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Theoretical Study of N–N Cleavage in 1,2-Diaza Compounds: Evidence of Anchimeric Assistance Leading to Azaphenonium Ion

G. Subramaniam

Department of Chemistry, Pennsylvania State University, Hazleton, Pennsylvania 18201

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Theoretical Investigation of N–N bond cleavage in acyclic *N,N*-dimethylhydrazonium salts reveals it to proceed with anchimeric assistance from aryl substituent, leading to an aza analog of ethylenephenonium ion, spiro[2.5]-1-aza-1,4,6-octatrienyl cation **5**. This is the first theoretical evidence of an interesting phenyl-bridged nitrenium ion. Formation of **5** from acyclic salts is a relatively low-energy process (E_a = 49 kcal/mol). Experimental results show the cyclic analogs to resist N–N cleavage. Semiempirical calculations reveal it to have a high activation barrier (E_a = 65 kcal/mol) with no anchimeric assistance from the aryl ring. The absence of assistance is presumed to be due to the excess strain that would have been associated with the transition state for such a process involving a fused spiro tricyclic system.

Introduction

Electron-deficient nitrogens—nitrenes and nitrenium ions—have been accepted as reactive intermediates by logical deduction in a variety of rearrangements, photochemical reactions, and synthesis[1–4] and have been recently postulated as the reason for the carcinogenicity of aromatic amines and mutagenicity of *N*-alkoxy-*N*-acetoxyamides.[5–7] There remains as yet no proof that they are distinct species even under favorable conditions. Recent work reveals ways of generating nitrenium ions if there is mesomeric stabilization from a heteroatom or phenyl substituent.[8–12] Again, this experimental evidence strongly supports the nitrenium ion as the potential intermediate, even though no direct proof for its existence was given. The techniques and methods used successfully to prove the existence of carbonium ions seem to fail in the case of nitrogen species.[13]

Theoretically one should expect the nitrenium ions to be very similar to carbonium ions but more reactive due to the higher electronegativity of nitrogen. The higher electrophilicity may well be the reason for its elusiveness, for it rearranges to the more stable carbonium ions in most of the cases. In fact, major products from most of the reactions postulated to involve nitrenium ions are C–N rearranged products. The current thinking is to use the absence of C–N rearranged products as strong positive evidence for the nonintermediacy of a nitrenium ion in the given reaction. However, this counter argument may not be true at all. There may be a number of reactions which may require the formation of electron-deficient nitrogen, but may not lead to C–N rearranged products. Investigation of such a reaction may lead us to a way of proving the distinct existence of these elusive species.

Are such reactions known? Yes. There seem to be many such reactions, most of them being thermal decompositions.[14,15] Thermolyses of 1,2-diaza compounds proceed with N–N bond breaking at some point in the reaction, but no C–N rearranged products were isolated in all cases studied. Of particular interest are the hydrazonium salts **1** and their cyclic analogs **2**. Thermolyses of **1** have been shown to lead to 2,6-diaryl-3,5-dimethylpyridines **3** (Scheme I) and are an attractive route to synthesize complex symmetrically substituted pyridines.[15,16] Formation of **3** from **1** requires a N–N cleavage but with no C–N rearrangement. This observation suggests that the N–N cleavage occurs either in a concerted way and no electron-deficient nitrogen species is produced or a nitrenium ion **4** (or a nitrene) forms and does not undergo rearrangement under the reaction conditions. So, this reaction seems to be an ideal system for detailed study. The study becomes all the more interesting from the observation that **2**, the cyclic analogs, do not undergo N–N cleavage even under severe conditions of thermolysis.[17]

As a first step, we decided to do a theoretical study on these two compounds to explore the possible pathways for N–N cleavage and for the resistance of **2** toward N–N bond breaking. This paper describes the results of the semiempirical study of these two systems by the MNDO approach.

Choice of Method. Most of the semiempirical methods, especially the most commonly used MNDO,[18] AM1,[19] and most recently introduced PM3,[20] use only a limited number of molecules as their basis and not the whole gamut of molecules. Since a wide range of 1,2-diaza compounds was not included in the initial evaluation, we wanted to

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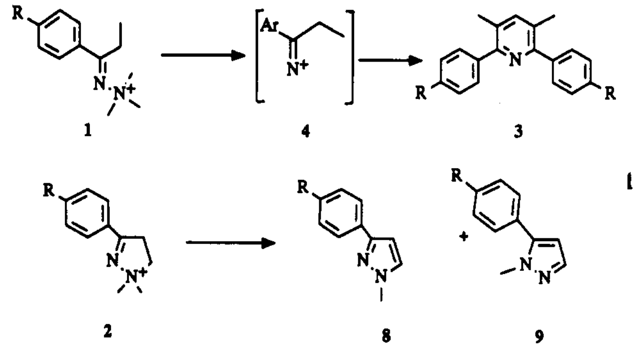
Scheme I



do a preliminary investigation to see the relative merits of the above mentioned three methods in predicting their properties and structure. Calculations were carried out on a number of 1,2-diaza compounds with known experimental heats of formation using these three approaches. Our results clearly revealed AM1 did poorly by overestimating the heats of formation; MNDO and PM3 performed comparably and very well in their predictions.[21] For example, the heats of formation of pyrazole as calculated by MNDO, AM1, and PM3 were 43.4, 65.6, and 48.8 kcal/mol, respectively. The experimental heat of formation is 43.3 kcal/mol. AM1 overestimates by 22.5 kcal whereas MNDO by only 0.1 kcal. We preferred MNDO to PM3, since it has been shown to perform reasonably well and agrees with ab initio methods in its prediction of the trends and relative stabilities of various isomeric cationic nitrogen species.[22] Even though we did not include any nitrenes in our set, earlier calculations on thermal decomposition of diazenes and azoalkanes show that the MNDO estimates of energies of activation (with 2 × 2 CI) agree well with experimental values.[5]

Calculations were carried out using MOPAC-5[23] package and using MNDO approach. The geometries of all stable species were optimized with respect to all geometrical variables using the Broyden–Fletcher–Goldfarb–Shanno algorithm incorporated in the program. The reaction pathways (transition states) were calculated using the best suited reaction coordinate, viz. N–N bond lengths. Force constant calculations were done on transition-state geometry to verify that there is only one negative eigenvalue. Most of the calculations were carried out using the Ohio Supercomputer Center CRAY/Y-MP machine and using the Penn State University IBM ES/3090-600S computer.

Results and Discussion

At first, the geometries of 1, 2, and their derivatives were optimized. To find out exactly what happens during and after the N–N bond fission, reaction coordinate calculations were done by stretching the N–N bond in 1 and its derivatives. The energy profile for this cleavage is shown in Figure 1.

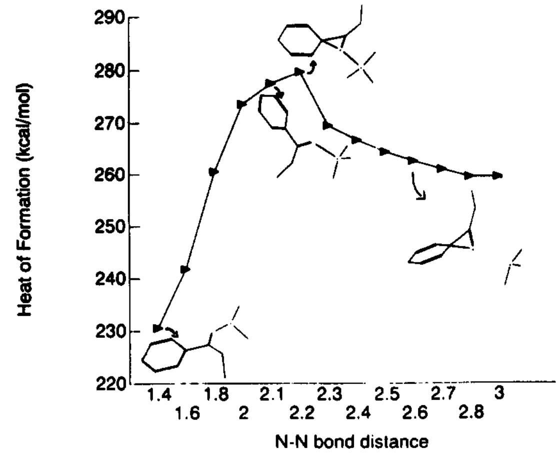
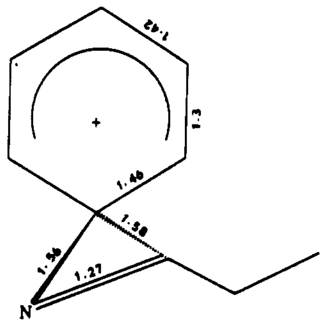


Figure 1. Reaction coordinate for N–N bond breaking in 1.



5

Figure 2. Geometry of 5.

As the N–N bond distance is increased, a decrease in the C_{ipso}–N_{sp2} distance was noticed, and the geometry of the molecule when the bond is stretched to 2.2 Å is suggestive of anchimeric assistance by the phenyl ring. A close inspection of the change in C_{ipso}–N_{sp2} distance and dihedral angle C_{ortho}–C_{ipso}–C_1–N_{sp2} (or C_2) as a function of N–N bond length shows them to change 10–15% for every 0.1-Å change in the initial stages of the reaction, 50–60% then to 100% increase for every 0.01 Å towards approaching the transition state confirming assistance by aryl ring. The geometry of the intermediate formed is that of an aza analog of phenonium ion 5 (Figure 2).

This ion is analogous to the ethylenephenonium ion observed by Olah and co-workers[24] and to the sulfenyl analog suggested as intermediate in the photochemical decomposition of sulfonyl azides.[25] This can also be considered as a monoaza analog of the proposed diazaphenonium ion to explain the ^{15}N interchange in diazonium ions.[26] In fact this ion 5 has been suggested possibly as an intermediate in Beckmann rearrangement in poorly ionizing mediums even though no definite evidence for its existence is given.[27] This is the first definite theoretical evidence for the existence of 5 to the best of our knowledge. Various stages of N–N cleavage leading to 5 are shown by three representative geometries along the reaction coordinate in Figure 1. The energy of activation (E_a) for this process is 49.2 kcal/mol.

Further evidence and confirmation for anchimeric assistance came from the reaction coordinate calculations of various para-substituted derivatives of 1. The results of these calculations are shown in Table I.

Theses data clearly show E_a to be dependent upon the nature of the para-substituent, and it increases steadily with decreasing electron donation to the aryl ring. A plot of E_a vs σ^+ of the substituents (Figure 3) shows a linear

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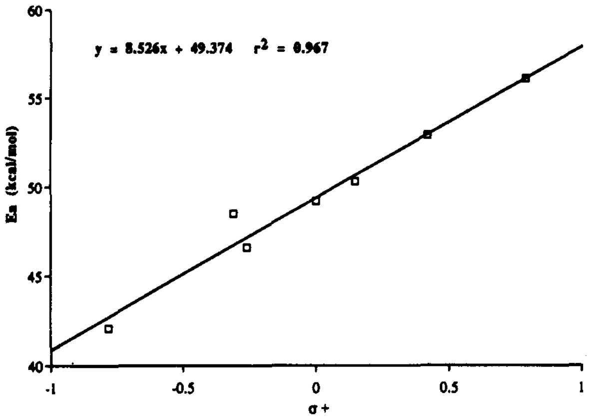


Figure 3. $E_a - \sigma^+$ plot for **1** and its derivatives.

Table I. E_a for **1** and **2** and Their Derivatives

R	1	2
-OMe	42.1	70.8
-Me	48.5	65.2
-CMe$_3$	46.6	
-H	49.2	65.1
-Br	50.3	72.3
-COOH	52.9	
-NO$_2$	56.1	73.1

correlation with a correlation coefficient of 0.967 strongly supporting assistance by aryl for N–N cleavage. The calculated value of the reaction constant of −14.4 (from the plot of ln K vs σ^+, Figure 7) is high and is very similar to the value reported for electrophilic aromatic substitution.[29,30] This is what one would expect if one views this reaction as an electrophilic attack of $=N^+$ on the aromatic ring. The methyl substituent seems to deviate slightly from the linear relation. The reason for this deviation is not clearly understood.

A second indirect proof came from the study of the *Z*-isomer of **1**. The *Z*- or syn-isomer **6** does not have the necessary anti-orientation of the phenyl ring for assistance. So one would expect the N–N cleavage to have relatively high E_a. Reaction coordinate calculation and an inspection of the geometries at various stages of bond breaking do not reveal any sign of anchimeric assistance. The E_a was calculated to be 55.1 kcal/mol, showing that the transition state for this process is 6 kcal/mol higher in energy than that of **1**.

These calculations demonstrate the formation of cationic intermediates, at least, in the gas phase. Formation of **3** was postulated to proceed through the imine **7** formed by a concerted 1,3-hydride shift and N–N bond fission. This concerted pathway (involving a thermally disallowed reaction) rather than the stepwise formation of an electron-deficient nitrogen was proposed mainly because of the absence of C–N rearranged products from these thermolyses. Assuming that one can extrapolate the gas-phase results to solution phase with reasonable confidence, it is very likely that the actual intermediate formed is **5** which leads to **7** by a regiospecific hydride addition as shown in Scheme II based on the evidence given.[15,16] Our calculations also show the ΔH of this proposed hydride transfer to be −69.7 kcal. Our calculations show the alternative route leading to **11** to be equally likely (ΔH −71.9 kcal), even though no C–N rearranged products were isolated.

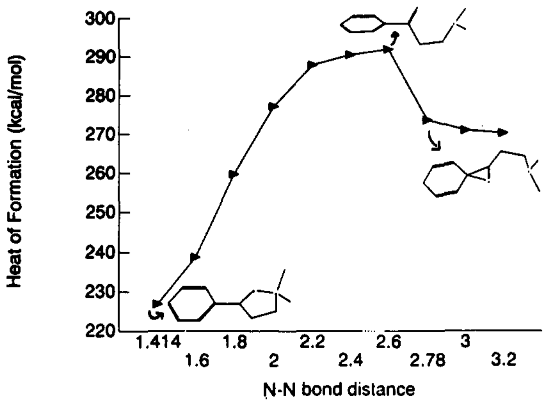
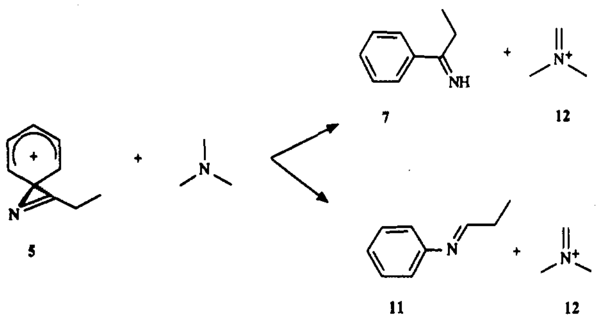


Figure 4. Reaction coordinate for N–N bond breaking in **2**.

Scheme II



Formation of the imine **7** is supported by actual trapping studies and by mixed thermolytic studies.[28] At this point, it is not clear as to why the aryl ring does not migrate to nitrogen and what may be the reason for this regiospecific hydride attack. However, these calculations hint anchimeric assistance to be the reason for the exothermic decomposition of **1**.

On the other hand, the cyclic analogs (**2**) resist decomposition and can only be decomposed over a long period by heating to 300–350 °C. The major products isolated were pyrazole derivatives **8** and **9** (Scheme I) showing the reluctance of **2** to N–N cleavage. The geometry of **2** closely resembles **1** and since it is cyclic it has its aryl ring nicely locked in the favorable anti orientation for assistance. So one would expect it to undergo the anchimerically assisted N–N cleavage. However, reaction coordinate (Figure 4) calculation reveals this bond breaking to proceed with a high E_a = 65.1 kcal/mol, 16 kcal more than that of **1**. If one studies the change in geometry as a function of N–N bond distance as was done for **1**, one sees only a 2–3% change, for example, in C_{ipso}–N_{sp2} distance (as opposed to 15% in **1**) in the initial stages and only 20–25% change approaching the transition state. There is no sign of assistance by phenyl ring up to 2.6 Å, the point of "breaking" of the N–N bond. Table II lists some of the properties of the N–N bond breaking for **1** and **2**.

A few representative geometries along the reaction coordinate are also shown in Figure 4. When calculations were repeated for various p-substituted derivatives of **2**, no $E_a - \sigma^+$ correlation was observed (Figure 5).

Table I lists the calculated E_a for **2** and its derivatives. The absence of linear correlation between E_a and σ^+ and the relatively high E_a suggests the absence of assistance by the aryl ring in **2** and its derivatives. It is puzzling at

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Table II. Calculated Properties of the Ground and the Transition States for the N-N Cleavage of 1 and 2

	1		2	
	GS	TS	GS	TS
ΔH^a	230.47	279.70	226.78	291.75
N-N^b	1.414	2.2001	1.414	2.680
ν^c		353		384

^{a} Energy in kcal/mol. ^{b} N-N bond length in Å. ^{c} Imaginary mode in cm^{-1}.

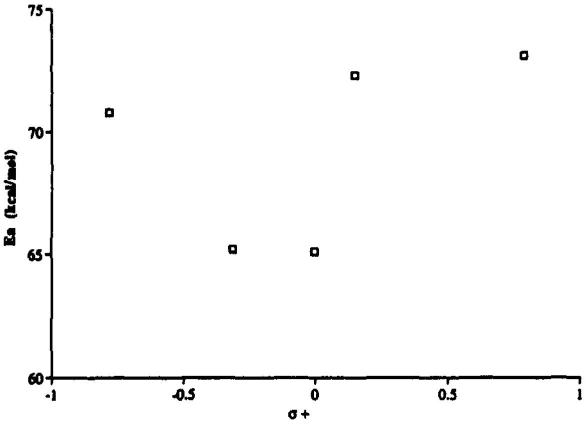
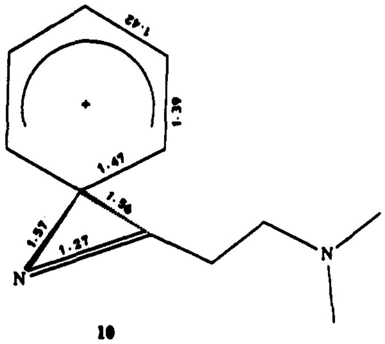


Figure 5. E_a - σ^+ plot for 2 and its derivatives.



10

Figure 6. Geometry of 10.

first sight to see this much contrast between 1 and 2. However, visualizing a transition structure with phenyl assistance for 2 shows a spiro-fused tricyclic (consisting of 5-, 3-, and 6-membered rings) system with a considerable amount of angle strain making the assisted pathway more energy demanding than the unassisted pathway. In order to get a rough estimate of this excess strain in the transition state of the cyclic system if it were to form with anchimeric assistance, we estimated its heat of formation by the use of constraints. The N-N, C=N, and all C-C bond lengths of aryl and azacyclopropyl rings from the transition-state geometry of 1 were used as constraints, and the results show ca. 5 kcal/mol to be the strain energy associated with the transition state of 2.

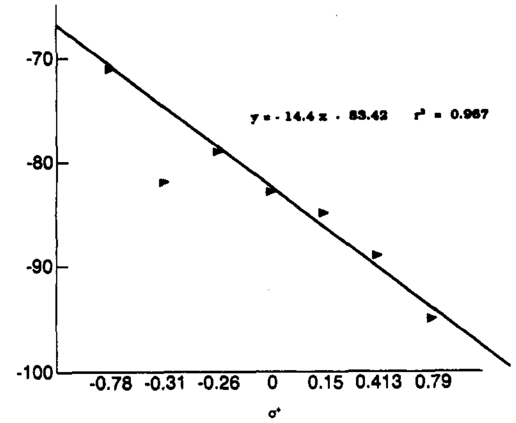


Figure 7. ln K - σ^+ Plot for 1 and its derivatives.

Another interesting observation was that despite the nonparticipation of the phenyl ring during bond breaking, after the N-N bond is completely "broken", the phenyl stabilizes the cationic nitrogen by delocalization. The geometry of the intermediate **10** (Figure 6) resembles closely that of **5**. This is easily comprehended in view of the fact that once the ring is open the structure of **2** resembles that of **1** to start with and the angle strain has, therefore, been eliminated.

Conclusion

These calculations were able to show that the absence of anchimeric assistance might be the reason for the higher energy barrier of N-N fission of **2** relative to its acyclic counterpart, **1**. It is also of interest to prove that the azaphenonium ion **5** is a distinct species, if not under thermolytic conditions, at least under stable ion conditions at low temperatures. Future work will revolve around the design of model compounds that could be directly ionized to give **5**. Success in producing **5** and getting spectral evidence for its existence would also serve as a touchstone to the validity and reliability of these gas-phase calculations as well as their extrapolation to the solution phase.