THE MECHANISM OF THE BENZIDINE REARRANGEMENT

PART I

THE REARRANGEMENT OF p-HYDRAZOTOLUENE

PART II

THE REARRANGEMENT OF m-HYDRAZOANILINE

Thesis by

James Stanley Clovis

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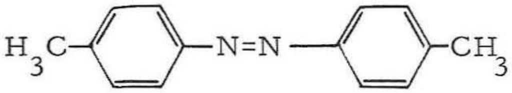
ABSTRACT

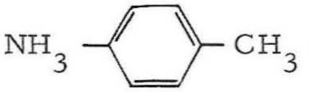
PART I

A number of unsuccessful experiments were carried out in an attempt to show that the benzidine rearrangement proceeds through intermediate cation radicals. The rearrangement of p-hydrazotoluene (HzT), which has been reported to give rise to p-toluidine, p-azotoluene, and 2-amino-4,5'-dimethyldiphenylamine (an o-semidine) in a 2:1:2 weight ratio, was extensively investigated.

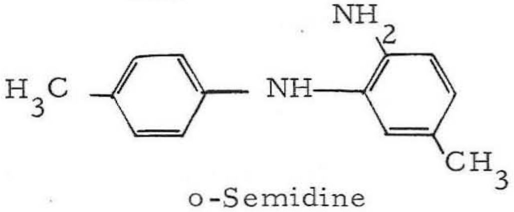
HzT



p-Azotoluene



p-Toluidine



o-Semidine

Attempts to initiate polymerization by intermediates formed during the rearrangement of HzT (and hydrazobenzene) failed. The product solution that was obtained after all of the HzT had reacted was found to oxidize N,N,N',N'-tetramethyl-p-phenylenediamine to Wurster's Blue. The kinetics of this oxidation were investigated.

The composition of the mixture of products obtained from HzT was re-examined by the technique of isotope dilution. The

results showed that p-toluidine, p-azotoluene, and the o-semidine account for only 90% of starting material and are actually formed in a 3:2:4 weight ratio. An additional product (or products) must account for 10% of the reaction of HzT.

Radioactive HzT was rearranged in the presence of a number of added compounds. The presence of hydrazobenzene was found to reduce the yield of p-azotoluene, but not to alter the formation of p-toluidine and the o-semidine. These results show that p-azotoluene is formed by an intermolecular process, while the remaining products probably originate from intramolecular paths.

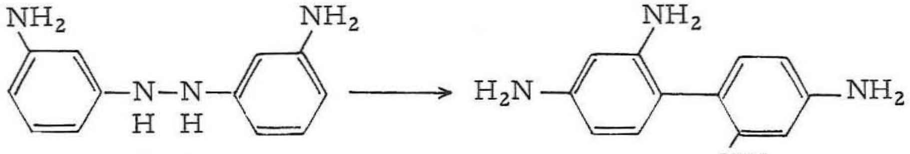
The rearrangement of p,p'-ditrideuteromethylhydrazobenzene-4,4'-C^{14} was investigated and found to be unaffected by the presence of the deuterium.

An unknown compound was isolated in very small quantities from the product mixture obtained from the rearrangement of HzT. This compound was in the form of an oil and was only partially characterized.

A possible explanation for the formation of the 10% of unknown product is that it arises from coupling of the para carbon atoms of HzT.

PART II

The rearrangement of m-hydrazoaniline (HzA) to 2,2'-diaminobenzidine has been investigated. The reaction rate exhibits an


HzA

inverse dependence upon hydrogen ion. As HzA is a diacidic base, the observed rate law requires that the transition state of the rearrangement involve a monoconjugate acid of HzA.

HzA-N^{15}H-N^{15}H- was prepared and rearranged at four acid concentrations, three of which were within the concentration range used to determine the acid dependence of the rearrangement. The N^{15} content of the o-amino groups of the resulting benzidine was found to increase as the acidity of the rearrangement solutions was increased. In terms of coupling reactions the results showed that the extent of ortho coupling that occurred in the formation of the benzidine varied from approximately 35% at the lowest acid concentration to 44% at the highest. As only one hydrogen is involved in the transition state of the rearrangement, a metastable intermediate must be formed which can either collapse to product or be attacked by a second proton. The results are consistent with a mechanism which involves initial heterolysis of the N-N bond to give Dewar's "π-complex." This complex can either collapse to product or can be attacked by proton to form a pair of cation radicals which will also collapse to product.

Starting material was recovered after a rearrangement had proceeded to 50% completion and the N^{15} content of the hydrazo linkage was found to be unchanged.

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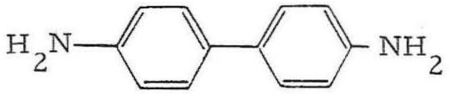
HISTORICAL

For the past sixty years elucidation of the mechanism of the benzidine rearrangement has proved to be one of the most difficult problems that has faced organic chemists. A very significant amount of information about the rearrangement of substituted and unsubstituted hydrazobenzene may be found in the literature to testify to the efforts of numerous researchers. The early work on this subject dealt principally with product studies, while in more recent years kinetic investigations have dominated the picture.

The acid catalyzed rearrangement of aromatic hydrazo compounds gives rise to five types of products, although no more than four have ever been formed in any one rearrangement. Examples of these products are listed below along with the nomenclature employed by Jacobson (1).

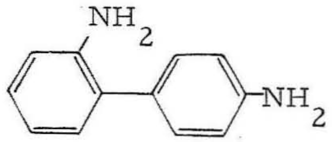
FIGURE I

a.



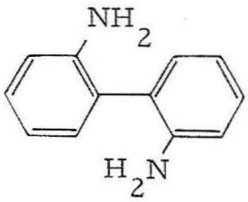
benzidine

b.



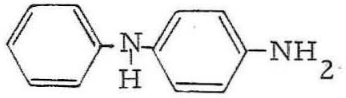
diphenyline

c.



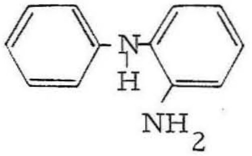
2,2'-diaminobiphenyl

d.



p-semidine

e.



o-semidine

Rearrangements a-c are often referred to as diphenyl rearrangements while d and e are referred to as semidine rearrangements.

Disproportionation products have also been observed. Carlin and Wich (2) have reported that the rearrangement of p-hydrazotoluene produces a mixture of p-toluidine, p-azotoluene, and 2-amino-4',5-dimethyldiphenylamine (an o-semidine) whose composition remains constant throughout the reaction. This result requires that a description of the formation of disproportionation products be included in any comprehensive discussion of the mechanism of the benzidine rearrangement.

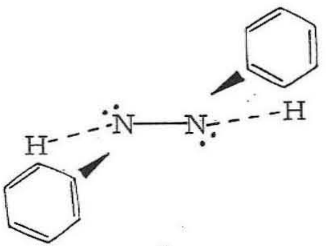
Several mechanistic schemes were proposed at an early date to explain the formation of these various products. Some were modified and some were completely discarded when the rearrangement was shown to be intramolecular. Jacobson (1) first pointed out that in none of his extensive studies did he ever find any indication of crossed products. Wheland and Schwartz (3) rearranged 2-methyl-2'-ethoxyhydrazobenzene which contained C^{14} in the methyl group. The product was worked up with 3,3'-dimethylbenzidine as a carrier, and the recovered dimethylbenzidine contained essentially no activity. In a similar experiment Bloink and Pausacker (4) investigated the rearrangement of hydrazobenzene-2-carboxylic acid and found no evidence of any nonacidic or dibasic benzidine.

These experiments do not exclude the possibility of an initial heterolytic cleavage of the N-N bond which would always take place in the same direction. As fragments of like charge should not couple, no symmetrical products would result from the rearrangement of an unsymmetrical hydrazobenzene. However, Ingold and Kidd (5) rearranged a mixture of 2,2'-dimethoxy- and 2,2'-diethoxyhydrazobenzene and found no crossed products. As these two compounds have similar rates of rearrangement, crossed products should have been found if free fragments were present in solution.

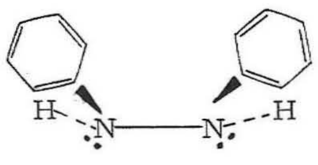
Many of the early mechanistic postulates assumed that the rearrangements were first order with respect to hydrogen ion. However, Hammond (6) showed that at constant ionic strength the rearrangement of hydrazobenzene in 75 percent ethanol-water is second order with respect to the hydrogen chloride concentration. This result was subsequently confirmed by Carlin et al. (7) and Croce and Gettler (8), who used slightly different solvent compositions.

With these and other results in mind various speculators have covered practically the entire field of mechanistic possibilities. Ingold (9, 10, 11) has repeatedly, although not dogmatically, championed a concerted mechanism. This mechanism implies that carbon-carbon bond formation is concurrent with N-N bond cleavage, although the two processes need not be completely synchronous. Seemingly, any practical configuration of the neutral hydrazo molecule will cause the para carbon atoms to be significantly farther apart than the 1.5-2 Å necessary for sigma bonding. Two favorable configurations are represented below (Fig. II).

FIGURE II



1

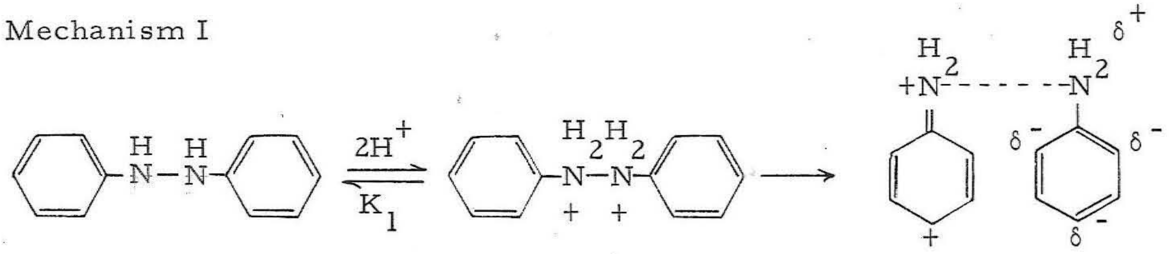


2

The para carbon atoms in these structures should be a minimum of 5 Å apart. To bring them closer in structure 2 would produce considerable strain in the N-N-C bond angle. However, Ingold feels that such restrictions do not apply to the diprotonated form of hydrazobenzene. For some nebulous reason he argues that this symmetrical distribution of charge leads to a partial heterolysis of the N-N bond as it is stretched (Fig. III), and that such a bond may retain its integrity at distances of 5-7 Å .

FIGURE III

Mechanism I



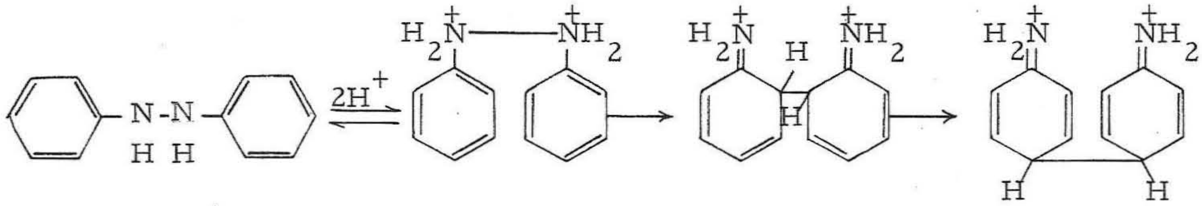
Transition state

Furthermore, Hammick and Mason (12) have calculated that highly polar structures may be easily deformed so that the para carbon atoms of a diprotonated hydrazo molecule may readily come as close as 2 Å to each other. With these results in mind Ingold feels that the stereochemical challenge of the benzidine rearrangement has been met.

An extension of the concerted mechanism is the "leap frog" mechanism (Fig. IV) of Brownstein, Bunton, and Hughes (13). Theirs is essentially a two-step, concerted mechanism which is somewhat analogous to the para Claisen rearrangement.

FIGURE IV

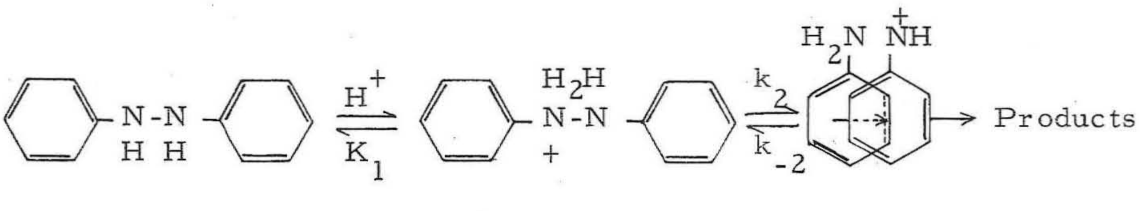
Mechanism II



Dewar (14, 15, 16) has proposed a heterolytic mechanism which involves an intermediate formation of a "π-complex" as a separate step between the dissociation of the N-N bond and the formation of the C-C bond. In his first papers (14, 15) Dewar assumed that the rearrangement was first order in hydrogen ion and that the complex was formed in the rate-determining step. After Hammond reported that the reaction actually exhibits a second order dependence upon hydrogen ion, Dewar modified his mechanism (16) to make the rate-determining step the attack of proton on the "π-complex" (Fig. V). He clearly required that this step also be product determining.

FIGURE V

Mechanism III



Dewar argues that the products are determined by the orientation of the fragments of the "π -complex" and that the results are in good agreement with molecular orbital theory. The most favorable orientation of the complex derived from hydrazobenzene is the one in which the two nitrogen atoms of the parallel rings are eclipsed. This would lead to the formation of benzidine. Rotation of the fragments could produce the next most stable "π-complex" which would be the one which leads to diphenyline. This argument may also be extended to include the formation of o- and p-semidines from substituted hydrazobenzenes.

There are numerous precedents for the proposed "π-complex." Stable complexes of aromatic molecules which are strongly polarizing (acceptors) with ones which are readily polarized (donors) have been isolated and characterized. Polynitro aromatics such as picric acid, trinitrobenzene, and trinitrofluorenone are known for example to form stable molecular complexes with numerous aromatic hydrocarbons. The presence of such substituents as methyl, hydroxyl, and amino on the donor molecule generally increase the stability of the complexes (except where steric factors are important). The opposite effect is observed if these substituents are on the acceptor (17). For obvious reasons π-complexes are also referred to as charge-transfer or donor-acceptor compounds. Complexes which are of a less stable nature than those described above have been postulated to explain the observations that solutions of iodine in benzene exhibit abnormal color and dipole moments, and that aromatic hydrocarbons dissolve in anhydrous hydrogen fluoride to give colored solutions, while paraffins and olefins are insoluble (18). The driving force for the formation of these complexes would be the energy that is gained from the overlap of electron-rich π-molecular orbitals of one molecule with electron-poor orbitals of another molecule (or ion).

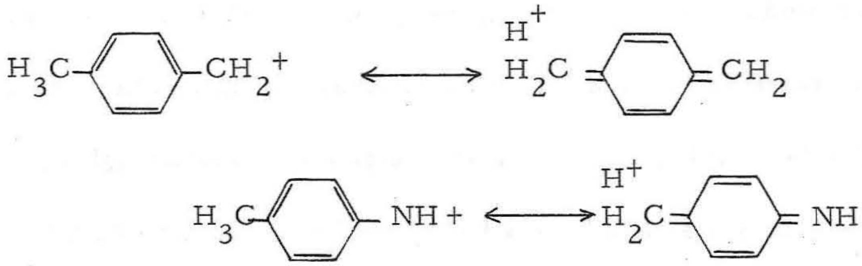
Dewar has not attempted to describe the benzidine rearrangement as unique, but has included it in the whole series of rearrangements of N-substituted anilines which he proposes to proceed through intermediate "π-complex" formation. He postulates that the stability of the complex will vary inversely with the stability of the positive ion. The observed intramolecularity of the benzidine rearrangement is then explained by stating that the unstable phenylimino cation would be too strongly held to allow dissociation of the complex. In contrast, the observed intermolecularity of the rearrangement of N-chloroacetanilide is consistent with the hypothesis that the chlorine positive ion is sufficiently stable to depart from the influence of the aromatic nucleus.

In a brief kinetic study (15) Dewar found that the accelerating effect of substituents upon the rates of rearrangement of hydrazobenzenes decreases in the following order.

$$o\text{-}CH_3 > p\text{-}CH_3 > m\text{-}OCH_3 > H$$

These rearrangements were not conducted under identical conditions, but the results do show that an electron-donating group accelerates the rate of reaction. Presumably, reactions involving the formation of a phenylimino cation would be subject to substituent effects similar to those observed for reactions involving benzyl carbonium ions (Fig. VI).

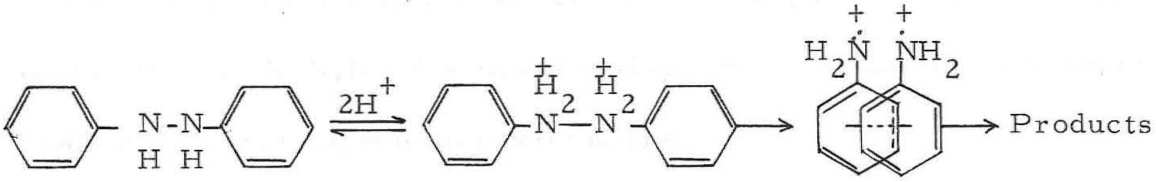
FIGURE VI



A fourth mechanism was proposed as early as 1903 by Tichwinsky (19), who advocated the formation of intermediate phenylamino cation radicals. This idea was discarded on the basis of the observed intramolecularity of the rearrangement. Hammond, although never in print, has revived the radical mechanism. He has proposed that the cation radicals form a complex, that is somewhat analogous to Dewar's "π-complex," which may collapse directly to the observed products (Fig. VII).

FIGURE VII

Mechanism IV



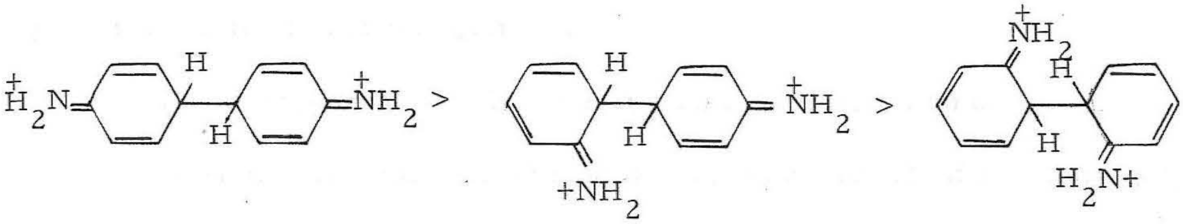
Considerable evidence exists to lend support to this proposal. There are a number of reactions in which benzidines are formed from what is in all probability phenylamino cation radicals. Oxidation of diphenylamine in acetic acid solution with concentrated sulfuric acid and sodium dichromate gives good yields of diphenylbenzidine (20). If the oxidation is carried out in neutral or alkaline medium, tetraphenyltetrazine is obtained in high yield (21). α-Naphthylamine (22) and N,N-dimethylaniline (23) have also been oxidized to the corresponding benzidines. As further evidence Hammond and Seidel (24) have observed that tetraphenyltetrazine is decomposed in ether-hydrogen chloride at -20°C to give diphenylbenzidine and a polymer which is paramagnetic. These results indicate that phenylamino cation radicals tend to couple at carbon atoms, while neutral radicals couple at nitrogen.

The radical mechanism offers a ready explanation for the formation of disproportionation products. If the complexed cation radicals break apart and become "free," they would be expected to readily oxidize unrearranged starting material. Aromatic hydrazo compounds are known to be quite susceptible to air oxidation, and the present study has shown that the cation radical (Wurster cation) formed by oxidation of N,N,N',N'-tetramethyl-p-phenylenediamine will readily oxidize p-hydrazotoluene to p-azotoluene.

The probability that two positively charged cation radicals could form a "π-complex" might at first seem to be quite low; however, Hausser (25) has presented evidence that the Wurster cation can exist in such a form. Moreover, Neuman and Hammond (26) have observed that the efficiency factor for the decomposition of the di-protonated form of azobisisobutyroamidine is 0.65 as compared to 0.45 for the neutral form. While the geminant radical pair produced in the former case has a greater tendency to dissociate, the charge repulsion has not prevented a high percentage of combination of these radicals within their initial "solvent cage."

The observed product distributions may be qualitatively accounted for by the concerted and radical mechanisms. In these schemes positive charges are placed on initially adjacent nitrogen atoms. The formation of benzidines would result in minimum charge repulsion by placing the charges a maximum distance apart. Furthermore, coupling at the para carbon atoms would produce two para-quinoid structures which would be preferred to the ortho-quinoid forms. This argument would predict that diphenyline would be the second most favorable product and that the formation of 2,2'-diamino-diphenyl would be unfavorable (Fig. VIII).

FIGURE VIII



Each of the mechanisms that has been presented suffers from major deficiencies when considered in light of the large body of kinetic information that has been gathered. Objections may be raised to the role that the second proton plays in each of the four mechanisms. As the neutral hydrazo molecule is itself a weak base, addition of a second proton to a site that is adjacent to a positively charged center would seem intuitively quite unfavorable. Yet Mechanisms I, II, and IV all require the formation of the diconjugate acid of hydrazobenzene. The possibility exists that this step could be rate-determining, and indeed Hammond (27) has shown that the rearrangement of hydrazobenzene in 50% ethanol-water exhibits general acid catalysis. However, Ingold (11) has investigated the rearrangement of hydrazobenzene, 1- and 2-naphthylphenylhydrazine, and o-hydrazotoluene in 60% aqueous dioxan and found that the rates are a linear function of H_o. A slope of approximately 2.1 was obtained from the plot of log k vs. H_o for all four cases. Ingold (11) also studied the effect of replacing the water of the aqueous dioxan solvent with deuterium oxide. The k_D/k_H ratio was greater than one in all four cases and was as high as 4.8 for the rearrangement of hydrazobenzene. These two sets of results demand that the second proton be completely transferred to the hydrazo compound prior to its rearrangement.

The contrasting results of Hammond and Ingold could be accommodated if the rate-determining step were attack of the conjugate bases on the second conjugate acid (eq. 1). However, Hammond and

$$R = k[BH_2^{++}][A^-] = k'[BH^+][H^+][A^-] = k''[BH^+][HA] \qquad (1)$$

Grundemeier (28) have shown that hydrazobenzene-4,4'-d_2 rearranges at the same rate as hydrazobenzene.

This disparity of results could be attributed to the difference in solvent systems employed. Perhaps the steps involving deprotonation and rearrangement of the second conjugate acid are of sufficiently similar rates that their importance could be varied with a change of solvent composition (eq. 2).

$$\begin{array}{l} BH^+ + HA \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} BH_2^{++} + A^- \\ \qquad\qquad\qquad\qquad \downarrow k_3 \\ \qquad\qquad\qquad\quad \text{complex} \end{array} \qquad (2)$$

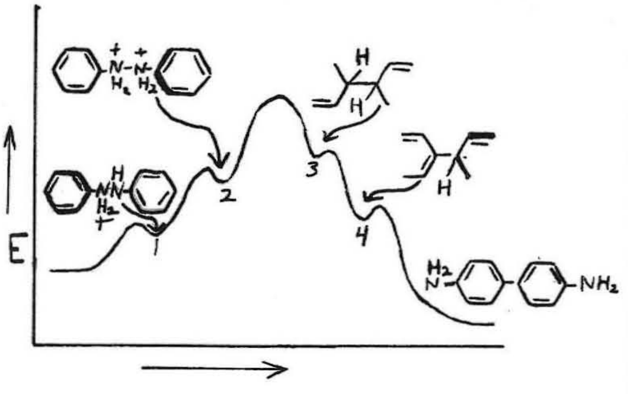
$$R = \frac{k_2[BH^+][HA]}{k_{-2}[A^-] + k_3}$$

If $k_3 \gg k_2 [A^-]$, general acid catalysis would be observed; and if $k_2[A^-] \gg k_3$, catalysis by lyonium ion would occur.

The results of Ingold are certainly examples of cases where an equilibrium exists between a first and second conjugate acid of the hydrazobenzene. While this observation may be felt to detract from mechanisms I, II, and IV, it is completely incompatible with the proposed form of mechanism III. As written, this mechanism requires that addition of the second proton to the complex be rate-determining. This process would be solely consistent with general acid catalysis and could be reconcilable with the results of Ingold only if two different mechanisms were operative.

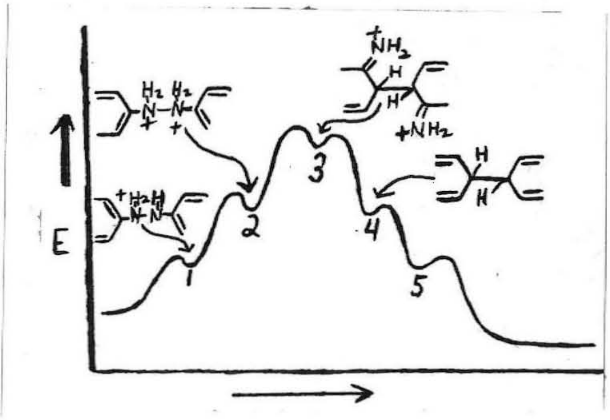
Any discussion of the mechanism of the benzidine rearrangement should include a description of the reaction profile. Mechanisms I-IV could be described by the energy surfaces that are shown below (Figs. IX-XII).

FIGURE IX



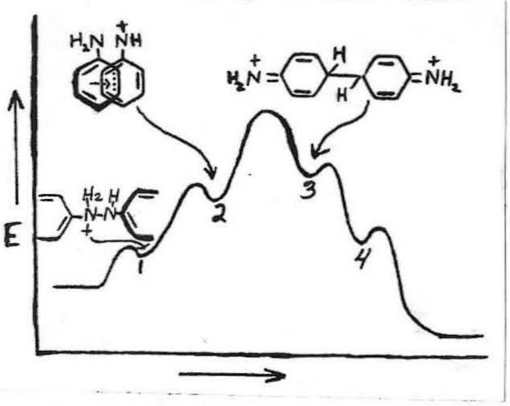
Mech. I

FIGURE X



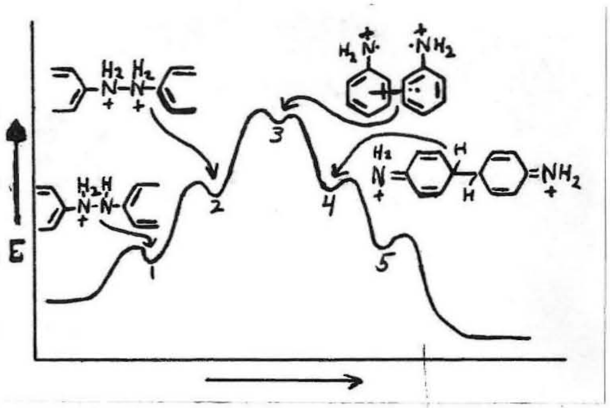
Mech. II

FIGURE XI



Mech. III

FIGURE XII



Mech. IV

The energy separation between most of the various valleys and crests is a rather arbitrary matter and is probably more a function of one's prejudices than any experimental observations. However, certain limitations must be placed upon the separation between the second valley and the transition state described by mechanisms I and III (Figs. IX and XI). Carlin showed that the distribution of products obtained from the rearrangement of p-hydrazotoluene (2) and hydrazobenzene (7) remains constant over the 0-20° temperature range studied in the former case, and the 0-25° range in the latter. Hydrazotoluene produces the o-semidine, p-toluidine, and azotoluene in a 2:4:1 mole ratio (29); while hydrazobenzene rearranges to give benzidine and diphenylene in a 70:30 ratio. In mechanisms I and III the product-determining and rate-determining steps are identical. There must be several of these steps which are competitive in the rearrangement of hydrazobenzene and p-hydrazotoluene as several products are formed in both cases. An extreme coincidence would be required for the activation energies from "valley 2" to the transition states of these various steps to be identical, yet a significant temperature change does not alter their relative importance. If, however, the energy separations between "valley 2" and these transition states are quite small compared to the total activation energy, a temperature variation would not be expected to significantly alter the relative rates of the various product-determining steps.

Estimation of the importance of this critical energy separation in Mechanism III would be quite difficult, as little can be definitively said about the energetics of the protonation of the "π-complex." The energy gap from "valley 2" to the transition state of Mechanism I, however, is determined by certain well-defined conditions. In this concerted reaction an N-N bond is being broken, the aromatic character of two benzene rings is being destroyed, the N-N-C bond angles are being greatly distorted, and the two rings are brought within 2-3 Å of each other.

The final condition alone should involve significant energy requirements. Brown (3) has shown that the benzene rings in di-p-xylene (2,2-paracyclophane) are buckled, presumably as a result of the interference between the π-electron clouds of the two rings. Even in those cases where complexes are formed, the two aromatic rings remain farther apart than 3 Å. Powell (3) has determined the structure of the p-iodoaniline-s-trinitrobenzene complex in which the two rings are found to be parallel. The average distance between the two rings was found to be 3.6 Å, and was never less than 3.5 Å.

Seemingly, a significant amount of energy would have to be supplied to bring the two rings close enough to allow the para- (or ortho-para-) carbon atoms to initiate binding. The only factor which could begin to compensate for all of the requirements of the final step would be the energy gained from formation of the C-C bond. That this energy gain could lower the activation energies of the final steps to relatively insignificant values seems extremely unlikely. This arguments weighs heavily against the first concerted mechanism and inherently implies that there must be an intermediate that is formed prior to the product-determining step. Mechanism III need not have a separation between the rate-determining and product-determining steps as the final hump on the upper slope of the energy surface could be a small one.

Mechanisms II and IV are both compatible with the above argument. In each of them a high energy intermediate is formed in the rate-determining step which precedes the product-determining step. As the products are formed on the downhill part of the energy profile, their relative rates of formation should not be significantly influenced by a temperature variation.

An investigation of entropies of activation for the rearrangement of a number of hydrazobenzenes reveals valuable information which must be related to the mechanism of the rearrangement. The following table gives a summary of entropy data that has been obtained.

TABLE I

Activation Entropies for the Rearrangement of Several Hydrazobenzenes

No.	Hydrazo Compound	Solvent	Reference	ΔS e.u.
1	2-MeO	90% EtOH	8	-25*
2	2-EtO	"	8	-19*
3	2,2',3,3'-Me	"	8	- 1.7
4	3,3'-Me	"	8, 32	-1.3[8], +3.2[32]
5	2,2'-Me	"	8	+ 1.3
6	3,3'-MeO	"	8	+ 2.8
7	Unsubstituted	70[8], 90[8], 85%	8, 7	7.0[8], -2.8[8], +2.9[7]
8	4,4'-Me	95% EtOH	2	+ 6.6

*These rearrangements are exceptionally fast and the rate data is quite inaccurate. Moreover, the dependence of the rates on acid concentration has apparently not been determined; and the rates may be first rather than second order with respect to hydrogen ion.

The activation entropies for #1 and #2 cannot be dismissed as completely irrelevant, but they do seem to be exceptions to the more general tendency of near zero entropies of activation that are observed in the other six cases.

The near zero entropy values seem quite incompatible with both Mechanisms I and II. Each requires that in the transition state two positive charges be on adjacent atoms. This would necessitate a reorganization of solvent molecules in order to better solvate the two centers. The negative entropy of solvation that would result should be a significant part of the total entropy of activation. Moreover, both of these mechanisms require that there be at least some degree of simultaneous bonding between two nitrogen atoms and between two carbon atoms. Many of the degrees of freedom that were associated with the ground state of the hydrazobenzene will have been lost as the transition state becomes essentially that of a four-center reaction. These two factors are difficult to compensate for, and they lead to the conclusion that both Mechanisms I and II would require a significant negative entropy of activation.

The entropies of activation associated with Mechanisms III and IV should not be so low as those associated with Mechanisms I and II; however, an accurate prediction of the entropy values of the former pair would be rather difficult to make. Mechanism III would be more likely to have the higher entropy of activation of the two as the transition state involves conversion of the "π-complex" to product. In this step the two positive charges are separated and the restriction of movement placed upon the two fragments is lessened.

The discussion so far has tended to exclude Mechanisms I, II, and III from consideration. As the first two are concerted, little can be done to modify them. The insertion or modification of a step, however, could readily make the third and fourth mechanisms more compatible with the experimental data. As written, neither of the last two mechanisms is consistent with Carlin's (33) observation that the rearrangement of o-hydrazotoluene is 1.6 order in acid rather than second. Two possible explanations for this result readily come to mind. One is that there could be two competitive mechanisms, one of which is first order in hydrogen order and the other second order. The pseudo first order rate constant would then be

$$k_o = k_o [H^+] + k_2 [H^+]^2 \qquad (3)$$

Mechanisms III can be used to explain a second possibility.

$$B + H^+ \overset{K_1}{\rightleftarrows} BH^+ \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \text{"}\pi\text{"} \xrightarrow[k_3]{[H^+]} P$$

If a steady state concentration is assumed for the π-complex, the following rate expression is obtained.

$$R = \frac{k_3 k_2 K_1 [H^+]^2 [B]}{k_{-2} + k_3 [H^+]} \qquad (4)$$

When $k_3 [H^+] >> k_{-2}$, the rearrangement would exhibit a first order dependence upon hydrogen ion; and when $k_{-2} >> k_3 [H^+]$, second order dependence would be observed. For a rearrangement which exhibits mixed order dependence upon hydrogen ion, equation 4 predicts that an increase in hydrogen ion concentration would decrease the order in acid. The opposite result is predicted by equation 3. An increase in hydrogen ion concentration would increase the second term more rapidly than the first. The rearrangement would then show an increase in order with respect to hydrogen ion as the acid concentration is increased.

Ingold (11) has made a careful study of several aromatic hydrazo compounds which exhibit an intermediate order with respect to hydrogen ion. All of his results show that the dependence upon hydrogen ion approaches second order as the hydrogen ion concentration is increased. The following table gives the transitional dependence upon hydrogen ion that he has observed.

TABLE II

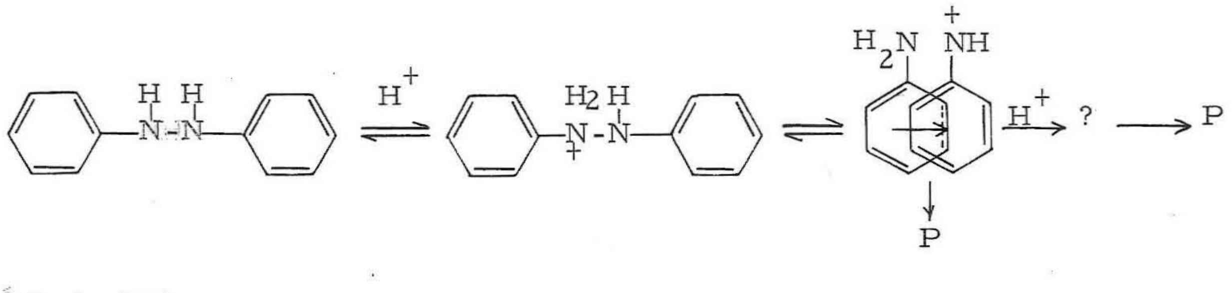
Observed Dependence upon Hydrogen Ion for the Rearrangement of Several Hydrazobenzenes in Aqueous Dioxan (11)

Substrate	Order
α-$C_{10}H_7NHNHC_{10}H_7$-α	1.0
α-$C_{10}H_7NHNHC_{10}H_7$-β	1.0
β-$C_{10}H_7NHNHC_{10}H_7$-β	1.0-1.2
α-$C_{10}H_7NHNHC_6H_5$	1.0-ca. 2.0
β-$C_{10}H_7NHNHC_6H_5$	1.1-ca. 2.0
o-$MeC_6H_5NHNHC_6H_5Me$-o	1.3-ca. 2.0
$C_6H_5NHNHC_6H_5$	2.0

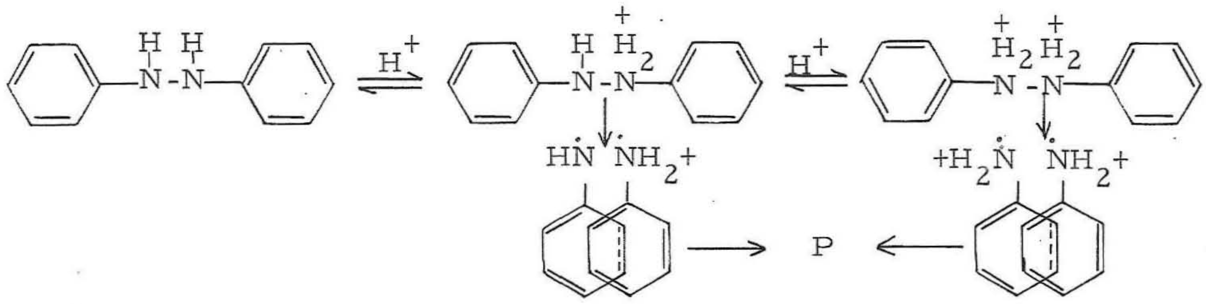
The arguments that have been presented seem to exclude all four mechanisms. Mechanism IV could be resurrected by allowing the monoconjugate acid of hydrazobenzene to cleave directly into a complex of a neutral and a positively charged radical. This complex could then collapse to products. Mechanism III would be suitably modified if the "π-complex" could collapse directly to products as well as undergo the proposed protonation. This second protonation, however, must not lead directly to products as hydrogen ion would then have to be transferred in the rate-determining step. Such a postulate is not consistent with the results of Ingold (see pp. 9 and 10) which require that the second proton be transferred prior to the rate-determining step. For one mechanism to accommodate Ingold's results and the general acid catalysis observed by Hammond, the second protonation must lead to an additional intermediate. Either the formation of this intermediate or its collapse to products would be rate-determining. Mechanisms III and IV may be rewritten as follows (Fig. XIII).

FIGURE XIII

Mech. III'



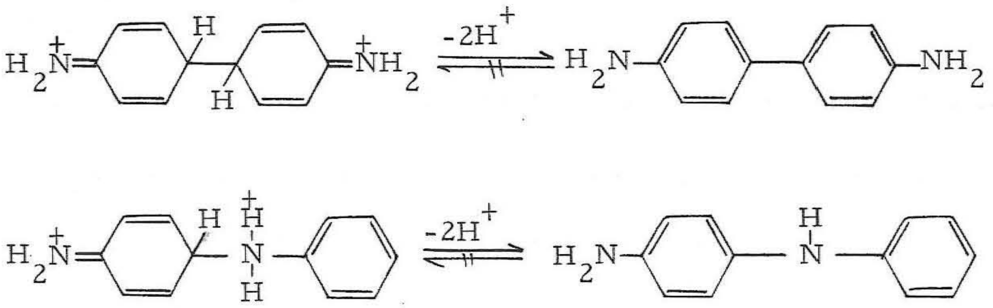
Mech. IV'



To make III' complete the second intermediate should be described. A possible candidate would be the radical complex of Mechanisms IV and IV'. The question of the nature of any intermediate, however, must remain an academic one until information about its structure can be obtained.

An important question to consider when discussing any of the proposed mechanisms is whether or not the carbon-carbon bond formation is reversible. Presumably, once tautomerization of the quinoid-type coupling products has occurred, the resulting diphenyls or semidines would be stable (Fig. XIV). For example, Carlin (2) has shown that the purified products obtained from p-hydrazotoluene are not affected when allowed to stand individually or in pairs under the conditions of the rearrangement. This observation, however, says nothing about the stability of the C-C (or C-N) bonds in the quinoid form of the products. Reversible formation of the C-C bonds would have to be competitive with tautomerization. Substitution of hydrogen

FIGURE XIV



with deuterium at one of the coupling centers should decrease the rate of the tautomerization and hence decrease the yield of the corresponding product. This decrease would be complimented by increased formation of the other product(s). Hammond and Ingold have investigated the rearrangement of 4,4'-dideutero (28, 11) and 2,2',3,3'- (11) tetradeuterohydrazobenzene. The benzidene-diphenyline ratio was found to be unaffected by the deuterium substitution. From these results the conclusion is drawn that C-C bond formation in the products is irreversible. This observation would tend to cast further doubt on the "leap frog" mechanism (II). However, the tautomer of 2,2'-diaminobiphenyl is described as a very high energy species and need not be subjected to the same rules which apply to the tautomers of the products.

There are some observations for which a ready explanation is not easily found. A number of workers (2, 6) have observed a strong positive salt effect upon the rates of rearrangement of various hydrazobenzenes. Such a result would be predicted for any two proton mechanisms; however, Ingold (11) reports that a large effect is also observed for the rearrangement of α- and β-hydrazonaphthalenes. As the transition states for the rearrangement of these compounds involves but one proton, the origin of the salt effect is not readily apparent. Ingold (11) also reports that an increase in water content of mixed solvents accelerates the rearrangement of hydrazobenzenes and that the same effect is observed in the rearrangement of α- and β-hydrazonaphthalene. Again the results are difficult to explain, but Ingold's observations are not completely valid. A comparison of the results of Carlin (7) and Hammond (6) shows that hydrazobenzene rearranges much more rapidly in 95% ethanol than in 75% ethanol-water.

The substituent effect upon the rates of rearrangement of hydrazobenzenes is an additional point of interest and confusion. Croce and Gettler (8) and Dewar (15), to mention but a few workers, have observed that electron-withdrawing substituents retard the rearrangements while electron-donating substituents accelerate it. These effects are extremely widespread and do not correlate well at all with Hammett sigma constants, although they do indicate that the value of "ρ" must be very large and negative. No rigorous attempt has been made, however, to relate the rates of rearrangement to a suitable set of sigma constants.

The information that has been presented shows that the benzidine rearrangement is no simple reaction. A very qualitative attempt has been made in this discussion to relate the observed rearrangement products to the four mechanisms that have been presented. One need only refer to Jacobson's summary (1), however, to realize that this is perhaps the most confusing phase of the whole rearrangement, and that a more rigorous explanation of the product-determining factors is needed.

EXPERIMENTAL

Acrylonitrile.--Seventy-five milliliters of practical grade acrylonitrile was washed with 65 ml. of 1N sulfuric acid, 95 ml. of 5% sodium carbonate, and 95 ml. of water. It was dried over calcium chloride and then distilled. The distillate was kept over calcium chloride and the desired aliquots were removed from this and distilled under reduced pressure before they were used.

Styrene.--Styrene, reagent grade, containing t-butylpyrocatechol, was purified by distillation at 42.5°C under 18 mm. of pressure. The distillate was recrystallized three times at temperatures induced by dry ice-isopropanol.

Hydrazobenzene.--Hydrazobenzene was prepared by the method described in "Laboratory Experiments in Organic Chemistry" (34).

p-Hydrazotoluene.--Hydrazotoluene (HzT) was synthesized by the method of Carlin (2). The crude HzT is separated from filtered zinc and zinc oxides by treatment with hot benzene. Large quantities of benzene had to be used to obtain the yields reported by Carlin.

Phenylhydroxylamine.--Phenylhydroxylamine was prepared by the method described in "Organic Syntheses" (35).

Wurster Blue Perchlorate.--The salt was prepared from N,N,N',N'-tetramethyl-p-phenylenediamine hydrochloride by the procedure of Michaelis and Granick (36).

p-Aminobenzyl Alcohol.--p-Aminobenzyl alcohol was synthesized by the method of Fischer and Fischer (37). The crude product was sublimed to give approximately a 30% yield, m.p. 63-65° (reported, 65°).

p-Aminobenzyl Chloride Hydrochloride.--p-Aminobenzyl alcohol hydrochloride was prepared by treating a solution of 0.48 g. of p-aminobenzyl alcohol in 15 ml. of chloroform with hydrogen chloride. Two neutralization equivalents of the resulting precipitate were determined by potentiometric titration. Calc. 159.6; found 159.5, 159.7.

To a 100 ml. 3-necked round-bottom flask equipped with a reflux condenser, an addition funnel, a magnetic stirrer, and a gas inlet tube was added 25 ml. of chloroform (which had been distilled at 60° and dried over magnesium sulfate) and 0.353 g. of p-aminobenzyl alcohol. The stirred solution was treated for several minutes with hydrogen chloride which was first passed through concentrated sulfuric acid. The mixture was heated to reflux with an oil bath, and then treated over a one-half hour period with 21 ml. of a solution of 2 ml. of thionyl chloride (which had been purified by distillation at 76°) in 20 ml. of chloroform. The solution soon became yellow and after about ten minutes the oil bath was shut off and the mixture was allowed to cool to room temperature. The product mixture was stirred for a total of three hours and filtered to give 0.446 g. of a light yellow solid which lost none of its color when washed with chloroform.

Two potentiometric titrations gave neutralization equivalents of 95.2 and 95.4; calculated for p-aminobenzyl chloride hydrochloride, 89.0. Precipitation of a white solid always occurred between a pH of 4 and 5. The precipitate would burn and would not give a positive chlorine test when heated on a copper wire.

The solutions which had been titrated to determine the neutralization equivalent were filtered and acidified with 5 ml. of 6F nitric acid. They were then heated to near boiling and silver chloride was precipitated by the addition of a solution of silver perchlorate. If the observed neutralization equivalent was assumed to be due to both the hydrochlorides of p-aminobenzyl alcohol and p-aminobenzyl chloride, then the two samples should give 70.4 and 56.3×10^{-5} moles of silver chloride. Actually obtained were 69.6 and 55.5×10^{-5} moles, respectively.

p-Aminobenzyl Acetate.--The preparations were carried out in a dry box. To 0.2 g. (4.4×10^{-3} moles) of a 53% sodium hydride suspension in 5 ml. of ether was added 0.2 g. (1.63×10^{-3} moles) of p-aminobenzyl alcohol. After all of the alcohol had been added and bubbling had ceased, 0.25-0.4 ml. of acetic anhydride was added. The resulting mixture was filtered and the filtrate was coooled in dry ice-acetone. Crystals formed but could not be visibly separated by filtration. A few ml. of chloroform was poured over the sintered-glass filtering funnel. An infrared spectrum was taken of the chloroform and showed strong carbonyl absorption, medium N-H absorption, and weak O-H absorption. Addition of the ether solution to a solution of the Wurster base in ethanol gave little or no oxidation.

p-Aminobenzyl Tosylate.--The preparations were carried out in a dry box. To 1 gram (2.2 x 10^{-2} moles) of a 53% sodium hydride suspension in ether was added 0.19 g. (1.54 x 10^{-3} moles) of p-aminobenzyl alcohol. After one half hour 0.32 g. (1.68 x 10^{-3} moles) of p-toluenesulfonyl chloride was added and the mixture was swirled for twenty minutes. The mixture was filtered and diluted to 250 ml. with ether. Fifteen milliliters of a solution of 17.9 g. of silver perchlorate in 50 ml. of ethanol was added to 25 ml. of the ether solution which had been mixed with 25 ml. of ethanol. A precipitate which weighed 21.8 mg. was separated by filtration and redissolved with ammonium hydroxide. Addition of nitric acid to the ammonium hydroxide solution reprecipitated 19.2 mg. of silver chloride. A precipitate of 20 mg. of silver chloride corresponds to an ether solution that is 5.6 x 10^{-3} molar in p-toluenesulfonyl chloride. The maximum concentration that could have been present if no reaction had occurred and if no sodium chloride were present would have been

6.7×10^{-3} m/ℓ. Apparently little or no tosylate of p-aminobenzyl alcohol actually formed.

Bindschedler's Green.--Bindschedler's Green was prepared by the method described by Dewar (15).

p-Azotoluene.--p-Azotoluene (AzT) was recovered from rearrangements of HzT and purified by recrystallization from ethanol, ethanol-water, and ethanol again. Sublimation at 60-70° and 1 mμ was sometimes performed.

o-Semidine.--This compound could be most easily obtained in a relatively pure state by the rearrangement of HzT in the presence of a limited excess of added hydrochloric acid. For example, a solution of 2.5 g. (0.0118 moles) of purified HzT, in 150 ml. of nitrogen-flushed 95% ethanol was initially treated with 0.5 ml. (0.006 moles) of concentrated hydrochloric acid. After fifteen to twenty minutes another 0.5 ml. of acid was added. The resulting solution was stirred for another 30 minutes, cooled with ice-water, and filtered to remove precipitated p-azotoluene. Fifty ml. of water was then added to the filtrate and more p-azotoluene was deposited. The yellow-orange solid was separated and the resulting filtrate was neutralized with 2.5F sodium hydroxide. The light orange-brown o-semidine which precipitated was separated and weighed 0.5 g. Purification was effected by recrystallization from ethanol-water, sublimation at 70° and 1 micron, and another recrystallization from ethanol-water. The wet product was dried under vacuum, m.p. 110°.

p-Toluidine.--Practical grade p-toluidine was purified by four to five recrystallizations from 85-100° ligroin, m.p. 42-43°.

Potassium t-Butoxide.--Twenty grams of potassium metal was added in chunks to 200 ml. of t-butyl alcohol. After most of the potassium had reacted, the product mixture was heated under reduced pressure to remove the excess t-butyl alcohol. The resulting solid was heated under vacuum for an additional three days during which time solid sublimed on the walls of the container.

Ethanol-O-D.--Ethanol-O-D was prepared by the reaction of sodium ethoxide with deuterium oxide.

A mixture of 14 g. of freshly cut sodium, 55 g. of ethyl phthalate, and 2 liters of absolute ethanol was refluxed for several hours. The dried ethanol was then recovered by distillation. To 1300 ml. of the center cut of the distillate was cautiously added 155-160 g. of freshly cut sodium. The mixture was refluxed until all of the sodium had reacted. The excess ethanol was then removed first by distillation at atmospheric pressure and finally by distillation at about 0.01 mm. until no more ethanol collected in the dry ice traps. The neutralization equivalent was found to be 69.4, calcd. 68.1.

To 100 g. of heavy water ($>99.5\%$ D_2O) was added 110-120 g. of sodium ethoxide. The liquid was distilled under vacuum from the resulting sludge. The ethanol-water solution that was collected was then distilled through a spinning band column and about 60 ml. of ethanol was collected at 78°. An infrared spectrum showed little or no O-H absorption and exhibited the expected O-D absorption.

p-Nitrotoluene-1-C^{14}.--Forty milligrams of toluene-1-C^{14} which had an activity of 0.5 millicuries was distilled under vacuum into 20 ml. of purified reagent grade toluene that was contained in a receiver immersed in dry ice-acetone. This solution was transferred with numerous washings to a 250 ml. volumetric flask which was then filled to the mark.

Thirty grams of the toluene was nitrated by the procedure described in "Organic Syntheses with Isotopes" (38). The compounds of the product solution were separated by vacuum distillation through a spinning band column. Recrystallization of the para isomer from 95% ethanol gave 6.8 g. of product, m.p. 50-51°. Yield, 15%.

p-Hydrazotoluene-4,4'-C^{14}.--The p-nitrotoluene-1-C^{14} was reduced by the procedure of Carlin (2), which was scaled down by a factor of 17. The yield was 68.5%.

Benzoic acid-1-C^{14} was prepared by permanganate oxidation (39) of toluene-1-C^{14}. Yields of 90-98% were obtained. The highest yield was obtained when the reaction mixture was kept just below the reflux temperature.

Methyl benzoate-1-C^{14} was prepared in virtually quantitative yield by the reaction of diazomethane with benzoic acid.

Copper chromite was prepared by the method of Vogel (40).

Attempted Preparation of Toluene-α-D_3-1-C^{14}.--All hydrogenations were carried out in a 500 cc. bomb. The product compositions were determined by gas chromatography with an Apiezon-J Column.

TABLE III

Hydrogenation of Methyl Benzoate in the Presence of Copper Chromite[a]

No.	Solvent	Grams of methyl benzoate	Press.[b] of H_2 in Psi	Temp.	Time	Product Composition[c]		
						MeOBz	φCH_2OH	φCH_3
1	EtOH 195 ml. abs.	25	1450-1500	190[d]	15 hrs.	100	-	-
2	"	"	1500	250-90	12 hrs.	67	28	25
3	EtOH 200 ml. abs.	"	"	"	67 hrs.	-	30	70
4	"	"	1450	320-40	64 hrs.	-	< 2	>98
5	Methyl-cyclohexane 200 ml.	27	"	"	63 hrs.	100	-	-
6	-	18[e]	1500	"	41 hrs.	1 g.	-	sm.
7	-	27	"	"	140 hrs.	60-70	-	30-40
8[f]	EtOH 250 ml. abs.	25	1650[f]	"	73 hrs.	-	trace	> 98

[a] Ten grams of catalyst was used in all runs except No. 6.

[b] This refers to the initial pressure of the gas before the bomb was heated. The pressure was never allowed to drop below 1100 psi. Considerable amounts of hydrogen dissolved in ethanol, but very little went into methylcyclohexane or methyl benzoate. It is felt that higher pressures of hydrogen would have significantly shortened the reaction time. The practice runs were, however, governed by the size of the bomb and the supply of deuterium gas.

[c] All values are approximate and as no other products were detected by VPC, it was assumed that starting material was completely accounted for by the compounds listed here.

[d] It is estimated that 5-6 hours are required for the contents of the bomb to reach the temperature indicated by the thermocouple.

[e] Five grams of catalyst were used.

[f] Reaction of radioactive methyl benzoate with deuterium. As toluene and ethanol form an azeotrope, the two were separated by addition of an equal volume of water to the solution followed by extraction of the resulting mixture with pentane. The separated pentane solution was then dried with calcium chloride, and the toluene was recovered by distillation. The infrared spectrum of the radioactive toluene obtained from the actual deuteration showed only a trace of possible C-D absorption around 2100 cm^{-1} and the usual C-H absorption of the methyl group in the 2000-3000 cm^{-1} region.

Benzyl Alcohol-α-D_2-1-C^{14}.--A solution of 38 g. (0.316 M) of benzoic acid-1-C^{14} in several hundred ml. of ether was added with stirring over a period of 1.5 hours to 20 g. (> 0.45 M) of LiAlD (> 95% purity) in 650-700 ml. of ether. The mixture was stirred for a total of fourteen hours, after which time it was worked up by standard techniques. A total of 28.7 g. (83.5% yield) of benzyl alcohol-α-D_2-1-C^{14} was isolated (b.p. 95° at 10 mm.).

Benzyl Chloride-α-D_2-1-C^{14}.--To 50 ml. of thionyl chloride (0.69 M) in 50 ml. of ether was added the 28.7 g. (0.26 M) of benzyl chloride in 45 ml. of ether. The resulting solution was stirred at room temperature for seven hours and then distilled. The gas that was evolved during distillation probably came from either the formation and resulting decomposition or from the decomposition of the previously formed benzyl chlorosulfite. Thirty grams (91% yield) of benzyl chloride-α-D_2-1-C^{14} was collected at 92-93°, at a pressure of 50 mm.

Toluene-α-D_3-1-C^{14}.--To 5.69 g. (0.234 M) of magnesium turnings in 80 ml. of anhydrous ether was added gradually over a 20 minute period the 30 g. (0.234 M) of benzyl chloride. It was necessary to apply gentle heat to initiate the reaction which was then controlled by intermittent cooling with an ice water bath. After all of the benzyl chloride had been added, the reaction mixture refluxed spontaneously for 10-15 minutes; heat was then applied for another 25 minutes to continue the reflux action. After this time 25 g. of D_2O (1.25 M) was added over a 30 minute period. The magnesium salts soon coagulated and left a clear ether solution. The mixture was stirred for 100 minutes under gentle reflux and was then worked up. A total of 19.6 g. (88% yield) of toluene-α-D_3-1-C^{14}, which contained a trace of ether, was isolated. Analysis by n.m.r. showed 0.15 atoms of deuterium per molecule of toluene in the ring. No hydrogen could be detected in the methyl group by n.m.r. while the infrared spectrum indicated a possible trace. The overall yield based on the 30 g. of starting toluene-1-C^{14} was 63%.

p-Aminohydrazobenzene.--p-Aminohydrazobenzene was prepared by the method of Ruggli and Holze (41). A solution of 0.3 g. of p-aminoazobenzene in 2 ml. of ethanol was heated gently and treated with small portions of concentrated ammonium hydroxide and zinc dust. The addition of the latter materials was continued until the solution appeared colorless. About 5 ml. of ethanol was then added and the mixture was filtered and cooled in ice water. Water was then added dropwise to the cold swirled solution. Fine crystals formed if the water was added carefully, but only an oil would result if the addition was too fast. The yields were generally about 50%. The compound was quite unstable and would quickly darken on exposure to air.

Potassium Nitrate-N^{15}.--Potassium nitrate-N^{15} was prepared by the neutralization of 6.15 ml. of 5.41F nitric acid-N^{15} (Isomet Corporation) of 99.7% isotopic purity. The end point was determined with a pH meter. A solution of 3.38 g. of potassium nitrate in 25 ml. of water was added to the neutralized solution which was then evaporated to dryness to give 6.71 g. of potassium nitrate. The nitrogen-15 content was approximately 50%.

m-Nitromethylbenzoate-$N^{15}O_2$.--A solution of the 6.71 g. (0.066 moles) of potassium nitrate in 30 ml. of concentrated sulfuric acid was added dropwise over a one hour period to 9.00 g. (0.066 moles) of methyl benzoate. The resulting mixture was stirred for an additional 90 minutes and then poured onto 50 g. of ice. The precipitated solid was separated by filtration and stirred for several hours at zero degrees in 9 ml. of methanol. The meta-isomer, which was separated by filtration, weighed 8.57 g. (72% yield), m.p. 79°.

n-Nitrobenzoic Acid-$N^{15}O_2$.--The 8.57 g. of m-nitromethyl-benzoate-N^{15} was added to 3.8 g. of sodium hydroxide in 20 ml. of water which was then heated until solution was completed. The solution was heated for an additional 5 minutes, after which time it was cooled to room temperature and poured into 20 ml. of cold concentrated hydrochloric acid. The resulting white precipitate was separated and dried to give 7.57 g. (yield, 96%).

m-Nitroaniline-$N^{15}O_2$.--The 7.57 g. (0.054 m.) of m-nitrobenzoic acid-$N^{15}O_2$ was dissolved in a mixture of 30 ml. of chloroform, 15 ml. of concentrated sulfuric acid, and 11 ml. of 30% oleum. A total of 3.90 g. (0.064 m.) of sodium azide was added to the stirred mixture which was then refluxed for three hours, cooled to room temperature, and poured onto 100 g. of ice. The resulting solution was neutralized with a concentrated solution of sodium hydroxide and the precipitate was separated by filtration. The dried m-nitroaniline-$N^{15}O_2$ weighed 5.40 g. (86.5% yield), m.p. 111.5-111.8°. The filtrate was extracted with ether which was then dried with magnesium sulfate. Removal of the ether left a residue which was sublimed to give 0.34 g. of a yellow-orange solid, m.p. 80-112°. This solid was dissolved in dilute hydrochloric acid and reprecipitated by the addition of aqueous sodium hydroxide to give 0.24 g. of m-nitroaniline-$N^{15}O_2$, m.p. 110-111°.

m-Phenylenediamine-$N^{15}O_2$.--m-Phenylenediamine was prepared by the method of Pietra (42). A solution of 0.161 g. of m-nitroaniline-$N^{15}O_2$ in 3 ml. of absolute ethanol and 0.2 ml. of hydrazine hydrate was heated to 40-50°. To this was added in small portions a total of 5 mg. of 5% palladium on carbon. The mixture was then heated at 80° until gas evolution ceased and the solution appeared colorless. Filtration, removal of the solvent under vacuum, and sublimation of the residue gave 83 mg. (68% yield) of the desired product, 75 mg. of which had a m.p. of 62.8-63.1°; reported, 62.8°.

m-Hydrazoaniline-$N^{15}H$-$N^{15}H$.--m-Hydrazoaniline-$N^{15}H$-$N^{15}H$ (HzA) was prepared by the electrolytic reduction of m-nitroaniline-$N^{15}O_2$ (43). A porous porcelain cylinder was placed in a one-liter beaker. The cathode, which was a cylinder of platinum gauze, was placed inside of the cylinder while a lead plate which served as the anode was placed between the wall of the beaker and the porcelain cup. The anode was connected directly to the current source while the cathode was connected to the source through an ammeter and a 40 ohm variable resistor. A solution of 2.0 g. of m-nitroaniline-$N^{15}O_2$ and 2.5 g. of sodium acetate in 20 ml. of water and 140 ml. of 95% ethanol was placed inside the porcelain cylinder while a concentrated sodium carbonate solution was placed in the anode compartment. Four amps of current were then applied for 60 minutes. Ethanol was added occasionally to maintain the volume of the boiling solution. The reaction mixture was then cooled by an external application of ice water and 2.5 amps were applied for another 70 minutes. The resulting mixture was filtered to give 0.76 g. of m-hydrazoaniline-$N^{15}HN^{15}H$, m.p. 151-158°. The filtrate was treated with an equal volume of water and concentrated to give 0.34 g. of crude m-azoaniline (AzA). A clean electrode surface and the stipulated amount of sodium acetate were necessary for complete reduction. In one reduction of labeled material only AzA was formed. The reduction to HzA was completed by bubbling hydrogen through a solution of 60-70 mg. of AzA in 5-10 ml. of ethanol to which platinum dioxide had been added. When the mixture became colorless, it was filtered. The resulting solution was then rearranged under the desired conditions.

2, 2'-Diaminobenzidine Tetrahydrochloride.--The acid salt of 2, 2'-diaminobenzidine was prepared by dissolving 0.4-0.5 g. of HzA in 5-10 ml. of glacial acetic acid which was then heated and treated with hydrogen chloride. The resulting mixture was treated with ethanol and more hydrogen chloride to complete the reaction and the precipitation of the hydrochloride salt of the benzidine. Approximately 90% yields were generally obtained. The salt could be purified by recrystallization from an ethanol-water hydrochloric acid solution. The neutralization equivalent of the salt was found to be 90.7 as compared with a theoretical value of 90.0 for the tetrahydrochloride of diaminobenzidine. The ultraviolet spectrum of the neutralized salt was the same as that of the product obtained from the rearrangement of HzA in ethanol.

2,7'-Diaminocarbazole Dihydrochloride.--2,7'-Diaminocarbazole was prepared by the method of Taüber (44). A solution of 0.100 g. of the hydrochloride of diaminobenzidine was heated in 2-4 ml. of 6F hydrochloric acid for 10 hours at 180-190°. The product solution was heated to dryness and the resulting solid was dissolved in a few milliliters of water and purified by adding zinc dust and concentrated hydrochloric acid in small portions. The light yellow solution that was obtained on filtration was treated with a few more milliliters of concentrated hydrochloric acid to precipitate the dihydrochloride of the diaminocarbazole. This salt could be further purified by recrystallization from ethanol-ether. Greater than 90% of the theoretical chloride content was recovered as silver chloride from 23.5 mg. of the acid salt of the carbazole. As high as 97% of the theoretical nitrogen content could be obtained by a Kjeldahl conversion to ammonia. The ultraviolet spectrum of the carbazole showed maxima at 3300 and 2425 Å, a shoulder at 2600 and a minimum at 2850 Å. The spectra of the carbazole obtained from the numerous conversions of diaminobenzidine were used as an indication of the purity of the carbazole. The diaminocarbazole could be converted in low yields to N-nitrosocarbazole by diazotization with nitrous acid and subsequent reduction with hypophosphorous acid.

Azobenzene-N^{15}=N^{15}-. --m-Azoaniline-N^{15}=N^{15}- was deaminated to azobenzene-N^{15}=N^{15}- by diazotization with nitrous acid and subsequent reduction of the diazonium salt with hypophosphorous acid. A typical deamination consisted of the solution of 50 mg. of AzA in several milliliters of water which contained 0.09 ml. of concentrated hydrochloric acid. The solution was cooled in ice-water and 32 mg. of sodium nitrite in a milliliter of cold water was added to the AzA solution by means of a dropper placed below the surface of the AzA solution. After about ten minutes 23 ml. of 50% hypophosphorous acid was added. The resulting solution was kept at near zero temperatures for three to six hours. The final mixture was extracted with ether which was then dried over calcium chloride. The ether was removed and the residue was sublimed at 35-40° and less than 1 micron. The best yields were about 25%. Direct addition of solid sodium nitrite resulted in much lower yields.

Sodium Hypobromite. --Sodium hypobromite was prepared by the procedure described by Rittenberg (45). Half of a solution of 50 g.

of sodium hydroxide in 75 ml. of water was added to a 200 ml. 3-necked round-bottom flask immersed in an ice bath. Then 14-15 ml. of bromine was added over a 10-minute period to the rapidly stirred solution. The remainder of the sodium hydroxide solution was then added and the yellow mixture was filtered and stored in the refrigerator. After several days the solution was filtered to remove the sodium bromide which had precipitated.

m-Chloronitrosobenzene.--Nine grams of m-chloronitrobenzene which had been recrystallized from ethanol was dissolved in a warm solution (50-60°) of 30 ml. of absolute ethanol and 30 ml. of water which contained 3.5 g. of ammonium chloride. Ten grams of 95% zinc dust was then carefully added over a 5-10 minute period. Vigorous frothing accompanied the addition of zinc. The resulting mixture was stirred for 15-20 minutes and then filtered to remove the light gray mixture of zinc and zinc oxide. The filtrate was added to a suspension of 18.5 g. of anhydrous ferric chloride in a mixture of 400 ml. of water and several hundred grams of ice. Filtration of the resulting mixture gave a light brown solid which was subjected to steam distillation until no more green liquid distilled. The collected solid was recrystallized from 95% ethanol to give 2.8 g. (35% yield) of m-chloronitrosobenzene, m.p. 71.5-72.5° (reported, 72°, 99°).

m-Chloro, m'-nitroazobenzene.--A typical preparation of this compound involved the addition of 0.912 g. (0.066 moles) of m-nitroaniline and 0.931 g. (0.066 moles) of m-chloronitrosobenzene to 20 ml. of acetic acid. Crystals of the azo compound separated after 5-10 hours. After 24-48 hours the mixture was filtered. More product was obtained by addition of water to the filtrate. The combined fractions weighed 1.29 g., m.p. 96-97°. Yields of 75-90% were generally obtained.

m-Chloro, m'-aminoazobenzene.--m-Chloro, m'-nitroazobenzene was reduced to m-chloro, m'-aminobenzene by the general procedure of Charrier and Beretta (46). A solution of 1.39 g. of m-chloro, m'-nitroazobenzene in 25 ml. of 95% ethanol was heated to 70°. To this stirred solution was added slowly a solution of 6.5 g. of sodium sulfide nonahydrate in 4-5 ml. of water. The reddish mixture that resulted was stirred for an additional thirty minutes at 70° and was then allowed to stand overnight. Sulfur was separated by filtration and 75-100 ml. of water was added to the filtrate. The resulting yellow suspension was placed in the refrigerator until the solution became clear and deposited a yellow-orange precipitate. Filtration gave a rather gummy solid which was sublimed at 80-90°, 0.001 mm. A total of 0.63 g. (50% yield) of solid was collected. The product was dissolved in ether from which it was precipitated as the hydrochloride by the addition of 0.85F ethanolic hydrogen chloride. A neutralization equivalent was determined by potentiometric titration. Found, 269; calc., 268.

When the hydrochloride was added to water, a large amount of the free base would form and not dissolve. The remainder of the free base could be precipitated by the addition of dilute sodium hydroxide. The purified m-chloro, m'-aminoazobenzene melted at 88°.

m-Chloro, m'-aminohydrazobenzene.--A solution of 5.35 mg. of m-chloro, m'-aminoazobenzene in 5 ml. of ethanol was treated with a few drops of glacial acetic acid and sufficient zinc dust to reduce the azo compound. The solution quickly became colorless and was then filtered. The filtrate was diluted to 50 ml. Three 10-ml. aliquots were withdrawn and titrated with a solution of Bindschedler's green that had been standardized with HzT. A molecular weight of 232 ± 2 was determined from the titration. The calculated value is 233. The reductions could be carried out on a larger scale or could be effected by passing hydrogen gas through a solution of the azo compound in ethanol. Platinum oxide was used as a catalyst for the reduction.

Kinetics and the Formation of the Wurster Cation.--The oxidation of the Wurster base by a solution of rearranged HzT was followed by observing the increase in absorption at 6140 Å. A Beckman DU spectrophotometer which was maintained at 26.3°C was employed. The various solutions containing HzT, and the Wurster base were brought to this temperature before they were mixed. Prior degassing of the solutions did not affect the rate constants obtained.

A typical reaction mixture was prepared by adding 10 ml. of 0.0133F hydrogen chloride in ethanol and 5 ml. of a solution of 51.7 mg. of the Wurster base in 10 ml. of ethanol to 4.6 mg. of HzT. The Wurster cation was shown to react quickly with HzT in a 2 to 1 mole ratio of salt to HzT. Thus buildup of the cation did not occur until virtually all of the HzT had reacted.

Reproduction of the kinetic Data of Carlin and Wich (2).--The kinetic procedure used by Carlin was repeated carefully in all rearrangements with but few modifications. A nitrogen purification train was constructed in which the nitrogen was passed over a copper pile heated to 450-500°C and then through Fieser's solution. The gas was then passed through saturating solutions of ethanol and ethanol-hydrogen chloride of the same concentration as that to be employed in the rearrangement. The acid catalyst was prepared by diluting the calculated amount of standardized ethanol-hydrogen chloride to 50 ml. This solution was maintained at the temperature of the constant temperature bath and treated with nitrogen at the same time the other solutions were being flushed. The nitrogen treatment was continued for 1-2 hours, after which time 25 ml. of the catalyst solution was added to a volumetric flask. This flask was placed in the constant temperature bath for a few more minutes and then its contents were added to a solution of approximately 35 mg. of HzT in 250 ml. of 95% ethanol. Before the catalyst was added, the nitrogen was passed through ethanol, the ethanol-HzT solution, the ethanol-hydrogen chloride saturating solution, and finally through the catalyst solution. After the catalyst had been added, the nitrogen was passed from ethanol to ethanol-acid and finally to the HzT solution.

The rate of disappearance of HzT was followed by two methods. One was that of Carlin in which 2 ml. aliquots of the reaction solution were withdrawn at various time intervals and added to 2 ml. of water, 1 ml. of 0.3188F sodium hydroxide and sufficient ethanol to give a final volume of 25 ml. Ultraviolet readings were taken at 2350, 2500, 2750, and 2950 Å. The data of Carlin were used without any modifications to calculate the concentrations of the various components. The second method was that of direct titration of the HzT with aqueous solutions of approximately 150 mg. of Bindschedler's Green per liter of water. Ten-ml. aliquots were withdrawn, partly neutralized with aqueous sodium hydroxide and titrated.

For all rearrangements for which the t_o concentrations were obtained before the catalyst was added, the intercepts of the plotted line were significantly above the points for the initial concentrations. This result was attributed to the presence of the excess local acid concentration that occurred on addition of the catalyst. In support of this idea was the observation that the deviation was lowered by use of a lower acid concentration.

The use of water in the quenching solution seemed to give a shift in the absorption pattern. The calculated p-toluidine concentration was proportional to the amount of water and thus seemed to be in error. The use of sodium hydroxide in ethanol as the quenching solution (with no extra water) did not give this trouble and a decent check of the apparent product composition with that reported by Carlin was obtained. The following table gives apparent percentage composition of the various products after 5 hours (5-6 half lives) of rearrangement of the starting material at zero degrees.

TABLE IV

Percentage Composition of the Products of the Rearrangement of HzT*

#	Azotoluene	p-Toluidine	o-Semidine
1	22	40	38
2	19	41	41
3	21	40	39
4	20	41	39

*There is always some HzT left after 5 hours, but these compositions are calculated only on the basis of the total product and do not include starting material.

The best data were obtained when a fresh blank solution was prepared at the time of sampling the rearrangement solution. Distilled 95% ethanol was used in most of the rearrangements.

Kinetics of the Rearrangement of HzA.--The acid dependence of the rate of rearrangement of HzA was determined by rearranging 0.1 g. samples of this compound in 280 ml. of 95% ethanolic hydrogen chloride at 40.2-40.5°. The added acid concentration was varied from 0.01 to 0.0442F. The reaction was found to be too slow at zero degrees to observe any rearrangement over the period of 12-24 hours. The disappearance of HzA was followed by titration with Bindschedler's Green.

One rearrangement was carried out in the presence of an added acid concentration of 0.002F. The observed first order rate constant was 1.84×10^{-2} min.^{-1}, which corresponds to a half life of 37.6 minutes. A 67.21 mg. sample of HzA was used which corresponds to 1.12×10^{-3} moles per liter. As the concentrations of HzA and added acid were so close together, a corrected acid concentration and a corrected rate constant could not be accurately calculated.

Kinetics of the Rearrangement of m-Chloro, m'-aminohydrazobenzene.--m-Chloro, m'-aminoazobenzene was reduced to the corresponding hydrazo compound by the methods described earlier. The solutions containing the m-chloro, m'-aminohydrazobenzene were diluted to 250 ml. with 95% ethanol. The diluted solution was brought to the desired temperature and was flushed with nitrogen which passed through a saturating solution of ethanol or hydrogen chloride in ethanol.

Water-cooled condensers were attached to the various flasks through which the nitrogen passed. After one-half to one hour a specific concentration of hydrogen chloride in 25 ml. of 95% ethanol was added to the solution of the hydrazo compound. The rearrangements were carried out at 40° and 60°. At the former temperature the rate of rearrangement was followed by titration of unreacted starting material with solutions of Bindschedler's Green. At 60° the rate of rearrangement was followed by observing the absorption at 2450 Å of the neutralized aliquots of the solutions of the rearranging hydrazo compound. A [illegible] plot of $1/A_t - A_\infty$ vs. t was used to obtain the rate constants. "A_∞" is the final (minimum) absorption while "A_t" is the absorption at any time t. The data that were obtained are shown below in Table V.

TABLE V

Rate Data Obtained from the Rearrangement of m-Chloro, m'-aminohydrazobenzene

#	Temp., °C	$[H^+]$	$k_o \times 10^4$ min.$^{-1}$
1	40	0.0100	1.47
2	40	0.03665	1.72
3	60	0.03600	17.6
4	60	0.0100	18.3
5	60	0.03600	15.6
6	60	0.06600	21.0

Water was used in the constant temperature bath. As a result the temperature regulation was quite poor.

Rearrangement of Hydrazobenzene in the Presence of Acrylonitrile.--A solution of 216 ml. of denatured ethanol, 5.7 ml. of acrylonitrile, and 5.1 g. of hydrazobenzene was placed in a 500 ml. flask and treated with nitrogen. To this solution was added slowly 72 ml. of nitrogen-treated 0.89F hydrochloric acid. The concentrations of the reactants were 0.1M, 0.29M, and 0.22F for hydrazobenzene, acrylonitrile, and hydrochloric acid, respectively.

After several hours, 55 ml. of concentrated hydrochloric acid was added to the reaction solution. A white solid was separated and dissolved in hot water. The aqueous solution of the salt was added to a 10% sodium hydroxide solution which contained 200 g. of ice. The resulting solid was separated and recrystallized from ethanol-water. The infrared spectrum of this material was identical to that of reagent grade benzidine. No solid other than benzidine could be obtained from the product solution. Polymer would not have been soluble in ethanol-water and both α- and β-anilinopropionitrile are reported to be insoluble in ethanol-water.

Rearrangement of Hydrazotoluene (HzT) in the Presence of Acrylonitrile.--To a nitrogen-treated solution of 13.7 g. of HzT in 600 ml. of 95% ethanol and 22.5 ml. of acrylonitrile was added 120 ml. of concentrated hydrochloric acid. The concentrations of the reactants were 0.087M, 0.46M, and 1.9F for HzT, acrylonitrile and hydrochloric acid, respectively. After 45 minutes the solution was chilled with ice-water and then filtered to give an orange-yellow compound. The filtrate was diluted with 800 ml. of water to give further precipitation of the yellow solid. The filtrate obtained from this mixture was neutralized with 120 ml. of 15F ammonium hydroxide and the resulting yellowish-brown solid was separated by filtration. The final filtrate was extracted with ether which was then dried with sodium sulfate. The first two fractions had a combined weight of 3.1 grams and melted from 130-139°; while the third fraction weighed 5.2 grams and melted from 91-99°. Infrared spectra were taken of the solid fractions and of the reddish residue that remained after evaporation of a portion of the ether extracts. Only the latter compound indicated the presence of a nitrile group. The first two compounds were identified as p-azotoluene and the o-semidine.

The red residue was dissolved in an ether-pentane mixture and passed through an alumina chromatography column. The column was eluted with pentane-ether mixtures, ether, methanol, and benzene. The spectra of the various fractions, which had a combined weight of about 3 grams, as well as of the original material, were virtually identical to that of p-toluidine. Several spectra showed what was possibly a weak carbonyl absorption and the final minor fractions that were collected showed the presence of the nitrile group along with the peaks of p-toluidine.

Rearrangement of HzT in the Presence of Styrene.--To 250 ml. of nitrogen flushed 95% ethanol were added 10 ml. of purified styrene, 4 g. of HzT, and 25 ml. of 0.228F hydrogen chloride in 95% ethanol. The concentrations of the reactants were 0.066M, 0.30M, and 0.02F in HzT, styrene, and hydrochloric acid, respectively. No polymer formation was visibly observed and removal of solvent left a solid residue which was not analyzed but was characteristic of the products of the normal rearrangement and gave no indication of the presence of telomer or of polymer.

Attempted Production of Benzidine by the Reaction of Phenylhydroxylamine with Titanium Trichloride.--To a solution of 10 g. (0.092 moles) of phenylhydroxylamine in 100 ml. of methanol was added over a 2 minute period a solution which contained 48 ml. of 3F hydrochloric acid and 100 ml. of quite impure aqueous titanium trichloride. The titanium trichloride solution was later determined to be approximately 0.4F. The reaction mixture was 0.33M in phenylhydroxylamine, 0.5F in acid, and about 0.13F in titanium trichloride. The purple color of titanium(III) disappeared immediately. The solution which had originally been yellow became an opaque brown, and a dark green solid formed. The separated solid turned blue when it was washed with water or dilute alkali. Sublimation of the solid gave a yellow compound whose infrared spectrum and melting point (34-35°) were the same as those of azoxybenzene. Aqueous sodium hydroxide was used to precipitate titanium from the product solution. The titanium hydroxide was removed by filtration and the filtrate was extracted with ether which was then dried with magnesium sulfate. The ether was removed and the remaining oil was treated with benzoyl chloride, benzene, and pyridine. A solid was obtained which had an infrared spectrum quite similar to that of benzanilide.

A solution of 2.00g. (0.0183 moles) of phenylhydroxylamine in 100 ml. of ethanol and 1 ml. of concentrated hydrochloric acid was titrated with a 1.9F titanium trichloride solution. A total of 18.8 ml. (0.0358 moles) of the latter solution was added before the titanium color persisted. The stoichiometry of the reaction was 2 moles of titanium to one of phenylhydroxylamine. Only aniline was isolated from the reaction mixture.

A solution of hydroxylamine hydrochloride and acrylonitrile in methanol was treated with titanium trichloride. A gelatinous white precipitate formed. An infrared spectrum of a mull of this precipitate was quite similar to a spectrum of polyacrylonitrile which had been prepared by the reaction of acrylonitrile with potassium persulfate and titanium trichloride. The spectra of both solids showed sharp nitrile bands. An attempt to initiate the polymerization of acrylonitrile with phenylhydroxylamine and titanium trichloride gave no visible polymer formation.

Rearrangement of HzT in the Presence of Formic Acid.--Five milliliters of 1.5F hydrochloric acid was added to a solution of 2 g. of HzT in 200 ml. of 95% ethanol and 20 ml. of formic acid (98-100%). No gas was evolved and the reaction solution gradually became darker until it was an almost opaque brown color.

A cursory investigation indicated that Bindschedler's Green (an organic cation) would react with neither formic acid nor formate ion in an aqueous medium.

Numerous experiments were carried out in which HzT was rearranged in neat 98-100% formic acid to which potassium formate had often been added. Infrared spectra were taken of the gas that was evolved. Absorption characteristic of formic acid and carbon dioxide was detected. A similar absorption of carbon dioxide was observed from a spectrum of the vapors of a formic acid control experiment in which no HzT was present. In a number of the runs formic acid was added (in an apparatus sealed from the atmosphere) from a dropping funnel to HzT. In other runs the addition was reversed. The agitation produced by the addition process was sufficient to cause evolution of formic acid vapors.

Attempted Detection of Intermediate Radicals by Electron Spin Resonance.--One and a half milliliters of a solution of 0.436 g. of HzT in 95% ethanol and one and a half milliliters of a solution of

2.6 ml. of 1.5F hydrochloric acid diluted to 100 ml. with 95% ethanol were degassed and then mixed after they had warmed to room temperature. The resulting solution was initially 0.069M in HzT and 0.0195F in hydrochloric acid. After three minutes the solution was frozen and scanned in the electron spin resonance machine. No signal was obtained. However, the concentrations of the reactants were quite unfavorable for the production of a significant steady state concentration of radicals.

Rearrangement of HzT in the Presence of N-Phenylhydroxylamine.--To each of two 500-ml. flasks was added 200 ml. of ethanol and 1.9 g. of HzT. To one of the flasks was added 0.8 g. of phenylhydroxylamine. Two 50-ml. portions of acid, which consisted of 16.5 ml. of 1.5F hydrochloric acid, and 33.5 ml. of water, were treated with nitrogen and then added to the two stirred HzT solutions which had also been flushed with nitrogen. The solutions were thus initially 0.1F in acid, 0.03M in phenylhydroxylamine, and 0.035M in HzT.

After 15 minutes the control run was an opaque brown color while the solution containing the phenylhydroxylamine was not much darker than the original yellow color of the HzT solution.

About 0.68 g. (33%) of p-azotoluene, m.p. 138-147°, was isolated by addition of 300 ml. of water to the rearrangement solution which contained precipitated p-azotoluene. The filtrate was neutralized with concentrated ammonium hydroxide to give 0.50 g., m.p. 79-83°, of a light colored precipitate which gradually became darker.

The basic filtrate was extracted with ether, which was then dried with magnesium sulfate. The yellow ether solution was concentrated to several milliliters. Portions of this were analyzed by vapor phase chromatography. An Apiezon-J column was used at 175°. All of the peaks that were formed had the same retention time as those produced by a mixture of azoxybenzene and p-toluidine in ether. The azoxybenzene gave several peaks which were probably due to its decomposition products. Infrared analysis of the solid residue that remained after the ether was removed showed all of the peaks that could be attributed to p-toluidine and azoxybenzene.

The Stability of Phenylhydroxylamine.--A solution of phenylhydroxylamine identical to the one which was rearranged was prepared, except that no HzT was added. The solution was divided into separate portions, one of which was neutralized with ammonium hydroxide. The acidic and neutralized solutions were worked up by the procedure used for the HzT-phenylhydroxylamine solution. The final solid residues were found by infrared analysis to be mixtures of phenylhydroxylamine and azoxybenzene. The ultraviolet spectrum of an aliquot of phenylhydroxylamine in ethanol which was made alkaline with aqueous sodium hydroxide was found to be identical to that of nitrosobenzene.

Rearrangement of HzT in the Presence of N,N,N',N'-Tetramethyl-p-phenylenediamine Dihydrochloride (Wurster Base). -- Three milliliters of a solution of 93.3 mg. of HzT in 250 ml. of nitrogen-flushed 95% ethanol was added to one compartment of a three-compartment vessel. Five milliliters of a solution of 2.91 ml. of 1.5F hydrochloric acid diluted to 250 ml. with 95% ethanol were added to the second compartment and 14.5 mg. of the Wurster base was added to the third. The latter compound was always used as the dihydrochloride. The solutions were degassed five times and the Wurster base was then dissolved in the ethanol-acid solution. The two solutions were then mixed. Within thirty minutes the solution had changed from yellow to a clear blue. The initial reaction mixture was 6×10^{-4}M in HzT, 7.7×10^{-3}M in the added Wurster base, and 1.1×10^{-2}F in added acid.

A control was run in which no HzT was added. The solution was initially light blue and did not visibly darken.

Two grams of HzT (1.7×10^{-2}M) were rearranged in 275 ml. of nitrogen-flushed ethanol that was 0.11F in hydrochloric acid and 7.7×10^{-3}F in the Wurster base. After one minute the originally yellow solution began to darken and in another minute had turned very dark blue.

Determination of the Basicity Constants for the Wurster Base.-- The necessary data were obtained by ultraviolet analysis. The extinction coefficients for the neutral and diprotonated forms were determined at 260 mμ and 262.5 mμ. Each sample was run against a blank of the same solvent composition.

The extinction coefficients for the neutral form were obtained by adding an excess of 1F sodium hydroxide to a solution of the Wurster base in 250 ml. of 95% ethanol. Average values of ϵ_{260} of $1.60 \pm 0.015 \times 10^4$ liters mole^{-1} cm.$^{-1}$ and $\epsilon_{262.5}$ of $1.58 \pm 0.012 \times 10^4$ liters mole^{-1} cm.$^{-1}$ were obtained.

The extinction coefficients for the diprotonated form were determined in 1:1 ethanol-concentrated hydrochloric acid. The absorption maximum for a given sample composition had reached a minimum at this acid concentration. The result for ϵ_{260} was $3.01 \pm 0.01 \times 10^2$ and for $\epsilon_{262.5}$ was $1.77 \pm 0.03 \times 10^2$.

The extinction coefficients for the monoprotonated form were determined only approximately as the $\lambda_{max.}$ for the neutral (260 mμ) and monoprotonated (262.5 mμ) were quite close. Various samples of 3.2 mg. of the Wurster base in 250 ml. of 95% ethanol were checked over the acidity range of 4.1×10^{-4} to 8.2×10^{-4} F. In this manner ϵ_{260} and $\epsilon_{262.5}$ were found to be 2.06×10^4 and 2.15×10^4, respectively.

The equilibrium constant ($K_1 = [BH^+]/[B][H^+]$) for the first protonation was determined in solutions of low acidity where no diprotonated base existed. Similarly, the second equilibrium constant (K_2) was measured in solutions of rather high acidity where no neutral base was present. Three samples of 3.0, 3.7, and 2.7 mg./250 ml. ethanol of the Wurster base were checked at 260 and 262.5 mμ. The acid concentration is twice the concentration of the added base as the latter was added as the dihydrochloride. The concentrations of the neutral and monoprotonated base were determined from the absorption data and three values of K_1 were calculated. They were 5.7×10^4, 4.5×10^4, and 15.2×10^4 for the 3.0, 3.7, and 2.7 mg. samples, respectively. Two samples of 1.4 mg. of the Wurster base in 250 ml. 0.1F and 0.2F ethanol-hydrochloric acid were prepared.

TABLE VI

#	Conc. of sample	$[H^+]$	Absorption 260	Absorption 262.5	Calculated sum of mono- and diprotonated form	K_2
1	5.90×10^{-5}	0.1F	0.942	0.976	8×10^5 m/ℓ.	10
2	"	0.2F	0.552	0.570	6.6×10^{-5} m/ℓ.	7.5

The data are quite crude. An approximate value of 7 was chosen for K_2. The value of 7.5 corresponds to data which give a mass balance that is about 12% too high, while the data for sample #1 give a mass balance that is 50% in excess of that actually present.

Stability of the Oxidizing Agent. --A solution of 5.0 mg. of HzT in 10 ml. of 0.0134F hydrogen chloride in ethanol was prepared. After 26 minutes this solution was neutralized with a sodium ethoxide solution. After a total of 91 minutes 5 ml. of a solution of 49.8 mg. of the Wurster base in 10 ml. of ethanol which contained 2 drops of concentrated hydrochloric acid was added. Approximately a two minute induction period occurred and a maximum absorbency (A_∞) of 1.20 was observed. A value of the extinction coefficient for Wurster's Blue perchlorate was determined and found to be 1.13×10^4. The concentration of HzT based on the final volume of solution was 1.57×10^{-3} m/ℓ. while the Wurster Blue was about 1.1×10^{-4} m/ℓ.

A solution of 5.3 mg. of HzT in 10 ml. of 0.0134F hydrogen chloride in ethanol was prepared. After 90 minutes 5 ml. of a solution of 50.8 mg. of the Wurster base in 10 ml. of ethanol was added. A maximum absorbence of 0.600 was obtained. The concentration of HzT was 1.67×10^{-3} m/ℓ. while the first concentration of the Wurster Blue was 5.3×10^{-5} m/ℓ.

Ten milliliters of 0.0133F ethanol-acid was added to 14.8 mg. of HzT. After 35 minutes 10 ml. of a solution of 104.3 mg. of the Wurster base (the dihydrochloride) in 15 ml. of 0.0296F sodium hydroxide in ethanol was added. After a total of 95 minutes 20 ml. of 0.0133F ethanol-acid was added. Increase in absorption at 6140 Å did not occur until approximately one half hour had passed. A maximum of 0.052 was obtained. The concentration of HzT was 1.74×10^{-4} m/ℓ.

Attempted Oxidation of the Wurster Base by p-Aminobenzyl Alcohol.--A solution of one milligram of p-aminobenzyl alcohol in 10 ml. of nitrogen-flushed ethanol was placed in one compartment of the degassing apparatus. In another compartment was placed a solution of approximately 50 mg. of the Wurster base in 5 ml. of ethanol. The two solutions were degassed and mixed and part of the resulting soltion was poured into a uv cell. Some oxidation did occur at a very slow rate as indicated by the absorption at 6140 Å. In two and one-half hours the optical density had reached 0.280 and after 24 hours it was 0.376. The concentration of p-aminobenzyl alcohol was 8.15×10^{-4} m/ℓ. and that of the Wurster salt, 3.33×10^{-5} m/ℓ.

Attempted Oxidation of the Wurster Base by the Product of the Neutralization of p-Aminobenzyl Chloride Hydrochloride.--p-Aminobenzylchloride hydrochloride was soluble in dimethyl sulfoxide and ethanol. It appeared to dissolve and reprecipitate from dimethyl formamide and was insoluble in benzene. The salt seemed to undergo a heterogeneous modification while in contact with benzene. Addition of a benzene-potassium-t-butoxide solution of the hydrochloride in dimethyl sulfoxide produced an orange to deep red solution, the intensity of which depended upon the initial concentration of the hydrochloride. These solutions would oxidize the Wurster base at a rate that was qualitatively much faster than that observed with the unknown obtained from HzT. The solvent compositions were, of course, different in the two cases. A blank of benzene-potassium-t-butoxide gave only a light yellow solution. Ultraviolet absorption spectra were quite indefinite. The basic solution had a small maximum at 3650 Å and a larger one at 2700 Å which may have been due to benzene. The acidified solution exhibited small maxima at 3360 and 4000 and the larger one at 2400 Å.

Addition of the hydrochloride to a solution of the Wurster base in ethanol gave no oxidation other than that which could be attributed to air oxidation. Neutralization of a solution of the hydrochloride in ethanol resulted in a precipitate which appeared to be the same as that obtained upon neutralization of aqueous solutions. Apparently the solution of the hydrochloride in ethanol was either accompanied or followed by its polymerization. Addition of a solution of the hydrochloride in dimethyl sulfoxide to a solution of the Wurster base in ethanol resulted in no oxidation.

Attempted Oxidation of the Wurster Base by p-Tolylhydroxylamine.--To a solution of 0.125 g. of the Wurster base dihydrochloride in 25 ml. of 95% ethanol was added 0.55 mg. of p-tolylhydroxylamine (prepared by the procedure used for the preparation of phenylhydroxylamine). The concentration of the Wurster base was 2.11×10^{-2}M, of hydrogen ion approximately 2.11×10^{-2}F, and of p-tolylhydroxylamine 1.79×10^{-4}. After twenty-five minutes at 27° the absorption had increased only 0.05 units. Approximately two minutes were required for a similar increase in absorption in the oxidation of the Wurster base (2.11×10^{-2}M) by a solution of HzT (6.92×10^{-4}M) the acid concentration of which was 2.96×10^{-2}F.

Photolysis of p-Aminobenzyl Alcohol.--Several 0.01M solutions of p-aminobenzyl alcohol in benzene were photolyzed in the presence and absence of acetophenone (1M). The photolyses were carried out with an immersion reactor with 3130 Å light. In both cases a reddish gelatinous precipitate quickly formed. It was not possible to analyze this material which was probably of polymeric nature.

Photolysis of Aniline.--Two solutions of 0.1M aniline in ethanol were photolyzed in the immersion reactor with unfiltered light. One was made 1.0F in nitric acid and was saturated with sodium nitrate. The second was made 0.3F in trichloroacetic acid. The first solution quickly turned dark red and was not analyzed while the second solution became dark more slowly and gave only a red gummy material upon removal of solvent. Only the second solution was degassed.

An aqueous solution that was 1F in sodium sulfate, 0.2F in sodium bisulfate, and 1M in aniline was irradiated after it had been degassed and filled with nitrogen. A dark colored precipitate soon deposited. An infrared spectrum of a mull of this material was quite poor but was certainly different from that of benzidine sulfate.

Another solution that was 1F in sodium sulfate, 5×10^{-3}F in sodium bisulfate, and 1M in aniline was carefully degassed and then subjected to flash photolysis. Another solution that was slightly more concentrated with respect to aniline was subjected to flash photolysis with a low pressure xenon lamp. Both solutions were flashed 100 times and nothing more than a slight color change in the second solution was observed.

Rearrangement of HzT in Ethanol-O-D.--To a solution of 1 g. of HzT and 2 g. of sodium perchlorate in 50 ml. of nitrogen-flushed 95% ethanol was added one gram of the Wurster base. This gave an approximate initial acid concentration of 0.084F. After 20 minutes 25 ml. of water was added and the resulting mixture was chilled and filtered free from the precipitated AzT, which weighed 0.30 g. The filtrate was treated with 2 ml. of concentrated ammonium hydroxide and 75 ml. of water to give another 0.23 g. of a light yellow precipitate. The light yellow filtrate was extracted with ether which was then dried with magnesium sulfate. The ether was removed and the resulting oil was dissolved in methanol-ether and passed over an alumina column. The column was eluted first with ether which removed the Wurster base and then with methanol which removed p-toluidine. A few milligrams of pure p-toluidine were obtained by thermal sublimation of the residue left after removal of the methanol. Infrared spectra were taken of all three fractions. No C-D absorption was observed.

Procedure Used for the Recovery of the Products of the Rearrangement of Radioactive HzT in the Isotope Dilution Analyses.--Approximately 35 mg. of HzT was rearranged at zero degrees in 275 ml. of 95% ethanol which was 0.015F in hydrogen chloride. After 5 hours AzT, p-toluidine, and o-semidine were added in 40, 80, and 80 mg. amounts, respectively. The ethanol was removed by distillation under vacuum and the residue was treated with 10 ml. of water. The resulting mixture was filtered and the orange AzT was dissolved in ether which was then dried with calcium chloride. The filtrate was neutralized with sodium hydroxide to precipitate o-semidine which was separated by filtration. This second filtrate was then extracted with ether which was dried with sodium hydroxide.

The AzT was purified by chromatography over alumina with pentane and ether, sublimation at 60°, and finally recrystallization from 95% ethanol.

o-Semidine was purified by one or two careful fractional recrystallizations from ethanol-water and sublimation at 60-70°. The resulting solid was white and melted in the range 108-110°.

p-Toluidine was recovered in two forms. One method involved removal of the ether to give crude p-toluidine which was purified by sublimation at 30-40°, m.p. 42-43°. The second method involved the addition of 0.5 ml. of acetic anhydride to the dried ether solution. The solution was then heated to produce the anilide and to evaporate the ether. In one reaction the Wurster base was added along with the three non-labeled products. In this case the Wurster base was separated from the anilide by bubbling hydrogen chloride through the ether solution. The filtered ether solution was concentrated to 1-2 ml. and water was added to dissolve the acetic acid and acetic anhydride, and to precipitate p-acetotoluide. The latter compound was easily purified by one or two recrystallizations from benzene.

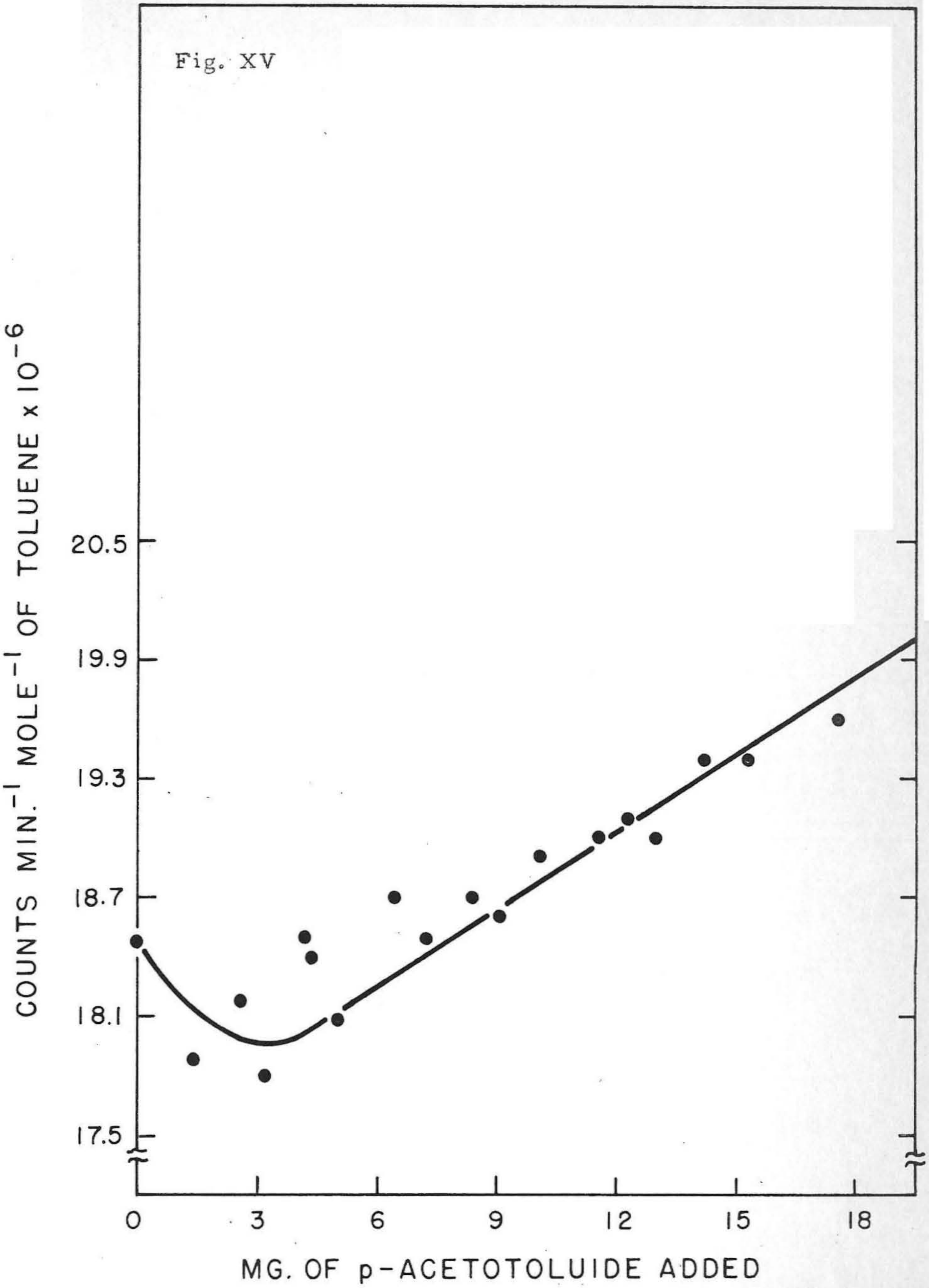
Several rearrangements were carried out in which a large excess of hydrazobenzene was added prior to introduction of the acid catalyst. After the AzT, p-toluidine and o-semidine were added, the resulting solution was concentrated to 50-75 ml. at which point benzidine was precipitated by the addition of concentrated sulfuric acid. The filtrate from this mixture was concentrated to dryness and the residue was treated with 20-30 ml. of water. The resulting mixture was heated on the steam bath for several minutes and then filtered to remove the insoluble azobenzene and azotoluene. These compounds were dissolved in ether which was then dried with calcium chloride, concentrated and chromatographed over alumina with ether. The ether was removed and the residue was sublimed at 40° and 1 micron to remove azobenzene and then at 60° to obtain AzT which was then recrystallized from ethanol. The filtrate obtained during separation of azobenzene and azotoluene was neutralized with aqueous sodium hydroxide to precipitate o-semidine and some diphenyline. The solid material thus obtained was sublimed, fractionally recrystallized from ethanol-water, and finally sublimed a second time. The resulting solid melted in the range 108-110°. The filtrate that was obtained after o-semidine had been removed was completely neutralized and then extracted with ether. The ether solution was dried with sodium hydroxide and treated with 1 ml. of acetic anhydride. The solution was then concentrated to several milliliters and treated with water to precipitate the aceto derivatives. The resulting solid was sublimed at less than 1 micron and about 110°. The p-acetotoluide which had sublimed was further purified by one or two recrystallizations from benzene.

Calibration of the Liquid Scintillation Counter Against the Rearrangement Products.--The solvent system used in this work is comprised of a solution of 3.5 g. of PPO (2.5-diphenyloxazole) and 0.1 g. of POPOP (p-bis[2-(5-phenyloxazolyl)]-benzene) in one liter of toluene. The two scintillators in some way aid in the conversion of beta rays into light emissions which are picked up and recorded. The compounds studied in these experiments acted as fluors and quenchers. Thus data had to be obtained which would show the effect of the concentration of the various compounds on the detection of the emitted beta rays. To accomplish this their effect upon toluene of a predetermined specific activity was measured. The samples to be counted were prepared by dissolving weighed amounts of the various compounds in 20 ml. of the toluene scintillation solution. They were then counted at zero degrees with a tri-carb liquid scintillation counter (Packard Instrument Company). Reproducible data were determined on different days and a plot was made of the specific activity of the radioactive toluene vs. the milligrams of the rearrangement product added. Figures XV - XVIII show the data that were plotted.

Determination of the Yields of the Products of the Rearrangement of HzT by Isotope Dilution.--Radioactive HzT was rearranged under various conditions. The weights of the radioactive samples that were counted were chosen so as to correspond to the most reproducible or to the most nearly level portions of the graphs shown in Figures XV - XVIII. In six runs a 2 ml. aliquot was withdrawn after 5 hours of rearrangement and just prior to the addition of the inactive diluents. This aliquot was checked by ultraviolet analysis to give the product concentrations as determined by the method of Carlin.

Investigation of the Product Mixture Obtained from the Rearrangement of HzT.-- To a solution of 2.5 g. of purified HzT in 150 ml. of nitrogen-flushed 95% ethanol was added slowly 0.5 ml. of concentrated hydrochloric acid. After 15 minutes another 0.5 ml. of acid was added. The initial concentration of HzT was 0.079M and the total added acid concentration was 0.08F. A solid (p-azotoluene) precipitated from the product solution which was chilled in ice-water and then filtered. The

Fig. XV


COUNTS MIN.$^{-1}$ MOLE^{-1} OF TOLUENE x 10^{-6}
20.5
19.9
19.3
18.7
18.1
17.5
0
3
6
9
12
15
18
MG. OF p-ACETOTOLUIDE ADDED

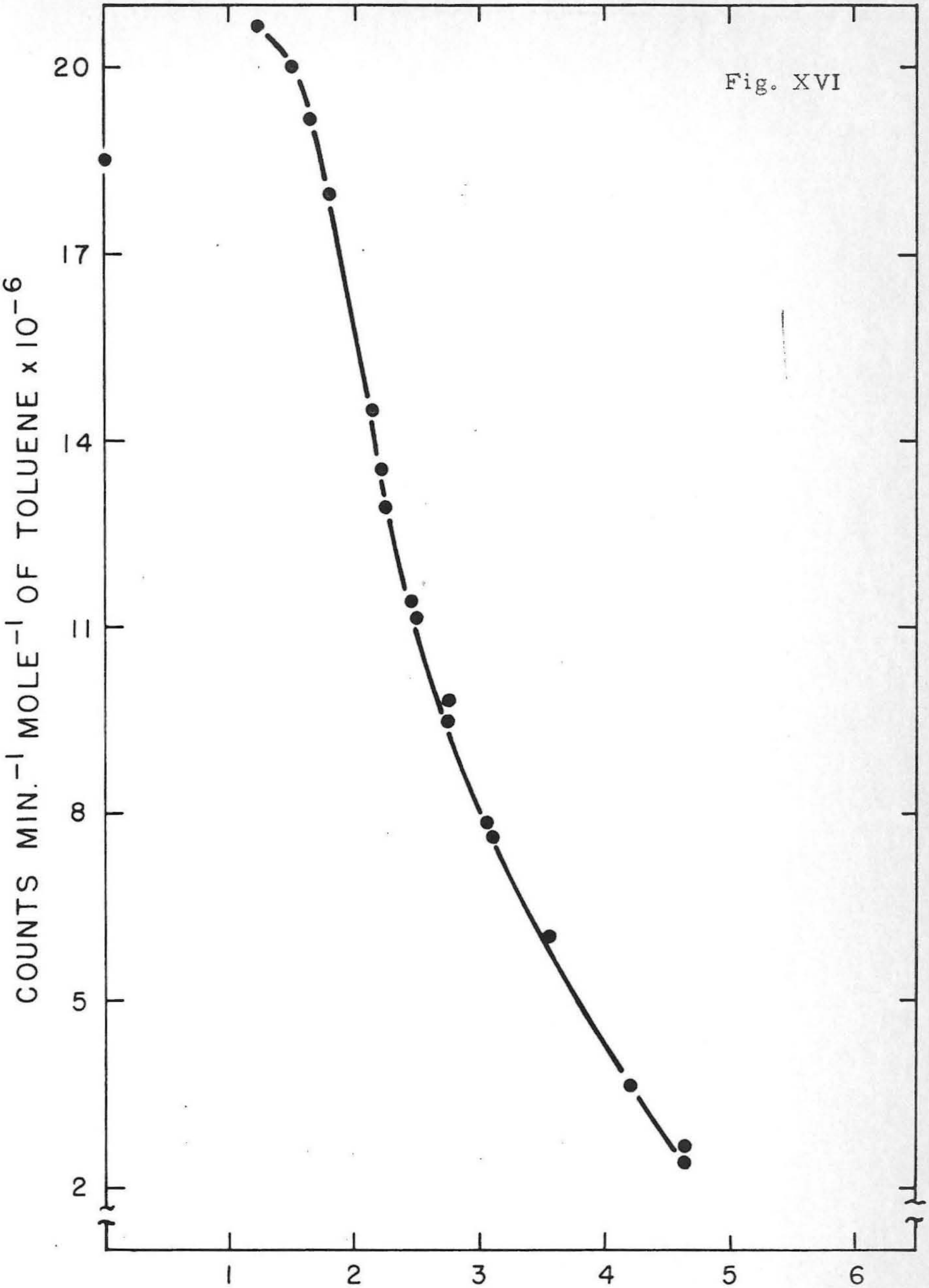
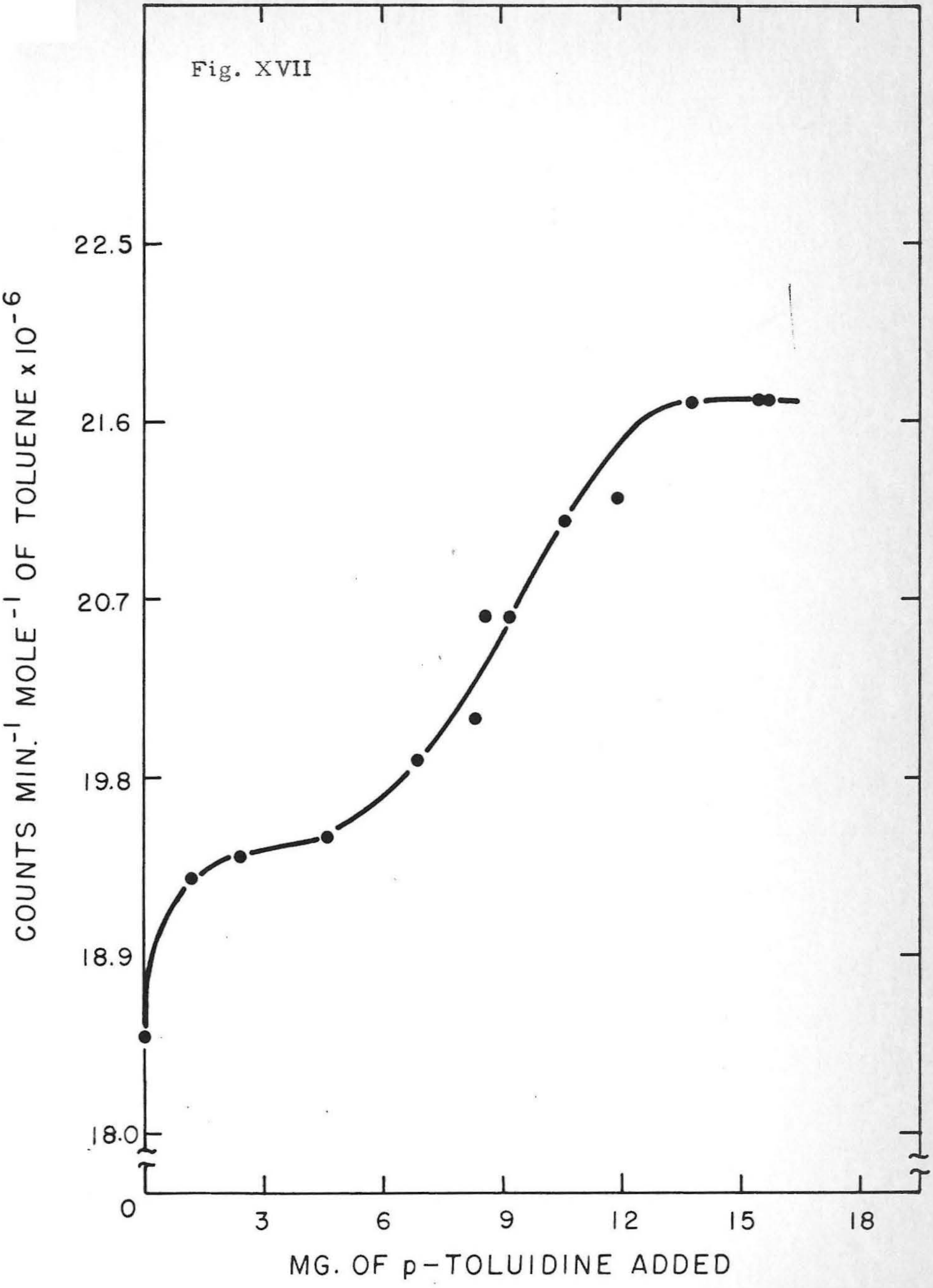


Fig. XVI
COUNTS MIN.$^{-1}$ MOLE^{-1} OF TOLUENE x 10^{-6}
20
17
14
11
8
5
2
1
2
3
4
5
6
MG. OF p-AZOTOLUENE ADDED

Fig. XVII


COUNTS MIN.$^{-1}$ MOLE^{-1} OF TOLUENE x 10^{-6}
22.5
21.6
20.7
19.8
18.9
18.0
0
3
6
9
12
15
18
MG. OF p-TOLUIDINE ADDED

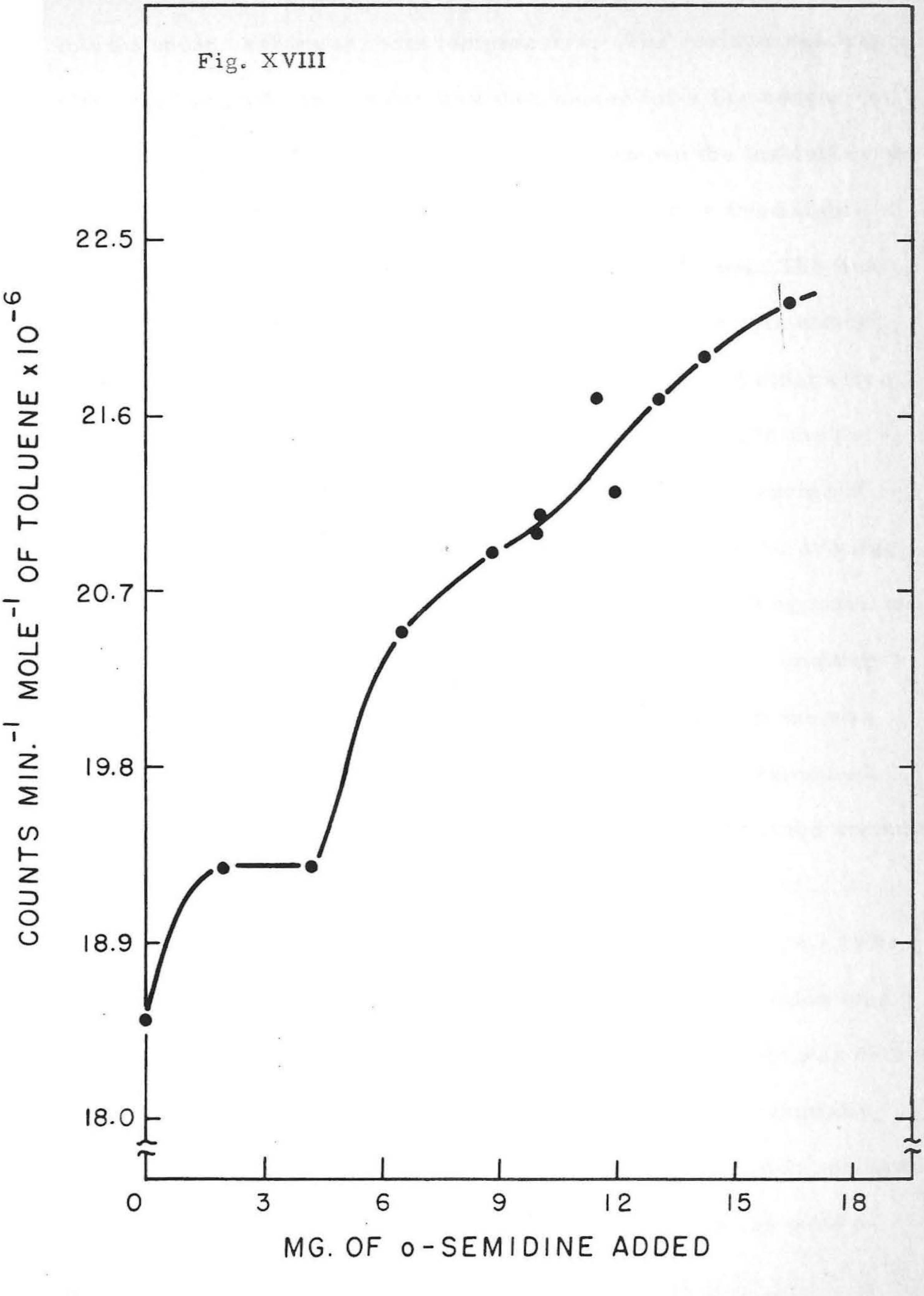


Fig. XVIII

COUNTS MIN.$^{-1}$ MOLE^{-1} OF TOLUENE x 10^{-6}
22.5
21.6
20.7
19.8
18.9
18.0
0
3
6
9
12
15
18
MG. OF o-SEMIDINE ADDED

clear orange filtrate was concentrated to dryness by removing the solvent under vacuum at room temperature. The residue was treated with 10-15 ml. of water which was then heated for a few seconds on a steam bath. The mixture was filtered to remove the insoluble compounds. The filtrate was neutralized to precipitate a third light-colored solid fraction which was separated by filtration. The final filtrate was extracted with ether which was then dried with either sodium hydroxide or potassium hydroxide. Removal of ether left a solid residue whose color depended upon the care taken in the performance of the individual steps of the procedure. In a series of eight experiments the four solid fractions accounted for an average of 26, 12, 20, and 31 percent, respectively, of the starting material.

The first solid fraction was readily identified by its melting point (140-145°) and infrared spectrum. If this p-azotoluene was slowly sublimed, a milligram or so of a brown residue remained. The residue generally contained some p-azotoluene and could account for but a trace of the total products.

The second solid fraction was seen by infrared analysis to be a mixture of p-azotoluene and the o-semidine. No absorption other than that which could be attributed to these two compounds was detected.

The infrared spectrum of the third fraction was essentially identical to that of pure o-semidine. Very weak absorption appeared at about 1685 $cm.^{-1}$ that was not present in spectra of the pure o-semidine.

The infrared spectrum of the final fraction was that of p-toluidine. Not characteristic of p-toluidine were a small shoulder in the C-H stretching region and a weak band at about 1690 cm.$^{-1}$ The p-toluidine was slowly removed by sublimation at room temperature. The residue was in the form of an oil. In the numerous experiments that were performed the color of this oil varied from red to yellow. When the final rearrangement solution was a dark color, or the workup procedure had not been carefully followed, the oil was of a reddish color.

An infrared spectrum was taken of the oil. A strong carbonyl group was present in the 1680-1685 cm.$^{-1}$ region. Four strong C-H stretching bands from 2840-3020 cm.$^{-1}$ were present. Three of these bands were identical to those present in p-toluidine. The fourth band (2963 cm.$^{-1}$) was not present in spectra of p-toluidine or the o-semidine. The n.m.r. spectrum of the oil in carbon tetrachloride showed the presence of aromatic and vinyl protons, N-H protons, methyl, and possibly methylene protons. At least four aliphatic C-H bearing groups were present. One or two of these were split although no pattern could be established. One of the signals was only 9 cps downfield from the reference band of tetramethylsilane (external standard). The chemical shifts of one or two of the groups presumed to be methyl because of the appearance of signals at relatively high field were quite similar to the shifts of the methyl groups of p-toluidine and the o-semidine.

Hydrogenations of the oil (ca. 30 mg. in 10 ml. of ethanol) were carried out at 150-200° and 1500-2000 psi in the presence of Raney nickel. Infrared spectra of the residues obtained from various hydrogenations were rather ambiguous. Some showed the presence of an O-H group at about 3620 $cm.^{-1}$ and absence of a carbonyl band, while one spectrum showed no O-H absorption and a doublet carbonyl absorption that occurred at about 1725-1750 $cm.^{-1}$ Strong C-H bands were observed at 2855 and 2933 $cm.^{-1}$ (The starting material had bands at 2863 and 2926 $cm.^{-1}$) A broad band in the N-H stretching region (3200-3500 $cm.^{-1}$) was also observed.

Two molecular weight determinations were carried out by the technique of isothermal distillation. Constant volumes of liquid in the two compartments of the distillation apparatus could not be achieved. Two molecular weights were determined with a specially constructed osmometer (47). Average resistance changes of 154 and 462 ohms were observed for samples of 17 mg. of the oil in 2.35 g. of acetone and 15 mg. of oil in 0.72 g. of acetone, respectively. These values correspond to molecular weights of 267 and 257, respectively. The samples were prepared by vacuum sublimation of p-toluidine and addition of acetone to the resulting residue. The weight of the oil was taken as the difference between the weight of the flask before acetone was added and the weight of the flask after it had been rinsed with acetone and dried.

A control experiment was carried out in which 0.800 g. of p-azotoluene, 0.802 g. of the o-semidine, and 0.901 g. of p-toluidine (all three solids were previously purified) were added to 150 ml. of nitrogen-treated 95% ethanol. One milliliter of concentrated hydrochloric acid was added to the resulting solution which was then worked up by the procedure used to isolate the unknown oil. The residue that was left after the p-toluidine had been removed from the fourth fraction showed none of the characteristics of the unknown oil. The four fractions accounted for 24, 32, 9, and 30 percent, respectively, of starting material. The second fraction is large and the third small because addition of water to the residue that remained after solvent had been removed was not accompanied by application of sufficient heat to dissolve much of the o-semidine.

Rearrangement of p-Aminohydrazobenzene.--A solution of 30 mg. of p-aminohydrazobenzene in 250 ml. of nitrogen-flushed 95% ethanol was treated at zero degrees with 25 ml. of ethanolic hydrogen chloride. The initial concentration of the hydrazobenzene was 5.5×10^{-4} M and of acid was 7.5×10^{-3} F. An aliquot of the solution was withdrawn immediately after the acid had been added and was titrated with an aqueous solution of Bindschedler's Green. No more of the oxidant was used than would be required for a blank titration.

Several rearrangements of 0.2-0.3 g. samples of p-aminohydrazobenzene were carried out in ethanol which had been acidified with either hydrochloric, acetic, or sulfurous acid. Water was added to the residue that remained after solvent had been removed from the product solution. p-Aminoazobenzene hydrochloride that did not dissolve was separated by filtration. The filtrate was neutralized to give more p-aminoazobenzene, but no compound resembling 4,4'-diaminodiphenylamine (a p-semidine) could be isolated.

Procedure for the Determination of the N^{15} Content of the Various Compounds.--The analytical procedure followed was that described by Rittenberg (45). The procedure involves conversion of the nitrogen of the organic compounds to ammonia by the Kjeldahl method. The ammonia was then trapped in dilute hydrochloric acid. The resulting solution was concentrated to a few milliliters and then mixed with 2 ml. of sodium hypobromite solution in the evacuated collection apparatus. Nitrogen was evolved and then compressed into a 10-ml. glass bulb with a modified Toeppler pump. The mercury column was lowered a few centimeters below the neck of the bulb which was then pulled off by application of a torch. The other end of the bulb was equipped with a 14/35 joint and a break seal. The samples were analyzed with a mass spectrometer (Consolidated Electrodynamics, Model 21-620). The formula used to calculate the percentage of N^{15} was

$$\% N^{15} = \frac{N^{29} + 2N^{30}}{2(N^{28} + N^{29} + N^{30})}$$

The heights of the peaks at 28, 29, and 30 were directly used to measure the abundance of the various isotopes. The N^{28} peak was corrected for air contamination by measuring the peak at 32. This peak was multiplied by 4.9 to give the contamination of the N^{28} peak with atmospheric nitrogen. This factor was determined from the ratio of the peak heights at 28 and 32 of a sample of ordinary air.

Kjeldahl Conversions of the Nitrogen Present in the Various Compounds Studied.--An apparatus identical to that used by Rittenberg (45) was used for the formation and collection of ammonia. All of the compounds that were treated, except diaminocarbazole, were dissolved in 3 ml. of concentrated sulfuric acid to which had been added 1 g. of potassium sulfate and a crystal of copper sulfate pentahydrate. Dextrose and selenium were used in a number of the conversions. The amounts of the various compounds used are listed in the tables below. The mixtures were digested at 350-380 for various time intervals. The samples which contained N^{15} were digested for 12-15 hours. Diaminocarbazole was treated in 5 ml. of concentrated sulfuric acid to which had been added 0.2-0.5 g. of copper sulfate pentahydrate. The cooled digestion solutions were treated with 25 ml. of water and neutralized with 40% sodium hydroxide. The ammonia was driven off with heat and a gentle air stream which passed into a flask containing 25 ml. of 0.01F hydrochloric acid. The heating process was carried out for about 45 minutes although only about 5 minutes were required to turn the originally blue or green mixture to a dirty brown. The final hydrochloric acid solutions were titrated with 0.01409F sodium hydroxide. The labeled samples were converted under the conditions which gave the best recovery of ammonia. Practice conversions were not carried out on m-phenylenediamine. The labeled m-phenylenediamine was treated under the same conditions as was m-nitroaniline.

TABLE VII

Kjeldahl Conversion of m-Nitroaniline

#	wt. of sample	wt. of dextrose	digest. time	$N_{calc.}$	N_{found}
1	5.27 mg.	70 mg.	1 hr.	1.08 mg.	0.95 mg.
2	5.32	70	3	1.08	1.01
3	5.50	97	3	1.11	0.97
4	5.30	65	10	1.07	0.91
5	5.13	50	10	1.04	1.05
6	5.54	50	12	1.19	1.09

TABLE VIII

Kjeldahl Conversion of Diaminocarbazole

#	wt. of sample	wt. of dextrose	wt. of selenium	wt. of copper sulfate$\cdot 5H_2O$	digest. time
1	5.00 mg.	60 mg.	12 mg.	-	1 hr.
2	4.80	79	15	-	3
3	4.92	91	18	-	12
4	4.95	100	20	0.32 g.	12
5*	4.38	77	18	0.30 g.	14
6*	4.02	73	15	0.28	14

#	$N_{calc.}$	N_{found}
1	1.065 mg.	0.805 mg.
2	1.022	0.902
3	1.048	0.972
4	1.053	1.010
5	0.682	0.614
6	0.625	0.532

* #5 and #6 were run on the dihydrochloride rather than on the neutral base.

TABLE IX

Kjeldahl Conversion of Azobenzene

#	wt. of sample	wt. of dextrose	wt. of selenium	digest. time	$N_{calc.}$	N_{found}
1	6.77 mg.	68 mg.	-	10 hr.	1.04 mg.	0.41 mg.
2	6.72	55	-	3	1.03	0.26
3	6.50	70	15 mg.	10	1.00	0.98
4	6.39	70	16	12	0.982	0.97

Rearrangement of HzA-N^{15}H-N^{15}H.--Weighed amounts (60-70 mg.) of HzA-N^{15}H-N^{15}H were rearranged in ethanolic hydrogen chloride at 40.2-40.5°. The acid concentration was varied and the rearrangements were carried to 97-99 percent completion. Reaction times were 5 hours to 14 days, depending on the acid concentrations. The solvent was removed under vacuum and the residue that remained was converted to diaminocarbazole by the procedure described earlier.

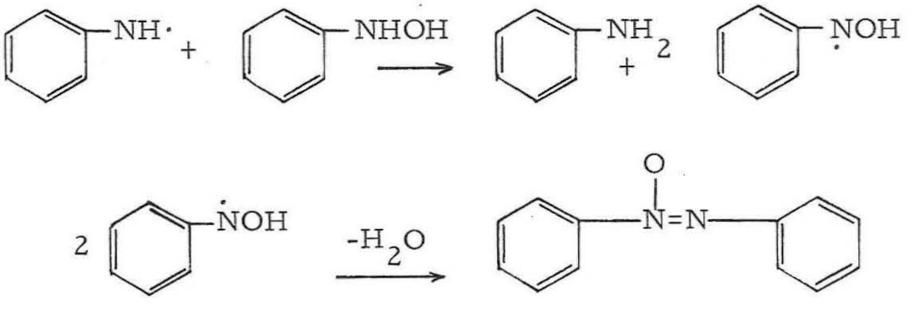
Partial Rearrangement of HzA-N^{15}H-N^{15}H and Conversion of the Unrearranged HzA to AzA.--Solutions of HzA-N^{15}H-N^{15}H (0.100 g.) were rearranged to 50% completion. The solutions were partly neutralized and treated with solutions of ethanol containing weighed amounts of Wurster's Blue perchlorate that were equivalent to unrearranged HzA. Solvent was then removed and the residue was treated with about 5 ml. of water. Some of the hydrochloride of AzA did not dissolve and it was separated by filtration. That which did dissolve was precipitated by the addition of aqueous sodium hydroxide. The Wurster base did not precipitate if the solutions were carefully neutralized. The combined AzA fractions were dissolved in dilute aqueous hydrochloric acid and precipitated by addition of aqueous sodium hydroxide. The dried AzA (35-40 mg.) was deaminated by the procedure described earlier.

Attempted Preparation of 2,7-Diaminocarbazole from the Product of the Rearrangement of m-Chloro,m'-aminohydrazobenzene.-- A number of experiments were carried out in an attempt to convert the product residue (in the form of a hydrochloride) obtained from the rearrangement of m-chloro,m'-aminohydrazobenzene to 2,7-diaminocarbazole. This residue was heated in water and in dimethylformamide at temperatures ranging from 100° to 240°. The acid concentration was varied over a wide range. Several reactions were carried out in which the neutral product of the rearrangement was heated at 180° in nitrobenzene to which had been added copper powder. The hydrochloride form of the rearrangement product was also treated in various solutions of sodamide or potassium amide dissolved in liquid ammonia. In none of these experiments was any product isolated that resembled 2,7-diaminocarbazole.

RESULTS OF PART I

Attempts to Show the Presence of an Intermediate in the Rearrangement of Aromatic Hydrazo Compounds. Hydrazobenzene and p-hydrazotoluene (HzT) were each rearranged in the presence of acrylonitrile. A rearrangement of HzT was also carried out in the presence of styrene. In none of these experiments was any polymerization observed.

An attempt to produce benzidine from the reaction of phenylhydroxylamine with titanium trichloride in acidic ethanol (positively-charged amino radicals are presumably formed from the reaction of titanium trichloride with hydroxylamine in acid solution (48)) was unsuccessful, but did lead to the formation of azoxybenzene. The explanation was advanced that a radical process could account for this reaction. Attacks of intermediate phenylamino radicals on unreacted phenylhydroxylamine could produce N-phenylhydroxylamino radicals. Coupling of two of the latter radicals with subsequent

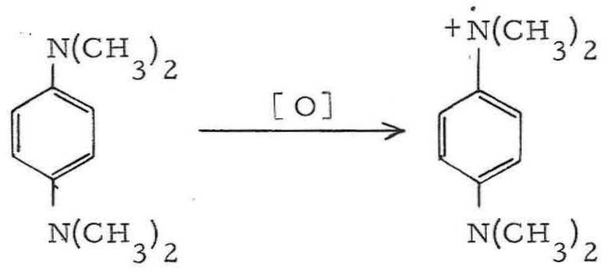


elimination of water would give azoxybenzene. Although a later investigation showed that the sole product of the complete reaction of titanium trichloride with phenylhydroxylamine was aniline, the suggestion initially occurred that phenylhydroxylamine might be an excellent scavenger for intermediate radicals produced from the rearrangement of HzT. Two solutions that were 0.1F in hydrochloric acid and 0.035M in HzT were prepared. Phenylhydroxylamine (0.03 molar) was added to one of the solutions. After a few minutes the control run was an opaque brown, while the reaction solution containing phenylhydroxylamine was a light brownish yellow. Workup of the reaction solution afforded azoxybenzene. Similar treatment of a solution of phenylhydroxylamine in acidic ethanol also gave azoxybenzene.

HzT was rearranged in neat formic acid and in ethanol to which formic acid had been added. No carbon dioxide was evolved.

A solution of HzT in acidic ethanol was frozen with liquid nitrogen and scanned with an EPR machine. No signal was detected.

When HzT was rearranged in the presence of N,N,N',N'-tetramethyl-p-phenylenediamine dihydrochloride (the Wurster base), a blue solution resulted. This color was attributed to the Wurster cation (I). The blue color was observed under conditions that



I

ordinarily resulted in an opaque product solution and under conditions in which lower concentrations of HzT resulted in a clear yellow product solution. Careful degassing of the acidic ethanol prior to addition of HzT did not prevent formation of the cation.

Kinetics of the Oxidation of the Wurster Base by Solutions of Rearranged HzT. The rate of formation of Wurster's Blue was followed spectrophotometrically. A typical first order plot of the rate data (Figure XIX) shows that there is an induction period. Since the Wurster cation readily oxidizes HzT, this induction corresponds to the period of time in which unrearranged HzT is still present. The induction period depended on the hydrogen ion concentration and was generally less than 25 minutes under the conditions employed. The ionic strength and the concentration of hydrogen ion and of the Wurster base were varied for the different runs, while the concentration of HzT was kept constant. The results that were obtained are listed below in Table X. These data show that the rate and amount of oxidation are increased by an increase in ionic strength (runs 5-8). The rate of oxidation appears to be dependent on the hydrogen ion concentration (runs 9, 10), while the amount of oxidation of the Wurster base

TABLE X

Run	Hydrazo-toluene	[Cl$^-$]	μ -	[H$^+$]^1	[W.B.]^2	k_a in sec.^{3}	A_∞^{5}
1	6.92×10^{-4}	4.15×10^{-2}	4.15×10^{-2}	2.92×10^{-2}	1.06×10^{-2}	9.42×10^{-2}	0.805
2	"	4.17×10^{-2}	4.17×10^{-2}	2.93×10^{-2}	1.06×10^{-2}	10.2×10^{-2}	0.800
3	"	5.44×10^{-2}	5.44×10^{-2}	2.96×10^{-2}	2.11×10^{-2}	7.03×10^{-2}	0.815
4	"	5.46×10^{-2}	5.46×10^{-2}	2.97×10^{-2}	2.11×10^{-2}	7.10×10^{-2}	0.815
5	"	25.5×10^{-2}	25.5×10^{-2}	2.97×10^{-2}	2.11×10^{-2}	9.64×10^{-2}	1.040
6	"	5.5×10^{-2}	25×10^{-2}	2.97×10^{-2}	2.11×10^{-2}	12.2×10^{-2}	1.200
7	"	45.5×10^{-2}	45.5×10^{-2}	2.97×10^{-2}	2.11×10^{-2}	10.9×10^{-2}	0.975
8	"	5.5×10^{-2}	44.5×10^{-2}	2.97×10^{-2}	2.11×10^{-2}	17.1×10^{-2}	1.360
9	"	5.22×10^{-2}	5.22×10^{-2}	1×10^{-2}	2.11×10^{-2}	4.31×10^{-2}	0.81
10	"	5.22×10^{-2}	5.22×10^{-2}	3×10^{-3}	2.11×10^{-2}	3.11×10^{-2}	0.80
11	"	7.32×10^{-2}	7.32×10^{-2}	1.86×10^{-2}	3.16×10^{-2}	4.75×10^{-2}	0.81
12	"	9.44×10^{-2}	9.44×10^{-2}	1.77×10^{-2}	4.22×10^{-2}	4.49×10^{-2}	0.83
13^4	"	9.44×10^{-2}	9.44×10^{-2}	1.77×10^{-2}	4.22×10^{-2}	4.48×10^{-2}	0.67

1) Determined on the basis of 5×10^4 and 7 as the equilibrium constants for $W.B. + H^+ - + W.B.H^+ + H^+ -$.

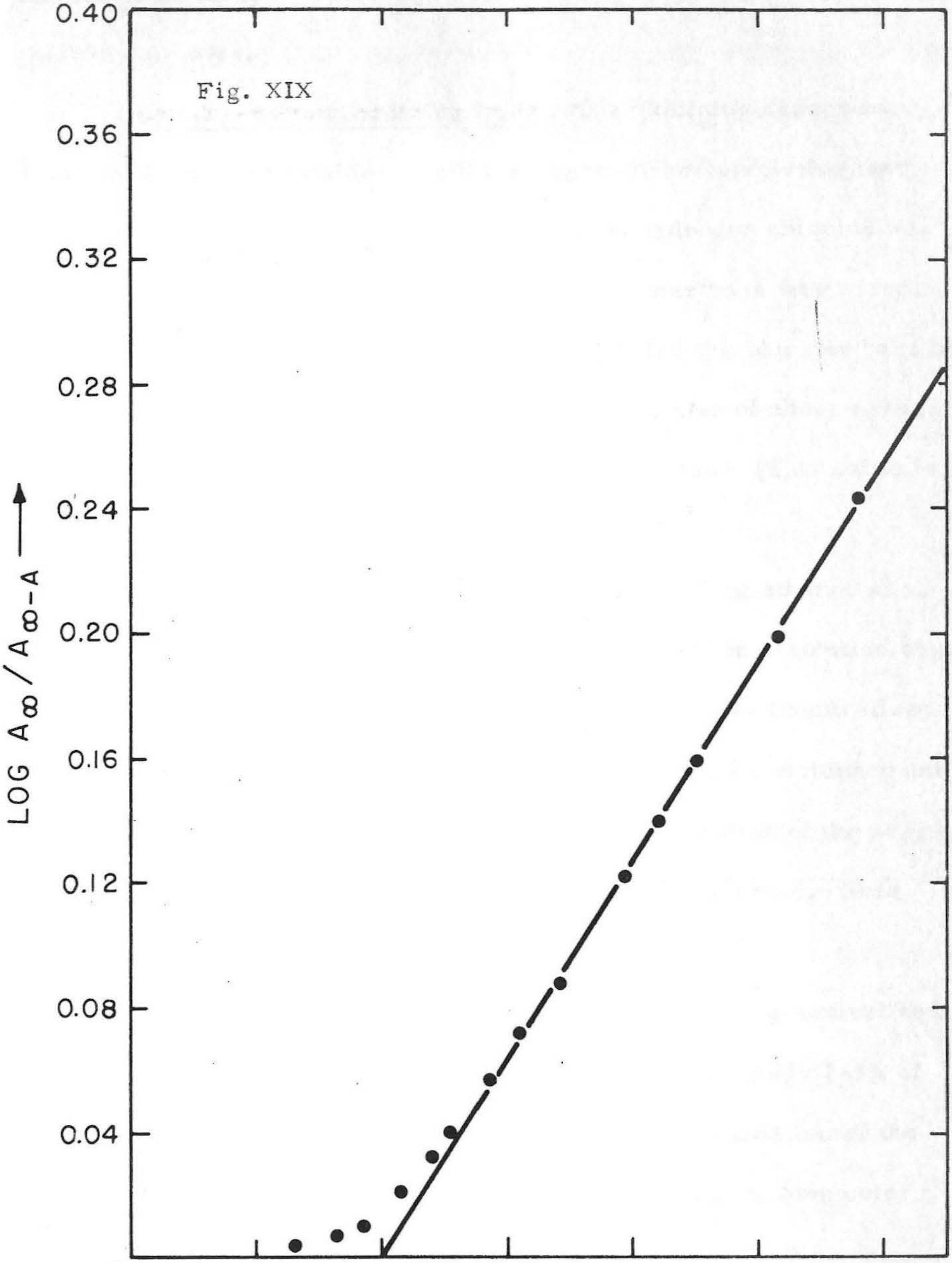
2) Wurster base concentration.

3) Calculated by dividing the observed rate constant by the total concentration of the Wurster base.

4) Run 13 was allowed to stand for ten minutes before adding the Wurster base.

5) These have to be estimated as the blue color gradually disappears. The reaction cells were allowed to stand for a period equal to the time it had taken to reach the observed A_∞. One half of the decrease in absorption was added to the observed A_∞ to obtain the A_∞ given here.

Fig. XIX


0.40
0.36
0.32
0.28
0.24
0.20
0.16
0.12
0.08
0.04
0
100
200
300
400
500
600
LOG A∞ / A∞-A →
SECONDS →

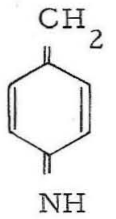
is seen to be independent of the concentration of hydrogen ion and of the Wurster base.

Stability of the Oxidizing Agent. The oxidizing agent was found to be rather unstable in acidic ethanol. When a solution that was 1.67×10^{-3}M in HzT and 1.34×10^{-2}F in hydrogen chloride was allowed to stand for 90 minutes before the Wurster base was added, the maximum absorbence reached was 0.60. Had the Wurster base been added at the beginning of the rearrangement, a value of about 1.9 for the maximum absorbence should have been observed. (This value is calculated from the data in Table X.)

The stability of the oxidizing agent in alkaline ethanol was determined to be greater than in acidic ethanol. When a solution of HzT (1.57×10^{-3}M) in acidic ethanol (1.34×10^{-2}F) was neutralized after rearrangement was virtually complete, and then reacidified and treated with the Wurster base 90 minutes after initiation of the rearrangement, a maximum absorbence of 1.200 was observed. This compared with a predicted value of about 1.80.

Reacidification after 90 minutes of reaction of a neutralized solution of the Wurster base and rearranged HzT gave only 2-3% of the maximum predicted absorbence. Accordingly, oxidation of the Wurster base occurred in alkaline solution, although no blue color developed.

Attempts to Synthesize the Unknown Oxidizing Agent. The idea was advanced that the unknown oxidizing agent might be a simple derivative of p-benzoquinone imine methide (II) or might even be the imine methide itself. Likely derivatives would be p-aminobenzyl alcohol or the ethyl ether of p-aminobenzyl alcohol. p-Aminobenzyl alcohol was found, however, to be stable in the presence of the Wurster base.



II

Attempts were made to prepare the acetate and tosylate of p-aminobenzyl alcohol. The alcohol was treated in ether with a sodium hydride-oil suspension. Acetic anhydride or p-toluenesulfonyl chloride was added to the resulting mixture. The ether solutions that were obtained upon filtration of the final reaction mixture would not oxidize the Wurster base in acidic ethanol. No conclusive evidence was obtained to prove that the desired derivatives were formed, although an infrared spectrum of some of the product of the acetate synthesis showed the presence of a primary amino and a carbonyl group.

p-Aminobenzyl chloride hydrochloride was synthesized and treated in dimethyl sulfoxide with potassium t-butoxide in an attempt to eliminate two moles of hydrogen chloride per mole of the benzyl chloride and thus form the imine methide II. A deep red solution was obtained from the reaction. This solution would oxidize the Wurster base in ethanol, but no relation could be established between this oxidation and the one that accompanied rearrangement of HzT. Attempted solution of p-aminobenzyl chloride hydrochloride in benzene and in dimethylformamide apparently resulted in heterogeneous polymerization of the acid salt. Neutralization of a solution of the hydrochloride in ethanol and in water was accompanied by the formation of insoluble compounds. Apparently polymerization occurred in these two solutions.

A final attempt to prepare p-benzoquinone imine methide involved photolysis of p-aminobenzyl alcohol in benzene. Acetophenone was added to one of the solutions that was irradiated. A red precipitate of polymeric nature was obtained in both cases.

Rearrangement of HzT in Ethanol-O-D. Ethanol-O-D was prepared by the reaction of sodium ethoxide with deuterium oxide. An infrared spectrum of the resulting ethanol showed little or no O-H absorption. A solution that was 0.93M in HzT, approximately 0.084F in the Wurster base, and 3.3F in sodium perchlorate was rearranged. p-Azotoluene, p-toluidine, and the o-semidine were separated from the product mixture. Infrared spectra showed that no detectable deuterium had been incorporated in the methyl groups of any of the three compounds.

Kinetics of the Rearrangement of HzT. The spectrophotometric procedure that Carlin used to determine the rate of rearrangement of HzT was repeated. The absorption data that he determined for starting material and the three products were used without modification. The disappearance of HzT was also followed by titration with aqueous solutions of Bindschedler's Green. The data in Table XI show that both methods gave good agreement with the kinetic results obtained by Carlin.

TABLE XI

Pseudo First Order Rate Constants for the Rearrangement of HzT

#	T, °C	Method	$k \times 10^2 \text{ min.}^{-1}$ (1)	$[H^+]$	$k \times 10^2 \text{ min.}^{-1}$ obtained by Carlin
1	0	uv	1.23	0.0150	1.15
2	"	"	1.23	"	"
3	"	"	1.21	"	"
4	"	B.G. (2)	1.24	"	"
5	"	"	1.28	0.0155	1.22
6	"	"	1.25	0.0150	1.15
7	20.4	uv	11.7	"	11.6
8	"	B.G.	12.3	0.0146	11.1

1) The reactions reported by Carlin were at slightly lower ionic strength.
2) Bindschedler's Green.

The product compositions that were indicated by ultraviolet analysis were also in good agreement with the values obtained by Carlin. He reported that the product mixture consisted of 40.4±3.1% p-toluidine, 36.5±5.7% o-semidine, and 22.7± 2.8% p-azotoluene.

The apparent results obtained in the repetition of his work were 40.5 ± 0.5%, 39.2 ± 0.8%, and 20.5 ± 1.0%, respectively. (These values were not corrected for the few percent of azotoluene present in the starting material.) The method of analysis employed in these experiments differed in one respect from Carlin's procedure. In his work the aliquots were quenched in 95% ethanol to which aqueous sodium hydroxide had been added. As the presence of water was found to cause a shift in the absorption spectrum of HzT, the quenching solutions used in a number of experiments consisted of sodium hydroxide dissolved only in 95% ethanol. When this procedural modification was employed, the calculated product composition tended to give better agreement with Carlin's data.

Determination of the Yields of the Products of the Rearrangement of HzT by Isotope Dilution. As none of the reported products of the rearrangement of HzT will oxidize the Wurster base, an additional compound must be formed. Carlin's spectrophotometric results showed that the sum of the concentrations of the products and of unrearranged starting material was equal to the initial concentration of HzT. The amount of Wurster cation formed from the Wurster base, however, indicated that the oxidizing agent accounts for 5-10% of starting material. As this observation cast doubt upon the validity of Carlin's results, the product yields were checked by isotope dilution.

Radioactive HzT was rearranged at zero degrees in 95% ethanol. After 5 hours (5-6 half-lives) of reaction, the product composition was determined by ultraviolet analysis. At the same time weighed amounts of inactive p-toluidine, o-semidine, and p-azotoluene were dissolved in the reaction solution. The three compounds were recovered and counted with a liquid scintillation counter. The yields of p-toluidine, o-semidine, and p-azotoluene as determined by the two methods are given in Table XII.

TABLE XII

Yields of the Products from the Rearrangement of HzT as Determined by Ultraviolet and Isotope Dilution Analysis.

	Azotoluene %			p-Toluidine % 1)			o-Semidine %		
#	C^{14} dil'n.	2)Corr. dil'n.	UV	C^{14} dil'n.	2)Corr. dil'n.	UV	C^{14} dil'n.	2)Corr. dil'n.	UV
1	22.1	18.9	20.8	28.5	29.4	40.0	32.7	33.7	39.2
2	23.2	21.0	-	26.8	27.6	-	38.8	40.3	-
3	23.2	20.8	18.8	27.6	28.5	41.0	41.4	42.7	40.2
4	23.2	20.9	20.5	27.4	28.3	39.4	38.3	39.5	40.2
5	21.2	18.7	21.1	28.8	29.7	40.4	35.7	36.8	38.5
6	22.7	20.3	20.4	28.1	29.0	39.7	38.2	39.3	39.9
Ave	22.6± 0.6	20.1± 0.9	20.3± 0.6	27.9± 0.6	28.8± 0.6	40.1± 0.5	37.5± 2.2	38.7± 2.4	39.6± 0.6

1) Counted as p-toluidine
2) These columns represent a corrected concentration for each constituent if it is assumed that the starting material contained at least 3% p-azotoluene. This assumption was derived from the ultraviolet data obtained from the time zero aliquots.

A comparison of the two sets of results shows that ultraviolet analysis gives a value for p-toluidine that is 10% too large (33 relative percent).

Attempts to Alter the Product Composition. Radioactive HzT was rearranged in the presence of added hydrazobenzene, p-toluidine, and o-semidine. In one experiment the Wurster base was added after five hours of reaction. The yields of the products that were determined are given in Table XIII.

The results of runs 7-13 show that the addition of p-toluidine, the o-semidine, and the Wurster base had no significant effect upon the yields of the products of the reaction of HzT. The addition of hydrazobenzene clearly reduced the formation of p-azotoluene. Since less p-azotoluene was formed a greater percentage of HzT would rearranged to p-toluidine, o-semidine, and the unknown. From the amount of p-azotoluene formed in these experiments and from the results given in Table XII, the amounts of p-toluidine and o-semidine which should be formed can be calculated. The results which were obtained are in rather good agreement with the predicted values of 44-52% for the o-semidine and 34.5-37.5% for p-toluidine. As p-toluidine and o-semidine formation is effectively unaltered, the unknown product must also be formed according to prediction.

Rearrangement of p,p'-Ditrideuteromethylhydrazobenzene-4,4'-C^{14}. Some of the radioactive toluene that was used as a precursor of

TABLE XIII

Effect of the Addition of Various Compounds on the Yields of the Products Obtained from the Rearrangement of HzT as Determined by Isotope Dilution Analysis.

#	AzT-%	p-Toluidine[1]-%	o-Semidine-%	Conditions
7	22.3	26.5	-	After 5 hrs. 0.784 g. of the Wurster base was added
8	-	25.9	-	Nothing added
9	27.4	25.2,[2] 25.9[1]	40.4	32.71 mg. of o-semidine at start of rearrangement
10	29.1	26.4	35.0	80.63 mg. of o-semidine
11	28.0	26.3	36.1	80.00 "
12	28.6	26.7	35.5	80.71 "
13	26.8[3]	26.9	36.6	Nothing added
14	7.7[4]	35.4 (38.3[5])	44.5 (48.3)	0.10096 g. of hydrazobenzene initially added
15	4.4	36.3 (38.0)	42.9 (44.9)	0.30165 "
16	3.6	36.4 (37.7)	43.7 (45.3)	0.5000 "
17	22.8	29.1	37.3	80.94 mg. of p-toluidine added at start

---

1) Counted as p-acetotoluide.

2) Counted as p-toluidine.

3) Runs 9-12 were performed with HzT which had aged 5 weeks since runs 7 and 8 had been performed. Run 13 was carried out to determine whether or not the p-azotoluene content of the starting material had increased. The value of 26.8% obtained for p-azotoluene shows that this increase had occurred.

4) Purified HzT which contained no more than 3% p-azotoluene was used for runs 14-17.

5) The numbers in parentheses give the percentage composition of the total products, other than p-azotoluene, represented by the compounds in question. If the data from Table XII are used, the values for o-semidine and p-toluidine would be predicted to lie between 44-52 and 34.5-37.5%, respectively. These values are subject to uncertainty that arises from a lack of knowledge of the amount of p-azotoluene present in the starting material.

HzT was converted to toluene-α-D_3-1-C^{14}. An infrared spectrum showed that only trace amounts of hydrogen were present in the methyl group. No methyl hydrogen signal could be detected by n.m.r. HzT which was prepared from this deuterated toluene was rearranged. The product yields were determined and are listed in the table below.

TABLE XIV

Product Yields from the Rearrangement of p, p'-Ditrideuteromethylhydrazobenzene-4, 4'-C^{14}.

#	p-Azotoluene-%	p-Toluidine-%	o-Semidine-%
18	19.5	28.7	40.3
19	20.0	29.9	39.9
Ave.	19.75±0.25%	29.3±0.6%	40.1±0.2%

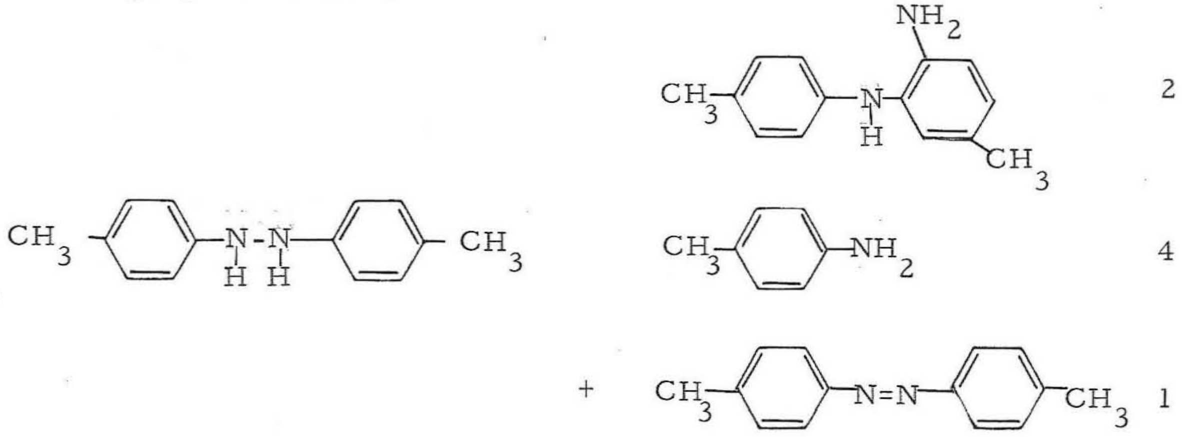
The presence of deuterium in the methyl groups of HzT did not affect the product distribution. The pseudo first order rate constant for the rearrangement of the deuterated HzT was found to be 1.40×10^{-2} min.^{-1} at an acid concentration of 0.0154F. This value is essentially the same as that which would be obtained for HzT itself. These results show that deuteration of the methyl group has not affected the course of the rearrangement of HzT.

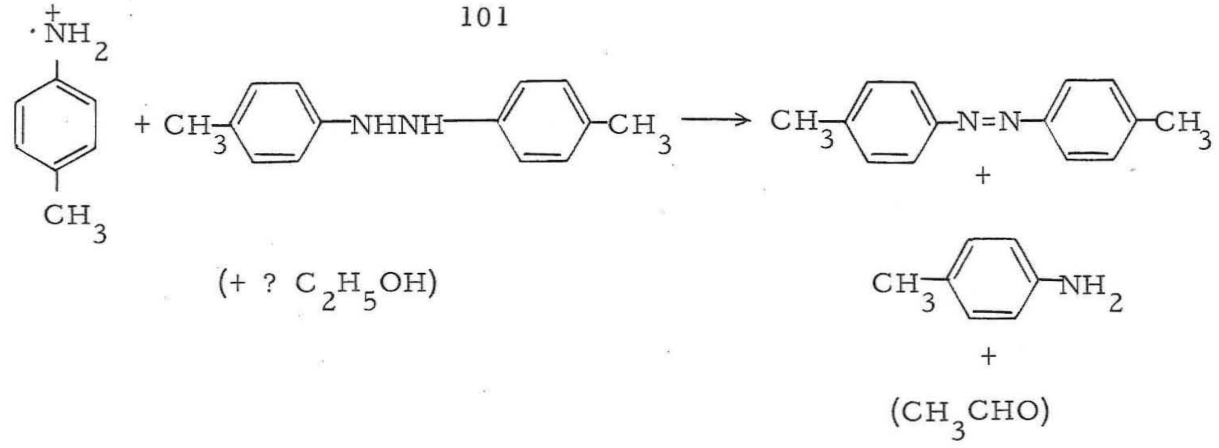
Isolation of an Unknown Product from the Rearrangement of HzT. A careful investigation of the p-azotoluene, o-semidine, and p-toluidine fractions obtained from the reaction of HzT revealed the presence of an unknown oil. The water solubility of the three main products makes their separation possible. p-Azotoluene is completely water insoluble, while the o-semidine is soluble in acid, but insoluble in neutral or basic solution. p-Toluidine has an appreciable water solubility and may be recovered from water by extraction with ether. When the p-toluidine fraction was subjected to vacuum sublimation at room temperature, a small amount (15-30 mg. from 2.5 g. of HzT) of an oily residue was obtained. Infrared spectra of the oil contained a band indicative of a conjugated carbonyl group (1680-1685 cm.$^{-1}$) and a doublet of a primary amine (3400-3500 cm.$^{-1}$). The spectra indicated that no p-toluidine or o-semidine was present in the oil. Four C-H stretching bands occurred between 2840 and 3020 cm.$^{-1}$ Only one of these bands (2963 cm.$^{-1}$) was not present in the spectrum of p-toluidine. This band was also absent in spectra of the o-semidine. N.m.r. spectra of the oil in carbontetrachloride contained signals which indicated thepresence of a number of methyl (or methylene) groups. One of these signals was only 9 cps downfield from the reference band of tetramethylsilane and was significantly more important than the rest of the signals. No assignment could be made to the various signals that were observed. The molecular weight of the oil was determined with a molecular weight osmometer and was found to be approximately 260. Attempts to hydrogenate the oil and obtain further structural information proved unsuccessful. A control experiment in which purified p-azotoluene, p-toluidine, and the o-semidine were treated by the same procedure used to isolate the unknown oil gave none of the latter product.

DISCUSSION OF RESULTS
OF PART I

The possibility that the benzidine rearrangement proceeds by way of a radical mechanism had never been rigorously investigated until the inception of the work described in this thesis. The observed intramolecularity of the acid-catalyzed rearrangements of aromatic hydrazo compounds has long been thrown up as a barrier to any serious consideration of a radical process. This barrier is certainly a weak one on several counts. The rearrangement products could be formed from geminant radical ions which never escape from the solvent cage in which they are formed. Furthermore, there is no requirement that intermediate radicals must couple once they have escaped from their initial solvent cage. These "free" radicals might instead react with unrearranged starting material to give rise to the disproportionation products that have been observed in a number of rearrangements. Many of the arguments that may be raised for and against a radical mechanism must remain academic ones until some sound experimental evidence can be obtained that will either prove or disprove such a process. In this light the initiation of the polymerization of a monomer such as acrylonitrile would be an excellent test for the presence of intermediate radicals.

The observation that the rearrangements of hydrazobenzene and of HzT in the presence of acrylonitrile (and styrene) do not give rise to polymerization certainly does not exclude the possibility that a radical mechanism could be operative. As the products that arise from the rearrangement of hydrazobenzene (benzidine and diphenyline) are certainly formed by an intramolecular path, the absence of polymerization could simply mean that no radicals have escaped from their initial solvent cage. The case for HzT must, however, be explained in a somewhat different manner. This compound seemed to be an ideal one to study. Not only are disproportionation products formed during the rearrangement of HzT, but also Carlin reported that there is more hydrogen in the products than was present in the starting material. The disproportionation products are formed in a 4 to 1 mole ratio (p-toluidine to azotoluene) rather than a 2 to 1 ratio which would be required to satisfy the balance of hydrogen between products and starting material. The only likely source of hydrogen other than HzT would be the solvent ethanol. If radicals are responsible for the

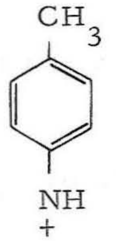




disproportionation products, then the HzT system should certainly be an excellent one to initiate polymerization. Since the polymerization of neither styrene nor acrylonitrile was initiated, the radical mechanism seemed on shaky ground. If the disproportionation products had been formed in a 2 to 1 mole ratio, the lack of polymerization would be compatible with the postulate that HzT is a much better scavenger for the p-tolylamino radicals than are styrene and acrylonitrile. These monomers should, however, be competitive with ethanol (if the latter compound is a source of hydrogen for intermediate radicals) and one would at least expect to observe telomer, if not polymer, formation. The conclusion may be drawn that either no free radicals were formed (and hence the mechanism is not free radical) or that the product composition reported by Carlin is incorrect. The third alternative, that the proposed radical intermediates will not initiate polymerization, must be considered, however unlikely it may seem. Results to be discussed below revealed that Carlin's work actually was in error so that the scavenging properties of HzT relative to styrene and acrylonitrile could be sufficient to explain the absence of polymerization that was observed.

As HzT appeared to be a better trap than acrylonitrile or styrene for whatever intermediates are formed during the rearrangement, the possible requirement that any added scavenger be structurally similar to HzT was realized. Phenylhydroxylamine seemed a likely candidate for such a scavenger and was interestingly found to have a marked effect upon the final color of a solution of rearranged HzT. Instead of an opaque brown solution, a clear yellow one resulted. The fate of the phenylhydroxylamine in this reaction could not be determined, as it is unstable under the conditions used to work up the product solution.

As the p-tolylimino cation (III), which would no doubt prefer to react with solvent rather than with acrylonitrile, might have been responsible for the disproportionation reaction, HzT was rearranged in the presence of formic acid. As the latter is a good hydride donor and as no carbon dioxide was evolved, the p-tolylimino cation must not have reacted with solvent if it were ever formed at all. Educated intuition would say that such a species should prefer to undergo an electrophilic attack on solvent rather than oxidize HzT.

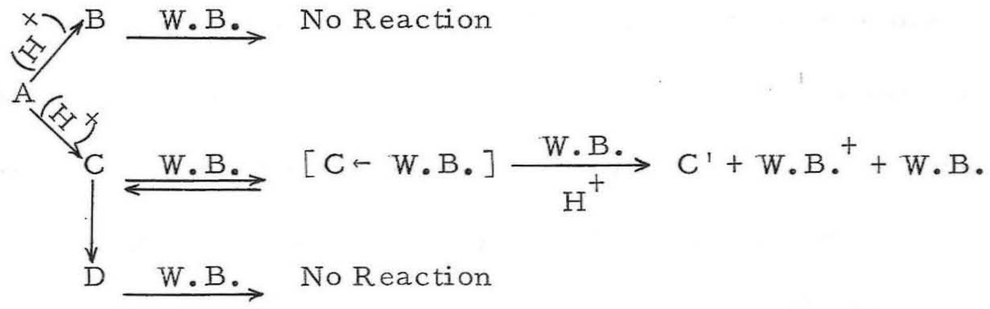


III

When the Wurster base was added as a scavenger, the Wurster cation was formed. As the cation readily oxidizes HzT to azotoluene, its formation would not be observed until virtually all of the HzT had rearranged. The length of the induction period that occurred before the blue color of the cation began to develop agreed approximately with the amount of time predicted for complete reaction of HzT. No conclusion can be drawn as to whether or not intermediate radicals oxidize the Wurster base, but the results do show that a fourth product has been formed from the rearrangement of HzT in addition to the three already reported.

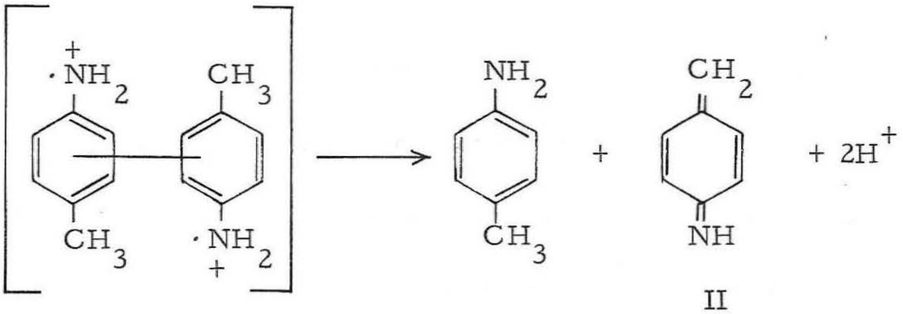
The kinetic and absorption data of Table X show that the rate of formation of Wurster's Blue is increased by both an increase in ionic strength and in acid concentration. The amount of the cation that is formed is independent of the concentration of the Wurster base and of the acid concentration, while an increase in ionic strength increases the amount of oxidation that occurs. Furthermore, the oxidizing agent has been shown to be unstable in acid solution. The reaction scheme given below (Fig. XX) may be used to discuss these observations.

FIGURE XX



There are at least two paths by which the unknown oxidizing agent (C) or its precursor can react, as the amount of Wurster's Blue ($W.B.^+$) that is formed can be varied with a change in ionic strength. If C were to be formed directly from HzT, the extent to which it could decompose by any particular path, including the oxidation reaction, would depend on the concentration of the Wurster base (W.B.). As the amount of the observed oxidation is independent of the concentration of the Wurster base, there must be a precursor (A) of C which has at least two modes of reaction (including formation of C). The observation that the amount of Wurster's Blue and hence the amount of C that is formed is independent of the acid concentration indicates that all of the paths by which A may react have the same dependence upon hydrogen ion concentration. As the oxidizing agent has been shown to be consumed in acid solution (at a rate which is competitive with but slower than the oxidation of the Wurster base) in the absence of the Wurster base, there must be some method other than reaction with the latter compound by which it could disappear (such as formation of D). However, when the Wurster base is present, this additional mode (or modes) of reaction cannot be competitive with the oxidation process. Otherwise the extent of the Wurster's Blue formation would be dependent upon the concentration of the Wurster base. If, however, the Wurster base, which is present in large excess, complexes all of C [$C \leftarrow W.B.$], the oxidation of the former compound could be the only reaction path available to the latter one. If this complex decomposed directly into the Wurster cation and C', the rate of formation of the cation would be independent of the concentration of the Wurster base. Since this is not the case, the complex is shown (in Fig. XX) to be reacting with an additional molecule of the Wurster base in the slow step of the overall sequence. To satisfy the observed acid catalysis, a proton is also inserted in this final step. This whole scheme is far from being a simple one and is certainly not proposed as an unequivocal answer to the question of the process of the formation and destruction of the unknown oxidizing agent. Perhaps the most important conclusion that can be reached from all of these data is that the unknown oxidizing agent is formed from a product of the rearrangement of HzT rather than directly from HzT itself.

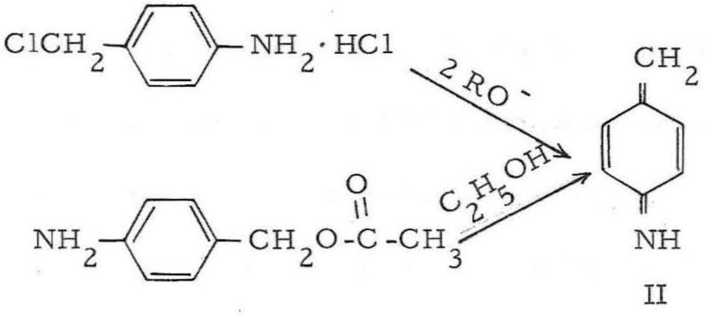
In an attempt to explain the origin of the unknown oxidizing agent and of the imbalance of hydrogen between products and starting material, the idea was advanced that two caged p-tolylamino cation radicals could disproportionate to give p-toluidine and p-benzoquinone imine methide (II). The latter compound or a derivative of it could be



II

the unknown oxidizing agent. If II were reduced to p-toluidine by some compound other than HzT, the problem of the imbalance of hydrogen would also be solved.

If the oxidizing agent were a derivative of II, p-aminobenzyl alcohol or its ethyl ether would be a likely candidate for this derivative. However, p-aminobenzyl alcohol was found to be stable in the presence of the Wurster base. A number of reactions such as neutralization of the hydrochloride of p-aminobenzyl chloride and solvolysis of p-aminobenzyl acetate (and tosylate) were carried out in an attempt to produce the desired p-benzoquinone imine methide and show that it would oxidize the Wurster base at the same rate as the unknown oxidizing agent. The failure of these experiments to produce the desired results could just as well have been an indication that direct generation of II had not been accomplished as it could have been proof that II was not related to the unknown oxidizing agent.



II

To reduce II to p-toluidine, an atom of hydrogen from the reducing agent must be incorporated into the methyl group of p-toluidine. Accordingly, rearrangement of HzT in ethanol-O-D should have given rise to p-toluidine with deuterium in the methyl group if the proposed reduction had been operative. As no deuterium was incorporated, the conclusion was reached that if p-benzoquinone imine methide is the unknown oxidizing agent, its reduction product could not be p-toluidine.

The possibility that p-tolylhydroxylamine could be the unknown oxidizing agent was ruled out by the very slow formation of Wurster's Blue that occurred in the presence of the former compound.

All of the results that had been obtained from the HzT system cast doubt upon the validity of Carlin's spectrophotometric data. While repetition of Carlin's work gave good agreement with his results, the isotope dilution experiments showed that there was an inherent error in his spectrophotometric procedure. The rate data are valid, but the product data are not. p-Toluidine, p-azotoluene, and the o-semidine were found to account for 90% of starting material rather than 100%, the difference being that p-toluidine accounted for about 30% of starting material rather than 40%. The isotope dilution and ultraviolet data were in rather good agreement for p-azotoluene and the o-semidine. The results obtained from the tracer experiments are felt to be unequivocal. The data obtained for p-toluidine are certainly beyond doubt as this compound was counted both as the free base and as its derivative, p-acetotoluide. The data obtained for the two compounds were in good agreement.

The 10% of starting material that is not accounted for by the known products must certainly be related to the unknown oxidizing agent. In run number 8 (Table X) approximately 1.2×10^{-4} moles of Wurster's Blue was formed. This number corresponds to about 8.5% (mole percent) of starting material if the unknown is assumed to be a two electron oxidant. Perhaps under the proper conditions the oxidizing agent could account for the entire 10% of HzT which does not give rise to p-toluidine, p-azotoluene, and the o-semidine.

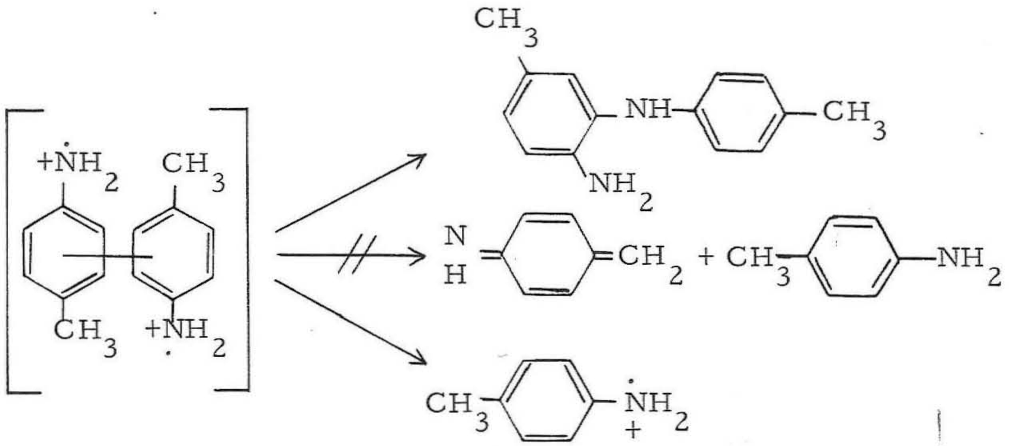
A number of rearrangements of radioactive HzT were carried out in the presence of compounds which had been added in an attempt to alter the course of the product-forming steps of the reaction (Table XIII). Neither p-toluidine nor the o-semidine had any important effect upon the product distribution. The p-azotoluene yield was somewhat higher than usual in the o-semidine runs but this observation can be readily explained. The o-semidine should be a sufficiently strong electron donor to be susceptible to attack by the unknown oxidizing agent. The probability for this attack to occur would be much higher in the experiments in which a large excess of the o-semidine had been added than in those reactions in which the only source of the o-semidine was the rearranging HzT. The oxidized o-semidine would not be stable and might well oxidize unrearranged HzT to p-azotoluene. In this manner an increased amount of p-azotoluene would be produced.

In one experiment the Wurster base was added after 5-6 half lives of reaction of HzT. Wurster's Blue was formed as usual, a fact which showed that the oxidizing agent had been reduced. The formation of p-toluidine was unaffected by the reduction. This experiment simply confirms the earlier results which showed that the oxidizing agent is not reduced to p-toluidine.

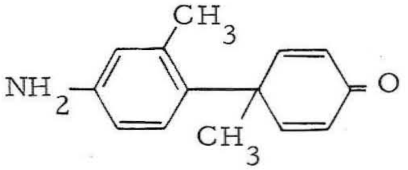
The rearrangements of radioactive HzT that were carried out in the presence of an excess of hydrazobenzene resulted in decreased formation of p-azotoluene. This result may be explained in one of two ways. Hydrazobenzene either traps an intermediate oxidizing agent that is responsible for p-azotoluene formation, or it reduces p-azotoluene back to HzT. Both of these processes would cause an increased percentage of HzT to react to give the o-semidine, p-toluidine, and the unknown. Accordingly, an increased yield of these compounds would be (and actually was) observed. As HzT reacts at least 100 times as rapidly as hydrazobenzene under the conditions employed (2, 7), only a few percent of the latter compound will have rearranged when the inactive diluents are added. If reduction of radioactive p-azotoluene by hydrazobenzene were responsible for the decreased yield of the former compound, the unlabeled p-azotoluene which had been added as diluent should also be reduced. This reduction would result in the formation of unlabeled HzT and accordingly more unlabeled p-toluidine and o-semidine would be present than had been added (as diluents). The net result would be a low calculated yield of p-toluidine and o-semidine. In actuality, the percentage of HzT that rearranged to p-toluidine and the o-semidine (and the unknown) was unaffected by the addition of hydrazobenzene. These results show that not only is p-azotoluene formed by the intramolecular attack of some intermediate that is produced during the rearrangement of HzT, but also this oxidizing agent is not a precursor of the one that is reduced by the Wurster base. Although the conclusion is not unequivocal, the results strongly indicate that the o-semidine and the unknown (more probably its precursor) are formed by intramolecular processes.

The formation of azo compounds during the rearrangement of hydrazobenzenes is most easily envisioned as proceeding by an intermolecular path. However, until the above-described work had been performed, only one piece of experimental evidence existed that might be interpreted as actual proof of such a process. Krolik and Lukashevich (49) prepared hydrazobenzene dihydrochloride by passing dry hydrogen chloride through a solution of hydrazobenzene in ether. When the salt was treated with o-hydrazoanisole (the conditions of this reaction are not given), azobenzene and anisidine were formed. Perhaps o-hydrazoanisole underwent an acid-catalyzed decomposition into fragments which reacted with hydrazobenzene to give the observed products.

While Carlin's product data have been found to be in error, the isotope dilution experiments have shown that the p-toluidine to p-azotoluene weight ratio is still larger than the 1 to 1 value that would be required to satisfy the stoichiometry of a disproportionation reaction. The excess of p-toluidine appears to be related to the unknown oxidizing agent since there is apparently a balance of hydrogen between products and starting material. This excess of p-toluidine is at the same time probably unrelated to the p-toluidine and p-azotoluene that are formed by a normal disproportionation reaction. The fact that the oxidizing agent is not reduced to p-toluidine says nothing about the possibility that p-toluidine might be formed by disproportionation of two p-tolylamino cation radicals. The data show only that if p-benzoquinone imine methide or some derivative of it is formed, that the product of its reduction is not p-toluidine. To determine whether or not p-toluidine is in part formed by disproportionation of p-tolylamino radicals, p,p'-ditrideuteromethylhydrazobenzene was rearranged. As the yields of the various products were not affected by the deuterium, the conclusion may be drawn that the proposed disproportionation reaction is not operative. A sizeable isotope effect on the product forming steps of the reaction should have been observed if one of these steps involved abstraction of hydrogen from a methyl group.

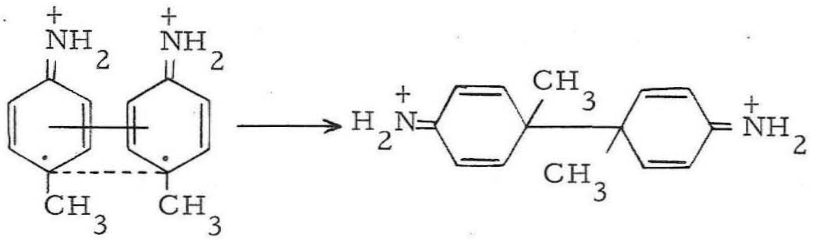


A careful product investigation was carried out in an attempt to isolate some compound that would be related to the unknown oxidizing agent. An unknown oil that was isolated was found to have an amino group and a conjugated carbonyl group. The molecular weight of the oil (ca. 260) showed that it was at least equivalent to a molecule of HzT (whose molecular weight is 212). The n.m.r. spectra of the oil showed the presence of a very high field resonance that was only 9 cps downfield from the reference band of tetramethylsilane. The hydrogen of this group was clearly present in a greater amount than the hydrogen of any other group of the unknown oil. Aromatic and probably vinyl protons as well as several methyl (and methylene) groups were indicated. The purity of the oil was not known and the very strong possibility exists that more than one species and even polymer were present in the various samples of the oil that were studied. An ultraviolet spectrum of the oil was rather similar to that of p-toluidine with only a weak maximum at 3000 Å (with a very long tail) and a much stronger one at 2325 Å. A possible structure for the oil is shown below. This compound could obviously not account for all of the oil.



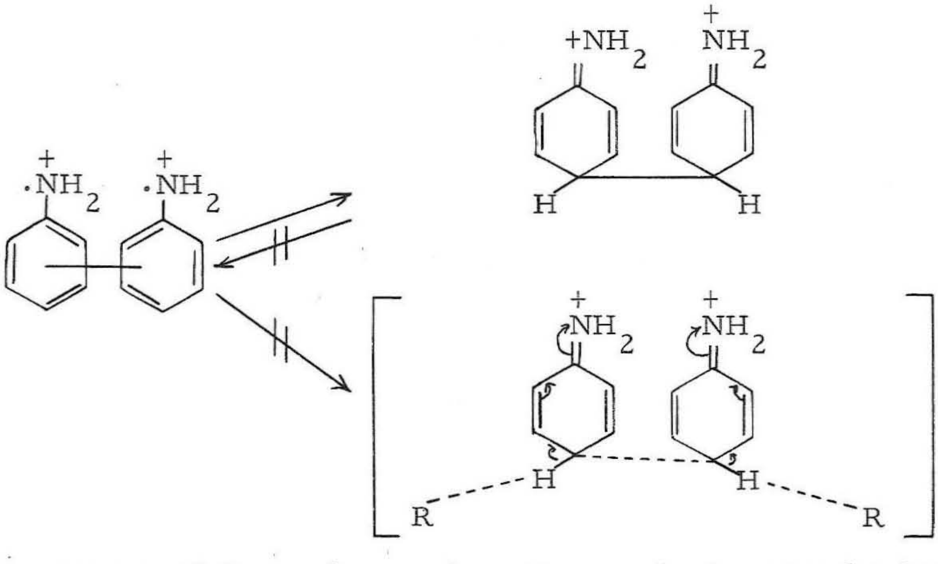
It does, however, contain a conjugated carbonyl and a primary amino group. The methyl group of the dieneone ring could be responsible for the high field n.m.r. signal. This group would be near to, but well out of, the plane of the aromatic ring. As benzene and other aromatics have a large diamagnetic susceptibility perpendicular to the ring, the methyl group could be subjected to considerable diamagnetic shielding and might thus be shifted to high field relative to the normal methyl resonance position (50). A number of objections might be raised as to the validity of the proposed structure. If is certainly inconsistent with the complete n.m.r. spectrum, the molecular weight that was determined, and the ultraviolet spectrum of the oil. (An unsaturated ketone would have been expected to absorb strongly around 3000 Å.) The proposed structure, however, does serve as a guide for further speculation and also presents an explanation of the origin of the high field signal that was observed.

The evidence that has already been discussed indicated that the unknown product of the rearrangement is formed by an intramolecular process. This conclusion, which is far from being unequivocal, was based on the observation that the presence of hydroazobenzene does not affect the formation of a fourth compound (in addition to the reported products) from the rearrangement of HzT. This compound or a derivative of it has been shown to possess rather strong oxidizing properties. The very strong possibility exists that the unknown component of the rearrangement is formed by coupling of the para carbon atoms of HzT.



The steric origin of the high field methyl group is accounted for by the resulting compound as is the saturation necessary for oxidation of the Wurster base. The aromatic ring which has been postulated as the cause of the diamagnetic shift of the methyl group could result from a dieneimine rearrangement which is analogous to a dieneone rearrangement. Furthermore, hydrolysis of an imine group could give rise to the conjugated carbonyl group whose presence was indicated by infrared spectra of the unknown oil.

The proposed coupling at substituted para positions has a number of good precedents. In Jacobson's (1) summary of the rearrangement of hydrazobenzenes are included examples in which benzidines (para-para coupling products) are formed from para-substituted hydrazobenzenes. Chlorine, bromine, iodine, and carboxyl are among the groups which have been displaced. The only factor which would hinder the para-para coupling in HzT (relative to hydrazobenzene) would be a steric one. The electron density at the para carbon atoms would certainly not be decreased by the presence of a methyl group. The rearrangements of deuterium substituted hydrazobenzene (see pp. 23-24) that were performed by Hammond and Ingold showed that carbon-carbon bond formation is irreversible. These experiments also showed that tautomerization (to give an aromatic ring) does not occur simultaneously with the carbon-carbon bond formation. As a



consequence of these observations the conclusion may be drawn that coupling at the para carbon atoms of HzT should not be hindered by the inability of the coupling product to tautomerize to an aromatic compound.

The original work of Carlin on HzT seemed to be rather straightforward. The important observation was made that p-toluidine and p-azotoluene formation are subject to the same rate law as is o-semidine formation. The work described in this thesis shows that in reality the HzT system is far from straightforward and that Carlin's values for the yield of p-toluidine are in error. This latter result, however, should not render invalid the conclusion that the disproportionation reaction follows the same rate law as the o-semidine rearrangement. Carlin's work left unanswered the question of the cause of the high p-toluidine to p-azotoluene ratio. The results described in this thesis show the actual ratio to be lower (3:2 by weight) than reported by Carlin (2:1), but still to be higher than the value that would be predicted for a stoichiometric disproportionation (1:1). The origin of the excess of p-toluidine remains unexplained, although it is probably related to the unknown component(s) of the rearrangement and not to the disproportionation reaction.

While this study of HzT has yielded much new information, it has done little to push aside the barriers that surround the transition state of the benzidine rearrangement. The failure of attempts to detect intermediate radicals by EPR and to produce benzidine from phenylamino cation radicals, is no more a proof of the nonexistence of a radical mechanism than it is of its existence. In fact, the only result of this work that may be used to interpret the mechanism is the observation that the disproportionation reaction is intermolecular. The only logical candidate for the species that oxidizes HzT would be the tolylamino radical. This proposal is an old one but has been perhaps somewhat strengthened by the above-described results.

RESULTS OF PART II

Rearrangement of p-Aminohydrazobenzene. p-Aminohydrazobenzene was found to react instantaneously in acidic ethanol at zero degrees. Only disproportionation products were apparently formed and no compound such as 4,4'-diaminodiphenylamine (a p-semidine) could be isolated.

Kinetics of the Rearrangement of HzA. The rearrangement of HzA was carried out in ethanolic hydrogen chloride (95% ethanol) and was followed by titration of unreacted HzA with aqueous solutions of Bindschedler's Green. The rate data were fitted to a first order plot. The results are given in the following table.

TABLE XV

Rate Data Obtained from the Rearrangement of HzA at 40.2-40.5°
in 95% Ethanol Solution

#	$[H^+] \times 10^2$	$[H^+]_c \times 10^2$(1)	$k_o \times 10^4$(2) min.$^{-1}$	$k_o \times [H^+]_c \times 10^6$ min.$^{-1}$	$u \times 10^2$(3)	half life in hours
1	1.47	1.14	5.50	6.26	1.94(4)	21.0
2	2.94	2.61	2.10	5.50	10.0(4)	55.0
3	2.94	2.61	2.49	6.50	10.0	46.3
4	1.47	1.13	5.50	6.21	10.0	21.0
5	4.42	4.08	1.67	6.83	10.0	69.2
6	2.21	1.88	3.30	6.20	10.0	35.0
7	1.00	0.67	8.71	5.84	10.0	13.3
8	2.94	2.61	2.32	6.05	10.0(4)	49.7
9	1.47	1.14	4.90	5.59	1.94(4)	23.5

Ave. 6.11 ± 0.37

1) The added hydrogen ion concentration was corrected by assuming that HzA was virtually completely diprotonated in all runs.
2) "k_o" is the observed first order rate constant.
3) "u" refers to the ionic strength.
4) Lithium chloride was added in runs 1, 2, 9, 10. Lithium perchlorate was added in the other five runs.

A rearrangement was carried out at an added acid concentration of 0.002F. The observed rate constant was 1.84×10^{-2} min.$^{-1}$, which corresponds to a half life of 37.6 minutes. "$k_o \times [H^+]_c$" could not be calculated as a lack of knowledge of the equilibrium constants for the protonation of the amino groups of HzA prohibited determination of a corrected hydrogen ion concentration ($[H^+]_c$).

While the data are not very accurate, the rate of rearrangement clearly exhibits an inverse dependence upon hydrogen ion concentration. The maximum deviation of observed rate constants is greater than five-fold while the maximum deviation of the corrected rate constants is only about 20%. The average deviation of the corrected rate constants is approximately 6%. The inability to obtain highly reproducible rate data is a consequence of the kinetic procedure. Exact endpoint determination is difficult as the color of the solution changes from the yellow of m-azoaniline to the green of Bindschedler's Green. Moreover, the titrant solution is not completely stable over the period of time required for determination of the rate data.

If variation of the ionic strength has affected the rearrangement, the effect is within the experimental error of the rate data.

Total N^{15} Content of HzA and N^{15} Content of the Hydrazo Linkage. The analytical procedure that was used involved conversion of the nitrogen of the various samples to ammonia. The ammonia was trapped in dilute hydrochloric acid and was then oxidized to nitrogen with sodium hypobromite. The nitrogen was analyzed with a mass spectrometer.

The total amount of N^{15} that was incorporated into m-nitroaniline (and consequently into HzA) was determined. To eliminate any ambiguity that might result from incomplete conversion of the nitrogen of m-nitroaniline, the latter compound was converted to m-phenylenediamine. As both nitrogen groups of m-phenylenediamine are equivalent, incomplete conversion to ammonia could not confuse the results. The values that were obtained are listed in Table XVI. The attenuation of the mass spectrometer was set at ten for the N^{28} and N^{29} peaks and at three for the N^{30} peak.

TABLE XVI

N^{15} Content of m-Nitroaniline and m-Phenylenediamine.

#	Sample	% N^{15}(1)	Atoms of N^{15} per Molecule
1	m-nitroaniline	24.5	0.480
2	"	24.3	0.486
3	m-phenylenediamine	24.8	0.496
4	"	24.9	0.498
5	"	24.2	0.484
6	"	24.5	0.490
	Ave.	24.5 ± 0.2	0.491 ± 0.006

1) This refers to the percentage composition of the total nitrogen of the molecule that is represented by N^{15}.

As the N^{15} content of m-nitroaniline and m-phenylenediamine was found to be the same, the Kjeldahl procedure used to decompose m-nitroaniline may be assumed to be adequate.

Three different reductions (A, B, C) of labeled m-nitroaniline to HzA were carried out. In one of these (Synthesis B) no HzA formed and only m-azoaniline could be recovered from the synthetic mixture. Some of the HzA obtained from Synthesis A was rearranged for one half life. The unreacted HzA was oxidized to m-azoaniline which was recovered and purified. m-Azoaniline was isolated from the product solution of Synthesis A. A sample of the HzA obtained fron Synthesis C was oxidized to m-azoaniline. All of the m-azoaniline samples were deaminated to azobenzene and the N^{15} content of the latter compound was determined. The results that were obtained are listed in Table XVII.

The N^{15} of the hydrazo linkage of the sample of HzA that was rearranged to 50% completion is given by the N^{15} content of samples 7-10. The value of 97.3 atom percent is essentially the amount of N^{15} that should be present (ca. 98.0%) in the hydrazo linkage had no shuffling occurred during electrolytic reduction of m-nitroaniline-$N^{15}O_2$. This result shows that no equilibration of the nitrogen groups of HzA had occurred prior to its rearrangement.

As the N^{15} content of the azo linkage of the various samples of azobenzene is in most cases lower than the total possible content,

TABLE XVII

N^{15} Content of Azobenzene Obtained from Deamination of m-Azoaniline.

#	Sample	% N^{15}	Atoms of N^{15} per Molecule	Source
7	Azobenzene	48.3	0.966	A
8	"	49.6	0.992	"
9	"	48.8	0.976	"
10	"	47.9	0.958	"
	Ave.	48.7±0.5	0.973±0.009	
11	Azobenzene	44.9	0.898	A_1
12	"	45.8	0.916	"
13	"	45.5	0.910	"
	Ave.	45.4±0.3	0.908±0.007	
14	Azobenzene	47.1	0.942	B
15	"	47.2	0.944	"
16	"	47.4	0.948	"
17	"	48.6	0.972	"
	Ave.	47.6±0.5	0.951±0.01	
18	Azobenzene	46.5	0.930	C
19	"	46.8	0.936	"
20	"	47.2	0.944	"
	Ave.	46.8±0.2	0.937±0.005	

1) "A_1" refers to the m-azoaniline recovered from the product solution of Synthesis A.

some shuffling of the label must have occurred during the electrolytic reductions. The difference of the N^{15} content of the samples obtained from sources A and A_1 indicates that HzA is formed by some path other than, or in addition to, direct reduction of m-azoaniline. The mass spectrometer was attenuated at ten for all three nitrogen peaks. As the N^{30} peak of the nitrogen of m-nitroaniline (and m-phenylenediamine) was attenuated at three, a small error could result in the comparison of the N^{15} content of azobenzene with that of m-nitroaniline.

N^{15} Content of 2,7-Diaminocarbazole that was Obtained from the 2,2'-Diaminobenzidine Formed during the Rearrangement of HzA-N^{15}H-N^{15}H- at Different Acid Concentrations. HzA-N^{15}H-N^{15}H- was rearranged at four different acid concentrations. The solvent was removed after 5-6 half lives of reaction (as determined from the kinetic data of Table XV) and the residue was converted to 2,7-diaminocarbazole. The N^{15} content of the carbazole was determined. The mass spectrometer was attenuated at ten, ten, and three for the N^{28}, N^{29}, and N^{30} peaks, respectively. The O^{32} peak for all samples investigated was attenuated at three. The results that were obtained are listed below in Table XVIII.

Kinetics of the Rearrangement of m-Chloro,m'-aminohydrazobenzene. m-Chloro,m'-aminohydrazobenzene was prepared by reduction of the corresponding azobenzene with hydrogen and platinum

TABLE XVIII

N^{15} Content of 2,7-Diaminocarbazole Samples

Rearrangement No.	Sample No.	Synthesis	[HzA] x 10^3	$[H^+]$ total	% N^{15}	Atoms of N^{15} per Molecule
1	21	A	1.12	0.00200	26.7	0.801
"	22	"	"	"	26.9	0.807
"	23	"	"	"	27.3	0.819
"	24	"	"	"	26.8	0.804
"	25	"	"	"	26.4	0.792
				Ave.	26.8$\pm$0.2	0.805$\pm$0.007
2	26	C	1.14	0.00200	27.0	0.810
"	27	"	"	"	27.1	0.813
"	28	"	"	"	27.2	0.816
"	29	"	"	"	26.2	0.786
				Ave.	26.9$\pm$0.3	0.806$\pm$0.010
3	30	A	1.17	0.0100	26.6	0.798
"	31	"	"	"	26.5	0.795
				Ave.	26.55$\pm$0.005	0.797$\pm$0.001
4	32	A	1.10	0.0100	26.2	0.786
"	33	"	"	"	26.6	0.798
"	34	"	"	"	26.7	0.801
				Ave.	26.5$\pm$0.2	0.795$\pm$0.006
5	35	C	1.12	0.0200	26.1	0.783
"	36	"	"	"	26.2	0.786
"	37	"	"	"	26.7	0.801
"	38	"	"	"	26.0	0.780
"	39	"	"	"	25.3	0.759
				Ave.	26.1$\pm$0.3	0.782$\pm$0.010
6	40	C	1.13	0.0200	26.1	0.783
"	41	"	"	"	26.1	0.783
				Ave.	26.1$\pm$0.00	0.783$\pm$0.000

TABLE XVIII (continued

Rearrangement No.	Sample No.	Synthesis	[HzA] x 10^3	$[H^+]$ total	$\%N^{15}$	Atoms of N^{15} per Molecule
7	42	A	1.17	0.0400	25.5	0.765
"	43	"	"	"	25.9	0.777
"	44	"	"	"	25.5	0.765
"	45	"	"	"	25.8	0.774
"	46	"	"	"	25.5	0.765
				Ave.	25.6±0.2	0.769±0.005
8	47	B(1)	1.09	0.0400	25.3	0.759
"	48	"	"	"	25.3	0.759
				Ave.	25.3±0.0	0.759±0.000

1) m-Azoaniline was reduced to HzA with hydrogen and platinum dioxide.

dioxide or with zinc and acetic acid. The hydrazo compound was rearranged at 40° and at 60°. At the former temperature the rearrangement was followed by titration with Bindschedler's Green and at the latter by observation of the change in absorption at 2450 Å. The rather crude rate data that were obtained at both temperatures (Table V) show that the rate of the rearrangement is independent of the acid concentration within the limits of the experimental error.

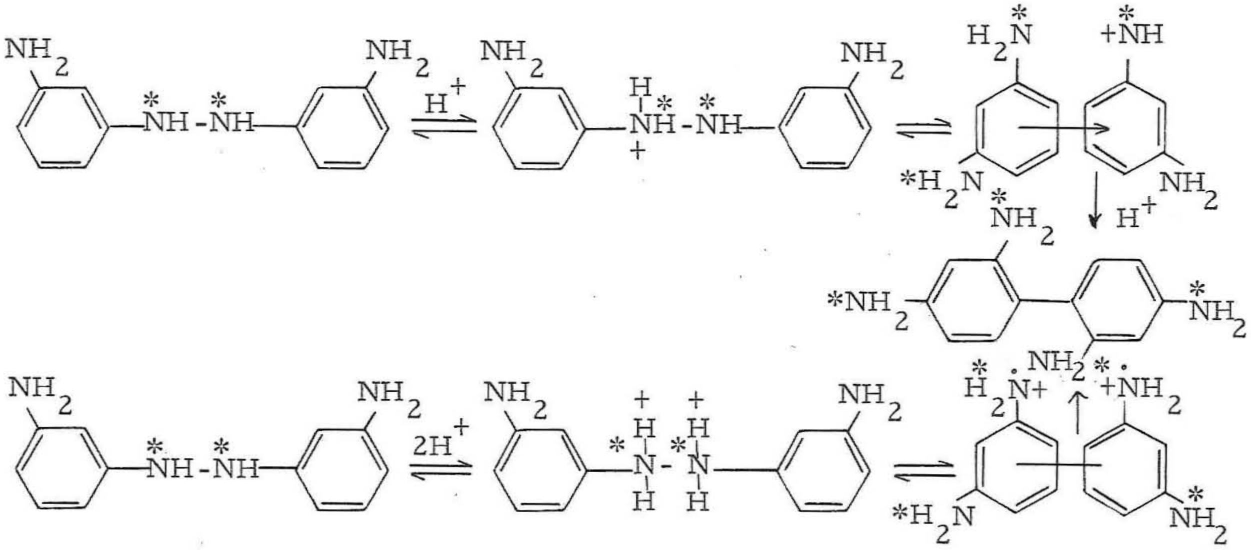
All attempts to convert the product of the rearrangement to 2,7-diaminocarbazole failed.

DISCUSSION OF PART II

The mechanism of an organic reaction may be placed into one of two general categories (excluding tunneling). Either the product of the reaction will be formed in the same step as that in which the starting material disappears (a concerted mechanism), or an unstable intermediate will be produced which can be converted into the stable product of the reaction. If the existence of an intermediate can be proved, a concerted mechanism can be automatically eliminated from consideration. However, a concerted mechanism is not proved by the failure to identify a reaction intermediate. The possibility must be considered, however unlikely it may seem, that there is no such thing as a concerted mechanism. Reactions whose mechanisms have been defined as concerted may instead involve the formation of intermediates so unstable that they defy detection.

The benzidine rearrangement has long existed in a class of its own. While a great deal of shouting has been done for and against a concerted mechanism, the cautious chemist has long realized that neither he nor anyone else knows the mechanism of the benzidine rearrangement. Extremely frustrating to the pragmatic chemist is the realization that no one (at least in recent years) has attempted to prove the existence of the intermediate which he has proposed. A very legitimate stumbling block to the investigation of the presence of an intermediate has been the lack of a system which might be unequivocally studied.

Amino-substituted hydrazobenzenes present very interesting possibilities for the detection and description of an intermediate. The system that was found to be most convenient for study was that of m-hydrazoaniline (HzA). The information that might be obtained from an investigation of the rearrangement of HzA which contains N^{15} in the hydrazo linkage (or in the amino groups) may be illustrated by use of the heterolytic (16) and homolytic mechanisms.



The "π-complex" of the heterolytic mechanism is composed of one symmetrical and one unsymmetrical fragment. If the complex is not completely rigid, its equilibration with starting material will be accompanied by shuffling of the label throughout the various nitrogens of the molecule. Both starting material and products would show a high (or perhaps complete) degree of randomization of the N^{15}.

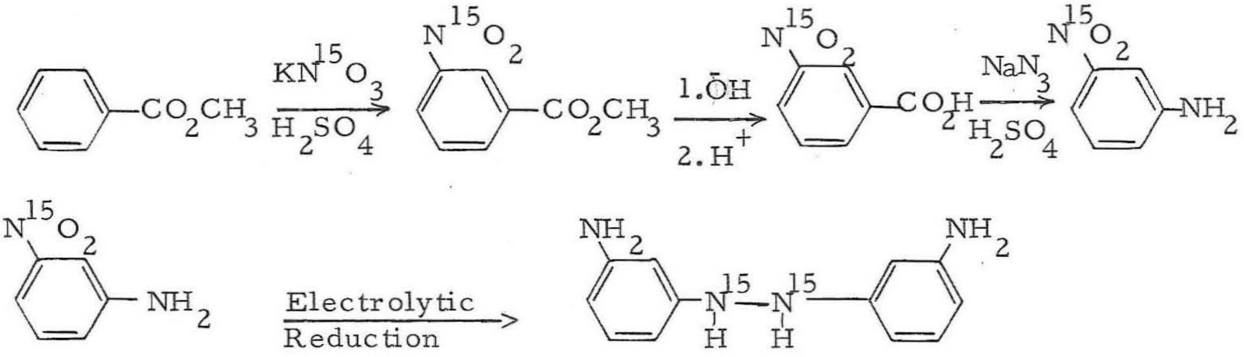
The homolytic mechanism predicts somewhat different results. Both fragments of the proposed complex would be completely symmetrical. As the complex is not necessarily equilibrated with starting material, randomization of the N^{15} would occur only in the products.

In the discussion of these two mechanisms the transition state has been assumed to consist of a diconjugate acid of HzA. If both of the amino groups are protonated under the conditions of the rearrangement, an actual zero order dependence of the rate upon the hydrogen ion concentration should be observed. When the kinetics of the rearrangement were investigated, the rate was found instead to be inversely proportional to the hydrogen ion concentration. Consequently, a monoconjugate acid of HzA, rather than a diconjugate acid, is involved in the transition state of the rearrangement. Mixed order dependence upon hydrogen ion concentration has been observed in the case of o-hydrazotoluene (33) while mixed and complete first order have been reported for several naphthylhydrazo systems (11). HzA is, however, the first hydrazobenzene that has been found to rearrange to benzidine products by way of a transition state that involves only a monoconjugate acid of the hydrazo compound.

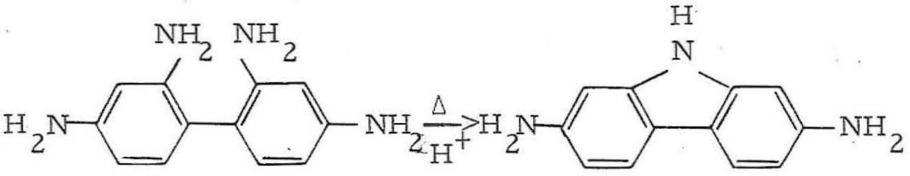
If HzA is not a bastard hydrazo compound which rearranges by a unique process, the complexion of the heterolytic and homolytic mechanisms, as written above, must be changed. As both of these mechanisms have been discussed at some length in the historical section of this thesis, a repetition of arguments will be avoided. Suffice it to say that the heterolytic mechanism would no longer require shuffling of the label in starting material as "π -complex" formation could be rate determining. Moreover, if a radical complex is formed which consists of a neutral and a positively charged radical, complete randomization of the label need not occur in the product benzidine. In fact, there is no real distinction between the "π -complex" proposed by Dewar and a singly-charged complex of phenylamino radicals.

An additional ambiguity of the HzA system that must be recognized is the fact that diphenyline formation (which arises from coupling of ortho and para carbon atoms) cannot be distinguished from benzidine formation. The two compounds are in this case structurally identical. Thus ortho coupling could be a result of diphenyline formation or of benzidine formation from an intermediate in which the ortho and para carbon atoms are equivalent.

While the above observations detract somewhat from the beauty of a study of HzA, there are other features which made this an extremely interesting and simple one to investigate. The synthesis of $HzA\text{-}N^{15}H\text{-}N^{15}H\text{-}$ was straightforward.



The N^{15} content of the hydrazo linkage and consequently of the amino groups was readily ascertained. Determination of the N^{15} content of each of the amino groups of the rearrangement product (2,2'-diaminobenzidine) was also quite straightforward. 2,2'-Diaminobenzidine was converted to 2,7-diaminocarbazole by displacement of one half of the ortho amino groups of the benzidine.



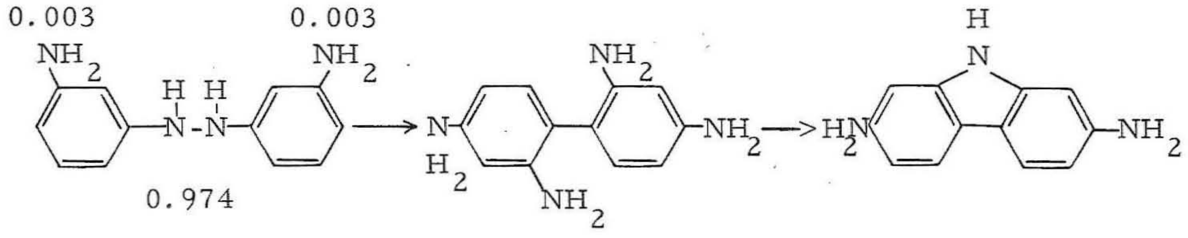
If kinetic isotope effects on the ring closure are ignored, the difference between the N^{15} content of the carbazole and of the benzidine corresponds to one half the N^{15} content of the ortho amino groups. Consequently, the N^{15} content of the para amino groups is also determined.

When HzA-N^{15}H-N^{15}H- was rearranged to 50% completion, the hydrazo linkage of the recovered starting material (recovered as m-azoaniline) was found to have lost none of its N^{15} content. This result requires that any symmetrical reaction intermediate, if present, be formed during (or perhaps after), but not prior to, the rate-determining step of the rearrangement.

If HzA rearranged with 100% para coupling, all of the N^{15} of the hydrazo linkage would be retained in the diaminocarbazole which is formed from the rearrangement product. If 100% ortho coupling occurs, the diaminocarbazole would contain only 50% of the N^{15} of the hydrazo linkage. The exact values that would be observed for these limiting cases can be predicted from the data in Tables XVI and XVII. A maximum of 0.98 and a minimum of 0.49 atoms of N^{15} per molecule of diaminocarbazole is calculated for the respective cases. The former value would be somewhat lower and the latter somewhat higher as a consequence of the small amount of shuffling that occurred during reduction of m-nitroaniline-$N^{15}O_2$. The results that are given in Table XVIII are clearly intermediate to the values that are calculated for the two extreme cases.

The most striking feature of the data of Table XVIII is the decrease in the N^{15} content of 2,7-diaminocarbazole that accompanies an increase in acid concentration of the rearrangement solutions. The number of atoms of N^{15} per molecule of 2,7-diaminocarbazole can be used to express the amount of ortho coupling that has occurred in the formation of 2,2'-diaminobenzidine. The latter expression should enable a more meaningful description of the course of the rearrangement. The following calculations illustrate the manner in which the degree of ortho coupling was determined. The difference between the N^{15} content of the hydrazo linkage as given in Table XVII and the total N^{15} content of HzA (taken as 0.980) was taken as the amount of N^{15} in the meta amino groups.

Synthesis A:



Limits

A. If all para coupling occurs, 0.974+0.003 atoms of N^{15} would be incorporated in the carbazole.
Total = 0.977.

B. If all ortho coupling occurs, 0.487+0.006 atoms of N^{15} would be incorporated in the carbazole.
Total = 0.493.

Let

x = fraction of HzA which rearranges to para coupling products

y = fraction of HzA which rearranges to ortho coupling products

$x + y = 1$

Let

z = the observed atoms of N^{15} per molecule of diaminocarbazole

Then

$$0.977(x) + 0.493(y) = z$$

$$0.977(1-y) + 0.493(y) = z$$

$$y = \frac{0.977-z}{0.484} \qquad (5)$$

For Synthesis B

$$y = \frac{0.966-z}{0.462} \qquad (6)$$

For Synthesis C

$$y = \frac{0.958-z}{0.466} \qquad (7)$$

The data calculated with these formulae are presented in the following table.

TABLE XIX

Percent Ortho Coupling Obtained at the Four Acid Concentrations

Rearrangement No.	Sample No.	$[H^+]_c$ (1)	Synthesis	Percent Ortho Coupling (2)
1	21-25	$<<0.002$	A	35.7
2	26-29	$<<0.002$	C	33.9
3	30-31	7.66×10^{-3}	A	37.6
4	32-34	7.80×10^{-3}	A	37.6
5	35-39	1.78×10^{-2}	C	39.2
6	40-41	1.77×10^{-2}	C	39.2
7	42-46	3.77×10^{-2}	A	43.2
8	47-48	3.77×10^{-2}	B	44.8

1) The added hydrogen ion concentration was corrected by assuming that HzA was completely diprotonated in all runs except the two at the lowest acidity.
2) The "z" values used to calculate the percent ortho coupling were based on the average values of the percent of N^{15} in the total nitrogen content of 2,7-diaminocarbazole. (See column 4 of Table XVIII.)

The amount of coupling of the ortho carbon atoms of HzA that occurs in the formation of 2,2'-diaminobenzidine is seen to increase as the acidity of the rearrangement solution is increased. Of the four acid concentrations studied, three lie in the acidity range used to determine the acid dependence of the rearrangement rate. As a variation of hydrogen ion concentration affects the product-forming step of the rearrangement, but not the rate-determining step, the two processes must be different. Consequently, a metastable intermediate must be formed during the rate-determining step of the rearrangement. This intermediate can either collapse directly to product or it can be protonated with subsequent product formation by a path which does not require proton attack.

$$\begin{tikzcd}
[\text{Intermediate}] \arrow[r, "k"] \arrow[d, "k'"', "H^+"] & \text{Benzidine} \\
\text{Benzidine} &
\end{tikzcd}$$

Since the rearrangement of HzA involves an intermediate, it can obviously not be concerted. The task then remains to describe the intermediate. Approximation of the corrected acid concentration for the rearrangements carried out at an added acid concentration of 0.00200F should prove instructive. An upper limit for this value may be calculated from the equation derived by the following procedure.

$$\begin{tikzcd}
B + H^+ \arrow[r, shift left, "K_1"] & BH^+ \arrow[l, shift left] \arrow[d, "k_3"] & BH^+ + H^+ \arrow[r, shift left, "K_2"] & BH_2^{++} \arrow[l, shift left] \\
& \text{Product} & &
\end{tikzcd}$$

$$\frac{-dB}{dT} = k_o [T_b] = k_3 [BH^+] \qquad (8)$$

$$[T_b] = [BH^+] + [BH_2^{++}] \qquad (9)$$

In these equations "B" refers to HzA. "K_1" is the sum of the equilibrium constants for the formation of the monoconjugate acids of HzA. "$[BH^+]$" is the sum of the concentrations of all of the monoconjugate acids of HzA and "$[BH_2^{++}]$" refers to the diconjugate acid of HzA. "k_o" is the observed first order rate constant and "$[T_b]$" represents the total concentration of HzA regardless of the form in which it exists. The concentration of neutral HzA is assumed to be negligible.

$$K_2 = \frac{[BH_2^{++}]}{[BH^+][H^+]} \qquad (10)$$

$$[BH_2^{++}] = [T_b] - [BH^+] \tag{11}$$

Insertion of equation 11 into equation 10 gives

$$[BH^+] = \frac{[T_b]}{1 + K_2[H^+]} \tag{12}$$

Insertion of equation 12 into equation 8 gives

$$\frac{-dB}{dT} = k_o\,[T_b] = \frac{k_3[T_b]}{1+K_2[H^+]} \tag{13}$$

Thus

$$k_o = \frac{k_3}{1 + K_2[H^+]} \tag{14}$$

The ratio of the observed rates of rearrangement, k_o and k_{o1}, at any two acid concentrations, is given by equation 15.

$$\frac{k_o}{k_{o1}} = \frac{1 + K_2\,[H^+]_1}{1 + K_2\,[H^+]_o} \tag{15}$$

The ratio of the observed rate constants for a rearrangement of HzA which was carried out at an added acid concentration of 0.00200F to the corresponding rate constant for a rearrangement conducted at a corrected acid concentration of 0.00670F (Table XV) is 21.1. The corrected hydrogen ion concentration for the former rearrangement may be approximated with the following formula which is obtained from equation 15.

$$[H^+]_o = 0.000317 - \frac{20.1}{21.1\ K_2} \qquad (16)$$

The corrected hydrogen ion concentration which must be present to cause a rearrangement of HzA to proceed 21.1 times as rapidly as another rearrangement carried out at an acidity of 0.00670F can be calculated for any value of K_2. The upper limit for the corrected acidity of the rearrangement solution which was 0.00200F in added hydrogen chloride is 3.17×10^{-4}. This value corresponds to a value of K_2 of 10^6 or greater. Probably a more realistic value of K_2 would be 10^4. This would correspond to a hydrogen ion concentration of 2.17×10^{-4} instead of 3.17×10^{-4}.

The relationship between the relative hydrogen ion concentrations and the average percent ortho coupling observed for the four sets of rearrangements is given in the following table.

TABLE XX

Relationship between Hydrogen Ion Concentration and Percent Ortho Coupling

Rearrangement No.	Relative $[H^+]_c$ (1)	Average Percent Ortho Coupling
1, 2	≤ 1	34.8 ± 0.9
3, 4	24	37.6 ± 0.0
5, 6	56	39.2 ± 0.0
7, 8	119	44.0 + 0.8

1) Corrected hydrogen ion concentration.

There is at least a 24-fold variation in acid concentration between the first two sets of data and a 5-fold variation between the second and fourth sets. The maximum difference in percent ortho coupling in the former case is 3.7% (absolute) while the minimum difference in the latter case is 5.6%. The most likely and obvious explanation for the observation that the greater variation in acid concentration is accompanied by a smaller increase in percent ortho coupling is that 34.8% is the minimum amount of ortho coupling that can occur. This means that at the low acidity the step in which the metastable intermediate collapses directly to product is sufficiently faster than the step involving protonation of the intermediate that the latter process cannot be detected. Thus 34.8% is the amount of ortho coupling that occurs when the metastable intermediate collapses directly to product.

Comparison of the variation in the ortho coupling among the second, third, and fourth sets of rearrangements is somewhat discomforting. The variation of acidity between the second and third, and third and fourth, sets of data is essentially the same (2.3 and 2.1, respectively) while the ortho coupling differences between these sets are rather large (1.6 and 3.8%, respectively). Since the amount of ortho coupling must approach some upper limit, the variation in ortho coupling should have decreased rather than increased with the approximately equal variation in acid concentrations. The data would at least appear to be more physically real if the value of 39.2% were increased and that of 44.0% decreased. This disparity of results is felt to be due principally to the experimental error that arose in determination of the N^{15} content of 2,7-diaminocarbazole and of the various azobenzene samples. A two-tenths of a percent error (absolute percent) in the N^{15} content of the carbazole, for example, could vary the amount of ortho coupling by more than one percent (absolute).

A quantitative determination of the amounts of ortho coupling that occur in the two product-forming steps should be theoretically possible.

Let u = mole fraction of ortho coupling in the acid-promoted step

x = fraction of ortho coupling that occurs in the acid-promoted step

$1-u$ = mole fraction of benzidine formed by direct collapse of the intermediate

y = fraction of ortho coupling that occurs in the direct step

z = total fraction of ortho coupling

Then

$$xu + y(1 - u) = z \tag{17}$$

Since the benzidine is formed by two competitive steps,

$$\begin{tikzcd}
\text{[Intermediate]} \arrow[r, "k_1"] \arrow[d, "H^+"', "k_2"] & \text{Benzidine (A)} \\
\text{Benzidine (B)} &
\end{tikzcd}$$

the following expression may be written.

$$\frac{B}{A} = \frac{u}{1-u} = \frac{k_2[H^+]}{k_1} = \alpha[H^+] \qquad \alpha = \frac{k_2}{k_1} \tag{18}$$

Solving for u and substitution of the resulting expression into equation 17 gives

$$x\alpha[H^+] + y = z + z\alpha[H^+] \tag{19}$$

When the three sets of values for z and $[H^+]_c$ (rearrangements 3-8) were substituted into equation 19, a negative value (which is physically unreal) for α was obtained. If the assumptions underlying the derivation of equation 12 are valid, this result is a consequence of the sensitivity of equation 19 to small differences in the values of z. A real value for α could have been obtained if the percent ortho coupling were a bit larger in runs 5 and 6 and a bit smaller in 7 and 8. This observation is not independent of the one that was made about the data of Table XX. It does seem more rigorous, however, as a mathematical, rather than an intuitive, approach to the data was used. The experimental data thus do not permit a quantitative determination of the two limiting values (x and y) for the percent ortho coupling. Unfortunately, the slowness of the rearrangement at high acid concentrations prevented the determination of an experimental value for y.

A semiquantitative description of the maximum amount of ortho coupling may be carried out by the following method in which the minimum amount of ortho coupling is taken as 34.8%. If values for the maximum amount of ortho coupling are assumed, the percent ortho coupling that should be observed for the third and fourth sets of rearrangements (numbers 5-8) can be predicted from the data of the first two sets. In equation 17 let $y = 0.348$ and assume x to be 0.500. For rearrangements 3 and 4, z is equal to 0.377. Therefore,

$$\begin{aligned} 0.5u + 0.348(1-u) &= 0.377 \\ u &= 0.191 \qquad (20) \\ 1-u &= 0.809 \end{aligned}$$

The acid concentration is varied by a factor of 2.3 between the second and third sets of data (Table XX). The product-forming step which is acid-promoted will be increased by this amount while the other step will remain unchanged. The former path would thus account for 35.3% of the reaction and the latter would account for 64.7%. As the two paths are assumed to proceed by 50% and 34.8% ortho coupling, respectively, a total of 40.2% ortho coupling would be predicted. Similarly, the predicted amount of ortho coupling for rearrangements run at the highest acid concentration is 43.0 . In the following table the predicted values for the percent of ortho coupling for $x = 0.5$, 0.75, and 1.00 are compared with the observed values.

TABLE XXI

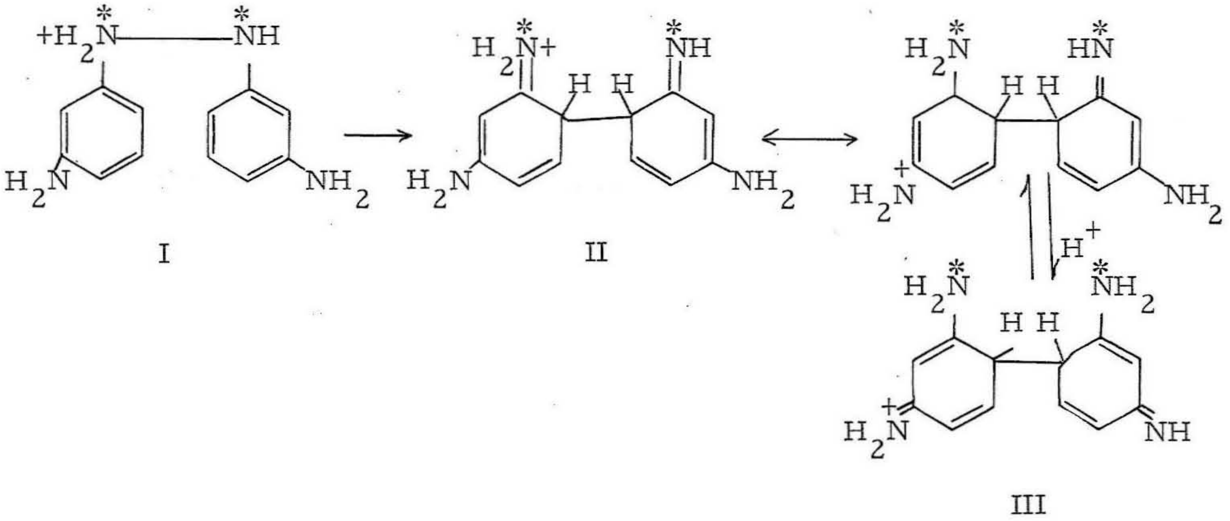
Comparison of Predicted and Observed Amounts of Ortho Coupling(1)

x(2)	$[H]_S$ (3) x 10^2	Percent Ortho Coupling		
		Predicted	Observed	Predicted-Observed(4)
0.50	1.78	40.2	39.2	+1.0
"	3.77	43.0	44.0±0.8	-1.0±0.8
0.75	1.78	40.9	39.2	+1.7
"	3.77	45.8	44.0±0.8	+1.8±0.8
1.00	1.78	41.1	39.2	+1.9
"	3.77	47.1	44.0±0.8	+3.1±0.8

1) Minimum possible ortho coupling taken as 34.8%
2) Assumed maximum possible ortho coupling
3) Values taken from Table XX
4) Difference between the predicted and observed values

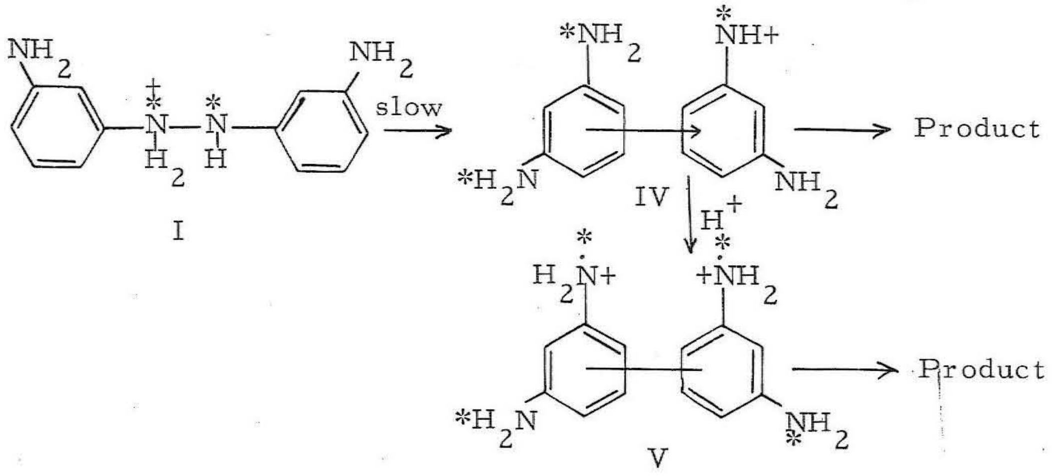
The agreement between predicted and observed values of ortho coupling is the best for the case where x is 0.500. Earlier in this discussion the observation was made that the experimental data would seem to be more physically real if the value of 39.2% were higher and that of 44.0% were lower. These changes would result in better agreement at both acid concentrations of the predicted and observed values of ortho coupling in the case x = 0.5. For the other two cases (x = 0.75, 1.00), the agreement would be better for the lower of the two acid concentrations, but worse for the higher. The overall picture of the experimental data thus indicates that 50% ortho coupling occurs in the product-forming step of the rearrangement which is promoted by acid. This conclusion is certainly not unequivocal. It is far from being rigorously justified by the data of Table XXI. In addition, limiting values of ortho coupling need not be multiples of 0.25, although the latter assumption is not an unreasonable one. Finally, the interpretation of the data has been based on the assumption that the product-forming step which is acid-promoted is first order in attacking hydrogen ion. Again the assumption is reasonable, but it is not rigorously justified by the experimental data.

The preceding discussion of the coupling reactions which occur upon rearrangement of HzA has pointed out that a minimum of 35% and a possible maximum of 50% of the ortho carbon atoms of HzA can be present in the carbon-carbon bond which joins the two aromatic rings of 2, 2'-diaminobenzidine. These observations are incompatible with the "leap frog" mechanism of Brownstein, Bunton, and Hughes (13), which would be written as follows.



As proton exchange among the various nitrogen atoms of the intermediate (II) should be more rapid than carbon-carbon bond breakage, all of the possible isomers of II would be equivalent. Accordingly, a minimum value of 50% ortho coupling would occur in the formation of 2, 2'-diaminobenzidine. This prediction is incompatible with the observed minimum of 35%.

With the elimination of intermediates of the type represented in the "leap frog" mechanism, there remains only the logical possibility that the intermediate is formed by a cleavage of the N-N bond of HzA that is accompanied by no simultaneous C-C sigma bond formation. The heterolytic mechanism of Dewar offers a good explanation for the formation and for the structure of the intermediate. This mechanism could readily involve a step in which the intermediate collapses directly to product. Moreover, in the Dewar scheme the second proton attacks the intermediate, although the nature of this attack has never been described. The following mechanism, which is but an extension of the Dewar mechanism, is compatible with the results obtained in the study of HzA-$N^{15}H$-$N^{15}H$- and also describes the nature of the proton attack on the intermediate.



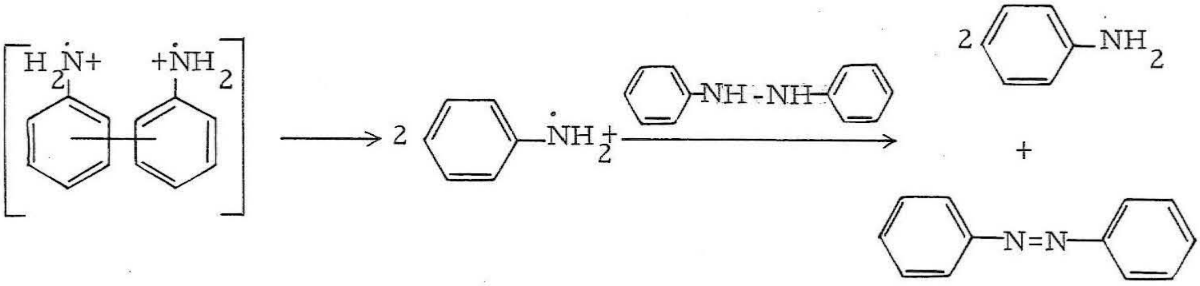
Instead of one intermediate, two are proposed, the second resulting from attack of proton on the first. Intermediate IV is composed of one symmetrical and one unsymmetrical fragment. If 20% of the ortho carbon atoms and 80% of the para carbon atoms of the unsymmetrical ring attack equally the ortho and para carbon atoms of the symmetrical ring, the observed requirement of a minimum of 35% ortho coupling would be satisfied. Attack of proton on IV would result in the formation of intermediate V which is composed of two completely symmetrical cation radicals. Formation of benzidine from V would thus occur with equal amounts of ortho and para coupling.

Dewar's "π-complex" (IV) is strongly supported by the results of the study of HzA. The experimental data show that an intermediate is formed which is a monoconjugate acid of HzA and that this intermediate is capable of direct collapse to product with 35% ortho coupling. The Dewar intermediate is also singly charged and would collapse directly to benzidine with at least 25% ortho coupling. The observed value of 35% is not at all surprising as exclusive attack on the phenylenediamine fragment by the para carbon atom of the unsymmetrical half of the complex would seem unlikely. The weakest part of the Dewar mechanism has always been the attack of proton on the "π-complex." As an attack of this nature is clearly observed, this step of the heterolytic mechanism can no longer be objected to.

The results of the N^{15} study in no way demand that proton attack on IV lead to the formation of an additional intermediate, let alone that this intermediate be a pair of caged cation radicals. The only condition that these results do demand is that protonation of the reaction intermediate lead to benzidine formation with a fraction of ortho coupling that appears to approach 0.50. In addition, the experimental data are not sufficiently accurate to require that 50% be a limiting value for the maximum amount of ortho coupling that can occur. Intermediate V is simply consistent with, but not demanded by, the results of the investigation of the rearrangement of HzA-N^{15}H-N^{15}H-.

Proposal of V is dictated to a large extent by the information that has been obtained from reactions of hydrazo compounds other than HzA. The possibility must be recognized that HzA reacts by an entirely different mechanism than do other hydrazobenzenes whose rearrangements exhibit second rather than first order dependence upon hydrogen ion. This observation is a precautionary one and will not be extensively elaborated upon in the following discussion.

In the historical section of this thesis an objection was raised to the timing of the proposed attack of proton on Dewar's "π-complex." For rearrangements which are second order in hydrogen ion, no provision has been made for this step to be other than rate (and product) determining. Ingold (11), however, showed that at least in several cases (including hydrazobenzene) the second proton can be transferred prior to the rate-determining step. This condition is a consequence of the observations that the rates of rearrangement of the compounds that he studied are faster in D_2O-dioxan than in H_2O-dioxan, and that the rates are a linear function of H_o and not of the hydrogen ion concentration. For the Dewar mechanism to be compatible with these results, the protonation of the "π-complex" would have to lead to the formation of a second intermediate which (in the cases that Ingold studied) would undergo transformation in the rate-determining step of the reaction. If the rearrangement of HzA proceeds by the same reaction sequence as the rearrangement of hydrazobenzene, the attack of proton on the intermediate (IV) would have to result in the formation of a second intermediate. A very likely candidate for the second intermediate would be a caged pair of cation radicals. The observation that the ortho and para coupling reactions that lead to the formation of 2, 2'-diaminobenzidine become of more nearly equal importance as the concentration of hydrogen ion is increased is in good agreement with this proposal. Virtually all of the arguments that were advanced in the historical section in support of a homolytic mechanism may be applied to the proposal that the second intermediate (V) is a pair of caged (or complexed) cation radicals. For example, one of the strongest points in favor of a radical intermediate is the observed formation of disproportionation products from hydrazobenzenes. The Dewar mechanism offered no good explanation for their formation which is certainly compatible with a radical process.



An interesting feature of the two intermediate mechanism is that it is essentially a blend between the heterolytic mechanism of Dewar and the homolytic one that Hammond has favored. This compromise is not a result of any weakness of principles on the part of either camp, but is a direct consequence of experimental observations.

There exists an area of difference between the rearrangement of HzA and rearrangements of aromatic hydrazo compounds which exhibit mixed order dependence upon hydrogen ion. In the historical section it was pointed out that the transitional dependence upon hydrogen, that is sometimes observed, is a consequence of the existence of two competitive rate-determining steps, one of which is first order in hydrogen ion concentration and the other second order. This conclusion was reached as a result of the observation that the order of the

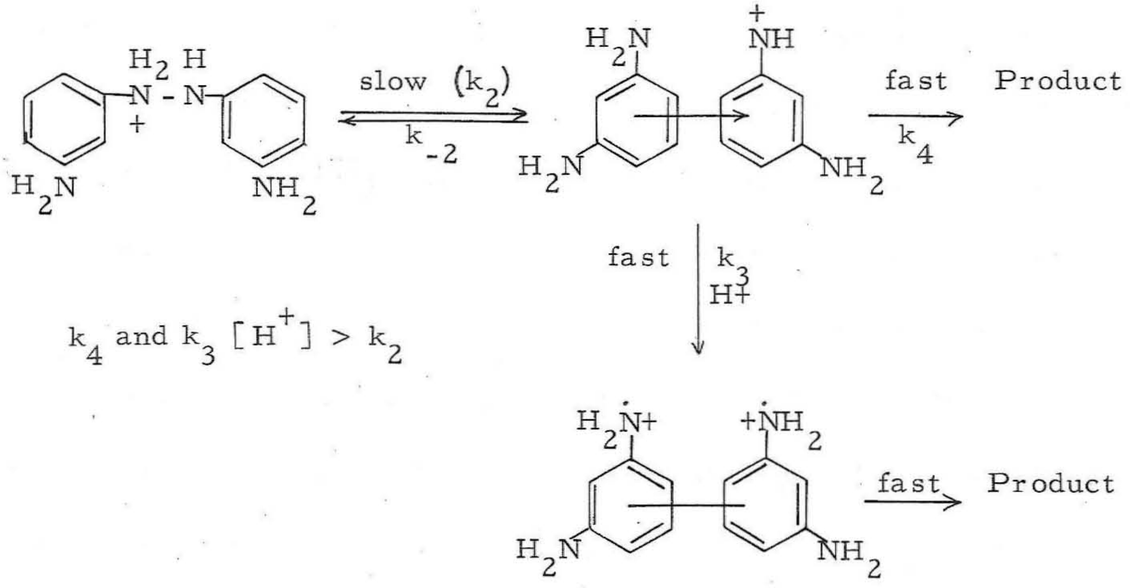
$$k_o = k_1 [H^+] + k_2 [H^+]^2$$

rearrangements in question increased with an increase in acid concentration. This result ruled out the possibility that the transitional dependence upon hydrogen ion was due to a similarity between the rate of reversal of Dewar's "π-complex" to starting material and the rate of attack of proton on the complex. Were this situation to have

$$BH^+ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [\pi\text{-complex}] \xrightarrow[H^+]{k_3}$$

$$k_{-2} \simeq k_3 [H^+]$$

existed, an increase in acidity should have been accompanied by a decrease in the order of the rearrangements (which exhibited transition dependence) with respect to the hydrogen ion concentration. Thus the observed results show that "π-complex" formation could not be rate-determining for the reactions in question. The results also indicated that there should be two product-forming steps, one of which would be first order in hydrogen ion and the other second order. This latter conclusion was actually observed in the rearrangement of HzA. However, since attack of hydrogen ion on the reaction intermediate occurs after the rate-determining step, the formation of the intermediate must take place in the slow step of the reaction.

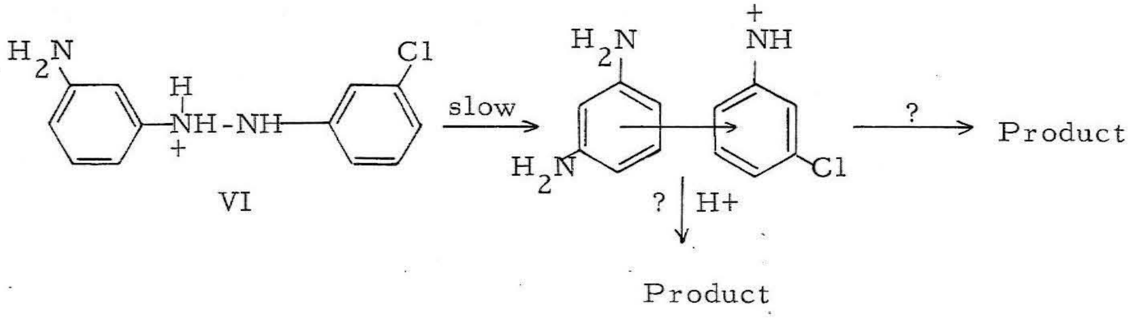


$$k_4 \text{ and } k_3\,[H^+] > k_2$$

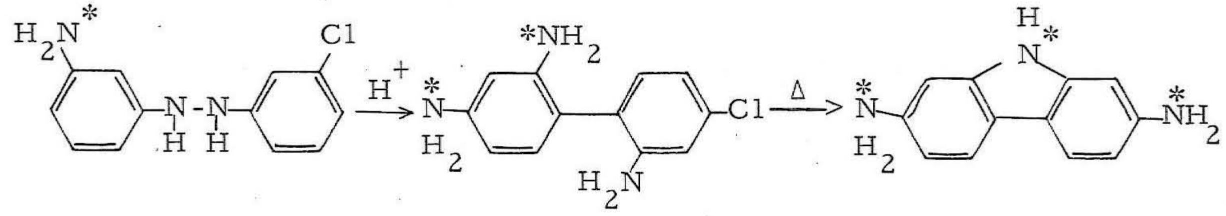
Whereas in other cases $k_{-2} > k_4 \sim k_3[H^+]$, k_{-2} is now less than k_4 and $k_3[H^+]$. This result must be due to the influence of the meta amino groups. These groups could be important in several possible ways. "k_4" might well be increased (relative to k_4 for other rearrangements) because the neutral half of the "π -complex" has available for attack two equivalent positions which are subjected to the strong ortho- and para-directing effects of two amino groups. These amino groups should also aid in the formation of the radical complex.

Taft (51) has observed unusually large substituent effects upon the rates of oxidation of meta- and para-substituted anilines. He has proposed a sigma-bond effect which cannot occur with carbonium ions and carbanions. Taft concluded that the greater the cation radical character of the transition state, the greater will be the enhanced resonance effects of meta and para substituents. For the meta-substituted anilines he found that the group whose effect was most pronounced relative to that of a normal substituent effect was an amino group. The application of this study of Taft's to the rearrangement of HzA is quite apparent. In fact, the suggestion readily comes to mind that a study of the kinetics of a series of meta-substituted hydrazobenzenes should prove quite interesting. Finally, the meta amino groups might serve to increase the stability of the "π-complex" relative to starting material and in this way decrease k_{-2} in comparison with k_{-2} values for other rearrangements.

These arguments that have been presented to explain the effect of the meta amino groups on the kinetics of the rearrangement led to a study of m-chloro,m'-aminohydrazobenzene. The observed first order rate constant for the rearrangement of this compound was found to be independent of the hydrogen ion concentration in the range of acidities investigated. Thus, the transition state for this mono aminohydrazobenzene also involves a monoconjugate acid. Again, the observed acid dependence must be a consequence of the amino group.

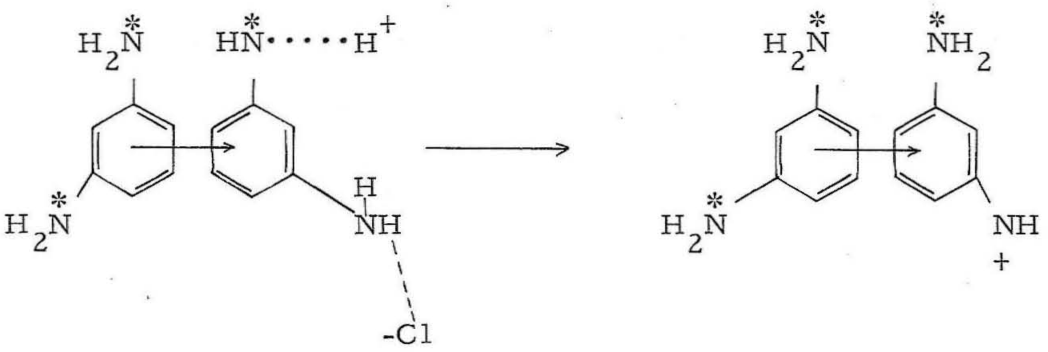


If the arguments used to explain the behavior of HzA are correct, then complex VII should be formed in the rate-determining step of the rearrangement of VI. Accordingly, the two amino groups of the symmetrical ring should be equivalent. Attempts were made to find an analytical procedure to check this prediction, but they all proved unsuccessful.



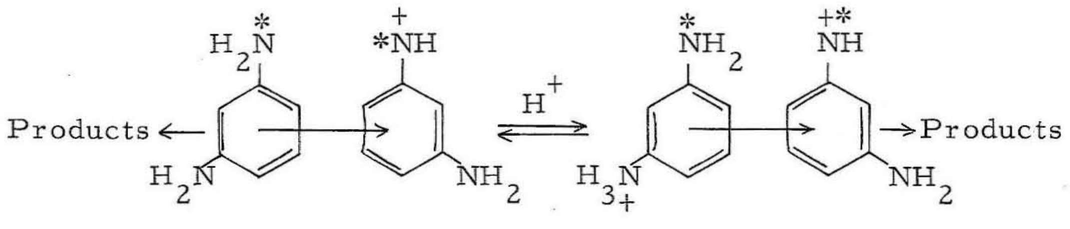
If the diaminocarbazole could have been formed, it could have been converted to carbazole with nitrous acid and hypophosphorous acid.

It is only fair to point out that the most important results of the study of HzA were not anticipated before the investigation was commenced. By no means were the steps which involve direct collapse of the reaction intermediate to product and proton attack on the intermediate expected to be competitive. While sound logic has been used to advance the idea that a radical intermediate is formed by the latter process, the skeptic will no doubt point out that the results of the N^{15} study are consistent with a hydrogen exchange reaction which would cause all of the nitrogen atoms to become equivalent.



This process cannot be distinguished from the proposed radical process by any chemical test (EPR studies would probably prove negative regardless of whether or not a radical intermediate is formed). The proton exchange is in no way related to the benzidine rearrangement. The radical process, however, offers a good explanation for the use of the second proton that is required for the rearrangement of most hydrazobenzenes.

The final possibility exists that the role of the attacking hydrogen ion could simply be to protonate one of the amino groups of the "π-complex."



IV

VIII

That collapse of VIII to the corresponding benzidine should be at all competitive with collapse of IV is extremely unlikely and will be considered no further.

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PROPOSITION I

An investigation of the mechanism of elimination reactions which are induced by weak bases is proposed. The substrates of interest are the various isomers of 2-deutero-4-t-butylcyclohexyl tosylate and 2-phenylcyclopentyl tosylate.

In recent years a number of examples of elimination reactions which are induced by such weak bases as chloride, bromide, and thiophenoxide have appeared in the literature. Eliel (1-4) has made an extensive study of the reaction of sodium thiophenoxide with a number of substituted cyclohexyl bromides and tosylates. All of the reactions are first order in the cyclohexyl-derivative and first order in thiophenoxide. The following tables summarize the data that Eliel obtained.

TABLE I

Reaction of Various Tosylates with Sodium Thiophenoxide in 87% Ethanol at 25.1°C

Tosylate of	$10^5 k_t$(a)	% Elimination
Cyclohexanol	18.35	45
cis-4-t-Butylcyclohexanol	70.19	49
trans-4-t-Butylcyclohexanol	1.78	40
cis-4-Methylcyclohexanol	46.20	61
trans-4-Methylcyclohexanol	2.58	~ 0 (b)
cis-3-Methylcyclohexanol	2.41	~ 0 (b)
trans-3-Methylcyclohexanol	59.30	45
4,4'-Dimethylcyclohexanol	19.04	0 (b)

a) "k_t" is measured in liters mole^{-1} sec.$^{-1}$ and represents the sum of $k_{subst.} + k_{elim.}$ The reaction was followed acidimetrically to give the total rate of reaction, while the fraction of elimination was determined by iodometric titration of unreacted thiophenoxide.

b) The validity of these values may be questioned. Eliel originally reported (2, 3) that the trans isomer of t-butylcyclohexanol gave only substitution products when treated with thiophenoxide. He reinvestigated (4) this experiment and found approximately 40% elimination.

TABLE II

Reaction of Various Bromides with Sodium Thiophenoxide in 87% Ethanol at 25.1°C

Bromide	$10^5 k_t$	% Elimination
cis-4-t-Butylcyclohexyl	9.44	49
trans-4-t-Butylcyclohexyl	0.154	46
cis-4-Methylcyclohexyl	6.40	51
Cyclohexyl	2.28	47

Eliel also reported (1) that the elimination rates of cyclohexyl tosylate and cis-4-t-butylcyclohexyl tosylate are ten times faster with thiophenoxide than with hydroxide.

Winstein and Darwish (5, 6) have investigated the elimination reactions of cis- and trans-4-t-butylcyclohexyl tosylate in acetone. Several bases were studied and all were found to linearly accelerate the rate of elimination. The results obtained are listed below in Table III.

TABLE III

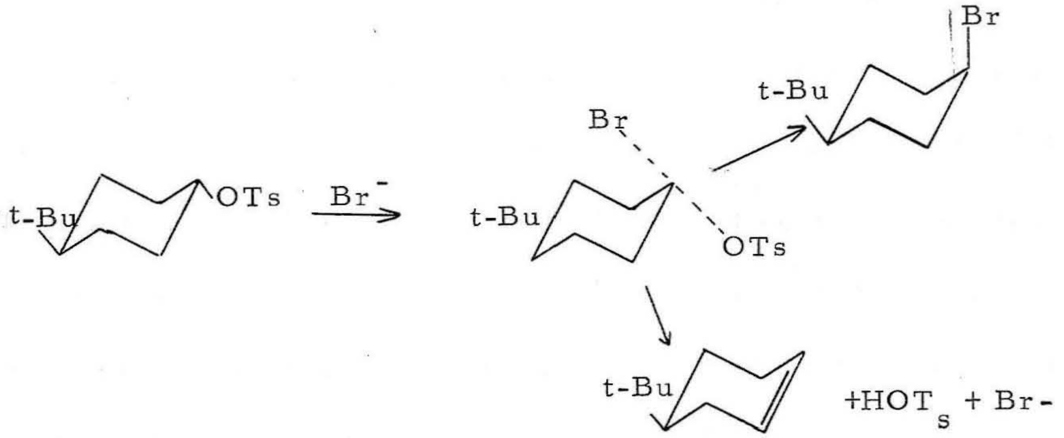
Substitution and Elimination of cis- and trans-4-t-Butylcyclohexyl Tosylate in Acetone at 75°

Salt	Relative Rate (a)	n(b)	F_e	
			trans ROTs	cis ROTs
LiCl	1	3.04	0.30	-
Bu_4NBr	10	3.89	0.25	-
LiBr	5	3.89	0.25	0.57
NaI	5	5.04	ca. 0.10	0.41
NaS	-	high	ca. 0	0.48

a) This refers to the total second order rate constant.
b) Nucleophilic constants of the anions--see G. Swain, *J. Am. Chem. Soc.*, *75*, 141 (1953).
c) Fraction of elimination.

Winstein discussed the possible mechanisms and concluded that none of the common explanations could satisfy his results. As lithium perchlorate was 10 to 90 times less effective in inducing elimination than the bases studied, he argued that a salt-promoted ionization (S_n1, E_1 mechanism) which does not involve direct participation of the added anion could not be operative. The E_2 mechanism is precluded for the elimination reaction of the trans isomer, as the equatorial tosylate group and the hydrogen trans to it are not coplanar. Nor could substitution followed by elimination be compatible with the results as the substitution product is several powers of ten less reactive than the tosylate.

Winstein advanced an interesting mechanism (the "merged mechanism") to account for these observations. He proposed that the added anion attacks the 1-carbon atom to form an "S_n2 like" intermediate which can collapse either to substitution or elimination products (Fig. I). He feels that the leaving group probably pulls off an axial proton to give the elimination product.



Bunnett (7) has investigated the elimination reactions of benzyldimethylcarbinyl chloride and the derivative in which the methylene hydrogens are replaced by deuterium. The reactions were carried out in methanol at 75.8° in the presence of added sodium perchlorate, sodium methoxide, and sodium thioethoxide. These salts affect the overall rate of reaction in the following increasing order. $NaOCH_3 < NaClO_4 < NaSC_2H_5$. Sodium perchlorate did not alter the product distribution that was observed for the unimolecular solvolysis reaction. However, the formation of the two possible olefins was linearly dependent upon the concentration of added sodium methoxide or sodium thioethoxide. The deuterium isotope effect upon the formation of the more substituted olefin was 2.6 (k_H/k_D) for the reaction with sodium methoxide and 2.4 for the reaction with sodium thioethoxide. The isotope effect for the formation of the terminal olefin was 0.86 for the reaction with methoxide and 1.24 for the reaction with thioethoxide. The isotope effect for the combined base induced eliminations was 1.86 in both cases. The isotope effects of 2.6 and 2.4 are much lower than the more common values of 6-7 for E_2 mechanisms (8). Bunnett has interpreted his results in terms of an E_2 mechanism, the transition state of which involves extensive carbon-halogen separation and only slight carbon-hydrogen bond breakage. Bunnett seems to doubt that the "merged mechanism" of Winstein is ever operative. He argues that thioethoxide is a stronger base kinetically than methoxide, even though it is a weaker thermodynamic one.

Darwish and Winstein (6), however, have as yet kept out of the literature some very interesting results that give strong support to the "merged mechanism." They have investigated the second order reaction of 3-methyl-2-butyl tosylate and the 3-deutero derivative with tetra-n-butylammonium bromide in acetone at 75°. The non-deuterated substrate gives rise to 56% substitution product and 44% olefin, of which at least 99.5% is 2-methyl-2-butene. The deuterium-substituted isomer reacts to give 80% substitution product and 20%

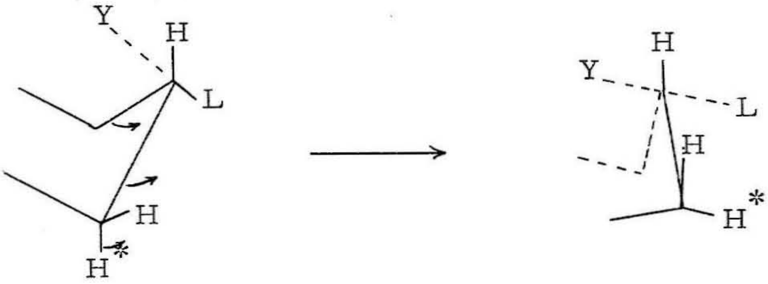
elimination. The k_H/k_D ratio for olefin formation is 2.71 and for substitution is 0.88, while the isotope effect on the overall reaction rate is 1.26. A rigorous interpretation of all of these numbers is somewhat difficult to make; however, the results do show that the rate of substitution is increased at the expense of the rate of elimination, which is decreased much more than is the overall rate of the reaction. These results strongly indicate that the substitution and elimination reactions are linked by a common intermediate.

The results that have been presented in this discussion strongly support the "merged mechanism" that Winstein has proposed. No authors, however, have paid any real attention to the actual nature of the elimination reactions of the cyclic substrates. Eliel's results (Table I) show that the thiophenoxide induced elimination reaction of cis-4-t-butylcyclohexyl tosylate (trans elimination) is only 36 times as fast as the corresponding reaction of the trans isomer. Trans eliminations are known to be generally favored over cis eliminations by several powers of ten. For example, DePuy (9) has found that in potassium-t-butoxide in t-butanol cis-2-phenylcyclohexyl tosylate undergoes elimination at least 10^4 times as rapidly as does the trans isomer. This remarkable effectiveness of thiophenoxide (and other weak bases) to produce elimination with such compounds as trans-4-t-butylcyclohexyl tosylate brings one to a very important question.

Do these eliminations that are induced by weak bases have any relation to ordinary E_2 eliminations or must one devise a completely new set of rules.

An investigation of the Winstein intermediate leads to an interesting observation. As the nucleophile attacks the substituted carbon atom, the steric configuration at this carbon atom begins to invert. This process of inversion brings the three permanent bonds into a common plane. In the cyclohexyl case the bonds cannot rotate. As a result, the hydrogens of the two unsubstituted carbon atoms will eclipse the leaving group and the hydrogen atom of carbon-1. The hydrogen atom that was originally cis to the leaving group will become coplanar with it (Fig. II).

FIGURE II



Trans eliminations have long been known to be favored over cis eliminations (10). However, the possibility exists that, where the leaving group cannot be trans-coplanar with a hydrogen atom, cis coplanarity can result and lead to elimination. Such eliminations could well be of importance in the reactions mentioned in this discussion.

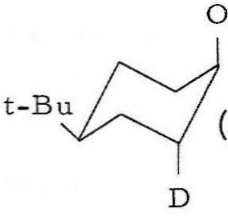
Evidence exists to support cis-coplanar elimination. DePuy (9) has investigated the elimination reaction of cis- and trans-2-phenylcyclopentyl tosylate in potassium t-butoxide-t-butyl alcohol, and has found that the cis isomer undergoes elimination only 14 times as rapidly as the trans isomer. The ratio for the corresponding cyclohexyl isomers is greater than 10^4. DePuy argues that this great difference in the ratios for the two systems is a result of the greater ease with which cis coplanarity can be achieved in the cyclopentyl tosylate. As the dihedral angle between hydrogen and the departing anion is much smaller in the trans-2-phenylcyclopentyl tosylate than in the corresponding cyclohexyl compound, much less energy would be required to produce coplanarity in the former compound than in the latter (Fig. III).

FIGURE III

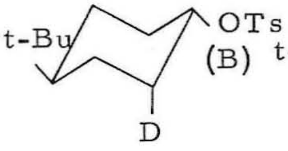
Cyclopentyl--cis elimination

Cyclohexyl--cis elimination

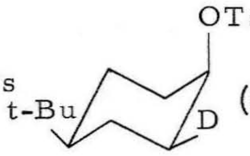
To establish the stereochemistry of the elimination reactions of cis- and trans-cyclohexyl tosylates, which are induced by strong nucleophiles, but weak bases, it is proposed to investigate the elimination (and substitution) reactions of the four 2-deutero-4-t-butylcyclohexyl tosylates (A-D).



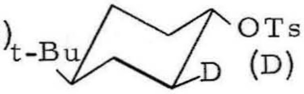
(A)



(B)



(C)



(D)

The "merged mechanism" would predict a large isotope effect on the formation of olefin from B. This olefin should show less deuterium than its precursor. In contrast, the formation of olefin from D should be only slightly affected, and should contain just as much deuterium as starting material. While the results obtained from tosylates B and D would be quite important, the significance of the results obtained from tosylates A and C cannot be too strongly emphasized. The effect of weak bases on elimination from the cis isomer must surely be similar to the effect on the trans isomer. If the "merged mechanism" holds for tosylates A and C, the equatorial and not the axial hydrogen should be lost. Such a result would exclude any ordinary E_2 mechanism and would lend very strong support to Winstein's "merged mechanism."

Even if the experiments with the deuterium-substituted cyclohexyl tosylates show that the elimination reactions are of a cis nature, they will not show the importance of the coplanarity of the departing anion and hydrogen on an adjacent carbon atom. If such coplanarity is of extreme importance to the elimination reaction, the strongly nucleophilic and weakly basic halides and thio-oxides should be extremely efficient in promoting elimination from cyclopentyl derivatives. Not only should coplanarity of vicinal cis substituents be more easily achieved for cyclopentyl derivatives than for the corresponding cyclohexyl compounds, but also the former substrates are known to be more susceptible to nucleophilic attack than the latter (11). It is therefore proposed to investigate the elimination reactions of cis- and trans-cyclopentyl tosylates (for example, cis- and trans-2-phenylcyclopentyl tosylate) with a series of weakly basic nucleophiles such as have been mentioned in the discussion of this propostion.

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PROPOSITION II

It is proposed to investigate the photochemical decomposition of phenylhydroxylamine.

The homolytic cleavage of 0-0 and N-N bonds in organic peroxides and hydrazines has received considerable attention. Both processes have been effected by thermal and photochemical means (1-4).

In comparison, the study of the homolytic cleavage of N-O bonds is still in its infancy. This bond has been thermally fragmented in various nitrite and nitrate esters. The resulting products have been accounted for in terms of an initial homolytic cleavage of the N-O bond (5, 6). Recently, Walling (7) has investigated the thermal and photochemical decomposition of diacylhydroxylamines. Product analysis and polymerization initiation both lead to the conclusion that the N-O bond underwent a homolytic fragmentation. (Thermal reactions are complicated by Lossen rearrangements.)

The bond dissociation energy of the N-O bond may be correlated with the energies of the O-O bond in hydrogen peroxide and the N-N bond in hydrazine. Walling (8) lists these energies as 52 and 60 kilocalories, respectively. Pauling (9) has derived the rather empirical formula

$$D(A-B) = [D(A-A)D(B-B)]^{\frac{1}{2}} + 30(X_a - X_b)$$

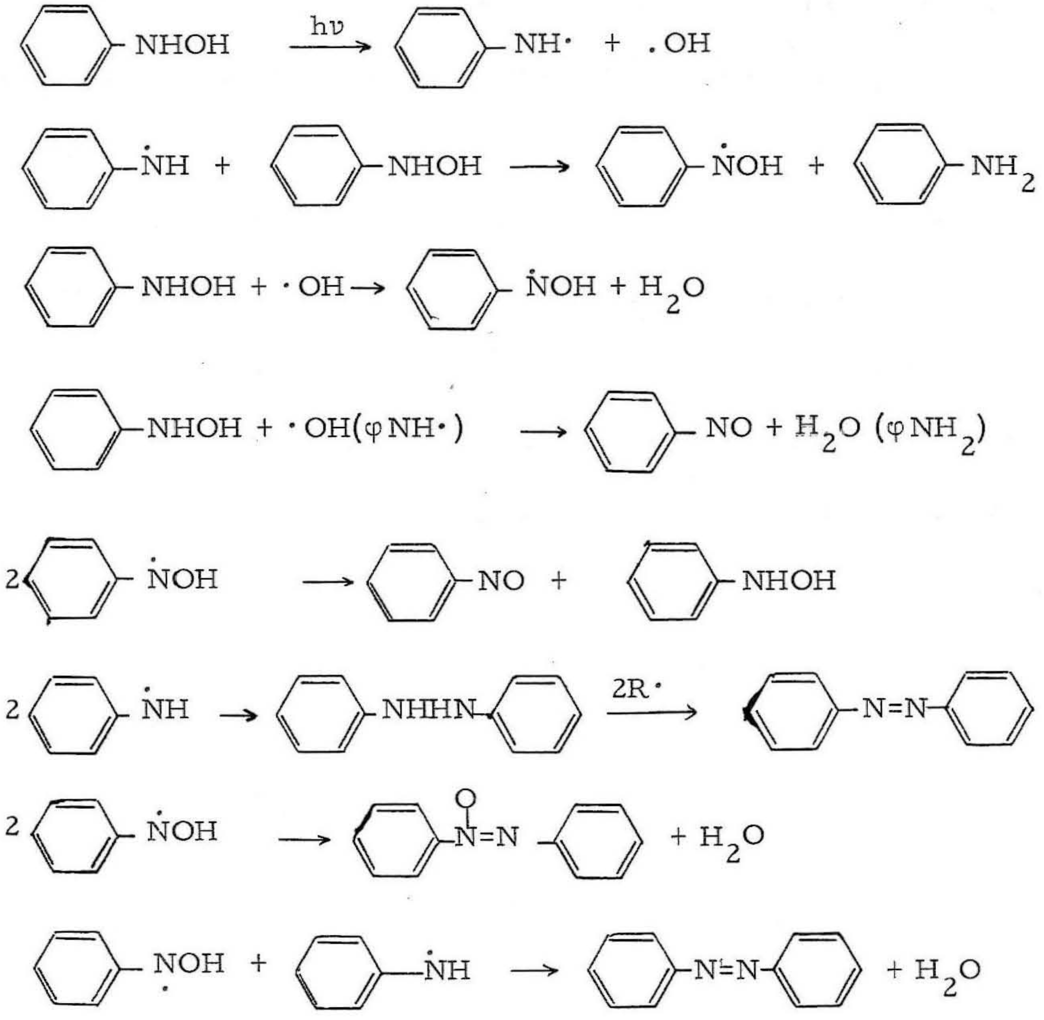
to calculate average bond energies. The final term of the equation is included to account for the added stabilization that results from the electronegativity difference, $X_a - X_b$, of the bonded atoms. Since bond dissociation energies as well as average bond energies have been used to determine the empirical electronegativity factor, this equation should give a fair approximation of the N-O bond dissociation energy of hydroxylamine. The calculated value is 63 kilocalories.

Bond dissociation energies (for the N-O bond) of substituted hydroxylamines should be related to those of substituted hydrazines or peroxides. The heat of dissociation of hydrazobenzene is estimated to be between 32 and 37 kilocalories (10). This corresponds to a value of 12-14 kilocalories of resonance energy per phenyl group. The energy of the N-O bond of phenylhydroxylamine would be estimated to be approximately 50 kilocalories.

As phenylhydroxylamine absorbs appreciably from 2000-3000 Å and since the N-O bond energy is well below the amount of energy absorbed in this region, a study of the photolysis of this compound was felt to have interesting possibilities.

Photolysis of a 0.01M solution of phenylhydroxylamine in benzene or 95% ethanol was found to be virtually complete within two and one half hours. One half hour of photolysis with the light below 2800 Å filtered out produced a color change in the solution, but gave rise to no chemical change that could be detected by ultraviolet analysis. The ultraviolet spectra of the successfully irradiated solutions indicated that aniline, nitrosobenzene, azobenzene, and possibly azoxybenzene might all have been formed.

It is proposed that homolytic cleavage of the N-O bond has occurred and that the resulting products would be formed by the following paths.

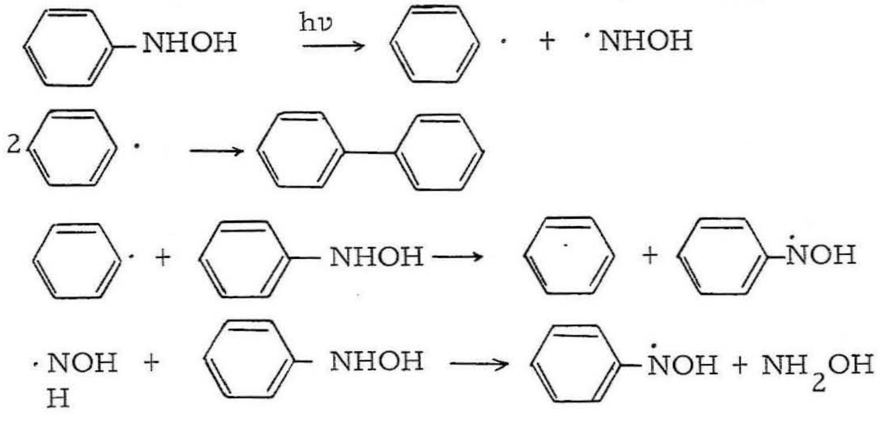


Careful experimental techniques would have to be developed to show that azobenzene and azoxybenzene, if present, are formed by radical coupling processes.

In this process the radical source is also an excellent radical scavenger. This system would thus probably be a poor one to initiate polymerization. More suitable radical scavengers than phenylhydroxylamine would have to be chosen to divert the course of the reaction. Tributyltin hydride should be a good candidate. An investigation of the photodecomposition of N, N-diphenylhydroxylamine should eliminate some of the experimental difficulties encountered with phenylhydroxylamine.

The observation that the photolysis is apparently as efficient in benzene as in ethanol is quite interesting. Since benzene absorbs virtually all of the light below 2800 Å , the phenylhydroxylamine molecules may well receive energy via collision with activated benzene molecules.

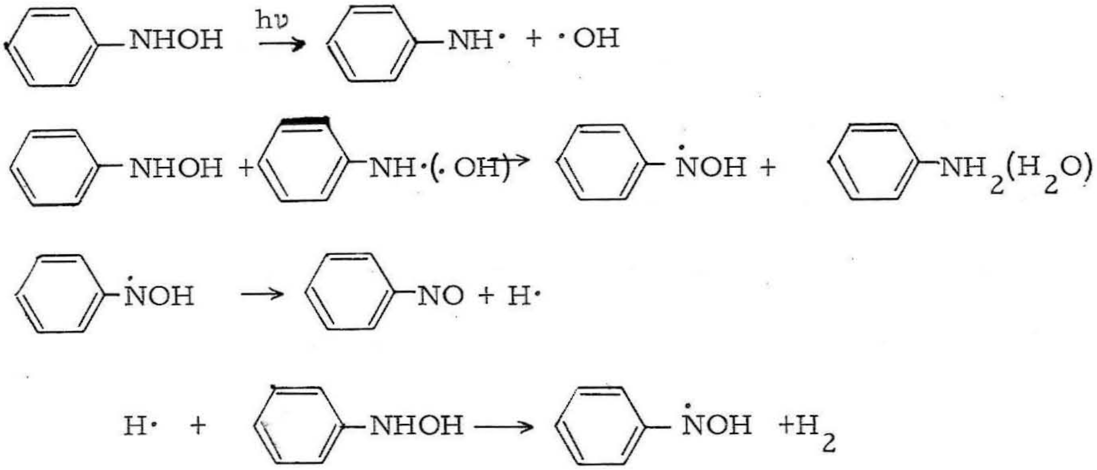
Product analysis is essential for proof of the above mechanism and would be used to either advance or discount the following possible mechanisms for the observed decomposition.



The remaining steps would be similar to those given in the proposed mechanism.

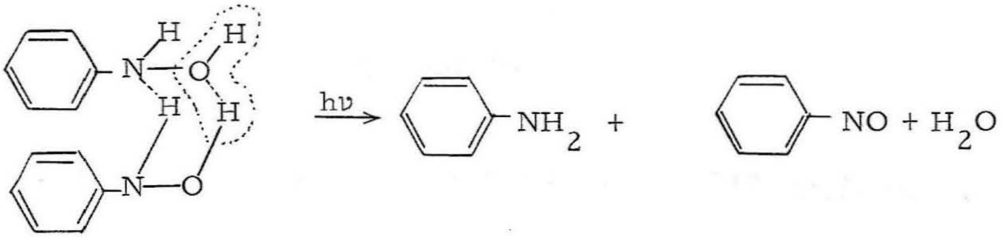
Since the energy absorbed by the molecule at 2537 Å (the strongest emission band of mercury) is greater than that of either the C-N or N-O bond, the possibility of C-N bond cleavage must be considered. The absence of benzene, biphenyl, and hydroxylamine would eliminate such a process.

A chain process must also be considered.



This mechanism would require formation of hydrogen, a product which should not be difficult to detect. Absence of hydrogen would discount any mechanism involving cleavage of a C-H, N-H, or O-H bond.

As aniline and nitrosobenzene could be produced by a concerted dismutation reaction, the possibility must be considered that no radicals are ever formed.



This is clearly a bimolecular path. A kinetic analysis of the reaction should thus be quite informative. As molecules of phenylhydroxylamine should associate much more in benzene than in ethanol, the above concerted mechanism might partially account for the apparent similarities of photolysis in the two solvents.

Determination of the quantum yield in the presence and in the absence of radical traps should give a result pointing to or away from a chain process. The quantum yields in benzene and in ethanol would show the efficiency of cleavage in the two solvents. This study might well prove a separate problem in itself, as it could lead to a description of intra- and intermolecular energy transfer. A similar or greater quantum yield in benzene as compared to ethanol would be good evidence against photoionization as this process would be expected to be much more efficient in the latter solvent.

Extension of the proposed study to include O-substituted N-phenylhydroxylamines should prove interesting. A large number of alkoxy and carboxy radicals might be produced by photolysis of such compounds.

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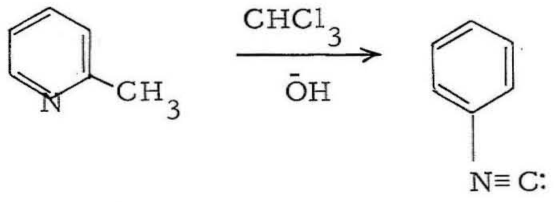
PROPOSITION III

Mechanisms are proposed to explain the formation of phenylisocyanide from 2- and 4-methylpyridine.

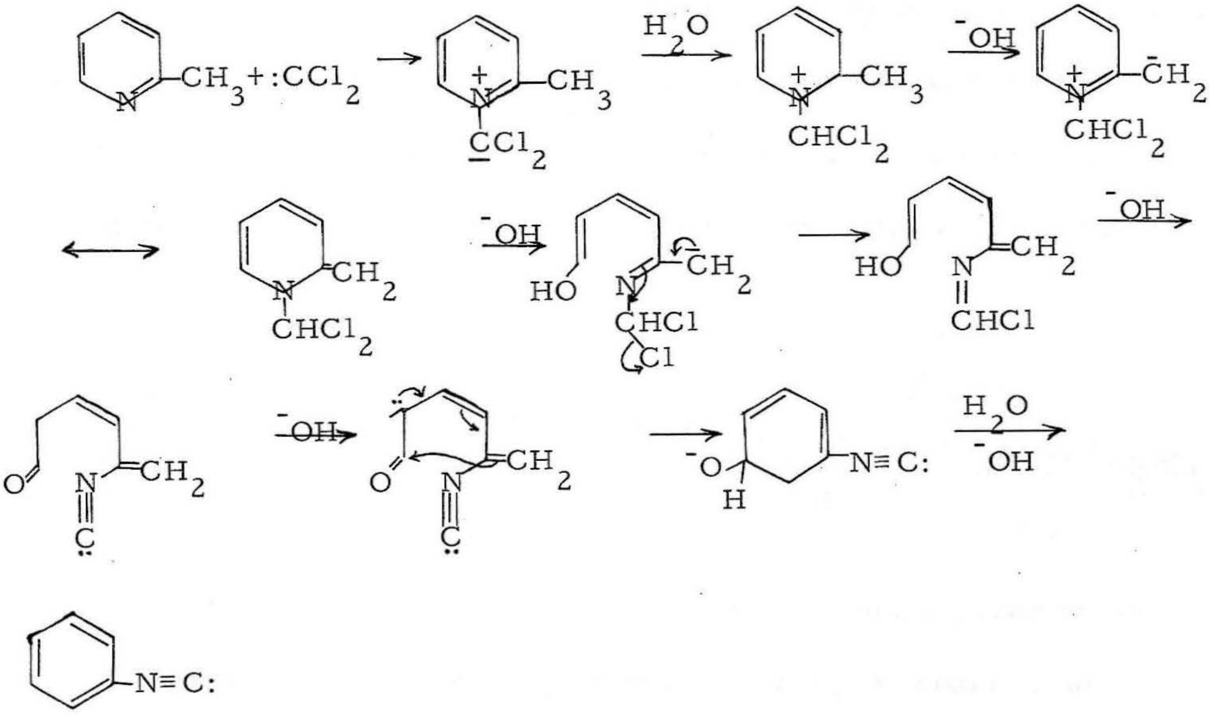
Ploquin (1) has reported that treatment of certain methyl substituted pyridines with chloroform and strong alkali leads to the formation of phenylisocyanides. The details of the experimental procedure are quite sketchy. The isocyanides were identified by their characteristic odor. Phenyl isocyanide has such a strong and disagreeable odor that its detection should be unmistakable. The isocyanides were hydrolyzed to amines which were then diazotized. The diazonium salts were coupled with β-naphthol to give colored compounds. The fact that colored coupling products were formed was advanced as evidence of the aromatic character of the isocyanides. Care was taken in the purification of the pyridines to remove any traces of amines which could easily give rise to the observed isocyanides. The starting material was characterized by its boiling point and by the melting point of the picrate derivative.



Ploquin has proposed an amazing mechanism that does not consider the intermediacy of dichlorocarbene and that includes a pentavalent nitrogen and apparently a bivalent carbon that is linked to nitrogen by a double bond. No consideration will be given to his mechanism except to note that he has postulated a methylenecyclopentene-type intermediate (in the rearrangement of 4-methylpyridine) that would not be too remote from the bicyclic ring advanced in this proposition.

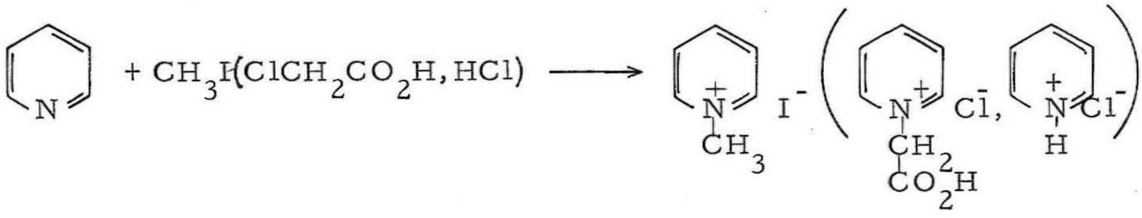
The following mechanism is proposed for the formation of phenyl isocyanide from the reaction of 2-methylpyridine with chloroform and strong alkali.

$$CHCl_3 + {}^{-}OH \longrightarrow :CCl_2 + H_2O + Cl^-$$

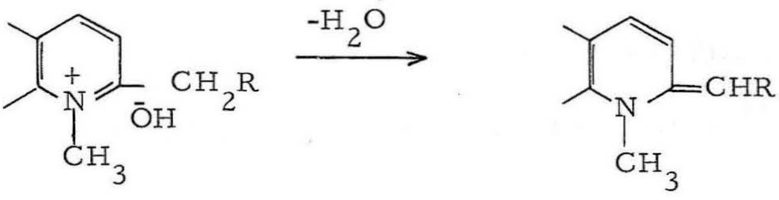


The order in which the various steps are written is not meant to imply the exact timing of the different phases of the reaction. The principal steps are attack by dichlorocarbene, formation of the methylene group (or zwitterion), ring opening by base, and finally ring closure. Ploquin's observation that 3-methylpyridine does not form an aromatic isocyanide supports the step which involves ring opening by attack of base on the zwitterion. The latter form could not be obtained from 3-methylpyridine.

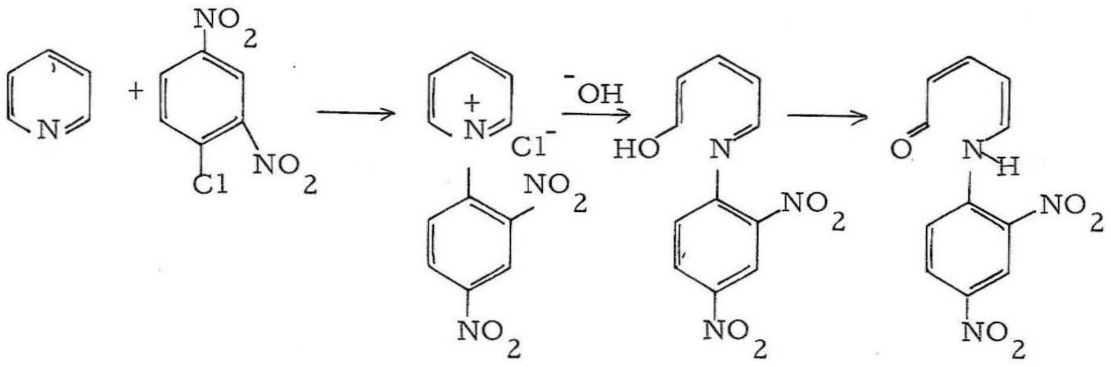
Virtually all of the steps that are proposed in this mechanism have good precedents. A summary of pyridine chemistry may be found in Sidgwick's "Organic Chemistry of Nitrogen" (2). As the unshared pair of electrons of nitrogen is available for bonding, pyridine behaves like a tertiary amine, forming quaternary compounds with methyl iodide, dimethyl sulfate, and acids, to mention a few examples. As dichlorocarbene is certainly the intermediate that attacks primary



amines to form isocyanides, reaction between the nucleophilic pyridine and dichlorocarbene to form a quaternary derivative should occur readily. Methyl substituted quaternary hydroxides that are derived from pyridine readily lose water to form anhydro bases which resemble intermediate IV (IV') of the proposed mechanism.



Finally, ring opening of N-substituted pyridine by hydroxide has been observed. The substitution product of the reaction of pyridine with 2,4-dinitrochlorobenzene when treated with alkali forms an unsaturated aldehyde.



The attack of hydroxide ion at the 2-carbon atom would be similar to the proposed reaction of the zwitterion IV with hydroxide.

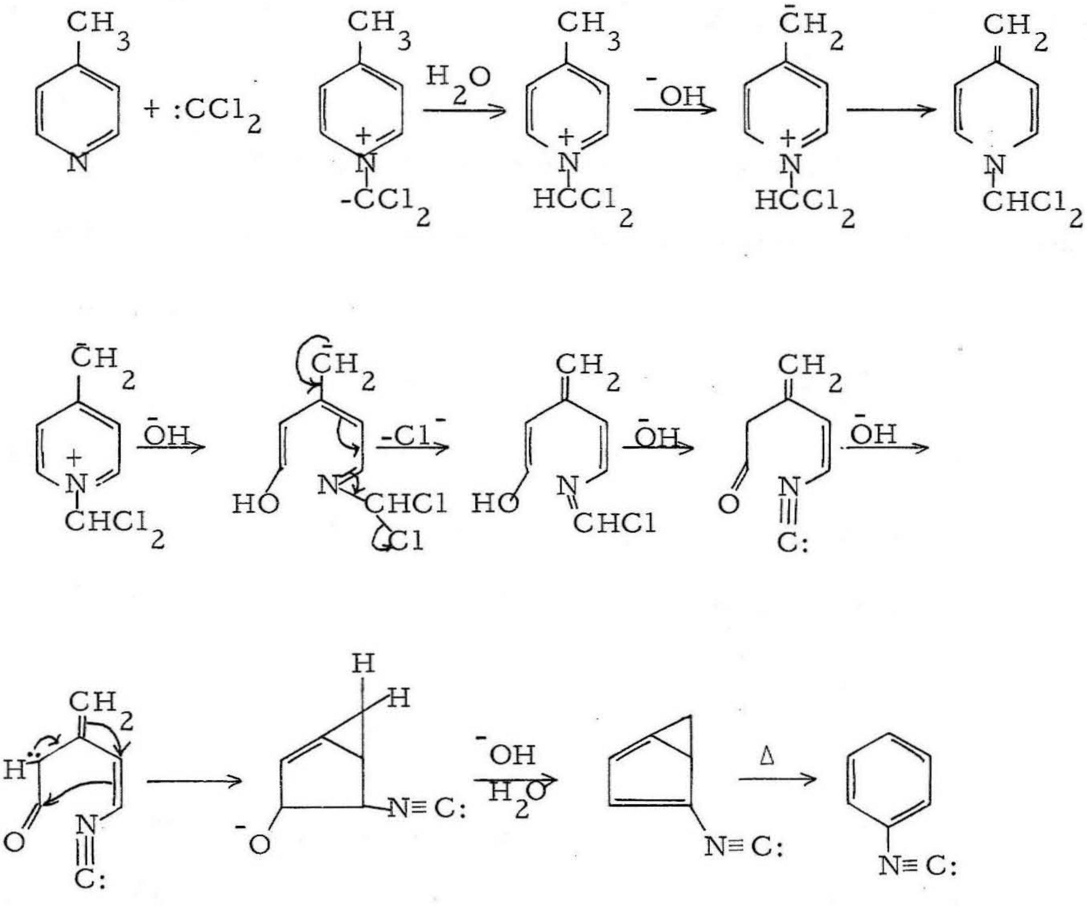
The final identity of the methyl group could be determined by tagging it with C^{14}. The proposed mechanism would require that all of the label be in the ortho carbon atoms of the resulting phenyl isocyanide. This mechanism is straightforward and does not present any great challenge. The mechanism for the conversion of 4-methylpyridine to phenyl isocyanide is certainly more complex, but still should be similar to the reaction sequence for 2-methylpyridine.

Discussion of the latter mechanism is therefore necessary before the more unusual reaction of 4-methylpyridine can be discussed.

It is proposed to study the conversion of 4-methylpyridine to phenyl isocyanide by tagging the 4-methyl group with C^{14} and observing the distribution of the label throughout the ring. Labeling of the ring atoms would also prove instructive.

The following mechanism is proposed.

$CHCL_3 + \bar{O}H \longrightarrow :CCl_2 + H_2O + Cl^-$



This reaction sequence is identical to the one first proposed until the final three steps are reached. The attack of the CH_2^- group on the double bond is simply a Michael addition. The ring closure that accompanies the Michael addition leads to a strained bicyclic structure which should quickly eliminate water and expand to an aromatic system.

If the methyl group is labeled, all of the C^{14} should be in C_3 of the resulting phenyl isocyanide. If C_3 of the 4-methylpyridine were instead tagged, 50% of the total activity would be found in C_2 and 50% in C_3 of the product isocyanide.

Degradation of the isocyanide could be accomplished by acid hydrolysis to the amine which could then be degraded by the method of Roberts et al. (3).

If randomization other than that proposed in this discussion should occur, it should be of a symmetrical nature. A back-door (product to starting material) approach to the mechanism should be possible.

Investigation of the dimethylpyridines should lead to the clarification of any mechanistic ambiguity.

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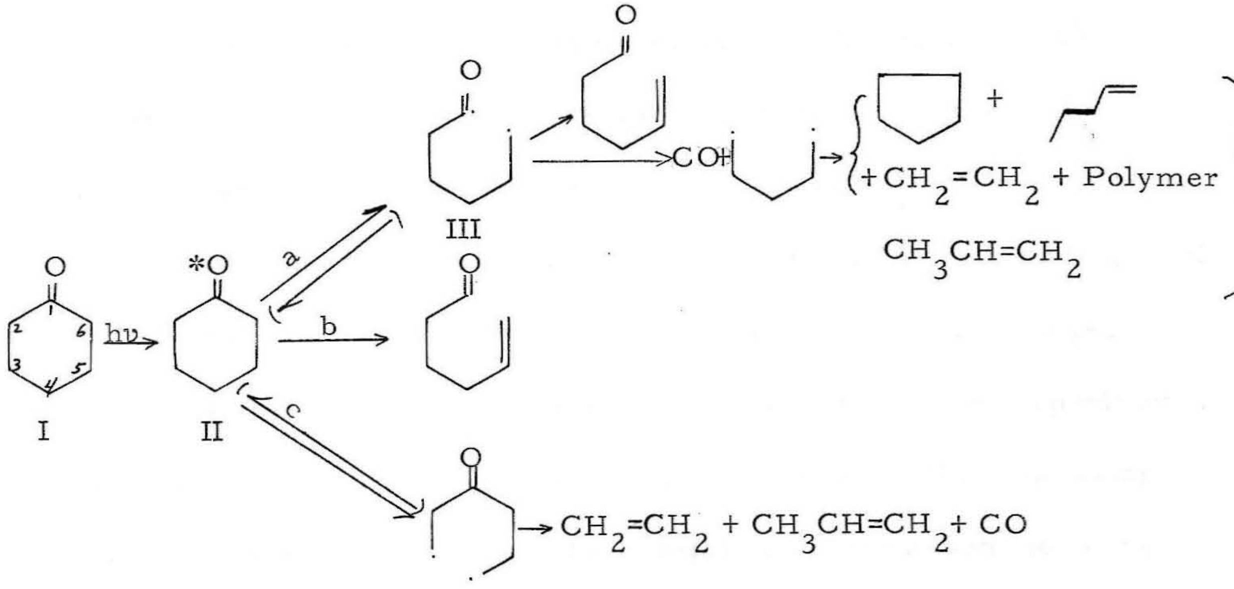
PROPOSITION IV

It is proposed to investigate several aspects of the photolysis of cyclic ketones by employing the technique of measuring the change in optical activity of a ketone whose asymmetric center is involved in the bond breaking.

The products formed from the vapor phase photolysis of several cyclic ketones have been rather clearly determined (1-4). Cyclohexanone, for example, gives rise principally to 5-hexenal, carbon monoxide, cyclopentane and 1-pentene; while ethylene, propylene, and polymer are formed in minor amounts. Similar products are obtained from 2-methylcyclohexanone, cyclopentanone, and cycloheptanone. Several possible schemes which might account for the observed products are shown below (Fig. I).

FIGURE I



Srinivasan (4) has investigated the photolysis of cyclohexanone at different temperatures and pressures. The results that be obtained are given in Table I.

TABLE I (4)

Photolysis of Cyclohexanone at 3130 Å

Pressure mm.	Time min.	Temp. °C	Φ CO(1)	Φ_{hexenal}	Remarks
4.8	120	28.9	0.046	0.16	
3.7	60	25.8	---	0.17	$P_{O_2} = 21.0$ mm.
4.7	120	28.8	0.022	0.19	$P_{CO_2} = 18.0$ mm.
5.0	120	100.0	0.108	0.12	
25.5	30	100.0	0.087	0.16	
47.0	30	100.0	0.061	0.12	

1) "Φ" refers to quantum yield

An increase in temperature clearly produces an increase in the quantum yield (Φ) of carbon monoxide, while in contrast an increase in pressure is accompanied by a reduced quantum yield of carbon monoxide. The effect of these variables upon the formation of hexenal is not clearly defined. Srinivasan feels that a pressure increase results in a higher quantum yield of hexenal, although the experimental data do not seem to compel such an interpretation. The conclusions may be drawn, however, that the quantum yield of carbon monoxide is more sensitive to temperature variation than is the quantum yield of hexenal, and that the quantum yield for the decomposition of cyclohexanone is increased with an increase in temperature.

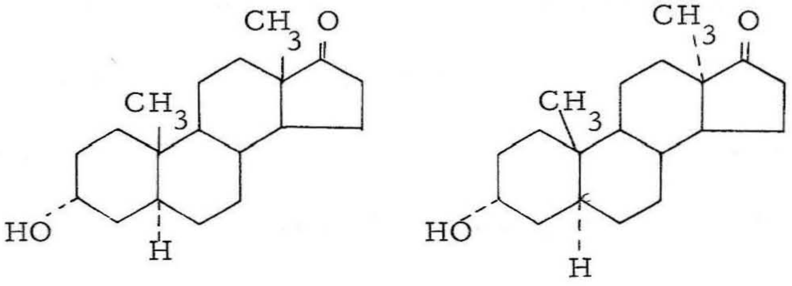
Srinivasan (5) observed a similar temperature dependence for the photolysis of cyclopentanone. A rigorous investigation of the effect of pressure (6, 7) upon the yields of carbon monoxide and pentenal showed that the former product decreases and the latter increases with an increase in pressure. The quantum yield of cyclopentanone decomposition does not vary more than 13%, although a maximum is indicated at a pressure of 53 mm. of the ketone.

Srinivasan has concluded that the vibrational energy possessed by the molecule in the upper electronic state at the instant of decomposition will determine the products that are formed. As a pressure increase favors pentenal formation at the expense of carbon monoxide, the conclusion is drawn that the former molecule is formed from a lower vibrational state than the latter.

Srinivasan seems to doubt that a diradical is ever formed as the addition of oxygen does not divert the course of the product-forming reactions. He feels instead that the various products are probably formed by a concerted mechanism.

The possibility that a concerted mechanism is operative in the photolysis of cyclic ketones seems quite improbable. A great deal of imagination would be necessary to explain the formation of such products as 1-pentene by a concerted path. Why cyclic ketones should not give radical fragments upon photolysis when aliphatic ketones most certainly do is an extremely difficult question to answer. In support of a diradical mechanism is Butenandt's (8) observation that the photolysis of androsterone produces lumiandrosterone which is simply the former compound with the opposite configuration at C_{13} (Fig. II).

FIGURE II



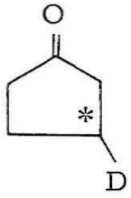
The bond between C_{13} and C_{17} must break and reform to allow the observed inversion of configuration.

If a radical mechanism is assumed, at least two important questions are left unanswered. First, does an increase in temperature increase the quantum yield of formation of the diradical (III) or does it aid in the breaking of the 1-2 bond of the diradical. Similarly, does the pressure increase lead to the deactivation of II or of III. If the effect of an increase in temperature is to aid in the ejection of carbon monoxide from the diradical, then the conclusion follows that the initial bond-breaking process is reversible. Under the proper conditions an increase in pressure may effect the reversibility of the initial bond cleavage. The process of reversible bond cleavage could be readily studied by irradiating optically active cyclic hexanones in which C_2 was made the asymmetric center. The change in activity of the unreacted ketone would aid in the description of the various steps that lead to the observed products.

It is therefore proposed to investigate the photolysis of optically active 2-deuterocyclohexanone at various temperatures and pressures and accordingly study the change in activity of the recovered starting material. This system is essentially the same as cyclohexanone, but suffers from the drawback that the optical activity will be small. If this proved too much of a problem, a related compound of greater specific rotation could be studied. For example, 2-methylcyclohexanone appears to give results similar to those obtained with cyclohexanone.

The technique of measuring the change in optical activity may be used to investigate the nature of formation of ethylene and propylene. The yield of these olefins is quite small in the case of cyclohexanone, but the photolysis of cyclopentanone produces ethylene in 62% yield (2). If these compounds are formed by path c (Fig. I), one might expect to observe a change in activity of recovered ketone in which C_3 was the asymmetric center.

Ex.



If the experiments show no change in activity of recovered starting material, one of two conclusions is possible. Either initial bond cleavage is irreversible or a concerted mechanism is operative. The latter process could be substantiated or eliminated by photolysis of pure cis (or trans) 2,3-dideuterocyclic ketones. The products of photolysis would show entirely the same spatial orientation of the deuterium atoms as the starting material if diradicals were never formed.

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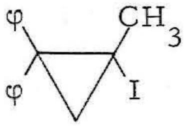
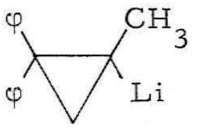
PROPOSITION V

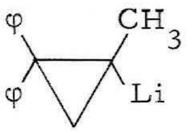
It is proposed to investigate the process of halogen-metal interchange in the system



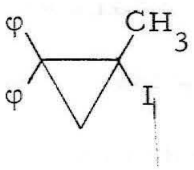
I



II



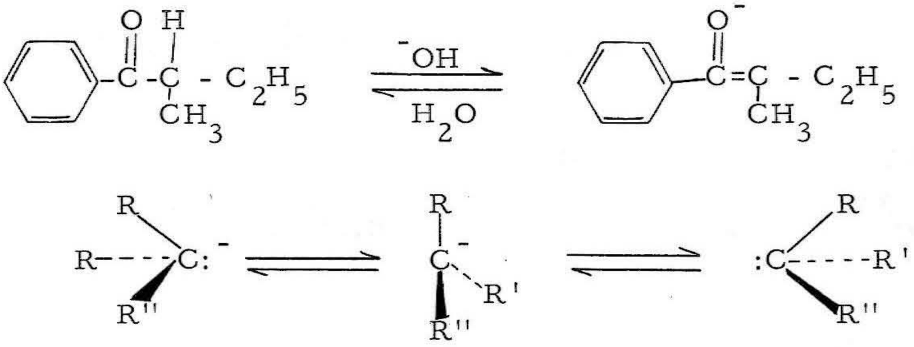
I'



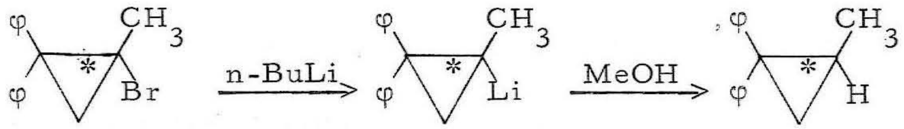
II'

The optical stability of organometallics has long been a question of interest to organic chemists. The nature of the carbanion, of the solvent, and of the metal are all important in determining whether an organometallic compound can preserve the optical activity that was present in its precursor (1). The carbanion center of these compounds must become planar before racemization can occur. Planarity could be achieved by resonance stabilization of the negative charge or by a simple inversion such as occurs with amines (Fig. I).

FIGURE I



The ease of inversion must certainly be affected by the amount of carbanionic character that the organometallic possesses. If the carbon-metal bond is essentially covalent, the organometallic cannot undergo racemization by a simple flipping of a carbanion, which is not even present. If, however, the carbon-metal bond has appreciable ionic character, a relatively free carbanion will be present which can undergo inversion of configuration. Organosodium compounds are highly ionic and organomercury compounds are quite covalent. The former never preserve activity while the latter are found to exhibit a high degree of optical stability. Intermediate in ionic character are organolithium compounds. In his text (1) Eliel gives several examples of organolithiums which have been found to retain at least some of the optical stability of their precursors. Perhaps the most stable of these is 2,2-diphenyl-1-methylcyclopropyllithium (II), which was prepared by the reaction of the corresponding bromide (III) with n-butyllithium in ether-benzene-petroleum ether at 5-6°C (2). Mixing of the reactants required 20 minutes. After an additional 15 minutes, the reaction mixture was quenched with methanol to give 2,2-diphenyl-1-methylcyclopropane (IV).



III II IV

The optical activity of the product corresponded to 60% retention of configuration and 40% racemization. The optical stability of the cyclopropyllithium compound is most certainly increased by the barrier to inversion of the three-membered ring.

Curtin (3) has shown that solvent polarity strongly influences the optical stability of organolithium compounds. He prepared 2-butyllithium by the reaction of 2-octyllithium with (-)-di-2-butylmercury. After 30 minutes of reaction at -8° in ether-free pentane, the mixture was carbonated to give 2-methylbutyric acid with about 50% retention of configuration. When the preparation was carried out in pentane which contained 6% ether, the methylbutyric acid that was obtained was totally racemic. The addition of ether to pentane increases the polarity of the solvent. This solvent change should increase the ionic character of the carbon-metal bond and, accordingly, a greater degree of racemization should result.

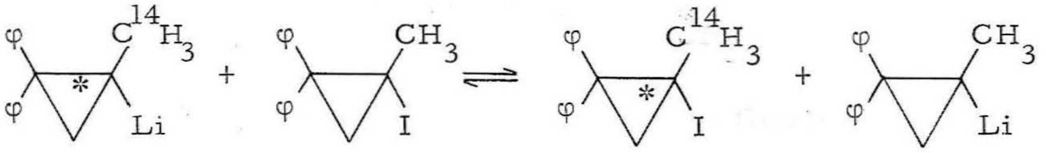
These results show that under the proper conditions optically stable organolithiums can be readily prepared and handled. With choice of the proper system investigations of the stereochemical fate of organolithium reagents should be possible.

One common question that comes to mind is when and how do organometallics racemize. A particular phase of this problem is that of metal-halogen interconversion.

$$R\text{-}Li + R'X \longrightarrow R'Li + RX$$

Such reactions are quite common where X is iodide or bromide. With the proper reagents the exchange is rapid and reversible (4). Equilibration is probably complete within 30 minutes for the reaction of n-butyllithium with ethyl iodide in ether at -75°. Whether or not racemization may accompany the exchange reaction between organolithiums and organohalides is simply not known. Obviously, exchange can be accompanied by retention of configuration as the optically active cyclopropyllithium compound described above was prepared by an exchange reaction between an optically active cyclopropyl bromide and n-butyllithium. Since the n-butyl carbanion is certainly much more basic than the cyclopropyl carbanion, the latter species would probably have no more freedom during the exchange than when it is bonded to lithium. That this exchange reaction does proceed with retention of configuration accordingly says nothing about the fate of an asymmetric center that is involved in an exchange reaction between substrates which can produce carbanions of equal (or nearly equal) basicities.

To gain an understanding of halogen-metal interconversion, it is proposed to investigate the exchange reaction between 2,2-diphenyl-1-iodo-1-methylcyclopropane (racemic) and optically active 2,2-diphenyl-1-methylcyclopropyl lithium which is also radioactive.



In order to obtain a maximum of information, the study is to include the exchange reactions in which the two labels are both incorporated into the halide or one into the halide and one into the cyclopropyllithium. As the reaction is reversible, the radioactivity will approach a constant level for the two compounds. The optical activity will of course drop to zero. If the cyclopropyl iodide (or cyclopropyllithium) is used in large excess, the back reaction (at least for the equilibration of the radioactive label) will be of little importance throughout most of the reaction. A plot of the change in optical activity vs. the change in radioactivity for the various substrates should prove quite instructive. As the slope of this line should be independent of the concentration of the reactants (for at least the early stages of the exchange), the study will not be affected by side reactions such as elimination and coupling. An additional advantage of this system is that the basicities of the carbanions involved in the exchange reaction are equal.

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