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Abstract
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Nuwan De Silva, Soohaeng Y. Willow, and Mark S. Gordon* 

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ABSTRACT: Solvent effects on the electronic spectra of formamide and trans-N-methylacetamide are studied using four different levels of theory: singly excited configuration interaction (CIS), equations of motion coupled-cluster theory with singles and doubles (EOM-CCSD), completely renormalized coupled-cluster theory with singles and doubles with perturbative triple excitations (CR-EOM-CCSD(T)), and time-dependent density functional theory (TDDFT), employing small clusters of water molecules. The simulated electronic spectrum is obtained via molecular dynamics simulations with 100 waters modeled with the effective fragment potential method and exhibits a blue-shift and red-shift, respectively, for the $n \rightarrow \pi^*$ and $n_{ab} \rightarrow \pi^*$ vertical excitation energies, in good agreement with the experimental electronic spectra of amides.

I. INTRODUCTION

The study of solvent effects on the electronic absorption spectra of amides provides an excellent benchmark for implementing an accurate solvent representation of proteins. Therefore, the electronic transition energies of formamide (HCONH$_2$) and trans-N-methylacetamide (NMA) have been of considerable interest, both experimentally$^{1-6}$ and theoretically.$^{7-12}$ The previous studies were motivated by the role of amides as a model for the underlying repeating unit in protein backbones. HCONH$_2$ is an important prototype molecule, being the simplest unsubstituted unit to contain the peptide linkage in proteins. Meanwhile, NMA can serve as the simplest substituted unit in the peptide linkage. HCONH$_2$ and NMA provide important prototypes for the calculation and interpretation of electronic excitation energies of proteins. Interactions between these prototype molecules and surrounding water molecules can give insight into the complex intermolecular interactions that occur when proteins are solvated.

Experimentally, the gas phase electronic spectra of amides are well understood. In general, amides exhibit five main absorption bands in the gas phase:$^{2}$ (1) an intense band, the $V_1$ band, due to the $n \rightarrow \pi^*$ transition; (2) a less intense band, the $W$ band (due to the $n \rightarrow \pi^*$ transition); (3), (4) two sharp bands, $R_1$ and $R_2$ (due to Rydberg transitions); and (5) a $Q$ band (due to Rydberg transitions with a superposition of two Rydberg states).$^{6,13,14}$

The absorption spectra of amides in the condensed phase exhibits interesting solvatochromic effects depending on the type of amide and the solvent. In the electronic absorption spectrum of HCONH$_2$, in aqueous solution, the $n \rightarrow \pi^*$ and $n_{ab} \rightarrow \pi^*$ transitions were found to be blue- and red-shifted by 0.27 and 0.50 eV, respectively, relative to the gas phase HCONH$_2$. Nielsen and Schellman$^4$ measured the absorption curves for a series of amides including NMA in cyclohexane and water. The position of the $n_{ab} \rightarrow \pi^*$ band in NMA was measured, and a very small red-shift was observed when changing the solvent from cyclohexane to water (0.07 eV). Considering the $n_{ab} \rightarrow \pi^*$ excitation energy of NMA in gas phase (6.81 eV) measured by Kaya et al.$^3$ and NMA in aqueous solution (6.67 eV) measured by Nielsen et al.,$^4$ a 0.14 eV red-shift was observed in the aqueous phase. The experimental gas phase data for the $n \rightarrow \pi^*$ transition of NMA is not available. However, when NMA is placed in cyclohexane the $n \rightarrow \pi^*$ band appeared to be 5.46 eV$^{15}$ and in aqueous solution, the $n \rightarrow \pi^*$ band shifted to 5.85 eV$^4$ with a 0.39 eV blue-shift. The electronic spectrum shifts in different directions and with different magnitudes, depending on the nature of the solvent and solute–solvent interactions.$^{16-18}$

Two approaches are commonly used to model solvent effects, the continuum (implicit) approach$^{19,20}$ and the discrete (explicit) approach.$^{21,22}$ The continuum model requires some choice for the geometry of the molecular cavity, which is intended to reflect the size of the solvated molecule. Popular continuum methods include the polarizable continuum method (PCM)$^{20,23}$ the conductor-like screening model (COSMO)$^{24,25}$ the solvation model $x$ (SM$x$)$^{26-28}$ where $x$ denotes a specific parametrization of a particular solvent model, the solvation with volume polarization (SVP)$^{29}$ and the self-consistent reaction field (SCRF) model.$^{30}$ A review article for the continuum solvation models can be found in refs 31 and 32. In the discrete approach, the individual solvent molecules are explicitly present, modeled either by some level of electronic structure theory or by a model potential. The individual solvent–solvent interactions are explicitly accounted for.

Both the continuum and discrete approaches have advantages and disadvantages. The continuum approach is
relatively fast and is designed to mimic bulk properties of the solution. However, the continuum approach does not describe the specific interactions (e.g., hydrogen bond) between the solute and solvent molecules. In addition, the continuum approach can be very sensitive to the cavity parameters. The discrete approach treats solute–solvent interactions explicitly. However, the discrete approach generally requires extensive configurational sampling. Therefore, the discrete approach can be computationally demanding, especially if fully ab initio potentials are used.

Commonly used discrete methods include the effective fragment potential (EFP) method, the simple point charge/extended (SPC/E) method, and the three-, four-, and five-point transferable intermolecular potentials (TIP3P, TIP4P, and TIP5P), all-atom optimized potentials for liquid simulations (OPLS)-AA, dissipative particle dynamics (DPD), smooth particle hydrodynamics (SPH), and the particle-based simulation technique often called stochastic rotation dynamics (SRD). The approach taken in the present work for representing the solvent explicitly is the effective fragment potential method for water (EFP1). The EFP1 method, which includes self-consistent polarization effects, has been shown to accurately treat the interactions between solute and solvent molecules. The EFP1 method, a quantum mechanics (QM)-based method that includes self-consistent induction, was introduced to study aqueous solvent effects. Most of the above discrete methods can be considered to be variants of quantum mechanics/molecular mechanics (QM/MM) simulations in which the electronic structure of the solute is treated as QM and the solvent molecules are treated as MM.

The computational modeling of solvent effects on the electronic spectra of amides has primarily examined the effects of up to three explicit water molecules. The singlet excited configuration interaction (CIS) method with a minimal STO-3G basis set was used to calculate the $n\rightarrow\pi^*$ excited state of HCONH$_2$ in the presence of one and two water molecules. These authors concluded that the formation of a hydrogen bond with the carbonyl oxygen of HCONH$_2$ could destabilize the $n\rightarrow\pi^*$ state and change the magnitude of the blue-shifted $n\rightarrow\pi^*$ transition energy. The geometries of the ground state and the first excited singlet and triplet states of HCONH$_2$ in vacuo and in the presence of three EFP water molecules were explored by Krauss and Webb using the multicombinatorial self-consistent-field (MCSCF) method with the DH(d,p) basis set. The vertical transition of HCONH$_2$ in vacuo and in the presence of three EFP water molecules was reported to be 5.66 and 6.14 eV, respectively. It was also shown that the EFP1 water calculations accurately reproduced the fully ab initio excited state geometry and the interaction energy between HCONH$_2$ and water.

The complete active space self-consistent field (CASSCF) and multiconfigurational second-order perturbation theory (CASPT2) methods have been used to study the $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ states of HCONH$_2$ with one water molecule, using a double-$\zeta$ plus polarization basis set. Relative to isolated HCONH$_2$, the $n\rightarrow\pi^*$ state was predicted to be blue-shifted by 0.18 eV upon the addition of a water molecule, while the $\pi_{ab}\rightarrow\pi^*$ state was predicted to be red-shifted by 0.15 eV. The CASSCF and CASPT2 methods, with an ANO basis set, have also been used to calculate the ground state and excited state energies of HCONH$_2$ in the presence of one, two, and three water molecules. The HCONH$_2$ with one, two, and three water molecules undergoes a blue-shift of 0.36, 0.48, and 0.50 eV, respectively, in the $n\rightarrow\pi^*$ transition, whereas the $\pi_{ab}\rightarrow\pi^*$ transition undergoes a red-shift of 0.15, 0.15, and 0.25 eV, respectively, relative to isolated HCONH$_2$.

Besley and Hirst have reported a theoretical investigation of the solvent effects on the valence electronic spectra of NMA and HCONH$_2$ using the CASSCF and CASPT2 methods for the solute and a self-consistent reaction field model for the solvent. The experimental $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ excitation energies were reproduced to within 0.15 eV accuracy. A red-shift was predicted for the $\pi_{ab}\rightarrow\pi^*$ excitation energy. However, in contrast to the experimental data, no significant blue-shift was found for the $n\rightarrow\pi^*$ excitation energy. Recently, a polarizable embedding (PE) QM/MM method was developed by Olsen et al. They have computed gas-to-aqueous solvent induced shifts of the lowest $n\rightarrow\pi^*$ vertical excitation energy in acetone and acrolein and the lowest $\pi\rightarrow\pi^*$ vertical excitation energy in acrolein, pyridine, uracil, coumarin 151, and coumarin 153. They have used a QM/MM (PE-DFT) approach in which the solute is treated using DFT (CAM-B3LYP functional) and the solvent molecules are represented by a PE potential. The aug-cc-pVQZ basis set was used in the calculations of excitation energies of all the molecules except a smaller 6-31+G* basis was used in the calculations on coumarin 153. The PE model was applied by Sneskov et al. to the $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ excitation energies of HCONH$_2$ and NMA in vacuum and water solution using the CCSDR(3) with the aug-cc-pVQZ basis set. Even though Sneskov et al. predicted acceptable solvent-induced blue-shift $n\rightarrow\pi^*$ transitions in both HCONH$_2$ and NMA, they failed to predict the solvent-induced red-shift $\pi_{ab}\rightarrow\pi^*$ transitions in NMA within 0.15 eV accuracy. (The $\pi_{ab}\rightarrow\pi^*$ transition of NMA was predicted to give a large blue-shift (+ 0.67 eV) instead of a small red-shift.)

The temperature effects on the electronic spectra of amides (HCONH$_2$, N-methylformamide, acetamide, and NMA) have been studied using a combination of molecular dynamics (MD) simulations and TDDFT in the gas phase by Besley et al. The valence $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ transitions in both HCONH$_2$ and NMA, they failed to predict the solvent-induced red-shift $\pi_{ab}\rightarrow\pi^*$ transitions in NMA within 0.15 eV accuracy. (The $\pi_{ab}\rightarrow\pi^*$ transition of NMA was predicted to give a large blue-shift ($+0.67$ eV) instead of a small red-shift.)

The temperature effects on the electronic spectra of amides (HCONH$_2$, N-methylformamide, acetamide, and NMA) have been studied using a combination of molecular dynamics (MD) simulations and TDDFT in the gas phase by Besley et al. The authors have also calculated the electronic spectrum of HCONH$_2$ in the presence of 16 water molecules around each gas phase MD configuration. Overall, a blue-shift was predicted for the $n\rightarrow\pi^*$ state and red-shift was predicted for the $\pi_{ab}\rightarrow\pi^*$ state of HCONH$_2$ with respect to HCONH$_2$. The mean values for the $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ excitation energies of HCONH$_2$ have been blue- and red-shifted by +0.52 and −0.33 eV, respectively, compared to the gas phase at 300 K. The authors also noted that structural changes in the amides contribute to the $\pi_{ab}\rightarrow\pi^*$ red-shift.

In the present study, solvent effects on the electronic absorption spectra of amides are considered for the $n\rightarrow\pi^*$ and $\pi_{ab}\rightarrow\pi^*$ vertical excitations. The $n\rightarrow\pi^*$ state originates primarily from a carbonyl oxygen lone pair $n$ into the antibonding C=O $\pi^*$ orbital. Experimentally the $n\rightarrow\pi^*$ excitation of amides exhibits a blue-shift in an aqueous environment. The $\pi_{ab}\rightarrow\pi^*$ excitation from a nonbonding $\pi$ orbital into an antibonding $\pi^*$ orbital is particularly
interesting since the $\pi_{ab} \rightarrow \pi^*$ transition has an intense band and exhibits a red-shift in an aqueous environment.\textsuperscript{4,5} Since amides can act as models for the underlying repeating unit in a protein, understanding solvent effects on amides helps to design and develop an accurate solvent representation of proteins. In this article, a qualitative interpretation of solvent-induced shifts of amides is obtained via examination of the change in the solute HOMO and LUMO electronic energies of solute:water complexes at four different levels of theory: CIS, EOM-CCSD, CR-EOM-CCSD(T), and TDDFT. QM/MM molecular dynamics simulations are employed to provide the simulated electronic spectrum and quantitative values of solvent-induced blue-shift and red-shift, respectively, for $n \rightarrow \pi^*$ and $\pi_{ab} \rightarrow \pi^*$ vertical excitations using an explicit solvent model. An important aspect of this article is to demonstrate that the sophisticated EFP method can capture the observed solvent shifts. This is important since EFP has been shown previously to predict ground state properties at a level that is equivalent to MP2.\textsuperscript{49,50,80,81}

II. COMPUTATIONAL DETAILS

For QM-EFP applications, an EFP1 water is described by one-electron potentials, representing electrostatic (Coulomb), induction (polarization), and exchange repulsion + charge transfer, that are added to the QM Hamiltonian. The Coulomb interaction is modeled with multipoles (through octopoles) located at atoms and bond midpoints. The polarization effects are described by dipole polarizability tensors located at the centroids of localized orbitals: bonds and lone-pairs. The repulsive terms (exchange repulsion + charge transfer) are represented by exponential functions placed at the atom centers and the center of mass, with the exponents fitted to the water dimer potential energy surface. There are two QM-EFP1 variants; Hartree–Fock (HF)-based (EFP1/HF)\textsuperscript{41,42} and density functional theory (DFT)-based (EFP1/DFT).\textsuperscript{43} The B3LYP\textsuperscript{84,85} functional was used for the DFT version. Recently, Yoo et al.\textsuperscript{44} interfaced time-dependent density functional theory (TDDFT) with the EFP1/DFT model to describe the excited states of molecules solvated by water. This combined TDDFT/EFP1/DFT method was used to calculate the solvent-induced shifts of molecular electronic excitations of acetone. The calculated solvent effect on the $n \rightarrow \pi^*$ vertical excitation energy is in good agreement with the experimental blue-shift.

All calculations in the present work are performed with the GAMESS\textsuperscript{84,85} electronic structure code. First, the solute with one, two, and three water molecules located at the ground state global minima are fully optimized with second order perturbation theory (MP2)\textsuperscript{86} and the 6-311++G(2d,2p) basis set, in C$_1$ symmetry. Using the optimized geometries, vertical excitation energy calculations are carried out with CIS\textsuperscript{87} equations of motion coupled-cluster with singles and doubles (EOM-CCSD),\textsuperscript{88} completely renormalized coupled cluster theory with single and double and perturbative triple excitations (CR-EOMCCSD(T)),\textsuperscript{89} and TDDFT\textsuperscript{90,91} with the PBE0 functional and using the cc-pVDZ\textsuperscript{92,93} basis set. Only vertical singlet-to-singlet transitions are considered here.

The hybrid QM/EFP scheme is employed to calculate the solvent induced shifts of the amides.\textsuperscript{44} The solute is treated quantum mechanically using DFT and the PBE0 functional with the cc-pVDZ basis set. The solvent is treated using 100 EFP1/DFT solvent water molecules. Therefore, MD simulations with 100 waters explicitly modeled with the EFP method in GAMESS can be described as a QM/MM (PBE0/EFP1) variant. The MD simulations were carried out for both the gas phase and the aqueous phase (100 EFP1 water molecules) at 300 K, with a time step of 1 fs. The simulation was carried out for 60 ps with 50 ps equilibration, and configurations were extracted every 10 steps after equilibration was achieved. Therefore, a total of 1000 configurations were used to compute the TDDFT(PBE0)/cc-pVDZ vertical excitation energies.

The simplest ab initio electronic structure implementation for calculating vertical excitation energies is CIS. TDDFT has become a popular method for calculating electronic excitation spectra because it is able to produce accurate vertical absorption energies for some types of molecular systems, at a relatively modest computational cost.\textsuperscript{4–9} Of the methods used in this work, CR-EOM-CCSD(T) is expected to provide the most accurate excitation energies and also to be the most computationally expensive.

III. RESULTS AND DISCUSSION

The MP2/6-311++G(2d,2p) optimized structures of the HCONH$_2$:n(H$_2$O) complexes ($n = 0–3$) are shown in Figures 1 and 2, respectively. In general, the water molecules are more likely to form hydrogen bonds to the carbonyl oxygen than to the amide group.

The calculated vertical $n \rightarrow \pi^*$ ($\omega_1$) and $\pi_{ab} \rightarrow \pi^*$ ($\omega_2$) excitation energies of the amides and amide:water complexes are shown in Tables 1 and 2, respectively. The blue (or red)-shifted energy values are given in parentheses. In general, $n \rightarrow \pi^*$ excitations are blue-shifted, and $\pi_{ab} \rightarrow \pi^*$ excitations are red-shifted at all levels of theory. One exception is the TDDFT
Figure 2. MP2/6-311++G(2d,2p) optimized structures of NMA:n(-H₂O) complexes (n = 0–3); a and b refer to different isomers of the complexes. The relative energies of isomers in each HCONH₂:n(H₂O) complex are given in kcal/mol.

<table>
<thead>
<tr>
<th>Complex</th>
<th>CIS</th>
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<th>TD-PBE0</th>
<th>exp</th>
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<td>HCONH₂</td>
<td>6.48(0.00)</td>
<td>5.78(0.00)</td>
<td>5.41(0.00)</td>
<td>5.65(0.00)</td>
<td>5.58</td>
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<td>HCONH₂:1H₂Oa</td>
<td>6.84(0.36)</td>
<td>6.04(0.26)</td>
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<td>7.08(0.31)</td>
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Table 1. ω₁(n → π*) Vertical Excitation Energies (eV) for HCONH₂:n(H₂O) and NMA:n(H₂O), n = 0–3, with the cc-pVDZ Basis Set Using the MP2/6-311++G(2d,2p) Geometry; the Vertical Excitation Energy Differences between the Amide and Amide/Water Complex Are Provided in Parentheses; a and b Refer to Different Isomers of the Complexes (See Figures 1 and 2)

*NMA in cyclohexane (the experimental data for NMA are not available for the n–π* state).

The πₐ → π* transition in HCONH₂:2H₂Oa. However, the predicted solvent-induced shifts for these species are small at all levels of theory. EOM-CCSD and CR-EOMCCSD(T) give essentially the same vertical excitation energies.

The MD simulated spectra of HCONH₂ and NMA are shown in Figure 3a,b, respectively. The ω₁(n → π*) spectra are shown in solid bars, and ω₂(πₐ → π*) spectra are shown in open bars. In each spectrum, the green color represents the amide with 100 EFP1 waters, and the orange color represents the amide without EFP1 waters. The average excitation energy of the ω₁(n → π*) transition is blue-shifted, and the average ω₂(πₐ → π*) transition is red-shifted in both HCONH₂:100EFP1 and NMA:100EFP1, relative to the HCONH₂ and NMA without EFP1 waters present.

Each geometric configuration (snapshot) in an MD trajectory shows different electronic properties. Hence, the ω₁(n → π*) and ω₂(πₐ → π*) vertical excitation energies are different for one geometric configuration to another. Therefore, it is important to average the excitation energies. The computed average vertical excitation energy values and shifts are given in Table 3. The computed shifts are in reasonable agreement with the experimental data.4,5

The physical origin of the solvatochromic shifts of ω₁(n → π*) and ω₂(πₐ → π*) can be correlated with molecular orbital characteristics if the CIS wave function is in reasonable agreement with the more reliable levels of theory (e.g., the EOM-CC methods), and if the CI wave function is dominated by just one orbital excitation, such as n → π* and πₐ → π*. It may be seen in Tables 1 and 2 that although the absolute CIS excitation energies are too high relative to the more accurate methods, they are consistently so. Consequently, the CIS method is in consistently good agreement with the shifts that are predicted by the EOM-CC methods. In addition, the CIS expansion coefficient for the n → π* and πₐ → π* excitations are greater than 0.9 in most of the complexes and always greater than 0.8, so, a qualitative orbital-based argument is reasonable here.

The πₐ,n, and π* Hartree—Fock orbitals of HCONH₂ and NMA molecules are shown in Figure 4a,b, respectively. Schematic representations of the molecular orbitals and vertical excitation of amides are provided in Figure 5. According to Figures 4a,b and 5, the electron densities of both the lone pair orbital n and the antibonding π* orbital are distributed mainly on the carbonyl group of the amide. Most of the electron density in the n orbital is located on the oxygen, while in the π* orbital most of the electron density is located on the carbonyl carbon. The nonbonding orbital πₐ has a nodal plane on the carbonyl carbon atom. Therefore, the electronic density of the

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**Note:** The page contains a table and a figure, which are not visually represented here. The textual content discusses the electronic structure and properties of amides in various solvent environments, focusing on the vertical excitation energies and their dependencies on the solvent. It also contrasts the computational methods used, such as CIS and EOM-CC, and their predictions against experimental data.
Table 2. $\omega_2(\pi_{nb} \rightarrow \pi^*)$ Vertical Excitation Energies (eV) for HCONH$_2$:n(H$_2$O) and NMA:n(H$_2$O), $n = 0$–3, with the cc-pVDZ Basis Set Using the MP2/6-311++G(2d,2p) Geometry; the Vertical Excitation Energy Differences between the Amide and Amide/Water Complex Are Provided in Parentheses; a and b Refer to Different Isomers of the Complexes (See Figures 1 and 2)

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<th></th>
<th>CIS</th>
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<th>CR-EOMCCSD(T)</th>
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<td>NMA</td>
<td>8.94(0.00)</td>
<td>7.68(0.00)</td>
<td>7.17(0.00)</td>
<td>7.57(0.00)</td>
<td>6.81$^3$</td>
</tr>
<tr>
<td>NMA:1H$_2$Oa</td>
<td>8.96(0.03)</td>
<td>7.70(0.01)</td>
<td>7.23(0.05)</td>
<td>7.72(0.15)</td>
<td></td>
</tr>
<tr>
<td>NMA:1H$_2$Ob</td>
<td>8.87(0.07)</td>
<td>7.64(0.04)</td>
<td>7.15(0.02)</td>
<td>7.47(0.10)</td>
<td></td>
</tr>
<tr>
<td>NMA:2H$_2$Oa</td>
<td>8.89(0.04)</td>
<td>7.58(0.10)</td>
<td>7.08(0.09)</td>
<td>7.54(0.03)</td>
<td></td>
</tr>
<tr>
<td>NMA:2H$_2$Ob</td>
<td>8.88(0.05)</td>
<td>7.63(0.05)</td>
<td>7.14(0.03)</td>
<td>7.56(0.01)</td>
<td></td>
</tr>
<tr>
<td>NMA:3H$_2$Oa</td>
<td>8.84(0.10)</td>
<td>7.50(0.19)</td>
<td>6.99(0.18)</td>
<td>7.54(0.03)</td>
<td></td>
</tr>
<tr>
<td>NMA:3H$_2$Ob</td>
<td>8.83(0.11)</td>
<td>7.54(0.14)</td>
<td>7.05(0.13)</td>
<td>7.56(0.01)</td>
<td></td>
</tr>
</tbody>
</table>

π$_{nb}$ orbital is primarily on the nitrogen atom and on the oxygen atom.

As illustrated in Figure 6, the schematic energy level diagrams are designed for the solvent effects on the vertical excitations using two possible interactions (interaction type I and interaction type II), of water with amides. Figure 7 shows the configuration (snapshot) of HCONH$_2$ in EFP1 water during a MD simulation.

Table 3. Average Vertical Excitation Energies of $\omega_1$ and $\omega_2$ Are Given in eV for HCONH$_2$ and NMA at the TD-PBE0/cc-pVDZ Level of Theory

<table>
<thead>
<tr>
<th></th>
<th>$\omega_1(n \rightarrow \pi^*)$</th>
<th>$\omega_2(\pi_{nb} \rightarrow \pi^*)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCONH$_2$</td>
<td>5.75</td>
<td>8.74</td>
</tr>
<tr>
<td>HCONH$_2$:100EFP1</td>
<td>6.08</td>
<td>8.31</td>
</tr>
<tr>
<td>QM/EFP1 shift</td>
<td>0.33</td>
<td>−0.43</td>
</tr>
<tr>
<td>experimental shift</td>
<td>0.27$^a$</td>
<td>−0.50$^b$</td>
</tr>
<tr>
<td>NMA</td>
<td>5.74</td>
<td>7.52</td>
</tr>
<tr>
<td>NMA:100EFP1</td>
<td>6.15</td>
<td>7.51</td>
</tr>
<tr>
<td>QM/EFP1 shift</td>
<td>0.42</td>
<td>−0.01</td>
</tr>
<tr>
<td>experimental shift</td>
<td>0.39$^c$</td>
<td>−0.07$^d$</td>
</tr>
</tbody>
</table>

$^a$ Obtained using the $n \rightarrow \pi^*$ absorption spectra of HCONH$_2$ in gas phase (5.58 eV)$^3$ and HCONH$_2$ in aqueous solution (5.85 eV)$^4$.

$^b$ Obtained using the $\pi_{nb} \rightarrow \pi^*$ absorption spectra of HCONH$_2$ in gas phase (7.31 eV)$^5$ and HCONH$_2$ in acetonitrile solution (6.81 eV)$^5$.

$^c$ Obtained using the $n \rightarrow \pi^*$ absorption spectra of NMA in cyclohexane (5.46 eV)$^{15}$ and NMA in aqueous solution (5.85 eV)$^4$.

$^d$ Obtained using the $\pi_{nb} \rightarrow \pi^*$ absorption spectra of NMA in cyclohexane (6.74 eV)$^3$ and NMA in aqueous solution (6.67 eV)$^4$. MD simulation. This shows how the EFP1 water molecules spherically surround the solute molecule. One can determine the optimum number of EFP1 waters that are required for solvation by successively adding EFP1 water molecules and calculating the properties. The solutes HCONH$_2$ and NMA (not shown) are relatively small, so 100 EFP1 water molecules are sufficient for complete solvation. The structural pattern of water molecules surrounding the solutes shown in Figure 7 is close to that of the solute:n(H$_2$O) in gas phase shown in Figures 1 and 2.

Interaction Type I. In Figure 6a, one of the hydrogen atoms in a water molecule involves a hydrogen bond interaction with the amide carbonyl oxygen. In this interaction type, the water oxygen atom donates the hydrogen to the carbonyl oxygen acting as the hydrogen acceptor. Both the occupied (n and π$_{nb}$) and virtual (π*) amide orbitals are stabilized due to the favorable electronic interaction between the partially positive water hydrogen atom and the electronic density on the carbonyl group. However, one can deduce that the amide n orbital would be more stabilized than the π* orbital since the n orbital has more electron density localized on the carbonyl group.
oxygen than does the \( \pi^* \) orbital. Therefore, the \( n-\pi^* \) energy gap increases in the presence of the water, relative to the isolated amide molecule. This interaction results in a blue-shifted \( n \rightarrow \pi^* \) vertical excitation. However, the amide occupied \( \pi_{ab} \) orbital will be slightly less stabilized than that of the \( \pi^* \) orbital because the \( \pi_{ab} \) electron density is distributed between the nitrogen and oxygen atoms. Therefore, the \( \pi_{ab}-\pi^* \) energy gap slightly decreases in the presence of a water molecule, relative to the isolated amide molecule, giving rise to a red-shift upon solvation.

**Interaction Type II.** In Figure 6b, a water oxygen atom forms a hydrogen bond interaction with an amide \((N-H)\) hydrogen atom. In this interaction type, the water oxygen atom is the hydrogen atom acceptor, and the \(N-H\) amide group is the hydrogen donor. Since the electron densities on the occupied orbitals \((n\) and \(\pi_{ab}\)) and the virtual \(\pi^*\) orbital cause a destabilizing electronic interaction between the partially negative water oxygen atom and the partially negative amide nitrogen atom, each of the \(\pi_{ab}\), \(n\), and the \(\pi^*\) orbital energies increase in the presence of a water molecule, relative to an isolated amide. One can deduce that the \(\pi_{ab}\) orbital will be destabilized more than the \(\pi^*\) due to the larger electron density of the \(\pi_{ab}\) localized on the amide nitrogen atom than that of \(\pi^*\) orbital. Therefore, the \(\pi_{ab}-\pi^*\) energy gap decreases with a water present, relative to the isolated amide molecule. This gives rise to a red-shifted \(\pi_{ab} \rightarrow \pi^*\) vertical excitation.

In summary, the blue (or red)-shift vertical excitations are mainly due to the different electron density distributions between the \(n\) (or \(\pi_{ab}\)) and the \(\pi^*\) orbitals of amides that interact with different solvent configurations via hydrogen bonding.
IV. CONCLUSIONS

Four different levels of theory CIS, EOM-CCSD, CR-EOMCCSD(T), and TDDFT (PBE0 functional) with cc-pVDZ basis set are used to study the explicit solvent effect on the electronic spectra for the HCONH$_2$·n(H$_2$O) and NMA·n(H$_2$O) complexes (n = 1–3). These computational results provide the qualitative interpretation of the solvent effects on the electronic absorption spectra of amides. In addition, the simulated electronic spectra are calculated through the QM/EFP1MD simulation combined with TDDFT/EFP1. The calculated water solvent effect on the n → $\pi^*$ and n_d → $\pi^*$ vertical excitations exhibits quantitative blue- and red-shifts in the amides, which are consistent with the experimental observation.

The schematic energy level diagrams (Figure 6) are used to understand the solvent induced blue- and red-shift vertical excitation of the amides. In summary, the physical origin of the solvent effect on n → $\pi^*$ (blue-shift) and n_d → $\pi^*$ (red-shift) vertical excitations of amides could be understood as to how the energies of occupied molecular orbitals are changed relative to that of the $\pi^*$ due to stabilizing (or destabilizing) electronic interaction of water with the electronic densities of the amides.

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Notes
The authors declare no competing financial interest.

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REFERENCES


