QM/MM non-adiabatic decay dynamics of formamide in polar and non-polar solvents

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Non-adiabatic on-the-fly dynamics simulations of the photodynamics of formamide in water and n-hexane were performed using a QM/MM approach. It was shown that steric restrictions imposed by the solvent cage do not have an influence on the initial motion which leads to the lowest energy conical intersection seam. The initial deactivation in water is faster than in n-hexane and in the gas phase. However, most of the formamide molecules in water do not reach the ground state. The reason for the deactivation inefficiency in water is traced back to a decrease of close CO·−HOH and NH·−OH2 contacts which fall in the range of hydrogen bonds. The energy deposition into H-bond breaking events leaves molecules with less energy for surmounting the CN dissociation barrier. In both solvents, after hopping to the ground state, the solvent cage keeps the HCO and NH2 fragments or CO and NH3 products in close proximity. Consequently, the number of trajectories where fast recombination happens is augmented with delayed recombinations that start when the dissociation fragments hit the cage wall and return back.

The hot ground state formamide is formed in an internal conversion process identical to the path leading to CN photodissociation. In the case of aqueous formamide, good agreement with experimental results is achieved by combining dynamics simulations starting from the S1 and the S2 excited states collecting high and low energy trajectories, respectively.

Introduction

Formamide is the simplest prototype of the –NH–CO– bond which is the sole covalent linkage between amino acids in the linear back-bone structure of proteins. Besides this direct significance to the structure and function of biomolecules in live organisms, formamide is also relevant for exo-biological questions as a molecule that could be one of the precursors of small prebiotic molecules. Namely, it is observed in interstellar medium, star-forming regions and in the comet Hale–Bopp. Since UV and VUV radiation is an important energy source for intriguing synthesis under the conditions that are similar to that in primitive Earth or the interstellar medium, the detailed understanding of excited states of formamide and their photochemical and photophysical properties can add to understanding of life’s origins. Due to this reason as well as many other implications in fields such as laser surgery, investigation of how the formamide interacts with irradiation has received considerable scientific attention.

Photochemical experiments in the gas phase, at 150 °C showed that irradiation of formamide with light at 206.2 nm (6.01 eV) leads to formation of CO, H2 and NH3 with quantum yields of 0.8, 0.6 and 0.2, respectively. Based on product composition, three major processes (CN dissociation, CH dissociation and direct formation of NH3 + CO) were proposed as primary reactions. The same primary photodissociation processes were also found to follow irradiation of formamide by a 193 nm nanosecond laser pulse in noble gas matrices. In Ar, excitation led to the formation of a weakly bound NH2 + HCO radical pair. In the Xe matrix, H2 and HNCO were detected due to a strong external heavy atom effect which induced intersystem crossing to the triplet state. More recently, cleavage of the CH bond following excitation to the triplet state was investigated by measuring laser induced fluorescence spectra upon irradiation at 205 nm. Of special interest to the present study is a recent femtosecond photolysis investigation of aqueous formamide. In this work it was shown that the majority of formamide molecules (80%) decay to the vibrationally excited ground state, followed by efficient dissipation of vibrational energy to the water cage in a few picoseconds. The remaining fraction of the excited...
formamide molecules (about 20%) switched to the ground state as \( \text{CHO} \cdots \text{NH}_2 \) radical pairs, of which 50% underwent recombination.\(^\text{10}\)

To supplement experiments and to shed light on mechanisms of photoprocesses in formamide, numerous calculations have also been performed. They were focused on characterisation of the lowest excited singlet states,\(^\text{11–13}\) stationary points on the excited-state potential energy surfaces,\(^\text{8,14}\) location of low lying conical intersection seams,\(^\text{15}\) description of deactivation paths and exploring the dynamics of the dissociation process in the gas phase.\(^\text{15,16}\) The effect of protonation\(^\text{17}\) and methylation\(^\text{18}\) on formamide’s photoprocesses was also explored. A comprehensive overview of these results is given in ref. 19 and 20. Briefly, on the basis of these studies five main photodeactivation channels for formamide excited in the \( S_1 \) singlet state and related conical intersection seams where non-adiabatic \( S_1/S_0 \) crossing is possible were identified and fully characterized. The corresponding minima on the crossing seams (MXSs) are visualised in Fig. 1.

Four deactivation channels correspond to excited-state dissociation of CN, CO, CH or NH bonds while one is related to the OCN bending. Among them the channel involving CN bond cleavage was shown to be the lowest in energy. Surface-hopping dynamics simulations of formamide in the gas phase\(^\text{15}\) confirmed that the major deactivation process involves conical intersections related to the seam represented with MXSCN. After hopping to the ground state the energy is mostly transferred to the translational motion of the HCO and \( \text{NH}_2 \) fragments.

Since most of the chemical and biophysical processes involving the peptide linkage take place in the solvent or within complex biological systems (e.g. enzymes), understanding of the role of complex environments in shaping and directing their photochemistry and photophysics is particularly challenging. In the recent study of matrix-controlled photofragmentation of formamide\(^\text{21}\) using a non-adiabatic OM/MM approach,\(^\text{22,23}\) we have shown that embedding of formamide in an argon matrix had a significant influence on the outcome of the photochemical process. Upon approaching the conical intersection along the C–N stretch coordinate, the molecule dissociates into the weakly bound \( \text{NH}_2 \) + \( \text{CHO} \) radical pair. After decay to the ground state the radical pair undergoes hydrogen transfer from the \( \text{CHO} \) to the \( \text{NH}_2 \) fragment affording \( \text{NH}_3\cdot\cdot\cdot\text{CO} \) complexes. As already indicated in femtosecond photolysis of formamide in water,\(^\text{10}\) a similarly strong impact of solvation on the outcome of photolysis was observed. The main goal of the work described in the present paper was to shed light on the mechanisms of the initial process following excitation of formamide in water to the lowest excited singlet states. This is of considerable importance since one of the basic questions posed by Petersen and colleagues\(^\text{10}\) was whether the excited formamide molecules follow the same potential energy surface to dissociation, whereupon some molecules recombine to ground state formamide or whether the hot formamide ground state is formed in an internal conversion process different from the path leading to dissociation of the molecule. An answer was not possible from the experimental data\(^\text{10}\) calling for additional experimental and/or computational investigations. In addition, we thought it of interest to extend this study to the non-polar environment using \( n \)-hexane as solvent. In contrast to water, which could affect the photodissociation process through steric restrictions imposed by caging and electrostatic interactions between solute and water molecules, in \( n \)-hexane only steric restrictions are possible. By comparing the results for \( n \)-hexane and water we shall provide more thorough insight into relative importance of these two factors on the studied photodissociation process. Besides mechanistic description, we shall comment on the effect of solute confinement on the deactivation rate.

**Computational details**

The formamide molecule (QM region) was included in a spherical cluster (sphere = 13.43 Å) of 300 water molecules (MM region). The initial packing was performed using the VEGA-ZZ program\(^\text{24}\) with default maximum overlap (0.80 Å) between solute and neighbouring water molecules. In the case of \( n \)-hexane, the solvent cluster was built from 150 molecules by using the PACKMOL\(^\text{25}\) program. The radius of its sphere was set to 38.45 Å in order to keep the experimental density of 0.651 g L\(^{-1}\).

The solvent structure was then thermalized and relaxed around individual solute structures at the MM level keeping the molecule in the QM region at the frozen structure (time of thermalization 100 ps). The van der Waals parameters, intramolecular parameters and effective charges for formamide and the non-polar solvent molecules were taken from the OPLS/AA force field,\(^\text{26}\) while for water the TIP3P model was applied. The molecular mechanics calculations were performed using TINKER.\(^\text{27}\) After thermalization, statistically independent sample geometries of the solvent were selected from a thermalized ground state trajectory in steps of 1 ps with the QM region left frozen at the starting structure. Initial conditions for formamide were calculated using a Wigner distribution of a quantum harmonic oscillator using the B3LYP/SV(P) frequencies of the ground state equilibrium structure optimized at the same level of theory. The initial formamide structure along the C–N stretch coordinate, the molecule dissociates into the weakly bound NH\(_2\) + CHO radical pair. After decay to the ground state the radical pair undergoes hydrogen transfer from the CHO to the NH\(_2\) fragment affording NH\(_3\)····CO complexes. As already indicated in femtosecond photolysis of formamide in water,\(^\text{10}\) a similarly strong impact of solvation on the outcome of photolysis was observed. The main goal of the work described in the present paper was to shed light on the mechanisms of the initial process following excitation of formamide in water to the lowest excited singlet states. This is of considerable importance since one of the basic questions posed by Petersen and colleagues\(^\text{10}\) was whether the excited formamide molecules follow the same potential energy surface to dissociation, whereupon some molecules recombine to ground state formamide or whether the hot formamide ground state is formed in an internal conversion process different from the path leading to dissociation of the molecule. An answer was not possible from the experimental data\(^\text{10}\) calling for additional experimental and/or computational investigations. In addition, we thought it of interest to extend this study to the non-polar environment using \( n \)-hexane as solvent. In contrast to water, which could affect the photodissociation process through steric restrictions imposed by caging and electrostatic interactions between solute and water molecules, in \( n \)-hexane only steric restrictions are possible. By comparing the results for \( n \)-hexane and water we shall provide more thorough insight into relative importance of these two factors on the studied photodissociation process. Besides mechanistic description, we shall comment on the effect of solute confinement on the deactivation rate.

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embedded in each of individual solvent clusters was replaced by one of the displaced structures of the Wigner distribution. Finally, the MM region of each of these sample structures was than thermalized around its frozen, displaced QM-region structure so as to adapt the cavity to the slightly changed new structure. The relaxation of the solvent cavity was performed for 10 ps with 1 fs step size using Newton-X. The Andersen thermostat was used to simulate 298 K and a collision frequency of 0.2 fs⁻¹.

Mixed quantum chemical dynamics calculations were conducted with on-the-fly computation of the energies, gradients and non-adiabatic coupling vectors at the complete active space self-consistent field level of theory with ten electrons distributed in eight orbitals and a 6-31G(d) basis set. A set of active orbitals comprised, two non-bonding lone pairs, one pair of π/π* orbitals and two σ/σ* pairs, which was proved to be a good compromise for adequate characterization of the low-lying valence states and the photodissociation process of formamide in ref. 11 and 15. The three lowest singlet states of formamide in the gas phase and in the argon matrix, intermediate Rydberg states were not taken into account. By comparison with the MR-CISD and MR-CISD+P calculations this approach was proven to be well suited for the accurate description of formamide’s surfaces as well as for use in the molecular dynamics calculations in our previous study on photodynamics of isolated formamide. For the sake of illustration we only mention here that excitation energy of the first singlet state of formamide change by 0.01 and 0.06 eV when the 6-31G(d) basis set is replaced with 6-311G(d) and 6-31+G(d,p) basis sets.

Nuclear motions were represented by classical trajectories with numerical integration of the Newtonian equations using the velocity Verlet algorithm. Non-adiabatic transition probabilities between electronic states were calculated by means of a modified Tully’s fewest switches approach. Decoherence correction to the state probabilities was used. Two batches of dynamics simulations (in water and n-hexane) with the Andersen thermostat turned on (298 K) were performed starting from the S₁ valence excited state. To not interfere with the non-adiabatic treatment, the action of the thermostat was restricted to the solvent molecules. For each of the batches 100 trajectories were calculated with the step size for the integration of 0.5 fs and a maximum allowed simulation time of 2000 fs. Additional dynamics simulations in water with the S₂ (ππ* initial valence excited state and the temperature kept constant at 298 K) were conducted. In the latter trajectory batch, the maximum simulation time was decreased to 500 fs since the photodynamic processes are much faster. Also, one batch of trajectories starting from S₁ in the gas phase by using the same initial conditions created for water, current time-step and time window of 2000 fs were also carried out in order to produce reference values.

All CASSCF calculations were carried out with the COLUMBUS program package. The atomic orbital gradients and gradient integrals were computed with program modules taken from the DALTON program. The molecular mechanics calculations of energy and gradients were performed using TINKER. The combination of the hybrid energies and gradients, the integration of the equations of motion and the time-dependent Schrödinger equation and the surface hopping were performed using the NEWTON-X package of programs.

### Results and discussion

#### Solvatochromic effects

Solvatochromic effects were deduced from the difference of average vertical excitation energies sampled from the initial geometries in dynamics simulation of formamide in the gas phase and the employed solvents. Since a Wigner distribution for the quantum harmonic oscillator in the gas phase ground state was used for solute geometry, calculated solvatochromic effects reflect only the effect of solvent on the electronic structure. In other words, contribution of structural changes induced by solvation is not included. It is important to note in this regard that in a previous QM/MM study of the electronic spectra of amides, Besley et al. showed that the effect of structural changes on the maxima of the ππ* (S₁) and πn* bands (S₂) of formamide on passing from the gas phase to water is negligible as compared to electrostatic interactions. Hence, it should be expected that in spite of neglecting the structural changes the calculated values provide reasonable insight into solvatochromic effects.

Comparison of the calculated average vertical excitation energies for the S₁ excited state for formamide in n-hexane and in the gas phase (Table 1) reveals that the effect of solvation by non-polar solvent n-hexane is negligible. On the other hand, immersion of formamide in water cluster causes a shift of the S₁ average vertical excitation energy toward higher energies by 0.27 eV.

In the linear absorption spectrum of formamide in aqueous solution, a weak absorption band extends from 210 to 230 nm. It is very difficult to determine its maximum due to overlap with the more intense band around 180 nm (6.9 eV). If the maximum of aqueous formamide is supposed to be in the middle of the wavelength range, somewhere around 220 nm (5.63 eV), a comparison to the gas phase experimental value of vertical excitation located at 5.8 eV would give a blue solvatochromic shift of 0.17 eV. Similarly, a blue shift of approximately 0.2–0.4 eV for the πn* transition of amides upon replacing non-polar solvent with water was reported by Nielsen and Schelman. Our calculated shift in water is in

<table>
<thead>
<tr>
<th>Ref.</th>
<th>E_{exc, vert}/eV</th>
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</thead>
<tbody>
<tr>
<td>Gas phase</td>
<td>S₁</td>
</tr>
<tr>
<td>n-Hexane</td>
<td>5.81</td>
</tr>
<tr>
<td>Water</td>
<td>5.79</td>
</tr>
<tr>
<td>Gas phase (experiment)</td>
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<tr>
<td>Water (experiment)</td>
<td>5.8</td>
</tr>
<tr>
<td>Acetonitrile (experiment)</td>
<td>5.9</td>
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</tbody>
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Table 1: Average vertical excitation energies at the initial geometries of the dynamics.
agreement with these experimental estimates. It is also in accord with calculations by Hirst and coworkers who applied a semicontinuum approach based on combination of explicitly defined solvent and continuum description.\(^{39}\) It is interesting to mention in this regard that the same authors did not found significant blue shift using a continuum solvent model.\(^{39}\)

In contrast to the \(S_1\) excited state, the average vertical excitation energy calculated for the \(S_2\) excited state exhibits a red shift of 0.26 eV (the values of average excitation energies are 8.09 eV and 8.35 eV in water and in the gas phase, respectively). The calculated shift is in the correct direction, but lower than the experimentally observed one (ca. 0.5 eV) in water and acetonitrile.\(^{10,41}\) Inspection of the results presented in Table 1 shows this to be consequence of a more pronounced overestimation of the calculated average vertical excitation energies in water than that in the gas phase. Overestimation of the vertical excitation energy for the \(S_2\) excited state is a well known phenomenon and it is due to a lack of major dynamical electron correlation effects inherent to the CASSCF approach used in the present work. Its consequences on photodynamics from the \(S_2\) state of formamide were previously noted \(^{15}\) and discussed in more detail in our previous studies on photodissociation of formamide \(^{21}\) as well as by others for variety of systems.\(^{42}\)

In the case of a non-polar \(n\)-hexane environment, similarly to what was found for the \(n\pi^*\) state, there is no change in \(\pi\pi^*\) state vertical excitation with respect to the gas phase. The difference between water and \(n\)-hexane solvatochromic effects is not surprising due to the ability of the water to form strong H-bonds with the carbonyl oxygen and nitrogen atoms of formamide, a feature which is not present in the non-polar media. Besides, the contribution of the electrostatic bulk effects is also prominent due to large change in dipole moment between ground and excited states.\(^{13}\)

**Dynamics calculations from the \(S_1\)**

**Deactivation time constants.** The evolution of the excited state population for the dynamics simulations of formamide in the gas phase, \(n\)-hexane and water with the \(S_1\) as the initial state is compared in Fig. 2. In order to assure straightforward comparison, we recalculated deactivation time constants for photodissociation of formamide \(^{15}\) in the gas phase using the same starting geometry for generating initial conditions as in solvents, diabatic populations were corrected for decoherence effects and the simulation time window was elongated from 1000 to 2000 fs. The excited state lifetimes were calculated by fitting the average adiabatic \(S_1\) population of the decay part of the curve as a function of time with the delayed exponential function given in eqn (1)

\[
f(t) = f_0 + (1 - f_0) \exp\left(-\frac{t}{\tau_d}/\tau_c\right)
\]

**Fig. 2** Fraction of trajectories for each state as a function of time after excitation of formamide in (a) gas phase, (b) embedded in \(n\)-hexane and (c) embedded in water. The \(S_1\) (\(n\pi^*\)) valence excited state was used as an initial state in all dynamics batches of trajectories. The dashed lines represent the exponential fitting curves. The error bars correspond to the rms of the fitting procedure.
where \( \tau_d \) is the initial delay or latency time and \( \tau_e \) is the decay constant. The present fitting function accounts better than one used in ref. 15 for the fact that some trajectories stay in the excited state what is particularly important for the dynamics simulations in water where the largest fraction of the excited molecules (57%) remains in the \( S_1 \) state minimum and does not decay to the ground state. The excited state lifetime for the ultrafast deactivation process is calculated as the sum of \( \tau_d \) and \( \tau_e \) values. The parameter \( f_0 \) denotes the fraction of trajectories that does not deactivate within the simulation time. Calculated lifetimes and fitting parameters are summarised in Table 2.

The dynamics of formamide in the gas phase shows a latency time of 21 fs before starting the exponential non-adiabatic decay to the ground state with a decay constant of 732 fs. This gives an excited lifetime of 753 fs, which differs somewhat from the 517 fs calculated and reported in ref. 21. It should be noted, however, that a direct comparison of these two results has to be made with care because of the significantly longer simulation time used here for fitting and because in the present study the average vertical excitation energy was lower by \( \approx 0.3 \) eV due to differences in the starting geometry used for selecting initial conditions.

Simulations in water revealed a considerable shortening of the lifetime as compared to the gas phase and \( n \)-hexane (Table 2). The main reason behind that lies in diminishing of the decay constant, while the latency time is essentially the same as in \( n \)-hexane. Another important feature worth noting concerns the fact that the decay process in water becomes practically inhibited at 1000 fs and the population of the \( S_1 \) state stabilizes at 60% (Fig. 2c). In other words, the initial deactivation is faster, but becomes inefficient since most of the formamide molecules do not return to the ground state.

**Description of trajectories.** In concordance with previously reported gas phase results,\(^{15} \) in the majority of deactivated trajectories starting from the \( S_1 \) state of formamide in the gas phase excitation energy is transferred to strong vibrational stretching and bending modes. In fact, the most prominent initial motion is stretching of the CN bond which is also the key motion that leads toward hopping points related to the lowest energy \( S_1/S_0 \) crossing seam denoted MXS\(_{CN} \) (86% of hopping points has structure very similar to the structure of MXS\(_{CN} \), Table 3). In a smaller fraction of trajectories, the formamide switches to the ground state via conical intersections related to other seams (related to MXS\(_{SCN} \) (7%), MXS\(_{CH} \) (3.5%) and MXS\(_{CO} \) (3.5%)). The results of simulations in \( n \)-hexane and in water summarized in Table 3 show a similar pattern. The deactivation process from the \( S_1 \) state via the MXS\(_{CN} \) is active in 100% and 95% of deactivated trajectories in \( n \)-hexane and water, respectively. The only notable difference concerns

| Table 2 | Summary of the fitting parameters for the \( S_1 \) excited state occupations in different environments |
|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | \( f_0 \) | \( \tau_d / \)fs | \( \tau_e / \)fs | \( \tau \) |
| Gas phase | 0.19 | 21 | 732 | 753 |
| Argon\(^{21} \) | 0.15 | 78 | 650 | 728 |
| \( n \)-Hexane | 0.29 | 68 | 667 | 735 |
| Water | 0.57 | 75 | 229 | 305 |

The fraction of trajectories belonging to the Type I is the largest for dynamic simulations started in the gas phase (67%). There are only few trajectories (4) among them where the CN bond dissociation is followed by CO + NH\(_3\) formation. Upon embedding formamide into solvent the number of trajectories of Type I generally decreases. The decrease is small in \( n \)-hexane and more prominent in water where only in 10% of trajectories dissociation of the CN bond takes place. It should also be noted that, in contrast to the gas phase, H atom abstraction from the HCO radical and formation of CO + NH\(_2\) in the ground state are not found at all in \( n \)-hexane. It is more likely in water in spite of the smallest fraction of trajectories of Type I.

| Table 3 | The decomposition of photodeactivation paths differentiated by conical intersection seams responsible for deactivation observed in the dynamics calculations with the \( S_1 \) as an initial state |
|----------------|-----------------|-----------------|-----------------|-----------------|
| | No\(^{a} \) | MXS\(_{CN} \) | MXS\(_{CO} \) | MXS\(_{CH} \) | MXS\(_{SCN} \) |
| Gas phase | 85 | 86% | 3.5% | 3.5% | 7% |
| Gas phase\(^{b} \) (from ref. 15) | 81 | 89% | 1% | 4% | 6% |
| \( n \)-Hexane | 66 | 100% | — | — | — |
| Water | 43 | 95% | 5% | — | — |

\(^{a}\) Number of deactivated trajectories. \(^{b}\) Total number of trajectories taken into analysis is 96.
The most striking difference between the Type I trajectories in the gas phase and solvents concerns the observation that in the gas phase, the excitation energy is transferred to the translational motion of the HCO and NH$_2$ or NH$_3$ and CO fragments which fly apart while in solvents these fragments stay in close proximity within the cage. This is illustrated in Fig. 4, where the evolution of the CN distances along trajectory runs is shown for all trajectories in the gas phase and in water. In the gas phase, the distance between C and N atoms after hopping to the ground state increases from 2 to 10 Å within a few hundreds of femtoseconds, while in water restrictions imposed by the water cage hold the fragments close to each other. In the latter case, the separation of the fragments, characterized by the C⋯N distance, does not reach 6 Å.

Comparison of the C⋯N distances plotted against time, for Type I trajectories in n-hexane and in water is also of some interest (Fig. 5). The distance between the C and N atoms after dissociation in n-hexane is in the range of 3–8 Å. In some trajectories (5%) the distance becomes even larger than 9 Å, indicating that dissociated fragments penetrate into the solvent cage. The average separation of the NH$_2$ and HCO fragments increases continuously during the deactivation time (100–1300 fs) and reaches an equilibrium value of ca. 5.5 Å between 1400 and 1800 fs. On the other hand, the increase in the average separation of these fragments in Type I trajectories in water is much faster than in n-hexane due to the shorter time constant for the deactivation process. It occurs between

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Fig. 3 Decomposition of trajectories in dynamics simulations following excitation to the S$_1$ state of formamide (a) in gas phase, (b) embedded in n-hexane and (c) embedded in water.

Fig. 4 Evolution of C–N distances for all trajectories in (a) gas phase and (b) water at 298 K. Mean value is denoted with black colour.

Fig. 5 Evolution of C–N distances for trajectories of Type I in (a) n-hexane and (b) water. Mean value is denoted with black colour.
100 and 600 fs, when it reaches the equilibrium value. Moreover, the C⋯N distances in water oscillate within a narrower range (between 2.75 and 5 Å) and the mean value is significantly smaller than in n-hexane (around 3.75 Å). This in turn suggests that the hexane cage is more flexible and explains the higher portion of trajectories in Type I as compared to water.

Next we turn to trajectories of Type II which lead to non-dissociated formamide in the ground state. From Fig. 3 it is evident that the ratio of the deactivated trajectories of this type and the total number of deactivated trajectories (Type I and Type II) significantly increases upon immersion of formamide into the solvent cage. It is the largest in the case of water where in most of the deactivated trajectories (31) HCO and NH₂ fragments recombine to the parent formamide. To shed more light on the mechanism of deactivation, plots of C⋯N distances vs. time for Type II trajectories for isolated formamide and formamide immersed in water are compared in Fig. 6. We note that the CN distances in the hopping points (indicated by black triangles) in most of the trajectories in both systems are in the range between 1.7 and 2.5 Å as expected for the activation of the MXS-CN reaction path. In the gas phase, most of these points correspond to the largest CN distance displacements from the equilibrium value or are very close to it. In other words, the reversion of the HCO and NH₂ fragments to the starting structure in the S₀ state is fast. On the other hand, in the water cage (Fig. 6b) in addition to this type of trajectories we also observe a significant fraction of trajectories (10) in which separation between HCO and NH₂ fragments after hopping to the ground state assumes values as high as 3–5 Å. The recombination of the formamide structure occurs in these trajectories with a small delay relative to those in which HCO and NH₂ fragments remain at distances close to the equilibrium value. We thus speculate that recombination of formamide structures in this type of trajectories occurs following collision of the dissociated fragments with the cage wall. It is interesting to mention that a similar feature is also observed in n-hexane (not shown here), but only in three trajectories. Consequently, their contribution to the fraction of recombined structures is negligible. We assume that the reason for this unique situation in water should be ascribed to the lower flexibility of the cage walls caused by the presence of hydrogen bonding. As stated above, in trajectories of Type III formamide molecules do not decay to the ground state and do not dissociate within the simulation time of 2000 fs. Their fraction is almost doubled in n-hexane and becomes the dominant pattern in the water cage (Fig. 3). The observed trend cannot be explained by steric hindrance imposed by the solvent cage since the average value of the C⋯N distance in the hopping points in all three media is very similar (2.2, 2.3 and 2.1 Å for gas phase, n-hexane and water, respectively). In order to provide a rationale for this result we initially explored the effect of microsolvation with water on the energy barrier for CN dissociation in the S₁ state, using a cluster of formamide with two water molecules as a model. The calculated value of 0.34 eV was found to be somewhat lower (0.45 eV) than that for the isolated formamide. Concomitantly, this factor can also not be responsible for the observed trend.

Next we considered the possibility that part of the energy is transferred to the environment through stretching motions of hydrogen bonds leaving less energy in the system to surmount the energy barrier. For this purpose we analysed the mutual distances between formamide and the neighbouring water molecules in more detail. All CO⋯HOH and NH⋯OH₂ contacts, shorter than 2.5 Å, have been counted in all trajectories since these contacts might be considered as possible H-bonds. Average numbers of contacts per structure for the O and N site of the formamide molecule are 2.03 and 1.90 for the initial ground state structures at the beginning of the simulation (see Fig. 7). A decrease to a value of 1.5 is clearly visible for CO⋯OH contacts in the time window of 600 fs. On the NH₂ side of the formamide molecule the decrease is less pronounced, but still noticeable. Obviously, there are less hydrogen bonds present in the excited state. Hence, some amount of energy is deposited into H-bond breaking processes leaving molecules with less energy for crossing the excited state energy barrier for CN stretching. More molecules remain trapped in the S₁ state minimum and less molecules approach the vicinity of the MXS-CN conical intersection seam where hopping to the ground state takes place.

Dynamics calculations for the small formamide–water cluster. It should be noted that in an electrostatic embedding approach, water molecules are unpolarizable in the fixed charge representation. Therefore, dynamic solvent effects due to fast electronic
reorganization in the solvent molecules cannot be described by this model. Mutual polarisation effects between solute and solvent as well as the charge transfer effects to water might play a significant role in strong H-bonding systems. For instance an example of high importance of polarization effects on photodissociation dynamics is provided by the Na\(^+\)I\(^–\) ion pair within small water clusters.\(^{45}\) Namely, in this particular case highly ionic ground state opposes the reversed polarity of the covalent first excited state. This certainly is not the case in the present study and therefore we do not expect a pronounced change in the decay channels by using the polarizable force field. Strong support in favour of such expectation is provided by the recent study of photodynamics of microsolvated zwitterionic glycine where the QM/MM approach with electrostatic embedding is tested on the glycine–water clusters.\(^{46}\) Substitution of water molecules with point charges left the reaction pathways in the first excited state of zwitterionic glycine essentially the same as the ones calculated using the CASSCF method.

To gain further insight into importance of hydrogen bonding between formamide and directly bound water molecules, we performed additional set of dynamics simulations in which pure formamide in the QM region was replaced by the formamide–(H\(_2\)O\(_2\)) cluster and embedded within a shell of 300 H\(_2\)O molecules within the MM part. The optimized structure of the cluster is shown in Fig. 8.

Initial conditions were generated in the same way as that for the isolated formamide. The orbitals included in the CASSCF(10,8)/6-31G(d) calculation were localized on the formamide molecule within the cluster. 50 trajectories were computed with a simulation time window of 1000 fs. The evolution of the excited state population for the dynamics simulations of the two set of calculations with the S\(_1\) as the initial state is compared in Fig. 9.

Inspection of Fig. 9 clearly shows that the presence of two polarisable water molecules in the QM part did not substantially affect neither the speed of the deactivation process or the fraction of deactivated trajectories (38\% vs. 43\%). The mechanism of deactivation also remained unaltered – most of the hopping points are found to be structurally similar to the MXSCN with the average CN bond length of 2.12 Å.

The distribution of the calculated trajectory types (not shown) is also very similar to that observed for the formamide inserted into the water cage: type I 10\%, type II 28\% and type III 62\%, what is statistically insignificant. All these facts demonstrate that the results obtained for the formamide–(H\(_2\)O\(_2\)) cluster are in qualitative agreement with the results for formamide reported above.

**Dynamics calculations from the S\(_2\)**

We next turn to the simulation of the photodissociation process of aqueous formamide with S\(_2\) as an initial state. The average occupation of the adiabatic states as a function of time derived from the dynamics calculations is illustrated in Fig. 10.

In the early stage of the dynamics simulation, ultrafast S\(_2\) \(\rightarrow\) S\(_1\) population transfer with a time constant of 45 fs is observed. After 150 fs, the fraction of trajectories occupying S\(_2\) drops to ca. 2%. The average occupation of the intermediate S\(_1\) state reaches its maximum at 60–75 fs and then it slowly drops to less than 10% at the end of the simulation time. The first trajectory hops to the ground state at 17 fs. After that, the occupation of the S\(_0\) state increases strongly, reaching 94% at
the end of simulation time. The excited state lifetime is estimated by fitting the S_0 occupation with the function \( g(t) = 1 - f(t) \) where \( f(t) \) is the fitting function (eqn (1)) used for fitting the average occupation of the S_1 state in the dynamics calculations described above when the initial state was S_1. The calculated lifetime for formamide when excited to the S_2 state is 118 fs (21 fs contribution from \( \tau_d \) and 97 fs contribution from \( \tau_v \)) if the fitting range spans from 20 to 500 fs. The population flow from the S_1 to the S_0 state is faster with respect to the S_1 \( \rightarrow \) S_0 transition in dynamics simulation starting from the S_1 initial state. The same trend was previously observed in dynamics simulations of formamide in the gas phase\(^{15} \) and in the argon matrix,\(^{21} \) where it was ascribed to the presence of a S_2/S_1 conical intersection in the vicinity of the Franck–Condon region and overshooting of the S_2 vertical excitation energy at the present level of theory.

The mechanism of deactivation of aqueous formamide starting the dynamics from the S_2 state (Fig. 11) is identical to that observed starting from the S_1 state (Fig. 3). The initial motion follows the CN stretching mode and formamide initially dissociates to HCO and NH\(_2\) fragments in 95% of trajectories. In 27% of trajectories, the energy is afterwards passed to additional C–H dissociation and transfer of H atoms from HCO to NH\(_2\) fragment forming CO + NH\(_3\) photo products. In 25% of trajectories, the dissociated fragments after hopping to the ground state PES recombine into the parent molecule. At the end of the simulation time, the ratio between the number of recombinations and the number of trajectories where CN dissociation occurs is approximately 1:3. It is decreased with respect to dynamic simulations from the S_1 as an initial state where this ratio is approximately 2:1.

It is interesting to note that the decomposition pattern in a water environment differs from that observed in the gas phase,\(^{15} \) where CO bond stretching was identified as the initial motion in two types of trajectories. In 13% of trajectories CO dissociation proceeds accompanied by a concomitant merging of all three potential energy surfaces along the trajectory while in 19% of trajectories the CO bond recombines followed by the energy transfer to the CN stretching mode. This type of initial motion is completely suppressed in the water environment.

**Comparison with experiment**

As mentioned in the Introduction section the available experimental data for aqueous formamide obtained by Keiding’s group\(^{10} \) showed that most of the formamide molecules (80%) decayed to the vibrationally excited ground state, followed by efficient dissipation of vibrational energy to the water cage in a few picoseconds. The remaining fraction of the excited formamide molecules (about 20%) switched to the ground state as CHO \(-\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\cdot\......

**Fig. 10** Fraction of trajectories for each state as a function of time after excitation of formamide embedded in water into the S_2 initial state. The dashed line shows the exponential fitting curve.
exponentially observed ratio of 80 : 20. This clearly demonstrates that there is a significant energy dependence on the dynamics results. The careful selection of the energy window in creating initial conditions is crucial to explain the experimentally observed results.

Conclusions

The results of non-adiabatic on-the-fly dynamics simulations of the photodynamics of formamide in the solvents water and n-hexane were presented and compared with the photodissociation process in the gas phase. Calculations in the condensed media were performed using a recently developed non-adiabatic photodynamics QM/MM approach.

Steric restrictions imposed by a non-polar or an inert environment on the deactivation rate are negligible since embedding of formamide in n-hexane does not have an influence on the time constant of the ultrafast decay process from the S1 state. This leads to the conclusion that the initial motion which leads to the lowest energy conical intersection seam is not prevented by the solvent cage. The initial deactivation is faster in water due to the smaller energy barrier for CN dissociation caused by electrostatic effects. However most of the molecules in this solvent do not return to the ground state. The reason for the deactivation inefficiency is traced back to the decrease of close CO···HOH and NH···OH2 contacts (possible H-bonds). The energy is deposited into H-bonds breaking, thus leaving molecules with less energy for surmounting the CN dissociation barrier.

In all examined media the primary deactivation process from the S1 state was found to be dissociation of the C–N bond in agreement with available experimental data. The only noticeable solvent effect is steric hindrance to CN bond elongation after hopping to the ground state, resulting in prevention of the separation between HCO and NH2 or CO and NH3 products in deactivated trajectories. A careful analysis of trajectories resulting in hot ground state formamide shows that the starting structure is formed in an internal conversion process identical to the path leading to CN photodissociation of the molecule. All recombinations of HCO and NH2 fragments are very fast after hopping events in the gas phase. In solvents, the number of trajectories where fast recombination happens is augmented with delayed recombinations that start when one of the fragments hits the cage and returns back.

The dynamic simulations initiated in the S2 state of formamide immersed in the water cage are characterized by the CN initial elongation. The MXS\textsubscript{CO} deactivation path present in the gas phase is completely suppressed.

The last point, worth mentioning is the significant energy dependence on the dynamics results. Namely, correspondence with experimental results is achieved after new analysis of the MD simulations employing new sorting criteria, which better account for the experimental initial conditions. This is achieved by collecting high and low energy trajectories from calculations starting from the S1 and the S2 initial state, respectively. An adequate selection of the energy window in creating initial conditions is necessary to explain experimental results where laser pulse can populate two different excited states.

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Notes and references

