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Understanding the stereo- and regioselectivities of the polar Diels–Alder reactions between 2-acetyl-1,4-benzoquinone and methyl substituted 1,3-butadienes: a DFT study

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The polar Diels–Alder (DA) reactions of 2-acetyl-1,4-benzoquinone (acBQ) with methyl substituted 1,3-butadienes have been studied using DFT methods at the B3LYP/6-31G(d) level of theory. These reactions are characterized by a nucleophilic attack of the unsubstituted ends of the 1,3-dienes to the β conjugated position of the acBQ followed by ring-closure. The reactions present a total regioselectivity and large *endo* selectivity. The analysis based on the global electrophilicity of the reagents at the ground state, and the natural bond orbital (NBO) population analysis at the transition states correctly explain the polar nature of these cycloadditions. The large electrophilic character of acBQ is responsible for the acceleration observed in these polar DA reactions. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: polar Diels–Alder reactions; benzoquinones; electrophilicity; transitions states

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.[1,2] In this process, a 1,3-diene reacts with an olefinic or acetylenic dienophile to form a six-membered 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 presence of electron-withdrawing substituents in the dienophile and electron-releasing subtituents in the diene or vice versa can drastically accelerate the process. Furthermore, this type of substitution favors an asynchronous concerted mechanism.[3–6] In addition, adequate substitution on the diene and dienophile, which can favor the stabilization of charges of opposite signs, can give a stepwise mechanism with a large polar character.[7] Therefore, the molecular mechanism of these polar DA reactions are borderline between a highly asynchronous concerted mechanism and a stepwise process with a large polar character.

The use of quinones as dienophile component in DA reactions provides access to a range of biologically active natural products.[8] In this context, the 2-acetyl-1,4-benzoquinone (acBQ) **1** has been used as an electron-deficient quinone in a wide variety of methodological syntheses.[9–11] On the other hand, this compound has been used as an efficient dienophile in DA reactions to afford policyclic systems. The most remarkable property of this quinone is its high selectivity to build tri- and tetracyclic linear and angularly fused compounds. These structures are part of the fundamental skeleton of natural products and biologically actives compounds.[12–14] On the other hand, the DA reaction of acBQ **1** with unsymmetrical methyl substituted dienes takes place with a high yield[15,16] to form a unique cycloadduct. For these cases, the selectivity is related to two regioisomeric channels: the *ortho* and *meta* channels for 1,3-pentadiene **3**, and the *meta* and *para* channels for 2-methyl-1,3-butadiene **4** (refer Scheme 1).

For polar DA reactions two mechanisms have been characterized: one corresponding to a one-step process through a highly asynchronous transition structure (TS),[17–21] and other corresponding to a two-step mechanism via a zwitterionic intermediate.[22,23] These studies point out a relationship between the decrease of the activation barrier of the cycloaddition and the charge transfer (CT) along an asynchronous bond-formation process. Thus, the increase of the electron-rich character of the diene (the nucleophile) together with the increase of the electron-poor character of the

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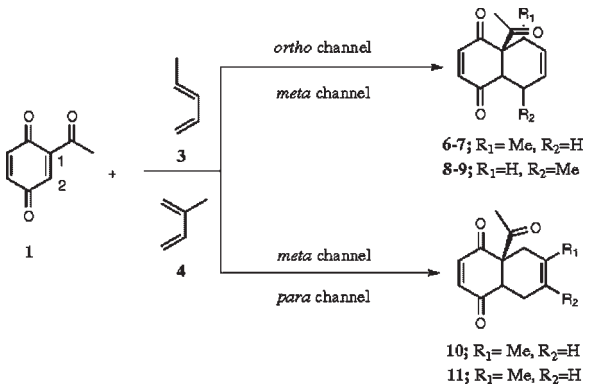


Scheme 1. Regioisomeric channels of the DA reaction between 2-acetyl-1,4-benzoquinone **1** and the methyl substituted 1,3-butadienes **3** and **4**

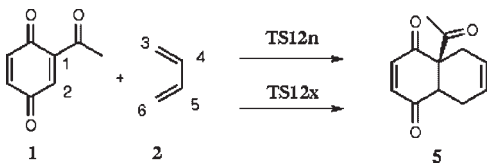
ethylene derivative (the electrophile), or vice versa, results in an increase of the CT and a decrease of the activation barrier.

The global electrophilicity index ω proposed by Parr *et al.*[24] has been used to classify the dienes and dienophiles currently used in DA reactions within a unique scale of electrophilicity.[25,26] A good correlation between the difference in electrophilicity of the diene and dienophile pair, $\Delta\omega$, and the feasibility of the cycloaddition was found. In addition, the static CT model proposed by Pearson[27,28] gave a good correlation with the actual CT found at the corresponding highly asynchronous TSs.[25] 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,[29] ω_k, 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,[30] f_k^-, allow the identification of the most electrophilic and nucleophilic centers in the reactants, respectively.[29]

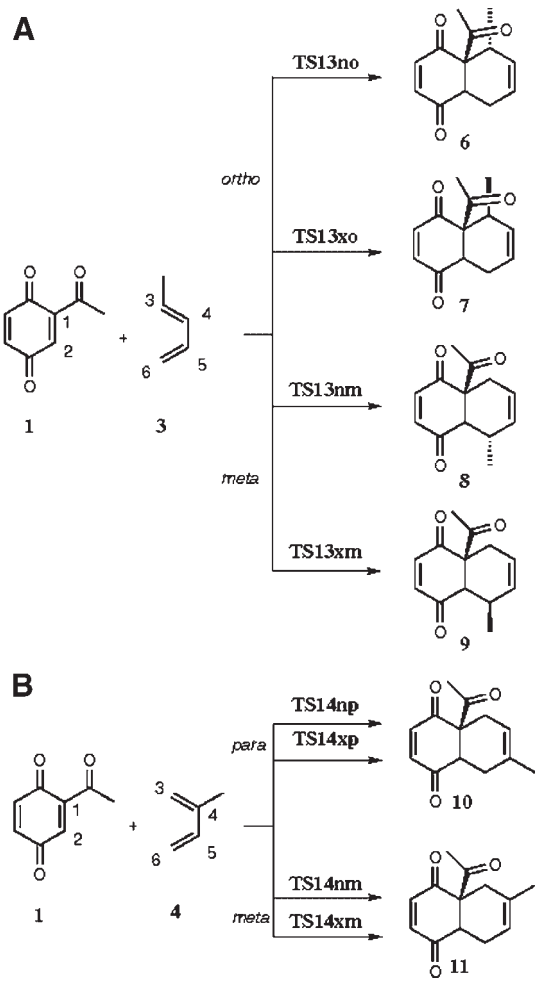
In this work, we present a theoretical study on the mechanisms of the polar DA reactions of acBQ **1** with 1,3-butadiene **2** (refer Scheme 2), with 1,3-pentadiene **3**, and 2-methyl-1,3-butadiene **4** (refer Scheme 3). Firstly, an analysis of the reactivity indices of the reagents was performed in order to establish the polar character and the regioselectivity of these cycloadditions. Then, the mechanisms of DA reactions between **1** and the dienes **2**–**4** will be analyzed. The purpose of our work is to contribute to a better understanding of the high reactivity and selectivity displayed by acBQ **1** in these polar DA reactions and to shed some light on the mechanistic details of these polar cycloadditions.

COMPUTATIONAL DETAILS

DFT calculations were carried out using the B3LYP[31,32] exchange-correlation functional, together with the standard



Scheme 2. Stereoisomeric channels of the DA reaction between 2-acetyl-1,4-benzoquinone **1** and 1,3-butadiene **2**



Scheme 3. Stereo- and regioisomeric reactive channels of the DA reactions between 2-acetyl-1,4-benzoquinone **1** and (a) 1,3-pentadiene **3** and (b) 2-methyl-1,3-butadiene **4**

6-31G(d) basis set.[33] Since some species involved in these DA reactions have some zwitterionic character, the effects of the diffuse functions on the energies were analyzed by using the 6-31+G(d,p) basis set[33] for the reaction between acBQ **1** and **2**. The optimizations were carried out using the Berny analytical gradient optimization method.[34,35] The intrinsic reaction coordinate (IRC)[36] path was traced to check the energy profiles connecting each TS to the two associated minima of the proposed mechanism by using the second-order González–Schlegel integration method.[37,38] All calculations were carried out with the Gaussian 03 suite of programs.[39] The stationary points were characterized by frequency calculations. The electronic structures of TSs were analyzed in term of the bond orders (BOs), Wiberg indexes,[40] and the natural charges obtained from the natural bond orbital (NBO) method[41,42] 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.[43–46] Several studied devoted to polar DA reactions have indicted that the inclusion of solvent effects on the geometry optimization produce minor changes relative to the gas-phase calculations.[21,47] Since the solvent is usually toluene, we used a dielectric constant value $\varepsilon = 2.37$.

Global reactivity indexes such as the electronic chemical potential, μ, chemical hardness, η, and electrophilicity ω, were approximated in terms of the one electron HOMO and LUMO energies, ε_H and ε_L, using the expressions $\mu \approx (\varepsilon_H + \varepsilon_L)/2$ and $\eta \approx (\varepsilon_L - \varepsilon_H)$ and $\omega = \mu 2/2\eta$, respectively, at the ground state of the molecules.[48,49] The local electrophilicity,[29] ω_k, condensed to atom k is easily obtained by projecting the global quantity onto any atomic center k in the molecule by using the electrophilic Fukui function, f_k^+,[30] and the expression $\omega_k = \omega f_k^+$.

RESULTS AND DISCUSSION

Global and local electrophilicity analysis

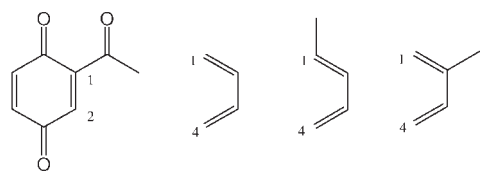
The DA reactions between acBQ **1** and the dienes **2**–**4** have been analyzed using reactivity indexes defined in the context of conceptual DFT.[50,51] Recent studies devoted to DA reactions have shown that the global indexes are a powerful tool to understand the behavior of the polar cycloadditions.[25,26] In Table 1, we report the static global and local properties, namely electronic chemical potential μ, chemical hardness η, and global electrophilicity ω, fukui functions and local electrophilicity ω_k for the acBQ **1** and the dienes **2**–**4**.

The electronic chemical potential of 1,3-butadiene **2** ($\mu = -0.1257$ au), 1,3-pentadiene **3** ($\mu = -0.1164$ au), and 2-methyl-1,3-butadiene **4** ($\mu = -0.1226$ au) are higher than the electronic chemical potential of acBQ **1** ($\mu = -0.2042$ au), thereby indicating that along a polar DA reaction, the net CT will take place from the dienes **2**–**4** toward **1**, in qualitative agreement with the CT analysis performed at the TSs (*vide infra*).

The acBQ **1** has an electrophilicity of 4.64 eV, and therefore it may be classified as a strong electrophile.[25,26] On the other hand, the electrophilicity values of the dienes **2**–**4** are 1.04, 0.91, and 0.98 eV, respectively; values that fall within the range of moderate electrophiles within the ω scale.[25,26] Inclusion of an electron-releasing methyl group on the diene system decreases slightly the electrophilcity of 1,3-butadiene **2**. This trend accounts for the increase of the nucleophilic character of the diene system by methyl substitution. The high $\Delta\omega$ value for these DA reactions indicates that they will have a high polar character (*vide infra*).

Recent studies devoted to cycloadditions with a large polar character have shown that the analysis based on the local electrophilicity ω_k[29] at the electrophilic reagent and the nucleophilic fukui function f_k^- at the nucleophilic allows one to explain the regioselectivity experimentally observed.[47] The analysis of local electrophilicity on acBQ **1** indicates that the C2 positions is the more electrophilic center of the molecule ($\omega_{C2} = 0.64$ eV) in good agreement with the regioselectivity experimentally observed.[15,16] The dienes present high nucleophilicity at the positions where the fukui function f_k^- present its higher values. For instance, 1,3-pentadiene **3** has the larger nucleophilic activation at C4, $f_k^- = 0.309$, and 2-methyl-1,3-butadiene **4** at the C1, $f_k^- = 0.380$, thereby indicating that these positions are the most reactive sites for nucleophilic attack.

Table 1. Electronic chemical potential μ (in au), chemical hardness η (in au), and global electrophilicity ω (in eV)



1 **2** **3** **4**

	μ	η	ω		f_k^+	f_k^-	ω_k
1	−0.2042	0.1222	4.64	1	0.108	0.080	0.50
				2	0.138	0.011	0.64
2	−0.1257	0.2064	1.04	1	0.322	0.338	0.33
				4	0.322	0.338	0.33
3	−0.1164	0.2024	0.91	1	0.302	0.296	0.28
				4	0.321	0.309	0.30
4	−0.1226	0.2069	0.98	1	0.304	0.380	0.31
				4	0.341	0.289	0.35

Nucleophilic Fukui function f_k^-, electrophilic Fukui function f_k^+ are dimensionless quantities; local electrophilicity ω_k (in eV).

Study of the Diels–Alder reactions between acBQ 1 and the dienes 2–4

Energy aspects

The DA reaction between acBQ **1** and 1,3-butadiene **2** can take place along two stereoisomeric reactive channels: the *endo* and *exo* approach modes. An analysis of the stationary point found on the potential energy surface (PES) for these cycloadditions indicates that these DA reactions are asynchronous concerted C—C bond-formation processes. Therefore, two TSs, **TS12n** and **TS12x**, associated with the two stereoisomeric reactive channels and one cycloadduct, **5**, were located and characterized (refer Scheme 2). Note that the *endo* and *exo* stereoisomeric reactive channels yield the same stereoisomeric [4+2] cycloadduct **5**. The total and relative energies corresponding to the stationary points associated with these reaction channels are summarized in Table 2.

The B3LYP/6-31G(d) activation barriers associated with the two stereoisomeric channels are 13.1 kcal/mol for **TS12n** and 14.2 kcal/mol for **TS12x**. The *endo* approach mode is favored by 1.1 kcal/mol with respect to the *exo* adduct. The activation barrier associated with *endo* channel is 9.3 kcal/mol lower than that associated with the DA reaction between 1,3-butadiene + ethylene;[52] as a consequence of the large electrophilic character of acBQ **1**. Formation of the cycloadduct **5** is exothermic by −29.9 kcal/mol.

Table 2 reports the B3LYP/6-31+G(d,p) total and relatives energies for the DA reaction between **1** and **2**. The incorporation of diffuse functions produces an increase in the activation barriers and a decrease of the exothermic character of these DA reactions about 2 and 9 kcal/mol, respectively. On the other hand, inclusion of diffuse functions does not substantially modify the *endo* selectivity. Therefore, despite the polar character of these cycloadditions, we can conclude that the inclusion of diffuse functions does not modify substantially the 6-31G(d) results. A similar trend is found for the DA reaction between **2** and ethylene where the inclusion of diffuse functions at 6-31+G(d,p) level raises the relative energy of the TS and cycloadduct in 2.5 and 5.6 kcal/mol, respectively. Note that for this DA reaction, the

Table 2. B3LYP with different basis sets. The total energies (E in au), relative[a] energies (ΔE in kcal/mol), in vacuum and in toluene, for the stationary points of the DA reaction of 2-acetyl-1,4-benzoquinone **1** with 1,3-butadiene **2**

	6-31G(d)				6-31+G(d,p)	
	E	ΔE	E_{sol}	ΔE_{sol}	E	ΔE
1 + 2	−690.085237		−690.092497		−690.135542	
TS12n	−690.064412	13.1	−690.072464	12.6	−690.111331	15.2
TS12x	−690.062595	14.2	−690.070429	13.8	−690.109764	16.2
5	−690.132900	−29.9	−690.139499	−29.5	−690.169331	−21.2

[a] Energy values relative to the separated reagents.

computed B3LYP/6-31G(d) activation barrier and the reaction enthalpies are in reasonable agreement with the experimental values.[52]

Due to the low symmetry of acBQ **1** and the methyl substituted dienes **3** and **4** four reactive channels are feasible. They are related to the *endo* and *exo* stereoisomeric channels and the two regioisomeric channels: the *ortho* and *meta* channels for 1,3-pentadiene **3**, and the *para* and *meta* channels for 2-methyl-1,3-butadiene **4**. An exhaustive exploration of the PES for these DA reactions indicates that they are associated with highly asynchronous C—C bond-formation processes. Four TSs and the corresponding [4+2] cycloadducts associated with the four reactive channels of the DA reactions of acBQ **1** with the dienes **3** and **4** were located and characterized (as shown in Scheme 3). Note that while the stereoisomeric channels associated with the DA reactions of **1** with **3** give a pair of diastereomeric [4+2] cycloadducts as a consequence of the formation of an additional asymmetric C3 center, the *endo* and *exo* stereoisomeric channels associated with the DA reactions of **1** with **4** give the same stereoisomeric [4+2] cycloadduct. The total and relative energies corresponding to the stationary points associated with these reaction channels are summarized in Table 3.

The activation barriers associated with the reactions between acBQ **1** and 1,3-pentadiene **3** are 9.5 kcal/mol for **TS13no**, 11.3 kcal/mol for **TS13xo**, 14.8 kcal/mol for **TS13nm**, and 16.9 kcal/mol for **TS13xm**. These energy results indicate that the *endo* approaches are 1.8 and 2.1 kcal/mol more favorable than the *exo* ones. In addition, the *ortho* channels are 5.3 and 5.6 kcal/mol more favorable than the *meta* ones. Therefore, the DA reaction between **1** and **3** presents a complete *ortho* regioselectivity and a large *endo* stereoselectivity. Furthermore, the activation barrier for the more favorable *endo*/*ortho* channel via **TS13no** is 3.6 kcal/mol lower in energy than that associated with the DA reaction between **1** and **2** via **TS12n**. This result may be traced to the higher nucleophilicity displayed by the methyl substituted diene **3** as compared to 1,3-butadiene **2**. These results are in reasonably good agreement with the observed selectivities. All of these DA reactions are highly exothermic:

Table 3. B3LYP/6-31G(d) total energies (E in au), relative[a] energies (ΔE in kcal/mol), in vacuum and in toluene, of the stationary points for the DA reactions of 2-acetyl-1,4-benzoquinone **1** with the methyl substituted 1,3-butadienes **3** and **4**

	E	ΔE	E_{sol}	ΔE_{sol}
1 + 3	−729.405349		−729.412663	
TS13no	−729.390256	9.5	−729.398016	9.2
TS13xo	−729.387275	11.3	−729.391621	13.2
6	−729.442867	−23.5	−729.449030	−22.8
7	−729.439093	−21.2	−729.445442	−20.6
TS13nm	−729.381716	14.8	−729.388984	14.9
TS13xm	−729.378261	16.9	−729.374325	24.1
8	−729.434087	−18.1	−729.440137	−17.2
9	−729.443976	−24.4	−729.450274	−23.6
1 + 4	−729.403543		−729.410570	
TS14np	−729.385084	11.6	−729.392573	11.3
TS14xp	−729.383689	12.5	−729.390746	12.4
10	−729.445834	−26.5	−729.451392	−25.6
TS14nm	−729.382435	13.2	−729.390170	12.8
TS14xm	−729.382221	13.4	−729.389499	13.2
11	−729.452812	−30.9	−729.459768	−30.9

[a] Energy values relative to the separated reagents.

between −18.1 and −24.4 kcal/mol. Inclusion of diffuse functions on the optimization of the *endo* TSs shows also minor changes on the regioselectivity; at the B3LYP/6-31+G(d,p) level **TS13no** is 5.9 kcal/mol less energetic than **TS13nxo**.[53]

For the DA reactions between acBQ **1** and 2-methyl-1,3-butadiene **4** the activation barriers associated with the cycloaddition processes are 11.6 kcal/mol for **TS14np**, 12.5 kcal/mol for **TS14xp**, 13.2 kcal/mol for **TS14nm**, and 13.4 kcal/mol for **TS14xm**. As in the case of the DA reactions between **1** and **3**, these energy results show that the more favorable reactive channel corresponds to the *endo/para* approach mode of acBQ **1** to the diene **4**, via **TS14np**. Both stereo- and regioselectivity are lower than those observed for the reactions between **1** and **3**. As a result, a more complex reaction mixture is expected. These energy results indicate that both selectivities increase with the polar character of the cycloaddition (*vide infra*), that is with the nucleophilic character of the diene. These DA reactions are also highly exothermic: −26.5 kcal/mol (**10**) and −30.9 kcal/mol (**11**).

As these DA reactions have a polar character, and solvent can stabilize some species, solvent effects of toluene were considered by means of single point energy calculations on the gas-phase optimized geometries using the PCM method.[41,42] The total and relative energies in toluene are given in Tables 2 and 3. As expected, solvent effects stabilize more effectively the TSs than reagents due to their zwitterionic character. The decrease in activation energy amounts is 0.5 kcal/mol to the DA reaction between acBQ **1** and 1,3-butadiene **2**. These marginal solvent effects on the activation barriers may be traced to the low polarity of toluene. However, at the DA reaction between **1** and **3** the solvent effects increase the stereo- and regiochemistry as a consequence of the large stabilization of the more favorable TSs. Consequently, in toluene this DA reaction presents a complete *endo/ortho* selectivity. Finally, as in the case of the DA reaction between **1** and **2**, solvent effects are predicted to have a low incidence on the activation barriers and selectivities of the DA reaction between **1** and **4** (as shown in Table 3).

Geometries and electronic structures of the transitions states

The geometries of the TSs associated with the DA reaction between acBQ **1** and 1,3-butadiene **2** are given in Fig. 1. The lengths of the C1—C3 and C2—C6 forming bonds at the TSs are 2.694 and 1.975 Å at **TS12n**, and 2.904 and 1.969 Å at **TS12x**, respectively. The extent of the synchronicity 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, that is, $\Delta d = d(\text{C2—C6}) - d(\text{C1—C3})$. The calculated values are 0.71 at **TS12n** and 0.93 at **TS12x**, thereby suggesting that they correspond to high asynchronous C—C bond-formation processes. The C2—C6 forming bond at the conjugated C2 position of acBQ **1** is being formed to a larger extent, probably as a consequence of the large electrophilic activation of the C2 position of acBQ **1**. The more unfavorable **TS12x** is more asynchronous than **TS12n**.

The geometries of the TSs associated with the DA reaction between acBQ **1** and 1,3-pentadiene **3** are given in Fig. 2. The lengths of the C1—C3 and C2—C6 forming bonds at the TSs associated to the *ortho* channels are 2.885 and 1.973 at **TS13no**, and 2.925 and 2.014 Å at **TS13xo**, respectively. For the TSs associated to the *meta* channels the length C2—C3 and C1—C6 forming bonds are 2.489 and 2.016 Å at **TS13nm** and 2.482 and 2,046 Å at **TS13xm**, respectively. The extent of the asynchronicity on the bond formation at the TS structures, 0.91 at **TS13no**, 0.93 Å at **TS2xo**, 0.47 Å at **TS13nm**, and 0.43 Å at **TS13xm**, indicates that the TSs associated with the more favorable *ortho* approaches are more asynchronous than those associated with the *meta* ones.

The analysis of the IRC path from **TS13no** to the cycloadduct **6** indicates that the more favorable *endo/ortho* reactive channel has a *two-stage* mechanism.[54] On going from the TS to cycloadduct, the reaction progresses with the unique formation of the C1—C3 bond, and only when it is completely formed, begins the C2—C6 bond formation. Therefore, the increase of the nucleophilic character of 1,3-pentadiene **3** does not only reduce the activation barrier for **TS13no**, but also changes the mechanism from a asynchronous concerted to a *two-sage* mechanism. Note that the more unfavorable *meta* regioisomeric channels have concerted mechanisms.

Finally, the geometries of the TSs associated with the DA reaction of acBQ **1** and 2-methyl-1,3-butadiene **4** are shown in Fig. 3. The lengths of the C1—C3 and C2—C6 forming bonds at the *para* TSs are 2.802 and 1.984 Å at **TS14np**, and 3.032 and

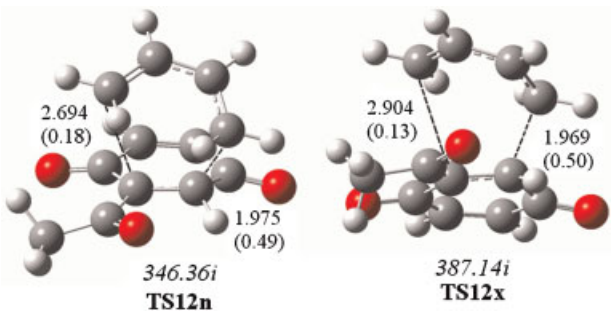


Figure 1. Geometries of transition states of the DA reaction between 2-acetyl-1,4-benzoquinone **1** and 1,3-butadiene **2**. The imaginary frequencies are given in cm^{-1} and bond distances in Å units. Bond order values are given in parenthesis

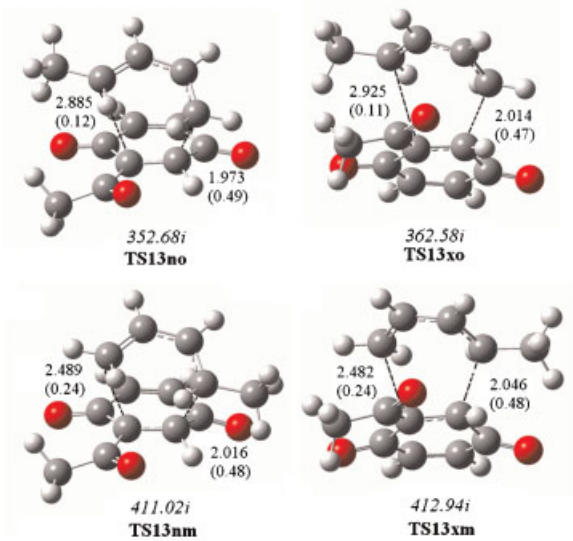


Figure 2. Geometries of transition states of the DA reactions between 2-acetyl-1,4-benzoquinone **1** and 1,3-pentadiene **3**. The imaginary frequencies are given in cm^{-1} and bond distances in Å units. Bond order values are given in parenthesis

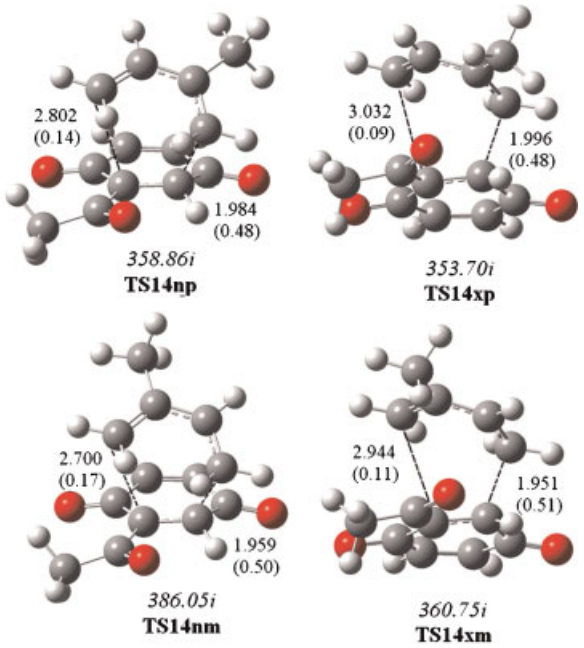


Figure 3. Geometries of transition states of the DA reactions between 2-acetyl-1,4-benzoquinone **1** and 2-methyl-1,3-butadiene **4**. The imaginary frequencies are given in cm^{-1} and bond distances in Å units. Bond order values are given in parenthesis

1.996 Å at **TS14xp**, respectively, while for the *meta* TSs the length of C2—C3 and C1—C6 forming bonds are 2.700 and 1.959 Å at **TS14nm** and 2.944 and 1.951 Å at **TS14xm**, respectively. The extent of the asynchronicity on bond formation at the *para* TSs are 0.85 at **TS14np** and 1.03 at **TS14xp**, while for the *meta* TSs these values are 0.74 at **TS14nm** and 0.99 at **TS14xm**. These results indicate that these TSs also correspond to highly asynchronous bond-formation processes.

The extent of bond formation along a reaction pathway may be assessed by the BO[39] index. At the TSs associated with the DA reaction between **1** and **2**, the BO values for the C1—C3 and C2—C6 forming bonds are: 0.18 and 0.49 at **TS12n** and 0.13 and 0.50 at **TS12x**, respectively.

At the *ortho* TSs associated with the DA reaction between **1** and **3**, the BO values of the C1—C3 and C2—C6 forming bonds are 0.12 and 0.49 at **TS13no** and 0.11 and 0.47 at **TS13xo**, respectively, while at *meta* TSs the BO values of the C1—C6 and C2—C3 forming bonds are 0.24 and 0.48 at **TS13nm** and **TS13xm**, respectively.

Finally, At the *para* TSs associated with the DA reaction between **1** and **4**, the BO values of the C1—C3 and C2—C6 forming bonds are 0.14 and 0.48 at **TS14np** and 0.09 and 0.48 at **TS14xp**, respectively, while for the *meta* TSs the BO values of the C1—C6 and C2—C3 forming bonds are 0.17 and 0.50 at **TS14nm** and 0.11 and 0.51 at **TS14xm**.

These BO values indicate that at these asynchronous processes, the C—C bond formation at the C2 position of acBQ **1** is more advanced than that at the C1 position. This behavior may be traced to the large electrophilic activation of the C2 position of acBQ **1**, which corresponds with the β conjugated position of the acetyl susbtituent. The natural population analysis (NPA) allows us to evaluate the CT along these cycloadditions. The natural charges at the TSs appear shared between the electron acceptor acBQ **1** and the electron donor butadienes **2**–**4**. At **TS12n** and **TS12x**, the CT from the diene **2** to **1** is 0.29 and 0.28 e, respectively. These values indicate that these structures may have some zwitterionic character. These values are larger than those obtained at the TS associated with the DA reaction between butadiene/acroleyn, 0.11 e;[24] a result that may traced again to the larger electrophilicity of acBQ **1**. At the TSs of the DA reaction between **1** and **3** the CT from the diene **3** to **1** is 0.34 e at **TS13no**, 0.32 e at **TS13xo**, 0.29 e at **TS13nm**, and 0.28 e at **TS13xm**. At the TSs associated to the more favorable *ortho* reactive channels the CT is slightly larger that at the *meta* TSs. This behavior accounts for the larger solvation of the *ortho* TSs, and consequently the increase of the regioselectivity in toluene. At the more favorable *ortho* TSs the CT is slightly larger than that at **TS12n**, as a consequence of the larger nucleophilic character of 1,3-pentadiene **3** as compared to 1,3-butadiene **2**. At the TSs of the DA reaction between **1** and **4**, the CT from the diene **4** to **1** is 0.31 e at **TS14np** and 0.29 e at **TS14xp**, **TS14nm**, and **TS14xm**. The CT at the more favorable **TS14np** is slightly lower that that at **TS13no**.

At the more favorable reactive channel of these DA reactions, the increase of the CT at the corresponding TS, **TS12n** (0.28 e) < **TS14nm** (0.29 e) < **TS13no** (0.34 e), results in a decrease of the activation barrier of the cycloaddition, **TS12n** (13.1 kcal/mol) > **TS14nm** (11.6 kcal/mol) > **TS13no** (9.5 kcal/mol). This behavior can be related to the increase of the polar character of the DA reaction as a consequence of the increase of the nucleophilic character of the corresponding diene, **2** < **4** < **3**.

Note that at the more favorable regioisomeric channels of these DA reactions, the CT at the lesser energetic *endo* TSs is slightly larger than at the *exo* ones; that is the process is slightly more polar. However, the *endo* TSs are slightly less asynchronous than the *exo* ones as a consequence of the shortening of the C1—C3 distance. This behavior can be related to the favorable coulumbic interactions that appear between the opposite charged fragments at the more favorable zwitterionic *endo* TS that stabilized the electronic energies relative to the *exo* ones. Note that at the *endo* TSs, the positively charged diene framework is located over the negatively charge benzoquinone moiety, while at the *exo* ones, they are far apart. These charge interactions appear to be responsible for the larger CT found at the *endo* TSs, and for the *endo* selectivity found in these polar DA reactions.

CONCLUDING REMARKS

The mechanisms of the polar DA reaction of acBQ with 1,3-butadiene and with two unsymmetrical methyl substituted 1,3-butadienes have been studied using DFT methods at the B3LYP/6-31G(d) level of theory. Both *endo*/*exo* stereo- and regioselectivity have been studied. The theoretical results obtained may thus provide a useful tool for the interpretation of the experimental findings and a useful guide for understanding the mechanism of other analogous reactions involving electron-deficient quinones with electron-rich dienes. The analysis based on the electrophilicity index of the reagents correctly explains the polar nature of these cycloaddition reactions. The strong electrophilic character of acBQ is responsible for the large acceleration found in these polar DA reactions. We have found that these reactions are characterized by a nucleophilic attack type of the end of the dienes to the β conjugated position of acBQ with concomitant ring-closure. These DA reactions present a total

regioselectivity and large *endo* selectivity. No significant solvent effects by toluene were found. Finally, despite the polar character of these DA reactions, the inclusion of diffuse functions at the 6-31+G(d,p) level does not improve the relative energies obtained with the standard 6-31G(d) basis set.

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