Understanding the mechanism of polar Diels–Alder reactions

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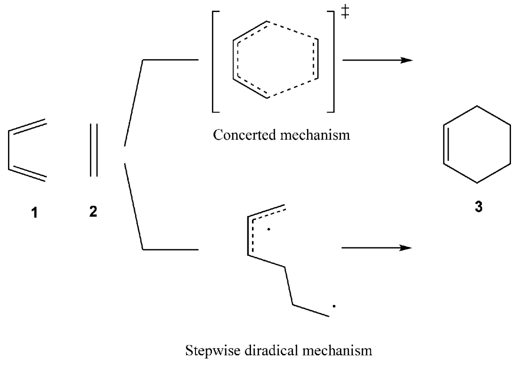
Received 15th May 2009, Accepted 12th June 2009
First published as an Advance Article on the web 10th July 2009
DOI: 10.1039/b909611f

A good correlation between the activation energy and the polar character of Diels–Alder reactions measured as the charge transfer at the transition state structure has been found. This electronic parameter controls the reaction rate to an even greater extent than other recognized structural features. The proposed polar mechanism, which is characterized by the electrophilic/nucleophilic interactions at the transition state structure, can be easily predicted by analyzing the electrophilicity/nucleophilicity indices defined within the conceptual density functional theory. Due to the significance of the polarity of the reaction, Diels–Alder reactions should be classified as non-polar (*N*), polar (*P*), and ionic (*I*).

I. Introduction

The Diels–Alder (DA) reaction is arguably one of the most powerful reactions in the arsenal of the synthetic organic chemist.[1] By varying the nature of the diene and dienophile, many different types of carbocyclic structures can be built up. However, not all possibilities occur easily. For instance, the DA reaction between butadiene (**1**) and ethylene (**2**) must be forced to take place: after 17 hours at 165 °C and 900 atmospheres, it gives a 78% yield.[2] Nevertheless, the presence of electron-withdrawing groups in the dienophile and electron-releasing groups in the diene or *vice versa* can drastically accelerate the process.[3]

The actual mechanism of DA reactions has been the subject of controversy for some time.[4] The archetypal DA reaction of butadiene (**1**) and ethylene (**2**) is exothermic by 40 kcal/mol and has a reaction barrier of 27.5 kcal/mol.[5] It may occur either through a synchronous concerted mechanism associated with a pericyclic process or through a stepwise mechanism involving the formation of diradical intermediates,[4] although both mechanisms are very unfavorable (see Scheme 1). In general, for DA reactions to be reasonably fast, the electronic features on the substituents at the diene and the dienophile should be opposite. This type of substitution favors an asynchronous concerted mechanism; thus, adequate substitution on the diene and dienophile, which can favor the stabilization of charges of the opposite sign, can produce a stepwise mechanism with highly polar character.[3] Therefore, the electronic features of both reagents play a central role in the development of the reaction.



Scheme 1

For many years our group has studied the molecular mechanism of DA reactions.[6–7] The results of these studies indicate that there is *a direct relationship between the decrease of the cycloaddition activation barrier and the charge transfer (CT) throughout a non-synchronous bond-formation process*.[7] Thus, the increase of the electron-rich character of the diene (the nucleophilicity), together with the increase of the electron-deficient character of the dienophile (the electrophilicity), or *vice versa*, results in an enhancement of the CT that is accompanied by a lowering of the activation barrier.[7]

Recently, we have performed a theoretical study[8] on the polar DA reactions between cyclopentadiene (**4**) and the series of cyanoethylenes **5–10** which had been studied experimentally by Sauer.[9] In this series of DA reactions, for which experimental kinetic data is available,[9] a clear relationship between the observed acceleration rate and the polar character of the DA reaction was established (see Table 1). A very good correlation (R^2 = 0.99) between the CT at the B3LYP/6-31G* transition state structure (TS) and the logarithm of the experimental rate constant is shown in Fig. 1. Both experimental[9] and theoretical[8] studies indicated that, while the largest acceleration caused by the cyano group substitution corresponds to the DA reaction between cyclopentadiene (Cp) and the unsymmetrical substituted 1,1-diacyanoethylene (**8**), the fastest reaction is that between Cp and

Table 1 Experimental rate constants (k) and CT (in e) at the TSs associated with the Diels–Alder reactions of Cp (**4**) with ethylene (**2**) and with the cyanoethylene series **5–10**

	k [M^{-1} s^{-1}]^a	CT^b
Ethylene (**2**)	10^{-5}	0.03
Acrylonitrile (**5**)	1.04	0.15
trans-1,2-Dicyanoethylene (**6**)	81	0.24
cis-1,2-Dicyanoethylene (**7**)	91	0.25
1,1-Dicyanoethylene (**8**)	4.5×10^4	0.28
Tricyanoethylene (**9**)	4.8×10^5	0.36
Tetracyanoethylene (**10**)	4.3×10^7	0.43

[a] Ref. 9 [b] Ref. 8

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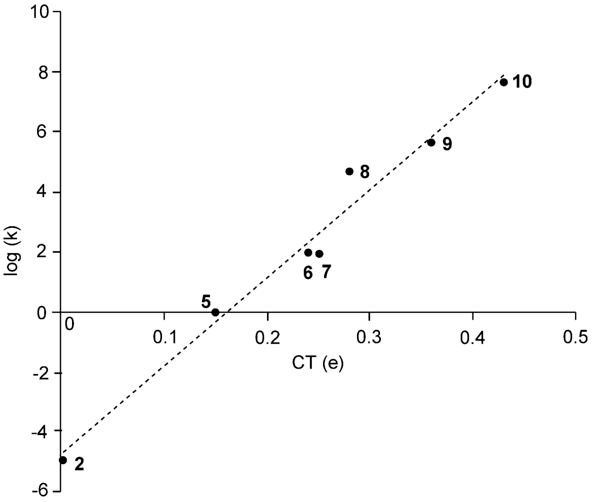
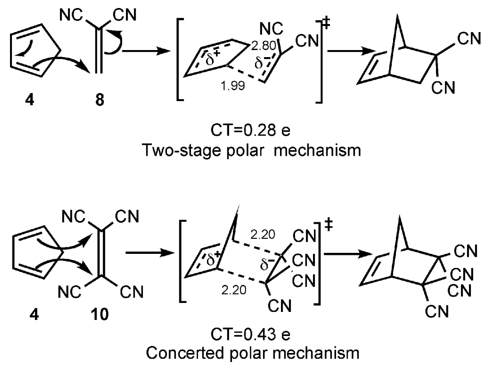


Fig. 1 Plot of the logarithm of the experimental rate constant *vs.* the charge transfer (CT), $R^2 = 0.99$, for the Diels–Alder reactions of Cp (**4**) with ethylene (**2**) and with the cyanoethylene series **5–10**.

tetracyanoethylene (**10**), which is the most electrophilic species of this series (see Table 1). Interestingly, while the reaction with 1,1-diacyanoethylene (**8**) takes place through a highly asynchronous TS associated with a *two-stage* mechanism,[10] the reaction with tetracyanoethylene (**10**) takes place through a synchronous concerted TS that geometrically resembles that of the butadiene (**1**)/ethylene (**2**) reaction (see Scheme 2). We thus concluded that *the synchronicity of the bond-formation process cannot be related with reaction rate*.[8]

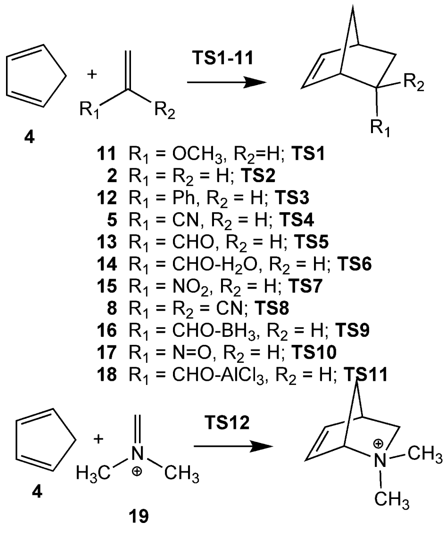


Scheme 2

Few years ago, Domingo, in collaboration with Contreras and Perez, initiated a series of studies devoted to the application of the reactivity indices defined within the conceptual density functional theory (DFT)[11] to the study of polar cycloadditions. The initial goal was to correlate the global electrophilicity index proposed by Parr,[12] ω, with the activation barriers of the polar DA reactions studied previously in our laboratory. Thus, they classified for the first time the common dienes and dienophiles involved in DA reactions in a unique electrophilicity scale.[13] The $\Delta\omega$ of the diene/dienophile pairs was proposed as a measure of the polar character of the reactions.[13] We have very recently introduced a simple empirical (relative) nucleophilicity index, N,[14] based on the HOMO energies obtained within the Kohn–Sham scheme.[15] Current studies of polar cycloadditions, including the participation of quadricyclane as a nucleophile in polar [2σ+2σ+2π] cycloadditions,[10b] indicated that the index N aptly characterizes the nucleophilic behavior of organic molecules.

In the polar model, the DA reactions are characterized by the dominant electrophile–nucleophile interaction.[13] In these reactions, the progress of the CT throughout the cycloaddition and, therefore, the latter's feasibility, is well established once the nucleophilic and electrophilic behaviors of the reagents involved in the reaction have been identified by their position within the electrophilicity scale.[13] In this reactivity model, the regioselectivity is clearly rationalized by the most favorable polar interaction between the most highly electrophilic center of the electrophile and the most highly nucleophilic center of the nucleophile during a two-center interaction. The local descriptors, namely the local electrophilicity index[16] (ω_k) and the local nucleophilicity index[17] (N_k), aid in the characterization of these relevant sites in a molecule.

This paper is our latest comparative study of the DA reactions between Cp and a series of twelve substituted ethylenes with different levels of electronic activation (see Scheme 3). Some of them have already been studied separately[18,19] and represent a wide sample of experimental DA reactions. It is worth noting that no previous studies[19] have stressed the relevance of the polar character of these DA reactions, and, in consequence, they have not examined Cp and these ethylene derivatives as nucleophiles and electrophiles interacting in a polar reaction. The aim of the present study is to emphasize the high correlation found between the activation barriers associated with these significant organic reactions and the polar character of the TSs, and to state also the electronic reorganization along the polar DA reactions.



Scheme 3

II. Computational and theoretical methods

DFT calculations were carried out with the B3LYP[20] exchange-correlation functional, together with the standard 6-31G* basis set.[21] This level of theory has been shown to be suitable for the analysis of both geometric and electronic properties of DA reactions.[11b] The optimizations were carried out with the Berny analytical gradient optimization method.[22] The stationary points were characterized with the aid of frequency calculations in order to verify that the TSs had one and only one imaginary frequency. The CT at the TSs were analyzed with the Natural Bond Order (NBO) method.[23] All calculations were carried out with the Gaussian 03 suite of programs.[24]

The global electrophilicity index,[12] 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:

$$\omega = (\mu^2/2\eta)\ \text{(eV)}$$

in terms of the electronic chemical potential μ and the chemical hardness η. Both quantities may be calculated in terms of one of the electron HOMO and LUMO energies, ε_H and ε_L, as $\mu \approx (\varepsilon_H + \varepsilon_L)/2$ and $\eta \approx (\varepsilon_L - \varepsilon_H)$, respectively.[25] Recently, we introduced an empirical (relative) nucleophilicity index, N, based on the HOMO energies obtained within the Kohn–Sham scheme[15] and defined as:[14]

$$N = E_{\text{HOMO(Nu)}} - E_{\text{HOMO}(\mathbf{10})}\ \text{(eV)}.$$

This nucleophilicity scale takes tetracyanoethylene **10** as a reference. This choice allows us to handle a nucleophilicity scale with only positive values.[14]

Concepts like electronic chemical potential, global and local electrophilicity indices and nucleophilic Fukui functions have started to be introduced in modern texts of organic chemistry,[26] and therefore they are expected to be incorporated into the current language of the organic chemistry community.

III. Results and discussion

Firstly, we performed an analysis of the energies, geometries, and electronic structures of the TSs involved in the selected DA reactions. After that, an analysis of the global reactivity indices at the ground state (GS) of the reagents was carried out.

III.1 Mechanistic study of the DA reactions between Cp and the series of selected ethylene derivatives

In order to identify the more relevant behaviors of polar DA reactions, we first performed a comparative study of the mechanistic details of this type of reaction between Cp and a series of selected ethylene derivatives of increasing electrophilicity (see Scheme 3). For the $CH_2{=}CHR$ unsymmetrically substituted ethylenes, two stereoisomeric approach modes to the diene system of Cp are feasible: the *endo* and the *exo* modes. For the present mechanistic study, we considered only the *endo* reactive channel. In addition, some cycloaddition reactions afford isomeric [4 + 2], [2 + 4],[27] and even [4 + 3][28] cycloadducts, but due to thermodynamic considerations, we focused on the formation of the corresponding formally [4 + 2] cycloadducts. An exhaustive exploration of the potential energy surface (PES) of these DA reactions indicates that they are one-step reactions ranging from a concerted mechanism for the DA reaction of Cp (**8**) with ethylene (**2**) to the *two-stage* mechanism[10] of the most of the polar cycloadditions.

III.1.1 Energies. The total and relative energies of the stationary points involved in the DA reactions between Cp and the series of ethylene derivatives are given in Table 2. The activation barriers ($\Delta E^{\#}$) range from 22.0 kcal/mol for the least favorable DA reaction between Cp and the electron-rich methyl vinyl ether (**11**), to −5.1 kcal/mol for the most favorable DA reaction between Cp and the iminium cation **19**. Such a wide range of $\Delta E^{\#}$ values (27 kcal/mol) is interesting by itself, but several of the values even deserve further examination. The DA reaction between Cp and ethylene **2**, for example, has a $\Delta E^{\#} = 19.9$ kcal/mol. This value, which is only *ca.* 4 kcal/mol lower than that for the butadiene (**1**)/ethylene (**2**) DA reaction,[4a] indicates that this DA reaction should take place under drastic experimental conditions (high temperatures and/or pressures). Note that this high activation energy together with the unfavorable activation entropy associated with the bimolecular process, $\Delta S^{\#} = -44.8$ eu, arise the free activation energy $\Delta G^{\#}$ for the Cp/ethylene DA reaction to 40.0 kcal/mol (150 °C). Likewise, the inclusion of a phenyl group on the ethylene moiety does not favor the DA reaction between Cp and styrene (**12**), which has a $\Delta E^{\#} = 20.7$ kcal/mol.

Table 2 Total[a] (E, in au) and relative energies (ΔE, in kcal/mol) of the stationary points involved in the Diels–Alder reactions of Cp (**4**) with the substituted ethylene series. CT (in e) is the charge transfer at the corresponding TSs

Reagents		TSs				Cycloadducts	
No.	E	No.	E	ΔE	CT	E	ΔE
11	−193.110421	**TS1**	−387.176463	22.0	−0.05	−387.243704	−20.2
2	−78.587457	**TS2**[8,19a,c]	−272.656774	19.9	0.03	−272.727382	−24.4
12	−309.648259	**TS3**[19b]	−503.716295	20.7	0.06	−503.776348	−17.0
5	−170.831550	**TS4**[8,19e,d]	−364.906426	16.4	0.15	−364.967787	−22.1
13	−191.911974	**TS5**[19d]	−385.987062	16.3	0.15	−386.042653	−18.6
14	−268.334996	**TS6**	−462.414536	13.5	0.20	−462.465441	−18.4
15	−283.087910	**TS7**	−477.169714	12.1	0.20	−477.228297	−24.7
8	−263.062684	**TS8**[8,19a]	−457.148957	9.3	0.28	−457.195379	−19.8
16	−218.557189	**TS9**	−412.641800	10.3	0.26	−412.688367	−18.9
17	−207.872878	**TS10**	−401.964921	5.7	0.20	−402.011728	−23.7
18	−1815.198008	**TS11**	−2009.295849	2.0	0.37	−2009.330496	−19.7
19	−173.623137	**TS12**[18]	−367.732355	-5.1	0.45	−367.760228	−22.6

[a] The total energy of Cp (**8**) is-194.101064 au.

The most unfavorable DA reaction is that between Cp and the electron-rich ethylene **11**, which has a $\Delta E^{\#}$ value of 22.0 kcal/mol. This result can be explained by the poor capability of Cp to act as an electrophile (see below). Therefore, the lone substitution on the diene[29] or dienophile by one electron-releasing group is unfavorable for DA reactions.

The inclusion of an electron-withdrawing group like -CN or -CHO in ethylene has a remarkable effect on the activation barriers of the DA reactions between Cp and both acrylonitrile (**5**) ($\Delta E^{\#}$ = 16.4 kcal/mol) and acrolein (**13**) ($\Delta E^{\#}$ = 16.3 kcal/mol). An even more remarkable effect is produced by the inclusion of a second electron-withdrawing -CN group in 1,1-dicyanoethylene (**8**), which decreases the $\Delta E^{\#}$ value to 9.3 kcal/mol.[8,19a]

A similar acceleration is found when a Lewis acid (LA) coordinates to the carbonyl oxygen atom of acrolein, decreasing the $\Delta E^{\#}$ of the catalyzed DA reactions to 10.3 (Cp/**16**) and 2.0 (Cp/**18**) kcal/mol.[30] These results, which illustrate the greater LA potential of $AlCl_3$ over BH_3, are in clear agreement with the increase of the electrophilicity of the corresponding complexes (see below).[31] It is worth noting that in the DA reaction between Cp and the acrolein·H_2O complex (**14**) a reduction of the activation energy by *ca.* 3 kcal/mol occurs with the hydrogen-bond formation. This is most likely related to the increased polar character of the reaction.[32]

Finally, for the DA reaction between Cp and the iminium cation **19**, **TS12** is located −5.1 kcal/mol below the reagents.[18,33] Note that the analysis of the PES of this reaction shows the presence of a molecular complex located below reagents and TS and, in consequence, this reaction presents a positive activation barrier.[18,33] As this cycloaddition involves cationic species, this particular reaction should be classified as an ionic DA (*I*-DA) reaction. Interestingly, the majority of the reported [4 + 2^+] DA reactions are referred to as "polar [4 + 2^+] Diels–Alder cycloadditions".[34] Our goal is to distinguish *polar DA reactions*, which merely present a charge separation during the cycloaddition reaction, from *I-DA reactions*, in which the ionic character of the reagents remains the same throughout the cycloaddition. It is worth noting that there are also *I*-DA reactions promoted by anionic species,[35] but they are quite unusual. Unlike cationic DA reactions, these reactions require the counterpart reagent to have some electrophilic character so that an efficient charge delocalization can occur during the cycloaddition.

All these DA reactions are exothermic processes. The corresponding [4 + 2] cycloadducts are located between −18.4 and −24.7 kcal/mol below the reagents. Therefore, the electronic characteristics of the dienophiles have a greater influence over the kinetic parameters, with $\Delta E^{\#}$ values falling within a 27 kcal/mol range, than over thermodynamic parameters, with ΔE_r values in a 7 kcal/mol range.

III.1.2 Geometries. The geometries of the TSs involved in these DA reactions are given in Fig. 2. Only the DA reaction between Cp and ethylene (**2**), **TS2**, presents a synchronous bond-formation process. The synchronicity of the process is broken by the unsymmetric substitution of ethylene, with the shorter lengths corresponding to the bond-formation at the β-conjugated position of the electrophilically activated ethylenes.

The extent of the synchronicity of the bond-formation can be measured as the difference between the lengths of the two σ bonds formed in the reaction, *i.e.*, Δd = dist1 − dist2. The asynchronicity ranges from Δd = 0.0 for the DA reaction of Cp (**4**) with ethylene (**2**) up to Δd = 1.17 for the DA reaction of Cp (**4**) with the iminium cation **19**. Although there is not a strict linear relationship between asynchronicity and the polar character of the reaction, an increase in the polar character of the reaction seems to be accompanied by an increase in its asynchronicity.

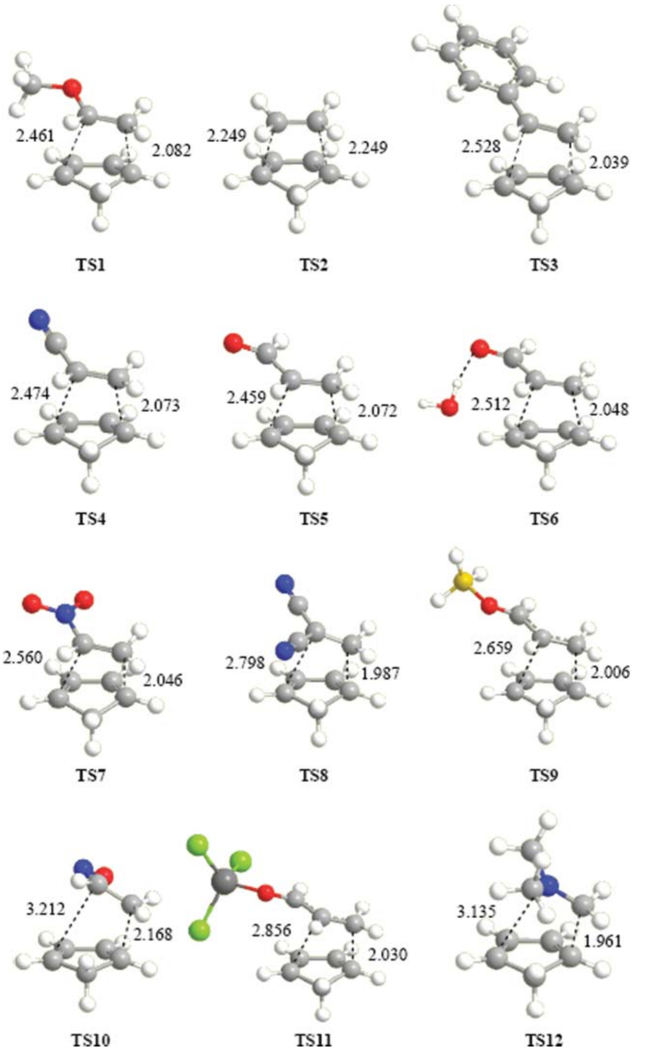


Fig. 2 Geometries of the transition structures involved in the Diels–Alder reactions of Cp (**4**) and the substituted ethylene series. The distances are given in Å.

At the highly asynchronous TSs, *e.g.* $\Delta d > 0.5$, the analysis of the IRC from the TSs to the cycloadducts indicates that such cycloadditions have a *two-stage* mechanism.[10] At the first stage of the reaction, a C–C bond is formed through a nucleophilic/electrophilic interaction. These TSs are associated with a two-center interaction. After the first C–C bond is formed, the formation of the second C–C bond begins, thus initiating the second stage of the reaction. Stabilizing factors for a feasible zwitterionic intermediate, including charge delocalization[33] or solvent effects,[6c,32] may change the *two-stage* mechanism into a stepwise one.

III.1.3 CT analysis of the TSs. The polar character of the DA reactions has been related to the CT at the corresponding

TS.[7] The natural charges at the TSs are shared between the Cp fragment and that of the ethylene derivative. The charges at the Cp fragments are given in Table 2. In the DA reaction between Cp and ethylene **2**, the CT at the TS is 0.03 e (**TS2**), a very low value which indicates that this reaction has a non-polar character. Inclusion of a phenyl group in styrene (**12**) does not substantially modify the non-polar character of the DA reaction, which has a CT = 0.06 e (**TS3**). On the other hand, the presence of an electron-releasing methoxy group on methyl vinyl ether (**11**) does not increase the CT as a consequence of the low electrophilic character of Cp (CT = –0.05 e) (**TS1**). The sign of the charge at the Cp framework of **TS1** indicates an inversion of the flux of the electron density, which in this case goes from the electron-rich ethylene **11** to Cp. In spite of the nucleophilic character of vinyl ether **11**, the poor electrophilic character of Cp leads to this low value (see below). A clear increase of the CT from Cp to the electron-deficient ethylene series was found for the rest of the DA reactions, in which the CT increased from 0.15 e at **TS4** to 0.45 e at **TS12**.

Fig. 3 shows a significant linear correlation ($R^2 = 0.89$) between the CT at the TSs and the calculated activation barriers associated with these DA reactions. This finding supports the observation that an increase in the CT at the TSs (*i.e.*, an increase in the polar character of the cycloaddition) is accompanied by an acceleration of the reactions. Looking at this figure, we can see that the non-polar DA reactions are located at the top left region while the ionic DA reactions are in the lower right region. The feasibility of a DA reaction can thus be foreseen by predicting the polar character of the process that is, by taking into account the electrophilic/nucleophilic character of the reagents (see below). Note that *I*-DA reactions, in which one of the reagents is a cation or anion, have the most polar mechanism, thus presenting the largest CT at the TS involved in the DA reaction.

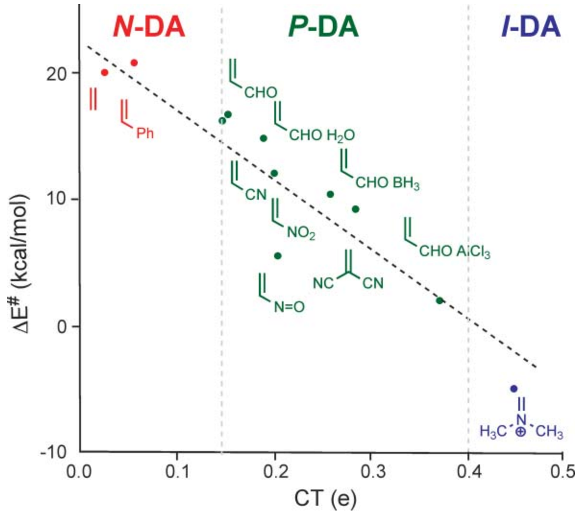
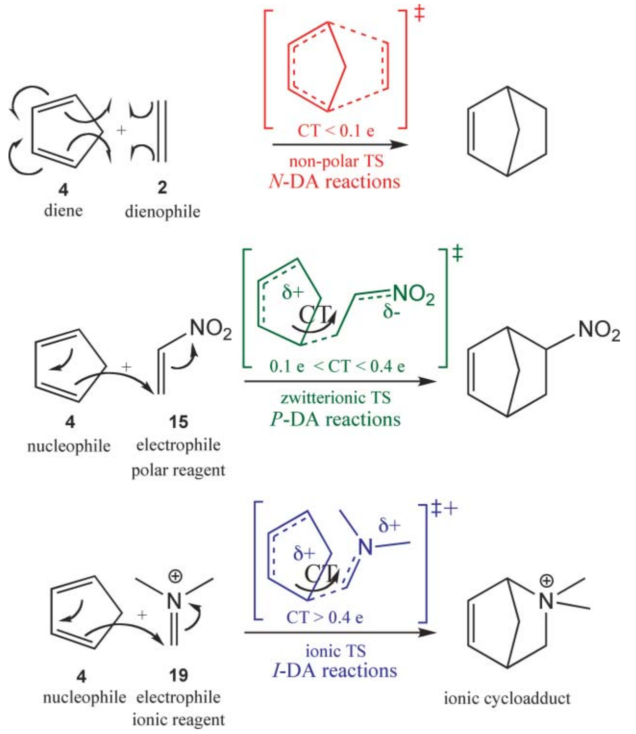


Fig. 3 Plot of the activation barriers ($\Delta E^{\#}$) *vs.* the charge transfer (CT), $R^2 = 0.89$, for the Diels–Alder reactions of Cp (**4**) with the substituted ethylene series.

Fig. 3 shows the distinguishing features of three types of DA reactions: a) those with a non-polar character (CT < 0.15 e and $\Delta E^{\#}$ higher than 18 kcal/mol), referred as *N*-DA reactions; b) those with a polar character (0.15 e < CT < 0.40 e and $\Delta E^{\#}$ ranging from 17 to 5 kcal/mol), called *P*-DA reactions, and those with an ionic character (CT > 0.40 e and negative $\Delta E^{\#}$), named *I*-DA reactions. Note that the reactions with a CT *ca.* 0.15 e are located at the borderline between *N*-DA and *P*-DA reactions, but they represent a reduced group of DA reactions. Most of the *P*-DA reactions have a CT >0.20 e with an activation barrier <15 kcal/mol. A schematic representation of examples of each of these DA reaction modes is given in Scheme 4, in which the electron movement throughout the cycloaddition is shown with arrows. While the *N*-DA reaction between Cp and ethylene presents a symmetric movement with a radical character,[36] the *P*-DA and *I*-DA reactions present an asymmetric electron movement, which is associated with nucleophilic/electrophilic two-center interactions. In Scheme 4, the arrows plotted are intended to show the electron density changes along the first part of the reaction. Note that the half-arrows used in the *N*-DA emphasise the homolytic π break-bond required to achieve the formation of the two new σ bonds.[36] This picture for the *N*-DA reactions diverges from that proposed in the pericyclic mechanism, in which all bonds are made or broken around a circle. It is interesting to note that at the *P*-DA reactions, which have *two-stage* mechanisms, after the first C–C bond is formed there is a back-donation process during the ring closure. It should be noted that concepts as non-polar and polar DA reactions are widely used in the literature.



Scheme 4

III.2 Analysis of the global reactivity indices at the GS of Cp and the ethylene derivative series

Recent studies carried out on DA reactions have shown that the reactivity indices defined within the conceptual DFT[11] are powerful tools for establishing the polar character of such reactions.[13] Table 3 shows the static global properties, which include electronic chemical potential (μ), chemical hardness (η),

Table 3 Electronic chemical potential, μ, chemical hardness, η, global electrophilicity, ω, and global nucleophilicity, N, for Cp (**4**), 1,3-butadiene (**1**), ethylene (**2**), the iminium cation (**19**) and the substituted ethylene series

	μ/au	η/au	ω/eV	N/eV
Strong electrophiles				
19	−0.4107	0.2780	8.25	−5.84
18	−0.2190	0.1412	4.62	1.24
17	−0.1673	0.1163	3.28	2.98
16	−0.1887	0.1516	3.20	1.92
8	−0.2074	0.2075	2.82	0.65
15	−0.1958	0.2001	2.61	1.07
14	−0.1722	0.1929	2.09	1.81
13	−0.1611	0.1921	1.84	2.12
5	−0.1728	0.2329	1.74	1.25
Moderate electrophiles				
12	−0.1261	0.1911	1.13	3.09
1	−0.1270	0.2083	1.05	2.83
4	−0.1107	0.2016	0.83	3.37
Marginal electrophiles				
2	−0.1239	0.2855	0.73	1.86
11	−0.0902	0.2572	0.43	3.17

global electrophilicity (ω), and global nucleophilicity (N), of cyclopentadiene (**4**), ethylene (**2**), styrene (**12**), the electrophilically activated ethylene series, and the nucleophilically activated methyl vinyl ether (**11**).

Since the electronic chemical potential of cyclopentadiene (**4**) ($\mu = -0.1107$ au), is higher than those of the electron-deficient ethylenes, which range from −0.1270 to −0.4107 au, the net CT during a polar DA reaction will occur from Cp to the electron-deficient ethylenes. Our model further predicts that the DA reaction between Cp and the electron-rich dienophile **11**, for example, which has the lowest electronic chemical potential of this series ($\mu = -0.0902$ au), will present an inversion of the flux of electron density, which should go from **11** to Cp. Finally, the electronic chemical potential of ethylene **2** ($\mu = -0.1239$ au) is slightly lower than that of Cp. In this case, the very low CT during the cycloaddition will progress from Cp to **2**.

In Table 3, the reagents involved in this series of DA reactions have been listed in order of decreasing electrophilicity (ω) values.[13] Cp (**4**), which presents a low electrophilicity value of $\omega = 0.83$ eV, is thus classified as a moderate electrophile within the electrophilicity scale.[13] Indeed, Cp is located at the limit between the moderate and the marginal electrophiles (nucleophiles); therefore, it is probable that it could act as a nucleophile in polar DA reactions with strong electrophiles. This behavior is in agreement with the high nucleophilicity of Cp (**4**) ($N = 3.37$ eV). It should be noted that Cp is the best nucleophile of this series and that it has a higher nucleophilicity than 1,3-butadiene (**1**), which has $N = 2.83$ eV. Therefore, Cp should be more reactive as nucleophile than **1** in polar DA reactions, a hypothesis that is in clear agreement with the high reactivity experimentally observed for this reagent in DA reactions.

Ethylene (**2**) presents a low electrophilicity of $\omega = 0.73$ eV and is thus classified as a marginal electrophile within electrophilicity scale.[13] For this reason, the $\Delta\omega$ for the reaction Cp (**4**)/**2** has the very low value of 0.10 eV and is expected to have a non-polar character. Since ethylene (**2**) also has a low nucleophilicity value ($N = 1.86$ eV), it will be a poor nucleophile as well. In addition, inclusion of a phenyl group on the ethylene **12** produces a very low electrophilic activation. As a result, the DA reaction between Cp and styrene (**12**), which has a $\Delta\omega = 0.30$ eV, should have a very low polar character and, consequently, a high activation energy.[19b] On the other hand, due to the large nucleophilicity of styrene (**12**) ($N = 3.09$ eV), it should be able to act as a good nucleophile.

The electron-deficient substituted ethylenes have electrophilicity values ranging from 1.74 eV for acrylonitrile (**5**) to 8.25 eV for the iminium cation **19**. Several interesting conclusions can be drawn from these values. For example, inclusion of an electron-withdrawing group like -CN or -CHO increases the electrophilicity of acrylonitrile (**5**) and acrolein (**13**) to 1.74 and 1.84 eV, respectively. Therefore, their corresponding DA reactions should have a heightened polar character. The inclusion of a second electron-withdrawing -CN group on the 1-position of acrylonitrile (**5**) considerably increases the electrophilicity of 1,1-dicyanoethylene (**8**) to $\omega = 2.82$ eV. The $\Delta\omega$ of the DA reaction between Cp and **8** (1.99 eV) indicates that this reaction will have a highly polar character and, as a result, the reaction should experience a high acceleration.[8,19a] This prediction is in clear agreement with the experimental results.[9]

Hydrogen-bond formation between a water molecule and the carbonyl oxygen atom of acrolein (**13**) increases the electrophilicity of the acrolein·H_2O complex **14** to 2.09 eV. Recent DFT studies have shown that formation of non-classical[32,37] ($C{=}O\cdots H{-}C$) and classical[38] ($C{=}O\cdots H{-}O$) hydrogen-bonds to carbonyl compounds accelerate DA reactions through their conversion into more polar processes. This acceleration can thus be associated with the electrophilicity increase of the carbonyl compound as a result of the hydrogen-bond formation, which raises the polarity of the process.[31]

Coordination of a LA to the carbonyl oxygen atom of acrolein (**13**) produces a highly electrophilic activation in complexes **16** ($\omega = 3.20$ eV) and **18** ($\omega = 4.62$ eV). These values are in agreement with the LA character of $AlCl_3$, which is greater than that of BH_3.[31] Our reactivity model accurately accounts for the effects of the LA on the polar DA reactions. LA-catalyzed DA reactions experience a high acceleration as a consequence of the increase in the electrophilicity of the carbonyl compound, which favors the DA reaction through a more polar process.[28,30]

The ammonium cation **19** has the highest electrophilicity value ($\omega = 8.25$ eV). The corresponding DA reaction should thus have an ionic character and, as a result, the nucleophilic addition of Cp to **19** should have an insignificant activation barrier.[18]

The electron-rich methyl vinyl ether (**11**) has very low electrophilicity ($\omega = 0.43$ eV) and has been classified as a marginal electrophile within the electrophilicity scale.[13] Our model predicts that the DA reaction between Cp and **11** will have a low polar character and high activation energy. In addition, the electronic chemical potentials and electrophilicities of both Cp and the electron-rich ethylene **11** indicate that there will be an inversion of the electron flux, which in this case will go from **11** to Cp, with the latter acting as an electrophile. In spite of the low polar character of this DA reaction, an analysis of its electronic chemical potentials and electrophilicities aptly predicts the direction of the CT for this cycloaddition. Methyl vinyl ether (**11**) has a high nucleophilicity index ($N = 3.17$). This electron-rich ethylene has been used as an effective nucleophile in polar DA reactions with electron-deficient π molecules such as nitroethylene (**15**).[7] It is worth noting that Cp has a nucleophilicity index N similar to that of the vinyl derivative **11**; they are thus classified as strong nucleophiles.

Finally, a representation of the activation barriers ($\Delta E^{\#}$) with respect to the electrophilicity values of the corresponding substituted ethylenes is shown in Fig. 4. There is a good correlation between the increase of the electrophilicity of the ethylene derivative and the reduction of the activation barrier associated with these DA reactions ($R^2 = 0.92$). Therefore, the proposed classification can be related to the electrophilic character of the reagents, expressed as $\Delta\omega$. In the case of the series of DA reactions of Cp examined here, the classification is related to the electrophilicity of the substituted ethylene. The subgroup of *N*-DA reactions includes molecules with an electrophilicity lower than 1.2 eV while the subgroup of *P*-DA reactions includes molecules with an electrophilicity between 1.7 and 5.0 eV. Finally, the subgroup of *I*-DA reactions includes molecules with an electrophilicity higher than 5.0 eV. Note that the subgroups of *P*- and *I*-DA reactions include molecules classified as moderate and strong electrophiles within the electrophilicity scale.[13]

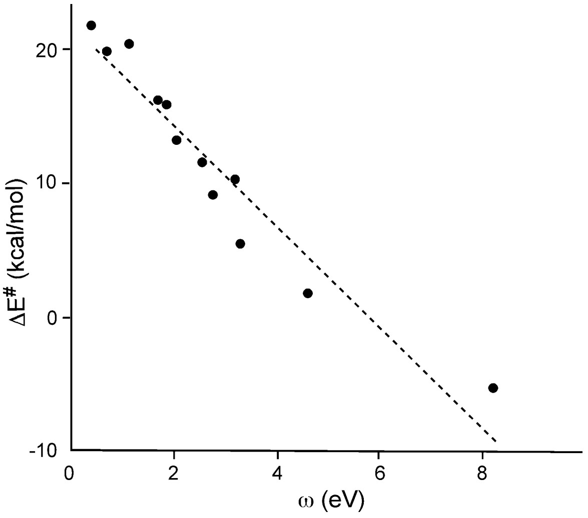


Fig. 4 Plot of the activation barriers ($\Delta E^{\#}$) *vs.* the electrophilicity index (ω) of the ethylenes, $R^2 = 0.92$, for the Diels–Alder reactions of Cp (**4**) with the substituted ethylene series.

IV. Concluding remarks

A good correlation between the activation energies of DA reactions and the polar character of the cycloaddition as measured by the charge transfer at the corresponding TSs has been established. This behavior can be accurately predicted analyzing the reactivity indices defined within the conceptual DFT at the ground state of the reagents. Our studies have shown that the polarity of the cycloaddition controls the reaction rates of this relevant chemical process to a greater extent than recognized structural features such as the asynchronicity of the bond formation, which represents the concerted or stepwise character of the mechanism.

In order to affirm this correlation, the electronic features of the TSs involved in the Diels–Alder reactions of cyclopentadiene with twelve substituted ethylenes of increasing electrophilicity, ω, were analyzed with the aid of DFT at the B3LYP/6-31G* level of theory. Based on the results obtained, the DA reactions should be classified into three separate groups: non-polar (*N*), polar (*P*), and ionic (*I*). Note that concepts as non-polar and polar DA reactions are being used in the modern literature. Analysis of the electrophilicity and nucleophilicity reactivity indices of the reagents clearly allows the classification of any given DA reaction into one of these groups. While the *N*-DA reactions require drastic experimental conditions, the increase in the polar character of the cycloaddition accelerates the *P*-DA reactions, allowing the reactions to take place at room temperature, and even at temperatures as low as −78 °C in the case of *I*-DA reactions or *P*-DA reactions involving strong electrophiles.

Acknowledgements

This work was supported with research funds provided by the Ministerio de Educación y Ciencia of the Spanish Government (project CTQ2006-14297/BQU).

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