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A theoretical study of the influence of BF$_3$ on the reaction path of the [4+2] cycloaddition of vinylketene with formaldimine

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Abstract—A comprehensive B3LYP/6-31+G* study of the influence of BF$_3$ on the [4+2] cycloaddition of vinylketene with formaldimine was conducted. For this purpose, the complete pathway was determined and changes in different magnetic properties (magnetic susceptibility, χ, magnetic susceptibility anisotropy, χ_{anis}, and the nucleus-independent chemical shifts, NICS) were monitored along the reaction profile with a view to estimate the aromatization associated to the process. We have also applied the ACID (anisotropy of the current-induced density) method with the same intention.
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1. Introduction

The structures, reactions and use of ketenes in organic synthesis are been widely studied[1] since they are discovered by Staudinger in 1905.[2] The [2+2] cycloadditions of ketenes have been of great utility in synthetic methodology. An example for this is the cycloaddition with imines in order to obtain β-lactam antibiotics.[3] In the last years, the [4+2] cycloadditions where the ketene has a dienophile behaviour have been investigated. Yamabe et al. have provided NMR evidence for the [4+2] cycloadditions involving the carbonyl of the ketene with dienes.[4]

Birney and Zhou[5] have found a concerted pathway for the reaction of vinylketene with formaldimine at B3LYP/6-31G* level. They concluded a pericyclic nature of this cycloaddition on the basis of the geometric and electronic structures of the transition state and the energy barrier. In a previous paper,[6] we have observed this pericyclic behaviour but we have found at B3LYP/6-31+G* level a two-step process. Moreover, for the cyclization process, two possible transition states with similar energy (the difference of energy is less than 2 kcal mol^{-1}) were found. The basic difference

between the two structures was its conrotatory (TS2Aconr) or disrotatory (TS2Adisr) nature.

Due to the special characteristics of this reaction, we have thought that the BF$_3$ may have important effects on its behaviour. The BF$_3$, as Lewis acid, can form complex with chemicals containing oxygen, nitrogen, sulfur and other electron pair donors. In this case, we have studied two possible complexations: with the oxygen or with the π cloud of the vinylketene.

Pseudopericyclic reactions were originally defined by Lemal et al. as concerted transformations whose primary changes in bonding compass a cyclic array of atoms, at one (or more) of which nonbonding and bonding atomic orbitals interchange roles.[7,8] This interchange means a disconnection in the cyclic array of overlapping orbitals. The problem of this definition seems to be that the orbital description is not unique.

Birney et al. have studied a large number of pseudopericyclic reactions.[9–15] They have found three common characteristics: very low activation energies, planar transition states and a pseudopericyclic reaction is always orbital symmetry allowed, regardless of the number of electrons involved.

Other studies[16] have employed the aromatic character of the transition states as an argument to explain the difference between pericyclic and pseudopericyclic reactions. The cyclic loop of pericyclic reactions is known to give rise to aromatic

transition states,[17–21] and the orbital disconnection in the pseudopericyclic reactions prevents this aromaticity.

However, an aromatic character of a transition state does not imply the impossibility of pseudopericyclic reaction, as we have demonstrated in a previous paper.[22] This affirmation indicates the need to study the whole process and not only the transition structure in order to define a process as pericyclic or pseudopericyclic. In addition, we have stood out the importance of the study of the magnetic properties along the reaction profile in this controversial matter.[23] For this reason, this work carries out a comprehensive study of the aromaticity along the reaction profile of the whole process of [4+2] cycloaddition of formaldimine with vinylketene in the presence of BF_3. This aromaticity was examined in terms of magnetic susceptibility, χ, magnetic susceptibility anisotropy, χ_{anis}, and the nucleus-independent chemical shifts, NICS, reported by Schleyer et al.[24]

Herges and Geuenich[25] have recently developed a method based on the magnetic properties, which seems to be a good tool in order to distinguish between coarctate and pseudocoarctate and pericyclic and pseudopericyclic as we have indicated in other papers.[22,23,26] This method is referred as ACID (anisotropy of the current-induced density) method and it has been employed in this study.

2. Results and discussion

2.1. Reactions paths

The relevant stationary points found in the potential energy surfaces are presented in Scheme 1 and their energies are indicated in Table 1. As we can observe at B3LYP/6-31+G* level we have found a two-step process.
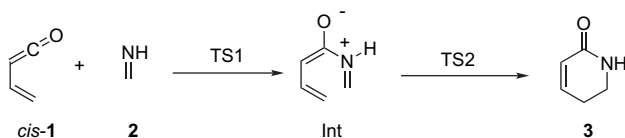
Scheme 1. Reaction paths for the process with BF_3.

Figure 1 and Table 1 show the differences in the reaction path when BF_3 is included in the reaction. We may observe as the points of higher energy correspond to the reaction path

Table 1. Calculated relative energies in kcal mol^{-1} of the stationary points

Structure	Relative energy		
	Without BF_3[a]	π–BF_3	O–BF_3
TS1	9.27	3.58	3.71
Int	9.69	−1.01	−14.33
TS2	Conr: 12.65 Disr: 10.82	3.90	−2.46
3	−51.13	−50.92	−67.36

The values are relative to the reactive conformation of reactants and corrected with ZPE.
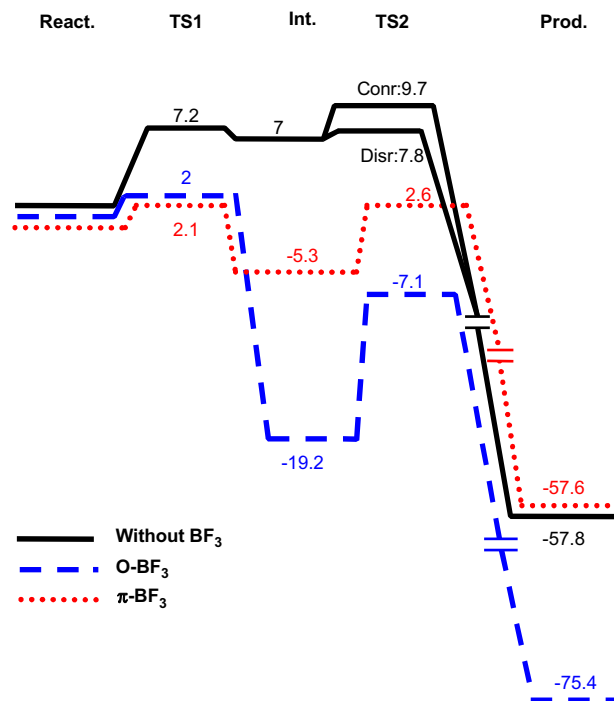[a] Ref. 6.

Figure 1. Energy profiles for the three cycloadditions. The energy values are in kcal mol^{-1} and referred to the reactive conformation of reactant.

without catalyst. Moreover, without BF_3, the higher energy barrier corresponds to the nucleophilic attack of the imine nitrogen on the ketene, but for the complexes with BF_3, the electrocyclic ring closure has a higher barrier. It is worth pointing out the stabilization of the zwitterion by complexation with BF_3, especially in the O–BF_3 case. Therefore, we should emphasize the strong catalytic effect of BF_3.

2.2. Magnetic properties along the reaction path: susceptibility, anisotropy and NICS

In the ring closure step, we can study the possible development of aromaticity and the pericyclic or not nature of the cyclization. This is the reason why we have monitored the variation of magnetic properties only in this part of the reaction profile. Figure 2 shows the variation of magnetic susceptibility (χ), magnetic susceptibility anisotropy (χ_{anis}) and nucleus-independent chemical shift (NICS) during the electrocyclization process. For pericyclic reactions, a marked minimum is observed near the transition structure, indicating its special aromaticity.

In our case, the graphics for susceptibility and its anisotropy seem to lead us to different conclusions. For the anisotropy of the susceptibility, we observe minima for the four studied cases, but this is not the behaviour of the susceptibility. This contradicting behaviour between isotropic magnetic susceptibility and anisotropy can be a consequence of the different role the *zz* component of the magnetic susceptibility tensor plays in both properties. The shielding associated with aromatization is mainly due to the *zz* (perpendicular to the molecular plane) component of the magnetic susceptibility. The anisotropy responds more readily to changes in *zz* component than mean magnetic susceptibility does, probably leading to the differences thus noted.
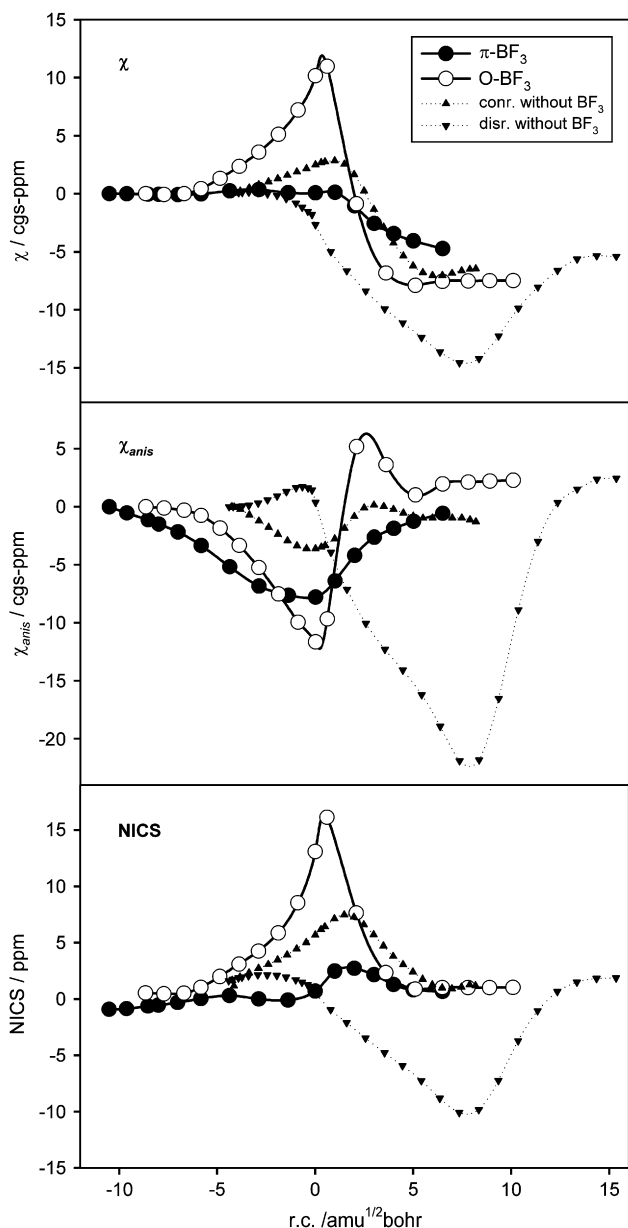
Figure 2. Variation of magnetic properties along the reaction path.

reaction, minimum close to transition state is not present in the NICS curves, indicating the absence of special aromaticity in the transition state. On the basis of this behaviour, the reactions should be classified as pseudopericyclic.

2.3. ACID (anisotropy of the current-induced density) method

In order to carry out a deeper study of the nature of this reaction, the ACID method[24] was employed. This is a recently published method to investigate the delocalization and conjugation effects in molecules. It provides a powerful way to visualize the density of delocalized electrons and quantify conjugation effects. The ACID approach has several advantages: it is a scalar field, which is invariant with respect to the relative orientation of the magnetic field and the molecule, it is not a simple function of the overall electron density, it has the same symmetry as the wave function and it can be plotted as an isosurface. Some examples have demonstrated the applicability of this method to distinguish between pericyclic/pseudopericyclic and coarctate/pseudocoarctate reactivities.[22,23,25–28]

Figure 3 presents the ACID isosurface of the transition states for these reactions at an isosurface value of 0.03 au. Current density vectors are plotted onto the ACID isosurface. The ACID figures for the conrotatory and the O–BF$_3$ processes show a paratropic ring current. This points out an antiaromatic character of the transition state and explains the higher barrier and the maximum of the magnetic properties near this structure. For the structure corresponding to the disrotatory reaction path without BF$_3$, we may observe a diatropic ring current, indicating an aromatic character and a pericyclic behaviour. Finally, for the π complexation with BF$_3$, we can observe a disconnection in the ring current, pointed out by a pseudopericyclic behaviour.

We have to emphasize that the results obtained by the study of the NICS along the reaction path and by the ACID method are in perfect agreement.

3. Conclusions

The effect of the complexation with BF$_3$ on the [4+2] cycloaddition of vinylketene with formaldimine was studied by performing B3LYP/6-31+G* calculations. Reactants, intermediates, products and transition states were located and characterized by means of a vibrational analysis. Also, intrinsic reaction coordinate calculations have been performed and the changes on magnetic properties along the reaction path were studied for the cyclization process.

The complexation with BF$_3$ does not vary the two-step character of this cycloaddition, but we have observed important differences in the reaction profile by complexation, especially the stabilization of the zwitterion intermediate in O–BF$_3$ case.

The variation of magnetic properties, especially NICS, along the IRC presents a different behaviour for the π or O complexation. For the O-case a very marked maximum is showed near transition state, similar to conrotatory process
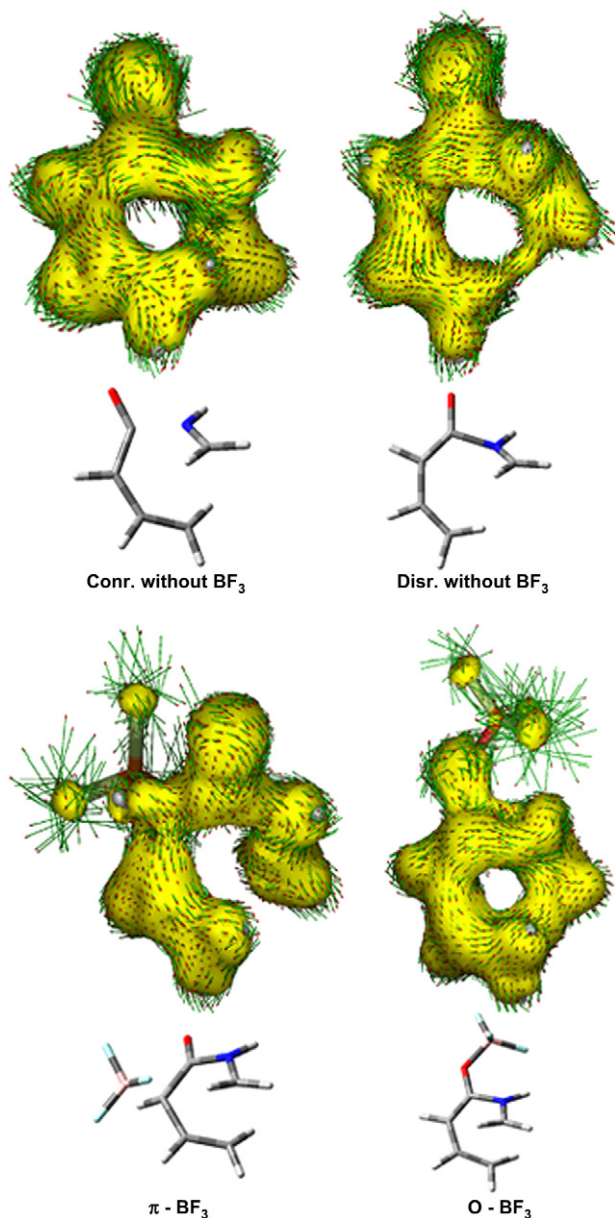
In any case, it should be remembered that some caution must be present when analyzing results from magnetic susceptibility or its anisotropy, since they correspond to global properties, and effects not directly involved in aromatization could distort the observed behaviour.

For this reason, we have also employed another way of measuring aromaticity: the NICS index proposed by Schleyer, which is defined as the negative value of the magnetic shielding.[24] This property can be evaluated at a single point of the molecule, avoiding some of the problems related to global properties such as susceptibility and anisotropy. In our case, the NICS values were calculated in the geometric centre of the forming ring.

The NICS for the O–BF$_3$ reaction presents a maximum near the transition state and the positive NICS values near transition state point out its antiaromatic character. For the π–BF$_3$

Figure 3. ACID plots for the transition structures of the studied reactions.

without BF$_3$, indicating an antiaromatic character of the transition state. While, for the π complexation, we do not observe any minimum or maximum (any special aromaticity) according to a pseudopericyclic behaviour.

The ACID isosurfaces of the transition states for the reaction with BF$_3$ do not have the diatropic cyclic topology, which characterizes to aromatic structures. The O–BF$_3$ case presents a paratropic ring current, indicating an antiaromatic character. The complexation of BF$_3$ and the π cloud of the transition state produce the loss of this character, showing a disconnection in the ring current in the ACID figure.

We have to stand out the important difference with the complexation type: the complexation with the π cloud produces the loss of the antiaromatic character of the transition state and the change from a pericyclic to a pseudopericyclic behaviour.

4. Computational methods

Geometries were optimized at the Density Functional Theory (DFT) level with the 6-31+G* basis set. Becke's three-parameter exchange functional (B3)[29] was employed in conjunction with the Lee–Yang–Parr (LYP) correlation functional.[30] All points were confirmed as minima or transition states by calculating the harmonic vibrational frequencies at B3LYP/6-31+G* level, using analytical second derivatives. In addition, the path for the reaction was obtained using the intrinsic reaction coordinate (IRC)[31–33] at same theoretical level.

The ketene object of our study presents different conformations. The reactant for the cycloaddition is the *s*-cis conformation (*cis*-**1**).

Magnetic properties: nucleus-independent chemical shift (NICS), magnetic susceptibility (χ) and magnetic susceptibility anisotropy (χ_{anis}) were calculated at different points along the IRC. In the magnetic susceptibility calculations, the NMR shielding tensors have been computed with a larger basis set (6-311+G(2d,p)). In order to obtain the NICS along the reaction path at B3LYP/6-31+G* level, we have employed the GIAO (Gauge-Independent Atomic Orbital) method[34] but this method does not provide information about magnetic susceptibility, so χ and χ_{anis} were calculated using the IGAIM (Individual Gauges for Atoms in Molecules) method,[35,36] which is a slight variation of the CSGT (Continuous Set of Gauge Transformations) method.[35–37] Finally, CSGT method at B3LYP/6-31+G* level of theory was employed in ACID calculations, carried out with the programme supplied by Herges and Geuenich.[25]

All calculations were performed with the Gaussian98 software package.[38]

Acknowledgements

Supplementary data

Listings of optimized geometries of reactants, products, intermediates and transition states for the reaction in presence of BF$_3$. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet. 2007.09.005.

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