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Density functional based reactivity parameters: Thermodynamic or kinetic concepts?

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ABSTRACT

The Density Functional Theory of chemical reactivity has provided and effective way to develop a mathematical framework for many empirical chemical concepts. In this work, the relation of some of the proposed indexes with the thermodynamic and kinetic effects on a chemical reaction will be discussed. In order to give a numerical support to the discussion, families of S_N2 reactions and Diels–Alder reactions have been studied. It is concluded that the theoretical proposed indexes represent neither thermodynamic nor kinetic effects but a combination of both depending on the type of reaction.

1. Introduction

Some of the most important empirical concepts used in Chemistry come as a duality. Acid–base, electrophile–nucleophile and oxidation–reduction. They have been for a long time used in almost all fields of Chemistry [1]. Although they have been always associated with experimental quantities there is not an absolute scale to measure them, and their definitions are not linked to an experimental observable as defined in quantum mechanics. However, there is a traditional accepted distinction among them. It is usually established that acid–base are concepts related to the thermodynamic of a chemical reaction and electrophile–nucleophile are associated to the kinetic aspects of a chemical reaction. Oxidation–reduction concepts are more linked to electrochemical reactions where ions gain or lose a whole electron charge. All of them are included in the more general concepts of electron donor or electron acceptor system. The distinction between thermodynamic and kinetic effects has been followed for the attempts to define quantitative scales based in the possible separation of those effects [2–5]. Hence, nucleophilicity scales are associated to reaction rates, an experimental observables related to the kinetic of the reaction, and basicity scales are associated to equilibrium constants, like proton affinities, associated to the thermodynamic aspects of a chemical reaction. However, a sharp separation of the competitive effects is not possible.

From a theoretical point of view, there is no way to separate between observables depending on kinetic effects and observables depending only on thermodynamic effects. Usually, both effects are entangled. However, there have been various attempts to elucidate the point [6–8], and this work goes also on this direction. Specially, the conclusions of Ref. [6] will be reinforced. Chattaraj et al. [6] emphasized the fact that the reactivity indexes and the model of the quadratic dependence of the energy with respect to the number of electrons give perfectly account of the HSAB (Hard Soft Acid Base) principle which fulfils both thermodynamic and kinetic considerations.

Density Functional Theory has been the most accepted theoretical framework to develop and generalize a chemical reactivity theory [9–11]. Starting from the pioneer works of Parr and others who proposed first, the negative of the chemical potential as a measure of the absolute electronegativity [12], then the derivative of the chemical potential with respect to the number of electrons as a measure of the chemical hardness [13], and later an electrophilicity scale [14]. All of them are directly based in the empirical quadratic formula for the variation of the energy with respect to the number of electrons:

$$\Delta E = \mu \Delta N + \frac{1}{2}\eta \Delta N^2 + \dots \quad (1)$$

where the gain or lose of energy of a molecule, ΔE, associated with en electron charge transfer of ΔN, is expanded as a Taylor series. The first derivative, μ, is the chemical potential:

$$\mu = \left(\frac{\partial E}{\partial N}\right)_v \quad (2)$$

where the derivative is taken at constant external potential v. For every system in a stable equilibrium the chemical potential is negative, and its absolute value has been proposed as a formal defini-

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tion of an absolute electronegativity. The second derivative of the energy with respect to the electron charge transfer is known as the hardness η:

$$\eta = \left(\frac{\partial^2 E}{\partial N^2}\right)_v \quad (3)$$

Higher order derivatives have been defined but they are of interest only in special circumstances [15,16]. Following a model of Maynard et al. [17], Parr et al. [14] reasoned that the electrophilicity power of a system should be given for its capacity of gaining energy, according to Eq. (1), in presence of an ideal electron donor, i.e., an electron sea of zero chemical potential and hardness. In this way they proposed the electrophilicity, ω, as:

$$\omega = \frac{\mu^2}{2\eta} \quad (4)$$

Unfortunately, no one of the derivatives can be calculated in an exact way, and different options to approximate them have been discussed. The impact of those chemical descriptors in the development and applications of a chemical reactivity theory has been widely documented [10,18]. We would like now only to recall that they are based on a series expansion and the principle of minimum energy. Therefore, their prediction capability is at the beginning of a chemical reaction, and favor the evolution toward an equilibrium state of minimum energy. Generalizations and modifications of the equations to include other related concepts like nucleophilicity and electron donor power have been also proposed [19,20]. It is important here to notice that they do not contain any indication about kinetic or thermodynamic effects, which are both interconnected. Therefore, the electrophilicity index is able to correlate well with kinetic parameters as well as with thermodynamic parameters [6]. The recently proposed nucleophilicity index is also able to correlate with kinetic and thermodynamic parameters depending on the type of reaction [8].

In this work, in order to study further the relationship between these factors some well known S_N2 reactions in gas phase have been studied. The reactivity parameters of a variety of identity reactions of the type $X^- + RX \rightarrow RX + X^-$ have been calculated. The known reaction path is according to scheme 1, where one can see that the first step, the formation of the ion–molecule complex, is only affected by the thermodynamic reaction enthalpy denoted by $\Delta H_{\mathrm{therm}}$. Since in this step there is no reaction barrier there is no kinetic influence, therefore, any descriptor based on kinetic models should fail in correlating with the reaction enthalpy. On the other side, the second step is only governed by the reaction barrier because the reactants and products have the same energy. Hence it is only kinetic controlled, and any descriptor based on a thermodynamic model should fail. It is important to notice that the studied mechanism is valid for the gas phase reactions. In solution other type of effects do not considered in this work can be important.

In order to evaluate with more detail the relationship between the reactivity and energetic parameters, the Diels–Alder reactions have also been studied. These reactions are characterized by a strong nucleophilic/electrophilic interaction at the first stages of the reaction, where a 1,3-diene is added to an olefinic or acetylenic dienophile. For these reactions two mechanisms have been characterized: one corresponding to a one-step process through an asynchronous transition structure (TS) to form an adduct with a six-member ring, and other corresponding to a two-step mechanism via a zwitterionic intermediate. Hence, we have considered the Diels–Alder reactions with a one-step process. An analysis of the PES for these DA reactions indicates that they correspond to a one-step process. In this case, the reaction is affected by kinetic and thermodynamic effects. To be sure that the comparison of results is not erroneous because of different numerical details the reactivity indexes as well as the kinetic and thermodynamic energy differences have been calculated at the same level of theory.

The main interest of this work is the confrontation and possible separation of kinetic and thermodynamic effects. The used examples, S_N2 and Diels Alder reactions, are completely arbitrary. Therefore, we do not intend to obtain exhaustive or novel results for these reactions, and we do not make any comparison with experimental data. It is also important to stress that the evidence based on numerical data is not conclusive, and should be only used as a new example reinforcing the point that, from a theoretical side, on a chemical reaction one cannot separate the thermodynamic from the kinetic effects.

2. Results and discussion

All the calculated reactivity parameters are based in the values of the chemical potential, Eq. (2), and the chemical hardness, Eq. (3). They have been calculated using the finite difference and the frozen orbital approximations, which yields them in terms of the highest occupied molecular orbital energy, HOMO (ε_H), and the lowest unoccupied molecular orbital energy, LUMO (ε_L). They are:

$$\mu = \epsilon_H - \epsilon_L$$

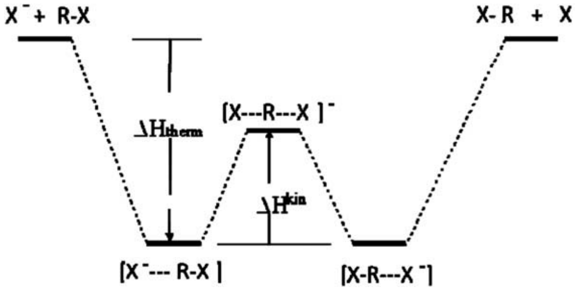
and

$$\eta = -(\epsilon_H + \epsilon_L)$$

All calculations were performed using the Gaussian 03 program package [21] within the context of DFT using the B3LYP functional. With the aim of evaluating the dependence of the indexes of reactivity with the basis set, all electron calculations were done for first- second- and third-row atoms with three basis sets 6-31+G(d,p), 6-311++G(d,p) and 6-311++G(2df,2pd), while for Iodine atom the aug-cc-pVTZ-PP basis set [22] with the Stuttgart's pseudopotential [23] was used .

2.1. Bimolecular nucleophilic substitution reaction S_N2

The S_N2 reactions have been the subject of a considerable number of experimental [24–40] and theoretical studies [41–53], and its mechanism in gas phase is therefore well established. In this work, we have considered the identity nucleophilic substitution at saturated carbon, $X^- + CH_3X \rightarrow CH_3X + X^-$ [49,52,54–57], at saturated oxygen $X^- + HOX \rightarrow HOX + X^-$ (X = F, Cl, Br, I) [58], at saturated nitrogen, $X^- + NH_2X \rightarrow NH_2X + X^-$ [59,60], and at nitrogen $X^- + N(CH_3)_2X \rightarrow N(CH_3)_2X + X^-$ [61], where X is a halogen atom. They are all described by a double-well potential curve (Scheme 1). The reaction involves an initial formation of a reactant ion–molecule complex $[X^-\text{–}R\text{–}X]$ (R = CH_3, OH, NH_2 and $N(CH_3)_2$) , with a complexation energy $\Delta H_{\mathrm{therm}}$ relative to the separated reactants.



Scheme 1. Schematic energy profile for the $X^- + RX$ identity exchange reaction (R = CH_3, NH_2, $N(CH_3)_2$, OH and X = F, Cl, Br, I).

Table 1
Reactivity global indexes of the RX (R = CH_3, NH_2, $N(CH_3)_2$, OH and X = F, Cl, Br, I) calculated with B3LYP functional and various basis sets (B1, B2 and B3).[a]

Reactants	μ[b] (eV)			η[c] (eV)			S[d] (1/eV)			ω[e] (eV)		
	B1	B2	B3	B1	B2	B3	B1	B2	B3	B1	B2	B3
CH_3F	−4.66	−4.94	−4.93	4.95	4.74	4.75	0.20	0.21	0.21	2.20	2.58	2.56
CH_3Cl	−4.16	−4.36	−4.35	4.04	3.90	3.90	0.25	0.26	0.26	2.14	2.44	2.43
CH_3Br	−4.13	−4.26	−4.25	3.50	3.45	3.47	0.29	0.29	0.29	2.44	2.64	2.60
CH_3I	−4.13	−4.20	−4.20	2.93	2.86	2.87	0.34	0.35	0.35	2.92	3.08	3.08
NH_2F	−4.18	−4.34	−4.30	3.87	3.73	3.75	0.26	0.27	0.27	2.26	2.52	2.47
NH_2Cl	−4.44	−4.48	−4.41	2.96	2.97	3.01	0.34	0.34	0.33	3.33	3.38	3.23
NH_2Br	−4.58	−4.64	−4.56	2.60	2.59	2.65	0.38	0.39	0.38	4.02	4.16	3.93
NH_2I	−4.57	−4.59	−4.59	2.21	2.21	2.22	0.45	0.45	0.45	4.74	4.77	4.74
$N(CH_3)_2F$	−3.51	−3.70	−3.68	3.55	3.37	3.37	0.28	0.30	0.30	1.73	2.03	2.01
$N(CH_3)_2Cl$	−3.95	−3.96	−3.87	2.76	2.78	2.83	0.36	0.36	0.35	2.83	2.83	2.65
$N(CH_3)_2Br$	−4.20	−4.25	−4.16	2.47	2.41	2.47	0.41	0.42	0.40	3.57	3.75	3.49
$N(CH_3)_2I$	−4.26	−4.28	−4.28	2.08	2.08	2.09	0.48	0.48	0.48	4.37	4.41	4.38
OHF	−5.72	−5.77	−5.60	3.43	3.45	3.53	0.29	0.29	0.28	4.77	4.83	4.44
OHCl	−5.38	−5.46	−5.26	2.70	2.70	2.79	0.37	0.37	0.36	5.37	5.52	4.97
OHBr	−5.37	−5.49	−5.31	2.34	2.31	2.40	0.43	0.43	0.42	6.17	6.55	5.87
OHI	−5.19	−5.21	−5.19	1.99	1.98	2.00	0.50	0.50	0.50	6.77	6.86	6.73

[a] B1, B2 and B3 corresponding a 6-31+G(d,p), 6-311++G(d,p) and 6-311++G(2df,2pd), respectively. Iodine was calculated using aug-cc-pVTZ-PP basis set with their corresponding Stuttgart's pseudopotential [23].

[b] Chemical potential.

[c] Chemical hardness.

[d] Chemical softness.

[e] Electrophilicity index.

This complex must then overcome a central activation barrier ΔH^{kin} to reach a symmetrical transition structure **[X–R–X]**$^-$. The latter then breaks down to give the product ion–molecule complex which finally dissociates into the separated products. We have selected the reagent RX to evaluate the reactivity global indexes: chemical potential (μ), chemical hardness (η), chemical softness (s) and electrophilicity index (ω). The values of these indexes are summarized in Table 1. Inspection of Table 1 shows that the reactivity indexes for the species RX (R = CH_3, OH, NH_2, $N(CH_3)_2$ and X = F, Cl, Br, I) are rather insensitive to the basis set used. Analysis of the linear correlation of the reactivity indexes calculated with different basis set shows that there is not dependence on the basis set. The results show very good correlations and a slope very near to one for all indexes. Chemical potential: $\mu(B2) = 0.973\mu(B1)–0.218$ ($R^2 = 0.983$); $\mu(B3) = 0.898$ $\mu(B1)–0.493$ ($R^2 = 0.969$) and $\mu(B3) = 0.926$ $\mu(B2)–0.281$ ($R^2 = 0.992$), with B1, B2 and B3 the basis set 6-31+G(d,p), 6-311++G(d,p) and 6-311++G(2df,2pd), respectively. For chemical softness and electrophilicity the results are similar: $s(B2) = 0.972$ $s(B1) + 0.014$ ($R^2 = 0.997$); $s(B3) = 0.946$ $s(B1) + 0.018$ ($R^2 = 0.993$) and $s(B3) = 0.974$ $s(B2) + 0.004$ ($R^2 = 0.997$). $\omega(B2) = 0.975$ $\omega(B1) + 0.264$ ($R^2 = 0.994$); $\omega(B3) = 0.890$ $\omega(B1) + 0.408$ ($R^2 = 0.986$) and $\omega(B3) = 0.910$ $\omega(B2) + 0.177$ ($R^2 = 0.987$).

Because the results are independent of basis set, we will analyze only our results calculated by the 6-31+G(d,p) basis set. The data in the Table 1 show that chemical softness and electrophilicity values for a specific group RX have an increasing pattern from F to I: RF < RCl < RBr < RI, while chemical potential values do not show the same trend for all groups RX. For the groups CH_3X and OHX the chemical potential ($\chi = -\mu$) is driven by the electronegativity of the halogen atom (i.e., μ(R F) < μ(RCl) < μ(RBr) < μ(RI)), while for the groups NH_2X and $N(CH_3)_2X$ the order is the opposite one (i.e., μ(RF) > μ(RCl) > μ(RBr) $\sim$ μ(RI)), the only difference being the relative order for RBr and RI. It is also observed from the results reported in Table 1 that for a specific halogen atom with varying group R, the chemical softness presents a regular pattern. The values increase in the order: $CH_3 < NH_2 < N(CH_3)_2 <$ OH (i.e., S = 0.35 eV for CH_3I < S = 0.45 eV for NH_2I < S = 0.49 eV for $N(CH_3)_2I$ < S = 0.50 eV for OHI). Based on these analysis and remembering that the electrophilicity index (Eq. (4)) is defined in terms of chemical potential and chemical softness (inverse of chemical hardness), we may conclude that the order obtained for ω is mainly driven by the chemical softness of the halogen atom.

Table 2 compares the linear correlations between the thermodynamic and kinetic parameters of S_N2 reactions $X^- + RX \rightarrow RX + X^-$ and various reactivity indexes calculated for free reactants RX. The thermodynamic energy corresponds to enthalpies of reaction ΔH_{therm} for the formation of the ion–molecule complex from the separated reactants. The kinetic energy ΔH^{kin} corresponds to enthalpies of activation to reach a symmetrical transition structure from ion–molecule complex. The values of ΔH_{therm} and ΔH^{kin} calculated at the G2(+) (298 K) level [49,62] were obtained for four series of reactions from CH_3X [49], NH_2X [60], $N(CH_3)_2X$ [61] and OHX [58]. The obtained results are organized in two data groups (see Table 2). The first group shows the correlation of the indexes with the energetic parameters for the series of reactions varying the radical R(Fig. 1), whereas the second group shows the same correlations varying the halogen atom X. The results show that for the first data group there is a well defined linear relationship between the ΔH_{therm}

Table 2
Linear correlations of various reactivity indexes (μ,s,ω)[a] calculated for the species RX with energetic parameters (ΔH_{therm} and ΔH^{kin})[b] of $X^- +$ R–X identity reactions (R = CH_3, NH_2, $N(CH_3)_2$, OH and X = F, Cl, Br, I).

R	R^2					
	μ		s		ω	
	ΔH_{therm}	ΔH^{kin}	ΔH_{therm}	ΔH^{kin}	ΔH_{therm}	ΔH^{kin}
CH_3	0.921	0.004	0.900	0.352	0.655	0.624
NH_2	0.968	0.626	0.874	0.812	0.903	0.903
$N(CH_3)_2$	0.998	0.182	0.915	0.377	0.953	0.360
OH	0.940	0.816	0.831	0.970	0.970	0.790
X	μ		s		ω	
	ΔH_{therm}	ΔH^{kin}	ΔH_{therm}	ΔH^{kin}	ΔH_{therm}	ΔH^{kin}
F	0.424	0.141	0.606	0.796	0.784	0.477
Cl	0.686	0.063	0.685	0.649	0.948	0.280
Br	0.969	0.024	0.537	0.470	0.977	0.148
I	0.984	0.008	0.561	0.411	0.965	0.112

[a] All indexes (μ chemical potential, s chemical softness, ω electrophilicity index) calculated at B3LYP/6-31+G(d,p) level of theory (see Table 1).

[b] Energetic parameters, ΔH_{therm} (enthalpies of reactions) and ΔHkin (enthalpies of activation), were obtained from Ref. [48,57,59,60].

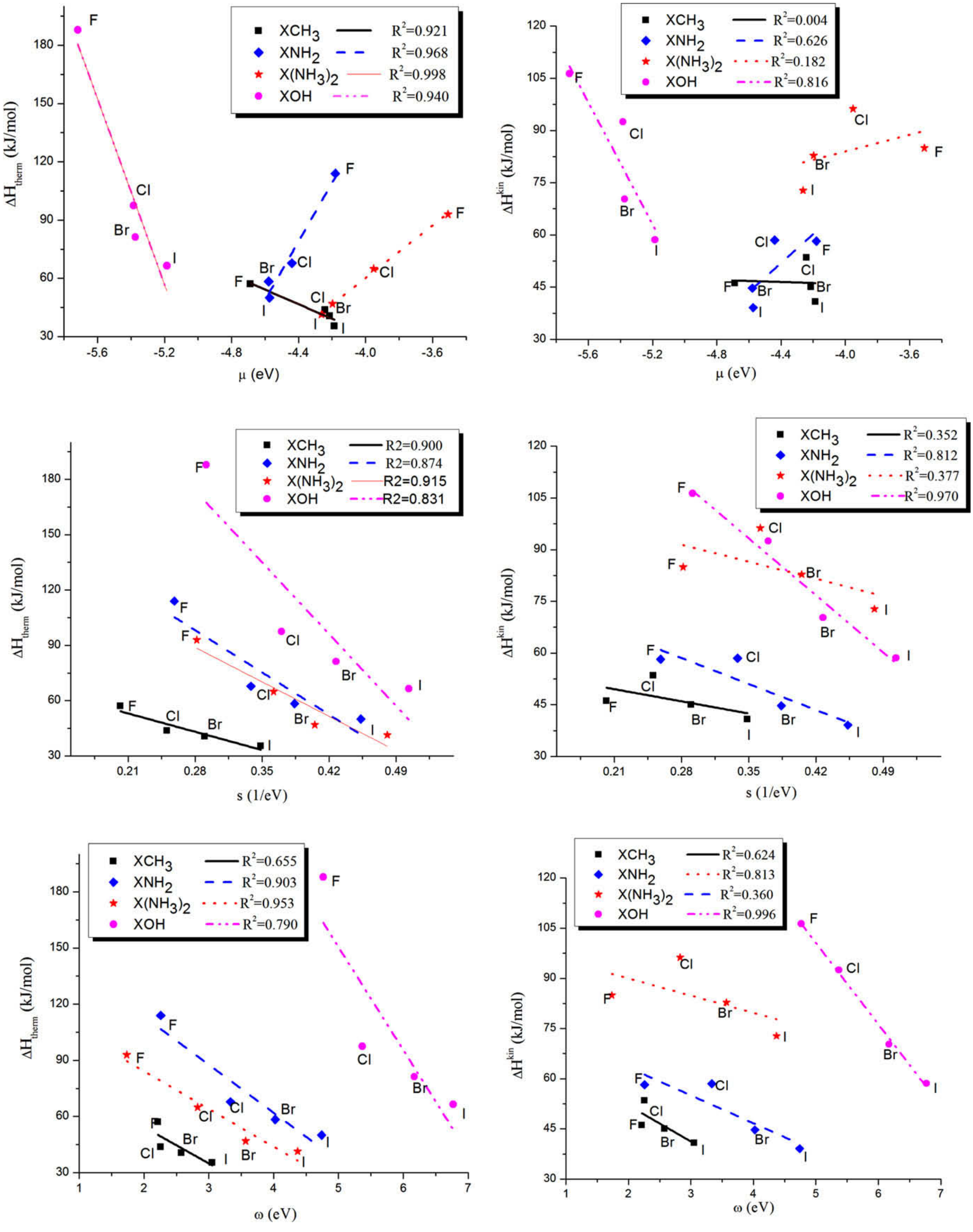


Fig. 1. Plot of energetic parameters ΔH_{therm} (enthalpies of reaction) and ΔH^{kin} (energy of activation) of $X^- + RX$ identity reactions (R = CH_3, NH_2, $N(CH_3)_2$, OH and X = F, Cl, Br, I) vs. reactivity indexes of the RX species.

and all reactivity indexes: chemical potential ($R^2 = 0.921$ for CH_3, $R^2 = 0.968$ for NH_2, $R^2 = 0.998$ for $N(CH_3)_2$ and $R^2 = 0.940$ for OH) , chemical softness and electrophilicity, with the exception of the correlation between ΔH_{therm} and ω for radicals CH_3 ($R^2 = 0.655$). However, the correlation between the kinetic parameter (ΔH^{kin}) and the reactivity indexes is very poor. We find no correlation at CH_3, NH_2

and $N(CH_3)_2$ between ΔH^{kin} and chemical potential ($R^2 = 0.004$, $R^2 = 0.626$ and $R^2 = 0.182$, respectively). Likewise, we find no correlation for substitution at CH_3 and $N(CH_3)_2$ between ΔH^{kin} and chemical softness ($R^2 = 0.352$ and $R^2 = 0.377$, respectively). There is also a bad linear correlation between the kinetics parameter at CH_3 and $N(CH_3)_2$ and electrophilicity index ($R^2 = 0.624$ and $R^2 = 0.360$, respectively). In general, the linear correlation between energetic parameters for substitution reactions and reagents reactivity indexes is lower for ΔH^{kin} than for ΔH_{therm}, with the only exception of the chemical softness for substitution at OH ($R^2 = 0.970$ and $R^2 = 0.831$ for ΔH^{kin} and ΔH_{therm}, respectively) and the electrophilicity for the substitution at NH_2, where the correlation is the same with ΔH^{kin} and ΔH_{therm} ($R^2 = 0.903$). The second data group shows the correlation between energetic parameters for the reactions varying R (CH_3, OH, NH_2, $N(CH_3)_2$) and the reactivity indexes from the corresponding reagent RX (Fig. 2). In this case, as in the first group, the thermodynamic parameters present a better correlation than the kinetic ones, exception made of the chemical softness in the series of reactions with fluorine atom ($R^2 = 0.606$ for $\Delta H_{therm} < R^2 = 0.796$ for ΔH^{kin}). Note, that unlike the first group, in this second group of data the correlation between the chemical softness and the thermodynamic parameter is poor for the four series of reactions (F, Cl, Br and I). Hence, the correlations between the thermodynamic parameter and chemical softness do not depend on the halogen atom. Nevertheless, such a correlation breaks down for $N(CH_3)_2$ (Fig. 2b), but there is still a definite linear correlation for CH_3, NH_2 and OH (e.g., $R^2 = 0.951$, 0.899, 0.924 and 0.947 for the series of reactions F, Cl, Br and I, respectively). For the kinetic parameter the poor correlation with chemical softness is not dependent on any specific radical R. In general, for the chemical potential and electrophilicity indexes the correlation with the thermodynamic parameter is good. It has been also checked whether there is a correlation between the energetic parameter and the recently proposed nucleophilicity index (ω^-) [19]. The nucleophilicity index has been evaluated for the ion X^- relative to species RX. We found here that there is a well defined linear relationship with thermodynamic parameter for F, Cl and I ($R^2 = 0.925$, 0.918, 0.834, respectively), but not for Br ($R^2 = 0.753$) (Fig. 3). The correlation with kinetic parameter is very poor for Cl, Br and I ($R^2 = 0.47$, 0.29, 0.22, respectively), but for F is better ($R^2 = 0.81$). In general, we find that the nucleophilicity index correlates better with the thermodynamic parameter. The indexes of reactivity calculated for the free reactant RX correlate well with the thermodynamic parameter which is the first energetic change in relation with the separated reactants, whereas the correlation with the kinetic parameter, which correspond to the second energetic change regarding separated reactants, is not so good.

2.2. Diels–Alder reactions

The Diels–Alder reaction, probably the most widely used methodology in organic synthesis [63], contributes greatly to the development of mechanistic and theoretical organic chemistry. They are characterized by the reaction of a 1,3-diene with an olefinic or acetylenic dienophile to form an adduct with a six-member ring. In the reaction two new σ-bonds are formed at the expense of two π-bonds [64–66] (Scheme 2 and 3). Many different types of carbocyclic structures can be built up varying the nature of the diene and dienophile. Mostly used is the so-called Normal Electron Demand Diels–Alder reaction (NED reaction) where the diene contains electron-donating groups and the alkene or alkino electron-withdrawing groups. Its counterpart, the Inverse Electron Demand Diels–Alder reaction (IED reaction), is favored by opposite properties of the substituents on diene and alkene. In this work, we have considered the NED reaction. Three Diene–dienophile cycloaddition reactions series have been studied: The Cycloaddition reaction of the 1,3-butadiene toward a series of activated dienophiles (see Scheme 2 and Table 3) and Diels–Alder reactions of two strong activated dienophiles, acrolein–BH_3 complex and 1,1-dicyanoethylene with a series of dienes. The results are shown in Table 4 (see Scheme 3). The last two reactions series present different regioselectivity patterns which are well documented in the literature

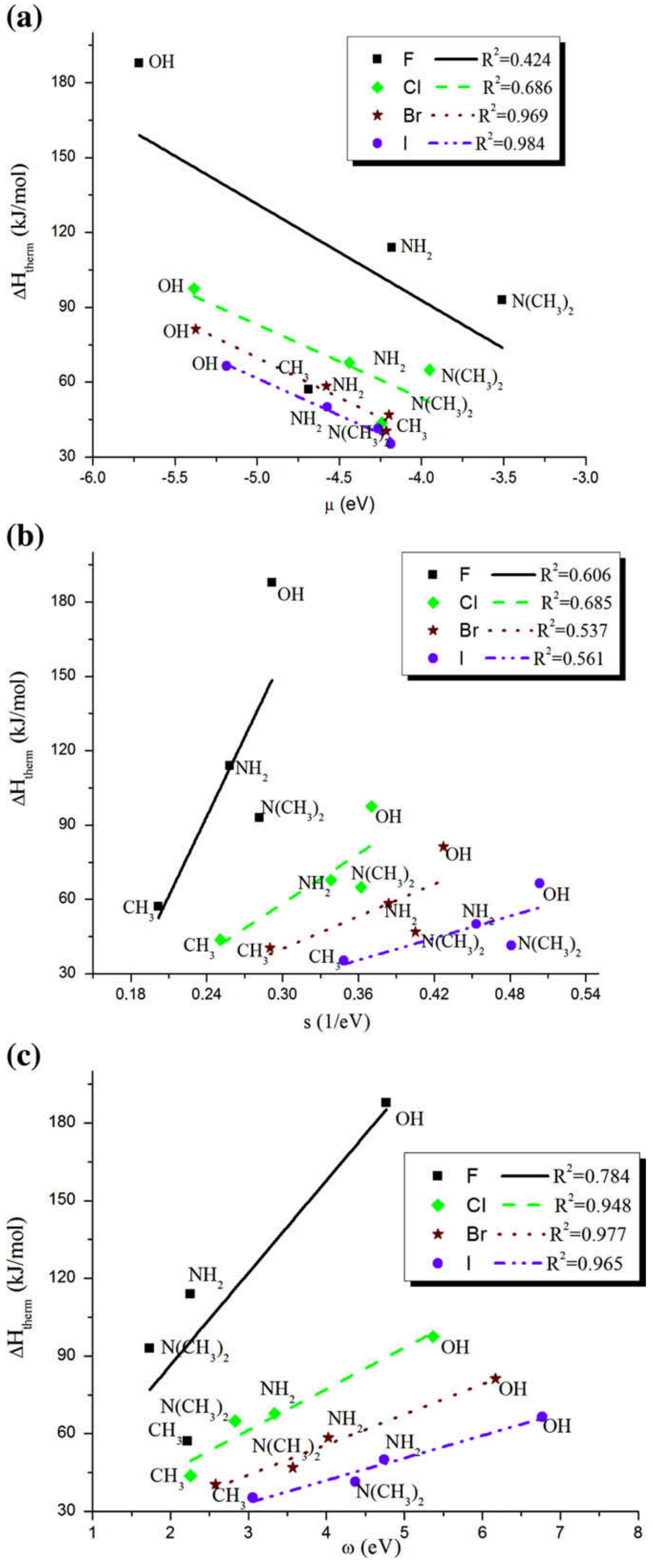
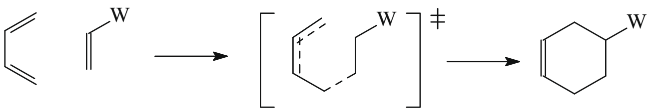


Fig. 2. Plot of enthalpies of reaction (ΔH_{therm}) of X^- + RX identity reactions (R = CH_3, NH_2, $N(CH_3)_2$, OH and X = F, Cl, Br, I) vs. reactivity indexes, (a) chemical potential μ, (b) chemical softness s and (c) electrophilicity ω, of the RX species.

[67–69]. The interaction between unsymmetrical dienes and dienophiles can give two isomeric adducts depending upon the relative position of the substituent in the cycloadducts head-to-head or head-to-tail (see Scheme 3). For these polar cycloadditions, the most favorable regioisomeric pathways can be associated with bond formation at the electrophilic and nucleophilic sites of unsymmetrical dienophile and diene reagents, respectively. Recent Density Functional Theory (DFT) studies devoted to the Diels–Alder reaction have shown that whereas the global electrophilicity index [14] is useful in classifying the electrophilic power of a series of dienes and dienophiles within a unique relative scale [68], the local counterpart [69] helps to identify the relevant electrophilic sites for predicting the regioselectivity patterns. We relay on these results to select the most favorable interaction between the pair dieno/dienophile. In the cycloadditions of the dienophiles **1** and **2** with the dienes **12** and **14** the ortho cycloadduct is considered, whereas with dienes **13**, **15** and **16** the para cycloadduct. In both reactions series, we have considered only the exo approach of the group (W) relative to the π system of the diene.



Scheme 2. Dienophiles listed in Table 3.

Table 3 summarizes the results on the DA reaction of the 1,3-butadiene toward a series of dienophiles. The reactivity global indexes evaluated for the dienophiles are: chemical potential (μ), Chemical hardness (η) and electrophilicity index (ω). ΔE_{kin} corresponds to the energy barrier to reach the transition state structure and ΔE_{therm} is the thermodynamic energy involved in the formation of the Diels–Alder product from separated pair diene/dienophile. DFT calculations were carried out using the B3LYP exchange–correlation functional, together with the standard 6-31G(d) basis set. This level of theory has been shown suitable to provide good enough performance in the analysis of both geometric and electronic properties of DA reactions [70]. The dienophiles are given in decreasing order of the ω value (fifth column in Table 3). At the top of this table appears acrolein–BH_3 complex, which is classified as a strong electrophile (ω = 3.20 eV), while at the end is methyl acrylate (ω = 1.51 eV). Note that coordination of a BH_3 to the carbonyl oxygen atom of Acrolein (ω = 1.84 eV) noticeably increases the electrophilicity of the corresponding com-

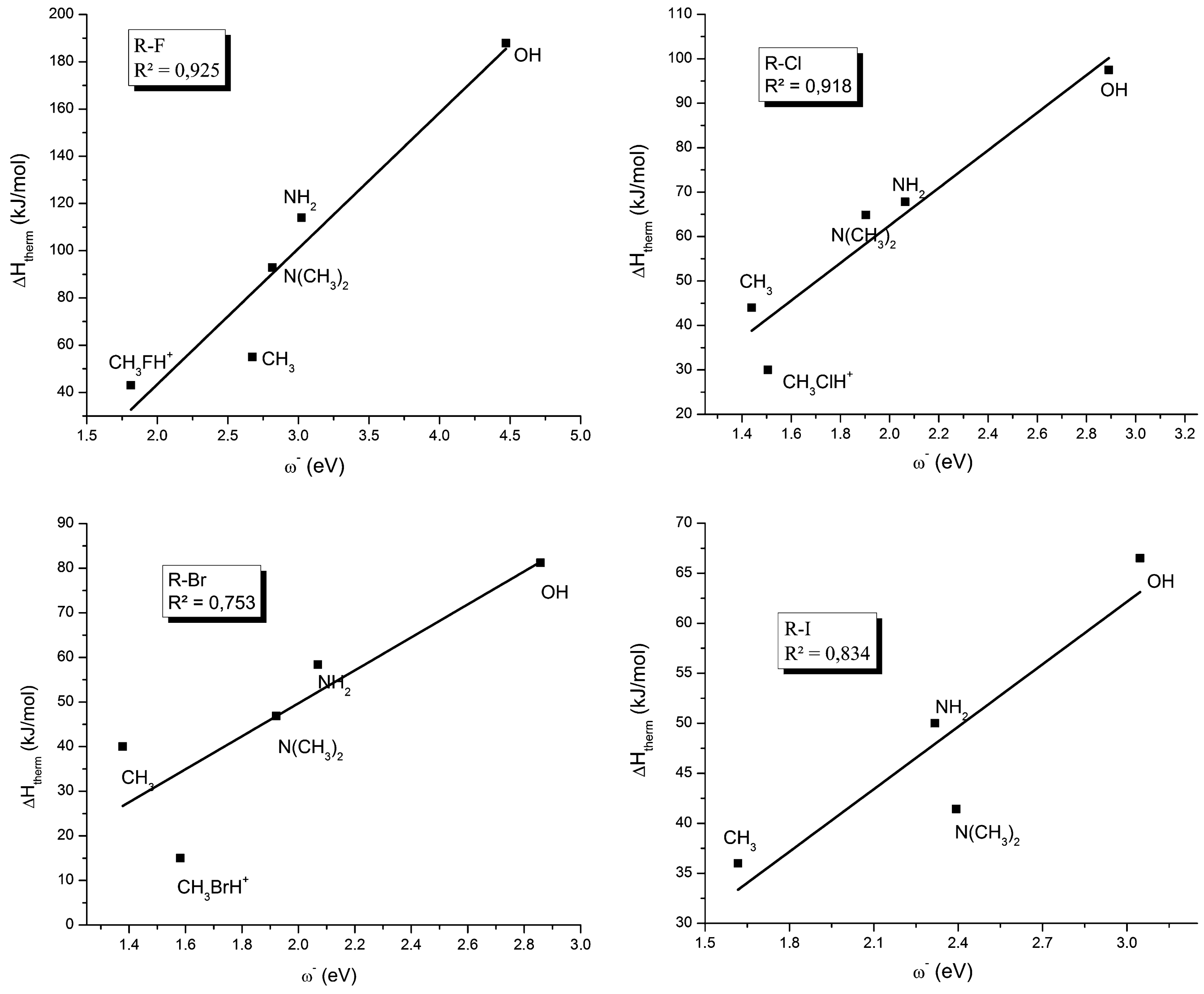
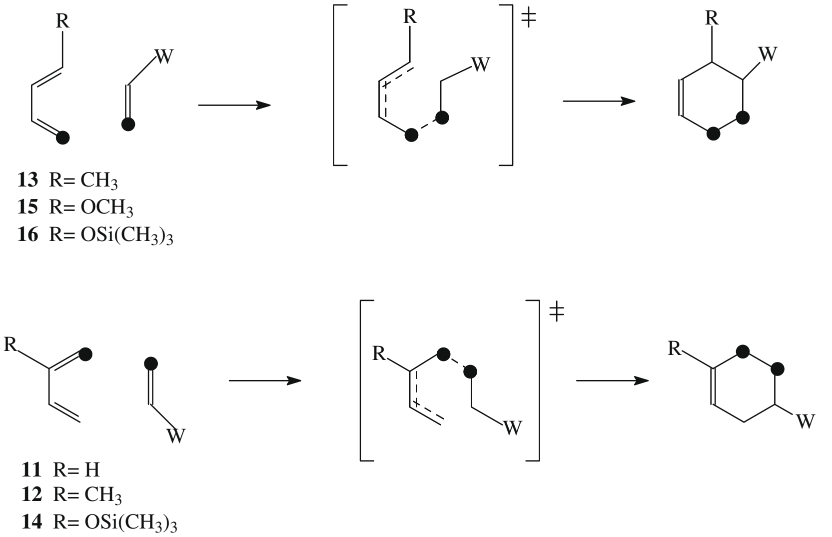


Fig. 3. Plot of enthalpies of reaction (ΔH_{therm}) of the X^- + RX identity reactions (R = CH_3, NH_2, $N(CH_3)_2$, OH, CH_3XH^+ and X = F, Cl, Br, I) vs. nucleophilicity index of the species X^- relative at RX.



13 R= CH_3
15 R= OCH_3
16 R= $OSi(CH_3)_3$

11 R= H
12 R= CH_3
14 R= $OSi(CH_3)_3$

Scheme 3. Dienes listed in Table 4 and acrolein–BH_3 complex and 1,1-dicyanoethylene dienophiles.

Table 3
Reactivity global indexes (μ, η, ω)[a] of dienophiles and the activation (ΔE_{kin}) and reaction (ΔE_{therm}) energies involved in Diels Alder reactions with 1,3-butadiene. Calculated at B3LYP/6-31G(d) level of theory.

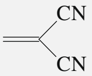
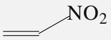
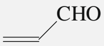
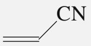
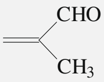
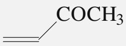
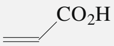
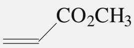
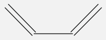
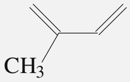
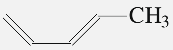
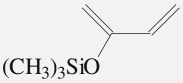
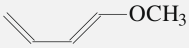
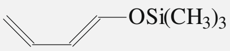
	Molecule	μ(eV)	η(eV)	ω(eV)	ΔE_{kin} (kJ/mol)	ΔE_{therm} (kJ/mol)
1	 Acrolein-BH_3 complex	−5.14	4.13	3.20	42,30	−159.08
2	 1,1-dicyanoethylene	−5.64	5.65	2.82	45,39	−159.95
3	 Nitroethylene	−5.33	5.45	2.60	51,52	−189.52
4	 Acrolein	−4.38	5.23	1.84	66,13	−159.1
5	 Acrylonitrile	−4.70	6.34	1.74	66,96	−174.38
6	$CH_3OOC—C\equiv C—COOCH_3$ Dimethylacetylenedicarboxylate DMAD	−4.68	6.37	1.72	64,80	−268.39
7	 1-methyl Acrolein	−4.27	5.36	1.70	73,20	−140.16
8	 Methyl vinyl ketone	−4.15	5.20	1.65	69,53	−159.33
9	 Acrylic acid	−4.46	6.22	1.60	67,06	−165.54
10	 Methyl acrylate	−4.31	6.17	1.51	66,27	−167.76

Table 4
Reactivity global indexes (μ, η, ω^-)[a] of dienes and the activation energies ($\Delta E^{kin}_{[1]}$, $\Delta E^{kin}_{[2]}$) involved in Diels Alder reactions with the acrolein–BH$_3$ complex and 1,1-dicyanoethylene, respectively. Calculated at B3LYP/6-31G(d) level of theory.

	Molecule	μ(eV)	η(eV)	ω(eV)	ω^-[1] (eV)	ω^-[2] (eV)	$\Delta E^{kin}_{[1]}$ (kJ/mol)	$\Delta E^{kin}_{[2]}$ (kJ/mol)
11	 1,3-butadiene	−3.46	5.67	1.05	0.083	0.106	49.55	45.39
12	 2-methyl-1,3-butadiene	−3.30	5.77	0.94	0.099	0.122	47.07	41.00
13	 (*E*)-1,3-pentadiene	−3.22	5.54	0.93	0.109	0.130	35.57	35.05
14	 2-trimethylsilyloxy-1,3-butadiene	−3.12	5.39	0.90	0.121	0.141	31.77	25.66
15	 1-methoxy-1,3-butadiene	−2.86	5.26	0.77	0.155	0.172	26.88	15.21
16	 1-trimethylsilyloxy-1,3-butadiene	−2.79	5.33	0.73	0.164	0.180	22.16	18.47

Nucleophilicity index relative at acrolein–BH$_3$ complex (ω^-[1]) and 1,1-dicyanoethylene (ω^-[2]).

[a] μ chemical potential, ηchemical hardness, ω electrophility and ω^- nucleophilicity indexes.

Table 5
Linear correlations of the reactivity indexes (μ, η, ω), calculated for the dienophile, with the energetic parameters (ΔH_{therm} and ΔH^{kin}) of 1,3-butadiene + dienophile[a] cycloadditions.

Index	$R^2(\Delta E^{kin})$ [b]	$R^2(\Delta E_{therm})$ [c]		
		(**1**)	(**2**)	(**3**)
μ	0.82	0.02	0.02	0.37
η	0.25	0.21	0.20	0.59
ω	0.93	0.01	0.01	0.15

[a] Dienophiles listed in Table 3.

[b] Indexes and kinetic parameter calculated at B3LYP/6-31G(d) level of theory (see Table 3).

[c] (**1**) Indexes and thermodynamic parameter calculated at B3LYP/6-31G(d) level of theory, (**2**) Indexes calculated at B3LYP/6-31G(d) level of theory and thermodynamic parameter calculated at CBS-QB3 level of theory, (**3**) Indexes and thermodynamic parameter calculated at CBS-QB3 level of theory.

Table 6
Linear correlations of the reactivity indexes (μ, η, ω, ω^-), calculated for the diene, with the activation energy (ΔH^{kin}) of dienea + acrolein–BH$_3$ complex and diene [a]+1,1-dicyanoethylene cycloadditions .[b]

Index	R^2 (ΔE^{kin})	
	acrolein–BH$_3$	1,1-dicyanoethylene
μ	0.91	0.94
η	0.87	0.91
ω	0.85	0.87
ω^-	0.90	0.93

[a] Dienes listed in table 4.

[b] Indexes and activation energy calculated at B3LYP/6-31G(d) level of theory (see Table 4).

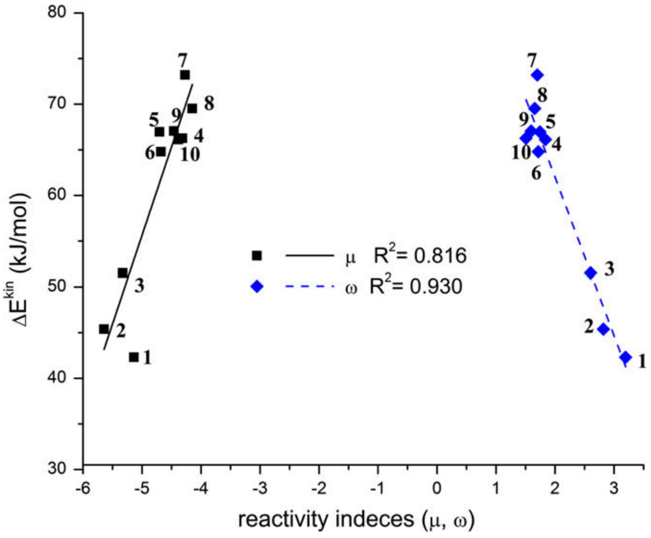


Fig. 4. Plot of activation energy (ΔE^{kin}) of the Diels Alder reactions (scheme 1) vs. chemical potential (μ) and electrophilicity (ω) indexes of dienophiles. Values listed in Table 3.

plex Acrolein–BH$_3$ (ω = 3.20 eV). The ω values for the dienophiles are higher than that for the 1,3-butadiene (ω = 1.05 eV, see Table 4). Therefore, for all cases the dienophile/1,3-butadiene interacting pair corresponds to the electrophile/nucleophile pair (NED reaction). These results are consistent with chemical potential values (third column in Table 3 and Table 4). The chemical potential value for 1,3-butadiene (μ = −3.46 eV) is higher than the chemical potential values of the dienophiles. Hence the electron transfer is from the 1,3-butadiene to the dienophiles.

The dienes reactivity indexes, chemical potential (μ), chemical hardness (η), electrophilicity (ω) and nucleophilicity (ω^-, see appendix), are given in Table 4. The nucleophilicity index is evaluated relative to acrolein–BH$_3$ complex (ω^-[1]) and 1,1-dicyanoethy-

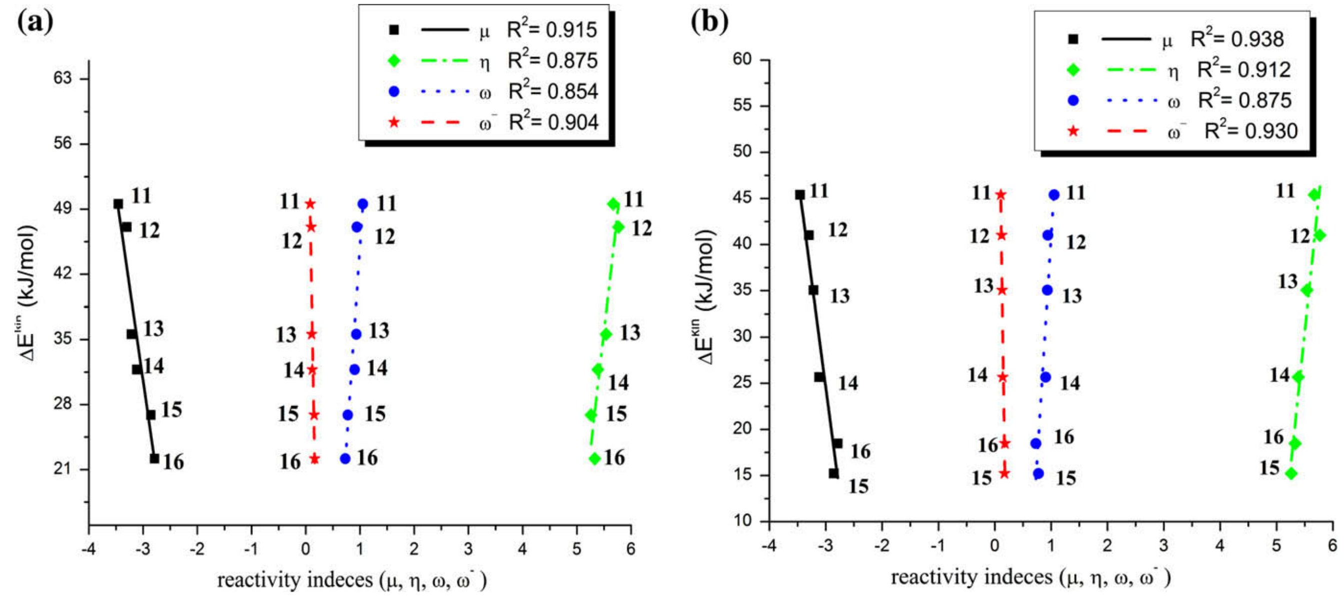


Fig. 5. Plot of activation energy (ΔE^{kin}) of the Diels Alder reactions (scheme 2) of (a) Acrolein–BH_3 complex and (b) 1,1-dicyanoethylene dienophiles with the dienes listed in table 4 vs. chemical potential (μ), chemical hardness (η), electrophilicity (ω) and nucleophilicity (ω^-) of dienes.

lenen ($\omega^-[2]$) dienophiles (sixth and seventh columns in Table 4, respectively). The kinetic parameters, $\Delta E^{\mathrm{kin}}_{[1]}$ and $\Delta E^{\mathrm{kin}}_{[2]}$, correspond to energetic barriers to reach the transition state structure for the cycloadditions of the acrolein–BH_3 complex and 1,1-dicyanoethylene dienophiles, respectively. In this Table the dienes are given in decreasing order of the ω value (fifth column). At the top is the 1,3-butadiene (ω = 1.05 eV) and at the end is 1-trimethylsilyloxy-1,3-butadiene (ω = 0.73 eV). By examining the nucleophilicity index ω^- for the diene relative to acrolein–BH_3 complex and 1,1-dicyanoethylene, we found that the 1,3-butadiene ($\omega^-[1]$ = 0,083 eV and $\omega^-[2]$ = 0.106 eV) is the worst nucleophiles of this series, while 1-trimethylsilyloxy-1,3-butadiene ($\omega^-[1]$ = 0.164 eV and $\omega^-[2]$ = 0.180 eV) represents the best one. Clearly, there is an inverse relationship between the electrophilicity ω and the nucleophilicity ω^- indexes. These results are consistent with the expected reactivity pattern.

For the studied Diels–Alder reactions a linear correlation between the reactivity indexes and energetic parameters has been found. Table 5 shows the linear correlation for the reactions between 1,3-butadiene and the dienophiles series listed in Table 3. The kinetic parameter ΔE^{kin} displays a reasonable linear correlation with the indexes of reactivity (Fig. 4): chemical potential (R^2 = 0.82), electrophilicity (R^2 = 0.93) and nucleophilicity (R^2 = 0.91), exception made of the chemical hardness (R^2 = 0.25). On the other side, with the thermodynamic parameter $\Delta E_{\mathrm{therm}}$ there is no linear correlation with any reactivity indexes (Table 5). In the process of the review of this work, a referee called our attention on the poor accuracy of the B3LYP calculations to describe the thermochemistry of these reactions. We recalculated the thermodynamic parameter $\Delta E_{\mathrm{therm}}$ for the reactions between 1,3-butadiene and the dienophiles series using the method CBS-QB3 [71]. Table 5 (column 4 and 5) shows the results. It is observed that the correlations are almost the same. We also checked whether there is a correlation between the kinetic parameter and reactivity indexes for the cycloadditions of the dienes series (Table 4) toward the Acrolein–BH_3 complex and 1,1-dicyanoethylene. Our results show that there is a good correlation whit all reactivity indexes (μ, η, ω and ω^-) in both reactions series (see Table 6, Fig. 5). These results show again that the free reactant reactivity indexes correlate well with the first energetic change in relation to the separated reactants, in this case the kinetic parameter. The correlation with the second energetic change regarding separated reactants is very poor, which for these Diels–Alder reactions corresponds to the thermodynamic parameter.

In summary, for both set of reactions some density functional reactivity indexes have been compared with kinetic and thermodynamic energy differences. All the numbers have been calculated under similar conditions and numerical accuracy. Hence, the comparisons are not affected by calculation artifacts or neglected effects. The results show that the reactivity indexes correlate well with the first energy difference, independent of whether this is kinetic barrier energy or a thermodynamic energy. The correlation of the reactivity indexes with thermodynamic parameters is good for S_N2 reactions, whereas for Diels–Alder reactions there is no correlation. On the other side, the correlation between the reactivity indexes and kinetic parameters is poor for S_N2 reactions, whereas for Diels–Alder reactions a reasonable linear correlation was found. Therefore, one could conclude that the reactivity indexes are neither kinetic nor thermodynamic. They are just derived by perturbation theory arguments indicating only the "very beginning" of the reaction.

Acknowledgements

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Appendix A

In this appendix, the nucleophilicity index which has been proposed in Ref. [19] will be introduced as an extension of the model used by Parr et al. [14] to propose the electrophilicity index. Most of the equations are already known but it is the first time that both concepts, electrophilicity and nucleophilicity are proposed together starting from the same model. Consider a molecule **A** reacting with a molecule **B** to give as a product **AB**:

$$\mathrm{A} + \mathrm{B} \rightarrow \mathrm{AB} \tag{A1}$$

Suppose now that one is looking only to the charge transfer ignoring completely the variations in the potential energy felt by **A** and **B**. One can think the process in two parts. First, they interchange charge at constant chemical potential, and then at constant electron charge the chemical potential is varied to reach the final equilibrium. In this case, one can use the Taylor series expansion of Eq. (1) for each subsystem **A** and **B** in the molecule **AB**. Therefore, the energy change due to the electron transfer associated to the process of Eq. (A1) will be

$$\Delta E_{\mathrm{AB}} = (\mu_{\mathrm{A}} - \mu_{\mathrm{B}})N + \frac{1}{2}(\eta_{\mathrm{A}} + \eta_{\mathrm{B}})N^2 + \ldots \tag{A2}$$

N representing the gain or lose of electron charge of the system **A** which has the opposite sign for the system **B**. Now, the amount of charge that atoms **A** and **B** are able to interchange will be the one which minimize the energy, and it is given by

$$N = \frac{\mu_A - \mu_B}{\eta_A + \eta_B} \tag{A3}$$

The sign of *N* will be dictated by the chemical potential difference indicating which system acts as a donor of charge and which one as an acceptor of charge. Once *N* is fixed the new formed molecule **AB** seeks to optimize the chemical potential in order to get to the equilibrium state. The process occurs at constant number of electrons and external potential and the changes are obtained optimizing the grand potential with respect to the variation of μ

$$\Delta\Omega_M = -N\Delta\mu - \frac{1}{2}S_M\Delta\mu^2 + \ldots \tag{A4}$$

where *M* refers to the species **A** or **B**, *N* is given by Eq. (A3) and S_M is the softness of species *M*. One obtains

$$\Delta\mu = -N\eta_M \tag{A5}$$

and the resulting potential is

$$\Delta\Omega_M = \frac{1}{2}N^2\eta_M \tag{A6}$$

The optimal value of the grand potential can be interpreted as the capacity of the system to accept or donate charge and, in the case of a donor of charge corresponds to the nucleophilicity concept quoted by the symbol, ω^-. Inserting the value of *N* from Eq. (A3) and writing now ω^-, one gets

$$\omega_M^- = \frac{(\mu_{\mathrm{A}} - \mu_{\mathrm{B}})^2}{2(\eta_{\mathrm{A}} + \eta_{\mathrm{B}})^2}\eta_M \tag{A7}$$

Note that the variation of the chemical potential at constant external potential is in the direction of optimizing the effect on the grand potential. Let us then consider the reactivity of **A** with respect to any other molecule **B**. Of course, the chemical potential difference dictates which one acts as a donor or an acceptor of charge. In the limit case of **B** being an “electron reservoir”, i.e. a system able of giving any amount of electrons without changing in any significant way the chemical potential, one has μ_{B} and η_{B} going to zero, and the system **A** will react as an electron acceptor. In this case, the variation of the grand potential is:

$$\Delta\Omega_A = \frac{\mu_A^2}{2\eta_A} \tag{A8}$$

which is exactly the Parr’s definition of the electrophilicity index of Eq. (4). This index has been widely used and its importance in chemistry recently reviewed [18]. This is, like the chemical potential and the hardness, an absolute index, in the sense that it depends only on the reactant **A** independent of the partner **B**. Therefore, it has been possible to do absolute scales ordering family of molecules according to their ability to act as an acceptor of charge. Unfortunately, it is not possible to do a similar model for the dual concept. For a molecule acting as a donor of charge, there is no a counterpart for the limiting case of the “electron reservoir”. While it is always possible to think of a system donating any amount of electron charge, it does not exist a system which can receive any amount of charge. This lack of symmetry between the concepts of electron donor and electron acceptor is only one more consequence of the discontinuity of the energy derivative with respect to the number of electrons. Hence, at least using the model of Eq. (A1), for the case of molecule **A** acting as an electron donor its ability as a donating will depend on the partner **B** as dictated by Eq. (A7), which has been proposed [19] as a measure of the nucleophilicity of molecule **A** in presence of molecule **B**.

References

[1] L. Pauling, The Nature of the Chemical Bond, University Press, 1960.
[2] J. Edwards, R. Pearson, J. Am. Chem. Soc. 84 (1962) 16.
[3] C. Swain, C. Scott, J. Am. Chem. Soc. 75 (1953) 71.
[4] C. Richie, Acc. Chem. Res. 5 (1972) 348.
[5] A. Legon, D. Millen, J. Am. Chem. Soc. 109 (1987) 356.
[6] P.K. Chattaraj, U. Sarkar, D. Roy, M. Elango, R. Parthasarthi, V. Subramanian, Ind. J. Chem. A 45A (2006) 1099.
[7] E. Uggerud, Chem. Eur. J. 12 (2006) 1127.
[8] P. Jaramillo, P. Pérez, P. Fuentealba, J. Phys. Org. Chem. 20 (2007) 1050.
[9] R.G. Parr, W. Yang, Density Functional Theory of Atoms and Molecules, Oxford Press, 1989.
[10] P. Geerling, F. de Proft, W. Langaenecker, Chem. Rev. 103 (2003) 1793.
[11] P. Ayers, J. Anderson, L. Bartolotti, Int. J. Quantum Chem. 101 (2005) 520.
[12] R.G. Parr, R. Donelly, M. Levy, W. Palke, J. Chem. Phys. 68 (1978) 3801.
[13] R.G. Parr, R. Pearson, J. Am. Chem. Soc. 105 (1983) 7512.
[14] R.G. Parr, L. von Szentpaly, S. Liu, J. Am. Chem. Soc. 121 (1999) 1922.
[15] P. Fuentealba, R.G. Parr, J. Chem. Phys. 94 (1991) 5559.
[16] E. Chamorro, R. Contreras, P. Fuentealba, J. Chem. Phys. 113 (2000) 10861.
[17] A.T. Maynard, M. Huang, W.G. Rice, D.G. Covell, Proc. Natl. Acad. Sci. USA 95 (1998) 11578.
[18] P.K. Chattaraj, U. Sarkar, D. Roy, Chem. Rev. 106 (2006) 2065.
[19] P. Jaramillo, P. Pérez, R. Contreras, W. Tiznado, P. Fuentealba, J. Phys. Chem. A 110 (2006) 8181.
[20] J.L. Gazquez, A. Cedillo, A. Vela, J. Phys. Chem. A 111 (2007) 1966.
[21] M.J. Frisch et al., Gaussian 03, Revision E.01, Gaussian, Inc., Wallingford CT, 2004.
[22] K.A. Peterson, B.C. Shepler, D. Figgen, H. Stoll, J. Phys. Chem. A 110 (2006) 13877.
[23] K.A. Peterson, D. Figgen, E. Goll, H. Stoll, M. Dolg, J. Chem. Phys. 119 (2003) 11113.
[24] M.J. Pellerite, J.I. Brauman, J. Am. Chem. Soc. 105 (1983) 2672.
[25] G. Caldwell, T.F. Magnera, P.J. Kebarle, J. Am. Chem. Soc. 106 (1984) 959.
[26] J.A. Dodd, J.I. Brauman, J. Phys. Chem. 90 (1986) 3559.
[27] S.E. Barlow, J.M. Van Doren, V.M. Bierbaum, J. Am. Chem. Soc. 110 (1988) 7240.
[28] J.M. Van Doren, C.H. DePuy, V.M. Bierbaum, J. Phys. Chem. 93 (1989) 1130.
[29] C.H. DePuy, S. Gronert, A. Mullin, V.M. Bierbaum, J. Am. Chem. Soc. 112 (1990) 8650.
[30] S.T. Graul, M.T. Bowers, J. Am. Chem. Soc. 113 (1991) 9696.
[31] A.A. Viggiano, J.S. Paschkewitz, R.A. Morris, J.F. Paulson, A. Gonzalez-Lafont, D.G. Truhlar, J. Am. Chem. Soc. 113 (1991) 9404.
[32] B.D. Wladkowski, K.F. Lim, W.D. Allen, J.I. Brauman, J. Am. Chem. Soc. 114 (1992) 9136.
[33] D.M. Cyr, G. Scarton, M.A. Johnson, J. Chem. Phys. 99 (1993) 4869.
[34] S.T. Graul, M.T. Bowers, J. Am. Chem. Soc. 116 (1994) 3875.
[35] A.A. Viggiano, R.A. Morris, T. Su, B.D. Wladkowski, S.L. Craig, M. Zhong, J.I. Brauman, J. Am. Chem. Soc. 116 (1994) 2213.
[36] R.A.J. O’Hair, G.E. Davico, J. Hacaloglu, T.T. Dang, C.H. DePuy, V. Bierbaum, J. Am. Chem. Soc. 116 (1994) 3609.
[37] W.N. Olmstead, J.I. Brauman, J. Am. Chem. Soc. 99 (1997) 4219.
[38] J.V. Seeley, R.A. Morris, A.A. Viggiano, H. Wang, W.L. Hase, J. Am. Chem. Soc. 119 (1997) 577.
[39] M.L. Chabinyc, S.L. Craig, C.K. Regan, J.I. Brauman, Science 279 (1998) 1882.
[40] R. Gareyev, S. Kato, V.M. Bierbaum, J. Am. Soc. Mass Spectrom. 12 (2001) 139.
[41] M.V. Basilevsky, V.M. Ryaboy, Chem. Phys. Lett. 129 (1986) 71.
[42] S.R. Vande Linde, W.L. Hase, J. Am. Chem. Soc. 111 (1989) 2349.
[43] S.C. Tucker, D.G. Truhlar, J. Am. Chem. Soc. 112 (1990) 3338.
[44] X.G. Zhao, S.C. Tucker, D.G. Truhlar, J. Am. Chem. Soc. 113 (1991) 826.
[45] G.D. Billing, Chem. Phys. 159 (1992) 109.
[46] S. Shaik, H.B. Schlegel, S. Wolfe, Theoretical Aspects of Organic Chemistry, The S_N2 Mechanism, Wiley, New York, 1992.
[47] W.L. Hase, Science 266 (1994) 998.
[48] I. Lee, C.K. Kim, D.S. Chung, B.-S. Lee, J. Org. Chem. 59 (1994) 4490.
[49] N.M. Glukhovtsev, A. Pross, L. Radom, J. Am. Chem. Soc. 117 (1995) 2024.
[50] G.H. Peslherbe, H. Wang, W.L. Hase, J. Am. Chem. Soc. 118 (1996) 2257.
[51] H. Wang, W.L. Hase, Int. J. Mass Spectrom. Ion Processes 167 (1997) 573.
[52] S. Timothy, W. Haobin, W.L. Hase, J. Phys. Chem. A 102 (1998) 9819.
[53] J. Zhang, U. Lourderaj, S.V. Addepalli, W.A. de Jong, W.L. Hase, J. Phys. Chem. A 113 (2009) 1976.
[54] S. Hoz, H. Basch, J.L. Wolk, T. Hoz, E. Rozental, J. Am. Chem. Soc. 121 (1999) 7724.

[55] P.O. Staneke, G. Groothuis, S. Ingemann, N.M.M. Nibbering, J. Phys. Org. Chem. 9 (1996) 471.
[56] C. Li, P. Ross, J.E. Szulejko, T.B. McMahon, J. Am. Chem. Soc. 118 (1996) 9360.
[57] S. Gronert, Acc. Chem. Res. 36 (2003) 848.
[58] Y. Ren, J.L. Wolk, S. Hoz, Int. J. Mass Spectrom. 220 (2002) 1.
[59] N.M. Glukhovtsev, A. Pross, L. Radom, J. Am. Chem. Soc. 117 (1995) 9012.
[60] Y. Ren, J.L. Wolk, S. Hoz, Int. J. Mass Spectrom. 221 (2002) 59.
[61] R. Yi, H. Basch, S. Hoz, J. Org. Chem. 67 (2002) 5891.
[62] N.M. Glukhovtsev, A. Pross, M.P. McGrath, L. Radom, J. Chem. Phys. 103 (1995) 1878.
[63] W. Carruthers, Cycloaddition Reactions in Organic Synthesis, Pergamon Press, Oxford, 1990.
[64] J. Sauer, R. Sustmann, Angew. Chem., Int. Ed. Engl. 19 (1980) 779.
[65] I. Fleming, Frontier Orbitals and Organic Chemical Reactions, John Wiley and Sons, New York, 1976.
[66] I. Fleming, Pericyclic Reaction, Oxford University Press, Oxford, 1999.
[67] L.R. Domingo, M. Arnó, R. Contreras, P. Pérez, J. Phys. Chem. A 106 (2002) 952.
[68] L.R. Domingo, M.J. Aurell, P. Pérez, R. Contreras, Tetrahedron 58 (2002) 4417.
[69] L.R. Domingo, M.J. Aurell, P. Pérez, R. Contreras, J. Phys. Chem. A 106 (2002) 6871.
[70] D.H. Ess, G.O. Jones, K.N. Houk, Adv. Synth. Catal. 348 (2006) 2337.
[71] J.A. Montgomery Jr., M.J. Frisch, J.W. Ochterski, G.A. Petersson, J. Chem. Phys. 110 (1999) 2822.