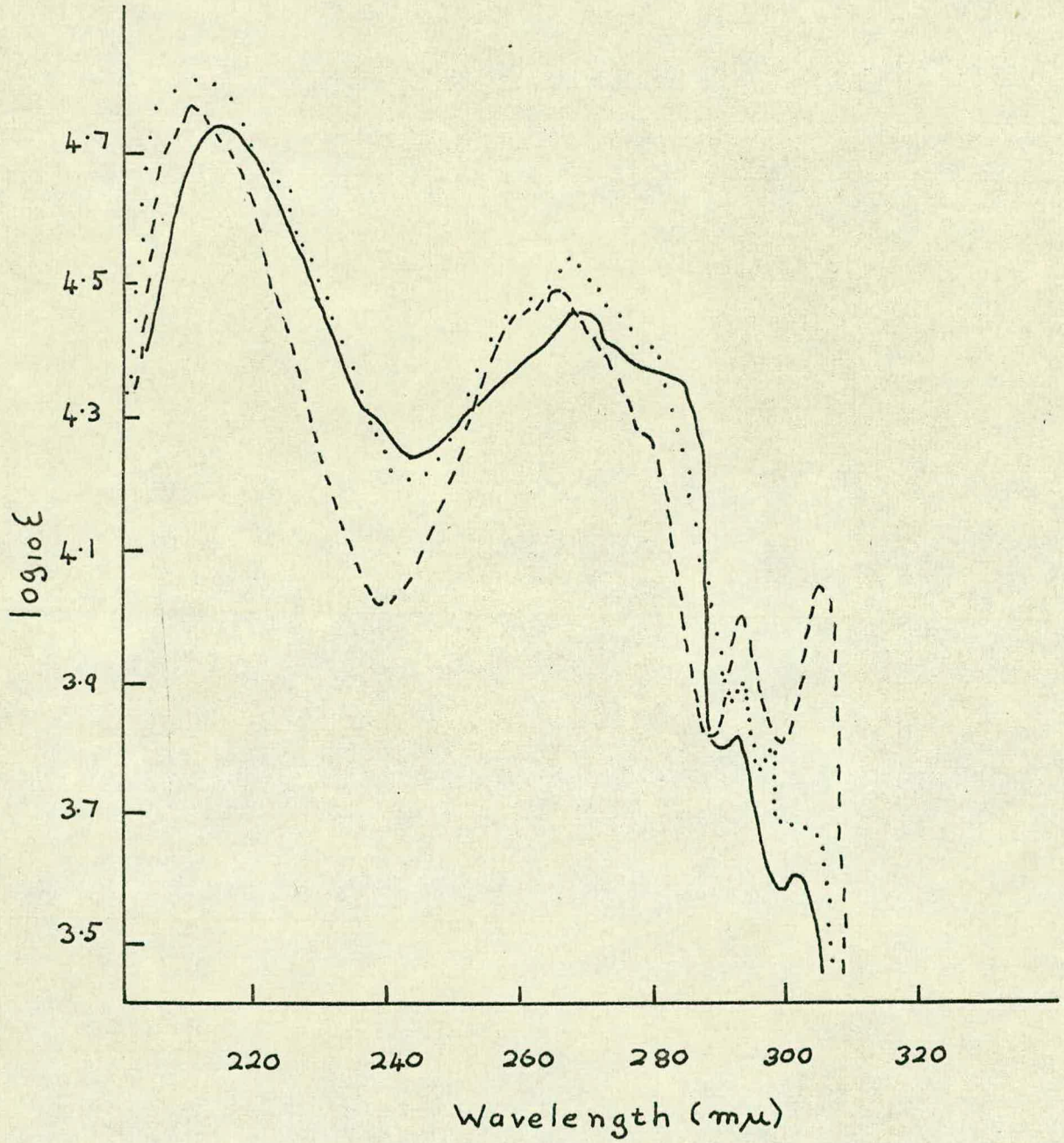
Refluxing the amide in a lithium aluminium hydride suspension in tetrahydrofuran unexpectedly gave the dinitrile, 9,9′-dicyano-9,9′-bifluorene (LXXVI). This dinitrile had been previously obtained[42] by a lengthy procedure [see opposite page] involving the treatment of bis-fluorenylacethydrazide chloride (LXXVII) with sodium ethoxide.

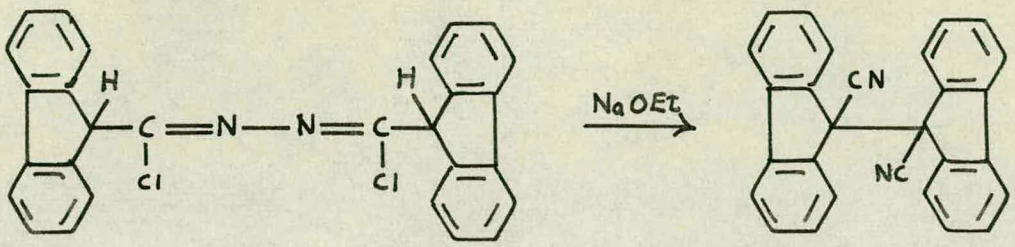
FIG. 1

9,9'-BIFLUORENE (LXXXVI) - - -

9-CYANO-9,9'-BIFLUORENE (LXXIII) .....

9,9'-DICYANO-9,9'-BIFLUORENE (LXXVI) ——

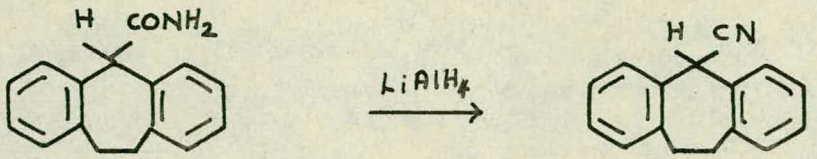




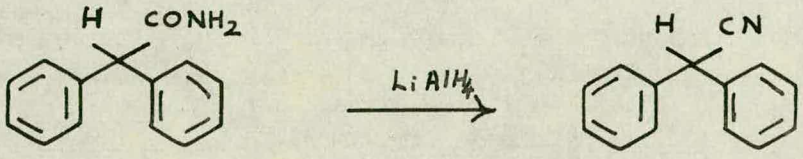
LXXVII LXXVI

The product (LXXVI) obtained by this procedure melted at 242°C and appears to be impure since the dinitrile obtained by the dehydration of 9-carbamoylfluorene melted at 266-68°C. Boiling the dinitrile with sodium in ethanol gave 9,9′-bifluorene. The nuclear magnetic resonance spectrum of 9-cyano-9,9′-bifluorene (LXXIII) showed a sharp absorption at 5·11τ, assigned to the 9-methylene proton, whereas that of the dinitrile (LXXVI) showed no absorptions at fields above 3·0τ. The ultraviolet spectra of (LXXIII) and (LXXVI) were similar to that of 9,9′-bifluorene [Fig. I].

The unusual dehydration and dimerisation of 9-carbamoylfluorene in the presence of lithium aluminium hydride has no direct parallel in the literature, as far as the present author is aware. Humber and Davis[43] reported the unexpected formation of the nitriles (LXXVIII) and (LXXIX) during the attempted lithium aluminium hydride reduction of the corresponding amides, but the combination of dehydration and dimerisation appears to be new.

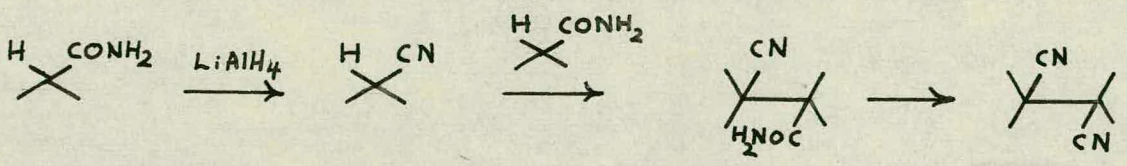


LXXVIII



LXXIX

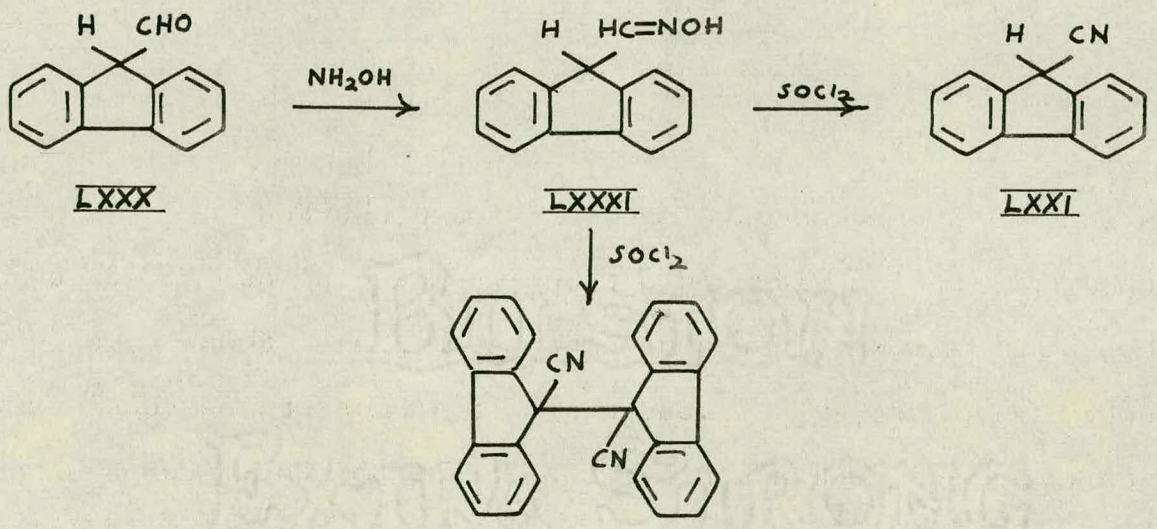
The similarity between the structures of 9-carbamoylfluorene and these two amides is obvious, and the slightly acidic methylene hydrogen present in all three compounds could possibly be involved in an intermediate common to all three. Why 9-carbamoylfluorene should undergo both dehydration and dimerisation is difficult to explain. The following mechanism is tentatively offered.



The nitrile formed initially by dehydration being more acidic than the amide could attack the 9-methylene hydrogen of the latter to yield a product which could undergo further dehydration to the dinitrile.

PART II: The oximes of 9-formylfluorene

The failure of the reduction of 9-carbamoylfluorene to give 9-fluorenemethylamine, necessitated the search for a different route to the amine. A further attempt was therefore made to synthesise and reduce 9-cyanofluorene (LXXI). Wislicenus and Russ[44] reported the preparation of the nitrile from 9-formylfluorene (LXXX).

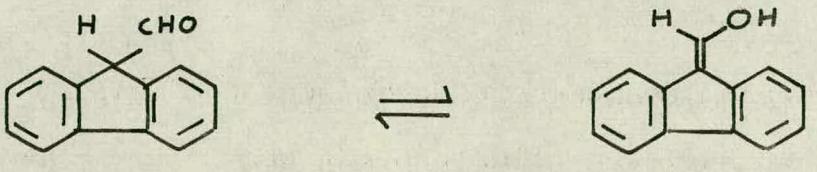


LXXX LXXXI LXXI

LXXVI

9-Formylfluorene on oximation yielded a mixture of oximes (LXXXI), which on dehydration with thionyl chloride gave 9-cyanofluorene (LXXI). This route to the nitrile proved satisfactory except on one occasion when the dinitrile 9,9´-dicyano-9,9´-bifluorene (LXXVI) was obtained. This unusual dehydration prompted an investigation into the nature of the oximes of 9-formylfluorene in an attempt to find a reason for the formation of the dinitrile.

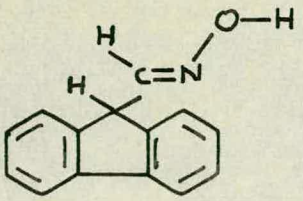
9-Formylfluorene (LXXX) is prepared by the formylation of fluorene[44]. Enolisation of the aldehyde is apparently considerable, and the infrared spectrum of the compound shows a strong absorption at 1675cm^{-1}., characteristic of an exocyclic double bond.



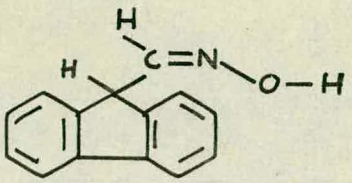
LXXX LXXXa

The aldehyde is readily oximated with hydroxylamine in alcohol solution to yield a mixture of α-and β-oximes (LXXXI).

Wislicenus and Russ claimed to have separated the two oximes by recrystallisation of the mixture from ligroin. The α-isomer dissolved in the boiling solvent and separated on cooling as fine white needles m.p.132-33°, whereas the β-isomer was insoluble in boiling ligroin and was removed by filtration. Recrystallisation of this isomer from boiling toluene gave white crystals m.p. 166-67°. The higher melting β-isomer was also formed from the α-isomer by rearrangement with hydrogen chloride. Adopting the conventions of Hantzsch these workers wrongly assigned an anti configuration to the α-isomer, and a syn configuration to the β-isomer. Meisenheimer and others[45] later proved that for a pair of stereoisomeric aldoximes the higher melting β-isomer has the anti configuration.



α-syn oxime



β-anti oxime

Contrary to the results of Wislicenus, the present author obtained a white crystalline product, m.p. 130-50°, on recrystallising the oximes of 9-formylfluorene from ligroin. The n.m.r. spectrum of the product showed it to be a mixture of α- and β-isomers. Nuclear magnetic resonance has recently been introduced as a reliable technique for assigning syn and anti configurations to stereoisomeric oximes. Lustig[46] examined the spectra of two p-chlorobenzaldoximes in dimethyl sulphoxide solution, and found that the signal from the hydrogen on the oximino carbon (-CH = N-OH resonance) of the syn isomer appeared at lower field than that of the anti isomer. The configuration of both isomers of p-chlorobenzaldoxime had been determined previously through X-ray diffraction studies.[47] In a more extensive study of p-substituted benzaldoximes, Pejkovic[48] confirmed that the -CH = NOH resonance of the syn isomer appears at lower field. Pejkovic suggested that in the syn isomer the proximity of the oxygen atom induces a paramagnetic shift on the aldehydic proton. This reasoning was supported by the observation[49] that the signals from the ring protons ortho to the oximino function in the anti isomer of isonicotinaldehyde oxime appeared at lower field than those of the syn isomer.

The crude oxime mixture of 9-formylfluorene gave a n.m.r. spectrum in acetone solution with four distinct absorptions (doublets) at field values greater than 2·6τ. These were assigned as follows, on the basis of the studies just mentioned.

τ 5·20 α-9-fluorene proton J = 7·2 c/s

τ 4·21 β-9-fluorene proton J = 6·6 c/s

τ 3·44 β-H-C=NOH proton J = 6·6 c/s

τ 2·75 α-H-C=NOH proton J = 7·2 c/s

Attempts were made to separate the two isomers with ligroin as described by Wislicenus, but the n.m.r. spectra of the products showed that both the α- and β-oximes were soluble in petrol to only a limited extent, and that although the α-isomer was indeed the more soluble, the Wislicenus product was a mixture and not pure α-isomer. Ether and petrol mixtures effected no improvement in separation. The β-isomer, however, was obtained 100% pure by repeated recrystallisation from ethanol. The n.m.r. spectrum of this isomer showed a doublet at 4·21τ, J = 6·6 c/s (9-fluorene proton) and a doublet at 3·44τ, J = 6·6 c/s (H-C=NOH proton), which corresponds with the assignments given above. Concentration of the ethanol mother liquors failed to give the pure α-isomer.

In certain cases the use of infrared spectroscopy has also led to correct assignments of configuration to α- and β-oxime isomers. Palm and Werbin[50] in an extensive study of the spectra of aromatic aldoximes found that the bonded hydroxyl stretching frequency occurred at 3250cm^{-1}. for the α-isomer, and at 3115cm^{-1}. for the β-isomer. These figures refer to solid state spectra. The infrared

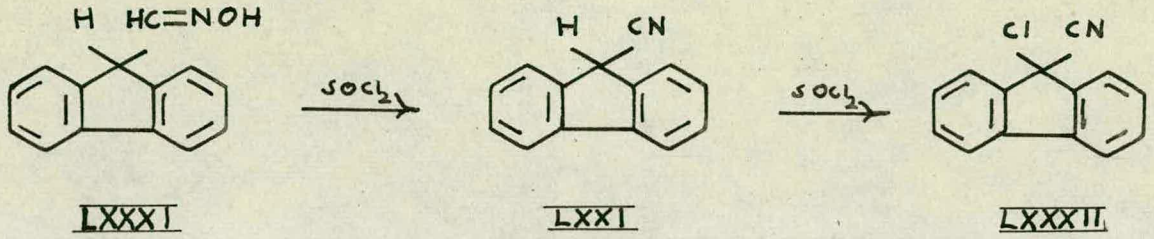
spectrum of the β-isomer of 9-formylfluorene oxime showed a strong absorption at 3200cm^{-1}., indicating the limited use of infrared spectroscopy in determining the configurations of oxime isomers.

The acetyl derivatives of α- and β-oxime isomers are known to behave in a different manner towards base. Shaking the α-acetyl derivative with sodium carbonate regenerates the α-oxime, whilst the β-acetyl derivative undergoes elimination under the same conditions to give the corresponding nitrile. This seemed a neat method of separating the oxime isomers of 9-formylfluorene. Acetic anhydride reacted with a mixture of the oximes to yield a crystalline product which did not display the normal characteristics of acetyl derivatives of oximes. The infrared spectrum of the product showed a weak carbonyl peak at 1740cm^{-1}., a strong broad band at 1640cm^{-1}., and a weak broad band at 3250-3100cm^{-1}. Boiling the product with sodium carbonate solution gave a similar crystalline compound, from which no 9-cyanofluorene could be isolated. Washing with dilute sodium hydroxide failed to remove any α-oxime. Treatment of pure β-oxime with acetic anhydride and sodium carbonate did not give the expected 9-cyanofluorene. It seems possible that acetic anhydride oxidises the oximes at the 9-methylene group, and attempts to separate the isomers by this method were abandoned.

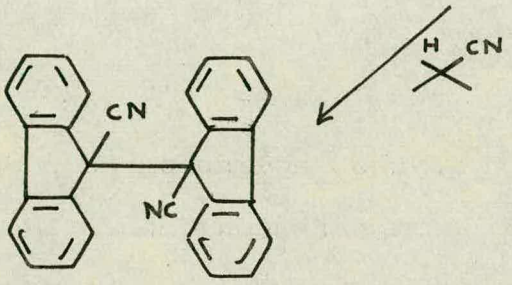
PART III: Possible mechanisms for the formation of 9,9´-dicyano-9,9´-bifluorene from 9-formylfluorene oxime.

As already mentioned thionyl chloride dehydration of the mixture of oxime isomers of 9-formylfluorene yielded 9-cyanofluorene, except on one occasion when 9,9´-dicyano-9,9´-bifluorene was obtained. The percentage of α- to β-isomer present in the mixture to be dehydrated was conveniently determined by the intensity of the signals from the hydroxyl protons in the n.m.r. spectrum of the mixture. The hydroxyl proton of the α-isomer resonates at -0·11τ, and that of the β-isomer at -0·66τ. Measurement of the ratio of the intensities of these singlets gave the proportion of α/β isomer in the mixture. 9-Cyanofluorene was formed on dehydrating mixtures with α/β composition varying from 0% [i.e. 100% β-isomer] to 90% α-isomer. 9,9´-Dicyano-9,9´-bifluorene was formed from a mixture containing 60% α-isomer. As attempted repetition of this latter dehydration on other mixtures containing 60% α-isomer gave solely the mononitrile, it appears that the formation of dinitrile does not depend on the α/β composition of the mixture to be dehydrated, and that the two isomers react in a similar manner with thionyl chloride. Dehydration of pure β-isomer gave the mononitrile, as did dehydration of a mixture containing 90% α-isomer.

By analogy with the mechanism proposed for the preparation of 9-cyano-9,9´-bifluorene, it was thought that the dinitrile obtained by dehydration of the oxime mixture may be formed by alkylation of initially formed mononitrile in the following manner.

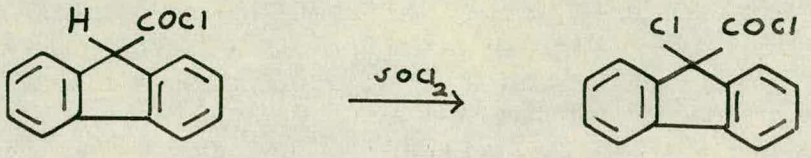


LXXXI LXXI LXXXII



LXXVI

The proposed chlorination of 9-cyanofluorene by thionyl chloride has no direct parallel in the literature, as far as the present author is aware. Ethyl fluorene-9-carboxylate, for example, has not been reported to react with thionyl chloride in a similar manner. However, 9-chlorofluorene-9-carbonyl chloride (LXXXIV) has been prepared[51] by refluxing fluorene-9-carbonyl chloride (LXXXIII) with excess thionyl chloride for several days.



LXXXIII LXXXIV

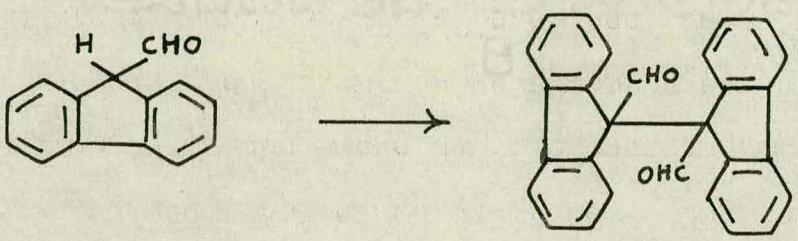
Alkylation of 9-substituted fluorene derivatives with slightly acidic methylene hydrogens has already been mentioned [p.29]. To test this proposed mechanism 9-cyanofluorene was stirred in ethereal solution in the presence of excess thionyl chloride for 12 hours. The mononitrile was recovered unchanged. A similar result was obtained after three days stirring.

Varying the time of dehydration and the quantity of thionyl chloride used in excess failed to give any insight into the mechanism of dinitrile formation. As previously mentioned, the dinitrile was formed from one batch of the oxime mixture [60% α-isomer], and attempts to repeat this preparation by changing the above variables were unsuccessful, mononitrile being repeatedly obtained in both sets of experiments. The latter was obtained on dehydrating a mixture of 60% α-isomer for 1-24 hour periods. Varying the quantity of thionyl chloride from 1 molar excess to 10 molar excess similarly gave mononitrile on each occasion.

A series of experiments were conducted to see if the time lag between preparation and oximation of 9-formylfluorene had any bearing on the course of subsequent dehydration of the oxime. The aldehyde was oximated after standing for periods of 2,4,6 and 8 days in ethereal solution. The four oxime batches thus obtained, all

mixtures of α- and β-isomers as determined from their n.m.r. spectra, were dehydrated in the normal manner. All four batches yielded 9-cyanofluorene and no dinitrile.

During this procedure, it was found that an ethereal solution of 9-formylfluorene, after standing for 30 days, deposited fine white prisms of 9,9´-diformyl-9,9´-bifluorene (LXXXV).

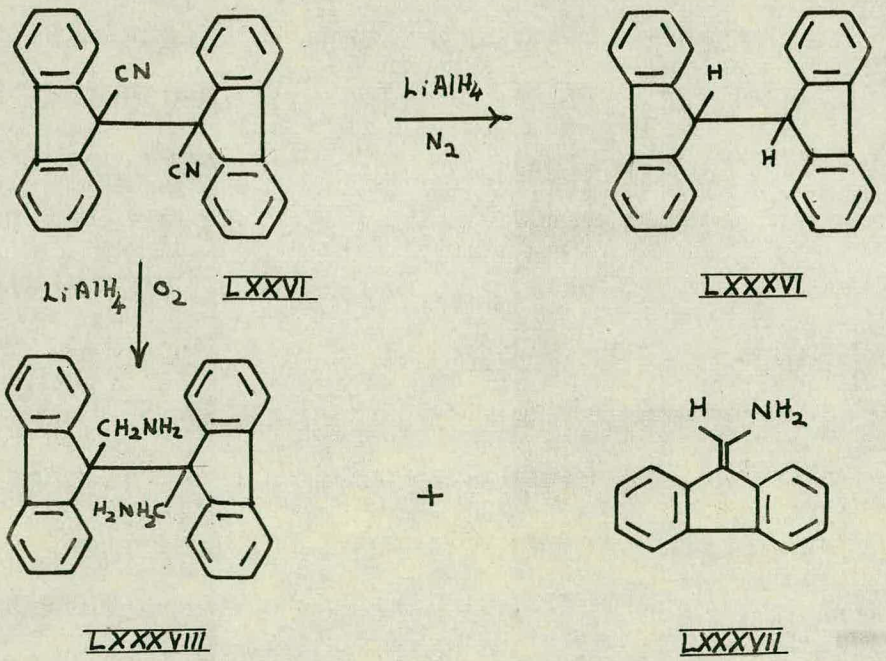


LXXX LXXXV

This dialdehyde was identified by its n.m.r. and infrared spectra, and a molecular weight determination confirmed the dimeric nature of the compound. Wislicenus and Russ[44] prepared (LXXXV) by oxidation of 9-formylfluorene with ferric chloride, but attempts to repeat this procedure proved unsuccessful. The dialdehyde was prepared by the method of Greenhow,[52] by refluxing freshly prepared 9-formylfluorene in thionyl chloride. It seemed possible that 9,9´-diformyl-9,9´-bifluorene (LXXXV) might be an intermediate in the unusual dehydration of 9-formylfluorene oxime which yielded the dinitrile (LXXVI). Accordingly an attempt was made to oximate the dialdehyde in the normal manner with hydroxylamine in ethanol solution. No dioxime was obtained indicating that should any dialdehyde be formed during the formylation of fluorene it is unlikely that it would be responsible for the subsequent formation of the

dicyano-compound. The dialdehyde was extremely insoluble in ethanol and it seems likely that if any of the compound was present in a sample of 9-formylfluorene, it would precipitate on dilution of the aldehyde with ethanol prior to treatment with hydroxylamine. No separation of the dialdehyde was witnessed on any occasion when oximation was performed.

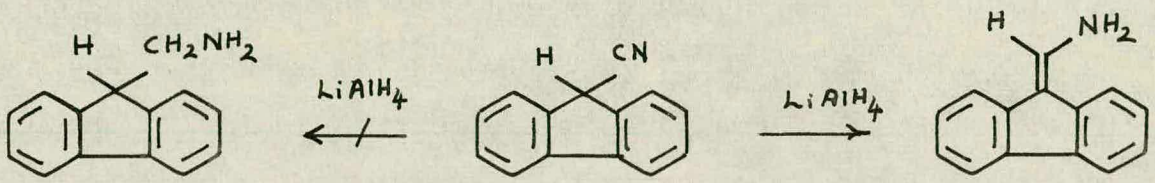
Reduction of 9,9´-dicyano-9,9´-bifluorene (LXXVI) by lithium aluminium hydride gave different products under different reaction conditions.



Reduction in an atmosphere of nitrogen gave a 30% yield of 9,9´-bifluorene (LXXXVI) and 30% of a high-melting (>310°C) polymeric compound. Reduction in the absence of nitrogen gave a mixture of 9-aminomethylenefluorene (LXXXVII) and the diamino-compound (LXXXVIII). The latter compound could not be obtained 100% pure, owing to difficulty involved in removing the unsaturated amine (LXXXVII). Both reductions were conducted in tetrahydrofuran as solvent.

PART IV: The reduction of 9-cyanofluorene.

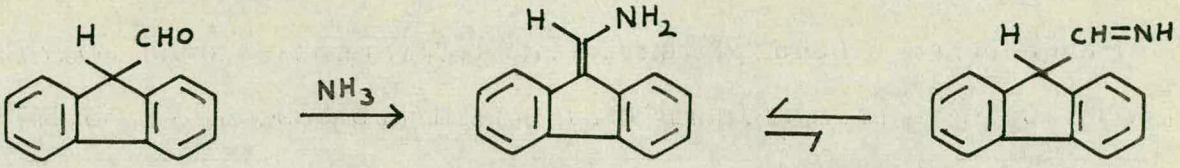
Reduction of 9-cyanofluorene (LXXI), obtained by the dehydration of 9-formylfluorene oxime, offered a route to the required 9-fluorenemethylamine. Lithium aluminium hydride reduction of the nitrile in tetrahydrofuran as solvent unexpectedly gave 9-aminomethylenefluorene (LXXXVII)



LXXII LXXI LXXXVII

This compound was obtained as yellow-white needles m.p. 149-151°. The infrared spectrum of the amine showed two absorptions at 3500cm^{-1}. and 3400cm^{-1}. characteristic of a free-NH_2 grouping, and a strong absorption at 1655cm^{-1}. characteristic of an olefinic double bond; the n.m.r. spectrum had a broad amine peak at 5·36τ, and aromatic absorptions from 2·0 -2·8τ. The olefinic proton resonated at less than 2·8τ, and was lost in the aromatic region of the spectrum.

9-Aminomethylenefluorene has been prepared[44,53] by bubbling ammonia through a benzene solution of 9-formylfluorene. Von and Wagner[53] established the structure of the amine by its ozonolysis to fluorenone and formamide.



LXXX LXXXVII LXXXVIIa

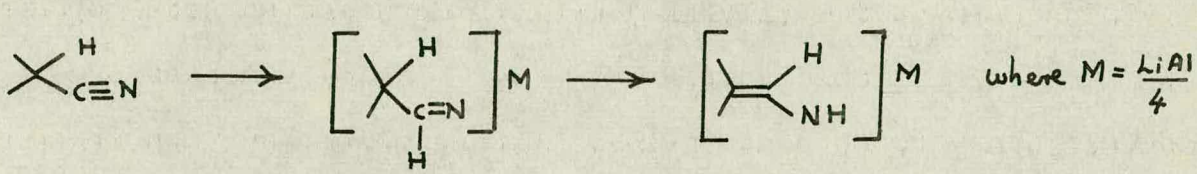
Miller and Wagner[54] proved using ultraviolet spectral data that the amine existed as the enamine form (LXXXVII) rather than as the ketimine tautomer (LXXXVIIa). The ultraviolet spectrum of the amine closely resembled that of 9-[N-piperidinomethylene]fluorene (LXXXIX), and was totally different from that of 9-[9-methyl-fluorenyl]methyl ketoxime (XC), these compounds being adopted as reference compounds for the enamine and ketimine forms respectively.

LXXXIX XC

The infrared spectrum of the amine strongly suggests an enamine structure, and the lack of a proton absorption at 5-6τ in the n.m.r. spectrum characteristic of the 9-fluorene methylene proton supports the absence of a ketimine form. It is to be expected that the amine would exist in the enamine form, as this structure would be jointly stabilised by the lability of the hydrogen attached to the 9-carbon

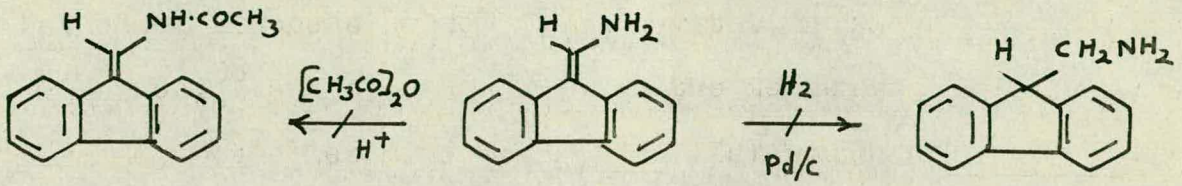
atom of fluorene, the conjugation of the 9,α-double bond with the unsaturated fluorene system[55], and by the proton-binding character of nitrogen,[56] and as a consequence the tendency of (LXXXVII) to isomerise to the ketimine form (LXXXVIIa) would be depressed.

The formation of the unsaturated amine by the lithium aluminium hydride reduction of 9-cyanofluorene, probably occurs[57] by rearrangement of the initially formed imine to the very stable enamine.



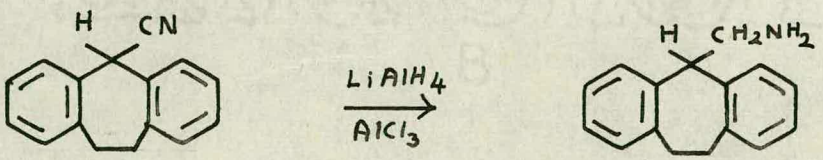
Catalytic reduction of (LXXXVII) proved extremely difficult. The unsaturated amine was shaken in an atmosphere of hydrogen, at 20° and atmospheric pressure, with 10% palladium-charcoal and W2 Raney Nickel as catalysts, but no reduction occurred. Hydrogenation at 5 atmospheres in a Parr low-pressure hydrogenator with palladium-charcoal and platinum oxide as catalysts similarly failed to effect reduction.

Von and Wagner[53] prepared the acetyl derivative (XCl) of the unsaturated amine by dissolving the amine in acetic anhydride, and removing excess of the latter in a vacuum desiccator. They failed to cyclise the product to a 2-azafluoranthene derivative using normal Bischler-Napieralski conditions. Attempted preparations of 9-acetaminomethylenefluorene (XCI) by the above procedure and by the normal acid-catalysed acetic anhydride method were unsuccessful and so no cyclisation was attempted.



XCI LXXXVII LXXII

The use of lithium aluminium hydride-aluminium chloride mixtures has been reported[58] as an improved method for the reduction of nitriles. 9-Cyanofluorene (LXXI), when treated with a 1:1 molar solution of this reduction mixture, unaccountably yielded 9,9′-dicyano-9,9′-bifluorene (LXXVI). The formation of the dinitrile was totally unexpected since the acidic medium would be expected to retard such a dimerisation. Reduction of the nitrile (XCII) under the same conditions proceeded in excellent yield.[43]

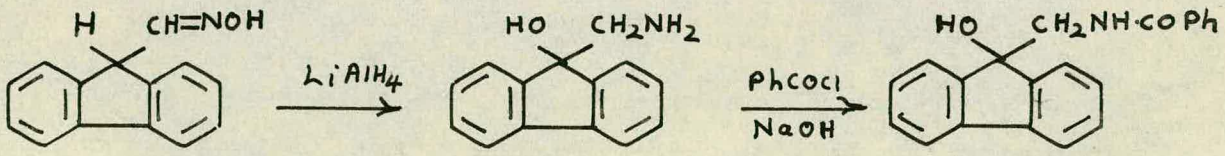


XCII

Attempted reduction of 9-cyanofluorene (LXXI) with Raney alloy in alcoholic alkali merely resulted in recovery of starting material. Staskun and vanEs[59] successfully reduced several aromatic nitriles by this procedure, the reduction being effected without application of heat.

PART V: The reduction of 9-formylfluorene oxime.

Lithium aluminium hydride reduction of oximes has proved an excellent procedure for the preparation of the corresponding amine.[60] Reduction of a mixture of the oximes of 9-formylfluorene gave a white crystalline solid m.p. 140-41°, which was identified from its elemental analysis and spectral data as 9-hydroxy-9-fluorenemethylamine (XCIII). The infrared spectrum showed a strong sharp absorption at 3610cm^{-1}. attributed to a hydroxyl group, and a strong broad peak at 3410cm^{-1}. which was assigned to a hydrogen-bonded primary amine grouping. The n.m.r. spectrum in deuterochloroform contained a degenerate aromatic region from 2·16 -2·58τ, a singlet at 7·18τ, and a broad peak with a small shoulder at 7·57τ which was assigned to a combination of hydroxyl and amino absorptions. The singlet at 7·18τ and the signals from the aromatic region integrated



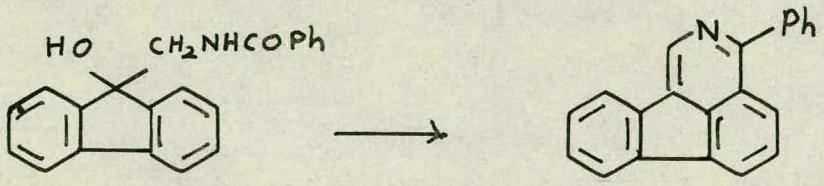
LXXXI XCIII XCIV

in the ration 1:4, which corresponds to the structure (XCIII), where the methylene group is considered responsible for the singlet absorption. The elemental analysis for the compound agreed with the proposed structure, as did the molecular weight determination, which ruled out the possibility of dimerisation having occurred.

Benzoylation of the hydroxyamine gave a hydroxyamide, and the elemental analysis, infrared and n.m.r. spectra of this compound agreed with structure (XCIV), which supported the assignment of (XCIII) to the initial reduction product. The hydroxyamine (XCIII) failed to give an acetyl derivative. An attempt was made to reduce the hydroxyl group with hydriodic acid[61] to give 9-fluorenemethylamine, but this yielded a white solid product m.p.200-30°, soluble in hydrochloric acid, which could not be purified.

The formation of (XCIII) from 9-formylfluorene oxime probably occurs by simultaneous reduction of the oxime function and oxidation of the 9-methylene hydrogen. Aerial oxidation of the 9-position of fluorene has frequently been observed.[62]

Cyclisation of the β-hydroxyethylamide (XCIV) by the Pictet-Gams procedure [p.18] offered a convenient synthesis of 3-phenyl-2-azafluoranthene.



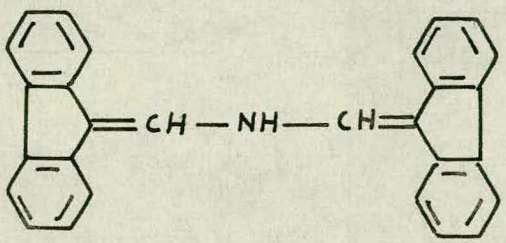
XCIV

Heating a mixture of the amide and phosphorus pentoxide for 3 hours at 150-160° with xylene as solvent failed to effect cyclisation, the product obtained being an acid-insoluble tar. A similar cyclisation with phosphorus pentoxide and polyphosphoric acid was

also unsuccessful. The Pictet-Gams procedure is normally carried out by refluxing the β-hydroxyamide with phosphorus oxychloride [p. 18], but this method was too mild to cyclise (XCIV), no aza-fluoranthene being isolated. Phosphorus pentoxide in boiling tetralin has occasionally been used to cyclise unactivated amides, but again only acid-insoluble tarry products were obtained when this procedure was applied to the cyclisation of (XCIV).

Attempted reduction of 9-formylfluorene oxime (LXXXI) with Raney alloy in alcoholic alkali at room temperature[59] resulted in deoximation, the product being identified as 9-formylfluorene (LXXX) by comparison of infrared spectra and the formation of a 2,4-dinitro-phenylhydrazone. Staskun[59] reported complete deoximation to the aldehyde form on refluxing benzophenone oxime, and various other oximes, with Raney alloy in alkaline solution. 9-Formylfluorene oxime is apparently deoximated at lower temperatures.

9-Fluorenone oxime is readily reduced to 9-fluorylamine by boiling with granulated zinc in dilute acetic acid.[63] Application of this procedure to 9-formylfluorene oxime gave 1,1′-difluoren-9-ylidene-dimethylamine (XCV) m.p. 313-15°.

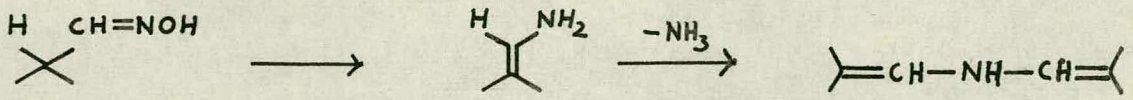


XCV

The infrared spectrum of the product showed a very sharp strong absorption at 1650cm^{-1}. similar to the absorption assigned to the enamine double bond of 9-aminomethylenefluorene (LXXXVII) [p.43]. The electronic spectrum contained intense absorptions in the visible region at 415 mμ and 436 mμ, attributable to the highly unsaturated system of (XCV). The molecular weight, as determined by mass spectrometry, and the elemental analysis of the compound supported the structure (XCV). No n.m.r. spectrum could be obtained owing to the insolubility of the substance in common organic solvents. The compound was extremely resistant to acid and basic hydrolysis.

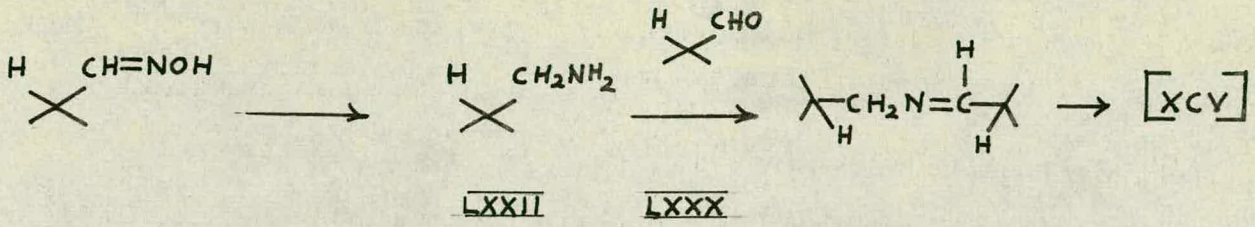
1,1'-Difluoren-9-ylidene-dimethylamine has been obtained[44,53] as a by-product in the synthesis of 9-aminomethylenefluorene (LXXXVII) from 9-formylfluorene (LXXX). The unsaturated amine (LXXXVII) is readily converted into (XCV) by the action of heat or acid. The structure of the divinylamine (XCV) was assigned by Kuhn and Neugebauer.[64]

The formation of (XCV) from 9-formylfluorene oxime probably occurs by elimination of ammonia from the initially formed unsaturated amine (LXXXVII).[53]



LXXXVII

An alternative mechanism involves condensation between the amine (LXXII) and the aldehyde (LXXX) [formed by hydrolysis of oxime], followed by loss of hydrogen from the Schiff base to give (XCV).

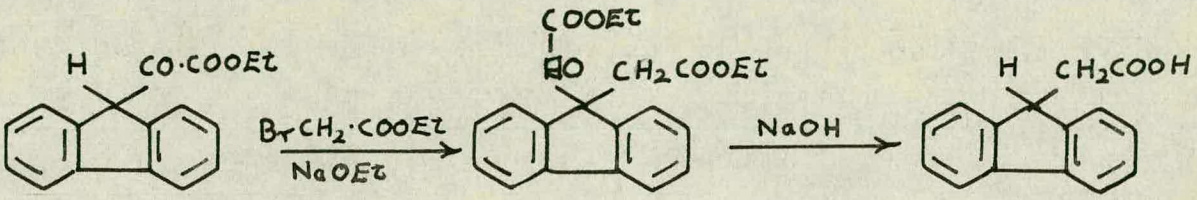


LXXII LXXX

The former mechanism appears more probable, as there is more precedent for the loss of ammonia from (LXXXVII), than there is for the loss of hydrogen from the Schiff base.

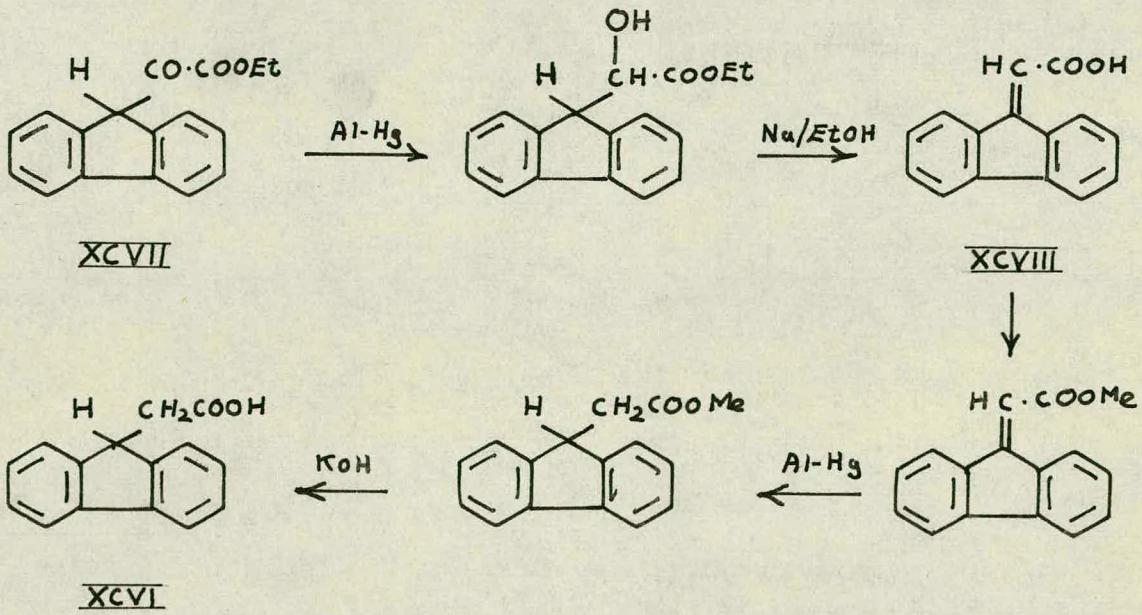
PART VI: The degradation of 9-fluoreneacetic acid.

Degradation of 9-fluoreneacetic acid (XCVI) by a Curtius, Hofmann or Schmidt reaction seemed a convenient route to 9-fluorenemethylamine (LXXII). 9-Fluoreneacetic acid has been prepared by several different procedures. Mayer,[65] and Wislicenus and Elbe,[66] synthesised the acid by the treatment of ethyl 9-fluorylglyoxalate (XCVII) with ethyl bromoacetate in alcoholic alkali as outlined below.



XCVII XCVI

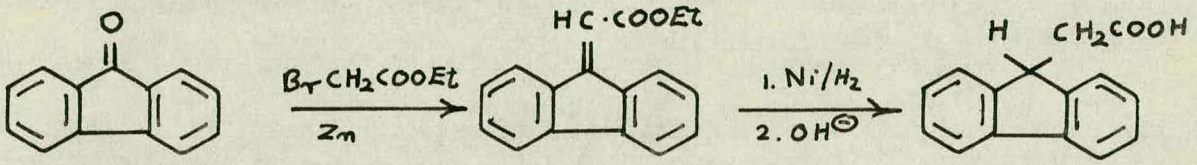
Sieglitz and Jassoy[67] obtained the acid from (XCVII) via the intermediate 9-fluorenylideneacetic acid (XCVIII).



XCVII XCVIII XCVI

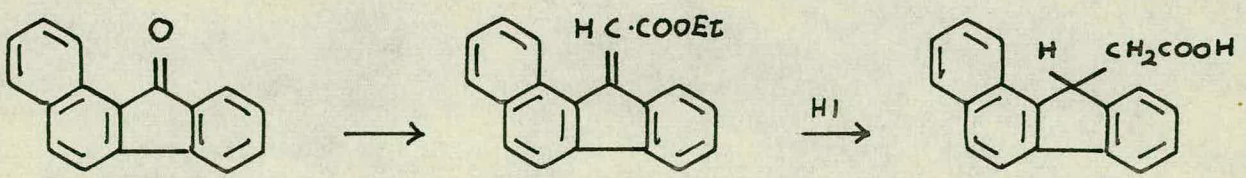
Aluminium-amalgam reduction of methyl 9-fluorenylideneacetate gave methyl 9-fluoreneacetate, which was readily hydrolysed to the acid (XCVI). Both these procedures involved several time-consuming processes and a more direct route to the acid seemed desirable.

Sieglitz and Jassoy,[67] and Anton and von Braun[1] prepared (XCVI) from fluorenone through the Reformatsky reaction.



XCIX XCVI

Sieglitz reduced ethyl 9-fluorenylideneacetate (XCIX) with aluminium amalgam; Anton reduced the ester in an autoclave with nickel as a catalyst. The Reformatsky reaction on 1,2-benzfluorenone (C) followed by reductive hydrolysis with hydriodic acid of the crude unsaturated ester, gave 1,2-benzfluorenyl-9-acetic acid (CI) in high yield.[68]

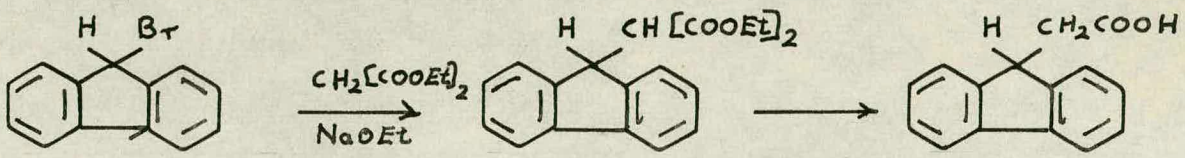


C CI

A similar reductive hydrolysis of (XCIX) to 9-fluoreneacetic acid, seemed preferable to the methods of decomposition outlined above.

Preparation of (XCVI) in this manner gave a 35% yield of the acid. The hydriodic acid hydrolysis of (XCIX) occurred very smoothly, but the initial Reformatsky reaction on fluorenone gave only a 50% yield of the ester. This was surprising as Campbell[69] reported a 90% yield for this reaction.

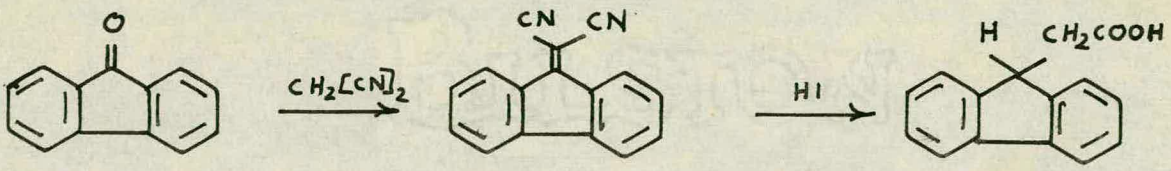
9-Fluoreneacetic acid has also been prepared in excellent yield from 9-bromofluorene (LXX) through the malonic ester synthesis.[70]



LXX XCVI

This seemed potentially the best procedure for the preparation of the acid, but it was not used in the present work because of the toxicity of 9-bromofluorene [p. 30].

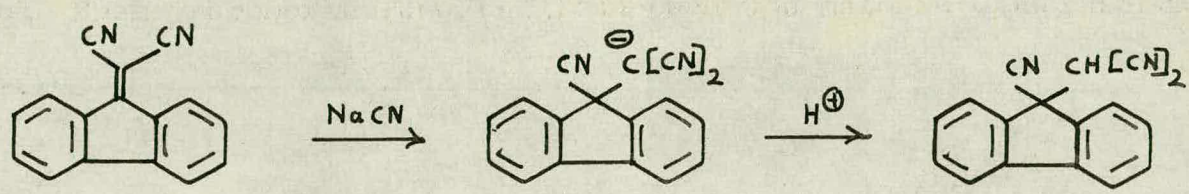
A solution of 9-fluorenone and malononitrile in ethanol at room temperature rapidly deposits a quantitative yield of 9-dicyanomethylenefluorene (CII) on addition of a few drops of piperidine.[71]



CII XCVI

D. Reid[72] hydrolysed (CII) with hydriodic acid and glacial acetic acid to 9-fluoreneacetic acid (XCVI) in 60% yield. This procedure involved only two simple stages and gave a very pure product, and proved to be the most efficient method for the preparation of (XCVI).

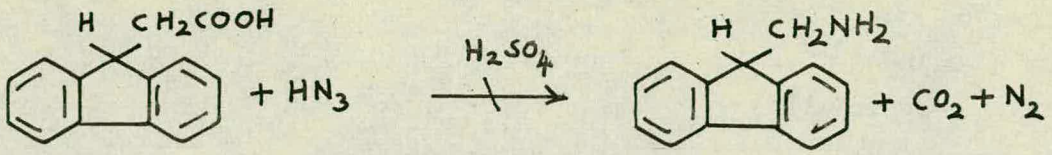
Hartzler[73] added cyanide ion to (CII) to give the anion of 9-cyanofluorenemalononitrile, from which the free acid (CIII) was obtained. R. Macpherson in this department[74] converted this compound



CII CIII

into 9-fluoreneacetic acid by acid hydrolysis to a tricarboxylic acid and subsequent decarboxylation with alkali, but this process, although proceeding in 40% yield was unreliable and less efficient than the method of Reid. It should be noted that 2 moles of sodium cyanide were required to convert (CII) into the anion of (CIII), and not 1 mole as reported by Hartzler.[73]

In the Schmidt reaction,[75] equimolar quantities of hydrazoic acid and a carboxylic acid interact in the presence of strong mineral acid to give an amine of one less carbon atom. Stirring a mixture of 9-fluoreneacetic acid (XCVI) and hydrazoic acid in chloroform solution with concentrated sulphuric acid as catalyst failed to give 9-fluorenemethylamine (LXXII).



XCVI LXXII

As the original acid could not be recovered from the aqueous phase after dilution of the chloroform solution with ammonium hydroxide, it is probable that (XCVI) was sulphonated. For acids which are readily sulphonated Smith[76] suggested the use of only two molar equivalents of sulphuric acid with one of the carbonyl compound in trichloroacetic acid as solvent. m-Toluic acid gave m-toluidine in good yield by this procedure.

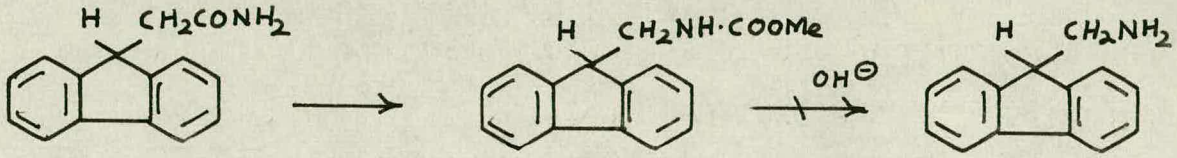
Adding 1 mole of 9-fluoreneacetic acid to a mixture of 2 moles of sulphuric acid, 1 mole of sodium azide and excess trichloroacetic acid at 60°C unexpectedly gave trichloroacetamide. Trichloroacetic acid reacted readily with sodium azide in the absence of other acids to give trichloroacetamide. No report could be found in the literature of the formation of trichloroacetamide when using trichloroacetic acid as a solvent for the Schmidt reaction.

Amides are converted into amines by treatment with bromine and alkali [Hofmann[77]].

$$RCONH_2 + Br_2 + 4OH^- \longrightarrow RNH_2 + CO_3^{--} + 2Br^- + 2H_2O$$

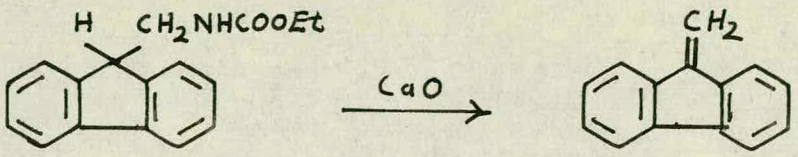
The reaction generally is carried out by dissolving the amide in a very slight excess of cold aqueous hypohalite solution in alkali, followed by rapid warming to give the amine. A valuable modification, usually employed with high molecular weight amides, consists in carrying out the reaction in methanolic solution, with subsequent hydrolysis of the urethane so obtained.

9-Fluoreneacetamide gave an excellent yield of methyl 9-fluorenemethylurethane (CIV) by the latter procedure.



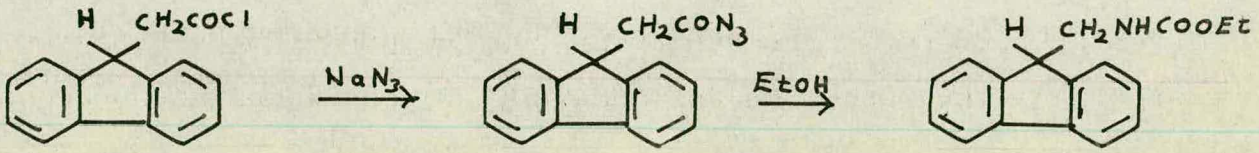
CIV LXXII

The urethane could not be hydrolysed to the amine (LXXII) with aqueous or alcoholic alkali. Sieglitz and Jassoy[67] prepared ethyl 9-fluorenemethylurethane (CV) and failed to decompose it to the amine (LXXII) with concentrated hydrochloric acid, sulphuric acid or concentrated ammonia. Distillation of the urethane with calcium oxide at low pressure and in an atmosphere of hydrogen gave an appreciable yield of 9-methylenefluorene (CVI).[78]



CV CVI

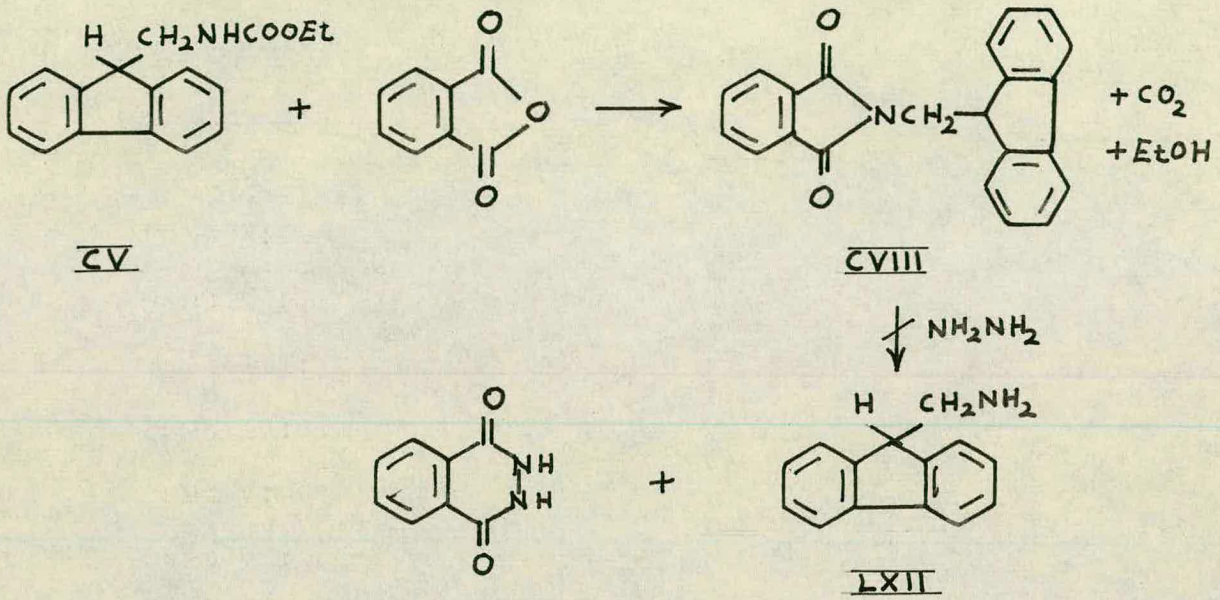
The urethane (CV) was prepared from 9-fluoreneacetic acid by the Curtius reaction.[79] 9-Fluoreneacetyl chloride was reacted with sodium azide activated by Nelles' procedure[80] in benzene to give the azide (CVII), which was boiled with ethanol to give (CV).



CVII CV

The azide (CVII) was also prepared by adding an aqueous solution of sodium azide to a solution of the acid chloride in acetone. The latter procedure gave a higher yield of product, but the urethane so obtained was contaminated with traces of inorganic material. The urethane resisted attempts to decompose it to the amine (LXXII), confirming the report of Sieglitz[67] to this effect.

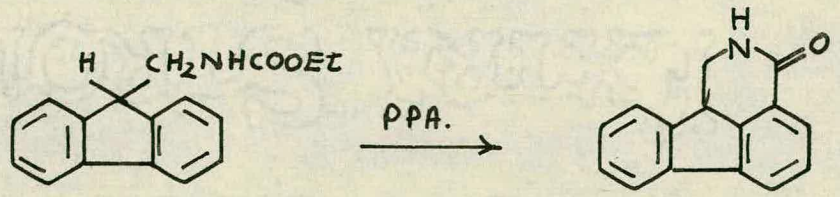
Ing and Manske[81] developed an essentially non-hydrolytic method for cleaving urethanes. The carbalkoxy group of the urethane is first replaced by the phthalyl group, usually in excellent yields by fusion with phthalic anhydride. The resulting phthalimides are readily split into amines and sec-phthalylhydrazide by warming with alcoholic hydrazine. The phthalylhydrazide is easily removed by virtue of its sparing solubility in most solvents. Occasionally the reaction halts with formation of an addition compound between hydrazine and the phthalimide, which, however, can be decomposed to the amine hydrochloride and phthalylhydrazide by the addition of dilute hydrochloric acid.



CV CVIII LXII

Fusion of (CV) with phthalic anhydride gave an excellent yield of the phthalimide (CVIII). Decomposition of the latter failed to give 9-fluorenemethylamine, the only product isolated being an acid-insoluble tar.

Urethanes such as (CV) have been cyclised with polyphosphoric acid[18,43] to give isocarbostyrils. This procedure is essentially a modification of the Bischler-Napieralski reaction [p.19] yielding a 1-hydroxy-isoquinoline derivative.



CV CIX

Heating ethyl 9-fluorenemethylurethane at 120-150° for 2 hours with polyphosphoric acid failed to effect cyclisation to (CIX). The oily product obtained was chromatographed on 10% deactivated alumina, but no crystalline product could be isolated.

PART VII: The infrared spectra of 9-substituted fluorene derivatives.

It was found that many of the 9-substituted and 9,9'-di-substituted fluorenes obtained by the methods outlined in the previous sections exhibited two bands of nearly equal intensity in the 1980-1940 and 1930-1880cm^{-1} regions of the infrared spectrum. These bands are quite characteristic and are probably related to those groups of bands in the 2000-1600cm^{-1} region which can be used to distinguish between different types of ring substitution in the benzene series.[137]

The bands in this region have been shown to be summation bands of the CH out-of-plane fundamentals which occur between 1000 and 700cm^{-1}. The intensities and numbers of the bands are relatively more significant than the precise wavelengths at which they occur, and they have been useful in distinguishing between various simple disubstituted, trisubstituted and higher-substituted benzenes. These absorptions are not so useful in distinguishing between substituted polycyclic hydrocarbons as the patterns resulting from the combined effects of two or more rings are generally not easily resolved.

Nevertheless, of the many 9-substituted fluorene compounds examined (see experimental section), the majority displayed two absorptions of equal intensity in the regions mentioned. Fluorenone-1-carboxylic acid, 1-substituted fluorenes, and 2,2'-dicarbomethoxy-biphenyl showed a more complex set of absorptions in the same region. 9-Substituted fluorenes in which the substituent contained a benzene ring, e.g. 9-benzylfluorene, also showed a complex pattern

of absorptions of different intensities.

These observations appear to indicate that the simple absorption patterns of 9-substituted fluorenes are related to the more symmetrical structure of these compounds than those with substituents in the benzenoid rings of fluorene, with a consequent decrease in the number of out-of-plane CH fundamentals.

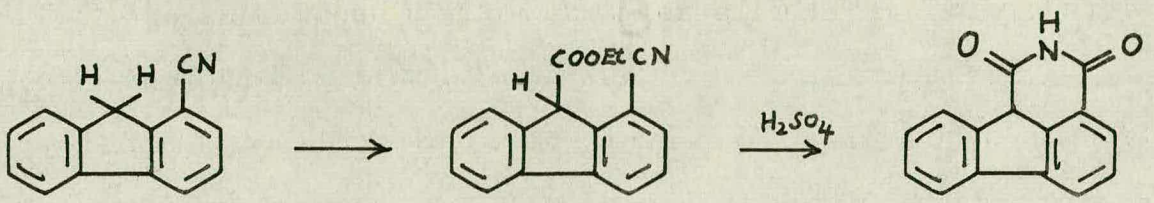
It should be noted, however, that both fluorene and 9,9′-bifluorene do not show the characteristic absorptions of the simple 9-substituted fluorene compounds.

SECTION II.

Attempts to prepare 2-azafluoranthene by a condensation involving carbon atoms 1 and 3 of the potential heterocyclic ring.

Attempts to prepare 2-azafluoranthene by a condensation involving carbon atoms 1 and 3 of the potential heterocyclic ring.

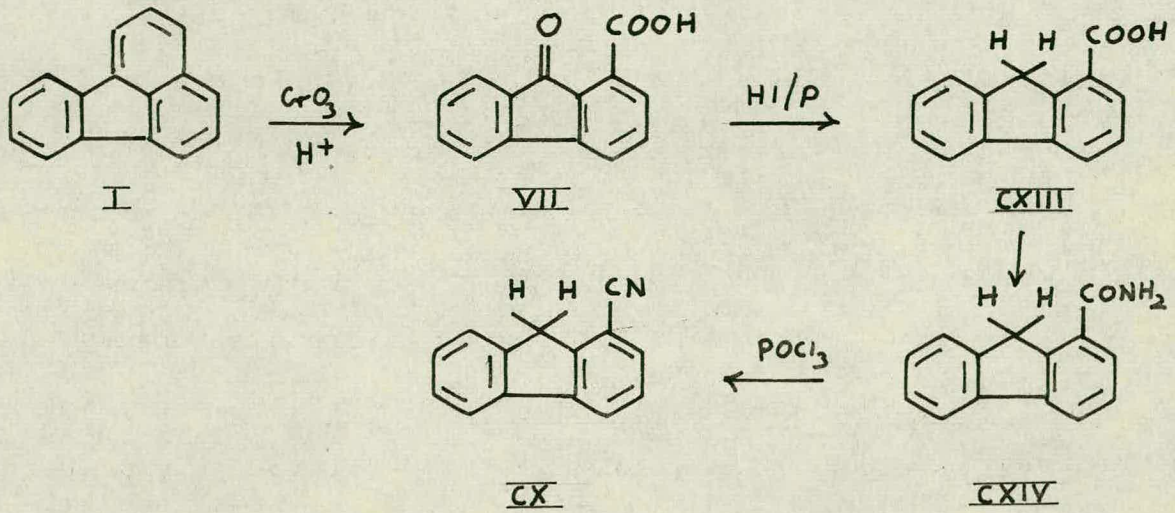
As mentioned in the "Introduction" [p.22] homophthalimide derivatives are readily converted into isoquinolines, and are often used as intermediates in the preparation of the latter. A possible route to 2-azafluoranthene involved the synthesis of (CXII) from 1-cyanofluorene (CX).



CX CXI CXII

The acid-catalysed condensation of a carbethoxy group with a cyano group to yield a pyridine ring has been reported.[82]

1-Cyanofluorene (CX) was obtained from fluoranthene as outlined in the following formulae.

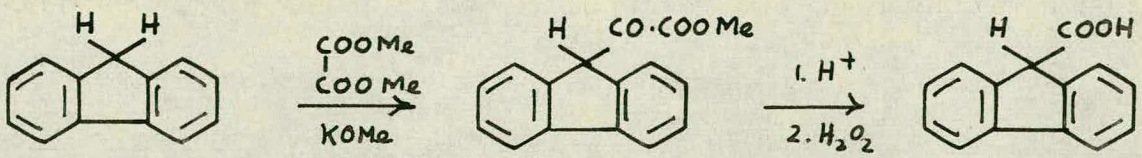


I VII CXIII

CX CXIV

Fluorenone-1-carboxylic acid (VII), obtained by the oxidation[83] of fluoranthene (I), was reduced in 90% yield to fluorene-1-carboxylic acid (CXIII). Of the several reported methods for reducing the ketonic function of (VII), the method of Morrison[84] using red phosphorus and hydriodic acid in glacial acetic acid was found to be the most successful. Dehydration of 1-fluorenecarboxamide (CXIV) with phosphorus oxychloride[85] gave 1-cyanofluorene (CX) in 50% yield. An attempt to dehydrate (CXIV) with the milder reagent thionyl chloride gave a mixture of nitrile and recovered amide. A dimethylformamide-thionyl chloride mixture[86] at 60° similarly failed to completely dehydrate the amide.

A carboxyl group can be introduced at the 9-position of fluorene by a Claisen Ester condensation. Treatment of 1 mole of fluorene with 2 moles of dimethyl oxalate and 2 moles of potassium methoxide in methanol gives methyl 9-fluoreneglyoxalate (CXV).[87] Hydrolysis to the glyoxylic acid and treatment of the latter with hydrogen peroxide yields 9-fluorenecarboxylic acid.



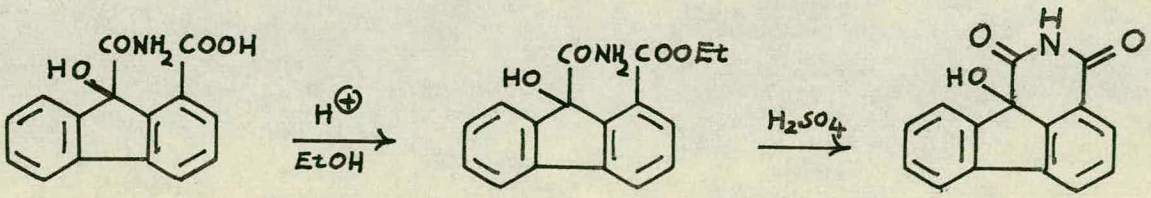
CXV

Application of this procedure to 1-cyanofluorene proved unsuccessful, no acylation occurring at the 9-position of the nitrile. Boiling a mixture of the nitrile, potassium metal and dimethyl oxalate in

methanol did not give a homogeneous solution. The potassium salt of the nitrile was essentially insoluble in methanol. The use of benzene and potassium methoxide produced a more homogeneous mixture, but no condensation was observed, 1-cyanofluorene being recovered from the benzene solution on addition of water. Diethyl oxalate and sodium ethoxide in benzene also failed to acylate (CX), although a completely homogeneous solution was obtained. The nitrile was recovered unchanged. It seems possible, therefore, that the condensation was unsuccessful for steric reasons.

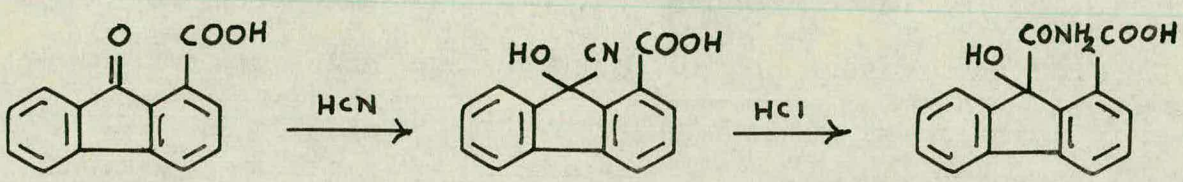
A carboxyl group has been introduced at the 9-position of fluorene by the carbonation of 9-fluorenylmagnesium bromide or 9-fluorenyl-lithium.[88] This procedure was not applied to 1-cyano-fluorene owing to the possible complications involving addition of ethylmagnesium bromide or butyl-lithium to the nitrile grouping.

Kuhn[89] prepared 9-carbamoyl-9-hydroxyfluorene-1-carboxylic acid (CXVI) from fluorenone-1-carboxylic acid, and it was intended to convert this compound into the ester (CXVII) and cyclise the latter with sulphuric acid to the homophthalimide (CXVIII).



CXVI CXVII CXVIII

Addition of hydrogen cyanide to fluorenone-1-carboxylic acid (VII) gave the cyanohydrin (CXIX), which was hydrolysed with hydrochloric acid and acetic acid to the amide (CXVI), m.p. 150-51°. The elemental analysis of the compound obtained indicated that it was the monohydrate of (CXVI), and repeated recrystallisation from water failed to raise the melting point.



VII CXIX CXVI

Kuhn reported a melting point of 215° for the monohydrate of (CXVI), and a melting point of 182-89° for the monohydrate of the corresponding 9-hydroxy-1,9-dicarboxylic acid. Hydrolysis of the carbamoyl compound melting at 150-51° gave a hydroxyacid m.p. 181-83°.

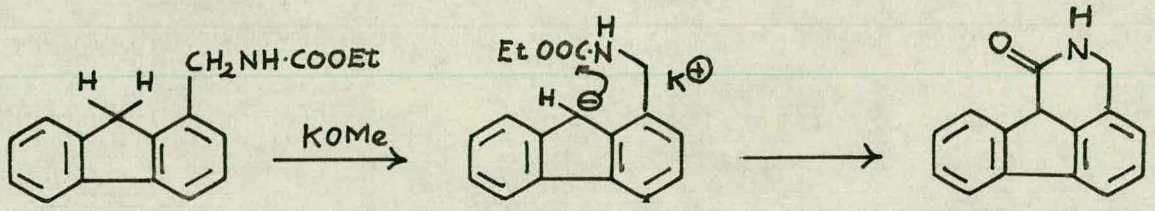
Esterification of (CXVI) with ethanol and concentrated sulphuric acid gave an excellent yield of ethyl 9-carbamoyl-9-hydroxyfluorene-1-carboxylate (CXVII). Warming (CXVII) with 60% sulphuric acid failed to give the homophthalimide derivative (CXVIII). Pouring the acidic solution into water gave only a tarry product, from which no crystalline compound could be isolated.

SECTION III.

Attempted preparation of 2-azafluoranthene using a Dieckmann cyclisation.

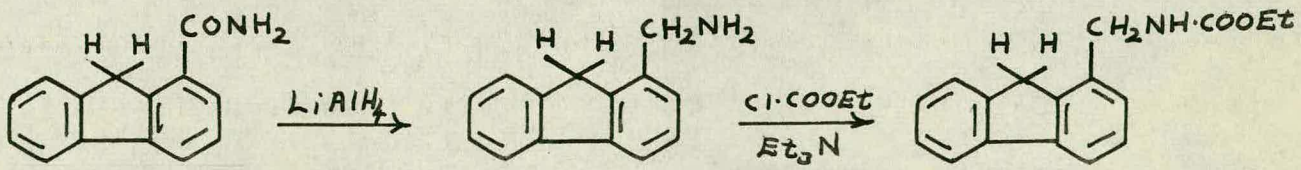
Attempted preparation of 2-azafluoranthene using a Dieckmann cyclisation.

Condensation between a reactive hydrogen of the 9-methylene group and the carbethoxy group of the urethane (CXX) to give (CXXI), offered a possible route to 2-azafluoranthene.



CXX CXXa CXXI

Ethyl 1-fluorenemethylurethane (CXX) was synthesised as outlined in the following formulae.



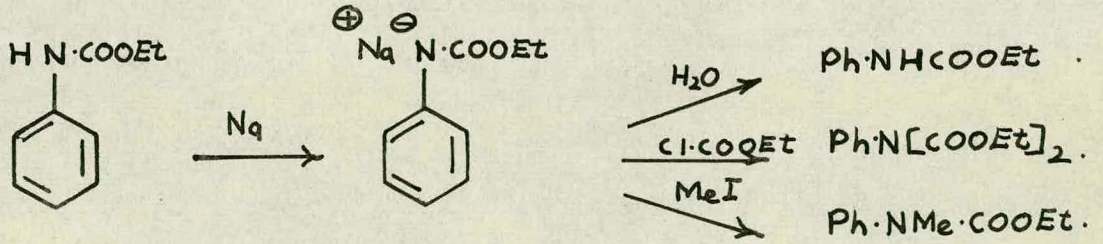
CXIV CXXII CXX

Lithium aluminium hydride reduction of 1-fluorenecarboxamide (CXIV) gave 1-fluorenemethylamine (CXXII) which was converted into (CXX) by reaction with ethyl chloroformate in toluene.

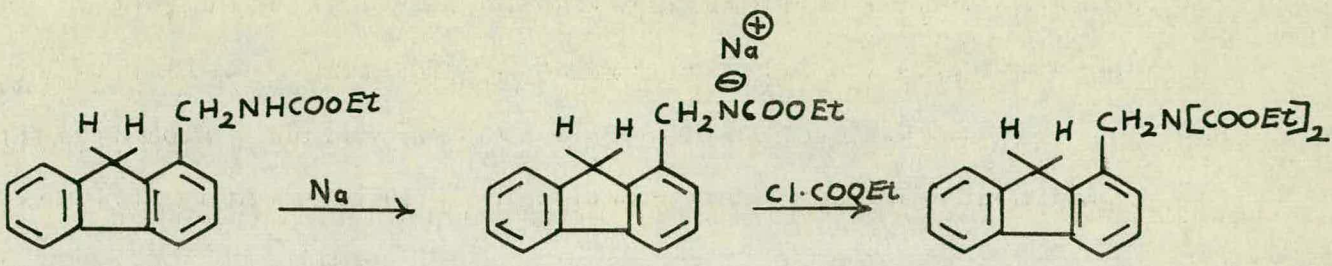
The urethane was boiled with potassium methoxide in ether for three hours. The ether solution initially developed a deep

red colour, which disappeared after 15 minutes with separation of a white solid. Shaking with water produced a homogeneous two-phase system. Acidification of the aqueous phase failed to yield a product; evaporation of the ether phase yielded unreacted urethane. A similar attempted cyclisation using triphenylmethyl-sodium as base was unsuccessful. Again a red colour was initially observed which disappeared with a simultaneous precipitation of a white solid product. These observations appeared to indicate that the white precipitate was the insoluble potassium [or sodium] salt (CXXa) of the urethane, which after failing to cyclise was hydrolysed to (CXX).

It is known, however, that unsubstituted N-monoalkyl or -arylurethanes can have the hydrogen on the nitrogen atom replaced by alkali metals.[90]



These alkali metal derivatives react with water, ethyl chloroformate and methyl iodide with replacement of the metal by -H, -COOEt, and -Me respectively. The possibility therefore existed that in the attempted cyclisations of ethyl 1-fluorenemethylurethane, the base was reacting with the amide hydrogen to form an alkali metal derivative (CXXIII).



CXX CXXIII CXXIV

To test this hypothesis the urethane was boiled in ether in the presence of freshly cut sodium wire for five hours, and ethyl chloroformate was added to the mixture. The urethane (CXX) was recovered unchanged, and no formation of (CXXIV) could be detected. A similar result was observed on replacing sodium with potassium methoxide.

It therefore appears that the solid which precipitated during the attempted cyclisation was the alkali metal salt (CXXa) of the urethane. As there appears to be no steric factor inhibiting cyclisation, it is likely that the insolubility of the alkali metal salt of (CXX) in ether renders cyclisation difficult. The use of a solvent in which the salt is more soluble may result in cyclisation occurring.

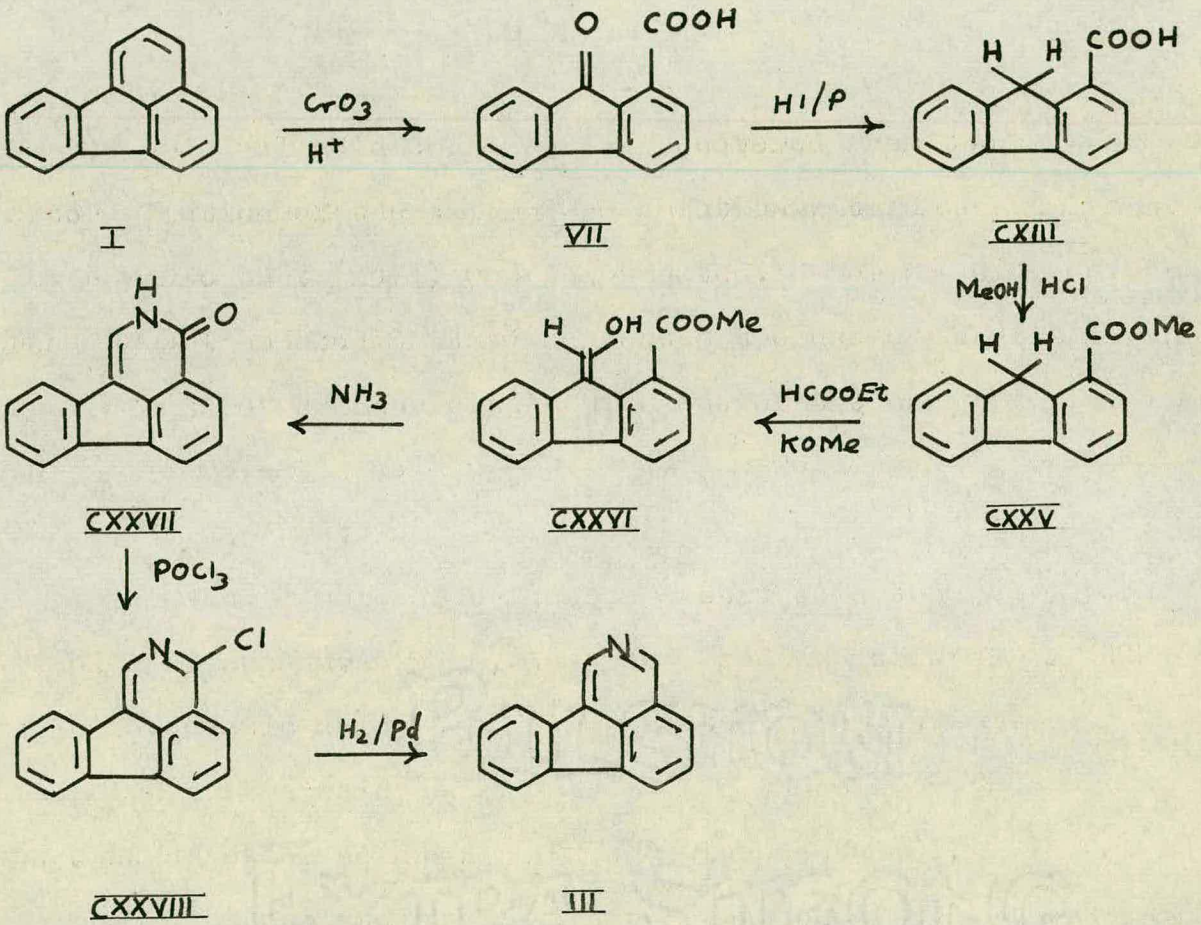
Sodium methylsulphinate and dimethyl sulphoxide may be a suitable combination of base and solvent.

SECTION IV.

The synthesis and properties
of 2-azafluoranthene.

PART I: The synthesis of 2-azafluoranthene

2-Azafluoranthene (III) was prepared by the following synthetic scheme:

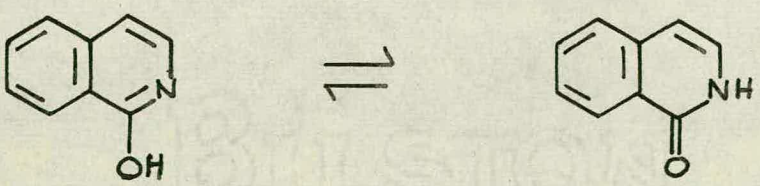


Oxidation of fluoranthene (I) gave fluorenone-1-carboxylic acid (VII), which was reduced to fluorene-1-carboxylic acid (CXIII). Esterification of (CXIII) gave methyl fluorene-1-carboxylate (CXXV). Formylation of the ester yielded the hydroxymethylene compound (CXXVI), which on treatment with ammonia gave 2-azafluoranth-3[2H]-

one (CXXVII). Boiling the latter with phosphorus oxychloride gave 3-chloro-2-azafluoranthene (CXXVIII), which was hydrogenolysed to the parent hydrocarbon, 2-azafluoranthene (III). The conversion of fluoranthene into its 2-aza- derivative occurred in 15% yield.

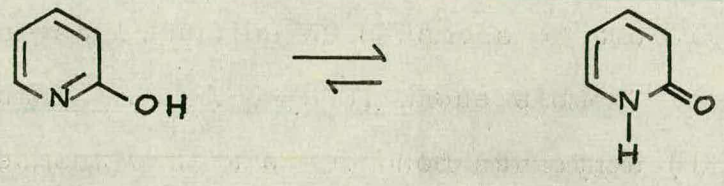
The degradation of fluoranthene to fluorene-1-carboxylic acid (CXIII)[83,84] has been described [p. 63]. The ester[83] (CXXV) was obtained in 40% overall yield from fluoranthene. Formylation[53] of (CXXV) gave an oily product which was immediately cyclised to (CXXVII). Recrystallisation of a sample of the oil from ligroin gave white crystals m.p.= 175-78°C, whose elemental analysis was in reasonable agreement with the proposed structure (CXXVI). Ungnade[24] transformed hydroxymethylene esters such as (CXXVI) directly into isocarbostyril derivatives with aqueous ammonia. Boiling (CXXVI) with concentrated aqueous ammonia gave the isocarbostyril (CXXVII) m.p. 287-89°.

Isocarbostyril is known to exist as a tautomeric mixture of the hydroxyisoquinoline (CXXIX) and isoquinolone (CXXX) compounds.



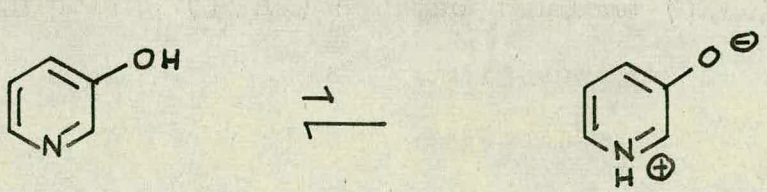
CXXIX CXXX

This tautomerism is a feature of N-heteroaromatics with a hydroxyl group α or γ to a nitrogen atom.[91] Extensive investigation of the exact nature of 2- and 4-hydroxypyridines has shown that both in neutral solution and in the solid state, these compounds exist mainly in the pyridinone form (CXXXII) rather than in the form (CXXXI).



CXXXI CXXXII

However, 3-hydroxypyridine possesses the normal structure (CXXXIII) rather than that of the zwitterion (CXXXIV).

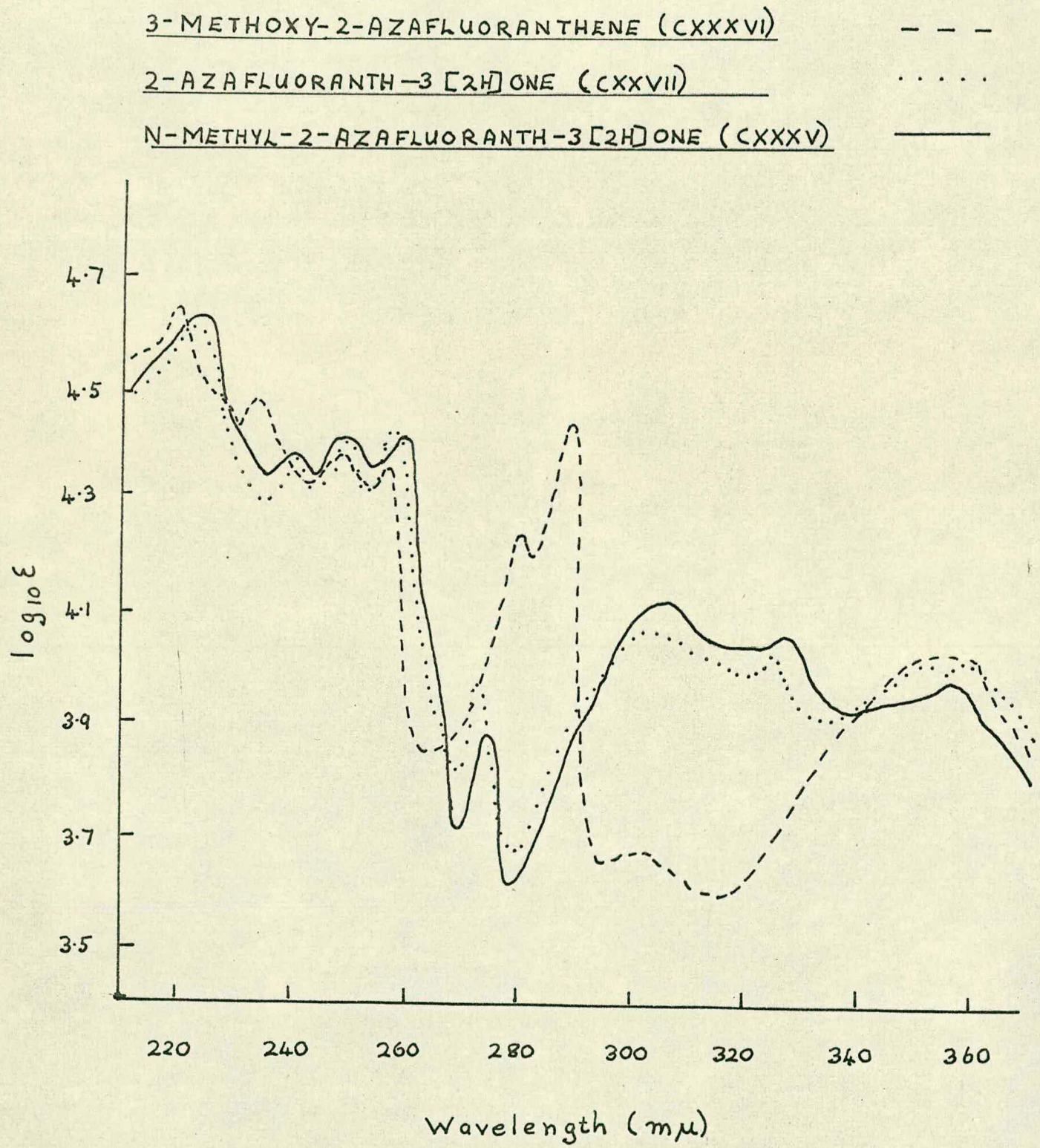


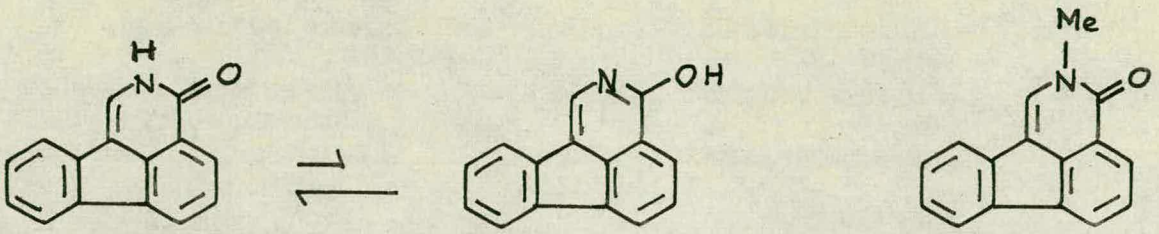
CXXXIII CXXXIV

These statements are supported by physical evidence.

On the basis of the available infrared and ultraviolet spectral data, the isocarbostyril (CXXVII) appears to exist predominantly in the amide [pyridone] form (CXXVII) rather than in the form (CXXVIIa).

FIG. 2


3-METHOXY-2-AZAFLUORANTHENE (CXXXVI)
2-AZAFLUORANTH-3[2H]ONE (CXXVII)
N-METHYL-2-AZAFLUORANTH-3[2H]ONE (CXXXV)
4·7
4·5
4·3
4·1
3·9
3·7
3·5
log10ε
220
240
260
280
300
320
340
360
Wavelength (mμ)



CXXVII ⇌ CXXVIIa CXXXV

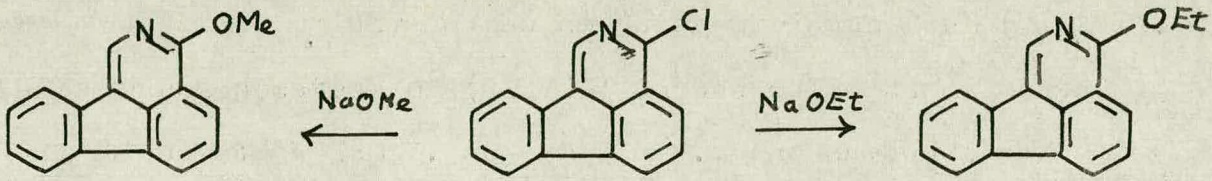
Mason[92] showed that the solid state infrared spectra of heterocycles with a hydroxyl group α or γ to a nitrogen atom contained N-H absorptions in the region 3300-3100cm^{-1}., and carbonyl absorptions in the region 1700-1630cm^{-1}., indicating that these compounds exist mainly in the amide or pyridone form (CXXXII). The infrared spectrum of (CXXVII) in the solid state contained N-H absorptions at 3175cm^{-1}. and 3040cm^{-1}., and carbonyl absorptions at 1690cm^{-1}. and 1672cm^{-1}. [The peak at 1672cm^{-1}. may be an olefimic double bond absorption].

Mason[93] also showed that N-heteroaromatic hydroxy compounds with a hydroxyl group α or γ to a ring nitrogen atom have an ultraviolet spectrum similar to that of their N-methyl derivative and different from that of their O-methyl derivative both in organic and in aqueous solvents indicating that they tautomerise predominantly to the amide form under these conditions. The ultraviolet spectra of the isocarbostyril (CXXVII) and its N-methyl (CXXXV) and O-methyl (CXXXVI) derivatives in ethanol solution are shown in Fig.2. The similarity of the spectra of (CXXVII) and (CXXXV) indicates that (CXXVII) exists predominantly in the amide form.

The N-methyl derivative (CXXXV) was prepared by boiling (CXXVII) with dimethyl sulphate and alkali in methanol. The O-methyl derivative (CXXXVI) was prepared as indicated below.

Compound (CXXVII) should, therefore, correctly be named 2-azafluoranth-3[2H]one and not 3-hydroxy-2-azafluoranthene (CXXVIIa).

Boiling (CXXVII) with phosphorus oxychloride gave a quantitative yield of 3-chloro-2-azafluoranthene (CXXVIII). Boiling the chlorocompound with sodium in methyl or ethyl alcohol gave the extremely fluorescent 3-methoxy- and 3-ethoxy-2-azafluoranthenes, (CXXXVI) and (CXXXVII) respectively.



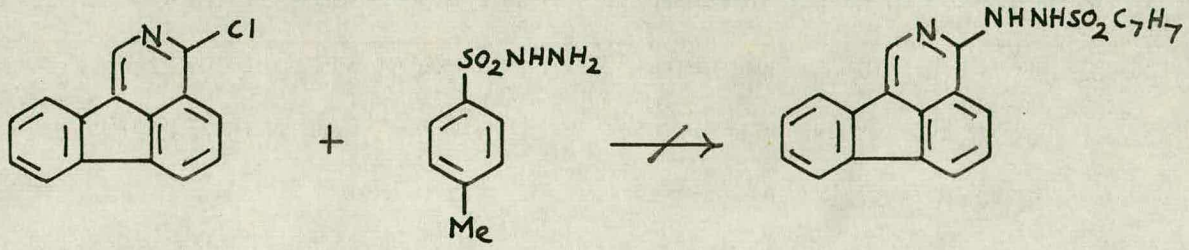
CXXXVI CXXVIII CXXXVII

The n.m.r. spectra of 3-chloro-2-azafluoranthene and its two ethers showed a singlet at 1·55-1·75τ and degenerate aromatic absorptions from 2·0-2·9τ, which integrated in the ratio 1:7. The low field singlet absorption is characteristic of a proton α or γ to the ring nitrogen atom of N-heteroaromatic compounds. The two ethers were readily hydrolised with 6N hydrochloric acid to 2-azafluoranth-3-[2H]one.[94]

Hydrogenolysis of 3-chloro-2-azafluoranthene over 10% palladium on charcoal in ethanol solution in the presence of one

molar equivalent of potassium hydroxide gave a 60% yield of 2-azafluoranthene, and smaller quantities of 3-ethoxy-2-azafluoranthene (CXXXVII) and 2-azafluoranth-3[2H]one (CXXVII). The presence of alkali was found to promote hydrogenolysis,[95] although it appears that some nucleophilic replacement of the chlorine in (CXXVIII) occurred, by attack from hydroxyl and ethoxyl anions.

A boiling chloroform solution of 3-chloro-2-azafluoranthene and toluene-p-sulphonylhydrazide failed to give a precipitate of the corresponding toluene-p-sulphonylhydrazino compound (CXXXVIII).

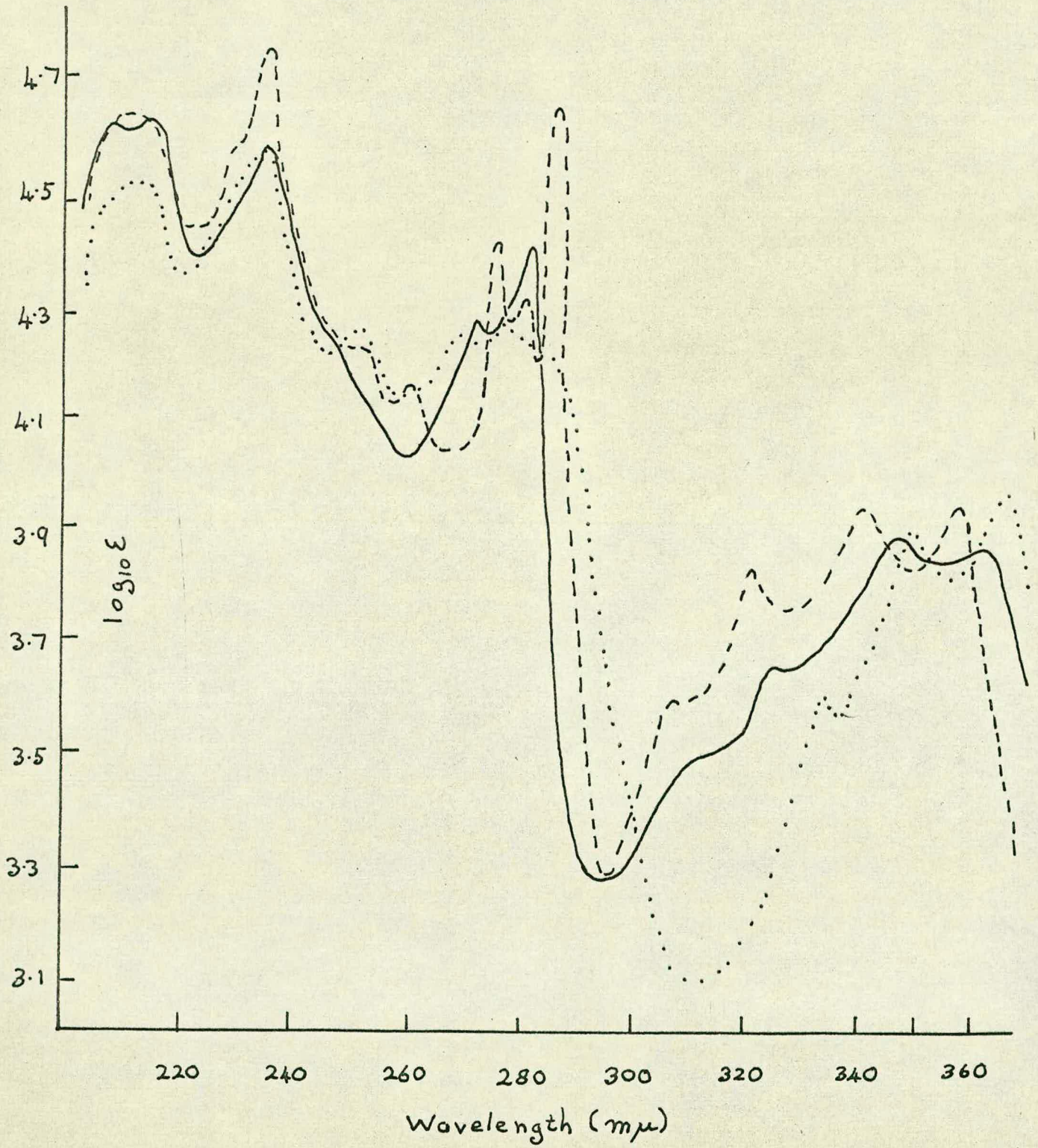


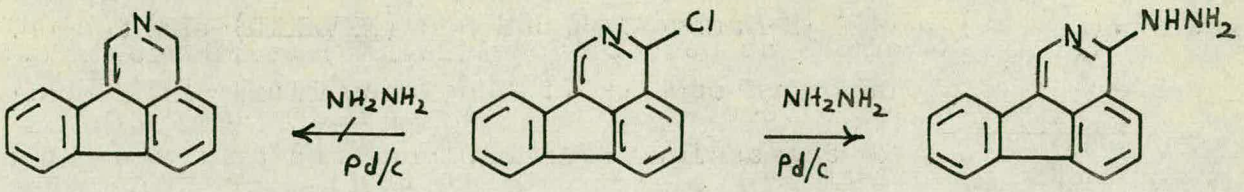
CXXVIII CXXXVIII

Reactive halogen atoms have been removed from chloroacridines, chlorocinnolines, chloroquinazolines and chlorophthalazines by reaction with toluene-p-sulphonylhydrazide and decomposition of the product with alkali.[96] The chlorine atom of (CXXVIII) is probably not sufficiently reactive to condense with the hydrazide. The chlorine atom of 4-chlorocinnoline is known to be much more reactive than that of 4-chloroquinoline or 1-chloroisoquinoline.[97]

Boiling a mixture of (CXXVIII), hydrazine hydrate and 10% palladium on charcoal in ethanol failed to effect hydrogenolysis to 2-azafluoranthene. 3-Hydrazino-2-azafluoranthene (CXXXIX) was recovered from the ethanol solution.

FIG. 3


FLUORANTHENE
1-AZAFLUORANTHENE
2-AZAFLUORANTHENE
4·7
4·5
4·3
4·1
3·9
3·7
3·5
3·3
3·1
log10 ε
220
240
260
280
300
320
340
360
Wavelength (mμ)



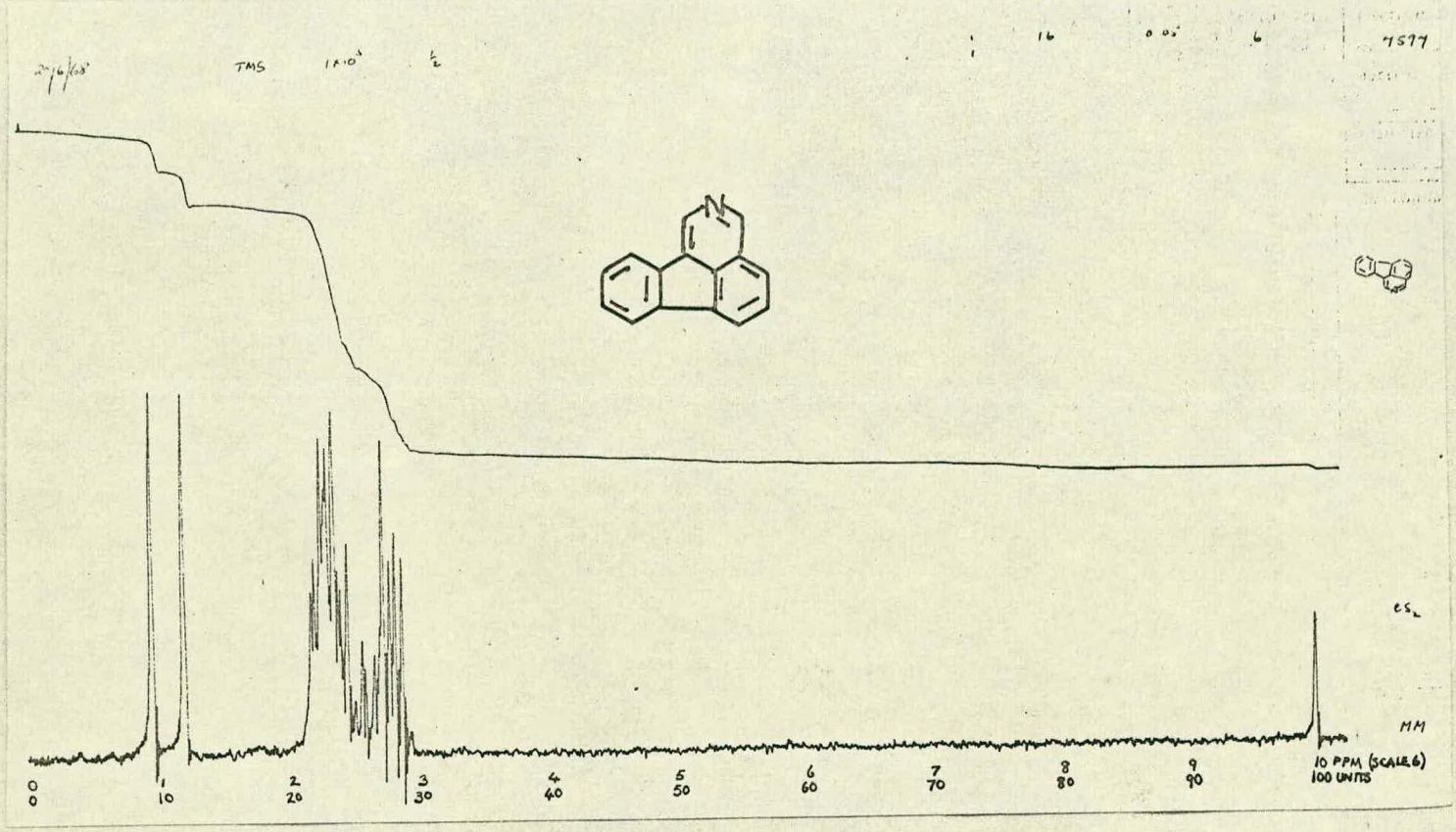
III CXXVIII CXXXIX

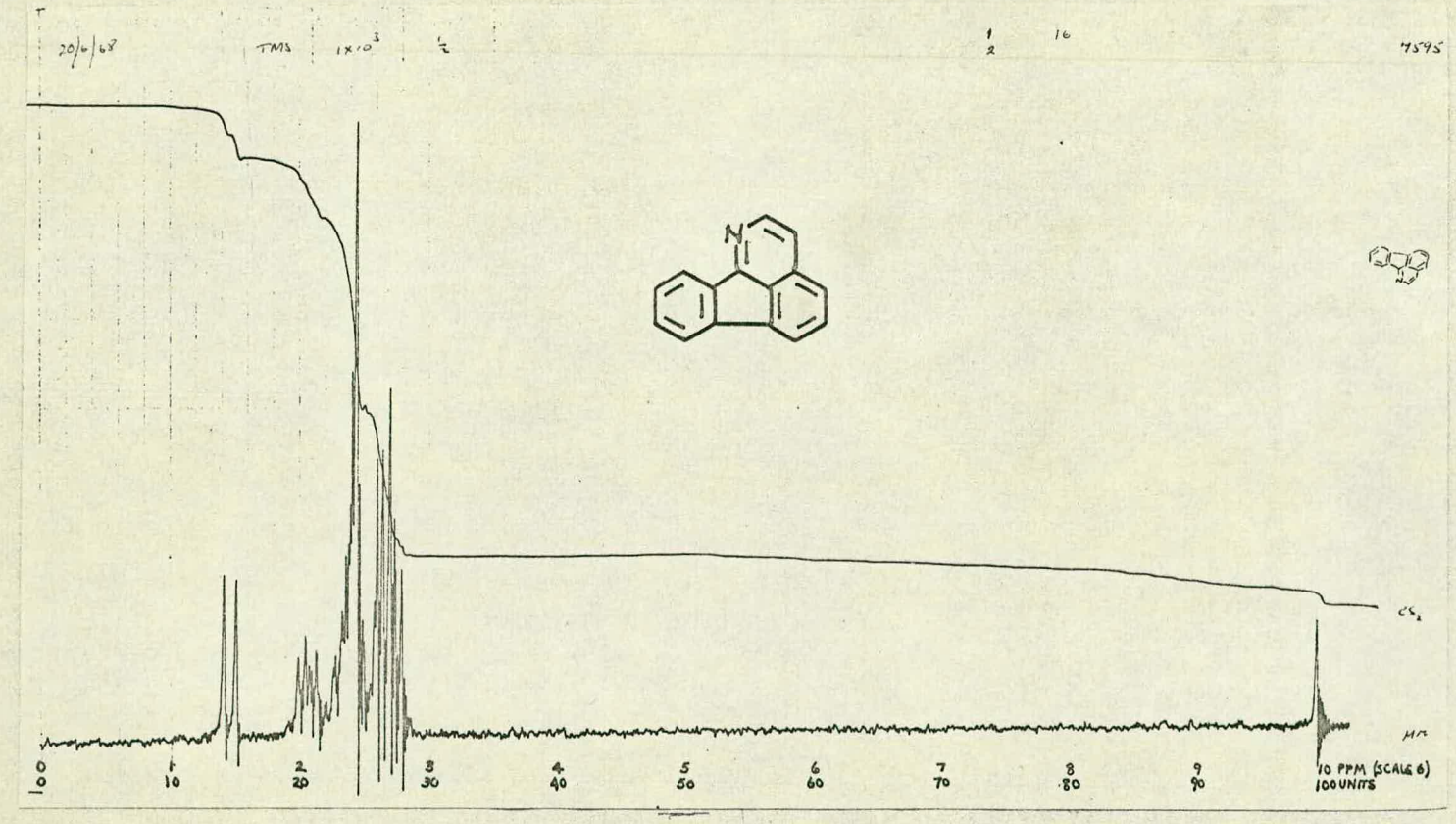
Mosby[98] reported a neat laboratory procedure for the dehalogenation of haloheterocycles using hydrazine hydrate and palladium. The hydrazino compound (CXXXIX) was prepared by boiling (CXXVIII) with hydrazine in ethanol.

2-Azafluoranthene crystallised as pale yellow needles from petroleum ether [40-60°], m.p. 62-63°. It distilled at 150-55° at a pressure of 1·0 mm. It readily formed a picrate and a trinitrobenzene complex in ethanol, and a methiodide in boiling methyl iodide. Bubbling dry hydrogen chloride through a solution of the base in benzene gave a yellow hydrochloride which was exceedingly hygroscopic.

The ultraviolet spectrum of 2-azafluoranthene is very similar to that of fluoranthene and 1-azafluoranthene, Fig.3. It is a feature of polycyclic azacompounds that generally the replacement of a methine group by a nitrogen atom results in relatively little change in the spectrum of the hydrocarbon.[99] On the other hand, Stubbs and Tucker[100] from a study of the spectra of methoxyfluoranthenes found that a methoxy group in the benzenoid ring has much less effect on the fluoranthene spectrum than the same group in a

FIG. 4


TMS
7577
10 PPM (SCALE 6)
100 UNITS


20/6/68
TMS
7595
10 PPM (SCALE 6)
100 UNITS

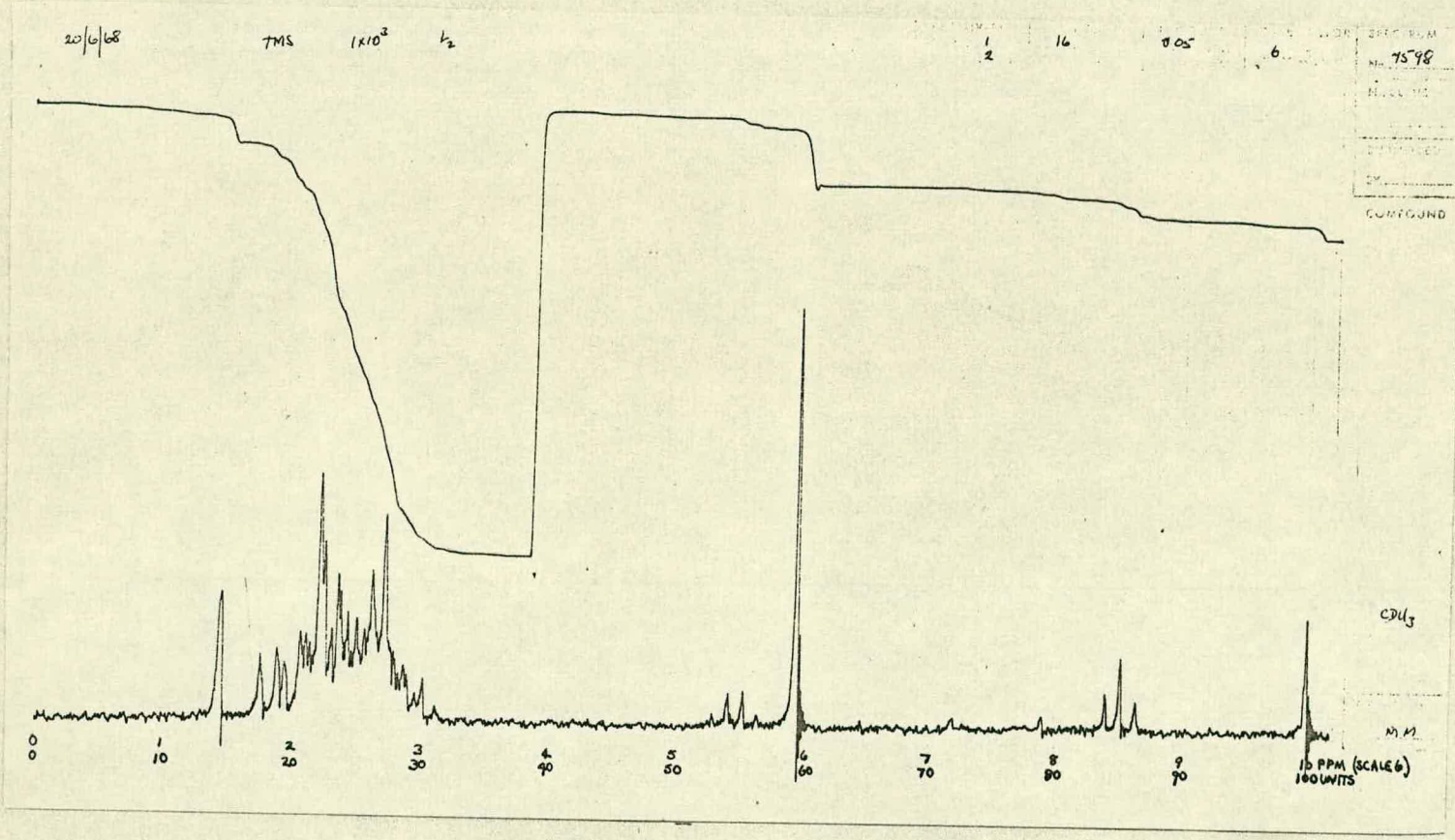
naphthenoid ring. They concluded that "p-absorption in fluoranthene is located in the naphthalene ring system". On this basis it may be expected that the spectra of the azafluoranthenes, with a nitrogen atom in the naphthalene ring system, would differ significantly from the spectrum of fluoranthene.

The spectrum of the methiodide of 2-azafluoranthene shows a considerable bathochromic shift of the long-wavelength absorption with an associated increase in intensity. This shift has been attributed to the formation of a charge-transfer complex between the iodide ion and the pyridinium ring.[101]

The n.m.r. spectrum of 2-azafluoranthene, Fig.4., contains two sharp singlet absorptions at 0·91τ and 1·17τ and degenerate aromatic absorptions from 2·10 -2·82τ, which integrate in the ratio 1:1:7. The two low field signals are characteristic of protons adjacent to the nitrogen atom of an N-heteroaromatic compound. The 1- and 3-protons of isoquinoline[102] similarly resonate at low field values. There is no detectable spin-spin coupling between the 1- and 3-protons of 2-azafluoranthene; the 1-proton of isoquinoline is normally found as a singlet since J_{13} is small. The methiodide of 2-azafluoranthene similarly shows no coupling between the 1- and 3-protons.

A comparison with the n.m.r. spectrum of 1-azafluoranthene is of interest. This heterocycle is a 1,8-disubstituted isoquinoline. The 2-proton is found as a doublet [J = 5·9c/s] at 1·5τ, whilst the 3-proton is immersed in the aromatic absorptions of the spectrum. The coupling constant J_{34} = 6·0 cycles/second is characteristic of simple isoquinolines.[102]

FIG. 5


20/6/68
TMS
1x10²
½
1/2
16
0.05
6
No. 7598
COMPOUND
CDCl₃
0 0
1 10
2 20
3 30
4 40
5 50
6 60
7 70
8 80
9 90
10 PPM (SCALE 6)
100 UNITS

The ultraviolet spectrum of 2-azafluoranthene shows the relation of the base to fluoranthene, whilst the n.m.r. spectrum shows its relation to isoquinoline.

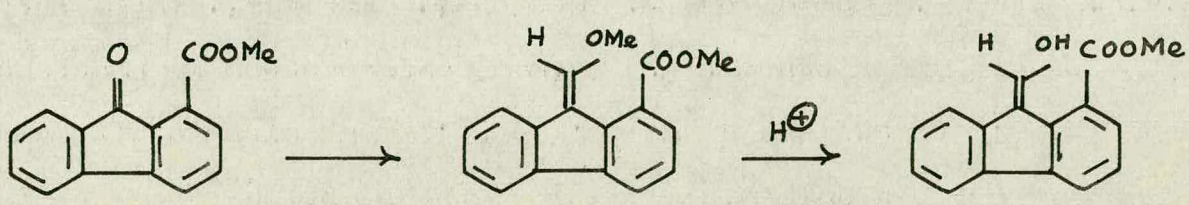
The conversion of the hydroxymethylene ester (CXXVI) into 2-azafluoranth-3[2H]one (CXXVII) with boiling aqueous ammonia occurred in poor yield. An improved procedure involved boiling (CXXVI) for 24 hours in a solution of ammonium carbonate and glacial acetic acid. Cooling deposited white needles of (CXXVII) in 50% yield; pouring the filtered acetic acid solution onto water yielded a yellow crystalline product, m.p. 235-36°, whose structure could not be determined. The infrared spectrum of the compound showed a weak absorption at 3050cm^{-1}. and four intense absorptions at 1725cm^{-1}., 1675cm^{-1}., 1635cm^{-1}., and 1620cm^{-1}. The n.m.r. spectrum in dueterochloroform, Fig. 5, contained a singlet at 1·43τ, aromatic signals from 1·75 - 3·0τ and a singlet at 5·9τ. These signals integrated in the ratio 1:15:2. The spectrum also contained weak signals at 5·44τ [doublet J = 8 c/s] and at 8·52τ [triplet J = 8 c/s]. The doublet at 5·44τ and the strong singlet at 5·9τ integrated in the ratio 3:10. The sample was chromatographed on alumina and then dried for eight hours at 120° at a pressure of 15 mm. before the spectrum was taken. A molecular weight determination gave a value of 338 mass units. The ultraviolet spectrum of the compound consisted of three poorly resolved broad peaks at 220 mμ, 235 mμ and 343 mμ [log ε = 4·59, 4·60, 4·17].

The yellow compound was recovered unchanged after boiling with concentrated hydrochloric acid. Boiling the compound with

alcoholic alkali gave an orange acidic compound, m.p. 195-210°, soluble in sodium bicarbonate, which on boiling in methanol with a few drops of concentrated sulphuric acid yielded 2-azafluoranth-3-[2H]one (CXXVII). Boiling the compound melting at 235-36° with sodium and ethanol also gave (CXXVII).

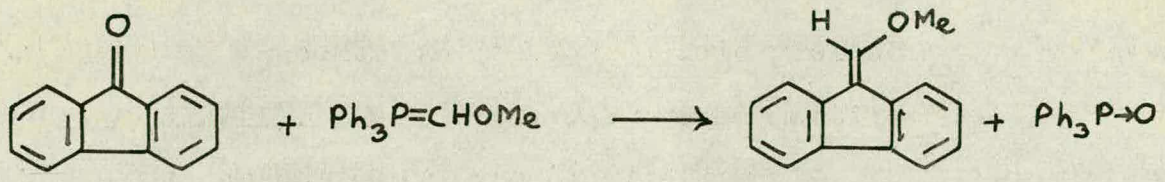
An attempt was made to deoxygenate (CXXVII) directly to 2-azafluoranthene using triethyl phosphite.[103] 2-Azafluoranth-3[2H]one was recovered unchanged after boiling with triethyl phosphite for twenty four hours.

A possible alternative procedure for the preparation of (CXXVI) involves a Wittig reaction[104] on methyl fluorenone-1-carboxylate (CXL).



CXL CXXVI

Wittig[105] prepared 9-methoxymethylenefluorene (CXLI) by the interaction of 9-fluorenone and methoxymethylenetriphenylphosphorane, although he made no attempt to hydrolyse the product to 9-formylfluorene with acid.[106]

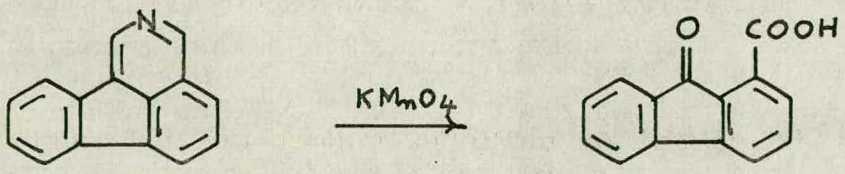


CXLI

This procedure did not appear to offer an increased yield of (CXXVI), or a decrease in the time required to convert fluorenone-1-carboxylic acid (VII) into the hydroxymethylene ester (CXXVI) and, therefore, it was not employed.

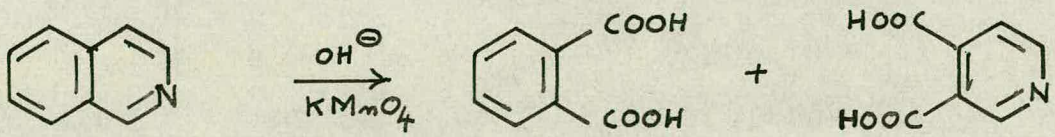
PART II: The oxidation of 2-azafluoranthene

Oxidation of 2-azafluoranthene with aqueous potassium permanganate gave fluorenone-1-carboxylic acid (VII) as the sole product



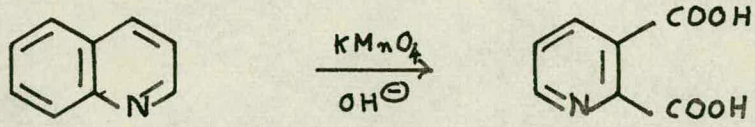
III VII

The fission of the pyridine ring was unexpected. In the oxidation of N-heteroaromatic compounds it is usually the benzenoid ring which is preferentially attacked.[107] Isoquinoline itself gives a mixture of phthalic (CXLII) and cinchomeric (CXLIII) acids upon oxidation with alkaline permanganate;[108]



CXLII CXLIII

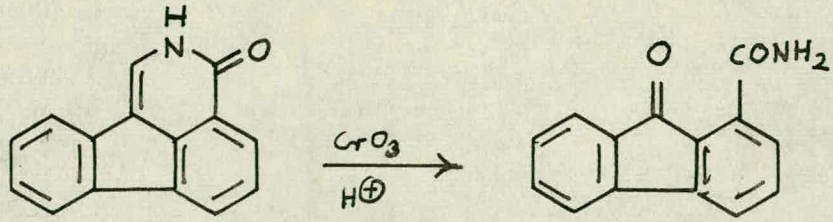
oxidation of quinoline with alkaline permanganate[109] gives quinolinic acid (CXLIV).



CXLIV

Oxidation of 1-azafluoranthene (p. 3) with potassium permanganate gives fluorenone-1-carboxylic acid and 4-azafluorenone-1-carboxylic acid; oxidation of 3-azafluoranthene (p. 5) gives 2-azafluorenone-1-carboxylic acid; and oxidation of 7-azafluoranthene (p. 4) with permanganate gives 4-azafluorenone-8-carboxylic acid, and 1-azafluorenone-8-carboxylic acid.

Oxidation of 2-azafluoranthene with chromium trioxide in acetic acid gave a high melting ($>300^{\circ}$) polymeric yellow compound which could not be purified. The infrared spectrum of the compound showed a strong sharp absorption at $1610 cm^{-1}$., and a complete lack of carbonyl absorptions. Oxidation of 2-azafluoranth-3 (2H) one, (CXXVII) with chromium trioxide gave fluorenone-1-carboxamide (CXLV).

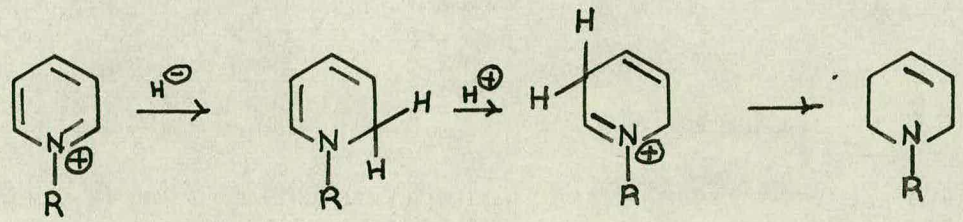


CXXVII CXLV

The amide was not hydrolysed during the reaction. Hydrolysis to fluorenone-1-carboxylic acid (VII) readily occurred by boiling with concentrated hydrochloric acid. No report could be found of the oxidation of isocarbostyril.

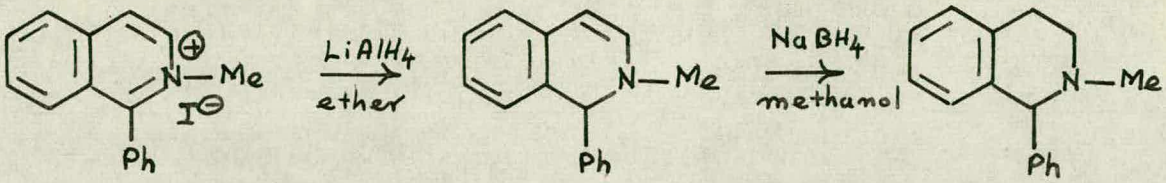
PART III: The reduction of 2-azafluoranthene

The reduction of nitrogen heterocycles with complex metal hydrides has been thoroughly reviewed by Lyle and Anderson.[110] On the basis of the products obtained from the sodium borohydride reduction of pyridinium ions in protonic solvents they proposed that attack by hydride ion occurs at the carbon atom adjacent to the quaternary nitrogen if steric interferences do not occur, and that the dienamine [or enamine] system thus formed undergoes attack by a proton from the solvent at the 3-position of the dienamine system provided that the nitrogen lone-pair of electrons is in an orbital overlapping only with the π-bonds of the dienamine system, and also provided that there is no substituent at this 3-position. The immonium system thus formed is reduced to a tetrahydropyridine.



From these observations Lyle and Anderson proposed that reduction of isoquinolines and quinolines with lithium aluminium hydride in aprotic solvents would yield dihydrocompounds, which could be further reduced to tetrahydro-compounds with sodium borohydride in protonic solvents. The 1,2-dihydro-intermediate (CXLVII) formed by the lithium aluminium hydride reduction of 1-phenyl-2-methylisoquinolinium iodide (CXLVI) was reduced to the

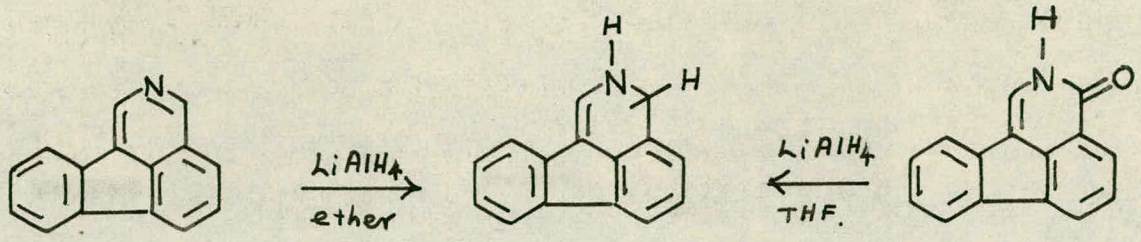
1,2,3,4-tetrahydroisoquinoline (CXLVIII) with sodium borohydride in methanol.[111]



CXLVI CXLVII CXLVIII

Reduction of isoquinoline itself with lithium aluminium hydride in ether[112] gave 1,2-dihydroisoquinoline [60%],1,2,3,4-tetrahydroisoquinoline [16%], 4-hydroxyisoquinoline [<5%] and a high melting compound [<5%]. The formation of the tetrahydroisoquinoline was accounted for by a proposed addition of hydrogen to the enamine grouping of the dihydroisoquinoline, although no proton source was apparently present.

Reduction of 2-azafluoranthene with lithium aluminium hydride in ether gave a white solid product m.p. 110-115°, which rapidly darkened on storage in a desiccator. The product could not be crystallised from common organic solvents. The solid formed a picrate m.p. 271-74°, whose elemental analysis was in reasonable agreement with that calculated for the picrate of 2,3-dihydro-2-azafluoranthene (CXLIX).



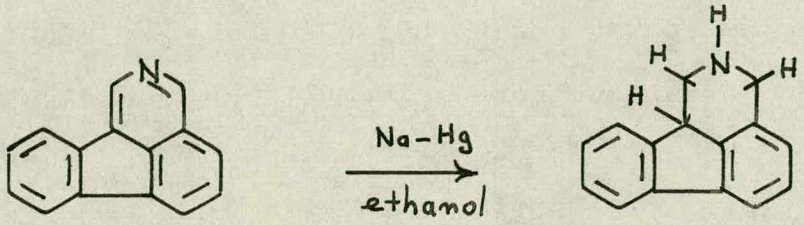
III CXLIX CXXVII

The n.m.r. spectrum of the compound, however, contained only aromatic absorptions in the region 2·0-3·0τ. Reduction of 2-aza-fluoranth-3[2H]one with lithium aluminium hydride in tetrahydro-furan gave a similar unstable compound m.p. 102-120°. The picrate of this product, m.p. 270-75°, showed no melting point depression on admixture with the above picrate, m.p. 271-74°.

The instability of the reduction product is analogous to the instability of 1,2-dihydroisoquinoline.[112] The poor crystallinity of the product may have resulted from the presence of some tetrahydro-2-azafluoranthene, although the formation of this compound is unlikely. Attack by hydrogen at the enamine double bond of (CXLIX) in a similar manner to the proposed attack of the 3,4-double bond of 1,2-dihydro isoquinoline[112] would be unlikely, because of both the steric crowding at this position and the necessary disruption of the strongly conjugated fluorenylidene system. The presence of a tetrahydro-compound should be readily detected from the n.m.r. spectrum of the reduction product, but no absorptions were evident at fields greater than 3·0τ.

Reduction of 2-azafluoranthene with sodium amalgam in ethanol solution gave a white solid product m.p. 125-130°, which also proved

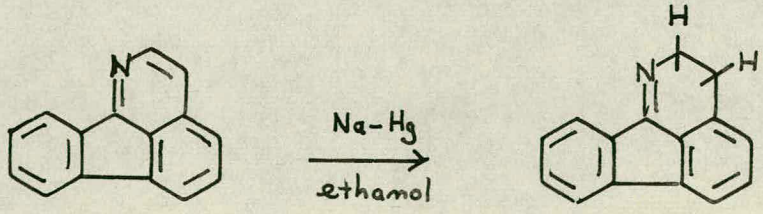
difficult to obtain in a crystalline form. The n.m.r. spectrum contained only aromatic absorptions in the region 1·8-2·8τ. The compound formed a crystalline picrate, m.p. 192-95°, whose elemental analysis was in reasonable agreement with that calculated for 10a,1,2,3-tetrahydro-2-azafluoranthene (CL).



III CL

The assignment of (CL) as the structure of the reduction product can be only tentative, as the expected high field absorptions [4-7τ] for the saturated pyridine ring in the n.m.r. spectrum were not observed.

Reduction of isoquinoline with sodium and alcohol[113] gave 1,2,3,4-tetrahydroisoquinoline. Reduction of 1-azafluoranthene [p.11] with sodium amalgam in ethanol gave 2,3-dihydro-1-azafluoranthene.

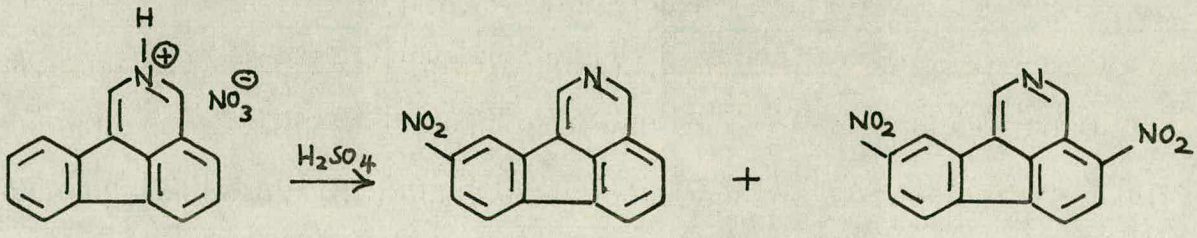


SECTION V.

The nitration of 2-azafluoranthene.

The nitration of 2-azafluoranthene.

2-Azafluoranthene was nitrated by dissolving the nitrate (CLI) in concentrated sulphuric acid, and allowing nitration to proceed at room temperature for ninety minutes and at 60° for twenty minutes. This procedure gave 30% of 9-nitro-2-azafluoranthene (CLII), m.p. 198-200°, and 35% of 4,9-dinitro-2-azafluoranthene (CLIII), m.p. 304-305°.

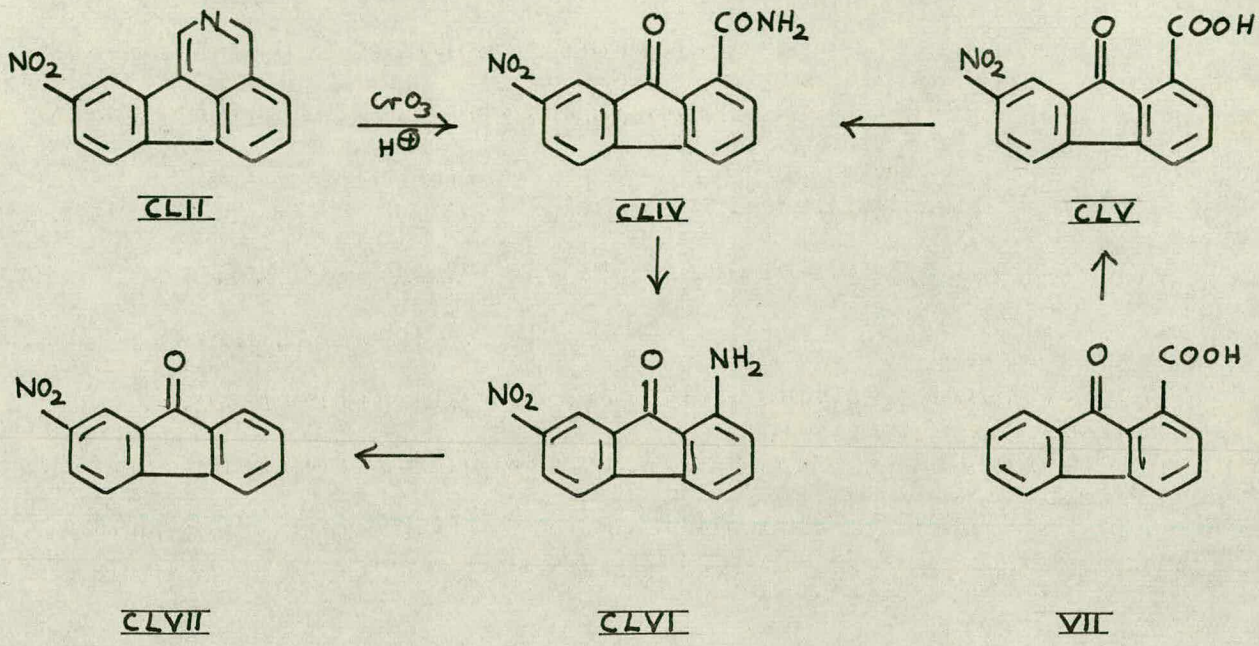


CLI CLII CLIII

The orientation of the nitro groups in (CLII) and (CLIII) was determined as follows.

9-Nitro-2-azafluoranthene.

Oxidation of (CLII) with chromium trioxide in glacial acetic acid gave 7-nitrofluorenone-1-carboxamide (CLIV). The amide was identified by both its synthesis from fluorenone-1-carboxylic acid (VII), and its degradation to 2-nitrofluorenone (CLVII).



The acid (CLV) has been synthesised from (VII) by two different methods. Garascia[114] prepared the acid by the addition of fluorenone-1-carboxylic acid (VII) to a mixture of concentrated sulphuric and nitric acids, the nitration mixture being maintained at 35° for 1 hour. In the present author's hands this procedure gave a nitrofluorenone-1-carboxylic acid m.p. 255-75°, and not 245-46° as reported. Decarboxylation of this acid gave the known 2,7-dinitrofluorenone. Koelsch and Steinhauer[5] prepared (CLV) by the addition of a solution of sodium nitrate in concentrated sulphuric to a solution of (VII) in the same acid at room temperature. This procedure gave an excellent yield of (CLV), m.p. 242-44°. Decarboxylation of the acid with copper and quinoline gave 2-nitrofluorenone (CLVII).[115] The amide (CLIV) of 7-nitrofluorenone-1-carboxylic acid was identical with the product obtained from the

oxidation of 9-nitro-2-azafluoranthene.

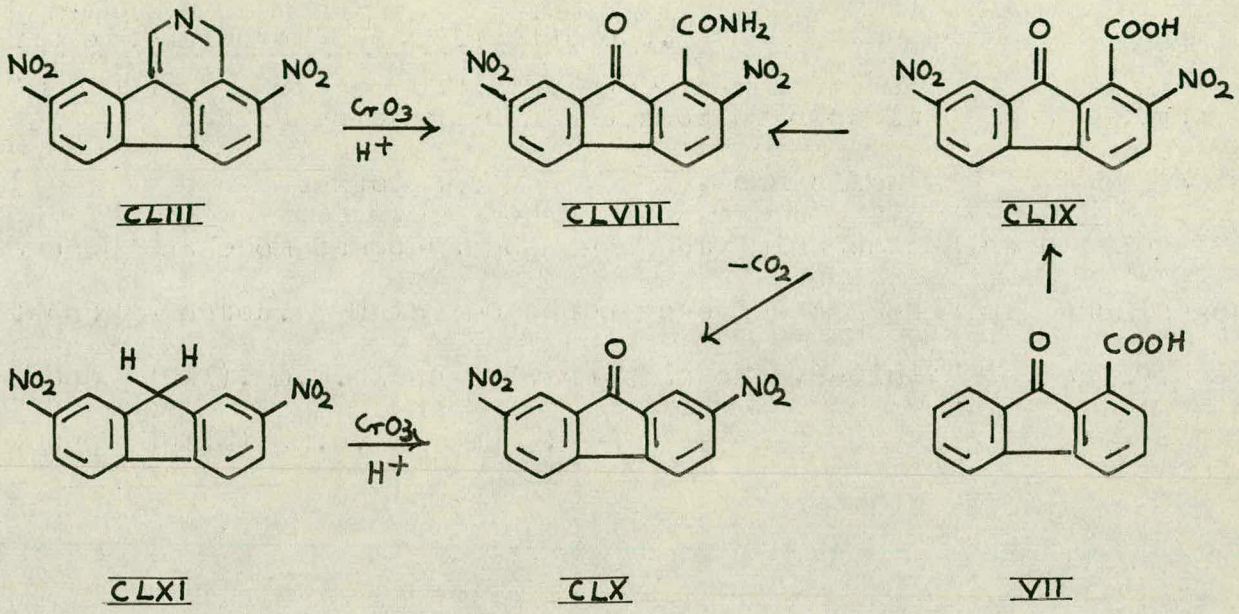
The Hofmann reaction on the amide (CLIV) obtained from the oxidation of (CLII) gave 1-amino-7-nitrofluorenone (CLVI), which was diazotised [sulphuric acid and sodium nitrite] and deaminated [hypophosphorous acid] to 2-nitrofluorenone (CLVII).

The isolation of (CLIV) from the oxidation of 9-nitro-2-azafluoranthene with chromium trioxide was unexpected. The oxidation of 2-azafluoranthene by this procedure gave a polymeric compound. The oxidation possibly occurs through the intermediate formation of a hydroxy-2-azafluoranthene. Oxidation of 2-azafluoranth-3[2H]one [or 3-hydroxy-2-azafluoranthene] with chromium trioxide gave fluorenone-1-carboxamide (CXLV) [p.81]. Apparently the amide function of (CLIV) and (CXLV) is not hydrolysed to the acid under the oxidation conditions employed. Both amides were hydrolysed to the corresponding acids by boiling with concentrated hydrochloric acid.

Attempted oxidation of 9-nitro-2-azafluoranthene with aqueous potassium permanganate gave a 40% recovery of starting material, no 7-nitrofluorenone-1-carboxylic acid was isolated [p.80].

4,9-dinitro-2-azafluoranthene

Oxidation of (CLIII) with chromium trioxide in glacial acetic acid gave 2,7-dinitrofluorenone-1-carboxamide (CLVIII).



The amide was identified by its synthesis from fluorenone-1-carboxylic acid (VII).[9]

Potassium nitrate was added to a solution of (VII) in concentrated sulphuric acid, and nitration was allowed to proceed at room temperature for five minutes, and then at 80° for a further five minutes to give 2,7-dinitrofluorenone-1-carboxylic acid (CLIX). Decarboxylation of the acid gave 2,7-dinitrofluorenone (CLX), which was prepared by the oxidation of 2,7-dinitrofluorene (CLXI).[116] The amide of (CLIX) was identical to the product obtained from the oxidation of 4,9-dinitro-2-azafluoranthene (CLIII).

This amide was extremely resistant to hydrolysis. It was recovered unchanged after boiling with concentrated hydrochloric acid and glacial acetic acid; a 1:1:1 mixture of concentrated sulphuric acid, water and acetic acid; and a solution of nitrous acid in acetic acid.[117] Unlike 7-nitrofluorenone-1-carboxamide,

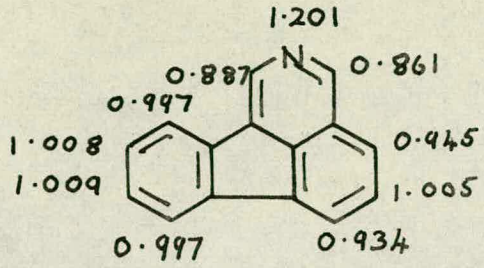
(CLVIII) could not be converted into an aminonitrofluorenone by the Hofmann reaction. The failure of this reaction and the resistance of (CLVIII) to acid hydrolysis is probably a result of steric interference between the nitro group at the 2-position of the amide and the intermediates involved in those reactions.

Treatment of a solution of 2-azafluoranthene in concentrated sulphuric acid with potassium nitrate gave mainly 4,9-dinitro-2-azafluoranthene. The nitration mixture was kept at room temperature for twenty hours. A small quantity, about five per cent, of mononitro-2-azafluoranthene was isolated.

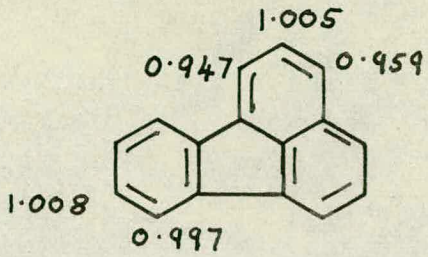
Treatment of 2-azafluoranthene with fuming nitric acid at room temperature for twenty hours gave a product consisting in a mixture of nitrocompounds melting from 250-310°. No pure mono-nitro- or dinitrocompounds could be isolated.

These nitration experiments were carried out in order to examine the behaviour of 2-azafluoranthene towards electrophilic substitution; that is, whether the base is to be regarded as a substituted fluoranthene or whether it demonstrates its relationship to isoquinoline. Before embarking on such a discussion, however, a brief comment will be made on the relevance of the results of these experiments to the calculations of Michl and Zahradnik[8][p.10].

The calculated π-electron densities for 2-azafluoranthene (III) indicate that the highest density is at the 8-position, although the density at the 9-position is only minimally smaller.



III



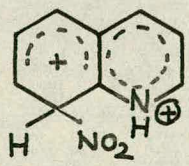
I

This would seem to predict that the 8-position of the base is slightly more reactive to electrophilic attack than the 9-position. The position of highest π-electron density in both the isomeric 1- and 3-azafluoranthenes is the 9-position. Nitration of these heterocycles gave the 9-nitroazafluoranthenes. The isolation of 9-nitro-2-azafluoranthene but no 8-nitro-2-azafluoranthene from the nitration of (III) emphasises the difficulty involved in using π-electron densities as a measure of reactivity towards electrophiles. It should be stressed, however, that some 8-nitro-compound may have been formed during the nitration, and was not isolated by the separation techniques which were used.

Recent investigations[118] have indicated that the most appropriate index of reactivity of a particular position in an aromatic molecule is the "Cation Localisation Energy", which is defined as the energy required to re-organise the π-electrons of the nucleus so as effectively to localise an electron-pair at that position, or alternatively, as the difference in π-electron energy between the ground state and the transition state [the "Wheland" intermediate] involved in substitution at this position.

The application of this index to fluoranthene itself has proved remarkably successful. Nitration of fluoranthene in acetic acid[119] indicated that the experimentally determined order of reactivities for the hydrocarbon, 3>8>7>1>2, was in fair agreement with the order predicted from the calculated localisation energies, 3>7>8>1>2. Electron density calculations, on the other hand, predicted the 8-position as the most reactive[120] with the 3-position considerably less reactive. [see diagram (1) p. 92]

Allowance has been made in the calculation of localisation energies for N-heteroaromatic compounds for the protonation which occurs during electrophilic substitution in strong acid. Localisation energy calculations for the dications, such as (CLXII), formed during the nitration of quinoline are in good agreement with experiment.[121]



CLXII

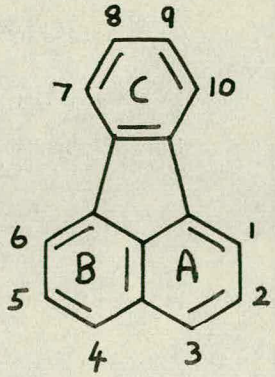
Similar calculations for the azafluoranthenes are required before any definite relation between theoretical calculations and experimental results can be proposed.

Returning to the question of whether 2-azafluoranthene behaves as a fluoranthene or an isoquinoline towards electrophilic substitution, it is first necessary to outline the behaviour of

monosubstituted derivatives of these two compounds.

Campbell and Keir[122] proposed two general rules for the orientation of a group entering a monosubstituted fluoranthene. If the substituent in the 3-position is meta-directing the second group will enter the 9-position; while if it is ortho-para directing the second group will enter the 8-position. These rules were based upon the following experimental evidence: mono-bromination of 3-nitro-, 3-cyano-, 3-carboxy-, and 3-carbomethoxyfluoranthene[122] in each case gave the corresponding 9-bromofluoranthene; further acetylation of 3-acetylfluoranthene[123] gave 3,9-diacetylfluoranthene; disulphonation of fluoranthene[122] gave the 3,9-disulphonic acid; and bromination of 3-bromofluoranthene[124] gave 3,8-dibromofluoranthene. Campbell and Keir suggested the following explanation for these results.

Fluoranthene can be considered as a diphenyl derivative containing the diphenyl nuclei AC and BC.



Since orientation in the diphenyl series is dominated by the phenyl groups, so that substitution in most cases occurs in the second ring in the 2′ and 4′-position[125] irrespective of the nature and position of the group already present in the first ring, it was postulated that whilst each of the rings A and B, unsubstituted, will direct an entering group predominantly to the "para-position" in ring C, i.e. to positions 8 and 9 respectively, a meta-directing group will decrease the directive power of ring A so that ring B dominates further substitution which therefore occurs at C_9 [and possibly C_7], but an ortho-para directing group in ring A will increase the directive power of this ring, with consequent substitution at C_8 [and possibly C_{10}].

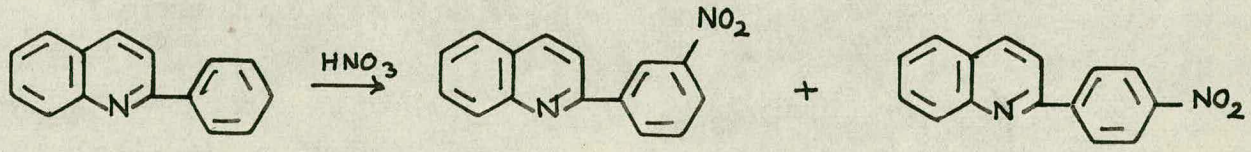
Kloetzel, King and Menkes[126] suggested that this explanation was oversimplified to the extent that it did not take into account the effects of intensely activating substituents. Nitration of 3-acetylaminofluoranthene gave 3-acetylamino-2—nitrofluoranthene in excellent yield. Bromination of 3-acetylaminofluoranthene in pyridine[127] later was shown to give 3-acetylamino-2-bromofluoranthene.

Andrew[128] investigated the effect of weaker electron-releasing groups than acetamido- on further substitution. He found that nitration of 3-tosyloxy-, 3-acetoxy-, and 3-methylfluoranthene gave mainly the 8-nitrofluoranthene and a small quantity of the 2-nitrofluoranthene. These results are in accordance with the rule of Campbell and Keir.

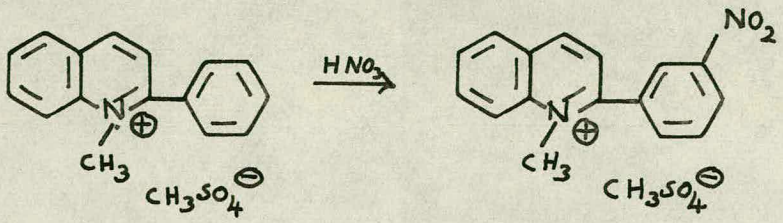
Charlesworth[129] brominated 2-nitrofluoranthene to give 9-bromo-2-nitrofluoranthene, and brominated 2-acetylaminofluoranthene to give 2-acetylamino-3-bromofluoranthene. These results demonstrate that Campbell and Keir's rule for deactivating substituents and the rule

of Kloetzel et al. for strongly activating substituents are also applicable to substituents in the 2-position. This feature of fluoranthene substitution is obviously relevant to the substitution behaviour of 2-azafluoranthene.

Schofield and Swain[130] summarised the results of the nitration of substituted quinolines and isoquinolines. Of more importance to the present discussion is the information which has been derived from the nitration of the phenyl-substituted quinolines and isoquinolines. Nitration of 2-phenylquinoline[131] with fuming nitric acid at 0° furnished a mixture of 2-[m-nitrophenyl]-quinoline (CLXIII) and 2-[p-nitrophenyl]-quinoline (CLXIV) in 40 and 60% yield respectively, whilst nitration, under identical conditions, of 2-phenylquinolinium methosulphate gave solely 2-[m-nitrophenyl]-quinolinium methosulphate (CLXV).

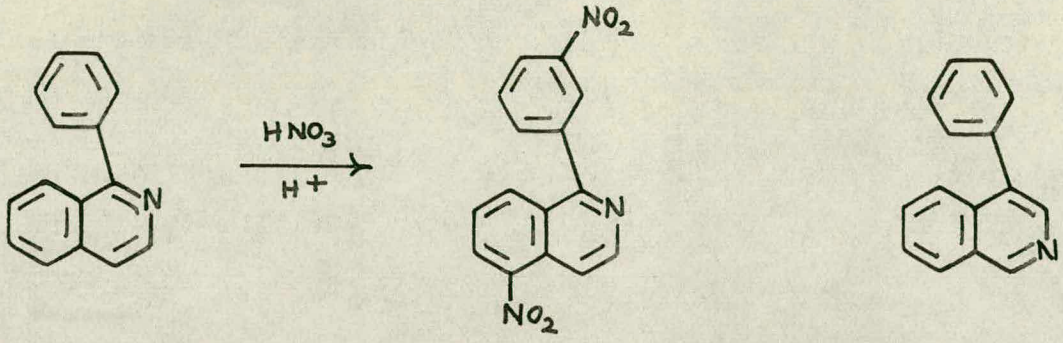


CLXIII CLXIV



CLXV

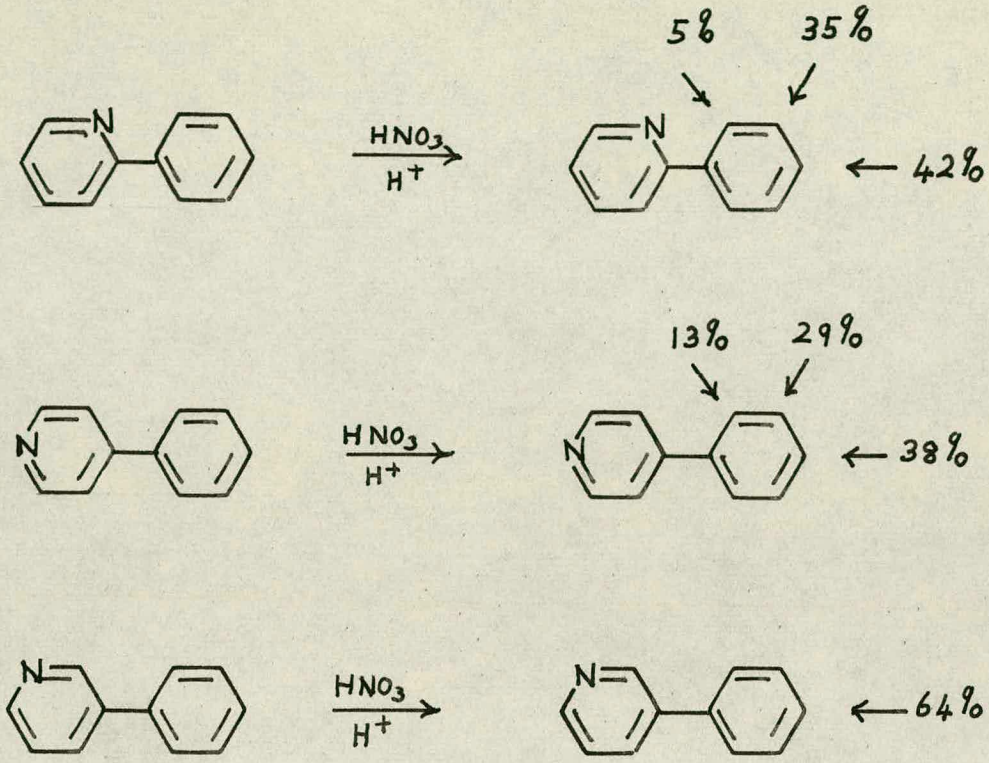
Nitration of 1-phenylisoquinoline[132] gave 1-[m-nitrophenyl]-5-nitroisoquinoline (CLXVI).



CLXVI CLXVII

No report could be found of the nitration of 4-phenylisoquinoline (CLXVII) which is structurally similar to 2-azafluoranthene.

In the same way that fluoranthene is regarded as a diphenyl derivative, 2-azafluoranthene can be considered as a diphenyl or a 3-azadiphenyl derivative. As previously mentioned, the outstanding feature in the behaviour of substituted diphenyls towards further substitution, is the fact that orientation of the entering group is dominated by the ortho-para directing influence of the phenyl group, and does not depend on the nature and position of the first substituent. For instance, 2- and 4-nitrodiphenyls are further nitrated in the 2′ - and 4′ -positions of the second ring.[133] However, in passing to the azadiphenyls, a different state of affairs is observed and although substitution still occurs predominantly in the ortho- or para position considerable quantities of m-nitrocompounds are isolated in the nitration[134] of 2- and 4-azadiphenyls.

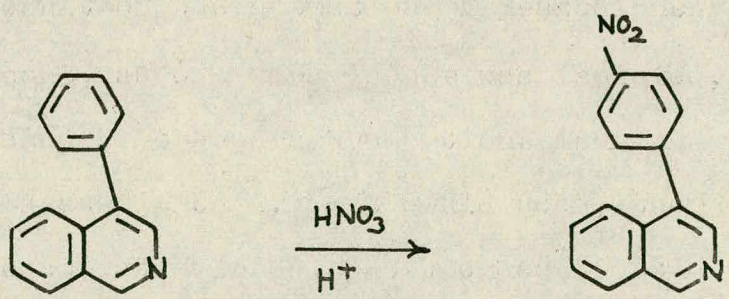


The result of the nitration of 3-azadiphenyl appears to be very significant, as 64% para-isomer was isolated, which is higher than the combined ortho-para proportions isolated from the nitration of the 2- or 4-azadiphenyl. It would seem, therefore, that not merely the deactivating ring, but the deactivating protonated nitrogen atom in the 2- and 4-azadiphenyls is the meta-orienting group, whilst in the 3-azadiphenyl the location of the heteroatom meta to the phenylpyridine linkage occasions its diminished orienting capacity. The occurrence of ortho-para substitution in the 2- and 4-azadiphenyls, is presumably a result of nitration of the unprotonized forms of these compounds.

These observations explain the nitration of the phenyl-quinolines and phenylisoquinolines. In the nitration of 2-phenyl-

quinoline, 60% "para-compound" is isolated from the nitration of the unprotonised quinoline, and 40% meta-nitro compound is isolated from the protonised form. In the nitration of 2-phenyl-quinolinium methosulphate the meta-orienting influence of the quinolinium ion is thorough, and 90% 2-[m-nitrophenyl]-quinolinium methosulphate is isolated. Nitration of 1-phenylisoquinoline gives solely 1-[m-nitrophenyl]-5-nitroisoquinoline, indicating that the nitration is of a form more comparable to 2-phenyl quinolinium methosulphate than 2-phenylquinoline; this latter result is in accordance with the increased basicity of isoquinoline over quinoline.

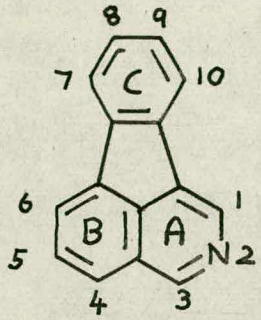
It would therefore be expected that nitration of 4-phenyl-isoquinoline would give solely 4-[p-nitrophenyl]-isoquinoline (CLXVIII) and very little 4-[m-nitrophenyl]isoquinoline, nitrogen meta to the phenylpyridine linkage having a diminished orienting capacity.



CLXVII CLXVIII

In other words, if 2-azafluoranthene is to behave as a derivative of isoquinoline, nitration should most likely give 8-nitro-2-azafluoranthene. If, on the other hand, the heterocycle behaves as a substituted fluoranthene, the nitrogen atom in the 2-position

would deactivate ring A and nitration should give 9-nitro-2-azafluoranthene, as predicted by the Campbell-Keir rule.[122]



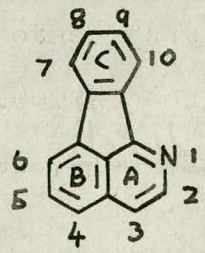
The isolation of 9-nitro-2-azafluoranthene would appear to indicate that 2-azafluoranthene does indeed behave as a substituted fluoranthene in accordance with the Campbell-Keir rule, but other factors must be considered. Firstly, the mononitroazafluoranthene is readily converted into 4,9-dinitro-2-azafluoranthene, indicating that the 9-position in the unsubstituted base is only little more reactive than the 4-position in the mononitro derivative. The 5- and 8-positions of isoquinoline and quinoline are readily nitrated, and the behaviour of 2-azafluoranthene tends to emphasise its relation to the former heterocycle. It will be recalled [p. 97] that nitration of 1-phenylisoquinoline gave 1-[m-nitrophenyl]-5-nitroisoquinoline; the structurally related 1-azafluoranthene[6] readily gave a dinitroazafluoranthene under scarcely less forcing conditions than those used to effect mononitration.

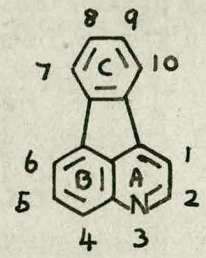
Secondly, as the basic assumption of the Campbell-Keir rule is that the orientation of the entering group of a substituted diphenyl is independent of the position of the first substituent, the

fact that in the case of the nitration of the azadiphenyls the orientation depends on the position of the heteroatom, necessitates the cautious use of this rule to the azafluoranthene system.

In conclusion, the nitration of 2-azafluoranthene indicates the relationship of the base to both the heterocycle isoquinoline and the condensed aromatic hydrocarbon fluoranthene.

Both 1-azafluoranthene[6] and 3-azafluoranthene[5] give 9-nitro-azafluoranthenes. These results can be regarded as an example of the Campbell-Keir rule, with the reservations mentioned above, or they can be attributed to the protonated heteroatom in the ortho- and para-position to the phenylpyridine linkage directing the substituent group to the 9-[meta]position of ring C.

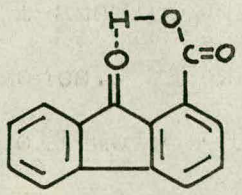




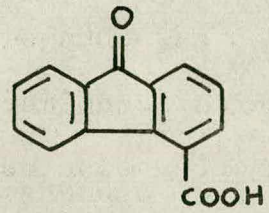
The spectra of the nitrofluorenone-1-carboxylic acids.

The spectra of 7-nitrofluorenone-1-carboxylic acid (CLV) and 2,7-dinitrofluorenone-1-carboxylic acid (CLIX) are of interest in relation to the publication by Demmering and Dörr[135] on the spectra of the fluorenone-carboxylic acids. The infrared spectrum of fluorenone-1-carboxylic acid contains two carbonyl absorptions at 1735cm^{-1}. and 1665cm^{-1}. which were originally assigned[136] to the carbonyl stretch of the fluorenone group and the carbonyl stretch of the carboxyl group respectively. Dörr assigned the 1735cm^{-1}. peak

to the carboxyl group and the 1665cm^{-1}. peak to the fluorenone group. He attributed this unusual assignment to the formation of an intramolecular hydrogen-bonded 7-membered ring as in (CLXIX), which decreased the double bond character of the 9-carbonyl group and increased the double bond character of the 1-carbonyl group.



CLXIX



CLXX

The infrared spectra of fluorenone-4-carboxylic acid (CLXX), on the other hand, contained two peaks at 1715cm^{-1}. and 1675cm^{-1}. which were assigned to the 9-carbonyl and the 4-carbonyl groups respectively, no chelation being possible in this acid.

The infrared spectrum of 7-nitrofluorenone-1-carboxylic acid contains two peaks at 1730cm^{-1}. and 1665cm^{-1}., which are very similar to the absorptions of fluorenone-1-carboxylic acid. The spectra of both acids contain sharp OH-absorptions in the 2750-2630cm^{-1}. region characteristic of the intramolecular 7-membered ring.(CLXX) contains only broad absorptions in this region. It appears, therefore, that the 7-nitro group of (CLIV) does not interfere with the chelation across the 1- and 9-positions.

The spectrum of 2,7-dinitrofluorenone-1-carboxylic acid contains only a single carbonyl absorption at 1720cm^{-1}., and broad hydroxyl absorptions in the 2750-2600cm^{-1}. region, indicating that

FIG. 7

$n-\pi^*$ ABSORPTIONS OF NITROFLUORENONE-1-CARBOXYLIC ACIDS.

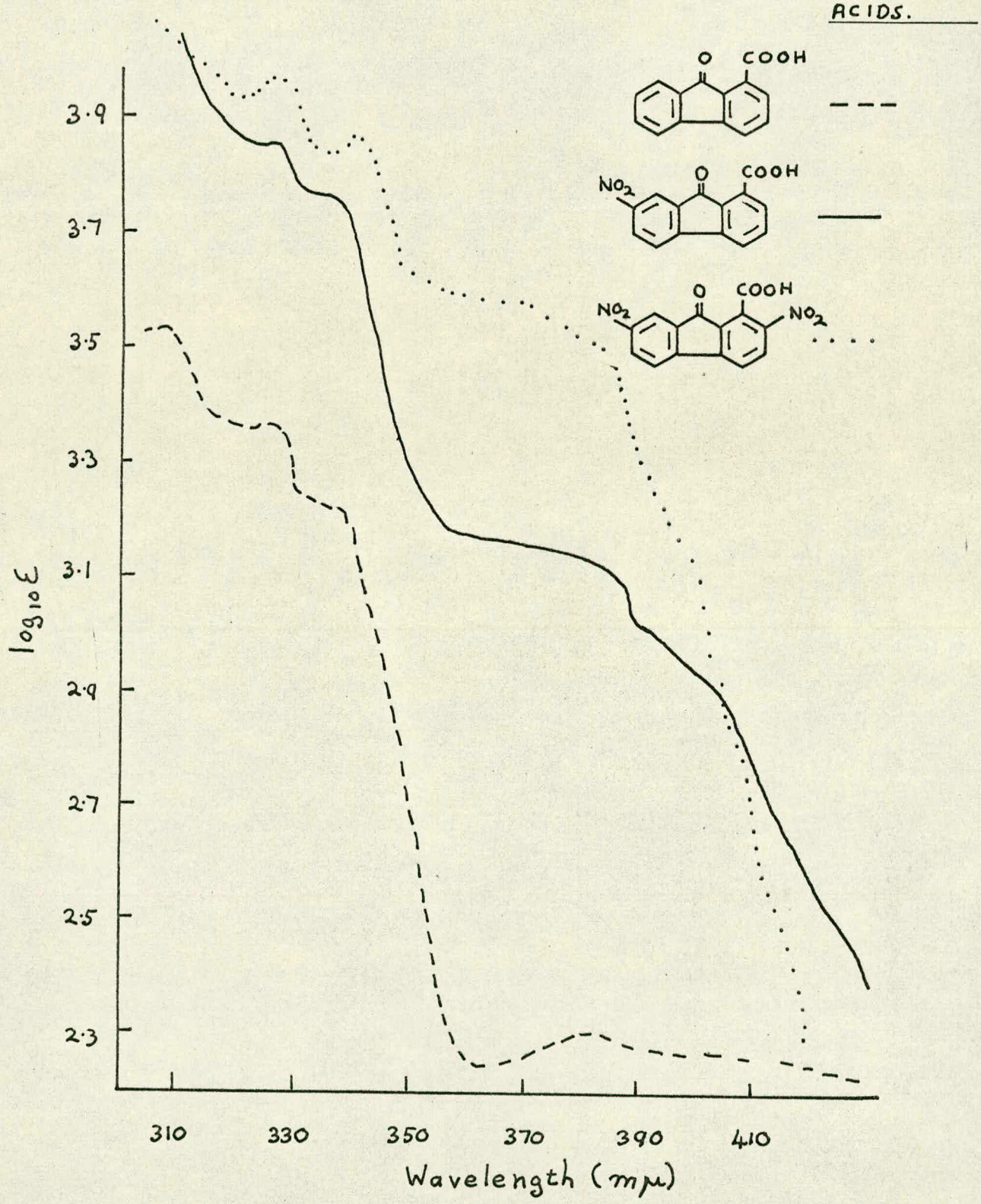
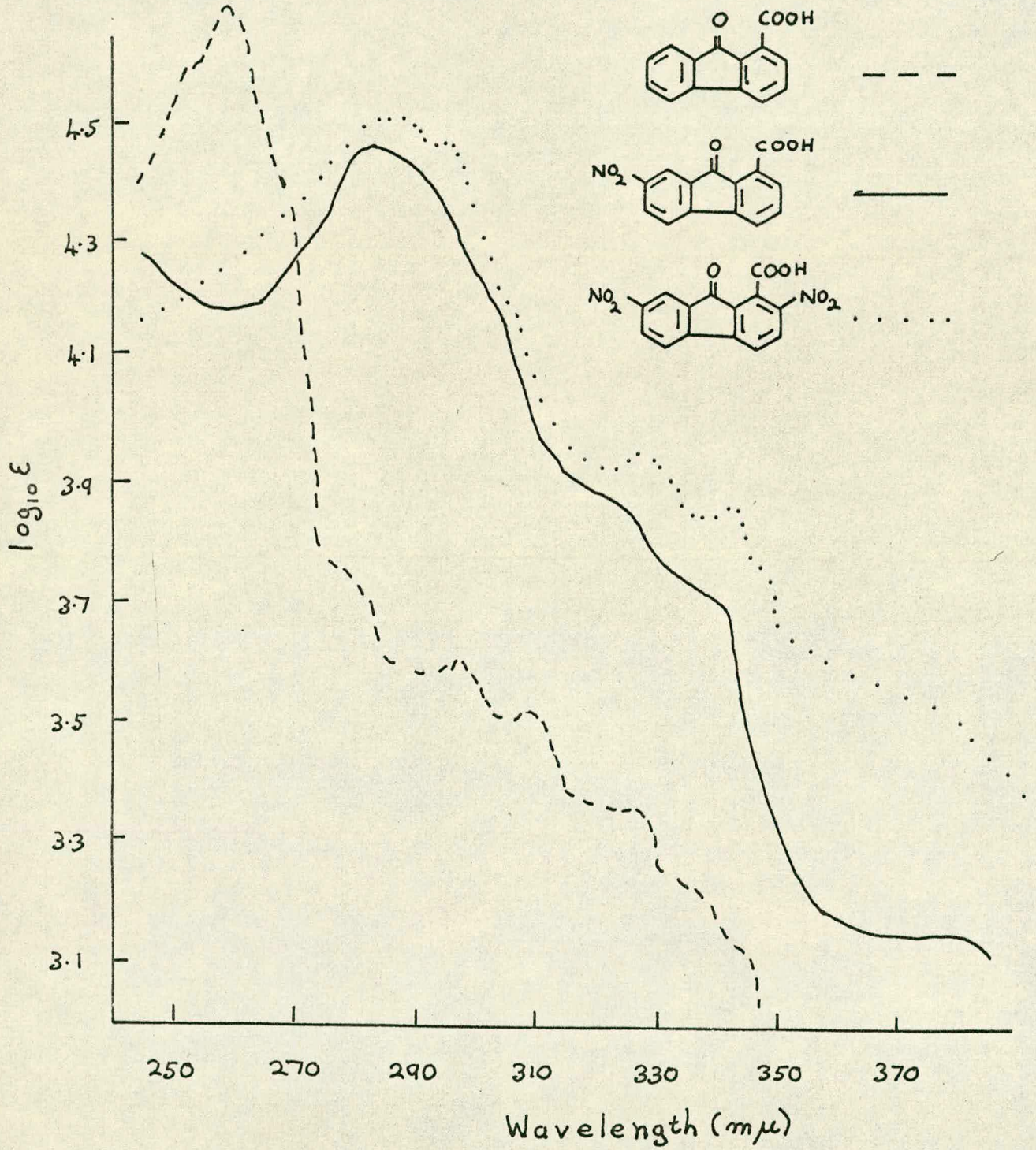


FIG. 6

ELECTRONIC SPECTRA OF NITROFLUORENONE-1-CARBOXYLIC ACIDS



the 2-nitro group is probably interfering sterically with the 7-membered chelate ring.

The spectra of the acid chlorides and amides of the acids (CLIV) and (CLIX) show distinctly separate and characteristic acid chloride carbonyl [1790-1780cm^{-1}.] and amide carbonyl [1670-1645cm^{-1}.] absorptions; the spectra of the ethyl esters show a single absorption at 1725cm^{-1}. These derivatives, as expected, show no sign of chelation.

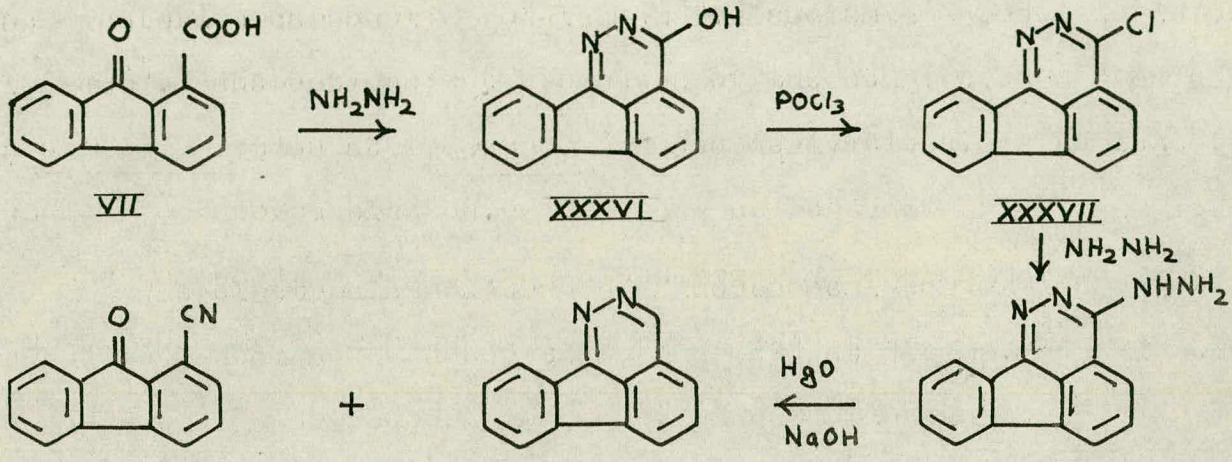
The electronic spectrum of fluorenone-1-carboxylic acid contains a weak n-π^* absorption [logε <3] at 380 mμ.[135] In the spectra of 7-nitrofluorenone-and 2,7-dinitrofluorenone-1-carboxylic acids this absorption becomes completely submerged by the π-π^* absorptions [logε >3], which undergo a bathochromic and hyperchromic shift, Figs. 6 and 7. These shifts are greater for the dinitro acid.

SECTION VI.

The nitration of 1,2-diazafluoranthene.

The nitration of 1,2-diazafluoranthene.

1,2-Diazafluoranthene, pyridazino[4,5,6-m,1]fluorene, was prepared by the method of Dokunikhin and Mikhalenko[10,11][p.13].



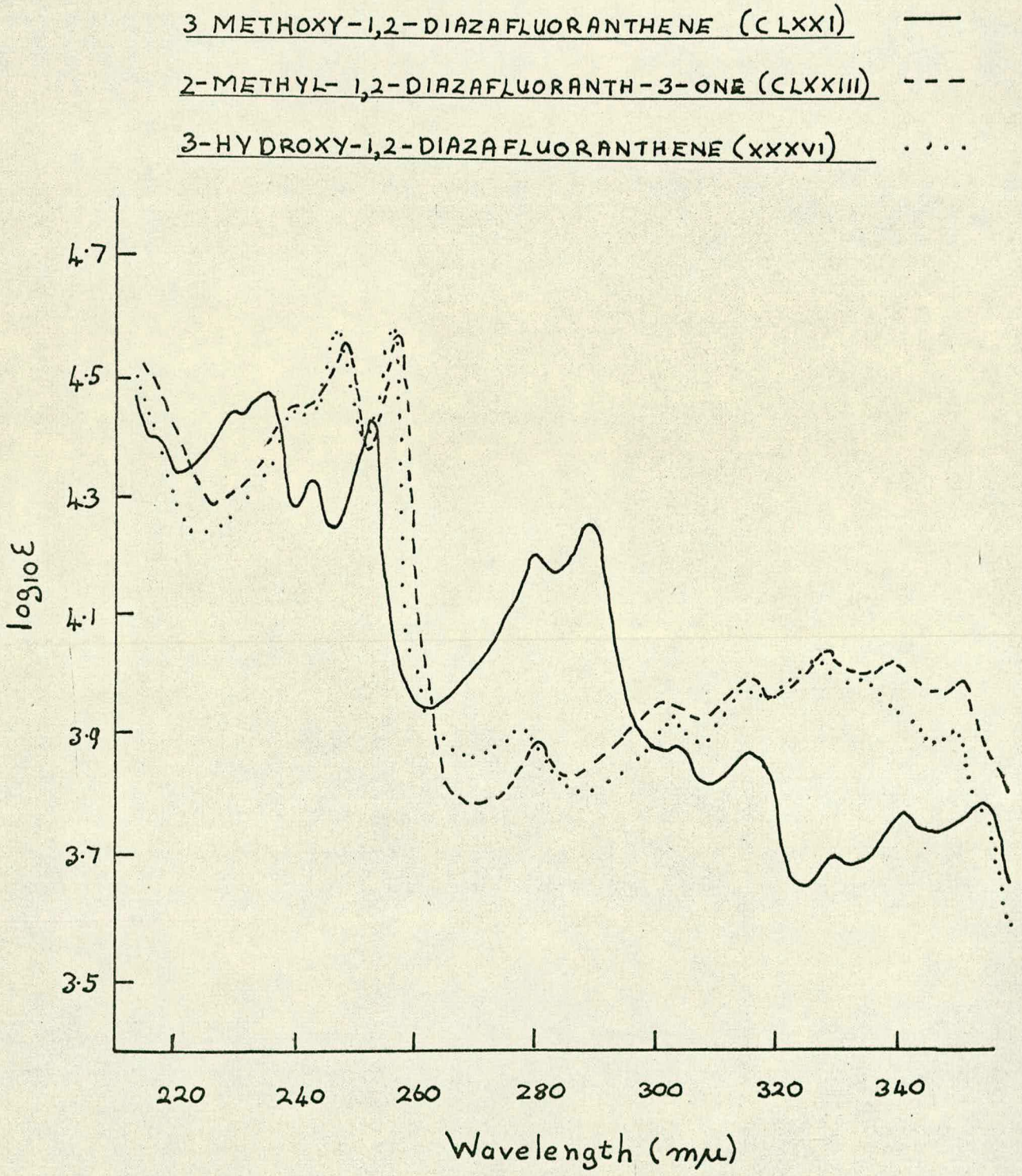
VII XXXVI XXXVII

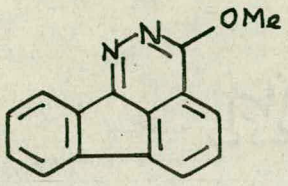
XXXIX XXXIV XXXVIII

Conversion of (XXXVI) into (XXXVII) did not proceed as smoothly as was reported.[11] Boiling the hydroxy-compound with phosphorus oxychloride gave a brown solid product which contained a considerable quantity of (XXXVI). Chromatography of the product on alumina gave 3-chloro-1,2-diazafluoranthene in 50% yield. Decomposition of excess phosphorus oxychloride with sodium carbonate solution had to be conducted very carefully, because in solutions with pH>9, the chlorocompound was hydrolysed to (XXXVI).

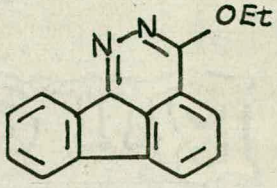
Refluxing (XXXVII) with sodium in methyl or ethyl alcohol gave the corresponding 3-methoxy- and 3-ethoxy-1,2-diazafluoranthenes, (CLXXI) and (CLXXII) respectively. Boiling a mixture of (XXXVI), 4N sodium hydroxide and dimethyl sulphate in methanol gave 2-methyl-1, 2-diazafluoranth-3-one (CLXXIII). The ultraviolet spectrum of

FIG. 8

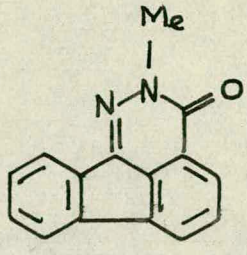

3 METHOXY-1,2-DIAZAFLUORANTHENE (CLXXI)
2-METHYL-1,2-DIAZAFLUORANTH-3-ONE (CLXXIII)
3-HYDROXY-1,2-DIAZAFLUORANTHENE (XXXVI)
4·7
4·5
4·3
4·1
3·9
3·7
3·5
log10ε
220
240
260
280
300
320
340
Wavelength (mμ)



CLXXI

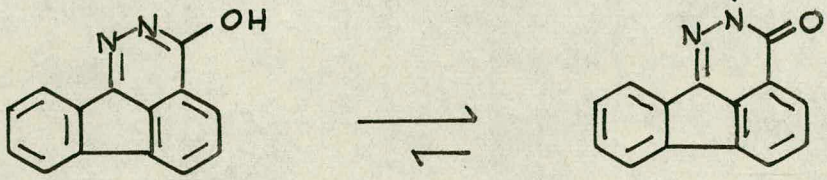


CLXXII



CLXXIII

(XXXVI) resembled that of its N-methyl derivative (CLXXIII) and was different from that of its O-methyl derivative (CLXXI), [Fig.8]. 3-Hydroxy-1,2-diazafluoranthene, like 3-hydroxy-2-azafluoranthene [2-azafluoranth-3[2H]one], obviously exists predominantly in the amide form (XXXVIa) rather than in the form (XXXVI).



XXXVI XXXVIa

The infrared spectrum of (XXXVI) contains two absorptions at 3200 and 3090cm^{-1}. in the NH region and absorptions at 1670 and 1640cm^{-1}. in the carbonyl region.

Attempted hydrogenolysis of 3-chloro-1,2-diazafluoranthene (XXXVII) in a benzene-methanol mixture with palladium on charcoal as a catalyst[138] failed to give 1,2-diazafluoranthene. p-Toluenesulphonylhydrazide and (XXXVII) could not be made to condense in

FIG. 9

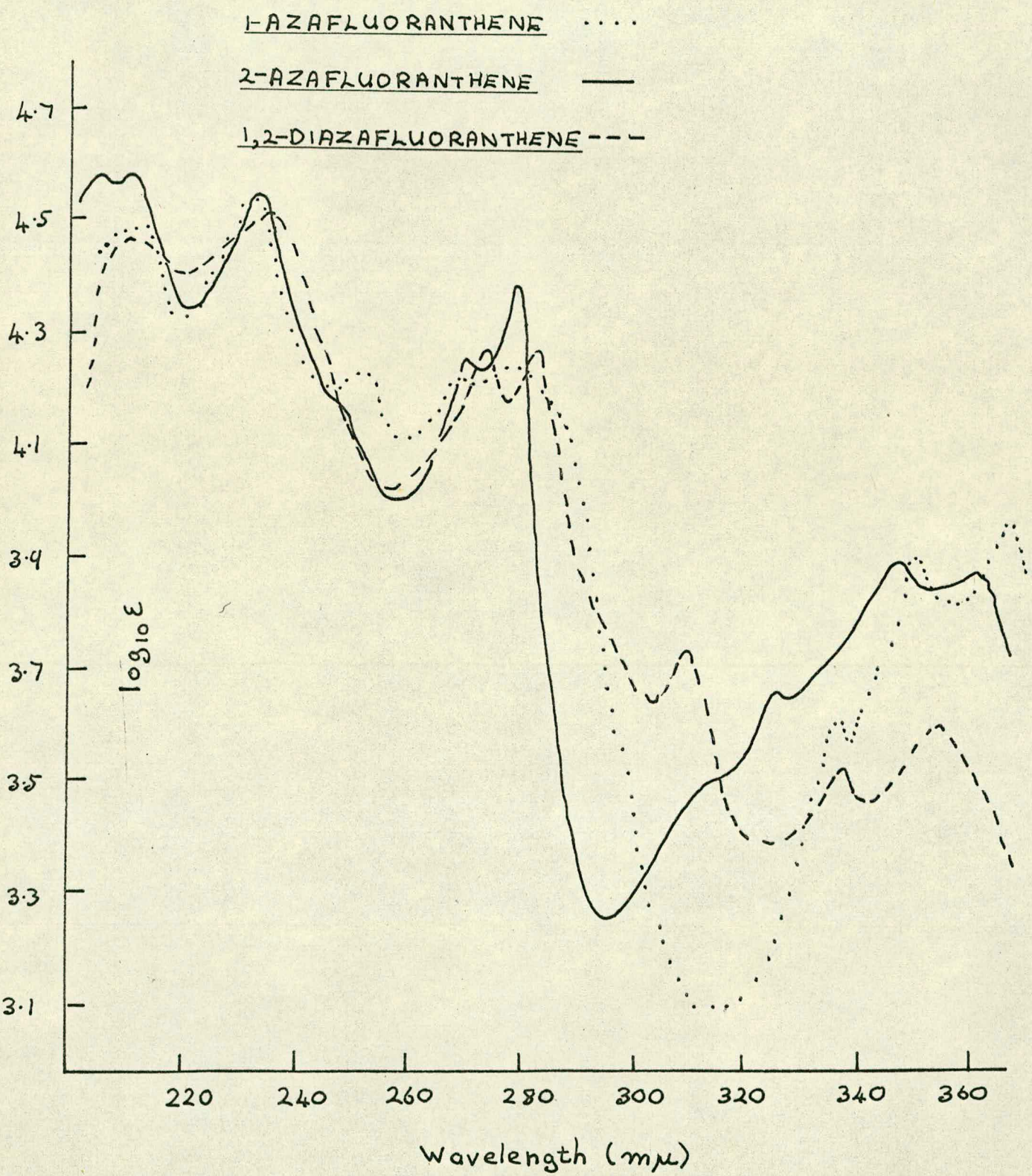
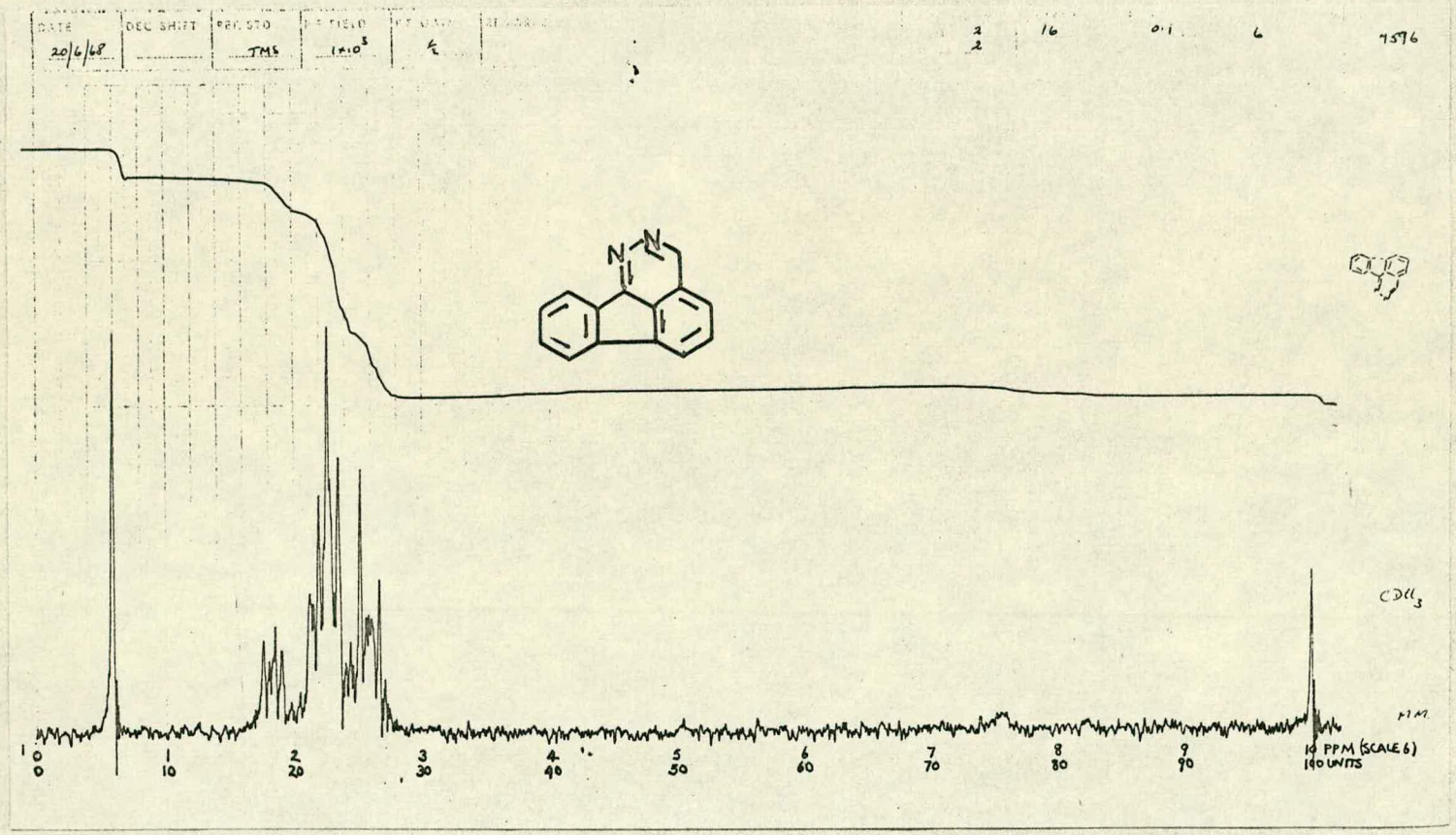

1-AZAFLUORANTHENE
2-AZAFLUORANTHENE
1,2-DIAZAFLUORANTHENE
4·7
4·5
4·3
4·1
3·9
3·7
3·5
3·3
3·1
log10 ε
220
240
260
280
300
320
340
360
Wavelength (mμ)

FIG. 10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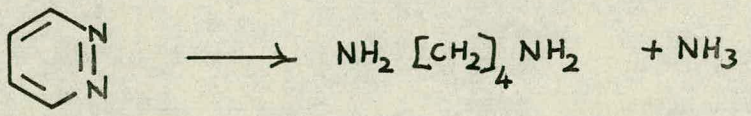
boiling chloroform. This is surprising since 1-chlorophthalazine is readily converted[139] into phthalazine by this procedure.

The hydrazino-compound (XXXVIII) was stirred with sodium hydroxide and mercuric oxide in ethanol to give 10% 1-cyanofluorenone (XXXIX) and 50% 1,2-diazafluoranthene (XXXIV). Dokunikhin and Mikhalenko did not report the formation of the cyano-compound during the above oxidation, although it was obtained in 85% yield by the oxidation of (XXXVIII) with aqueous copper sulphate. 1,2-Diazafluoranthene was recovered unchanged after boiling with alcoholic alkali for 16 hours, and so it appears that the cyanide (XXXIX) is not formed by fission of (XXXIV) with alkali during the oxidation of (XXXVIII). Marquis[140] obtained 1,4-diaminobutane and ammonia on boiling pyridazine (CLXXIV) with sodium and ethanol.



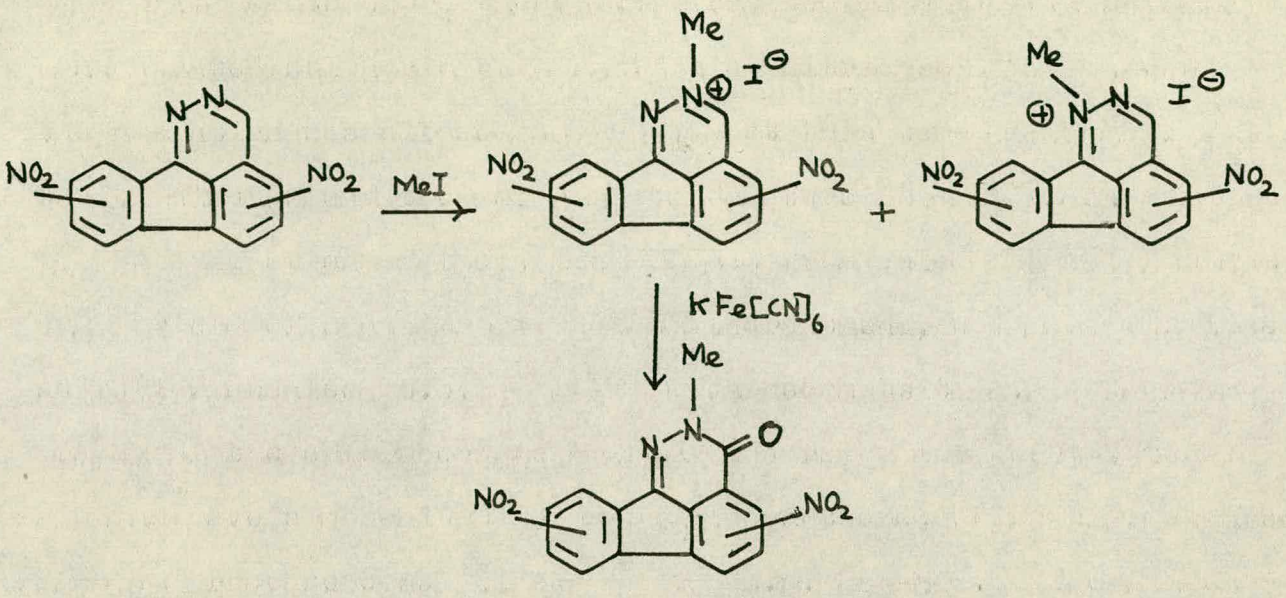
CLXXIV

The ultraviolet spectrum of 1,2-diazafluoranthene is similar to that of the 1- and 2-azafluoranthenes [Fig.9]. The nuclear magnetic resonance spectrum,[Fig.10] contained a sharp singlet at 0·49 τ and a complex aromatic multiplet from 1·68 - 2·6 τ, the signals integrating in the ratio 1:7.

1, 2-Diazafluoranthene was dissolved in a mixture of concentrated sulphuric acid and fuming nitric acid at 0°, and the nitration was allowed to proceed at this temperature for twenty minutes and then at room temperature for one hour. Recrystallisation of the crude product from chlorobenzene gave a 20% yield of a dinitro-1, 2-diazafluoranthene, which crystallised as yellow needles, m.p. 280-305° with decomposition. Chromatography of the chlorobenzene mother liquors on 10% deactivated alumina gave a suspected mononitro-1, 2-diazafluoranthene, which crystallised from chlorobenzene as yellow needles m.p. 248-50°. The fingerprint regions of the infrared spectra of the two nitro-compounds were totally different.

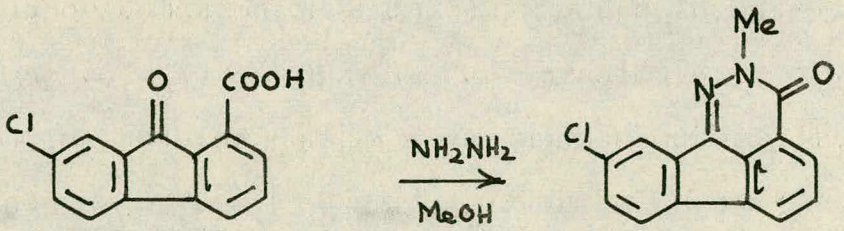
Oxidation of the dinitro-compound, m.p. 280-305°, with chromium trioxide in glacial acetic acid gave a mixture of nitrocarboxylic acids, m.p. 285-90°, which could not be separated owing to the small quantity of material obtained.

The orientation of the nitro groups in nitrophthalazines was determined[141] by potassium ferricyanide oxidation of the corresponding methiodides to give known N-methylphthalazinones. This procedure offers a means of determining the position of the nitro groups in the nitro-1, 2-diazafluoranthenes.



CLXXV

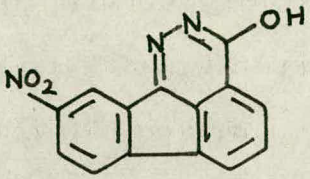
Dokunikhin[142] prepared several 2-methyl-1,2-diazafluoranthones such as (CLXXVII) with a substituent in one of the benzenoid rings by adding hydrazine hydrate in methanol to a solution of the corresponding fluorenone-1-carboxylic acid (CLXXVI) in acetic acid.



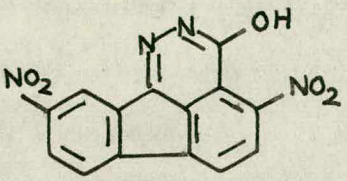
CLXXVI CLXXVII

Similar compounds with nitro groups in the benzenoid rings, required to establish the position of the nitro group (or groups) in the oxidation product (CLXXV), could be prepared in this manner. Alternatively they could be prepared by the methylation of compounds

such as (CLXXVIII) and (CLXXIX) with dimethyl sulphate in aqueous sodium hydroxide and 2-methoxyethanol, or[142] with the same reagent in trichlorobenzene and potassium carbonate. 3-Hydroxy-9-nitro-1,



CLXXVIII



CLXXIX

2-diazafluoranthene[143] (CLXXVIII) and 3-hydroxy-4,9-dinitro-1,2-diazafluoranthene (CLXXIX) were prepared by the addition of hydrazine hydrate to 7-nitrofluorenone-1-carboxylic acid (CLV) and 2,7-dinitrofluorenone-1-carboxylic acid (CLIX) respectively.

Neither (CLXXVIII) nor (CLXXIX) could be converted into the corresponding nitro-3-chloro-1,2-diazafluoranthenes, both compounds failing to react with a boiling phosphorus oxychloride-phosphorus pentachloride mixture, and so the attempted syntheses of 9-nitro- and 4,9-dinitro-[and other nitro-] 1,2-diazafluoranthenes were abandoned.

Insufficient time was left to carry out the necessary experimental work to determine the position of the nitro groups in the nitro-1,2-diazafluoranthenes obtained. On the basis of the theories expounded on the nitration of 2-azafluoranthene, and bearing in mind that 1,2-diazafluoranthene is a phthalazine derivative [nitrated at the 5-position[141]], it is likely that the two nitro-compounds are the 9-nitro- and 4,9-dinitro-1,2-diaza-fluoranthenes.

EXPERIMENTAL RESULTS.

Introduction to Experimental Section.

1. Melting points were determined on a Kofler micromelting-point apparatus with a calibrated thermometer, and fitted with a polariser.

2. Infrared (IR) spectra were recorded on a Unicam S.P.200 Spectrophotometer. The intensity of the absorption maxima are indicated by strong (s), medium (m), and weak (w). The group corresponding to the particular absorption maximum is written after the absorption wave number. Spectra were measured for nujol suspensions unless otherwise stated.

3. Ultraviolet (UV) spectra were recorded on a Unicam S.P.800 UV Spectrophotometer. In the UV data given, the wavelengths of absorption maxima are expressed in mμ [$\log_{10} \varepsilon_{max}$ in parenthesis]. Spectroscopic ethanol was used as solvent unless otherwise stated.

4. Nuclear magnetic resonance (NMR) spectra were recorded on a Perkin Elmer R10 (60 m/c) instrument. In the NMR data given, the numbers of protons assigned to particular signals, were the integral ratios for that spectrum. Spectra were measured in dueterochloroform with tetramethylsilane as internal standard unless otherwise stated.

5. Alumina was of Type-H as supplied by Peter Spence and Sons, Widnes. 10% Deactivated alumina was prepared by shaking 100 g. of alumina with 10 ml. of a 10% glacial acetic-water system. Solvents were distilled before use on alumina columns. Light petroleum refers to that fraction with b.p. 60-80°, unless otherwise stated. Solutions were dried over anhydrous sodium sulphate.

6. Analyses were carried out by Drs. Weiler and Strauss, Oxford: A.H. Baird Ltd., Edinburgh: or A. Bernhardt, Max-Planck Institut, Mülheim [Ruhr], W. Germany.

SECTION I - PART I

The unexpected formation of 9-cyano-9,9′-bifluorene and 9,9′-dicyano-9,9′-bifluorene.

9-Bromofluorene (LXX).

N-Bromosuccinimide (5·5g.) was added to a solution of fluorene (5g.) in carbon tetrachloride (50ml.), and the mixture was boiled for 3 hours. The resulting precipitate of succinimide was removed by filtration, and the residue taken up in boiling light petroleum. Cooling caused long needle-like crystals of 9-bromofluorene to precipitate.

m.p. 101-103°. (Lit.[34] m.p. 103-104°).

Yield: 4·1g. (68%).

9-Cyano-9,9′-bifluorene (LXXIII).

Potassium cyanide (0·7g.) dissolved in the minimum quantity of water was added to a solution of 9-bromofluorene (2g.) in the minimum quantity of ethanol, and the mixture was boiled for 3 hours. On cooling, a crystalline product separated, which was filtered and thoroughly washed with water to remove inorganic material. Recrystallisation from glacial acetic acid gave colourless prisms, m.p. 228°, of (LXXIII). (Lit.[36] m.p. 233-34°).

Yield: 1·2g.

Analysis: found: C: 90·5% H: 4·8% N: 3·7%

$C_{27}H_{17}N$ requires: C: 91·3% H: 4·8% N: 3·9%

IR Spectrum: 2230cm^{-1}.(m) (CN)

UV Spectrum: 210(4·81)268(4·53)274(4·39)293(3·86)304(3·66)

NMR Spectrum: τ 2·37-2·90 (complex. 16 aromatic protons).

τ 5·20 (singlet. 9-fluorene proton).

9-Carbamoyl-9,9′bifluorene (LXXIV).

Nitrile (LXXIII), (1g.), was heated at 55° for 3 hours with 15ml. of a 3:1 mixture of 10% hydrogen peroxide and 6N sodium hydroxide, and 15ml. of ethanol. Cooling deposited colourless crystals of the amide. Recrystallisation from glacial acetic acid gave 0·5g.(48%) of colourless prisms, m.p. 275-76°.

Analysis: found: N: 3·4%

$C_{27}H_{19}NO$ requires: N: 3·8%.

IR Spectrum: 3420cm^{-1}.(m) and 3220cm^{-1}.(m) (NH_2)

1680cm^{-1}(s) (amide C=O).

NMR Spectrum: τ 2·41-2·97 (complex. 16 aromatic protons).

τ 4·82 (broad singlet. (NH_2) protons).

τ 5·24 (singlet. 9-fluorene proton).

Fluorene-9-carboxylic acid.

The acid was prepared[144] by the addition of an ethereal solution of phenyl-lithium to a solution of fluorene in ether, followed by carbonation of the 9-fluorenyl-lithium compound so obtained, m.p. 227-28°. (Lit.[87] m.p. 220-25°).

Yield: 40%.

9-Carbamoylfluorene (LXXV).

Fluorene-9-carboxylic acid was boiled with excess thionyl chloride for 1 hour. Thionyl chloride was distilled under reduced pressure, and the residual (liquid) acid chloride was

dissolved in dry benzene. Concentrated aqueous ammonia was carefully added to the chilled solution, and the solid which separated was removed by filtration, and thoroughly washed with water. Recrystallisation from acetic acid gave colourless needles of 9-carbamoylfluorene, m.p. 245-47°, (Lit.[145] m.p. 250°). Yield: 80%.

9,9´-Dicyano-9,9´-bifluorene (LXXVI).

The dinitrile was prepared by the reduction of 9-carbamoylfluorene. Because of the low solubility of the amide in ether and tetrahydrofuran, the reduction was carried out by means of a Soxhlet extractor arranged between the reaction flask, in which was placed 1·3g. of lithium aluminium hydride and 150ml. of dry tetrahydrofuran. In the extractor there was placed 3·0g. of the amide. The hydride suspension was maintained at a moderate rate of boiling for 20 hours, during which time 2·1g. of amide was introduced into the reaction flask. The reaction complex and excess of the hydride were decomposed by the successive dropwise addition of 1·5ml. of water, 1·5ml. of 15% sodium hydroxide and 4·5ml. of water. Inorganic material was removed and the filtrate was evaporated to dryness to yield a black tar (1·9g.). Trituration with methanol gave 0·3g. of white prisms of the dinitrile, m.p. 266-68°, after recrystallisation from benzene-light petroleum. The methanol mother liquors were evaporated to dryness and the residue dissolved in benzene and chromatographed on alumina. Development with benzene gave a further 0·8g. of the dinitrile, m.p. 266-68°.

Analysis: found: C: 88·2% H: 4·0% N: 7·3% M.W. 366.

$C_{28}H_{16}N_2$ requires: C: 88·4% H: 4·2% N: 7·4% M.W. 380.

IR Spectrum: 2240cm^{-1}.(m) (CN).

UV Spectrum: 212(4·72)269(4·43)281(4·34)290(3·76)302(3·52)

NMR Spectrum: τ 2·40-2·82 (complex. aromatic protons).

The dinitrile (0·2g.) was boiled for 3 hours with sodium (0·3g.) and ethanol (15ml.). Pouring onto water gave 9,9 -bifluorene (0·13g.) m.p. 242-45°. (Lit.[146] m.p. 244-45°).

SECTION I - PART II

The oximes of 9-formylfluorene.

9-Formylfluorene (LXXX).

Fluorene (15g.) and ethyl formate (6·7g.) were condensed[53] by the method of Von and Wagner. The crude yellow oil which was obtained was used at once in the preparation of the oximes of formylfluorene. A sample of the crude product distilled at 138-140° at 0·5mm.

IR Spectrum: 1710cm^{-1}.(s) (C=O carbonyl of keto tautomer).
1675cm^{-1}.(s) (C=C exocyclic double bond of enol tautomer).

Yield: 80%.

9-Formylfluorene oximes[44] (LXXXI).

9-Formylfluorene (crude, 10g.) was dissolved in ethanol (100ml.), and to the solution was added sodium (1·4g.) in ethanol (20ml.) followed by hydroxylamine hydrochloride (4·8g.) in water (20ml.). Sodium chloride separated from the solution which was heated at 50° for one hour. The temperature was then raised to 60-65°, and enough water added at the same temperature to produce a turbid solution which on cooling, yielded 9-formylfluorene oxime as long white needles (8·2g.).

The oxime was obtained as a mixture of the α- and β-isomers.

(i) NMR Spectra of oxime mixture

(Acetone soln.)

τ -0·66 (singlet. β-OH proton).

τ -0·11 (singlet. α-OH proton).

τ 1·96-2·64 (complex. aromatic protons).

τ 2·75 (doublet. J = 7·2 c/s. α-H-C=N proton).

τ 3·44 (doublet. J = 6·6 c/s. β-H-C=N proton).

τ 4·21 (doublet. J = 6·6 c/s. β-9-fluorene proton).

τ 5·20 (doublet. J = 7·2 c/s. α-9-fluorene proton).

These signals were assigned on the basis of the observations outlined in the "Discussion" section, [p. 35].

(ii) Attempted separation of oxime mixture.

The oxime mixture (80mg.) was added to light-petroleum (10ml.) and the mixture boiled for 10 minutes and then filtered hot. The insoluble material (38mg.) melted from 135°-158°; the filtrate deposited white needles (30mg.) m.p.130-145°. The n.m.r. spectra of the products indicated that they were both mixtures of the α- and β-oximes. Evaporation of the filtrate to smaller volumes in each case gave mixtures of the two oxime isomers. Repeated recrystallisation of the product, m.p. 130-145°, from light petroleum failed to give pure α-isomer (indicated by n.m.r. spectra).

The oxime mixture (1g.) was dissolved in ether (25ml.) at room temperature, and sufficient light petroleum was added to produce a turbid solution. The solution was filtered and allowed to evaporate. The material which initially separated melted in the range 130°-170°. When the solution had evaporated to a volume of 5ml., the insoluble material was removed and the filtrate was evaporated to dryness. The residue (16mg.) melted over the range 130°-150°, and its n.m.r. spectrum showed the presence of both α- and β-oximes.

A sample of the oxime mixture (1g.) was recrystallised from

95% ethanol four times to give white needles, m.p. 171-72°; the n.m.r. spectrum of the product (0·15g.) indicated that it was pure β-isomer. Concentration of the ethanol mother liquors failed to give pure α-isomer.

(iii) IR spectra of oximes.[50]

β-isomer: 3200cm^{-1}.(s) (bonded OH).

α/β-mixture: 3250-3200cm^{-1}.(s) (broad) (bonded OH).

(iv) Attempted separation of oxime isomers using acetic anhydride.

The oxime mixture (2g.) was added to acetic anhydride (4ml.), and after warming at 25° for 5 minutes the solid dissolved. The solution was left at 18-20° for 24 hours. Dilution of the solution with concentrated aqueous sodium carbonate deposited a yellow oil, which was extracted with chloroform. The chloroform extract was washed thoroughly with water and dried, evaporation giving a yellow oil which crystallised from benzene-light petroleum as colourless prisms, m.p. 112-120°.

IR Spectrum: 3250-3000cm^{-1}.(m) (broad) (bonded OH).
1720cm^{-1}. (m) (acetyl C=O).
1640cm^{-1}. (s)

NMR Spectrum: τ 1·85-2·73 (complex. aromatic protons).

Boiling the product with sodium carbonate solution gave a similar crystalline compound, from which no nitrile could be extracted. The solid product was boiled for 15 minutes with 5% aqueous sodium hydroxide, and the oil which separated on cooling was extracted into chloroform and the two phases were separated.

Carbon dioxide was bubbled through the aqueous phase. No oxime

was precipitated. The chloroform solution was washed with water and dried, evaporation giving a yellow oil which crystallised from benzene-light petroleum as an amorphous, colourless, solid, which melted between 95-110°. The IR and n.m.r. spectrum of the product were very similar to those of the starting-material.

Treatment of β-9-formylfluorene oxime in a similar manner as above gave a white crystalline product, which melted between 130-45°. The infrared spectrum was similar to that of the above products, and showed no indication of a nitrile absorption.

The absorption at 1640cm^{-1}. in the IR spectra of these products suggests that possible oxidation at the 9-methylene position occurred.

(v) Dehydration of the oxime mixture.

The oxime mixture (5g.) was dissolved in dry ether (80ml.) and the solution was well dried by being allowed to stand over anhydrous sodium sulphate for 60 minutes. The filtered solution was then treated with thionyl chloride (5ml.), and the mixture allowed to stand for 12 hours. Evaporation of the ether gave a solid product (3g.), which was crystallised from ethanol to give white prisms, m.p. 150-51°, of 9-cyanofluorene (LXXI) (Lit.[44] m.p. 151-152°, with previous softening).

IR Spectrum: 2230cm^{-1}. (m) (CN).

NMR Spectrum: τ 2·19-2·69 (complex. 8 aromatic protons).

τ 5·18 (singlet. 9-fluorene proton).

On one occasion dehydration of the oxime mixture under identical conditions as outlined above gave a 60% yield of 9,9 -dicyano-9,9 -bifluorenyl (LXXVI), m.p. 266-68°. From the ratio of the intensities

of the OH protons in the n.m.r. spectrum, the α/β composition of the oxime mixture was determined as 60% α-isomer.

SECTION I - PART III

Possible mechanisms for the formation of 9,9'-dicyanobifluorene.

Table I.

Batch	% α-isomer	% β-isomer	m.p. of product
1	0	100	151-52°
2	20	80	150-52°
3	40	60	149-51°
4	60	40	150-52°
5	90	10	148-50°

Five batches of the oxime mixture with α/β composition varying from 0% (i.e. 100% β-isomer) to 90% α-isomer were dehydrated in dry ether for 12 hours with 2 molar equivalents of thionyl chloride. 9-Cyanofluorene, m.p. 150-52°, was obtained in each case.

Table II.

Q_{SOCl_2}	T_{Ox}-T_{Al}	T_D	Product
1m.	1 hr.	1 hr.	9-Cyanofluorene.
2m.	2 days	2 hrs.	9-Cyanofluorene.
4m.	4 days	6 hrs.	9-Cyanofluorene.
6m.	6 days	12 hrs.	9-Cyanofluorene.
10m.	8 days	24 hrs.	9-Cyanofluorene.

Five batches of the oxime mixture containing approximately 60% α-isomer were dehydrated for 12 hours with quantities of thionyl chloride (Q_{SOCl_2}) varying from 1-10 molar equivalents. In each case 9-cyanofluorene was recovered on removing solvent and excess thionyl chloride.

The time gap (T_{Ox}-T_{Al}) between preparation and oximation of 9-formylfluorene was varied from 1 hour - 8 days. The oxime mixtures thus obtained, approximately 60% α-isomer, were dehydrated with thionyl chloride (2 molar excess) for 12 hours. In each case 9-cyanofluorene was obtained.

The time of dehydration (T_D) of the oxime mixture, 60% α-isomer, was varied from 1 - 24 hours. Two molar equivalents of thionyl chloride were used. 9-Cyanofluorene was recovered in each case.

Attempted chlorination of 9-cyanofluorene with thionyl chloride.

9-Cyanofluorene (0·2g.) was dissolved in dry ether (15ml.), and thionyl chloride (1ml.) was added. The solution was kept at room temperature for 12 hours. Evaporation gave a colourless oil, which crystallised from ethanol as needles, m.p. 150-52° alone or on mixing with 9-cyanofluorene. A similar result was obtained on standing for 3 days.

9,9′-Diformyl-9,9′-bifluorene (LXXXV).

An ethereal solution of 9-formylfluorene, on standing at room temperature for 30 days, deposited fine crystals of (LXXXV). Recrystallisation from glacial acetic acid gave colourless prisms, m.p. 218-22°.

Analysis: found: C: 85·6% H: 4·7% M.W. 398

$C_{28}H_{18}O_2$ requires: C: 87·0% H: 4·7% M.W. 386

IR Spectrum: 2830cm^{-1}.(w) and 2720cm^{-1}.(w) (aldehyde C-H).

($CHCl_3$) 1715cm^{-1}.(s) (aldehyde C=O).

NMR Spectrum: τ 0·12 (singlet. 1 aldehydic proton).

τ 2·39-3·08 (complex. 8 aromatic protons).

The dialdehyde was prepared[52] by boiling an ethereal solution of 9-formylfluorene with thionyl chloride.
Yield: 25%. m.p. 217-18° (Lit. 217-18°).

The dialdehyde was extremely insoluble in ethanol. A solution of the dialdehyde (1·0g.) in ethanol (120ml.) was treated with a mixture of sodium (0·12g.) in ethanol (4ml.) and hydroxylamine hydrochloride (0·35g.) in water (4ml.). Sodium chloride separated from the solution which was heated at 60° for two hours. The mixture was concentrated to 50ml. and the precipitated sodium chloride was filtered. Cooling deposited crystals (0·6g.), m.p. 128-150°. Recrystallisation from aqueous ethanol gave colourless crystals, m.p. 132-148°.
IR Spectrum: 3400cm^{-1}.(m) and 3250cm^{-1}.(m) (OH).
no carbonyl absorption.
NMR Spectrum: τ 0·10 (singlet. 1 hydroxyl proton).
(Acetone) τ 2·4-3·1 (complex. 20 aromatic protons).

The IR and NMR spectra failed to give conclusive evidence for the formation of a dioxime.

The product from the attempted oximation (0·3g.) was dissolved in dry ether (50ml.), and thionyl chloride (2ml.) was added. The mixture was kept at room temperature for 4 hours. Evaporation gave a colourless solid product (0·26g.), m.p. 225-230°, which could not be purified. The IR and NMR spectra failed to show the presence of a nitrile.

Reduction of 9,9′-dicyano-9,9′-bifluorene.

(a) In an atmosphere of nitrogen.

The dinitrile (0·2g.) and lithium aluminium hydride (0·1g.) were mixed in dry tetrahydrofuran (20ml.), and the mixture was boiled in an atmosphere of nitrogen for 12 hours. Excess hydride and the reaction complex were decomposed in the normal manner. The tetrahydrofuran solution thus obtained was concentrated to small volume, and then poured into water. The oil which separated was extracted into chloroform.

The chloroform solution was washed with water, dried and evaporated to give an oil (0·2g.), which was boiled with benzene (3ml.). On cooling, a white solid product (80mg.), m.p. >300°, separated.

IR Spectrum: 1665cm^{-1}.(s) (C=C).

The product appeared to be a polymeric compound.

The benzene mother liquors were chromatographed on an alumina column (10g.) made up in light petroleum. Elution with light petroleum gave a colourless solid product (52mg.). Recrystallisation from light petroleum gave colourless needles of 9,9 -bifluorenyl, m.p. 242-45° (Lit.[146] m.p. 244-45°).

NMR Spectrum: τ 2·42-3·22 (complex. 8 aromatic protons).

τ 5·31 (singlet. 9-fluorene proton).

(b) Reduction in the absence of nitrogen.

The dinitrile (0·4g.) and lithium aluminium hydride (0·2g.) were boiled in tetrahydrofuran (40ml.) for 12 hours. The oil (0·3g.) obtained was dissolved in boiling benzene. Addition of light petroleum deposited a solid product (0·15g.), which

crystallised from aqueous ethanol as colourless prisms, m.p. 258-60°, with softening from 140°.

IR Spectrum: 3500cm^{-1}.(m) and 3400cm^{-1}.(m) (NH_2).
($CHCl_3$) 1655cm^{-1}.(s) (enamine C=C).

NMR Spectrum: τ 2·0-2·84 (complex. aromatic protons).
τ 5·33-5·47 (complex. methylene and (NH_2)protons).
Absorptions integrate in the ratio 13:3.

The spectral data indicates that the product is a mixture of 9,9′-diaminomethyl-9,9′-difluorene (LXXXVIII) and 9-aminomethylenefluorene (LXXXVII). The melting point indicates that (LXXXVIII) is the principal component of the mixture.

Analysis: found: N: 6·3%.
$C_{28}H_{24}N_2$ requires: N: 7·2%

SECTION I - PART IV

Reduction of 9-cyanofluorene with lithium aluminium hydride.

A solution of 9-cyanofluorene (5g.) in tetrahydrofuran (30ml.) was added slowly to a well-stirred suspension of lithium aluminium hydride (1·9g.) in tetrahydrofuran (50ml.) at 20°. After all the nitrile had been added, the mixture was boiled for 2 hours. The reaction complex and excess hydride were decomposed in the normal manner.

The tetrahydrofuran filtrate was evaporated to yield a solid product which crystallised from benzene-light petroleum as light yellow needles (2·6g.) of 9-aminomethylenefluorene,[53] m.p. 151-52°. The crystals became discoloured when kept in a desiccator, and after several weeks were dark brown.

IR Spectrum: 3500cm^{-1}.(s) and 3400cm^{-1}.(s) (NH_2).
($CHCl_3$) 1655cm^{-1}.(s) (C=C).

NMR Spectrum: τ 2·00-2·82 (complex. 8 aromatic and 1 olefinic protons).
τ 5·36 (broad doublet. 2(NH_2) protons).

UV Spectrum: 241(4·70)298(4·16)328(4·02)344(4·00)410(2·35)424(2·37).

The product was identical (IR spectrum and mixed melting point) with the amine obtained by bubbling ammonia through a benzene solution of 9-formylfluorene.[53]

A boiling acetic acid solution of the amine deposited yellow-orange needles of bis-[9-fluorenylmethylene]amine (XCV). Recrystallisation from tetralin gave needles, m.p. 313-15° (Lit.[44] m.p. 316-317°).

9-Aminomethylenefluorene (0·3g.) was boiled for 5 minutes with 0·5ml. acetic anhydride containing a trace of concentrated sulphuric

acid. Addition of water failed to precipitate 9-acetaminomethylenefluorene. The acetyl derivative could not be prepared by the method of Von and Wagner.

Attempted hydrogenation of 9-aminomethylenefluorene.

(1) The amine (2·0g.) was dissolved in ethyl acetate (75ml.) and 10% palladium on charcoal (0·1g.) was added. The mixture was shaken at room temperature in an atmosphere of hydrogen (1 atmosphere) for 4 hours, but no uptake of hydrogen was observed. The catalyst was removed and evaporation of the filtrate yielded 9-aminomethylenefluorene.

The use of W2 Raney nickel as catalyst similarly failed to reduce the enamine double bond.

(2) The amine (1·0g.) in ethyl acetate (40ml.) was shaken for 16 hours at room temperature in an atmosphere of hydrogen (4·6 atmospheres) with 10% palladium on charcoal as catalyst. No uptake of hydrogen was observed. 9-Aminomethylenefluorene was recovered after filtration and evaporation of the solvent.

The use of platinum oxide as catalyst at 3·4 atmospheres also failed to hydrogenate the amine.

Attempted reduction of 9-cyanofluorene with lithium aluminium hydride and aluminium chloride.

9-Cyanofluorene (6g.) dissolved in ether (100ml.) was added over 1 hour to a mixture of lithium aluminium hydride (0·74g.) and aluminium chloride (2·6g.) in ether (150ml.). The mixture was boiled for 2 hours then allowed to remain at 20° for 16 hours. Concentrated hydrochloric acid (13ml.) and water (100ml.) were added and the ether was removed by distillation. The yellow oil

which separated was extracted into ether. The ether solution was washed (water) and dried, evaporation giving a yellow oil, which crystallised from benzene-light petroleum as colourless prisms of 9,9′-dicyano-9,9′-bifluorene (2·8g.), m.p. 266-68°, identified by IR spectrum and mixed melting point.

Attempted reduction of 9-cyanofluorene with Raney alloy in alkaline solution.[59]

Raney alloy (1·5g.) was added in one portion to a (magnetically) stirred solution of the nitrile (1g.) in ethanol (20ml.) and 2N sodium hydroxide (20ml.). No external cooling was used and the stirring was continued for 1 hour. The mixture was extracted with chloroform. The chloroform solution was washed with water and dried, evaporation giving colourless crystals of 9-cyanofluorene, m.p. 150-52°.

SECTION I - PART V

Reduction of 9-formylfluorene oxime with lithium aluminium hydride; preparation of 9-hydroxy-9-fluorenemethylamine (XCIII).

A mixture of 9-formylfluorene oximes (6g.) dissolved in ether (300ml.) was added slowly to a well-stirred suspension of lithium aluminium hydride (3g.) in ether (100ml.). The resulting brown mixture was boiled for a further 17 hours, and then poured into iced-water. Dilute hydrochloric acid (1:1v/v) was added and the acidic aqueous phase was separated and made basic with 10% sodium hydroxide. The solid which precipitated was extracted into ether. The ether solution was washed thoroughly with water, dried, and treated with hydrogen chloride to yield the hydrochloride of the amine (5·8g.), m.p. 210-213°.

Decomposition of the hydrochloride with hot sodium hydroxide (5%) gave the amine, which crystallised from benzene-light petroleum as long flat colourless prisms, m.p. 140-41°.

Yield: 4·8g. (80%).

Analysis: found: C: 80·1% H: 5·7% N: 6·9% M.W.218

$C_{14}H_{13}NO$ requires: C: 79·6% H: 6·2% N: 6·6% M.W.211

IR Spectrum: 3600cm^{-1}.(m) (free OH).

($CHCl_3$) 3400cm^{-1}.(m) (broad) (bonded NH_2).

UV Spectrum: 209(4·50)220(4·36)228(4·37)235(4·25)275(4·15)296(3·68) 306(3·52).

NMR Spectrum: τ 2·16-2·58 (complex. 8 aromatic protons).

τ 7·18 (singlet. 2 methylene protons).

τ 7·57 (broad singlet. 3 protons, (OH),(NH_2)).

The amine (0·3g.) was boiled with acetic anhydride. Addition of water did not give an acetyl compound.

The benzoyl derivative of the amine was prepared in the normal manner (Schotten-Baumann method). Recrystallisation from benzene-light petroleum gave colourless prisms, m.p. 185-86°.

Analysis: found: C: 79·6% H: 5·5% N: 4·6%.

$C_{21}H_{17}NO_2$ requires: C: 80·0% H: 5·4% N: 4·4%.

IR Spectrum: 3395cm^{-1}.(s) (N-H).

3300cm^{-1}.(m) (broad) (bonded OH).

1642cm^{-1}.(s) (amide C=O).

UV Spectrum: 208(4·64)221(4·52)227(4·54)235(4·47)275(4·14)295(3·64) 307(3·33).

NMR Spectrum: τ 2·20-2·67 (complex. 13 aromatic protons).

τ 3·31 (broad singlet. 1 (OH) proton).

τ 5·98 (singlet. 1 (NH) proton).

τ 6·19 (doublet. J = 6 c/s. 2 methylene protons).

Attempted reduction of 9-hydroxy-9-fluorenemethylamine.

Amine (0·3g.) was boiled for 30 minutes with a mixture of glacial acetic acid (5ml.) and hydriodic acid (S.G.1·94:3·0ml.), and the resulting solution was poured into aqueous sodium metabisulphite. The clear solution was made alkaline with 10% sodium hydroxide, and the precipitate was extracted into chloroform. Evaporation gave a white solid, which crystallised from benzene-light petroleum as colourless crystals, m.p. 220-235°.

Analysis: found: C: 82·3% H:6·3% N: 5·8%.

$C_{14}H_{13}N$ requires: C: 86·1% H: 6·7% N: 7·2%.

IR Spectrum: 3380cm^{-1}.(m) (broad) (NH_2).

NMR Spectrum: τ 2·42- 3·20 (complex. aromatic protons).

The product was obviously a mixture of compounds.

Attempted preparation of 3-phenyl-2-azafluoranthene by the Pictet-Gams procedure.

(i) The amide (XCIV), m.p. 185-86°, (0·2g.) was boiled for 2 hours in phosphorus oxychloride (5ml.). Excess phosphorus oxychloride was distilled, (2ml.), and the residue poured into iced-water (10ml.) to which concentrated hydrochloric acid (1ml.) had been added. A quantity of tar was deposited. The mixture was shaken with chloroform, and the organic phase was washed with water, dried and evaporated to give a black tar, from which no crystalline product could be isolated. The aqueous acidic phase was made alkaline with 10% sodium hydroxide. No product separated.

(ii) The amide (0·2g.) was dissolved in sulphur-free xylene (6ml.) and phosphorus pentoxide (0·5g.) was added to the solution. The mixture was heated at 150° for 2 hours and then poured into 10ml. of dilute hydrochloric acid (1:10 v/v). A brown oil separated which was extracted into chloroform. Washing, drying and evaporation gave an oil from which no crystalline product could be isolated. The aqueous acidic phase gave no product on basification with 10% sodium hydroxide.

(iii) The amide (0·2g.) was heated for 1 hour at 160° in a solution of phosphorus pentoxide (0·5g.) in polyphosphoric acid (2ml.). The mixture was poured into dilute hydrochloric acid. The only product isolated was an acid-insoluble gum.

(iv) The amide (0·2g.) was added to a stirred mixture of phosphorus pentoxide (0·5g.) and tetralin (3ml.) at 150°. The mixture was kept at this temperature for 30 minutes, and then boiled for a further 30 minutes. The mixture was poured into dilute hydrochloric acid. Once again the product was an acid-insoluble tar.

Reduction of 9-formylfluorene oxime with zinc in acetic acid: preparation of 1,1´-difluoren-9-ylidene-dimethylamine (XCV).

A solution of the oxime (3g.) in warm glacial acetic acid (9ml.) was diluted with water (3ml.) and heated to 100°. Active[147] zinc wool -cut up into 0·2cm. strands - was added and a brisk effervescence occurred. After 5 minutes an orange solid separated from the solution. The mixture was boiled for a further 2 hours, and then poured into a hot solution of concentrated hydrochloric acid (9ml.) in water (25ml.). The cooled mixture was filtered. Recrystallisation of the product from tetralin gave yellow-orange needles of bis-(9-fluorenylmethylene)amine, m.p. 313-15°.

Analysis: found: C: 90·4% H: 5·2% N: 4·4%.

$C_{28}H_{19}N$ requires: C: 91·0% H: 5·2% N: 3·8%.

Molecular Weight: found: 369 (from mass spectrum).

$C_{28}H_{19}N$ requires: 369.

IR Spectrum: 1650cm^{-1}.(s) (enamine C=C).

UV Spectrum: 252(4·83)290(4·13)301(4·08)415(4·70)

(dioxane) 436(4·81).

Because of the gross insolubility of the product in normal solvents a NMR spectrum could not be obtained.

The compound was identical with the product obtained by boiling

9-aminomethylenefluorene in glacial acetic acid [p.125] (mixed melting point, IR and UV spectra).

The amine was insoluble in boiling concentrated hydrochloric acid. It dissolved in a boiling mixture of 2-methoxyethanol and 10% sodium hydroxide. Dilution of the solution with water yielded starting-material.

Attempted reduction of 9-formylfluorene oxime with Raney alloy in alkaline solution.[59]

Raney alloy (1·5g.) was added to a stirred solution of the oxime (1g.) in ethanol (20ml.) and 2N sodium hydroxide. After 1 hour, the mixture was extracted with chloroform. Evaporation gave a yellow oil, whose IR spectrum was identical with that of 9-formylfluorene. An ethanolic solution of the oil gave a 2,4-dinitrophenylhydrazone, m.p. 205-8°. (Lit.[148] m.p. 208°).

SECTION I - PART VI

Preparation of 9-fluoreneacetic acid (XCVI).

(i) By the Reformatsky reaction.

A mixture of fluorenone (10g.) and ethyl bromoacetate (10g.) in dry benzene (100ml.) was slowly added to activated zinc wool[147] (4g.) and a crystal of iodine. The mixture was stirred and refluxed in an atmosphere of nitrogen for 3 hours. The cooled mixture was filtered through glass wool and poured onto a mixture of ice and concentrated sulphuric acid (10ml.); ether was added and the organic layer washed with water, aqueous sodium bicarbonate and saturated sodium chloride solution. The solvents were carefully distilled and the residual unsaturated ester (5g.) was then refluxed for 24 hours with 24 ml. of hydriodic acid (S.G.1·71) and 100ml. of glacial acetic acid. About 70ml. of acetic acid was then distilled off and the residue poured into iced sodium metabisulphite. The oil which separated was extracted into ether. The ether solution was washed thoroughly with water, dried and evaporated to yield a yellow oil, which crystallised from benzene-light petroleum as colourless needles (3·8g.), m.p. 134-35°. There appears to be a lack of agreement in regard to the melting point of this acid. Values of 128-129° (Mayer,[65]), 132-33° (Bachmann and Sheehan,[70]), 137° (Sieglitz and Jassoy,[67]), and 138-39° (Wislicenus and Elbe,[66]) have been recorded. Recrystallisation from dilute acetic acid gave needles, m.p. 135-36°.

Yield: 35%.

IR Spectrum: 1705cm^{-1}.(s) (carboxyl C=O).

NMR Spectrum: τ 2·18-2·81 (complex. 8 aromatic protons).

τ 5·59 (triplet. J = 7 c/s. 9-fluorene proton).

τ 7·14 (doublet. J = 7 c/s 2 methylene protons).

A sample (0·2g.) of the crude unsaturated ester was dissolved in ethanol. Cooling gave colourless needles, m.p. 74-76°. (Lit.[67] m.p. 77°).

IR Spectrum: 1720cm^{-1}.(s) (ester C=O).

1610cm^{-1}.(w) (C=C).

(ii) By the hydrolysis of 9-dicyanomethylenefluorene (CII).

A solution of malononitrile (6·6g.) in ethanol (100ml.) was added to a solution of fluorenone (18g.) and piperidine (0·5ml.) in ethanol (800ml.). The solution turned deep red at once and within five minutes a precipitate of fine red needles separated. After standing for 12 hours the solution was filtered to give 16g. of 9-dicyanomethylenefluorene, m.p. 212-14°, (Lit.[71] m.p. 213°).

The product (10g.) was added to a solution of hydriodic acid (S.G. 1·94: 100ml.) in glacial acetic acid (100ml.), and the mixture was boiled for 12 hours. The cooled solution was poured into iced water, and the solid which separated was filtered and washed thoroughly with water. Recrystallisation of the product from benzene-light petroleum gave colourless needles of 9-fluoreneacetic acid, m.p. 133-35°.

Yield: 6·0g. (60%).

(ii) By the hydrolysis of 9-cyano-9-dicyanomethylenefluorene (CIII).

A slurry of 9-dicyanomethylene fluorene (23g.), sodium cyanide (10g.), water (100ml.), and ethanol (200ml.) was stirred (magnetically) at room temperature. The system became homogeneous after 30 minutes. The yellow solution was cooled in ice and

acidified with cold, dilute hydrochloric acid. Filtration gave 16g. of 9-cyano-9-dicyanomethylenefluorene, m.p. 151-53°, after recrystallisation from ethanol. (Lit.[73] m.p. 152-53°).
Yield: 62%.

It should be noted that the use of less than 2 moles of sodium cyanide in the above reaction resulted in the recovery of a quantity of starting-material. (Hartzler[73] used only 1 mole).

The product (10g.) was boiled for 12 hours in a mixture of concentrated sulphuric acid (100ml.), glacial acetic acid (100ml.) and water (100ml.). The cooled mixture was poured into 300ml.of iced water, and the product (5g.), m.p. 192-96°, which separated was filtered.
IR Spectrum: 1705cm^{-1}.(s) (C=O).

The product (4·5g.) was boiled for 12 hours with 10% sodium hydroxide (50ml.). Acidification with dilute hydrochloric acid gave 3·9g. of 9-fluoreneacetic acid, m.p. 131-33°.
Yield: 38%.

The use of smaller quantities of the acidic hydrolysis mixture gave a product, m.p. 180-200°. Hydrolysis of this acid with 10% sodium hydroxide gave impure 9-fluoreneacetic acid.

Schmidt reaction on 9-fluoreneacetic acid.

(i) Sodium azide (0·5g.) was slowly added to a well-stirred solution of 9-fluoreneacetic acid (1g.) and concentrated sulphuric acid (3ml.) in chloroform (20ml.) at 45-50°. After all the azide had been added, the solution was stirred at this temperature for a further 1 hour. The mixture was poured onto iced water (100ml.) to which

concentrated ammonia (10ml.) had been added. Chloroform (50ml.) was added and after thorough shaking, the organic phase was separated, washed with water and dried. Evaporation gave only a small quantity (5mg.) of an oily product. Acidification of the aqueous phase with hydrochloric acid failed to give a product.

(ii) The addition of a solution of hydrazoic acid in chloroform to a solution of 9-fluoreneacetic acid in concentrated sulphuric acid at 30-35°, also failed to yield a product. No basic or acidic compound could be recovered.

(iii) Sodium azide (0·85g.) was added all at once to a solution of 9-fluoreneacetic acid (3g.) and concentrated sulphuric acid (0·9ml.) in trichloroacetic acid (15g.) at 60°. The mixture was stirred and heated at this temperature for 3 hours. The hot solution was carefully poured onto iced ammonium hydroxide, and the solid which separated was extracted into ether. The ether solution was washed with water, dried and evaporated to give a solid product, which crystallised from benzene-light petroleum as colourless plates, m.p. 141-42°. Yield: 0·60g.

IR Spectrum: 3500cm^{-1}.(m) and 3400cm^{-1}.(m) (NH_2).
1725cm^{-1}.(s) (C=O)

The infrared spectrum contained no aromatic absorptions. Elemental analysis indicated that the product was trichloroacetamide, (Lit.[149] m.p. 141°).

The same compound was obtained by adding sodium azide (0·8g.) to trichloroacetic acid (15g.) at 60°. Heating at 60° for 2 hours and pouring into ammonium hydroxide gave trichloroacetamide (0·7g.), m.p. 140-41°.

Hofmann reaction on 9-fluoreneacetamide.

9-Fluoreneacetamide was prepared in the normal manner from 9-fluoreneacetic acid.

m.p. 187-88°. (Lit.[1] m.p. 189°).

Yield: 92%.

Bromine (1·6g.) was added rapidly to a solution of the amide (3·4g.) and sodium (1·0g.) in methanol (80ml.), and the mixture was refluxed for 30 minutes. Methanol (50ml.) was distilled off, and the residue cooled in ice. Sharp needles of methyl 9-fluorene-methylurethane (2·8g.), (73%), separated. Recrystallisation from light petroleum gave colourless needles, m.p. 138-40°.

IR Spectrum: 3450cm^{-1}.(m) (N-H).

($CHCL_3$) 1700cm^{-1}.(s) (C=O).

NMR Spectrum: τ 2·20-2·79 (complex. 8 aromatic protons).

τ 5·38 (broad singlet. NH proton).

τ 5·75-6·02 (complex. 9-fluorene proton, 9-methylene protons).

τ 6·31 (singlet. 3 methyl protons).

The urethane (1g.) was boiled for 2 hours with 10% sodium hydroxide (15ml.). Cooling gave a 90% return of starting-material.

Boiling the urethane with alcoholic potassium hydroxide failed to give 9-fluorenemethylamine. The urethane was also recovered unchanged after boiling with sodium in methanol for 12 hours.

Curtius reaction on 9-fluoreneacetic acid.

9-Fluoreneacetic acid (3g.) was boiled with thionyl chloride (30ml.) for 2 hours. Excess thionyl chloride was distilled off

and the residual acid chloride was dissolved in dry benzene. Sodium azide (0·9g.), activated by Nelles' procedure,[80] was added to the solution and the mixture was boiled under anhydrous conditions for 12 hours. The cooled mixture was filtered, and the filtrate was evaporated to give a clear oil, which was dissolved in ethanol (100ml.) and boiled for 6 hours. Ethanol (80ml.) was distilled off, and the residue was cooled in ice. The solid product which separated was recrystallised from benzene-light petroleum to give (0·9g.),(25%), of ethyl 9-fluorenemethylurethane, m.p. 111-12°, (Lit.[67] m.p. 112-13°).

IR Spectrum: 3310cm^{-1}. (s) (N-H).
1690cm^{-1}.(s) (C=O).

NMR Spectrum: τ 2·20-2·77 (complex. 8 aromatic protons).
τ 5·38 (broad singlet. NH proton).
τ 5·80-6·04 (complex. 9-fluorene proton, 9-methylene protons).
τ 6·29 (quartet. J = 7 c/s. 2 methylene protons).
τ 8·84 (triplet. J = 7 c/s. 3 methyl protons).

The same urethane was prepared by adding a 25% aqueous solution (3ml.) of sodium azide to a solution of 9-fluoreneacetyl chloride (2·2g.) in acetone (10ml.). The mixture was stirred at room temperature for 30 minutes, and then diluted with water (30ml.). The azide which precipitated was dissolved in ether (40ml.), and the ethereal solution was dried and then poured into 30ml. of ethanol. The solution was concentrated to 40ml. by distillation on a water-bath, and then boiled under reflux for 12 hours. The solution was concentrated to 15ml. and cooled. Colourless needles

of ethyl 9-fluorenemethylurethane (1·2g.), (47%), separated. The crystals melted at 110-12°, although an inorganic residue remained on the hot plate to temperatures of 230-50°.

The urethane was recovered unchanged after boiling with alcoholic potassium hydroxide for 3 hours. Boiling with concentrated hydrochloric acid gave an acid-insoluble oil.

N-9-fluorenemethylphthalimide (CVIII).

The urethane (0·4g.) was fused with phthalic anhydride (0·6g.) in a metal bath at 230° for 1 hour. The bath temperature was lowered to 100°, and ethanol (6ml.) was added to the reaction mixture. The slurry obtained was decanted into dilute sodium bicarbonate solution (5ml.). The solid product obtained was dissolved in boiling ethanol. Animal charcoal, (10mg.) was added and the mixture was boiled for 10 minutes. The hot solution was filtered, and the cooled filtrate deposited needles (0·25g.), (43%). Recrystallisation from benzene gave colourless needles m.p. 145-46°.

Analysis: found: C: 80·5% H: 5·1% N: 4·7%.

$C_{22}H_{15}NO_2$ requires: C: 81·1% H: 4·7% N: 4·3%.

IR Spectrum: 1780cm^{-1}.(m) (C=O).

1740cm^{-1}.(s) (C=O).

The phthalimide (0·24g.) was warmed with hydrazine hydrate (0·25ml.) in ethanol (5ml.). The phthalimide dissolved after 5 minutes at 50°, and the solution was boiled for 30 minutes. A white gelatinous precipitate separated, which was decomposed with dilute hydrochloric acid. The precipitate of phthalylhydrazide, m.p.>300°, was filtered, and thoroughly washed with water. Excess

ethanol (3ml.) was distilled from the filtrate, and a brown oil separated. The mixture was made alkaline with 5% sodium hydroxide and the oily product extracted into chloroform. No crystalline product could be isolated from the oil obtained on evaporation of the chloroform solution.

Attempted cyclisation of ethyl 9-fluorenemethylurethane (CV).

The urethane (0·6g.) was heated with polyphosphoric acid (6ml.) at 130-40° for 2 hours. The hot mixture was poured onto iced-water (30ml.), and a brown oily product separated. The mixture was made alkaline with 10% sodium hydroxide, and the oily product extracted into chloroform. The chloroform solution was washed, dried, and evaporated, but the product oil could not be made to solidify. The gum was dissolved in benzene and chromatographed on a column of 10% deactivated alumina (10g.) made up in light petroleum. Elution with a 2:1 benzene-light petroleum mixture gave a brown gum, from which no crystalline product could be isolated.

SECTION I - PART VII

Infrared spectra of 9-substituted fluorene derivatives.

In the following table the medium in which the individual spectra were recorded is designated (n) for nujol suspensions, and (s) for chloroform solutions. The ratio of the intensity of the low wavelength band to the high wavelength band is represented by "I".

Compound	Medium	Frequency (cm^{-1}.)	I
Fluorene	(s)	1960, 1920	2:1
Fluoranthene	(s)	1940, 1880	2:1
2,2′-Dicarbomethoxybiphenyl	(s)	1960, 1930	1:2
9-Methylfluorene	(s)	1950, 1900	1:1
9-Hydroxy-9-methylfluorene	(s)	1950, 1890	1:1
9-Hydroxy-9-ethylfluorene	(s)	1950, 1890	1:1
9-Benzylfluorene	(s)	1945, 1905	2:1
9-Phenyl-3,6-dimethoxyfluorene	(s)	1945, 1880	1:2
9-Bromofluorene	(n)	1950, 1910	1:1
9-Formylfluorene	(s)	1955, 1915	1:1
β-9-Formylfluorene oxime	(n)	1960, 1920	1:1
9-Cyanofluorene	(s)	1955, 1920	1:1
9,9′-Dicyano-9,9′-bifluorene	(s)	1960, 1915	1:1
9,-Cyano-9,9′-bifluorene	(n)	1955, 1915	1:1
9-Carbamoyl-9,9′-bifluorene	(n)	1950, 1910	1:1
9,9′-Diformyl-9,9′-bifluorene	(s)	1950, 1915	1:1
9,9′-Bifluorene	(n)	1965, 1920	1:2
9-Aminomethylenefluorene	(s)	1940, 1890	1:1
9-Fluorenecarboxylic acid	(n)	1950, 1915	1:1
9-Carbamoylfluorene	(n)	1950, 1900	1:1
9-Fluoreneacetic acid	(n)	1970, 1915	1:1
9-Fluoreneacetamide	(s)	1960, 1920	1:1
Methyl 9-fluorenemethylurethane	(s)	1950, 1910	1:1
Ethyl 9-fluorenemethylurethane	(n)	1955, 1905	1:1
Methyl 9-fluorylglyoxalate	(s)	1950, 1910	1:1
9-Hydroxy-9-fluorenemethylamine	(s)	1970, 1930	1:1
Fluorenone-1-carboxylic acid	(n)	weak	
Fluorene-1-carboxylic acid	(n)	peaks	
1-Carbamoylfluorene	(n)	1960, 1925	3:1
1-Cyanofluorene	(s)	1960, 1930	4:1
1-Fluorenemethylamine	(s)	1930	
Ethyl-1-fluorenemethylurethane	(s)	1920	
Methyl-1-fluorenecarboxylate	(s)	1940, 1910	3:1

SECTION II

Attempts to prepare 2-azafluoranthene by a condensation involving carbon atoms 1 and 3 of the potential heterocyclic ring.

Fluorenone-1-carboxylic acid (VII).

The acid was prepared[83] by the oxidation of fluoranthene (100g.) with chromium trioxide in acetic acid.

m.p. 194-95°. (Lit. m.p. 197-98°).

Yield: 55g. (50%).

Fluorene-1-carboxylic acid (CXIII).

The acid was prepared[84] by the method of Morrison. A solution of fluorenone-1-carboxylic acid (40g.) in 3 litres of glacial acetic acid was mixed with red phosphorus (70g.) and hydriodic acid (S.G. 1·7. 72ml.) and the mixture was boiled for 48 hours. Excess acetic acid (2000ml.) was distilled, the residue poured into water (7000ml.), filtered, dissolved in sodium carbonate solution, separated from phosphorus and acidified to give 35g. (91%) of (CXIII).

m.p. 240-44°. (Lit. m.p. 242-47°).

Fluorene-1-carboxamide (CXIV).

The amide was prepared from fluorene-1-carboxylic acid (10g.) by the normal procedure via the acid chloride.

m.p. 248-49°. (Lit.[83] m.p. 251-53°).

Yield: 7g. (70%).

1-Cyanofluorene (CX).

Fluorene-1-carboxamide (5g.) was boiled in freshly distilled phosphorus oxychloride (20ml.) for 2 hours. Excess phosphorus

oxychloride was distilled off under reduced pressure, and the residue was poured onto iced water. The mixture was made distinctly alkaline with 5% sodium hydroxide, and the solid which separated was extracted into chloroform. The chloroform solution was washed (water), dried and evaporated and the residue was dissolved in benzene and chromatographed on a column of alumina (100g.) made up in light petroleum. Elution with light petroleum gave a solid which crystallised from ethanol as colourless needles.
m.p. 91-93°. (Lit.[85] m.p. 92-95°).
Yield: 2·7g. (59%).

Boiling 1-carbamoylfluorene (1g.) with thionyl chloride for 2 hours gave a mixture of the nitrile and unreacted amide.

A solution of the amide (0·4g.) in dimethylformamide (15ml.) and thionyl chloride (3ml.) was stirred at 60° for 2 hours. Pouring the solution into water gave a mixture of the nitrile and unreacted amide.

Attempted acylation of 1-cyanofluorene.

(1) Potassium (0·4g.) was dissolved in anhydrous methanol (20ml.), 1-cyanofluorene (1g.) and dimethyl oxalate (1·2g.) were added and the mixture was heated and shaken in an attempt to obtain a homogeneous solution. The mixture, which became red in colour, was then boiled for 2 hours. The mixture was evaporated to dryness and stirred in 10% sodium hydroxide (10ml.). The basic solution was filtered and the filtrate acidified with hydrochloric acid. No precipitate separated. The material insoluble in alkali, m.p. >290°, was stirred in dilute hydrochloric acid, and then extracted with ether. The organic phase was washed (water),

dried and evaporated to give 1-cyanofluorene, m.p. 92-93° from ethanol.

(ii) 1-Cyanofluorene (0·7g.) was added to a mixture of dimethyl oxalate (3g.) and potassium methoxide (from 0·3g. of potassium) in benzene (20ml.), and the mixture was boiled for 2 hours. A reasonably homogeneous solution was obtained. The cooled mixture was extracted with water (20ml.), and the aqueous phase was acidified with dilute sulphuric acid. No precipitate separated, The organic phase was washed (water), dried and evaporated to give 1-cyanofluorene (0·6g.)

(iii) 1-Cyanofluorene (1·0g.) was added to a mixture of diethyl oxalate (1·4g.) and potassium ethoxide(from 0·4g. of potassium) in benzene (30ml.), and the mixture was boiled in an atmosphere of nitrogen for 2 hours. A homogeneous solution was obtained. Addition of water to the cooled solution and work up of the reaction as in (ii) gave solely 1-cyanofluorene (0·9g.).

9-Carbamoyl-9-hydroxyfluorene-1-carboxylic acid.[89] (CXVI).

Anhydrous hydrogen cyanide (7 ml.) was added to a solution of fluorenone-1-carboxylic (5g.) in anhydrous pyridine (50ml.). The solution was heated on a water bath at 50° for 5 minutes, and then evaporated to dryness at the same temperature (1·0mm.). Acetic acid (35ml.), water (13ml.) and concentrated hydrochloric acid (20ml.) were added to the residue, and the mixture was heated at 100° for 3 hours. Addition of ether (100ml.) to the cooled solution caused colourless crystals to separate. These were removed by filtration, and recrystallised from water to give prisms of (CXVI), m.p. 150-52°, (Lit. m.p. 215°).

Yield: 0·9g. (22%).

Analysis: found: C: 62·6% H: 5·0% N: 5·1%

$C_{15}H_{11}NO_4.H_2O$ requires: C: 62·7% H: 4·6% N: 4·9%

IR Spectrum: 3490cm^{-1}.(m) and 3390cm^{-1}.(m) (NH_2).

1685cm^{-1}.(s) (carboxyl C=O).

1665cm^{-1}.(s) (amide C=O).

Evaporation of the ether phase gave fluorenone-1-carboxylic acid (3·8g.).

The carbamoyl-compound (CXVI), (0·05g.), was heated with acetic anhydride (1·5ml.) containing a trace of concentrated sulphuric acid. Addition of water gave colourless prisms of an acetyl compound, m.p. >310°.

Analysis: found: C: 62·2% H: 5·1% N: 3·7%

$C_{17}H_{13}NO_5.2H_2O$ requires: C: 62·0% H: 4·6% N: 4·2%

The acetyl compound was recrystallised from a large volume of water for analysis.

IR Spectrum: 1710cm^{-1}.(s) (ester C=O) ($CHCl_3$)

The carbamoyl-compound (0·2g.) was heated at 100° with 5ml. of a 5:3:2 mixture of acetic acid, concentrated hydrochloric acid, and water for 24 hours. The cooled solution was evaporated to dryness, and the residue was dissolved in boiling water (10ml.). Cooling gave colourless crystals (0·14g.) of 9-hydroxy-fluorene-1,9-di-carboxylic acid, m.p. 181-83°. (Lit.[89] m.p. 182-89°).

IR Spectrum: 3300cm^{-1}.(m) and 2650cm^{-1}.(m) (bonded OH).

1700cm^{-1}.(s) (carboxyl C=O).

Ethyl 9-carbamoyl-9-hydroxyfluorene-1-carboxylate (CXVII).

The carbamoyl-compound (CXVI), (0·35g.), was boiled in ethanol (5ml.) containing 2 drops of concentrated sulphuric acid for 12 hours. On cooling, colourless crystals were deposited. Recrystallisation from glacial acetic acid gave prisms (0·2g.) (67%), m.p. 243-45° with previous softening.

Analysis: found: C: 68·6% H: 5·1% N: 5·5%.

$C_{17}H_{15}NO_4$ requires: C: 68·7% H: 5·1% N: 4·7%.

IR Spectrum: 3400cm^{-1}.(m) and 3300cm^{-1}.(m) (NH_2).

1690cm^{-1}.(s) (ester C=O).

1670cm^{-1}.(s) (amide C=O).

The product (0·2g.) was gently warmed at 50° with 60% (by vol.) sulphuric acid (2ml.) for 30 minutes. The solution was poured into iced-water, and an oily product separated which was extracted into chloroform. The chloroform solution was washed (water), dried, and evaporated to give a tar, from which no crystalline product could be isolated.

SECTION III

Attempted preparation of 2-azafluoranthene using a Dieckmann cyclisation.

1-Fluorenemethylamine (CXXII).

1-Fluorenecarboxamide (5·2g.) was placed in the thimble of a Soxhlet extractor, and extracted into a suspension of lithium aluminium hydride (3·25g.) in tetrahydrofuran (250ml.). The purple mixture obtained was boiled for 12 hours, by which time the colour had changed to deep brown. The reaction complex and excess hydride were decomposed with alkali in the normal manner. The tetrahydrofuran solution was evaporated to small volume and then poured onto iced water (200ml.). The oil which separated was extracted into chloroform. The chloroform solution was thoroughly washed with water, dried and evaporated to give a solid product, 4·7g. (95%), m.p. 95-102°.

A small quantity of the product was recrystallised from methanol to give colourless prisms, m.p. 101-103°.

Analysis: found: C: 82·2% H: 6·5% N:7·0%.

$C_{14}H_{13}N$ requires: C: 86·0% H: 6·7% N:7·2%.

IR Spectrum: 3350cm^{-1}(m) and 3270cm^{-1}.(m) (NH_2). ($CHCl_3$).

NMR Spectrum: τ 2·18-2·80 (complex. 7 aromatic protons).

τ 6·11 (2 x 9-fluorene protons).

τ 6·31 (2 methylene protons).

τ 8·32 (2 (NH_2) protons).

The crude product from this reaction was used to prepare (CXX).

Ethyl 1-fluorenemethylurethane (CXX).

A solution of 1-fluorenemethylamine (4·1g.) and triethylamine (2·1g.) in toluene (100ml.) was slowly added to a solution of ethyl chloroformate (2·3g.) in toluene at 0°. A precipitate of triethylamine hydrochloride separated at once. After all the amine solution had been added, the mixture was stirred at 0° for 30 minutes and then at 60° for 1 hour. The cooled mixture was filtered and evaporated, and the residue was dissolved in boiling methanol. On cooling colourless needles separated, 2·6g.(41%), m.p. 124-25°.

Analysis: found: C: 76·0% H: 6·4% N: 5·2%.

$C_{17}H_{17}NO_2$ requires: C: 76·4% H: 6·4% N: 5·4%.

IR Spectrum: 3360cm^{-1}.(m) (NH).

($CHCl_3$) 1700cm^{-1}.(s) (C=O).

NMR Spectrum: τ 2·28-3·01 (complex. 7 aromatic protons).

τ 5·04 (broad singlet. 1 (NH) proton).

τ 5·64 (doublet. J = 6 c/s. 2 methylene protons).

τ 5·94 (quartet. J = 7 c/s. 2 methylene protons).

τ 6·25 (singlet. 2 x 9-fluorene protons).

τ 8·85 (triplet. J = 7 c/s. 3 methyl protons).

Attempted cyclisation of ethyl 1-fluorenemethylurethane.

(i) With potassium methoxide.

Ethyl 1-fluorenemethylurethane (1g.) was added to a mixture of potassium methoxide (from 0·2g. potassium) in ether (50ml.), and the mixture was boiled under anhydrous conditions for 3 hours. A red colour appeared initially, but disappeared after 10 minutes with a simultaneous separation of a white solid. The cooled mixture was shaken with water (50ml.), and the transparent two-

phase system was separated. The aqueous phase was extracted with two 10ml. portions of ether, and then acidified with dilute sulphuric acid. A small quantity of oil (20mg.) separated, and was extracted into ether. Evaporation of the ether solution gave an orange oil which could not be made to crystallise.

The combined ether solutions (60ml.) were washed (water), dried, and evaporated to give 0·8g. of recovered urethane.

(ii) With triphenylmethylsodium.

The urethane (1g.) was added to 50ml. of a solution of triphenylmethylsodium in ether (0·11 mole/litre), and the mixture was boiled for 5 hours under an atmosphere of nitrogen. The deep red colour of the triphenylmethyl anoin disappeared after 10 minutes with a simultaneous precipitation of a white solid. The cooled mixture was shaken with water (50ml.), the insoluble material disappearing. The aqueous phase was acidified with dilute sulphuric acid. No product separated. The ether solution was washed (water), dried, and evaporated, and the solid residue was dissolved in benzene (10ml.). The benzene solution was chromatographed on a column of 10% deactivated alumina (30g.) made up in light petroleum. Elution with light petroleum gave 1·0g. of triphenylmethane, m.p. 90-95° (Lit. m.p. 94°). Elution with benzene gave recovered urethane (0·7g.), (identified by mixed melting point and IR Spectrum).

Attempted metalation of ethyl 1-fluorenemethylurethane at the amide hydrogen.

(i) With sodium.

Freshly cut sodium wire (0·05g.) was added to a solution of the urethane (0·5g.) in boiling ether (25ml.), and the mixture was boiled

for 5 hours under anhydrous conditions. The sodium did not dissolve. Ethyl chloroformate (0·22g.) was added to the mixture, and boiling was continued for a further 15 hours. The cooled inhomogeneous mixture was poured onto water. The ether phase was evaporated, and the residue recrystallised from ethanol to give recovered urethane (0·45g.).

(ii) With potassium methoxide.

The urethane (1g.) was added to a mixture of potassium methoxide (from 0·2g. of potassium) in anhydrous ether (50ml.). After boiling for 2 hours, ethyl chloroformate (0·44g.) was added and the mixture was boiled for a further 3 hours. The inhomogeneous mixture was cooled and poured onto water (50ml.). Evaporation of the dried ether phase gave 0·9g. of recovered urethane.

SECTION IV - PART I

Synthesis of 2-azafluoranthene.

Fluorenone-1-carboxylic acid[83] (VII).

Oxidation of fluoranthene (100g.) gave 55g. of the acid.

Fluorene-1-carboxylic acid[84] (CXIII).

Reduction of fluorenone-1-carboxylic acid (55g.) gave 50g. of (CXIII).

Methyl 1-fluorenecarboxylate (CXXV).

A solution of fluorene-1-carboxylic acid (50g.) in absolute methanol (800ml.) was saturated with hydrogen chloride, and then boiled for 3 hours. Methanol (500ml.) was distilled off and the residue was cooled. Long needles (45g.) of the ester separated. The product was removed by filtration and thoroughly washed with sodium bicarbonate solution and then with water. The dried solid was dissolved in anhydrous benzene (200ml.) and chromatographed on a column of alumina (1kg.) made up in light petroleum. Elution with a 4:1 mixture of light petroleum-benzene gave 42gm. of the ester. Recrystallisation from methanol gave colourless needles, m.p. 86-88°. (Lit.[83] m.p. 86-87°).

Yield: 40g. (76%).

IR Spectrum: 1710cm^{-1}.(s) (ester C=O).

NMR Spectrum: τ 2·05-2·82 (complex. 7 aromatic protons).

τ 5·88 (singlet. 2 x 9-fluorene protons).

τ 6.15 (singlet. 3 methyl protons).

Methyl 9-formylfluorene-1-carboxylate (CXXVI).

A mixture of methyl 1-fluorenecarboxylate (25g.), ethyl formate (8·2g.) and potassium methoxide (from 4·5g. of potassium) was boiled in ether (700ml.) for 3 hours. The cooled mixture was extracted with water (700ml.), and the aqueous phase was extracted with a further two 70ml. portions of ether. The aqueous phase was acidified with 10% (by vol.) sulphuric acid, and the oil which separated was extracted into ether (700ml.). The ether phase was washed with two 300ml. portions of water, dried, and evaporated to yield a yellow oil (15g.), (53%).

Recrystallisation of a sample of the product from light petroleum gave colourless crystals, m.p. 175-78°.

Analysis: found: C: 73·2% H: 4·9%.

$C_{16}H_{12}O_3$ requires: C: 76·2% H: 4·8%.

IR Spectrum: 2680cm^{-1}.(w) (aldehyde CH).

1710cm^{-1}.(s) (broad) (C=O).

2-Azafluoranth-3[2H]one. (CXXVII).

(i) The crude product (6·0g.) from the previous reaction was boiled with concentrated aqueous ammonia (70ml.) for 12 hours. On cooling, a solid product separated, which was recrystallised from tetralin to give long colourless needles 0·7g. (13%), m.p. 287-89°.

Analysis: found: C: 81·9% H: 4·6% N: 6·2%.

$C_{15}H_9NO$ requires: C: 82·2% H: 4·2% N: 6·4%.

IR Spectrum: 3150cm^{-1}.(m) and 3040cm^{-1}.(m) (NH).

1680cm^{-1}.(s) (amide C=O).

1655cm^{-1}.(s) (olefinic C=C).

UV Spectrum: 222(4·60)240(4·37)248(4·38)257(4·42)272(3·96)
302(4·06)325(4·01)358(4·02).

NMR Spectrum: τ 2·07-2·77 (complex. aromatic protons).
(TFA.)

(ii) Crude methyl 9-formylfluorene-1-carboxylate (15g.) was dissolved in glacial acetic acid (170ml.), and powdered ammonium carbonate (50g.) was carefully added to the solution. The mixture was boiled for 12 hours, and on cooling, fine colourless crystals separated and were removed by filtration. The product was thoroughly washed with water, and dried. Recrystallisation from tetralin gave colourless needles, 7·8g. (60%), m.p. 287-89°.

2-Azafluoranth-3[2H]one (0·2g.) was boiled with 4N sodium hydroxide (2ml.), dimethyl sulphate (1ml.) and methanol (10ml.) for 2 hours. Excess methanol was removed and the residue was poured onto iced water to give (0·15g.) of N-methyl-2-azafluoranth-3[2H]one (CXXXV). Recrystallisation from ethanol gave pale yellow needles, m.p. 179-81°.

Analysis: found: C: 82·4% H: 4·6% N: 6·2%.
$C_{16}H_{11}NO$ requires: C: 82·4% H: 4·8% N: 6·0%.

IR Spectrum: 1665cm^{-1}.(s) (amide C=O).
1630cm^{-1}.(m) (olefinic C=C).
1610cm^{-1}.(m) (aromatic C=C).

UV Spectrum: 224(4·61)240(4·37)248(4·40)259(4·41)273(3·87)
303(4·11)325(4·04)357(3·97).

NMR Spectrum: τ 1·79-2·82 (complex. 7 aromatic protons,
1 olefinic proton).
τ 6·42 (singlet. 3 methyl protons).

3-Chloro-2-azafluoranthene (CXXVIII).

2-Azafluoranth-3[2H]one (7·8g.) was boiled with freshly distilled phosphorus oxychloride (120ml.) for 5 hours. Excess phosphorus oxychloride was removed under reduced pressure and the residue was poured onto cracked ice. The mixture was made alkaline with dilute ammonium hydroxide, and the yellow precipitate was filtered and washed with water. Recrystallisation from ethanol gave pale yellow needles, 6·9g. (82%), m.p. 135-36°.

Analysis: found: C: 75·5% H: 3·7% N: 6·3% Cl: 14·8%.

$C_{15}H_8NCl$ requires: C: 75·8% H: 3·4% N: 5·9% Cl: 14·9%.

IR Spectrum: 1615cm^{-1}.(m) (aromatic C=C). ($CHCl_3$).

UV Spectrum: 211(4·63)238(4·58)274(4·27)284(4·39)325(3·71)351(3·99) 366(3·96).

NMR Spectrum: τ 1·59 (singlet. 1-H proton).

(CS_2) τ 2·06-2·83 (complex. 7 aromatic protons).

Boiling a solution of 3-chloro-2-azafluoranthene with excess sodium in methanol gave 3-methoxy-2-azafluoranthene (CXXXVI). Recrystallisation from a 3:1 mixture of light petroleum-benzene gave colourless fluorescent prisms, m.p. 154-55°.

Analysis: found: C: 82·8% H: 4·8% N: 5·8%.

$C_{16}H_{11}NO$ requires: C: 82·4% H: 4·8% N: 6·0%.

IR Spectrum: 1625cm^{-1}.(m) (aromatic C=C).

(CS_2) 1240cm^{-1}.(s) (OMe).

UV Spectrum: 219(4·63)232(4·47)246(4·37)256(4·35)279(4·02) 289(4·43)302(3·66)355(4·01).

NMR Spectrum: τ 1·70 (singlet. 1-H proton).

(CS_2) τ 2·03-2·85 (complex. 7 aromatic protons).

τ 5·91 (singlet. 3 methyl protons).

Boiling a solution of 3-chloro-2-azafluoranthene with sodium in ethanol gave 3-ethoxy-2-azafluoranthene (CXXXVII). Recrystallisation from light petroleum gave colourless fluorescent needles, m.p. 100-101°.

Analysis: found: C: 82·6% H: 5·4% N: 5·8%.

$C_{17}H_{13}NO$ requires: C: 82·6% H: 5·3% N: 5·7%.

IR Spectrum: 1625cm^{-1}.(m) (aromatic (C=C).

(CS_2) 1240cm^{-1}.(s) (OEt).

UV Spectrum: 218(4·61)231(4·45)246(4·36)255(4·36)280(4·03) 290(4·45)301(3·64)356(4·00).

NMR Spectrum: τ 1·75 (singlet. 1-H proton).

τ 2·11-2·94 (complex. 7 aromatic protons).

τ 5·33 (quartet. J = 7 c/s. 2 methylene protons).

τ 8·62 (triplet. J = 7 c/s. 3 methyl protons).

3-Ethoxy-2-azafluoranthene (0·2g.) was boiled with 6N hydrochloric acid (3ml.) for 30 minutes. The ether dissolved in the acidic solution to give a clear solution, and after five minutes a white precipitate separated. The mixture was poured into water, giving 0·15g. of 2-azafluoranth-3[2H]one, m.p. 287-89°.

3-Methoxy-2-azafluoranthene also gave 2-azafluoranth-3[2H]one on boiling with 6N hydrochloric acid.

2-Azafluoranthene (III).

A solution of 3-chloro-2-azafluoranthene (5g.) and potassium hydroxide (1·2g.) in ethanol (500ml.) was treated with 0·25g. of 10% palladium on charcoal and shaken in an atmosphere of hydrogen (1 atmosphere) at room temperature for 7 hours. During this time 700ml. of hydrogen was absorbed (calculated 520ml.). The catalyst

was removed by filtration, and the filtrate was made slightly acidic with dilute hydrochloric acid. The acid solution was evaporated to small volume, and made alkaline with 5% sodium hydroxide. The product which separated was extracted into chloroform, and the chloroform solution was washed (water), dried and evaporated. The residue was extracted with 100ml. of light petroleum, 0·3g. of material being filtered off. Recrystallisation of the latter from tetralin gave 2-azafluoranth-3[2H]one.

The petrol solution was chromatographed on a column of alumina (150g.) made up in light petroleum (40-60°). Elution with a 1:1 mixture of benzene-light petroleum (40-60°) gave (0·4g.) of 3-ethoxy-2-azafluoranthene, m.p. 101-2°. Elution with a 4:1 mixture of benzene-light petroleum (40-60°) gave 2·6g. of 2-azafluoranthene. Recrystallisation from light petroleum (40-60°) gave pale yellow needles, m.p. 62-63°.

The base distilled at 150-55° at 1·0 mm.

Yield: 60%.

Analysis: found: C: 87·2% H: 4·6% N: 7·0%.

$C_{15}H_9N$ requires: C: 88·6% H: 4·5% N: 6·9%.

IR Spectrum: 3050cm^{-1}.(m) (aromatic C-H).

(CS_2) 1625cm^{-1}.(m) (aromatic C=C).

UV Spectrum: 210(4·58)235(4·54)272(4·16)281(4·37)324(3·63) 346(3·87)360(3·83).

NMR Spectrum: τ 0·91 (singlet. 1-H proton).

τ 1·15 (singlet. 3-H proton).

τ 2·10-2·81 (complex. 7 aromatic protons).

The 1-H proton is assigned to the signal at 0·91 because of the deshielding effect of steric interaction with 10-H proton.

Methiodide: prepared in boiling methyl iodide. Recrystallisation from ethanol gave orange-yellow needles, m.p. 266-68°.

Analysis: found: N: 4·1% I: 35·9%.

$C_{16}H_{12}NI$ requires: N: 4·0% I: 36·8%.

UV Spectrum: 217(4·66)245(4·65)266(4·09)283(3·81)304(3·64)370(3·93).

NMR Spectrum: τ 0·54 (singlet. 1-H proton).

(TFA). τ 1·21 (singlet. 3-H proton).

τ 1·67-2·54 (complex. 7 aromatic protons).

τ 5·29 (singlet. 3 methyl protons).

Picrate: prepared in ethanol. Recrystallisation from nitromethane gave yellow needles, m.p. 273°(dec.).

Analysis: found: C: 58·3% H: 3·2% N: 13·0%.

$C_{21}H_{12}N_4O_7$ requires: C: 58·3% H: 2·8% N: 13·0%.

Trinitrobenzene complex: prepared in ethanol. Recrystallisation from ethanol gave pale yellow prisms, m.p. 152-54°.

Analysis: found: N: 14·5%

$C_{21}H_{12}N_4O_6$ requires: N: 13·5%

Hydrochloride: precipitated from a benzene solution of the base. Recrystallisation from ethanol-light petroleum gave pale yellow prisms, m.p. 205-8°. The hydrochloride was very hygroscopic.

Analysis: found: Cl: 12·0%

$C_{15}H_{10}NCl$ requires: Cl: 14·8%

2-Azafluoranthene was analysed several times after repeated purification by column chromatography but the percentage of carbon was persistently low.

Attempted preparation of 3-toluene-p-sulphonylhydrazino-2-azafluoranthene (CXXXVIII).

3-Chloro-2-azafluoranthene (1·0g.) and p-toluenesulphonylhydrazide were boiled in chloroform (20ml.) for 2 hours. The blood red solution was kept at 0° for a further 48 hours.

No material precipitated from the solution. The solution was evaporated to dryness to give a red oil, which crystallised from ethanol as pink needles, m.p. 132-34°. Two recrystallisations from benzene gave yellow needles of 3-chloro-2-azafluoranthene, m.p. 135-36°.

Attempted hydrogenolysis of 3-chloro-2-azafluoranthene with hydrazine hydrate and palladium-charcoal.

3-Chloro-2-azafluoranthene (0·6g.), hydrazine hydrate (1·8ml), and 10% palladium on charcoal (0·24g.) were boiled in ethanol (60ml.) for 3 hours. The cooled solution was filtered free off catalyst, and the filtrate evaporated to small volume and poured into water. The product which separated was removed by filtration, washed with water, and dried. Recrystallisation from amyl acetate gave orange-yellow needles (0·46g.) of 3-hydrazino-2-azafluoranthene, m.p. 210-13°.

Analysis: found: C: 77·2% H: 5·1% N: 17·8%.

$C_{15}H_{11}N_3$ requires: C: 77·2% H: 4·8% N: 18·0%.

IR Spectrum: 3320cm^{-1}.(m) (broad) (NH.NH_2).

NMR Spectrum: τ 1·58 (singlet. 1-H proton).

(DMSO). τ 1·84 (complex. 7 aromatic protons).

The hydrazino-compound was prepared directly by boiling 3-chloro-2-azafluoranthene (0·2g.) and hydrazine hydrate (0·7ml.) in ethanol (20ml.) for 2 hours.

Attempted deoxygenation of 2-azafluoranth-3[2H]one with triethyl phosphite.

2-Azafluoranth-3[2H]one (0·5g.) was boiled with triethyl phosphite (25ml.) under an atmosphere of nitrogen for 15 hours. The solution was cooled to yield crystals, 0·4g., of starting-material. The filtrate was evaporated to dryness at 50° (1·0mm.) to give 0·1g. of 2-azafluoranth-3[2H]one.

Unusual product obtained during the cyclisation of methyl 9-formylfluorene-1-carboxylate with ammonium carbonate in acetic acid.

The hydroxymethylene ester (15g.) was boiled with ammonium carbonate (50g.) in glacial acetic acid (120ml.) for 12 hours. On cooling, colourless crystals of 2-azafluoranth-3[2H]one (8g.) separated and were removed by filtration. The filtrate was poured into water (300ml.) and the yellow solid which separated was filtered and washed with water. Recrystallisation from acetic acid gave yellow needles (2·5g.), m.p. 235-36°.

Analysis: found: C: 81·1% H: 4·5% N: 3·9% M.W.: 338

IR Spectrum: 3050cm^{-1}.(w) (aromatic CH).
1725cm^{-1}.(s) (ester C=O?).
1675cm^{-1}.(s) (amide C=O?).
1635cm^{-1}.(s) (olefinic C=C).
1620cm^{-1}.(s) (aromatic C=C).

UV Spectrum: 220(4·59)235(4·60)343(4·17).

NMR Spectrum:	τ -values		integral ratios
(see Fig.5)	1·43	(singlet. proton adjacent to N)	1
	1·75-3·0	(complex. aromatic protons)	15
	5·90	(singlet. methyl protons)	2
	5·44	(doublet. J = 8 c/s. methylene protons).	0·6
	8·52	(triplet. J = 8 c/s. methyl protons).	1

The product, m.p. 235-36°, was recovered unchanged after boiling with concentrated hydrochloric acid.

The compound (0·4g.) was boiled with ethanol (15ml.) and 10% sodium hydroxide (15ml.) for 2 hours. The deep red solution obtained was diluted with water and acidified with concentrated hydrochloric acid. An orange solid (0·3g.) separated, and was removed by filtration, and washed with water and warm ethanol. The product could not be recrystallised because of its insolubility in common organic solvents. It was dissolved in dilute sodium bicarbonate. Acidification with concentrated hydrochloric acid gave orange crystals, m.p. 195-210°.

IR Spectrum: 2650cm^{-1}.(m) (broad) (bonded OH).
1690cm^{-1}.(s) (carboxyl C=O).
1640cm^{-1}.(s) (olefinic C=C).

NMR Spectrum: τ 1·20-2·65 (complex. aromatic protons) (DMSO).

The acidic product (0·25g.) was boiled with methanol (40ml.) and concentrated sulphuric acid (1ml.) for 2 hours. Methanol (20ml.) was distilled off, and the remaining solution was poured into water (80ml.). The oil which separated was extracted into

chloroform (200ml.). The chloroform solution was washed with dilute sodium bicarbonate, then with water, dried, and evaporated to give 0·18g. of 2-azafluoranth-3[2H]one, m.p. 287-89°.

Boiling a solution of the unknown compound, m.p. 235-36°, with excess sodium in ethanol gave a pink solution. On pouring the solution into water, 2-azafluoranth-3[2H]one separated.

SECTION IV - PART II

The oxidation of 2-azafluoranthene.

Oxidation of 2-azafluoranthene

(i) With potassium permanganate.

2-Azafluoranthene (0·3g.) was suspended in 10ml. of water, and a 3% aqueous potassium permanganate solution (90ml.) was added over a period of 1 hour to the boiling mixture. The suspension was boiled for a further 2 hours, and then cooled and filtered to remove precipitated manganese dioxide. The filtrate was made slightly acidic with dilute nitric acid, and the precipitated orange solid was removed by filtration. Recrystallisation from glacial acetic acid gave 0·15g. of fluorenone-1-carboxylic acid, m.p. 194-96°. The acidic oxidation filtrate was made slightly basic with 10% sodium hydroxide. No precipitate separated.

(ii) With chromium trioxide.

2-Azafluoranthene (0·2g.) was boiled with chromium trioxide (0·5g.), water (0·5ml.) and glacial acetic acid (15ml.) for 1 hour. The green solution obtained was poured into iced water (30ml.). The solid which precipitated was removed by filtration and thoroughly washed with water to give 0·11g. of orange-yellow crystals which did not melt below 300°. The product could not be recrystallised owing to its insolubility in common organic solvents.

IR Spectrum: 1615cm^{-1}. (s) (olefinic C=C).

Oxidation of 2-azafluoranth-3[2H]one.

2-Azafluoranth-3[2H]one (0·4g.) was boiled with chromium trioxide (1·6g.), water (2ml.) and glacial acetic acid (25ml.) for 2 hours. Excess acetic acid (15ml.) was distilled off and the green solution poured into water (50ml.). The solid which separated was removed by filtration and recrystallised from acetic acid to give orange-yellow needles (0·25g.) of fluorenone-1-carboxamide, m.p. 230-32°.

The compound was identified by a mixed melting point determination (m.p. 230-32°) with a sample of fluorenone-1-carboxamide prepared[83] from fluorenone-1-carboxylic acid via the acid chloride in the normal manner.

Boiling the amide with concentrated hydrochloric acid for one hour gave fluorenone-1-carboxylic acid.

SECTION IV - PART III

The Reduction of 2-azafluoranthene.

Reduction of 2-azafluoranthene with lithium aluminium hydride.

A solution of 2-azafluoranthene (0·5g.) in ether (25ml.) was added to a suspension of lithium aluminium hydride (0·25g.) in ether (10ml.) at room temperature, and the mixture was boiled for 4 hours. The reaction complex and excess hydride were decomposed with alkali in the normal manner, and the ethereal filtrate was evaporated to dryness to give 0·45g. of a white solid product. The product crystallised in amorphous form, m.p. 110-115°, from a 2:1 benzene-light petroleum mixture. The compound rapidly darkened on storage in a desiccator.

IR Spectrum: τ 3305cm^{-1}. (m) (NH).

1620cm^{-1}. (m) (enamine C=C).

NMR Spectrum: τ 2·02-3·12 (complex. aromatic protons).

The compound failed to give an acetyl derivative on boiling with acetic anhydride.

The product formed a picrate in ethanol solution. Recrystallisation from glacial acetic acid gave yellow plates, m.p. 271-74°.

Analysis: found: C: 58·6% H: 3·0% N: 11·8%.

$C_{21}H_{14}N_4O_7$ requires: C: 58·1% H: 3·3% N: 12·9%.

Reduction of 2-azafluoranth-3[2H]one with lithium aluminium hydride.

2-Azafluoranth-3[2H]one (0·5g.) and lithium aluminium hydride (0·25g.) were combined in tetrahydrofuran and boiled for 13 hours to give a white solid product (0·4g.), m.p. 102-120°. The compound crystallised in amorphous form, m.p. 105-118°, from

benzene-light petroleum.

IR Spectrum: 3300cm^{-1}. (m) (NH).

1625cm^{-1}. (m) (enamine C=C).

NMR Spectrum: τ 2·15-2·91 (complex. aromatic protons).

The product formed a picrate in ethanol solution, m.p. 270-75°. A mixed melting point with the picrate, m.p. 271-74°, of the product from the reduction of 2-azafluoranthene was not depressed.

Reduction of 2-azafluoranthene with sodium amalgam.

2-Azafluoranthene (0·5g.) was dissolved in gently refluxing ethanol (20ml.) and 5% sodium amalgam (10g.) was added in portions, over ca. 10 minutes. The mixture was boiled for 3 hours, concentrated to 12 ml, and concentrated hydrochloric acid added to bring it to near neutral point before being poured into water (100ml.). The oil which separated was extracted into chloroform, and the chloroform solution was washed, dried and evaporated. The oily product was dissolved in benzene and chromatographed on an alumina column (25g.) made up in light petroleum. Elution with benzene gave an amorphous solid (0·3g.), m.p. 125-30°.

IR Spectrum: 3300cm^{-1}. (m) (broad) (NH).

1610cm^{-1}. (w) (aromatic C=C).

NMR Spectrum: τ 1·81-2·79 (complex. aromatic protons).

The product formed a picrate in ethanol solution. Recrystallisation from ethanol gave yellow plates, m.p. 192-95°.

Analysis: found: C: 57·4% H: 3·7% N: 11·7%.

$C_{21}H_{16}N_4O_7$ requires: C: 57·8% H: 3·7% N: 12·8%.

SECTION V

The Nitration of 2-azafluoranthene.

Nitration of 2-azafluoranthene.

2-Azafluoranthene (2g.) was added to 10% (by vol.) nitric acid (40ml.) and the mixture heated to 35° for 5 minutes to give a clear solution. Cooling in ice gave a yellow solid, which crystallised from ethanol as yellow needles of 2-azafluoranthene nitrate (2·1g.), m.p. 175-81°.

Analysis: found: N: 11·4%.

$C_{15}H_{10}N_2O_3$ requires: N: 10·5%.

NMR Spectrum: τ 1·47 (singlet. 1-H proton).

(D_2O) τ 2·47 (singlet. 3-H proton).

τ 2·60-3·32 (complex. 7 aromatic protons).

The nitrate (2·0g.) was added slowly to concentrated sulphuric acid (10ml.), with cooling of the solution to room temperature. When the addition was complete the solution was set aside at room temperature for 90 minutes and then heated for 20 minutes at 60°, and poured into water (200ml.). The precipitate was removed by filtration, and then boiled with potassium carbonate solution. The product was collected, dried thoroughly, and then boiled with toluene (250ml.). The boiling mixture was filtered to remove insoluble material, and then allowed to cool to room temperature. A yellow solid (0·4g.) separated, m.p. 230-90°, and was removed by filtration. The filtrate was evaporated to dryness to give a yellow solid (0·7g.), which crystallised from ethanol as yellow needles (30%) of 9-nitro-2-azafluoranthene, which sublimed at 198-200°.

The nitrocompound (0·2g.) was dissolved in benzene and chromatographed on a short column of 10% deactivated alumina (10g.). Elution with light petroleum (40-60°) gave a single band (0·16g.) of 9-nitro-2-azafluoranthene. The product was sublimed in a small sublimation apparatus, and the sublimate was recrystallised from benzene to give yellow needles subliming at 198-200°.

Analysis: found: C: 71·6% H: 3·6% N: 10·9%.

$C_{15}H_8N_2O_2$ requires: C: 72·6% H: 3·2% N: 11·3%.

IR Spectrum: 1530cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

UV Spectrum: 226(4·55)267(4·22)302(4·27)358(4·03)376(4·08).

NMR Spectrum: τ 0·60-1·75 (degenerate) (aromatic protons).

(TFA)

The material (1·3g.) insoluble in toluene was heated in a sublimation apparatus at 160° and 1·0mm. for 3 hours. The sublimate of 9-nitro-2-azafluoranthene was removed and the residue was recrystallised twice from nitrobenzene and once from chlorobenzene to yield 4,9-dinitro-2-azafluoranthene, m.p. 304-5°. The dinitro-compound was dissolved in xylene and chromatographed on a column of neutral alumina (30g.) made up in benzene. Elution with benzene gave 1·0g.(35%) of 4,9-dinitro-2-azafluoranthene, which crystallised from chlorobenzene as yellow needles, m.p. 304-305°.

Analysis: found: C: 62·4% H: 2·8% N: 13·8%.

$C_{15}H_7N_3O_4$ requires: C: 61·4% H: 2·4% N: 14·3%.

IR Spectrum: 1535cm^{-1}.(s) and 1350cm^{-1}.(s) (NO_2).

UV Spectrum: 225(4·57)255(4·31)298(4·28)372(4·16).

NMR Spectrum: τ 0·58-0·85 (complex. 3 aromatic protons 1-H, 3-H, and H-ortho to (NO_2))
(TFA) τ 1·10-1·72 (complex. 4 aromatic protons).

It should be noted that, as can be seen from the analyses figures, the two nitro-compounds were not 100% pure. This is probably a result of a slightly imperfect separation of the mono- and dinitro-compounds, which proved to be a difficult procedure. However, as can be seen from the work outlined below, the amount of impurity was very low.

Oxidation of 9-nitro-2-azafluoranthene.

The nitrocompound (0·4g.) was boiled with chromium trioxide (0·8g.), water (0·4ml.) and glacial acetic acid (15ml.) for 2 hours. The cooled solution was poured into water (80ml.), and the precipitate which separated was removed by filtration. Recrystallisation from glacial acetic acid gave pale yellow needles (0·2g.) of 7-nitrofluorenone-1-carboxamide, m.p. 283-85°. The product did not depress the melting point of a sample of the above amide prepared by the method of Koelsch and Steinhauer.[5] The IR spectra of the two amides were identical.

A suspension of the product (0·16g.) from the above oxidation in water (0·3ml.) was treated with potassium hypobromite from 0·04ml. of bromine, 2·8ml. of water and 0·21g. of potassium hydroxide. The mixture was shaken for 90 minutes, then mixed with 0·3g. of potassium hydroxide and heated for 1 hour at 80°. The cooled solution was poured into water (20ml.) and the solid which precipitated was removed by filtration. The product was washed with water and dried to give 0·04g. of orange-red crystals,

m.p. 255-59°, of 1-amino-7-nitrofluorenone (Lit.[5] m.p. 261-63°).

IR Spectrum: 3500cm^{-1}. (w) and 3350cm^{-1}. (w) (NH_2).
1700cm^{-1}. (s) (9-fluorenone C=O).
1530cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

A solution of the nitroaminoketone (0·036g.) in concentrated sulphuric acid (1ml.) was treated with glacial acetic acid (0·4ml.). The resulting solution was cooled in an ice-salt bath and treated with finely powdered sodium nitrite (0·020g.). The mixture was shaken occasionally and kept at 0° for 30 minutes. Ice-cold 50% hypophosphorous acid (1ml.) was then added and the solution was kept at 0° for a further 24 hours. Gas evolution was detected during the first 4 hours.

The solution was poured into water (25ml.), and the precipitate which separated was extracted into chloroform. The chloroform solution was washed with dilute sodium bicarbonate, then with water, dried and evaporated to give a yellow oil (0·016g.). The oil was dissolved in benzene and chromatographed on a column of alumina (5g.) made up in light petroleum. Elution with benzene gave a yellow oil (0·008g.) which crystallised from light petroleum as yellow needles of 2-nitrofluorenone, m.p. and mixed m.p. with an authentic sample,[115] 220-22°.

Preparation of 7-nitrofluorenone-1-carboxylic acid (CLV).

(i) By the method of Garascia.[114]

Finely divided fluorenone-1-carboxylic acid (2·0g.) was added in small portions with constant stirring at room temperature to a mixture of concentrated sulphuric acid (10ml.) and concentrated nitric acid (10ml.)(d.1·42) over a period of

20 minutes. The mixture was then stirred for an additional 1 hour at 35°, cooled and poured into iced water. The precipitate was removed, washed with water, dried and recrystallised from glacial acetic acid to yield yellow crystals (1·6g.), m.p. 255-75°. Garascia claimed to isolate yellow needles of 7-nitrofluorenone-1-carboxylic acid, m.p. 245-46°, by this procedure.

The nitration product (1·0g.) was dissolved in quinoline (5ml.) and copper powder (0·1g.) was added. The mixture was heated in an oil bath for 30 minutes at 175-80°, filtered hot, and poured into 20% (by vol.) hydrochloric acid (100ml.). The product was filtered, stirred in 10% sodium hydroxide solution, washed with water, dried and dissolved in toluene. The toluene solution was chromatographed on alumina (30g.). Development with benzene yielded a bright yellow band, which gave yellow needles (0·4g.) of 2,7-dinitrofluorenone,[116] m.p. and mixed m.p. 290-92°.

(ii) By the method of Koelsch.[5]

A solution of fluorenone-1-carboxylic acid (1·9g.) in concentrated sulphuric acid (5ml.) was stirred and kept <30° while a solution of sodium nitrate (0·75g.) in concentrated sulphuric acid (4·5ml.) was added. After 1 hour, the mixture was poured into water, and the precipitate removed and boiled with 10% sodium hydroxide (30ml.). The resulting solution was cooled and filtered, and the residue was dissolved by boiling with 1·0g. of sodium hydroxide in 350ml. of water. Filtration then removed a dark impurity, and acidification gave a yellow solid,

(1·3g.). Recrystallisation from glacial acetic acid gave golden-yellow needles, m.p. 243-45°. (Lit. 242-44°). Decarboxylation with copper in quinoline gave 2-nitrofluorenone,[115] m.p. 220-22°.

Analysis: found: C: 62·1% H: 2·9% N: 5·4%.

$C_{14}H_7NO_5$ requires: C: 62·5% H: 2·6% N: 5·2%.

IR Spectrum: 2760cm^{-1}. (m) and 2630cm^{-1}. (m) (bonded OH).

1730cm^{-1}. (s) (carboxyl C=O).

1665cm^{-1}. (s) (9-fluorenone C=O).

1530cm^{-1}. (s) and 1340cm^{-1}. (s) (NO_2).

Acid chloride.

Acid (0·4g.) boiled with thionyl chloride (10ml.) for 2 hrs. Excess thionyl chloride was removed and the yellow residue was triturated with light petroleum and filtered. The product was recrystallised from benzene to give yellow cubic prisms (0·3g.), m.p. 198-205°.

Analysis: found: Cl: 12·2%.

$C_{14}H_6NO_4Cl$ requires: Cl: 12·3%.

IR Spectrum: 1775cm^{-1}. (s) (acid chloride C=O).

1715cm^{-1}. (s) (9-fluorenone C=O).

1530cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

Amide.

Acid chloride (0·25g.) was stirred overnight in concentrated ammonia (10ml.), and the mixture was filtered, and the product washed thoroughly at the filter with water. Drying and recrystallisation from acetic acid gave pale yellow needles (0·20g.), m.p. 283-85°.

Analysis: found: C: 62·6% H: 3·2% N: 10·3%.

$C_{14}H_8N_2O_4$ requires: C: 62·7% H: 3·0% N: 10·5%.

IR Spectrum: 3390cm^{-1}. (m) and 3195cm^{-1}. (m) (NH_2).

1708cm^{-1}. (s) (9-fluorenone C=O).

1645cm^{-1}. (s) (amide C=O).

1542cm^{-1}. (s) and 1348cm^{-1}.(s) (NO_2).

A mixed melting point with the product obtained from the oxidation of 9-nitro-2-azafluoranthene with chromium trioxide showed no depression. The IR spectra of the two amides were identical.

Ethyl Ester.

Acid chloride (0·11g.) was boiled with ethanol for 2 hours. The cooled solution deposited a yellow solid, which crystallised from ethanol as pale yellow prisms (0·09g.), m.p. 144-46°.

Analysis: found: C: 64·2% H: 3·7% N: 4·3%.

$C_{16}H_{11}NO_5$ requires: C: 64·6% H: 3·7% N: 4·7%.

IR Spectrum: 1725cm^{-1}. (s) (broad) (ester C=O and 9-fluorenone C=O).

1535cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

NMR Spectrum: τ 1·38-2·28 (complex. 6 aromatic protons).

(TFA) τ 5·33 (quartet. J = 7 c/s. 2 methylene protons).

τ 8·48 (triplet. J = 7 c/s. 3 methyl protons).

It is interesting that the ethyl 7-nitrofluorenone-1- carboxylate obtained by Garascia[114] melted at 149°. It appears that he did indeed synthesise the 7-nitro-acid, but the present author found that his method was not reproducible.

Boiling 7-nitrofluorenone-1-carboxyamide with concentrated hydrochloric acid gave 7-nitrofluorenone-1-carboxylic acid.

Oxidation of 4,9-dinitro-2-azafluoranthene.

Nitro-compound (0·4g.) was boiled with chromium trioxide (0·8g.), water (0·4ml.) and glacial acetic acid (15ml.) for 2 hours, and then poured onto water. The precipitate was filtered, and recrystallised from nitrobenzene to give pale yellow needles (0·25g.) of 2,7-dinitrofluorenone-1-carboxamide, m.p. 320-25°. The product did not depress the melting point of a sample of the amide prepared from 2,7-dinitrofluorenone-1-carboxylic acid. The IR spectra of the two amides were identical.

Preparation of 2,7-dinitrofluorenone-1-carboxylic acid[9] (CLIX).

Potassium nitrate (2g.) was added over a period of 5 minutes to a well-stirred solution of fluorenone-1-carboxylic acid (2g.) in concentrated sulphuric acid (10ml.) at room temperature. After a further 5 minutes stirring, the mixture was warmed on a water bath to 80°, maintained at this temperature for 5 minutes, and then poured into iced water (200ml.). The yellow solid which separated was filtered, washed thoroughly with water and dried. Recrystallisation from glacial acetic acid gave yellow cubic prisms (1·2g.), m.p. 268° (dec.).

Analysis: found: C: 53·6% H: 2·3% N: 9·0%.

$C_{14}H_6N_2O_7$ requires: C: 53·6% H: 1·9% N: 8·9%.

IR Spectrum: 2680cm^{-1}. (w) (broad) (bonded OH).

1725cm^{-1}. (s) (broad) (carboxyl C=O and 9-fluorenone C=O).

1540cm^{-1}.(s) and 1355cm^{-1}.(s) (NO_2).

Preparation of the acid by the method of Temple,[150] in which the reaction mixture was heated at 80° for 1 hour prior to pouring

into water, gave a product of poor crystalline quality, m.p. 190-260°.

Acid chloride.

Acid (1·0g.) was boiled with thionyl chloride for 2 hours to give yellow cubic prisms (0·8g.), m.p. 205-210° (from benzene).

Analysis: found: Cl: 10·8%.

$C_{14}H_5N_2O_6Cl$ requires: Cl: 10·7%.

IR Spectrum: 1790cm^{-1}. (s) (acid chloride C=O).

1730cm^{-1}. (s) (9-fluorenone C=O).

1545cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

Amide.

Prepared by stirring acid chloride (0·3g.) overnight in concentrated ammonia. Recrystallisation from nitrobenzene gave pale yellow needles (0·2g.), m.p. 320-25° (dec.).

Analysis: found: C: 53·7% H: 2·7% N: 13·2%.

$C_{14}H_7N_3O_6$ requires: C: 53·7% H: 2·3% N: 13·4%.

IR Spectrum: 3430cm^{-1}. (s) and 3310cm^{-1}. (s) (NH_2).

1710cm^{-1}. (s) (9-fluorenone C=O).

1670cm^{-1}. (s) (amide C=O).

1545cm^{-1}. (s) and 1355cm^{-1}. (s) (NO_2).

A mixed melting point with the amide obtained from the oxidation of 4,9-dinitro-2-azafluoranthene with chromium trioxide showed no depression. The IR spectra of the two amides were identical.

Ethyl Ester.

Prepared by boiling the acid chloride (0·3g.) with ethanol for 1 hour. Recrystallisation from ethanol gave pale yellow

needles (0·2g.), m.p. 188-9°.

Analysis: found: C: 56·2% H: 3·3% N: 8·1%.

$C_{16}H_{10}N_2O_7$ requires: C: 56·1% H: 3·0% N: 8·2%.

IR Spectrum: 1740cm^{-1}. (s) (broad) (ester C=O and 9-fluorenone C=O).

1540cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

NMR Spectrum: τ 1·21-1·35 (complex. 3 aromatic protons).

(TFA) τ 1·77-1·96 (complex. 2 aromatic protons).

τ 5·14 (quartet. J = 7 c/s. 2 methylene protons).

τ 8·42 (triplet. J = 7 c/s. 3 methyl protons).

Decarboxylation of 2,7-dinitrofluorenone-1-carboxylic acid.

The acid was decarboxylated with quinoline and copper powder at 175-80°. The product was chromatographed on alumina to yield yellow crystals of 2,7-dinitrofluorenone, m.p. 290-92°.

The dinitroketone was prepared for comparison by the oxidation of 2,7-dinitrofluorene. The latter nitrocompound was obtained from the nitration[116] of fluorene by the method of Courtot, and was shown from a melting point determination to be free from contamination by 2-nitrofluorene, m.p. 154°. 2,7-Dinitrofluorene crystallised from nitrobenzene as light orange needles, m.p. 290-95°(dec.), and was oxidised with chromium trioxide in glacial acetic acid to yield yellow needles of 2,7-dinitrofluorenone, m.p. 290-92° (from glacial acetic acid); mixed m.p. 290-92° with product from decarboxylation.

2,7-Dinitrofluorenone prepared by the nitration[151] of fluorenone with fuming nitric acid was found to contain 2-nitrofluorenone, m.p. 220-22°, as an impurity, which could not be efficiently removed by repeated recrystallisation from glacial acetic acid.

Attempted hydrolysis of 2,7-dinitrofluorenone-1-carboxamide.

(i) Hydrochloric acid/acetic acid.

The amide (40mg.) was boiled with glacial acetic acid (2·0ml.) and concentrated hydrochloric acid (1·0ml.) for 20 minutes. A further 4·0ml. of concentrated hydrochloric acid was added to the boiling mixture over a period of 30 minutes, and boiling was continued for a further 1 hour. The cooled mixture was poured onto iced water to give 30mg. of starting-material.

(ii) Acetic acid/sulphuric acid/water.

The amide (30mg.) was boiled with 2ml. of a 1:1:1 mixture of acetic acid:sulphuric acid: and water for 2 hours, and then poured into iced water. Filtration gave 25mg. of recovered amide, m.p. 320-25°.

(iii) Nitrous acid in acetic acid.[117]

Hydrogen chloride was bubbled through a solution of the amide (40mg.) in acetic acid (30ml.). Isoamyl nitrite (0·20ml.) was added to the solution, which was then set aside at room temperature for 1 hour. The temperature was raised to 80° for 1 hour, and finally the mixture was boiled for 90 minutes. Acetic acid (20ml.) was distilled off, and the residue poured into water to yield (30mg.) of starting-material, m.p. 318-325°.

Attempted Hofmann degradation of 2,7-dinitrofluorenone-1-carboxamide.

(i) Concentrated hydrochloric acid (10ml.) was added to potassium permanganate (1·08g.), and the chlorine gas evolved was passed into an ice-cold solution of sodium hydroxide (4·32g.) in water (80ml.). The amide (0·16g.) was added to 2·2ml. of this solution and the mixture kept ice-cold and stirred for 2 hours. The mixture

was then heated at 80° for 3 hours, cooled and made strongly basic by the addition of 50% sodium hydroxide solution. The product was filtered, washed with water and dried to yield 0·11g. of starting-material.

(ii) The amide was recovered unchanged after heating with potassium hypobromite [p.168] at 80° for 2 hours.

Attempted oxidation of 9-nitro-2-azafluoranthene with potassium permanganate.

A suspension of the nitro-compound (0·2g.) in water (5ml.) was boiled while 3% aqueous potassium permanganate (35ml.) was slowly added over a period of 2 hours. The mixture was boiled for a further 3 hours, cooled, and treated with sulphur dioxide until all the precipitated manganese dioxide had dissolved. A precipitate of 80mg. of 9-nitro-2-azafluoranthene, m.p. 196-98°, separated.

The filtrate was concentrated to 15ml., but no organic material separated.

Reduction of 9-nitro-2-azafluoranthene.

Hydrazine hydrate (2ml.) and 10% palladium-charcoal were added to a solution of the nitro-compound (0·2g.) in a mixture of ethanol (20ml.) and toluene (60ml.) at 90°. The mixture turned deep red in colour, and was heated on a boiling water bath for 3 hours. The cooled mixture was filtered, and the filtrate evaporated to dryness. The residue was diluted with water (20ml.), and the product was filtered and dissolved in toluene (10ml.). The toluene solution was chromatographed on a column of 10%

deactivated alumina (10g.) made up in light petroleum. Elution with a 4:1 mixture of benzene-light petroleum gave orange crystals, which crystallised from benzene as orange needles (40mg.) of 9-amino-2-azafluoranthene, m.p. 173-75°.

Analysis: found: N: 13·9%.

$C_{15}H_{10}N_2$ requires: N: 12·8%.

IR Spectrum: 3405cm^{-1}. (m) and 3295cm^{-1}. (m) (NH_2).

As suggested from the analysis figures the amine was probably contaminated with a trace of diamino-compound.

Hydrogenation of the nitro-compound in ethyl acetate with 10% palladium-charcoal as catalyst gave a mixture of amino- and nitro-compounds, as indicated by the IR spectrum of the product.

Nitration of 2-azafluoranthene with potassium nitrate in sulphuric acid.

Potassium nitrate (0·1g.) was slowly added to a solution of 2-azafluoranthene (0·2g.) in concentrated sulphuric acid (2ml.). The mixture was set aside at 17-20° for 20 hours, poured into water and the aqueous suspension made alkaline with sodium carbonate. The crude product (0·21g.) was washed with water, dried and extracted with 20ml. of boiling benzene. The filtered benzene solution was evaporated to dryness, and the residue crystallised from benzene-light petroleum to give 10mg. of 9-nitro-2-azafluoranthene, subliming at 197-200°. The insoluble material was recrystallised from chlorobenzene to give 90mg. of 4,9-dinitro-2-azafluoranthene, m.p. 304-5°.

Nitration of 2-azafluoranthene with fuming nitric acid.

2-Azafluoranthene (0·2g.) was dissolved in nitric acid (sp.gr.1·5; 2ml.) and the solution kept at 17-20° for 20 hours, then poured carefully into sodium carbonate solution. The crude product (0·22g.) was washed with water and dried, to give a yellow solid m.p. 250-310°.

IR Spectrum: 1540cm^{-1}. (s) and 1355cm^{-1}. (s) (NO_2).

The mixture of nitro-compounds was extracted with boiling chlorobenzene. The filtered chlorobenzene solution was cooled, and a brown solid product m.p. 255-300° separated. Attempted re-crystallisations from tetralin and nitrobenzene gave similar mixtures, m.p. 250-300°. No further attempts at purification were made.

SECTION VI

The nitration of 1,2-diazafluoranthene.

3-Hydroxy-1,2-diazafluoranthene[9](XXXVI).

Hydrazine hydrate (12ml.) was added to a solution of fluorenone-1-carboxylic acid (20g.) in dioxan (120ml.) and the mixture was boiled for 2 hours and then cooled. The product was recrystallised from glacial acetic acid to give colourless needles, 12g. (60%), m.p. 266-67°. (Lit. m.p. 267°).

IR Spectrum: 3200cm^{-1}. (m) and 3100cm^{-1}. (m) (NH).
1670cm^{-1}. (s) (amide C=O).
1640cm^{-1}. (s) (C=N).

UV Spectrum: 213(4·51)238(4·44)246(4·57)255(4·58)277(3·92)
302(3·93)313(3·98)325(4·03)348(3·89).

The product (0·2g.) was boiled with 4N sodium hydroxide (1ml.), dimethyl sulphate (0·3ml.) and methanol (5ml.) for 2 hours, and then poured into water to give (0·15g.) of 2-methyl-1,2-diazafluoranth-3-one (CLXXIII). Recrystallisation from ethanol gave pale yellow prisms, m.p. 153-55°. (Lit.[142] m.p. 154-55°).

IR Spectrum: 1665cm^{-1}. (s) (C=O).
1630cm^{-1}. (s) (C=N).

UV Spectrum: 214(4·53)238(4·44)246(4·54)257(4·58)279(3·88)
302(3·97)313(3·99)325(4·04)349(3·96).

NMR Spectrum: τ 2·01-2·75 (complex. 7 aromatic protons).
τ 6·15 (singlet. 3 methyl protons).

3-Chloro-1,2-diazafluoranthene (XXXVII).

3-Hydroxy-1,2-diazafluoranthene (12g.) was boiled with phosphorus oxychloride (100ml.) for 3 hours. Excess phosphorus

oxychloride was removed under reduced pressure and the residue poured onto water and brought to pH 8-9 with 10% sodium carbonate solution. The product was dissolved in xylene and chromatographed on alumina (300g.). Development with benzene gave 6g. of yellow needles, m.p. 185-87°. (Lit.[11] m.p. 187-88°).

Boiling a solution of 3-chloro-1,2-diazafluoranthene with sodium in methanol gave colourless needles of 3-methoxy-1,2-diazafluoranthene (CLXXI), m.p. 204-5°. (Lit.[11] 207-8°).

UV Spectrum: 212(4·49)228(4·44)235(4·48)243(4·34)252(4·45)
278(4·21)288(4·27)315(3·89)329(3·72)340(3·77)354(3·79).

Boiling a solution of 3-chloro-1,2-diazafluoranthene with sodium in ethanol gave colourless needles of 3-ethoxy-1,2-diazafluoranthene (CLXXII), m.p. 150-52°.

Analysis: found: N: 11·2%.

$C_{16}H_{12}N_2O$ requires: N: 11·3%.

UV Spectrum: 213(4·47)227(4·42)236(4·45)244(4·21)252(4·43)277(4·19)
288(4·25)316(3·87)327(3·71)339(3·77)355(3·76).

3-Chloro-1,2-diazafluoranthene (0·64g.) and toluene-p-sulphonylhydrazide (0·55g.) were boiled in chloroform for 3 hours, and the blood-red solution was set aside at 0° for 3 days. Evaporation, and crystallisation of the residue from benzene gave 3-chloro-1,2-diazafluoranthene, m.p. 186-88°.

<u>3-Hydrazino-1,2-diazafluoranthene[10](XXXVIII).</u>

3-Chloro-1,2-diazafluoranthene (4·0g.) was boiled with hydrazine hydrate (60ml.) for 15 hours. Cooling caused red needles (3·7g.), to separate.

m.p. 250-55°. (Lit. m.p. 255-56°).

1,2-Diazafluoranthene (XXXIV).

3-Hydrazino-1,2-diazafluoranthene (3·7g.) was stirred with ethanol (300ml.), sodium hydroxide (7·4g.), and mercuric oxide (3·2g.) for 1 hour. The mixture was diluted with water (500ml.) and filtered. The filtrate was concentrated to 500ml. and extracted with chloroform (500ml.). The chloroform solution was washed (water), dried, and evaporated to yield a dark oil, which was dissolved in benzene. The benzene solution was chromatographed on a column of alumina (120g.) made up in light petroleum. Elution with a 4:1 mixture of benzene-light petroleum gave yellow needles (0·35g.), m.p. 178-80°, of 1-cyanofluorenone. (Lit.[10] m.p. 180-81°). Elution with benzene gave 1·8g. of impure 1,2-diazafluoranthene. This was dissolved in boiling ethanol and added to a boiling solution of picric acid (2·0g.) in ethanol. An orange-yellow picrate, m.p. 220-22°, separated. This was shaken with 5% sodium hydroxide solution (25ml.), and the product was extracted into chloroform. Evaporation of the chloroform solution gave a yellow oil, which was dissolved in benzene and chromatographed on alumina (30g.). Elution with benzene gave 1·7g. (53%) of 1,2-diazafluoranthene, pale yellow needles from benzene, m.p. 123-24°. (Lit.[10] 123-25°).

IR Spectrum: 1640cm^{-1}. (m) and 1620cm^{-1}. (w) (aromatic C=C,C=N).

UV Spectrum: 210(4·47)235(4·52)274(4·27)282(4·28)308(3·73) 335(3·51)352(3·58).

NMR Spectrum: τ 0·60 (singlet. 3-H proton).

τ 1·76-2·68 (complex. 7 aromatic protons).

1,2-Diazafluoranthene was recovered unchanged after boiling with 10% ethanolic potassium hydroxide for 16 hours. A similar result was obtained on boiling with excess sodium in ethanol for 10 hours.

Attempted hydrogenolysis of 3-chloro-1,2-diazafluoranthene.

The chloro-compound (0·56g.) was dissolved in dry benzene (90ml.) and treated with sodium acetate (0·21g.) in anhydrous methanol (20ml.), and 0·2g. of 10% palladium on charcoal. The mixture was agitated in an atmosphere of hydrogen (1 atmosphere) at room temperature for 5 hours during which time 100ml. of hydrogen was absorbed, (theoretical 80ml.). The mixture was filtered and the filtrate evaporated. The residue was made alkaline with 5% sodium hydroxide, and the product was extracted into chloroform. The chloroform solution was washed (water), dried, evaporated and the residue dissolved in benzene and chromatographed on alumina (20g.). Development with benzene gave a dark oil, which would not crystallise from benzene-light petroleum mixtures.

Nitration of 1,2-diazafluoranthene.

1,2-Diazafluoranthene (0·5g.) was dissolved in a mixture of concentrated sulphuric acid (2·5ml.) and fuming nitric acid (s.g. 1·50; 2·5ml.) at 0°. The mixture was maintained at this temperature for 20 minutes and then allowed to warm to room temperature during 1 hour. The yellow solution was poured into iced-water (25ml.), and the mixture partly neutralised with 10% sodium hydroxide, and finally made alkaline with 10% sodium carbonate.

The dark green product (0·59g.) was filtered. The mixture of nitro-compounds was extracted with boiling chlorobenzene (50ml.). The filtered chlorobenzene solution deposited yellow needles (0·11g.) on cooling, m.p. 280-305°(dec.).

Analysis: found: C: 57·3% H: 2·2% N: 18·9%.

$C_{14}H_6N_4O_4$ requires: C: 57·2% H: 2·1% N: 19·0%.

IR Spectrum: 1535cm^{-1}.(s) and 1355cm^{-1}.(s) (NO_2).

The chlorobenzene mother liquors were chromatographed on a column of 10% deactivated alumina (10g.) made up in light petroleum. Elution with a 2:1 mixture of benzene-light petroleum gave a yellow solid, which crystallised from chlorobenzene as yellow prisms (0·035g.), m.p. 248-50°.

Analysis: found: C: 64·3% H: 2·4% N: 17·8%.

$C_{14}H_7N_3O_2$ requires: C: 67·5% H: 2·8% N: 16·9%

IR Spectrum: 1535cm^{-1}(s) and 1345cm^{-1}(s) (NO_2).

The fingerprint regions of the IR spectra of the two nitro-compounds were different.

Oxidation of dinitro-1,2-diazafluoranthene.

The nitrocompound (60mg.) was boiled with chromium trioxide (0·2g.), water (0·2ml.) and acetic acid (3ml.) for 1 hour, and the mixture poured into water. A yellow acidic compound (10mg.) separated, m.p. 280-295°.

Analysis: found: N: 15·8%

Obviously a mixture of nitro-acids.

IR Spectrum: 3310cm^{-1}.(w) (broad) (bonded OH).

1700cm^{-1}.(s) (carboxyl C=O).

1540cm^{-1}.(s) and 1355cm^{-1}.(s) (NO_2).

3-Hydroxy-9-nitro-1,2-diazafluoranthene.[143] (CLXXVIII).

7-Nitrofluorenone-1-carboxylic acid (10g.) was dissolved in dioxan (200ml.) and hydrazine hydrate (20ml.) was added. The mixture was boiled for 1 hour, and an orange-yellow solid (7·3g.) separated, m.p.>320°.

IR Spectrum: 3180cm^{-1}. (m) and 3110cm^{-1}. (m) (NH).
1700cm^{-1}.(s) (amide C=O).
1540cm^{-1}.(s) and 1350cm^{-1}.(s) (NO_2).

3-Hydroxy-4,9-dinitro-1,2-diazafluoranthene (CLXXIX).

Hydrazine hydrate (2ml.) was added to a solution of 2,7-dinitrofluorenone-1-carboxylic acid (0·8g.) in dioxan (20ml.) and the mixture boiled for 1 hour. Red crystals (0·4g.) separated, m.p. >320°.

Analysis: found: N: 18·2%.
$C_{14}H_6N_4O_5$ requires: N: 18·1%.

IR Spectrum: 3390cm^{-1}. (m) and 3200cm^{-1}. (m) (NH).
1685cm^{-1}. (s) (amide C=O).
1540cm^{-1}. (s) and 1350cm^{-1}. (s) (NO_2).

Both (CLXXVIII) and (CLXXIX) were extremely insoluble in benzene, toluene, chlorobenzene and acetic acid. They were both recovered unchanged after boiling with a mixture of phosphorus oxychloride and phosphorous pentachloride.

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