

On the Hardness Evaluation in Solvent for Neutral and Charged Systems

G. De Luca,[†] E. Sicilia,[†] N. Russo,^{*†} and T. Mineva[‡]

Contribution from the Dipartimento di Chimica, and Centro di Calcolo ad Alte Prestazioni per Elaborazioni Parallele e Distribuite-Centro d'Eccellenza MURST, Università della Calabria, I-87030 Arcavacata di Rende (CS), Italy, and Institute of Catalysis, Bulgarian Academy of Sciences, Bul G. Bonchev bl.11, 1113 Sofia, Bulgaria

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Abstract: The influence of water on the hardness values of a series of neutral and charged molecules has been studied in the framework of density functional theory using the polarizable continuum model to take into account solvent effects. Three working formulas already widely tested in gas-phase have been used and the results compared. Two of the methods employed going from gas phase to solvent phase give values that do not change, while the results of the third method show remarkable changes. To check the reliability of the hardness behavior found, a test based on the hard-soft/acid-base principle and the calculation of the free energy of reaction has been applied using the adopted procedures.

Introduction

Qualitative concepts such as hardness (η), softness (S), and chemical potential (μ), which have proved useful in many ways, have found a rigorous theoretical definition in the framework of density functional theory (DFT).¹ It has been demonstrated by Parr and co-workers² that the chemical potential and the hardness represent the first and second derivative of the energy (E) with respect to the number of electrons (N). Since these derivatives are difficult to evaluate for atomic or molecular systems, several working formulas have been proposed. Most of these formulas, within DFT,¹⁻⁵ HF,⁶ or semiempirical approaches,⁷ are based on the finite difference approximation, in which the change of one electron is usually involved $\Delta N = \pm 1$. Employing an integer electron change, rather than an infinitesimally small change on N , often leads to misleading chemical interpretations^{8,9} due to the rough approximation in the calculation of these derivatives. Other computational schemes^{10,11} have been proposed to improve the previous

approach, using fractional occupation numbers based on the Janak's extension of DFT.¹²

These theoretical and working definitions have been widely applied in gas phase to describe many chemical phenomena,¹³⁻²³ but the role of solvent interactions in modifying reactivity indices, undoubtedly of fundamental importance, has not yet been treated in depth.^{14,15,24-29} Since chemical reactions occur mainly in solution, taking into account the changes of reactivity indices, going from gas to solvent phase, permits the elucidation of the actual reactivity of the compounds.

This work is an attempt to quantitatively examine, for the first time, the changes in the hardness values induced by the presence of the solvent. Several approaches have been applied and the differences in their results compared. The performance of the hardness working formulas have been tested against some chemical reactions for which the hard and soft acids and bases

[†] Università della Calabria.

[‡] Bulgarian Academy of Sciences.

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(HSAB)³⁰ principle is verified. In these reactions, a series of soft bases³¹ is used to remove a hard base from a soft acid. As a result, the free energy of reaction gives a measure of the softness of the base. Taking into account the solute–solvent interactions, the hydration free energies have been computed, within DFT, using the polarizable continuum model (PCM).³² As a consequence of the improved reliability of quantum-mechanical tools in treating solvent effects,^{33–35} a quantitative correlation between the softness of the bases, computed with the same methods and hydration free energies can be now established.

To achieve this goal, the hardness of several neutral and charged systems have been calculated to underline the main theoretical differences between the approaches used. The first operational formula used was the classical finite difference approximation, in which the change of N is made equal to one, to evaluate the second-order derivative of the energy with respect to the number of electrons.² Setting N equal to one implies that electron affinity and ionization potential, experimentally available properties, can be used in these formulas, (EA/IP). The second is based on Koopman's theorem, which allows us, according to MO theory, to use the HOMO and LUMO energies rather than the ionization potentials and electron affinities (H/L). As a third method a computational scheme dealing with fractional occupation numbers, the internally resolved hardness tensor approach (IRHT),^{10,11} has been employed.

The choice of these operational methods, but it is connected to the problems that these approaches show when they are applied in solution.³⁶ Indeed, the comparison between the results of the aforesaid methods can give a better insight into their performance in solution. At the same time, this comparative study could pave the way to improve the early basic approximation to use the gas-phase values of η also in solution.

Method

Parr has shown that for every chemical system, there is a quantity μ called the electronic chemical potential, which must be constant everywhere in such a system. He has also shown that μ is the first derivative of the total energy with respect to the number of electrons N :

$$\mu = (\partial E/\partial N)_v = (\partial E/\partial \rho)_v \quad (1)$$

thus, μ is simply the instantaneous value of the slope of E vs N at any value of N . The method of finite differences can be used to estimate this slope:

$$\mu = (\partial E/\partial N)_v \approx \frac{E(N+h) - E(N-h)}{2h} \quad (2)$$

Since we only know the experimental energy for integral values of N , from data such as ionization potentials (I) and electron affinities (A), it is useful to set h equal to one, and then through a simple rearrangement, we can obtain the following expression:

$$\mu = \frac{E(N+1) - E(N-1)}{2} = -\frac{I+A}{2} \quad (3)$$

The chemical potential changes as the number of electrons changes; thus, from the finite difference method, these changes (the curvature) are equal to $(I-A)$ with $h = 1$. This curvature is strictly connected to the HSAB principle and gives the rigorous definition of hardness:

$$\eta = \frac{1}{2} \left(\frac{\partial \mu}{\partial N} \right)_v = \frac{1}{2} \left(\frac{\partial^2 E}{\partial N^2} \right)_v \quad (5)$$

and according to the three-point finite difference approximation, we obtain the working formula:

$$\eta = \frac{I-A}{2} \quad (6)$$

In the context of molecular orbital theory, using Koopman's approximation, eqs 3 and 6 can be further simplified using the negative of the eigenvalues (ϵ) of the highest occupied (ϵ_{HOMO}) and lowest unoccupied (ϵ_{LUMO}) orbitals instead of I and A . Therefore, the previous definitions become:

$$\begin{aligned} \mu &= \frac{\epsilon_{\text{LUMO}} + \epsilon_{\text{HOMO}}}{2} \\ \eta &= \frac{\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}}{2} \end{aligned} \quad (7)$$

In formulas 6 and 7 the change of one electron is considered, and as has already been mentioned,⁸ inconsistent behavior of the reactivity indices can be observed. Moreover, concerning the latter definitions we need to consider that, in the framework of DF theory, the Kohn–Sham orbitals are different from the canonical molecular orbitals.¹

A proven method for the construction of the internally resolved hardness tensor (IRHT)¹⁶ within DFT formalism has been employed to calculate global hardness. The main scheme of the IRHT procedure is outlined below.

The generalization of Slater's³⁷ transition state approach through Janak's theorem

$$\epsilon = \left(\frac{\partial E}{\partial n_i} \right)_{i=1,\dots,N} \quad (8)$$

has introduced the possibility to extend DFT to noninteger occupation numbers and has provided the physical and mathematical justification for expanding the energy functional in a Taylor series around the state characterized by the corresponding set of occupation numbers $n^0 = (n_1^0, n_2^0, \dots, n_k^0)$ and by the corresponding KS-eigenvalues $\epsilon^0 = (\epsilon_1^0, \dots, \epsilon_k^0)$. In this series, the first derivatives of the energy functional with respect to the occupation numbers have the meaning of the KS-eigenvalues, and the second derivatives:

$$\frac{\partial^2 E}{\partial n_i \partial n_j} = \eta_{ij} \quad (9)$$

give the hardness matrix elements.

It is then simple to express the hardness matrix elements as the derivatives of the KS-orbitals (i.e., the ij th element of the hardness matrix can be now obtained as the first derivative of ϵ_i with respect to n_j):^{10,16}

$$\eta_{ij} = \frac{\partial \epsilon_i}{\partial n_j} \quad (10)$$

and to approximate them numerically using the finite difference formula:

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$$\eta_{ij} = \frac{\epsilon_i(n_j - \Delta n_j) - \epsilon_i(n_i)}{\Delta n_j} \quad (11)$$

The latter expression takes into account the energy variation of the i th orbital due to the j th occupation number variation.

From the hardness matrix, one can calculate the total hardness value via the calculation of the softness matrix, that is:

$$[s_{ij}] = [\eta_{ij}]^{-1} \quad (12)$$

Since the total softness is obtained as an integral of the local softness, S can be obtained from the following approximation:

$$S = \sum_{ij} s_{ij} \quad (13)$$

thus the total hardness becomes:

$$\eta = \frac{1}{S} = \frac{1}{\sum_{ij} s_{ij}} \quad (14)$$

Computational Details

Two kinds of approaches are commonly used to theoretically treat solute–solvent interactions: classical ensemble and quantum mechanical continuum models.³² In continuum methods, the solvent is considered as a continuum with a uniform dielectric constant (ϵ) surrounding a solute molecule, which is placed in a cavity, and the proposed approaches differ only in the way the cavity and the reaction field of the solvent are defined. In this work we have adopted the model proposed by Tomasi and co-workers,^{32,38} the polarized continuum model (PCM). The cavity is defined as interlocking atomic spheres constructed using van der Waals radii, and the effect of the polarization of the solvent is calculated by numerical differentiation. To bypass the arbitrary choice of the cavity, implicit in this model, we carried out the fitting of the radii with respect to experimental free-solvation energy of the studied systems, to find the optimal radii. In all the calculations water was chosen as the solvent.

The results presented here have been obtained using the Gaussian 98 software package³⁹ and a modified version of the deMon code⁴⁰ called deMonCs, which includes the PCM algorithm and the possibility to set fractional occupation numbers which are needed to calculate global hardness and softness with the IRHT method. We have chosen the PCM method as the tool to study solvent effects because it is implemented in both of the codes used.

All calculations were performed employing the gradient-corrected functional of Becke⁴¹ and Perdew⁴² (B88-P86), whereas the Coulomb energy was calculated by a variational fitting procedure.^{43,44} For the

Table 1. Calculated Hardness, in eV, from Internally Resolved Hardness Tensor (η_{IRHT}), HOMO–LUMO Energy Gap ($\eta_{\text{H/L}}$), and Finite Difference Approximation ($\eta_{\text{EA/IP}}$) for Neutral Systems

system	η_{IRHT}		$\eta_{\text{H/L}}$		$\eta_{\text{EA/IP}}$	
	gas	sol	gas	sol	gas	sol
H ₂ O	8.49	8.49	4.01	4.37	8.35	4.72
NH ₃	7.60	7.84	3.72	4.06	7.52	4.18
HCN	6.97	6.92	3.97	4.03	8.25	4.92
CH ₃ OH	5.84	6.02	3.57	3.81	7.14	4.01
CH ₃ NH ₂	5.31	5.46	3.36	3.59	6.67	3.60
CH ₃ SH	4.70	4.79	2.66	2.76	5.94	3.27

Table 2. Calculated Hardness, in eV, from Internally Resolved Hardness Tensor (η_{IRHT}), HOMO–LUMO Energy Gap ($\eta_{\text{H/L}}$), and Finite Difference Approximation ($\eta_{\text{EA/IP}}$) for Cations

system	η_{IRHT}		$\eta_{\text{H/L}}$		$\eta_{\text{EA/IP}}$	
	gas	sol	gas	sol	gas	sol
H ₃ O ⁺	10.02	10.07	5.44	5.50	10.07	5.94
NH ₄ ⁺	9.02	8.99	7.38	7.28	11.44	7.90
CH ₃ NH ₃ ⁺	6.05	6.09	5.05	5.39	8.55	5.93
CH ₃ OH ₂ ⁺	5.85	6.67	4.04	4.09	7.73	4.40
CH ₃ SH ₂ ⁺	5.04	5.05	3.86	3.87	7.35	4.30

Table 3. Calculated Hardness, in eV, from Internally Resolved Hardness Tensor (η_{IRHT}), HOMO–LUMO Energy Gap ($\eta_{\text{H/L}}$), and Finite Difference Approximation ($\eta_{\text{EA/IP}}$) for Anions

system	η_{IRHT}		$\eta_{\text{H/L}}$		$\eta_{\text{EA/IP}}$	
	gas	sol	gas	sol	gas	sol
OH [−]	7.64	7.84	2.91	3.80	6.95	3.42
NH ₂ [−]	5.83	5.89	2.44	3.08	5.93	2.68
CH ₃ O [−]	5.29	6.09	3.18	3.54	6.00	3.10
CN [−]	4.91	5.06	2.64	3.32	6.73	3.42
CH ₃ S [−]	4.57	3.46	2.04	2.60	4.91	2.57

fitting of the density function the A3 auxiliary basis set was coupled with the TZVP⁴⁵ orbital basis set.

All molecular structures were fully optimized in the gas-phase and in the solvent using analytical energy gradients and the Beryni quasi-Newton update with redundant internal coordinates.⁴⁶ The structure optimization convergence, in both environments, was based on the gradient thresholds of 4×10^{-5} and the displacement vectors with thresholds of 10^{-4} , whereas the energy convergence threshold for the self-consistent field procedure was set to 10^{-7} .

To calculate hardness values with the IRHT approach only occupied valence orbitals have been taken into account, setting the variation of the occupation number, Δn , equal to 0.25. The vertical values of I and A have been calculated by the energy difference method, where separate calculations were carried out for neutral and ionic species.

Results and Discussion

The hardness values for a series of neutral molecules, cations, and anions are reported in Tables 1, 2 and 3, respectively.

It can be seen at once that the η values, obtained by IRHT and H/L methods, are nearly unchanged in solution with respect to the gas-phase, whereas the $\eta_{\text{EA/IP}}$ values show a noticeable difference. However, the variations given by the H/L method are slightly more significant than those obtained by the IRHT. After an analysis of these tables, two important aspects clearly appear: the trend in the variation is seen for both charged and

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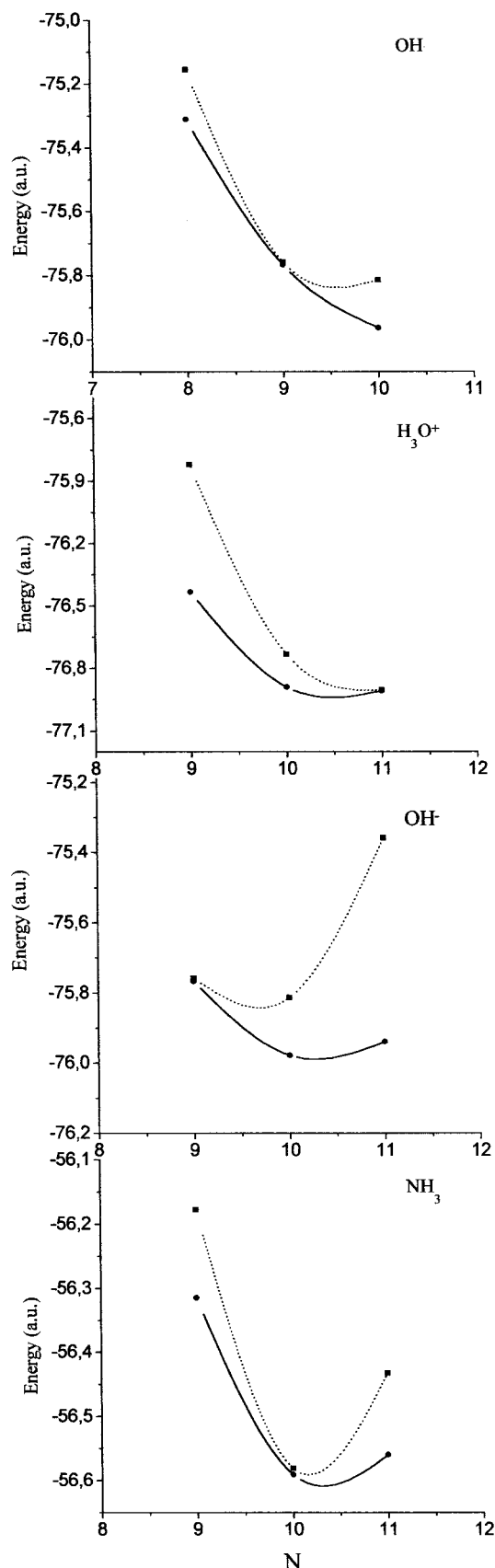


Figure 1. Plot of the gas-phase (dot line) and solvent (solid line) free energy (kcal/mol) as a function of number of electrons (N) for neutral (NH_3), anionic (OH^-), cationic (H_3O^+), and radical ($\text{OH}\cdot$) systems.

neutral systems and the ordering of the hardness values is conserved for neutral and partially conserved for charged

compounds, for each method used in going from the gas to the solution phase.

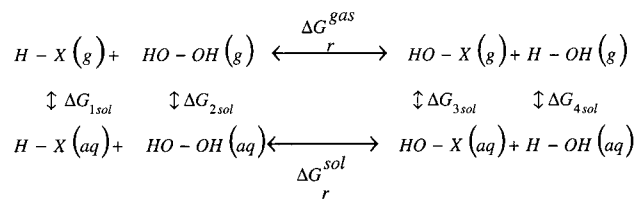
Concerning the observed variation in the case of the $\eta_{\text{EA/IP}}$ values, the results of our computations both confirm, and extend to charged systems, the conclusion of Pearson that the compounds seem much softer in water than in the gas phase.^{13,36} Intuitively, this behavior for neutral molecules can be understood because of the stabilization induced by the solvent on the resultant charged species. Analogous behavior, although less obvious,²⁵ has been found for charged systems. If a plot of the free energy as a function of N , for a series of neutral, charged, and radical systems is drawn (see Figure 1, a, b, c, and d), it is evident that the curvature ($\partial^2 G/\partial N^2$) in solvent is smaller in all cases.

The negligible change of the η_{HL} values agrees with the trend previously surmised^{13,36} on the basis of solvation effects on the absorption maxima in vis/UV spectra. The important energy difference between the ground state and the excited state remains about the same, even if from our computations we note that the orbital energies are shifted upward by the same small amount in solvent.

To understand the hardness pattern obtained through the IRHT approach we need to bear in mind that this method is based on the calculation of the hardness matrix, whose elements are defined according to eq 11. In this case, differences in energy between the perturbed orbitals are involved but, similar to those from the H/L method, these differences both in the gas phase and in solution remain almost equal.

Considering the pronounced variations of $\eta_{\text{EA/IP}}$ values, we can conclude that the approaches involving energy differences among orbitals, perturbed or not, do not give substantial changes, whereas if total energy differences are considered then marked changes are observed. The $\eta_{\text{EA/IP}}$ values in solution obtained as a result of these changes, have little practical utility, as previously pointed out by Pearson,³⁶ who suggests, in absence of any definitive information, the use of the EA/IP formula with the gas electron affinity and ionization potential values. Therefore, we may construct a quantitative test to fill this gap in our knowledge.

Since many molecules and ions have already been labeled as hard or soft as a result of their chemical behavior³¹ and it has been shown that several theoretical evaluations of hardness are also possible,^{15,16,19,25} a correlation between the two ways to classify molecules as hard or soft can be explored. Driven by this aim, we have selected several reactions in which a soft base removes a hard base from a soft acid. The bases have been chosen by taking into account their general classification into two groups, which reflects their chemical properties.³¹ The general scheme of the selected reactions is



In Table 4 the hydration free energies (ΔG_{sol}) of the reactants, $\text{H}-\text{X}$, and the products, $\text{HO}-\text{X}$, and the reaction free energy in the gas-phase, ΔG_r^{gas} , and in solution, ΔG_r^{sol} , are reported.

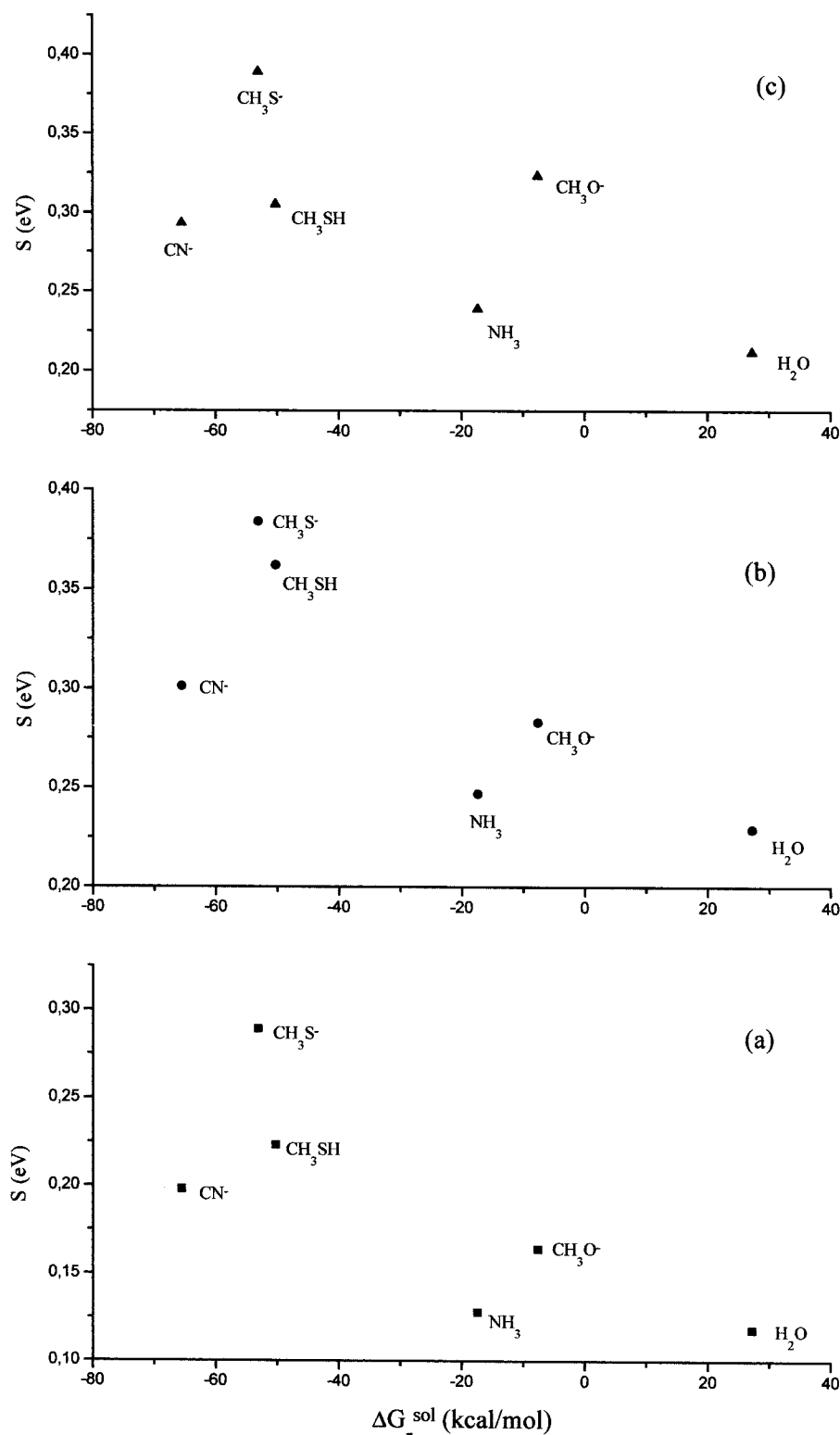


Figure 2. Softness values, in eV, calculated with IRHT (a), H/L (b), and EA/IP (c) methods, respectively as a function of solvation free energies, in kcal/mol, of probe bases (CN⁻, CH₃S⁻, CH₃SH, NH₃, CH₃O⁻ and H₂O).

The corresponding reaction free energy in water can be calculated the thermodynamic cycle:

$$\Delta G_r^{\text{sol}} = -\Delta G_{1\text{sol}} - \Delta G_{2\text{sol}} + \Delta G_r^{\text{gas}} + \Delta G_{3\text{sol}} + \Delta G_{4\text{sol}} \quad (15)$$

where $\Delta G_{2\text{sol}}$ and $\Delta G_{4\text{sol}}$ are respectively calculated to be -7.6 and -8.4 kcal/mol. The use of eq 15, rather than a direct

calculation of reaction free energy in the solvent, allows the different energetic contributions to this process to be highlighted. The calculated DF ΔG_r^{sol} values mirror the early classification of bases as soft or hard and are reported in the literature. As a consequence, this scheme can be used as a tool to test the methods used. According to the above scheme, we would image that the more negative ΔG_r^{sol} the softer the base X. Finally, in

Table 4. Calculated BP86 Hydration Free Energies of Reactants and Products and Reaction Free Energies^a in Gas Phase and in Solution

system (X)	ΔG_{1sol}	ΔG_{2sol}	ΔG_r^{gas}	ΔG_r^{sol}
CN ⁻	-3.7	-10.1	-58.3	-65.5
CH ₃ S ⁻	-1.7	-5.7	-48.3	-53.1
CH ₃ SH	-73.3	-74.0	-48.8	-50.2
NH ₃	-82.2	-85.7	-13.2	-17.4
CH ₃ O ⁻	-5.7	-5.3	-7.2	-7.6
H ₂ O	-98.2	-89.6	19.4	27.2

^a All the values are in kcal/mol.

Table 5. Calculated Softness (eV) from Internally Resolved Hardness Tensor (S_{IRHT}), HOMO–LUMO Energy Gap ($S_{H/L}$), and Finite Difference Approximation ($S_{EA/IP}$) for Neutral Systems and Reaction Free Energies in Solution (kcal/mol)

system (X)	S_{IRHT}	$S_{H/L}$	$S_{EA/IP}$	ΔG_r^{sol}
CN ⁻	0.20	0.30	0.29	-65.5
CH ₃ S ⁻	0.29	0.38	0.39	-53.1
CH ₃ SH	0.22	0.36	0.31	-50.2
NH ₃	0.13	0.25	0.24	-17.4
CH ₃ O ⁻	0.16	0.28	0.32	-7.6
H ₂ O	0.12	0.23	0.21	27.2

Table 5 the softness values of the probe bases, calculated using the working formulas are shown, while the Figure 2 shows a plot of ΔG_r^{sol} versus softness value.

The results reported in Figure 2 clearly show that, in agreement with the classical arrangement of compounds based on their chemical behavior, it is possible to place the probe bases into two groups, using the IRHT and H/L approaches, although the softness trend in each group is not well reproduced. On the other hand, the chemical classification into two groups does not work with the EA/IP method. It is worth noting that the driving force of the considered reactions is the intrinsic softness of the bases, while the solvation energies, which even though they contribute to ΔG_r^{sol} , are less relevant.^{13,29} In this way, the

correlation between softness and the solvation free energy can be considered reliable to test the working formulas for softness quantification.

From the results obtained in this work, it seems clear that the EA/IP formula applied in solution must be used with caution, as underlined by Pearson.³⁶ Moreover, it is desirable that the performance of other methods for the calculation of global hardness be tested with respect to the chemical reactivity, before predictions of hardness changes on going from the gas to the solvent phase are made.

Conclusion

This work has highlighted that, for both neutral and charged species, using methods based on the orbital energies (IRHT, H/L), there is a small dependence of hardness values on the solvent environment. The method based on total energy differences (EA/IP) does not, however, give the same results.

A complete theoretical scheme, based on the calculation of ΔG_r^{sol} , can provide a useful tool to verify if the working formulas employed for hardness computations give results compatible with the general classification of compounds as hard or soft, based on their chemical behavior. Consequently, from the correlation between such ΔG_r^{sol} values and the theoretical hardness, it follows that the IRHT and H/L results give a screening of the examined bases according to the expectations based on the qualitative chemical description of such systems. On the contrary, this is not true for the EA/IP method. Since none of the applied approaches provides a more accurate grading, then an improvement of the operational definitions of hardness in solvent should be formulated.

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