Ab Initio Study of the Effect of CH ··· O Hydrogen Bonding on the *Exo/Endo* Stereoselectivity of Diels–Alder Reactions of 2-Substituted-1,3-Dienes with Sulfur Dioxide

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ABSTRACT

Ab initio calculations at the MP2/6-31G*//HF/3-21G* level have been carried out to study Diels–Alder reactions of 2-substituted-1,3-dienes with sulfur dioxide. The CH ··· O electrostatic interaction detected in some of the transition structures located could be decisive in the control of the *exo/endo* stereoselectivity of this type of reaction. © 1996 John Wiley & Sons, Inc.

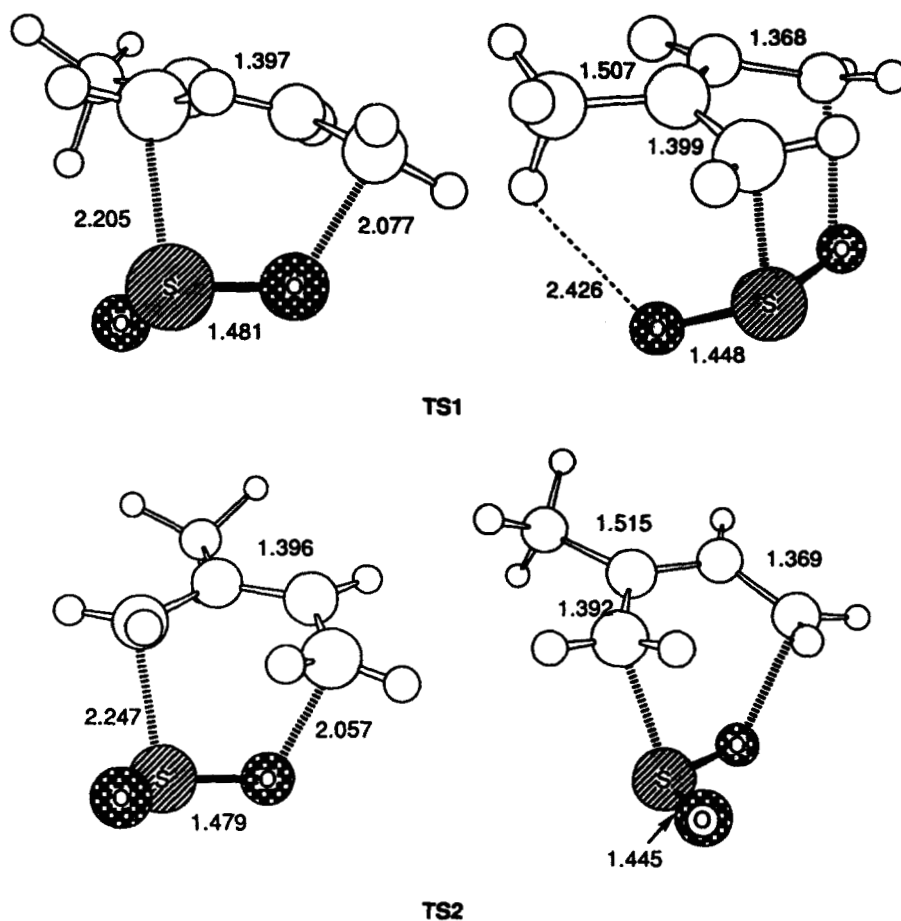* To whom correspondence should be addressed.

FIGURE 1. "*Meta*"–*endo* (**TS1**) and "*meta*"–*exo* (**TS2**) transition structures for the cycloaddition of isoprene to sulfur dioxide (see [6]). The broken line in **TS1** between an oxygen of SO_2 and a hydrogen of the substituent group at C-2 of 1,3-butadiene corresponds to the CH $\cdots$ O interaction discussed in the text. Distances are in angstroms.

Introduction

The Diels–Alder reaction has been the object of a number of both experimental [1] and theoretical [2] studies after its discovery by O. Diels and K. Alder [3] almost seven decades ago. It has been only recently that hetero-Diels–Alder reactions have attracted the attention of experimentalists [4] and theoreticians [5].

We recently studied the thermal and Lewis acid-catalyzed reactions of 1,3-dienes with sulfur dioxide both in the gas phase [6] and in solution [7]. Such reactions have been shown to proceed through a concerted mechanism in which the Lewis acid catalysis and the presence of an electron-releasing methyl group in the 1,3-dienes play an

important role. Also, the electrostatic solvent effect has been predicted to be important in the control of selectivity of these cycloadditions.

One of the most important aspects of the Diels–Alder reactions is the understanding of the factors influencing the *exo/endo* stereoselectivity [1]. We previously showed that both Lewis acid catalysts [6] and solvent effects [7] enhance the stereoselectivity of reactions of 1,3-dienes with sulfur dioxide. On the other hand, the remarkable role played by CH $\cdots$ O interactions [8] in the stereo- and regioselectivity of the cycloaddition reaction of isoprene with sulfur dioxide has also been pointed out [6].

In this article, we present the results of ab initio calculations on the effect of CH $\cdots$ O hydrogen bonds on the *exo/endo* stereoselectivity of
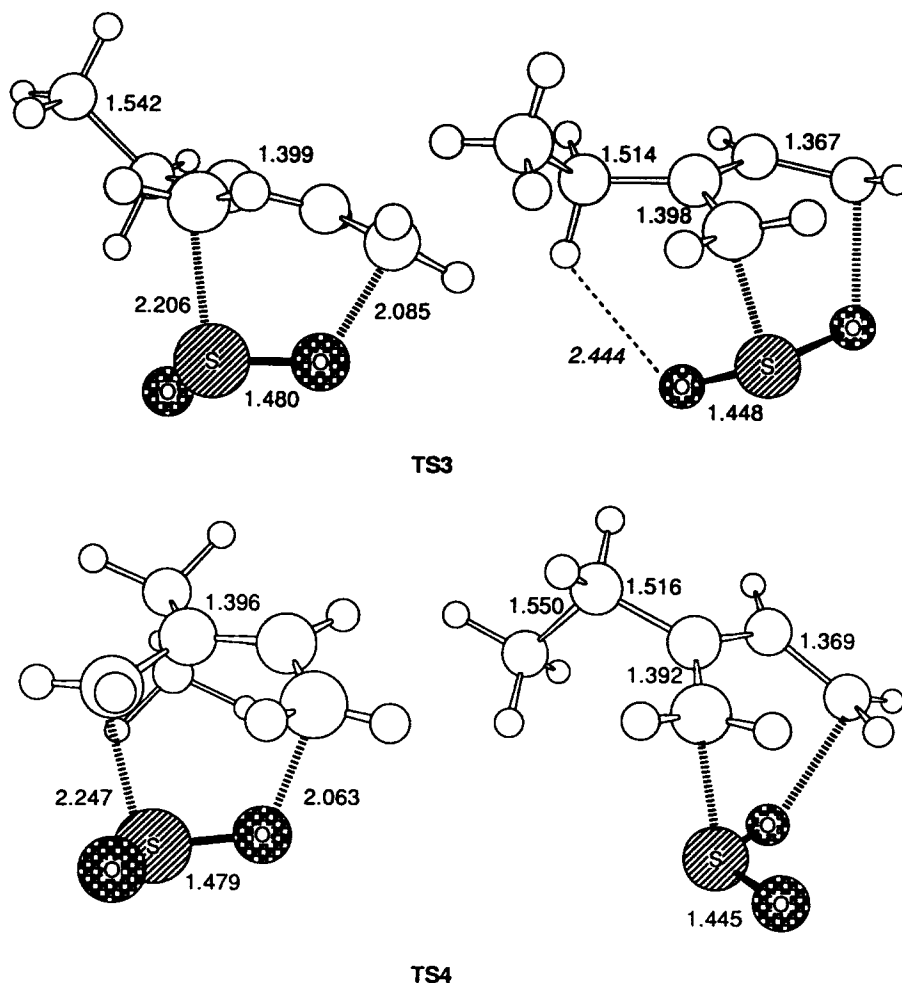
FIGURE 2. "*Meta*"-*endo* (**TS3**) and "*meta*"-*exo* (**TS4**) transition structures for the cycloaddition of 2-ethylbutadiene to sulfur dioxide. The broken line in **TS3** between an oxygen of SO_2 and a hydrogen of the substituent group at C-2 of 1,3-butadiene corresponds to the CH $\cdots$ O interaction discussed in the text. Distances are in angstroms.

Diels–Alder cycloadditions of 2-substituted-1,3-dienes with sulfur dioxide.

Method

Ab initio calculations were carried out at the Hartree–Fock (HF) level of theory using the GAUSSIAN 92 package of programs [9]. Structures were fully optimized with the 3-21G* basis set [10a], followed by vibrational frequency calculations which confirmed that reactants and transition structures (located by means of Schlegel's algorithm [11]) have zero and one imaginary frequency, respectively. In addition, single-point HF/6-31G* [10b] calculations were carried out on all the HF/3-21G* geometries. The correlation en-

ergy contribution was estimated by performing second-order Møller–Plesset [12] calculations (MP2) on the HF/3-21G* geometries with the 6-31G* basis set (MP2/6-31G*//HF/3-21G*).

To characterize the nature of the CH $\cdots$ O bonding found in some of the transition structures located, we computed some bond properties [electronic density, $\rho(r_c)$; Laplacian of electron density, $\nabla^2\rho(r_c)$; and bond ellipticity, ε] at the bond critical points (r_c) which have been shown to be a useful tool for such a purpose [13].

Results and Discussion

Figures 1–5 depict the HF/3-21G* transition structures corresponding to the two stereoisomers
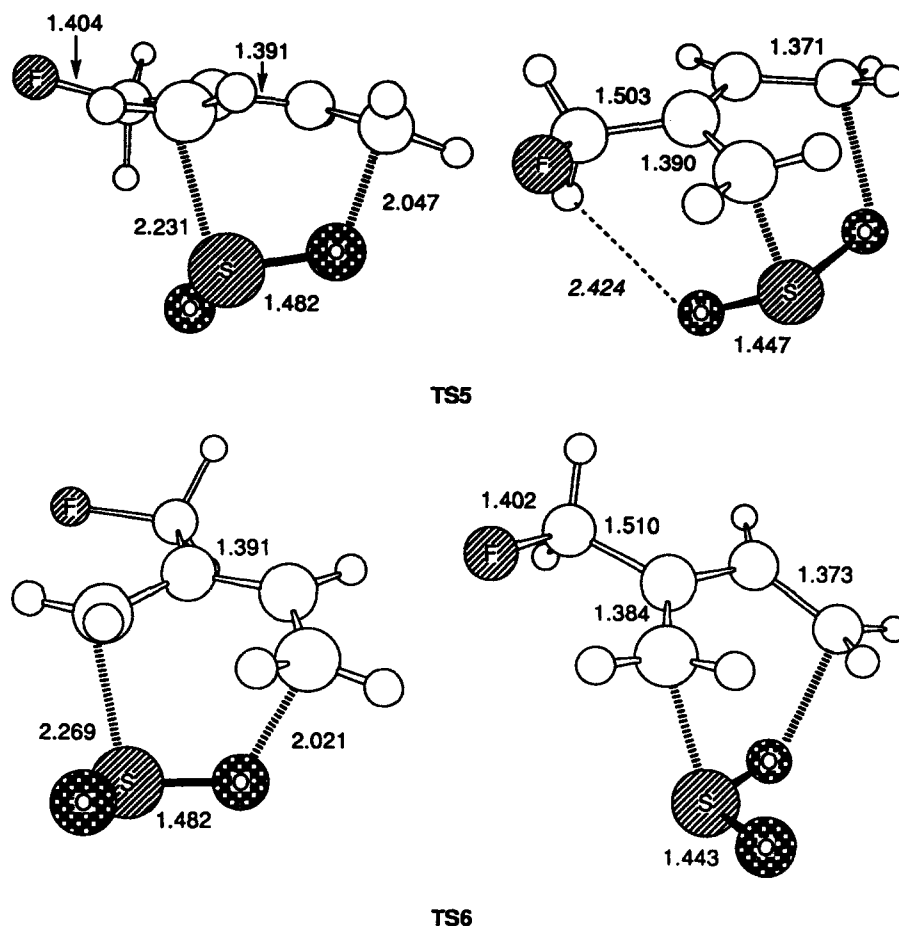
TS5

TS6

FIGURE 3. "*Meta*"–*endo* (**TS5**) and "*meta*"–*exo* (**TS6**) transition structures for the cycloaddition of 2-fluoromethylbutadiene to sulfur dioxide. The broken line in **TS5** between an oxygen of SO_2 and a hydrogen of the substituent group at C-2 of 1,3-butadiene corresponds to the CH $\cdots$ O interaction discussed in the text. Distances are in angstroms.

(*exo, endo*) of the reactions between sulfur dioxide and isoprene (**TS1, TS2**) [6], 2-ethylbutadiene (**TS3, TS4**), 2-fluoromethylbutadiene (**TS5, TS6**), 2-cyanomethylbutadiene (**TS7, TS8**), and 2-aminobutadiene (**TS9, TS10**), respectively. The "*meta*" regioisomers were considered in all cases as from our previous study on the reaction of sulfur dioxide with isoprene, they resulted to be lower in energy than the corresponding "*para*" regioisomers [6]. In the cases of 2-fluoromethyl- and 2-cyanomethylbutadiene, apart from the transition structures **TS5** and **TS7**, two other transition structures (higher in energy), corresponding to the conformers obtained from rotation of the fluoro- and cyanomethyl groups, were located. In Table I, the activation energies for the transition structures **TS1–TS10** considered in this work, as computed

at different theory levels, are given, and Table II collects the bond properties [13] corresponding to the CH $\cdots$ O interaction present in the **TS1**, **TS3**, **TS5**, and **TS7** structures.

It was shown in a previous article [6] that the CH $\cdots$ O electrostatic interaction contributes to the stabilization of the *endo* transition structure for the cycloaddition reaction of isoprene with sulfur dioxide by 2.0 kcal/mol (HF/6-31G*//HF/3-21G*).

To study the influence of the substitution at the C-2 of the diene on the *exo/endo* preference, we chose a pair of electron-releasing and electron-withdrawing groups. Thus, in the case of the reaction of 2-cyanomethylbutadiene with sulfur dioxide, the presence of the strong electron-withdrawing cyano group causes the *endo* transition structure (**TS7**) to be more stable than is the
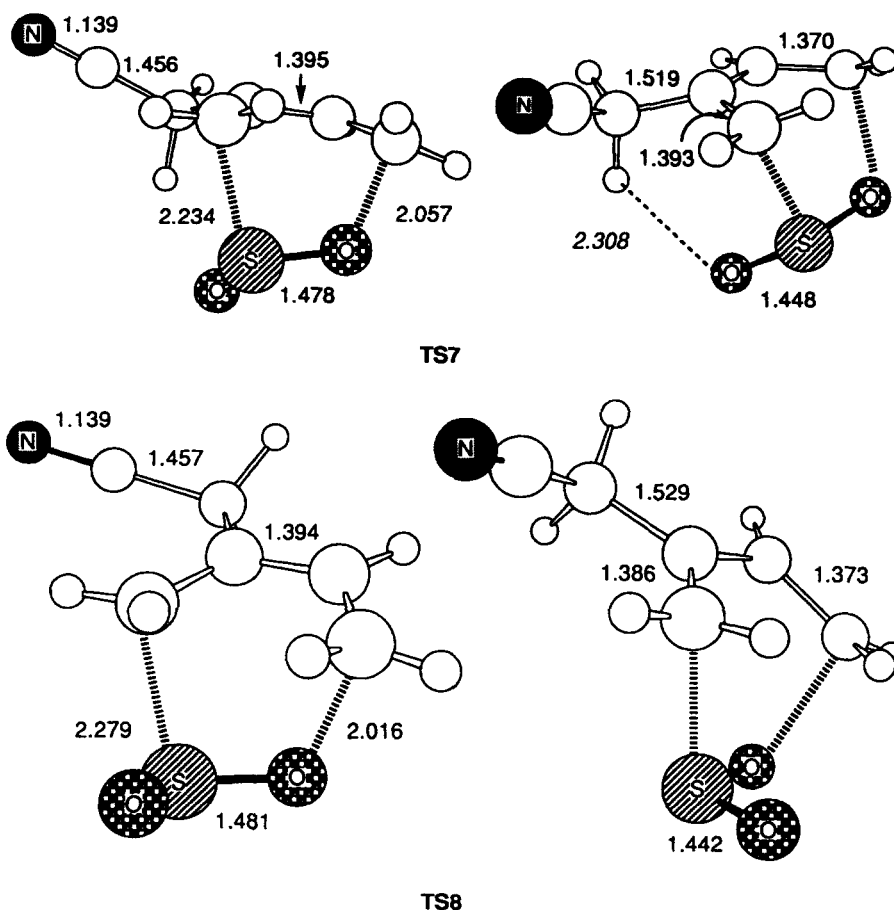
FIGURE 4. "*Meta*"–*endo* (**TS7**) and "*meta*"–*exo* (**TS8**) transition structures for the cycloaddition of 2-cyanomethylbutadiene to sulfur dioxide. The broken line in **TS7** between an oxygen of SO_2 and a hydrogen of the substituent group at C-2 of 1,3-butadiene corresponds to the CH ··· O interaction discussed in the text. Distances are in angstroms.

exo one (**TS8**) by 3.5 kcal/mol. This represents a 1 kcal/mol increase of the *exo/endo* preference when compared with the reaction of isoprene with sulfur dioxide. On the other hand, when the electron-releasing methyl group is used (**TS3, TS4**), the *exo/endo* preference is lowered by 1.2 kcal/mol as compared with the reaction involving isoprene. In both cases, a Bader-type density analysis [13] indicates (see Table II) the existence of a bond critical point associated with the electrostatic interaction between an oxygen of the dienophile and a hydrogen of the X group of the diene (see Table II). The previously described effects of the cyano and methyl groups can be rationalized in terms of such an electrostatic interaction. Indeed, an electron-releasing group makes the carbon atom attached to the C-2 of the diene more electron-rich, thus disfavoring the CH ··· O electrostatic interaction, while

an electron-withdrawing group is expected to favor this interaction. In the case of the reaction of 2-fluoromethylbutadiene, where the CH ··· O electrostatic interaction is also present (see Table II), the *exo/endo* preference is quite similar to the one found for the isoprene case, which could be explained as the result of the competing effects of the fluorine electronegativity and the presence of lone electron pairs in that atom.

Finally, in the case of the reaction of 2-aminobutadiene, a NH ··· O electrostatic interaction could also be possible. However, Table II clearly shows that no critical point was found. An examination of the geometry of the corresponding transition structures (see **TS9** and **TS10** in Fig. 4) shows an sp^2 hybridation of the nitrogen, the two hydrogens being in the plane of the diene in order to favor conjugation of the nitrogen lone pair with
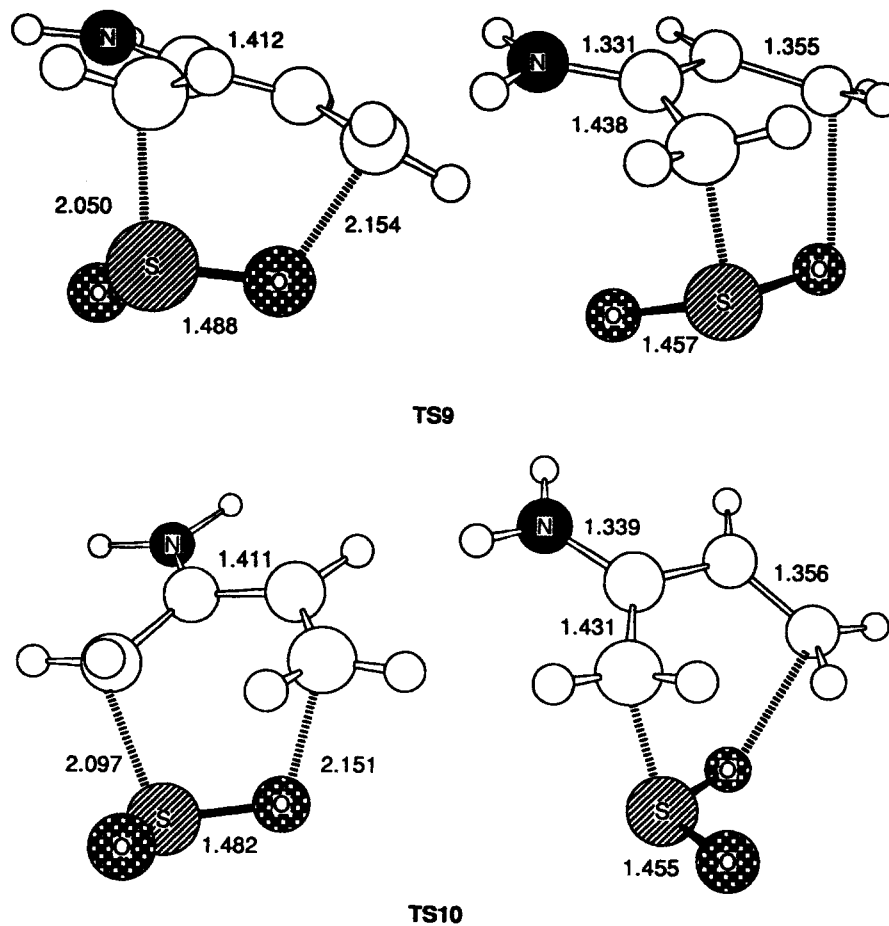
TS9

TS10

FIGURE 5. *"Meta"–endo* (**TS9**) and *"meta"–exo* (**TS10**) transition structures for the cycloaddition of 2-aminobutadiene to sulfur dioxide.

TABLE I

Activation energies (kcal / mol) at different theory levels of the *"meta"* transition structures for the Diels – Alder of 2-substituted-1,3-butadienes with sulfur dioxide.

Diene	Transition structure	HF / 3-21G*	HF / 6-31G*// HF / 3-21G*	MP2 / 6-31G*// HF / 3-21G*
Isoprene[a]	TS1 (*endo*)	18.0	29.2	11.6
	TS2 (*exo*)	22.2	32.3	14.1
2-Ethylbutadiene	TS3 (*endo*)	18.3	28.9	11.4
	TS4 (*exo*)	21.0	31.2	12.7
2-Fluoromethylbutadiene	TS5 (*endo*)	17.5	29.5	10.7
	TS6 (*exo*)	21.9	32.8	13.4
2-Cyanomethylbutadiene	TS7 (*endo*)	18.4	30.9	11.2
	TS8 (*exo*)	24.1	35.2	14.7
2-Aminobutadiene	TS9 (*endo*)	9.2	16.3	7.8
	TS10 (*exo*)	11.3	19.4	9.7

[a] See [6].

TABLE II

Bond properties[a] for the XH $\cdots$ O interaction (X = CH_2, CH_3CH, FCH, NCCH, NH) in the "*meta*"– *endo* transition structures leading to the sultines considered in this work.

Diene	Transition structures	R(XH $\cdots$ O)	$\rho(r_c)$	$\nabla^2\rho(r_c)$	ε
Isoprene	TS1 (*endo*)	2.426	0.0121	0.0595	0.2026
2-Ethylbutadiene	TS3 (*endo*)	2.444	0.0104	0.0539	0.3263
2-Fluoromethylbutadiene	TS5 (*endo*)	2.424	0.0108	0.0572	0.3893
2-Cyanomethylbutadiene	TS7 (*endo*)	2.308	0.0134	0.0686	0.1772
2-Aminobutadiene	TS9 (*endo*)	3.005	—	—	—

[a] See [13].

the π-diene orbitals. This conformation of the amino group precludes the N $\cdots$ O interaction and, therefore, a lowering in the *exo/endo* preference, as compared with the reaction involving isoprene, should be expected, in agreement with the data in Table I.

Conclusions

The effect of the CH $\cdots$ O hydrogen bonding on the *exo/endo* stereoselectivity of hetero Diels–Alder reactions of 2-substituted-1,3-dienes with sulfur dioxide has been studied ab initio at the MP2/6-31G*//HF/3-21G* level of theory. As the *exo/endo* preference in Diels–Alder reactions is usually on the order of a few kcal/mol[1], the CH $\cdots$ O electrostatic interaction reported in this work, which represents contributions of about 2 kcal/mol [6], could be decisive in the control of the *exo/endo* stereoselectivity of these reactions.

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