Ab initio study of the potential energy functions relevant for hydrogen transfer in formamide, its dimer and its complex with water

Andrzej L. Sobolewski

Institute of Physics, Polish Academy of Sciences, 02-668 Warsaw, Poland

Abstract

The potential energy (PE) functions of the electronic ground state and the lowest $n\pi^*$ and $\pi\pi^*$ excited singlet states of formamide, its dimer and its complex with water have been characterized theoretically along the proton transfer (PT) reaction coordinate. The calculations were performed using the ab initio complete-active-space self-consistent-field (CASSCF) method and second-order perturbation theory employing the CASSCF wavefunction as the reference state. The results suggest that the photoinduced PT reaction in an isolated molecule occurs via successive dissociation and association of the hydrogen atom, whereas in hydrogen-bonded complexes, the PE functions along the PT reaction coordinate are qualitatively the same as for the PT reaction along the intramolecular hydrogen bond. Some implications concerning biological molecules containing peptide linkages are discussed.

Keywords: Potential energy functions; Hydrogen transfer; Formamide; Dimer

1. Introduction

The crucial role played by the N–H....O=C hydrogen bond in determining the structures and properties of proteins and nucleic acids means that its theoretical characterization may be of great importance for an understanding of the basic processes of life. The light hydrogen nucleus moving between two heavy (nitrogen and oxygen) atoms, and being chemically bonded to one of them and forming a hydrogen bond with the other, and vice versa, can be viewed as the simplest model of a tautomerization reaction. Tautomeric structures can govern the chemical and biochemical activities of proteins or nucleic acids and may play a role in spontaneous genetic mutations [1–3].

Formamide is the simplest molecule containing the essential features of the peptide linkage and is often used as a model. The tautomeric equilibrium of formamide thus represents the simplest model of the keto–enol equilibrium. A knowledge of the energetics of tautomerization in this prototype system in the ground and electronically excited states may provide useful information on the intrinsic photochemical stability of other biologically important tautomers as well as their photochemical behaviour. Since formamide contains both carbonyl and amino groups, it is expected to form

a strong binary complex with water. As such, the formamide–water complex provides the simplest model for the hydration of proteins. Finally, the dimer of formamide may be viewed as a simple model of the pairing of nucleic acid bases. Its tautomerization thus represents the simplest double proton transfer reaction which may be responsible for generating the less likely tautomeric forms of nucleic acid bases that are suspected to be responsible for spontaneous genetic mutations [1–3].

Due to its simplicity, formamide and its clusters have been the subject of a large number of theoretical ab initio studies [4–15]. Some of these investigations concern the relative stabilities of formamide [5,6,10–14], its complex with water [11] and its dimer [6], but exclusively in the ground state. The only theoretical ab initio studies of electronically excited states, to our knowledge, concern the energies of vertical electronic excitations [16] and the nuclear geometries in the lowest excited electronic states of formamide [17].

In the present work, we report an investigation of the potential energy (PE) functions in the ground and first excited singlet states, which are relevant for the proton transfer (PT) reaction in formamide, its dimer and its cyclic complex with water, using the complete-active-space self-consistent-field (CASSCF) method [18]

and second-order perturbation theory with the CASSCF wavefunction as the reference state (CASPT2) [19,20]. This is one of the first applications of the novel CASPT2 method to study the PE functions of polyatomic molecules. Thus the results obtained and, in particular, their comparison with those obtained using the well-founded CASSCF method are of importance for the future application of the CASPT2 method to larger systems for which it has been especially designated. In this respect, formamide and its clusters are not themselves considered as the particular subject of this study. They are rather treated as representing part (the PT reaction centre) of a larger system. Such an assumption imposes some restrictions on the considered system and on the sophistication of the theoretical treatment. Firstly, full molecular geometry optimization along the reaction path makes no particular sense, since formamide and its clusters may appear to be very labile in this respect and may change their geometry significantly; this could never happen if they were fragments of a larger system (a heteroaromatic ring for instance). This particularly concerns the excited states in which large out-of-plane deformations of formamide might be expected [17]. The steric hindrance present in large systems imposes large constraints on the deformation of the peptide linkage. Thus, in this paper, we retain the C_s symmetry (the plane) along the PT reaction coordinate in order to mimic the properties of such systems closely. Moreover, formamide itself also appears to be very labile with respect to in-plane deformations compared with larger systems containing the peptide linkage. Thus the PE functions calculated along the PT coordinate, including the full geometry relaxation of formamide, may not be very representative for larger systems. In order to avoid such difficulties, we have decided to use the concerted reaction path concept in which the vector of internal displacements (bond lengths and bond angles), that extrapolates linearly between the equilibrium geometries of the reactant and the product, defines the reaction coordinate. A number of intermediate nuclear configurations along this reaction coordinate were generated and the energies of the ground and lowest excited singlet states were calculated. More details concerning this approach can be found in Refs. [21–23]. This is not the best approach since we cannot extract from our results the quantitative information important for a description of the reaction dynamics (e.g. barrier heights), but it seems to be the only solution which can give a qualitative picture of the phenomenon. The second important limitation concerns the sophistication of the theoretical treatment. Considering formamide itself, it is obvious that we can use extended basis sets in the optimization of its geometry as well as in the PE function calculations, but such basis sets cannot be applied to larger systems. Thus, in this work, we have decided to use a moderate basis set, the double-

zeta-valence (DZV) gaussian basis set of Dunning and Hay [24] with polarization functions added (DZVP). The exponents of the polarization functions are 0.75, 0.80, 0.85 and 1.0 for carbon, nitrogen, oxygen and hydrogen atoms respectively.

2. Method of calculation and results

It is well established that the CASSCF method [18] is especially useful in describing a process in which the electronic structure varies strongly as a function of the nuclear geometry. It accounts for all near-degeneracy effects, which are rather common along the reaction coordinates, and includes full orbital relaxation. The remaining, so-called dynamic electron correlation effects are added in a subsequent step using second-order perturbation theory with the CASSCF wavefunction as the reference state (CASPT2) with a non-diagonal zero-order hamiltonian [19,20].

In order to define the intramolecular coordinate for the concerted PT reaction, we need the nuclear geometries of the two tautomeric forms of interest (see, for instance, Refs. [22,23]). Both tautomeric forms of formamide and its clusters are stable (or metastable) in the ground state; therefore, in the following, we use their nuclear geometries optimized in the ground state. The ground and excited PE functions calculated in this work can thus be considered as representing a one-dimensional section of the PE hypersurface between the points defined by the ground state geometries of both tautomeric forms. For the purpose of a qualitative characterization of the PE surfaces along the PT reaction coordinate, the precise nuclear geometries of the reactant and the product forms are, however, of secondary importance. Thus, in the following, we have optimized all the structures in the restricted Hartree–Fock approximation using the DZV gaussian basis set of Dunning and Hay [24] with polarization functions added (HF/DZVP). All geometry optimizations were performed with the CADPAC program package [25]. In the CASSCF and CASPT2 energy calculations, the same basis set was used with (DZVP) and without (DZV) polarization functions. The CASPT2 calculations were performed with respect to CASSCF wavefunctions which were optimized for each state independently. MOLCAS-2 software [26] was used for the CASSCF and CASPT2 energy calculations.

2.1. Formamide molecule

The two tautomeric forms of formamide optimized in the ground state are shown in Fig. 1. Our results indicate that both forms are stable in C_s symmetry at the HF/DZVP level of approximation with the keto form (1a) being 0.55 eV lower in energy than the enol
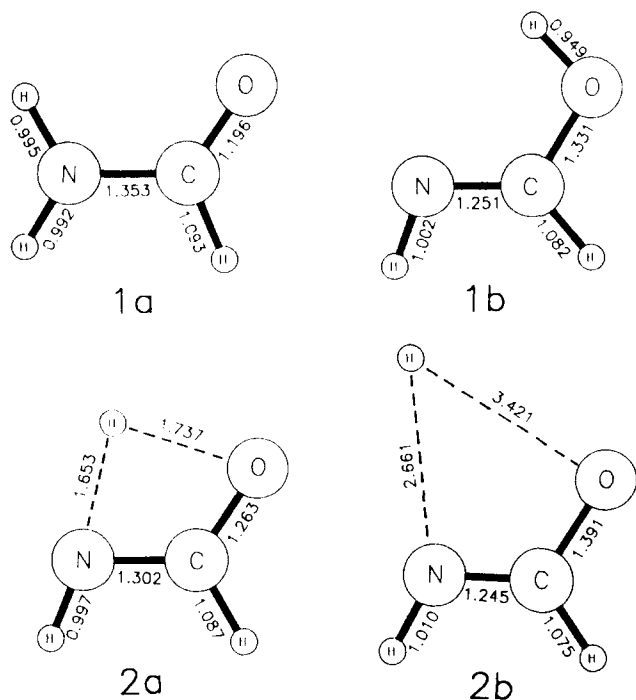
Fig. 1. The keto (1a) and enol (1b) forms of formamide and their transient structures (2a and 2b). The numbers indicate the optimized bond lengths (see text for details).

form (1b). The inclusion of electron correlation effects at the Moller–Plesset perturbation theory level (MP2/DZVP) in the optimization of the molecular geometry gives an imaginary frequency for the NH_2 wagging vibration of the keto form ($\omega = 127$ cm^{-1}). This point has been extensively discussed in the literature [4,7,11], and it has been shown that the out-of-plane stabilization of formamide is very small (1 kcal mol^{-1} or less) due to pyrimidization of the $-NH_2$ group. In the following, we retain the C_s symmetry along the PT reaction coordinate according to the arguments presented in Section 1.

In the calculations of the ground and excited state energies of formamide, ten electrons (of a total number of 24) have been correlated within seven orbitals in the CASSCF reference wavefunction. The active space is denoted as (7,0/4,3), where the first two numbers denote the numbers of closed (doubly occupied in each configuration) molecular orbitals, and the second two numbers denote the number of active orbitals of a' and a" symmetry respectively in the C_s point group. The first-order interaction space in the CASPT2 calculations has dimensions of about 3.4×10^4 and 1.4×10^5 in the DZV and DZVP basis sets respectively. The calculated energies, as well as the energies and oscillator strengths for vertical excitations from the S_0 state, are listed in Table 1. For all states, the weight of the CASSCF reference in the first-order wavefunction exceeds 0.84. The transition energies and the oscillator strengths are relatively little modified by the inclusion

of polarization functions into the basis set and they reproduce quite well the experimental observation [27]. Our best estimate for the relative stability of the two tautomers ($\Delta E = 0.42$ eV) is in good agreement with other theoretical results [5,6,10–14].

The two tautomeric forms of formamide (the keto form (1a) and the enol form (1b)) define the beginning ($Q = 0$) and the end ($Q = 1$) of the reaction coordinate for the PT reaction. The resulting CASSCF and CASPT2 PE functions calculated along this reaction coordinate are presented in Fig. 2. We can see that the two tautomeric forms are separated by a moderate barrier on the ground state PE surface, as expected. It should be noted that the molecular geometry at the top of the ground state barrier has not been optimized; thus the calculated barrier is somewhat higher than the energy of the saddle point on the ground state PE surface ($\Delta E \simeq 2$ eV [11]). The PE functions of the excited A"($n\pi^*$) and A'($\pi\pi^*$) singlet valence states are qualitatively different from that of the ground state. They clearly show an additional local minimum located roughly at the position of the top of the ground state barrier ($Q \simeq 0.5$). All the basic features of the PE function of formamide are already present at the CASSCF/DZV level of approximation (Fig. 2(a)). Inclusion of dynamic correlation effects in the CASPT2/DZV approximation decreases the excitation energies as well as the barriers, but retains all the qualitative features of the PE functions (Fig. 2(b)). Inclusion of the polarization functions into the basis set (CASPT2/DZVP) gives only a slight modification of the relative energies. Thus we can safely conclude that, in this case, we have indeed obtained saturated results with respect to the sophistication of the method as well as the basis set.

It is interesting to note that the PE functions of formamide calculated along the PT reaction coordinate retain all the essential features found previously for 2-hydroxypyridine (2-HP) [28]. Moreover, as with 2-HP, an attempt to optimize the nuclear geometry at the intermediate ($Q = 0.5$) local minimum on the A"($n\pi^*$) PE surface leads to dissociation of the mobile hydrogen atom. The optimization was performed at the CASSCF level with the 3-21G split-valence basis set [29] using GAMESS program software [30]. The active space used in the optimization can be denoted as (9,1/2,2) in the C_s point group. The optimization was stopped at the structure 2b of Fig. 1 when the default tolerance for the gradient of GAMESS (5×10^{-5} hartree bohr^{-1}) was reached. This molecular structure has no other meaning than representing a transient structure for the dissociation of hydrogen. Using the two structures 2a and 2b of Fig. 1, we can define the reaction coordinate for dissociation of the hydrogen atom and calculate the PE functions along this coordinate. The resulting CASPT2/DZV PE functions are presented in Fig. 3.

Table 1

The CASPT2 energies of the ground and lowest excited singlet states (E), weights of the CASSCF reference in the renormalized first-order wavefunctions (ω) and energies (ΔE) and oscillator strengths (f) for dipole transitions from the ground state of the two tautomeric forms of formamide calculated with the DZV and DZVP basis sets. Energies and transition dipole moments were calculated at the equilibrium geometries of the given form in the ground state

Parameter	DZV			DZVP		
	S_0	$A''(n\pi^*)$	$A'(\pi\pi^*)$	S_0	$A''(n\pi^*)$	$A'(\pi\pi^*)$
Keto form						
E (a.u.) [a]	− 1.1881	− 0.9773	− 0.9042	− 1.4538	− 1.2388	− 1.1718
ω	0.925	0.920	0.888	0.896	0.888	0.866
ΔE (eV)	–	5.73	7.72	–	5.85	7.67
f	–	0.001	0.279	–	0.001	0.317
Enol form						
E (a.u.) [a]	− 1.1638	− 0.9252	− 0.8594	− 1.4385	− 1.2086	− 1.1406
ω	0.922	0.916	0.852	0.894	0.886	0.840
ΔE (eV)	(0.66) [b]	6.49	8.28	(0.42) [b]	6.67	8.10
f	–	0.013	0.334	–	0.010	0.346

[a] Energies relative to − 168.0 a.u.

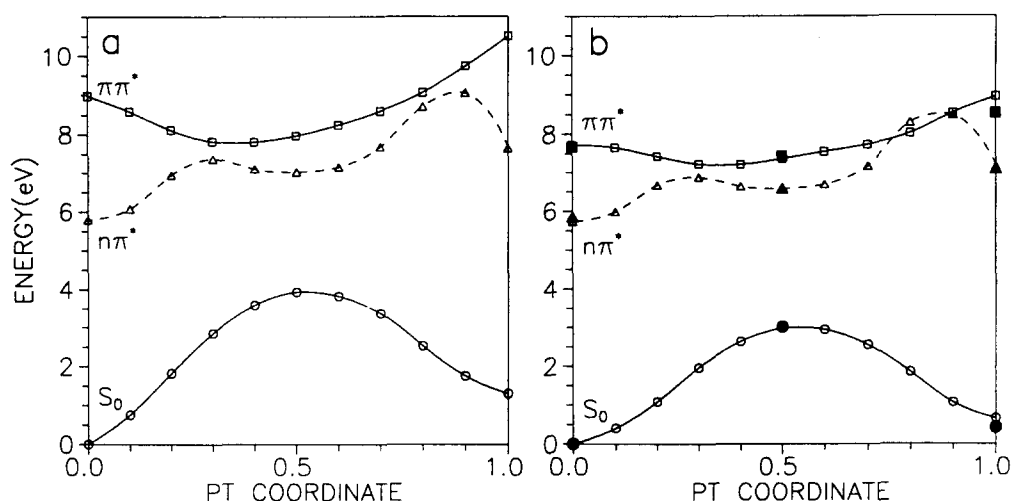[b] Relative to the S_0 state of the keto form.

Fig. 2. Potential energy functions of the PT reaction coordinate of the ground (circles) and lowest $n\pi^*$ (triangles) and $\pi\pi^*$ (squares) excited singlet states of formamide obtained at the CASSCF/DZV (a) and CASPT2/DZV (b) levels of approximation. The filled symbols denote the energies calculated using the CASPT2/DZVP approximation.

They are very similar to the corresponding PE functions calculated for 2-HP [28]. The only difference is that, in formamide, the $A''(n\pi^*)$ state approaches asymptotically the ground state along the dissociation path, whereas in 2-HP an intersection has been found. It is difficult to decide at present whether the intersection found in Ref. [28] is real or is an artifact resulting from the limited precision of the method. The question of the existence of an intersection or not is not very crucial for the photophysical dynamics, which should be very similar in both systems.

There are two important implications of the above-mentioned similarity of the PE surfaces of formamide and 2-HP. Firstly, the qualitative picture of the PT reaction derived in Ref. [28] at the CASSCF level as typical for the PT reaction in isolated systems without

an intramolecular hydrogen bond, has found confirmation at the CASPT2 level of theory. Secondly, all the essential features of the PE surfaces of 2-HP with respect to the PT reaction are already present in a much simpler system (formamide) which contains the essential reaction centre (N–C–OH). This is a very promising conclusion which provides strong support that the results obtained below for clusters of formamide may also be representative of more complex systems.

2.2. Formamide–water complex

Of the several isomers of the formamide–water (F–H_2O) complex, the cyclic structure stabilized by a pair of hydrogen bonds formed between water and the amino and carbonyl groups of formamide is the most
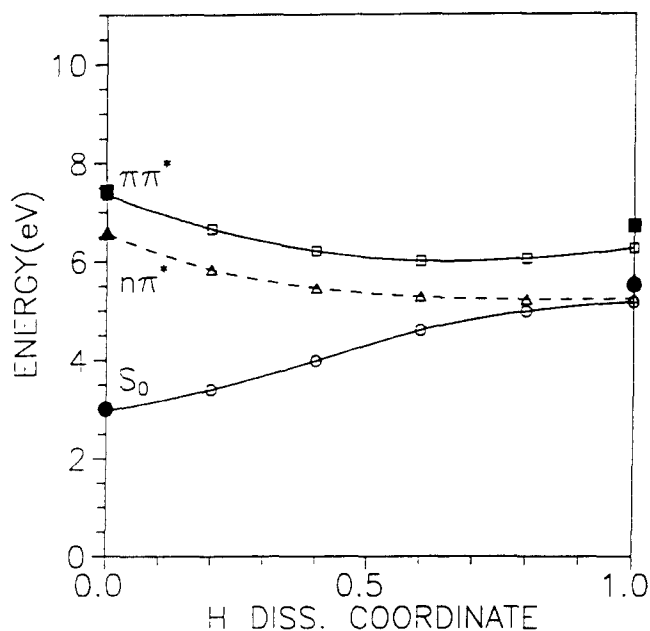
Fig. 3. The same as in Fig. 2, but calculated along the reaction coordinate to the mobile hydrogen dissociation between the transient structures 2a and 2b of Fig. 1.

stable [8]. The ground state optimized tautomeric forms of the F–H$_2$O cyclic complex are presented in Fig. 4. The keto form (3a) is 0.51 eV more stable than the enol form (3b) in the HF/DZVP approximation. Both tautomeric forms optimized at the HF/DZVP level are non-planar in their ground state with one hydrogen atom of water tilted out of plane. This has, however, a minor effect on the energy. The C_1 optimized structures

are more stable compared with the C_s optimized structures by 33 cm^{-1} and 141 cm^{-1} for the keto and enol forms respectively. In the following, we use the C_s optimized structures with the parameters indicated in Fig. 4.

The active space used in the CASSCF reference correlates ten electrons (of a total number of 34) in eight orbitals and is denoted as (12,0/4,4). The dimension of the first-order interaction space in the CASPT2 calculations is about 1.2×10^5 and 5.6×10^5 for the DZV and DZVP basis sets respectively. The absolute energies of the ground and first excited singlet states, as well as the energies and oscillator strengths for vertical transitions from the ground state, are listed in Table 2. The weight of the CASSCF reference in the first-order wavefunction is slightly decreased compared with the case of formamide (Table 1), but still exceeds 0.82 for all states. Hydration of formamide slightly decreases the energy difference between the tautomers. It also shifts the energies of the vertical transitions from the ground state in a characteristic way: the $S_0 \rightarrow n\pi^*$ transition is shifted to the blue (hypsochromic shift), whereas the $S_0 \rightarrow \pi\pi^*$ transition is shifted to the red (bathochromic shift), as expected.

The PE functions calculated in the CASPT2 approximation along the PT reaction coordinate are presented in Fig. 5(b). They look qualitatively rather different from those obtained for the formamide molecule (Fig. 2). This is not surprising, however, because the PT reaction coordinates are very different in both cases. In the F–H$_2$O complex, the PT reaction proceeds along pre-existing hydrogen bonds as a synchronous transfer
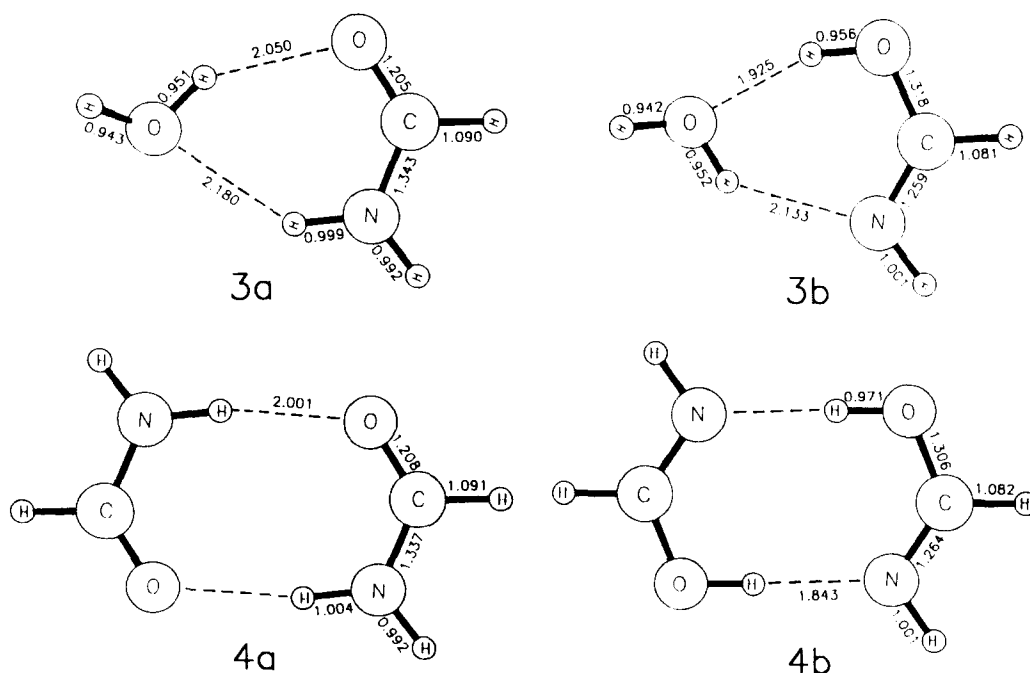

Fig. 4. The keto (3a and 4a) and enol (3b and 4b) forms of the formamide–water complex and formamide dimer respectively. The numbers indicate the optimized bond lengths.

Table 2
The CASPT2 energies of the ground and lowest excited singlet states (E), weights of the CASSCF reference in the renormalized first-order wavefunctions (ω) and energies (ΔE) and oscillator strengths (f) for dipole transitions from the ground state of the two tautomeric forms of the formamide–water complex calculated with the DZV and DZVP basis sets. Energies and transition dipole moments were calculated at the equilibrium geometries of the given form in the ground state

Parameter	DZV			DZVP		
	S_0	$A''(n\pi^*)$	$A'(\pi\pi^*)$	S_0	$A''(n\pi^*)$	$A'(\pi\pi^*)$
Keto form						
E (a.u.) [a]	−0.3426	−0.1226	−0.0590	−0.7144	−0.4928	−0.4378
ω	0.898	0.888	0.853	0.859	0.847	0.827
ΔE (eV)	–	5.98	7.71	–	6.03	7.52
f	–	0.001	0.352	–	0.001	0.337
Enol form						
E (a.u.) [a]	−0.3203	−0.0694	−0.0181	−0.7009	−0.4463	−0.4036
ω	0.897	0.884	0.853	0.859	0.846	0.820
ΔE (eV)	(0.61) [b]	6.87	7.22	(0.37) [b]	9.92	8.09
f	–	0.014	0.389	–	0.011	0.370

[a] Energies relative to −245.0 a.u.
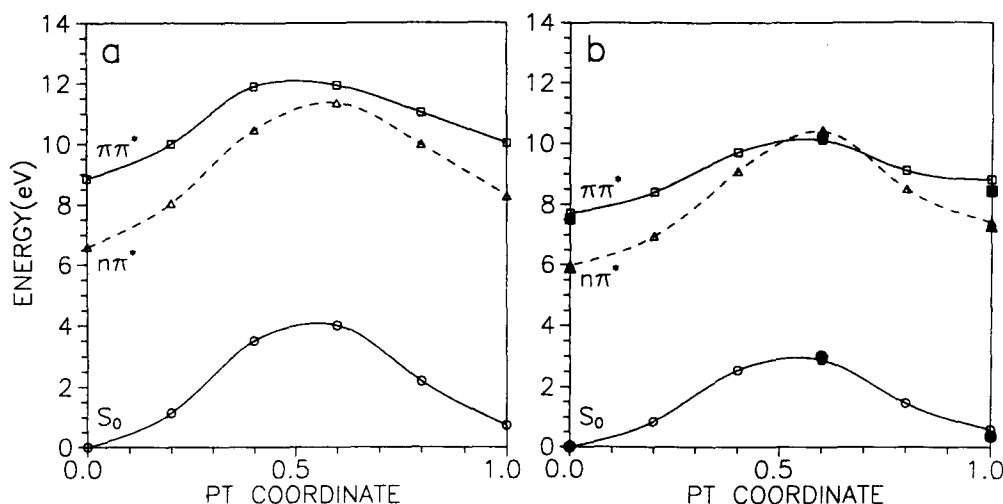[b] Relative to the S_0 state of the keto form.

Fig. 5. The same as in Fig. 2, but calculated along the PT reaction coordinate for the formamide–water complex.

of two hydrogen atoms. Indeed, the PE functions for the PT reaction in the F–H₂O complex are qualitatively similar to those obtained for the PT reaction occurring in systems with an intramolecular hydrogen bond [22,23].

In the case of the F–H₂O complex, dynamic correlation effects, mostly neglected in the CASSCF approximation (Fig. 5(a)), have a more significant influence on the PT functions (Fig. 5(b)). This is a direct consequence of the fact that fewer electrons have been correlated in the CASSCF reference as compared with the formamide case. This is also reflected by the smaller values of the reference weights in the first-order wavefunction presented in Table 2. Inclusion of polarization functions into the basis set does not introduce any significant changes in the PE functions as is revealed by the results of benchmark calculations presented in Table 2 and marked in Fig. 5(b).

2.3. Formamide dimer

The tautomeric forms of the formamide dimer (F–F) optimized using the HF/DZVP approximation, imposing a D_{2h} symmetry constraint, are presented in Fig. 4. The keto form (4a) is 0.92 eV more stable than the enol form (4b) at this level of theory. In the energy calculations, the CASSCF reference correlates 12 electrons (of a total number of 48) within ten orbitals. The active space is denoted as (8,8,0,0/2,2,3,3) in the D_{2h} point group with irreducible representations A_g, B_g, A_u and B_u respectively. The dimension of the first-order interaction space in the CASPT2 calculations is about 1.4×10^5 and 6.7×10^5 with the DZV and DZVP basis sets respectively. The absolute energies of the ground and first excited singlet states, as well as the energies and oscillator strengths for vertical transitions from the

Table 3

The CASPT2 energies of the ground and lowest excited singlet states (E), weights of the CASSCF reference in the renormalized first-order wavefunctions (ω) and energies (ΔE) and oscillator strengths (f) for dipole transitions from the ground state of the two tautomeric forms of the formamide dimer calculated with the DZV and DZVP basis sets. Energies and transition dipole moments were calculated at the equilibrium geometries of the given form in the ground state

Parameter	DZV					DZVP				
	S_0	$B_g(n\pi^*)$	$A_u(n\pi^*)$	$A_g(\pi\pi^*)$	$B_u(\pi\pi^*)$	S_0	$B_g(n\pi^*)$	$A_u(n\pi^*)$	$A_g(\pi\pi^*)$	$B_u(\pi\pi^*)$
Keto form										
E (a.u.) [a]	−0.4106	−0.1865	−0.1856	−0.1703	−0.1592	−0.9232	−0.6977	−0.6969	−0.6821	−0.6709
ω	0.837	0.822	0.822	0.725	0.727	0.809	0.782	0.783	0.717	0.697
ΔE (eV)	–	6.09	6.12	6.54	6.85	–	6.13	6.15	6.56	6.86
f	–	–	0.003	–	0.693	–	–	0.002	–	0.681
Enol form										
E (a.u.) [a]	−0.3686	−0.1223	−0.1179	−0.1156	−0.0982	−0.8803	−0.6348	−0.6311	−0.6297	−0.6241
ω	0.836	0.818	0.819	0.753	0.748	0.801	0.773	0.774	0.722	0.724
ΔE (eV)	(1.14) [b]	6.70	6.82	6.88	7.35	(1.17) [b]	6.68	6.78	6.82	6.97
f	–	–	0.028	–	0.887	–	–	0.021	–	0.832

[a] Energies relative to −338.0 a.u.

[b] Relative the S_0 state of the keto form.

ground state, are listed in Table 3. Dimerization splits the excited electronic states into the gerade and ungerade components. Only the ungerade states carry oscillator strength for dipole transitions from the ground state. As expected, dimerization shifts the excited states of different orbital nature in a manner similar to hydration, i.e. lowers the energy of the S_0 $\pi\pi^*$ transition and raises the energy of the S_0 $n\pi^*$ transition. Inclusion of the polarization functions into the basis set does not change the quality of the results. This is a very promising result with respect to future applications to large polyatomic systems where a reasonable compromise between the quality of the basis set and the sophistication of the theoretical treatment is needed. Our results indicate that the DZV basis set may be a reasonable choice when treating such systems at the level of CASPT2.

The CASSCF and CASPT2 PE functions calculated along the PT reaction coordinate are presented in Fig. 6. We can see that they are qualitatively similar to those obtained for the F–H_2O complex (Fig. 5), i.e. they are rather typical of an intramolecular PT reaction. There is a significant effect of the dynamic electron correlation on the PE functions, even stronger than in the case of the F–H_2O complex. This results from the further decrease in the percentage of electrons correlated in the CASSCF reference as compared with the systems considered above. In effect the dynamic correlation significantly lowers the excited state energies and makes the PE functions much flatter. Energetic barriers for the PT reaction on the ground and excited PE surfaces of the formamide dimer (Fig. 6) are smaller than those obtained for the formamide–water complex (Fig. 5). This results from steric differences in the geometry of the hydrogen bonds of the two systems.

The PE functions of the gerade $n\pi^*$ and $\pi\pi^*$ states follow those of their ungerade partners along the PT reaction coordinate, and so are not presented in Fig. 6.

3. Discussion of results

The extensive ab initio calculations of the PE surfaces reported in this work have been performed with the intention to develop a better understanding of some aspects of the photochemistry of proton transferring systems. In this section, we discuss the relevance of the PE surface data.

Let us consider at the beginning the formamide example. The excited state intramolecular proton transfer (ESIPT) mechanism that emerges from our calculations is basically the same as found previously for 2-HP [28]. In other words, the ESIPT reaction in an isolated molecule or a molecule embedded in a condensed inert medium can take place via a photon-induced dissociation–association (PIDA) mechanism. The optically prepared wave packet on the bright (allowed for dipole transitions from the S_0 state) $A'(\pi\pi^*)$ PE surface of a given tautomeric form will spread over the surface, and will also transfer to the dark (almost strictly forbidden for dipole transitions from the S_0 state) $A''(n\pi^*)$ PE surface due to the vibronic coupling between the quasi-degenerate states. Part of the wave packet (perhaps the dominant part) will follow the gradients in the direction of the tautomeric minima in both S_1 and S_2 states, relaxing the nuclear geometry. This non-reactive part of the wave packet will eventually come back to the S_0 state via fluorescence or internal conversion. The reactive part
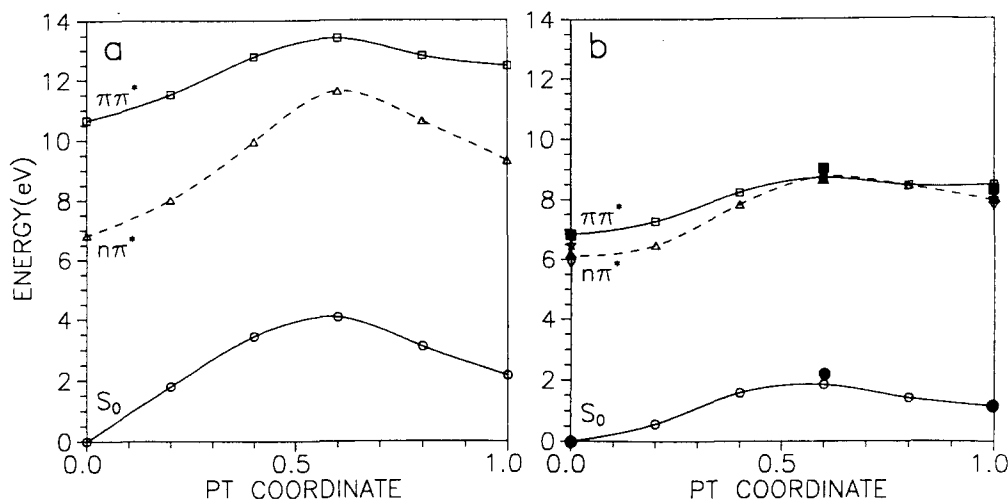
Fig. 6. The same as in Fig. 2, but calculated along the PT coordinate for the formamide dimer.

of the wave packet will feel a significant gradient towards dissociation of the hydrogen atom either on the $A'(\pi\pi^*)$ or $A''(n\pi^*)$ PE surfaces. This can eventually lead to the actual dissociation of the mobile hydrogen. On the other hand, the wave packet moving on the excited state PE surface towards dissociation of the hydrogen atom can also jump to the ground state PE surface either due to fluorescence or internal conversion induced via vibronic interactions between the close-lying electronic states. As the net effect, there is a finite probability for the system to reach a ground state near its barrier ($Q \approx 0.5$ in Fig. 2), and thus to settle down in a minimum of the PE surface different from the initial one. Thus photoinduced tautomerization takes place.

We can argue, however, that the scheme of the ESIPT reaction via the PIDA mechanism sketched above is too crude and does not consider in detail the nuclear geometry relaxation following electronic excitation, which may have a significant influence on the dynamics of the process. This is certainly true, and we can expect large changes in the nuclear geometry of formamide in the excited electronic states [17]. This is also reflected by the relatively long vibronic progressions observed in the absorption bands [27]. It has already been pointed out that an out-of-plane distortion of 2-HP [28] and o-hydroxybenzaldehyde [22] along the reaction path to their prefulvenic forms may strongly influence the ESIPT dynamics of these systems. This may be responsible for the fact that, in 2-HP, the keto to enol photoinduced tautomerization is observed exclusively [31] instead of a practically reversible reaction predicted by a simple PIDA mechanism [28]. To some extent this also concerns formamide. Thus a full characterization of its PE surfaces in the complete internal coordinate space may be of great importance with respect to its own excited state dynamics, but is not particularly representative for more complex systems for the reasons indicated in Section 1.

The dimerization of formamide or its complexation with a protic solvent such as water changes qualitatively the mechanism of the ESIPT process. Now the PT reaction can occur as a synchronous transfer of two hydrogen atoms along pre-existing intramolecular hydrogen bonds. The excited state dynamics of the PT reaction in formamide clusters are thus basically the same as in other molecular systems with intramolecular hydrogen bonds [22,23]. The important feature of the process is that it is exclusively a one-way reaction, transferring effectively the nominal enol form into its keto partner. In other words, the ESIPT process is strongly exothermic with respect to the enol-to-keto transformation. The keto form of formamide is energetically preferred over the enol form on the ground and lowest excited state PE surfaces (Figs. 5 and 6). The PT reaction in the excited states of formamide clusters is even more endothermic than in the ground state. In the case of clusters of formamide, this means that once we have the rare enol form in the ground state it is easily transformed to the native keto form either thermally or via optical excitation.

It should be noted that the native forms of nucleic acid bases (adenine, cytosine, guanine and thymine) contain the keto ($=O$) and amino ($-NH_2$) groups, while their rare forms, which are suspected to play a role in mutagenesis [1-3], contain the enol ($-OH$) and imino ($=NH$) groups. If it is true that formamide can mimic the properties of more complex systems containing the peptide linkage, e.g. nucleic acid bases, then their pairs should be, after electronic excitation, even more stable in the native structure than in the rare structure. The same concerns their complexes formed with protic solvents by analogy with the formamide-water complex. The last point has recently been confirmed by theoretical results obtained for a hydrogen-bonded complex of cytosine with water [32]. Finally, we can conclude that our results indicate that the hypothesis of Löwdin [1],

i.e. the phototautomerization of complementary pairs of DNA may be responsible for mutagenesis, seems to be questionable. We cannot exclude, however, phototautomerization as a mutagenic factor. One such possibility is the photoinduced transformation of some (mutagenic) compounds which can drive (or catalyse) the tautomerization reaction of nucleic acid bases to their rare forms (see, for instance, Ref. [33]).

Acknowledgements

References

[1] P.-O. Löwdin, Rev. Mod. Phys., 35 (1963) 724.

[2] B. Pullman and A. Pullman, Adv. Heterocycl. Chem., 13 (1971) 77.

[3] G.E. Schulz and R.H. Schirmer, Principles of Protein Structure, Springer, New York, 1979.

[4] L. Radom and N.V. Riggs, Aust. J. Chem., 33 (1980) 249.

[5] H.B. Schegel, P. Gund and E.M. Fluder, J. Am. Chem. Soc., 104 (1982) 5347.

[6] T.J. Zielinski and A. Poirer, J. Comput. Chem., 5 (1984) 466.

[7] J.E. Boggs and Z. Niu, J. Comput. Chem., 6 (1985) 46.

[8] P.G. Jassien and W.J. Stevens, J. Chem. Phys., 84 (1986) 3271.

[9] A.M. Sapse, L.M. Fugler and D. Cowbourn, Int. J. Quantum Chem., 29 (1986) 1241.

[10] J.S. Kwiatkowski, R.J. Bartlett and W.B. Person, J. Am. Chem. Soc., 110 (1988) 2353.

[11] X.-Ch. Wang, J. Nichols, M. Feyereisen, M. Gutowski, J. Boatz, A.D. Haymet and M.J. Frisch, J. Phys. Chem., 95 (1991) 10 419.

[12] M.W. Wong, K.B. Wiberg and M.J. Frisch, J. Am. Chem. Soc., 114 (1992) 1645.

[13] J.S. Kwiatkowski and J. Leszczynski, J. Mol. Struct., 270 (1992) 67.

[14] S. Dapprich and G. Frenking, Chem. Phys. Lett., 205 (1993) 337.

[15] X.-C. Wang, J.C. Facelli and J. Simons, Int. J. Quantum Chem., 45 (1993) 123.

[16] L.B. Harding and W.A. Goddard III, J. Am. Chem. Soc., 97 (1975) 6300.

[17] Y. Li, R.L. Garrel and K.N. Houk, J. Am. Chem. Soc., 113 (1991) 5895.

[18] B.O. Roos, Adv. Quantum Chem., 69 (1987) 399.

[19] K. Andersson, P.-A. Malmqvist, B.O. Roos, A.J. Sadley and K.J. Wolinski, J. Phys. Chem., 94 (1990) 5483.

[20] K. Andersson, P.-A. Malmqvist and B.O. Roos, J. Chem. Phys., 96 (1992) 1218.

[21] W.H. Miller, B.A. Ruf and Y.-T. Chang, J. Chem. Phys., 89 (1988) 6298.

[22] A.L. Sobolewski and W. Domcke, Chem. Phys. Lett., 211 (1993) 82.

[23] A.L. Sobolewski and W. Domcke, Chem. Phys., 184 (1994) 115.

[24] T.H. Dunning and P.J. Hay, in H.F. Schaefer III (ed.), Methods of Electronic Structure Theory, Plenum, New York, 1977.

[25] R.D. Amos and J.E. Rice, Cambridge Analytic Derivatives Package, Issue 4.0, Cambridge, 1987.

[26] K. Andersson, M.P. Fuelscher, R. Lindh, P.-A. Malmqvist, J. Olsen, B.O. Roos, A.J. Sadlej and P.-O. Widmark, MOLCAS Version 2, User's Guide, University of Lund, Sweden, 1991.

[27] H. Basch, M.B. Robin and N.A. Kuebler, J. Chem. Phys., 49 (1968) 5007.

[28] A.L. Sobolewski, Chem. Phys. Lett., 211 (1993) 293.

[29] J.S. Binkley, J.A. Pople and W.J. Here, J. Am. Chem. Soc., 102 (1980) 939. M.S. Gordon, J.S. Binkley, J.A. Pople, W.J. Pietro and W.J. Here, J. Am. Chem. Soc., 104 (1982) 2797.

[30] M. Dupuis, D. Spangler and J.J. Wendoloski, Nat. Resour. Comput. Chem. Software Cat. 1, Prog. QC01 (GAMESS), 1980.

[31] M.J. Nowak, L. Lapinski, J. Fulara, A. Les and L. Adamowicz, J. Phys. Chem., 96 (1992) 1562.

[32] A.L. Sobolewski and L. Adamowicz, J. Chem. Phys., 102 (1995).

[33] A.L. Sobolewski and L. Adamowicz, Chem. Phys. Lett., 234 (1995) 94.