Global and Local Analysis of the Gas-Phase Acidity of Haloacetic Acids

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The relative gas-phase acidity of halosubstituted acetic acids CH_2XCO_2H, CHX_2CO_2H and CX_3CO_2H ($X =$ F, Cl, and Br) is analyzed in terms of global and local descriptors of reactivity. The model is based on the analysis of proton-transfer equilibria with reference to acetic acid CH_3CO_2H. The relative acidity pattern displayed by this series is rationalized in terms of the hard and soft acids and bases principle. The relative stability between the neutral species and the corresponding anions is in agreement with the maximum hardness principle. Charge transfer between the conjugated bases present in the proton-transfer equilibria is correctly accounted for by using a classical ion-transport model that introduces the electronic chemical potential of transfer. The local reactivity analysis based on regional Fukui functions and local softness displays a good correlation with the experimental gas-phase acidity within the series.

1. Introduction

It has been well-established that the relative acidity of haloacetic acids with reference to acetic acid in the gas phase is determined by the electronic substituent effects promoted by the presence of an increasing number of halogen groups in the molecule.[1−3] The gas-phase acidity of acetic acid and derivatives may be quantitatively represented by the proton affinity (PA), defined as the enthalpy change for the heterolytic cleavage reaction 1

$$RCO_2H \rightleftharpoons RCO_2^- + H^+; \quad PA = \Delta H \qquad (1)$$

for $R = CH_3$, CH_2X, CHX_2, and CX_3; $X =$ F, Cl, and Br. This series may be used as a useful source to study the intrinsic effects of the substituents on equilibrium 1. Substituent effects on the acidity of this series have been studied in detail by Charton.[4,5] This author reported that the effect of an sp^3 carbon atom between the substituent and the π-bonded carboxylic moiety was sufficient to prevent the delocalization effect. The acidity pattern displayed by these compounds may then be almost completely determined by the electronic inductive effects promoted by substitution at the alkyl group. However, the linear free energy analysis performed by Charton was based on the pK_a values of these acids, and therefore it contained in some implicit way the effect of the solvent. Gas-phase acidity data for some members of this series are available from the experimental work reported by Topsom, Taft, et al.[6] Therein, it was shown that the intrinsic acidity pattern was also strongly dependent on the inductive effect of the substituent, with the possibility that a small polarizability effect could be also operative in the gas phase. Another pertinent experimental source for the study of the intrinsic acidity pattern in the halosubstituted acetic acids is that reported by Kebarle et al.[7] In that work, the gas-phase acidity of aliphatic carboxylic acids, including some haloacetic species, was studied from proton-transfer equilibria data recorded from pulsed electron high-pressure mass spectrometer (PHPMS) experiments. The proton-transfer equilibria with reference to acetic acid is shown in eq 2

$$CH_3CO_2H + RCO_2^- \leftrightarrow CH_3CO_2^- + RCO_2H; \quad \Delta H^\circ = \delta PA \quad (2)$$

where $\delta PA = PA(CH_3CO_2^-) - PA(RCO_2^-)$. The main results obtained from that study were the following: (a) In the absence of solvent effects, the polarizability of the substituent becomes very important. The increasing polarizability of these groups leads to the enhanced gas-phase acidity. (b) Within the CHX_2CO_2H series, the introduction of a second X group provides a somewhat smaller increase of acidity than the first one. This result was associated with the effective decrease of the negative charge on the CO_2^- moiety promoted by the X_2 substituents, which attenuates the stabilizing effect of their polarizabilities. (c) On the basis of these results, almost equal acidity in the CX_3CO_2H acids for $X =$ F, Cl, and Br was predicted.[7]

Theoretical studies on the substituent effects and their relationship with the gas-phase acidity in the haloacetic series have been presented in the literature.[8−10] For instance, in a recent study, Geerlings et al.[8] proposed a simple model to explain both gas- and solution-phase acidity of the substituted acetic acids CH_2XCO_2H, based on group hardness and electronegativity analysis. Calculated parameters, which are a measure of local hardness and softness, were used to interpret the acidity pattern of substituted acetic acids, in the framework of the hard and soft acids and bases (HSAB) principle. In the gas phase, local softness at the X group plays an important role in the relative acidity shown by these systems.[8]

In this work we propose a global and local analysis of the relative gas-phase acidity displayed by the series RCO_2H; for

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$R = CH_2X$, CHX_2, and CX_3; X = F, Cl, and Br, with reference to the unsubstituted acetic acid (CH_3CO_2H). The global analysis is performed on the basis of the electronic chemical potential changes associated with the proton-transfer process described in eq 2. This analysis permits a closer approach to the experimental results reported in ref 7. The local analysis is performed on the basis of the regional Fukui function and local softness condensed to the basic oxygen atom in the RCO_2^- species. The results are discussed in the framework of a local HSAB rule.

2. Model Equations

The electronic chemical potential is defined in the framework of the density functional theory formulation of Parr, Pearson, and Yang (PPY-DFT)[11,12] as

$$\mu = \left[\frac{\partial E}{\partial N}\right]_{v(\mathbf{r})} \tag{3}$$

which is defined for any atomic or molecular system with N electrons and electronic energy E, at constant external potential $v(\mathbf{r})$. This quantity may be approached by a finite difference method, in terms of the ionization potential I and the electron affinity A, or in terms of the energies ϵ_H and ϵ_L of the HOMO and LUMO frontier molecular orbitals, respectively[11]

$$\mu \approx -\left(\frac{I + A}{2}\right) \approx \frac{\epsilon_H + \epsilon_L}{2} \tag{4}$$

Other useful global descriptors of reactivity are the global hardness and global softness. The former is defined within the PPY-DFT as the derivative of the electronic chemical potential with respect to the number of electrons, at constant external potential.[11,12] Chemical hardness has been also approached in terms of the quantities I and A, or using Koopman's theorem, in terms of the ϵ_H and ϵ_L quantities as follows:

$$\eta \approx \frac{(I - A)}{2} \approx \frac{\epsilon_L - \epsilon_H}{2} \tag{5}$$

Chemical softness S is defined as the inverse of global hardness, namely, $S = 1/\eta$.[11,12] Chemical hardness and softness are usually used in connection with the maximum hardness principle (MHP).[13−15] This empirical rule establishes a relationship between changes in global hardness and energy changes: minimum energy states usually coincide with states of maximum hardness, so that the MHP has become a useful and complementary criterion to discuss relative stability within a series of molecules. Also, these global descriptors of chemical reactivity have been used to quantitatively describe Pearson's hard and soft acids and bases (HSAB) principle.[16] This empirical rule states that soft−soft (ss) and hard−hard (hh) acid−base interactions proceed with a more favorable enthalpy than the crossed hs or sh interactions. A local version of the HSAB principle has been tested for a number of systems.[17,18] It has been proved to be a useful tool to discuss regional or group affinity between an acid−base pair, thereby allowing the selectivity concept to be discussed on a more quantitative basis.[17,18] The local application of the HSAB rule requires the definition of local descriptors of reactivity. One of the most used local reactivity indexes is the Fukui function, which is defined in the PPY-DFT as[11]

$$f(\mathbf{r}) = \left[\frac{\delta\mu}{\delta v(\mathbf{r})}\right]_N = \left[\frac{\partial\rho(\mathbf{r})}{\partial N}\right]_{v(\mathbf{r})} \tag{6}$$

The second equality of eq 6 defines $f(\mathbf{r})$ as the change in electron density $\rho(\mathbf{r})$ with the total number of electrons, at constant external potential $v(\mathbf{r})$. Local softness $s(\mathbf{r})$ may be defined in terms of the Fukui function and global softness as

$$s(\mathbf{r}) = f(\mathbf{r})S \tag{7}$$

Local softness is an additive (extensive) property of the system in the sense that integration of $s(\mathbf{r})$ over the $\mathbf{r}$ space yields the global softness S, namely

$$\int \mathrm{d}\mathbf{r}\, s(\mathbf{r}) = S = {}^1/\eta \tag{8}$$

The charge transfer associated with proton transfer may be successfully described in terms of the electronic chemical potential changes for process 2. The electronic chemical potential of transfer may be obtained from a suitable model of proton transfer.[19] We may, for instance, consider the PT reaction between RCO_2^- and $CH_3CO_2^-$, as the motion of a proton in the field of an applied external potential. This external potential is determined by the chemical environment of the proton, and it may be represented by the proton affinity difference (δPA) between the conjugated bases RCO_2^- and $CH_3CO_2^-$.[19] The electronic chemical potential of transfer ($\Delta\mu_t$), describing the amount and direction of charge transfer during the PT process, will be given by

$$\Delta\mu_t = \mu(CH_3CO_2^-) - \mu(RCO_2^-) \tag{9}$$

We will show below that the set of global and local quantities may be used in connection with the empirical MHP and HSAB rules to yield a simple reactivity model to explain the electronic substituent effect on the gas-phase acidity of haloacetic acids, on a more quantitative basis. Within the present approach, the electronic substituent effect is assessed as local responses at the basic oxygen atom, in terms of the variations of the Fukui function or local softness at that site. This aspect of the model has the potential advantage with respect to other theoretical models based on the group property analysis, in the sense that the transferability of group properties, namely, group hardness and electronegativity, is not required. This makes our approach more general in the sense that it could be applied to other systems presenting quite different chemical functionalities.

3. Results and Discussion

3.a. Energetic aspects. The structures for the series of 10 haloacetic acids, including acetic acid, were optimized at B3LYP/6-311G** level of theory, using the GAUSSIAN94 package of programs.[20] The corresponding anions were also optimized at the same level of theory. Proton affinity values were calculated as $PA \cong \Delta E = E(RCO_2^-) - E(RCO_2H)$. The relative PA value, δPA, calculated at this level of the theory reproduces quite well the experimental trends[1] (see Table 1). For instance, for the monosubstituted subseries the predicted gas-phase relative acidity order as measured by the δPA quantity, CH_2FCO_2H (10.8 kcal/mol) < CH_2ClCO_2H (16.8 kcal/mol) < CH_2BrCO_2H (17.7 kcal/mol), is in agreement with the experimental gas-phase acidity order reported by Cumming and Kebarle.[1] For the series of disubstituted haloacetic acids, the predicted order, CHF_2CO_2H (18.4 kcal/mol) < $CHCl_2CO_2H$ (26.0 kcal/mol) ≈ $CHBr_2CO_2H$ (26.3 kcal/mol), is also in close agreement with the experimental results reported in ref 1. Unfortunately, for the series of trisubstituted acetic acids, only experimental data for CF_3CO_2H are available. However, according to ref 7, the effective decrease of electronic charge at

TABLE 1: Comparison between Experimental and Predicted δPA Values (in kcal/mol), Electronic Chemical Potential of Transfer $\Delta\mu_t$ (in eV), Global Softness *S* (in eV^{-1}), and the Charge Transfer, ΔN (in electron units), for the Proton-Transfer Reaction between RCO_2^- and $CH_3CO_2^-$ Species

R	$\delta PA_{exp}{}^a$	$\delta PA_{pred}{}^b$	$\Delta\mu_t$	*S*	ΔN^c
CH_3	0.0	0.0	0.0	0.3230	0.0
CH_2F	10.3	10.8	0.3015	0.3000	0.0234
CHF_2	17.9	18.4	0.4838	0.2865	0.0367
CF_3	25.8	25.3	0.6424	0.2691	0.0472
CH_2Cl	12.4	16.8	1.2141	0.3368	0.1001
$CHCl_2$	20.3	26.0	2.0410	0.3783	0.1778
CCl_3		33.4	2.7504	0.4029	0.2465
CH_2Br	14.5	17.7	1.6383	0.3746	0.1421
$CHBr_2$	20.0	26.3	2.5537	0.4393	0.2377
CBr_3		33.8	3.3037	0.4792	0.3182

[a] Experimental PAs from ref 1. [b] Predicted δPA values from B3LYP/6-311G** calculations. [c] ΔN values predicted from Pearson's equation.

the CO_2^- group due to the field effect of the X_2 substituents reduces the stabilizing effect of their polarizabilities, and on the basis of this result, almost equal acidity in CX_3CO_2H for X = Cl and Br was predicted.[7] Our theoretical gas-phase acidity order, CF_3CO_2H (25.3 kcal/mol) < CCl_3CO_2H (33.4 kcal/mol) $\approx$ CBr_3CO_2H (33.8 kcal/mol), confirms this prediction advanced by Kebarle et al.[7] (see Table 1). Another relevant result follows from the analysis of global softness variations. As stated by Kebarle et al.,[7] the increasing polarizability of halogen groups leads to an enhanced gas-phase acidity. Polarizability has been related to global softness:[21,22] high (low) polarizability is associated with high (low) values of global softness. If we make the assumption that increasing the polarizability of the group will result in an increase in global softness of the RCO_2^- species, then the following relationship between gas-phase acidity and global softness may be proposed (the global softness value is given in parentheses, see Table 1): for the monosubstituted subset the acidity order is CH_2FCO_2H (0.3000 eV^{-1}) < CH_2ClCO_2H (0.3368 eV^{-1}) < CH_2BrCO_2H (0.3746 eV^{-1}). For the disubstituted series the following order relationship is obtained: CHF_2CO_2H (0.2865 eV^{-1}) < $CHCl_2CO_2H$ (0.3783 eV^{-1}) < $CHBr_2CO_2H$ (0.4393 eV^{-1}). For the trisubstituted series the following order is predicted: CF_3CO_2H (0.2691 eV^{-1}) < CCl_3CO_2H (0.4029 eV^{-1}) < CBr_3CO_2H (0.4792 eV^{-1}). Note that in the softness scale the prediction that trisubstituent species should display similar gas-phase acidity is lost. This may be due to the fact that there is no linear relationship between energy and global softness variations.

3.b. Electronic Chemical Potential and Charge Transfer. As proposed in section 2, the charge transfer associated with the proton-transfer process given in eq 2 may be described as the motion of a charged particle in an applied external potential.[19] Within the present approach, this applied external potential is represented by the proton affinity difference $\delta PA = PA(CH_3CO_2^-) - PA(RCO_2^-)$. In section 3.a, it was shown that the driving potential δPA assesses well the gas acidity pattern displayed by the haloacetic acid series. On the other hand, it is well-known that associated with the proton migration in a PT process, there is always a charge transfer (CT) in the opposite direction.[23,24] To understand the CT pattern associated with the PT reaction described in eq 2, we introduce a classic ion-transport model discussed elsewhere.[19] Since the net PT process 2 may be regarded as a direct proton transfer from RCO_2^- toward the reference $CH_3CO_2^-$ species, the charge transfer may be conveniently described in terms of the electronic chemical potential of transfer $\Delta\mu_t$ defined in eq 9. The electronic chemical potentials of the individual species involved in eq 9 were evaluated using eq 4. From Table 1, third column, it may be seen that $\delta PA = PA(CH_3CO_2^-) - PA(RCO_2^-) > 0$ for all the acetic acid haloderivatives, indicating that the PA of the reference $CH_3CO_2^-$ is always greater than that of the corresponding RCO_2^- derivatives. The proton transfer is therefore predicted to take place from RCO_2^- toward the $CH_3CO_2^-$ species. The $\Delta\mu_t$ values for this series are also displayed in Table 1, fourth column. It may be seen that $\Delta\mu_t > 0$ for the whole series, which entails that $\mu(CH_3CO_2^-) > \mu(RCO_2^-)$, and the charge transfer is consistently predicted to occur from $CH_3CO_2^-$ toward RCO_2^-, i.e., in the opposite direction to that of the proton motion.

TABLE 2: Comparison between Energy (in kcal/mol) and Hardness Variations (in eV) for the Acid−Base Equilibria of Acetic Acid (Eq 10), Haloderivatives (Eq 11), and the Net PT Reaction (Eq 2)[a]

R	ΔE_1	ΔE_2	δPA	$\Delta\eta_1$	$\Delta\eta_2$
CH_3	364.2		0.0	−0.81	
CH_2F		−353.4	10.8		0.59
CHF_2		−345.8	18.4		0.22
CF_3		−338.9	25.3		0.06
CH_2Cl		−347.3	16.8		0.97
$CHCl_2$		−338.9	26.0		0.79
CCl_3		−330.8	33.4		0.90
CH_2Br		−346.5	17.7		0.94
$CHBr_2$		−337.9	26.3		0.82
CBr_3		−330.4	33.8		0.62

[a] See the text for definitions.

It is useful to analyze the amount of charge transferred in terms of the well-known Pearson's equation, namely, $\Delta N = \Delta\mu_t/\partial\eta_t$,[13] where the electronic chemical potential of transfer is defined by eq 9 and the total hardness by $\eta_t = \eta(CH_3CO_2^-) + \eta(RCO_2^-)$. The results are also included in Table 1, last column. It may be seen that the charge-transfer pattern predicted from Pearson's equation confirms the one predicted by the electronic chemical potential of transfer.

3.c. Proton Affinity and Hardness Variation: Probing the Maximum Hardness Principle. According to the net PT reaction described in eq 2, the energy variations associated with the PT equilibrium with reference to the gas dissociation reaction of acetic acid is directly given by the quantity $\delta PA = \Delta E_{pt}$. For the gas-phase reference reaction we write

$$CH_3CO_2H \rightarrow CH_3CO_2^- + H^+; \quad \Delta E_1 = PA(CH_3CO_2^-) \tag{10}$$

which is to be combined with the protonation reaction of the haloacetic acid

$$RCO_2^- + H^+ \rightarrow RCO_2H; \quad \Delta E_2 = -PA(RCO_2^-) \tag{11}$$

to yield the net PT reaction described in eq 2. In fact, addition of eqs 10 and 11 yields eq 2 with $\Delta E_{pt} = \Delta E_1 + \Delta E_2 = \delta PA$. Associated with the energy variations ΔE_1 and ΔE_2, we may define the hardness variations $\Delta\eta_1 = \eta(CH_3CO_2^-) - \eta(CH_3CO_2H)$ and $\Delta\eta_2 = \eta(RCO_2H) - \eta(RCO_2^-)$ for the processes described in eqs 10 and 11, respectively. Chemical hardness of the individual species was evaluated using eq 5. In Table 2 we summarize the calculated values of ΔE_1, ΔE_2, $\Delta\eta_1$, $\Delta\eta_2$, and δPA. We first compare the energy and hardness variations for processes 10 and 11; for the reference reaction 10, it may be seen that $PA(CH_3CO_2^-) = \Delta E_1 > 0$ entails a negative variation in global hardness $\Delta\eta_1 = -0.81$ eV, a result consistent with the maximum hardness principle.[13−15] On the other hand, the analysis of the energy-hardness variations for the processes described in eq 11 shows that ΔE_2 defined as $\Delta E_2 =$

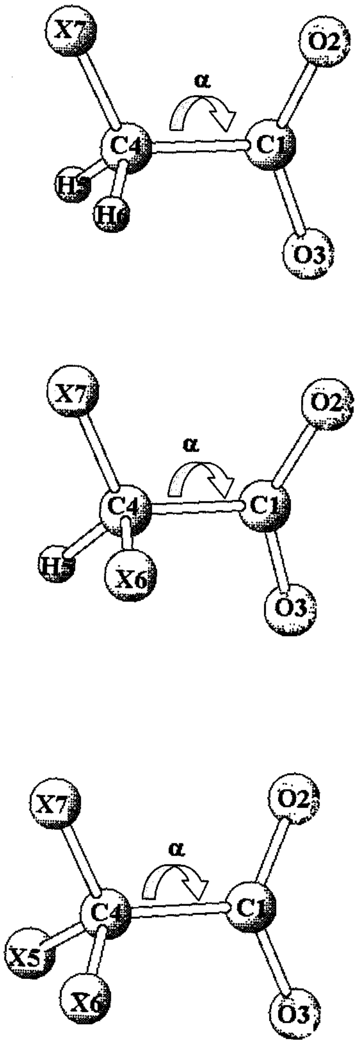

Figure 1. Atom numbering for the mono-, di-, and trisubstituted haloacetate ions.

$-PA(RCO_2^-)$ is always negative because the PA is a positively defined quantity. Negative values of ΔE_2 are associated with positive variations of the corresponding $\Delta\eta_2$ quantities, again in agreement with the MHP.

3.d. Local Analysis: Probing the HSAB Principle. Local reactivity indices are useful descriptors of site reactivity.[25−27] For instance, the Fukui function defined in eq 6 has been recently proposed as the key reactivity index to discuss chemical reactivity within a generalized HSAB rule.[28] However, a still more useful formulation of the Fukui function is that condensed to atoms or groups. Condensed Fukui functions may be easily available from a three-points finite difference approximation,[27] which is expressed as differences in the electron population between the systems with N, $N + 1$, or $N - 1$ electrons. An alternative way to obtain condensed-to-atoms Fukui functions from single-point calculations has been recently proposed.[17] In that approach, the regional or condensed-to-atom Fukui function is directly obtained from the electron density of the highest occupied molecular orbital HOMO. They are expressed in terms of the HOMO coefficients and the overlap matrix for an electrophilic attack.[17] This last approach is used here. From the knowledge of $f(\mathbf{r})$, the local (or condensed-to-atoms) softness $s(\mathbf{r})$ (S_k^-) may be readily obtained through eq 7. To complete the local analysis in the framework of a local HSAB principle, an operational formula for local hardness is desirable. Unfortunately, unambiguous definitions of this local reactivity index are at present unavailable. However, it has been shown that local softness and hardness may be at least inversely proportional to each other.[29,30] We will then assume here that those regions presenting a maximum (minimum) value in local softness will be characterized by a minimum (maximum) value in local hardness.

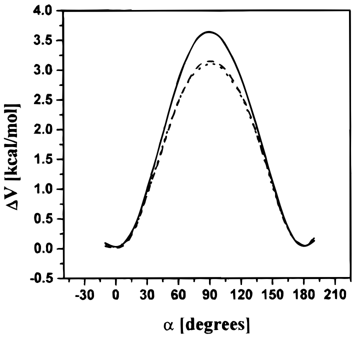

Figure 2. Energy potential profiles for monosubstituted acetate ions: X = F (solid line), X = Cl (dotted line), and X = Br (dashed line).

Atom numbering is defined in Figure 1 for the mono-, di-, and trisubstituted ion derivatives. All the systems studied here present barrierless rotation around the C1−C4 bond described by the torsional variable α (defined as the dihedral X7−C4−C1−O3 angle), except the monosubstituted ion derivatives that present low rotational barriers ranging from 3.1 to 3.7 kcal/mol (see Figure 2) at the B3LYP/6-311G** level of theory. MP2/6-311G** calculations confirm this result. Other global properties such as electronic chemical potential and chemical hardness show marginal variations with α.

Despite the absence of energy barriers for the rotation around the C1−C4 bond, the Fukui function at the basic centers O2 and O3 does show significant variations with the torsional variable α (see Figures 3−5) for the mono-, di-, and trisubstituted derivatives, X = F, Cl, and Br. To fix a criterion to discuss the local effect of chemical substitution at the basic oxygen atoms of the haloacetate ions, we propose to take as a reference configuration the one at which the Fukui function at O2 and O3 becomes equal. This choice guarantees that both centers remain as equivalent potential sites toward protonation.

For $FCH_2CO_2^-$, the estimated value of the Fukui function at the basic centers is approximately 0.46 (see Figure 3a). Introduction of a second fluorine atom (Figure 3b) reduces the value of the Fukui function to ca. 0.35. For the case of the trifluoro derivative, the Fukui function at both oxygen atoms increases to a value of 0.46 (see Figure 3c).

For the monochloroacetate the estimated Fukui function at both basic sites is approximately 0.46 (see Figure 4a), which is approximately the same value obtained for the monobromoacetate species (see Figure 5a). These results indicate that in the monosubstituted species the Fukui function at the basic oxygen centers of the conjugated bases $CH_2XCO_2^-$ is not sensitive to the halogen atom replacement. However, gas-phase acidity for the monosubstituted series may be discussed in terms of a local HSAB principle[28] using local softness as descriptor. Local softness at the oxygen site is readily obtained by multiplying the Fukui function value of 0.46 by the global softness of the corresponding $CH_2XCO_2^-$ species shown in Table 1. The following results are obtained: S_O^-(0.17 eV^{-1}; X = Br) > S_O^-(0.15 eV^{-1}; X = Cl) > S_O^-(0.14 eV^{-1}; X = F), i.e., the same order shown by the gas-phase acidity. This result is consistent with a local HSAB rule: the increasing local softness at the equivalent oxygen centers in going from F to Br may be interpreted as a decrease in local hardness at that

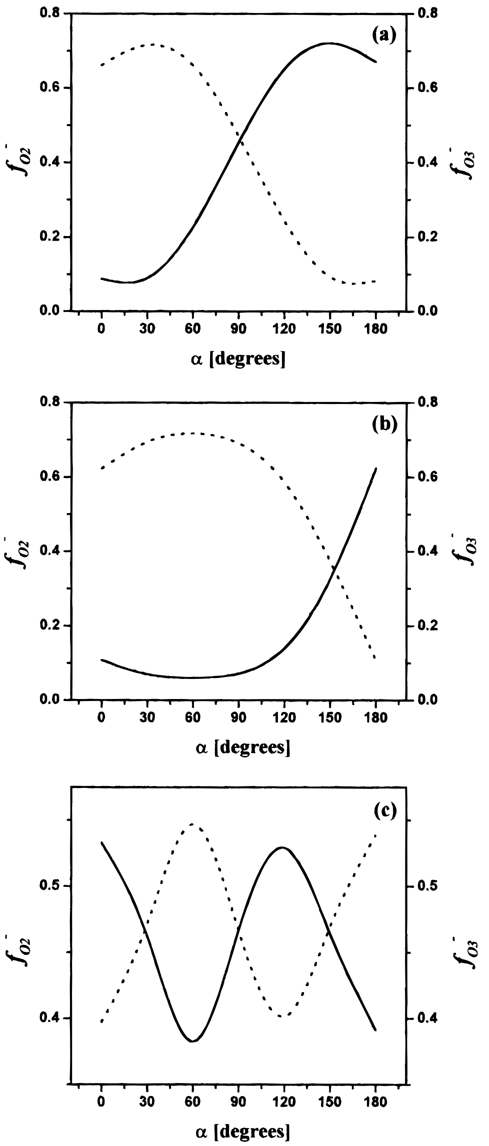

Figure 3. Fukui function profiles for fluoroacetate ions with respect to the torsional coordinate α at O2 (solid line) and O3 (dotted line): (a) $CH_2FCO_2^-$, (b) $CHF_2CO_2^-$, and (c) $CF_3CO_2^-$.

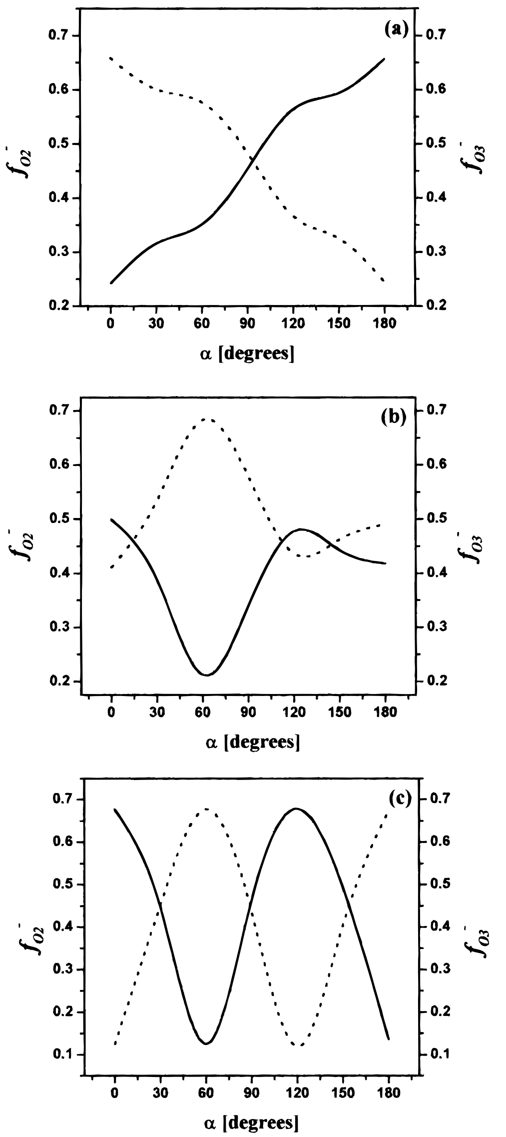

Figure 4. Fukui function profiles for chloroacetate ions with respect to the torsional coordinate α at O2 (solid line) and O3 (dotted line): (a) $CH_2ClCO_2^-$, (b) $CHCl_2CO_2^-$, and (c) $CCl_3CO_2^-$.

site.[31-33] A decrease in local hardness means that the interaction with a proton will be unfavorable (HSAB rule), thereby stabilizing the conjugated base $CH_2XCO_2^-$ and therefore increasing the gas-phase acidity.

For the series of disubstituted haloacetate ions, the Fukui functions at the basic center for X = Cl and Br are 0.46 and 0.45, respectively. Having in mind the Fukui function value of 0.35 for the oxygen atom in $CHF_2CO_2^-$, we can repeat the same procedure described above to obtain the local softness at the basic sites. The following results are obtained: $S_O^-(0.20\ \mathrm{eV}^{-1}$; X = Br) > $S_O^-(0.17\ \mathrm{eV}^{-1}$; X = Cl) > $S_O^-(0.10\ \mathrm{eV}^{-1}$; X = F), indicating again that the gas-phase acidity order follows the same trend given by an increasing local softness pattern or a decreasing local hardness pattern, so that the gas-phase acidity order may be again explained on the basis of a local HSAB rule.

For the trisubstituted acetate ions, the values of the Fukui function at the basic centers are 0.45, 0.43, and 0.37 for X = F, Cl, and Br, respectively. The transformation to the local softness scale using the values of global softness quoted in Table 1 yields the following order relationship: $S_O^-(0.18\ \mathrm{eV}^{-1}$; X = Br) > $S_O^-(0.17\ \mathrm{eV}^{-1}$; X = Cl) > $S_O^-(0.12\ \mathrm{eV}^{-1}$; X = F), in close agreement with the gas-phase acidity pattern predicted for this series on the basis of proton affinity values.

In summary, the gas-phase acidity order for the series of mono-, di-, and trisubstituted haloacetic acids may be explained on the basis of a global and local HSAB rule, showing that the increasing acidity pattern results from a substituent electronic effect that renders the basic oxygen atoms softer in going from fluorine to bromine substitution. In a recent study on the basicity of para-substituted phenolates,[34] it was found that when the basicity increases the condensed softness at the oxygen atom increases, in agreement with our results. However, these results do not suggest that the relative gas-phase acidity is controlled by hardness variations. While the gas-phase acidity of haloacetic acids is consistent with both global and local HSAB rules, the relative order of PAs remains primarily controlled by electrostatic effects, which are assessed here by changes in electronic chemical potential of transfer. As a consequence of this electrostatic inductive effect, the regional softness at the active site increases, thereby canceling the extra stabilization coming from the interaction with the proton, which is absolutely hard.

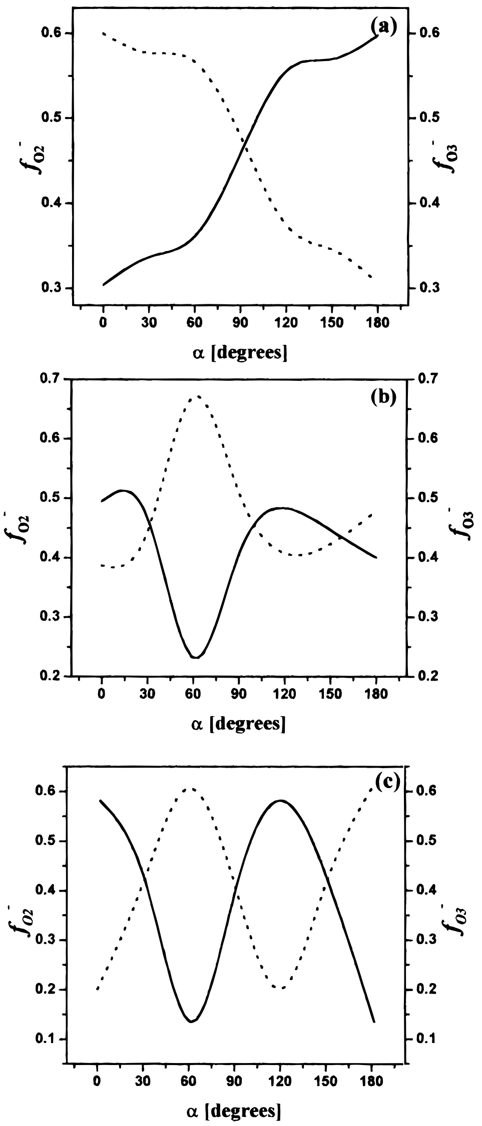

Figure 5. Fukui function profiles for bromoacetate ions with respect to the torsional coordinate α at O2 (solid line) and O3 (dotted line): (a) $CH_2BrCO_2^-$, (b) $CHBr_2CO_2^-$, and (c) $CBr_3CO_2^-$.

Note that the electrostatic substituent effects encompassed in the electronic chemical potential of transfer are confirmed by the charge-transfer pattern derived from Pearson's equation.

4. Concluding Remarks

A complete global and local analysis of the gas-phase acidity of a series of haloacetic acids has been presented. B3LYP/6-311G** calculations quantitatively reproduce the gas-phase acidity pattern as described by proton affinity variations within the series. Our results confirm the prediction advanced by Kebarle et al.[7] that the CCl_3CO_2H and CBr_3CO_2H should present almost equal acidity. The analysis of charge transfer performed on the basis of the electronic chemical potential of transfer shows that there is a charge transfer in the opposite direction to the proton migration. Positive energy variations associated with proton transfer with reference to acetic acid are associated with negative variations in the chemical hardness, in agreement with the maximum hardness principle. The local analysis performed on the basis of electrophilic Fukui function and local softness suggests that the gas-phase acidity order within the series may be explained in the context of a global and local HSAB principle. Increasing substitution results in an increase in global softness and local softness at the basic center of the conjugated bases, thereby stabilizing the haloacetate ions.

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