Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Photochemistry and Photobiology A: Chemistry 173 (2005) 365–374
Journal of Photochemistry and Photobiology A:Chemistry
www.elsevier.com/locate/jphotochem

Theoretical study of the photoinduced intramolecular proton transfer and rotational processes in 2-(2′hydroxyphenyl)-4-methyloxazole in gas phase and embedded in β-cyclodextrin

Ricard Casadesús, Miquel Moreno *, José M. Lluch

Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain

Available online 10 May 2005

Abstract

The intramolecular proton transfer and the internal rotations of the 2-(2′hydroxyphenyl)-4-methyloxazole (HPMO) in the first electronically excited singlet state (S_1) have been theoretically studied. Electronic calculations have been carried out within an all-single configuration interaction scheme (CIS). Time-dependent DFT (TDDFT) calculations have been performed to correct the energies of the proton transfer as CIS tends to overestimate the energy barriers. The effect of confinement of the HPMO molecule inside the cavity of β-cyclodextrin (β-CD) has also been studied. The ONIOM hybrid method is used to deal with the large host–guest system. Within the ONIOM procedure two levels of calculation are defined: CIS or TDDFT for the HPMO and the semiempirical PM3 method for the β-CD. A comparison of the electronic energies reveals that the proton-transfer process has a lower energy barrier than the subsequent internal rotation of the keto tautomer, both in the isolated system and in the host–guest complex. However, the initial energy of the wavepacket accessed upon photoexcitation (vertical transition) is high enough to surpass both barriers, so that electronic energies alone are not able to explain the different reaction times found for both processes by means of time-resolved (femtosecond) fluorescence experiments. A dynamic method based on the RRKM statistical theory has been used to account for this difference. The so calculated rate constants also reproduce the increment in the time for the internal rotation process when HPMO is confined inside the β-CD cavity. Analysis of the different factors that contribute to the rate constant disclose that this delay is due to the increment of rigidity of HPMO that takes place upon encapsulation.

Keywords: 2-(2′Hydroxyphenyl)-4-methyloxazole; Host–guest complexes; β-cyclodextrin; Intramolecular proton-transfer; RRKM theory

1. Introduction

The study of reactions in nanocavities is presently a hot topic that embraces virtually all the fields of chemistry [1–8]. Such nanostructures are usually formed through weak non-covalent bonding between the (usually small) reactive substrate (the guest) and a large molecule (the host) that possesses a cavity (a “molecular pocket”) that wraps up the guest. Among the best known hosts are cyclodextrins (CDs) [2,3,9]. CDs are cyclic oligosacharides with a small number of glucose units. The best known CDs are α-, β- and γ-cyclodextrin that differ in the number of D-glucopyranose ($C_6H_{10}O_5$) units: 6, 7 and 8, respectively. The hydrophobic nanocavity of CDs allows the experimental study of size-controlled nanoenvironment effects such as reduced degrees of freedom of the guest [8].

In the recent past a considerable effort has been devoted to the study of CD complexes with aromatic organic molecules [3,5,10–12]. These experimental studies usually show the effects of molecular restrictions in the photophysical and photochemical properties of the encapsulated guest. These effects are usually attributed to the cavity size of the host and the protection of the guest provided by the CD cavity and its low polarity relative to that of water [7,13–18]. Therefore the chemistry inside CDs can be very rich, and applications that would be of interest at the industrial level have been proposed [6,19–22]. The understanding of the fundamental chemical processes taking place inside CDs is then one of the main goals of the physical chemistry studies on these

* Corresponding author. Tel.: +34 935812174; fax: +34 935812920.
E-mail address: mmf@klingon.uab.es (M. Moreno).

1010-6030/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jphotochem.2005.04.016

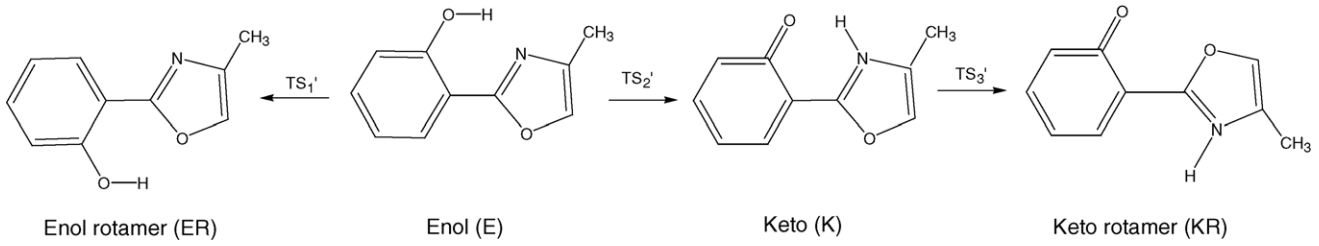

Fig. 1. Scheme of the intramolecular proton transfer and the internal rotations of reactant and product.

systems. Among them the works that make use of femtochemistry techniques are remarkable in that they provide a real-time picture of the molecular motions [8,23–26].

A paradigm of the different photochemistry exhibited by a molecule in gas phase (or apolar media) and inside a cavity is the system 2-(2′hydroxyphenyl)-4-methyloxazole (HPMO), an heterocyclic molecule with two moieties, capable of establishing an intramolecular hydrogen bond. Upon irradiation to the first excited singlet state, the molecule undergoes an ultrafast intramolecular proton-transfer reaction. This process can be tracked down from the observation of a large Stokes shift (ca. 10,000 cm^{-1}) in the emission spectrum of HPMO [27]. In Fig. 1 a scheme of the molecule is shown. The enol form (E) is the most stable in the ground state but electronic promotion to the first singlet excited state (S_1) implies an electronic redistribution that makes the keto tautomer (K) more stable. Femtosecond studies in gas phase or apolar media have revealed that the excited state intramolecular proton transfer (ESIPT) in S_1 is an ultrafast process taking place in less than 300 fs [16–27]. Later on detailed studies of the caging effect on the dynamics of the ESIPT were carried out by Douhal et al. First, the effect of encapsulating HPMO inside one molecule of β-CD was studied [14]. Later on the effect of other hosts such as micelles or proteins was also considered [8,28]. By using a femtosecond pump pulse at 325 nm that excited HPMO to the S_1 state and recording the time-resolved fluorescence spectra at different wavelengths, Douhal et al. observed two groups of time-resolved fluorescence emission transients overlapping at 430 nm. At short wavelengths all the transients show fast decays after the initial rise (l00–250 fs), whereas at longer wavelengths the transient shows a competition between rise and decay. To explain this behavior two different trajectories for the direct proton-transfer reaction have been proposed [28]. A direct one in which the proton transfer takes place directly within less than 300 fs and a second one where the system evolves along two different coordinates: the proton-transfer motion at earlier times and the twisting motion of the heterocyclic moieties later on. This last motion would account for the slower rise component (on the order of a few picoseconds) found at long interrogated wavelengths. Upon confinement of the guest by CD or protein, the times along the second trajectory become significantly longer. These results seem to suggest that encapsulation does not alter much the intramolecular H-bond but, because of the confinement, it greatly affects the rigidity of the guest. This fact is also accounted for by the anisotropy time decays measured for HPMO in the different environments, that show a considerable increment as the rigidity of the guest increases [8,28].

Some time ago, we performed theoretical calculations on the ESIPT reaction in HPMO in gas phase [27] and encapsulated in β-CD [29]. We found no significant differences between both media, a result which is in agreement with the femtosecond results just discussed. The internal rotations were studied in the isolated HPMO system though no much attention was paid to them [27]. No attempt was made to study the effect of encapsulation on these rearrangements. In this paper we undertake such a work aimed at understanding how the intermolecular host–guest interactions are affecting the internal rotation process, that is, how can we explain at the molecular level the increment of rigidity of HPMO upon encapsulation. As it will be shown later on, some kind of dynamic calculations have to be carried out to account for the experimental facts. We have adopted a strategy based on the statistical RRKM model. Of course statistical models are not expected to accurately deal with ultrafast processes such as the ones studied here, but the use of more sophisticated dynamic calculations is beyond the present computer capabilities because of the complexity of the whole process, as inferred from the femtosecond results, that would require the consideration of a too large number of degrees of freedom.

2. Calculational details

For the isolated HPMO molecule an ab initio method has been considered. In particular the ground electronic state S_0 is studied by the restricted Hartree-Fock (RHF) method with the split-valence 6-31G(d) basis set that includes a set of d-polarization functions on atoms other than hydrogens [30]. To deal with the first electronically excited singlet state (S_1) we have used an all-single configuration interaction (CIS) scheme with a spin-restricted HF reference ground state [31]. Stationary points have been located through the minimization procedure of Schlegel [32] by using redundant internal coordinates. The energy of the stationary points corresponding to the ESIPT reaction in S_1 has been recalculated through the time-dependent formalism within the density functional theory (TDDFT) [33–35]. In particular we have used the three parameter hybrid functional of Becke with the correlation

functional of Lee et al. (B3LYP) [36–38]. The basis set chosen for the TDDFT calculations was also the 6-31G(d).

For the HPMO encapsulated in a β-CD molecule the hybrid ONIOM method has been used [39]. In this method one can define up to three layers of atoms that are to be dealt at different levels. We have restricted the layers to only two (high and low levels). The obvious choice is to put the HPMO in the high level layer and the whole CD in the low level layer. In order to have results that can be readily compared with the gas phase calculations, the high level is the same used to deal with the isolated HPMO molecule. That is: RHF for the ground state and CIS and TDDFT for the first electronically excited singlet state always with the 6-31G(d) basis set. For the lower level we have picked the semiempirical PM3 method of Stewart [40]. All the quantum electronic calculations have been performed with the GAUSSIAN 98 series of programs [41].

To account for the dynamics in the excited state S_1 we have considered the statistical transition state theory. As in the excited state there is no thermodynamic equilibrium, the temperature is not well defined, so that a microcanonical ensemble that takes the energy as a fixed value comes into play. In this way the well-known RRKM methodology has been applied [42]. Within the RRKM formalism the rate constant can be obtained through the expression:

$$k(E) = \frac{N(E)}{hN_0'(E)} \tag{1}$$

where $N(E)$ and $N_0'(E)$ are the integral densities of states for the transition state and for the reactant molecule, respectively. Specifically

$$N(E) = \sum_{\boldsymbol{n}} h(E - \varepsilon_{\boldsymbol{n}}^{\ddagger}) \tag{2}$$

$$N_0(E) = \sum_{\boldsymbol{n}} h(E - \varepsilon_{\boldsymbol{n}}) \tag{3}$$

where h is the usual step function and $\varepsilon_{\boldsymbol{n}}^{\ddagger}$ and $\varepsilon_{\mathbf{n}}$ are the vibrational energy levels of the transition state and the reactant molecule. As usual we have assumed that they are obtained as a set of separable harmonic oscillators (the vector **n** contains the vibrational numbers of all the vibrational modes).

Both values have been calculated through direct count of the vibrational states at a given energy using the Beyer–Swinehart algorithm [43]. The rotational states have not been included in the calculation. In the original formulation of Eq. (1) $N(E)$ is zero when the energy falls below the adiabatic energy barrier V^{AG} (including the zero point energy correction). For the proton-transfer reaction it is necessary to include the tunneling effect [44]. This implies that the numerator in Eq. (1) has to be substituted by $P(E)$, the one-dimensional tunneling probability as a function of the energy along the reaction coordinate. This probability has been evaluated by assuming a generalized Eckart potential [45] whose parameters are fitted to the energy of the stationary points along the proton-transfer reaction. Within this approximation the tunneling probability can be analytically calculated (the final expressions can be found in Ref. [44]).

3. Results and discussion

In a previous letter [29] we presented the results for the ESIPT reaction of HPMO in the ground (S_0) and first electronically excited singlet (S_1) states. Both the isolated HPMO (gas phase) and the molecule encapsulated inside β-CD, were studied. In both cases the S_1 state comes from a $\pi \rightarrow \pi^*$ transition which is also the HOMO-LUMO excitation. Both π orbitals are delocalized between the two aromatic rings. A careful conformational analysis was carried out for the host–guest complex aimed at finding the more stable geometries of the enol tautomer (the only stable structure in S_0) inside β-CD. Different minima were localized for the whole complex. Here we will only consider the most stable one depicted in Fig. 2. In this structure the oxazole ring is sequestered by the CD cavity, the phenol ring resting mostly out of the CD cavity. This geometry agrees with the experimental evidence based on analysis of the ^{1}H-NMR spectra [16]. This structure was also used as a starting point to locate all the stationary points along both S_0 and S_1 electronic states. In this paper we consider both the intramolecular proton-transfer reaction and the following inter-ring rotation of the keto tautomer. In addition to the initial geometry of E inside β-CD, Fig. 2 shows the geometries of the keto tautomer K′ and its rotameric form KR′ in S_1 (where the ESIPT takes place) along with the two transition states labeled TS_2' (ESIPT) and TS_3' (internal rotation on the keto side). The primes in the names are used to identify excited state geometries.

As we discussed in the previous work [29], it is not easy to analyze the nature of the intermolecular forces that make the host–guest complex a stable structure. The intramolecular O–H–N bond remains almost unperturbed upon encapsulation. HPMO retains also its planarity inside the cavity. A clue to the stabilization is given by the dipole moments of the host and the guest, 1.78 and 2.47 D, respectively, and the angle between them (119°), as a value larger than 90° indicates a favorable dipole–dipole interaction [46,47].

As for the energies of the internal rearrangements of HPMO, the most reliable results obtained are schematized in Figs. 3 and 4. Fig. 3 shows the energy profiles for the HPMO molecule alone, so that these results are to be used to explain the behavior of HPMO in gas phase or inside an apolar solvent. Fig. 4 gives an identical scheme for the HPMO-β-CD complex. In both figures the energy profiles for both S_0 and S_1 states are given.

Prior to analyze the results, some words have to be said about the methodology used to obtain the energies shown in Figs. 3 and 4. For the ground state the energies are from the RHF method (as explained in the previous section). This level of calculation could be easily improved but we are not really interested in S_0 as, of course, the photoreaction takes place in the excited electronic state. The accuracy of the the-

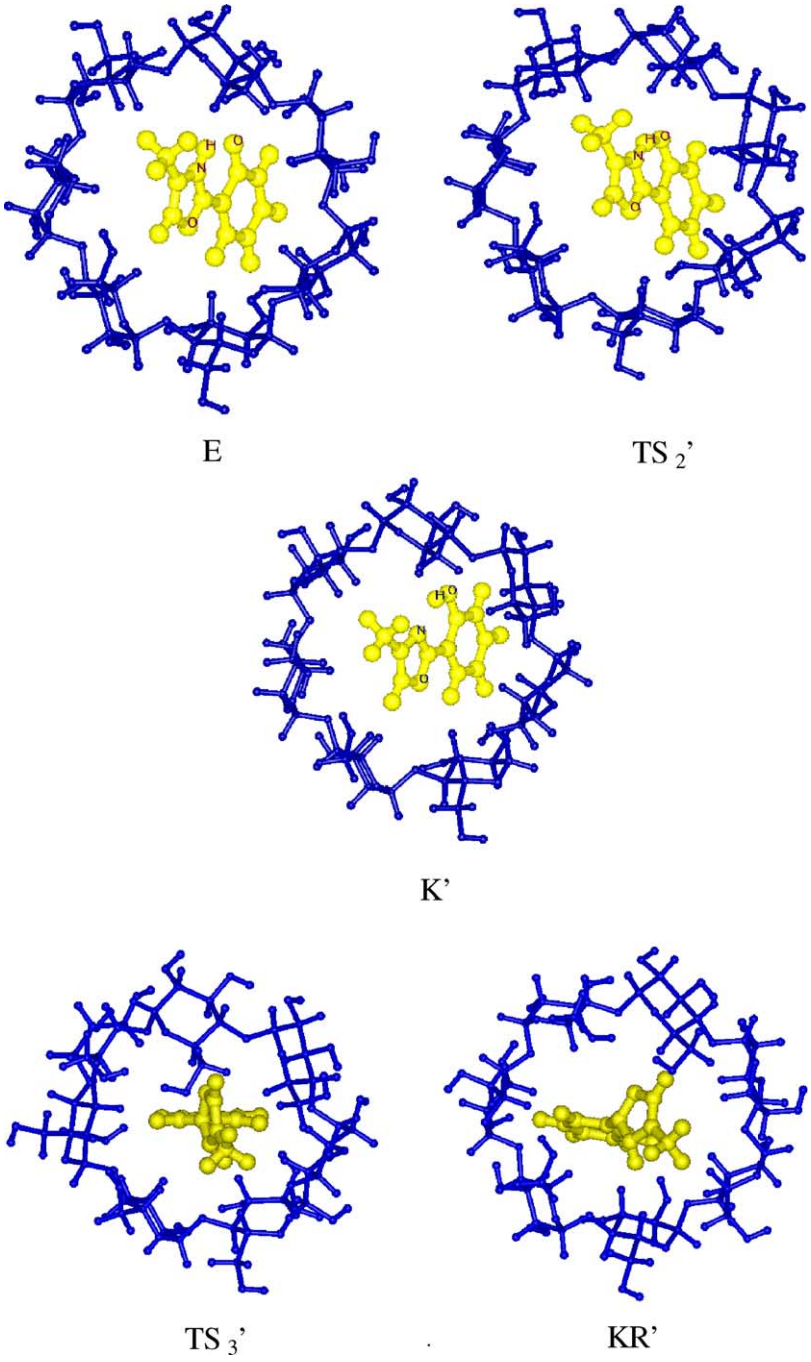

Fig. 2. Structures of the enol tautomer (E) in the ground state S_0 and the stationary points in the first electronically excited singlet state S_1 that correspond to the intramolecular proton transfer and the subsequent internal rotation of the keto tautomer for HPMO embedded in β-cyclodextrin.

oretical electronic methods that deal with excited states is far below the one that can be obtained in the ground state. Besides, calculations are much more computationally expensive in the excited state, a fact that prevents the use of the CASSCF/CASPT2 method, the most reliable method up to now for excited states, to study the host–guest complex. As explained in the methodological section, the single configuration interaction method (CIS) has been used to optimize the geometries in the excited state. The CIS method is known to greatly overestimate the energy barriers for proton-transfer reactions [48,49]. An alternative to the use of CIS is the so-called TDDFT method that is based in a DFT calculation of the ground electronic state and a time-dependent evaluation of the electronic excitation. This method has been proved much more reliable when dealing with intramolecular proton-transfer reactions [48–50] but it has serious problems when used to study excited states that come from an intramolecular charge transfer [51,52]. We have performed single-point

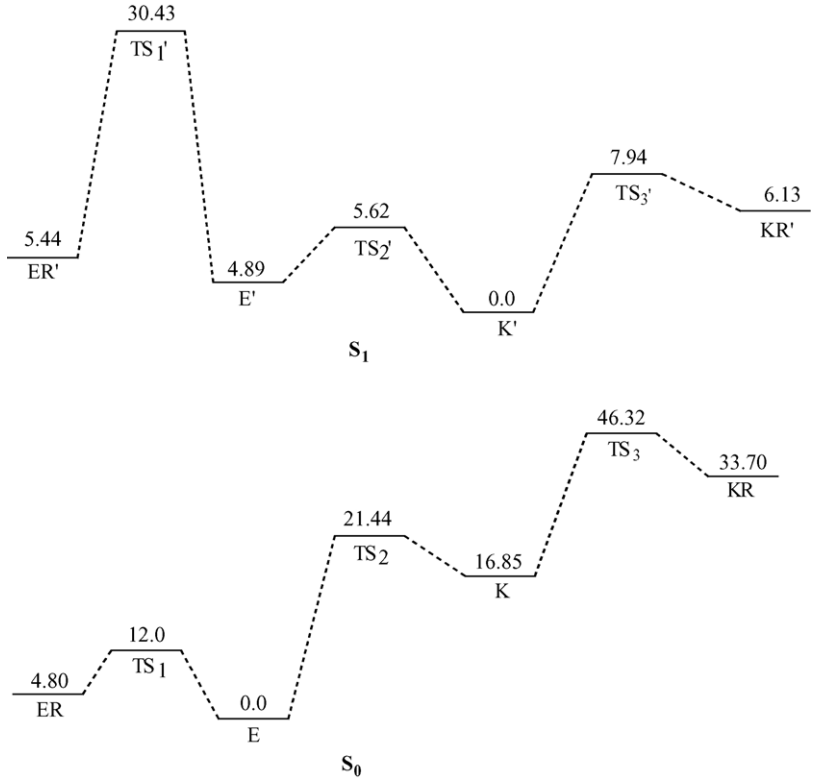

Fig. 3. Schematic energy profile for the intramolecular proton transfer and the C─C inter-ring rotations of isolated HPMO in the ground state S_0 and the first electronically excited singlet state S_1. Energies are given in kcal/mol.

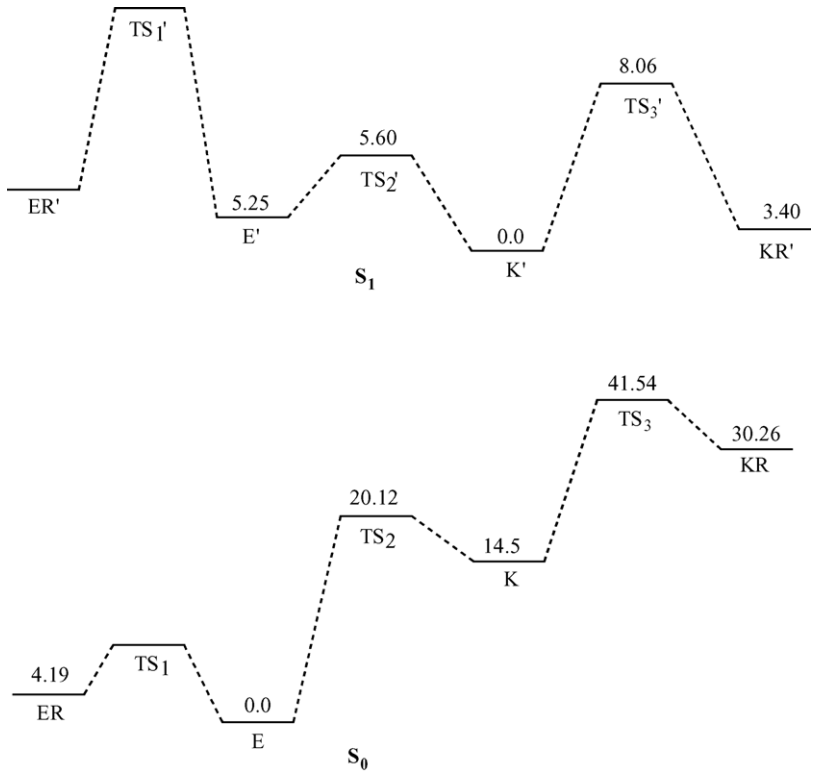

Fig. 4. Schematic energy profile for the intramolecular proton transfer and the C─C inter-ring rotations of HPMO/β-CD complex in the ground state S_0 and the first electronically excited singlet state S_1. Energies are given in kcal/mol.

TDDFT calculations over CIS geometries for all the stationary points located in S_1. For the proton-transfer process the TDDFT calculations show a clear lowering of the energy barrier (as expected). Surprisingly TDDFT calculations find that the rotamer and the transition state for the internal rotation are more stable than the initial keto form obtained from the ESIPT process. Analysis of the orbitals and the electronic excitations along the inter-ring rotation discloses that there is a crossing between the initial $\pi\rightarrow\pi^*$ state and an $n\rightarrow\pi^*$ one where the *n* orbital is fully located in the oxygen that has lost the hydrogen. The crossing takes place in the transition state that is a mix of both excitations. This change from a localized orbital to a greatly delocalized one seems to be badly described by the TDDFT method. Given these facts we have opted to use the TDDFT energies for the ESIPT process but we have kept the CIS results to study the internal rotation. These are the energies represented in Figs. 3 and 4.

First of all we consider the energies in the ground state. The intramolecular proton transfer in S_0 is clearly endoergic with a high energy barrier, so that tautomerization is not taking place in S_0. Inside the cyclodextrin the energy barrier and the endoergicity are lowered but the energy barrier is still too high to allow the transfer. As for the internal rotation of the keto tautomer, it is also clearly impeded in the ground state (both in isolated and encapsulated HPMO). Again the rotation is more favorable in the host–guest complex but, even there, there is a considerable energy barrier to be surpassed (27.04 kcal/mol). More interesting it is to note that the energy barrier for the reverse process from KR to K has also a noticeable energy barrier (12.62 and 11.28 kcal/mol in gas phase and encapsulated, respectively) so that if the keto rotamer KR is obtained after photoreaction in S_1 and ulterior deactivation to S_0, it could be quite stable opening the door to the use of HPMO as a memory device.

Let us now turn our attention to the excited state where the intramolecular proton transfer and the inter-ring rotation may take place. As already noted in previous works, the relative stability of both tautomers is reversed and the relative energy of the transition state is also greatly lowered so that the energy barrier for the $E'\rightarrow K'$ process is only 0.73 kcal/mol in gas phase and 0.35 kcal/mol in the host–guest complex. Even if this small energy barriers seem enough to justify the ultrafast nature of the ESIPT process, as experimentally found, it has to be taken into account that, according to the Franck–Condon principle, the initial geometry of the reaction in S_1 is not the minimum of the enol tautomer in the excited state E′ but the geometry of E, the minimum energy structure in S_0 as the electronic excitation is too fast to allow for the nuclei to rearrange. The energy of this structure in S_1 (vertical excitation) is 13.23 and 13.78 (gas phase and host–guest complex, respectively) relative to the keto K′ structure, the more stable one in S_1. As for the subsequent internal rotation of K′, relative energies of the transition states are quite similar in both phases, whereas the stability of the rotamer KR′ is greater inside the cavity. In any case, the transition state TS'_3 is, in both phases, clearly below the initial energy of the wavepacket, so that after photoexcitation the internal rotation may also take place in an ultrafast fashion.

Figs. 3 and 4 also show (on the left-most side) the energies corresponding to the internal rotations of the enol tautomer. The transition states in both S_0 and S_1 electronic states are high enough to disregard the possible role of this process in the whole dynamics of HPMO. In fact, the transition states have only been located in the isolated HPMO but the energies corresponding to the encapsulated enol tautomer ER′ are not greatly affected when the host is included, so that no major differences are to be expected upon encapsulation.

In order to have a theoretical evaluation of the real-time dynamics of the process in the excited state, we have performed statistical RRKM calculations. The use of a microcanonical ensemble here is compulsory as the temperature is not well defined in the excited state. Given the ultrafast nature of the reactions it may well be that the actual behavior of the process is not statistically driven. That is, the molecule may not have enough time to randomly rearrange its internal vibrational energy, which is a basic assumption of the RRKM method. However, the time resolved fluorescence experiments systematically show a rising component of 100–250 fs in the region of the keto emission. This observation indicates that vibrational energy redistribution occurs within this time scale [8,28]. Of course RRKM assumes a statistical distribution of all degrees of freedom which is hardly obtained after such a small period of time. In any case, given that the measured times for the ESIPT are of the same order and the internal rotation much slower (5–10 ps) the use a statistical model for the dynamics may be expected to give qualitatively correct results. To really analyze the time evolution of the system, a nuclear dynamics method should come to play. Such a study would require a very deep analysis of the potential energy surface and the design of a dynamical model that include the two or three more relevant nuclear coordinates (a full dimensional treatment is not computationally feasible up to now). In a previous work the dynamics of the ESIPT process in HPMO was studied using a quite simplified potential energy surface [53] but the host–guest complex is clearly too large to use such a formalism. The dynamics of the internal rotation was not considered in this previous work [53].

As explained in the methodological section, the rate constant has been evaluated making use of a direct count method of vibrational states (rotation is not accounted for) by means of the Beyer–Swinehart algorithm [43]. We have considered both the ESIPT ($E'\rightarrow K'$) and the subsequent inter-ring rotation of the keto tautomer ($K'\rightarrow KR'$). For the proton-transfer reaction, tunneling has been included through a simple one-dimensional model assuming an Eckart potential. As usual, we have analyzed and compared the gas phase system and the host–guest complex. The rate constants at different energies have been obtained and results are shown in Fig. 5. As in Figs. 3 and 4 the energy is given relative to the one of K′, the more stable structure in S_1.

As somehow expected, the rate constant for the proton transfer k_{ESIPT} is clearly greater than the one for the internal

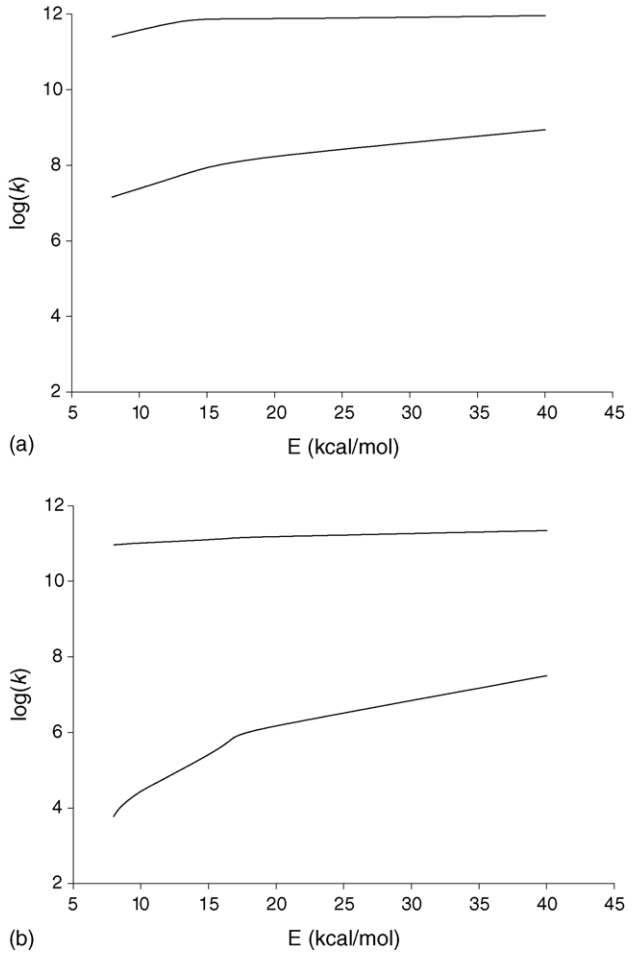

Fig. 5. RRKM rate constants (in s^{-1}) for the intramolecular proton transfer (k_{ESIPT}) and internal rotation of the keto tautomer in S_1 (k_{IR}). Energies are relative to the keto minimum in S_1. (a) Isolated HPMO; (b) host–guest complex.

rotation of the keto tautomer k_{IR}. The inverse of this rate constant gives, of course, the mean times of the reactions. At the energy of the vertical transitions $k_{ESIPT} = 6.51 \times 10^{11}\ s^{-1}$ and $k_{IR} = 5.68 \times 10^{7}\ s^{-1}$ in gas phase. In the host–guest complex the corresponding values are $k_{ESIPT} = 1.27 \times 10^{11}\ s^{-1}$ and $k_{IR} = 1.82 \times 10^{5}\ s^{-1}$. Comparing our results with the time-resolved fluorescence experiments [14,28], it is first noted that theoretical rate constants give too low reaction mean times (the inverse of the rate constant). Taking into account the large number of approximations, results are not so bad for the ESIPT process that is predicted to take place on the picosecond time range rather than the subpicosecond order experimentally found. As for the keto internal rotation, expected to take place in few picoseconds, it falls down to the nanosecond scale or below in our model. These discrepancies could be in principle attributed to the inability of the statistical RRKM strategy to deal with such a processes. However the previous dynamical work, that does not make any statistical assumption, also find mean times for the ESIPT process in HPMO of around 4–5 ps [53]. Then the inability to correctly reproduce the observed reaction times is to be found more likely in the electronic calculations as excited electronic states energies are far less reliable than ground state ones. In any case, our results account for the most interesting results of the precedent femtosecond studies. That is, the internal rotation process is much slower than the intramolecular proton transfer. What is more relevant, comparing the rate constants obtained in isolated HPMO with the host–guest system, is that the ESIPT process is not much affected by the confinement (k_{ESIPT} is lower in the complex but of the same order). Conversely, the internal rotation is dramatically slowed down upon encapsulation of the HPMO as k_{IR} drops by more than two orders of magnitude.

It is quite interesting to analyze what are the factors that lead to such a different rate constants for the same process in different media. We can also extend this discussion to the understanding of the different rates for the two elementary processes. In the experimental work the different rates observed for the ESIPT and the subsequent internal rotation of the keto product is attributed to the fact that the first process is barrierless, whereas the second one involves the crossing of an energy barrier [28]. This energy barrier would be higher in the encapsulated HPMO thus accounting for the slower rate of the internal rotation inside the cavity. Within our theoretical calculations, both processes are in practice barrierless. In fact, there is an energy barrier from the corresponding minimum in S_1 for both elementary processes but the initial energy is clearly above, so that from the statistical point of view the wavepacket does not "see" any barrier (of course at the molecular level the wavepacket does not evolve along a one dimensional path so that the actual process might not be barrierless). However, the higher energy of TS_3' with respect to TS_2' implies that the number of states available for the system to cross the barrier ($N(E)$ in Eq. (1)) is lower for the internal rotational process than for the intramolecular proton transfer.

To acquire a deeper understanding of what are the factors that govern such difference of rate constants for the two reactions, it is interesting to use here the simplified expression for the rate constant that can be obtained assuming a continuum of vibrational states which gives the "classical" expression for the RRKM rate constant [44]:

$$k(E) = \frac{\prod_{i=1}^{s} \upsilon_i}{\prod_{i=1}^{s-1} \upsilon_i^{\ddagger}} \left(\frac{E - V^{AG}}{E} \right)^{s-1} \tag{4}$$

where the two productories are over all the real frequencies for the reactants and the transition state. At the vertical transition energy, we have verified that this simple expression gives not much different results than the more exact direct count used by us. Eq. (4) clearly shows that two factors account for the magnitude of the rate constant: the quocient of the productory of the frequencies and the quocient of energies. In a thermodynamic language, the first quocient is to be related with the entropic factor and the second one with

the enthalpic barrier. We have calculated the two factors for each reaction. More interesting that the actual figures is the comparison of the different terms so that we have evaluated the two factors in the k_{ESIPT}/k_{IR} relationship using Eq. (4). For the isolated HPMO molecule at the vertical transition energy the frequency factor is 8.72, whereas the energy term amounts to 32.59. As usual the energy factor is more important than the entropic term. For the HPMO molecule inside the CD, the frequency factor is higher (32.69) and the energy one also higher (85.02). Then both factors contribute, more or less equally, to the larger difference in the reaction times of both processes upon encapsulation. At first sight, it is surprising to see such a large increment of the energy term in the host–guest complex as the electronic energies of the involved reactants and transition states are quite invariant upon confinement (compare Figs. 3 and 4). The difference is to be found in the frequencies of the transition state for the rotation of the keto tautomer as they are globally larger in the host–guest complex than in absence of the CD. This fact leads to a smaller frequency factor in Eq. (4) but also to a small energy factor, as the zero point energy of the transition state in the host–guest complex is also higher. The zero point energies have not been considered in the energy profiles of Figs. 3 and 4 but they have to be included when evaluating the rate constant through Eqs. (1) and (4) as indicated in Eqs. (2) and (3). Then our results point to an increment of the rigidity of the HPMO molecule inside the CD cavity as the reason behind the lowering of the internal rotation rate constant upon encapsulation by the cyclodextrin. This increment of rigidity comes from the subtle intermolecular forces that emerge between host and guest when the complex is formed. The nature of these intermolecular forces was discussed in a previous work [29].

Fig. 5 also shows that a further increment of the total energy above the vertical transition one (12–13 kcal/mol) does not produce a large increment of the rate constant for the ESIPT. Conversely, the rate constant for the internal rotation noticeably increases, though it always lies clearly below the rate for the proton-transfer process. At lower energies, both rate constants are also lowered the effect being again much more prominent for the internal rotation rate constants. The curves in Fig. 5 do not go down beyond 8 kcal/mol as this is the energy of TS'_3, the transition state for the internal rotation. At energies below that, k_{IR} falls down to zero (no tunneling is to be expected for the internal rearrangement) whereas the k_{ESIPT} would remain over the $10^{10}\,s^{-1}$ value for a while as TS'_2 lies below 6 kcal/mol and tunneling is not neglectful here. This means that the slower rise component observed in the fluorescence transients would eventually disappear if the energy of the initial excitation (the pump) were further lowered. Fig. 6 depicts the quotient of both rate constants as a function of the energy, where the different dependence of both rates on energy is more clearly seen. At low energies, k_{ESIPT} tends to rapidly increase relative to the k_{IR}, whereas at high energies the dependency of the quocient on the energy is less noticeable. In any case, we note that k_{IR} is always more than two orders of magnitude below k_{ESIPT} and the difference between both is more prominent in the host–guest complex (note the change of the scale factor in the *y*-axis between Fig. 6(a) and (b)).

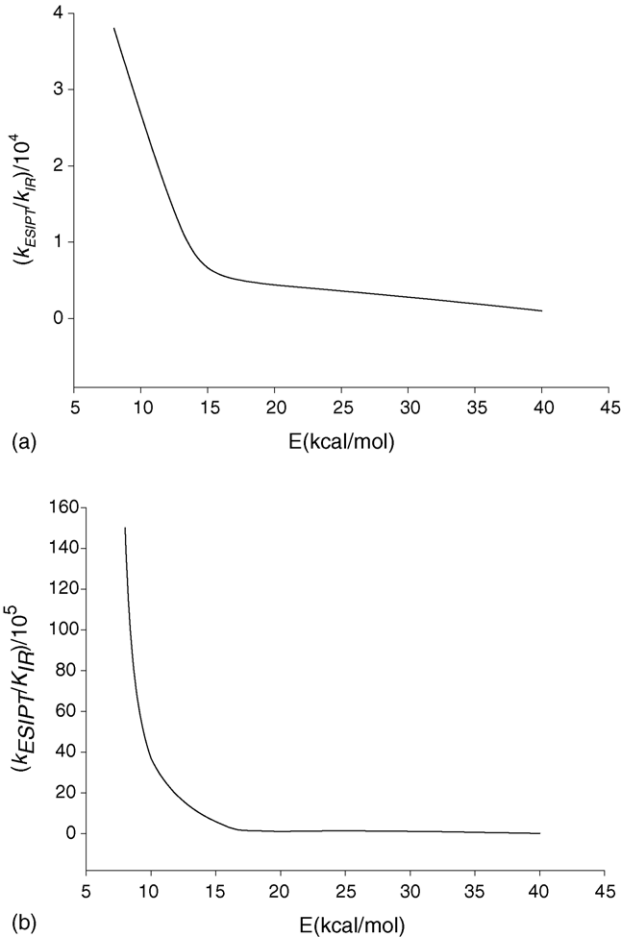

Fig. 6. Quocients of the RRKM rate constants as a function of the total energy relative to the keto minimum in S_1 K′. (a) Isolated HPMO; (b) host–guest complex.

4. Conclusions

We have theoretically analyzed the intramolecular proton transfer in the first electronically excited singlet state (S_1) for the 2-(2′hydroxyphenyl)-4-methyloxazole (HPMO) system. Both the molecule alone (gas phase) and embedded inside the cavity of one β-cyclodextrin (β-CD) have been considered. We have also studied the internal rotation of the keto tautomer which is the more stable form in S_1. Electronic calculations disclose that, in both cases the proton-transfer reaction takes place with a small energy barrier, whereas the internal rotation has a slightly larger barrier. In any case, the energy of the initial wavepacket obtained through photoexcitation of the enol tautomer in the ground electronic state (the vertical transition according to the Franck–Condon principle) is high enough to surpass both energy barriers. Femtosecond-

resolved fluorescence experiments indicate two trajectories for the chemical reaction in S_1 following the initial photoexcitation: a fast process (100–250 fs) consisting on the proton transfer and a slower motion that would also imply the internal rotation of the two rings of HPMO. Electronic energies cannot be held fully responsible for this difference, as the relative energies for reactant and transition state are not noticeably affected by the confinement. To account for the dynamics of these two processes, we have chosen a statistical RRKM procedure to calculate the rate constants for both the proton-transfer reaction (k_{ESIPT}) and the internal rotation of the keto rotamer (k_{IR}). Even if the ultrafast nature of the reaction may cast some doubts on the validity of the statistical assumptions of the RRKM method, the obtained results correctly reproduce the order of the time scale for the proton-transfer reaction, though the internal rotational process is predicted to be much slower than experimentally found. Our calculations also account for the internal rotation of the keto tautomer being clearly slowed down upon confinement of the HPMO inside the β-CD cavity. The increment of rigidity of the HPMO molecule in the host–guest complex leads to globally larger vibrational frequencies. As a consequence, the zero point energy for the transition state of the inter-ring rotation is higher and there is also a lowering in the number of states that allow the crossing of the barrier at a given energy. Both factors contribute almost equally to the slowing down of the internal rotation in the host–guest complex. A further increment of the intermolecular forces between host and guest would produce a more dramatic lowering of the internal rotation rate. This is probably what happens when HPMO is embedded in the human serum albumin protein [28,54], as in that case femtosecond experiments find a larger delay of the rotational process.

Acknowledgement

We are grateful for financial support from the Spanish 'Ministerio de Ciencia y Tecnología' and the 'Fondo Europeo de Desarrollo Regional' through Project No. BQU2002-00301.

References

[1] K.E. Drexler, Nanosystems: molecular machinery, in: Manufacturing and Computation, Wiley, New York, 1992.
[2] J. Szetjli, Cyclodextrins and Their Inclusion Complexes, Académiai Kiadó, Budapest, 1982.
[3] Special issue (5) on cyclodextrins, Chem. Rev. 98 (1998).
[4] J. Szetjli, Cyclodextrin Technology, Kluwer Academic Publishers, Dordrecht, 1988.
[5] G. Wenz, Angew. Chem. Int. Ed. Engl. 33 (1994) 803.
[6] P. Bortolus, S. Monti, in: D.C. Neckers, D.H. Volman, G. Von Bunau (Eds.), Advances in Photochemistry, Wiley, New York, 1996.
[7] A. Douhal, Ber. Bunsenges. Phys. Chem. 102 (1998) 448.
[8] A. Douhal, Chem. Rev. 104 (2004) 1955.
[9] Z.-P. Yi, H.-L. Chen, Z.-Z. Huang, Q. Huang, J.-S. Yu, J. Chem. Soc., Perkin Trans. 2 (2000) 121.
[10] J.L. Szetjtli, in: J.L. Atwood, J.E.D. Davies, D.D. MacNicol, F. Vögtle (Eds.), Comprehensive Supramolecular Chemistry, vol. 3, Pergamon Press, New York, 1996.
[11] Supramolecular Chemistry, in: J.M. Lehn (Ed.), Concepts and Perspectives, VCH Publishers, New York, 1995.
[12] V. Balzani, F. Scandolla (Eds.), Supramolecular Chemistry, Ellis Horword, London, 1991.
[13] A. Douhal, F. Amat-Guerri, A.U. Acuña, Angew. Chem. Int. Ed. Engl. 36 (1997) 1514.
[14] A. Douhal, T. Fiebig, M. Chachisvilis, A.H. Zewail, J. Phys. Chem. A 102 (1998) 1657.
[15] M. Milewski, W. Augustyniak, A. Maciejewski, J. Phys. Chem. A 102 (1998) 7427.
[16] I. García-Ochoa, M.-A. Díez-López, M.H. Viñas, L. Santos, E. Martínez-Ataz, F. Amat-Guerri, A. Douhal, Chem. Eur. J. 5 (1999) 897.
[17] W.M. Nau, X. Zhang, J. Am. Chem. Soc. 121 (1999) 8022.
[18] G. Grabner, K. Rechthaler, B. Mayer, G. Köhler, K. Rotkiewicz, J. Phys. Chem. A 104 (2000) 1365.
[19] J.A. Thoma, L. Stewart, in: R.L. Whistler, E.F. Paschall (Eds.), Starch: Chemistry and Technology, Academic Press, New York, 1965.
[20] G. Li, L.B. McGown, Science 264 (1994) 249.
[21] F. Cacialli, J.S. Wilson, J.J. Michels, C. Daniel, C. Silva, R.H. Friend, N. Severin, P. Samori, J.P. Rabe, J.M. O'Connell, P.N. Taylor, H.L. Anderson, Nature Mater. 1 (2002) 160.
[22] A.V. Kabashin, M. Meunier, C. Kingston, J.H.T. Luong, J. Phys. Chem. B 107 (2003) 4527.
[23] A.H. Zewail, Femtochemistry – Ultrafast Dynamics of the Chemical Bond, vols. I and II, Word Scientific, New Jersey and Singapore, 1994.
[24] A.H. Zewail, J. Phys. Chem. A 104 (2000) 5660.
[25] M.A. El-Sayed, I. Tanaka, T.N. Molin (Eds.), Ultrafast Processes in Chemistry and Biology – Chemistry for the 21st Century, Blackwell Scientific, Oxford, 1994.
[26] E. Schreiber (Ed.), Femtosecond Real-Time Spectroscopy of Small Molecules and Clusters, Springer, New York, 1998.
[27] V. Guallar, J.M. Lluch, M. Moreno, F. Amat-Guerri, A. Douhal, J. Phys. Chem. 100 (1996) 19789.
[28] A.H. Zewail, A. Douhal, D. Zhong, Proc. Natl. Acad. Sci. U.S.A. 97 (2000) 14056.
[29] R. Casadesús, M. Moreno, J.M. Lluch, Chem. Phys. Lett. 356 (2002) 423.
[30] P.C. Hariharan, J.A. Pople, Mol. Phys. 27 (1974) 209.
[31] J.B. Foresman, M. Head-Gordon, J.A. Pople, M.J. Frisch, J. Phys. Chem. 96 (1992) 135.
[32] H.B. Schlegel, J. Comput. Chem. 17 (1996) 49.
[33] R. Bauernschmitt, R. Ahlrichs, Chem. Phys. Lett. 256 (1996) 454.
[34] M.E. Casida, C. Jamorski, K.C. Casida, D.R. Salahub, J. Chem. Phys. 108 (1998) 4439.
[35] R.E. Stratmann, G.E. Scuseria, M.J. Frisch, J. Chem. Phys. 109 (1998) 8218.
[36] C.T. Lee, W.T. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.
[37] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.
[38] P.J. Stephens, F.J. Devlin, C.F. Chabalowski, M.J. Frisch, J. Phys. Chem. 98 (1994) 11623.
[39] S. Dapprich, I. Komáromi, K.S. Byun, K. Morokuma, M.J. Frisch, J. Mol. Struct. (Theochem.) 461/462 (1999) 1.
[40] J.J.P. Stewart, J. Comput. Chem. 10 (1989) 209.
[41] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennuci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick,

A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B.G. Johnson, W. Chen, M.W. Wong, J.L. Andrés, M. Head-Gordon, E.S. Replogle, J.A. Pople, Gaussian 98, Gaussian Inc., Pittsburgh, PA, 1998.
[42] J.I. Steinfeld, J.S. Francisco, W.L. Hase, Chemical Kinetics and Dynamics, Prentice Hall, Englewood Cliffs, NJ, 1989.
[43] T. Beyer, D.A. Swinehart, ACM Commun. 16 (1973) 379.
[44] W.H. Miller, J. Am. Chem. Soc. 101 (1979) 6810.
[45] H.S. Johnston, Gas Phase Reaction Rate Theory, Ronald Press, New York, 1966.
[46] M. Kitagawa, M. Sakurai, H. Hoshi, Chem. Lett. (1988) 895.
[47] D.M. Davies, J.R. Savage, J. Chem. Res. (S) (1993) 94.
[48] O. Vendrell, M. Moreno, J.M. Lluch, J. Chem. Phys. 117 (2002) 7525.
[49] R. Casadesús, O. Vendrell, M. Moreno, J.M. Lluch, Chem. Phys. Lett. 405 (2005) 187.
[50] O. Vendrell, R. Gelabert, M. Moreno, J.M. Lluch, Chem. Phys. Lett. 396 (2004) 202.
[51] A. Dreuw, J.L. Weisman, M. Head-Gordon, J. Chem. Phys. 119 (2003) 2943.
[52] A.L. Sobolewski, W. Domcke, Chem. Phys. 294 (2003) 73.
[53] V. Guallar, V.S. Batista, W.H. Miller, J. Chem. Phys. 113 (2000) 9510.
[54] O. Vendrell, M. Moreno, J.M. Lluch, S. Shames-Schiffer, J. Phys. Chem. B 108 (2004) 6616.