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Why α-Azido Five-membered Heterocycles Decompose So Fast? An Ab Initio Molecular Orbital Study [1]

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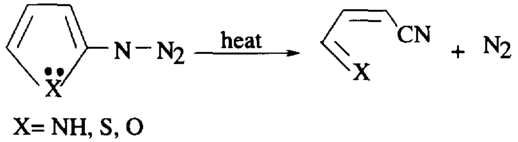
Abstract

Thermal decomposition process in the ground singlet state of several five-membered α-azido heterocycles analogous of azido-pyrazoles producing molecular nitrogen and ring-opened species has been investigated via ab initio molecular orbital theory at the MP2/6-31G(d,p) level. In most cases the decomposition is calculated to be a concerted but asynchronous process on the closed-shell singlet ground state of the azides. The five-membered ring is in fact found to be intact at the transition state. The activation barriers for the decomposition are found to decrease in the order: thiophenes>furans>pyrroles. Decomposition of phenyl azide is found to be more difficult to achieve than those of five-membered heterocycles. The higher energy demand for phenyl azide decomposition is probably due to smaller charge transfer between the azido group and the ring when compared to those of five-membered heterocycles during the decomposition. The stability of the transition state due to an internal electrostatic force was also found to be larger in the case of the five-membered heterocycles. The fate of the different products has not been considered. © 1997 Elsevier Science Ltd.

INTRODUCTION

The chemistry of α-azido five-membered heterocycles continues to attract the attention of organic chemists due to their very high rate constants for thermal decomposition process as compared to azido-benzenes. For example, simple azido-benzenes require a temperature of about 433K to achieve their halflife of 1 hour while several α-azido heterocycles can decompose to the same extent even below 333K.[1-3] From the point of view of rate constant, a typical 5-azidopyrazole 1-phenyl-3-methyl derivative reacts $\sim 3\times 10^3$ times faster than azido-benzene at 353K. The reason for this puzzling behaviour of α-azido five-membered heterocycles is still unclear. An explanation which is often put forward is that the ring-opening is concerted with the loss of N_2, and as a consequence, the high-energy nitrene species is not apparently formed (Scheme 1).



Scheme 1

An alternative explanation was recently presented by L'abbé *et al*[4]. According to these authors, the transition state is stabilised by internal electrostatic attraction between X^+ and N^-, where X is the heteroatom (Scheme 2). The mechanism in Scheme 2 however suggests that the reaction passes through

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[1] In memory of Professor Gerrit L'abbé

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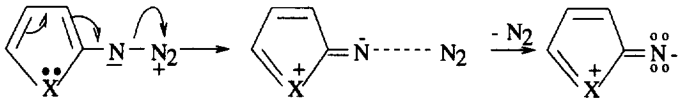
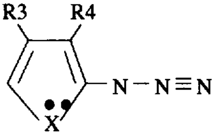


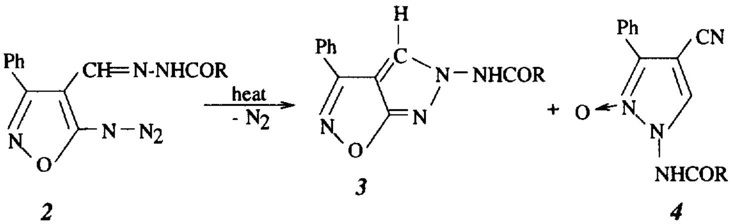
Scheme 2

a stable nitrene intermediate.

Effect of substituents at the positions 3 (R3) and 4 (R4) of the α -azido heterocycles on their thermal decomposition is another interesting phenomenon (see structure 1). With an appropriate substitution it is possible to obtain products which are formed with and/or without ring-opening.[5]



1



2 *3* *4*

Scheme 3

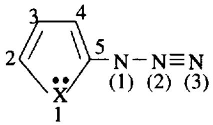
While the ring **4** is the product formed via ring-opening upon decomposition of **2**, **3** is that via cyclisation (Scheme 3). Several experimental results show that while substitution at the 4-position of **1** has a large effect, substitution at the 3-position has a very small effect on the thermal decomposition of α-azido five-membered heterocycles.[1,4] The above experimental facts and interpretations lead to the questions of how the transition state would look like, whether or not the decomposition process is concerted and how the charge distributions of various atoms in the molecules are.

About two years ago, Professor Gerrit L'abbé from our department brought this problem to our attention and asked us whether quantum chemical calculations could provide us with an answer. Subsequently, we have carried out theoretical studies and enjoyed many stimulating discussion with him and our other experimental colleagues. Sadly, Gerrit L'abbé untimely passed away in August 1996 leaving this study unfinished! We wish to dedicate this paper to his memory. In the present work, therefore, our objective is to rationalise some of the experimental facts using ab initio molecular orbital (MO) theory. Since the higher level ab initio calculations with the α-azido heterocycles **1** with larger substituents are

Table 1: Activation barriers in kcal/mol for the decomposition process, calculated at the MP2/6-31G(d,p)+ ZPE level and the decomposition rate constants relative to that of **6c** for several five-membered α-azido heterocycles.

Molecule	Activation barrier	Relative Rate constant
5a	28.2	7.5×10^{6}
5b	31.0	3.0×10^{6}
5c	34.4	2.1×10^{3}
6a	33.6	6.2×10^{3}
6b	38.0	240
6c	40.2	1
7a	29.5	7.8×10^{5}
7b	31.6	1.0×10^{5}
7c	35.1	4.7×10^{2}

computationally more demanding even with the modern high speed computers, we have performed our calculations on rather simple model five-membered heterocycles such as **5**, **6** and **7**.



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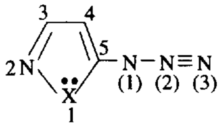

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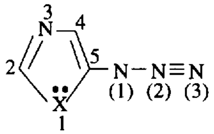


7

X = NH *a*
= O *b*
= S *c*

Firstly, we consider the mechanism of thermal decomposition process and calculate the corresponding activation barriers. Then, on the basis of charge distribution, attempts will be made to rationalise effect of substituents at two different positions (R3 and R4) on the rate of decomposition.

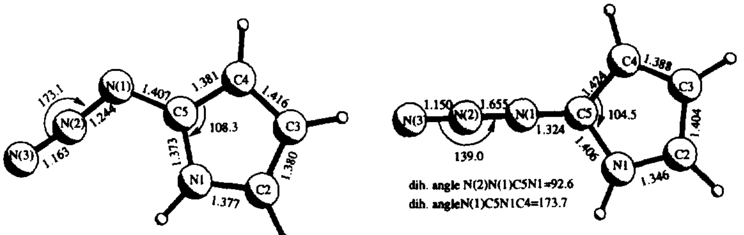
AB INITIO CALCULATIONS AND RESULTS

All calculations were performed using the Gaussian 92 program package.[6] Ground states of the azides considered here are closed-shell singlet (S_o). Initial geometry optimizations and calculations of vibrational wavenumbers in S_o surface were carried out at the Hartree-Fock (HF) level with 6-31G(d,p) basis set. Geometries of the stationary points were then reoptimized with the same basis set at the second-order Moller-Plesset perturbation theory (MP2) level where all electrons were included in the correlation calculations. Table 1 summarizes the zero point energy corrected activation barriers of the decomposition for all five-membered heterocycles considered at the MP2/6-31G(d,p) level. The relative rate constants for the decomposition process at 350K using Arrhenius equation are also shown in Table 1.

Fig.1 shows geometries of the azide **5a** and the transition structure for its thermal decomposition. Structures of other azides are not shown as they look almost similar either for equilibrium or transition structure. Table 2 records the charge on the atoms in the reactants, and their changes while going from a reactant to the corresponding transition structure. It is important to recall that energetic results obtained from MP2/6-31G(d,p)+ZPE level are not quantitatively accurate. Therefore, we do not attach much importance to the absolute values of energy barriers. On the contrary, the relative ordering between them is expected to be meaningful and appropriate for our comparative purpose. Similarly, the charge distribution within the molecule is strongly dependent on quality of the wavefunction and the model employed. Here we consider only the qualitative trend in going from one structure to the other. It should also be noted that we have not examined the final products generated from the ring-opened structure as they are not expected to influence the decomposition kinetics.

DISCUSSION

The equilibrium structures of α-azides are planar. At the transition state however, there is appreciable change in the structure, particularly at the azido moiety. The N(1)-N(2) bond length becomes 1.655Å from an initial value of 1.244Å in the reactant and the N(1)-N(2) bond becomes almost perpendicular to the plane of the five-membered ring (Fig.1). This may be due the donation of the ring π-electrons into the anti-bonding N(1)-N(2) orbital. C5 also shows a slight pyramidal character at the transition state. This can be viewed as the larger lobe of the hybrid orbital is in cis orientation with respect to the N(1)-N(2) bond. Most interestingly, the transition structure does not show any indication of ring-opening. This prompted us to look for the equilibrium structure of the nitrene in its closed-shell singlet state. We found that in all cases, except for the nitrene derived from **6a**, there is no stable



5a

Transition State

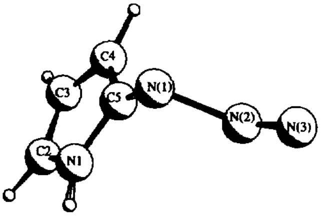


Fig.1. Geometrical parameters of α-azido pyrole **5a** and transition structure for the decomposition process calculated at the MP2/6-31G(d,p) level. Bond lengths and angles are in angstroms and degrees, respectively. Another view of the transition structure is also presented to show the non-planarity of the azido group with respect to the ring.

Table 2: Charge on each atom, using MP2 density, of the equilibrium and transition structures for decomposition of several α-azido heterocycles.

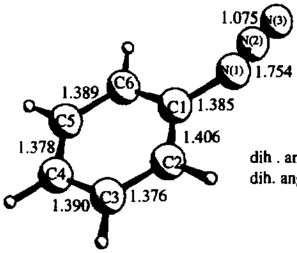
Molecule	Atom	Reactant	TS	Change in charge
5a	N1	-0.570	-0.491	+0.079
	C2	+0.048	+0.078	+0.030
	C3	-0.175	-0.174	+0.001
	C4	-0.162	-0.116	+0.046
	C5	+0.436	+0.398	-0.038
	N(1)	-0.379	-0.482	-0.103
	N(2)	+0.284	+0.096	-0.188
	N(3)	-0.177	-0.039	+0.138
Charge	ring+H	+0.272	+0.428	+0.156
Charge	Azido group	-0.272	-0.428	-0.156
5b	O1	-0.455	-0.396	+0.059
	C2	+0.110	+0.148	+0.038
	C3	-0.181	-0.179	+0.002
	C4	-0.166	-0.115	+0.051
	C5	+0.490	+0.443	-0.047
	N(1)	-0.404	-0.457	-0.053
	N(2)	+0.313	+0.111	-0.202
	N(3)	-0.149	-0.021	+0.128
Charge	ring+H	+0.241	+0.367	+0.126
Charge	azido group	-0.241	-0.367	-0.126
5c	S1	+0.306	+0.325	+0.019
	C2	-0.332	-0.309	+0.023
	C3	-0.095	-0.102	-0.007
	C4	-0.101	-0.056	+0.045
	C5	-0.018	+0.016	+0.034
	N(1)	-0.339	-0.422	-0.083
	N(2)	+0.292	+0.105	-0.187
	N(3)	-0.154	-0.019	+0.135
Charge	ring+H	+0.201	+0.336	+0.135
Charge	azido group	-0.201	-0.336	-0.135

Table 2 (cont'd)

Molecule	Atom	Reactant	TS	Change in charge
6a	N1	-0.411	-0.317	+0.094
	N2	-0.252	-0.226	+0.026
	C3	+0.034	+0.032	-0.002
	C4	-0.211	-0.164	+0.047
	C5	+0.485	+0.426	-0.059
	N(1)	-0.374	-0.461	-0.087
	N(2)	+0.285	+0.109	-0.176
	N(3)	-0.155	-0.016	+0.139
Charge	ring+H	+0.246	+0.370	+0.124
Charge	azido group	-0.246	-0.370	-0.124
6b	O1	-0.370	-0.305	+0.065
	N2	-0.114	-0.084	+0.030
	C3	+0.029	+0.033	+0.004
	C4	-0.220	-0.162	+0.058
	C5	+0.549	-0.477	-0.072
	N(1)	-0.394	-0.417	-0.023
	N(2)	+0.318	+0.118	-0.200
	N(3)	-0.124	-0.001	-0.123
Charge	ring+H	+0.201	+0.301	+0.100
Charge	azido group	-0.201	-0.301	-0.100
6c	S1	+0.454	+0.475	+0.021
	N2	-0.464	-0.447	+0.017
	C3	+0.017	+0.014	-0.003
	C4	-0.104	-0.058	+0.046
	C5	-0.039	-0.023	+0.016
	N(1)	-0.324	-0.386	-0.064
	N(2)	+0.291	+0.107	-0.184
	N(3)	-0.137	-0.002	+0.135
Charge	ring+H	+0.170	+0.281	+0.111
Charge	azido group	-0.170	-0.281	-0.111
7a	N1	-0.568	-0.495	+0.073
	N2	-0.252	-0.226	+0.026
	C3	+0.034	+0.032	-0.002
	C4	-0.211	-0.164	+0.047
	C5	+0.485	+0.426	-0.059
	N(1)	-0.374	-0.461	-0.087
	N(2)	+0.285	+0.109	-0.176
	N(3)	-0.155	-0.016	+0.139
Charge	ring+H	+0.246	+0.370	+0.124
Charge	azido group	-0.246	-0.370	-0.124

Table 2 (cont'd)

Molecule	Atom	Reactant	TS	Change in charge
7b	O1	-0.370	-0.305	+0.065
	N2	-0.114	-0.084	+0.0303
	C3	+0.029	+0.033	+0.004
	C4	-0.220	-0.162	+0.058
	C5	+0.549	+0.477	-0.072
	N(1)	-0.394	-0.417	-0.023
	N(2)	+0.318	+0.118	-0.200
	N(3)	-0.124	-0.001	+0.123
Charge	ring+H	+0.201	+0.301	+0.100
Charge	azido group	-0.201	-0.301	-0.100
7c	S1	+0.297	+0.319	+0.022
	C2	-0.114	-0.109	+0.005
	N3	-0.354	-0.350	+0.004
	C4	+0.054	+0.101	+0.047
	C5	-0.022	+0.077	+0.029
	N(1)	-0.337	-0.404	-0.067
	N(2)	+0.296	+0.108	-0.188
	N(3)	-0.142	-0.006	+0.136
Charge	ring+H	+0.183	+0.303	+0.120
Charge	ring+H	-0.183	-0.303	-0.120
Phenyl azide	C1	+0.199	+0.209	+0.010
	C2	-0.114	-0.125	-0.011
	C3	-0.130	-0.126	+0.004
	C4	-0.116	-0.116	-0.000
	C5	-0.133	-0.131	+0.006
	C6	-0.119	-0.113	+0.006
	N(1)	-0.391	-0.378	+0.013
	N(2)	+0.309	+0.200	-0.109
	N(3)	-0.166	-0.040	+0.126
Charge	ring+H	+0.248	+0.218	-0.030
Charge	azido group	-0.248	-0.218	+0.030



dih . angle N(2)N(1)C1C2=148.6
dih. angle N(1)C1C2C3=170.0

Fig.2. Geometrical parameters of approximate transition structure for phenyl azide decomposition calculated at the MP2/6-31G(d,p) level. Bond lengths and angles are in angstroms and degrees, respectively.

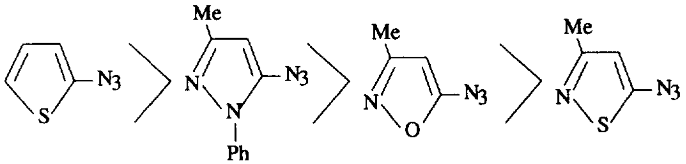
structure corresponding to closed-shell singlet nitrene. Optimization of the expected closed-shell singlet nitrene structure invariably leads to a ring-opened structure. However, triplet states of these nitrenes are found to be stable and expected to be their ground electronic state. It is not possible to carry out calculations of the nitrenes in an open-shell singlet in the UHF framework. Due to the fact that our calculations for the decomposition process were carried out from the ground singlet state of azides and to the inability of the UHF method to calculate open-shell singlet nitrene, we are unable to predict whether the reaction produces directly the ring-opened structure or proceeds via a nitrene intermediate after crossing the transition state. However, possibility for a product formation via an open-shell singlet nitrene is likely to be dependent upon the magnitude of coupling between the S_o and S_1 potential energy curves at their crossing point after the transition state has passed.

Table 2 shows that net transfer of charge takes place from the ring to the azido group in going from an equilibrium to a transition state. In all cases, charge is primarily being depleted from the hetero atom, X and the carbon atom of the ring C4 to the azido group. The nearest nitrogen atom, N(1) has gained appreciable amount of charge at the transition state. This indicates that both N(1).....X1 and N(1)......C4 internal electrostatic repulsions are reduced at the transition state. Such reduction along with the net charge transfer to azido group, could give rise to a certain degree of stabilisation to the transition state.

At this stage it is interesting to compare the thermal decomposition process of α-azido five-membered heterocycles with that of phenyl azide. Experimental results suggest that the former decomposes about 10^3 times faster than the latter.[1-3] Our calculations on phenyl azide in its singlet ground state show that elimination of N_2 is a direct dissociation producing closed-shell singlet phenylnitrene without having a transition state along the energy path. The associated dissociation energy amounts to about 60 kcal/mol which is much higher than the activation barrier of similar process in five-membered α-azido heterocycles at the same level of theory (Table 1). To get further insight into the reason for higher activation barrier in phenyl azide decomposition, we calculated the charges on all the atoms of phenyl azide assuming a transition state where N(1)-N(2) is 1.75Å (see Fig. 2). We have chosen this distance due to the fact that the N(1)-N(2) distance at the transition structure for all five-membered α-azides is approximately 1.7Å. It should be pointed out that an energy barrier of 56 kcal/mol was found by considering this pseudo-transition state structure; such value is also much higher than the corresponding process in five-membered azides. In phenyl azide, charge transfer takes place from azido group to the phenyl ring (Table 2). Moreover, the amount of charge transfer ($0.03e^-$) is much smaller than those in the five-membered α-azido heterocycles (minimum $0.1e^-$). The larger degree of charge transfer in five-membered α-azido heterocycles is likely to provide higher stability of the transition state. A look at the changes in net charges at the C2, C6 and N(1) during phenyl azide decomposition listed in Table 2 reveals that while C2 gains more negative charge, C6 and N(1) actually lose electron in contrast to those in five-membered heterocycles. The changes in charges at the C2, C6 and N(1) are also much smaller compared to the equivalent atoms in five-membered azides. This indicates further that stabilisation of the transition structure due to internal electrostatic force is stronger for five-membered azides, thereby resulting in lower activation barriers.

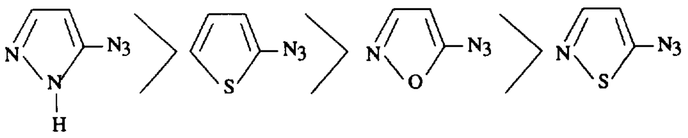
A closer look at the Table 2 also reveals that the change in charges at C3 is much smaller compared to that at C4 in all α-azido heterocycles, suggesting that substitution at C4 will have a more pronounced effect on the decomposition than that at C3. In fact, recent experimental studies on thermolysis of 5-azido isoxazoles and 5-azido pyrazoles reveal larger effects of substitution at C4 on rate constant than that at C3.[1,4]

The activation barriers for the decomposition process of α-azido heterocycles as shown in Table 1 decrease in the order, X = S > O > N. This trend was found for all the five-membered heterocycles studied here. Overall charge transfer from ring to the azido group is larger for compounds with X=N than those with X=O. Moreover, stability of the transition state due to internal electrostatic forces is also larger for the former due to the larger charge transfer at N(1) and N1. These two factors could give rise to lower activation barriers for the compounds with X=N. Transfer of charge from the ring to the azido group for compounds with X=S is larger compared to that with X=O, but the stability of the transition state due to internal electrostatic force in the former will be much smaller due to the longer C5-S1 distance compared to the C5-N1 and C5-O1 distances, and less charge transfer at S1 (see Table 2). This could be the reason for very high activation barriers for the sulphur containing compounds. Experimental studies on various substituted five-membered heterocycles showed the following trend in rate constants at 353K :



5c *9* *10* *11*

Our calculations however predicts the following trend:



6a *5c* *6b* *6c*

It can be seen that theoretical calculations predict the rate constant of **6a** to be larger than that of **5c**. Experimental results show that the rate constant of **9** is lower than that of **5c**.[7] Such disagreement might be due to the fact that phenyl substitution could play a role in determining the thermolysis rate constant. Recently,[7] experiment has been carried out for a molecule where the phenyl group of **9** has been replaced by a methyl group. Rate constant measurement shows that there is more than two fold increase in the thermolysis rate constant when methyl group was used in place of phenyl. We therefore could suggest that if experiments were carried out on the model molecule **6a**, it could be possible to match both theoretical results and experimental observations.

CONCLUSIONS

Thermal decomposition of several five-membered α-azido heterocycles has been studied using ab initio MO calculations. The reaction can be characterised as a concerted but asynchronous process between N_2 departure and ring-opening on the S_o surface of the azides. In fact, in the transition structure, the five membered ring remains almost intact. A ring opening takes place only after the transition state. We, however, remain inconclusive whether the reaction proceeds via an open-shell singlet nitrene or directly to the ring-opened product after the transition state is passed. Faster decomposition of five-membered α-azido heterocycles as compared to phenyl azide arises probably from a larger charge transfer from a five-membered ring to the azido group. This can provide some degrees of stabilisation to the transition state. The stability of the transition state due to internal electrostatic force is presumably larger in case of five-membered heterocycles than in phenyl azide.

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