J. Am. Chem. Soc. **1983,** *105,* 31-40

Conclusions

We have demonstrated that markedly enhanced photocurrents can be obtained from illuminated TiO_2 suspensions when methyl viologen dication is present in the suspension. The observation of this behavior is consistent with electron trapping by MV^{2+}, thus preventing deleterious (e^-h^+) recombination. This behavior has led to insight into the energetics of TiO_2 particles in that shifting of Fermi level with pH can be observed, and the location of the Fermi and quasi-Fermi levels can be estimated. Methyl viologen is useful in these studies as it is soluble over a wide range of pH values, unlike previously reported electron trapping agents Fe^{3+} and Cu^{2+} which form insoluble compounds in basic solutions. These measurements emphasize the utility of electrochemical techniques in characterizing heterogeneous photocatalysts. In agreement with the photochemical results of Gratzel et al.,[22] photogenerated electrons in anatase preparations are sufficiently negative to cause proton reduction.

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Registry No. TiO_2, 13463-67-7; NaOAc, 127-09-3; MV^{2+}, 4685-14-7.

Theoretical Models for Solvation and Catalysis in Carbonyl Addition

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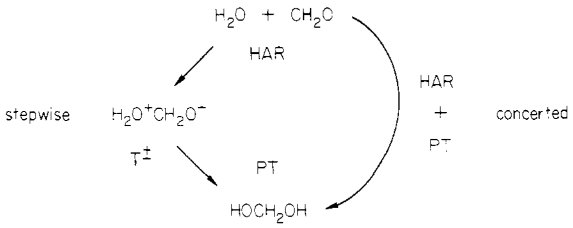
Abstract: Alternative modes of catalysis of formaldehyde hydration by a single ancillary water molecule are investigated by ab initio calculations at the STO-3G level. A cyclic transition state ($FW2^{\ddagger}$) involving formaldehyde with two molecules of water is characterized and is only 0.8 kcal mol^{-1} higher in energy than the isolated reactants. The results indicate that gas-phase formaldehyde hydration probably proceeds via $FW2^{\ddagger}$ in a concerted mechanism with a Gibbs free energy of activation of 27 kcal mol^{-1}. Addition of a water dimer to formaldehyde via $FW2^{\ddagger}$ is predicted to occur in water with a Gibbs free energy of activation of 16 kcal mol^{-1}, in agreement with experiment. Empirical extrapolation to the liquid phase of entropies of activation calculated for reaction of one or two waters in the gas phase suggests that a mechanism involving three water molecules would be consistent with experiments for dioxan solution. Specific solvation by four water molecules is predicted to stablize the zwitterionic adduct $H_2O^+CH_2O^-$ (an unbound state in the gas phase) by 111 kcal mol^{-1} relative to $H_2O^+CH_2O^-$ and $4H_2O$ or by 37 kcal mol^{-1} relative to $(H_2O)_3$ and $CH_2O{\cdot}2H_2O$. Thus a stepwise mechanism for formaldehyde hydration also may be feasible, although the energy barrier to formation of a solvated zwitterionic intermediate has not yet been calculated.

Nucleophilic addition of water to formaldehyde may be envisaged as occurring either by stepwise or concerted mechanisms to yield methanediol. If the processes (see Scheme I) of heavy-atom reorganization (HAR), i.e., C—O σ-bond making and C=O π-bond breaking, are accomplished in an initial step followed by the necessary proton transfer (PT) in a second step, then a zwitterionic intermediate $T^{\pm}$ is involved. However, a recent theoretical study[2] suggests that the structure corresponding to $T^{\pm}$ does not exist as a bound chemical species in the gas phase. In this case, PT cannot occur before $T^{\pm}$ dissociates to reactants, and thus the stepwise mechanism is not feasible. Instead, the HAR and PT processes must occur concertedly: the mechanism is enforced[3] as concerted.

In aqueous solution the situation differs from this simple gas-phase scheme as the result of interactions between the reacting system and its environment. Within a transition-state theoretical framework, the effect of solvation upon the mechanism of carbonyl addition may be studied by consideration of the environmental influences acting upon the reactant, intermediate, product, and transition-state structures involved in the gas-phase mechanistic scheme. However, the possible existence of new intermediate or transition-state structures involving solvent molecules, which may open new channels for reaction, ought also to be admitted. A complete treatment of solvation effects upon mechanism should include the influence not only of the cybotactic region of the solvent, whose structure is modified by the presence of the solute, but also of the bulk solvent. Such a project is, however, currently beyond the scope of this work. In the present theoretical study, *specific interactions of small numbers of ancillary solvent water molecules* have been considered with regard to the mechanism of formaldehyde hydration. In particular, a dramatic reduction of the energy barrier to concerted addition, effected by a *single* ancillary water molecule, and stabilization of the zwitterionic intermediate $T^{\pm}$ by four or six solvent water molecules, are reported herein.

Scheme I



Computational Methods and Results

Ab initio SCF-MO calculations with the STO-3G basis[4] were employed throughout this work. Preliminary calculations were

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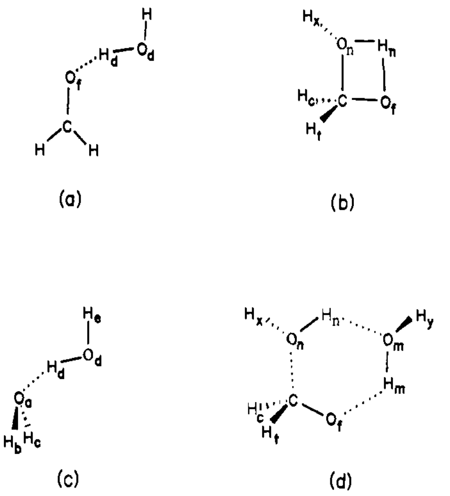

Figure 1. Schematic structures for species whose geometries are given in Table I.

performed with the GAUSSIAN70 program[5] as implemented on the Honeywell 66/60 of the University of Kansas Academic Computer Center, and supporting calculations were carried out with this program as implemented on the IBM 370/165 of the University of Cambridge. Most of the geometries reported in this work were optimized by using a version of the HONDO/G program on the VAX 11/780 at the NRCC. Table I contains optimized geometries and energies for structures pertinent to the following discussion, and the key to the atomic labeling system adopted is provided by Figure 1. ORTEP molecular drawings are presented in Figure 2 for some novel structures of particular significance.

Transition-State Characterization. A transition-state structure, FW2‡, for the concerted addition $2H_2O + CH_2O \rightarrow CH_2(OH)_2 \cdot H_2O$ was determined by a novel gradient-search procedure[6] following preliminary calculations[7] using the distinguished coordinate method.[8] This structure, shown in Figures 2b and 2c, corresponds to a true saddle point on the 24-dimensional potential energy surface (i.e., a point at which the force-constant matrix has one and only one negative eigenvalue). The optimized geometry for FW2‡ is given under entry 8 of Table I. The atoms of the making and breaking O–C and O–H bonds form a six-membered ring that assumes an envelope-like conformation: the hydrogen-bonded chain O_n–H_n–O_m–H_m–O_f (cf. Figure 1d) is very nearly coplanar; the carbon atom lies out of this plane (see Figure 2c). The two hydrogen bonds O_n–H_n–O_m and O_m–H_m–O_f have angles of 156.5° and 150.5°, respectively, and it is presumed that their near linearity subjects the ring to a strain that is best accommodated by a coplanar arrangement of the atoms involved. The exocyclic hydrogen atoms H_x and H_y are staggered with respect to each other, thereby minimizing steric repulsion and allowing for optimal interaction of the lone-pair electrons on the nucleophilic oxygen O_n with the π^* orbital of the carbonyl group.

The STO-3G energy of FW2‡ is 6.7 kcal mol^{-1} higher than that of $(H_2O)_2 + CH_2O$. Therefore, the presence of the ancillary water molecule that serves as a bifunctional catalyst reduces the potential energetic barrier to reaction by 35.5 kcal mol^{-1} relative to the uncatalyzed addition via FW1‡, which has an energy 42.2 kcal mol^{-1} above that of $H_2O + CH_2O$ in STO-3G.

Diagonalization of the mass-weighted force-constant matrix for FW2‡ using ^1H, ^{12}C, and ^{16}O isotopes yielded normal coordinates and vibrational frequencies. A frequency of 547 cm^{-1} was found for the reaction coordinate vibrational mode, whose atomic displacement vectors (non mass weighted) are shown by the arrows in Figure 2b. It can be seen that the dominant motions are those of (a) the endocyclic protons, which are transferring between the oxygen atoms, and (b) the carbon atom, which is moving out of the plane of formaldehyde toward the nucleophilic oxygen atom. Not only is proton transfer coupled with HAR but the motions of both protons have equal amplitudes and are thus mutually coupled. The processes of bond making and bond breaking are both kinetically and dynamically coupled[9] in FW2‡. The motions in the reaction-coordinate mode of the two water moieties (viewed individually) are small rotations relative to each other and to the formaldehyde moiety, and it is of interest to note that the magnitude of the imaginary frequency, $|\nu^{‡}|$, is of the same order as that for librational modes in pure water.[10]

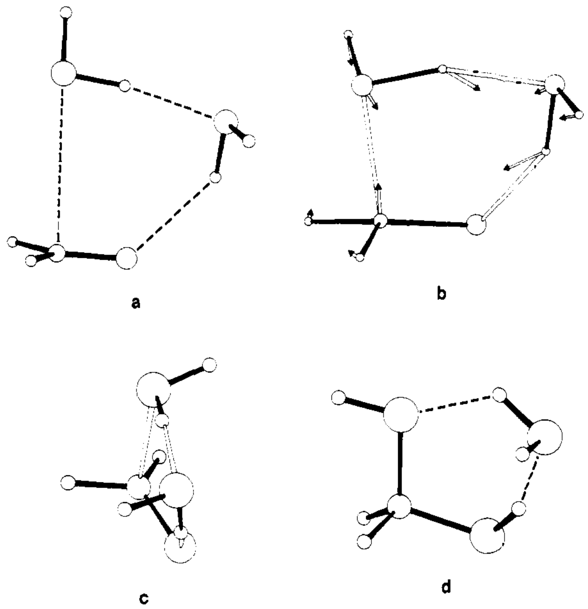

Figure 2. ORTEP drawings for species invovled in concerted formaldehyde hydration catalyzed by a single ancillary water molecule: (a) reactant complex $(H_2O)\cdot CH_2O$; (b) FW2‡ with the reaction coordinate motion indicated by arrows—newly forming bonds are unshaded; (c) FW2‡ showing the coplanarity of the hydrogen-bonded fragment of the cyclic structure—newly forming bonds are unshaded; (d) product complex $CH_2(OH)_2 \cdot H_2O$.

Calculations of Thermodynamic Quantities. Relative Gibbs free energies were calculated according to eq 1, where E is the STO-3G

$$\Delta G^\circ = \Delta E + \Delta E_{zp} - RT\,\Delta \ln (q_t^\circ q_r q_v) \qquad (1)$$

potential energy, E_{zp} is the zero-point energy, q_t, q_r, and q_v are molecular partition functions for translational, rotational, and vibrational motions (assumed to be separable), and the superscript degree refers to a standard state of 1 atm. The zero-point energies and partition functions were evaluated within the ideal gas, rigid rotor, and harmonic oscillator approximations, and hindered internal rotational motions were treated as torsional vibrations.[11] Rotational partition functions were evaluated by using a symmetry for each species given as $h/2$, where h is the order of the point group of the molecular species; thus chiral species were properly accounted for.[12] The force constants employed in the normal coordinate calculations were initially obtained by numerical differentiation of analytical first derivatives of the STO-3G energy with respect to Cartesian coordinates by using the HONDO program. These force constants were then transformed to an internal valence coordinate basis and scaled by a factor of 0.7, a value chosen to provide reasonable agreement between STO-3G calculated and observed frequencies for the water and formaldehyde molecules.[6]

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(12) (a) Coulson, D. R. *J. Am. Chem. Soc.* **1978**, *100*, 2992–2996. (b) See also: Pollak, E.; Pechukas, P. *Ibid.* **1978**, *100*, 2984–2991.

Table I. STO-3G Geometries and Energies

entry	species	figure	total energy, hartrees	bond lengths, Å		bond angles, deg		dihedral angles, deg	
1	H_2O		−74.965 90	O-H	0.989	H-O-H	100.0		
2	CH_2O		−112.354 35	C-O	1.217	H-C-H	114.5		
				C-H	1.101				
3	$CH_2O\cdot HOH$[a]	1a	−187.325 55	O_f-O_d	2.88	C-O_f-O_d	119		
						O_f-O_d-H_d	1		
4	[$FW1^{\ddagger}$]	1d	−187.252 96	O_n-C	1.674	O_n-C-O_f	90.6	O_f-O_n-C-H_t	123.4
				C-O_f	1.307	O_n-C-H_t	101.4	O_f-O_n-C-H_c	−123.1
				C-H_t	1.109	O_n-C-H_c	102.7	O_f-C-O_n-H_x	105.6
				C-H_c	1.111	C-O_n-H_x	114.7	O_f-C-O_n-H_n	0.0
				O_n-H_x	0.992	C-O_n-H_n	75.5		
				O_n-H_n	1.064				
5	$CH_2(OH)_2$	cf. 1b	−187.389 41	O_n-C	1.429	O_n-C-O_f	112.0	O_f-O_n-C-H_t	122.6
				C-O_f	1.429	O_n-C-H_t	106.2	O_f-O_n-C-H_c	−119.3
				C-H_t	1.101	O_n-C-H_c	112.0	O_f-C-O_n-H_x	59.8
				C-H_c	1.102	C-O_n-H_x	104.0	O_f-C-O_n-H_n	−25.7
				O_n-H_x	0.991	C-O_n-H_n	50.0		
				O_n-H_n	2.502				
6	$(H_2O)_2$	1c	−149.941 24	O_a-O_d	2.740	O_d-H_d-O_a	179.7	H_e-O_d-H_d-O_a	125.9
				O_a-H_b	0.987	H_d-O_a-H_b	110.9	H_e-O_d-O_a-H_b	−126.8
				O_a-H_c	0.987	H_d-O_a-H_c	111.0	H_e-O_d-O_a-H_c	121.9
				O_d-H_d	0.990	H_b-O_a-H_c	100.9		
				O_d-H_e	0.988	H_d-O_d-H_e	100.4		
7	$2H_2O\cdot CH_2O$[a]	2a, cf. 1d	−262.300 95	O_n-C	2.978	O_n-C-O_f	96.7	O_n-C-O_f-O_m	14.2
				O_m-O_f	2.876	O_n-C-H_t	78.2	O_f-O_n-C-H_t	122.1
						O_n-C-H_c	94.5	O_f-O_n-C-H_c	−123.8
						C-O_n-H_x	150.4	O_f-C-O_n-H_x	79.8
						C-O_n-H_n	81.2	O_f-C-O_n-H_n	−15.1
						C-O_f-O_m	110.7	C-O_f-O_m-H_m	179.8
						O_f-O_m-H_m	26.3	C-O_f-O_m-H_y	88.1
						O_f-O_m-H_y	100.3		
8	[$FW2^{\ddagger}$]	2b, 2c, cf. 1d	−262.284 90	O_n-C	1.808	O_n-C-O_f	106.6	O_f-O_n-C-H_t	123.7
				C-O_f	1.264	O_n-C-H_t	91.6	O_f-O_n-C-H_c	−125.2
				C-H_t	1.109	O_n-C-H_c	96.3	O_f-C-O_n-H_x	78.1
				C-H_c	1.107	C-O_n-H_x	109.7	O_f-C-O_n-H_n	−30.0
				O_n-H_x	0.986	C-O_n-H_n	98.4	O_n-C-O_f-O_m	26.5
				O_n-H_n	1.036	C-O_f-O_m	97.2	C-O_f-O_m-H_m	156.2
				O_m-O_f	2.420	O_f-O_m-H_m	17.6	C-O_f-O_m-H_y	86.0
				O_m-H_m	1.018	O_f-O_m-H_y	110.7		
				O_m-H_y	0.983				
9	$CH_2(OH)_2\cdot H_2O$	2d, cf. 1d	−262.363 53	O_n-C	1.442	O_n-C-O_f	109.1	O_f-O_n-C-H_t	122.7
				C-O_f	1.417	O_n-C-H_t	109.2	O_f-O_n-C-H_c	−119.0
				C-H_t	1.109	O_n-C-H_c	110.9	O_f-C-O_n-H_x	174.7
				C-H_c	1.102	C-O_n-H_x	104.7	O_f-C-O_n-H_n	−38.9
				O_n-H_x	0.989	C-O_n-H_n	107.0	C-O_n-H_n-O_m	5.6
				O_n-H_n	1.973	O_n-H_n-O_m	127.2	O_n-H_n-O_m-H_m	14.8
				O_m-O_f	0.987	H_n-O_m-H_m	93.6	O_n-H_n-O_m-H_y	−100.4
				O_m-H_m	0.987	H_n-O_m-H_y	101.4		
				O_m-H_y	1.673				

[a] Geometry optimization of intermolecular degrees of freedom only was performed by axial iteration using GUASSIAN70; intramolecular coordinates were constrained to their isolated molecule values.

Table II. Thermodynamic Changes[a] along Catalyzed and Uncatalyzed Reaction Paths

species	ΔH, kcal mol^{-1}	$\Delta S°$, eu	$\Delta G°$, kcal mol^{-1}
$CH_2O + 2H_2O$	(0.0)	(0.0)	(0.0)
$CH_2O + (H_2O)_2$	−4.0	−22.7	+2.8
$FW1^{\ddagger}$	43.1	−34.8	+53.4
$FW2^{\ddagger}$	5.5	−70.2	+26.5
$CH_2(OH)_2\cdot H_2O$	−42.8	−62.1	−24.3
$CH_2(OH)_2 + H_2O$	−39.6	−34.3	−29.4

[a] Relative to formaldehyde and two free water molecules.

Force constants were not calculated for the association complexes $H_2O\cdot CH_2O$ and $2H_2O\cdot CH_2O$, and hence Gibbs free energies for these species are not available. Relative enthalpies were calculated according to eq 2, where Δn is the change in stoichiometry and

$$\Delta H = \Delta E + \Delta E_{zp} + 4RT\Delta n + RT^2\Delta(\partial \ln q_v/\partial T) \qquad (2)$$

entropies from $\Delta S° = (\Delta H - \Delta G°)/T$. The values of these quantities are given in Table II.

To correct the ideal-gas-phase values of ΔH^*, ΔS^*, and ΔG^* to values in aqueous solution, we use a simple relationship between the gas-phase entropies in small molecules and their entropies of solvation in water, recently proposed by Wertz.[13a] He based his method upon the observations that the entropy of liquid water at 25 °C is 46% less than that of gaseous water at a concentration of 55.5 M and that the entropies of solvation of ammonia, methane, and water in water are almost identical. With the assumptions that (a) changes in the entropy of water do not contribute to the entropy of solvation and (b) all molecules lose the same fraction of their entropy when transferred from the gas phase to water, the entropy of solvation ΔS_s of any solute (including water) in water at 25 °C may be calculated from the ideal-gas entropy $S°_g$ of the solute, at 25 °C and 1 atm, by the expression in eq 3 (see also ref 13b). Application of this expression

$$\Delta S_s = -0.46(S°_g - 14.3) \text{ eu} \qquad (3)$$

to each component of an ideal-gas system at equilibrium allows the entropy change for the same equilibrium in aqueous solution

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(13) (a) Wertz, D. H. *J. Am. Chem. Soc.* **1980**, *102*, 5316–5322. (b) Abraham, M. H. *Ibid.* **1981**, *103*, 6742–6744.

Table III. STO-3G Calculated Activation Parameters for Formaldehyde Hydration in Gaseous and Aqueous Phases at 25 °C[a]

reactants	transition state	gas phase[b]			aqueous phase[c]		
		$\Delta H_g^\ddagger$	$\Delta S^\circ{}_g^\ddagger$	$\Delta G^\circ{}_g^\ddagger$	$\Delta H^+{}_{aq}^\ddagger$	$\Delta S^+{}_{aq}^\ddagger$	$\Delta G^+{}_{aq}^\ddagger$
$H_2O + CH_2O$	$FW1^\ddagger$	43.1	−34.8	53.4	43.6	−11.1	46.9
$2H_2O + CH_2O$	$FW2^\ddagger$	5.5	−70.2	26.5	6.7	−22.4	13.4
$(H_2O)_2 + CH_2O$	$FW2^\ddagger$	9.5	−47.5	23.7	10.1	−18.7	15.7

[a] Enthalpies and Gibbs free energies in kcal mol^{-1}; entropies in eu. [b] Standard state 1 atm. [c] Standard state 1 M.

Table IV. STO-3G Calculated Activation Parameters for Carbonyl Hydration in Dioxane at 25 °C[a]

reactants	transition state	$\Delta S^+{}_g^\ddagger$	$\Delta S^+{}_d^\ddagger$	E_a
$H_2O + CH_2O$	$FW1^\ddagger$	−28.5	−23.0	44.2
$2H_2O + CH_2O$	$FW2^\ddagger$	−57.5	−46.5	7.3
$(H_2O)_2 + CH_2O$	$FW2^\ddagger$	−41.2	−32.9	10.7
$3H_2O + (ClCH_2)_2CO$	exptl		−68[b]	5
$3H_2O + Cl_3CCHO$	exptl		−64[c]	2

[a] Entropies in eu at standard state 1 M, energies in kcal mol^{-1}. [b] Mean of two values given in ref 31. [c] Mean of four values given in ref 32.

to be calculated; excellent agreement between calculated and experimental equilibrium entropy changes for formaldehyde hydration may thus be obtained.[14] The same expression may also be applied tentatively to the components of reacting systems assuming that the method holds also for transition states, thereby allowing calculation of activation entropies for reactions in aqueous solution. Appropriate standard states for the components involved in the hydration of formaldehyde in aqueous solution are 1 M for the reactant formaldehyde and for $FW1^*$ or $FW2^*$, 55.5 M for monomeric water, and 55.5/2 M for dimeric water. Conversions of ideal-gas-phase solute entropies to aqueous-phase entropies at 25 °C and the appropriate standard state may thus be effected by the following relations (in eu):

$$S^+{}_{aq}\ (1\ M) = 0.54S^\circ{}_g + 0.24 \qquad (4)$$

$$S''_{aq}\ (55.5\ M) = 0.54S^\circ{}_g - 7.74 \qquad (5)$$

$$S'_{aq}\ (55.5/2\ M) = 0.54\ S^\circ{}_g - 6.99 \qquad (6)$$

Since for reactions in solution the $P\Delta V^*$ term may be neglected, the enthalpy of activation $\Delta H_{aq}{}^*$ for a reaction in aqueous solution of molecularity γ is given in terms of the ideal-gas-phase enthalpy of activation $\Delta H_g{}^*$ by relation 7. Values of $\Delta H_{aq}{}^*$, $\Delta S_{aq}{}^*$, and

$$\Delta H_{aq}{}^* = \Delta H_g{}^* - (1 - \gamma)RT \qquad (7)$$

$\Delta G_{aq}{}^*$ are presented in Table III. Wertz's method for estimation of entropies of solution in water may be extended to the solvent dioxane in the same manner as it was applied by Wertz to 1-octanol. Thus at 25 °C, the entropy of liquid dioxane[15] is 77% of the entropy of gaseous dioxane[15] at a concentration (11.73 M) equal to the density of the liquid,[16] and therefore the entropy of any solute in dioxane at 25 °C and 1 M is given by eq 8. The

$$S^+{}_d\ (1\ M) = 0.77S_g - 3.76\ \text{eu} \qquad (8)$$

Arrhenius activation energy E_a is given in terms of the ideal-gas-phase activation enthalpy by eq 9. Calculated values of $\Delta S^+{}_d$ and E_a for reactions in dioxan are given in Table IV.

$$E_a = H_g{}^* + RT \qquad (9)$$

Partial Optimization of a Solvated Zwitterion. Figure 3 illustrates an arrangement of six solvent water molecules around a water–formaldehyde zwitterionic adduct with a straddled structure. Three of the ancillary water molecules serve as proton donors in hydrogen bonds to the carbonyl oxygen atom, a fourth is a proton donor in a hydrogen bond to the nucleophilic oxygen atom, and two further solvent water molecules are hydrogen bonded as proton acceptors to the nucleophilic water molecule. Some further degree of structure is present in the six-water cage by virtue of hydrogen bonds between solvent molecules, themselves hydrogen bonded to the zwitterion such that the nucleophilic and electrophilic moieties are linked via hydrogen-bonded chains of solvent water molecules. This array of solvent molecules represents a plausible structure such as might occur instantaneously in aqueous solution. Such an array need not constitute a global minimum energy structure nor even a local minimum energy structure. However, some optimization is in order to ensure a total configurational energy that allows for a reasonable extent of statistical occurrence in the appropriate ensemble of solvent-cage solute structures.

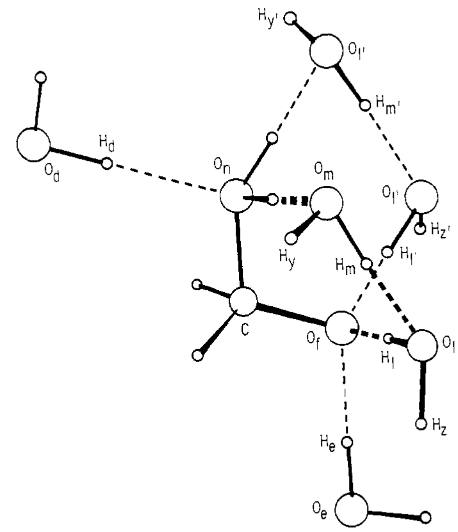

Figure 3. ORTEP drawing of a partially optimized structure of a solvated zwitterion $(H_2O^+CH_2O^-)\cdot 6H_2O$.

The geometry of a straddled water–formaldehyde adduct (cf. ref 2) optimized within the constraint of C_s symmetry and with O_n–C = 1.6 Å was taken as the starting point for this calculation. The solvent waters were fixed in their isolated-molecule geometries, all zwitterion–solvent hydrogen bonds were constrained to be linear, and the spatial distribution of the carbonyl bond and the three hydrogen bonds about the atom O_f was taken as being tetrahedral. Similarly, a tetrahedral angle was assumed between the O_n–C bond and the hydrogen bond from O_n to the proton-donor water molecule. The values chosen for the various dihedral angles defining the solvent-cage structure are given in Table V with the group of constrained coordinates. As is apparent from Figure 3, the original symmetry plane of the unsolvated zwitterion is maintained in the solvated structure and throughout the optimization in order to reduce the number of independent degrees of freedom. The four distinct zwitterion–solvent hydrogen-bond O···O distances were optimized in turn by finding the minimum in a parabola fitted to three energies calculated for structures in which the particular O···O length was suitably incremented. The resulting values for these hydrogen-bond lengths are given in Table V as the group of partially optimized coordinates. Subsequently, five independent coordinates were optimized to within 0.01 Å for bond lengths and 1° for angles, namely the O_n–C and C–O_f bond

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Table V. Partially Optimized STO-3G Geometry for Solvated Zwitterion[a]

Constrained Coordinates

C-H, 1.12; O_n-H, 0.99; solvent O-H, 0.99; H-C-H, 108; H-O_n-H, 103; solvent H-O-H, 100; C-O_n-O_d, C-O_f-O_e, C-O_f-O_l, 109; O_n-H_d-O_d, O_f-H_e-O_e, O_f-H_l-O_l, O_n-H-O_m, 180; O_m-H_m-O_l, $O_{m'}$-$H_{m'}$-$O_{l'}$, 171; O_n-O_m-H_y, O_n-$O_{m'}$-$H_{y'}$, 117; C-O_n-O_m-H_y, −79; C-O_n-O_m-H_m, 21; C-O_f-O_l-H_z, 100; C-O_n-$O_{m'}$-$H_{y'}$, 79; C-O_n-$O_{m'}$-$H_{m'}$, −21; C-O_f-$O_{l'}$-$H_{z'}$, −100

Partially Optimized Coordinates

O_f-O_e, 2.69; O_f-O_l, O_f-$O_{l'}$, 2.34; O_n-O_d, 2.77; O_n-O_m, O_n-$O_{m'}$, 2.49

Optimized Coordinates

O_n-C, 1.52; C-O_f, 1.36; O_n-C-O_f, 110; C-O_n-O_m, C-O_n-$O_{m'}$, 112; O_n-C-H, 102

[a] See Figure 3; bond lengths are in Å, bond angles and dihedral angles are in degrees.

Table VI. STO-3G Energies for Solvated Zwitterions

species[a]	O_n-C, Å	total energy, hartrees
six-water solvated zwitterion $H_2O^+CH_2O^-\cdot 6H_2O$	1.47	−637.209 12
	1.52	−637.211 32
	1.57	−637.209 47
six-water solvent cage	1.47	−449.778 38
	1.52	−449.785 33
	1.57	−449.790 76
four-water solvated zwitterion	1.47	−487.264 86
	1.52	−487.264 91
	1.57	−487.264 94
four-water solvent cage	1.47	−299.847 25
	1.52	−299.854 13
	1.57	−299.859 52
unsolvated zwitterion ($H_2O^+CH_2O^-$)	1.47	−187.215 99
	1.52	−187.226 16
	1.57	−187.234 08

[a] Species in parentheses is an unbound state.

lengths, the O_n–C–O_f angle, and the angles between the O_n–C bond and the planes of the nucleophilic water moiety and the methylene group, respectively. The values of these or equivalent optimized coordinates are also given in table V. These coordinates appear to describe the internal structure of the zwitterion, but owing to the nature of the constraints employed, they also determine the structure of the solvent cage to a certain extent. The overall result of the partial geometry optimization may be judged by consideration of the calculated energy change for dissociation of six water molecules from the solvated zwitterion to yield isolated water molecules and an unsolvated (and unbound) zwitterion having the same geometry as in the solvated adduct. The energy required for this process increased from 71 kcal mol^{-1} initially to 119 kcal mol^{-1} after optimization, while the total energy of the solvated adduct decreased by about 28 kcal mol^{-1}.

Table VI contains STO-3G energies calculated for the partially optimized structure of the water–formaldehyde zwitterion solvated by six water molecules depicted in Figure 3, the six-water solvent cage (minus the zwitterion), and the zwitterion (minus the solvent cage), each of the latter two structures having the same geometry as in the solvated structure. Energies are also given for corresponding structures in which the O_n–C bond length is incremented and decremented by 0.05 Å. A further set of energies is presented for homologous structures in which the two water molecules lying in the symmetry plane are removed. The geometry adopted for this zwitterion solvated by four water molecules is the same as the partially optimized structure with six water molecules.

Discussion

Bifunctional Catalysis by a Single Ancillary Water Molecule. Figure 4 shows STO-3G potential energies for structures along the reaction paths for both uncatalyzed and bifunctionally catalyzed concerted additions of water to formaldehyde. The energies are given relative to a noninteracting system of a formaldehyde molecule with two free water molecules.

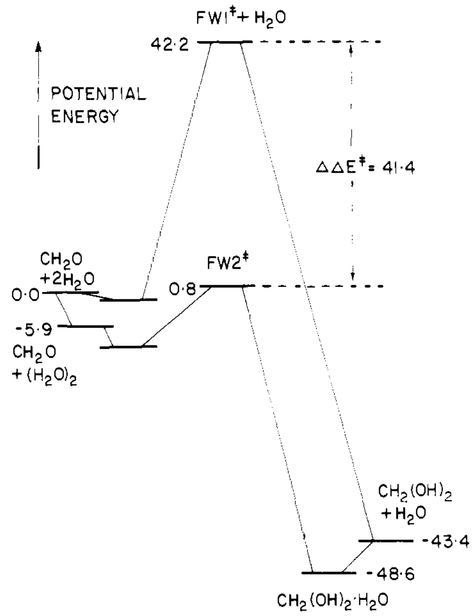

Figure 4. Relative STO-3G potential energies (kcal mol^{-1}) for catalyzed (via FW2‡) and uncatalyzed (via FW1‡) gas-phase formaldehyde hydration.

Along the uncatalyzed path through FW1‡, one of these water molecules remains noninteracting throughout while the other interacts nucleophilically with the formaldehyde molecule Figure 4 indicates initial formation of a weekly bound dipole-dipole adduct $H_2O \cdot CH_2O$ stabilized by 1.1 kcal mol^{-1} with a 43.3 kcal mol^{-1} barrier to formation of the product methanediol via FW1‡, which lies 42.5 kcal mol^{-1} above the energy of the separated reactants (see ref 2 and 7 for detailed discussion of the structure of FW1‡). Calculations with larger basis sets[6] indicate that the 43.4 kcal mol^{-1} stabilization of methanediol relative to water and formaldehyde is grossly overestimated in an STO-3G basis; but the transition-state energy of 42.2 kcal mol^{-1} is shown by the same calculations to be a reasonable estimate. Thus, for the purposes of the present discussion of catalysis of the forward process, namely hydration, these relative STO-3G energies provide adequate estimates of the energetics of transition-state formation.

Along the catalyzed path through FW2‡, initial formation of a water dimer stabilized by 5.9 kcal mol^{-1} followed by weak association of the water dimer with formaldehyde results in a cyclic complex stabilized by 9.3 kcal mol^{-1}. This complex then proceeds across a barrier of 10.1 kcal mol^{-1} through FW2‡ to the product methanediol–water complex. The potential energy difference between FW1‡ and FW2‡ is 41.4 kcal mol^{-1}.

To understand the energetics of this catalysis by a second, bifunctional water molecule in a way most relevant to experimental chemistry, we need an estimate of the Gibbs free energies, rather than the potential energies. Values of $\Delta H^\ddagger$, $\Delta S^\ddagger$, and $\Delta G^\ddagger$, calculated as described above, are given in Table II. A dramatic portrayal of the catalytic function of the second water molecule in FW2‡ emerges from these data, as is shown in Figure 5. The insertion of the additional water molecule into the structure of FW1‡ (eq 10)

$$FW1^\ddagger + H_2O \rightarrow FW2^\ddagger \qquad (10)$$

reduces the free energy of this species and thus the barrier to reaction by 26.9 kcal mol^{-1}, corresponding to a catalytic acceleration factor of about 10^{20} at 298 K. This effect arises from an extremely *unfavorable entropy change* of −35.4 eu, consistent with a substantial restriction of mobility as the free water molecule becomes "frozen" into the cyclic structure, and an extremely *favorable enthalpy change* of −37.6 kcal mol^{-1}. The favorable enthalpy change doubtless derives from a series of factors, in-

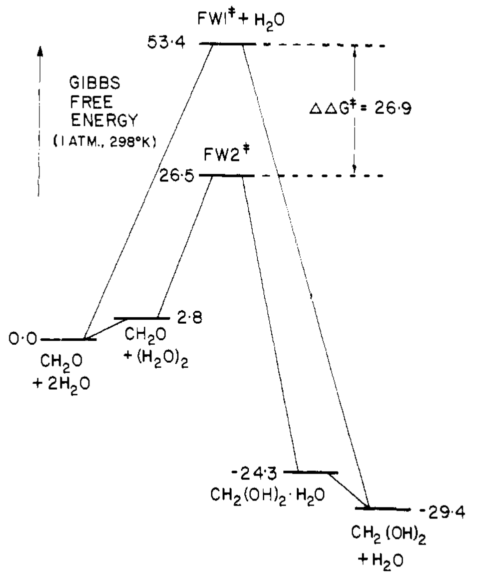

Figure 5. Relative STO-3G Gibbs free energies (kcal mol^{-1}) for catalyzed (via $FW2^{\ddagger}$) and uncatalyzed (via $FW1^{\ddagger}$) gas-phase formaldehyde hydration at 25 °C and 1 atm.

cluding bond formation, strain relief, etc., that are considered in greater detail below. Part of the enthalpy release (10.7 kcal mol^{-1}) is "utilized", in Jenck's terminology,[17] to repay the unfavorable entropy of association of $FW1^{\ddagger}$ and the catalytic water molecule. The remaining 26.9 kcal mol^{-1} is then "expressed" in transition-state stabilization.

It is notable that only the transition state has this capacity for extraordinary stabilization, since the enthalpy of association in reactant and product states is insufficient to repay the entropy cost. Thus, water-dimer formation in the reactant state is unfavorable ($\Delta G° = +2.8$ kcal mol^{-1}) in spite of a favorable enthalpy of hydrogen-bond formation ($\Delta H° = -4.0$ kcal mol^{-1}) because the entropy cost of −22.7 eu is too great. Similarly, association of water with methanediol in the product state leads to a net Gibbs free energy consumption of 5.1 kcal mol^{-1} ($\Delta H = -3.2$ kcal mol^{-1}; $\Delta S° = -27.8$ eu).

This model thus exhibits an essential property of catalytic systems: a capability for strong transition-state stabilization by a catalytic species that at the same time either fails to stabilize reactant and product states or effects a much smaller stabilization of these states.

Energetic Analysis of the Bifunctional Catalytic Effect. An understanding of the way in which the bifunctional water molecule produces a stabilization of $FW2^{\ddagger}$ relative to $FW1^{\ddagger}$ can be obtained from an analysis of the energetic components related to the assembly of the two transition states. This is most straightforwardly accomplished in terms of potential energy rather than free energy. The use of potential energy should not be objectable, however, for the following reasons. First, the entropic difference between $FW1^{\ddagger}$ and $FW2^{\ddagger}$ arises in large part from the loss of transitional and rotational entropy of a free water molecule upon its incorporation into $FW2^{\ddagger}$. This is overcompensated for by a large enthalpic term that in effect produces the catalysis by more than repaying the entropy costs (vide supra). Hence, it is the enthalpic difference between $FW1^{\ddagger}$ and $FW2^{\ddagger}$ that is the source of catalysis and is therefore most useful to analyze. Second, the enthalpic stabilization of $FW2^{\ddagger}$ relative to $FW1^{\ddagger}$ (37.6 kcal mol^{-1}) is quite close to the potential energy stabilization (41.4 kcal mol^{-1}). This means that the effects of zero-point energy and excited vibrational states (accounted for in the enthalpy but missing from the potential energy) are minor compared to the pure potential energy effects. Thus, we conclude that an analysis in terms of potential energy should be sufficient to elucidate the origins of the catalytic effect.

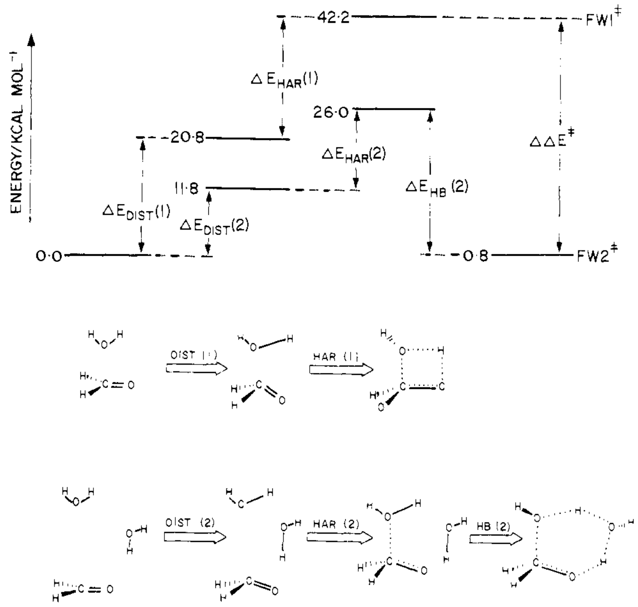

Figure 6. Subelementary steps in (1) uncatalyzed formaldehyde hydration via $FW1^{\ddagger}$ and (2) bifunctionally catalyzed formaldehyde hydration via $FW2^{\ddagger}$. STO-3G energies (kcal mol^{-1}) are expressed relative to isolated reactants $H_2O + CH_2O$ or $2H_2O + CH_2O$. Total catalytic effect:

$$FW1^{\ddagger} + H_2O \rightarrow FW2^{\ddagger} \qquad (10)$$

Our analysis will involve the *formal decomposition*, into discrete conceptual steps, of the process of transition-state formation from reactants for $FW1^{\ddagger}$ and $FW2^{\ddagger}$. For $FW2^{\ddagger}$, these steps are the following: (1) Distortion of the formaldehyde and the two water molecules into the configurations they will possess in the transition state. The calculation is carried out with the individual molecules in isolation so that only the pure distortion energy in the absence of intermolecular interactions is obtained. This energy is called ΔE_{DIST}. (2) Assembly of the distorted reactant-derived parts of $FW2^{\ddagger}$ (i.e., formaldehyde and the nucleophilic water molecule) into the positions they occupy in the transition state. Since these species have previously been distorted, the energy of assembly reflects simply the sum of bonded and nonbonded interactions as the electrophile and nucleophile come together. This energy change we denote ΔE_{HAR}. (3) Incorporation of the catalytic water molecule, which has also been distorted in advance. Thus, the energy change calculated here—ΔE_{HB}, for the "hydrogen bonding"—gives the net bonding and nonbonding interactions generated by incorporation of the catalytic entity into $FW2^{\ddagger}$. For $FW1^{\ddagger}$, only the distortion and reactant assembly steps are involved.

The results of this analysis are given in Figure 6. The distortion energy calculations show that a part of the catalytic effect of 41.4 kcal mol^{-1} derives from decreased distortion energy in the formation of $FW2^{\ddagger}$, representing a savings of 9 kcal mol^{-1}. This is possible because incorporation of the catalyst has (a) shifted the structure of the reactant-derived domain of the transition state in the direction of reactant-like structure and (b) permitted relief of strain in the four-membered ring of $FW1^{\ddagger}$ (see Figure 1b and ref 2, 6, and 7). Thus, formaldehyde and the nucleophilic water in $FW2^{\ddagger}$ are substantially closer in structure to their reactant forms than in $FW1^{\ddagger}$. Even when the distortion energy of the catalytic water molecule of $FW2^{\ddagger}$ is included, the resulting total distortion energy is 9 kcal mol^{-1} short of the distortion energy cost for the formation of $FW1^{\ddagger}$.

A further part of the catalytic effect derives from the less unfavorable energy of reactant assembly of $FW2^{\ddagger}$ compared to $FW1^{\ddagger}$, namely $\Delta(\Delta HAR) = 7.2$ kcal mol^{-1}. Presumably here again, the operative factor is the more reactant-like structure of $FW2^{\ddagger}$. The greater distance between the component fragments reduces the nonbonded repulsions, which dominate the energetics at this point along the reaction pathway.

Finally, the largest part of the catalysis (25.2 kcal mol^{-1} of the total 41.4 kcal mol^{-1}) emerges as the catalytic water molecule is

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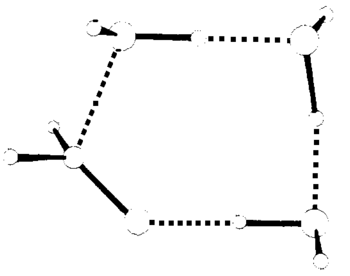

Figure 7. Hypothetical cyclic-transition-state structure of FW3‡.

added to the reactant assembly to form FW2‡. This can be thought of as arising from a very strong hydrogen-bonding interaction between the catalyst and the reactant-derived structure. Strong hydrogen bonds in charged systems are well-known:[18] the stabilization energies of $(H_2O\cdots H\cdots OH_2)^+$ relative to $H_2O + H_3O^+$ and of $(HO\cdots H\cdots OH)^-$ relative to $H_2O + OH^-$ have been estimated experimentally at 36 and 25 kcal mol^{-1}, respectively.[19] Strong hydrogen bonds also exist between neutral species having large dipoles: a 4-31G calculation yields a hydrogen-bond strength of 22.7 kcal mol^{-1} between ammonia and nitric acid.[20] In the present case, two hydrogen bonds are formed between the catalyst and the partially charged parts of the reactant-derived fragment. A Mulliken population analysis for the reactant-derived structure alone, with a geometry as in FW2‡, suggests that the amount of charge transfer from the nucleophile to the electrophile is about 0.2 of an electronic charge. Nonlinearity of the two hydrogen bonds may cause a reduction in stabilization, but cooperativity between them could roughly compensate for this effect. On balance, it seems that the value of ~25 kcal mol^{-1} for the strength of the hydrogen-bonding interaction in FW2‡ is not unreasonable and may be rationalized without need to invoke any peculiar properties for the transition state.

Probable Mechanisms in Gas and Aqueous Phases. The present calculations indicate that it is unlikely that any substantial fraction of the actual gas-phase hydration of formaldehyde passes through FW1‡ due to its large activation energy and to the fact that introduction of a single ancillary water molecule to form FW2‡ yields a reduction of 27 kcal mol^{-1} at 25 °C in the Gibbs free energy of activation (corresponding to a rate acceleration of nearly 10^{20}). The question then becomes, could the introduction of even more water molecules stabilize the transition state sufficiently to compensate for the unfavorable entropy term resulting from the higher molecularity?

Transition state FW2‡ presumably involves a certain amount of strain in its cyclic structure as evidenced by the coplanarity of the nonlinear hydrogen bonds. This strain might be relieved by incorporation of a second ancillary water molecule into the cyclic hydrogen-bonded structure. However, the Gibbs free energy of activation for formation of a transition state FW3‡ (Figure 7) for such a system would be lower than that for FW2‡ only if the attendant reduction in potential energy were greater than the increase in free energy of activation (from entropic sources) implied by the involvement of a fourth molecule. A rough estimate of this entropic cost is available form the difference in entropies of formation of FW1‡ and FW2‡ (Table II), which is 35.4 eu and corresponds to a free energy increment of 10–11 kcal mol^{-1}, at 25 °C and 1 atm standard state. Since it is not expected that relief of strain energy from nonlinear hydrogen bonds would amount to 10–11 kcal mol^{-1}, it seems unlikely that processes involving two or more ancillary water molecules would lead to enhanced catalysis. *It seems likely therefore that transition state FW2‡ provides the major channel for hydration of formaldehyde in the gas phase.* Although it is known that there exists an equilibrium between formaldehyde and methanediol in the gas phase,[21] the kinetics of gas-phase hydration do not appear to have been studied experimentally. Thus, confirmation of this prediction must await future experimental investigations.

It is also of interest to enquire as to the smallest number of ancillary water molecules required in order essentially to "bridge the gap" between gas-phase and solution behavior in formaldehyde hydration. Could it be that FW2‡, involving only a single ancillary water molecule, is an adequate model of a transition state for the reaction in aqueous solution as well as in the gas phase? There is, in fact, evidence from a recent Monte Carlo[22] computer simulation of formaldehyde in dilute aqueous solution that a cyclically hydrogen-bonded reactant complex $2H_2O{\cdot}CH_2O$ (Figure 2a and entry 7 in Table I) is a plausible structure. Figure 13 in Mehrotra and Beveridge's paper[22] shows a sample structure (described as "provisionally representative") of formaldehyde and its first hydration shell: inspection of this stereographic view reveals two water molecules situated in positions not dissimilar from those shown in Figure 2a of the present work and thus they are possible candidates for the roles of nucleophile and bifunctional catalyst as in FW2‡.

A comparison of the calculated results for FW1‡ and FW2‡ with experimental observations for aqueous solution can be effected by the following procedure. First, an estimate of $\Delta G^‡$ is obtained from experimental data. Second, $\Delta H^‡$, $\Delta S^‡$, and $\Delta G^‡$ are calculated for gas-phase reactions proceeding through FW1‡ and FW2‡, respectively. Third, these values are corrected by an empirical method to yield values appropriate for aqueous solution. Finally, calculated values of $\Delta G^‡$ for FW1‡ and FW2‡ are compared with the experimental estimate.

The rate constant for methanediol dehydration in aqueous solution at 25 °C was found by Bell and Evans[23] to be 5.1×10^{-3} s^{-1}, and a value of 4.4×10^{-4} was measured polarigraphically by Valenta[24] for the equilibrium constant $[CH_2O]/[CH_2(OH)_2]$ at 20 °C. Application of the van't Hoff equation using the value $\Delta H = -8.4$ kcal mol^{-1}, reported by Zavitsas et al.[25] for formaldehyde hydration allows the pseudo-first-order rate constant for formaldehyde hydration at 25 °C to be estimated as 9.2 s^{-1}. The Gibbs free energy of activation calculated from this rate constant is 16 kcal mol^{-1}. The temperature dependence of the rate constant for methanediol dehydration (or formaldehyde hydration) in aqueous solution does not appear to have been measured, and thus experimental values for the enthalpy and entropy of activation are not available.

Table III contains enthalpies, entropies, and Gibbs free energies of activation calculated with scaled STO-3G force constants with STO-3G-optimized geometries (see also Table II) for formaldehyde hydration in the gas and aqueous phases proceeding by means of three model mechanisms. Application of Wertz's method (as described above) to the calculation of entropies of solvation leads to substantial reductions in the adverse entropies of activation for each of the model mechanisms in aqueous solution and consequently to appreciable reductions in the corresponding Gibbs free energies of activation. Comparison of the calculated values for $\Delta G_{aq}^‡$ given in Table V with the experimental value of 16 kcal mol^{-1} clearly shows that the mechanism of formaldehyde hydration via FW1‡ is not acceptable for the reaction in aqueous solution. On the other hand, on the basis of the agreement between the theoretical and experimental Gibbs free energies of activation, addition of a water dimer to formaldehyde via FW2‡ would appear to be a feasible model for the mechanism of formaldehyde hydration in aqueous solution. Indeed, in order to account for the observed linearity of a Brønsted plot for acid–base catalysis of

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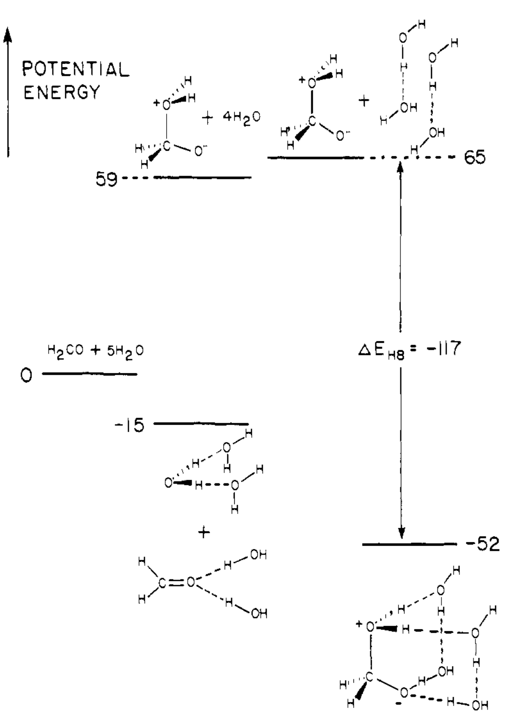

Figure 8. Analysis of STO-3G energetic factors (kcal mol^{-1}) leading to stabilization of a zwitterionic adduct $(H_2O^+CH_2O^-)\cdot 4H_2O$.

methanediol dehydration over a very wide pK range, Bell[23,26] proposed that this reaction might proceed by means of a concerted mechanism involving several water molecules in a cyclic hydrogen-bonded structure homologous with FW2*. He did not, however, speculate as to the number of water molecules involved in such structures. Mechanisms of this type, in which the water molecules serve bifunctionally, were suggested earlier by Eigen.[27]

Carbonyl Hydration in Aprotic Media. In principle, the use of an aprotic medium for carbonyl hydration permits direct determination of the number of water molecules in the transition state. For example, the number of water molecules involved in the hydration of 1,3-dichloroacetone in dioxan and acetonitrile solutions was estimated by Bell et al.[28] from measurements of the apparent kinetic orders with respect to water. For hydration in both solvents, a kinetic order of 3 was found. This may be interpreted qualitatively as the amount by which the number of water molecules present in the transition state exceeds the number associated with the reactant carbonyl compound. Since, in dilute solutions of water in aprotic solvents, 1,3-dichloroacetone is unlikely to be solvated to any great extent (for instance, by water molecules hydrogen bonded to the carbonyl oxygen atom), it appears that there are indeed three molecules of water present in the transition state for its hydrogen in aprotic media. This result was corroborated by Bell and Critchlow,[29] who also argued, from the results of experiments with $H_2O + D_2O$ mixtures in dioxan, that the number of exchangeable protons in this transition state was at least six, in accord with a mechanism involving three molecules of water in a cyclic structure such as shown in Figure 7. A semiempirical theoretical analysis of such a transition state by Critchlow[30] suggested, however, that the three proton transfers were not all synchrotrons with HAR (in a fully concerted mechanism) but that transfer of only one proton was coupled with HAR in an "intimate stepwise" mechanism.[29]

Activation parameters have been reported by Bell and Sörensen[31] for the hydration of 1,3-dichloroacetone in dioxan and by Sörensen[32] for hydration of chloral also in dioxan. Entropy changes and activation energies calculated by using Wertz's method[13a] extended to dioxan (as described above) are given in Table IV for the three models of formaldehyde hydration considered above relative to a standard state of 1 M for each component. This table also contains the experimental Arrhenius parameters for hydration of 1,3-dichloroacetone and chloral in dioxan at 25 °C. Not surprisingly, the models for formaldehyde hydration involving either one or two molecules of water do not accord well with the experimental results for carbonyl hydration involving three molecules of water, but nonetheless several points are worthy of note. The difference between the calculated entropies of activation $\Delta S^{+}{}_{d}{}^{*}$ for $H_2O + CH_2O$ and $2H_2O + CH_2O$ in dioxan is about −23 eu; if this increment is added to the entropy of activation for $2H_2O + CH_2O$, then the value predicted for $3H_2O + CH_2O$ in dioxan is about −69 eu, which does accord with the experimental entropies of activation. This extrapolation lends further support to the proposition that three water molecules are involved in the transition state for carbonyl hydration in aprotic media. Sörensen[31] did propose that four molecules might be involved, but extrapolation of the calculated entropy of activation as above would not support this. For a mechanism involving three molecules of water to be preferred over one involving only two water molecules requires that it must have an activation energy lower by about 7 kcal mol^{-1} in order to compensate for the extra entropic disadvantage of 23 eu.

Although the calculated and experimental activation energies given in Table IV do refer to different reactions, nevertheless it does seem that the experimental energies are indeed lower than the activation energy calculated for $2H_2O + CH_2O$. Both Bell and Sörensen[31,32] noted that the activation energy increased with water concentration in the dioxan solution, which corresponded with increased association of the water. The calculated results bear out this finding in that the activation energy for $(H_2O)_2 + CH_2O$ is significantly higher than that for $2H_2O + CH_2O$.

Thus, although the mechanism involving a water dimer as reactant appears to be a better model for carbonyl hydration in aqueous solution than that involving two monomeric water molecules, it seems that the reverse is true in an aprotic solvent such as dioxan. Moreover, it seems likely that the system $3H_2O + CH_2O$ would be a still better model. The hydrogen bonds in such cyclic structures, as shown in Figure 7, may be accommodated with proton-donor–acceptor arrangements much closer to linearity than is possible in FW2*, and the attendant relief of strain energy might well amount to 7 kcal mol^{-1} (in contrast to the 15 kcal mol^{-1} required in the gas phase as discussed above). The hypothetical, homologous, transition state FW3* would involve a cyclic system of eight atoms in accord with the preferred requirement for intramolecular proton transfer postulated by Gandour.[33] Theoretical studies on the $3H_2O + CH_2O$ system are currently in progress in our laboratories.

A mechanism, related to that described in this paper for formaldehyde hydration via FW2*, has been previously suggested for ester aminolysis in aprotic media. Burshtein and Khurgin[34] performed a quantum mechanical study of the ammonolysis of methyl acetate catalyzed by a second molecule of ammonia that was hydrogen bonded in a cyclic structure between the nucleophile and the leaving methoxy group. The resulting complex was calculated by the CNDO/BW method to be more stable than either the reactants or products; however, such semiempirical methods are very unreliable for the description of chemically reacting systems such as this (cf. ref 2). On the other hand, recent ab initio calculations by Oie et al.[35] on the ammonia-catalyzed reaction of ammonia with formic acid have yielded similar results

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Table VII. Variation of Components of Interaction Enegy for Four-Water Solvated Zwitterion with Bond Length O_n-C[a]

O_n-C, Å	intrinsic inter-action[b]	solvent cage strain energy[c]	solvation energy[d]	total inter-action energy[e]
1.47	65.4	10.3	−126.5	−50.8
1.52	59.0	5.9	−117.1	−52.1
1.57	54.1	2.6	−107.5	−50.9

[a] All energies in kcal mol^{-1}; four-water solvated zwitterion is a substructure of the partially optimized geometry for the six-water solvated zwitterion given in Table VI. [b] $E(H_2O^+CH_2O^-) - E(H_2O) - E(CH_2O)$. [c] $E(\text{solvent cage}) - 4E(H_2O)$. [d] $E(\text{solvated zwitterion}) - E(\text{solvent cage}) - E(H_2O^+CH_2O^-)$. [e] $E(\text{solvated zwitterion}) - 4E(H_2O)$.

to those obtained in the present work. Moreover, they obtained multiple transition states, as might be expected in such a more complicated system.

A Zwitterionic Intermediate in Aqueous Solution? As we have seen, these calculations suggest that the gas-phase hydration of formaldehyde proceeds through a concerted, two-water process, with the zwitterionic intermediate for the two-step addition of one water not being a bound species.[2,7] Data for liquid-phase processes have also been found consistent with multiple-water participation, although the degree of "concertedness" is not experimentally well-defined. We should like to consider the significance of our calculations on zwitterionic stabilization by water aggregates, presented in the results section, to the question of whether such species might also be reaction intermediates in aqueous media.

Mechanistically, calculations of solvation by either six-water or four-water aggregates are equally informative,[36] and thus we will confine our discussion to the simpler four-water case. The four-water solvated zwitterion is stabilized relative to the unsolvated zwitterion and the four-water cage by 117 kcal mol^{-1}. This remarkable stabilization may be analyzed into components as illustrated in Figure 8. Formation of an unsolvated zwitterion-like structure with O_n–C = 1.52 Å is unfavorable by 59 kcal mol^{-1} with respect to isolated water and formaldehyde molecules. Assembly of the four water molecules into the solvent-cage structure shown in Figure 3 is also unfavorable to the extent of a further 6 kcal mol^{-1}. This is due to an unfavorable parallel alignment of water dimer fragments that are themselves favorably hydrogen bonded. It should be noted that the solvent-cage structure was quite deliberately not fully optimized for reasons stated earlier; such optimization would, of course, lead to an increase in the predicted stability of the solvated zwitterion with respect to its isolated components. Part of the favorable interaction energy of the zwitterion with the four-water solvent cage arises from the unfavorable interactions within the solvent cage; the solvated zwitterion is stablized by 111 kcal mol^{-1} relative to the unsolvated species and four isolated water molecules but by 117 kcal mol^{-1} relative to the unsolvated species and the solvent cage.[37]

An alternative analysis of the zwitterion solvation can be obtained by imagining initial formation of an open-chain water trimer, in which the nucleophilic water molecule serves as the proton donor in both hydrogen bonds, and of a hydrogen bonded complex of formaldehyde with two molecules of water (Figure 8). The water trimer is stabilized by 9.33 kcal mol^{-1} in STO-4G[38] and the doubly solvated formaldehyde by 5.88 kcal mol^{-1} in a minimal Slater basis.[39] Addition of these two solvated reactants yields the solvated zwitterion with a further stabilization of about 37 kcal mol^{-1}, and this adduct is in a potential energy well with respect to dissociation to the solvated reactants.

Compression of the O_n–C bond in the solvated zwitterion is accompanied by an increasingly unfavorable intrinsic energy of interaction between the nucleophile and formaldehyde and by an increasingly favorable solvation energy between the zwitterion and the solvent cage, as may be seen from the data given in Table VII. A force constant of about 7 mD Å^{-1} for stretching of the O_n–C bond may be evaluated from this data, which is about equal to the STO-3G force constant for the O–C bond in methanediol; it should be noted, however, that extension and compression of the O_n–C bond of the solvated zwitterion in the present calculation is accompanied by change in the structure of the solvent cage since the nucleophilic and electrophilic moieties each "carry" two solvent molecules as in the solvated reactants.

The present STO-3G calculations suggest that a four-water solvated zwitterion of water and formaldehyde is energetically stable with respect to dissociation to five molecules of water and one of formaldehyde in the gas phase, neglecting entropic factors. The magnitude of this stabilization energy is probably overestimated in the minimal basis description just as the stability of methanediol relative to water and formaldehyde is overestimated.[40] Guthrie[41] has estimated the (dimensionless) equilibrium constant K^z for addition of water to formaldehyde to yield a zwitterionic adduct in aqueous solution at 25 °C and has reported a value of $\log K^z = -8.5$. The corresponding Gibbs free energy change for zwitterion formation in aqueous solution would be 112 kcal mol^{-1}. Assuming that the entropy change in this process is equal to that which accompanies neutral methanediol formation in the hydration equilibrium,[25] the enthalpy change may be calculated to be approximately +8 kcal mol^{-1}.

To enable comparison between this estimated enthalpy of zwitterion formation, derived from experimental data, and the corresponding calculated potential energy change, one must correct the gas-phase four-water solvated zwitterion stabilization energy by an amount equal to the solvation energy of five molecules of water and one molecule of formaldehyde in aqueous solution. Data given by Rowlinson[42] for the molar residual energy of water at 20 and 40 °C (the energy change for transfer from the gas to the liquid phase at the same temperature) may be interpolated to give a value of −9.9 kcal mol^{-1} for the solvation energy of water in water at 25 °C. Mehrotra and Beveridge[22] have calculated the partial molar internal energy of transfer of formaldehyde into water to be −16.7 ± 11.67 kcal mol^{-1}. Thus, transfer of five molecules of water and one of formaldehyde from the gas phase into aqueous solution at 25 °C would be accompanied by an energy change of about −66 kcal mol^{-1}, and the calculated energy of the four-water solvated zwitterion relative to aqueous formaldehyde would be approximately $-52 - (-66) = 14$ kcal mol^{-1}. This calculated energy is at least of the same order of magnitude as the experimentally derived value of 8 kcal mol^{-1}, although the calculation

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[36] The stabilization of the six-water solvated zwitterion (Figure 3) as calculated from the values given in Table VI relative to the unsolvated (and unbound) zwitterion and the six-water solvent cage is 125 kcal mol^{-1} for the partially optimized structure with O_n–C = 1.52 Å. The partial positive charge on the nucleophilic moiety of the zwitterion is stabilized by interactions with solvent molecules serving as proton acceptors, and the partial negative charge on the carbonyl oxygen atom is stabilized by interactions with solvent molecules serving as proton donors in hydrogen bonds. Presumably, therefore, the water molecule hydrogen bonded as a proton donor to the nucleophilic oxygen atom contributes little, if anything, to the total stabilization energy. The four-water structure was obtained from the partially optimized six-water solvated zwitterion structure by removal of the two water molecules lying in the symmetry plane, leaving the remainder of the structure unaltered. The stabilization of the four-water solvated zwitterion relative to the unsolvated zwitterion and the four-water solvent cage is 117 kcal mol^{-1}. This stabilization energy differs from that effected by the six-water solvent cage by only 8 kcal mol^{-1}, which is roughly the same energy as the combined hydrogen-bond strengths in a water dimer and a formaldehyde-water adduct (see data in Table I). Thus the two water molecules removed from the six-water solvated zwitterion together contribute no more to the stability of the zwitterion than they would to isolated, neutral, water and formaldehyde molecules.

[37] A close analogy exists between this situation and the concept of intrinsic binding energy of a substrate to an enzyme (cf. ref 17): binding of the zwitterion (substrate) to the solvent (enzyme) yields a solvated zwitterion (enzyme-substrate complex) in which the solvent structure is strained by an amount equal to the difference between the observed binding energy and the intrinsic binding energy.

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[40] Compare ΔE(STO-3G) = −43.4 kcal mol^{-1} with ΔE(4-31G) = −16.8 kcal mol^{-1}.[2,7,8]

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has neglected the energy of transfer of the solvated zwitterion from the gas phase into aqueous solution.

Guthrie[41] has applied Marcus theory to carbonyl hydrations and has found that observed rate constants for uncatalyzed hydration may be correlated satisfactorily with equilibrium constants for formation of a zwitterionic adduct but not with equilibrium constants for neutral adduct formation by a concerted mechanism. He argued that uncatalyzed hydration of carbonyl compounds generally proceeds by a stepwise mechanism involving rate-determining formation of a zwitterionic adduct followed by fast proton transfer to yield the neutral product; the concerted mechanism would become important only for extremely unreactive compounds. The present calculations for solvated zwitterions consider only the overall energy change in forming a zwitterionic intermediate, and no information is available concerning the energy barrier to this process. However, if this rate-determining transition state involves the same number of water molecules as does the solvated zwitterion, then the four-water solvated zwitterion may represent a good model for such an intermediate. This model would predict an additional three molecules of water associated with the transition state as over the doubly solvated reactant formaldehyde, in accord with the findings of Bell and his coworkers[28,29,31,32] (in aprotic solvents).

Funderburk, Aldwin, and Jencks,[43] in contrast, have given an argument for concerted, nonbifunctional uncatalyzed hydration proceeding by the equivalent of general-base catalysis. They have pointed out that observed rate constants for uncatalyzed (i.e., water catalyzed) formaldehyde hydration (and hemiacetal formation) lie nearer to the extrapolated Brønsted line for general-base catalysis than for general-acid catalysis. They have also pointed out that bifunctional catalysis by water cannot be important since there is no significant positive deviation of points for catalysis by carboxylate anions that cannot act as bifunctional catalysts. These authors concluded that uncatalyzed formaldehyde hydration represents general-base catalysis by water, possibly by means of a one-encounter involving a cyclic structure (cf. Figure 7) but not involving synchronous proton transfers in a fully concerted mechanism. Furthermore, it was argued that a zwitterionic intermediate has such a short lifetime that general catalysis is enforced and that the processes of HAR and PT must be coupled in a concerted mechanism.

Summary

Gas-phase formaldehyde hydration is probably a termolecular reaction proceeding by means of a concerted mechanism involving $FW2^{\ddagger}$. The single ancillary water molecule has a dramatic effect that may be understood in terms of a strong hydrogen-bonding interaction between the bifunctional catalyst and the (unbound) zwitterionic adduct of the nucleophilic water with formaldehyde.

In aprotic solvents, carbonyl addition probably involves three molecules of water in a cyclic transition state rather than just two as in $FW2^{\ddagger}$. As yet the structure of this transition state in unknown, and it is unclear whether the mechanism is fully concerted (involving synchronous motions of all the transferring protons) or "intimate stepwise" (involving at least two steps but occurring within a single encounter; one of the steps may involve coupled HAR and PT as in general acid–base catalysis). A theoretical study of the system $3H_2O + CH_2O$ is in progress in our laboratories.

In aqueous solution it is not all clear whether the mechanism is stepwise (involving a solvated zwitterion) or concerted. It may be that not just a single mechanism is involved but that several competing mechanisms may be significant. Analysis of the experimental kinetic data is not a simple matter and may perhaps be assisted by evidence from appropriate theoretical studies of model systems.

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Electronic Interactions in Mixed-Valence Molecules As Mediated by Organic Bridging Groups

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Abstract: The preparations, spectroscopic properties, and electrochemistry of a number of new complexes with the general formula $[(Ru(NH_3)_5)_2L]^{n+}$ (n = 4, 5, 6) are reported, where L is a rigid organic bridging ligand (including pyrimidine, the dicyanobenzenes, 3- and 4-cyanopyridine, and dicyanonaphthalenes). These complexes and others are used to illustrate several aspects of the effect of bridging ligand structure on metal–metal interactions in polymetallic systems. The observed trends are predicted theoretically by combining a molecular orbital description of the bridging ligand with a semiempirical measure of metal–ligand charge-transfer interactions. The relationship of bridging ligand size, orientation of substituents, interplanar distances, and saturation to metal–metal interaction is demonstrated both theoretically and experimentally. Bridging ligand effects in intramolecular electron transfer are considered in the context of nonadiabatic theories and electronic interactions between redox sites. The relationship between the characteristics of the bridging group and the comproportionation constant, K_c, is discussed.

Numerous binuclear mixed-valence (MV) complexes based on ruthenium ammines have been reported[1-10] since the synthesis of the Creutz ion, $[(Ru(NH_3)_5)_2\text{pyrazine}]^{5+}$.[11] Examples of both localized[2-5,10,12] and delocalized (valence averaged)[1,8,9] systems

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