Two state reactivity mechanism for the rearrangement of hydrogen peroxynitrite to nitric acid

Renato Contreras [a,b,c,*], Marcelo Galván [b], Mónica Oliva [c], Vincent S. Safont [c], Juan Andrés [c], Doris Guerra [d], Arie Aizman [d,*]

[a] Departamento de Química, Facultad de Ciencias, Universidad de Chile, Casilla 653-Santiago, Chile
[b] Departamento de Química, División de Ciencias Básicas e Ingeniería, Universidad Autónoma Metropolitana-Iztapalapa, A.P. 55-534, México, D.F. 09340, Mexico
[c] Departament de Química Física i Analítica, Universitat Jaume I, Avda. Sos Baynat s/n, 12071 Castelló, Spain
[d] Departamento de Química, Universidad Técnica Federico Santa María, Casilla 110-V, Valparaíso, Chile

ABSTRACT

For the isomerization of HOONO to nitric acid, a spin triplet reactive intermediate [3]HOONO* was identified on a two state reactivity (TSR) potential energy surface. This bi-radical is postulated as one of the possible activated species responsible for the potent oxidant activity attributed to H-peroxynitrite. A theoretical analysis based on spin density-dependent reactivity indices consistently explains the observed reactivity of this molecule in biological and model systems.

1. Introduction

Peroxynitrite ($OONO^-$) is a potent oxidant in biological systems. The protonated form, HOONO is stable at pH $\sim$ 6, and reported as one of the first peroxyacid that can be produced in vivo [1]. Up to date, there are two possible mechanisms that might account for the observed oxidizing potential of H-peroxynitrite. The first one considers homolysis of the protonated species HOONO to form the hydroxyl radical which would be the proximate oxidant. The second mechanism involves a putative reactive intermediate, HOONO*, which has been proposed to be the proximate oxidant [1–4]. This HOONO* activated species appears on the potential energy surface as a transient meta stable intermediate during the decomposition of HOONO to nitric acid [1–4].

The nature of the HOONO* intermediate has been theoretically studied by Houk et al. [2,4] Based on B3LYP/6-31G(d) calculations they have discarded the hypothesis that the isomerization of peroxynitrous acid to nitric acid takes place via a concerted rearrangement, in view of the huge barrier of 60.0 kcal/mol including solvent corrections, calculated by Cameron et al. for this mechanism [5]. Instead, they have proposed that the HOONO* species may correspond to hydrogen bonded radical pairs located at minima on the potential energy surface of a stepwise route for the conversion of

HOONO into nitric acid. These species are proposed to arise from the homolysis of HOONO followed by recombination to yield hydrogen bonded bi-radicals which are almost degenerate in energy. These hydrogen bonded complexes have free energies that are *c.a.* 15.0 kcal/mol above the ground state of cis-peroxynitrous acid [4]. The resulting energy barriers fall very close to the experimental free energy of activation (17.0 kcal/mol) estimated for the rearrangement [1].

In this work we report new calculations on this system that suggests that the intermediate HOONO* (which we shall call [3]HOONO*(TSR) hereafter) may be a spin triplet reactive intermediate located after assuming a two state reactivity (TSR) mechanism for the isomerization of peroxynitrous acid to nitric. The two state reactivity concept was formerly proposed by Schroder, Shaik and Schwarz to explain reaction mechanisms in organometallics [6]. The TSR paradigm suggests that there may be more than one spin surface connecting reactants and products. In other words, a thermal reaction which involves spin crossover along the reaction path from reactants to products should be described in terms of two state reactivity, if product formation arises from an interplay of spin polarization and the respective barrier heights on both spin surfaces. Thus, a TSR mechanism may provide lower energy activation paths for otherwise too high activation channels in such a manner that the spin inversion junction can act as an effective rate bottleneck (if the spin crossover occurs before the transition state on the energy surface of starting materials) or as a product distributor (if the spin crossover occurs after the transition state on the energy surface of starting materials). For the present case, the spin crossover from singlet to triplet channels leads to locate a reactive

* Corresponding authors. Address: Departamento de Química, Facultad de Ciencias, Universidad de Chile, Casilla 653-Santiago, Chile. Fax: +56 2 2713888 (R. Contreras); fax: +5632 654258 (A. Aizman).

E-mail addresses: rcontrer@uchile.cl (R. Contreras), arie.aizman@usm.cl (A. Aizman).

intermediate, which we propose here to be the proximate oxidant HOONO* species. The TSR paradigm is framed on a general quantum theory of chemical reactions [7,8]. The TSR model has already been applied to the study of oxidation reactions catalyzed by Cytochrome P450 [9,10]. The TSR energy results are complemented with reactivity analyses based on global and local reactivity indexes; these are defined in the context of the spin polarized density functional theory. The analysis based on reactivity indexes provides a coherent picture that correctly accounts for the oxidizing and nitrating potentials of the ^{3}HOONO*(TSR) species.

2. Model equation and computational details

Within the spin polarized version of density functional theory, the electronic chemical potential μ_N corresponds to the first-order partial derivative of the energy, with respect to the total number of electrons at constant external potential $v(\mathbf{r})$ and spin number N_S [11–13]

$$\mu_N = \left(\frac{\partial E}{\partial N}\right)_{N_S, v(r)} \tag{1}$$

This quantity can be evaluated by using the finite difference formula proposed by Galván et al. as [11,12]

$$\mu_N \approx \frac{1}{2}\left(\mu_N^+ + \mu_N^-\right), \tag{2}$$

where μ_N^+ and μ_N^- are chemical potentials in the direction of increasing and decreasing the electron numbers, respectively. These indices can be approximated by [11,12]:

$$\mu_N^+ \approx \frac{1}{2}\left(\varepsilon_L^\alpha + \varepsilon_L^\beta\right), \quad \mu_N^- \approx \frac{1}{2}\left(\varepsilon_H^\alpha + \varepsilon_H^\beta\right), \tag{3}$$

where ε_L^α, ε_L^β, ε_H^α and ε_H^β are the one electron orbital energies of the α and β LUMO and HOMO orbitals, respectively.

The generalized hardness η_{NN} is the equivalent of the chemical hardness in the spin-restricted case, except, again, that the derivative is evaluated at a fixed spin number N_S. It can be approximated as [11]

$$\eta_{NN} \approx (\mu_N^+ - \mu_N^-). \tag{4}$$

The generalized Fukui functions $f_{NN}^\pm(\mathbf{r})$ are the analogous of the electrophilic (+) and nucleophilic (−) counterparts defined within the spin-restricted DFT [11]. They describe the response of electron density to a constrained charge transfer processes. These Fukui functions can be evaluated using the approximations proposed by Galván et al. as follows [11]:

$$f_{NN}^+(r) \approx \frac{1}{2}\left[|\phi_L^\alpha|^2 + |\phi_L^\beta|^2\right] \text{and} \quad f_{NN}^-(r) \approx \frac{1}{2}\left[|\phi_H^\alpha|^2 + |\phi_H^\beta|^2\right], \tag{5}$$

where $\phi_L^\alpha(\mathbf{r})$, $\phi_L^\beta(\mathbf{r})$, $\phi_H^\alpha(\mathbf{r})$ and $\phi_H^\beta(\mathbf{r})$ are the α and β LUMO and HOMO orbitals.

The spin-philicity (ω_S^+) and spin-donicity (ω_S^-) indices were introduced by Contreras et al. to describe the philicity of the system to undergo spin polarization in the direction of increasing (+) and decreasing (−) multiplicity, respectively [14]. These indices are expressed as follows:

$$\omega_S^+ = \frac{(\mu_S^+)^2}{2\eta_{SS}^0} \quad \text{and} \quad \omega_S^- = \frac{(\mu_S^-)^2}{2\eta_{SS}^0}, \tag{6}$$

where μ_S^+ and μ_S^- are the spin-potentials in the direction of increasing and decreasing multiplicity, respectively, and η_{SS}^0 is the spin hardness. These quantities can be evaluated by using the finite difference formulae proposed by Galván et al. as [11–13]:

$$\mu_S^+ \approx \frac{\varepsilon_L^\alpha(M) - \varepsilon_H^\beta(M)}{2} \quad \text{and} \quad \mu_S^- \approx \frac{\varepsilon_H^\alpha(M') - \varepsilon_L^\beta(M')}{2}; \tag{7}$$

in terms of the one-electron energies of the HOMO and LUMO orbitals for the system in the lower (M) and upper (M') spin multiplicities. The spin-hardness (η_{SS}^0) can be obtained from the spin potentials as follows:

$$\eta_{SS}^0 = \frac{\mu_S^- - \mu_S^+}{2}. \tag{8}$$

For the study of local chemical reactivity it is necessary to introduce the corresponding local descriptors. For instance, local spin philicity and spin donicity index are easily obtained from their global counterpart as follows [15,16]:

$$\omega_S^+(\mathbf{r}) = \omega_S^+ f_{SS}^+(\mathbf{r}) \quad \text{and} \quad \omega_S^-(\mathbf{r}) = \omega_S^- f_{SS}^-(\mathbf{r}), \tag{9}$$

where $f_{SS}^\pm$ is the Fukui function for increasing spin number (+) and decreasing spin number (−). These spin Fukui functions can also be evaluated using the approximations proposed by Galván et al. [11]:

$$f_{SS}^+(r) \approx \frac{1}{2}\left[|\phi_L^\alpha|^2 + |\phi_H^\beta|^2\right] \quad \text{and} \quad f_{SS}^-(r) \approx \frac{1}{2}\left[|\phi_H^\alpha|^2 + |\phi_L^\beta|^2\right]. \tag{10}$$

Relative energies for the different chemical species present in both the triplet and singlet potential energy surface (PES), including the minimum energy crossing points (MECP) were obtained at the B3LYP/6-311G(d,p) level of theory, using the Gaussian03 package of programs [17]. The intrinsic reaction coordinate (IRC) method has been used to describe the minimum energy paths connecting the TSs with the corresponding minima [18]. Structures of the singlet–triplet crossing points were found using Harvey's algorithm [19,20]. The search of the MECP between non-interacting PES, requires energies and analytical energy gradients between both hypersurfaces involved. Starting from the TS closest to the crossing seams, the reaction pathway may be traced down to the corresponding minimum. Thereafter, each point optimized along the IRC path is submitted to a single point energy calculation with the other spin multiplicity. In this manner it is possible to obtain structures that have identical geometry and commensurate energy in the singlet and triplet states. At this point, Harvey's algorithm is applied and the minimum energy crossing points (MECP) are located [19]. This algorithm has been previously used in our groups to study the gas phase reactions of organometallic systems [21,22] and the cycloaddition of triplet carbene to alkenes [23].

Global and local quantities like chemical hardness, spin potential, spin hardness, electrophilicity, spin philicity and a set of generalized Fukui functions were obtained from a single point calculation at the B3LYP/6-311G(d,p) level of theory, at the relevant stationary structures involved in the rate determining step of the TSR pathway (i.e. that involving HOONO ground state, and the ^{3}HOONO*(TSR) intermediate), using Eqs. (1)–(10). The condensed to-atom quantities $f_{NN}^\pm(k)$, and $f_{SS}^\pm(k)$ as well as those that are defined in terms of them used in the present work, may easily be obtained by a method described elsewhere [24,25].

3. Results and discussion

3.1. Energy aspects

The potential energy surface for the rearrangement of H-peroxynitrite to nitric acid has been calculated by several authors [2,4,5,26–32]. We have recalculated this potential energy surface using the B3LYP/6-311G(d,p) method. The optimized geometrical parameters of the relevant stationary points involved in the rearrangement are summarized in Table 1. Table 2 contains the corresponding total energies and the harmonic vibrational analysis for each species (NIMAG is the number of imaginary frequencies found after the frequency analysis). The singlet transition state HOON-O(TS,S) structure shows a single, yet very loose (729.8 i cm^{-1})

Table 1
Geometrical parameters of the optimized structures of the stationary points and non stationary (MECP) structures involved in the TSR H-peroxynitrite to nitric acid rearrangement[a]

Parameter	HOONO	MECP(HOONO)	HOONO(TS,S)	^{3}HOONO* (TSR)	MECP(HNO$_3$)	HNO$_3$
Bond lengths						
O1N2	1.158	1.185	1.167	1.190	1.187	1.194
N2O3	1.480	1.198	1.172	1.198	1.195	1.209
O3O4	1.424	2.110	2.454	2.918	2.947	2.224
O4H5	0.969	0.972	0.969	0.976	0.974	0.971
Bond angles						
O1N2O3	114.6	133.0	139.9	134.0	135.0	130.5
N2O3O4	112.1	104.1	70.5	93.8	49.6	35.0
O3O4H5	102.2	89.8	80.7	40.2	71.7	73.6
Torsional angles						
O1N2O3O4	−5.3	−1.0	−72.7	−27.3	−174.9	−180.0
N2O3O4H5	92.5	173.5	−163.2	149.8	−174.6	180.0

[a] Bond distances in Angstroms and angles in degrees.

Table 2
Total energies and harmonic vibrational analysis for the concerted rearrangement of hydrogen peroxynitrite to nitric acid at B3LYP/6-311G(d,p) level of theory[a]
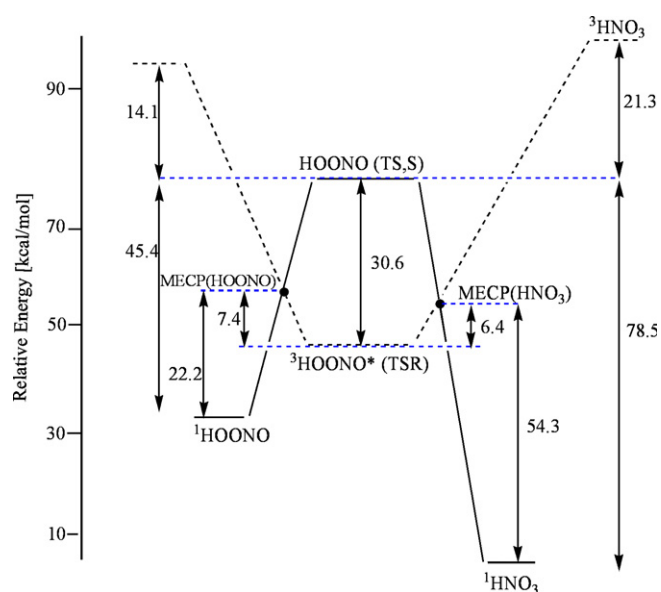
Species	NIMAG	Spin multiplicity	Imaginary frequency	−Energy
HOONO	0	Singlet	–	280.914695
	2	Triplet[b]	−450.75	280.819863
			−398.27	
MECP(HOONO)	1	Singlet	−94.35	280.879249
	2	Triplet	−219.81	280.879271
			−123.09	
HOONO(TS,S)	1	Singlet	−729.79	280.842323
HOONO(TS$_V$,T)[c]	3	Triplet[b]	−418.20	280.878243
			−216.01	
			−99.85	
^{3}HOONO*(TSR)	0	Triplet	–	280.891104
MECP(HNO$_3$)	1	Singlet	−216.52	280.880877
	2	Triplet	−300.26	280.880875
			−138.40	
HNO$_3$	0	Singlet	–	280.967374
	2	Triplet[b]	−820.56	280.808320
			−541.48	

[a] Energy values in hartrees, frequency values in cm^{-1}.
[b] Vertical energy evaluated at the external potential of the singlet.
[c] The HOONO(TS$_V$,T) structure is not a true TS structure. It corresponds to a structure obtained by a vertical calculation using the optimized HOONO(TS,S) structure, see the text for further details.


Fig. 1. Relative energies between all the species involved as probable intermediates along the TSR mechanism for the H-peroxynitrite to nitric acid rearrangement at B3LYP/6-311G(d,p) level of theory. The point of reference is the energy of the ground state of **HNO$_3$**.

imaginary frequency. We have next considered a non relaxed triplet state HOONO(TS$_V$,T) obtained by a single point calculation performed at the frozen geometry of the HOONO(TS,S) structure to obtain the HOONO(TS$_V$,T) energy. Note that this structure is not a true TS structure because it was obtained from a vertical calculation performed on the geometry of the HOONO(TS,S) and therefore is not a geometry stationary state for the spin triplet; note also that it further shows two imaginary frequencies (see Table 2). Surprisingly, the HOONO(TS$_V$,T) structure is strongly stabilized with respect to the HOONO(TS,S), thereby suggesting a possible *intersystem crossing* mechanism for the rearrangement of H-peroxynitrite to nitric acid. Hence, we have explored the IRC path down from the HOONO(TS,S) in both directions, by making at each point a vertical calculation for the triplet state. In such a way we have located the crossing points along the IRC, that have then been used as starting points in the search of the two corresponding MECPs, namely MECP(HOONO) and MECP(HNO$_3$). From both MECPs, a common triplet minimum, ^{3}HOONO*(TSR) has been found, and hence the isomerization mechanism from HOONO to HNO$_3$ can be described as a two state reactivity process involving the singlet and triplet PES, *via* MECP(HOONO), a reactive intermediate

^{3}HOONO*(TSR) and MECP(HNO$_3$). The energy gap between HOONO and MECP(HOONO), 22 kcal/mol, agrees fairly well with the experimental energy barrier, 17 kcal/mol [1] and also with the H-bonded radical pairs model proposed by Houk et al. [2,4]. The relative energies between all these species are depicted in Fig. 1. In summary, according to the TSR energy analysis the isomerization of peroxynitrous acid to nitric acid is proposed to proceed according to the mechanism shown in Scheme 1.

Starting from the HOONO singlet ground state, the system evolves towards the first singlet triplet crossing point which is 22 kcal/mol higher in energy. This MECP(HOONO) acts as an effective energy barrier to the isomerization. This structure relaxes to the reactive intermediate ^{3}HOONO*(TSR), which is a minimum in the triplet PES. From this state, the system changes to a second crossing point MECP(HNO$_3$) with an energy barrier of 6.4 kcal/mol. Finally, the system relaxes along the singlet channel towards the HNO$_3$ ground state. Note that the proposed mechanism does not require the homolysis step leading neither to the separated HO· and ·NO$_2$ radicals nor to the cage pair radical HOONO* proposed earlier [2,4]. The proposed mechanism is also consistent with the experimental data reported by Koppenol et al. [1] who
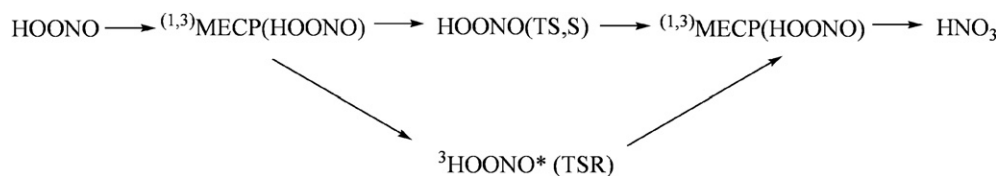
**Scheme 1.** Two state reactivity mechanism proposed for the conversion of HOONO into nitric acid.

suggested that H-peroxynitrite may react with different compounds by at least two distinct mechanisms and that the hydroxyl radical is not involved in either. This result has been later confirmed by Pryor et al. [3].

3.2. Global and local reactivity aspects

The proposal that ^{3}HOONO*(TSR) species may correspond to one of the possible activated form of H-peroxynitrite may be conveniently reinforced by a global and local reactivity analysis that consistently explains the evolution of the system from the HOONO to the HNO$_3$ ground states on one hand, and that coherently explain the known chemistry of H-peroxynitrite. For the global analysis, the pertinent quantities are the chemical hardness η_{NN}, the spin potentials μ_S^+ and μ_S^- associated with the energy change in the direction of increasing and decreasing multiplicity, respectively, and the spin hardness η_{SS}^0 measuring the resistance of the system to modify its spin multiplicity all them defined in Eqs. (2)–(4), (8).

The global analysis is summarized in Table 3. The vertical energy gap $\Delta E_V = {}^3E - {}^1E$ is included to help in the understanding of the meaning of the other reactivity indices as for instance the spin potentials in the direction of increasing (+) and decreasing (−) multiplicities. A first pertinent remark is that the generalized chemical hardness η_{NN}, is in the order HOONO > ^{3}HOONO* (TSR), thereby confirming that the triplet activated species are effectively softer and therefore more reactive than the HOONO ground state, as it should be expected from the maximum hardness and minimum polarizability principles [33–35]. The value of the spin potentials in both directions needed to build up the spin philicity and spin donicity indexes ω_S^+ and ω_S^-, respectively, are also quoted in Table 3. These indices suggest that the philicity of the ground state to undergo spin polarization towards the activated triplet species is significant ($\omega_S^+ = 2.55$ eV), as well as the philicity of the activated species to undergo spin polarization towards the singlet ground state of the product HNO$_3$ ($\omega_S^- = 1,32$ for the ^{3}HOONO*(TSR)). In summary, the ^{3}HOONO*(TSR) activated species proposed as intermediate during the conversion of peroxynitrous acid into nitric acid is consistently predicted to be electronically softer than the HOONO ground state, and with a bigger propensity to change their spin multiplicity towards the singlet product HNO$_3$ (as it may be seen from the μ_S^- values quoted in Table 3).

The local analysis of the structures involved in the TSR potential energy surface for the concerted rearrangement of H-peroxynitrite to nitric acid, may give some important clues about the experimentally known reactivity pattern displayed by these species. We will focus on two important reactions experimentally studied by Pryor et al. [36] that include oxidation and nitration of phenol (ArOH) by
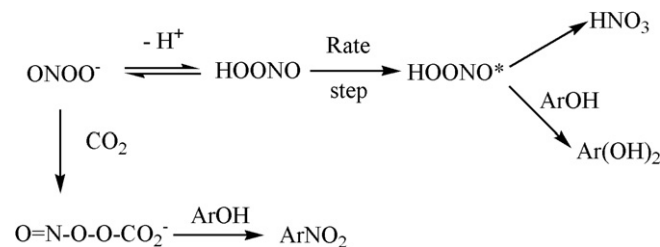
Scheme 2. Reaction scheme for the isomerization and hydroxylation reactions (right branch) and for the formation of the nitrating nitrosoperoxocarboxylate intermediate (left branch) proposed in Ref. [35].

the activated HOONO* species. The mechanism proposed by Pryor et al. is shown in Scheme 2.

HOONO* may isomerizes towards HNO$_3$ or undergo a one electron oxidation to yield biphenol (See right branch in Scheme 2). On the other hand, and in the presence of carbonate, the HOONO* species may form the $O = NOO – CO_2^-$ intermediate which acts as a nitrating agent. Note that the proposed mechanism for the formation of this intermediate consider the deprotonation of peroxynitrous acid to yield peroxynitrite which is the species that bind CO_2 to yield the nitrating $O = NOO – CO_2^-$ intermediate [36].

This reactivity pattern may be described by looking at the local or regional reactivity indexes that depends on the electronic and spin distributions. The relevant points of the TSR potential energy surface to be considered are: the singlet ground state HOONO structure and the activated ^{3}HOONO*(TSR) intermediate. These structures are included in Fig. 2 for atom numbering. The local reactivity parameters are quoted in Table 4.

We first consider the electrophilic interaction of peroxynitrite with CO_2 leading to the formation of the nitrosoperoxocarboxylate $O = NOO – CO_2^-$ intermediate, by a nucleophilic attack to the carbon atom of CO_2 (see Scheme 2) [36]. The regional nucleophilic Fukui function $f_{NN}^-(k)$ of the activated ^{3}HOONO*(TSR) structure show its highest value at the hydroxyl Oxygen center O4, (see Table 4 column 4). Note that even though this reaction has been proposed to involve the base $^-$OONO, [36] the activated form of peroxynitrite ^{3}**HOONO*(TSR)** is predicted to be a still active species to form the transient intermediate nitrosoperoxocarboxylate $O = NOO – CO_2^-$, according to the mechanism shown in Scheme 3.

It is however the radical activity of H-peroxynitrite what makes this system to be the object of increasing interest. Spin reactivity may be conveniently described with the aid of the generalized spin Fukui function $f_{SS}(k)$ defined in Eq. (10). Values of this index for the singlet ground state HOONO, and the activated ^{3}HOONO*(TSR)

Table 3
Summary of global DFT-SP indices evaluated at the B3LYP/6-311G(d,p) level of theory for the relevant species involved in the TSR mechanism[a]

Species	ΔE_V (kcal/mol)	μ_S^+	μ_S^-	η_{SS}^0	ω_S^+	ω_S^-	μ_{NN}	η_{NN}
HOONO	59.5	2.65	−0.10	−1.38	2.55	–	−5,44	5,29
^{3}HOONO*(TSR)	−37.1	0.74	−1.85	−1.29	–	1.32	−5,92	4,69

[a] Spin reactivity index (in eV units) evaluated in the singlet to triplet direction (+) and in the triplet to singlet direction (−).
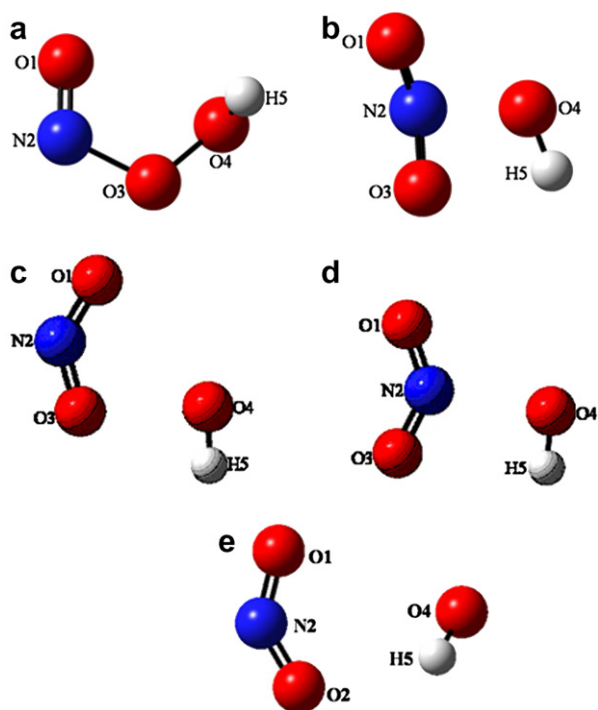
Fig. 2. Structures of the relevant points in the B3LYP/6-311G(d,p) TSR potential energy surface for the H-Peroxynitrite to nitric acid rearrangement: a. the singlet ground state **HOONO;** b. the singlet HOONO(TS,S) structure; c. the first minimum energy singlet–triplet crossing point MECP (HOONO); d. the second minimum energy triplet–singlet crossing point MECP (HNO$_3$) and e. the activated ^{3}HOONO*(TSR) intermediate. Atom numbering is included for the local analysis.

Table 4

Generalized (regional) Fukui functions for the HOONO ground state and the activated triplet structure[a]

Species	Site (k)	$f_{NN}^+(k)$	$f_{NN}^-(k)$	$f_{SS}^+(k)/f_{SS}^-(k)$
HOONO	O1	0.3465	0.3243	0.3354
	N2	0.5553	0.2191	0.3872
	O3	0.0890	0.2404	0.1647
	O4	0.0064	0.2118	0.1091
	H5	0.0028	0.0045	0.0037
Normalization	$\sum_k$	1.0000	1.0000	1.0000
^{3}HOONO*(TSR)	O1	0.1320	0.1422	0.1424
	N2	0.2427	0.1885	0.1852
	O3	0.1273	0.1402	0.1399
	O4	0.4908	0.5170	0.5196
	H5	0.0072	0.0122	0.0128
Normalization	$\sum_k$	1.0000	1.0000	1.0000

[a] The $f_{SS}^+(k)$ and $f_{SS}^-(k)$ values applies to the singlet and triplet structures, respectively.
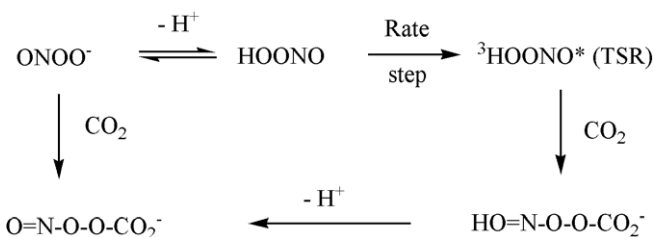
Scheme 3. Possible reaction scheme for the for the formation of the nitrating O $=$ NOO $-$ CO$_2^-$ intermediate proposed here after the local reactivity analysis.

intermediate are also summarized in Table 4. At the ground state HOONO, the spin Fukui function is almost entirely distributed over

the ONO moiety. Taking the group property as the sum of the regional spin Fukui function over the atoms belonging to the ONO and OH groups, it may be seen that the radical activity is almost concentrated at the ONO moiety (f_{SS}^+(ONO) $= 0.89$ and f_{SS}^+(OH) $= 0.11$). Upon activation towards the ^{3}HOONO*(TSR) intermediate, a partial spin transfer from the ONO unit is observed, thereby leaving the OH moiety as an additional active center for a radical attack (f_{SS}^+(ONO) $= 0.47$ and f_{SS}^+(OH) $= 0.53$). The results of the local analysis with respect to the ^{3}HOONO*(TSR) intermediate indicates that the oxidizing potential of H-peroxynitrite involves the activated form of this species and that the most probable site for one electron oxidation processes would be the OH• moiety, in the form of a hydroxyl radical *activated* by the presence of the NO$_2$ group. In summary, the local reactivity analysis performed on the ^{3}HOON-O*(TSR) biradical structure is consistent with well known potential exhibited by this system as a potent nitrating and hydroxylating agent [36–39].

4. Concluding remarks

The potential energy surface for the concerted rearrangement of H-peroxynitrite to nitric acid has been revisited, using high level density functional theory. New features regarding the activation energies for this rearrangement have been found. For instance, the isomerization of H-peroxynitrite (Hydrogen oxoperoxonitrate (-1)) to nitric acid may be described as a two state reactivity process with two minimum energy crossing points (MECP). The first one from the singlet to the triplet surface occurs before reaching the singlet transition state, thereby producing a net kinetic effect that lowers the energy barrier from 45 to 22 kcal/mol. After the first spin crossover, a triplet reactive intermediate ^{3}HOONO*(TSR) was located. This biradical is postulated here as one of the possible activated species responsible for the potent oxidant activity attributed to H-peroxynitrite. The proposed TSR mechanism does not require the homolysis step leading neither to the separated HO· and ·NO$_2$ radicals nor to the cage pair radical HOONO* postulated earlier.

The local reactivity analysis performed on the ^{3}HOONO*(TSR) biradical structure of the activated form of H-peroxynitrite is consistent with the well known reactivity pattern exhibited by this system as a potent oxidant and nitrating agent.

References

[1] W.H. Koppenol, J.J. Moreno, W.A. Pryor, H. Ischiropoulos, J.S. Beckman, Chem. Res. Toxicol. 5 (1992) 834.
[2] K.N. Houk, K.R. Condroski, W.A. Pryor, J. Am. Chem. Soc. 118 (1996) 13002.
[3] W.A. Pryor, X. Jin, G.L. Squadrito, J. Am. Chem. Soc. 118 (1996) 3125.
[4] Y. Zhao, K.N. Houk, L.P. Olson, J. Phys. Chem. A 108 (2004) 5864.

[5] D.R. Cameron, A.M.P. Borrajo, B.M. Bennett, G.R.J. Thatcher, Can. J. Chem. 73 (1995) 1627.

[6] D. Schroder, S. Shaik, H. Schwarz, Acc. Chem. Res. 33 (2000) 139.

[7] G.A. Arteca, O. Tapia, J. Math. Chem. 37 (2005) 389.

[8] G.A. Arteca, O. Tapia, Int. J. Quant. Chem. 107 (2007) 382.

[9] D. Kumar, S.P. de Visser, S. Shaik, J. Am. Chem. Soc. 126 (2004) 5072.

[10] D. Kumar, S.P. Visser, P.K. Sharma, S. Cohen, S. Shaik, J. Am. Chem. Soc. 126 (2004) 907.

[11] M. Galván, A. Vela, J.L. Gázquez, J. Phys. Chem. 92 (1988) 6470.

[12] M. Galván, R. Vargas, J. Phys. Chem. 96 (1992) 1625.

[13] R. Vargas, M. Galván, A. Vela, J. Phys. Chem. A 102 (1998) 3134.

[14] P. Pérez, J. Andrés, V.S. Safont, R. Contreras, O. Tapia, J. Phys. Chem. A 109 (2005) 4178.

[15] F. De Proft, S. Fias, C.V. Alsenoy, P. Geerlings, J. Phys. Chem. A. 109 (2005) 6335.

[16] D. Guerra, R. Castillo, J. Andrés, P. Fuentealba, A. Aizman, R. Contreras, Chem. Phys. Lett. 424 (2006) 437.

[17] M.J. Frisch, et al., Gaussian 03, Revision D.01, Gaussian, Inc., Wallingford CT, 2004.

[18] C. Gonzalez, H.B. Schlegel, J. Chem. Phys. 90 (1989) 2154.

[19] J.N. Harvey, M. Aschi, H. Schwarz, W. Koch, Theor. Chem. Acc. 99 (1998) 95.

[20] J.N. Harvey, R. Poli, K.M. Smith, Coord. Chem. Rev. 238 (2003) 347.

[21] L. Gracia, J.R. Sambrano, V.S. Safont, M. Calatayud, A. Beltrán, J. Andrés, J. Phys. Chem. A 107 (2003) 3107.

[22] L. Gracia, J. Andrés, V.S. Safont, A. Beltrán, Organometallics 23 (2004) 730.

[23] P. Pérez, J. Andrés, V.S. Safont, R. Contreras, O. Tapia, J. Phys. Chem. A 109 (2005) 4178.

[24] R. Contreras, P. Fuentealba, M. Galván, P. Pérez, Chem. Phys. Lett. 304 (1999) 405.

[25] P. Fuentealba, P. Pérez, R. Contreras, J. Chem. Phys. 113 (2000) 2544.

[26] G.V. Shustov, R. Spinney, A. Rauk, J. Am. Chem. Soc. 122 (2000) 1191.

[27] R. Sumathi, S.D. Peyerimhoff, J. Chem. Phys. 107 (1997) 1872.

[28] K. Doclo, U. Rothlisberger, J. Phys. Chem. A 104 (2000) 6464.

[29] R.D. Bach, M.N. Glukhovtsev, C. Canepa, J. Am. Chem. Soc. 120 (1998) 775.

[30] D. Zhang, R.Y. Zhang, J. Park, S.W. North, J. Am. Chem. Soc. 124 (2002) 9600.

[31] D.A. Dixon, D. Feller, C.G. Zhan, J.S. Francisco, J. Phys. Chem. A 106 (2002) 3191.

[32] R.D. Bach, O. Dmitrenko, C.M. Estevez, J. Am. Chem. Soc. 125 (2003) 16204.

[33] R.G. Pearson, Acc. Chem. Res. 26 (1993) 250.

[34] P.K. Chattaraj, A. Poddar, J. Phys. Chem. A 102 (1998) 9944.

[35] P.K. Chattaraj, P. Fuentealba, B. Gómez, R. Contreras, J. Am. Chem. Soc. 122 (2000) 348.

[36] J.N. Lemercier, S. Padmaja, R. Cueto, G.L. Squadrito, R.M. Uppu, W.A. Pryor, Arch. Biochem. Biophys. 345 (1997) 160.

[37] A. Denicola, B.A. Freeman, M. Trujillo, R. Radi, Arch. Biochem. Biophys. 333 (1996) 49.

[38] G. Merényi, J. Lind, Chem. Res. Toxicol. 10 (1997) 1216.

[39] M.G. Bonini, R. Radi, G. Ferrer-Sueta, A.M. Da C. Ferreira, A. Ohara, J. Biol. Chem. 274 (1999) 10802.