Kinetic Basicities of Aqueous Binary Mixtures: A Surprisingly Good Linear Correlation with the Gas Phase Basicity of the Organic Cosolvent

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Abstract. A remarkably good correlation between the rate of proton transfer from excited protonated 1-aminopyrene and the gas phase basicities of the organic component in water: organic solvent binary mixtures has been found. We suggest that use of ammonium acids minimizes the effect of anion solvation and Coulomb interactions and enables the influence of the organic cosolvent on the proton transfer to be clearly observed. The model proposed is one in which the proton is always transferred to a water molecule and a concerted proton transfer to a water molecule solvated by the organic cosolvent also occurs. The cosolvent influence is then on this latter species via hydrogen bond interactions. The correlation holds in pure water but not in pure organic solvents where, clearly, the proton must be transferred to the organic molecule.

INTRODUCTION
Photoacids are excellent model molecules for general acid–base research in aqueous solutions. Förster was first to suggest, some 40 years ago, that the electronic excitation shifts the acid–base equilibrium to a new value which may be characterized thermodynamically (the "Förster Cycle"). Indeed, photoacid dissociations are generally reversible and occur on a vibrationally relaxed excited state under conditions very close to thermal equilibrium. Recently, we reported that in aqueous solutions the rate of the proton transfer from protonated 1-aminopyrene, a cationic photoacid, increases when water was mixed with a wide range of organic solvents. The proton transfer rate was measured by monitoring the fluorescence decay of the excited 1-aminopyrene solutions following short pulse excitation using time-correlated single-photon counting detection. A broad maximum in the proton transfer rate was found for water:organic solvent mole ratios between 2:1 and 1:1, and its magnitude varied from one organic cosolvent to the other. Further decrease in the water content resulted in the opposite trend, i.e., the proton transfer rate progressively slowed down up to the pure organic solvent limit. In the pure organic solvents the rate was much slower than in pure water and varied greatly from one solvent to the other. We found that in many binary mixtures (but not in pure organic solvents) the acidity constant of the photoacid (pKₐ) and the proton solvation free-energy exhibited a similar dependence on the solution composition. We further refer to water mixtures which exhibit such effects on proton dissociation as "normal water mixtures".

A useful characterization of normal water mixtures is that they are made of water and a strong hydrogen bond acceptor (HBA) solvent of a greater gas phase proton affinity (basicity), but of a lesser liquid phase basicity. It follows, that while such HBA solvents are able to interact strongly with water via hydrogen bond interactions, they are unable to directly solvate the proton in the presence of excess water. Here we report, for the first time, a surprisingly good one-variable correlation (r = 0.99) between the excited-state proton transfer rate of 1-aminopyrene and the gas phase basicity (proton affinity) of 11 common HBA cosolvents which form normal water mixtures. The 2:1 water:organic solvent mixture was used as a standard state and the measured dissociation rates were normalized with the organic solvent concentration at that composition (Fig. 1). The correlation thus found is insensitive to the choice of the standard solution composition in the water-rich region of the binary mixtures. This essentially free-energy relationship implies that all the correlated reactions belong to the same

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series of acid–base Brønsted-type proton transfers.\textsuperscript{14} It also implies that in this particular case solvation effects other than hydrogen bond interactions are either very small or tend to cancel out.\textsuperscript{6,8} Indeed, the proton transfer reaction from 1-aminopyrene is an isoelectronic and an isoelectrostatic process\textsuperscript{15} and the functional amine group as well as the proton are preferentially solvated by water so they are not affected directly by the cosolvent. Finally, solvation effects on the large aromatic residue cancel out, as it is largely unaffected by the proton transfer.\textsuperscript{8}

Scheme 1 shows a likely mechanism for 1-aminopyrene dissociation in water:organic solvent mixtures:

\[
\begin{align*}
\text{HN} & \quad \text{H} \\
\text{RN–H} \cdots \text{O–H} + (\text{H}_2\text{O}) & \leftrightarrow \text{RN} \cdots \text{H–O} + (\text{H}_3\text{O})\text{S}
\end{align*}
\]

Scheme 1

where $S$ is an organic cosolvent and $k_d$ is the proton dissociation rate. Apart from $S$, Scheme 1 is identical with the accepted scheme for the dissociation of protonated amines in pure water.\textsuperscript{11,16} In both schemes the reaction is assumed to proceed without desolvation of the reaction site. This implies a transition state with minimal solvent rearrangement activation energy.\textsuperscript{17} It follows that in this case, direct proton transfer to an organic cosolvent is also unfavorable kinetically. Another feature in Scheme 1 is that in accordance with the greater basicity of water, the proton is assumed to reside in solution on a water molecule. Further solvation of the $\text{H}_3\text{O}^+$ moiety is dominated by hydrogen bond interactions\textsuperscript{18} which involve the participation of the organic cosolvent. In this model, ion pairing is considered unimportant as the proton transfer rate was unaffected by either the protonating agent concentration ($\text{HClO}_4, 10^{-1} - 10^{-3}\text{ M}$) or by variation in the static dielectric constant of the solution ($80 \leq \varepsilon_s \leq 20$).

Further support for our model comes from the finding that the correlation shown in Fig. 1 holds for pure water (in this case, the rate was normalized assuming $c = 55.3\text{ M}$) but breaks down at the pure organic solvent composition where the proton must be transferred directly to the organic cosolvent. In this case, no apparent correlation was found between either the gas phase proton affinity or the photoacid $pK_a$ and the normalized proton dissociation rates. In addition, organic solvents which are comparable in basicity to water so they are able to directly solvate the proton and the amine group\textsuperscript{12} and solvents which are also strong hydrogen bond donors (HBD solvents)\textsuperscript{16} still roughly conform with the correlation (i.e., within the same class of solvents the stronger the gas phase basicity, the faster the rate of proton transfer). However, it seems that a multivariable analysis is needed to correlate these additional classes of cosolvents together, a practice which is commonly found in the literature of solvent effects.\textsuperscript{11,19} In this short note, we stress the point that our one-variable analysis correlates the indirect solvent effect for a large and important class of organic solvents. The model stresses the role of hydrogen bonding in water solvation, a role which is usually masked by many other solvation effects.\textsuperscript{11,20} Furthermore, the linear correlation found may prove useful in estimating the reactivity of protonated amine groups in biochemical environments where water molecules serve as the “background” solvent. As a step in this direction we have recently studied the excited-state proton transfer of protonated 1-aminopyrene complexed with $\beta$-cycloexetrin.\textsuperscript{21} The rate of proton transfer is increased by a factor of 2–3 compared to pure water. The inclusion complex resembles a water–ethanol mixture near the 75% by volume alcohol composition. In complete analogy with the model proposed here we suggest that the water near the cavity rim of $\beta$-cycloexetrin is modified by the OH groups in such a way as to increase its basicity. Such effects may play a role in acid–base catalytic activity of enzymes.
REFERENCES AND NOTES


(12) For selective values of equilibrium constants for solvent replacement around the proton see: Marcus, Y. Ion Solvation, Wiley: New York, 1985, Ch. 7.


(17) For a discussion see: Bell, R.P. In Faraday Symp. Chem. Soc. No. 10. (Proton transfer), 1975, p. 7 and the following lectures and discussions.


