

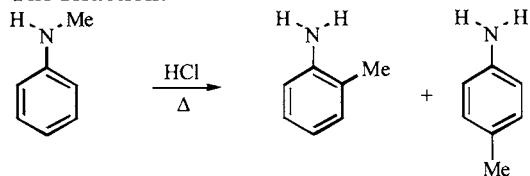
## **Sem 4 - Remaining Portion of the Syllabus**

- **Migration from nitrogen to ring carbon:**

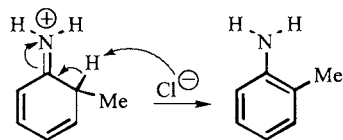
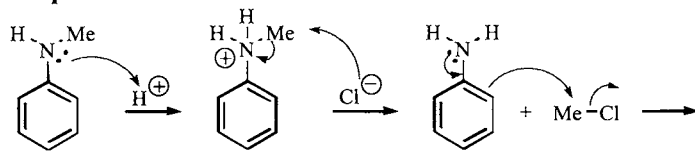
1. Hofmann-Martius rearrangement,
2. Sommelet Hauser rearrangement,
3. Fischer-Hepp rearrangement,
4. N-azo to C-azo rearrangement,
5. Bamberger rearrangement,
6. Orton rearrangement
7. Benzidine rearrangement.

## Hofmann-Martius Rearrangement

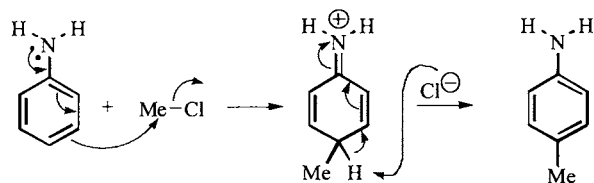
### The Reaction:



### Proposed Mechanism:



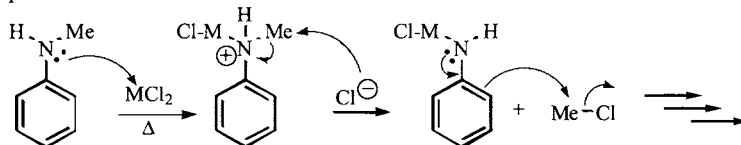
OR



### Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5<sup>th</sup> ed., John Wiley and Sons, Inc., New York, 2001, p. 729.

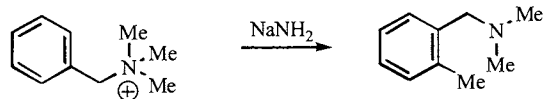
The **Reilly-Hickinbottom Rearrangement** uses  $\text{CoCl}_2$ ,  $\text{CdCl}_2$  or  $\text{ZnCl}_2$  and the amine rather than protic acid and the amine salt.



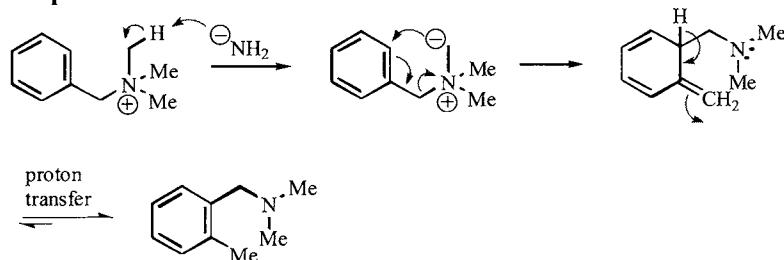
M = Co, Cd, Zn;  $\Delta = 200\text{-}350\text{ }^\circ\text{C}$

## Sommelet-Hauser Rearrangement

### The Reaction:

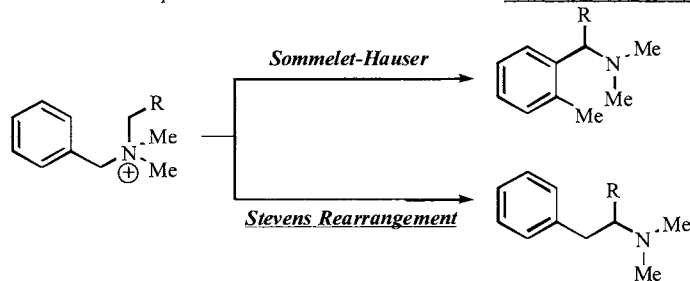


### Proposed Mechanism:



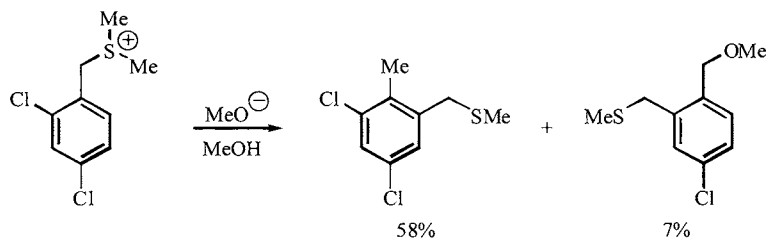
### Notes:

There can be competition between *Sommelet-Hauser* and *Stevens Rearrangement* mechanisms:

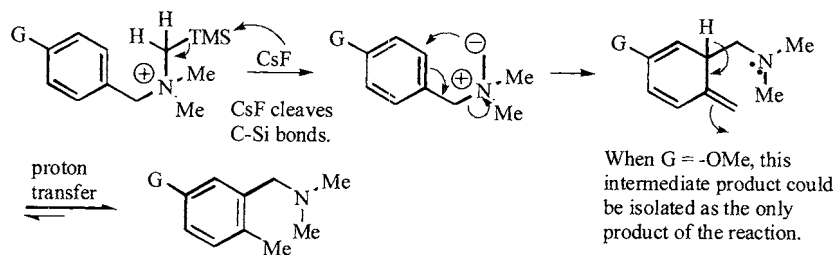


M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5<sup>th</sup> ed., John Wiley and Sons, Inc., New York, 2001, pp. 877, 1420, 1455; S. H. Pine, *Organic Reactions* **18**, 4

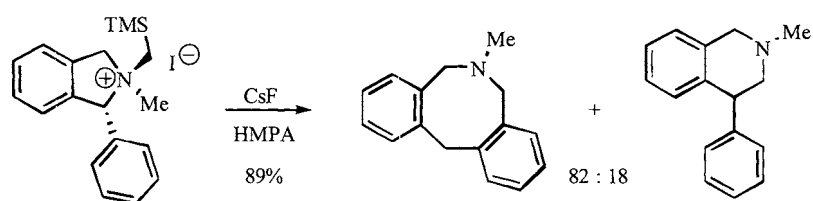
### Examples:



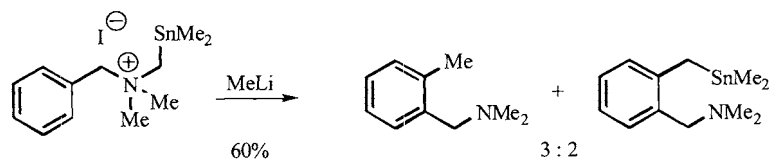
T.-J. Lee, W. J. Holtz, *Tetrahedron Letters* **1983**, *24*, 2071



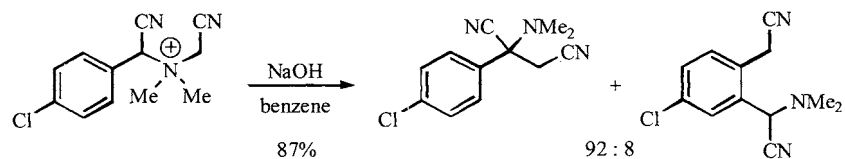
N. Shirai, Y. Watanabe, Y. Sato, *Journal of Organic Chemistry* **1990**, 55, 2767



A. Sakuragi, N. Shirai, Y. Sato, Y. Kurono, K. Hatano, *Journal of Organic Chemistry* **1994**, 59, 148



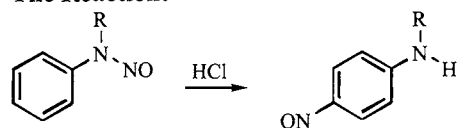
Y. Maeda, Y. Sato, *Journal of Organic Chemistry* **1966**, 61, 5188



A. Jonczyk, D. Lipiak, *Journal of Organic Chemistry* **1991**, 56, 6933

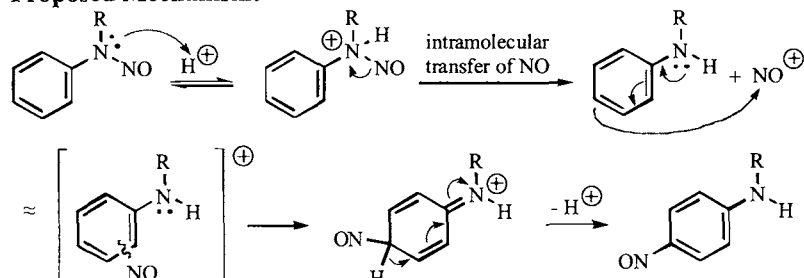
## Fischer-Hepp and Related Rearrangements

### The Reaction:



HCl is the preferred acid.

### Proposed Mechanism:



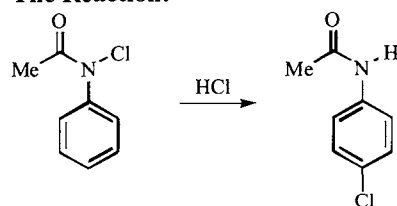
See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5<sup>th</sup> ed., John Wiley and Sons, Inc., New York, 2001, pp. 728-730 for the **Fischer-Hepp Rearrangement** as well as the **Orton and Hofmann-Martius Rearrangements**.

D. L. H. Williams, *Tetrahedron* **1975**, 31, 1343

See similarity to:

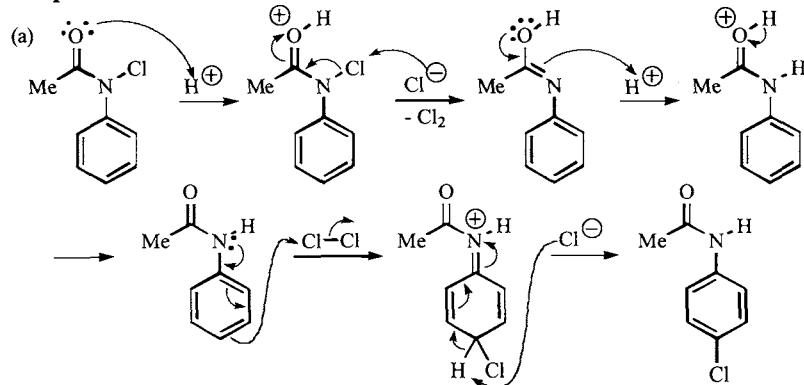
### Orton Rearrangement

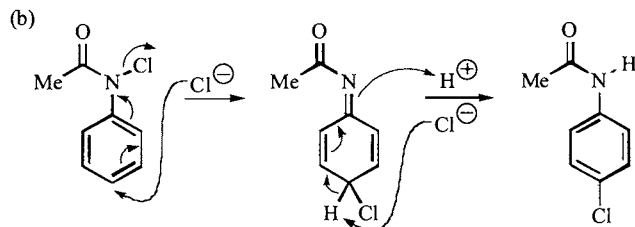
#### The Reaction:



D. L. H. Williams, *Tetrahedron* **1975**, 31, 1343 comments on the similarities.

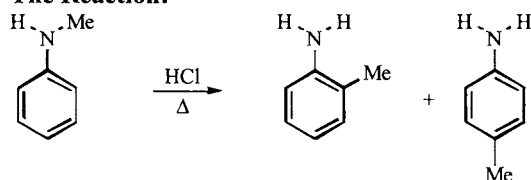
### Proposed Mechanism:



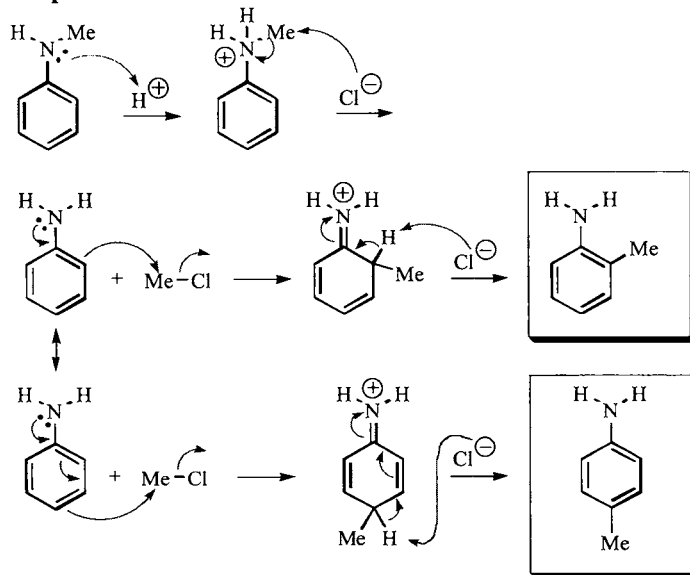


### Hofmann-Martius Rearrangement

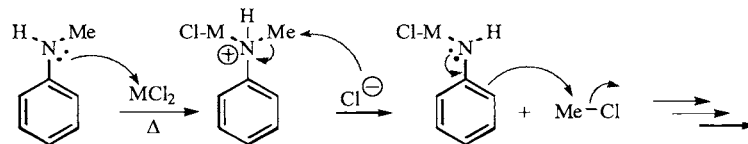
#### The Reaction:



#### Proposed Mechanism:



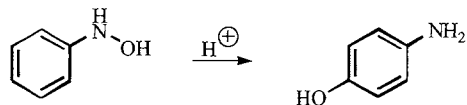
**Reilly-Hickinbottom Rearrangement** - uses Lewis acids and the amine rather than protic acid and the amine salt.



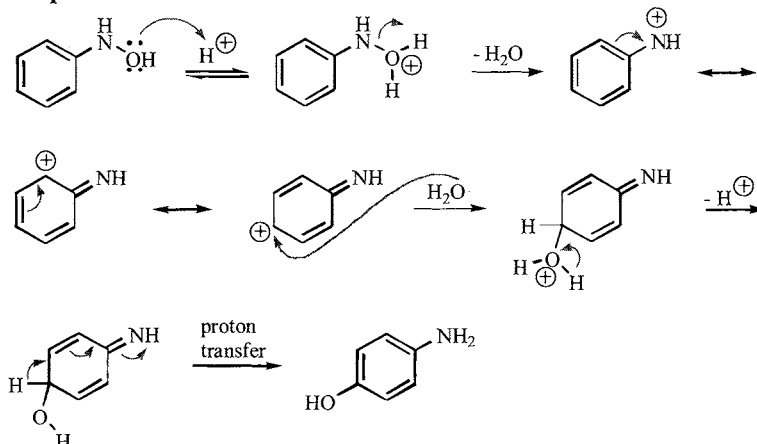
M = Co, Cd, Zn

## Bamberger Rearrangement

### The Reaction:



### Proposed Mechanism:

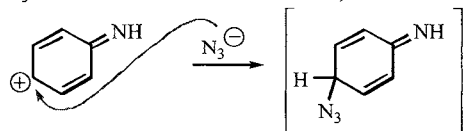


See discussion in: N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, *114*, 9795

### Notes:

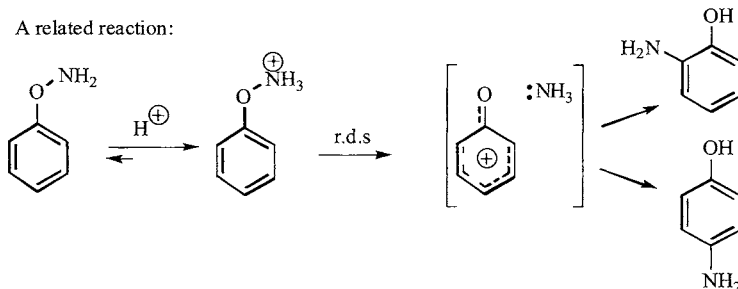
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5<sup>th</sup> ed., John Wiley and Sons, Inc., New York, 2001, p. 878; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 449

By addition of azide ion to the reaction, the intermediate can be competitively trapped:



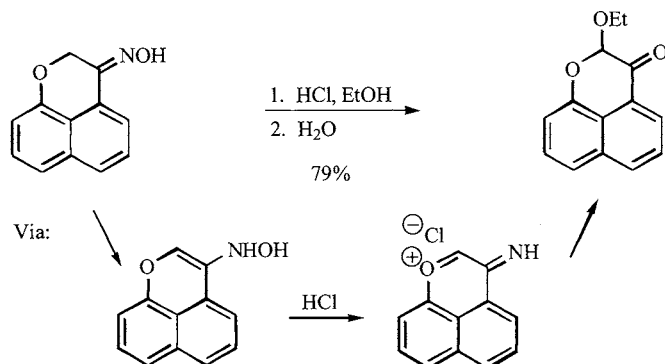
J. C. Fishbein, R. A. McClelland, *Journal of the American Chemical Society* **1987**, *109*, 2824

A related reaction:

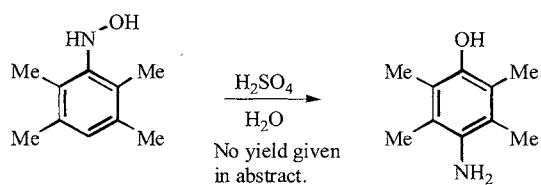


N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, *114*, 9795

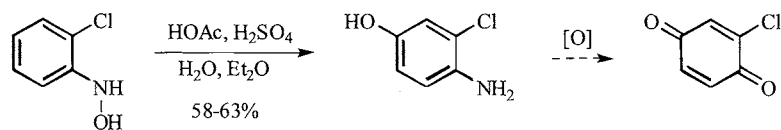
## Examples:



J. C. Jardy, M. Venet, *Tetrahedron Letters* **1982**, 23, 1255



G. G. Barclay, J. P. Candlin, W. Lawrie, P. L. Paulson, *Journal of Chemical Research Synopses* **1992**, 245

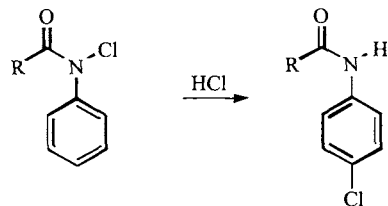


R. E. Harman, *Organic Syntheses* CV4, 148

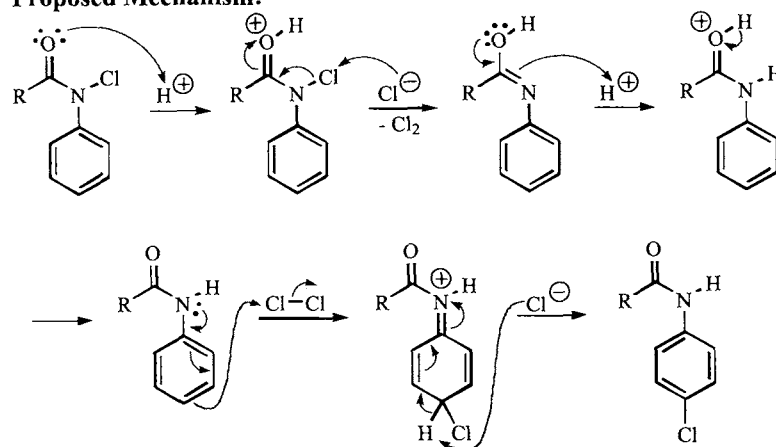


## Orton Rearrangement

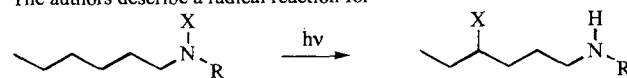
### The Reaction:



### Proposed Mechanism:



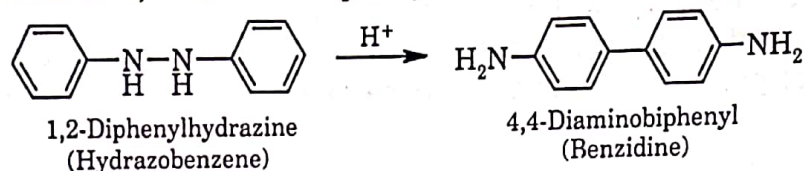
R. S. Neale, N. L. Marcus, R.G. Schepers, *Journal of the American Chemical Society* **1966**, 88, 305  
The authors describe a radical reaction for



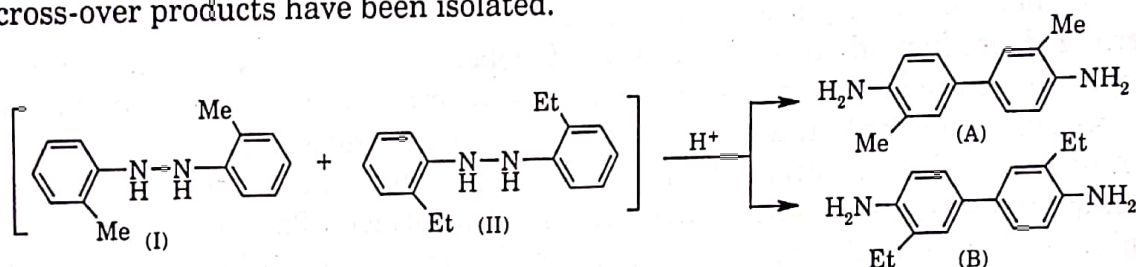
See: R. S. Neale, N. L. Marcus, *Journal of Organic Chemistry* **1969**, 34, 1808 for related reactions of *N*-halo-cyano compounds. A radical process is discussed.

## BENZIDINE-SEMIDINE REARRANGEMENT

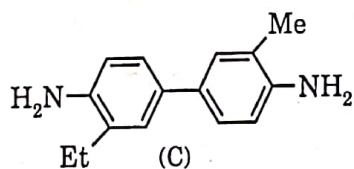
The acid-catalysed rearrangement of hydrazobenzenes to benzidines and semidines is called 'Benzidine-semidine rearrangement'. For example, when 1,2-diphenylhydrazine (hydrazobenzene) is treated with protic acid, it rearranges primarily to benzidine 4,4'-Diaminobiphenyl.



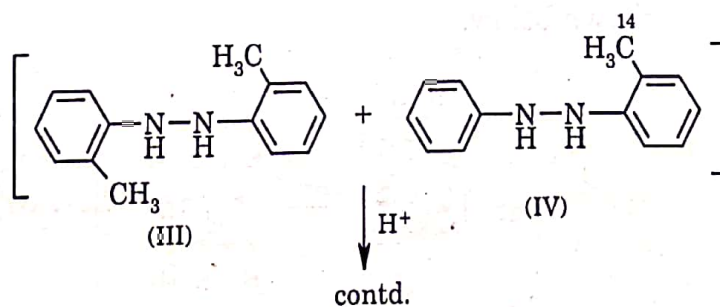
The rearrangement is found to be intramolecular in nature because when a mixture of two different hydrazobenzenes is subjected to this rearrangement, then no cross-over products have been isolated.

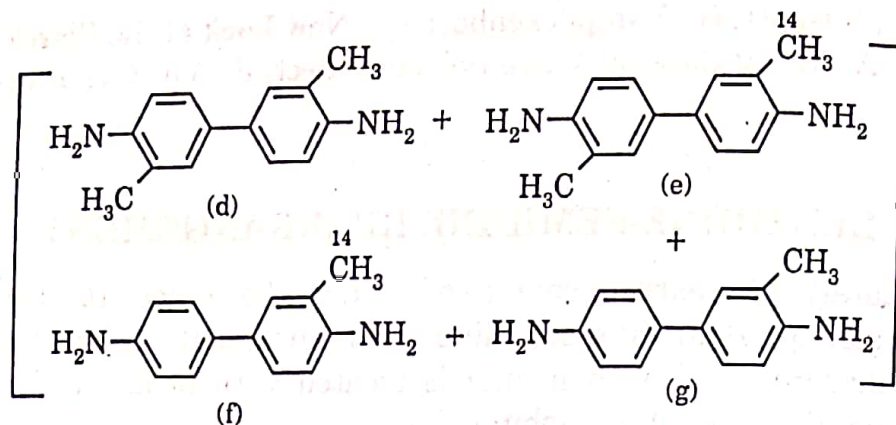


The product (A) has been originated from the compound (I) and (B) from the compound (II). The possible cross-over product (C) has not been isolated, and thus eliminates the possibility of intermolecular reaction.



To prove further that the reaction is intramolecular in nature, experiments were carried out with isotopically labeled compounds, as shown below.

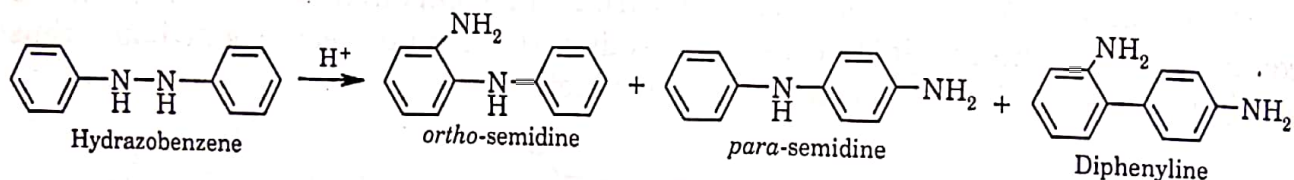




In the above experiments, the normal intramolecular products would be (d) and (f). It is to be noted that the potential cross-over product (e) is chemically identical with the normal product (d) and the other cross-over product (g) with the normal product (f).

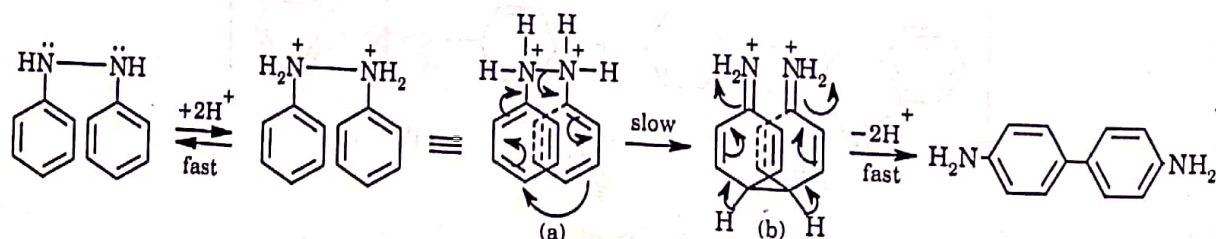
After the meticulous separation of the reaction products using column chromatography, followed by measurements of the specific activity of each, it is found that the specific activity of (f) is identical with that of (IV), i.e. no dilution of the  $^{14}\text{C}$  label has taken place on rearrangement. This has also been found that the rearranged product (d) has no trace of  $^{14}\text{C}$  label. Since the experiments with the isotopically labeled compounds give no trace of cross-over products, it has been unequivocally concluded that the rearrangement is intramolecular in nature.

Along with the formation of the rearranged products benzidines, another class of compounds, isomeric with benzidines, is also formed. They have been named 'semidines'. During the rearrangement small amount of diphenylenes are also formed.



### Mechanism:

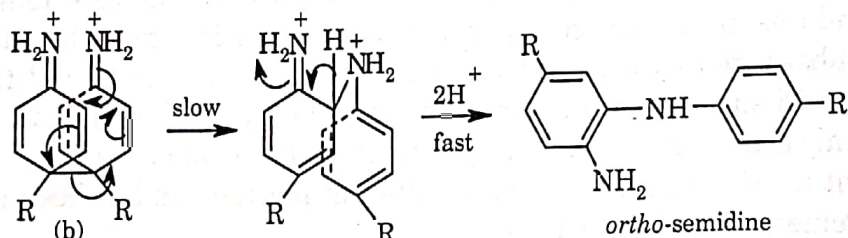
The mechanism of benzidine-semidine rearrangement has been investigated in details and two different suggestions emerged. One involves the protonation on both the nitrogen atoms of the hydrazine part of the hydrazobenzene and the second one is protonation on one of the nitrogen atoms and other on the benzene ring. Both of these mechanisms are shown below.



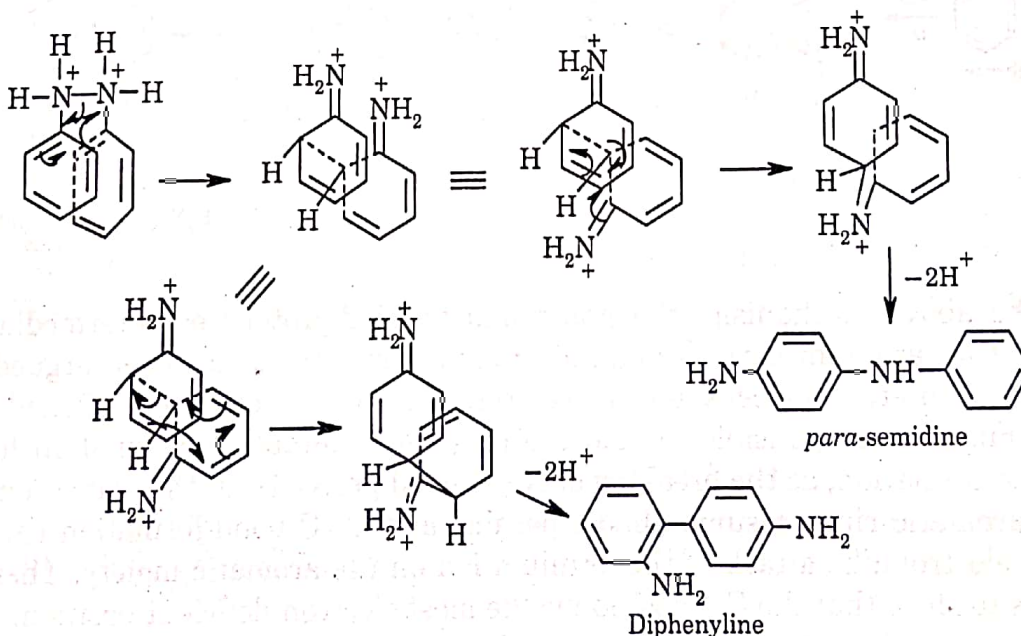
In the above mechanism, it may be assumed that the easy cleavage of the N-N bond in the diprotonated species is due to electrostatic repulsion between the two positively charged nitrogen atoms.

When the reaction is carried out *p, p'*-dideuterated hydrazobenzene, the rate of the reaction is nearly the same as in the case of non-deuterated hydrazobenzene. This suggests that the para-hydrogens become detached from the ring carbons after, rather than during, the rate determining step. It, therefore appears that the rate-determining step involves only the double conjugated acid of the substrate.

When both the para positions of the hydrazobenzene are substituted then ordinary benzidine rearrangement fails because aromatisation in the last step of the reaction is not possible. Then the intermediate 'b' undergoes a second rearrangement to produce *ortho*-semidine.

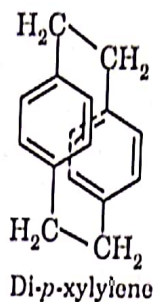


The formation of *para*-semidine and diphenylenes probably also occur in stages. These are shown below.



Two very pertinent questions have been raised regarding the mechanism of benzidine rearrangement discussed above. First is what forces hold the two benzene rings so close to each other in parallel position in the transition state of the slow step and within a distance of about 3.7Å to form a  $\sigma$ -bond. Such a parallel arrangement of two benzene rings will make the system unstable due to

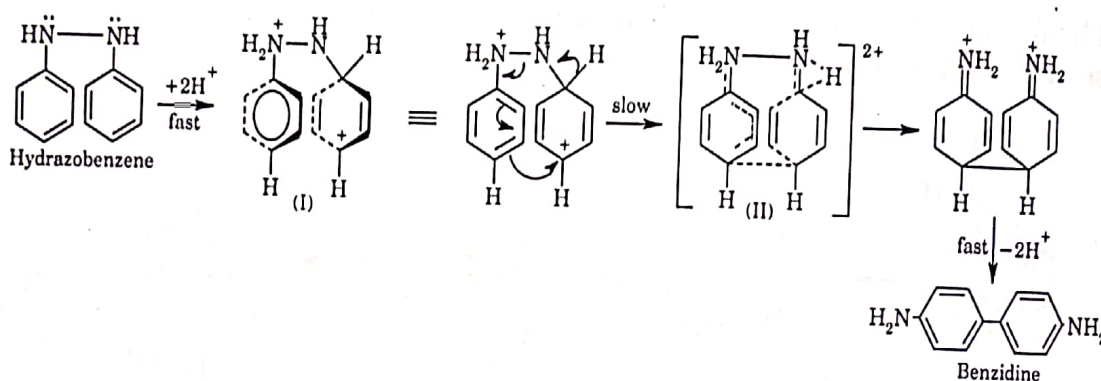
interference between the  $\pi$ -electron clouds of the two rings. In fact that has been observed in the case of di-*p*-xylylene.



It has been suggested that the transition state in the benzidine rearrangement and in related rearrangements is subjected to exceptional stabilization by resonance. But the cause of this 'extra resonance' is not well understood because transition state cannot assume a very planar structure to enhance resonance stabilization.

The second question is raised regarding the manner in which the substituent in singly *para*-substituted hydrazobenzene direct predominant course of the reaction. For example, *p*-Cl substituent favours rearrangement to a diphenylene, *p*-Me group produces mainly *ortho*-semidine, and a *p*-NH<sub>2</sub> gives *para*-semidine.

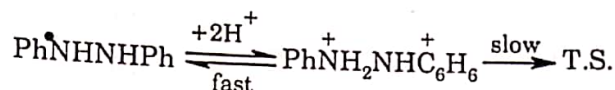
To account for these shortcomings, a different mechanism has been proposed for this rearrangement. This is given below.



In the above mechanism, the non-symmetrical diprotonated intermediate (I) consists of an arenium part and an aromatic moiety. It has been argued that electrostatic interaction between an electron rich and an electron deficient ring-systems might be responsible to hold the rings in a suitable conformation for the C-C bond formation, as the breaking of N-N bond proceeds. In the transition state (II) the aromatic rings assume almost parallel and C-C bond-formation can then occur by electrophilic attack of the arenium ion on the aromatic moiety. There are evidences to show that the C-4 position is the most electron-deficient position.

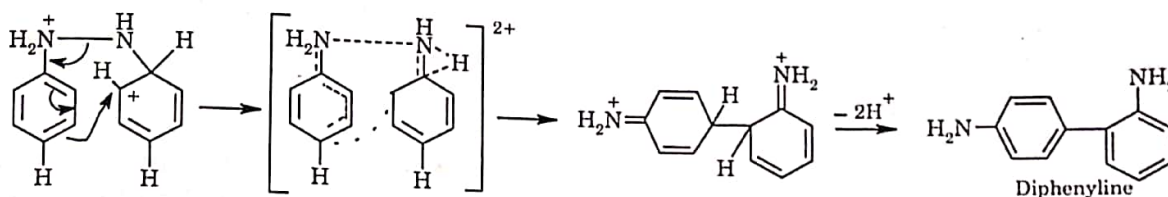
When the acid catalysed rearrangement is carried out in D<sub>2</sub>O in place of H<sub>2</sub>O, the reaction rate is speeded up. It has been observed experimentally that when the reaction is separately carried out in 60% dioxane /40% D<sub>2</sub>O and 60% dioxane and 40% H<sub>2</sub>O in 0.19M HClO<sub>4</sub>, then  $k_{D_2O} / k_{H_2O} = 4.8$ . This is because D<sub>3</sub>O<sup>+</sup> in D<sub>2</sub>O is a stronger acid than H<sub>3</sub>O<sup>+</sup> in H<sub>2</sub>O. This fact confirms the following pathway for the

reaction. Thus, the initial protonation is not the rate determining step in this reaction.



Hydrazobenzene itself normally follows the second order with respect to  $[\text{H}^+]$  and first order with respect to  $[\text{PhNHNHPh}]$ . Thus the reaction is overall third order. The rate equation is:  $\text{Rate} = k[\text{PhNHNhPh}][\text{H}^+]^2$ ,  $k$  = rate constant.

The formation of good amount of diphenylene during the rearrangement can be also be explained through a similar transition state.



### References:

1. Smith, Schwartz, and Wheland, *J. Am. Chem. Soc.* **1952**, 74, 2282.
2. Hammond and Shine, *J. Am. Chem. Soc.* **1950**, 72, 220.
3. Blackadder and Hinshelwood, *J. Chem. Soc.* **1957**, 2898.
4. Cohen and Hammond, *J. Am. Chem. Soc.* **1953**, 75, 880.
5. Hammond and Grundemeier, *J. Am. Chem. Soc.* **1955**, 77, 2444.
6. Brown, *J. Chem. Soc.* **1953**, 3265, 3278.