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Kinetics of Exchange Between Zero-, One-, and Two-Hydrogen-Bonded States of Methyl and Ethyl Acetate in Methanol

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Abstract

It has recently been shown that the ester carbonyl stretching vibration can be used as a sensitive probe of local electrostatic field in molecular systems. To further characterize this vibrational probe and extend its potential applications, we studied the kinetics of chemical exchange between differently hydrogen-bonded (H-bonded) ester carbonyl groups of methyl acetate (MA) and ethyl acetate (EA) in methanol. We found that while both MA and EA can form zero, one, or two H-bonds with the solvent, the population of the 2hb state in MA is significantly smaller than that in EA. Using a combination of linear and non-linear infrared measurements and numerical simulations, we further determined the rate constants for the exchange between these differently H-bonded states. We found that for MA the chemical exchange reaction between the two dominant states (i.e., 0hb and 1hb states) has a relaxation rate constant of 0.14 ps⁻¹, whereas for EA the three-state chemical exchange reaction occurs in a predominantly sequential manner with the following relaxation rate constants: 0.11 ps⁻¹ for exchange between 0hb and 1hb states, 0.12 ps⁻¹ for exchange between 1hb and 2hb states.

Keywords

Chemical exchange; Hydrogen bond; Solvation dynamics; 2D IR; Ester stretching vibration

1. INTRODUCTION

A hydrogen bond (H bond) is not only an energetic and structural determinant of biological molecules, but can also play a key role in many biological functions. For example, a H-bond network involving several bound water molecules in bacteriorhodopsin is responsible for pumping protons across a membrane.¹ Similarly, a H-bonded water wire in the influenza A virus M2 channel is believed to facilitate conduction of protons across the viral membrane envelop when the channel is activated upon endosomal acidification.^{2–3} In addition, various H-bond networks, especially those involving water, are commonly found at the active or binding sites of proteins.^{4–5} Since a H-bond, unlike a covalent bond, is an intrinsically weak

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interaction and hence can break and form on an ultrafast timescale (within picoseconds) in the condensed phase, steady-state and transient infrared (IR) spectroscopy is often a preferred method to study H-bonding dynamics.^{6–15} In order to probe the H-bonding dynamics of proteins in a site-specific manner, however, a local IR probe is needed.^{16–19} Recently, Pazos *et al.* showed that the ester C=O stretching vibration of L-aspartic acid 4-methyl ester (D_M) and L-glutamic acid 5-methyl ester (E_M) is a convenient and sensitive probe in this regard, as the frequency of this vibration shows a linear correlation with the number of H-bonds that the ester carbonyl forms.²⁰ To further characterize how this probe interacts with protic solvents, herein we study the H-bond dynamics of two esters, methyl acetate (MA), which is the sidechain mimic of D_M , and ethyl acetate (EA) in methanol.

The carbonyl moieties of MA and EA can populate zero-, one-, and two-H-bonded states (herein after referred to as 0hb, 1hb and 2hb) in methanol.²¹ Thus, the characterization of the underlying H-bonding dynamics of these states will not only provide quantitative information needed to help interpret results obtained with more complex molecular systems (e.g., proteins), but can also yield new insights into solvation dynamics of small molecules, a subject of extensive experimental and theoretical investigations.^{22–24} In particular, we focus on determining the chemical exchange kinetics between these differently H-bonded states. While many previous studies have employed non-linear IR spectroscopy to investigate the kinetics of various ultrafast chemical exchange processes, they have focused primarily on two-state systems.^{8,25–31} For example, using two-dimensional (2D) IR spectroscopy Hochstrasser and coworkers²⁵ have studied the exchange kinetics between the H-bonded and free states of CH_3CN in methanol, while Fayer and coworkers²⁶ have investigated the equilibrium dynamics of phenol complexation with benzene in solution, where the phenol is either weakly-bound to benzene or is in an unbound state. Thus, studying systems with increased complexity that involve more than one dynamic equilibrium is not only a natural extension of these previous studies, but can also help refine the analytical procedures used to extract kinetic information from congested 2D IR spectra.³²

The vibrational relaxation dynamics of the carbonyl stretching mode of MA in methanol have been studied by Tominaga and coworkers.³³ Their results indicate that H-bond formation with the solvent can lead to a significant decrease in the vibrational lifetime of this mode, which is in agreement with the current study. In addition, Righini and coworkers³⁴ have used *ab initio* molecular dynamics simulations to show that such H-bonds have a lifetime of 0.5 to 2 ps. Here, we expand the scope of these previous studies by further characterizing the chemical exchange kinetics between differently H-bonded states of MA and EA molecules in methanol under equilibrium conditions. We anticipate that our results described below are interesting from the perspective of understanding three-state chemical exchange reactions in small molecular systems and advancing the application of ester carbonyl vibrational probes.

2. EXPERIMENTAL SECTION

Sample Preparation

A solution of 0.1 M of either MA or EA in dehydrated methanol (Acros Organics) was freshly prepared before each measurement and diluted as needed. The solution was placed between two 2 mm CaF_2 windows separated by a 50 μm spacer.

Linear IR Measurements

Linear infrared absorption spectra were collected on a Thermo Nicolet 6700 FTIR spectrometer at the resolution of 0.25 cm^{-1} at room temperature. For all the spectra shown, a solvent background has been subtracted. In addition, for both MA and EA, a series of FTIR measurements indicated that the carbonyl absorption lineshape does not change in the concentration range of 20–100 mM.

Time-Resolved IR Measurements

The experimental setup for nonlinear and time-resolved IR spectroscopic measurements has been described in detail elsewhere.³⁵ Briefly, ultrashort IR pulses ($\omega_0 = 1730\text{ cm}^{-1}$, $\omega = 200\text{ cm}^{-1}$, $\tau = 75\text{ fs}$, and $\varepsilon = 300\text{ nJ}$) were generated via a home-built setup involving an optical parametric amplifier and a difference frequency generation stage pumped by a commercial regenerative amplifier (Coherent, Libra). Polarization of the electric field of each pulse was controlled independently with a combination of zero-order waveplates (Karl Lambrecht) and polarizers (Specac) placed as a last optical element before the sample to avoid any potential depolarization of light upon reflection.^{36–37} In the pump-probe experiments the intensity of the probe pulse was attenuated to 5% of the pump pulse intensity. The signal was collected on a 64 elements liquid nitrogen-cooled MCT array detector (Infrared Associates) coupled to a spectrograph equipped with a 50 gr/mm grating. In the two-dimensional experiments, which used the BOXCARS configuration, the signal was heterodyned with the local oscillator pulse, which preceded the signal by 1 ps. The coherence time intervals scanned in all of the 2D experiments were from -6 to 6 ps with 4 fs steps. The rephasing and non-rephasing spectra were collected during separate scans and the absorptive spectra were obtained by adding the two, while matching their projections to the corresponding pump-probe spectra.³⁸ Note, that in order to match a traditional notation used in 2D-IR spectroscopy, both pump-probe and 2D-IR spectra are presented with ground state bleach and stimulated emission signals having positive amplitude.

3. RESULTS AND DISCUSSION

Solvent-solute interaction is a widely studied topic in chemistry and physics, as it plays a critical role in determining many of the chemical and physical properties of the solute. In order to arrive at a molecular-level understanding of a specific solvent-solute system, however, one needs to characterize not only the thermodynamic but also the dynamic aspect of the underlying interactions. This is because, even under equilibrium conditions, individual solute molecules can experience various environmental fluctuations as well as transitions from one thermodynamic state to another. Herein, we use linear and 2D IR spectroscopy, in conjunction with theoretical modeling, to characterize the vibrational

dynamics of the C=O stretching vibrations of two esters (MA and EA) in methanol and also the dynamics of the H-bonds formed between this vibrator and the solvent.

Linear IR Spectra

As shown (Figure 1), the FTIR spectra of MA and EA in the ester C=O stretching frequency region consist of three overlapping but resolvable bands, arising from 0hb, 1hb, and 2hb species.²¹ Interestingly, these results indicate that changing the methyl group to a larger ethyl group is sufficient to induce a change in the relative populations of these species and also their corresponding carbonyl stretching frequencies. To better quantify these changes, we fit each spectrum to a sum of three Lorentzian functions and the resulting fitting parameters are listed in Table 1. In comparison to those of MA, the C=O stretching frequencies of the 0hb and 1hb species of EA are red-shifted by approximately 5.7 and 3.2 cm^{-1} , respectively, whereas the frequency of the 2hb species is blue-shifted by approximately 6.7 cm^{-1} . In addition, the percentage (ca. 40%) of the 2hb species of EA, calculated using its band area, is significantly increased from that (<5%) of MA. These spectroscopic differences can be qualitatively explained by the differences in the molecular properties of the methyl and ethyl groups. Because an ethyl group is more strongly electron-donating than a methyl group, the ester oxygen in EA should have a higher electron density, compared to that of MA. The relatively higher electron density is expected to lengthen and weaken the C=O bond and, as a result, cause the C=O stretching frequency to shift to a lower wavenumber (for the 0hb species), as observed. For the H-bonded species, besides this electron-withdrawing effect, we also need to consider the size difference between the methyl and ethyl groups. As shown (Figure 2a), there are two possibilities to form one H-bond between the ester carbonyl and a methanol molecule.³⁴ For MA, both configurations are likely to be (nearly) equally populated, whereas for EA, favorable interactions between the solvent's methyl group and the larger ethyl group could preferentially stabilize the β configuration in Figure 2a. This notion is consistent with the fact that the relative population of the 2hb species of EA is larger than that of MA, as the additional stabilizing interaction in EA can help compensate the entropic loss associated with the formation of two H-bonds. A simple calculation using the band areas of the 1hb and 2hb species to estimate the corresponding equilibrium constant suggests that the increase of the 2hb population of EA requires an additional stabilizing energy of approximately 1.4 kcal/mol. Further evidence supporting this picture is that the frequency of the 2hb species of EA is blue-shifted from that of MA, and that the corresponding red-shift (i.e., 3.2 cm^{-1}) of the 1hb species is less than that (i.e., 5.7 cm^{-1}) of the 0hb species, as the aforementioned interactions between the methyl and ethyl groups will likely distort the respective H-bond (i.e., β configuration in Figure 2a).

Finally, to determine how H-bond formation affects the oscillator strength (μ) of the C=O stretching vibration, we carried out concentration dependent FTIR measurements of MA and EA in methanol (Figure 1c and 1d). As expected, the integrated areas of all IR bands show a linear dependence on solute concentration. However, for MA the slope of the straight line, which is proportional to μ^2 , increases with the number of H-bonds. As indicated (Table 1), the trend is in qualitative agreement with a previous theoretical study,³⁴ which showed that upon H-bond formation the transition dipole moment of the C=O stretching vibration of MA

is increased.³⁹ For EA, the transition dipole moments were found to be similar for the 0hb and 1hb species, whereas formation of two H-bonds slightly decreases the transition dipole moment (see Table 1).

Vibrational Lifetime and Rotational Diffusion Constant of MA

To determine the lifetimes of the ester C=O stretching vibrations of MA and EA in methanol, we carried out frequency-resolved pump-probe measurements under magic-angle polarization conditions. As shown (Figure 3a), the time-resolved spectra of MA consist of, as expected, mainly signals arising from the 0hb and 1hb species, and exhibit frequency-dependent decay kinetics. For example, the transient signal at $\omega=1748\text{ cm}^{-1}$, which arises mostly from ground state bleaching of the 0hb species, has a decay time constant of about 4 ps, whereas the signal at $\omega=1710\text{ cm}^{-1}$, which corresponds to mostly the excited state absorption of the 1hb species (see below), decays in about 1 ps. These results are consistent with a previous study³³ indicating that H-bond formation with solvent can significantly affect the vibrational lifetime of this vibrator.

To provide a more accurate assessment of the C=O stretching vibrational lifetimes of these differently H-bounded species, we further analyzed the time-resolved spectra using the singular value decomposition (SVD) method. Following the approach used in similar applications,^{40–41} we decomposed the time-resolved spectra, $S(\omega, T)$, into a set of basis spectra via $S(\omega, T) = U(T)\sigma R^\dagger V^\dagger(\omega)$, where σ is a diagonal singular-value matrix, $V(\omega)$ is a frequency-dependent matrix composed of the eigenstates of $S(\omega, T)$, $U(T)$ is a time-dependent matrix composed of the corresponding time evolution traces, and R is a unitary operator, which is used to transform the SVD results to a proper basis for further interpretation. Because the signal arising from the 2hb species is negligible, we chose to use a 2×2 rotation matrix $R(\theta)$ to act on the two eigenstates of $S(\omega, T)$, namely $V_i(\omega)$ and $V_j(\omega)$, that have the highest weights σ_{ii} and σ_{jj} . Since the vibrational lifetime of the 0hb species is significantly longer than that of the 1hb species, we can assume that the transient spectra collected at longer delay times (e.g., 5 ps) arise mostly from the 0hb species. Thus, the rotation angle θ was determined by fitting the high-frequency principal component (i.e., the one corresponding to the transient spectrum of the 0hb species) as represented in the new basis $\tilde{V}(\omega, \theta) = R(\theta)V^\dagger(\omega)$ to the normalized time-resolved spectrum obtained at 5 ps. As shown (Figure 3b), excellent match was found between the spectrum at 5 ps (black line) and decomposed principal component representing 0hb species (blue line), indicating that the SVD analysis adequately captures the spectral evolutions of the 1hb and 0hb species.⁴¹

As expected (Figure 3c), the normalized time profiles of the two spectral principal components, which were obtained from the columns of the matrix $\tilde{U}(T) = U(T)\sigma R^\dagger(\theta)$, exhibit different decay kinetics. More specifically, the high-frequency component, which is associated with the 0hb species, follows single-exponential decay with a time constant of 4.0 ps. On the other hand, the decay of the low-frequency component, which arises from the 1hb species, cannot be described satisfactorily by a single-exponential function; instead, it can be fit by a bi-exponential function with the following time constants (relative amplitudes): 0.4 ps (0.4) and 1.7 ps (0.6). Interestingly, a previous study⁴² found that the vibrational relaxation kinetics of the carbonyl stretching mode of MA in CCl_4 also occur in a bi-

exponential manner and attributed this phenomenon to the solvent memory effect. In the current case, the bi-exponential decay kinetics can be potentially caused by the dynamic exchange between the 0hb and 1hb species. However, as shown below, this chemical exchange process takes place on a much slower timescale, making it unlikely. While further studies are required to determine the molecular origin of this bi-exponential relaxation behavior, one possibility is that the fast component (~ 0.4 ps) is reflective of a rapid chemical exchange between the two aforementioned conformers of the 1hb species (Figure 2a), and the other is that the excited vibrational state is in dynamic equilibrium with a dark state.⁴³ In addition, both principal components decay to essentially zero at long delay times (i.e., >10 ps), suggesting that intermolecular excitation transfer^{44–46} and overall heating effects are negligible in the present case.

As shown (Figure 3d), the anisotropy of the pump-probe signal, $r(t)$, measured at 1748 cm^{-1} , follows a single-exponential decay with a time constant of 1.0 ps. This result indicates that, when not H-bonded to methanol, MA has a rotational diffusion constant of $D_{\text{MA}} = 0.17\text{ ps}^{-1}$, if a spherical rotor model is assumed. Formation of H-bonds with solvent is expected to slow down the rotational diffusion of the solute.⁴⁷ However, owing to the spectral congestion, a direct experimental assessment of the anisotropy decay of the 1hb species is challenging. Therefore, in the subsequent analyses we use the value of 0.17 ps^{-1} as an upper limit for the rotational diffusion constant of the 1hb species.

Vibrational Lifetime and Rotational Diffusion Constant of EA

As expected, the time-resolved spectra of EA contain more spectral features than those of MA (Figure 4a). In addition, the transient signal at $\omega = 1745\text{ cm}^{-1}$, which arises predominantly from the 0hb species, has a decay time constant of approximately 2.8 ps, whereas that at $\omega = 1695\text{ cm}^{-1}$, which reflects mostly the decay of the H-bonded species, has a time constant of approximately 1.1 ps. Following the protocols outlined above, we also carried out SVD analysis to better assess these time-resolved spectra. However, due to the smaller difference in the vibrational lifetimes of differently H-bonded species of EA, the transformation matrix $R(\theta, \phi, \varphi)$ cannot be simply determined as was done in the case of MA. To circumvent this difficulty, we took advantage of the fact that the underlying chemical exchanges processes are relatively slow (see below) and resorted to the 2D IR spectra obtained at early waiting times (see below) to determine this reference. Specifically, we used the 2D IR spectrum collected at a waiting time of $T = 0.25\text{ ps}$ to generate the reference spectrum used to determine $R(\theta, \phi, \varphi)$, which corresponds to a trace along the probe frequency axis (ω_p) at a pump frequency corresponding to the excitation of the 0hb species ($\omega_\tau = \omega_{0hb}$).

As shown (Figure 4b), the SVD analysis yielded three principal components, corresponding to the time-resolved spectra of the 0hb, 1hb, and 2hb species. It is clear that the principal component that represents the 0hb species matches well with its transient spectrum determined from the 2D IR measurement, indicating that the corresponding SVD spectral decompositions are adequate. As shown (Figure 4c), the decay of the principal component corresponding to the 0hb species follows a single-exponential function with a time constant of 2.8 ps. Similar to that observed for MA, the decays of the components corresponding to

the H-bonded species can be described by a double-exponential function with the following time constants (relative amplitudes): 0.5 ps (0.7) and 2.0 ps (0.3) for 1hb species; 0.6 ps (0.7) and 1.9 ps (0.3) for 2hb species.

As done in the case of MA, the rotational dynamics of the 0hb EA species was assessed by fitting the anisotropy decay at 1745 cm^{-1} to a single-exponential function (Figure 4d), which yielded a rotational time constant of 1.6 ps or a rotational diffusion constant of $D_{\text{EA}} = 0.1\text{ ps}^{-1}$, indicating that rotational diffusion of EA molecule is slower than that of MA.

Chemical Exchange Kinetics of MA

The ultrafast exchange kinetics between different chemical or molecular states can be directly assessed by 2D IR spectroscopy if the exchange process of interest results in well-isolated cross peaks in the 2D spectra.^{26, 32} In the current case, however, due to spectral congestion, significant difference in the vibrational lifetimes of different states, and relatively slow exchange rate, the spectral signature associated with exchange between differently H-bonded states is manifested only as a change in the spectral lineshape of the diagonal peak of the longer-lived species. Therefore, in order to determine the underlying exchange kinetics, one must invoke theoretical modeling.

As shown (Figure 5a), the 2D IR spectra of MA collected under magic-angle polarization conditions indicate that at earlier waiting times (e.g., $T = 0.3\text{ ps}$) two positive diagonal peaks, centered at $\omega_{\tau} = 1748\text{ cm}^{-1}$ and $\omega_{\tau} = 1730\text{ cm}^{-1}$, which correspond to the 0hb ($S_{0\text{hb},0\text{hb}}^{\text{MA}}$), and 1hb ($S_{1\text{hb},1\text{hb}}^{\text{MA}}$) species, respectively, are clearly observable. On the other hand, due to the much smaller population, the 2D spectral signatures arising from the 2hb species are not clearly detectable. Thus, in the following analysis we will ignore its contribution and only consider the exchange process between the 0hb and 1hb species. In addition, the anharmonicity values obtained from these 2D IR results (Table 1) are consistent with previous studies.^{33, 39, 42}

The conversion of 1hb species to 0hb species should yield a positive cross peak centered at $\omega_{\tau} = 1730\text{ cm}^{-1}$ and $\omega_t = 1748\text{ cm}^{-1}$ ($S_{1\text{hb},0\text{hb}}^{\text{MA}}$). However, due to the aforementioned reasons, it only results in a build-up as a shoulder in the positive diagonal peak (Figure 5c). For the same reasons, the reverse process, i.e., 1hb formation, does not produce a distinct cross peak either in the 2D spectra.

In order to estimate the exchange rate between the 1hb and 0hb species, we carried out numerical simulations of the 2D IR spectra using third-order response function theory,^{48–49} as the decay rates of the corresponding diagonal peaks contain important information about the exchange kinetics.³² First, we used IR lineshape analysis to estimate the parameters of the underlying frequency fluctuation correlation function, $\xi(t)$, of the respective excited vibrational state. Because the 2D lineshapes of these vibrational transitions do not show significant spectral diffusion or inhomogeneous broadening, which could be quantified by tracking the evolution of the 2D peak lineshape, we assumed that $\xi(t)$ follows Bloch dynamics, i.e., $\xi(t) = \Gamma t + 0.5\sigma^2 t^2$. The appearance of the shoulder in $S_{0\text{hb},0\text{hb}}^{\text{MA}}(T)$ peak likely arises from the $S_{1\text{hb},0\text{hb}}^{\text{MA}}(T)$ cross-peak build-up but not from the spectral diffusion of

$S_{0hb,0hb}^{MA}(T)$. As shown (Figure 6a), we were able to satisfactorily describe the linear absorption spectrum of MA, which excludes the contribution from the 2hb species, using linear response functions and the experimentally determined vibrational lifetimes and rotational diffusion constants of the 0hb and 1hb species, along with those fitting parameters in Table 1.

Second, we estimated the exchange rates numerically by minimizing the total sum of the relative square differences between the peak volumes ($S_{0hb,0hb}^{MA}(T)$, $S_{1hb,1hb}^{MA}(T)$, and $S_{1hb,0hb}^{MA}(T)$), of the simulated and measured 2D IR spectra at each waiting time using the following kinetic model:

$$\dot{P}_{ii}(T) = -(k_{ii} + k_{ij}) P_{ii}(T) + k_{ji} P_{ij}(T) \quad (1)$$

$$\dot{P}_{ij}(T) = -(k_{jj} + k_{ji}) P_{ij}(T) + k_{ij} P_{ii}(T) \quad (2)$$

where the indices i and j represent either the 0hb or 1hb species. $P_{ii}(T)$ corresponds to the probability that state i at time $T = 0$ will remain in the same state at a later time T , while $P_{ij}(T)$ corresponds to the probability that state i at time $T = 0$ will be in state j at a later time T . In addition, k_{ii} (k_{jj}) correspond to the vibrational relaxation rate constant of state i (j) (as those given in Table 1), whereas k_{ij} (k_{ji}) corresponds to the rate constant of the process that converts state i (j) to j (i). Specifically, for various values of k_{ij} and k_{ji} (determined from k_{ij} using the respective equilibrium constant in Table 1), the above rate equations were solved numerically using the fourth-order Runge-Kutta propagation method, where the convergence of the solution was controlled by the comparison to the fifth-order solution. The relative populations determined from the linear IR spectrum (Table 1) were used as the initial conditions, and the time-dependent vibrational relaxation rates $k_{ii}(T)$ for the H-bonded molecules were found by numerical differentiation of the decay curves obtained from the SVD analysis of the pump-probe data (see Figure 3c). The resultant probabilities, $P_{ii}(T)$ and $P_{ij}(T)$, were then used as time-dependent multiplicative factors for the third-order response functions⁴⁸ to compute the waiting time dependent 2D spectra. The exchange dynamics during the coherence and detection time intervals were neglected.⁵⁰

As shown (Figure 7), the best fit yielded an exchange rate constant of

$k_{x01}^{MA} = k_{0hb,1hb}^{MA} + k_{1hb,0hb}^{MA} = 0.14 \text{ ps}^{-1}$. The 95% confidence interval was determined by applying the model comparison F-test to be between 0.08 ps^{-1} and 0.22 ps^{-1} . Furthermore, we found that the numerically simulated 2D IR spectra obtained using this chemical exchange rate are in close agreement with those measured experimentally (Figure 5). For instance, the simulated spectra reproduce the appearance of the shoulder in the diagonal peak as a manifestation of the chemical exchange between the 0hb and 1hb states of the MA molecule (Figure 5d). On the other hand, when this chemical exchange processes was excluded by setting $k_{x01}^{MA} = 0$, the simulated 2D IR spectra lack this feature. Thus, this comparison provides further validation of the simulation results.

Chemical Exchange Kinetics of EA

A series of 2D IR spectra of EA in methanol were collected for waiting times ranging from 0.25 to 8 ps. As shown (Figure 8a), unlike MA, the 2D IR spectrum of EA collected at $T = 0.25$ ps consists of three positive diagonal peaks at $\omega_{\tau} = 1744, 1727$, and 1716 cm^{-1} , corresponding to the 0hb ($S_{0\text{hb},0\text{hb}}^{\text{EA}}$), 1hb ($S_{1\text{hb},1\text{hb}}^{\text{EA}}$), and 2hb ($S_{2\text{hb},2\text{hb}}^{\text{EA}}$) molecules. This result is consistent with the linear IR measurement (Figure 1b) and also indicates that the fraction of the molecules in the 2hb state in EA is significantly larger than that in MA. The corresponding negative peaks appear at the anharmonically-shifted frequencies $\omega_{\tau-}$ and the estimated anharmonicity values are summarized in Table 1. As in the case of the MA, the diagonal peaks decay as a function of waiting time by two mechanisms: (1) vibrational relaxation, which is faster for the H-bonded molecules than for the 0hb ones, and (2) chemical exchange processes. In principle, all three chemical exchange reactions between the 0hb and H-bonded EA molecules can lead to the growth of cross-peaks in the 2D spectra measured at later waiting times. However, in the following analysis we will focus only on cross-peaks that appear in less congested regions of the 2D IR spectra, and, therefore, are easier to identify. These peaks include $S_{1\text{hb},0\text{hb}}^{\text{EA}}$, $S_{0\text{hb},1\text{hb}}^{\text{EA}}$, $S_{2\text{hb},1\text{hb}}^{\text{EA}}$, and $S_{2\text{hb},0\text{hb}}^{\text{EA}}$, which correspond to dissociation of a 1hb complex, formation of 1hb complex, dissociation of one of the H-bonds in a 2hb complex, and simultaneous dissociation of both H-bonds in a 2hb complex, respectively.

We first consider the cross-peak $S_{2\text{hb},0\text{hb}}^{\text{EA}}$, i.e. the chemical exchange between the 2hb and 0hb EA molecules. If the contribution of this exchange was significant, one would expect, in addition to the appearance of a positive peak centered at $\omega_{\tau} = 1716 \text{ cm}^{-1}$ and $\omega_t = 1747 \text{ cm}^{-1}$, a gradual build-up of a negative peak (i.e., the corresponding $v = 1$ to $v = 2$ transition) at $\omega_t = 1727 \text{ cm}^{-1}$. Therefore, this exchange process would result in a faster decay of the diagonal peak arising from the 2hb species (i.e., $S_{2\text{hb},2\text{hb}}^{\text{EA}}$) as the negative part of $S_{2\text{hb},0\text{hb}}^{\text{EA}}$ will interfere destructively with the positive part of $S_{2\text{hb},2\text{hb}}^{\text{EA}}$, and, eventually, at sufficiently long waiting times will overwhelm it. As indicated (Figures 7a and 7c), such effect is not observed in the experimental 2D IR data as they clearly show that the positive part of the $S_{2\text{hb},2\text{hb}}^{\text{EA}}$ peak is still present even at long waiting times. Therefore, in order to simplify the kinetic model, we assume that the chemical exchange process between the 2hb and 0hb molecules occurs on a timescale that is significantly slower than the time window of the experiment and set the corresponding rate constant, $k_{\text{X02}}^{\text{EA}}$, to 0. In addition, based on the linear IR measurements (Figure 1), an equilibrium constant ($K_{0\text{hb},1\text{hb}}^{\text{EA}}$) of 1 was used for this reaction in the following simulations.

The chemical exchange kinetics of EA was analyzed using the same approach as discussed above. First, we fit the linear absorption spectrum of EA using linear response theory (Figure 6b) and the resultant fitting parameters were listed in Table 1. Similar to that observed for MA, no measurable inhomogeneous contribution to $S_{0\text{hb},0\text{hb}}^{\text{EA}}$ lineshape was obtained. Second, we determined the chemical exchange rates by tracking the evolutions of the relevant peak volumes extracted from the waiting time dependent 2D IR spectra via

simulation of the corresponding 2D IR spectra. As shown (Figure 9a and b), the best fit to the kinetic model that includes exchanges between 0hb and 1hb and between 1hb and 2hb molecules yielded the least square values of $k_{x01}^{EA} = k_{0hb,1hb}^{EA} + k_{1hb,0hb}^{EA} = 0.11 \text{ ps}^{-1}$ and $k_{x12}^{EA} = k_{1hb,2hb}^{EA} + k_{2hb,1hb}^{EA} = 0.12 \text{ ps}^{-1}$, respectively. Figure 9c shows a two-dimensional map demonstrating the dependence of the sum of the weighted square distances between the experimental data and fits on the exchange rates. As indicated by the dash line in the figure, the 95% confidence intervals of these exchange rate constants are 0.05 ps^{-1} ; 0.15 ps^{-1} and 0.01 ps^{-1} ; 0.28 ps^{-1} , respectively. Furthermore, the 2D IR spectra simulated with these best-fit exchange rate constants are in good agreement with the experimental data (Figure 8b). Finally, a close comparison between the simulated and experimentally determined 2D IR spectra in the cross-peak regions (Figures 8c, 8d, and 8e) provided clear indication that the chemical exchange between the 1hb and 2hb EA molecules cannot be excluded.

Because H-bonding to the solvent plays a central role in many complex molecular systems, we anticipate that our results for the H-bond dynamics of ester groups in small molecules will be valuable for further successful applications of ester side-chains as vibrational probes of the solvation dynamics in proteins and peptides. Generally, different ester probe environments may give rise to different shifts of the corresponding transition frequencies, and different protein conformations give rise to the states with a different number of H-bonded molecules of the solvent. We anticipate that in such cases the ability to understand systems with multiple states involved in the chemical exchange reactions will be highly important.

4. CONCLUSIONS

In conclusion, we have studied the kinetics of chemical exchange reactions between differently H-bonded states of ester carbonyl groups of MA and EA in methanol. Our results show that the carbonyl of MA has a nearly equal probability of forming either 0hb or 1hb with methanol, while the fraction of molecules that simultaneously form two H bonds with the solvent is small. On the other hand, the probabilities of forming 0hb, 1hb, and 2hb between the EA carbonyl group and methanol are nearly equal. By numerically simulating the waiting time dependent 2D IR spectra, we have also determined the chemical exchange rates between differently H-bonded states. Specifically, we found that the conversion from the 1hb to 0hb state occurs with a rate constant of $(k_{1hb,0hb}^{MA})^{-1} = (14 \text{ ps})^{-1}$ for MA and $(k_{1hb,0hb}^{EA})^{-1} = (18 \text{ ps})^{-1}$ for EA, whereas the conversion from the 2hb to 1hb state for EA occurs with a rate constant of $(k_{2hb,1hb}^{EA})^{-1} = (17 \text{ ps})^{-1}$. These elementary exchange reactions proceed slower than the analogous reactions of the H-bond dissociation in *N*-methylacetamide (12 ps)⁸ and acetonitrile (8 ps)²⁵ in methanol. In addition, we found that among the different possible chemical exchange reaction pathways between the three differently H-bonded states of EA, the most probable is the sequential one. In other words, on the timescale of the present experiment, the probability for the transition between the 0hb and 2hb states without occupying the 1hb state transiently is relatively low.

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Figure 1.

Linear spectroscopy of MA and EA. Absorption spectra of 0.1 M MA (a) and EA (b) in methanol in the carbonyl stretching vibrational band region with the solvent background subtracted. Thick grey line – experimental data, thin black line – fit to Lorentzian lineshapes. In each case, the individual components shown in blue, green and red represent the high-, middle- and low-frequency conformations of the molecule, or 0hb, 1hb and 2hb states, respectively. The integrated areas (open circles) of these Lorentzian components obtained for the 0hb, 1hb, and 2hb states for different solute concentrations are given in (c) for MA and (d) for EA. Solid lines of matching colors show linear fits to the experimental data points. For MA, we did not include the 2hb state because of its relatively rare occurrence.

Figure 2.

Schemes representing the chemical exchange processes discussed in the text. (a) Dynamic equilibrium between the states α and β involving one H-bonded solvent molecule. Here R stands for either methyl or ethyl group. (b) Equilibrium between the states involving different number of H-bonded solvent molecules. Notation of rate constants determined in the present work is indicated.

Figure 3.

Frequency-resolved pump-probe spectroscopy of MA in methanol. (a) Normalized pump-probe signal as a function of waiting time. (b) Normalized spectral principal components obtained with the singular value decomposition method. Blue and green lines are the principal components involving high-frequency transitions (0hb) and low-frequency transitions (1hb), respectively. Purple and black lines are the non-decomposed spectra collected at $T = 0.25$ ps and 5 ps, respectively. Black line is in a perfect overlap with the blue one (see text for details). (c) Time profiles of the corresponding high-frequency (blue circles) and low-frequency (green circles) components as shown in (b). Black lines show a single-exponential and double-exponential fits respectively (see text for details). (d) Polarization anisotropy measured at $\omega = 1748$ cm⁻¹, representing $\nu = 0$ to $\nu = 1$ transition of the 0hb molecules.

Figure 4.

Frequency-resolved pump-probe spectroscopy of EA in methanol. (a) Normalized pump-probe signal as a function of waiting time. (b) Normalized spectral principal components obtained with the singular value decomposition method. Blue, green, and red lines correspond to principal components representing 0hb, 1hb, and 2hb species, respectively. Black line shows a trace of the 2D spectrum at $T = 0.25$ ps along the probe frequency axis ω , taken at the pump frequency $\omega_p = 1745$ cm⁻¹. (c) Blue, green, and red circles - time profiles of the corresponding principal components as shown in (b) with matching colors extracted with SVD method. Black lines show a single-exponential and double-exponential fits respectively (see text for details). (d) Polarization anisotropy measured at $\omega = 1745$ cm⁻¹, representing $v = 0$ to $v = 1$ transition of the 0hb molecules.

Figure 5.

2D-IR spectroscopy of MA in methanol. (a) Series of the 2D spectra collected at the waiting times as indicated on top of the panels. (b) Numerically simulated 2D spectra with third-order response functions and chemical exchange rate of $k_{x01}^{\text{MA}} = 0.14 \text{ ps}^{-1}$. (c) Cross-peak region of the experimentally measured spectra in (a). This cross-peak indicates chemical exchange between the 1hb and 0hb molecules. (d) Cross-peak region of the numerically simulated spectra in (b). (e) Same as in (d) but with chemical exchange excluded from the simulations, by setting $k_{x01}^{\text{MA}} = 0$. All spectral amplitudes are normalized to a maximum value of the positive peak.

Figure 6.

Linear response functions model absorption lineshapes. The model includes 0hb, and 1hb states for the case of MA (a) and 0hb, 1hb, and 2hb states for the case of EA (b). Thick grey line – experimental data with the solvent background subtracted, thin black line – results of the fit to the response-function-based model. The lineshape parameters obtained from the fit are summarized in Table 1.

Figure 7.

Chemical exchange kinetics of MA in methanol. (a) Normalized waiting time dependence of the volumes of the 2D spectral peaks of MA as in Figure 5: black circles – diagonal peak $S_{0hb,0hb}^{MA}$; blue circles – diagonal peak $S_{1hb,1hb}^{MA}$; red circles - cross-peak $S_{1hb,0hb}^{MA}$. See text for the corresponding transition frequencies. Solid lines show results of the corresponding numerical simulations with $k_{X01}^{MA} = 0.14 \text{ ps}^{-1}$. (b) Sum of square distances between the experimental data shown in (a) and simulated results for varying values of k_{X01}^{MA} . The least squares value is obtained at $k_{X01}^{MA} = 0.14 \text{ ps}^{-1}$, dash line - 95% confidence level.

Figure 8.

2D-IR spectroscopy of EA acetate in methanol. (a) Series of the 2D spectra collected at the waiting times as indicated on top of the panels. (b) Numerically simulated 2D spectra with the third-order response functions and chemical exchange rates of $k_{x01}^{\text{EA}} = 0.11 \text{ ps}^{-1}$ and $k_{x12}^{\text{EA}} = 0.12 \text{ ps}^{-1}$ (c) Cross-peak region of the experimentally measured spectra in (a). This cross-peak indicates chemical exchange between the 2hb and 1hb molecules. (d) Cross-peak region of the numerically simulated spectra in (b). (e) Same as in (d), but with chemical exchange between 2hb and 1hb molecules excluded from the simulations, by setting $k_{x12}^{\text{EA}} = 0$, but keeping the exchange between 1hb and 0hb molecules at $k_{x01}^{\text{EA}} = 0.11 \text{ ps}^{-1}$. All spectral amplitudes are normalized to a maximum value of the positive peak.

Figure 9.

Chemical exchange kinetics of EA in methanol. (a) Normalized waiting time dependence of the volumes of the 2D spectral peaks of EA as in Figure 8: black circles – diagonal peak $S_{0hb,0hb}^{EA}$; blue circles – diagonal peak $S_{1hb,1hb}^{EA}$; red circles - cross-peak $S_{1hb,0hb}^{EA}$; green circles - cross-peak $S_{0hb,1hb}^{EA}$. Solid lines show results of the corresponding numerical simulations with $k_{X01}^{EA}=0.11$ ps⁻¹ and $k_{X12}^{EA}=0.12$ ps⁻¹. (b) Same as in (a): blue circles - diagonal peak $S_{2hb,2hb}^{EA}$; red circles - cross-peak $S_{2hb,1hb}^{EA}$. (c) Sum of square distances between the experimental data shown in (a) and simulated results for varying values of k_{X01}^{EA} and k_{X12}^{EA} . The least squares value is shown in black cross, dash line - the 95% confidence contour.

Table 1

Parameters of vibrational dynamics and chemical exchange kinetics of differently H-bonded states of MA and EA in methanol obtained from spectroscopic measurements and numerical simulations.

	MA			EA		
	0hb	1hb	0hb	1hb	2hb	
ω_0 , cm^{-1}	1748.4	1729.9	1742.7	1726.7	1713.8	
ν , cm^{-1}	20	15	20	30	20	
μ^2/μ_{0hb}^2	1.0	1.4	1.0	1.0	0.9	
$K_{0hb,1hb}$	1.1			1		
$K_{1hb,2hb}$	-			1		
$K_{2hb,0hb}$	-			1		
k_{X01} , ps^{-1}	0.14			0.11		
k_{X12} , ps^{-1}	-			0.12		
Vibrational and Rotational Relaxation						
a_1	1	0.4	1	0.7	0.7	
a_2	4	0.4	2.8	0.5	0.6	
a_2	-	0.6	-	0.3	0.3	
τ_2 , ps	-	1.7	-	2.0	1.9	
D , ps^{-1}	0.17			0.1		
$\xi(t) = \langle \delta\alpha(0)\delta\alpha(t) \rangle$						
Γ , ps^{-1}	0.8	0.5	0.7	0.3	0.3	
α , ps^{-1}	0	0.9	0.0	0.5	0.7	