Potential Energy Profile for Gas-Phase, Unimolecular Reactions of Ionized Acetic Acid and Its Enol. The Barrier to a 1,3-Hydrogen Migration

## Helmut Schwarz,* [1a,b] Dudley H. Williams,* [1b] and Chrysostomos Wesdemiotis [1a]

Contribution from the University Chemical Laboratory, Cambridge, United Kingdom, and the Department of Organic Chemistry, Technical University, D 1000 Berlin 12, West Germany. Received March 28, 1978

Abstract: The relatively slow unimolecular reactions undergone by ionized acetic acid (1) and its enol form (5) have been studied. Both 1 and 5 undergo loss of OH and H_2O. It is established that 5 undergoes a rate-determining 1,3-hydrogen shift to 1 prior to OH loss. This rate-determining reaction is accompanied by a primary deuterium isotope effect, and the subsequent dissociation then occurs with excess energy in the transition state (as established from the kinetic energy release accompanying dissociation). In contrast, 5 loses water directly to give ionized ketene. The experiments allow a potential energy profile for the unimolecular reactions of ionized acetic acid and its enol form to be constructed.

Introduction

Recent reviews[2] and earlier work[3] have summarized the information which may be obtained regarding the energetics of unimolecular, gas-phase reactions of organic ions by the study of metastable peaks. We outline only briefly therefore the principles which are relevant to the present study.

Metastable peaks arise when ions, generated in the gas phase in a mass spectrometer, decompose some 10^8 vibrations after they have been energized. The passage of such a long time (ca. 10^{-5} s) relative to the time scale for energy redistribution in a molecule (ca. 10^{-12} s) ensures that metastable peaks arise from decomposing ions which have little excess energy in the transition state. Primary deuterium isotope effects establish that these excess energies are comparable to, or less than, those occurring in solution reactions near to room temperature.[2b,3a] Additionally, the shapes of metastable peaks give a direct picture of the kinetic energy released during the unimolecular dissociation. Mutual repulsion of an ionic and neutral product (from the dissociation of an ion) produces a flat-topped or dished metastable peak (A) if the kinetic energy released (T)

(B)
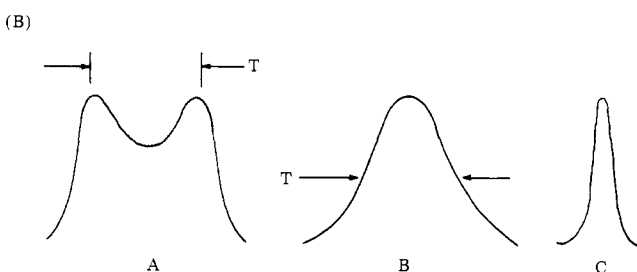
is essentially single valued (or not very different from this simple case). If a wide range of kinetic energies is released upon dissociation, then the metastable peak is broad (B), and clearly different from the narrow peaks (C) which result when the kinetic energy release is very small or negligible. When a wide range of kinetic energies is released it is conventional to quote the kinetic energy release T from the width at half-height (B).
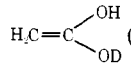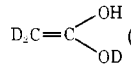
Until recently, the chemical reasons for the difference in peak shapes typified by B and C were not understood. However, it has now been shown[2b] that if the gas-phase ion undergoes a rate-determining isomerization prior to a more energetically facile dissociation of the rearranged form, excess energy will be present in the transition state for the dissociation step. Some of this excess energy may flow into the reaction coordinate as the transition state for dissociation is passed, with

the result that a relatively wide range of kinetic energies is released (B). In contrast, if the rearranged form (from which dissociation occurs directly) is produced by a route which requires less energy than its dissociation, then the direct dissociation produces a narrower metastable peak (e.g., C). The phenomenon of rate-determining isomerization appears to be a general cause of metastable peak broadening, and the principle involved should be further clarified by the application of the criterion in this paper.

Thus, a mass spectrometer is an excellent device for determining, through the study of metastable peaks, the most energetically facile unimolecular reaction(s) of a selected gas-phase ion. Moreover, through the measurement of appearance potentials (i.e., the minimum energy required from the electron beam to produce the metastable peak for the fragmentation concerned), the approxiate activation energy for the rate-determining step can be determined. Owing to inherent inaccuracies in the determination of appearance potentials, derived activation energies may be subject to errors of a few kilocalories per mole, but, as will be seen, the derived values are extremely useful.

The measurement of transition-state energies, as outlined above, in conjunction with heats of formation of reactants and products,[4] allows potential energy profiles to be constructed for unimolecular reactions of gas-phase ions of selected atomic composition.[2b] Such potential energy profiles may indicate which of a number of isomeric structures exist in potential wells. The conclusions may then be independently checked by examination of collisional activation (CA) mass spectra. In this technique, it is convenient to use a mass spectrometer in which the magnetic sector precedes the electric sector. It is then possible to select, by mass analysis, the ion of interest; its dissociations in the field-free region between the two sectors (again ca. 10^8 vibrations after its energization) can be followed by sweeping the electric sector voltage. With progressive reduction of the electric sector voltage, product ions arising by dissociation of the selected precursor ion via loss of increasing (neutral) masses are successively focused at the collector. The resulting spectrum is known as a mass-analyzed ion kinetic energy spectrum (MIKES).[5] It is an experiment which is easy to perform, and highly informative since it establishes the unimolecular chemistry of a selected ion when it has just enough energy to undergo the most favored reaction(s). If a collision gas is then introduced between the two sectors, then the unimolecular reactions which occur are normally of a greater variety. Many of the reactions are now so highly energetic and fast that isomerization before fragmentation is precluded—providing that there is a barrier to isomerization.

Table I. Competition between Hydroxyl Radical and Water Elimination from Ionized Acetic Acid (1), the Ionized Enol Form (5), and Deuterated Analogues[a,b]

| ion structure	neutral lost				
	·OH	·OD	H_2O	HDO	D_2O
H_3COOH (1)	92		8		
H_3COOD (1b)		91		9	
D_3COOH (1c)	95		5		
D_3COOD (1d)		95			5
$H_2C{=}C(OH)_2$ (5)[c]	32		68		
$H_2C{=}C(OD)_2$ (5a)		30			70
$D_2C{=}C(OH)_2$ (5b)[c]	31		69		
H,C=C<OH OD (5c)[c]	9	22		69	
D,C=C<OH OD (5d)[c]	8	21		71	

[a] Competition undergone in metastable transitions, with the total metastable ion current normalized to 100 units. The data are the average of at least three measurements, and were obtained using the MIKES technique.[5] [b] **5a, 5b, 5c,** and **5d** were generated by fragmentation of butyric-*4,4,4-d₃* acid-*O-d*, butyric-*2,2-d₂* acid, butyric acid-*O-d* (or butyric-*4,4,4-d₃* acid), and butyric-*2,2-d₂* acid-*O-d*, respectively. [c] Data for these compounds are in good agreement with those already published.[6]

Thus, the resulting (CA) spectrum is believed to be characteristic for each species that exists in a potential well.[2a,8]

Much useful information with regard to chemical bonding and the energy barriers to reaction can be obtained from this type of work. Additionally, the absence of solvent removes a variable whose influence often complicates the analysis. In general, the reactions which are observed could not be studied in solution since they would normally be circumvented by more favorable bimolecular reactions. This paper reports a detailed study of the reaction of gas-phase ionized acetic acid, and its enol form, and the potential energy profile which results from such a study. The principles applied are those outlined in the Introduction.

Discussion

If acetic acid is ionized, then metastable ions are observed corresponding to the competing losses of OH and H_2O in the ratio 92:8 (Table I). Thus, these two reactions are the energetically most facile from ionized acetic acid (1). As expected, the approximate activation energies determined from appearance potentials measurements are similar, and are 19 (H_2O loss) and 21 kcal mol⁻¹ (OH loss). These values are probably not reliable to better than ±6 kcal mol⁻¹, but, as will be seen later, the approximate values are extremely useful. Since CH_3COOD^+· (1b) loses specifically OD and HDO (Table I), then the unlabeled ionized acetic acid (1) undergoes no isomerization to its enol prior to OH or H_2O loss and (2) H_2O loss probably gives rise to ionized ketene (3).

H,CC<O+ OH → H,CC≡O+ + OH (2)

→ H,C=C=O⁺ + H,O (3)
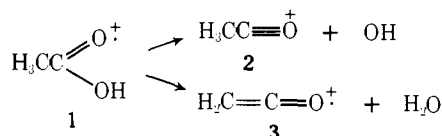
From the ionization potential of acetic acid, the heat of formation of **1** ($\Delta H_f \simeq 141$ kcal mol⁻¹) is available. The potential energy maxima associated with H_2O and OH losses from **1** are therefore available by adding the above activation energies for these processes (19 and 21 kcal mol⁻¹, respectively) to 141 kcal mol⁻¹.

Thus, the above measurements of approximate transition
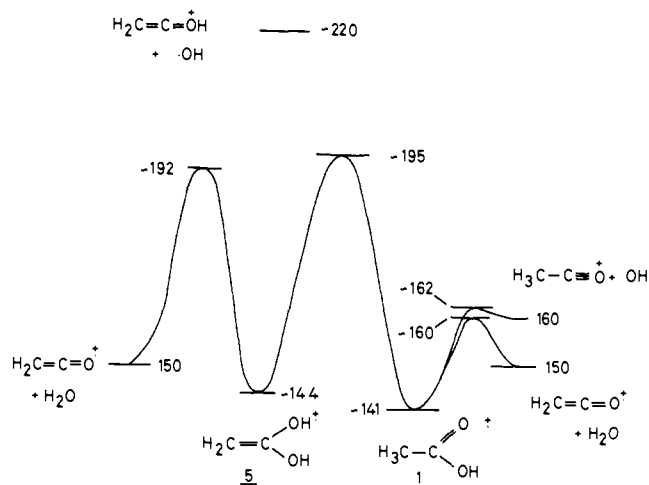
Figure 1. Potential energy profile (kcal mol⁻¹) for unimolecular reactions of ionized acetic acid (1) and its enol form (5).

state energies, in conjugation with thermochemical data for the heats of formation of the products,[4] give rise to the right-hand portion of the potential energy surface reproduced in Figure 1. Within the limits of accuracy of our measurements, the hydroxyl radical loss does not appear to have a significant reverse activation energy, in contrast to the water loss. The occurrence of a significant reverse activation energy in the loss of a stable neutral, but not in loss of a radical, is a situation that frequently (but not always) occurs.[3]

If the elimination of water from ionized acetic acid involves stretching of a C–H bond in the transition state for the rate-determining step (e.g., **4**), then ionized D_3CCOOH (1c) and D_3CCOOD (1d) should show discrimination against HDO and D_2O losses (relative to OH and OD losses, respectively) due to an isotope effect. This is the case, the relative rates of H_2O and HDO (or D_2O) losses being ca. 1.7:1 in metastable transitions [as measured by the ability of these processes to compete with OH or OD losses (Table I)].
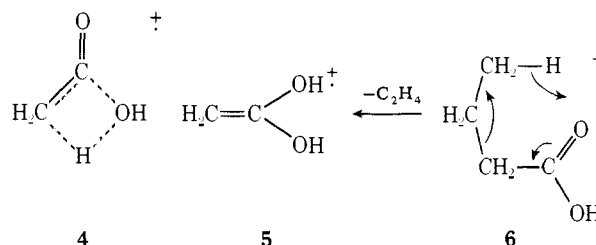
An earlier study[6] has established that the ionized enol (5) of acetic acid, generated, for example, by fragmentation of ionized butyric acid (6), exists in a potential well and that there is a considerable barrier to its conversion to **1**. This study[6] established that **5** loses OH and H_2O in the approximate ratio 30:70 (see also Table I) and that the H_2O loss is a specific 1,2-elimination to give ionized ketene (3), without prior isomerization to ionized acetic acid (1). This conclusion is confirmed in the present work, **5a**, for example, losing only D_2O (Table I). It was also concluded[6] that **5** loses OH via the ionized acetic acid configuration **1**. This conclusion is based on the preference for **5c** and **5d** to lose OD rather than OH (ratio ca. 2.5:1, Table I), reflecting a dominance of **5c → 1b** over **5c → 1e** (for example) due to a primary deuterium isotope effect (Scheme I).

All the data for the deuterated analogues given in Table I are consistent with this interpretation, and moreover demand that the isomerization of the ionized enol to the acetic acid form **1** must not be reversible prior to OH loss from **1**. Thus it must

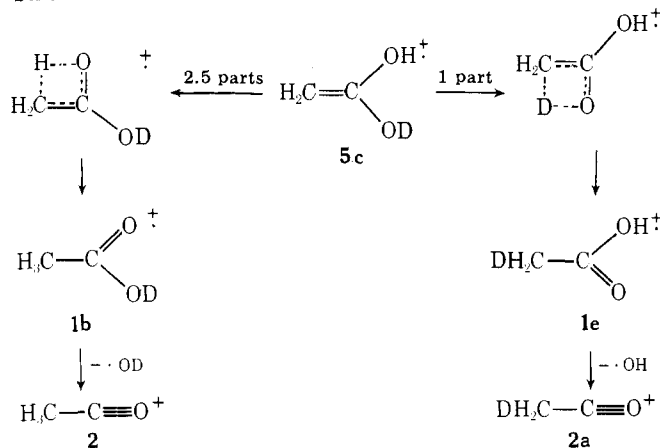**Table II.** Transition State Energies for OH and H_2O Losses from 1 and 5

	loss	
ion	OH	H_2O
$H_3CCOOH^+\cdot$ (1)	162 ± 6	160 ± 6
$H_2C=C(OH)_2^+\cdot$ (5)	195 ± 10	192 ± 10

Scheme I

be concluded that (1) the direct water loss from the enol form 5 is competitive with the 1,3-hydrogen shift given in Scheme I, and (2) ionized acetic acid produced by such a 1,3 shift will contain internal energy in excess of that required for dissociation to $H_3C\equiv O^+$ and $\cdot OH$. Two consequences which can be subjected to experimental test follow from the latter conclusion: (1) the total energy content for 5 → 1 must be greater than 162 kcal mol^{-1} (Figure 1) and (2) the metastable peak for $\cdot OH$ loss from 1 must be broader occurring through the sequence 5 → 1 → $H_3CC\equiv O^+$ than through the direct process 1 → $H_3CC\equiv O^+$. The latter prediction follows from the conclusion[7] that a rate-determining isomerization prior to dissociation allows excess energy to flow into the reaction coordinate for dissociation thus increasing the average kinetic energy released in dissociation.

Our experimental results have confirmed the above two predictions. The transition state energies for OH and H_2O losses from 1 and 5 (as measured from appearance potentials) are summarized in Table II.

The data for 5 are incorporated in the potential energy profile given in Figure 1. The heat of formation of 5 ($\Delta H_f \simeq$ 144 kcal mol^{-1}) is derived on the assumption that its production from ionized butyric acid does not involve a reverse activation energy i.e., $\Delta H_f \simeq$ 144 kcal mol^{-1} corresponds to the appearance potential of 5 from ionized butyric acid. This seems likely to be a good approximation since the reaction 6 → 5 can be formulated as a symmetry-allowed process proceding through a relatively strain-free six-membered transition state. Consistent with our approximation is the observation that C_2H_4 loss from ionized 6 occurs with only a very small average release of kinetic energy (0.3 kcal mol^{-1}). If ΔH_f (5) is significantly in error then the quoted value should be too high.

The average kinetic energy releases for the relevant hydroxyl radical losses are given in Table III; those for H_2O losses are also included.

The data are in accord with the presence of excess energy in the transition state for the dissociation 1 → $H_3CC\equiv O^+$ when 1 is formed from 5. Although it is established from the deuterium labeling data (Table I) that 1 and 5 both lose water directly to give ionized ketene, it is noteworthy that the reaction from the latter releases, on average, much more kinetic energy (Table III). This is in accord with the much larger reverse

Table III. Kinetic Energy Releases for OH and H_2O Losses from 1 and 5[a]

	loss	
ion	OH	H_2O
$H_3CCOOH^+\cdot$ (1)	0.3	0.7
$H_2C=C(OH)_2^+\cdot$ (5)	2.2	6.1

[a] Values are in kcal mol^{-1}, and represent the average of six measurements in the first field-free region of a double-focusing mass spectrometer.

Table IV. CA Spectra of $C_2H_2O^+\cdot$ (*m/e* 42)[a]

CA fragment	*m/e* 42 from 1	*m/e* 42 from 5[b]	*m/e* 42 from diketene
41	61	67	66
40	7.0	6.6	6.6
29	5.7	4.8	5.2
28	6.2	5.1	5.7
14	13	12	12
13	4.9	4.8	4.7

[a] The relative abundances are normalized to $\sum_{13}$ = 100%. [b] 1on 5 was produced by fragmentation of *n*-butyric acid (6).

activation energy ($\sim$42 kcal mol^{-1}) associated with H_2O loss from 5 (Figure 1). However, the broad metastable peak for this process is still approximately Gaussian, suggesting that water loss from 5 may not be a highly synchronous process. Thus, for example, it is possible that this process may involve $\cdot CH_2COO^+H_2$ as a discrete intermediate; ΔH_f for this possible intermediate is estimated[14] as 147 kcal mol^{-1}. Its dissociation to $H_2C=C=O^+\cdot$ and H_2O would therefore be only slightly endoergic (see Figure 1), and its production rate determining from 5 via a 1,3-hydrogen shift. The dissociation of this possible intermediate would therefore occur with excess energy in the transition state and account for the occurrence of a broad metastable peak (Table III).

Further support for the structures of the products of dissociation of 1 and 5 by H_2O loss is derived from the results of collisional activation (CA) mass spectra.[2a,8] Thus CA mass spectra of ketene ions produced by fragmentation of molecular ions of diketene were compared with CA spectra of the ions produced by loss of H_2O from both 1 and 5 (Table IV).

The CA spectra are the same within experimental error. In particular, no *m/e* 25 ($HC=C^+$) fragment is produced upon collisional activation of ions produced by water loss from 5, suggesting that no $HC\equiv COH^+\cdot$ ions are produced from 5 even in source reactions.

Several interesting features are evident from the energy profile produced in Figure 1.

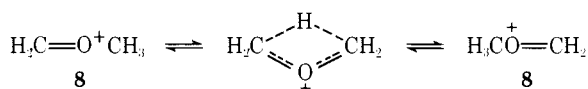(1) Direct OH loss from 5 would produce the hydroxyvinylium ion which is a canonical form of protonated ketene (7).

$$H_2C=C(OH)_2^+ \cdot \rightarrow H_2C=C=^+OH + \cdot OH$$
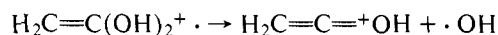
The heat of formation of 7 has been estimated using the heat of formation of the vinylium cation, and Franklin's group equivalents[10] in conjunction with increments given for α-substituted vinyl cations.[11] We obtain $\Delta H_f(7) + \Delta H_f(OH) \simeq$ 220 kcal mol^{-1}. Thus the activation energy for this reaction, which is not observed, should be ca. 80 kcal mol^{-1}. Since a 1,3-H shift in 5 (or H_2O loss from 5) is energetically preferable ($E_a \simeq$ 51 kcal mol^{-1}) it occurs and OH loss is then facile from the resulting structure 1. Evidently, when dissociation of 1 occurs with excess energy, H_2O loss is unable to complete significantly with OH loss, as might be expected since H_2O loss requires an ordered transition state.

(2) If H_2O is added to ionized ketene through the reverse of the pathways leading to its elimination from **1** and **5**, it is clear that addition across the C=C bond has a much lower activation energy than addition across the C=O bond.

(3) The activation energy for the conversion of the ionized enol **5** to ionized acetic acid is relatively large (~51 kcal mol^{-1}). An estimate of the heat of formation of the intermediate which should be involved if **5** → **1** went via two successive 1,2-H shifts, viz., via $H_2C^+CH(OH)O\cdot$, ΔH_f(est) 205 kcal mol^{-1}, indicates that this pathway is feasible, but appears unlikely on energetic grounds. Thus, owing to the relatively large barriers to 1,3-H shifts, ionized enols are relatively stable species in the gas phase. From recent ab initio calculations[12] it has been deduced that the barrier to the conversion of an isolated molecule of vinyl alcohol to acetaldehyde is ca. 85 kcal mol^{-1}. It might reasonably be expected that barriers to 1,3 shifts would be somewhat lower in the open-shell [as opposed to the closed-shell (even-electron) system studied theoretically] ionized enol studied in the present work. A further closed-shell system which has been studied is the degenerate 1,3-hydrogen shift in **8**; it was concluded[7] that the energy requirements of

$$H_2C=O^+CH_3 \rightleftharpoons H_2C{\overset{H}{\underset{O^+}{\diagdown\diagup}}}CH_2 \rightleftharpoons H_3CO^+=CH_2$$
$$\quad\;\;\textbf{8} \qquad\qquad\qquad\qquad\qquad\qquad\qquad \textbf{8}$$

this reaction were ≥58 and ≤83 kcal mol^{-1}.

Experimental Section

The MIKES and CA spectra were recorded on a Varian MAT 311A instrument (reverse Nier-Johnson geometry), at an ionization energy of 70 eV, emission current of 20 mA, and an ion source temperature of 200 °C; the collision gas (for the CA spectra) was air.

Ionization efficiency curves were obtained on both Varian MAT 711 and AEI MS 902 mass spectrometers, and appearance potentials derived by application of the semilogarithmic plot method.[13] The CD$_3$-labeled acetic acid was commercially available, and partially deuterated butyric acid (the precursor of labeled analogues of **5**) was synthesized by unexceptional methods. The H/D exchange of car-boxylic acid protons was carried out in the inlet system of the mass spectrometer.

References and Notes

(1) (a) Technical University Berlin; (b) University Chemical Laboratory, Cambridge.
(2) (a) K. Levsen and H. Schwarz, *Angew. Chem.*, **88**, 589 (1976); *Angew. Chem., Int. Ed. Engl.*, **15**, 509 (1976); (b) D. H. Williams, *Acc. Chem. Res.*, **10**, 280 (1977).
(3) (a) D. H. Williams and I. Howe, "Principles of Organic Mass Spectrometry", McGraw-Hill, New York, N.Y., 1972; (b) R. G. Cooks, J. H. Beynon, R. M. Caprioli, and G. R. Lester, "Metastable Ions", Elsevier, Amsterdam, 1973; (c) J. L. Holmes and F. M. Benoit in "Mass Spectrometry, MTP International Review of Science", A. Maccoll, Ed., Butterworths, London, 1973.
(4) H. M. Rosenstock, K. Draxl, B. W. Steiner, and J. T. Herron, "Energetics of Gaseous Ions", National Bureau of Standards, Washington, D.C., 1977.
(5) (a) J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger, and T. Y. Ridley, *Anal. Chem.*, **45**, 1023A (1973); (b) U. P. Schlunegger, *Angew. Chem., Int. Ed. Engl.*, **14**, 679 (1975); (c) J. H. Beynon and R. G. Cooks in ref 3c.
(6) K. Levsen and H. Schwarz, *J. Chem. Soc., Perkin Trans. 2*, 1231 (1976).
(7) G. Hvistendahl and D. H. Williams, *J. Am. Chem. Soc.*, **97**, 3097 (1975).
(8) (a) W. F. Haddon and F. W. McLafferty, *J. Am. Chem. Soc.*, **90**, 4745 (1968); (b) K. R. Jennings, *Int. J. Mass Spectrom. Ion Phys.*, **1**, 227 (1968); (c) F. W. McLafferty, R. Kornfeld, W. F. Haddon, K. Levsen, I. Sakai, P. F. Bente III, S.-C. Tsai, and H. D. R. Schuddemage, *J. Am. Chem. Soc.*, **95**, 3886 (1973).
(9) F. P. Lossing, *Can. J. Chem.*, **49**, 357 (1971).
(10) J. L. Franklin, *Ind. Eng. Chem.*, **41**, 1070 (1949).
(11) Y. Apeloig, P. v. R. Schleyer, and J. A. Pople, *J. Am. Chem. Soc.*, **99**, 1291 (1977).
(12) W. T. Bouma, D. Poppinger, and L. Radom, *J. Am. Chem. Soc.*, **99**, 6443 (1977).
(13) F. P. Lossing, A. W. Tickner, and W. A. Bryce, *J. Chem. Phys.*, **19**, 1254 (1951).
(14) ΔH_f(CH$_3$COO$^+$H$_2$) has been reported (F. M. Benoit, A. G. Harrison, and F. P. Lossing, *Org. Mass Spectrom.*, **12**, 78 (1977); F. M. Benoit and A. G. Harrison, *J. Am. Chem. Soc.*, **99**, 3980 (1977)); this value, in conjunction with D(H–CH$_2$CO$_2$H), gives ΔH_f($\cdot$CH$_2$COO$^+$H$_2$) = 147 kcal mol^{-1}.

Lactim–Lactam Tautomeric Equilibria of 2-Hydroxypyridines. 1. Cation Binding, Dimerization, and Interconversion Mechanism in Aprotic Solvents. A Spectroscopic and Temperature-Jump Kinetic Study

O. Bensaude, M. Chevrier, and J. E. Dubois*

Contribution from the Institut de Topologie et de Dynamique des Systèmes de l'Université Paris VII, associé au C.N.R.S., 1, rue Guy de la Brosse, 75005 Paris, France. Received March 20, 1978

Abstract: When the temperature of an appropriate 2-hydroxypyridine solution in a polar aprotic solvent is raised, the lactam tautomer content increases with a reciprocal relaxation time proportional to the pyridine concentration. Therefore, the tautomeric interconversion is supposed to occur through the intermediate dimerization of the lactam and the lactim tautomers. The dimerization step is rate encounter controlled in agreement with previous works by ultrasonic attenuation. The sodium salt, added to ensure the electrical conductance of the media, decreases the relaxation time at constant substrate concentration. Indeed, it is shown by infrared spectroscopy that the binding of the sodium ion to the carbonyl group of the lactam tautomer inhibits the dimerization, thereby explaining the kinetic results. It is also shown, by ultraviolet spectroscopy, that cation binding strongly favors the lactam tautomer; this result may cast a new light on the theory of spontaneous mutagenesis.

Understanding the tautomerism of nitrogen heterocycles is of great importance in biochemistry. Indeed, tautomeric systems are often present in enzyme active sites as histidine residues or as pyridoxal phosphate coenzyme (vitamin B$_6$) and might contribute to the catalytic steps occurring there. The theory of spontaneous mutagenesis is also relevant to the tautomerism of nucleic acid bases.

In aqueous solutions, tautomeric interconversions are fast