Effect of solvation on the condensed Fukui function and the generalized philicity index

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Abstract

Condensed Fukui functions (FF) and philicity provide vital information about functionally reactive sites in molecules. The effect of solvation on the condensed FF and philicity has been assessed by computing these local quantities in both gas and solvent media. The various population schemes used to calculate condensed quantities have several limitations viz., computational time, multiplicity problem and interpretation of negative values. To overcome this we used the direct method to evaluate the condensed quantities in both gas and solvent media. Hirshfeld population scheme has also been employed to avoid negative FF values. The implications of the results are discussed.
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1. Introduction

Numerous computational methods have been carried out to correlate the electronic structure and chemical reactivity [1–16]. Conceptual density functional theory [1,2] has been successfully exploited to unravel chemical reactivity and site selectivity. Various global and local quantities used to analyze the chemical reactivity have been discussed in the literature [2]. It is well known that chemical reactivity of any molecular system depends on the surrounding solvent medium [3]. Fukui function (FF) is one of the widely used local density functional descriptors to model chemical reactivity and site selectivity [4,5]. The atom with the highest FF is highly reactive compared to the other atoms in the molecule. FF is defined as the derivative of the electron density $\rho(\vec{r})$ with respect to the total number of electrons N in the system, at constant external potential $v(\vec{r})$ acting on an electron due to all the nuclei in the system [4,5]

$$f(\vec{r}) = [\delta\mu/\delta v(\vec{r})]_N = [\partial\rho(\vec{r})/\partial N]_{v(\vec{r})}, \tag{1}$$

where μ is the chemical potential of the system. The electronic chemical potential is the derivative of the total energy E with respect to the electron density. It is more convenient to represent the FF values around each atomic site into a single value that characterizes the atoms in a molecule. Depending on the electron transfer, three types of FF are defined [4].

$$f^+(\vec{r}) = \rho_{N+1}(\vec{r}) - \rho_N(\vec{r})$$
for nucleophilic attack, (2a)

$$f^-(\vec{r}) = \rho_N(\vec{r}) - \rho_{N-1}(\vec{r})$$
for electrophilic attack, (2b)

$$f^0(\vec{r}) = \lfloor\rho_{N+1}(\vec{r}) - \rho_{N-1}(\vec{r})\rfloor/2$$
for radical attack. (2c)

The condensed FF are calculated using the procedure proposed by Yang and Mortier [9] based on a finite difference method

$$f_k^+ = q_k(N+1) - q_k(N)$$
for nucleophilic attack, (3a)

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$$f_k^- = q_k(N) - q_k(N-1)$$

for electrophilic attack, (3b)

$$f_k^0 = [q_k(N+1) - q_k(N-1)]/2$$

for radical attack, (3c)

where q_k is the electronic population of atom k in a molecule.

There are number of factors which influence the calculated FF values using the above scheme. The choice of treatment levels (Hartree–Fock (HF)/post HF methodologies/density functional approaches (DFT)), population scheme and basis set used in the calculation are some of the important factors which influence the calculated values of FF indices [6–8]. In conventional FF calculation method, three different calculations need to be carried out for the molecule and also for its cation and anion. The problems in the calculation of FF using various population schemes have their own merits and demerits. The main problem in this type of calculation arises due to the spin multiplicity of the electronic state, which may lead to some computational difficulties. In order to overcome the difficulties associated with the calculation of FF using the scheme proposed by Yang and Mortier [9], Contreras et al. [10] have developed a direct scheme based on the relationship between local reactivity and frontier molecular orbital theory. This simple formalism has been tested for several benchmark model reactions that are well documented [11].

In the calculation of molecular geometry and electronic properties, the effects of solvation can be included using self-consistent reaction field (SCRF) models. Tomasi and coworkers [12] have developed a variety of continuum based SCRF models to analyze non-specific solvation effects. Subramanian and coworkers [13] have made detailed analysis on the importance of solvent in the calculation of Fukui functions using SCRF method employing dipole level approximation. Since this method is based on the spherical cavity, appropriate modeling of molecular shape is necessary in addition to the associated electrostatics. The polarizable continuum model (PCM) takes care of some of the limitations of SCRF method based on dipole model. In this investigation an attempt has been made to probe the effect of solvation on the local quantities using PCM employing the direct scheme for the calculation of FF. Pal and coworkers [14] have discussed the issues related to the negativity of FF. Since negative value of FF indicates that the electron density is depleted from any particular site (or atom in the case of condensed definition). Hence it is institutive to look for positive valued Fukui function. Roy et al. [14,15] have made detailed analysis on the various factors influencing the condensed FF values. According to the analytical definition, the FF is valid at the limit of $\delta N \to 0$. However in the calculation of FF

using condensed method, we are allowing a change of the electron number by a large value i.e., 1. As a consequence there will be a drastic change in the electron distribution due to large relaxation in the corresponding cation or anion. This may cause depletion (accumulation) of electron density from a particular site. The other factor, which influences the condensed FF values, is the population scheme. The realistic charge partitioning is necessary to obtain proper FF from the condensed approach. The well-known population analysis schemes fail in some cases due to improper charge partitioning. The success of the Hirshfeld scheme is thoroughly analyzed by Roy et al. [14,15]. In the Hirshfeld's stockholder partitioning, the molecular charge density at each point is divided among the atoms of the molecule in proportion to their respective contributions to the promolecular density at the point. Hence, like partners in a stockholders corporation, each atom partakes of the local gain or loss in direct proportion to its share in the capital investment and hence yields positive FF values in all the cases and provides reliable rank ordering of reactivity. Due to above mentioned inherent nature of partitioning, the FF obtained from the Hirshfeld scheme are positive. Hence an attempt has also been made to compute the FF in both gas and water media using Hirshfeld scheme applying conventional approach.

Local quantities such as FF and local softness define the reactivity/selectivity of a specific site in a molecule. When two molecules interact, which one will behave as an electrophile (nucleophile) will depend on which has higher (lower) electrophilicity index. This global trend originates from the local behavior of the molecules or precisely the atomic site that is prone to be an electrophile (nucleophile). To analyze the local reactivity in terms of a general reactivity and selectivity index, Chattaraj et al. [16] have proposed a generalized philicity index. The unified treatment of philicity is based on a resolution of identity, encompassing electrophilic, nucleophilic and radical reactions. Since the local philicity is a product of the FF and the global electrophilicity, it will take care of the local intramolecular reactivity and selectivity and also give necessary details regarding the local intermolecular (unlike FF) reactivity and site selectivity. In addition it provides insight into the global electrophilicity [16]. In this investigation an attempt has also been made to verify the unified treatment of philicity as well as the effect of solvation on the local reactivity indices.

2. Theoretical background

2.1. Direct calculation of FF

An exact definition for the FF, has been proposed by Senet within the Kohn–Sham (KS) theory given by [17]:

$$f_S^\alpha(\vec{r}) = |\phi_f^\alpha(\vec{r})|^2, \tag{4}$$

where $\alpha = -$ (i.e., $\Delta N < 0$, for electrophilic attack) and $\alpha = +$ (i.e., $\Delta N > 0$, for nucleophilic attack). The subscript f in Eq. (4) indicates whether the HOMO or LUMO frontier molecular orbital (FMO) $\phi(\vec{r})$ is to be considered, respectively. Eq. (4) was obtained under the condition that the KS potential is kept constant. This condition entails that not only the external potential is frozen (Eq. (1)), but also the electron repulsion, namely the Hartree potential and the exchange-correlation potential, are kept fixed in the process of deriving the electron density with respect to the number of particles. However, Eq. (4) is indeed a useful result when it is interpreted within the DFT, under the frozen orbital approximation.

Contreras et al. [10] have developed a simple scheme of calculation for direct evaluation of regional FFs in molecules starting from Eq. (4) by involving a single-point calculation of the electronic structure, without resorting to additional calculations involving ionic species of different spin multiplicity and arrived at a condensed-to-site-k FF given by

$$f_k^\alpha = \sum_{\mu \in k} f_\mu^\alpha, \tag{5}$$

where

$$f_\mu^\alpha = |c_{\mu\alpha}|^2 + c_{\mu\alpha} \sum_{v \neq \mu} c_{v\alpha} S_{\mu v}. \tag{6}$$

$S_{\mu v}$ is the overlap integral between the basis functions. Eq. (5) and Eq. (6) were completely equivalent to the FF derived by Komorowski and co-workers [18], from a quite different approach based on the group analysis of atoms in molecules.

The (f_k^α) function conserves the normalization condition:

$$\sum_k f_k^\alpha = \sum_k \sum_{\mu \notin k} \left[|c_{\mu\alpha}|^2 + \sum_{v \neq \mu} c_{\mu\alpha} c_{v\alpha} S_{\mu v} \right] = 1. \tag{7}$$

Eq. (5) directly provides condensed FFs for electrophilic ($\alpha = -$) and nucleophilic ($\alpha = +$) attacks, involving in each case the HOMO and LUMO FMO coefficients, respectively. For the case of radical attacks, we take simply their average, namely, $f_k^0 = \frac{1}{2}[f_k^+ + f_k^-]$.

The global electrophilic power [19] of atoms and molecules has been given by

$$\omega = \mu^2 / 2\eta. \tag{8}$$

$\mu \approx -(I + A)/2$ and $\eta = (I - A)$ are the electronic chemical potential and the chemical hardness of the ground state of atoms and molecules, respectively, approximated in terms of the vertical ionization potential I and electron affinity A. It is also possible to define a local quantity called philicity [16] associated with a site k in a molecule with the aid of the corresponding condensed FF f_k^α, as

$$\omega_k^\alpha = \omega f_k^\alpha, \tag{9}$$

where ($\alpha = +, -$ and 0) represents local philic quantities describing nucleophilic, electrophilic and radical attacks. Eq. (9) predicts that the most electrophilic site in a molecule is the one providing the maximum value of f_k^+. This site also coincides with the softest region in a molecule.
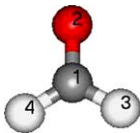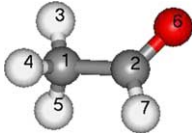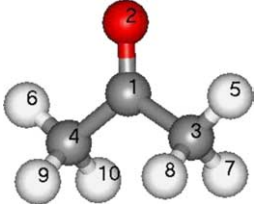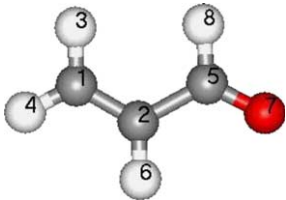
3. Computational details

It is evident from the previous work of De Proft et al. [6] that B3LYP and B3PW91 methods provide comparatively good results on FF indices. Hence in the present investigation, all computations have been made using B3LYP method. The geometries for formaldehyde (HCHO), acetaldehyde (CH$_3$CHO), acetone (CH$_3$COCH$_3$) and acrolein (CH$_2$CHCHO) molecules were optimized using 6–31+G* basis set in the framework of Becke's three-parameter hybrid method using LYP correlation functional (B3LYP) [20] theory. The atomic charges for all the above molecules have been obtained in the framework of B3LYP theory using Mulliken population analysis (MPA) [21] (Direct calculation of FF values [10]). DENSITY = CURRENT option has been used in all the calculations of atomic charges. All the calculations have been performed using G98W suite of programs [22]. To assess the importance of solvation on the FF, calculations have been carried out using PCM developed by Tomasi and coworkers [12]. The geometries of the above molecules are minimized using PCM method in water environment. It is now established that the FF values obtained from various population schemes provide negative values whereas Hirshfeld's Stockholder population scheme [23] yields positive FF values. Hence, Hirshfeld partitioning scheme [23] employing BLYP/DND method, which is implemented in the DMOL^3 program [24], has also been used to derive the atomic charges in gas phase and solvent medium to calculate FF for the above systems for comparison. COSMO solvation model [25] as included in the DMOL^3 is used to compute charges in the solvent environment.

4. Results and discussion

The optimized structures of all the considered systems with atom numbering are presented in Table 1. The aim of our present study is to assess the overall performance of the 'philicity', proposed by Chattaraj et al. [16] and solvation effects on the local quantities. The calculated FF indices for formaldehyde using both direct calculation (MPA scheme [21]) and conventional calculation (Hirshfeld scheme [23]) are shown in Figs. 1a and 2a. It

Table 1
Optimized structure of the selected systems with atom numbering

Molecules	Molecular structure with atom numbering
Formaldehyde (HCHO)	
Acetaldehyde (CH₃CHO)	
Acetone (CH₃COCH₃)	
Acrolein (CH₂CHCHO)	

is evident from the FF values that C and O are possible sites for nucleophilic and electrophilic attacks, respectively. The presence of water medium does not significantly enhance the intrinsic chemical reactivity. Only very marginal changes in both nucleophilicity and electrophilicity have been noted. Based on the electrostatic potential of various molecular systems in solvent environment, it is possible to conclude that there is a simultaneous enhancement of reactivity upon solvation

[26]. Such trend is not evident from the FF indices obtained from direct calculations using MPA scheme. Since direct method also suffers from the drawback of predicting negative FF, calculations have also been made using Hirshfeld method to obtain FF in both gas and solvent media. It is interesting to observe from the FF indices in solvent medium calculated from the Hirshfeld scheme for formaldehyde that there is a simultaneous enhancement in the nucleophilicity (5%) and electrophilicity (1.9%) at C and O sites, respectively.

FF values for acetaldehyde calculated using various population schemes are shown in Figs. 1b and 2b. It is seen from the FF values that C2 and O6 are possible sites for nucleophilic and electrophilic attacks, respectively. In the presence of solvent environment the intrinsic chemical reactivity increases the nucleophilic attack by 1.6% and 10.8% for direct [10] and Hirshfeld [23] methods, respectively, at C2 site whereas there is small decrease (0.9%) (increase by 6.9%) in the electrophilic attack at O6 site in direct calculation (Hirshfeld) methods. Also it can be noted that direct FF calculation scheme provides negative FF values for C1 site both in gas and solvent environments.

In the case of acetone, the FF values calculated using various population schemes are shown in Figs. 1c and 2c. The FF values obtained from direct calculation predict C1 and O2 as possible sites for nucleophilic and electrophilic attacks, respectively. But Hirshfeld scheme predicts O2 as the possible site for both nucleophilic and electrophilic attacks. Inclusion of water medium enhances the intrinsic chemical reactivity towards nucleophilic attack by 8.1% at C1 site for direct calculation method whereas there is small decrease (1%) (increase 10%) in the electrophilic attack at O2 site in direct calculation (Hirshfeld) methods.

For acrolein, the calculated FF values using various population schemes are shown in Figs. 1d and 2d. The FF values thus obtained predict C5 and O7 as possible sites for nucleophilic and electrophilic attacks, respectively. Solvation effect reduces the intrinsic chemical reactivity by 1% (enhances by 3%) towards nucleophilic
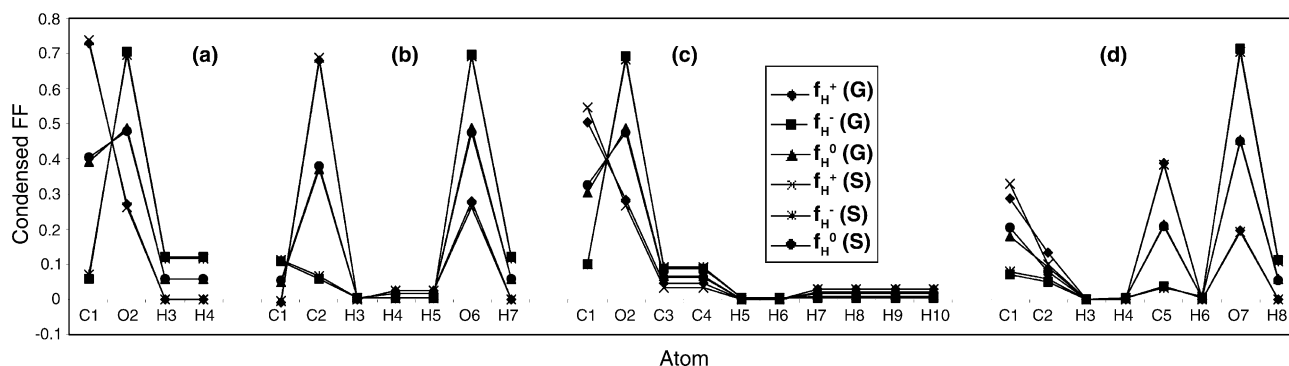

Fig. 1. Condensed Fukui function values: (a) Formaldehyde, (b) Acetaldehyde, (c) Acetone and (d) Acrolein using Direct (MPA) calculation. (G-Gas phase, S-Solution phase).
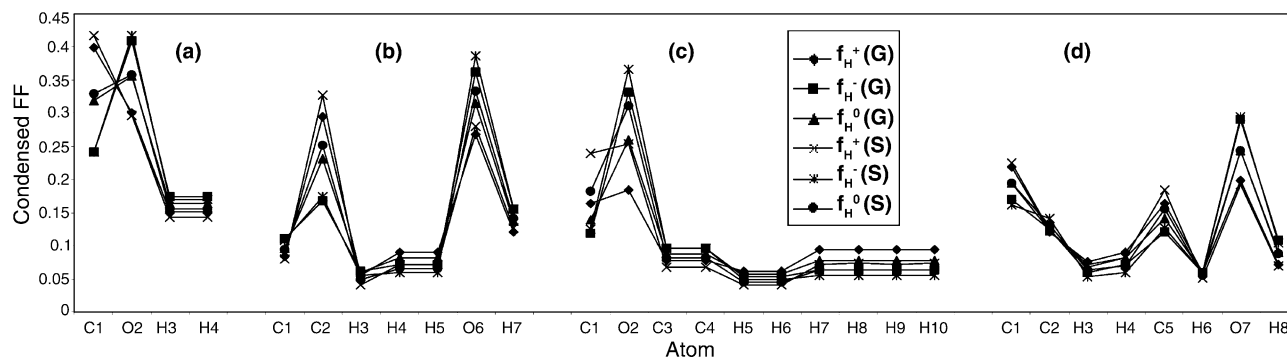
Fig. 2. Condensed Fukui function values: (a) Formaldehyde, (b) Acetaldehyde, (c) Acetone and (d) Acrolein using Hirshfeld population schemes. (G-Gas phase, S-Solution phase).

Table 2
The Calculated values of dipole moment and C=O bond length for the selected systems in gas and water media

Molecules	Dipole Moment (D)		C=O distance (Å)	
	Gas phase	Solvent (water) phase	Gas phase	Solvent (water) phase
Formaldehyde	2.52	3.08	1.209	1.214
Acetaldehyde	2.99	3.91	1.214	1.222
Acetone	3.19	4.28	1.219	1.227
Acrolein	3.53	4.65	1.218	1.227

attack at C5 site and reduces the chemical reactivity for electrophilic attacks at O7 site for direct calculation by 0.8% (enhances by 1.7% in Hirshfeld) methods.

The analyses of the results show that FF indices do not show any drastic change in the chemical reactivity of the molecules upon solvation. A maximum of 10% enhancement in the nucleophilicity at the C atomic site has been observed in the case of acetone. The direct calculation of FF indices greatly helps to perform calculations with less computational cost and provides quick guess about the probable site, which are influenced by the solvent environment. One of the limitations of the direct method stems from the fact that MPA scheme has been used in the computation of FF indices. As a consequence the direct method of calculation of FF does also suffer from yielding negative values for FF. The combination of direct algorithm of FF with Hirshfeld population scheme may solve some of the problems related to the computation of FF indices.

Table 2 presents the values of dipole moment and bond length for the selected systems in gas and water media. We see that there is an enhancement in the values of the dipole moment in the solvent environment compared to gas phase. Previous studies have shown carbonyl stretching vibration as one of the most solvent-sensitive infrared stretching vibrations. In a solvent of high dielectric constant, the dipolar resonance of a carbonyl compound is stabilized. This has been reflected by a larger degree of charge separation and lengthening of the C=O [23]. The C=O (R (1,2)) of formaldehyde is

lengthened by 0.005 Å in going from the gas phase to aqueous phase. The increase in CO (double bond) length will lead to a decrease in the force constant of the carbonyl group. Also in moving from gas to solution phase the change in dipole moment is found to be 0.569 D. It is interesting to note that formaldehyde is more stable in the solution phase than that in the gas phase.

In the case of acetaldehyde, C=O (R (2,6)) bond length is increased by 0.008 Å with a dipole moment change of 0.925 D in going from gas to solution phase. Like formaldehyde, acetaldehyde also exists as a stable system in solution phase compared to gas phase. C=O bonds in acetone (R (1,2)) and acrolein (R (5,7)) are also stretched by 0.008 Å in the solvent environment compared to gas phase with a dipole moment change of 1.09 and 1.122 D, respectively. Among the considered systems, acetone has got the highest stabilization energy in the solution phase compared to the gas phase.

A plot of philicity [16] with atoms in gas and solution phases using direct calculation for formaldehyde is shown in Fig. 3a. The f_k^+ value for C1 is the highest among all the atoms in the molecule whereas f_k^- value of O is the highest among all the atoms in the molecule for both the calculations (MPA and Hirshfeld) (see Fig. 1a and Fig. 2a). So the carbon and oxygen are the possible sites for nucleophilic and electrophilic attacks, respectively. According to the generalized concept of philicity proposed by Chattaraj et al. [16], the preferred site for nucleophilic addition of a molecule is one for which the ω_k^+ value is highest. For electrophilic (or radical) addi-
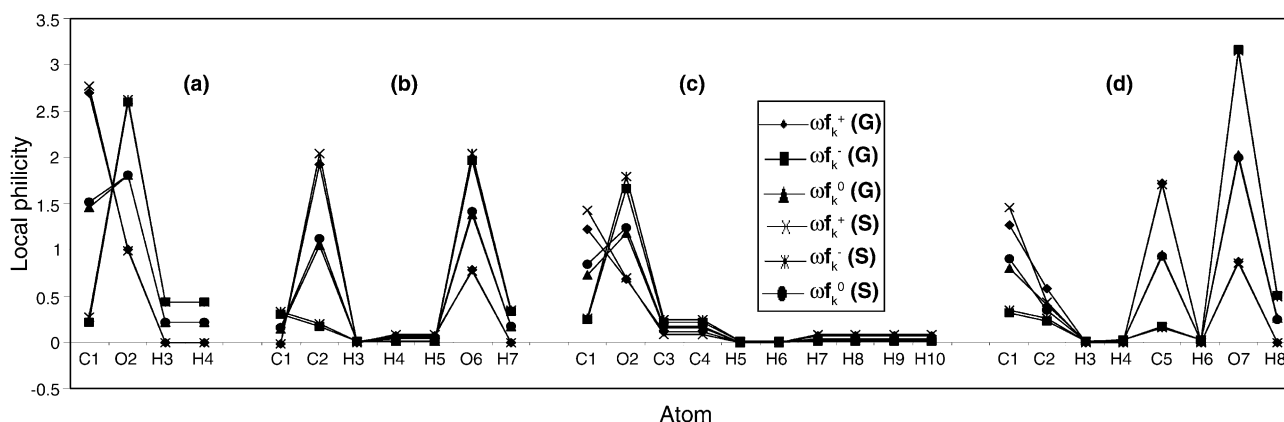
Fig. 3. Local philicity of: (a) Formaldehyde, (b) Acetaldehyde, (c) Acetone and (d) Acrolein using direct calculation (G-Gas phase, S-Solution phase).

tion the site, which has the maximum ω_k^- (or ω_k^0) value will be preferred. From Fig. 3a we see the ω_k^+ value of C1 atom is the highest whereas the ω_k^- value of O2 atom is the highest. So the C1 site is the preferred site for nucleophilic attack and O2 site is the preferred site for electrophilic attack, which is in conformity with the experimental observation. The inclusion of solvent changes ω_k^- and ω_k^0 value of C1 slightly, but has no significant effect for other atoms. The ω_k^- value does not change appreciably in gas and solution phases. One can see that the electrophilic nature of C1 site is enhanced by about 3.4% in going from gas to solution phase.

Fig. 3b represents the local philicity index in gas and solution phases for acetaldehyde. It is clear from the figure that the C2 atom has the highest ω_k^+ value whereas O6 atom has the highest ω_k^- value. That means atomic sites C2 and O6 are favorable for nucleophilic and electrophilic attacks, respectively. Local philicities are slightly increased for C2 and O6 atom in solvent medium. There is 6.8% increase in the electrophilic nature in the solvent environment.

Local philicity index with atoms in gas and solution phase for acetone is depicted in Fig. 3c. The maximum, ω_k^+ value is for C1 atom and ω_k^- is for O2 atom. So C1 atom is the preferred site for nucleophilic addition and O2 atom is the preferred site for electrophilic addition. The condensed FF, using Hirshfeld scheme shows that O2 atom is the favorable site for both nucleophilic and electrophilic attacks. But the preferred site for nucleophilic addition is known [27] to be the C1 atom of acetone. So local philicity index gives the better result. It is interesting to note that there is a drastic increase (about 17.4%) in the value of ω_k^+ in moving from gas to solution phase. For acrolein, a plot of local philicity index with atoms in gas and solution phases is shown in Fig. 3d. From the figure we see that C5 and O7 sites are the favorable sites for nucleophilic and electrophilic attacks, respectively. The ω_k^+ and ω_k^- values of C5 and O7 atoms decrease in the solvent medium. These results confirm the usefulness of the generalized concept of local philicity.

5. Conclusion

A systematic investigation has been made to study the effect of solvation on the local philicity indices using B3LYP scheme employing direct calculation method. Due to the negativity of the FF indices calculated using direct approach, the results have also been compared with those values obtained from Hirshfeld population scheme. It is possible to observe from the results that solvation marginally influences the local reactivity profiles. We have also made an attempt to verify the unified philicity indices proposed by Chattaraj et al. It is evident from the results that ω^α (where $\alpha = +, -$, and 0) values could describe effectively the reactivity as well as site selectivity when compared to the other local quantities in gas phase as well as in solvent environment. The solvent continuum around the solute molecules marginally influences the local quantities. Maximum changes in the local quantities are observed in acetone whereas minimum variations are noted in formaldehyde. The FF indices derived from BLYP/DND Hirshfeld population scheme using conventional FF method are positive and marginal increase in the local quantities are also observed from the calculations based on solvent environment.

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