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Article

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Negligible Isotopic Effect on Dissociation of Hydrogen Bonds

Chuanqi Ge[1,2]¶,Yuneng Shen[2,5]¶, Gang-Hua Deng[2], Yuhuan Tian[2], Dongqi Yu[1],

Xueming Yang[2], Kaijun Yuan[2]*, Junrong Zheng[2,3,4]*

[1]School of Physics and Electronic Technology, Liaoning Normal University, Dalian
116029, China

[2]State Key Laboratory of Molecular Reaction Dynamics, Dalian Institute of the
Chemical Physics, ChineseAcademy of Sciences, Dalian 116023, Liaoning, China

[3]Department of Chemistry, Rice University, Houston, Texas, USA

[4]College of Chemistry and Molecular Engineering, Beijing National Laboratory for
Molecular Sciences, Peking University, Beijing 100871, China

[5]University of the Chinese Academy of Sciences, Beijing 100049, China

¶The authors have equal contribution.

*To whom correspondence should be addressed:

kjyuan@dicp.ac.cn; junrong@rice.edu

Abstract

Isotopic effects on the formation and dissociation kinetics of hydrogen bonds are studied in real time with ultrafast chemical exchange spectroscopy. The dissociation time of hydrogen bond between phenol-OH and p-xylene (or mesitylene) is found to be identical to that between phenol-OD and p-xylene (or mesitylene) in the same solvents. The experimental results demonstrate that the isotope substitution (D for H) has negligible effects on the hydrogen bond kinetics. DFT calculations show that the isotope substitution doesn't significantly change the frequencies of vibrational modes that may be along the hydrogen bond formation and dissociation coordinate. The zero point energy differences of these modes between hydrogen bonds with OH and OD are too small to affect the activation energy of the hydrogen bond dissociation in a detectible way at room temperature.

1. Introduction

Hydrogen bonds are of fundamental importance in nature. It plays an important role in defining the three dimensional structures, dynamics, and functions of chemical and biochemical molecular systems.[1-6] Traditionally, hydrogen bonds exist between electronegative atoms (e.g., O, N, F and Cl) and H atoms covalently bound to similar electronegative atoms.[7] Recently this concept has been extended to unusual acceptors such as π systems which this work focuses on.[8] Most of these two types of hydrogen bonds are substantially weaker than a typical covalent bond and have a wide range of binding energies from about 4 to 40 kJ/mol.[9-11] Therefore, they can frequently dissociate and reform at room temperature (RT). This reversible nature of hydrogen-bond formation play a critical role in biological processes which depend upon hydrogen-bonding, such as DNA replication, protein folding, drug-receptor, and other recognition interactions.[4,11] To comprehensively understand their mechanisms involved in the dynamics, obtaining hydrogen-bond formation and dissociation rates is desired. Because of the advent of ultrafast IR techniques, researchers can measure these kinetic processes of relatively weak hydrogen bonds (<5 kcal/mol) at RT under thermal equilibrium conditions with adequate time resolution.[9,11-30] A series of studies on the lifetimes of hydrogen bonds between phenol-OD (and silanol-OD) and hydrogen bond acceptors using the method of ultrafast 2D-IR vibrational echo chemical exchange spectroscopy show that the dissociation rates of the weak hydrogen bonds are strongly correlated with their formation enthalpies[9,13-15,31,32], which can be described by an equation similar to the Arrhenius equation.

The majority of the studies mentioned above were performed on systems with deuterated hydrogen bonds (OD…acceptor).[9,13-15,32] Studies at the same quantitative level on regular hydrogen bond (OH…acceptor) dissociation kinetics have not been conducted. Though chemically very similar, deuterated and regular hydrogen bonds can have different dissociation kinetics. It is well known that many processes involving hydrogen bonds or the transfer of a proton have different kinetics if the proton is replaced by a deuterium. For example, the dissociation of C-H can be several times faster than that of C-D[33], and the vibrational relaxation of OD is much longer than that of OH in water solution.[34-36] If the zero point energies of vibrational modes associated with hydrogen bond dissociations are significantly affected by the D-H replacement, isotope effects observed in regular chemical reactions can also occur in hydrogen bonds.

In this work, we performed both experiments and ab initio calculations to study the isotope effects on hydrogen bond dissociation kinetics. Ultrafast chemical exchange spectroscopy was applied to monitor the real time formation and dissociation dynamics of both deuterated and regular hydrogen bonds. Ab initio calculations were performed to compute the binding energy, zero point energy, and normal mode analyses of the hydrogen bond systems. Both experimental and theoretical studies suggest that isotope effects at room temperature are negligible in these systems investigated: 0.6 wt% phenol or phenol-OD in the mixed p-xylene/CCl_4 (1:7 wt) solvent, 0.6 wt% phenol or phenol-OD in the mixed mesitylene/CCl_4 (1:7 wt) solvent. An issue needs to be clarified here. The donor/acceptor interaction of the π

H-bonds investigated here has two contributions: (1) the H-bond between H and the π electrons; and (2) the interaction between the lone electron pairs of oxygen atoms and the π electron orbitals. If the latter was dominant, our experimental results could not reflect the isotope effect of H-bond kinetics. Luckily, previous and current experiments have suggested that the interaction between the effect of lone electron pairs of oxygen atoms and the π electron orbitals on affecting the donor/acceptor dissociation/association kinetics is negligible, compared to that of the H-bond between H and the π electrons[13,14,37]. In a series of phenol/benzene, phenol/tolunene, phenol/p-xylene, and phenol/mesitylene complexes, the H-bond donor (phenol) is the same. The acceptors are different with more methyl groups adding to the benzene ring: benzene has no methyl group, toluene with one, p-xylene with two, and mesitylene with three. It is well known that the methyl group is electron donating, which can enhance the electronic density of the benzene ring and increase its H-bond accepting ability. On the other hand, more methyl groups must weaken the ability of the benzene orbitals accepting the lone electrons of oxygen of phenol because electrons repulse each other. If the interaction of benzene orbitals and the lone electrons of oxygen of phenol is dominant, one would observe that the dissociation is fastest in the phenol/mesitylene complex and slowest in the phenol/benzene complex in the order of phenol/mesitylene (fastest) >phenol/p-xylene > phenol/toluene > phenol/benzene (slowest). If the H-bond is dominant, the opposite trend would be observed. Experimentally, the dissociation of phenol/benzene is fastest and that of phenol/mesitylene is slowest with the dissociation time constants: 9ps (phenol/benzene), 15ps (phenol/tolunene), 22ps (phenol/p-xylene), and 31ps (phenol/mesitylene). The results indicate that the π H-bond dissociation/association kinetics is dominated by the H-bond and that of the interaction of benzene orbitals and the lone electrons of oxygen of phenol is negligible.

2. Experimental methods

The experimental setup has been described elsewhere.[38-42] Briefly, the experimental setup consisted of a Ti:Sapphire oscillator (~400 mw, ~800nm with a band width ~45 nm,<35 fs, ~76 MHz, LIGHTHOUSE PHOTONICS sprout combining QUANTRONIX Ti-Light), two Ti:Sapphire regenerative amplifiers and two optical parametric amplifier (OPA) systems. The oscillator pumps the two Ti:Sapphire regenerative amplifiers,90% power entering a picosecond amplifier(~3.5 W, ~800 nm with a band width ~0.6 nm, ~1.3 ps, 1 kHz, QUANTRONIX Integra-C) and 10% to a femtosecond amplifier (~3.5 W, ~800 nm with a band width ~26 nm, ~40 fs, 1 kHz, QUANTRONIX Integra-C) respectively. We use ~2.8Wof the picosecond amplifier to pump a picosecond OPA(TOPAS-800) plus non-collinear difference frequency generator (NDFG) system to producing ~1.4ps (vary from 1.0~1.5ps in different frequencies) mid-IR pulses with a bandwidth ~15cm^{-1} in a tunable frequency range from 500cm^{-1} to 4000cm^{-1} with energy1~40μJ/pulse at 1 KHz.We also use ~2.8Wof the femtosecond amplifier to pump another femtosecond OPA (TOPAS-Prime) and NDFG system producing ~140fs mid-IR pulses with a bandwidth ~200cm^{-1} in a tunable frequency range from 500cm^{-1} to 4000 cm^{-1} with energy1~40μJ/pulse at 1 KHz. In the 2D IR experiments, the ps IR pulse excites the vibrations of the molecules and its excitation power is adjusted based on need. The fs IR pulse is the probe beam. It is frequency resolved by a spectrograph and then is collected on a 2×32 pixel mercury cadmium telluride (MCT) detector (Infrared Associates)yielding the ω_m axis of a 2D spectrum. The optical resolution used was 4-7 cm^{-1} (depending on the used grating). Scanning the pump frequency yields the ω_τ axis of the spectrum. Two polarizers are inserted into the probe beam pathway, one is located immediately behind the sample to selectively measure the parallel or perpendicular polarized signal relative to the pump beam and the other is before the sample rotating the polarization of the probe pulse 45° with respect to that of the pump pulse. The entire system is computer controlled. The IR pump probe signal $P(t)$ is collected by measuring the transmission of the probe beam through the sample by chopping the pump beam at 500 Hz. For a given delay time t (the delay between the IR pump and the IR probe pulse was changed by changing the optical path length travelled using a translation stage), the IR pump probe signal is defined by $P(t)=[I_{pum\text{-}on} - I_{pump\text{-}off}](t)/I_{pump\text{-}off}=\Delta I(t)/I$ where I is the transmission of the probe beam. Vibrational lifetimes are obtained from the rotation-free signal $P_{life} = P_{//} + 2\times P_{\perp}$, where $P_{//}$ and $P_{\perp}$ are parallel and perpendicular data, respectively.

Phenol was purchased from SIGMA-ALDRICH. P-xylene was purchased from Tianjin Kemiou Chemical Reagent Co., Ltd.. Mesitylene was purchased from Tianjin Guangfu Fine Chemical Research Institute. Carbon tetrachloride was purchased from Xilong Chemical Industry Incorporated Co. Ltd..These samples were used without further purification.

To obtain the deuterated hydroxyl (OD) of the phenol, phenol was dissolved in methanol-OD (1g/10g) and stirred using magnetic stirring apparatus for 0.5 h. After the deuterium exchange completed, the solvent was then drew away by pump. Meanwhile the sample was under vacuum. The procedure was repeated many times until the compounds with >90% deuteration of the OH were obtained. The experimental liquid samples were contained in sample cells with Teflon spacers that provide suitable sample thickness according to their optical densities. The cell windows were made of two ~2 mm CaF_2 and provided sufficiently low group velocity dispersion. Experiments were performed at RT.

Density functional theory (DFT) calculations[43] of the structures of the intermolecular hydrogen bonded complexes were performed by using (DFT/B3LYP) method with the 6-311+G(d,p) or 6-31G* basis set level. All the DFT calculations were performed using Gaussian 09 program package. In our calculations, we don't include the surrounding solvent. Therefore all results reported in our paper are for the isolated molecules.

3. Results and discussions

3.1.FTIR spectra and the complex/free concentration ratios

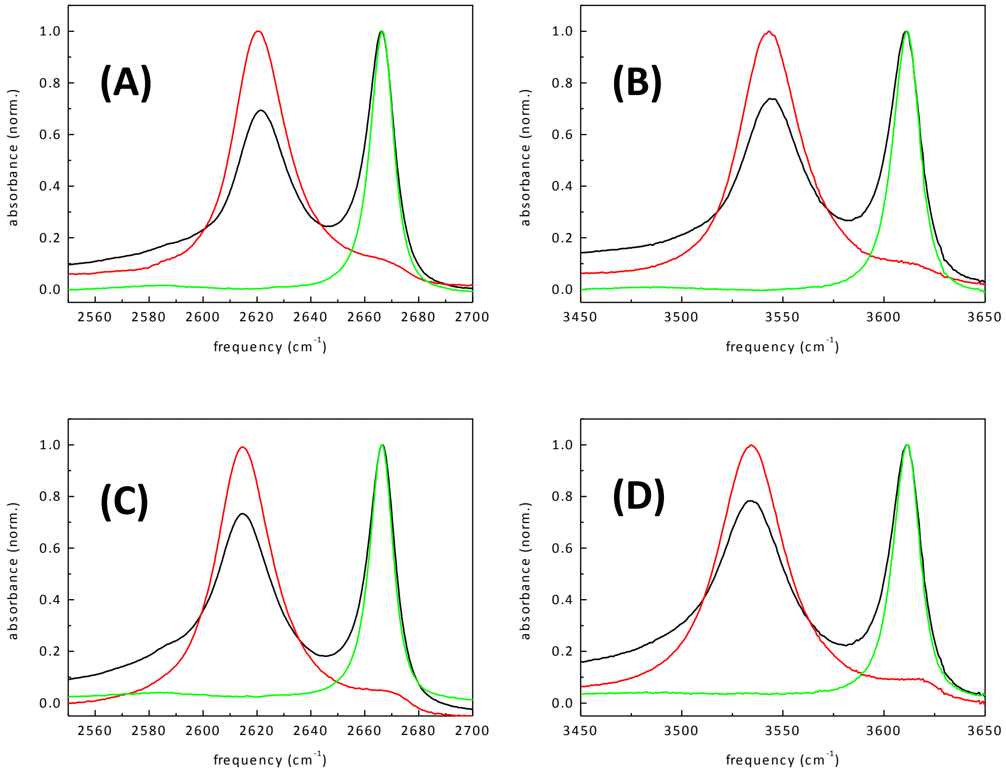

Figure 1.*FTIR absorption spectra of (A)the OD (hydroxyl H replaced with D) stretch and (B)the OH stretch of phenol in CCl_4 (free species, green curve), in p-xylene (complex species, red curve), and in the mixed p-xylene/CCl_4 solvent, which displays absorptions for both free and complex species (black curve).FTIR absorption spectra of (C) the OD stretch and (D) the OH stretch of phenol in CCl_4 (free species, green curve), in mesitylene (complex species, red curve), and in the mixed mesitylene/CCl_4 solvent (free and complex species, black curve).*

The studied systems are 0.6 wt% phenol-OD or phenol in the mixed p-xylene/CCl_4 (1:7wt) solvent, and 0.6 wt% phenol-OD or phenol in the mixed mesitylene/CCl_4 (1:7wt) solvent. In the solutions, the solutes have very low concentration, which ensures that resonant energy transfer between the phenol-OD or phenol species is negligible. In these solvent mixtures, the OD or OH stretching band separates into two distinguishable peaks, a broad resonance at low energy corresponding to phenol molecules that donate a hydrogen bond to the π-system of a neighboring aromatic molecule (the structures are presented in fig. 4&5) and a narrower high frequency resonance assigned to molecules with no hydrogen bonding partner. Experimental evidence for the formation of complexes is the shift of the OD (or OH) stretch frequency of phenol-OD (or phenol) to a lower frequency in p-xylene or mesitylene compared to that in CCl_4. Fig.1 (A) shows the FTIR spectra of phenol-OD in pure CCl_4, pure p-xylene, and a mixed p-xylene/CCl_4 solvent. When phenol-OD is dissolved in CCl_4, the solute is free and has no hydrogen bonding partner. The OD stretch is at 2666 cm^{-1} and its peak is relatively narrow with the half-width of 14 cm^{-1}. When phenol-OD is dissolved in p-xylene, solute molecules form a π hydrogen-bonded complex with solvent molecules. The frequency of OD stretch redshifts to 2621 cm^{-1} and its fwhm becomes 30 cm^{-1}. When phenol-OD is dissolved in mixed p-xylene/CCl_4 solvent, both free phenol-OD and complex exists with thermal equilibrium. Fig.1 (B) shows the FTIR spectra of phenol in the same solvents as phenol-OD in fig.1 (A). The free OH stretch is at 3610 cm^{-1} with half-width of 14.5 cm^{-1}. The OH stretch of complex is at 3544 cm^{-1} with half-width of 39 cm^{-1}. Fig.1 (C) shows the FTIR spectra of phenol-OD in pure CCl_4, in pure mesitylene, and in a mixed mesitylene/CCl_4 solvent. The free OD stretch is at 2666 cm^{-1}, while the complex OD stretch is at 2614 cm^{-1}. Fig.1 (D) shows the FTIR spectra of phenol in the same solvents as phenol-OD in fig.1 (C). The free OH stretch is at 3610 cm^{-1}, and the complex OH stretch is at 3533 cm^{-1}.

From the above FTIR spectra, we can also obtain the complex/free concentration ratios. The method is given in the below. The transition dipole moment of complex (free) phenol in pure solvent is assumed to be the same as complex (free) in the mixed solvent. Then we can use them (solutes in pure solvents) to divide the transition dipole moment and obtain the molar ratio of complex/free in mixed solvent, which is based on the fact that the FTIR signal of mixed solvent is $I_{FTIR}^{m}=kC_1\mu^2$ and that of pure solvent is $I_{FTIR}^{p}=kC_2\mu^2$, where I is the integration of the band, k is constant, C_1 is the unknown concentration of complex or free in mixed solvent, C_2 is the known concentration of complex or free in pure solvent and μ is the transition dipole moment. Based on this procedure, the complex/free concentration ratios are calculated to be 1.17, 1.22, 1.2 and 1.19 in phenol-OD/p-xylene/CCl_4 (0.6 wt%, 1:7 wt), phenol/p-xylene/CCl_4 (0.6 wt%, 1:7 wt), phenol-OD/mesitylene/CCl_4 (0.6 wt%, 1:7 wt), phenol/mesitylene/CCl_4(0.6 wt%, 1:7 wt) solutions, respectively (The detailed calculation is provided in SI.) From the results, we find that the equilibrium constant of the solute is almost same with that of deuterated one within experimental uncertainty.

3.2. 2DIR spectra of chemical exchange

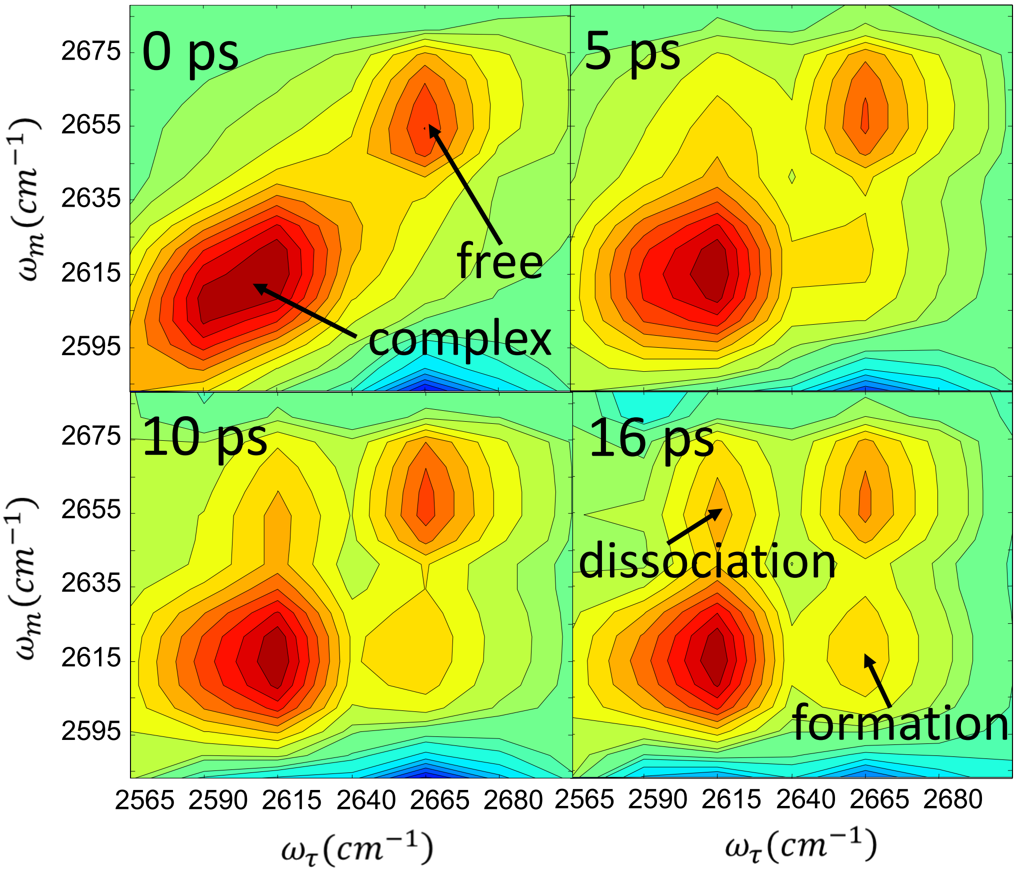

Figure 2.*Time dependent 2DIR vibrational spectra (measured for parallel polarization) of hydroxyl stretch of phenol-OD in the mixed mesitylene/CCl_4 solvents (0.6 wt%, 1:7 wt). The red contours on the diagonal (positive) are from the 0-1 vibration transitions, and the blue contours off the diagonal(negative, displayed partly) are from the 1-2 vibrational transitions. Each spectrum has been normalized to its largest peak for each time. Each contour is a 10% change. At 0 ps, there are two peaks on the diagonal (red). With time increasing, dissociation and formation of the phenol-OD-mesitylene complex causes two additional red peaks on the off-diagonal to grow in. Between 0 ps and 5ps, the peaks change shape because of spectral diffusion. Therefore, the time for spectral diffusion is<5 ps.*

Fig. 2 displays four 2DIR spectra (only the 0-1 transition region is shown) of phenol-OD in a mesitylene/CCl_4 mixture for a very short time (0 ps) and three long (5, 10, 16 ps) reaction period. At 0 ps, the red peaks (the 0-1 vibration transitions of the free phenol-OD and the phenol-OD-mesitylene complex) appear only on the diagonal positions in the 2DIR spectrum, showing that dissociation and formation of the complex has not occurred and the complex or free species in the sample are unchanged. The red peaks correspond to the absorption bands shown in fig. 1(C) for the mixed solvent. As time increases, off-diagonal peaks appear due to chemical exchange. At long time, 16 ps, extensive dissociation and formation of the complex has occurred, then causes additional peaks which can be seen clearly to grown in. The peak labeled as “dissociation” has its ω_τ (initial frequency) at the lower frequency, showing that the initial structure was complex phenol-OD. Its ω_m (final frequency) is at higher frequency, which shows the final structure is free phenol-OD. This off-diagonal peak arises from complex species converting to free species. The peak labeled as “formation” is the exact opposite of “dissociation”. The molecules in the two diagonal peaks are the same species, and they have either remained the same or have exchanged an even number of times during the chemical exchange process.

At short time, it is shown that the 2D vibrational spectrum is elongated along the diagonal. This is caused by inhomogeneous broadening.[9,13-15,44] By 5 ps they have become symmetrically rounded about the diagonal. The change in the 2D line shape is caused by spectral diffusion.[9,13-15,44]

The time dependent growth of the off-diagonal peaks provides direct data for us to inspect the chemical exchange process. From fig.2 we can see that the two off-diagonal peaks grow in at the same rate, showing that the rate of formation equals the rate of dissociation. As a result, the system is in equilibrium. However, it is difficult for us to directly compare the chemical exchange dynamics of the four systems with the 2DIR spectra (from the following sections, we can know that their chemical exchange times are too close to see difference in their 2DIR spectra). So we only present the 2DIR spectra for the phenol-OD/mesitylene/CCl_4 system to illustrate the chemical exchange process.

3.3. Chemical exchange kinetic model

Usually, we should analyze the peak volumes of the 2DIR spectra to extract the chemical exchange kinetic.[9,13,45] However, if the chemical exchange rate is much slower than spectral diffusion, we can use the peak intensities of 2DIR spectra to obtain the chemical exchange dynamics.[9,13] In this way, we can determine the chemical exchange rate more easily, and it only introduce small uncertainty. In our experiments we use peak intensities to fit chemical exchange times (the following sections will show that chemical exchange times of our studied systems are much longer than spectral diffusion). We use a kinetic model which include all dynamic processes.[13,14,38,39,45,46] The method is illustrated schematically for the complex species (CC) converting to free species (CF).

$$\xleftarrow{k_C}\left[CC\right]\underset{k_a}{\overset{k_d}{\rightleftarrows}}\left[CF\right]\xrightarrow{k_F}$$

where [CC] denotes the population of excited complex molecules, and [CF] denotes the population of excited free molecules. It should be noted that dependence on orientational relaxation of population is eliminated using rotation-free operation ($P_{life} = P_{//} + 2 \times P_{\perp}$, see the details in experimental methods section). k_d represents the rate constant for dissociation of the complex and k_a represents the rate constant for the association of the complex. $1/k_C$ and $1/k_F$ are the vibrational lifetimes of [CC]and[CF], respectively, which can be single or biexponetial.[38,39] When we separate one species into two subgroups, the weighing factor of each subgroup is determined by the prefactor of the bi-exponential. Each subgroup has a single-exponential-decay lifetime time. Each subgroup can exchange population with other species, but the subgroups can’t exchange population with each other (this follows the assumed physical picture of bi-exponential: the sub-components can be considered as independent species). In the model, the effects of dynamics such as spectral diffusions, vibrational decays and vibrational exchanges within each species are simply treated as apparent vibrational decays as experimentally measured. This is because not only the relaxation of the diagonal peaks is complex, but also the chemical exchange process is independent of the origin of the relaxation. Therefore, in our experiments we focus on the off-diagonal peaks which arise from the chemical exchange, and this treatment will not affect the value of chemical exchange lifetime we want to obtain.

According to the scheme showed above, we have kinetic equations:

$$\begin{cases} \dfrac{d\left[CC\right]}{dt} = -k_d\left[CC\right] + k_a\left[CF\right] - k_C\left[CC\right] \\ \dfrac{d\left[CF\right]}{dt} = -k_a\left[CF\right] + k_d\left[CC\right] - k_F\left[CF\right] \end{cases} \quad \text{eq. 1}$$

In the equations, the time dependent populations were obtained from the chemical exchange measurements (the method is described in the supporting information). In calculating the data, the apparent lifetimes determined by pump/probe experiments were used as initial input values and allowed them to vary at most 20%. Because the systems are in equilibrium, the rate of formation equals the rate of dissociation.[13] Therefore, the rate ratio k_d/k_a is determined by the complex/free concentration ratio (D). The dissociation rate constant k_d of complex is independent of concentration, and therefore, it is reported and discussed. $k_a = Dk_d$ is the association rate constant. The association rate is k_a [free]. Because the concentration ratio (D) is known, we can assume the single unknown parameter is k_d .

3.4.Hydrogen bond lifetimes of hydroxyl and deuterated hydroxyl for solute/solvent complexes are equal

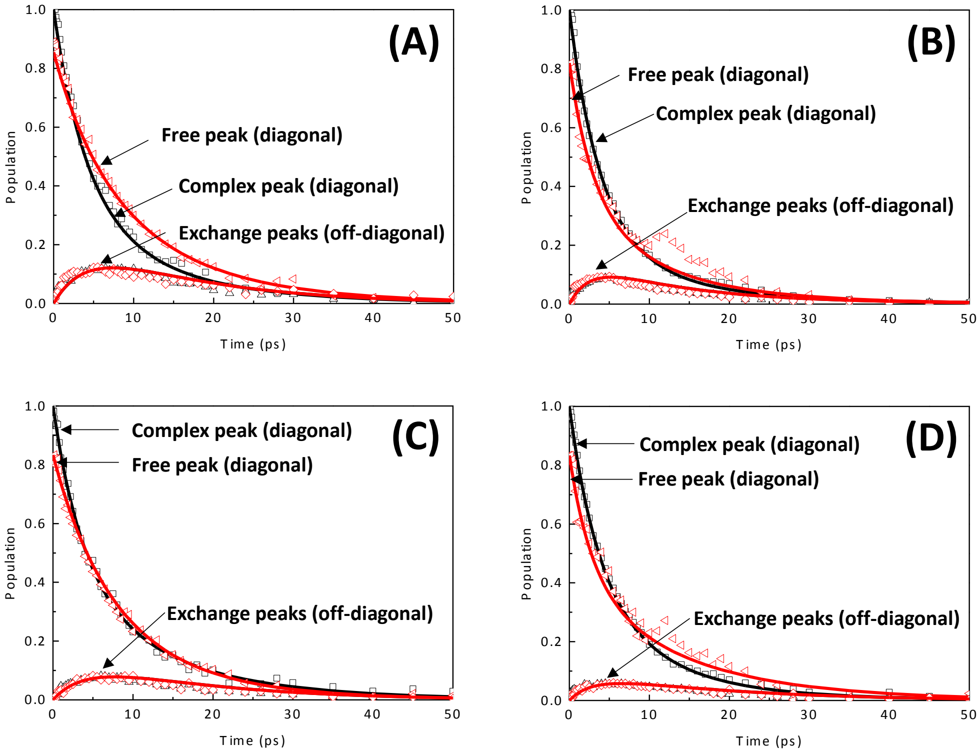

Figure 3.*Time dependent data (symbols) of the 2 off-diagonal and 2diagonal peak intensities in the 0-1 portion of the pump probe vibrational spectra for (A) phenol-OD in the p-xylene/CCl_4 mixture, (B) phenol in the p-xylene/CCl_4 mixture, (C) phenol-OD in the mesitylene/CCl_4 mixture and (D) phenol in the mesitylene/CCl_4 mixture. In each figure, we use the solid curves calculated from the chemical exchange kinetic model with one adjustable parameter, k_d, to fit the experimental data. Other parameters in the model are determined experimentally. Using these parameters, we can obtain $1/k_d$=19±2ps, 20±3p, 31±2ps and 33±3ps for(A), (B), (C) and (D), respectively.*

Figure 3A shows the peak intensity data for the 0-1 transition region which consists of four peaks: the two diagonal peaks for the complex and free phenol-OD species, and the two off-diagonal peaks (complex species convert to free species and free to complex). With the time increasing, the off-diagonal peaks grow in because of complex dissociation and formation. By inputting the known constants in the kinetic equations, we can fit the four peaks with a single adjustable parameter, the complex dissociation time, $1/k_d$. For the phenol-OD/p-xylene/CCl_4system, the input parameters used are listed in table 1. All the vibrational lifetimes in table 1 are experimentally determined in individual solution with pure solvent and all behave like biexponential. As can be seen from fig. 3A, the calculated solid curves fit in very well with the time dependent data of all of the peaks. From the fits, the dissociation time(hydrogen bond lifetime) for the phenol-OD/p-xylene complex is obtained and is listed in table 1.

Table 1.The complex/free concentration ratios, the vibrational lifetimes and its corresponding weighing factors of each subgroup and the dissociation rate constants of complexes in the four mixtures. (A), (B), (C) and (D) correspond to the solutions in fig.3, respectively.

	Complex/free concentration ratio *D*	Complex species				Free species				$1/k_d$ (ps)
		Fast process		Slow process		Fast Process		Slow process		
		$1/k_{C\text{-fast}}$ (ps)	$A_{C\text{-fast}}$	$1/k_{C\text{-slow}}$ (ps)	$A_{C\text{-slow}}$	$1/k_{F\text{-fast}}$ (ps)	$A_{F\text{-fast}}$	$1/k_{F\text{-slow}}$ (ps)	$A_{F\text{-slow}}$	
(A)	1.17	4.6	0.454	12.3	0.546	11	0.3	20	0.7	19±2
(B)	1.22	5	0.8	20	0.2	3.5	0.51	20	0.49	20±3
(C)	1.2	4	0.5	16	0.5	8	0.3	14	0.7	31±2
(D)	1.19	4	0.55	12.3	0.45	3	0.465	21	0.535	33±3

When analyzing the data in Figure 3, we assumed that the equilibrium constants and the exchange rates were not disturbed by vibrational excitation. This is supported by the following evidence. Such as both off-diagonal peak intensities (triangles and squares in Figure 3) have the same time dependence, the rates of complex formation and dissociation are equal. Namely, the aggregate populations of free and complex species in the mixtures are not affected by the excitation sequence. Other further tests by comparing time evolution of the 1-2 and 0-1 transition regions showing that the systems are in equilibrium have been presented for the phenol/benzene system[13] and many other systems[9,14,15].

For the phenol/p-xylene/CCl_4system (Figure 3B), the input parameters used are listed in table 1. As shown in fig. 3B, the calculated solid curves of the free diagonal peak misses a little with the time dependent data of that peak. However, the calculated solid curves of the other three peaks fit in very well with the time dependent data of those peaks. It should be noted that not only the free diagonal peak data in mixed solvent has a recurrence on its experimental curve at 12 ps, but also the diagonal peak data in pure solvent has the same phenomenon. Details are provided in SI. The recurrence is very interesting, but its origin is not known at this moment which is subject to future studies. The recurrence has little effect on the determination of the dissociation time, because the dissociation time is mainly determined by the growth of the off-diagonal peaks.[15] From the fits, the dissociation time for the phenol/p-xylene complex (hydrogen bond lifetime) is obtained and listed in table 1.

It is interesting that the measured chemical exchange rates show that the hydrogen bond lifetimes of the two systems (OH…p-xylene and OD…p-xylene) are equal within experimental uncertainty. There is a negligibly small isotopic effect on chemical exchange dynamics of phenol solutions.

Using the same method, we also obtain the dissociation times for the phenol-OD/mesitylene/CCl_4 system (Figure 3C) and the phenol/mesitylene/CCl_4 system (Figure 3D).The used input parameters and the results are listed in table 1. As can be seen from fig. 3C&D, the calculated solid curves fit in very well with the time dependent data of all of the peaks. The chemical exchange experiment results again show that the hydrogen bond lifetimes of the two systems are equal within experimental uncertainty.

3.5.DFT calculation results for solute/solvent complexes of hydroxyl and deuterated hydroxyl are almost identical

The gas-phase structures for hydrogen bonds have been determined by DFT calculations. The results show that the phenol donate a hydrogen bond to the π-system of a neighboring aromatic molecule in the mixed solvents and all of the complexes have a similar T-shaped structure. In addition, the T-shape structure is identical for both deuterated and regular hydrogen bonds. The structures of phenol/p-xylene and phenol/mesitylene complexes are displayed in figure 4&5. In a previous work[31], for the phenol/benzene complex, the T-shape structure has been confirmed by high-level electronic structure calculations and full molecular dynamic simulations of phenol in the benzene/CCl_4 solvent. Because of the consistency between the simulations and the electronic structure calculations for the phenol/benzene system, the electronic structure calculations for the other complexes provide a reasonable description of their structures.[9,13,14]

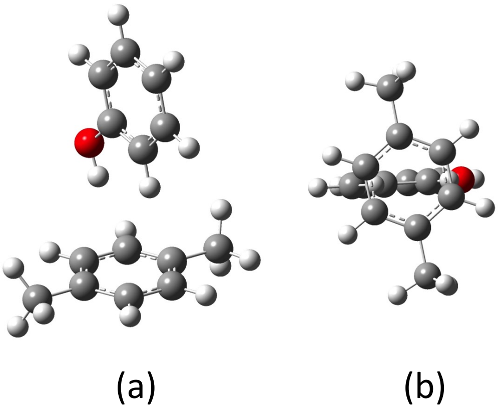

Figure 4.*Two views of the hydrogen bond structure of the phenol-p-xylene complex or phenol-OD-p-xylene complex calculated with DFT at B3LYP/6-31+G(d,p) level for isolated molecules (calculations show that the structures of the two complexes are almost identical). The binding energies of the two complexes are same, and are predicted to be -2.7 kcal/mol without any solvent molecules (with zero point energy correction).*

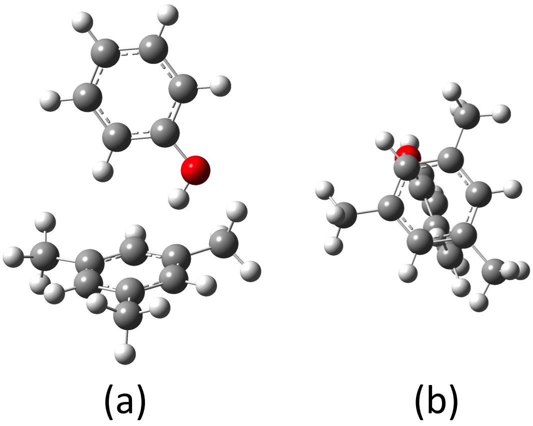

Figure 5.*Two views of the hydrogen bond structure of the phenol-mesitylene complex or phenol-OD-mesitylene complex calculated with DFT at B3LYP/6-31G* level for*

isolated molecules(calculations show that the structures of the two complexes are almost identical). The binding energies of the two complexes are same, and are predicted to be-3.9 kcal/mol without any solvent molecules (with zero point energy correction)

We then used calculations to analyze the vibrational modes of the hydrogen bonded complexes to obtain the directions and the zero point energies of the vibrations, investigating the principles leading to the observed negligible isotope effect on hydrogen bond dissociations. It is well known that, if a vibration is along the reaction coordinate, its zero point energy (the zero-point energy is defined by $\frac{1}{2}h\nu$, where ν is the 0-1 transition vibrational frequency.) can affect the activation energy of the reaction, leading to a remarkable isotope effect on the reaction kinetics.[47]The idea can be simply illustrated in Figure 6.

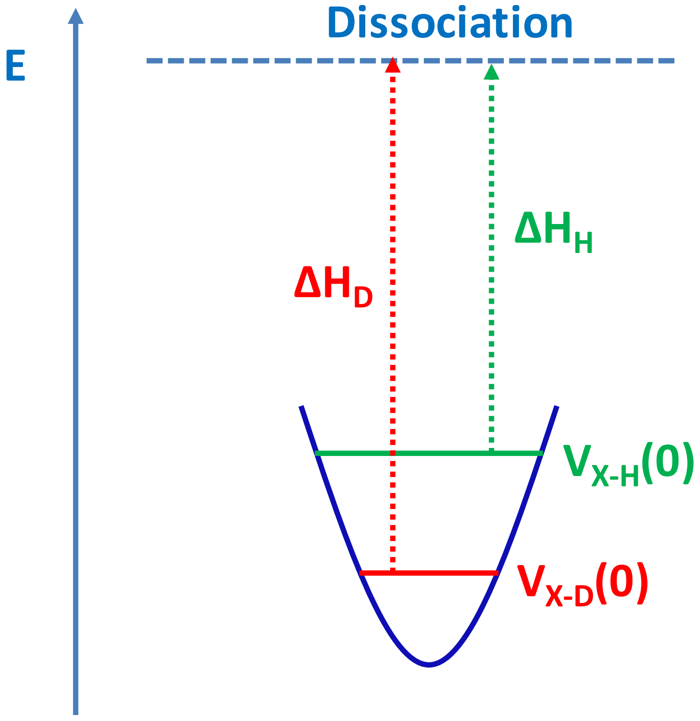

Figure 6. *Illustration of isotope effect caused by the zero point energy difference between X-H and X-D stretches for the dissociation of X-H and X-D bonds. The lower zero point energy of X-D stretch results in a larger dissociation enthalpy and a slower kinetics. The tunneling effect is not considered here.*

Table 2. *Vibrations of phenol-p-xylene and phenol-OD-p-xylene complexes that can be involved in hydrogen bond dissociation*

Vibrations (cm^{-1})	1	2	3	4	5	6	7
Phenol/p-xylene	12.33	15.92	30.50	38.14	43.67	71.57	310.46
phenol-OD/p-xylene	12.28	15.89	30.42	37.79	43.32	71.2	308.59

Table 3. *Vibrations of phenol-mesitylene and phenol-OD-mesitylene complexes that can be involved in hydrogen bond dissociation*

Vibrations (cm^{-1})	1	2	3	4	5	6	7	8	9
Phenol/mesitylene	13.51	21.32	28.52	37.62	52.44	82.39	225.64	233.46	237.85
phenol-OD/mesitylene	13.49	21.28	28.48	37.35	52.02	81.87	225.22	232.99	235.78

The frequencies of vibrations (0-1 transition) that can be involved in hydrogen bond dissociation of phenol/p-xylene, phenol-OD/p-xylene, phenol/mesitylene, and phenol-OD/mesitylene are listed in tables 2&3 (the corresponding pictures for vibrations are provided in SI.). The largest frequency difference between deuterated and regular hydrogen bonds is 2.07 cm^{-1} (No.9 in table 3), corresponding to a zero point energy difference 1.04 cm^{-1}. The calculated phenol/mesitylene hydrogen bond dissociation enthalpy is 3.9 kcal/mol (1362 cm^{-1}). At RT, according to the Arrhenius equation, the zero point energy difference only causes 0.5% difference in dissociation rate which is about 0.2ps for the dissociation (33ps) of phenol/mesitylene. The difference 0.2ps is smaller than our experimental uncertainty 2-3 ps, and therefore was not detected in the experiments. Our calculations also show that the total zero point energy difference between phenol/mesitylene and phenol-OD/mesitylene is 0.04/kcal/mol. Even if the total zero point energy completely contributes to the hydrogen dissociation activation energy, at room temperature the energy difference only causes a rate difference of 2ps which is still within our experimental uncertainty. The result for the phenol/p-xylene and phenol-OD/p-xylene is similar. The calculated total zero point energy difference between them is only 0.03kcal/mol. The energy difference only causes a rate difference of 1ps. Here, it is worth to emphasize that the calculated complexes in the gas phase may not have the same structures as those in real liquids. However, the main purpose of the calculations is to examine whether the H/D replacement will cause any frequency shifts of those low frequency vibrations when one phenol and one benzene derivative form a complex. Therefore, whether the calculated structures are close to real structures is expected not to affect the conclusions drawn from current calculations that much. In fact, MD simulations show that structure of a phenol/benzene complex calculated in this way is actually close to that in liquids in the MD simulations[48,49].

In summary, the ab initio calculations show that the values of zero energy of vibrations that can contribute to the dissociations of regular and deuterated hydrogen bonds are very similar. The differences are too small to cause detectible dissociation rate changes in our experiments. The experimental results also indicate that the hydrogen bond strengths are very similar for the OH and OD complexes studied in this work. This is somewhat different from that D_2O has stronger H-bonds than H_2O.[50] However, DFT calculations performed in this work cannot provide information to address this issue. Future theoretical studies by considering nuclear quantum effects can be very helpful[51].

4. CONCLUDING REMARKS

In this work, isotopic effects on the formation and dissociation kinetics of hydrogen bonds are studied in real time with ultrafast chemical exchange spectroscopy. The dissociation time 20ps (33ps) of hydrogen bond between phenol-OH and p-xylene (or mesitylene) is found to be identical to that between phenol-OD p-xylene (or mesitylene) in the same solvents. The experimental results demonstrate that the isotope substitution (D for H) has negligible effects on the hydrogen bond kinetics. DFT calculations show that the isotope substitution doesn't significantly change the frequencies of vibrational modes that may be along the hydrogen bond formation and dissociation coordinate. The zero point energy differences of these modes between hydrogen bonds with OH and OD are very small. The change of the hydrogen bond dissociation rate caused by the energy difference is smaller than 2ps at room temperature, which is within our experimental uncertainty. We expect the conclusion that the isotope effect is very small for hydrogen bond dissociation kinetics at room temperature is not only limited in the phenol systems investigated here. It should be general for a large number of other hydrogen bonds if the zero point energy difference is the only reason responsible for the isotope effect, because the zero point energy changed by deuteration is too small, compared to the thermal energy at room temperature. It is interesting to note that the H-bond strength can vary upon isotope exchange in some systems, which may also affect its dissociation and association kinetics.[50] This topic will be subject to future studies.

Conflicts of interest

The authors declare no competing financial interest.

Associated content

Supporting Information

The calculation parameters of the figures containing kinetic model calculations.

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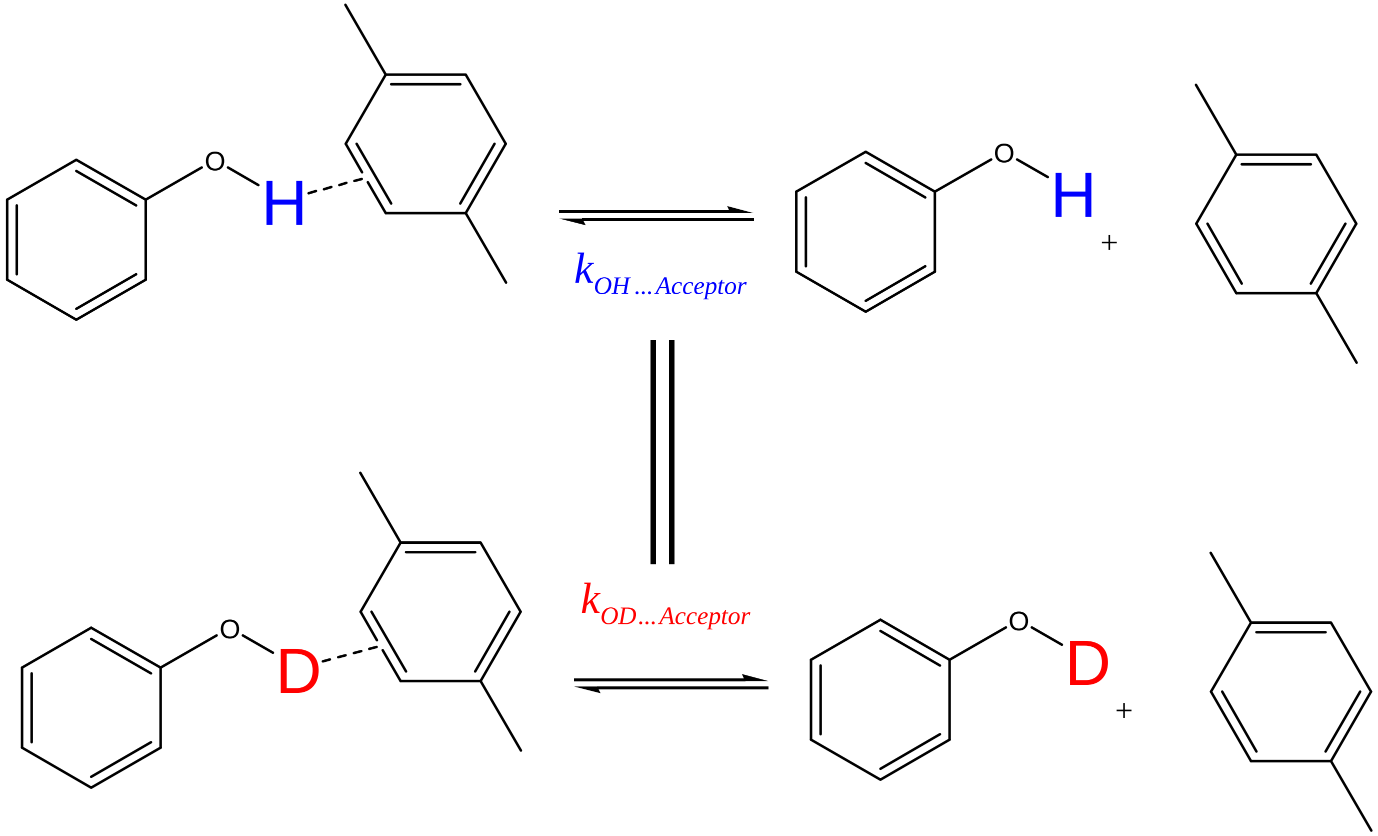

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