Water Deficient Environment Accelerates Proton Exchange: Acetone−Water Reaction Catalyzed by Calix[4]hydroquinone Nanotubes

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Calix[4]hydroquinone nanotubes possess the unique property to catalyze proton exchange between water and acetone. Since concerted proton transfer mechanisms could be excluded previously, stepwise proton transfer via ionic intermediates created by predissociation of CHQ OH groups is studied using state-of-the-art quantum chemical methodology. In fact, the presence of charged species, protonated acetone or deprotonated hydroquinone, leads to a substantial decrease of the proton transfer energy barrier and to calculated reaction rates that provide an explanation for the experimentally observed proton exchange. Furthermore, our quantum chemical investigation demonstrates that the catalytic activity of CHQ aggregates is not based on a reduction of the energy barrier connected with proton transfer but on the desolvation of acetone and prevention of solvent water cluster formation.

1. Introduction

Self-assembling organic hollow and tubular structures have attracted considerable interest as prospective functional materials in the areas of catalysis, electrochemistry, molecular recognition, and drug discovery.[1−5] Recently, tubular self-assembling nanostructures of calix[4]hydroquinone (CHQ) monomers have been discovered (Figure 1A).[6,7] In contrast to mostly covalently bound architectures, these tubular structures consist of bowl-shaped CHQ monomers linked only by hydrogen bonds (H-bond). Bridging water molecules link the OH-groups of CHQ in a quasi one-dimensional (1D) H-bond chain along the axis of the tubular structure (Figure 1A). In general, the molecular assembly into these CHQ nanotubes is predetermined by a delicate interplay of H-bonding and $\pi-\pi$ interactions similar to the situation found in biological systems, such as ion channels in lipid membranes and membrane proteins.[8,9]

The hollow bowl shape of the aromatic CHQ constituents lead to the unusual chemical properties of the tubular nanostructures. Most importantly, these nanotubes can specifically trap small organic molecules like acetone, 2-propanol, and 2-methyl-2-propanol,[10−12] where typically one molecule is bound to one CHQ bowl. A particularly astonishing property of the tubular CHQ structures is their catalytic function in acetone−water proton exchange (PE),[13] which has been observed at ambient conditions in NMR spectra displayed in Figure 1B. It is apparent that proton exchange between deuterated acetone and water takes place on a time scale of a few days. In analogous NMR experiments, acetone−water PE has also been observed catalyzed by nontubular CHQ aggregates in water deficient environment. On the contrary, a control experiment on an aqueous solution of hydroquinone (QH₂), acetone, and water revealed no proton exchange,.[14]

In a previous theoretical investigation,[14] we have studied the catalytic function of tubular and nontubular CHQ aggregates in the proton exchange between acetone and water employing high-level ab initio methods. Since acetone−water PE was not observed in the control NMR experiment on a solution of QH₂, acetone, and water, simple acid catalysis of keto−enol tautomerism by QH₂ has been ruled out as the principle mechanism. It was thus assumed that the PE reaction occurs via concerted keto−enol tautomerism (KET) of trapped acetone molecules without the intermediate formation of ionic species.

In that investigation, the influence of individual water molecules on the acetone−water PE in acetone···H₂O clusters and in QH₂···(H₂O)ₙ···acetone complexes was elucidated in detail, and it was shown that three or four water molecules seem to be optimal to catalyze the PE reaction, whereas additional solvent water molecules decrease the efficiency and show an anticooperative effect. Thus, the limited number of water molecules present (i.e., the water deficiency in the tubular and nontubular CHQ aggregates) appears to be an important feature of their catalytic function in the acetone−water PE reaction. However, the rate constant of the most efficient concerted KET occurring in the acetone·3H₂O complex with the activation energy of 29.1 kcal mol⁻¹ has only a very small value of 10^{-13} M⁻¹ s⁻¹. This is clearly too low to explain the observation of proton exchange in the NMR experiment on CHQ aggregagtes, and hence, KET via concerted proton transfer assisted by a few OH groups cannot be the mechanism of the proton exchange phenomenon.[14]

Since the limited number of water molecules is an important factor favoring concerted KET in CHQ aggregates compared to solution, a natural question to ask is thus, whether the water deficiency also supports ionic mechanisms in CHQ relative to aqueous solution, for the latter were previously excluded based on the NMR experiments. If this would be the case, it could provide an explanation of the observation of acetone−water PE in CHQ in contrast to solution via ionic mechanisms. To clarify that issue, we have extended our investigation on catalytic role

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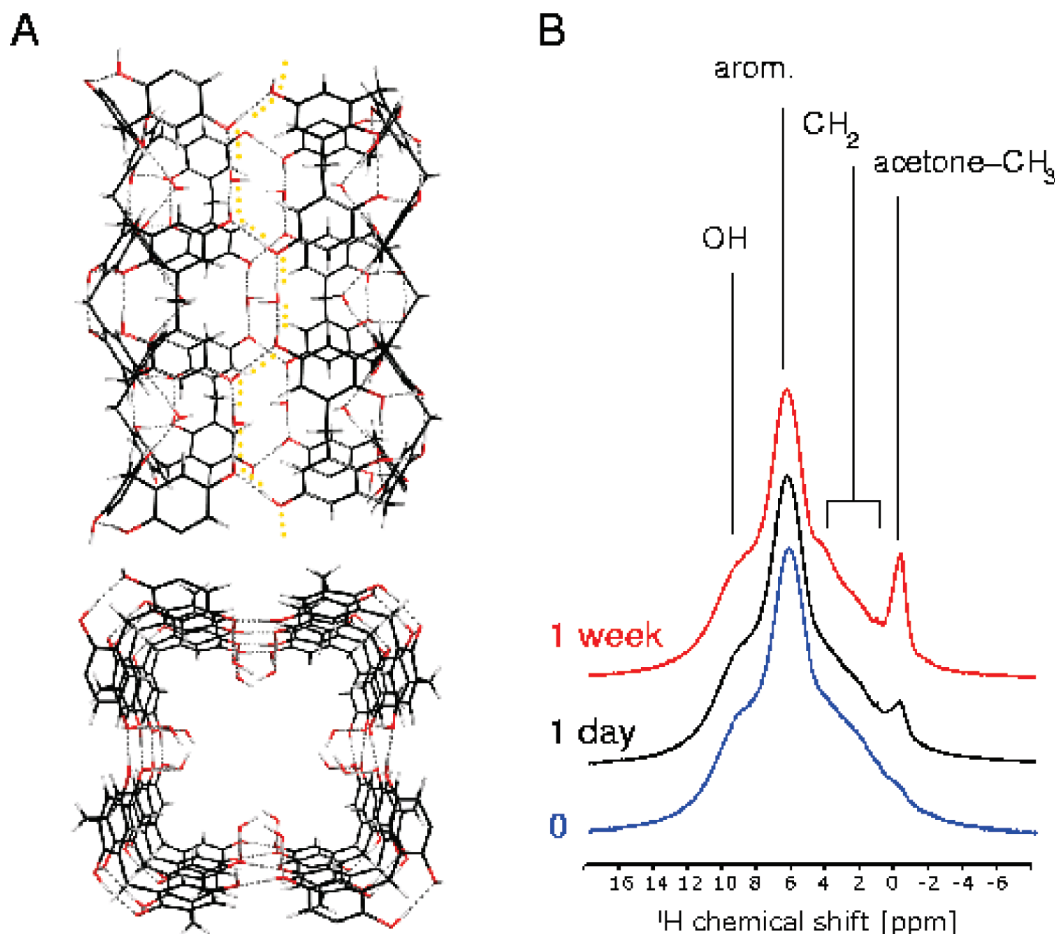‡ Max Planck Institute for Polymer Research.
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10396   *J. Phys. Chem. C, Vol. 113, No. 24, 2009*

Zakharov et al.

Figure 1. Structure of tubular CHQ (A) and time evolution of the solid state ^{1}H NMR spectrum of tubular CHQ trapping C_3D_6O (B).

of CHQ in acetone−water PE to ionic mechanisms following dissociation of the CHQ OH group.

The paper is organized as follows. In the section 2, our theoretical methodology is outlined. Section 3 starts with preliminary considerations, which allow us to suggest two possible mechanistic scenarios for acid-catalyzed PE. The results of our calculations on proton transfer via several ionic intermediates are outlined and discussed in sections 3.2−3.5. Some implications of our results for acid-catalyzed proton exchange in aqueous solution of acetone are presented in section 3.6. Finally, Section 4 summarizes the major conclusions of this paper.

2. Theoretical Methods

The description of proton transfer reactions generally requires a quantum treatment of electronic structure at highly correlated level, coupled with nuclear dynamics. However, for the large systems of interest such calculations are not feasible, and one has to resort either to combination of computationally inexpensive electronic structure methods with nuclear dynamics or to static calculations employing correlated ab initio theory. Since former methods often fail to describe noncovalent interactions even qualitatively, we have chosen to take the latter route.

The entire CHQ−water−acetone molecular complex is by far too large for high-level correlated quantum chemical methods, and therefore molecular models have been selected for this study. We have chosen hydroquinone (QH$_2$) as model, since it represents a substructure of CHQ and has been successfully employed in our previous study.[14] The acidity of QH$_2$ and CHQ can be expected to be essentially identical

exhibiting similar pK_a values of approximately 10. Indeed, DFT calculations of their deprotonation energies at B3LYP/6-31G** theory level yield values of 361 and 369 kcal mol^{-1}, respectively. This confirms that QH$_2$ and CHQ have practically identical chemical properties in proton transfer processes.

Second order Møller−Plesset perturbation (MP2) theory[15,16] is capable to treat the long-range interactions,[17] as well as dispersion, polarization and covalent effects associated with hydrogen bonding[18] with sufficient accuracy. The location of transition state structures and zero-point vibrational energy (ZPVE) corrections required the computation of analytical second derivatives of the energy. Unless indicated otherwise, the stationary point searches and harmonic vibrational frequencies were performed at the MP2 level[19,20] with the moderate 6-31G** basis set, while energy barriers for proton transfer were improved by means of single-point calculations with the larger cc-pVTZ basis set.[21] Deprotonation enthalpies have been computed as the difference of the total energies between the neutral molecule and its deprotonated anion, corrected for ZPVE. Proton affinities are given as energy difference between the protonated and neutral molecules, corrected for ZPVE. Comparison with available experimental data for the reaction barrier of acid-catalyzed acetone KET indicates that such a practical approach is accurate enough for this study.[22]

In our previous work,[14] we applied the counterpoise (CP) correction to the binding energies for the basis set superposition error (BSSE). Here the CP correction is not employed since we are dealing with charged species, and in such cases a specification of the charge distribution over the fragments in integer values is required. However, the distribution of the
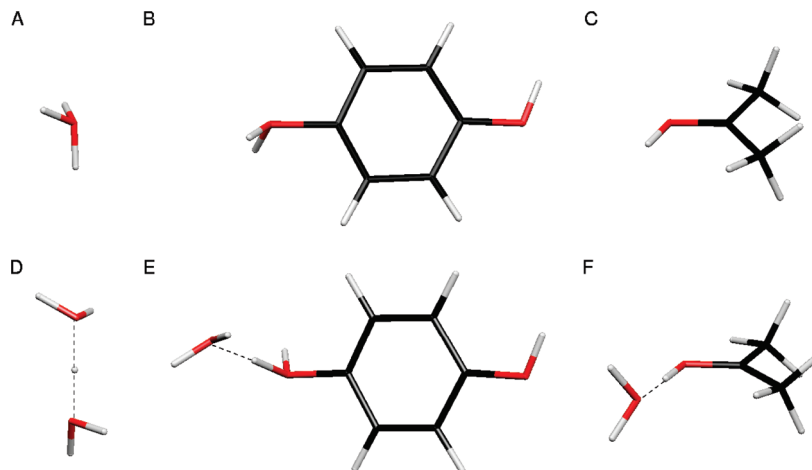
Figure 2. Molecular structure of the protonated water $[H_3O]^+$ (A), hydroquinone $[QH_3]^+$ (B) and acetone $[C_3H_6O]^+$ (C), water dimer $[(H_2O)_2-H]^+$ (D), monohydrated hydroquinone $[QH_2\cdots H_2O-H]^+$ (E), and monohydrated acetone $[C_3H_6O\cdots H_2O-H]^+$ (F).

charge over the dissociating fragments is not unambiguous and, as a consequence, so is the application of CP correction scheme.[23] In order to avoid the imbalance in the calculation of CP corrected protonation and deprotonation energies of the ionic clusters, we decided to not correct for BSSE.

MP2 natural orbital occupation number (NOON) analysis[24,25] gives insight into the multireference character of the wave functions, which can increase during bond-breaking reactions. The NOON analysis of all of the transition state structures studied in this work did not reveal appreciable multireference character. Hence, the closed-shell MP2 calculations with a single reference are clearly adequate for the study of all model systems. This is not surprising, since the dissociating species are closed-shell fragments. Because the ZPVE correction is slightly overestimated within the harmonic approximation compared to that calculated with corrected anharmonic potentials, we have scaled the harmonic ZPVE correction by a factor of 0.9.[26]

Most of the calculations were performed with the GAMESS-US[27] software package while partial charges analyses are done with the Gaussian 03 package of programs.[28]

3. Acetone/Water Proton Exchange in CHQ Aggregates

3.1. Relative Stability of the Charged Clusters. As a first step of our theoretical investigation of ionic PE mechanisms in CHQ, let us consider suitable model systems and possible scenarios that are needed to be taken into account. Since the OH group of CHQ (or in our model complexes including QH_2) dissociates first due to its higher acidity, the initial question to address is where does the proton go after dissociation? To answer this question, we have studied selected protonated molecules and their complexes with water and computed the proton affinities of the corresponding parent neutral molecules. By inspection of the proton transfer networks present in the tubular CHQ aggregates a few possible protonation sites can be identified. The most likely proton acceptors are monomers (water, CHQ, or acetone), or their complexes like $(H_2O)_2$, $QH_2\cdots H_2O$, $C_3H_6O\cdots H_2O$, and so on (Figure 2). In principle, one cannot a priori exclude that larger water complexes are present in CHQ aggregates. However, NMR experiments on tubular as well as nontubular CHQ aggregates have shown that they correspond to water deficient media. Therefore, one can thus safely assume that additional "free" water molecules that are not bound in the H-bond network of the tubular assembly are scarce and most likely spread evenly forming H-bonds to the OH-groups of CHQ. As a consequence, the amount of

TABLE 1: Zero-Point Energy Corrected Proton Affinities (PA) and Deprotonation Energies (DE) (kcal mol^{-1}) of Potential Proton Acceptors (See Text)[a]

| Complex	PA (ZPE) [kcal/mol]	DE (ZPE) [kcal/mol]
H_2O	−165.7 (+8.4)	
QH_2	−179.2 (+7.9)	+353.2 (−9.0)
C_3H_6O	−192.5 (+8.1)	+373.0 (−8.8)
$[C_3H_6O-H]^+$		+201.3 (−7.7)
$(H_2O)_2$	−197.8 (+7.2)	
$QH_2\cdots H_2O$	−203.2 (+7.5)	
$C_3H_6O\cdots H_2O$	−211.5 (+7.7)	

[a] All values were calculated as single-point MP2/cc-pVTZ energies on the MP2/6-31** optimized structures. ZPE has been computed at the MP2/6-31** level and is given in parentheses.

multihydrated molecular complexes in tubular and nontubular CHQ aggregates is probably negligible.

Geometry optimizations of the selected protonated complexes at the level of MP2/6-31G** theory produced the equilibrium structures shown in Figure 2. Proton affinities of these complexes, calculated at the MP2/cc-pVTZ level as differences in the total energies of the protonated and neutral systems are presented in Table 1. One can see that acetone has a higher PA than water and QH_2 by about 27 and 13 kcal mol^{-1}, respectively. Upon addition of one water molecule to each monomer, the acetone complex $C_3H_6O\cdot H_2O$ still remains the best proton acceptor, but the energetic differences between the complexes decrease. The PA of the water complexes $QH_2\cdot H_2O$ and the water dimer are only 8 and 14 kcal mol^{-1} smaller, respectively.

The comparison of PA values of the selected monomers and their monohydrated complexes suggest that the proton originating from CHQ will attach to the carbonyl group of acetone. In that situation, a zwitterionic intermediate would be formed which triggers back proton transfer with a PE step between the methyl group of acetone and water. This mechanism is sketched in Scheme 1. The created zwitterionic intermediate is probably quite high in energy and thus makes the initial CHQ dissociation energetically unfavorable, whereas the PE step should be essentially barrierless.

However, as PA increases with addition of water molecules to the cluster, one may suspect that further aggregation will lead to the protonation of pure water clusters rather than acetone. Indeed, this behavior has been previously reported for the water dimer that can abstract a proton from protonated alkenes, in contrast to a single water molecule whose proton affinity is not sufficient.[29]

SCHEME 1: Sketch of the Proposed Mechanism of Acetone Methyl−Water Proton Exchange Initiated by OH-Group Dissocation of QH_2 Leading to the Formation of a Zwitterionic Intermediate[a]
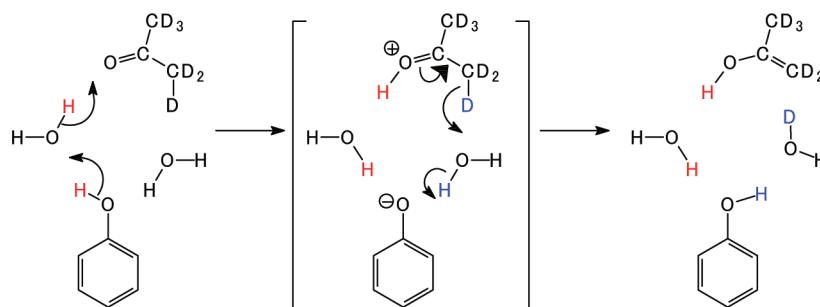
[a] Finally a methyl deuteron is transferred to a nearby water molecule in a back proton transfer step.
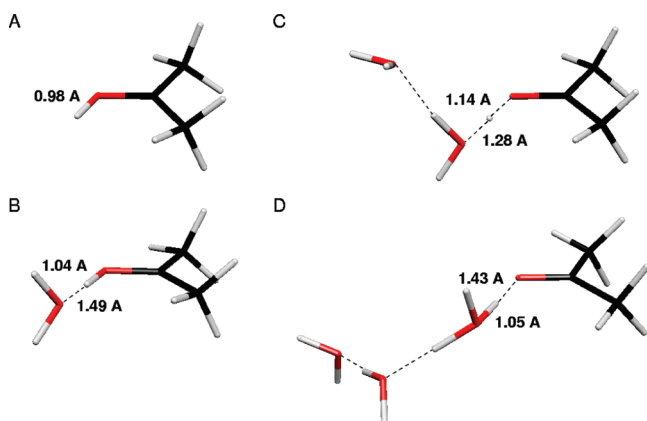

Figure 3. Optimized structures of protonated acetone (A) and protonated clusters of acetone hydrated by one (B), two (C), and three (D) water molecules.

Figure 4. Optimized structures of the protonated clusters $[C_3H_6O−H\cdots(H_2O)\cdots QH_2]^+$ (A) and $[C_3H_6O\cdots H−(H_2O)_2\cdots QH_2]^+$ (B).

SCHEME 2: Sketch of Proposed Mechanism of Acetone Methyl−Water Proton Exchange Catalyzed by a Deprotonated CHQ Moiety, Where the Proton Has Been Transferred to the Environment and Is Not Immediately Present

To check for that possibility, the structures of protonated acetone−water clusters with up to three water molecules have been optimized. The structures have been generated by addition of the *n*th water to the optimized structure of the $[C_3H_6O−H\cdots(H_2O)_{n-1}]^+$ cluster followed by a reoptimization step. From the comparison of the optimized geometries (Figure 3) one can see that only upon the addition of the third water molecule the proton migrates from the acetone to the adjacent water molecule. In the case of $[C_3H_6O−H\cdots(H_2O)]^+$, the proton is clearly bound to the carbonyl group of acetone exhibiting a typical bond length of 1.04 Å. Addition of one more water molecule to the $[C_3H_6O−H\cdots(H_2O)_2]^+$ cluster results in a small shift of the proton to the water. However, it is still located more closely to the acetone molecule with an extended bond length of 1.14 Å. Finally, in the cluster exhibiting three water molecules $[C_3H_6O\cdots H−(H_2O)_3]^+$, the proton is transferred entirely to the adjacent water molecule. This is in agreement with our finding that a cluster of three water molecules has larger proton affinity than acetone·H_2O complex. Summarizing, the protonated acetone is stable in water deficient environment (e.g., in CHQ nanotubes), whereas in excess of water molecules around (such as in aqueous solution), protonated acetone becomes unstable and the proton moves to the water molecules.

To confirm this effect in CHQ aggregates, we optimized protonated clusters of acetone, QH_2, and one or two water molecules (Figure 4). While in the $[C_3H_6O−H\cdots(H_2O) \cdots QH_2]^+$ cluster (Figure 4A) the proton is still bound to the carbonyl group of acetone, addition of the second water molecule results in hydroxonium cation and neutral acetone in the $[C_3H_6O\cdots H−(H_2O)_2\cdots QH_2]^+$ complex (Figure 4B). Therefore, the proton can be released into the environment, when sufficient water molecules are available. In that case, the proton
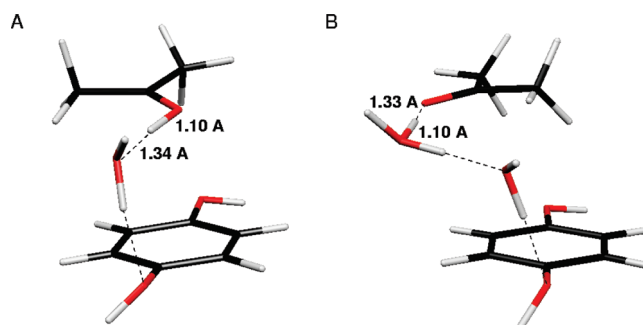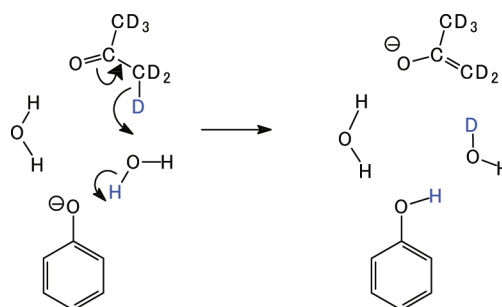
is not involved in the acetone−water PE, which is catalyzed by the anionic QH^- moiety (Scheme 2).

In summary, two general ionic scenarios are to be considered in our investigation of proton exchange between acetone and water in water deficient CHQ aggregates: (1) The predissociated proton of the OH group of QH_2 remains in the vicinity and protonates acetone leading to a zwitterionic intermediate and (2) the proton is released into the environment and is not directly involved in the proton exchange. In the following sections, we will investigate these two possibilities in detail.

3.2. Proton Exchange via Zwitterionic Intermediate. The quantum chemical description of the proton exchange reaction mechanism via zwitterionic intermediates (Scheme 1) consisting of a protonated cationic acetone molecule and deprotonated QH^- anion presents a challenge, since the zwitterionic structure does not correspond to a local minimum on the potential energy surface. A partial geometry optimization of the zwitterionic structures is possible when geometrical constraints are imposed in order to keep the hydrogen atom covalently bonded to the
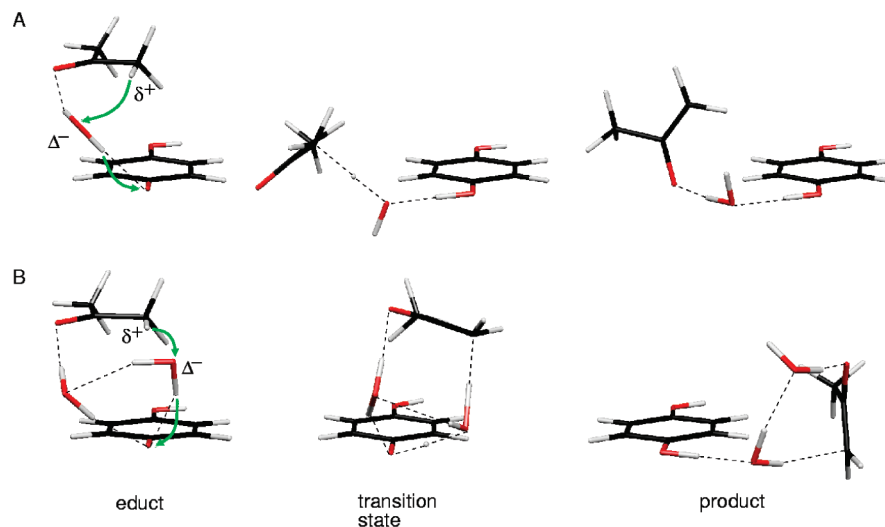
Water Deficient Environment Accelerates Proton Exchange

J. Phys. Chem. C, Vol. 113, No. 24, 2009 **10399**

Figure 5. Reactants, transition states and products of the proton transfer pathways from the acetone methyl group to deprotonated hydroquinone $[QH]^-$ in $[C_3H_6O\cdots H_2O\cdots QH]^-$ (A) and $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ (B) clusters, respectively. The arrows highlight the proton transfer pathway.

oxygen atom of the acetone molecule. For example, the energy of a partially optimized $[C_3H_6OH^+\cdots H_2O\cdots QH^-]$ cluster is found to be only 24 kcal mol^{-1} above the neutral complex. Since the obtained energies constitute an upper bound, they reveal the feasibility of the zwitterionic catalytic pathway at ambient temperatures. Indeed, this is readily corroborated by the liquid phase NMR experiment on the admixture of CHQ, acetone and water from our previous study, where proton exchange between the −OH groups of CHQ and water has been indicated (Figure 2B of ref 14): it is possible since the resolution of the liquid state NMR signal is greater than that of the solid state. Therefore, we assume in our further analysis that the formation of the zwitter-ionic intermediates occurs with the same probability as the deprotonation of QH$_2$ in water. Taking the pK_a value of the weak acid QH$_2$ of 9.8 into account, one recognizes that a fraction of only 10^{-5} of the present QH$_2$ molecules are deprotonated. Therefore, calculated rates of proton transfer starting from an educt generated by deprotonation of QH$_2$ must be scaled with 10^{-5} to account for the preceding deprotonation step. Here, it is reasonable to assume that the deprotonation step is independent of the presence of acetone.

Owing to the reasons given above, the zwitterionic complexes technically cannot be employed as defined starting points to study proton transfer from the acetone methyl group to the attached water molecule within a minimum energy pathway picture. Therefore, a different strategy has been chosen to study the energetics of the zwitterionic mechanism and to obtain reasonable values for the energy barriers and reaction rates. Within this strategy, the neutral, as whole, zwitterionic complex (Scheme 1) was decomposed into two ionic fragments. On one hand, anionic complexes of neutral acetone, one or two water molecules and deprotonated QH$^-$ are used to investigate the influence of QH$^-$ on that mechanism (Figure 5). At the same time, this anionic complex serves a model for the second anionic mechanism introduced in the previous section and depicted in Scheme 2. On the other hand a positively charged model complex of protonated acetone, one water molecule and neutral QH$_2$ has been employed to study the role of protonated acetone in the transfer step (Figure 6). It is clear that both the protonated acetone as well as the QH$^-$ anion together energetically support the proton transfer step. Therefore, the obtained energy barriers for proton transfer in the cationic and anionic model complexes are each higher than they are in the initial
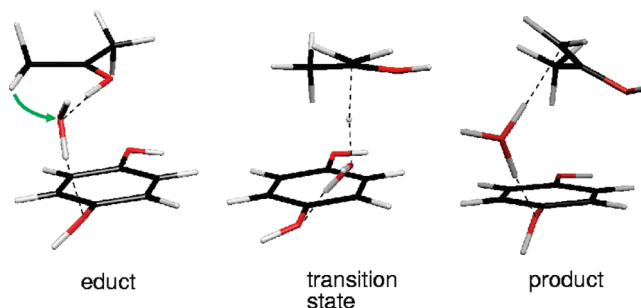

Figure 6. Reactant, transition state and product of the proton transfer between the methyl group of protonated acetone cation and water in the cationic complex $[C_3H_6OH\cdots(H_2O)\cdots QH_2]^+$. The green arrow highlights the proton transfer pathway.

zwitterionic intermediate (Scheme 1), while the barriers for proton transfer in the anionic complex correspond to the true barrier in case of the anionic mechanism (Scheme 2).

3.3. Proton Exchange via Anionic Intermediates. To begin the investigation of the possible role of anionic clusters in PE, we have constructed the complex $[C_3H_6O\cdots H_2O\cdots QH]^-$ (Figure 5A). Computation of the minimum energy path for the proton transfer from the methyl group of acetone to the water molecule reveals a concerted double proton transfer of a second water proton to the $[QH]^-$ anion via the transition state depicted in Figure 5A. The product of this reaction path is a complex of neutral QH$_2$, and acetone anion $[C_3H_5O]^-$ with a H-bonded neutral water molecule between them. The calculated activation enthalpy for the concerted proton transfer via the transition state shown in Figure 5 amounts to 13.9 kcal mol^{-1} (Table 2) at MP2/cc-pVTZ//MP2/6-31G**+ZPVE level of theory. The concerted mechanism can be rationalized by comparison of the deprotonation energy of acetone and the proton affinity of water, the potential intermediates of a stepwise process (Table 1). Since they are about 207 kcal mol^{-1} higher in energy than the barrier for concerted transfer, stepwise proton transfer via an intermediate hydronium cation H$_3$O$^+$ is very unlikely to occur.

Our previous study revealed that additional water molecules can have significant influence on the reactivity of the neutral complexes.[14] Following the same logics here, we studied the anionic model complex $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ (Figure 5B). Concerted double-proton transfer is observed for this complex as well. The proton is transferred from the methyl group of

TABLE 2: Energy Difference between Educt and Product (ΔE_{equil}), Energy Barriers (ΔE_{PT}), Free Activation Energies (ΔG_{PT}), and Transfer Rates (k_{PT}) Calculated at Ambient Temperature ($T = 298.15$ K) for the Proton Transfer in $[C_3H_6O\cdots H_2O\cdots QH]^-$, $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$, and $[C_3H_6OH\cdots H_2O\cdots QH_2]^+$ Model Clusters[a]

complex	ΔE_{equil}	ΔE_{PT}	ΔG_{PT}	k_{PT}
$[C_3H_6O\cdots H_2O\cdots QH]^-$	4.2 (−0.4)	13.9 (−3.5)	13.0	1.8×10^3
$[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$	9.2 (−0.2)	16.3 (−3.7)	16.8	2.9
$[C_3H_6OH\cdots(H_2O)\cdots QH_2]^+$	25.8 (−0.7)	25.6 (−2.1)	25.1	2.6×10^{-6}
$[C_3H_6O\cdots(H_2O)_3]$	11.5 (−1.2)	29.1 (−1.7)	32.0	2.3×10^{-13}

[a] The energies are given in kcal mol^{-1} and have been computed at MP2/cc-pVTZ level at MP2/6-31** optimized geometries. Zero-point energy corrections are calculated at the MP2/6-31** level and given in parentheses.

acetone, and simultaneously the second proton is transferred from the water to QH$^-$ via the transition state shown in Figure 5B. The product of this reaction presents a complex of deprotonated acetone and a neutral QH$_2$ molecule bridged by two water molecules. The calculated activation enthalpy for this pathway is 16.3 kcal mol^{-1}. Compared to the complex $[C_3H_6O\cdots H_2O\cdots QH]^-$ containing only one bridging water molecule, the barrier is higher by 2.5 kcal mol^{-1}. Thus, the additional water molecule exhibits an anticooperative effect within the anionic mechanism.

The physical reason for the increased efficiency of proton transfer in the anionic complexes compared to the neutral complexes studied previously[14] can be traced to the polarization of the proton donating and accepting groups by the negatively charged QH$^-$ anion. This is evidenced by the comparison of the Mullicken charges obtained for the anionic model cluster $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ and its neutral counterpart $[C_3H_6O\cdots(H_2O)_2\cdots QH_2]$. The difference of the Mullicken charges between the methyl proton of acetone and the accepting oxygen atom of the adjacent water molecule is 0.77 in the anionic species (Figure 6B), and only 0.65 in the corresponding neutral cluster.[14] This correlates with the difference in the free energy barriers for the proton transfer: 16.8 kcal mol^{-1} in case of the anionic complex versus 32.2 kcal mol^{-1} in case of the neutral cluster.

3.4. Proton Exchange via Cationic Intermediates. Let us now turn to the investigation of proton transfer in cationic model complexes of protonated acetone, water and neutral QH$_2$. The minimum energy path of the proton transfer in the model cluster $[C_3H_6OH\cdots H_2O\cdots QH_2]^+$ is shown in Figure 6. The products of this PE are the neutral enol-form of acetone, a hydronium cation H$_3$O$^+$ and neutral QH$_2$. In this pathway, the H-bond between the protonated carbonyl group of acetone breaks and another one is created between the hydronium cation and the methylene group of the neutral enol-form of acetone. The activation enthalpy for the proton transfer in this pathway is calculated to be 25.6 kcal mol^{-1} (Table 2). In comparison, proton transfer between neutral acetone and one water molecule is characterized by an energy barrier of 37.5 kcal mol^{-1}.[14] Obviously, the positive charge on the acetone increases the rate of proton transfer similar to the negative charge on QH$^-$ described in the previous section. However, in the protonated acetone cluster $[C_3H_6OH\cdots H_2O\cdots QH_2]^+$ the decrease of the barrier is not due to polarization, but due to decreased deprotonation energy of the methyl group of the protonated acetone cation vs neutral acetone molecule (Table 1). While the deprotonation energy has a value of 373 kcal mol^{-1} for neutral acetone, it is only 201 kcal mol^{-1} for protonated acetone. The larger deprotonation energy of neutral acetone can be explained by stronger electrostatic attraction between the proton and the remaining anion, which is weaker in the case of protonated acetone, since the remaining acetone is neutral.

3.5. Calculated Rate Constants for the Proton Exchange. We employed the Arrhenius equation to calculate proton transfer rates for the three model complexes $[C_3H_6O\cdots H_2O\cdots QH]^-$, $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ (Figure 5A and B) and $[C_3H_6OH\cdots(H_2O)\cdots QH_2]^+$ (Figure 6) studied above. The computed free activation energies for the model complexes are 13.0 and 16.8 kcal mol^{-1} for the anionic complexes $[C_3H_6O\cdots H_2O\cdots QH]^-$ and $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$, respectively, and 25.1 kcal mol^{-1} for the cationic complex $[C_3H_6OH\cdots(H_2O)\cdots QH_2]^+$ at 298.15 K. Comparison of these barrier heights with the lowest one obtained for proton transfer between neutral acetone and water via keto−enol tautomerism of 32.0 kcal mol^{-1} already demonstrates that the ionic intermediates reduce the energy barrier substantially. The computed proton transfer rates for the ionic complexes are 1.8×10^3, 2.9, and 2.3×10^{-6} M^{-1}s^{-1} for the complexes $[C_3H_6O\cdots H_2O\cdots QH]^-$, $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ and $[C_3H_6OH\cdots(H_2O)\cdots QH_2]^+$, respectively. However, these values must be scaled by the equilibrium concentrations of deprotonated QH$_2$ and the protons, which can be easily estimated to be ca. 10^{-5} from the QH$_2$ pK_a value of 9.8, since QH$_2$ is a weak acid. This leads to the effective rates of 1.8×10^{-2}, 2.9×10^{-5}, and 2.3×10^{-11} M^{-1} s^{-1} respectively. The rates for the anionic mechnism are comparable with the results of NMR experiments on CHQ aggregates, and thus explain the observation of acetone−water proton exchange in CHQ aggregates.

3.6. Catalysis of Acetone−Water Proton Exchange by Strong and Weak Acids in Aqueous Solution. Based on our finding, we can now make several remarks on general acid catalysis of acetone−water PE reaction mechanism. Judging from computed deprotonation energies and proton affinities (Table 1), no protonated acetone species are present in aqueous solution of acetone and weak (or strong) acids, since protonated water clusters are more stable than protonated acetone−water clusters. Therefore, one can assume that catalysis through the anion of the dissociated acid (in our case QH$^-$), is the dominating process under acidic conditions. Furthermore, our calculations on the anionic model complexes $[C_3H_6O\cdots H_2O\cdots QH]^-$ and $[C_3H_6O\cdots(H_2O)_2\cdots QH]^-$ have shown the energy barrier for proton transfer will increase by 2.5 kcal mol^{-1} with the addition of a second solvent water molecule. Due to this anticooperative effect of extra water molecules, we can estimate the barrier for proton exchange in aqueous solution to be ca. 20 kcal mol^{-1}. In fact, the energy barrier for keto−enol tautomerism of acetone catalyzed by perchloric acid has been measured previously to be 20 kcal mol^{-1}.[22] This energy barrier leads to a rate constant of about 10^{-2} M^{-1} s^{-1} for the rate-limiting proton transfer step from the methyl group of acetone to the anion of the dissociated acid. In analogy with CHQ, the observed rate of proton transfer depends on the concentration of anions, i.e., $k_{PT}^{eff} = 10^{-2}$ M^{-1} s^{-1} [A$^-$]. This allows us to distinguish between the limiting cases of weak and strong acids. In the former case only a fraction of the acid molecules is dissociated, while in the latter case essentially all acid molecules are dissociated so that the PE rate is faster, and needs not be scaled with a predissociation rate as in the case of weak acids. Consequently, in the presence of a strong acid proton exchange between acetone and water occurs with the rate close to 10^{-2} M^{-1} s^{-1} and should thus be easily observable in appropriate NMR experiments. In the presence of weak acids like QH$_2$, the reaction is much slower and in 1 M solution the calculated

Water Deficient Environment Accelerates Proton Exchange

J. Phys. Chem. C, Vol. 113, No. 24, 2009 **10401**

rate has to be scaled with a factor of 10^{-5}. This leads to a substantial decrease of the rate.

4. Summary and Conclusions

In our previous theoretical investigation[14] we had studied concerted proton transfer between acetone and water in calix[4]hydroquinone (CHQ) aggregates via keto−enol tautomerism to explain their catalytic function in the observed proton exchange between acetone and water. The lowest free Gibbs activation energy for concerted proton transfer in a complex of acetone and three water molecules $C_3H_6O\cdots(H_2O)_3$ had been predicted to be 32.0 kcal mol^{-1}, resulting in PE rate of only 2.3×10^{-13} M s^{-1}. This rate is clearly too low to explain the observation of proton exchange between acetone and water in CHQ aggregates. Therefore, we studied three alternative, ionic mechanisms of proton transfer between acetone and initiated by the dissociation of CHQ OH-groups. Based on the structure of the CHQ nanotubular aggregates and their H-bond networks, protonated and deprotonated model clusters have been built and possible proton transfer pathways have been investigated using Møller−Plesset perturbation theory. The computed energy barriers for ionic proton transfer were substantially smaller than that for concerted transfer with activation free energies of only 13.0 and 16.8 kcal mol^{-1} in the most favorable cases of $[C_3H_6O\cdots(H_2O)\cdots QH)]^-$ and $[C_3H_6O\cdots(H_2O)_2\cdots QH)]^-$. The corresponding proton transfer rates are 1.8×10^{-2} and 2.9×10^{-5} M^{-1} s^{-1} taking CHQ predissociation into account. These rates are high enough to explain the observation of proton exchange between acetone and water during several hours of the NMR experiment. Herein, depending on the hydration of CHQ -OH groups, two principal ionic mechanisms either involving the anionic complexes like $[C_3H_6O\cdots(H_2O)_2\cdots QH)]^-$ or zwitterionic complex $[C_3H_6OH^+\cdots(H_2O)_2\cdots QH^-]$ can take place in CHQ aggregates. The latter mechanism should be more efficient or even barrierless than the former one due to the presence of uncompensated protonated acetone cation.

Our findings also have implications for acetone−water proton exchange in aqueous solution catalyzed by weak and strong acids. We have shown that protonated acetone is unlikely to be present in aqueous solution, and thus it is the anion of the dissociated acid that most probably catalyzes the proton transfer from the methyl group of acetone to water molecule. The solvent water molecules lead to the increase in the proton transfer energy barrier. While in the weak acids the concentration of the anion is reducing the PE rate, in strong acids it should be observable experimentally. The proton transfer is significantly more efficient in water deficient CHQ aggregates than in aqueous solution of QH$_2$, acetone and water, similarly to the neutral mechanism, studied previously.[14]

In summary, the unique property of CHQ aggregates to catalyze proton exchange between acetone and water originates from the interplay of two factors: (1) only one acetone molecule is bound to one bowl-shaped CHQ monomer,[11,12] thus embedding it into a H-bonded chain that can efficiently mediate the proton exchange between acetone and incorporated water molecules, and (2) CHQ aggregates are water deficient. Only a few water molecules are bound to the CHQ monomers and mediate the formation of CHQ nanotubes. Water deficiency is one of the key factors for efficient proton transfer since additional solvent water molecules may increase in the corresponding energy barrier. In other words, the catalytic activity of CHQ is due to the restriction on the formation of the large water clusters, characterized by an anticooperative effect. In general, one can expect that proton exchange is observable in isolated acetone−water−QH$_2$, or protonated acetone−water

clusters in the gas-phase, since destabilizing solvent water molecules are not present.

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