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Are the Local Electrophilicity Descriptors Reliable Indicators of Global Electrophilicity Trends?

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Density functional theory based global and local electrophilicity descriptors are used to study the reliability of local electrophilicity values of the strongest electrophilic sites in generating global intermolecular electrophilicity trends. The evaluated values on 15 different organic chlorides show that, for systems having more than one comparatively strong electrophilic site, the local electrophilicity value of the strongest site does not produce a reliable global intermolecular electrophilicity trend. But for systems having one distinctly strong electrophilic site it does. The analytical explanation in favor of the above observation is also provided. Thus, what was argued in an earlier study (Roy, R. K. *J. Phys. Chem.* **2004**, *108*, 4934) is established strongly by numerical demonstrations as well as analytical reasoning in the present one.

I. Introduction

Conceptual density functional theory (DFT)[1,2] has given birth to several global and local reactivity descriptors in the past two decades.[3−10] These global reactivity descriptors are used to predict intermolecular reactivity trends, whereas local descriptors have potential use in predicting intramolecular reactivity trends (i.e., site selectivity). Prompted by a qualitative suggestion of Maynard et al.,[11] a new definition of global electrophilicity was defined by Parr et al.[12] as

$$w = \frac{\mu^2}{2\eta} \tag{1}$$

Here, *w* can be thought of as the electrophilic power of the concerned chemical species because of its analogy to that of the equation of power (i.e., Power = V^2/R of classical electricity, where *V* and *R* represent the potential difference and resistance, respectively). In eq 1, μ is the "chemical potential" and η is "global chemical hardness" of the concerned chemical species.

A more broad and very general local electrophilicity indicator has been proposed by Chattaraj et al.,[13] which can be considered as a local manifestation of *w*. This new local reactivity descriptor is named as "philicity" index and claims to be very reliable in predicting intermolecular electrophilicity (or nucleophilicity) trends between two molecules when they react with each other. The argument was that the global trend of electrophilicity (or nucleophilicity) originates from the local behavior of the molecules, or precisely of that atomic site which is most prone to electrophilic (or nucleophilic) attack. However, one of the present authors, in a subsequent study,[14] has argued that the above argument is logical for systems having only one distinctly strong site (electrophilic or nucleophilic) but does not hold true for systems having more than one site of comparable strength.

In the present study a thorough investigation is carried out to justify the above argument. This is done both by numerical demonstrations as well as by analytical explanation using 15 different organic chlorides. The chlorides are chosen in such a way that they have required structural features relevant for the present study and so have been divided into several subgroups, keeping in mind the structural variation (for details see section IVA).

This article is organized as follows: a brief theoretical background of global and local electrophilicity indicators is presented in different subsections of section II. The computational methods used are elaborated in section III. In section IVA the generated electrophilicity trends, in terms of the global and local electrophilicity values of the chosen systems (along with their subgroupings), are discussed. Situations where local reactivity descriptors can reflect the global reactivity trends, as well as the situations where it cannot, are established through formal analysis in section IVB. Finally, in the concluding section (i.e., section V), the net outcome of the work is summarized and the direction of future study is pointed out.

II. Global Reactivity Descriptors

In the equation of global electrophilicity (eq 1) the analytical and operational definitions of μ and η are given as follows:[3]

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{\nu(\bar{r})} \cong -\frac{(\mathrm{IP} + \mathrm{EA})}{2} \tag{2}$$

$$\eta = \left(\frac{\partial^2 E}{\partial N^2}\right)_{\nu(\bar{r})} \cong \frac{(\mathrm{IP} - \mathrm{EA})}{2} \tag{3}$$

The notations IP, EA, and $\nu(\bar{r})$ used in eqs 2 and 3 represent the first vertical ionization potential, first vertical electron affinity, and the external potential (i.e., the potential due to the positions of the nuclei plus applied external field, if any) at position $\bar{r}$, respectively. The inverse of η is known as global softness, *S*, and is represented as

$$S = \frac{1}{2\eta} \cong \frac{1}{(\mathrm{IP} - \mathrm{EA})} \tag{4}$$

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A. The Philicity Index. The local (or site) reactivity (selectivity) of a chemical species is represented by local reactivity descriptors. One such descriptor is Fukui function index and is defined as below:[6]

$$f(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial N}\right)_{\nu(\bar{r})} = \left(\frac{\partial \mu}{\partial \nu(\bar{r})}\right)_N \tag{5}$$

Here, N and $\rho(\bar{r})$ represent, respectively, the number of electrons and the electron density at position $\bar{r}$ of the chemical species. It is named so because of its conceptual similarity with Fukui's frontier molecular orbital theory.[15] After taking care of the discontinuities in the $f(\bar{r})$ versus N plot, the "condensed-to-atom" approximations of $f(\bar{r})$, when multiplied by global softness (S), provide three local softness values represented by[7]

$$s_k^+(\bar{r}) = [p_k(N+1) - p_k(N)]S = f_k^+ S \tag{6a}$$

$$s_k^-(\bar{r}) = [p_k(N) - p_k(N-1)]S = f_k^- S \tag{6b}$$

$$s_k^0(\bar{r}) = \frac{1}{2}[p_k(N+1) - p_k(N-1)]S = f_k^0 S \tag{6c}$$

Here, in eqs 6a−c, $p_k(N)$, $p_k(N+1)$, and $p_k(N-1)$ represent the condensed electronic populations on atom 'k' for neutral, anionic and cationic systems, respectively. So, s_k^+, s_k^-, and s_k^0 represent the condensed local softness values of atom 'k' toward nucleophilic, electrophilic, and radical attack on it, respectively. We were able to come to eqs 6a−c because of following analytical relations:

$$s(\bar{r}) = \left(\frac{\partial \rho(\bar{r})}{\partial \mu}\right)_{\nu(\bar{r})} = \left(\frac{\partial \rho(\bar{r})}{\partial N}\right)_{\nu(\bar{r})}\left(\frac{\partial N}{\partial \mu}\right)_{\nu(\bar{r})} = f(\bar{r})S \tag{7}$$

Equations 6a−c can be represented by a generalized expression as follows:

$$s_k^{\alpha} = f_k^{\alpha} S \tag{8}$$

where, α is $+$, $-$, and 0.

Chattaraj et al.[13] proposed the existence of a local electrophilicity index $w(\bar{r})$ that varies from point to point in an atom, molecule, ion, or solid and is defined as

$$w = \int w(\bar{r})\, d\,\bar{r} \tag{9}$$

where, w is the global electrophilicity index as proposed by Parr et al.[12]

By using the normalization condition of $f(\bar{r})$ [i.e., $\int f(\bar{r})\, d\bar{r} = 1$], the best choice of $w(\bar{r})$ was proposed to be

$$w = w\int f(\bar{r})\, \mathrm{d}\bar{r} = \int w f(\bar{r})\, \mathrm{d}\bar{r} = \int w(\bar{r})\, \mathrm{d}\bar{r} \tag{10a}$$

where

$$w(\bar{r}) = w f(\bar{r}) \tag{10b}$$

To take care of all types of reactions, three different forms of $w(\bar{r})$ were defined as

$$w^{\alpha}(\bar{r}) = w f^{\alpha}(\bar{r}) \tag{11}$$

where, $\alpha = +, -,$ and 0 for nucleophilic, electrophilic, and radical attacks, respectively. As $w^{\alpha}(\bar{r})$ takes care of all types of reactions [this is because in the presence of a physicochemical perturbation some particular atom (or atoms) is (are) better equipped toward electrophilic (or nucleophilic) attack on it], it is more general and is named the "philicity" index. The corresponding condensed-to-atom forms of the philicity index for atom k can be written as

$$w_k^{\alpha} = w f_k^{\alpha} \tag{12}$$

B. Relative Electrophilicity and Relative Nucleophilicity. To find out the most preferable site (or atom) to be attacked by a nucleophile (or electrophile), Roy *et* al.[8] proposed two new reactivity descriptors. These are defined as follows. (i) Relative electrophilicity $= s_k^+/s_k^-$, the highest value of which represents the most preferred atom in a molecule to be attacked by a nucleophile. (ii) Relative nucleophilicity $= s_k^-/s_k^+$, the highest value of which represents the most preferred atom in a molecule to be attacked by an electrophile.

The argument in favor of the above proposition is that the individual values of s_k^+ and s_k^- are strongly influenced by the basis set and correlation effects. But the ratios of s_k^+ and s_k^-, involving two differences of electron densities of systems differing by one in their number of electrons at constant nuclear framework, are expected to be less sensitive to the basis set and correlation effects. Several of the subsequent studies[16−21] established the superiority of these newly proposed descriptors over those of s_k^+ and s_k^-. It should be mentioned here that in some studies few exceptions and inadequacies have been reported regarding the reliability of s_k^+/s_k^- and s_k^-/s_k^+ in predicting intramolecular[22] and intermolecular[23] reactivity trends. Tishchenko et al.[22] reported the failure of s_k^-/s_k^+ in predicting a preferable site of protonation in halogen-substituted phenols. But whether this failure is due to inadequacy in s_k^-/s_k^+ or in the charge evaluation scheme used (which is electrostatic potential derived charge here) to evaluate s_k^-/s_k^+ (and other local reactivity descriptors) is not studied thoroughly. Roy et al.[17−19,21] have demonstrated clearly (both using numerical demonstrations and analytical reasoning) that the best results are obtained when s_k^+/s_k^- and s_k^-/s_k^+ are evaluated through Hirshfeld population analysis (HPA). Olah et al.[23] claimed that s_k^+/s_k^- and s_k^-/s_k^+ are found not to have any special advantage over other local reactivity descriptors. The cause of failure of s_k^+/s_k^- in predicting the electrophilicity order of the B atom in BH_3, BCl_3, and BF_3 (in the study of Olah et al.) is probably due to the presence of the Jahn−Teller effect in the BH_3 molecule, which affects the evaluation of s_k^+/s_k^-. Fuentealba and Contreras[24] have raised questions regarding the lack of universality of s_k^+/s_k^- and s_k^-/s_k^+ because these two reactivity descriptors are applicable only to those sites which have high s_k^+ (or s_k^-) values. But this lack of universality does not deter these two descriptors to be used to find out the strongest electrophilic (or nucleophilic) site because, by initial screening, insignificant sites [i.e., sites which have low s_k^+ (or s_k^-) values] are eliminated. Apart from the objections just mentioned, no question has been raised until now regarding the conceptual validity of s_k^+/s_k^- and s_k^+/s_k^-.

III. Computational Details

The chemical systems chosen in the present study (15 in all) are aliphatic chlorides. In some of these systems there are aromatic moieties (i.e., Ph rings), and in some cases double or triple bonds (i.e., unsaturation) are present. The presence of a Ph ring and unsaturation creates more than one strong electrophilic site (i.e., atoms) and thus the systems become ideal to verify the doubt raised in the previous study.[14] For the convenience of study, these systems are then divided into seven different series (see section IV). It is clear that some systems are present in more than one series. This is done keeping in mind the structural variation of the chlorides in a particular series so that the difference in the electrophilicity trends among the members of individual series could be clearly established.

The geometries were initially optimized at the semiempirical level using Chem3D program system,[25] followed by re-optimization at the RHF/6-31G(d,p) level using Gaussian 98.[26] Also, the geometries are re-optimized at the BLYP/dnp level using the DMOL^3 program package.[27] The "dnp" level basis set is of double-numeric quality (i.e., approximately two atomic orbitals for each one occupied in the free atom) augmented with polarization functions (i.e., functions with angular momentum one higher than that of the highest occupied orbital in the free atom). The dnp basis set is as included in DMOL^3 program package.

The global electrophilicity values were evaluated using eq 1, and the operational forms of μ and η are as in eqs 2 and 3, respectively. The local philicity indices of the individual atoms (i.e., w_k^α) are computed through eq 12, in which the f_k^α part comes from eq 6a. The charge values were evaluated by Hirshfeld population analysis (HPA)[28] using the DMOL^3 program and by Mulliken population analysis (MPA)[29] using the Gaussian program. The conceptual advantage of HPA over MPA is discussed in detail in refs 17−21. To enhance the reliability, the MPA-based charges are evaluated using a new technique adopted in ref 20. In this new technique the charges on the H atoms are summed on the heavy atom (i.e., C atom here) to which they are bonded. The charges evaluated in this way are found to be more reliable than charges evaluated in the normal "condensed-to-individual-atom" way.[7]

IV. Results and Discussion

A. Observed Intermolecular Electrophilicity Trends. Let us first do a comparative analysis of the trends of electrophilicity as expected from evaluation of various qualitative parameters (e.g., electronegativity, $\pm I$ and $\pm R$ effect, presence of unsaturation, etc.) with those generated by the global (w) and local (w_k^+) electrophilicity values.

Series I. In this series the systems were chosen in such a way that the first system contains an aromatic group, the second and third systems contain unsaturation, and the fourth system is a saturated chloride. The systems are

$$C_6H_5CH_2Cl \qquad (i)$$

$$CH{\equiv}C{-}CH_2Cl \qquad (ii)$$

$$CH_2{=}CH{-}CH_2Cl \qquad (iii)$$

$$CH_3CH_2Cl \qquad (iv)$$

(The numbers in parentheses, e.g., *i*, *ii*, *iii*, *iv*, refer the system for the convenience of future discussion). Here, the electrophilicity of the first system should be highest because the carbon atom adjacent to a Ph ring can easily accommodate an extra electron (if situation warranted, for example, when a nucleophile approaches it) through extended resonance. The second system (i.e., $CH{\equiv}C{-}CH_2Cl$) can also accommodate an extra electron because of the presence of unsaturation (i.e., triple bond), but is less effective than the Ph ring. The third one contains the allyl group and so has the ability to accommodate an extra electron due to the presence of a C=C bond, but is less effective than system *i* or *ii*. The system that is least effective (or not effective at all) in the series in accommodating an extra electron is ethyl chloride (i.e., *iv*). This is because there is no unsaturation in the system to disperse the negative charge. So, the electrophilicity trend generated by these systems should be as follows:

$$C_6H_5CH_2Cl > CH{\equiv}C{-}CH_2Cl > CH_2{=}CH{-}CH_2Cl > CH_3CH_2Cl$$

TABLE 1: Global (w) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

chloride compounds	atomic centers	methods[b]			
		MPA/6-31G(d,p)		HPA/dnp	
		w	w_k^+	w	w_k^+
i	C_{C-Cl}	0.0398	0.0043	0.0633	0.0038
ii	C_{C-Cl}	0.0266	0.0076	0.0589	0.0073
iii	C_{C-Cl}	0.0249	0.0027	0.0577	0.0055
iv	C_{C-Cl}	0.0206	0.0059	0.0451	0.0062

[a] Here *i*, *ii*, *iii*, and *iv* represent the chloride systems belonging to series I (see the text). Values are in atomic units. [b] Because the systems chosen here have more than one comparatively strong electrophilic site (i.e., for systems *i*, *ii*, *iii*) the w values reproduce the expected intermolecular electrophilicity trend but w_k^+ values (of C_{C-Cl}) do not (true for both MPA/6-31G(d,p) and HPA/dnp methods).

The observed electrophilicity trend from Table 1 clearly shows that only w (i.e., the global electrophilicity descriptor) generates the expected trend. The w_k^+ values of the C_{C-Cl} (which is supposed to be the strongest electrophilic center) are unable to generate the expected trend. The failure of w_k^+ values to generate the expected global electrophilicity trend vis-à-vis the success of w in doing so could be attributed to the presence of more than one strong electrophilic site in systems *i*, *ii*, and *iii* (i.e., the Ph ring carbon atoms in *i* and the C atoms attached to the double and triple bond in systems *ii* and *iii*, respectively). It is worth mentioning here that although the numerical values differ by very small amounts (varying in the second or third decimal places), they are not negligible when we consider the fact that the values are in atomic units and 1 au = 27.2114 eV (in ref 12, Parr et al. have reported the values in eV).

Series II. The systems chosen in this series differ by the number of branchings as well as the position of branching (i.e., α− and β−). These are

$$CH_3CH_2CH_2CH_2Cl \qquad (v)$$

$$CH_3CH(CH_3)CH_2Cl \qquad (vi)$$

$$CH_3CH_2CH(CH_3)Cl \qquad (vii)$$

$$CH_3C(CH_3)_2Cl \qquad (viii)$$

The major contribution to the overall electrophilicity will come from C_{C-Cl} as there is no other strong electrophilic atom in these systems. Now, if the $+I$ effect of the $-CH_3$ groups on the C_{C-Cl}, the distance between $-CH_3$ groups and C_{C-Cl}, and the numbers of such $-CH_3$ groups are considered together, the intermolecular electrophilicity trend in the series should be as follows:

$$CH_3CH_2CH_2CH_2Cl > CH_3CH(CH_3)CH_2Cl > CH_3CH_2CH(CH_3)Cl > CH_3C(CH_3)_2Cl$$

The w_k^+ values generated by MPA/6-31G(d,p) reproduce the expected trend, whereas those generated by HPA/dnp show the trends as $v \approx vi > vii \approx viii$ (see Table 2). When we consider

TABLE 2: Global (*w*) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

		Methods[b]			
		MPA/6-31G(d,p)		HPA/dnp	
chloride compounds	atomic centers	w	w_k^+	w	w_k^+
v	C_{C-Cl}	0.0199	0.0058	0.0428	0.0044
vi	C_{C-Cl}	0.0202	0.0057	0.0450	0.0044
vii	C_{C-Cl}	0.0203	0.0025	0.0425	0.0036
viii	C_{C-Cl}	0.0216	-0.0009	0.0476	0.0036

[a] Here *v*, *vi*, *vii*, and *viii* represent the chloride systems belonging to series II (see the text). Values are in atomic units. [b] Because the systems chosen here have only one strong electrophilic site (i.e., C_{C-Cl}), the w_k^+ values (of C_{C-Cl}) reproduce the expected (from ±*I* effects, electronegativity, etc.) intermolecular electrophilicity trend. However, *w* values do not (true for both MPA/6-31G(d,p) and HPA/dnp methods).

TABLE 3: Global (*w*) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

		methods[b]			
		MPA/6-31G(d,p)		HPA/dnp	
chloride compounds	atomic centers	w	w_k^+	w	w_k^+
i	C_{C-Cl}	0.0398	0.0043	0.0633	0.0038
ix	C_{C-Cl}	0.0230	0.0003	0.0551	0.0028

[a] Here 1 and 9 represent the chloride systems belonging to series III (see the text). Values are in atomic units. [b] Here, although the Ph ring contains some highly electrophilic C atoms, it is common to both the systems 1 and 9. Thus, both *w* and w_k^+ values (of C_{C-Cl}) reproduce the expected intermolecular electrophilicity trend [true for both MPA/6-31G(d,p) and HPA/dnp methods] although they differ by one intervening $-CH_2-$ moiety (present in system *ix*) between C_{C-Cl} and the Ph ring.

TABLE 4: Global (*w*) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

		methods[b]			
		MPA/6-31G(d,p)		HPA/dnp	
chloride compounds	atomic centers	w	w_k^+	w	w_k^+
ii	C_{C-Cl}	0.0266	0.0076	0.0589	0.0073
x	C_{C-Cl}	0.0164	0.0044	0.0432	0.0042

[a] Here *ii* and *x* represent the chloride systems belonging to series IV (see the text). Values are in atomic units. [b] Here, although the $CH{\equiv}C-$ moiety contains a highly electrophilic C atom, it is common to both systems *ii* and *x*. Thus, both *w* and w_k^+ values (of C_{C-Cl}) reproduce the expected intermolecular electrophilicity trend [true for both MPA/6-31G(d,p) and HPA/dnp methods] although they differ by one intervening $-CH_2-$ moiety (present in system *x*) between the C_{C-Cl} and $CH{\equiv}C-$ moieties.

TABLE 5: Global (*w*) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

		methods			
		MPA/6-31G(d,p)		HPA/dnp	
chloride compounds	atomic centers	w	w_k^+	w	w_k^+
iii	C_{C-Cl}	0.0249	0.0027	0.0577	0.0055
xi	C_{C-Cl}	0.0121	0.0033	0.0452	0.0040

[a] Here *iii* and *xi* represent the chloride systems belonging to series V (see the text). Values are in atomic units. [b] Here, although the $-CH_2{=}CH-$ moiety contains a highly electrophilic C atom, it is common to both the systems *iii* and *xi*. Thus, both *w* and w_k^+ values (of C_{C-Cl}) reproduce the expected intermolecular electrophilicity trend [for *w* true in both MPA/6-31G(d,p) and HPA/dnp methods, and for w_k^+ true only in the HPA/dnp method] although they differ by one intervening $-CH_2-$ moiety (present in system *xi*) between C_{C-Cl} and $-CH_2{=}CH-$ moieties.

the position of branching in *vi* (which is absent in *v*) and of an extra branching in *viii* (than in *vii*), the trend generated by HPA/dnp may not look that problematic (i.e., the extra +*I* effect of the $-CH_3$ group in *vi* and in *viii* differ negligibly compared to those present in *v* and *vii*, respectively). More discussion regarding the observed trend in this series is done at the end of subsection IVB.

Series III, IV, and V. The systems chosen in a particular series in this case differ from each other by the presence of an extra intervening $-CH_2-$ moiety. The presence of this extra $-CH_2-$ moiety lowers the electrophilicity of the C_{C-Cl} and thus causes the difference in global electrophilicity between the members within a series (this is true for all three series considered here). The expected trends in the three series are as follows:

Series III: $C_6H_5CH_2Cl$ (*i*) > $C_6H_5CH_2CH_2Cl$ (*ix*)

Series IV: $CH{\equiv}C-CH_2Cl$ (*ii*) > $CH{\equiv}C-CH_2CH_2Cl$ (*x*)

Series V: $CH_2{=}CH-CH_2Cl$ (*iii*) > $CH_2{=}CH-CH_2CH_2Cl$ (*xi*)

The evaluated *w* and w_k^+ values (of C_{C-Cl}) (from Tables 3, 4, and 5) show that the intermolecular electrophilicity trends are as expected in series III and IV. For series V, although the *w* values generate the expected trend, w_k^+ values fail when evaluated by MPA/6-31G(d,p). However, w_k^+ values generate the expected trend when evaluated by the HPA/dnp method.

Series VI and VII. The systems within a particular series differ from each other in the position of the Cl atom (i.e., α- or β-) with respect to the functional group. In the first system for both the series, the Cl atom is attached to the α carbon atom, i.e., the carbon atom present near the functional group. In the second system the Cl atom is attached to the β carbon. So the dispersion of the partial positive charge (i.e., δ+) of C_{C-Cl} is difficult in the first system (for both the series VI and VII). This could be attributed to the presence of strong electron withdrawing groups (i.e., an ester and a carbonyl group in series VI and VII, respectively) adjacent to C_{C-Cl}. Thus, in both series, the first system is expected to be more electrophilic than the second one. So, the expected electrophilicity trend within a series should be as follows:

Series VI: $CH_3CH(Cl)COOC_2H_5$ (*xii*) > $ClCH_2CH_2COOC_2H_5$ (*xiii*)

Series VII: $CH_3CH(Cl)COC_2H_5$ (*xiv*) > $ClCH_2CH_2COC_2H_5$ (*xv*)

From Tables 6 and 7 we see that the values of *w*, generated by both MPA/6-31G(d,p) and HPA/dnp methods, reproduce the expected intermolecular electrophilicity trend (in a particular series). But the w_k^+ values of C_{C-Cl} generate the expected trend when evaluated by HPA/dnp but not by MPA/6-31G(d,p).

B. Explanation of the Observed Intermolecular Electrophilicity Trends. A thorough analysis of the trends generated by the seven series given above clearly demonstrates that for those series in which the systems have more than one comparatively strong electrophilic site, comparison of the w_k^+ value of the strongest site (i.e., C_{C-Cl} in the present study) will not always generate the expected intermolecular electrophilicity trend.

Analytically this observation can be explained as follows. For any two systems A and B, let the global electrophilicity

TABLE 6: Global (w) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

chloride compounds	atomic centers	methods MPA/6-31G(d,p) w	methods MPA/6-31G(d,p) w_k^+	methods HPA/dnp w	methods HPA/dnp w_k^+
xii	C_{C-Cl}	0.0389	0.0019	0.0611	0.0041
xiii	C_{C-Cl}	0.0193	0.0048	0.0522	0.0035

[a] Here *xii* and *xiii* represent the chloride systems belonging to series VI (see the text). Values are in atomic units. [b] Here, although the $-COOC_2H_5$ moiety contains a highly electrophilic C atom ($C_{C=O}$), it is common to both the systems *xii* and *xiii*. Thus, both w and w_k^+ values (of C_{C-Cl}) reproduce the expected intermolecular electrophilicity trend [for w true in both MPA/6-31G(d,p) and HPA/dnp methods, and for w_k^+ true only in HPA/dnp method] although they differ by one intervening $-CH_2-$ moiety (present in system *xiii*) between the C_{C-Cl} and $-COOC_2H_5$ moieties.

TABLE 7: Global (w) and Local (w_k^+ of C_{C-Cl}) Electrophilicity Values of the Systems Studied[a]

chloride compounds	atomic centers	methods MPA/6-31G(d,p) w	methods MPA/6-31G(d,p) w_k^+	methods HPA/dnp w	methods HPA/dnp w_k^+
xiv	C_{C-Cl}	0.0340	0.0013	0.0661	0.0044
xv	C_{C-Cl}	0.0139	0.0034	0.0526	0.0035

[a] Here *xiv* and *xv* represent the chloride systems belonging to series VII (see the text). Values are in atomic units. [b] Here, although the $-COC_2H_5$ moiety contains a highly electrophilic C atom ($C_{C=O}$), it is common to both systems *xiv* and *xv*. Thus, both w and w_k^+ values (of C_{C-Cl}) reproduce the expected intermolecular electrophilicity trend [for w true in both MPA/6-31G(d,p) and HPA/dnp methods, and for w_k^+ true only in HPA/dnp method] although they differ by one intervening $-CH_2-$ moiety (present in system *xv*) between the C_{C-Cl} and $-COC_2H_5$ moieties.

values are represented by W^A and W^B, respectively. Also, let W_i^A and W_j^B represent the philicity of the individual atoms in systems A and B, respectively. If the strongest sites (either electrophilic or nucleophilic) are k (i.e., $i = k$) and l (i.e., $j = l$), then the corresponding philicity values are represented by W_k^A and W_l^B, respectively. Then we can write (from eq 12)

$$W_i^A = W^A f_i^A \tag{13}$$

$$W_j^B = W^B f_j^B \tag{14}$$

Also,

$$\sum_{i=1}^{M} W_i^A = W^A \sum_{i=1}^{M} f_i^A = W^A \quad \left(\text{as} \sum_{i=1}^{M} f_i^A = 1\right) \tag{15}$$

$$\sum_{j=1}^{N} W_j^B = W^B \sum_{j=1}^{N} f_j^B = W^B \quad \left(\text{as} \sum_{j=1}^{N} f_j^B = 1\right) \tag{16}$$

Here, M and N represent the total number of atoms present in systems A and B, respectively.

Now suppose that $W^A > W^B$, i.e., the global electrophilicity (or nucleophilicity) of system A is higher than that of B. From eqs 15 and 16 it is obvious that in such a situation W_k^A (i.e., the philicity value of the strongest center in species A) may or may not be greater than W_l^B (i.e., the philicity value of the strongest center in species B). Only if the corresponding strongest atom contribution is much greater than any other atoms (i.e., $W_k^A \gg W_i^A$, where $i \neq k$, and $W_l^B \gg W_j^B$, where $j \neq l$) will W_k^A be greater than W_l^B and we will get the expected intermolecular electrophilicity or (nucleophilicity) trends from the philicity index values of the corresponding strongest atoms. But if several W_i^A values make comparatively high contribution to the overall W^A, whereas only one particular W_j^B (which is W_l^B in this case) contributes distinctly very high to the overall W^B, then, although $W^A > W^B$, the highest W_i^A may not be greater than the highest W_j^B. In such a situation we will not get the expected intermolecular electrophilicity or (nucleophilicity) trend from the philicity index values of the corresponding strongest atoms.

It is obvious from eqs 13 and 14 that if $W^A > W^B$ and $f_i^A > f_j^B$, then $W_i^A > W_j^B$. In the present study we will see that in series I, although global electrophilicity (i.e., W) values reproduce the expected trend, the local electrophilicity values of the strongest electrophilic center (i.e., $W_{C_{C-Cl}}$) fail. This indirectly means that f_i values (and also the s_i values) are unable to generate the correct trend. The failure of local softness (and so Fukui function) to generate the expected intermolecular electrophilicity (or nucleophilicity) trend is not new. It was argued that[8,30] as local softness (and also Fukui function) are frontier orbital electron density based reactivity descriptors, they are best suited to explain intramolecular reactivity (i.e., site selectivity). To explain intermolecular reactivity, local hardness was found to be more reliable. The above argument is based on a suggestion by Klopman who, in a classic paper,[31] showed (with the help of polyelectronic perturbation theory) that hard−hard interactions are charge controlled and soft−soft interactions are orbital controlled. So, at the initial stage of a reaction (either nucleophilic or electrophilic), when two reagents approach each other, charge will play a major role in determining the reactivity, i.e., intermolecular reactivity will better be explained by the hardness-based reactivity descriptor. Once the reaction starts, frontier orbitals play the major role in determining the reactivity of a particular site (or atom), i.e., intramolecular reactivity will better be explained by softness-based reactivity descriptors. This is why philicity indices fail to generate reliable intermolecular reactivity trends although they are conceptually superior to local softness or Fukui function indices (because philicity indices take care of the global effect by global electrophilicity to some extent, see eq 12).

On the basis of the analytical reasoning just stated above we can explain why in series I the w_k^+ (which are evaluated using frontier orbital electron density, see eq 12) values of the C_{C-Cl} atoms are unable to generate the expected intermolecular electrophilicity trend although the w (a hardness-based quantity) values can do that. The presence of more than one comparatively strong electrophilic sites in the Ph ring (system *i*) and on either end of C≡C (system *ii*) and C═C (system *iii*) bonds makes that happen as these sites also contribute significantly to the overall w. In series III, IV, and V the situation is simple as the number of strong electrophilic sites is same in both systems (within a particular series) except for the presence of one extra $-CH_2-$ moiety in one of them. That is why we see that the trends generated by w and w_k^+ (of C_{C-Cl}) are the same and as expected from other qualitative parameters. In series V, although the w_k^+ values of C_{C-Cl} generated by MPA/6-31G(d,p) are unable to produce the expected trend, this is corrected when generated by HPA/dnp. Also, in both the series VI and VII, the two systems differ by the presence of one intervening $-CH_2-$ moiety. This should cause the difference in $w_k{}^+$ values of C_{C-Cl} present in these two series. Although the w_k^+ values for $C_{C=O}$ (present in the $-COOC_2H_5$ group in series VI and in the $-COC_2H_5$ group in series VII) are also comparatively high, these are common to both the members in a particular series and thus expected to exert equal electronic effect on C_{C-Cl}. This can be the reason of expected intermolecular electrophilicity trends generated by w_k^+ values when evaluated by the HPA/dnp method (although the trends generated by MPA/6-31G(d,p)-based w_k^+ values fail to do that). The w values, evaluated by both MPA/6-31G(d,p) and HPA/dnp methods, reproduce the expected intermolecular electrophilicity trends in both the series VI and VII. Thus, although there are more than one strong electrophilic sites in series V, VI, and VII, the intermolecular electrophilicity trends generated by w_k^+ values of C_{C-Cl} (in the HPA/dnp method) are as expected because of the presence of an identical chemical environment in the rest of the molecule (except they differ by the presence of one $-CH_2-$ moiety). The systems belonging to series II have only one strong electrophilic site, and that is the C_{C-Cl}. Thus, the w_k^+ values of C_{C-Cl} produce the intermolecular electrophilicity trend as expected from other qualitative parameters (i.e., the $+I$ effect of the $-CH_3$ groups and their numbers and position). The fact that the values of w, generated by either of the two methods, are unable to produce the expected trend merely indicates that the present definition of global electrophilicity indicator is not the role model and has limitation in it (in ref 14 there are more examples where w could not produce reliable trends).

V. Conclusion

In the present study a particular aspect of reactivity is considered and that is the electrophilicity, which is an electronic factor. The overall reactivity, however, consists of electronic, energetic, and steric factors. The study shows that for systems having more than one comparatively strong electrophilic site, the philicity index of the strongest electrophilic atom k (i.e., w_k^+) will not generate reliable intermolecular electrophilicity trends in all types of chemical systems. The situations where it cannot (e.g., series I) as well as the situations where it can (series III, IV, V, VI, VIII by HPA/dnp method and series III and IV by MPA/6-31G(d,p) method) generate the intermolecular electrophilicity trends are discussed in detail. However, for systems having only one distinctly strong electrophilic site, w_k^+ will be more reliable (series II). This has been clearly demonstrated by numerical results and also supported by analytical reasoning. Thus, what was doubted in an earlier study[14] is established more strongly in the present one.

The present study also explains (eqs 13−16) why local softness-based reactivity descriptors are not reliable in generating intermolecular reactivity trends. Following the argument of Klopman (that hard−hard interactions are charge-controlled and soft−soft interactions are orbital-controlled),[31] and its extension by Langenaeker et al.[30] and Roy et al.[8] to explain the different stages of a chemical reaction, it is understood that reliable intermolecular reactivity trends can be generated by local hardness-based descriptors. Thus, although philicity indices are superior to local softness or Fukui function (because of the "global electrophilicity" part in the definition, eq 12), they are not reliable in generating an intermolecular reactivity sequence. Local softness (and so Fukui function) will be more trustworthy in generating an intramolecular reactivity sequence (i.e., site selectivity) because these are based on frontier orbital electron density.

Finally, from the "power" analogy, one would expect that when there are two electrophilic centers in the same molecule, the overall electrophilicity would behave in the way resistances behave in a parallel circuit; i.e., reciprocals would add to give the reciprocal of the overall. A thorough investigation in this direction is sought.

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