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DFT-Based Linear Solvation Energy Relationships for the Infrared Spectral Shifts of Acetone in Polar and Nonpolar Organic Solvents

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Linear solvation energy relationships (LSER) established using solvation free energy and density functional theory (DFT)-based reactivity descriptors are for the first time documented in this study. The solvent-induced shifts of the carbonyl (C═O) stretching frequency of acetone in 21 organic solvents including polar protic, dipolar aprotic, and nonpolar solvents are examined. Results of the multiple regression analysis have shown that four descriptors, namely, (1) the solvation free energy of solute in continuous dielectric medium, (2) the global interaction energy of the solute−solvent system, (3) the maximum electrostatic potential on the hydrogen atom of the solvent molecule, and (4) the maximum condensed nucleophilic Fukui function (or nucleophilic condensed local softness) of the solvent molecule, those which considered both the nonspecific and specific effects of solute−solvent interactions, can be incorporated in a multiparameter equation for constructing the present DFT-based LSER.

I. Introduction

Solvent fulfills several important functions during a chemical reaction; hence, the solute−solvent interaction plays an essential role in a variety of chemical and physical processes in solution. Physicochemical properties in solution can often be correlated/predicted by so-called linear free energy relationships (LFER) or linear solvation energy relationships (LSER). Conventionally, one of the best-known LFERs is the Koppel−Palm multiparameter equation.[1] The equation describes both the nonspecific and specific components of solute−solvent interactions.

In order to explore the solute−solvent interactions, there has been great interest in applying infrared spectral measurements for the solvent-induced frequency shifts (SIFS) of solutes.[2−8] Fawcett et al. have studied the induced shifts of the C≡N stretching frequency (ν_2) of acetonitrile in various organic solvents.[3] Both the electrophilicity (Gutmann's acceptor number[9a]) and electrodonicity (Gutmann's donor number[9b,c]) of the solvent were considered with respect to those of the solute. They concluded that the major contribution to the variation observed for the C≡N stretching frequency between different solvents arises from specific solute−solvent interactions. This work was later extended using the Koppel and Palm multiparameter equation.[4,5] Four solvent parameters were considered in examining the solvent dependence of the induced frequency shifts of solutes. These are the Gutmann's acceptor number as a measure of solvent acidity, the Gutmann's donor number for solvent basicity, solvent polarity defined from the static dielectric constant, and solvent polarizability calculated from the solvent's refractive index. It was shown that a precise quantitative description of SIFS is possible only when one considers both specific effects (electrophilicity and electrodonicity) and nonspecific solvation effects which depend on the bulk dielectric properties of the solvent.[4a]

Kamlet, Taft, and their colleagues proposed a type of linear free energy relationship, called the linear solvation energy relationship.[10] The approach relates a bulk property to molecular parameters thought to account for cavity formation, dipole moment/polarizability, and hydrogen-bonding effects. The cavity term is a measure of the energy needed to overcome cohesive solvent−solvent molecule interactions to form a cavity for the solute molecule. The dipolarity/polarizability terms are measures of the energy of solute−solvent dipole and induced dipole interactions which contribute to solution formation. Hydrogen-bonding terms measure the energy of interaction when a solute−solvent complex is formed.

The original LSER descriptors were derived from UV−vis spectral shifts of indicator dyes. Because of their empirical origin, their ability to make a priori predictions has been somewhat limited. Abraham and co-workers,[11] and separately Carr and co-workers, have extended the original LSER by using gas chromatography instead of UV−vis spectral shifts to determine the LSER descriptors and added a term modeled by the gas−hexadecane partition coefficient to consider dispersion-type interactions.

Famini, Wilson, and co-workers have developed a new set of quantum-chemical-derived parameters to model conventional LSER terms.[12−14] A molecular volume is used to model the cavity term that measures the energy required to create a solute-molecule-sized cavity in the solvent. The dipolarity/polarizability term, which attempts to account for dispersion, is modeled by the polarizability index. This index is defined as the average molecular polarizability divided by the molecular volume. Hydrogen bonds are modeled using covalent and electrostatic terms by the frontier molecular orbital energies and maximum partial charges, respectively.

Politzer, Murray, and co-workers have done considerable work on using electrostatic potentials to interpret the *solvatochromic* parameters in Kamlet−Taft−Abraham (KTA) LSER and further developing a general interacting properties function (GIPF) for solute−solvent interactions.[15] It has been found that the surface maxima of the electrostatic potential, $V_{s,max}$, can measure the hydrogen-bond-donating tendency (or hydrogen-

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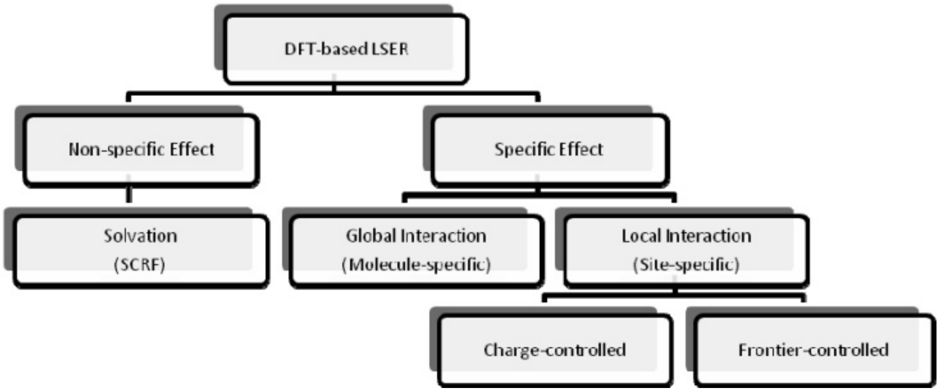
SCHEME 1: Partitioning Scheme of the Present DFT-Based Linear Solvation Energy Relationships



bond acidity) of a molecule.[15a] Based on the electrostatic potential, the GIPF methodology of Politzer and Murray is the ab initio alternative to the KTA LSER and the Famini and co-workers theoretical LSER (TLSER). Where comparisons have been made between the GIPF and the TLSER, the regressions have generally been comparable.

Density functional theory (DFT)-based reactivity descriptors have been extensively used in interpreting properties and reactions and in predicting site selectivities of various molecular and catalyst surface systems.[16−23] By using a local hard−soft acid−base (HSAB) principle, Chandrakumar and Pal presented several detailed studies on the calculations of the interaction energy for single-site-based and multiple-site-based intermolecular interactions.[16−18] Deka and co-workers[19] have investigated the interaction of small molecules with zeolite cluster models by using the concept of relative electrophilicity and relative nucleophilicity developed by Roy et al.[20] Chattaraj et al.[21] have proposed a generalized concept of philicity containing electrophilic, nucleophilic, and radical reactions. Recently, Padmanabhan and co-workers presented a series of studies for the applications of global and local reactivity descriptors.[22,23] They especially emphasized the importance of the electrophilicity index in the quantitative structure−activity relationship (QSAR) studies and the charge-transfer analyses. The applicability of local philicity, group philicity, and multiphilic descriptors was also discussed.

The aim of this study is to use DFT-based reactivity descriptors to elucidate the properties of polar and nonpolar organic solvents and, as illustrated in Scheme 1, to establish a feasible LSER for accurately predicting the variations of carbonyl ($C{=}O$) stretching frequencies of acetone in various organic solvents by coupling nonspecific dielectric effects, global interactions (molecular-specific), and local reactivity descriptors (site-specific).

II. Computational Methods

All calculations are performed using the Gaussian 03 software package.[24] The molecular geometries are optimized at the three-parameter hybrid functional B3LYP level using split-valence basis sets 6-31G(d,p). The Onsager self-consistent reaction field (SCRF) model[25] with a spherical cavity is used for modeling the nonspecific dielectric effects of 21 organic solvents on acetone solute. Optimizations are performed without constraints starting from structures optimized previously in the gas phase at the same level of theory. The cavity radius used by the SCRF calculation is estimated by a VOLUME calculation on the optimized geometry in gas phase. Vibrational frequencies are computed on the optimized geometries in all media. Frequency calculations also yield thermodynamic information about the molecule. The solvation free energy $\Delta G^\circ_{\mathrm{sol}}$ is defined as $\Delta G^\circ_{\mathrm{sol}} = G^\circ_{\mathrm{SCRF}} - G^\circ_{\mathrm{gas}}$.

The ionization potential (IP) and electron affinity (EA) are evaluated using the difference of separate SCF energies of neutral and corresponding anionic and cationic systems. The anionic and cationic system calculations are carried out at the same geometry to fulfill a constant external potential requirement. The restricted method is used for the calculation of energy of the neutral systems, and for the corresponding anionic and cationic systems, the restricted-open doublet spin method is used. When the IP and EA are obtained, the chemical potential (μ) is calculated using $\mu = -((\mathrm{IP} + \mathrm{EA})/2)$, and the global hardness (η) is calculated using $\eta = (\mathrm{IP} - \mathrm{EA})/2$.

The solute−solvent global interaction energy $\Delta E_{\mathrm{int}} = \Delta E_\nu + \Delta E_\mu$. The term $\Delta E_\nu = -(^1/_2)[(\mu(\mathrm{solvent}) - \mu(\mathrm{solute}))^2/(\eta(\mathrm{solute})] + \eta(\mathrm{solvent}))$ is derived from the electronegativity equalization principle, indicating the energy release by an electron transferred from donor to acceptor at constant external potential. The second term $\Delta E_\mu = -(^1/_4)[\lambda/(S(\mathrm{solvent}) + S(\mathrm{solute}))]$ is related to the charge reshuffling process within the solute−solvent system at constant chemical potential, to manifest the principle of maximum hardness, where the global softness (S) is defined as $1/(2\eta)$. Since the exact value of λ was difficult to obtain with a simple model, there were several different definitions in the literature.[16−18,26−31] Chandrakumar and Pal have related λ as the change in the electron population at the interacting site before and after the interaction process.[16−18] An alternate approach has been employed by using the fractional number of charges transferred (ΔN) as λ.[16] In this study, the value of λ is assumed to be a constant ($\lambda = 1$) as proposed by Gazquez et al. and Geerlings and co-workers.[29−31] They have used the value of λ as 1 and 0.5 for certain organic reactions.

For the calculations of local reactivity descriptors, the atomic partial charge (ρ) is calculated using Mulliken population analysis.[32] The electrostatic potential (V) is defined as $V_{\mathrm{Y}} = V(R_{\mathrm{Y}}) = \sum_{\mathrm{A}\neq\mathrm{Y}}(Z_{\mathrm{A}}/|R_{\mathrm{Y}} - R_{\mathrm{A}}|) - \int (\rho(r')/|R_{\mathrm{Y}} - r'|)\,\mathrm{d}r'$.[33] Where Z_{A} is the charge on nucleus A, located at R_{A}, $\rho(r)$ is the electronic density function, and r' is a dummy integration variable. In this study, Y represents the hydrogen atom for solvent molecules. The condensed nucleophilic Fukui function (f^+) is calculated via $[q(N + 1) - q(N)]$, where $q(N)$ and $q(N + 1)$ denote the Mulliken gross population of an atom in the neutral and anionic systems, respectively. The nucleophilic condensed local softness (s^+) is calculated using $s^+ = f^+S$, where S is the global softness.

TABLE 1: B3LYP/6-31G(d,p) Calculated Results of the Solvation Free Energy of Acetone and the Global Reactivity Descriptors of Solvent Molecules[a]

solvent	ΔG°_{sol} (kcal mol^{-1})	μ (a.u.)	η (a.u.)	ΔN (a.u.)	ΔE_ν (kcal mol^{-1})	$\Delta E_{\mu(\lambda=1)}$ (kcal mol^{-1})	$\Delta E_{int(\lambda=1)}$ (kcal mol^{-1})
acetone	−1.35	−0.130	0.219	0.000	0.00	−34.30	−34.30
dimethyl sulfoxide	−1.41	−0.096	0.224	0.039	−0.83	−34.69	−35.53
chloroform	−1.01	−0.187	0.221	−0.064	−2.24	−34.49	−36.73
dichloromethane	−1.20	−0.167	0.241	−0.039	−0.89	−35.96	−36.85
1,2-dichloroethane	−1.23	−0.160	0.238	−0.033	−0.62	−35.73	−36.34
acetonitrile	−1.40	−0.153	0.291	−0.022	−0.31	−39.19	−39.50
benzonitrile	−1.37	−0.161	0.186	−0.038	−0.73	−31.49	−32.22
nitromethane	−1.40	−0.190	0.234	−0.066	−2.44	−35.48	−37.92
nitrobenzene	−1.39	−0.184	0.177	−0.068	−2.29	−30.66	−32.96
benzene	−0.60	−0.124	0.210	0.007	−0.03	−33.58	−33.61
hexane	−0.49	−0.120	0.273	0.011	−0.08	−38.09	−38.17
diethylether	−0.96	−0.092	0.254	0.040	−0.96	−36.86	−37.83
dimethylformamide	−1.40	−0.105	0.231	0.029	−0.47	−35.24	−35.70
dimethylacetamide	−1.40	−0.099	0.223	0.036	−0.71	−34.66	−35.37
hexamethylphosphoramide	−1.38	−0.079	0.206	0.061	−1.99	−33.28	−35.27
propylene carbonate	−1.43	−0.133	0.263	−0.003	0.00	−37.46	−37.47
methanol	−1.39	−0.113	0.280	0.017	−0.19	−38.52	−38.71
ethanol	−1.36	−0.110	0.269	0.021	−0.27	−37.84	−38.11
propan-1-ol	−1.35	−0.109	0.266	0.022	−0.31	−37.66	−37.97
propan-2-ol	−1.33	−0.111	0.258	0.020	−0.25	−37.14	−37.38
t-butanol	−1.24	−0.112	0.249	0.019	−0.22	−36.49	−36.71

[a] ΔG°_{sol}, solvation free energy of solute (acetone) molecule in polar and nonpolar organic solvents calculated using the Onsager SCRF model; μ, chemical potential ($\mu = -((\mathrm{IP} + \mathrm{EA})/2)$; η, global hardness ($\eta = (\mathrm{IP} - \mathrm{EA})/2$); IP, ionization potential; EA, electron affinity; ΔN, fractional number of charges transferred ($\Delta N = {}^1/_2((\mu(\mathrm{solvent}) - \mu(\mathrm{solute}))/(\eta(\mathrm{solute}) + \eta(\mathrm{solvent})))$; $\Delta E_{int(\lambda=1)}$, solute−solvent global interaction energy with $\lambda = 1$, $\Delta E_{int(\lambda=1)} = \Delta E_\nu + \Delta E_{\mu(\lambda=1)}$.

III. Results and Discussion

The solvation free energy of solute (ΔG°_{sol}), the chemical potential (μ), and global hardness (η) of the solvent, and the fractional number of charges transferred (ΔN) and interaction energy (ΔE_ν, $\Delta E_{\mu(\lambda=1)}$, $\Delta E_{int(\lambda=1)}$) of the solute−solvent system are listed in Table 1. Within the framework of conceptual DFT, electronic chemical potential measures the escaping tendency of electron density in a molecule, whereas global hardness determines the resistance of the molecular species to lose electrons. The negative chemical potential can be called the absolute electronegativity. According to Sanderson's electronegativity equalization principle,[34] when two systems are brought together, electrons transfer from a less electronegative region to a more electronegative region until both regions have the same chemical potential value. It results in an equal electronegativity for each atom in a molecule. In this study, the fractional number of electrons transferred, ΔN, can be represented by $\Delta N = {}^1/_2((\mu(\mathrm{solvent}) - \mu(\mathrm{solute}))/(\eta(\mathrm{solute}) + \eta(\mathrm{solvent})))$. The electron transfer is driven by the difference of chemical potential but resisted by the sum of global hardness. If $\Delta N < 0$, charge flows from solute to solvent (solvent acts as electron acceptor), and if $\Delta N > 0$, charge flows from solvent to solute (solvent acts as electron donor).

From the values of ΔN shown in Table 1, it can be readily seen that chlorinated (chloroform, dichloromethane, 1,2-dichloroethane), nitrile (acetonitrile, benzonitrile), and nitro (nitromethane, nitrobenzene) solvents act as electron acceptors, and amide (dimethylformamide, dimethylacetamide) and alcoholic (methanol, ethanol, propan-1-ol, propan-2-ol, *t*-butanol) solvents act as electron donors, in their global interaction with acetone. It is evident that the amount of charge transfer increases with an increase in the number of electronegative chlorine substituents (chloroform > dichloromethane). Moreover, the results of charge transfer vary depending on the electron-withdrawing and electron-donating strength of substituents. For electron-accepting solvents, the tendency of charge transfer from acetone can be enhanced by increasing the electron-withdrawing strength of substituted groups in solvent molecules (nitro > nitrile), and for electron-donating solvents, the tendency of charge transfer to acetone can be enhanced by increasing the electron-donating strength of substituted groups in solvent molecules (amide > alcohol). However, the molecular interactions involve nonspecific dielectric effects and site-specific local interactions besides global electron transfer. ΔN is not the exact amount of electrons transferred but is still useful in unraveling the initial orbital interaction between solute and solvent systems.

By analyzing the contribution of the energy terms (ΔE_ν, $\Delta E_{\mu(\lambda=1)}$) to the global interaction energy ($\Delta E_{int(\lambda=1)}$) (Table 1), it reveals that the interacting strength between solute and solvent systems (molecule-specific) in the present study is mostly affected by the charge reshuffling process ($\Delta E_{\mu(\lambda=1)}$) rather than the process due to the electronegativity equalization (ΔE_ν). This result is quite consistent with the literature predictions.[16,17,30] As a consequence, according to the definition of $\Delta E_{\mu(\lambda=1)}$, the global softness ($S$) can be considered as a governing parameter in determining the strength of the solute−solvent global interactions. From the values of global hardness ($\eta = 1/(2S)$), it is obvious that aromatic solvents (benzonitrile, nitrobenzene, benzene) have smaller hardness so that the global interaction energy is substantially lower than other solvents. To go into details, additional trends can also be obtained: (i) the global hardness of substituted aromatics (benzonitrile, nitrobenzene) is smaller than that of nonsubstituted aromatics (benzene) and (ii) the global hardness of nitro-substituted aromatics (nitrobenzene) is smaller than that of nitrile-substituted aromatics (benzonitrile). With an increase in the number of chlorine substituents, the hardness will be decreased (dichloromethane > chloroform). Besides, the alcoholic solvents (methanol, ethanol, propan-1-ol, propan-2-ol, *t*-butanol) have in general a larger value of global hardness.

The local reactivity descriptors of solvent molecules (site-specific), namely, the maximum positive charge on the hydrogen atom of solvent molecule ($\rho^+_{max(H)}$), the maximum electrostatic potential on the hydrogen atom of solvent molecule ($V_{max(H)}$),

TABLE 2: B3LYP/6-31G(d,p) Calculated Results of the Local Reactivity Descriptors of Solvent Molecules (Given in Atomic Units)[a]

solvent	$\rho^{+}_{\max(\mathrm{H})}$	$V_{\max(\mathrm{H})}$	$f^{+}_{\max}$	$s^{+}_{\max}$	site[b]
acetone	0.139	−1.098	0.223	0.510	O
dimethyl sulfoxide	0.157	−1.082	0.428	0.957	S
chloroform	0.241	−1.036	0.325	0.735	Cl
dichloromethane	0.205	−1.059	0.385	0.800	Cl
1,2-dichloroethane	0.177	−1.080	0.306	0.644	Cl
acetonitrile	0.168	−1.067	0.291	0.499	C
benzonitrile	0.115	−1.086	0.128	0.346	C
nitromethane	0.172	−1.057	0.288	0.615	O
nitrobenzene	0.139	−1.084	0.177	0.501	O
benzene	0.084	−1.116	0.134	0.321	H
hexane	0.101	−1.137	0.123	0.225	H
diethylether	0.118	−1.126	0.192	0.378	H
dimethylformamide	0.159	−1.092	0.258	0.559	C
dimethylacetamide	0.143	−1.097	0.203	0.454	C
hexamethylphosphoramide	0.125	−1.116	0.161	0.391	P
propylene carbonate	0.138	−1.080	0.243	0.462	C
methanol	0.306	−1.015	0.598	1.067	H
ethanol	0.304	−1.016	0.516	0.960	H
propan-1-ol	0.304	−1.016	0.480	0.902	H
propan-2-ol	0.299	−1.018	0.400	0.776	H
t-butanol	0.295	−1.020	0.311	0.625	H

[a] $\rho^{+}_{\max(\mathrm{H})}$, the maximum positive charge of the hydrogen atom in solvent molecules; $V_{\max(\mathrm{H})}$, the maximum electrostatic potential of the hydrogen atom in solvent molecules; $f^{+}_{\max}$, the maximum condensed nucleophilic Fukui function; $s^{+}_{\max}$, the maximum nucleophilic condensed local softness. [b] Site: the atomic site with the maximum value of condensed nucleophilic Fukui function.

the maximum condensed nucleophilic Fukui function ($f^{+}_{\max}$) of the solvent molecule, and the maximum nucleophilic condensed local softness ($s^{+}_{\max}$) of the solvent molecule, are listed in Table 2. In light of the Klopman's concept[35] concerning chemical reactivity, the local reactivity descriptors can be grouped into two types such as charge-controlled ($\rho^{+}_{\max(\mathrm{H})}$, $V_{\max(\mathrm{H})}$) and frontier-controlled ($f^{+}_{\max}$, $s^{+}_{\max}$), connected with hard−hard and soft−soft interactions, respectively.

By considering the importance of electrostatic forces (hard−hard interactions) in solute−solvent systems, the atomic partial charge has been widely used to elucidate the intermolecular interactions in solution.[36] In a recent study, the atomic partial charge has been verified as a reliable local reactivity descriptor for the selectivity criteria of protonation reactions of several organic compounds.[37]

In a previous study from Galabov and Bobadova-Parvanova,[38] the hydrogen bonding between hydrogen fluoride and two series of molecules (nitrile and carbonyl compounds) was investigated using electrostatic potential as reactivity index. The results demonstrated that the electrostatic potential correlates excellently with the energy of hydrogen-bond formation.

From the values of the maximum positive charge ($\rho^{+}_{\max(\mathrm{H})}$) and maximum electrostatic potential ($V_{\max(\mathrm{H})}$) on the hydrogen atom shown in Table 2, it reveals that alcoholic solvents (methanol, ethanol, propan-1-ol, propan-2-ol, *t*-butanol) possess larger values of the maximum positive charge and maximum electrostatic potential on the hydrogen atom due to the strong bond polarity of the oxygen−hydrogen bond (O−H). For the chlorinated solvents, with an increase in the number of electronegative chlorine substituents, the maximum positive charge and maximum electrostatic potential on hydrogen atom will be increased (chloroform (0.241 and −1.036) > dichloromethane (0.205 and −1.059)). Furthermore, the electron delocalization carried out in the aromatic ring plays a role in reducing the electron-withdrawing capability of the substituted group ($-NO_2$ or $-C{\equiv}N$) in substituted aromatic solvents so that substantial trends in the values of the maximum positive charge and maximum electrostatic potential on hydrogen atom can be found as nitrobenzene (0.139 and −1.084) < nitromethane (0.172 and −1.057), benzonitrile (0.115 and −1.086) < acetonitrile (0.168 and −1.067).

Due to the high electron density on the carbonyl group in an acetone molecule, previous literature has shown that the most important property of organic solvents in interacting with acetone solute should be their Lewis acidity.[2c,5,13] The Lewis acidity of solvents can be conventionally explained by the Gutmann's acceptor number[9a] and has revealed the fact that active sites in solvents are those which are prone for nucleophilic attack. Therefore, the condensed nucleophilic Fukui function and nucleophilic condensed local softness are analyzed in the present study. For soft−soft interactions, the active site in a molecule should have the highest value of the Fukui function within the Li−Evans rules.[39] The atomic sites with the maximum condensed nucleophilic Fukui function obtained from the B3LYP/6-31G(d,p) method are also given by Table 2.

Multiple regression analyses have been carried out, and the regression equations are summarized in Table 3, considering the experimental carbonyl (C=O) stretching frequency data ($\nu_{\mathrm{C=O}}$)[5] as a dependent variable, and the solvation free energy ($\Delta G^{\circ}_{\mathrm{sol}}$), global interaction energy ($\Delta E_{\mathrm{int}(\lambda=1)}$), and local reactivity descriptors ($\rho^{+}_{\max(\mathrm{H})}$, $V_{\max(\mathrm{H})}$, $f^{+}_{\max}$, $s^{+}_{\max}$) as independent variables. The quality of the linear regression models is indicated by the coefficient of determination (R^2), standard deviation (SD), and ANOVA F-statistic (F). The ANOVA F-statistic is a ratio of the *variability between groups* divided by the *variability within groups*, testing if the means of the groups formed by values of the independent variable (or combinations of values for multiple independent variables) are different enough not to have occurred by chance. A larger F-statistic indicates that if we ran the test again we would come to the same results. F-statistic also reflects the effect of the independent variable (descriptors) on the dependent variable (observations). If the group means do not differ significantly then it is inferred that the independent variables did not have an effect on the dependent variable.[40] In this study, the F-statistic serves as a guide to determine which parameters produce statistically significant improvements in the fits.

As shown in Table 3, a poor correlation is obtained when the nonspecific solvation free energy is used as an only independent variable (eq 1). The R^2 is 0.464, SD is rather large (2.481), and F is rather small (16.449). For the Onsager's SCRF model, the solvent was represented as a continuous dielectric medium, characterized by a static dielectric constant. A reaction field in the solvent was induced by the dipole of the solute, which in turn interacted with the dipole. The reaction field was updated iteratively until self-consistency was achieved. This treatment met with limited success because the model did not give information about the site-specific effects in solute−solvent interactions.

Therefore, four single-parameter fits using local reactivity descriptors to consider the site-specific effects are further examined (eqs 2−5). In terms of charge-controlled descriptors ($\rho^{+}_{\max(\mathrm{H})}$, $V_{\max(\mathrm{H})}$), the use of $V_{\max(\mathrm{H})}$ ($R^2 = 0.691$, SD $= 1.883$, $F = 42.543$) is superior to that of $\rho^{+}_{\max(\mathrm{H})}$ ($R^2 = 0.555$, SD $= 2.261$, $F = 23.701$), and in terms of frontier-controlled descriptors ($f^{+}_{\max}$, $s^{+}_{\max}$), the use of $s^{+}_{\max}$ ($R^2 = 0.727$, SD $= 1.771$, $F = 50.541$) is superior to that of $f^{+}_{\max}$ ($R^2 = 0.624$, SD $= 2.079$, $F = 31.480$). However, the quality of these fits cannot arrive at the goal for the present quantitative predictions. By combining the nonspecific solvation free energy with the site-

TABLE 3: DFT-Based Linear Solvation Energy Relationships and the Regression Results[a]

eq	DFT-based LSERs	R^2	SD	F	N
1	$\nu_{C=O} = 8.50\Delta G^\circ_{sol} + 1722.8$	0.464	2.481	16.449	21
2	$\nu_{C=O} = -32.881\rho^+_{max(H)} + 1718.4$	0.555	2.261	23.701	21
3	$\nu_{C=O} = -70.759V_{max(H)} + 1636.5$	0.691	1.883	42.543	21
4	$\nu_{C=O} = -19.535f^+_{max} + 1718.0$	0.624	2.079	31.480	21
5	$\nu_{C=O} = -11.988s^+_{max} + 1719.5$	0.727	1.771	50.541	21
6	$\nu_{C=O} = 6.11\Delta G^\circ_{sol} - 25.802\rho^+_{max(H)} + 1724.6$	0.769	1.673	29.984	21
7	$\nu_{C=O} = 4.91\Delta G^\circ_{sol} - 56.150V_{max(H)} + 1658.2$	0.816	1.492	39.996	21
8	$\nu_{C=O} = 5.49\Delta G^\circ_{sol} - 15.282f^+_{max} + 1723.6$	0.787	1.606	33.319	21
9	$\nu_{C=O} = 4.73\Delta G^\circ_{sol} - 9.638s^+_{max} + 1724.0$	0.842	1.382	48.127	21
10	$\nu_{C=O} = 5.52\Delta G^\circ_{sol} - 11.822\rho^+_{max(H)} - 9.557f^+_{max} + 1724.1$	0.806	1.578	23.544	21
11	$\nu_{C=O} = 4.82\Delta G^\circ_{sol} - 8.005\rho^+_{max(H)} - 7.501s^+_{max} + 1724.3$	0.853	1.373	32.942	21
12	$\nu_{C=O} = 4.78\Delta G^\circ_{sol} - 36.392V_{max(H)} - 7.050f^+_{max} + 1681.3$	0.841	1.426	30.083	21
13	$\nu_{C=O} = 4.33\Delta G^\circ_{sol} - 27.935V_{max(H)} - 6.086s^+_{max} + 1691.4$	0.878	1.250	40.876	21
14	$\nu_{C=O} = 5.34\Delta G^\circ_{sol} - 0.53\Delta E_{int(\lambda=1)} - 33.569\rho^+_{max(H)} + 1705.9$	0.838	1.444	29.208	21
15	$\nu_{C=O} = 4.16\Delta G^\circ_{sol} - 0.43\Delta E_{int(\lambda=1)} - 67.112V_{max(H)} + 1630.0$	0.866	1.311	36.639	21
16	$\nu_{C=O} = 4.05\Delta G^\circ_{sol} - 0.72\Delta E_{int(\lambda=1)} - 22.160f^+_{max} + 1697.6$	0.901	1.128	51.453	21
17	$\nu_{C=O} = 4.04\Delta G^\circ_{sol} - 0.41\Delta E_{int(\lambda=1)} - 11.294s^+_{max} + 1709.2$	0.889	1.192	45.503	21
18	$\nu_{C=O} = 4.05\Delta G^\circ_{sol} - 0.74\Delta E_{int(\lambda=1)} - 13.738\rho^+_{max(H)} - 15.714f^+_{max} + 1697.5$	0.926	1.005	49.992	21
19	$\nu_{C=O} = 4.00\Delta G^\circ_{sol} - 0.54\Delta E_{int(\lambda=1)} - 15.590\rho^+_{max(H)} - 7.666s^+_{max} + 1705.1$	0.925	1.009	49.533	21
20	$\nu_{C=O} = 3.43\Delta G^\circ_{sol} - 0.70\Delta E_{int(\lambda=1)} - 34.199V_{max(H)} - 14.232f^+_{max} + 1658.6$	0.949	0.838	73.722	21
21	$\nu_{C=O} = 3.34\Delta G^\circ_{sol} - 0.51\Delta E_{int(\lambda=1)} - 36.503V_{max(H)} - 7.060s^+_{max} + 1663.0$	0.948	0.846	72.249	21

[a] R^2, the coefficient of determination; SD, standard deviation; F, ANOVA F-statistic; N, sample numbers.

specific local reactivity descriptors (eqs 6−9), although all of the R^2's and SDs are moderately improved, the ANOVA F-statistic does not exhibit significant increases. In addition, when combining the charge-controlled and frontier-controlled descriptors (eqs 10−13), the R^2 and SD can be slightly improved, whereas the ANOVA F-statistic does not show obvious increases in these cases. In comparison the regressive results of eqs 6−9 with those of eqs 14−17, when the global interaction energy ($\Delta E_{int(\lambda=1)}$) is introduced (eqs 14−17), only the regressive equation containing f^+_{max} (eq 16) is satisfactory for the ANOVA F-statistic increment ($F = 51.453$, as compared with eq 8, $F = 33.319$).

Consequently, the solvation free energy, global interaction energy, and both the charge-controlled and frontier-controlled local reactivity descriptors are combined together (eqs 18−21). The statistical results show that the regressive equations containing $V_{max(H)}$ are superior to those containing $\rho^+_{max(H)}$. The R^2's are 0.949 and 0.948, SDs are 0.838 and 0.846, and F's are 73.722 and 72.249 for eqs 20 and 21, respectively. In order to determine the cross-correlation of the descriptors and to show the predictive capability for eqs 20 and 21, the variance inflation factor (VIF), t score, and cross-validated R^2 (R_{cv}^2) are provided in Table 4. The variance inflation factor is defined as $\text{VIF}_j = 1/(1 - R_j^2)$, where R_j is the correlation coefficient for that particular descriptor j in terms of the others.[41] As determined by the VIF, the cross-correlation of descriptors is minimized (the closer to 1.0 the better). A value of under 5.0 is considered acceptable, and over 10.0 reveals an unstable regression where the cross-correlation of the descriptors is existed. The observed and predicted (using eqs 20 and 21) values with residuals are listed in Table 5. These results thus demonstrate the feasibility of eqs 20 and 21 for predicting carbonyl (C═O) stretching frequencies of acetone in various organic solvents.

TABLE 4: Variance Inflation Factor (VIF), *t* Score, and Cross-Validated R^2 (R_{cv}^2) for Eqs 20 and 21

parameter		eq 20	eq 21
ΔG°_{sol}	VIF	1.3	1.4
	t score	4.17	4.01
$\Delta E_{int(\lambda=1)}$	VIF	1.6	1.3
	t score	−5.77	−4.60
$V_{max(H)}$	VIF	3.4	3.2
	t score	−3.85	−4.22
f^+_{max} (or s^+_{max})	VIF	4.0	3.1
	t score	−5.06	−4.99
R_{cv}^2 [a]		0.903	0.897

[a] R_{cv}^2: cross-validated R^2 ($R_{cv}^2 = 1 - (\sum_i(Y_i^{pred} - Y_i^{obs})^2)/(\sum_i(Y_i^{obs} - Y^{mean})^2)$), where Y_i^{obs}, Y_i^{pred}, and Y^{mean} are the observed, predicted, and the observed mean values of the dependent variables, respectively. For calculating Y_i^{pred}, the leave-one-out (LOO) method is adopted (ref 22c).

As mentioned earlier, three basic terms of contributions to solute−solvent interactions have been proposed in previous literatures: volume, dipolarity/polarizability (for dispersion interaction), and hydrogen-bonding terms. Kamlet and co-workers suggested that the volume term is an energetic measure needed to form a cavity for the solute in the solvent.[42] However, Abraham and other authors later suggested that the volume term also contains the contribution in dispersion.[43] Despite the statistical significance of polarizability-related descriptors in previous correlations, the C═O stretching frequency decreases with the Koppel−Palm polarizability calculated from the solvent's refractive index and the KTA LSER dipolarity/polarizability (π^*), whereas it increases with Famini and co-workers TLSER polarizability index (π_I).[13] In addition, the Kamlet−Taft expression has been criticized for not separating specific and nonspecific effects.[4a] Alternative approaches that separate specific and nonspecific effects have also been addressed by Koppel and Palm,[1a] Fawcett,[4a] Reichardt,[44] and by Drago and co-workers.[45] Furthermore, the frontier molecular orbital (FMO) theory has been proven to fail to describe the reactivity and regioselectivity in particular organic reactions. As an alternative to FMO theory, the formulation of the interaction energy in terms of DFT and the HSAB principle has been used to study reactivity and regioselectivity in 1,3-dipolar cycloaddition reactions.[30a] It has been found that the interaction energy is dominated by the reshuffling of the charge distribution term instead of the charge-transfer process. Charge reshuffling interaction is more important to rationalize the reactivity and regioselectivity than FMO.

TABLE 5: Observed and Predicted Carbonyl (C═O) Stretching Frequencies (in cm^{-1}) of Acetone in Various Organic Solvents with Residual Using Eqs 20 and 21

solvent	observed[a]	eq 20		eq 21	
		predicted	residual	predicted	residual
acetone	1711.8	1712.4	−0.6	1712.5	−0.7
dimethyl sulfoxide	1709.1	1709.5	−0.4	1709.2	−0.1
chloroform	1710.3	1711.7	−1.4	1711.0	−0.7
dichloromethane	1711.8	1711.0	0.8	1710.8	1.0
1,2-dichloroethane	1712.4	1712.4	0.0	1712.3	0.1
acetonitrile	1712.9	1713.8	−0.9	1713.9	−1.0
benzonitrile	1712.3	1711.8	0.5	1712.1	0.2
nitromethane	1712.0	1712.4	−0.4	1711.9	0.1
nitrobenzene	1712.3	1711.5	0.8	1711.2	1.1
benzene	1715.4	1716.3	−0.9	1716.6	−1.2
hexane	1721.3	1720.8	0.5	1720.7	0.6
diethylether	1718.7	1717.6	1.1	1717.5	1.2
dimethylformamide	1713.5	1712.5	1.0	1712.4	1.1
dimethylacetamide	1713.0	1713.2	−0.2	1713.2	−0.2
hexamethylphosphoramide	1713.0	1714.4	−1.4	1714.4	−1.4
propylene carbonate	1713.5	1713.4	0.1	1713.5	0.0
methanol	1707.2	1707.1	0.1	1707.6	−0.4
ethanol	1708.2	1708.0	0.2	1708.2	0.0
propan-1-ol	1708.2	1708.5	−0.3	1708.6	−0.4
propan-2-ol	1709.7	1709.3	0.4	1709.3	0.4
t-butanol	1711.2	1710.5	0.7	1710.4	0.8

[a] Observed C═O stretching frequency (ν_3) of acetone from ref 5.

Through the present approach, the solute−solvent interactions may be described in terms of the nonspecific and specific effects, vindicating Koppel and Palms' concept. The positive coefficient for $\Delta G°_{\text{sol}}$ indicates that the C═O stretching frequency decreases with increase of the dielectric screening effects of solvents on a solute (i.e., more negative the solvation free energy). For molecular-specific effects, many important concepts and useful indices for understanding chemical reactivity have been rationalized within the framework of conceptual DFT. The results based on the electronegativity equalization principle and the principle of maximum hardness may be very useful to analyze the inherent chemical reactivity of a given solute−solvent system, because it leads to reasonable estimates of the global interacting energy between the solute and the solvent. The negative coefficient for $\Delta E_{\text{int}(\lambda=1)}$ indicates the C═O stretching frequency decreases with increase of the softness (or polarizability) of solute and solvent molecules (i.e., less negative the global interaction energy). It is consistent with the results predicted using the Koppel−Palm polarizability calculated from the solvent's refractive index and the KTA LSER dipolarity/polarizability.

By employing the Klopman's concept and the Li−Evans rules, the present approach elucidates the local charge-controlled and frontier-controlled contributions for solvent acidity. DFT-based local reactivity descriptors are useful to study site-specific effects. From the knowledge of the local properties of isolated species, they may provide information about the behavior of the different reactive sites of a chemical species with respect to different reactants. The Fukui function represents how the local electron density rearranges as a change in the total number of molecular electrons. The local softness represents the sensitivity of the local electron density to a change in electronic chemical potential and describes both the local charge redistribution within the reactants themselves and the local charge transfer between the reactants. The coefficients for $\rho^{+}_{\max(\text{H})}$ (or $V_{\max(\text{H})}$) and $f^{+}_{\max}$ (or $s^{+}_{\max}$) can be interpreted in terms of the properties of the solute. The negative coefficients indicate the C═O stretching frequency decreases with increase in the charge-controlled and frontier-controlled contributions for solute basicity, respectively.

IV. Conclusions

This work represents the application of the conceptual DFT in constructing LSER for predicting carbonyl (C═O) stretching frequencies of acetone in various organic solvents. Four-parameter regressive models based on the nonspecific solvation free energy, global interaction energy, maximum electrostatic potential of the hydrogen atom, and maximum condensed nucleophilic Fukui function (or maximum nucleophilic condensed local softness), calculated with the hybrid functional B3LYP method, have been derived and were shown to have excellent predictive power.

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