

Excited-State Proton Transfer in Chiral Environments. 1. Chiral Solvents

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Proton transfer is arguably the most important chemical process in nature. The careful control of rate and specificity relies on a complex architecture of interacting stereocontrolled sites. We now report the first example of excited-state proton transfer to solvent (PTTS) that exhibits diastereoselectivity through the action of independent chiral centers.

As a bimolecular process, proton transfer from an achiral acid to a chiral base should exhibit no stereoselection. Conversely, in proton transfer to chiral solvent, interactions between solvent molecules may lead to diastereomeric transition states and, hence, differences in proton-transfer rates between racemic and enantiopure solvents. Our development of “super” photoacids such as 5,8-dicyano-2-naphthol (DCN2) allows us to investigate proton transfer to alcohols,¹ as opposed to aqueous solvents. In the simplest (non-tritiated or deuterated) chiral alcohol, 2-butanol, we observe a marked distinction of proton-transfer rates in racemic and enantiopure solvents.

The dynamics of PTTS from DCN2 to the optical isomers of 2-BuOH were investigated using the combination of steady-state and time-resolved fluorescence spectroscopy. Details of the experimental setup have been described previously.^{1d} (*R,S*)-2-Butanol (99.5%) and (*R*)-(-)- and (*S*)-(+)-2-butanols (99%) were purchased from Fluka and Aldrich. Dielectric permittivity and losses for all alcohols were measured as described elsewhere.²

The steady-state emission spectrum of 5,8-dicyano-2-naphthol in (*R,S*)-2-butanol exhibits both anion and neutral emission spectra in a ratio of 0.5. When the same spectrum is recorded in (*S*)-(+)-butanol, the anion emission intensity is increased and is identical to that recorded in (*R*)-(-)-butanol (see Figure 1). Time-resolved emission spectra of the neutral (460 nm) and anionic (660 nm) species for all three systems were obtained. These revealed the source of the difference. That is, a noticeable slow-down of fluorescence kinetics was observed in racemic 2-butanol as compared to its enantiopure forms.

We have demonstrated experimentally and theoretically that a two-step reaction model (Scheme 1) adequately describes the nonexponential fluorescence decay of some rapidly dissociating naphthols, particularly “super” photoacids.^{1b–h} In this scheme, initially excited naphthol (R^*OH) undergoes reversible photodissociation with a rate constant k_d , forming solvent contact ion pair (CIP) $R^*O^- \cdots H^+$. The latter can undergo both adiabatic and nonadiabatic recombination with rate constants k_a and k_q , respectively. The second step in Scheme 1 involves diffusional separation of CIP from the contact radius, a , to infinity. R^*OH and R^*O^- experimental kinetic curves were fitted to the numeric solutions of

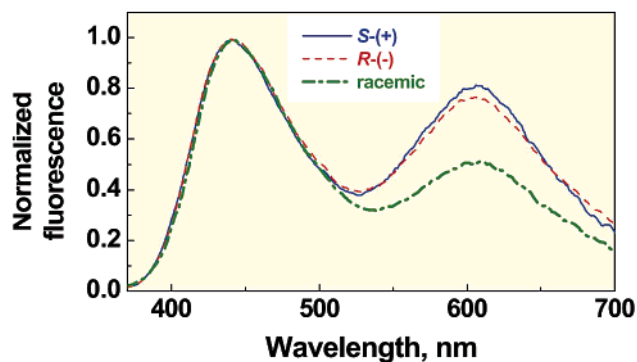


Figure 1. Steady-state emission spectra of DCN2 in 2-butanol.

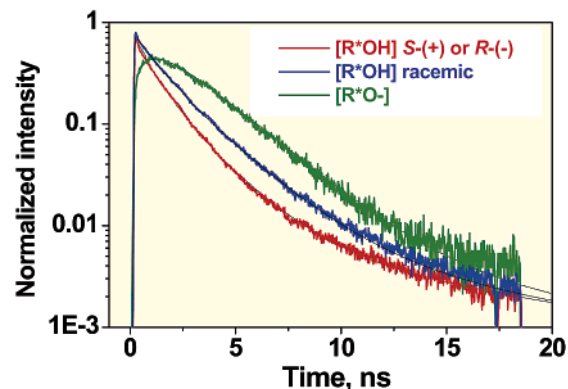
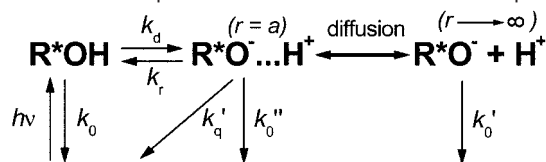


Figure 2. Emission kinetics of DCN2 in 2-butanols. Experimental data (color points, normalized) are composed with the theoretical DSE (black lines), using the parameters of Table 1.

Scheme 1. Two-Step Reaction Scheme of PTTS from Naphthols



the time-dependent Debye–Smoluchowski equation (DSE) using the approach used previously.^{1d,f,3,4} We provide the fundamentals of our method in the Supporting Information.

Figure 2 demonstrates the experimental and theoretical kinetic data, using the parameters given in Table 1. The data for (*R*)-(-)- and (*S*)-(+)-isomers are identical. One can see from the fit that the only parameter responsible for the difference in fluorescence decays of DCN2 in racemic and optical active 2-butanols is the protolytic dissociation rate constant k_d . What, then, is the effect of chirality?

First, the fluorescence lifetimes and emission maxima of DCN2 anion were the same in all 2-butanols, which form a similar microenvironment near the vibrationally relaxed R^*O^- anion.

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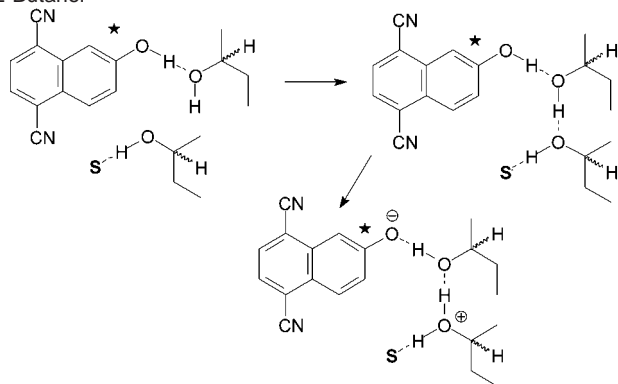
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Table 1. Parameters Used in Fitting the Fluorescence Decay of DCN2 to the Debye–Smoluchowski Equation and Calculated pK_a^* Values in 2-Butanols

2-BuOH	τ_D , ns	k_d , 1/ns	k_r , Å ³ /ns	a , Å	τ_0 , ns ^b	τ_0' , ns	D , Å ² /ns ^c	R_D , Å ^d	$pK_a^* e$
(<i>R,S</i>)	0.52	0.83	500	6.0	7.5	2.2	90	35.8	2.22
(<i>R</i>)-(–)	0.50	1.2	500	6.0	7.5	2.2	90	34.5	2.05
(<i>S</i>)-(+)	0.53	1.2	500	6.0	7.5	2.2	90	34.5	2.05

^a For kinetic analysis of Scheme 1 and definition of parameters, see Supporting Information. Relative error for parameters determination is 10%; $k_d = 0$, $\tau_0(\cdot) = 1/k_0(\cdot)$. ^b Lifetime of *O*-methyl ether of DCN2 in racemic 2-butanol. ^c Mutual diffusion coefficient $D = D_{H^+}/D_{R^*O^-}$. Values of D_{H^+} were determined by using the Nernst equation: $D_{H^+} = RT\lambda^0/F^2$, where λ^0 is the limiting proton mobility and F is Faraday's constant. The value for HCl in 2-butanol was taken from Lisi, R.; Goffredi, M.; Liveri, V. T. *J. Chem. Soc., Faraday Trans. 1* **1976**, 72, 436. The value of $D_{R^*O^-}$ in water (75 Å²/ns)^{1d} was multiplied by the water/2-butanol viscosity ratio. ^d At room temperature, the Debye radius $R_D = 566/\epsilon$ Å. Static dielectric permittivity ϵ is measured by us. ^e Calculated as $pK_a^* = -\log[k_d/10^{27} \exp(-R_D/a)/(k_r N_A)]$.

Scheme 2. Proposed Mechanism of PTTS from DCN2 to 2-Butanol^a



^a S is a bulk solvent molecule.

Thus, the observed difference in k_d is directly related to the structural and energetic distinctions between various optical isomers of 2-BuOH, although details of the nature of the primary proton acceptor and the possible geometry of the DCN2/2-BuOH reactive complex remain elusive.

We have speculated that the nonlinear dependence of proton-transfer rate upon acceptor (water) concentration^{1f} is due to the requirements for hydrogen-bonding with solvent molecules in the transition state. For instance, DCN2 in tetrahydrofuran/methanol exhibits similar nonlinearity. 2-Butanol represents a classical example of a self-associated liquid. We expect that hydrogen-bonding between 2-butanol molecules should lead to differences between an *R,R* and an *R,S* transition state (see Scheme 2 as the simplest case of proton transfer to alcohol aggregates). Several possible structures of 2-BuOH multimers, including linear and cyclic oligomers of different molecularity, have been detected experimentally.⁵

Herndon and Vincenti have observed a dependence of hydrogen bond strength upon the stereochemistry of 2-butanol dimers in chlorinated solvents,⁶ leading to stronger hydrogen bonds for the homochiral solvents than for the racemic ones by 2.76 kJ/mol at 23 °C. Although their dilute alcohol conditions are not directly comparable to our neat solvent conditions, faster proton transfer in the more strongly hydrogen-bonding solvent may reflect the importance of such aggregates the transition state. Conversely, Iwahashi et al.⁷ saw no difference between H-bonding for chiral and racemic 2-butanols.

King and Howard established experimentally and confirmed by ab initio calculations that, in the gas phase, the most stable hydrogen-bonded linear dimer of 2-butanol is heterochiral in

composition.⁸ The *R,S*-dimer is 1.46 kJ/mol higher in energy. However, it is very interesting that another recent theoretical paper predicts that heterochiral cyclic dimers of α -amino alcohols are more stable in the gas phase, while in solutions for several cases the relative stability is reversed and homochiral dimers become stable.⁹

The complex self-associative nature of alcohols and its influence on PTTS dynamics can be detected in temperature measurements. We have found^{1b,c,e-g} that for the PTTS of “super” photoacids in an array of alcohols two distinct temperature regimes exist. At temperatures near ambient, the rate of PTTS is almost temperature independent, whereas at lower temperatures the rate exhibits a large temperature dependence. In the latter case, the rate constant is proportional to the dielectric relaxation rate of the solvent and has similar activation energy. In the case of racemic and enantiopure 2-butanol, the longest and dominant relaxation time τ_D provides information on association dynamics.¹⁰ We experimentally have found it to be 510 ± 20 ps, regardless of solvent enantiopurity¹¹ (see Table 1). Extrapolating our published data to the experimental conditions of our work, we predict that the PTTS of DCN2 in 2-butanols at room temperature is in the transitional temperature regime. This is consistent with a proton-transfer rate that is twice the solvent relaxation rate.

Assuming a simple statistical model in which a single proton interacts with a solvent heterodimer or homodimer with equal probability, $50\% \times 1.2 = 0.6/\text{ns}$ represents the rate of proton transfer to homodimer in the racemic solvent. Thus, the 1.2/0.83 proton-transfer ratio in the two solvents translates into a $0.6/(0.8 - 0.6) = \sim 3:1$ preference for the homodimer. This preference is not due to solvent reorganization but rather to a preference for the homodimer in the transition state itself. In a more highly constrained environment, of course, this effect will only be multiplied.

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Supporting Information Available: Dielectric measurements procedure, analysis of the kinetic Scheme 1, and details of fitting procedure (PDF). This material is available free charge via the Internet at <http://pubs.acs.org>.

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