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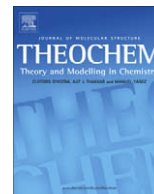**79** PUBLICATIONS **1,690** CITATIONS

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A comparison between theoretical and experimental models of electrophilicity and nucleophilicity

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ABSTRACT

Four different theoretical models of electrophilicity and nucleophilicity has been discussed in the light of experimental available evidence for a series of 20 benzhydrylium ions taken as reference electrophilic systems and 16 primary and secondary amines as nucleophilic systems. It is shown that the theoretical scales are linearly related to the well-known experimental ones based on the electrophilicity (E) and nucleophilicity (N and s) parameters derived by Mayr from the rate constants $k_{20\,°C}$ associated to general electrophile–nucleophile combinations, $\log k_{20\,°C} = s(N + E)$.

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1. Introduction

Electrophilicity and *nucleophilicity* are chemical concepts of great usefulness in the rationalization of electronic aspects of reactivity, selectivity, substituent effects, and solvent effects [1–10]. Despite these two quantities are known to depend on several factors, including the nature of substrate, the reagent, solvent, etc, that preclude the existence of unique and absolute indexes that could be applied to any chemistry situation [11–14], *relative* scales intended to categorize such reactivities have been proposed to be defined in terms of free energy relationships [11,15]. In this sense, and within an experimental perspective, Mayr et al. have emphasized that [7,9,15–31] benzhydrylium ions and quinone methides can be used as reference electrophiles [29,32,33] for characterizing a large variety of π-nucleophiles (e.g., alkenes, arenes, enol ethers, ketene acetals, enamines, allyl compounds, transition metal complexes, diazoalkanes, and delocalized carbanions), n-nucleophiles (e.g., amines, alcohols, alkoxides, phosphanes, inorganic anions, and pyridines), and σ-nucleophiles (e.g., hydrides) [19,20,22,31,34–40]. In their approximation, the rate constants have been correlated through,

$$\log k_{20\,°C} = s(N + E) \tag{1}$$

where $k_{20\,°C}$ is the second-order rate constant in units of $M^{-1}\,s^{-1}$, s is a nucleophile specific slope parameter, N is the nucleophilicity parameter, and E is the electrophilicity parameter. For a set of reference electrophiles, Eq. (1) defines nucleophilicity N values as

the intercept of the correlation line with the abscissa, and the slopes of these correlations yield the s parameters. This last number can be indeed neglected in qualitative considerations [41]. A comprehensive list of nucleophiles and electrophiles in terms of their N and E parameters is available spanning several hundreds of order of magnitude in terms of the associated experimental rate constants. An internet database containing a compilation of published reactivity parameters has been also made available [42]. It has been shown that the derived nucleophilicity orders also holds for reactions of these nucleophiles with non-charged electrophiles such as quinone methides [43].

Several theoretical efforts have been devoted to get qualitative and quantitative insights rationalizing these central concepts. Within this perspective and from a theoretical point of view, it has been emphasized that density functional theory (DFT) provides a powerful framework for the development and exploration of a chemical reactivity theory [44–55]. The electrophilicity index ω defined by Parr et al. [56] in terms of the electronic chemical potential and the chemical hardness [44], has shown to be a fruitful tool in the light of such proposal (see for instance Refs. [57–67] for recent examples). A review covering several application and extensions of this density functional theory descriptor is also available [68]. Extensions of such kind of descriptors into the framework of spin-polarized version of DFT have been also recently explored [69–76]. Within the interests of the current work we would like to emphasize that the electrophilicity index ω have been found linearly related to Mayr's electrophilicity E parameters for a series of reference benzhydryl cations [77]. The ω index has recently been successfully applied to quantitatively categorize in a simple scale both global [78] and local [79] reactivities of diene

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and dienophile reagents participating in DA reactions, dipole and dipolarophile pairs in 1,3-dipolar cycloadditions [80] and cycloaddition reactions of substituted *captodative* ethylenes [81,82]. It has also shown that ω is an important index to get further understanding on the reactivity of singlet carbenes and its electrophilic pattern [83]. Within a continuum model of solvent effects, it has been shown that the electrophilicity power of neutral electrophilic ligands becomes enhanced but it is attenuated in charged and ionic electrophiles [84]. There have also been many important attempts to define a theoretical quantity as an intrinsic nucleophilic index. Roy et al. [85] have proposed the direct use of local DFT reactivity descriptors such as hardness and softness [44] to predict both intramolecular an intermolecular nucleophilic attacks on carbonyl compounds. In a more general strategy, the (local) philicity concept introduced by Chattaraj et al. [66] emphasizes the idea of a unique generalized index, which can be applied to electrophilic, nucleophilic, and radical reactions [63,86] by projecting the global electrophilicity [56] through the electronic Fukui functions [44]. Dual and multiphilic descriptors have also been introduced describing the reactivity and selectivity [58,87–90]. These descriptors are intended to simultaneously give the electrophilicity and nucleophilicity proclivities of a given molecular system. A nucleophilicity index derived from a perturbation model for the interaction between a nucleophile and a positive test charge was presented [91]. Such model was validated for a series of neutral nucleophiles with a known nucleophilic pattern [91]. The use of point charges to study nucleophilicity has previously received a detailed attention within the context of energy changes in a perturbative framework [47,51,92–95]. In addition, nucleophilicity and electrophilicity of active radicals have been discussed using a variety of models proposed in the literature [96]. Recently, some of us have proposed an empirical nucleophilicity index for soft–soft interactions [97]. Such index is written in terms of frontier molecular orbitals, and it has been successfully validated against experimentally available kinetic data for amines, diimines, anilines, alcohols, ethers, alkenes, and π- and n-nucleophiles [97–99]. The appealing linear correlation found between the global electrophilicity and the nucleophilicity scales suggests that these concepts are indeed inversely related along related series of simple substituted systems [96]. A simple and useful model of nucleophilicity has demonstrated its usefulness for categorizing cycloadduct reagents [81,100]. The local extension of such nucleophilicity index was recently explored in the context of predicting substituent director effects in electrophilic aromatic substitution reactions [101].

Following our ongoing interest in to gain more insights into and to extend the range of applicability of theoretical models devoted to rationalize and quantify the electrophilicity and nucleophilicity concepts [77–82,97–101], in this work we further explore the theoretical basis defining electrophilicity and nucleophilicity quantities within the density functional theory framework. Our aim is to test the suitability of simple models (as presented in Section 2) of electrophilicity and nucleophilicity that arises from a variational perturbative approximation of a given system in interaction with an appropriate donor or acceptor environment. We mostly focus on the performance of the simplest approximations to these models in comparison to the well-established experimental Mayr's parameters [7,15–17,21,29–33] of electrophilicity and nucleophilicity.

2. Theory

Let us start by examining the recent discussion presented very recently by Gázquez et al. [102] within the conceptual framework provided by DFT [45,56,68]. It has been emphasized that the development of theoretical models for intrinsic electrophilicity and nucleophilicity powers can be derived from the examination of energy changes associated to a system in interaction with a "bath" simulating a given chemical environment. At first glance the bath can be considered as a reservoir for donating/accepting a finite number of electrons to/from the system. Thus, at global level this interaction can be considered to produce a net charge transfer, ΔN, between the system and the environment, will be modulated by the difference in chemical potentials between the bath and the system, $\mu_{bath} < 0$ and $\mu^{\pm} < 0$, respectively. Given the discontinuity of the energy with respect to the number of electrons, and considering that the responses of a system to accept/donate charge should be different, Gázquez et al. [102] have stressed that both the electroaccepting (e.g., intrinsic electrophilicity) and electrodonating (e.g., intrinsic nucleophilicity) powers of a given species can be defined by minimizing the change in the grand-potential energy $\Delta\Omega^{\pm} = \Delta E^{\pm} - \mu_{bath}\Delta N$ with respect to this amount of charge transfer, ΔN. Hence, such optimum transferred charge making stationary the grand canonical potential changes is,

$$(\Delta N)^* = \frac{\mu_{bath} - \mu^{\pm}}{\eta^{\pm}}. \tag{2}$$

This expression emphasizes that under the validity associated to such simple system–environment interaction, the difference in the chemical potentials *between the bath and the system* is the driven force for such charge transfer process. The system's energy change, ΔE, consequently is given by,

$$\Delta E^{\pm}(\Delta N^*) = \frac{\mu_{bath}^2 - (\mu^{\pm})^2}{2\eta^{\pm}}. \tag{3}$$

Eq. (3) say implies that this energetic change is negative (e.g., $\Delta E^+ < 0$) for a process where the system acts as an *electrophile* (i.e., by accepting charge from the bath, $\Delta N^* > 0$), and it is positive (e.g., $\Delta E^- > 0$) when the system acts as a *nucleophile* (i.e., donating charge to the bath, $\Delta N^* < 0$) as pictorially represented in Scheme 1. Note also that Eq. (3) incorporates the explicit dependence of the system's energy change in relation to the reaction partner, intrinsically represented at global level in terms of the bath's chemical potential. Note also in this point that Eqs. (2) and (3) are associated to a zero hardness chemical hardness, e.g., there is not resistance from the bath to charge transfer. Hence, electroaccepting/electrodonating powers have been [102] associated to the *intrinsic* system's contribution to its energy change,

$$\omega^{\pm} \equiv \frac{(\mu^{\pm})^2}{2\eta^{\pm}}. \tag{4}$$

The electrophilicity index first proposed by Parr et al. [56],

$$\omega \equiv \frac{\mu^2}{2\eta} = \frac{1}{8}\frac{(I+A)^2}{(I-A)} \quad \text{(Model I)} \tag{5}$$
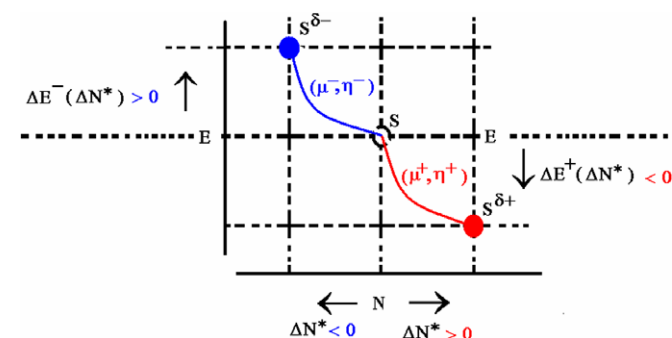
Scheme 1. The system's chemical potential and hardness quantities are negative and positively valued (e.g., $\mu^{\pm} < 0$, $\eta^{\pm} > 0$) for both the process of charge accepting and charge donation. The electrophilic systems' response (i.e., $\Delta N^* < 0$), raises its energy $\Delta E^- > 0$, whereas the nucleophilic one (i.e., $\Delta N^* > 0$), lowers it $\Delta E^+ < 0$.

can be recovered within this perspective under the consideration of a zero-chemical potential bath (e.g., a perfect donor), and taking the chemical potential at the N electron system to be an average between the slopes of the two straight lines connecting such state to those with $N-1$ and $N+1$ electrons in an exact theory [103,104,55,105,48], e.g., $\mu = -\frac{1}{2}(I+A)$. The associated hardness is therefore approximated as $\eta = I - A$ within a finite-difference scheme. Note however that within an exact theory $\mu^+ = -A$, and $\mu^- = -I$, and therefore $\eta^{\pm} = 0$. Gázquez et al. [102] have explicitly considered alternative interpolation schemes to both sides of the $E(N)$ curve by assuming different quadratic energy fits for the system's energy during charge accepting and charge donating processes. Their procedure yields to $\mu^+ = -\frac{1}{4}(I+3A)$ and $\mu^- = -\frac{1}{4}(3I+A)$, also supposing the same "curvature" for the two energy responses, i.e., $\eta^+ = \eta^- = 1/2(I-A)$. Hence, from Eq. (4) we have,

$$\omega^+ = \frac{(I+3A)^2}{16(I-A)}, \quad \omega^- = \frac{(3I+A)^2}{16(I-A)} \text{ (Model II)} \tag{6}$$

Within the spirit of Eq. (4), we note now that using an average hardness for the N electron system as above, an alternative scheme arises if we use directly that $\mu^+ = -A$, and $\mu^- = -I$, i.e.,

$$\omega^+ = \frac{A^2}{(I-A)}, \quad \omega^- = \frac{I^2}{(I-A)} \text{ (Model III)} \tag{7}$$

Eq. (7) is not absent of discussion, as it can be regarded as a component of Eq. (5). Alternatively, and only on intuitive basis, the "resistance" to the electron transfer from/towards the system could be related directly just to the chemical potential indicating the opposite electron charge process, e.g., $\eta^+ = |\mu^-| = |I|$ and $\eta^- = |\mu^+| = |A|$. This approach is presented here as an *ansatz,* yielding Eq. (4) to be rewritten as,

$$\omega^+ = \frac{A^2}{2|I|}, \quad \omega^- = \frac{I^2}{2|A|} \text{ (Model IV)} \tag{8}$$

Note again that Eqs. (7) and (8) are in fact naive modifications to the approximation given in Eq. (5). Eq. (4) and the above approximated models say simply that the intrinsic electrophilicity or

Scheme 2. Benzhydrylium cations used as electrophilic examples. Experimental electrophilicity parameters E_{Mayr} are available from Ref. [31].

nucleophilicity of a given system is driven by its propensity to accept or donate charge, e.g., $(\mu^{\pm})^2$, modulated by the "resistance" against such process, i.e., $2\eta^{\pm}$. We must note however that inclusion of electronegativity should be not regretted in such context, being an important component in more complete models of electrophilicity and/or nucleophilicity. In the following sections, we pursue on the performance of such models in contrast to the experimentally well-established Mayr's parameters determined within the validity of Eq. (1) [7,16,17,21,29,32,33,106].

3. Computational details

Scheme 2 displays 20 electrophiles chosen as reference by Mayr in the establishment of experimental nucleophilicity and electrophilicity scales. These systems will be used for testing the electrophilicity models derived from Eqs. (4)–(7). Scheme 3 depicts 16 primary and secondary amines, selected to test the different nucleophilicity models. Geometry optimization of selected systems were performed at the B3LYP/6-31G(d) and HF/6-31G(d) level of theory using the Gaussian03 package of programs [107]. This level is enough suitable for the analysis of relative qualitative reactivity trends as intended in the present work. The molecular orbital energies as the simplest approximation scheme to the calculation of these reactivity indexes (e.g., $\mu^{\pm}$ and $\eta^{\pm}$) are here used as approximations to ionization potentials and electron affinities in the above formulation. We note however that within the Kohn–Sham DFT scheme, the orbital energies do not have any physical meaning except to that implied from the Janak's theorem (e.g., the derivative of the total energy with respect to the orbital occupation number). Nevertheless from the long-range behavior of electron density and being expected for the exact effective potential in a DFT theory, one could expect that the energy of the highest occupied molecular orbital to be the exact ionization potential. Within approximate functionals of current DFT, negative values for the HOMO and LUMO energy can be considered as very initial approximations to the ionization potential and electron affinity, respectively [95,108–110]. Within the Hartree–Fock framework this fact is justified in terms of the scope of validity of Koopmans' theorem.
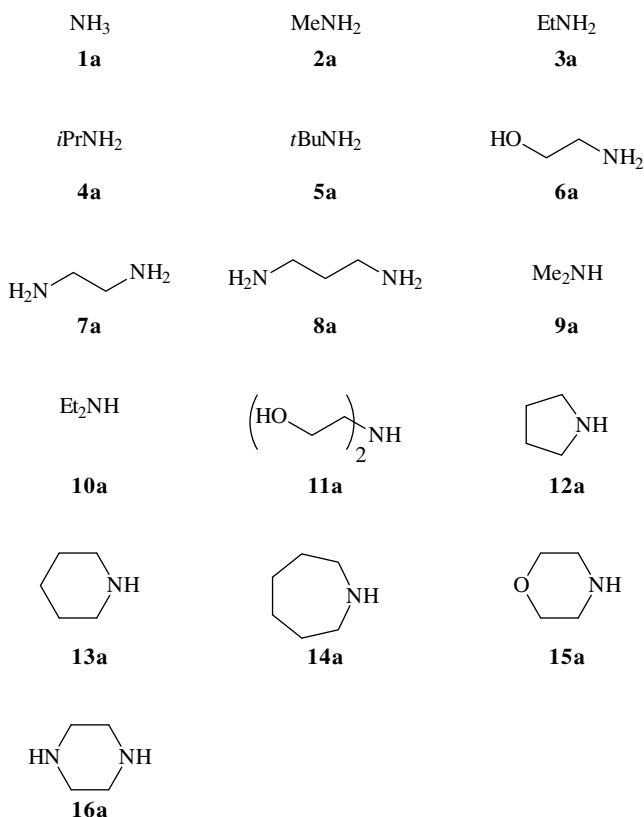
4. Results and discussion

Tables 1 and 2 report the global electrophilicity and nucleophilicity values as well as the Mayr's electrophilicity and nucleophilicity parameters, respectively, obtained from the four theoretical models in Eqs. (5)–(8). B3LYP and HF results are reported as first and second entries, respectively. More than a quantitative agreement between the theoretical and experimental data, it is interesting to explore the general linear relationship among these independent reactivity scales. It would provide support to the idea that the electrophilicity/nucleophilicity values along a series of related systems could be straightforwardly obtained by only using simple theoretical calculations. Fig. 1a and b shows linear correlations found between the Mayr's electrophilicity (E) parameters and the electrophilicity index calculated at both levels of theory, for the four models being tested. As it can be observed good correlations

NH$_3$

1a

MeNH$_2$

2a

EtNH$_2$

3a

iPrNH$_2$

4a

tBuNH$_2$

5a

HO–CH$_2$CH$_2$–NH$_2$

6a

H$_2$N–NH$_2$

7a

H$_2$N–NH$_2$

8a

Me$_2$NH

9a

Et$_2$NH

10a

(HO–)$_2$NH

11a

pyrrolidine NH

12a

piperidine NH

13a

azepane NH

14a

morpholine O NH

15a

piperazine HN NH

16a

Scheme 3. Primary and secondary amines used as nucleophilic examples. Experimental nucleophilic parameters N_{Mayr} are available from Ref. [38].

Table 1
Electrophilicity values for a series of benzhydryl cations from different theoretical Models (I–IV) at the B3LYP (first entry) and HF (second entry) level using a 6-31G(d) basis set. The Mayr electrophilicity parameter (E_{Mayr}) is also reported.

Benzhydryl	E_{Mayr}[a]	Model I [eV]	Model II [eV]	Model III [eV]	Model IV [eV]
		14.36	24.33	20.3	2.79
1b	6.02	4.63	5.44	2.23	0.84
		13.00	21.53	17.49	2.66
2b	5.90	4.35	4.94	2.23	0.74
		13.15	21.86	17.83	2.68
3b	5.60	4.37	4.96	2.25	0.74
		13.30	22.61	18.94	2.56
4b	2.90	3.73	4.05	1.68	0.58
		12.62	20.92	16.99	2.59
5b	4.59	4.16	4.66	2.06	0.69
		12.29	20.36	16.54	2.52
6b	3.63	3.98	4.42	1.91	0.65
		12.06	19.98	16.22	2.47
7b	2.11	3.78	4.11	1.70	0.59
		11.79	19.55	15.89	2.42
8b	1.48	3.67	3.97	1.63	0.56
		11.61	19.4	15.92	2.33
9b	0.61	3.43	3.65	1.44	0.51
		11.45	19.01	15.48	2.34
10b	0.00	3.46	3.68	1.46	0.51
		11.24	18.71	15.29	2.28
11b	−1.36	3.36	3.57	1.40	0.49
		10.59	17.64	14.42	2.15
12b	−3.85	2.99	3.28	1.39	0.47
		10.08	16.78	13.71	2.05
13b	−5.53	2.82	2.94	1.06	0.39
		9.85	16.32	13.25	2.02
14b	−7.02	2.76	2.78	0.96	0.35
		9.50	15.71	12.72	1.96
15b	−5.89	2.65	2.61	0.87	0.32
		9.53	15.79	12.84	1.95
16b	−8.76	2.60	2.57	0.86	0.32
		9.40	15.54	12.6	1.93
17b	−8.22	2.59	2.55	0.84	0.32
		9.35	15.41	12.44	1.93
18b	−7.69	2.60	2.55	0.84	0.31
		9.09	15.01	12.15	1.88
19b	−9.45	2.50	2.45	0.80	0.30
		8.87	14.6	11.77	1.84
20b	−10.04	2.41	2.31	0.71	0.27

[a] E_{Mayr} values are taken from Ref. [31].

Table 2
Nucleophilicity values for a series of primary and secondary amines from different theoretical models (I–IV) at the B3LYP (first entry) and HF (second entry) level using a 6-31G(d) basis set. The Mayr nucleophilicity parameter (E_{Mayr}) is also reported.

Amines	N_{Mayr}[a]	Model I (eV)	Model II (eV)	Model III (eV)	Model IV (eV)
		0.31	2.37	5.24	11.02
1a	9.48	0.21	2.84	7.46	10.76
		0.23	1.97	4.55	8.43
2a	13.85	0.13	2.36	6.54	8.76
		0.23	1.98	4.57	8.55
3a	12.87	0.13	2.36	6.52	8.75
		0.26	2.08	4.68	9.33
4a	12.00	0.15	2.43	6.58	9.05
		0.30	2.19	4.81	10.48
5a	10.48	0.17	2.52	6.68	9.46
		0.30	2.21	4.87	10.44
6a	12.61	0.15	2.47	6.71	9.20
		0.24	2.01	4.60	8.79
7a	13.28	0.13	2.34	6.49	8.67
		0.22	1.93	4.46	8.27
8a	14.02	0.13	2.30	6.40	8.54
		0.19	1.76	4.17	7.26
9a	17.12	0.10	2.10	6.01	7.73
		0.18	1.73	4.14	7.09
10a	14.68	0.10	2.07	5.96	7.63
		0.28	2.10	4.62	9.86
11a	13.00	0.12	2.24	6.25	8.28
		0.20	1.80	4.22	7.60
12a	17.21	0.11	2.12	6.03	7.83
		0.19	1.78	4.19	7.46
13a	18.13	0.10	2.09	5.97	7.70
		0.23	1.90	4.33	8.36
14a	18.29	0.12	2.16	6.04	7.98
		0.22	1.91	4.42	8.20
15a	15.62	0.11	2.16	6.13	7.96
		0.21	1.82	4.23	7.74
16a	17.22	0.10	2.06	5.91	7.60

[a] N_{Mayr} values are taken from Ref. [38].

Fig. 1. Plot of the theoretical electrophilicity index (ω_m^+) calculated at (a) B3LYP/6-31G(d) and (b) HF/6-31G(d) levels of theory for Model I ($\bullet$), Model II ($\blacksquare$), Model III ($\blacktriangle$), and Model IV ($\blacktriangledown$), vs. the Mayr's electrophilicity (E_{Mayr}) parameters for a series of reference benzhydrylium cations. Experimental electrophilicity (E_{Mayr}) parameters taken from Ref. [31].

between the theoretical electrophilicity models with the Mayr's parameters within a range of the regression coefficient R^2 = 0.90–0.98, and positive slopes can be found. From Eq. (3) it is clear that higher electrophilicities are associated to higher stabilization of the system's energy in the process of acquiring charge. Electron-withdrawing substituents increase the electrophilic reactivity of the reference benzhydrylium cations, and this is correctly incorporated by all theoretical models. Otherwise, electron-releasing substituents excerpt the opposite effect on the carbocation, lowering its global electrophilic power. The experimental E parameters and the theoretical approaches used to estimate the electrophilicity power are directly related. Using the theoretical values as independent variables, we can rewrite these regression equations at the DFT level as: $E = 3.57\omega_I^+ - 41.60$, $E = 2.08\omega_{II}^+ - 40.42$, $E = 2.44\omega_{III}^+ - 38.66$, and $E = 20.0\omega_{IV}^+ - 47.2$ for Models I–IV, respectively. At the HF level of theory the results are: $E = 8.33\omega_I^+ - 29.67$, $E = 5.88\omega_{II}^+ - 22.76$, $E = 10.00\omega_{III}^+ - 6.10$, and $E = 33.33\omega_{IV}^+ - 18.33$, respectively. Thus by examining the correlation results along the series of selected electrophilic systems and under the validity of approximations used to evaluate Eqs. (5)–(8), a high slope in the E vs. ω^+ plot is associated to a narrow scale relating the experimental and theoretical electrophilicity values. In that sense, the broadness of such theoretical scale at the DFT level of theory follows the order $\omega_{IV}^+ < \omega_I^+ < \omega_{III}^+ < \omega_{II}^+$, whereas that $\omega_{IV}^+ < \omega_{III}^+ < \omega_I^+ < \omega_{II}^+$ is at the HF level of theory. Note in this point that Models I–III essentially differs in the weights involved in the terms: $(\varepsilon_H)^2/(\varepsilon_L - \varepsilon_H)$, $\varepsilon_H\varepsilon_L/(\varepsilon_L - \varepsilon_H)$, and $(\varepsilon_L)^2/(\varepsilon_L - \varepsilon_H)$. These weights are, respectively, 0.125, 0.250, and 0.125 for Model I; 0.0625, 0.375, and 0.5625 for Model II; and 0.000, 0.000, and 1.000 for Model III. Thus, it is clear that Model IV using the simplest ansatz for hardness yields the narrowest
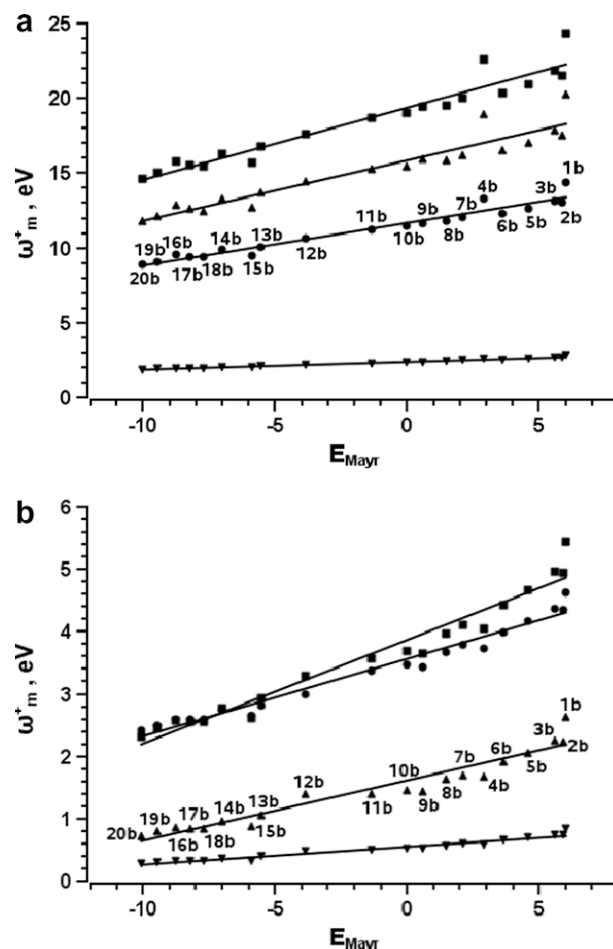
scale discriminating the experimental electrophilicity along the series of selected benzhydryl cations, while Models II and III with increasing weights for those terms associated to the square of LUMO energy seem to be slightly better than the Parr's electrophilicity index. In this sense, note also that such electrophilicity scales defined within a B3LYP model become certainly broader than those arising from HF calculations within the validity of the tested models of Eqs. (5)–(8).

Fig. 2a and b reports on the other hand linear correlations between the Mayr's nucleophilicity (N) parameters for selected amines shown in Scheme 2 and the nucleophilicity indexes obtained from Eqs. (5)–(8) at both B3LYP and HF levels of theory, respectively. As compared to the above electrophilicity results, the agreement between experimental and theoretical nucleophilicities is still fairly suitable, although of low significant linear quality. In this case, regression coefficients (R^2) are in the range 0.60–0.79. The negative slopes for these correlations indicate an inverse relationship between the theoretically determined and the experimental nucleophilicities values. This fact can be understood again in terms of Eq. (3) where it is clear that poorer nucleophiles are associated to higher values of the theoretically determined ω^- index i.e., the system's energy increases due to the donating charge process. A detailed discussion concerning structure-nucleophilicity ordering is avoided in the present section, but we only stress that the theoretical models, both at the HF and B3LYP level of theories,
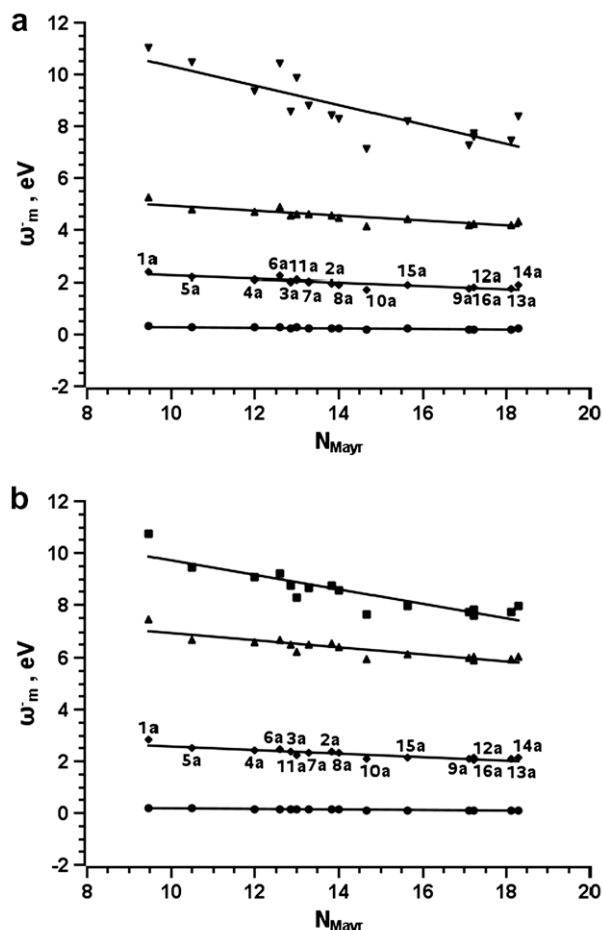
Fig. 2. Plot of the theoretical nucleophilicity index (ω_m^-) calculated at (a) B3LYP/6-31G(d) and (b) HF/6-31G(d) levels of theory for Model I (●), Model II (■), Model III (▲), and Model IV (▼), vs. the Mayr's nucleophilicity (N_{Mayr}) parameters for a series of primary and secondary amines taken as nucleophile examples. Experimental nucleophilicity parameters (N_{Mayr}) taken from Ref. [38].

behave fairly good giving the experimental N_{Mayr} trends. The ordering is essentially the same. The regression equations can be summarized at the DFT level as: $N = -100.00\omega_I^- + 41.00$, $N = -16.77\omega_{II}^- + 46.83$, $N = -10.00\omega_{III}^- + 59.30$, and $N = -2.63\omega_{IV}^- + 37.13$ for Models I–IV, respectively. The results at the HF level are correspondingly: $N = -100.00\omega_I^- + 27.00$, $N = -14.29\omega_{II}^- + 46.86$, $N = -7.69\omega_{III}^- + 63.62$, and $N = -3.57\omega_{IV}^- + 44.68$. In this case, the broader scale relating the experimental and theoretical nucleophilicity values is predicted to be that arising from the naive Model IV both for the B3LYP and HF theories. This broadness of nucleophilicity scale follows the order $\omega_I^- < \omega_{II}^- < \omega_{III}^- < \omega_{IV}^-$. Now, the above mentioned terms, e.g., $(\varepsilon_H)^2/(\varepsilon_L - \varepsilon_H)$, $\varepsilon_H\varepsilon_L/(\varepsilon_L - \varepsilon_H)$, and $(\varepsilon_L)^2/(\varepsilon_L - \varepsilon_H)$, entering in the operational definitions of models in Eqs. (5)–(8) have weights of 0.125, 0.250, and 0.125, respectively, for Model I; 0.5625, 0.375, and 0.0625 for Model II; and 1.000, 0.000, and 0.000 for Model III. Models II and III give an increasing weight to the HOMO energy, in comparison to those in Model I, for which the narrow scale for nucleophilicity is associated. Thus, in contrast to the electrophilicity prediction, the nucleophilicity trends seem to be better described using a simple ansatz such as Models III and IV, proposed in this work. These models with increasing weights for those terms associated to the square of HOMO energy seem to be significantly better than the electrophilicity index of Eq. (4). In this sense, we have also noted that as the contribution of the HOMO energies are implied in the present qualitative level, such nucleophilicity scales can be obtained at

B3LYP or HF calculations with good confidence within the general assessment provide by all models. It is important to note in this point and in the context of model in Eq. (8), that correlations using the simple HOMO and LUMO energies (data not explicitly reported here) also yields acceptable qualitative results at the current level of theory for the reference systems investigated in this work. The agreement is better for electrophilicity than for nucleophilicity, although the LUMO energies are in principle less reliable quantities than the electron affinity itself. The above results indicate that the simplest approximations used here are enough suitable for qualitative comparisons of relative reactivity trends along the selected series of electrophilic and nucleophilic systems. This is important because the electrophilic systems are indeed the reference benzhydrylium cations used by Mayr et al. [31] for the establishment of comprehensive experimental [2,19,21,31] electrophilicity and nucleophilicity scales [21,106]. The finding of linear relationships between theoretical and experimental electrophilicity and nucleophilicity parameters further validates the simple theoretical models based on the variational result summarized in Eq. (4). Further work to validate these results on a large series of systems whose experimental parameters are available [2,18–21,31,34,38,111] is desirable. These results constitutes a strong support to purely theoretical electrophilicity and nucleophilicity models that could be certainly used to build independent electrophilicity and nucleophilicity scales routed in the spirit of Mayr equation, by providing further insights about the theoretical basis of the underlying experimental correlations.

5. Concluding remarks

This work reports further evidence in favor of the usefulness of simple electrophilicity and nucleophilicity models derived within a variational perturbative approximation to the chemical reactivities, namely, Eq. (3). On the basis of simplest model calculations associated to Eqs. (3) and (4), e.g., Eqs (5)–(7), it has been shown that such theoretical electrophilicity and nucleophilicity scales are linearly related to the well-known experimental ones based on the Mayr's parameters. Based on the present results, the DFT calculations along the use of Models II and III seems to yield broader electrophilicity scales as compared to the Parr et al. index (Model I). Those models incorporating higher weights for the LUMO energies (e.g., Gázquez et al. related models) perform better agreements in such direction. Concerning nucleophilicity scales, both B3LYP and HF calculations are enough suitable within the simple approximations used in this work (i.e., the explicit consideration of HOMO energies). This work further extends recent findings on the establishment of nucleophilicity scales in terms of the negative of the ionization potential. These models have been shown valuable by categorizing qualitatively a large series of substituted alkenes, substituted aromatic compounds in simple nucleophilic molecules, as well as captodative ethylenes series [81,96,100]. The availability of linear correlations between theoretical and experimental scales of electrophilicity and nucleophilicity reported in the present work, further validate the general approximation model of Eq. (4). This fact broadens the possibilities of using such variational approaches as a suitable tool to predict the electrophilic and nucleophilic behavior, establishing correctly the qualitative reactive trends of a wider range of these species. Further studies in such context on a broad range of electrophiles and nucleophiles are in progress in our group.

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