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PM3–CI calculation of Diels–Alder transition structures of hetero dienophile addition to butadiene: comparison with PM3 and ab initio generated transition structures

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Abstract

Transition structures for Diels–Alder addition of formaldehyde, formaldimine, diazene, and nitrosyl hydride to butadiene were studied with ab initio and PM3–CI methods. Activation energies were evaluated and compared with the different methods. The order of the reactivity of the hetero dienophiles was predicted on the basis of the frontier orbital energies, and ab initio and semiempirical calculations of the reaction barriers were performed. These energies were used to predict the stereoselectivity of the reactions. It was concluded that the ab initio calculations tend to generate transition structures with a very small degree of asynchronicity, whereas, PM3–CI on the other hand, tends to generate highly asynchronous transition structures. That is specially pronounced in the case when one of the two new forming bonds in the transition structures is C–N. All of the studied methods predict high endo vs. exo N–H addition of hetero dienophiles to butadiene thus suggesting the usefulness of these reactions in stereoselective organic syntheses.

1. Introduction

Interest in the synthetic and theoretical study of hetero Diels–Alder reactions have increased considerably because they are a powerful tool for the preparation of heterocyclic compounds [1]. These reactions are generally assumed to be concerted, asynchronous cycloadditions, although a stepwise zwitterionic mechanism is also possible for polar dienophiles or for catalyzed processes. There are only a few mechanistic [2] and theoretical [3,4] studies of hetero Diels–Alder reactions although

the all-carbon Diels–Alder reactions have been studied extensively [5]. Here we present our results on hetero dienophile addition to butadiene.

2. Computational methods

The calculations were carried out with the restricted Hartree–Fock method, using the GAUSSIAN 92 program [6]. The transition structures were located and optimized [7] prior to any ab initio calculations with PM3 [8] from the MOPAC [9] computational package. These transition structures were then fully optimized with the 3-21G basis set [10]; each transition structure was confirmed by having only one imaginary frequency. These ab initio optimized transition structures

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were then again optimized by PM3 and PM3–CI [11] methods.

3. Results and discussion

In continuation of our interest in the hetero Diels–Alder reactions we have studied theoretically the addition of hetero dienophiles to cyclic dienes such as cyclopentadiene [12], furan [13], and 4H-pyrazole [12] by ab initio methods. In the all-carbon Diels–Alder addition of symmetrical dienes to either butadiene or cyclopentadiene [5], a concerted synchronous transition structure was generated by both semiempirical [14], and ab initio [5(b),5(c)] methods. When the dienophile is unsymmetrical the transition structure in the concerted mechanism is expected to be asynchronous. In the case of symmetrical hetero dienophile addition to cyclopentadiene, furan, and 4H-pyrazole synchronous transition structures have been generated by ab initio calculations. To our surprise Houk and coworkers [4] obtained an asynchronous transition structure for the addition of cis-diazene to butadiene calculated by RHF/3-21G. This prompted us to study the hetero Diels–Alder reactions with butadiene by taking into account the electron correlation.

The following questions in this PM3–CI study of the hetero Diels–Alder reactions were addressed: What will the CI calculation predict with regard to the order of reactivity of the hetero dienophiles toward butadiene, the geometry of the transition structures, and the stereoselectivity? Second, the reliability of this method compared to ab initio RHF/3-21G and MP2/6-31G* levels of calculation. To secure that the ab initio and semiempirical calculations will, at one time, in the calculations lead to the same structure, the transition structures of the addition of ethylene, formaldehyde, formalimine, cis- and trans-diazene were first optimized by 3-21G and then these optimized structures were used as input files for PM3 and PM3–CI optimizations. The PM3–CI optimized transition structures are presented in Fig. 1 (the bond lengths calculated by the other methods are also given).

Several general conclusions can be made from the geometries of the transition structures. All

Table 1

Degree of asynchronicity in the formation of the two new bonds

Transition structure	$\Delta r/\text{\AA}$			
	RHF/3-21G	MP2/6-31G* ^a	PM3	PM3–CI
1	0		0.003	0.007
2	0.121		0.126	0.128
3	0.427	0.283	0.532	0.576
4	0.285	0.002	0.452	0.462
5	0.330		0.356	0.365
6	0.128		0.077	0.077
7	0.167		0.156	0.157
8	0.207		0.492	0.504
9	0.081		0.299	0.341

^a Ref. 4(b).

transition structures, even the transition structure for ethylene addition to butadiene, are asynchronous and the asynchronicity is more pronounced than in the case of the ab initio calculations. The asynchronicities of the transition structures are presented in Table 1.

The degree of asynchronicity in the formation of the new bonds in the Diels–Alder reactions has been long debated. It has been stated that the all-carbon Diels–Alder reaction is synchronous but asymmetric substitution causes the transition structure to be asynchronous [5]. With PM3 and PM3–CI methods all transition structures are asynchronous. It is interesting to mention that all three methods agree with the asynchronicity of the ethylene and formaldehyde addition to butadiene. Although the discrepancies between the ab initio and semiempirical methods are very small, PM3–CI predicts a higher asynchronicity in both cases by 0.007 Å than RHF/3-21G. The highest degree of asynchronicity was obtained in the case of N–H endo formalimine addition to butadiene. The asynchronicity calculated with PM3–CI is 0.576 Å.

Surprisingly, MP2/6-31G* calculation actually generated structures with lower asynchronicity than both the semiempirical methods and RHF/3-21G. For example, in the case of N–H exo formalimine addition (4), MP2/6-31G* predicts $\Delta r = 0.002$ Å, while, PM3–CI predicts a highly asynchronous transition structure (Table 1). In the addition of N–H endo cis-diazene, the transition structure 5 is asynchronous with the higher

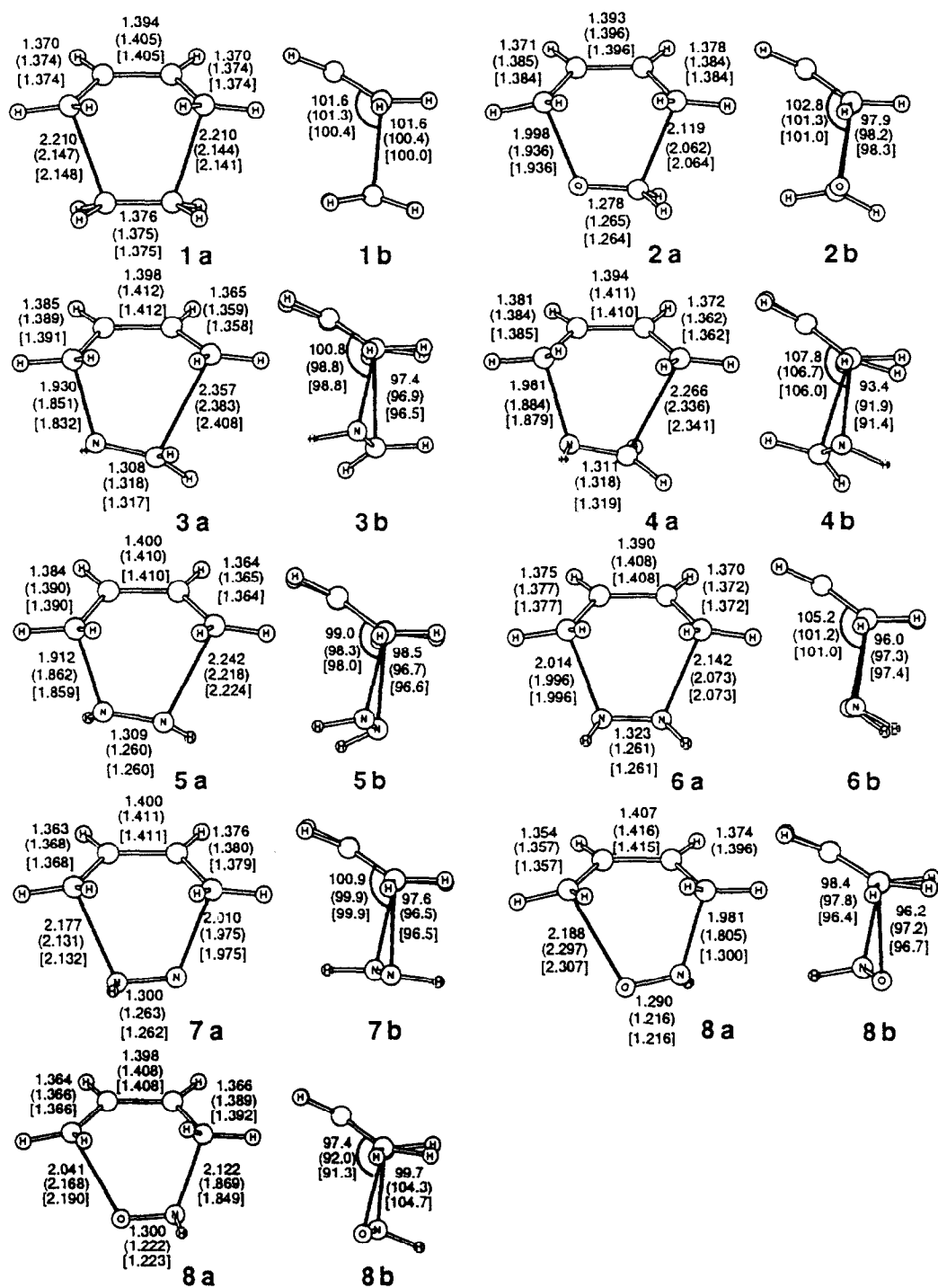


Fig. 1. Transition structures for the reaction of butadiene with hetero dienophiles. The bond lengths (ångströms) and angles (degrees) were generated by RHF/3-21, (PM3), [PM3-CI].

degree of asynchronicity again predicted by PM3–CI (0.365 Å). This is in contrast to the transition structure **6** for the exo isomer. PM3–CI predicts a slightly asynchronous transition structure (0.077 Å), whereas ab initio RHF/3-21G prefers a more asynchronous transition structure (Table 1). The same trend is present for the transition structure of trans-diazene addition, but the values for the asynchronicity are much more uniform.

One more interesting feature of the PM3–CI is its prediction of the new C–N bond formation. It is much shorter than predicted by both RHF/3-21G and MP2/6-31G*. This is nicely demonstrated on the example of N–H exo addition of nitrosyl hydride to butadiene. RHF/3-21G predicts that the new formed C–O bond is longer than the C–N bond by 0.081 Å, but PM3–CI predicts that the C–N forming bond is now shorter than the C–O forming bond by 0.341 Å.

The repulsion interactions between the hetero atom lone-pair of the dienophile and the π orbitals of butadiene are overestimated in the transition structures generated by RHF/3-21G. On the other hand, PM3–CI predicts higher endo N–H interactions with butadiene of the transition structure. That is demonstrated in all eight transition structures with the hetero dienophiles, but can be readily explained for the example of cis-diazene addition to butadiene. Transition structure **5** represents the exo addition of cis-diazene. The NCC angle, with a shorter N–C new forming bond, is predicted to be smaller by PM3–CI than by RHF/3-21G (Fig. 1) due to overestimation of the N–H interactions with the π system of butadiene.² On the other hand, transition structure **6**, for N–H exo cis-diazene addition to butadiene, demonstrates that PM3–CI underestimates the n – π repulsion interactions which causes the NCC angle to be 4.2° smaller than in the transition structure generated by RHF/3-21G (Fig. 1).

The reactivity of the hetero dienophiles in the Diels–Alder reaction can be explained in terms of the energy difference of frontier orbitals [15] of the diene and dienophile. According to the PM3–CI calculated HOMO–LUMO energy

Table 2

Frontier orbital energies (kcal mol^{−1}) of butadiene and hetero dienophile calculated by PM3–CI

Compound	HOMO	LUMO	A ^a	B ^b
Butadiene	−9.468	0.263		
Ethylene	10.642	1.229	10.697	10.905
Formaldehyde	−10.630	0.827	10.295	10.893
Formaldimine	−10.013	0.996	10.464	10.276
cis-Diazene	−9.585	0.532	10.000	9.848
trans-Diazene	−9.616	0.497	9.879	9.965
Nitrosyl hydride	−9.842	−0.071	9.539	10.105

^a A = LUMO_{dienophile} − HOMO_{butadiene}.

^b B = LUMO_{dienophile} − HOMO_{butadiene}.

differences (Table 2), the reactivity order is nitrosyl hydride ($\Delta E = 9.539$ kcal mol^{−1}), cis-diazene ($\Delta E = 9.848$ kcal mol^{−1}), trans-diazene ($\Delta E = 9.879$ kcal mol^{−1}), formaldimine ($\Delta E = 10.276$ kcal mol^{−1}), formaldehyde ($\Delta E = 10.295$ kcal mol^{−1}), and ethylene ($\Delta E = 10.697$ kcal mol^{−1}). If ethylene is not considered, the PM3–CI frontier orbital prediction of reactivity order is exactly the same as was obtained for the N–H endo addition of the same hetero dienophile to butadiene by MP2/6-31G*/RHF/3-21G [4(a)]. One of the limitations of the frontier orbital theory is that it does not take into account the steric and orbital interactions of the reactants in the transition structures. Although on the basis of the HOMO–LUMO energy difference formaldehyde is more reactive than ethylene, the MP2/6-31G*/RHF/3-21G energy estimation shows that ethylene is indeed more reactive due to the n – π repulsion interactions present in the transition structure with formaldehyde.

The activation energies calculated by both PM3 and PM3–CI do not show the reactivity order predicted by the frontier orbitals and by MP2/6-31G*/RHF/3-21G (Table 3).

It is known experimentally that butadiene does not react with ethylene and formaldehyde, but derivatives of formaldimine, diazene, and nitrosyl hydride react readily with dienes [1]. Although frontier orbital theory predicts that formaldehyde should be more reactive than ethylene, MP2/6-31G*/3-21G, and PM3 and PM3–CI suggest the opposite. That can be explained by the n – π

² For discussion of n – π repulsions on the structures and energies of the transition states see [4,12,13].

Table 3

Calculated energies (kcal mol⁻¹) of the hetero Diels–Alder transitions structures with respect to reactants

Transition	3-21G	MP2/6-31G*//3-21G ^a	PM3	PM3–CI
1	35.8	17.6	27.2	27.1
2	32.5(0.0)	20.9(0.0)	36.8(0.0)	36.8(0.0)
3	31.1(-1.4)	15.2(-5.7)	28.4(-8.4)	28.3(-8.5)
4	36.4(3.9)	20.1(-0.8)	31.0(-5.8)	31.0(-5.8)
5	27.4(-8.4)	6.0(-14.9)	35.3(-1.5)	35.3(-1.5)
6	39.9(4.1)	17.6(-2.3)	38.8(2.0)	38.7(1.9)
7	29.5(-6.3)	9.0(-11.9)	37.0(0.2)	37.0(0.2)
8	19.8(-16.0)	1.8(-19.1)	31.6(-5.2)	31.4(-5.4)
9	27.3(-8.5)	9.9(-11.9)	35.6(-1.2)	35.5(-1.3)

^a Ref. 4(a).

repulsion interaction between the lone-pair of formaldehyde and the π system of butadiene. These kinds of interactions are not present in transition structure 1 in the reaction of ethylene with butadiene. Because all the hetero dienophiles studied have lone pairs we have chosen formaldehyde as reference for comparison of the activation barrier with the other dienophiles (Table 3). According to both the ab initio method and PM3–CI frontier orbital theory, the most reactive hetero dienophile in this series is nitrosyl hydride, but both semiempirical methods predict that actually formaldimine is the most reactive of all hetero dienophiles studied. Thus it seems that both fail to predict correctly the reactivity of the hetero dienophiles.

The ability to predict the stereoselectivity of the hetero Diels–Alder reactions is a very important goal in the preparation of heterocyclic natural products [11]. Thus it is of great interest to determine if PM3–CI can correctly predict the stereoselectivity of the Diels–Alder reactions. The results of endo–exo comparison for different methods are presented in Table 4. Although the energy differences for both semiempirical methods are considerably lower than for ab initio calculations, all four

considered methods favour the correct isomer. That is quite different from the case of the all-carbon Diels–Alder reactions, where the semiempirical methods constantly predict the formation of the wrong stereoisomer (exo) [14]. This large calculated endo preference can be useful in the design of reagents for stereoselective hetero Diels–Alder reactions. Recently it was reported that α -chloro nitroso compounds undergo hetero Diels–Alder reactions with very high enantioselectivity.

4. Conclusion

The transition structures of hetero dienophile addition to butadiene calculated by PM3–CI have a much higher degree of asynchronicity than the ones calculated by ab initio methods. If the RHF/3-21G generated transition structures are used as reference, then the higher level of ab initio calculation, MP2/6-31G* tends to bring the asynchronous transition structure very close to a synchronous one, while the PM3–CI tends in the opposite direction and generates a highly asynchronous transition structure. PM3–CI activation energies of the hetero Diels–Alder reactions vary in

Table 4

Calculated endo preferences (kcal mol⁻¹) of hetero dienophile addition to butadiene

Dienophile	3-21G	MP2/6-31G*//3-21G	PM3	PM3–CI
Formaldimine	5.3	4.9	2.6	2.7
cis-Diazene	12.5	11.6	3.5	3.4
Nitrosyl hydride	7.5	8.1	4.0	4.1

a narrow energy range for a wide variety of hetero dienophiles. That makes the prediction of the order of reactivity for different hetero dienophiles inaccurate. Nevertheless, the PM3–CI method seems to be reliable in predicting the correct stereoisomer in the reaction, and if the dienophile has different structural isomers, which of them will be more reactive. The combination of frontier orbital energies for reactants and the activation barriers for the isomeric transition structures can be used for prediction of the order of reactivity and stereoselectivity, respectively.

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