On the role of water in intermolecular proton transfer reactions

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Abstract

We study the mechanism of proton transfer (PT) between the photo-acid (8-hydroxy-1,3,6-pyrenetrisulfonic acid (HPTS)) and the base acetate using femtosecond vibrational spectroscopy. By probing the vibrational resonances of the photo-acid, the accepting base, and the hydrated proton we find that intermolecular PT in this systems involves the transfer of the proton across several water molecules linking the donor-acceptor pair by hydrogen bonds (H-bonds). We find that at high base concentration the rate of PT is not determined by the mutual diffusion of acid and base, but rather the rate of Grotthuss-like conduction of the proton between molecules. This long-range PT requires an activated solvent configuration to facilitate the charge-transfer.

Introduction

Proton transfer (PT) constitutes a fundamental class of chemical transformation and is ubiquitous as an elementary process throughout nature[1]. Two important examples are the reaction of Brønsted acids and bases, and the conduction of protons along "water-chains" in the trans-membrane proton pumps of living cells[2]. Especially in protic solvents these reactions can be extremely complicated due to the involvement of the solvent molecules.

Since the pioneering work of Eigen and Weller, the qualitative framework in which bimolecular proton transfer reactions in solution have been understood is the following. First, diffusive motion transports the acid and base to a particular intermolecular separation (the reaction contact radius) at which an encounter pair/reactive complex is formed. Second, the chemical event of PT takes place within this reactive complex at some intrinsic rate. If the first stage is rate limiting (or strongly rate

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influencing), then the reaction is termed diffusion limited (or diffusion-influenced). The reaction mechanism is typically referred to as outer-sphere or inner-sphere depending on whether PT within the encounter complex occurs between solvent separated or direct hydrogen-bonded species.

The quantitative implementation of the Eigen-Weller framework has typically been based on Smoluchowski's theory of diffusion-controlled reactions[3], extended to include a finite reaction rate at contact[4,5]. In this case, the model is called Smoluchowski-Collins-Kimball (SCK) in recognition of all those involved. While the SCK model has been successfully applied to various reaction types, there are significant deficiencies when applied to intermolecular PT. First, spherical symmetry is assumed for the reactive encounter complex. However, acidic molecules are in general not isotropically reactive, and important orientational constraints have to be satisfied before the reaction can proceed. Such constraints can be included in the Smoluchowski picture by introducing a 'steric probability factor' multiplying the on-contact rate[6] (i.e. the probability of forming a reactively favourable encounter complex through diffusion). However, under these circumstances it becomes extremely difficult to interpret the effective on contact rate in terms of elementary mechanisms given the large number of degrees of freedom entering this single parameter. In addition – in light of modern work on the nature of the proton in water[7-10] – it is not evident that PT should be limited to occur at a fixed reaction radius, at least in aqueous solutions. A final difficulty is that continuum approaches ignore the discrete nature of the solvent and the organization of the aqueous hydrogen bond network, both of which are important in PT since bond breaking/making is an essential feature of these charge-transfer reactions (unlike outer-sphere electron transfer),

In recent years, the development of time-resolved spectroscopic techniques has stimulated considerable research on proton-transfer reactions. In these studies, proton transfer is triggered by optical excitation of a so-called photo-acid[11-13]; a molecule that is more strongly acidic in an excited electronic state than in the ground state. Many of the time-resolved studies on proton transfer have concentrated on the photo-acid pyranine: 8-hydroxy-1,3,6-pyrenetrisulfonic acid trisodiumsalt (HPTS). HPTS forms an ideal system with which to study PT reactions, since absorption of a photon leads to an enhancement in the molecule's acidity by as much as a factor 10^6. HPTS has been used to study the dynamics of acid dissociation[14-19] and acid-base reactions[20-26] using different time-resolved spectroscopic techniques like transient fluorescence, optical absorption spectroscopy, and vibrational absorption spectroscopy[22-26].

In several of the early time-resolved spectroscopic studies of photoacid dissociation[13,14] and PT between photoacid and base[21,22], the observed dynamics were successfully modeled using the SCK approach. However, in recent femtosecond mid-infrared spectroscopic studies on HPTS-acetate (or n-chloro-acetate) in aqueous solution performed by the Pines and Nibbering groups[22-26], it was found that the SCK model required refinement in order to explain the observations and fit the experimental data. In these studies the PT reaction was measured by probing the vibrations of the HPTS photo-acid, a proton-accepting carboxylate base and an apparent reaction intermediate. In these studies three distinct components to the proton transfer kinetics were identified. The fastest component, with a time constant of ~150 fs, was assigned to PT in a population of hydrogen bound HPTS-acetate complexes already formed in the ground-state. A second slower component, with a time constant of 6 to several tens of picoseconds, was assigned

to PT in a population of solvent-separated HPTS-acetate "loose" complexes. The third (and slowest) component – with a time constant of tens of picoseconds up to nanoseconds – was ascribed to the diffusive formation of tight and solvent-separated loose complexes. Only this third component was modeled inside of the SCK framework.

In this paper we present new information on the mechanism of proton transfer between HPTS and acetate in aqueous media by studying the isotope effect of the proton transfer, and by directly probing the broad-band infrared response of the hydrated proton/deuteron with femtosecond mid-infrared laser pulses. These measurements motivate a new view of intermolecular PT in aqueous solution, and lead to the development of a model that is a significant departure from the SCK approach described above. This new model allows all PT in solvent separated donor-acceptor pairs to be handled inside the same framework in a consistent manner; i.e. it is not necessary to distinguish between different solvent separated sub-populations as was done previously. We find that PT between HPTS and acetate in aqueous solution involves a distribution of solvent separated complexes differing in the number of water molecules separating the acid and the base. The proton is transferred inside these complexes via Grotthuss-like conduction through a hydrogen bound chain of water molecules connecting HPTS and acetate at a distance dependent rate that decreases by a factor of 5 for each additional water molecule separating the acid and the base.

Experimental Methods

We have used femtosecond UV-pump, mid-infrared probe spectroscopy to investigate the dissociation reaction of the photoacid HPTS and the microscopic mechanisms involved in

intermolecular excited state proton transfer (ESPT) in aqueous solutions (both H_2O and D_2O). Briefly, in these experiments a 400 nm, ~100 fs pump pulse is used to instantaneously switch the aciditiy of HPTS molecules in solution and at variable time-delays afterwards the microscopic aspects of acid dissociation and proton transfer are probed using mid-infrared pulses in several wavelength bands between 1400 cm^{-1} and 3000 cm^{-1}. The 400 nm pump pulse has an energy of ~5 μJ and is produced through frequency doubling the output of a Ti:sapphire amplifier (SpectraPhysics Hurricane) using a β-barium borate (BBO) nonlinear optical crystal. The amplifier delivers pulses with a central wavelength of 800 nm, an energy of 1 mJ at a repetition rate of 1 kHz. The dynamics and mechanism of the proton transfer are studied by probing the dynamics of the vibrational resonances of the photo-acid, the proton/deuteron and the base with a second, weak, tunable femtosecond mid-infrared pulse. This probe pulse has an energy of ~0.1 μJ, a pulse duration of ~150 fs, and is tunable between 2.5 and 8 μm. The probe pulse is generated via Optical Parametric Amplification in a BBO crystal followed by difference frequency mixing in a $AgGaS_2$ crystal. The foci of the pump and probe pulses have a diameter of 400 and 200 μm, respectively. The spectral bandwidth of the probe pulse is ~200 cm^{-1}. The probe pulse is dispersed by a spectrograph and the different frequency components are detected using a 2x32 HgCdTe array detector. The frequency resolution is 16 cm^{-1} per pixel of the array. The probe polarization is at the magic angle (54.7°) with respect to the polarization of the pump to remove the effects of molecular reorientation.

The photo-acid pyranine: 8-hydroxy-1,3,6-pyrenetrisulfonic acid trisodiumsalt (HPTS, 98%) and the sodiumacetate ($NaCH_3COO$) were purchased from Aldrich and are

used without further purification. We have studied the intermolecular proton transfer reaction between these species at sodium acetate concentrations of 0, 0.5, 1, 2, and 4 M in both normal water and deuterated (99.8 %) water. In most of the experiments we used a concentration HPTS of 10 mM. Part of the HPTS (with a maximum of ~50% at 4 M acetate) reacts with acetate to form the conjugate base (PTS⁻) in these self-buffering solutions. To rule out the involvement of PTS⁻ in the observed signals, we have performed control experiments on solutions containing only the conjugate base and found no signal following excitation at 400 nm, except during temporal overlap of the 400 nm excitation pulse and the mid-infrared probing pulses (i.e. <200 fs). We have also performed experiments on pH balanced solutions (obtained by adding small amounts of acetic acid), and the results were found to be identical to those presented here. The sample solution (10 – 50 μm thick, depending on the solution) is flowed between two CaF_2 windows.

Results

In Fig 1a, the transient infrared spectra observed in the frequency range 1460 – 1580 cm^{-1} are shown for several pump-probe delays from 3 – 170 ps for a 10 mM solution of HPTS in H_2O. The aromatic ring distortional modes in this frequency range are sensitive to the protonation state of HPTS. The spectrum at early delays shows strong increases in absorption at 1480 and 1540 cm^{-1}. These induced absorptions reflect the changes of the aromatic ring system that are directly induced by the electronic excitation. With increasing delay, the amplitude of the bands at 1480 and 1540 cm^{-1} decreases and a new vibrational band centered at 1503 cm^{-1} arises. This latter band marks the strong change in

the vibrational spectrum upon the acid dissociation of HPTS; i.e. the rise in population of the conjugate base (HPTS anion). This assignment is consistent with that of previous studies[22]. A time-trace of this band intensity is shown in Fig. 1b along with a single exponential fit to the data. The effective dissociation rate obtained, 90 ± 5 ps, is in excellent agreement with the rate of HPTS dissociation obtained from femtosecond fluorescence and absorption spectroscopies[18]. However, in addition to the bands associated with the modes of the HPTS molecule, the transient spectra show a surprising infrared continuum absorption throughout the $1400 - 3000$ cm^{-1} region that appears within the temporal resolution of the experiment (~200 fs). The continuum absorption cannot be caused by multi-photon excitation, since it is linear in pump intensity. The continuum shows a partial decay on the same timescale as HPTS dissociation in H_2O (Fig. 1b). A similar continuum is observed for HPTS in D_2O, which exhibits a partial decay with a time constant of ~250 ps. This timescale is in excellent agreement with that found for HPTS dissociation in D_2O solution using time-resolved fluorescence spectroscopy[14]. The continuum absorption is therefore ascribed to the photoacidic proton/deuteron. Further evidence for this assignment is presented below, and discussed in the following section.

In a previous study of HPTS dissolved in H_2O a continuum signal was also reported[25]; however, a complete decay on a time scale of hundreds of picoseconds was reported, so the signal was not assigned to the proton. This complete decay could be due to the fact that in that study a higher concentration of HPTS of 15-20 mM was used. We find that the dynamics of the continuum signal strongly depend on the concentration of HPTS. In Figure 2 a full decay of the continuum in ~300 ps is observed for a solution

containing 50 mM of HPTS, but only a partial decay for 2 and 10 mM solutions. The complete decay at higher concentrations shows the occurrence of self-quenching of the excitation. Self-quenching results from the mutual interaction of excited HPTS and/or conjugated photo base molecules and thus strongly depends on concentration. The de-excited PTS^- ions that result from the quenching will take up the hydrated protons leading to a decay of the continuum signal.

With the addition of a strong base (proton/deuteron acceptor), the dynamics of proton transfer between donor-acceptor pairs in aqueous solution can be studied. Acetate was chosen as the base, since the acidic form (acetic acid) has a well separated vibrational mode associated with the C=O stretch vibration that can be monitored as a marker for when the proton/deuteron arrives at the base. This is illustrated in Figure 3 for the case of 10 mM HPTS, 2 M acetate in D_2O solution. The acetic acid C=O band centered at 1710 cm^{-1} grows in as a function of time after photoexcitation of the HPTS molecules. This observation is in close agreement with the results of Ref. 22. In addition we observe again the IR continuum for which we find that the dynamics are precisely opposite to those of the acetic acid band (Fig. 3, inset).

The continuum response was measured in all experimentally accessible wavelength regions throughout the 1400-3000 cm^{-1} region, and in all these regions the same dynamics were observed. An uninterrupted transient continuum spectrum across this entire region cannot be presented because of the presence of solvent modes (bending, stretching bands), acetate and acetic acid modes and the HPTS transient spectra. The spectral density of the continuum is small (<250 μOD) so it is obscured by these other contributions where they overlap. There is also a heating response – showing very

different dynamics than the continuum – that is observable in the wavelength regions near the stretching and bending modes of the solvent. In contrast to the continuum response, the heating response is independent of acetate concentration and remains constant on the nanosecond time scale of the experiment. The region of the deuteron spectrum shown in Fig. 3 is relatively free from these other contributions, since this spectral region is between the stretch and bend bands of the D_2O solvent.

As reported previously[22], part of the HPTS forms direct contact pairs with acetate in the ground state. Proton transfer in these direct complexes occurs extremely fast (<150 fs)[22,23], so after ~ 1 ps these direct contact pairs no longer contribute to the observed dynamics. The presence of such complexes is recognized in our data as a strong signal of the acetic acid band immediately following photoexcitation. It should be noted that the observed continuum absorption cannot be due to direct HPTS-acetate contact pairs, because the continuum shows dynamics on a very different timescale than PT in such complexes. Moreover, the continuum absorption is also observed in the absence of acetate. Of particular importance for the current study is that the separation of timescales between PT in direct contact pairs and solvent separated species means that we can distinguish the dynamics of initially solvent separated donor-acceptor pairs by considering the signals at delay times >1.5 ps.

Figure 4 compares the decay of the infrared continuum for solutions of 10 mM HPTS and 2M acetate in H_2O and D_2O. In both solutions the decay is observed to be highly non-exponential. The data also show a significant isotope effect. The effective early-time (<10 ps) decay constants obtained from these data show an isotope effect of ~1.4 (Fig. 3, inset).

Figure 5 compares the decay of the infrared continuum for several acetate concentrations. The decay clearly becomes significantly faster with increasing base concentration. All solutions show a similar early time isotope effect of ~1.4.

Mechanism of intermolecular proton transfer in aqueous environments

In Figures 1 and 3 it was observed that directly after excitation a broad-band infrared absorption arises, and that this absorption shows dynamics on the same timescale as PT/DT. Broad-band infrared absorption is an expected feature of solvated protons in water[27], where the absorption results from O-H stretch vibrations of different solvation structures of the proton in water. Limiting cases of these solvation structures are the so-called Zundel ($H_5O_2^+$) and Eigen ($H_9O_4^+$) cations. However, in the present experiment, hydrated protons are expected to be generated at the same rate as HPTS dissociation (~90 ps for H_2O, ~280 ps for D_2O), and not on the sub-200 fs timescale. Thus, the source of the IR continuum absorption observed instantaneously with photoexcitation of HPTS cannot be fully solvated protons. It should be realized that continuous IR absorption is a feature of many systems in which strongly polarizable H-bonds are present[28,29]. Strongly polarizable H-bonds occur when a shallow double-well potential energy surface (PES) or a PES with a flat broad well is present along the H-bond (or proton transfer) coordinate. Evidently the photoexcitation with 400 nm leads to a significant softening of the covalent bond in the OH group in HPTS and a strengthening of the H-bond to the solvating water, i.e. $ROH \cdots OH_2 \overset{h\nu}{\Rightarrow} RO^{-*} \cdots H^+ \cdots OH_2$, where the HPTS molecule has been denoted *ROH*. In earlier measurements of fluorescence intensities by Weller it was also found that the excitation of HPTS leads to a strengthening of the hydrogen bond[29]. Hence,

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immediately after photoexcitation the O-H bond is weakened by the proton/deuteron remains close to the oxygen atom of the hydroxyl group of the HPTS molecule. This is the first stage of acid dissociation. In the second stage the proton moves away from the HPTS to a fully hydrated state, which is observed to lead to a ~50% decrease of the absorption of the infrared continuum (Fig. 1b). This two-stage picture is confirmed by a theoretical study in which it was found that the photo-excitation of HPTS does not directly lead to a strong transfer of charge from the oxygen atom of the hydroxyl group of HPTS to the aromatic rings. When the proton leaves the excited HPTS molecule, the negative charge on the oxygen atom is no longer stabilized and full charge transfer to the aromatic rings occurs, thereby turning the conjugated PTS into a weak base[18]. Only after this charge transfer does the optical absorption and fluorescence spectra acquire the shapes that are characteristic for the conjugated photo-base of the HPTS molecule. This picture also offers an explanation for the decrease in absorption of the infrared continuum accompanying the transfer of the proton to the fully hydrated state. In the loosely bound state, the proton vibration is close to a strongly negatively charged oxygen atom. As a result, the derivative of the dipole moment with respect to the vibrational coordinate, and thus the transition dipole moment, will likely be enhanced in this state. This enhancement vanishes when the proton leaves the HPTS.

For the solutions containing acetate the infrared continuum absorption decays completely (Fig. 3, inset), since the proton is taken up by the acetate. The isotope ratio of 1.4 is very similar to the square root of the mass ratio of the deuteron and the proton. It should be noted that the isotope ratio of 1.4 does not point at tunneling as being essential

in the proton/deuteron reaction, because the tunneling rate depends exponentially on the mass; tunneling will in general show a much stronger isotope effect.

The isotope effect of 1.4 is roughly the same as has been observed for the ratio of the proton and deuteron mobilities in pure H_2O/D_2O. Previous theoretical[7-9] and experimental[10] work showed that in pure water protons/deuterons are transferred via Grotthuss conduction. The observation of the same isotope ratio of 1.4 in the present study suggests that the elementary reaction mechanism facilitating PT between donor-acceptor pairs in water at these early delay times is the transfer of protons/deuterons via a Grotthuss-like process rather than the translational diffusion of the molecular species. In the Grotthuss mechanism the proton is transported through a process of structural diffusion via the interchange of covalent and H-bonds[7,8]. As a result, not the proton itself, but rather its charge is being transferred between the donor and acceptor. This also means that the proton transfer can take place between an acid and a base that are separated by several water molecules.
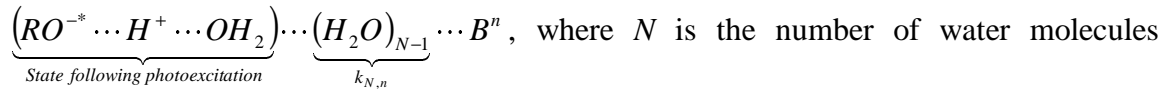
It should be noted that the transfer of a proton from acid to base via Grotthuss conduction has been proposed before, for instance in the autodissociation and recombination of H_3O^+ and OH^- in water[8] and in the adiabatic proton transfer picture developed by Ando and Hynes[31]. In recent femtosecond mid-infrared spectroscopy studies of proton transfer between HPTS and (chloro)acetate, Grotthuss conduction was also proposed as a possible mechanism by which protons/deuterons were transferred across a single water molecule connecting acid and the base[24], and within diffusively formed reactive encounter complexes[23] In all these processes the solvent molecules must both establish a wire of hydrogen bonds connecting the acid and the base, and generate

local electric fields favoring the products (and destabilizing the reactants) to facilitate the PT. Hence, the reaction rate will strongly depend on the time scale of the structural fluctuations of the solvent. The solvent controlled destabilization of the reactant configuration, stabilization of the product configuration, and the conduction of the proton from the acid to the base through a hydrogen bound chain of water molecules, could in principle each show different isotope effects. The similarity of the observed isotope effect with that of the conduction of protons/deuterons in neat liquid water suggests that for the present reaction the conduction through the water chain is rate limiting, or that other elements of the reaction show a similar isotope effect (i.e. depend on similar degrees of freedom as those involved with bulk proton diffusion). For other reactions (with for instance weaker bases and/or acids) it could of course be that a different kinetic isotope effect will be observed. This is likely, for example, if tunneling of the proton/deuteron is an essential feature of the reaction..

An important question is how many water molecules are involved in the Grotthuss conduction of the proton from HPTS to the base. For a base concentration of 2 M acetate in H_2O, the signal associated with the solvent-separated complexes decays ~50% in the delay time range <10 ps (Fig. 4). This signal decay is much larger than the statistical fraction of HPTS-acetate complexes that are separated by a single water molecule. Hence, the proton transfer likely involves conduction through several water molecules. When we also realize that in this brief time interval there is very little diffusion of the reactants[32], it follows that a significant fraction of the PT events have to occur in HPTS-acetate complexes that are separated by several water molecules.

Grotthuss hopping model for intermolecular proton transfer

We have developed a model in keeping with this picture that is based on a H-bond network starting at the active site of the acid (Fig. 6). The system of excited photo-acid and base is described as a distribution over reactive species of the type $\underbrace{\left(RO^{-*}\cdots H^{+}\cdots OH_2\right)}_{State\ following\ photoexcitation}\cdots\underbrace{\left(H_2O\right)_{N-1}}_{k_{N,n}}\cdots B^n$, where N is the number of water molecules separating the acetate (B) from the active site of the acid, which we call the shell number, and n is the number acetates in that shell. The initial distribution of these configurations (i.e. the distribution of initial water chain lengths) depends strongly on acetate concentration, and is determined assuming random site occupancy statistics. In the scheme of hydrogen network branching considered (Fig. 6) there are 2^N oxygen atoms (or available sites) in the Nth shell. The fraction of initial configurations with HPTS separated by N waters from n acetate molecules can be written as

$$g(N,n,t=0) = P_w(1 \rightarrow N-1) \cdot P_a(N,n), \qquad (1)$$

where $P_w(1 \rightarrow N-1)$ is the probability of having only water in the first N-1 shells and $P_a(n, N)$ is the probability of having n acetate molecules in the Nth shell. In terms of the probability that a given site in the H-bond network is occupied by a water molecule, p_w, (computed from the molarity of the solution)

$$P_w(1 \rightarrow N-1) = p_w^{\left(\sum_{i=1}^{N-1} 2^i\right)} \qquad (2)$$

$$\text{and } P_a(N,n) = \binom{2^N}{n} \cdot p_w^{2^N-n} \cdot (1-p_w)^n, \qquad (3)$$

where $\dbinom{2^N}{n}$ represents the binomial coefficient. It is important to note that $g(N, n, t{=}0)$

is normalized, i.e. $\displaystyle\sum_{N}\sum_{n=1}^{2^N} g(N,n,t=0) = \sum_{N} p_w^{\left(\sum_{i=1}^{N-1} 2^i\right)} \sum_{n=1}^{2^N} \binom{2^N}{n} \cdot p_w^{2^N-n} \cdot (1-p_w)^n = 1$.   The

implicit assumption is that PT always occurs between HPTS and the closest acetate

molecule, and that the number and distribution of acetate molecules in higher shells is

irrelevant. Using this framework, the initial distribution of water chain lengths for a 2M

and a 4M solution of acetate is shown in Fig. 8.

   We make no apriori determination for the number of H-bonds over which a

proton can be transferred in the model, but do take the rate constant for PT as a function

of shell and acetate number, $k_{N,n}$, to decrease exponentially with the number of water

molecules

$$k_{N,n} = nk_o \exp[-(N-1)/N_o] = nk_o\Delta^{N-1} \quad, \tag{4}$$

where k_o is the instrinsic rate of PT across a single water molecule and N_o is a parameter

that describes the distance dependence of PT that is to be determined. Δ is the factor by

which the proton-transfer rate decreases with each extra water molecule separating donor

and acceptor by H-bonds. The rate goes down with a factor Δ for every additional

element (=hydrogen bond), because conduction of the proton from the acid to the base is

only possible when all N water molecules possess the right hydrogen-bond configuration

to enable the transfer. This hydrogen-bond configuration is produced by spontaneous

fluctuations and the inverse rate $(k_{N,n})^{-1}$ forms the characteristic time the system has to

wait until the complete connecting chain of water molecules acquires a hydrogen-bond

configuration that enables conduction of the proton. As soon as such a configuration arises, the conduction itself has to rapid as this configuration will be very short-lived.

At early times the survival probability of protonated HPTS molecules can be written as

$$S(t) = \sum_{N} \sum_{n=1}^{2^N} g(N,n,t=0)\exp(-k_{N,n}t).$$ (5)

It is important to note that in liquid solution the separation of donor-acceptor pairs can change in time. In this model we account for particle diffusion by discretizing Eq. 5) over finite timesteps. This is accomplished by taking $g(N,n,\Delta t) = g(N,n,t=0)\exp(-k_{N,n}\Delta t)$, then allowing acetate molecules to redistribute between shells by hopping (i.e. $g(N,n,\Delta t) \to g'(N,n,\Delta t)$), and repeating the procedure for the next timestep. The assumption is that the PT event occurs much faster than the diffusive motion of the reactants. Acetate hopping is taken to occur at a rate given by the Einstein relation, $\tau = l^2/6D$, where l^2 is taken to be the average O-O distance in water (~2.8 Å) and D is the diffusion constant of acetate, 1.5×10^{-9} m^2/s. We ensure that the hopping between shells at equilibrium (before the reaction takes place) results in no net flux across the shell boundaries. PT reactions, however, will alter the distribution function $g(n,N,t)$ by preferentially removing the configurations in which the photo-acid and the base are closely spaced, since these react fastest. Hopping within the resulting nonequilibrium distribution leads to a net flux of the acetate molecules from higher N shells to lower N shells, in the same way as concentration gradients lead to Fickian diffusion. In this discretized manner it is possible to compute $S(t)$ given the initial (concentration dependent) distribution of reactants, $g(N,n,t=0)$.

Data Analysis

Assuming the acetate to be statistically distributed over the liquid, each base concentration results in a different initial distribution of HPTS-acetate distances and thereby in a different distribution of proton transfer rates. As mentioned in the results section, by fitting the model to the data at delays >1.5 ps we exclude the contribution to the proton transfer of the direct contact pairs and focus on the solvent separated donor-acceptor pairs. Least-squares fitting of this model to the experimental data show an optimal set of parameters in the space spanned by $\{k_o, \Delta\}$. In the case of H_2O/D_2O these are $\{(1.2 \text{ ps})^{-1}, 0.21 \pm 0.02 \}/\{(1.8 \text{ ps})^{-1}, 0.21 \pm 0.02\}$. Decay curves computed using this approach and the parameters $\{k_o, \Delta\}$ mentioned above are compared with the experimental data in Figs. 4,5 and 7. In Fig. 7 the data measured for deuteron transfer at different base concentrations are compared with decay curves calculated with both the Grotthuss hopping model and the SCK model used (and described) in previous work[21,23]. We have used SCK model parameters equivalent to those in previous studies to compute the curves in Fig. 7; the on-contact reaction radius, a = 6.3 Å, on-contact reaction rate, k_o = 4×10^{10} $M^{-1}s^{-1}$ and 8×10^{10} $M^{-1}s^{-1}$, and mutual diffusion constants of 1.5 (1M) , 1 (2M) and 0.8 (4M) 10^{-9} m^2/s. We find that the SCK model can provide either a good fit of the early delay-time data or of the later delay-time data, but never of both. Figures 4, 5 and 7 illustrate that the Grotthuss hopping model provides an excellent description of the proton/deuteron transfer at all delay times and concentrations.

The optimal parameters of $k_o = (1.2 \text{ ps})^{-1}$ for H_2O and $k_o = (1.8 \text{ ps})^{-1}$ for D_2O can be compared with hopping times of the proton/deuteron over a single water molecule in

pure water/heavy water. These values are in excellent agreement with the hopping times in pure water determined from NMR measurements, which find $\tau_p \sim 1.5$ ps for bulk water[33], and simple estimates for these times from the diffusion constants which give $\tau_p \sim$ 1.3 ps and $\tau_d \sim 1.7$ ps. It should be noted that the close correspondence of the values of k_o (derived for the aqueous reaction between HPTS and acetate) with the hopping rates of the proton/deuteron in neat liquid water is likely a mere coincidence. The value of k_o is expected to depend quite strongly on the driving force of the reaction, and thus on the combination of acid and base. The distribution of PT-reaction complexes (the distribution of intermolecular separations over which PT occurs) can be determined by keeping track of the reactant configurations in the Grotthuss hopping model. The results of this analysis are shown in Fig. 8 for solutions containing 2M and 4M of acetate. It is seen that the distribution of PT/DT closely follows the initial distribution of acetate. The fraction of PT/DT events is only smaller than the fraction of initial configurations for HPTS-acetate separations of more than 4 water molecules. For these larger separations diffusion acts to bring the reactants closer before PT/DT occurs. However, the small difference between the distribution of reaction complexes in H_2O/D_2O and the initial distribution of intermolecular separations shows that diffusive transport of the reactants plays a minor role in both PT and DT at these concentrations.

Discussion

We find that ~90% of PT/DT takes place between donor-acceptor pairs that are separated from one another by 1 to 4 water molecules in the base concentration range of 1 to 4 M (Fig. 8). To some extent this finding agrees with the original speculation of Eigen[34].

Eigen inferred that the optimal distance for proton transfer was ~ 0.75 nm, which corresponds to a configuration in the acid and the base are separated by two water molecules. There are important differences with this original picture, however. First, there is not a single distance at which proton transfer occurs, but a whole range which differ in the number of water molecules separating the acid and the base. The non-exponential character of the proton transfer is thus a direct consequence of the distribution of reactive complexes that differ in the number of water molecules separating the acid and the base. Second, diffusion does not play a significant role in the reaction for configurations with HPTS-acetate separated by less than ~5 water molecules, since these configurations are already 'reactive complexes'. Diffusion will clearly play a dominant role for the reaction dynamics as soon as the acid and the base are separated by more than 5 water molecules. Thus, in the limit of low reactant concentrations (when the average reactant separation is much larger than the lengthscale for PT) the model yields results consistent with the Eigen-Weller framework. The present approach, therefore, can be seen as an extension of the Eigen-Weller framework for general bimolecular PT in solution. In some respects, the Grotthuss mechanism we discuss can be considered to be the reaction mechanism responsible for PT inside the Eigen-Weller "encounter complex". Our results suggest that the average 'size' of this encounter complex is determined by interplay between the distance dependent reaction rate and the diffusion constants of the reactants.

In a previous study of the HPTS-acetate system using visible pump-probe spectroscopy[21], the concentration dependence of the reaction was described in the conventional SCK model for proton-transfer reactions. As the diffusion of acetate and

HPTS through H_2O/D_2O differ only slightly, the isotope effect observed in the data required a very large isotope effect of 4 for the on-contact reaction rate. This isotope effect is larger than for HPTS dissociation in water (~2.7), which is surprising as kinetic isotope effects (KIE) are expected to go *down* as the reaction asymmetry increases (or the reaction barrier is reduced). The present results show that diffusion of the reactants in fact plays a minor role at the base concentrations used in that study[21], and that the large difference in PT/DT rates can be explained from the isotope effect in the proton/deuteron conduction through the intervening H_2O/D_2O molecules.

In recent femtosecond mid-infrared spectroscopic studies by the groups of Pines and Nibbering it was also found that the SCK framework does not provide a complete description of the observed proton-transfer dynamics[22-26]. Our results are consistent with this finding; however, our observations of the continuum due to the loosely-bound proton have lead to quite different conclusions regarding the PT mechanism in particular and the appropriate framework for understanding PT reaction dynamics in general. In the work on HPTS-Acetate (or n-chloroAcetate) in aqueous solution performed by the Pines and Nibbering groups, the approach taken was to introduce several sub-populations (of empirically determined magnitude) that were handled outside of the SCK framework. In studies on acetate and chloro-acetate, one of the additional sub-populations was a metastable reaction intermediates of the type: PTS-H_3O^+-(chloro)acetate. The presence of only a single water molecule in the reactive loose complexes of HPTS and acetate/chloro-acetate was inferred from the presence of a transient narrow absorption band that was assigned to the protonic vibration of a PTS-H_3O^+-(chloro)acetate intermediate. In this study diffusive motion of the reactants was thought to be essential

for reactant separations larger than one water molecule. In studies on a weaker base, trichloroacetate, similar data suggested that the reaction involves not one, but several loose complexes that differ in the number of water molecules separating HPTS and the base[26]. No evidence for such 'long-range' PT, however, was found for acetate and chloroacetate. This finding is perhaps surprising, since it suggests that PT between HPTS and the weaker base (tri-chloro-acetate) involves longer-range reaction pathways than does PT between HPTS and the stronger bases (acetate and chloroacetate).

In the current work we find no evidence for intermediates in the reaction between HPTS and acetate. With acetate as a base, there is observable delay between the proton leaving the HPTS molecule (leading to the rise of the conjugate photo-base) and the arrival of the proton at the base (leading to the rise of acetic acid); i.e. the PT occurs rapidly, and there is no buildup of a partially charge-transferred intermediate. We also find that PT in this system is essentially long-range in character, involving reaction pathways with acid-base separated by 1-5 water molecules, not just one. In fact, we find that such short-range PT is inconsistent with our data. In the framework proposed here there is no *apriori* distinction between particular configurations or population types, the alternative pursued has been to propose that PT occurs at a distance dependent rate. All configurations with HPTS and acetate connected through the water H-bond network are in principle reactive. However, with every additional water molecule separating the acid and the base, the solvent configurations that facilitate rapid conduction of the protonic charge to the base become more unlikely. The larger the donor-acceptor distance, the longer the system has to wait before an activated solvent configuration arises that allows for the rapid conduction of the proton from the acid to the base. When analyzed in such a

framework, the data show that translational diffusion of the reactants plays only a limited role in the dynamics at high base concentrations (> 1M). The solvent fluctuations that facilitate long-range intermolecular PT and the distribution of intermolecular separations are much more important in determining the effective rate.

The present results are of also of relevance for other important systems involving PT. For instance, there are many (inhomogeneous) chemical and biological systems where the separation between the acid and the base is less than five water molecules and/or where water molecules are more ordered than in bulk liquid water[35]. It has been proposed that PT in these systems also proceeds via Grotthuss conduction. The same mechanism has also been invoked to explain many Excited-State Intramolecular PT (ESIPT) reactions[36] with little direct experimental evidence for this interpretation. Our results show the significant degree to which long-range PT between functional groups can be facilitated by the intervening water (and its fluctuations).

Conclusions

We studied the mechanism of proton transfer (PT) in aqueous environments between the photoacid 8-hydroxy-1,3,6-pyrenetrisulfonic acid (HPTS) and acetate. By directly probing the broadband infrared absorption of the proton it was possible to follow the intermolecular PT reaction along its trajectory from its initial loosely bound state localized primarily near the HPTS donor to its eventual position on the acetate acceptor.

This data has motivated a new model for proton transfer in liquid water that includes the site-specific nature of the PT reaction and allows for long-range transfer of the proton through the H-bond network of water. We find that the rate of proton transfer

is determined by the number of water molecules separating the acid and the base and the hydrogen-bond network fluctuations that facilitate the long range transfer. The rate of PT is found to be consistent with a Grotthuss-like mechanism, in which the transfer of the protonic charge between the donor-acceptor pair proceeds similarly to proton diffusion in bulk water. We find that translational diffusion of the reactants does not play a significant role in the reaction for configurations with HPTS-acetate separated by less than 5 water molecules. This mechanism is consistent with previous spectroscopic observations and fully explains the observed isotope effect and concentration dependence of the proton transfer.

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32. The root-mean-square-length over which acetate molecules diffuse in a time interval of 10 ps is less than the distance separating two water molecules.

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Figure Captions

Figure 1. HPTS acid dissociation. a) Acid dissociation viewed through the vibrational modes of the aromatic ring structure. The band that grows in at 1503 cm^{-1} marks when the proton leaves the active site of the HPTS molecule. **b)** Comparison of the dynamics of the deprotonation of HPTS with the relaxation of the IR continuum signal.

Figure 2. HPTS concentration dependence of the proton continuum decay (HPTS in H$_2$O). At HPTS concentrations higher than ~20mM self-quenching competes with acid dissociation as a de-excitation channel. At a HPTS concentration of 50mM, this leads to a complete decay of the continuum signal similar to that observed in previous work[24].

Figure 3. Intermolecular DT from the perspective of the deuteron.   Transient spectra showing the progress of the ESPT reaction between HPTS and acetate (2M) in D$_2$O solution. The IR continuum signal due to the loosely bound deuteron is observed within our experimental temporal resolution (~200 fs), and decays on the same timescale as the acetic acid band grows in.

Figure 4. Isotope effect in ESPT between HPTS and acetate in H$_2$O and D$_2$O solutions. Decay curves for the proton and deuteron continuum in 10 mM HPTS, 2 M acetate solutions in H$_2$O/D$_2$O. Early time dynamics (inset) are fit to single exponentials functions. The single exponential time constants are 4.5 ps (proton) and 6.3 ps

(deuteron), showing an isotope effect of ~1.4. The solid curves are calculated using the Grotthuss hopping model described in the text.

Figure 5. ESPT between HPTS and Acetate in aqueous solution: Concentration dependence. a) Acetate concentration dependence of deuteron transfer (in D_2O). **b)** Acetate concentration dependence of proton transfer (in H_2O). The solid curves are calculated with the Grotthuss hopping model described in the text

Figure 6. Grotthuss hopping model of PT in aqueous solution. Schematic picture of proton transfer from HPTS to acetate via a hydrogen-bonded (black dotted lines) water network. Proton transfer results from the migration of the protonic charge between donor and acceptor along the connecting hydrogen bonds via a Grotthuss-like mechanism (blue arrows).

Figure 7. Comparison of Grotthuss and SCK models. The decay of the deuteron continuum (HPTS survival probability) for HPTS in D_2O at acetate concentrations of 1M, 2M and 4M are compared with calculations using the Grotthuss hopping and SCK models. Two SCK decay curves are shown, one for the on contact rate parameter $k_o = 4 \times 10^{10}$ $M^{-1}s^{-1}$ and one for $k_o = 8 \times 10^{10}$ $M^{-1}s^{-1}$ (other SCK model parameters are described in the text). The SCK model is unable to reproduce the strong nonexponentiality of the data over the first 40 ps.

Figure 8. Proton/Deuteron transfer reaction pathways. The fraction of intermolecular PT/DT events that occur to each solvation shell. **a)** 2M acetate. **b)** 4M acetate. Also shown is the initial (statistical) distribution of acetate molecules. The small difference between this distribution and the distribution of proton/deuteron transfer pathways illustrates the limited degree to which diffusion of the reactants plays a role in the proton/deuteron transfer.
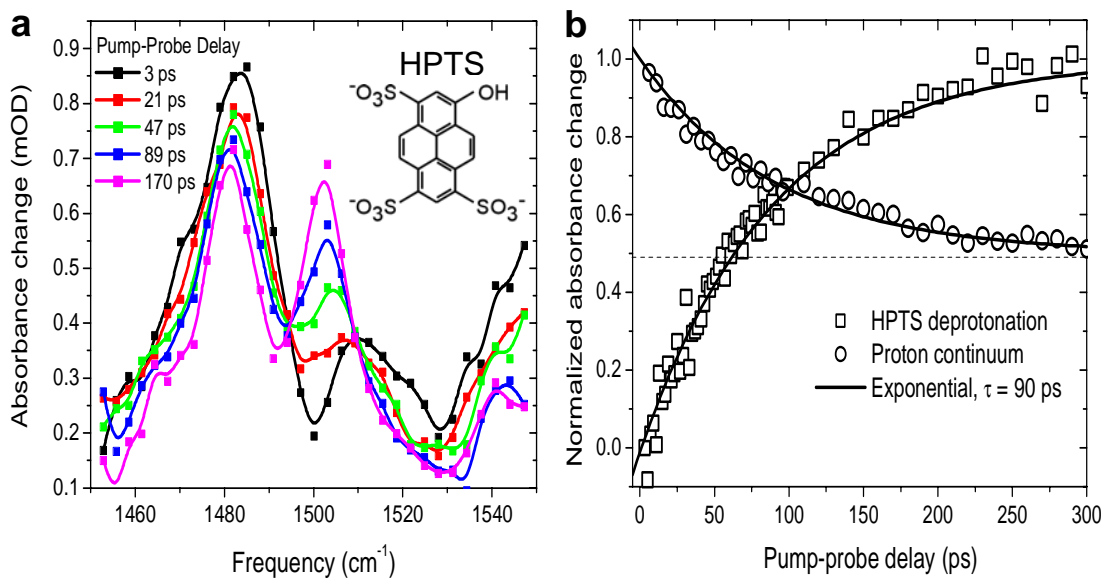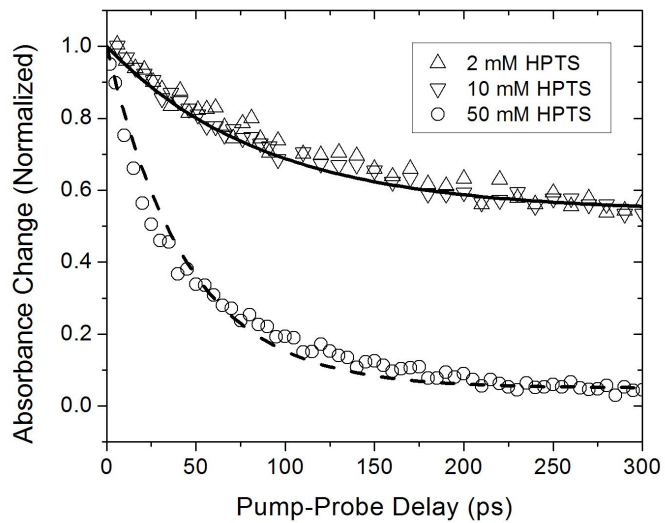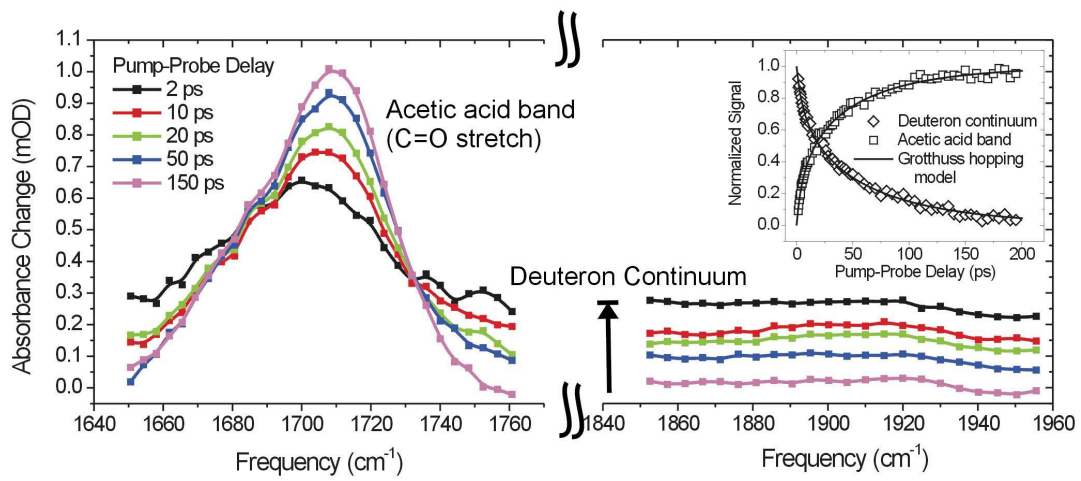
a — Pump-Probe Delay: 3 ps, 21 ps, 47 ps, 89 ps, 170 ps; HPTS structure with ^-O_3S, OH, ^-O_3S, SO_3^- groups; Absorbance change (mOD) vs Frequency (cm^{-1})

b — Normalized absorbance change vs Pump-probe delay (ps); HPTS deprotonation, Proton continuum, Exponential, τ = 90 ps

Figure 1.

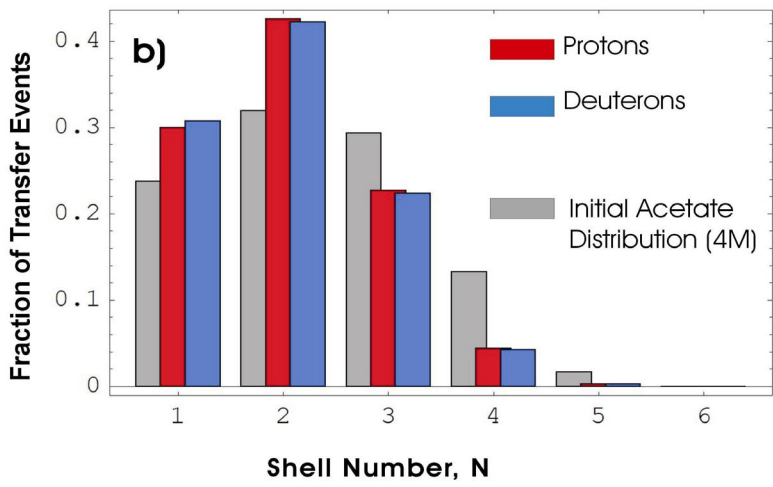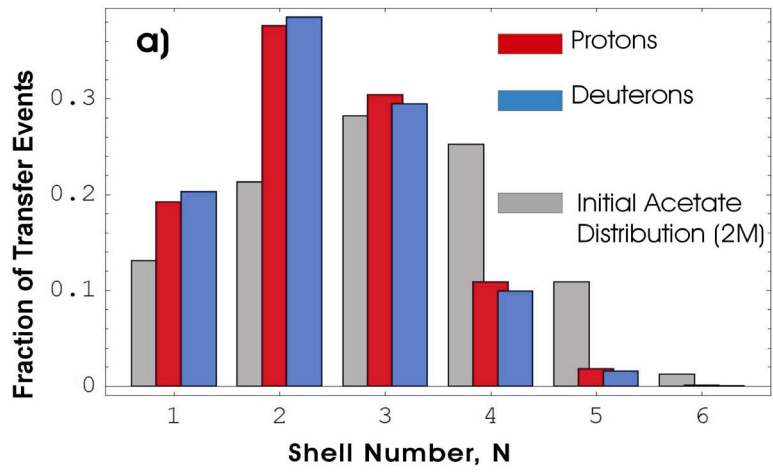**Figure 2.**

Figure 3.
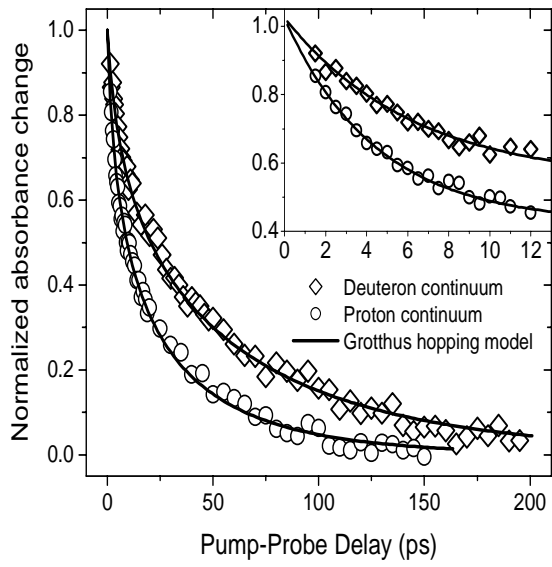
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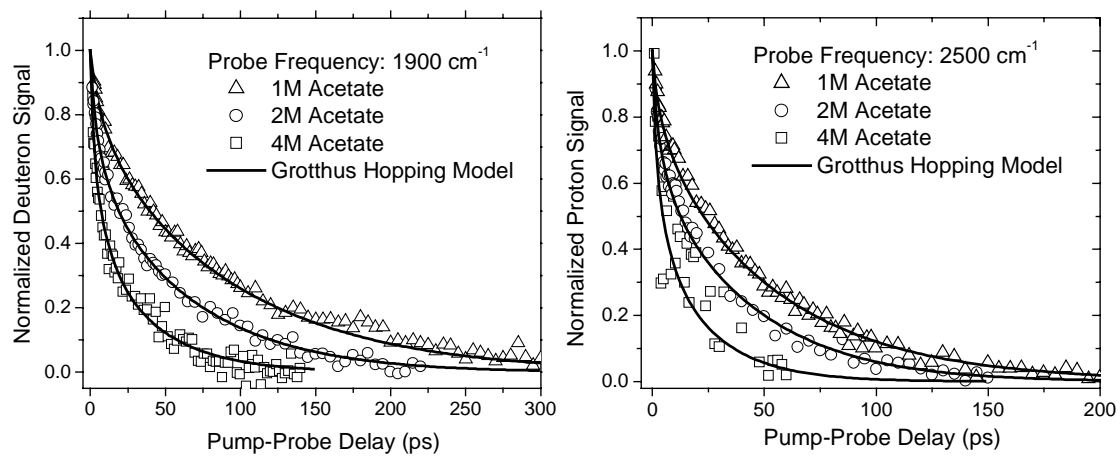
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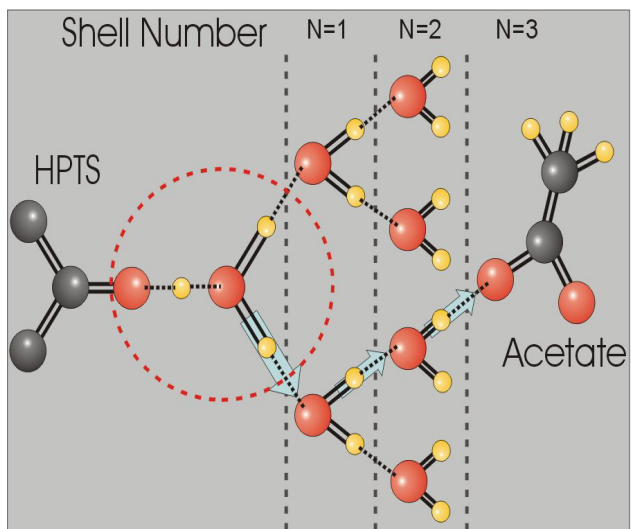
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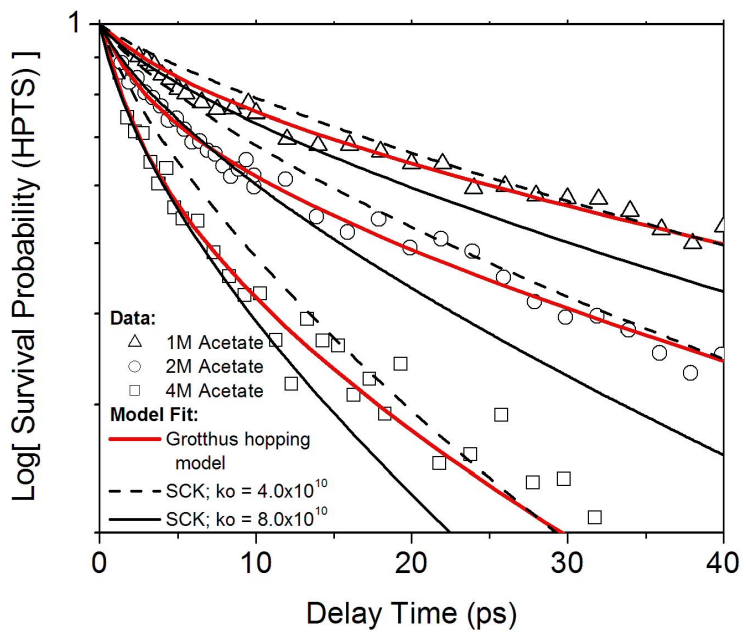
Figure 7.

Figure 8.

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