A STUDY OF THE NITRATION OF AMINES AND N-OXIDES OF PHENANTHRIDINE, ACRIDINE AND QUINOLINE

A Thesis

by

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GENERAL INTRODUCTION

As recently as 1950 Schofield (1) was able to state that the electrophilic substitution of heterocyclic compounds lacked a comprehensive explanation. Since then considerable progress has been made both on the experimental and on the theoretical side, but there still remain many problems to clarify.

The systematic investigations of Ochiai and den Hertog on the properties of heterocyclic N-oxides presented interesting new possibilities. In particular the demonstration of the greatly enhanced reactivity towards electrophilic reagents imparted to such molecules as pyridine and quinoline by the introduction of an N-oxide function prompted this study of the nitration of phenanthridine N-oxide and of 6-methylphenanthridine and its N-oxide. The latter compound however could not be studied as no convenient method of synthesis could be found.

The second phase of the project involved the preparation of nitramines as the continuation of a work which has been in progress for several years in this laboratory. To this effect nitration studies of the following materials were made: 6-aminophenanthridine, 9-aminoacridine and 3-aminoquinoline.

Coupled with this research an examination of the infrared spectra of a number of these substances was performed.

HISTORICAL

Mechanism of nitration

A great deal of attention has been given to nitration in the past fifteen years and, with the development of a theory of the electronic structure of molecules, our knowledge of this type of reaction has been greatly improved.

Ideas about the nature of the nitrating entity had been proposed by Euler as far back as 1903 (2), but it took almost half a century to demonstrate unequivocally the existence of the nitronium ion. The present understanding of the situation is based on four independent proofs (3):

a) cryoscopic measurements of sulphuric acid-nitric acid mixtures.

b) Raman and infrared investigations of such solutions.

c) preparation of crystalline nitronium salts.

d) X-ray analysis of such salts.

The mechanism of formation of the nitronium ion is considered to be a two-stage reaction:

$$HNO_3 + H^+ \underset{\text{fast}}{\rightleftharpoons} H_2NO_3^+$$

$$H_2NO_3^+ \xrightarrow{\text{slow}} H_2O + NO_2^+$$

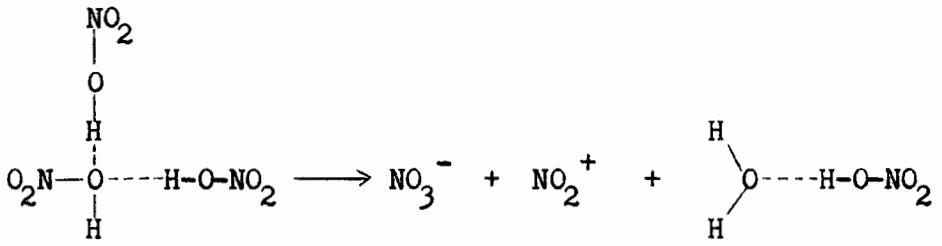
The proton in the first step can be supplied either by another molecule of nitric acid or by an appropriate solvent such as sulphuric acid. The second step is a unimolecular heterolysis, and being slow it is the rate determining one (4).

In some cases sulphuric acid has been replaced by acetic acid or acetic anhydride. The mechanism of formation of the nitronium ion is then slightly different.

Investigations of freezing point-concentration curves of acetic acid-nitric acid mixtures have clearly demonstrated the existence of a compound CH_3-COOH, HNO_3 (5). The Raman spectra of mixtures from 24 to 74% nitric acid consisted of the superposition of the spectra of the two acids (6) but neither the line at 1050 $cm.^{-1}$ nor at 1400 $cm.^{-1}$, characteristic of the nitronium ion, was observed. Finally the absence of ions in these solutions was confirmed by the negligible electrical conductivity of dilute solutions of nitric acid in acetic acid (7, 8).

The kinetic study of nitration, under these conditions, of mesitylene, p-xylene, ethylbenzene and toluene (9) showed that the reaction follows a zeroth-order law. In other words the rate is independent of the concentration and nature of the aromatic compound. This observation implies that the reaction must include some rate-determining stage which does not involve the aromatic compound and it excludes the possibility that this stage is dependent on any particular chemical transformation of the solvent. The zeroth-order must thus be due to a reaction in which the nitric acid produces some other nitrating agent. The only slow reaction that nitric acid itself can reasonably be assumed to undergo is a heterolytic fission with formation of the nitronium ion. This takes place in a group of associated nitric acid molecules, probably with a preceding or simultaneous proton transfer from one nitric acid molecule to that undergoing fission, and combination of the formed water molecule with another nitric acid

molecule (10). The process can be represented schematically as follows:



I II

When nitration is carried out in acetic anhydride, the mixture is often referred to as "acetyl nitrate" since the latter is formed to some extent according to the equation (11):

$$(CH_3\text{-}CO)_2O + HNO_3 \rightleftharpoons CH_3\text{-}COOH + CH_3\text{-}CO\text{-}ONO_2$$

However, it appears that acetyl nitrate is not completely stable, but that it is in equilibrium with small amounts of the acid anhydride and dinitrogen pentoxide. The following equilibrium was shown for instance to exist in the case of benzoyl nitrate (12, 13):

$$2\ C_6H_5\text{-}CO\text{-}O\text{-}NO_2 \rightleftharpoons (C_6H_5\text{-}CO)_2O + N_2O_5$$

It is probably the dinitrogen pentoxide thus formed (either in the molecular form or ionised to give the nitronium ion) that is responsible for the nitrating power of the acyl nitrates (14).

The process by which the nitronium ion attacks the aromatic ring and replaces one of its hydrogens has been explained by two different theories. One is that the introduction of the nitronium ion and the elimination of the proton by an external base, constitute a single-stage thermonuclear reaction represented by the equation:

$$NO_2^+ + ArH + A^- \longrightarrow NO_2\text{-}Ar + HA$$

On the other hand Ingold and collaborators (15) demonstrated that ionic charges are neither formed nor destroyed in the rate-determining stage of the entry of the nitronium ion into the aromatic molecule. Consequently the above mentioned mechanism has to be rejected.

The second, and the accepted theory, considers two stages. The first involving a slow uptake of the nitronium ion followed by the rapid transfer of a proton:

$$NO_2^+ + ArH \xrightarrow{slow} Ar^{+}\!\!\begin{array}{l}H\\ \diagdown\\ NO_2\end{array}$$

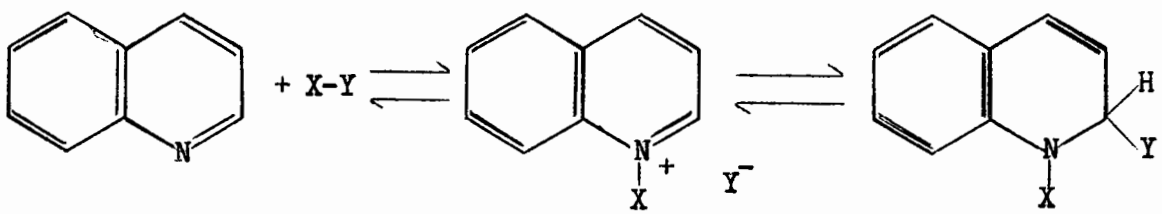
$$Ar^{+}\!\!\begin{array}{l}H\\ \diagdown\\ NO_2\end{array} + A^- \xrightarrow{fast} Ar\text{-}NO_2 + HA$$

Much of our knowledge of the mechanism of nitration in the benzene series can be carried over unchanged to heterocyclic substances, but with the introduction of a nitrogen atom in the ring certain complications arise.

In a strongly acidic solution, pyridine for example, must exist mostly as the pyridinium cation, which means that at least in a sulphuric acid medium the entity being nitrated is probably the conjugated acid. This consideration entrains the important consequence that the electronic distribution in the molecule is now going to be slightly different, so that the results of theoretical calculations made on the free bases have to be used with certain reservations. Furthermore, as Dewar and Maitlis pointed out (16), the positive charge on the nitrogen can very well hinder

the approach of the nitronium ion to the α position and thus considerably reduce the proportion of α-nitro isomer that one would otherwise expect.

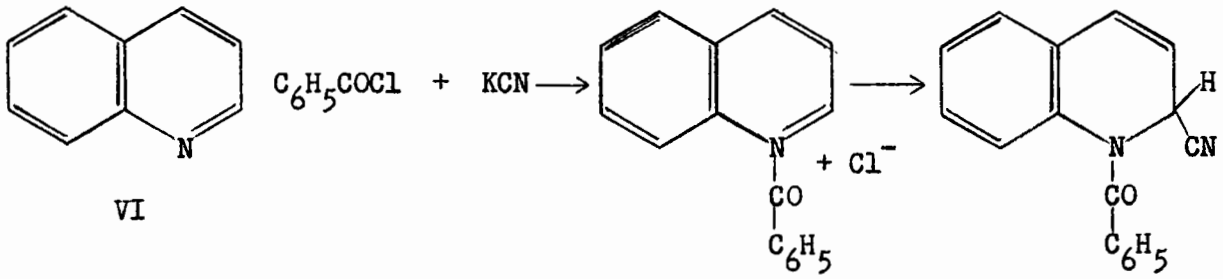
In acetic anhydride solution the nitration of heterocyclics proceeds in a fashion entirely different from the course followed by benzene derivatives, as shown by the case of quinoline. Whereas nitration of quinoline under normal conditions produces the 5- and 8-nitro isomers, a fact established by many workers (16 to 25), the use of acetic anhydride and nitric acid, lithium nitrate or nitrogen tetroxide was claimed by certain investigators (26, 27, 28) to yield mainly the 7-nitroquinoline. However a careful reexamination of the question by Dewar and Maitlis (29) demonstrated that no appreciable amount of 7-nitroquinoline was produced but the 3-nitroisomer was isolated as well as the 6- and 8-. The presence of 3-nitroquinoline can be considered indicative of the fact that the entity being nitrated is not quinoline itself. Indeed it seems necessary to assume the existence of an intermediate if one considers that the 3 position of quinoline will not be attacked easily by an electrophilic reagent, since its reactivity would not be expected to be greatly different from that of the equivalent position in pyridine, the inertness of which is well known (30). A likely mechanism, suggested by the authors is based on the assumption that at first there is formation of a 1,2 dihydro-quinoline derivative by the addition of the reagent to the 1,2 bond:



III IV V

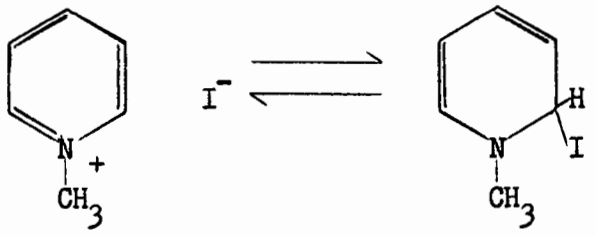
The adduct V would be an aniline derivative and would be nitrated ortho and para to the nitrogen atom, i.e. the 6 and 8 positions; while addition of oxides of nitrogen to the styrene-like double bond of V followed by elimination could give the 3 isomer. (3 nitroquinoline was formed only under conditions where oxides of nitrogen were present initially or could have been formed by reduction of nitric acid.)

The formation of an intermediate such as V is quite reasonable. A similar adduct is postulated in the Reissert reaction (31):



VI VII VIII

The nature of the reagent X-Y is not quite definite, but the authors believed it to be an acyl nitrate. Although no direct evidence could be obtained for the addition of acetic anhydride to quinoline, there existed in the literature another interesting analogy. Kosower (32) showed by the study of ultraviolet spectra that an equilibrium exists between 1-methylpyridinium iodide and 1,2-dihydro-2-iodo-1-methylpyridine:

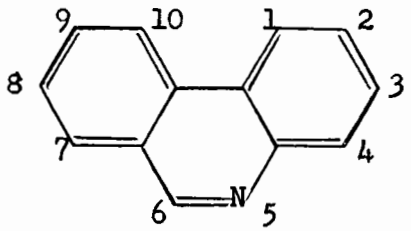


IX X

On this basis Dewar and Maitlis concluded that similar equilibria exist in other heterocyclic systems and that other polar molecules (e.g. acetyl nitrate) can form similar adducts.

Nitration of Phenanthridine and Phenanthridinone

Nomenclature. Several systems of numbering have been used for the phenanthridine ring. Since 1937 Chemical Abstracts has adhered to the following which we have adopted:



XI

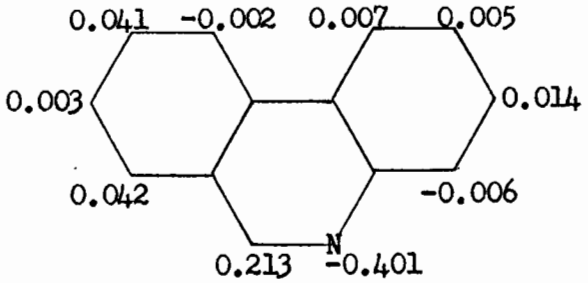
Phenanthridone and its derivatives will be named phenanthridinones, the numbering system being the same as that of phenanthridine.

With nine non-equivalent positions available for substitution the nitration of phenanthridine constitutes a rather complex problem.

The first attempt to solve the question was made in 1932 by Morgan and Walls (33). By dissolving anhydrous phenanthridinium nitrate in concentrated nitric acid at 0° and heating the solution to 100°, a mixture of mononitrophenanthridines was obtained. Three fractions were separated from the complex product: A, m.p. 163°; B, m.p. 158°; C, m.p. 263°. No effort was made to identify the various materials. Elderfield (34) assumed product C to be 8-nitrophenanthridine because of its high

melting point and sparing solubility. Oxidation of B with alkaline permanganate furnished a good yield of phthalic acid and thus located the nitro group in ring B. Elderfield concluded that since the aminoquaternary salt derived from it was yellow and not red the resonance positions 2 and 4 would be excluded. Its most likely location was thus 1 or 3. In 1945 Ritchie (35) prepared two nitrophenanthridines by nitration of 5-acetyl-6 dihydrophenanthridine, hydrolysis and oxidation. The author suggested that one (m.p. 178°) was the 8-nitro isomer and the other (m.p. 263°) 2-nitrophenanthridine. The latter seemed to be compound C of Morgan and Walls, although Elderfield reasoned that it should correspond to the structure of 8-nitrophenanthridine.

At this point Longuet-Higgins and Coulson (36) developed a method to calculate the electron densities of heterocyclic molecules using the corresponding arene molecule as a basis and applying the first order perturbation theory. The fundamentals of the method had been established earlier by Wheland and Pauling (37). In a second paper (38) the English workers extended their calculations to two and three ring systems containing one or two nitrogen atoms. The results for phenanthridine are given below:



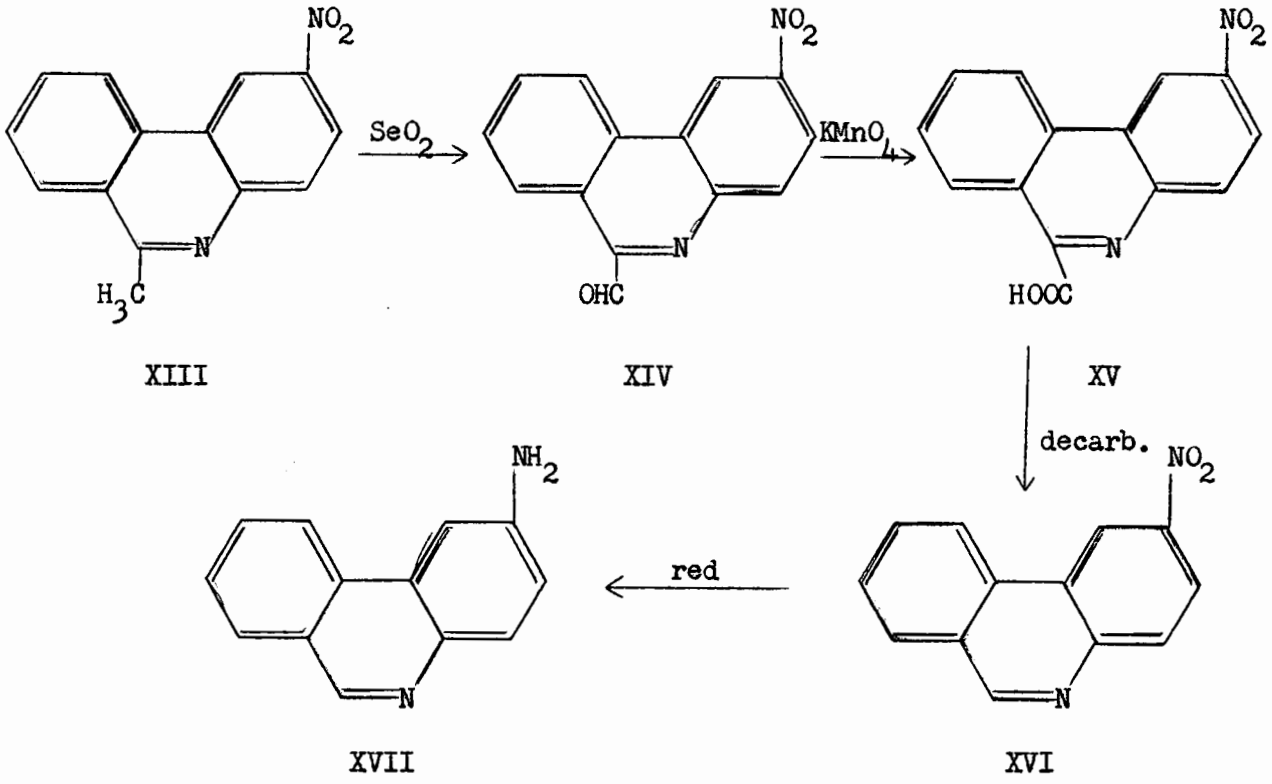
XII

These figures represent a relative value of electron densities, so that the negative positions ought to be attacked first by an electrophilic reagent. One would thus expect positions 4 and 10 to be most readily nitrated.

In 1952 Caldwell and Walls (39) published a paper which solved the problem entirely. The nitration of phenanthridines was carried out as previously described (33) and the mixture of the mononitrophenanthridines was isolated in the same manner. Extraction with boiling benzene gave a fraction A. The residue recrystallized from ethanol afforded a crystalline mass from which "well-defined transparent brownish-yellow prisms" were separated by hand-sorting. This constituted substance B. By crystallization of the residue from glacial acetic acid a third fraction C was obtained. (B and C were found in approximately equal amounts and formed the major fraction). The acetic acid mother-liquor from the crystallization of C slowly deposited solids of a compound D. After elimination of D the acetic acid was diluted with water. By fractional recrystallizations from the precipitate more B and C was obtained and also a fifth fraction E. In another experiment the authors found that if, after the removal of A, B and C from the benzene solution, the latter was evaporated, the residue dissolved in ethanol and sulphuric acid added to this solution, clumps of ill-defined crystals separated. They could then be converted into another base F. The three original fractions isolated by Morgan and Walls had thus been resolved into six isomers.

A was identified as 2-nitrophenanthridine by a mixed melting point determination with synthetic material. Further evidence was obtained

by reduction to the amino derivative and comparison with the synthetic product prepared by the following series of steps:

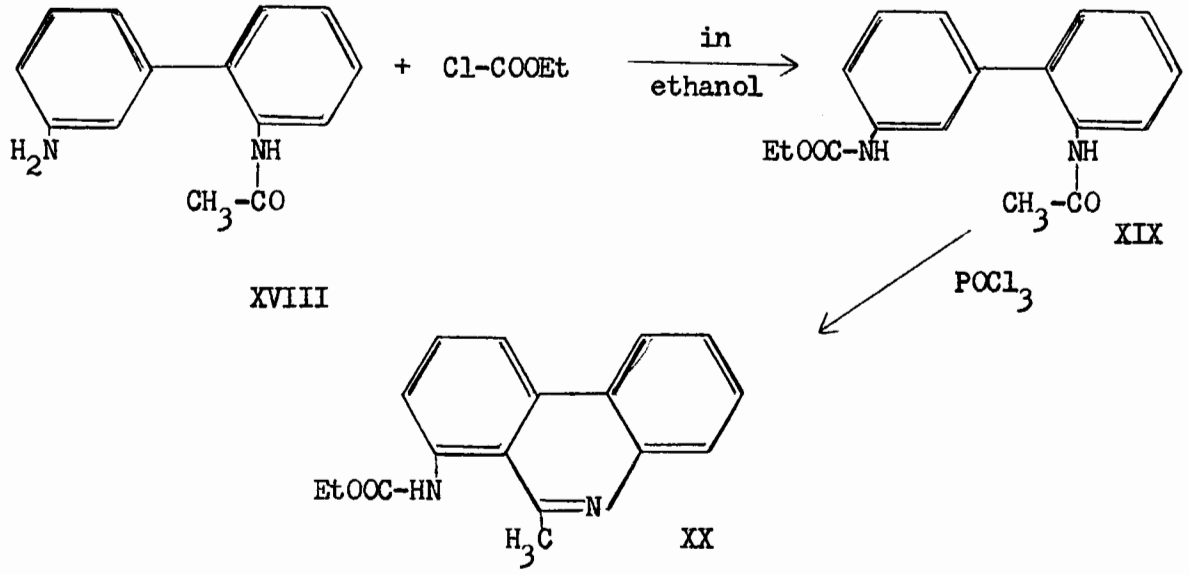


The selenium dioxide oxidation was a method described by Ritchie (40) and Caldwell (41). The conditions for the reduction of the nitro group were established by Caldwell and Walls whereas the other steps were well known in the chemistry of phenanthridine.

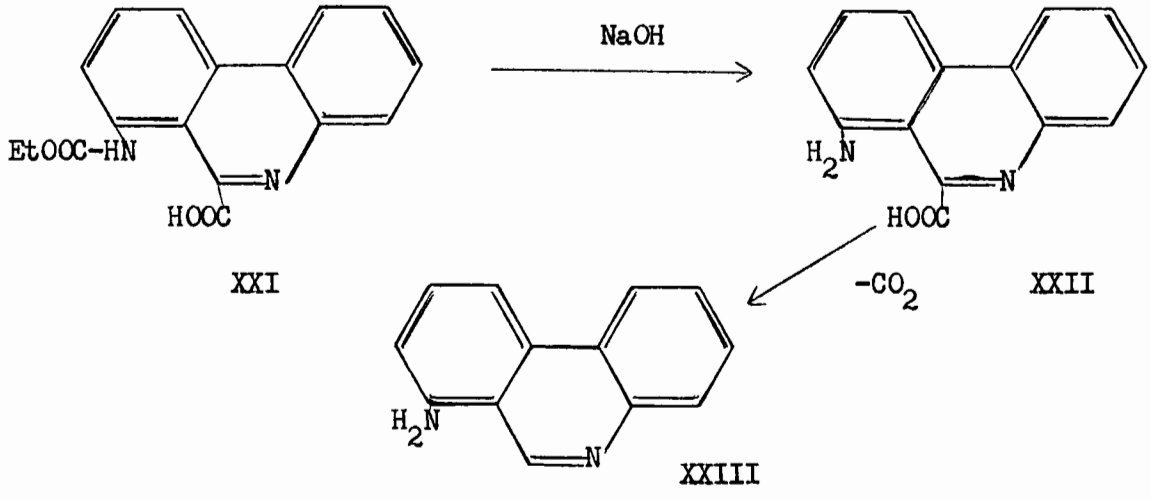
In a similar fashion fractions D, E and F were identified respectively as 3-, 4- and 8-nitrophenanthridine.

Compound C gave a good yield of phthalic acid on oxidation with permanganate and therefore it had to be 1-nitrophenanthridine, the nitro group occupying the only available position in that ring. Compound B

did not give an identifiable product on oxidation, but the amine obtained from it by reduction was different from synthetic 7-, 8- and 9-aminophenanthridines and thus by exclusion had to be the 10-nitrophenanthridine. The synthesis of 7-aminophenanthridine (and also the 8-, and 9-) was achieved by way of the carbethoxyamino-6-methylphenanthridines (42) as follows:



After oxidation of the methyl group the carbethoxyamino function was hydrolyzed and decarboxylation was achieved:



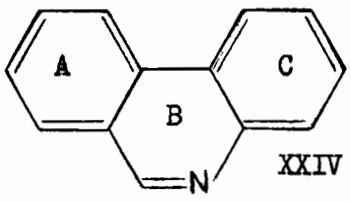
All isomers obtained by Caldwell and Walls are thus identified. The results are summarized in Table I.

Nitrophenanthridines

Substitution position	Melting point	% formed
1	160.5-161.5°	26.
2	266 -267°	3.
3	194 -195°	6.
4	190°	1.
8	159 -161°	11.
10	166 -166.5°	21.

One might note that the nitrophenanthridine obtained by Ritchie (35) was correctly assumed to be the 2-nitro isomer. The most obvious discrepancy with the theoretical calculations is the small amount of isomer 5 found experimentally. Longuet-Higgins and Coulson themselves had pointed out two possible causes of error, namely that the polarization of the sigma bonds due to the introduction of a nitrogen atom in the ring had been neglected and that the entity being nitrated, the phenanthridinium ion, had an appreciably different electron distribution from phenanthridine itself. But probably the most important effect is the repulsion of the nitronium ion by the electrostatic field resulting from the positive charge on the nitrogen.

To explain the large percentage of isomer 1 let us consider the

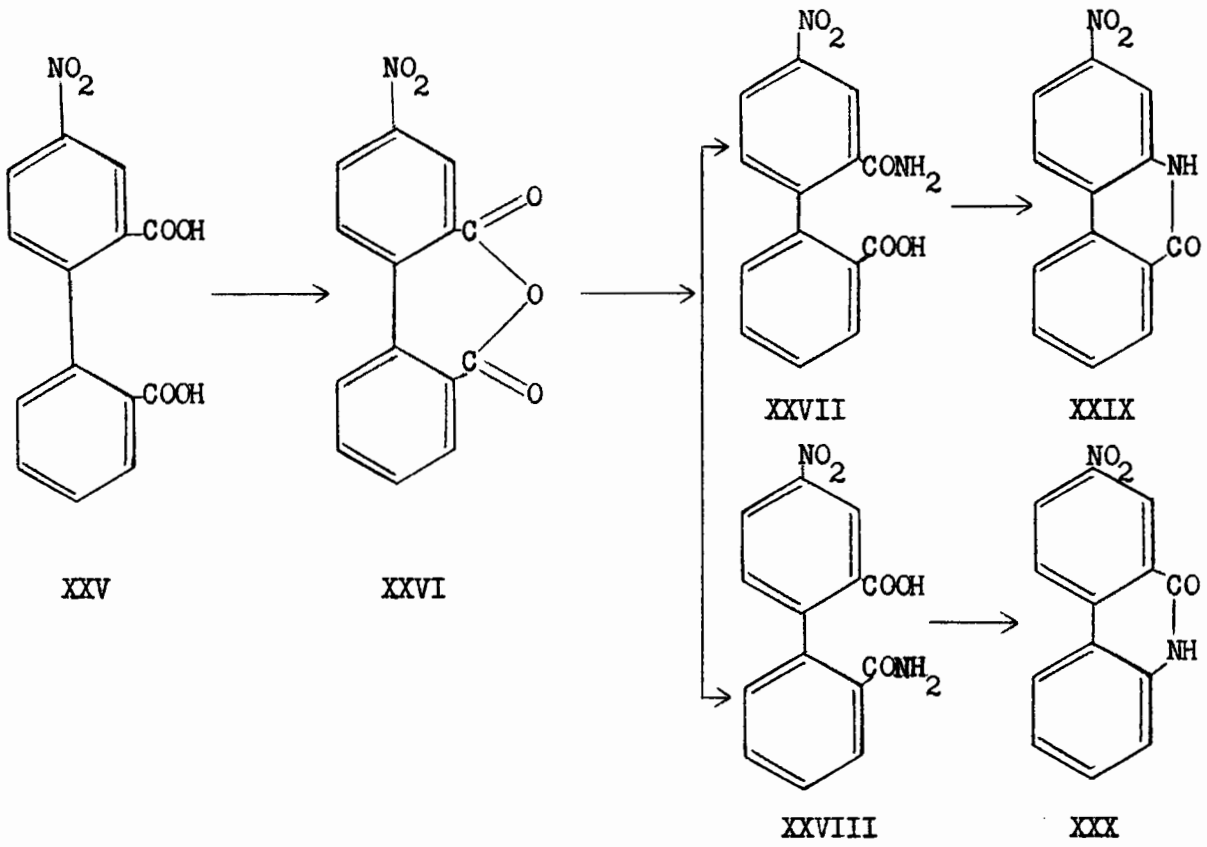


XXIV

B and C rings of phenanthridine as forming a quinoline system. In this assumption the 1 position of phenanthridine becomes the 5 position of quinoline which as mentioned previously gives mainly the 5-nitro isomer on nitration. The large proportion of 10-nitrophenanthridine can be similarly explained by considering A and B as forming an isoquinoline system, whose nitration gives almost exclusively 5-nitroisoquinoline (43 to 47).

The first reported nitration of phenanthridinone was published by Moore and Huntress in 1927 (48). The aim of the authors was to prepare several mononitrophenanthridinones which they attempted by various methods, one of them being the direct nitration of phenanthridinone. Two products were isolated. Comparison of the materials with synthetic products seemed to show that they differed from the expected 3- and 8-nitrophenanthridinone. These two isomers were prepared by a method proposed by Graebe and Wander (49) and also used by other workers (50, 51). 3-Nitrodiphenic acid (XXV) was transformed into the corresponding anhydride (XXVI) which then reacted with ammonium hydroxide at low temperature gave two isomeric diphenamic acids (XXVII, XXVIII). Each of these compounds was then cyclized to 3- (XXIX) and 8-nitrophenanthridinone (XXX) respectively by the use of alkaline hypobromite.

In 1935 Walls (52) prepared the 2-nitro isomer by oxidation of 6-methyl-2-nitrophenanthridine and Stepan and Hamilton (53) in 1949 oxidized 6-methyl-4-nitrophenanthridine to the corresponding phenanthridinone. Finally Caldwell and Walls (39) demonstrated that the product formed in the smallest amount in the nitration of phenanthridinone by Moore and Huntress,



was 4-nitrophenanthridinone. The second material was never further investigated. The following table summarizes the available information on nitrophenanthridinones (Table II)

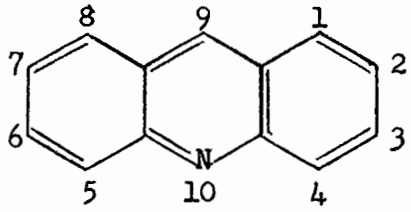
Isomer	Melting point
1	325 - 327°
2	380 - 383°
3	349°
4	265 - 267°
8	324 - 326°
10	316 - 318°

It is apparent that the problem of the direct nitration of phenanthridinone requires more investigation. The formation of the 4-nitro

isomer can be explained by considering the effect of the group -NH-COR- where R is the phenyl ring A. The 4 position is activated by the powerful ortho-para orienting group -NH-COR- (demonstrated in the quinoline series by Diskhoorn (25)), and concomittently the reactivity in the C ring is depressed by a -CO-NH-R' group where R' is the C ring.

Nitration of Acridine and 9-Aminoacridine

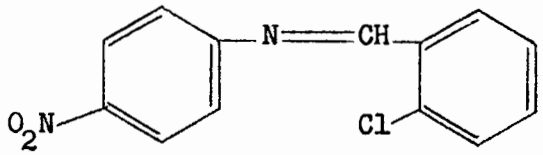
Nomenclature. From the ten different systems of numbering of the acridine ring (54), we have chosen to use the one adopted by the Chemical Abstracts since 1937:



Acridine was first nitrated over seventy five years ago by Graebe and Caro (55). The reaction was carried out at an elevated temperature (unspecified) in nitric acid alone. Three fractions were isolated, a so-called α-nitroacridine, a β-nitroacridine, and a dinitroacridine. The authors however did not attempt to elucidate their structures.

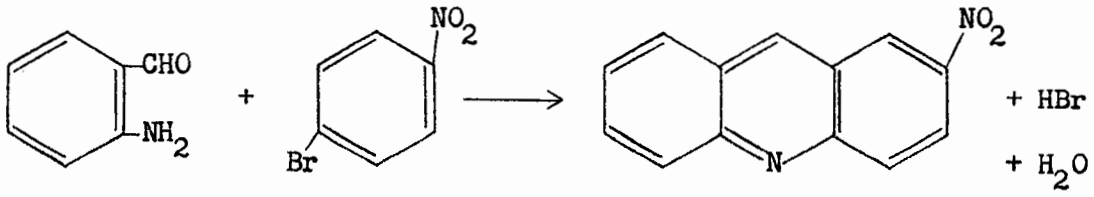
Jensen and Friedrich repeated this work in 1927 (56). The same products were found but slightly higher melting points were obtained by several recrystallizations. The β-isomer of Graebe and Wander formed only in a small amount was identified with the 4-nitroacridine prepared earlier by Mayer and Stein (57) through the condensation of o-nitroaniline with o-chlorobenzene using copper powder as a catalyst. To ascertain the structure of the α-isomer it was now necessary to synthesize it in such a way

that no doubt would be left about the position of the nitro group. The method of Meyer and Stein could not be applied to the 2- and 3-isomers since in these cases the amino group of the nitroaniline condenses with the aldehyde function instead of with the chlorine atom giving with p-nitroaniline e.g.:



XXXII

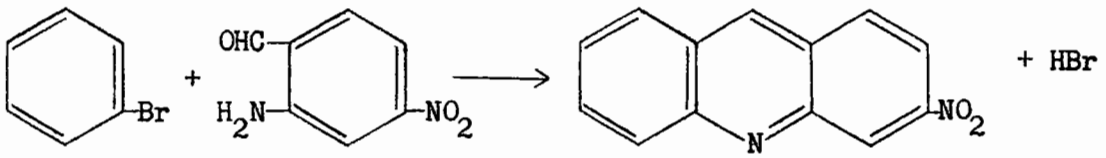
Any of the known methods at the time for the preparation of acridine derivatives either did not apply to the nitrocompounds or gave very poor yields (58 to 63). For this reason a new synthesis was developed involving the condensation of o-aminobenzaldehyde with bromonitrobenzenes. The o-bromonitrobenzene gave the already described 4-nitroacridine. p-Bromonitrobenzene afforded the 2-nitroacridine (XXXV):



XXXIII XXXIV XXXV

Mixed melting point determinations proved it to be identical with the α-nitroacridine of Graebe and Caro. m-Bromonitrobenzene gave two products one of which was 3-nitroacridine, the other 1-nitroacridine. The authors however were not able to differentiate them. The careful work of Lemstedt (64) demonstrated that the β-nitroacridine was in fact a eutectic mixture of 2- and 4-nitroacridine in the ratio of 1 to 3. Furthermore he isolated from

the nitration of acridine a product which seemed to have escaped the efforts of the other investigators. Oxidation of this material to an acridine derivative gave a compound which turned orange when dissolved in alcoholic potassium hydroxide. Since it had been shown previously (65) that this colour reaction was characteristic of the 1-nitro isomer its structure was defined. Further proof was obtained by conversion of 1-nitroacridine to 9-chloro-1-nitroacridine with phosphorus oxychloride and comparison with a synthetic sample. A fourth isomer was found in very small quantities and by elimination was 4-nitroacridine, a conclusion borne out by comparison with a synthetic sample prepared by a variation of the Jensen and Friedrich method:



XXXVI XXXVII XXXVIII

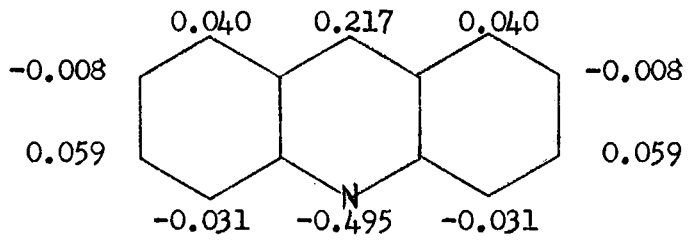
Lemstedt (66) demonstrated an elegant method of separation of the mononitroacridines based on the finding that the 2- and 4-nitroacridines were oxidized readily whereas the rate of oxidation of the 1- and 3-nitro isomers was quite slow.

The nitration of acridine thus produces mainly 2-nitroacridine with small amounts of 1-, 3- and 4-nitroacridine. These results are summarized in Table III:

TABLE III

nitroacridine	Melting point	Proportion
1	154°	5 parts
2	214°	130 "
3	183°	1 "
4	167°	25 "

The calculations of Longuet-Higgins and Coulson (38) give the following electronic distribution for acridine:



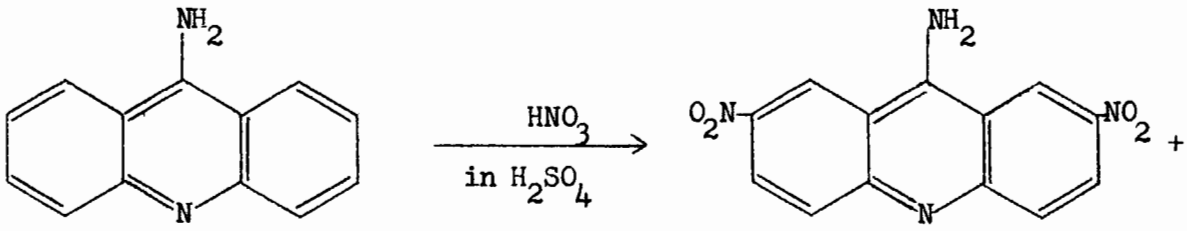
XXXIX

The greater reactivity of the 2 position, experimentally proved, can be explained by considering that during the reaction the acridinium cation is formed and consequently the positively charged nitrogen will hinder the approach of the nitronium ion.

While the mononitration of acridine seems to have been pretty well elucidated, the dinitration is still unsolved. Apart from an unsubstantiated statement by Lemstedt (66) that the dinitro compound obtained by Graebe and Caro is a mixture and aside from the fact that the proportion of dinitro isomers can be minimized by nitrating in sulphuric acid, the question of the polynitration of acridine remains open.

Previous to the work of Hampton and Magrath (67) only one report of a direct nitration of 9-aminoacridine existed. It consisted of the formation of an unidentified dinitro derivative obtained by Meister et al. (68).

Hampton and Magrath studied the di- and trinitration of 9-aminoacridine with the object of preparing polyamino derivatives. They isolated 9-amino-2,7-dinitroacridine (XLI), 9-amino-4,2,7-trinitroacridine (XLII) and 2,4,7-trinitroacridone (XLIII):



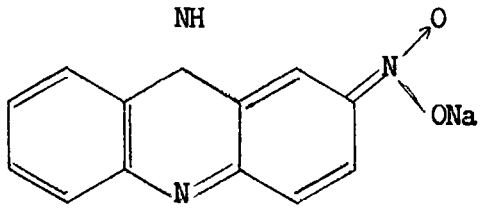
XL XLI

XLII XLIII

All compounds were identified with certainty by comparison with synthetic samples.

The mononitration of 9-aminoacridine was never investigated although the various mononitro isomers were known through synthetic procedures (69, 70, 71). An interesting property of 9-amino-2-nitroacridine described

by Albert and Ritchie (72) is the fact that it forms a purple nitronate (XLIV) when dissolved in alcoholic potassium hydroxide:

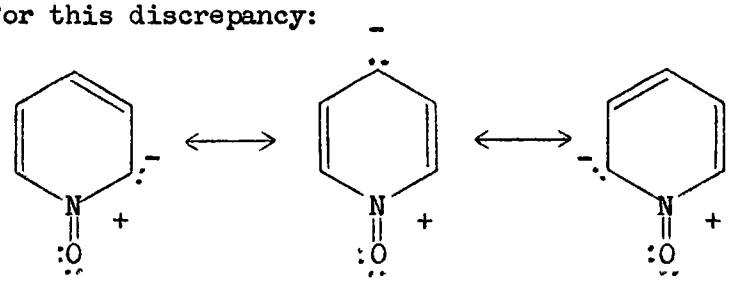


XLIV

The other isomers show no colour change under similar conditions.

Reactivity of heterocyclic N-oxides

Little interest was taken in the chemistry of heterocyclic N-oxides until about fifteen years ago. In 1940 Linton (73) determined experimentally the dipole moment of several aliphatic and aromatic tertiary amines and found the dipole moment of pyridine N-oxide to be 4.28 D compared with the calculated value of 6.6 D. He concluded that the contribution to the resonance hybrid of structures of the following type was responsible for this discrepancy:



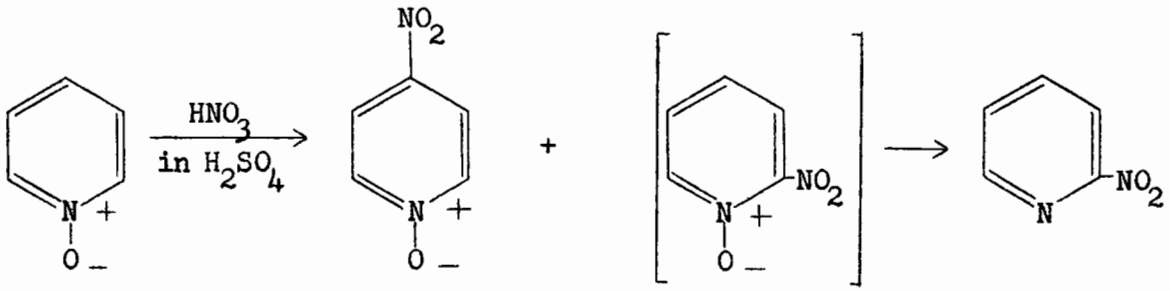
XLV XLVI XLVII

The implications of these results caught the interest of two workers: Ochiai in Japan and den Hertog in Holland. Many of Ochiai's most significant publications antedate den Hertog's. Ochiai's work however was

not known outside of Japan before 1953 at which time a summary of the research was published in English (74) and the Dutch investigations were performed independently. Since then a considerable number of papers has appeared. Part of these were reviewed by Katritsky in 1956 (75). Our aim is not to review the entire topic but rather to select a few typical cases of nitration in this series and also present the work pertaining to the N-oxide rearrangement.

Nitration of N-oxides

The mononitration of pyridine N-oxide produced two compounds, 4-nitropyridine N-oxide and 2-nitropyridine (76, 77). The former was identified by its reduction to 4-aminopyridine, the latter by comparison with an authentic sample prepared according to Kirpal and Boem (78). The yield of 2-nitropyridine was only 0.4% but it could be increased to 7.6% by raising the reaction temperature. In this case the yield of 4-nitropyridine N-oxide fell with simultaneous formation of 4-nitropyridine in 27% yield (79). It was further established that 4-nitropyridine N-oxide was deoxygenated by heating it with potassium nitrate in concentrated sulphuric acid (80). The presence of 2-nitropyridine in the nitration product resulted from the fact that at this temperature the originally formed 2-nitropyridine N-oxide was more easily deoxygenated than its 4-nitro isomer. In short, nitration of pyridine N-oxide produced mostly 4-nitropyridine N-oxide (XLIX) and some 2-nitropyridine (LI):



XLVIII XLIX L LI

den Hertog (81) carried out the reaction at a lower temperature and found only 4-nitropyridine N-oxide. It is likely that because of the milder conditions the rate of nitration in the 2 position is slow enough so that no appreciable amount is formed.

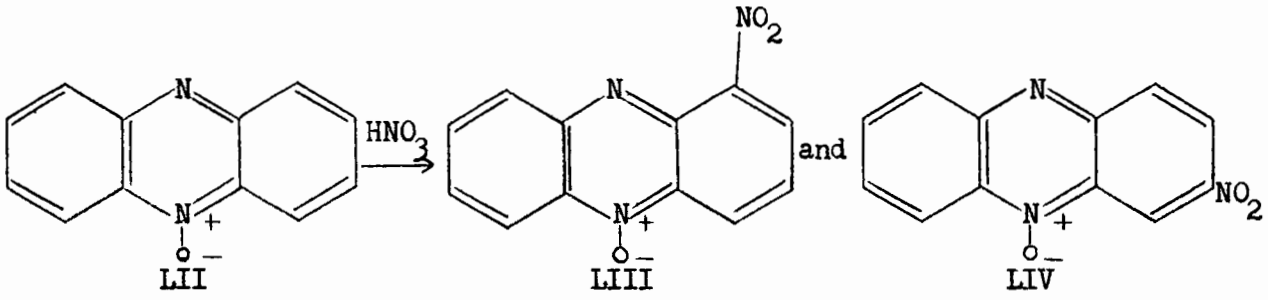
Quinoline N-oxide was nitrated even more easily than pyridine N-oxide. An important feature of this reaction is the striking temperature dependence of the position taken by the nitro group (82). At 0°-10° the 5- and 8-nitroquinoline N-oxides are formed. Above 40° the 4 position becomes reactive and at 65-70° mainly the 4-nitro derivative is produced. Deoxygenation of the N-oxide function begins to occur around 100° and at 120-130° the formation of 4-nitroquinoline N-oxide is much decreased with the simultaneous production of quinoline and 5- and 8-nitroquinoline in small amounts. If quinoline N-oxide is allowed to stand at room temperature for a long time in the presence of potassium nitrate in fuming sulphuric acid, 4,8-dinitroquinoline N-oxide is obtained beside the 5- and 8-nitro derivatives (83). Summarizing, it can be said that the nitration of quinoline N-oxide in sulphuric acid produces the 5- and 8-nitroquinoline N-oxides at 0°-10°, whereas around 70° 4-nitroquinoline N-oxide is mainly obtained. At higher temperatures deoxygenation takes place. The formation of a 2-nitro derivative was never observed.

A fairly recent publication (84) dealing with the nitration of quinoline N-oxide with acetyl nitrate in acetic anhydride reports the formation of 4-hydroxy-3,6,8-trinitroquinoline.

Isoquinoline N-oxide was studied by Ochiai and Ishikawa (85). The product of nitration was 5-nitroisoquinoline N-oxide.

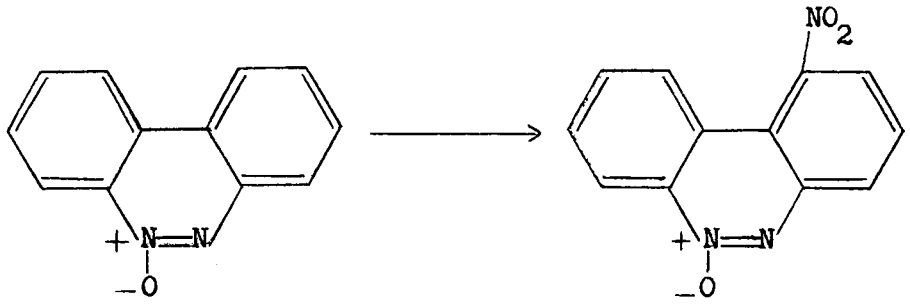
These nitration experiments show that at least in a number of cases the polar effect of the N-oxide function is quite considerable. In pyridine for instance the para position is greatly activated by the mesomeric effect of the N-oxide group. The reactivity of the ortho position is also sometimes noticeable, but it is much reduced owing to the inductive effect of the N-oxide function. The situation was compared by Ochiai (74) to that existing in chlorobenzene. The chlorine atom directs electrophilic substitution to ortho and para positions with an ortho:para ratio of approximately 1 to 5 (86). Direction to the ortho and para positions is a consequence of its mesomeric effect but deactivation particularly of the ortho position is caused by its inductive effect.

Little is known about the behaviour of N-oxides of three-ring systems. In phenazine N-oxide nitration takes place in the 1 and 3 positions (87).



LII LIII LIV

King and King reported a nitration of benzo(e)cinnoline N-oxide (same numbering as in phenanthridine) which they found to give chiefly 2-nitrobenzo(e)cinnoline N-oxide and a small amount of the 3-nitro derivative (88). The positions of substitution were determined by hydrogenation to triaminobiphenyls which were cyclized to give the known aminocarbazoles. Smith and Ruby doubted the orientation reported by the previous workers because of dipole moment measurements in contradiction with their conclusions (89). They repeated the work and now identified the major nitration product as being 1-nitrobenzo(c)cinnoline N-oxide (LVI). Two minor products were also isolated but not identified (90).

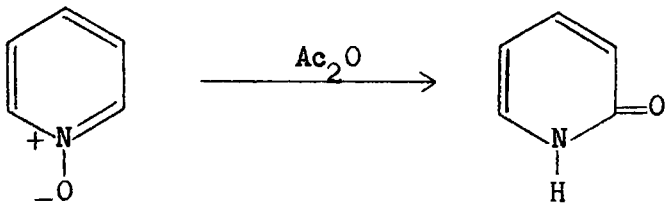


LV LVI

Iwai in a study of the nitration of benzo(h)quinoline N-oxide demonstrated that the 7, 9 and 10 positions were attacked (91) whereas Simpson isolated four products from the nitration of 4-phenylcinnoline N-oxide, none of which was identified (92).

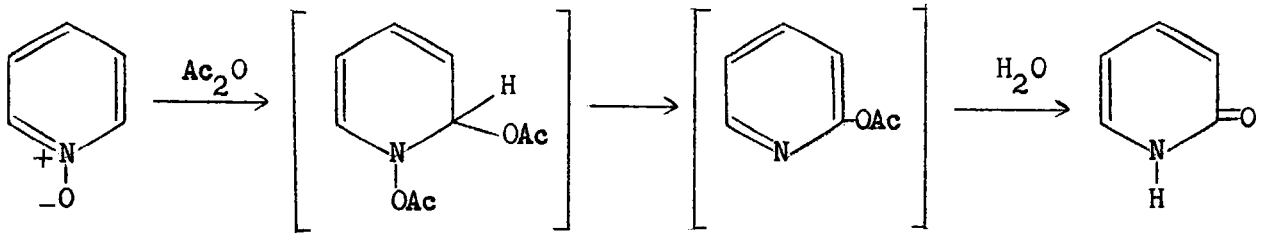
Rearrangement of N-oxides

All heterocyclic N-oxides seem to undergo a rearrangement when heated with an acid anhydride. The transformation can be illustrated by the case of pyridine N-oxide which is converted to 2(1H)-pyridone (LVIII):



LVII LVIII

In an investigation of the mechanism of this reaction (93, 94) pyridine N-oxide was heated with acetic anhydride at 140-150° and the reaction mixture directly hydrogenated using a palladium-on-charcoal catalyst. A lively absorption of hydrogen occurred and α-piperidone was isolated in almost quantitative yield. In a control experiment 2(IH)-pyridone was analogously treated but there was no uptake of hydrogen and the starting material was recovered. Since 2(IH)-pyridone can only be acetylated with complete exclusion of water and consequently since α-acetoxypyridine is saponified on contact with water, Ochiai concluded that the course of the reaction is as follows:

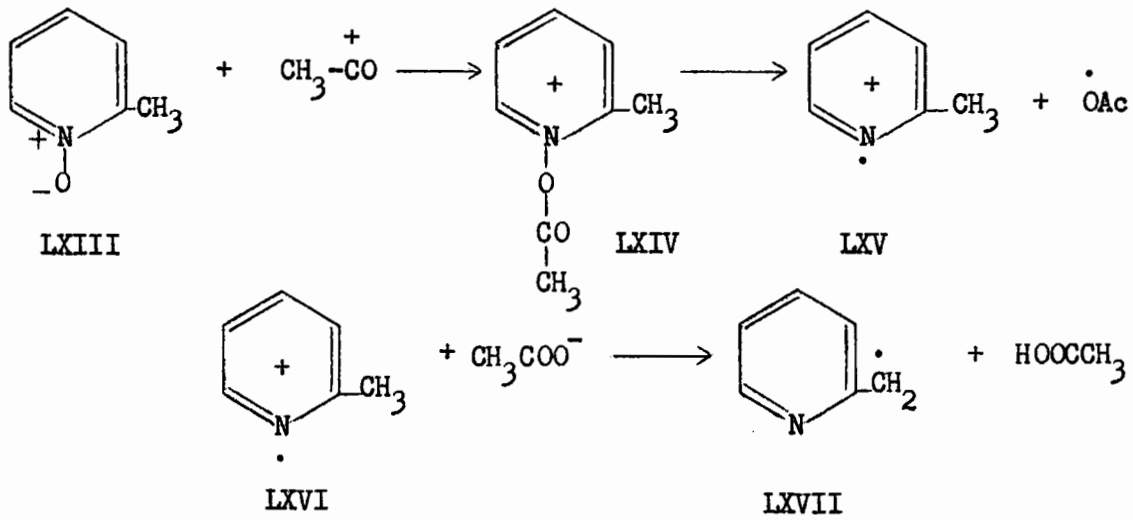


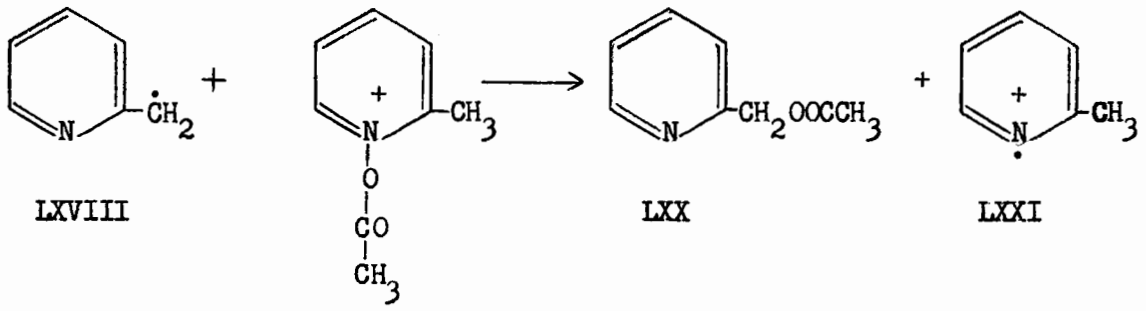
LIX LX LXI LXII

Ochiai and collaborators showed that this rearrangement will also take place with N-oxides of quinine, dihydroquinine and benzo(h)-quinoline (95, 96). Robinson and Robinson obtained 1- and 4-isocarbo-

styryl derivatives from the rearrangement of 3-methylisoquinoline N-oxide (97).

Bockelheide and Linn investigated alkyl substituted N-oxides under similar conditions and found the products to be pyridylcarbinol compounds (98). A similar reaction had been described previously with alkyl quinolines (99). 2-Methylpyridine N-oxide was shown to yield 2-pyridinemethanol acetate (LXV). A careful study of the reaction led to the conclusion that it proceeded via a mechanism by radicals (100). A very elegant experimental proof, consisting of reacting the materials in the presence of styrene, was devised. Polymerisation of the styrene occurred, whereas the styrene remained unaffected when either the N-oxide or the acetic anhydride was omitted. Likewise a mixture of pyridine and acetic anhydride in boiling benzene was entirely ineffective in polymerizing the styrene. Consequently the polymerization must have been due to an intermediate formed during the rearrangement and was not caused by any of the individual constituents or by an acyl ammonium ion. Bockelheide and Harrington thus suggested the following mechanism:





LXVIII LXIX LXX LXXI

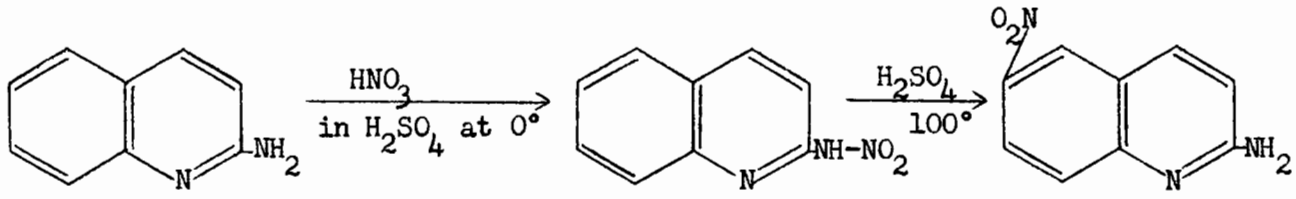
The last two steps would constitute a cycle and account both for the occurrence of an induction period sometimes observed and the exothermic nature of the reaction. Finally, the authors claimed that their kinetic measurements, yet unpublished, had shown that the rate of rearrangement was little affected by the polarity of solvent, a fact difficult to explain on the basis of an ionic mechanism.

Nitration of aminoquinolines

The investigations of Tschitschibabin and co-workers had shown by 1920 that the nitration of aminopyridines gave compounds in which the amino group was nitrated, providing the reaction temperature was kept low enough. Such "Nitramids" as the old German literature called them or "nitramines" in the modern nomenclature can be rearranged in sulphuric acid so that the nitro group migrates to the ring.

In 1920 Tschitschibabin and Sazepina published a preliminary paper on the nitration of 2-aminoquinoline in which they showed that a nitramine could be obtained and then rearranged in hot sulphuric acid (101).

In a second publication, the rearranged product was isolated and purified (102). Its structure was ascertained by transforming it into a nitrocarbostyryl by diazotization followed by heating. The product was identified as 2-hydroxy-6-nitroquinoline by comparison with a synthetic sample. Consequently the 2-amino-x-nitroquinoline carried its nitro group in the 6 position. The nitration of 2-aminoquinoline can thus be represented by:



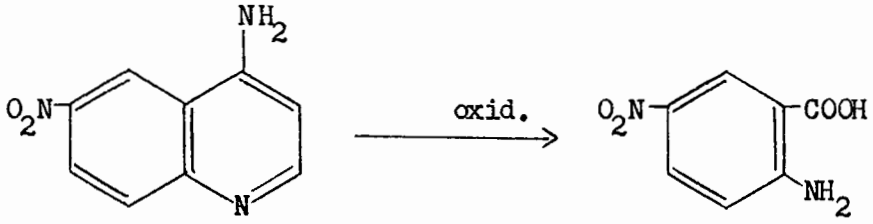
LXXII LXXIII LXXIV

The nitration of 4-aminoquinoline was first performed by Claus and Frobenius in 1897 (103). Nitric acid (d. 1.3) in cold acetic acid or in a warm solution only produced 4-aminoquinoline nitrate. With fuming nitric acid at low temperature there was still no reaction but when the mixture was heated on a water bath for 2 to 4 hours a yellow product not melted at 300° was isolated which the authors claimed was the same as the one obtained from the nitration of 4-hydroxyquinoline (104).

The identity of these two compounds was based on solubilities and crystalline form only. Nitration at 0° in sulphuric acid with fuming nitric acid afforded a dinitro derivative. It was found that the substance could be dissolved in concentrated sodium hydroxide to form a sodium salt and acidification of the latter yielded the original dinitro product. The logical conclusion that one of the nitro groups was attached to the amino function in a nitramine fashion seems to have escaped the authors. Since

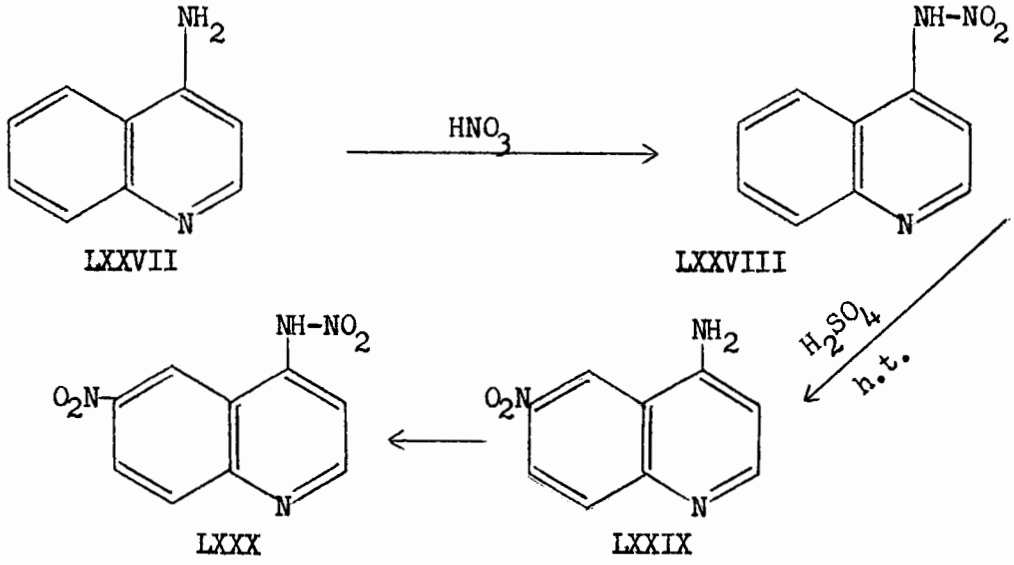
the position of one nitro group was known from the mononitration product and since the second bit of evidence placed the other nitro group the structure was actually completely defined.

Over twenty-five years later Tschitschibabin, Witkovsky and Lapschin (102) reexamined these results. They conducted the nitration at 0° with nitric acid of specific gravity 1.4. The reaction was allowed to stand for one hour and was then quenched with ice water. The product obtained melted at 207° instead of 203° as found by Claus and Frobenius but had the same solubility properties. Tschitschibabin and co-workers also showed that the compound could be rearranged. The structure of the rearrangement product was determined by oxidation to 2-amino-5-nitrobenzoic (LXXVI) acid. Hence the nitro group occupied the 6 position in the quinoline ring.



LXXV LXXVI

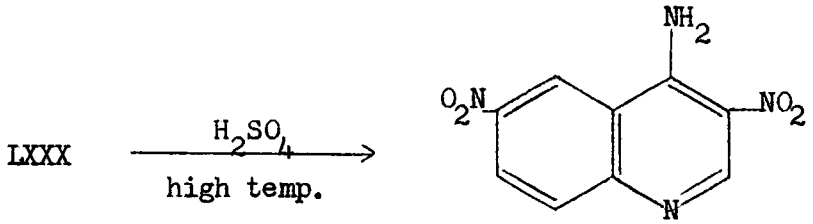
Summarizing we can write the various stages of nitration:



LXXVII LXXVIII LXXX LXXIX

In 1948 Simpson and Wright (105) in trying to prepare 4-amino-6-nitroquinoline by nitration and rearrangement discovered certain discrepancies between their results and Tschitschibabin's work. They were not able to isolate LXXIX by any simple procedure. Furthermore, although the Russian authors claimed to have established the orientation of LXXIX for which they recorded a melting point of 272°, they found that 4-amino-6-nitroquinoline prepared from 4-chloro-6-nitroquinoline (106) had a melting point of 312°.

A complex mixture seemed to have formed during the nitration of LXXVII, and although a complete separation of the products was not possible they were able to isolate LXXIX after prolonged fractionation. They also isolated LXXX which they isomerized. The structure of this rearrangement product could not be ascertained in any simple way but there was some evidence suggesting that the second nitro group was in position 3. In this eventuality the rearrangement can be represented by:



LXXXI

Infrared Spectroscopy

Aza-aromatic compounds

The similarity of the spectra of benzene and pyridine had been remarked in 1929 by Ganesan and Venkateswaran (107). Many workers made

similar observations in the ensuing years. Turkevitch and Stevenson made the first precise measurements of the infrared spectrum of pyridine in the vapor state (108) and Kline and Turkevitch located most of the fundamental frequencies of the molecule (109). Further work was carried out along these lines by the study of deuterated pyridines in the vapor state (110, 111, 112). The spectra of quinoline and isoquinoline have been reported (113, 114), but comparatively few derivatives have been studied. Among the three ring systems, the spectra of acridine and phenanthridine have been published by Cannon and Sutherland (115). The analysis of the data was rather sketchy. It is thus apparent that most of our knowledge of the infrared absorption of aza-aromatic compounds is based on the observations made on pyridine, quinoline and isoquinoline derivatives.

C-H stretching region. In much the same way as benzene derivatives pyridine and the picolines all show C-H absorptions in the range 3070-3020 $cm.^{-1}$ (109, 116). A number of alkaloids examined by Marion, Ramsay and Jones also presented an absorption in this region (117). Katritsky and co-workers showed in three papers published recently (118, 119, 120) and covering one hundred and ten 2-, 3- and 4-substituted pyridines that the C-H absorption occurs in these compounds in the range 3000-2930 $cm.^{-1}$ The authors found that electron attracting substituents tend to raise the frequency whereas electron releasing groups produce a shift in the opposite direction.

Combination and overtone region. Young, Duvall and Wright discovered average absorption patterns for benzene in the 2000-1600 $cm.^{-1}$ region that were typical with respect to the position and number of substituent groups (121). Cook and Church (122) noted such characteristic patterns in over thirty

mono-, di- and trisubstituted pyridines and showed that the shape of these bands was almost constant. No other work of this nature seems to have been carried out on heterocyclic molecules.

C=C and C=N region. The C=C and C=N vibrations appear, as one would expect from the evidence from benzenoid structures, in the range 1600-1400 cm.$^{-1}$ In many pyridine derivatives two bands about 100 cm.$^{-1}$ apart were observed, both at slightly lower frequencies than those of benzene. In some cases the higher frequency band was accompanied by a second absorption peak on the lower frequency side (123, 124). Cook and Church (122) showed that for monosubstituted alkylpyridines the average separation of the two bands could be used to differentiate 2- or 3-monosubstituted pyridines from the corresponding 4-substituted compounds. In the former the average separation of the two bands could be used to differentiate 2- or 3-monosubstituted pyridines from the corresponding 4-substituted compounds. In the former the average separation was about 20 cm.$^{-1}$ whereas in the latter there was a 40 cm.$^{-1}$ separation. Katritsky and co-workers (118, 119, 120) found two bands between 1650 cm.$^{-1}$ and 1550 cm.$^{-1}$, the latter usually of lower intensity. They noted that the intensity of both bands seemed to be a function of the Is effect of the substituents.

All the above mentioned investigators described bands between 1500 cm.$^{-1}$ and 1400 cm.$^{-1}$ In most cases two peaks of variable intensity appeared.

Quinolines and isoquinolines being larger molecules give more

complex patterns. Bellamy found as many as four bands in the interval 1600-1500 cm.$^{-1}$ in substituted dimethylquinolines (114).

A peak at 1330-1280 cm.$^{-1}$ was observed by Cook and Church (122) in the spectra of 32 out of the 34 pyridines examined. They suggested that it corresponded to an overtone of a fundamental occurring near 650 cm.$^{-1}$

Ring vibrations and hydrogen deformations. Bands can usually be found in the range 1200-1000 cm.$^{-1}$ which appear to persist throughout a series. For 2-monosubstituted pyridines a vibration arose at 1152-1145 cm.$^{-1}$ and 3-monosubstituted pyridines absorbed at 1196-1180 cm.$^{-1}$ (122). 4-Monosubstituted pyridines (27 examples studied) gave a band at 1112-1096 cm.$^{-1}$ of medium intensity except in the halogen derivatives when a very strong peak was found (120). Other bands at higher frequencies seemed to occur but were obscured by the solvent. None of the substituted quinolines examined by Bellamy (114) showed any strong absorption in this region.

The remaining characteristic region is that between 900 cm.$^{-1}$ and 700 cm.$^{-1}$ in which C-H deformations occur. It was shown (detailed discussion in Ref. 114 Chap. 5) in the case of benzene derivatives that the strongest band in this region originated from C-H out-of-plane vibrations and that its frequency was determined by the number of hydrogen atoms adjacent to one another. The limited number of molecules studied suggests that a similar situation is encountered in the aza-aromatics. Pyridine was found to absorb at 750 cm.$^{-1}$, 2-picoline at 755 cm.$^{-1}$, 3-picoline at 790 cm.$^{-1}$ and 4-picoline at 800 cm.$^{-1}$ (114), corresponding to the ortho-, meta- and para-substituted benzene derivatives respectively. Similar observations

were made on over fifty alkyl pyridines examined by Cook and Church (122) and by Shindo and Ikekawa (123).

The C-H out-of-plane deformation correlation still appears to be valid in quinoline and isoquinoline compounds. For example 2,6- and 2,7-dimethylquinolines only have two adjacent hydrogen atoms in each of the rings. Both materials absorbed strongly at 831 $cm.^{-1}$ and 835 $cm.^{-1}$ respectively, corresponding to para-substituted aromatics (114).

Heterocyclic N-oxides

Clemo and Daglish proposed two bands corresponding to the N-oxide absorption, one around 1390-1350 $cm.^{-1}$ and one in the range 1090-1040 $cm.^{-1}$ (125).

Costa and collaborators investigating a large number of such compounds suggested that a usually strong band appearing in the range 1300-1200 $cm.^{-1}$ corresponded to an N-oxide function (124, 126, 127). Japanese workers examining over thirty N-oxides noted the presence of the same band, often accompanied by a satellite band or presenting an inflexion around the main peak. They showed that the position of this peak is determined by the Is effect of the surrounding substituents and the mesomeric effect. Their studies also demonstrated the presence of two bands of variable intensity at 780-720 $cm.^{-1}$ and at 880-840 $cm.^{-1}$ These were assigned to N-O bending modes (128, 129, 130).

Katritsky and co-workers (131, 132) studied twenty-four 2-substituted pyridine N-oxides and the corresponding twenty-four 4-substituted

compounds. They located the N-oxide absorption between 1300 cm.$^{-1}$ and 1240 cm.$^{-1}$ This frequency was found to be raised by electron-accepting groups and the intensities increased with increasing electron-withdrawing ability of the substituents. The 2-substituted derivatives showed a shoulder or subsidiary band on the high frequency side. In the lower frequencies a band of variable intensity occurred at 860-842 cm.$^{-1}$ for the 4-substituted pyridine N-oxides and at 866-834 cm.$^{-1}$ for the corresponding 2-substituted materials.

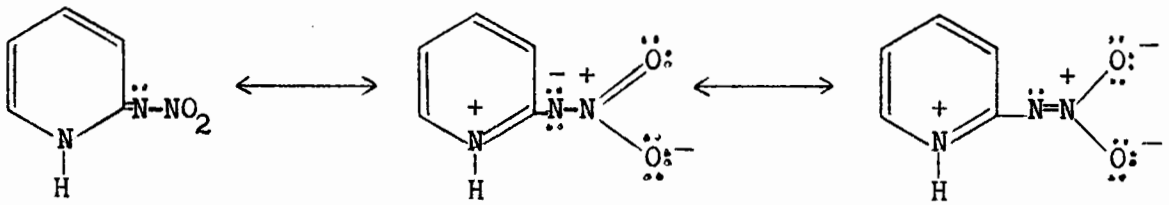
Nitramines

Lieber, Levering and Patterson (134) examined seventeen N-nitro compounds of various types and found the symmetric nitro vibration to be reasonably constant within the range 1315-1260 cm.$^{-1}$ The asymmetric frequencies, on the other hand, fell in a wide range (1640-1540 cm.$^{-1}$) and appeared to be more influenced by the nature of the substituents.

A study of the near infrared region (1 - 2μ) of nine arylnitramines by Salyamon and Yaroslavskii (135) showed that these compounds were true nitro derivatives and that thus their structure was represented by R-NH-NO_2 rather than by R-N-NOOH. They based their conclusion on the fact that no band appeared at 7143 cm.$^{-1}$, a characteristic of the OH group.

Taurins in 1958 considering the possibility of tautomerism existing in heterocyclic nitramines investigated the infrared absorption of six such pyridine and thiazole derivatives (136). He showed that the N-H band normally found in the region 3400-3200 cm.$^{-1}$ was absent and that instead a

wide band appeared between 2880 and 2550 cm.$^{-1}$ The conclusion drawn from this observation was that 2-nitraminopyridine, for example, existed in the nitrimino betaine form. Structures (LXXXIII) and (LXXXIV) will thus predominate in the resonance hybrid.



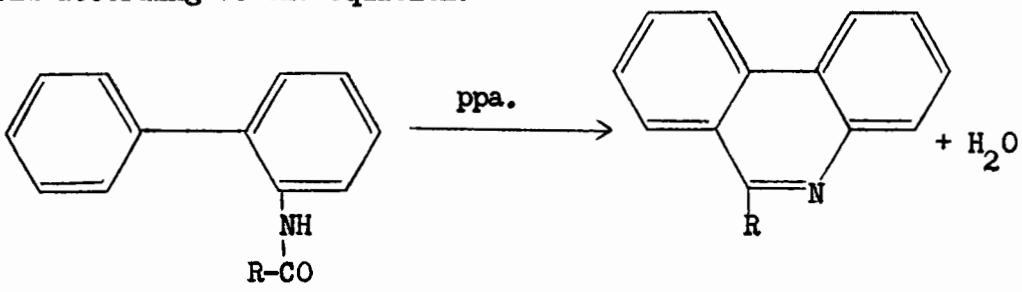
LXXXII LXXXIII LXXXIV

This interpretation explained the shift of the N-H absorption to lower frequencies. The possibility that such a shift was the result of association of the N-H group with the oxygen of the nitro function was eliminated by comparison with the spectrum of n-butylnitramine where a peak was observed at 3300 cm.$^{-1}$

DISCUSSION

Synthesis of phenanthridines

As a first step in this work it was necessary to select a convenient method of preparation of phenanthridine and its 6-alkyl derivatives. A few trials soon demonstrated that the pyrolysis of N-methylcarbazole, a method described by Diesbach and Aeschbach (149) and recommended by Theobald and Schofield (150), produced mostly acridine whereas the cyclization of o-amidobiphenyls with zinc chloride, originally proposed by Pictet and Hubert (151), afforded very low yields, owing to the drastic conditions of the reaction. The method chosen for the preparation of phenanthridines was that proposed by Taylor and Kakuda (138) involving the ring closure of o-amidobiphenyls with polyphosphoric acid according to the equation:

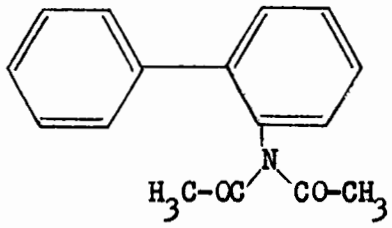


LXXXV LXXVI

Preparation of o-amidobiphenyls

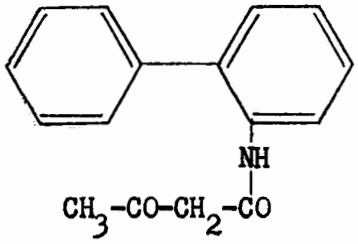
o-Formamidobiphenyl and o-propionamidobiphenyl were formed by the action of the respective anhydrides on o-aminobiphenyl. On the other hand it was claimed by Bell (143) that o-acetamidobiphenyl could not be prepared by acetylation with acetic anhydride because of the formation of

oils which could not be crystallized. The authors proposed an alternate route consisting of acetylation with acetyl chloride. It was found here that the reaction of 1.5 equivalent of acetic anhydride with o-aminobiphenyl gave an oily product, but the latter crystallized either by allowing it to stand for 24 hours or by adding a small amount of water and stirring rapidly while cooling the mixture on an ice bath. An unexpected feature of this reaction was the formation of a di-acetyl compound when under similar conditions o-aminobiphenyl was reacted with three equivalents of acetic anhydride. The compound was found to hydrolyze to the monoacetyl derivative by merely dissolving it at room temperature in orthophosphoric acid. The infrared spectrum presented no N-H absorption at all and consequently its structure had to be (LXXXVII):



LXXXVII

This last piece of evidence eliminated the possibility of the material being the substituted acetoacetic acid amide (LXXXVIII)



LXXXVIII

whose melting point (83.5-85°) is quite close to the one of this substance (87°).

Cyclization of o-amidobiphenyls

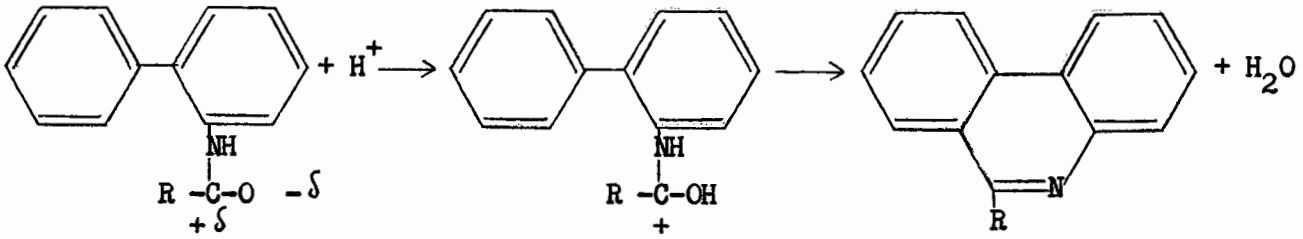
The ring closure was achieved by heating the o-amidobiphenyls with polyphosphoric acid. The synthesis of phenanthridine achieved by cyclizing o-formamidobiphenyl had to be repeated several times to provide enough starting material for this investigation. A certain experience in this procedure was thus gained and some important experimental factors were discovered. First, it was found that a thorough mixing of the reagents before heating the mixture was essential. Yields as low as 10% were recorded whenever this condition was not fulfilled. Second, the operations did not have to be carried out in a dry atmosphere, although the polyphosphoric acid is quite hygroscopic. Third, consistently higher yields were obtained when clear polyphosphoric acid was used as opposed to the semi-liquid, semi-crystalline mixture that develops on standing for long periods of time.

The method was extended to the preparation of 6-methylphenanthridine and 6-ethylphenanthridine. The object of the latter synthesis was not to prepare 6-ethylphenanthridine as a basic material for further investigation but only to test the applicability of the procedure to the formation of phenanthridines carrying a larger alkyl group in the 6 position.

The 6-methyl derivative was obtained under much milder conditions than phenanthridine itself with an equivalent yield; the 6-ethyl compound only formed in very small amounts and was extremely difficult to purify.

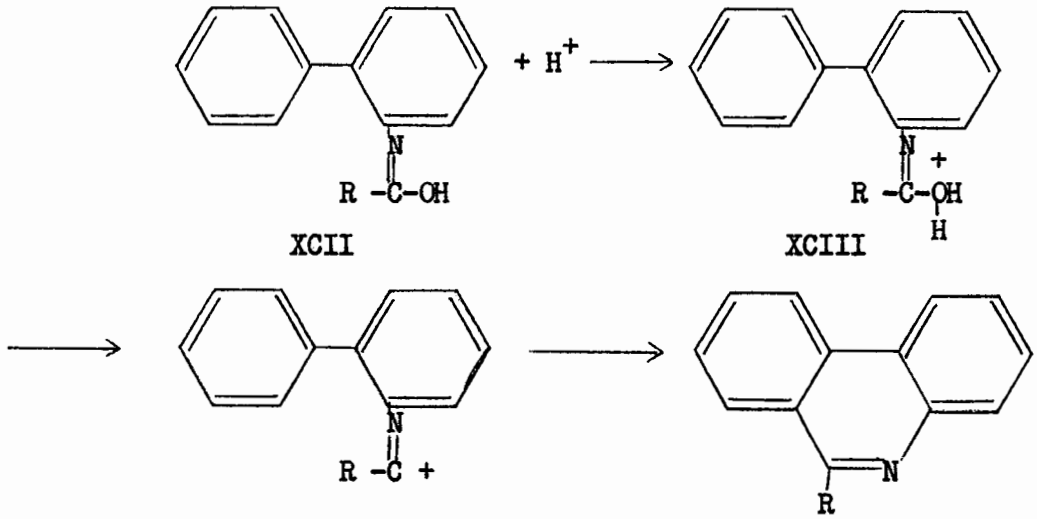
Theobald and Schofield (150) suggested that such a ring closure

proceeded through the intermediate formation of a carbonium ion. If this is the case, the stability of the ion will control the reaction. A priori one can imagine two ways in which such a carbonium can be formed. In the first one there is addition of a proton to the partially negative oxygen of the carbonyl group of (LXXXIX) to give the intermediate (XC) which then loses the elements of water to form the product (XCI).



LXXXIX XC XCI

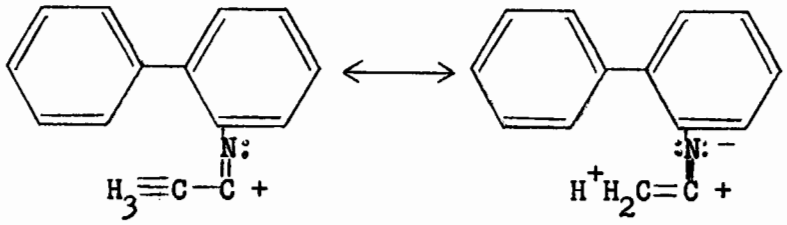
The other route consists in the addition of a proton to the enolic tautomer of (XCII) followed by the elimination of water to give the carbonium ion (XCIV) which subsequently cyclizes to (XCV).



XCII XCIII XCIV XCV

The experimental fact that the 6-methyl derivative is formed with

much more ease supports the second mechanism. Indeed, if R=CH_3 in the preceding formulae, one can see that the resulting carbonium ion will be stabilized by hyperconjugation of the methyl group with the double bond between carbon and nitrogen.



XCVI XCVII

When R = H or CH_2-CH_3 no such hyperconjugation can take place and consequently the intermediate will be formed with greater difficulty. This reaction scheme thus explains the different degrees of reactivity of the three substances whereas the first mechanism does not. However, the extremely low yields obtained for 6-ethylphenanthridine are somewhat surprising.

Nitration of phenanthridine N-oxide

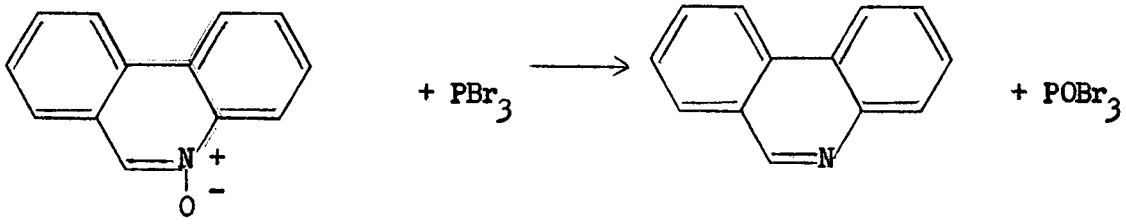
Two methods were reported in the literature for the oxidation of phenanthridine to its corresponding N-oxide. Mitsuhashi (140) proposed the use of hydrogen peroxide in acetic acid as oxidizing agent. The Japanese procedure could only be reproduced with a yield of less than 5% against the 45% claimed by the author. On the other hand, reaction with an ethereal solution of monoperphthalic acid, as described by Petrow (141) proved to be a simple and rapid way to obtain phenanthridine N-oxide. Whereas Petrow carried out the reaction at 0° for several days, this

investigation showed that comparable yields could be obtained by allowing the materials to react at room temperature for 24 hours. The modified procedure thus provided a way of preparing phenanthridine N-oxide in a short time, with a good yield and from easily accessible starting materials. Furthermore it presented no purification problems.

Reactivity of phenanthridine N-oxide

Two characteristic chemical properties of heterocyclic N-oxides are the easy reduction by phosphorus halides and the rearrangment of the N-oxide function. No data existed in the literature as to the behaviour of phenanthridine N-oxide under these conditions.

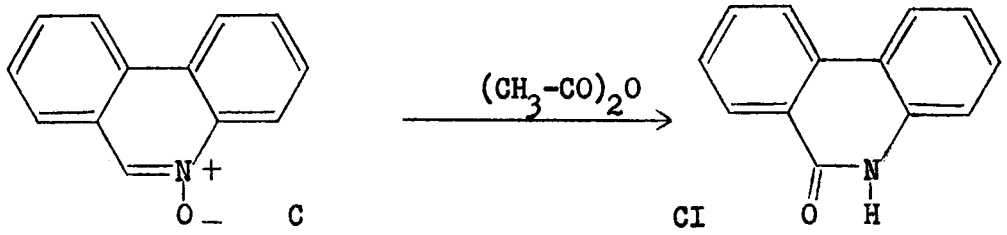
The reduction was carried out in chloroform solution with phosphorus tribromide according to the equation:



XLVIII XLIX

An almost instantaneous reaction took place as demonstrated by the immediate formation of a precipitate of phosphorus oxybromide.

The rearrangement was performed in acetic anhydride and yielded, as predicted, phenanthridinone (CI):



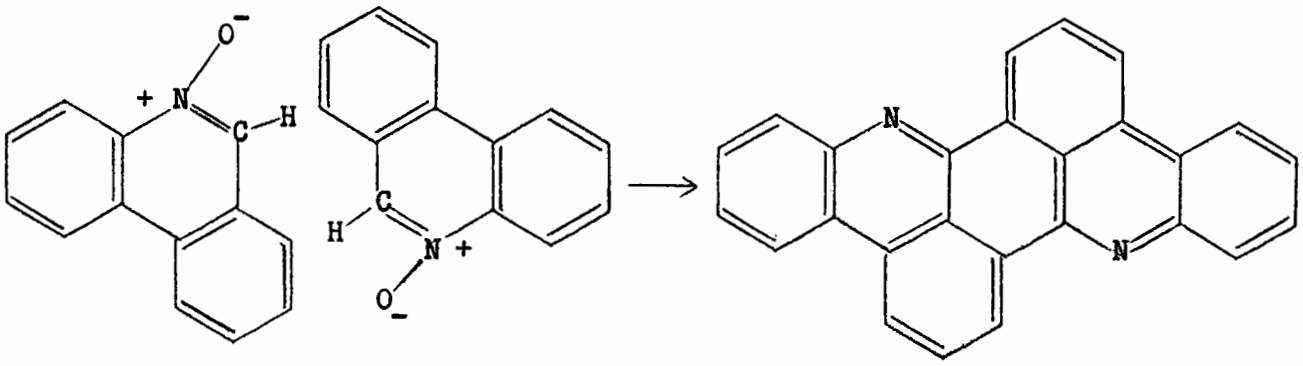
C CI

In order to test the claim that such a rearrangement does not occur by heating with organic acid and to determine the stability of the N-oxide function in hot acetic acid, such a solution was refluxed for one hour. Phenanthridine N-oxide was recovered unchanged. A significant fact observed during the course of this reaction was that after eliminating part of the solvent by distillation crystals formed which dissolved as soon as they came in contact with the air. The solids must have been phenanthridine N-oxide acetate which hydrolyzed in the presence of moist air. Whereas the parent hydrocarbon is a base of some strength the N-oxide is a much weaker base but strong enough to form an acetate in a water-free medium.

Nitration of phenanthridine N-oxide

Sulphuric acid is usually classified as a fast solvent of nitration and in most cases the reaction has to be conducted at low temperature. Phenanthridine N-oxide however could not be nitrated in concentrated sulphuric acid either at 0° or at 45°. This lack of reactivity is not too surprising if one considers that phenanthridine itself cannot be directly nitrated but that it is first necessary to prepare a mono- or dinitrate which then on heating in sulphuric acid produces nitro derivatives. The starting material recovered from the low temperature reaction was slightly yellow, an indication that at least a small amount of product was formed. The high temperature nitration afforded a gum of undefined character which could not be solubilized. The type of reaction that seems most likely to produce such a gum is a condensation. Although there is no proper evidence to this effect it brings up the possibility

of a condensation between two N-oxide molecules to give (CIV):



CII CIII CIV

The existence of such a compound was postulated by Elderfield (146) as the structural formula of a by-product occurring during the preparation of 6-aminophenanthridine.

The conclusion emerging from these data is that whereas at low temperature no reaction can be detected, at the temperature favourable to nitration there are competitive reactions whose rates are high enough to obliterate any signs of nitration.

The lack of success with sulphuric acid led to trials with glacial acetic acid. At room temperature no product was formed, as one could have predicted from the results of the previous experiments. A characteristic feature of the reaction, which reappeared in all other nitrations of phenanthridine N-oxide, was the formation of a precipitate soon after the addition of the nitrating mixture to the acetic acid solution had been completed. Since these solids dissolved when the mixture was poured into water and since the material isolated was phenanthri-

dine N-oxide, i.e. no irreversible reaction had taken place, the structure of the precipitate had to be that of a salt, which hydrolyzed immediately on coming into contact with an aqueous medium. Furthermore, the salt had to be phenanthridine N-oxide nitrate.

Nitration was achieved by raising the reaction temperature to 70-75°. To determine the optimum conditions successive runs were made with one, two and three equivalents of nitric acid 70%, all other factors being equal. The course of the reaction in all cases was similar. At first the precipitate already mentioned formed. Then as the temperature was increased the solids solubilized rapidly between 65° and 70°. After a period of time ranging from three to six minutes the nitration product started to precipitate. The same material was isolated every time and consequently, as the analysis showed, it had to have the structure of a mononitro derivative. The different variables are recorded in Table IV.

TABLE IV

Nitration of phenanthridine N-oxide

Medium	Nitrating agent	Equivalents	Yield (in %)
CH_3-COOH	HNO_3 70%	1	36
CH_3-COOH	HNO_3 70%	2	62
CH_3-COOH	HNO_3 70%	3	65
$(CH_3\text{-}CO)_2O$	HNO_3 70%	1	38.5
CH_3-COOH	HNO_3 fuming	1	27.5

The yields increase with the number of equivalents of nitric acid but there is no linear relationship between the two parameters. Whereas two equivalents give a yield of less than twice that obtained with one the results are only slightly better with three. This set of conditions thus corresponds to the optimum.

The effect of the concentration of the nitric acid and of the presence of small amounts of water was evaluated by doing a run with fuming nitric acid. The reaction was found to proceed in the same way as previously and afforded the same material. The yield was appreciably lower but this effect was probably due to a shorter total reaction time. An experiment performed in acetic anhydride showed that no benefit could be obtained by working in this medium since an almost identical yield was recorded.

A dilute solution of phenanthridine N-oxide in acetic acid gave the same product on nitration with three equivalents of 70% nitric acid. A striking difference however resided in the fact that the reaction was considerably slower, the latter conclusion being drawn from the observation of the rate of formation of the second precipitate in the reaction mixture. Although not a quantitative determination, this reduced rate was quite definite. This meant that the reaction did not follow a zeroth-order law but that it did in fact depend on the concentration of the reagents. In this respect it differed from the findings of Ingold and Benford (9) concerning the nitration of toluene and analogous materials. One is thus led to the assumption that in contradistinction with toluene, this nitration must include some rate-determining stage involving the

heterocyclic molecule.

Summarizing one can say that the nitration of phenanthridine N-oxide in acetic acid or acetic anhydride produces one mononitro compound and that an optimum yield is attained with three equivalents of 70% nitric acid.

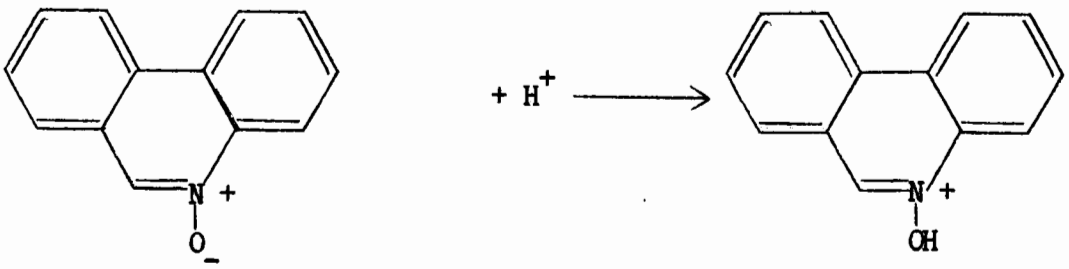
Purification of the product was in most cases extremely difficult. Even after several recrystallizations and a sublimation the product charred to a rather large extent before melting at 382-383°, a sure indication of the presence of some impurities. Chromatography was thought to be a possible means of achieving complete purification. Adsorption of the substance on alumina and subsequent elution with hot pyridine did indeed separate a brick-red compound from the bulk of the material. Its structure could not be ascertained since it could not be desorbed from the alumina. The nitro derivatives after going through this separation retained the same melting point but no blackening was detected on heating.

Reduction of the product either with phosphorus trichloride or phosphorus tribromide failed altogether. The conclusion emerging from this piece of information was that the substance was not an N-oxide. The next most probable structure was that of a nitrophenanthridine, but an examination of the melting points of the nitrophenanthridines ruled out this possibility. On the other hand, the melting point of this material corresponded to that of 2-nitrophenanthridinone. Furthermore the infrared spectrum did not seem to have an N-oxide band and exhibited a strong absorption peak at 1670 $cm.^{-1}$ suggestive of a carbonyl group. 2-Nitrophen-

anthridinone was therefore prepared by synthetic means, and comparison of the infrared spectra of the latter and of the compound obtained by nitration of phenanthridine N-oxide proved them to be identical. It thus appears that not only was the molecule nitrated but that a rearrangement of the N-oxide function also took place.

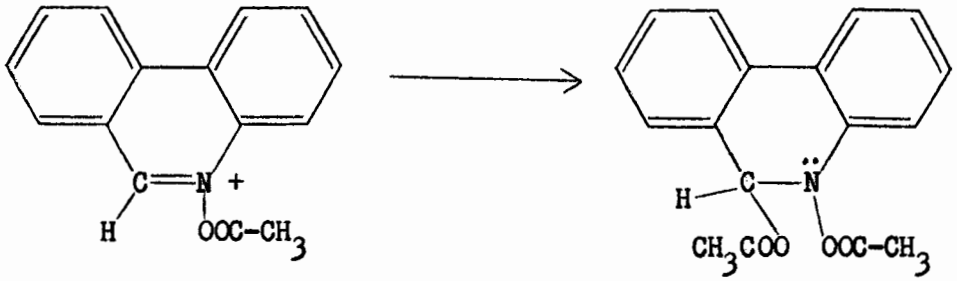
The first question to be answered in examining the possible mechanism of such a reaction is whether the rearrangement preceded, followed or was concomitant with the nitration. The first case can be eliminated immediately, since it is known that phenanthridinone is nitrated mainly in the 4 position. The second possibility involving a nitration before rearrangement does not seem to be more likely since no resonance structure can be written showing a negative charge in the 2 position. Any displacement of π electrons in the molecule will bring a negative charge on the 1 or 3 positions and consequently a positive charge on carbon 2. It is thus necessary to assume that both rearrangement and nitration proceed simultaneously; in other words that while the system is rearranging an intermediate is produced which will direct the nitronium ion in the 2 position.

As established previously the primary step of the reaction is the formation of a phenanthridine N-oxide salt (CVI), the first precipitate.



CV CVI

This precipitate solubilizes when the temperature is raised. Considering the mechanism proposed by Ochiai for the rearrangement of N-oxide and keeping in mind the accepted mechanism of formation of the so-called Reissert compounds as well as the work of Kosower (32) on the structure of methylpyridinium iodide, it seems logical to assume that the proton fixed on the oxygen of (CVI) is replaced by an acetyl group and that the carbon 6 is attacked by an acetate group. For clarity the process can be represented by two stages, although no claim is made that two distinct steps actually occur:



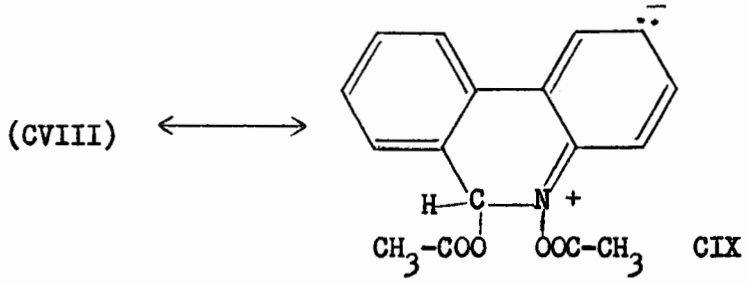
CVII CVIII

The addition of the acetyl group to the N-oxide function results in an increased partial positive charge on the carbon 6 due to the strong -Is effect of the nitrogen bearing a full positive charge. Hence a facile addition of the acetate group in this position.

Such a mechanism evidently presupposes the existence in the solution of both acetate and acetyl ions. There is no difficulty in explaining the presence of the former. The existence of the latter may seem unlikely in the face of the results obtained from eutectic curves, Raman spectra and electrical conductivity (see Historical). However all of these measurements were made at or below room temperature and conseq-

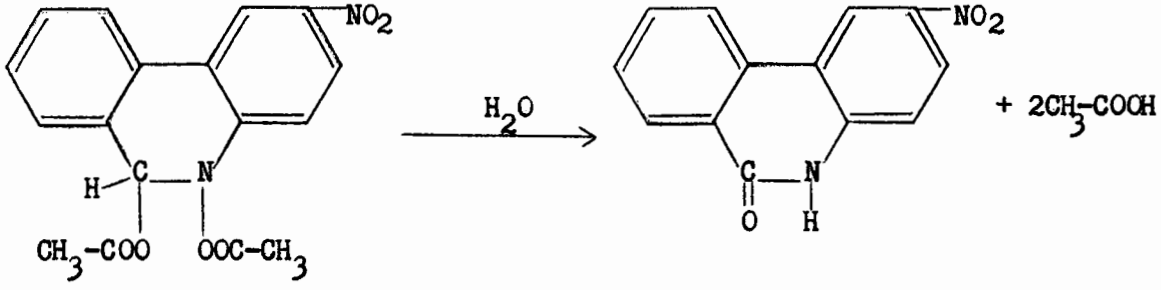
uently the conclusions reached cannot be extrapolated to the relatively high temperature of this reaction. Furthermore any explanation of the rearrangement of the N-oxide function seems to involve necessarily the formation of acetyl ions.

Nitration of the intermediate (CVIII) will now proceed in position 2. That this is the preferred site of electrophilic substitution can be understood by considering the right side of the molecule as an aniline derivative. Indeed as an aniline analogue one would expect nitration in ortho and para to the nitrogen atom, corresponding to the 4 and 2 position of the phenanthridine nucleus. No evidence of the 4-isomer was found but it is quite possible that the rate of substitution in the 2 position was considerably higher than in the 4 position. One important resonance structure of the intermediate (CVIII) is thus (CIX).



CIX

The last step then consists in the hydrolysis of the nitro compound (CX) to give 2-nitrophenanthridinone (CXI).



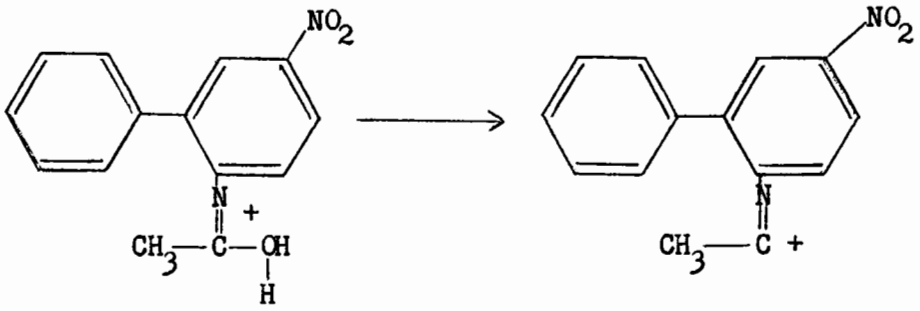
CX CXI

This mechanism based on analogies with similar systems explains all the experimental data. It accounts for the initial precipitate, the rearrangement of the N-oxide function and the orientation of the nitro group.

Note on the synthesis of 2-nitrophenanthridinone

Two methods of synthesis were available in the literature. One involved the nitration of 2-acetamidobiphenyl, followed by cyclization to 6-methyl-2-nitrophenanthridine and oxidation of the latter. The first step, described by Bell (143), could not be duplicated and for this reason it was necessary to adopt the other route, somewhat longer but more reliable.

2-p-Toluenesulfonamidobiphenyl, prepared from 2-aminobiphenyl by a standard procedure, was nitrated with 70% nitric acid in acetic acid. The use of one equivalent of nitric acid prevented the formation of any dinitro derivative, a simpler and more efficient way than operating in a dilute solution as recommended by Bell (143). 5-Nitro-2-p-toluene-sulfonamidobiphenyl was then hydrolyzed to 2-amino-5-nitrobiphenyl which in turn was acetylated. Cyclization to 6-methyl-5-nitrophenanthridine was achieved with remarkable ease by an extension of the method of Taylor and Kakuda (138). Heating the material in polyphosphoric acid for less than five minutes gave a yield of over 50%. Such a facile reaction must be due to the -Is effect of the nitro group in the 2 position which tends to weaken the carbon-oxygen bond in (CXII) and thus renders the formation of the intermediate carbonium ion (CXIII) easier.



CXII CXIII

6-Methyl-2-nitrophenanthridine was then oxidized to the corresponding phenanthridinone by a procedure described by Walls (52).

Nitration of 6-methylphenanthridine

One would expect the reactivity of 6-methylphenanthridine to be very similar to that of phenanthridine itself and consequently it would be reasonable to predict the formation of the same isomers in roughly the same proportion during a nitration.

The direct nitration of phenanthridine is not possible. Instead it is necessary to prepare first a mono- or dinitrate and then by heating this salt in sulphuric acid a mixture of nitro isomers can be isolated (see Historical). In this respect the 6-methyl derivative behaves in an identical fashion. Dissolving 6-methylphenanthridine nitrate in sulphuric acid and keeping the solution at 70-75° for one hour produced two isomers labelled A and B. The former having a relatively low melting point and soluble in ethanol analyzed for a mononitro derivative; the latter melting at a much higher temperature and insoluble in ethanol but soluble in acetic acid gave an analysis corresponding to a dinitro compound. Its presence proved that the 6-methylphenanthridine nitrate used as starting

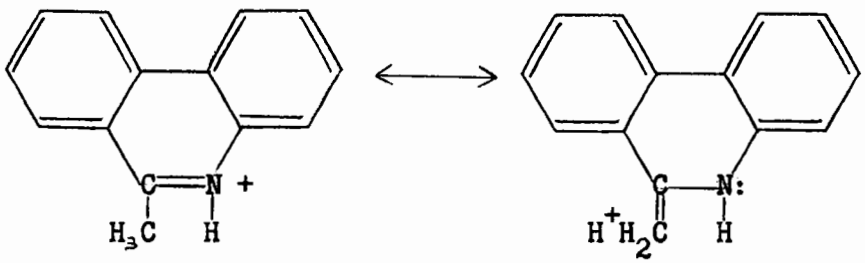
material was not a pure mononitrate but that it contained a certain amount of dinitrate, a phenomenon also observed in the case of phenanthridine.

With the object of trying to identify these fractions they were oxidized to the corresponding phenanthridinones.

Compound A reacted with sodium dichromate in acidic solution gave an easily crystallizable material melting at 265-267°. It was not soluble in ethanol any more and its infrared spectrum showed a strong wide band at 1690 $cm.^{-1}$ indicative of a carbonyl function. Both of these facts coupled with the results of the elemental analysis pointed to a phenanthridinone structure. An examination of the melting points of the six known nitrophenanthridinones showed it to be the 4-nitro isomer. Consequently fraction A resulting from the nitration of 6-methylphenanthridine was 6-methyl-4-nitrophenanthridine.

Compound B oxidized in the same manner to give a substance soluble only in boiling acetic acid and whose infrared spectrum displayed a carbonyl band at 1680 $cm.^{-1}$ No dinitrophenanthridinone having been described previously the substance could not be identified by comparison with an already synthesized compound. Furthermore since none of the diaminophenanthridinones were described and since only 2,8-diamino-6-methylphenanthridine and 3,8-diamino-6-methylphenanthridine had been reported, there seemed to be no other relatively simple way of elucidating the structure of fraction B.

The formation of a 4-nitro derivative in the nitration of 6-methylphenanthridine in a large proportion is somewhat surprising since the nitration of the parent compound only produces this isomer to the extent of 1%. It is significant however that the theoretical calculations of Longuet-Higgins and Coulson (38) predict the 4 position as being the most reactive one of phenanthridine in an electrophilic substitution. The discrepancy was accounted for by Dewar (see Historical). The introduction of a methyl group in the 6 position of phenanthridine probably does not disturb appreciably the electronic distribution in the benzene rings of the phenanthridine system and consequently one can assume that the 4 position of 6-methylphenanthridine will still be the most negative one. With this in mind let us examine the 6-methylphenanthridinium ion which is the entity being nitrated. The methyl group is in direct conjugation with the double bond existing between the nitrogen and the carbon atoms. This results in hyperconjugation as shown in structure (CXV).

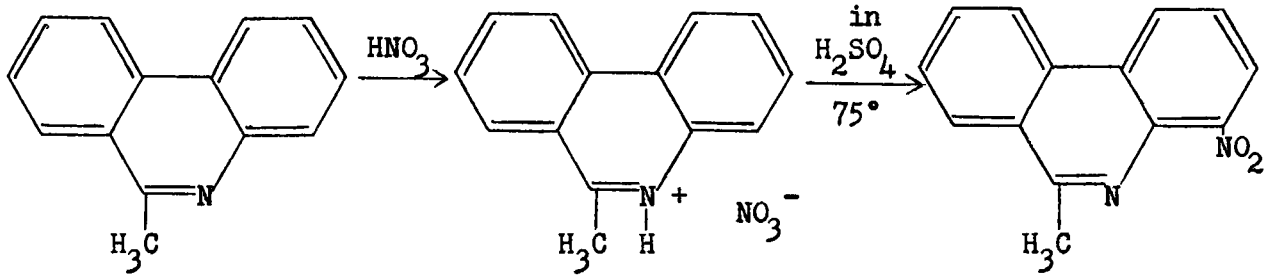


CXIV CXV

The net effect of this phenomenon is to decrease the positive charge carried by the nitrogen atom. Furthermore the methyl group possesses a +Is effect so that the electrons will be even more delocalized toward the nitrogen and thus minimize the positive charge of the nitrogen

atom. In the light of these considerations it becomes apparent that, contrary to what is found with phenanthridine, the nitronium ion will be able to attack the 4 position with greater facility, since the positive electrostatic field in this region will be much decreased.

The mononitration of 6-methylphenanthridine can thus be summarized by the equations:



CXVI CXVII CXVIII

Nitration of 6-aminophenanthridine

6-Aminophenanthridine was prepared by the reaction of sodamide with phenanthridine according to Morgan and Walls (145). Commercial sodamide was used and since this grade of material was always decomposed to some extent it was necessary to react four equivalents with one equivalent of phenanthridine to obtain a good yield.

The mononitration was carried out first at -15° with the object of preparing the corresponding nitramine. This low temperature was chosen to minimize as much as possible the rearrangement of the eventual product, a process whose rate was shown by Kasman (152) to be relatively rapid at 0° in some cases. The product obtained was identical to the one isolated

from a reaction which was allowed to stand at room temperature for ten minutes before quenching it with water. The infrared spectrum of both substances showed a band at 3460 $cm.^{-1}$ with shoulders at 3400$cm.^{-1}$ and 3340 $cm.^{-1}$ The presence of these absorption maxima coupled with the fact that a room temperature reaction produced the same substance as a low temperature reaction suggested a nitro-amino structure rather than a nitramine. The possibility that a stable nitramine had formed can be eliminated since it was shown later that in the presence of an excess of nitric acid a dinitro compound could be obtained. Indeed, the formation of a non-rearrangeable nitramine supposes that either no vacant position exists in the system or that neither of them is sufficiently reactive to accommodate the nitro group. The first alternative does not have to be considered here since there are eight substitutable carbons in the molecule. In the second case the formation of a dinitro compound would be extremely unlikely because the replacement of one of the hydrogens of the amino group by a nitro group results in a decreased +Is effect with the consequence that the flow of electrons towards the rings is restrained. None of the ring carbons will thus become more negative and substitution by a second nitro group will be impossible.

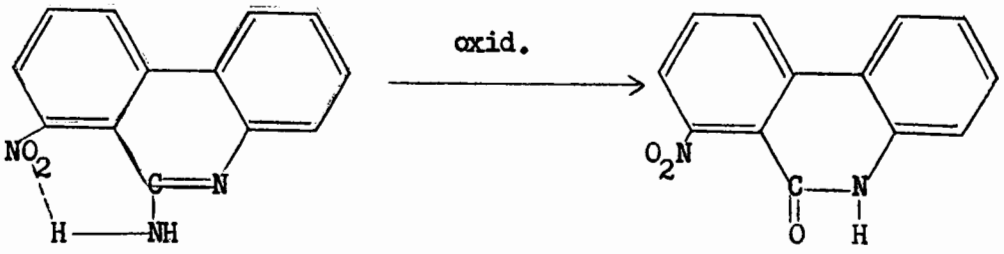
Nitration with an excess of reagent was carried out at low and at relatively high temperature. The course of the reaction was similar in both instances and the same product was isolated. Analysis showed it to be an aminodinitrophenanthridine. An attempt to rearrange the material by heating it in concentrated sulphuric acid to 50° failed, indicating that its structure was that of a nitro-amino compound. The presence of two

bands one at 3380 cm.$^{-1}$ and one at 3280 cm.$^{-1}$, characteristic of an amino group supported this view.

In an effort to identify the mononitration product a procedure described by Morgan and Walls (145) to transform 6-aminophenanthridine into phenanthridinone was applied. The product of the reaction analyzed for a nitrophenanthridinone and its infrared spectrum showed a carbonyl band at 1685 cm.$^{-1}$ To verify the claim made by Morgan and Walls (145) that the amino group in the 6 position of phenanthridine does not diazotize a drop of the reaction mixture was tested after two hours with β-naphthol. A negative reaction was obtained demonstrating the absence of diazonium salt in the solution.

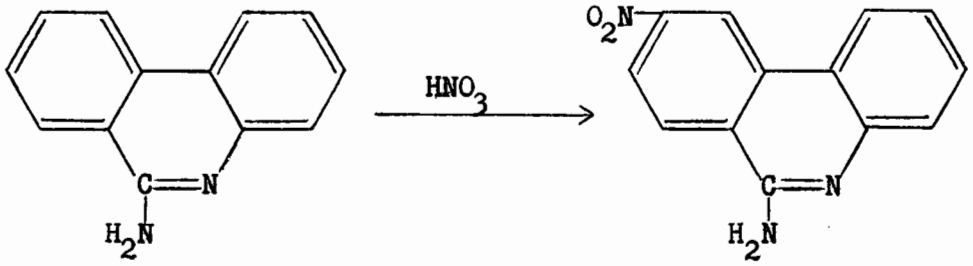
The melting point of the product was checked against those of the six already known nitrophenanthridinones and was found to be considerably higher than any of these. Therefore the compound had to be either 7- or 9-nitrophenanthridinone. A choice can be made by considering the evidence obtained from infrared spectroscopy. The asymmetric nitro band of the aminonitrophenanthridine appears at 1497 cm.$^{-1}$ and in the corresponding phenanthridinone the absorption peak is observed at 1495 cm.$^{-1}$, i.e. almost at the same frequency. Gilman and Eisch (153) showed that in 4-nitrophenanthridinone the asymmetric nitro group absorption occurred at a lower frequency than the corresponding vibration in 2-nitrophenanthridinone. This shift was attributed to the fact that in the 4-isomer intramolecular hydrogen bonding took place between the oxygen of the nitro group and the hydrogen of the N-H function, whereas no such bonding could take place in the 2-nitro derivative.

If the nitro product obtained here were 6-amino-7-nitrophenanthridine a certain amount of hydrogen bonding could occur (CXIX) and consequently a fairly substantial shift of the nitro group absorption peak would be expected in 7-nitrophenanthridinone (CXX) where this situation does not exist.

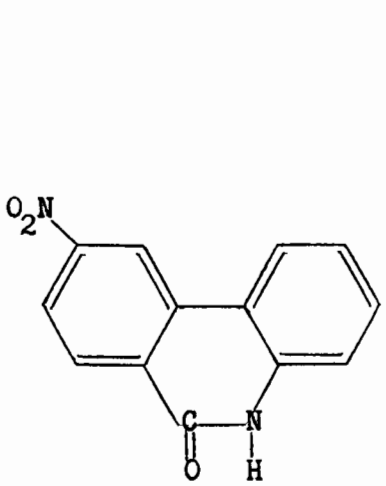


CXIX CXX

It must thus be concluded that nitration of 6-aminophenanthridine (CXXI) produced 6-amino-9-nitrophenanthridine (CXXII) which on oxidation gave 9-nitrophenanthridinone (CXXIII).



CXXI CXXII

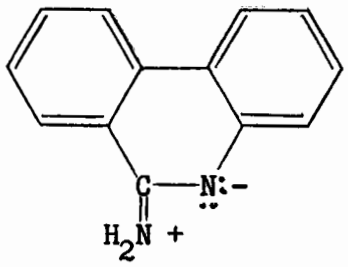


CXXIII

The structure of the dinitro product (fraction B) could not be elucidated since, as in the case of 6-methylphenanthridine, none of the related derivatives are known.

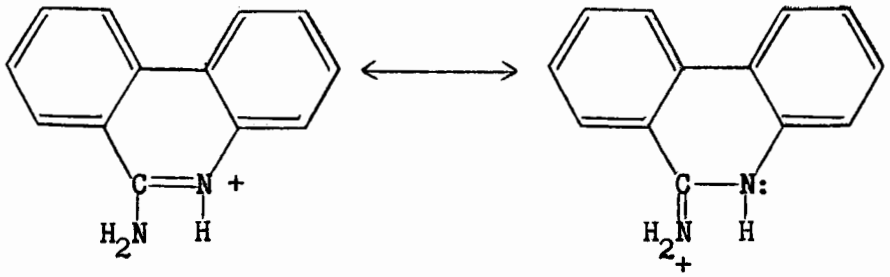
Helpful evidence can be found in a study of the infrared spectrum of 6-aminophenanthridine to determine the reason why this material did not furnish any nitramine even when the reaction was carried out at -15°. Reese (154) investigating the infrared absorption of 6-aminophenanthridine found that the compound existed predominantly in the amino form, in other words that no imino structure could be detected. In this work two absorption peaks were observed in the spectrum of 6-aminophenanthridine which indicated that the classical amino structure did not correspond exactly to reality (see also Infrared Section).

The first peak at 2760 $cm.^{-1}$ was low enough to suggest that the nitrogen of the NH_2 group carried a full or partial positive charge. The other absorption at 1685 $cm.^{-1}$ was very strong and indicated a C=N type of bonding. The conclusion stemming out of these observations is that the structure of 6-aminophenanthridine is a resonance hybrid to which a structure like (CXXIV) makes an important contribution.

(CXXI) $\longleftrightarrow$ 

(CXXIV)

During nitration a phenanthridinium ion will be formed which will be stabilized by resonance in the same manner.



CXXV CXXVI

The result of this phenomenon will be that the nitrogen of the amino group will carry a partial positive charge large enough to prevent substitution by a nitronium ion and thus no nitramine will be formed.

Nitration of 9-aminoacridine

Technical grade acridine was used and it was necessary to purify it before further processing. The method employed was one recommended by Elderfield (146) consisting in the formation of the dichromate salt, easy to obtain in a pure form, and then liberation of the free base by alkalinization. 9-Aminoacridine was synthesized from acridine by a Tschitschibabin type of reaction described by Bauer (147). The substance was obtained in a fairly good yield by using three equivalents of commercial sodamide.

9-Aminoacridine was nitrated at -15° with one equivalent of 70% nitric acid in concentrated sulphuric acid with the object of preparing the nitramine. Two fractions were isolated. The largest one, labelled A,

was deep yellow in acidic solution and turned red at the equivalence point. The analysis showed it to be a 9-aminomononitroacridine. It was easily crystallizable and gave an instantaneous purple coloration when placed in a 1 N alcoholic potassium hydroxide solution. Fraction B obtained in very small amount was isolated only once. When the reaction was repeated it could not be detected again.

Nitration with one equivalent at high temperature (50°) produced a compound exhibiting the same properties as fraction A of the previous experiment. A slightly higher yield was recorded.

A large excess of nitric acid at low temperature gave an 80% yield of a material identical with the above-mentioned fraction A, and a second fraction in small amount which analyzed for a 9-aminotrinitro-acridine. At high temperature (70°) the yield of mononitro compound fell to 16% but the trinitro derivative was obtained in a 42.5% yield.

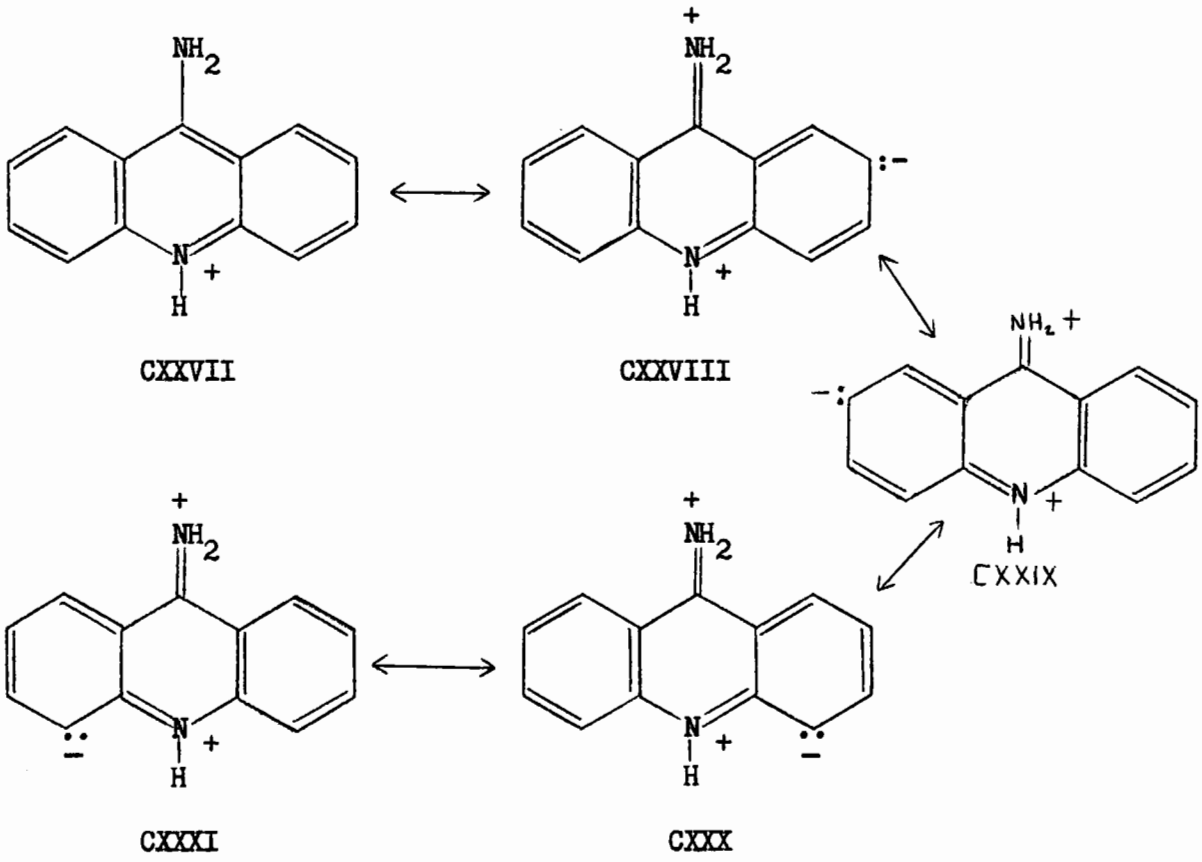
The change from yellow to red by varying the pH of a solution containing fraction A pointed to an aminonitroacridine structure. The infrared spectrum showed a band at 3470 $cm.^{-1}$ with a very weak shoulder at 3380 $cm.^{-1}$ Although the last absorption was ill-defined the absence of any band between 2900 $cm.^{-1}$ and 2500 $cm.^{-1}$ was considered sufficient evidence that the compound was an aminonitro derivative. The melting point eliminated the possibilities of it being either 9-amino-1-nitro-acridine or 9-amino-4-nitroacridine, but since no definite melting points were given in the literature for the 2- and 3-nitro analogues, it was not possible to differentiate by this method. However, the fact that our

material gave a purple coloration in alcoholic potassium hydroxide identified it definitely as being 9-amino-2-nitroacridine, since in this series only the 2-isomer gives such a colour reaction.

The trinitro derivative was identified by its melting point, reported by Hampton and Magrath (67), as being 9-amino-2,4,7-trinitroacridine. The infrared spectrum showed the NH_2 stretching vibrations at 3380 $cm.^{-1}$ and 3280 $cm.^{-1}$

It thus appears that while raising the temperature does not affect sensibly the yield of the mononitration, the same change in the nitration with a large excess of nitric acid results in a sharp decrease in the amount of 9-amino-2-nitroacridine produced with a simultaneous increase in the proportion of 9-amino-2,4,7-trinitroacridine.

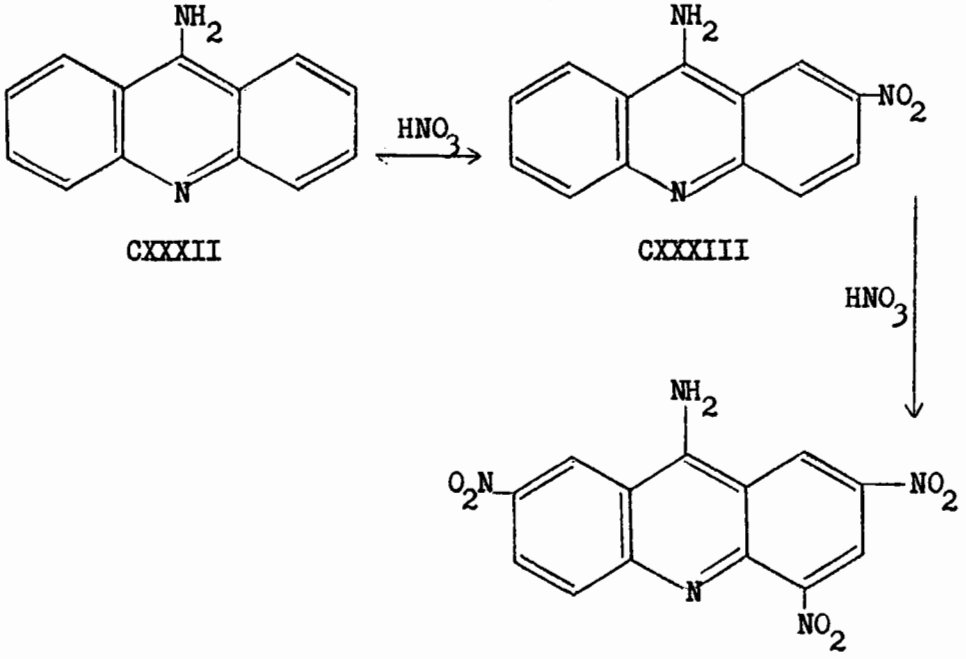
No nitramine was formed even with reaction temperatures as low as -15°. As in the case of 6-aminophenanthridine an explanation of this behaviour can be found by an examination of the spectroscopic data. Short (155) concluded from his study of the infrared absorption of 9-aminoacridine in chloroform solution that it existed predominantly in the amino form. Russian workers (156) by carrying out a similar study came to the opposite conclusion that it existed in the imino form but their arguments are ambiguous. Moreover the investigations of Irvin and Irvin (157) on the ultraviolet absorption of 9-aminoacridine and its derivatives in acidic solution supported the amino structure rather than the imino hypothesis. The latter view will be adopted here. The acridinium cation (CXXVII) is a resonance hybrid with structures (CXXVIII), (CXXIX), (CXXX) and (CXXXI) making important contributions:



CXXVII CXXVIII CXXIX

CXXXI CXXX

The formation of 9-amino-2-nitroacridine (CXXXIII), and 9-amino-2,4,7-trinitroacridine (CXXXIV) is thus explained.



CXXXII CXXXIII

CXXXIV

Furthermore since all the resonance structures carry a positive charge on the nitrogen belonging to the amino group it is readily understood that the nitronium ion will not be able to attack the amino group and that consequently no nitramine will be formed.

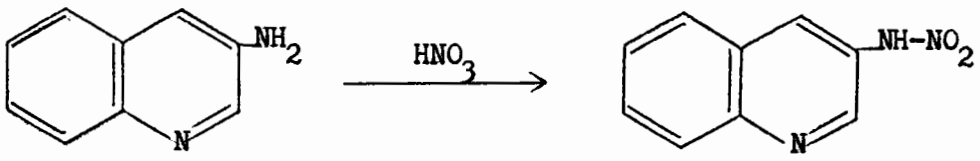
Nitration of 3-aminoquinoline

The 3-aminoquinoline used in this work was a pure sample purchased from Fisher Scientific Company.

Nitration of the material at -15° with one equivalent of 70% nitric acid gave a 65% yield of a mononitro compound melting at 141-142° (A). Heating it in concentrated sulphuric acid produced a new substance melting at 251-252° (B). A sodium salt could be prepared by dissolving it in a concentrated solution of sodium hydroxide. A room temperature reaction gave a 36.5% yield of a product identical with B and a 14% yield of A.

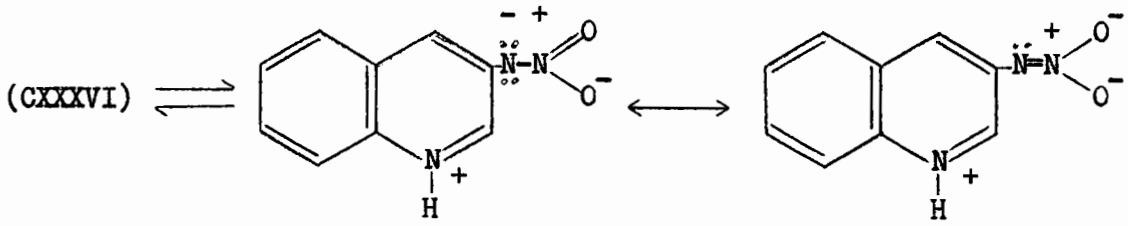
Reaction with an excess of nitric acid 70% at low temperature furnished a 51% yield of a substance exploding at 173° (C) which formed a sodium salt when dissolved in a hot concentrated solution of sodium hydroxide. At high temperature the yield of C dropped to 12.9% and a gum which could not be further processed was formed.

The transformation of A into B by heating in concentrated sulphuric acid and the fact that it produces a sodium salt, are ample proof that the material is in fact a nitramine. The first step of the reaction can thus be represented by the equation:



CXXXV CXXXVI

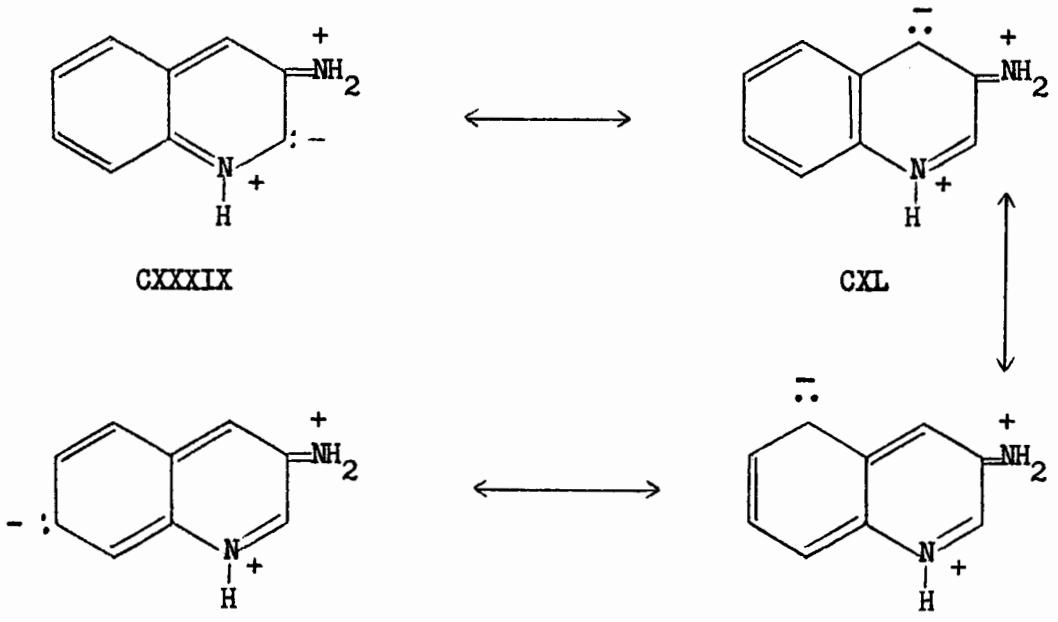
The infrared spectrum of this compound shows a wide band between 2900 cm.$^{-1}$ and 2300 cm.$^{-1}$, and there is no sign of any N-H band in the 3500 cm.$^{-1}$ - 3200 cm.$^{-1}$ region. This situation is exactly the one observed by Taurins (see Historical) for the corresponding pyridines and thiazoles. It leads to the conclusion that the substance is a resonance hybrid of the tautomer form of (CXXXVI). An examination of structures (CXXXVII) reveals that these formulae cannot be written without separation of charges and consequently the compound is a betaine.



CXXXVII CXXXVIII

In the light of these considerations it becomes apparent that the compound has to be renamed 3-nitrimino-(1H)quinolinium betaine.

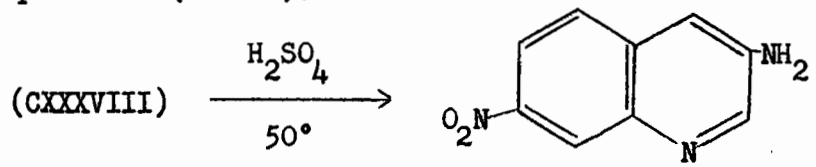
In order to decide on the position of the nitro group in material B let us consider the resonance formulae of the 3-aminoquinolinium ion. Four main structures take part in the formation of the hybrid:



CXXXIX CXL

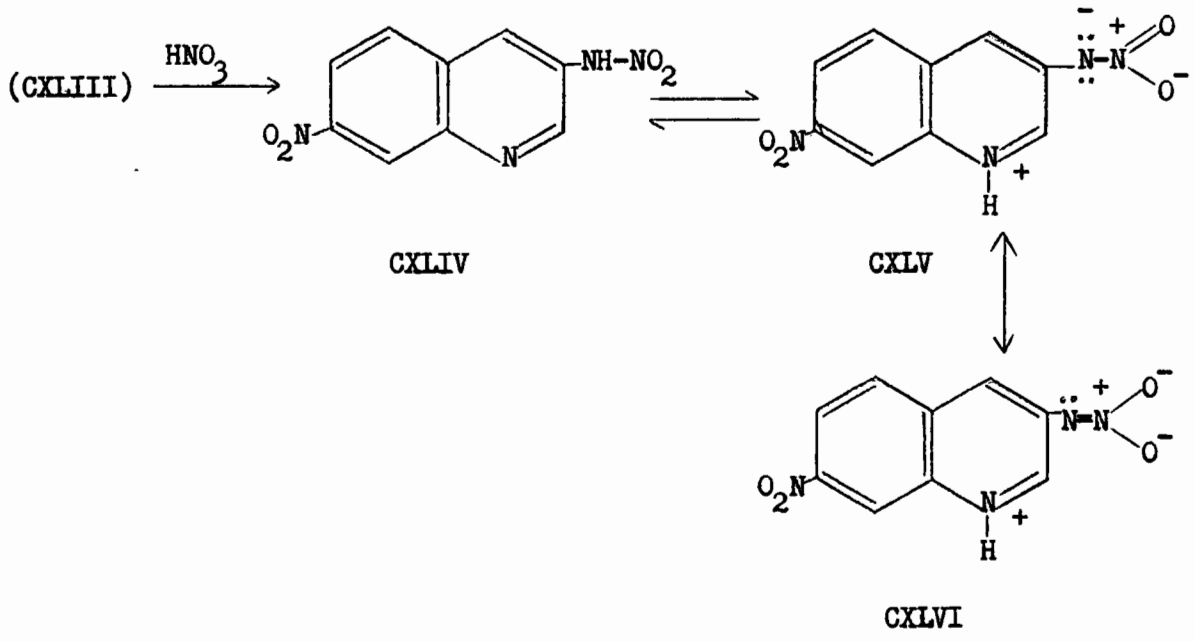
CXLII CXLI

The stability of (CXXXIX) will be least since a negative charge in α to the -Is effect group $\overset{+}{N}$-H is quite unlikely. The importance of (CXLI) must be small because the nitro group in B is not in the 5 position, a conclusion drawn from the comparison of its melting point with that of 3-amino-5-nitroquinoline given by Kaslow and Buchner (158). A choice can be made between (CXL) and (CXLII) by considering that the strong -Is effect of the $\overset{+}{N}$-H group will deactivate the pyridine ring of the molecule and by noticing that the deep yellow colour of B is better explained by an important contribution to the resonance hybrid of a quinoid structure of the type of (CXLII). This argument thus leads to the conclusion that the rearrangement of 3-nitrimino-(1H)quinolinium betaine (CXXXVIII) gives 3-amino-7-nitroquinoline (CXLIII).



(CXXXVIII) $\xrightarrow[50°]{H_2SO_4}$ CXLIII

C does not rearrange but it forms a sodium salt, a definite proof that the compound is a nitramine. It does not seem to be stable at higher temperatures in acidic solution since it either forms gums or carbonizes. Its infrared spectrum, very much like in the case of A, does not have any absorption in the N-H stretching region, but it shows a wide band between 3100 $cm.^{-1}$ and 2700 $cm.^{-1}$. The structure of the molecule must thus be considered as being that of a resonance hybrid of the tautomer form of (CXLIV).



CXLIV CXLV

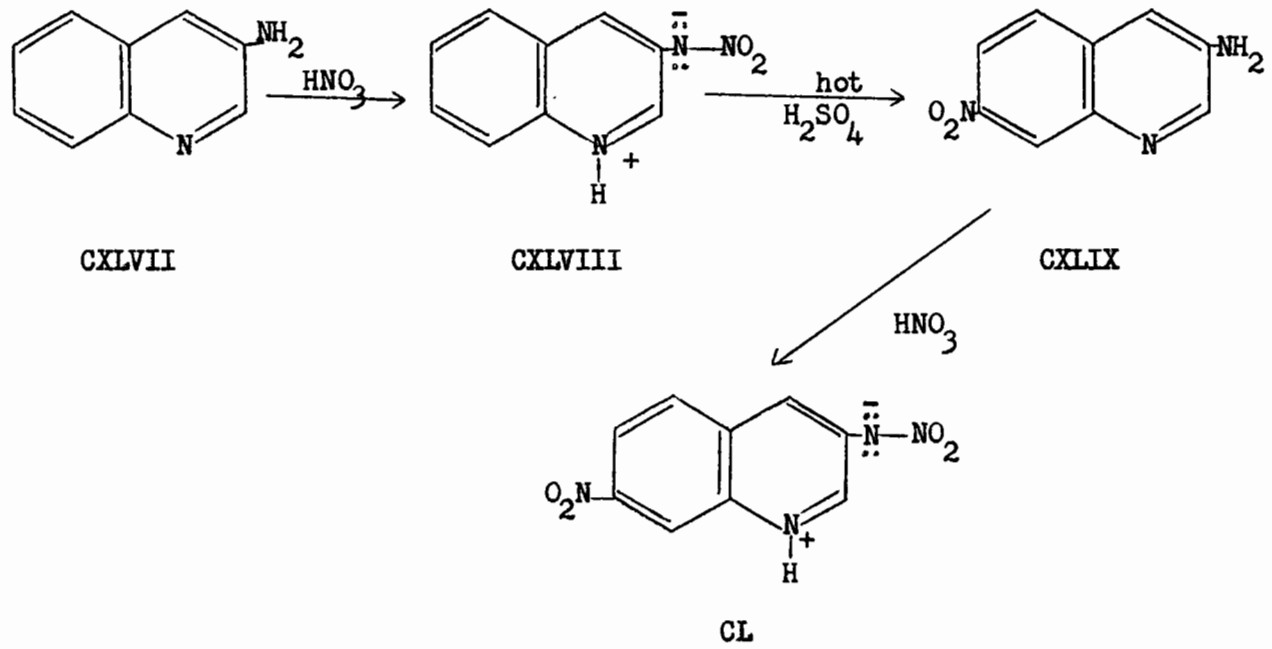
CXLVI

Once again the spectroscopic evidence leads to renaming the compound to 3-nitrimino-6-nitro-(1H)quinolinium betaine.

Two of the most important structures are shown in (CXLV) and (CXLVI) but it is evident that more can be written, e.g. Kekule structures and structures involving the nitro group located on the benzene part of the molecule. This strong resonance is responsible for both the stability

and the peculiar copper-like colour of the crystals.

The following series of reactions summarizes this study of the nitration of 3-aminoquinoline:



CXLVII CXLVIII CXLIX

CL

Infrared Spectroscopy

Experimental technique

All the spectra were recorded with a Perkin-Elmer Model 21 double beam spectrophotometer.

Solid phase studies were done by preparing a potassium bromide pellet in the following manner. The substance was placed with potassium bromide in a 1 ml. glass-stoppered tube with five steel balls and vibrated

for three minutes in a magnetic vibrator. The powder was then submitted to a pressure of 20.000 lb./sq.in. for two minutes.

Solutions were prepared by dissolving a weighed amount of material in 1 ml. of either carbon tetrachloride or carbon disulphide and subsequently they were introduced into a 1 mm. cell with sodium chloride windows.

Phenanthrene, phenanthridine and 6-methylphenanthridine (TABLE XII)

The spectra of these three substances were obtained in carbon disulphide solution.

The aromatic CH stretching absorption is found in the range 3040-3080 $cm.^{-1}$ Phenanthrene shows a definite shoulder at 2950 $cm.^{-1}$ and the two other compounds have a sharp band at approximately the same frequency.

The CH stretching absorption of the methyl group in 6-methylphenanthridine appears at 2920 and 2850 $cm.^{-1}$, the first peak being approximately twice as strong as the second.

About a dozen absorption maxima are found in the combination and overtone region (2000-1650 $cm.^{-1}$). Some of these bands are accounted for by using the method suggested by Whiffen (159) consisting of the addition two by two of all peaks observed in the range 1000-700 $cm.^{-1}$ In phenanthrene (Table V) six bands are shown to be the result of such combinations, one of them also corresponding to an overtone. In phenanthridine (Table VI) thirteen out of the fourteen bands are explained by a similar process

TABLE V

Phenanthrene

a	b	a + b or ab Calc.	a + b or ab Found
1002	946	1948	1950
2 x 975	(overtone)	1950	1950
975	857	1932	1830
946	857	1803	1800
975	805	1780	1776
946	805	1751	1748
857	805	1662	1668

TABLE VI

Phenanthridine

a	b	a + b or ab Calc.	a + b or ab Found
1000	951	1951	1955
1000	924	1924	1920
2 x 951	(overtone)	1902	1900
951	924	1875	1876
2 x 924	(overtone)	1842	1846
1000	824	1824	1823
924	881	1805	1802
951	824	1775	1775
1000	759	1759	1760
2 x 881	(overtone)	1762	1760
2 x 864	(overtone)	1728	1730
951	785	1736	1730
1000	711	1711	1715
881	824	1705	1705
951	740	1690	1687
864	824	1688	1687
924	759	1683	1687

and four bands are accounted for in the 6-methyl derivative (Table VII).

TABLE VII

6-Methylphenanthridine

a	b	a + b or ab Calc.	a + b or ab Found
1002	948	1950	1955
1002	750	1752	1756
1002	715	1717	1720
948	776	1724	1720
948	750	1698	1700

In the range 1200-700 cm.$^{-1}$ the three compounds have nine bands of medium to strong intensity in common. Their position varies from 10 to 20 cm.$^{-1}$ around the following frequencies 1200, 1160, 1140, 1095, 1040, 1000, 950, 855, 710 cm.$^{-1}$, but the general shape is usually retained and thus makes identification possible. It may be pointed out that Bellamy also noted bands around 1200, 1100 and 1140 cm.$^{-1}$ in pyridine derivatives.

Still in the same region absorptions are found at 750 cm.$^{-1}$ for phenanthrene, 730 cm.$^{-1}$ for phenanthridine and 760 cm.$^{-1}$ for its methyl derivative. All bands are very strong and wide. By analogy with the situation found in benzenoid molecules, these peaks must be attributed to the four neighbouring hydrogens on each of the benzene rings of the phenanthridine system. Indeed each of these rings can be considered as an ortho disubstituted benzene and hence the characteristic absorption

here is very strong because there are twice four such hydrogens.

Phenanthrene shows a strong wide band at 810 cm.$^{-1}$ whereas phenanthridine has a rather weak and sharp peak at 825 cm.$^{-1}$ and its methyl analogue does not show any absorption in this region. This behaviour suggests that the first band is due to the two neighbouring hydrogens of the middle ring of phenanthrene acting as a 1,2,3, 4 tetrasubstituted benzene. The 825 cm.$^{-1}$ peak of phenanthridine can then be related to the one hydrogen on carbon 6 and evidently the absence of hydrogen in this position in the methyl derivative results in the absence of absorption.

Note on the intensity of the combination bands of phenanthridine and 6-methylphenanthridine

A study of range 2000-1650 cm.$^{-1}$ was done in carbon tetrachloride solution. Concentrations of 10 to 100 mg. per ml. were considered for 6-methylphenanthridine. In the case of phenanthridine the resolution of the bands was not sharp enough at concentrations above 50 mg. per ml. to permit quantitative determinations.

The peak appearing at 1850 cm.$^{-1}$ was selected for the study of phenanthridine and in the 6-methyl derivative the absorption maximum at 1958 cm.$^{-1}$ was chosen. The intensity of the latter is expressed as the difference between the transmittance at 1985 cm.$^{-1}$ and the transmittance at 1958 cm^{-1}. Similarly the intensity of absorption for phenanthridine is the difference between the values of the transmittance at 1865 cm.$^{-1}$ and

at 1850 cm.$^{-1}$

The results are given in Tables VIII and IX. Both substances show a linear relationship between concentration and intensity up to 50 mg. per ml. In other words Beer's law is observed and consequently these two bands can be used for a quantitative analysis.

Phenanthridine, phenanthridine N-oxide, 6-methylphenanthridine and nitro derivatives (TABLE XIII)

All these spectra were obtained in the solid state.

Between 1600 and 1400 cm.$^{-1}$, the region of C=C and C=N vibrations, phenanthridine, its N-oxide and its 6-methyl analogue have seven peaks in common located within ± 10 cm.$^{-1}$ of 1615, 1590, 1580, 1525, 1490, 1465, 1445 cm.$^{-1}$

Comparing the spectra of phenanthridine and its methyl derivative in the solid phase to those obtained in solution it is found that in the case of the parent compound a shift of 15 to 20 cm.$^{-1}$ occurs toward the lower frequencies; for the other substance the shift is only of the order of 5 cm.$^{-1}$

The symmetric CH deformation frequency of CH_3 in the methyl derivative appears at 1373 cm.$^{-1}$ The corresponding asymmetric vibration could be at 1446 cm.$^{-1}$ but this assignment is uncertain since phenanthridine has a band at 1452 cm.$^{-1}$

TABLE VIII

Phenanthridine in CCl_4 - Band at 1850 $cm.^{-1}$

mg./ml.	mole/l.	Intensity of absorption
10	0.056	5
30	0.168	14.5
50	0.288	21.5

TABLE IX

6-Methylphenanthridine in CCl_4 - Band at 1958 $cm.^{-1}$

mg./ml.	mole/l.	Intensity of absorption
10	0.052	9
30	0.156	21
50	0.259	31
70	0.365	37
100	0.517	47

The N-oxide absorption in phenanthridine N-oxide must be placed at 1318 cm.$^{-1}$ because all other strong bands in this region are common to the other molecules.

The symmetric NO_2 vibrations of the two nitromethylphenanthridines occur both at 1525 cm.$^{-1}$ but the asymmetric frequency appears at 1374 cm.$^{-1}$ for 6-methyl-4-nitrophenanthridine and drops to 1319 cm.$^{-1}$ in the dinitro compound.

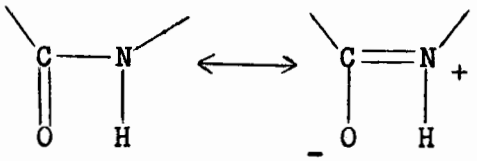
In the region below 850 cm.$^{-1}$, the weak band at 800 cm.$^{-1}$ in phenanthridine, assigned to the isolated hydrogen of carbon 6 appears at 799 cm.$^{-1}$ in the N-oxide. Three strong bands between 775 and 725 cm.$^{-1}$ in phenanthridine and its N-oxide, reduced to two in the methyl derivative probably correspond to four adjacent hydrogens. In the nitro compounds the situation being more complex it is difficult to present an interpretation.

Phenanthridinone and its nitro derivatives (TABLE XIV)

The N-H stretching vibration is found as a weak and broad band at 3500-3450 cm.$^{-1}$ except in 9-nitrophenanthridinone where it is sharp. Another peak appears at 3210-3170 cm.$^{-1}$ indicating a hydrogen bonding between the amide functions.

The aromatic CH stretching occurs at 3090-3040 cm.$^{-1}$.

Absorptions in the range 3000-2730 cm.$^{-1}$ suggest that in all these substances the amide function resonates between structures (CLI) and (CLII).



CLI CLII

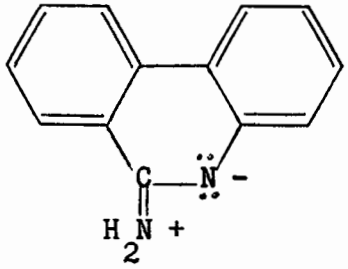
The carbonyl absorption is fairly constant in the range 1685-1665 cm.$^{-1}$ In three of the compounds another strong band exists at 1615-1610 cm.$^{-1}$ There seems to be no peak corresponding to the amide II band occurring usually around 1550 cm.$^{-1}$

The asymmetric NO_2 vibration appears in the range 1530-1525 cm.$^{-1}$ and the symmetric one is present at 1350-1340 cm.$^{-1}$

Below 800 cm.$^{-1}$ a large number of bands are found. We shall only note that the strongest absorption appears at 754 cm.$^{-1}$, corresponding to a system with four adjacent hydrogens.

6-Aminophenanthridine and its nitro derivatives (TABLE XV)

The N-H stretching vibrations are located in the 6-amino-nitrophenanthridines between 3500 and 3300 cm.$^{-1}$ indicating the absence of hydrogen bonding. In 6-aminophenanthridine there is a strong band at 3240 cm.$^{-1}$ with a shoulder at 3350 cm.$^{-1}$, and absorptions are also observed at 2940 and 2760 cm.$^{-1}$ These data suggest that 6-aminophenanthridine is a resonance hybrid, one of the important contributing structures being (CLIV).



CLIV

The N-H deformation mode shows up as a strong band in the range 1685-1665 cm.$^{-1}$ The C-N vibration is a strong band located at 1315-1305 cm.$^{-1}$ in the nitro derivatives and of medium size in the unsubstituted amino compound. The NO_2 bands are found around 1500 cm.$^{-1}$ and 1325 cm.$^{-1}$

In the region below 800 cm.$^{-1}$ the strongest band in 6-amino-phenanthridine is the one at 750 cm.$^{-1}$ already mentioned for analogous derivatives. In the mononitro compound it is much weaker and in the dinitro it seems to have disappeared, indicating that both benzene rings are now substituted.

Anthracene and Acridine (TABLE XVI)

The spectra were measured in carbon disulphide solution.

The CH aromatic appears at 3055 cm.$^{-1}$ in anthracene and at 3050 cm.$^{-1}$ in acridine. The latter spectrum also presents shoulders at 2930 cm.$^{-1}$ and 2860 cm.$^{-1}$

The combination and overtone region displays a rather complicated pattern. By applying the method described by Whiffen (159) three bands in anthracene are accounted for, and eleven are explained for acridine (see Tables X and XI).

In the region from 1300 cm.$^{-1}$ down it is quite striking that anthracene has fewer bands than acridine. There are however seven common peaks within 5 cm.$^{-1}$ located at 1315, 1270, 1165, 1145, 1000, 955 and 725 cm.$^{-1}$ The last absorption seems to correspond to the one found at 750 cm.$^{-1}$

TABLE X

Anthracene

a	b	a + b or ab Calc.	a + b or ab Found
1001	954	1955	1942
2 x 954		1908	1902
1001	751	1752	1757
2 x 874		1748	1757
954	751	1705	1700

TABLE XI

Acridine

a	b	a + b or ab Calc.	a + b or ab Found
1000	955	1955	1950
2 x 976		1946	1950
973	955	1928	1927
1000	902	1902	1906
2 x 955		1910	1906
955	920	1875	1875
902	973	1875	1875
955	902	1857	1855
920	902	1822	1820
973	845	1818	1820
955	845	1800	1802
2 x 902		1804	1802
973	783	1756	1753
955	783	1738	1735
920	814	1734	1735
973	902	1716	1710
920	783	1703	1710
2 x 845		1690	1685
902	783	1685	1685

in phenanthridine derivatives.

9-Aminoacridine and its nitro derivatives (TABLE XVII)

9-Aminoacridine has NH stretching bands at 3350 and 3200 cm.$^{-1}$, 9-amino-2-nitroacridine shows absorptions at 3470 and 3380 cm.$^{-1}$, and 9-amino-2,4,7 trinitroacridine at 3380 and 3270 cm.$^{-1}$

The aromatic CH vibration is not discernible in 9-aminoacridine but shows up at 3080-3060 cm.$^{-1}$ in the two other compounds.

The NH deformation is stable at 1665-1660 cm.$^{-1}$

The asymmetric NO_2 is found as a rather weak band at about 1540 cm.$^{-1}$; the symmetric NO_2 appears as a very strong band in both materials at 1330 cm.$^{-1}$

A band of medium intensity at 1260-1250 cm.$^{-1}$ corresponds to a C-N vibration.

In the 750 cm.$^{-1}$ region two strong bands appear in 9-aminoacridine, one weak band remains in 9-amino-2-nitroacridine and two strong peaks are observed about 25 cm.$^{-1}$ below the ones of 9-aminoacridine in 9-amino-2,4,7-trinitroacridine.

3-Aminoquinoline and its nitrimino derivatives (TABLE XVIII)

Whereas 3-aminoquinoline shows three absorptions in the NH stretching region at 3460, 3320 and 3180 cm.$^{-1}$ the two other materials show none, but a wide band is observed in the mononitro compound between 3000

and 2300 cm.$^{-1}$, and in the dinitro substance between 3100 and 2700 cm.$^{-1}$ These two wide bands indicate a nitrimino structure as pointed out in the discussion of the nitration of 3-aminoquinoline.

In the N-H deformation region two absorptions occur in 3-aminoquinoline one at 1623 cm.$^{-1}$ and the other at 1612 cm.$^{-1}$ The mononitro derivative shows a peak at 1610 cm.$^{-1}$ and the dinitro at 1604 cm.$^{-1}$ Consequently the band at 1623 cm.$^{-1}$ is probably related to the N-H absorption whereas the peak at 1612 cm.$^{-1}$ and 1610 cm.$^{-1}$ and 1604 in the derivatives corresponds to a C=N vibration.

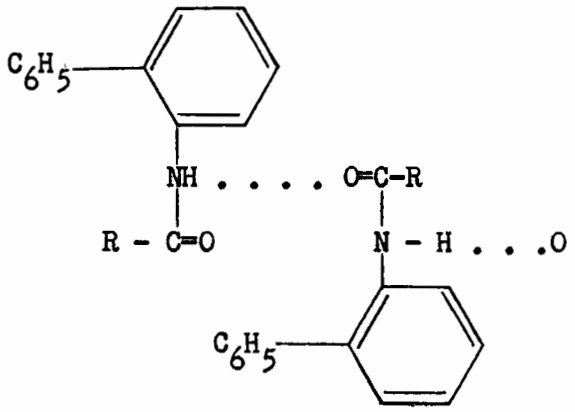
3-Nitrimino-(1H)quinolinium betaine has NO_2 absorptions at 1475 cm.$^{-1}$ and 1320 cm.$^{-1}$ In the dinitro substance both are shifted to higher frequencies, 1520 cm.$^{-1}$ and 1345 cm.$^{-1}$

The two strongest peaks below 850 cm.$^{-1}$ are found at 774 cm.$^{-1}$ and 755 cm.$^{-1}$ In 3-nitrimino-(1H)quinolinium betaine these two absorptions are located at 770 cm.$^{-1}$ and 751 cm.$^{-1}$ Apart from two weak bands on either side, at 785 and 735 cm.$^{-1}$ this region of the spectrum has the same general appearance. Since this range of absorption is sensitive to ring substitution the similarity between the two spectra can be considered as additional evidence that the structure is indeed that of a nitramine. 3-Nitrimino-7-nitroquinoline of course presents an entirely different pattern with peaks at 827, 799, 763 and 745 cm.$^{-1}$

2-Amidobiphenyls (TABLE XIX)

The N-H stretching is found at 3270-3240 cm.$^{-1}$ in 2-formamido-2-

acetamido and 2-propionamidobiphenyls. It is an indication that the molecules are hydrogen bonded in a trans fashion, as shown in (CLV)



CLV

where R = H, CH_3, CH_3-CH_2

The diacetyl compound has no absorption in this region.

No peak corresponding to an aromatic CH stretching is observed in the formamido derivative; the others all absorb at 3130 $cm.^{-1}$

The CO absorption seems around 1700 $cm.^{-1}$ except in the diacetyl compound where one strong band appears at 1653 $cm.^{-1}$ In 2-acetamidobiphenyl and in the diacetyl derivative the CO absorption is doubled.

An amide II band is found between 1530-1515 except of course in the diacetyl molecule.

2-(N-diacetylamino)-biphenyl has a very strong band at 1245$cm.^{-1}$ The same absorption but weaker exists in the monoacetyl compound and can be attributed to C-C vibrations.

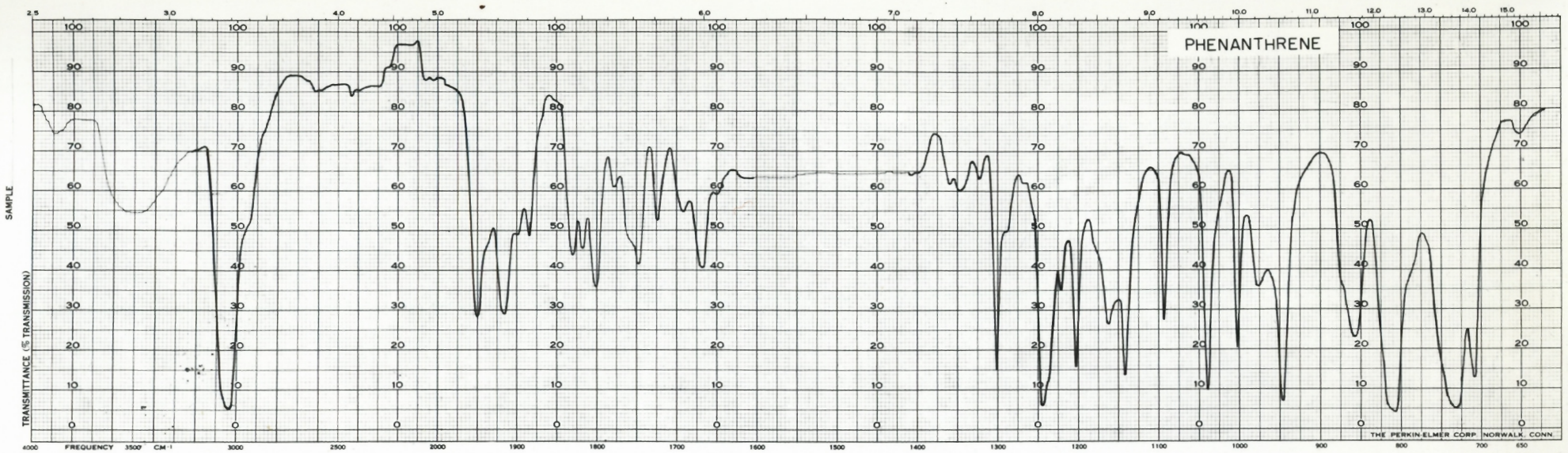
In the region below 800 cm.$^{-1}$ two strong bands are found for 2-formamidobiphenyl. The number of peaks increases with the size of the substituent.

FIG. 1

Infrared spectra of

Phenanthrene in carbon disulphide (0.1 gm./ml. of solution)

Phenanthridine in carbon disulphide (0.05 gm/ml. of solution)


PHENANTHRENE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

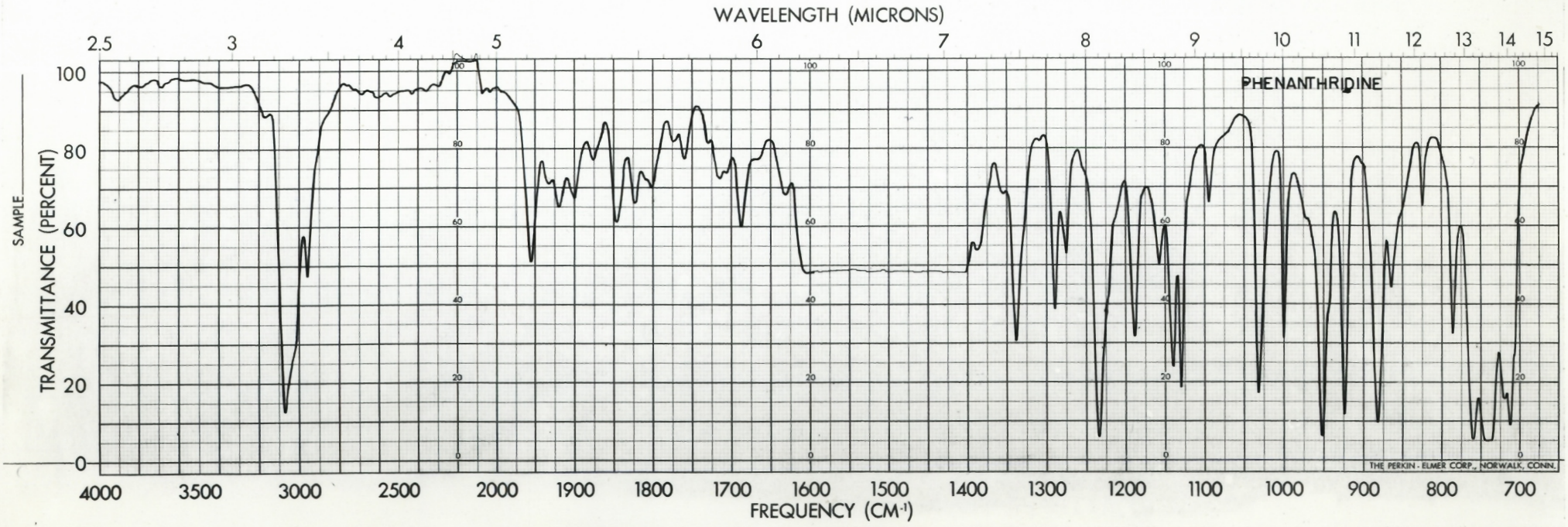
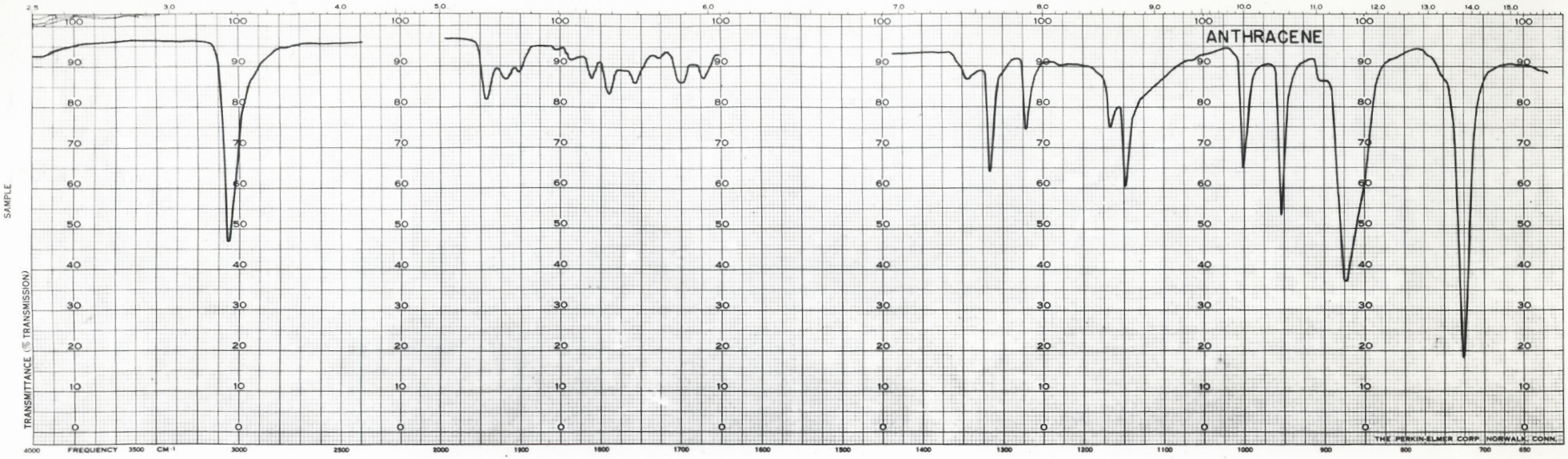

WAVELENGTH (MICRONS)
PHENANTHRIDINE
SAMPLE
TRANSMITTANCE (PERCENT)
FREQUENCY (CM-1)
THE PERKIN-ELMER CORP., NORWALK, CONN.

FIG. 2

Infrared spectra of

Anthracene in carbon disulphide (0.01 gm./ml. of solution)

Acridine in carbon disulphide (0.1 gm./ml. of solution)


ANTHRACENE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

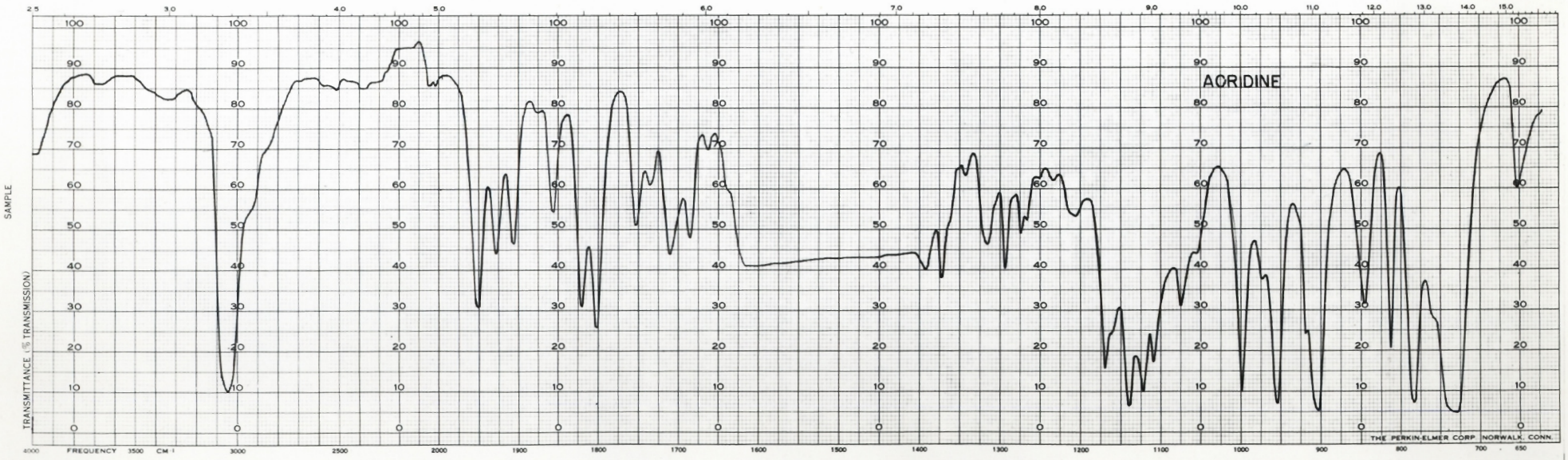
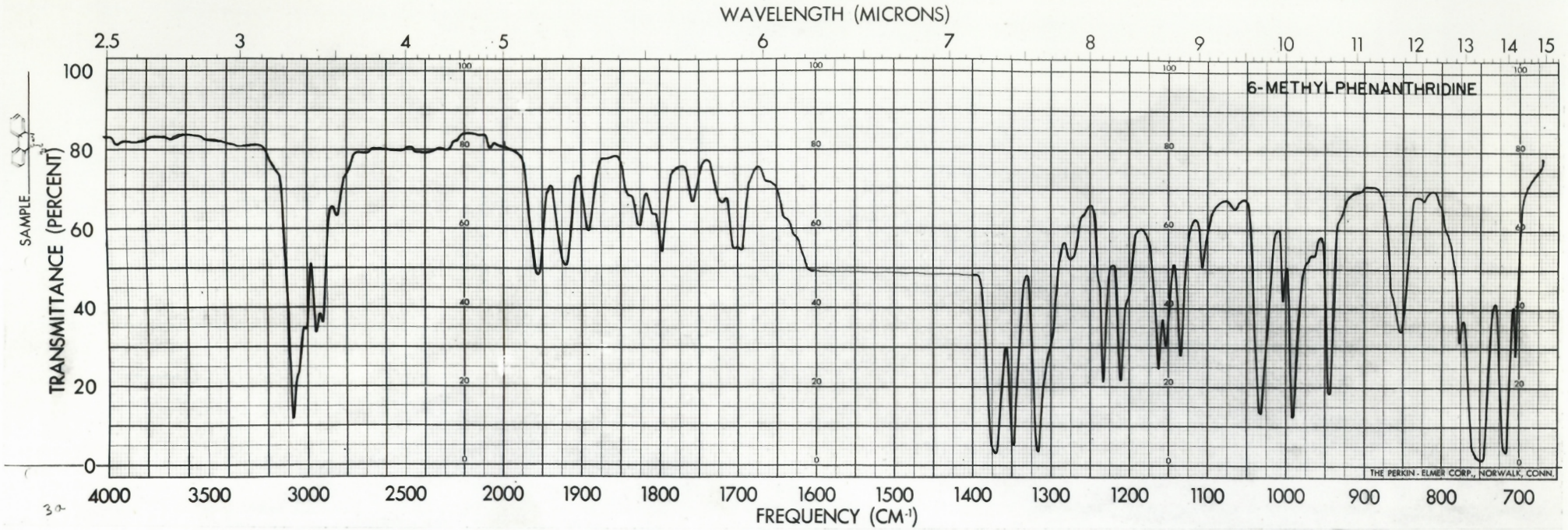

ACRIDINE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

FIG. 3

Infrared spectra of

6-Methylphenanthridine in carbon disulphide (0.05 gm./ml. of solution)

6-Aminophenanthridine in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
100 80 60 40 20 0
TRANSMITTANCE (PERCENT)
SAMPLE
6-METHYLPHENANTHRIDINE
4000 3500 3000 2500 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)
THE PERKIN-ELMER CORP., NORWALK, CONN.

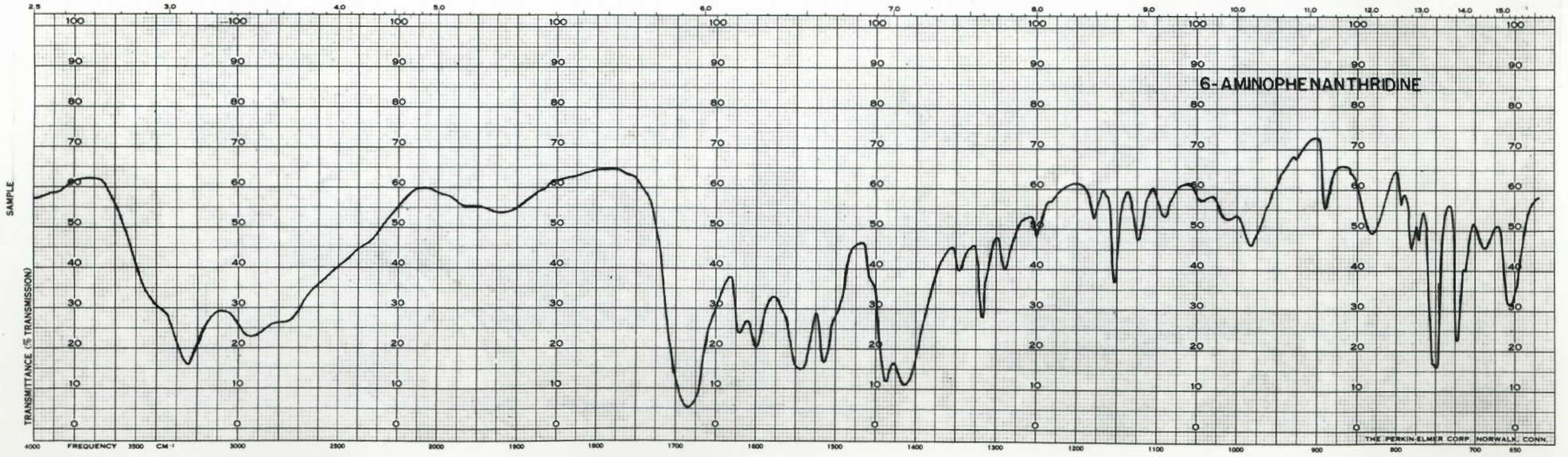
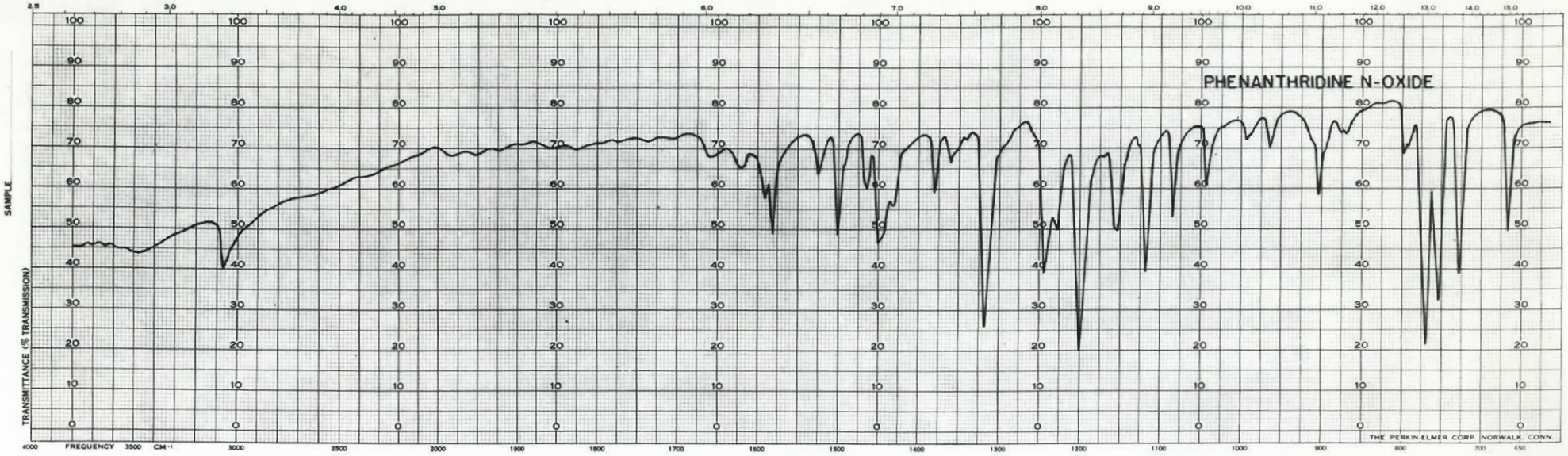

6-AMINOPHENANTHRIDINE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

FIG. 4

Infrared spectra of

Phenanthridine N-oxide in potassium bromide pellet

Phenanthridinone in potassium bromide pellet.


PHENANTHRIDINE N-OXIDE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

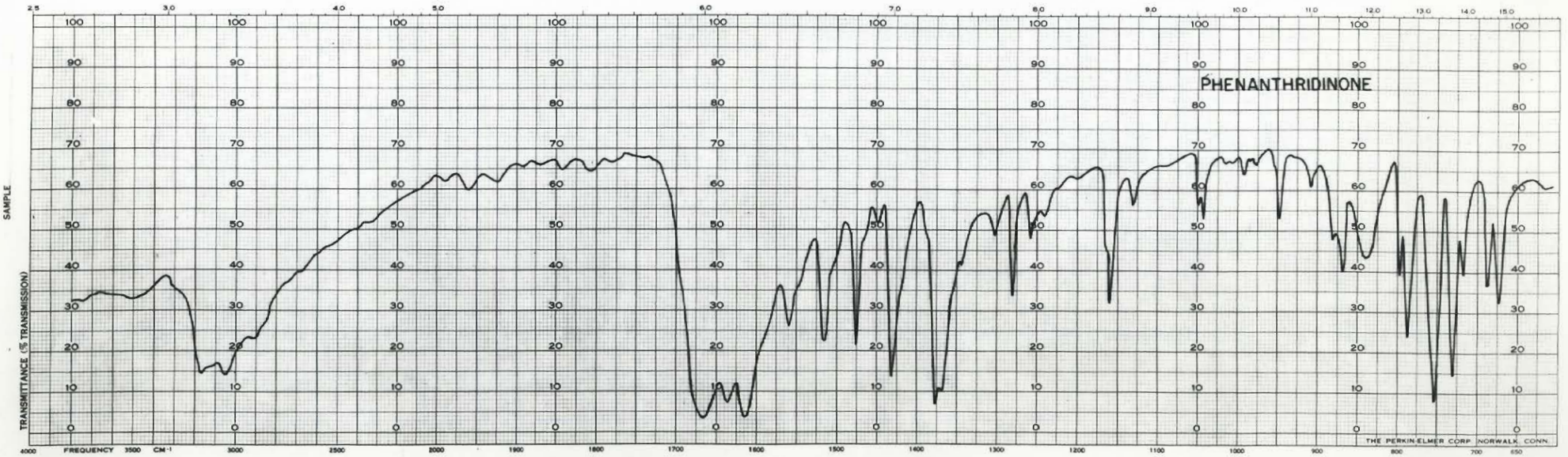
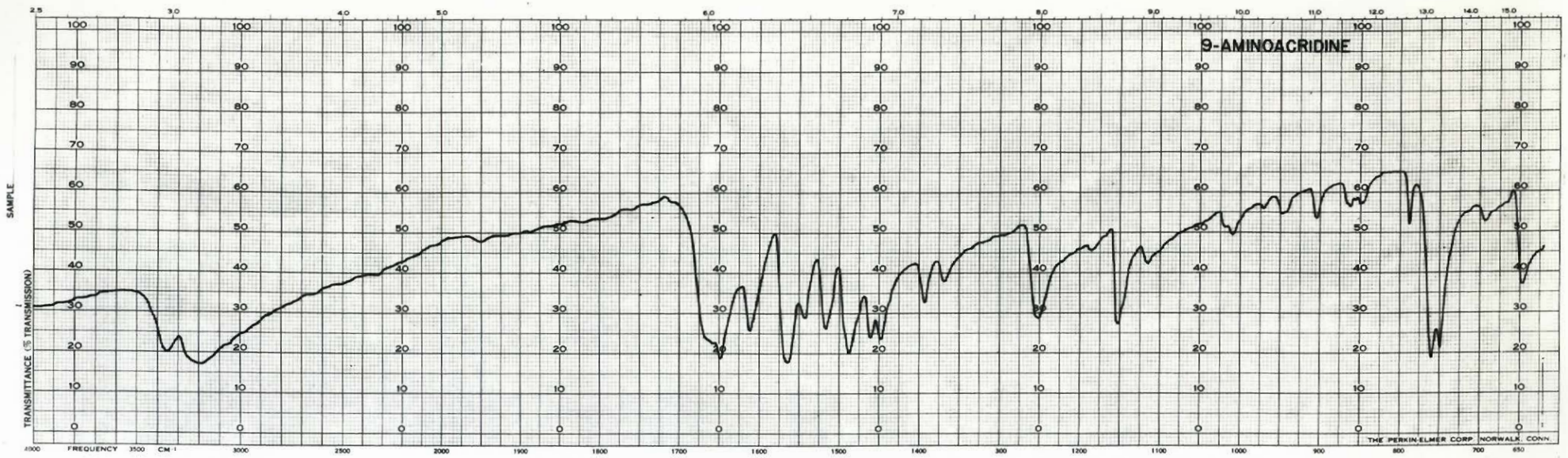

PHENANTHRIDINONE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

FIG. 5

Infrared spectra of

2-Nitrophenanthridinone in potassium bromide pellet

9-Aminoacridine in potassium bromide pellet.


9-AMINOACRIDINE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

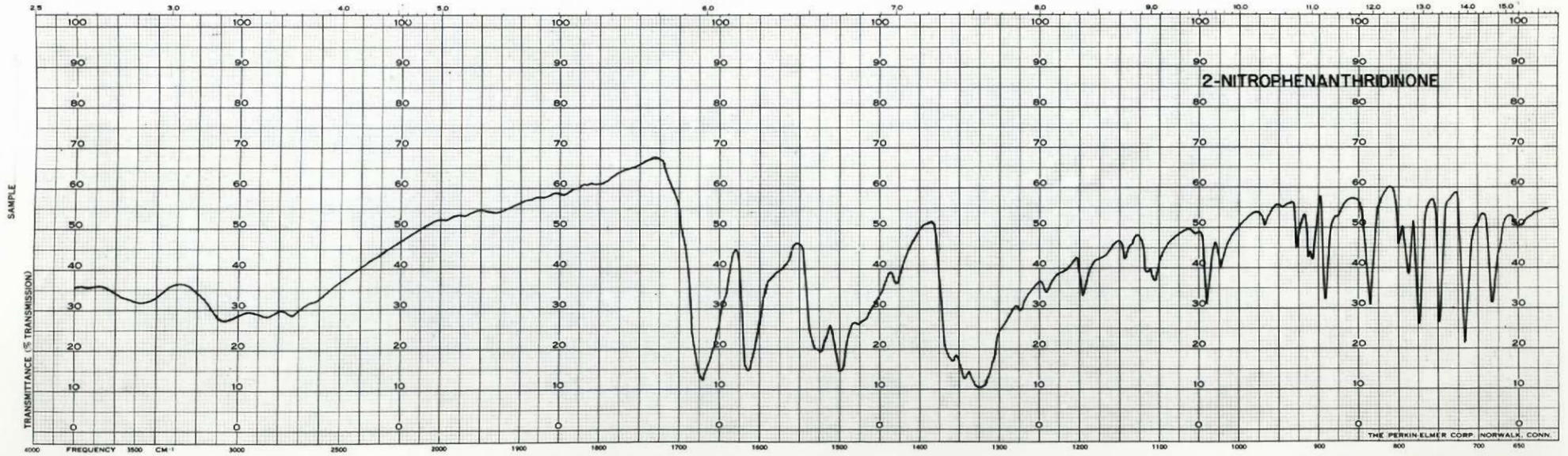

2-NITROPHENANTHRIDINONE
SAMPLE
TRANSMITTANCE (% TRANSMISSION)
FREQUENCY 3500 CM-1
THE PERKIN-ELMER CORP. NORWALK, CONN.

TABLE XII

Phenanthrene[1]	Phenanthridine[2]	6-Methylphenanthridine[3]
3040 vS	3070 s	3070 vS
2950 sh.	2960 m	3010 sh.
		2960 m
		2920 m
		2850 m
1950 S	1955 m	1955 m
1915 S	1932 w	1920 m
1885 m	1920 w	1890 m
1830 m	1900 w	1825 w
1817 m	1876 w	1797 m
1800 m	1846 m	1756 w
1776 w	1823 w	1720 w
1748 m	1802 w	1700 m
1725 m	1775 w	
1692 m	1760 w	
1668 m	1730 w	
	1715 w	
	1705 vw	
	1687 m	
1300 S	1338 m	1370 S
1245 S	1290 m	1347 S
1220 w	1275 m	1315 S
1202 m	1234 s	1275 w
		1232 m
		1210 m

(continued)

TABLE XII (cont'd.)

Phenanthrene[1]	Phenanthridine[2]	6-Methylphenanthridine[3]
1161 m	1188 m	1161 m
1141 S	1156 w	1152 m
	1139 m	1133 m
	1156 w	1105 w
	1140 s	
	1130 s	
1093 m	1094 w	1031 m
1040 S	1030 s	1002 w
1002 m	1000 m	990 m
975 w	952 s	
946 S	924 s	
857 m	881 s	852 m
805 vS	864 w	
	824 w	
730 vS	785 m	776 m
708 S	760 s	750 vS
	740 s	715 vS
	711 s	704 m

1 in carbon sulphide (0.1 g./ml.)

2 in carbon sulphide (0.05 g./ml.)

3 in carbon sulphide (0.05 g./ml.)

TABLE XIII

Phenanthridine	Phenanthridine N-oxide	6-Methylphenanthridine	6-Methyl-4-nitrophenanthridine	6-Methyldinitrophenanthridine
3060 w	3070 w	3060 w	3080-2820 w	
1624 m	1660 w	1611 m	1605 w	1615 w
1595 m	1620 w	1584 m	1586 m	1580 m
1580 m	1590 w		1566 w	1520 s
1532 m	1580 m		1523 s	1510 s
	1525 w			
	1500 m			
1495 m	1465 w	1485 m	1485 w	1440 w
1463 m	1450 m	1465 w	1453 w	1405 w
1452 m	1431 w	1445 w		
1407 m				
1350 w	1380 w	1373 m	1375 s	1368 m
1296 w	1360 w	1320 w	1350 w	1344 s
1250 m	1318 s	1240 w	1331 w	1310 w
1235 w	1244 s	1213 w	1305 w	1288 w
1200 m	1227 m		1276 w	1262 w
	1200 s			1220 w
1152 w	1155 m	1155 w	1198 w	1192 w
1141 m	1119 s	1035 w	1176 w	1100 w
1040 m	1085 m	995 w	1080 w	985 w
976 m	1044 m	945 w	1025 w	902 w
	994 w		1000 w	
	965 w		956 w	
	904 m			
897 m	875 w	855 w	860 w	883 w
875 w			831 s	855 w
835 w			822 s	839 w
800 w				819 m
780 m	799 w	749 s	777 w	789 w
755 s	770 s	719 s	764 s	780 w
726 s	755 s	705 w	749 m	765 w
716 w	728 s	650 w	744 s	745 w
	666 m		655 w	734 w
				716 m
				650 w

All compounds in solid state.

TABLE XIV

Phenanthridinone	2-Nitrophenanthridinone	4-Nitrophenanthridinone	7- or 9-Nitrophenanthridinone	Dinitrophenanthridinone
3170 m	3060 w	3200 w	3460 m	3220 m
3050 m	2860 w	3140 w	3080 m	3090 w
2910 w	2740 w	2870 w	2900 m	2940 w
1990 w				
1960 w				
1925 w				
1890 w				
1870 w				
1843 w				
1805 w				
1780 w				
1665 s	1670 s	1679 s	1685 s	1690 s
1635 s	1615 s	1610 m	1614 s	1625 w
1615 s	1525 s	1530 s	1522 s	1611 m
1560 m	1500 s			1532 s
1515 m				
1476 m	1428 w	1440 w	1495 s	1493 w
1431 s	1358 s	1350 s	1460 w	1476 w
1376 s	1344 s		1425 w	1450 w
1369 s	1325 s		1345 s	1393 w
1303 w				1350 s

(continued)

TABLE XIV (cont'd.)

Phenanthridinone	2-Nitrophenanthridinone	4-Nitrophenanthridinone	7- or 9-Nitrophenanthridinone	Dinitrophenanthridinone
1280 m	1273 w	1245 w	1258 w	1248 m
1258 w	1241 w	1170 w	1230 w	1156 m
1240 w	1195 w	1155 w	1150 w	
1110 m	1143 w	1100 w	1130 w	
1130 w	1115 w	1005 w	1105 w	
1050 m	1105 w			
1042 m	1040 m			
	1023 w			
992 w	927 w	895 w	900 w	960 w
948 m	913 w	848 w	845 m	900 w
908 w	907 w	832 w		850 w
880 m	892 m	814 w		830 w
869 m	835 m			
840 m	800 w			
798 m	787 w	795 w	795 m	795 w
787 s	774 m	774 w	745 w	774 m
754 s	749 m	739 w	718 w	740 m
730 s	717 m	726 m		730 w
717 m	683 m	675 w		705 w
689 m		649 w		650 w
674 m				

All compounds in solid state.

TABLE XV

6-Amino-phenanthridine	6-Amino-7- or 9-nitro-phenanthridine	6-Amino-dinitrophe-nanthridine
3350 sh.	3410 m	3480 m
3240 s	3300 sh.	3350 w
2940 w	3060 m	3110 m
2760 w		
1685 s	1665 s	1669 s
1620 m	1605 s	1607 s
1600 m	1588 s	1593 w
1545 m	1517 s	1572 s
1515 m		1519 s
		1505 s
1437 s	1498 s	1488 s
1413 s	1481 s	1430 w
1345 w	1465 w	1410 w
1317 m	1425 m	1325 s
	1345 s	1307 s
	1333 s	
	1322 s	
	1308 s	
1290 w	1226 m	1227 w
1250 w	1147 w	1200 w
1179 w	1124 w	1126 w
1153 m	1102 m	1103 m
1124 w		
1090 w		
1045 w		
1013 w		
983 m	910 w	895 w
890 m	895 w	840 m
830 m	839 m	813 m
795 w	791 m	792 m
780 w	745 w	756 w
771 w	714 w	743 w
750 s		711 m
723 s		
687 w		
655 m		

All compounds in solid state.

TABLE XVI

Anthracene[1]	Acridine[2]
3050 S	3040 vS
	2950 sh.
1943 w	1950 S
1918 w	1927 m
1902 vw	1906 m
1855 vw	1955 m
1835 vw	1820 S
1810 w	1802 S
1790 w	1753 m
1757 w	1735 w
1727 vw	1710 m
1700 w	1685 m
1670 w	
	1373 m
1344 w	1343 vw
1316 m	1315 m
1220 m	1294 m
	1275 w
	1265 w
	1205 w
1166 w	1170 s
1148 m	1140 s
1001 m	1123 s
	1110 s
	1075 w
	1000 s
954 m	973 w
900 w	955 s
874 s	920 w
	902 s
	845 m
	814 s
751 vs	783 s
	735 s
	652 m

1 in carbon sulphide (0.01 g./ml.)

2 in carbon sulphide (0.1 g./ml.)

TABLE XVII

9-Amino-acridine	9-Amino-2-nitroacridine	9-Amino-2,4,7-trinitroacridine
3350 m	3470 w	3440 sh.
3200 m	3380 sh.	3380 w
3050 vw	3060 w	3280 w
		3180 w
1655 sh.	1660 m	1665 m
1649 s	1618 s	1615 m
1612 m	1582 m	1580 m
1565 s	1535 m	1537 m
1542 m		1500 m
1516 m		
1487 m	1493 s	1432 w
1460 m	1330 s	1398 w
1448 m		1330 s
1393 m		
1369 w		
1250 m	1260 m	1248 m
1157 m	1215 w	1202 w
1115 w	1145 w	1130 w
1010 w	1095 w	1095 w
		1032 w
949 w	900 w	937 w
905 w	840 m	900 w
861 w	827 w	845 w
850 w		823 m
789 w	744 m	797 w
760 s		740 m
750 s		726 m
745 w		
648 m		

All compounds in solid state.

TABLE XVIII

3-Amino-quinoline	3-Nitrimino-(1H)-quinolinium betaine	7-Nitro-3-Nitrimino-(1H)quinolinium betaine
3460 w	3080 w	3080-2700 w
3320 w	3000-2300 w	
3180 w		
1623 s	1610 m	1603 s
1610 s	1587 s	1520 s
1495 m	1475 m	1469 w
1470 w	1450 w	1440 w
1434 m		1420 w
1385 m	1395 w	1345 s
1350 m	1360 s	1300 s
1298 m	1318 s	1250 w
1240 w	1280 s	1205 m
1220 w	1230 s	
1188 w	1140 s	1170 w
1149 w	1012 w	1148 w
1120 w		1085 w
1015 w		1007 w
982 w	970 w	950 w
955 w	910 m	899 m
874 m		880 m
849 m		827 m
779 m	785 w	799 m
755 m	770 m	767 w
	751 m	745 m
	735 w	

All compounds in solid state.

TABLE XIX

2-Formamido-biphenyl	2-Acetamido-biphenyl	2-(N,N-diacetyl-amino)biphenyl	2-Propionamido-biphenyl
3270 m	3260 w	3030 w	3240 m
3060 sh.	3030 w		3030 w
2880 w			2980 sh.
1975 w	1990-1950 w	1985 w	1955 w
1937 w	1915 w	1950 w	1910 w
1885 w	1890 w	1830 w	1882 w
1810 w	1825 w		1800 w
	1765 w		
1690 s	1710 s	1713 s	1652 s
1660 s	1690 s	1698 s	
1580 s	1657 s		
1513 s	1560 m	1507 w	1585 m
	1530 s		1530 s
1490 w	1476 m	1485 m	1480 m
1460 w	1450 w	1457 w	1451 w
1445 s	1435 m	1440 m	1435 m
1395 s	1415 w	1415 m	1377 m
1300 m	1369 s	1370 s	
1274 w	1292 s	1298 m	1299 w
1244 w	1242 s	1245 s	1280 s
1220 w	1210 w	1212 m	1232 m
1176 w	1185 w	1185 w	1202 m
1166 w	1155 w		1156 w
1150 w	1110 w		1112 w

(continued)

TABLE XIX (cont'd.)

2-Formamido-biphenyl	2-Acetamido-biphenyl	2-(N,N-diacetyl-amino)biphenyl	2-Propionamido-biphenyl
1073 w	1075 w	1075 w	1073 m
1023 w	1035 w	1056 w	1050 w
1010 m	1010 m	1035 w	1020 w
992 w	974 w	1020 m	1010 m
950 w	955 w	955 w	934 w
923 w	940 w	904 w	924 m
	921 w		
	903 w		
856 w	875 w	875 w	860 w
850 w	778 m	776 m	845 w
791 w	767 m	766 m	802 w
763 s	743 s	743 s	775 m
700 s	705 s	706 s	755 s
		638 m	740 s
			725 m
			702 s

All compounds in solid state.

EXPERIMENTAL

Preparation of 2-aminobiphenyl (137)

2-Nitrobiphenyl (50 g; 0.25 mole) dissolved in 100 ml. of ethanol was placed together with 180 g. of stannous chloride (0.78 mole) in 600 ml. of hydrochloric acid in a one liter flask fitted with a reflux condenser. The mixture was boiled for three hours. The milky suspension which had formed at first, slowly cleared up to give a perfectly transparent solution after approximately half an hour. At the end of the heating period the solution was cooled and large crystals of hydrochloride deposited. The supernatant liquid was decanted and the remaining hydrochloride solubilized by addition of 300 ml. of water. Alkalinization with a 10% sodium hydroxide solution gave a milky suspension which was extracted four times with 100 ml. of ether. Evaporation of the ether left a white residue which was recrystallized from dilute ethanol. In this manner 35 g. of 2-aminobiphenyl melting at 43-44° was obtained. Yield: 82%.

Preparation of 2-formamidobiphenyl

The starting material for this preparation was either prepared by the above mentioned procedure or it was obtained as a commercial product. In the latter case, the substance had to be purified by distillation under reduced pressure (10 mm Hg; 250°) before use.

2-Aminobiphenyl (84 g; 0.5 mole) dissolved in 150 ml. of formic acid (85%) was placed in a 500 ml. flask fitted with a condenser. The

solution was refluxed for ninety minutes, after which the water and excess formic acid was eliminated by vacuum distillation. The residue recrystallized from 150 ml. of 65% ethanol, gave 95 g. of o-formamidobiphenyl melting at 74-75°. Yield: 98%.

Preparation of phenanthridine by cyclization of 2-formamidobiphenyl

The best results on this preparation, described by Taylor and Kakuda (138), were obtained by proceeding as follows: Polyphosphoric acid (300 g.) of commercial origin was placed together with o-formamidobiphenyl (20 g; 0.118 mole) in a 500 ml. three-necked flask, fitted with a mechanical stirrer, a thermometer and a glass stopper. After thorough mixing, the white suspension was heated on an oil bath to 150°, and kept at 140-160° for one hour. Foam started to form at a temperature of about 130°. The foamhead disappeared after five minutes and a clear solution resulted which turned brownish by the end of the heating period. The mixture was poured into 1000 ml. of ice-water and made slightly alkaline with a 20% sodium hydroxide solution. During neutralization the temperature was kept below 40° at all times. The pH was then carefully adjusted to 10 by addition of dilute sodium hydroxide. An oil formed which solidified on standing overnight. The pink solids filtered and washed with plenty of cold water, were dried and recrystallized from ligroin (b.p. 90-120°). Phenanthridine was thus obtained in white crystals melting at 105-107°. Yield: 75%.

Preparation of 2-acetamidobiphenyl

2-Aminobiphenyl (30 g; 0.178 mole), freshly distilled, was refluxed for one hour with 25 g. of acetic anhydride (0.245 mole) in a 100 ml. flask. The excess acetic anhydride and the acetic acid produced during the reaction were removed by vacuum distillation. The residue was dissolved in 100 ml. of boiling ethanol and 50 ml. of water added. After standing for 24 hours, 30 g. of white crystals formed, melting at 117°. Yield: 80%. Acetylation by means of an acid chloride was also used. 2-Aminobiphenyl (15 g; 0.089 mole) dissolved in 50 ml. of pyridine was placed in a 100 ml. flask guarded by a calcium chloride tube. The solution was cooled in ice, while acetyl chloride (105 g; 0.133 mole) was added dropwise over a period of fifteen minutes. A crystalline substance was formed during the addition. The mixture was allowed to stand for half an hour and then poured in 100 ml. of hydrochloric acid (10%). The solid was isolated by filtration and crystallized from dilute ethanol in white needles melting at 119°.

Preparation of 2-(N,N diacetylamino)biphenyl

2-Aminobiphenyl (56.5 g; 0.33 mole), freshly distilled was refluxed for one hour with 100 g. of acetic anhydride (1 mole). The excess anhydride and the acetic acid were distilled off and the residue heated with 100 ml. of ethanol to which 50 ml. of water was added. Addition of the water precipitated instantaneously 20 g. of white crystals. A sharp melting point was observed at 86-87°. Yield: 24%.

Anal. Calc. for $C_{16}H_{15}NO_2$ C, 75.86; H, 6.59; N, 5.57%

Found C, 75.94; H, 6.18; N, 5.43%.

When a few milligrams of the substance were heated with 5 ml. of sulphuric acid 70%, a distinctive smell of acetic acid was perceived. On the other hand, when one gram of the material was dissolved in 10 ml. of orthophosphoric acid, the solution diluted with 10 ml. of water, a precipitate came down whose melting point was 118°.

Preparation of 6-methylphenanthridine by cyclization of 2-acetamidobiphenyl

The optimum conditions for the reaction were found to be as follows:

o-Acetamidobiphenyl (10 g; 0.06 mole) and 150 grams of polyphosphoric acid were placed in a 500 ml. flask. thoroughly mixed and heated to 125-130° while stirring rapidly. The system was kept at this temperature for ten minutes, after which the brownish solution that had formed was poured in 1000 ml. of ice water. Addition of solid sodium carbonate until a slightly alkaline solution was obtained produced an oil which solidified after standing overnight. The solid was filtered, washed with plenty of water and dried in a vacuum dessicator. Purification was best achieved by dissolving the material in 100 ml. of ether, filtering and evaporating the solvent. The residue was then dissolved in 25 ml. of ethanol at the boiling point and water was added until a beginning of cloudiness. On standing 24 hours a total of 6.5 grams of 6-methylphenanthridine melting at 85° was collected. Yield: 71%.

Preparation of 2-propionamidobiphenyl

2-Aminobiphenyl (49 g; 0.29 mole) and propionic anhydride (100 g;

0.85 mole) placed in a 250 ml. flask were refluxed for one hour. The excess anhydride and the propionic acid were then removed by vacuum distillation. The residue was dissolved in 100 ml. of boiling ethanol and water was added until a beginning of cloudiness. White crystals deposited after 48 hours standing. A melting point of 63-65° was recorded. Yield: 75%.

Preparation of 6-ethylphenanthridine by cyclization of 2-propionamidobiphenyl

2-Propionamidobiphenyl (1 g; 0.004 mole) and 15 grams of polyphosphoric acid were placed in a 100 ml. flask and thoroughly mixed. Heating the system for one hour at 140-160° produced a brown solution which was poured in 100 ml. of water. A 20% solution of sodium hydroxide was added until slightly alkaline reaction. The oil formed in this manner was extracted twice with 100 ml. of ether and the ether removed by distillation. The oily residue was dissolved in 25 ml. of ethanol and a few ml. of water added. Allowed to stand for 48 hours, the solution deposited 0.25 gram of slightly brown solids of 6-ethylphenanthridine melting at 51°. Repeated crystallizations did not seem to increase the purity of the sample. Yield: 30%.

Preparation of monoperphthalic acid (139)

A 15% solution of sodium hydroxide (275 g; 1 mole) was placed in a one liter round-bottomed flask equipped with a stirrer and cooled in an acetone-dry ice bath. After cooling to -5° approximately one mole of hydrogen peroxide 30% (115 g.) was added in one portion. The heat of reaction

caused the temperature to rise to about 30°. When the temperature had dropped to -5°, powdered phthalic anhydride (75 g; 0.5 mole) was added as quickly as possible with vigorous stirring. After five minutes the solution was acidified with 250 ml. of sulphuric acid 20% (0.5 mole) previously cooled. The acid solution was filtered through glass wool and extracted successively with 500, 250 and 250 ml. of ether. The combined extracts were dried over 25 grams of anhydrous sodium sulphate. The peracid content was determined by adding 2 ml. of the ethereal solution to 30 ml. of potassium iodide 20% and titrating after ten minutes with 0.05 N thiosulphate solution.

On a number of experiments, an average yield of 0.003 gram of active oxygen per ml. of ethereal solution was obtained.

Preparation of phenanthridine N-oxide

A. Oxidation with hydrogen peroxide (140). Phenanthridine (4 g; 0.002 mole) was dissolved in 75 grams of glacial acetic acid and hydrogen peroxide 30% (3.75 g; 0.033 mole) was added. The mixture was heated for four hours at 70-72° on an oil bath. At the end of this period powdered manganese dioxide (1 g) was added to destroy the excess hydrogen peroxide. After filtration the solvent was evaporated to dryness and the residue taken up with 200 ml. of a saturated solution of sodium carbonate. Filtration of the latter left a residue which was dried and then boiled with 200 ml. of chloroform. The solvent was evaporated to dryness and the residue recrystallized from 25 ml. of ethanol diluted with 10 ml. of water. In this way 0.2 gram of faintly coloured crystals of phenanthridine N-oxide was

obtained. A melting point of 218° was found. Yield: 4.6%.

The reaction was also carried out at 50°, 65-70°, 75° and 100° without better success.

B. Oxidation with monoperphthalic acid (141). Phenanthridine (20 g; 0.115 mole) was dissolved in 700 ml. of dry ether and poured into 850 ml. of a monoperphthalic acid ethereal solution containing a total of 2 grams of active oxygen (0.125 mole). A slight turbidity appeared at first and a few minutes later a deep yellow solution was obtained. It was allowed to stand at room temperature for 24 hours. At this time the ether was decanted and the solids, which had deposited at the bottom of the flask, shaken with 100 ml. of ammonium hydroxide 5%. After filtration the residue was dissolved in 100 ml. of ethanol and 50 ml. of water was added. On cooling in ice 15.5 grams of white crystals of phenanthridine N-oxide formed melting at 208°. This represented a 70% yield.

Successive recrystallizations from ethanol and ethyl acetate gave a melting point of 220-222°. The picrate prepared by the standard method was recrystallized from ethanol m.p. 193°. The following table gives the conditions for five runs:

Active Oxygen (g.)	Phenanthridine (g.)	in ml. ether	Time (at room temp.)	Yield
2.65	18.	550.	24 hrs	62.%
1.4	9.	250.	24 hrs	65.%
3.6	31.	600.	24 hrs	45.%
2.	20.	700.	24 hrs	70.%

Anal. Calc. for $C_{13}H_9NO$ C, 80.00; H, 4.65; N, 7.18%

Found: C, 79.55; H, 4.33; N, 6.92%.

Reduction of Phenanthridine N-oxide

Phenanthridine N-oxide (1 g; 0.005 mole) was dissolved in 25 ml. of chloroform. The solution was cooled in ice and phosphorus tribromide (2 g; 0.009 mole) was added. Immediate precipitation of a yellow solid took place and the temperature rose to 30°. The mixture was then refluxed on a steam bath for thirty minutes, during which time the amount of precipitate increased. The chloroform was distilled off and 50 ml. of water was added. A small amount of precipitate formed at this point and was removed by filtration. The filtrate made alkaline with a saturated solution of sodium carbonate gave a milky suspension which on standing 24 hours deposited white crystals. These solids were isolated and dried. Recrystallization from petroleum ether (b.p. 90-120°) gave 0.45 gram of phenanthridine with a melting point of 107°. Yield: 50%.

Rearrangement of phenanthridine N-oxide

Phenanthridine N-oxide (1 g; 0.005 mole) was dissolved in 50 ml. of glacial acetic acid and refluxed for one hour. Approximately half the volume of acetic acid was then removed by distillation under reduced pressure. The residual solution on cooling with ice deposited white crystals. When it was attempted to filter these crystals they dissolved on the filter. The solution was neutralized by addition of solid sodium carbonate and diluted with water to 100 ml. A white precipitate formed which recrystallized from dilute ethanol gave 0.9 gram of crystals of phenanthridine N-oxide. m.p. 220°.

Phenanthridine N-oxide (1 g; 0.005 mole) was placed with 50 ml. of

acetic anhydride 95%, in a one-necked 100 ml. flask fitted with a condenser. The solution was refluxed for one hour, at the end of which period all of the N-oxide had solubilized. On cooling long white needles (0.73 g.) formed which were filtered, washed with water and recrystallized from acetic acid. m.p. 287°. Yield: 73.%. The mother-liquor was made alkaline with a concentrated solution of sodium hydroxide. The precipitate which formed at this point was filtered and recrystallized from dilute ethanol. In this fashion 0.2 gram of phenanthridine N-oxide was recovered. m.p. 220°.

Preparation of phenanthridinone (142)

o-Biphenylisocyanate. Phosgene (56. g; 0.57 mole) was dissolved in 280 grams of toluene previously dried over sodium wire. The solution was then placed in a 500 ml. three-necked flask fitted with condenser, calcium chloride tube and separatory funnel. 2-Aminobiphenyl (19 g; 0.113 mole) purified by vacuum distillation was dissolved in 100 ml. of dry toluene, placed in the separatory funnel and added over a period of half an hour. The flask was slightly heated during the addition and a considerable amount of gas was evolved. The mixture was then refluxed for three hours, allowed to stand overnight and refluxed one more hour. At this stage the evolution of gas had ceased almost completely. The toluene and excess phosgene were distilled off. In order to take up any phosgene vapours a flask with a 20% sodium hydroxide solution was placed after the receiver. The residue was heated for a few minutes with 80 ml. of carbon tetrachloride, and the latter eliminated by distillation. The final residue distilled under vacuo (6 mm Hg) gave 18 grams of a pale yellow liquid. Yield: 81%.

Cyclization of o-biphenylisocyanate. Aluminum chloride (13.5 g; 0.1 mole) was suspended in 70 ml. of o-dichlorobenzene in a 100 ml. flask fitted with a thermometer, a separatory funnel and a stirrer. O-Biphenylisocyanate (18 g; 0.092 mole) was added over a period of twenty minutes, keeping the temperature between 70-80°. At first a deep violet colour developed which slowly turned to blue and bluish-grey. When the addition was completed the mixture was stirred for another 45 minutes, at which time the temperature had dropped to 29°. The solids were filtered, washed with 50 ml. of o-dichlorobenzene and triturated in 100 ml. of hydrochloric acid 15%. The precipitate turned white instantaneously. The material was then suspended in 75 ml. of ethanol and stirred rapidly for a few minutes. The white solids (12.5 g.) were collected and dried at 50° for one hour. They were recrystallized from 300 ml. of glacial acetic acid. Phenanthridinone melted at 289°. Yield: 70%.

Attempted nitration of phenanthridine N-oxide

Sulphuric acid medium - Low temperature. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 10 ml. of concentrated sulphuric acid. The brownish solution was cooled to 0°, and a mixture of nitric acid 70% (0.9 g; 0.01 mole) and 1 ml. of concentrated sulphuric acid, previously cooled, was added dropwise with rapid stirring. During the addition the temperature was always kept below 5°. After standing one hour at 0°, the reaction mixture was poured into 100 ml. of ice water. A yellow precipitate appeared immediately. It was filtered off, washed with water and dried. Several recrystallizations from dilute ethanol afforded 1.5 gram of slightly yellow starting material, melting at 220°. Alkalinization of the filtrate with

solid sodium carbonate resulted in the formation of more precipitate (0.3 g.). It was filtered, dried and recrystallized three times from dilute ethanol. A melting point of 218-220° was recorded.

Sulphuric acid medium - High temperature.

A. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 10 ml. of concentrated sulphuric acid. Nitric acid 70% (0.9 g; 0.011 mole) in 1 ml. of concentrated sulphuric acid was added dropwise with stirring to the brownish solution. A red colour appeared immediately and the temperature rose to 45°. The reaction mixture was allowed to stand for one hour and was then poured into 100 g. of ice water. A yellow substance precipitated at this stage and was filtered. It was recrystallized three times from dilute ethanol, treated with charcoal and recrystallized again. In this way 1.5 gram of starting material was recovered melting at 218-220°.

The acidic filtrate was made alkaline and diluted with an equal amount of water. The precipitate which deposited was filtered. Three recrystallizations from dilute ethanol gave 0.25 g. of starting material melting at 218-220°.

B. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 10 ml. of concentrated sulphuric acid. Nitric acid 70% (0.9 g; 0.011 mole) in 1 ml. concentrated sulphuric acid was added dropwise with stirring. When the addition was completed the mixture was placed on a water bath and heated to 60°. After fifteen minutes at that temperature the solution had turned to a deep red and nitrogen oxide gases were being evolved. On pouring into 100 ml. of ice water a gummy material precipitated. This substance was

filtered. It hardened rapidly in contact with the air and could not be solubilized.

Acetic acid medium - Room temperature. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved at room temperature in 10 ml. of glacial acetic acid. A mixture of nitric acid 70% (0.99 g; 0.01 mole) and 1 ml. of glacial acetic acid was then added dropwise with stirring to the solution. Approximately thirty seconds after the addition was completed a large amount of precipitate formed. After standing for fifteen minutes 100 ml. of ice water was added which resulted in the dissolution of the first precipitate immediately followed by the formation of a second precipitate. This was filtered and recrystallized once from dilute ethanol to give 1.8 gram of the starting material, m.p. 218-220°. Neutralization of the acidic filtrate with solid sodium carbonate produced another 0.1 gram of material. One recrystallization from ethanol gave phenanthridine N-oxide melting at 218-220°.

Nitration of phenanthridine N-oxide in acetic acid

One equivalent. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 10 ml. of glacial acetic acid. The nitrating mixture consisting of nitric acid 70% (0.99 g; 0.01 mole) and 1 ml. of glacial acetic acid was added dropwise with rapid stirring. After a few seconds a precipitate started to form which did not disappear on further addition of 10 ml. of glacial acetic acid. The mixture was placed on an oil bath and the temperature slowly brought up to 75°. At 70°, the precipitate dissolved rapidly and three minutes later yellow solids began to form. After fifteen minutes at 75°, nitric fumes started to evolve and the reaction was stopped by

pouring it in about 100 grams of ice water. The precipitate which formed was isolated by filtration and dried. It was then treated with 30 ml. of boiling ethanol for a few minutes and filtered. The insoluble fraction (0.86 g.) was recrystallized twice from nitrobenzene. The substance melted at 380-382°, but started carbonizing at 285°. Further purification could be achieved by subliming the material slowly at 280° with a pressure of 0.5 mm Hg m.p. 382-383°. Yield: 36%. By alkalinization of the acidic filtrate with solid sodium carbonate to 0.22 gm. of phenanthridine N-oxide was recovered. When the ethanolic solution was concentrated to one third of its volume, another 0.16 gm. of material was obtained which recrystallized from dilute ethanol proved to be starting material.
N.B. During the recrystallization of the nitration product (m.p. 380-382°) from nitrobenzene it was found that if the solution was kept at the boiling point for more than a few seconds carbonization occurred.

Two equivalents. Phenanthridine N-oxide (5 g; 0.025 mole) was dissolved in 25 ml. of glacial acetic acid and a mixture of nitric acid 70% (4.95 g; 0.05 mole) and 2 ml. of glacial acetic acid was added dropwise with stirring. Phenanthridine N-oxide dissolved completely. After a short time a precipitate started to form. The mixture was then slowly heated. At 65° complete solution took place. The temperature was allowed to rise to 75°, and approximately four minutes later, yellow solids began to form. After another two minutes the reaction mixture seemed to turn into a solid mass. Two hundred ml. of ice water were made. A product precipitated immediately and was filtered. Drying followed by two recrystallizations from nitrobenzene gave 3.6 gm. of a brownish substance melting at 380-382°. Yield: 62%. Slow sublimation (280°; 1 mm Hg) raised the melting point to 382-383°.

The acidic filtrate was made alkaline with solid sodium carbonate. The precipitate (1 g.) which formed was filtered and recrystallized from dilute ethanol. The melting point 218-220° proved it to be unreacted phenanthridine N-oxide.

Three equivalents. Phenanthridine N-oxide (2 g; 0.01 mole) was dissolved in 10 ml. of glacial acetic acid. To the light brown solution which resulted nitric acid 70% (2.97 g; 0.03 mole) in 2 ml. of glacial acetic acid was added dropwise with stirring. The solution turned dark brown and the usual precipitate only started to form after five minutes. The temperature was then raised to 75°. The solids solubilized rapidly around 65° and after six minutes at 75° the second precipitate began to form. Three minutes later the amount of solids seemed to have reached a maximum. The mixture was poured into 100 ml. of ice water and filtration afforded a yellow residue which was dried and recrystallized successively from nitrobenzene, acetic acid and nitrobenzene. In this manner 1.6 gm. of yellow crystals melting at 381-383° was obtained. Yield: 65%.

The acidic filtrate was treated with solid sodium carbonate to alkaline reaction. The resulting precipitate (0.2 g.) dried and recrystallized from dilute ethanol proved to be starting material (m.p. 218-220°).

Dilute solution. Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 50 ml. of glacial acetic acid. The nitrating mixture consisting of nitric acid 70% (2.97 g; 0.03 mole) in 2 ml. of glacial acetic acid was added to the orange solution dropwise with stirring. twelve minutes after the addition the initial precipitate started forming. Another eight minutes were required before the precipitation was completed. The mixture was then

heated on an oil bath to 75°. Complete solution took place around 65° and nitric fumes were evolved. Soon after yellow solids appeared and continued to form for approximately eight minutes. At this time the reaction was quenched with 100 ml. of ice water. The precipitate which formed was isolated and treated with 30 ml. of boiling ethanol. The insoluble material (1.3 g.) was filtered off and recrystallized twice from nitrobenzene. m.p. 381-382°. Yield: 54%.

The acid filtrate was treated as previously with sodium carbonate. In this fashion 0.4 gm. of starting material was recovered.

Nitration of phenanthridine N-oxide with fuming nitric acid

Phenanthridine N-oxide (2 g; 0.011 mole) was dissolved in 10 ml. of glacial acetic acid. To this solution a mixture of fuming nitric acid (0.63 g; 0.01 mole) and 1 ml. of glacial acetic acid was added dropwise with stirring at room temperature. A few seconds after completion of the addition a considerable amount of white precipitate came down. The reaction mixture was heated on an oil bath to 75°. At 69° the precipitate dissolved to give a dark brown solution. After one minute at 75°, the usual yellow precipitate began to form and two minutes later the reaction seemed to have attained equilibrium. It was then poured into 100 ml. of ice water. The golden yellow precipitate which resulted was filtered, dried and then treated with 30 ml. of boiling ethanol for a few minutes. The insoluble fraction was filtered off and recrystallized twice from nitrobenzene. This procedure gave 0.664 gram of material melting at 381-382°. Yield: 27.5%. By concentration of the ethanolic solution 1.3 gm. of starting material was

recovered. Also, neutralization of the acidic filtrate afforded another 0.145 gm. of a substance which recrystallized from dilute ethanol proved to be phenanthridine N-oxide. m.p. 218-220°.

Nitration of phenanthridine N-oxide in acetic anhydride

Phenanthridine N-oxide (2 g; 0.011 mole) was placed in 10 ml. of acetic anhydride. The material did not dissolve at room temperature and even when heated to 70°, a certain amount remained in suspension. The nitrating mixture was made up by adding one gram of acetic anhydride to 0.99 gram of nitric acid 70% (0.01 mole). It was added dropwise with stirring to the phenanthridine N-oxide suspension. At first nitric fumes were evolved and then the solids still in suspension dissolved completely to give place to a dark brown solution. At the same time the temperature rose to 75°. After approximately three minutes at 70-75° with constant stirring a yellow precipitate started to form and after two more minutes the reaction seemed to be completed. It was allowed to stand for five minutes and then poured into 100 ml. of ice water. Yellow solids precipitated and were filtered. They were treated with 30 ml. of boiling ethanol for a few minutes. The insoluble fraction was collected. Its melting point, 232-236°, was raised to 381-382° by three recrystallizations from nitrobenzene. In this manner 0.94 gm. of material was obtained. Yield: 38.5%.

By concentration of the ethanolic solution one gram of starting material was recovered. On the other hand, the initial acidic filtrate was neutralized with solid sodium carbonate, which resulted in the precipitation of a very small amount of a reddish powder not further investigated.

Attempted reduction of the nitration product of phenanthridine N-oxide

The mononitration product of phenanthridine N-oxide of melting point 380-382° (0.2 g; 0.0008 mole) was dissolved in 50 ml. of dioxane and 1 ml. of phosphorus tribromide (2.85 g; 0.0105 mole) was added. The reaction mixture was refluxed for thirty minutes. At the end of this period the solution was cooled and diluted with 50 ml. of water. The white solid which precipitated was collected. Recrystallized from dilute ethanol it gave 0.18 gm. of the starting material. m.p. 218-220°. The same reaction was tried with phosphorus trichloride. Again the starting material was recovered unreacted.

Chromatography of the nitration product of phenanthridine N-oxide

A column .64 cm. high and with a diameter of 5 cm. was used. It was filled with chromatographic alumina, acid washed, up to about five centimeters from the top. First the adsorbent was wetted with 25 ml. of pyridine and then a solution of 1 gm. of the nitration product (m.p. 380-382°) in 75 ml. of pyridine was poured on it. A deep red band approximately 2 cm. long formed almost immediately and did not seem to move afterwards. Elution was carried out at the beginning with cold pyridine, then with hot pyridine. After eluting for eight hours in this fashion the column appeared as follows: starting from the top there was a red band about 2 cm. long and 3 cm. of an orange band. A break of approximately 30 cm. almost perfectly white was followed by a continuous yellow column 15 cm. long. The bottom section was isolated and the alumina heated with 300 ml. of pyridine. Evaporation of the solvent however did not leave any residue.

The adsorbent was then treated with 200 ml. of hot nitrobenzene, but after filtration and cooling no solid crystallized. Finally, the alumina was mixed with 200 ml. of concentrated sulphuric acid. Filtration afforded a dark solution which was diluted with half its volume of water. A small amount of white precipitate was filtered out and the solution cooled with ice was neutralized with ammonium hydroxide. A yellow precipitate formed. It was filtered, washed with water and dried. The substance (0.2 g.) melted at 382-383° and no appreciable change in colour could be noticed before its melting point.

Synthesis of 2-nitrophenanthridinone

Preparation of 2-p-toluenesulfonamidobiphenyl. 2-Aminobiphenyl (17.5 g; 0.104 mole) dissolved in 75 ml. of pyridine was placed in a 250 ml. flask. To this solution p-toluenesulfonyl chloride (29.5 g; 0.155 mole) was added. The reaction mixture was refluxed for thirty minutes and then poured onto 300 gm. of ice. At first an oil appeared but on cooling the system on dry ice for a few moments and scratching the walls of the beaker with a spatula this oil solidified. It was filtered, washed with plenty of water and recrystallized from 200 ml. of ethanol without previous drying. Thirty-one grams of product melting at 97° were thus obtained. Yield: 94%.

Nitration of 2-p-toluenesulfonamidobiphenyl (143). 2-p-Toluenesulfonamidobiphenyl (31 g; 0.078 mole) was dissolved in 100 ml. of glacial acetic acid and placed in a 250 ml. flask fitted with a condenser and a thermometer. The nitrating mixture consisting of nitric acid 70% (7 g; 0.078 mole) in 5 ml. of glacial acetic acid was added in one portion and the solution heated

to 95° on an oil bath. A dark red colour appeared and an exothermic reaction set in. The oil bath was removed immediately but the temperature still reached 110°. The system was allowed to cool over a period of half an hour. At this time the crystals which had formed during the cooling process were filtered and washed with water. The yellow-orange crystals (26 g.) melted at 166°. Yield: 74%.

Hydrolysis of 5-nitro-2-p-toluenesulfonamidobiphenyl (144). 5-Nitro-2-p-toluenesulfonamidobiphenyl (26 g; 0.07 mole) was placed in a 250 ml. flask together with 100 ml. of concentrated sulphuric acid diluted with 25 ml. of water and heated to 125° for thirty minutes. At the end of the heating period the solid had completely dissolved. The solution was poured onto 200 grams of ice. A yellow oil formed and solidified after standing a few minutes. The solid was collected and recrystallized from 100 ml. of ethanol. Ten grams of material were thus obtained with a melting point of 125°. Yield: 65%.

Acetylation of 2-amino-5-nitrobiphenyl. 2-Amino-5-nitrobiphenyl (10 g; 0.047 mole) was dissolved in 20 ml. of glacial acetic acid and 10 ml. of acetic anhydride (13.9 g; 0.136 mole) was added to this solution. The mixture was refluxed for thirty minutes and poured onto 50 gm. of ice. An oil appeared first and solidified a few moments later. The solids were filtered, washed with water and recrystallized from 50 ml. of ethanol. This procedure afforded 10 grams of slightly coloured solids melting at 131°. Yield: 84%.

Cyclization of 2-acetamido-5-nitrobiphenyl. 2-Acetamido-5-nitrobiphenyl (2 g; 0.0084 mole) was thoroughly mixed at room temperature with 40 grams of commercial polyphosphoric acid. The temperature of the system was then rapidly brought to 130° and maintained for approximately five minutes while stirring constantly. The heating was then stopped and the greenish solution poured into 200 ml. of ice water. Alkalinization with a solution of sodium hydroxide 30% precipitated brown solids. These were filtered, washed with water and after overnight drying in a dessicator were recrystallized from benzene. One gram of very slightly brown material was obtained m.p. 200°. Yield: 54%.

Oxidation of 6-methyl-2-nitrophenanthridine (52). 6-Methyl-2-nitrophenanthridine (0.5 g; 0.002 mole) was dissolved in 5 ml. of hot glacial acetic acid. Sodium dichromate dihydrate (1.5 g; 0.005 mole) was added to the hot solution in small portions over a period of ten minutes. A vigorous reaction occurred and a red powder separated. The mixture was refluxed for one hour. After cooling, filtration left a brick-red residue (0.35 g.) melting at 375°. Yield: 50%.

The substance was slowly sublimed at 275° and 0.5 mm Hg. This operation raised the melting point to 382-383° (without previous blackening).

Preparation of 6-methylphenanthridine nitrate

6-Methylphenanthridine (10 g; 0.052 mole) was placed in 135 ml. of nitric acid 7 N (50 ml. of nitric acid 70% in 85 ml. of water). It was heated to 50° and kept at this temperature until all solids had dissolved.

On standing overnight crystals formed and were filtered. Treated with 25 ml. of water and filtered after five minutes, the crystals were then dissolved in 50 ml. of boiling ethanol. On cooling seven grams of long white needles formed, melting at 130°.

Attempted nitration of 6-methylphenanthridine

6-Methylphenanthridine nitrate (7 g; 0.029 mole) was dissolved in 12 ml. of concentrated sulphuric acid keeping the temperature between -5 and 0°. The mixture was then allowed to come to room temperature and was left standing for one hour with occasional stirring. It was then poured into 100 ml. of ice water and made slightly alkaline with ammonium hydroxide, always keeping the temperature below 5°. An orange oil formed. After standing 24 hours at room temperature, the pH was raised to 10 by further addition of ammonium hydroxide. The oil solidified immediately to give slightly yellow crystals (6.5 g.). These were dissolved in 50 ml. of ethanol and the solution treated with charcoal. After filtration of the latter, the ethanolic solution was heated to its boiling point and 25 ml. of water added. On cooling white crystals of 6-methylphenanthridine formed. m.p. 82°.

6-Methylphenanthridine nitrate (5 g; 0.02 mole) was dissolved in 10 ml. of concentrated sulphuric acid keeping the temperature at 0°. The mixture was then heated rapidly to 100° on an oil bath, and allowed to cool. On pouring into 100 ml. of ice water a very small amount of precipitate formed and was removed by filtration. The filtrate was made alkaline with dilute sodium hydroxide. The substance which precipitated

at this stage was isolated, washed with plenty of water and dried (3.5 g.). By recrystallization from dilute ethanol 6-methylphenanthridine, melting at 82°, was recovered.

Nitration of 6-methylphenanthridine

6-Methylphenanthridine nitrate (11 g; 0.043 mole) was dissolved in 50 ml. of concentrated sulphuric acid at 0°. The solution was then heated on an oil bath to 70-75° and kept at that temperature for one hour. At the end of this period the reaction mixture was poured in 300 ml. of ice water and made slightly alkaline by addition of a sodium hydroxide solution. (The total volume at this point was one liter.) Alkalinization produced both an oil and a precipitate. The oil was decanted as well as possible and the precipitate was filtered, washed with water and dried.

The oil was dissolved in 100 ml. of ethanol. A certain amount of precipitation took place when the oil was poured in the alcohol. These white solids were removed by filtration and proved to be non-combustible. The ethanolic solution was evaporated to one third of its volume and on standing deposited yellowish crystals melting at 115°. Three recrystallizations from dilute ethanol afforded 4 grams of yellow crystals of melting point 149-150° (fraction A). Yield: 29.5%.

Anal. Calc. for $C_{14}H_{10}N_2O_2$ C, 70.6; H, 4.23, N 11.76%

Found: C, 70.52; H, 4.39; N, 11.79%.

The initial precipitate was recrystallized from dilute acetic acid to give 0.5 gm. of a solid melting at 258°. (fraction B).

Anal. Calc. for $C_{14}H_9N_3O_4$ C, 59.07; H, 3.22; N, 14.94%
Found: C, 60.01; H, 3.14; N, 14.2%.

Oxidation of fraction A

One gram (0.004 mole) of the impure product (m.p. 115°) was dissolved in 20 ml. of glacial acetic acid. Approximately 2.5 gm. of sodium dichromate dihydrate (0.008 mole) was added to the solution portionwise. After a few minutes a strongly exothermic reaction set in, which kept the system at boiling point for ten minutes. It was allowed to cool and stand at room temperature for 24 hours. Finally it was refluxed for one hour. The addition of 50 ml. of water caused a yellow solid to precipitate. It was filtered, washed with water and dried. Purification was achieved by recrystallizing three times from acetic acid. The 0.6 gram of material obtained in this way was further purified by sublimation at 200° and 0.5 mm Hg followed by one recrystallization from acetic acid. A stable melting point of 265-267° was found. Yield: 59.5%.

Anal. Calc. for $C_{13}H_8N_2O_3$ C, 65.; H, 3.35; N, 11.66%
Found: C, 64.91; H, 3.33; N, 11.76%.

Oxidation of fraction B

One gram (0.0035 mole) of the impure product (m.p. 245°) was placed in 20 ml. of glacial acetic acid. Partial solution was achieved. To this mixture 2.5 gm. of sodium dichromate dihydrate (0.008 mole) was added portionwise and the system was refluxed for two hours. A precipitate started to form after a few minutes of heating and increased slowly as the

reaction proceeded. After standing at room temperature for 24 hours, the precipitate was filtered and washed with water to eliminate all inorganic salts. By addition of water (50 ml.) to the filtrate more yellow precipitate came down. It was isolated and added to the first crop. Sublimation at 220° and 0.5 mm Hg produced 0.4 gram of material which was then recrystallized three times from glacial acetic acid. A sharp melting point of 350-351° was registered. Yield: 40%.

Preparation of 6-aminophenanthridine (145)

Phenanthridine (5 g; 0.028 mole) was dissolved in 25 ml. of xylene previously dried over sodium wire and placed in a 100 ml. flask. Sodium amide (5 g; 0.128 mole) of commercial origin, ground to a fine powder was introduced in the reaction vessel which was fitted with a reflux condenser equipped with a calcium chloride tube. The system was heated to 120-130° for five and a half hours. The liberation of hydrogen which began around 110° had almost ceased at the end of this period. The reaction mixture, now a black paste, was decomposed with about 100 grams of ice. The resulting greenish suspension was filtered and after drying, dissolved in 50 ml. of ethanol. On cooling bright yellow crystals (3.25 g.) formed melting at 185°. A higher degree of purity was reached by dissolving the compound in a minimum of glacial acetic acid, treating with charcoal at its boiling point and reprecipitating 6-aminophenanthridine by addition of dilute ammonium hydroxide. After this operation the melting point had risen to 193°. Yield: 60%.

Mononitration of 6-aminophenanthridine

A. 6-Aminophenanthridine (4 g; 0.023 mole) was dissolved in 20 ml. of concentrated sulphuric acid at room temperature and then cooled to -15° by means of a dry ice-acetone bath. A mixture of 2 ml. of concentrated sulphuric acid and nitric acid 70% (1.95 g; 0.023 mole) was added dropwise with rapid stirring to the green solution. During the addition the temperature was maintained between -15° and -10°. The clear brown solution was stirred and kept at low temperature for two more minutes and it was then poured onto 100 grams of ice. A yellow precipitate appeared. It was filtered, washed and dried. Three recrystallizations from acetic acid gave 1.5 gm. of a yellow product melting at 357-358°. Recrystallized once more from nitrobenzene and then sublimed at 250° and 0.5 mm Hg, it melted at 320-321°. Yield: 30%.

B. 6-Aminophenanthridine (0.2 g; 0.001 mole) was dissolved in 5 ml. of concentrated sulphuric acid and then cooled to -15°, at which temperature the nitrating mixture, consisting of 1 ml. of concentrated sulphuric acid and nitric acid 70% (0.1 g; 0.001 mole), was added dropwise with stirring. When the addition was completed the temperature was allowed to rise to room temperature. After ten minutes, it was poured into 20 ml. of ice water. The yellow precipitate was collected, washed and dried. The filtrate made alkaline with a 20% sodium hydroxide solution produced more precipitate. Both crops were combined and two recrystallizations from acetic acid followed by one from nitrobenzene gave 0.125 gm. of a material melting at 357-358°. Yield: 50%.

Anal. Calc. for $C_{13}H_{10}N_3O_2$ N, 17.7%

Found: N, 18.4%.

Dinitration of 6-aminophenanthridine

A. 6-Aminophenanthridine (3.7 g; 0.019 mole) was dissolved in 20 ml. of concentrated sulphuric acid and cooled to -15°. The nitrating mixture consisting of 5 ml. of nitric acid 70% (large excess) and 5 ml. of concentrated sulphuric acid was added dropwise with stirring, the temperature being maintained between -15° and -10°. The solution was stirred for two more minutes and then poured onto 100 grams of ice. Yellow solids precipitated immediately and after standing for half an hour were filtered, washed with water and dried overnight in a vacuum dessicator. Recrystallization from nitrobenzene gave 2.15 grams of yellow crystals melting at 315-317° (dec.). Neutralization of the acidic filtrate with dilute ammonium hydroxide did not produce a precipitate. Yield: 40%.

B. 6-Aminophenanthridine (1.4 g; 0.007 mole) was dissolved in 10 ml. of concentrated sulphuric acid and subsequently cooled to-15° by means of a dry ice-acetone bath. A mixture of 5 ml. of concentrated sulphuric acid and 5 ml. of nitric acid 70% (large excess) was added dropwise with vigorous stirring. The system was stirred for another ten minutes after completion of the addition. By this time the colour had turned from an initial green to brown and the temperature had risen to 0°. The solution was poured onto 50 grams of ice. Immediate precipitation of yellow solids took place. They were filtered after half an hour, washed and dried. Recrystallization from nitrobenzene and treatment with charcoal followed by a second recrystallization from nitrobenzene gave 1.35 gm. of deep yellow crystals melting at 315-317° (dec.). Yield: 60%.

Anal. Calc. for $C_{13}H_9N_4O_4$ C,54.92; H, 2.83; N, 19.7%

Found: C,55.81; H, 2.83; N, 19.83%.

Oxidation of 6-aminomononitrophenanthridine

6-Aminomononitrophenanthridine (1 g; 0.004 mole) was dissolved in 5 ml. of concentrated sulphuric acid and cooled to 0°. A solution of sodium nitrite (1 g; 0.0145 mole) in 3 ml. of water was added in one portion. The reaction mixture was placed in a frigidaire for 24 hours (temperature between 0° and 5°), then brought to boiling point and filtered hot. The residue of the filtration was washed with warm 3 N sulphuric acid to remove all traces of unreacted aminocompound. After drying it was recrystallized several times from ethanol and treated with charcoal. Finally 0.4 gm. of bright yellow crystals of mononitrophenanthridinone were isolated giving a sharp melting point of 414°. Yield: 40%.

Anal. Calc. for $C_{13}H_9N_2O_3$ N, 11.66%

Found: N, 10.84%.

One drop of the cold solution of 6-aminomononitrophenanthridine and sodium nitrite after two hours of reaction time was placed on a filter paper and one drop of a dilute alkaline solution of β-naphthol was placed next to it. At the point of junction no coloration was observed.

Attempted oxidation of 6-aminodinitrophenanthridine

6-Aminodinitrophenanthridine (1 g; 0.0035 mole) was dissolved in 5 ml. of concentrated sulphuric acid and cooled to 0°. Sodium nitrite (1 g; 0.0145 mole) in 3 ml. of water was added in one portion. The solution was kept at 0° for 24 hours and then heated to its boiling point for a few minutes. The solution was cooled and made alkaline with a dilute sodium

hydroxide solution. The material that precipitated was filtered, washed with water and thoroughly dried (0.9 g.). Recrystallization from nitrobenzene gave yellow crystals of starting material melting at 345°.

Attempted rearrangement of the nitration products of 6-aminophenanthridine

A. 6-Aminomononitrophenanthridine (0.5 g; 0.002 mole) was dissolved in 5 ml. of concentrated sulphuric acid at 0°. The light brown solution was heated to 50° and kept at this temperature for fifteen minutes. At the end of this period the solution, whose colour had not changed, was cooled and made slightly alkaline with solid sodium carbonate. The yellow precipitate that formed (0.4 g.) was isolated and recrystallized from nitrobenzene. Its melting point (357-358°) showed it to be starting material.

B. 6-Aminodinitrophenanthridine (0.5 g; 0.0017 mole) was dissolved in 5 ml. of concentrated sulphuric acid at 0°. The brown solution was then treated to 50° for twenty minutes. After cooling it was made alkaline with solid sodium carbonate. The resulting yellow precipitate was filtered, washed with water and dried. Recrystallization from nitrobenzene gave 0.45 gram of starting material melting at 315-317°.

Purification of technical acridine (146)

Acridine (Eastman, technical grade) (5 g.) was dissolved in 100 ml. of concentrated sulphuric acid diluted with 100 ml. of water. The solution was cooled to room temperature and 25 grams of sodium dichromate dihydrate (approximately 3 equivalents) in 50 ml. of water was added.

(N.B. If the dichromate is added when the temperature of the acidic acridine solution exceeds 30° a violent oxidation to acridone takes place.) A precipitate of acridine dichromate formed immediately. It was filtered after a few minutes and washed with water. The solids were then suspended in 150 ml. of water, made alkaline with ammonium hydroxide and heated for a few minutes on a hotplate. The yellowish solids were then filtered and dried. They were dissolved in 50 ml. of ethanol and treated with decolorizing charcoal. After filtration of the latter the alcoholic solution was heated and water was added to turbidity. On standing overnight it deposited 3 grams of long pale yellow needles melting at 107°.

Preparation of 9-aminoacridine (147)

Purified acridine (18 g; 0.1 mole) was dissolved in 150 ml. of dimethylaniline placed in a 25 ml. flask fitted with a condenser and a calcium chloride tube. Finely powdered commercial sodium amide (16 g; 0.325 mole) was added and the system heated to 150-160° by means of a heating mantle. This temperature was kept for four hours after which the evolution of hydrogen had almost ceased. The mixture was rapidly filtered and washed with 25 ml. of ether, previously dried over sodium wire, to eliminate most of the dimethylaniline. The solids were then added portionwise to 200 ml. of ice water while stirring rapidly. After standing for 2 hours the brownish solids which had settled at the bottom of the flask were filtered and dried. The product was dissolved in 50 ml. of ethanol at room temperature, decolorizing charcoal added and the solution boiled for a few minutes. The carbon black was filtered, the solution again brought to boiling and water added to turbidity. On cooling 12 grams of

yellow crystals deposited melting at 227°. Yield: 61.5%. Further purification could be achieved by the following method. The material was dissolved in 10 ml. of concentrated sulphuric acid and poured in an equal volume of water. The resulting precipitate was filtered, dissolved in 50 ml. of hot water, filtered again and the solution made alkaline with a dilute sodium hydroxide solution. The 9-aminoacridine thus treated melted at 231-232°.

Nitration of 9-aminoacridine

One equivalent - Low temperature. 9-Aminoacridine (1 g; 0.0052 mole) was dissolved in 5 ml. of concentrated sulphuric acid. When the solution was complete, which took about fifteen minutes, the temperature was lowered to -15° by means of a dry ice-acetone bath. The nitrating mixture consisting of nitric acid 70% (0.47 g; 0.0052 mole) and 1 ml. of concentrated sulphuric acid was added dropwise with stirring. During this operation the temperature was maintained between -15° and -10°. The reaction mixture was kept at -10° for ten more minutes and then poured on ice. A yellow precipitate formed and was filtered (fraction A). The filtrate made alkaline with ammonium hydroxide, yielded a brown precipitate (fraction B).

Fraction A was suspended in 25 ml. of water and a few ml. of concentrated ammonia added. The solids turned red immediately. Filtered and dried the precipitate weighed 0.75 gram. Yield: 61%. Recrystallized from nitrobenzene the product formed a red crystalline powder melting at 346-347° with decomposition. A few milligrams placed in a 1N alcoholic potassium hydroxide solution gave an instantaneous purple coloration.

Anal. Calc. for $C_{13}H_9N_3O_2$ N, 17.57%

Found: N, 17.75%.

Fraction B was recrystallized twice from 2 ml. of ethanol diluted with three or four drops of water. The final product (0.100 g.), greenish needles which turned red on drying in vacuum melted at 228-229°.

One equivalent - High temperature. 9-Aminoacridine (0.95 g; 0.0049 mole) was dissolved in 5 ml. of concentrated sulphuric acid. The temperature rose to 50°. After cooling to 30° a mixture of nitric acid 70% (0.46 g; 0.049 mole) and 1 ml. of concentrated sulphuric acid was added dropwise with stirring. The temperature rose to 50° and maintained itself for ten minutes. At the end of this period the solution was poured on ice. An abundant yellow precipitate formed and was filtered (fraction A). The pH of the filtrate was brought up to 2.5 by careful addition of dilute sodium hydroxide solution. A second yellow precipitate formed and was isolated (fraction B). The filtrate was made strongly alkaline. A purple precipitate came down and was filtered (fraction C).

Fraction A was placed in 50 ml. of glacial acetic acid. On heating it dissolved almost completely. The insoluble was filtered out and after cooling ammonium hydroxide was added until strongly alkaline. The precipitate filtered and dried weighed 0.987 gram. Yield: 67%. Purification was accomplished by one recrystallization from 25 ml. of nitrobenzene followed by one recrystallization from ethanol. The product decomposed at 346°.

Fraction B was placed in ammonium hydroxide, triturated, filtered

and dried. In this way 0.95 gram of a yellowish solid was obtained melting at 155°. Fraction C was treated in the same way and provided 0.037 gram of a solid melting at 145°. Fractions B and C were combined and several recrystallizations from ethanol gave crystals melting at 230° (starting material).

Excess - Low temperature. 9-Aminoacridine (0.97 g; 0.005 mole) was dissolved in 5 ml. of concentrated sulphuric acid. The dark solution was cooled to -15° by means of a dry ice-acetone bath and a mixture of nitric acid 70% (2.5 ml.; large excess) in 2.5 ml. of concentrated sulphuric acid was added dropwise with stirring. During this addition the temperature was kept between -15° and -10°. After approximately half of the nitrating solution had been added a large amount of solid precipitated. Three minutes after completion of the addition the mixture was poured into 75 ml. of ice water. The abundant yellow precipitate was filtered (fraction A). The filtrate was made alkaline with a dilute sodium hydroxide solution. At a pH of 6.5 a large amount of yellow precipitate had formed which turned purple when the pH was further raised. The solids were filtered (fraction B).

Fraction A was dissolved in 500 ml. of methanol and one gram of solid sodium hydroxide added. The solution turned purple. It was evaporated to half its volume and 50 ml. of water added. On cooling brick-red crystals formed which were filtered and dried. The material (0.95 g.) was recrystallized twice from ethanol. A melting point of 346-347° was registered and the infrared spectrum was identical to that of the product obtained by the low temperature mononitration of 9-aminoacridine. Yield: 80%.

Fraction B recrystallized twice from ethanol gave 0.175 gram of a compound melting at 288-289°, and whose infrared showed it to be different from fraction A. The compound had an amino group as proved by bands at 3270 $cm.^{-1}$ and 3370 $cm.^{-1}$

Excess - High temperature. 9-Aminoacridine (0.3 g; 0.0016 mole) was dissolved in 2 ml. of concentrated sulphuric acid and one ml. of nitric acid 70% added. The mixture was left at room temperature for twenty minutes and then poured in 20 ml. of ice water. The yellow precipitate was collected, dissolved in 50 ml. of boiling water and made alkaline with ammonium hydroxide. The brick-red precipitate which formed (0.06 g.) was recrystallized from ethanol to give a substance melting at 368-370° (dec.). Yield: 16%.

The filtrate made alkaline produced a red precipitate which was recrystallized from ethanol to give 0.2 gram of an aminotrinitroacridine whose melting point and infrared spectrum were identical with those of fraction B isolated from the nitration at low temperature with an excess of reagent. Yield: 42.5%.

Anal. Calc. for $C_{13}H_6N_6O_8$ C, 47.42; H, 2.14; N, 21.27%
Found: C, 46.58; H, 2.72; N, 20.57%.

Nitration of 3-aminoquinoline

One equivalent - Low temperature. 3-Aminoquinoline (2 g; 0.0138 mole) was dissolved in 10 ml. of concentrated sulphuric acid at room temperature. The solution was cooled to -15° and the nitrating mixture, nitric acid 70% (1.2 g; 0.0138 mole) in 2 ml. of concentrated sulphuric acid, was added dropwise

with stirring. The yellow solution was stirred for another two minutes, keeping the temperature at -15°, and then it was poured onto 100 grams of ice. There was no precipitation even after standing for one hour. The pH of the solution was brought to 2.5 with 20% sodium hydroxide. An orange oil formed which solidified after fifteen minutes. Filtration and drying produced 1.7 grams of yellow solids. Two recrystallizations from dilute ethanol gave a melting point of 141-142° (dec.). Yield: 65%.

The nitration product (0.1 g; 0.0007 mole) was dissolved in 25 ml. of 30% sodium hydroxide at the boiling point. On cooling bright yellow crystals deposited. They were filtered and dried in a vacuum dessicator. The solids were then dissolved in 20 ml. of ethanol and precipitated out by addition of 5 ml. of chloroform. The white precipitate was recrystallized from 5 ml. of ethanol with 2 ml. of chloroform. White microscopic needles (0.08 g.) formed melting at 294-295°.

Anal. Calc. for $C_3H_6N_3O_2Na$ N, 19.9%

Found: N, 20.15%.

The nitration product (m.p. 141-142°) (0.5 g; 0.0035 mole) was dissolved in 5 ml. of concentrated sulphuric acid at 0°. The solution was then heated to 50° and kept at this temperature for ten minutes. It was poured on 10 grams of ice and made alkaline with sodium hydroxide. The yellow precipitate was collected and recrystallized twice from dilute ethanol. The final melting point was 251-252°.

Anal. Calc. for $C_9H_7N_3O_2.2H_2O$ C, 48; H, 4.88; N, 18.66%

Found: C, 48.19; H, 4.79; N, 19.37%.

One equivalent - Room temperature. 3-Aminoquinoline (2 g; 0.0138 mole) was dissolved in 10 ml. of concentrated sulphuric acid at room temperature. After cooling to -15° a mixture of nitric acid 70% (1.2 g; 0.0138 mole) in 2 ml. of concentrated sulphuric acid was added dropwise with stirring. The temperature was allowed to rise to 25°. At the same time the colour changed from light yellow to dark orange. It was poured on ice after fifteen minutes. An orange precipitate formed. It was collected and recrystallized twice from dilute ethanol (0.95 g.). A melting point of 251-252° was registered. Yield: 36.5%.

The acidic filtrate was brought to pH 2.5 with sodium hydroxide. The orange precipitate which formed was collected and recrystallized from dilute ethanol (0.37 g.). m.p. 141°. Yield: 14%.
Total Yield: 50.5%.

Excess - Low temperature. 3-Aminoquinoline (2 g; 0.0135 mole) was dissolved in 10 ml. of concentrated sulphuric acid at room temperature. The system was cooled to -15° and the nitrating mixture, nitric acid 70% (5 ml.; large excess) in 5 ml. of concentrated sulphuric acid was added dropwise with stirring over a period of fifteen minutes. At the end of the addition the orange mixture had a pasty like appearance. The reaction was allowed to proceed for two more minutes and was subsequently poured on 100 ml. of ice water. An orange precipitate formed after a few minutes. It was filtered and dissolved in one liter of boiling water. On standing overnight orange needles mixed with some amorphous material deposited (1.65 g.). These were dissolved in 30 ml. of ethanol, heated with charcoal and after

elimination of the latter 20 ml. of water was added to the boiling solution. On cooling and standing for a few hours copper like needles formed. With fast heating the material exploded at 173°, but slow heating resulted in slow decomposition starting around 160°. Yield: 51%.

Anal. Calc. for $C_9H_6N_4O_4$ C, 46.4; H, 2.6; N, 23.2%

Found: C, 46.3; H, 2.87; N, 22.93%

The nitration product (0.1 g; 0.0004 mole) was dissolved in 15 ml. of sodium hydroxide 5% at the boiling point. It was allowed to cool and three pellets of sodium hydroxide were added. Precipitation of a yellow material followed. It was recrystallized three times from n-butyl alcohol to give 0.1 gram of crystals of the sodium salt exploding at 311°. Yield: 92%.

The sodium content was determined by oxidizing the organic material with boiling sulphuric acid and weighing the sodium sulphate formed.

Calc. for $C_9H_5N_4O_4Na$ Na, 9%

Found: Na, 8.7%.

Excess - High temperature. 3-Aminoquinoline (1 g; 0.007 mole) was dissolved in 5 ml. of concentrated sulphuric acid. The solution was cooled to -15° and addition of nitric acid 70% (2.5 ml.; large excess) in 2.5 ml. of concentrated sulphuric acid was carried out dropwise with stirring. The temperature was allowed to rise to 20° and the colour of the solution changed progressively from yellow to dark red. The temperature continued to rise spontaneously to 75°, with considerable evolution of white gases. After half an hour, the solution was poured on ice. The orange precipitate which formed was filtered and dried (0.11 g; fraction A). The filtrate on

standing deposited more solids (0.1 g; fraction B). After elimination of the latter the filtrate was made alkaline with solid sodium carbonate. This operation produced a gum which could not be purified. Fractions A and B were combined and recrystallization from dilute ethanol gave a material exploding at 173°. Yield: 12.9%.

Purification of commercial anthracene (148)

Anthracene was purified according to the following method for infrared spectroscopy purposes.

Preparation of anthracene dibromide. Crude anthracene 90% (10 g.) was dissolved in 50 ml. of hot pure carbon tetrachloride. The solution was cooled to 0° and treated with 4 ml. of bromine added portionwise. A precipitate started to form almost immediately. The reaction mixture kept at 10° was allowed to stand in the sunlight for one hour. The solids were then filtered and dried. Recrystallization from 150 ml. of benzene to which 100 ml. of petroleum ether (b.p. 60-115°) had been added gave colourless plates with a greenish tinge (3 g.). Yield: 20.5%.

Decomposition of the dibromide. Anthracene dibromide (3g.; 0.0115 mole) was placed in 60 ml. of ethanol and 2.25 g. of Zn was added. The mixture was kept at 55° for fifteen hours and then filtered hot. The filtrate was evaporated to half its volume and the white plates which formed were recrystallized from ethanol (2 g.). Yield: 98%.

SUMMARY AND CONTRIBUTIONS TO KNOWLEDGE

1. The cyclization of 2-amidobiphenyl with polyphosphoric acid was extended to the preparation of 6-methylphenanthridine, 6-methyl-2-nitrophenanthridine and 6-ethylphenanthridine. A mechanism was proposed for the cyclization.

2. A new substance, 2-(diacetylamino)biphenyl, was obtained and its structure ascertained.

3. Phenanthridine N-oxide was shown to be easily prepared by the action of monoperphthalic acid on phenanthridine at room temperature.

4. Phenanthridine N-oxide was reduced to phenanthridine with phosphorus tribromide and rearranged to phenanthridinone with acetic anhydride.

5. The nitration of phenanthridine N-oxide was studied in acetic acid and acetic anhydride. It was shown that in all cases one product formed and that its structure was that of 2-nitrophenanthridinone. The best yields were obtained with three equivalents of 70% nitric acid. The rate of the reaction depended on the concentration of the reagents. A mechanism consistent with all the experimental data was proposed.

6. The synthesis of 2-nitrophenanthridinone was improved appreciably.

7. 6-Methylphenanthridine was nitrated to give the unknown 6-methyl-4-nitrophenanthridine, identified by oxidation to the corresponding phenanthridinone, and a dinitro compound. The presence of 6-methyl-4-nitrophenanthridine was accounted for.

8. 6-Aminophenanthridine was nitrated under various conditions. A product identified as 6-amino-7-nitro- or 6-amino-9-nitrophenanthridine was isolated. The evidence from infrared spectroscopy indicated that the nitro group was located in the 9 position. A dinitro compound was also obtained. The absence of nitramine was explained in terms of the spectroscopic data.

9. A study of the nitration of 9-aminoacridine showed that 9-amino-2-nitroacridine and 9-amino-2,4,7 trinitroacridine were formed. The absence of any nitramine was accounted for.

10. The low temperature nitration of 3-aminoquinoline gave a substance identified as 3-nitrimino-(1H) quinolinium betaine. Rearrangement produced a compound whose structure is probably that of 3-amino-7-nitroquinoline. Dinitration afforded 3-nitrimino-7-nitro-(1H) quinolinium betaine, not rearrangeable. The sodium salts of both nitrimino compounds were prepared.

11. The infrared spectra of 26 substances were recorded and discussed. It was shown that a number of bands appearing in the 2000-1650 $cm.^{-1}$ region of phenanthrene, phenanthridine, 6-methylphenanthridine, anthracene and acridine can be explained as combinations of the bands found between 1000-700 $cm.^{-1}$

12. Investigations in carbon tetrachloride solution of the 1850 $cm.^{-1}$ band of phenanthridine and the 1958 $cm.^{-1}$ band of methylphenanthridine showed that both these absorption maxima follow Beer's Law up to concentrations of 50 mg. per ml.

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