

**AB INITIO STUDY OF DIELS-ALDER REACTIONS OF
1,3,4-OXADIAZOLE WITH ETHYLENE, ACRYLONITRILE,
MALEONITRILE, FUMARONITRILE AND
1,1-DICYANOETHYLENE. INVERSE ORDER AND RATIO OF
ENDO/EXO REACTIVITY**

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Transition structures for the Diels-Alder reactions of 1,3,4-oxadiazole with ethylene, acrylonitrile, maleonitrile, fumaronitrile, and 1,1-dicyanoethylene were located with *ab initio* molecular orbital calculations with the RHF/3-21G theoretical model. The activation energies were calculated by single-point calculations with the RHF/6-31G* and MP2/6-31G* theory levels on the RHF/3-21G geometries. Geometries of two transition structures and the corresponding reactants were generated at the MP2/6-31G* and the energies evaluated at the MP3/6-31G* level. The values obtained are comparable to those generated by MP2/6-31G*/3-21G. The asynchronicity of the transition structures follow the same trend as the corresponding all-carbon Diels-Alder reactions with buta-1,3-diene and cyclopentadiene, but the activation energies are almost in opposite correlation. This behavior is explained by the oxadiazole nitrogen lone pair repulsion with the π -orbitals of the nitrile groups.

INTRODUCTION

The Diels-Alder reaction continues to be an important method for the preparation of a wide variety of products. The usefulness of the Diels-Alder reaction in synthesis arises from its versatility and its high regio- and stereoselectivity. Numerous dienes and dienophiles bearing various functional groups can be used, and many different types of ring structures built. Not all the atoms involved in the ring closure need be carbon atoms, so that both carbocyclic and heterocyclic rings can be obtained by these reactions. Moreover, it is frequently found that although the reaction could conceivably give rise to a number of structurally stereoisomeric products, only one isomer is formed exclusively or at least in a preponderant amount.¹ These synthetic advantages of the Diels-Alder reaction make it an important subject for computational studies. Significant progress has been made in understanding the nature of the transition states and the level of *ab initio* theory required to reproduce experimental kinetic data.² These reactions are generally assumed to be

concerted cycloadditions, although a stepwise radical mechanism has been proposed,³ but has been rejected by high level *ab initio* calculations.⁴ There are only a few examples of the synthetic application of 1,3,4-oxadiazolium salts as dienes in Diels-Alder reactions. The adducts are not stable and produce the corresponding heterocyclic compounds in a retro-Diels-Alder reaction.⁵ Because a wide variety of substituted 1,3,4-oxadiazoles can be prepared in high yields from simple and not expensive materials,⁶ they are excellent materials for the preparation of other heterocyclic compounds via Diels-Alder and retro-Diels-Alder reactions. We have been successful in transforming 1,3,4-oxazoles and activated dienes to corresponding furan derivatives.⁷ Here we report a computational study of 1,3,4-oxadiazole as a diene in Diels-Alder reactions.

COMPUTATIONAL METHODS

The structures of the compounds were built with the Chem-X⁸ computational package and saved as

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MOPAC⁹ files for PM3¹⁰ semi-empirical calculations. The transition states¹¹ were initially located with MOPAC and refined by Bartel's NLLSQ method. The geometries obtained were used as input files for the Gaussian system of computer programs.¹² Structures were fully optimized without symmetry restrictions with the RHF/3–21G theoretical model, followed by vibrational frequency calculations. The energies were computed at the restricted Hartree–Fock and restricted second-order Möller–Plesset perturbation theory with the 6–31G* basis set.¹³

RESULTS AND DISCUSSION

A concerted, but not necessarily synchronous, reaction mechanism was assumed. For the prototypical Diels–Alder reactions of butadiene with ethylene derivatives, semi-empirical, RHF, MP2 and MCSCF calculations all predict concerted transition structures with remarkably similar geometries.¹⁴ However, the energy estimates indicate that semi-empirical^{15,16} and

small basis set *ab initio* calculations cannot predict the correct isomer in the cycloaddition reactions.¹⁶ Although RHF/3–21G calculations generally give reasonable transition structures compared with higher level *ab initio* calculations, such as MP2/6–31G* and MCSCF, the higher levels are required to obtain accurate activation energy.^{16,17} For the Diels–Alder reaction, MP2 overestimates the effect of electron correlation in the transition state structure and lowers the activation energy too much. For example, in the reaction of cyclopentadiene with ethylene at the MP2/6–31G*//HF/6–31G* level,¹⁷ ΔE^\ddagger is 11.8 kcal mol⁻¹ (1 kcal = 4184 kJ) less than the experimental¹⁸ activation energy. Nevertheless, the MP2/6–31G* relative energies should give a reasonable estimation of the effect of substituents, since the magnitude of the correlation energy is largely dependent on the number of electrons involved in bonding changes.²

In this work seven transition structures were located for five dienophiles, since two of the reactions have both *endo* and *exo* transition states. The concerted transition structures were found for all reactions.

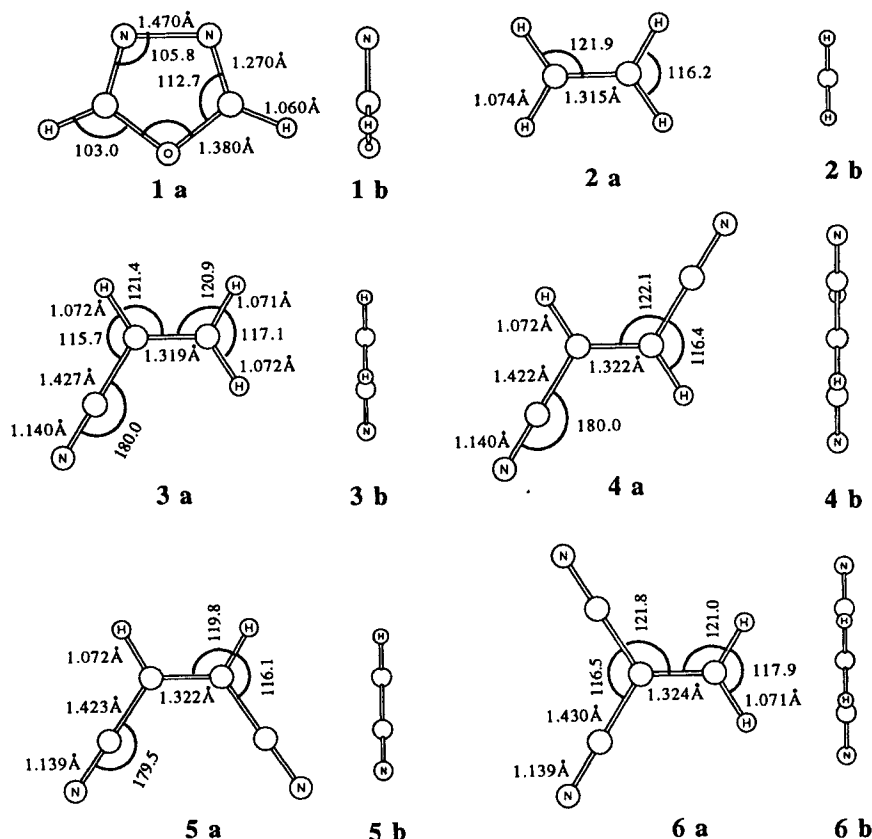


Figure 1. Front (a) and side (b) views of the reactants calculated with the RHF/3–21G theoretical model

Geometry features of the reactants

The RHF/3-21G structures of the reactants and the transition structures are shown in Figures 1 and 2, respectively. All reactants are planar. The nitrile groups and the carbon to which they are connected are linear and the molecules show the highest symmetry of all structures considered. The calculated structural parameters for ethylene and cyanoethylene are identical with those obtained by Houk *et al.*¹⁶ and agree with data obtained from microwave spectroscopy for 1,3,4-oxadiazole.¹⁹

Ethylene or maleonitrile as dienophiles give rise to fully symmetrical transition state structures (7, 11 and 12). Compared with the butadiene reaction with the

same dienophiles, the new forming bonds are much shorter. For example, the new forming bond in transition structure 7 is 0.114 Å shorter than in the case of butadiene,¹⁶ optimized with the same model chemistry. On the other hand, unsymmetrical dienes give rise to unsymmetrical transition structures. In both the *exo* (8) and the *endo* (9) transition state structures of acrylonitrile addition to 1,3,4-oxadiazole, the new forming carbon-carbon bond on the cyano side is slightly shorter than the other. The asynchronicity (Δr) is 0.104 Å for the *exo* and 0.086 Å for the *endo* addition, which is considerably lower than that calculated for the cyclopentadiene-acrylonitrile adduct (0.159 and 0.158 Å, respectively).¹⁶ The transition-state structure for 1,3,4-oxadiazole-fumaronitrile (10) has a very low

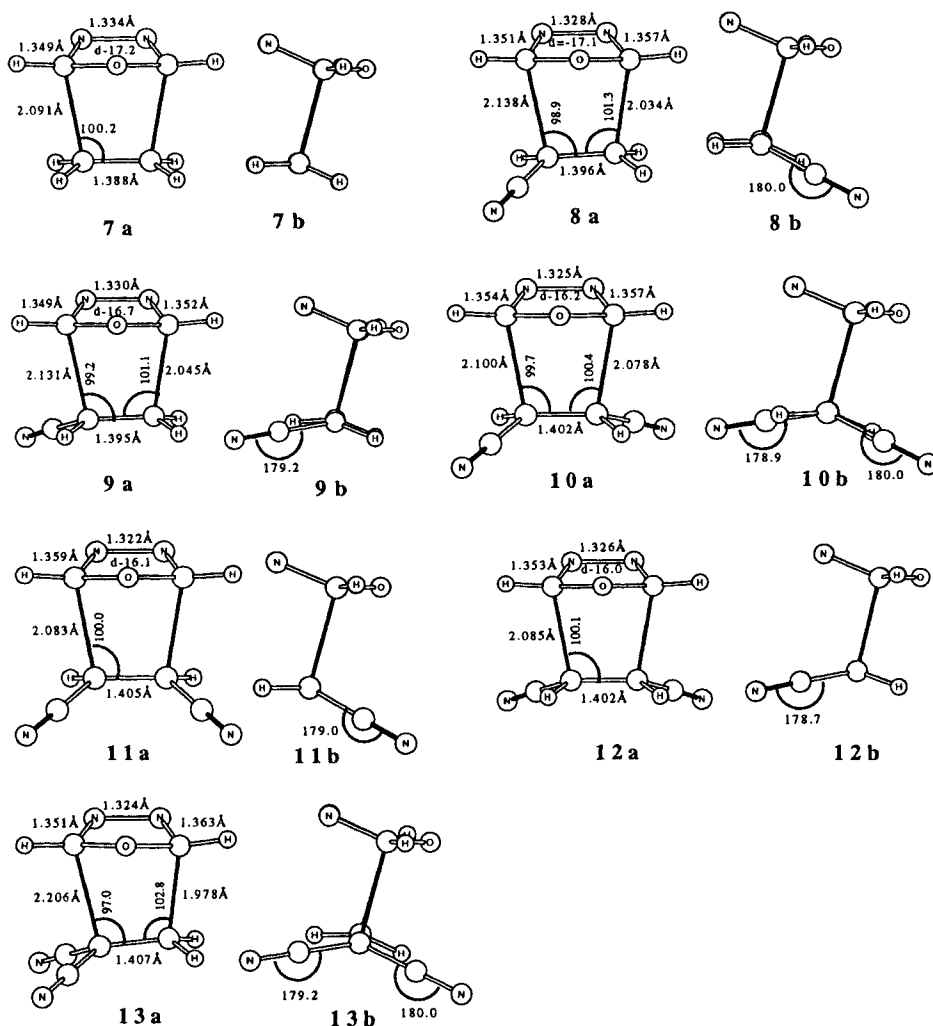


Figure 2. Front (a) and side (b) views of the transition-state structures calculated with the RHF/3-21G theoretical model

degree of asynchronicity ($\Delta r = 0.022 \text{ \AA}$), with the endo cyanide forming bond being shorter. This is similar to the butadiene–fumaronitrile structural parameters.¹⁶

Energetics of the transition structures

The calculated total energies for the reactants and the transition state structures and the activation energies are given in Tables 1 and 2, respectively. According to the calculated activation energies for all model chemistries employed, the most reactive of all dienophiles in the addition to 1,3,4-oxadiazole is ethylene. This result is different to, for example, the order of reactivity in the cyanoethylene additions to cyclopentadiene obtained experimentally and by similar *ab initio* calculations.¹⁷ In all cases of cyanoethylene additions to butadiene, the calculated activation energy for the *endo* transition structures is always lower than or very close to that for the isomer with the hydrogen in the *exo* position.¹⁷ For example, the calculated RMP2/6–31G**//RHF/6–31G* *exo*–*endo* difference is 0.07 kcal mol⁻¹. In two cases, the *endo* isomer is preferred by all studied theoretical models by at least 1.5 kcal mol⁻¹. The higher activation energy for the *endo* isomer in comparison with

the *exo* isomer can be explained as being caused by interactions of the oxadiazole nitrogen lone pair with the π -orbitals of the nitrile groups. This explanation can also help in understanding the order of the reactivity. The most reactive dienophile is the one without a nitrile group, and the energetically favored isomer is the one that has an *exo* cyano group. This is opposite to what is known to be the case in the Diels–Alder reaction of cyanoethylenes with both buta-1,3-diene, and cyclopentadiene.^{16,17} Because the difference in these systems is the heteroatoms in the cyclopentadiene ring, this unusual behavior can be attributed to the nitrogen lone pair interactions in the transition structures.

Evaluation of the reactivity with correlated methods

In order to confirm the order of the dienophile reactivity in these cycloaddition reactions, higher levels of theory were employed for the ethylene and the *endo* acrylonitrile addition to 1,3,4-oxadiazole. These two examples were chosen because, in the Diels–Alder addition with normal electron demand, the activation energy for the acrylonitrile addition is considerably

Table 1. Total energies (au) of reactants and transition-state structures for the Diels–Alder reaction of 1,3,4-oxadiazoles with cyanoethylenes

Species	HF/3–21G	HF/6–31G**//HF3–21G	MP2/6–31G**//HF3–21G
1	-259.12387	-260.60463	-261.35775
2	-77.60099	-78.03169	-78.28410
3	-168.82040	-169.76775	-170.29326
4	-260.03294	-261.49537	-262.29687
5	-260.03133	-261.49308	-262.29687
6	-260.02773	-261.49002	-262.29528
7	-336.66416	-338.56589	-339.61648
8	-427.88208	-430.29988	-431.62634
9	-427.87948	-430.29703	-431.62361
10	-519.09074	-522.02327	-523.62785
11	-519.09110	-522.02321	-523.62818
12	-519.08665	-522.01854	-523.62383
13	-519.08779	-522.02036	-523.62492

Table 2. Calculated activation energies (kcal mol⁻¹) for the Diels–Alder reactions with 1,3,4-oxadiazole (relative to the ethylene addition, in parentheses)

Dienophile	TS	HF/3–21G	HF/6–31G**//HF3–21G	MP2/6–31G**//HF3–21G
Ethylene	7	38.1 (0.0)	44.2 (0.0)	15.9 (0.0)
Acrylonitrile, <i>exo</i>	8	39.0 (0.9)	45.5 (1.3)	15.5 (-0.4)
Acrylonitrile, <i>endo</i>	9	40.7 (2.6)	47.3 (3.1)	17.2 (1.3)
Fumaronitrile	10	41.4 (3.3)	48.1 (3.9)	16.3 (0.4)
Maleonitrile, <i>exo</i>	11	40.2 (2.1)	46.8 (2.6)	16.6 (0.7)
Maleonitrile, <i>endo</i>	12	43.0 (4.9)	49.7 (5.5)	19.3 (3.4)
1,1-Dicyanoethylene	13	40.0 (1.9)	46.6 (2.4)	17.6 (1.7)

lower than the activation energy for the ethylene addition. As demonstrated by evaluating the energies at the RMP2/6-31G*//RHF/3-21G level, this effect is opposite with 1,3,4-oxadiazole as diene. To confirm this finding, the transition structures **7** and **9** and their reactants (**1**, **2** and **3**) were optimized at the correlated MP2/6-31G* theoretical level (Figure 3). As expected, the geometries of both the reactants and the transition structures differ from those calculated at RHF/3-21G. The bond distances are within a range of 5%, while the changes in the angles are below 3%.

The calculated total energies at the three different theory levels for these two transition structures and reactants involved in the reactions on MP2/6-31G* geometries are presented in Table 3.

The calculated activation energies are presented in Table 4. It is reasonable to expect that the values for the activation energies will differ for the different levels of calculation. However, it is interesting that the

RHF/6-31G* energy evaluation on the MP2/6-31G* geometries (Table 4) is almost identical with that calculated on the RHF/3-21G* geometries (Table 2). That is not so surprising because the geometries are only slightly different and RHF/6-31G* does not account for the correlation interactions.

At the correlated levels these differences are slightly higher. MP2/6-31G* on the RHF/3-21G geometries predicts approximately 1.6 kcal mol⁻¹ lower activation energies than the energies on the MP2/6-31G* geometries. Nevertheless, at all levels of theory, including the highest employed, MP3/6-31G*//MP2/6-31G*, the *endo* addition of acrylonitrile to 1,3,4-oxadiazole has a higher activation barrier than the ethylene addition. This was already explained in the previous discussion as a result of the repulsion interactions between the oxazole nitrogen lone pair and π -orbitals of the nitrile groups in transition structure **9**. This demonstrates that our initial model chemistry can be successfully applied

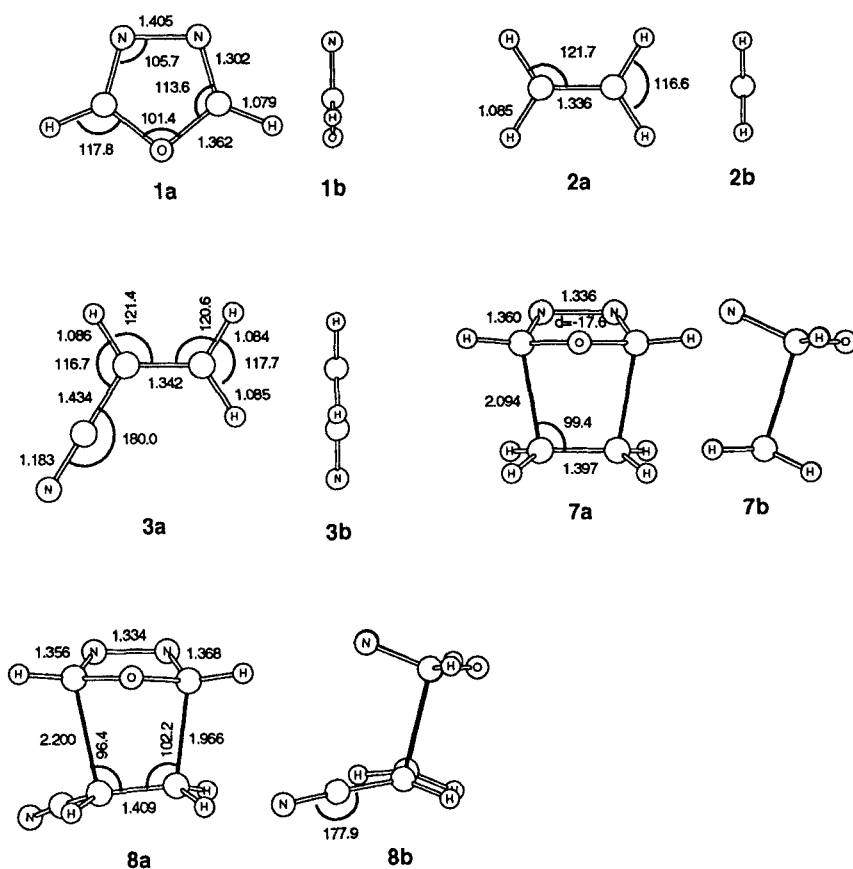


Figure 3. Top (a) and side (b) views of the the transition-state structures calculated at the MP2/6-31G* theory level. The numbering of the structures is the same as in Figures 1 and 2

Table 3. Total energies (au) of reactants and transition-state structures for ethylene and *endo* acrylonitrile cycloaddition to 1,3,4-oxadiazole

Species	HF/6-31G*//MP2/6-31G*	MP2/6-31G*	MP3/6-31G*//MP2/6-31G*
1	-260.60628	-261.36352	-261.36532
2	-78.03098	-78.28503	-78.30597
3	-169.76162	-170.29816	-170.30840
7	-338.56675	-339.61941	-339.62636
9	-430.29192	-431.63072	-431.62448

 Table 4. Calculated activation energies (kcal mol⁻¹) for the Diels–Alder reactions with 1,3,4-oxadiazole

Dienophile	TS	HF/6-31G*//MP2/6-31G*	MP2/6-31G*	MP3/6-31G*//MP2/6-31G*
Ethylene	7	44.2 (0.0)	18.3	28.2 (0.0)
Acrylonitrile, <i>endo</i>	9	47.7 (3.5)	19.4 (1.1)	30.9 (2.2)

to these systems, especially when only the relative reactivity is considered. It is apparent that the geometries at the SCF level give reasonable values for the energies calculated at the correlated levels. This does not mean that the values obtained for the activation energies are those which would be expected from experimental data. For such purposes, the calculations need to be performed at levels hardly available on the present computational resources.

CONCLUSION

The transition structures for the Diels–Alder reaction of 1,3,4-oxadiazole with cyanoethylenes are similar to those reported previously by others^{16,17} for the all-carbon Diels–Alder reactions (e.g. buta-1,3-diene and cyclopentadiene). The substitution of CH by two nitrogens and CH₂ by oxygen does not exert a substantial effect on the asynchronicity of the transition-state structures, but does change the activation energy of the reactions. Consequently, the stereoselectivity of the Diels–Alder reactions is opposite to that of the corresponding all-carbon reactions, and the reactivity of the cyanoethylenes decreases with increasing number of cyano groups. Such reactivity seems to be caused by repulsions between the π -orbitals of the nitrile groups and the lone pairs of the nitrogens in the oxadiazole rings.

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