Density Functional Theory Study of a Lewis Acid Catalyzed Diels−Alder Reaction. The Butadiene + Acrolein Paradigm

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Abstract: The four transition structures (TS's) of the reaction between butadiene and acrolein, both uncatalyzed and catalyzed by BF_3, have been theoretically studied taking into account electron correlation effects by means of DFT (B3LYP) calculations. In both the uncatalyzed and catalyzed reactions, the *endo s-cis* is the most stable of the four possible transition structures. In the case of the catalyzed reaction, the inclusion of electron correlation in the search for this transition structure indicates the classical [4+2] reaction path, instead of that corresponding to a [2+4] inverse electron, demands hetero-Diels−Alder reaction, as happens when the Hartree−Fock level of theory is used. The B3LYP/6-31G(d) calculations lead to activation energy values close to those experimentally found. The origin of the *endo/exo* selectivity, both in the presence and in the absence of the catalyst, is discussed.

Introduction

It is well-known that the use of Lewis acids leads to significant changes in rate and regio, *endo/exo*, and diastereofacial selectivities of Diels−Alder reactions in comparison with the uncatalyzed processes. This fact has led to a huge amount of experimental work, in which a wide variety of homogeneous and heterogeneous Lewis acids have been used to improve the results of different Diels−Alder reactions.[1] In spite of the important role of the catalyst, theoretical studies dealing with Lewis acid-catalyzed carbo-Diels−Alder reactions are rather scarce.

The role of BH_3 as the Lewis acid was first considered by Birney and Houk[2] for the reaction between 1,3-butadiene and acrolein, and more recently, the roles of BF_3 and $AlCl_3$ have been theoretically studied for the same reaction by Yamabe *et al.*[3] In the latter work, however, only the *s-cis* conformation of the dienophile was considered. Birney and Houk based their discussion on RHF/6-31G(d)//3-21G results, whereas Yamabe *et al.* performed transition structure (TS) searches at the RHF level using a splicing 6-31G(d) & 3-21G (the latter for the Lewis acid) basis set, and then they carried out single point calculations up to the MP3/6-31G(d) level. In addition, these authors investigated the reaction pathways by carrying out Intrinsic Reaction Coordinate (IRC) calculations at the RHF level. One of the most striking conclusions of the study by Yamabe *et al.* was that the *endo s-cis* TS of the reaction catalyzed by BF_3 corresponds to a [2+4] hetero-Diels−Alder cycloaddition, instead of the expected [4+2] Diels−Alder cycloaddition. Dai *et al.* have considered the effect of BF_3 on the reaction of 1,1-dimethyl-1,3-butadiene with acrolein and *trans*-crotonaldehyde by means of RHF/3-21G calculations.[4] González *et al.* have considered the role of H^+ as a hard Lewis acid in the reaction of cyclopentadiene with fumaric acid derivatives by means of RHF/3-21G calculations.[5] Finally, during the preparation of the present manuscript, Branchadell and co-workers have published a study on the role of $AlCl_3$ in the Diels−Alder reaction of a chiral dienophile with cyclopentadiene.[6]

Recently, we have demonstrated[7] that the inclusion of electron correlation effects in the geometry optimization step, using second-order Møller−Plesset theory through MP2/6-31G(d)//MP2/6-31G(d) calculations, changes the nature of the *endo s-cis* TS of the reaction between 1,3-butadiene and acrolein, catalyzed by BF_3. In this case the TS becomes a true [4+2] TS, which has been further confirmed by IRC calculations at the same theory level. This result highlights the important role that electron correlation effects play in the correct description of the TS geometries and energies of this reaction. Density Functional Theory methods have been shown to be a computationally economical yet efficient methodology to incorporate electron correlation effects to complex systems, as are chemical reactions. Therefore, we consider it timely to complete the former study by calculating all four possible TS's of the BF_3-catalyzed reaction between 1,3-butadiene and acrolein, using a Density Functional Theory (DFT) method, based on the increasingly popular hybrid Becke three-parameter correlation functional plus the Lee−Yang−Parr exchange functional, B3LYP.[8] DFT methods have already been shown to be useful to describe

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TS's of Diels−Alder reactions,[9,10] but to the best of our knowledge, their performance to describe Lewis acid catalyzed processes has only very recently been considered in the work of Branchadell and co-workers.[6]

For the sake of completeness, we have also calculated the corresponding transition structures of the uncatalyzed reaction at the same theoretical level to gain a deeper insight into the role of the catalyst by comparison between the uncatalyzed and catalyzed processes.

Computational Methods

All the *ab initio* theoretical calculations described in this work were carried out with the Gaussian 94 program.[11]

Geometrical optimizations, including transition structure searches, were carried out with the standard 6-31G(d) basis set by using the three-parameter hybrid functional developed by Becke[8a] in the formulation implemented in the Gaussian 94 program (B3LYP), which is slightly different from the original proposed by Becke. The presence of a stationary point was confirmed in all cases by the correct number of negative eigenvalues of the Hessian matrix. In the case of the TS, the vibration associated with the imaginary frequency was checked to correspond with a movement in the direction of the reaction coordinate. In the case of the *endo s-cis* TS of the BF_3-catalyzed reaction, a mass-weighted Cartesian coordinate IRC calculation was carried out at the B3LYP/6-31G(d) level, using the method of González and Schlegel,[12] to confirm that this TS leads to the [4+2] cycloadduct.

Single point energy calculations were carried out on all the stationary points found at the B3LYP/6-311+G(2d,p) level, based on the corresponding B3LYP/6-31G(d) geometry.

Results

Geometries of the Transition Structures. There are four possible transition structures (TS) for the uncatalyzed reaction, depending on the approach of the diene with respect to the carbonyl group of the dienophile, and on the conformation of the latter: *endo s-cis*, *endo s-trans*, *exo s-cis*, and *exo s-trans*. Following the convention previously established,[2] we will denote these TS's as NC, NT, XC, and XT, respectively. For the catalyzed reaction, there are also four possible TS's on keeping the BF_3 in its most stable disposition, *i.e.* in a *syn* position with respect to the carbonyl hydrogen atom, as in the reactant. By analogy, we will denote these structures as BNC, BNT, BXC, and BXT.

Some selected geometrical parameters of the calculated TS's are shown in Figures 1 and 2. In the case of the uncatalyzed process (Figure 1), all the TS's correspond to a concerted, but asynchronous, reaction pathway. The extent of the synchronicity can be measured by means of the difference between the distances of the bonds that are being formed in the reactions, *i.e.* $\Delta d = (C_1{-}C_2) - (C_5{-}C_6)$, with the first always being longer.

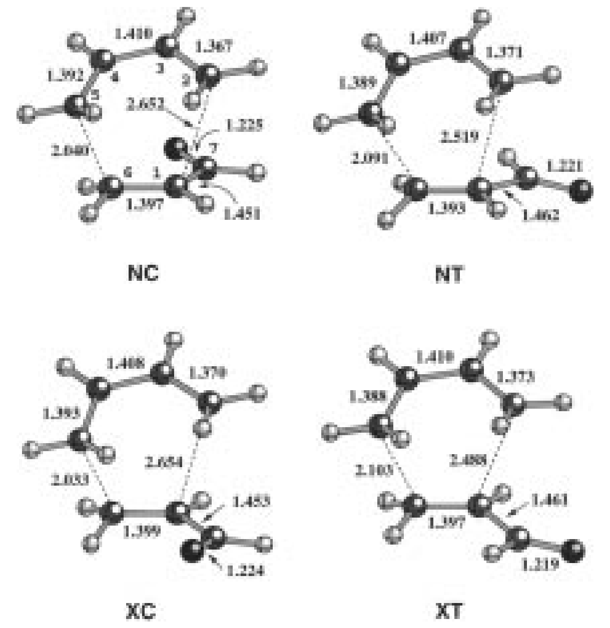

Figure 1. Some selected distances of the transition structures of the reaction between acrolein and 1,3-butadiene, calculated at the B3LYP/6-31G(d) theory level.

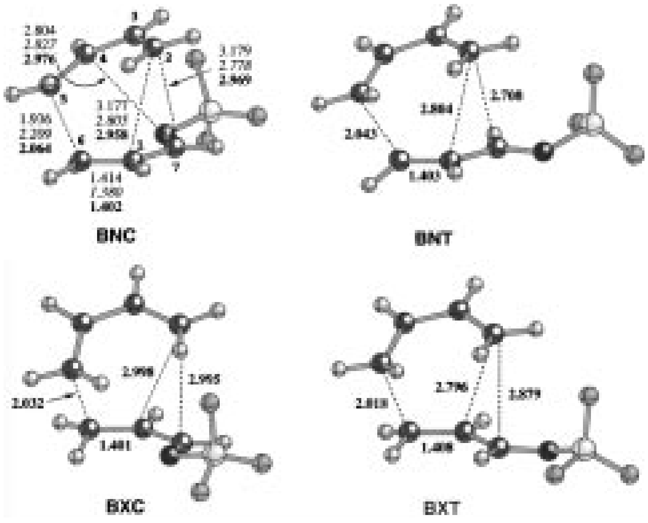

Figure 2. Some selected distances of the transition structures of the reaction between acrolein and 1,3-butadiene, catalyzed by BF_3, calculated at the B3LYP/6-31G(d) theory level. For BNC, some HF/6-31G(d) (plain text) and MP2/6-31G(d) (italic) values, taken from ref 7, are also given.

As it can be seen, the *s-trans* TS's are always more synchronous than the *s-cis* TS's, which has previously been explained in terms of the differences in the LUMO coefficients of the acrolein in its *s-cis* and *s-trans* conformation.[13]

As far as the catalyzed process is concerned (Figure 2), the first question to be addressed is the special nature of BNC. As already reported,[3] this TS corresponds to a [2+4] hetero-Diels−Alder reaction when the calculations are performed at the Hartree−Fock level of theory. However, when electron correlation is considered through the MP2 scheme, the corresponding BNC TS leads to the expected [4+2] cycloadduct.[7] Therefore, it is necessary to assess the behavior of B3LYP with regard to this very special system. From a purely geometrical viewpoint, the B3LYP TS lies approximately halfway between

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Table 1. Relative Energies and Thermodynamic (at 298.15 K) Properties (in kcal mol^{-1}) of the Transition Structures of the Reaction between 1,3-Butadiene and Acrolein, Uncatalyzed and Catalyzed by BF_3, Calculated at the B3LYP/6-31G(d) Theory Level

TS	$\Delta\Delta E_0$[a]	$\Delta\Delta E_{298}$	$\Delta\Delta H_{298}$	$\Delta\Delta G_{298}$
NC	0.00 (0.00)	0.00	0.00	0.00
NT	1.45 (1.37)	1.24	1.24	1.27
XC	0.01 (0.22)	0.06	0.06	−0.01
XT	2.12 (1.74)	1.93	1.93	1.82
BNC	0.00 (0.00)	0.00	0.00	0.00
BNT	2.29 (2.32)	2.25	2.25	2.50
BXC	1.66 (1.93)	1.72	1.72	1.48
BXT	5.72 (5.49)	5.61	5.61	5.14

[a] Values in parentheses correspond to single point energy calculations at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level.

Table 2. Activation Energies, Enthalpies, and Free Energies (in kcal mol^{-1}) of the Reaction between 1,3-Butadiene and Acrolein, Uncatalyzed and Catalyzed by BF_3, Calculated at the B3LYP/6-31G(d) Theory Level

TS	$\Delta E^{\ddagger}_0$[a]	$\Delta E^{\ddagger}_{298}$	$\Delta H^{\ddagger}_{298}$	$\Delta G^{\ddagger}_{298}$
NC	17.9 (21.5)	19.7	19.1	32.7
NT	19.4 (22.9)	20.9	20.4	33.9
XC	17.9 (21.7)	19.8	19.2	32.7
XT	20.1 (23.3)	21.6	21.0	34.5
BNC	7.3 (11.2)	9.3	8.7	23.2
BNT	9.6 (13.5)	11.6	11.0	25.7
BXC	9.0 (13.2)	11.0	10.4	24.3
BXT	13.0 (16.7)	14.9	14.3	28.3

[a] Values in parentheses correspond to single point energy calculations at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level.

the corresponding RHF and MP2 TS's (Figure 2). However, if one compares the C_1-C_2 and the C_4-O distances, it can be seen that the B3LYP TS is indeed more similar to the MP2 TS, in both cases C_4-O being longer than C_1-C_2. The frequency analysis corroborates this first impression. When the imaginary frequency (338.4i cm^{-1}) of the B3LYP TS is graphically represented, it can be seen that the two couples C_1-C_2 and C_4-O have a bonding movement in the TS. However, the vector modulus for the C_1-C_2 movement is greater (0.316) than that corresponding to the C_4-O movement (0.154). Finally, a mass-weighted Cartesian coordinate IRC calculation[12] confirms that the B3LYP TS leads to a [4+2] cycloadduct, as happens with the MP2 calculation. It can then be concluded that the inclusion of electron correlation effects in the TS optimization step is essential to correctly describe the reaction course.

It is worth noting that, apart from the particular values for the C_1-C_2 distance and the result of the IRC calculation, there are no other special geometrical differences between the RHF BNC TS and the B3LYP BNC TS's.

With regard to the uncatalyzed reaction, the B3LYP TS's of the catalyzed process are always more asynchronous, which is mainly due to longer C_1-C_2 distances.

Birney and Houk[2] have pointed out the flexibility of the TS's of the BH_3-catalyzed reaction between acrolein and butadiene. This flexibility is also observed in the TS's of the BF_3-catalyzed process. In particular, the value of the dihedral angle $C_2-C_5-C_6-C_1$ corresponding to BNT is 26.0°, whereas those values corresponding to BNC, BXC, and BXT (0°, 10°, and 3°, respectively) are closer to planarity, *i.e.*, there is a considerably greater degree of twisting about the stronger forming bond, which indicates a behavior particular to this TS.

Energies of the Transition Structures. The calculated total energies of the reactants (in their most stable conformations) and the TS's of the uncatalyzed and catalyzed processes [at the B3LYP/6-31G(d) and B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) levels] are given in the Supporting Information. The relative energies of the TS's (relative to NC and BNC) are gathered in Table 1. The computed thermodynamic properties of reactants and TS's for the same reactions, from B3LYP/6-31G(d) frequency calculations, are given in the Supporting Information, whereas the relative values for the TS's (relative to NC and BNC) are gathered in Table 1.

With regard to the uncatalyzed reaction, the calculated energy order of the TS's is NC < XC < NT < XT. With regard to the catalyzed process, the energy order is BNC < BXC < BNT < BXT, *i.e.*, the presence of the Lewis acid does not change the relative energies of the TS's. As a general conclusion, *s-cis* and *endo* TS's are always more stable than their *s-trans* and *exo* counterparts, respectively.

From a quantitative viewpoint, the energy differences between the TS's are magnified by the presence of BF_3. In particular, BXT appears to be relatively less stable in comparison to the other TS's.

Discussion

Activation Barriers. The calculated activation barriers for the four TS's of the uncatalyzed and catalyzed processes are gathered in Table 2, together with the activation enthalpies and free energies calculated from the thermodynamic properties at 298.15 K.

The experimental value of the activation enthalpy in the gas phase of the reaction between 1,3-butadiene and acrolein is 19.4 kcal mol^{-1}.[14] Also, the activation free energy of the reaction between cyclopentadiene and acrolein in the gas phase is 25.5 kcal mol^{-1}.[14]

The B3LYP/6-31G(d) calculations lead to a value for the activation enthalpy (19.1 kcal mol^{-1}) that is in excellent agreement with the experimental value for the same reaction in the gas phase. Also, the calculated activation free energy (32.7 kcal mol^{-1}) seems to be in reasonable agreement with the experimental value for the reaction between cyclopentadiene and acrolein when the greater reactivity of cyclopentadiene with respect to the 1,3-butadiene is taken into account. Finally, the B3LYP value of the activation energy (17.9 kcal mol^{-1}) is also close to the 16.8 kcal mol^{-1} calculated for the same reaction at the MP3/6-31G(d)//RHF/3-21G level.[3]

The use of a more extended basis set does not improve the results, so the essential features of these TS's seem to be well represented by the medium-sized 6-31G(d) basis set. Therefore, as other authors have concluded previously,[9,10] the B3LYP/6-31G(d) level seems to constitute an excellent compromise between computational cost and accuracy of the energetic results for the study of Diels−Alder reactions.

Although there are no experimental values for the catalyzed reaction, we can compare the calculated values with the activation enthalpy experimentally determined for the reaction between 1,3-butadiene and methyl acrylate, catalyzed by $AlCl_3$ (10.4 ± 1.9 kcal mol^{-1}).[15] From this comparison, it seems reasonable to conclude that B3LYP barriers are in good agreement with the experimental values also in the case of the catalyzed reaction.

With regard to the uncatalyzed reaction, the activation barriers are always lower, which reflects the accelerating effect of the Lewis acid. The decrease in the activation barrier is of *ca.* 10 kcal mol^{-1} for BNC in comparison to NC.

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Table 3. Decomposition of the Potential Energy Barriers (in kcal mol^{-1}) for the Reaction between 1,3-Butadiene and Acrolein, Catalyzed by BF_3, Calculated at the B3LYP/6-31G(d) Theory Level

	deformation				interaction				
TS	acrolein	BF_3	butadiene	total	acrolein/BF_3	diene/dienophile	total	*s-cis*/*s-trans*	$\Delta E^{\ddagger}$
BNC	11.4	9.8	12.1	33.3	−16.8	−11.0	−27.8	1.8	7.3
BNT	10.1	10.1	15.4	35.6	−14.5	−11.5	−26.0		9.6
BXC	12.5	9.7	12.5	34.7	−15.3	−12.2	−27.5	1.8	9.0
BXT	8.9	11.1	16.4	36.4	−12.7	−10.7	−23.4		13.0

Zero-point and thermal corrections tend to slightly increase the activation energies, but the relative differences between TS's remain unchanged. The use of extended basis sets also tends to increase the activation energies, but once again, the energy differences between the different TS's do not change very much.

The partition of the activation potential energy can be useful to rationalize the origin of the decrease in the activation barriers induced by the Lewis acid. However, the decomposition of the activation potential energy is not straightforward in the case of the catalyzed process. This is due to the fact that the dienophile is not a single molecule, but a complex. Thus, the difference between the energy of the complex in its ground state and in the TS geometry consists not only of the deformation energy, but also any differential interaction between the acrolein and the BF_3. To circumvent this situation, we have considered a somewhat more complicated scheme, in which the acrolein and the BF_3 moieties of the complex are considered independently. In this form, we can calculate the pure deformation energy for each part of the TS (acrolein, BF_3, and butadiene), the enhanced interaction energy between acrolein and BF_3 when passing from the ground state to the TS geometry, and the interaction energy between the diene and dienophile moieties. The results of this analysis are gathered in Table 3.

The significant values of the enhanced interaction energy between the acrolein and the BF_3 on passing from the reactant to the TS should be noted. If the deformation energy is discounted, the enhanced acrolein−BF_3 interaction in the TS results in a stabilization of 7 kcal mol^{-1}, *i.e.* most of the decrease in the activation barrier observed on passing from the uncatalyzed to the catalyzed reaction (*ca.* 10.5 kcal mol^{-1}) can be explained on the basis of this effect. A similar effect has previously been described in the case of the interaction between methyl vinyl ketone and water molecules, using a very different methodology.[16] On passing from the reactant to the TS, the hydrogen bond interaction increases, resulting in a differential solvation of the TS, and hence in a decrease of the activation barrier.

Energy Differences between the TS's (Selectivities). It has already been reported for other related systems[17−19] that the *s-trans* TS's are more *endo* selective than the *s-cis* TS's. This has generally been explained due to the particular instability of the *exo s-trans* TS. In the case of the reactions of cyclopentadiene, this instability has often been ascribed to steric interactions between the methylene group of the diene and the dienophile.[17,18] These steric interactions are more difficult to justify in the case in which 1,3-butadiene is used as the diene, but the energy difference between NT and XT is also smaller (for example, 1.1 kcal mol^{-1} as opposed to 2.4 kcal mol^{-1} between NT and XT in the reaction of cyclopentadiene with methyl vinyl ketone, calculated at the same theoretical level).[20] This particular behavior of XT has also been reported for the reaction of 1,3-butadiene with methyl acrylate.[19]

This situation also holds in the case of the B3LYP/6-31G(d) calculations for the uncatalyzed and catalyzed reactions. Thus, the *s-trans* TS's are always more *endo* selective than their *s-cis* counterparts. In the case of the uncatalyzed process, if one accepts that most of the reaction goes through the *s-cis* TS's, there is no *endo* selectivity at all. This result indicates that the secondary orbital interactions, if they exist, must be of relatively little importance from an energy viewpoint. On the other hand, in the case of the catalyzed process, both *s-cis* and *s-trans* TS's display *endo* selectivity, although this is more important for the latter. Therefore, the role of secondary orbital interactions cannot be ruled out in these cases. We will return on this point below.

There have been several attempts to explain the origin of the relative energies of the TS's of Diels−Alder reactions. Some authors have described that, for unsymetrically substituted dienophiles, the more asynchronous the TS, the lower the barrier.[20,21] Although it is difficult to find a rigorous theoretical justification for this result, it has become an empirical rule that holds for a variety of Diels−Alder reactions. It has been recently described that kinetic isotope effects calculated at the B3LYP/6-31G* level for Diels−Alder reactions of maleic anhydride are essentially coincident with the corresponding experimental values,[22] so that the degree of synchronicity calculated by this method is highly reliable. Therefore, we can use our results to test if the above mentioned empirical rule is also of general validity in the present system.

As can be seen from Figure 1, in the case of the uncatalyzed process, the *s-trans* TS's are always more synchronous than their *s-cis* counterparts ($\Delta d = 0.428$ *vs* 0.612 for the *endo* TS's, and 0.385 *vs* 0.621 for the *exo* TS's), so it would be expected that they were also higher in energy, as is indeed the case (Table 2). On the other hand, following this criteria, XC should be slightly more stable than NC, which is not the case, given that at this level both TS's have practically the same energy.

This discrepancy is even enhanced in the case of the catalyzed process. As in the precedent case, the *s-trans* TS's are always more synchronous than their *s-cis* counterparts ($\Delta d = 0.761$ *vs* 0.894 for the *endo* TS's, and 0.385 *vs* 0.621 for the *exo* TS's; see Figure 2), which is in agreement with their higher energy. However, following the same assumption, BXC should be clearly more stable than BNC, and BXT slightly more stable than BNT, which is not the case.

As a conclusion, the empirical rule that relates the degree of synchronicity with the relative energies of the TS's lacks general validity, above all in the case of catalyzed systems.

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The relative stability of the *endo* over the *exo* TS's in the case of the catalyzed process deserves particular comment. The Lewis acid induces a strong polarization of the dienophile molecular orbitals, and changes their energies, giving rise to higher interactions with the diene, and for this reason, the role of the possible secondary orbital interaction must be considered. "Classical" secondary orbital interactions are only possible between C_3 and C_7 for *endo* TS's BNC and BNT. In the case of BNC, a C_4-O interaction can be expected on the basis of the nature of the RHF TS and the MP2 and B3LYP IRC calculations, which show that these atoms are close to each other during a large part of the reaction path. A third possibility lies in a new type of orbital interaction, postulated by Singleton[23] for the *endo s-trans* TS of the reaction studied by Birney and Houk.[2] The so-called "[4+3] interaction" is a bonding interaction between C_2 and C_7, and has been explained on the basis of frontier molecular orbital considerations.[23] Although this interaction was not discerned for the corresponding *exo* TS's in the above-mentioned work, there is no geometrical reason, at least in principle, by which this interaction should discriminate between *endo* and *exo* TS's. In fact, examination of the C_2-C_7 distances in the four TS's (Figure 2) reveals that this distance is similar to C_1-C_2 in the case of BNC and BXC, and is even shorter in the case of BNT. Only in the case of BXT is C_2-C_7 longer than C_1-C_2.

One possibility to test the existence and relative importance of all the aforementioned interactions lies in the values of the Mulliken overlap polulation. The analysis of the SCF density in the case of the B3LYP calculations reveals that the "classical" C_3-C_7 interaction in the endo TS's (0.000 for BNT and 0.009 for BNC) cannot account for any change in the selectivity of the reaction. In the case of BNC, there is a significant C_4-O overlap (0.031), although it is weaker than the C_1-C_2 overlap (0.056). The C_2-C_7 overlap is more important in the case of BXC and BNT (0.041) than for BNC and BXT (0.028), which clearly shows that this secondary interaction is possible in both *endo* and *exo* TS's. Finally, the new C_1-C_2 bond presents a more important overlap in the case of the most synchronous TS, *i.e.* in BXT the value is larger (0.102) than in the TS's BXC (0.060) and BNT (0.067).

Another possibility lies in the examination of the integrated electron density of the TS's. Figure 3 shows the results obtained from the B3LYP/6-31G(d) calculations as an isovalue surface at the 0.013 au level. As can be seen, the C_2-C_7 interaction is present in all cases, whereas the C_3-C_7 interaction is not detectable at this level. In the case of BNC, the C_4-O interaction is also visible as an overlap density zone (marked with an arrow in Figure 3). One method to qualitatively estimate the importance of these interactions is to examine the isovalue surfaces at higher levels, *i.e.* enclosing lower proportions of the total electron density. On doing this, it can be observed that, at the 0.016 level, the C_4-O interaction is no longer visible in BNC, whereas both the C_2-C_7 and C_1-C_2 interactions appear as a single connection between the diene and dienophile moieties, just in the middle between the two "bonds". The same situation occurs at this level in the case of BXC. Increasing the representation level to 0.018 au results in the total disappearance of all the interactions between the diene and the dienophile (except, of course, that of the most formed bond, C_5-C_6) in the case of BNC and BXC, whereas both the C_2-C_7 and the C_1-C_2 interactions are still clearly visible in BNT, with only C_1-C_2 visible in BXT.

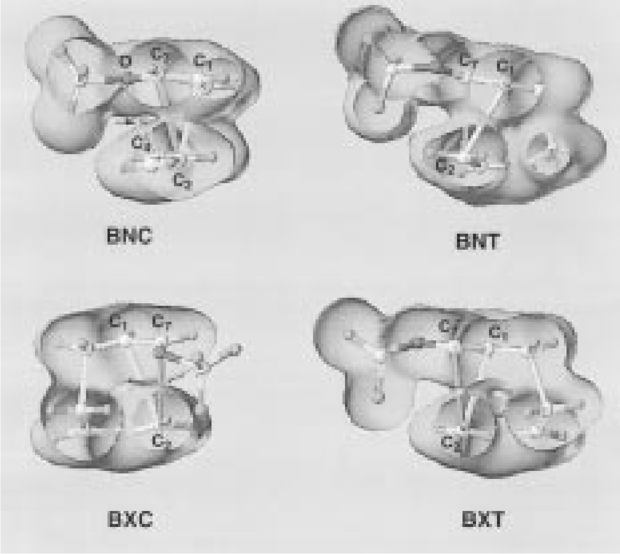

Figure 3. Electron density isovalue surfaces (at the 0.013 au level) of the transition structures of the reaction between acrolein and 1,3-butadiene, catalyzed by BF_3, calculated at the B3LYP/6-31G(d) theory level.

Finally, at the 0.020 au level, only the interactions between C_2-C_7 and C_1-C_2 are visible in the case of BNT and these are only weak.

From this analysis, it seems that the strongest C_2-C_7 secondary interaction occurs in BNT, which is in agreement with the Mulliken overlap population results and, above all, with the geometrical differences found for this TS (C_2-C_7 distance shorter than C_1-C_2, higher $C_2-C_5-C_6-C_1$ torsion angle). In the case of BXT, the only detectable interaction is that of the second C−C bond formed in the reaction, again in agreement with the geometric and Mulliken overlap population results. BXC and BNC also display a secondary C_2-C_7 interaction but, in each case, this is weaker than that observed for BNT. Finally, a C_4-O interaction is clearly present in BNC, although it seems to be weaker than the C_2-C_7 interaction.

It then can be concluded that the energy differences between the four TS's will depend in part on the number and strength of the secondary interactions. Thus, in BXT only the "primary" C_1-C_2 interaction is present, with the C_2-C_7 interaction being either non-existent or very weak. BNT benefits from the strongest C_2-C_7 interaction, although the C_1-C_2 interaction is probably less important than in BXT. BXC also exhibits both the C_2-C_7 and the C_1-C_2 interactions, but its relative weakness (in comparison to BNT) does not agree with its relative energy. Finally, BNC does not have any clearly dominant interaction, but this TS does have the largest number of interactions: C_1-C_2, C_2-C_7, and C_4-O. This observation adds new value to the "maximum accumulation of unsaturations" idea, present in the original Alder rule, and will be subject of further investigations.

Conclusions

Several conclusions can be drawn from the results described for the uncatalyzed process. First of all, the activation barrier of the reaction, calculated at the B3LYP/6-31G* theoretical level, is in excellent agreement with the experimental value in the gas phase.

The energy ordering of the four TS's is NC = XC < NT < XT. The relative energies of NC and XC point to a negligible role of "classical" secondary orbital interactions for the uncatalyzed reaction.

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[23] Singleton, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6563.

In the case of the catalyzed reaction, we have demonstrated that the inclusion of electron correlation effects in the search for the TS is absolutely necessary to describe BNC as a TS leading to a [4+2] cycloaddition. In this respect, the B3LYP method is suitable for describing this kind of system, and computationally much more economical than the MP2 scheme, previously reported.

The B3LYP calculations predict greater asynchronicity of the catalyzed reaction in comparison to the uncatalyzed process, as well as a significant decrease of the activation barrier. Both results agree with that expected from frontier orbital theory. The decomposition of the activation energy shows that most of this decrease comes from the enhanced acrolein−BF_3 interaction in the TS with respect to the reactants.

In a similar way to that found for the uncatalyzed reaction, the energy odering of the four TS's of the catalyzed reaction is BNC < BXC < BNT < BXT. In this case, these energy differences seem to be modulated by secondary orbital interactions. In this respect, "classical" secondary interactions do not play any significant role in this reaction. However, an interaction between the carbonyl atom of the dienophile and the carbon atom of the diene, involved in the later C−C forming bond (the "[4+3] interaction" postulated by Singleton), appears to be a general possibility, both for *endo* and *exo* TS's, and its participation in other Diels−Alder reactions cannot be ruled out. However, the *endo* rule seems to keep its validity in this particular system, because the secondary interactions are globally more important in the *endo* TS, due to their number and/or strength.

Finally, as a consequence of the results described above, B3LYP/6-31G(d) constitutes a more than acceptable compromise between computational cost and quality in the description of the system, and should be routinely used for the study of transition structures of both uncatalyzed and catalyzed Diels−Alder reactions.

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Supporting Information Available: Cartesian coordinates for all the B3LYP/6-31G(d) TS's described in the paper; B3LYP/6-31G(d)//B3LYP/6-31G(d) and B3LYP/6-311+G-(2d,p)//B3LYP/6-31G(d) total energies for all the reactants and TS described in the paper; and computed thermodynamic (at 298.15 K) properties of all the reactants and TS described in the paper, calculated at the B3LYP/6-31G(d) level (5 pages). See any current masthead page for ordering information and Web access intructions.

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