On the Reliability of Global and Local Electrophilicity Descriptors

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Received: December 28, 2003; In Final Form: March 30, 2004

The global electrophilicity index w (as defined by Parr et al. *J. Am. Chem. Soc.* **1999**, *121*, 1992) and local "philicity" index, w_k^α (as defined by Chattaraj et al. *J. Phys. Chem. A* **2003**, *107*, 4973) of some carbonyl compounds are evaluated on the basis of Mulliken population analysis (MPA) and Hirshfeld population analysis (HPA) schemes. It is observed that the local electrophilicity indices (i.e., w_k^+), extracted from both HPA and MPA based charge, produce reliable intermolecular electrophilicity trends except in one case each. However, the reliability is lost in some cases when w is used. It is also shown both through numerical demonstrations and analytical proof that for generating intramolecular reactivity trends "philicity" index does not provide any extra reliability over local softness or Fukui function values. "Relative electrophilicity" and "relative nucleophilicity", as defined by Roy et al. (*J. Phys. Chem. A* **1998**, *102*, 3746), generate the most reliable intramolecular reactivity (i.e., site selectivity) sequences.

1. Introduction

In the last two decades, several global and local reactivity descriptors, based on density functional theory (DFT), have been proposed. Prominent among those are global hardness and softness,[1] local hardness,[2,3] local softness[3] and Fukui function,[4] and the corresponding condensed forms,[5] "relative electrophilicity" and "relative nucleophilicity",[6] "global electrophilicity",[7] and most recently the "philicity" index.[8] Although the global reactivity descriptors are supposed to provide intermolecular reactivity trends, the local counterpart generates the intramolecular reactivity sequence or site selectivity of an individual chemical system.

In a recent article, Parr et al.[7] have proposed a new definition of global electrophilicity, which may be regarded as a quantitative formulation of the model of Maynard et al.[9] A successful application of this newly defined global reactivity descriptor was made by Domingo et al.,[10] who could characterize quantitatively the global electrophilicity power of common diene/dienophile pairs used in Diels−Alder reactions. In a separate interesting study,[11] the same group has extended the concept of global electrophilicity index to define the local electrophilicity index and successfully explained the regioselectivity in Diels−Alder reactions. Solvent effects on this electrophilicity index were studied by Pérez et al.[12] In this context, it should also be mentioned that intermolecular reactivity trends in carbonyl compounds and organic acids was explained successfully by Krishnamurty and Pal[13] using "group softness" as the reactivity parameters. Chandrakumar and Pal[14,15] have proposed a model, based on the local hard and soft acid−base (HSAB)[16] principle, which explains the preferable site of attack considering both single site[14] and multiple site[15] interactions. For a detailed descritption and for the most authentic information on the development of all aspects of the hard and soft acid−base concept, the recent review by Geerlings et al.[17] is highly recommended.

Based on this global electrophilicity index as defined by Parr et al.,[7] very recently Chattaraj et al.[8] proposed a more broad and very general local reactivity descriptor. This is named as the "philicity" index, which encompass all types of reactions (i.e., electrophilic, nucleophilic, and radical reactions). This local philicity is promised to be a more powerful quantity than global reactivity indicators because the former contains the information of the later in addition to the site selectivity of a molecule toward electrophilic, nucleophilic, and radical attacks. Also, according to the argument of the authors, "because the global electrophiliciy of two different molecules are different, best sites of two different molecules for a given reaction can be explained only in terms of the 'philicity' and not Fukui function".

In the present study, an investigation is carried out on the relative reliability of the global electrophilicity index as proposed by Parr et al.[7] and the philicity index as proposed by Chattaraj et al.[8] in predicting intermolecular reactivity sequence. Also to generate intramolecular reactivity sequence (i.e., site selectivity), a comparative study of the "philicity" index with "relative electrophilicity" and "relative nucleophilicity", as proposed by Roy et al.,[6] is performed.

The article is structured as follows. A brief theoretical background of the global electrophilicity indicator, local philicity index, "relative electrophilicity", and "relative nucleophilicity" is presented in different subsections of section 2. The computational techniques and methodologies adopted and the details of the systems chosen are elaborated in section 3. In section 4, the results are presented and the generated trends in terms of the global and local reactivity descriptors are analyzed. An effort is made to explain the observed trends from the analytical expressions of the reactivity descriptors. Finally, in the concluding section (i.e., section 5), the net outcome of the work is summarized. Potential areas of future development are also pointed out.

2. Reactivity Descriptors

A. Global Electrophilicity Indicators. Prompted by a qualitative suggestion by Maynard et al.,[9] a new reactivity

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10.1021/jp038025i CCC: $27.50

indicator was proposed by Parr et al.[7] This new reactivity indicator is named the electrophilicity index (w) (or, better called the global electrophilicity) of the concerned chemical species and is defined as

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

The above notation and nomenclature is justified because of its analogy to that of the equation of Power = (V^2/R) of classical electricity (where, V and R represent the potential difference and resistance, respectively). Thus w can be thought of as the electrophilic power of the chemical species. In eq 1, μ is the chemical potential (i.e., negative of elctrophilicity[18]), and η is the global chemical hardness of the concerned chemical system. The analytical and operational definitions of μ and η are given as follows:[1]

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

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

The notations IP, EA, and $v(\bar{r})$, in eq 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

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

B. Local Philicity Index. The local (or site) reactivities (selectivities) of a chemical species are represented by local reactivity descriptors. One such descriptor is Fukui function indices (it is named so because of its conceptual similarity with Fukui's frontier molecular orbital theory[19]) proposed by Parr and Yang[4] as

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

here, N and $\rho(\bar{r})$ represent respectively the number of electrons and the electron density at position $\bar{r}$ of the chemical species. After taking care of the discontinuities in the $f(\bar{r})$ versus N plot, the "condensed to atom" approximations of FF indices, when multiplied by global softness (S), provide three local softness values which are represented by

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

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

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

In eq 6a–c, $p_k(N)$, $p_k(N+1)$, and $p_k(N-1)$ represent the condensed electronic populations of atom k for neutral, anionic and cationic systems, respectively. So, s_k^{+}, s_k^{-}, and s_k^{0}, represent the condensed local softness values indicating that atom k is more susceptible toward attack by a nucleophile, electrophile, and radical on it, respectively. We could come to eqs 6a–c because of the following analytical relation:

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

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

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

where $\alpha = +, -$, and 0.

One important property of Fukui function indices $f(\bar{r})$ is that they obey the normalization condition

$$\int f(\bar{r})\,\mathrm{d}\bar{r} = 1 \tag{9}$$

Chattaraj et al.[8] argued that the global trend (of electrophilicity and nucleophilicity) originates from the local behavior of the molecules or precisely of those atomic sites which are prone to electrophilic (or nucleophilic attack). So, they 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

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

here, w is the global electrophilicity index as proposed by Parr et al.[7]

By using the resolution of identity as represented by equation,[9] the best choice of $w(\bar{r})$ was proposed to be

$$w = w\int f(\bar{r})\,\mathrm{d}\bar{r} = \int wf(\bar{r})\,\mathrm{d}\bar{r} = \int w(\bar{r})\,\mathrm{d}\bar{r} \tag{11a}$$

where

$$w(\bar{r}) = wf(\bar{r}) \tag{11b}$$

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

$$w^{\alpha}(\bar{r}) = wf^{\alpha}(\bar{r}) \tag{12}$$

where $\alpha = +, -$, and 0 are for attacks by a nucleophile, electrophile, and radical, respectively. It is obvious that eq 12, when integrated, generates w, i.e., the global electrophilicity as defined by Parr et al.[7] This is true for $\alpha = +, -$, and 0. However, in the presence of a physicochemical perturbation, some particular atom (or atoms) is (are) better equipped toward electrophilic (or nucleophilic) attack on it. As $w^{\alpha}(\bar{r})$ takes care of all types of reactions, it is more general and is called the local philicity index. The corresponding condensed-to-atom forms of the philicity index for atom k can be written as

$$w_k^{\alpha} = wf_k^{\alpha} \tag{13}$$

C. 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.[6] proposed two new reactivity descriptors. These are defined as follows:

(i) Relative electrophilicity = s_k^{+}/s_k^{-} which represents the most preferred atom to be attacked by a nucleophile.

(ii) Relative nucleophilicity = s_k^{-}/s_k^{+}, which represents the most preferred atom to be attacked by an electrophile.

Arguments in favor of the proposition of these two new descriptors were given in detail in ref 6. Several of the

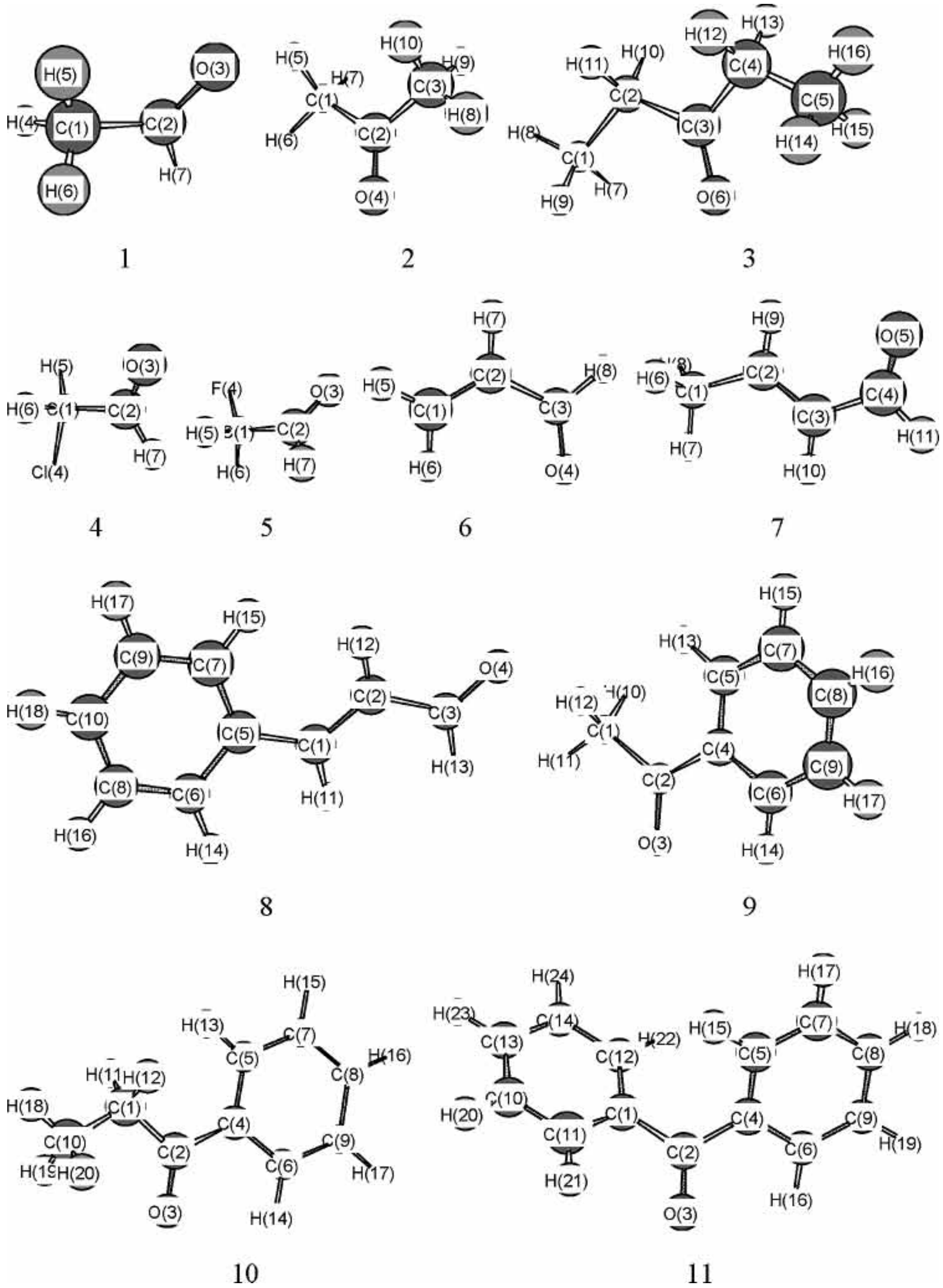

Figure 1. Carbonyl compounds (with numbering of atoms) chosen in the present study.

subsequent studies[20−25] established the superiority of these newly proposed descriptors over those of s_k^+ and s_k^- .

3. Methodology and Computational Details

Altogether 11 carbonyl compounds are chosen in the present study. These belong to aromatic and aliphatic and saturated and unsaturated category. For convenience of study these systems are then grouped into four homologous series as follows:

(i) CH_3CHO, CH_3COCH_3, $C_2H_5COC_2H_5$

(ii) CH_2ClCHO, CH_2FCHO

(iii) $CH_2=CHCHO$, $CH_3CH=CHCHO$, $C_6H_5CH=CHCHO$

(iv) $C_6H_5COCH_3$, $C_6H_5COC_2H_5$, $C_6H_5COC_6H_5$

Incidentally, Roy et al. used the same systems and similar groupings in ref 6. The picture of the systems along with the atom-numberings are demonstrated in Figure 1. These pictures are generated by the CHEM-3D program system.[26] The geometries were initially optimized at the semiempirical level using the same program followed by re-optimization at the BLYP/dnd and BLYP/dnp levels using the DMOL^3 program.[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 free atom). The dnd level basis set is similar to dnp basis except that no p functions are used on hydrogen. Both dnd and dnp are 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 eq 2 and 3. The local philicity indices of the individual atoms (i.e., w_k^α) are

TABLE 1: MPA and HPA Based w and w_k^+ Values of $C_{C=O}$ (i.e., carbon atom of the carbonyl group) of the Systems Studied[a]

		Methods		
			w_k^+	
carbonyl compounds	atomic centers	w	MPA/dnp	HPA/dnp
1	$C_{C=O}$	0.0525	0.0149	0.0156
2	$C_{C=O}$	0.0470	0.0082	0.0101
3	$C_{C=O}$	0.0449	0.0077	0.0090
4	$C_{C=O}$	0.0717	0.0136	0.0147
5	$C_{C=O}$	0.0600	0.0129	0.0148
6	$C_{C=O}$	0.0891	0.0117	0.0157
7	$C_{C=O}$	0.0760	0.0093	0.0120
8	$C_{C=O}$	0.0920	0.0061	0.0081
9	$C_{C=O}$	0.0731	0.0065	0.0070
10	$C_{C=O}$	0.0720	0.0068	0.0067
11	$C_{C=O}$	0.0788	0.0054	0.0052

[a] Here 1, 2, 3, etc. represent the systems (see Figure 1). Values are in atomic units.

computed through eq 13, in which the f_k^α part comes from eq 6a,b. The charge values were evaluated by both Hirshfeld population analysis (HPA)[28] and Mulliken population analysis (MPA)[29] to study the comparative performance between these two charge partitioning schemes. Superiority of HPA over that of MPA is discussed in details in refs 21−25.

4. Results and Discussion

A. Comparison of Intermolecular Electrophilicity Trends. *(i) Through Global Electrophilicity (w).* The carbonyl systems chosen in the present study should have the following intermolecular electrophilicity order within a homologous series:

(i) $CH_3CHO > CH_3COCH_3 > C_2H_5COC_2H_5$

(ii) $CH_2ClCHO > CH_2FCHO$

(iii) $CH_2 = CHCHO > CH_3CH = CHCHO > C_6H_5CH = CHCHO$

(iv) $C_6H_5COCH_3 > C_6H_5COC_2H_5 > C_6H_5COC_6H_5$

The above trend is based on the expected electrophilicity of only the $C_{C=O}$ (i.e., carbon atom of the carbonyl group) and considering a multitude of effects, e.g., inductive, resonance, polarizability, etc., exerted by other parts of the chemical system on it. The expected trends (as demonstrated above) could be reproduced by using the local hardness parameter as proposed by Langenaeker et al.[30] According to this proposition local hardness is defined through Thomas−Fermi−Dirac model of density functional theory as follows:

$$\eta_D^{TFD}(\bar{r}) = -\frac{V_{el}(\bar{r})}{2N} \qquad (14)$$

here, $V_{el}(\bar{r})$ is the electronic contribution to the molecular electrostatic potential at position $\bar{r}$ and N is the number of electrons of the concerned system.

In the present study, the global electrophilicity values (w) of all of the systems are evaluated by using both BLYP/dnd and BLYP/dnp methods. Because the generated values of w in both the methods produce similar trends, except that they differ numerically, the values only at the BLYP/dnp level are presented in Table 1. As the reactivity of a chemical system toward a reactant depends primarily on the reactivity of the most reactive center (i.e., the atom being attacked), a reasonable approximation to the comparison of the intermolecular electrophilicity would also be to compare the electrophilicity values of only the most reactive center of the systems in a homologous series. As in the studied systems, the most reactive (i.e., electrophilic) center is $C_{C=O}$ the evaluated w_k^α values (according to eq 13) of this center are also shown in Table 1 (for both MPA/dnp and HPA/dnp methods).

When the w values of the systems are compared, we observe the following global electrophilicity trends of the four homologous series:

(i) $CH_3CHO > CH_3COCH_3 > C_2H_5COC_2H_5$

(ii) $CH_2ClCHO > CH_2FCHO$

(iii) $C_6H_5CH = CHCHO > CH_2 = CHCHO > CH_3CH = CHCHO$

(iv) $C_6H_5COC_6H_5 > C_6H_5COCH_3 > C_6H_5COC_2H_5$

The above trends are observed for both the basis sets (i.e., for both dnd and dnp). Although, it is gratifying to note that the global electrophilicity trends are as expected in almost all of the four series, the unexpected outcome for the first inequalities in series (iii) and (iv) requires some plausible explanations. One reason for the unexpected outcome may be the fact that for extended systems (having more than one highly reactive centers) the global reactivity trend cannot be directly correlated to the reactivity of an individual reactive center (i.e., atom), even if it is the predominant one. Apart from $>C{=}O$, in both the cases, the Ph group is involved [in series (iii) this is the sole Ph group in $C_6H_5CH = CHCHO$ and in series (iv) an extra Ph-group in $C_6H_5COC_6H_5$ is present], which also has reasonably strong electrophilic sites (see Table 2) apart from $C_{C=O}$. The existence of these multiple strong electrophilic sites will contribute to the global electrophilicity, and as a result w values of these two systems are higher than those of the other members in the corresponding homologous series.

(ii) Through Philicity Index (w_k^+). The w_k^+ values of the $C_{C=O}$ and other important atoms (having w_k^+ values in the higher range), generated at BLYP/dnp level and based on both MPA and HPA, are also shown in Table 1. It is worth mentioning here that, although the numerical values differ by a very small amount (varying in the second or third decimal points), they are not negligible when we consider the fact that the values are in atomic units and 1 au = 27.2114 eV (in ref 7, Parr et al. have reported the values in eV). The following trends of electrophilicity of the four series become apparent when we analyze the w_k^+ values of the $C_{C=O}$ generated at the BLYP/dnp level and based on HPA:

(i) $CH_3CHO > CH_3COCH_3 > C_2H_5COC_2H_5$

(ii) $CH_2ClCHO \approx CH_2FCHO$

(iii) $CH_2 = CHCHO > CH_3CH = CHCHO > C_6H_5CH = CHCHO$

(iv) $C_6H_5COCH_3 > C_6H_5COC_2H_5 > C_6H_5COC_6H_5$

It is encouraging to note that the trends generated by the w_k^+ values are as expected for series (i), (iii), and (iv). Only in series (ii), $C_{C=O}$'s of both the systems have almost identical w_k^+ values, wrongly projecting the systems to be equally electrophilic. It is also obvious from Table 1 that for MPA based calculations the trends are not as expected in series (iv).

TABLE 2: MPA and HPA Based Charges w_k^+, s_k^+, and s_k^+/s_k^- Values of Atoms Having the w_k^+ Values in the Higher Range[a]

carbonyl systems	atomic centers	MPA/dnp w_k^+	MPA/dnp s_k^+	MPA/dnp s_k^+/s_k^-	HPA/dnp w_k^+	HPA/dnp s_k^+	HPA/dnp s_k^+/s_k^-
1	$C_{C=O}$	0.0149	0.6514	4.1618	0.0156	0.6816	1.8210
	$O_{C=O}$	0.0120	0.5271	0.5798	0.0142	0.6229	0.7069
2	$C_{C=O}$	0.0082	0.4186	4.9714	0.0101	0.5162	1.8580
	$O_{C=O}$	0.0104	0.5316	0.5886	0.0112	0.5742	0.6709
3	$C_{C=O}$	0.0077	0.4289	3.9768	0.0090	0.5024	2.0273
	$O_{C=O}$	0.0092	0.5142	0.6327	0.0097	0.5395	0.7349
4	$C_{C=O}$	0.0136	0.4633	3.4546	0.0147	0.4982	2.0148
	$O_{C=O}$	0.0126	0.4292	0.6848	0.0149	0.5048	0.8293
	Cl	0.0177	0.6024	0.6269	0.0185	0.6273	0.6822
5	$C_{C=O}$	0.0129	0.4784	3.1618	0.0148	0.5458	1.7711
	$O_{C=O}$	0.0114	0.4228	0.5901	0.0140	0.5162	0.7389
	F	0.0025	0.0935	0.2456	0.0046	0.1700	0.4728
6	C_1	0.0149	0.4519	1.4274	0.0182	0.5526	1.2489
	$C_{C=O}$	0.0117	0.3545	2.2203	0.0157	0.4765	1.4626
	$O_{C=O}$	0.0154	0.4681	0.6028	0.0163	0.4957	0.6513
7	C_2	0.0085	0.3087	1.6716	0.0112	0.4076	1.3241
	$C_{C=O}$	0.0093	0.3390	2.5102	0.0122	0.4437	1.4935
	$O_{C=O}$	0.0119	0.4327	0.5947	0.0126	0.4606	0.6437
8	C_1	0.0049	0.1788	1.7097	0.0072	0.2665	1.6424
	$C_{C=O}$	0.0061	0.2260	2.1613	0.0081	0.2975	1.2475
	$O_{C=O}$	0.0104	0.3811	0.6011	0.0111	0.4068	0.6501
9	$C_{C=O}$	0.0065	0.2652	2.7813	0.0070	0.2848	1.7288
	$O_{C=O}$	0.0089	0.3635	0.6256	0.0090	0.3661	0.6698
10	$C_{C=O}$	0.0068	0.2826	2.6111	0.0067	0.2796	1.8164
	$O_{C=O}$	0.0084	0.3518	0.6324	0.0084	0.3509	0.6813
11	C_8	0.0028	0.1170	1.1613	0.0050	0.2077	1.1152
	C_{13}	0.0028	0.1170	1.1613	0.0051	0.2087	1.1204
	$C_{C=O}$	0.0054	0.2210	2.2667	0.0052	0.2136	2.0467
	$O_{C=O}$	0.0074	0.3056	0.7231	0.0072	0.2965	0.7415

[a] Here 1, 2, 3, etc. represent the systems (see Figure 1). The w_k^+ and s_k^+ values are in atomic units.

B. Comparison of Intramolecular Electrophilicity Trends. In Table 2, the w_k^+, s_k^+, and s_k^+/s_k^- values (generated by both MPA/dnp and HPA/dnp methods) of atoms having electrophilicity in the higher range (as evidenced by high s_k^+ values) are shown. It is obvious from w_k^+ and s_k^+ values that the trends generated by comparing the s_k^+ values (and so f_k^+ values) will be similar to those obtained by comparing w_k^+ values also. This is because w_k^α and s_k^α are analytically related as follows:

$$w_k^\alpha = wf_k^\alpha = \frac{\mu^2}{2\eta} f_k^\alpha = \mu^2 S f_k^\alpha = \mu^2 s_k^\alpha$$

(from eqs 13, 1, 4, and 8 respectively for the four consecutive equalities)

$$w_k^\alpha = \mu^2 s_k^\alpha \tag{15}$$

Thus, condensed philicity index is obtained after multiplying the condensed local softness by a constant multiplier (i.e., μ^2), which varies from system to system. So, although w_k^+ and s_k^+ values vary numerically, intramolecular electrophilicity trends generated by them remain identical. Which means that for comparison of intramolecular reactivity (or site selectivity), w_k^+ will not provide any extra information than what we get from s_k^+ or f_k^+.

Coming back to the comparison of intramolecular electrophilicity, we notice that in several cases the trends are not as expected (i.e., $C_{C=O}$ is not emerging as the strongest electrophilic center) when w_k^+ values are compared. Thus in systems 2, 3, 4, 6, 7, 8, 9, 10, and 11, for both HPA/dnp and MPA/dnp methods, the generated w_k^+ or s_k^+ values do not project $C_{C=O}$ to be the strongest electrophilic center. As was shown by Roy et al. (in ref 6), in the present study also (although here we are using DFT methods), s_k^+/s_k^- appears to be much more reliable than either w_k^+ or s_k^+ values. This is because $C_{C=O}$ emerged to be the strongest electrophilic center in all of the systems using these s_k^+/s_k^- values generated by both HPA and MPA (see Table 2). Needless to mention that the expected trends from w_k^+/w_k^- values will also be as reliable as those obtained from s_k^+/s_k^- values because of the analytical relation shown by eq 15.

TABLE 3: MPA and HPA Based w_k^-, s_k^-, and s_k^-/s_k^+ Values of Important Nucleophilic Atoms in the Chosen Carbonyl Compounds[a]

carbonyl systems	atomic centers	MPA/dnp w_k^-	MPA/dnp s_k^-	MPA/dnp s_k^-/s_k^+	HPA/dnp w_k^-	HPA/dnp s_k^-	HPA/dnp s_k^-/s_k^+
1	$C_{C=O}$	0.0036	0.1565	0.2403	0.0085	0.3743	0.5491
	$O_{C=O}$	0.0207	0.9092	1.7249	0.0201	0.8812	1.4146
2	$C_{C=O}$	0.0017	0.0842	0.2012	0.0054	0.2779	0.5382
	$O_{C=O}$	0.0179	0.9141	1.7195	0.0168	0.8559	1.4906
3	$C_{C=O}$	0.0019	0.1079	0.2515	0.0044	0.2478	0.4933
	$O_{C=O}$	0.0145	0.8127	1.5805	0.0131	0.7342	1.3608
4	$O_{C=O}$	0.0184	0.6268	1.4602	0.0179	0.6087	1.2058
	Cl	0.0283	0.9609	1.5951	0.0271	0.9194	1.4658
5	$O_{C=O}$	0.0194	0.7165	1.6947	0.0189	0.6987	1.3535
	F	0.0103	0.3805	4.0714	0.0097	0.3596	2.1152
6	C_1	0.0104	0.3166	0.7006	0.0146	0.4424	0.8007
	$O_{C=O}$	0.0256	0.7766	1.6590	0.0251	0.7612	1.5355
7	C_3	0.0056	0.2040	4.9333	0.0091	0.3335	1.2526
	$O_{C=O}$	0.0199	0.7276	1.6815	0.0196	0.7155	1.5536
8	C_3	0.0028	0.1046	0.4627	0.0065	0.2385	0.8016
	C_3	0.0029	0.1450	1.1316	0.0065	0.2405	0.9661
	$O_{C=O}$	0.0172	0.6341	1.6637	0.0170	0.6257	1.5381
9	C_7	0.0032	0.1311	1.4194	0.0058	0.2351	1.0662
	C_9	0.0031	0.1281	1.4828	0.0056	0.2291	1.0491
	$O_{C=O}$	0.0143	0.5809	1.5984	0.0134	0.5467	1.4931
10	C_7	0.0030	0.1263	1.3125	0.0055	0.2306	1.0464
	C_9	0.0030	0.1233	1.4138	0.0054	0.2249	1.0332
	$O_{C=O}$	0.0133	0.5563	1.5812	0.0123	0.5151	1.4679
11	C_7	0.0023	0.0943	1.5263	0.0043	0.1768	1.1405
	C_9	0.0024	0.0975	1.5790	0.0044	0.1814	1.1050
	$O_{C=O}$	0.0102	0.4226	1.3830	0.0097	0.3999	1.3486

[a] Here 1, 2, 3, etc. represent the systems (see Figure 1). The w_k^- and s_k^- values are in atomic units.

While comparing the intramolecular nucleophilicity, it is found that w_k^- values are not always very reliable. The s_k^-/s_k^+ values (and so will be w_k^-/w_k^+), however, generate the correct intramolecular reactivity trends projecting $O_{C=O}$ to be the strongest nucleophilic center in most of the systems (see Table 3). The only exception noticed is in series (ii), where generated s_k^-/s_k^+ values of halogen atoms, at the HPA/dnp method, are highest, indicating these two atoms to be the strongest nucleophilic centers. Although, for CH_2ClCHO it may be so, in the case of CH_2FCHO, it is difficult to accept. It should also be mentioned here that the MPA/dnp based values of s_k^-/s_k^+ indicate that $O_{C=O}$ in systems 7 and 11 also (apart from 4 and 5 as in case of HPA/dnp) is not the strongest electrophilic center. This also points to the fact that MPA is not as reliable as HPA.

5. Conclusion

The present article makes one significant revealation regarding the correlation between global and local reactivity descriptors. Comparatively higher global electrophilicity values (w) of $C_6H_5CH = CHCHO$ and $C_6H_5COC_6H_5$, than other members in the respective series, points to the fact that it may not always be logical to approximate the global reactivity to the local reactivity of the predominant site (or atom). This will, especially, be true for systems having more than one comparatively strong reactive sites (e.g., different positions of the Ph group in the above two systems). For example, position C_1 in $C_6H_5CH = CHCHO$ and positions C_8 and C_{13} in $C_6H_5COC_6H_5$ (see Figure 1) have comparatively high w_k^+ values (C_8 position in systems 9 and 10 also has high w_k^+ values, but in system 11 an extra position, i.e., C_{13}, also has high w_k^+ value). A thorough and rigorous study in this direction is sought for.

The HPA generated trends of local electrophilicity of the $C_{C=O}$ by philicity index (w_k^+), as proposed by Chattaraj et al.,[8]is as expected in almost all of the systems categorized in four different series [only in series (ii) the w_k^+ values of $C_{C=O}$ are approximately equal in both CH_2ClCHO and CH_2FCHO]. This is important in the sense that evaluation of w_k^+ is comparatively faster and less involved than the local hardness parameters used to evaluate the same electrophilicity trends by Roy et al. in their earlier study.[6]

Also, through numerical demonstrations and analytical expressions, it is shown that the philicity index (w_k^α) is not that good of an intramolecular reactivity descriptor as it is for intermolecular reactivity. On the contrary relative electrophilicity (s_k^+/s_k^-) and relative nucleophilicity (s_k^-/s_k^+), as proposed by Roy et al.,[6] are still the most reliable intramolecular reactivity indices (and for the same reason will be w_k^+/w_k^- and w_k^-/w_k^+, respectively). Also, the strongest nucleophilic centers in the studied systems, i.e., $O_{C=O}$, (except CH_2ClCHO and CH_2FCHO, in which cases these are the Cl and F atoms, respectively) could be reproduced by only s_k^-/s_k^+ (and so w_k^-/w_k^+) values using the HPA/dnp method.

Acknowledgment. The author is grateful to his colleagues at Birla Institute of Technology and Science (BITS), Pilani, for helpful discussions from time to time. Sincere thanks also to one of the referee for making constructive suggestions and pointing out some delicate issues, which has helped to improve the standard of the manuscript. Partial computational support by Prof. Kimihiko Hirao of the University of Tokyo is also gratefully acknowledged.

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