Understanding the influence of Lewis acids in the regioselectivity of the Diels–Alder reactions of 2-methoxy-5-methyl-1,4-benzoquinone: A DFT study

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ABSTRACT

The mechanisms of the Diels–Alder (DA) reactions of 2-methoxy-5-methyl-1,4-benzoquinone 1 with 2-methyl-1,3-butadiene 2, in the absence and in the presence of LA catalysts, have been studied using the DFT method at the B3LYP/6-31G(d) level of theory. The uncatalyzed DA reactions between 1 and 2 take place via synchronous concerted TSs. The large activation barrier as well as the low stereo and regioselectivity associated with the uncatalyzed process are in clear agreement with the non-polar character of the cycloaddition. Coordination of the LA catalysts, BF3 or SnCl4, to the oxygen atoms of the benzoquinone 1 produces a large acceleration of the reaction, which can be associated with the large polar character of the cycloaddition. The different coordination modes of BF3 and SnCl4 LA catalysts to the oxygen atoms of benzoquinone 1 allow explaining the reverse para/meta regioselectivity observed in these LA-catalyzed DA reactions. The analysis based on the global and local electrophilicity indices of the reagents correctly explains the polar nature of the title reactions, as well as the change of regioselectivity experimentally observed.

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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]. In this process a 1,3-diene reacts with an olefinic or acetylenic dienophile to form a six-member ring adduct. The usefulness of DA reactions arises from its versatility and from its remarkable stereochemistry. By varying the nature of the diene and dienophile many types of carbocyclic structure can be built up.

The use of quinones as dienophile component in DA reactions provides access to a range of structures that are part of the fundamental skeleton of natural products and biologically active molecules [2]. The effects of the substituents on the quinone system are important because they determine the regiochemistry of the DA reactions. Electron-releasing substituents effects, CH3O > CH3, on the quinone decrease the reactivity of the double bond to which they are attached. In addition, the methoxy group produces an influence on the orientation at the unsubstituted double bond [3]. The interactions between unsymmetrical dienes can give two isomeric cycloadducts, depending upon relative positions of the substituent in the cycloadduct. For 1-substituted dienes head-to-head interactions corresponds to orto channel and head-to-tail interactions corresponds to meta channel. For 2-substituted dienes, head-to-head corresponds to meta channel and head-to-tail corresponds to para channel. This substitution usually directs the DA reaction with 2-substituted dienes to give the para cycloadducts.

Tou and Reusch [4] reported that the regiochemistry of 2-methoxy-5-methyl-benzoquinone 1 with alkyl-substituted dienes like 2-methyl-1,3-butadiene 2 can be directed to favor either of the regiosomeric adducts by using appropriate Lewis acid (LA) catalysts (Scheme 1a). Thus, while the use of BF3·OEt2 produce a 2:4:1 ratio of the para/meta regioisomeric cycloadducts, thereby indicating that this cycloaddition proceeds with very low regioselectivity; the use of SnCl4 produces an inverse relationship with a higher regiochemistry in favor of the meta regioisomeric cycloadduct 1:20 para/meta. In absence of a LA, the para and meta cycloadducts are formed in a 1:1 ratio [4].

The activation energy associated to the DA reactions has been related with the polar character of the TS involved in such processes [5,6]. The characterization of the electrophilic/nucleophilic character of the reagents allows predicting the polar character of the reaction and in consequence the feasibility of the process. In this context, it is worth noting that the LA-catalyzed DA reactions take place through TSs with a larger zwitterionic character [7,8].

The global electrophilicity index Ω proposed by Parr et al. [9] has been used to classify the dienes and dienophiles currently used in DA reactions within a unique scale of electrophilicity [10,11].

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A good correlation between the difference in electrophilicity of the diene and dienophile pair, \( \Delta \omega \), and the feasibility of the cycloaddition was found. A high electrophilicity at the dienophile and a high nucleophilicity at the diene will in general result in a highly polar transition state, associated with a favorable diene–dienophile interaction, thereby facilitating the cycloaddition [10]. In addition, the static charge transfer (CT) model proposed by Pearson [12] gave a good correlation with the actual CT found at the corresponding highly asynchronous TSs [10]. Therefore, \( \Delta \omega \) for a diene/dienophile pair is a valuable tool to predict the polar character of a DA reaction. In addition, the local counterpart condensed to atom \( k \), \( \omega_k \) [13], has been found to be a useful tool that correctly explains the regioselectivity of the polar DA reactions. The local electrophilicity together with the Fukui functions for electrophilic attack, \( \mu_x \), allow the identification of the most electrophilic and nucleophilic centers in the reactants [13].

Recently, we have studied the DA reactions of 2-acetyl-1,4-benzoquinone 3, an electrophilically activated benzoquinone, with methyl substituted 1,3-butadienes [15] (Scheme 1b). These reactions were characterized by the nucleophilic attack of the unsubstituted ends of 1,3-dienes to the \( \beta \) conjugated position of the 2-acetyl-1,4-benzoquinone followed by a ring-closure. These DA reactions have low activation energies, between 9.5 and 14.8 kcal/mol (B3LYP/6-31G(d)), [16] and a large endo selectivity.

In this work we present a theoretical study about the mechanisms of the DA reactions of 2-methoxy-5-methyl-benzoquinone 1 with 2-methyl-1,3-butadiene 2, in the absence and in the presence of LA catalysts, BF\(_3\) and SnCl\(_4\) (see Scheme 2). We first make a reactivity analysis based on static reactivity indices to discuss the origin of the polar character and the regioselectivity of these cycloadditions. Then, the mechanism of DA reactions between the benzoquinone 1 and the 2-methylbutadiene 2 in absence and in the presence of LA catalysts coordinated to different positions of the benzoquinone 1 is discussed. The purpose of our work is to contribute to a better understanding of the changes in the regiochemistry due to different modes of LA coordination in these DA reactions and to shed some light on the mechanistic details of these polar cycloadditions.

2. Methodology

DFT calculations were carried out using the B3LYP [17,18] exchange-correlation functional, together with the standard 6-31G(d) basis set [19] for hydrogen, carbon, oxygen, boron, fluorine and chlorine and the Hay–Wadt small-core effective core potential (ECP) including a double-\( \zeta \) valence basis set for Tin [20] (LandL2DZ keyword). The optimizations were carried out using the Berny analytical gradient optimization method. [21] The intrinsic reaction coordinate (IRC) [22] path was traced 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 [23,24]. All calculations were carried out with the Gaussian 03 suite of programs [25]. The stationary points were characterized by frequency calculations. The electronic structures of TSs and ground states were analyzed in term of the bond orders (BO) [26] and the natural charges obtained from the natural bond orbital (NBO) method [27,28] at the same calculation level. Solvent effects were evaluated by performing single-point B3LYP/6-31G(d) calculations at the gas-phase stationary points involved in the reaction using the polarizable continuum model (PCM) of Tomasi's group [29,30]. Since the solvent is usually dichloromethane, we used a dielectric constant value \( \varepsilon = 8.93 \).

Global reactivity indexes such as the electronic chemical potential, \( \mu \), chemical hardness, \( \eta \), and electrophilicity \( \omega \), were approximated in terms of the one electron energies of the frontier molecular orbital (FMO) HOMO and LUMO, \( \varepsilon_{\text{HOMO}} \) and \( \varepsilon_{\text{LUMO}} \), using the expressions \( \mu = (\varepsilon_{\text{HOMO}} + \varepsilon_{\text{LUMO}})/2 \) and \( \eta = (\varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}) \) and \( \omega = \mu^2/2\eta \), respectively, at the ground state of the molecules [32]. The local electrophilicity [10], \( \omega_x \), condensed to atom \( k \) is easily obtained by

\[
\omega_x = \frac{\mu_x^2}{2\eta_x} = \frac{\mu_x^2}{2\eta_x} = \frac{\mu_x^2}{2\eta_x}
\]
For the SnCl$_4$ LA catalyst only one coordination mode has been considered, namely double coordination to the carbonyl oxygen in benzoquinone, while in SnCl$_4$ increases the electronic chemical potential value of SnCl$_4$ for the oxygens in benzoquinone.

3. Global electrophilicity analysis

3.1. Results and discussion

Recent studies carried out on DA reactions [5–8,15] have shown that the reactivity indices defined within the conceptual density functional theory [34,35] are powerful tools to study the polar character of the cycloaddition. In Table 1, we report the static global properties, namely, electronic chemical potential $\mu$, chemical hardness $\eta$, and global electrophilicity $\omega$ for the system 1–2 and the LA coordinated systems 4–6.

The electronic chemical potential of 2-methylbutadiene 2 ($\mu = -0.1226$ au) is higher than that of benzoquinone 1 ($\mu = -0.1848$ au), thereby indicating that along a polar DA reaction, the net CT will take place from the diene 2 toward the benzoquinone 1, in qualitative agreement with the CT analysis performed at the TS structures (vide infra). Coordination of the LA catalysts, BF$_3$ or SnCl$_4$, to the carbonyl oxygen atoms of benzoquinone 1 decreases the electronic chemical potential value of 1 to $-0.2199$ au for 4, $-0.1980$ au for 5 and $-0.2355$ au for 6.

The electrophilicity of benzoquinone 1 is 3.21 eV, a value that falls within the range of strong electrophiles in the $\omega$ scale. [10] Note that the electrophilicity of 1 is lower than that of 2-acetyl1,4-benzoquinone 3 $\omega = 4.64$ eV [15] probably as a consequence of the substitution by the electron-withdrawing acetyl group present in 3 compared to the electron-releasing methoxy group in 1.

Coordination of BF$_3$ to the carbonyl 09 oxygen in 4 increases the electrophilicity of 1 to 4.39 eV, while coordination to O7 oxygen in 5 results in an electrophilic activation to 3.87 eV. On the other hand, coordination of SnCl$_4$ to carbonyl O7 and methoxy O8 oxygen atoms increases the electrophilicity of 6 to 6.42 eV due to the larger acid character of SnCl$_4$, and a decrease of the electron-releasing ability of the methoxy oxygen atom with the LA coordination. The difference in electrophilicity of the diene and dienophile pair $\Delta \omega$ for DA reactions has been used to predict the polar character of the cycloadditions [10]. The $\Delta \omega$ values for uncatalyzed DA reaction between 1 and 2 is 2.32 eV, while for the LA-catalyzed reactions, these values raise to 3.95 eV, 2.89 eV and 5.44 eV for 4, 5 and 6, respectively. The larger $\Delta \omega$ values found for the LA-catalyzed DA reactions indicate that they will present a strong polar character.

### Table 1

<table>
<thead>
<tr>
<th>$\mu$ (in a.u.)</th>
<th>$\eta$ (in a.u.)</th>
<th>$\omega$ (in eV)</th>
<th>$\omega_k$ (in eV) for</th>
<th>C$_2$</th>
<th>C$_3$</th>
<th>C$_5$</th>
<th>C$_6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$-0.1848$</td>
<td>0.1446</td>
<td>3.21</td>
<td>0.28</td>
<td>0.16</td>
<td>0.40</td>
<td>0.27</td>
</tr>
<tr>
<td>4</td>
<td>$-0.2193$</td>
<td>0.1325</td>
<td>4.93</td>
<td>0.51</td>
<td>0.10</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>5</td>
<td>$-0.1980$</td>
<td>0.1380</td>
<td>3.87</td>
<td>0.29</td>
<td>0.21</td>
<td>0.52</td>
<td>0.27</td>
</tr>
<tr>
<td>6</td>
<td>$-0.2355$</td>
<td>0.1176</td>
<td>6.42</td>
<td>0.38</td>
<td>0.47</td>
<td>0.93</td>
<td>0.27</td>
</tr>
<tr>
<td>2</td>
<td>$-0.1226$</td>
<td>0.2069</td>
<td>0.98</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
a larger polar character at the TS. In addition, it may be anticipated that the DA reaction between 2 and 6 will present the largest polar character and the largest acceleration.

Recent studies on cycloadditions with a large polar character have shown that the analysis based on the local electrophilicity $\omega_k$ [13] allows one to explain the regioselectivity experimentally observed. The analysis of local electrophilicity on benzoquinone 1 indicates that the C5 position is the more electrophilic center of the molecule ($\omega_{C5} = 0.40$ eV). This result is not in agreement with the regioselectivity experimentally observed for uncatalyzed reaction (vide infra). However, coordination of 1 with BF$_3$ in 4 produces a similar activation at C5 and C6 ($\omega = 0.47$ eV), in good agreement with the low regioselectivity experimentally observed for this catalyzed DA reaction. On the other hand, the coordination at carbonyl O7 oxygen with BF$_3$ in 5 and SnCl$_4$ in 6 produces a large activation at C5 position ($\omega_{C5} = 0.52$ eV and $\omega_{C5} = 0.93$ eV) respectively. The regioselectivity predicted for 6 is in close agreement with the experiment.

3.2. Study of the uncatalyzed Diels–Alder reaction between 2-methoxy-5-methyl-benzoquinone 1 and 2-methylbutadiene 2

The DA reaction between benzoquinone 1 and 2-methylbutadiene 2 can take place along four reactive channels: the two endo and exo stereoisomeric channels and the two ortho and meta regioselective channels. An exhaustive exploration of the PES for these DA reactions indicates that they are associated with concerted C–C bond-formation processes. One TS and the corresponding [4+2] cycloadduct associated with the four reactive channels was located and characterized (see Scheme 2a).

The total and relative energies corresponding to the stationary points associated with these reactive channels are summarized in Table 2. The activation barriers associated with the cycloaddition processes are 22.5 kcal/mol for TS1np, 24.3 kcal/mol for TS1xp, 22.8 kcal/mol for TS1nm and 24.3 kcal/mol for TS1xm. These energy results indicate that the endo approaches are 1.8 and 1.5 kcal/mol more favorable than the exo ones. On the other hand, the ortho and meta channels present almost similar activation energies, thereby correctly suggesting a 1:1 product distribution. These values point out to the low asynchronicity that is present in concerted processes. These results indicate that these TSs correspond to concerted but slightly asynchronous bond-formation processes.

The natural population analysis (NPA) allows evaluating the CT along these cycloadditions [10]. The natural charges at the TSs appear shared between the donor 2-methylbutadiene 2 and the acceptor benzoquinone 1 frameworks. The CT from the diene 2 to 1 at the TSs are 0.18e at TS1np and TS1nm and 0.16e at TS1xp and 0.17e at TS1nm. These values are slightly larger than those obtained at the TS associated with the non-polar DA reaction between butadiene/acroleine, 0.11e [10] and account for the large activation energy associated with these DA reactions.

3.3. Study of LA-catalyzed Diels–Alder reactions between 2-methoxy-5-methyl-benzoquinone 1 and 2-methylbutadiene 2

Previous studies on benzoquinones bearing electron-withdrawing substituents have shown that these DA reactions present endo selectivity. [15] In addition, the endo and exo stereoisomeric reactive channels leading to the same regioisomeric cycloadduct. In consequence, for the catalyzed DA reactions only the endo approaches modes of the diene system of 2 over the benzoquinone system of 1 have been studied. For DA reactions catalyzed with BF$_3$, two coordination modes of the LA to each one of the two carbonyl oxygen atoms have been considered (see Scheme 2b). The total and relative energies associated with the processes are summarized in Table 3. The activation barriers associated with the BF$_3$ catalyzed DA reactions are 13.9 kcal/mol for TS2np and 13.6 kcal/mol for TS2nm, 15.8 kcal/mol for TS3np and 16.0 kcal/mol for TS3nn. Therefore, a large acceleration with the LA coordination is found for the catalyzed process as a consequence of the enhancement in electrophilicity of 4 and 5 relative to 1. These en-

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### Table 2

<table>
<thead>
<tr>
<th>$E\Delta E/\text{E}_{\text{total}}$</th>
<th>$\text{E}_{\text{total}}$</th>
<th>$\Delta E_{\text{total}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>−730.611835</td>
</tr>
<tr>
<td>TS1np</td>
<td>−730.575479</td>
<td>22.5</td>
</tr>
<tr>
<td>TS1xp</td>
<td>−730.573138</td>
<td>24.3</td>
</tr>
<tr>
<td>CAp</td>
<td>−730.656873</td>
<td>28.3</td>
</tr>
<tr>
<td>TS1nm</td>
<td>−730.576022</td>
<td>22.8</td>
</tr>
<tr>
<td>TS1xm</td>
<td>−730.573125</td>
<td>24.3</td>
</tr>
<tr>
<td>CAm</td>
<td>−730.656347</td>
<td>27.9</td>
</tr>
</tbody>
</table>

*a* Energy values relative to the separated reagents.
energy barriers show that the coordination of BF₃ to the carbonyl O₉ oxygen at 4 is more favored than coordination at the carbonyl O₇ oxygen in 5, in good agreement with the larger electrophilicity activation predicted for the LA complex 4 than that for the LA complex 5. The effect of the LA catalyst is therefore revealed at the transition state structure. For instance, in the energy profile, complex 4 appears 5.9 kcal/mol below complex 5. These energy results indicate that the reactive channels via TS₂np and TS₂nm are favored over those via TS₃np and TS₃nm. For the SnCl₄ catalyzed DA reaction, the two endo regioisomeric channels were studied. The activation barriers are 14.7 kcal/mol for TS₄np and 13.1 kcal/mol for TS₄nm. A change of the regioselectivity is found with the 2-endo transition states (see Table 2).

As expected, a solvent polar effect will stabilize more effectively the TSs when this structure presents a polar character. Therefore, for the LA-catalyzed DA reactions solvent effects produce a large acceleration as a consequence of a larger stabilization of the polar TSs than reagents. These results are a consequence of the increase in the electrophilicity of the corresponding LA complex. This behavior allows explaining the large acceleration observed in these polar DA reactions.

The geometries, lengths of the forming bonds and bond order of the TSs associated with the DA reaction of the BF₃ LA complexes 4 and 5 and SnCl₄ LA complex 6 with the diene 2 are shown in Fig. 2. The extents of the asynchronousity on bond-formation at the TSs are 0.74 at TS₂np, 0.64 at TS₂nm, 0.68 at TS₃np, 0.80 at TS₃nm, 0.80 at TS₄np and 0.83 at TS₄nm. These large values point to highly asynchronous TSs associated with two-center additions. These results indicate that these TSs correspond to highly asynchronous bond-formation processes.

Finally, the CT at the TSs associated to the LA-catalyzed DA reactions are 0.33 at TS₂np, 0.34e at TS₃np and 0.39e at TS₄np, for the meta TSs, the calculated CT are 0.30e at TS₂nm, 0.37e at TS₃nm and 0.41e at TS₄nm. These values indicate that these structures have a large zwitterionic character. Coordination of the LAs to the benzoquinone 1 results in a large increase of the CT at the TSs as a consequence of the increase in electrophilicity of the corresponding LA complex. This behavior allows explaining the large acceleration observed in these polar DA reactions.

As these LA-catalyzed DA reactions have a polar character, and solvent can stabilize some species, solvent effects by dichloromethane were considered by means of single point energy calculations on the gas-phase optimized geometries using the PCM method [31]. Several studies devoted to polar DA reactions have indicated that the inclusion of solvent effects on the geometry optimization produce only minor changes relative to the gas-phase calculations [5,6]. The total and relative energies in dichloromethane are given in Tables 2 and 3, respectively. For the DA reaction between the benzoquinone 1 and 2-methylbutadiene 2 the decrease in activation barrier is only 0.5 kcal/mol. This marginal solvent effect on the activation barriers may be traced to the low polarity of the TSs (see Table 2).

<table>
<thead>
<tr>
<th>Reaction</th>
<th>E₄ antidepressant energy (E in a.u.), relative energy (ΔE in kcal/mol), in vacuum and in dichloromethane, of the stationary points for the DA reactions of 2-methyl-1,4-benzoquinone in presence of LA 4, 5 and 6 with the 2-methyl-1,3-butadiene 2.</th>
</tr>
</thead>
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<tr>
<td>4 + 2</td>
<td>-1055.185649 (E) - 1055.203572 (ΔE) - 1055.250675 (ΔE relative to the separated reagents)</td>
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<tr>
<td>TS₂np</td>
<td>-1055.163413 (E) - 1055.183829 (ΔE) - 1055.230675 (ΔE relative to the separated reagents)</td>
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<tr>
<td>CA₂p</td>
<td>-1055.233921 (E) - 1055.233921 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>TS₂nm</td>
<td>-1055.163904 (E) - 1055.183511 (ΔE) - 1055.230675 (ΔE relative to the separated reagents)</td>
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<tr>
<td>CA₂m</td>
<td>-1055.233687 (E) - 1055.250541 (ΔE) - 1055.233687 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>5 + 2</td>
<td>-1055.176265 (E) - 1055.189476 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>TS₃np</td>
<td>-1055.151012 (E) - 1055.173768 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>CA₃p</td>
<td>-1055.221488 (E) - 1055.233921 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>TS₃nm</td>
<td>-1055.150779 (E) - 1055.172713 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
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<tr>
<td>CA₃m</td>
<td>-1055.221788 (E) - 1055.233921 (ΔE) - 1055.233921 (ΔE relative to the separated reagents)</td>
</tr>
<tr>
<td>6 + 2</td>
<td>-2574.925740 (E) - 2574.947337 (ΔE) - 2574.925740 (ΔE relative to the separated reagents)</td>
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<td>TS₄np</td>
<td>-2574.902321 (E) - 2574.928543 (ΔE) - 2574.925740 (ΔE relative to the separated reagents)</td>
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<tr>
<td>CA₄p</td>
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<td>TS₄nm</td>
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<td>CA₄m</td>
<td>-2574.968763 (E) - 2574.986988 (ΔE) - 2574.925740 (ΔE relative to the separated reagents)</td>
</tr>
</tbody>
</table>

a Energy values relative to the separated reagents.

Fig. 2. Geometries of endo transition states of the DA reactions between 2-methoxy-5-methyl-1,4-benzoquinone with BF₃ OEt2 as LA 4, 5 and with SnCl₄ as LA 6 and 2-methyl-1,3-butadiene 2. The imaginary frequencies are given in cm⁻¹ and bond distances in Å units. Bond order values are given in parenthesis.
tivity, in clear agreement with the experimental result. In dichloromethane, TS2np is 0.2 kcal/mol lesser in energy than TS2nm as a consequence of a large solvation of the former. Note that even through in dichloromethane the activation barrier associated with TS3np, 9.8 kcal/mol, is lower than that for TS2np, 12.8 kcal/mol, the larger stability of complex 4 compared to complex 5, –8.9 kcal/mol, causes the reaction channel to follow the pathway through TS3np. This result is in agreement with the Curtin–Hammett principle [37].

In summary in dichloromethane the BF3 catalyzed DA reaction presents a low para regioselectivity. However, the SnCl4 catalyzed DA reaction presents a large meta selectivity. An inversion of the regioselectivity with respect the BF3 catalyzed process is found in good agreement with the experimental results.

4. Concluding remarks

The mechanisms of the Diels–Alder reactions of 2-methoxy-5-methyl-1,4-benzoquinone 1 with 2-methyl-1,3-butadiene 2, in the absence and in the presence of LA catalysts have been studied using DFT method at the B3LYP/6-31G(d) level of theory. For the uncatalyzed reaction both endo/exo stereo and para/meta regioselectivity channels have been studied. These DA reactions take place via synchronous concerted TSs. The larger activation barrier associated with the uncatalyzed process is in good agreement with the non-polar character of the cycloaddition. The uncatalyzed reaction presents a low regioselectivity. Coordination of the LA catalysts, BF3 or SnCl4, to the oxygen atoms of the benzoquinone 1 produces a large acceleration of the reaction, which can be associated with a larger polar character of the cycloadduct. The uncatalyzed reaction presents a low regioselectivity. Coordination of the LA catalysts, BF3 or SnCl4, to the oxygen atoms of the benzoquinone 1 allows explaining the reverse para/meta regioselectivity observed in these LA-catalyzed DA reactions.

The theoretical results obtained may thus provide a useful tool for the interpretation of the reaction mechanisms. The analysis based on the electrophilicity index of reagents correctly explains the polar nature of the LA-catalyzed DA reactions. The strong electrophilic character of LA complexes of the methoxybenzoquinone 1 accounts for the larger acceleration found in these DA reactions. Finally, the analysis based on the local electrophilicity index at the LA complexes allows explaining the reverse regioselectivity experimentally observed in the presence of the BF3 and SnCl4 LA catalysts. Solvent effects are consistently predicted as marginal in the uncatalyzed mechanism because the non-polar character of the TSs. On the other hand, significant solvent effects on the reaction barriers are consistently predicted for polar TSs induced by the presence of LA catalysts. The polarity of the LA coordinated TSs in turn display high values of electrophilicity index difference.

Acknowledgments

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References

[16] Despite the polar character of DA reaction of quinones, the incorporation of polarized and diffuse functions with 6-31+G(d,p) basis set produce an increase in the activation energies and a decrease in the exothermic character of these reactions. On the other hand, it does not substantially modify the selectivities. See Ref. [15].