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Quantitative characterization of the global electrophilicity power of common diene/dienophile pairs in Diels–Alder reactions

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Abstract—The global electrophilicity power, ω, of a series of dienes and dienophiles commonly used in Diels–Alder reactions may be conveniently classified within a unique relative scale. Useful information about the polarity of transition state structures expected for a given reaction may be obtained from the difference in the global electrophilicity power, $\Delta\omega$, of the diene/dienophile interacting pair. Thus the polarity of the process can be related with non-polar ($\Delta\omega$ small, pericyclic processes) and polar ($\Delta\omega$ big, ionic processes) mechanisms. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Organic reactions fall into one of the three general categories of processes that include polar, radical and pericyclic reactions.[1] In a bimolecular polar reaction, one component called the nucleophile provides a pair of electrons to the other, called the electrophile, to form a new bond.[1] The pericyclic processes on the other hand, shares the feature of having cyclic transition states, with a concerted movement of electrons simultaneously breaking and forming bonds. In the pericyclic reactions neither component may be associated with the supply of electrons to any of the new bonds formed during the concerted process. Within the wide variety of pericyclic processes well characterized in the Organic Chemistry literature, the cycloaddition reactions are the largest class. Cycloaddition reactions involve the approach of two components presenting a π system to form two new sigma bonds within a cyclic structure. The range of reactions, the stereochemistry, and regioselectivity present in these processes are by far the most abundant and useful of all pericyclic reactions.[1] Diels–Alder (DA) reactions are the largest family of cycloaddition processes. In a DA reaction one π component, named the dienophile, adds to a 1,3-diene system to afford a six-membered ring product. The usefulness of the DA reaction arises from its versatility and from its remarkable stereochemistry.[2,3] By varying the nature of the diene and dienophile many different types of carbocyclic structures can be built up. However, not all possibilities take place easily. For instance, the DA reaction between butadiene and ethylene must be forced to take place: after 17 h at 165°C and 900 atm, it does give a yield of 78%.[1,4–7] The presence of electron-releasing substituents in the diene and electron-withdrawing in the dienophile or vice versa can drastically accelerate the process.

The mechanism of the DA reaction has been controversial for some time.[8,9] The archetypal DA reaction of butadiene and ethylene is exothermic by 40 kcal/mol and has a reaction barrier of 27.5 kcal/mol.[10,11] It may occur via either a synchronous concerted mechanism along a pericyclic transition state or a stepwise mechanism involving the formation of diradical intermediates.[8] The butadiene+ethylene reaction, however, is not the typical case. In general, the DA reaction requires opposite electronic features in the substituents at the diene and the dienophile for being reasonably fast. Recent studies point out that this type of substitution on diene and dienophile favors the charge transfer along with an asynchronous mechanism.[12–16] Furthermore, the reaction mechanism changes progressively from a concerted, asynchronous to a polar stepwise pathway with increasing ability of the dienophile to stabilize a negative charge. Under suitable conditions, the intermediates of the stepwise process were trapped.[17] At this point the 1,3-diene and the ene systems clearly behave as an nucleophile/electrophile pair.

Recently, we have studied the mechanism of several DA reactions of pyrrole and furan derivatives, as electron-rich dienes, with acetylenes having electron-withdrawing

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Table 1. Global electrophilicity scale and global properties for some common reagents involved in DA reactions

Molecule		Global properties			
		ω	μ	η	$\Delta N_{\max}$
(I) *Strong electrophiles*					
1	*N*-Methylmethyleneammonium cation	8.97	−0.4348	0.2867	1.516
2	Tetracyanoethylene	5.96	−0.2586	0.1529	1.695
3	Hexafluorothioketone	4.77	−0.2122	0.1285	1.651
4	Maleic anhydride	3.24	−0.2082	0.1822	1.143
5	Acrolein–BH_3 complex	3.20	−0.1837	0.1516	1.245
6	1,1-Dicyanoethylene	2.82	−0.2074	0.2075	1.000
7	Nitroethylene	2.61	−0.1958	0.2001	0.979
8	Dimethyl acetylenedicarboxylate	2.27	−0.1831	0.2007	0.910
9	Dimethyl 2-methylenemalonate	1.93	−0.1703	0.2048	0.832
10	Acrolein	1.84	−0.1610	0.1922	0.838
11	Acrylonitrile	1.74	−0.1726	0.2329	0.740
12	Methyl vinyl ketone	1.65	−0.1524	0.1910	0.789
13	Methyl propiolate	1.52	−0.1624	0.2363	0.690
14	Methyl acrylate	1.51	−0.1586	0.2268	0.699
(II) *Moderate electrophiles*					
15	1-Acetoxy-1,3-butadiene	1.10	−0.1259	0.1957	0.643
16	1,3-Butadiene	1.05	−0.1270	0.2083	0.610
17	2-Methyl-1,3-butadiene	0.94	−0.1212	0.2120	0.572
18	(*E*)-1,3-Pentadiene	0.93	−0.1182	0.2037	0.580
19	2-Trimethylsilyloxy-1,3-butadiene	0.88	−0.1135	0.1999	0.568
20	*N*-Methylmethanimine	0.86	−0.1259	0.2504	0.503
21	4-Methyl-1,3-pentadiene	0.86	−0.1137	0.2048	0.560
22	Cyclopentadiene	0.83	−0.1106	0.2016	0.550
(III) *Marginal electrophiles (nucleophiles)*					
23	1-Methoxy-1,3-butadiene	0.77	−0.1028	0.1875	0.548
24	Ethylene	0.73	−0.1239	0.2855	0.430
25	1-Trimethylsilyloxy-1,3-butadiene	0.73	−0.1024	0.1958	0.523
26	Furan	0.59	−0.1024	0.2441	0.420
27	*N*,*N*-Dimethyl-1,3-butadien-1-amine	0.57	−0.0867	0.1801	0.481
28	Acetylene	0.54	−0.1148	0.3344	0.343
29	2-Methylfuran	0.52	−0.0946	0.2358	0.400
30	Methyl vinyl ether	0.42	−0.0894	0.2564	0.350
31	Pyrrole	0.31	−0.0753	0.2525	0.298
32	Dimethylvinylamine	0.27	−0.0680	0.2390	0.290

Global electrophilicity, ω, in eV; electronic chemical potential, μ, and chemical hardness, η, in au; and $\Delta N_{\max}$ in *e*. See the text for definitions.

substituents.[18–22] These studies point out a relationship between the increase of the reaction rate and the charge transfer along an asynchronous bond-formation process. Thus, the increase of the electron-rich character of diene, the nucleophilicity, together with the increase of the electron-poor character of the acetylene derivative, the electrophilicity, results in an increase in the charge transfer, with an enhancement of the reaction rate. This pattern, which is extensible to other DA reactions,[16,23–25] allows us to approach the reactivity of these activated cycloadditions in terms of the electrophilicity power displayed by the dienophile/diene pair. Thus, depending on the electrophilicity potential displayed by the dienophile/diene pairs, the mechanisms for these DA reactions will have a more or less marked polar character. This polarity pattern, which may be predicted from a static model based on the difference in electrophilicity power of the electrophile/nucleophile interacting pair, is expected to manifest itself at the transition state structures in the DA reactions.

In order to quantitatively establish the static electrophilicity power of the reagents participating in DA cycloaddition processes, it is therefore desirable to have an electrophilicity scale that can help in the design of the transition state structures involved in the mechanism of cycloaddition reactions. In this work, the global electrophilicity index recently proposed by Parr et al.[26] is used to classify the electrophilicity power of a series of dienophiles and dienes currently present in DA reactions. Some well-known DA reaction mechanisms are revisited and reinterpreted within the present model.

2. Global properties

Global electronic indexes, as defined within the density functional theory of Parr, Pearson and Yang[27,28] are useful tools to understand the reactivity of molecules in their ground states. For instance, the electronic chemical potential μ describing the changes in electronic energy with respect to the number of electrons is usually associated with the charge transfer ability of the system in its ground state geometry. It has been given a very simple operational formula in terms of the one electron energies of the frontier molecular orbital HOMO and LUMO, ε_H and ε_L, as[27]

$$\mu \approx \frac{\varepsilon_H + \varepsilon_L}{2} \tag{1}$$

Besides this index, it is also possible to give a quantitative representation to the chemical hardness concept introduced by Pearson,[28] which may be represented as[27]

$$\eta \approx \varepsilon_L - \varepsilon_H \quad (2)$$

Recently, Parr et al.[26] have introduced a new and useful definition of global electrophilicity, ω, which measures the stabilization in energy when the system acquires an additional electronic charge ΔN from the environment. The electrophilicity power has been given the following simple expression[26]:

$$\omega = \frac{\mu^2}{2\eta}; \quad (3)$$

in terms of the electronic chemical potential μ and the chemical hardness η, defined in Eqs. (1) and (2). The electrophilicity index encompasses both, the propensity of the electrophile to acquire an additional electronic charge driven by μ^2, and the resistance of the system to exchange electronic charge with the environment described by η, simultaneously. A high value of μ and a low value of η therefore characterize a good electrophile. On the other hand, the maximum amount of electronic charge that the electrophile system may accept is given by[26]

$$\Delta N_{\max} = -\frac{\mu}{\eta} \quad (4)$$

The ω index is a useful descriptor of reactivity that allows a quantitative classification of the global electrophilic character of a molecule within a relative scale.

3. Computational details

The global electrophilicity power for a series of the most common dienes and dienophiles systems quoted in Table 1 was evaluated using Eq. (3). The electronic chemical potential μ, and chemical hardness η were evaluated in terms of the one electron energies of the frontier molecular orbitals (FMO) HOMO and LUMO using the Eqs. (1) and (2), respectively, at the ground state (GS) of the molecules using the B3LYP/6-31G* level of theory,[29,30] implemented in the GAUSSIAN98 package of programs.[31] With these values, the global electrophilicities have been obtained via Eq. (3). The global maximum charge transfer towards the electrophile is evaluated using Eq. (4).

Finally, the TSs corresponding to the cycloaddition reaction between 1,3-butadiene and nine selected dienophiles of increasing electrophilicity have been studied using B3LYP/6-31G* calculations in order to estimate the polarity of the process, ΔN. This has been obtained from a natural bond orbital[32,33] (NBO) analysis at the TSs sharing the natural charges between the electron-donor 1,3-butadiene and the electron-acceptor dienophile.[21–25]

4. Results and discussion

4.1. Global electrophilicity scale

A wide series of reagents commonly used in DA reactions have been classified in a unique scale of the decreasing electrophilicity power (ω) in Table 1. Some global properties as the values of electronic chemical potential (μ), chemical hardness (η), and maximum charge transfer ($\Delta N_{\max}$) are also included. In the absence of an accurate definition of nucleophilicity, we will assume that high nucleophilicity and high electrophilicity are opposite ends of a simple scale and thus, a molecule presenting a low electrophilicity power may be considered as a nucleophile, yet the inverse relationship between global electrophilicity and nucleophilicity has not been well established.[26]

Within the Table 1 there are three groups including strong electrophiles (**I**), compounds **1–14**, moderate electrophiles (**II**), compounds **15–22**, and marginal electrophiles (nucleophiles) (**III**), compounds **23–32**. For instance, there is a first group of strong electrophiles ranging from *N*-methylmethyleneammonium cation **1** (ω=8.97 eV) to methyl acrylate **14** (ω=1.51 eV), with a larger electrophilicity power than 1.50 eV. A second group of reagents that display a moderate electrophilicity power goes from 1-acetoxy-1,3-butadiene **15** (ω=1.10 eV) to cyclopentadiene **22** (ω=0.83 eV). They present an electrophilicity power between 1.5 and 0.8 eV. Finally, the third group goes from 1-methoxy-1,3-butadiene **23** (ω=0.77 eV) to dimethylvinylamine **32** (ω=0.27 eV) with marginal electrophilicity power, so that they can be classified as nucleophiles. They present an electrophilicity power lesser than 0.80 eV. Within this unique scale of electrophilicity power several DA reagents like nitroethylene **7** and furan **26** are correctly classified as strong electrophile and nucleophile, respectively, yet they can act as dienes or dienophiles in polar DA cycloadditions. Note that in the first group of strong electrophiles, the maximum charge $\Delta N_{\max}$ that these systems may acquire from the environment consistently decrease with the global electrophilicity power, from 1.5*e*, *N*-methylmethyleneammonium cation **1**, to ca. 0.7*e*, methyl acrylate **14**. This trend is conserved in the second and third group of reagents (see Table 1).

4.2. Normal-electron-demand DA reactions

Most of the structural and electronic features induced by chemical substitution are often reflected as responses in the global reactivity indexes.[34] We claim that the global electrophilicity index encompasses most of the relevant information that may roughly account for the global reactivity pattern observed in the DA reactions. In a normal-electron-demand (NED) DA reaction, the ethylene component (dienophile) usually bears one or more electron-withdrawing groups that enhance both the reaction rate and the yield of the kinetic control products.[1,4–7] For instance, taking ethylene/butadiene system as reference, we expect that increasing substitution by electron-withdrawing groups in the dienophile should be reflected in an increase in the electrophilicity power of the ethylenic moiety as measured by the ω index. For instance, substitution of one hydrogen atom in ethylene **24** by the electron-withdrawing –CHO group brings the electrophilicity power of the ethylenic moiety from 0.73 eV in ethylene **24** to 1.84 eV in acrolein **10**. The reaction of 1,3-butadiene **16** with acrolein **10** takes place within half an hour in quantitative yield, compared to the 78% yield obtained in the ethylene/1,3-butadiene reaction under more extreme external conditions.[1,10] The dimerization of 1,3-butadiene **16** on the other hand (85% yield after 10 days at 150°C), is very much slower than its reaction

Table 2. Relationship between polarity and the difference in electrophilicity power for some diene/dienophile pairs involved in DA reactions between several dienophiles and 1,3-butadiene **16**

Dienophile	Static polarity, ΔN^{0a}	$\Delta\omega^{b}$	Polarity at TS, ΔN
Ethylene **24**	0.01	−0.32	0.00
Acrolein **10**	0.08	0.79	0.11
Acrylonitrile **11**	0.10	0.69	0.12
Dimethyl 2-methylenemalonate **9**	0.10	0.88	0.21
1,1-Dicyanoethylene **6**	0.19	1.77	0.24
Acrolein–BH_3 complex **5**	0.16	2.15	0.21
Hexafluorothioketone **3**	0.26	3.72	0.23
Tetracyanoethylene **2**	0.37	4.91	0.39
N-Methylmethyleneammonium cation **1**	0.63	7.92	0.56

[a] Polarity values (ΔN^0, in e) are the static values calculated from Pearson's equation (see the text for details), polarity at the TS (ΔN, in e) from NBO population analysis (see the text).

[b] The electrophilicity difference ($\Delta\omega$, in eV) is evaluated with reference to the electrophilicity power of butadiene (ω=1.05 eV, see Table 1).

with acrolein **10**. It is interesting to note that the electrophilicity power of 1,3-butadiene **16** (ω=1.05 eV) is lower than that shown by acrolein **10**, according to the classification given in Table 1. Methyl acrylate **14** and methyl vinyl ketone **12** that bear electron-withdrawing substituent of comparable power and that react at a similar rate, display very similar values of global electrophilicity (ω=1.51 and 1.65 eV, respectively, see Table 1). Nitroethylene **7** a well known powerful dienophile containing one of the most powerful electron-withdrawing groups,[35] shows one of the highest value in electrophilicity power (ω=2.61 eV) among the neutral dienophiles, as well as dimethyl 2-methylenemalonate **9** (ω=1.93 eV). The thioketone **3** that shows a very high electrophilicity power (ω=4.77 eV) readily reacts with 1,3-butadiene **16** in almost quantitative yield at low temperature (−78°C).[36]

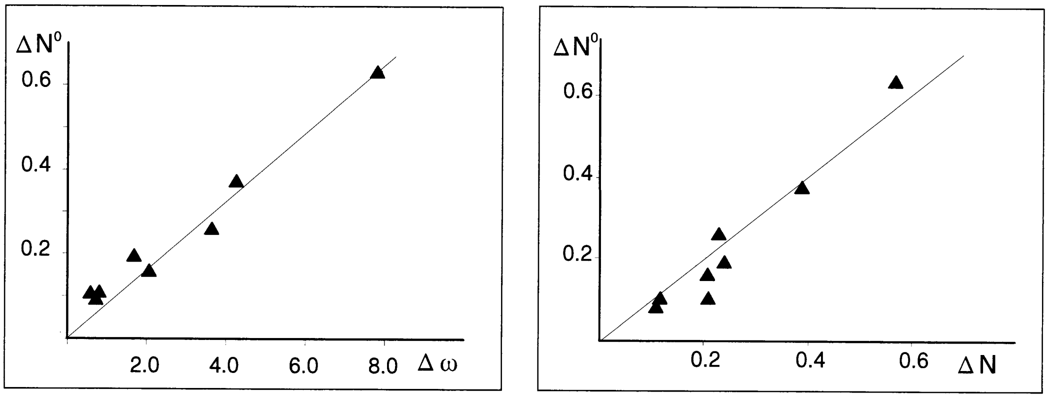
The electrophile/nucleophile interaction in NED-DA reactions may also be enhanced by chemical substitution on the diene by an electron-releasing group. It is experimentally known that even a weak electron-releasing methyl group makes this diene more reactive than 1,3-butadiene. A methoxy group on the diene makes them still more reactive. For instance, it has been experimentally established that acrolein **10** reacts with 1,3-pentadiene **18** by heating up to 130°C with 80% yield after 6 h.[1] Replacement of the methyl group by methoxy at the same position enhances the reaction rate keeping approximately the same yield after 2 h. Acrolein **10** also reacts with 2-methyl-1,3-butadiene **17** in very similar conditions to that of compound **18**.[4] Substitution of one methyl by the trimethylsilyloxy group in **17** to give compound **19** lowers the reaction rate, maintaining a similar yield (81%) after 24 h.[4] According to our model, chemical substitution in the diene with electron-releasing groups make it less electrophilic (i.e. more nucleophilic) in global terms. For instance, substitution of one terminal hydrogen atom in 1,3-butadiene **16** by methyl groups brings the electrophilicity power from ω=1.05 eV in **16** to ω=0.93 eV in 1,3-pentadiene **18**, and to ω=0.86 eV in 4-methyl-1,3-pentadiene **21**. Replacement of one terminal hydrogen in 1,3-butadiene **16** by a more electron-releasing methoxy group in compound **23**, lowers even more the electrophilicity power (ω=0.77 eV) making the derivative a more powerful nucleophile than 1,3-butadiene. Note that cyclopentadiene **22** (ω=0.83 eV) is correctly predicted as the alkyl substituted butadiene that present the lowest electrophilicity power (i.e. the highest nucleophilicity), as compared to the methyl substituted butadienes.[4]

4.3. Inverse-electron-demand DA reactions

The above examples correspond to a NED-DA reaction, where the charge transfer takes place from the electron-rich diene (the nucleophile) to the electron-poor dienophile (the electrophile). However, it is also possible to have the electron-releasing substituent on the dienophile and the electron-withdrawing substituent on the diene. Such reactions are said to have an inverse-electron-demand (IED). They are much less common, because having the substituent with the inverse inductive effects order is not as effective as having them in the usual way (i.e. the electron-withdrawing group on the dienophile and the electron-releasing group on the diene).[1] This is for instance the case of the interaction of nitroethylene **7** (ω=2.61 eV) with either methyl vinyl ether **30** (ω=0.42 eV) or dimethylvinylamine **32** (ω=0.27 eV).[37] Nitroethylene, which was classified as strong electrophile, may be also considered as a heterodiene, where the C1 and C2 carbon atoms of 1,3-butadiene have been substituted by oxygen and nitrogen atoms, respectively. According to the electrophilicity scale of Table 1, this heterodiene will act as electrophile (in a NED-DA reaction, the diene is usually the nucleophile), while methyl vinyl ether **30** or dimethylvinylamine **32** will act as nucleophiles.[23] The IED may be better visualized in this case by looking at the values of electronic chemical potential. From Table 1, it may be seen that the μ value for nitroethylene **7** (μ=−0.1958 a.u.) is less than the corresponding values of μ for methyl vinyl ether **30** or dimethylvinylamine **32** (μ=−0.0894 and −0.0680 a.u., respectively), thereby indicating that the electron flux will take place this time from the electron-rich substituted ethylene to the heterodiene, i.e. in the opposite direction to that expected in the NED-DA reaction.[23]

4.4. Lewis acid catalyzed DA reactions

Lewis acid (LA) catalysis has a relevant role on the DA reaction. It is well know that the presence of LAs increases both rate and regioselectivity. As a consequence, most of the LA catalyzed DA reactions take place at lower temperature that the uncatalyzed process. In a catalyzed NEDDA reaction the LA is coordinated to the electron-poor dienophile thereby markedly decreasing its LUMO energy, and



(a) (b)

Figure 1. (a) Correlation between the static polarity ΔN^0 (in e) evaluated from Pearson equation and the electrophilicity difference $\Delta\omega$ (in eV); (b) correlation between the static polarity ΔN^0 (in e) evaluated from Pearson equation and polarity calculated from a NBO population analysis ΔN (in e), at the corresponding transition structures.

increasing the ionicity of the process. The acroleine–BH_3 complex/cyclopentadiene is one of most studied LA catalyzed Diels–Alder reaction.[38] Table 1 shows that the presence of BH_3 coordinated to acroleine, acroleine–BH_3 complex **5**, increases the electrophilicity power in 1.36 eV relative to acroleine **10**, in agreement with the more polar character of the LA catalyzed cycloaddition. A greater increase in electrophilicity is found for the protonated iminium cation **1** (ω=8.97 eV) relative to the imine **20** (ω=0.86 eV). The imine **20** shows an electrophilicity power ten times lesser than its protonated parent **1**. Thus, if we consider the proton as the strongest Lewis acid in nature, this highest increase of electrophilicity power is in agreement with the large acceleration of the DA reaction of imines in an acidic medium.[39] Therefore, this enhancement in the reaction rate may be again explained by the strong increase of the electrophilicity power of the dienophile induced by protonation at the nitrogen atom.[25]

In consequence, the effect of the LA catalyst on the DA reactions can be explained by an increase of the electrophilicity of the electron-poor DA component which acts as the dienophile on a NED-DA reaction and as the diene in an IED-DA reaction. The enhancement in electrophilicity entails an increase of the ionicity of the process, which is usually accompanied by a decrease of the activation energy for the cycloaddition.

4.5. Polarity of the DA reactions

The classification based on the global electrophilicity scale presented in Table 1, to describe the substituent effects on the diene/dienophile pairs interactions including IED interactions, may be complemented with a static analysis of the charge transfer pattern expected for transition state structures involved in DA reactions. This aspect is useful to discuss the more or less polar character of these species that helps to rationalize the reaction mechanisms. Consider for instance the ethylene/1,3-butadiene interaction, **24/16**, as reference. Since both ethylene and 1,3-butadiene are classified as a marginal and a moderate electrophile in Table 1 the reaction will present a charge transfer pattern mostly consistent with a non-polar process associated to a pericyclic transition state. According to our classification, the acrolein/1,3-butadiene interaction, **10/16**, on the other hand, is expected to show a slightly different picture that follows from their more markedly difference in electrophilicity power: acrolein **10** is expected to act as electrophile and 1,3-butadiene **16** as nucleophile, and the reaction mechanism is expected to be more polar in character. This prognosis based on the difference in ω is reinforced by the corresponding values in electronic chemical potential quoted in Table 1: it may be seen that the electronic chemical potential in acrolein **10** (μ=−0.1610 a.u.) is less than the electronic chemical potential of 1,3-butadiene **16** (μ=−0.1270 a.u.); thereby indicating that the net charge transfer will take place from the diene towards the dienophile. Note that 1,3-butadiene **16** and ethylene **24** have a similar electronic chemical potential (μ=−0.1270 and −0.1239 a.u., respectively), and therefore, neither of them tend to provide charge to the other, in agreement with a non-polar pattern.

The more polar character of the acrolein/1,3-butadiene interaction, **10/16**, with respect to the ethylene/1,3-butadiene interaction, **24/16**, may be also drawn from a static charge transfer model, as for instance Pearson's equation of charge transfer.[28] Within this model, the charge transfer from the nucleophile towards the electrophile may be easily represented in terms of an Ohm's like equation that uses the electronic chemical potential and chemical hardness of the isolated interacting pairs, namely, $\Delta N^0 = (\mu_{\mathrm{NU}^-} - \mu_{\mathrm{E}^+})/(\eta_{\mathrm{NU}^-} + \eta_{\mathrm{E}^+})$. Using the values of μ and η quoted in Table 1, we obtain ΔN^0=0.08e for the acrolein/1,3-butadiene interaction, **10/16**, compared to ΔN^0=0.01e for the ethylene/1,3-butadiene interaction, **24/16**, thereby predicting a slightly more polar character for the former.

The apparent relationship between static polarity of the electrophile/nucleophile interaction, ΔN^0, and the difference in global electrophilicity power, $\Delta\omega$, for a series of electron-poor dienophiles used in NED-DA reactions is depicted in Table 2 and Fig. 1(a). Furthermore, LA catalyzed DA reactions, represented by the acrolein–BH_3 complex/1,3-butadiene interaction (compounds **5** and **16** in Table 1), have been found to react through a more polar mechanism as compared to the uncatalyzed process, **10/16**. The charge transfer pattern for the LA catalyzed processes may also be estimated by the Pearson's equation, using the values of electronic chemical potential and chemical hardness for the acrolein–BH_3 complex **5** and 1,3-butadiene **16** quoted in Table 1. Thus, for the catalyzed cycloaddition process, **5/16**, the estimated charge transfer is $\Delta N^0=0.16e$. Note that the enhancement in charge transfer for the LA catalyzed process results from both, an increase in the chemical potential difference $\Delta\mu=0.87$ eV in the acrolein/1,3-butadiene interaction, **10/16**, to $\Delta\mu=1.49$ eV in the acrolein–BH_3 complex/1,3-butadiene interaction, **5/16**, and by a simultaneous lowering in the chemical hardness of the acrolein–BH_3 complex **5** (see Table 1).

The NED-DA reactions of 1,3-butadiene with the nine dienophiles presented in Table 2 is an useful example to establish the qualitative relationship between the difference of the electrophilicity power for the dienophile/diene pair and the polarity of the process. The difference in electronic chemical potential between the electrophile/nucleophile pair in the dimethyl 2-methylenemalonate/1,3-butadiene interaction, **9/16**, becomes 1.13 eV with a total resistance to the charge transfer $\eta=10.94$ eV. These figures yield an expected charge transfer of about $\Delta N^0=0.10e$ for the interaction between 1,3-butadiene, **16**, and dimethyl 2-methylenemalonate, **9**, compared to the value $\Delta N^0=0.16e$ for the acrolein–BH_3 complex/1,3-butadiene, **5/16**, and with the value $\Delta N^0=0.01e$ for ethylene/1,3-butadiene **24/16**, interactions. Moreover, the increase of the polarity within the series of the mono-, di- and tetracyanoethylene derivatives **11**, **6**, and **2**, $\Delta N^0=0.10$, 0.19 and $0.37e$, respectively (see Table 2), is in complete agreement with the increase of the electrophilicity power of the corresponding dienophile, $\omega=1.74$, 2.82 and 5.96 eV, respectively (see Table 1), and also with the increase of the rate reaction.[40] The extreme case of *N*-methylmethyleneammonium cation/1,3-butadiene interaction, **1/16**, presents the highest polarity ($\Delta N^0=0.63e$) that corresponds with highest value in the difference of electrophilicity ($\Delta\omega=7.92$ eV, see Table 2).

Finally, the feasibility to anticipate the polarity of a transition state structure for a cycloaddition as given from the static values estimated by the Pearson's equation, has been tested by comparing the predicted values, ΔN^0, with those obtained from a NBO population analysis at the corresponding B3LYP/6-31G* TSs, ΔN (see Table 2). A comparison of the static polarities calculated and those obtained from the corresponding TSs shows a good agreement between both values (see Fig. 1(b)). Note that for this short series of electron-poor dienophiles used in NED-DA reactions, the order relationship in the expected charge transfer: acrolein<acrylonitrile≈dimethyl 2-methylenemalonate<acrolein–BH_3 complex<1,1-dicyanoethylene<hexafluorothioketone<tetracyanoetylene<*N*-methylmethyleneammonium, is approximately consistent with the difference in electrophilicity power, $\Delta\omega$, displayed by the diene/dienophile pair (see Table 2 and Fig. 1(a)). Therefore, the relationship between the electrophilicity difference of the dienophile/diene pair and the static polarity may be an useful tool to describe the electronic pattern expected for the transition state structures involved in DA reactions, describing non polar ($\Delta\omega$ small) or polar ($\Delta\omega$ big) mechanisms.

These results are consistent with those reported by Cramer and Barrows[41,42] for the cycloaddition reactions of hydroxyallyl cations and dienes of varying nucleophilicity, as well as cycloaddition reactions between *s-cis*-1,3-butadiene with oxyallyl cations of varying electrophilicity. The effect of the electrophilicity pattern on the different mechanisms (stepwise or concerted) that may be developed in a DA reaction has been also addressed by Mayr et al.[43] The electrophilicity power of molecules being described therein by a relative empirical electrophilicity scale based on kinetic parameters.[44]

On the other hand, the stepwise vs concerted nature of the DA cycloaddition reactions has been previously analyzed by Sauer and Sustmann.[45] These authors rationalize the mechanistic aspects of DA reactions based on the basis of the FMO Klopman's equation[46] of reactivity, that introduces the coefficients and the frontier energy levels of the diene/dienophile pair. Our approach is quite different, in the sense that it does not needs the electronic properties of the interacting diene/dienophile pair to set up a unique scale of electrophilicity in these systems. The present approach is rather a static reactivity picture developed around the frontier energy levels defining the electronic chemical potential that correctly describes the direction of the charge transfer in normal and inverse electron demand processes on one hand, and that introduces a unique absolute electrophilicity scale that correctly predicts the reactivity in many DA reactions where one or both reagents are widely functionalized. The present scale provides a simple way to assess the more or less polar character of the interaction, on the basis of the difference in the electrophilicity gap between the reacting partners. This is achieved within a simple model where the information encompassed in the MO coefficients is implicitly self contained in the electron density according to the density functional formalism.

5. Concluding remarks

In summary, the global electrophilicity index introduced by Parr et al. becomes a useful quantity to classify the electrophilicity power of a series of dienes and dienophiles within a unique relative scale. Useful information about the polarity of the transition state structure expected for a given reaction may be obtained from the difference in the global electrophilicity of the diene/dienophile interacting pair. Thus, small electrophilicity differences can be related with non-polar (pericyclic processes) mechanisms, while big electrophilicity differences can be related with polar (ionic processes) mechanisms. Finally, recent density functional theory studies devoted to Diels–Alder reactions have shown that this global electrophilicity scale is a powerful tool to explaining the substituent effects on the diene/dienophile pair.[47–50]

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