THE JOURNAL OF PHYSICAL CHEMISTRY B

Article

pubs.acs.org/JPCB

Ground-State Proton Transport along a Blended-Alcohol Chain: Accelerated by Accumulated Proton-Donating Ability

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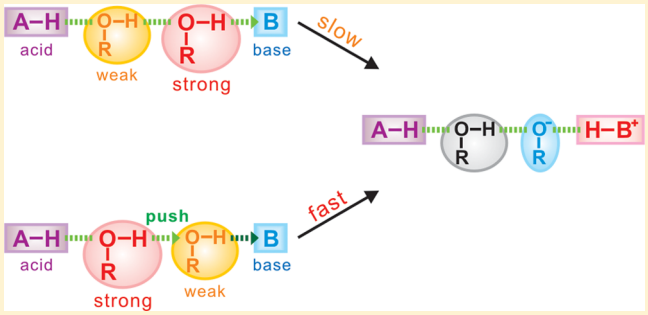
Supporting Information

ABSTRACT: The ground-state reverse proton transfer (GSRPT) of 7-hydroxyquinoline (7HQ) along a hydrogen (H)-bonded mixed-alcohol chain made of different two alcohol molecules having dissimilar proton-donating abilities, designed as a biomimetic system of a proton wire composed of various amino acids, has been investigated in nonpolar aprotic media of *n*-alkanes using time-resolved transient-absorption spectroscopy with variation of alcohol combinations and medium viscosities. Solvent-inventory experiments have been carried out by varying the composition of alcohols systematically in the heterogeneous H-bonded alcohol chain to understand the molecular dynamics and the elementary mechanisms of GSRPT. Similarly to excited-state proton transfer, GSRPT takes place concertedly without accumulating any reaction intermediate but asymmetrically via a rate-determining tunneling process, and GSRPT is accelerated by the accumulated proton-donating abilities of two alcohol molecules participating in the H-bond chain by push-ahead effect. However, in the ground state, the reorganization of the H-bond bridge in a cyclic 7HQ·(alcohol)$_2$ complex to form an optimal precursor configuration for efficient proton tunneling takes place prior to intrinsic proton transfer, and the rate constant of GSRPT is governed mainly by configurational optimization. Consequently, the large contribution of the configurational optimization to GSRPT leads to the weaker push-ahead effect and the less-asymmetric character of GSRPT than the respective ones of excited-state proton transfer whose rate constant is determined mostly by tunneling.



1. INTRODUCTION

Intercellular signal transduction, which controls vital phenomena of living organisms, takes place by the chemical and physical interactions among biomolecules such as proteins, carbohydrates, nucleic acids, and ions.[1−4] Proteins, particularly, are at the center of intercellular signal transduction, and their binding properties determine the functions of biological systems.[1−3] On the other hand, principal biological processes of proteins usually involve prototropic reactions, and proton transfer plays a crucial role in most of prototropic biological processes, e.g. enzymatic catalysis and proton pumping through membrane protein channels.[5−8] Biological proton relay often occurs through a long-ranged hydrogen (H)-bonded chain consisting of various amino acids and water, which is generally called a proton wire.[7−11] Accordingly, mechanistic and dynamic studies on such long-ranged proton relay in proteins should be performed preferentially to understand the functions and the structural dynamics of proteins. Nonetheless, due to the structural complexity and the massive size of proteins as well as the technical difficulties of in vivo experiments, it is tremendously difficult to investigate the molecular mechanism and dynamics of biological proton transfer along a proton wire composed of diverse amino acids directly.[6−12] Thus, a simple biomimetic system is demanded to explore multiple proton transport at the molecular level. Proton transport is commonly mediated by polar solvent molecules which can accept or donate protons, and its dynamics is determined mainly by the structure, the size, and the motion of mediating solvent molecules.[6,13−16] In this regard, we have focused on the role of mediating solvent molecules, which would be amino acids in biological proton-relay systems, so that we have employed a heterogeneous H-bonded chain consisting of different solvent molecules as a model system of the proton wire.

Hydroxyquinolines, having both photoacidic enol and photobasic imine, have been attracting considerable attention because they are good experimental models to study biological proton-relay processes.[17−28] 7-Hydroxyquinoline (7HQ), in particular, is well-known to undergo excited-state proton transfer (ESPT) via H-bonded solvent molecules;[20−26] because two prototropic groups of 7HQ, which are photoacidic enol and photobasic imine, are far from each other, they cannot donate or accept a proton directly. Accordingly, protic solvent molecules such as water or alcohol molecules are required to mediate proton transfer from the enolic group to the imino

Received: June 13, 2012
Revised: July 25, 2012
Published: August 16, 2012

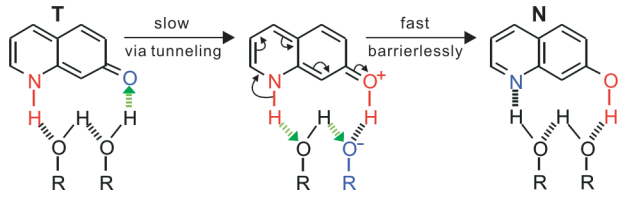
   dx.doi.org/10.1021/jp305769n | *J. Phys. Chem. B* 2012, 116, 10915−10921

group of 7HQ.[20−26] It has been already reported many times that in a nonpolar aprotic medium, a 7HQ molecule and two protic solvent molecules form a H-bonded cyclic 1:2 complex stably in the ground state.[22,27] 7HQ in an alcohol-added *n*-alkane undergoes ESPT along a H-bonded alcohol chain,[21−23,26] so that intrinsic proton-transfer dynamics can be explored directly without interference by solvent reorganization to form the cyclic 7HQ·(alcohol)$_2$ complex. Thus, cyclically complexed 7HQ·(alcohol)$_2$ can be a good biomimetic system to study the molecular mechanism of solvent-mediated multiple proton transfer. We have already reported that in the ESPT of the cyclic 7HQ·(alcohol)$_2$ complex, the proton-donating ability (acidity) rather than the proton-accepting ability (basicity) of the alcohol determines the rate constant of ESPT mainly.[22,23] In other words, proton transfer from an adjacent alcohol molecule to the imino group of 7HQ, which is the rate-determining step of ESPT, takes place first, and subsequent rapid proton relay from the enolic group of 7HQ to the deprotonated alkoxide moiety completes ESPT (Scheme S1 of the Supporting Information). Considering this result which designates an important role of the alcohol acidity in ESPT, we have previously investigated the ESPT of 7HQ along a mixed-alcohol chain of two different alcohol molecules having dissimilar acidities, i.e., proton-donating abilities, and reported the result to *J. Am. Chem. Soc.* in 2010.[23] The result has revealed that the accumulated proton-donating abilities of two alcohol molecules in the H-bonded chain of a cyclic 7HQ·(alcohol)$_2$ complex induce the acceleration of ESPT; at the rate-determining step which is the protonation of the imino group, proton donation of the adjacent alcohol molecule to the imino group is pushed by the other alcohol molecule bound to the enolic group from the backside along the proton-relay pathway, and we have described this as the push-ahead effect.[23]

While the dynamics of ESPT has been extensively investigated for various photoacids,[13−28] the dynamics of ground-state proton transfer has been scarcely explored due to experimental difficulty and explanatory intricacy.[26,29−31] In an exoergic reaction having an asymmetric double potential well, ESPT is usually expedited by a tunneling process and completed within a nanosecond.[22−24] In contrast, most of the molecules showing ultrafast ESPT kinetics undergo slow ground-state proton transfer on a time scale of microseconds.[26,32,33] In our previous work,[31] proton-inventory experiments for the ground-state reverse proton transfer (GSRPT) of cyclic 7HQ·(alcohol)$_2$ complexes have been reported; GSRPT takes place on a time scale of microseconds and its dynamics is controlled mostly by configurational optimization prior to intrinsic proton tunneling whereas the dynamics of ESPT is governed mostly by tunneling.[31]

As already mentioned above, the ESPT of 7HQ along a blended-alcohol chain has been found to be accelerated by push-ahead effect.[23] However, such acceleration has not been observed in the excited-state deuteron transfer;[34] because the mass of a deuteron is larger than that of a proton and the energy barrier of deuteron transfer is higher than that of proton transfer, it is hard for a deuteron to transfer via tunneling even in the excited state. Moreover, due to the low H-bonding ability and the weak acidity of deuterated alcohols, two deuterated-alcohol molecules participating in the H-bond chain hardly accumulate their deuteron-donating abilities.[34] Then, it would be an issue of whether the GSRPT of 7HQ along a mixed-alcohol chain is accelerated by the push-ahead effect. Thus, here we report the GSRPT dynamics of cyclically H-bonded 7HQ·(alcohol)$_2$ complexes (Scheme 1) by performing solvent-inventory experiments, which are altered proton-inventory experiments, with variation of the composition of alcohols. To tell the conclusion briefly first, similarly to the ESPT,[23] the GSRPT of the cyclic 7HQ·(alcohol)$_2$ complex takes place concertedly without accumulating any intermediate species but asymmetrically with the rate-determining tunneling process, and GSRPT is also accelerated by the accumulated proton-donating abilities of alcohol molecules participating in the H-bond bridge of 7HQ·(alcohol)$_2$. However, in the ground state, the reorganization of the H-bond bridge in the cyclic complex to form an optimal precursor configuration for efficient proton tunneling is more inevitable prior to intrinsic proton transfer. As a result, the large contribution of configurational optimization to GSRPT leads to the weaker push-ahead effect and the less-asymmetric character of GSRPT than the respective ones of ESPT.

Scheme 1. GSRPT of 7HQ along H-Bonded Alcohol Molecules



2. EXPERIMENTAL SECTION

7HQ (99%) was used as purchased from Acros, and alcohols (anhydrous, ≥99.5%) and *n*-alkanes (anhydrous, ≥99%), purchased from Sigma-Aldrich, were stored over molecular sieves of 4 Å prior to use. Alcohol molecules of 7HQ·(alcohol)$_2$ were varied for solvent-inventory experiments by changing the mole fractions of two different alcohols in a *n*-alkane containing 7HQ; the concentration of 7HQ was 0.2 mM, and the total concentration of two alcohols was kept at 600 mM. Time-resolved transient-absorption kinetic profiles were obtained by monitoring transmittance changes of a Xe lamp (Spectral Energy, LH150) beam of 75 W passing through a sample, which was excited at 355 nm by a pulsed beam (1 mJ, 6 ns, 10 Hz) from a Nd:YAG laser (Quantel, Brilliant). The wavelength of the Xe lamp beam was selected by using a monochromator of 0.15 m (ARC, SP150) and a double monochromator of 0.20 m (Kratos, GM200). The probe beam was detected with a photomultiplier tube (Hamamatsu, R928) and digitized with an oscilloscope of 1 GHz (Lecroy, Wavepro950). Samples were flowed during kinetic measurements using a peristaltic pump (ISCO, 1612) to avoid sample decomposition. Kinetic profiles were collected at intervals of 5 nm to generate time-resolved transient-absorption spectra. All measurements were carried out at room temperature.

3. RESULTS AND DISCUSSION

The steady-state absorption spectra of 7HQ in alcohol-added *n*-heptane show only the absorption band of the normal species (**N**) of 7HQ with the maximum around 330 nm and shift to the red, losing their vibronic structures, with the concentration increment of the alcohol (Figure S1 of the Supporting Information). This suggests that 7HQ molecules associate with alcohol molecules via H bonding to form 7HQ−alcohol

dx.doi.org/10.1021/jp305769n | *J. Phys. Chem. B* 2012, 116, 10915−10921

complexes in *n*-heptane.[22,23,31] The formation constant (K) of H-bonded 7HQ–alcohol complexes can be deduced from linear relationship between the squared reciprocal molar concentration of an alcohol ($[\text{alcohol}]^{-2}$) versus the reciprocal of absorbance (A^{-1}),[28] indicating that the association of a 7HQ molecule with two alcohol molecules produces a 7HQ·$(\text{alcohol})_2$ complex (see the Supporting Information for details). Of note is that the most stable structure of the 7HQ·$(\text{alcohol})_2$ complex in the ground state is reported to have the cyclic geometry.[27] Table S1 of the Supporting Information shows that the K value of the 7HQ·$(\text{alcohol})_2$ complex decreases with the structural complexity of the H-bonding alcohol but increases with the proton-donating ability (α), rather than the proton-accepting ability (β), of the alcohol. This designates that not only the structural complexity but also the α value of the alcohol plays an important role in the formation of the cyclic 7HQ·$(\text{alcohol})_2$ complex. On the other hand, in spite of the increasing concentration of an alcohol added in *n*-heptane, the absorption band of the tautomeric species (**T**) of 7HQ, which presumably grows around 410 nm,[30,35] does not appear.[23,31] This implies that although cyclic 7HQ·$(\text{alcohol})_2$ complexes exist stably in the ground state, they do not undergo ground-state proton transfer to generate **T**.[21,28] However, upon excitation of the cyclic 7HQ·$(\text{alcohol})_2$ complex at 345 nm, not only **N*** fluorescence at 370 nm but also **T*** fluorescence at 530 nm appears; this suggests that the cyclic complex undergoes proton transfer in the excited state.[22,23,31] **T*** fluorescence grows as the α value of the alcohol increases, indicating that the 7HQ·$(\text{alcohol})_2$ complex having the more acidic alcohol can undergo ESPT more facilely.[22,23,31] The relaxation of **T*** generated by the ESPT of **N*** brings about the ground-state population of **T** transiently, and **T** undergoes ground-state proton transfer to replenish photodepleted **N**. Thus, by investigating **T**-depletion kinetics, we can study the GSRPT dynamics of 7HQ along a H-bonded alcohol chain (Scheme 1).

Figure 1 shows the time-resolved transient-absorption spectra of 7HQ·$(\textit{tert}\text{-butanol})_2$ in *n*-heptane; the transient

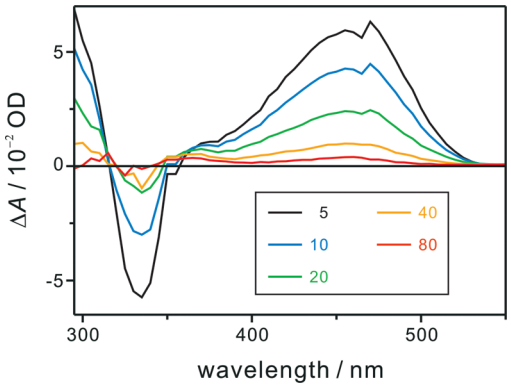


Figure 1. Time-resolved transient-absorption spectra, excited at 355 nm, of 0.2 mM 7HQ in *n*-heptane having *tert*-butanol of 600 mM. Time delays after excitation are indicated inside in units of microseconds.

absorption band at 450 nm, which is attributed to ground-state **T**, diminishes with increasing delay time, whereas the absorption bleach band at 330 nm, which is ascribed to ground-state **N**, recovers with delay time. The spectral features as well as the band maxima of the transient-absorption spectra do not vary with delay time, and thus, we infer that only one transient species, i.e., **T**, exists in the ground state. Figure 1 also shows that the bleach band of **N** at 330 nm recovers concomitantly with the decay of the transient **T** band at 450 nm; the recovery time of the bleach band at 330 nm, arising from photodepleted **N**, matches well with the fast-decay time of **T** at 450 nm (Figure S2 of the Supporting Information), indicating that the depletion of **T** replenishes **N** directly. In other words, the GSRPT of 7HQ along a H-bonded alcohol chain takes place in a concerted manner, rather than in a stepwise manner, without accumulating any intermediates. Accordingly, we can infer that the reciprocal of the observed decay time of **T** at 450 nm corresponds to the rate constant of the GSRPT (k_{pt}) of 7HQ·$(\text{alcohol})_2$ complexes. On the other hand, the slow-decay time (100 μs) of **T** at 450 nm arises from the relaxation of triplet-state **T**.[31] The kinetics as well as the existence of triplet-state **T** has been already discussed in our previous work,[31] so that we neglect the slow-decay component of **T** with a small fractional amplitude in the present work.

Time-resolved transient-absorption kinetic profiles of 7HQ·$(\text{alcohol})_2$ in *n*-heptane with variation of alcohols are shown in Figure 2a. The decay time of **T** observed at 450 nm,

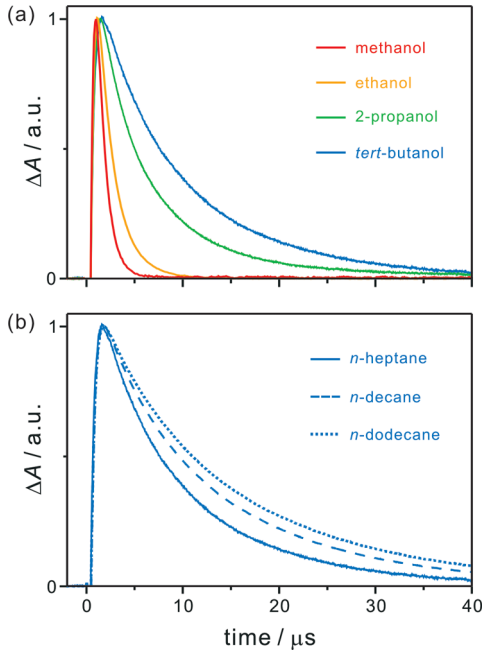


Figure 2. Time-resolved transient-absorption kinetic profiles of 0.2 mM 7HQ in *n*-heptane having indicated alcohols (a) and those of 0.2 mM 7HQ in indicated *n*-alkanes having *tert*-butanol (b). The alcohol concentration of each sample was kept at 600 mM, and samples were excited at 355 nm and probed at 450 nm.

i.e., the GSRPT time of 7HQ·$(\text{alcohol})_2$, does not vary with the alcohol concentration, supporting that the cyclic complex of 7HQ·$(\text{alcohol})_2$, which can undergoes ESPT to form **T***, exists already at the moment of excitation; the collision-induced formation of the cyclic 7HQ·$(\text{alcohol})_2$ complex does not occur to conduct ESPT within the lifetime of **N***. Considering that the decay time of **T** (k_{pt}^{-1}) becomes shorter with the increasing α value of the alcohol in the cyclic complex (Table S1 of the Supporting Information), we suggest that proton transfer from the adjacent alcohol molecule to the keto group of **T** is the rate-determining step of the GSRPT of 7HQ·$(\text{alcohol})_2$ (Scheme

dx.doi.org/10.1021/jp305769n | J. Phys. Chem. B 2012, 116, 10915–10921

1). If the rate-determining step was the proton transfer from the amino group of **T** to the directly H-bonded alcohol molecule, k_{pt} should depend on the β value, rather than the α value, of the alcohol, and *tert*-butanol having the largest β value among all of the employed alcohols should give the shortest GSRPT time. Thus, the proton donation of the alcohol molecule H-bonded directly to the keto group of **T** plays a key role in GSRPT (see below). We inform that this is in line with the ESPT of 7HQ·(alcohol)$_2$ in which the rate constant is also determined by the α value, not the β value, of the alcohol.[23]

It is noteworthy that in alcohol-added *n*-heptane, the GSRPT time of 7HQ is longer by 4 orders of magnitude than the ESPT time (Table S1 of the Supporting Information).[23] 7HQ is less polar in the ground state than in the excited state while the energy barrier of proton transfer is larger in the ground state than in the excited state; with the photoexcitation of 7HQ, both the acidity of the enolic group and the basicity of the imino group increase immensely. Accordingly, it is hard for the cyclic complex of 7HQ·(alcohol)$_2$ to undergo proton transfer in the ground state without any assistance to make proton transfer operative. In other words, the reorganization motions of the H-bond bridge in the cyclic complex to form an optimal precursor configuration having proper bond angles and lengths are required prior to intrinsic proton transfer in the ground state (see below). The decay time of **T** becomes longer with the viscosity of the host medium, i.e., *n*-alkane (Figure 2b and Table S1 of the Supporting Information). In the viscous medium, solvent fluctuation, which plays a decisive role in the reorganization of the H-bond bridge in the cyclic 7HQ·(alcohol)$_2$ complex, is reduced, so that configurational optimization prior to proton tunneling is slowed down. As a result, the GSRPT time of 7HQ·(alcohol)$_2$ increases with the medium viscosity; the overall rate of proton transfer is governed mainly by configurational optimization in the ground state. Intrinsic proton transfer via tunneling is isotopically sensitive whereas configurational optimization for efficient proton tunneling is isotopically insensitive. Thus, configurational optimization is orthogonal to intrinsic proton transfer in the reaction coordinates of the potential hypersurface. Accordingly, as the contribution of configurational optimization to GSRPT increases, the contribution of tunneling to GSRPT decreases relatively.[30,31]

As mentioned above, in biological systems, proton relay often takes place through a proton wire made of H-bonded diverse amino acids.[7−11] Thus, considering such proton wire, we have employed a blended-alcohol chain composed of two different alcohol molecules having dissimilar acidities, as a simple biomimetic system. There are two possible cases in accordance with the sequence of two different alcohol molecules in the H-bonded chain of a cyclic 7HQ·(alcohol)$_2$ complex: which one of two alcohol molecules having dissimilar α values is H-bonded directly to the keto group of **T**. One case is that the relatively strong-acidic alcohol molecule (**S**) having the larger α value is bound to the keto group to donate a proton, and the other case is that the relatively weak-acidic alcohol molecule (**W**) having the smaller α value is bound to the keto group (Figure 3). Then, one would wonder whether the rate constants of those two cases are the same. Besides, if the rate constants of two cases are different from each other, it would be a major concern which case takes place faster. Recall that the ESPT of 7HQ along a H-bonded mixed-alcohol chain has been already reported to be accelerated by the accumulated proton-donating abilities of alcohol molecules;[23] the rate constant of

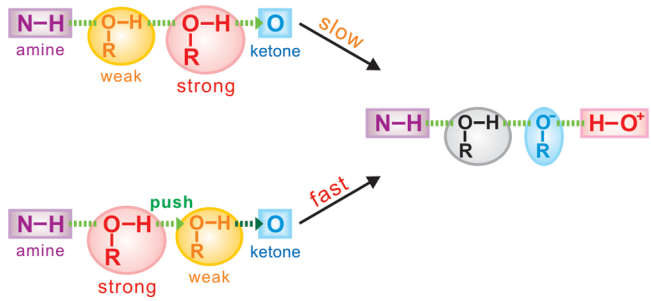


Figure 3. Schematic diagram showing the acceleration of proton transfer via a blended-alcohol chain by push-ahead effect. At the rate-determining step that is the proton acceptance of a base from a directly H-bonded alcohol molecule, when the relatively weak-acidic alcohol molecule (**W**) is bound to the basic keto group directly, the accumulated proton-donating abilities of two alcohol molecules accelerates proton transfer because the deprotonation of **W** is pushed by the relatively strong-acidic alcohol (**S**) from the backside along the proton-transfer pathway. However, in the opposite case, i.e., when **S** is bound to the keto group directly, **W** hardly helps the deprotonation of **S**, so that **S** donates a proton for itself.

the ESPT is larger when **W**, rather than **S**, is H-bonded directly to the imino group of 7HQ to donate a proton because the proton donation of **W** to the imino group is pushed by **S** from the backside along the ESPT pathway to accumulate proton-donating abilities of **S** and **W**. Then, it would attract great attention to whether such acceleration of proton transfer by the push-ahead effect also appears in the ground-state. Hence, in the present work, we have investigated the GSRPT dynamics of 7HQ along a blended-alcohol chain using solvent-inventory experiments. To tell the conclusion first, similarly to ESPT,[23] the k_{pt} value of the latter case, in which **W** is bound to the keto group, is larger than the k_{pt} value of the former case, in which **S** is bound to the keto group (Figure 3). Considering the same result to ESPT, we suggest that such push-ahead effect is also operative in GSRPT. However, the strength of the push-ahead effect is reduced in GSRPT compared with that in ESPT because configurational optimization occurring prior to intrinsic proton transfer is more decisively required in the ground state (see below).

To understand the molecular mechanism and dynamics of GSRPT along a mixed-alcohol chain, we have performed solvent-inventory experiments,[23,34] which are altered proton-inventory experiments,[22,24,31,36−39] for the GSRPT of 7HQ·(alcohol)$_2$ by varying the mole fractions of two alcohols systematically in a sample. Five combinations of two different alcohols having dissimilar α values are employed: methanol and ethanol (**C1**), methanol and 2-propanol (**C2**), methanol and *tert*-butanol (**C3**), ethanol and *tert*-butanol (**C4**), and 2-propanol and *tert*-butanol (**C5**). In proton-inventory experiments, three protic hydrogen atoms are varied,[36−39] whereas in solvent-inventory experiments, two alcohol molecules (**S** or **W**) as solvent molecules mediating GSRPT are varied.[23,34] Figure 4 and Figure S3 of the Supporting Information show that the decay of transient **T** absorption becomes slower with the increment of X_W, which is [**W**]/([**S**] + [**W**]), indicating that k_{pt} decreases as X_W increases. In proton-inventory experiments,[36−39] all the three protic hydrogen atoms participating in proton transfer should be considered because any of them can be either ^{1}H or ^{2}H. However, in solvent-inventory experiments, the proton of the amino group of **T** remains the same regardless of which alcohol molecules are H-bonded to

dx.doi.org/10.1021/jp305769n | J. Phys. Chem. B 2012, 116, 10915−10921

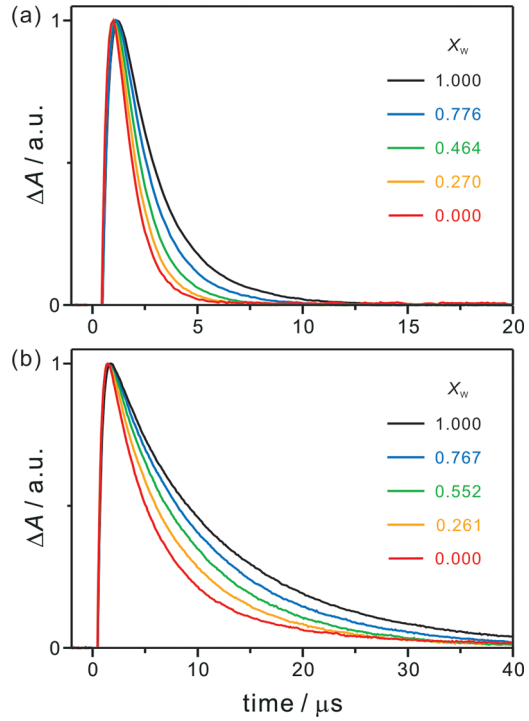


Figure 4. X_W-dependent transient-absorption kinetic profiles of 0.2 mM 7HQ in *n*-heptane having methanol and ethanol (a) and 2-propanol and *tert*-butanol (b). The total concentration of two alcohols in each sample was kept at 600 mM, and samples were excited at 355 nm and probed at 450 nm.

7HQ.[23,34] Thus, only two alcohol molecules are varied in the solvent-inventory experiments although all the three protic hydrogen atoms transfer along a H-bonded chain. Accordingly, 7HQ·(alcohol)$_2$ can have four different types of alcohol exchange: **SS**, **WS**, **SW**, and **WW**, where two successive characters represent two alcohol molecules H-bonded to the amino group of **T** in turn (Scheme 1 and Figure 3).

The k_{pt} values of the above four types of 7HQ·(alcohol)$_2$ are denoted as k^{SS}, k^{WS}, k^{SW}, and k^{WW}, respectively. As $X_S = 1 - X_W$, we can deduce eqs 1 and 2 in accordance with the alcohol H-bonded to the keto group of 7HQ; the rate-determining step of GSRPT is the proton donation of the adjacent alcohol molecule to the keto group.

$$d[*S]/dt = -\{(1 - X_W)k^{SS} + X_W k^{WS}\}[*S] \quad (1)$$

$$d[*W]/dt = -\{(1 - X_W)k^{SW} + X_W k^{WW}\}[*W] \quad (2)$$

where * denotes either **S** or **W**. Because the association constant, i.e., *K*, of 7HQ·(alcohol)$_2$ varies with alcohols (Table S1 of the Supporting Information), we have calibrated X_S and X_W with consideration of different *K* values of **S** and **W**.[23,34] When X_W is 0.5, the calibrated value becomes 0.464 for **C1**, 0.452 for **C2**, 0.405 for **C3**, 0.440 for **C4**, and 0.451 for **C5**. The decay component of transient **T** absorption (k_{pt}^{-1}) can be further decomposed into two decay components of k^S and k^W as eq 3.

$$\exp(-k_{pt}t) = X_S \exp(-k^S t) + X_W \exp(-k^W t) \quad (3)$$

where k^S and k^W consist of the four different k_{pt} values according to eqs 4 and 5, respectively.

$$k^S = k^{SS} + (k^{WS} - k^{SS})X_W \quad (4)$$

$$k^W = k^{SW} + (k^{WW} - k^{SW})X_W \quad (5)$$

The linear correlations of k^S and k^W with calibrated X_W (Figure 5 and Figure S4 of the Supporting Information) yield k^{SS}, k^{WS},

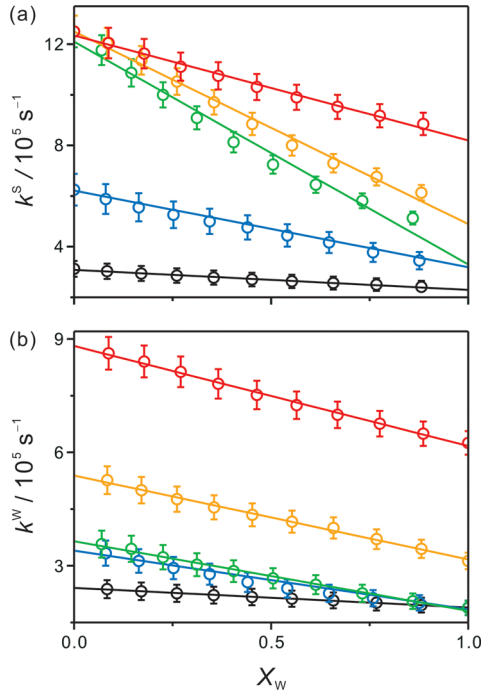


Figure 5. Plots of k^S (a) and k^W (b) with variation of X_W for the GSRPT of 0.2 mM 7HQ in *n*-heptane having diverse alcohol combinations: methanol and ethanol (red), methanol and 2-propanol (yellow), methanol and *tert*-butanol (green), ethanol and *tert*-butanol (blue), and 2-propanol and *tert*-butanol (black). Solid lines are the best linear fittings to obtain k^{SS}, k^{WS}, k^{SW}, and k^{WW}. The total concentration of two alcohols in every sample was kept at 600 mM.

k^{SW}, and k^{WW} for five combinations (Table 1). If GSRPT occurs concertedly and synchronously, then, according to the rule of the geometric mean, $k^{WS} = k^{SW} = (k^{SS}\, k^{WW})^{1/2}$ should hold.[23,34] However, our results show that $k^{WS} \neq k^{SW} \neq (k^{SS}\, k^{WW})^{1/2}$ in all of the five combinations, suggesting that although the GSRPT of 7HQ·(alcohol)$_2$ occurs concertedly without accumulating any intermediates, the GSRPT takes place asymmetrically with a rate-determining tunneling process, similarly to ESPT.[23]

Recall that on the basis of α-dependent k_{pt}, the rate-determining step of the GSRPT of cyclic 7HQ·(alcohol)$_2$ complexes is considered to be proton transfer from the adjacent alcohol molecule to the keto group (Scheme 1). Accordingly, in the GSRPT of 7HQ along a blended-alcohol chain, at first glance, k^{WS} was seemed to be larger than k^{SW}. However, Table 1 shows that k^{WS} is significantly smaller than k^{SW} for all of the explored alcohol combinations, and this result is in line with ESPT as reported already.[23] Thus, we suggest that similarly to the ESPT,[23] push-ahead effect is also operative in the GSRPT of the cyclic 7HQ·(alcohol)$_2$ complex (Figure 3); in other words, the reaction is accelerated by the accumulated proton-donating abilities of alcohol molecules participating in the H-bonded chain of the cyclic complex. The relative strength of the push-ahead effect can be estimated by comparing the ratios of k^{SW}/k^{WS} (Table 1).[23] All of the ratios are larger than unity for all the explored alcohol combinations in all the three *n*-alkanes, showing that there is significant push-

dx.doi.org/10.1021/jp305769n | J. Phys. Chem. B 2012, 116, 10915−10921

Table 1. Rate Constants Extracted from Solvent-Inventory Experiments for the GSRPT of 7HQ·(alcohol)$_2$ Complexes in *n*-Alkanes Having Various Combinations of Alcohols

medium[a]	alcohol combination[b]	$(k^{SS})^{-1}/\mu s$	$(k^{WS})^{-1}/\mu s$	$(k^{SW})^{-1}/\mu s$	$(k^{WW})^{-1}/\mu s$	k^{SW}/k^{WS}
n-heptane	MeOH and EtOH (**C1**)	0.81	1.22	1.13	1.62	1.08
	MeOH and PrOH (**C2**)	0.80	2.04	1.86	3.16	1.10
	MeOH and BuOH (**C3**)	0.83	3.03	2.74	5.54	1.11
	EtOH and BuOH (**C4**)	1.61	3.14	2.94	5.42	1.07
	PrOH and BuOH (**C5**)	3.24	4.36	4.14	5.28	1.05
n-decane	MeOH and BuOH (**C3′**)	0.90	3.09	2.89	6.16	1.07
n-dodecane	MeOH and BuOH (**C3″**)	0.96	3.16	3.01	6.81	1.05

[a]The viscosities of *n*-heptane, *n*-decane, and *n*-dodecane at 25 °C are 0.39, 0.84, and 1.38 cP, respectively.[40,41] [b]MeOH, EtOH, PrOH, and BuOH indicate methanol, ethanol, 2-propanol, and *tert*-butanol, respectively.

ahead effect. Moreover, as a gap between the α values[42−44] of two alcohols in a combination increases, the ratio increases; this indicates that the dependence of the GSRPT rate constant on the push-ahead effect increases with the gap. On one hand, comparing three combinations of **C3**, **C4**, and **C5** involving *tert*-butanol as **W**, we have found out that the ratio of k^{SW}/k^{WS} increases as the α value of **S** increases; the larger α value **S** has, the stronger the push-ahead effect is. On the other hand, comparing three combinations of **C1, C2,** and **C3** involving methanol as **S**, we have figured out that k^{WS} increases with the increasing α value of **W**. Thus, two alcohol molecules transport protons concertedly by accumulating their proton-donating abilities in the ground state as well as in the excited state, resulting in the acceleration of proton transfer.

It is noteworthy that the strength of the push-ahead effect, i.e., the ratio of k^{SW}/k^{WS}, is slightly weaker in GSRPT than in ESPT,[23] and we attribute this to the large contribution of configurational optimization to GSRPT. It has been reported already that even in the ESPT of 7HQ·(alcohol)$_2$, proton tunneling is vibrationally enhanced by heavy-atom motions and that under the glass temperature of the host medium, ESPT does not occur due to the absence of solvent fluctuation.[22] Thus, in GSRPT whose energy barrier is higher than the barrier of ESPT, the reorganization of the H-bond bridge in the cyclic complex of 7HQ·(alcohol)$_2$ to form an optimal precursor configuration having optimal bond angles and distances is a prerequisite to efficient proton tunneling. On the other hand, the asymmetric character of triple proton transfer has been observed to be weaker in the ground state than in the excited state. As mentioned above, when the rule of the geometric mean, i.e., $k^{WS} = k^{SW} = (k^{SS}\ k^{WW})^{1/2}$, holds, it can be inferred that triple proton transfer takes place in a symmetrically concerted fashion. However, our results show that $k^{WS} \neq k^{SW}$ although GSRPT takes place without accumulating any reaction intermediate. Thus, we have suggested that GSRPT occurs in an asymmetrically concerted manner, not a stepwise manner. Meanwhile, the smaller ratio of k^{SW}/k^{WS} in GSRPT than in ESPT signifies that the k^{SW} value is less different from the k^{WS} value in the ground state than in the excited state.[23] Accordingly, we consider that GSRPT shows less-asymmetric character than ESPT does, and we attribute this to the larger contribution of configurational optimization than the contribution of tunneling in the ground state; intrinsic proton transfer via tunneling, which is isotopically sensitive, is orthogonal to configurational optimization prior to tunneling, which is isotopically insensitive, in the reaction coordinates of the potential hypersurface, so that the contribution of tunneling to GSRPT decreases as the contribution of configurational optimization to GSRPT increases. The result that the ratio of k^{SW}/k^{WS} decreases slightly with the viscosity of the host medium of *n*-alkane (Table 1) also supports the large contribution of configurational optimization to GSRPT. In the more viscous medium, solvent fluctuation, which plays an important role in configurational optimization, is reduced, so that configurational optimization becomes slower.

Considering these results, we conclude that the overall rate constant of the GSRPT of 7HQ along a blended-alcohol chain is dependent mostly on configuration optimization and that the contribution of push-ahead effect to the determination of the proton-transfer rate is relatively reduced in the ground state than in the excited state. We suggest that at the rate-determining step of proton transfer, push-ahead effect assists a proton in passing through the energy barrier via tunneling facilely in both the ground and the excited states. As we have already reported,[34] push-ahead effect has not been observed in deuteron transfer even in the excited state, so that push-ahead effect is considered to be isotope-sensitive. Thus, our suggestion that push-ahead effect gets involved in proton tunneling, which is isotope-sensitive, rather than in configurational optimization, which is isotope-insensitive, is plausible. Our results can give a clue at the molecular level on the fundamental mechanistic elucidation of proton relay through long-ranged solvent networks such as a proton wire consisting of diverse amino acids in biological processes as well as in chemical processes.

4. CONCLUSIONS

The GSRPT of 7HQ along a blended-alcohol chain consisting of different two alcohol molecules with dissimilar acidities has been investigated in *n*-alkanes with variation of alcohol combinations and medium viscosities by conducting solvent-inventory experiments. As a result, it has been found out that GSRPT takes place concertedly without accumulating any reaction intermediate but asymmetrically with a rate-determining tunneling process. Similarly to ESPT, GSRPT has been observed to be accelerated by the accumulated proton-donating abilities of two alcohol molecules in the H-bonded chain of 7HQ·(alcohol)$_2$ by push-ahead effect; at the rate-determining step which is the protonation of the keto group, proton donation of the adjacent alcohol molecule to the keto group is pushed by the other alcohol molecule bound to the amino group from the backside along the proton-relay pathway. However, in GSRPT whose energy barrier is higher than the barrier of ESPT, the reorganization of the H-bond bridge in the cyclic complex of 7HQ·(alcohol)$_2$ to form an optimal precursor configuration for efficient proton tunneling is a prerequisite to intrinsic proton transfer. As a consequence, due to the larger contribution of configurational optimization to proton transfer

in the ground state than in the excited state, both the push-ahead effect and the asymmetric character of GSRPT become weaker than the respective ones of ESPT.

■ ASSOCIATED CONTENT

Supporting Information

Association constants, GSRPT time constants, ESPT scheme, steady-state absorption spectra, wavelength-dependent and X_W-dependent transient-absorption kinetic profiles, and X_W-dependent k^S and k^W. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by a research grant through the National Research Foundation (NRF) of Korea by the Ministry of Education, Science, and Technology (2007-0056095). D.-J.J. is also thankful for a NRF Grant (2011-0028981).

■ REFERENCES

(1) Osses, L. R.; Godoy, C. A. *Plant Physiol. Biochem.* **2006**, *44*, 226−235.
(2) Yamada, H.; Otsuka, M.; Hayashi, M.; Nakatsuka, S.; Hamaguchi, K.; Yamamoto, A.; Moriyama, Y. *Diabetes* **2001**, *50*, 1012−1020.
(3) Galkina, S. I.; Sudina, G. F.; Dergacheva, G. B.; Margolis, L. B. *FEBS Lett.* **1995**, *374*, 17−20.
(4) Thomas-Reetz, A.; Hell, J. W.; During, M. J.; Walch-Solimena, C.; Jahn, R.; Camilli, P. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 5317−5321.
(5) Kohen, A.; Cannio, R.; Bartolucci, S.; Klinman, J. P. *Nature* **1999**, *399*, 496−499.
(6) Silverman, D. N. *Biochim. Biophys. Acta* **2000**, *1458*, 88−103.
(7) Royant, A.; Edman, K.; Ursby, T.; Pebay-Peyroula, E.; Landau, E. M.; Neutze, R. *Nature* **2000**, *406*, 645−648.
(8) Mathias, G.; Marx, D. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 6980−6985.
(9) Higashi, N.; Tanimoto, K.; Nishioka, M.; Ishikawa, K.; Taya, M. *J. Biochem.* **2008**, *144*, 77−85.
(10) Faxen, K.; Gilderson, G.; Adelroth, P.; Brzezinski, P. *Nature* **2005**, *437*, 286−289.
(11) Pomes, R.; Roux, B. *Biophys. J.* **2002**, *82*, 2304−2316.
(12) Lu, D.; Voth, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 4006−4014.
(13) Mohammed, O. F.; Pines, D.; Nibbering, E. T. J.; Pines, E. *Angew. Chem., Int. Ed.* **2007**, *46*, 1458−1461.
(14) Moilanen, D. E.; Fenn, E. E.; Wong, D.; Fayer, M. D. *J. Phys. Chem. B* **2009**, *113*, 8560−8568.
(15) Spry, D. B.; Fayer, M. D. *J. Phys. Chem. B* **2009**, *113*, 10210−10221.
(16) Maroncelli, M.; Fleming, G. R. *J. Chem. Phys.* **1987**, *86*, 6221−6239.
(17) Douhal, A.; Angulo, G.; Gil, M.; Organero, J. A.; Sanz, M.; Tormo, L. *J. Phys. Chem. B* **2007**, *111*, 5487−5493.
(18) Yu, H.; Kwon, O.-H.; Jang, D.-J. *J. Phys. Chem. A* **2004**, *108*, 5932−5937.
(19) Park, S.-Y.; Yu, H.; Park, J.; Jang, D.-J. *Chem.—Eur. J.* **2010**, *16*, 12609−12615.
(20) Bardez, E.; Chatelain, A.; Larrey, B.; Valeur, B. *J. Phys. Chem.* **1994**, *98*, 2357−2366.
(21) Kohtani, S.; Tagami, A.; Nakagaki, R. *Chem. Phys. Lett.* **2000**, *316*, 88−93.
(22) Kwon, O.-H.; Lee, Y.-S.; Yoo, B. K.; Jang, D.-J. *Angew. Chem., Int. Ed.* **2006**, *45*, 415−419.
(23) Park, S.-Y.; Jang, D.-J. *J. Am. Chem. Soc.* **2010**, *132*, 297−302.
(24) Park, S.-Y.; Lee, Y.-S.; Kwon, O.-H.; Jang, D.-J. *Chem. Commun.* **2009**, 926−928.
(25) Nakagawa, T.; Kohtani, S.; Itoh, M. *J. Am. Chem. Soc.* **1995**, *117*, 7952−7957.
(26) Konijnenberg, J.; Ekelmans, G. B.; Huizer, A. H.; Varma, C. A. G. O. *J. Chem. Soc., Faraday Trans. 2* **1989**, *85*, 39−51.
(27) Fang, W.-H. *J. Am. Chem. Soc.* **1998**, *120*, 7568−7576.
(28) Chou, P.-T.; Wei, C.-Y.; Wang, C.-R. C.; Hung, F.-T.; Chang, C.-P. *J. Phys. Chem. A* **1999**, *103*, 1939−1949.
(29) Lavin, A.; Collins, S. *Chem. Phys. Lett.* **1993**, *204*, 96−100.
(30) Park, S.-Y.; Kwon, O.-H.; Kim, T. G.; Jang, D.-J. *J. Phys. Chem. C* **2009**, *113*, 16110−16115.
(31) Park, S.-Y.; Lee, Y.-S.; Jang, D.-J. *Phys. Chem. Chem. Phys.* **2011**, *13*, 3730−3736.
(32) Tokumura, K.; Watanabe, Y.; Udagawa, M.; Itoh, M. *J. Am. Chem. Soc.* **1987**, *109*, 1346−1350.
(33) Lee, S.-I.; Jang, D.-J. *J. Phys. Chem.* **1995**, *99*, 7537−7541.
(34) Park, S.-Y.; Jang, D.-J. *Phys. Chem. Chem. Phys.* **2012**, *14*, 8885−8891.
(35) Kwon, O.-H.; Kim, T. G.; Lee, Y.-S.; Jang, D.-J. *J. Phys. Chem. B* **2006**, *110*, 11997−12004.
(36) Schowen, R. L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1434−1438.
(37) Klein, O.; Aguilar-Parrilla, F.; Lopez, J. M.; Jagerovic, N.; Elguero, J.; Limbach, H.-H. *J. Am. Chem. Soc.* **2004**, *126*, 11718−11732.
(38) Gerritzen, D.; Limbach, H.-H. *J. Am. Chem. Soc.* **1984**, *106*, 869−879.
(39) Kwon, O.-H.; Zewail, A. H. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 8703−8708.
(40) *CRC Handbook of Chemistry and Physics*, 78th ed.; Lide, D. R., Ed.; CRC Publishing Co.: Boca Raton, FL, 1999.
(41) Kim, K.-S.; Lee, H. *J. Chem. Eng. Data* **2002**, *47*, 216−218.
(42) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877−2887.
(43) Abboud, J.-L. M.; Sraidi, K.; Guiheneuf, G.; Negro, A.; Kamlet, M. J.; Taft, R. W. *J. Org. Chem.* **1985**, *50*, 2870−2873.
(44) Frange, B.; Abboud, J.-L. M.; Benamou, C.; Bellon, L. *J. Org. Chem.* **1982**, *47*, 4553−4557.