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The Synthesis and Diazotization of
Some Aminophenanthrenes

by

Tommy Clark Singleton

A THESIS
SUBMITTED TO THE FACULTY
IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
Doctor of Philosophy

Houston, Texas
May, 1954
ACKNOWLEDGMENT

The author wishes to express his sincere appreciation to Dr. E. S. Lewis who conceived this problem and guided the work to its completion.
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INTRODUCTION

Diazonium salts were first prepared by Griess (1) in 1858 by the reaction of aromatic amines and nitrous acid. In a series of later publications (2) he reported that phenols and aromatic halides are formed by the decomposition of these diazonium salts. However it was not until 1884 that Sandmeyer discovered the ability of cuprous salts to catalyze the conversion of diazonium salts to aryl chlorides and aryl bromides (3). Since this time this reaction, which bears his name, has been used in most of the preparative work involving the replacement of the diazonium group by these atoms. From the time of their discovery until the present time these reactions have been the object of the study of many organic chemists. The original purpose of this research project was to offer new evidence for the mechanism of these reactions.

The decomposition of diazonium salts in aqueous media in the absence of a metallic catalyst may in general be formulated stoichiometrically:

\[
\text{ArN}_2\text{X} + \text{H}_2\text{O} \rightarrow \text{ArOH} + \text{N}_2 + \text{HX}
\]  

(1)

where \( \text{Ar} \) represents an aromatic nucleus and \( \text{X} \) an acid radical. In cases where \( \text{X} \) is a halogen varying amounts of the aryl halide may result from the reaction.
\[
\text{ArN}_2\text{X} + \text{ArX} + \text{N}_2
\]  \hspace{1cm} (2)

The Sandmeyer reaction may be represented as:

\[
\text{ArN}_2\text{Y} \xrightarrow{\text{CuY}} \text{ArY} + \text{N}_2
\]  \hspace{1cm} (3)

where \(Y\) is chloride, bromide or cyanide. The diazonium iodides react to produce aryl iodides in the absence of a copper catalyst.

Diazonium salts can be decomposed in alcohols and organic acids to give respectively aryl alkyl ethers and aryl esters \((4, 5, 6)\).

\[
\text{ArN}_2\text{X} + \text{ROH} \rightarrow \text{ArOR} + \text{EX} + \text{N}_2
\]  \hspace{1cm} (4)

\[
\text{ArN}_2\text{X} + \text{RCOOH} \rightarrow \text{RCOAr} + \text{HX} + \text{N}_2
\]  \hspace{1cm} (5)

The most important side reactions are the reduction to hydrocarbons, formation of biphenyls and formation of azo compounds. The production of azo compounds usually is more favorable in alkaline solutions than in acidic media.

The first attempt at formulating a mechanism for the uncatalyzed decomposition of diazonium salts was made in 1900 by Hantzsch \((7)\) who suggested that the reaction proceeds via an addition product of the diazonium salt and hydrogen chloride. This then decomposes to the azohalide followed by elimination of nitrogen to give the aryl
halide.

\[
\begin{array}{cccccc}
\text{Ar} & \text{Cl} & \text{Ar} & \text{Cl} & \text{Ar} & \text{Cl} \\
\text{N≡N} & + & \text{N≡N} & + & \text{N≡N} & + \\
\text{Cl} & \text{H} & \text{Cl} & \text{H} & \text{Cl} & \text{H} \\
\end{array}
\]

This mechanism is unfavorable on the basis of modern structural theories.

More recently Pfeil (8) has postulated a mechanism for this reaction which is nothing more than a modification of the mechanism of Hantzsch. He suggested that a solvated diazonium ion is converted to a covalent diazohalide which loses nitrogen to form a neutral aryl radical and halogen atom which then react to give the aryl halide.

The phenols are said to be formed by a similar reaction of water molecules on the diazonium ions. The only experimental evidence which Pfeil offered to support this mechanism is the ratios of p-nitrophenol and p-nitrochlorobenzene formed in the presence of varying chloride ion concentrations and at different pH's. However this evidence is of doubtful validity because of his unreliable methods of product analysis. For a better discussion of Pfeil's work see the Ph.D. thesis of W. H. Hinds (9).

In disagreement with the bimolecular mechanisms of Hantzsch and Pfeil is the fact that the decomposition of benzenediazonium ion in dilute water solution is found to be a first-order reaction in the diazonium salt (10). It has been shown that in moderate concentra-
tions other ions have very small effects on the rate of the reaction (6). This kinetic evidence has led Waters (11) to propose an $S_N1$ type mechanism (12) involving a rate-determining decomposition of the diazonium ion with loss of nitrogen to form a phenyl cation. This cation then reacts rapidly with water or chloride ion to give respectively phenol or chlorobenzene.

$$\text{C}_6\text{H}_5\text{N}_2^+ + \text{N}_2 \rightarrow \text{C}_6\text{H}_5^+ + \text{N}_2$$  \hspace{1cm} (7)

$$\text{C}_6\text{H}_5^+ + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_5\text{O}_2^+ + \text{C}_6\text{H}_5\text{OH} + \text{H}^+$$  \hspace{1cm} (8)

$$\text{C}_6\text{H}_5^+ + \text{Cl}^- \rightarrow \text{C}_6\text{H}_5\text{Cl}$$  \hspace{1cm} (9)

One objection to this mechanism is the fact that the phenyl cation formed is not stabilized by the type of resonance available in other compounds where reactions are believed to proceed by this type of mechanism. However the formation of the stable nitrogen molecule may compensate for the lack of stability of this phenyl cation. Waters points out that this is the only reaction that the diazonium cation can undergo in which nitrogen is lost without an electron transfer from outside the ion. He neglected to mention the possibility of an $S_N2$ type of displacement (12) of nitrogen by water, which in this case could not be distinguished kinetically from the $S_N1$ mechanism.
In a recent publication Lewis and Hinds (13) reported that a second-order displacement of nitrogen from p-nitrobenzenediazonium fluoborate takes place in the presence of large concentrations of bromide ion. From this evidence it may be concluded that both SN1 and SN2 displacements of nitrogen can occur in this reaction. It has been demonstrated that in numerous other cases nucleophilic displacement reactions in aromatic systems are enhanced by the presence of an electron withdrawing substituent in the para position (14). The decrease in electron density of the aromatic ring could also inhibit the release of electrons to the nitrogen and thus decrease the rate of the first-order decomposition of the diazonium ion. This electron withdrawing effect of the nitro group may explain why a second-order reaction is noticed in this case but not in the case of the unsubstituted benzenediazonium salts.

At this same time Lewis and Miller (15) investigated the effect of different alkyl substituents on the rate of decomposition of benzenediazonium salts. They observed in para alkyl compounds the order 
\[ \text{H} > \text{t-butyl} > \text{s-butyl} > \text{isopropyl} > \text{methyl}. \]
They found that although meta alkyl substituents enhanced the decomposition of diazonium salts, the order of reactivity of t-butyl faster than methyl was observed in this series also.

The fact that para alkyl compounds react more slowly than the unsubstituted diazonium salts could be explained by the stabilization of the diazonium ion by the following type of resonance.
This concept of hyperconjugation has been used to explain other effects of alkyl groups (16). Since this resonance cannot take place in the meta alkyl compounds the accelerating effect of these substituents might be explained on the inductive effect alone. The increase in electron density of the ring due to the inductive effect of these groups may enhance the release of electrons to the nitrogen and form a more stable aryl cation. However no definite conclusion about the relative effects of the different alkyl groups could be made because it was found that the entropies of activation for these substituents are not constant. Hammett (17) has shown that the entropies of activation must be constant for the different groups in a series of reactions of this type in order to hold the potential energy effects responsible for the differences in rates of the reactions.

In a recent publication DeTar and Relyea (18) have presented further evidence for the existence of both the $S_N1$ and $S_N2$ mechanisms in this reaction. They found that when 2-benzoylbenzenediazonium fluoroborate ($R_1 = R_2 = H$) was thermally decomposed in acidic solution, 2-hydroxybenzophenone and fluorenone were produced.
They found that the 4′-methyl derivative (R₁ = H, R₂ = CH₃) also gave the corresponding hydroxybenzophenone and fluorenone in about the same proportions as in the case of the unsubstituted compound. However when the diazonium salt of the 3′-nitro derivative (R₁ = NO₂, R₂ = H) was decomposed, the yield of the hydroxybenzophenone was greatly increased while the yield of the fluorenone was much lower. This was offered as evidence for the primary formation of an aryl cation which then reacted to give the phenol or fluorenone. In the case of the 3′-nitro derivative the nitro group deactivates the ring to electrophilic substitution and therefore a higher yield of the hydroxybenzophenone resulted.

This 4′-methyl derivative was also decomposed in 6.2 M sodium chloride and found to give some 2-chloro-4′-methylbenzophenone and a lower yield of 2-hydroxy-4′-methylbenzophenone but the yield of the fluorenone did not differ from that produced in the absence of chloride ion. This would indicate that there was no S_N2 displacement
of nitrogen by chloride ion. However when this reaction was carried out in the presence of the same concentration of bromide ion, a larger yield of the halogen derivative resulted and the yield of the fluorenone decreased. This indicates that some S_N2 displacement by the more nucleophilic bromide ion may be occurring in this case.

The mechanisms that have been proposed for the more complex Sandmeyer reaction (19, 20, 21) fall into two classes - the free radical mechanism and the ionic mechanism.

Hodgson (21) has suggested that the nitrogen of the diazonium group undergoes an S_N2 displacement by a cuprous halide complex and Cowdry and Davies (19, 20) have proposed the formation of a complex of the diazonium ion and a CuCl_2^- ion which then reacts further to give the aryl chloride.

\[ \text{ArN}_2^+ + \text{CuCl}_2^- \rightarrow (\text{ArN}_2\cdot\text{CuCl}_2) \rightarrow \text{ArCl} + \text{CuCl} + \text{N}_2 \]  

They have also written a series of equations in which this intermediate complexes with another diazonium ion followed by reactions to give the observed by-products.

Waters has suggested that the initiating step in the reaction is the reduction of the diazonium cation to a neutral aryl radical and free nitrogen by the cuprous ion (11). This neutral aryl radical can then react with a halide ion to form the aryl halide with the release of an electron which reduces the cupric ion back to the
cuprous state.

\[ \text{ArN}_2^+ + \text{Cu}^+ \rightarrow \text{Ar}^+ + \text{N}_2 + \text{Cu}^{++} \]  \hspace{1cm} (12)

\[ \text{Ar}^+ + \text{Cl}^- \rightarrow \text{ArCl} + e \]  \hspace{1cm} (13)

\[ \text{Cu}^{++} + e \rightarrow \text{Cu}^+ \]  \hspace{1cm} (14)

Waters suggests that these three steps are occurring simultaneously in the reaction. He justifies this mechanism on the basis of the low oxidation potential of the cuprous ion. Waters offers this same type of mechanism for the replacement of a diazo group by iodine since the oxidation potential of iodine is close to that of the cuprous ion. Also in a recent publication Relyea and DeTar (22) suggested that the Sandmeyer reaction goes at least in part by a free radical mechanism. As evidence for this they reported an intramolecular chain transfer in the Sandmeyer reaction on diazotized 2-amino-4'-methyl-benzophenone.
The production of these two isomers can be explained most readily on the basis of free radical intermediates.

The original purpose of this research project was to prepare a compound in which stereochemical evidence could be used to determine whether these reactions proceeded by way of a back side displacement of nitrogen or by way of an intermediate which would lead to racemization of the product. Newman (23, 24) has described a type of optical activity resulting from the substitution of alkyl groups in the 4- and 5- positions of phenanthrene. This optical activity results from these substituents being forced out of the plane of the phenanthrene nucleus because of steric hindrance and thus forming an asymmetric molecule.

Models of 4-amino-5-methylphenanthrene (Figure 1) have shown that there is enough hindrance between these two groups that they are forced out of the plane of the aromatic rings in the same manner as in 4,5-dimethylphenanthrene and therefore it is theoretically capable of
possessing optical activity. It was hoped to resolve this compound into its optical isomers and then observe whether the products from the diazonium salts were optically active. By this method it might be possible to determine whether nitrogen is displaced in a manner in which the asymmetry of the molecule is retained or in a manner which leads to racemization of the product.

If the reactions of the diazonium salt from this amine had shown promise, a greater effort would have been made to resolve the amine. However the desired products were not obtained from this reaction and also the first attempts to resolve the amine proved to be unsuccessful so this project was not pursued further. It was found however that some information about the uncatalyzed decomposition of the phenanthrenediazonium salts could be obtained by comparing the rates of evolution of nitrogen from diazotized 4-amino-5-methylphenanthrene and the less hindered 4-phenanthrenediazonium salt. Also this steric hindrance between the groups in the 4- and 5- positions led to an interesting study of this effect on the acid and base strengths of some acids and amines in the phenanthrene series.

In 1944 the concept of B-strain was introduced by H. C. Brown (25) to explain the relatively weak base strength of trialkylamines as compared to mono- and dialkylamines. Brown suggested that in trivalent nitrogen derivatives the bond angles are slightly greater than the normal tetrahedral angles because the fourth position in the valence shell is not occupied. However when a fourth group is added
to this position, the nitrogen atom is forced toward a tetrahedral configuration. In the case of ammonia, methylamine and dimethylamine the molecules are unhindered and thus the bond angles can approach the tetrahedral configuration. In this case the base strength increases on going from ammonia to dimethylamine due to the negative inductive effect of the alkyl groups. However trimethylamine is found to be almost as weak as ammonia. Brown explains this on the basis that the nitrogen cannot approach the tetrahedral configuration so easily in this case as in the other less substituted amines because of hindrance from the alkyl groups. Since the hindrance in this case is from the back of the nitrogen the term "B-strain" is applied. It might be noted that this B-strain depends only on the steric requirements of the amine involved and is independent of the steric requirements of the acid.

At this same time Brown introduced the term "F-strain" to explain the base weakening effect caused by the steric requirements of both the amine and the acid. He found that if the proton is used as the comparison acid, $\alpha, \alpha'$-lutidine is a stronger base than pyridine. However the reverse order of acidity is noticed if boron trifluoride is used as the acid, and $\alpha,\alpha'$-lutidine shows no basic properties whatever toward trimethylboron. Since the approach of these large acids is hindered by a face-to-face interference of these bulky groups, the term F-strain was applied to this effect.

However in 1948 Spitzer and Pitzer (26) calculated the strain
energy in ammonia, methyamine, dimethylamine and trimethylamine by spectrographic data and found that the B-strain involved in these molecules is very small. This suggestion that B-strain is unimportant has recently been confirmed by Pearson and Williams (27) who made some rate studies on the reactions of some amines with nitroethane. In this work they found that although triethylamine is a weaker base in aqueous solutions than either ethylamine or diethylamine, the rate of reaction of these amines with nitroethane is in the order: triethylamine > diethylamine > ethylamine. This indicates that the basicity toward nitroethane is governed only by the inductive effect of the alkyl groups. They suggested that the weakly basic character of trialkylamines in aqueous solutions is simply due to hindrance involved in solvation of the trialkylammonium ion and not due to B-strain as suggested by Brown.

In this same work Pearson and Williams demonstrated this solvation effect more conclusively by determining the base strength of the methylanilines in different solvents. They found that in ethanol, a good solvating material, the basicity is in the order aniline > N-methylaniline > N,N-dimethylaniline. However in m-cresol and chloro-benzene this order of base strength is reversed. This reverse order of basicity cannot be explained by B-strain alone since this effect should not change on going from polar to non-polar solvents. This hindrance to solvation might be regarded as another example of F-strain.

Part of this research project was devoted to determining the
acid base strengths of some hindered phenanthroic acids and phenanthrylamines. From the acid and base strengths of some of these compounds it was hoped to get more information about the effect of steric hindrance on these properties. In addition to this work this thesis is concerned with the preparation and attempted resolution of 4-methyl-5-phenanthroic acid and 4-amino-5-methylphenanthrene and with the reactions of diazonium salts derived from some aminophenanthrenes. A small amount of time was also given to the investigation of the specific adsorption properties of specially prepared silica gel as a means of resolution of optically active compounds.
II
DISCUSSION

Pyrene was used as the starting material for the preparation of 4-methyl-5-phenanthroic acid and 4-amino-5-methylphenanthrene. The synthesis is a modification and refinement of the method used by L. L. Bott (28). On ozonolysis of pyrene and reduction of the ozonide with hydrogen over platinum oxide, 4,5-phenanthrenedialdehyde was formed. This aldehyde was not isolated in this work but was previously isolated from this reaction and identified by Bott (28). The dialdehyde was converted to the sodium salt of 4-hydroxymethyl-5-phenanthroic acid by the Cannizzaro reaction. On acidification, the lactone (I) of this acid was formed. Also produced from this reaction was a small amount of 5-formyl-4-phenanthroic acid (II) which Fieser (29) synthesized by the ozonization of pyrene. It was later shown by Badger and co-workers (30) that this compound exists as the pseudo acid rather than the true aldehyde acid.

The lactone of 4-hydroxymethyl-5-phenanthroic acid (I) was found to be reduced by hydrogen in the presence of large quantities of platinum oxide catalyst to 4-methyl-5-phenanthroic acid (III). A better method suggested by Dr. M. S. Newman was the reduction of a solution of the lactone of 4-hydroxymethyl-5-phenanthroic acid with hydrogen over palladium chloride and charcoal. The yield of acid was higher in the latter case. Infrared spectra and a mixed melting point showed
these two acids to be identical. By further reduction over the same 
palladium catalyst, 9,10-dihydro-4-methyl-5-phenanthroic acid (IV) 
was formed.

The Curtius reaction (31) was chosen for the conversion of this 
acid (III) to 4-amino-5-methylphenanthrene (V) since sulfonation of 
the phenanthrene nucleus would likely take place under the conditions 
of the Schmidt reaction (32). The method used in this reaction was 
the conversion of the acid chloride to the acid azide and thermal 
de decomposition to the isocyanate. The amine was obtained by conversion 
of the isocyanate to the ethyl urethane followed by alkaline hydrolysis. 
This same method was used for the conversion of the dihydro acid (IV) 
to 9,10-dihydro-4-amino-5-methylphenanthrene (VI). These phenanthrene 
derivatives all have typical phenanthrene absorption spectra in the 
ultraviolet region (Figure 3) while the dihydro acid (IV) has an ultra-
violet absorption spectrum similar to that of 9,10-dihydrophenanthrene 
(Figure 4). The reactions involved in the preparation of these com-
 pounds are given on the flow sheet on the following page. The paren-
thetical Roman numerals correspond to those given for the above-men-
tioned compounds.

The syntheses of 1-aminophenanthrene (VII) and 4-aminophenanthrene 
(VIII) were accomplished by the method of Langenbeck and Weissenborn 
(33) who prepared these amines by treating the oximes of 1- and 4-
ketoo-1,2,3,4-tetrahydrophenanthrene respectively with hydrogen chloride
\[ \text{Ozonide} \xrightarrow{\text{H}_2/\text{PtO}_2} \text{(II)} \text{ m.p. 274-276°} \]

\[ (I), 33.5\% \text{ m.p. 176-177°} \]

\[ (I) \xrightarrow{\text{H}_2/\text{PdCl}_2} \text{COOH} \xrightarrow{\text{C}_2\text{H}_5\text{OH}} \text{Curtius} \]

\[ (III), 84.5\% \text{ m.p. 236-237°} \]

\[ (IV), 94\% \text{ m.p. 204.5-206.0°} \]

\[ 2 \xrightarrow{\text{H}_2/\text{PdCl}_2} \text{COOH} \xrightarrow{\text{C}_2\text{H}_5\text{OH}} \text{Curtius} \]

\[ (V), 70\% \text{ m.p. 112-114°} \]

\[ (VI), 82\% \text{ m.p. 59-62°} \]
and acetic anhydride in acetic acid solution.

An attempt was made to resolve 4-methyl-5-phenanthroic acid into its optical isomers by forming the salts of a number of optically active bases. However only in the case of 1-quinine could a crystalline salt be obtained, but this salt was insoluble in all solvents tried and could not be recrystallized. The salt obtained by mixing one mol of quinine with two mols of the acid only gave a racemic acid when hydrolyzed with alkali. In the case of the other bases a crystalline salt could not be obtained.

When equivalent amounts of 4-amino-5-methylphenanthrene and d-camphor sulfonic acid were dissolved in ethanol and cooled, only the free amine crystallized. This difficulty in forming a salt presumably is due to the weakly basic character of the amine which will be discussed later. Attempts to form a salt with d-dibenzoyltartaric acid also failed.

When equivalent amounts of the amine and d-camphor sulfonic acid were dissolved in anhydrous non-polar solvents, a solid material slowly crystallized. However treatment of this compound with alkali gave a solid material which was insoluble in water and organic solvents. On further examination this material proved to have all the characteristics of a ketimine. This ketimine could be produced by the reaction of the amino group and the carbonyl oxygen of the camphor sulfonic acid.
The sodium salt of this compound could be expected to be insoluble in water because of its high molecular weight. This type of compound has been reported by Schreibner and Shriver to be formed under equilibrium conditions from the camphor sulfonate salts of other primary amines in anhydrous solvents. A solution of this compound in anhydrous ethanol was found to have a high negative rotation which did not change over a period of several hours. However when 80% ethanol was used as a solvent, a slow mutarotation to a dextrorotatory value was observed. This observation may be explained by the hydrolysis of the ketimine to the amine and d-camphor sulfonic acid in the presence of water. If this compound were the camphor sulfonate salt of the amine, the mutarotation to the value of d-camphor sulfonic acid would be expected in anhydrous ethanol as well as in 80% ethanol.
Since this amine could not be resolved by recrystallization of the camphor sulfonate salt, an attempt was made to resolve it by chromatographic adsorption on an optically active adsorbent. One method tried was chromatography on sucrose but this was unsuccessful. One reason for the failure in this case might be due to the low adsorption power of sucrose. The method used was based on that of Prelog (35) who resolved Tröger's base by chromatographic adsorption on lactose.

Another adsorbent used in this attempted chromatographic resolution was silica gel which was prepared in a manner that was expected to give it an optically active surface. It has been demonstrated by Dickey (36) that silica gel prepared by precipitating silicic acid from a sodium silicate solution in the presence of methyl orange had a greater adsorption affinity for methyl orange than for ethyl orange (p-diethylaminophenylazobenzene-p'-sulfonic acid), propyl orange or butyl orange. Also in the case of the other dyes the silica gel had a greater adsorption affinity for the dye in the presence of which it was precipitated than for the other dyes. An investigation was conducted to determine whether silica prepared in the presence of an optically active compound in this manner would exhibit a similar effect in adsorbing one optical isomer more tenaciously than its optical antipode.

It was found that silica gel precipitated in the presence of
d-camphor sulfonic acid failed to resolve 4-amino-5-methylphenanthrene by a chromatographic method similar to that used in the case of the sucrose. Also attempts to resolve dl-camphor sulfonic acid and α-phenylethanol by this method were unsuccessful. The only indication that the surface of the silica gel was influencing the adsorption under these conditions was the observation that α-phenylethanol was absorbed to a greater degree on the silica precipitated in the presence of l-ephedrine than on that from the d-camphor sulfonic acid. This may be explained by the fact that ephedrine has a structure more closely related to that of α-phenylethanol.

Finally this experiment was repeated by preparing the silica in the presence of d-α-phenylethylamine and using this silica in an attempt to resolve dl-α-phenylethylamine but again this experiment failed. Since this seemed to be a very favorable case for resolution, this project was pursued no further.

The pK's of the acids and amines in this series of compounds were determined in the hopes of obtaining more information about the effect of steric hindrance on these properties. The pKa's of the acids studied were determined in 60% ethanol (by volume) and are listed in Table 1. The pKa of benzoic acid was measured in this solvent as a reference acid. These pKa's are the pH's of half neutralized solutions of the acids.
TABLE 1

<table>
<thead>
<tr>
<th>Acid</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzoic acid</td>
<td>6.08</td>
</tr>
<tr>
<td>4-Methyl-5-phenanthroic acid</td>
<td>6.12</td>
</tr>
<tr>
<td>9,10-Dihydro-4-methyl-5-phenanthroic acid</td>
<td>6.25</td>
</tr>
</tbody>
</table>

In aromatic acids in which the carboxyl group is attached directly to the ring the following acid weakening resonance may take place:

\[
\begin{array}{c}
\text{O-H} \\
\text{C} \\
\text{O} \\
\end{array} \quad \leftrightarrow \quad + \begin{array}{c}
\text{O-H} \\
\text{C} \\
\text{O} \\
\end{array}
\]

This increase in electron density of the carboxyl group causes the proton to be released with greater difficulty than if this resonance did not exist. However the negative inductive effect of the phenyl group tends to offset this resonance effect and thus it is seen that benzoic acid is of the same order of base strength as acetic acid.

It is found that if a methyl group is placed in the para position to the carboxyl group, the acidity is weakened by the electron
donating effect of the methyl group.

Also a methyl group in the meta position slightly decreases the acidity due to electron donating inductive effect of the methyl group. However when the methyl group is in the ortho position to the carboxyl group, the acid strength is enhanced (37). This may be explained by the fact that these resonance structures require a planar configuration of the molecule. In the case of the ortho isomer this planar configuration is inhibited by the steric hindrance of the adjacent methyl group and therefore the acid is not weakened by resonance with the aromatic ring to as great an extent as in the unsubstituted compound.

In 4-methyl-5-phenanthroic acid (III) the resonance dampening effect due to steric hindrance of the methyl group may be an acid strengthening factor which does not exist to so large an extent in the 9,10-dihydro analogue (IV). In the case of (IV) the carboxyl group is not hindered so much as in (III) because of the distortion of the ring system due to the dimethylene bridge. Also this dimethyl-
ene bridge (IV) is a meta alkyl group which tends to further weaken the acid. From these effects alone it would be expected that (III) would be a stronger acid than (IV). However because of the small differences in acid strengths and the non-equivalence of the aromatic systems in these acids, no definite conclusion could be made about the importance of these effects.

Resonance with the ring can also be used to explain the weak basicity of aromatic amines as compared to aliphatic amines.

\[
\begin{align*}
\begin{array}{c}
\text{NH}_2 \\ \text{(amine)}
\end{array}
\quad & \leftrightarrow \\
\begin{array}{c}
\text{\textsuperscript{+}NH}_2 \\ \text{(cation)}
\end{array}
\end{align*}
\]

This resonance effect of the amino group is electron donating and therefore the increase in positive character of the nitrogen tends to weaken the base strength of aromatic amines.

The pKa's of the amine hydrochlorides studied were determined in 60% ethanol (by volume) and are listed in Table 2. The pK's of the naphthylamines were determined in this solvent as reference bases. These pKa's are the pH's of half neutralized solutions of the amine hydrochlorides.
TABLE 2

<table>
<thead>
<tr>
<th>Amine Hydrochloride</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Naphthylamine</td>
<td>3.88</td>
</tr>
<tr>
<td>α-Naphthylamine</td>
<td>3.60</td>
</tr>
<tr>
<td>1-Aminophenanthrene</td>
<td>3.45</td>
</tr>
<tr>
<td>9,10-Dihydro-4-amino-5-methylphenanthrene</td>
<td>3.16</td>
</tr>
<tr>
<td>4-Aminophenanthrene</td>
<td>3.09</td>
</tr>
<tr>
<td>4-Amino-5-methylphenanthrene</td>
<td>2.98</td>
</tr>
</tbody>
</table>

In this series of amines there are competing effects on the relative base strengths. In the case of 4-amino-5-methylphenanthrene (V) the resonance of the amino group with the aromatic ring may be dampened to a small extent because of the non-planarity of the system. This resonance inhibition would tend to increase the electron density in the vicinity of the nitrogen and thus enhance its ability to attract a proton. Also the inductive effect of the methyl group would tend to increase the negative character of the ring and exert a base strengthening effect.

This hindrance due to the methyl group however can also be a base weakening factor. It can be seen from models of (V) that the least hindered position of the amino group is the position in which the
unshared pair of electrons is adjacent to the methyl group (Figure 1). Because of this position of the amino group the approach of a proton to the unshared pair of electrons on the nitrogen will be hindered by the methyl group. This is a type of hindrance that corresponds neither to Brown's B-strain nor F-strain. Also the ion formed by the addition of a proton to this amine cannot be solvated easily due to this hindrance. As pointed out by Pearson and Williams (27) this can be a base weakening factor. Because of the small difference in base strengths of (V) and 4-aminophenanthrene (VII) no definite conclusion could be made about the relative importance of these effects.

In the case of the dihydro amine (VI) it can be seen from models (Figure 2) that there is less strain between the amino and methyl groups than in the case of (V) and therefore the effect of steric hindrance should not be so noticeable as in (V). However since these aromatic systems are not equivalent, no conclusion could be drawn from the small difference in these pK's either.

The stronger basic character of 1-aminophenanthrene may be due to the fact that it is the least hindered of the phenanthrylamines studied, although the 1- and 4- positions of the phenanthrene molecule are not structurally equivalent so no direct comparison can be made in this case. However it is seen from these pK values that the general decreasing order of base strength is closely related to the amount of steric hindrance throughout.
When the Sandmeyer reactions were carried out on (VII) and (VIII), small amounts of the corresponding chlorophenanthrenes were isolated from the reactions. The isolation of these halogen derivatives is contradictory to the observation of Bachmann and Boatner (38) who reported that halogen derivatives could not be obtained from the Sandmeyer reactions on the aminophenanthrenes. The 1-chlorophenanthrene had a melting point corresponding to that of the compound which Bachmann and Boatner reported to be produced by the fusion of the complex of mercuric chloride and 1-phenanthrenediazonium chloride (38). The 4-chlorophenanthrene has not previously been reported. Considerable quantities of a dark red material were also isolated from these reactions. These compounds probably are coupling products from the diazonium salt as the phenanthrene nucleus is very susceptible to substitution reactions.

When the diazonium salts of these amines were decomposed in the absence of a copper catalyst, the corresponding phenanthrols were produced along with the same type of dark red neutral by-products. The neutral material from 4-phenanthrenediazonium chloride was subjected to vacuum sublimation with a small amount of orange oil distilling out. It is possible that this orange material contains 4,5-diazapyrene as it would be expected to be more volatile than the coupling products from two mols of the diazonium salt. This compound could be formed by the electrophilic displacement of a proton from the 5-position.
of the phenanthrene nucleus by the terminal nitrogen of the diazo group.

\[ \begin{array}{c}
\text{N=N} \\
\text{N} \\
\text{N=N} \\
\text{N} \\
\end{array} \rightarrow \begin{array}{c}
\text{N=N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\end{array} \rightarrow \begin{array}{c}
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\end{array} + H^+ \] (17)

The ultraviolet and visible spectra of this orange oil failed to reveal any definite information about its structure. On the basis of the bathochromic shifts in the absorption spectra on going from naphthalene to cinnoline (Figure 5) and from phenanthrene to 3,4-benzocinnoline (Figure 6), it would be expected that the spectrum of 4,5-diazapyrene would be shifted to longer wave lengths than that of pyrene since these two compounds bear the same structural relationship as 3,4-benzocinnoline and phenanthrene. It was found that the spectrum of this orange oil extends into the visible region well beyond that of pyrene (Figure 7) but its spectrum in the ultraviolet region bears a closer resemblance to that of phenanthrene derivatives than to pyrene. From this information no definite conclusion could be made about the structure of this material.
In the case of 4-amino-5-methylphenanthrene the only isolable products from both the Sandmeyer reaction and the uncatalyzed decomposition of the diazonium salt were 4,5-methylenephenanthrene and an unidentified brown substance. In neither case could an acidic nor halogen containing compound be isolated from the reaction mixture. The chloride and bromide Sandmeyer reactions and the decomposition in the presence of iodide ion were carried out on this diazonium salt. Also the diazonium salt was treated with cupric chloride in the hopes of obtaining 4-chloro-5-methylphenanthrene but 4,5-methylenephenanthrene again resulted.

Since the failure to resolve this amine into its optical isomers and to obtain the desired products from the diazonium salts made it impossible to gain any stereochemical evidence about these reactions, some kinetic experiments were carried out on the decomposition of the diazonium salts obtained from (V), (VII) and (VIII). No crystalline diazonium fluoborates could be isolated from these compounds so the rate measurements were carried out on the diazotized amines in dilute hydrochloric and acetic acid solutions. It was found that at 26° nitrogen was evolved most rapidly from 1-phenanthrenediazonium chloride and most slowly from 4-phenanthrenediazonium chloride. The first order rate constants at 26° are given in Table 3.
TABLE 3

<table>
<thead>
<tr>
<th>Diazonium Salt</th>
<th>$k \times 10^2$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-Phenanthrediazonium chloride</td>
<td>0.27 ± 0.04</td>
</tr>
<tr>
<td>5-Methyl-4-phenanthrediazonium chloride</td>
<td>1.1 ± 0.3</td>
</tr>
<tr>
<td>1-Phenanthrediazonium chloride</td>
<td>1.8 ± 0.6</td>
</tr>
</tbody>
</table>

The values of the rate constants for the diazonium salts from (V) and (VII) could not be determined accurately because of the rapid rates of decomposition.

Although the decomposition of the 1-phenanthrediazonium ion cannot be compared directly to the others due to the structural nonequivalence of the 1- and 4- positions, a conclusion about the mechanism of this reaction can be made by comparing the kinetic results from the decomposition of the diazonium salts from (V) and (VIII).

If the loss of nitrogen from these compounds were the result of an $S_{N}2$ type of displacement of the nitrogen by a nucleophilic reagent, it would be predicted that the more hindered diazonium ion would react more slowly than the less hindered one. However if the mechanism of this reaction is the primary loss of nitrogen to give an aryl cation
which reacts further to give the observed products, then one would ex-
pect the hindered diazonium ion to react more slowly. This latter
order of reactivity is similar to the observation of Bartlett (39)
who found that the more hindered tertiary alkyl chlorides such as
triisopropylmethyl chloride and tri-t-butyldimethyl chloride undergo
first-order solvolysis more rapidly than t-butyl chloride. This
order of reactivity is also observed in these two diazonium salts.
This may be explained by the theory that the loss of nitrogen from
5-methyl-4-phenanthrenediazonium ion is enhanced by the strained con-
figuration of these groups. Also the stabilization of the diazonium
ion by resonance with the aromatic ring is inhibited because of the
requirements of a planar configuration for this resonance.

The SN1 mechanism for the reactions in this series is also sup-
ported by the fact that 4,5-methylene-phenanthrene is produced from
all reactions involving 5-methyl-4-phenanthrenediazonium salts. The
most likely path for this reaction is the loss of nitrogen to give
the aryl cation which then displaces a proton from the methyl group.
An alternative mechanism for this reaction may be the displacement of nitrogen from the diazonium ion by water to give 5-methyl-4-phenanthrol which then dehydrates to the observed product, but this mechanism is not in agreement with the order of reactivity of these diazonium salts. The intramolecular displacement of nitrogen by the methyl group seems very unlikely because of the poor nucleophilic character of alkyl groups. It has been reported that fluorene is formed by this same type of reaction from diazotized 1-amino-1'-methylbiphenyl (40).

The isolation of 4,5-methylenephenanthrene from the Sandmeyer reactions as well as from the uncatalyzed decomposition of diazotized 4-amino-5-methylphenanthrene might be regarded as evidence for the primary formation of a complex between the diazonium ion and the cuprous halide. The diazo group in this compound may be hindered to the extent that the formation of the complex is prevented and there-
fore the diazonium ion reacts in the same manner as in the absence
of a catalyst. Since Relyea and DeTar (22) offered evidence for the
existence of a free radical intermediate, the mechanism may be the
formation of a complex with the cuprous halide followed by decomposi-
tion to an aryl radical and halogen atom which combine to give the
aryl chloride. The outcome of the experiments conducted in this re-
search gave no further information about this reaction.
III

FIGURES
Figure 1. 4-Amino-5-methylphenanthrene
Figure 2

9,10-Dihydro-4-amino-5-methylphenanthrene
Figure 3. Ultraviolet Spectra

A. Lactone of 4-hydroxymethyl-5-phenanthroic acid (raised one log unit)
B. 4-Methyl-5-phenanthroic acid
C. N-Acetyl-4-amino-5-methylphenanthrene (lowered one log unit)
Figure 4. Ultraviolet Spectra

A. 9,10-Dihydro-4-methyl-5-phenanthroic acid
B. 9,10-Dihydrophenanthrene (lowered one log unit) (41)
Figure 5. Ultraviolet Spectra

A. Cinnoline (42)
B. Naphthalene (lowered one log unit) (43)
Figure 6. Ultraviolet Spectra

A. 3,4-Benzocinoline (44)

a. Phenanthrene (lowered one log unit) (45)
Figure 7. Ultraviolet Spectra

A. Neutral material from diazotized 4-aminophenanthrene
B. Pyrene (raised one log unit)
Figure 8. Decomposition of 1-phenanthrenediazonium chloride at 26°.

\[ k = (1.8 \pm 0.6) \times 10^{-2} \text{ sec}^{-1} \]
Figure 9. Decomposition of 5-methyl-4-phenanthrene-diazonium chloride at 26°.

\[ k = (1.1 \pm 0.3) \times 10^{-2} \text{ sec}^{-1} \]
Figure 10. Decomposition of 4-phenanthrenediazonium chloride at 26°C.

\[ k = (0.27 \pm 0.04) \times 10^{-2} \text{ sec}^{-1} \]
IV
EXPERIMENTAL

A. Physical Measurements

1. Melting points: The melting points were taken in capillary tubes in an aluminum melting point block with a 300° A.S.T.M. partial immersion thermometer. This apparatus was calibrated by comparing the melting points of a series of compounds to the melting points observed for the same samples on a calibrated Hershberg melting point apparatus. Unless otherwise indicated, all melting points reported are corrected by this calibration.

2. Optical rotations: The optical rotations reported were measured on an O.C. Rudolph High Precision polarimeter with sodium and mercury vapor lamps.

3. Ultraviolet and visible spectra: These spectra were measured on a Beckmann Model DU Quartz Spectrophotometer.

4. Infrared spectra: These spectra were taken on a Perkin-Elmer Model 12C Infrared Spectrophotometer.

5. pH measurements: These measurements were made on a Beckmann Model H2 pH meter with standard glass and calomel electrodes.

B. Purification of Materials

1. Pyrene: Equal weights of pyrene (Matheson, pract.) and C.P. picric acid were mixed and crystallized three times from benzene (Baker,
reagent) giving dark red needles of pyrene picrate, m.p. 227-228°. By concentrating the mother liquors and recrystallizing the picrate until the above melting point was reached, a total yield of 85% of pyrene picrate was obtained. The pyrene could be recovered by treating the pyrene picrate with dilute sodium hydroxide and extracting with benzene. After washing the benzene solution with water until free of base and evaporating to dryness, the pyrene was obtained as yellow crystals. This pyrene was further purified by dissolving in dry benzene and passing through a column of Alcoa F-20 alumina. On evaporation of the benzene, the pyrene was recovered in 80% yield as light yellow crystals, m.p. 151.5-152.2°.

2. Solvents: Ethyl acetate (Baker, reagent), used as a solvent in the ozonolysis of pyrene, was passed through a column of Alcoa F-20 alumina before using. A lower yield of the product was obtained by using ethyl acetate which was not treated in this manner. It is possible that the effectiveness of this treatment was simply the removal of acetic acid from the ethyl acetate by the base present in the crude alumina.

For the chromatographic adsorptions petroleum ether (Baker, reagent, b.p. 35-60°) was redistilled before use. The methanol was boiled under reflux over magnesium methoxide for 8 hours and redistilled. The ether was dried over sodium for several hours before using.
C. Preparation of Compounds

1. Lactone of 4-hydroxymethyl-5-phenanthroic acid (I): A solution of 12 g. of pyrene (0.06 mol) in 300 ml. of ethyl acetate and 20 ml. of methanol was cooled to -15° in a salt-ice mixture and treated with a stream of ozone for a length of time calculated to ozonize 80% of the pyrene. The solution of the ozonide was then reduced with hydrogen over 50 mg. of platinum oxide catalyst for 1 hour giving 4,5-phenanthrenedialdehyde. After removal of the catalyst by filtration, the ethyl acetate solution was extracted with dilute sodium bicarbonate and washed with water. The ethyl acetate was replaced with benzene as a solvent by evaporating to a small volume under an atmosphere of nitrogen and diluting with benzene. This operation was repeated three times. The solution was not evaporated to dryness because of the difficulty in getting all the material back into solution.

The benzene solution containing 4,5-phenanthrenedialdehyde was then boiled under reflux with a solution of 15 g. of sodium hydroxide in 200 ml. of water for one hour after which the aqueous layer had a dark brown color. On acidification of the alkaline solution, 7.0 g. of brown crystals of the lactone was obtained. From this reaction 2.1 g. (14.7%) of pyrene was recovered from the benzene solution.

The crude brown material from this reaction was partially dissolved in 150 ml. of boiling benzene and treated with charcoal. After
removal of the charcoal, the solution was cooled to room temperature giving a white flocculent precipitate of pseudo-5-formyl-4-phenanthroic acid (II). After recrystallization from ethyl acetate it melted at 274-276° (uncorr.). Reported in literature: 279-280° (29). The benzene solution was concentrated on a steam bath until crystallization began and then allowed to crystallize overnight at 0-5° giving some more of (II) in addition to some rust colored crystals of (I). These compounds were separated mechanically by swirling the mixture, allowing the crystalline lactone to settle out and then decanting the mother liquor and pseudo acid. By adding the mother liquor to the crystalline material and repeating this operation two more times, a good separation of the lactone and pseudo acid was effected. By concentrating the mother liquors, a total of 5.5 g. of the rust colored lactone was obtained. This product when crystallized twice from 20% acetone in benzene gave 4.7 g. (33.5%) of pure white crystals of (I), m.p. 176-177°.

A sample of this compound was prepared for analysis by vacuum sublimation at 150° and 0.2 mm. Calc. for C_{16}H_{10}O_2: C, 82.04%; H, 4.30%. Found: C, 82.07%; H, 4.36%. (Clark Microanalytical Laboratory).

2. 4-Methyl-5-phenanthroic acid (III): A solution of 4 g. (0.017 mol) of (I) in 500 ml. of absolute ethanol and 2 ml. of 10% palladium chloride in hydrochloric acid was added to 2 g. of charcoal and reduced
with hydrogen at 60° until 0.017 mol of hydrogen above that required for the reduction of the catalyst had been absorbed. At this point the reduction was stopped and after removal of the charcoal and catalyst, the solution was evaporated to dryness leaving the crude acid. This acid was dissolved in ether and extracted with dilute sodium bicarbonate. The sodium bicarbonate extract was then filtered through celite and on acidification gave (III). This sodium bicarbonate extraction was repeated a second time and on acidification gave (III) in 84.5% yield, m.p. 231-233°.

This acid was also prepared by reducing 4 g. of (I) under the same conditions with 1 g. of platinum oxide but (III) was obtained only in 55% yield. A mixture of the acids prepared by these two methods showed no depression in melting point. Also the infrared spectra of mineral oil mulls of these acids were identical.

A sample of (III) was prepared for analysis by recrystallizing twice from a benzene-alcohol mixture and drying at 80° and 0.2 mm. The acid was obtained as white crystals, m.p. 236-237°. Calc. for C₁₆H₁₂O₂: C, 81.34%; H, 5.12%. Found: C, 81.25%, H, 5.40%. (Clark Microanalytical Laboratory).

Neutralization equivalent: Calc. for C₁₆H₁₂O₂, 236; found, 238.

An etheral solution of (III) was treated with diazomethane. After washing the ether solution with dilute sodium bicarbonate and
evaporating to dryness, a gummy yellow solid material was left. After chromatographic adsorption on alumina a gummy colorless material was obtained. This product was assumed to be the methyl ester of (III) although it was not further identified.

3. 9,10-Dihydro-4-methyl-5-phenanthroic acid (IV): This acid was prepared by the reduction of (I) over palladium chloride in the same manner as in the preparation of (III) except that the reduction was allowed to proceed until twice the amount of hydrogen was absorbed as in the other synthesis. (IV) was obtained in 94% yield by precipitation from sodium bicarbonate solution. This acid when crystallized twice from toluene was isolated as white crystals, m.p. 204.5-206.0°.

**Neutralization equivalent:** Calc. for C_{16}H_{14}O_{2}, 238; found, 238.

The ultraviolet spectrum was taken on a 3 x 10^{-5} molar solution of (IV) in absolute alcohol (Figure 4).

4. 4-Amino-5-methylphenanthrene (V): The acid chloride of (III) was prepared by heating 1 g. of (III) on a steam bath with 15 ml. of thionyl chloride for 1 hour after which the excess thionyl chloride was evaporated under reduced pressure. To a cold solution of this acid chloride in 30 ml. of acetone was added a solution of 1 g. of sodium azide (Eastman, pract.) in 3 ml. of water. After standing for 1 hour with frequent agitation, 100 ml. of water was added and then allowed to stand overnight at 0-5°. The acid azide was then
extracted with 100 ml. of benzene and dried for 4 hours over anhydrous sodium sulfate after which it was boiled under reflux on a steam bath for 2 hours. At this time 50 ml. of absolute alcohol was added to the solution and heated an additional 30 minutes. After evaporating to dryness, the residue of ethyl 4-(5-methyl)-phenanthrylurethane was hydrolyzed by heating under reflux with 100 ml. of 1 N sodium hydroxide in 90% methanol for 24 hours. The methanol was then dispelled from the flask by heating on a steam bath and water added giving a precipitate of (V). After vacuum sublimation at 110° and 0.05 mm., and recrystallization from ethanol, 0.61 g. (70%) of (V) was obtained as light yellow crystals, m.p. 112-114°. Calc. for C₁₅H₁₃N: C, 86.92%; H, 6.32%; N, 6.76%. Found: C, 85.93%; H, 6.32%; N, 6.86%. (Clark Microanalytical Laboratory).

Acetyl derivative: m.p. 198-199°. Benzoyl derivative: m.p. 156.5-158.5°.

Since a satisfactory analysis could not be obtained for this amine, the acetyl derivative was prepared by heating (V) with an excess of acetic anhydride. After recrystallization four times from alcohol, N-acetyl-4-amino-5-methylphenanthrene was obtained as white crystals, m.p. 198-199°. Calc. for C₁₇H₁₅NO: C, 81.90%; H, 6.06%; N, 5.62%. Found: C, 81.81%; H, 6.03%; N, 5.68%. (Elek Microanalytical Laboratories, 4763 W. Adams Blvd., Los Angeles 16, Calif.)

5. 9,10-Dihydro-4-amino-5-methylphenanthrene (VI): This com-
pound was prepared from 1 g. of (IV) by the same procedure that was used for the preparation of (V). From the sublimation, 0.72 g. (82%) of the amine was obtained as white crystals, m.p. 59-62°.

6. l-Aminophenanthrene (VII) and 4-aminophenanthrene (VIII):
These amines were prepared respectively from the oximes of 1-keto-1,2,3,4-tetrahydrophenanthrene and 4-keto-1,2,3,4-tetrahydrophenanthrene by the procedure of Langenbeck and Weissenborn (33). Each of the amine hydrochlorides was obtained in 30% yield from the ketone. The free amines were obtained by dissolving the amine hydrochloride in hot dilute hydrochloric acid, filtering and precipitating with ammonium hydroxide. M.p. of (VII): 145-147°; (VIII): 65-66°. The keto-tetra-hydrophenanthenes were prepared by the procedure of Wilds and Close (46).

7. dl- and d-α-phenylethylamine (IX): This compound was prepared and resolved by the methods given in "Organic Syntheses" (47).

D. Attempted Resolution of 4-Methyl-5-Phenanthroic Acid.
Equimolar quantities of (III) and l-brucine were dissolved in methanol but no crystallization was observed on cooling. Only a gummy residue was obtained on evaporation of the solvent. This residue solidified when cooled in liquid nitrogen but melted again when warmed to 0°. Attempted crystallization from ethanol, ethyl acetate, chloroform and ethyl acetate-ethanol and chloroform-iso-octane mixtures failed to give a crystalline salt.
Attempted resolutions with strychnine, ephedrine, cinchonine, cinchonidine and d-α-phenylethylamine produced the same type of gummy materials.

When equimolar quantities of (III) and l-quinine were dissolved in methanol, a crystalline material formed very rapidly. However this substance was insoluble in methanol, ethanol, isopropyl alcohol, ethyl acetate and acetone and could not be recrystallized. After hydrolyzing with sodium hydroxide and removal of the quinine by filtering through celite, the alkaline solution of the acid was found to be optically inactive.

The formation of a salt by mixing 2 mols of (III) and 1 mol of quinine also failed to effect a resolution of (III).

E. Attempted Resolution of 4-Amino-5-Methylphenanthrene.

1. Camphor Sulfonic Acid: Equimolar quantities of (V) and d-camphor sulfonic acid were dissolved in alcohol but only the amine crystallized on cooling. After washing with cold alcohol, this amine was found to be optically inactive in alcohol solution.

The camphor sulfonate salt of (V) was formed by dissolving 0.50 g. of (V) and 0.56 g. of d-camphor sulfonic acid in the minimum amount of hot benzene. After a few seconds the salt precipitated in light yellow crystals. The benzene was then heated to boiling and chloroform added dropwise until the salt dissolved. After cooling overnight no crystallization had occurred so the solution was diluted with iso-
octane and cooled for 2 to 3 days. After this time 0.52 g. of yellow
crystals was isolated. Treatment of this material with sodium hydrox-
ide only produced solid material which was insoluble in both water
and organic solvents.

This material was found to have the following optical rotation
in absolute ethanol: \( l = 1, c = 0.0058 \text{ g./ml.}, \alpha^{25}_{5461} = -0.254^\circ, \)
\( [\alpha]^{25}_{5461} = -43.8^\circ. \) After standing 24 hours the rotation did not change.
A solution of this material in 80% ethanol was found to slowly muta-
rotate to a positive value. These optical rotations are given in
Table 4.

**TABLE 4**

\[ l = 1, c = 0.0103 \text{ g./ml.} \]

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>( \alpha^{25}_{5461} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-0.440°</td>
</tr>
<tr>
<td>2</td>
<td>-0.370°</td>
</tr>
<tr>
<td>3</td>
<td>-0.330°</td>
</tr>
<tr>
<td>11</td>
<td>-0.106°</td>
</tr>
<tr>
<td>13</td>
<td>-0.086°</td>
</tr>
<tr>
<td>17</td>
<td>-0.040°</td>
</tr>
<tr>
<td>21</td>
<td>-0.010°</td>
</tr>
<tr>
<td>26</td>
<td>+0.016°</td>
</tr>
<tr>
<td>36</td>
<td>+0.052°</td>
</tr>
</tbody>
</table>
After 36 hours the solution had become too dark for an accurate reading. Recrystallization of this material from alcohol gave a white solid, m.p. 280-283° (uncorr.).

2. d-Dibenzoyltartaric acid: Equimolar amounts of (V) and d-dibenzoyltartaric acid were dissolved in alcohol but only the amine crystallized on cooling. The same result was noticed when benzene was used as a solvent.

3. Chromatographic adsorption on sucrose: To 50 g. of powdered sucrose was added 100 ml. of hot chloroform and the mixture stirred for several minutes. The sucrose was then separated by filtration and washed with an additional 100 ml. of hot chloroform. After drying at room temperature, the sucrose was thoroughly pulverized and sifted through a 200 mesh sieve. It was then dried at 75° and 0.2 mm. for 12 hours.

A solution of 0.001 g. of (V) in 1 ml. of petroleum ether was added to 30 g. of this sucrose in an ordinary chromatographic column. The column was then eluted with petroleum ether and the eluent collected in 0.5 ml. fractions. By diluting these fractions tenfold and measuring the optical density at 340 mμ, it was found that the bulk of the amine was displaced from the column in the first 5 ml. of the eluent. Since this small amount of (V) was so weakly adsorbed on the sucrose, no attempt was made to resolve a larger quantity of the amine by this method.
F. **pK Determinations.**

The pK's of the acids were determined by titrating a solution of 0.05 g. of the acid in 15 ml. of alcohol and 10 ml. of water with 0.05 N sodium hydroxide in 60% alcohol (by volume). The pKa of the acid was taken as the pH of the solution at the point where half of the acid was neutralized. The pKa's of the amine hydrochlorides were determined in the same manner by titrating a solution of 0.05 g. of the amine in 12 ml. of alcohol, 8 ml. of water and 5 ml. of 0.05 N hydrochloric acid in 60% alcohol with the standard alkali used for the acids.

G. **Diazotization of Amines.**

1. **1-Aminophenanthrene:** A solution of 0.2 g. of (VII) in 10 ml. of acetic acid and 5 ml. of water was cooled in an ice bath and diazotized with a cold solution of the equivalent amount of sodium nitrite. This solution was then diluted with 15 ml. of concentrated hydrochloric acid and 75 ml. of water and allowed to stand at 0-5° for 24 hours. The precipitate which had formed was extracted with ether and the ether extract washed with 6 N hydrochloric acid and then with dilute sodium hydroxide. After drying the ether solution over anhydrous sodium sulfate and evaporating to dryness, a dark red solid material was obtained. The alkaline extract on acidification gave a small amount of impure 1-phenanthrol, m.p. 150-155°. Picrate, m.p. 179-181° (48).
The Sandmeyer reaction was carried out on 0.2 g. of (VII) by diazotizing in the same manner as before and adding a solution of 0.103 g. of cuprous chloride in 5 ml. of concentrated hydrochloric acid. After standing at 0-5° overnight, it was extracted with ether and the ether extract washed with 6 N hydrochloric acid and then with dilute sodium hydroxide. This ether solution was treated with charcoal to remove the red color and evaporated to dryness, leaving a gummy yellow residue. After purification of this material by chromatographic adsorption on base free alumina and recrystallization from alcohol, 0.009 g. (4%) of 1-chlorophenanthrene was obtained, m.p. 121.5-122.5°.

2. 4-Aminophenanthrene: This amine was diazotized in the same manner as in the case of (VII). From 0.2 g. of (VIII) there was isolated a small amount of brown solid which was assumed to be 4-phenanthrol. This material was methylated by treating with dimethyl sulfate and potassium hydroxide in methanol. After chromatographic adsorption on alumina, the 4-methoxyphenanthrene was identified by its picrate, m.p. 185-188° (49).

The neutral red material from this reaction was subjected to vacuum sublimation at 180° and 0.01 mm. with a small amount of orange oil distilling out. The ultraviolet and visible spectra were taken on an alcoholic solution of this oil (Figure 7). The extinction coefficient of this compound was estimated by comparing the optical
density at the absorption maximum with that of the other compounds in this series.

The Sandmeyer reaction was carried out on (VIII) by the same procedure that was used for (VII). From 0.2 g. of (VIII) there was isolated 0.023 g. (11%) of 4-chlorophenanthrene, m.p. 59-60°.

3. 4-Amino-5-methylphenanthrene: This amine was diazotized by the same procedure that was used for (VII) and (VIII). The only isolable products from this reaction were 4,5-methylenephenanthrene and an unidentified brown material. After purification by chromatographic adsorption on alumina, the 4,5-methylenephenanthrene was isolated as white crystals, m.p. 115-117°. Picrate, m.p. 164.5-166.0° (50,51). The ultraviolet spectrum of this compound in an alcoholic solution was identical to that reported by Friedel and Orchin (52).

The chloride Sandmeyer reaction was carried out on this compound in the same manner as for (VII) and (VIII) but the only isolable product from the reaction was 4,5-methylenephenanthrene. The bromide Sandmeyer reaction was carried out on (V) in this same manner by replacing the hydrochloric acid with hydrobromic acid and using an equivalent amount of cuprous bromide, but 4,5-methylenephenanthrene again resulted. This same product was also obtained by treating the diazonium salt with an equivalent amount of potassium iodide. The same product was isolated from the reaction catalyzed by cupric chloride. The yields of 4,5-methylenephenanthrene isolated ranged from 25% in
the case of the broxide Sandmeyer reaction to 60% from the decomposi-
tion of the diazonium salt in the absence of a catalyst.

H. Kinetic Measurements.

The apparatus used for the rate measurements of the decomposi-
tion of the diazonium salts was identical to that described by Lewis
and Hinds (13). The reaction vessel was thermostated at 26° by run-
ing tap water through the system and the nitrogen was collected in
a 10 ml. burette. The rate measurements for all the diazonium salts
were made in the same manner. A solution of 0.1 g. of the amine in
10 ml. of acetic acid and 5 ml. of water was cooled in an ice bath
and diazotized by addition of a solution of an equivalent amount of
sodium nitrite. This solution was added to the reaction vessel and
diluted with 10 ml. of concentrated hydrochloric acid and 70 ml. of
water. The shaker was then started and allowed to run a few seconds
before the collection of nitrogen was begun. The volume of nitrogen
evolved was measured at 1 minute intervals from the time the collect-
tion was started. The first-order rate constants were determined
by straight lines drawn for conventional logarithmic plots (Figures
8, 9, 10).

I. Attempted Resolution by Chromatographic Adsorption on Silica Gel.

1. Silica gel prepared in the presence of d-camphor sulfonic
acid: To a solution of 100 ml. of water glass (40° Be) and 5 g. of
d-camphor sulfonic acid in 500 ml. of water was added 100 ml. of
glacial acetic acid with vigorous stirring. The gel which formed immediately was broken into small lumps and heated on a steam bath under water pump pressure until all of the water was driven off. This operation usually required about 24 hours. The resulting silica was then pulverized and washed with water until the washings showed no optical rotation in a ½ dcm. polarimeter tube. After washing with methanol and drying on a steam bath, the silica was sifted through copper sieves with the fraction between 50 mesh and 100 mesh being saved for this experiment.

A solution of 0.01 g. of (V) in 5 ml. of petroleum ether was absorbed on 5 g. of this silica in a small chromatographic column. The displacement of the amine from the column was effected by eluting with 5% ether in petroleum ether. The amount of amine being displaced was determined by collecting the eluent in small fractions and measuring the optical density at 340 mμ after tenfold dilution with petroleum ether. A graph made by plotting the optical density against the volume of eluent had a broad peak with only one maximum range indicating that the two isomers were equally adsorbed on the silica.

A solution of 0.5 g. of dl-camphor sulfonic acid (53) in 10 ml. of water was mixed with 4 g. of this silica and allowed to stand for 1 hour. The silica was then removed by filtration and the solution found to be optically inactive.
Another experiment was carried out in which 1 g. of this silica was added to a solution of 0.250 g. of d-camphor sulfonic acid in 250 ml. of water. This same experiment was repeated with 0.250 g. of d,l-camphor sulfonic acid. After 1 hour the optical densities of these solutions were measured at 284 m\(\mu\) and found to be the same for each solution, indicating that no preferential adsorption had occurred. The same results were noticed when methanol was used as the solvent.

To a column packed with 6 g. of this silica was added 1 g. of \(\alpha\)-phenyl-ethanol. On eluting with petroleum ether, approximately half of the \(\alpha\)-phenylethanol was displaced from the column. This alcohol was found to have no optical activity when dissolved in 10 ml. of ethanol. On elution of the column with ether, a material was displaced which proved to be styrene formed by the dehydration of \(\alpha\)-phenylethanol.

2. Silica gel prepared in the presence of l-ephedrine: Some silica was prepared from 100 ml. of water glass in the presence of 6 g. of l-ephedrine in the same manner as before except that the silica was washed with dilute hydrochloric acid until free of the ephedrine. The attempted resolution of \(\alpha\)-phenylethanol was repeated with this silica giving the same results that were noticed in the previous case. The only difference was that the \(\alpha\)-phenylethanol had to be displaced with 1½ ether in petroleum ether. The first and last fractions of
the \( \alpha \)-phenylethanol coming off of the column were found to be optically inactive.

3. Silica gel prepared in the presence of \( d-\alpha \)-phenylethylamine: Some silicic acid was precipitated from 70 ml. of water glass by addition of 2.5 g. of \( d-\alpha \)-phenylethylamine in 70 ml. of acetic acid. The silica was prepared for use in the same manner as in the case of the 1-ephedrine. An attempt to resolve 1 ml. of \( dl-\alpha \)-phenylethylamine by chromatographic adsorption on 12 g. of this silica also failed. It was necessary to elute the column with 2% methanol in petroleum ether in order to displace the amine.

Some of this silica gel was added in small fractions to a solution of 2 g. of \( dl-\alpha \)-phenylethylamine in 100 ml. of cyclohexane until the optical density of the solution at 260 \( \text{m}\) was reduced to half its original value. This solution was then filtered and the solvent removed by evaporation. The residue of \( \alpha \)-phenylethylamine was found to have no optical activity when dissolved in 10 ml. of ethanol.
V

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