Water-Mediated Proton Transfer: A Mechanistic Investigation on the Example of the Hydration of Sulfur Oxides

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Received: October 20, 2000; In Final Form: February 21, 2001

We outline general mechanistic features of "water-mediated proton transfer" in the example of the isomerization reaction in hydrogen-bonded sulfur oxide−water supermolecules containing up to three water molecules. The nucleophilic attack of a water oxygen on the sulfur atom occurs concertedly with the (multiple) proton-transfer event(s). The protons are transferred according to the well-known hydrogen-bond compression mechanism. However, contrary to "pure" multiple proton-transfer reactions, the protons are transferred asynchronously. These mechanistic features force the reaction to be classical rather than quantum-tunneling-dominated down to rather low temperatures. In the quantum-dominated temperature region, tunneling takes place only if all protons tunnel through the barrier. Straight line corner cutting (large curvature tunneling) does not dominate at any temperature, as the reduced mass corresponding to reaction coordinate motion does not drop to values low enough in the reaction barrier region. The asymmetric nature of the potential energy surface even allows different mechanisms involving transient H_3O^+ rotation termed "molecular swing" and a H_2SO_3 isomerization to be favorable compared to water-mediated triple proton transfer in the case of three participating water molecules.

1. Introduction

In the literature water has been shown to be important as a catalyst mediating proton transfer. In many proteins hydrogen atoms are transferred more or less linearly for distances of about 10−50 Å between different amino acid residues along so-called "proton wires". Lately, light has been shed on the way protons are drawn through proteins on the example of ferredoxin I by a combined fast-scan voltammetry, high-resolution crystallography, and molecular dynamics study.[1] Similar transmembrane proton pumps or proton relays are ubiquitous in biochemistry. Bacteriorhodopsin,[2−6] alcohol dehydrogenases,[7−10] ATP synthase,[11−13] cytochrome *c* oxidase,[14−19] rhodobacter sphaeroides,[20,21] ribonucleotide reductase,[22,23] and carbonic anhydrase[24−31] are just a few examples of proteins having hydrogen-bond networks serving the function of long-distance proton transport. The function of the water molecules is to both accept and donate a proton. A similar transfer mechanism along proton wires (commonly referred to as Grøtthus mechanism) is thought to be the reason for the extraordinarily high conductivity in liquid water.[32−41]

Another possibility for the protons to be transferred is in a cyclic rather than linear manner. Such mechanisms referred to as "water-mediated proton transfer", "bifunctional water catalysis", or "water-assisted hydration" were demonstrated to be of relevance in many organic and anorganic reactions. In principle, water can be replaced by any hydroxylic solvent, e.g., alcohols, so that "solvent-assisted" or "solvent-mediated" proton-transfer reactions can also be assigned to this type of reaction. Again, a wealth of examples is known for this category. These examples range from *tautomerization* and *proton shifts* (e.g., in DNA/RNA-base analogues like formamidine,[42−45] 7-azaindole,[46−50] 7-hydroxyquinoline[51−53] and others,[54−57] in DNA/RNA-bases,[58−50] in peptides,[63,64] or in formic acid[65−67] as well as the Cope[68] and Beckmann[69] rearrangements), *hydration of double bonds* (e.g., of carbon dioxide,[70,71] sulfur oxides,[72−76] carbonyl compounds,[77,78] ketene imines, or carbodiimides[79,80]), *hydrolyses* (e.g., of carboxylic acid esters[81] or methyl chloride[82]), to *nucleophilic substitutions* (e.g., the decomposition of chlorine nitrate[83−88]).

Experimental and theoretical studies nowadays focus on a general, atomistic understanding of the involved proton-transfer processes. In this theoretical study we analyze in detail the reaction mechanism and the influence of tunneling on the example of the hydration of sulfur dioxide and sulfur trioxide in gas-phase supermolecules constituted of up to three water molecules. Recently, we have shown that in our atmosphere sulfur trioxide is hydrated rather than the much more abundant sulfur dioxide.[76] Furthermore, the best agreement in terms of reaction rate constants with reaction chamber flow studies is obtained in SO_3/H_2O complexes of 1:2 and 1:3 stoichiometry.[75] Now, we want to show how the proton-transfer mechanism and the multidimensional tunneling effect are altered when investigating such an "impure" proton-transfer reaction, i.e., proton-transfer reaction accompanied by a nucleophilic attack, rather than a "pure" proton-transfer reaction, which we investigated previously by the same method for cyclic water clusters[89,90] and the formic acid dimer.[91]

2. Methods

2.1. Stationary Points. Geometry optimization of the equilibrium structures and the transition states was performed both by hybrid density functional theory (B3LYP/6-31+G(d))[92] and by second-order perturbation theory (MP2/aug-cc-pVDZ),[93] as implemented in Gaussian98.[94] The nature of these stationary points was verified by calculating vibrational frequencies. The Hessian matrix contains exclusively positive eigenvalues for

10.1021/jp0038862 CCC: $20.00
Published on Web 05/04/2001

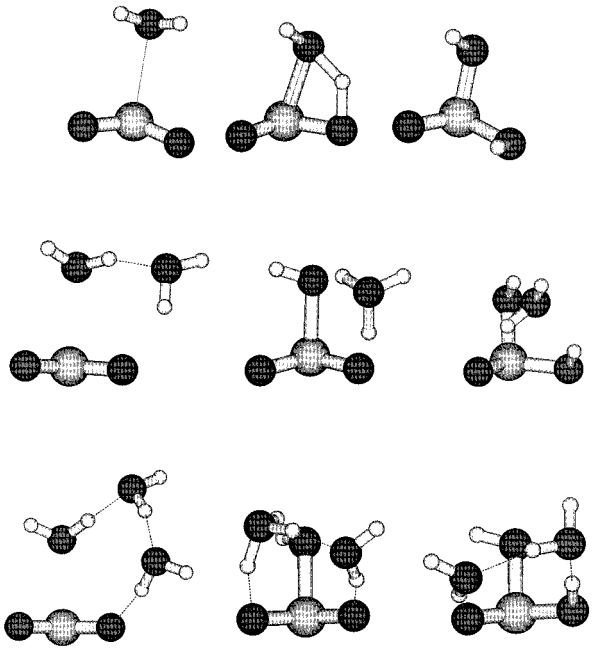

Figure 1. Stationary structures involved in the unimolecular conversion from sulfur dioxide (SO_2) to sulfurous acid (H_2SO_3) in the presence of one (top), two (middle), and three water molecules (bottom) as found at the B3LYP/6-31+G(d) level of theory.

minima and exactly one single negative eigenvalue for transition states. Predictions of reaction dynamics critically depend on the reaction barrier, i.e., the difference in electronic energy between transition state and minima, and the tunneling correction factor. We employed single-point energy calculations at the CCSD-(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ[95] level of theory to validate the accuracy of the barrier height, where computationally feasible.

2.2. Ab Initio Reaction Path. Starting from the transition state the reaction path was generated as the steepest descent path in mass-scaled coordinates employing a scaling mass of 1 amu throughout. This path, called minimum energy path (MEP) or intrinsic reaction coordinate (IRC), was generated by using the Page−McIver algorithm[96] by employing a step size of 0.05 bohr (1 bohr corresponds to 0.53 Å). The distance of a point on the potential energy surface to the transition state is denoted *s* and given a "+" sign if on the product side and a "−" sign if on the educt side. Vibrational frequencies and partition functions were calculated every third point on the hypersurface. On both branches of the reaction coordinate the path was stopped when stable minima structures were reached, i.e., when the gradient vanished. This required altogether about 400 points and was done using hybrid density functional theory (B3LYP/6-31+G(d)), which was designed to incorporate electron correlation at a cost comparable to Hartree−Fock calculations, which do not incorporate electron correlation effects. The use of such a procedure was found to be successful for "pure" proton-transfer reactions, which are more difficult to describe in terms of quantum tunneling.[90,91,97]

2.3. Quantum Mechanical Tunneling and Corner Cutting. The tunneling correction factor was calculated in the framework of canonical variational transition state theory (CVTST). Four different correction schemes were employed. The Wigner correction[98] is calculated directly from the imaginary frequency at the transition state without using any information on the reaction path. Zero-curvature tunneling (ZCT) involves tunneling along the minimum energy path, small-curvature tunneling (SCT)[99−101] involves adiabatic tunneling at the inner turning

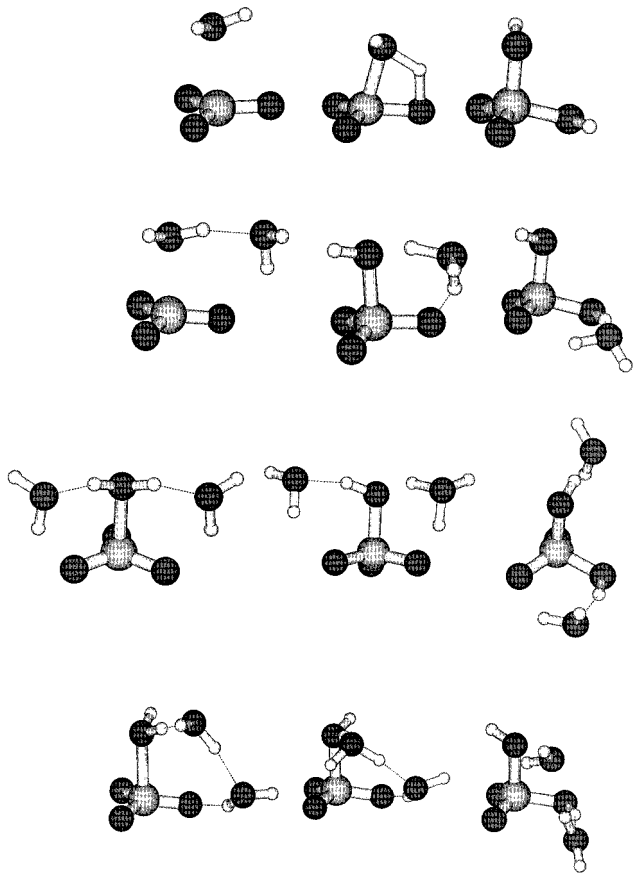

Figure 2. Stationary structures involved in the unimolecular conversion from sulfur trioxide (SO_3) to sulfuric acid (H_2SO_4) in the presence of one (top), two (second from top), and three (second from bottom and bottom) water molecules as found at the B3LYP/6-31+G(d) level of theory. The mechanism in the third row corresponds to water-mediated double proton transfer assisted by a rather rigid third water molecule. The mechanism in the bottom row corresponds to a single proton transfer, rotation of a H_3O^+ like transient subspecies, and a second single proton transfer.

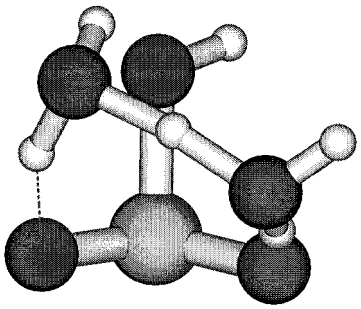

Figure 3. Transition state interconverting two isomers of the dihydrate of sulfurous acid as found at B3LYP/6-31+G(d) level of theory.

points of the concave side of the minimum energy path,[102] and large-curvature tunneling (LCT) involves vibrationally nonadiabatic straight line tunneling through the reaction swath[103−106] by allowing tunneling into all available vibrationally excited states.[103−105,107,108] The latter three corrections were all calculated by employing the semiclassical approximation[109] as implemented in the program Polyrate8.2,[110,111] written at the University of Minnesota in the group of Donald Truhlar. SCT and LCT allow us to take reaction paths different from the MEP, which are shorter, but more demanding in terms of energy. Such paths may be favored compared to the MEP, as they involve more hydrogenic motion and are, therefore, accelerated by quantum mechanical tunneling.

TABLE 1: Electronic Energies (kcal/mol) for the Hydration of SO_x ($x = 2, 3$) Assisted by $n = 1-3$ Water Molecules, Respectively

		B3LYP/6-31+G(d)	MP2/aug-cc-pVDZ	CCSD(T)/aug-cc-pVDZ	MP2/aug-cc-pVTZ
			Sulfur Dioxide Hydration		
$n = 1$	SO_2/H_2O	5.26	4.50	5.00	4.34
	$SO_2 \cdot H_2O$	0.00	0.00	0.00	0.00
	TS	33.34	35.44	34.19	34.40
	H_2SO_3	6.94	11.59	6.82	9.00
$n = 2$	$SO_2/2H_2O$	16.60	14.01	14.74	
	$SO_2 \cdot (H_2O)_2$	0.00	0.00	0.00	
	TS	19.96	22.95	22.12	
	$H_2SO_3 \cdot H_2O$	5.77	9.38	4.47	
$n = 3$	$SO_2/3H_2O$	27.86	23.54		
	$SO_2 \cdot (H_2O)_3$	0.00	0.00		
	TS	13.02			
	$H_2SO_3 \cdot (H_2O)_2$	5.52	8.31		
			Sulfur Trioxide Hydration		
$n = 1$	SO_3/H_2O	9.96	8.72	9.09	
	$SO_3 \cdot H_2O$	0.00	0.00	0.00	
	TS	27.60	28.11	28.15	
	H_2SO_4	−7.03	−3.74	−6.74	
$n = 2$	$SO_3/2H_2O$	22.48	19.40	19.81	
	$SO_3 \cdot (H_2O)_2$	0.00	0.00	0.00	
	TS	10.03	11.61	11.34	
	$H_2SO_4 \cdot H_2O$	−7.71	−4.60	−7.70	
$n = 2 + 1$	$SO_3/3H_2O$	36.50	31.39		
	$SO_3 \cdot (H_2O)_3$	0.00	0.00		
	TS	9.35			
	$H_2SO_4 \cdot (H_2O)_2$	−6.44			
$n = 3$	$SO_3/3H_2O$	36.43	31.12		
	$SO_3 \cdot (H_2O)_3$	0.00	0.00		
	TS	3.99			
	$H_2SO_4 \cdot (H_2O)_2$	−3.22			

[a] In each group, the first lines correspond to the separated SO_x and nH_2O molecules, the second lines correspond to the $SO_x \cdot nH_2O$ minima (set to 0.00 kcal/mol by definition), the third lines correspond to the transition states to the concerted nucleophilic attack/proton-transfer reaction (TS), and the last lines correspond to the $H_2SO_{x+1} \cdot (n-1)H_2O$ minima. CCSD(T) energies rely on MP2/aug-cc-pVDZ geometries.

3. Results

3.1. Stationary Structures. The educt minimum, the product minimum, and the transition state found after full geometry optimization at the B3LYP/6-31+G(d) level of theory are depicted in Figure 1 for the SO_2 hydration and in Figure 2 for the SO_3 hydration. Additionally, a transition state interconverting $H_2SO_3 \cdot 2H_2O$ structures is shown in Figure 3. A main difference between the two reactions is that SO_3 hydration is exothermic and SO_2 hydration is endothermic (cf. Table 1). As observed experimentally, "sulfurous acid" is unstable in any hydration state by at least 5 kcal/mol relative to loosely hydrated sulfur dioxide species. Zero-point correction tends to further increase this instability by approximately 1 kcal/mol. Nevertheless, it is still possible that oligomeric "sulfurous acid" $(H_2SO_3)_n$ species are approximately as stable as loosely hydrated sulfur dioxide species. Such a situation occurs for structurally similar carbon dioxide hydrates and carbonic acid dimers $(H_2CO_3)_2$.[112] According to the Hammond postulate[113,114] exothermic reactions exhibit early transition states resembling educts, whereas endothermic reactions exhibit late transition states resembling products. In this case the postulate proves to be useful. For SO_3 hydration the nucleophilic attack is still in its initial stages at the transition state. The SO_3 subunit is not distorted very much from the planar coordination toward a tetrahedral coordination in the transition state. On the other hand the nucleophilic attack is more or less complete in the transition state in the case of SO_2 hydration. This can be seen best on the example of three participating water molecules in Figures 1 and 2. For the thermoneutral isomerization reaction the proton is positioned exactly in the middle between the two oxygen atoms (cf. Figure 3).

The reaction barrier to SO_x hydration (as summarized in Table 1) clearly decreases in going from single proton transfer ($n =$ 1) to water-mediated double proton transfer ($n = 2$) and double proton transfer alleviated by a "molecular swing" ($n = 3$). The decrease on going from $n = 1$ to $n = 2$ is directly explainable by ring strain in the transition state. Whereas in the case of $n = 1$ an unfavorable four-membered transition state is encountered, a six-membered transition state is involved in the case of $n = 2$, which is more free of ring strain. The amount of ring strain of cyclobutane compared to cyclohexane is lower by 26 kcal/mol,[115] which is clearly more than the calculated barrier reduction of 12 kcal/mol (SO_2) and 17 kcal/mol (SO_3). This is probably due to the sulfur atom, which is not restricted to a tetrahedral coordination geometry as is the case for carbon atoms

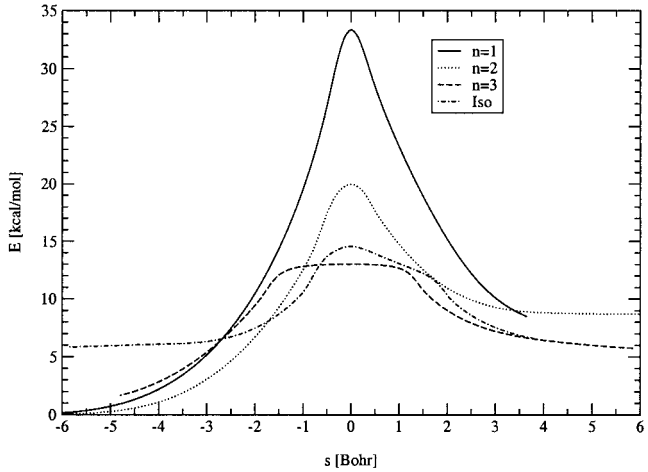

Figure 4. Electronic energy along the minimum energy path for the conversion from sulfur dioxide to sulfurous acid, as calculated at the B3LYP/6-31+G(d) level of theory.

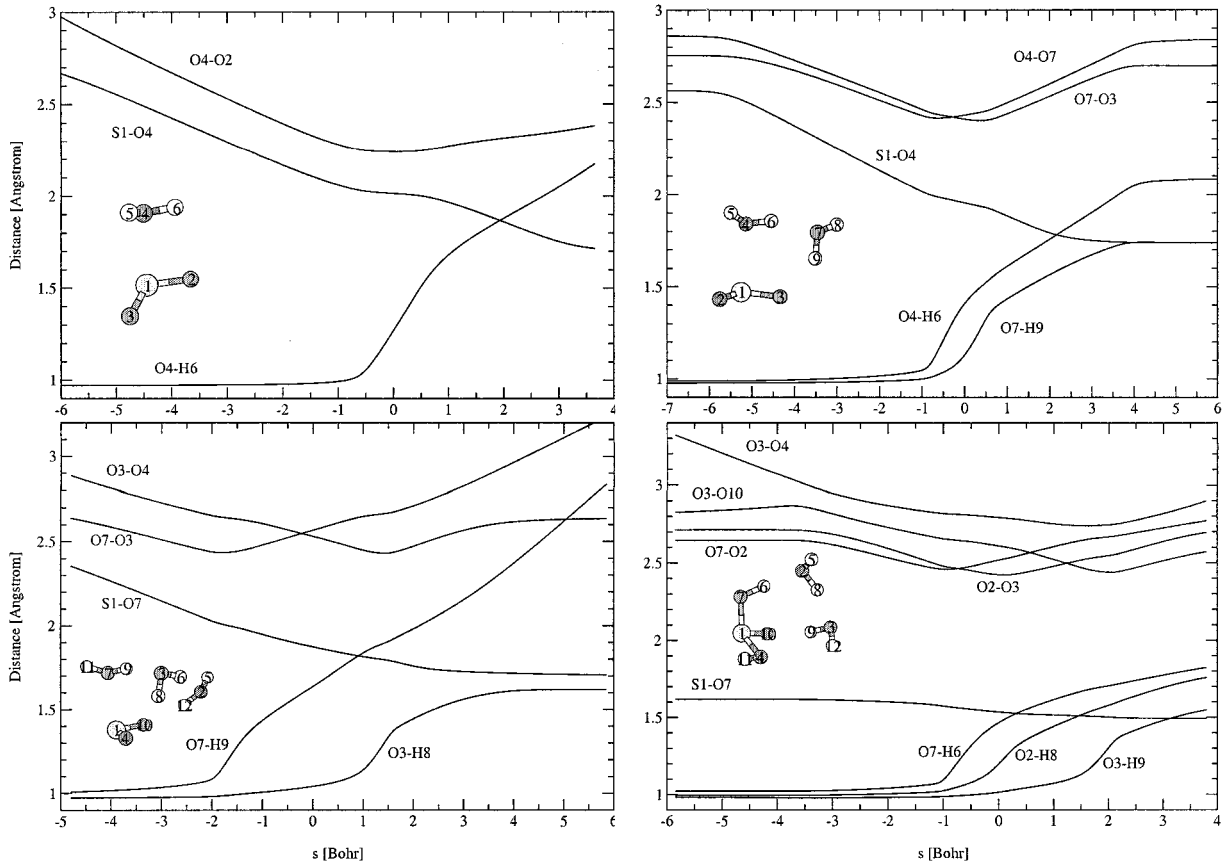

Figure 5. Distances (Å) between two selected atoms along the minimum energy path (bohr) for the hydration of sulfur dioxide by one (top left), two (top right), or three (bottom left) water molecules and for the isomerization of "sulfurous acid" in the presence of two water molecules (bottom right). The numbering scheme is shown as an inset in the respective plots.

due to the missing d orbitals. The reduction of the reaction barrier on going from $n = 2$ to $n = 3$ amounts to 6−7 kcal/mol. This reduction is supposedly due to a different reaction mechanism (described in the next section) bringing the system to an energetically favorable atomic arrangement in the transition state region.

Another low-energy transition state (cf. Figure 3) that can be found in the $H_2SO_3 \cdot 2H_2O$ water system corresponds to the transfer of a hydrogen atom of "sulfurous acid" via double proton transfer along a two water chain to the oxygen atom previously double bonded to the sulfur atom. Of course the educts and products of this isomerization are energetically equal, as seen in Figure 4. Nevertheless, this mechanism provides a possibility for oxygen isotope exchange. The marked *O atom moves from the hydroxy group (H*O)(O═S)(OH) to the double-bonded position (HO)(*O═S)(OH). The reaction barrier to this process amounts to about 9 kcal/mol, which is clearly lower than all hydration barriers. However, using the $SO_2 \cdot 3H_2O$ complex as the zero of energy, as exemplified in Figure 4, it becomes clear that the barrier-top for hydration ($n = 3$) lies lower by about 1.5 kcal/mol. When taking into account zero-point correction for both structures, the barrier-top to isomerization is lower by 0.5 kcal/mol. This similarity in absolute energies of the transition states indicates that for the backward reaction there is a competition between isomerization and decomposition to sulfur dioxide. Indeed, the geometries found on the minimum energy path are absolutely identical for both reaction channels between 6 and 4 bohr. At the reaction coordinate of about 4 bohr there is a point at which the system "decides" statistically or from the available distribution of thermal energy into vibrational excitations, which path will be tracked.

3.2. "Classical" Reaction Coordinate. All investigated hydration reactions involve concerted atomic movement, because no additional transition states besides the one at $s = 0.0$ bohr can be found. From the mechanistic viewpoint this means that the nucleophilic attack of oxygen on sulfur and all involved proton transfers happen in a single step without any intermediates existing for longer than a vibrational period.[116] However, the multiple proton-transfer steps occur not synchronously, but rather asynchronously. Both for the $n = 2$ and $n = 3$ reactions two protons are transferred at different reaction coordinates. This is quite surprising for the SO_x hydration involving three water molecules, as one could suspect the triple proton transfer along three water molecules to be favored most from ring strain considerations. Obviously, the task of the third water molecule must be a different one.

In Figures 5 and 6 selected distances between pairs of atoms are depicted along the classical reaction coordinate for the different hydration reactions of SO_x and the isomerization of the unstable dihydrate of sulfurous acid. Commonly, the protons involved in OH···O hydrogen bonds stay at a rather constant distance of slightly less than 1 Å from the donor oxygen atom for a great portion of the reaction coordinate. At the same time the O- -O distance reduces from the equilibrium distance of 2.7−2.9 Å to about 2.5 Å. Then there is a point on the reaction coordinate where the proton suddenly starts the transfer to the acceptor oxygen atom, which can be seen from the sudden increase of the proton distance to the acceptor oxygen atom. After the proton transfer has been accomplished, the O- -O distance again relaxes to the equilibrium distance of 2.7−2.9 Å. Obviously, the proton transfer is triggered by very short O- -O distances. This phenomenon has been noted both by NMR

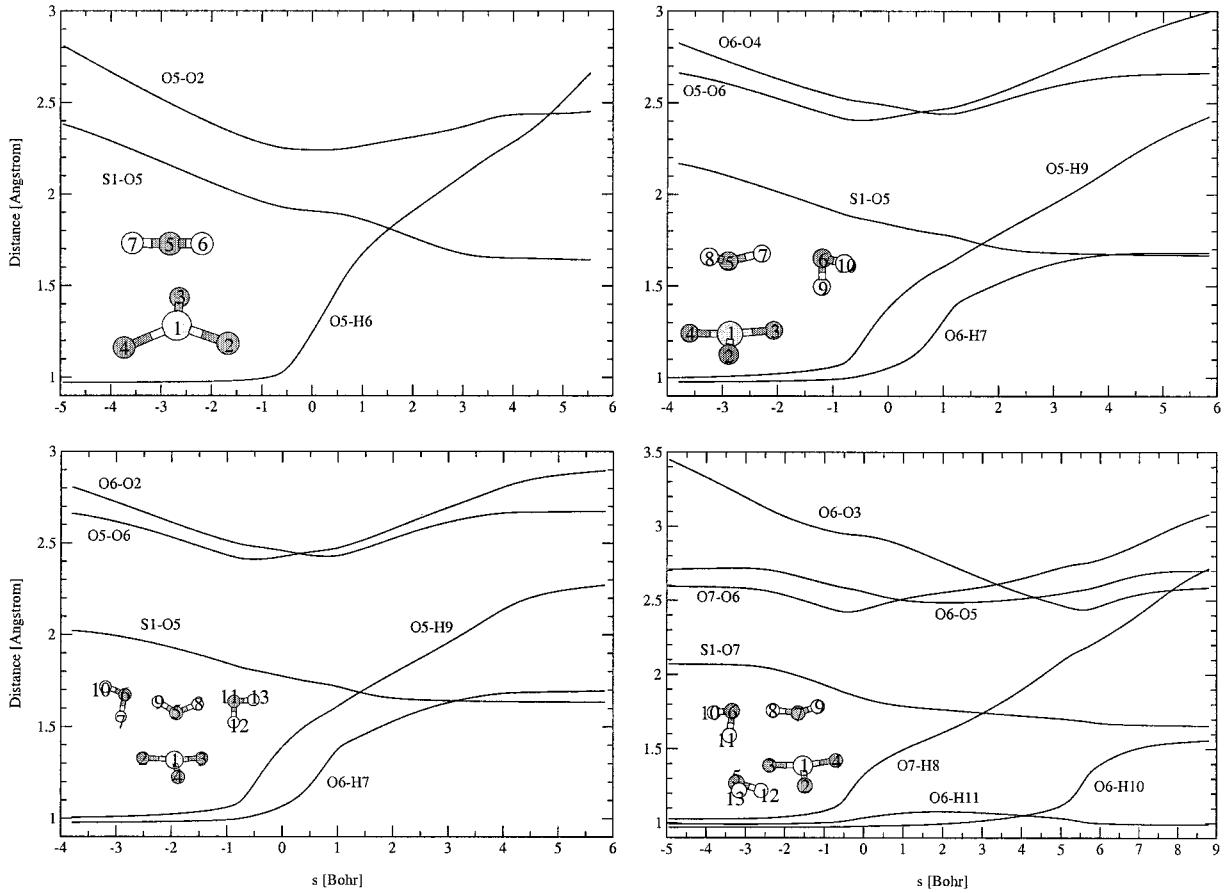

Figure 6. Distances (Å) between selected two atoms along the minimum energy path (bohr) for the hydration of sulfur trioxide by one (top left), two (top right), two active and one passive (bottom left), or three water molecules (bottom right). The numbering scheme is shown as an inset in the respective plots.

methods and from electronic structure calculations for many different hydrogen bonds in the literature and received the name "hydrogen-bond compression mechanism".[117−120] It has been shown in numerous publications that the potential describing the proton-transfer process changes from a double-well potential involving a barrier to a single-well potential involving no barrier on decreasing the distance of the donor and acceptor atoms subsequently.[121−129] When more than one proton has to be transferred, all O- -O distances vary at the same time; i.e., the process becomes highly cooperative. The accomplishment of the first proton transfer yields a H_3O^+ containing, unstable transient species. To reach a stable state again, the next proton transfer is triggered and so forth. According to IUPAC nomenclature such a behavior is called *asynchronous*.[130] On inspecting the S- -O distance, which decreases along the whole hydration coordinate, it becomes clear that the proton transfer is *concerted* with the nucleophilic attack.

This hydrogen-bond compression mechanism, which works best in linear OH···O arrangements and at O- -O distances of 2.5 Å, explains why H9 is transferred to O10 rather than to O4 in the case of H_2SO_3 isomerization. Whereas the O3−O4 atom pair can only reach a distance of 2.8 Å, the O3−O10 atom pair can reach a better orientation for hydrogen transfer. The hydrogen atom takes its way to the potential valley corresponding to the isomerization channel, therefore. The S1- -O7 distance varies by ≈0.1 Å, corresponding to rehybridization from a formal single bond (S−O) to a double bond (S═O).

For the $n = 3$ cases a reaction mechanism clearly distinct from the $n = 2$ and $n = 2 + 1$ cases can be observed, which we term the "molecular swing mechanism". Instead of "classical" water-mediated proton transfer, the hydronium ion like subpart of the supermolecule performs a slight rotational movement in order to bring one proton to a position from which transfer to the neighbor oxygen atom is energetically favorable. Although the third water molecule acts as spectator, i.e., remains in about the same position during the whole reaction, it has the important function of stabilizing the H_3O^+ subunit by providing the oxygen atom O2 (SO_2 case), which acts as hydrogen-bond acceptor. Figuratively spoken, this oxygen atom is the anchor for the second hydrogen bridge "rope" to which the molecular water "swing" carrying a proton is fastened. And when the "swing" reaches the highest point, the proton has gained enough energy to be able to "jump" to the oxygen atom O10 (SO_2 case). A mechanism differing in this way from water-mediated triple proton transfer is possible, as the reaction takes place on a highly complex potential energy surface showing many valleys and ridges because of the energy asymmetry of the reaction and the according "impurity" of the proton transfer. The "rope" function can also be seen in Figure 6. Whereas the O6- -O5 distance remains rather constant after the transfer of the first proton, the O6- -O3 distance is shortened. Atom H10 rotates into the O6- -O3 line and is transferred, when the O6- -O3 distance reaches 2.5 Å. A slight elongation of the O6- -H11 bond is required to make this rotation energetically feasible. Instead of H11 being transferred to O5 the second proton switch involves H10 being transferred to O3, therefore.

3.3. Influence of Quantum-Tunneling and Corner-Cutting. Now the question remains, how long is "classical" reaction coordinate motion expected to be the dominating motion compared to other motions significantly enhanced by quantum-

TABLE 2: Tunneling Correction Factors κ at 100, 200, and 300 K to the Rate Constants Obtained from Classical Transition State Theory for the Reaction $SO_x \cdot nH_2O \rightleftharpoons H_2SO_{x+1} \cdot (n-1)H_2O$ ($x = 2, 3$; $n = 1-3$)

	temp, K	Wigner	ZCT	SCT	LCT
		Sulfur Dioxide Hydration			
$n = 1$	100	24.9	9.9×10^{17}	6.4×10^{23}	4.1×10^{21}
	200	7.0	1.3×10^{3}	1.9×10^{5}	7.4×10^{4}
	300	3.7	13.3	76.4	27.1
$n = 2$	100	7.9	4.4×10^{4}	6.0×10^{7}	4.7×10^{8}
	200	2.7	6.3	39.1	68.2
	300	1.8	2.1	4.2	3.3
$n = 3$	100	1.1	3.4	20.9	25.8
	200	1.0	1.4	1.6	1.5
	300	1.0	1.2	1.2	1.2
iso	100	4.1	6.1	5.8×10^{2}	3.9×10^{4}
	200	1.8	1.4	2.1	5.1
	300	1.3	1.2	1.3	1.4
		Sulfur Trioxide Hydration			
$n = 1$	100	24.9	2.7×10^{21}	4.8×10^{26}	6.1×10^{24}
	200	7.0	6.5×10^{3}	1.1×10^{6}	3.1×10^{5}
	300	3.7	19.2	113.4	35.3
$n = 2$	100	3.7	3.2×10^{3}	1.9×10^{6}	3.8×10^{6}
	200	1.7	3.3	8.9	7.2
	300	1.3	1.6	2.2	1.8
$n = 2 + 1$	100	3.9	6.1×10^{3}	2.6×10^{6}	8.3×10^{6}
	200	1.7	4.5	17.0	15.1
	300	1.3	1.8	2.9	2.2
$n = 3$	100	1.7	1.5	2.0	3.4
	200	1.2	1.1	1.2	1.3
	300	1.1	1.0	1.1	1.1

[a] B3LYP/6-31+G(d) was employed throughout.

tunneling? Obviously, the answer to this question depends on the temperature. In Table 2 the magnitude of the quantum-mechanical tunneling correction κ to the classical rate constant is listed for the hydration reactions of SO_2 or SO_3 and the isomerization mechanism (labeled Iso) described above at three temperatures (100, 200, and 300 K). There is a clear correlation between the magnitude of the imaginary frequency at the transition state and the tunneling correction factor. For the lowest imaginary frequency observed, namely 124i cm^{-1} for the SO_2 hydration involving three water molecules, tunneling is rather unimportant. In the direct corner-cutting (LCT) mechanism, the reaction is accelerated by a factor of 25.8 at 100 K. At higher temperatures tunneling ceases, i.e., κ approaches 1.0. In comparison the isotope exchange mechanism is preferred by tunneling. This can be explained by the thinner energy barrier in Figure 4 and the higher absolute value of the imaginary frequency, namely 597i cm^{-1}. Similarly, for the SO_3 hydrations, on increasing the number of microsolvating water molecules the importance of quantum mechanical tunneling diminishes due to the broadening nature of the reaction barrier, which can be seen in the decrease of the "imaginary frequency" from 1663i to 564i cm^{-1} (582i cm^{-1}) and 288i cm^{-1} for $n = 1$, $n = 2$ ($n = 2 + 1$), and $n = 3$, respectively. Most tunneling enhancement is observed for the classically slowest reactions involving one and two water molecules. Especially at 100 K acceleration factors of 10^{24} and 10^{8} are found from the calculation for $n = 1$ and $n = 2$, respectively. However, this acceleration is still not sufficient to outweigh the classical disadvantage in terms of reaction rates. Assuming uncertainties of 1 kcal/mol in the reaction barrier leading to uncertainties of a factor of 5 (300 K), 12 (200 K), and 150 (100 K) in the classical rate constant, it becomes clear that tunneling is a negligible effect for $n = 3$ down to 100 K, important below about 250 K for $n = 2$, and important even above room temperature for $n = 1$. The LCT tunneling corrections are not significantly higher than the SCT corrections. This is in strict contrast to the results found in carboxylic acid dimers,[91] cyclic HF,[97,131] and water clusters.[90] Whereas these systems involve "pure" proton transfer of reduced mass 1 amu, in the case of sulfur oxide hydration, heavy atom movement accompanies the reaction. This renders the proton transfer "impure", so that the effective reduced mass becomes 1 amu nowhere along the reaction coordinate and even does not drop below 5 amu in the $n = 1$ systems, although a proton is transferred.

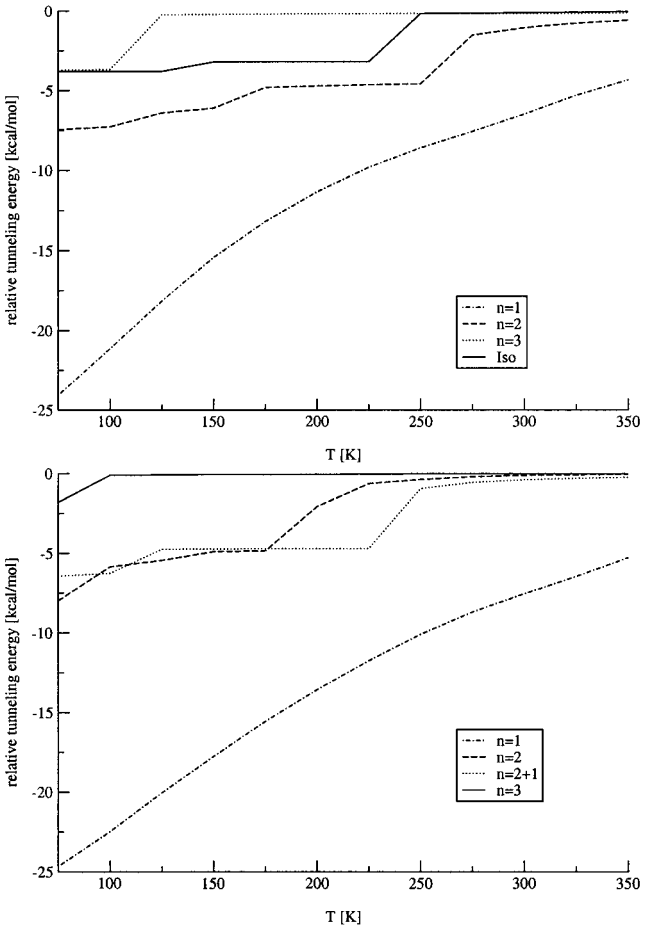

Figure 7. Representative relative tunneling energy referring to the barrier top as the zero of energy for the hydration reactions of SO_2 (top) and SO_3 (bottom) in water clusters of different sizes.

TABLE 3: Approximate Crossover Temperatures above Which the Classical Over-Barrier Reaction Dominates and below Which Quantum-Mechanical Tunneling through the Barrier Dominates, As Calculated by the Multidimensional Optimized Tunneling Method at a B3LYP/6-31+G(d) Hypersurface

	SO_2	SO_3
$n = 1$	375 K	350 K
$n = 2$	225 K	175 K
$n = 3$	100 K	75 K
iso/$n = 2 + 1$	175 K	200 K

In Table 3 the crossover temperatures, i.e., the border temperatures between overbarrier and tunneling-dominated reaction, are summarized. Especially for the larger supermolecules investigated here the crossover temperatures are very low. Even for the $n = 1$ reactions the crossover temperatures are still about 100 K lower than the crossover temperatures found for "pure" proton-transfer reactions.[91,131]

In Figure 7 the representative tunneling energies relative to the barrier top are depicted. An energy of 0 kcal/mol implies

an overbarrier mechanism, whereas negative values indicate tunneling. It can be seen that for $n = 2$ and $n = 3$ the overbarrier mechanism prevails down to rather low temperatures. The kinks seen in this plot are indicative of the sudden change to tunneling of all transferred protons. For $n = 1$ the representative tunneling energy changes rather continuosly to lower values on decreasing the temperature, as the whole temperature region shown is in the tunneling domain.

The difference in tunneling mechanisms compared to "pure" proton transfer also has consequences for the choice of the method of calculating the tunneling correction. Whereas for "pure" proton-transfer reactions LCT is clearly the dominant tunneling contribution, in the case of "impure" proton transfer SCT is the dominant tunneling mechanism (even for $n = 1$). Only in some cases does the LCT scheme provide slightly higher corrections, e.g., for $n = 2$ at 100 K. However, the additional effort for the calculation is not outweighed by such a marginal increase. The other corrections (ZCT and Wigner) are clearly insufficient to describe tunneling enhancement of such proton-transfer reactions properly. As a consequence, we recommend employing the LCT scheme for "pure" proton-transfer reactions and to employ the SCT scheme for "impure" proton transfer in order to reach agreement with experimental data.

4. Conclusions

We have investigated the hydration reactions of sulfur dioxide and sulfur trioxide in water clusters, which are examples of active solvent catalysis through water-mediated proton transfer with the aid of variational transition state theory and multidimensional tunneling methods. The examination revealed that such reactions belong to the category of "impure" proton transfer. That is, the reaction coordinate is near the classical minimum energy path down to rather low temperatures, which corresponds to asynchronous (i.e., at different reaction coordinates) proton-transfer events concerted with the nucleophilic attack following the rules of the hydrogen-bond compression mechanism. The influence of tunneling is smaller compared to the "pure" proton transfers, as can be seen from the rather low crossover temperatures. However, as demonstrated on the example of the smaller clusters, the tunneling effect cannot be treated negligible a priori. Direct corner cutting (LCT) does not play a dominant role compared to corner cutting on the concave side of the classical reaction path (SCT), as the reduced mass of the reaction coordinate mode does not drop to 1 amu anywhere. On the contrary, in the case of "pure" proton transfer, direct corner cutting takes place along the directions involving hydrogenic motion only, i.e., with a reduced mass of 1 amu. This explains why the reaction swath region on the potential energy surface is not crossed in the case of "impure" proton transfer. Furthermore, we could show that the asymmetry (impurity) brought into the potential energy surface due to net heavy atom motion leads to transient, i.e., not stabilized, formation of ions on the reaction coordinate. It is possible that in condensed phases, e.g., in aqueous solution, such ions can be stabilized to change the mechanism from concerted to stepwise. This could be of importance, e.g., in explaining mutation probabilities of DNA bases. In addition, this complexity of the potential energy surface opens new mechanistic possibilities, as demonstrated by the "molecular swing" mechanism ($n = 3$) and by the isomerization channel in the $H_2SO_3 \cdot 2H_2O$ system. It is our belief that these general features also apply to many other reactions in diverse fields ranging from biochemistry, organic chemistry, and inorganic chemistry to atmospheric chemistry.

Acknowledgment. We are grateful to Markus Loferer for help in the initial stage of the work. Support by the Austrian Science Fund (project no. P14357-TPH) is gratefully acknowledged. T.L. is indebted to the Austrian Academy of Sciences (DOC-program) for financal support.

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