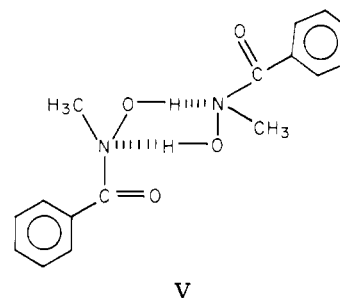


effects. When  $R_2 = H$  or  $CH_3$ , resonance forms II and III apply, with III taking on increased importance for  $R_2 = CH_3$ . When  $R_2 = C_6H_5$ , then resonance forms II-IV apply. These resonance forms may be used to consider the net enhancement of the molecular dipole on ionization and thus to rationalize the observed trends of  $\Delta H_a$  and  $\Delta S_a$  in terms of solvation effects. Although it is generally agreed that little C-N double bond character exists in the neutral hydroxamic acids,<sup>1a</sup> resonance form III for the hydroxamate anion has C-N double bond character which can lock the anion into the rotamer shown for maximum molecular dipole moment. Resonance form III is expected to have the maximum relative importance when  $R_2 = CH_3$ . We note that the *N*-methyl-substituted hydroxamic acids are those with the most negative  $\Delta S_a$  and least positive  $\Delta H_a$  values, suggesting a stronger interaction with the solvent. When  $R_2 = C_6H_5$  resonance form IV must be considered as a resonance contributor. Contributions from resonance form II-IV may then represent a conjugate base anion with a lower molecular dipole (relative to consideration of only form II and III) and hence a lesser interaction with the solvent. This is consistent with an interpretation of  $\Delta S_a$  and  $\Delta H_a$  being strongly influenced by solvation effects since when  $R_2 = C_6H_5$ , the  $\Delta S_a$  values are the least negative and  $\Delta H_a$  the most positive of the series reported here.

In considering the physical characterization data for the *N*-methyl-substituted hydroxamic acids in nonaqueous solvents, we conclude that dimerization takes place in nonpolar media where the intermolecular forces are due to hydrogen bonding. This is consistent with the observation of multiple  $^1H$  NMR signals in the *N*-methyl region for  $CH_3C(O)N(OH)CH_3$  and  $C_6H_5C(O)N(OH)CH_3$  in

$CDCl_3$  solvent. Molecular weight data in toluene and gas chromatography-mass spectra results in  $Et_2O$  for  $C_6H_5C(O)N(OH)CH_3$  further substantiate the existence of a monomer  $\rightleftharpoons$  dimer equilibrium. The molecular weight data may be used to calculate an approximate dimerization equilibrium quotient of  $20 M^{-1}$  for  $C_6H_5C(O)N(OH)CH_3$  in toluene at 25 °C. A tentative structural assignment for the hydrogen bonded dimer for the  $C_6H_5C(O)N(OH)CH_3$  system is as shown in V. Apparently a good electron donor



$R_2$  substituent is necessary for a significant amount of dimer to form. Furthermore, H-bonded association is not expected to occur in polar solvents such as  $H_2O$ .

**Acknowledgment** is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

**Registry No.**  $CH_3C(O)N(OH)H$ , 1113-25-3;  $C_6H_5C(O)N(OH)H$ , 495-18-1;  $CH_3C(O)N(OH)C_6H_5$ , 1795-83-1;  $C_6H_5C(O)N(OH)C_6H_5$ , 304-88-1;  $CH_3C(O)N(OH)CH_3$ , 13115-24-7;  $C_6H_5C(O)N(OH)CH_3$ , 2446-50-6.

## Proton Inventory of the Water-Catalyzed Hydrolysis of 1-Acetyl-1,2,4-triazole. Examination of Ionic Strength Effects<sup>1,2</sup>

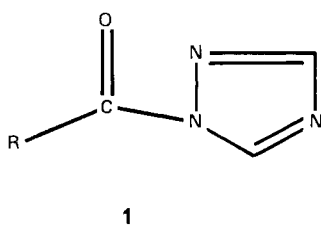
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Proton inventories of the water-catalyzed hydrolysis of 1-acetyl-1,2,4-triazole have been completed under a variety of conditions. The solvent deuterium isotope effect,  $k_{H_2O}/k_{D_2O}$ , determined at pH 4.7 or the equivalent point on the pD rate profile at 25 °C by using acetic acid-acetate buffers at 1 M ionic strength was 3.18. The solvent deuterium isotope effects determined at ionic strengths of 1 and 0.5 M by using  $10^{-3}$  M HCl (DCl) to control the pH(D) were 3.13 and 3.07, respectively. In all cases the proton inventories exhibit significant downward curvature and are, within experimental error, consistent with a cyclic transition state structure involving four water molecules. The equation  $k_n = k_0(1 - n + 0.75n)^4$  describes the proton inventories where the value of the isotope fractionation factor for the four "in-flight" protons is 0.75. These inventories are compared to an earlier study done with no ionic strength control,<sup>4</sup> and several alternative transition states are considered in detail.

The mechanism of the neutral hydrolysis of 1-acyl-1,2,4-triazoles (1) has recently been probed by Karzijn and



Engberts using the proton inventory technique.<sup>4</sup> A study of the "water reaction" of 1-acetyl-1,2,4-triazole (1,  $R = CH_3$ ) completed by us at about the same time<sup>1</sup> and recently expanded upon lends itself to a slightly different interpretation. We report our results and point out the differences in the two studies. These differences and similarities should be of particular interest to anyone contemplating a proton inventory investigation.

(2) This research was supported by the Robert A. Welch Foundation and the National Institutes of Health (Grant No. 1 R01 GM 2543301).

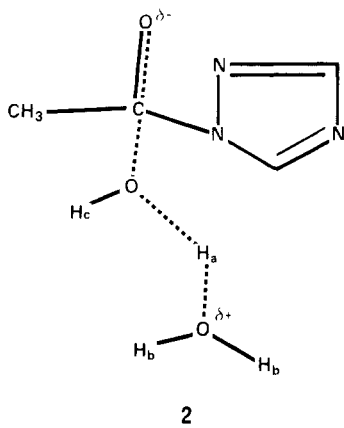
(3) (a) Recipient of a Robert A. Welch Foundation Predoctoral Fellowship. (b) Recipient of a Robert A. Welch Foundation Undergraduate Scholarship.

(4) Karzijn, W.; Engberts, J. B. F. N. *Tetrahedron Lett.* 1978, 1787-90.

(1) Taken in part from the M.S. Thesis of Jacob F. Patterson, Texas A&M University, 1978.

Fox and Jencks had previously shown that 1-acetyl-1,2,4-triazole exhibited a pH-independent "water reaction" between pH 3 and 7 at 25 °C<sup>5</sup> ( $\mu = 1.0$  M, KCl). The reaction was found to be subject to general-base catalysis ( $\beta = 0.34$ ). Our previous investigation of the mechanism of hydrolysis of the 1-acetylimidazolium ion, using the proton inventory technique, spurred us to investigate 1-acetyl-1,2,4-triazole.<sup>6,7</sup> We also chose to investigate the influence of reaction conditions (e.g., ionic strength) upon the magnitude of the solvent deuterium isotope effect and the shape of the proton inventory. The latter studies were prompted by some initial discrepancies between our values and those reported by Karzijn and Engberts.<sup>1,4</sup>

The proton inventory for 1-acetyl-1,2,4-triazole determined by Karzijn and Engberts was interpreted in terms of a transition-state structure involving one water molecule assisting, in a general-base fashion, the attack of another water molecule on the carbonyl carbon (2).<sup>4</sup> There were



several precedents for this type of transition state in ester and amide hydrolyses on the basis of previous proton inventory studies.<sup>8-5</sup>

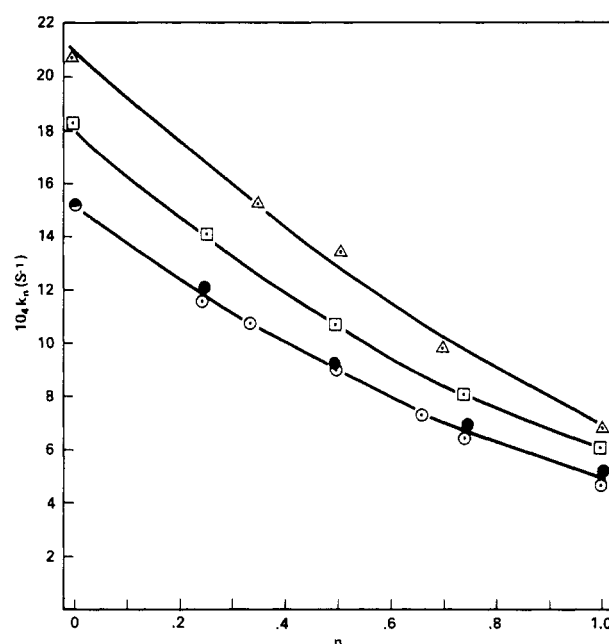
The theory of the proton inventory technique has been well documented in the literature.<sup>9-11</sup> In essence, the rate constant,  $k_n$ , in protium oxide–deuterium oxide mixtures of atom fraction of deuterium  $n$  is related to the rate constant in pure protium oxide,  $k_0$ , by eq 1. The param-

$$k_n = k_0 \frac{\prod_i^{\text{TS}} (1 - n + n\phi_i^*)}{\prod_j^{\text{RS}} (1 - n + n\phi_j)} \quad (1)$$

eters  $\phi_i^*$  and  $\phi_j$  represent the isotopic fractionation factors for the  $i$ th transition-state (TS) site and the  $j$ th reactant-state (RS) site, respectively. In most cases, the values of  $\phi_j$  are unity, and eq 1 reduces to eq 2. Such is the case

$$k_n = k_0 \prod_i^{\text{TS}} (1 - n + n\phi_i^*) \quad (2)$$

in the present study. Thus a plot of  $k_n$  vs.  $n$  (i.e., a proton inventory) will yield information about the identity and number of transition-state protons giving rise to isotope effects. In general, downward curvature in proton inven-



**Figure 1.** Collected proton inventories for the water-catalyzed hydrolysis of 1-acetyl-1,2,4-triazole determined under a variety of conditions: pH 3–5, no buffers or ionic strength control ( $\Delta$ );<sup>4</sup> pH 4.7, acetic acid–acetate buffers,  $\mu = 1.0$  M ( $\circ$ ); pH 3, HCl–DCl,  $\mu = 0.5$  M ( $\square$ ); pH 3, HCl–DCl,  $\mu = 1.0$  M ( $\bullet$ ). The symbols used to represent data points encompass the error bars.

**Table I.** Values of  $k_n$  for the Water-Catalyzed Hydrolysis of 1-Acetyl-1,2,4-triazole in H<sub>2</sub>O–D<sub>2</sub>O Mixtures of Atom Fraction of Deuterium  $n$  at 25.00 ± 0.05 °C Determined by Using Buffered Solutions<sup>a</sup>

$n$	$10^6 k_n$ , <sup>b</sup> s <sup>-1</sup>	$n$	$10^6 k_n$ , <sup>b</sup> s <sup>-1</sup>
0.000	1536 ± 14	0.659	728 ± 8
0.247	1163 ± 16	0.742	663 ± 7
0.330	1082 ± 16	0.989 <sup>c</sup>	483 ± 7
0.495	901 ± 3		

<sup>a</sup> Determined at pH 4.7 by using acetic acid–acetate buffers at 1.0 M ionic strength (KCl). The buffer concentration was varied from  $10^{-2}$  to  $2 \times 10^{-1}$  M. <sup>b</sup> Error limits are standard deviations. <sup>c</sup> Atom fraction of deuterium in "100%" deuterated buffer solution as determined by Mr. Josef Nemeth.<sup>14</sup>

tories is indicative of multiple-proton contributions in the transition state to the observed solvent deuterium isotope effect. It then becomes necessary to try and fit various chemically reasonable transition-state structures to the observed proton inventory. This procedure will be illustrated for the hydrolysis of 1-acetyl-1,2,4-triazole (1, R = CH<sub>3</sub>).

## Results

We chose initially to determine the proton inventory by extrapolating the observed rate constants in protium oxide–deuterium oxide mixtures to zero buffer concentration to obtain values for  $k_n$ , the rate constant for the water-catalyzed reaction. Figure 1 (open circles) shows a plot of the rate constant for the "water reaction" of 1-acetyl-1,2,4-triazole vs. the atom fraction of deuterium ( $n$ ) in the solvent determined at pH 4.7 at 25.00 ± 0.05 °C by using acetic acid–acetate buffers. The values of  $k_n$  are the linear least-squares intercepts of plots of the observed rate constant vs. total buffer concentration. The total buffer concentration was varied between  $10^{-2}$  and  $2 \times 10^{-1}$  M, with a minimum of five different concentrations being used to make each plot. The buffer plots were linear over this

(5) Fox, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* 1974, 96, 1436–49.

(6) Hogg, J. L.; Phillips, M. K.; Jergens, D. E. *J. Org. Chem.* 1977, 42, 2459–61.

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(9) Schowen, K. B. In "Transition States of Biochemical Processes"; Gandour, R. D., Schowen, R. L., Eds.; Plenum: New York, 1978; Chapter 6.

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(11) Alberty, J. In "Proton Transfer Reactions"; Caldin, E., Gold, V., Eds.; Wiley: New York, 1975; Chapter 9.

Table II. Values of  $k_n$  for the Water-Catalyzed Hydrolysis of 1-Acetyl-1,2,4-triazole in  $\text{H}_2\text{O}$ - $\text{D}_2\text{O}$  Mixtures of Atom Fraction of Deuterium  $n$  at  $25.00 \pm 0.05^\circ\text{C}$  Determined by Using Unbuffered HCl-DCl Solutions<sup>a</sup>

$n$	$10^6 k_n, \text{ s}^{-1}$	
	$\mu = 1.0 \text{ M}$	$\mu = 0.5 \text{ M}$
0.000	$1533 \pm 16$	$1814 \pm 24$
0.247	$1200 \pm 7$	$1417 \pm 20$
0.493	$916 \pm 7$	$1076 \pm 20$
0.740	$686 \pm 5$	$808 \pm 10$
0.986 <sup>c</sup>	$491 \pm 11$	$591 \pm 12$

<sup>a</sup> Determined by using  $10^{-3} \text{ M}$  HCl-DCl solutions with the ionic strength ( $\mu$ ) controlled with potassium chloride. Each value is the average of between three and nine runs, with the error limits being standard deviations. <sup>c</sup> Atom fraction of deuterium in "100%" deuterated solution as determined by Mr. Josef Nemeth.<sup>14</sup>

Table III. Values of  $k_n$  for the Water-Catalyzed Hydrolysis of 1-Acetyl-1,2,4-triazole in  $\text{H}_2\text{O}$ - $\text{D}_2\text{O}$  Mixtures of Atom Fraction of Deuterium  $n$  at  $25.00 \pm 0.05^\circ\text{C}$  Determined<sup>a</sup> by Engberts and Karzijn<sup>4</sup>

$n$	$10^6 k_n, \text{ s}^{-1}$	$n$	$10^6 k_n, \text{ s}^{-1}$
0.00	2090	0.70	1000
0.35	1540	1.00	688
0.50	1330		

<sup>a</sup> Determined at pH 3-5 (HCl). The ionic strength was not controlled.

concentration range. The ionic strength was maintained constant at 1 M with potassium chloride.

Table I gives the values of  $k_n$  and  $n$  used to make the plot of Figure 1. The solvent deuterium isotope effect determined by using this method was  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 3.18$ . Initial visual inspection of the proton inventory of Figure 1 reveals significant downward curvature similar to that seen in the previous study.<sup>4</sup> The secondary  $\beta$ -deuterium isotope effect determined under these conditions for deuteration of the acetyl group was  $k_{3\text{H}}/k_{3\text{D}} = 0.93 \pm 0.02$ .

Figure 1 also shows proton inventories for the hydrolysis of 1-acetyl-1,2,4-triazole determined in a manner similar to that used by Karzijn and Engberts<sup>4</sup> but with the ionic strength rigorously controlled. These inventories were determined by using  $10^{-3} \text{ M}$  HCl-DCl, with the ionic strength being controlled at 1.0 M (filled circles) and at 0.5 M (squares). Table II lists the values of  $k_n$  and  $n$  used to make these plots. The values of the solvent deuterium isotope effect determined by using this method were  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 3.13$  ( $\mu = 1.0 \text{ M}$ ) and  $3.07$  ( $\mu = 0.5 \text{ M}$ ).

### Discussion

The values of  $k_n$ , the rate constant for the water-catalyzed hydrolysis of 1-acetyl-1,2,4-triazole, determined in this study are clearly different than those reported by Karzijn and Engberts.<sup>4</sup> Table III lists the data previously reported for this compound. Two points are easily made which illustrate the differences in the data sets. First, the rate constants determined by Karzijn and Engberts in pure protium oxide and deuterium oxide are significantly larger than any of those determined in the present study under a variety of conditions. Second, the solvent deuterium isotope effect of  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 3.04$  is smaller than any of those determined in the present study.

Closer inspection of the data reveals an interesting trend, however. The rate constants decrease with increasing ionic strength. At 1.0 M ionic strength the values of  $k_n$  are consistent regardless of whether they were obtained in the experiment utilizing acetic acid-acetate buffers or in the

Table IV. Comparison of Values for  $k_{\text{H}_2\text{O}}$  for the Hydrolysis of 1-Acetyl-1,2,4-triazole Obtained under a Variety of Conditions

$10^4 k_{\text{H}_2\text{O}}, \text{ s}^{-1}$	conditions	ref
15	$\mu = 1.0 \text{ M}$ (KCl)	5
15.4	$\mu = 1.0 \text{ M}$ (KCl), extrapolation to zero buffer concentration	present study
15.3	$\mu = 1.0 \text{ M}$ (KCl), $10^{-3} \text{ M}$ HCl	present study
15.7	$\mu = 1.0 \text{ M}$ (KCl), $10^{-3} \text{ M}$ HCl	personal communication from J. B. F. N. Engberts
17.2	$\mu = 1.0 \text{ M}$ ( $(\text{CH}_3)_4\text{N}^+\text{Cl}^-$ )	5
18.3		12
20.9	ionic strength uncontrolled, $10^{-3} \text{ M}$ HCl	4
22.0	ionic strength uncontrolled, $10^{-3} \text{ M}$ HCl	present study

experiment utilizing  $10^{-3} \text{ M}$  HCl (DCl) solutions to control pH(D). We have collected the values of  $k_{\text{H}_2\text{O}}$  from the literature along with ours in Table IV. It is clear that under identical conditions of ionic strength control the values of  $k_{\text{H}_2\text{O}}$  are consistent. Thus, there is no doubt that the ionic strength influences these rate constants significantly.

We were, therefore, concerned that the ionic strength effect could alter the shape and, hence, the interpretation of the proton inventory. Recall that the isotope effect is only slightly dependent upon the ionic strength. Figure 1 collects the proton inventories obtained under four sets of conditions for the hydrolysis of 1-acetyl-1,2,4-triazole, three curves which merely reflect the different values of the ionic strength result. It then becomes necessary to ask the following question: "Is the same transition-state model consistent with all three proton inventories?"

Karzijn and Engberts interpreted their proton inventory in terms of the transition-state model (2) and found that eq 3 would satisfactorily reproduce their experimental

$$10^4 k_n = 20.9(1 - n + 0.43n)(1 - n + 0.87n)^2 \quad (3)$$

proton inventory.<sup>4</sup> The equation is the appropriate form of eq 2 for the transition-state model 2. It is of the form of eq 4 where  $\phi_a^*$  and  $\phi_b^*$  represent the isotopic fraction-

$$k_n = k_0(1 - n + n\phi_a^*)(1 - n + n\phi_b^*)^2 \quad (4)$$

ation factors for the indicated protons in the catalytic proton bridge transition state 2. This transition state is reasonable on the basis of the Brønsted  $\beta$  value of 0.36 for general-base catalysis of hydrolysis and the large negative entropy of activation ( $-36 \text{ eu}$ ).<sup>4,5</sup>

If we assume that  $\phi_b^* = (0.69)^\beta$  we can use the known Brønsted  $\beta$  value to calculate  $\phi_b^*$ . This value can be used with eq 4 along with the data collected at 1.0 M ionic strength to calculate a value for  $\phi_a^*$  and, thus, generate eq 5. Figure 2 shows that this equation which, within

$$10^4 k_n = 15.4(1 - n + 0.41n)(1 - n + 0.87n)^2 \quad (5)$$

experimental error, utilizes fractionation factors identical with those of Karzijn and Engberts does not generate enough curvature to be consistent with our experimental proton inventories at 1.0 M ionic strength. Thus, the traditional catalytic proton bridge transition state does not appear to be consistent with the proton inventory at  $\mu = 1.0 \text{ M}$ . If one does not consider the isotopic fractionation

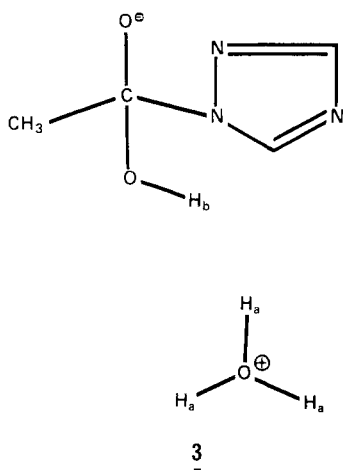
factor to be unity for the proton  $H_c$  (although this is the usual assumption), one might argue that **2** is a "four-proton" model. This would require the inclusion of another term in the general equation (eq 4) with a fractionation factor  $\phi_c^*$  for  $H_c$ . It is generally argued that the fractionation factor for such a proton will not differ significantly from unity, so this factor will not be considered further.<sup>9</sup>

It is also possible that one could generate more curvature by adding an additional term to eq 5 to take into account a possible differential medium effect for solvation differences between the reactant and transition state.<sup>11</sup> It does not appear that the present data lend themselves to ready interpretation in terms of such an effect, however. The addition of another term to eq 5 merely provides one more variable to be adjusted in fitting a model and does not appear warranted by the data available.

In general, more curvature will be induced in a proton inventory if the contributions of additional protons are included or if the contributions become more nearly equal. The latter model can be easily checked. It is easily shown that a "three-proton" model with three equal fractionation factors will reproduce our proton inventories at both ionic strengths ( $\mu = 1.0$  and  $0.5$  M). Thus, eq 6 with  $\phi_a^* = 0.69$

$$k_n = k_0(1 - n + n\phi_a^*)^3 \quad (6)$$

generates a line which is consistent with the proton inventories obtained in our study. Such a model could correspond to a very late transition state for formation of a tetrahedral intermediate as shown in **3**. The three

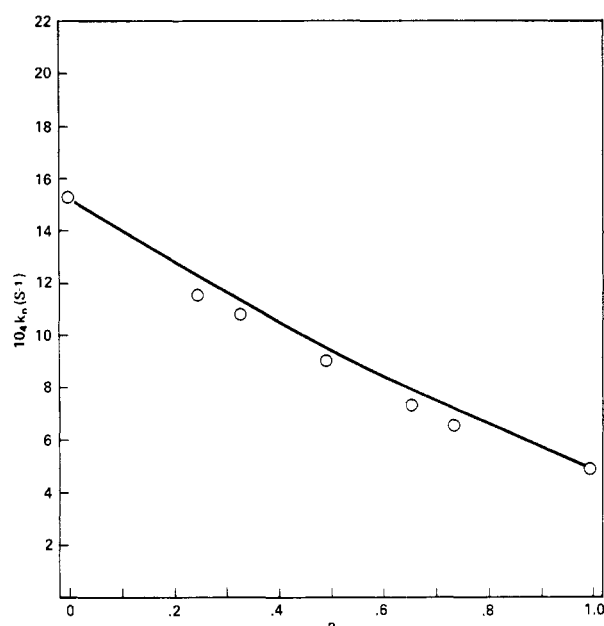


protons labeled  $H_a$  in this transition-state structure would be expected to have isotopic fractionation factors of 0.69 which is the value for a hydronium ion. However, one must now include a greater than unity fractionation factor for the gem-diol type proton  $H_b$  in this structure. Such protons have been shown to have fractionation factors of about 1.25.<sup>9</sup> Thus, eq 6 would really require an additional term of the form  $(1 - n + 1.25n)$  to be consistent with **3**. The inclusion of such a term would only diminish the curvature and serve to further emphasize the lack of consistency of **3** with the observed proton inventories. Such a late transition state also appears to be inconsistent with the Brønsted  $\beta$  value.

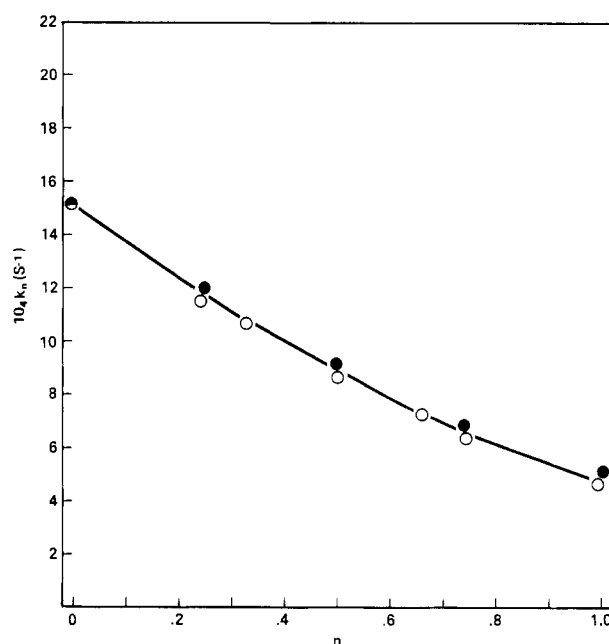
Although the quality of fit for a "four-proton" model is not dramatically different than the "three-proton" model, we would like to consider this transition-state model in detail. Equation 7 fits the experimental proton inventory

$$k_n = k_0(1 - n + n\phi_a^*)^4 \quad (7)$$

slightly better than the three-proton model as seen by the solid line of Figure 3. The quality of the data is not good



**Figure 2.** Comparison of the line generated by eq 5 with the experimental proton inventory determined at 1.0 M ionic strength by using buffers.<sup>1</sup> This is the line for the "catalytic proton bridge" transition state of **2**.



**Figure 3.** Comparison of the line generated by eq 7 with the experimental proton inventory determined at 1.0 M ionic strength by using buffers.<sup>1</sup> This line is consistent with a "four-proton" transition state such as those shown in **4** and **5**.

enough to make a statistical argument in favor of such a model, but we believe that a strong chemical argument can be made. A "four-proton" model with all four protons having fractionation factors of 0.75 generates the solid line of Figure 3. This model clearly duplicates the proton inventory very well. In fact, this model duplicates the proton inventory done at 0.5 M ionic strength as well. This implies that although the absolute values of the rate constants change with ionic strength, the curvature of the proton inventory is the same as that in our studies at different ionic strengths. The data of Table V show that the ratio of  $k_n(\mu = 0.5 \text{ M})$  to  $k_n(\mu = 1.0 \text{ M})$  is constant within experimental error. The "salt effect" appears to be constant as a function of  $n$  and does not affect deu-

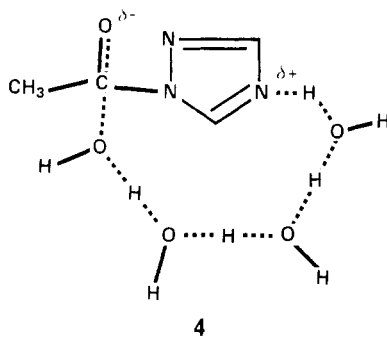
Table V. Ratio of  $k_n(\mu = 0.5 \text{ M})$  to  $k_n(\mu = 1.0 \text{ M})$  as a Function of  $n^a$ 

$n$	$k_n(\mu = 0.5)/k_n(\mu = 1.0)$	$n$	$k_n(\mu = 0.5)/k_n(\mu = 1.0)$
0.000	$1.18 \pm 0.02$	0.740	$1.18 \pm 0.02$
0.247	$1.18 \pm 0.02$	0.986	$1.20 \pm 0.04$
0.493	$1.17 \pm 0.02$		

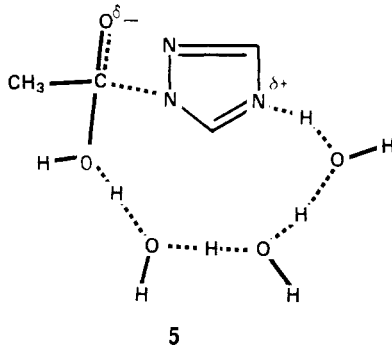
<sup>a</sup> Data taken from Table II.

terium oxide solutions differently than protium oxide solutions.

Thus, our proton inventories obtained under a variety of experimental conditions are all consistent with a "four-proton" transition-state model. Such a transition state could be envisioned as in 4. Such a transition state could be involved in either attack to form the tetrahedral intermediate or in breakdown of the tetrahedral intermediate as shown in 5. In 4 the attack of water on the



carbonyl carbon is assisted in a 12-membered-ring transition state by the triazole ring nitrogen. In 5 the loss of



triazole from the tetrahedral intermediate is assisted via protonation at N-4 through the chain of water molecules. Protonation is expected to occur at N-4 on the basis of the arguments of Jencks and Fox.<sup>5</sup> Both transition states involving four water molecules are feasible on the basis of space-filling models whereas a transition state involving three water molecules is hard to accommodate. Komiyama and Bender have recently proposed a similar transition-state structure for the water-catalyzed hydrolysis of *p*-nitrofluoroacetanilide.<sup>13</sup>

The suggested transition state is different from that proposed earlier by us for the water-catalyzed hydrolysis of the 1-acetyl-1,2,4-triazolium ion.<sup>6,7</sup> However, the  $pK_a$  of 10.3 for 1,2,4-triazole could explain the requirement for pro-

tonation of the leaving group as in 5.<sup>5</sup> Jencks has pointed out that "triazole is not as good a leaving group as might be expected from the  $pK_a$  of triazolium ion because the intermediate product of the reaction is the isomer of 1,2,4-triazole with the proton on the 4-position, which is tenfold less stable than the 1-protonated isomer". Thus, it is reasonable to expect a transition state such as that shown in 5.

## Conclusion

The proton inventory investigations presented here are consistent with a "four-proton" transition-state structure for the water-catalyzed hydrolysis of 1-acetyl-1,2,4-triazole such as that shown in 4 and 5. Although our data are not good enough to absolutely rule out a "three-proton" transition-state structure proposed earlier (or, for that matter, to exclude possible transition states involving more than four protons), we feel the evidence favors the "four-proton" model. We have shown that the proton inventory is independent of ionic strength in the region 0.5–1.0 M and of the method of determination provided the ionic strength is controlled. Perhaps, in the absence of any ionic strength control the transition-state structure may be slightly different due to differences in the water structure. This could explain the differences between our results and those published earlier.<sup>4</sup> Additional experiments designed to probe this question are currently planned or underway in our laboratories and in Engberts' laboratories.

## Experimental Section

**Materials.** 1-Acetyl-1,2,4-triazole was prepared by a slightly modified version of a literature procedure and had a melting point of 40–41 °C (lit.<sup>12</sup> mp 40–42 °C). 1-Acetyl-*d*<sub>3</sub>-1,2,4-triazole was prepared in like fashion by using acetyl-*d*<sub>3</sub> chloride (Aldrich) and had a melting point of 38–40 °C. Analysis indicated 92% deuteration of the acetyl group.<sup>14</sup> Deuterium oxide (Aldrich, 99.8 atom % deuterium) was glass distilled before use as was the protium oxide. Acetonitrile (Fisher) was distilled from calcium hydride and stored under nitrogen. Deuterium chloride (20% solution in D<sub>2</sub>O; Aldrich) was used as obtained. Potassium chloride was oven dried before use.

**Buffer Solutions.** Stock buffer solutions (0.2 M total buffer) were prepared by dissolving equimolar quantities of potassium acetate and acetic acid in protium oxide and deuterium oxide. The ionic strength of these solutions was adjusted to 1 M with potassium chloride. Less concentrated buffer solutions were prepared by dilution with 1 M potassium chloride solution. The appropriate volume of these solutions was mixed in the cuvette prior to each run for H<sub>2</sub>O–D<sub>2</sub>O mixtures.

**Kinetics.** The hydrolysis of 1-acetyl-1,2,4-triazole was monitored by observing the decrease in absorbance at 222 nm with a Cary 118C ultraviolet–visible spectrophotometer equipped with a constant-temperature cell compartment. The temperature was controlled at 25.00 ± 0.05 °C.

Reactions were initiated by injecting 25 μL of a solution which was 6 × 10<sup>−3</sup> M 1-acetyl-1,2,4-triazole in acetonitrile into 3.00 mL of the appropriate buffer solution or HCl (DCl) solution at the required ionic strength. Reactions were followed for 3–4 half-lives, and infinity absorbances were taken at 10 half-lives. The pH(D) was measured after each run by using a Corning Model 130 pH meter. Rate constants were determined by using a nonlinear least-squares computer program. Plots of log ( $A_t - A_\infty$ ) vs. time were used in a confirmatory fashion.

**Registry No.** 1 (R = CH<sub>3</sub>), 15625-88-4; 1 (R = CD<sub>3</sub>), 74930-01-1.

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