RESEARCHES IN THE AZAFLUORANTHENE SERIES.

by

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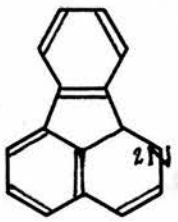
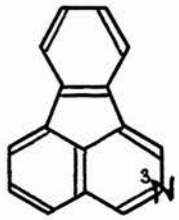
I N D E X

INTRODUCTION.

Of the five theoretically possible, isomeric mono-azafluoranthenes (formulae I-V), there was known, at the commencement of the studies detailed in this thesis, only the 2-azafluoranthene (I). This polynuclear heterocycle



I



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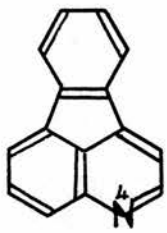

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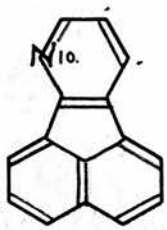

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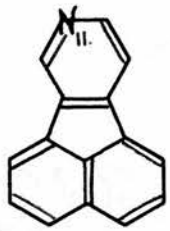
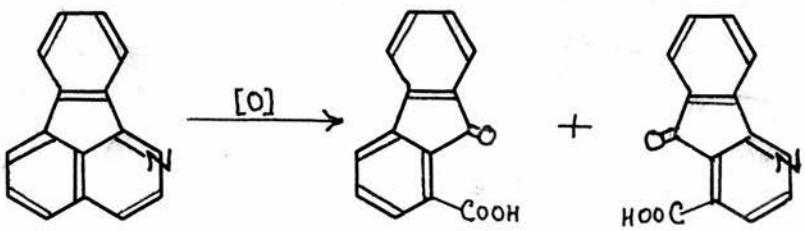


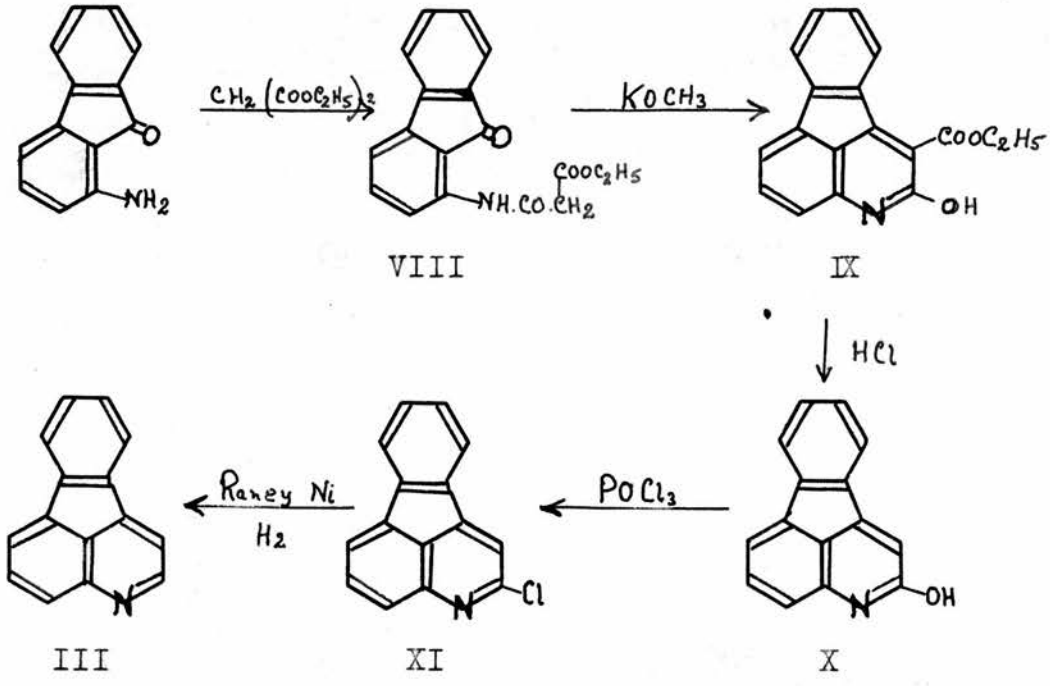
V

had been isolated from the high-boiling, fluoranthene-pyrene fraction of coal tar by Kruber (1) who had elucidated its structure, using potassium permanganate to effect its oxidative break-down into the known fluorenone-1-carboxylic acid (VI) and 4-azafluorenone-1-carboxylic acid (VII).

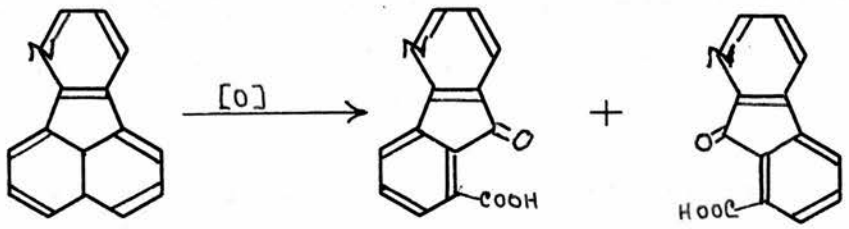


I VI VII

Since then, the total synthesis of 4-azafluoranthene (III) by Koelsch and Steinhauer (2), and the discovery by Oberkobusch (3) of 10-azafluoranthene (IV) in coal tar have been announced. The course of the synthesis of the 4-isomer, followed by Koelsch and Steinhauer, was taken independently by Cook and Moffatt (4) who proceeded as far as the 3-chloro compound (XI), with which they condensed ammonia and a variety of amines. Both pairs of workers reacted diethyl malonate with 1-amino-fluorenone to obtain (VIII) which was then cyclized under the influence of sodium methoxide to the ester of 3-hydroxy-4-azafluoranthene-2-carboxylic acid (IX), which in turn yielded (X). Reduction of the 3-chloro compound, obtained by the action of phosphoryl chloride on (X), was carried through by the former pair of workers who thus isolated the parent heterocycle.



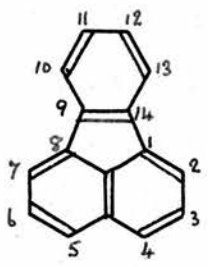
Oberkobusch established the structure of 10-azafluoranthene by oxidation with potassium permanganate, obtaining the 5-aza- and 8-aza-fluorenone-1-carboxylic acids, (XII) and (XIII), respectively; the former he decarboxylated to the known 4-azafluorenone.



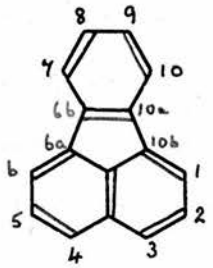
IV XII XIII

2-Azafluoranthene is a pale yellow compound, m.p. 91-92°C and not 83°C as stated initially by Kruber. It does not appear to possess the two melting-points, 83°C and 91°C, as Oberkobusch has reported (loc.cit.), and indeed Dr. Kruber in a personal communication has confirmed that the sample melting at 83°C was contaminated with the 10-isomer. So also, the picrate melts at 239°C, not at 223°C. 4-Azafluoranthene is a yellow compound, m.p. 102-103°C; and the 10-isomer a colourless compound, m.p. 96-97°C.

As for fluoranthene itself, there are two current systems of numbering the nitrogen and carbon atoms of the azafluoranthenes, and these are shown in formulae A and B.



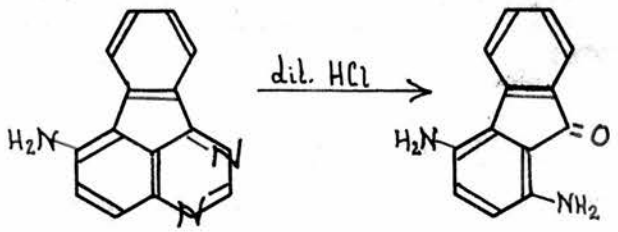
A



B

The former is adopted by European chemists and is in accordance with the Richter system of notation; the latter is employed in Chemical Abstracts, but enumerations based upon it have, in this thesis, been translated into those conforming to system A.

The only simple polyazafluoranthene known is the 2,4-diazafluoranthene, obtained by Cook and Moffatt (loc.cit.) in low yield, by reacting 1-aminofluorenone with boiling formamide. The monoazafluoranthenes, as so far studied, are not susceptible to hydrolytic fission by mineral acids but the 2,4-diazafluoranthene nucleus is rapidly cleaved by hot, dilute hydrochloric acid, as illustrated by 7-amino-2,4-diazafluoranthene which yields 1,4-diaminofluorenone:-



The researches on the azafluoranthenes were undertaken with the ultimate aim of examining the effects of the nuclear

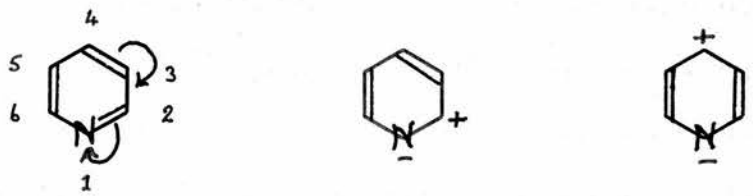
hetero atom upon the fluoranthene structure, and particularly the correlative interactions of the nitrogen atom and the five-membered ring; however, the more immediate object has been the exploration of routes leading to the syntheses of the heterocycles.

Of the five monoazafluoranthenes, the 2- and 3-isomers may be regarded as 1,8-(o-phenylene)- and 4,5-(o-phenylene)-isoquinoline respectively; the 4-isomer as 4,5-(o-phenylene)-quinoline; and the 10- and 11-isomers as respectively the 2,3- and 3,4-(1:8 acenaphthenyl)-pyridines. Accordingly, although the strong electron-attracting nature of the five-membered ring may be supposed to influence the behaviour of the nitrogen atom, it is likely that the azafluoranthenes will possess properties, and enter into reactions, which consist with their formal relationships to the heterocycles isoquinoline, quinoline and pyridine respectively, and the remainder of this Introduction will be such an account of the chemistry of these simple heterocycles, and of fluoranthene, as may be thought to justify an a priori consideration of the chemistry of the azafluoranthenes themselves. Deviations from the expected behaviour will be considered in the Discussion of the present author's own experimental results. For convenience, the succeeding account will be under the heads: Substitution Reactions; Behaviour of Substituent Groups; Reduction; Quaternary Salts; and, Methods of Ring Cleavage.

SUBSTITUTION REACTIONS.

a) Of Pyridine.

The powerful electron attraction of the ring nitrogen atom results in an electron displacement from the 2- and 4-positions of the pyridine nucleus, the 3-position being considerably less affected. Accordingly, pyridine suffers

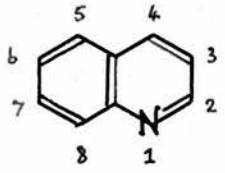


electrophilic (cationoid) substitution (nitration, bromination, sulphonation and mercuration) at the latter position, though with much greater difficulty than benzene, whilst nucleophilic (anionoid) reagents, such as sodamide, alkali hydroxides and organo metallic compounds, attack preferentially the 2-position. The former type of substitution is greatly facilitated by the presence, in the nucleus, of o,p-directing groups, though never to such an extent that an activated pyridine will undergo the Friedel-Crafts reaction; on the other hand, the presence of a +E group will so deactivate the system that further electrophilic substitution is difficult or impossible, unless a -E group also is present. In this connection, it is evident that such substitution will be retarded in a protonating medium, relative to a neutral medium, for in the former case it is the positively charged pyridinium ion that is being attacked.

Substitution of the pyridine nucleus by free radicals is illustrated by the Gromberg-Bachmann coupling reaction with phenyldiazonium chloride (5), in which the main product is 2-phenyl pyridine, the 3- and 4-isomers being formed but in low yield. Bromination of pyridine at 500 C, by supposed free radical substitution, furnishes the 2-bromo and 2,6-dibromo compounds (6).

b) Of Quinoline.

The behaviour of the hetero ring of the quinoline nucleus towards nucleophilic and electrophilic reagents parallels that of pyridine itself, so that electrophilic reagents, excepting the halogens, attack the benzene ring.



The exceptional mode of substitution by halogen gives rise to the 2- or 3-halogen derivative, depending on the halogenating reagent and on the reaction temperature. Thus quinoline is brominated in the vapour phase over pumice at 300°C to furnish 3-bromoquinoline in 25% yield; at 450-500°C the product is 2-bromoquinoline, obtained in 50-60% yield (7).

Although electrophilic substitution does take place in the benzene ring, no conclusive rationalization of the behaviour of quinoline in such substitution reactions has been hitherto achieved. The attempt at generalization made

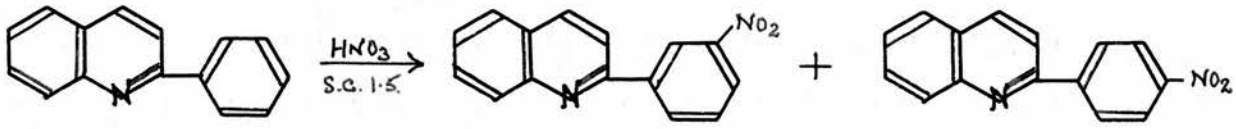
by Huisgen (8) is, therefore, perhaps best omitted here, and the mere facts which seem to be most relevant to a correlation of quinoline and the azafluoranthenes, alone given.

Nitration of quinoline in mixed acid produces a mixture of the 5-nitro- and 8-nitroquinolines; further nitration, under forcing conditions, gives rise to the 5,7- and 6,8-dinitro derivatives respectively, the nitro group initially present exerting a normal meta-orienting influence. However, this same influence is modified to some extent during the further nitration, again under forcing conditions, of 6-nitro- and 7-nitroquinoline respectively, this resulting in the production of the two mixtures, namely, of 5,6- and 6,8-dinitroquinoline, and of 5,7- and 7,8-dinitroquinoline (9).

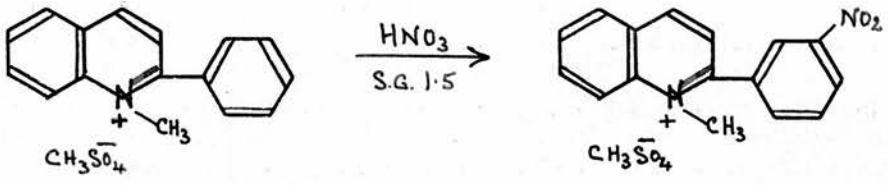
The results of the nitration of quinolines bearing one substituent other than the nitro group again have elicited no satisfactory theoretical explanation; in general, however, the 8-position is most liable to substitution, the 5- and 6-positions also, and in that order, showing a degree of reactivity. Extraordinarily, the 2- and 4-hydroxyquinolines are nitrated in the 3-position, in the absence of sulphuric acid. The results have been summarized by Schofield and Swain (10).

Of more importance to the present discussion is the information which has been derived from the nitration of the 2- and 4-phenylquinolines (11,12). The 2-phenyl derivative (I), on being treated with fuming nitric acid at 0°C, yields a mixture of 2-(m-nitrophenyl)-quinoline (II) and 2-(p-

nitrophenyl)-quinoline (III) in 40 and 60% yield respectively, whilst nitration, under identical conditions, of 2-phenyl-quinolinium methosulphate (IV) yields solely 2-(m-nitrophenyl)-quinolinium methosulphate (V).

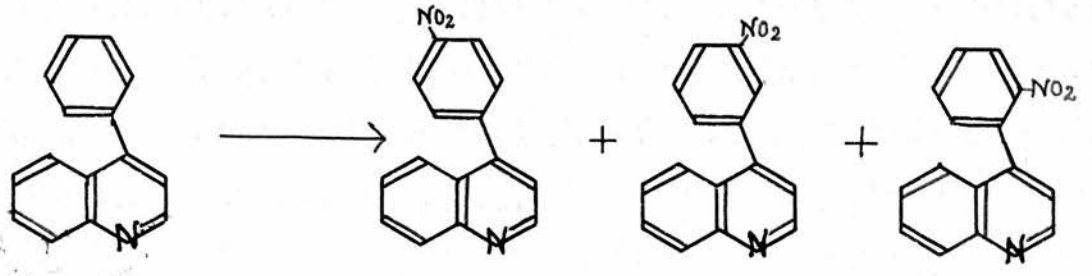


I II 40% III 60%



IV V

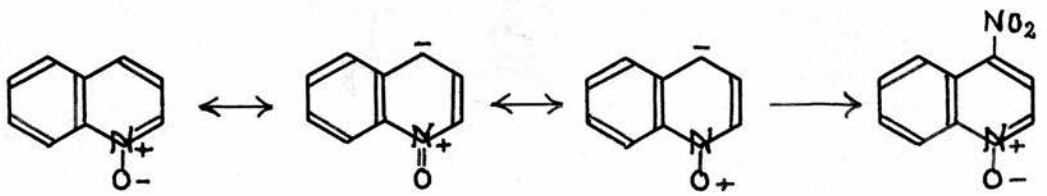
This difference is attributable to the fact that in the latter case the meta-orienting influence of the quinolinium ion is thorough, whereas in the former it is operative only to the extent to which the phenylquinolinium nitrate is formed in the nitrating solution. The sulphonation of 2-phenyl-quinoline is explicable in the same way (13). By analogy, to the three products of the nitration of 4-phenylquinoline (VI) obtained in 50, 40 and 5% yield respectively, it would seem plausible to assign the following structures:



VI 50% 40% 5%

Nevertheless, so long as the above assignment is solely by analogy, no determined comparison of the result of the nitration of 4-phenylquinoline with that of the nitration of 4-azafluoranthene can be made.

A final case of electrophilic substitution, which merits notice, is the nitration of the N-oxide of quinoline (VII), giving rise to 70% of the 4-nitro compound (VIII) and but small amounts of the 5- and 8-nitro derivatives (14). It has been suggested (15) that this substitution at the 4-position is to be ascribed to the contributing resonance forms VII, VIIa, VIIb.



VII VIIa VIIb VIII

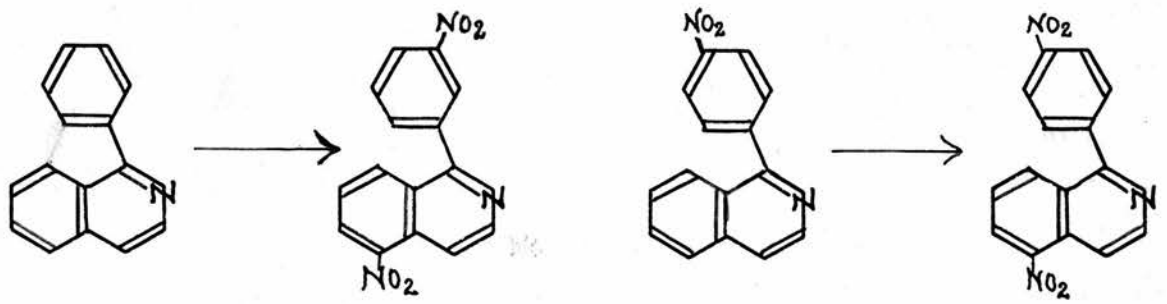
c) Of Isoquinoline.

Towards nucleophilic reagents, of the two positions ortho to the nitrogen atom of isoquinoline, only the 1-position

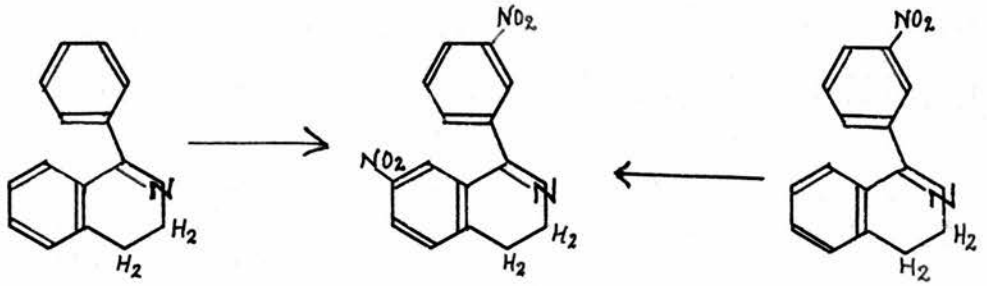
is reactive. This is consistent with the fact that in the neutral isoquinoline molecule the pi-electron density at C_1 is less than at C_3 (16), but the reason for the exclusiveness of substitution at the 1-position is the greater stability of the intermediate transition state leading to the reaction product.

Electrophilic substitution has been observed only at the 5-, 8- and 4-positions. Thus, nitration and sulphonation favour the 5-, then the 8-position; bromination (by heating the perbromide of isoquinoline or its salts (17,18)), and mercuration (19) occur anomalously at the 4-position, nor has a satisfactory explanation been advanced to account for these results.

Nitration (20) of 1-phenylisoquinoline (IX) furnishes the 1-(m-nitrophenyl)-5-nitroisoquinoline (X), whilst 1-phenyl-3,4-dihydroisoquinoline (XI) is nitrated in the 7- and 3'-positions to give (XII) which is also the product of the nitration of 1-(m-nitrophenyl)-3,4-dihydroisoquinoline (XIII). The 1-(p-nitrophenyl)-isoquinoline (XIV) yields the 5-substituted product (XV). Reference to these results will be made later.



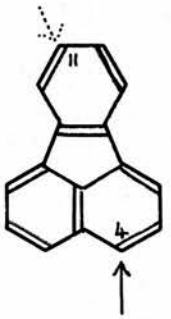
IX X XIV XV



XI XII XIII

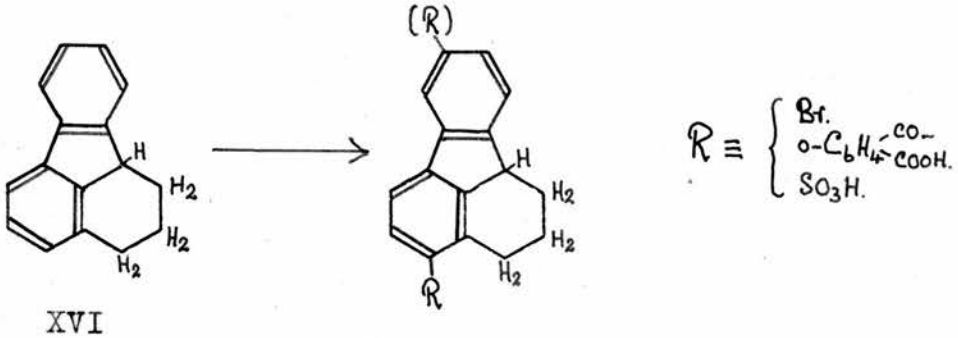
d) Of Fluoranthene.

The preferred site of electrophilic mono-substitution of fluoranthene is the 4-position, although the 11-position also



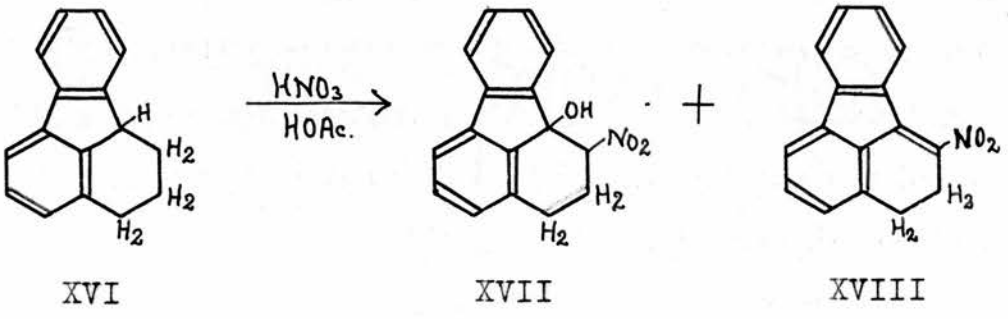
is affected to an extent which varies with the nature of the attacking reagent (21). Thus nitration gives mainly the 4-derivative, but Friedel-Crafts benzoylation results in the formation of approximately equal quantities of the 4- and 11-isomers.

Chlorosulphonation, bromination, and the Friedel-Crafts reaction with phthalic anhydride, occur mainly at the 5-position of 1,2,3,4-tetrahydrofluoranthene, though small amounts of the 11-isomers also are formed (22).

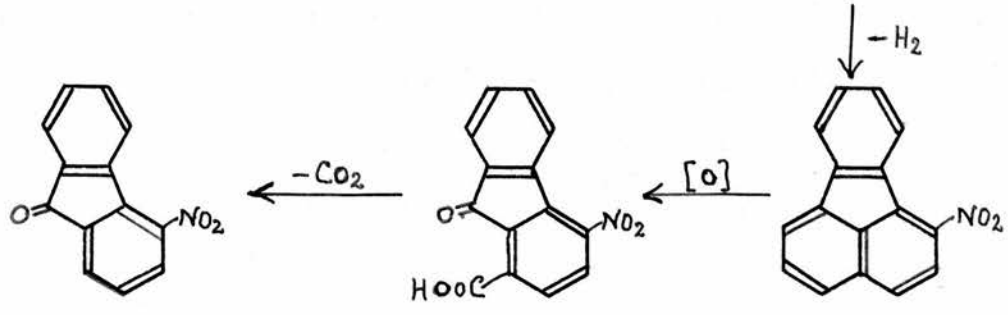


XVI

The course of nitration, however, has been shown to be different from that of the other three,reactions (23), for treatment of the tetrahydrofluoranthene (XVI) with nitric acid in acetic acid gave rise to a mixture of two products, namely 2-nitro-1-hydroxy-1,2,3,4-tetrahydrofluoranthene (XVII), and its dehydration product, 2-nitro-3,4-dihydrofluoranthene (XVIII). The structure of the latter was proved by its dehydrogenation to give 2-nitrofluoranthene (XIX) which was oxidized to the acid (XX), decarboxylation then yielding the 4-nitrofluorenone (XXI).



XVI XVII XVIII



XXI XX XIX

The orientation of a group entering a mono-substituted fluoranthene is still somewhat problematic, but two general rules have been proposed, namely, that if the substituent in the 4-position is meta-directing the second group will enter the 12-position; and that, if it is ortho-para-directing, the second group will enter the 11-position (24). These rules are based upon the facts, 1) that if the 4-substituent is the nitro, cyano, carboxyl, or methoxy-carbonyl group, the compound afforded by mono-bromination is the 12-bromo derivative; 2) that further acetylation of 4-acetylfluoranthene affords the 4,12-diacetylfluoranthene, and disulphonation of the hydrocarbon produces the 4,12-disulphonic acid; and 3) that if the 4-substituent is the bromo, further bromination yields 4,11-dibromofluoranthene. As a possible explanation of these results, Campbell and Keir have suggested the following.

Fluoranthene is 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,

irrespective of the nature and position of the group already present in the first ring, it has been 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 11 and 12 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_{12} (and possibly C_{10}), but an ortho-para-directing group in ring A will increase the directive power of this ring, with consequent substitution at C_{11} (and possibly C_{13}).

It has been suggested recently by Kloetzel, King and Menkes (25) that this explanation is an oversimplification; these authors have effected the nitration of 4-acetylamino-fluoranthene to obtain in very high yield the 3-nitro derivative; that is, the rule proposed by Campbell and Keir appears not to cover the case of intensely activating substituents.

BEHAVIOUR OF SUBSTITUENT GROUPS IN PYRIDINE, QUINOLINE AND ISOQUINOLINE.

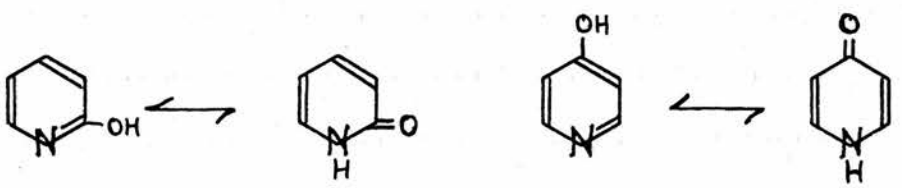
Alkyl, hydroxyl and amino groups, and halogens, in the 2- and 4-positions of pyridine and quinoline, and in the 1-position of isoquinoline, behave differently from the corresponding substituents in aromatic carbocycles, and similarly, the correspondingly substituted azafluoranthenes may be expected to differ from their fluoranthene analogues.

The chemistry of the alkyl groups is determined by the fact that the ring nitrogen atom creates an electron deficit

at these positions, thereby imparting an acidic nature to the hydrogen atoms of an adjacent methyl or methylene group. Consequently, such a group displays a reactivity in typical aldol-type condensation reactions that is not to be met with in the usual carbocyclic derivatives. Further examples of this reactivity are the replacements of such active hydrogen atoms by sodium and lithium, from sodamide and lithium phenyl respectively.

For the same reason, halogen substituents are unusually labile; facilitated attack at the same positions, by nucleophilic reagents such as amines and alkali hydroxides and alkoxides, results in the expulsion of halogen under exceptionally mild conditions. It has been demonstrated (2,4) that the chlorine atom of 3-chloro-4-azafluoranthene is subject to such ready replacement.

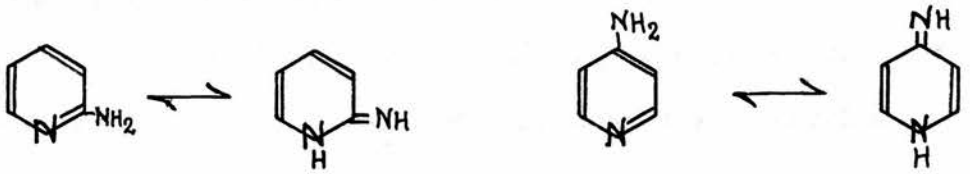
The anomalous behaviour of the hydroxyl groups may be illustrated in the cases of 2- and 4-hydroxy pyridine: it arises from tautomerism (26,27) between the true hydroxypyridine forms (Ia, IIa) and the pyridone forms (Ib, IIb) respectively, and the products of the reactions entered into by the hydroxypyridines conform predominantly to one or other form.



Ia Ib IIa IIb

Thus, methylation of 2-hydroxypyridine with diazomethane yields the 2-methoxypyridine only, but with methyl iodide and a base N-methyl-2-pyridone is obtained. Again, the expected behaviour of the 3-hydroxy group in the substituted 4-azafluoranthene has been observed (2).

Similarly, the 2- and 4-aminopyridines exist tautomerically with the corresponding pyridonimines (IIIb, IVb).



IIIa IIIb IVa IVb

In this case, the effects of the tautomerism are more striking than in the previous one: the 3-aminopyridine forms a di-hydrochloride salt, whilst the 2- and 4-amino pyridines form only a mono-hydrochloride; the 3-isomer undergoes normal diazotisation but the 2-isomer does not, rather furnishing 2-hydroxypyridine; and methylation of the 2-isomer gives rise to the N-methylpyridonimine or the 2-methylaminopyridine, according as the base employed is silver oxide or sodamide.

Two other points may be mentioned here: in general, 2- and 4-alkoxyquinolines display exceptional susceptibility towards acid hydrolysis, to yield the hydroxyquinolines (28); and secondly, it is true that the methyl group in the 3-position of isoquinoline is activated also, though not to the same extent as is that in the 1-position.

REDUCTION.

a) Of Pyridine.

Reduction of pyridine and its derivatives generally results in the formation of the corresponding piperidines, and it is the exceptional cases which merit further remark. Neither 2-hydroxy- nor 2-aminopyridine has been reduced to the piperidine; the former absorbs but two moles of hydrogen to yield the 2-piperidone, the latter appears to yield either pentamethylenediamine (from hydrogenolysis of the ring) or 2-imino-piperidine (29,30).

Certain carboxylic acid or ester derivatives of pyridine have been reduced to the dihydro compounds by amalgamated aluminium in moist ether (31), but the position of the reduced bond is in some doubt, though it does not involve the hetero atom, since varied attempts at acylation have failed. In other cases, sodium hydrosulphite, sodium amalgam and lithium aluminium hydride serve to produce dihydropyridines (32). Sodium and ethanol reduce the fully aromatic ring in certain cases to give tetrahydropyridines in small amount (33). It appears to be likely that the remaining double bond is located in the 3:4-position, and indeed Δ^3-tetrahydropyridines are reported to be difficult to reduce - a noticeable result, when it is remembered that piperidines are the normal reduction products from pyridines.

b) Of Quinoline and Isoquinoline.

Although isoquinoline is reduced by the common reducing

agents (hydrogen plus metal catalyst; metal-hydroxylic solvent combinations) somewhat more difficulty than quinoline, these two heterocycles behave otherwise very similarly towards hydrogenation. The hetero ring is reduced preferentially, and further reduction, that is, of the benzene nucleus, is accomplished with difficulty. Usually the stable products of hydrogenation are the 1,2,3,4-tetrahydro-quinolines and -isoquinolines. It appears that no 3,4-dihydro compound of either series has ever been isolated as the product of reduction; however, consistent with the idea that the 1,2 "double bond" is the first to be saturated, is the fact that 1,2-dihydro-quinolines have been formed (34). On the other hand, Knowles and Watt (35) who have studied the reduction of quinolines by sodium, and sodium and ammonium bromide, in liquid ammonia, have suggested that the dihydroquinolines formed are the 1,4-addition products, arguing that if the products of reaction were the 1,2-dihydro derivatives, subsequent reduction of the C-C double bond conjugated with the benzene ring would be expected to occur, whereas an isolated 2,3-double bond would not [in the quinoline series] be susceptible to reduction. An explanation of these various findings has, therefore, still to be proposed.

N-substituted 1,2-dihydroquinolines and -isoquinolines have been prepared through the reducing action, particularly of lithium aluminium hydride, on the corresponding quaternary salts; the 3,4-double bond is unaffected (36). These compounds, the 3,4-dihydroisoquinolines obtained synthetically (37),

and the quaternary salts of the fully aromatic heterocycles, can all be reduced to the corresponding 1,2,3,4-tetrahydro derivatives with ease.

c) Of Fluoranthene.

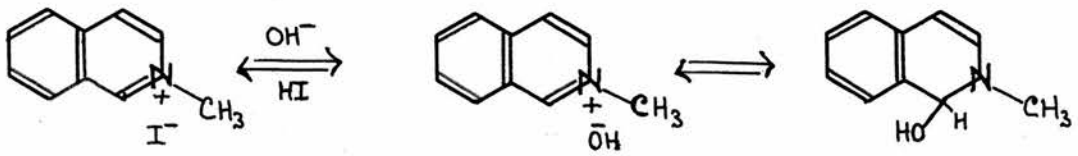
The first product from the reduction of fluoranthene by sodium amalgam and ethanol, or phosphorus and hydriodic acid, or hydrogen over 20 per cent palladium charcoal, is the 1,2,3,4-tetrahydrofluoranthene. Subsequent reduction by the latter two combinations, or by sodium in ethanol, gives the 1,2,3,4, 9,10,11,12,13,14-decahydro derivative, whilst the perhydrofluoranthene results from the sustained catalytic hydrogenation (38).

That is, hydrogen adds primarily to ring A, then to ring C, finally to ring B.

QUATERNARY SALTS.

A reaction, characteristic of the quaternary salts of quinoline and isoquinoline and, to a smaller degree, of pyridine, is the transformation, in alkaline solution, into the corresponding carbinols, or pseudo bases. This is

illustrated in the case of isoquinoline methiodide:

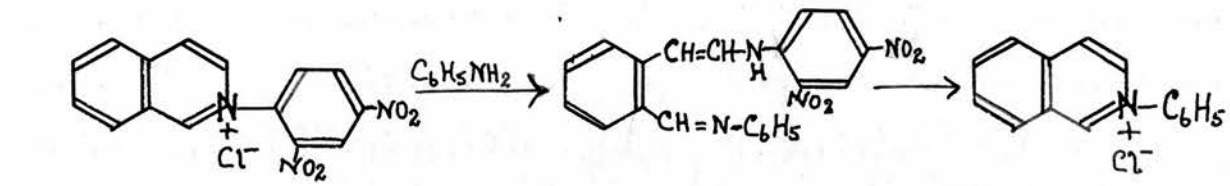


A B C

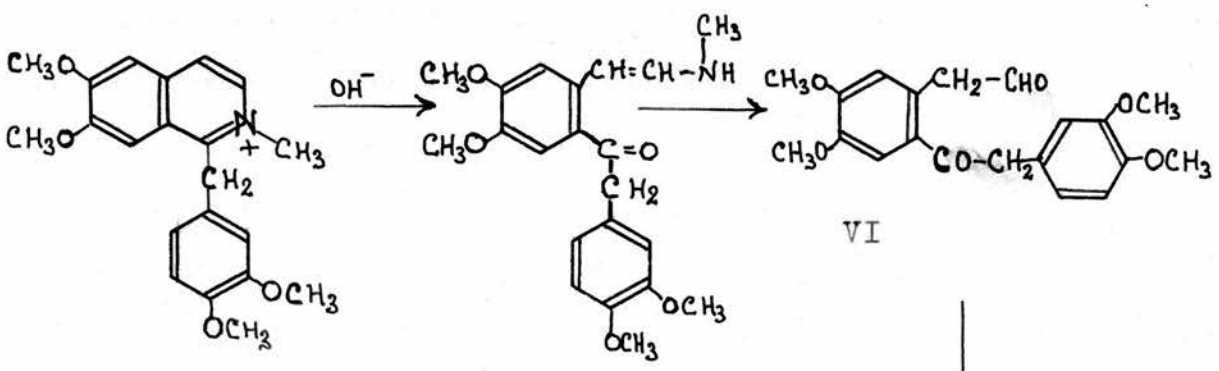
Formula B represents the true base, or ammonium form; formula C represents the pseudo base, or carbinol form, and as the transformation of the salt into the latter is accompanied by the loss of aromaticity throughout the hetero ring, it will occur more readily with quinoline and isoquinoline compounds than with pyridines, where the loss of aromaticity is complete. In fact, the examination of the equilibrium positions in the quaternary ammonium hydroxide: pseudo base interconversions for pyridine, quinoline and isoquinoline respectively, and also for the analogous conversion of the 3,4-dihydroisoquinolinium ion (39,40), demonstrated that the quaternary ammonium hydroxide form is most stable for pyridine, decreasingly so for quinoline, isoquinoline and 3,4-dihydroisoquinoline. Owing to the greater readiness with which the transformation occurs for the two last-named compounds, these have been fairly extensively studied to provide information bearing on the phenomenon; accordingly, evidence relating to the interconversion in their case, will be stated briefly.

Treatment of N-methyl isoquinolinium salts with silver iodide produces the alkaline quaternary ammonium hydroxide which is gradually transformed into the ether-soluble pseudo base;

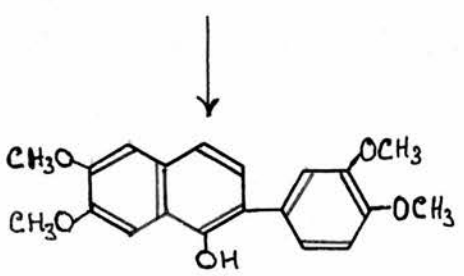
and, a solution of the latter in benzene renders strongly alkaline an aqueous layer in contact with it, the indicated mobile equilibrium between the two forms, ionic and non-ionic, explaining the results obtained in conductance and ultra-violet absorption studies. Evidence exists, however, that the cyclic pseudo base isomerizes to an open-chain form which possesses aldehydic properties: thus oxime formation is possible (41); again, boiling aniline transforms N-(2,4-dinitrophenyl)isoquinolinium chloride (I) into N-phenyl isoquinolinium chloride (III), almost certainly through the open-chain form (II) (42); and the aldehydic form (VI) must be an intermediate in the alkali-induced conversion (43) of the N-methyl papaverinium cation (IV) into the naphthalene derivative (VII).



I II III

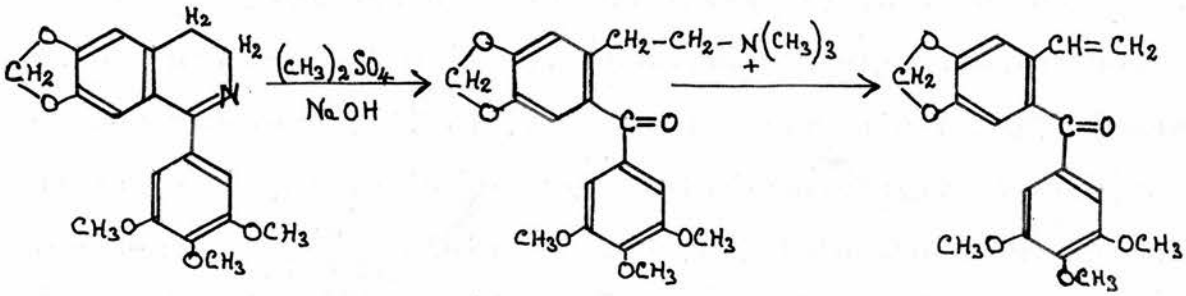


IV V VI



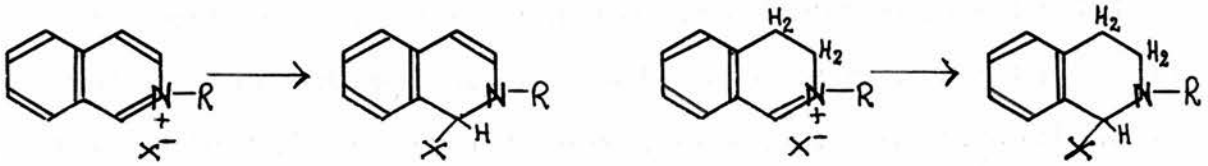
VII

The evidence for the transformation occurring with 3,4-dihydroisoquinolinium salts on their being treated with alkali, is similar to that described above, and there is an obvious parallel between the dihydro and the fully aromatic compounds; and again, the possibility of an open-chain form is encountered. Thus treatment of (VIII) with excess dimethyl sulphate and alkali results in the formation of the vinyl ketone (X), through (IX) undergoing a Hofmann elimination (44).

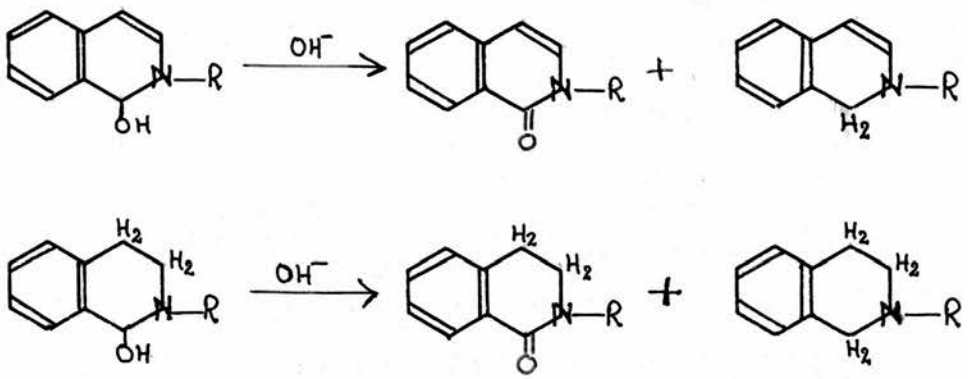


VIII IX X

Since the formation of pseudo bases of cyclic structure can be regarded as a nucleophilic attack by hydroxyl anion at the electron deficient 1-position, whether of the isoquinolinium ion or the 3,4-dihydroisoquinolinium ion, it is to be expected that other anions, for example, the cyanide and ethoxide, whose electronic stabilities more or less resemble that of the hydroxyl ion, will participate in similar nucleophilic additions. This has been realized, with the preparation of a variety of 1-substituted 1,2-dihydroisoquinolines and 1,2,3,4-tetrahydroisoquinolines respectively. Treatment of these compounds with mineral acid (supplying a stable anion) usually regenerates the ammonium ion.



The pseudo bases also undergo disproportionation on treatment with strong alkali to yield the corresponding isocarbostyrils and 1,2-dihydro isoquinolines; and the 1-keto tetrahydroisoquinolines and tetrahydroisoquinolines (45).

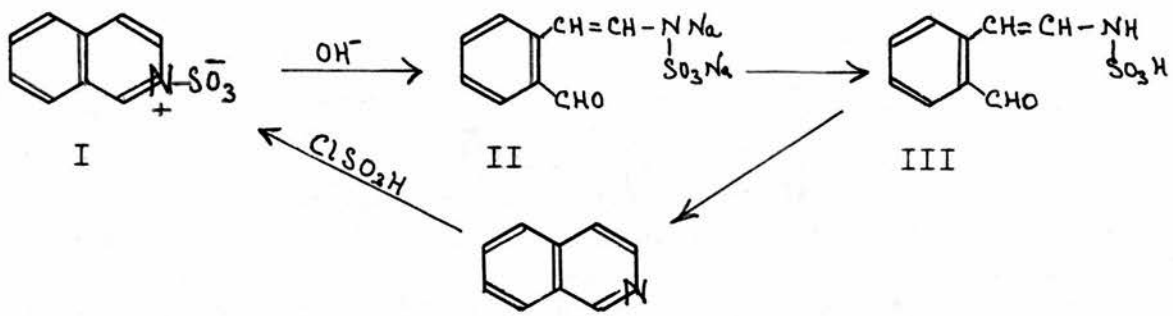


METHODS OF RING CLEAVAGE.

There are a number of general methods by which the hetero ring may be opened, and these are classified according as it is the unreduced or the reduced ring that is involved.

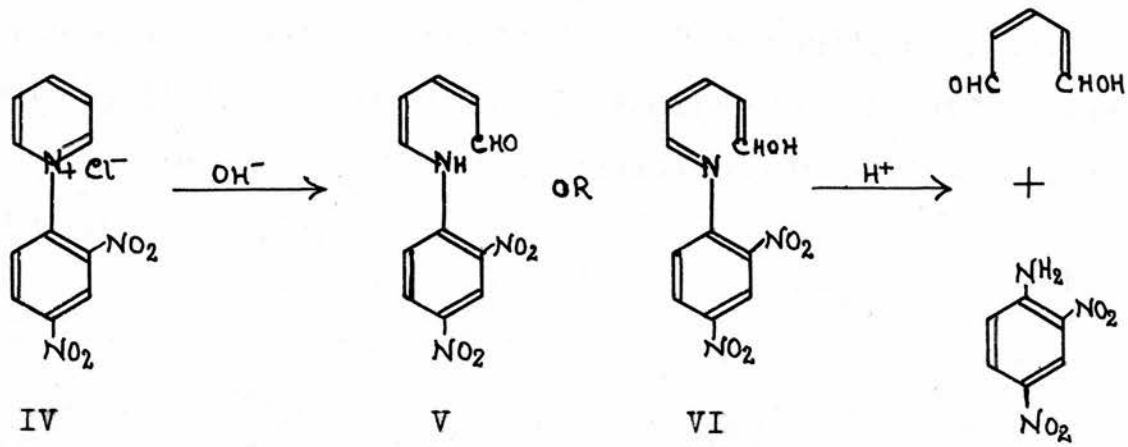
It has been already pointed out that there are certain reactions of the pseudo bases which must be interpreted as proceeding through open-chain intermediates, and in a number of cases the open-chain form has been stabilized through the formation of a suitable derivative, for example, an oxime or a phenylhydrazone. But further, the hetero ring adds at the

nitrogen atom various reagents, notably 2,4-dinitrochlorobenzene, cyanogen bromide, and chlorosulphonic acid, and the resulting compounds are usually susceptible to alkaline hydrolysis, just as are the normal pseudo bases. Thus isoquinoline reacts with chlorosulphonic acid in chloroform solution to yield the N-sulphonate (I), which is readily transformed by sodium hydroxide into a compound, assigned the structure (II). Treatment of (II) with mineral acid produces the sulphonic acid (III); this decomposes in boiling water to isoquinoline (46).



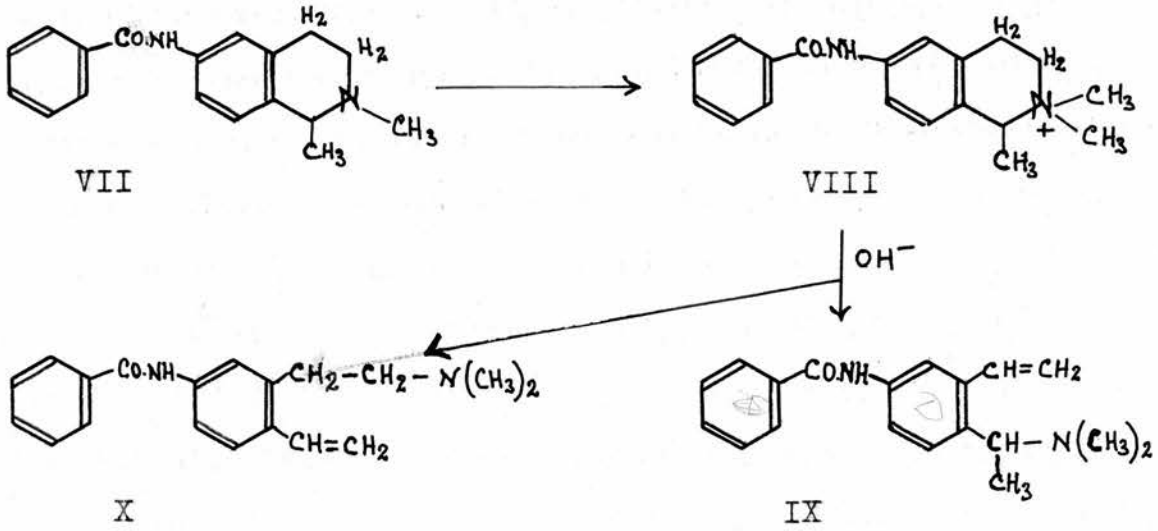
Ring cleavage by means of the above-mentioned reagents is, however, of more importance in the pyridine series itself, since the simple quaternary salts do not as easily undergo the transformation to the pseudo bases (and hence to the corresponding ring-opened compounds) as do the analogous quinoline and isoquinoline derivatives. For example, N-methyl pyridinium hydroxide evolves methylamine but very slowly when it is treated with boiling alkali; in contrast, 2,4-dinitrophenylpyridinium chloride (IV) rapidly goes over to a deep-red substance almost certainly (V) or (VI), in the presence of cold alkali (47). This is hydrolysed by acid to 2,4-dinitroaniline

and glutaconic dialdehyde. It is noticed that the ease of hydrolysis of these more complex pyridinium compounds is attributable to the presence of the strongly electron-attracting group on the nitrogen atom.

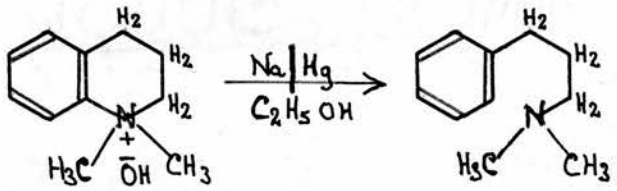


IV V VI

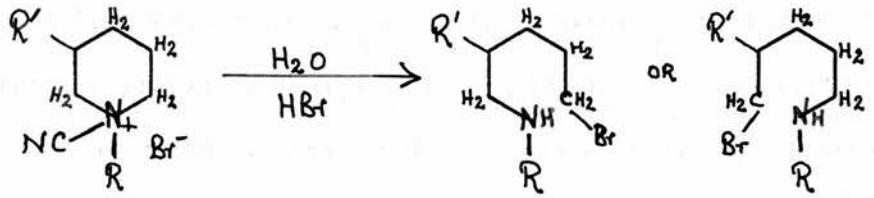
Opening of the fully reduced hetero ring in the pyridine, quinoline and isoquinoline series can be effected by one or other of five general methods, which may be illustrated as follows. 1) The quaternary hydroxide (VIII), obtained from (VII), using silver oxide and methyl iodide as the methylating combination, yields on dry distillation the two possible products (IX) and (X) (48).



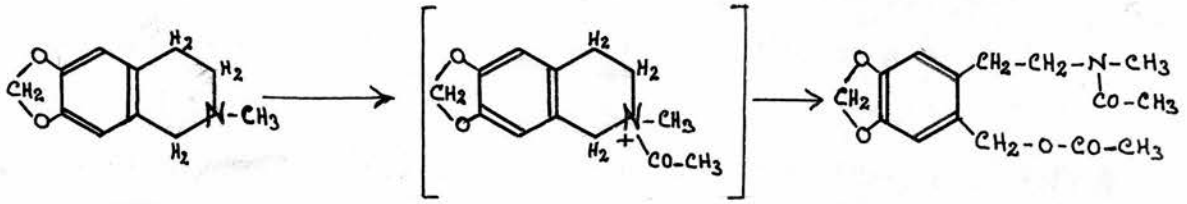
2) The Emde reductive cleavage by sodium amalgam and ethanol, of the tetrahydroquinoline quaternary hydroxide (XI) leads to the dimethyl-(γ-phenyl) propylamine (XII)



The piperidine ring can be opened by either method introduced by von Braun (49,50). Thus 3) N-benzoyl piperidine on being treated with phosphorous pentachloride gives an imino chloride which is readily hydrolysed to ∈-benzoylamino, amyl chloride; and 4) alkyl and aryl piperidines react with cyanogen bromide, the resulting quaternary salts being vulnerable to hydrolysis in one or other of the two theoretically possible ways:



5) Finally, N-methyl tetrahydro isoquinolines may be ruptured under acylating conditions (51); for example, hydrohydrastinin (XIII) furnishes (XIV) by interaction with acetic anhydride.



XIII XIV

It is true that the hetero ring in both quinolines and isoquinolines may be opened by oxidation, for example by potassium permanganate (in acid, rather than in alkaline, solution); however, the course of the degradative oxidation of a particular substituted quinoline or isoquinoline depends greatly upon the nature of the substituent group, as well as its position and it is hardly possible to predict with accuracy whether it will be the hetero or the benz ring that will be degraded in preference. Oxidation of the parent heterocyclic compounds is primarily of the latter ring, in conformity with other electrophilic reactions, although permanganate readily disrupts isoquinoline to both phthalic and cinchomeronic acids. Pyridine is very resistant to cleavage by oxidation.

Fluoranthene is oxidized to fluorenone-1-carboxylic acid, or, under less drastic conditions, fluorenone-1(β-propionic) acid.

EXPERIMENTAL.

In the following section, the melting points recorded were determined by means of a Kofler micro-melting point apparatus, unless otherwise stated.

Chromatographic separations were carried out on columns prepared from B.D.H. alumina, and fluorescence observations were made in ultra-violet light generated in a Hanovia lamp.

Analyses were performed by Drs. Weiler and Strauss, Oxford.

EXPERIMENTAL PART I.

The Schmidt reaction on fluoranthene-3:4-quinone.

PREPARATION OF FLUORANTHENE-3:4-QUINONE.

The method of preparation was that outlined by Goldschmiedt (Ber., 10, 2029 (1877)), who, however, did not give the experimental details. The following procedure was found to be effective. Fluoranthene (10 g.) was dissolved in glacial acetic acid (150 ml.), and a solution of chromic anhydride (15 g.) in water (10 c.c.) and glacial acetic acid (10 ml.) added in such a way that the temperature of the reaction mixture did not exceed 50°C. The mixture was then heated on the water-bath at 45-50°C until the solution assumed a deep green colour (18 hr.), when it was poured into water (1·5 l.). The precipitated brown-red powder was washed thoroughly with hot water and dissolved in chloroform. The chloroform solution was then extracted twice with 10 per cent sodium carbonate solution to remove fluorenone-1-carboxylic acid, washed with warm water, and dried (Na_2SO_4). Acidification of the sodium carbonate extracts yielded 4·0 g. of fluorenone-1-carboxylic acid. The quinone was purified from unchanged fluoranthene by chromatography. The dried chloroform solution was evaporated to small volume, and passed down a column of alumina, firstly with benzene to remove the hydrocarbon, then with benzene:chloroform solution (1:1 v/v), as eluant. The eluate was concentrated to small volume,

diluted with benzene to about thrice this volume, and finally concentrated until the quinone just commenced to crystallize from the hot solution. The product was obtained as beautiful deep red needles (1·5 g.), m.p. 194°C (Goldschmiedt gives m.p. 188-189°C for fluoranthene-3:4-quinone). The quantity of fluoranthene recovered was 2·0 g.

Analysis. Found: C = 82·6; H = 3·2%,

$C_{16}H_8O_2$ required: C = 82·8; H = 3·4%.

The quinoxaline derivative of the quinone was prepared by adding a hot ethanolic solution of o-phenylene diamine to a hot solution of the quinone in glacial acetic acid. Recrystallization of the quinoxaline from acetic acid gave yellow needles, m.p. 229°C.

Analysis. Found: C = 86·6; H = 3·8; N = 8·9%,

$C_{22}H_{12}N_2$ required: C = 86·8; H = 4·0; N = 9·2%.

ACTION OF HYDRAZOIC ACID ON FLUORANTHENE-3:4-QUINONE.

The action of hydrazoic acid on the quinone was examined under a variety of experimental conditions as follows.

a) Fluoranthene quinone (1·4 g.; 0·006 mol.) was dissolved in trichloracetic acid (20 g.) at 60°C, and sodium azide (1·2 g.; 0·018 mol.) added in small amounts, and with constant stirring, so that the temperature of the reaction mixture was kept at 60°C. After all the azide had been added, the solution was heated at the same temperature for one hour, then poured into ice-cold water (ca. 70 ml.). The resulting

suspension was allowed to stand for several hours, until a clear supernatant liquid was obtained, the yellow-brown solid was collected at the filter, washed free of acid, and dried. Sublimation at 190-200°C/0·1-0·5 mm. yielded 0·350 g. of the imido compound which crystallized from ethanol-acetic acid as yellow needles, m.p. 256·5-257°C.

Analysis. Found: C = 77·5; H = 3·8; N = 6·1%,
$C_{16}H_9NO_2$ requires: C = 77·7; H = 3·6; N = 5·7%.

b) The quinone (0·7 g.; 0·003 mol.) was dissolved in concentrated sulphuric acid (9 ml.) and the stirred solution maintained at 55-60 C while sodium azide (0·57 g.; 0·009 mol.) was added in small portions. When all the azide had been added, the solution was heated at 60°C for 15 minutes, then poured carefully into ice-cold water. The light-brown precipitate was collected at the filter, washed free of acid, and dried. The yield of crude product was 0·68 g. Crystallization from toluene gave 0·41 g. of yellow needles, m.p. 256°C. That this product was identical with that obtained in a) above was confirmed by mixed melting-point and by analysis.

Analysis. Found: C = 77·5; H = 3·9; N = 5·6%,
$C_{16}H_9NO_2$ requires: C = 77·7; H = 3·6; N = 5·7%.

c) The quinone (0·5 g.) was dissolved in concentrated sulphuric acid (9 ml.) and the stirred solution maintained at 50-55°C while a solution of sodium azide (0·4 g.) in water (1·5 ml.) was added, drop-wise. The reaction mixture was poured into

water, the product collected and purified as in b). It was identical with the compound obtained in b).

ACTION OF HYDRAZOIC ACID ON THE PRODUCT OF THE SCHMIDT REACTION.

a) The imide (0·3 g.) obtained in the above-detailed experiments a), b) and c), was dissolved in concentrated sulphuric acid (10 ml.) and the temperature of the solution kept at 50-55°C while sodium azide (0·2 g.) was added as rapidly as possible, with stirring. The reaction mixture was thereafter worked up as in b) above: the starting material was recovered.
b) The imide (0·23 g.) was dissolved in trichloracetic acid (5 g.) and the temperature of the solution maintained at 115-120°C while sodium azide (0·22 g.) was added in small amounts. When the addition was complete, the reaction mixture was poured into water. The precipitated solid proved to be the starting material, causing no depression in the m.p. of an authentic sample of the imide.

HYDROLYSIS OF THE IMIDE FROM THE SCHMIDT REACTION.

All attempts to open the imide ring by acid hydrolysis failed. The attempts were made with concentrated hydrochloric acid; a concentrated hydrochloric acid-ethanol mixture (1:1 v/v); 50% aqueous sulphuric acid; a sulphuric acid-water-acetic acid mixture (1:1:1 v/v); and concentrated sulphuric acid at room temperature. In all cases except the last

starting material was recovered, although the presence of sulphuric acid caused the formation of small amounts of a gum-like material. The concentrated sulphuric acid sulphonated the imide, and no useful product could be isolated.

The rupture of the imide ring was finally achieved thus. The imide (0·2 g.) was refluxed with 20% sodium hydroxide (14 ml.) for 17 hours. On acidification of the solution with hydrochloric acid a white precipitate was obtained, and this was washed with water and dried. The white solid was extracted with a small volume of toluene and the residual silicic acid discarded. On cooling the toluene solution, which was charcoal-screened, deposited 0·15 g. of fluorene-1-carboxylic acid, m.p. 249-250°C (Bergmann and Orchin give 246-249°C; J. Amer. Chem. Soc., 71, 1111, (1949)). It produced no depression when mixed with an authentic sample of fluorene-1-carboxylic acid prepared by the method of Forrest and Tucker (J. Chem. Soc., 1948, 1137).

PREPARATION OF FLUORENE-9-OXALESTER.

cf. v. Auwers and Frühling, Ann., 422, 223 (1920).

To a solution of potassium (4 g.) in absolute ethanol were added successively a solution of diethyl oxalate (14·5 g.) in dry ether (35 ml.), and a solution of fluorene (14 g.) in dry ether (130 ml.). Almost immediately after the addition of the latter solution, a yellow precipitate of the potassium salt of the ethyl fluorene oxalate was obtained. The mixture was heated under reflux for 30 minutes, then shaken thoroughly

with water; the aqueous layer was acidified and extracted with ether. Removal of the ether from the dried solution (sodium sulphate) left a yellow oil which was dissolved in a minimum volume of benzene. Addition of petrol-ether to the hot benzene solution induced crystallization of yellow ethyl fluorene-9-oxalate, m.p. 85-87° C. Yield = 20·0 g. (Wislicenus and Weitemeyer (Ber., 33, 771 (1900)) give m.p. 74-76°C).

PREPARATION OF FLUORENE-9-OXYACETIC ACID.

cf. Wislicenus and Weitemeyer, Ann., 436, 1 (1924).

Clean, granulated zinc (40 g.) was treated for 1 hour with a 5% mercuric chloride solution (80 c.c.) and the resulting amalgam collected and washed with water. Ethyl fluorene-9-oxalate (10 g.) was refluxed for 12 hours with the amalgamated zinc in diluted hydrochloric acid (1:1 v/v) and the cooled acid solution extracted with ether. Removal of the ether by evaporation left a white residue which was crystallized from nitrobenzene as white needles, m.p. 205-206°C. Yield = 9·5 g. (Wislicenus and Weitemeyer give m.p. 194-195°C).

DEHYDRATION OF FLUORENE-9-OXYACETIC ACID TO ββ'-BIPHENYLENE ACRYLIC ACID.

cf. Wislicenus and Weitemeyer, Ber., 54, 979 (1921).

The dehydration of fluorene-9-oxyacetic acid to the biphenylene acrylic acid may be effected rather more speedily than by the procedure of Wislicenus and Weitemeyer, as follows.

The acid was dissolved in 20% NaOH, and almost immediately the acrylic acid was formed, as indicated by the production of a yellow colour in the alkaline solution. The solution was boiled for several minutes, cooled and made acid with hydrochloric acid. The precipitated ββ'-biphenylene acrylic acid was crystallized from benzene as yellow needles, m.p. 228-229°C (Wislicenus and Weitemeyer give m.p. 222-223°C).

NOTE: The m.p.s. of the compounds, fluorene-9-oxalester, fluorene-9-oxyacetic acid and ββ'-biphenylene acrylic acid, respectively, as given by Wislicenus and Weitemeyer, are not stated to be corrected. The m.p.s given here are corrected.

ACTION OF ALKALI ON ββ'-BIPHENYLENE ACRYLIC ACID.

The acrylic acid (0·2 g.) was refluxed for 6 hours with sodium hydroxide (2·0 g.) in water (20 ml.). The white sublimate of fluorene which gathered in the water condenser was removed by ether. Evaporation of the ether left a residue of fluorene (0·05 g.), the identity of the material being established by m.p. and mixed m.p. determinations. On acidification of the basic solution, ββ'-biphenylene acrylic acid (0·120 g.) was recovered.

Hence, based upon the quantity of acid unrecovered, the percentage yield of fluorene = 83.

The experiment was repeated with fluorene-9-oxyacetic acid (0·3 g.), other conditions being unaltered. Again, fluorene (0.075 g.) was obtained, and ββ'-biphenylene acrylic acid

(0·148 g.) recovered. Based upon the quantity of acid unrecovered, the percentage yield of fluorene = 77.

When ββ'-biphenylene acrylic acid (0·2 g.) was refluxed for 30 hours in water (15 ml.) with piperidine (2 ml.) added, no fluorene was obtained. The acid was recovered.

No fluorene was obtained by refluxing the acrylic acid (0·2 g.) in water (20 ml.) for 6 hours; or by refluxing the acid in water (20 ml.) with concentrated hydrochloric added (3 ml.), for 17 hours. In each case, the acrylic acid was recovered.

OXIMATION OF FLUORANTHENE-3:4-QUINONE.

The quinone (0·7 g.; 0·003 mol.) was dissolved in pyridine (10 ml.) containing hydroxylamine from hydroxylamine hydrochloride (0·24 g.; 0·003 mol.), and the solution heated at 100°C for 30 minutes. On cooling, it was poured into dilute hydrochloric acid, and the resulting yellow precipitate collected and washed with dilute hydrochloric acid, followed by water. Yield of crude material = 0·75 g. On crystallization from toluene, 0·4 g. of material, m.p. 204-205°C, was obtained. Further crystallization from dilute acetic acid yielded a mixture of two compounds, from which, by mechanical means, were obtained yellow needles, m.p. 205-207° C (with decomposition) and orange-red needles, m.p. 205-207° C (with decomposition). No separation of the two forms was achieved in the recrystallizations, and it was not certain that they did represent two pure substances, as a mixed m.p. showed no depression.

EXPERIMENTAL PART 2.

Unsuccessful attempts to synthesise 2-azafluoranthene 4-phenyl-3-azafluoranthene; 3-azafluoranthene; and 1-azafluorene, with a view to the synthesis of 10-azafluoranthene.

ATTEMPTED SYNTHESIS OF 2-AZAFLUORANTHENE.

PREPARATION OF FLUORENONE OXIME.

Fluorenone oxime was prepared in good yield by the procedure given by Schmidt (Ber., 40, 4257 (1907)). The product obtained was sufficiently pure for immediate use in the subsequent reaction.

REDUCTION OF FLUORENONE OXIME TO 9-FLUORENYLAMINE.

The reduction of fluorenone oxime (40 g.) to 9-fluorenylamine was effected according to the procedure given by Ingold and Wilson (J. Chem. Soc., 1933, 1499). The product was obtained as the amine hydrochloride (31-32 g.). The amine (m.p. 59-62°C) readily absorbs carbon dioxide to give the carbonate, and for the subsequent reaction with chloroacetyl chloride, the amine was generated immediately before the reaction.

PREPARATION OF α-CHLOROACETO-9-FLUORENYLAMIDE.

Fluorenylamine hydrochloride (45 g.) was added to sodium

hydroxide overlaid with benzene, contained in a separating funnel, and the mixture shaken vigorously until the reaction was complete. The benzene layer was washed free of alkali with water, dried by azeotropic distillation of the water from the solution, and dry benzene added to the latter until the volume was approximately 100 ml. The solution was shaken continuously, while chloroacetyl chloride (25 g.) was added fairly rapidly, and cooled in ice-water so that the temperature did not exceed 40°C. When the addition was complete, the solution was set aside for five minutes, then heated on the water-bath for 30 minutes and finally poured into water. The precipitate was collected at the filter, washed with cold water and dried. The fluorenylamine hydrochloride produced in the reaction was separated from the fluorenylamide by boiling the mixture with benzene, in which only the latter is soluble. The amide was recrystallized from toluene to give long, colourless needles, m.p. 239-240°C. The yield was quantitative.

Analysis. Found: N = 5·4; Cl = 13·7%,

$C_{15}H_{12}NOCl$ requires: N = 5·5; Cl = 13·8%.

ATTEMPTED RING-CLOSURE OF α-CHLOROACETO-9-FLUORENYLAMIDE.

Four attempts were made as follows.

i) The amide (1 g.) was heated with stannic chloride (2·6 g.) for 3 hours in an oil-bath at 130°C. There was no observed evolution of HCl. The cooled solution was poured into water

(25 ml.), the undissolved solid collected at the filter and dried. Recrystallization from benzene (charcoal) gave white needles, m.p. 238° C which did not depress the m.p. of a sample of the amide.

ii) The amide (1 g.) and aluminium chloride (1·3 g.) were heated as an intimate mixture which became molten at 125 C. The heating was continued at 140° C until the evolution of HCl ceased, and the cooled melt decomposed with dilute hydrochloric acid. The dark brown residue was collected at the filter, then boiled with ethanol to extract organic matter. The ethanolic solution was filtered hot, but yielded no product when cooled, and but a trace of material when diluted with water. This could not be purified.

iii) The amide (1 g.) was heated with aluminium chloride (1·3 g.) in nitrobenzene (5 ml.) to the lowest temperature (ca.130°C) at which HCl was evolved. The reaction was stopped after 60 minutes but on being worked up, yielded no product. A similar attempt, in which the solvent was tetrachloroethane, likewise resulted in the formation of only organic debris.

iv) The amide (1 g.) was heated with zinc chloride (1·3 g.). The mass became mobile at 170° C, without evolving HCl gas. The temperature of the mixture was raised gradually to 220 C, when the darkening melt solidified. No hydrogen chloride was evolved throughout and the charred material, on being worked up, gave no homogeneous substance.

ATTEMPTED SYNTHESIS OF 4-PHENYL-3-AZAFLUORANTHENE.

PREPARATION OF 9-FORMYLFLUORENE.

cf. Von and Wagner, J. Org. Chem., 9, 155 (1944).

Fluorene (45 g.), potassium methoxide (20 g.) and ethyl formate (21·1 g.) were added to anhydrous ether (200 ml.) and the mixture heated on the water-bath for five hours. The cooled ether solution was then shaken with water, and the aqueous layer extracted with a small volume of ether, then acidified with dilute sulphuric acid. The formylfluorene thus liberated was taken up in ether, the ether layer was washed with sodium bicarbonate, then with water, and finally dried (sodium sulphate). Removal of the solvent by evaporation left a yellow oil which was used at once in the preparation of the oxime of formylfluorene. (On standing in the cold, and more readily on warming, formylfluorene polymerizes to an amorphous yellow material which interferes with purification processes).

PREPARATION OF 9-FORMYLFLUORENE OXIME.

cf. Wislicenus and Russ, Ber., 43, 2719 (1910).

9-Formylfluorene (crude, 48 g.) was dissolved in ethanol (400 ml.), and to the solution was added sodium (5·6 g.) in ethanol (80 ml.) followed by hydroxylamine hydrochloride (20 g.) in water (80 ml.). Sodium chloride separated from the solution which was heated at 50°C for 16 hours. The temperature was then raised to 60-65°C, and enough water at the same

temperature added to produce a turbid solution which, on cooling, yielded 9-formylfluorene oxime as long white needles (43 g.). A further crop (5 g.), only slightly less pure, was obtained by re-heating the solution and adding water as before, and allowing the turbid solution to cool.

The oxime exists in two forms: the α-oxime has the m.p. 132-133° C, the β-oxime has m.p. 166-7° C. For the reduction described below, the product obtained directly from the oximation was used.

PREPARATION OF 9-FLUORENYLMETHYLAMINE.

To a well-shaken suspension of lithium aluminium hydride (3 g.) in dry ether (100 ml.), contained in a flask fitted with a reflux condenser, was added slowly a solution of 9-formylfluorene oxime (5 g.) in dry ether (250 ml.). The resulting brownish-orange suspension in ether was refluxed for a further 17 hours, then poured carefully into ice-water. The aqueous layer was made acid with dilute hydrochloric acid (1:1 v/v) and the free amine passed into the acid layer. The ether layer was extracted once with hydrochloric acid (1:1 v/v). The combined acid portions were overlaid with ether and made alkaline with 10% sodium hydroxide. The ether layer was washed with water to remove alkali and treated directly with hydrogen chloride to yield the hydrochloride of 9-fluorenylmethylamine, 5·15 g.

The free amine crystallized from petrol ether (60-80° C) as white needles, m.p. 139-141° C. The amine hydrochloride

crystallizes from ethanol-petrol ether as white needles, m.p. 223-225°C (dec.).

Analysis. Found: N = 5·9; Cl = 15·1%,

$C_{14}H_{14}NCl$ requires: N = 6·1; Cl = 15·3%.

The benzoyl derivative of 9-fluorenylmethylamine was prepared in the usual way from the amine hydrochloride. Recrystallization from benzene-petrol ether gave white prisms, m.p. 185-186°C.

Analysis. Found: C = 79·7; H = 5·6; N = 4·3.

$C_{21}H_{17}ON$ requires: C = 84·3; H = 5·7; N = 4·7%.

ATTEMPTED PREPARATION OF 4-PHENYL-1,2-DIHYDRO-3-AZAFLUORANTHENE.

i) Benzoyl-9-fluorenylmethylamine (1 g.) was dissolved in sulphur-free xylene (30 ml.) and phosphorus pentoxide (5 g.) and phosphoryl chloride (10 ml.) added to the solution. The two-phase reaction mixture was heated gently at 140°C for 3 hours, then poured carefully into ice-cold water to which concentrated hydrochloric acid (4-5 ml.) had been added. The xylene was thoroughly shaken with the aqueous layer, and a quantity of tar was deposited. The xylene and aqueous layers were then separated; the aqueous was covered with benzene, and made alkaline with sodium hydroxide. The benzene layer was shaken with the aqueous, washed with water and dried over sodium sulphate. There was no precipitate when it was finally treated with dry hydrogen chloride. The xylene deposited

only a quantity of tar.

ii) The amide (2 g.) was stirred into a solution of phosphorus pentoxide (10 g.) in phosphoric acid (10 ml.) at 160°C, and the stirred solution maintained at this temperature for 1·25 hours. The cooled solution was poured onto ice, the aqueous solution made strongly acid with hydrochloric acid, warmed to ca. 50°C and filtered. The residue consisted of reddish-brown resinous material, insoluble in concentrated hydrochloric acid. The filtrate was rendered alkaline with potassium hydroxide, but yielded no precipitate.

During the attempted ring-closure, a very small sublimate of benzoic acid formed on the upper parts of the reaction vessel.

iii) The amide (2 g.) was added to a stirred mixture of phosphorous pentoxide (15 g.) and tetralin (25 ml.) at 150°C. The resulting mixture was kept at this temperature for 30 minutes, the temperature was then raised fairly rapidly to 200°C. After a further 30 minutes, during which time the stirring had to be stopped as the phosphorous pentoxide set solid, the mixture was allowed to cool. The tetralin layer was poured into cold water acidified with hydrochloric acid; the phosphorous pentoxide residue was decomposed with water, and the aqueous solution made strongly acid with hydrochloric acid. The two acid solutions were combined (after the one had been separated from the tetralin layer and the other filtered from reddish-brown resinous material), and the combined solution made alkaline; again, no precipitate was obtained.

ATTEMPTED SYNTHESIS OF 3-AZAFLUORANTHENE.

PREPARATION OF FLUORENONE-1-CARBOXYLIC ACID.

Fluorenone-1-carboxylic acid was prepared by the oxidation of fluoranthene (45 g.), according to the method given by Fieser and Seligman (J. Amer. Chem. Soc., 57, 2174 (1935)). The yield of the rather impure product was 34 g.; that of the material recrystallized from acetic acid was 25 g.

PREPARATION OF FLUORENE-1-CARBOXYLIC ACID.

Fluorenone-1-carboxylic (20 g.) was reduced to fluorene-1-carboxylic acid (17 g.; m.p. 240-245°C) by the procedure given by Forrest and Tucker (J. Chem. Soc., 1948, 1137). These authors give the m.p. 245°C; Bergmann and Orchin (J. Amer. Chem. Soc., 71, 1111 (1949)) give the m.p. 246-249°C. For the preparation of the methyl ester, the acid was purified by extracting it with barium carbonate solution.

The methyl ester was prepared by refluxing a solution of fluorene-1-carboxylic acid (4 g.) in methanol (80 ml.) saturated with hydrogen chloride, for 3 hours. Concentration of the methanolic solution gave a somewhat impure product (4·3 g.). Recrystallization from methanol gave colourless needles, m.p. 86-88°C (Bergmann and Orchin (loc.cit.) give m.p. 86·6-87·4°C).

PREPARATION OF FLUORENE-1-CARBOXYLIC ACID HYDRAZIDE.

cf. Bergmann and Orchin (loc.cit.).

Methyl fluorene-1-carboxylate (4·3 g.) was refluxed with 98% hydrazine hydrate (6 ml.) in ethanol (30 ml.) for 17 hours. During the reaction colourless hydrazide was deposited from the solution. The solution was concentrated, and the white product collected at the filter, washed with potassium carbonate solution then with water, and dried. Yield, 3·4 g., m.p. 215-218°C (Bergmann and Orchin give m.p. 216·6-218°C).

PREPARATION OF FLUORENE-1-CARBOXYLIC ACID-p-TOLUENESULPHONYL-HYDRAZIDE.

Fluorene-1-carboxylic acid hydrazide (3·4 g.) was dissolved in anhydrous pyridine (25 ml.) and to the solution was added p- toluenesulphonyl chloride (2·9 g.), slowly and with constant shaking. The mixture was set aside at room temperature for 3 hours, poured into an ice-dilute hydrochloric acid mixture, and the precipitate washed thoroughly with ice-cold dilute hydrochloric acid and dried. The crude p-toluenesulphonyl hydrazide (5·6 g.) was recrystallized from dioxan-ethanol-petrol as white prisms (4·5 g.), m.p. 220-222° C, with evolution of gas.

Analysis. Found: N, 6·8; S, 7·5%,

$C_{21}H_{18}N_2SO_3$ requires: N, 7·4; S, 8·5%.

PREPARATION OF FLUORENE-1-ALDEHYDE.

The p-toluenesulphonylhydrazide (1·9 g.) was dissolved in ethylene glycol (25 ml.) at 160°C, and thoroughly dried sodium

carbonate (1·4 g.) added as rapidly as effervescence permitted. The reaction was allowed to continue for a further 75 seconds then stopped abruptly by the addition of hot water. The cooled aqueous mixture deposited a brown oil which was extracted with three portions of ether. The combined ether solution was washed with water, dried (sodium sulphate) and charcoal screened. Evaporation of the solvent left a brown solid which was extracted with petrol-ether. The removal of the petrol gave crude fluorene-1-aldehyde (0·35 g.). Recrystallization at low temperature from ether-petrol ether solution gave white needles, m.p. 88-90°C (uncorr.), which became discoloured on standing, and more rapidly on being dried at 60°C for analysis.

Analysis. Found: C, 85·8; H, 5·1%,

$C_{14}H_{10}O$ requires: C, 86·6; H, 5·2%.

The 2,4-dinitrophenylhydrazone was prepared in the usual way in ethanol. Recrystallization of a sample from acetic acid, in which it is very insoluble, gave reddish-orange needles, m.p. 298°C (dec.).

Analysis. Found: N, 14·7,

$C_{20}H_{14}N_4O_4$ requires: N, 15·0%.

ATTEMPTED FORMYLATION OF METHYL FLUORENE-1-CARBOXYLATE.

Methyl fluorene-1-carboxylate (1·4 g.), potassium methoxide (0·5 g.), and ethyl formate (1·5 ml.) were heated together for 1·5 hours in a solution of anhydrous methanol (5 ml.) and

anhydrous ether (25 ml.). During the reaction the solution assumed a yellow colour. The mixture was shaken with water and the yellow aqueous layer was separated and shaken, with a small portion of ether to remove unchanged ester. The aqueous layer was acidified with hydrochloric acid, extracted with ether, and the yellow ether solution separated, washed and dried (sodium sulphate). Evaporation of the solvent yielded only a trace of a yellow oil which could not be condensed with ammonia in anhydrous methanol solution contained in a sealed tube at 120°C for 16 hours. The original methyl ester was recovered from its ether solution.

A second attempt to formylate methyl fluorene-1-carboxylate was made by refluxing for 3 hours a mixture of the ester (1·1 g.), potassium methoxide (0·36 g.) and ethyl formate (1 ml.) in anhydrous ether (20 ml.). The solution was worked up as before; and the small amount of yellow product was treated with concentrated ammonium hydroxide for 1 hour at 100°C. Only a minute quantity of a yellow acidic material could be recovered.

ATTEMPTED PREPARATION OF 3-AZAFLUORANTHENE-N-OXIDE.

Fluorene-1-aldehyde (2·1 g.), potassium methoxide (1 g.) and ethyl formate (3 ml.) were heated for 2·5 hours in refluxing anhydrous ether (35 ml.). The solvent and the excess of ethyl formate were removed by distillation at reduced pressure, and the deep red residue was dissolved in anhydrous pyridine (10 ml.) and anhydrous ethanol (10 ml.).

To the red solution was added hydroxylamine hydrochloride (2 g.); the resulting yellow solution was diluted with anhydrous ethanol (10 ml.) and refluxed for 18 hours, concentrated under reduced pressure, and poured into water. The yellow precipitate (1·3 g.) was insoluble in hot water, alkali and concentrated hydrochloric acid. It could not be recrystallized; a sample, purified by charcoal-screening in chloroform solution, had the m.p. 195-201°C (dec.).

Analysis. Found: C, 85.0; H, 4.9%.

ATTEMPTED SYNTHESIS OF 1-AZAFLUORENE.

PREPARATION OF 5,6-BENZ-QUINOLINE.

cf. Skraup and Cobenzl, Monatsh., 4, 436 (1883).

β-Naphthylamine (56 g.), nitrobenzene (26 g.) concentrated sulphuric acid (80 g.) and anhydrous glycerol (100 g.), were heated under reflux on an oil bath. The initially viscous mass became mobile at approximately 90°C, and dark-brown in colour. Heating was continued until the temperature of the solution had risen to 150°C, when a very vigorous reaction commenced. When this had subsided, the reaction flask was replaced in the oil-bath and the solution heated for five hours between 150-160°C. To the mixture was added water (420 ml.) then a concentrated solution of sodium hydroxide (40 g.), and the resulting tarry mass was filtered through a bed of filter cel. The filtrate was overlaid with ether and

made just alkaline with sodium hydroxide. The ether layer was separated, dried over potassium carbonate and the solvent was removed by distillation to yield the dark-brown, crude benz-quinoline. This was most readily purified by extracting it with refluxing petrol-ether: two layers formed, the upper consisting of the benz-quinoline in the petrol, the lower of tar. The upper layer was decanted, and on cooling it deposited a slightly discoloured product. Recrystallization from petrol ether (charcoal) gave 5,6-benz-quinoline as colourless plates, m.p. 90°C. (Skraup and Cobenzl give the m.p. 90°C (uncorr.)).

OXIDATION OF 5,6-BENZ-QUINOLINE.

cf. Skraup and Cobenzl (loc.cit.).

5,6-Benz-quinoline (5 g.) was added to hot water (700 ml.) and the molten suspension vigorously stirred while the temperature fell to 40-50°C. A cold saturated aqueous solution of potassium permanganate (12 g.) was added in small amounts to the vigorously stirred solution, an addition being made only when the mixture had been decolourized. The solution was filtered, the manganese dioxide was extracted repeatedly with hot water, and the combined filtrate concentrated under reduced pressure to ca. 150 ml. A small amount of benz-quinoline gathered in the condenser. The aqueous solution was neutralized with sulphuric acid; addition of an equal volume of ethanol precipitated the potassium sulphate which was removed by filtration. The filtrate was evaporated to dryness, sufficient water added just to dissolve the residue,

and the solution was made just acid with dilute hydrochloric acid. The light-brown, fine-grained precipitate was collected at the filter (1·5 g.). Recrystallization from hot water (charcoal) gave white prisms, m.p. 212-213°C. (Skraup and Cobenzl give m.p. 207°C (uncorr.)).

Analysis. Found: C, 63·9; H, 3·8; N, 5·8%,

$C_{13}H_8NO_4$ requires: C, 64·2; H, 3·7; N, 5·8%.

ATTEMPTED CYCLIZATION OF 2-CARBOXY-3-(o-CARBOXYPHENYL)-PYRIDINE.

Several unsuccessful attempts to effect the cyclization of 2-carboxy-3-(o-carboxyphenyl)-pyridine to 1-azafluorenone-5-carboxylic acid were made. The most forceful conditions used are described in the following procedure. The acid (1 g.) was dissolved in concentrated sulphuric acid (3 ml.) at 150°C. After 8 hours, the solution was cooled, poured into water and made neutral with potassium hydroxide. The potassium sulphate was removed as described above and the aqueous ethanol solution evaporated to dryness. The residue was dissolved in a minimum volume of water, and the solution made just acid with dilute hydrochloric acid. 2-Carboxy-3-(o-carboxyphenyl)-pyridine (0·9 g.) was recovered. Similarly, polyphosphoric acid (phosphoric acid:phosphorus pentoxide 1:1 w/w) failed to effect the cyclization.

EXPERIMENTAL PART 3.

The syntheses of 2-azafluoranthene and 3,4-benz-2-azafluoranthene.

SYNTHESIS OF 2-AZAFLUORANTHENE.

PREPARATION OF 1,2,3,4-TETRAHYDRO-FLUORANTHENE.

cf. v. Braun and Manz, Ber., 63, 2612 (1930).

Fluoranthene (55 g.) was dissolved in gently refluxing ethanol (1700 ml.), and 5% sodium amalgam (760 g.) added in small pieces over 45 minutes. The mixture was refluxed for a further 24 hours, the ethanol solution reduced to ca. 1 litre and then made neutral to litmus, with the addition of concentrated hydrochloric acid. It was poured into 4 litres of water and the aqueous suspension of 1,2,3,4-tetrahydrofluoranthene set aside for 24 hours. The product was collected at the filter and dried. Recrystallization from ethanol gave 42·5 g. of white needles, m.p. 77-78°C. (v. Braun and Manz give the m.p. 74-75°C).

PREPARATION OF FLUORENONE-1-(β-PROPIONIC)-ACID.

cf. Kruber, Ber., 64, 84 (1931).

1,2,3,4-Tetrahydrofluoranthene (16 g.) was dissolved in glacial acetic acid (90 ml.) and the solution stirred mechanically at 60°C, while a solution of sodium bichromate (38 g.) in acetic acid (230 ml.) was run in slowly over about

1 hour. The mixture was heated for a further 5 hours at 60°C, then poured into water. The aqueous solution was thoroughly extracted with ether-chloroform solvent (1:1 v/v) and the organic solvent layer in turn was shaken with sodium carbonate solution. Acidification of the latter with hydrochloric acid precipitated fluorenone-1-(β-propionic) acid which was extracted into ether-chloroform solvent. The solution was dried (sodium sulphate) and the solvent removed by evaporation leaving 12·5 g. of fairly pure acid. Recrystallization from 70% aqueous acetic acid yielded 10 g. of pure acid, yellow plates, m.p. 137-139°C. (Kruber gives m.p. 137-138°C, uncorr.).

HOFMANN REACTION ON FLUORENONE-1-(β-PROPIONIC) ACID.

The fluorenone-1-(β-propionic) acid chloride was formed according to the procedure given by Wilshire (Thesis, Edinburgh 1952). The acid (10 g.) dissolved in anhydrous ether (170 ml.) was treated with thionyl chloride (7 ml.) and pyridine (2 drops). The solution was set aside for 3 hours with occasional swirling, then the solvent and excess thionyl chloride were removed by evaporation, the last traces of the latter being removed by co-distillation with anhydrous benzene. The acid chloride was left as an orange-coloured oil.

The amide was prepared as follows. The acid chloride was dissolved in anhydrous ether (150 ml.) and into the stirred solution was bubbled dry ammonia gas for 45 minutes. The passing of the ammonia was accompanied by an immediate

precipitation of the yellow amide and of ammonium chloride. When the reaction was completed, the ether was removed by evaporation and the solid residue shaken thoroughly with cold water to dissolve the ammonium chloride. The amide was collected at the filter, and recrystallized from 70% aqueous ethanol to give fluorenone-1-(β)-propionamide as yellow needles (9·9 g.), m.p. 191-192° C. A second crystallization from the same solvent gave needles, m.p. 193-194° C.

Analysis. Found: C = 76·5; H = 5·4; N = 5·4%,
$C_{16}H_{13}NO_2$ requires: C = 76·5; H = 5·2; N = 5·6%.

The degradation of the amide to the amine was attempted under varied experimental conditions. Sodium hypochlorite failed to react with the amide; and no product was isolated when hypobromite was employed in methanol solution. Aqueous sodium hypobromite afforded at least small amounts of product, the highest yield being obtained by the following procedure. The amide (1·0 g.), finely powdered, was added with constant stirring to a hypobromite solution prepared from sodium hydroxide (1·0 g.), water (8 ml.) and bromine (0·26 ml.), the temperature of the mixture being maintained at 10°C. After 90 minutes at this temperature, the mixture, which contained some undissolved amide, was heated rapidly to 70-80° C, maintained between these limits for 20 minutes, then poured into water. The precipitate was dissolved in chloroform, the solution washed free of alkali with water and shaken with several portions of warm, dilute hydrochloric acid. The

undissolved amine hydrochloride was collected at the filter, along with precipitated amide (0·17 g.), from which it was freed by heating the mixture in water at 60°C. The filtered solution was combined with the acid extracts, and the entire solution made basic with alkali. The pale yellow suspension of 3,4-dihydro-2-azafluoranthene was shaken thoroughly with ether, the ether solution washed with water and dried (sodium sulphate). Removal of the ether by evaporation left a yellow oil (0·30 g.) which could not be crystallized and which failed to solidify. The 3,4-dihydro-2-azafluoranthene was characterized by its hydrochloride, methiodide and picrate.

3,4-Dihydro-2-azafluoranthene hydrochloride: prepared by passing dry hydrogen chloride into a solution of the base in ether. Recrystallization from petrol ether-ethanol gave orange needles, m.p. 193-194°C.

Analysis. Found: N = 5·0; Cl = 12·6%,

$C_{15}H_{12}HCl$ requires: N = 5·8; Cl = 14·7%.

Methiodide: prepared in methyl iodide solution of the base. Recrystallization from ethanol gave reddish-orange needles, m.p. 252-253°C.

Analysis. Found: I = 36·2%,

$C_{16}H_{14}NI$ requires: I = 36·6%.

Picrate: prepared in ethanol solution in the usual way. Recrystallization from ethanol gave orange needles, m.p. 229-230°C (dec.).

Analysis. Found: N = 12·6%,

$C_{21}H_{14}N_4O_7$ requires: N = 12·9%.

CURTIUS DEGRADATION OF FLUORENONE-1-(β-PROPIONIC) ACID.

It was found necessary to use sodium azide, activated according to the method of Nelles (Ber., 65, 1345 (1932)). The acid chloride was prepared as already described.

Fluorenone-1-(β-propionic) acid (10 g.) was converted into its acid chloride which was dissolved in anhydrous benzene (50 ml.). To the solution was added activated sodium azide (2·6 g.), and the mixture was heated under reflux for 20 hours, during which time care was taken to exclude moisture from the reactants. The cooled solution was filtered, the filtrate was introduced into a 500 ml. flask and concentrated hydrochloric acid (50 ml.) added. The two-phase reaction mixture was then heated on the boiling water-bath, and after 10-15 minutes a greenish-yellow precipitate began to separate. Heating was continued for a further 4 hours, and the mixture cooled. The precipitate of fluorenone-1-β-ethylamine hydrochloride was collected. Recrystallization of a small sample from dioxan containing a few drops of water gave greenish-yellow plates, m.p. 210-211° C.

Analysis. Found: C = 69·2; H = 5·4; N = 5·5; Cl = 13·6%,

$C_{15}H_{14}NOCl$ requires: C = 69·4; H = 5·4; N = 5·4; Cl = 13·7%.

The hydrochloride was treated with potassium hydroxide solution, and the precipitated 3,4-dihydro-2-azafluoranthene

taken up in ether. The ether solution was washed with water, dried (sodium sulphate) and removal of the solvent by evaporation gave the base (7.9 g.).

The 3,4-dihydro-2-azafluoranthene is not hydrolysed to the fluorenone-1-β-ethylamine hydrochloride by boiling it with dilute or concentrated hydrochloric acid. Thus after being heated on the water-bath at 100°C for 3 hours in concentrated acid, the 3,4-dihydro-2-azafluoranthene hydrochloride was recovered.

DEHYDROGENATION OF 3,4-DIHYDRO-2-AZAFLUORANTHENE.

3,4-Dihydro-2-azafluoranthene (0·3 g.) was dissolved in 1-methyl-naphthalene (5 ml.), 20% palladium/charcoal (0·05 g.) added, and the solution boiled gently for 3 hours in an atmosphere of carbon dioxide. The catalyst was removed at the filter, and washed with small quantities of benzene which were then added to the filtrate. The combined solution was shaken with concentrated hydrochloric acid, and the orange-coloured acid layer made alkaline with sodium hydroxide. The resulting pale yellow precipitate was taken up in ether, the ether solution was washed free of hydroxide and dried (sodium sulphate; sodium wire). Evaporation of the ether yielded the pale yellow 2-azafluoranthene (0·285 g.). Recrystallization from petrol-ether gave pale yellow needles, m.p. 91-92°C.

Analysis. Found: C = 88.7; H = 4·4; N = 7·0%,

$C_{15}H_9N$ requires: C = 88.7; H = 4·4; N = 6·9%.

Methiodide: prepared in refluxing methyl iodide. Recrystallization from ethanol gave deep-orange needles, m.p. 273°C (dec.).

Analysis. Found: N = 4·0; I = 36·6%,

$C_{16}H_{12}NI$ requires: N = 4·1; I = 36·8%.

Trinitrobenzene complex: prepared in ethanol. Recrystallization from ethanol gave pale yellow needles, m.p. 126-127°C.

Analysis. Found: N = 12·8%,

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

Picrate: prepared in ethanol. Recrystallization from dioxan gave orange-yellow needles, m.p. 239°C.

Hydrochloride: precipitated from an ether solution of the base. Recrystallization from petrol-ether-ethanol gave yellow needles, m.p. 208-209°C.

Analysis. Found: N = 5·0; Cl = 12·5%,

$C_{15}H_{10}NCl$ requires: N = 5·9; Cl = 14·8%.

2-Azafluoranthene is readily extracted from concentrated hydrochloric acid by chloroform.

SYNTHESIS OF 3,4-BENZ:2-AZAFLUORANTHENE.

PREPARATION OF 9-(o-CHLOROBENZAL)-FLUORENE.

Fluorene (16·6 g.) and potassium methoxide (7·2 g.) were refluxed in anhydrous ether (100 ml.) for 30 minutes to form

the insoluble potassium salt of fluorene. A solution of o-chloro-benzaldehyde (14·4 g.) in anhydrous ether (70 ml.) was then gradually added, and the resulting yellow solution refluxed for 2 hours. A precipitate of potassium hydroxide formed during the reaction and this was removed by filtration. The ether was removed from the yellow filtrate, leaving an oil which was used directly in the subsequent reaction.

PREPARATION OF 3,4-BENZFLUORANTHENE.

cf. I. G. Farbenindustrie A-G. Brit. Pat. 459, 108.

9-(o-Chlorobenzal)-fluorene (crude; 30 g.) was mixed with quinoline (180 g.) and potassium hydroxide (140 g.) in a special thick-walled flask, and the stirred mixture refluxed for 2·5 hours, then poured carefully into ice-hydrochloric acid. The brown precipitate was collected at the filter, washed with dilute potassium hydroxide, followed by water, and dried. Recrystallization from glacial acetic acid (charcoal) gave white needles, m.p. 166-167°C, yield, 7 g. (Quoted m.p., 167°C).

PREPARATION OF FLUORENONE-1-(o-BENZOIC) ACID.

cf. Kruber and Oberkobusch, Ber., 85, 436 (1952).

3,4-Benzfluoranthene (7 g.) was dissolved in glacial acetic acid (350 ml.) and the stirred solution maintained at 60°C while a solution of sodium bichromate (30 g.) in acetic acid (100 ml.) was added over ca. 1 hour. The mixture was

heated for a further 5 hours at the same temperature, poured into water (2·5 l.) and the precipitate taken up in chloroform. The chloroform solution (I) was shaken with sodium bicarbonate, the aqueous layer acidified with hydrochloric acid, and the yellow precipitate dissolved in chloroform. The chloroform solution (II) was washed with water and dried (sodium sulphate). Evaporation of the solvent gave almost pure fluorenone-1-(o-benzoic) acid, 3·0 g. Recrystallization from toluene-petrol ether gave yellow needles, m.p. 202-203°C. (Kruber and Oberkobusch give m.p. 203°C).

The chloroform solution (I) was washed with water and dried. Removal of solvent gave 3,4-benzfluoranthene (2·0 g.), white needles from acetic acid.

PREPARATION OF 3,4-BENZ-2-AZAFLUORANTHENE.

Fluorenone-1-(o-benzoic) acid (1·0 g.) was refluxed in thionyl chloride (5 ml.) for 45 minutes. The excess of thionyl chloride was distilled under reduced pressure, the last traces being co-distilled with anhydrous benzene. The acid chloride, a yellow oil, was dissolved in anhydrous acetone (23 ml.) and the stirred solution kept at 0-5°C while a solution of sodium azide (0·3 g.) in water (1·0 ml.) was added drop-wise. Sodium chloride was precipitated at once. The suspension was kept at 0-5°C for 45 minutes, with occasional swirling, water (50 ml.) added, and the precipitated acid azide taken up in ether. The ether solution was washed with water,

reduced to small volume and concentrated hydrochloric acid (25 ml.) added. The mixture was heated slowly from 20°C to 100°C, the ether being allowed to evaporate. The acid solution was finally boiled vigorously for 15-20 minutes, and poured into potassium hydroxide solution. The yellow precipitate was dissolved in ether, the ether solution washed free of alkali and dried (sodium sulphate). Removal of the solvent yielded 0·71 g. of a yellow solid. Recrystallization from petrol-ether gave 3,4-benz-2-azafluoranthene, pale yellow needles, m.p. 168-169°C.

Analysis. Found: C = 89·8; H,= 4·4; N = 5·5%,

$C_{19}H_{11}N$ requires: C = 90·1; H = 4·3; N = 5·5%.

3,4-Benz-2-azafluoranthene is weakly basic as is shown by its inability to form a stable hydrochloride. Chloroform readily extracts the base from concentrated hydrochloric acid.

EXPERIMENTAL PART 4.

The preparation of 12-nitro-2-azafluoranthene, 5,12-dinitro-2-azafluoranthene and a dinitro-10-azafluoranthene.

PREPARATION OF 12-NITRO-2-AZAFLUORANTHENE.

2-Azafluoranthene was dissolved in dilute nitric acid and the solution evaporated under reduced pressure to dryness. The tacky residue was triturated with warm ethanol, and the yellow product collected at the filter. Recrystallization from ethanol gave yellow needles of 2-azafluoranthene nitrate, m.p. 179°C.

Analysis. Found: C = 67·8; H = 3·8; N = 11·2%,

$C_{15}H_{10}N_2O_3$ requires: C = 67·7; H = 3·8; N = 10·5%.

2-Azafluoranthene nitrate (3·6 g.) was added slowly to concentrated sulphuric acid (18 ml.), with cooling of the solution to room temperature. When the addition was complete the solution was set aside at room temperature for 1·5 hours, then heated for 20 minutes at 60°C, and poured into water. The precipitate was collected at the filter, then boiled with potassium carbonate solution. The product was collected, dried thoroughly, and recrystallized once from toluene to give 2·0 g. of fairly pure 12-nitro-2-azafluoranthene. 0·7 g. of material, insoluble in the toluene, was removed by filtration. Recrystallization of the 12-nitro-2-azafluoranthene from benzene gave yellow needles, m.p. 250-252°C.

Analysis. Found: C = 71·7; H = 3·4; N = 11·0%,
$C_{15}H_8N_2O_2$ requires: C = 72·6; H = 3·2; N = 11·3%.

OXIDATION OF 12-NITRO-2-AZAFLUORANTHENE METHIODIDE.

12-Nitro-2-azafluoranthene (0·8 g.) was heated in excess methyl-p-toluene sulphonate for 1 hour at 100°C. The mixture was extracted twice with hot benzene and once with ether. The crystalline residue was collected at the filter, 12-nitro-2-azafluoranthene metho-p-toluene sulphonate (1·0 g.) yellow needles, m.p. 218-220°C (uncorr.). For subsequent work, the more readily recrystallized methiodide was prepared from an aqueous solution of the metho-p-toluene sulphonate by precipitation with aqueous potassium iodide. Recrystallization from aqueous ethanol gave reddish-violet needles, m.p. 254-255°C.

Analysis. Found: N = 7·1; I = 32·1%,
$C_{16}H_{11}N_2IO_2$ requires: N = 7·2; I = 32·6%.

12-Nitro-2-azafluoranthene methiodide (0·9 g.) was stirred in a dilute potassium hydroxide solution (32 ml.) at 60°C while a solution of potassium permanganate (2 g.) in water (100 ml.) was added drop-wise over 4 hours. The heating was continued for a further hour, the temperature of the mixture was then raised to 90-100°C, and the solution filtered. The manganese dioxide was extracted once with boiling water, and the filtrates combined and made acid. The fine yellow precipitate was dissolved in chloroform, the chloroform

solution washed with water, and dried (sodium sulphate). The solution was evaporated to 1-2 ml. and the product precipitated by addition of petrol ether, 0·050 g. of yellow acid. Recrystallization from glacial acetic acid gave yellow needles, m.p. 245-247°C (dec.). The acid did not depress the m.p. of an authentic sample of 7-nitro-fluorenone-1-carboxylic acid, prepared by the method of Garascia, Fries and Ching (J. Org. Chem., 17, 226 (1952)).

PREPARATION OF 5,12-DINITRO-2-AZAFLUORANTHENE.

2-Azafluoranthene (0.5 g.) was dissolved in nitric acid (sq. gr. 1·5; 5 ml.) and the solution kept at 17-20°C for 20 hours, then poured carefully into sodium carbonate solution. The crude product (0·62 g.) was washed with water and dried. Recrystallization from chlorobenzene gave 5,12-dinitro-2-azafluoranthene (0·37 g.), yellow needles, m.p. 300-301°C.

Analysis. Found: C, 61·8; H, 2·4; N, 14·3%,

$C_{15}H_7N_3O_4$ requires: C, 61·4; H, 2·5; N, 14·3%.

The same dinitro-2-azafluoranthene was the sole product from the nitration of 2-azafluoranthene (0·1 g.) in glacial acetic acid (0·5 ml.) and nitric acid (sq. gr. 1·42; 1·0 ml.). The nitration mixture was refluxed gently for 1 hour, poured into water, and the yellow precipitate recrystallized from chlorobenzene as yellow needles, m.p. 300-303°C.

The following procedure also yielded 5,12-dinitro-2-azafluoranthene: 2-azafluoranthene (1·0 g.; 0·005 mol.) was

dissolved in concentrated sulphuric acid (5 ml.) and powdered potassium nitrate (0·52 g.; 0·005 mol.) added in small amounts. The mixture was set aside at 17-20°C for 20 hours, poured into water and the aqueous suspension made alkaline with sodium carbonate. The yellow product (1·2 g.) was dried and crystallized.from chlorobenzene in yellow needles (0·5 g.), m.p. 288-292°C. A second recrystallization gave yellow needles, m.p. 298-300°C.

Analysis. Found: C, 62·9; H, 2·5; N, 14·1%,

$C_{15}H_7N_3O_4$ requires: C, 61·4; H, 2·5; N, 14·3%.

The mother liquor from the first recrystallization was chromatographed on a column of alumina (15" x 0·5") with benzene:chlorobenzene (4:1 v/v) as eluant. The appearance of the column, soon after development was begun, was as is illustrated in Fig.I; the appearance towards the end of the development was as illustrated in Fig.II.

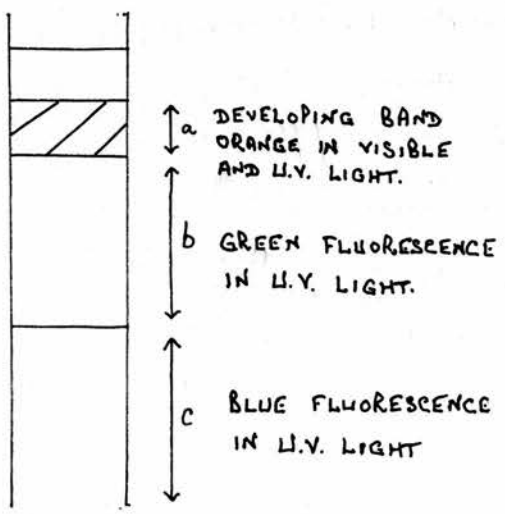


Fig.I

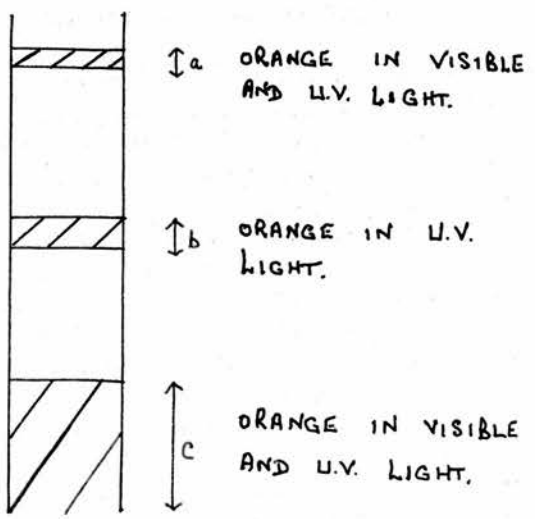


Fig.II

The green fluorescence (Fig.Ib) was due to 2-azafluoranthene. Four fractions were taken from the eluted band (Fig.IIc) and these were concentrated to very small volume giving:-

i. Yellow material, m.p. range 195-250°C.

ii. Yellow material, m.p. range 210-225°C.

iii. Yellow material, m.p. range 215-235°C.

iv. Orange material, very impure.

No further resolution of these fractions was attempted. It is probable that they were mixtures of the 5- and 12-nitro-2-azafluoranthenes.

ATTEMPTED OXIDATION OF 5,12-DINITRO-2-AZAFLUORANTHENE.

Several attempts to oxidize 5,12-dinitro-2-azafluoranthene were made, and these were almost entirely unsuccessful. Typical procedures followed ~~XXX~~ are given in i. and ii., a small amount of an acidic product being obtained by that given in ii.

i. To a solution of the dinitro-2-azafluoranthene (0·2 g.) in glacial acetic acid (10 ml.) was added chromic anhydride (1·0 g.) and the mixture was boiled for 90 minutes. Acetic acid (4 ml.) was distilled and the green solution then poured into water (30 ml.). The precipitate was collected at the filter, treated with alkali and the alkaline solution filtered. The residue consisted of starting-material.

The acid filtrate was reduced to small volume and made neutral with a concentrated solution of alkali. No organic

acid was precipitated before the neutral point was reached.

The alkaline filtrate was acidified; no precipitate was obtained.

ii. To a well-stirred suspension of the dinitro-2-azafluoranthene (1·4 g.) in water (42 ml.) was added a 3% solution of potassium permanganate (200 ml.). The mixture was maintained at reflux temperature, and the oxidant was added in 5-10 ml. portions over ca. 4 hours. The solution was filtered, and the residue treated with sulphurous acid to yield starting-material. The filtrate was concentrated, and acidified carefully with dilute hydrochloric acid to give a solution of pH 3-1. Acidic material (0·01 g.) was isolated, pale yellow, m.p. 250-260°C. It could not be purified.

PREPARATION OF 5,12-DINITRO-3,4-DIHYDRO-2-AZAFLUORANTHENE.

3,4-Dihydro-2-azafluoranthene (1 g.) was dissolved in nitric acid (sq. gr. 1·5; 8 ml.), and the solution set aside at 17-20°C for 17 hours. It was poured into a stirred solution of potassium carbonate, the yellow precipitate was collected at the filter, washed with water and dried. The crude material (1·38 g.) was recrystallized from petrol ether-toluene to give brownish-yellow needles (0·7 g.), m.p. 278-284°C. 5,12-Dinitro-3,4-dihydro-2-azafluoranthene begins to darken at 170-180°C, and the final m.p. depends on the rate of heating.

Analysis. Found: C, 61·4; H, 2·9; N, 13·8%,

$C_{15}H_9N_3O_4$ requires: C, 61·0; H, 3·1; N, 14·2%.

DEHYDROGENATION OF 5,12-DINITRO-3,4-DIHYDRO-2-AZAFLUORANTHENE.

Attempted dehydrogenation of 5,12-dinitro-3,4-dihydro-2-azafluoranthene (0·43 g.) in gently refluxing 1-methylnaphthalene (6 ml.), with 20% palladium: charcoal (0·15 g.) gave, after 1 hour, a dull red solid which was chromatographed on a column of alumina. The separation, with benzene-chlorobenzene as eluant, was difficult. A red material adhered to the top of the column while an orange substance spread slowly down. The column was cut and the orange portion extracted to give impure orange material (0·095 g.), m.p. 260-280° C.

The dehydrogenation was accomplished during an attempt to oxidize 5,12-dinitro-3,4-dihydro-2-azafluoranthene with chromic anhydride. The dinitro-dihydro-2-azafluoranthene (0.9 g.) was dissolved in acetic acid (25 ml.) and a solution of chromic anhydride (1·2 g.) in acetic acid (5 ml.) and water (5 ml.) added. The mixture was heated under reflux until it had assumed a deep green colour, then poured into water. The yellow precipitate was collected at the filter, washed, dried and chromatographed, with chlorobenzene:benzene (1:1 v/v) as eluant.

Four fractions were collected, yielding a total of 0.08 g. of yellow crystals. The m.p. of each fraction lay within the range 295-301° C. Recrystallization from toluene-chlorobenzene gave yellow needles, m.p. 300-301° C, and a mixed m.p. with the dinitro-2-azafluoranthene obtained by the nitration of

2-azafluoranthene showed no depression.

Analysis. Found: C, 61·2; H, 2·2; N, 14·0%,

$C_{15}H_7N_3O_4$ requires: C, 61·4; H, 2·5; N, 14·3%.

OXIDATION OF 5,12-DINITRO-3,4-DIHYDRO-2-AZAFLUORANTHENE.

5,12-Dinitro-3,4-dihydro-2-azafluoranthene (0·75 g.) was dissolved in 30% sulphuric acid (ca. 75 ml.) and potassium permanganate (2 g.) added all at once. The mixture was refluxed until decolorization of the permanganate was complete, and then treated with an excess of sulphurous acid. The precipitate was extracted into chloroform, most of the solvent was distilled off and the solution diluted with petrol ether to precipitate the acid. This was purified by dissolution in sodium bicarbonate and re-precipitation with hydrochloric acid from the filtered solution. The yellow precipitate was taken up in chloroform and the concentrated solution yielded, on addition of petrol ether, a small quantity of compound which was recrystallized from chlorobenzene-acetic acid-petrol ether as yellow needles, m.p. 265-268°C. A mixed m.p. determination with a sample of 2,7-dinitrofluorenone-1-carboxylic acid prepared by the procedure of Campbell and Stafford (J. Chem. Soc., 1952, 299) gave the m.p. 262-267°C. The re-solidified material in each case melted at a higher temperature (270-275°C), owing to decarboxylation of the acid to 2,7-dinitrofluorenone, m.p. 290-292°C.

An attempted decarboxylation of crude 2,7-dinitrofluorenone-1-carboxylic acid with copper-bronze and quinoline

gave a yellow powder (ca. 0·015 g.) which could not be recrystallized. It had the m.p. 275-280° C.

PREPARATION OF A DINITRO-10-AZAFLUORANTHENE.

10-Azafluoranthene (1 g.) was dissolved in nitric acid (sp. gr. 1·5; 10 ml.) and the solution set aside at 19-21°C for 18 hours, then heated at 60°C for 25 minutes, before being poured into potassium carbonate solution. The crude product (1·2 g.) was collected at the filter, washed with warm water and dried. Recrystallization from chlorobenzene-acetic acid (charcoal) gave yellow needles (0·59 g.) which did not melt below 350°C.

Analysis. Found: C, 61·2; H, 2·4; N, 14·3%,

$C_{15}H_7N_3O_4$ requires: C, 61·4; H, 2·5; N, 14·3%.

EXPERIMENTAL PART 5.

The reduction of 2-azafluoranthene, and miscellaneous experiments.

REDUCTION OF 2-AZAFLUORANTHENE TO 3,4-DIHYDRO-2-AZA-FLUORANTHENE.

2-Azafluoranthene (2 g.) was dissolved in gently refluxing ethanol (80 ml.) and 5% sodium amalgam (40 g.) added in small portions, over ca. 10 minutes. The solution was refluxed for 1·75 hours, concentrated to 50 ml., and concentrated hydrochloric acid added to bring it to near neutral point before being poured into water (400 ml.). The aqueous suspension was extracted with ether and the ether solution dried (sodium sulphate), charcoal-screened, and concentrated. The residual oil was chromatographed on a column of alumina, with petrol-ether as eluant. The eluate yielded firstly 3,4-dihydro-2-azafluoranthene (1·14 g.), then starting material (0·28 g.). The 3,4-dihydro-2-azafluoranthene was characterized by its picrate, methiodide and hydrochloride.

A second reduction was effected as follows: 2-azafluoranthene (2 g.) was boiled in ethanol (80 ml.) with 5% sodium amalgam (55 g.) for 14 hours, and the mixture worked up as before. From the chromatographed solution of reaction product, four fractions were collected. The fractions I-III yielded a total of 0·855 g. of 3,4-dihydro-2-azafluoranthene; the fraction IV yielded an impure, low melting solid (0·44 g.)

which failed to give a methiodide with methyl iodide. Acetylation with acetic anhydride in glacial acetic acid gave a dark coloured oil which could not be purified.

PREPARATION OF 1,2,3,4-TETRAHYDRO-2-AZAFLUORANTHENE.

3,4-Dihydro-2-azafluoranthene hydrochloride (0·5 g.) was dissolved in boiling concentrated hydrochloric acid (20 ml.) and to the solution was added granulated tin (10 g.). The solution was refluxed until it was nearly colourless, concentrated hydrochloric acid (5 ml.) was added and heating continued until a completely colourless solution was obtained. The cooled solution was decanted, the flask rinsed with hot water, and the combined solution made alkaline with potassium hydroxide. The mixture was extracted with several portions of ether, the combined ether solutions washed with water and dried (sodium sulphate). Evaporation of solvent left crude 1,2,3,4-tetrahydro-2-azafluoranthene (0·2 g.). Recrystallization from petrol ether gave white needles, m.p. 74-76°C (uncorr.). The compound, which became discoloured on being dried for analysis, was characterized by its hydrochloride and picrate.

Hydrochloride: prepared by passing dry hydrogen chloride into an ether solution of the base. Recrystallization from ethanol-petrol ether gave white prisms which became discoloured towards the m.p. 258-260°C (dec.).

Analysis. Found: N, 5·6; Cl, 14·2%,

$C_{15}H_{14}NCl$ requires: N, 5·8; Cl, 14·6%.

Picrate: prepared in ethanol solution. Recrystallization from ethanol gave yellow needles, m.p. 225-228°C (dec.).
Analysis. Found: N, 12·8%,
$C_{21}H_{16}N_4O_7$ requires: N, 12·8%.

An attempt to hydrogenate 3,4-dihydro-2-azafluoranthene (1·5 g.) in ethanol solution (35 ml.) using hydrogen (3 atm.) and 30% palladium:charcoal (0·25 g.), yielded, after 21 hours, only starting material (1·45 g.).

Reduction of 2-azafluoranthene (0·5 g.) with tin (10 g.) and concentrated hydrochloric acid (20 + 5 ml.) was effected according to the procedure detailed in the case of the 3,4-dihydro-2-azafluoranthene. The hydrochloride of 1,2,3,4-tetrahydro-2-azafluoranthene (0·23 g., m.p. 258-260°C (dec.)) was isolated from the reaction which, however, furnished a quantity of gum-like material and which did not proceed as readily as the reduction of the dihydro-2-azafluoranthene.

Attempted reduction of 2-azafluoranthene (1·3 g.) in refluxing ether (45 ml.) with lithium aluminium hydride (0·3 g.) yielded, after 3 hours, the starting material. The reaction mixture was decomposed with saturated ammonium chloride solution.

ATTEMPTED REDUCTION OF 3,4-BENZ-2-AZAFLUORANTHENE.

i) 3,4-Benz-2-azafluoranthene (2 g.) was dissolved in refluxing ethanol (100 ml.) and to the solution was added 5% sodium amalgam (50 g.) fairly rapidly. The mixture was

refluxed for a further 2 hours, brought nearly to neutral point with hydrochloric acid and poured into water. The suspension was extracted with ether, the ether solution washed and dried (sodium sulphate). Evaporation of the solvent left a pale yellow substance. An attempt to form a -toluene sulphonyl derivative in pyridine solution failed; and the chromatographing of a portion of the substance, with petrol ether-ether (9:1 v/v) as eluant, achieved no resolution of material. Four fractions were collected; each yielded starting material, as proved by mixed m.p. determinations.
ii) 3,4-Benz-2-azafluoranthene (0·8 g.) was refluxed with tin (10 g.) and concentrated hydrochloric acid (35 ml.). Soon after reaction had begun the benz-2-azafluoranthene was absorbed into an orange complex, presumably with stannic chloride; this complex was insoluble in the acid solution, and at the conclusion of the reaction was decomposed with potassium hydroxide to yield the starting-material.

OXIDATION OF 3,4-BENZ-2-AZAFLUORANTHENE.

Attempted oxidation, by either sodium bichromate or chromic anhydride, of 3,4-benz-2-azafluoranthene in glacial acetic acid, was hindered through the immediate precipitation of an insoluble complex. Only traces of an organic acid were isolated, while the complex could be decomposed with potassium hydroxide to yield the starting-material. The degradation of 3,4-benz-2-azafluoranthene by potassium permanganate was effected as follows.

3,4-Benz-2-azafluoranthene (1 g.) was dissolved in analar glacial acetic acid (25 ml.) at 80-87°C, and to the stirred solution was added, in small amounts, powdered potassium permanganate (5 g.). The addition of the permanganate occupied 2 hours, and the oxidation was complete after a further hour. The acid solution was concentrated and the residue extracted thoroughly with dilute potassium hydroxide. The combined alkaline filtrates were made just acid with careful addition of hydrochloric acid, and the suspension thoroughly extracted with chloroform. The combined chloroform solution was washed with water, dried (sodium sulphate) and concentrated to 2-3 ml. Addition of petrol-ether precipitated a yellow acidic material (0·07 g.) which on sublimation gave pale yellow needles, m.p. 185-190°C.

The manganese dioxide residue was treated with sulphurous acid; 3,4-benz-2-azafluoranthene (crude; 0·2 g.) was recovered.

Analysis. Found: C = 67·2; H = 3·7; N = 0·8%.

The above acid (0.07 g.) was heated for 2 hours under reflux with 90% hydrazine hydrate (0·2 ml.) in dioxan (2 ml.). The cooled solution deposited a colourless compound, prisms, m.p. 350°C (dec.).

Analysis. Found: C = 58·4; H = 3·3; N = 17·3%.

REACTION OF 3,4-DIHYDRO-2-AZAFLUORANTHENE WITH ALKALI AND DIMETHYL SULPHATE.

3,4-Dihydro-2-azafluoranthene (1·8 g.) was suspended in a vigorously stirred solution of sodium hydroxide (20 g.) in water (105 ml.) at 100°C. To the suspension was added dropwise dimethyl sulphate (7·5 ml.). Almost immediately an orange precipitate was formed, which rapidly became orange-brown. The reaction was continued for 15 hours, the orange-brown material was collected at the filter and washed free of alkali. The filtrate had a pronounced odour of trimethylamine. The product was dried and extracted with benzene; the benzene solution (charcoal) on cooling yielded a yellow substance (0·72 g.) which could not be recrystallized. It contained no nitrogen. A sample was prepared for analysis by charcoal-screening a sample of the powder dissolved in chloroform, reprecipitating it with petrol-ether, and repeating this process with the precipitate. The sample softened at 215-220°C (dec.).

Analysis. Found: C, 84·6; H, 5·2%,

$C_{15}H_{10}O$ requires: C, 87·4; H, 4·9%.

ACTION OF HYDROXYLAMINE AND ALKALI ON (1) 3,4-DIHYDRO-2-AZAFLUORANTHENE METHIODIDE; (2) 2-AZAFLUORANTHENE METHIODIDE.

(i) To a suspension of 3,4-dihydro-2-azafluoranthene methiodide (1 g.) in ethanol (60 ml.) was added hydroxylamine hydrochloride (2·1 g.) and a solution of sodium hydroxide (1·4 g.) in water

(10 ml.). The mixture, which was distinctly alkaline, was heated under reflux for 18 hours, the hot solution was filtered from inorganic salts and concentrated to ca. 20 ml. On cooling, it deposited colourless needles; recrystallization from ethanol-petrol ether gave colourless needles, m.p. 194°C (dec.). The mother liquor was diluted with water and the resulting aqueous suspension extracted with ether. The ether solution yielded a further quantity of discoloured product (ca. 0·2 g.). The aqueous solution was evaporated under reduced pressure to dryness and the small residue dissolved in water (1-2 ml.). Acidification with hydriodic acid produced no precipitate.

The colourless reaction product was insoluble in water; treatment with hydrochloric acid produced no colouration.

Analysis. Found: C, 76·8; H, 6·3; N, 10·4%,

$C_{16}H_{16}N_2O$ requires: C, 76·2; H, 6·3; N, 11·1%.

(ii) 2-Azafluoranthene methiodide (0·9 g.), hydroxylamine hydrochloride (1·9 g.) and sodium hydroxide (1·3 g.) were heated together in a refluxing solution of water (9 ml.) and ethanol (56 ml.) for 18 hours. The hot solution was filtered and concentrated to ca. 15 ml. A dark-coloured oil separated. The solution was diluted with water, and the oily suspension evaporated to dryness under reduced pressure. The dark, rather tarry residue was stirred with a little water, then solution made acid with hydriodic acid and extracted several times with chloroform. On evaporation to dryness the aqueous

layer yielded inorganic material. The chloroform solution was evaporated to dryness and the tarry residue stirred with potassium iodide solution (6 ml.). A quantity of tar remained undissolved.

PREPARATION OF i. 6,7-BENZ-4-HYDROXY-2,3-DIAZAFLUORANTHENE; ii. 12-NITRO-4-HYDROXY-2,3-DIAZAFLUORANTHENE.

(i) 3,4-Benzfluorenone-1-carboxylic acid (0·2 g.) was heated for 2 hours in a refluxing solution of 90% hydrazine hydrate (1 ml.) in dioxan (5 ml.). The cooled solution deposited 6,7-benz-4-hydroxy-2,3-diazafluoranthene (0·14 g.) as yellow needles which did not melt below 350°C,

Analysis. Found: C, 78·4; H, 3·4;

$C_{18}H_{10}N_2O$ requires: C, 80·0; H, 3·7%.

(ii) 7-Nitrofluorenone-1-carboxylic acid (0·2 g.) was heated for 1·5 hours in a refluxing solution of 90% hydrazine hydrate (1 ml.) in dioxan (5 ml.). The cooled solution deposited 12-nitro-4-hydroxy-2,3-diazafluoranthene as reddish-orange needles which did not melt below 350°C.

Analysis. Found: C, 61·8; H, 3·2; N, 16·4%,

$C_{14}H_7N_3O_3$ requires: C, 63·4; H, 2·6; N, 15·9%.

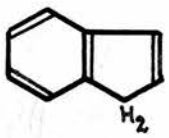
Both of these diazafluoranthenes were very insoluble in boiling concentrated hydrochloric acid; and the nucleus proved to be stable to hydrolytic fission by boiling concentrated hydrochloric acid.

DISCUSSION.

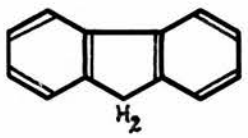
INTRODUCTION.

The carbocyclic cyclopentadiene system (I) and the five-membered rings incorporated in its benz- and dibenz homologues, indene (II) and fluorene (III) respectively, do not exhibit aromatic character.

I



II



III

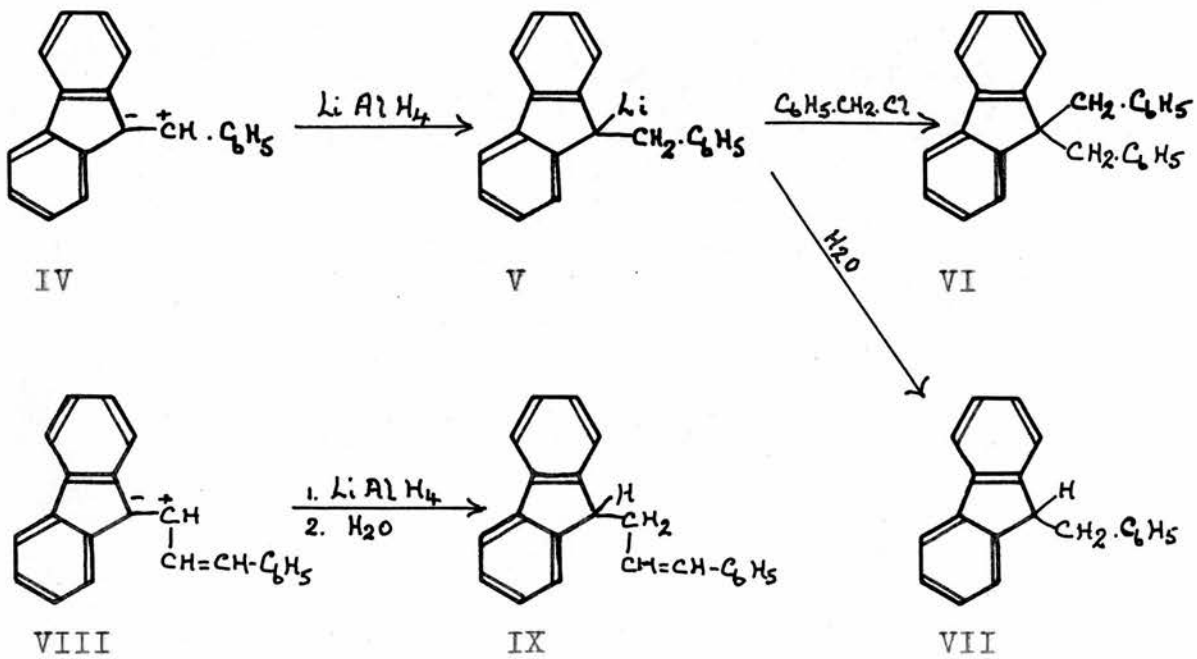
However, the methylene group in each case does behave markedly differently from methylene groups situated between C=C double bonds in open-chain systems and in ring systems other than the five-membered; for example, the hydrogen atoms are readily replaced by alkali metals, and, dependent upon this replacement, the methylene group displays a capacity for condensing with carbonyl compounds; and the accepted explanation for the unusually great acidity of these hydrocarbons, that is, for the stability of their corresponding anions, is that the negative charge participates in the ensuing delocalization, throughout the five-membered system, of an aromatic sextet of π-electrons (52). Thus, although the five-membered ring itself is not aromatic in character, the methylene group is strongly hyperconjugated with the two flanking double bonds, and the hyperconjugation readily passes into fully aromatic conjugation, on the replacement

of either acidic hydrogen atom by an alkali metal atom. The degree of hyperconjugation, and the stability of the anion, decrease in the order, cyclopentadiene, indene and fluorene, since the presence of the benzene rings reduces the symmetry of the π-electron system of the incipiently or the fully charged five-membered ring.

Consistent with this explanation of the activity of the methylene group in these three hydrocarbons are the properties of the compounds derived from them by substitution of the active hydrogen atoms. The class of such compounds hitherto the most extensively studied is the fulvenes, obtained by the condensation of carbonyl compounds with the methylene group. The fairly extensive studies of the dipole moments of fulvenes confirm that the moment is directed towards the five-membered ring, and that it decreases with annellation of the benzene rings (53). Annellation also produces an increase in the infrared valence frequencies (54) and a hypsochromic displacement in the visible and ultra-violet spectrum, as relating to the semicyclic bond. The theoretically-derived low bond order of this bond, lowest for cyclopentadiene, is evidenced by the fact that in very few cases have geometrically isomeric fulvenes been isolated, and it appears that it is only with the dibenzofulvenes that isomerism can occur. Thus p-nitrobenzylidene-2-nitrofluorene and -2-bromofluorene, and benzylidene-2-aminofluorene have been shown to exist in the respective isomeric forms (55).

Certain of the chemical properties of the fulvenes further illustrate the enhanced polar nature of the semicyclic double bond.

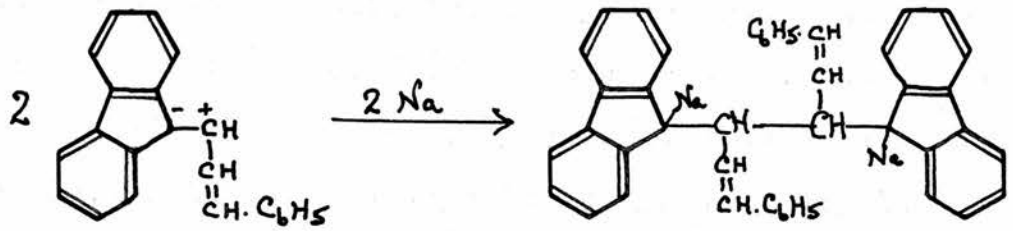
Compounds containing activated methylene groups undergo Michael condensation with the semicyclic bond, and hydrogen atoms attached to the positively charged exocyclic carbon atom are acidic, so that the exocyclic methylene group itself enters into aldol condensations. Yet more striking is the susceptibility of fulvenes to reduction by lithium aluminium hydride, and the mode of the addition of the lithium hydride fragments, as illustrated in the sequences IV—VII, VIII—IX, is at once explicable by the polarization of the subsequently reduced double bonds (56).



IV V VI

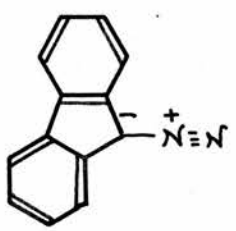
VIII IX VII

Again, sodium metal reacts with dibenzofulvenes, the resulting radicals dimerizing so as to form the corresponding disodio derivatives:

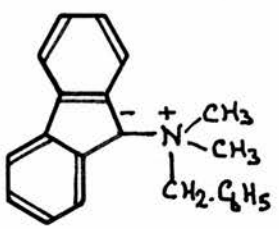


The fulvene ketones, derived formally by the replacement of the active methylene hydrogen atoms by oxygen, show marked dissimilarity from other ketones only in the cases of the cyclopentadienones and the indenones. It is true that the electronic spectrum of fluorenone shows absorption at considerably longer wave-length than benzophenone, and that the infra-red carbonyl frequency is higher than in aromatic ketones, indicating a decrease in the ionic character of the carbonyl double bond; nevertheless, the chemical properties of fluorenone differ little from those of aliphatic and aromatic ketones, and as it is as derivatives of the fluorene molecule that the azafluoranthenes are to be considered, no further mention of the fulvene ketones need be made.

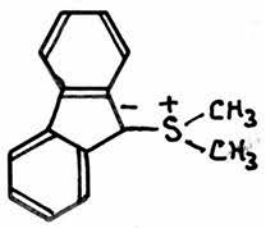
There are three compounds derived from fluorene, by the replacement of a hydrogen atom with a hetero group, which further illustrate, and remarkably, the delocalization of electrons that is found in the cyclopentadienide-ion type; these are given in formulae X-XII:



X

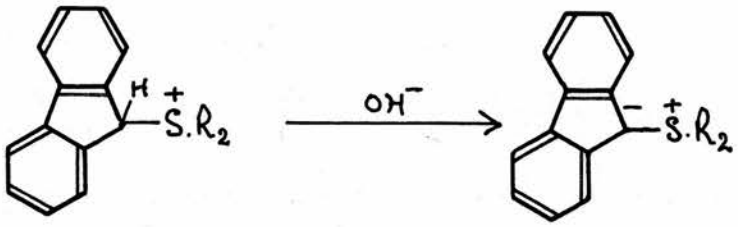


XI



XII

Compounds of the type, (XI) and (XII), are formed when quaternary 9-fluorenylammonium salts and 9-fluorenylsulphonium salts, respectively, are treated with alkali. Especially



noteworthy are the sulphonium compounds; thus the large dipole moment of (XII), which has been investigated in detail, indicates that the negative charge is almost entirely absorbed into the five-membered ring, although the sulphur atom would inherently tend to develop its unoccupied orbitals (57).

It has been already suggested (p.5) that the presence of the five-membered ring in the azafluorenthene structure will tend to modify the chemical properties and effects of the hetero atom, and an attempt can be now made to present the theoretical basis of the suggestion. Theoretical attempts to solve the problem of chemical reactivity in conjugated organic molecules have proceeded along one or other of two distinct lines. In the first case, the assumption is made that, in a reaction, whether ionic or neutral, the susceptibility of a position to attack is determined by the π-electron density at the position at the moment of reaction. The π-electron density at that moment differs from that of the same position when the molecule is not in the vicinity of the attacking reagent, and the reason

is that the attacking particle will perturb the π-, that is, the mobile electron system of the molecule. This perturbability effect is considerably more important when the particle is ionic than when it is a neutral molecule or a radical. There is a further effect, the localizability effect, which operates, and while the perturbability of the π-electron system at a position will tend to dominate the course of attack by an ionic particle, this second effect will be the more important when the attacking entity is neutral and, probably, when the perturbabilities of two or more of the reactive positions are the same, or nearly the same. The localizability effect increases directly with the free valence of a position, and while this latter quantity appears to be devoid of a permanent physical significance, it is associated with the physically significant fact that the atom has not participated in bonding to its (numerical) capacity. A particle then, which has approached close to the conjugated system will be held by the incipient bond formed between the reacting position and itself, and as the strength of the bond increases, a resulting change in the hybridization of the position - from the sp^2 to the sp^3 type - will take place. That is to say, at the reacting position there is a break-down of the electronic delocalization, reflected in the change of hybridization, and the greater the free valence, the smaller will be the required change in the π-electron energy, that is, the more favourable will be the position towards attack.

In the second of the two approaches to the problem of chemical reactivity, the emphasis is laid on the determination of energies

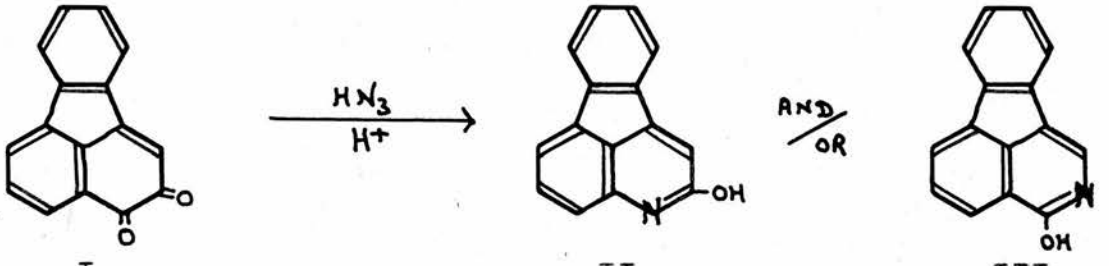
of activation of the various positions in a molecule, the activation being that of a position in the unattacked molecule to the state in which the π-electrons at that position are completely localized. The most reactive position is considered to be that which possesses the smallest localization energy, (the residual molecule having the lowest π-electron energy), and the value of this is the difference in the energies of the residual and the unattacked molecule. This being so the position, or positions, at which localization is complete are, in effect, removed from the conjugated, residual molecule - it being assumed that the interaction of the π-electrons of the residual molecule with the σ-electrons of the localized positions is a constant which may be ignored. In certain reactions, and the Diels-Alder reaction is an example, the complete localization is actually achieved with the formation of the reaction product, but generally, the complete localization will represent merely a transition state in the reaction sequence. The critical transition state in the sequence is, of course, that for which the energy of the π-electron system of the residual molecule is the greatest, and hence it may, and in most cases does, correspond to a partial localization, the complete localization referring to a somewhat smaller energy of the residual π-electron system, that is, to a less activated complex.

Now, the fact that emerges from this restricted statement of the approaches to the question of chemical reactivity is, that in each case the response of a position to an attacking

reagent involves the break-down of aromaticity at that part of the molecule. In the second of the two approaches it is admittedly complete; in the first it is at least partial, the extent depending upon one or other of the two possible controlling effects, the perturbability and localizability effects. Considering, then, the azafluoranthene structure in which the hetero atom is in the 2,-3- or 4-position, it is evident that reaction which involves the hetero ring at one or more of the three adjacent attackable carbon atoms, will result in the partial or complete localization of π-electrons at these positions, with the consequent realization of the identity of the fluorene or fulvene system, this realization increasing with the measure of π-electron localization. Accordingly, the presence of the forming five-membered aromatic ring may be expected to affect significantly the reactions, associated with the nitrogen atom, which involve attack of a neighbouring carbon atom. The significance of the directive effect of the forming ring in nucleophilic reactions, for example of 3-azafluoranthene, requires to be established experimentally; in other cases, it should be possible to predict the actual course of reaction; thus, while quinoline is reduced with lithium aluminium hydride to the 1,2-dihydroquinoline, one mole of the same reagent should reduce 3- and 4-azafluoranthene to the corresponding tetrahydro derivatives. However, the chief interest of the matter lies in the influence of the forming five-membered aromatic system on the development of the incipient bonds at the competing sites of reactivity.

THE SCHMIDT REACTION ON FLUORANTHENE-3:4-QUINONE.

The Schmidt reaction, in which a carbonyl compound is reacted with hydrazoic acid in the presence of a strong acid, has been applied to o-quinones in only a very few cases, and from 9,10-phenanthraquinones alone have the corresponding heterocyclic compounds been obtained (58). Phenanthraquinone gives phenanthridone; retenequinone, 1-methyl-7-isopropyl-phenanthridone; and chrysenequinone, 1,2-benzphenanthridone. It was considered that the application of the reaction to fluoranthene-3:4-quinone (I) might furnish either 3-hydroxy-4-



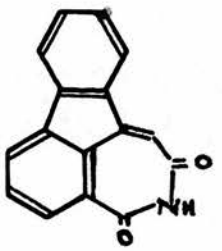
I II III

azafluoranthene (II) or 4-hydroxy-3-azafluoranthene (III) or, possibly, a mixture of (II) and (III), and, in any event, the result of the application might be expected to throw some light on the potentialities of the reaction and on its mechanism.

The reaction conditions were slightly more forcing than those used by Badger and Seidler (59) in their re-examination of the reaction on chrysenequinone; that is, a solution of the quinone (1 mole) in concentrated sulphuric acid at 50-60°C was treated with sodium azide (3 moles), the reacting hydrazoic acid being generated *in situ*. Trichloroacetic acid was, on occasion,

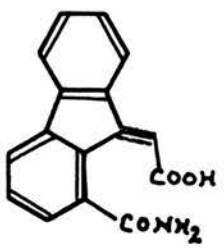
employed as solvent, in place of sulphuric acid, however, with a decrease in the yield of product. The former solvent possessed one advantage, namely, it could be used at higher temperatures, whereas sulphonation of the fluoranthenequinone accompanied the use of sulphuric acid at temperatures above 60-65°C.

The reaction product was, for each set of conditions employed, the imide (IV), and attempts to convert (IV) into

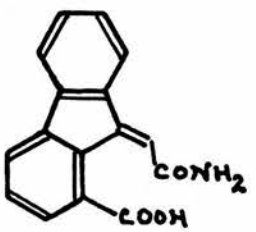


IV

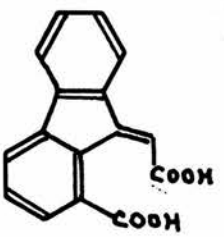
the 3- or 4-azafluoranthene system, by treating it with hydrazoic acid at elevated temperatures, were unsuccessful; the imide was recovered in each case. Such a conversion would require the rupture of the imide ring with the formation of one or both of the amido acids (V) and (VI), or of the dicarboxylic acid (VII), followed by the application of the Schmidt



V



VI

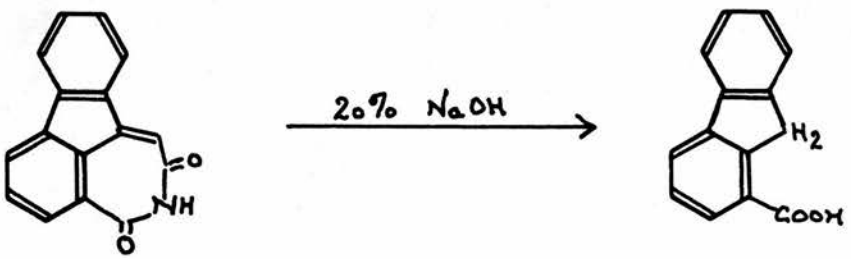


VII

reaction. An attempt was made to combine this reaction sequence with the examination of the reaction under conditions which, by themselves, might occasion the formation of V or VI as an isolable reaction product, and to this end the reaction was carried out in aqueous sulphuric acid (85%). The imide, however, was again obtained.

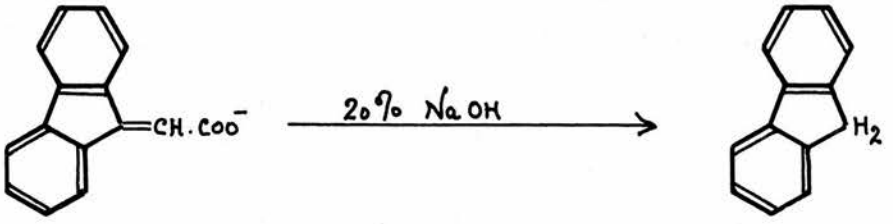
One possible hindrance to the transformation of V to 4-hydroxy-3-azafluoranthene, which required to be considered, was the unstable nature of the vinylamine group (60) which would be produced in the Schmidt reaction on the acid; this group displays a readiness towards polymerization in acid medium. Still, it was probable that neither V nor VI would be isolated from the deliberate hydrolysis of the imide, and of the two carboxyl groups in VII, the 1-carboxyl group, rather than that attached to the fulvene system, appeared to be more susceptible to the proton attack, which is assumed to be the initial step in the Schmidt degradation of a carboxyl group.

All attempts to cleave the imide ring by acid hydrolysis failed; in contrast, hydrolysis with 20% sodium hydroxide gave fluorene-1-carboxylic acid (VIII) in good yield. The smoothness



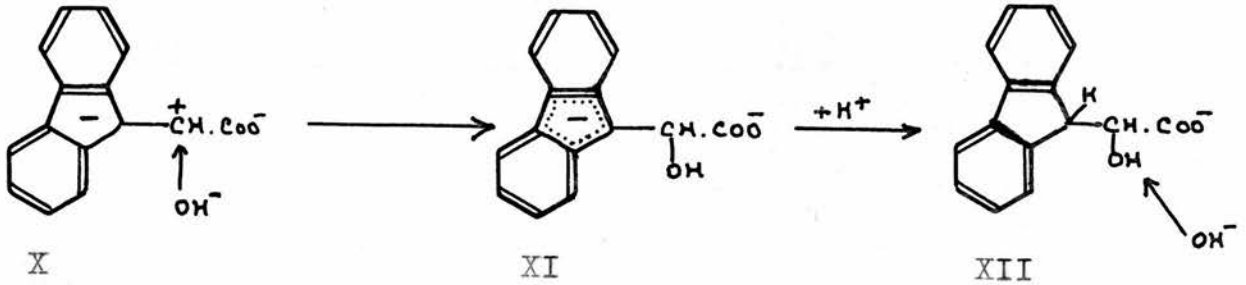
IV VIII

of the transformation, imide to fluorene-1-carboxylic acid, suggested its occurrence by way of a regular mechanism, and this was confirmed by the fact that ββ'-biphenyleneacrylic acid (IX) could be degraded to fluorene, by 20% sodium hydroxide.

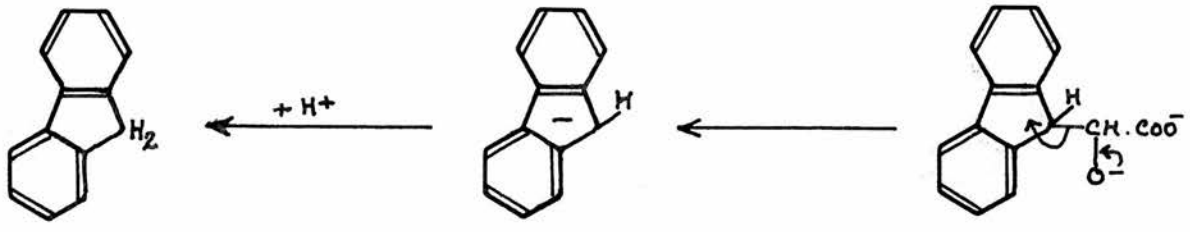


IX

It seems reasonable to attribute this unusual cleavage by alkali of, formally, a carbon-carbon double bond, to the great extent to which, in fact, this bond will be polarized. In both the imide and ββ'-biphenyleneacrylic acid, the semicyclic bond will be polarized in the usual sense indicated in (X), and hydroxyl



X XI XII

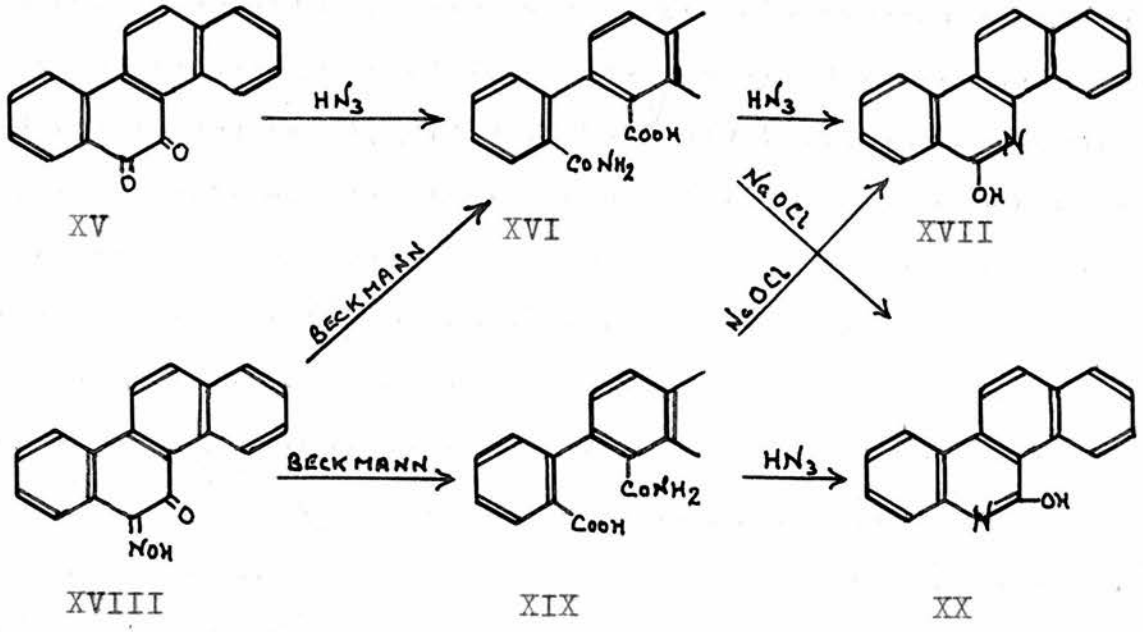


XIII XIV

ion may be expected to add to the positive centre, with the ultimate formation of fluorene-9-oxyacetic acid (XII). Although (XII) will undergo ready dehydration to (X), so that in the sequence (X)-(XII) the equilibrium will be displaced far towards (X), the delocalization of the negative charge in the anion (XI) will stabilize this intermediate, and the dehydration of (XII) will not be an irreversible process. The acid (XII) will undoubtedly participate in the base-catalysed aldol reverse reaction expressed in the sequence (XII)-(XIV), of which the step (XIII)-(XIV) may be regarded as irreversible((XIV) will not be stable in aqueous solution). The dependence on the presence of hydroxyl ion of the conversion of ββ'-biphenyleneacrylic acid to fluorene was established by the fact that no fluorene was produced when the acid was refluxed in neutral or acid medium.

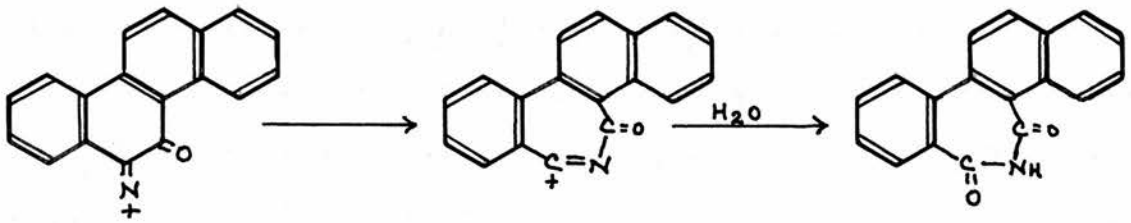
Reverting to the matter of the hydrolysis of the imide, it is evident that cleavage of the ring may have been preceeded either by hydroxyl attack at the polarized C-C bond, or by attack at the carbonyl group attached to this bond.

The significance of the fact that an imide, rather than a heterocyclic system, was the Schmidt reaction product, remains for consideration. The most detailed examination of a case of the reaction, which has actually furnished a heterocycle as the product, is that undertaken by Badger and Seidler on chrysenequinone (XV) which, with one mole of sodium azide, yielded 2-(o-benzamido)-1-naphthoic acid (XVI), but with two moles of



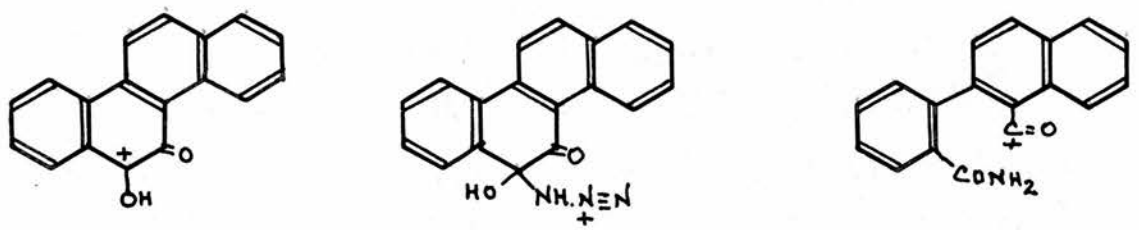
azide, yielded 1,2-benzphenanthridone (XVII) which was also the product of the Schmidt reaction on (XVI). The implications of these reactions are compared with the implications of the result of the Beckmann rearrangement of the quinone oxime (XVIII), which was carried out by Graebe (61). By the rearrangement, the two acids (XVI) and 2-(o-carboxyphenyl)-1-naphthamide (XIX) were obtained, convertible by the Hofmann procedure to (XVII) and 7,8-benzphenanthridone (XX) respectively, the latter being formed also by the Schmidt reaction on (XIX). In suggesting a mechanism for the Schmidt reaction on o-quinones, based upon their results, Badger and Seidler emphasise the fact that the quinone (XV) undergoes the Schmidt reaction to give but one amido acid (XVI), whereas its mono-oxime (XVIII) undergoes the Beckmann transformation to give the two possible amido acids (XVI) and (XIX), and they accommodate this difference in their

proposed mechanisms for respectively the Schmidt reaction on the quinone and the Beckmann conversion of the quinone oxime.



XXI XXII XXIII

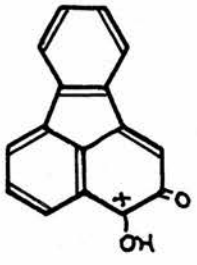
The latter is considered to proceed by way of the nitrogenium ion (XXI) which rearranges to the carbonium ion (XXII), and whilst the addition of one mol. of water would give the imide (XXIII), the addition of two moles will give the two amido acids (XVI) and (XIX). On the other hand, (XXI) cannot be an intermediate in the Schmidt reaction, as only one amido acid is obtained. The carbonium ion (XXIV), as the first intermediate,



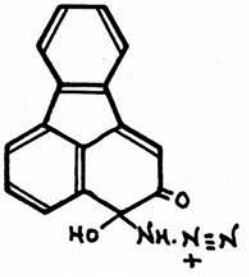
XXIV XXV XXVI

is considered to add hydrazoic acid to yield (XXV) which loses nitrogen, with fission of the C-C bond, to give (XXVI). Addition of one mole of water to (XXVI) would result in the formation of the amido acid (XVI), while addition of a further mole of hydrazoic acid would lead to formation of 1,2-benz-phenanthridone (XVII).

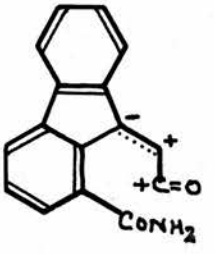
If the general validity of this mechanism is accepted with reservation, since it is founded upon but one investigation, an attempt may be made to apply it to the Schmidt reaction on fluoranthene-3:4-quinone. Since proton addition is almost certain to occur at the 4-position, the corresponding intermediates will be (XXVII), (XXVIII) and (XXIX), and the latter ion will be very unstable, for in fact, the polarization of the



XXVII

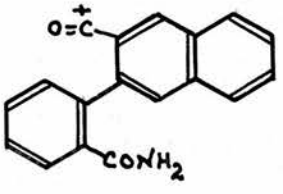


XXVIII



XXIX

semicyclic bond will occasion the presence of two adjacent positive charges. Hence, the rapid loss of a proton, with the consequent formation of the imide (IV), must be expected, and this will be aided by the spatial configuration of (XXIX) in contrast to that of the ion (XXVI) which may be represented as



XXVIa

in XXVIa. That is, the carbonium carbonyl group will, in general, be closer to the amido group in (XXIX) than in (XXVI).

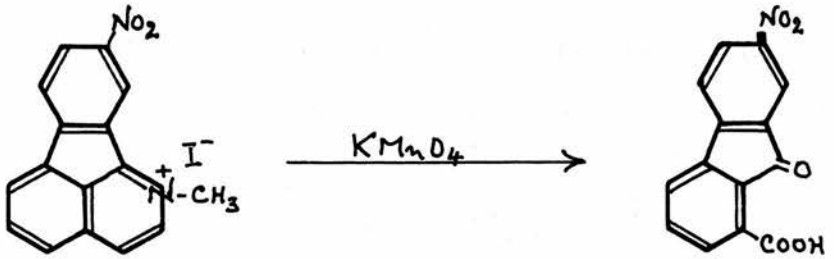
The fact that the Schmidt reaction cannot be successfully

applied to a number of acids, and gives anomalous results when carried out on certain ketones, is itself an indication that it may have limited applicability to o-quinones, for the development of the reaction course will depend upon the reactivity to hydrazoic acid of the carbonium intermediates. For example, the electronic environment of such an intermediate, or the steric arrangement of the postulated intermediate carbonium ion, which must allow of ready rearrangement of the ion to the isocyanate form, may, in fact, be unfavourable towards the development of the reaction to give the amine. Since the reaction is hindered by electrophilic groups, it may be expected that further reaction of ion (XXIX) with hydrazoic acid would be inhibited by the adjacent positive charge of the exocyclic carbon atom; in this case the reaction product would necessarily be the imide (IV). The operation of such factors is indicated by the observation that the Schmidt reaction on 1:2:5:6-dibenzanthra-3:4-quinone furnishes two amido acids, although only one phenanthridone has been isolated (62).

THE NITRATION OF 2-AZAFLUORANTHENE.

Depending upon the reaction conditions employed, attempts to nitrate 2-azafluoranthene yielded two different products, namely, 12-nitro-2-azafluoranthene and 5,12-dinitro-2-azafluoranthene. The former was obtained by dissolving 2-azafluoranthene nitrate in concentrated sulphuric acid, and allowing the nitration to proceed at room temperature for ninety minutes and at 60°C for

twenty minutes. The position of substitution was determined by the permanganate oxidation, in alkaline solution, of the 12-nitro-2-azafluoranthene methiodide, from which 7-nitro-fluorenone-1-carboxylic acid was isolated.

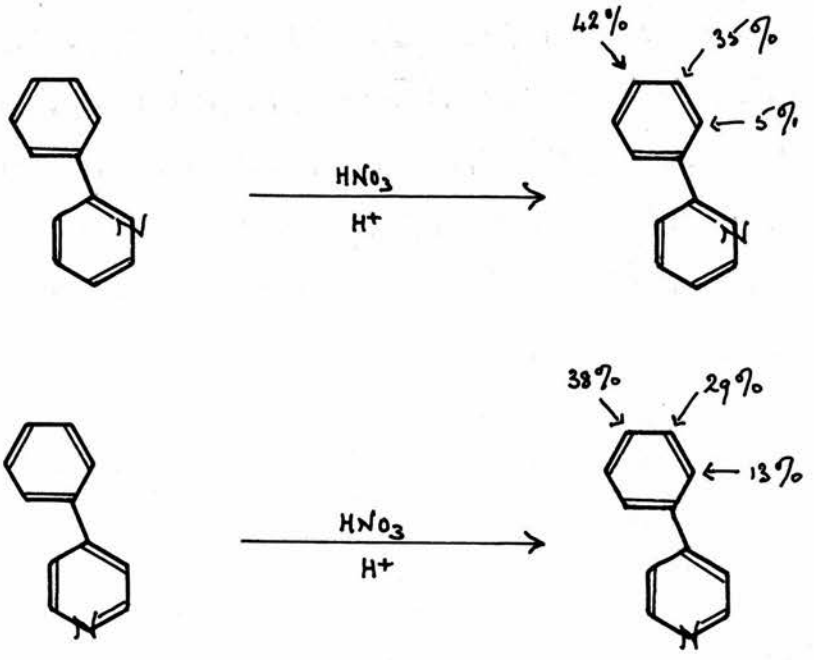


In contrast to this result of mono-nitration, treatment of a solution of 2-azafluoranthene in concentrated sulphuric acid with one mole of potassium nitrate, yielded mainly 5,12-dinitro-2-azafluoranthene, when the reaction temperature was 17-20°C, and the time of reaction was 20 hours. The same dinitro derivative was obtained from the nitration of the base with 1) fuming nitric acid at room temperature and 2) a refluxing acetic acid-concentrated nitric acid mixture. The time of reaction was in 1) twenty hours; in 2) one hour. The orientation of the two nitro groups was determined as follows: 3,4-dihydro-2-azafluoranthene, obtained in the course of the synthesis of the parent heterocycle, was nitrated in fuming nitric acid to yield 5,12-dinitro-3,4-dihydro-2-azafluoranthene, the structure of which was elucidated by permanganate oxidation to 2,7-dinitro-fluorenone-1-carboxylic acid. Dehydrogenation of (III) gave a dinitro-2-azafluoranthene identical with the product of nitration.

These 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; the question, indeed, being part of the entire problem of conjugation between linked aromatic systems, which concerns the relative effects on an aromatic nucleus of an ortho-condensed benzene or heterocyclic ring, as in naphthalene or quinoline, and of a linearly-conjugated phenyl or heterocyclic group, as in diphenyl or the mono-azadiphenyls. In 2-aza-fluoranthene it is the latter type of conjugated system that is being considered.

It was pointed out (p.14) that the orientation of a group entering a mono-substituted fluoranthene has been considered from the point of view that fluoranthene is, formally, a diphenyl derivative. In the same way, 2-azafluoranthene contains both a diphenyl and a 2-azadiphenyl nucleus, and hence a comparison of the behaviour of these compounds towards electrophilic substitution should give an indication of the accuracy of regarding the heterocycle as a substituted fluoranthene. The outstanding fact in the behaviour of mono-substituted diphenyls towards further substitution is that, in the main, the nature and position of the first group does not control the orientation of the entering group. Thus the meta-orienting effect of the nitro groups in 2- and 4-nitrodiphenyl and in 2,4-dinitrodiphenyl, is submerged, and the substituted phenyl group acts as a unity which is ortho-para-directing (63). Apparently, however, the

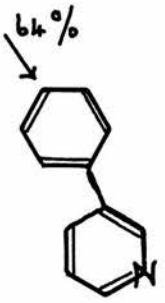
2- and 4-pyridyl groups in 2- and 4-azadiphenyl (2- and 4-phenyl pyridine respectively) are, in measure, meta-directing, for



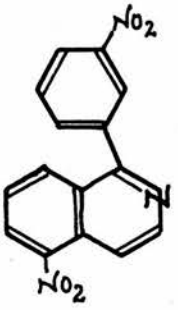
nitration of these compounds furnishes a significant amount of the meta-isomers (64). Presumably, it is the protonated pyridyl ring or hetero atom which is meta-directing, whilst the non-ionized ring is still able to function as an ortho-para-directing group, and this explanation accords with the behaviour towards substitution of 2-phenyl quinoline, 2-phenylquinolinium methosulphate and possibly of 4-phenylquinoline, as recorded earlier (p.9).

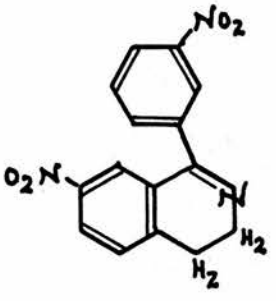
These results, however, do not confirm whether or not the protonated nitrogen atom or the protonated hetero ring is the controlling group, and this distinction - that is, whether or not the effect of the positive charge on the hetero atom is being relayed by conjugation to the phenyl ring - must be

clarified before 2-azafluoranthene can be regarded as a derivative of fluoranthene or of isoquinoline in substitution reactions. The result of the nitration of 3-phenylpyridine does lend strength to the latter view, for in this case the para-isomer has been isolated in 64% yield, which, it will be observed, is higher than the combined ortho-para proportions isolated from the nitration of the 2- or 4-phenylpyridine.



That is to say, it appears that not merely the deactivated ring but the deactivating protonated nitrogen atom in the 2- and 4-phenylpyridines is the meta-orienting group, whilst in the 3-phenylpyridine the location of the hetero atom meta to the phenyl-pyridine linkage occasions its diminished orienting capacity, according to the normal rules of benzene substitution. This conclusion is further promoted by the observations made on the nitration of 1-phenylisoquinoline and 1-phenyl-3:4-dihydro-isoquinoline (p.11): the phenyl ring is substituted in the





former in the same position as it is in the latter, that is, meta to the nitrogen atom, nor has the nitration of the fully aromatic compound furnished any 2'- or 4'-nitrophenylisoquinoline. It is, perhaps, difficult to appreciate why this last fact stands; as compared with quinoline (K_b, $3{\cdot}2 \times 10^{-10}$) it can be argued that isoquinoline (K_b, 2×10^{-9}) will be protonated more readily, so that the nitration is of a form more comparable to 2-phenylquinolinium methosulphate than 2-phenylquinoline; but a similar argument is not valid where the comparison is made, with pyridine (K_b, $2{\cdot}3 \times 10^{-9}$), and the fact serves to indicate the complexity of the entire problem of such conjugated systems.

The fact that nitration of 2-azafluoranthene with one equivalent of potassium nitrate in sulphuric acid gave, after twenty hours at 17-20°C, a considerable amount of 5,12-dinitro-2-azafluoranthene, while the 12-nitro-2-azafluoranthene was formed under scarcely less forcing conditions, indicates that the 12-position in the unsubstituted base is only little more reactive than the 5-position in the mono-nitro derivative. Now, although the decisive significance of this would depend upon its examination quantitatively, the present inference is, that if the nitro group in ring C (formula I) is deactivating ring B in comparison with the unsubstituted ring C, so also must

I

II

the hetero atom in 2-azafluoranthene be exercising a deactivating influence on ring C (formula II) which, therefore, is attacked at the meta or 12-position. Accordingly, although the orientation of the nitro group in 12-nitro-2-azafluoranthene is consistent with the hypothesis that ring B in 2-azafluoranthene controls the mono-substitution, the orientation itself does not constitute a proof of the hypothesis, and there is more direct evidence that, in fact, the hetero atom, or its protonated form, is the directing group. This conclusion, if valid, suggests that the normal rule of benzene substitution, namely, that an activating rather than a deactivating substituent will control further substitution, has limited applicability to condensed aromatic systems. This indeed can be recognized in the fact that the deactivating substituent, in 4-bromofluoranthene directs a second substituent into the 11-position (p.14); evidently, the temporary, that is, the electromeric effect of the 4-bromo group is successfully relayed to dominate the observed substitution at the 11-position, in preference to the control of substitution at the 12-position, which would be exercised by the non-deactivated, unsubstituted ring B (formula III).

III

The conclusion that is thus favoured is that the behaviour towards nitration of 2-azafluoranthene is to be ascribed to its relationship to isoquinoline.

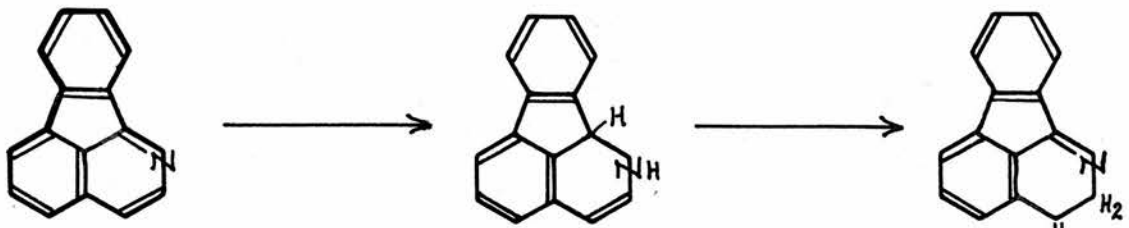
On the other hand, 3:4-dihydro-2-azafluoranthene is nitrated in the 5- and 12-positions, according to its formal relationship to diphenyl (or fluorene).

THE REDUCTION OF 2-AZAFLUORANTHENE.

The reduction of 2-azafluoranthene with 5% sodium amalgam in refluxing ethanol yielded 3:4-dihydro-2-azafluoranthene. The crude reaction mixture was chromatographed in order to remove starting material, and the oily product was characterized as the 3:4-dihydro compound. Further reduction of this to 1:2:3:4-tetrahydro-2-azafluoranthene was very readily effected by means of tin and concentrated hydrochloric acid, which was also effective in the conversion of the parent heterocycle to 1:2:3:4-tetrahydro-2-azafluoranthene. The attempted reduction of 3:4-benz-2-azafluoranthene with sodium amalgam and ethanol or with tin and hydrochloric acid was unsuccessful; so also was the attempt to reduce 2-azafluoranthene to 1:2-dihydro-2-azafluoranthene by means of lithium aluminium hydride in boiling ether.

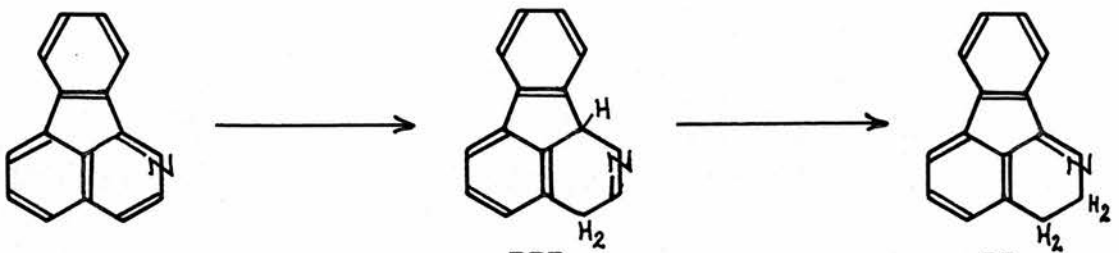
Since fluoranthene is reduced primarily to 1:2:3:4-tetrahydrofluoranthene (p.20), and no 3:4-dihydro derivative appears to have been obtained from the reduction of the fully aromatic heterocycles, quinoline and isoquinoline (p.19), the course of the reduction of 2-azafluoranthene by sodium amalgam in ethanol

would seem to be anomalous. An attempt will therefore be made to examine the possible courses by which this result has been reached. Excluding the direct addition of hydrogen to the 3:4-carbon-carbon "double bond," the observed result could be achieved either by 1:2-addition of a mole of hydrogen, which is known to occur in the quinoline and isoquinoline series, followed by migration of the 3:4-double bond, or by 1:4-addition



I II

of a mole of hydrogen, as occurs during the reduction of naphthalene, followed by migration of the 2:3-double bond.



III II

A decision as to which reaction course is the more probable may be sought in the application of current views on the mechanism of reduction by metal-hydroxylic solvent combinations. The essential step in the reduction of the double bond A=B is considered by Birch (65) to be either 1) the addition of one

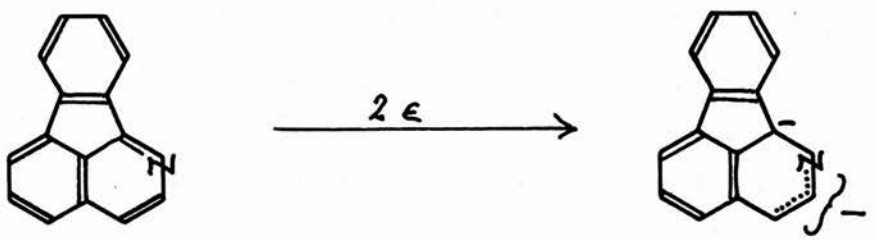
1) $A=B \longrightarrow \bar{A}-\dot{B}$

2) $A=B \longrightarrow \bar{A}-\bar{B}$

electron from the metal to give an anion radical, or 2) the addition of two electrons to give a charged anion, succeeding addition of protons completing the reaction. On the other hand, the theory has been developed (66) in which the metal is regarded as an electronic gas enclosed in potential walls from which electrons can escape only by way of an adsorbed electrophilic cation or molecule. The cation may be simply a proton, or it may be a cation formed by the initial addition of a proton to the negative pole of an unsaturated polarized group. The molecule, to be reducible, must possess a positive centre, created by a polarizing group, so that the necessary initial adsorption onto the metal surface occurs, and in a system in which the polarizing group is part of an extended conjugated system the electrons taken up may be distributed to any point throughout the system. It is held, then, that irrespective of the exact moment when the first proton enters the reducible system, whether before, during or after the assumption by the molecule of electrons, the process of electron uptake will be attended by the addition of a proton; and in the usual case when two electrons have been taken up - so that octets are completed - the entire operation will have been equivalent to the addition of the hydride anion, H^-. In the resulting anionic

system, the final proton will add to the most nucleophilic centre, so that the orientation is normally kinetically, not thermodynamically, controlled: the addition of both protons is considered to be an irreversible procedure, for under the reaction conditions usually employed, prototropic equilibrium is negligible.

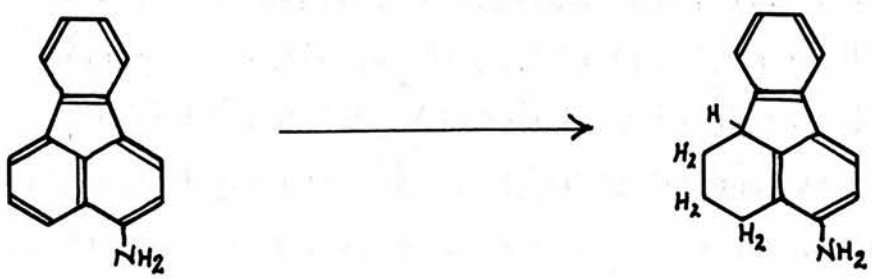
Since the details of the mechanism of reduction are not fully established, neither of the above explanations can be applied rigorously; however, for a conjugated system such as is being considered in 2-azafluoranthene, both explanations support the view that the initially formed intermediate will be a mesomeric anion, and the evident requirement is the determination of the identity of the anion. From the fact that the five-membered ring, which would be developing with the adsorption of the molecule onto the metal, is intensely electrophilic, it is almost certain that adsorption will occur at this point, and the first electron to be assumed will be held at the 1-position, whilst the second will resonate between positions 2,3 and 4. This is further supported by the fact



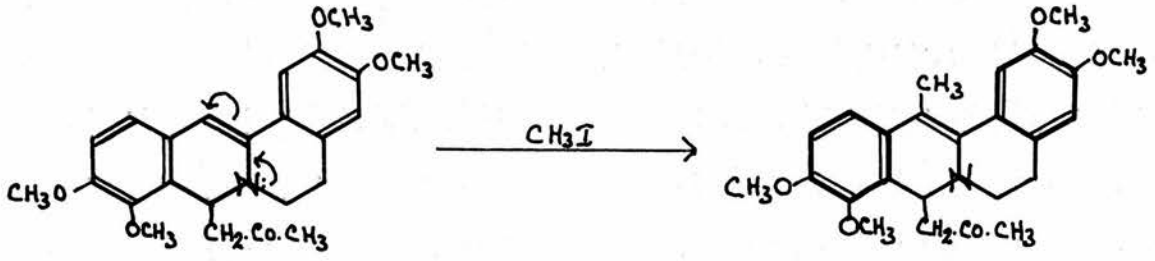
IV

(67) that 4-aminofluoranthene is reduced by sodium amalgam in ethanol to yield the 5:6:7:8-tetrahydro derivative; clearly,

the most electrophilic centre is the "1-position" which is not para to the nucleophilic amino group - in reality, the 8-position. The location of the initially assumed proton cannot

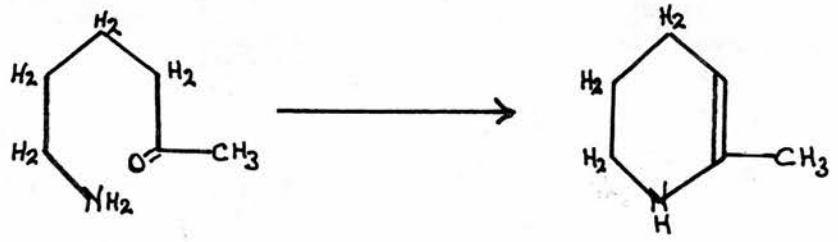


be determined with certainty, because, although the 1-position is the most nucleophilic, bearing a full negative charge, if in fact the uptake of the proton occurs during adsorption, it will do so at the most negative of the three remaining free positions. The problem of assigning the highest negative density to one or other of these positions is somewhat difficult, for, in competition with the essentially negative character of the nitrogen atom, is the tendency of the benzene nucleus to draw into conjugation with itself the mesomeric residue, so that the 4-position would be the most nucleophilic. However, it is probable that the capacity of the hetero atom to conjugate, by means of its lone pair of electrons, with a double bond located in the 3:4-position, will stabilize this configuration and accordingly, the most negative 4-position will add the proton. Such stabilization by conjugation in a hetero-enoid system is common; for example, it explains the methylation at the 4-position of the isoquinoline derivative (V) and the formation



V

of the tetrahydropyridine (VII) from the ring-opened compound (VI) (the methyl group would be hyperconjugated with either the 1:2- or the 2:3-double bond).

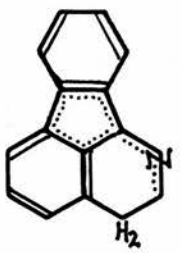


VI VII

If the addition of the first proton occurs after the charged anion (the 2-azafluoranthene system bearing two charges) has been desorbed, it will be to the 1-position, and subsequent proton addition will furnish the 1:4-dihydro-2-azafluoranthene which must undergo alkali-induced isomerization to yield the actually obtained 3:4-dihydro derivative. Whilst an express stipulation of the second of the above-stated theories is that the thermodynamically stable product is not obtainable from the less stable product, under the usual reaction conditions, it may be expected that the presence of the more than usually acidic hydrogen atom at the 1-position will result in an equally unusually facile isomerization to the thermodynamically stable

3:4-dihydro-2-azafluoranthene, and to test this, an attempt to obtain the 1:2-dihydro-2-azafluoranthene (which will be more resistant than the 2:3-isomer to isomerization) was made, but without success.

On the other hand, if the first proton adds while the charged anion is still adsorbed to the metal, it will to the 4-position, with the formation of the mesomeric anion (VIII) which is precisely the anionic intermediate which would be



VIII

produced during the alkali-induced isomerization of the 1:4-dihydro-2-azafluoranthene. Therefore, unless the present discussion of the problem is fundamentally inaccurate, it must be concluded that this anion is sufficiently stable to occasion an appreciable prototropic equilibrium between the kinetically and thermodynamically oriented reduction products, or even to occasion the direct formation of the thermodynamically more stable 3:4-dihydro-2-azafluoranthene, rather than permit the second proton to be oriented kinetically.

It will be evident from this discussion that the nitrogen atom in 2-azafluoranthene has not influenced the course of the mechanism which could be applied in detail to the reduction by sodium amalgam in ethanol of fluoranthene itself. However, the

fact that fluoranthene is readily reduced to the 1:2:3:4-tetrahydro derivative contrasts with the observation that 3:4-dihydro-2-azafluoranthene is at least fairly resistant to further reduction by this agent (it cannot be affirmed as yet that it is completely resistant). Any sufficient explanation of this resistance must take into account the three contrasting facts, namely, that 3:4-dihydroisoquinolines normally undergo ready reduction with sodium amalgam in ethanol; that if it is in fact an intermediate in the reduction of fluoranthene, the 3:4-dihydrofluoranthene is readily reduced to the tetrahydro compound; and that 3:4-dihydro-2-azafluoranthene is readily reduced to the tetrahydro derivative in concentrated hydrochloric acid solution. These appear to be adequately considered in the following explanation: the polarized dihydro-2-azafluoranthene will be adsorbed onto the metal in the usual way; however, if the 1:2-"double bond" is a low energy bond (and there is reason to believe that it is), despite the small work function of the reducing metal, the electronic uptake will be achieved with difficulty and may proceed only to the extent of one electron being added to the system. That is, the situation will be similar energetically to the "pinacol reduction" of a ketone by magnesium. Since dimerization of the bulky anion-radical is unlikely, the fact that the 1:2-double bond is of low energy will occasion the ready loss, to a proton from the medium, of the single added electron. It must be emphasized that the complete absorption into the system of the electron will represent the most extreme case, and in fact the electron may

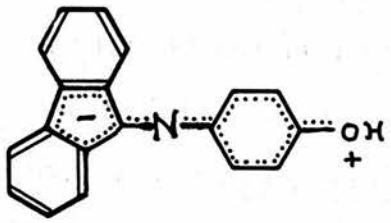
never become entirely free of the metal - that is, outwith the influence of the "potential walls."

If this explanation is valid, the above-mentioned contrasted facts are readily understood: 1) whilst in the dihydro-2-azafluoranthene the hetero atom will be conjugated by means of its lone pair to a negatively charged, aromatic five-membered ring so that further positive polarization of the nitrogen atom will be inhibited, the hetero atom in 3:4-dihydroisoquinolines is conjugated with a neutral benzene ring, which still possesses the capacity to absorb a further electron and act as the characteristically negative pole of a polarized, conjugated system involving the now positive nitrogen atom. Accordingly, the uptake of two electrons will be a considerably facilitated process in the dihydroisoquinolines, as compared with 3:4-dihydro-2-azafluoranthene, 2) in 3:4-dihydrofluoranthene, which is essentially a fulvene, the exocyclic carbon atom, without the capacity possessed by its hetero counterpart to conjugate by means of a lone pair, will be significantly more positive than the nitrogen atom so that, under the given reducing conditions, its behaviour is comparable to 3) that of the nitrogen atom protonated in acid solution. Hence, the reduction of 3:4-dihydrofluoranthene by the metal sodium (low work function) is comparable to that of 3:4-dihydro-2-azafluoranthene in acid medium, in which the protonated and, therefore, fully charged, nitrogen atom facilitates reduction by a metal of higher work function, such as tin.

In connection with the general theory of reduction,

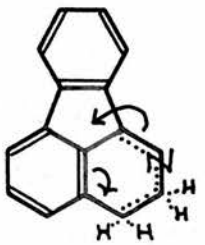
perhaps the above discussion gives implicit emphasis to one point, namely, that the detailed mechanism applicable to a particular reaction must be considered especially in the view of the molecule's electronic configuration under the given conditions of hydrogenation. For this reason, differences in the nature of products obtained under different conditions of reduction (cf. p.19) are readily to be expected, and perhaps it is not naive to remember that, from the mechanistic view-point, the reducible substance is as much a "reagent" as the other.

Since the offered explanation of the resistance to reduction of 3:4-dihydro-2-azafluoranthene depends on the consideration of the 1:2-double bond as of low energy, this section will be concluded by the statement of an observation which lends support to the idea. It has been found that the Schiff's bases, obtained by condensing fluorenone with primary aliphatic amines and certain primary aromatic amines, are readily hydrolysed to their components by means of warm dilute or cold concentrated hydrochloric acid. Thus, when the amine is β-ethanolamine, even cold dilute acid effects the cleavage; and warm dilute or cold concentrated acid cleaves the bond when the amines are aniline or para-toluidine. On the other hand, 3:4-dihydro-2-azafluoranthene and the anil from para-hydroxyaniline (69) are stable to prolonged treatment with hot concentrated acid. In the latter case, it appears that the hydroxy group stabilizes the bond in question by entering, by means of its lone electron pair, into conjugation with the electrophilic five-membered ring.

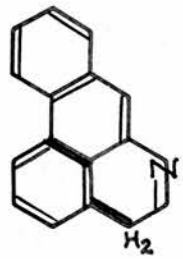


IX

The consequent delocalization pervading the C-N linkage (formula (IX)) will resemble that which characterizes the acid-stable azomethine linkage in a fully aromatic heterocycle such as 2-azafluoranthene itself. In the same way, the greater stability of the linkage in 3:4-dihydro-2-azafluoranthene, as compared with the C-N bond in the open-chain anils, may be attributable to increased hyperconjugation, with the electrophilic five-membered ring, of the methylene group in the 3-position. The planar configuration of the cyclic dihydro derivative will enable this methylene group to satisfy the geometrical requirements of first-order hyperconjugation which, in this case, will be considerable, and which will be aided also by the greater symmetry of the cyclic system. The consequent electron delocalization again may be assumed to produce the necessary degree of stabilization, and the C-N bond will be of low energy. Moreover, the hyperconjugation will be enhanced electromerically on the approach of a proton, the addition of which to the nitrogen atom will be the first step in the acid hydrolysis of a Schiff base. There may be a contribution to the hyperconjugative stabilization



X

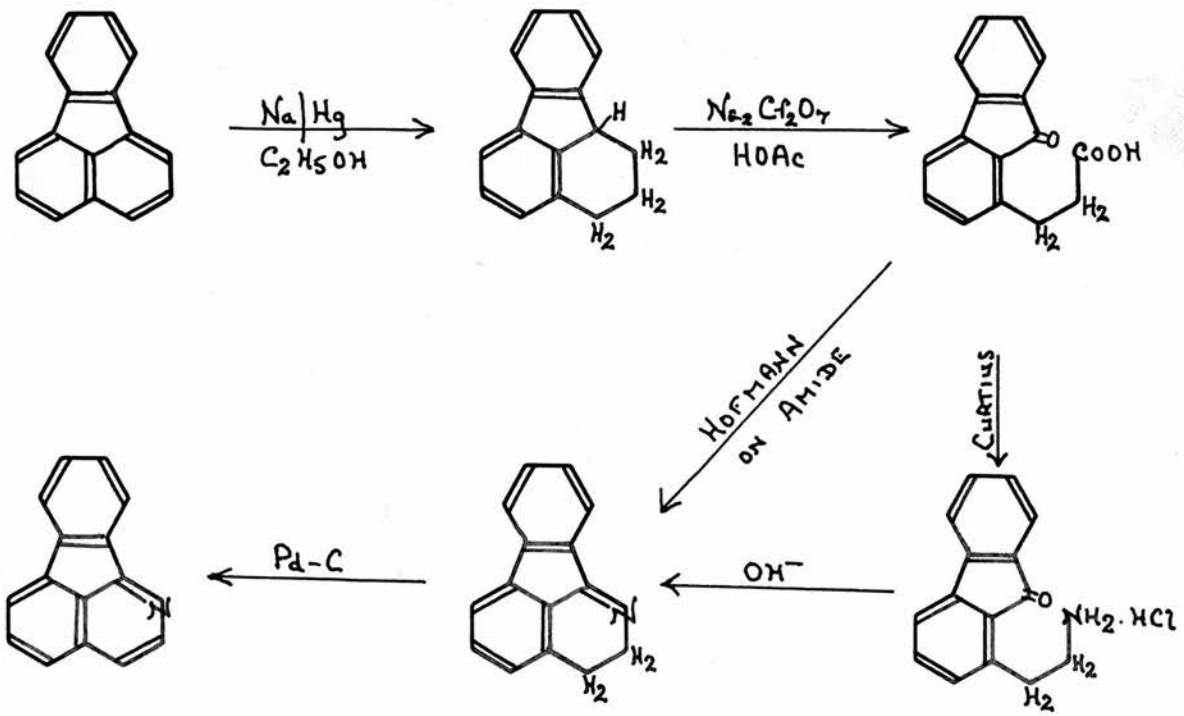


Xa

from the methylene group at the 4-position, as indicated in formula (X), but unless the possibility of mesomerism, involving the benzene ring and leading partially to the π-electron state to be found in (Xa), actually occasions an extraordinary ionization of the hydrogen atoms at C_4, such a contribution must be regarded as being negligible.

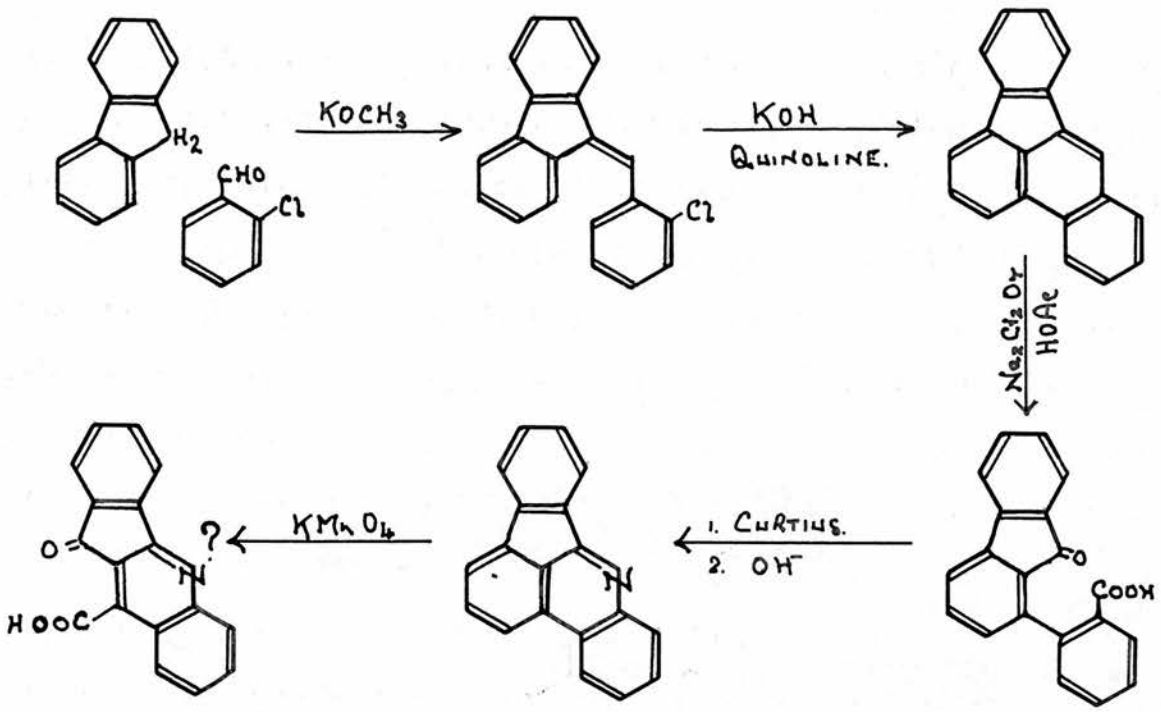
SYNTHESES OF 2-AZAFLUORANTHENE AND 3:4-BENZ-2-AZAFLUORANTHENE.

The synthesis of 2-azafluoranthene was carried out in accordance with the following scheme.



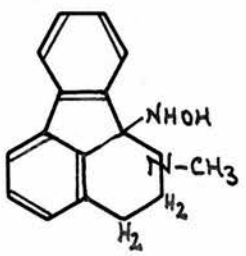
The yield of product at each stage in the synthesis was satisfactory, except for the Hofmann degradation of fluorenone-1-(β-propionic) acid amide to the dihydro-2-azafluoranthene; at this stage the maximum yield obtained was 40% of the theoretical. However, when this method of converting the acid to the base was replaced by the Curtius reaction, the yield was raised to about 90% of the theoretical. The Schmidt reaction cannot be applied to achieve the conversion since, in conformity with the rule that under the reaction conditions a ketonic group is attacked in preference to a carboxyl, the expected product is a phenanthridone, or a mixture of the two possible isomeric phenanthridones (cf. Cook and Moffatt, loc.cit.).

The synthesis of 3:4-benz-2-azafluoranthene was undertaken with the dual purpose of examining its behaviour under conditions of hydrogenation, and of finding an easy route to 2:3-benz-4-azafluorene. The attempted reduction of the heterocycle has been considered; the oxidation of the heterocycle proved to be difficult and only small amounts of a pale yellow acid were obtained. The structure of this has not been established, although its interaction with hydrazine to yield a colourless, high-melting nitrogen-containing compound indicates that it is 2:3-benz-4-azafluorenone-1-carboxylic acid. The synthesis of 3:4-benz-2-azafluoranthene was effected in accordance with the following scheme.



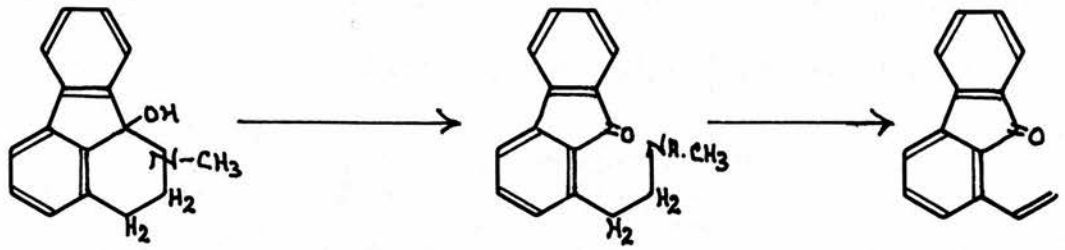
MISCELLANEOUS.

a) As preliminary experiments on the quaternary salts of 2-aza- and 3:4-dihydro-2-azafluoranthene, the methiodides of both the fully aromatic and the dihydro compound were reacted with excess hydroxylamine in alkaline solution. No identifiable product was obtained from the former, but the latter yielded a colourless substance, the analysis of which is in fairly good agreement with that required for 1-hydroxylamino-2-methyl-3:4-dihydro-2-azafluoranthene (I).



I

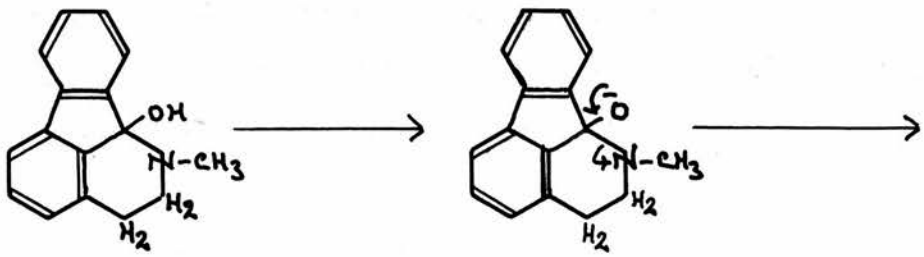
The compound does not show a tendency to isomerize to the yellow ring-opened oxime. In contrast, the pseudo base (II), formed during the reaction of dimethyl sulphate and excess alkali on 3:4-dihydro-2-azafluoranthene, must have isomerized to



II III IV

the fluorenone derivative (III) which, on subsequent methylation, underwent a Hofmann elimination to furnish the nitrogen-free 1-vinylfluorenone (IV). It should be pointed out that this reaction sequence is presumed on the basis of the work of Gensler and Samour (44).

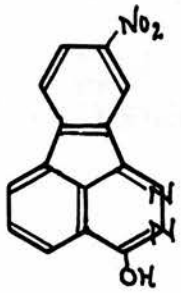
Although further experimentation is evidently required, it seems reasonable to suppose that the more strongly electronegative nature of the oxygen atom in the pseudo base (II) will permit a readier ionization of the proton than will occur for the nitrogen-bound hydrogen atom in (I). Hence, the formation of



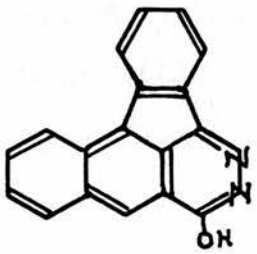
III

a C=O double bond and the associated ring-opening are more probable than the analogous transformations in the hydroxylamine derivative (I).

b) The ring system of 2:3-diazafluoranthene is readily formed, as has been previously demonstrated (68). From the corresponding derivatives of fluorenone-1-carboxylic acid, 12-nitro and 6:7-benz-4-hydroxy-2:3-diazafluoranthene, (V) and (VI) respectively, were prepared. Unlike that of 2:4-diazafluoranthene, the hetero



V



VI

nucleus of these 2:3-diazafluoranthenes is resistant to acid hydrolysis. However, the reduced basicity of the nitrogen atom in the 3-position, which is potentially amidic in character, will alter its behaviour towards proton attack, and, consequently, no explanation of this difference in resistance to acid hydrolysis can at present be offered.

SUMMARY.

1. The Schmidt reaction on fluoranthene-3:4-quinone has been carried out, and the results obtained have been discussed.

2. The mono-nitration and the dinitration of 2-azafluoranthene have been effected, and the orientation of the nitro groups in the products has been determined and discussed.

3. 2-Azafluoranthene and 3,4-benz-2-azafluoranthene have been synthesized.

4. Unsuccessful attempts to synthesize 2-azafluoranthene, 4-phenyl-3-azafluoranthene, 3-azafluoranthene and 1-azafluorene have been made.

5. The reduction of 2-azafluoranthene has been carried out, and the results obtained have been discussed. An unsuccessful attempt to determine the course of reduction of 3:4-benz-2-azafluoranthene has been made.

6. Miscellaneous experiments, including preliminary investigations into the behaviour of the quaternary salts of 2-azafluoranthene and 3,4-dihydro-2-azafluoranthene, have been carried out.

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