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Global and Local Reactivity and Activation Patterns of HOOX (X = H, NO_2, CO_2^-, SO_3^-) Peroxides with Solvent Effects

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A detailed analysis of the global and local reactivity patterns of neutral and charged peroxides, including hydrogen peroxide (HOOH), peroxynitric acid ($HOONO_2$), the peroxymonocarbonic ion ($HOOCO_2^-$), and the peroxymonosulfate ion ($HOOSO_3^-$) in the presence of a polar solvent (water) is presented. The polar solvent effects are included using an isodensity surface polarized continuum model (IPCM). The (1,2) hydrogen-shift reaction for these peroxides is studied. The transition states involved in the (1,2) hydrogen shift have been located and characterized at the B3LYP/6-311G** level of theory. The global analysis shows that, although the replacement of one hydrogen atom in HOOH by a neutral NO_2 group enhances both the global softness and global electrophilicity, the substitution of one hydrogen atom by charged CO_2^- and SO_3^- groups results in a significant electrophilic deactivation of $HOOCO_2^-$ and a moderate electrophilic activation of $HOOSO_3^-$. This result is observed in both the ground state and in some activated forms involved in the (1,2) hydrogen rearrangement. The local analysis, however, shows that the transition-state structures for the same rearrangement of HOOH and the $HOOCO_2^-$ ion display an electrophilicity-enhanced pattern at the oxygen atom that is being deprotonated, thereby suggesting that this activated form is more likely to be involved in the oxygen-transfer reactions. The site-activation analysis performed on the basis of the variations in local softness from the ground to the transition states is also consistent with this local reactivity picture.

1. Introduction

The oxidation reactions belong to an important group of chemical transformations. Particularly, the transfer of an oxygen atom involving oxygen−oxygen bond cleavage (oxo transfer) plays a crucial role in organic chemistry.[1,2] In addition, this process has been proposed as a possible oxidation mechanism of biological systems.[3] Even though the mechanism of oxidation by oxygen atom transfer is not completely understood, it is known that some reagents such as hydrogen peroxide (HOOH), peroxynitric acid ($HOONO_2$), the peroxymonocarbonic ion ($HOOCO_2^-$), the peroxymonosulfate ion ($HOOSO_3^-$), and organyl hydroperoxides are involved in such kinds of oxidation reactions.[2] Special attention has been devoted to the activity of hydrogen peroxide in these processes as well as a structural isomer of hydrogen peroxide that may occur as an intermediate in oxidation reactions initiated by the latter species. This isomer has been named oxywater or water oxide ($H_2O{-}O$).[4] In contrast to hydrogen peroxide, which has been widely studied both experimentally[5−10] and theoretically,[11−19] oxywater has seldom been considered to be a stable species in the literature. The first experimental indication that this molecular species might exist came from Bain and Giguere,[4] from the infrared spectra of hydrogen peroxide using isotopic substitution studies. They failed to observe an O−O stretching fundamental frequency, characteristic of hydrogen peroxide, and they concluded that the existence of a tautomeric form of the molecule, such as $H_2O{-}O$, was possible. Recent experimental evidence for the existence of neutral oxywater was provided by Schröder et al.,[20] using neutralization−reionization mass spectrometry.[21]

Many theoretical studies have been performed to demonstrate the existence of oxywater.[22] The first theoretical study of this activated form of hydrogen peroxide was made by Kalder and Shavitt in 1966.[23] In 1983, Pople et al.[24] studied several simple (1,2) hydrogen shifts, including the HOOH → $H_2O{-}O$ reaction, and they concluded that oxywater could not exist because this species was either a shallow potential minimum or it was not a minimum at all. These authors based this conclusion on their theoretical studies performed at the MP4SQD/6-31G**//HF/6-31G* level of theory. However, Meredith et al.[25] suggested that Pople's conclusion on the existence of oxywater was questionable because the optimization of structures was not performed at a high level of theory. Bach et al.[18,26] optimized hydrogen peroxide and oxywater structures at a higher level of theory and concluded that oxywater was a minimum in the potential energy surface. In 1996, Huang, Xie, and Schaefer,[27] using the CCSD(T)/TZ2P+f level of theory, showed that oxywater can live long enough to be detected experimentally. More recently, the singlet and triplet potential energy surfaces of the $^1[H_2, O_2]$ and $^3[H_2, O_2]$ systems were calculated by Schalley et al.[28] using the B3LYP/6-311++G(d,p) level of theory. The oxywater is contained in these surfaces. The neutral singlet oxywater was predicted to be stable in the gas phase by these authors.

The existence and stability of oxywater can give rise to many applications in chemistry. This molecule is not only of academic interest because of its hypervalent oxygen atom but also has been postulated as a possible intermediate in the oxidation of amines and sulfur compounds with hydrogen peroxide[29] or in

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metal-mediated oxidation reactions in biochemistry.[30,31] For this reason, it is interesting to explore the reactivity and activation patterns of oxywater and other peroxides that can display a (1,2) hydrogen shift, such as $HOONO_2$, $HOOCO_2^-$, and $HOOSO_3^-$.

Peroxynitric acid has potential importance in aqueous atmospheric chemistry,[32] and interest in its reactivity in water has recently increased.[33] In aqueous solution, $HOONO_2$ is a strong oxidizing agent, reacting rapidly with charged nucleophiles such as I^-, Br^-, Cl^-, and benzene.[33] The halide oxidation mechanism has not been investigated completely, but it is known that this involves a nucleophilic attack by the halide ion on the hydrogen-bearing oxygen atom in $HOONO_2$, yielding HOX (X = I, Cl, Br) and NO_3^- as the primary products. Experimental results show that $HOONO_2$ displays a kinetic pattern very close to that shown by $HOOSO_3^-$ as a halide oxidant.[34] Its reactivity is higher than that of hydrogen peroxide in such processes. In addition, mono- and dinitrobenzenes, nitrophenol, and quinone can be obtained from the reaction of benzene with peroxynitric acid.

Sulfide oxidations by peroxides, however are generally considered to proceed by the nucleophilic attack of a sulfide group at the electrophilic oxygen of peroxide. Kinetic experiments show that the peroxymonocarbonate ion is moderately reactive toward the oxidation of sulfides. This reactivity is intermediate between that shown by HOOH and by the peroxymonosulfate ion.[35] Oxidations by $HOOCO_2^-$ are also of interest in terms of the possible but rarely mentioned role of $HOOCO_2^-$ as a nonradical reactive oxygen species in biological systems.[36]

Peroxymonosulfate ion is a versatile anionic and water-soluble oxidant of sulfides to sulfoxides and eventually to sulfones and thioesters.[37−39] Ruff and Kucsman[40] have discussed possible mechanisms of sulfide oxidation by IO_4^-, which can be regarded as a nucleophilic attack by sulfur at one oxygen site, with the displacement of IO_3^-. A similar mechanism can be written for oxidation by $HOOSO_3^-$, including proton transfer with or after oxygen transfer.

In summary and as expected for a nucleophilic attack at an electrophilic oxidant, faster oxidation is observed if the nucleophilic power is increased. In this sense, oxywater and the products of the (1,2) hydrogen shift in $HOONO_2$, $HOOCO_2^-$, and $HOOSO_3^-$ could be better oxidants in these processes. To our knowledge, there are no theoretical studies oriented toward the elucidation of the chemical reactivity of these strongly oxidizing species in aqueous solution. Density functional theory (DFT) is a useful theoretical framework for the study of the electronic properties of molecular systems.[41] DFT has allowed the development of a conceptual scheme[42] that makes it possible to express many intuitive concepts used by experimental chemists, such as the electronegativity χ,[43] the global hardness η,[44,45] and the electrophilicity index ω,[46] establishing quantitative scales of reactivity. It is important to mention that the electronic density $\rho(\mathbf{r})$, the fundamental variable of the DFT, contains the information needed to describe a system in its ground state. In this sense, different parameters of local reactivity have been proposed on the basis of this variable. They include the Fukui function $f(\mathbf{r})$,[47,48] the local softness $s(\mathbf{r})$,[49] and the local electrophilicty $\omega(\mathbf{r})$. These indexes correctly assess the selectivity of a molecule in a chemical reaction.[50−52] Furthermore, the local softness and the Fukui functions, calculated in two different states of a molecule (ground and transition states), can be used as a model for site activation.[50−52]

Because the main chemical activity of oxidizing agents such as HOOH, $HOONO_2$, $HOOCO_2^-$, and $HOOSO_3^-$ takes place in aqueous solution, the inclusion of solvent effects in a chemical reactivity study is mandatory. In the particular case of species that display (1,2) hydrogen-shift reactions, the solvent effects have a strong influence on their stabilization.[24] In recent decades, two main techniques have been developed to include solvent effects in electronic calculations: continuum models[53] and discrete solvent models.[54] In continuum models, the solvent is described as an infinite isotropic dielectric surrounding a solute molecule that is placed in a cavity. In the discrete approach, solvent molecules are treated explicitly so that specific interactions between solute and solvent are taken into account.

In this work, we investigate the global and local reactivity and the activation patterns of HOOH, $HOONO_2$, $HOOCO_2^-$, and $HOOSO_3^-$ throughout the (1,2) hydrogen-shift reaction, including polar solvent effects with a continuum model, paying attention to the oxygen−oxygen region that is involved in oxygen-transfer reactions.[2]

2. Model Equations

2.1. Global Properties. Within the Parr−Yang formulation of DFT,[41] the energy is functional of both the total number of electrons N and the external potential $v(\mathbf{r})$ due to the compensating positive (nuclear) charges in the system. In this formulation, the changes in energy come from variations in both N and $v(\mathbf{r})$. These changes are expressed by the equation[41]

$$dE = \mu \, dN + \int \rho(\mathbf{r}) \, dv(\mathbf{r}) \, d\mathbf{r} \qquad (1)$$

where $\rho(\mathbf{r})$ is the electron density and the quantity μ is the electronic chemical potential, which is defined as[41]

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(\mathbf{r})} \qquad (2)$$

The electronic chemical potential is the natural descriptor of electron transfer, and its negative is related to the classical chemical concept of electronegativity.[41,43] Its first derivative is associated with Pearson's concept of hardness,[44,45] namely,

$$\eta = \left(\frac{\partial \mu}{\partial N}\right)_{v(\mathbf{r})} = \left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\mathbf{r})} \qquad (3)$$

The inverse of chemical hardness is the global softness, $S = {}^1/_\eta$, a quantity related to the electronic polarizability of the system.[55] Although the chemical hardness may be interpreted as a measure of the resistance of the system to exchange electronic charge with the environment,[45] the global softness is a measure of the ability of the system to exchange electronic charge. Both the electronic chemical potential and chemical hardness have a finite difference expression in terms of the vertical ionization potential and electron affinity, I and A, namely, $\mu \approx -(I + A)/2$ and $\eta \approx (I - A) \geq 0$, respectively. Another pertinent quantity is the global electrophilicity index recently introduced by Parr et al. as[46]

$$\omega = \frac{\mu^2}{2\eta} \qquad (4)$$

This reactivity index measures the corresponding stabilization in energy when the system acquires an additional charge, $\Delta N_{\max} = -{}^\mu/_\eta$, from the environment.

2.2. Local Quantities and Site Activation. The local response functions have been associated with the selectivity of molecules[50−52] (i.e., quantities that describe the reactivity pattern, dictated by the global quantities, which is developed at specific regions of molecules). One of the most useful local reactivity indexes is the Fukui function, which has been given by the following definition:[47,48]

$$f(\mathbf{r}) \equiv \left(\frac{\delta\mu}{\delta\upsilon(\mathbf{r})}\right)_N = \left(\frac{\partial\rho(\mathbf{r})}{\partial N}\right)_{\upsilon(\mathbf{r})} \tag{5}$$

This quantity measures how sensitive the electronic chemical potential is to a localized external perturbation $\delta\upsilon(\mathbf{r})$. It also quantifies the variations in electron density at each point in space when the system acquires or donates ΔN electrons during its interaction with the environment. Another pertinent local quantity is the local softness, defined as[49]

$$s(\mathbf{r}) \equiv \left(\frac{\partial\rho(\mathbf{r})}{\partial\mu}\right)_{\upsilon(\mathbf{r})} \tag{6}$$

The local softness and the Fukui function are related by $s(\mathbf{r}) = f(\mathbf{r})S$.[41] They contain the same information about the active sites in a molecule, yet the local softness encompasses additional information about the global electronic polarizability of the system. In other words, the global softness of a molecule is distributed following the Fukui function. Additional useful information may be obtained by looking at the variations in local softness from the ground state to the transition state. These variations may be associated with the electrophilic-, nucleophilic-, or radical-site activation of a molecule as it reaches the transition state,[56] namely,

$$\Delta s_k(\mathbf{r}) \approx f_k^0 \Delta S + S^0 \Delta f_k \tag{7}$$

The computational scheme of selectivity and site activation in a molecule is the following: selectivity may be normally expressed in terms of the Fukui function condensed to atom k,[57] and it can be approximated by

$$f_k^\alpha = \sum_{\mu\in k} f_\mu^\alpha = \sum_{\mu\in k}[|c_{\mu\alpha}|^2 + c_{\mu\alpha}\sum_{\nu\neq\mu} c_{\nu\alpha}S_{\mu\nu}] \tag{8}$$

where $c_{\mu\alpha}$'s are the molecular orbital coefficients of the frontier orbital α, $S_{\mu\nu}$'s are the atomic orbital overlap matrix elements, and α is positive or negative for nucleophilic or electrophilic attacks, respectively. The expression from eq 8 represents the condensed Fukui function approximated by Contreras et al.[58,59] as $f(\mathbf{r})^\alpha \approx |\phi_{\mathrm{KS}}^{\mathrm{F}}(\mathbf{r})|^2$, where F is the LUMO for f^+ or the HOMO for f^-.[60,61] At this point, it is important to mention that a local electrophilic pattern at the k site in a molecule, which is measured by the f_k^+ index, reveals the capacity of this site to receive nucleophilic attacks. However, a local nucleophilic pattern at the k site reveals the capacity of this site to receive electrophilic attacks, which is measured by thef_k^- index. With the regional Fukui function at hand, the regional softness may be immediately obtained as $s_k^\alpha = f_k^\alpha S$. Site activation may be quantified using eq 7 with reference to the properties of the transition-state structures by defining $\Delta S = S^\ddagger - S^\circ$ and $\Delta f_k^\alpha = f_k^{\alpha,\ddagger} - f_k^{\alpha,o}$, thereby introducing the global and local properties of the ground (o) and transition (‡) states of molecules.

3. Computational Details

The ground states of neutral and charged peroxides were fully optimized at the B3LYP/6-311G** level of theory using the Gaussian 98 suite of programs.[62] The transition state and the oxywater-like structures of peroxides were also located at the same level of theory. The transition state of each peroxide was characterized by a frequency analysis, showing only one negative eigenvalue of its Hessian matrix; that is, each transition state has only one single imaginary frequency. Intrinsic reaction coordinate (IRC) calculations were done in this work, and they indicated that all transition states are fundamentally concerted ones corresponding to the (1,2) hydrogen-shift reaction. The optimized transition-state geometrical parameters are available from the authors upon request. The polar solvent effects were included using the isodensity surface polarized continuum model (IPCM).[63] The IPCM method has been quite successful in the treatment of neutral molecules and single ions.[64,65] The optimized gas-phase geometries were used in the IPCM calculations to estimate the solvent effects. For this model, the dielectric constant of water was used, and the isodensity level was kept at 0.001 electrons per cubic bohr. Recently, Zhan and Chipman[65] have shown that for this value of isodensity adequate accuracy is obtained in the IPCM calculations. The global and local analysis was performed on the optimized ground-state, transition-state, and oxywater-like complexes. The calculation of chemical hardness was performed for each structure using Koopman's theorem, namely, $\eta = I - A \approx \epsilon_{\mathrm{L}} - \epsilon_{\mathrm{H}}$, in terms of the one-electron energy levels of the frontier molecular orbitals HOMO(H) and LUMO(L). The global softness was obtained as $^1/_\eta$. Regional electrophilic (+), nucleophilic (−), and radical (0) Fukui functions were evaluated for both the ground- and transition-state structures using eq 8 from single-point calculations in terms of the optimized molecular orbital coefficients $c_{\mu\alpha}$ and the overlap matrix $S_{\mu\nu}$.[58,59] With the ground- and transition-state properties at hand, the site-activation pattern for each species was evaluated using eq 7.

4. Results and Discussion

Several models have been developed to include solvent effects in electronic structure calculations, and they are reported in the literature.[53,54,63−65] The IPCM, which is available only for single-point calculations, and the SCIPCM, which is available for energy calculations and optimizations, are some of these solvation models. In this work, the ground state of HOOH was calculated using the SCIPCM model. The optimized structural parameters of hydrogen peroxide, obtained with this reaction field method, are shown in Figure 1. We can notice that there are no significant variations in these parameters with respect to those obtained in the gas phase. Within this work, we assume that this effect is preserved in the other peroxides. It is important to mention that the SCIPCM calculations are much more expensive than IPCM calculations. For these reasons, the IPCM model was used with gas-phase optimized structures in all calculations made in this work.

4.1. Energy and Global Reactivity Analysis of the Internal Rearrangement of Peroxides. The study of the potential energy surfaces (PES) for the internal rearrangement of the hydrogen atom ((1,2) hydrogen shift) in hydrogen peroxide, peroxynitric acid, the peroxymonocarbonate ion, and the peroxymonosulfate ion reveals that in the ground state the replacement of one hydrogen atom by NO_2, CO_2^-, or SO_3^- introduces slight geometrical changes in the O−O−H frame, as shown in Figure 1. However, one can note that whereas the ground state of HOOH is in the skew conformation[10] with respect to the O−O bond the ground states of the NO_2, CO_2^-, and SO_3^- derivatives are in the cis conformation, a result that is probably due to extra stabilization coming from intramolecular hydrogen bonding between the hydrogen atom of the O−O−H region and an oxygen atom of the substituents and from the additional extension of the delocalization zone favored by the planar structure. Another aspect of the PES in these systems is the internal rearrangement of the peroxides toward the oxywater

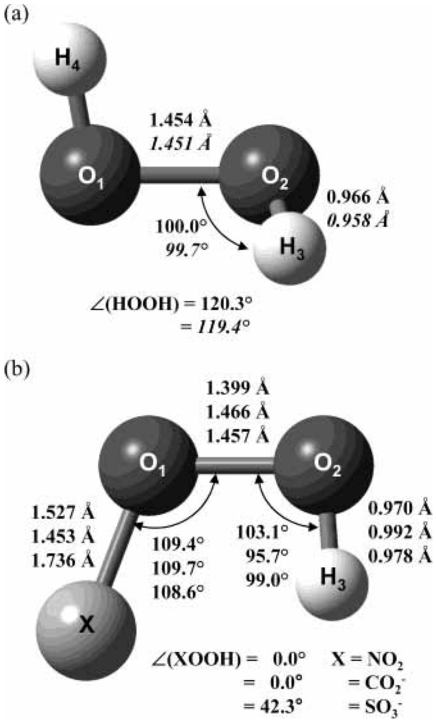

Figure 1. Structural parameters in the gas phase for the ground state of (a) hydrogen peroxide and (b) HOOX molecules ($X = NO_2$, CO_2^-, and SO_3^-) obtained at the B3LYP/6-311G** level of theory and used in the IPCM calculations. Values in italic correspond to the structural parameters obtained with the SCIPCM model.

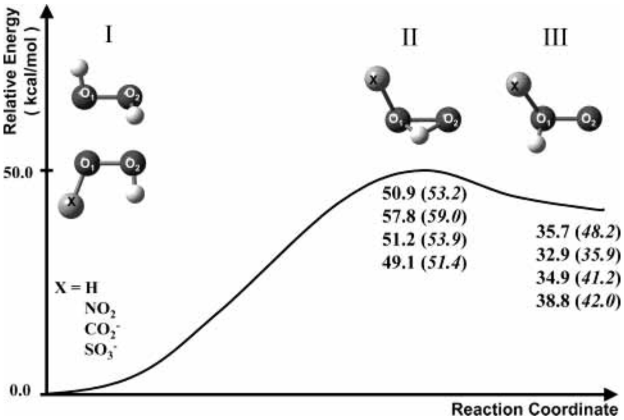

Figure 2. Structural conformations and comparison of the energetic features for the (1,2) hydrogen-shift reaction of peroxides calculated with the B3LYP/6-311G** model, including solvent effects with the IPCM model. Ground-state (**I**), transition-state (**II**), and oxywater-like complex (**III**) structures are shown. The relative energy values are referenced to the ground state without ZPVE correction. The values in parentheses are the relative energy values of the same systems in the gas phase.

TABLE 1: Vertical Singlet − Triplet Energy Differences (without ZPVE Correction) for Ground-State (I), Transition-State (II), and Oxywater-Like Complexes (III) of Peroxides and Harmonic Vibration Analysis of the Singlet TS Structures Involved in the (1,2) Hydrogen Shift[a]

	$\Delta E_{vertical}$ (kcal/mol)			singlet TS frequencies[b]
molecule	I	II	III	(cm^{-1})
HOOH	107.2	37.0	47.9	1000.85i
$HOONO_2$	103.5	63.7	12.5	1629.00i
$HOOCO_2^-$	95.4	51.8	73.1	1226.68i
$HOOSO_3^-$	96.7	46.4	68.4	1222.87i

[a] Singlet and triplet calculations include solvent effects. [b] For all cases in this work, the corresponding TS structure only has one imaginary frequency.

complex.[18−26] For the HOOH, $HOOCO_2^-$, and $HOOSO_3^-$ systems, the predicted barriers for the (1,2) hydrogen-shift isomerization reaction are ca. 50.0 kcal/mol. The energy barrier for the isomerization of the $HOONO_2$ derivative is a little higher by about 8.7 kcal/mol. The structural and energetic characterization of the isomerization reaction in the gas phase and in solution for all four peroxides is summarized in Figure 2. It includes the ground-state structure (**I**), the transition-state structure (**II**), and the oxywater-like complex (**III**). The calculations predict that the solvent induces a stabilization at least of 3 kcal/mol to the oxywater-like complexes, suggesting that a polar solvent can play a significant role in the isomerization reaction. This result agrees with the work of Okajima.[22] This author studied the isomerization of hydrogen peroxide to oxywater with the involvement of *n* molecules of water ($n = 0-3$), and he demonstrated that a protic solvent such as H_2O can play a significant role in accelerating the formation of oxywater.

It is important to notice that the transition state involved in the (1,2) hydrogen-shift reactions of peroxides has a three-center two-electron bond.[26] Gritsenko et al.[66] showed that some GGA functionals overestimate the stability of the transition state in reactions that involve three-center two- or four-electron bonds; however, they concluded that hybrid functionals such as B3LYP improve the energetic description of this reactions. To be more confident with our calculations, we compare our results with the PES calculated by Schaefer et al.[25,27] at the CCSD(T)/TZ2P+f level of theory for the $HOOH \rightarrow H_2O{-}O$ reaction in the gas phase. Schaefer's calculation predicts an activation energy of 52.4 kcal/mol. This energy is nicely reproduced by our calculations, 53.2 kcal/mol (Figure 2). In addition, the values of the energy gap between the transition state and the oxywater are 5.7 and 5.0 kcal/mol at the CCSD(T)/TZ2P+f[25,27] and B3LYP/6-311G** (this work) levels, respectively.

However, the ground states of all four peroxides as well as the corresponding transition-state structures and oxywater-like complexes are singlets, so the (1,2) hydrogen-shift process proceeds via the singlet channel. (The energy comparison between the triplet and singlet states quoted in Table 1 is made in terms of the vertical singlet/triplet energy difference.) Note that for all of the peroxides considered the singlet transition state is predicted to be largely stabilized with respect to the vertical triplet state ($\Delta E \geq 37.0$ kcal/mol). At this point, it is important to mention that the optimized triplet analogue of oxywater corresponds to a van der Waals complex of a water molecule and a triplet oxygen atom, which is weakly bound by ∼1 kcal/mol relative to the $H_2O + O$ (^3P) exit channel. This van der Waals complex is predicted to be ∼15 kcal/mol more stable than the singlet oxywater.

The global reactivity pattern of molecules may be conveniently described in terms of global response functions such as chemical hardness and softness[41,44,45] and global electrophilicity.[46] These quantities were evaluated for the ground- and transition-state (GS and TS, respectively) structures associated with the internal rearrangement of the peroxides considered in the present study. The results are summarized in Table 2. First, we observe that the GS hardness for all four peroxides is greater than the chemical hardness for the corresponding TS structures, a result consistent with the maximum hardness principle.[67] The activation softness, $\Delta S = S^{\ddagger} - S^{\circ}$, is also depicted in Table 2. It may be seen that the $HOONO_2$ displays the higher value in softness activation toward the formation of the corresponding NO_2-substituted oxywater complex; furthermore, this species

TABLE 2: Global Reactivity Indices of Peroxides Including Polar Solvent Effects[a]

molecule	state	ϵ_{HOMO}	ϵ_{LUMO}	μ	η	S	ΔS	ω
HOOH	I	−0.28	0.01	−0.13	**0.29**	3.43	***1.67***	**0.81**
	II	−0.28	−0.09	−0.18	0.20	5.09		2.35
	III	−0.23	−0.02	−0.13	0.21	4.66		1.00
$HOONO_2$	I	−0.33	−0.08	−0.21	**0.24**	4.11	***1.76***	**2.38**
	II	−0.28	−0.11	−0.20	0.17	5.87		3.10
	III	−0.26	−0.14	−0.20	0.12	8.34		4.63
$HOOCO_2^-$	I	−0.24	0.03	−0.10	**0.27**	3.67	***1.23***	**0.54**
	II	−0.23	−0.02	−0.13	0.20	4.91		1.07
	III	−0.18	0.04	−0.07	0.23	4.44		0.30
$HOOSO_3^-$	I	−0.27	0.00	−0.14	**0.27**	3.74	***1.11***	**0.95**
	II	−0.26	−0.06	−0.16	0.21	4.85		1.67
	III	−0.22	−0.04	−0.13	0.18	5.59		1.24

[a] All quantities are reported in atomic units except the global electrophilicity ω, which is expressed in eV.

TABLE 3: Regional Electrophilic (+), Nucleophilic (−), and Radical (0) Fukui Functions for the Species Involved in the (1,2) Hydrogen Shift of Peroxides[a]

		I			II			III		
molecule	site	f^+	f^-	f^0	f^+	f^-	f^0	f^+	f^-	f^0
HOOH	O_1	0.33	0.48	0.41	0.26	0.11	0.19	0.00	0.04	0.02
	O_2	0.33	0.48	0.41	0.63	**0.87**	0.75	0.30	**0.95**	0.62
$HOONO_2$	O_1	0.04	0.16	0.10	0.25	0.17	0.21	0.20	0.08	0.14
	O_2	0.00	0.47	0.24	0.11	**0.74**	0.42	0.27	**0.50**	0.39
$HOOCO_2^-$	O_1	0.41	0.39	0.40	0.31	0.14	0.22	0.01	0.09	0.04
	O_2	0.35	0.42	0.39	0.58	**0.77**	0.68	0.13	**0.86**	0.50
$HOOSO_3^-$	O_1	0.37	0.00	0.18	0.27	0.10	0.19	0.13	0.07	0.10
	O_2	0.36	0.00	0.18	0.60	**0.84**	0.72	0.10	**0.86**	0.48

[a] All quantities are expressed in atomic units.

presents at the same time the highest activation energy for the interconversion. This result may be traced to a significant polarization of the TS structure induced by the strong electron-withdrawing behavior of the neutral NO_2 group. For the remaining substituted systems, the negatively charged CO_2^- and SO_3^- groups exert a similar electron-releasing effect upon activation, but their activation energies are lower than that presented by the NO_2 derivative. The analysis of the global electrophilicity pattern predicted for these molecules reveals that whereas the GS of HOOH is moderately electrophilic the GS associated with the $HOONO_2$ derivative is highly electrophilic (Table 2). Charged peroxides $HOOCO_2^-$ and $HOOSO_3^-$ are also predicted to be moderate electrophiles. Note, however, that the electrophilicity of both HOOH and $HOONO_2$ is strongly enhanced in the TS structure (**II**) that connects them to the corresponding oxywater-like complexes. However, the transition-state structures associated with negatively charged peroxides $HOOCO_2^-$ and $HOOSO_3^-$ have smaller values. Additionally, the oxywater complex (**III**) shows slight electrophilic activation with respect to the HOOH ground state, and the corresponding oxywater complex (**III**) associated with the $HOONO_2$ derivative displays a large electrophilicity enhancement that is even more pronounced than that shown for the TS structure. This result is probably due to the strong electron-withdrawing effect promoted by the NO_2 group at the O_1 site.

4.2. Selectivity and Site Activation. To characterize the electrophilic, nucleophilic, and radical sites for the ground states and the activated forms of the peroxides, we performed an analysis of the local reactivity patterns in terms of the Fukui function. The effect of solvation on the condensed Fukui function has been discussed in the literature; for example, Fuentealba et al.[59] using a continuum model and Balawender et al.[68] using a discrete solvent model showed a negligible solvent effect on the Fukui function. Table 3 displays the results obtained for the whole series of peroxides considered in the present study. The symmetry of the ground state of HOOH maps out in the Fukui function. However, the asymmetric transition-state structure (**II**) shows high selectivity toward electrophilic attack at the O_2 site, which corresponds to the center that is being deprotonated in the process leading to the oxywater complex. This center is also the active site for nucleophilic and radical attacks. The oxywater structure (**III**) is of particular interest because this structure has been proposed as an intermediate in several chemical processes, including the epoxidation of alkenes.[69] This complex is characterized by high electrophilicity at the acidic protons (70% of the electrophilic potential is distributed in the hydrogen atoms attached to the O_2 center) and the complete deactivation of O_1. The local nucleophilic pattern, as measured by the f_k^- index, reveals a very strong propensity of the O_2 site to receive electrophilic attacks. The radical activity at this site is less than that presented for the transition-state structure (**II**). This result suggests that the oxywater complex is more likely to be involved in ionic rather than radical processes, a result that is consistent with the known reactivity reported for this species.[10] Another interesting observation concerning the local reactivity pattern of the oxywater complex is related to a possible epoxidation mechanism of alkenes that was recently proposed by Jursic.[69] This author suggests that the reaction mechanism involves the electrophilic attack of the O_2 atom in oxywater on the double bond of the alkenes, even thought the transition state for such a transformation has been located only at the semiempirical AM1 level of theory. This result is consistent with the exceptionally high value of the nucleophilic Fukui function at this center in the oxywater complex shown in Table 3. Note, however, that the TS structure (**II**) is also an activated form of hydrogen peroxide toward the electrophilic attack on the electron-rich π system of alkenes.

For the neutral $HOONO_2$ peroxide, the local reactivity analysis is also shown in Table 3. The ground state of this molecule is predicted to be active for electrophilic attacks on the O_2 site. Note, however, that the nucleophilic pattern at the O_2 site is slightly lower than the one presented by the reference HOOH molecule, so we may conclude that the replacement of one hydrogen atom by the neutral NO_2 group has a marginal deactivating effect at this site. The local electrophilic activity as measured by the f_k^+ index at both oxygen sites is marginal and significantly lower than the local electrophilicity pattern predicted for the HOOH molecule. Therefore, NO_2 substitution has a deactivating effect on nucleophilic attacks at these sites. The TS structure connecting the GS of this peroxide with the corresponding oxywater complex shows significant nucleophilic activation at the O_2 site, which is lower than the nucleophilic activation in the reference HOOH molecule at the same site. Note that the $HNO_2O{-}O$ derivative is predicted to be less activated than the oxywater at the O_2 site. The two negatively charged peroxides, $HOOCO_2^-$ and $HOOSO_3^-$, are predicted to be slightly electrophilic at the O_2 site in the ground state. However, their activated forms (i.e., structure **II** corresponding to the TS for the (1,2) hydrogen shift) appear to be even more activated toward electrophilic attacks at the O_2 site. Note that the electrophilicity pattern at this site measured by f_k^+ becomes closer to that shown by the TS structure of HOOH. On the basis of this result, one would expect both $HOOCO_2^-$ and $HOOSO_3^-$ peroxides to be efficient epoxidant agents in their reactions with alkenes. The corresponding CO_2^-- and SO_3^--substituted oxywater derivatives (structure **III**), however, show significant

TABLE 4: Local Electrophilic (+), Nucleophilic (−), and Radical (0) Activation Analyses of Peroxides[a,b]

molecule	site	$f_k^+\Delta S$	$S\Delta f_k^+$	Δs_k^+	$f_k^-\Delta S$	$S\Delta f_k^-$	Δs_k^-	$f_k^0\Delta S$	$S\Delta f_k^0$	Δs_k^0
HOOH	O_1	0.55	−0.23	0.31	0.81	−1.27	−0.46	0.68	−0.75	−0.07
	O_2	0.55	1.04	1.59	0.81	1.32	2.13	0.68	1.18	1.86
$HOONO_2$	O_1	0.01	0.44	0.45	0.28	0.05	0.33	0.17	0.45	0.63
	O_2	0.07	0.85	0.93	0.83	1.10	1.93	0.42	0.77	1.19
$HOOCO_2^-$	O_1	0.50	−0.36	0.14	0.48	−0.92	−0.44	0.49	−0.64	−0.15
	O_2	0.44	0.88	1.31	0.52	1.29	1.81	0.48	1.08	1.56
$HOOSO_3^-$	O_1	0.41	−0.36	0.05	0.00	0.38	0.38	0.20	0.01	0.21
	O_2	0.40	0.91	1.31	0.00	3.11	3.11	0.20	2.01	2.21

[a] All quantities are expressed in atomic units. [b] See the paragraph following eq 7 of the text for the definitions of the involved quantities.

nucleophilic activation at the O_2 site. Note also that in general the whole series of peroxides examined here shows a local reactivity pattern that is markedly ionic rather than radical, a result that is consistent with the observed activity of these compounds as efficient ionic oxidants.[10]

The analysis of site activation performed on the basis of local softness gives a complementary picture of the local reactivity patterns. It introduces, apart from the variations in the Fukui functions from the ground state to any activated form of molecules including the transition state, the effect of global activation measured, for instance, by the changes in global softness. Equation 7 is an example of how the site-activation analysis may be performed. The first entry in Table 4 shows the electrophilic-, nucleophilic-, and radical-site activation patterns as measured by the Δs_k^α quantities defined in eq 7 at the oxygen sites of hydrogen peroxide. For instance, electrophilic activation at the O_2 center is mainly driven by local activation that may be traced to a significant increase in the electrophilic Fukui function value at this site. The O_1 center, however, is slightly electrophilically activated, a result associated with moderate global electrophilic activation and moderate local electrophilic deactivation at that site. The nucleophilic activation analysis shows strong activation at the O_2 site that is mainly local in nature. The O_1 center is deactivated with a significant contribution from local effects. Note that the average effect measuring the activation pattern toward radical attacks is predicted to be lower than the nucleophilic activation pattern at the O_2 center but greater than the electrophilic activation at the same site. The O_1 center is deactivated for both electrophilic and radical attacks and marginally activated for a nucleophilic attack. Note that the $HOONO_2$ species shows marginal electrophilic activation as compared to that of the charged $HOOCO_2^-$ and $HOOSO_3^-$ peroxides. On the basis of the electrophilic activation pattern encompassing the global activation that results from the changes in global softness from the ground to the transition state, one would again expect these charged peroxides to act as efficient reagents in oxygen-transfer reactions. Note that the site-activation model based on the changes in local softness predicts that $HOONO_2$ will show moderate electrophilic activation at the O_2 site.

5. Concluding Remarks

The global and local reactivity patterns of a series of neutral and charged peroxides have been analyzed in detail, using the global and local descriptors of reactivity defined in the context of DFT, in their stable structures and in their corresponding activated forms ((1,2) hydrogen-shift structures and the involved TS). The global analysis shows that the electrophilic power of the ground and transition states as well as the oxywater-like complex of $HOONO_2$ are strongly activated with respect to hydrogen peroxide. However, $HOOCO_2^-$ is globally deactivated, but $HOOSO_3^-$ presents small variations. The local analysis at the transition state reveals strong electrophilic activation of the oxygen atom that is being deprotonated (O_2) in HOOH, $HOOCO_2^-$, and $HOOSO_3^-$ peroxides. In addition, nucleophilic behavior is always enhanced at the TS of the internal rearrangement. Both effects, global and local, always produce an increase in the condensed local softness at the O_2 site for electrophilic and nucleophilic reactions patterns; however, the migration of the hydrogen atom deactivates the O_1 site in most cases.

The energy barriers for the (1,2) hydrogen shift are modified by the presence of an explicit solvent[22] in a similar manner as when a nonexplicit solvent model is used. Therefore, the analysis performed in the present work can provide useful clues in the search for the transition-state structures of those processes where oxywater-like intermediates have been suggested, such as in the epoxidation reactions of alkenes.[69]

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