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Cation-Enhanced Deprotonation of Water by a Strong Photobase

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Abstract. We have used picosecond fluorescence spectroscopy to study the proton-dissociation dynamics of bulk water and H_2O molecules solvating Mg^{2+} ions in aqueous solutions. We have analyzed the photo-initiated proton-transfer reaction to a photobase 6-aminoquinoline by the Collins–Kimball approach and have modeled the ensuing bimolecular reaction dynamics by the Smoluchowski equation with radiation boundary conditions. We have found the on-contact proton transfer rate to follow the Marcus free-energy relation for proton transfer and estimate by this rate-equilibrium correlation the considerable enhancement in the acidity of the water molecules solvating the Mg^{2+} ion. Our findings may be used in the study of metalloenzymes such as carbonic anhydrases (CAs), which catalyze the reversible addition reaction of OH^- to CO_2 by increasing the reactivity of the zinc-bound water molecules by means of stabilizing the product of water dissociation, the OH^- anion.

INTRODUCTION

Approximately one-third of all proteins require a metal ion for their structure and function.[1] Positively charged metal ions stabilize negative charges in the transition state and are able to polarize nearby water molecules, which then interact with the substrate. One example is ATP, which most often reacts as a Mg^{2+} complex. A second example is carbonic anhydrases (CAs), which control the physiological pH by controlling the relative concentrations of the CO_2/HCO_3^- buffer by a reversible hydration/dehydration cycle and often use Zn^{2+} and sometimes Cd^{2+} as the main catalytic factor in the enzyme. The hydration of CO_2 by water is facilitated by the positively charged metal cation, which polarizes a nearby (coordinated) water molecule and stabilizes the nucleophilic attack of the negatively charged OH^- anion, the product of H_2O dissociation, on CO_2. The catalytic cycle produces a proton and the bicarbonate ion, which is stable under normal (slightly basic) physiological pHs.[2,3]

The study of cation-assisted proton transfer from water to electronically excited heterocyclic bases was pioneered by Weller[4] who investigated the proton abstraction reaction of excited acridine and 6-hydroxyquinoline in water. Heterocyclic bases, which are much stronger bases in their first excited singlet state than in their ground electronic state, have been since extensively studied in solution.[4–21]

Pines et al.[12] have used excited 6-methoxyquinoline and acridine bases as proton acceptors from water. They have found that cations with relatively high charge density (i.e., small or multi-charged cations such as

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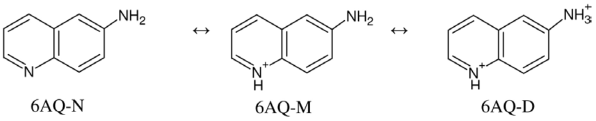
Li^+, Ca^{2+}, and Mg^{2+}) considerably accelerate the rate of proton transfer from water to the imine group, and have demonstrated by direct kinetic analysis that water molecules that are strongly interacting with metal cations are more acidic than bulk water. Picosecond fluorescence spectroscopy made it possible to investigate in real-time the ultrafast proton abstraction dynamics from water by imine protonation of the anionic (phenolate) form of 3-, 6-, and 7-hydroxyquinolines solutions.[14–20]

In this paper we use steady-state and time-resolved fluorescence spectroscopy to investigate the proton transfer reaction from water to a very strong photobase, 6-aminoquinoline, in concentrated solutions of Mg^{2+}. The biological importance of aminoquinolines is well recognized and their fluorescence properties have been reported in several papers.[6,7] A recent study reports on the role of the ring nitrogen and the amino group in the solvent dependence of the excited-state dynamics of 3-aminoquinoline.[21]

6-aminoquinoline (6AQ) is an amphoteric bifunctional compound characterized in the ground state by a weakly basic amine group with a pK_a of the protonated amine $-NH^{3+}$ equal to 1.2 and a more strongly basic imine group with a pK_a of the protonated imine group $=NH^+$ equal to 5.1 (Scheme 1).[7]



Scheme 1. Acid–base equilibria of 6-aminoquinoline (6AQ).

The basicity of the imine group of 6AQ-N strongly changes upon photoexcitation. As a result, 6AQ-M has a significantly higher pK_a^* value (13.3) of the protonated imine group than the previously investigated 6-methoxyquinoline (6MQ, $pK_a^* = 11.8$[12]) and acridine ($pK_a^* = 9.2$[13,22]) molecules.[12] We focus in this study on dynamics, not obtained previously, of the protonation of the neutral form of 6AQ in aqueous solution (6AQ-N) to determine the intrinsic rate of proton abstraction from Mg^{2+} hydrates and correlate this rate using the Marcus equation for proton transfer to find the pK_a of water molecules directly solvating the Mg^{2+} cation. We show that our approach yields for the enhanced acidity of the water molecules strongly interacting with Mg^{2+} pK_a^* values in agreement with previous experimental and theoretical estimations.

The general outline of this contribution is as follows: We first describe briefly the experimental setup we have used to study the protonation reaction of 6AQ-N in water following short laser-pulse excitation, we then characterize the photobasicity and the hydrogen-bonding interactions of 6AQ both in the ground state and in the first electronic excited state of the molecule. This we do by analyzing the absorption and fluorescence spectra of 6AQ in a set of some 19 solvents. We then define the pK_a scale we have used to correlate the proton transfer rate from water and the free-energy change of the reaction. In the following section we describe how we have obtained from the time-resolved measurements the intrinsic proton transfer rate within the various reaction complexes needed for the free-energy correlation. Finally, we discuss the general free-energy correlation between rate and equilibria we have found in proton transfer reactions in aqueous solutions and discuss how we use this correlation together with the kinetic data on the intrinsic proton transfer rates to obtain the $pK_a(H_2O)$ values in the bulk and in the presence of Mg^{2+} ions.

EXPERIMENTAL

6-Aminoquinoline was used as received from Aldrich. All solvents were of spectroscopic grade and were purchased from Aldrich. The steady-state spectra were recorded on a JASCO 570 spectrophotometer and Cary Eclipse Varian fluoremeter. Single-photon counting measurements were carried out with a setup similar to the one described before,[23] using a data acquisition card with 16000 channels (Gennie 2000 made by Canbera). Time resolution of the card was 1.5 ps per channel at the 25 ns full-scale of the apparatus. The kinetic decay curves were analyzed by convolution with the instrument response function using Matlab software version 7.2.

RESULTS

Steady-State Measurements

The photophysics of the 6-aminoquinoline molecule (6AQ-N), a bifunctional photobase, is richer than the photophysics of the previously studied 6-methoxyquinoline molecule,[12,17] where only the quinoline/quinolinium equilibrium is present. A cationic double-protonated form, 6AQ-D, a monoprotonated form, 6AQ-M, and a neutral form, 6AQ-N, are differentiated and identified by the position of their lowest absorption band.

The 6AQ-D, 6AQ-M, and 6AQ-N forms are predominantly present in highly acidic, slightly acidic, and neutral (alkaline) aqueous solutions, respectively, according to their corresponding acid–base equilibria (we have measured pK_a values of 1.8 and 5.1 for the double protonated and monoprotonated forms, respectively).

We measured the steady-state absorption spectra of 6AQ with different concentrations of a strong acid. In acetonitrile (not shown) acidified by concentrated $HClO_4$ the absorptions of the D-form, N-form, and M-form of 6AQ are at 312 nm, 351 nm, and 405 nm, respectively. Figure 1 shows the absorption spectra of 6AQ in aqueous solutions. The absorption maxima of

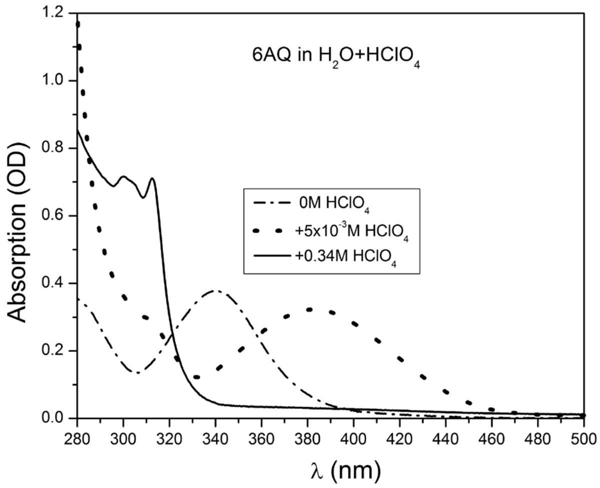


Fig. 1. Absorption spectra of 6AQ in water with different concentrations of $HClO_4$ (0 M, 5 × 10^{-3} M, and 0.34 M).

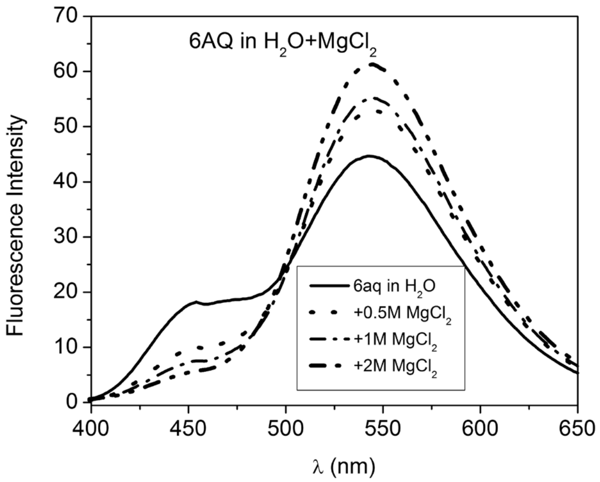


Fig. 2. Fluorescence spectra of 6AQ in water with 0 M, 0.5 M, 1 M, and 2 M $MgCl_2$. The excitation wavelength was 340 nm.

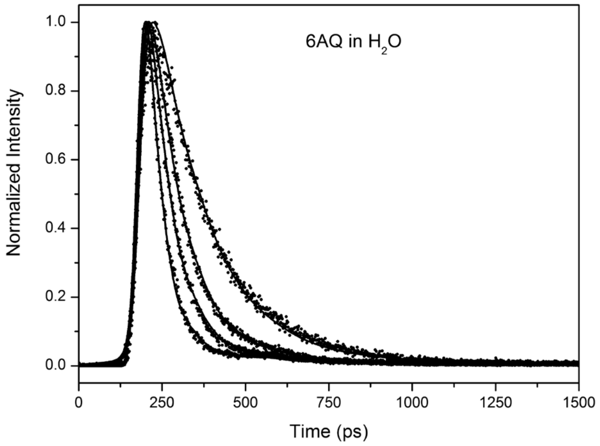


Fig. 3. Normalized fluorescence intensity of 6AQ as a function of time (dots). Top to bottom: 0 M, 0.5 M, 1 M, and 2 M of $MgCl_2$ in H_2O. The fluorescence decay was fitted using eqs 20 and 21 (solid lines).

6AQ-N and 6AQ-M are both blue-shifted in water to 341 nm and 382 nm, respectively, due to the combined effect of the hydrogen-bond accepting and donating ability of water. The absorption maximum of the 6AQ-N form shows a small continuous red-shift to lower energies and higher wavelengths with increasing solvent polarity and more so with the hydrogen-bond acceptor ability of the solvent reaching a value of 364 nm in DMSO, one of the strongest hydrogen-bond-acceptor (HBA) solvents. The absorption maximum indicates a reverse trend (moderate blue-shifting tendency) with increasing hydrogen-bond donor (HBD) ability of the solvent, as was also shown by Schulman et al. [7] in a smaller set of solvents.

Fluorescence emissions were identified at 398 nm, 540 nm, and 420 nm in acetonitrile and at 406 nm, 546 nm, and 454 nm in water for the D, M, and N forms of 6AQ, respectively. In pure water upon excitation of the N-form at 340 nm two emission bands are observed, which we assigned to the N-form at 454 nm and to the mono-protonated imine, M-form, at 546 nm (shown in Fig. 2). The fluorescence intensity of the N-form decreases and the intensity of M-form increases in higher $MgCl_2$ concentrations. Similar enhancement of the fluorescence of the 6AQ-M with increasing Mg^{2+} concentration was observed in heavy water (not shown).

TIME-RESOLVED MEASUREMENTS

The rates of protonation of the excited 6AQ-N in pure water, D_2O water, and in the presence of high concentrations of $MgCl_2$ have been determined by high-resolution time-correlated single-photon counting (TCSPC) techniques. We have collected the time-resolved fluorescence of the photobase at 440 nm, detuned from the fluorescence peak of the protonated photobase. Time-resolved measurements carried out at various $MgCl_2$ concentrations are shown in Fig. 3. In neat H_2O, the N-form of 6AQ decays with a time constant of $\tau_w = 130$ ps (the upper curve). In neat D_2O, the decay is significantly longer (Fig. 4), $\tau_w = 360$ ps. Similar measurements were carried out at 550 nm to monitor the emission rise and decay of the monoprotonated 6AQ, which is one of two products of the proton transfer reaction from H_2O to 6AQ, the other being the OH^- anion. We find a correlation between the appearance of the M-form and the disappearance of the N-form of 6AQ. Addition of high

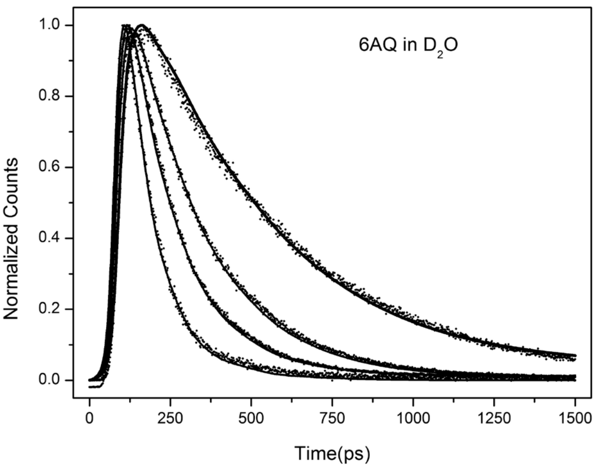


Fig. 4. Normalized fluorescence intensity of 6AQ as a function of time (dots). *Top to bottom*: 0 M, 0.5 M, 1 M, and 2 M of $MgCl_2$ in D_2O. The fluorescence decay was fitted using eqs 20 and 21 (solid lines).

concentrations of $MgCl_2$ led to a much faster decay of the 6AQ-N and to a faster rise in the population of 6AQ-D when dissolved in both H_2O and in D_2O (not shown).

DISCUSSION

Steady-State Measurements

The 6AQ-N molecule has two functional groups of comparable basic strength in the ground electronic state. The protonation order of these two groups is first the protonation of the internal imine group to form $–NH^+=$ and then the protonation of the external amine group to form $–NH_3^+$. To analyze and assign the multiple acid–base equilibria of the molecule and to establish the order of protonation we have assumed that each functional group retains its characteristic acid–base behavior, as found in analogue molecules having only one out of the two functional groups. For that end we have used the well-researched protonated acridine molecule (pK_a = 5.2 and pK^*_a = 9.2) as the benchmark for the acid–base behavior of the protonated imine group in 6AQ. The well-behaved cationic acid, the protonated aminopyrene molecule (pK_a = 3.2, pK^*_a = –0.34 by kinetic measurements),[24] has served as the benchmark for the characteristic acid–base behavior of the protonated $–NH_2$ group in 6AQ. To verify that the two functional groups when both present in 6AQ, behave as assumed we have analyzed the steady-state absorption and fluorescence spectra of the molecule in various solvents. Measurements in organic solvents as well as in water suggest that the absorption and the emission spectra of 6AQ-N are affected significantly by specific hydrogen-bonding interactions of the amino group and of the imine nitrogen atom,[7,13] as found for each of the functional groups in the analogous acridine and aminopyrene molecules. To analyze the solvent effect on the spectral properties of 6AQ-N we have used a multi-parameter (empiric) free-energy correlation suggested by Kamlet, Taft, and coworkers.[25] The Kamlet–Taft (KT)[25] analysis has been utilized often in order to separate the effect of specific hydrogen bonding interactions and the effect of nonspecific polar interactions on the spectral properties of a solute. In the KT analysis, solvatochromatic effects, such as the positions of the absorption and emission peak maxima in various solvents, are expressed as a linear combination of π^*, the effect of the solvent polarity parameter; α, the hydrogen-bond donating (HBD) ability of the solvent; and β, the hydrogen-bond accepting (HBA) ability of the solvent (eq 1):

$$\nu = \nu_0 + s\pi^* + a\alpha + b\beta \qquad (1)$$

where ν denotes the spectral peak frequency in a particular solvent, π^*, α and β denote the polarity, HBD and HBA properties of that solvent, respectively, and ν_0 denotes the peak frequency in a reference ($\pi^* = \alpha = \beta = 0$) nonpolar solvent arbitrarily assigned to *n*-hexane in the various KT solvent polarity scales. The coefficients s, a, and b are obtained by analyzing the spectrum of the fluorophore in a series of solvents and characterize the strength of the solute–solvent interactions. We have performed the KT analysis by a best-fit procedure using the Matlab 7.2 package for multiple regression of the position of the absorption and emission maxima of 6 AQ-N as a function of the solvent polarity parameters.

Upon best-fitting the KT function (eq 1) to the absorption and emission spectra of 6AQ-N in various solvents (Fig. 5) we have found out that the effect of HBA solvents, characterized by the large “b” parameter of 6AQ-N, is to almost equally red-shift the absorption and the emission spectra of 6AQ-N. Similar to the situation found with aminopyrene, we attribute this observation to the hydrogen-bond donating ability of the $–NH_2$ group of 6AQ-N, which retains its proton-donating ability in the excited state. In a marked contrast and similar to the observation in acridine, we have observed *blue-shifting* of the absorption spectra in HBD solvents, as characterized by the minus sign of the “a” parameter of 6AQ-N, and a much larger but opposite effect on the emission spectra, i.e., red-shifting of the emission spectra of 6AQ-N in HBD solvents. This indicates that the ground state of 6AQ is better stabilized by protic HBD solvents than the locally-excited singlet state of 6AQ. We attribute this observation to the polar interactions of the imine nitrogen, which is a mildly strong base in the ground state and hence strongly affected by HBD

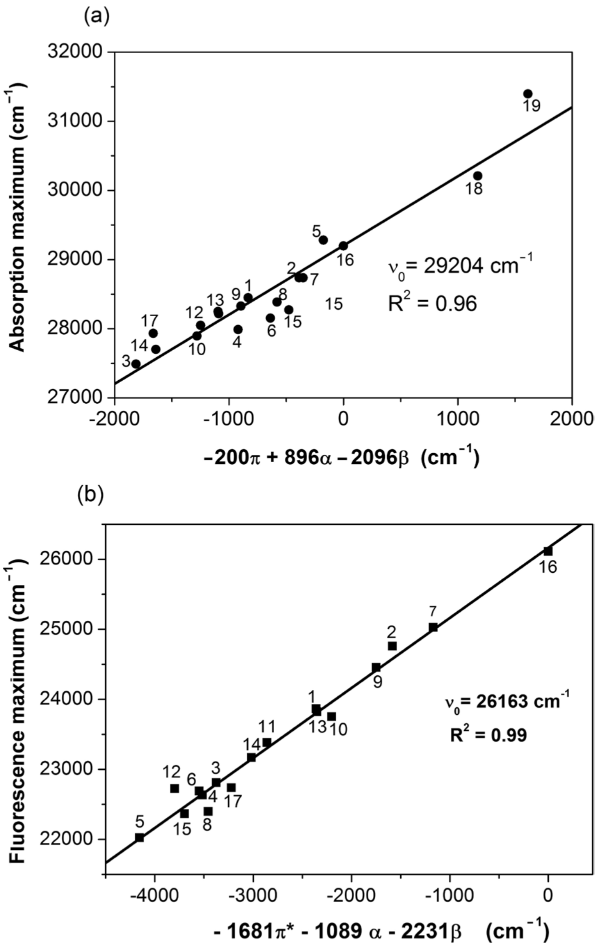


Fig. 5. KT analysis of the absorption (a) and fluorescence (b) frequencies taken at the peak of the spectra of 6 AQ in the following solvents: acetonitrile–1, dichloroethane–2, dimethylsulfoxide–3, ethanol–4, water–5 methanol–6, toluene–7, formamide–8, 1,4-dioxane–9, tetrahydrofuran–10, propylene carbonate–11, *n*-propanol–12, acetone–13, dimethylformamide–14, ethylene glycol–15, *n*-hexane–16, 1-butanol–17, tetrafluoroethanol–18, hexafluoropropanol–19.

solvents. Two additional observations are important for comprehending the KT analysis of the absorption and emission spectra of 6AQ: The polarity of the solvent has been found to be an important factor only for the emission spectrum, indicating an increase in the polarity of the emitting state as compared to the ground state of 6AQ, and the spectral shifts of the monoprotonated molecule, (6AQ-M), have been found to be much smaller than those of the neutral molecule.

A likely explanation for all these observations is that, similar to the situation encountered in acridine,[26] the photophysics of 6-aminoquinoline is controlled by the relative position of the three lowest-lying singlet states of the molecule, a relative position that may be reversed by internal conversion or by the presence of a solvent. State inversion may be caused by polar interactions between the lone (non-binding) electron pair on the nitrogen atom (of the imine group) and the solvent. In protic solvents, hydrogen-bonding interactions between the solvent and the lone electron pair on the nitrogen atom more strongly solvate the ground state of 6AQ relative to the excited state because the electron density on the nitrogen atom is smaller than that in the less-polar locally-excited state. This leads to hydrogen-bond weakening in a vertical excitation process when absorption from the ground state to a locally-excited singlet state happens with the solvent in an equilibrium configuration suitable for stabilizing the ground state but not the excited state.

While a ^1L_b or a n-π* state (with a small dipole) of low polarity could be the lowest S_1 state of 6AQ in the vapor and in some nonpolar solvents, a stabilized ^1L_a state (with a large dipole) becomes the S_1 state in polar and protic solvents following solvent relaxation around the excited 6AQ-N molecule because polar environment favors the more polar ^1L_a state. We attribute the enhanced photobasicity of the imine group to a property of an indirectly accessed polar electronic state, the ^1L_a state, which becomes the lowest-lying electronic state either following internal geometry relaxation or following intermolecular solvent relaxation. ^1L_b inversion to the ^1L_a state having a partial CT character has been invoked for a possible explanation for the observed enhanced photoacidity of pyranols and naphthols.[27–29] A state-inversion model explains the sign reversal of "a" between absorption and emission of 6AQ-N obtained by the KT analysis, Fig. 5. However, efficient vibronic coupling usually occurring between close-lying electronic states may render a two-level dynamics picture oversimplified. While typically "^1L_a", "^1L_b", and "n-π*" labels are used to designate the three most low-lying electronic levels in many heterocyclic aromatic molecules, it is not strictly correct to consider such energy levels as isolated electronic states. The S_1, S_2, and S_3 states may become considerably mixed because of vibronic coupling, and as a result, their specific polar or nonpolar character may also become mixed. A clearly distinctive two-state (one for absorption and the other, more polar, for emission) picture is certainly lost upon protonation of 6AQ, which is borne out by the relative insensitivity of the spectrum of 6AQ-M to the solvent polarity parameters. In this case one may invoke the idea that the emitting state is heavily mixed by the extra positive charge so absorption and emission occur to and from essentially the same state, which its intrinsic polarity may only slightly change by intermolecular interactions with the solvent.

The predicted acid–base properties of 6AQ were further verified by steady-state fluorescence measurements of 6AQ-N as a function of the pH. These measurement have revealed that in the excited state the acidity of the protonated amine group, $–NH_3^+$, and the basicity of the imine group, $–NH^+=$, are both enhanced, as expected from the analogous behavior of acridine and aminopyrene. Förster cycle calculations on naphthylamines indicate a slight increase in the acidity of the amine group ($RNH_2 \leftrightarrow RNH^- + H^+$) from about 14 to about $pK^*_a = 12$.[22] An increase of 7.7 pK_a units in the pK_a value of the imine group in the excited state as judged by the Förster cycle marks a remarkable increase in the basicity of 6AQ in the excited state. In strongly acidic solutions both basic groups of 6AQ may be protonated in the ground state resulting with the formation of the 6AQ-D form. The behavior of the 6AQ-D upon excitation is mainly proton dissociation from the protonated amine group to the solvent, resulting in the formation of the electronically excited monoprotonated 6AQ-M form. The acidity of 6AQ-D in the electronic excited state is comparable with the acidity of the strongest mineral acids.

USING 6AQ-N AS A VERY STRONG PHOTOBASE

In the present study we have utilized 6AQ-N as a novel very strong photobase. In order to do so, the solution was kept at slightly basic or neutral conditions so the molecule retained its unprotonated state while in the ground electronic state. Under such conditions the optical excitation of 6AQ-N in water and the lower alcohols has mainly resulted in rapid proton abstraction from the solvent. Enhancement of the acidity of water may be achieved by dissolving high concentrations of strong electrolytes such as $MgCl_2$ in water, which stabilizes the OH^- anion in solution. In the current study, the presence of dissolved cations has led to faster proton abstraction by 6AQ-N from water molecules solvating Mg^{2+} cations and to a substantial increase in the steady-state fluorescence emission from the monoprotonated form of 6AQ. The tendency of metal cation hydrates to donate a proton has been also explored in D_2O by probing the deuteration reaction of 6AQ and was qualitatively similar to the behavior of 6AQ in H_2O.

Proton transfer in pure water

The conventional way of describing the dissociation reaction of any Brønsted acid, HA, in water is given in Scheme 2:

$$HA = A^- + H^+$$

Scheme 2. The conventional acid–base equilibria of a Brønsted acid in water.

With an equilibrium constant, K_{PT}, given by

$$K_{PT} = [A^-][H^+]/[HA] \qquad (2)$$

Equation 2 is the basis for the common tables listing the dissociation constant of Brønsted acids. In this approach the self-concentration of water is simply omitted from the equation, a procedure that is usually rationalized by the large concentration of water being part of the equilibrium constant of the dissociation reaction. In reality, this procedure avoids dealing with problems imposed by treating the water solvent as a reactant, and the procedure is chemically allowed because of its balanced stoichiometry.

The situation is different when water directly enters the stoichiometry of an acid–base reaction, i.e., when it is a reactant in the reaction undergoing a chemical transformation. Such is the situation when 6AQ molecules undergo an excited-state protonation reaction in water according to Scheme 3:

$$B + H_2O \leftrightarrow BH^+ + OH^-$$

Scheme 3. The conventional acid–base equilibria of a Brønsted base in water.

With an equilibrium constant, K_{PT}, given by:

$$K_{PT} = [BH^+][OH^-]/[B][H_2O] \qquad (3)$$

where the chemical activity of water, which is poorly represented by its self-concentration value, $c(H_2O) = 55.3$ M at room temperature, explicitly enters the expression. This problem was already acknowledged by Brønsted and is briefly discussed by Bell in his classic book *The Proton in Chemistry*[30] without prescribing a procedure for avoiding this difficulty. A formal way out of this difficulty is to define the activity of water as unity by enlisting the thermodynamic definition of the standard state of pure solvents. This acidity scale is used in many modern physical chemistry textbooks without much discussion. Clearly, this procedure cannot be exact from a kinetic point of view, as it suggests that the rate of proton transfer to 1 M of water in water, a situation we encounter in this study, should be identical to the proton transfer rate to pure water. However, in order to use a universal acidity scale for both solvent and solute we adopt this procedure where the activity coefficient of each dissolved species at infinite dilution and the activity of water in its pure solvent form are defined as unity and are omitted from the mass equation. Using this definition of the acidity scale, eq 3 may be rewritten as

$$K_{PT} = [BH^+][OH^-]/B \qquad (3a)$$

For the acid dissociation reaction of water itself (water acting as a Brønsted acid) $H_2O \leftrightarrow OH^- + H^+$, the equilibrium constant of water dissociation is given by:

$$K_a(H_2O) = [H_3O^+][OH^-] = 10^{-14}\ (T = 293\ K) \quad (4)$$

where, as before, the activity of water and the activity coefficients of the ions are assumed to be unity and are omitted from the equation.

For the dissociation reaction of the protonated acceptor (the conjugate acid of the base) one retrieves the general expression for Brønsted acids equilibria, Scheme 4:

$$BH^+ \leftrightarrow B + H^+$$

Scheme 4. The conventional acid–base equilibria of a conjugate acid of a Brønsted base in water.

having a K_a defined by:

$$K_a(\text{protonated acceptor}) = [B][H^+]/[BH^+] \quad (5)$$

One obtains the equilibrium constant K_{PT} of the proton transfer reaction between H_2O and a base by dividing eq 4 by eq 5:

$$K_{PT} = K_a(H_2O)/K_a(\text{protonated acceptor}) \quad (6)$$

Equation 6 may be rewritten as:

$$pK_{PT} = pK_a(H_2O)–pK_a(BH^+) = 14–pK_a(BH^+) \quad (6a)$$

We note in passing that the equilibrium constant for the self-exchange of the proton in water may be viewed as the dissociation reaction of a protonated water molecule in water,

$$H_3O^+ + H_2O = H_2O + H_3O^+$$

Scheme 5. The self-exchange of the proton in water.

so in this acidity scale $pK_a(H_3O^+) = 0$. We note that this is indeed the value of $pK_a\ (H_3^+O)$ listed in Atkins' *Textbook of Physical Chemistry*.[31] In our opinion this approach describes more realistically the true acidities of H_3^+O and of H_2O in bulk water, and the pK_a values of 0 and 14 should be preferred over the more often used values of –1.74 and 15.74, which take into account the self-concentration of water.

The expression for a general proton transfer reaction between any proton donor and any proton acceptor in water is given by Scheme 6:

$$B + HA \leftrightarrow BH^+ + A^-$$

Scheme 6. A general reversible proton transfer reaction between a Brønsted base and a Brønsted acid.

with K_{eq} defined as:

$$K_{eq} = [A^-][BH^+]/[HA][B] \quad (7)$$

and

$$pK_{eq} = pK_a(HA) - pK_a(BH^+) = \Delta pK_a \quad (8)$$

where pK_{eq} is equal to the difference between the dissociation constant of the proton-donating acid and the dissociation constant of the conjugate acid of the proton-accepting base calculated in the logarithmic scale.

We note that for proton transfer from a photoacid to bulk water at room temperature we have $pK_a(BH^+) = 0$, and for proton transfer from bulk water to a photobase we have $pK_a(HA) = 14$.

DETERMINATION OF THE RATE OF PROTON ABSTRACTION FROM WATER MOLECULES SOLVATING THE Mg^{2+} ION

Base-hydrolysis of water results in water transferring a proton to a strong base. The hydrolytic process clearly depends on its intrinsic Brønsted acidity. The Brønsted acidity of the water molecule may be affected by the presence of nearby cations, which act to stabilize the OH^- anion. We have investigated the effect of cations on the Brønsted acidity of water using the strong photobase 6AQ. We analyze the ensuing proton transfer reaction between a photobase and water-solvating cations by utilizing the Eigen–Weller (EW)[4,32,33] two-stage reaction model, Scheme 7, which is outlined from the reactant side:

$$B + M(H_2O)_n \underset{k_{-D}}{\overset{k_D}{\longleftrightarrow}} B\cdots H\text{-}OH(M)(H_2O)_{n-1} \underset{k_{-r}}{\overset{k_r}{\longleftrightarrow}} BH^+ \cdots OH^-(M)(H_2O)_{n-1}$$

Scheme 7. The Eigen–Weller two-stage reaction model.

k_D and k_{-D} are the diffusion-limited rate constants for encounter and separation of the reactive complex, and k_r and k_{-r} are the unimolecular reaction rate constants for the reaction complex.

The equilibrium constant of the second (activated) reaction stage upon contact is given by:

$$K_{eq} = K_a(H\text{-}OH(M))/K_a(BH^+) \quad (9)$$

Making the steady-state approximation for the concentration of the reaction complex, the effective overall bimolecular rate constant of the proton transfer reaction, k_{PT}, is given by:

$$k_{PT} = \frac{k_D k_r}{k_{-D} + k_r} \quad (10)$$

Equation 10 may be applied directly to weak photobases that undergo slow protonation reaction while in the excited state. A typical weak base is acridine, which has been studied in the past in water and in water containing $MgCl_2$. For acridine the pK_a^* of its conjugate acid is 9.2[13,22] and $k_r << k_{-D}$, so the complex separation rate into free reactants is much faster than the intrinsic proton transfer rate within the reaction complex. Ignoring k_r in the denominator and making use of Fuoss's equation for uncharged reactants,[34] one gets for the overall bimolecular proton transfer rate constant:

$$k_{\mathrm{PT}} = \left(k_{\mathrm{D}}/k_{-\mathrm{D}}\right)k_{\mathrm{r}} = K_{\mathrm{Fuoss}}k_{\mathrm{r}} = \frac{4\pi r_0^{\,3}}{3}Nk_{\mathrm{r}} \qquad (11)$$

or solving for the unimolecular (intrinsic) reaction rate constant at contact separation, r_0, k_{r}, one has:

$$k_{\mathrm{r}} = \frac{3}{4\pi r_0^{\,3}N}k_{\mathrm{PT}} \qquad (12)$$

where N is Avogadro's number. We thus find k_{r}, the intrinsic proton transfer rate of the EW reaction model, to equal k_{PT}, the overall proton transfer rate, multiplied by the relative concentration of the reaction pair at contact separation.

Using eq 11 with the measured bimolecular reaction rate constant of acridine[12] $k_{\mathrm{PT}} = 79 \times 10^6$ $\mathrm{M^{-1}s^{-1}}$ and using $r_0 = 4.5$ Å, we could estimate the unimolecular proton transfer rate constant within the reaction complex between acridine and $\mathrm{Mg^{2+}}$ hydrate as $k_{\mathrm{r}} = 3 \times 10^8$ $\mathrm{s^{-1}}$.

THE SMOLUCHOWSKI–COLLINS–KIMBALL MODEL APPLIED TO THE PROTONATION REACTION OF 6AQ IN WATER

In the case of the strong photobase 6AQ, where the on-contact proton transfer rate is almost as fast as the diffusion-limited rate, and the steady-state approximation is not valid at early times of the proton transfer reaction, the description of the bimolecular proton transfer dynamics is not a trivial problem. In this case the starting point is the time-dependent Smoluchowski equation (SE)[35] with reactive boundary conditions introduced by Collins and Kimball,[36] where a finite on-contact reaction rate between proton donor and acceptor and the diffusion rates of the reactants determines the observed time-dependent proton transfer rate. The Smoluchowski–Collins–Kimball (SCK) approach has already been used to describe aqueous photoacid–base neutralization reactions.[37–41]

The time-dependent second-order (bimolecular) rate coefficient k(t) is calculated from the flux of the incoming reactants across the surface of the contact sphere having a radius r_0:

$$k(t) = 4\pi Da^2\frac{\partial\rho(r,t)}{\partial r}\Big|_{r=r_0} \qquad (13)$$

ρ is the density distribution function of the reactive pair (which is time dependent), and D is the relative diffusion coefficient between the two reactants, approximated by the sum of their respective diffusion coefficients, $D = D_{\mathrm{Mg(H_2O)_n}} + D_{\mathrm{6AQ}}$.

In the Smoluchowski–Collins–Kimball (SCK) approach[36] the reaction flux at contact is assumed to be proportional to the distribution function on contact. The proportionality constant k_0 is the intrinsic (bimolecular) rate constant of the reaction at contact separation.

$$4\pi Da^2\frac{\partial\rho(r,t)}{\partial r}\Big|_{r=r_0} = k_0\rho\left(r_0,t\right) \qquad (14)$$

For the case of zero Coulombic potential between the reactants ($\mathrm{Mg^{2+}}$ $\mathrm{(H_2O)_n}$ is charged, but 6AQ is uncharged in its neutral form), the Smoluchowski equation (SE) under radiative boundary conditions may be solved analytically. Collins and Kimball[36] have found an exact expression for the time-dependent rate constant, *k(t)*:

$$k(t) = \frac{k_{SD}k_0}{k_{SD}+k_0}\left[1 + \frac{k_0}{k_{SD}}\exp\left(\gamma^2 Dt\right)\;\; erfc\left(\sqrt{\gamma^2 Dt}\right)\right] \qquad (15)$$

where *erfc* is the complementary error function, k_{SD} is the diffusion-limited second-order rate constant for steady-state conditions at long times after the reaction onset,

$$k_{\mathrm{SD}} = 4\pi NDr_0 \qquad (16)$$

here, N is Avogadro's constant and is defined as:

$$\gamma = a^{-1}\left[1 + \frac{k_0}{k_{\mathrm{SD}}}\right] \qquad (17)$$

We consider the case of proton donors ($\mathrm{Mg^{2+}}$ $\mathrm{(H_2O)_n}$) having an average concentration c_0 in large excess over the proton acceptor (photobase). The survival probability, $\mathrm{S_B}(t)$, of a proton acceptor, B, surrounded by an equilibrium distribution of proton donor molecules with the initial condition $\mathrm{S_B}(0) = 1$, may be approximated according to the following kinetic equation:

$$\frac{dS_{\mathrm{B}}(t)}{dt} = -c_0k(t)S_{\mathrm{B}}(t) \qquad (18)$$

$k(t)$ is the time-dependent rate coefficient given by eq 15.

Integrating, the survival probability of the photobase is given by:

$$S_B(t) = \exp\left\{-c_0\int_0^t k(t')dt'\right\} \qquad (19)$$

The integral of *k(t)* has the following form:

$$\int_0^t k(t')dt' = \frac{k_{SD}k_0}{k_{SD}+k_0}\times$$
$$\left\{t + \frac{k_0}{k_{SD}D\gamma^2}\left[\exp\left(\gamma'^2 Dt\right)erfc\left(\sqrt{\gamma^2 Dt} + 2\sqrt{\gamma^2 Dt/\pi} - 1\right)\right]\right\} \qquad (20)$$

Taking into the account the parallel proton transfer reaction from bulk water to the photobase, we obtain the normalized decay of the photobase population $S_{\mathrm{B}}(t)$:

$$S_B(t) = \exp\left\{-k_w t - \int_0^t c_0k(t')dt'\right\} \qquad (21)$$

Figure 3 shows the time-resolved emission of 6AQ in $\mathrm{H_2O}$ in the presence of $\mathrm{MgCl_2}$. The measured decay of the photobase in neat water without the electrolyte was found to be single exponential with a decay rate $k_w = (130\ \text{ps})^{-1}$. In contrast, the decays of 6AQ in water containing high concentrations of $MgCl_2$ were faster and appeared to be highly nonexponential. The fits of the decay profiles of 6AQ in the presence of $MgCl_2$ have been carried out using eqs 20 and 21 and have been optimized by a global run of the kinetic data for the three $MgCl_2$ concentrations used, 0.5 M, 1 M, and 2 M. Figure 3 depicts the data fits using a uniform value for the intrinsic (bimolecular) SCK rate constant at contact, $k_0 = (25\ \text{ps})^{-1}\ \text{M}^{-1} = 4 \times 10^{10}\ \text{M}^{-1}\ \text{s}^{-1}$. Figure 4 shows the time-resolved emission of 6AQ in D_2O in the presence of $MgCl_2$. The measured decay of the photobase in pure deuterated water appears to be single exponential with a decay rate $k_w = (360\ \text{ps})^{-1}$. The kinetic isotope effect (KIE) of imine protonation in neat water for 6AQ is thus $k_w(D_2O)/k_w(H_2O) = 2.8$. Figure 4 shows the data fits using a uniform value for the intrinsic SCK rate constant at contact for all magnesium chloride concentrations in D_2O, $k_0 = (75\ \text{ps})^{-1}\ \text{M}^{-1} = 1.7 \times 10^{10}\ \text{M}^{-1}\ \text{s}^{-1}$, implying a KIE for the intrinsic proton transfer rate of 3.0. The contact radius used was $r_0 = 5.0$ Å for both H_2O and D_2O and the mutual diffusion coefficients of 6AQ and Mg^{2+} hydrate were $2.5 \times 10^{-9}\ \text{cm}^2\ \text{s}^{-1}$ and $1.4 \times 10^{-9}\ \text{cm}^2\ \text{s}^{-1}$ for H_2O and D_2O, respectively. The diffusion coefficient of Mg^{2+} hydrate was estimated from the known mobility of Mg^{2+} in water,[42,43] and was searched for and best-fitted in the range of ±10% around this value. The contact radius parameter *a* was searched for and best-fitted in the range of 5–6.5 Å, covering the accepted range for this parameter in typical acid–base reactions.[40,41,44–53]

To find the unimolecular proton transfer rate constant within the reaction complex *kr*, we have made use of the relation between the bimolecular reaction constant k_0 and the unimolecular reaction constant k_r, eq 22, first established by Shoup and Szabo.[54]

$$k_r = \frac{3}{4\pi r_0^3 N} k_0 \tag{22}$$

Equation 22 is identical to eq 10 when the overall bimolecular reaction rate k_{PT} is identical to the intrinsic bimolecular proton transfer rate k_0. This identity may only apply when k_r is much smaller than k_{-D}, as discussed earlier in the text.

It follows by eq 22 that k_r of the EW reaction model is equal to k_0 multiplied by the relative concentration of the reaction pair at contact separation. The unimolecular on-contact reaction rate found for the $6AQ–Mg^{2+}(H_2O)_n$, complex was $k_r = 1.2 \times 10^{11}\ \text{s}^{-1}$, which is almost 3 orders of magnitude faster than the one found for acridine,[12] $k_r = 3 \times 10^8\ \text{s}^{-1}$.

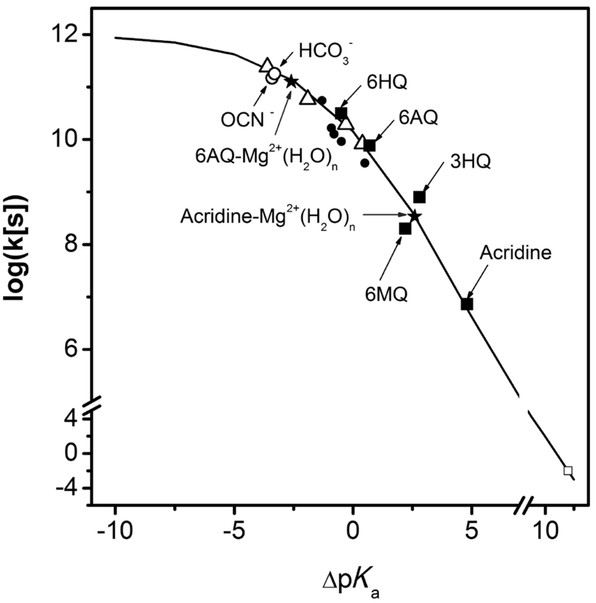


Fig. 6. Free-energy correlation: ΔpK_a (proton donor–protonated acceptor) vs. the proton transfer (PT) rate. The free-energy vs. reaction-rate curves are calculated using the Marcus equation for proton transfer (MBEBO) (solid line). Data points: PT from photoacids to water (solid dots); PT from pyranine to carboxylic bases (solid triangles); PT from 2N6,8S to HCO_3^- and OCN^- (open dots); protonation of photobases: acridine, 6MQ, 6HQ, 6AQ in water (solid squares); open square denotes water self-dissociation. Stars are PT rates from Mg^{2+} hydrate to acridine and 6AQ calculated using the parameters of the MBEBO equation.

UNIVERSAL FREE ENERGY CORRELATIONS FOR SOLVENT-ASSISTED PROTON TRANSFER REACTIONS IN AQUEOUS SOLUTIONS

Here we will show that the proton dissociation reaction from the water molecule follows a free energy relationship; the rate becomes larger when increasing the basicity of the proton acceptor or, equivalently, when lowering the pK_a of the conjugate acid of the proton acceptor.

We have estimated the $pK_a(H_2O)$ value of water molecules directly solvating the Mg^{2+} cation using the semi-empiric free-energy correlation of Marcus where the difference between the pK_a values of the proton donors and the pK_a values of conjugate acids of the proton acceptors were used to correlate the proton transfer rate between donors and acceptors (Fig. 6).

The simplest method to obtain the intrinsic proton transfer rate to 6AQ-N in pure water, k_r, is to determine the rate of the fluorescence decay of 6AQ-N in the absence of proton abstraction, k_f, by measuring the lifetime of 6AQ-N in alcoholic solvents in which 6AQ-N has radiative and nonradiative decay constants similar to the ones in water solutions but 6AQ-M is not formed. A good estimation could have been drawn from measurements in ethanol (6AQ-N is a strong enough photobase to abstract a proton from methanol). In ethanol the emission lifetime of 6AQ-N is 8.5 ns, almost 2 orders of magnitude longer than in water, so one can safely assume that the apparent fluorescence decay rate in H_2O and D_2O, k_w, is practically equal to the rate of proton (deuterium) abstraction, $k_r = k_w$.

The free-energy vs. reaction-rate curve is calculated using the MBEBO equation,[55] eqs 23–25, below:

$$k_r = k_r^0 \exp(-\Delta G_a/kT) \tag{23}$$

where the frequency factor, k_r^0, has been found to approach the reciprocal value of longitudinal relaxation time, τ_L, of the solvent (water), $\tau_L \approx 0.8$ps[56] and ΔG_a the activation free-energy of the proton transfer reaction and is given by the Marcus MBEBO equation, eq 24

$$\Delta G_a = \Delta G^o/2 + \Delta G^\#_o + \Delta G^\#_o \cosh[\Delta G^o \ln 2/(2\Delta G^\#_o)]/\ln 2 \tag{24}$$

In eq 24

$$\Delta G^o = \mathrm{RT}\log(10)\Delta \mathrm{p}K_a \tag{25}$$

Where $\Delta G^\#_o$ is the intrinsic activation free energy of the symmetric transfer when $\Delta \mathrm{p}K_a = 0$ and ΔG^o is equal to zero. The above semi-empiric model for proton dissociation is supported by the theoretical studies on proton-transfer reaction by Hynes and coworkers.[57–60]

For aqueous solutions, our study demonstrates that the rate of proton transfer is controlled by a free energy relationship common for both the acid and base side, irrespective of whether water acts as proton acceptor or as proton donor. This points to a common factor controlling both types of proton transfer reactions in water. The reaction parameters correlating the kinetic data, $k_r^0 = (1\text{ps})^{-1}$ and $\Delta G^\#_o = 2.5$ kcal (Fig. 6), may be identified with dynamic and thermodynamic parameters controlling the rearrangement of the hydrogen-bonding network of water along the proton transfer coordinate. The MBEBO intrinsic reaction parameters are extracted from the following proton transfer reactions and represent a graphic average over an ensemble of reaction parameters:

1. Photoacid (pyranine and naphthol derivatives) dissociation to water [24,61] (solid dots).
2. Proton transfer from photoacids to bases: pyranine reacting with carboxylate bases in a reactive complex consisting of $HPTS^{-}\cdots H_3O^{+}\cdots {}^{-}OOCCH_{(3-x)}Cl_x$ ($x = 0$–3) in D_2O (solid triangles),[50–52] 2N-6,8S reacting with cyanate OCN^- in H_2O,[53] and bicarbonate HCO_3^- bases in D_2O[62] (open dots). (The values obtained in D_2O were rescaled by a factor of 1.45 to approximate proton transfer.)
3. Proton abstraction from water to photobases: acridine and the following quinoline bases: 3-hydroxyquinoline (3HQ),[16] 6-methoxyquinoline (6-MQ),[17] 6-hydroxyquinoline (6HQ),[17] and 6-aminoquinoline (6AQ) (this work) (solid squares).
4. Water auto-dissociation[33] (open square).

The numeric values of the two reaction parameters, k_r^0 and $\Delta G^\#_o$, may be viewed as representing some specific "universal" properties of acid–base reactions in water when proton transfer involves water molecules acting both as one of the reactants and as the reaction medium.

Using this general correlation between rates and equilibriums for proton transfer reactions, we can directly estimate the acidity of water molecules solvating metal ions by measuring the proton transfer rate from the metal cation hydrates to a base of a known basicity. We estimate by this method that water molecules solvating the Mg^{2+} cation have a pK_a value about 3.3 units lower than that of bulk water using 6AQ as the Brønsted photobase (present study). A smaller decrease of 2.2 pK_a units is similarly extracted using the less accurate measurement of the protonation rate of acridine.[12] The pK_a value of the water molecules in Mg^{2+} hydrates, which was calculated in the present study, compares well with values indirectly obtained in concentrated solutions of strong electrolytes. In particular, it was reported that the pK_a of water decreases by 3.3 pK_a units in Mg^{2+} solution and by 6.5 pK_a units in Zn^{2+} solution.[63] Recently, Bernasconi et al.,[64] have studied the proton dissociation of water molecules coordinated to a divalent metal ion center, M^{2+} (Mg^{2+}, Zn^{2+}), using density functional theory (DFT) and ab initio molecular dynamics (AIMD) simulations. Bernasconi et al., have also computed the acidity of coordinated water molecules in solution using free-energy thermodynamic integration with constrained AIMD. This approach has yielded a value of 9.5 for the pK_a value of Mg^{2+} hydrate in the gas phase, which is about 4.5 units lower than the pK_a of bulk water, which is slightly larger than our estimate of a 3.3 pK_a unit reduction.

CONCLUSIONS

The intrinsic Brønsted acidity of strongly interacting water molecules in metal hydrates was directly determined by measuring ultrafast proton transfer rates from Mg^{2+} hydrates to strong amino-photobases in aqueous solution. These metal-hydrate cations significantly increase the acidic properties of the complexed water molecules. As a result, water in metal cation hydrates protonates basic species much more rapidly than bulk water. The rate of the hydrolytic process is controlled by a free energy relationship that we have found to be common for a large number of photoacids and photobases, when water either acts as the proton acceptor or the proton donor, respectively. The pK_a value of water molecules solvating Mg^{2+} ions is estimated to decrease by about 3.3 pK_a units as compared to bulk water, in very good agreement with values obtained in the past by several theoretical studies and experimental methods. We have extended a general method for determining the pK_a value of water to the case of metal cation hydrates in water. By doing so, we have introduced a general method for determining of acidity of water molecules in solution when interacting with ions, organic solutes or biological molecules. We expect our method also to be useful for the investigation of the reactivity of water in diverse biological environments.

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