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A DFT study of the Diels–Alder reaction between methyl acrolein derivatives and cyclopentadiene. Understanding the effects of Lewis acids catalysts based on sulfur containing boron heterocycles

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Abstract—The effects of Lewis acid catalysts based on sulfur containing boron heterocycles on the Diels–Alder reactions of two methyl acroleins with cyclopentadiene have been studied using DFT methods. These reactions take place along highly asynchronous concerted processes. While the reaction with crotonaldehyde leads to the expected *endo* adduct, the reaction with methacrolein leads to *exo* one in agreement with the experiments. The catalytic effect can be explained through the analysis of the electrophilicity index (ω) of the reagents, and the molecular structure of the corresponding transition structures.

1. Introduction

The Diels–Alder (DA) reaction is a powerful tool employed frequently in the synthesis of six-membered ring systems with excellent regio and stereoselective control.[1] The remarkable importance of the DA reaction in the synthesis of natural products and physiologically active molecules led to an upsurge in research activities aimed at developing newer methods to improve yields and selectivities of the [4+2] cycloaddition reactions.[1] In particular, the discovery in 1960 by Yates and Eaton,[2] that the Lewis acid (LA) $AlCl_3$ strongly accelerates the DA reaction encouraged the development of DA reactions of poorly reactive dienophiles[3] and several other carbon–carbon forming bond reactions.[4] LA catalyzed DA reactions can be considered one of the most investigated area in organic synthesis and many regio-, chemo-, diastereo-, and enantioselective DA reactions catalyzed by various LAs have been developed to date.[5]

The effect of LA catalysis in DA reactions has been the object of several theoretical[6–18] and experimental[19] studies employing semiempirical,[6,7,15,16] ab initio[8–12,17,18] and density functional theory (DFT) methods.[13,14a–f] They predict that the catalyst produces transition states (TSs) with significant zwitterionic character and it is related to the greater asynchronicity in the catalyzed reaction, as compared with the uncatalyzed one.[14a] Even, recent studies have also showed that cycloaddition reactions in the presence of LA can occur through a stepwise mechanism.[14b,c,f,16–18]

Carbonyl compounds can undergo DA reactions and the activation of ketones or aldehydes as poor dienophiles is achieved by coordination of LAs to oxygen atom of the carbonyl group, lowering the LUMO energy. Recently, some of us have reported that the ^{13}C NMR chemical shifts of the dienophile carbonyl groups show a deshielding effect of approximately 4–7 ppm, after the addition of LA catalyst on heterocycles containing boron, suggesting strong coordination and a concomitant activation effect in their chemical reactivity associated to DA reactions.[15] As a simple alternative to LA catalyst Rawal and Huang[20] have reported a significantly higher reaction rate for a hetero DA reactions involving aldehydes in Cl_3CH than in other aprotic organic solvents. To understand these solvent-assisted reactions, some of us have performed a theoretical investigation to assess how hydrogen bond-formation between Cl_3CH and the carbonyl oxygen atom influences the chemical reactivity of the hetero DA, making the carbonyl group a stronger hetero-dienophile.[21]

Keywords: Diels–Alder reactions; Lewis acid catalysts; Molecular mechanisms; Electrophilicity index; DFT analysis.

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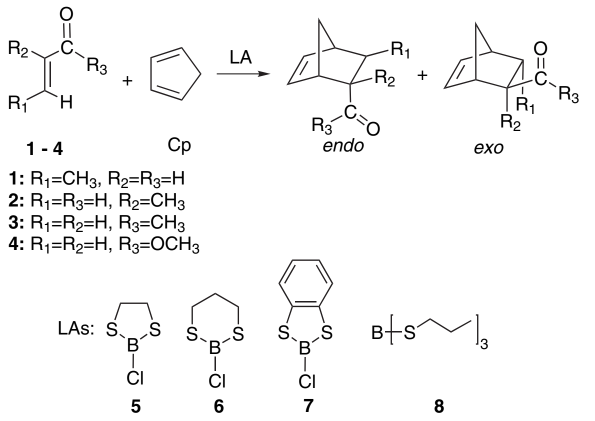
LAs catalysis based on catecholborane moiety have used in different types of DA reactions.[15,22b,c] In particular, Howarth et al.[22a] have carried out an extensive experimental study on the DA reactions between cyclopentadiene (Cp) with crotonaldehyde (**1**), methacrolein (**2**), methylvinyl ketone (**3**), and methylmethacrylate (**4**), that includes the presence of a wide range of LA catalysts based on heterocycles containing boron and sulfur atoms, **5**–**7**, and trialkythioboranes, **8** (see Scheme 1). Surprisingly, the DA reaction between methacrolein and methylmethacrylate lead to the unexpected *exo* adducts.[22a] These types of reactions are interesting, offering the possibility to carry out a complementary theoretical analysis to a better understanding about the key role of the LAs catalysts as well as challenging to study computationally due to the presence of competitive pathways, *endo* and *exo*. Thus, the present theoretical study has been undertaken to shed insight into the role of the sulfur containing boron heterocycle **5** as LA catalyst in the DA reactions between crotonaldehyde and methacrolein and Cp; in addition, the *endo* and *exo* reactive channels have been explored in order to explain the experimentally observed *endo*/*exo* stereoselectivity (see Schemes 2 and 3) using **5**, 2-chloro-1,3,2-dithioborolane, as LA catalyst. We have performed a systematic DFT study through the localization of the stationary points (reactants, TSs, and products) along the reaction pathway on the potential energy surface (PES) for these cycloadditions.



Scheme 1.

The article is structured as follows. The selected computational techniques and methodologies as well as the details of the model systems are listed in next section together with a brief theoretical background of the global electrophilicity index. Next, the results are presented and discussed on the basis of the generated trends in terms of global electrophilicity indexes and the analysis of stationary points on PES. This analysis allows to rationalize and to explain the experimental observations. Finally, in conclusions section, the net outcome of the work is summarized.

2. Computing procedures and model systems

Theoretical calculations based on DFT methods[23] have emerged as alternatives to traditional ab initio calculations in the study of structure and reactivity of chemical systems. DA reactions and related cycloadditions have been the object of several DFT studies showing that those that include gradient corrections and a hybrid functional, such as B3LYP,[24] with the 6-31G* basis set,[25] lead to activation energies in good agreement with the experimental results.[26]

The PESs have been calculated in detail to ensure that all relevant stationary points have been located and properly characterized. Stationary points on PES were characterized by frequency calculations. The optimization was carried out using the Berny analytical gradient optimization methods.[27–29] Finally, the nature of each stationary point was established by calculating analytically and diagonalizing the matrix of the second derivative of energy to determine the number of imaginary frequencies (zero for local minimum and one for TS). The transition vector (TV),[30] i.e., the eigenvector associated to the unique negative eigenvalue of the force constant matrix has been characterized.

The intrinsic reaction coordinate (IRC)[31] path was traced in order to check the energy profiles connecting each transition structure to the two associated minima of the proposed mechanism by using the second order González–Schlegel integration method.[32] The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method.[33] All calculations were carried out with the Gaussian 03 suite of programs.[34]

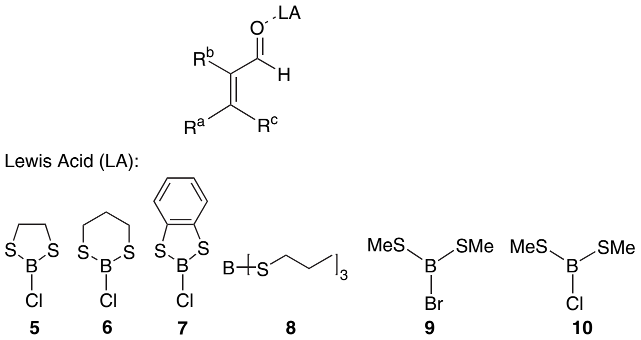
The values of the free energies have been calculated based on the total energies and the thermochemical analysis at the B3LYP/6-31G* level. The thermal contributions to the vibrational energy have been scaled by 0.96.[35] The free energies have been computed at -78 °C, and they were calculated with the standard statistical thermodynamic formulae.[25]

The solvent effects modeled as a continuum model have been analyzed by B3LYP/6-31G* single-point calculations on the gas-phase optimized geometries using a relatively simple self-consistent reaction field (SCRF)[36] based on the polarizable continuum model (PCM) of the Tomasi's group.[37] Since these cycloadditions are carried out in dichloromethane, we have selected its dielectric constant $\varepsilon=8.93$.

The global electrophilicity index,[38] ω, which measures the stabilization energy when the system acquires an additional electronic charge ΔN from the environment, has been given by the following simple expression,[38] $\omega=(\mu^2/2\eta)$, in terms of the electronic chemical potential μ and the chemical hardness η. Both quantities may be approached in terms of the one electron energies of the frontier molecular orbital HOMO and LUMO, ε_H and ε_L, as $\mu\approx(\varepsilon_H+\varepsilon_L)/2$ and $\eta\approx(\varepsilon_L-\varepsilon_H)/2$, respectively.[23a,39] Recent studies devoted to DA[40] and 1,3-dipolar cycloaddition[41] reactions have shown that the global indexes defined in the context of DFT[42] are a powerful tool to understand the behavior of polar cycloadditions. The difference of global electrophilicity between the reagent pair,[40] $\Delta\omega$, can be used to predict the polar character of the process and thereby the feasibility of the cycloaddition.

The DA reactions between Cp and crotonaldehyde (**1**), and methacrolein (**2**), in absence and in the presence of a LA catalyst, have been studied. The influence of the LA catalysts

Table 1. Global electrophilicity of the series of molecules included in this study



Entry	R^a	R^b	R^c	LA	ω (in eV)
1	H	H	H	**7**	5.66
2	Me	H	H	**7**	4.88
3	H	H	H	**10**	4.68
4	H	H	H	**9**	4.64
5	H	H	H	**5**	4.50
6	H	H	H	**6**	4.56
7	Me	H	H	**10**	4.12
8	Me	H	H	**9**	4.08
9	H	H	Me	**5**	4.10
10	H	Me	H	**5**	4.06
11	Me	H	H	**6**	4.01
12	Me	H	H	**5**	3.94
13	H	Me	Me	**5**	3.81
14	Me	H	Me	**5**	3.80
15	Me	H	H	**8**	3.67
16	Me	Me	H	**5**	3.54
17	H	H	H	—	1.84
18	H	Me	H	—	1.70
19	Me	H	H	—	1.65
20	Me	H	Me	—	1.59

The electrophilicity of Cp and 1,3-butadiene is 0.83 and 1.05 eV, respectively.[40]

has been modeled taking into account the formation of a complex between the boron atom of the LA catalyst **5** and the carbonyl oxygen atom of **1** or **2** (see **11** and **12** in Scheme 3 and Table 1).

3. Results and discussion

3.1. Global electrophilicity analysis

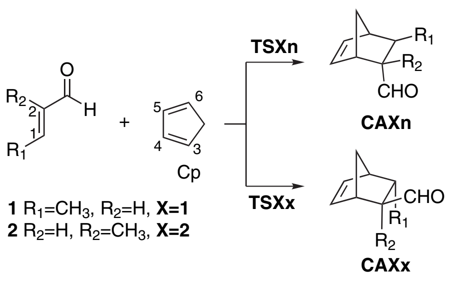
The global electrophilicity, ω, of crotonaldehyde **1**, methacrolein **2**, and a wide series of LA coordinated complexes studied by Howarth et al.[22a] are presented in Table 1. Acrolein, entry 17, has a global electrophilicity value of 1.84 eV and it may be classified as a strong electrophile within the electrophilicity scale.[40] Methyl substitution on the α and β positions of acrolein decreases the electrophilicity of crotonaldehyde **1** and methacrolein **2** to 1.65 and 1.70 eV, respectively (entries 19 and 18 in Table 1), as a consequence of the electron-releasing (ER) character of the methyl group. The presence of the methyl group on the β position of acrolein cause a large reduction of the electrophilicity.

Global electrophilicity scale was used to examine the effect of the LAs observed in the above reactions. Coordination of the boron based LAs, **5–10**, to the lone pair of the carbonyl oxygen atom of these acrolein derivatives increases notably the electrophilicity of the corresponding complex to 3.54–5.66 eV. Therefore, it is expected that these LA catalyzed DA reactions have a large polar character. Some conclusions can be obtained from the data given in Table 1. Electrophilicity of the complexes can be related to the electron-withdrawing (EW) ability of the corresponding LA, and the methyl substitution on the acrolein framework. Thus, the chloride derivative **10**, entries 3 and 7, has a more EW character than the bromide derivative **9**, entries 4 and 8, in clear agreement with more of the electronegative character of the chloride atom than the bromide one. The boron heterocycles **5** and **6** posses a lower EW effect than the LA **10** (see entries 3, 5, and 6), while the boron heterocycle derivative **7** possesses the largest EW effect of this series. Thus, coordination of the LA **7** to acrolein and crotonaldehyde raises the electrophilicity of the corresponding complexes to 5.66 and 4.88 eV, respectively (see entries 1 and 2). Finally, the trialkylthioborane **8** possesses a lower EW effect than the chloride derivative **10** as a consequence of the substitution of the chloride atom in **10** by the thioether in **8** (see entries 15 and 7).

In summary, the coordination of boron atom of LA catalysts, **5–10**, to the lone pair of the oxygen atom of the carbonyl group lowers the electron density at the oxygen atom and lowers the energy of the LUMO, the C=O π^* orbital, with concomitant increases of the electrophilicity index, ω, activating the α,β-unsaturated carbonyl group towards nucleophilic attack. On the other hand, substitution on the acrolein by an ER methyl group decreases slightly the electrophilicity of these methyl derivatives; the substitution on the β position being a large incidence than at the α one.

3.2. Analysis based on the exploration of the PES

3.2.1. Study of the uncatalyzed cycloaddition between 1+Cp and 2+Cp. For the DA reactions **1**+Cp and **2**+Cp, two reactive channels are feasible depending on the relative approach of the diene system of Cp to the carbonyl group of these acrolein derivatives: in the *endo* mode, the π system of Cp is near to the carbonyl group, while in the *exo* it is far. The two approach modes have been considered (see Scheme 2). Analysis of the results renders that these cycloadditions take place along asynchronous concerted processes. Thus, two TSs: **TSXn** and **TSXx**, corresponding to the *endo* and *exo* approach modes of Cp to **1** and **2** (**X**=**1** for **1** and **X**=**2** for **2**), named as **n** and **x**, respectively, for each one of the two DA reactions considered were located and characterized. The total and relative energies corresponding to these reactions are summarized in Table 2.



Scheme 2.

The activation energies associated to these processes are: 21.36 (31.59) kcal/mol for **TS1n**, 20.89 (31.11) kcal/mol

Table 2. B3LYP/6-31G* total and free energies (E, E_{sol} in dichloromethane and G, in au), relative[a] (ΔE, ΔE_{sol} in dichloromethane and ΔG, in kcal/mol) for the stationary points involved in the boron based LA catalyzed Diels–Alder reactions between crotonaldehyde **1** and methacrolein **2** with cyclopentadiene

	E	ΔE	E_{sol}	ΔE_{sol}	G	ΔG
1+Cp	−425.335246		−425.340522		−425.189182	
TS1n	−425.301209	21.36	−425.306480	21.36	−425.138847	31.59
TS1x	−425.301953	20.89	−425.307152	20.94	−425.139612	31.11
CA1n	−425.356793	−13.52	−425.359091	−11.65	−425.189657	−0.30
CA1x	−425.356769	−13.51	−425.359099	−11.66	−425.189689	−0.32
2+Cp	−425.334607		−425.337096		−425.188503	
TS2n	−425.302951	19.86	−425.307402	18.63	−425.140719	29.98
TS2x	−425.305044	18.55	−425.309862	17.09	−425.142765	28.70
CA2n	−425.355757	−13.27	−425.357823	−13.01	−425.188431	0.05
CA2x	−425.355737	−13.26	−425.357959	−13.09	−425.188440	0.04
11+Cp	−1785.490026		−1785.512254		−1785.283995	
TS1Bn	−1785.471382	11.70	−1785.496789	9.70	−1785.249002	21.96
TS1Bx	−1785.471171	11.83	−1785.496291	10.02	−1785.248244	22.43
CA1Bn	−1785.509928	−12.49	−1785.526306	−8.82	−1785.282560	0.90
CA1Bx	−1785.509647	−12.31	−1785.526155	−8.72	−1785.282371	1.02
12+Cp	−1785.486882		−1785.505385		−1785.280854	
TS2Bn	−1785.473595	8.34	−1785.496799	5.39	−1785.250934	18.78
TS2Bx	−1785.474854	7.55	−1785.498392	4.39	−1785.252491	17.80
CA2Bn	−1785.508233	−13.40	−1785.523384	−11.29	−1785.281000	−0.09
CA2Bx	−1785.506821	−12.51	−1785.521017	−9.81	−1785.279853	0.63

[a] Relative to **1**+Cp, **2**+Cp, **11**+Cp or **12**+Cp.

for **TS1x**, 19.86 (29.98) kcal/mol for **TS2n**, and 18.55 (28.70) for **TS2x** (values in parenthesis are relative free energy). The discrepancy between both values is associated to the negative values of activation entropies while the present results are clear that both uncatalyzed reactions present a *exo* selective. The large activation energy associated to these uncatalyzed processes prevents the corresponding DA reaction instead that these cycloadditions are exothermic in ca. 13 kcal/mol.

The geometries of the TSs are given in Figure 1. The lengths of the C1–C3 and C2–C6 forming bonds at the TSs are: 2.091 and 2.408 Å (**TS1n**), and 2.089 and 2.429 Å (**TS1x**), and 2.024 and 2.531 Å (**TS2n**), 2.005 and 2.643 Å (**TS2x**), respectively. The extent of the asynchronicity on the bond-formation can be measured by means of the difference between the lengths of the two σ bonds that are being formed in the reaction, i.e., $\Delta r = d(\mathrm{C2{-}C6}) - d(\mathrm{C1{-}C3})$. These values are in the range 0.31–0.63; they indicate that these TSs correspond with asynchronous bond-formation processes, where the C1–C3 forming bond at the β position of acrolein derivative is being formed in a large extension as a consequence of the large polarization of the C1–C2 double bond. The TSs associated to the DA reaction between **2** and Cp are more asynchronous that those associated to reaction between **1** and Cp. The hindrance of the C2 methyl group on **2** could be responsible for the large asynchronicity. In addition the *exo* TSs are slightly more asynchronous than the *endo* ones.

The analysis of the atomic motion at the unique imaginary frequency of the TSs (see the corresponding values in Fig. 1) indicates that they are mainly associated to the movement of the C1 and C3 atoms and the C2 and C6 along the C1–C3 and C2–C6 bond-formation. At these asynchronous TSs, the two forming bond processes are coupled.

The extent of bond-formation along a reaction pathway is provided by the concept of bond order (BO).[43] The BO values of the C1–C3 and C2–C6 forming bonds at the TSs are: 0.45 and 0.27 (**TS1n**), and 0.44 and 0.27 (**TS1x**), and 0.49 and 0.23 (**TS2n**), 0.49 and 0.21 (**TS2x**), respectively. These values indicate that at these asynchronous bond-formation processes the C1–C3 bond-formation is more advanced than the C2–C6 one.

The natural population analysis (NPA) allows us to evaluate the charge transfer (CT) along the cycloaddition of these acrolein derivatives. The natural charges at the TSs appear

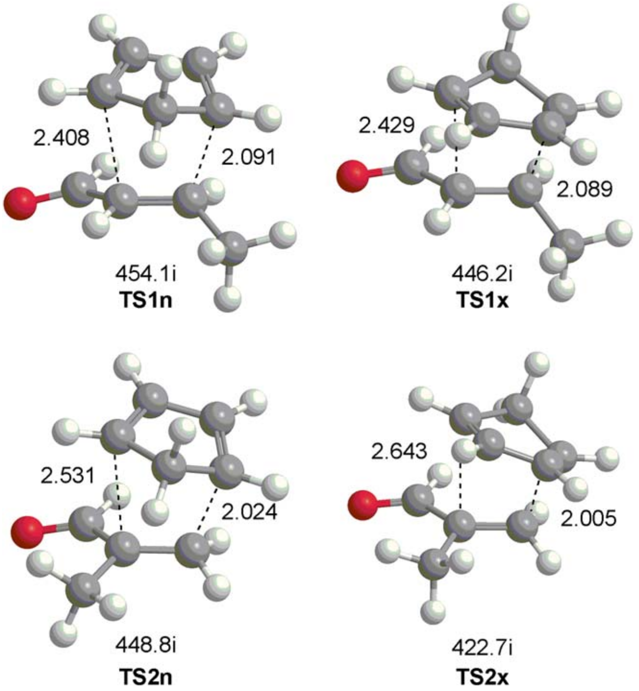
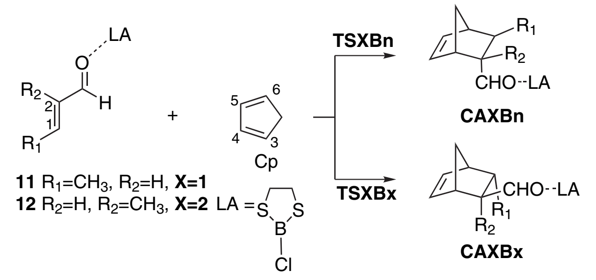


Figure 1. Geometries of the transition structures involved in the Diels–Alder reactions between crotonaldehyde **1** and methacrolein **2** with cyclopentadiene. The distances are given in Å. The unique imaginary frequencies in cm^{-1} are also given.

shared between the donor Cp and the acceptor methyl acrolein derivatives. The CT from Cp to **1** or **2** at the TSs are: 0.14 e at **TS1n**, **TS1x**, **TS2n**, and 0.13 e at **TS2x**. This values are slightly larger than that obtained at the TS associated to the DA reaction between butadiene/acrolein, 0.11 e.[40] Although acrolein is slightly more electrophile than the methyl derivatives **1** and **2**, see Table 1, Cp is better nucleophile than butadiene; note that $\Delta\omega$ for **1**+Cp and **2**+Cp DA reactions, 0.87 and 0.82 eV, respectively, are large than that for butadiene+acrolein DA reaction, 0.70 eV.[40]

3.2.2. Study of the Lewis acid catalyzed cycloaddition between 1+Cp and 2+Cp. The effect of LA catalyst could be confirmed with energetics of these cycloadditions. The *endo* and *exo* approach modes have been considered for the LA catalyzed DA reactions **1**+Cp and **2**+Cp (see Scheme 3). A complete exploration of the PES for the formal [4+2] cycloadditions between the complexes **11** and **12** with Cp affords that these reactions take place along highly asynchronous concerted processes, associated to the nucleophilic attack at the end of the 1,3-diene system of Cp to the β position of these LA coordinated acrolein derivatives. Therefore, these reactions can be considered a formally Michael-type addition. Thus, two TSs: **TSXBn** and **TSXBx** and two cycloadducts: **CAXBn** and **CAXBx**, corresponding to the *endo* and *exo* approach modes of Cp to the complexes **11** and **12** (**X**=**1** for **11** and **X**=**2** for **12**), named as **n** and **x**, respectively, for each one of the two DA reactions considered were located and characterized. The stationary points corresponding to these LA catalyzed DA reactions are shown in Scheme 3 together with the atom numbering. The total and relative energies are summarized in Table 2. The geometries of the TSs are given in Figure 2.



Scheme 3.

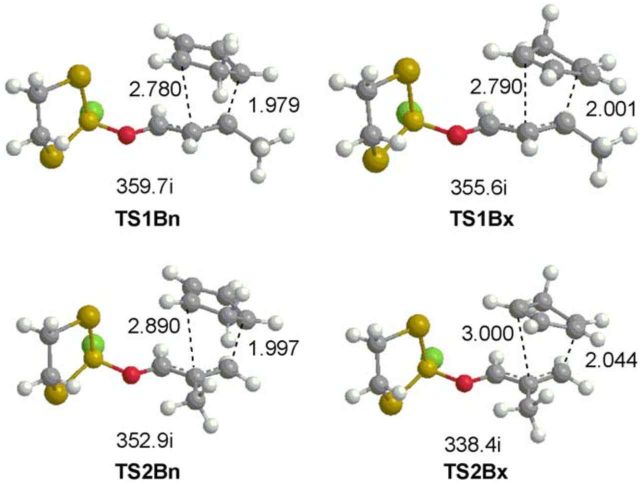


Figure 2. Geometries of the transition structures involved in the LA catalyzed Diels–Alder reactions between crotonaldehyde **1** and methacrolein **2** with cyclopentadiene. The distances are given in Å. The unique imaginary frequencies in $\mathrm{cm^{-1}}$ are also given.

The activation energies associated with these process are: 11.70 (21.96) kcal/mol for **TS1Bn**, 11.83 (22.43) kcal/mol for **TS1Bx**, 8.34 (18.78) kcal/mol for **TS2Bn**, 7.55 (17.80) kcal/mol for **TS2Bx**, (values in parenthesis are relative free energy). The inclusion of the LA catalyst **5** decreases of the activation energies associated to these DA reactions between 9–12 kcal/mol. For the DA reaction between complex **11** (LA **5** plus crotonaldehyde **1**) and Cp the difference between *endo*/*exo* energies is of 0.13 (0.48) kcal/mol (the *endo* pathway is slightly favored with respect *exo* channel). This value give a *endo*:*exo* proportion of 53:47 (62:38) that is in reasonable agreement with the experimental results of 87:13.[22a] On the other hand, for the DA reaction between the complex **12** (LA **5** plus methacrolein **2**), and Cp there is a change on the stereoselectivity; now **TS2Bx** is 0.79 (0.98) kcal/mol lesser in energy that **TS2Bn**, this value give a *endo*:*exo* proportion of 31:69 (27:73) in agreement with the experimental results of 8:92 (*endo*/*exo*).[22a] These LA catalyzed DA reactions are exothermic in 12–13 kcal/mol. However, the inclusion of thermal corrections to the energy and the entropic term makes the process endergonic in 0–1 kcal/mol.

The activation energy associated to the reaction of **12** with Cp is 4.15 kcal/mol lower than that associated to the reaction of **11** with Cp, while for the uncatalyzed processes this difference is 2.34 kcal/mol. Therefore, the presence of the ER methyl group on the β position of acrolein derivative **11** produces a lower catalytic effect on the activation energy value. Note that the methyl substitution produces an electrophilic deactivation of acrolein. This behavior can be also rationalized by means of the analysis of the ω values of **12** and **11**, 4.06 and 3.94 eV, respectively (see entries 10 and 12 in Table 1).

The geometries of the TSs are given in Figure 2. The lengths of the C1–C3 and C2–C6 forming bonds at the TSs associated to the nucleophilic attack of Cp to these LA coordinated acrolein derivatives are: 1.979 and 2.780 Å (**TS1Bn**), and 2.001 and 2.790 Å (**TS1Bx**), and 1.997 and 2.890 Å (**TS2Bn**), 2.044 and 3.000 Å (**TS2Bx**), respectively. The extent of the asynchronicity on the bond-formation, i.e., $\Delta r = d(\mathrm{C2{-}C6}) - d(\mathrm{C1{-}C3})$, is in the range 0.79–0.96. Coordination of the LA to the carbonyl oxygen atom increases the asynchronicity of the process. These TSs correspond with highly asynchronous bond-formation processes, where the C1–C3 forming bond at the β position of acrolein derivative is being formed in a large extension as a consequence of the large polarization of the C1–C2 double bond.

An analysis of molecular structure of **TS2Bn** shows that along the *endo* approach of Cp to methacrolein **12**, the methylene group of Cp is positioned close to the methyl group of **12**; the C(methylene)–C(methyl) distance is 3.370 Å. The sum of the van der Waals radius of the two groups is ca. 4.08 Å. Therefore, while for the **11**+Cp reaction the attracting electrostatic forces at the *endo* TS are responsible for the *endo* selecivity,[14a] the non-bonding interactions between the methylene group of Cp and the methyl group of methacrolein **12** are responsible for the *exo* selectivity experimentally observed.[22a]

The analysis of the atomic motion at the unique imaginary frequency of the TSs (see the corresponding values in Fig. 2) indicates that they are mainly associated to the movement of the C1 and C3 atoms along the C1–C3 bond-formation; the movement of the C2 and C6 atoms being negligible. This analysis reinforces the two-center interaction at these LA catalyzed DA reactions.

The BO values of the C1–C3 and C2–C6 forming bonds at the TSs are: 0.52 and 0.11 (**TS1Bn**), and 0.49 and 0.12 (**TS1Bx**), and 0.52 and 0.10 (**TS2Bn**), 0.46 and 0.09 (**TS2Bx**), respectively. These values indicate that at these asynchronous bond-formation processes the C1–C3 bond-formation is more advanced than the C2–C6 one. The *endo* TSs are slightly more asynchronous and more advanced than the *exo* ones.

To evaluate the CT along the nucleophilic attack of Cp to the LA coordinated acrolein derivatives, the natural charges at the TSs were shared between the donor Cp and the acceptor LA coordinated aldehyde **11** and **12**. The CT from Cp to the complexes **11** or **12** at the TSs are: 0.34 e at **TS1Bn**, 0.32 e at **TS1Bx**, at 0.33 e at **TS2Bn**, and 0.29 e at **TS2Bx**. These values indicate that these species have some zwitterionic character. These large values are in clear agreement with the increase of the difference of electrophilicity, $\Delta\omega$, between the reagents for these LA catalyzed DA reactions relative to the uncatalyzed ones. This behavior is a consequence of the large electrophile character of these LA coordinated acrolein derivatives and the CT at the *endo* TSs are slightly larger than that of the *exo* ones.

Finally, as these reactions were carried out in dichloromethane, and solvent effects can produce some alteration in both activation energies and stereoselectivity, they were considered by means of single-point calculations over the gas-phase optimized geometries using the PCM method. Table 2 reports the relative energies. Solvent effects stabilize all structures between 9–16 kcal/mol. The more stabilized species are the TSs as a consequence of their zwitterionic character. As a result, the electronic activation barriers decrease ca. 2 kcal/mol for the reaction of **11**, and ca. 3 kcal/mol for the reaction of **12**. A unlike behavior has the solvation on the stereochemistry of both DA reactions; while for the reaction between **11** and Cp, the *endo* TS is slightly more stabilized than the *exo* one, increasing the *endo* selectivity (*endo*:*exo* proportion of 58:42), for the reaction between **12** and Cp, the *exo* TS is slightly more stabilized, therefore increasing the gas-phase *exo* selectivity (*endo*:*exo* proportion of 27:73). These energetic results reinforce the gas-phase analysis. This value give a *endo*:*exo* proportion that is in reasonable agreement with the experimental results 87:13 and 8:92, respectively.[22a]

4. Conclusions

The present calculations using density functional theory, B3LYP/6-31G*, provide thermodynamic and kinetic information on the DA reaction between crotonaldehyde and methacrolein with Cp catalyzed by LAs based on sulfur containing boron heterocycles. The theoretical data obtained may thus provide a helpful tool for the interpretation of the experimental findings and a useful guide for understanding the mechanism of other analogous reactions. From the comprehensive study on these reaction pathways the following conclusions can be drawn:

(i) A DFT analysis based on the electrophilicity index, ω, of the reagents shows the large increase of the electrophilicity of crotonaldehyde and methacrolein with coordination of the sulfur containing boron heterocycles, as LA catalysts.

(ii) LAs were found to be extremely effective in promoting and accelerating the cycloaddition reactions. The large increase of $\Delta\omega$ values for these LA catalyzed DA reactions accounts for the polar character of these cycloadditions and the reduction of the corresponding activation energies. Then, these cycloadditions can be viewed as a nucleophilic attack.

(iii) The reaction pathways, *endo* and *exo*, associated with cycloaddition reactions of crotonaldehyde and methacrolein with cyclopentadiene (Cp) catalyzed by 2-chloro-1,3,2-dithioborolane as LA have been studied. The boron atom of LA catalysts is coordinated to the lone pair of the oxygen atom of the carbonyl group. This coordination lowers the electron density at the oxygen atom and increases ω value, activating the α,β-unsaturated carbonyl group towards nucleophilic attack.

(iv) These LA catalyzed cycloaddition reactions take place along highly asynchronous concerted bond-formation processes associated to the nucleophilic attack of Cp to the β position of the LA coordinated α,β-unsaturated carbonyl compounds. The DA reaction between crotonaldehyde and Cp leads the expected *endo* adducts, while the cycloaddition between methacrolein and Cp leads to the unusual *exo* adduct, in agreement with the experimental outcomes. While the attracting electrostatic forces at the ends of the zwitterionic *endo* TS associated to the reaction of crotonaldehyde with Cp are responsible for the *endo* selectivity, the hindrance between the methyl group of methacrolein and the methylene moiety of Cp in the *endo* TS is responsible for the *exo* selectivity found experimentally.

(v) Solvent effects of dichloromethane reinforce the gas-phase energetic results found for these polar cycloadditions.

(vi) The present computational study enhances our understanding on the reactivity of Cp with crotonaldehyde and methacrolein in sulfur containing boron heterocycles LA catalyzed DA reactions and would stimulate experimental interest. This efficient catalytic effect can be satisfactorily explained in terms of global electrophilicity scale as well as the analysis of the molecular structure of the corresponding transition structures.

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