
An *Ab Initio* Study of Heterodienophiles Addition to 2,3-Diaza-1,3-Butadiene: An Example of Endo-Lone-Pair Effect on the Reaction Energy Barrier

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ABSTRACT

Transition states for the Diels-Alder reactions of 2,3-diaza-1,3-butadiene with ethylene, formaldehyde, formalimine, *cis*- and *trans*- diazene, and nitrosyl hydride were located by *ab initio* molecular orbital calculations. The bond orders of the new forming bonds have been used to determine the asynchronicity of the reactions. *Ab initio* calculations show that the energy barrier for the hetero-Diels-Alder reactions is relatively high. The highest energy barrier of 34.76 kcal/mol calculated at the MP4/6-31G*//MP2/6-31G* level was found for the *exo-cis*-diazene addition to 2,3-diaza-1,3-butadiene. In all cases, when two diastereomeric transition structures are possible, the one with the endo hydrogen, exo lone pair was predicted to have a lower activation barrier. This behavior can be explained by the $n-\pi$ and $n-n$ lone pair repulsion interaction between the dienophile and diene heteroatoms in the corresponding transition state. The barrier is higher for those reactions which in the transition state have more lone electron pairs. Also, the barrier is higher when the lone pairs are endo oriented than when they are exo oriented in the transition state. © 1996 by John Wiley & Sons, Inc.

Introduction

The hetero-Diels-Alder reaction is one of the most widely used procedures for the preparation of heterocyclic compounds,¹ and often it is a key step in the stereoselective syntheses of natural

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†See also ref. 6f.

products.² These reactions take place through a concerted, synchronous cycloaddition pathway, although a stepwise, zwitterionic mechanism is also possible for polar dienophiles, especially when they are catalyzed by an acid. There are relatively few mechanistic³ and theoretical⁴ studies of hetero Diels-Alder reactions, contrary to extensive studies of the all-carbon Diels-Alder reactions.^{5,6} We have begun a general theoretical study of Diels-Alder reactions of hetero dienophiles with dienes that

contain a heteroatom.⁷ Here we would like to present an *ab initio* study of addition of ethylene, formaldehyde, formaldimine, *trans*-diazene, *cis*-diazene, and nitrosyl hydride to 2,3-diaza-1,3-butadiene. In our study, only a concerted mechanism of the cycloaddition reaction was considered because recent calculations with both *ab initio* and DFT methods prefer a synchronous concerted over biradical stepwise mechanism. At the QCISD(T)/6-31G* level, the synchronous concerted mechanism for ethylene addition to butadiene is predicted to be favored by 6 kcal/mol.⁸ Similar results were obtained by density functional theory (DFT) calculations⁹ that are in good agreement with experimental estimates of 2–7 kcal/mol.¹⁰

Methods

Ab initio molecular orbital calculations were performed with Gaussian 92.¹¹ Geometry optimizations without restrictions were carried out up to the MP2/6-31G* theoretical model, and single-point energy evaluations were performed at the MP4/6-31G*//MP2/6-31G* level.¹² Vibrational frequency calculations were utilized to characterize all stationary points either as minima or transition structures on the potential energy surface. Each transition state gave only one imaginary harmonic vibrational frequency, corresponding to the motion along the new forming C—C and C—X bonds. The bond order¹³ calculations were performed with Spartan at the same level as the geometry optimizations.

Results and Discussion

As has been proposed in the case of the heterodienophile addition to 1,3-butadiene,^{4a,4b} a concerted, but not necessarily synchronous, reaction mechanism was presumed. For the prototypical Diels-Alder reaction of 1,3-butadiene with ethylene, semiempirical, restricted Hartree-Fock (RHF), MP2, and multiconfiguration self-consistent field (MC-SCF) calculations all predict concerted transition state structures with remarkably similar geometries.⁵ Thermochemical estimates¹⁴ and MC-SCF calculations indicate that the diradical intermediates are 5 kcal/mol higher in energy than the concerted transition state in the case of the ethylene addition to butadiene. The forming CC bond lengths for the concerted structures at different

levels of theory range from 2.20 to 2.28 Å, with much smaller variations of the other bond lengths and angles. Likewise, the geometries of the cyclobutadiene ring opening are very similar regardless of the theory level employed.¹⁵ Again, the largest deviation in the bond lengths is found in the elongated cleaving C—C bond, which differs by 0.14 Å for the various calculations. At one extreme, MC-SCF predicts bond breaking at 2.238 Å, while at the other, RHF/STO-3G predicts bond breaking at 2.102 Å.

Transition state structures and geometrical features for the hetero dienophile addition to 2,3-diaza-1,3-butadiene are presented in Figure 1 and Table I. It has been shown that correlation gradient geometry optimizations are important for conformational analysis.¹⁶ These calculations support this finding, and a general trend observed for all structures is that the transition states occur earlier and they are more synchronous at the correlated levels than at lower levels of calculation (cf. values for A and C in Table I).

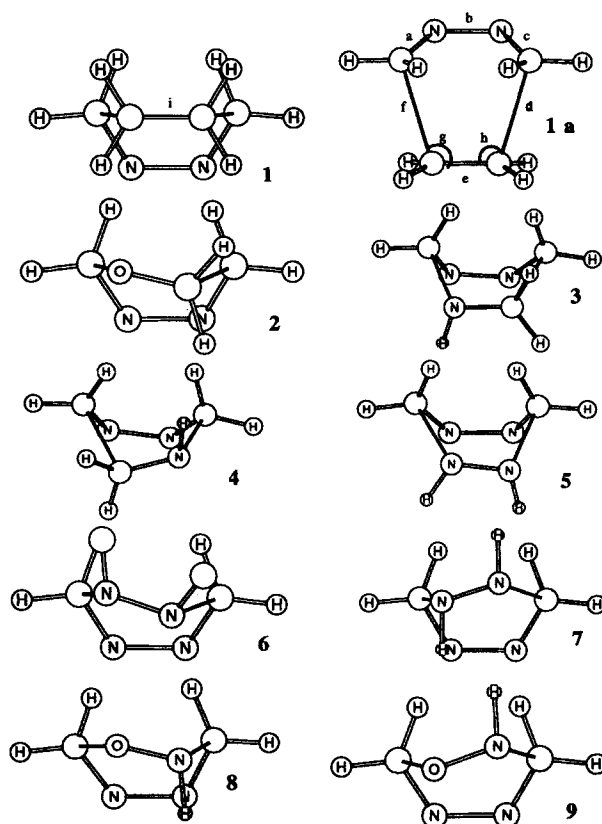


FIGURE 1. Geometries of transition state structures of heterodienophile addition to 2,3-diaza-1,3-butadiene generated at the MP2/6-31G* level.

TABLE I.
Geometrical Features of the Transition State Structures Obtained at Various Levels of Calculations.

		a	b	c	d	e	f	g	h	i
1	A	1.320	1.373	1.320	2.283	1.376	2.283	106.3	106.3	0.0
	B	1.306	1.309	1.306	2.167	1.379	2.167	106.6	106.6	0.0
	C	1.313	1.353	1.313	2.160	1.377	2.160	107.0	107.0	0.0
2	A	1.320	1.357	1.337	2.031	1.277	2.029	112.4	104.8	16.4
	B	1.319	1.300	1.314	2.076	1.253	1.892	114.7	103.4	18.3
	C	1.325	1.349	1.318	2.126	1.279	1.884	115.5	103.0	16.2
3	A	1.329	1.375	1.316	2.398	1.316	1.981	112.8	101.2	-12.7
	B	1.349	1.327	1.283	2.641	1.278	1.698	118.0	93.8	-27.6
	C	1.356	1.365	1.296	2.456	1.296	1.769	115.5	98.5	-25.0
4	A	1.329	1.362	1.325	2.048	1.322	2.219	103.0	108.8	-26.5
	B	1.304	1.300	1.400	1.545	1.283	2.510	89.2	118.4	-46.2
	C	1.315	1.338	1.428	1.571	1.291	2.452	99.9	116.9	-48.0
5	A	1.308	1.389	1.328	1.986	1.297	2.413	102.9	110.7	20.5
	B	1.282	1.330	1.358	1.633	1.242	2.531	95.9	115.7	34.3
	C	1.303	1.363	1.339	1.835	1.304	2.192	105.3	110.8	21.3
6	A	1.329	1.362	1.322	2.215	1.313	1.996	109.8	104.2	22.6
	B	1.355	1.303	1.300	2.379	1.247	1.657	114.5	94.5	44.0
	C	1.330	1.344	1.312	2.154	1.309	1.889	110.6	103.0	29.7
7	A	1.327	1.382	1.311	2.343	1.294	2.041	111.5	102.4	-22.8
	B	1.355	1.308	1.298	2.230	1.262	1.786	113.4	103.0	-24.0
	C	1.327	1.356	1.308	2.117	1.300	1.930	110.0	106.4	-22.5
8	A	1.303	1.397	1.325	2.008	1.255	2.496	100.0	114.2	21.8
	B	1.278	1.334	1.346	1.651	1.207	2.441	99.3	115.6	32.0
	C	1.300	1.367	1.322	1.929	1.290	2.081	109.4	108.0	27.1
9	A	1.317	1.374	1.320	2.121	1.279	2.137	108.0	106.5	-25.6
	B	1.314	1.300	1.312	2.013	1.244	1.922	112.0	107.2	-16.2
	C	1.311	1.356	1.309	2.070	1.300	1.964	112.4	106.6	-19.5

Distances in angstroms, angles in degrees. Denotations a, b, c, d, e, f, g, h, and i correspond to the bond lengths (angstroms) and angles (degrees) in structure 1, Figure 1; A—MP2/6-31G*; B—HF/6-31G*; C—HF/3-21G.

ASYNCHRONICITY OF THE TRANSITION STRUCTURES

The progress of a reaction and the extent to which a new bond has been formed can be followed by calculating the bond orders for the new forming bonds.¹³ The Mulliken and Löwdin bond orders for the new forming bonds are presented in Table II. In all cases, the Löwdin bond orders have a greater value, indicating a somewhat later stage of the bond formation. When the two new forming bonds are of the same nature, it is acceptable to compare the bond lengths and on that basis discuss the asynchronicity of the structure. On the other hand, when the new forming bonds are of a dissimilar nature because of the difference in orbital overlap, this can often give misleading conclusions as to the asynchronicity of the structures and reactions. An illustration of this can be given by examining structures 2 and 4. The difference of the bond lengths d and f in the former is 0.002 Å and in the latter 0.171 Å (D in Table III), suggesting that structure 2 is synchronous. However, comparing the bond orders, it is obvious that the reaction for the *exo*-formaldimine addition is slightly more synchronous than the formaldehyde addition.

It is known from the all-carbon Diels-Alder reactions that symmetric reactants gives rise to synchronous transition states, whereas asymmetric substitution in the reactants cause the transition state structure to be asynchronous.^{5,6} The case is the same here with transition state 1 of the ethylene addition, but not so with transition states 5 and 6 of *cis*-diazene addition to 2,3-diazabuta-1,3 diene. The transition states are asynchronous, especially 5. The greatest asynchronicity is observed in the formalimine addition, while the least asynchronous structure (except the ethylene addition) is obtained with nitrosyl hydride as dienophile. Similar asynchronicity is also obtained in the transition state structure for reaction of *cis*-diazene with butadiene.⁴

Comparison of the sum of the bond orders for the two new forming bonds gives direct evidence about which reaction has an early and which a late transition state. In other words, information on the relative reactivity can be obtained from the bond orders following the Hammond principle.¹³ The earliest transition state is predicted for the nitrosyl hydride reaction, followed by the *endo-cis*-diazene addition. The bond orders show that the formaldehyde addition has the latest transition state and

TABLE II.
Bond Orders for the New Forming Bonds in the Transition States.^a

	Mulliken				Löwdin			
	d	f	D	d+f	d	f	D	d+f
1	0.216	0.216	0.000	0.432	0.259	0.259	0.000	0.504
2	0.355	0.251	0.104	0.606	0.418	0.327	0.091	0.745
3	0.170	0.295	0.125	0.465	0.202	0.395	0.193	0.597
4	0.282	0.240	0.042	0.522	0.376	0.287	0.089	0.663
5	0.230	0.112	0.118	0.342	0.343	0.150	0.193	0.493
6	0.219	0.263	0.044	0.482	0.271	0.379	0.108	0.650
7	0.218	0.131	0.087	0.349	0.319	0.182	0.137	0.501
8	0.199	0.060	0.139	0.259	0.318	0.091	0.227	0.409
9	0.164	0.200	0.036	0.364	0.227	0.284	0.057	0.511

^a Denotations d and f correspond to the bond lengths (angstroms) in structure 1, Figure 1.

consequently the highest energy for the reaction. As expected, for example, the reactivity of *trans*-diazene is between the one for the endo and the exo additions of the cis isomer, although very close to the endo addition (cf. the sum of the Löwdin bond orders, 0.493, 0.501, and 0.650).

Since there are published data for the 1,3-butadiene additions with the same dienophiles,⁴ it is interesting to compare the corresponding structures. The differences in the bond lengths for the two new forming bonds are given in Table III. The general trend is that the dissimilarity of the new forming bond is greater in the case of the 2,3-diaza-1,3-butadiene additions, except in **8**. For example, with formaldehyde that is caused by a much shorter new forming C—O bond (1.998 Å vs. 1.884 Å), while this effect with formalimine is mainly caused by both longer C—C and a shorter C—N new forming bonds. Similar observations can be applied to all other transition states. It should be noted, however, that the comparisons are made on

structures calculated at the HF/3-21G level since the available data are for that theoretical model. The MP2/6-31G* structures can be different from the HF/3-21G (Table I), and comparison with the former model may give somewhat different results.

ENERGIES OF THE ACTIVATION BARRIERS

It is well known that conjugated dienes possessing the 2,3-diaza-1,3-butadiene system rarely participate in effective [4 + 2] cycloadditions. Typical efforts to promote the Diels-Alder cycloadditions of such systems with representative dienophiles afford 2:1 adducts or [3 + 2] criss-cross products.¹⁷ Selected examples include the highly delocalized diazabutadiene, as in reaction of **10** with dienophile **11**,¹⁸ or, if the diazabutadiene unit is a diene with normal electron demand, such as in **12**, then the dienophile **13** has to be strongly activated with electron withdrawing groups.¹⁹ Because the Diels-

TABLE III.
Differences in the New Forming Bond Lengths for the 1,3-Butadiene and 2,3-Diaza-1,3-Butadiene Additions.

TS	$\Delta r/\text{Å}$		$\Delta\Delta r/\text{Å}^a$
	1,3-Butadiene ^b	2,3-Diaza-1,3-butadiene	
1	0.000	0.000	0.000
2	0.121	0.242	0.121
3	0.427	0.687	0.260
4	0.285	0.881	0.596
5	0.330	0.357	0.027
6	0.128	0.265	0.137
7	0.167	0.187	0.020
8	0.207	0.152	-0.055
9	0.081	0.106	0.025

^a $\Delta\Delta r = \Delta r(2,3\text{-diaza-1,3-butadiene}) - \Delta r(1,3\text{-butadiene})$.

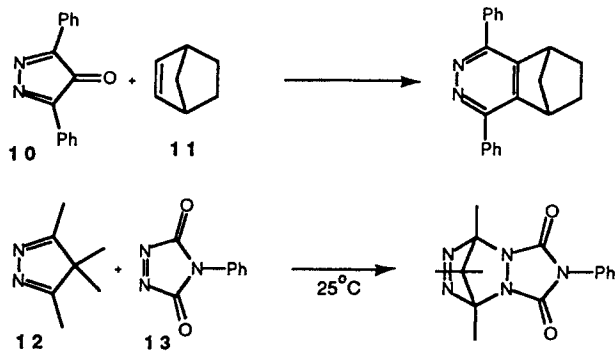
^b From refs. 4b and 15.

TABLE IV.
Calculated Energies for the Reactants and Transition States for the Diels-Alder Reaction of 2,3-Diaza-1,3-Butadiene with the Heterodienophiles.

	<i>E</i> 1	<i>E</i> 2	<i>E</i> 3	<i>E</i> 4	<i>E</i> 5	<i>E</i> 6	<i>E</i> 7	<i>E</i> 8
A	-185.82488	0.05903	-186.88600	0.06120	-187.45709	0.06002	-187.47722	-187.51146
B	-77.60099	0.04904	-78.03171	0.05003	-78.28503	0.05020	-78.30596	-78.31983
C	-113.22182	0.02579	-113.86633	0.02667	-114.16775	0.02631	-114.17285	-114.19202
D	-93.49478	0.03811	-94.02846	0.03954	-94.31521	0.03922	-94.32980	-94.34554
E	-109.34240	0.02621	-109.98350	0.02825	-110.30473	0.02684	-110.31470	-110.33340
F	-109.35477	0.02678	-109.99476	0.02871	-110.31518	0.02751	-110.32475	-110.34337
G	-129.03829	0.01323	-129.78607	0.01468	-130.12459	0.01337	-130.12468	-130.14805
H	-154.05946	0.09205	-154.91965	0.09154	-155.42266	0.08636	-155.45564	-155.48439
1	-263.35148	0.11214	-264.83682	0.11524	-265.70506	0.11336	-265.73095	-265.78750
2	-298.97130	0.08921	-300.66272	0.09250	-301.57623	0.09089	-301.58471	-301.65030
3	-279.25506	0.10130	-280.83786	0.10483	-281.73861	0.10313	-281.75626	-281.81705
4	-279.25147	0.10172	-280.83466	0.10578	-281.72922	0.10301	-281.74601	-281.80780
5	-295.10720	0.08998	-296.79304	0.09418	-297.73718	0.09061	-297.74913	-297.81297
6	-295.07921	0.08900	-296.76578	0.09306	-297.71404	0.09004	-297.72298	-297.78947
7	-295.11209	0.09047	-296.79518	0.09473	-297.74251	0.09124	-297.75384	-297.81820
8	-314.80779	0.07746	-316.59738	0.08128	-317.56006	0.07780	-317.56441	-317.63298
9	-314.79043	0.07690	-316.57771	0.08096	-317.54473	0.07722	-317.54527	-317.61576
I	-231.60321	0.13516	-232.87960	0.13711	-233.67910	0.13718	-233.71896	-233.76822

A — 2,3-Diaza-1,3-butadiene; B — Ethylene; C — Formaldehyde; D — Formaldimine; E — *cis*-Diazene; F — *trans*-Diazene; G — Nitrosyl hydride; H — *trans*-1,3-Butadiene; I — Transition structure for ethylene + 1,3-butadiene; *E*1 — RHF/3-21G; *E*2 — ZPVE RHF/3-21G, scaled by 0.89^{20a}; *E*3 — HF/6-31G*; *E*4 — ZPVE HF/6-31G*, scaled by 0.9135^{20b}; *E*5 — MP2/6-31G*; *E*6 — ZPVE MP2/6-31G*, scaled by 0.9646^{20b}; *E*7 — MP3/6-31G*//MP2/6-31G*; *E*8 — MP4/6-31G*//MP2/6-31G*.

Alder reaction in the case of **10** is with inverse electron demand, the conventional dienophiles, including maleic anhydride, dimethyl acetylenedicarboxylate, diphenylacetylene, and dimethyl fumarate, have failed to react.¹⁸ At the same time, derivatives of butadienes react with a wide variety of heterodienophiles in Diels-Alder reactions. Apparently, the differences in the reactivity are caused by the presence of the two nitrogens in the butadiene skeleton. To evaluate the reactivity of 2,3-diaza-1,3-butadiene in hetero Diels-Alder reactions, the energies of the species involved in the reactions were calculated. The calculated total energies of the reactants and the transition structures and activation energies are presented in Tables IV and V respectively.



An obvious conclusion from Table V is that the

energy barriers are always lower in all cases when the dienophile hydrogen is endo oriented in the transition structures than when it is exo. This has been rationalized on the basis of the $n-\pi$ repulsion interactions between the lone pairs of the dienophile heteroatoms and the π -orbitals of the diene. The first ones who suggested that the lower reactivity in the Diels-Alder reactions might be explained by repulsion of the reactants' electron field orbitals in the transition states were Coxon and co-workers²¹ and in the hetero Diels-Alder reactions Houk and co-workers,^{4a,4b} In this case, it is plausible to predict that besides these interactions, $n-n$ lone pair interactions between the dienophile and diene heteroatoms' lone pairs will further enhance these effects. It would be expected that the differences in the barriers for the endo-exo additions would be higher than when only $n-\pi$ interactions are possible.

The bond order prediction that nitrosyl hydride is the most reactive dienophile is confirmed with all employed theoretical models. MP4/6-31G*//MP2/6-31G* predicts that the activation barrier is only 16.65 kcal/mol, indicating that the reaction should be experimentally attainable, although to the best of our knowledge there is no such evidence.

The reaction with ethylene has a barrier of 27.48 kcal/mol at the highest level. The prototypical

TABLE V.
Calculated Activation Energies (kcal / mol) for the Diels-Alder Reaction of 2,3-Diaza-1,3-Butadiene with the Heterodienophiles.

Dienophile	TS	Ea1	Ea2	Ea3	Ea4	Ea5	Ea6	Ea7	Ea8
Ethylene	1	46.68	49.23	50.76	53.28	23.26	25.23	32.77	27.48
Formaldehyde	2	47.31	50.07	56.23	59.14	30.50	33.36	41.01	33.37
Formaldimine, endo H	3	40.54	43.15	48.07	50.63	21.14	23.58	31.85	25.07
Formaldimine, exo H	4	42.79	45.66	50.08	53.24	27.03	29.40	38.28	30.87
<i>cis</i> -Diazene, endo H	5	37.70	40.68	47.98	50.95	15.46	17.82	26.85	20.01
<i>cis</i> -Diazene, exo H	6	55.26	57.62	65.09	67.35	29.98	31.98	43.26	34.76
<i>trans</i> -Diazene	7	42.39	45.32	53.70	56.73	18.67	21.00	30.20	22.99
Nitrosyl hydride, endo H	8	34.75	38.01	46.87	50.26	13.57	16.33	23.53	16.65
Nitrosyl hydride, exo H	9	45.65	48.56	59.21	62.40	23.19	25.59	35.54	27.45
Ethylene + 1,3-butadiene ^a		35.92	39.64	45.03	47.83	17.94	18.33	26.76	22.59

Ea1 — RHF/3-21G; Ea2 — ZPVE RHF/3-21G; Ea3 — HF/6-31G*; Ea4 — ZPVE HF/6-31G*; Ea5 — MP2/6-31G*; Ea6 — ZPVE MP2/6-31G*; Ea7 — MP3/6-31G*//MP2/6-31G*; Ea8 — MP4/6-31G*//MP2/6-31G*.

^a See also ref. 6f.

reaction between ethylene and butadiene has an activation barrier of 27.5 kcal/mol.²² The calculated barrier at the MP4/6-31G*//MP2/6-31G* level is 22.59 kcal/mol.[†] Interestingly, the MP3/6-31G*//MP2/6-31G* is somewhat closer to the experimental value (Table V). On the other hand, the energy barrier for the ethylene addition to 2-aza-1,3-butadiene is predicted to be somewhat lower than the ethylene addition to 1,3-butadiene.²³ However, the calculations had been performed at the MP2/6-31G*//HF/3-21G level. The geometrical parameters, as was already stated, are very different for the structures optimized at the Hartree-Fock minimal basis set level and the ones at the Møller-Plesset theoretical level. The present results for the ethylene addition to 1,3-butadiene and 2,3-diaza-1,3-butadiene at the correlated levels clearly show that the introduction of the heteroatoms in the diene increases the energy barrier. The differences are from 4.9 to 6.9 kcal/mol at the correlated levels. This can be attributed to the lone pair interactions on the diene nitrogen with the π -orbitals of ethylene.

In the transition states of the two diastereomeric structures 3 and 4, there are three lone pairs, two of them located on the diene and one on the dienophile. The repulsion interactions between these three lone electron pairs are maximal in transition state 4, and state 4 is predicted to have 5.8 kcal/mol higher activation energy than 3 (Table V), favoring the structure with the nitrogen lone pair of formaldimine in the exo position. Due to these interactions, the reaction with the dienophile nitrogen lone pair in the endo position has a higher activation energy barrier in compari-

son to both the ethylene addition to 2,3-diaza-1,3-butadiene and to 1,3-butadiene.

The lone pair repulsion interactions also explain the lower reactivity of formaldehyde in comparison to formaldimine. In transition structure 2, there are four lone pairs. Two of them are located on the formaldehyde oxygen. Although one of the oxygen lone pairs is pointing away from the diene moiety in the transition state structure, there are still small repulsion interactions that are responsible for the higher reaction barrier in comparison to the exo hydrogen formaldimine reaction.

In the diazene addition to 2,3-diaza-1,3-butadiene, there are four lone pair electrons that can interact in the process of the reaction. In transition state 5, the two lone pairs located on the nitrogens of *cis*-diazene are in the exo position. State 5 is expected to have the least lone pair repulsion interactions and therefore the lowest energy barrier of all three isomeric transition states 5, 6, and 7. Second in reactivity should be *trans*-diazene because in transition state 7 one nitrogen lone pair of the dienophile is in the endo and the other in the exo position. Finally, transition state 6, with both nitrogen lone pairs in the endo position, has the highest activation barrier of all three reactions. The energy barrier for 7 is about 3 kcal/mol lower than for 5, while the energy barrier for 6 is almost 12 kcal/mol higher than for 7. The same conclusion that the energy barrier of 7 is closer to 5 than to 6 was reached on the basis of the bond orders.

The low reactivity of the heterodienophiles in Diels-Alder reactions with 2,3-diaza-1,3-butadiene

can be also explained by differences in orbital overlap for the C—C, C—N, and C—O bonds in the discussed transition states 2–9. This is certainly one of the factors. Additional effects are exerted from the postulated $n-\pi$ repulsion interactions, but also in this case lone pair–lone pair interactions seem to be a plausible explanation for the somewhat decreased reactivity. As with other Diels-Alder reactions, they can be facilitated if the density of electron pair is delocalized on the 2,3-diaza-1,3-butadiene or the heterodienophile substituents, as in diene **11** and dienophile **13**.

Conclusion

Calculations performed at MP4/6-31**//MP2/6-31G* show that the additions of ethylene, formaldehyde, formalimine, *cis*-diazene, *trans*-diazene, and nitrosyl hydride to 2,3-diaza-1,3-butadiene are less favorable than the same additions to 1,3-butadiene. When two diastereomeric transition structures are possible, the one with the endo hydrogen, exo lone pair was predicted to have a lower activation barrier. This behavior can be explained by the known $n-\pi$ repulsion interactions between the dienophile and the diene heteroatoms in the corresponding transition state, but in this case $n-n$ lone pair repulsion interaction also enhances these interactions. The barrier is higher for those reactions which in the transition state have more lone electron pairs.

The bond orders, rather than the bond lengths, are a more appropriate measure of the reaction asynchronicity. In some cases, they can be used to determine the relative reactivity of similar reactants.

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