# Intrinsic Relative Scales of Electrophilicity and Nucleophilicity

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# Intrinsic Relative Scales of Electrophilicity and Nucleophilicity

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Ⓢ *Supporting Information*

**ABSTRACT:** The formulation of the second-order perturbation approach to the stabilization energy of the A−B interacting species due to charge transfer is revisited. Intrinsic (i.e., electronic) theoretical indices for both relative electrophilicity and nucleophilicity are proposed for any electrophile (A)−nucleophile (B) pairs of combining species. By using the new descriptors, an electronic analogue to the Mayr−Patz linear free relationship has been successfully tested in the context of available experimental evidence reported for reactions of primary and secondary amines with benzhydrylium ions.
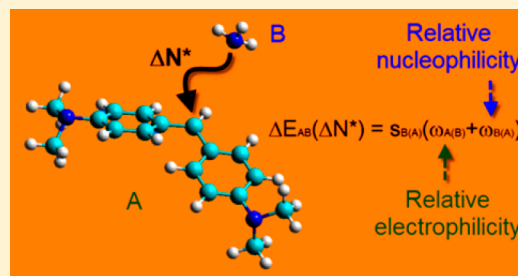
## ■ INTRODUCTION

Within the framework of density functional theory (DFT), Parr and Pearson first demonstrated[1] that the interaction of two species A and B having chemical potentials $\mu_B > \mu_A$ and with finite hardnesses (i.e., $\eta_B \neq 0, \eta_A \neq 0$), yields up to second order, to a global *decreasing* in the electronic interaction energy $\Delta E_{AB}$, due exclusively to flow of electrons from B to A, $\Delta N_{B \to A}$.[2] This is true only under the consideration of charge transfer effects. Indeed, minimization of $\Delta E_{AB}$ with respect to $\Delta N_{B \to A}$ provides simple expressions accounting for the *optimum amount* of charge transferring $\Delta N^*_{B \to A}$ which yield the maximum electronic stabilization $\Delta E_{AB}(\Delta N^*_{B \to A})$ associated to a given intended interaction between the pair species, namely,

$$\Delta N^*_{B \to A} = \frac{\mu_B - \mu_A}{\eta_B + \eta_A} > 0 \tag{1}$$

$$\Delta E_{AB}(\Delta N^*_{B \to A}) = -\frac{1}{2}\frac{(\mu_B - \mu_A)^2}{\eta_B + \eta_A} < 0 \tag{2}$$

In the limiting case of a perfect electron donor environment $B_0$ (i.e., $\mu_B = 0$, $\eta_B = 0$), the energy lowering predicted by eq 2 has been identified as the negative of the *intrinsic* electrophilicity power of species A, namely,[3]

$$\Delta E_{AB}(\Delta N^*_{B_0 \to A}) = -\mu_A^2/(2\eta_A) \equiv -\omega_A \tag{3}$$

It is worth mentioning that the electrophilicity definition in eq 3 provides an absolute scale that is based on a variational principle for an electrophile immersed in an electron sea provided by a perfect donor. This electrophilicity index has been demonstrated to be a key quantity to explore several aspects of both global and local reactivities,[4−6] in both spin-free[7−17] and spin-dependent representations.[18−20] Indeed, a *net electrophilicity*[8] scale has been introduced including both the electrophilic and nucleophilic character at each molecule and it

was defined as the electron-accepting power of a molecule in relation to its electron-donating ability. Nevertheless, a proper definition for a nucleophilicity index escapes from a variational principle behind the derivation of eq 3. The transfer of electronic charge from a given system will be always associated to an increase in its energy. Several difficulties are well-known when defining nucleophilicity and electrophilicity within a common framework, as exemplified from application of molecular electrostatic potential strategies,[21] minimum ionization potential approximations,[22] or using the definition of a nucleophilicity index based on a perturbation model for the interaction energy between the electron donor and a positive test charge.[23] During the last years many authors have been driving research on nucleophilicity models, although a definitive response indicator that incorporates all key effects still remains elusive. In this work we just focus on an electron-transfer piece of the interaction energy in order to define a nucleophilicity indicator. Our resulting theoretical model of electrophilicity and nucleophilicity thus encompasses only electronic charge-transfer effects, in a form that is consistent with validated experimental scales. The simplest approximations in eq 1 have been applied in several different key problems of chemical reactivity.[1,2,24−26] Recently, Roy and co-workers have enhanced[27−29] the usefulness of the analysis of the individual terms entering such decomposition of electronic stabilization energy given in eq 2, namely, those associated to the electronic energies of individual species A and B,[27−29]

$$\Delta E_{AB}(\Delta N^*_{B \to A}) = \Delta E_{A(B)}(\Delta N^*_{B \to A}) + \Delta E_{B(A)}(\Delta N^*_{B \to A}) \tag{4}$$

These authors have properly stressed that the electron acceptor (A) will undergo an energy lowering whereas the electron donor (B) will concurrently increase its electronic energy, i.e., $\Delta E_{A(B)} (\Delta N_{B\to A}^*) < 0$ and $\Delta E_{B(A)} (\Delta N_{B\to A}^*) > 0$ along the process of charge transferring yielding the net stabilization of the A−B pair interaction at constant external potential.[27−29] These energy terms, as well as the intrinsic electrophilicity $\omega_A$,[3−6] have been found linearly correlated to the particular step reaction rate constants. Roy et al. have particularly focused[27−29] on the usefulness of such quantities to locate the rate-determining step in multistep reactions, also to the analysis of intermolecular reactivity sequence between dienes and dienophiles, and to the analysis of the most stable structures between urea and *m*-nitrobenzoic acid within a supramolecular approximation.[27−29] Inspired by these discussions and following ongoing research interests[15−17,30−39] within the field of modeling chemical reactivity in the DFT context,[40−44] we here to resort to the analysis of a different partition of the *stabilization energy* that allows us to establish connections with experimental electrophilicity−nucleophilicity scales of reactivity.

**Scales of Electrophilicity and Nucleophilicity on the Basis of the Mayr−Patz Experimental Parameters.** The relative chemical response of electrophiles (i.e., electrophilicity) and nucleophiles (i.e., nucleophilicity) plays a central role in chemistry. These concepts are used to rationalize both global reactivity and local selectivity in most polar chemical reaction processes.[13,17,32,33,35,45−54] Several efforts have been aimed to develop both qualitative and quantitative models in order to obtain deeper insights and understanding concerning the nature of such reactive proclivities.[23,38,47,54−57] These reactivities are indeed associated to the examination of relative rate constants. Despite electrophilicity and (particularly) nucleophilicity, known to depend on several factors (e.g., physical chemistry nature of substrates, reagents, and solvents) precluding in principle the formal definition of unique and absolute associated descriptors,[47] there has been an intensive effort to introduce absolute scales that properly categorize these reactive responses in terms of linear free-energy relationships. In such a context and within a comprehensive experimental perspective, Mayr et al. have extensively emphasized[45−47,57,58] that for a wide range of chemical reactions between sets of electrophiles and nucleophiles, the second-order rate constants at 293.15 K, $k$ (in units of $M^{-1} s^{-1}$), are linearly related to only three parameters, i.e.,

$$\log k_{20°C} = s_B(N_B + E_A) \tag{5}$$

where $E_A$ corresponds to a *uniquely defined* solvent-independent *electrophilicity* parameter, and $s_B$ and $N_B$ are associated to *nucleophilicity*-dependent quantities. By choosing a reference set of charged (i.e., benzhydrylium ions) or neutral (i.e., quinone methides) electrophiles, their reactions with nucleophiles follow second-order rate laws. Least-squares adjustments of the second-order rate constants and the corresponding electrophilicity parameters, as indicated in eq 5, provide a way to obtain nucleophilicity indices for a large variety of $\pi$-, $n$-, and $\sigma$-nucleophiles, including alkenes, arenes, enol ethers, ketene acetals, enamines, allyl compounds, transition metal complexes, diazoalkanes, and delocalized carbanions, amines, alcohols, alkoxides, phosphanes, inorganic anions, pyridines, and hydrides. Discussions regarding the nature, scope, and limitations of the adjustment of experimental kinetic data to a given choice of the correlation equation have been recently

raised.[59,60] The Mayr's model has in fact enabled a comprehensive rationalization and categorization of electrophilicity−nucleophilicity responses driving polar organic reactions within a wide range of more than 30 orders of magnitude.[46] A database containing a compilation of available reactivity parameters is also available.[61] In this approximation, electrophilicity parameters become related with almost exclusively electronic effects, whereas nucleophilicity parameters also bear steric and solvent effect contributions associated to the activation energies. As we will see, our approximations will focus just on the electronic (intrinsic) components of both electrophilic and nucleophilic responses.

**Toward Theoretical Relative Intrinsic Scales of Electrophilicity and Nucleophilicity.** Note from eq 2 that the interaction energy can be explicitly written as

$$\Delta E_{AB}(\Delta N^*_{B\to A}) = -\frac{1}{2}\frac{\mu_B^2 - 2\mu_B\mu_A}{\eta_B + \eta_A} - \frac{1}{2}\frac{\mu_A^2}{\eta_B + \eta_A} \tag{6}$$

where the last term is thereafter identified as the negative of **relative electrophilicity power of species A in presence of nucleophile B**, i.e.,

$$\omega_{A(B)} \equiv \frac{1}{2}\frac{\mu_A^2}{\eta_B + \eta_A} \tag{7}$$

which is of course trivially related to the absolute or intrinsic electrophilicity index or Parr et al. given in eq 3, namely,

$$\omega_{A(B)} = \omega_A \frac{\eta_A}{\eta_B + \eta_A} \tag{8}$$

This fact indeed justifies that we can use the absolute index of electrophilicity (instead of the relative one given in eq 7) within the aim of characterizing the interaction between electrophiles and nucleophiles in analogy to the experimental approach explored by Mayr and co-workers. Thereafter, it is straightway easy to show that eq 6 can be rewritten in the form of eq 5, i.e.,

$$\Delta E_{AB}(\Delta N^*_{B\to A}) = s_{B(A)}(\omega_{B(A)} + \omega_A) \tag{9}$$

with

$$s_{B(A)} \equiv -\frac{\eta_A}{\eta_B + \eta_A} \tag{10}$$

and

$$\omega_{B(A)} \equiv \frac{1}{2}\frac{\mu_B^2 - 2\mu_B\mu_A}{\eta_A} \tag{11}$$

Equations 8−11 define an *electronic* analogue to the Mayr−Patz linear *free energy* relationship given by eq 5. Of most relevance, eq 11 defines, within the underlying limitations of current approximations, a relative **nucleophilicity index of species B in presence of electrophile A.** Note that the analogy is justified if the maximum stabilization energy of the interacting pair, $\Delta E_{AB}(\Delta N^*_{B\to A})$, can, in fact, be found linearly related to the experimental second-order rate constant for some set of interacting systems. We postulated that such a reactivity model establishes a straightway first approximation to the theoretical analysis of *electronic effects* controlling polar combinations of electrophiles and nucleophiles. These relationships, as previously discussed,[30,31] are aimed to obtain new

**Scheme 1. Electrophiles A (benzhydrylium ions Ar$_2$CH$^+$, 1−7) and Nucleophiles B (primary (a−r) and secondary (s−zz) amines) Examined in This Work**[a]
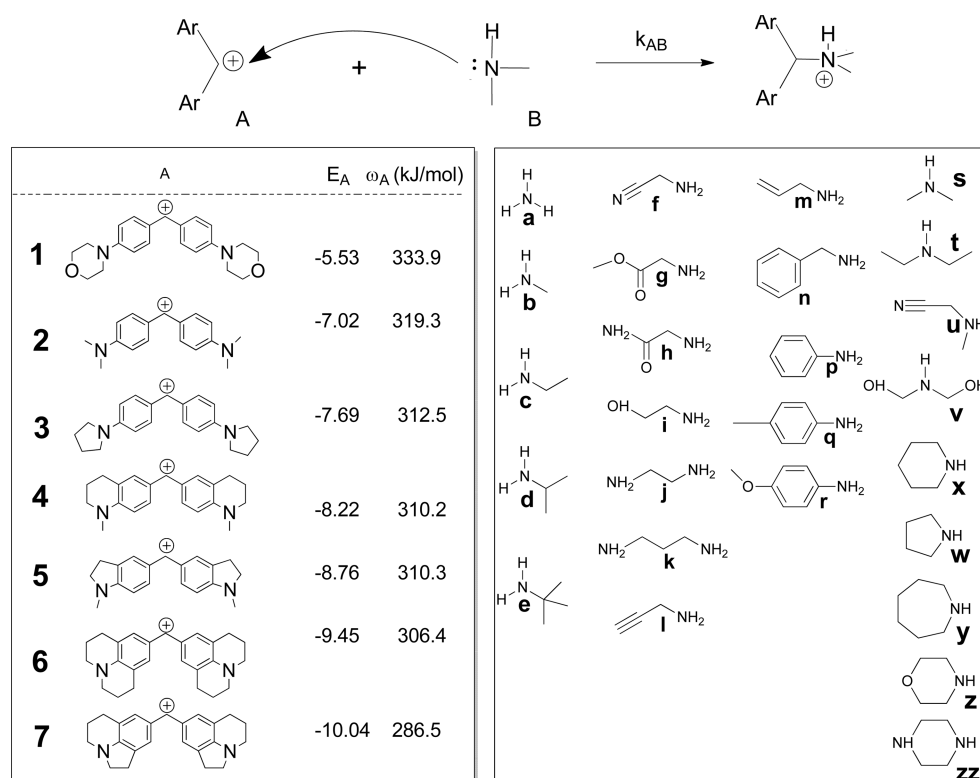


[a]$E_A$ taken from ref 62 and $\omega_A$ (eV) evaluated in this work from eq 3.

insights concerning the exploration and categorization of electronic effects driving the observed reactivity trends.

### COMPUTATIONAL DETAILS

As a practical test, the combination reactions of 7 benzhydrylium ions (electrophiles) with 26 primary and secondary amines (nucleophiles) have been chosen (see Scheme 1) in order to explore the suitability of proposed indices in eqs 8−11. Experimental kinetic constants in water are available for these reactions which have been discussed within the framework of Mayr's methodology.[62] Complete geometry optimizations of both electrophilic and nucleophilic systems were performed at the B3LYP/6-31G(d) level of theory using the Spartan 08 suite of programs.[63] This level of theory has been demonstrated to be suitable enough for the analysis of relative *qualitative* reactivity trends as it is the goal intended in the present work. Solvent effects were introduced within the context of the SM8 model approximations.[64−67] Within the general aim of the present work, we use the simplest approximation scheme (i.e., finite differences) to the calculation of chemical potential and hardness implied in eqs 5−8, namely,

$$\mu \approx -(I + A)/2 \text{ and } \eta \approx I - A \qquad (12)$$

which are evaluated in terms of the ionization potentials $I$ and electron affinities $A$. Further, highest occupied (HO) and lowest unoccupied (LU) molecular orbital (MO) energies have been used in our final operational formulas, i.e.,

$$I \approx -\varepsilon_{HOMO} \text{ and } A \approx -\varepsilon_{LUMO} \qquad (13)$$

Within the Kohn−Sham DFT scheme, the orbital energies do not have any physical meaning except to those implied from the Janak's theorem (e.g., the derivative of the total energy with respect to the orbital occupation number).[68] Nevertheless from the long-range behavior of electron density as expected for the effective potential in an exact DFT theory, the energy of HOMO will be the ionization potential. Within the Hartree−Fock framework such approximation is justified in terms of the validity of Koopmans' theorem. It is well-known that these quantities will strongly depend on the quality of the frontier molecular orbitals. Within approximate current DFT functionals, negative values for the HOMO and LUMO energy also can be considered as very initial approximations to $I$ and $A$, respectively, becoming useful just for qualitative analysis of *reactivity trends* of related chemical species, just the context of validity of our chemical reactivity model given by eqs 8−11.

### RESULTS AND DISCUSSION

Within the Mayr's methodology, a set of reference electrophiles is used for the construction of nucleophilicity scales by using eq 5. Two nucleophilicity parameters ($s_B$ and $N_B$) are obtained from a least-squares analysis of the log $k_{AB}$ against the single parameter $E_A$ for each electrophile. Absolute electrophilicities of the reference electrophiles, both from Mayr's work ($E_A$) and from the theoretical approximation given by eq 3, are also shown in Scheme 1. Both quantities are here found indeed linearly correlated, i.e., $E_A = (0.101 \pm 0.016)\omega_A - (39.534 \pm 5.057)$ with $R^2 = 0.8856$. Within the spirit of eq 9, we report in Table 1S for all possible pair combinations of chosen electrophiles and nucleophiles, the maximum amount of *charge transfer* (eq 1), in Table 2S the maximum electronic energy stabilization (eq 6), in Table 3S the *relative electrophilicity* (eq 7), and in Tables 4S and 5S *relative nucleophilicities* descriptors

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(eqs 10 and 11). Compilation of experimental kinetic data log $k_{AB}$ for all combinations A−B is available from ref 62 and it is summarized in Table 6S. The tiny maximum amount of charge transfer predicted (i.e., 0.06−0.23 e, Table 1S) for the interaction of primary and secondary amines with the reference electrophiles under the current approximation given by eq 1 is, as we show later, suitable enough within the interest of discriminating the electronic nature of observed nucleophilicities within the perspective of a perturbative approximation. For the interaction of each nucleophilic system along the screening in electrophilic power that represents varying from electrophile **1** to **7**, charge transferring is predicted to decrease. For the studied amines such proclivity moves within the range of 16−30%, being much greater only for primary amines **f** (i.e., 41%) and **g** (i.e., 44%), that appears indeed strongly deactivated. Along the process of charge transferring, a net electronic stabilization of the A−B pair interaction is evidenced as reported in Table 2S. Energy lowering is predicted to account for ~1.4 (i.e., couple g-7) kJ/mol to ~27.2 (couple t-1) kJ/mol. As evidenced for each nucleophile in Table 2S, such a stabilization electronic energy change decreases as the electrophilic power of the partner decreases. Table 3S reveals indeed that the ordering of the relative electrophilic power is always conserved, decreasing from **1** to **7** independent of the reaction nucleophilic partner. This fact follows from eq 8 showing the straightway connection of the relative $\omega_{A(B)}$ and absolute $\omega_A$ electrophilicity indices. Note however from Table 3S that relative indices allow us to seek for particular activation/deactivation of the reactive responses in virtue of the specific reaction partner and substitution pattern, in agreement with previous discussion in light of experimental results. As evidenced in Table 4S, the relative nucleophilicity slope parameter given by eq 10 remains tiny and almost constant (i.e., in the range −0.21 to −0.35) for all possible interactions of primary and secondary amines and the chosen electrophiles, providing a sound basis for the analysis of electronic nucleophilicities only on the basis given by the relative indices reported in Table 5S. Given the nucleophilic addition of B to A is the rate-determining step for the chosen series of reactions, $\Delta E_{AB}$ can be suitably employed in the context of the proposal relationship given by eq 9. In fact, it is found that when the experimental log $k_{AB}$ for the reactions of nucleophiles B with electrophiles A are plotted against the maximum stabilization energy $\Delta E_{AB}$, linear correlations are obtained (Figure 1) for all examined systems. It is consistently observed that the deeper the lowering in the interaction energy, the higher the kinetic constant, for each nucleophilic system interacting with the electrophilic series. This result implies that the electronic contributions to the nucleophilicity power on amines can be suitably assessed by using the stabilization energy. It has been argued[62] that given the kinetic constants of amines with electrophile **2** are within 4 orders of magnitude, structure−reactivity relationships might be based on reactivities toward that single electrophile. Henceforth, in order to assess the purely electronic components and to compare with the experimental results, we introduce the simple ratio of energy lowering $Q_{\Delta EAB} \equiv \Delta E_{AB}/\Delta E_{2B}$ with respect to such specific electrophile. This is illustrated in Figure 2 which, in general, reflects the observed experimental order of reactivity, e.g., secondary amines become more nucleophilic than primary ones, as previously discussed. Thereafter, being validated the quantity $\Delta E_{AB}$ as a suitable indicator of reactivity for the series of systems being examined, we probe that plots of $\Delta E_{AB}$ against
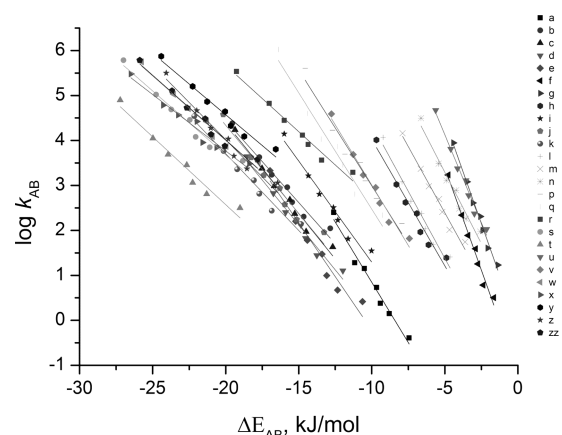


**Figure 1.** Plots of experimental rate constants log $k_{AB}$ for the reactions of amines with benzhydrylium cations vs the calculated B3LYP/6-31G(d) electronic stabilization energy, $\Delta E_{AB}$. For each nucleophile B, the deepest is the decreasing in electronic energy, the highest the kinetic constant, along the series of reactions with electrophiles A.
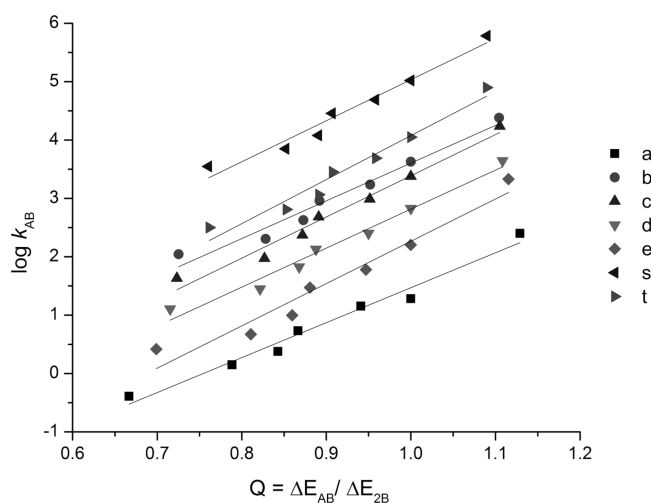


**Figure 2.** Plots of experimental rate constants log $k_{AB}$ for the reactions of amines with benzhydrylium cations vs the calculated B3LYP/6-31G(d) electronic stabilization energy ratio, $Q \equiv \Delta E_{AB}/\Delta E_{2B}$, arbitrarily chosen relative to the electrophilic system **2**. Reactivity scale reads at $Q = 1$.

the absolute electrophilicity $\omega_A$ for each nucleophilic system are linear (as exemplified in Figure 3) which will allow us to derive *absolute* electronic nucleophilicity parameters from the slope (i.e., $s_B$) and the intercept $s_B\omega_B$ for the examined amines. Note that these quantities ($s_B$ and $\omega_B$) are absolute in the sense that becomes determined from least-squares adjustment and will remain only valid within the interval of variation of global electrophilicity $\omega_A$ given by eq 3. Table 7S summarizes the corresponding linear fit regression results. Note immediately that absolute quantities such as single parameters predict the same order of *electronic nucleophilicity* that the *relative indices* defined in eqs 10 and 11. In the present case, given the small variation in the slopes ($s_{B(A)}$ and $s_B$) the order of *electronic* nucleophilic reactivity can be properly assessed by using both the relative (i.e., Table 5S) and absolute (Table 7S) approaches. The predicted order of electronic nucleophilicity in both cases is reported in Scheme 2, revealing that the theoretical model properly assesses that increasing branching in primary alkyl amines yields to a decrease in the *electronic nucleophilicities* of
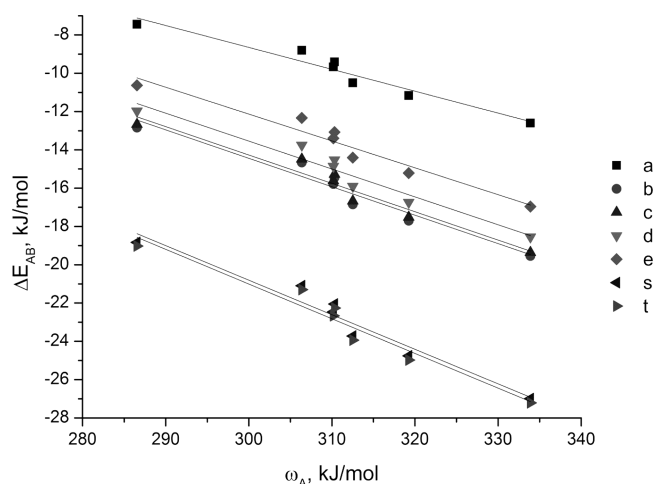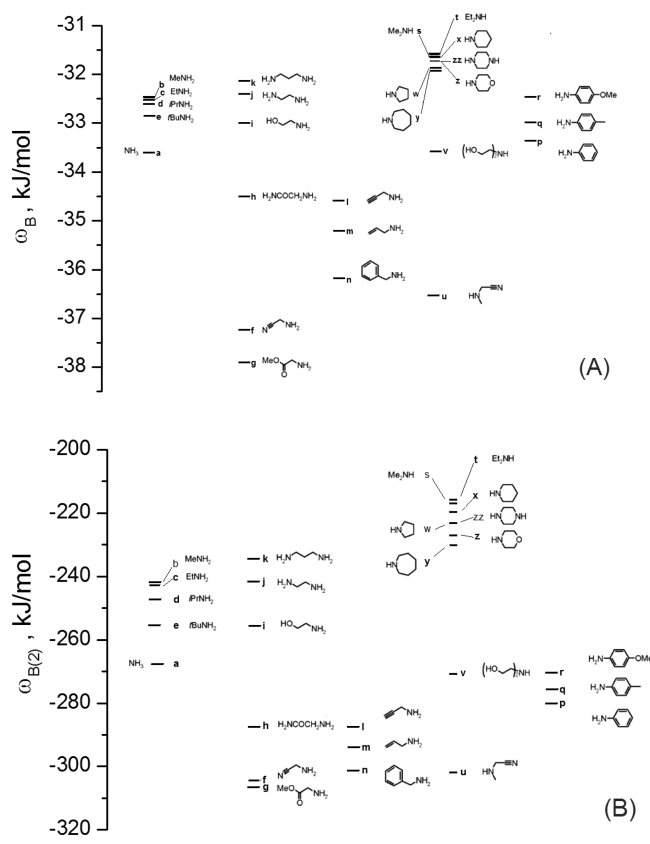
**Figure 3.** Plot of the electronic stabilization energy, $\Delta E_{AB}$, vs the global intrinsic electrophilicity $\omega_A$ at the B3LYP/6-31G(d) level of theory, associated to the electrophile−nucleophile pair combination A−B.

**Scheme 2. Comparison of Electronic Nucleophilicities Ordering of Amines in Water (A) Using the Absolute Nucleophilicity Index $\omega_B$ Reported in Table 7S and (B) Using the Relative Nucleophilicity Index $\omega_{B(A)}$ ($A = 2$), Reported in Table 5S**



implicit within the experimental parameters of nucleophilicity. Our results are thus consistent with a strong deactivating electronic effect on the −NH$_2$ caused by $\alpha$-ester or $\alpha$-cyano groups, than by $\alpha$-amido (**h**), or $\beta$-hydroxy groups (**i**). Our theoretical results are also consistent with the tiny effect on electronic nucleophilicities predicted by increasing the individual amino groups from aminoethane (**c**) to 1,2-diaminoethane (**j**) and 1,3-diaminopropane (**k**). The electronic effects confirm the previous inference regarding that individual amino groups exhibit essentially the same reactive response in all three compounds. Differences arise, however, when examining benzylamine (**n**), allylamine (**m**), and propargylamine (**l**) showing that replacement of the methyl group in aminoethane (**c**) by unsaturated hydrocarbon groups will decrease the intrinsic electronic nucleophilicity. Indeed our model evidence the stronger deactivating model of a benzyl group as compared to the propargylamine. The theoretical results are consistent with the observation of increasing nucleophilicity by replacement of hydrogens in ammonia (**a**) by one (MeNH$_2$, **b**) and two methyl groups (Me$_2$NH, **s**). In these cases, the intrinsic electronic effects of substituents seem to be playing the dominant role under the experimental conditions. However, electronic effects are predicted to be almost equivalent for dimethylamine (**s**) and diethylamine (**t**), allowing us to further stress the validity of previous conclusions regarding that steric factors play a considerably greater role for secondary amines than for primary amines. Our theoretical results also confirm that electronic effects in aniline (**p**) and ammonia (**a**) in water are similar. The same is observed for electronic effects on nucleophilicity in *p*-methoxyaniline (**r**) and ethylamine (**c**). Differences are discriminated through the slope $s_B$ values. These facts reveal that other effects will play the dominant role on the observed reactivities. The secondary cyclic amines (**w**, **x**, **y**, **z**, **zz**) are revealed (together Et$_2$NH, **t**) as the most nucleophilic systems in water. Electronic reactivities are also predicted to be similar, and the differences are explained in terms of $s_B$. These conclusions (i.e., electronic nucleophilicities in secondary amines are greater than in primary ones) are in complete agreement with experimental findings and the rationalization of nucleophilicities based on Mayr's work (eq 5). The theoretical rationalization based on the simple approximations of eqs 9−11 further contributes to obtain a deeper rationalization and understanding of nucleophilicities of primary and secondary amines in the underlying context of experimental approximations based on eq 5. On the basis of these preliminary results, we propose eqs 7−11 as *electronic* analogues to the Mayr−Patz linear *free energy* relationship eq 5. Within the limitations of naive approximations being used in this work, the relative nucleophilicity index of species B in the presence of electrophile A, eq 11, can be used to study the implicit electronic contributions in the experimental $N$ parameter. The justification for this claim is the observation that the maximum stabilization energy for the intended A−B interaction, $\Delta E_{AB}$ ($\Delta N^*_{B \to A}$), is linearly related to the associated experimental second-order rate constant. This formulation will enable a simple method for the theoretical analysis of *electronic effects* that drive *polar combinations* of electrophiles and nucleophiles. Within the general interest of this work, the relation of DFT key descriptors with thermodynamic and kinetic aspects of chemical reactions has been previously emphasized,[10,69] although there and here, formal argumentation about a rigorous connection between the

primary alkyl amines in water (i.e., MeNH$_2$ to *t*-BuNH$_2$), in agreement with the experimental observation. However, ammonia is not predicted to have the lowest *electronic* nucleophilicity but it is the strongly deactivated $\alpha$-ester (**g**) amine followed by the $\alpha$-cyano amine (**f**). We have to point out that our model only senses *intrinsic electronic effects* assumed

reactivity descriptors with kinetics remains an open question. Additional work on this particular subject is certainly desirable.

## CONCLUSIONS

This work introduces simple *relative* descriptors of electrophilicity and nucleophilicity, namely eqs 7−11, based on the second-order perturbation approach to the stabilization energy of any pair A−B of interacting species due to charge transfer. The usefulness of the intrinsic (i.e., electronic) theoretical scales of both absolute and relative electrophilicity and nucleophilicity have been probed on the examination of combination reactions of seven benzhydrylium ions with 26 primary and secondary amines (nucleophiles). The main results are in complete agreement with experimental findings, stressing that both absolute and relative electronic nucleophilicities predict the higher nucleophilic character of secondary amines over primary ones in water. We stress that the simple approximations behind the proposed partition of the *stabilization energy* constitute a first step of rationalization concerning the establishment of useful connections with the experimental electrophilicity−nucleophilicity scales of reactivity based on the experimental approach of Mayr and co-workers. Additional research on this direction is now in progress. Equations 7−11 are intended to explore for new insights concerning the categorization of electronic effects driving the experimental reactivity trends. It is expected that the present work extends the range of applications of conceptual DFT and broadens the possibility of extensions and interpretation of chemical reactivity in the context of density-functional theory.

## ASSOCIATED CONTENT

### Ⓢ Supporting Information

Tables reporting main reactivity results associated to the interaction of primary and secondary amines (B: **a−zz**) and benzhydrylium ions (A: **1−7**) in water, evaluated at the B3LYP/6-31G(d) level of theory using the SM8 solvation model, namely: the maximum amount of transferred electrons (Table 1S); the maximum stabilization in the electronic interaction energy (Table 2S); the relative electrophilicity of electrophiles A in presence of nucleophile B; the relative nucleophilicity slope parameters of nucleophiles B in the presence of electrophiles A (Tables 4S); the relative nucleophilicity of nucleophile B in the presence of electrophiles A (Table 5S); the logarithm of the experimental second order rate constant for the reaction of electrophiles A with nucleophiles B (Table 6S); and the summary of the linear adjustment between the maximum electronic interaction energy change and the absolute electrophilicity for each single nucleophile (B), including standard errors for the parameters and the coefficient of determination (Table 7S). This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

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