SYNTHESES AND INFRARED SPECTRA OF PHENAZINES

A Thesis

by

Chaim Stammer
(Chem. Eng., Politechnika Lwowska, Poland)

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This thesis is dedicated to my wife Felicia

whose encouragement made this work possible

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GENERAL INTRODUCTION

The structure and reactivity of aza-aromatic nitramines has been under study in this laboratory for several years. Since the chemical properties of phenazine place it between aromatic hydrocarbons and strongly electron-deficient aza-aromatics, the compound is especially interesting from the point of view of the behaviour of its nitramine derivatives. An investigation of the latter would bridge the gap between nitramines of the two groups of compounds.

2-Nitraminophenazine was prepared and was found to behave similarly to the known aza-aromatic compounds of this type. 1-Nitraminophenazine could not be isolated under the reaction conditions.

In the course of the investigation several phenazine compounds were prepared and their structure was elucidated.

It was hoped that the properties of derivatives with the nitramine function in position one and two of phenazine would reflect the difference in reactivity between these two positions. Mononitration of 1- and 2-aminophenazine which was investigated in the present work confirmed the higher reactivity of position one towards electrophilic attack. This has been predicted on the basis of molecular orbital calculations.

At the same time nitration studies of aminophenazines opened a new path for the syntheses of phenazines inaccessible by other means.

In some cases the methods described in the literature for the

syntheses of simple phenazines were unsatisfactory. Therefore, it was found necessary to devote considerable effort to the development of procedures for the preparation of the phenazines and aminophenazines required as starting materials.

A special method was developed also for the chromatographic purification of certain phenazines which were sparingly soluble in the majority of solvents commonly used in chromatography.

The present work was restricted to several basic reactions and not all of these reactions were explored under a variety of conditions. Consequently, it is felt that this investigation could be used as a basis for further study of some of the described reactions, and also for the preparation of a number of related compounds.

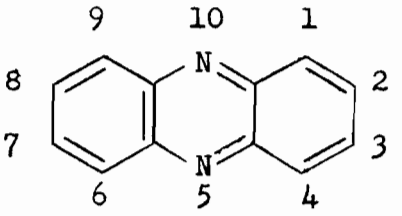
Infrared studies of the twenty-nine phenazines synthesized led to conclusions which are useful for determining the structure of unknown compounds of this series.

HISTORICAL INTRODUCTION

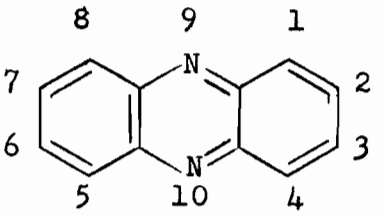
Introduction

a. Numbering and nomenclature of phenazines

Phenazine, a fused tricyclic heteroaromatic compound, is conveniently represented by structure I. The numbering system recommended for use by I.U.P.A.C. and used by Chemical Abstracts is shown in I. However many other publications, including current ones and Beilstein, number the phenazine molecule as shown in IA:

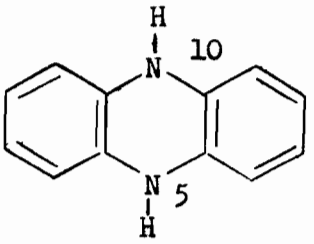


I



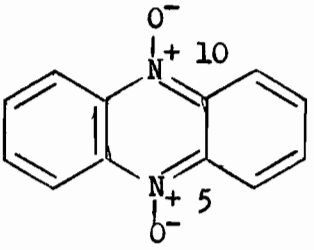
IA

Other phenazine derivatives are named as follows:



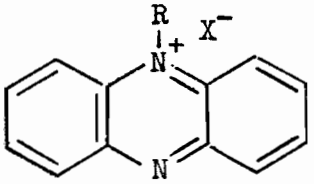
II

5,10-Dihydrophenazine



III

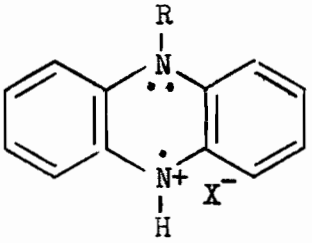
Phenazine-5,10-dioxide



IV

Phenazinium salt

R = H, alkyl, aryl etc.

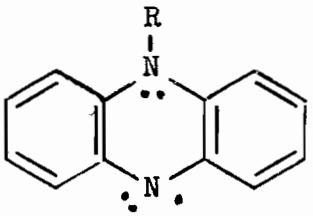


V

Phenazine semiquinone or

phenazyl salt

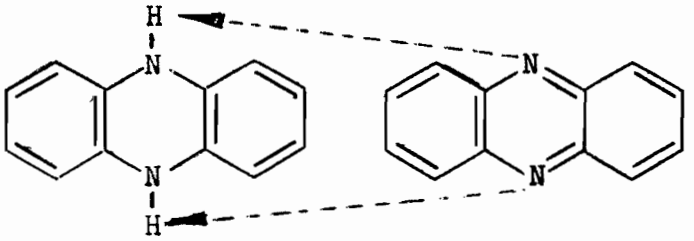
R = H, alkyl



VI

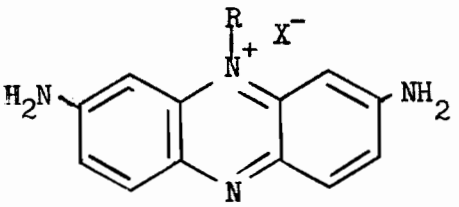
Phenazyl

R = H, alkyl



VII

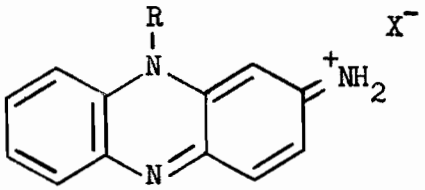
Phenazhydrin



VIII

Safranines

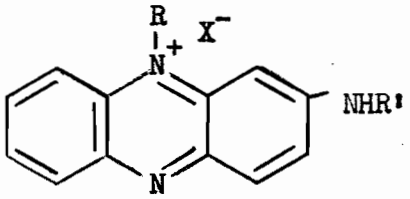
R = aryl, alkyl



IX

Aposafranines

R = aryl, alkyl



X

Indulines

R = aryl, alkyl

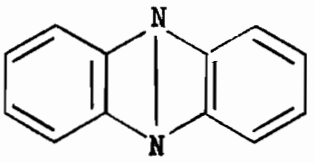
R^1 = aryl

The hydroxy-derivatives of phenazine are named phenazinols, the keto-derivatives phenazinones.

b. History of phenazines

Phenazine was first synthesized by Claus (1) in 1873, who prepared it by distilling calcium azobenzoate with calcium hydroxide. He named the

substance "azophenylene" and assigned to it the structure IB:



IB

The history of phenazine goes back as far as 1856 when Perkin (2) tried to synthesize quinine by the oxidation of allyltoluidine. This undertaking, based on the contemporary views about the structure of chemical compounds ended, understandably, in failure. However, from the tarry reaction product Perkin isolated a violet dyestuff that became known as mauveine. It was the first reported synthetic dyestuff as well as the first reported phenazine derivative.

The work of Fischer and Hepp (3,4,5) and Nietzki (6) led to elucidation of the structure of mauveine, pseudomauveine and of a series of new dyestuffs all of which were related to mauveine - these were classed as indulines, and were N-phenylphenazinium compounds having aminophenyl (or iminophenyl-)- groups in the benzene ring of the phenazine nucleus.

At the same time another group of phenazine dyestuffs, the safranines (VIII) were developed. This group differed from the indulines by the presence of an unsubstituted amino group on the carbocyclic ring of phenazine.

Owing to the great interest in the development of synthetic dyestuffs, the chemistry of phenazine derivatives belonging to the class

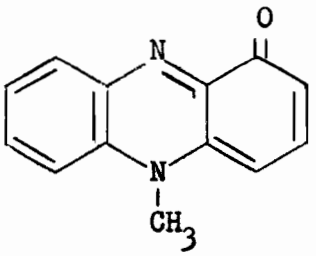
of "aniline dyestuffs" showed rapid growth at the end of the 19th century. The most eminent chemists of this period like W.H. Perkin, H. Caro, O. Fischer, E. Hepp, A.W. Hoffman, R. Nietzki and F. Kehrman (2-10) contributed to this development.

c. Biological activity of phenazines

The first application of phenazines in the biological field was for staining. Of particular interest in this regard is the specific coloration of subcellular particles by Janus Green and Neutral Red.

The bacterial pigments pyocyanine from Bacillus pyocyaneus, chlororaphine from Bacillus chlororaphis and iodinine from Chromobacterium iodinum are the only phenazine compounds found in nature. The structure of these phenazine derivatives has been established only recently.

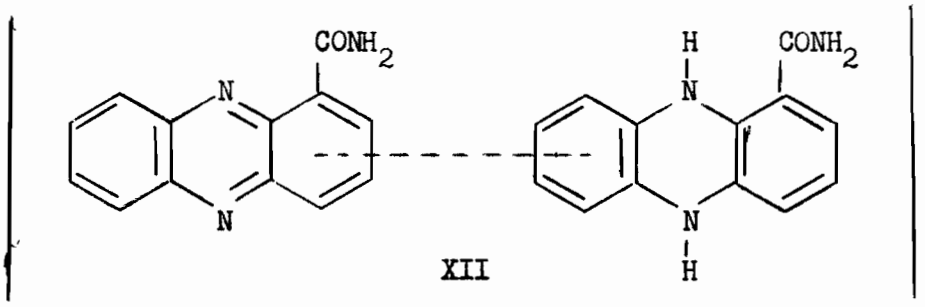
Pyocyanine was first synthesized by Wrede and Strack (14). The synthesis was also accomplished later by McIlwain (15). The structure of pyocyanine (XI), now accepted, was proven by the work of Michaelis (16,17).



XI

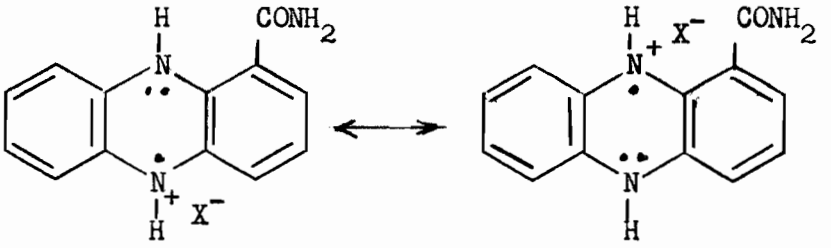
For over 30 years chemists have been involved in the elucidation of the structure of chlororaphine. Kögl and Postowsky (11) synthesized

phenazine-1-carboxamide, which on reduction in acidic medium yielded chlororaphine. Hence, they assigned for the latter in solid state a phenazhydrin structure. Clemo and McIlwain (12) suggested for this phenazhydrin the structure XII.



XII

Dufraisse, Etienne and Toromanoff (13) applying titration with iodine, found that chlororaphine in the solid state was a molecular compound of phenazine-1-carboxamide and its dihydro derivative in the ratio 3:1, and not 1:1 as shown in (XII). Elema (18) showed that in acid solution (pH 1) phenazine-1-carboxamide undergoes reversible reduction by two one-electron steps, in which an emerald green semiquinone (XIII) is formed first.

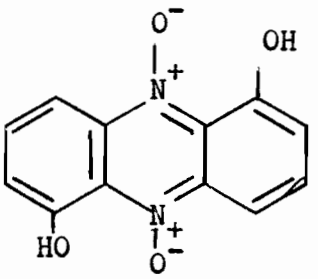


XIII

Further reduction of (XIII) yields an orange-yellow dihydro compound. In the pH range of 4-10, however, a two-electron one step reduction takes place with the formation of a phenazhydrin as the inter-

mediate reduction product.

Iodinine was proven to be 1,6-phenazinediol-5,10-dioxide (XIV)



XIV

by the work of quite a number of scientists with the significant contribution being made by McIlwain (19), Clemo and Daglish (20,21,22).

The reversibility of oxidation and reduction of phenazines at different pH values and oxidation-reduction potentials encounters their biological activity (23). Pyocyanine inhibits succinic dehydrogenaze from heart muscle (24) but accelerates aerobic oxidation of their respective substrates by malic, lactic and α-hydroxyglutaric dehydrogenases (23,25,26).

The inhibitory action of phenazine and a number of its synthetic derivatives against a variety of different organisms has been investigated, but the results have not been very promising. The azine dyes were found to have a very slight therapeutic effect against tuberculosis (27). Some phenazine derivatives exhibit fungistatic action (28). Phenazine has been found to be toxic to the clothes moth and some other insects, but has not been used as an insecticide for economic reasons (29).

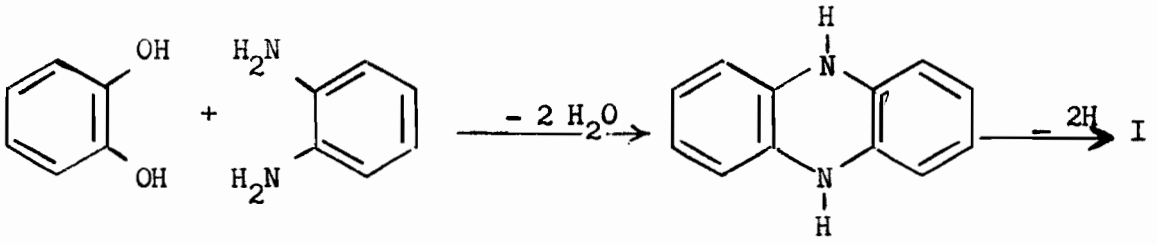
Finally it can be said that, although the biological effects of

many phenazine derivatives have been studied, up to the present time none of these compounds has proved to be of great practical value (30).

General Methods for Syntheses of Phenazines

a. 1,2-Cyclohexanedione and ortho-substituted benzene derivatives, such as catechol and o-quinone, when condensed with o-phenylenediamine, or ring substituted o-phenylenediamines, form phenazines (31-36).

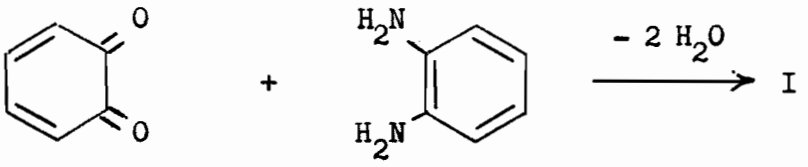
In 1886, Merz (31) synthesized 2-methylphenazine by heating 4-methylphenylenediamine and catechol to 200-210° in a sealed tube. Ris (32) applied the same procedure to obtain phenazine (I) from catechol and o-phenylenediamine. The reaction proceeds through the formation of the intermediate dihydrophenazine (II) which is easily dehydrogenated:



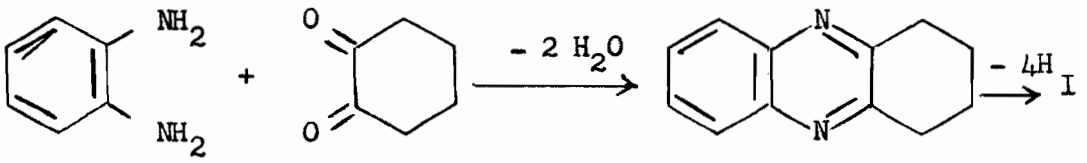
This synthesis provided convincing evidence for the basic ring structure of phenazine.

Morley (33) introduced a modification in the procedure. He employed an original type of oxidative sublimation of the dihydro-intermediate (II) and obtained phenazine (I) in a 55% over-all yield. The original procedure claimed a 35% yield.

Hinsberg (37) and Witt (38) showed that o-quinones react with o-aryldiamines to form phenazine structures (I):

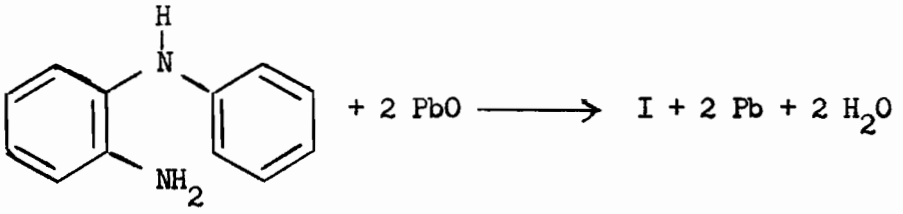


This general method was used for the syntheses of a variety of phenazine derivatives (34,39,40). A modification of this procedure introduced by Clemo and McIlwain (35) can be employed for the preparation of a number of substituted phenazines. Phenazine (I) is obtained by dehydrogenation of the condensation product of 1,2-cyclohexanedione and o-phenylenediamine:

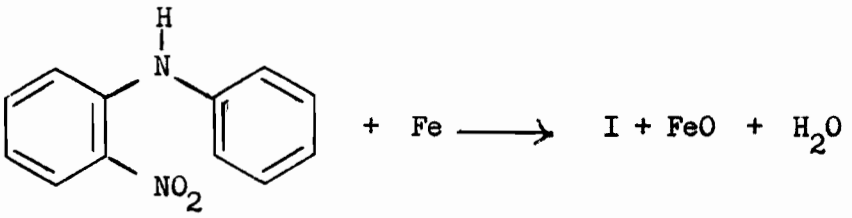


b. Phenazines also can be obtained from diphenylamines, bearing an amino- or nitro- group in the ortho-position, by ring closure.

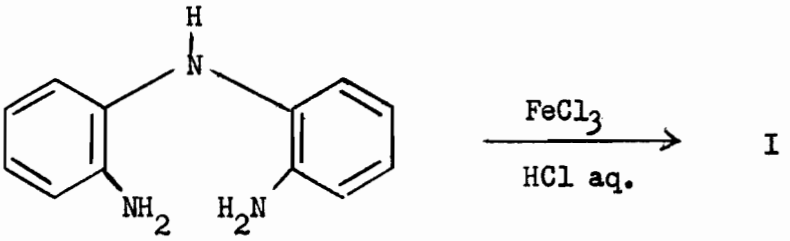
Fischer and Heiler (41,42) prepared phenazine (I) by leading 2-aminodiphenylamine in the vapour phase over red-hot lead oxide:



By combining the reduction and ring closure steps Waterman and Vivian (43,44) obtained phenazine (I) directly from the reaction of o-nitrodiphenylamine with iron metal:

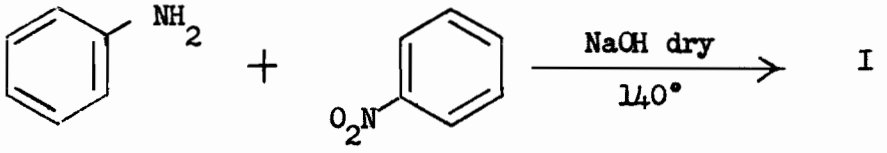


The synthesis of phenazine (I) by oxidation of 2,2'-diaminodiphenylamine with ferric chloride (45) is another modification of the general method:



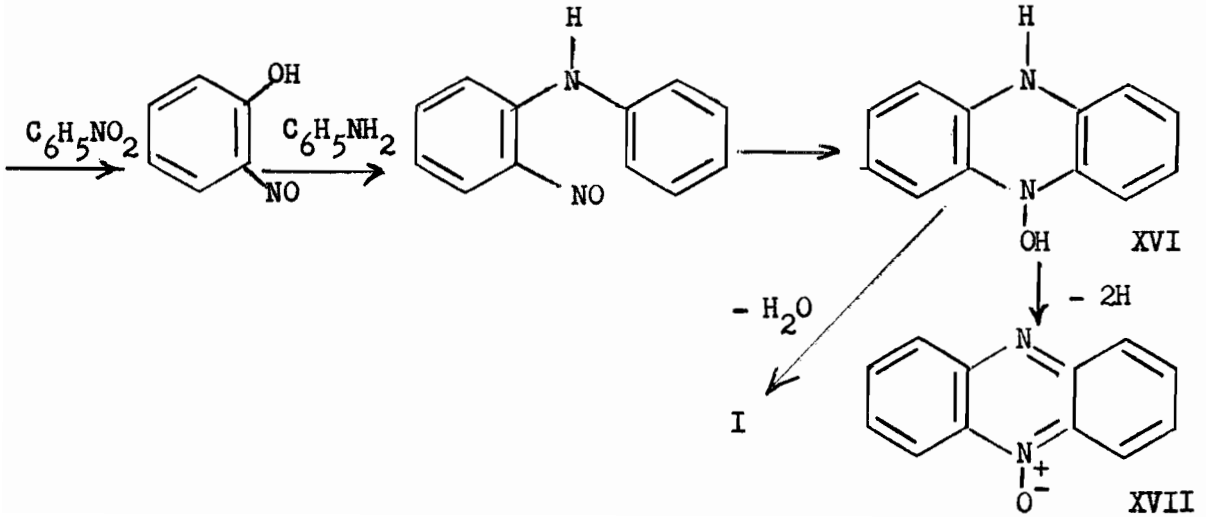
c. Among various other procedures for preparing phenazines, that of Wohl and Aue (46) should be mentioned because of its general applicability

(47-50). Aniline and nitrobenzene are heated with dry alkali hydroxides and phenazine (I) is formed:

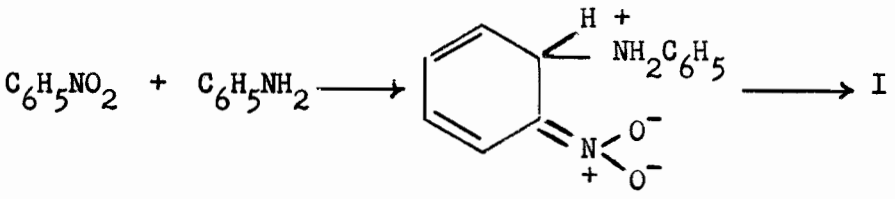


Phenazine N-oxide is produced as a co-product in this reaction. It can also be obtained as the main reaction product on changing the aniline : nitrobenzene ratio in favour of the latter and conducting the synthesis in an inert solvent (benzene).

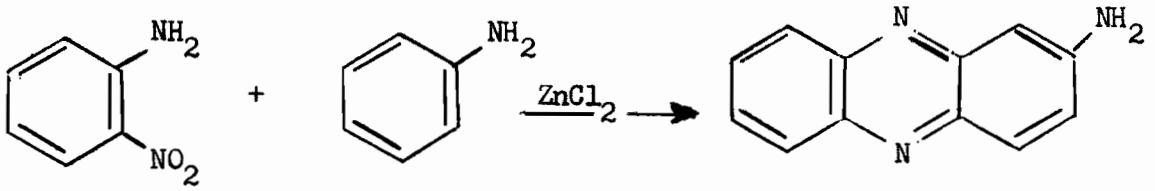
The mechanism suggested (46) for this reaction postulated a rearrangement of the nitrobenzene, under the influence of alkali, into o-nitrosophenol (o-quinone-monoxime) (XV). The latter then condensed with aniline and the resulting intermediate (XVI) either could be oxidized by excess nitrobenzene to phenazine-5-oxide (XVII), or could be converted to phenazine by loss of water:



This suggested mechanism is somewhat questionnable since o-nitrosophenol does not react with aniline under the Wohl-Aue conditions (51). An alternative explanation (52) is that the above reaction is started by a direct anionoid attack of aniline in the ortho-position of the nitrobenzene:

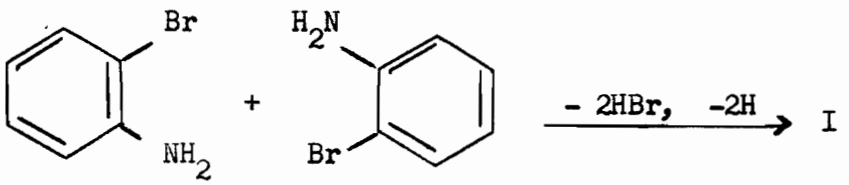


Another phenazine synthesis introduced by Wohl (53) consists of the formation of 2-aminophenazine (XVIII) by the reaction of o-nitroaniline with aniline hydrochloride in the presence of fused zinc chloride at 180-185°:

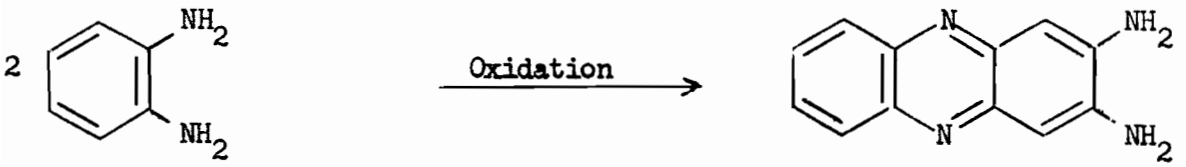


XVIII

Nitrobenzene is used as reaction medium and oxidant in the formation of phenazine (I) from o-bromoaniline (54).

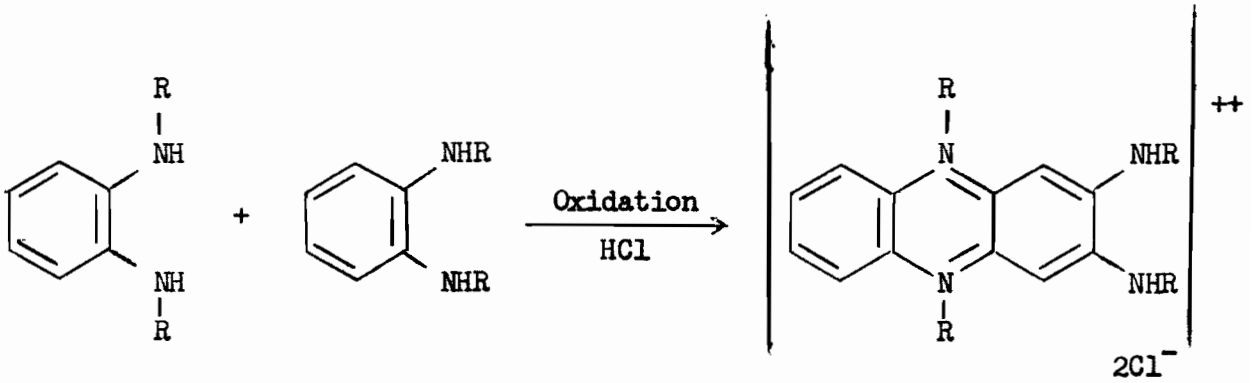


2,3-Diaminophenazine (XIX) is formed by oxidation of o-phenylenediamine under mild conditions (ferric chloride, iodine) (8,55,56):



XIX

In the case of N,N'-dialkyl- derivatives of o-phenylenediamine phenazinium compounds (XX) result (57):



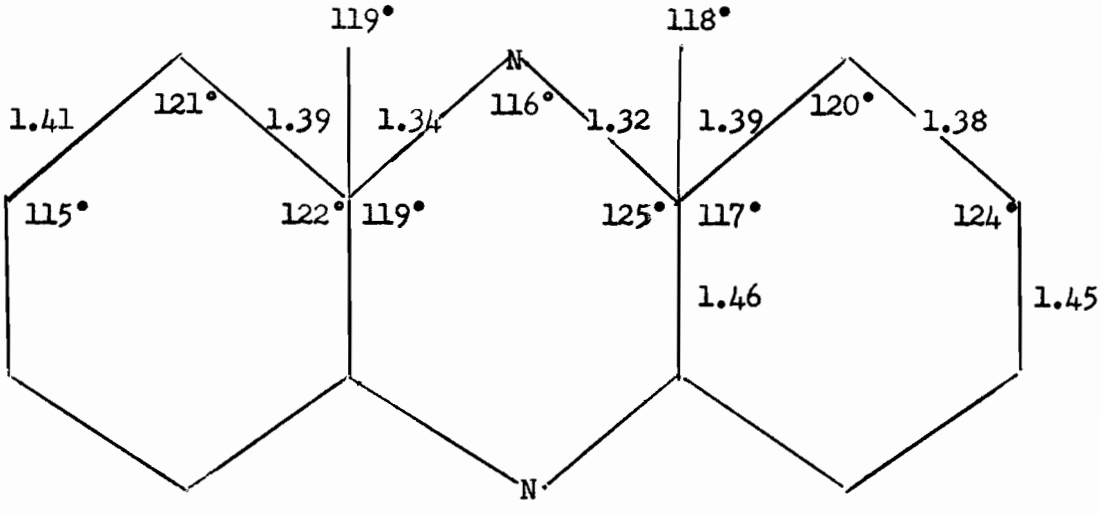
XX

Several other methods of synthesizing phenazine dyes by oxidation of mixtures of aromatic amines have been developed (2,7,58-60).

Physical Constants and Structure of Phenazine

Phenazine (I) sublimes without decomposition forming long, bright yellow needles, and melts at 176°. It is a very weak base, the pKa value

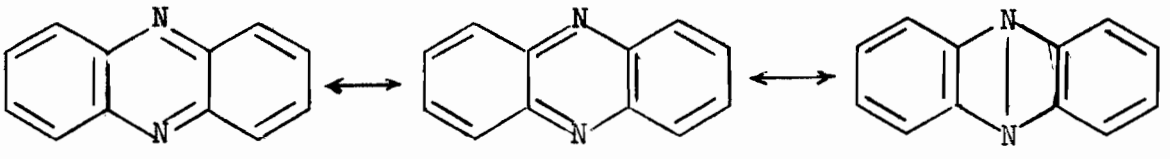
being 1.23 ± 0.10 (M/3000) (61). The values for bond lengths (Å) and bond angles in phenazine (I) have been determined by X-ray diffraction and are (62):



I

From these data it was concluded that the phenazine molecule is planar and that the two carbocyclic rings are not identical. However, the zero dipole moment of phenazine (63) is in keeping with a planar, symmetrical structure.

In terms of resonance theory, phenazine (I) could be represented as a resonance hybrid, the principal structures involved being A, B and C:



A B C

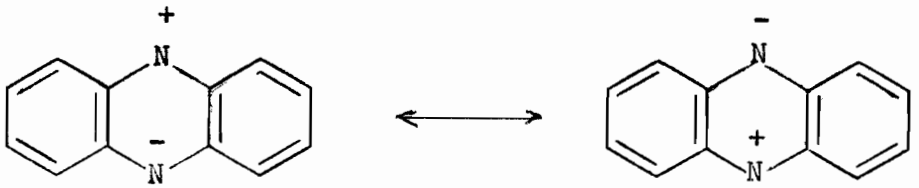
I

Throughout this thesis the base will, for convenience, be represented by only one of these formulae.

The structural relationship of phenazine with acridine and anthracene is clearly seen when the resonance energies of these compounds are considered. They are 105, 106 and 105 kcal/mole respectively (64).

Reactions of Phenazine

Phenazine (I), a very weak base, can be largely reprecipitated from solution in acids by dilution with water, due to hydrolysis of the salt. The very low basicity of phenazine (I) may be attributed to the facts (a) that the second nitrogen atom introduced into acridine (65) (pKa 4.3) is electron-attracting and therefore lessens the basicity, and (b) that in the phenazine molecule (I) an opportunity exists for the formation of exactly equivalent dipolar structures F and G:



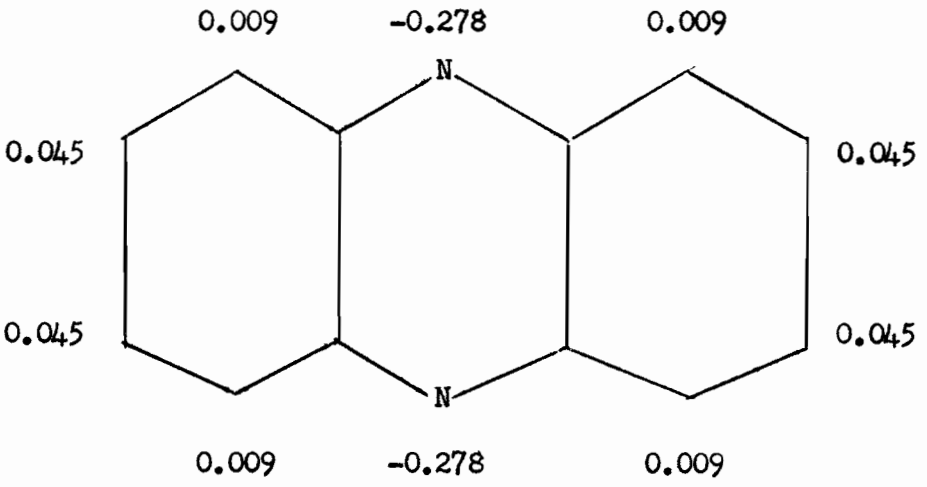
F G

I

which may strengthen the resonance of this species at the expense of the ion (61).

Longuet-Higgins and Coulson (66) determined, by the methods of molecular orbitals, the π-electron distribution in the molecule of phenazine (I). The calculations are based on the corresponding values for the parent hydrocarbon anthracene to which the first order perturbation treatment has

been applied. The authors (66) correlate the relative values of the net charges at different positions of the molecule (I) with the chemical behaviour of the compound in substitution reactions:



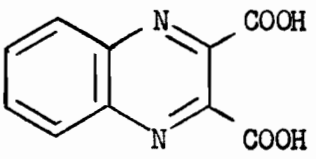
I

Thus position one of phenazine (I), with a lower net charge, should be more susceptible to electrophilic attack than position two. On quaternization of the nitrogen atom the difference in reactivity of these positions would be enhanced still further owing to the proportional increase of the charges.

Dewar and Maitlis (67) studied the reactivity in electrophilic substitutions of some six-membered nitrogen-heterocyclic compounds. They came to the same conclusion as Coulson had, estimating by molecular orbital treatment the difference (ΔE) between the relative π-electron energies of the parent aromatic compound and of the transition state. The values obtained for phenazine are: $\Delta E_1 = -13.5$ for the 1-position and $\Delta E_2 = -17.9$ for the 2-position. Consequently, the electrophilic substitution would be expected to occur at position one in preference to position two.

These theoretical calculations have been supported by the results of nitration experiments of phenazines conducted by Maffei and Aymon (68). Only α-nitrophenazines were formed in these reactions. The same investigators reported (69) that they obtained 1-chloro-, 1,4-dichloro-, 1,4,6-trichloro- and 1,4,6,9-tetrachlorophenazine, consecutively, on direct chlorination of phenazine (I) in hydrochloric acid solution.

Phenazine is oxidized to quinoxaline-2,3-dicarboxylic acid (XXI) on treatment with potassium permanganate in alkaline medium:



XXI

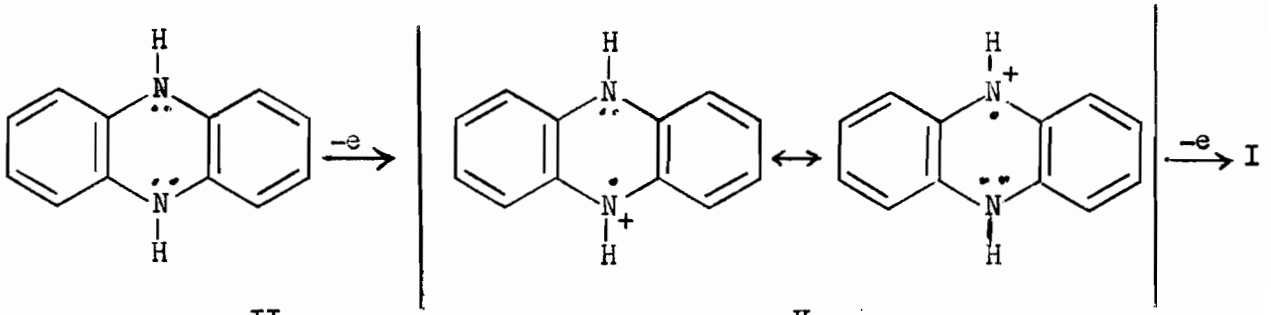
Pushkareva and Agibalova (70) obtained the acid (XXI) in a 75% yield, in this way.

The oxidation of a mixture of 1,6- and 1,9-dinitrophenazines under similar conditions resulted in the formation of pyrazinetetracarboxylic acid (68).

In reduction reactions phenazine behaves as an o-quinone derivative. There are two types of compounds on an oxidation level between phenazine and dihydrophenazine. One has a free radical structure (semiquinone), the other is a molecular compound of the two forms (phenazhydrin). The nature of these compounds was clarified by the potentiometric studies

of Michaelis (16,17) and Elema (18).

Dihydrophenazine (II) was titrated in acidic medium with p-quinone. The titration curve showed two distinctly separate steps which agreed perfectly in shape with two one electron titration curves, the normal potentials amounting to -0.086 and +0.254 volts in the solvent (50% acetic acid) used:

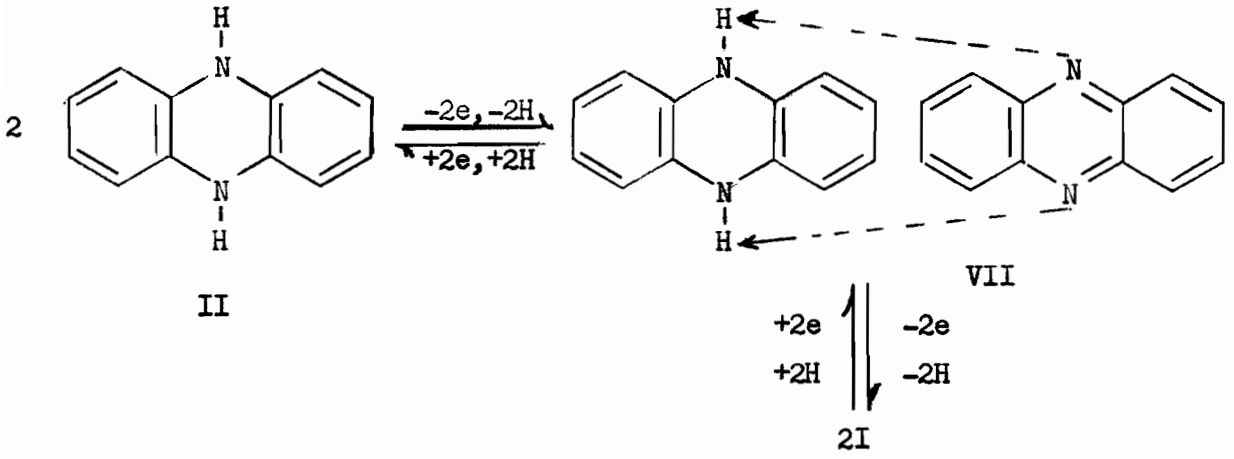


II V

Thus it was clear that the green intermediate compound (semiquinone (V)) was a free radical with an odd number of electrons and of the same molecular size as the fully reduced or fully oxidized form and not a molecular compound of phenazine and its dihydro-derivative in a ratio 1:1 (the phenazhydrin (VII)). This free radical (V) does not undergo partial dimerization in the way that triphenylmethyl partly associates to hexaphenylethane. The explanation of this is found in the fact that the semiquinone (V) is not only a free radical, but also a cation, and hence will repel a like radical-cation. In terms of resonance theory the semiquinone (V) is a resonance hybrid of two equivalent structures, which adds greatly to its stability.

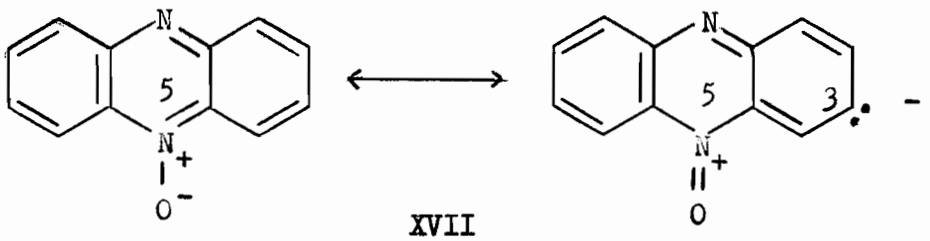
Phenazines when reduced in neutral or alkaline medium (or dihydrophenazines oxidized in the same medium) do not form the green intermediate, but undergo a one step two electron reduction (or oxidation).

As intermediates in these reactions molecular compounds of phenazines and their dihydro derivatives are formed, (the phenazhydrins) (VII),



which are considered to be combined in one molecule by means of hydrogen bonding (35). However, the exact structure of phenazhydrins must be regarded as not definitely established (17).

Phenazine-5-oxide (XVII) is formed simultaneously with phenazine (I) when aniline and nitrobenzene are heated with dry sodium or potassium hydroxide (46). The N-oxide (XVII) is generally more reactive towards electrophilic reagents than phenazine and, in contrast to the latter, is preferentially substituted in the 3-position. Both phenomena are explained by the polarization of the 5-oxide. The polarisation increases the electron density of the carboxylic rings as a whole, but especially of the 3-position which is in conjugation with the nitrogen atom in 5-position of the N-oxide (XVII).



Hirotaka Otomasu (71) nitrated the 5-oxide (XVII) at 0° and obtained mainly the 3-nitro derivative with some 1-nitrophenazine-5-oxide in a very good over-all yield. Phenazine, under the same conditions, did not react at all.

Mechanism of Nitration in Concentrated Sulphuric Acid Solution

Euler in 1903 (72) suggested that the nitronium ion (NO_2^+) was the nitrating entity in nitration mixtures. However, unequivocal proof for the existence of the nitronium ion in mixtures of nitric acid with sulphuric or other strong acids, as well as in pure nitric acid, was demonstrated by Hughes, Ingold and co-workers (73).

Nitronium ion formation is considered to be a two-stage reaction:

1) $HO{-}{-}NO_2 + H_2SO_4 \underset{\text{fast}}{\rightleftharpoons} H_2\overset{+}{O}{-}{-}NO_2 + HSO_4^-$ - protonation step

2) $H_2\overset{+}{O}{-}{-}NO_2 \xrightarrow{\text{slow}} H_2O + \overset{+}{N}O_2$

3) $H_2O + H_2SO_4 \longrightarrow H_3\overset{+}{O} + HSO_4^-$

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4) $HO{-}{-}NO_2 + 2H_2SO_4 \longrightarrow H_3\overset{+}{O} + \overset{+}{N}O_2 + 2HSO_4^-$

As it follows from equation (4) the measured freezing point depression of the solvent sulphuric acid caused by the solute nitric acid should be four times that of the ideal solute. This prediction is in

good agreement with experimental data.

Other evidence for the presence of nitronium ion in the mixtures of sulphuric and nitric acids was derived by the authors from Raman and infrared spectra, isolation of crystalline nitronium salts, and in X-ray analysis of the latter.

From cryoscopic measurements it can also be concluded that conversion of nitric acid, in sulphuric acid solution, into nitronium ion is quantitative. This fact explains the high reactivity of a nitric-sulphuric acid mixtures as a nitrating agent.

Kinetic measurements of the nitric acid nitration of nitrobenzene dissolved in sulphuric acid show (74) that it is a second-order process.

$$(1)\quad \text{Rate (in } H_2SO_4) = k_2 \left|ArH\right| \left|HNO_3\right|$$

The expression for the rate (1) shows also that the attacking species, if not nitric acid, is formed so rapidly from it that it bears a constant ratio to it.

The mechanism, now accepted, for the electrophilic attack by the nitronium ion on the aromatic ring and the formation of a nitro compound was proposed by Ingold and his collaborators (75). Two steps are involved in the mechanism, the first consisting of a slow uptake of the nitronium ion, and the second which is the rapid transfer of a proton:

$$ArH + \overset{+}{N}O_2 \xrightarrow{\text{slow}} Ar\overset{+}{\underset{NO_2}{\overset{H}{<}}}$$

$$Ar\overset{+}{\underset{NO_2}{\overset{H}{<}}} + A^- \xrightarrow{\text{fast}} Ar{-}{-}NO_2 + HA$$

Most of the theoretical concepts concerning the mechanism of nitration in the benzene series can be applied unchanged to aza-aromatic substances. Some complications do arise, however, due to changes in the π-electron distribution of the ring caused by the introduction of the nitrogen atoms into the aromatic system. The, to a certain extent, localized distribution of π-electrons in aza-aromatic compounds will make some of the ring positions more susceptible to electrophilic attack than others.

Nitramines

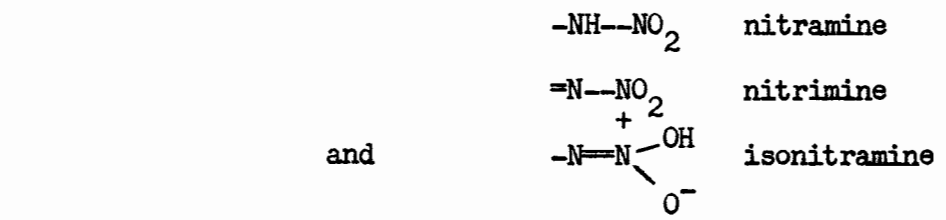
Nitramines are compounds derived from amines in which one of the hydrogen atoms of the amino-group is replaced by a nitro-group. Their names are formed in three ways:

a) by adding of the suffix nitramine to the name of the alkyl or aryl group (e.g. phenylnitramine, methylnitramine).

b) by putting the prefix nitramino before the name of the parent compound (e.g. 2-nitraminophenazine).

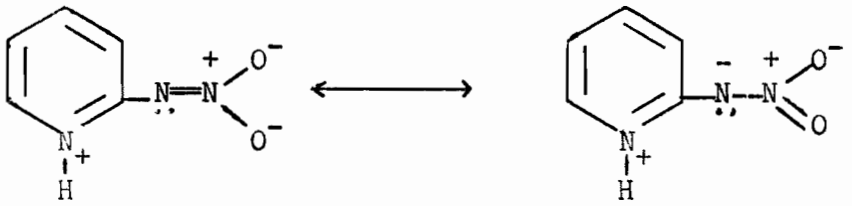
c) or using the prefix N-nitro attached to the name of the amine (e.g. N-nitropiperidine).

The structure of nitramines can be formulated as follows:



Recent studies on nitroguanidines by McKay (76) and the work on

heterocyclic nitramines by Taurins (77) and his co-workers (78,79) showed that these substances must be considered as dipolar nitrimino inner salts, where the presence of a basic nitrogen atom in the molecule favours the formation of such a zwitterion. As an example the suggested structure for 2-nitrimino-(1H)pyridinium inner salt (XXII) with structures A and B predominating in the resonance hybrid could be cited.



A B

XXII

The evidence for the structure (XXII) is based on an analysis of the infrared spectrum in the region 3500-2500 cm^{-1}, in which the presence of a $\overset{+}{N}$--H group is indicated by a characteristic absorption pattern. A study of the spectrum of n-butylnitramine excluded the alternative explanation that the N--H absorption was shifted because of association of the N--H group with the oxygen of the nitro-group.

Infrared Spectroscopic Studies

a. Aza-aromatic compounds

Our knowledge of the infrared spectra of aza-aromatic compounds at present is based on the investigation of spectra of pyridine and its derivatives by Shindo and co-workers (80-83). Turkevitch (83), Corrsin (85)

and Katritzky (86-89).

Some infrared work on quinoline and isoquinoline compounds has been reported by Shindo (90) and Tallent (91).

Among the three ring aza-aromatic compounds, the infrared spectra of acridine (92), and of phenanthridine (93) have been published.

The spectrum of 2-t.butylphenazine has been presented, without discussion by Teuber and Steiger (94), and Gagnon and his collaborators (95) have reported the infrared spectra of phenazine and some of its derivatives (in solid state).

The information at present available concerning absorption in the various spectral regions of aromatic and aza-aromatic compounds is outlined in the following paragraphs.

C-H stretching region

Similarly to benzene, pyridine and its derivatives show C-H stretching bands in the range 3070-3020 cm^{-1} (96).

Combination and overtone bands region

Young, Duvall and Wright (97) discovered average absorption patterns for benzene in the 2000 cm^{-1} region that were typical for the position and number of substituent groups. Whiffen (98) presented evidence showing that the stronger absorption bands in the region 2000-1600 cm^{-1} in benzene derivatives normally arise from summation tones of the out-of-plane C-H bending vibrations. Cook and Church (99) noted the

same characteristic patterns in over thirty mono-, di-, and tri- substituted pyridines and showed that the shape of those bands was almost constant.

C=C and C=N vibrations in aza-aromatic compounds occur, as would be expected, in the 1600-1400 cm^{-1} region giving rise to two bands about 100 cm^{-1} apart (100). In some cases the higher frequency band is accompanied by a second absorption peak at a slightly lower frequency. Cook and Church (99) have shown that for mono-substituted alkylpyridines, the average separation of the two bands can be used to differentiate 2- or 3- mono-substituted pyridines from the corresponding 4-substituted compounds. In the former, the average separation is about 20 cm^{-1}, whereas in the latter there is a 40 cm^{-1} separation. In most cases two peaks of variable intensity appear in the range 1500-1400 cm^{-1}.

Quinolines and isoquinolines show a more complex pattern due to the pyridine bands being superimposed on those arising from the benzenoid ring (100). 8-Hydroxyquinoline has major bands at 1577 cm^{-1} and 1495 cm^{-1} accompanied by weaker ones at 1563 cm^{-1} and 1504 cm^{-1}.

Skeletal and C-H in-plane deformations (1400-900 cm^{-1})

Cannon and Sutherland (93) pointed out that pyridine and the derivatives they examined showed a strong band near 1200 cm^{-1} and another between 1110-1000 cm^{-1}. 2-Methylpyridine exhibited two bands at 1240 cm^{-1} and 1043 cm^{-1}, the latter being especially strong. None of the substituted quinolines examined by Bellamy (101) showed any strong absorption in this region.

The C-H out-of-plane region (900-700 cm^{-1})

In benzene the strongest bands in this region originate from out-of-plane vibrations of the free hydrogen atoms of the ring (101). The main factor determining the frequency of these bands is the number of adjacent hydrogen atoms. When their number decreases, the band maxima are shifted to higher frequencies with an attendant decrease in intensity.

Five adjacent H-atoms give rise to a strong band in the range 770-730 cm^{-1} and another strong band at 700 $\pm$ 10 cm^{-1}.

Ortho-substituted benzenes with four adjacent hydrogen atoms have one strong band in the range 770-735 cm^{-1}. The reduction in the number of hydrogen atoms from five to four does not affect significantly the frequency of the absorption band.

Benzene derivatives with three adjacent hydrogen atoms show a strong absorption band at 810-750 cm^{-1}, which is accompanied by a second band of medium intensity in the region 725-680 cm^{-1}.

When there are two adjacent hydrogen atoms in the ring the band is shifted to 860-800 cm^{-1}.

One isolated ring hydrogen atom situated between two substituents gives rise to a band occurring in a frequency range 900-850 cm^{-1}.

A similar correlation is found in naphthalenes, quinolines and larger ring systems. Cannon and Sutherland (93) assigned the bands at 750 cm^{-1} in 9,10 dihydroanthracene and at 725 cm^{-1} in anthracene to the out-of-plane vibrations of the four adjacent hydrogen atoms.

Cencelj and Hadzi (102) found that in naphthalenes substituted in one of the rings the band positions were in relatively good agreement with the correlation rules outlined. The pattern of the bands in this region seemed to be characteristic of the type of substitution and independent of the nature of the substituent. The authors concluded that the presence of a band was not sufficient proof for the presence of the corresponding group of hydrogen atoms. However, the absence of a band required by a certain type of substitution seemed to exclude the latter. In naphthalene substituted in both rings the characteristic absorption bands are more difficult to identify.

Studies carried out on aza-aromatic compounds (101) have suggested the applicability of the foregoing correlation rules to these compounds. Pyridine (five adjacent hydrogen atoms) was found to absorb at 750 cm^{-1}; α-picoline (four) at 755 cm^{-1}, β-picoline (three) at 790 cm^{-1} and γ-picoline (two) at 800 cm^{-1}.

The rules appear to hold also in quinoline compounds if each ring is considered separately. 2,6-Dimethylquinoline with two adjacent, one single, and two adjacent H-atoms, absorbs strongly at 831 cm^{-1}, while the 2,7-derivative with two, two, and one, absorbs at 835 cm^{-1}. Both compounds show a weaker band in the 900-850 cm^{-1} region as well. The first band has been assigned to the two adjacent hydrogen atoms of each ring and the second band to the single isolated hydrogen atom.

2,3-Dimethylquinoline, with one single and four adjacent H-atoms and its 2,4-isomer also with one single, four adjacent H-atoms, exhibit a strong band at 755 cm^{-1} and 758 cm^{-1}, respectively, due to the four

adjacent hydrogen atoms of the carbocyclic ring. They also have a band between 900-850 cm^{-1} which has been assigned to the single hydrogen atom of the hetero-ring.

Isoquinoline with one single, and two, and four adjacent hydrogen atoms displays three bands in this region. The strongest, at 745 cm^{-1}, has been assigned to the four hydrogen atoms of the carbocyclic ring, the second, a weaker one, at 829 cm^{-1} and a third at 864 cm^{-1} have been linked to the presence of the two adjacent and the one single hydrogen atom of the pyridine ring, respectively.

b. Nitramines

Bellamy (103) has established that the stretching vibrations of the nitro-group in nitramines result in absorption in the range 1630-1550 cm^{-1} and 1300-1250 cm^{-1} (s). These bands were assigned to the asymmetric and symmetric vibration modes, respectively. Also a band of medium intensity observed in the region 790-770 cm^{-1} (103,104) has been considered characteristic for nitramines.

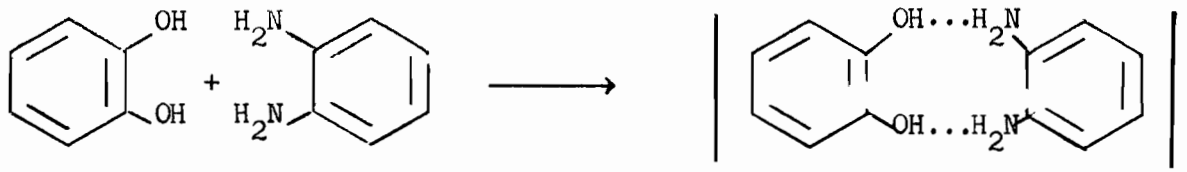
The N-H stretching frequency in n-butylnitramine occurs at 3300 cm^{-1} (77). Heterocyclic nitramines, the structure of which is described as nitrimino inner salts or betaines show broad absorption bands displaced towards lower frequencies, between 3200-2000 cm^{-1}. Taurins (77) has assigned these bands to the stretching vibrations of the $\overset{+}{N}$-H group.

DISCUSSION

Syntheses of 5,10-Dihydrophenazines and Phenazines

In a search for the most satisfactory method of the large-scale laboratory preparation of phenazine, several known methods were examined. Phenazine was synthesized from aniline and nitrobenzene by the procedure of Wohl and Aue (46) and from 2,2'-dinitrodiphenylamine as described by Eckert and Steiner (105) and by Tomlinson (45). However these methods were found inconvenient because of the unsatisfactory yield or too many reaction steps involved in the preparation. Further consideration of the problem led to an attempt to develop the procedure based on the use of catechol (XXIII) and o-phenylenediamine (31,32,33). Both starting materials were inexpensive and the reaction appeared to be straightforward.

In the first exothermic step of the reaction catechol (XXIII) and o-phenylenediamine (XXIV) formed a compound (XXV),

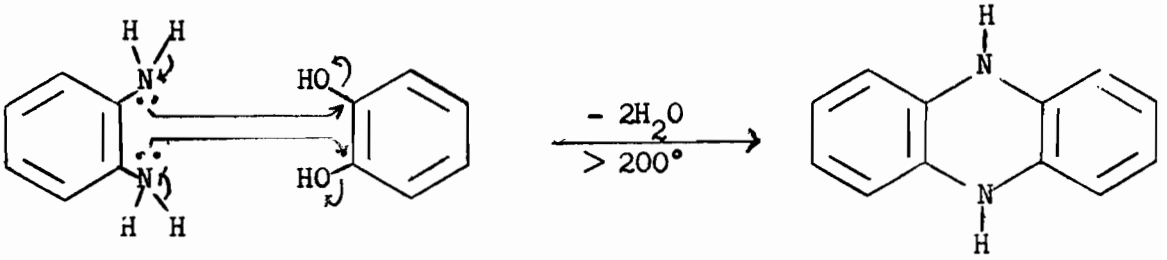


XXIII XXIV XXV

which when crystallized from benzene melted sharply at 87-88°, was relatively stable and could be sublimed in vacuo without decomposition. The infrared spectrum of (XXV) showed a broad band in the region 3500-2500 cm^{-1} usually observed with compounds containing $N\text{-}H^{+}$ groups. This

could indicate a partial ionic character of bonds involved in the formation of (XXV).

It is considered that the condensation reaction proceeds by an intramolecular rearrangement of (XXV) with the formation of the highly thermostable 5,10-dihydrophenazine (II).



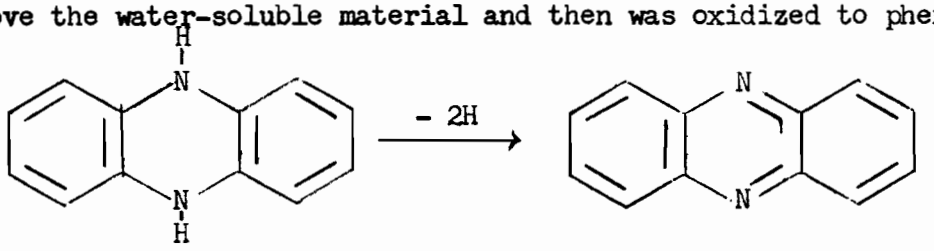
XXV II

The reaction was found to occur only at temperatures greater than 200°. All attempts to effect the condensation at temperatures below 200° in solution, using catalysts such as zinc chloride, boron and aluminum oxides, polyphosphoric and sulphanilic acids, failed. When the condensation reaction was carried out at temperatures over 200°, the addition of sulphanilic acid to the reaction mixture did not affect the rate of condensation.

These facts, and the high yield of product obtained in spite of the vigorous conditions employed, substantiated the intramolecular mechanism proposed for the reaction.

Thermal decomposition of (XXV) to 5,10-dihydrophenazine (II) and two molecules of water started at 200°. In the present work it was established that the optimum temperature for the thermal decomposition was in the range of 240-270°.

Cathechol (XXIII) and a 50% excess of o-phenylenediamine (XXIV) (which acts also as the reaction medium) were heated to the melting point with stirring. To avoid oxidation of the reactants, a slow stream of nitrogen was passed through the apparatus. The temperature of the reaction mixture was raised gradually from 240 to 270°. The water which formed during the process was distilled off slowly and collected in a graduated receiver. In this way it was possible to follow the course of the reaction and to determine when it was finished. Then the excess amine (XXIV) was distilled off at temperatures between 270° and 320° under normal pressure. In another experiment the excess amine (XXIV) was allowed to remain with the condensation product. In both cases the crude 5,10-dihydrophenazine (II) was washed thoroughly with warm water (50°) to remove the water-soluble material and then was oxidized to phenazine (I).



II I

The oxidation was accomplished by passing a stream of air through the suspension of 5,10-dihydrophenazine (II) in aqueous sodium hydroxide at the boiling temperature. The crude phenazine (I) was filtered off, washed with water and dried. The dry product was mixed with twice its weight of reduced iron powder and sublimed in a specially designed apparatus (Fig. 18). The proportion of iron powder required for sublimation depended on the purity of the crude phenazine and was increased, on occasion, as high as 5:1. Phenazine (I) sublimed in the form of yellow needles and had a melting point of 170-171°. The yield obtained was 64%.

Several oxidizing agents such as ferric chloride, potassium permanganate and hydrogen peroxide were tried for the oxidation of the crude 5,10-dihydrophenazine (II) but were found less convenient for this purpose; the yield did not increase and further purification of the product was more complicated. The time required for the oxidation varied depending on the reaction conditions (temperature, stirring, size of batch and vessel). It was necessary for the oxidation to be complete, otherwise the subsequent sublimation did not provide pure phenazine (I). Disappearance of the green colour, due to semiquinone formation, in a sample dissolved in dilute hydrochloric acid indicated complete oxidation.

The same procedure was used to synthesize 2-tert. butylphenazine, 2-methyl- and 1-methylphenazine from the correspondingly substituted catechols and o-phenylenediamine, and high yields were obtained. In these three cases it was possible to purify the phenazines by sublimation, as well as by precipitation from solution in dilute acid.

The procedure described can also be used for the preparation of pure 5,10-dihydrophenazine in the way of purification of the crude condensation product.

2-Aminophenazine (XVIII)

From among the few known procedures for preparing 2-aminophenazine (XVIII) the one described by Wohl and Lange (53) was selected for use in this work because the starting materials were readily available and inexpensive, the preparation was a straightforward reaction and the crude reaction product could be easily purified by two sublimations in the apparatus shown in Fig. 18. The amine (XVIII) was obtained in a high degree of purity and melted sharply at 279°.

The same compound (XVIII) was obtained by zinc-dust distillation of 2,3-diaminophenazine (XIX), but no particular advantage was found in using this procedure.

The ultraviolet spectrum of 2-aminophenazine (XVIII) has been examined by Kehrman and Sandoz (106); the infrared spectrum has not yet been reported.

In the infrared spectrum of 2-aminophenazine (XVIII) (Fig. 5, Table 8) there are three peaks at 3390, 3310 and 3200 cm^{-1}, in the region generally associated with N-H stretching vibrations. Bellamy and Williams (107) have established that the frequencies of symmetric and asymmetric N-H stretching modes in primary amines are directly related to each other by the equation:

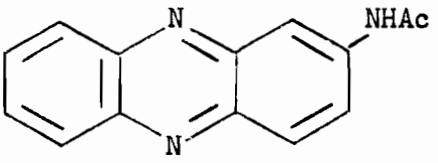
$$\nu_{sym} = 345.53 + 0.876\,\nu_{asym}$$

For the amine (XVIII) ν_{sym} calculated using the above equation would be 3315 cm^{-1}. This is in good agreement with the observed value of

3310 cm^{-1} since the standard deviation for 62 amino-compounds, studied by the above-mentioned investigators, was 4.8 cm^{-1}. The 3390 cm^{-1} and 3310 cm^{-1} frequencies might be assigned to the asymmetric and symmetric vibrations of the free amino-group. It is possible that small shifts in the absorption maxima towards lower frequencies have occurred because the spectra were taken in the solid state. The peak at 3200 cm^{-1} might be attributed to intermolecular association of the N-H---N- type. Flett (108) has noted that β-naphthylamine and 2-aminoanthraquinone, similarly, show three absorption peaks in the 3500-3000 cm^{-1} region.

No definite assignments of the absorption bands could be made in the 1650-1400 cm^{-1} range since phenazine itself exhibits a variety of absorption bands in this region. The strong absorption at 1335 cm^{-1} might arise from the C-N stretching vibrations of the amino group. The bands at 855 cm^{-1}, 825 cm^{-1} and 760 cm^{-1} are consistent with the presence of one single, and two and four adjacent hydrogen atoms, respectively, in the structure (XVIII).

In the spectrum of 2-N-acetylaminophenazine (XXVI) (Table 8, Fig. 12)



XXVI

there are two medium intensity peaks at 3300 cm^{-1} and 3200 cm^{-1} associated with the N-H stretching modes (109) and a weaker band at 3070 cm^{-1} the assignment of which remains uncertain since the aromatic C-H stretching band

appears in the same region. The strong bands at 1700 cm^{-1} and 1675 cm^{-1} could arise from C=O stretching modes. Here, as in the case of 2-aminophenazine, characteristic absorption for 2-substitution is observed in the 900-700 cm^{-1} region.

2-Nitraminophenazine

Formation and Rearrangement of Nitramines

Wright and his co-workers (110,111) have made an essential contribution to the understanding of the mechanism of nitramine formation. They applied colorimetric titration, using o-nitroaniline as the indicator, to determine the proton-attracting tendency of seventeen aliphatic amines, in acetic acid solution, with respect to perchloric and sulphuric acids. A comparison of the values obtained for the relative proton-attracting tendency of these amines with their behaviour in direct nitration with nitric acid showed that the poorest proton acceptors are the most easily nitrated to form nitramines.

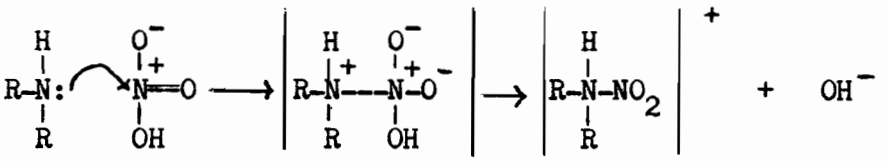
The proton-accepting tendency of an amine is represented by the following equilibrium:

$$R_2NH + HNO_3 \rightleftharpoons \left|R_2NH.HNO_3\right| \rightleftharpoons \left|R_2NH_2\right|^+ + \left|NO_3\right|^-$$

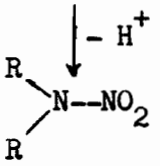
XXVII

Formation of the nitrate salt structure (XXVII) involving a hydrogen bridge would be characteristic of a strong amine. Therefore on the basis of its behaviour in nitration the salt (XXVII) is not the intermediate leading to the formation of a nitramine which contains a N-N bond.

Wright suggests that weak amines with electron donor properties first coordinate with nitric acid (XXVIII), then ionize into hydroxyl and nitrammonium ion (XXIX):



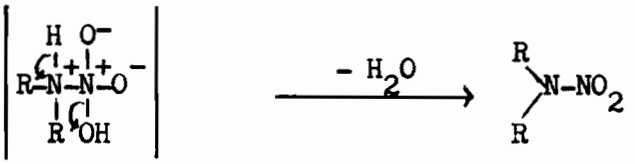
XXVIII XXIX



XXX

Loss of a proton from the nitrammonium ion (XXIX) provides the nitramine (XXX).

Direct formation of the nitramine (XXX) from the intermediate (XXVIII) by a trans-elimination of water could be considered as a possible variation of the mechanism:

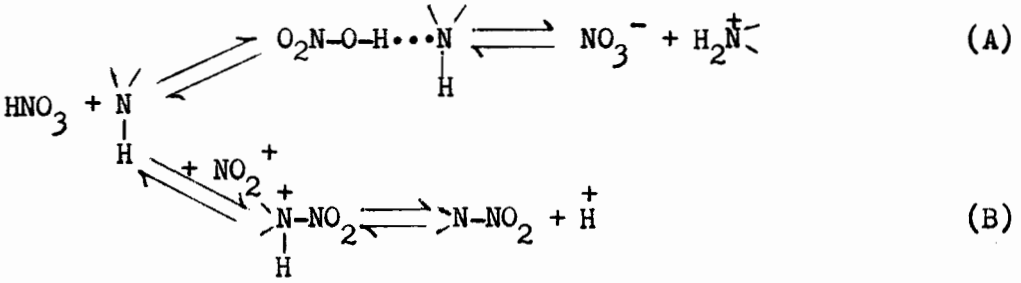


XXVIII XXX

In the case of weak amines the author considers, as an alternative possibility, the formation of nitramines by direct nitration of the free amine which exists in equilibrium with its salt. However, he is of the opinion that there is a certain necessity for salt formation as an adjunct to nitration. The very weak base diphenylamine will not form a nitramine, likewise diacetamides which do not form salts cannot be nitrated in the amino-group.

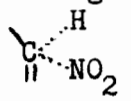
Wright's basic views on the mechanism of nitramine formation have been reformulated by Lamberton (112). The latter suggests that

Wright's nitrammonium ion (XXIX) is formed directly by co-ordination of a nitronium ion (NO_2^+) with the nitrogen atom of the free base. However, at the same time the author admits that the distinction involved in this modification of the nitramine formation mechanism is perhaps more apparent than real. The reaction of amines with nitric acid is summarized by Lamberton in the following scheme:



(A)

(B)

It is assumed that the nitration of amines (and amides) is a result of two competing reversible bimolecular reactions (A,B) followed, in one case, by the ejection of a hydrogen ion. Such a mechanism differs from that postulated for aromatic nitration in (1) the existence of a competing reaction (A) and (2) the comparative stability which might be attributed to $\overset{+}{N}H\text{-}NO_2$ in contrast with the transition state  (in aromatic nitration).

Strong bases may be converted almost wholly into the quaternary $\overset{+}{N}H_2$- form, and bases weaker than amides may not react with the nitronium ion. In neither case will nitramine formation occur.

The nitration of aromatic amines can take place in the nucleus as well as in the amino-group. The product of N-nitration, i.e. the nitramine, may undergo an acid-catalyzed rearrangement with migration of the nitro-group to the aromatic ring, thus yielding products of "indirect nitration". Which mechanism, or mechanisms, will prevail in the process

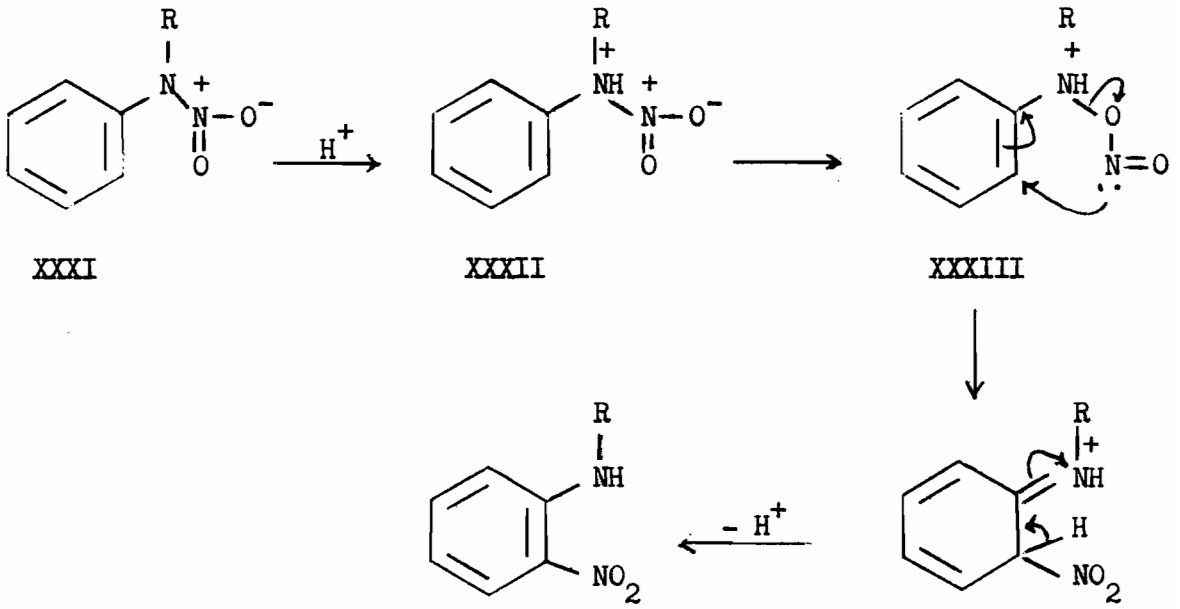
will depend on the reaction conditions, the basicity of the species undergoing nitration and the reactivity of different positions in the aromatic nucleus.

Hughes and Jones (113) nitrated aniline and rearranged nitraminobenzene under strictly comparable conditions in 85% sulphuric acid at a temperature near the freezing point of the mixture. They obtained 6, 34 and 59 per cent of ortho-, meta-, and para-nitroaniline, respectively, by nitration, and 93, 0 and 7 per cent of the same products, by rearrangement. These results left no doubt that direct nitration of aniline in 85% sulphuric acid and the rearrangement of phenylnitramine under the same conditions were two essentially independent processes (114).

Investigation of the acid-catalyzed rearrangement of aromatic nitramines by the above-mentioned investigators furnished evidence proving the essentially intramolecular character of this reaction. This had previously been suggested in the early work of Bamberger (115).

In order to explain the high percentage of ortho-isomer produced in the rearrangement of phenylnitramine, Hughes and Ingold (114) suggested an especially facile intramolecular route for this reaction involving an ortho-migration of the nitro-group.

The mechanism includes isomerization of the nitramine (XXXI) to a nitritoamine (XXXIII) which rearranges further through a cyclic transition state to ortho-nitroaniline (XXXIV). The isomerization is assumed to take place in the ionic conjugate acid (XXXII):



XXXI XXXII XXXIII XXXIV

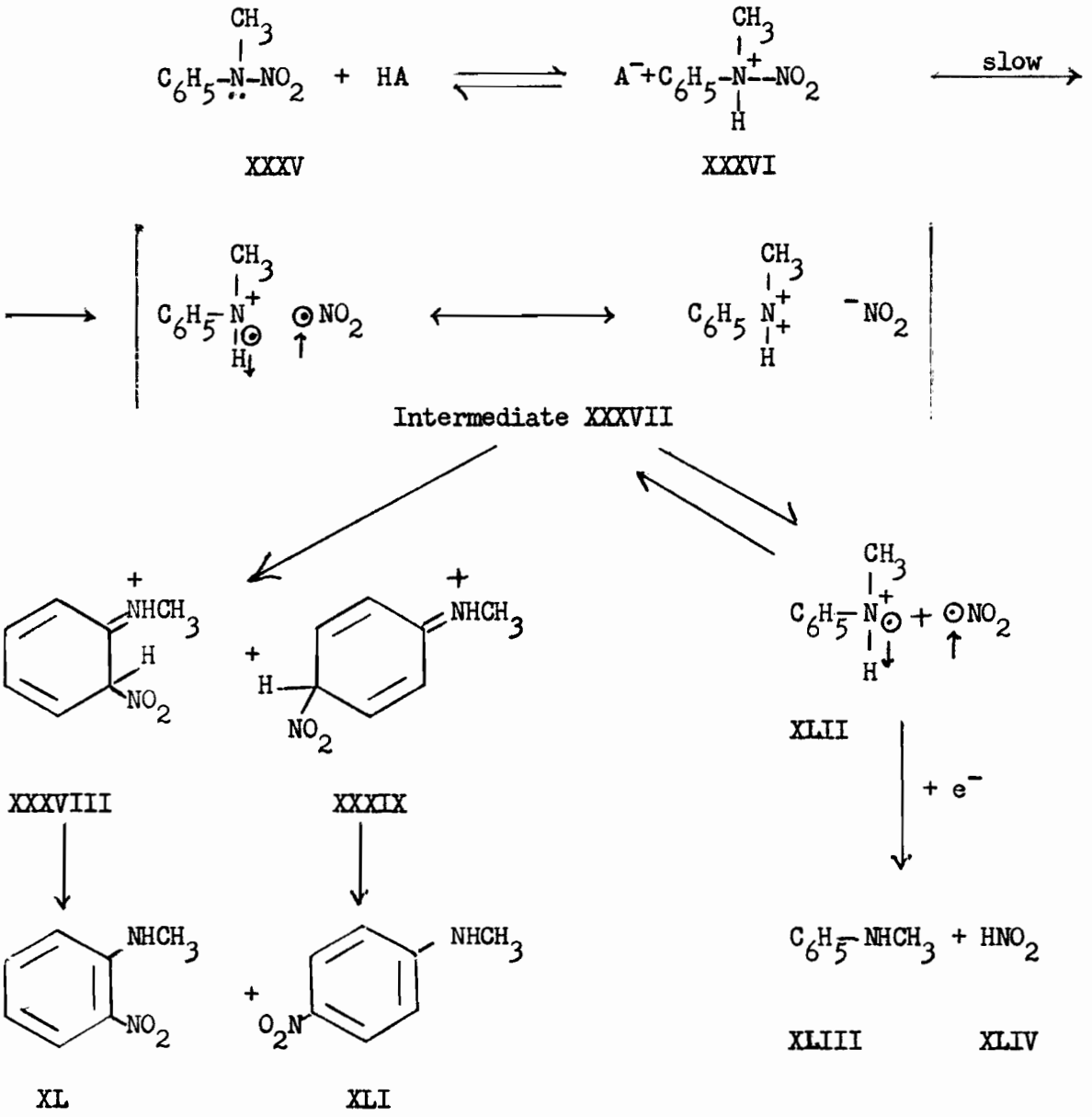
The weakness of the Hughes-Ingold mechanism, outlined above, lies in its restriction of the nitro-group to ortho-migration, while para-rearrangement of aromatic nitramines, which usually accompanies ortho-migration, has to be explained by a different mechanism.

Recently, White and co-workers (116) announced the completion of research which resulted in the proposal of a new mechanism for the acid catalyzed rearrangement of N-nitroanilines to o- and p-nitroanilines.

N-Nitro-N-methylaniline-C_{14} (XXXV) was treated with 0.1 N hydrochloric acid at 40°. The rearrangement product consisted of 52.1% ortho-nitro-N-methylaniline (XL), 30.9% para-nitro-N-methylaniline (XLI), 9.9% N-methylaniline (XLIII); no meta-nitro-N-methylaniline was formed. In addition 13% of nitrous acid (XLIV) was produced.

The mechanism suggested to explain these experimental results is

represented by the following scheme:



The main novelty of this mechanism is the structure of the intermediate (XXXVII). It is considered to be a radical molecular complex in which the bonding is realized by overlapping of the π-orbitals. Such radical π-complexes are described (117) as sandwich type structures in which both fragments participating in their formation lie in parallel

planes. The one unpaired electron of each fragment is in the π-orbital which extends throughout the conjugated atoms. The complex is stabilized by the interaction of π-electrons of the two fragments.

Radical π-complexes dissociate fairly readily. In solution they are in equilibrium with the components from which they are formed.

The formation of such an intermediate π-complex (XXXVII) which collapses to the two cyclohexanedieneimines (XXXVIII, XXXIX) explains the facile formation of ortho-, as well as para--nitroanilines (XL, XLI).

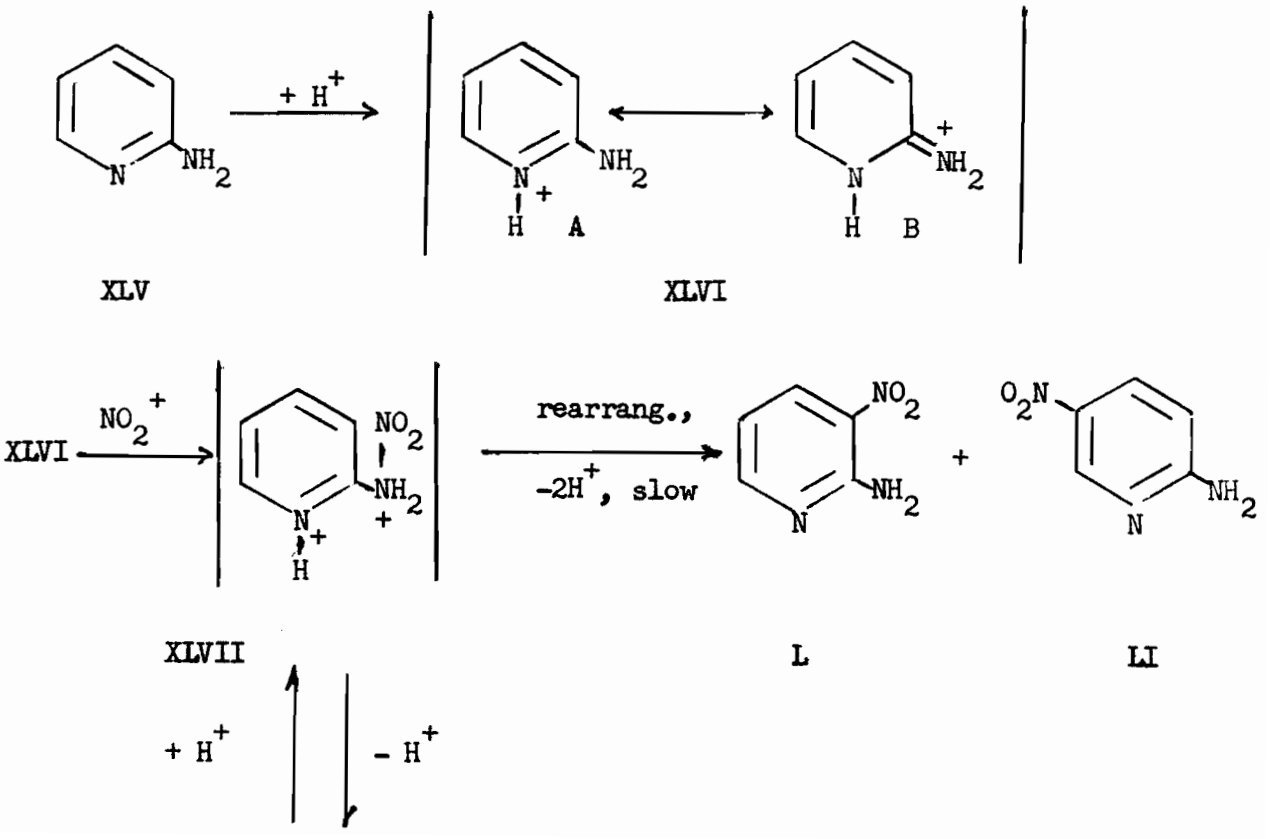
Rearrangement of N-nitro-N-methylaniline-2,6-d_2 yielded the same ratio of isomers in the reaction product as ordinary N-nitro-N-methylaniline. This fact is consistent with the proposed mechanism. If an ortho-shift (114) were involved in the rearrangement reaction the ratio would change due to a rate decrease of the competing deuteron loss from the ortho-intermediate.

The N-methylaniline (XLIII) and nitrous acid (XLIV) are formed on reduction of the free radical (XLII) which is in equilibrium with the π-complex (XXXVII). Rearrangement in the presence of aniline yielded emeraldine, a product of free radical oxidation of aniline. Hence, a free radical must have been present in the reaction mixture. Addition of a reducing agent like hydroquinone or α-naphthol resulted in an increase of N-methylaniline (XLIII) formation, but the over-all rate was unaffected, indicating that the nitramine does not react with the added reagent directly. Kinetic studies were cited which supported the suggested mechanism of acid-catalyzed nitramine rearrangement. Thus, a mechanism was offered which explains the facile route for the reaction including both

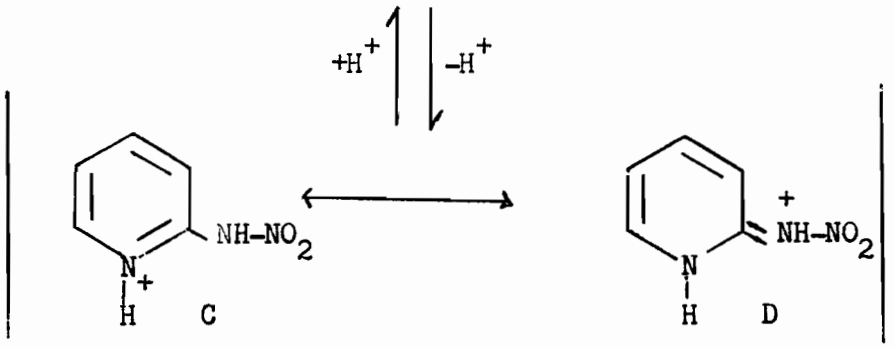
the ortho- and para-migration of the nitro-group.

Aromatic nitramines are unstable in acidic medium, therefore they are prepared by indirect means such as "dehydration" of amine nitrates with acetic anhydride or by oxidation of diazotates (118).

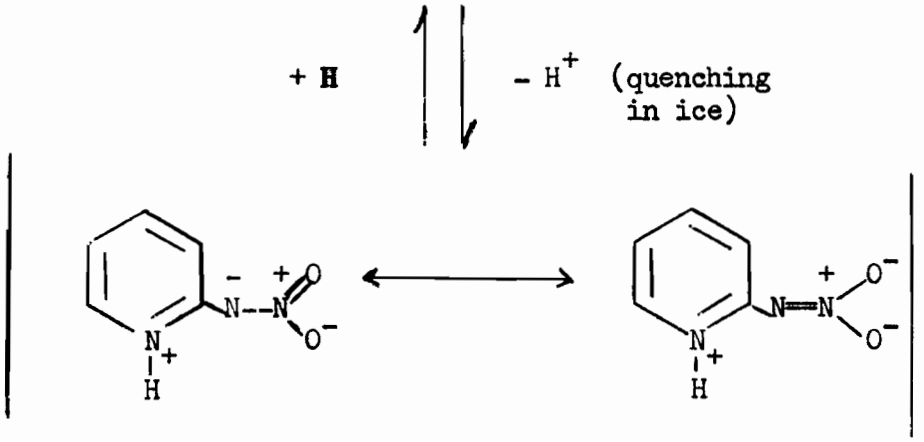
The aza-aromatic nitramines, on account of their much higher stability toward acids, are usually obtained by nitration of amines in sulphuric acid solution (119-123, 78). 2-Nitraminopyridine (XLIX) was prepared by the action of nitric acid on the amine (XLV) in concentrated sulphuric acid (119). On rearrangement of the nitramine (XLIX) in concentrated sulphuric acid a mixture of 2-amino-3-nitro- and 2-amino-5-nitropyridines (L, LI) was obtained. The same products could be obtained without isolating the nitramine (XLIX).



XLVII



XLVIII



XLIX

The principal basic centre in 2-aminopyridine (XLV) is the ring nitrogen (61). The cation (XLVI) formed on protonation of the amine (XLV) is stabilized by resonance between two canonical forms (A,B). In nitration in sulphuric acid this amine conjugate acid (XLVI) would be the most probable species for direct attack by the nitrating agent. The cation (XLVI) is a very weak base and thus, according to Wright (110), would fulfil the condition for nitrammonium ion (XLVII) formation via an intermediate complex with the nitrating agent, or by direct formation of (XLVII) through coordination with a nitronium ion (NO_2^+) (112). The nitrammonium ion (XLVII) can be stabilized (1) by slow rearrangement to

the two aminonitro-compounds (L, LI) or (2) by proton release and formation of the protonated nitramine (XLVIII), which acquires some stability due to resonance (C, D). The protonated nitramine (XLVIII) must be in equilibrium with the nitrammonium ion (XLVII) since in analogous conditions the same rearrangement products are obtained from the previously isolated nitramine (XLIX) as well as directly from the nitration mixture. The rearrangement reaction must be a slow process since, if the reaction is quenched at an early stage, the product isolated is the nitramine (XLIX).

The above-discussed behaviour of 2-aminopyridine in nitration is typical of other amino-derivatives of electron-deficient aza-aromatic compounds. It has been proven in many cases that the final nitration products are formed via rearrangement of the intermediate nitramines. A mixture of 2-N-methylamino-3-nitropyridine and its 5-nitro-isomer is obtained by isomerization of 2-N-methylnitraminopyridine (122). 2-Nitraminoquinoline is rearranged to 2-amino-6-nitroquinoline (120) and 2-nitraminothiazoles can be rearranged to 2-amino-5-nitrothiazoles (123).

Nitration of 2-Aminophenazine (XVIII)

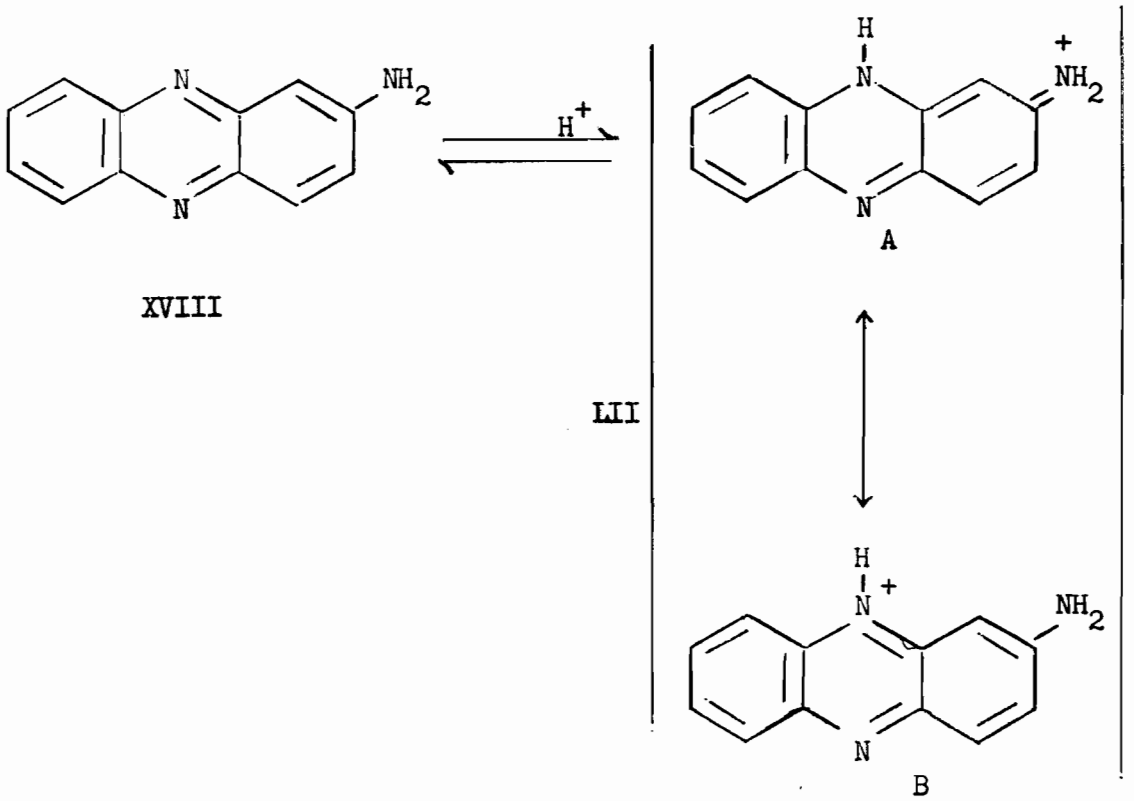
From the π-electron distribution in the phenazine (I) molecule it would be expected the 2-aminophenazine (XVIII) would behave in nitration reaction very much like the above-mentioned aza-aromatic amines.

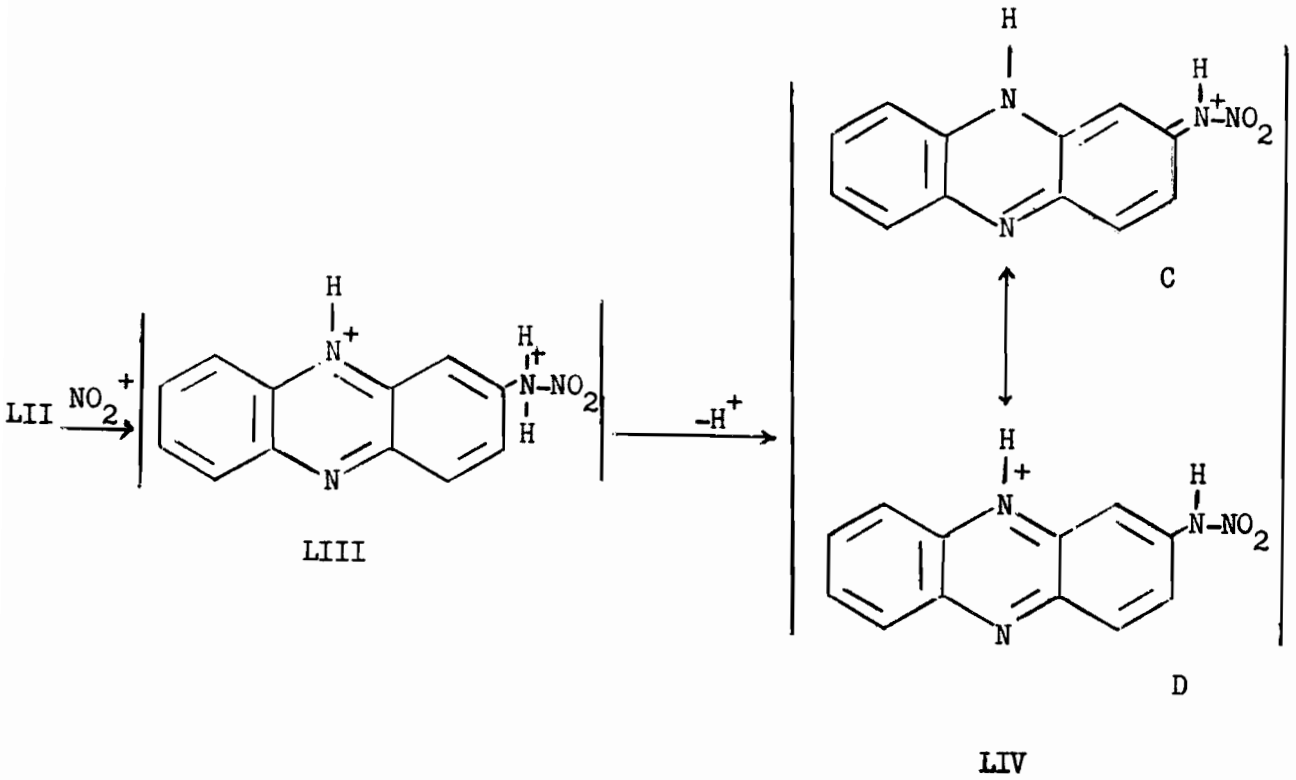
2-Aminophenazine (XVIII) was nitrated in concentrated sulphuric acid with nitric acid (sp. gr. 1.42) at temperatures between -50° and -15°. The formation of the nitramine (LV, LVI) occurred instantly and the

reaction was stopped by pouring the mixture onto ice. The yield of nitramine (LV, LVI) was nearly quantitative and the same whether a 10 or 66% excess of nitric acid was used.

The nitramine (LV, LVI) formed precipitated as an orange amorphous solid. This was dissolved in water with the addition of a few drops of ammonia and reprecipitated from the slightly alkaline solution with aqueous acetic acid.

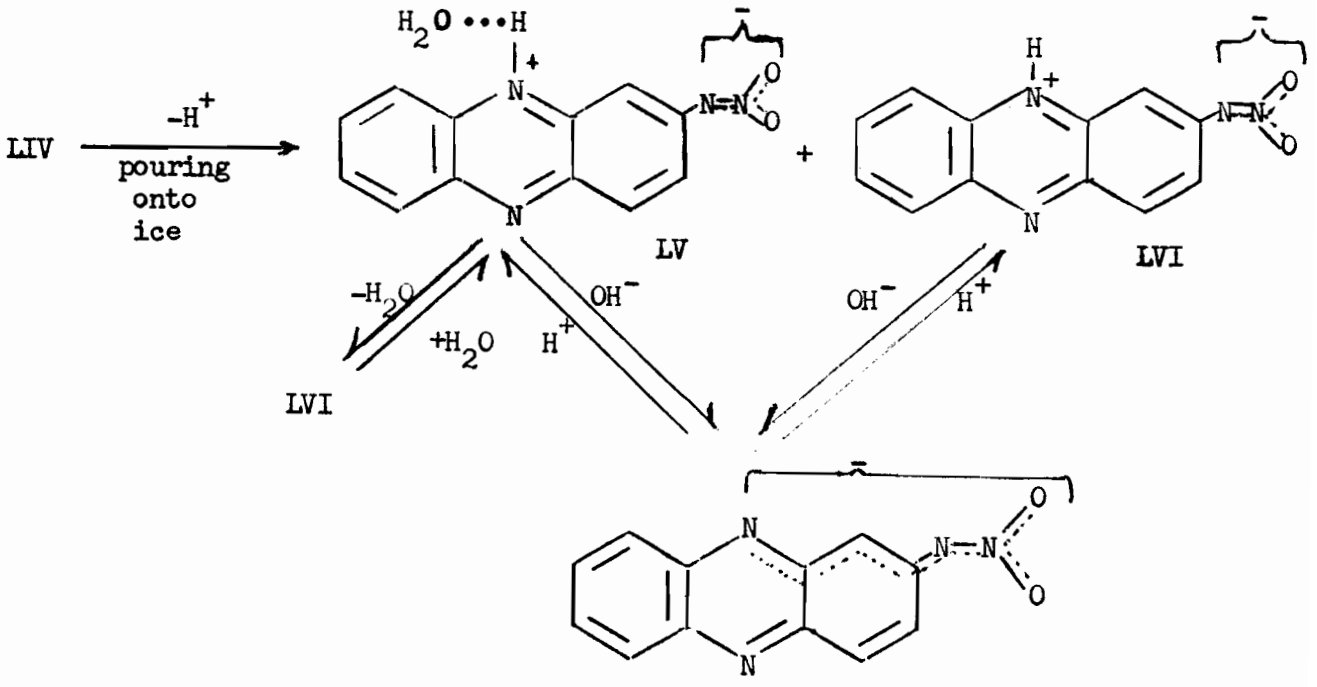
Schematically the preparation of 2-nitraminophenazine (LV, LVI) can be described as follows:





LIII

LIV



LVI

LVII

Since the main basic centre in 2-aminophenazine (XVIII) is the ring nitrogen (61,106), it will be protonated first. The conjugate amine acid (LII) is a resonance hybrid of two canonical structures (A, B) one of which bears a formal plus charge on the amino-group ($=\overset{+}{N}H_2$). Consequently, the basicity of the amino-group in the hybrid (LII) is greatly decreased. In spite of the high acidity of the reaction medium the low basicity of (LII) allows a part of it to be present in the non-protonated state (with a free NH_2-group) and to react with nitronium ions (NO_2^+) forming a covalent N-N-bond (LIII). The intermediate nitrammonium ion (LIII) releases a proton to yield the relatively stable protonated nitramine (LIV). The latter may owe its stability to the possibility of resonance (C, D). When the reaction is stopped by pouring the mixture onto crushed ice the nitramine (LV, LVI) is formed.

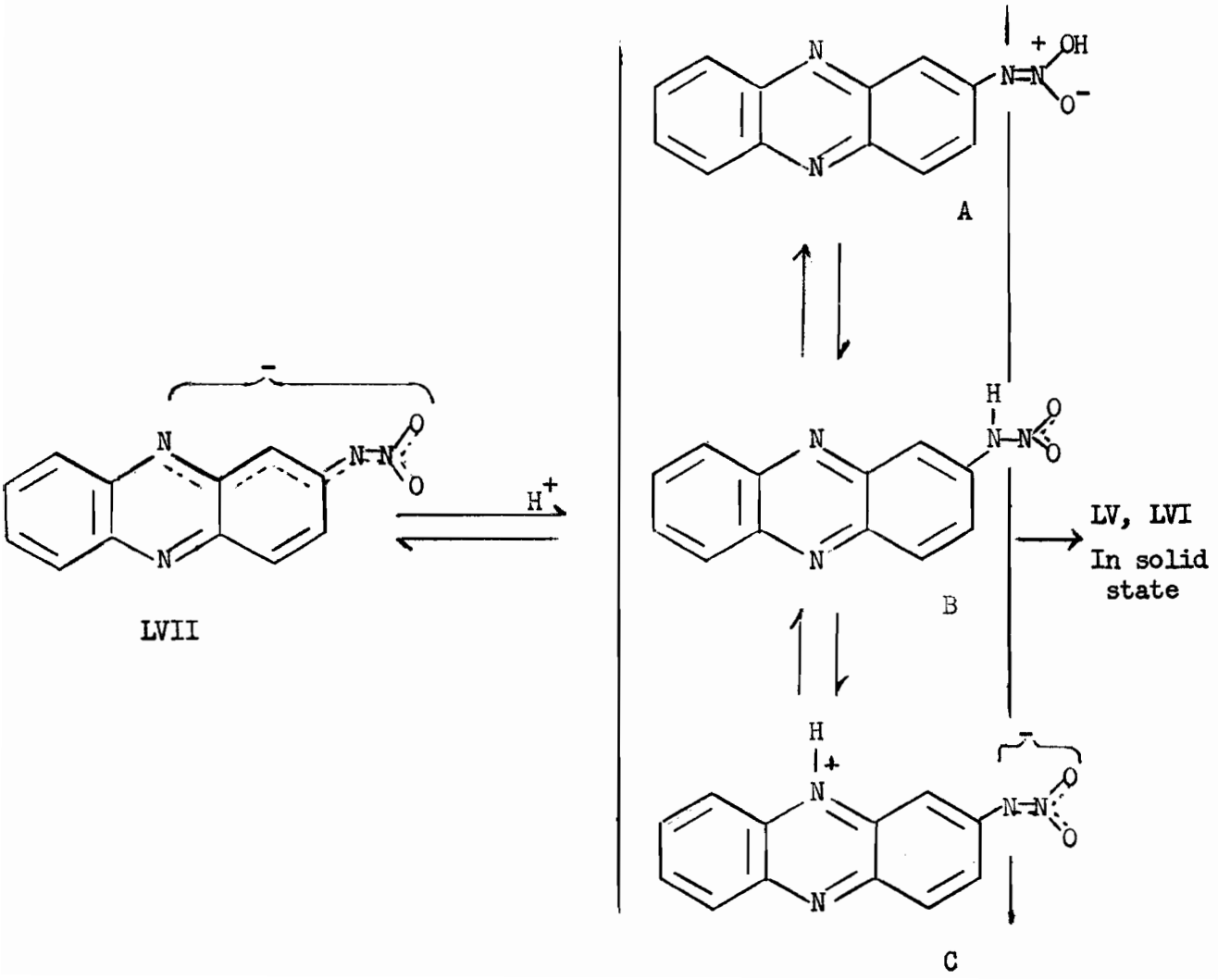
The 2-nitraminophenazine (LV, LVI) obtained in this way was a pure mixture of the monohydrate (LV) and the anhydrous nitramine (LVI), the former being the main component. On prolonged drying (for several days) the monohydrate (LV) was converted gradually to the anhydrous material (LVI).

The pure monohydrate (LV) was prepared by slow crystallization from a dilute acidic solution of the nitramine (LV, LVI). It precipitated in golden needles which could be dried apparently without loss of water of crystallization.

The monohydrate (LV) as well as the mixture of both forms (LV, LVI) when dried by the benzene distillation procedure at 50° yielded anhydrous nitramine (LVI) as a yellow amorphous powder.

Both forms dissolve readily in dilute alkali to produce the highly stable anion (LVII), which owes its stability to the delocalization of the negative charge over a large part of the molecule.

Three tautomeric forms of 2-nitraminophenazine are likely to be formed in solution on protonation of the anion (LVII), the isonitramine (A), the nitramine (B) and the nitrimino inner salt (C):



In solution the three tautomers (A, B, C) might be in equilibrium through the common anion (LVII). Of them the nitrimino-inner salt (C) would be the most likely to precipitate as a solid, being the least acidic (since the proton is attached to the most basic centre) and the least soluble. The primary protonation product (by H_3O^+) should be the monohydrate (LV) which might undergo partial dehydration yielding the anhydrous nitramine (LVI).

The evidence for the structure of the nitramines (LV, LVI) is based on their physical properties such as infrared spectrum and melting point. Another proof is derived from their chemical behaviour, i.e. acidic character, salt formation and acid-catalyzed rearrangement to 2-amino-1-nitrophenazine (LVIII).

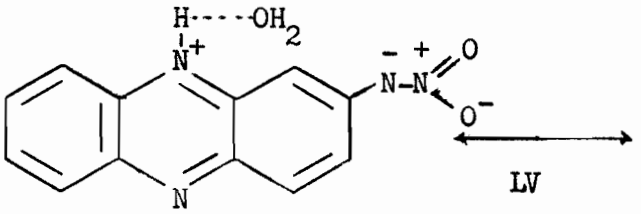
The infrared spectra of the two 2-nitraminophenazines are consistent with the structures proposed (Table 7, Fig. 6).

The monohydrate (LV) shows a broad band with maxima at 3540, 3400 and 3200 cm^{-1}. This absorption is attributed to the presence of the water of crystallization in the compound (LV). The weak, broad band at 2700 cm^{-1} is assigned to $\overset{+}{N}$-H-stretching modes. In the region of $-NO_2$ symmetrical vibrations, a strong band appears with two peaks at 1315 and 1300 cm^{-1}. The absorption pattern in the range 900-700 cm^{-1} is in agreement with a phenazine substituted in position two, the 880 cm^{-1} peak being assigned to the single 1-hydrogen atom, the band at 835 cm^{-1} to the two adjacent 3,4-hydrogen atoms and the strong band with peaks at 765, 755 and 745 cm^{-1} to out-of-plane deformations of the unsubstituted carbocyclic ring hydrogen atoms.

In the infrared spectrum of the anhydrous nitramine (LVI) the broad unresolved band between 3100 cm^{-1} and 2700 cm^{-1} is considered to be due to the $\overset{+}{N}$-H stretching vibrations. Taurins (77) has linked the band observed in this region in nitramines with the presence of a $\overset{+}{N}$-H group, when no absorption characteristic for =N-H is present at higher frequencies. Sandorfy (124) has found that the shift in frequency occurring on quaternization of an amine nitrogen is due to the electrostatic interaction of the type $\overset{+}{N}$-H.....X^-, where X^- is the anionic component of the structure. Any change in this interaction will cause, correspondingly, a change in the absorption pattern assigned to this group. Thus, the observed difference in frequency and shape of the bands assigned to the $\overset{+}{N}$-H stretching vibrations in the monohydrate (LV) and in the anhydrous nitramine (LVI) was expected, since the water molecule hydrogen-bonded with the $\overset{+}{N}$-H group in (LV) must have changed the electrostatic interaction between the latter group and the anionic component of the molecule ($-\overset{+}{N}=N\begin{matrix}O^- \\ O^-\end{matrix}$). The very weak band appearing at 3400 cm^{-1} is due to the presence of moisture in potassium bromide; the spectrum taken in "Nujol" does not show this absorption. The pattern of bands in the region 900-700 cm^{-1} is similar to that observed in the case of the monohydrate (LV) except for two new peaks at 855 cm^{-1} and 790 cm^{-1}. The latter absorption is especially significant since Bellamy (125) has noticed the occurrence of a band of medium intensity in the region 790-770 cm^{-1} in the spectra of nitramines, and other investigators have confirmed this observation (104). These two extra bands present in the spectrum of the anhydrous nitramine (LVI) and the difference in the spectra of the anhydrous and monohydrate forms over 2500 cm^{-1} provided an easy way for

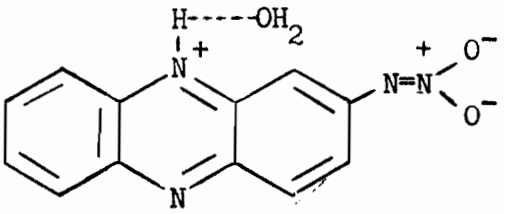
distinguishing between the two forms of 2-nitraminophenazine (LV, LVI).

The infrared analysis of 2-nitraminophenazine indicates that its structure would be best represented as a resonance hybrid (LV, LVI) of two canonical forms (A, B), as the main contributors:

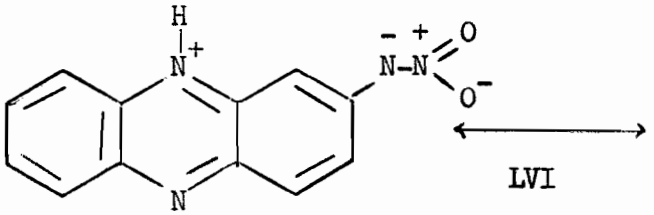


LV

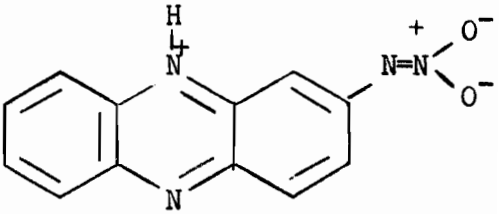
A



B



LVI



According to Taurins (77) these should be called 2-nitrimino-(1OH) phenazinium betaines or inner salts.

Both the monohydrate (LV) and the anhydrous nitramine (LVI) decompose rapidly when heated to 150-160°. This property confirms their structure as nitramines.

No differences have been observed in the chemical behaviour of the two forms (LV, LVI). They are weakly acidic, dissolve in dilute alkali and are reprecipitated from the solution with dilute acids. When treated with concentrated sulphuric acid the nitramine (LV, LVI) is rearranged to

2-amino-1-nitrophenazine (LVIII).

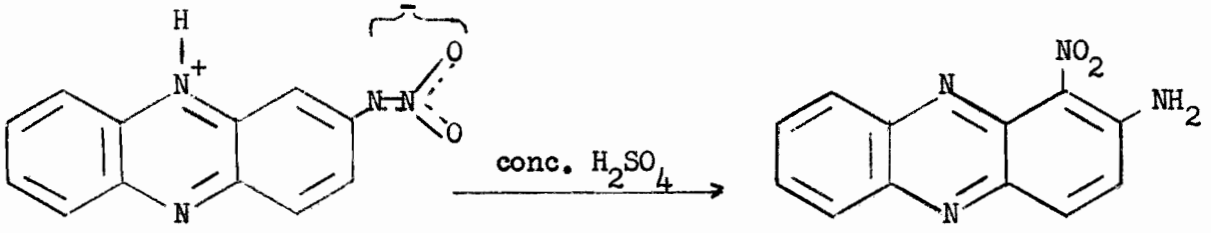
The ammonium, potassium and sodium salts of 2-nitrimino-(10H) phenazinium betaine (LV, LVI) crystallize out of the solution on addition of the corresponding acetates to a slightly alkaline solution of the nitramine in water. In the behaviour of the sodium salt an unexplained peculiarity has been observed. The nitramine (LV, LVI) is readily soluble in very dilute sodium hydroxide solution. On addition to this solution of a concentrated solution of sodium hydroxide, sodium acetate or sodium sulphate the nitramine sodium salt is precipitated instantly. Once precipitated the salt is no longer readily soluble in cold water. It dissolves only on prolonged boiling in water and does not crystallize back on cooling. In contrast to its slight solubility in cold water the nitramine (LV, LVI) sodium salt is readily soluble in absolute ethanol and dissolves in 1-butanol on being slightly heated.

The elemental analyses of the sodium, ammonium and potassium salts are consistent with their molecular formulae $C_{12}H_7O_2N_4.Na.2H_2O$, $C_{12}H_7O_2N_4.NH_4$ and $C_{12}H_7O_2N_4.K.H_2O$, respectively. The infrared spectra of the salts (Tables 7, 8; Fig. 7, 9) in the 900-700 cm^{-1} region show an absorption pattern that is in agreement with the phenazine substituted in position two, thus constituting additional evidence for the structure of the nitramine (LV, LVI).

Rearrangement of 2-Nitrimino-(1OH)phenazinium Betaine (LV, LVI)

The rearrangement of the nitramine (LV, LVI) was carried out in concentrated sulphuric acid at 0°. The reaction is slow but after three hours the isomerization was complete.

2-Amino-1-nitrophenazine (LVIII), the main rearrangement product, was obtained in 55% yield of pure material after chromatography.



LVI LVIII

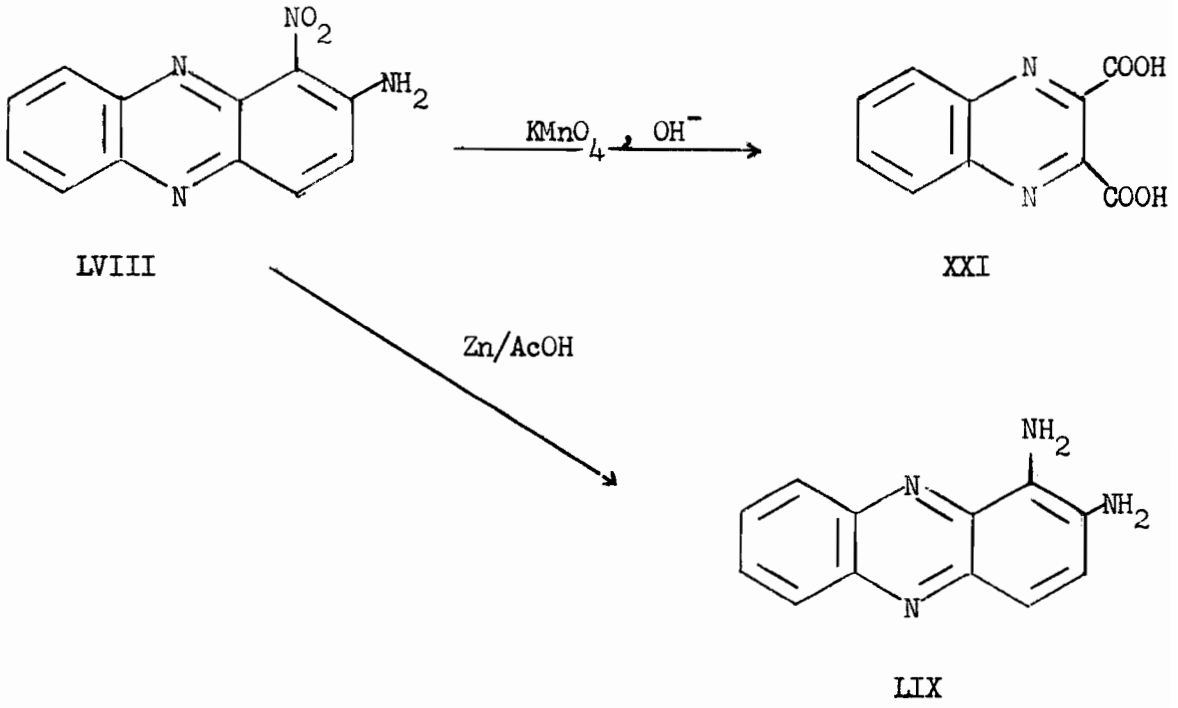
The compound (LVIII) is basic and is insoluble in aqueous alkali hydroxides but dissolves readily in 5% hydrochloric or sulphuric acid.

Direct nitration of 2-aminophenazine (XVIII), carried out under conditions similar to those of rearrangement, resulted in the formation of (LVIII) in a slightly lower yield. Since the nitramine (LV, LVI) was found to be formed instantly and quantitatively under the conditions employed, it is quite obvious that in the case of direct nitration the formation of the aminonitro-compound (LVIII) is accomplished also by way of rearrangement of the intermediate nitramine (LV, LVI). The fact that, in spite of the nitric acid being present in a 10% excess in the latter reaction, the yield of the nitro-product (LVIII) did not increase might be considered as

an argument in favour of the intramolecular mechanism for the rearrangement process (113,114,116).

The structure of 2-amino-1-nitrophenazine (LVIII) was proven in several ways.

(a) The compound (LVIII) when oxidized in alkaline medium with potassium permanganate yields quinoxaline-2,3-dicarboxylic acid (XXI). This proves that only one of the two carbocyclic rings in (LVIII) is substituted. The reduction of (LVIII) to 1,2-diaminophenazine (LIX), the only diamine which could be different from the known 1,3- and 2,3-diaminophenazines is conclusive evidence for the proposed structure of the aminonitrophenazine (LVIII).

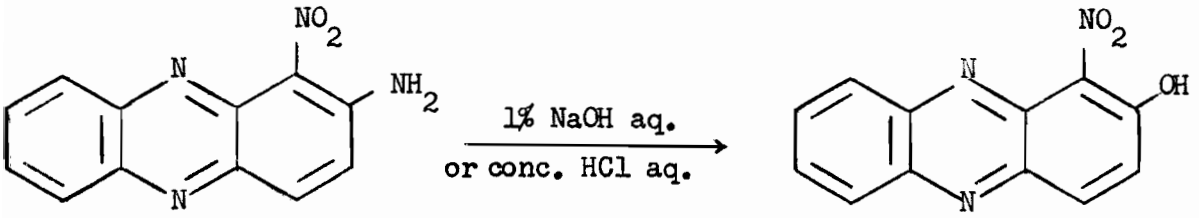


LVIII XXI

LIX

(b) The amino-group in (LVIII) is replaced by an hydroxyl-group on refluxing with concentrated hydrochloric acid or boiling with 1% aqueous sodium hydroxide. Thus, 2-hydroxy-1-nitrophenazine (LX) is obtained, a compound

which has previously been prepared by a different procedure (71):



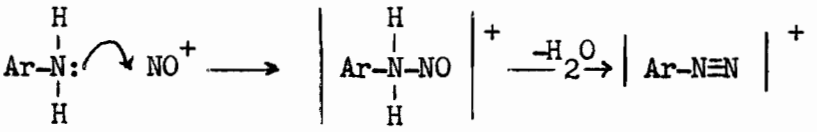
LVIII LX

(c) The infrared spectrum of 2-amino-1-nitrophenazine (LVIII) (Table 8, Fig. 8) exhibits three bands in the region of NH_2-stretching vibrations at 3430, 3290 and 3170 cm^{-1}. The first two frequencies are assigned to vibrations of the free amino-group and the third might be due to association of the group. The frequencies assigned to asymmetric and symmetric stretching modes of the free NH_2-group do not concur with the previously cited correlation found by Bellamy and Williams (107), although the latter correlation is obeyed in the case of 2-aminophenazine (XVIII). This may indicate hydrogen bonding between the amino-group and the ortho-nitro-group resulting in a shift of the corresponding frequencies. The peaks at 1520 cm^{-1} and 1280 cm^{-1} are correlated with the asymmetric and symmetric stretching vibrations, respectively, of the nitro-group. The lack of any bands between 900 cm^{-1} and 850 cm^{-1} and the presence of a peak at 802 cm^{-1} is consistent with the 1,2-substitution assigned to the structure (LVIII).

It was thought that additional evidence for the structure of the 2-amino-1-nitrophenazine (LVIII) could be obtained by replacing the amino-group with a hydrogen atom by diazotization. However, (LVIII), when treated

under the same conditions by which 2-aminophenazine (XVIII) had been instantly diazotized, resisted the reaction.

The mechanism of diazonium salt formation proposed by Kenner (126) postulates the formation of an intermediate nitrosoammonium ion (LXII) in the diazotization process. In this reaction the amine (LXI) is the nucleophilic reagent:



LXI LXII

Picramide, the amino-group of which has less nucleophilic character due to the electron withdrawal caused by the three ring-nitro-groups, resists diazotization. The same explanation can apply to the case of 2-amino-1-nitrophenazine, in which the nucleophilic character of the amino-group is greatly decreased due to conjugation with two strongly electron-attracting centres, the ring nitrogen and the ortho-nitro-group.

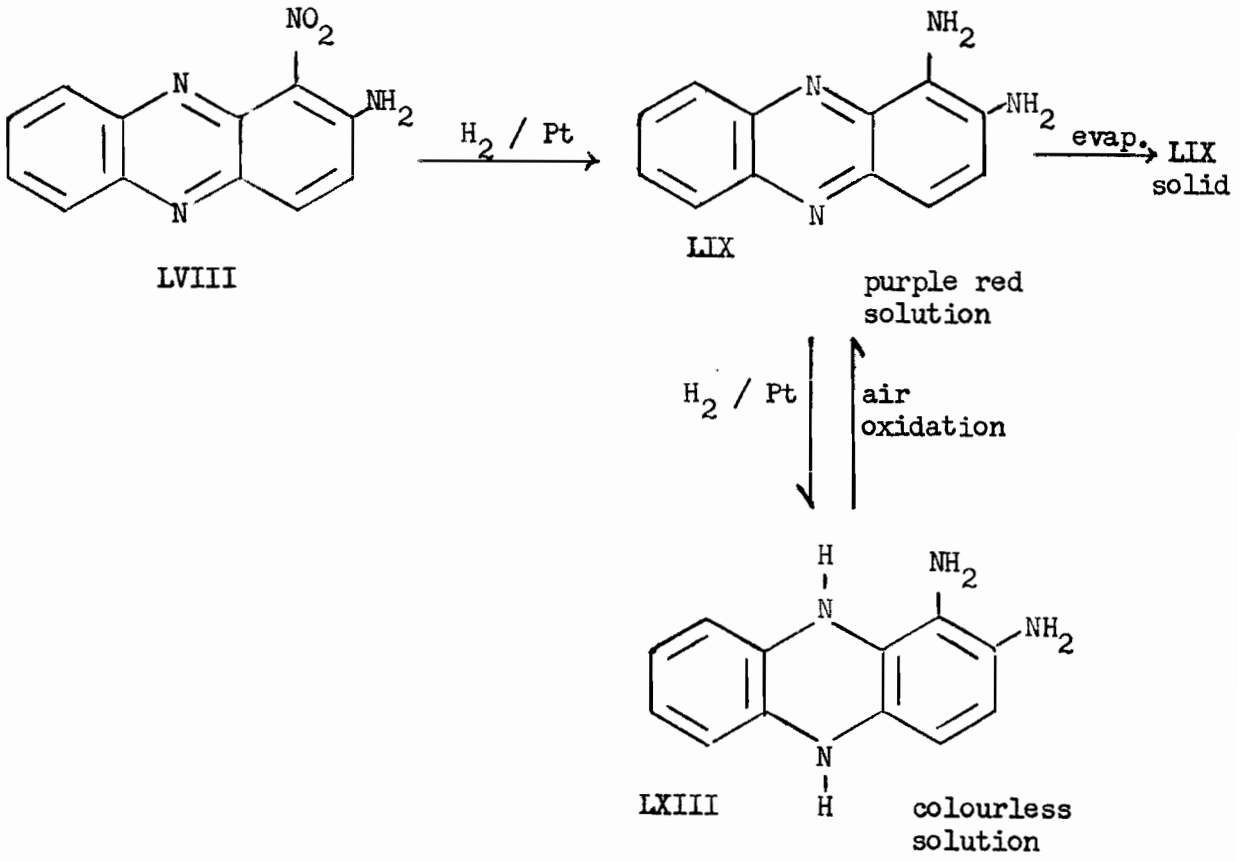
1,2-Diaminophenazine (LIX)

1,2-Diaminophenazine (LIX) was conveniently prepared in good yield by the zinc-acetic acid reduction of 2-amino-1-nitrophenazine (LVIII).

The same diamine (LIX) was also obtained by catalytic reduction of (LVIII). When the latter in methanolic solution was reduced with hydrogen in the presence of a platinum catalyst the colour of the liquid changed from brown to purple red to nearly colourless. On exposure to air

the colourless liquid turned purple red again and, when evaporated, left a residue which after sublimation yielded pure 1,2-diaminophenazine (LIX). The colourless methanolic solution was considered to contain a product of further hydrogenation, namely, the 1,2-diamino-5,10-dihydrophenazine (LXIII). Hydrogenation of both ring-nitrogen-atoms in (LIX) has destroyed the high degree of conjugation, responsible for the colour, and rendered the compound (LXIII) sensitive to oxidation by air. Any intermediate hydrogenation product structure for (LXIII) is excluded since phenazine-derivatives of this kind, the phenazhydrins, are coloured substances.

The catalytic reduction of (LVIII) is summarized in the scheme:



The 1,2-diaminophenazine (LIX) has a considerably lower melting point than the two known 1,3- and 2,3-diaminophenazines and sublimes more easily. The latter property of the diamine (LIX) facilitates its purification. The amine (LIX) reacts with dilute hydrochloric acid at room temperature to form a yellow solid which precipitates from the solution. From solution in dilute acetic acid, diamine (LIX) can be recovered by rendering the liquid alkaline with ammonia.

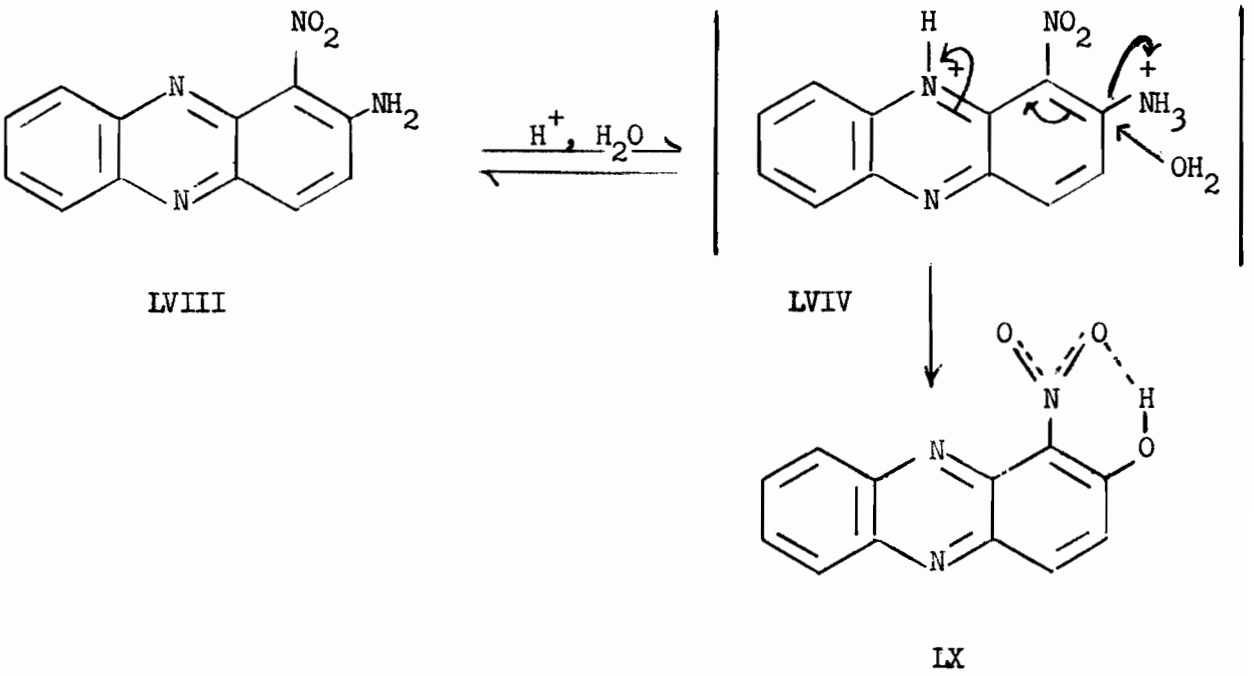
The infrared spectrum of 1,2-diaminophenazine (LIX) (Table 9, Fig. 9) exhibits a broad unresolved band with three maxima at 3390, 3300 and 3170 cm^{-1}. The first two frequencies agree satisfactorily with the Bellamy-Williams (107) correlation for asymmetric and symmetric NH_2 stretching vibrations. The third peak occurs at a slightly lower frequency than the corresponding band (at 3200 cm^{-1}) in 2-aminophenazine (XVIII). As expected, there is no absorption in the 1300-1270 cm^{-1} region which could be attributed to a nitro-function, indicating that the aminonitrophenazine (LVIII) has been reduced. The absorption pattern in the range 900-700 cm^{-1} does not show clear correlation with 1,2-substitution. Such a situation has been noted with other diamines (102). Nevertheless, the four adjacent hydrogen atoms of the unsubstituted carbocyclic ring are represented in the present instance by a strong band at 755 cm^{-1}.

2-Hydroxy-1-nitrophenazine (LX)

2-Hydroxy-1-nitrophenazine (LX), previously prepared (71) by nitration of 2-methoxyphenazine-10-oxide, was obtained by hydrolytic replacement of the amino-group in 2-amino-1-nitrophenazine (LVIII) in both

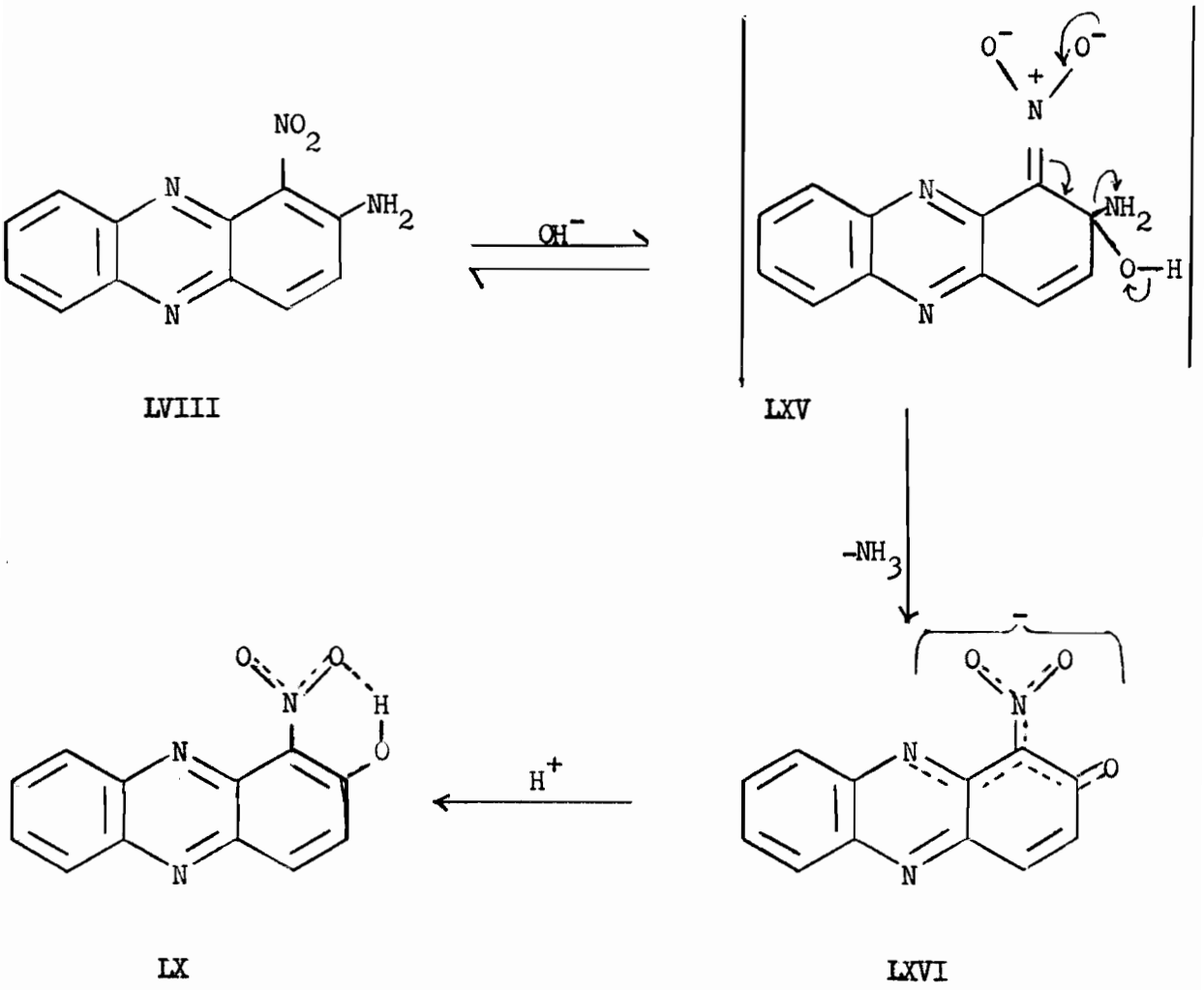
acidic and alkaline media.

(a) Reaction in acidic medium



The replacement of the amino-group in the amino-nitro-compound (LVIII) in acidic medium is facilitated by increased electron withdrawal from position two due to protonation of the ring nitrogen. Thus conditions favourable for an attack by the nucleophilic water molecule are created (LXIV). Another factor favouring the reaction is the higher stability of the reaction product (LX) achieved by chelation of the hydroxyl group with the ortho-nitro-function. The reaction in acidic medium is very slow. After 24 hours refluxing with concentrated hydrochloric acid the reaction was still not complete. The product obtained (LX) was contaminated and difficult to isolate in pure state.

(b) Reaction in alkaline medium



LVIII LXV

LX LXVI

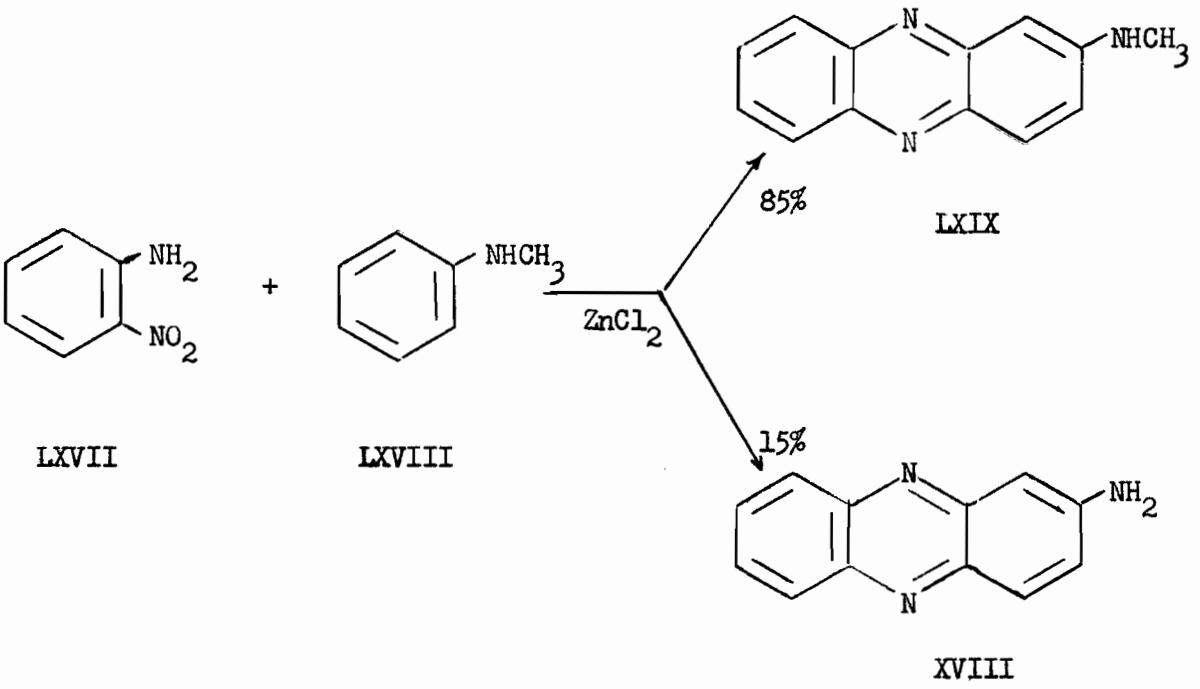
Replacement of the amino-group of (LVIII) in alkaline medium proceeded in a straight forward fashion. It was completed within 1-1/2 hours in a nearly quantitative yield. There are two factors which could explain the facile hydrolysis in alkaline medium. (1) The activation energy for the formation of the complex (LXV) must be low due to the possibility of charge distribution in the latter (LXV) by an electron shift in the ortho-nitro-group. (2) The high degree of stability of the primary reaction product, the anion (LXVI), which is achieved by the negative

charge distribution over a large part of the molecule.

The infrared spectrum of 2-hydroxy-1-nitrophenazine (LX) (Table 9, Fig. 8) has a broad strong band with a maximum at 3040 cm^{-1} indicating the presence of a hydrogen-bonded hydroxyl group in the structure (LX). In the region attributed to asymmetric NO_2-stretching vibrations two very strong bands appear at 1550 cm^{-1} and 1530 cm^{-1}. The absorption at 1250 cm^{-1} is assigned to the symmetric vibrations of the NO_2- group. Contrary to the case of 2-amino-1-nitrophenazine (LVIII) the intensity of the latter band is much less than that arising from asymmetric NO_2 vibrations. The absorption pattern in the range 900-700 cm^{-1} resembles very clearly that observed in the case of 2-amino-1-nitrophenazine (LVIII) indicating the same kind of substitution.

2-N-Methylaminophenazine (LXIX)

2-N-Methylaminophenazine (LXIX) was prepared by a modification of the Wohl-Lange procedure (53).

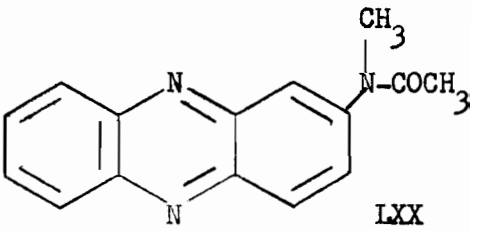


LXVII LXVIII LXIX XVIII

o-Nitroaniline (LXVII) was allowed to react with methylaniline hydrochloride (LXVIII) in the presence of fused zinc chloride. The tarry reaction product, which resulted, was extracted with dilute hydrochloric acid and the acidic extract was rendered alkaline with sodium hydroxide. The basic products recovered in this way were purified by several sublimations (app. Fig. 18). A mixture consisting of approximately 15% 2-aminophenazine (XVIII) and 85% 2-N-methylaminophenazine (LXIX) was obtained. The separation of these two amines was achieved on the basis of their different solubility in chloroform and by chromatography from alumina.

The infrared spectrum of 2-N-methylaminophenazine (LXIX) is consistent with the structure proposed (Table 10, Fig. 11). The single, medium band at 3260 cm^{-1} is assigned to the stretching vibrations of the N-H group. The band at 855 cm^{-1} indicates the presence of the single hydrogen atom in position one and the peak at 805 cm^{-1} is linked with the two adjacent 3,4-hydrogen atoms. The strong band at 755 cm^{-1} is due to the four adjacent hydrogen atoms of the unsubstituted carbocyclic ring.

Acetylation of the amine (LXIX) yields 2-N,N-acetylmethylamino-phenazine (LXX)

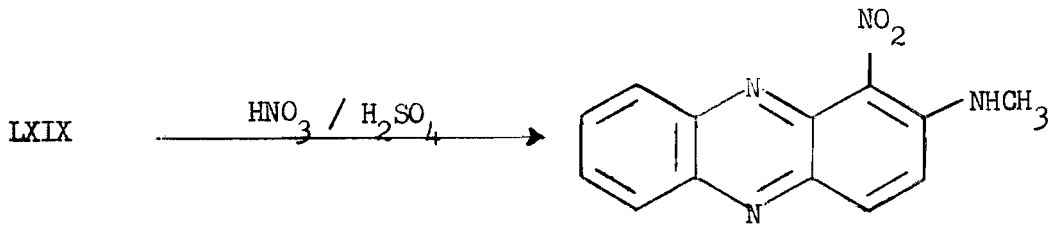
LXIX $\xrightarrow{AcOH\ /\ Ac_2O}$ 

LXX

which, as expected, does not show any absorption bands in the range 3500-3100 cm^{-1} (Table 10, Fig. 11) thus proving that both amino-group hydrogen atoms have been substituted. The spectrum of the compound (LXX) in the 900-700 cm^{-1} region is very similar to that of the parent amine (LXIX).

Nitration of 2-N-Methylaminophenazine (LXIX)

Nitration of 2-N-methylaminophenazine (LXIX) in concentrated sulphuric acid with 70% excess of nitric acid at temperatures below -20° resulted in the instant formation of 2-methylamino-1-nitrophenazine (LXXI).



LXXI

The latter (LXXI), isolated in a 65% over-all yield, was purified by means of chromatography. It is weakly basic and dissolves in 3.7% hydrochloric acid. Recovery from acidic solution can be achieved by rendering the latter neutral with ammonia. The substance can be sublimed in vacuo above 200°.

In connection with the formation of the 2-methylamino-1-nitro-phenazine (LXXI) the question arises whether the direct or indirect nitration mechanism is involved in this reaction. In nitration of aromatic amines, when direct mechanism is operative, usually meta-nitro-derivatives are formed, while in cases where the final product is obtained by rearrangement of the intermediate nitramines no meta-substituted products are found (113,116,118,127,128).

In direct nitration, considerable amounts of the meta-compounds are produced presumably by nitration of the amine conjugate acids in which the $N\text{-}H^{+}$-group should act as the meta-directing centre. Thus, certain conclusions about the reaction mechanism might be derived from a comparison of the composition of the reaction products, provided that proper reference data are available.

The nitration of electron deficient aza-aromatic amines has been found to proceed mainly by an "indirect route" (119-123). In cases in which the intermediate nitramine was not formed the amine resisted nitration.

2-Aminopyridine and 2-N-methylaminopyridine are easily nitrated in the 3- and 5-position through the intermediate nitramine (119,122), while 2-N-acetylaminopyridine, which will not form the corresponding nitramine, does not produce any nitro-compound under the same conditions (129). 3-Aminopyridine forms 3-nitraminopyridine and 3-N-methylaminopyridine is nitrated in the position two through the intermediate nitramine, but the more basic 3-N,N-dimethylaminopyridine and the less basic 3-N-acetyl- and 3-N-formylaminopyridines, which do not form nitramines, resist nitration (130). Thus the distinction between the "indirect" and direct nitration of electron deficient aza-aromatic amines is more obvious than in the case of aromatic amines. The first mechanism represents the "facile route" of the reaction with the characteristic very high rate, while the direct nitration of an aza-aromatic amine would proceed with a low rate, comparable with that for nitration of the aza-aromatic parent compound.

The nitration of 2-N-methylaminophenazine (LXIX) is considered to proceed <u>via</u> an intermediate nitramine which is very unstable in acidic medium.

The 2-N-methyl- and 3-N-methylaminopyridines are nitrated primarily in the amino-group in the same way as the parent 2- and 3-aminopyridines (119,122,130). The nitramines obtained from the N-methyl derivatives are considerably less stable and undergo acid-catalyzed rearrangement with remarkably greater ease than the corresponding parent nitramines. The explanation for this could be the increase in basicity of the nitramine due to the presence of the electron supplying methyl-group, which facilitates the protonation of the intermediate nitramine thus

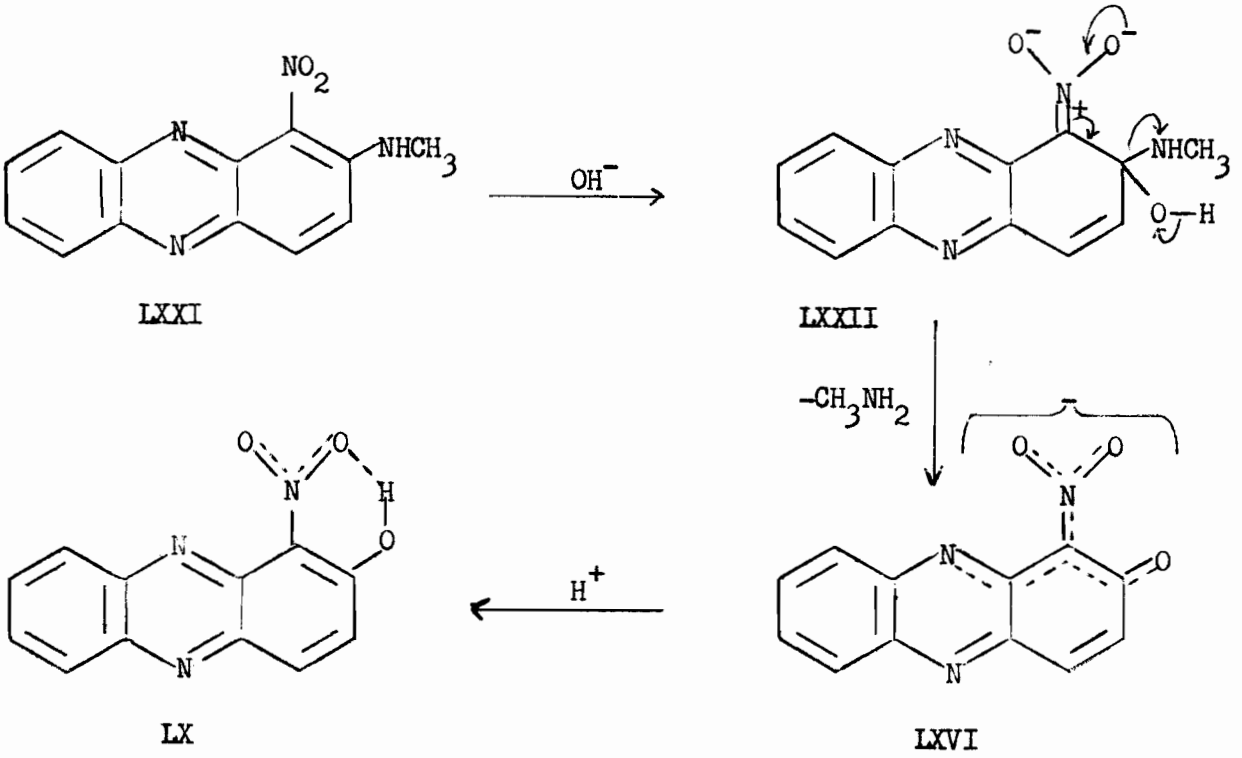
increasing the rate of rearrangement.

An analogous change in reactivity should occur when a methyl-group is introduced into the amino-group of 2-aminophenazine (XVIII). Since 2-nitraminophenazine (LV, LVI) is rearranged smoothly at 0°, the less stable nitramine derived from the 2-N-methylaminophenazine (LXIX) might undergo so fast a rearrangement that it could not be isolated under the given conditions.

The nitro-group shift to position one on rearrangement, identical with that observed in 2-nitraminophenazine (LV, LVI), indicates the probability of the same "indirect nitration" mechanism for 2-N-methylamino-phenazine (LXIX). The direct mechanism, on the other hand, would include the amine conjugate acid with the $-\overset{+}{N}H_2CH_3$ group which, being a meta-directing centre, would favour nitration in the meta-4-position before the ortho-1-position and would also decrease the general reactivity of the compound towards electrophilic attack. In both cases the opposite is observed. (Another alternative of a direct mechanism could be the nitration in one of the α-positions of the other carbocyclic ring.)

In the infrared spectrum of 2-methylamino-1-nitrophenazine (LXXI) (Table 10, Fig. 12) there is a strong band at 3340 cm^{-1} which is assigned to the stretching vibrations of the N-H-group. The very weak unresolved band at 2900 cm^{-1} is correlated with the presence of the methyl-group in the molecule. The very strong absorptions at 1515 cm^{-1} and 1265 cm^{-1} are considered to be due to the presence of the nitro-group. In the 900-700 cm^{-1} region the absorption pattern, similar to that of 2-amino-1-nitrophenazine (LVIII), indicates the same kind of substitution.

Further evidence for the structure of 2-methylamino-1-nitrophenazine (LXXI) was obtained by its transformation to 2-hydroxy-1-nitrophenazine (LX) by treatment with 1% sodium hydroxide solution. The latter (LX) had been prepared previously in an analogous reaction from 2-amino-1-nitrophenazine (LVIII). In this way the position one of 2-methylamino-1-nitrophenazine (LXXI) was proven.



LXXI LXXII

LX LXVI

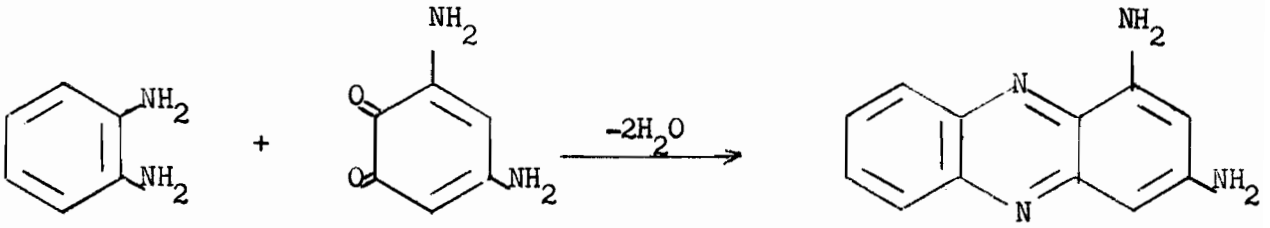
The mechanism involved in the hydrolysis would be analogous to that suggested for the reaction of 2-amino-1-nitrophenazine (LVIII) with aqueous alkali. It includes the formation of the intermediate (LXXII) (with a tetrahedral carbon atom in position two) which is stabilized by expulsion of the methylamine-substituent and formation of the anion (LXVI).

1-Aminophenazine (LXXVII)

The 1-aminophenazine (LXXVII) was prepared in two ways.

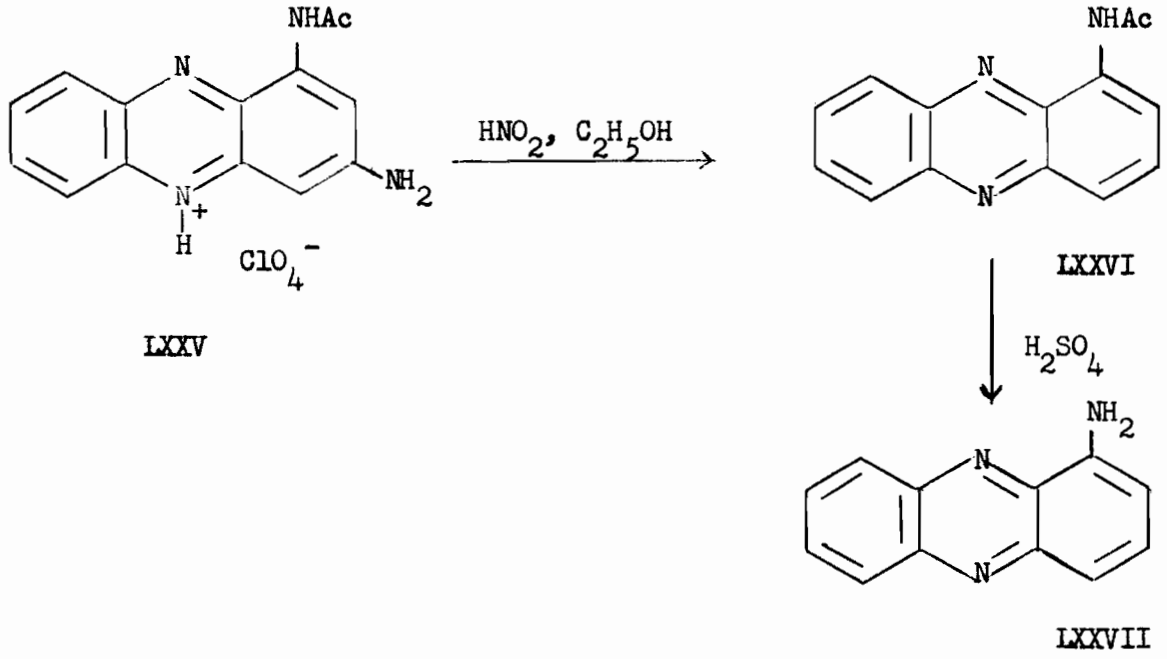
(a) Deamination of 1,3-diaminophenazine (LXXIV)

Following the procedure of Kehrman and Prunier (9), 3,5-diamino-1,2-benzoquinone (LXXIII) dissolved in glacial acetic acid was allowed to condense with ortho-phenylenediamine (XXIV) to form 1,3-diaminophenazine (LXXIV).



XXIV LXXIII LXXIV

The diamine (LXXIV), purified by sublimation, was obtained in a 60% yield. It was noted that in the original procedure the yield of (LXXIV) was not reported. The diamine (LXXIV) was transformed into its acetylperchlorate (LXXV). Deamination of 1-acetylamino-3-aminophenazine perchlorate (LXXV) by diazotization followed by reduction provided 1-acetylaminophenazine (LXXVI) which was hydrolyzed to 1-aminophenazine (LXXVII) by the action of 76% sulphuric acid:



LXXV

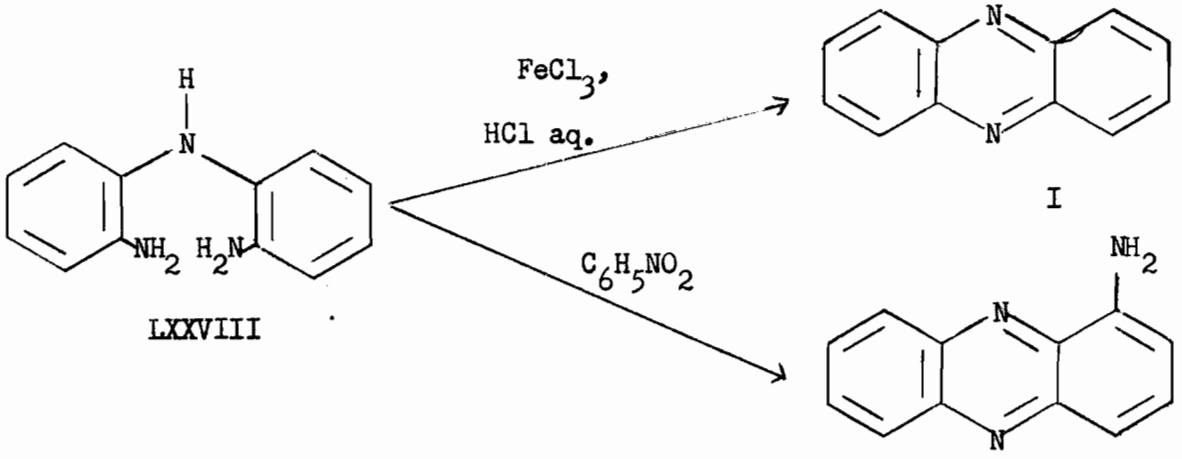
LXXVII

In the literature (9) the yield obtained in the deamination of 1-acetylamino-3-aminophenazine perchlorate (LXXV) is not reported. When this reaction was repeated under the same conditions the best yield obtained was 25% and difficulty was encountered in reproducing even this low yield. Although the procedure of Kehrman and Prunier makes 1,3-diaminophenazine (LXXIV) readily available, the difficulties involved in the deamination of the latter make this procedure inadequate for the preparation of 1-aminophenazine (LXXVII).

(b) Oxidation of 2,2'-diaminodiphenylamine (LXXVIII)

Tomlinson (45) has found that 2,2'-diaminodiphenylamine (LXXVIII) is oxidized in acid medium by ferric chloride to form phenazine (I) in a nearly quantitative yield with elimination of one amino-group. However,

Gray, Gertner and Holliman (131) claimed to obtain 1-aminophenazine (LXXVII), in a 50% yield, by refluxing the diamine (LXXVIII) with nitrobenzene.



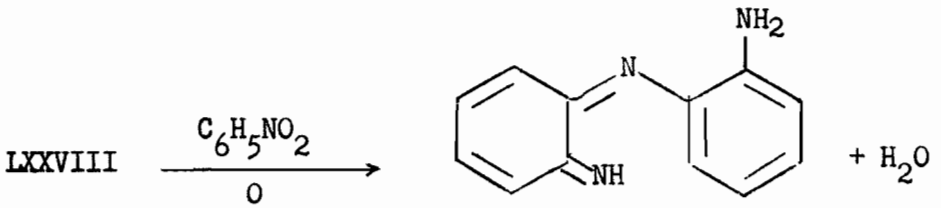
LXXVIII

LXXVII

No detailed reaction conditions were given by the authors and all attempts to repeat the oxidation by this method failed.

Numerous experiments carried out in the course of this investigation under different conditions resulted in establishing a procedure in which 1-aminophenazine (LXXVII) was produced in a good yield.

It was assumed that in the oxidation of 2,2'-diaminodiphenylamine (LXXVIII) with nitrobenzene an intermediate quinonediimine (LXXIX) and water are formed:



LXXIX

The intermediate (LXXIX) can react further with water or air which possibly would lead to undesired products. Therefore, the reaction was carried out

in such a way that both air and water were excluded. The water which formed was distilled off with nitrobenzene and the reacting mixture was protected from air by passing a stream of nitrogen through the reaction vessel. The changes observed in the distillate (Table 15) showed how far the reaction had proceeded and when it was finished. Pure 1-aminophenazine (LXXVII) was obtained in 40% yield calculated from the crude starting material (LXXVIII).

This procedure was used for preparing the main part of the 1-aminophenazine (LXXVII) investigated in this work.

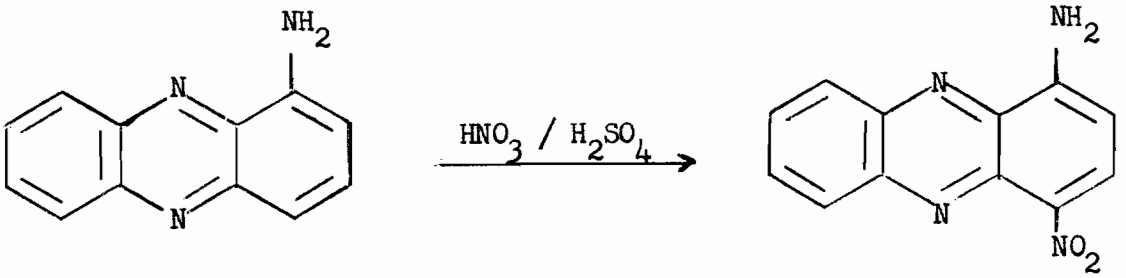
The infrared spectrum of 1-aminophenazine (LXXVII) is shown in Fig. 13 (Table 11). The two bands at 3480 cm^{-1} and 3340 cm^{-1} in the spectrum are assigned to the asymmetric and symmetric vibrations of the free NH_2-group, respectively. The discrepancy between the latter frequency and that calculated by means of the Bellamy-Williams equation (107) is minus 50 cm^{-1}. The substitution in position one in the amine (LXXVII) is confirmed by the strong absorption at 765 cm^{-1} (three adjacent H-atoms) and at 735 cm^{-1} (four adjacent H-atoms).

Nitration of 1-Aminophenazine (LXXVII)

The main mononitration product of 1-aminophenazine (LXXVII) in concentrated sulphuric acid was found to be 1-amino-4-nitrophenazine (LXXXI). The experiments, which have led to the establishment of the optimum conditions for the reaction are outlined in Table 16. When the excess of nitric acid used was less than 30% some starting material (LXXVII) was isolated from

the reaction mixture (No. 1, 2, Table 16). Nitration with a 30% excess of nitric acid (No. 3) was complete, however, the yield of the crude mononitration product, insoluble in ammonia, was lower than in the two previous experiments, while a considerable amount of an ammonia soluble substance was produced at the same time. The latter was assumed to be the 1-nitramino-4-nitrophenazine on the basis of its solubility in ammonia, rapid decomposition at its melting point temperature, relative stability with respect to dilute acids and the infrared spectrum of the crude product. Further investigation of this nitration product was not included in this work.

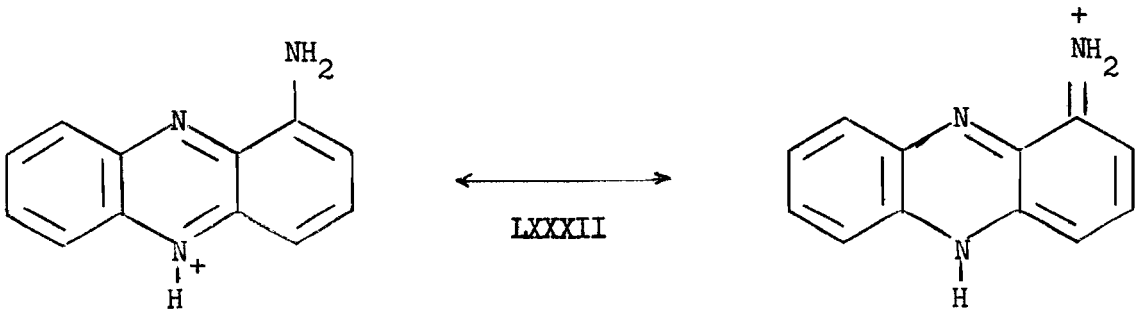
Complete nitration of the amine (LXXVII), with no detectable formation of polynitro-compounds soluble in ammonia, was achieved when a 70% excess of nitric acid was used. The reaction was stopped as soon as the amine (LXXVII) could no longer be detected in the reaction mixture by the specific colour test; the reaction was finished in two minutes (in previous experiments the time was one hour). The nitration product was extracted from the mixture with chloroform and purified by chromatography on alumina. In this way 1-amino-4-nitrophenazine (LXXXI) was obtained in a 47% yield.



LXXVII LXXXI

It is assumed that the above nitration reaction is an indirect process and involves the intermediate formation of a nitramine which undergoes acid catalyzed intramolecular rearrangement to give 1-amino-4-nitrophenazine (LXXXI).

The nitration of 1-aminophenazine (LXXVII) at 0° proceeded in two minutes while the same reaction with phenazine (I) is a very slow process (e.g. heating phenazine with a nitric and sulphuric acid mixture for 8 hours gave 1-nitrophenazine in 10% yield (68)). This fact clearly indicates activation of the ring under attack in the nitration of 1-aminophenazine (LXXVII). Since a protonated amino group is not likely to be the activating or active centre in electrophilic attack, it can be assumed that the reacting species possessed the free amino-group. Under strongly acidic reaction conditions, the amine conjugate acid (LXXXII) would most probably be the reacting intermediate.



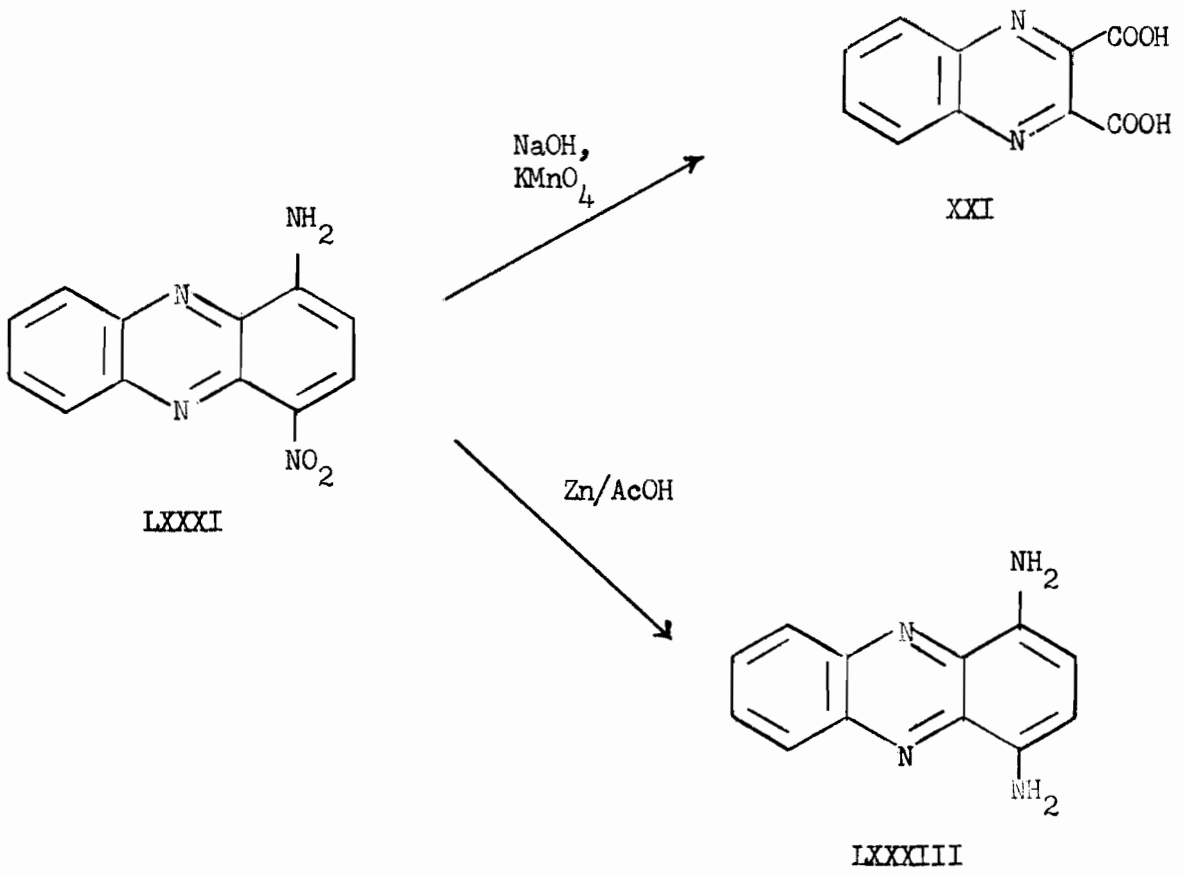
The attack of a nitronium ion (NO_2^+) on the free amino-group of the species (LXXXII) would be energetically preferred to the direct attack on the position four of the ring. The rapid rearrangement of the protonated nitramine formed would yield the final 1-amino-4-nitrophenazine (LXXXI). This reaction sequence would be the facile path in which the nitration could proceed. This accounts for the mild conditions and high rate of

the process. The direct nitration of the ring would be expected to proceed at a much slower rate and thus would be less important as a competing reaction.

Concerning the above discussion it should be emphasized that 3-N,N-dimethyl-, 3-N-acetyl-, and 3-N-formylaminopyridines, which do not form nitramines, resist nitration, although some activation of the pyridine ring due to those substituents might be expected. In contrast, 3-N-methylamino- and 3-aminopyridine are easily nitrated, to form nitramines under the same conditions (130).

1-Amino-4-nitrophenazine (LXXXI) is weakly basic; it is soluble in moderately concentrated acids but is practically insoluble in 5% hydrochloric or sulphuric acid. The structure of compound (LXXXI) was proven in several ways:

(a) When the substance (LXXXI) was oxidized in alkaline medium with potassium permanganate quinoxaline-2,3-dicarboxylic acid (XXI) was obtained. This proves that only one of the two carbocyclic rings bears substituents. The reduction product of the compound was neither 1,2-diamino (LIX)- nor 1,3-diaminophenazine (LXXIV), nor an intermediate which could be transformed into one of the two diamines. Consequently, the 1,4-substituted phenazine was left as the only possibility for (LXXXI).



LXXXI

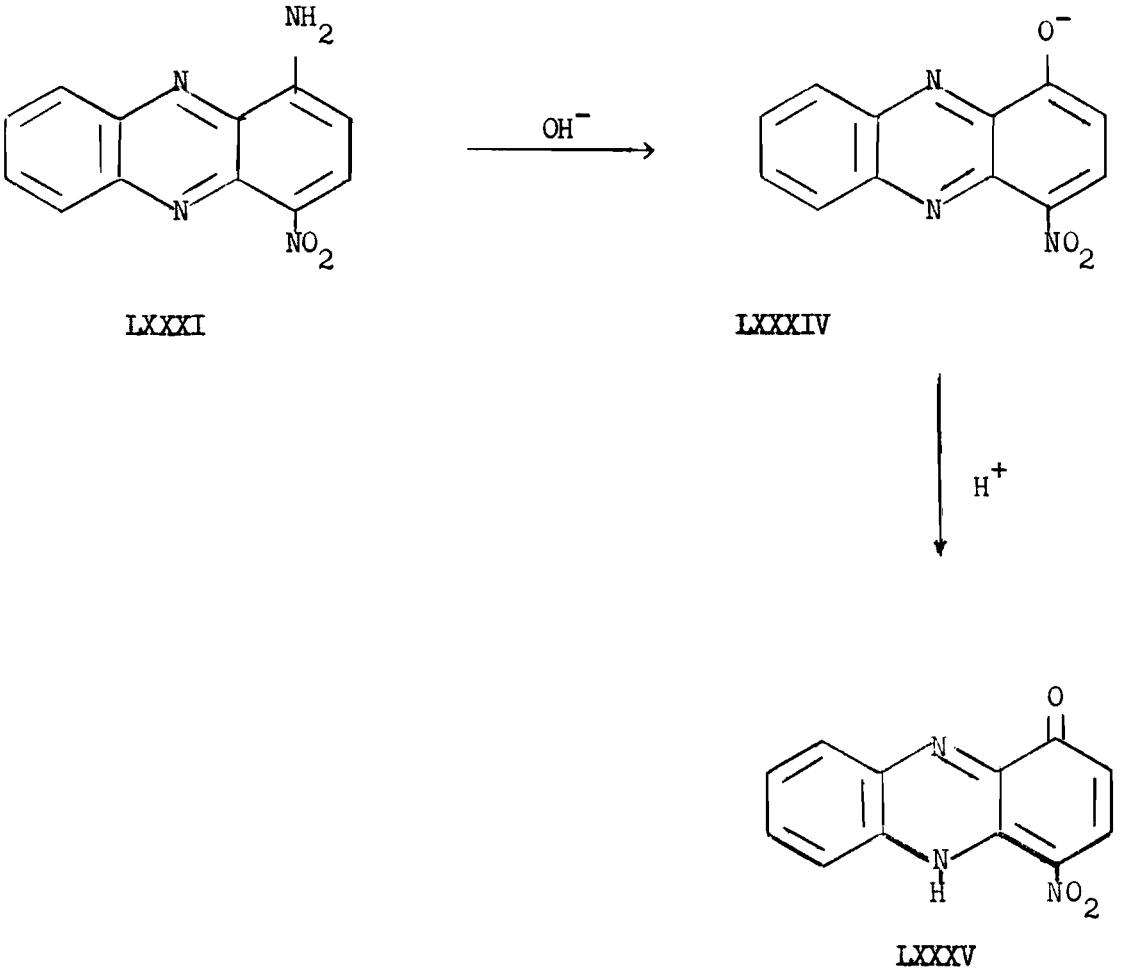
XXI

LXXXIII

(The assumed 1,4-diaminophenazine (LXXXIII) was not prepared in an analytically pure state and was not investigated further. However, the dark blue colour of the substance, its high melting point (it does not melt below 300°), its sensitivity towards oxidation by air when in solution, and its infrared spectrum indicate a different structure from that shown in the above scheme. In other words the structure (LXXXIII) has been used merely for the sake of simplicity).

(b) The amino-group in 1-amino-4-nitrophenazine was replaced on boiling with aqueous alkali, yielding 1-hydroxy-4-nitrophenazine in the form of its alkali salt (LXXXIV). On acidifying the water solution of the alkali salt, fine red crystals of 4-nitro-1(5H)-phenazinone (LXXXV) were

obtained:



LXXXI LXXXIV

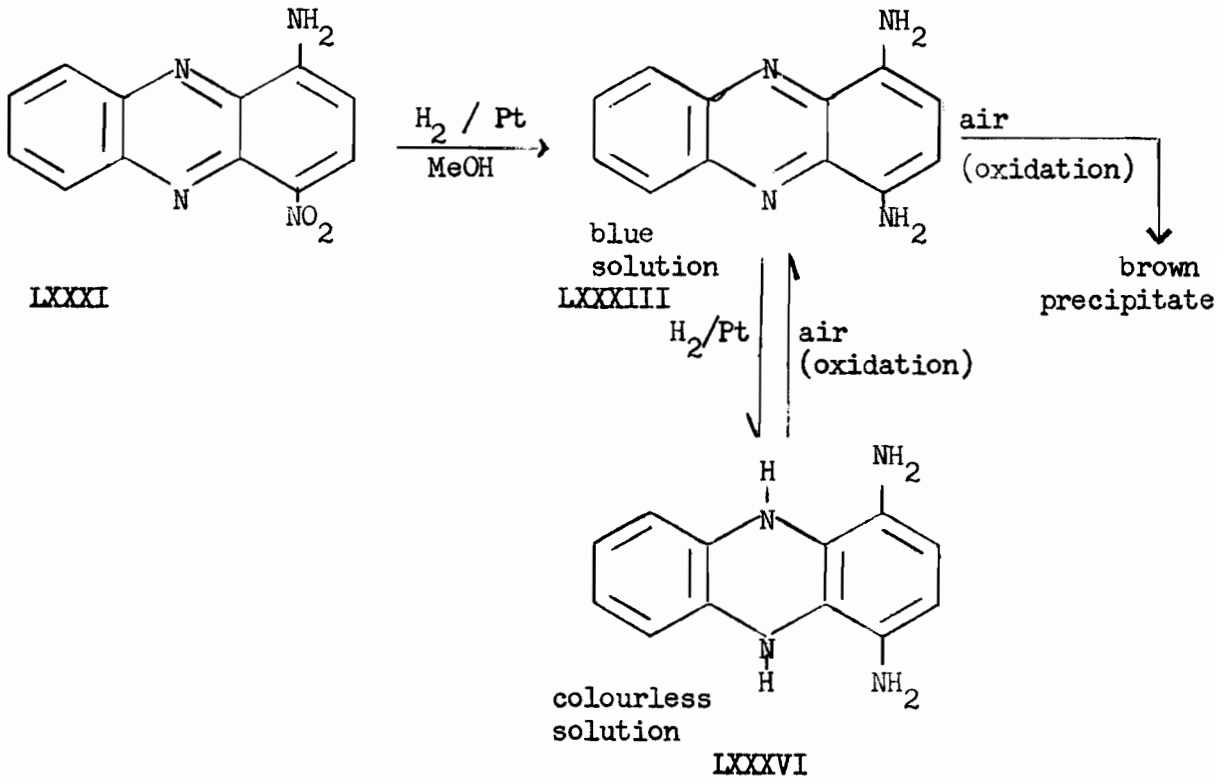
LXXXV

(c) The presence of a free amino-group in 1-amino-4-nitrophenazine (LXXXI) is indicated by the bands at 3430 cm^{-1} and 3290 cm^{-1} of the infrared spectrum (Table 11, Fig. 14). The strong absorptions at 1520 cm^{-1} and 1285 cm^{-1} are assigned to the asymmetric and symmetric NO_2-vibrations. The lack of bands between 900 cm^{-1} and 850 cm^{-1} with the simultaneous occurrence of a band at 802 cm^{-1} is consistent with the type of substitution having two adjacent hydrogen atoms in the ring; possible 1,4- or 1,2-substitution.

Reduction of 1-Amino-4-nitrophenazine (LXXXI)

1-Amino-4-nitrophenazine (LXXXI) was reduced catalytically (Pt) with hydrogen, in methanol solution. The initial brown colour of the solution changed during the process to blue and finally the solution became colourless. The colourless liquid, on exposure to air, turned blue again but soon changed to brown and a brown unidentified solid precipitated.

The following scheme is suggested as an explanation for the above reactions:



The final reduction product of 1-amino-4-nitrophenazine (LXXXI) which gave the colourless solution is assumed to be the 1,4-diamino-5,10-dihydrophenazine (LXXXVI). Both ring-nitrogen atoms in the compound

(LXXXVI) were hydrogenated which destroyed the high degree of conjugation responsible for the colour and also rendered the compound very sensitive to oxidation (by air). Any intermediate, between the structures (LXXXIII) and (LXXXVI), hydrogenation product would be a coloured phenazhydrin. The colourless solution of compound (LXXXVI) was rapidly oxidized by air to give the blue solution of the assumed 1,4-diaminophenazine (LXXXIII) which was also observed as the primary reduction product of (LXXXI).

This sequence of reactions excludes the possibility of an 1,2-substitution for the starting aminonitrophenazine (LXXXI), since in such a case the colourless substance (obtained in the reduction process) should be the 1,2-diamino-5,10-dihydrophenazine (LXIII) which on oxidation by air would give the previously identified 1,2-diaminophenazine (LIX). The 1,3-substitution is also excluded since the solution of 1,3-diamino-phenazine in methanol is purple red.

The behaviour of 1-amino-4-nitrophenazine (LXXXI) on reduction with zinc-acetic acid also confirms the 1,4-substituted phenazine as the only possible representation of the structure (LXXXI).

In this reaction the solution of the reduction product (LXXXIII) in acetic acid is violet, while the solutions of 1,2-diaminophenazine (LIX) and 1,3-diaminophenazine (LXXIV) are orange-brown and intense green, respectively. The amine (LXXXIII) was isolated from the acetic acid solution by rendering it alkaline with ammonia (in nitrogen atmosphere). The substance forms blue needles, soluble with blue colour in methanol. The colour of the solution changes to brown on exposure to air. No ways of purification of the crude product (LXXXIII) were found.

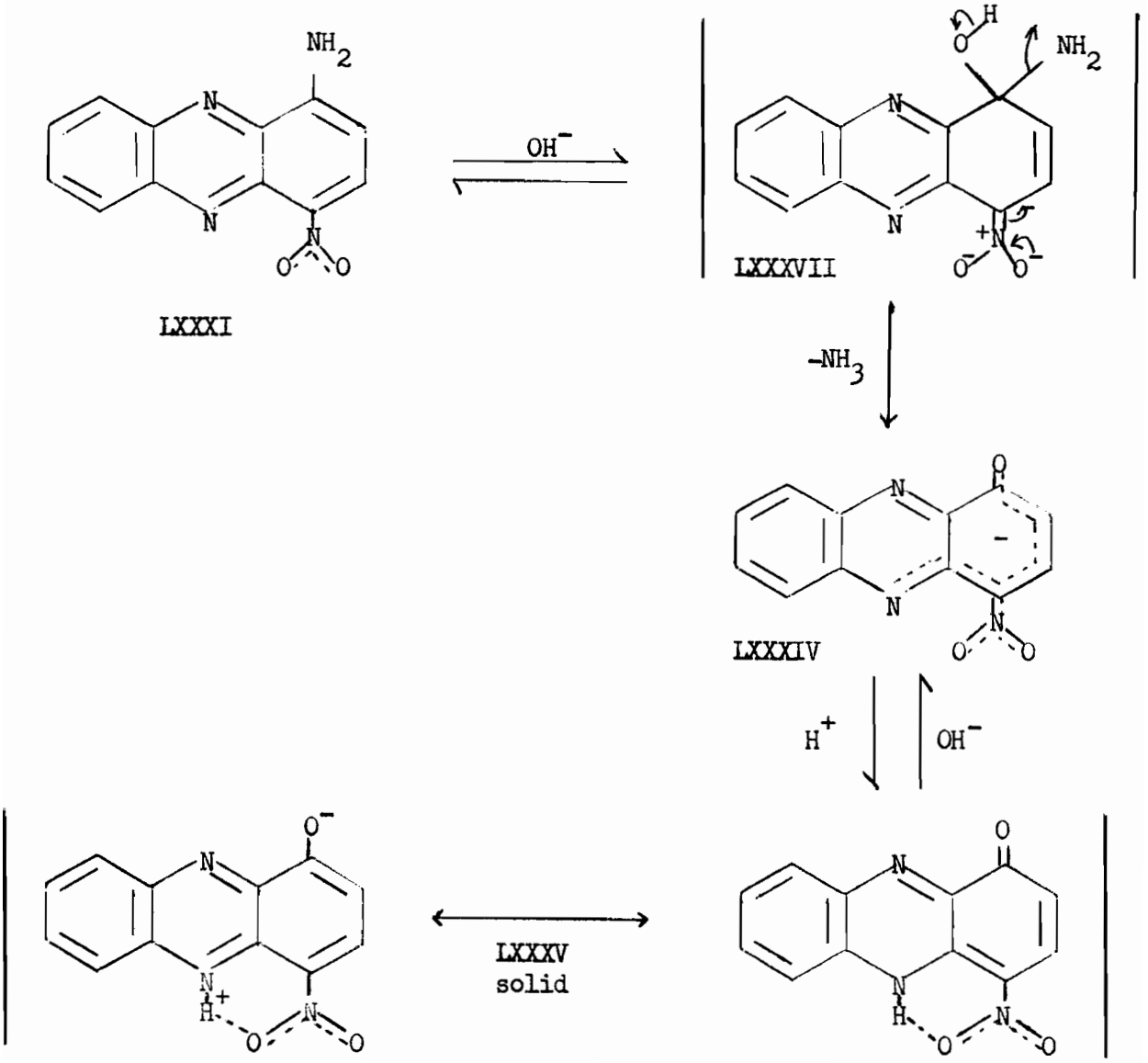
Attempted diazotization of 1-amino-4-nitrophenazine (LXXXI)

The diazotization of the compound (LXXXI) was attempted in order to substitute its amino group for a hydrogen atom. In this way, it was thought to obtain additional evidence for the structure (LXXXI). The reaction was carried out under conditions in which 1-aminophenazine (LXXVII) formed the diazonium salt instantly. However, 1-amino-4-nitrophenazine (LXXXI) was recovered unchanged from the reaction mixture. The reason for the resistance of the compound (LXXXI) to diazotization might be, similarly to the case of 2-amino-1-nitrophenazine (LVIII), the decrease of the nucleophilic character of its amino-group due to conjugation with the strongly electron-attracting nitro-group in position four.

1-Hydroxy-4-nitrophenazine and 4-Nitro-1(5H)-phenazinone

The Phenazinol-Phenazinone Tautomerism

When 1-amino-4-nitrophenazine (LXXXI) was refluxed with 1% sodium hydroxide solution, the sodium salt of 1-hydroxy-4-nitrophenazine (LXXXIV) was obtained, which yielded the 4-nitro-1(5H)-phenazinone (LXXXV) on treatment with hydrochloric acid. The mechanism suggested for this reaction is as follows:



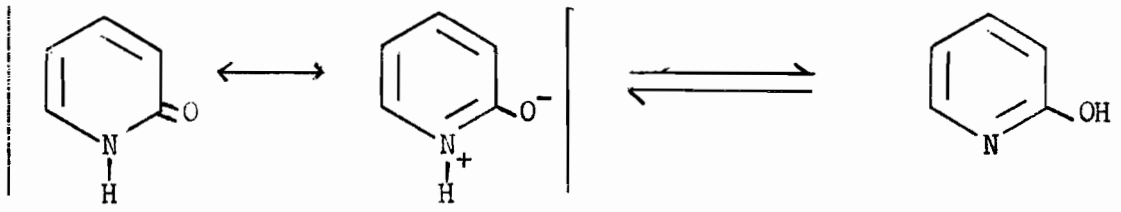
In the reaction an intermediate (LXXXVII) is formed which is stabilized by releasing of an ammonia molecule. The anion (LXXXIV) obtained has its negative charge delocalized over a large part of the structure. The preferred position for protonation in the anion (LXXXIV) is the nitrogen-atom in position five of the ring since in this case hydrogen bonding will be possible between the hydrogen and the nitro-group in position four. The stability of the six-membered ring formed is probably the factor responsible for the exclusive occurrence of the phenazinone (LXXXV) tautomer in the solid separated from acidic solutions.

The phenazinol-phenazinone tautomerism involved in the above reactions is an example of a general phenomenon observed with hydroxy-derivatives of aza-aromatic electron deficient compounds. The proto-tropic rearrangement of the hydroxy-tautomer, characteristic of positions with low electron density, gives a more stable molecule of the pyridone type (66). Albert (132) advises the use of the name "amide form" for these oxo-tautomers since their chemical properties are rather those of amides than of keto-compounds.

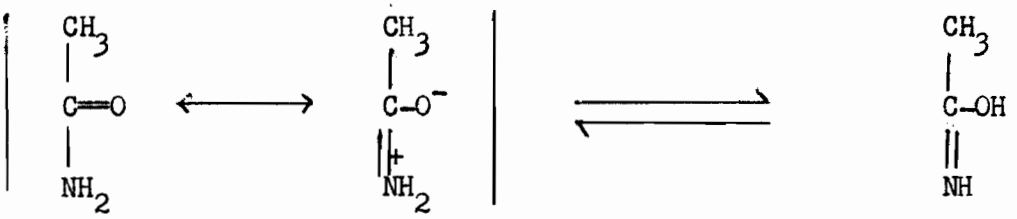
Investigation of these tautomeric equilibria is based on measure-ments of such physical properties as ionization constants, ultraviolet and infrared spectra, X-ray diffraction and dipole moment.

Aqueous solutions of 2- and 4-hydroxypyridine were found to contain mainly the corresponding amide forms (133). The oxo-tautomer of 2-hydroxypyridine (LXXXVIII) is considered to be a resonance hybrid of two canonical forms (A, B) and owing to this resonance the amide form

(LXXXVIII) is more stable than the hydroxy form (LXXXIX). The equilibrium between these two tautomers (LXXXVIII, LXXXIX) (132) resembles the analogous one of acetamide (XC, XCI):



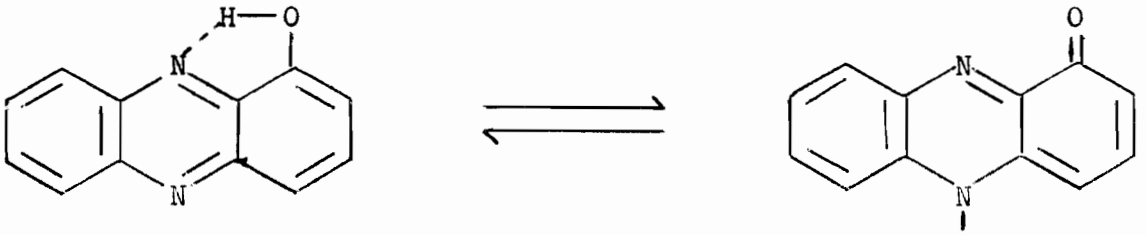
LXXXVIII LXXXIX



XC XCI

Albert (132) presents a review of experimental data and literature showing that α- and γ-hydroxy-derivatives of electron-deficient aza-aromatics in solid state exist mainly in the amide form.

1-Phenazinol (XCII) is tautomeric with 1(5H)-phenazinone (XCIII):

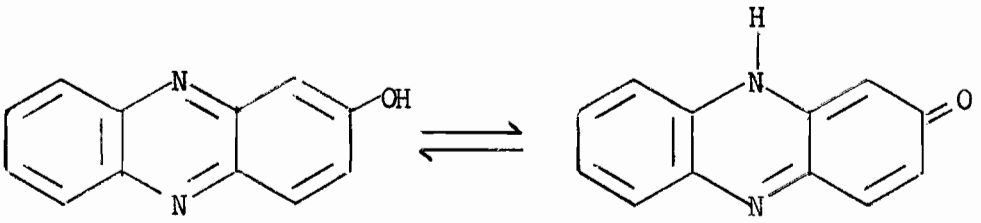


XCII XCIII

The infrared and ultraviolet spectra of 1-phenazinol suggest that it exists exclusively in the hydroxy-form (XCII). This fact is explained by

the stabilization of the proton in the position arising from hydrogen bonding of the 1-hydroxyl-group with the nitrogen atom in position ten of the ring (134). However, the naturally occurring bacterial pigment pyocyanine (XI) was found to be the 5-methyl-derivative of the amide-form (XCIII).

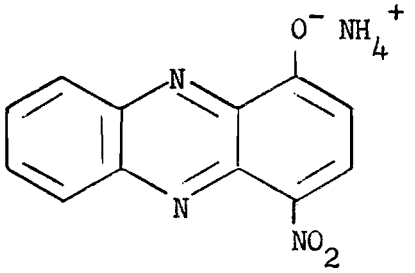
The ultraviolet spectra of 2-phenazinol (XCIV) showed that it is in equilibrium with the amide-tautomer (XCV). In alcoholic solution the former structure (XCIV) predominates, but in water the deeper colour of the latter (XCV) is apparent (134):



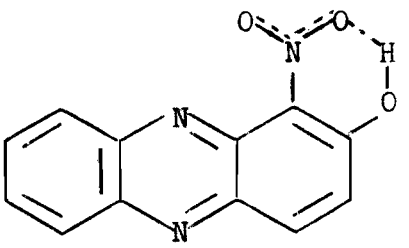
XCIV XCV

The two tautomeric forms of 1,3,4-trimethyl-2-phenazinol have been isolated, one being yellow (phenolic) and the other violet (amide) (135).

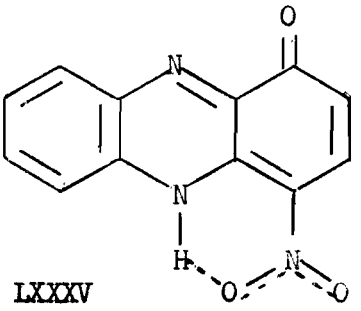
On acidification of the 1-hydroxy-4-nitrophenazine ammonium salt (XCVI) solution, 4-nitro-1(5H)-phenazinone (LXXXV) was the only solid tautomer obtained.



XCVI



LX



LXXXV

This fact, as well as the exclusive existence of the hydroxy-tautomer of 2-hydroxy-1-nitrophenazine (LX) in the solid state are both explained by the hydrogen bonding effect and the formation of the stable six-membered chelate ring.

Equally, the exclusive existence of the tautomer (LX, LXXXV) is good evidence for the position of the nitro-group in the molecule, for the stability of the hydroxy-tautomer in 2-hydroxy-1-nitrophenazine (LX) requires the nitro-group to be located in position one. Also, in the case of the 4-nitro-1(5H)-phenazinone (LXXXV), the nitro-group in position four is a necessary factor. The location of the nitro-group in position two, in the latter case, would stabilize the corresponding hydroxy-tautomer, in contrast to previous findings.

Evidence for the structure of phenazinone (LXXXV) is based on the reversible transformation of the compound (LXXXV) into the ammonium salt of 1-hydroxy-4-nitrophenazine (XCVI), the infrared spectra of both compounds (LXXXV, XCVI), and the study of the ultraviolet spectra of the phenazinone (LXXXV) in water solution.

The ammonium salt (XCVI) crystallized from a water solution of the phenazinone (LXXXV) in the form of yellow needles when treated with an excess of ammonia. The infrared spectrum of the salt (XCVI) (Table 10, Fig. 14) exhibits a broad unresolved band between 3600 cm^{-1} and 2700 cm^{-1}, usually observed with ammonium salts. The frequencies at 1530 cm^{-1} and 1265 cm^{-1} are assigned to the NO_2-group vibrations. The general absorption pattern in the 900-700 cm^{-1} region, similar to that of 1-amino-4-nitrophenazine (LXXXI) clearly indicates the same kind of substitution and analogous structure of the compounds (XCVI, LXXXI).

The medium strong band at 3120 cm^{-1} shown in the infrared spectrum of 4-nitro-1(5H)-phenazinone (LXXXV) (Table 10, Fig. 15) is attributed to the hydrogen bonded N-H group of the structure. The very strong absorption at 1655 cm^{-1} corresponds to the amide carbonyl group. The NO_2-frequencies appear practically at the same position as in the ammonium salt (XCVI). The entirely different absorption pattern of phenazinone (LXXXV) from that of 1-amino-4-nitrophenazine (LXXXI) and of the salt (XCVI) in the range 900-700 cm^{-1} indicates considerable differences in structure of the compounds discussed. This part of the spectrum (LXXXV) does not exhibit two very characteristic bands which appear in all phenazines previously discussed. (The band at 820 cm^{-1} ($\pm$ 10 cm^{-1}) is

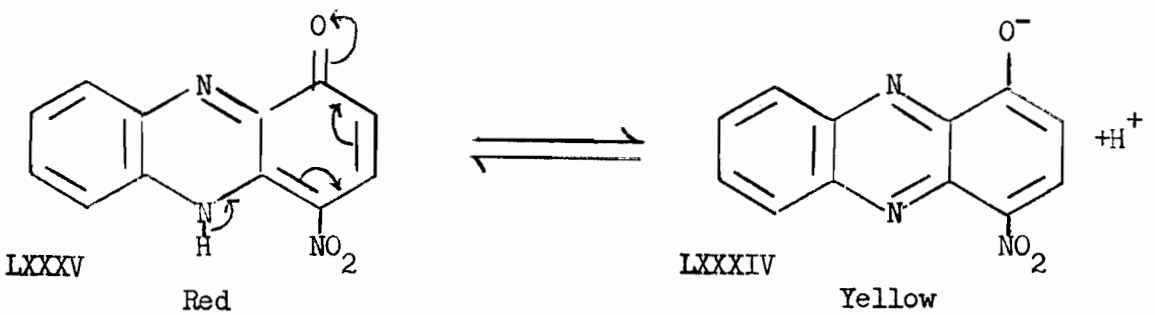
assigned to the phenazine skeleton deformations and the 750 cm^{-1} ($\pm$ 15 cm^{-1}) band arises from out-of-plane C-H vibrations of the unsubstituted carbocyclic ring.) Instead, a very strong peak is shown at 815 cm^{-1} and several weaker bands at other frequencies.

These differences in the spectrum in the region which is very sensitive to structural changes should be expected and can be considered as additional proof for the change from the phenazine- to the phenazinone-structure of the compound (LXXXV).

Ultraviolet Study of Aqueous Solutions of 4-Nitro-1(5H)-phenazinone (LXXXV)

The solubility of 4-nitro-1(5H)-phenazinone (LXXXV) in water at 25° is $\frac{1}{2}$ mg per ml. The solution is red with a slightly yellowish tinge, however, on diluting ten times the colour of the solution changes to pure yellow. The yellow solution may be evaporated to recover unchanged phenazinone (LXXXV) in the form of red crystals. In acidic media (pH < 2.0) compound (LXXXV) is much less soluble and the solution has pure red colour.

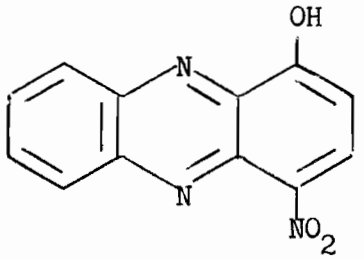
In order to explain this behaviour of phenazinone (LXXXV) the following equilibrium is assumed to be established in the water solution:



LXXXV Red ⇌ LXXXIV Yellow

On dissolving in water the compound (LXXXV) is mainly converted to the anion (LXXXIV) which accounts for its (LXXXV) much higher solubility in water than in acidic medium, where the equilibrium must be shifted to the left. On dilution, more of anion (LXXXIV) is formed which is accompanied by the change of colour to yellow.

This equilibrium was studied by means of ultraviolet spectroscopy. An attempt was made to establish the approximate equilibrium ratio of both species (LXXXV, LXXXIV). The possibility of the presence of 1-hydroxy-4-nitrophenazine (XCVII) in the water solution was ignored since the latter, being quite a strong acid, would be virtually completely



XCVII

dissociated in the low concentration solutions which were investigated.

The electronic spectrum of a water solution of phenazinone (LXXXV) (4.15×10^{-5} mole/litre) shows a maximum at 425 mμ with a molar extinction coefficient of 13970 (Fig. 16). No absorption was observed at wavelengths above 530 mμ. An alkaline solution of the compound (LXXXV) of equal concentration gave the same absorption curve (Fig. 16). Hence, it was concluded that, at the concentration of 4.15×10^{-5} mole/litre, the phenazinone (LXXXV) was already fully converted to the anion (LXXXIV).

An acidic solution of phenazinone (LXXXV) (2 drops of 3.7%

hydrochloric acid per 4 ml of the solution) of the same concentration as above, showed an electronic spectrum with a maximum at 400 mμ and a molar extinction coefficient of 12050 (Fig. 16). It also absorbed markedly at 530 mμ (ε = 3370). On the assumption that, in the rough approximation, the compound in the acidic solution is fully converted to the phenazinone form (LXXXV) it was found convenient to use the absorption at 530 mμ to measure the amount of species (LXXXV) present in equilibrium in water solutions of different concentrations.

Because of the high absorbance exhibited by the solutions studied, the differential method of measurement was applied; the reference cells were filled each time with alkaline solutions of phenazinone (LXXXV) of the same concentration. The differential absorbance shown at 530 mμ has been attributed to the presence of phenazinone (LXXXV) (the amide-form) in equilibrium.

The results obtained are summarized in Table 1.

TABLE 1

Amount of phenazinone (LXXXV) dissolved per litre of water, mole	Absorbance (A) measured at 530 mμ	Concentration (C) of species (LXXXV) in equilibrium $C = \frac{A}{3370}$ mole/l	% of the species (LXXXV) (amide-form) in equilibrium
2.075×10^{-3} saturated solution	0.52	1.54×10^{-4}	7
4.15×10^{-4}	0.03	0.89×10^{-5}	2
2.075×10^{-4}	0.00	0.00	Beyond the accuracy of the differential method
4.15×10^{-5}	0.00	0.00	Determined by direct measurement

The approximate ratio of phenazinone (LXXXV) to anion (LXXXIV) in a saturated water solution of 4-nitro-1(5H)-phenazinone was 7:93; on diluting five times the ratio fell to 2:98, and when ten times diluted no detectable amount of the first form (LXXXV) was found. The saturated solution is red due to the presence of 7% of the amide form (LXXXV). On further dilution the latter dissociates to form the yellow anion (LXXXIV).

Note on the Synthesis of Phenazyl Hydrochloride (V)

Phenazyl hydrochloride (V) is an intermediate in the reduction of phenazine (I) in acidic medium to 5,10-dihydrophenazine (II). It was prepared either by sodium amalgam reduction of phenazine (I) in acetic acid-hydrochloric acid solution (136) or from phenazine-N-oxide (XVII) reduced with stannous chloride-hydrochloric acid.

It was found that, when a solution of phenazine (I) in hydrochloric acid was treated with an excess of powdered iron metal, phenazyl hydrochloride (V) precipitated from the solution in the form of dark green needles. The preparation was simple and the product was obtained in a pure state in nearly quantitative yield.

Elemental analysis data concur with the formula $C_{12}H_9N_2 \cdot HCl \cdot H_2O$ for the compound (V). The formula assigned to the product from the sodium

amalgam reduction of phenazine (I) is $C_{12}H_9N_2 \cdot HCl$ (136).

The infrared spectrum of phenazyl hydrochloride (V)(Table 12, Fig. 15) shows a broad band with a maximum at 3400 cm^{-1}, assigned to the water molecule in the structure (V). The broad, unresolved absorption between 3100 cm^{-1} and 2400 cm^{-1} is correlated with the $\overset{+}{N}$-H-group. The absence of the 820 cm^{-1} band in the spectrum indicates a change in the phenazine structure (I) which affects the whole aromatic system, thus being the change to the semiquinone system (V).

Infrared Study of Phenazines

The infrared spectra of phenazines and its twenty-eight derivatives, including phenazine-d_8, were recorded in the region 3800-650 cm^{-1}. The spectra were taken in carbon disulphide and carbon tetrachloride solutions, and in the solid state in potassium bromide pellets. The latter were prepared either of a mixture of the compound investigated and potassium bromide, or the compound was sublimed onto a previously prepared pellet of pure potassium bromide. In some cases the sublimation technique resulted in much better resolution, especially in the region above 3000 cm^{-1}. The infrared spectra of phenazine and three alkylphenazines, and a spectrum of phenazine-d_8 are recorded in Tables 6 and 12, respectively (Figs. 1, 2, 3).

The 3100-3000 cm^{-1} region. Phenazine and alkylphenazines exhibit a strong infrared absorption band at 3065 to 3060 cm^{-1} in carbon disulphide and carbon tetrachloride solution. In the spectrum of phenazine-d_8 (in carbon tetrachloride) the corresponding band occurs at 2290 cm^{-1}; the substitution of hydrogen for deuterium resulted in a shift of the band by a factor of 0.7484.

The 3000-2800 cm^{-1} region. Phenazine shows a very weak band at 2890 cm^{-1}. 1-Methyl- and 2-methylphenazine exhibit four bands each (1-methylphenazine: 2970, 2950, 2912 and 2830 cm^{-1}; 2-methylphenazine: 2973, 2940, 2910 and 2845 cm^{-1}).

The 2000-1650 cm^{-1} region. In this region there is a complicated pattern of ten to twelve bands which can be studied best in the spectra obtained

with solutions of phenazines in carbon disulphide. These are the combination and overtone bands of the fundamental frequencies of the 1000 to 600 cm^{-1} out-of-plane deformation vibrations region.

The 1650-1300 cm^{-1} region. Phenazine shows, in this region, seven absorption bands at 1625, 1550, 1515, 1471, 1432, 1362, and 1329 cm^{-1}, most of them being recorded from the solid sample in a potassium bromide pellet. With the exception of the weak band at 1550 cm^{-1} all other bands are of medium or strong intensity. From the seven bands in this region the band at 1329 cm^{-1} may arise by CC distortion. All other bands originate from CC and CN stretching vibrations of the ring. In the infrared spectrum of phenazine-d_8 the same type of skeletal vibrations occur at 1620, 1492, 1387, 1308, 1257, and 1202 cm^{-1}. In alkyl-substituted phenazines there are additional bands due to asymmetric and symmetric vibrations of methyl groups.

The 1300-900 cm^{-1} region. Phenazine and substituted phenazines exhibit strong skeletal and C-H in-plane-deformation bands in the range 1215-1200 cm^{-1}, 1152-1132, 1122-1112, 1084-1074, 959-955, and others.

The 900-700 cm^{-1} region. The strongest absorption bands in this region might be assigned to the out-of-plane deformation vibrations of the phenazine ring hydrogen atoms. The most intense band at 760-745 cm^{-1} is assigned to the four unsubstituted C-H groups on a carbocyclic ring of phenazine. This band can be used for the analytical determination of phenazines since it is common to all substituted phenazines used in this investigation. The single, strong band appearing in the 810-750 cm^{-1} region is characteristic for 1-substitution in the phenazine molecule.

The bands at 860-800 cm^{-1} and 900-850 cm^{-1} are associated with 2-substituted phenazines and can be used for identification purposes.

The strong band, shown in all phenazines studied, at 820 cm^{-1} ($\pm$ 15 cm^{-1}) is assigned to skeletal deformations of the phenazine ring system. This band appears in all phenazines, independently of the type of substitution, in which the phenazine conjugated system is present. This frequency occurs also in phenazine-d_8, which proves that no C-H type vibrations are involved in this absorption. However, the 820 cm^{-1} band is not shown in 5,10-dihydrophenazine and phenazyl hydrochloride in which the conjugation of the phenazine system is disrupted. Consequently, this frequency can be used for determination of structural changes, which involve the conjugated system in phenazines.

The spectra of twenty-seven phenazines investigated for their absorption in the region 900-700 cm^{-1} substantiate the spectra-structure correlations (Table 2).

TABLE 2

Frequencies assigned to the type of substitution in phenazines

No.	Compound	System	Regions of expected bands cm^{-1}	Frequencies observed cm^{-1}	
1	Phenazine	4H	770-735	745 vs 752	Soln. in CS_2 and Solid in KBr
2	5,10-Dihydro-phenazine	4H	770-735	745 730(sh) vs 725	Solid in KBr
3	Phenazine Hydrochloride	4H	770-735	760 vs 740 vs	Solid in Nujol
4	Phenazyl Hydrochloride	4H	770-735	740 730(sh) vs	Solid in KBr
5	1-Methyl-phenazine	3H	810-750 725-680	792 m 777 s 700 w	Soln. in CS_2 and
		4H	770-735	767 758 vs 752	Solid in KBr
6	Phenazine-1-carboxylic acid	3H	810-750 725-680	795 s 675 m	Solid in KBr
		4H	770-735	755 740(sh) vs	
7	1-Amino-phenazine	3H	810-750 725-680	800 w 765 s 665 vw	Solid in KBr
		4H	770-735	735 vs	
8	1-N-Acetylamino-phenazine	3H	810-750 725-680	780 m 765 s 680 m	Solid in KBr
		4H		760 s 750 vs	

. . . .

TABLE 2 (cont'd.)

No.	Compound	System	Regions of expected bands cm^{-1}	Frequencies observed cm^{-1}	
9	2-Methyl-phenazine	1H	900-850	878 m 840 m	Soln. in CS_2
		2H	860-800	820 s	and
		4H	770-735	765 758 vs 750	Solid in KBr
10	2-tert-Butyl phenazine	1H	900-850	888 s 847 m	
		2H	860-800	830 s 820 s	Soln. in CS_2
		4H	770-735	755 vs	
11	2-Amino-phenazine	1H	900-850	865 w 855 ms 840 w	Solid
		2H	860-800	825 s	in
		4H	770-735	760 735 vs	KBr
12	2-N-Acetyl-aminophenazine	1H	900-850	875 860 m 830 s	Sublimed onto
		2H	860-800	802 ms	the KBr pellet
		4H	770-735	755 s	
13	2-N-Methyl-amino-phenazine	1H	900-850	855 ms 815 s	
		2H	860-800	805 s	Solid
		4H	770-735	755 750(sh)vs 735(sh)	in KBr
14	2-N,N-Acetyl-methylamino-phenazine	1H	900-850	860 ms	
		2H	860-800	830 s	
		4H	770-735	765 750 vs 740	Solid in KBr

. . . .

TABLE 2 (cont'd.)

No.	Compound	System	Regions of expected bands cm^{-1}	Frequencies observed cm^{-1}		
15	2-Nitrimino-(10H)phenazinium betaine anhydrous	1H	900-850	880 w 855 m		Solid in KBr
		2H	860-800	830 820	s	
		4H	770-735	765 750 740	vs	
16	2-Nitrimino-(10H)phenazinium betaine monohydrate	1H	900-850	880 m 835 m		Solid in KBr
		2H	860-800	820 s 765		
		4H	770-735	755 745	vs	
17	2-Nitramino-phenazine sodium salt	1H	900-850	885 870 vw		Solid in KBr
		2H	860-800	835 s 815 s		
		4H	770-735	750 735	vs	
18	2-Nitramino-phenazine potassium salt	1H	900-850	870 ms 835		Solid in KBr
		2H	860-800	825	s	
		4H	770-735	765 755 735	vs	
19	2-Nitramino-phenazine ammonium salt	1H	900-850	875 s 835 s		Solid in KBr
		2H	860-800	820 s		
		4H	770-735	750 735	vs	
20	2,3-Diamino-phenazine	1H	900-850	890 m		Solid in KBr
		1H	900-850	(broad)		
		4H	770-735	765 740(sh)	vs	
21	1,3-Diamino-phenazine	1H	900-850	855(sh)		Sublimed onto a KBr pellet
		1H	900-850	850	s	
		4H	770-735	760	vs	

. . . .

TABLE 2 (cont'd.)

No.	Compound	System	Regions of expected bands cm^{-1}	Frequencies observed cm^{-1}	
22	1,2-Diamino-phenazine	2H 4H	860-800 770-735	825 s (broad) 755 vs	Solid in KBr
23	2-Amino-1-nitro-phenazine	2H 4H	860-800 770-735	845 s 835 ms 802 ms 770 755 vs 740	Solid in KBr
24	2-Methyl-amino-1-nitro-phenazine	2H 4H	860-800 770-735	830 s 802 m 760 vs	Solid in KBr
25	2-Hydroxy-1-nitro-phenazine	2H 4H	860-800 770-735	840 vs 802 w 755 vs	Solid in KBr
26	1-Amino -4-nitro-phenazine	2H 4H	860-800 770-735	820 s 802 m 770 vs	Solid in KBr
27	1-Hydroxy--4-nitrophenazine ammonium salt	2H 4H	860-800 770-735	820 s 805 m 765 vs	Solid in KBr

Remarks:

The symbols 1H, 2H, 3H, 4H used in this table denote systems with one single, two, three or four adjacent hydrogen atoms, respectively, present in the substituted carbocyclic rings.

The regions of expected bands, assigned to different systems, are those summarized by Bellamy (137) with respect to benzene derivatives.

The substances listed in Table 2 bear substituents in only one of the two phenazine carbocyclic rings, the other ring having four adjacent hydrogen atoms. A comparison of the frequencies presented with the regions of expected bands shows that in all compounds the absorption bands exhibited can be assigned to the type of substitution.

Some difficulties in correlation may arise from the presence of bands other than those expected in the characteristic regions. In systems with four adjacent hydrogen atoms (unsubstituted ring) or three adjacent hydrogen atoms (substitution in position one), the intense characteristic bands which dominate in the regions are easy to identify. However, the phenazines substituted in position two absorb very near, or in some cases (Table 2, No. 11, 14) the characteristic band overlaps with the strong absorption at 820 cm^{-1} arising from phenazine skeletal deformations. Additional evidence for this type of substitution is obtained from the presence of a band in the 900-860 cm^{-1} region, characteristic of the single hydrogen atom (in position one) of the system.

The 1,2- and 1,4-substituted carbocyclic ring, with two adjacent hydrogen atoms present (Nos. 23, 24, 25, 26, 27, Table 2), shows the characteristic absorption in a narrow range between 805 cm^{-1} and 800 cm^{-1} (as compared with the band at 802 cm^{-1} of benzene with the same type of substitution). The simultaneous absence of any significant absorptions in the 900-860 cm^{-1} region can be considered as additional evidence for this type of substitution.

Frequencies assigned to the nitro-group in phenazines are recorded in Table 3. The assignment of the frequencies was based on a comparison of

the spectra of the nitrophenazines with those of the parent compounds, isomers, analogous structures or reduction products.

The nitro-group of aromatic compounds exhibits easily recognizable strong bands in the 1650-1500 cm^{-1} and 1350-1250 cm^{-1} regions (138), corresponding to asymmetric and symmetric stretching vibrations of the group. The nitrophenazines (Table 3, No. 1, 2, 3, 4) show the NO_2-frequencies in the range 1535-1515 cm^{-1} and 1285-1265 cm^{-1}, respectively. The intensities of the asymmetric and symmetric absorptions are comparable.

The nitramines (Table 3, No. 5, 6) have their symmetric NO_2-frequencies shifted towards higher values (1320-1295 cm^{-1}); the bands are of high intensity and exhibit two peaks. The asymmetric absorptions, at 1515-1510 cm^{-1}, are comparatively weak.

The NO_2-symmetric frequencies of the nitramine salts (Table 3, No. 7, 8, 9) are further shifted towards shorter wavelengths (1365-1325 cm^{-1}); the bands are of very high intensity and show two or three maxima.

Lieber et al. (104) have examined seventeen N-nitro-compounds of various types. In fourteen of these, the symmetric NO_2-vibrations are reasonably constant within the range 1315-1260 cm^{-1}, while the exceptions (which absorb at higher frequencies) are either acid or salt forms in which an ionic structure with the $-N{=}\overset{+}{N}\!\!<\!\!\begin{matrix}O^- \\ O^-\end{matrix}$ group might be expected to have marked influence. A similar ionic structure is considered to be one of the canonical forms of 2-nitrimino-(10H)phenazinium betaine (Table 3, No. 5, 6) resonance hybrid; hence the observed shift in the symmetric

NO_2-absorption of the nitramines is additional evidence for the suggested inner salt structure (LV, LVI). In the alkali salts (Table 3, No. 7, 8, 9), the still stronger ionic character of the nitro-group causes further shift of the symmetric frequencies towards higher wave numbers, in agreement with the suggestion cited.

The strong hydrogen bonding assigned to 2-hydroxy-1-nitrophenazine (Table 3, No. 11) is accompanied by a shift of the symmetric NO_2-frequency to 1250 cm^{-1} and by a relative increase of the asymmetric band intensity.

TABLE 4

Amino-group stretching frequencies of phenazines

No.	Compound	Frequency, cm^{-1}
1	1-Aminophenazine	3480 m 3340 m
2	1-Amino-4-nitrophenazine	3430 ms 3290 s
3	2-Aminophenazine	3390 m 3310 m 3200 ms
4	2-Amino-1-nitrophenazine	3430 m 3290 s 3170 w
5	1,2-Diaminophenazine	3390 s 3300 unresolved 3170
6	1,3-Diaminophenazine	3420 s 3300 s 3200 s
7	2,3-Diaminophenazine	3430 s 3300 unresolved 3160

All spectra taken in solid state in potassium bromide pellets.

The free NH_2-group frequencies of phenazines appear (Table 4) in the region 3480-3290 cm^{-1}; the separation of the two bands assigned to the asymmetric and symmetric vibrations, respectively, is from 80 to 140 cm^{-1}. The third absorption, present in 2-aminophenazines, is located between 3200 and 3160 cm^{-1}, and is assigned to an intermolecular association of the type N-H...N. The latter assignment is supported by the observed remarkably higher (100°) melting point of 2-aminophenazine, as compared with 1-aminophenazine.

TABLE 5

N-H-stretching frequencies of secondary amines and amides in phenazine series

No.	Compound	Frequency, cm^{-1}
1	2-N-Methylaminophenazine	3260 ms
2	2-Methylamino-1-nitrophenazine	3340 s
3	5,10-Dihydrophenazine	3400 (sh) 3360 s
4	1-N-Acetylaminophenazine	3370 ms
5	2-N-Acetylaminophenazine	3300 3200 (sh) ms

All spectra taken in solid state in potassium bromide pellets.

The N-H stretching frequencies, listed in Table 5, appear in the range 3400-3200 cm^{-1}. The bands are well resolved and reasonably sharp in contrast to the very broad (3100-2700 cm^{-1}) and unresolved absorption which is assigned to the $\gtrless\overset{+}{N}$-H-group of 2-nitrimino-(10H)phenazinium betaine (LV, LVI).

TABLES 6-12

Infrared Absorption Maxima of Phenazines

TABLE 6

Infrared frequences of phenazine, 1- and 2-methylphenazine, and 2-tert.-butylphenazine (in cm^{-1})

Phenazine[1]	1-Methyl-phenazine[2]	2-Methyl-phenazine[3]	2-tert.-Butyl-phenazine[4]
3065vs	3060vs	3060vs	3065vs
	2970(sh)s	2973s	2955s
	2950s	2940s	
2890vw	2912s	2910s	2895s
	2830m	2845s	2860s
2750vw	2750vw	2750w	2750vw
	2730vw	2730w	
	2620vw	2640vw	2640vw
		2600vw	
		2535vw	2550vw
	2460vw	2460vw	2460vw
	2410vw	2400vw	2400vw
2290vw	2290vw	2300vw	2290vw
2120vw	2120vw	2120vw	2120vw
	2060vw	2050vw	2040vw
2000vw	2005vw	2005vw	2005vw
1959m	1958ms	1958m	1957m
1934m	1935s	1927s	1932s
1912m	1911m	1912m	1910m
	1859m		
1840(sh)m	1835m	1837s	1835m
1831m			
1812m	1814m	1813m	1813m
	1783ms	1776m	1785m
1767m	1768(sh)m	1763(sh)m	1764m
1745w	1745(sh)m	1747s	1752m
	1735m		
1725m	1725m	1723m	1725w
1716m			
1704m	1710s	1707s	1707s
	1670w		
1625m	1627m	1630m	1627s
		1605w	1603m
1550w	1560w		1555vw
			1540vw
1515s	1525s	1515vs	1506s
1471m	1477m	1485m	1483m
	1450ms	1468w	1457w
1432ms	1432ms	1440s	1435s
	1420vw		
			1395w

TABLE 6 (cont'd.)

Phenazine[1]	1-Methyl-[2] phenazine	2-Methyl-[3] phenazine	2-tert.-Butyl-[4] phenazine
	1375s	1385m	1380(sh)m
1362vs		1360s	1365s
	1352s	1350s	1355(sh)m
1329m	1330w		
	1310w	1307m	
1280m	1280vw	1280w	1285w
1261w	1267w	1270w	1277w
		1260w	
			1247s
1240w	1240vw		
1213ms	1212m	1200m	1215m
			1202m
			1198ms
	1158vw	1162w	
1139vs	1132s	1149s	1152s
		1138m	
		1130s	
1112vs	1118s	1116s	1122s
1074ms	1074ms	1080w	1084s
	1050m		
1029vw	1037m	1037m	1025s
999s	1001m	1000m	1001ms
	969m	965(sh)m	967(sh)w
958s	959m	958m	955s
	919w	925vw	925w
905s	900vw	910m	910m
		878m	888s
858w	855m		847m
		840m	830s
820s	820ms	820s	820s
	792m	790m	795m
	777s		
752vs	767vs	765vs	
745vs	758vs	758vs	755vs
	752vs	750vs	
	700w		715m
655m	645w		

1) 3800-1650 cm^{-1} and 1400-650 cm^{-1} - 3% solution in carbon disulphide
1650-1400 cm^{-1} - solid in potassium bromide pellet

2) 3) 4)
3800-1650 cm^{-1} - 4% solution in carbon disulphide
1400-650 cm^{-1} - 2% solution in carbon disulphide
1650-1400 cm^{-1} - solid in potassium bromide pellet

TABLE 7

Infrared frequencies of 2-nitrimino-(1OH)phenazinium betaine monohydrate, 2-nitrimino-(1OH)phenazinium betaine anhydrous, 2-nitraminophenazine ammonium salt, and 2-nitraminophenazine potassium salt (in cm^{-1})

2-Nitrimino-(1OH)-phenazinium betaine monohydrate	2-Nitrimino-(1OH)-phenazinium betaine anhydrous	2-Nitramino-phenazine ammonium salt	2-Nitramino-phenazine potassium salt
3540)broad 3400)bands 3200) 2700 broad w	3400vw 3100)unresolv. to) broad 2700) band s	3450w 3150)broad s 3020)unresolv. 2880)band	3400vs broad band
1665w 1630m 1605s	1630s 1610s	1630m 1600w	1660m 1630m 1600m
1565w 1515w 1485m 1455m 1435s 1375vw 1315)broad 1300)band vs 1195s 1165m 1140)m 1130) 1025m 915w	1555w 1510s 1485ms 1445ms 1430s 1405m 1355ms 1320)broad 1295) vs 1220m 1205ms 1190w 1160m 1150w 1125ms 1040s 960w	1510m 1475s 1440)ms 1415) 1380ms 1345)vs 1325) 1295w 1285w 1215w 1200w 1150vw 1130s 1025s 955ms 915w	1560w 1480w 1460m 1445s 1415m 1385)vs 1365)broad 1355)band 1320) 1260m 1200ms 1125s 1010s 950vw 915w
880m 835m 820s	880vw 855w 830)s 820)	875s 835s 820s	870ms 835)s unresolv. 825)
765) 755)vs 745) 680m	790m 765) 750)vs 740) 675	750)vs 735)w 680w	795vw 765)vs 755)ms 735)w 690w

All spectra taken in solid state in potassium bromide pellets

TABLE 8

Infrared frequencies of 2-nitraminophenazine sodium salt, 2-aminophenazine, 2-N-acetylaminophenazine, and 2-amino-1-nitrophenazine (in cm^{-1})

2-Nitramino-phenazine sodium salt[1]	2-Amino-phenazine[2]	2-N-Acetyl-amino-phenazine[3]	2-Amino-1-nitro-phenazine[4]
		3300m	3430m
3340)vs broad	3390m	3200(sh)	3290s
3240)unresolv.	3310m	3070w	3170w
3140)band	3200ms		3040w
		1700s	
	1637s	1675s	1645vs
	1620(sh)	1630m	1615s
1700ms	1600s	1605m	1600ms
1630ms			
1600m		1570s	1555ms
	1525m	1545s	1540w
	1510ms	1505m	1520s
	1485s	1485ms	1495ms
	1475ms	1460ms	1480m
1515ms	1450s	1440s	1435ms
1480ms	1405w	1410vw	1380s
1465w	1365vw	1365s	1350m
1445s	1335s	1310s	1280vs
1415)	1232s	1285m	1215m
1400) vs	1215w	1255s	1175m
1360) vs broad	1200m	1200m	1130ms
1330) band	1130s	1180m	1005w
1300w	1120ms	1145 (sh)	975ms
1285w	1000w	1120s	905m
1215vw	950w	1035(sh)	
1200w	905w	1010ms	
1150w		955vw	
1125s		910w	
1030s			
960ms		875m	
915w	865vw	860m	
885s	855ms	830s	
870vw	840w	800m	845s
835s	825s		835ms
815s		755s	802ms
785w	785m	695w	795s
750vs)	760vs		770)w
735 w)	735w		755)vs
690w	705vw		740)w

1) 2) 4) Solid in potassium bromide pellet

3) Sublimed onto potassium bromide pellet

TABLE 9

Infrared frequencies of 2-hydroxy-1-nitrophenazine, 1,2-diaminophenazine, 1,3-diaminophenazine, and 2,3-diaminophenazine (in cm^{-1})

2-Hydroxy-1-nitrophenazine [1]	1,2-Diaminophenazine [2]	1,3-Diaminophenazine [3]	2,3-Diaminophenazine [4]
3040 broad s band	3390) broad 3300) unresolved 3170) band s	3420 s) 3300 s) broad 3200 s)	3430) broad 3300) unresolved 3160) s
		3050 vw	1645 s
		1640 vs	1565 m
1635 s	1630 vs	1600 (sh)	1495) vs broad
1605 s	1605 vs	1590 s	1470) s
		1560 m	1410 m
		1510 s	1370 w
1575) vs	1555 (sh)	1475 s	1340 s
1550) vs	1515 s	1450 s	1325 (sh)
1530) vs	1490 s	1410 (sh)	1230 s
1505 (sh)	1470 m	1395 m	1210 (sh)
1485 m	1440 vs	1370 (sh)	1140 m
1470 w	1390 w	1335 vs	1125 (sh)
1445 s	1355 w	1265 w	1005 vw
1415 vw	1320 s	1245 w	915 w
1385 w	1270 vw	1220 s	890 m
1370 w	1240 ms	1205 s	850 (sh)
1345 ms	1230 (sh)	1130 m	835 ms
1320 ms	1210 w	1110 w	765) vs
1300 ms	1165 m	1060 w	740 (sh))
1250 ms	1130 s	1000 vw	
1225 w	1005 vw	955 vw	
1175 s	955 m	910 w	
1150 m	905 m	855 (sh)) s	
1140 w		850)	
1120 ms		835 ms	
1045 m		825 ms	
1010 vw		800 w	
990 s		760 vs	
905) vw		685 vw	
895)			
840 vs	865 (sh)		
802 w	825 s		
	800 (sh)		
790 m	785 s		
775 m	755 vs		
755 vs	700 w		
740 w			
680 vw			

1) 2) 4) Solid in potassium bromide pellet

3) Sublimed onto potassium bromide pellet.

TABLE 10

Infrared frequencies of 2-N-methylaminophenazine, 2-NN-acetylmethylaminophenazine, 2-methylamino-1-nitrophenazine, 1-hydroxy-4-nitrophenazine ammonium salt, and 4-nitro-1(5H)phenazinone (in cm^{-1})

2-N-Methylamino-phenazine	2-NN-Acetylmethyl-aminophenazine	2-Methylamino-1-nitrophenazine	1-Hydroxy-4-nitro-phenazine ammonium salt	5-Nitro-1(5H)-phenazinone
3260 ms	3050 w	3340 s	3400 v. broad	3400 m
3050 w	2980 (sh)	3050 (sh)	3100 unresolved	3120 ms
1635 vs	2900 (sh)	2900 w	band	3060 (sh)
1605 s	1665 vs	1640 vs	1620 vs	1655 vs
1575 (sh)	1625 s	1610 s	1595 s	1640 (sh)
1550 s	1605 ms	1570 ms	1540 (sh)	1615 (sh)
1520 vs	1510 w	1515 vs	1530 s	1600 ms
1485 ms	1490 ms	1500 m	1510 (sh)	1575 m
1475 (sh)	1470 (sh)	1465 ms	1470 s	1545 (sh)
1440 s	1440 m	1445 w	1405 s	1535 vs
1425 ms	1415 m	1430 ms	1340 (sh)	1495 ms
1400 w	1385 m	1405 vw	1320 vs	1485 (sh)
1355 ms	1365 w	1375 (sh)	1265 vs	1445 w
1300 ms	1345 m	1365 (sh) broad	1215 w	1415 ms
1240 s	1320 (sh)	1360 s	1140 m	1390 m
1215 w	1300 (sh)	1340 w	1095 ms	1365 vw
1200 s	1250 w	1265 s	1025 ms	1335 s
1120 s	1200 m	1220 s	940 ms	1325 (sh)
1055 w	1160 (sh)	1175 s	900 w	1290 (sh)
1010 vw	1140 ms	1165 ms	820 s	1265 vs
980 vw	1120 m	1140 s	805 m	1235 (sh)
960 vw	1075 m	1130 (sh)	780 ms	1225 s
945 vw	1010 w	1085 s	765 vs	1185 s
905 m	980 ms	1015 s	740 ms	1160 ms
855 ms	900 ms	975 s	730 (sh)	1135 w
815 s	860 ms	960 w	705 ms	1090 m
805 s	830 s	905 m		1025 m

. . . .

TABLE 10 (cont'd.)

2-N-Methylamino-phenazine	2-NN-Acetylmethyl-aminophenazine	2-Methylamino-1-nitrophenazine	1-Hydroxy-4-nitro-phenazine ammonium salt	5-Nitro-1(5H)-phenazinone
780 m	765 vs	865 w		975 w
755 vs	760 (sh)	830 s		960 vw
750 (sh)	745 (sh)	802 m		940 w
735 (sh)	720 w	800 (sh)		900 w
	675 m	785 m		875 w
		760 vs		815 vs
		685 vw		810 (sh)
				800 (sh)
				780 m
				760 w
				750 w
				735 w
				700 ms

All spectra taken in solid state in potassium bromide pellets.

TABLE 11

Infrared frequencies of 1-aminophenazine, 1-N-acetylaminophenazine, phenazine-1-carboxylic acid, and 1-amino-4-nitrophenazine (in cm^{-1})

1-Amino phenazine	1-N-Acetyl-amino-phenazine	Phenazine-1-carboxylic acid	1-Amino-4-nitro-phenazine
3480 m	3370 ms	3600) broad	3430 ms
3340 m	1685 (sh)	to) unresolved	3290 s
1620 s	1675 vs	2000)	3080 w
1605 s	1630 m	1780 w	1630 vs
1590 (sh)	1610 vw	1730 vs broad	1610 s
1555 w	1565 m	1620 w	1590 s
1520 (sh)	1530) vs	1600 m	1520 vs
1510 m	1515)	1560 m	1490 w
1475 s	1485 ms	1525 s	1465 m
1420 m	1465 w	1470 vs broad	1425 m
1395 ms	1445 (sh)	1425 m	1350 vs
1355 s	1420 s	1410 w	1325 (sh)
1320 m	1410 ms	1360 m	1285 vs
1235 w	1380) s	1315 w	1220 m
1210 w	1375) (sh)	1290 w	1150 w
1135 m	1350 w	1270 ms	1135 vw
1070 vw	1305) w	1240 ms	1115 w
1000 m	1290) m	1220 m	1075 w
955 vw	1280) w	1185 m	1000) (sh)
910 w	1245 ms	1160 m	990) s
860 w	1210 w	1140 ms	970) (sh)
820 m	1170 w	1130 m	915 w
800 w	1140 w	1065 w	895 vw
765 s	1120 w	1050 w	820 s
735 vs	1080 w	995 m	802 m
665 vw	1050 w	965 vw	775) (sh)
	1035 vw	950 w	770) vs
	1010 w	925 w	765) (sh)
	985 (sh)	885 s	750 w
	960 w	865 s	725 m
	920 w	840 ms	705 m
	900 w	795 s	685 m
	855 m	755)	
	830 ms	740 (sh)) vs	
	815 w	675 m	
	780 m		
	765 s		
	760 s		
	750 vs		
	680 m		

All spectra taken in solid state in potassium bromide pellets.

TABLE 12

Infrared spectra of phenazine-d_8, phenazine hydrochloride, phenazyl hydrochloride, and 5,10-dihydrophenazine (in cm^{-1})

Phenazine-d_8 [1]	Phenazine hydrochloride [2]	Phenazyl hydrochloride [3]	5,10-Dihydrophenazine [4]
2290 m	2940) vs	3400 m broad	3400) (sh)
	2850)	3100) broad	3360) ms
	2180) ms broad	to)s unresolv.	3050 vw
1620 m	2090) unresolv.	2400)	1610 ms
1492 vs	1910) broad	1610 s	1515) vs
1415 w	1880) vs unresolv.	1590 s	1500)
1387 s	1800)	1545 (sh)	1460 vs
1308 m	1610 ms	1495 s	1300 vs
1257 m	1570 m	1475 s	1140 vw
1202 m	1520 ms	1460 (sh)	1120 m
1167 vs	1465 vs	1420 (sh)	1030 w
1047 w	1425 m	1405 ms	915) m
1025 m	1410 w	1355 ms	910) (sh)
1014 vw	1380 ms	1300 ms	820 vw
950 m	1355 ms	1275 s	745) vs
921 s	1330 w	1175 m	730 (sh))
903 s	1320 w	1155 w	725)
852 m	1290 w	1140 w	670 w
827 (sh) m	1265 w	955 w	
822 s	1240 vw	945 w	
818 s	1225 w	895 m	
777 (sh) m	1210 vw	845)vs	
773 s	1175 w	835)s	
757 s	1150 w	825)(sh)	
744 vs	1130 vs	775 w	
703 vw	1030 s	740 vs	
692 w	975 vw	730 (sh)	
	955 vw		
	920 vw		
	900 ms		
	880 w		
	825 ms		
	795 w		
	775 ms		
	760 vs		
	740 vs		

1) 3800-1400 cm^{-1} - 3% solution in carbon tetrachloride
1400-650 cm^{-1} - 3% solution in carbon disulphide

2) Solid state in "Nujol"

3) and 4) Solid in potassium bromide pellets.

FIG. 1

Infrared Spectra of

Phenazine

3800-1650 cm^{-1} and 1400-650 cm^{-1} - 3% solution in carbon disulphide

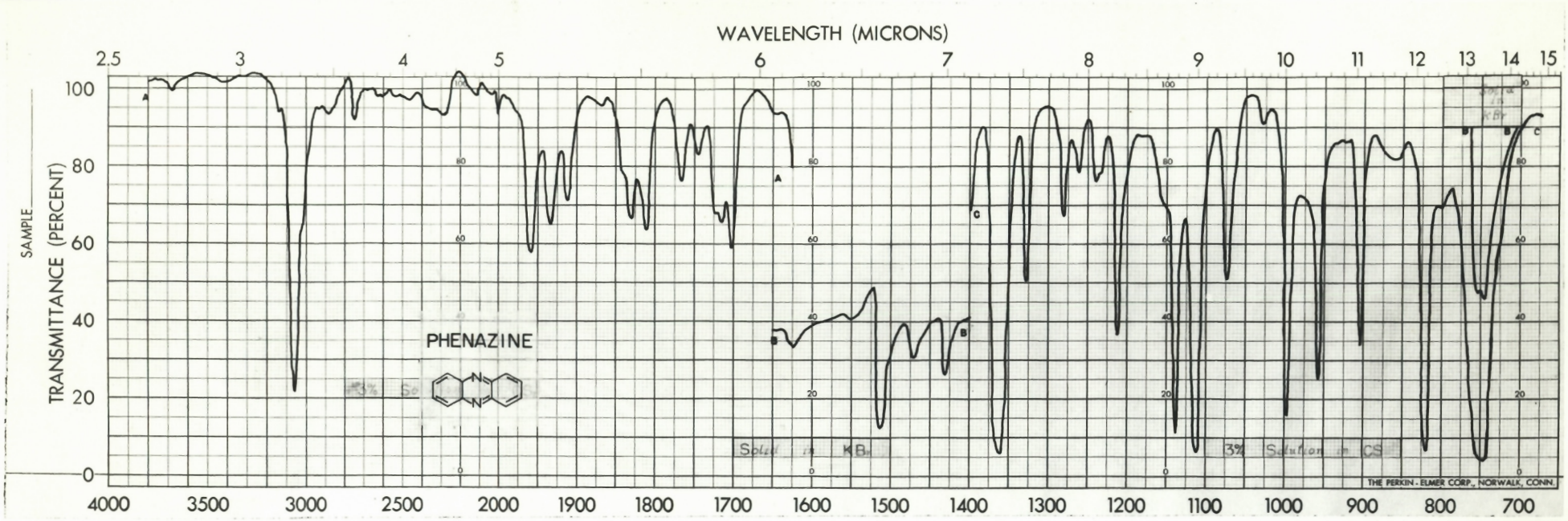
1650-1400 cm^{-1} - solid in potassium bromide pellet

and

Phenazine-d_8

3800-1400 cm^{-1} - 3% solution in carbon tetrachloride

1400-650 cm^{-1} - 3% solution in carbon disulphide


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

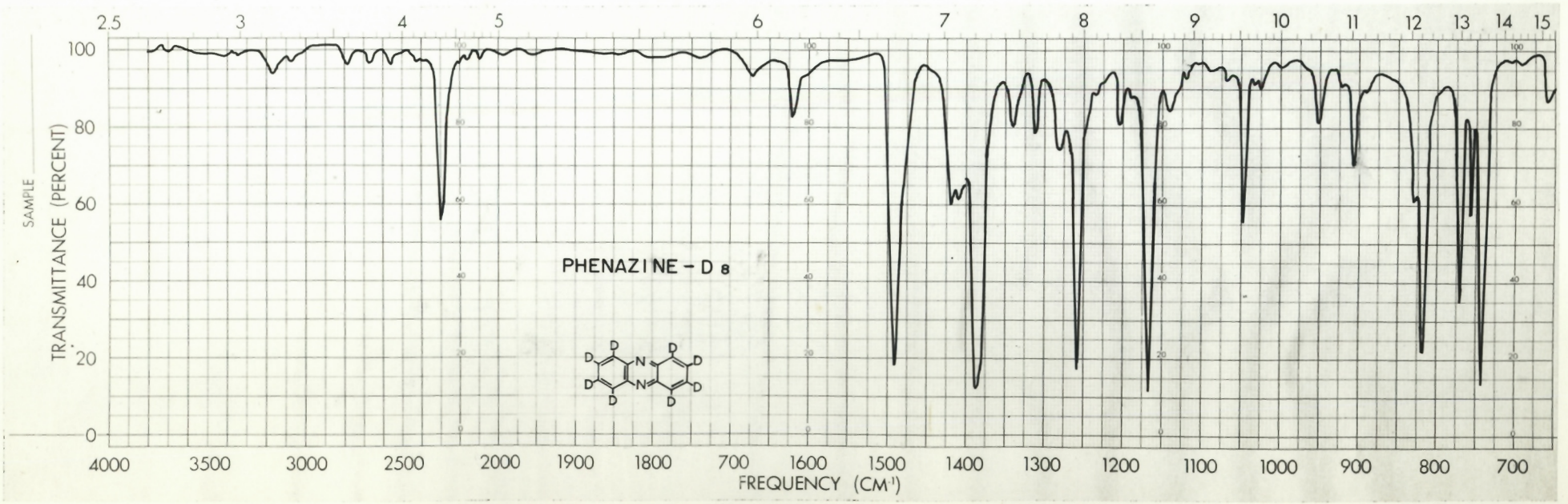

2.5
3
4
5
6
7
8
9
10
11
12
13
14
15
TRANSMITTANCE (PERCENT)
SAMPLE
100
80
60
40
20
0
PHENAZINE – D 8
D
N
4000
3500
3000
2500
2000
1900
1800
700
1600
1500
1400
1300
1200
1100
1000
900
800
700
FREQUENCY (CM⁻¹)

FIG. 2

Infrared Spectra of

1-Methylphenazine

3800-1650 cm^{-1} - 4% solution in carbon disulphide

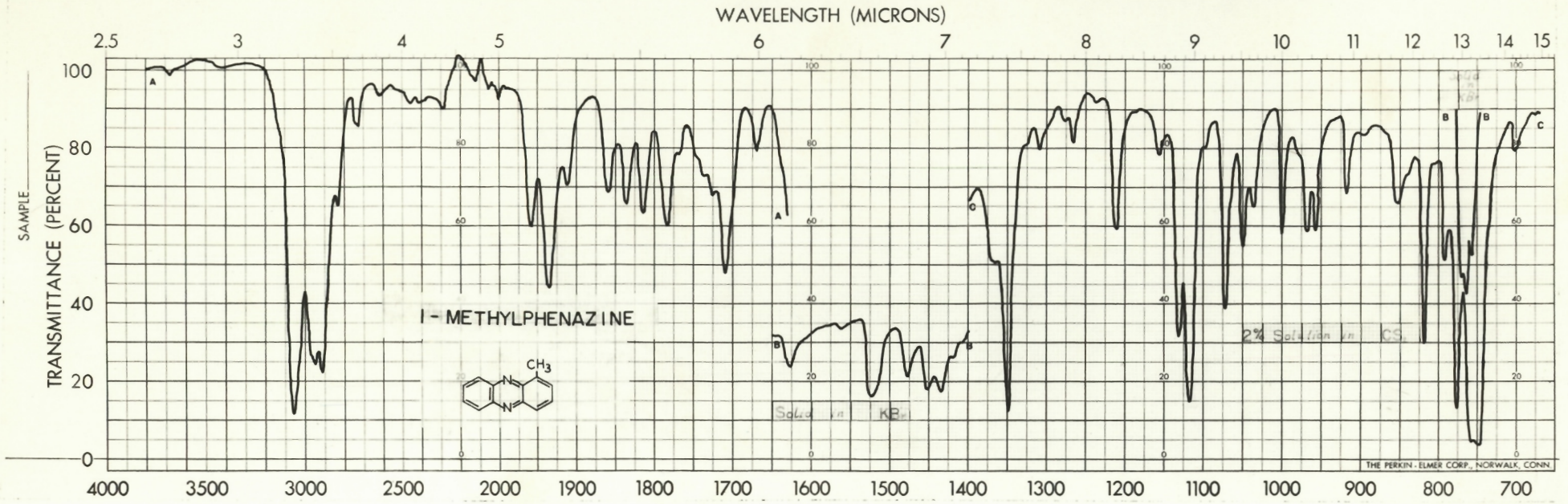
1400-650 cm^{-1} - 2% solution in carbon disulphide

1650-1400 cm^{-1} - solid in potassium bromide pellet

and

1-N-Acetylaminophenazine

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
SAMPLE
1-METHYLPHENAZINE
CH3
N
N
2% Solution in CS2
Solution in KBr
THE PERKIN-ELMER CORP., NORWALK, CONN.
4000 3500 3000 2500 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700

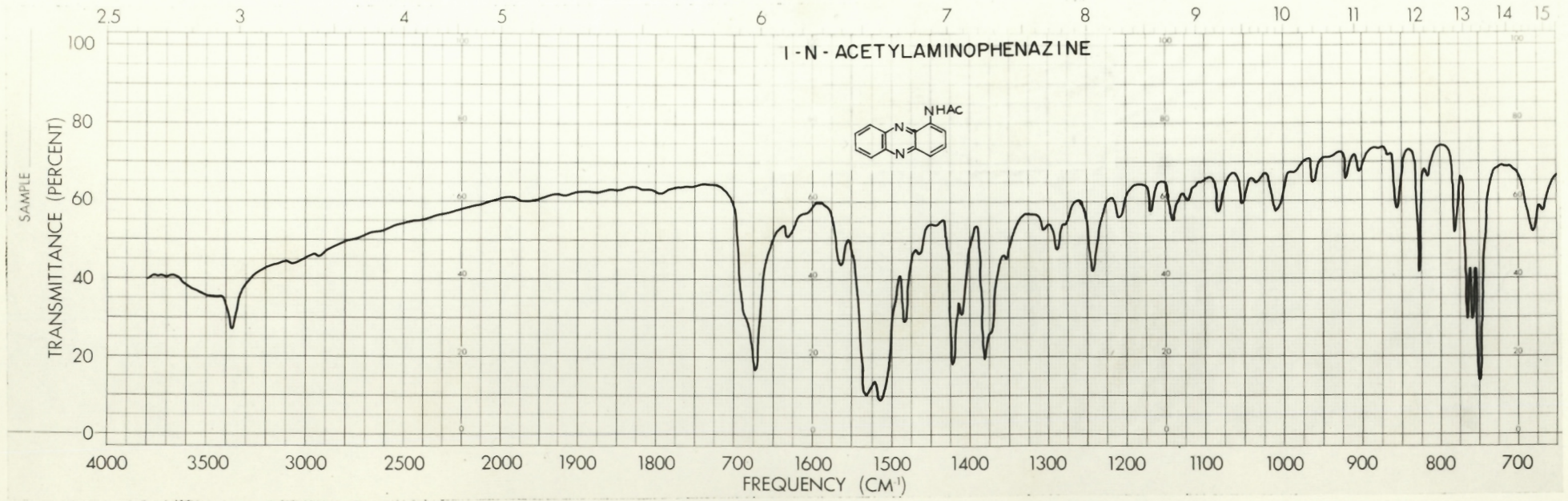

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
SAMPLE
1-N-ACETYLAMINOPHENAZINE
NHAC
N
N
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 3

Infrared Spectra of

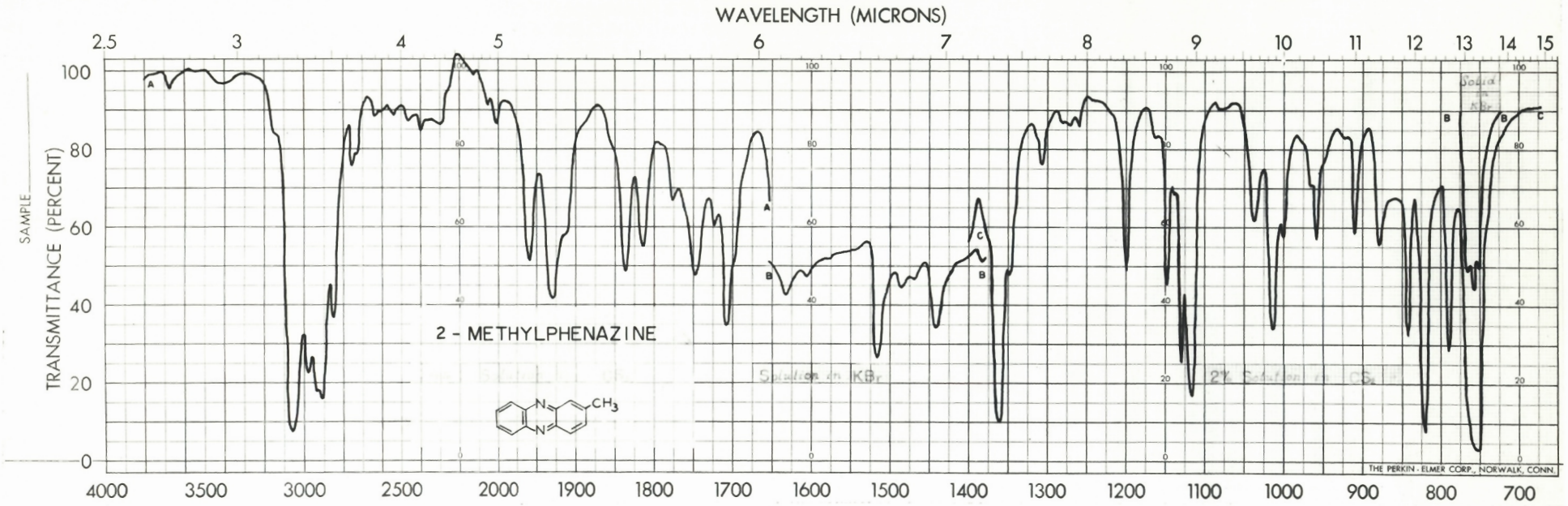
2-Methylphenazine and

2-tert.-Butylphenazine

3800-1650 cm^{-1} - 4% solution in carbon disulphide

1400-650 cm^{-1} - 2% solution in carbon disulphide

1650-1400 cm^{-1} - solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
SAMPLE
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700
2 - METHYLPHENAZINE
Solution in KBr
2% Solution in CS2
THE PERKIN-ELMER CORP., NORWALK, CONN.

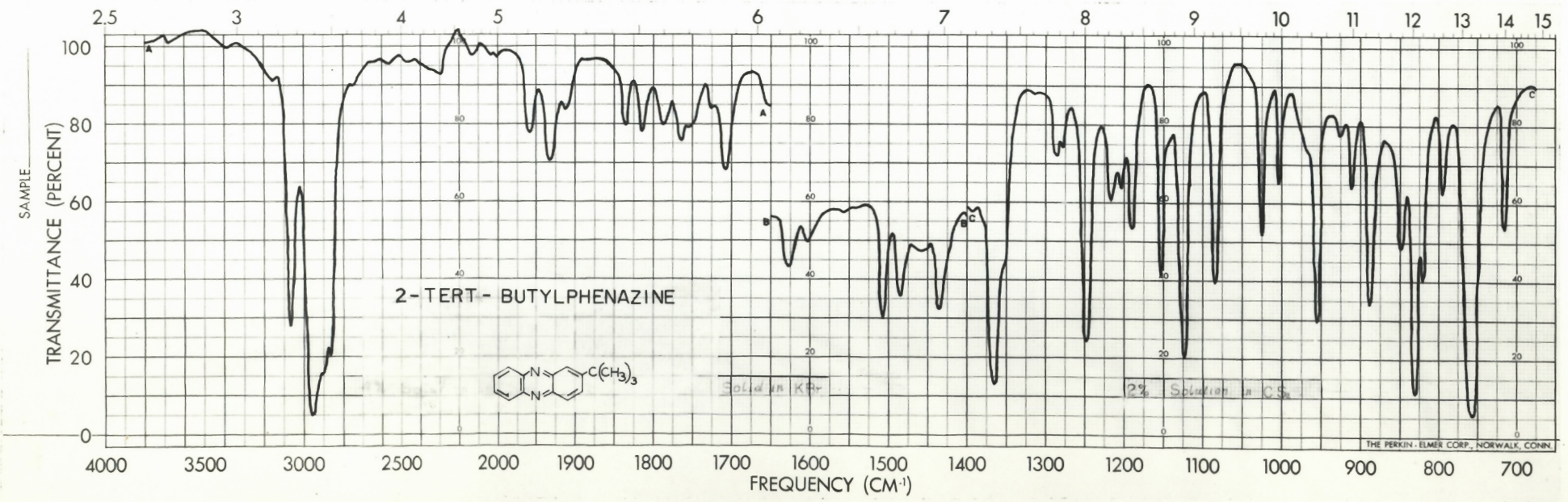

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
SAMPLE
100 80 60 40 20 0
2-TERT-BUTYLPHENAZINE
Solution in KBr
2% Solution in CS2
THE PERKIN-ELMER CORP., NORWALK, CONN.
4000 3500 3000 2500 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 4

Infrared Spectra of

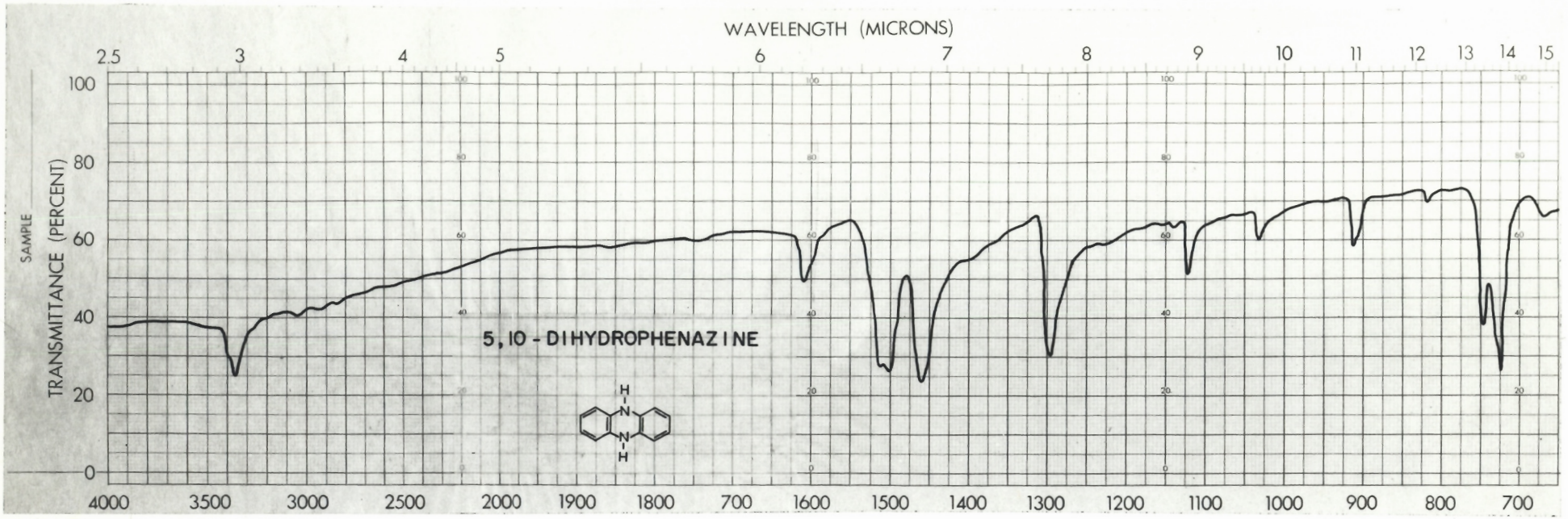
5,10-Dihydrophenazine

solid in potassium bromide pellet

and

Phenazine Hydrochloride

solid in "Nujol"


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
SAMPLE
100 80 60 40 20 0
5,10 - DIHYDROPHENAZINE
H
N
N
H
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

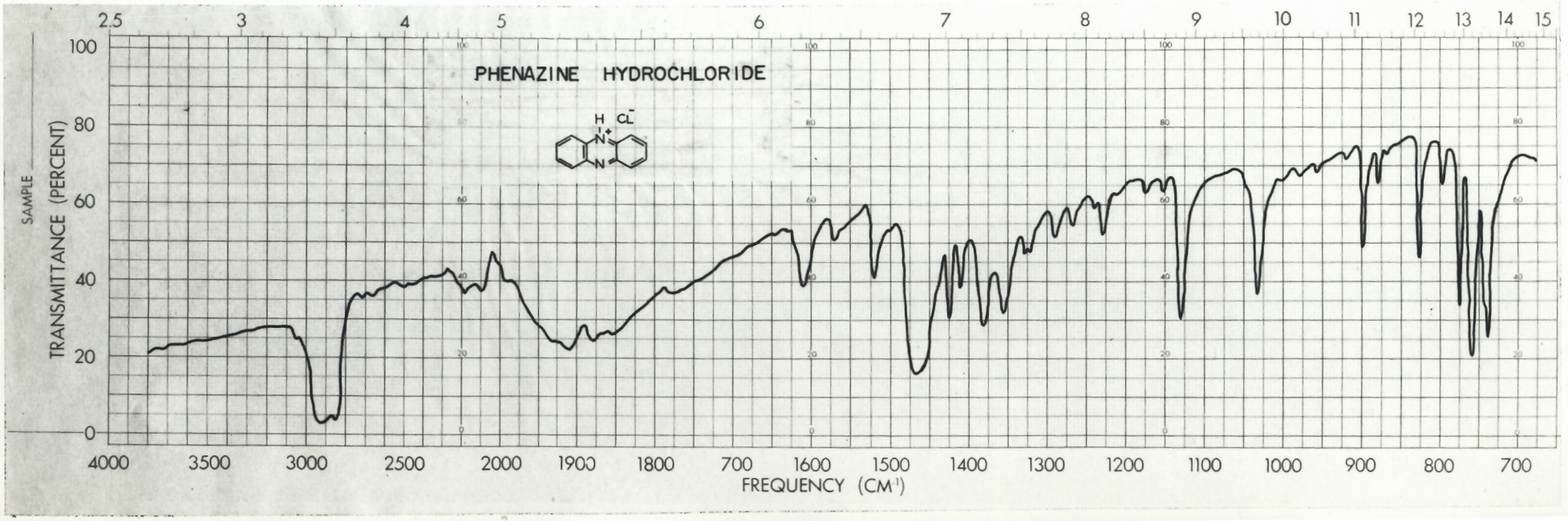

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
SAMPLE
100 80 60 40 20 0
PHENAZINE HYDROCHLORIDE
H CL
N
N
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 5

Infrared Spectrum of

2-Aminophenazine

solid in potassium bromide pellet

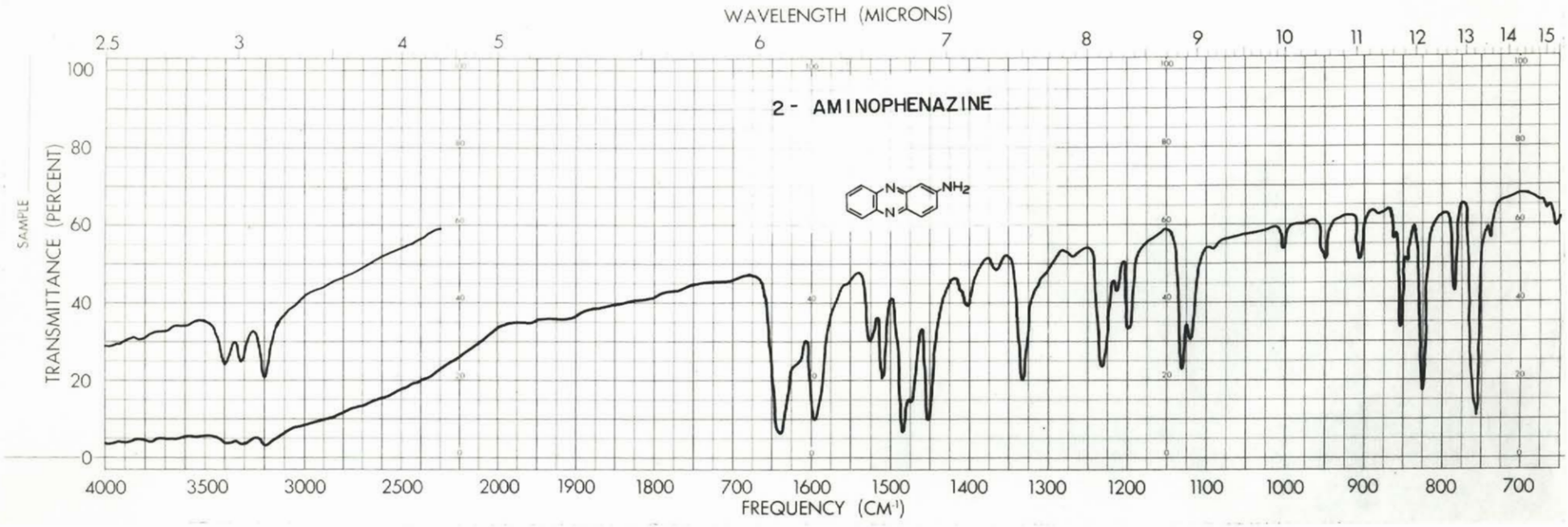

WAVELENGTH (MICRONS)
2.5
3
4
5
6
7
8
9
10
11
12
13
14
15
2 - AMINOPHENAZINE
NH2
N
N
SAMPLE
TRANSMITTANCE (PERCENT)
100
80
60
40
20
0
4000
3500
3000
2500
2000
1900
1800
700
1600
1500
1400
1300
1200
1100
1000
900
800
700
FREQUENCY (CM-1)

FIG. 6

Infrared Spectra of

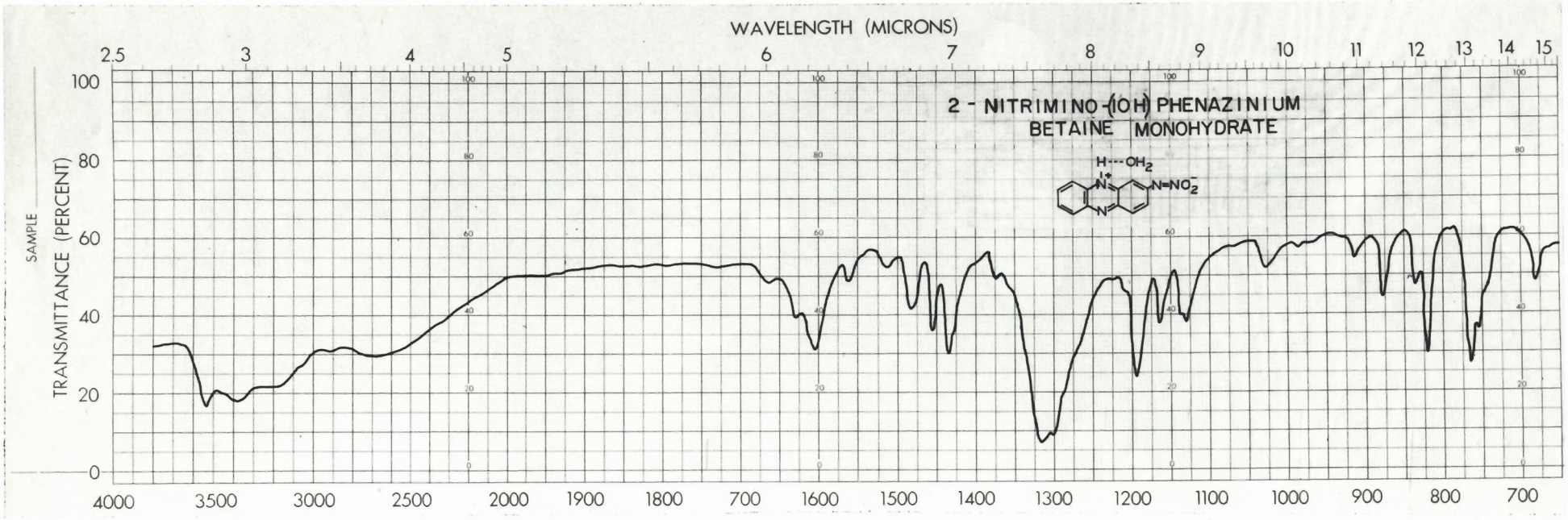
2-Nitrimino-(IOH)phenazinium Betaine

Monohydrate and

2-Nitrimino-(IOH)phenazinium Betaine

Anhydrous

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2 - NITRIMINO-(IOH) PHENAZINIUM
BETAINE MONOHYDRATE
H---OH2
N=NO2
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

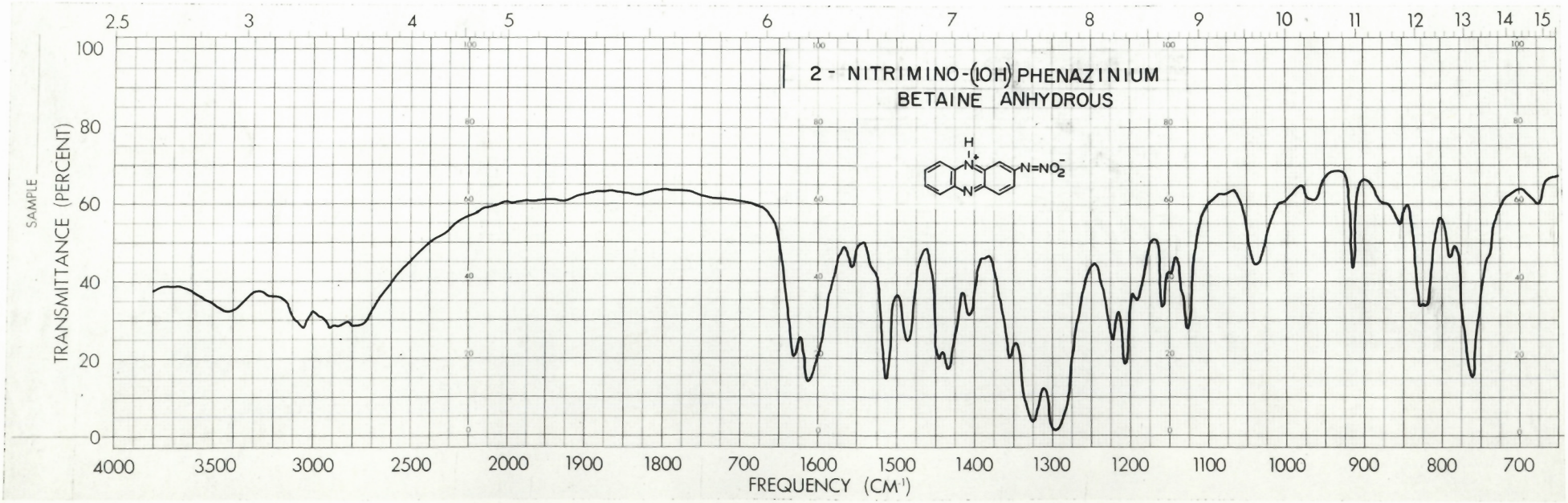

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2 - NITRIMINO-(IOH) PHENAZINIUM
BETAINE ANHYDROUS
H
N=NO2
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 7

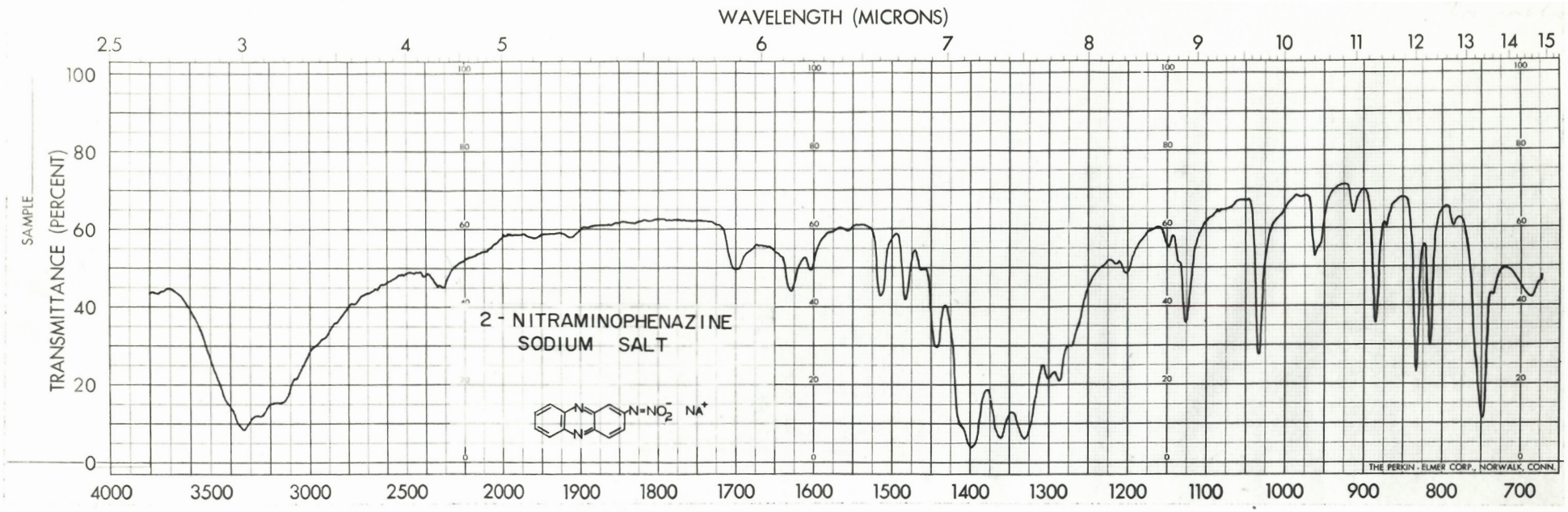
Infrared Spectra of

2-Nitraminophenazine Sodium Salt

and

2-Nitraminophenazine Ammonium Salt

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
SAMPLE
2 - NITRAMINOPHENAZINE
SODIUM SALT
N=NO2- NA+
4000 3500 3000 2500 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700
THE PERKIN - ELMER CORP., NORWALK, CONN.

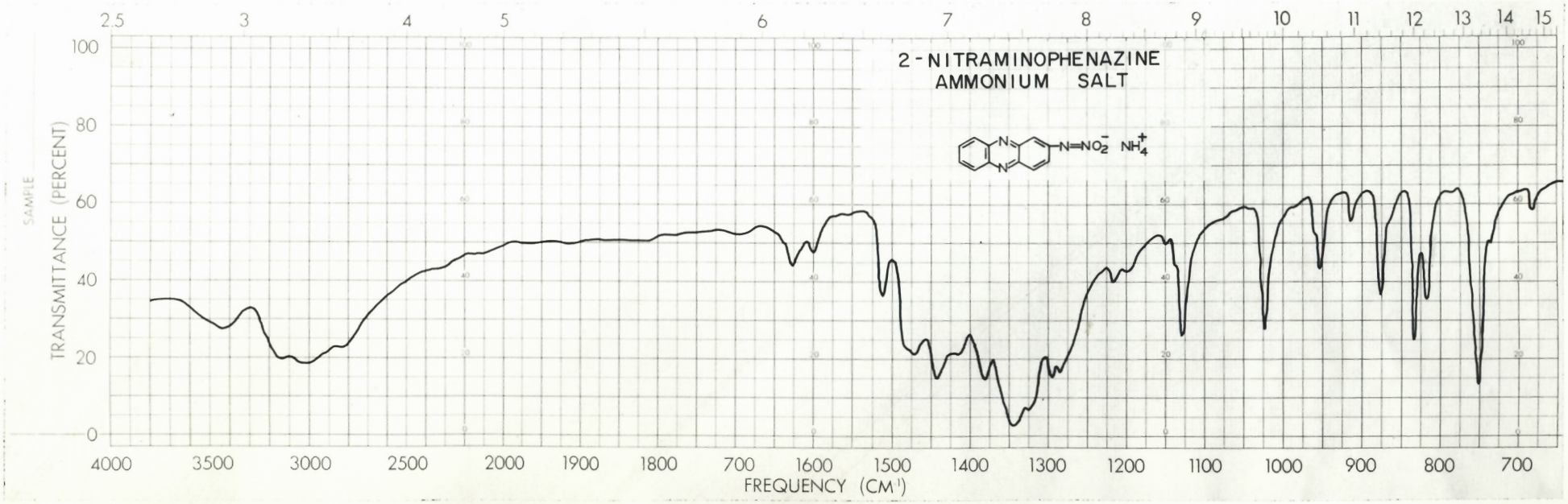

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
SAMPLE
2 - NITRAMINOPHENAZINE
AMMONIUM SALT
N=NO2- NH4+
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 8

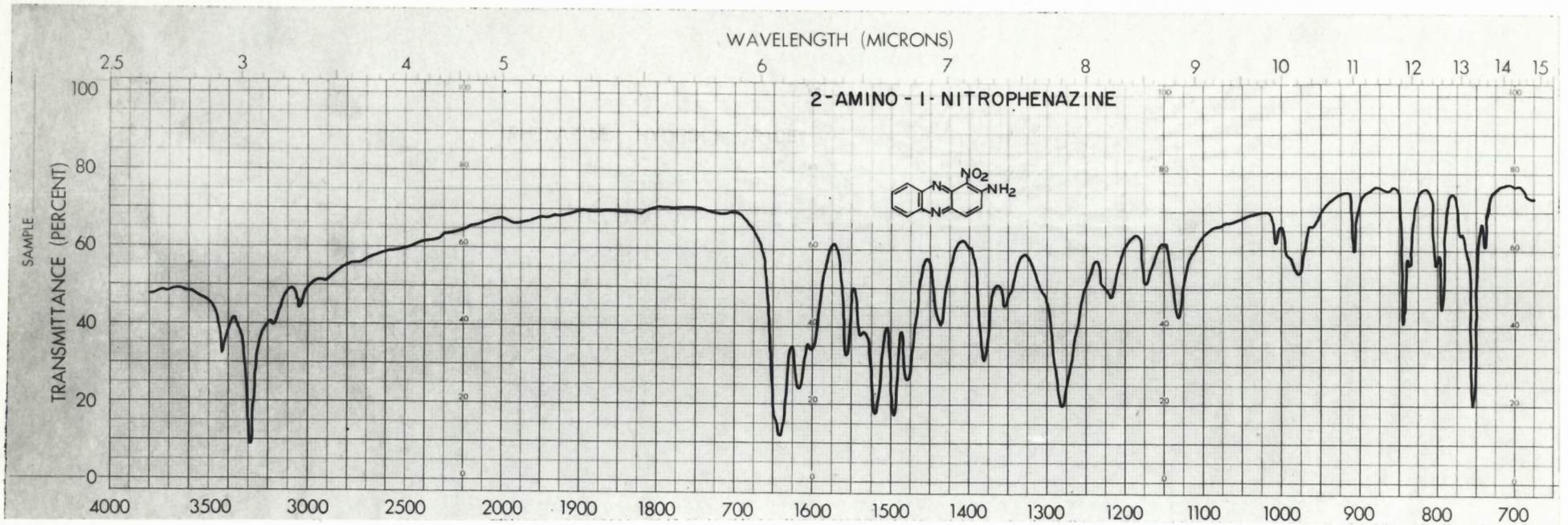
Infrared Spectra of

2-Amino-1-nitrophenazine

and

2-Hydroxy-1-nitrophenazine

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2-AMINO - 1- NITROPHENAZINE
NO2
NH2
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

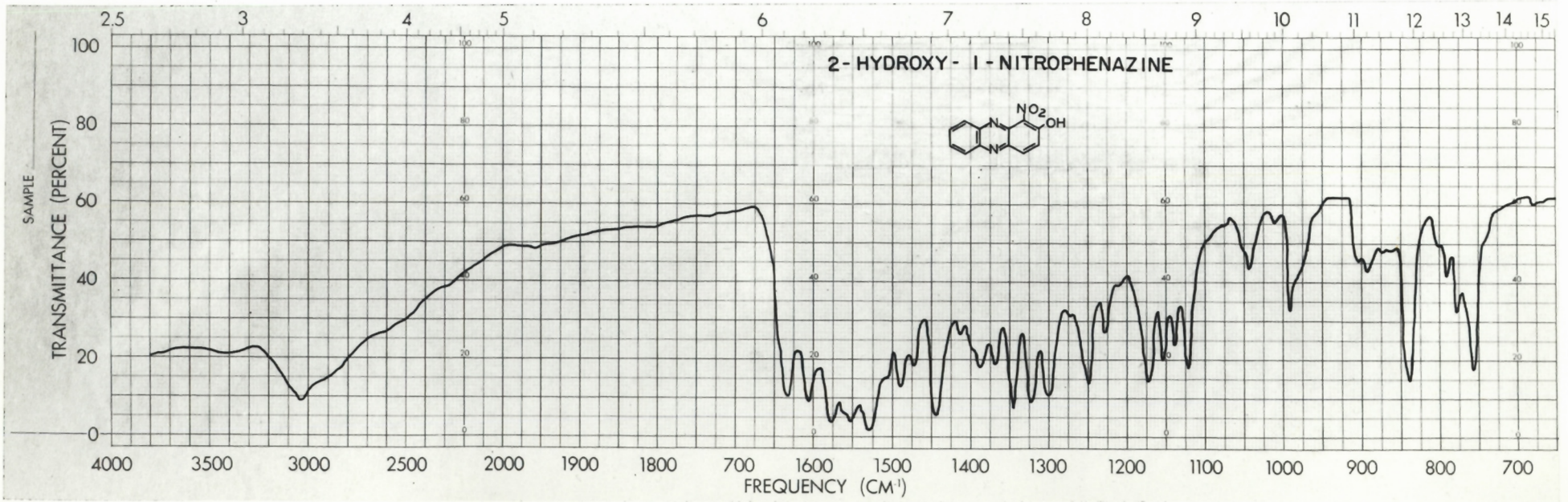

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2- HYDROXY - 1 - NITROPHENAZINE
NO2
OH
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 9

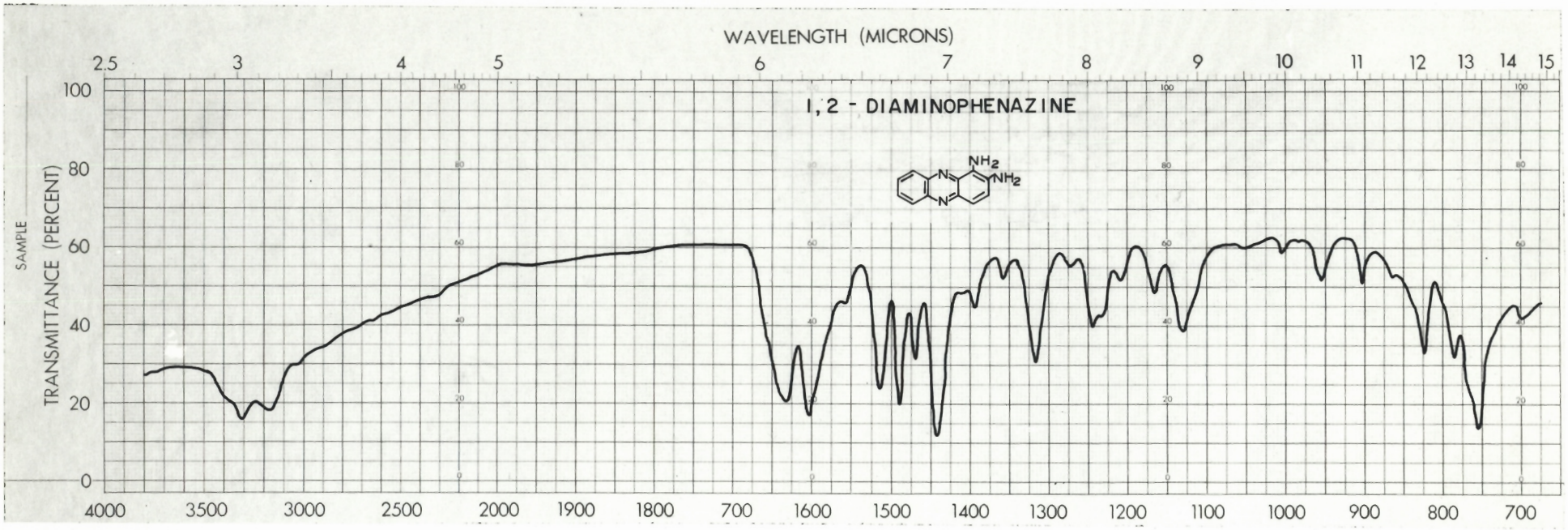
Infrared Spectra of

1,2-Diaminophenazine

and

2-Nitraminophenazine Potassium Salt

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
1, 2 - DIAMINOPHENAZINE
NH2
NH2
N
N
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

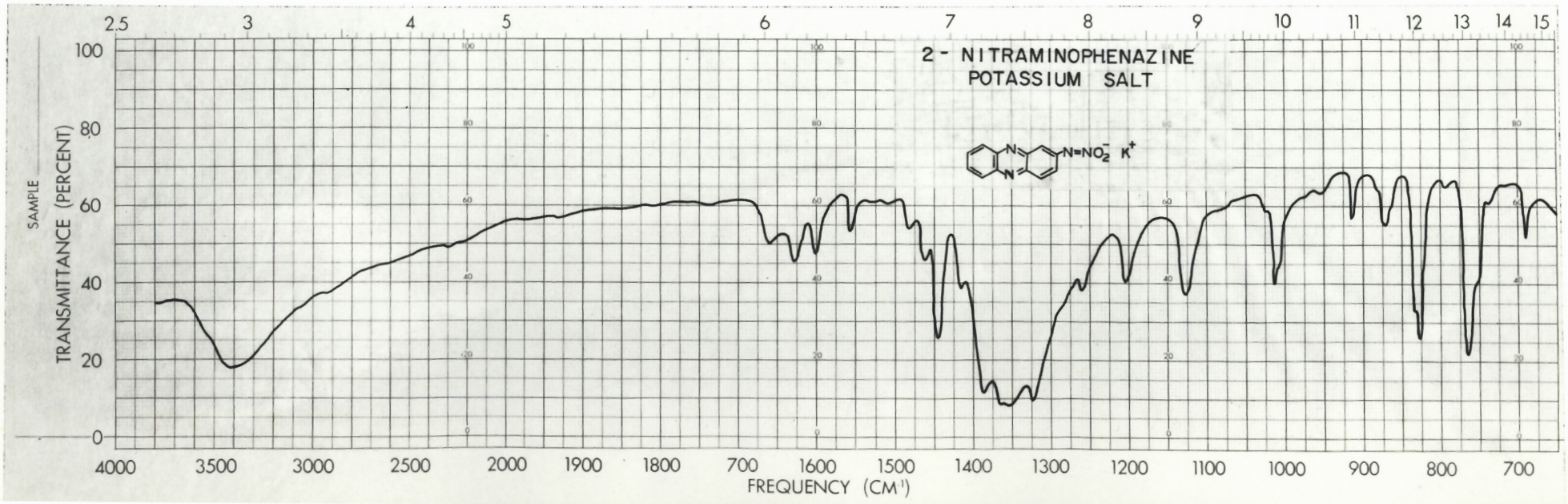

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2 - NITRAMINOPHENAZINE
POTASSIUM SALT
N
N
N=NO2 K+
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 10

Infrared Spectra of

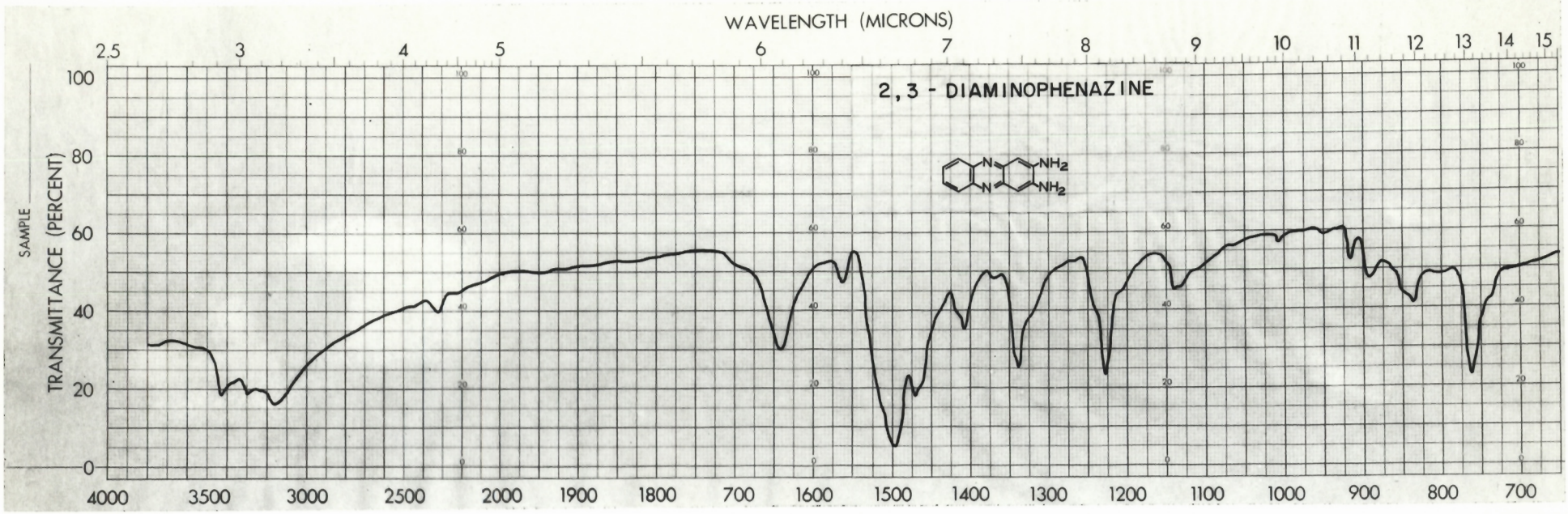
2,3-Diaminophenazine

solid in potassium bromide pellet

and

1,3-Diaminophenazine

solid sublimed onto potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2,3 - DIAMINOPHENAZINE
NH2
NH2
N
N
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

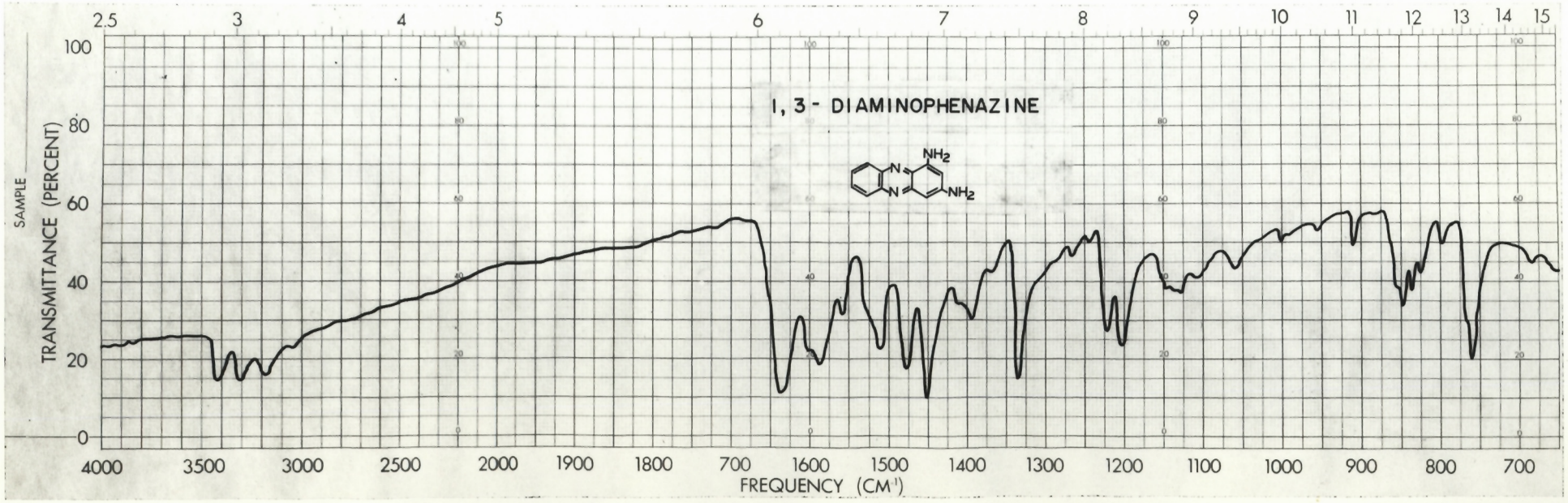

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
1,3 - DIAMINOPHENAZINE
NH2
NH2
N
N
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 11

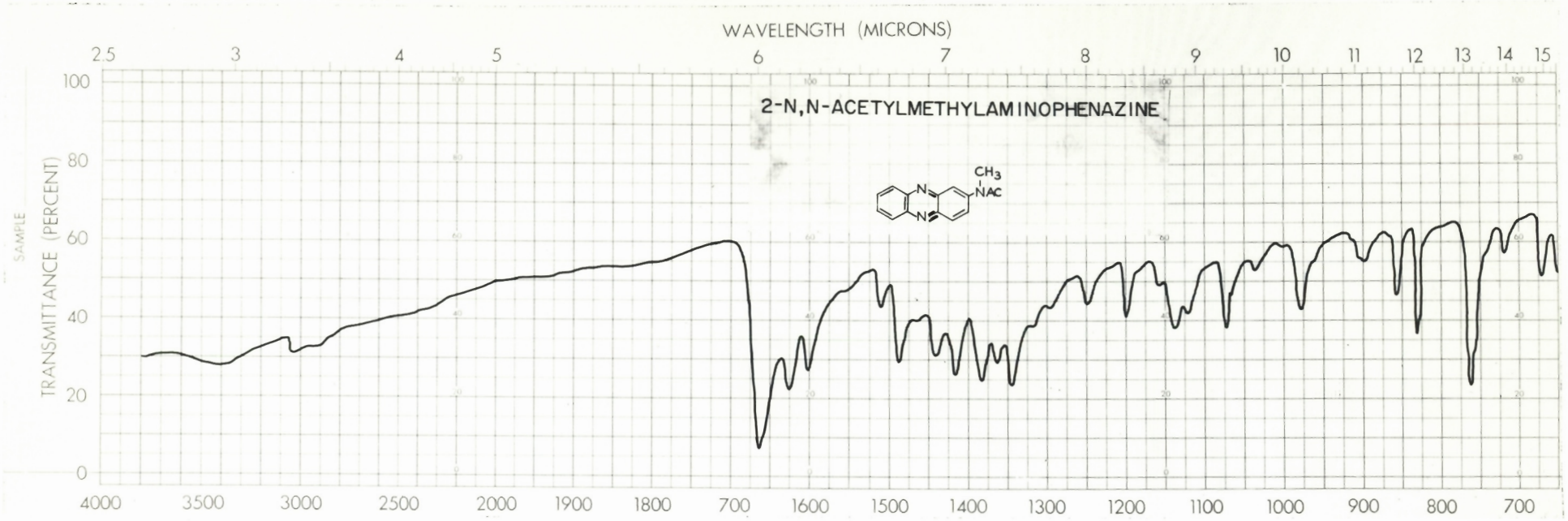
Infrared Spectra of

2-NN-Acetylmethylaminophenazine

and

2-N-Methylaminophenazine

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2-N,N-ACETYLMETHYLAMINOPHENAZINE
CH3
NAC
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

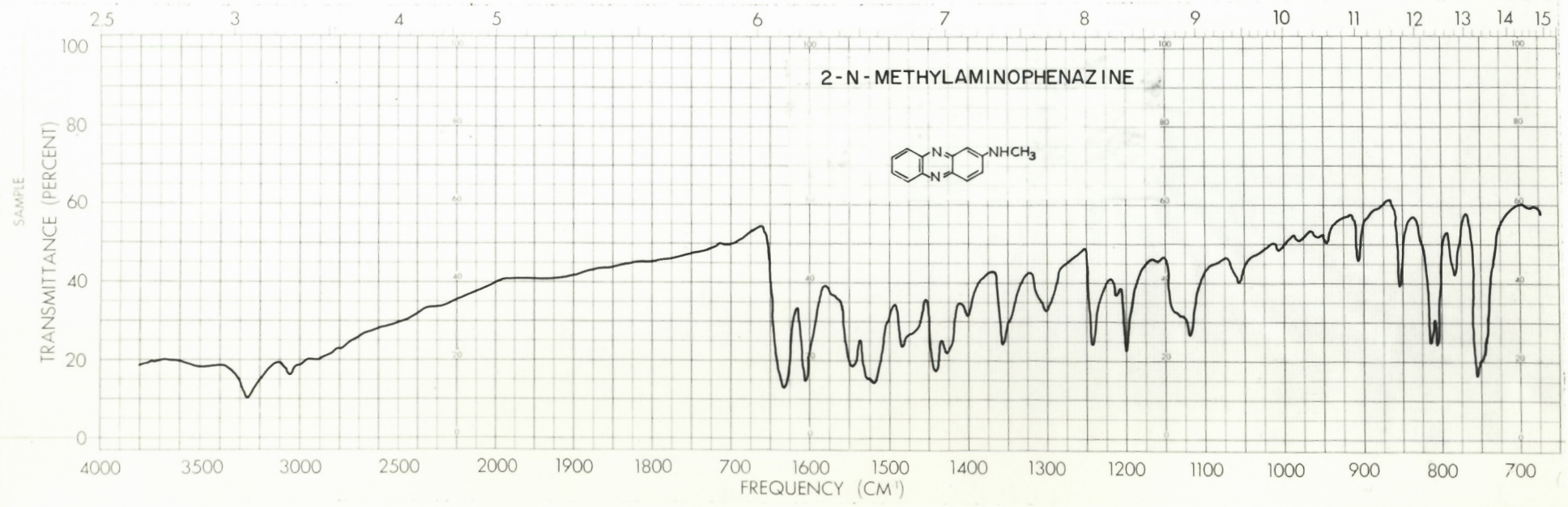

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2-N-METHYLAMINOPHENAZINE
NHCH3
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

FIG. 12

Infrared Spectra of

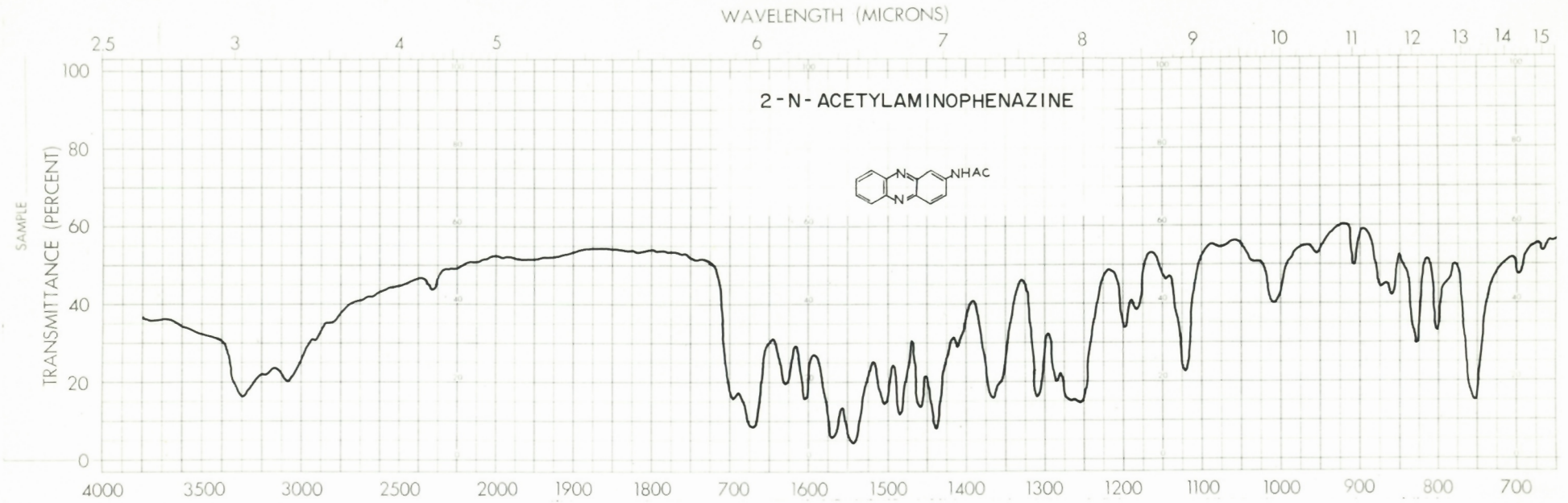
2-N-Acetylaminophenazine

solid sublimed onto potassium bromide pellet

and

2-Methylamino-1-nitrophenazine

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2-N-ACETYLAMINOPHENAZINE
NHAC
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

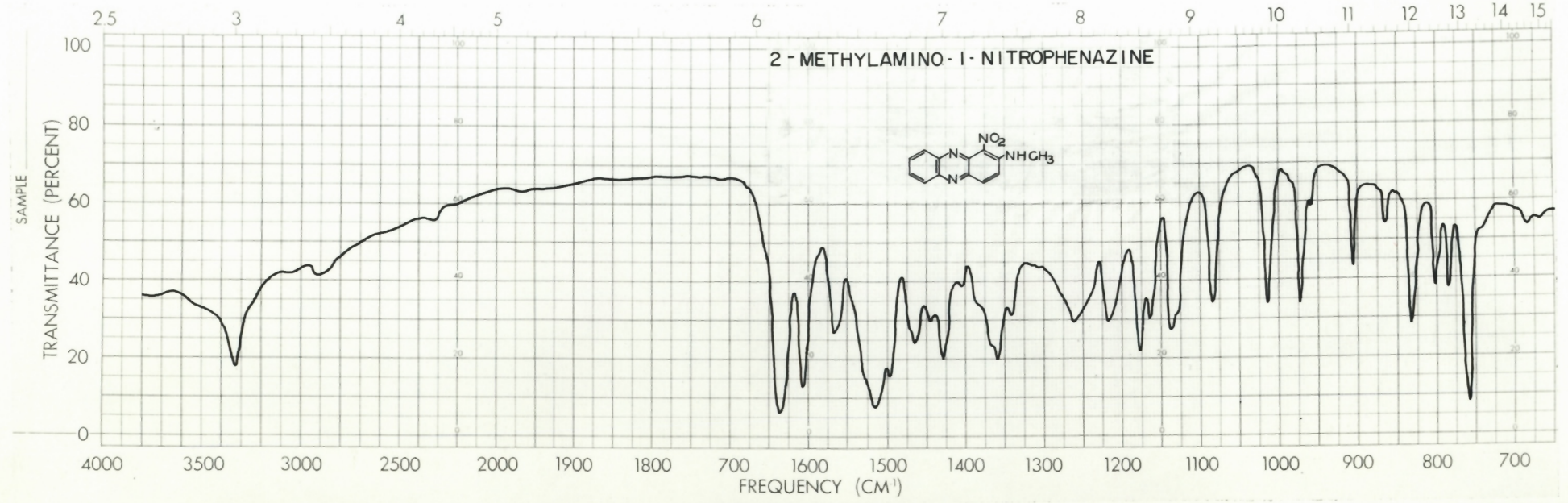

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
2-METHYLAMINO-1-NITROPHENAZINE
NO2
NHCH3
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM-1)

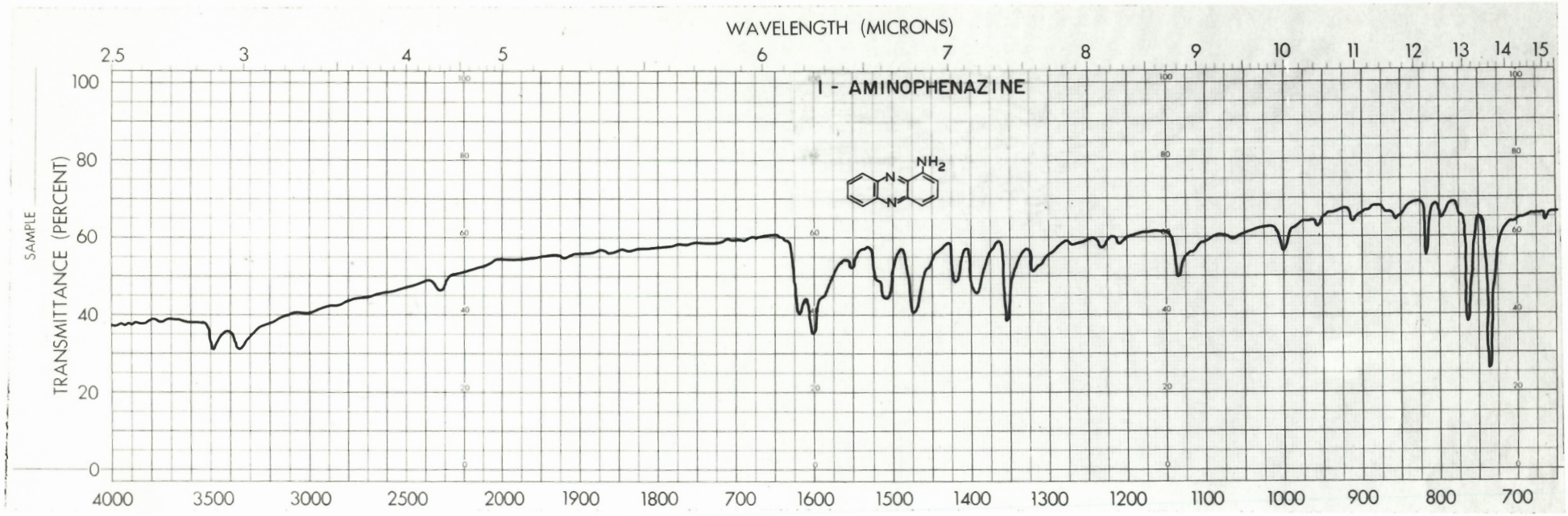
FIG. 13

Infrared Spectra of

1-Aminophenazine and

Phenazine-1-carboxylic acid

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5
3
4
5
6
7
8
9
10
11
12
13
14
15
1 - AMINOPHENAZINE
NH2
SAMPLE
TRANSMITTANCE (PERCENT)
100
80
60
40
20
0
4000
3500
3000
2500
2000
1900
1800
700
1600
1500
1400
1300
1200
1100
1000
900
800
700

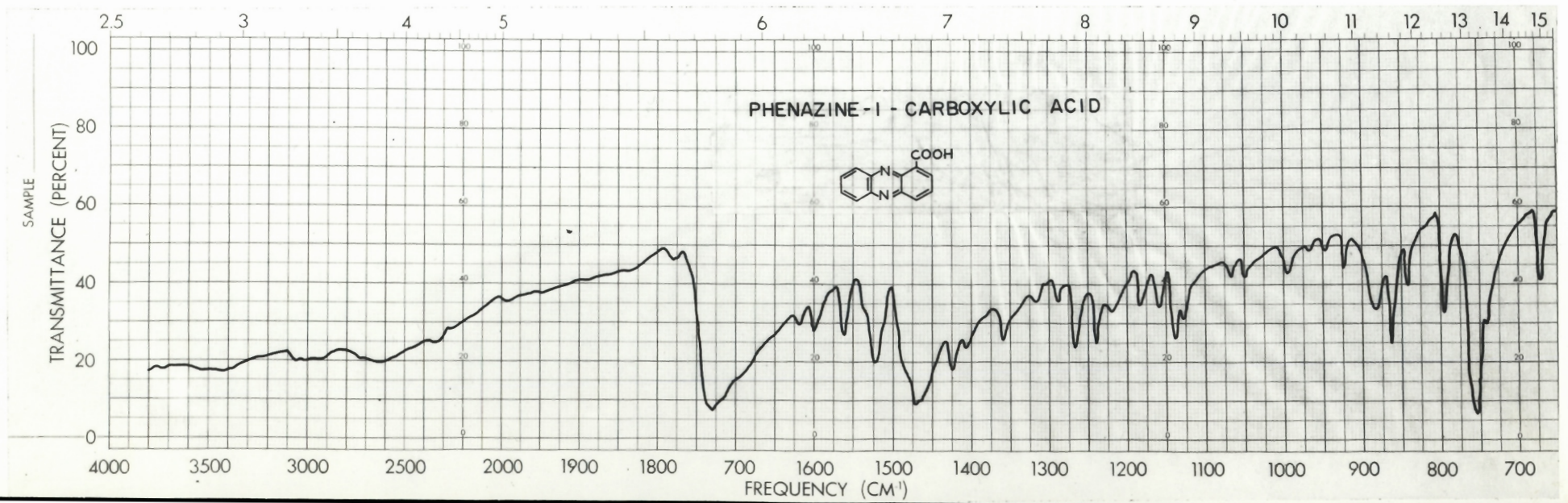

2.5
3
4
5
6
7
8
9
10
11
12
13
14
15
PHENAZINE-1-CARBOXYLIC ACID
COOH
SAMPLE
TRANSMITTANCE (PERCENT)
100
80
60
40
20
0
4000
3500
3000
2500
2000
1900
1800
700
1600
1500
1400
1300
1200
1100
1000
900
800
700
FREQUENCY (CM-1)

FIG. 14

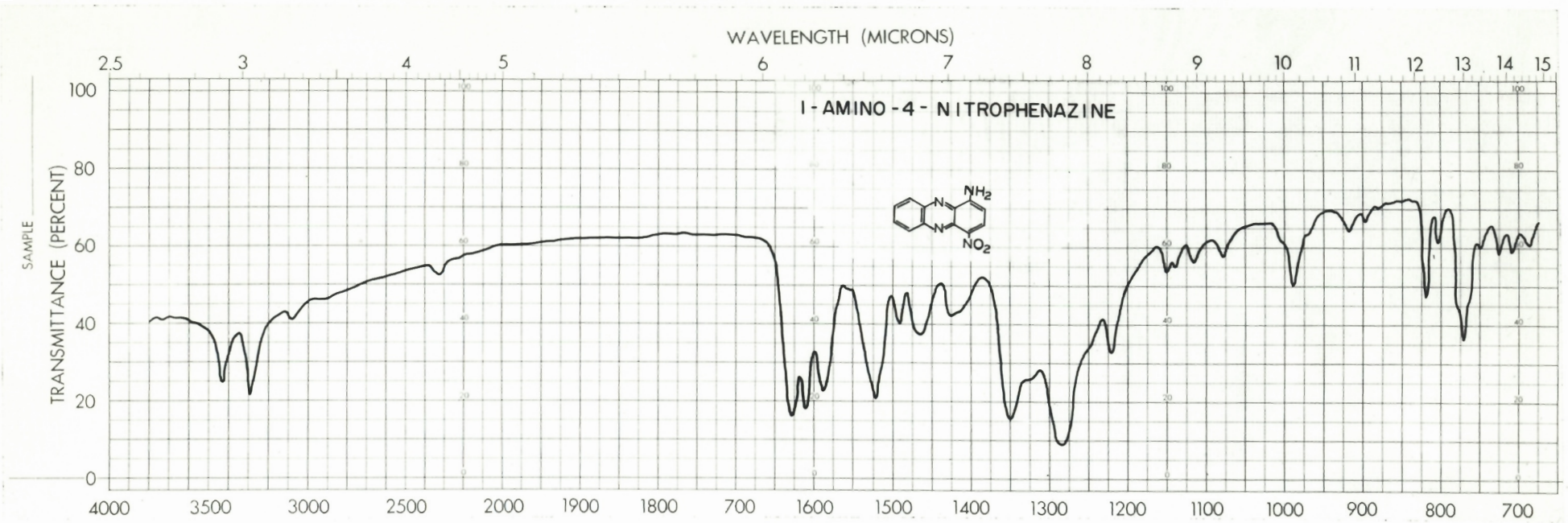
Infrared Spectra of

1-Amino-4-nitrophenazine

and

1-Hydroxy-4-nitrophenazine
Ammonium Salt

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
I - AMINO - 4 - NITROPHENAZINE
NH2
NO2
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

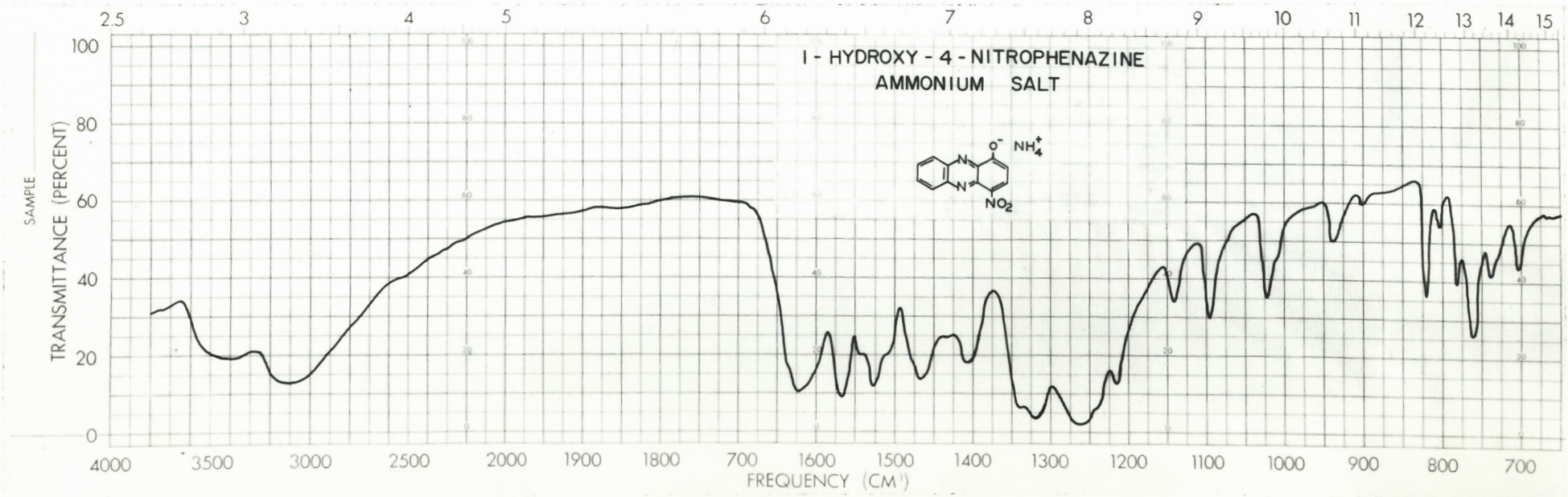

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
I - HYDROXY - 4 - NITROPHENAZINE
AMMONIUM SALT
O⁻ NH4⁺
NO2
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM⁻¹)

FIG. 15

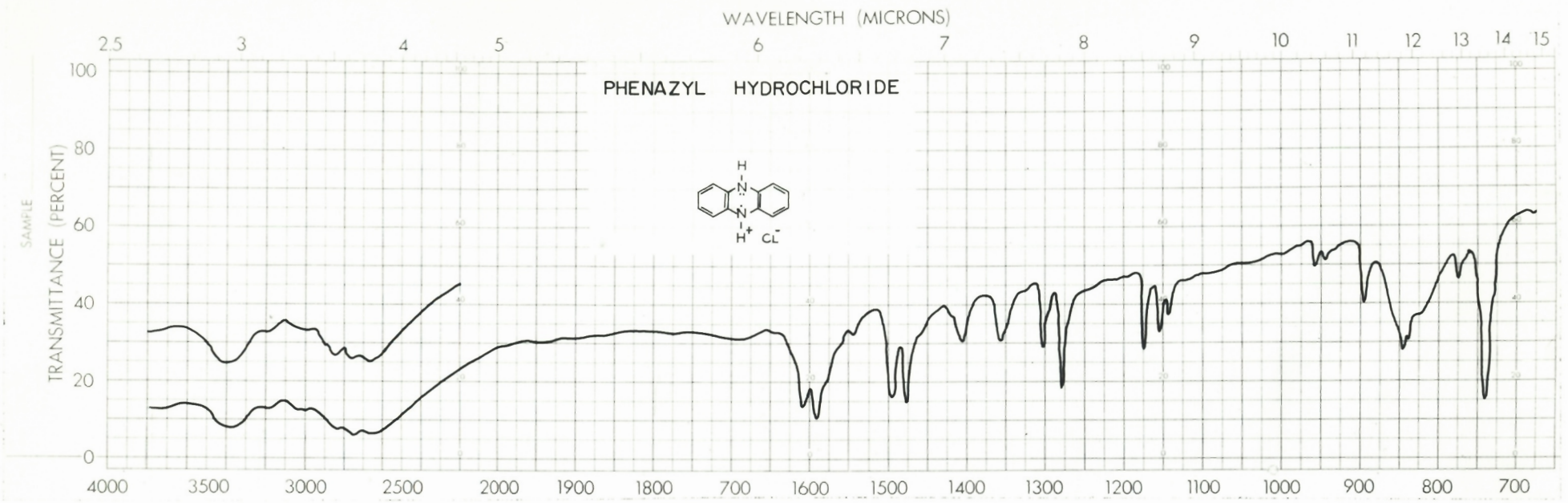
Infrared Spectra of

Phenazyl Hydrochloride

and

4-Nitro-1(5H)-phenazinone

solid in potassium bromide pellet


WAVELENGTH (MICRONS)
2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
PHENAZYL HYDROCHLORIDE
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700

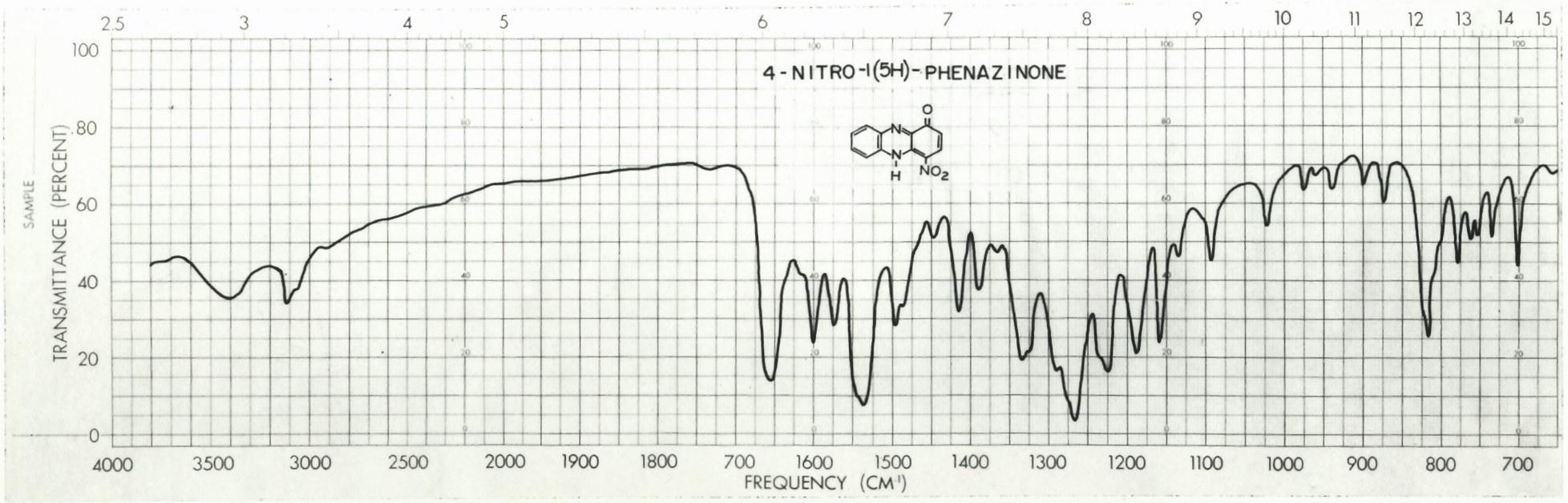

2.5 3 4 5 6 7 8 9 10 11 12 13 14 15
4-NITRO-1(5H)-PHENAZINONE
SAMPLE
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
4000 3500 3000 2500 2000 1900 1800 700 1600 1500 1400 1300 1200 1100 1000 900 800 700
FREQUENCY (CM⁻¹)

FIG. 16

Electronic Absorption Spectra of

4-Nitro-1(5H)-phenazinone

solution in water

(4.15×10^{-5} mole/litre)

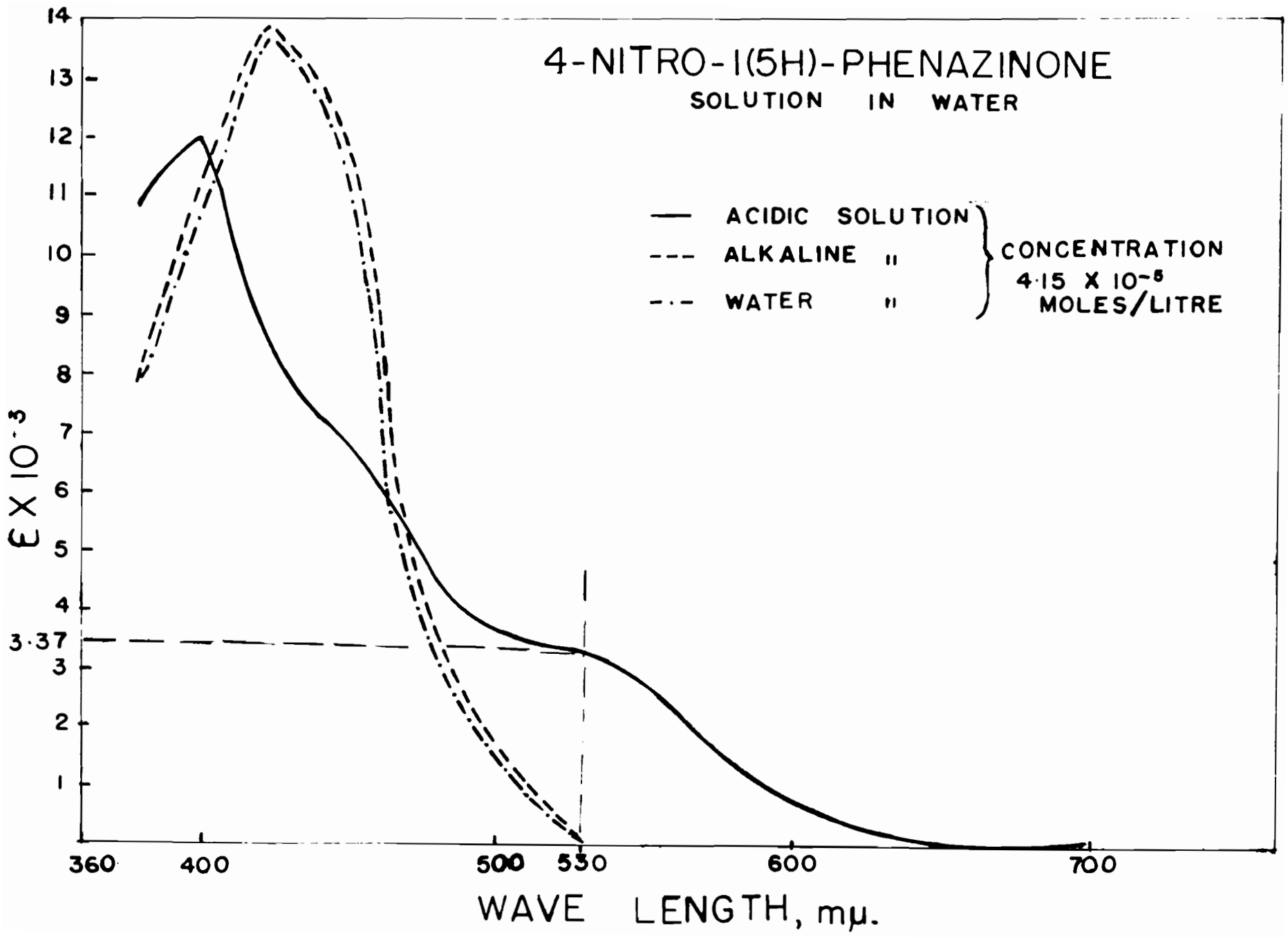

4-NITRO-1(5H)-PHENAZINONE
SOLUTION IN WATER
ACIDIC SOLUTION
ALKALINE "
WATER "
CONCENTRATION
4·15 X 10⁻⁵
MOLES/LITRE
ε X 10⁻³
14
13
12
11
10
9
8
7
6
5
4
3·37
3
2
1
360
400
500
530
600
700
WAVE LENGTH, mμ.

FIG. 17

Apparatus for Preparation of Phenazine

APPARATUS FOR PREPARATION OF PHENAZINE

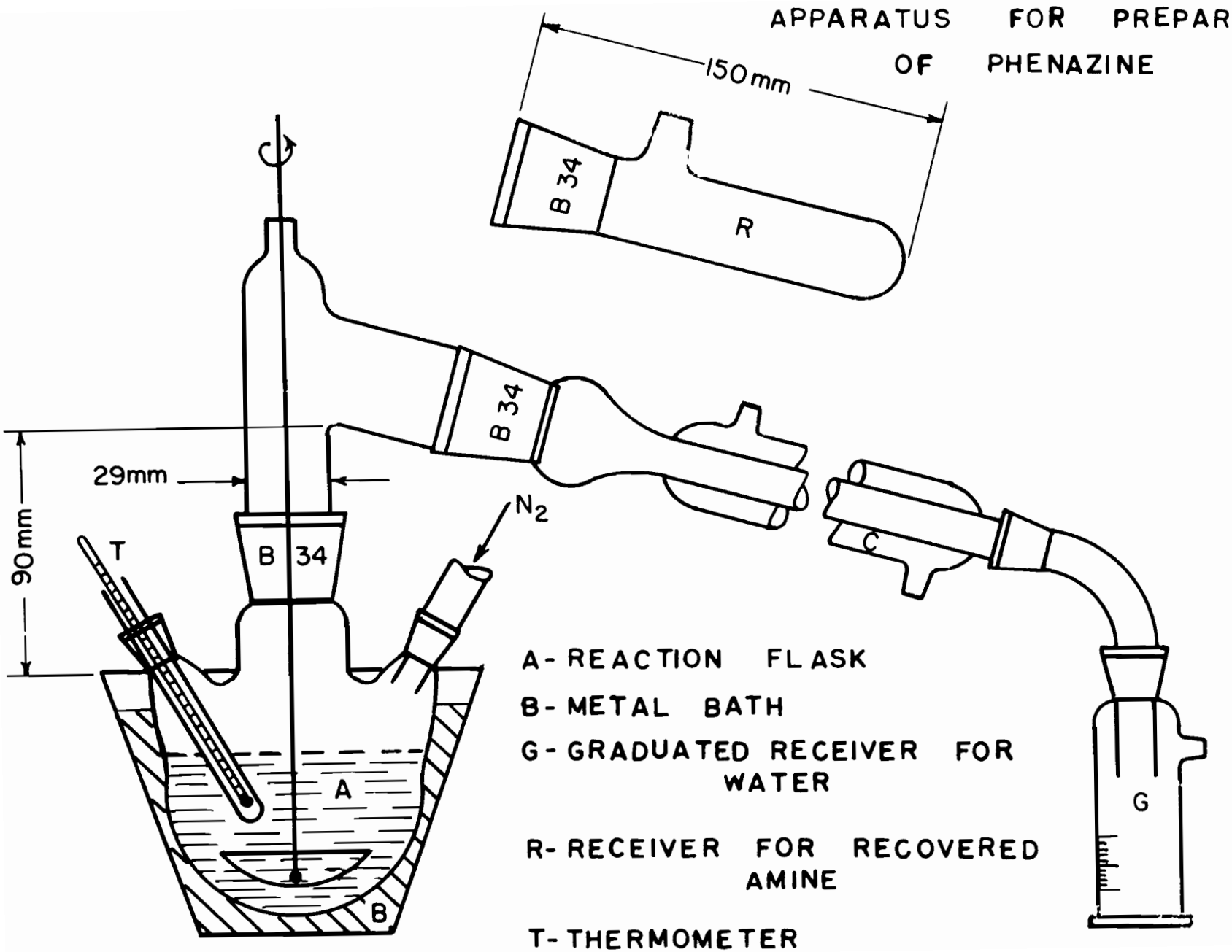
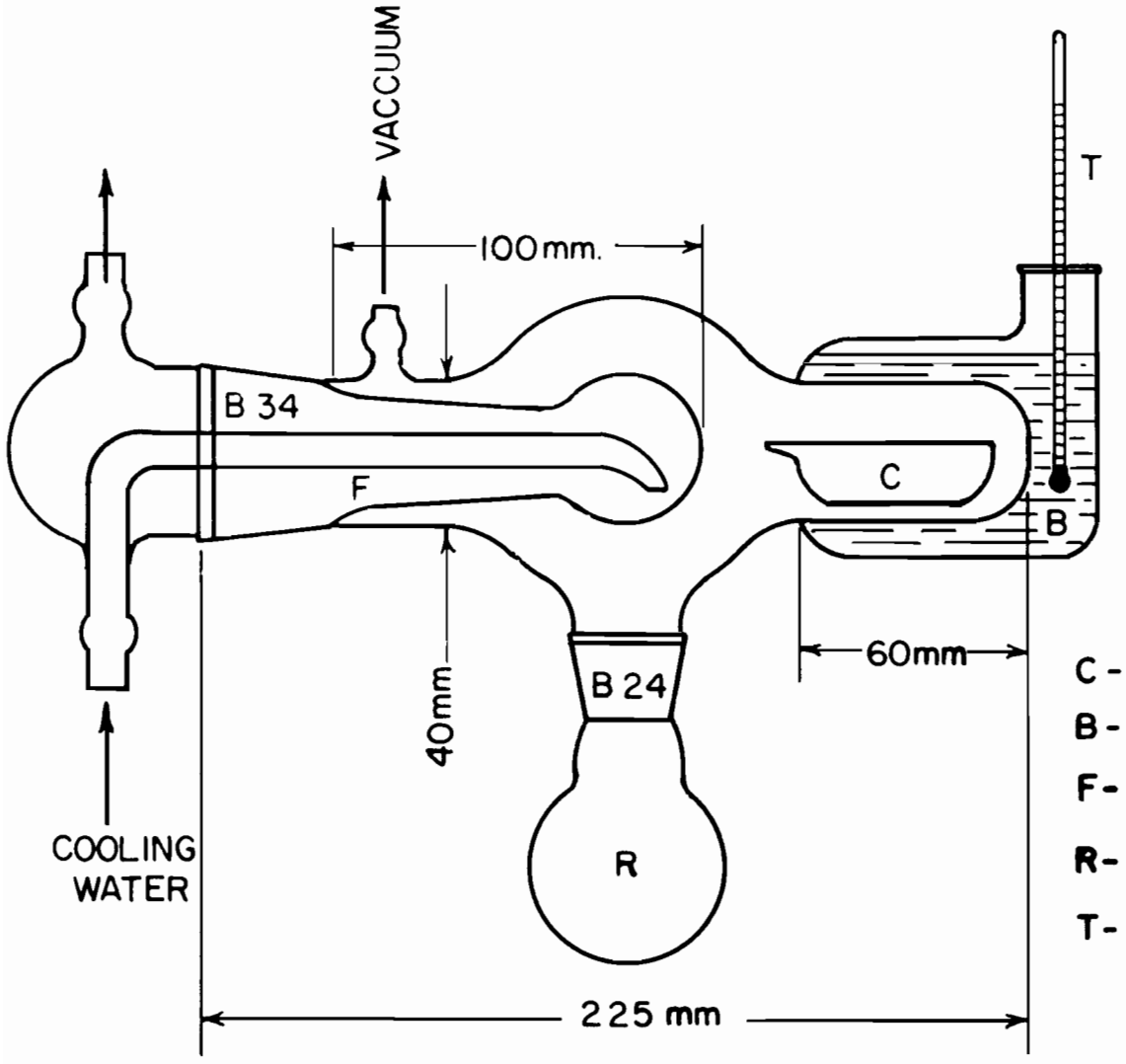


FIG. 18

Sublimation Apparatus

SUBLIMATION APPARATUS



C - SAMPLE BOAT

B - OIL BATH

F - COOLING FINGER

R - SUBLIMATE RECEIVER

T - THERMOMETER

EXPERIMENTAL

All melting points reported in this work are uncorrected and were determined in a Gallenkamp Melting Point Apparatus. The analyses were carried out in the C. Daessle laboratory, Montreal, Canada. The alumina used for chromatography was Aluminum Oxide Woelm, neutral for chromatography.

5,10-Dihydrophenazine

Catechol (38.5 g; m.p. 103-104°) and o-phenylenediamine (58 g; m.p. 101-103°) were melted together and poured into a reaction flask, which was then placed in the set-up shown (Fig. 17). The mixture was stirred vigorously and heated gradually to 240° while a stream of nitrogen, 40 ml per minute, was passed through the flask. The water formed in the reaction was collected in the graduated receiver. The gradual rise in temperature and the volume of water measured each hour is recorded (Table 13):

TABLE 13

Time, hours	Temperature, °C	Water formed, ml	Percentage of reaction completed, %
1	242	1.45	11.5
2	242	3.20	25.4
3	244	4.50	35.7
4	247	5.80	46.0
5	248	6.65	52.8
6	253	7.70	61.1
7	260	8.80	69.8
8	261	9.65	76.6
9	264	10.25	81.3
10	268	11.00	87.3
11	270	11.40	90.5
12	270	11.75	93.3

After 12 hours the temperature had risen to 270° and 11.75 ml of water had collected in the receiver (theoretical amount 12.6 ml). The water condenser was replaced by an air condenser and the receiver was changed. The excess o-phenylenediamine was distilled at temperatures from 270 to 320°. The distillation required 1/2 hour and 19.5 g of o-phenylenediamine was recovered. The recovered diamine could be used in the next preparation. The dark brown viscous residue was air-cooled with stirring in a nitrogen atmosphere. The yield of crude 5,10-dihydrophenazine, a greenish-gray crystalline substance, was 64.5 g.

Oxidation of 5,10-Dihydrophenazine

The crude condensation product (64.5 g) was ground finely, suspended in water (4 l), heated to 60° with stirring, and filtered hot. The solid substance on the filter was washed with water until the filtrate was colourless. The wet cake of 5,10-dihydrophenazine was suspended in 1.5 l of a 2.5% sodium hydroxide solution in a 3 l flask. The contents of the flask were stirred and boiled slowly while a stream of air was bubbled through the reaction mixture. The progress of the oxidation was checked by testing samples of the reaction mixture with dilute hydrochloric acid. The oxidation which was complete when the colour of the test solution turned from green to yellow, was finished within 20 hours. The reaction mixture was cooled and the solid material was filtered and washed thoroughly with water. The crude phenazine (57.0 g) was obtained in the form of a dark green microcrystalline mass.

Crude phenazine (10 g) was mixed with reduced iron powder (20 g) and sublimed in the specially designed apparatus (Fig. 18) under reduced pressure (12-15 mm) at 145°-150°. In this way pure phenazine (7.1 g) was obtained as long yellow needles, m.p. 170-171°. The over-all yield of the product from catechol was 64%.

1-Methylphenazine

In a similar way o-phenylenediamine (53.1 g; m.p. 101-103°) and 3-methylcatechol (38.0 g; m.p. 61-62°) were condensed to 1-methyl-5, 10-dihydrophenazine. The temperature of the reacting mass rose from 234° to 275° over a period of 9-1/2 hours. The excess o-phenylene-diamine (20 g) was distilled off in 1/2 hour by slowly raising the temperature above 275°. The progress of the condensation is outlined in Table 14.

TABLE 14

Time, hours	Temperature, °C	Water formed, ml	Percentage of reaction completed %
1	234	2.90	26.3
2	253	4.60	41.7
3	255	5.40	49.0
4	262	6.50	59.0
5	267	7.30	66.2
6	270	8.00	72.6
7	271	8.45	76.7
8	273	8.75	79.4
9	275	9.20	83.5
9-1/2	275	9.30	84.4

The yield of crude condensation product was 58.7 g. This was washed with water (4 l) at 50° and dried to give 55.5 g of material.

When 5 g of the latter, suspended in a 2.5% sodium hydroxide solution, was oxidized by air as described in the preparation of phenazine, 4.0 g of crude 1-methylphenazine was obtained. A mixture of the crude material sublimed in vacuo (1 mm pressure) with five times its weight of iron filings (Mallinckrodt, 40 Mesh) at 80-90° yielded 3.04 g of 1-methylphenazine, m.p. 103-5° (55% yield based on 3-methylcatechol).

2-Methylphenazine

The condensation of 4-methylcatechol (38.0 g; m.p. 61-62°) with o-phenylenediamine (53.1 g) was carried out as in the case of phenazine. When the condensation was complete the excess o-phenylenediamine was washed out with water (5 l) at 50° and 56.0 g of the crude dihydrophenazine was obtained.

This material (20.0 g) was suspended in a 2.5% sodium hydroxide solution (200 ml) and was oxidized by bubbling air through it for 72 hours at a temperature of about 50°. The crude 2-methylphenazine obtained (17 g) was purified by stirring it with 1400 ml of hydrochloric acid (1 volume of concentrated hydrochloric acid diluted with 9 volumes of water) for 1 hour at room temperature. The undissolved tarry residue was filtered off and washed with the same acid. The combined filtrates were made alkaline by adding an excess of dilute ammonia, with external cooling. The product precipitated in fine, yellow needles. After drying 16.0 g of

2-methylphenazine (63%), m.p. 108-111° was obtained.

2-t.-Butylphenazine

The condensation of 4-t.-butylcatechol (50.87 g; m.p. 58° obtained from Aldrich Co., U.S.A.) with o-phenylenediamine (53.1 g) was completed within 7-1/2 hours. The splitting off of water started at 205°. The temperature was increased gradually to 278°. Other reaction conditions were similar to those used in the previously described syntheses.

The crude condensation product (91.0 g, including the excess o-phenylenediamine) obtained, was crushed to a fine powder and suspended in cool water. Hot water was added gradually with stirring in such a way as to obtain a final volume of about 3 l and a temperature of 45°. The brown coloured suspension which resulted was filtered and the solid crystalline mass on the filter was washed with water (45°) until the filtrate was colourless. The wet cake was dried in vacuo. On exposure to air the wet product became oily, probably due to partial oxidation. The crude dihydrophenazine was obtained in a yield of 69.0 g.

Five grams of the condensation product was suspended in 2.5% sodium hydroxide solution (125 ml) and oxidized, in the usual manner, in a stream of air over a period of 20 hours on the steam-bath. The product obtained formed an oil, which solidified to a brown crystalline mass melting between 70° and 80°. In this way 4.4 g of crude 2-t.-butylphenazine was obtained. In order to purify, the product was stirred for 1 hour with 10% hydrochloric acid (520 ml) at room temperature and filtered. The

yellow filtrate was poured onto 500 g of ice and concentrated ammonia was added dropwise with stirring until precipitation ceased. At this stage the liquid was still slightly acidic. The fine, lemon yellow needles, which precipitated out of solution were filtered and dried. A first batch of 3.08 g of 2-t.-butylphenazine, m.p. 82-84° was obtained. The residue left after extraction of the main part of the phenazine, was ground with the 10% hydrochloric acid (130 ml) and treated in the same way as the major portion. Another 0.79 g of a product with m.p. 79-82° was recovered. The over-all yield based on t.-butylcatechol was 73%.

Preparation and Purification of 2-Aminophenazine

2-Aminophenazine was prepared by condensation of o-nitroaniline with aniline hydrochloride in the presence of fused zinc chloride as described by Wohl and Lange (53). The product which was separated by sublimation in a vertical sublimation apparatus was purified by repeated sublimation in the apparatus shown in Fig. 18.

The 2-aminophenazine obtained in the form of red needles with a bronze lustre melted sharply at 279° (sublimed) and was identified with the product of zinc dust distillation of 2,3-diaminophenazine (8) by a mixed melting point determination and infrared analysis.

ν_{max}^{KBr} 3390, 3310, 3200 cm^{-1} (NH_2); 855, 825, 760, 735 cm^{-1}.

2-N-Acetylaminophenazine

2-Aminophenazine (200 mg, m.p. 279°) was suspended in 2 ml of glacial acetic acid and acetic anhydride (1 ml) was added. The suspension was left at room temperature for 24 hours with occasional shaking. The amine dissolved gradually and a clear brown solution resulted. This was diluted with 5 ml of water and left for 3 hours at room temperature. The yellow crystalline solid which precipitated was recrystallized from 7 ml of hot ethanol and dried. The 2-N-acetylaminophenazine melted at 236°.

ν_{max}^{KBr} 3300 cm^{-1} (N-H); 1700, 1675 cm^{-1} (C=O);
875, 860, 830, 755 cm^{-1}.

2,3-Diaminophenazine (56)

2,3-Diaminophenazine was prepared by oxidation of o-phenylene-diamine with iodine. The amine purified by crystallization from water-dimethylformamide. was obtained in 80% yield.

ν_{max}^{KBr} 3430, 3300, 3160 cm^{-1} (NH_2); 890 cm^{-1}, 765, 740 cm^{-1}.

2,3-Diaminophenazine on distillation with zinc dust yielded 2-aminophenazine (8).

Preparation of 2-Nitrimino-(10H)phenazinium Betaine (2-Nitraminophenazine)

(a) Nitration with 10% excess of nitric acid

2-Aminophenazine (200 mg; m.p. 279°) purified by repeated sublimation, was powdered and dissolved in 2 ml of concentrated sulphuric acid. The brown solution was cooled to -50° in a dry ice-acetone bath and formed a thick paste. Nitric acid (0.073 ml; sp.gr. 1.42, 70% nitric acid) was added at once and the reaction mixture was stirred for 1-2 minutes until it changed to an orange liquid. The temperature rose to about -20°. Then the solution was poured onto 12.5 g of crushed ice, and stirred until the ice melted. The orange precipitate which formed was filtered quickly with suction. The wet cake was suspended in 100 ml of water and caused to go into solution by the addition of 16 drops of concentrated ammonia. The final pH of the solution was 8.0. It was filtered through a sintered glass plate and heated to 50°. On addition

of 20 drops of aqueous acetic acid (1:1) to the filtrate, the 2-nitrimino-(10H)phenazinium betaine precipitated in fine yellow needles.

After 24 hours drying in vacuo at room temperature, the product (243 mg) was shown by its infrared spectrum to consist mainly of the monohydrate of 2-nitrimino-(10H)phenazinium betaine. On prolonged drying in vacuo at room temperature the amount of the anhydrous form in the product increased. This was indicated by changes in the infrared spectrum.

(b) Nitration with 66% excess of nitric acid

2-Aminophenazine (200 mg), purified as in (a), was powdered and dissolved in 2 ml of concentrated sulphuric acid. The solution was cooled to -50° in a dry ice-acetone bath and 0.108 ml of nitric acid (sp.gr. 1.42) was added at once.

The reaction mass was then stirred for 1-2 minutes until an orange liquid was obtained (the temperature did not rise above -15°). The liquid was poured onto 12.5 g of crushed ice. The orange precipitate which formed was filtered off with suction, suspended in 100 ml of water, dissolved by the addition of 16 drops of concentrated ammonia and re-precipitated by the addition of 20 drops of aqueous acetic acid (1:1) at 50°. After drying in vacuo for 24 hours, 0.237 mg of 2-nitrimino-(10H) phenazinium betaine was obtained, mainly in its monohydrate form.

2-Nitrimino-(10H)phenazinium Betaine Monohydrate (pure)

The 2-nitrimino-(10H)phenazinium betaine (100 mg) obtained by procedures (a) or (b), consisting mainly of the monohydrate form, was dissolved in 200 ml of water and 6 drops of ammonia at 75°. The hot solution was acidified with 15 drops of aqueous acetic acid (1:2). 2-Nitrimino-(10H)phenazinium betaine monohydrate (98 mg, m.p. 150°-160° (explodes)) crystallized on gradual cooling in the form of golden needles.

ν_{max}^{KBr} 3540, 3400, 3200 cm^{-1} (O-H from water); 2700 cm^{-1} (NH); 1515, 1315, 1300 cm^{-1} (NO_2); 880, 835, 820, 765, 755, 745 cm^{-1}.

Anal. Calc. for $C_{12}H_8N_4O_2 \cdot H_2O$: C, 55.80; H, 3.95.
Found: C, 55.22; H, 4.16%.

2-Nitrimino-(10H)phenazinium Betaine Anhydrous

2-Nitrimino-(10H)phenazinium betaine monohydrate (100 mg) was ground and suspended in 50 ml of dry benzene. The suspension was heated to 50° for 2 hours with occasional swirling of the flask. Then approximately 35 ml of the benzene was distilled off under reduced pressure at a temperature not exceeding 50°. The solid anhydrous 2-nitrimino-(10H) phenazinium betaine (60 mg; decomposed at 150-160°) was filtered off and dried *in vacuo*.

ν_{max}^{KBr} 3100 to 2700 cm^{-1} ($\overset{+}{N}$-H); 1510, 1320, 1295 cm^{-1} (NO_2); 880, 855, 830, 820, 790, 765, 750, 740 cm^{-1}.

Anal. Calc. for $C_{12}H_8N_4O_2$: C, 59.98; H, 3.36; N, 23.33.
Found: C, 59.56; H, 3.40; N, 23.35%.

2-Nitrimino-(10H)phenazinium Betaine Monohydrate from the Anhydrous Form

Anhydrous 2-nitrimino-(10H)phenazinium betaine (100 mg) was dissolved in 100 ml of water and 4 drops of ammonia. The orange liquid was heated to 70° and acidified to pH = 5.0 by the addition of 22 drops of hot aqueous acetic acid (1:1). The liquid became reddish brown and upon slow cooling golden needles precipitated. These were filtered and dried in vacuo (106 mg). The identity of the 2-nitrimino-(10H)phenazinium betaine monohydrate obtained with the product prepared previously was demonstrated by its infrared spectrum.

The Sodium, Potassium and Ammonium Salts of 2-Nitraminophenazine

(a) Sodium Salt

2-Nitraminophenazine (100 mg) was dissolved in 15 ml of water to which 3 drops of 5% sodium hydroxide had been added. The orange liquid obtained was mixed at 60° with a solution of 2 g of sodium acetate in 15 ml of water and left overnight in a refrigerator. The sodium salt (90 mg) precipitated and was isolated in the form of a bright yellow crystalline powder. The same salt was obtained from solutions of 2-nitraminophenazine in aqueous concentrated sodium hydroxide or sodium sulphate.

ν_{max}^{KBr} 3340, 3240, 3140 cm^{-1} (H_2O); 1515, 1360, 1330 cm^{-1} (NO_2^-); 885, 835, 815, 750, 735 cm^{-1}.

Anal. Calc. for $C_{12}H_7N_4O_2Na.\ 2H_2O$: C, 48.30; H, 3.70; N, 18.80
Found: C, 46.11; H, 3.92; N, 18.95%.

(b) Potassium Salt

The potassium salt was obtained in the same manner by treating a solution of 2-nitraminophenazine (100 mg) in 15 ml of water and 3 drops of 5% potassium hydroxide, with a solution of 2 g of potassium acetate in 15 ml of water. The potassium salt was obtained in the form of yellow crystals (50 mg) which were readily soluble in water.

ν_{max}^{KBr} 3400 cm^{-1} (H_2O); 1365, 1355, 1320 cm^{-1} (NO_2^-); 870, 835, 825, 765, 755, 735 cm^{-1}.

Anal. Calc. for $C_{12}H_7N_4O_2K.H_2O$: C, 48.63; H, 3.06; N, 18.91.
Found: C, 46.60; H, 3.07; N, 19.07%.

(c) Ammonium Salt

The ammonium salt was obtained similarly by adding a solution of 2 g of ammonium acetate to a solution of 2-nitraminophenazine (100 mg) in 15 ml of water and 3 drops of dilute ammonia. The yellow salt (50 mg) isolated was readily soluble in water.

ν_{max}^{KBr} 3150, 3020, 2880 cm^{-1} (NH_4^+); 1510, 1345, 1325 cm^{-1} (NO_2^-); 875, 835, 820, 750, 735 cm^{-1}.

Anal. Calc. for $C_{12}H_7N_4O_2 \cdot NH_4$: C, 56.02; H, 4.31; N, 27.23.
Found: C, 55.31; H, 3.90; N, 26.89%.

Rearrangement of 2-Nitrimino-(10H)phenazinium Betaine

(a) Two hour reaction

2-Nitrimino-(10H)phenazinium betaine (500 mg) from nitration with a 66% excess of nitric acid was added gradually to 5 ml of concentrated sulphuric acid which had been cooled to -40° in a dry ice-acetone bath. The thick paste was stirred continuously. When the substance had dissolved, the viscous brown liquid obtained was kept in an ice-water bath for 2 hours. Then it was poured into 200 ml of ice water and allowed to stand until all the ice melted. The precipitate which formed was filtered and extracted with dilute ammonia (20 ml). The undissolved solid was filtered off (80 mg) leaving a clear orange filtrate which when acidified with acetic acid at 50° gave 20 mg of a yellow crystalline mass identified by its infrared spectrum as unchanged 2-nitrimino-(10H)phenazinium betaine. The brown filtrate from the first filtration when neutralized with ammonia at 60° gave 300 mg of a yellow precipitate the infrared spectrum of which was identical with that of 2-amino-1-nitrophenazine.

(b) Three hour reaction

2-Nitrimino-(10H)phenazinium betaine (500 mg) was added gradually to 5 ml of concentrated sulphuric acid which had been cooled to -40° in a dry ice-acetone bath. The thick paste was stirred continuously. When all

the substance had dissolved the viscous brown liquid which resulted was kept in an ice-water bath for 3 hours. The reaction mixture was diluted with 200 ml of ice water and the precipitate (90 mg) formed was filtered. On extraction of the precipitate with dilute ammonia no unchanged starting material was obtained. The brown acidic filtrate, on being heated to 60° and neutralized with ammonia gave 390 mg of a yellow-green substance which was identified by infrared analysis as crude 2-amino-1-nitrophenazine.

When the procedure was repeated starting from 1.5 g of 2-amino phenazine, 1.77 g of 2-nitrimino-(10H)phenazinium betaine was obtained, which on rearrangement gave 275 mg of an acid-insoluble product and 1.21 of crude 2-amino-1-nitrophenazine.

The crude 2-amino-1-nitrophenazine (400 mg) dissolved in 500 ml of chloroform (A.C.S.) was transferred to a chromatographic column packed with 90 g of alumina (activity grade I) in chloroform. Elution with methanol-chloroform (1:21) provided 341 mg of 2-amino-1-nitrophenazine, yellow needles, m.p. 264-5°, soluble in dilute acids, and subliming at temperatures over 200°.

ν_{max}^{KBr} 3430, 3290, 3170 cm^{-1} (NH_2); 1520, 1280 cm^{-1} (NO_2); 845, 835, 802, 795, 770, 755, 740 cm^{-1}.

Anal. Calc. for $C_{12}H_8O_2N_4$: C, 60.00; H, 3.40; N, 23.30.

Found: C, 60.25; H, 3.43; N, 23.53%.

(c) <u>In the nitration mixture</u>

2-Aminophenazine (200 mg) was dissolved in 2 ml of concentrated

sulphuric acid and the solution, on cooling in a dry ice-acetone bath (-40°), solidified to a thick paste. Nitric acid (0.073 ml, sp.gr. 1.42) was added to it at once. The reaction mass was stirred until an orange liquid was formed. The latter was left in an ice bath for 3 hours. After dilution with 40 ml of ice-water, 44 mg of a precipitate was filtered off. This material did not contain any ammonia-soluble compounds (i.e. no unchanged 2-nitraminophenazine left). The orange-brown filtrate when neutralized with ammonia gave 147 mg of a greenish-yellow precipitate the infrared spectrum of which indicated that the substance was 2-amino-1-nitrophenazine.

Oxidation of 2-Amino-1-nitrophenazine

To 2-amino-1-nitrophenazine (200 mg) purified by sublimation was added 3.5 ml of 10% hydrochloric acid. The mixture was heated on a steam-bath with stirring then rendered alkaline by the addition of a 40% sodium hydroxide solution. Potassium permanganate (0.9 g) dissolved in 13.5 ml of water and heated to 80-90° was added with stirring over a period of 45 minutes to the alkaline slurry which was being heated on the steam-bath. The initial orange colour of the reaction mixture changed gradually to dark brown. Test samples examined under the microscope showed a decreasing amount of the solid yellow unreacted starting material as the reaction progressed. After 7 hours heating on the steam-bath with stirring the hot slurry was filtered. The filtrate was acidified with an excess of concentrated hydrochloric acid and allowed to stand for 2 days in the refrigerator. An orange crystalline mass (82 mg) was formed, which on

being recrystallized from dilute hydrochloric acid gave almost colourless crystals (60 mg). The infrared spectrum of this product was found to be identical with the spectrum of quinoxaline-2,3-dicarboxylic acid prepared by the oxidation of phenazine (70) (m.p. 190°).

ν_{max}^{KBr} 3480 cm^{-1} (O-H); 1690 cm^{-1} (C=O);
1325, 1005, 840, 788, 770 cm^{-1}.

Reduction of 2-Amino-1-nitrophenazine with Zinc and Acetic Acid

A suspension of 2-amino-1-nitrophenazine (50 mg, purified by chromatography) in 9 ml of glacial acetic acid was prepared by grinding the substance with the acid in a mortar. To this 1.5 ml of water and then zinc powder (excess) in three small portions at 30° were added. The reaction mixture was shaken vigorously. The yellow suspension became orange-brown after a while and formed a clear solution with the excess zinc as the only solid present. The reaction mixture was filtered quickly with suction, washed with 8 ml of water and made alkaline by the gradual addition of 50 ml of concentrated ammonia. The liquid turned red-violet in colour and soon fine red-brown needles with a bronze lustre were deposited from solution.

The mixture was left for 3 hours in a refrigerator then was filtered and dried *in vacuo*. The crude product (41 mg) was sublimed twice *in vacuo* (1 mm) at 130-135°; the second time using the horizontal type of sublimation apparatus (Fig. 18). The pure 1,2-diaminophenazine was obtained

in the form of fine violet-red needles, m.p. 189-191° (in a closed m.p. tube).

ν_{max}^{KBr} 3390, 3300, 3170 cm^{-1} (NH_2);
825, 785, 755 cm^{-1}.

Anal. Calc. for $C_{12}H_{10}N_4$: N, 26.64.
Found: N, 26.68%.

Catalytic Reduction of 2-Amino-1-nitrophenazine

2-Amino-1-nitrophenazine (17 mg, purified by chromatography) was suspended in 5 ml of methanol and reduced with hydrogen in the presence of Adam's catalyst (14 mg of PtO_2). During the process the suspended particles dissolved and changes in colour from brown to purple red to nearly colourless were observed. The colourless solution on exposure to air became purple red again and after evaporation of the solvent 13 mg of reddish-brown solid was obtained. This crude product when sublimed gave a purple-red crystalline sublimate which was identified by its melting point and infrared spectrum as 1,2-diaminophenazine.

Reaction of 2-Amino-1-nitrophenazine with Aqueous Sodium Hydroxide

2-Amino-1-nitrophenazine (50 mg, purified by chromatography) was refluxed with 25 ml of 0.8% sodium hydroxide solution. After 40 minutes the solid dissolved yielding an orange solution. The refluxing was continued for another hour. The hot solution containing a tiny amount

of a sand-like precipitate was filtered and treated with 3.7% hydrochloric acid at 60° dropwise until a pH of 2.0 was reached. A bright yellow crystalline mass precipitated immediately.

After standing overnight in a refrigerator the solid was filtered and washed with slightly acidified water. It was then dissolved in 20 ml of hot water to which 4 drops of concentrated ammonia had been added. The orange solution obtained was filtered hot and acidified to pH = 2.0 by the dropwise addition of 3.7% hydrochloric acid at 80°. Instantly, bright yellow needles precipitated. After standing overnight in the refrigerator the crystals were filtered and washed with water. The 2-hydroxy-1-nitrophenazine melted at 238°. The yield was 46 mg.

ν_{max}^{KBr} 3040 cm^{-1} (O-H); 1550, 1530, 1250 cm^{-1} (NO_2); 840, 802, 755 cm^{-1}.

Anal. Calc. for $C_{12}H_7N_3O_3$: C, 59.75; H, 2.93; N, 17.42.
Found: C, 59.67; H, 3.29; N, 17.49%.

Reaction of 2-Amino-1-nitrophenazine with Concentrated Hydrochloric Acid

2-Amino-1-nitrophenazine (22 mg, purified by chromatography) was dissolved in 15 ml of concentrated hydrochloric acid. The solution was refluxed for 24 hours, during which period the colour of the liquid changed from red to orange to deep brown. The reaction product was filtered and ammonia was added to the hot filtrate until the pH was 3.0. The yellow needles which precipitated were filtered off (6 mg) and identified

as starting material by infrared analysis. After 2 days standing at room temperature an orange crystalline substance precipitated from the filtrate. These needles melted at 223° and were identified by the infrared spectrum as 2-hydroxy-1-nitrophenazine.

ν_{max}^{KBr} 3040 cm^{-1} (O-H); 1550, 1530, 1250 cm^{-1} (NO_2); 840, 802, 755 cm^{-1}.

Attempted Diazotization of 2-Amino-1-nitrophenazine (139)

2-Amino-1-nitrophenazine (30 mg, chromatographed material) was dissolved by heating in 10 ml of glacial acetic acid and 1 ml of water. The clear yellow solution was poured into a solution of nitrous acid (prepared from 1 ml of 2N sodium nitrite solution, 10 g of crushed ice and 3 ml of concentrated hydrochloric acid), and shaken vigorously until all the ice melted. No colour change in the reaction mixture was observed. The excess of nitrous acid was decomposed by the addition of urea. Then ammonia was added to the clear yellow solution until the pH was 5.0. A yellow crystalline mass separated (15 mg) which was identified as unchanged 2-amino-1-nitrophenazine by its infrared spectrum. When the filtrate was rendered alkaline with ammonia a further amount of the starting material was recovered.

Diazotization of 2-Aminophenazine

2-Aminophenazine (50 mg) was diazotized by the method described above. The deep red colour of the 2-aminophenazine hydrochloride solution

changed instantly to an orange colour indicating the formation of the diazonium salt. The latter coupled with an alkaline α-naphthol solution (20 ml; 1.2 g of α-naphthol dissolved in 150 ml of a 2.5% sodium hydroxide solution and 22 g of anhydrous sodium carbonate) at 0° to give a brown-red pigment.

2-N-Methylaminophenazine

Methylaniline hydrochloride (1.45 g, prepared by saturating a benzene solution of the amine with hydrogen chloride gas) and o-nitroaniline (1.40 g, recrystallized from 50% ethanol) were mixed together in a pyrex tube (200 x 25 mm) and heated in an oil bath. The mass melted between 80 and 90°. At 135° fused zinc chloride (4.5 g) was added to the reacting mass and the temperature was raised to 170° over a period of 1/2 hour. A sudden and vigorous reaction followed with water and o-nitroaniline vapours being evolved. The reaction subsided in a few seconds, but the mixture was stirred at 170° for a further period of 25 minutes. Then 20 ml of hot water was added with care and stirring was continued until the mixture had cooled to room temperature. The water layer was decanted from the tarry reaction mass. The latter was washed twice with 3 ml of water and then was ground with 20 ml of 2% hydrochloric acid. The acidic extract was filtered, and the residue on the filter was washed with 0.5% hydrochloric acid. The combined filtrates, cooled by means of an ice bath, were made alkaline with 20 ml of 20% sodium hydroxide and a voluminous red-brown mass precipitated. This was allowed to stand overnight then the precipitate was filtered with

suction and was washed with water until the latter gave a neutral reaction. After drying 1.2 g of a brown powder was obtained. It was sublimed using a vertical type sublimation apparatus. When the sublimation was carried out at temperatures up to 120° under reduced pressure (water aspirator), unchanged o-nitroaniline, identified by its melting point and characteristic odour, was obtained. In vacuo, and with the temperature being gradually raised to 160°, an orange sublimate (0.35 g) was collected. For further purification several batches of this sublimate (1.20 g) were combined and resublimed in vacuo using the horizontal sublimation apparatus (Fig. 18). At a temperature of 125-130° a sublimate consisting of o-nitroaniline and an oily substance was obtained, and at a temperature of 150-160° a mixture of orange and deep red crystals (0.77 g) sublimed. The latter mixture (1.76 g) was taken up in 176 ml of chloroform and filtered leaving 0.16 g of residue which was identified as 2-aminophenazine. The filtrate was transferred to a chromatographic column packed with 450 g of alumina (activity grade I) in chloroform. Elution with chloroform led to the development of a brown band from which was obtained 1.43 g of a substance in the form of orange needles melting at 198-201°. Purification by sublimation provided 2-N-methylaminophenazine m.p. 199-201°.

ν_{max}^{KBr} 3260 cm^{-1} (N-H); 855, 815, 805, 755, 750, 735 cm^{-1}.

Anal. Calc. for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08

Found: C, 74.73; H, 5.64; N, 20.16%.

From the second brick-red band 90 mg of 2-aminophenazine was recovered.

2-N,N-Acetylmethylaminophenazine

2-N-Methylaminophenazine (100 mg, purified by chromatography) was dissolved in 0.5 ml of glacial acetic acid and 0.5 ml of acetic anhydride was added. The solution was left for 24 hours at room temperature during which time a colour change from red to orange was noted. It was diluted with 2 ml of water, and evaporated to dryness under reduced pressure. The residue was recrystallized from aqueous ethanol providing 2-N,N-acetylmethylaminophenazine (75 mg) as light yellow crystals m.p. 155°.

ν_{max}^{KBr} 2980, 2900 cm^{-1} (CH_3); 1665 cm^{-1} (C=O); 860, 830, 765, 760, 745 cm^{-1}.

Anal. Calc. for $C_{15}H_{13}N_3O$: N, 16.69

Found: N, 16.78%.

Nitration of 2-N-Methylaminophenazine

2-N-Methylaminophenazine (200 mg, purified by chromatography) was dissolved in 2 ml of concentrated sulphuric acid. The clear brown solution was cooled to -50° in an acetone-dry ice bath, at which temperature solidification to a paste occurred. Nitric acid (0.11 ml, sp.gr. 1.42) was added at once, and the mixture was stirred until a red liquid was obtained (10-20 seconds). The latter was poured onto 12.5 g of crushed ice. A brown solution and a small amount of a black amorphous material was obtained. The latter was removed by filtration. The filtrate was treated with ammonia at 0° until the pH was 3.0-4.0. A yellow-brown

mass precipitated, was filtered, washed with water until the wash water gave a neutral reaction and dried. The crude nitration product (200 mg) was purified by dissolving in chloroform (45 ml) and chromatographing on a column packed with 80 g of alumina (activity grade I) in chloroform. Elution with methanol-chloroform (1:20) and recrystallization from chloroform gave 162 mg of 2-methylamino-1-nitrophenazine m.p. 278-280° (sublimed). A sample sublimed *in vacuo* at a temperature above 200° was analyzed.

ν_{max}^{KBr} 3340 cm^{-1} (N-H); 2900 cm^{-1} (CH_3); 1515, 1265 cm^{-1} (NO_2); 830, 802, 800, 785, 760 cm^{-1}.

Anal. Calc. for $C_{13}H_{10}N_4O_2$: N, 22.04.

Found: N, 22.14%.

Reaction of 2-Methylamino-1-nitrophenazine with Aqueous Sodium Hydroxide

2-Methylamino-1-nitrophenazine (20 mg) purified by chromatography was heated under reflux with 10 ml of 1% sodium hydroxide solution for two hours. The vapours which escaped during the process had the characteristic odour of methylamine and turned a red litmus paper blue. A small amount of a yellow solid was filtered off, and the hot, clear, orange filtrate was acidified with an excess of 3.7% hydrochloric acid. After several hours standing in a refrigerator the yellow brown crystalline solid which precipitated was separated by filtration and dried *in vacuo*. The product (16 mg) was identified by its infrared spectrum and mixed melting point as 2-hydroxy-1-nitrophenazine.

1,3-Diaminophenazine (9)

1,3-Diaminophenazine was obtained (1.2 g of crude diamine from 1.0 g of the o-quinone) by the condensation of o-phenylenediamine with 3,5-diamino-o-benzoquinone (10). The latter was prepared in a yield of 12.0 g from 25.0 g of the starting diacetylcatechol. The crude condensation product precipitated from the reaction mixture on addition of ammonia and was purified by sublimation (75% recovery) using the apparatus shown in Fig. 18. The pure diamine melted at 276-278°.

ν_{max}^{KBr} 3420, 3300, 3200 cm^{-1} (NH_2); 855, 850, 835, 825, 760 cm^{-1}.

1-N-Acetylaminophenazine and 1-Aminophenazine (9)

The monoperchlorate of 2,3-diaminophenazine (3.0 g of the o-quinone yielded 3.9 g of 2,3-diaminophenazine monoperchlorate) was precipitated by the addition of perchloric acid directly to the reaction mixture obtained from condensation of 3,5-diamino-o-benzoquinone with o-phenylenediamine. The perchlorate was acetylated with acetic anhydride to 1-acetylamino-3-aminophenazine monoperchlorate (4.3 g). Treatment of the latter with nitrous acid and ethanol resulted in the elimination of the amino-group and 1-N-acetylaminophenazine m.p. 171-172° was obtained (0.33 g from 1.2 g of the 1-acetylamino-3-aminophenazine perchlorate).

ν_{max}^{KBr} 3370 cm^{-1} (N-H); 1685, 1675 cm^{-1} (C=O);
830, 780, 765, 760, 750 cm^{-1}.

The acetylamine (0.25 g) was hydrolyzed with 76% sulphuric acid to the free amine. On sublimation 1-aminophenazine (0.2 g) m.p. 174-176°, was obtained.

ν_{max}^{KBr} 3480, 3340 cm^{-1} (NH_2); 820, 765, 735 cm^{-1}.

1-Aminophenazine from 2,2'-Diaminodiphenylamine

(This procedure was developed for the preparation of the compound on a laboratory scale).

2,2'-Dinitrodiphenylamine (105) was prepared in an 84% yield by the condensation of o-nitroaniline with 1-bromo-2-nitrobenzene. It was found that if the condensation temperature was maintained at 200°, instead of 180° as reported, the condensation could be accomplished in a more reasonable time. It was also more convenient to follow the progress of the reaction by measuring the amount of water split off than by the amount of carbon dioxide evolved.

The reaction product was purified by steam distillation during which the volatile unchanged starting materials were removed. The residue, crude 2,2'-dinitrodiphenylamine (40 g), was dissolved in 600 ml of glacial acetic acid. Zinc powder (160 g) was added to this solution in small portions and with vigorous stirring. During the reduction process the temperature was kept between 15° and 20° by cooling with an acetone-dry ice bath. When the reaction mixture had become nearly colourless, it was diluted with water to a volume of 4 l and 15 g of charcoal was added. The mixture was filtered. The slightly brown filtrate was cooled and 1 l. of aqueous ammonia (1:3) was added with stirring. The temperature was kept

at 0°. Some tarry material which precipitated was removed by treatment with 15 g of charcoal and filtration. The filtrate was neutralized by adding solid sodium acetate (1500 g) in portions with stirring at 0°. After addition of the acetate, the slurry was stirred for another 2-1/2 hours, while the reaction mixture reached room temperature. The crude diamine crystallized in nearly colourless leaflets. It was filtered, washed with water and dried in vacuo. The 2,2'-diaminodiphenylamine (17.8 g), a slightly brown crystalline powder, melted at 85-90°.

The crude 2,2'-diaminodiphenylamine (20 g), obtained by the procedure above, was heated and stirred with 200 ml of redistilled technical nitrobenzene. A stream of nitrogen (3 bubbles per second) was passed through the reaction vessel during the whole operation. The temperature of the oil bath was regulated (208-210°) so that a slow distillation of the nitrobenzene occurred. As the nitrobenzene was distilled off it was replaced continuously by the addition of fresh nitrobenzene. Table 15 has been included to show the progress of the reaction:

TABLE 15

Time, hours	Amount of nitrobenzene distilled off in ml	Amount of fresh nitrobenzene added in ml	Colour of distillate
1	40	40	Yellow, cloudy
2	55	40	Orange, cloudy
3	48	40	Orange, slightly turbid
4	55	40	Orange, clear
5	52	40	Orange, clear

When the reaction was complete, after 5 hours, the product (150 ml) was diluted with 850 ml of benzene and shaken in a separatory funnel with 500 ml of 3.7% hydrochloric acid. The emulsion formed was filtered with suction (250 mm Buchner funnel) and the black residue on the filter paper (7.0 g) was washed with another 200 ml of the same acid. The combined filtrates were transferred to a separatory funnel and the blue-green acidic layer was separated from the brown benzene layer. The latter was extracted twice with 150 ml of the acid. The combined acidic extracts (1 l) were filtered, diluted with an equal volume of water and boiled until no smell of nitrobenzene could be perceived. Then the liquid (1.2 l) was cooled and filtered. The amine was precipitated at room temperature by the gradual addition with stirring of anhydrous sodium acetate (150 g). After standing for 3 hours in the refrigerator, the solid product was filtered and dried in vacuo. A red crystalline mass of crude 1-aminophenazine (9.7 g, m.p. 172-178°) was obtained. This crude product was purified by two sublimations using the apparatus shown in Fig. 18, to provide 1-aminophenazine (7.76 g) red crystals with a bronze lustre, m.p. 181-2° identical with the deamination product of 1,3-diaminophenazine (9).

ν_{max}^{KBr} 3480, 3340 cm^{-1} (NH_2); 820, 765, 735 cm^{-1}.

Acetylation of 1-Aminophenazine

Acetylation of 1-aminophenazine with a glacial acetic acid-acetic anhydride mixture gave 1-acetylaminophenazine, yellow crystals, m.p. 171-2° (from aqueous acetic acid). This product was identical with that obtained

by deamination of 1-acetylamino-3-aminophenazine perchlorate (9).

ν_{max}^{KBr} 3370 cm^{-1} (N-H); 1685, 1675 cm^{-1} (C=O); 830, 780, 765, 760, 750 cm^{-1}.

Nitration of 1-Aminophenazine

The nitration experiments which were carried out to determine the optimum conditions for the reaction are outlined in the following Table 16. In each case, 200 mg of 1-aminophenazine was dissolved in 2 ml of concentrated sulphuric acid, the solution was cooled to a paste (-50°), then nitric acid was added at once and the mixture was stirred until it changed to a uniform liquid (-20°). In order to stop the reaction the nitration mixture was poured onto crushed ice (100 g). The reaction product precipitated and was removed by filtration or was extracted from the reaction mixture. The unreacted amine, when present, was recovered from the acidic filtrate by making the latter alkaline with ammonia.

TABLE 16

No.	Amount of nitric acid (sp.gr. 1.42) used in ml	Equivalent % of nitric acid	Procedure	Starting material recovered	Crude nitration product isolated		Amount of 1-amino-4-nitrophenazine purified by chromatography
					Soluble in dilute ammonia	Insoluble in dilute ammonia	
1	0.076	115	The nitration was allowed to proceed for an hour in an ice bath.	5 mg	8 mg (explodes at 240°)	155 mg	
2	0.080	120	As above.	2 mg	8 mg (explodes at 240°)	170 mg	
3	0.084	130	As above.		37 mg (explodes at 240°)	150 mg	
4	0.108	170	The nitration mixture was stirred for 20 seconds with the temperature being maintained below -20°, then was poured onto ice.	30 mg	The isolation was not carried out.		
5	0.108	170	The nitration mixture was stirred in an ice bath for 2 minutes. At this stage one drop of the mixture, when dissolved in ice water, gave a pure yellow colour. The reaction mixture was poured onto ice and the suspension obtained was stirred for 8 hours at room temperature. During this period the suspension changed in colour from yellow to brown-green. The product was extracted with chloroform and purified by chromatography.			194 mg	91 mg m.p. 280-282°
6	0.108	170	The nitration was carried out as in (5). The reaction mixture was poured onto ice, then neutralized with an excess of dilute ammonia at 0°. The solid which precipitated was filtered with suction. Acidification of the ammoniacal filtrate yielded a product which was extracted with chloroform.		7 mg (decompos. at 320-325°)	202 mg	96 mg m.p. 276-279°
7	0.108	170	Nitrated as in (5). The product, which precipitated when the nitration mixture was poured onto ice, was extracted with chloroform, and the extract obtained was chromatographed on alumina. The acidic liquid remaining after extraction with chloroform turned brown on standing and a tarry mass separated.				109 mg m.p. 281-282°

1-Amino-4-nitrophenazine

This procedure was developed on the basis of the above described (Table 16) experiments.

1-Aminophenazine (600 mg, m.p. 181-2°) was ground and dissolved in 6 ml of concentrated sulphuric acid. The solution was cooled to a paste (-50°) in a dry ice-acetone bath and 0.324 ml of nitric acid (sp.gr. 1.42) was added with stirring. The mixture was transferred to an ice-water bath and the stirring was continued for about 2 minutes until one drop of the now liquid nitration mixture, when mixed with ice-water, dissolved to form a yellow solution (the presence of 1-aminophenazine is indicated by a green colour). Then the nitration mixture was poured onto 300 g of crushed ice. The yellow suspension obtained, together with the remaining ice was transferred to a separatory funnel and extracted with four portions of chloroform (A.C.S., 200, 100, 50 and 50 ml). The temperature was maintained near 0°. The chloroform extracts were combined and allowed to pass through a column packed with 500 g of alumina (activity grade IV). The eluent was also chloroform. The main product was obtained first, and as an orange brown liquid (600 ml). On evaporation of the solvent to a volume of 25 ml a crystalline product was obtained. This was filtered with suction and washed with chloroform providing 320 mg of 1-amino-4-nitrophenazine, orange needles, m.p. 281-2° (sublimes).

ν_{max}^{KBr} 3430, 3290 cm^{-1} (NH_2); 1520, 1285 cm^{-1} (NO_2); 820, 802, 775, 770, 765 cm^{-1}.

Anal. Calc. for $C_{12}H_8O_2N_4$: N, 23.30.

Found: N, 23.11%.

Further concentration of the mother liquor to a 10 ml volume yielded 17 mg (m.p. 274-8°) of the same compound. The dark brown mother liquor from the latter was rechromatographed on alumina. In this way a third batch of 1-amino-4-nitrophenazine (7 mg, m.p. 278-81°) was obtained.

Evaporation of the mother liquor from the third batch to dryness left 95 mg of a brown crystalline powder, which melted at 140-5° with rapid decomposition. The infrared spectrum of this product was distinguished by a strong band at 2150 cm^{-1}.

Oxidation of 1-Amino-4-nitrophenazine

1-Amino-4-nitrophenazine (100 mg, purified by recrystallization from acetic acid-water) was ground with 2 ml of water and 4 drops of 40% sodium hydroxide solution to form a fine suspension. Potassium permanganate (0.45 g) was dissolved in 6 ml of water with heating, and the hot solution was added to the hot suspension of the aminonitro-compound in such a way that the violet colour caused by the addition of one drop disappeared before the next drop was added. The reaction mixture was well stirred during the addition and the temperature was kept close to the boiling point. After 1 hour the addition of potassium permanganate was completed and the yellow brown colour of the suspension changed to dark brown. No particles of unchanged starting material could be detected under the microscope. The reaction mixture was then stirred for another 1/2 hour and filtered hot. The orange filtrate was evaporated to a volume of 2 ml, then was cooled and acidified with an excess of hydrochloric acid. After standing overnight at room temperature, a mass consisting of tiny yellowish

and large brown crystals precipitated. A yield of 47 mg of dry material was obtained. The large brown crystals were separated from the mixture, and the infrared spectrum of this substance was found to be identical with the spectrum of quinoxaline-2,3-dicarboxylic acid prepared from phenazine (70).

ν_{max}^{KBr} 3480 cm^{-1} (O-H); 1690 cm^{-1} (C=O);
1325, 1005, 840, 788, 770 cm^{-1}.

Reduction of 1-Amino-4-nitrophenazine

(a) Catalytic

1-Amino-4-nitrophenazine (20 mg, m.p. 281-2°) was suspended in 5 ml of methanol and reduced with hydrogen in the presence of Adam's catalyst (14 mg of PtO_2). During the process the suspended particles dissolved and the liquid changed in colour from brown to dark blue and finally to light yellow. After filtration and on exposure to air, the nearly colourless solution turned instantly dark blue and after some time brown. A brown solid precipitated.

(b) Zinc-acetic acid in nitrogen atmosphere

Powdered 1-amino-4-nitrophenazine (50 mg, m.p. 281-2°) was suspended in 10.5 ml of acetic acid (9 ml of glacial acetic acid and 1.5 ml of water) and heated to 70°. After cooling to room temperature the process was continued in a nitrogen-filled dry box. The suspension was heated to 30°, and zinc powder in excess was added in two portions. The

reaction mixture was shaken vigorously until its colour changed to violet and no yellow particles of unchanged starting material could be noticed. The excess zinc powder was filtered off and the filtrate was diluted with 5 ml of water then made alkaline by the dropwise addition of 50 ml of concentrated ammonia. A mass of dark coloured needles precipitated from the alkaline liquid. It was allowed to stand 1 hour then was filtered, washed with water and dried in vacuo. A dark blue crystalline product (30 mg) was obtained, which when dry did not change remarkably on exposure to air but which turned brown when treated with a solvent in the air. (On long standing in the air the solid compound turns brown.) The substance did not melt below 300°.

Attempted Diazotization of 1-Amino-4-nitrophenazine

1-Amino-4-nitrophenazine (50 mg, m.p. 281-2°)was dissolved in 10 ml of glacial acetic acid with heating. The yellow solution was poured into a solution of nitrous acid, prepared from 1 ml of 2N sodium nitrite solution, 10 g of crushed ice and 3 ml of concentrated hydrochloric acid, and was shaken vigorously until all the ice melted. The excess nitrous acid was decomposed by the addition of urea. The reaction mixture was poured into 80 ml of ethanol and allowed to stand overnight. The yellow crystalline mass (40 mg) which precipitated, was filtered and dried. The melting point and infrared spectrum of this material indicated that it was quite pure 1-amino-4-nitrophenazine. The mother liquor, after concentration, provided another 3 mg of the same material.

Diazotization of 1-Aminophenazine

1-Aminophenazine (50 mg) was diazotized by the method described above. The blue-green colour of the 1-aminophenazine hydrochloride changed instantly to yellow indicating the formation of the diazonium salt. The latter coupled with an alkaline α-naphthol solution (20 ml; 1.2 g of α-naphthol dissolved in 150 ml of a 2.5% sodium hydroxide solution, and 22 g of anhydrous sodium carbonate) at 0° to give a red tarry substance which dissolved in ethanol to give a red solution and was insoluble in dilute acids.

Reaction of 1-Amino-4-nitrophenazine with Aqueous Sodium Hydroxide

(a) 4-Nitro-1(5H)-phenazinone

1-Amino-4-nitrophenazine (200 mg, m.p. 281-2°) was refluxed with 80 ml of a 1% solution of sodium hydroxide. The solid dissolved completely after 20 minutes and the brown solution which formed was refluxed for another hour, then was allowed to cool slowly (2 hours). A yellow precipitate settled out, which redissolved when the liquid was heated to about 60°. The hot liquid was filtered from a tiny amount of a brown amorphous solid, and the clear filtrate was acidified at room temperature by dropwise addition of 3.7% hydrochloric acid to pH 2.0. The liquid turned deep red and red crystals started to come out of solution. The mixture was left for 3 hours at room temperature, then the crystalline material (180 mg) was filtered, washed with water and dried *in vacuo*.

The crude product (75 mg) was heated to 40° with 150 ml of water, cooled to room temperature and filtered. The filtrate was acidified with 15 ml of 3.7% hydrochloric acid at room temperature. The orange red liquid turned deep red and became turbid. On standing a red crystalline substance precipitated. It was filtered, washed with water and dried in vacuo. The 4-nitro-1(5H)-phenazinone (60 mg) melts at 200° with decomposition.

ν_{max}^{KBr} 3120 cm^{-1} (N-H); 1655 cm^{-1} (C=O);
1535, 1290, 1265 cm^{-1} (NO_2); 815 cm^{-1}.

Anal. Calc. for $C_{12}H_7N_3O_3$: N, 17.42.
Found: N, 19.56%.

(b) Ammonium salt of 1-hydroxy-4-nitrophenazine

Fifty milligrams of crude 4-nitro-1(5H)-phenazinone was dissolved in 20 ml of water and rendered alkaline with 3 drops of ammonia. The solution was filtered from a small amount of an amorphous brown solid and treated with 14 drops of concentrated ammonia at 60°. The mixture was left overnight in a refrigerator. A precipitate (22 mg) consisting of pale yellow needles which decompose at 280° was collected. The infrared spectrum of this compound is consistent with the structure of the ammonium salt of 1-hydroxy-4-nitrophenazine.

ν_{max}^{KBr} 3400, 3100 cm^{-1} (NH_4^+); 1540, 1530, 1510, 1320, 1265 cm^{-1} (NO_2);
820, 805, 765 cm^{-1}

Anal. Calc. for $C_{12}H_{10}N_4O_3$: N, 21.70.
Found: N, 21.45%.

The mother liquor was acidified with 3.7% hydrochloric acid in such a manner that the addition of one drop of the acid changed the orange colour of the liquid to red. The final pH was 5.0-6.0. The liquid was heated until the yellow amorphous solid, which had precipitated, redissolved. The solution was left to cool at room temperature and yellow needles (27 mg) crystallized. These had the same infrared spectrum as the previously obtained ammonium salt of 1-hydroxy-4-nitrophenazine.

The ammonium salt was dissolved in water and the solution was acidified with dilute hydrochloric acid to pH 2.0. The red needles which crystallized out of solution were identified by infrared analysis as 4-nitro-1(5H)-phenazinone.

Phenazine-1-carboxylic acid

1-Methylphenazine was oxidized with a chromic acid-glacial acetic acid mixture (35). The carboxylic acid obtained was purified by sublimation (m.p. 234-5°).

ν_{max}^{KBr} 3600 to 2000 cm^{-1} (O-H); 1780, 1730 cm^{-1} (C=O); 840, 795, 755, 740 cm^{-1}.

Phenazyl Hydrochloride

Phenazine (1.0 g, m.p. 176°) was dissolved in 100 ml of 7.5% hydrochloric acid at 40°, and 0.14 g of reduced iron powder was added to the warm solution with stirring. Immediately dark green needles precipitated out of the solution. The reaction mixture was left at room temperature for

5 hours, then the crystalline material was filtered off, washed with 3.7% hydrochloric acid and anhydrous ether and dried *in vacuo*. The semiquinone obtained (1.1 g) did not melt but decomposed at 200° with sublimate formation. On exposure to air for a long time the crystals lost water and hydrogen chloride and long yellow needles of pure phenazine (IR) were formed on the surface.

ν_{max}^{KBr} 3400 cm^{-1} (O-H from water); 3100-2400 cm^{-1} ($\overset{+}{N}$-H); 845, 740 cm^{-1}.

Anal. Calc. for $C_{12}H_9N_2 \cdot HCl \cdot H_2O$: C, 61.13; H, 5.14.
Found: C, 61.53; H, 5.18%.

Phenazine Hydrochloride

A benzene solution of phenazine was saturated with gaseous hydrogen chloride. The hydrochloride which precipitated as an orange crystalline solid was filtered, washed with benzene, and dried *in vacuo*.

ν_{max}^{KBr} 2180, 2090, 1910, 1880, 1800 cm^{-1} ($\overset{+}{N}$-H); 825, 775, 760, 740 cm^{-1}.

Infrared Absorption Spectra

The infrared absorption spectra were determined with a Perkin-Elmer model 21 double beam spectrophotometer equipped with a sodium chloride prism. The settings of the instrument during the measurements were as follows: response 1, gain 5.0, speed 4.0 and suppression 0. The scale of

recording was 100 cm^{-1}/cm for the range 3800-2000 cm^{-1} and 100 cm^{-1}/4 cm for the range 2000-600 cm^{-1}.

The spectra had to be taken in solid state since the majority of the compounds are not sufficiently soluble in solvents used in infrared spectroscopy. However, some of them (phenazine and its alkyl derivatives) could be analyzed in solution as well. The pellets have been prepared by grinding 1-2 mg of the sample with 200-300 mg of spectro-grade potassium bromide (Harshaw Chem. Co., Cleveland) in a mortar, followed by compressing the mixture at 20,000 lb./sq.in. for two minutes. In some cases better resolution was achieved when the substance was sublimed onto a prepared disc of pure potassium bromide; the pellet was attached to the flat bottom of the sublimation apparatus' cylindrical finger by a specially designed holder and the substance was sublimed onto the surface of the pellet to form a microcrystalline layer. The sublimation was continued until a layer assuring optimum resolution was formed.

All samples analyzed were prepared in connection with this research work and were purified by sublimation, chromatography and crystallization. Deuteration of a sample of phenazine to phenazine-d_8 was done by the Merck Co., Canada.

Electronic Absorption Spectra

The electronic absorption spectra were determined by means of a Beckman Spectrophotometer Model DK-1. The settings of the instrument during the measurements were as follows: the scale expansion-absorbance

0-1, the scanning period - 3 min., chart speed - 2 in./min., the light source - tungsten lamp, detector - photomultiplier. The spectra were recorded in the range 700-380 mμ. The accuracy of absorbance determination was about ± 1 absolute per cent. The samples dissolved in water were of 2×10^{-5} - 2×10^{-4} mole/l concentration. The molar extinction coefficient ε was evaluated using the equation $\varepsilon = \frac{A}{c.l}$; where A is absorbance, c is concentration and l is the cell width, in this case equal 1 cm.

SUMMARY AND CLAIMS TO ORIGINAL RESEARCH

1. A two-stage procedure for the synthesis of phenazines was developed. First catechol was condensed with an excess of phenylenediamine at a temperature between 240 and 270°, in nitrogen atmosphere, to form crude 5,10-dihydrophenazine. The latter was subsequently oxidized in a stream of air to phenazine.

2. An intramolecular mechanism was postulated to explain the condensation of phenylenediamine with catechol.

3. Phenazine and three alkyl-phenazines were prepared by this method in a good over-all yield. This showed the general applicability of the procedure for the synthesis of phenazine derivatives. It is thought that pure dihydrophenazines could also be prepared by this procedure from the crude condensation product (crystallization from acetone in nitrogen atmosphere).

4. A special, horizontal type of sublimation apparatus was designed for the purification of phenazines. This apparatus possessed certain advantages over the usual vertical type; it was used successfully for the purification of several phenazine derivatives.

5. The Wohl-Lange procedure for preparing 2-aminophenazine was modified, and used for the synthesis of 2-N-methylaminophenazine. The latter amine was obtained by condensation of o-nitroaniline with methylaniline hydrochloride in the presence of fused zinc chloride. In the reaction a small amount of 2-aminophenazine also was formed as a result of

demethylation. The two amines were separated by crystallization from chloroform followed by chromatography from alumina. Evidence for the structure of 2-N-methylaminophenazine was furnished by the infrared spectra of the compound and its acetyl- and nitro-derivatives, and by the replacement of the methylamino-group in 2-methylamino-1-nitrophenazine by a hydroxyl-group. The known compound 2-hydroxy-1-nitrophenazine was obtained.

6. A method for the synthesis of 1-aminophenazine was established. The amine was prepared in good yield by the oxidation of 2,2'-diaminodiphenylamine. The latter was heated with nitrobenzene in nitrogen atmosphere and the water which formed during the course of the reaction was distilled off. This procedure made 1-aminophenazine readily available.

7. Phenazyl hydrochloride was obtained in a nearly quantitative yield by the reduction of phenazine, in acidic solution, with iron metal.

8. The nitration of 2-aminophenazine in concentrated sulphuric acid was found to proceed rapidly at temperatures between -50° and -15°. 2-Nitraminophenazine was obtained in a nearly quantitative yield when either 10 or 66% excess of nitric acid was used.

9. It was found that the 2-nitraminophenazine formed in the nitration reaction was a mixture of a monohydrate, and anhydrous nitramine. Both forms of 2-nitraminophenazine were prepared in pure state and each was converted into the other form. The pure anhydrous form was obtained from the monohydrate by distilling a suspension of the monohydrate in benzene at 50°, in this way removing a molecule of water. The anhydrous

form was transformed into the nitramine monohydrate by dissolving the former in a large volume of slightly alkaline water, acidifying the solution and allowing the product to crystallize slowly. The two forms of 2-nitraminophenazine differed in their crystalline form, the anhydrous being an amorphous yellow powder, and the monohydrate, fine golden needles. They could also be distinguished by different absorption bands in the 3000 and 900-700 cm^{-1} regions of their infrared spectra. No differences were observed in their chemical behaviour. On the basis of the infrared spectra of 2-nitraminophenazine a 2-nitrimino-(10H)phenazinium betaine structure was assigned as the most probable representation for the compound. The assignment of the structure was also based on (a) the infrared absorption pattern in the 900-700 cm^{-1} region which was in agreement with a phenazine structure substituted in position two of the ring; (b) rapid decomposition of the compound at melting point temperature; (c) its acidic character (salt formation) and (d) the acid-catalyzed rearrangement of the compound to the basic 2-amino-1-nitrophenazine.

10. Optimum conditions were found for the acid-catalyzed rearrangement of 2-nitrimino-(10H)phenazinium betaine. The rearrangement was complete when the nitramine dissolved in concentrated sulphuric acid had been maintained at 0° for 3 hours. The main rearrangement product, isolated in pure state (55% yield), was 2-amino-1-nitrophenazine. The structure of this rearrangement product was proven by (a) oxidation to quinoxaline-2,3-dicarboxylic acid, (b) reduction to 1,2-diaminophenazine, the only possible diamine different from the known 1,3- and 2,3-diaminophenazines, (c) conversion to the known 2-hydroxy-1-nitrophenazine by

both alkaline and acidic hydrolysis. Additional evidence for the structure of 2-amino-1-nitrophenazine was derived from its infrared spectrum.

11. The contemporary views concerning nitramine formation and acid-catalyzed rearrangement of aromatic nitramines were presented and were used to interpret the nitration of 2-aminophenazine.

12. The nitration of 2-N-methylaminophenazine in concentrated sulphuric acid with nitric acid at temperatures between -50° and -20° was found to occur instantly. The main nitration product, 2-methylamino-1-nitrophenazine, was isolated in a 65% yield. Evidence for the structure of the latter was obtained from its infrared spectrum and the transformation to 2-hydroxy-1-nitrophenazine by alkaline hydrolysis.

13. A mechanism was suggested for the alkaline hydrolysis of 2-amino- and 2-methylamino-1-nitrophenazines, a reaction which resulted in the formation of 2-hydroxy-1-nitrophenazine. The following factors were considered to facilitate the hydrolysis:

(a) the formation of an intermediate with the tetrahedral 2-carbon atom was supported by a corresponding shift of electrons in the nitro-group in position one of the ring,

(b) the stability, due to the high degree of charge delocalization, of the 1-hydroxy-1-nitrophenazine anion was the driving force of the reaction,

(c) the general electron deficiency of the positions of the carbocyclic rings in phenazines could be another factor facilitating the nucleophilic attack. Similar reasoning was used to explain the facile substitution of the amino- for an hydroxyl-group in the alkaline hydrolysis of 1-amino-4-nitrophenazine.

14. An "indirect" mechanism, involving an intermediate nitramine formation, was proposed for the nitration of 2-N-methylaminophenazine. The proposal was based on the observation that (a) the nitro-group was directed to position one of the ring as it had been in the acid-catalyzed rearrangement of 2-nitraminophenazine, (b) the reaction occurred at a very high rate and (c) the yield was also high (65%). The replacement of a hydrogen atom by a methyl-group in the amino-function was considered to decrease the stability of the corresponding intermediate nitramine to such an extent that it was not isolable under the reaction conditions. Direct nitration, on the other hand, would be expected to proceed at a slower rate, and to produce phenazine with the nitro-group in a position different from position one. This would occur as a result of the changed directing properties of the amine conjugate acid which presumably would have formed.

15. The nitration of 1-aminophenazine in sulphuric acid was studied. The optimum yield (47%) of the main reaction product, 1-amino-4-nitrophenazine, was obtained when 1-aminophenazine dissolved in concentrated sulphuric acid was treated with a 70% excess of nitric acid at 0° for 2 minutes. The structure of 1-amino-4-nitrophenazine was demonstrated by the following reactions. (a) Oxidation of the compound gave quinoxaline-2, 3-dicarboxylic acid which proved that both the amino- and nitro-groups of the compound were attached to the same carbocyclic ring. The reduction product of 1-amino-4-nitrophenazine was not 1,2- or 1,3-diaminophenazine, nor was it an intermediate which could be transformed into one of these two diamines. Consequently, the 1,4-substituted phenazine was left as the

only possible structure for 1-amino-4-nitrophenazine. (b) The amino-group in 1-amino-4-nitrophenazine was replaced by an hydroxyl-group *via* alkaline hydrolysis. The 1-hydroxy-4-nitrophenazine obtained was isolated and identified in the form of its ammonium salt. In acidic medium 1-hydroxy-4-nitrophenazine underwent immediately a tautomeric change to 4-nitro-1(5H)-phenazinone. The latter was the only tautomer isolated in solid state from acidic solutions. In order to explain the observed stability of the phenazinone tautomer the nitro-group must have been in position four of the ring. In this case a six-membered ring which assured the stability of the system was formed by hydrogen bonding between the hydrogen atom in position five of the ring and the nitro-group in position four. (c) The infrared spectrum of 1-amino-4-nitrophenazine offered support for the assignment of the structure to the compound.

16. Nitration of 2-amino-, 2-N-methylamino- and 1-aminophenazine showed the difference in reactivity of the α- and β-positions of phenazine towards electrophilic attack. The difference had been predicted on the basis of theoretical calculations. In each nitration experiment one α- and one β-carbon was in conjugation with the amino-group which meant that any change in electron density caused by the presence of the amino-group should affect both positions equally. However, since only the α-substituted nitro-compounds were isolated, it appeared that the β-positions possessed lower reactivity in nitration reactions. This confirmed the theoretical evaluation that there were lower π-electron densities at the β-carbon atoms of phenazine.

17. Diazotization attempts showed that 2-amino-1-nitrophenazine and

1-amino-4-nitrophenazine did not react under conditions in which 2- and 1-aminophenazine were diazotized instantly. It was considered that the decrease in the nucleophilic character of the corresponding amino-groups, due to conjugation with the nitro-groups, caused the observed inertness of the aminonitrophenazines in the diazotization reactions.

18. The tautomerism of hydroxy-derivatives of electron-deficient aza-aromatic compounds was discussed. The occurrence, in the solid state, of only one of the two possible tautomeric forms of 2-hydroxy-1-nitrophenazine (the phenazinol-form) and of 4-nitro-1(5H)-phenazinone (the phenazinone-form) were explained by a similar hydrogen bonding effect. In each case, the more stable of the two possible tautomers is that in which the proton is shifted to a position enabling the formation of a stable six-membered ring by hydrogen bonding with the nitro-group.

19. 4-Nitro-1(5H)-phenazinone was found to be the only solid tautomer isolable from acidic medium. However, in aqueous solution it was in equilibrium with the hydroxy-tautomer, the latter being present in the anionic form. This equilibrium was studied by means of ultraviolet spectroscopy. It was established that a saturated aqueous solution of 4-nitro-1(5H)-phenazinone contained only 7% of the compound in the unchanged phenazinone-form, the other 93% having been transformed into the anion of 1-hydroxy-4-nitrophenazine. On five-fold dilution the ratio fell to 2:98, and on ten-fold dilution full conversion into the anion occurred.

20. The infrared spectra of twenty-nine phenazines have been recorded and the frequencies tabulated. The specific group frequencies observed have been used as supporting evidence for the structures proposed throughout

this study. The specific NO_2-group frequencies of eleven phenazines, NH_2-group frequencies of seven phenazines and N-H-group frequencies of five phenazines have been tabulated separately.

The shift observed in the symmetric NO_2-frequencies of nitramines, as compared with other nitrophenazines, was attributed to the anionic character of the nitrimino-function of the 2-nitrimino-(10H)phenazinium betaine. This, together with the characteristic absorption pattern of the $\overset{+}{N}$-H-group around 3000 cm^{-1}, which was different from that exhibited by the N-H-group of other phenazines, allowed the assignment of the 2-nitrimino-(10H)phenazinium betaine structure to 2-nitraminophenazine.

The frequencies of twenty-seven phenazines in the 900-700 cm^{-1} region, presented separately, showed a reasonably good spectra-structure correlation. Therefore, this region was considered useful for the structural analysis of unknown phenazines.

It was found that the 820 cm^{-1} band in phenazines was associated with the skeletal vibrations of the phenazine system and that this frequency could be used for determining structural changes which involved the conjugated system of the phenazine molecule.

21. Chromatographic procedures for the purification of phenazines synthesized in the course of this research work were developed.

22. The following phenazine derivatives, not previously reported, were prepared and characterized:

a. 2-nitrimino-(10H)phenazinium betaine anhydrous

b. 2-nitrimino-(10H)phenazinium betaine monohydrate

c. 2-nitraminophenazine sodium salt

d. 2-nitraminophenazine potassium salt

e. 2-nitraminophenazine ammonium salt

f. 2-amino-1-nitrophenazine

g. 1,2-diaminophenazine

h. 2-N-methylaminophenazine

i. 2-NN-acetylmethylaminophenazine

j. 2-methylamino-1-nitrophenazine

k. 1-amino-4-nitrophenazine

l. 1-hydroxy-4-nitrophenazine ammonium salt

m. 4-nitro-1(5H)-phenazinone

n. phenazine-d_8.

REFERENCES

1. A. Claus, Ann., 168, 1-21 (1873).
2. W.H. Perkin, Jahresber., 756 (1859).
3. O. Fischer and E. Hepp, Ber., 21, 2617 (1888).
4. O. Fischer and E. Hepp, Ann., 272, 306 (1892).
5. O. Fischer and E. Hepp, Ber., 26, 1194 (1893).
6. R. Nietzki, Ber., 29, 1442 (1896).
7. H. Caro and C. Dale, Brit. Pat. 3307 (1863).
8. O. Fischer and E. Hepp, Ber., 22, 355 (1889).
9. F. Kehrman and P. Prunier, Helv. Chim. Acta, 7, 984 (1924).
10. R. Nietzki and F. Moll, Ber., 26, 2182 (1893).
11. F. Kögl and J.J. Postowsky, Ann., 480, 280 (1930).
12. G.R. Clemo and H. McIlwain, J. Chem. Soc., 738 (1935).
13. C. Dufraisse, A. Etienne and E. Toromanoff, Compt. rend., 235, 920 (1952).
14. F. Wrede and E. Strack, Z. Physiol. Chem. 181, 58 (1929); Chem. Abstracts, 23, 2717 (1929).
15. H. McIlwain, J. Chem. Soc., 1704 (1937).
16. L. Michaelis, J. Biol. Chem., 92, 211 (1931).
17. L. Michaelis, Chem. Reviews, 274-75 (1935).
18. B. Elema, Rec. trav. chim., 52, 569 (1933).
19. H. McIlwain, J. Chem. Soc., 322 (1943).
20. G.R. Clemo and A.F. Daglish, J. Chem. Soc., 1481 (1950).
21. G.R. Clemo and A.F. Daglish, Nature, 162, 776 (1948).
22. G.R. Clemo and A.F. Daglish, J. Chem. Soc., 2318 (1948).
23. W.A. Waters, Trans. Faraday Soc., 39, 140 (1943).
24. H. Weil-Malherbe, Biochem. J., 31, 299 (1937).

25. F. Dickens and H. McIlwain, Biochem. J., 32, 1615 (1938).

26. D.E. Green, L.H. Stickland and H.L.A. Tarr, Biochem. J., 28, 1812 (1934).

27. G. Meissner and E. Hesse, Arch. exptl. Path. Pharmakol., 147, 339 (1930); Chem. Abstracts, 24, 5066 (1930).

28. G.B. Marini-Bettolo and G. Borzini, Ist. botan. univ. lab. crittogam, Pavia, Atti, (5), 3, 261 (1947); Chem. Abstracts, 43, 8435 (1949).

29. L.E. Smith, Ind. Eng. Chem., 34, 499 (1942).

30. G.A. Swan and D.G.I. Felton, Phenazines, p. 203, Interscience Publishers Inc., New York, 1957.

31. V. Merz, Ber., 19, 725 (1886).

32. C. Ris, Ber., 19, 2206 (1886).

33. J.S. Morley, J. Chem. Soc. 4008-10 (1952).

34. F. Kehrman and C. Mermod, Helv. Chim. Acta, 10, 62 (1927).

35. G.R. Clemo and H. McIlwain, J. Chem. Soc., 1991 (1934).

36. G.R. Clemo and H. McIlwain, J. Chem. Soc., 261 (1936).

37. O. Hinsberg, Ber., 18, 1228 (1885).

38. O.N. Witt, Ber., 19, 914 (1886).

39. E. Diepolder, Ber., 42, 2916 (1909).

40. H. McCombie, H.A. Scarborough and W.A. Waters, J. Chem. Soc., 353 (1928).

41. O. Fischer and O. Heiler, Ber., 26, 378 (1893).

42. O. Fischer, Ber., 29, 1873 (1896).

43. H.C. Waterman and D.L. Vivian, U.S. Pat. 2,292,808 ; Aug. 11, 1942; Chem. Abstracts, 37, 892 (1943).

44. H.C. Waterman and D.L. Vivian, J. Org. Chem., 14, 289 (1949).

45. M.L. Tomlinson, J. Chem. Soc., 158 (1939).

46. A. Wohl and W. Aue, Ber., 34, 2442 (1901).

47. I.J. Pachter and M.C. Kloetzel, J. Am. Chem. Soc., 74, 971 (1952).

48. E.C. Soule, U.S. Pat. 2,332,179; Oct. 19, 1943; Chem. Abstracts, 38, 1534 (1944).

49. S. Maffei, S. Pietra and A. Cattaneo, Gazz. Chim. Ital., 83, 327 (1953).

50. S. Maffei, S. Pietra and A.M. Rivolta, Ann. chim. (Rome), 42, 519 (1952).

51. E.I. Abramova and I. Ya. Postovskii, Zhur. Obshchei Khim., (J. Gen. Chem.), 22, 502 (1952); Chem. Abstracts, 47, 2182 (1953).

52. W. Bradley and E. Lecte, J. Chem. Soc., 2129 (1951).

53. A. Wohl and M. Lange, Ber., 43, 2186 (1910).

54. H. Hillemann, Ber., 71B, 42 (1938).

55. P. Griess, J. prakt. Chem., (2), 3, 143 (1871).

56. E. Knoevenagel, J. prakt. Chem., (2), 89, 1-25 (1914).

57. O. Fischer, Ber., 37, 552 (1904).

58. O.N. Witt, J. Soc. Chem. Ind., London, 1, 255 (1882).

59. Ph. Barbier and L. Vignon, Bull. soc. chim. France, Mem., 48, 338 (1887).

60. Ger. Pat. 88,954; Frld., 4, 404 (1894-97).

61. A. Albert, R. Goldacre, and J. Philips, J. Chem. Soc., 40 (1948).

62. F.H. Herbstein and G.M. Schmidt, Nature, 169, 323 (1952).

63. E. Bergman, L. Engel and H. Mayer, Ber., 65B, 446 (1932).

64. J.B. Willis, Trans. Faraday Soc., 43, 97 (1947).

65. A. Albert, S.D. Rubbo and R. Goldacre, Nature, 147, 332 (1941).

66. H.C. Longuet-Higgins and C.A. Coulson, J. Chem. Soc., 971-80 (1949).

67. M.J.S. Dewar and P.M. Maitlis, J. Chem. Soc., 2521-28 (1957).

68. S. Maffei and M. Aymon, Gazz. Chim. Ital., 84, 667 (1954).

69. S. Maffei and M. Aymon, Gazz. Chim. Ital., 83, 327 (1953).

70. Z.V. Pushkareva and G.I. Agibalova, J. Gen. Chem. (U.S.S.R.), 8, 151 (1938); Chem. Abstracts, 32, 5404 (1938).

71. Hirotaka Otomasu, Pharm. Bull. (Jap.), 2, 283-7 (1954); Chem. Abstracts, 50, 1033a (1956).

72. H. Euler, Ann., 330, 280 (1903).

73. C.K. Ingold, Structure and Mechanisms in Organic Chemistry, p. 270, Cornell University Press, 1953.

74. H. Martinsen, Z. physik. Chem., 50, 385 (1904); ibid., 59, 605 (1907).

75. C.K. Ingold et al., Nature, 163, 599 (1949).

76. A.F. McKay, Chem. Reviews, 51, (2), 308 (1952).

77. A. Taurins, Can. J. Chem., 36, 465-72 (1958).

78. O. Harris, Ph.D. Thesis, McGill University, Montreal, Que., 1958.

79. R. Roberts, Ph.D. Thesis, McGill University, Montreal, Que., 1959.

80. H. Shindo, Pharm. Bull. (Jap.), 5, 472 (1957).

81. H. Shindo, ibid., 6, 117 (1958).

82. H. Shindo, ibid., 4, 460 (1956).

83. H. Shindo and N. Ikekawa, ibid., 4, 192 (1956).

84. J. Turkevitch, Stevenson, P.C., J. Ch. Phys. 12, 300 (1944).

85. L. Corrsin, B.J. Fax and R.C. Lord, J. Ch. Phys., 21, 1170 (1953).

86. A.R. Katritzky and J.N. Gardner, J. Chem. Soc., 2198 (1958).

87. A.R. Katritzky and A.R. Hands, ibid., 2202 (1958).

88. A.R. Katritzky, A.R. Hands and J.N. Gardner, ibid., 3165 (1958).

89. A.R. Katritzky, Quart. Rev., 13, 353 (1959) (Review).

90. H. Shindo and Sh. Tamura, Pharm. Bull. (Jap.), 4, 292 (1956).

91. W.H. Tallent and I.J. Sievers, J. Anal. Chem., 28, 953 (1956).

92. J. Lecomte and P. Lambert, Compt. rend., 208, 1148 (1939).

93. G.G. Cannon and G.B.B. Sutherland, Spectr. Acta, 4, 373 (1951).

94. H.J. Teuber and G. Steiger, Ber., 88, 802 (1955).

95. P.E. Gagnon, K.F. Keirstead and B.T. Newbold, Can. J. Chem. 35, 1423 (1957).

96. L.J. Bellamy "The Infrared Spectra of Complex Molecules", London, Methuen and Co. Ltd., 1958, p. 280.

97. C.W. Young, R.B. Duvall and N. Wright, Anal. Chem., 23, 709 (1951).

98. D.H. Whiffen, Spectr. Acta, 7, 253 (1955).

99. G.L. Cook and F.M. Church, J. Phys. Chem., 61, 458 (1957).

100. See ref. 96, p. 279.

101. See ref. 96, p. 280.

102. L. Cencelj and D. Hadzi, Spectr. Acta, 7, 274 (1955).

103. See ref. 96, p. 298 and p. 303.

104. E. Lieber, D.R. Levering and L.J. Patterson, Analyt. Chem., 23, 1594 (1951).

105. A. Eckert and K. Steiner, Monatsh., 35, 1153 (1914).

106. F. Kehrman and M. Sandoz, Helv. Chim. Acta, 3, 104-14 (1920).

107. L.J. Bellamy and R.L. Williams, Spectr. Acta, 9, 341 (1957).

108. M. St. C. Flett, J. Chem. Soc., 1441-8 (1948).

109. See ref. 96, p. 208.

110. G.E. Dunn, J.C. MacKenzie and G. Wright, Can. J. Res., 26B, 104-113 (1948).

111. G.S. Myers and G.F. Wright, Can. J. Res., 26B, 257-70 (1948).

112. A.H. Lamberton, Quart. Rev., 5, 75-98 (1951).

113. E.D. Hughes and G.T. Jones, J. Chem. Soc., 2678-84 (1950).

114. See ref. 73, p. 626-28.

115. E. Bamberger, Ber., 27, 586 (1894).

116. W.N. White, J.R. Klink, D. Lazdinz, C. Hathaway, J.T. Golden, H.S. White, J. Am. Chem. Soc., 83, 2024-5 (1961).

117. K.H. Hausser and J.M. Murrel, J. Chem. Phys. 27, 500-02 (1957).

118. E. Bamberger, Ber., 28, 399-403 (1895).

119. A.E. Tschitschibabin and B. Rasorenow, J. Russ. Phys. Ch. Soc., 47, 1286 (1915).

120. A.E. Tschitschibabin, D.P. Witkovsky and M. Lapshin, Ber., 58, 803-5 (1925).

121. A.E. Tschitschibabin and A.W. Kirsanov, Ber., 60, 2433 (1927).

122. A.E. Tschitschibabin and A.W. Kirsanov, Ber., 61, 1223 (1928).

123. S. Kasman, Ph.D. Thesis, McGill University, Montreal, Que., 1935.

124. P. Chevalier and C. Sandorfy, Can. J. Chem., 38, 2524, (1960).

125. See ref. 96, p. 303.

126. J. Kenner, Chem. and Ind. 60, 443-47 (1941).

127. G.A.F. Holleman, J.C. Hartogs and T. Van der Linden, Ber., 44, 704 (1911).

128. I. Glazer, E.D. Hughes, C.K. Ingold, A.T. James, G.T. Jones and E. Roberts, J. Chem. Soc., 2657-58 (1950).

129. E. Plazek and E. Sucharda, Ber., 61, 1813 (1928).

130. E. Plazek, A. Marcinkow, and C. Stammer, Roczniki Chem. 15, 365 (1935).

131. A. Gray, G. Gertner and F.G. Holliman, Tetrah. Letters, 7, 24 (1959).

132. A. Albert "Heterocyclic Chemistry", Univ. of London, The Athlone Press, 1959, p. 57-59.

133. H. Specker and H. Gawrosch, Ber., 75, 1338 (1942).

134. G.M. Badger, R.S. Pearce and R. Pettit, J. Chem. Soc. 3204 (1951).

135. W. John, Angew. Chem., A59, 188 (1947).

136. O. Hinsberg, H. Garfunkel, Ann., 292, 260 (1896).

137. See ref. 96, p. 65.

138. See ref. 96, p. 297.

139. K.H. Saunders, "The Aromatic Diazo-Compounds", p. 14, London, E. Arnold Co.