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Density Functional Reactivity Theory Study of S_N2 Reactions from the Information-Theoretic Perspective

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Abstract

As a continuation of our recent efforts to quantify chemical reactivity with quantities from the information-theoretic approach within the framework of density functional reactivity theory, the effectiveness of applying these quantities to quantify electrophilicity for the bimolecular nucleophilic substitution (S_N2) reactions in both gas phase and aqueous solvent is presented in this work. We examined a total of 21 self-exchange S_N2 reactions for the compound with the general chemical formula of $R_1R_2R_3C$-F, where R_1, R_2, and R_3 represent substituting alkyl groups such as -H, -CH_3, -C_2H_5, -C_3H_7, and -C_4H_9 in both gas and solvent phases. Our findings confirm that scaling properties for information-theoretic quantities found elsewhere are still valid. It has also been verified that the barrier height has the strongest correlation with the electrostatic interaction, but the contributions from the exchange-correlation and steric effects, though less significant, are indispensable. We additionally unveiled that the barrier height of these S_N2 reactions can reliably be predicted not only by the Hirshfeld charge and information gain at the regioselective carbon atom, as have been previously reported by us for other systems, but also by other information-theoretic descriptors such as Shannon entropy, Fisher information, and Ghosh-Berkowitz-Parr entropy on the same atom. These new findings provide further insights for the better understanding of the factors impacting the chemical reactivity of this vastly important category of chemical transformations.

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1. Introduction

In principle, the best way to evaluate chemical reactivity for a chemical reaction is through examining its associated transition state structure to obtain the activation energy (or barrier height), intrinsic reaction pathway, rate constant, etc. These numerical results nevertheless do not provide with us any conceptual framework for the insightful understanding about the origin, tendency, pattern, and factors governing the chemical reactivity of the molecular system. According to density functional theory,[1] any property of a molecule in the ground state including chemical reactivity is dictated by its electron density. The endeavor to make use of this density and its associated quantities such as density gradient and Laplacian as reactivity descriptors to establish a conceptual framework to quantitatively predict chemical reactivity is called density functional reactivity theory (DFRT).[1-4] It has been our ongoing efforts in the past few years to develop such a reliable framework under the umbrella of DFRT, which is able to accurately predict reactivity properties, such as acidity,[5-9] basicity,[5,10] nucleophilicity,[11-15] electrophilicity,[11,12,16] regioselectivity,[11-16] among others.[17-20]

Information-theoretic quantities such as Shannon entropy,[21] Fisher information,[22] Ghosh-Berkowitz-Parr entropy[23] and information gain[24,25] are all functions of the electron density and its associated quantities (e.g., density gradient and Laplacian, etc.), so they should be natural choices as reactivity descriptors in DFRT. Earlier, we examined their scaling behaviors with respect to the number of electron populations under different partition schemes of atoms in molecules.[26] Also, based on the *information conservation principle* recently introduced by us,[11] we proposed to use the information gain and Hirshfeld charge as a quantitative measure of both nucleophilicity and electrophilicity. Its effectiveness has been verified in a series of carbon[11] and nitrogen[12] containing systems. This idea has also been successfully applied to investigate the reactivity and regioselectivity for electrophilic aromatic substitution reactions. A novel explanation was provided to understand the nature and origin of the so-called *ortho/para* and *meta* group directing phenomena for this important category of reactions.[13-15]

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In this work, we apply the idea to study another extremely important category of chemical reactions, bimolecular nucleophilic substitution (S_N2).[27,28] The main difference between this work and our previous studies[13-15] is that our previous focus was on quantifying nucleophilicity with the information gain or Hirshfeld charge, but in the present study we instead work on quantifying electrophilicity,[16] the capability of an electrophile to accept as many electrons as possible, for S_N2 reactions. In a typical S_N2 reaction, when an incoming nucleophile such as halides tackles the central atom of a substrate, which often is an electrophilic atom such as an aliphatic sp^3 carbon center with an electronegative leaving group attached, one bond will be broken and another bond be formed synchronously with the inversion of the tetrahedral geometry at the central atom.[27,28] Kinetically, the rate of an S_N2 reaction is second order, as the rate-determining step depends on both the nucleophile concentration and the concentration of the substrate. The factors impacting the reactivity of S_N2 reactions include the incoming nucleophile, the size of the groups attached to the central atom, solvents, the nature of the leaving group, etc.[28] In an earlier study, we examined this kind of reactions and systematically looked into the question of which energy component dominates the barrier height of these reactions.[29] Here, we revisit these systems, trying to address the following issues from the information-theoretic perspective of DFRT. At first, we examine the behavior of Hirshfeld charge, information gain, and other DFRT quantities as descriptors to predict reaction barrier heights, and reveal strong linear correlations between the barrier height and these quantities. Secondly, with the tools we recently developed in quantifying chemical effects such as steric and electrostatic effects,[30] we decompose the barrier height and determine the energy components that play dominant and indispensable roles. Finally, we disclose scaling properties of information-theoretic quantities in these systems with respect to the electronic population at the entire molecular and atoms-in-molecules levels.[26] Put together, these novel results from this work should shed fresh light on further

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understanding the factors governing the reactivity for this vastly important category of chemical transformations.

2. Theoretical and Methodological Considerations

Earlier, we investigated the origin of barrier heights for S_N2 reactions from the perspective of the following two energy partition schemes.[29] One is the conventional approach in density functional theory (DFT), where the total energy difference ΔE between the transition state and reactant complex of an S_N2 reaction system is partitioned as follows,[1,29]

$$\Delta E[\rho] = \Delta T_s[\rho] + \Delta E_e[\rho] + \Delta E_{xc}[\rho] \qquad (1)$$

where T_s stands for the non-interacting kinetic energy, E_e denotes the electrostatic energy, and E_{xc} represents the exchange-correlation energy component with $\rho(\mathbf{r})$ as the ground state electron density of an N-electron system, which satisfies the normalization condition, $\int \rho(\mathbf{r}) d\mathbf{r} = N$. The electrostatic term consists of the nuclear-electron attraction, V_{ne}, classical electron-electron Coulombic repulsion, J, and nuclear-nuclear repulsion, V_{nn},

$$\Delta E_e[\rho] = \Delta V_{ne}[\rho] + \Delta J[\rho] + \Delta V_{nn}. \qquad (2)$$

Alternatively, a new partition scheme was recently proposed by one of us, [30]

$$\Delta E[\rho] = \Delta E_s[\rho] + \Delta E_e[\rho] + \Delta E_q[\rho] \qquad (3)$$

where the total energy difference comes from the contribution of three distinct but independent physiochemical effects, steric ΔE_s, electrostatic ΔE_e, and fermionic quantum due to exchange and correlation effects ΔE_q. The common term in these two schemes is the electrostatic contribution ΔE_e. The benefit of applying these formulas to examine energy differences is that contributions from energy components are directly related to the barrier height, so one will have a clear picture of which components contribute positively or negatively and dominantly or negligibly to ΔE, and whether or not there is any strong correlation of the barrier height to any of these energy components. Studies for a

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number of systems have shown that it is the electrostatic term ΔE_e that plays the dominant role in governing the total energy difference, but contributions from other terms, though less significant, are also indispensable.[31]

The second energy partition scheme, Eq. (3), was based on a solid physiochemical foundation, as has been previously showed.[30] The physical nature of this new quantification of the steric effect is based on the introduction of a new reference state, where electrons in atoms and molecules are assumed to behave like bosons. If the density of the hypothetical boson state is the same as that of the fermionic state, ρ(r), the total wave function of the hypothetical state will be √(ρ(**r**)/N), where N is the number of electrons. It measures the intrinsic dimensions peculiar to the system, when both the quantum and electrostatic effects are completely excluded. The total kinetic energy of the hypothetical state is simply the Weizsäcker kinetic energy $T_W[\rho]$,[32]

$$E_S[\rho] \equiv T_W[\rho] = \frac{1}{8}\int \frac{|\nabla\rho(\mathbf{r})|^2}{\rho(\mathbf{r})} d\mathbf{r}\ . \qquad (4)$$

with $\nabla\rho(\mathbf{r})$ being the density gradient. Notice that the definition of steric energy above is consistent with Weisskopf's original attribution of the steric effect to the "kinetic energy pressure" because steric energy in Eq. (4) is kinetic and its density has the dimension of pressure.[33] Further, it is exclusive because it is separate from the other effects, both quantum and electrostatic. E_S is non-negative everywhere and, therefore, repulsive in nature. In addition, it vanishes for the homogeneous electron gas. It is extensive, i.e., larger system the larger the steric energy, because it is homogeneous of degree one in density scaling.[34-40] This novel quantification of the steric effect has been applied to a number of systems[31,41-52], such as conformational changes of small molecules, S_N2 reactions, chained and branched alkanes, experimental electron densities of crystals, cis effect, the anomeric effect, water clusters, week interactions, etc.

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This quantification of steric energy in Eq. (4) is closely related to the Fisher information in information theory[22]

$$I_F = \int \frac{\left|\nabla\rho(\mathbf{r})\right|^2}{\rho(\mathbf{r})} d\mathbf{r} = 8 E_S[\rho]. \tag{5}$$

Other quantities from the information-theoretic approach in DFRT are the Shannon entropy,[21]

$$S_S = -\int \rho(\mathbf{r}) \ln \rho(\mathbf{r}) d\mathbf{r} \tag{6}$$

and the Ghosh-Berkowitz-Parr (GBP) entropy,[23]

$$S_{GBP} = \int \frac{3}{2} k\rho(\mathbf{r}) \left[c + \ln \frac{t(\mathbf{r};\rho)}{t_{TF}(\mathbf{r};\rho)}\right] d\mathbf{r} \tag{7}$$

where $t(\mathbf{r},\rho)$ is the kinetic energy density, which is related to the total kinetic energy T_S via

$$\int t(\mathbf{r};\rho) d\mathbf{r} = T_S, \tag{8}$$

and $t_{TF}(\mathbf{r};\rho)$ *is* the Thomas-Fermi kinetic energy density given by

$$t_{TF}(\mathbf{r};\rho) = c_K \rho^{5/3}(\mathbf{r}), \tag{9}$$

with *k* as the Boltzmann constant (set to be unity for convenience in this work),

$$c = \frac{5}{3} + \ln \frac{4\pi c_K}{3}, \text{ and } c_K = \frac{3}{10}(3\pi^2)^{2/3}. \tag{10}$$

Following the original literature,[15,16] we use

$$t(\mathbf{r};\rho) = \sum_i \frac{1}{8} \frac{\nabla\rho_i \cdot \nabla\rho_i}{\rho_i} - \frac{1}{8}\nabla^2\rho, \tag{11}$$

where ρ_i are the orbital densities. Shannon entropy measures the spatial delocalization of the electron density, whereas Fisher information is a gauge of the sharpness or concentration of the electron density distribution.[53] The GBP entropy was resulted from the reformulation the ground-state density-functional theory into a macroscopic local version of thermodynamics to describe the behavior of microscopic electrons with the introduction of the concepts of local temperature.[23]

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These three quantities, which were defined by the electron density ρ(**r**), can also be re-defined using the shape function σ(**r**), defined as σ(**r**)≡ ρ(**r**)/N, leading to the new information-theoretic quantities denoted by S_σ and I_σ, respectively,[26]

$$S_\sigma = -\int \sigma(\mathbf{r}) \ln \sigma(\mathbf{r}) d\mathbf{r} \tag{11}$$

and

$$I_\sigma = \int \frac{|\nabla \sigma(\mathbf{r})|^2}{\sigma(\mathbf{r})} d\mathbf{r} \, . \tag{12}$$

With the relationship between the electron density and shape function, one can readily prove that[18]

$$S_\sigma = \frac{S_S}{N} + \ln N \tag{13}$$

and

$$I_\sigma = \frac{I_F}{N} \, . \tag{14}$$

Recently, information gain I_G, also called Kullback–Leibler divergence, relative entropy, or information divergence, of a molecular system due to its formation from composing ingredients,

$$I_G = \sum_A \int \rho_A \ln \frac{\rho_A}{\rho_A^0} d\mathrm{r}, \tag{15}$$

was found to be a quantitatively reliable measure of electrophilicity, nucleophilicity, and regioselectivity.[11-15] In Eq. (15), ρ_A is the electron density on Atom (or Group) A in a molecule, whose total electron density is ρ, and ρ_A^0 is the counterpart of Atom (or Group) *A* in the reference state. This result was from the previous work by Nalewajski and Parr,[54-57] showing that minimizing Eq. (15) gives arise to the ‘‘stockholder partition’’ of the electron density proposed by Hirshfeld,[58]

$$\rho_A = \frac{\rho_A^0}{\sum_A \rho_A^0} \rho. \tag{16}$$

If a new variable, $x = (\rho_A - \rho_A^0)/\rho_A$, is introduced with the help that $\ln \frac{1}{1-x} \approx x$ as the first-order approximation, Eq. (15) can be simplified to become[11]

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$$I_G \approx \sum_A \int \left(\rho_A - \rho_A^0\right) dr = -\sum_A q_A \equiv 0 \qquad (17)$$

where q_A is the Hirshfeld charge on Atom (or Group) *A*. This result suggests that under the first-order approximation, the minimal information gain not only yields the Hirshfeld charge distribution but it also simply vanishes. We called this result the *information conservation principle*. Its effectiveness has been verified in a series and carbon and nitrogen containing systems.[11-12] It has also been successfully applied to examine the reactivity and regioselectivity for electrophilic aromatic substitution reactions. A novel explanation was obtained about the nature and origin of the so-called *ortho/para* and *meta* group directing phenomena for those reactions.[13-15]

In this work, we apply these formulations to bimolecular nucleophilic substitution (S_N2) reactions and examine their effectiveness of these quantities in predicting chemical reactivity for these systems. We are also interested in appraising the strong scaling properties for them in these systems and compare them with those unveiled from other systems reported elsewhere.

3. Computational Details

We considered, in this work, the transition state and reactant/product complex in both the gas phase and aqueous solvent for a total of 21 self-exchange S_N2 reactions of $R_1R_2R_3C$-F reacting with the fluorine anion, where R_1, R_2, and R_3 represent substituting alkyl groups such as -H, $-CH_3$, $-C_2H_5$, $-C_3H_7$, and $-C_4H_9$ groups (Scheme 1). We denote these systems in terms of three substituted groups in the format of ($R_1R_2R_3$). The S_N2 reaction in gas and solvent phases is known to proceed via a pre-transition state association type of the molecular complex.[27,28] All calculations were performed at the DFT B3LYP/6-311+G(d) level of theory.[59-61] Calculations of the reactions paths were performed with Gaussian 09 package version D01 [62] with tight SCF convergence and ultra-fine integration grids. For transition-state structure searches, the quadratic synchronous transit approach[63] was employed and single-point frequency calculation was followed to ensure that the final structure obtained has only one imaginary

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frequency and that the vibration mode of the negative frequency corresponds to the bond formation and bond breaking process of a S_N2 reaction. In addition, an intrinsic reaction coordinate (IRC)[64] run was ensued to verify the relevance of transition-state structures. As an example, Scheme 1 shows the IRC result for the system of $R_1=R_2=R_3=H$. To simulate the solvent effect, an implicit solvent model, the conductor-like polarizable continuum model (CPCM),[65] was utilized in this study.

The Multiwfn 3.2 program[66] developed by one of the present authors was used to calculate the information-theoretic quantities in Eqs. (4)-(17) using the checkpoint file from the above Gaussian calculations as the input file. To obtain the electron density for the isolated state, we employed the spherically-averaged electron density of the neutral atom at the same level of theory. Besides neutral molecules, we also examine the scaling properties of information-theoretic quantities for atoms in molecules. To that end, three schemes to perform the atomic partition, Becke's fuzzy atom approach,[67] Bader's zero-flux atoms-in-molecules criterion,[68] and Hirshfeld's stockholder approach,[58] are possible. As have been demonstrated earlier,[26] these three approaches yield similar results. In this work, we choose the Hirshfeld's stockholder approach[58] to partition atoms in molecules. The molecular and atomic values of the steric energy were obtained through Eq. (5). Other energetic components in Eqs (1) - (3) were gathered from the Gaussian calculation using the internal option keyword of IOp(5/33=1).

4. Results and Discussion

Table 1 exhibits the molecular value of Shannon entropy, Fisher information, GBP entropy and information gain for the 21 reactants of S_N2 reactions in aqueous solvent studied in this work. Also shown in the Table is the total number of electrons N in the systems as well as molecular values of the shape function counterpart for Shannon entropy and Fisher information, S_σ and I_σ. The correlation coefficient R^2 between N and these information-theoretic quantities is displayed in the last row of the

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Table. As can be seen from the Table, all quantities shown in the Table, S_S, S_σ, I_F, I_σ, S_{GBP}, and I_G, are positive. The correlation between N and S_S, I_F, and S_{GBP} is perfect, each with R^2=1.000, indicating that for systems studied in this work these three information-theoretic quantities are linearly extensive with respect to the total population of electrons and the system size. Correlations between N and S_σ, I_σ, and I_G are not perfect but they are still markedly strong. Similar linear strong relationships were found for reactions in the gas phase (results not shown).

Table 2 presents the atomic value of Shannon entropy, Fisher information, GBP entropy and information gain on the reactive carbon center for the 21 transition state structures of bimolecular nucleophilic substitution reactions in gas phase studied in this work. The atomic value was calculated using Hirshfeld's shareholder partition scheme.[58] Also shown in the Table is the Shannon entropy and Fisher information using the shape function as the local function, S_σ and I_σ, plus the Hirsheld charge and the total electron population, N_C, on the reactive carbon atom. In addition, the barrier height (activation energy) of these reactions is tabulated as well. The purpose of this Table is to correlate atomic values of those information quantities on the reactive carbon center with the reaction barrier height. Shown in the last row of the Table are the correlation coefficients R^2 of these relationships. One can see that all these quantities are remarkable indicators of the reaction barrier height, all with R^2 larger than 0.95. Recall that in our previous work,[14,15] the information gain and Hirshfeld charge were employed to quantify reactivity with strong correlations between them and the barrier height disclosed. Our results from this work suggest that for S_N2 reactions, at least for systems studied here, there are more descriptors of the reactivity from the information-theoretic approach. These results also indicate that atomic values of the quantities from the information-theoretic approach at the reaction center are strongly correlated. For example, the correlation coefficient between S_S and I_F, between I_F and S_{GBP}, and between I_σ and the Hirshfeld charge is 0.999, 0.999, 0.998, respectively. In agreement with our previous results,[14,15] these strong correlations among different quantities are merely another testament of the fact that the electron density determines everything in the ground state in density functional theory. All information-theoretic quantities are functions of the electron density, so it is not unusual that these quantities are interrelated, as have been theoretically proved[53] and numerically demonstrated elsewhere.[25,26] Given their vastly different analytical forms, this kind of correlations from information-theoretic quantities is not trivial and has never been reported in the literature. They serve as one of the main results in this work.

Do we have to make use of the quantities from the transition state structure to observe above correlations? Do they still work well if results from reactants are employed? What if the solvent effect is taken into consideration? It is well known that the solvent effect might have a huge impact on the reactivity indices.[69] To answer these questions, shown in Table 3 are the correlation coefficients of the above strong correlations with different structures in different conditions. In the Table, we employed both the reactant and transition state structures, and considered the condition in both gas phase and in aqueous solvent. In all the cases, the strong correlations discussed above are still in existence. We do not observe noticeable differences in their correlation coefficients. These results demonstrate that one does not have to use the transition state structure, nor does one have to do it in the gas or solvent phase. Indeed, the only exception in Table is information gain of the transition state structure in the aqueous solvent, whose R^2 is much smaller than others. In agreement with our previous work,[15] Table 3 shows that using the reactant alone, one is able to reliably predict the barrier height with the Hirshfeld charge and information gain. Moreover, this Table also suggests that other quantities from the reactant can do the similar job with the similar accuracy.

Shown in Figure 1 are the numerical results of three information-theoretic quantities, I_σ, S_{GBP}, and I_G, for a total of 346 carbon atoms from 21 reactant and transition state structures as a function of their total electron population in both gas (Fig. 1a - 1c) and solvent (Fig. 1d - 1f) phases. Again, we employed Hirshfeld's shareholder approach to perform the atom-in-molecule partition. These scaling

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results of atomic values with respect to the total electron population for Shannon entropy, Fisher information, and GBP entropy are similar to those shown in our previous study for other systems,[15,26] including transition state structures. What looks to be an exception is the result for the GBP entropy. In both the gas and solvent cases, R^2 values of S_{GBP} vs. N_C are both larger than 0.95, enough to claim that their correlations are strong. However, looking at Figs. 1b and 1e, it appears that there exist two parallel lines between S_{GBP} vs. N_C with the same slope but different intercepts. The origin of this bi-linearity might be coming from the fact that there exist two kinds of carbon atoms, one on the reaction center and the other from the substituting groups.[12]

Following our previous efforts,[30,31] we decomposed the reaction barrier height into three components using the two distinct energy partition schemes, Eqs. (1) and (3). The purpose of this analysis is to examine the origin of the activation energy by finding out (i) whether or not there is a dominant energy contributor and (ii) if there is a strong correlation between the barrier height and any of the energy components. Table 4 shows the numerical results for the 21 S_N2 substitution reactions studied in this work in aqueous solvent. Similar results were also obtained for these species in gas phase. As can be seen from the Table, we have the barrier height ΔE is always positive, $\Delta E > 0$, so are ΔE_e and ΔE_{xc} and $\Delta E_{S,}$ indicating that these three components are positively contributing to the existence of the barrier height. Correlations of these three components with the barrier height in both gas (a-c) and solvent (e-f) phases are shown in Fig. 2. For the gas phase, the correlation coefficient between ΔE and ΔE_S, between ΔE and ΔE_{xc}, and between ΔE and ΔE_e is 0.711, 0.965, and 0.990, respectively, whereas in aqueous solvent, it becomes 0.783, 0.824, and 0.944, respectively. There are two points to make in regard to the results in Fig. 2. At first, in both gas and solvent phases, it is the electrostatic effect that possesses the strongest linear correlation with the barrier height. This result is consistent with our results reported elsewhere for other systems.[31] Secondly, the reasonably strong correlation between ΔE and ΔE_S in both cases suggest that the steric effect is a good indicator of the chemical reactivity for this category of systems. The bigger the groups (R_1, R_2, and R_3) attached to the reactive center, the larger the barrier height and thus the slow the S_N2 reaction. This result agrees well with the experimental findings available in textbooks as well as our theoretical work in the literature.[29]

With the two energy components from Eqs. (1) and (3) to fit with the S_N2 reaction barrier height, we obtained slightly better results in both gas and solvent cases. Figure 3 exhibits the results, with R^2 equal to or better than 0.99 in gas phase and $R^2 > 0.95$ in aqueous solvent. These results are consistent with our previous studies for other systems such as conformational changes[31] and electrophilic aromatic substitution reactions,[16] confirming for one more time that the electrostatic interaction is the dominant contributor in determining the barrier height, but contributions from other effects such as exchange-correlation and steric interactions, though less significant, are indispensable.

Notice that, using virial theorem, the energy difference ΔE between two systems should satisfy[1]

$$\Delta E = -\Delta T = \tfrac{1}{2}\Delta V, \tag{18}$$

where T and V denote the total kinetic and potential energies, respectively, of the systems in concern. Eq. (18) suggests that ΔE is equal to either the entire kinetic energy difference or half of the total potential energy difference. These energy components are, however, not chemically meaningful. We often wish to obtain insights from such effects as steric, electrostatic, or quantum, which are missing in Eq. (18). More importantly, Eq. (18) does not work for density functional theory,[1-4] because a portion of the kinetic energy, $T_c[\rho]$, has already been incorporated in the exchange-correlation energy E_{xc}, making the DFT version of the viral theorem much more complicated.[71-74]

Before closing, we should caution the readers about the general applicability of these strong linear relationships obtained from this work to other systems. Based on the results we obtained previously, correlations from scaling properties[15,25,26] and energy partition analysis[29-31,41-51] shown in Figs. 1-3 should be generally applicable. However, for the strong correlations for the barrier height with various information-theoretic quantities, based on what we know for carbon and nitrogen systems,[11,12]

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it is highly possible that they are not generally applicable, same as what we have observed for the acidity case.[5-10] Many competing terms showing good linear correlations in one system might suggest that a complete picture is still lacking. The search for a more general quantification approach using these and other DFRT descriptors is still in the works.

5. Concluding Remarks

Can we make use of the quantities from the information-theoretic approach to reliably predict the reactivity for bimolecular nucleophilicity substitution (S_N2) reactions? Are the scaling properties observed in other systems for the quantities such as Shannon entropy, Fisher information, Ghosh-Berkowitz-Parr entropy and information gain still valid for S_N2 reactions? What is the origin of the barrier height of these reactions? To answer these questions, in this work, we examined a total of 21 self-exchange S_N2 reactions for compounds with the general formula of $R_1R_2R_3C$-F reacting with the fluorine anion, where R_1, R_2, and R_3 represent substituting alkyl groups such as -H, $-CH_3$, $-C_2H_5$, $-C_3H_7$, and $-C_4H_9$ groups. We confirmed that there existed similar scaling properties for information-theoretic quantities in these reactive systems. The barrier height of the S_N2 reactions can reliably be predicted by not only the Hirshfeld charge and information gain at the regioselective carbon atom, but also other reactivity descriptors such as Shannon entropy, Fisher information, and Ghosh-Berkowitz-Parr entropy at the same carbon atom. The energy decomposition analysis result is in excellent agreement with our previous work reported elsewhere for other systems, suggesting that it is the electrostatic interaction plays the dominant role, while the roles played by exchange-correlation and steric effects are less significant but indispensable. These novel findings provide additional insights for the better understanding of the chemical reactivity as well as the factors governing the chemical reactivity for this extremely important category of chemical transformations, which finds widespread applications in

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organic synthesis, enzyme chemistry, catalyst design and many other studies in different scientific disciplines.

Acknowledgements

CYR acknowledges support from the National Natural Science Foundation of China (21503076), the Chinese Scholarship Council, the Construct Program of the Key Discipline in Hunan Province, and the Aid Program for Science and Technology Innovative Research Team in Higher Educational Institutions of Hunan Province, PR China. PWA thanks NSERC for support from a Discovery Grant and an E. W. R. Steacie Fellowship.

References

1. R. G. Parr and W. T. Yang, *Density Functional Theory for Atoms and Molecules*, Oxford University Press, New York, 1989.
2. P. Geerlings, F. De Proft and W. Langenaeker, *Chem. Rev*., 2003, **103**, 1793.
3. P. K. Chattaraj, U. Sarkar and D. R. Roy, *Chem. Rev*., 2006, **106**, 2065.
4. S. B. Liu, *Acta Phys.-Chim. Sin*., 2009, **25**, 590.
5. S.B. Liu, and L.G. Pedersen, *J. Phys. Chem. A*, 2009, **113**, 3648.
6. S.B. Liu, C.K. Schauer, and L.G. Pedersen, *J. Chem. Phys*., 2009, **131**, 164107.
7. S.K. Burger, S.B. Liu, and P.W. Ayers, *J. Phys. Chem. A*, 2011, **115**, 1293.
8. Y. Huang, L.H. Liu, W.H. Liu, S.G. Liu, and S.B. Liu, *J. Phys. Chem. A*, 2011, **115**, 14697
9. D.B. Zhao, C.Y. Rong. D.L. Yin, and S.B. Liu, *J. Theor. Comp. Chem.,* 2013, **12**, 1350034.
10. Y. Huang, L.H. Liu, and S.B. Liu, *Chem*. *Phys. Lett.* 2012, **527**, 73-78.
11. S. B. Liu, C. Y. Rong and T. Lu, *J. Phys. Chem*. A, 2014, **118**, 3698.
12. X. Y. Zhou, C. Y. Rong, T. Lu and S. B. Liu, *Acta Phys.-Chim. Sin*., **2014**, 30, 2055.
13. S. B. Liu, *J. Chem. Phys*., 2014, **141**, 194109.
14. S. B. Liu, *J. Phys. Chem. A*, 2015, **119**, 3107.
15. W.J. Wu, Z.M. Wu, C.Y. Rong, Y. Huang, and S.B. Liu, *J. Phys. Chem. A*, **DOI:** 10.1021/acs.jpca.5b04309.

Physical Chemistry Chemical Physics Accepted Manuscript

16. R. G. Parr, L. von Szentpaly, and S.B. Liu, *J. Am. Chem. Soc.,* 1999, **121**, 1922.
17. S. Wu, S.B. Liu, S. Sim, and L.G. Pedersen, *J. Phys. Chem. Lett*., 2012, **3**, 2293.
18. P.P. Zhou, P.W. Ayers, S.B. Liu, and T.L. Li, *Phys. Chem. Chem. Phys*., 2012, **14**, 9890.
19. N. Kumar, S.B. Liu, and P.M. Kozlowski, *J. Phys. Chem. Lett*. 2012, **3**, 1035.
20. S.B. Liu, D. H. Ess, and C. K. Schauer, *J. Phys. Chem. A*, 2011, **115**, 4738.
21. C. E. Shannon, Bell Syst. Tech. J., 1948, 27, 379.
22. R. A. Fisher, Proc. Cambridge Philos. Soc., 1925, 22, 700.
23. S. K. Ghosh, M. Berkowitz and R. G. Parr, Proc. Natl. Acad. Sci. U. S. A., 1984, 81, 8028.
24. S. Kullback, *Information Theory and Statistics*, Dover, Mineola, NY, 1997.
25. C. Rong, T. Lu, P. K. Chattaraj and S. Liu, Indian J. Chem., Sect. A: Inorg., Bio-inorg., Phys., Theor. Anal. Chem., 2014, 53, 970.
26. C.Y. Rong, T. Lu, P.W. Ayers, P.K. Chattaraj, and S.B. Liu, *Phys. Chem. Chem. Phys*., 2015, **17**, 4977; *Phys. Chem. Chem. Phys***.**, 2015,**17**, 11110-11111.
27. J.E. McMurry, *Organic Chemistry*, Wadsworth, Belmont, 1992.
28. M.B. Smith, J. March, *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Wiley-Interscience, New York, 2007.
29. S. B. Liu, H. Hu and L. G. Pedersen, *J. Phys. Chem. A*, 2010, **114**, 5913.
30. S. B. Liu, *J. Chem. Phys*., 2007, **126**, 244103.
31. S. B. Liu, *J. Phys. Chem. A*, 2013, **117**, 962.
32. C. F. von Weizsäcker, Z. Phys., 1935, 96, 431.
33. V. F. Weisskopf, Science, 1975, 187, 605.
34. M. Levy and J. P. Perdew, *Phys. Rev. A: At., Mol., Opt. Phys*., 1985, **32**, 2010.
35. S. B. Liu, *Phys. Rev. A: At., Mol., Opt. Phys*., 1996, **54**, 1328.
36. S. B. Liu and R. G. Parr, *Phys. Rev. A: At., Mol., Opt. Phys*., 1996, **53**, 2211.
37. S. B. Liu, *Phys. Rev. A: At., Mol., Opt. Phys*., 1996, **54**, 1328.
38. S. B. Liu, R. C. Morrison and R. G. Parr, *J. Chem. Phys.*, 2006, **125**, 174109.
39. S. B. Liu, P. W. Ayers, and R. G. Parr, *J. Chem. Phys.*, 1999, **111**, 6197.
40. S. B. Liu and R. G. Parr, *J. Phys. Chem. A*, 2007, **111**, 10422.
41. S. B. Liu and N. Govind, *J. Phys. Chem. A*, 2008, **112**, 6690.
42. S. B. Liu, N. Govind, and L. G. Pedersen, *J. Chem. Phys*., 2008, **129**, 094104.
43. M. Torrent-Sucarrat, S. B. Liu, and F. De Proft, *J. Phys. Chem. A*, 2009, **113**, 3698.
44. D. H. Ess, S. B. Liu, and F. De Proft, *J. Phys. Chem. A*, 2010, **114**, 12952.

Physical Chemistry Chemical Physics Accepted Manuscript

45. V. G. Tsirelson, A. I. Stash, and S. B. Liu, *J. Chem. Phys*., 2010, **133**, 114110.
46. Y. Huang, A. G. Zhong, Q. S. Yang, and S. B. Liu, *J. Chem. Phys*. 2011, **134**, 084103.
47. R. O. Esquivel, S. B. Liu, J. C. Angulo, J. S. Dehesa, J. Antolin, and M. Molina-Espiritu, *J. Phys. Chem. A*, 2011, **115**, 4406.
48. D. B. Zhao, C. Y. Rong, S. Jenkins, S. R. Kirk, D. L. Yin, and S. B. Liu, *Acta Phys.-Chim. Sin*., 2013, **29**, 43.
49. V. G. Tsirelson, A. I. Stash, and S. B. Liu, *Comput. Theor. Chem*., 2013, **1006**, 92.
50. Y. J. Wang, D. B. Zhao, C. Y. Rong, and S. B. Liu, *Acta Phys.-Chim. Sin*. 2014, **29**, 2173.
51. D. Fang, J.-P. Piquemal, S. B. Liu, and G. A. Cisneros, *Theor. Chem. Acc*. 2014, **133**, 1484.
52. S.B. Liu, and C.K. Schauer, *J. Chem. Phys*., 2015, **142**, 054107.
53. S. B. Liu, *J. Chem. Phys*., 2007, **126**, 191107.
54. R. F. Nalewajski and R. G. Parr, *J. Phys. Chem. A*, 2001, **105**, 7391.
55. R. F. Nalewajski and R. G. Parr, Proc. *Natl. Acad. Sci. U. S. A*., 2000, **97**, 8879.
56. R. G. Parr, P. W. Ayers and R. F. Nalewajski, *J. Phys. Chem. A*, 2005, **109**, 3957.
57. P. W. Ayers, *Theor. Chem. Acc*., 2006, **115**, 370.
58. F. L. Hirshfeld, *Theor. Chem. Acc*., 1977, **44**, 129.
59. A. D. Becke, *J. Chem. Phys*., 1993, **98**, 5648.
60. C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys*., 1988, **37**, 785.
61. R. Ditchfield, W. J. Hehre and J. Pople, *J. Chem. Phys*., 1971, **54**, 724.
62. M. J. Frisch, G. W. Trucks and H. B. Schlegel, et al., Gaussian 09, Revision D. 01, Gaussian, Inc., Wallingford, CT, 2009.
63. C. Peng, P. Y. Ayala, H. B. Schlegel, and M. J. Frisch, *J. Comp. Chem.*, 1996, **17**, 49.
64. K. Fukui, *Acc. Chem. Res.*, 1981, **14**, 363.
65. M. Cossi, N. Rega, G. Scalmani, and V. Barone, *J. Comp. Chem.*, 2003, **24**, 669-81.
66. T. Lu and F. Chen, *J. Comput. Chem*., 2012, **33**, 580.
67. A. D. Becke, *J. Chem. Phys*., 1988, **88**, 2547.
68. R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, Oxford, 1990.
69. C. Y. Rong, S. X. Lian and S. B. Liu, *J. Nat. Sci. Hunan Norm. Univ*., 2014, **37**, 31.
70. M. Levy and J.P. Perdew, *Phys. Rev. A* 1985**, 32**, 2010.
71. S.B. Liu and R.G. Parr, *Phys. Rev. A* 1996**, 53**, 2211.
72. S.B. Liu, *Phys. Rev. A* 1996**, 54**, 1328.
73. S.B. Liu, A. Nagy, and R.G. Parr, *Phys. Rev. A* 1999**, 59**, 1131.
74. S.B. Liu, R.C. Morrison, and R.G. Parr, *J. Chem. Phys.,* 2006**, 125**, 174109.

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Table 1. The molecular value of Shannon entropy, Fisher information, GBP entropy and information gain for the 21 reactants of S_N2 reactions in aqueous solvent studied in this work. Also shown is the shape function counterpart of the Shannon entropy and Fisher information. The correlation coefficient R^2 between these information-theoretic quantities and the total electron number *N* of the molecules is displayed in the last row. Atomic units.

$R_1R_2R_3$	N	S_S	S_σ	I_F	I_σ	S_{GBP}	I_G
$C_2H_5C_2H_5C_2H_5$	76	78.457	5.363	2928.490	38.533	494.871	2.5051
$C_2H_5C_2H_5CH_3$	68	68.359	5.225	2676.706	39.363	442.883	2.3461
$C_2H_5C_2H_5H$	60	58.301	5.066	2425.464	40.424	391.018	2.2217
$C_2H_5CH_3CH_3$	60	58.255	5.065	2424.913	40.415	390.892	2.1888
$C_2H_5CH_3H$	52	48.056	4.875	2173.225	41.793	338.927	2.0186
C_2H_5HH	44	37.844	4.644	1921.361	43.667	286.927	1.8433
$C_3H_7C_2H_5C_2H_5$	84	88.639	5.486	3180.458	37.863	546.898	2.6594
$C_3H_7C_2H_5CH_3$	76	78.550	5.364	2928.701	38.536	494.918	2.5049
$C_3H_7C_2H_5H$	68	68.407	5.225	2677.132	39.370	442.982	2.3269
$C_3H_7C_3H_8C_2H_5$	92	98.829	5.596	3432.452	37.309	598.933	2.8204
$C_3H_7C_3H_7C_3H_7$	100	109.008	5.695	3684.408	36.844	650.957	2.9720
$C_3H_7C_3H_7CH_3$	84	88.735	5.487	3180.683	37.865	546.949	2.6609
$C_3H_7C_3H_7H$	76	78.661	5.366	2929.373	38.544	495.070	2.5183
$C_3H_7CH_3CH_3$	68	68.444	5.226	2676.913	39.366	442.927	2.3469
$C_3H_7CH_3H$	60	58.242	5.065	2425.211	40.420	390.960	2.1744
C_3H_7HH	52	48.039	4.875	2173.392	41.796	338.966	2.0016
C_4H_9HH	60	58.289	5.066	2425.606	40.427	391.043	2.1816
$CH_3CH_3CH_3$	52	48.138	4.877	2173.099	41.790	338.893	2.0283
CH_3CH_3H	44	37.998	4.648	1921.620	43.673	286.974	1.8974
CH_3HH	36	27.656	4.352	1669.378	46.372	234.892	1.6881
HHH	28	17.586	3.960	1418.115	50.647	182.985	1.6020
R^2		1.000	0.942	1.000	0.855	1.000	0.997

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Table 2. The atomic value of Shannon entropy, Fisher information, GBP entropy and information gain on the reactive carbon center for the 21 transition state structures of S_N2 reactions in gas phase studied in this work. Also shown is the shape function counterpart of the Shannon entropy and Fisher information. The Hirshfeld charge on the reaction carbon center and the barrier height of these reactions are tabulated as well. Atomic units except for the barrier height, which is in kcal/mol.

$R_1R_2R_3$	S_S	S_σ	I_F	I_σ	S_{GBP}	I_G	Hirshfeld	N_C	Barrier
$C_2H_5C_2H_5C_2H_5$	4.1304	2.4720	246.0801	42.1417	37.9468	0.0876	0.1607	5.8394	24.87
$C_2H_5C_2H_5CH_3$	4.1403	2.4737	246.0947	42.1415	37.9529	0.0880	0.1603	5.8397	25.48
$C_2H_5C_2H_5H$	4.4002	2.5204	246.5392	41.8373	38.3825	0.0952	0.1072	5.8928	19.04
$C_2H_5CH_3CH_3$	4.1558	2.4764	246.1133	42.1370	37.9640	0.0870	0.1592	5.8408	26.21
$C_2H_5CH_3H$	4.4445	2.5281	246.6084	41.8325	38.4137	0.0950	0.1049	5.8951	19.93
C_2H_5HH	4.7668	2.5844	247.1427	41.5653	38.8458	0.1021	0.0541	5.9459	14.04
$C_3H_7C_2H_5C_2H_5$	4.1300	2.4719	246.0733	42.1409	37.9457	0.0886	0.1607	5.8393	24.79
$C_3H_7C_2H_5CH_3$	4.1397	2.4736	246.0879	42.1413	37.9515	0.0878	0.1604	5.8396	25.39
$C_3H_7C_2H_5H$	4.3983	2.5201	246.5294	41.8395	38.3784	0.0962	0.1077	5.8923	19.13
$C_3H_7C_3H_8C_2H_5$	4.1296	2.4718	246.0665	42.1404	37.9444	0.0884	0.1608	5.8392	24.72
$C_3H_7C_3H_7C_3H_7$	4.1287	2.4717	246.0589	42.1407	37.9425	0.0883	0.1610	5.8390	24.65
$C_3H_7C_3H_7CH_3$	4.1386	2.4734	246.0788	42.1409	37.9496	0.0876	0.1606	5.8394	25.31
$C_3H_7C_3H_7H$	4.3956	2.5196	246.5137	41.8385	38.3753	0.0962	0.1080	5.8920	19.05
$C_3H_7CH_3CH_3$	4.1545	2.4762	246.1041	42.1368	37.9620	0.0869	0.1594	5.8406	26.10
$C_3H_7CH_3H$	4.4414	2.5275	246.5967	41.8366	38.4077	0.0962	0.1057	5.8943	20.03
C_3H_7HH	4.7634	2.5838	247.1247	41.5624	38.8432	0.1020	0.0541	5.9459	14.49
C_4H_9HH	4.7626	2.5837	247.1227	41.5620	38.8429	0.1019	0.0541	5.9459	14.87
$CH_3CH_3CH_3$	4.1739	2.4795	246.1366	42.1383	37.9734	0.0862	0.1588	5.8412	27.13
CH_3CH_3H	4.4647	2.5316	246.6172	41.8105	38.4417	0.0943	0.1015	5.8985	19.66
CH_3HH	4.8138	2.5924	247.2093	41.5587	38.8801	0.1016	0.0516	5.9484	14.67
HHH	5.2125	2.6606	247.8293	41.2701	39.3688	0.1056	-0.0051	6.0051	9.22
R^2	0.952	0.955	0.958	0.984	0.975	0.984	0.980	0.980	---

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Table 3. Correlation coefficients between the reaction barrier height and information-theoretic quantities for the S_N2 reactions studied in this work in both gas phase and aqueous solvent. The correlation is considered with respect to both the reactant complex and the transition state.

R^2	S_S	S_σ	I_F	I_σ	S_{GBP}	I_G	Hirshfeld	N_C
Reactant (gas)	0.945	0.946	0.955	0.946	0.952	0.974	0.951	0.951
TS (gas)	0.952	0.955	0.958	0.984	0.975	0.984	0.980	0.980
Reactant (solvent)	0.962	0.964	0.968	0.980	0.976	0.986	0.979	0.979
TS (solvent)	0.967	0.971	0.963	0.994	0.987	0.761	0.990	0.990

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Table 4. Energy component results from the two decomposition approaches, Eqs. (1) and (3), for a total of 21 S_N2 reaction systems in aqueous solvent studied in this work. Units in kcal/mol.

$R_1R_2R_3$	ΔT_s	ΔE_{xc}	ΔE_e	ΔE_s	ΔE_q	ΔE
$C_2H_5C_2H_5C_2H_5$	-46.58	18.53	43.53	77.91	-105.96	32.24
$C_2H_5C_2H_5CH_3$	-43.61	18.02	41.33	77.49	-103.07	32.50
$C_2H_5C_2H_5H$	-35.11	15.75	27.97	77.12	-96.49	27.07
$C_2H_5CH_3CH_3$	-44.33	18.06	42.62	79.07	-105.35	32.81
$C_2H_5CH_3H$	-35.42	16.50	31.93	76.66	-95.58	26.83
C_2H_5HH	-30.86	15.67	25.69	75.94	-91.14	22.36
$C_3H_7C_2H_5C_2H_5$	-47.67	18.77	44.42	78.07	-106.97	32.29
$C_3H_7C_2H_5CH_3$	-43.87	18.08	40.77	78.77	-104.56	32.49
$C_3H_7C_2H_5H$	-34.16	16.36	29.64	77.26	-95.06	26.80
$C_3H_7C_3H_8C_2H_5$	-47.49	18.62	43.93	78.23	-107.10	32.33
$C_3H_7C_3H_7C_3H_7$	-46.11	18.21	43.03	78.10	-106.00	32.35
$C_3H_7C_3H_7CH_3$	-44.81	18.21	41.77	78.91	-105.51	32.51
$C_3H_7C_3H_7H$	-34.79	15.82	28.34	77.13	-96.11	27.10
$C_3H_7CH_3CH_3$	-42.71	17.74	40.92	79.03	-104.00	32.82
$C_3H_7CH_3H$	-34.91	16.49	31.27	76.19	-94.60	26.86
C_3H_7HH	-29.95	15.43	24.59	75.72	-90.23	22.26
C_4H_9HH	-27.42	14.27	21.54	75.80	-88.95	22.27
$CH_3CH_3CH_3$	-41.79	17.16	41.80	78.70	-103.33	33.14
CH_3CH_3H	-34.46	15.16	29.32	74.20	-93.50	25.87
CH_3HH	-30.54	15.44	26.34	74.69	-89.79	22.56
HHH	-18.87	10.67	10.99	75.02	-83.22	18.56

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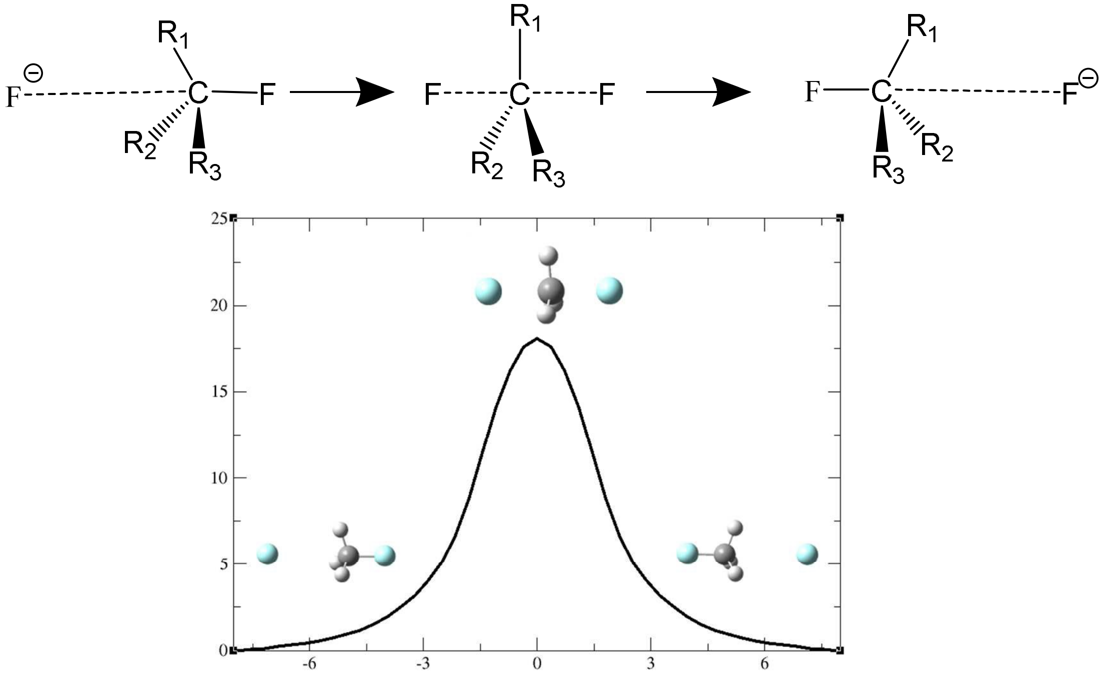

Scheme 1. The identity S_N2 reaction studied in this work. R_1, R_2, and R_3 are alky functional groups, which could be H, CH_3, C_2H_5, C_3H_8, or C_4H_{10}. The IRC calculation shown above was done at the B3LYP/6-311+G(d) level of theory for the system of R_1=R_2=R_3=H in aqueous solvent with the CPCM used as the implicit solvent model.

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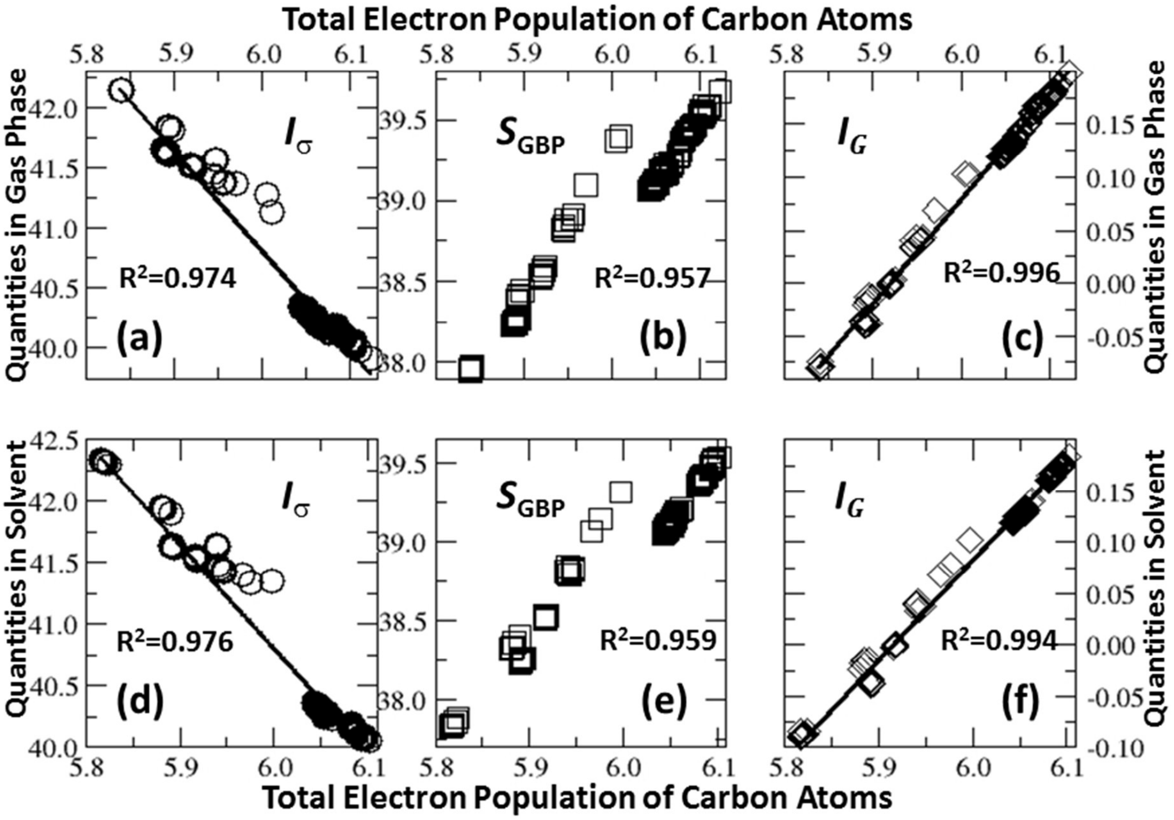

Figure 1. Strong linear scaling properties of informatics-theoretical quantities, I_σ, S_{GBP}, and I_G, obtained for a total of 346 carbon atoms from the 21 reactant and transition state structures with respect to the total electron populations on the carbon atom using Hirshfeld's shareholder partition scheme in both gas (a-c) and solvent (d-f) phases.

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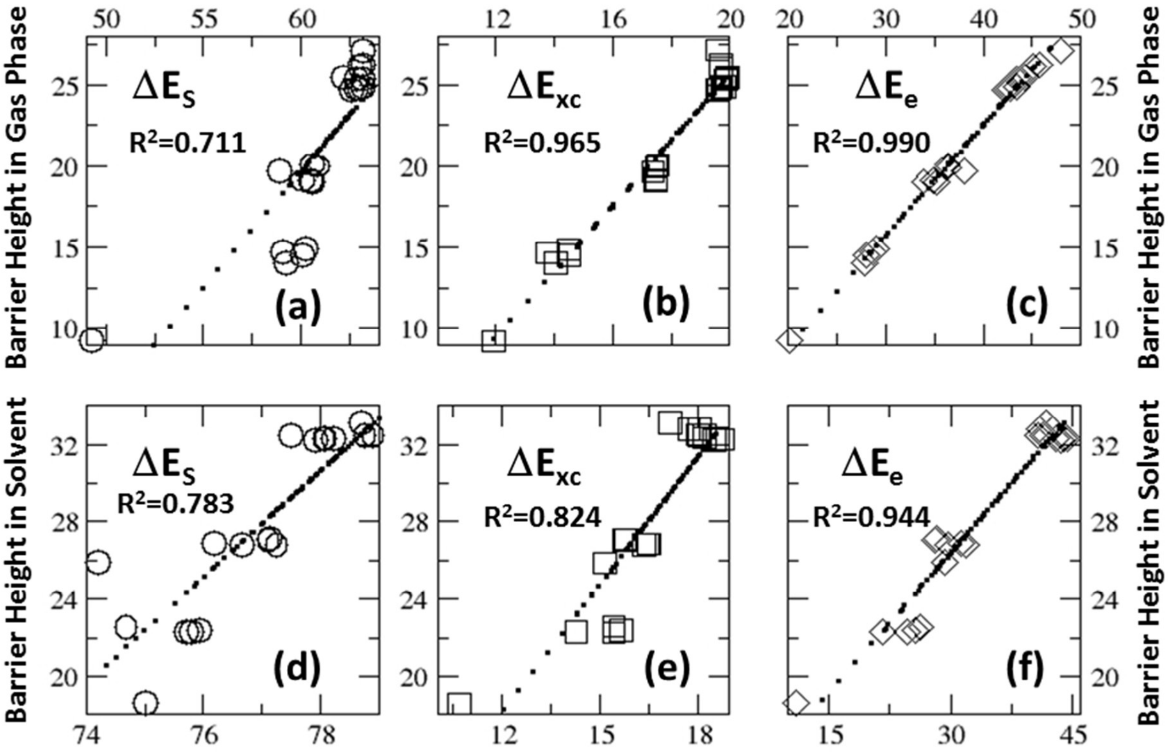

Figure 2. Strong linear correlations for 21 bimolecular nucleophilic substitution reactions between the computed barrier height and three individual energy components: (a,d) fitting with the steric energy component, ΔE_S; (b,e) fitting with exchange-correlation components ΔE_{xc}; and (c,f) fitting with the electrostatic term ΔE_e and steric energy components ΔE_s in both (a-c) gas and (d-f) solvent phases.

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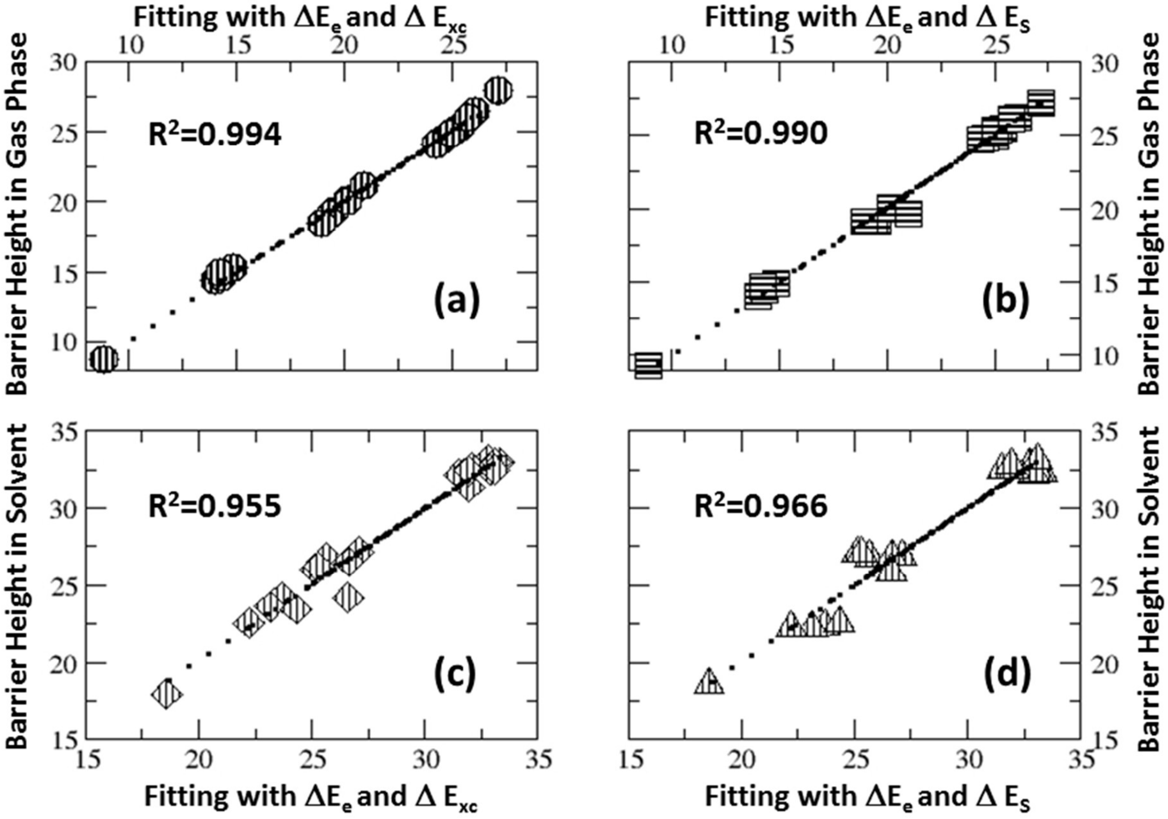

Figure 3. Strong linear correlations for 21 bimolecular nucleophilic substitution reactions between the computed barrier height and two-variable fitting: (a,c) with both electrostatic ΔE_e and exchange-correlation components ΔE_{xc} and (b,d): two-term fitting with both electrostatic ΔE_e and steric energy components ΔE_s in both (a-b) gas and (c-d) solvent phases.

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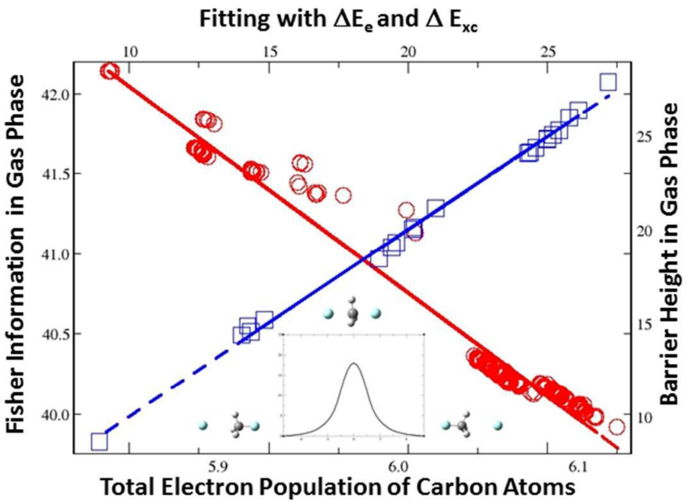
TOC Graphic



Strong linear correlations were unveiled between barrier heights of bimolecular nucleophilic substitution (S_N2) reactions and quantities from the information-theoretic approach.

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