Reactivity of the carbon–carbon double bond towards nucleophilic additions. A DFT analysis

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Abstract—The global and local electrophilicity indexes have been used to characterize the reactivity pattern of the C=C double bond towards nucleophilic addition reactions. A wide family of molecules including ketones, esters, anhydrides, nitriles and nitrocompounds containing appropriate substitution on the C=C double bond have been classified within an unique scale of reactivity. The predictive capability of the theoretical model is tested against a series of benzylidenemalononitriles and substituted α-nitrostilbenes.

1. Introduction

The soft π electron density present on the C=C double bond constitutes a reactive site on the hydrocarbon skeleton. In the case of unsubstituted alkenes, the two carbon atoms participating in the double bond present a negative charge because of the larger electronegativity of the carbon atom relative to the hydrogen atom (C=C–H). The more electronegative character of the sp[2] hybrid respect to the sp[3] one is an additional source for the better stabilization of a negative charge in the former case. Therefore, the expected reactivity pattern of the C=C functionality is the attack by electrophiles, E[+]. However, this behavior can be drastically modified by suitable substitutions. For instance, the presence of an electron-withdrawing substituent at the C=C double bond modifies the reactivity pattern of an adjacent carbonyl group, thereby leading to the well known result that the α,β-unsaturated carbonyl compounds usually undergo conjugate nucleophilic additions, named Michael additions. The nucleophilic activation of the α,β-unsaturated carbonyl compounds is a challenging problem involving intramolecular selectivity in polyfunctional systems, that may be conveniently treated in terms of local (regional) reactivity indexes within a simple model we shall discuss here.

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The study of polar processes involving the interaction of electrophiles and nucleophiles may be significantly facilitated if reliable scales of electrophilicity and nucleophilicity are available. The utility of such global reactivity scales is of great importance to answer some fundamental questions in chemistry such as reaction feasibility (whether or not a given reaction will take place) or intermolecular selectivity. An excellent source that illustrates this concept well is the review work recently published by Mayr et al.[1] The development of theoretical scales of nucleophilicity and electrophilicity on the other hand is also desirable, as a validated theoretical scale may be further used to project the global reactivity onto particular regions in the molecule, thereby allowing the intramolecular selectivity to be also assessed.

There are different ways to model the electrophilicity concept using the electronic structure of molecules. A suitable one is that based on Parr et al.'s definition of global electrophilicity[2] which will shortly be described in the next Section. This scale has been largely validated against the experimental scale proposed by Mayr's group[3] and other scales.[4] The validation has been done for a large number of organic molecules, including Diels–Alder (DA) reagents,[5] molecules participating in 1,3 dipolar cycloadditions,[6] carbenes,[7] as well as benzhydryl cations[8] and diazonium ions.[9] The electrophilicity index has been further shown to be almost insensitive to solvent effects.[10] The global electrophilicity index is also a useful tool to elucidate the reaction mechanism (concerted vs stepwise) in some

cycloaddition reactions.[5,6] For a long time we have been interested in the study of the molecular mechanism of the polar DA reactions. These cycloadditions and the Michael reactions are mechanistically related, as the first step of these stepwise cycloadditions may be viewed as a Michael process in several cases.[11] In this line, Mayr et al. has proposed that for the stepwise [2+2] cycloaddition between morpholinoisobutene and benzylidenemalononitrile (**9** see Chart 1) the first step may be viewed as Michael addition of morpholinoisobutene to **9**.[12] Adequate substitution on the diene/dienophile pair favors the cycloaddition through a polar process. For instance, α,β-unsaturated carbonyl compounds are commonly used as activated dienophiles. Coordination of a Lewis acid to the carbonyl oxygen atom increases the reactivity of these dienophiles through an enhancement of the global electrophilicity. These polar cycloadditions, which take place along highly asynchronous transitions states, can be described as a consecutive Michael type addition/cyclization processes to afford the final cycloadduct.

Previous effort to explain the nucleophilic activation of Michael acceptors has been recently presented.[13] In this work the authors performed a charge analysis at the ground state of the α,β-unsaturated carbonyl compounds and they showed that the two carbon atoms of the C=C double bond displayed negative charges, thereby preventing reactions towards nucleophiles. They further showed that local reactivity indexes like local softness and the electrophilic Fukui function (i.e. the Fukui function for nucleophilic attack) performed better in describing the nucleophilic activation for a series of six Michael acceptors. However, local softness and the Fukui function contain essentially the same information as the Fukui function corresponds to a normalized softness. Recently, Mayr and Lemek[12] presented a kinetic study on the reactivity of a series of benzylidenemalononitriles towards a wide variety of nucleophiles. These authors used an experimental scale of electrophilicity to predict the reactivity of these systems. Extensive kinetic work on the nucleophilic additions to activated olefins have been reported by Bernasconi et al.[14–17] They include the thiolate ion addition to substituted α-nitrostilbenes[14] and morpholine and piperidine additions to substituted benzylidenemalononitriles.[15] Both, Mayr's and Bernasconi's groups have provided experimental rate coefficients that will be used in this work to test the predictive capability of the theoretical electrophilicity scale based on Parr et al. definition of global electrophilicity.[2]

Our working hypothesis establishes that the electrophilicity indexes (both global and local) are better descriptors of reactivity that the global softness and the Fukui function, in the sense that other effects coming from the
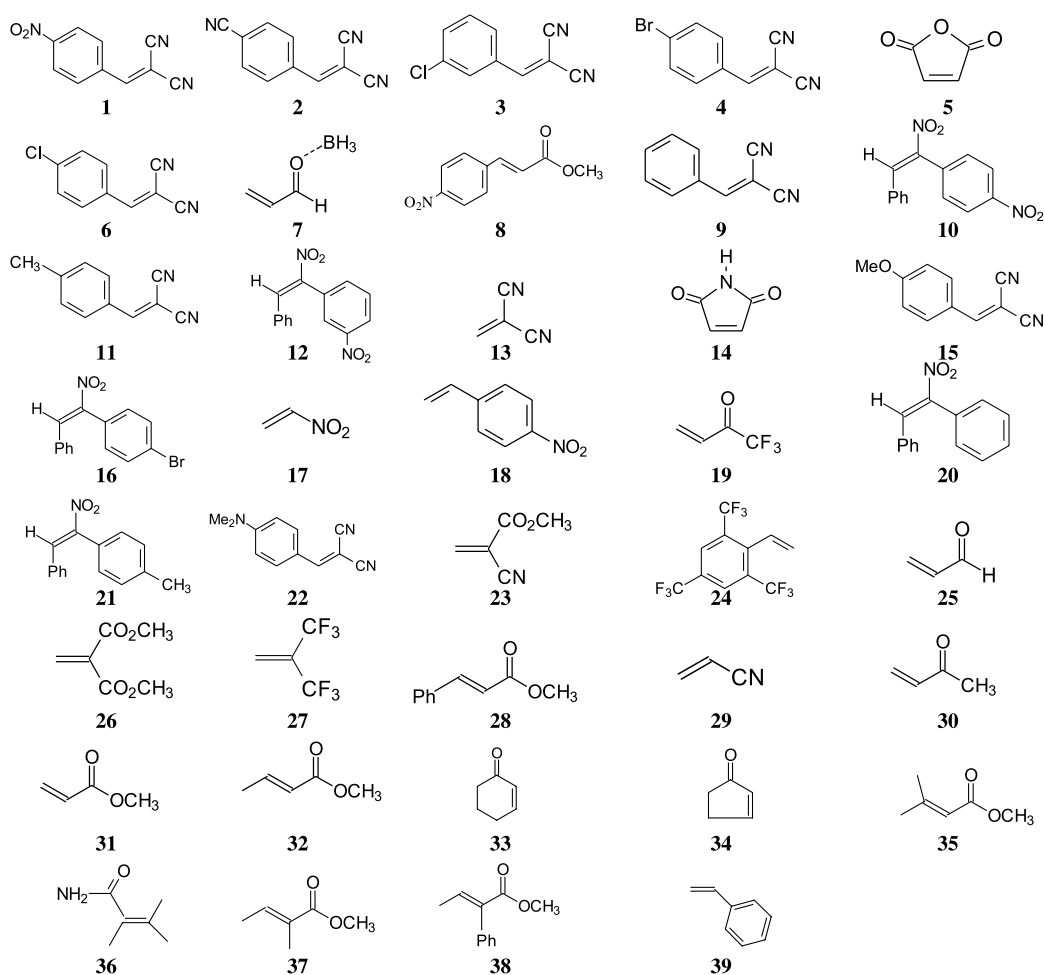

Chart 1. Series of molecules included in the present study.

electronegativity of the electron acceptors are incorporated in a single index encompassing the effect of the global softness.

In this work we present a systematic study on the global and local electrophilicity indexes for a wide family of substituted alkenes including α,β-unsaturated aldehydes, ketones, esters, anhydrides, nitriles and nitro derivatives as well as fluoroderivatives. We illustrate the usefulness of the global and local electrophilicity scales to explain the feasibility of the C=C double bond to react towards nucleophiles. Even though most of the members of the series included in the present study are Michael acceptors, some other cases are also considered.

2. The model

The concept of electrophilicity viewed as a reactivity index was introduced rather recently by Parr et al.[2] It is based on a second order expansion of the electronic energy with respect to the charge transfer ΔN at fixed geometry. Since electrophiles are species that stabilize upon receiving an additional amount of electronic charge from the environment, there exists a minimum of energy for a particular ΔN^* value. Using this simple idea Parr et al. performed a variational calculation that led to the definition of the global electrophilicity index as $\omega = -\Delta E(\Delta N^*)$, which may be recast into the more familiar form:[2]

$$\omega = \frac{\mu^2}{2\eta};\qquad(1)$$

in terms of the electronic chemical potential μ and the chemical hardness η. The ω index establishes an absolute scale of electrophilicity in the sense that the hierarchy of electrophilicity is built up from the electronic structure of molecules, independent of the nucleophilic partner, which is replaced by an unspecified environment viewed as sea of electrons.[2]

Beside the global electrophilicity index, it is possible to define its local (or regional) counterpart condensed to atoms. The local electrophilicity index ω_k condensed to atom k is easily obtained by projecting the global quantity onto any atomic center k in the molecule by using the electrophilic Fukui function (i.e. the Fukui function for nucleophilic attack, f_k^+). There result:[18]

$$\omega_k = f_k^+ \omega.\qquad(2)$$

The regional or condensed to atom electrophilicity index has been shown to correctly assess the regioselectivity in a number of cases.[7-9,18,19] In summary, while the global electrophilicity index categorizes within a unique scale the electron acceptor ability of molecules, its local or regional counterpart plays a key role in the elucidation of the intramolecular selectivity of the same systems. Note that site electrophilic activation may also be assessed as the variation in local electrophilicity induced for instance by chemical substitution or any source of external perturbation to the molecular system. Some applications that illustrate this concept have been already reported in the literature.[7-9,18,19]

3. Computational details

All the structures included in this study were optimized at the B3LYP/6-31G(d) level of theory using the Gaussian98 package of programs.[20] The calculation of the electronic chemical potential and the chemical hardness were obtained from the expressions $\mu \approx (\varepsilon_H + \varepsilon_L)/2$ and $\eta \approx \varepsilon_L - \varepsilon_H$, in terms of the one electron energies of the HOMO and LUMO frontier molecular orbitals, ε_H and ε_L, respectively.[21] With these quantities at hand, the global electrophilicity was obtained using Eq. 1. The local electrophilicity values are obtained from the global electrophilicity index and the electrophilic Fukui function using Eq. 2. The electrophilic Fukui function is evaluated from a single point calculation in terms of the molecular orbital coefficients and the overlap matrix using a procedure described elsewhere.[22,23]

4. Results and discussion

The systems considered in the present study are depicted in Chart 1, while the global electrophilicity valves are given in Table 1. Included in this series are the most common functionalities associated with the chemistry of the nucleophilic addition to the C=C double bond, namely aldehydes, ketones, esters, anhydrides, nitriles including a short series of benzylidenemalononitriles recently evaluated by Mayr et al.[12] as well as trifluoromethyl derivatives of ethylene, styrene and substituted α-nitrostilbenes.[14] Using the same criteria taken to classify the electrophilic power of dienes, dienophiles,[5] dipoles and dipolarophiles,[6] we may recognize a first subgroup of strong electrophiles with global electrophilicity values $\omega > 1.50$ eV (compounds 1–31 in Chart 1) and a second group of moderate electrophiles with $\omega < 1.50$ eV (compounds 32–39, in Chart 1). It is interesting to note that the electrophilicity hierarchy may be systematically rationalized in terms of the substituent effects induced by electron-withdrawing groups that result, as expected, in electrophilic activation, and the effect of electron-releasing groups leading to electrophilic deactivation. Consider for instance the series of carbonyl compounds. Starting from acrolein (25) we have on one hand a strong electrophilic activation induced by a Lewis acid (LA) catalyst modeled by BH_3 (7). Substitution of the aldehyde hydrogen atom in 25 by an electron-releasing methyl group to give methyl vinyl ketone (30) causes a moderate electrophilic deactivation. Substitution of this hydrogen atom by a methoxy group in methyl acrylate (31) produces an electrophilic deactivation. The π electron-releasing character of the $-OCH_3$ group overcome the σ electron-withdrawing one, and as a result, methyl acrylate (31) experiments a larger deactivation relative to acrolein 25. Note that substitution of the aldehyde hydrogen atom in 25 by the strong electron withdrawing CF_3 group to give compound 19 causes the opposite effect leading to a significant electrophilic activation.

For the carboxylic derivative series we take compound 31 as reference. Increasing substitution by methyl groups at the conjugated double bond to the carbonyl group consistently results in electrophilic deactivation (see compounds 32, 35, 37). Note however that while substitution of a hydrogen atom by a phenyl group in 32 to give 38 results in a moderate electrophilic deactivation, the substitution by a

Table 1. Global properties[a] and local electrophilicities of the series of electrophilically activated ethylenes **1-39**

Molecules	μ	η	ω	ω_k (Cβ)	ω_k (Cα)
1	−0.2112	0.1451	4.18	0.74	0.58
2	−0.2030	0.1454	3.85	0.90	0.61
3	−0.1907	0.1503	3.27	0.93	0.54
4	−0.1860	0.1447	3.25	0.92	0.52
5	−0.2083	0.1821	3.24	0.77	0.77
6	−0.1874	0.1472	3.24	0.92	0.52
7	−0.1837	0.1516	3.20	1.14	0.25
8	−0.1836	0.1533	2.99	0.34	0.20
9	−0.1832	0.1529	2.99	0.88	0.48
10	−0.1815	0.1501	2.99	0.67	0.25
11	−0.1774	0.1490	2.87	0.85	0.45
12	−0.1788	0.1536	2.83	0.63	0.24
13	−0.2074	0.2075	2.82	1.41	0.59
14	−0.1870	0.1740	2.73	0.61	0.61
15	−0.1672	0.1419	2.68	0.81	0.41
16	−0.1681	0.1463	2.63	0.59	0.22
17	−0.1958	0.2001	2.61	0.73	0.20
18	−0.1724	0.1577	2.56	0.26	0.05
19	−0.1865	0.1930	2.45	0.83	0.23
20	−0.1647	0.1504	2.45	0.53	0.22
21	−0.1614	0.1474	2.41	0.52	0.21
22	−0.1489	0.1279	2.36	0.70	0.33
23	−0.1907	0.2119	2.33	1.10	0.45
24	−0.1698	0.1985	1.97	0.26	0.08
25	−0.1610	0.1922	1.84	0.68	0.25
26	−0.1683	0.2135	1.80	0.82	0.33
27	−0.1872	0.2671	1.78	0.93	0.60
28	−0.1495	0.1706	1.78	0.39	0.33
29	−0.1726	0.2329	1.74	0.82	0.46
30	−0.1509	0.1929	1.60	0.60	0.23
31	−0.1586	0.2268	1.51	0.62	0.30
32	−0.1522	0.2144	1.47	0.59	0.24
33	−0.1423	0.1882	1.46	0.51	0.19
34	−0.1410	0.1933	1.40	0.54	0.20
35	−0.1474	0.2175	1.36	0.53	0.21
36	−0.1430	0.2125	1.31	0.52	0.32
37	−0.1418	0.2180	1.25	0.47	0.20
38	−0.1305	0.1923	1.20	0.39	0.17
39	−0.1261	0.1912	1.13	0.31	0.15

[a] Electronic chemical potential, μ, and chemical hardness, η, in atomic units; global, ω, and local, ω_k, electrophilicities, in eV. See the text for definitions.

phenyl group in **31** at the β position to give compound **28** results in an electrophilic activation. Substitution at the *para*-position by a nitro group of the phenyl moiety in **28**, to give compound **8**, results in an even higher electrophilic activation.

The presence of two electron-withdrawing substituents on the ethylene markedly increases the electrophilicity of the corresponding ethylene derivative. Thus, while cyano-ethylene (**29**) and methyl acrylate (**31**) are located on the bottom of the strong electrophiles subgroup, 1,1-dicyano-ethylene (**13**), methyl α-cyanoacrylate (**23**) and dimethyl fumarate (**26**) are classified as strong electrophiles. In this series the substitution by a −CN group produce a larger electrophilic activation than the −CO$_2$Me group. Note that acyl substitution results in an even higher electrophilic activation to give the maleic anhydride (**5**), located at the top of the scale, and malonoimide (compound **14**) within the series. However, the resulting symmetry in these compounds produces a significant lost of effectiveness as Michael acceptor, similar to the loss of reactivity already reported for the series of cyano-ethylenes.[19]

1,1-Ditrifluoromethylethylene **27** presents a larger electrophilic activation than ketones and esters which are usually used as Michael acceptors. In this case, the strong σ electron-withdrawing character of the CF$_3$ group is responsible for the larger electrophilic activation of ethylene. Furthermore, while styrene **39** is classified as a moderate electrophile, the substitution on the benzene moiety by three trifluoromethyl groups produces a strong electrophilic activation of the ethylene derivative **24**, which is classified as a strong electrophile within the present theoretical scale.

On the other hand, α-nitrostilbenes substituted at the α-phenyl ring present electrophilic activation when the hydrogen atom at the *para*-position of the aromatic ring in compound **20** is replaced by the strong electron-withdrawing group −NO$_2$ to give compound **10**. Note that the presence of an −Me group at the same position in compound **21** results in electrophilic deactivation.

The nitrile derivatives subseries is particularly interesting, since it contains a short series of benzylidenemalononitriles compounds (**9**, **15**, **22**), which have been kinetically evaluated by Mayr. For these compounds, there exist data for both the rate coefficients and the electrophilicity numbers (E).[12] This subseries will give us the opportunity to test the predictive value of our model. Consider for instance compounds **9**, **15** and **22**. The experimental order of electrophilicity (E) is **22**<**15**<**9**. Note that our predicted electrophilicity is in good qualitative agreement with this order. Unfortunately, the quantitative comparison is difficult since the experimental rate coefficients and electrophilicity values in comparable conditions (20 °C, H$_2$O/DMSO 1/1 v/v, piperidine as reference nucleophile) is only available for these three benzylidenemalononitriles (compounds **1a**−**c** in Ref. 12. Despite this limitation we compare in Figure 1 our predicted electrophilicity values with the experimental reaction rate coefficients reported by Mayr et al. It may be seen that the agreement is reasonably good. From the regression Eq. 3

$$\mathrm{Ln}\,(k) = 5.55\omega - 4.09 \tag{3}$$

we predict that the expected reaction rate coefficient for the reaction of compound **1** with piperidine would be about one
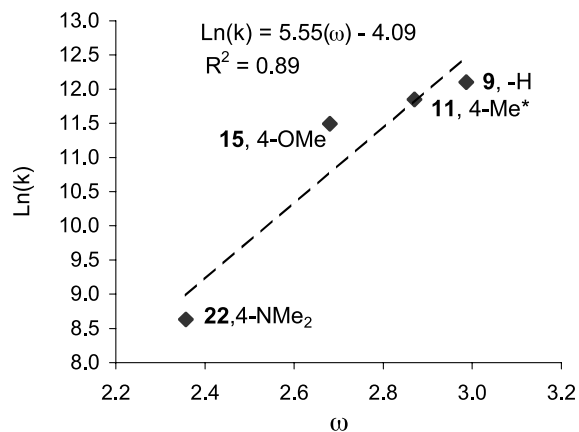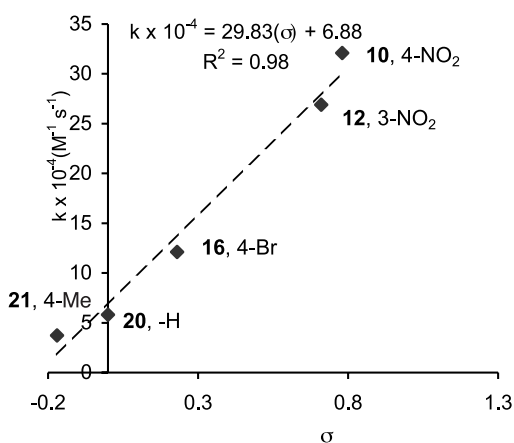
Figure 1. Plot of Ln(k) versus the electrophilicity index ω for the reaction of benzylidenemalononitriles series with piperidine. (∗) Predicted value. Rate coefficients k from Ref. 12.
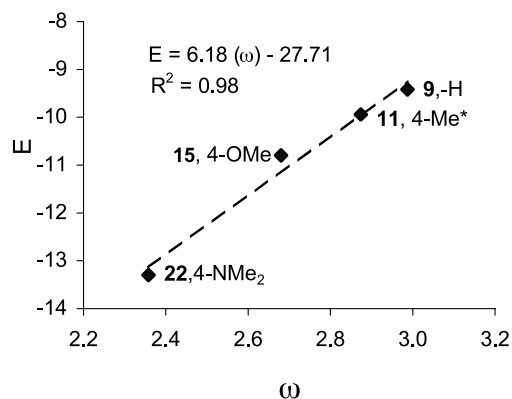
Figure 2. Plot of experimental electrophilic parameter E versus the electrophilicity index ω for the benzylidenemalononitriles series. ($*$) Predicted value. Rate coefficients k from Ref. 12.

thousand times faster than the reaction of piperidine with compound **9** (compound **1a** in Ref. 12). However, due to symmetry considerations that we will discuss below, such an enhancement should be significantly less than this figure. The predicted electrophilicity value for compound **1**, not evaluated in Mayr et al.'s database is $E=-1.88$ using the regression equation in Figure 2. However, this extrapolation is weak in view of the small number of experimental points available. A more reliable quantitative comparison may be obtained by an interpolation procedure for a compound that is expected to be bound, both in the experimental E scale and in the reaction rate coefficients. This is the case of compound **11**, whose predicted electrophilicity in the theoretical scale is $\omega=2.87$ eV. Using the regression Eq in Figure 2, this theoretical electrophilicity leads to the prediction that in the experimental scale compound **11** should show an E number around -9.94. Furthermore, the predicted rate coefficient for the reaction of this compound with piperidine in the same conditions should be bound by the rate coefficients of compounds **15** and **9** ($k\approx1.4\times10^5$ M^{-1} s^{-1}, obtained from the regression Eq. 3). Following a suggestion by a reviewer, regarding the incorporation of the experimental rate coefficients evaluated for compound **11** by Bernasconi's group in comparable experimental conditions,[15] the experimental value for the reaction of compound **11** with piperidine in a solvent

mixture 50% Me$_2$SO-50% H$_2$O is $k=2.14\times10^5$ M^{-1} s^{-1}, thereby showing the predictive capability of the global electrophilicity index.

Figure 3 shows the comparison between the rate coefficient and the Hammett substituent constant (σ) for the addition of HOCH$_2$CH$_2$S$^-$ to substituted α-nitrostilbenes reported by Bernasconi et al.[14] In a previous work, we have reported on a quantitative relationship between Hammett substituent constant (σ) for substituted ethylene and the global electrophilicity index.[24] Therefore it is not surprising to find a good correlation between Ln k and the global electrophilicity index ω, as shown in Figure 4.
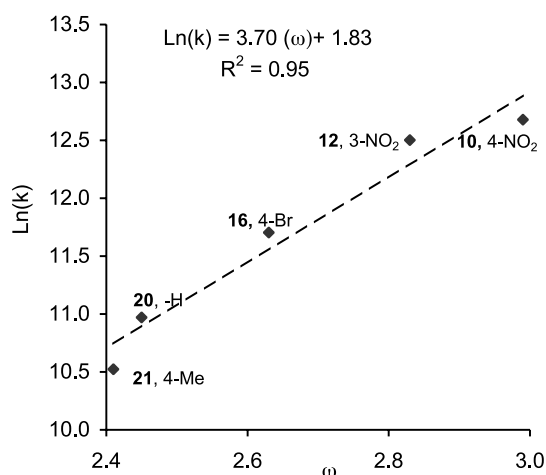
Figure 4. Plot of Ln(k) versus the electrophilicity index ω for the reaction of the addition of HOCH$_2$CH$_2$S$^-$ to substituted α-nitrostilbenes. Rate coefficients k from Ref. 14.

Following a remark addressed by a reviewer, we have incorporated 5 new substituted benzylidenemalononitriles[15] to the Mayr et al.'s series. The result of the comparison between Ln k and the global electrophilicity index ω is displayed in Figure 5. Note that this time the quantitative comparison between both quantities is not as good as the previously discussed correlation ($R^2=0.75$). The main factor that may account for this deviation may be traced

Figure 3. Plot of rate coefficients k versus Hammett substituent constant σ for the reaction of the addition of HOCH$_2$CH$_2$S$^-$ to substituted α-nitrostilbenes. Rate coefficients k from Ref. 14.
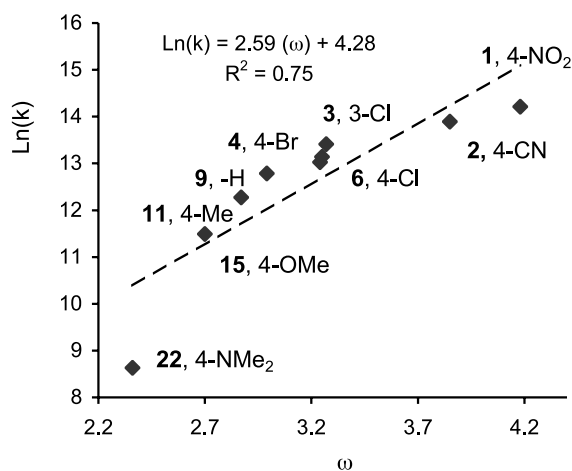
Figure 5. Plot of Ln(k) versus the electrophilicity index ω for the reaction of substituted benzylidenemalononitriles series with piperidine. Rate coefficients k from Ref. 15.

to solvent effects (not incorporated in the evaluation of the global electrophilicity index), preferentially affecting the highly polar electron releasing $-NMe_2$ group (compound **22**) and the highly polar electron withdrawing $-NO_2$ and $-CN$ groups (compounds **1** and **2**).[24] Thus, if we exclude the compound **22** of this series, the correlation improves considerably ($R^2=0.90$).

A final remark concerning the local reactivity picture is worth making. The local electrophilicity values ω_k, for the two carbon atom belonging to the $C{=}C$ double bond, named as $C\alpha$ and $C\beta$, of the series of 39 substituted ethylenes are given in Table 1. A joint analysis of the global electrophilicity of these molecules, and the projected local electrophilicity at the sites $C\alpha$ and $C\beta$, allows to obtain some additional conclusions: (i) in most of the cases the local electrophilicity value at the $C\beta$ position is larger than that at the $C\alpha$ position. In general, the ω_k value at the $C\beta$ is ca. 2.4 times the one localized at the $C\alpha$ position; (ii) the inclusion of a phenyl group at the $C\beta$ position decreases this relation to ca. 1.9 (see Mayr's subseries including compounds **9**, **15** and **22**). Note that for compound **1**, whose global electrophilicity is predicted to be drastically enhanced with respect to the parent compounds **9**, **15** and **22** by the presence of the $-NO_2$ group at the *para* position of the phenyl substituent, the $\omega_{C\beta}/\omega_{C\alpha}$ ratio decreases to 1.3. This result may suggest a loss of effectiveness of this molecule as a potential strong Michael acceptor in the sense that despite its high global electrophilicity it becomes at the same time less regioselective. This result is reminiscent of that obtained in the analysis of the cyanoethylene subseries.[19] Therein, the tetracyano derivative was shown to display the highest global electrophilicity, yet its reaction mechanism with cyclopentadiene was consistently predicted to proceed via a polar concerted synchronous pathway, not a stepwise one with a first step corresponding to a Michael addition.[19] Note that the same effect seems to be present in the symmetrically substituted compounds **5** and **14**, for which the $\omega_{C\beta}/\omega_{C\alpha}$ ratio approaches unity; (iii) the distribution of the local electrophilicity at the carbon atoms belonging to the $C{=}C$ double bond represents in most of the cases ca. 50% of the global electrophilicity of the molecule. Only in three out of the 39 cases considered here (compounds **8**, **18** and **24**), this distribution represents less than 30% of the global electrophilicity. This fact together with the large activation of the $C\beta$ position respect the $C\alpha$ one allows to conclude that the $C\beta$ site is the most electrophilically activated center of these electron-deficient substituted ethylenes, in complete agreement with experimentally observed regioselectivity shown by these molecules in the Michael addition reactions. Note that for the carbonyl and carboxyl derivatives given in this series the $\omega_{C\beta}/\omega_{C(carbonyl)}$ ratio is within the range of 1.4–2.4, the $C\beta$ position being more electrophilically activated than the $C(carbonyl)$ one.

5. Concluding remarks

The global electrophilicity index provides a quantitative classification of the absolute electrophilicity of α,β-unsaturated ketones, esters, anhydrides, nitriles, nitro-compounds and substituted styrenes and α-nitrostilbenes.

If we add to this database, the previously reported scale of global electrophilicity, including dienes, dienophiles, dipoles and dipolarophiles as well as the charged electrophiles including benzhydryl and diazonium cations, there results a useful theoretical scale. This scale may be used to explain, on a quantitative basis, the known reactivity of a significant body of organic compounds. The predictive power of the present scale of electrophilicity has been illustrated here for a short series of benzylidenemalono-nitriles and α-nitrostilbenes.

A validated theoretical reactivity scale on the other hand, is also a useful tool in the sense that this global property may be conveniently distributed in the molecule using the electrophilic Fukui function. The projected electrophilicity in turn, appears as a promising selectivity index. This has been illustrated in this work, by explaining the known regioselectivity displayed in the Michael's addition reaction.

References and notes

1. Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66.
2. Parr, R. G.; Szentpály, L. v.; Liu, S. *J. Am. Chem. Soc.* **1999**, *121*, 1922.
3. Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938.
4. Legon, A. C. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2686.
5. Domingo, L. R.; Aurell, M. J.; Pérez, P.; Contreras, R. *Tetrahedron* **2002**, *58*, 4417.
6. Pérez, P.; Domingo, L. R.; Aurell, M. J.; Contreras, R. *Tetrahedron* **2003**, *59*, 3117.
7. Pérez, P. *J. Phys. Chem. A* **2003**, *107*, 522.
8. Pérez, P.; Toro-Labbé, A.; Aizman, A.; Contreras, R. *J. Org. Chem.* **2002**, *67*, 4747.
9. Pérez, P. *J. Org. Chem. A* **2003**, *68*, 5886.
10. Pérez, P.; Toro-Labbé, A.; Contreras, R. *J. Am. Chem. Soc.* **2001**, *123*, 5527.
11. Domingo, L. R.; Picher, M. T.; Zaragozá, R. J. *J. Org. Chem.* **1998**, *63*, 9183.
12. Lemek, T.; Mayr, H. *J. Org. Chem.* **2003**, *68*, 6880.
13. Mondal, P.; Hazarika, K. K.; Deka, R. C. *Phys. Chem. Commun.* **2003**, *6*, 24.
14. Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506.
15. Bernasconi, C. F.; Killion, R. B., Jr. *J. Org. Chem.* **1989**, *54*, 2878.
16. Bernasconi, C. F.; Leyes, A. E.; Rappoport, Z. *J. Org. Chem.* **1999**, *64*, 2897.

17. Bernasconi, C. F.; Ketner, R. J.; Chen, X.; Rappoport, Z. *J. Am. Chem. Soc.* **1998**, *120*, 7461.
18. Domingo, L. R.; Aurell, M. J.; Pérez, P.; Contreras, R. *J. Phys. Chem. A* **2002**, *106*, 6871.
19. Domingo, L. R.; Aurell, M. J.; Pérez, P.; Contreras, R. *J. Org. Chem.* **2003**, *68*, 3884.
20. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; W. Gill, P. M.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A.; Gaussian 98, Revision A.6 Gaussian, Inc.: Pittsburgh PA, 1998.
21. Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.
22. Contreras, R.; Fuentealba, P.; Galván, M.; Pérez, P. *Chem. Phys. Lett.* **1999**, *304*, 405.
23. Fuentealba, P.; Pérez, P.; Contreras, R. *J. Chem. Phys.* **2000**, *113*, 2544.
24. Domingo, L. R.; Pérez, P.; Contreras, R. *J. Org. Chem.* **2003**, *68*, 6060.