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Theoretical study of azide anion addition to nonpolar and polar double and triple bonds

Branko S. Jursic*, Zoran Zdravkovski

Department of Chemistry, University of New Orleans, New Orleans, LA 70148, USA

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Abstract

Transition structures for the 1,3-polar addition of azide anion to hydrogen cyanide, formaldimine, nitrogen, *cis*- and *trans*-diazene, ethylene and acetylene were obtained at the MP2/6-31+G* theoretical model. The additions can be divided into two groups: addition to a triple bond, giving rise to an aromatic heterocyclic product, and addition to a double bond, forming a non-aromatic product. All transition structures correspond to a concerted mechanism for the polar cycloaddition. Symmetrical dienophiles, apart from *cis*-diazene, give rise to synchronous transition structures. The anomaly is explained in terms of strong n–n repulsion of the reactants in the transition structure. The reactivity of the compounds can be rationalized in terms of the bond orders of the newly forming bonds, from the frontier orbital energy differences and from the charge transfer from the azide anion to the dienophile. The quantitative correlation of the reactivity has been judged on the basis of the activation energies of the reactions calculated at MP2/6-31+G* and MP3/6-31+G*. It is predicted that the addition of azide to nitrogen is the slowest and that the additions to hydrogen cyanide and acetylene have the lowest barriers, in agreement with literature data.

Keywords: Ab initio calculation; Azide anion addition; Double bond; Transition structure; Triple bond

1. Introduction

One of the best synthetic procedures for the synthesis of triazole, tetrazole and pentazole and their saturated derivatives is the polar addition of the corresponding azide to the unsaturated compound [1]. By varying the substituents, for example on the dienophile and/or the azide, a wide variety of nitrogen-containing heterocyclic five membered compounds can be synthesized. 1,2,3-Triazole has been obtained by several direct and indirect synthetic approaches. The direct addition of azide anion in acidic media (hydrazoic acid) is a straightforward procedure but is somewhat dangerous [2]. Although the direct preparation of 1,2,3-triazole from acetylene and hydrazoic acid is experimentally feasible, the compound can be obtained from acetylenecarboxylic acid and sodium azide in acid media with cycloaddition and elimination in one synthetic step [3]. One of the adducts, pentazole, has very interesting properties. It should be an aromatic heterocycle with high acidity [4]. The chemistry of pentazole has developed in the last couple of decades because the compound is a

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* Corresponding author.

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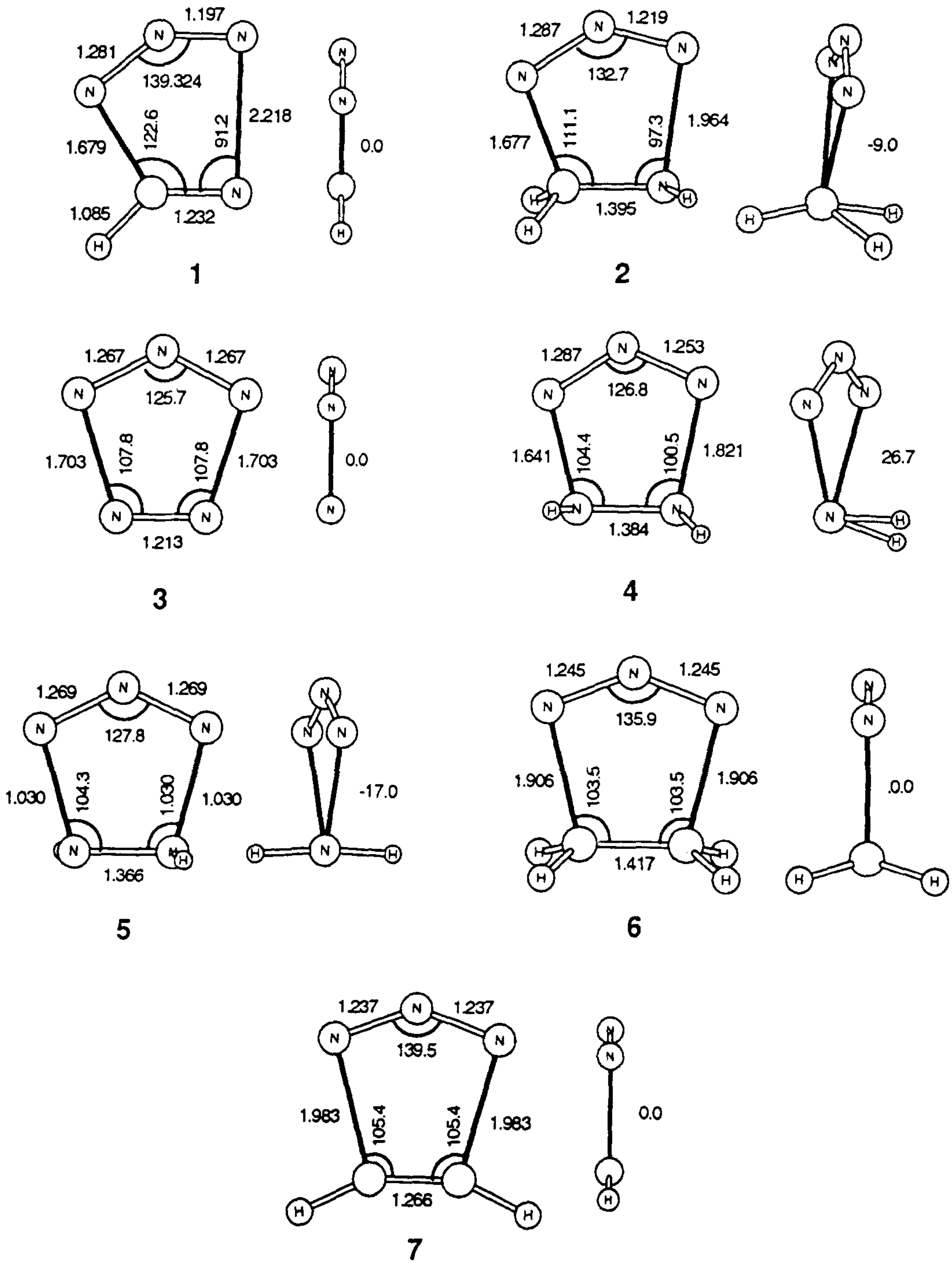

Fig. 1. Transition structures of polar azide addition to hydrogen cyanide (**1**), formaldimine (**2**), nitrogen (**3**), *cis*-diazene (**4**), *trans*-diazene (**5**), ethylene (**6**) and acetylene (**7**), calculated by MP2/6-31+G*.

very short lived species. Most of the mechanisms of azide anion cycloaddition to the N≡N triple bond is known from the reaction of azide with arenediazo compounds [5]. The addition of azide anion to non-polarized double and triple bonds requires drastic reaction conditions, whereas the addition to multiple CN bonds is straightforward [6].

Recently we have performed semiempirical and minimal basis set ab initio (RHF/3-21G) calculations of azide anion addition to organic cyanides [7]. The SCF AM1 approach and the employed ab initio calculations favor a two step cycloaddition reaction for the highly polar nitriles with formation of a C–N bond in the first step. It is of theoretical and experimental interest to determine the reactivity of different dienophiles towards the azide anion. Here we present our results of an ab initio study of azide addition to nonpolar and to polar double and triple bonds.

2. Methods

The ab initio program package Gaussian92 [8] was employed to optimize fully the geometries at the restricted Hartree–Fock [9] (HF) level with standard basis sets (3-21G and 6-31+G*). Electron correlation was incorporated by applying second-order Møller–Plesset theory [10] (MP2) for geometry optimization and the third-order equivalent (MP3) for energy evaluation, keeping the core electrons frozen (FC). Analytic vibrational frequencies were obtained up to the HF/6-31+G* level to determine the number of imaginary frequencies which characterize each stationary point (where minima have no imaginary frequency and transition structures have only one) and to obtain the zero point vibrational energies. The normal coordinates of the imaginary vectors of the transition structures have been carefully examined, and movements were visualized by a graphical program. The movements point in the direction of the minimum energy for the forward and backward reaction.

It was pointed out by one of the reviewers that comparison of the gas phase results with those from solution chemistry can be very tricky. We are aware of that; however, the methodology can be justified by the fact that in the course of the reaction there is no net change of charge. Consequently, it is reasonable to expect that the solvent stabilization effects on all species, reactants, transition state and products, would be the same and would cancel out.

3. Results and discussion

It might be expected that the 1,3-polar cycloaddition of the azide anion to nitriles and aldimines would be asynchronous or even a two-step reaction, owing to the polarity of both reactants. Our previous calculations [7] with AM1, in the case of azide anion addition to fluoroazide, predict an activation energy for the concerted reaction of 59.3 kcal mol^{-1}, 12.0 kcal mol^{-1} above that for the second transition structure in the two-step

Table 1
Bond orders [12] of the newly forming bonds in the azide anion addition calculated at the MP2/6-31+G* level

TS	Mulliken bond order				Lowdin bond order			
	a	b	a − b	a + b	a	b	a − b	a + b
1	0.683	0.380	0.303	1.063	0.833	0.387	0.445	1.220
2	0.784	0.597	0.187	1.381	0.895	0.637	0.258	1.532
3	0.790	0.790	0.000	1.580	0.893	0.893	0.000	1.786
4	0.793	0.751	0.042	1.544	0.939	0.815	0.124	1.754
5	0.766	0.766	0.000	1.532	0.861	0.861	0.000	1.722
6	0.679	0.679	0.000	1.358	0.714	0.714	0.000	1.428
7	0.562	0.562	0.000	1.124	0.601	0.601	0.000	1.202

Key: TS, transition structure; a, left forming bond of TS presented in Fig. 1; b, right forming bond of TS presented in Fig. 1.

addition. HF/3-21G was not able to determine either the first or the second transition structure. Both transition structures generated by AM1, after optimization by either the HF or the MP2 ab initio method, lead to synchronous asymmetric transition structures. The MP2/6-31+G* geometries are presented in Fig. 1. All of the structures represent a concerted transition state for the reaction. Some of them are asynchronous whereas the others are fully symmetrical.

Simple comparison of the bond lengths is not an adequate measure of the asynchronicity of the transition structures, i.e. the extent of bond formation when two different kinds of bonds are being formed (for example, C–N and N–N in **1** or **2**). In such cases the bond orders are a much better parameter for comparison [11]. The bond orders for the two incipient bonds are presented in Table 1 [12].

As expected from the symmetry of both reactants in the cycloaddition reaction, the transition structures for the addition of azide anion to hydrogen cyanide (**1**) and formaldimine (**2**) are highly asymmetric. The calculated differences of Mulliken bond orders are 0.303 and 0.187 respectively. The Lowdin bond order difference is slightly higher (Table 1). As the azide anion is planar and hydrogen cyanide attack occurs in the same plane, all atoms of transition structure **1** are also in one plane (Fig. 1). That is not the case with transition structure **2** because of the asymmetry of formaldimine. The dihedral angle (the angle between the two planes formed by the atoms involved in the bond formation) in transition structure **2** is −9.0° (Fig. 1).

To our surprise, transition structure **4** for azide anion addition to *cis*-diazene is asynchronous, even though both reactants have a plane of symmetry. The differences in the Mulliken and Lowdin bond orders are 0.042 and 0.124, respectively. The position of the hydrogen atom attached to the center with the shorter newly forming bond is pulled closer toward the azide moiety than the other hydrogen. This can be explained by the repulsive interactions between the lone pair orbitals of the azide anion and the *cis*-diazene molecule. The dihedral angle of 26.7° for the new bonds in transition structure **4** clearly demonstrates strong n–n repulsion interaction, indicated by pushing away the shorter newly formed N–N bond (Fig. 1). All other transition structures are fully symmetrical, as would be expected on the basis of the symmetry of the reactants. The dihedral angles are zero for all other transition structures except transition structure **5**, which has an electron pair located on each nitrogen atom from N_2. The repulsive interaction between these lone pairs and the occupied orbitals of the azide anion pushes the azide nitrogens away, making the dihedral angle −17.0° (Fig. 1) [13].

Qualitative evaluation of the facility of the reaction can be obtained based on the extent to which new bonds have been formed in the transition structures by applying the Hammond postulate [14]. It is reasonable to expect that the aromatic product obtained from azide anion addition to a triple bond will have lower energy than the reactants. Even products that are not aromatic, obtained by azide addition to the double bond, should be more stable than the reactants. Accordingly, two sets of reactivity can be obtained by comparing the sum of the two newly forming bond orders. In both cases a lower bond order means an earlier transition structure and a lower activation energy. Comparison of the sum of the Lowdin bond orders for the newly forming bonds gives the following sequence of reactivity for the aromatic series: **7**, **1**, **3**. However, from the Mulliken bond orders **1** is predicted to be the most reactive in this series. The reactivity in the non-aromatic series is **2**, **6**, **5**, **4**.

The reactivity in Diels–Alder and similar cycloaddition reactions has often been rationalized by comparison of the frontier orbital energies of

Table 2
Energy gap in kcal mol^{-1} between the HOMO of the azide anion and the LUMO of the dienophiles

TS	ΔE_{FMO^1}	ΔE_{FMO^2}	ΔE_{FMO^3}
1	5.88	4.41	4.11
2	5.04	4.15	4.21
3	5.23	5.51	5.17
4	4.29	4.83	4.60
5	4.41	4.89	4.64
6	5.25	4.53	4.58
7	6.15	4.26	4.30

Key: ΔE_{FMO^1}, RHF/3-21G; ΔE_{FMO^2}, RHF/6-31+G*; ΔE_{FMO^3}, MP2/6-31+G*.

the reactants [15]. In this reaction the azide anion is clearly the electron donor and its HOMO energy should be very low. The differences in the frontier orbital energies between the reactants are presented in Table 2.

According to frontier orbital theory, higher reactivity is predicted for the pair of reactants that have similar energies (smaller energy gap) of the HOMO of one reactant and the LUMO of the other [15]. All applied theoretical models predict that the reaction is LUMO dienophile controlled; however, the energy calculated at different theory levels predicts different reactivity orders. Comparison of the frontier orbital energy gaps obtained from the optimized structures at the highest theory level (MP2/6-31+G*) reveals that the most reactive dienophile is hydrogen cyanide, followed by formaldimine, acetylene, ethylene, *cis*-diazene, *trans*-diazene, and nitrogen.

It should be remembered that frontier molecular orbital theory considers only the separated reactants and does not take into account any other interactions, which can play a crucial role in determining the reactivity. A better picture, especially since ionic species are involved, can be obtained by following the charge transfer. In the course of these cycloadditions, the charge is transferred from the azide anion to the dienophile. The calculated transfer of Mulliken charge in the transition structures is presented in Table 3.

As demonstrated in Table 3, the charge transfer depends strongly on the theoretical model employed, and only the results from the higher level of calculation will be discussed here. A higher value means a higher electron affinity of the dienophile but, unlike the frontier orbital molecular (FMO) gap, it depends not only on the nature of the dienophile but also on the interactions in the transition state. The greatest transfer of charge takes place in the hydrogen cyanide transition structure, making it the most reactive, and the least reactive is nitrogen addition to the azide anion. The full order of reactivity is hydrogen cyanide, formaldimine, acetylene, *trans*-diazene, *cis*-diazene, ethylene, nitrogen. The reactivity is similar to that predicted by frontier molecular theory except for the position of the diazenes. *trans*-Diazene is shown to be more reactive than *cis*-diazene, and both are more reactive than ethylene. This is understandable, as the lone pair – hydrogen atom interactions are expected to be most pronounced in these dienophiles. A correlation of the reactivity predicted from frontier orbital energies and charge transfer in the transition states is presented in Fig. 2. The numbers are the same as for the transition structures presented in Fig. 1.

Table 3
Transfer of (Mulliken) negative charge from azide anion to dienophile

TS	$\Delta q1$	$\Delta q2$	$\Delta q3$
1	0.392	0.661	0.578
2	0.361	0.578	0.541
3	0.366	0.384	0.381
4	0.459	0.513	0.389
5	0.372	0.448	0.396
6	0.314	0.415	0.384
7	0.311	0.437	0.438

Key: $\Delta q1$, RHF/3-21G; $\Delta q2$, RHF/6-31+G*; $\Delta q3$, MP2/6-31+G*.

The most reliable available computational approach to the prediction of the reactivity of a reaction is that of estimation of the activation barriers [16]. The calculated total energies for the reactants and the transition states are presented in Table 4, and the activation energies of the reactions are reported in Table 5. As expected, the order of the reactivity strongly varies with the theoretical

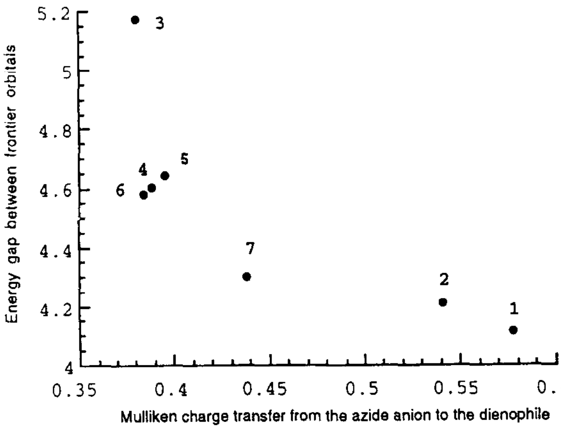

Fig. 2. Correlation of frontier orbital energy gap with charge transfer in the transition state calculated by MP2/6-31+G*.

Table 4
Total energies (a.u.) of reactants and transition structures for the polar hetero cycloaddition reactions

Species	*E*1	*E*2	*E*3	*E*4	*E*5
N_3^-	−162.27962	−163.28329	−163.26700	−163.82375	−163.77607
HCN	−92.35408	−92.87863	−92.87337	−93.16490	−93.16281
H_2CNH	−93.49478	−94.03267	−94.03059	−94.32314	−94.33692
N_2	−108.30095	−108.94702	−108.93824	−109.26193	−109.25139
cis-HNNH	−109.34240	−109.98738	−109.98288	−110.31258	−110.32175
trans-HNNH	−109.35477	−110.00008	−109.99522	−110.32487	−110.33347
H_2CCH_2	−77.60099	−78.03582	−78.03508	−78.29118	−78.31172
HCCH	−76.39596	−76.82307	−76.82065	−77.07326	−77.08189
1	−254.61240	−256.11092	−256.09872	−256.95716	−256.91455
2	−255.75087	−257.25307	−257.25157	−258.10328	−258.08459
3	−270.52728	−272.12226	−272.11881	−273.01225	−272.96749
4	−271.60548	−273.19658	−273.20023	−274.09048	−274.06944
5	−271.61780	−273.21076	−273.21828	−274.10814	−274.08621
6	−239.85104	−241.24851	−241.25145	−242.07565	−242.05769
7	−238.64810	−240.04249	−240.03848	−240.86984	−240.83080

Key: *E*1, RHF/3-21G; *E*2, RHF/6-31+G*; *E*3, RHF/6-31+G*//MP2/6-31+G*; *E*4, MP2/6-31+G*; *E*5, MP3/6-31+G*//MP2/6-31+G*.

model applied. The order of the calculated activation energies with the modest HF/3-21G is **4**, **5**, **1**, **7**, **2**, **6**, **3**, and at the correlated level (MP2/6-31+G*) it is **7**, **1**, **6**, **5**, **2**, **4**, **3**. Although the overall reactivity is quite different from that predicted by the charge transfer, it should be noted that in the case of isomers where FMO fails, such as the diazenes, better predictions can be made by calculating the charge transfers.

Examination of the activation energies at the MP3/6-31+G* level shows that the reaction should be experimentally feasible in all cases except for the addition of nitrogen ($E_a = 37.63$ kcal mol^{-1}) because the activation energies, for example, are below that calculated and experimentally obtained for the cycloaddition of ethylene to butadiene (25.6 kcal mol^{-1}) [18]. At this theory level the most reactive species is hydrogen cyanide which was also indicated from the Mulliken bond orders to form the earliest transition structure.

4. Conclusions

Calculations at the correlated theoretical levels predict that the addition of azide anion to triple bonds of acetylene and hydrogen cyanide will have a relatively low activation energy and that

Table 5
Calculated activation energies in kcal mol^{-1} for the azide anion cyloadditions

TS	E_a1	E_a2	E_a3	E_a4	E_a5	E_a6
1	13.36	14.51	32.00	33.45	19.76	15.27
2	17.77	19.12	39.46	40.71	27.37	17.83
3	33.44	34.64	67.78	69.02	46.08	37.63
4	10.38	12.14	46.50	48.09	28.78	17.81
5	10.41	12.25	45.57	47.38	25.41	14.64
6	18.55	19.57	44.30	45.47	24.65	18.89
7	17.24	19.00	40.08	40.62	17.05	17.04

Key: E_a1, RHF/3-21G; E_a2, RHF/3-21+ZPVE [17a]; E_a3, RHF/6-31+G*; E_a4, RHF/6-31+G*+ZPEV [17b]; E_a5, MP2/6-31+G*; E_a6, MP3/6-31+G*//MP26-31+G*.

the reaction should be very smooth. This has been confirmed with numerous experimental data [1]. On the other hand, the addition of azide anion to nitrogen is energetically unfavorable and experimentally will not be feasible. The reaction can be facilitated by decreasing the LUMO energy of the dienophile, for example in azonium salts, which readily react with the azide anion. The diazenes are predicted to have modest reactivity, and the product should be obtainable under vigorous reaction conditions.

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