of flotation; an aqueous potassium iodide solution was employed for this purpose.

The intensity data of all 4346 reflections with $2\theta \leq 140°$ were collected on the CAD-4 automatic diffractometer; Ni-filtered Cu K$\bar{\alpha}$ radiation (λ = 1.5418 Å) was employed at 22 °C. The data were obtained by $\theta - 2\theta$ scan techniques using variable scan width of $(1.0 + 0.1 \tan \theta)°$. The receiving aperture had a variable width of $(4.0 + 0.86 \tan \theta)$ mm, a height of 6 mm, and was at a distance of 173 mm from the crystal. A reflection was scanned for a maximum time of 50 s; two-thirds of this time was used to measure the peak intensity, and one-sixth of this time was spent on scanning each of the left and right background. A monitor reflection intensity was checked after every 25 measurements. Three orientation control reflections were centered after every 100 reflections. In the event that a change occurred in the orientation of more than 0.1° for any angle, a new orientation matrix was automatically obtained. Of the total reflections, 893 were considered indistinguishable from background, having $I < 2\sigma(I)$, where $I = P - 2(RB + LB)$ peak count, RB being the right background and LB being the left background. Lorentz and polarization corrections were applied to the intensity data, but no absorption corrections were made.

The program MULTAN[15] was used to solve the structure by direct methods. All non-hydrogen atoms were located from the E map calculated with 250 reflections with largest E values ($E \leq 1.5$). The structure was refined using a block-diagonal least-squares program[16] employing isotropic thermal parameters, to an R index of 0.160 ($R = \sum (|kF_o| - |F_c|) / \sum |kF_o|$). In the next stage, all the atoms were given anisotropic thermal parameters, and the structure was further refined to an R value of 0.100. A difference Fourier map calculated at this stage revealed all the hydrogen atom positions. The hydrogen atoms were assigned isotropic temperature factors and refined. The refinement was terminated when the maximum parameter shift was less than two-thirds of the corresponding standard deviation.

In all least-squares cycles, the quantity $\sum w_F(|kF_o| - |F_c|)^2$ was minimized, where $w_F = 1/\sigma_F 2$, and σ_F was obtained from the intensity statistics.[17] The scattering factors for carbon and oxygen atoms were taken from the International Tables for X-ray Crystallography,[18] and those for the hydrogen atoms were taken from the paper by Stewart and co-workers.[19] The final R index for all 4346 reflections was 0.056. The final difference Fourier map was featureless with maximum peak height of 0.11 e Å^{-3}.

Acknowledgment. Financial support of our study by The Air Force Office of Scientific Research (Grant No. AFOSR-84-0085), The Robert A. Welch Foundation (Grant B-963), The North Texas State University Faculty Research Committee, and the Faculty Research Fund, University of Oklahoma Research Council is gratefully acknowledged. The X-ray crystallographic structure determination of **9** was supported in part by a grant from the DHHS, National Cancer Institute, CA17562 (to D. van der Helm); we also thank the University of Oklahoma Computing Center for providing computing facilities and service in this connection.

Registry No. **3**, 40156-12-5; **4**, 90991-04-1; **5**, 90991-05-2; **7**, 90991-06-3; **8**, 90991-07-4; **9**, 90991-08-5; $Fe(CO)_5$, 13463-40-6.

Supplementary Material Available: Stereoviews of the single molecule of **9** and of the molecular packing of **9**, a listing of atomic parameters, bond angles, and observed and calculated structure factors for **9** (24 pages). Ordering information is given on any current masthead page.

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Mechanism of Hydrolysis and Alcoholysis of 2-Ethoxy-*N*-vinylpyrrolidiniminium Tetrafluoroborate[1]

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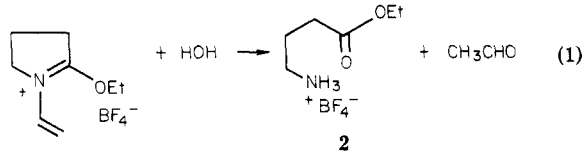
N-Vinyl-2-ethoxypyrrolidiniminium tetrafluoroborate, **1**, undergoes rapid hydrolysis to give acetaldehyde and ethyl 2-aminobutyrate, **2**. Imidate **1** reacts with methanol or ethanol, however, to give the *N*-(1-alkoxyethyl)-2-alkoxypyrrolidiniminium tetrafluoroborate **7** or **9**, respectively. Both hydrolysis and alcoholysis appear to be pseudo first order and the mechanism of each can be explained by initial formation of an "enamine-like" intermediate. The mechanism of both reactions is presented.

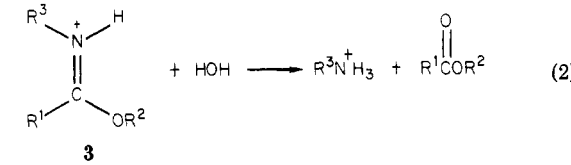
We have recently reported the preparation of a new imidate, *N*-vinyl-2-ethoxypyrrolidiniminium tetrafluoroborate, **1**, which undergoes remarkably facile hydrolysis under neutral conditions to give ethyl 4-aminobutyrate, **2**, and acetaldehyde, as shown in reaction 1.[2] This is



(1)

1 **2**

similar to the behavior of the related acyclic imidates **3** which undergo hydrolysis to give an amine and the corresponding ester. Such hydrolysis is normally slow except



(2)

3

under acidic conditions[3] and stands in contrast to the

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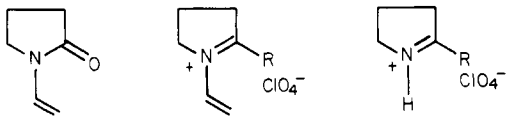
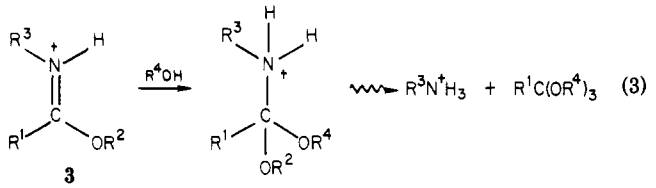
hydrolysis of 1 which proceeds to completion at neutral pH in under 30 min. The ability of the vinyl group to function as a latent aldehyde moiety finds precedent in the chemistry of lactams and imines. *N*-Vinyl-2-pyrrolidinone, 4, can be hydrolyzed to 2-pyrrolidinone and acetaldehyde but requires heating in 10% sulfuric acid.[4] *N*-Vinyl-2-alkylpyrrolidiniminim perchlorate 5 can also be hydrolyzed to 2-alkylpyrrolidiniminium perchlorate 6 and acetaldehyde but only under strongly acidic conditions.[5]



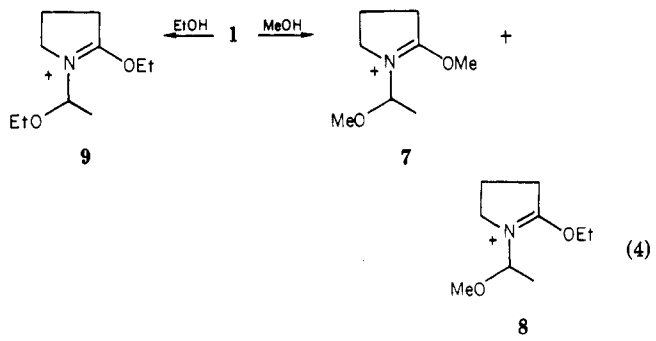
4 5 6

Imidate 3 has been shown to react with alcohols to give an amine and the ortho ester, as shown in reaction 3.[3a,6]



3 (3)

Although slow at ambient temperatures, the use of heat or excess alcohol accelerates reaction 3.[3a,6] Rather than forming the ortho ester analogue, via C–N bond cleavage, imidate 1 exhibited modified reactivity to give an *N*-(1-alkoxyethyl) imidate. Reaction with ethanol, for example, gave *N*-(1-ethoxyethyl)-2-ethoxypyrrolidiniminium tetrafluoroborate, 9, as shown in reaction 4. Likewise, reaction



9 7 8 (4)

with methanol gave a 3:1 mixture of *N*-(1-methoxyethyl)-2-methoxypyrrolidiniminium tetrafluoroborate, 7, and *N*-(1-methoxyethyl)-2-ethoxypyrrolidiniminium tetrafluoroborate, 8.[2]

The behavior of 1 toward hydrolysis and alcoholysis can be explained by intermediates which possess considerable *enamine character* and the "anomalous" reactions of 1 when compared to 3 represent an unique mixture of enamine and imidate chemistry. Further study has offered evidence for the presence of these key enamine-like intermediates and suggested a mechanism for the hydrolysis and alcoholysis of 1.

Synthesis and Reactions

Reaction of commercially available 4 with triethyloxonium tetrafluoroborate gave 1 as a crystalline solid in 72% isolated yield.[7] The hygroscopic nature of 1 was not surprising, but isolation of a sample of 1 after exposure to moist air indicated that a reaction had occurred. Subsequent dissolution of 1 in 100 equiv of water (neat, 25 °C, 20 h) followed by removal of water in vacuo gave ethyl 4-aminobutyrate tetrafluoroborate, 2, in 85% yield. The water which had been removed was treated with an ethanolic solution of 2,4-dinitrophenylhydrazine and sulfuric acid and yielded crystals of the 2,4-dinitrophenylhydrazone derivative of acetaldehyde. This confirmed that the vinyl group of 1 had been lost as acetaldehyde. Hydrolysis of 1 occurred with as little as 1 equiv of water although it appeared that about 4 equiv were required for complete and rapid conversion to 2. The rate of hydrolysis appeared to be slightly, but not significantly, faster with a large excess of water.

In addition to facile hydrolysis, reaction of 1 with 100 equiv of ethanol (neat, 25 °C, 20 h) and removal of excess ethanol, in vacuo, gave 9 in 86% yield, as a crystalline solid. Reaction of 1 with 100 equiv of methanol (neat, 25 °C, 20 h), however, gave a 3:1 mixture of 7 and 8, respectively, upon isolation. Imidate 8 was slowly converted to 7 over a period of 50 h but the initial 3:1 mixture was established within 30 min. Reaction of 1 with increasing amounts of methanol (up to 500 equiv) for 20 h indicated that the ratio of 7:8 changed only slightly. It appeared that formation of the mixture of 7:8 was relatively independent of the concentration of the alcohol.

Proton NMR was the best method to study the kinetics of hydrolysis and alcoholysis of 1. These studies were carried out in deuterium oxide or methanol-d_4, at 60 MHz, with a probe temperature of 35 °C. For both hydrolysis and alcoholysis, infrared and ultraviolet spectroscopy were unsuitable since no significant changes were observed during the course of the reactions. Loss of the vinyl signal and appearance of signals due to products were clearly visible in the NMR spectrum and was ideal for our study.

Results and Discussion

By ^{1}H NMR, loss of the vinyl protons at 6.82–7.32 ppm, appearance of an aldehyde proton at 9.5 ppm, and appearance followed by slow disappearance of a proton at 8.39 ppm were clearly discernable during the hydrolysis of 1, in D_2O. The location of this latter signal closely corresponds to the chemical shift noted for H_α of iminium salts such as 10, reported to be 8.3–8.4 ppm.[8] Imidate 3

10 13

was known to suffer addition of water across the C=N

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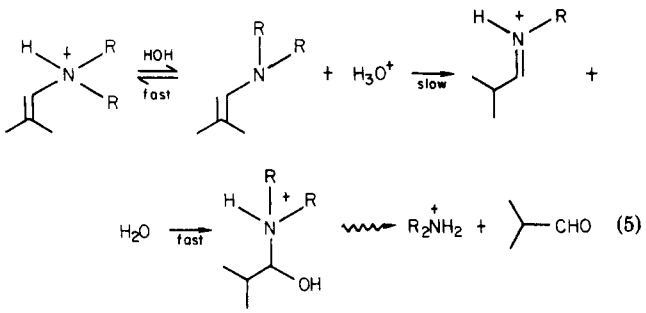
bond, as in reaction 3,[3a,6] and similar addition to 1 would give **12a** via the initial adduct 11. The ^1H NMR signal for H_a of enamine 13 was known to appear at 6.1 ppm,[9] and we assume a similar chemical shift for H_a of **12a**. It seems clear that the signal at 8.39 ppm is not due to **12a** but rather to the iminium salt **14a**. The "enamine" intermediate **12a** must, however, be an intermediate if 1 exhibits behavior similar to 3. This can be explained by initial formation of **12a** but slow transformation to **14a** during the course of the reaction. Indeed, this was found to be the case.

Addition of an alcohol to imidate 3 was known to be analogous to the addition of water and an intermediate such as 15 was anticipated, via **16a**. In the methanolysis reaction of 1, however, the signal at 8.39 ppm was clearly absent. This absence and the fact that addition of water to 3 was known to be fast led us to the conclusion that the vinyl signal at 6.82–7.32 ppm did not belong to 1. In fact, the initial addition of water or alcohol occurred too fast for observation in the NMR time scale and the ^1H NMR signals observed at 6.82–7.32 ppm were due to **12a** or **17a**, respectively. During hydrolysis slow transformation of **12a** to **14a** occurs prior to conversion to the observed products, acetaldehyde and 2. Methanolysis of 1 likewise gave **16a** and thereby, **17a**, which we observed at 6.82–7.32 ppm. Since we did not observe a signal at 8.39 ppm, **17a** did not undergo transformation to iminium salt 15 in significant concentrations and is the key intermediate for conversion to the observed products 7/8 or 9.

A striking similarity was noted in the hydrolysis of 1 and that of enamines.[10a,11] Reaction 5 shows the proposed



(5)

mechanism for hydrolysis of enamines[11] via addition of water to the intermediate iminium salt.[12] The solvent has a marked effect on the proportions of iminium salt/enamine species.[8a,10] In reactions of 1 the exclusive preference for enamine **17a**, in methanol, is contrasted with initial formation of enamine **12a** and slow conversion to **14a** in water. In part this is due to the greater ionizing and solvating power of water when compared to methanol. It is possible that 15 is an intermediate but reacts too fast for observation via NMR. Alternatively, **17a** may be the preferred intermediate but reacts too quickly to allow significant concentrations of 15 to accumulate. The conclusion that hydrolysis and alcoholysis of 1 follow a pathway analogous to enamines was inescapable but we sought evidence for the enamine/iminium salt equilibration in *both* reactions. We therefore allowed 1 to react with D_2O or methanol-d_4 in the solvent acetone-d_6. The effect of this solvent on the enamine/iminium salt concentration was clear since both deuterolysis and d_4 methanolysis exhibited an intermediate with an identical chemical shift of 8.7 ppm, 0.3 ppm downfield of the signal observed for reaction of 1, in neat D_2O. As expected, both reactions were much slower in acetone-d_6 than in the neat solvents but the loss of the vinyl group in the hydrolysis reaction was faster in acetone-d_6 than in neat water. The appearance of an intermediate in acetone-d_6 but not in neat methanol-d_4 can be explained by the rate of each reaction. In neat methanol the reaction is complete in about 1 h but requires 4 days in the acetone solution. This significant reduction in the rate at which **17** is lost allows a small amount of 15 to accumulate for observation in the NMR. Our results are consistent with the presence of iminium salts **14a** and 15 as intermediates for hydrolysis and methanolysis, respectively, in acetone-d_6, presumably via "enamines" **12a** and **17a**. If the mechanisms of reaction are the same in neat water or methanol as in the acetone solution, then the enamine-like intermediate is common to both reactions. These results were compelling evidence for initial fast addition of water or methanol to 1 and for the presence of 12, 14, and 17 as intermediates.

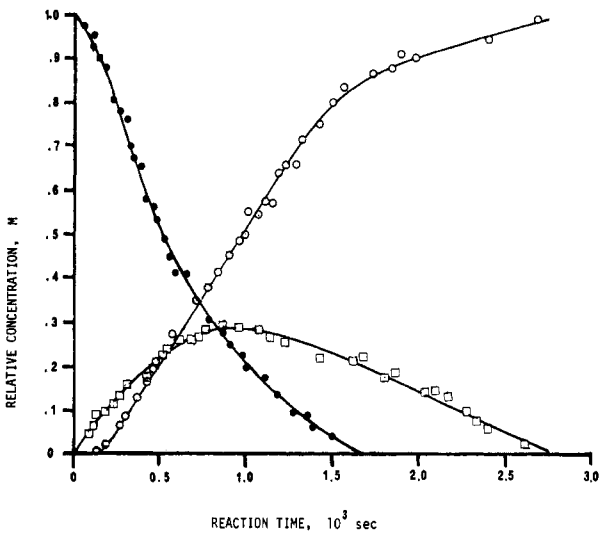


Figure 1. Plot of relative concentration of reaction products from a 1.0 M solution of 1 in D_2O, as determined by ^1H NMR: (●) [**12a**] based on signal at 6.82–7.32 ppm; (○) [CH_3CHO] based on signal at 9.5 ppm; (□) [**14a**] based on signal at 8.39 ppm.

If hydrolysis and alcoholysis proceed via similar mechanisms to give an initial enamine structure, **12a** or **17a**, the kinetics observed for loss of the vinyl signals in the NMR should also be similar. We therefore examined the rate of both hydrolysis and methanolysis by NMR. Figure 1 shows a plot of the reaction of 1 with D_2O as a function of time. Figure 2 shows the analogous plot for reaction of 1 with methanol-d_4. An examination of Figure 1 clearly shows that this reaction mimics the behavior of a series first-order reaction and plots of ln [**12a**] vs. time (s) for hydrolysis and ln [**17a**] for methanolysis were found to be linear to 85% completion. We were unable to plot ln [1] since addition of water or methanol to 1 was too fast for observation in the NMR. From these plots, values of $k_1(DOD) = 1.79 \times 10^{-3}$ s^{-1} and $k_1(CD_3OD) = 1.55 \times 10^{-3}$ s^{-1} were calculated. The similarity in k_1 for both processes was striking and is clearly consistent with a similar if not

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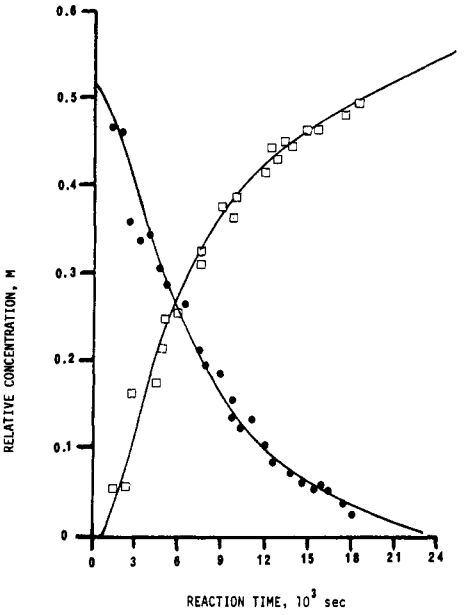
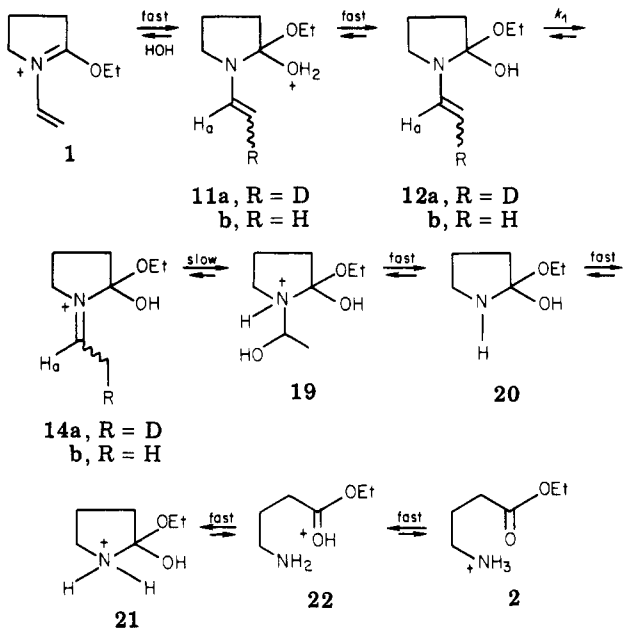


Figure 2. Plot of relative concentration of reaction products from a 0.52 M solution of 1 in CD_3OD as determined by ^1H NMR: (●) [17a] based on signal at 6.82–7.32 ppm; (□) [7] + [8] based on signal at 5.45 ppm.

Scheme I



common pathway for formation and loss of the enamine intermediate. Indeed, as shown in Scheme I, $k_1(D_2O)$ represents conversion of **12a** to **14a**. Likewise, $k_1(CD_3OD)$ is shown in Scheme II and corresponds to conversion of **17** to **18**. A very fast conversion of **17** to **15** followed by a fast conversion to **18** is also consistent with our results. Although one could calculate k_2 for these reactions by the use of Esson's equations,[13] assignment of k_2 to the pathways shown in Schemes I and II was ambiguous and uninformative, especially for the methanolysis reaction.

Since conversion of **11a** or **16a** to the observed intermediates requires a proton transfer, presumably to the water or methanol solvent, we examined the pH dependence of the hydrolysis of 1. Figure 3 shows the decrease

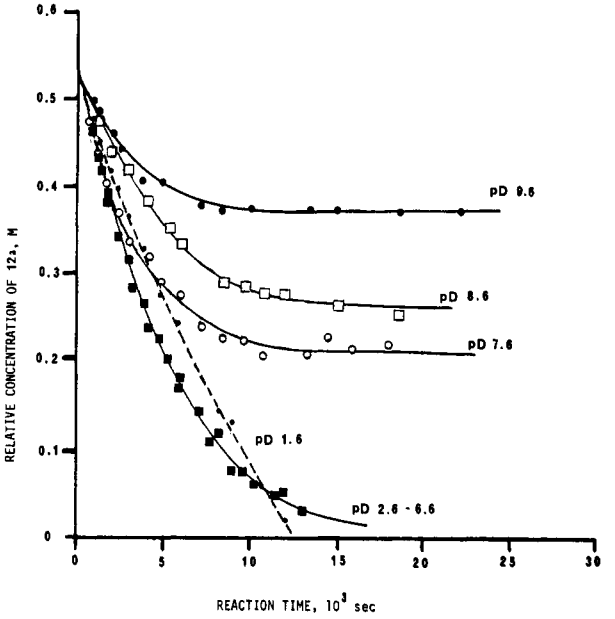


Figure 3. Plot of relative concentration of **12a** from reaction of 1 with D_2O, as a function of pD.

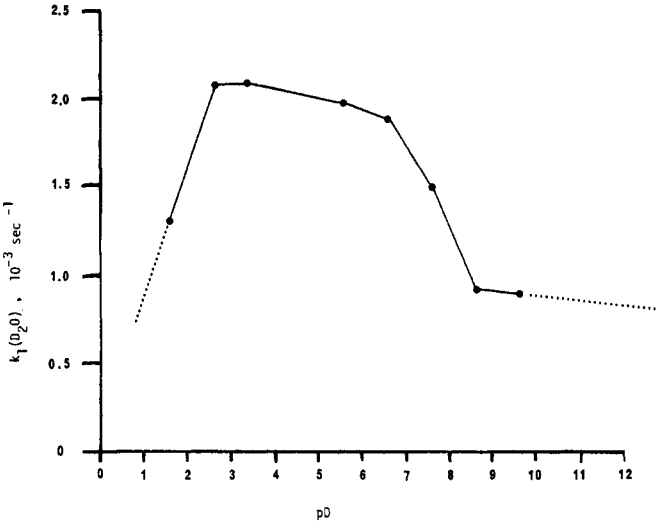


Figure 4. Plot of first-order rate constants for reaction of 1 with D_2O, as a function of pD.

in concentration of **12a** as a function of time in buffered D_2O. In D_2O, the pD is taken to be pD = pH − 0.4.[14] It is clear that the rate of hydrolysis is essentially independent of pH between pH 3–7 but undergoes a decrease in rate at pH 2. At basic pH, the final concentration of **12a** is dependent upon the pH and points to an equilibrium process favoring **12a**. This data is consistent with our conclusion that 1 is not observed in the ^1H NMR spectra of these reactions but is quickly converted to **12a** or **17a**. It is interesting to note that iminium salt **14a** appeared only at pH 2. When k_1 was calculated from the data in Figure 3 and plotted against pD, the "bell-shaped" curve shown in Figure 4 resulted and was virtually identical with those shown for the hydrolysis of imidate salts.[3c,f,g,15] The initial addition of water to 1, analogous to **3**, is therefore consistent with the pH study although these reactions do not appear to be acid catalyzed at neutral pH.

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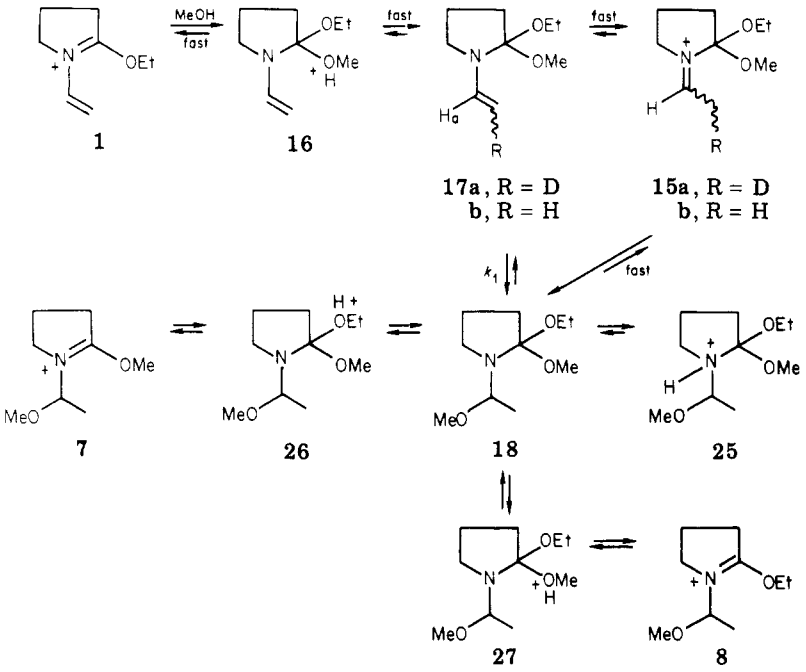
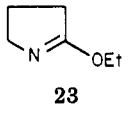
Scheme II

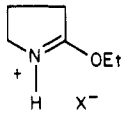


Mechanism

It appears that **14b** and **12b** are key intermediates in the hydrolysis of **1**, shown in Scheme I, and are clearly derived from the initial hydrated adduct **11b**. Enamine **12b** is formed from **11b** but is slowly converted to iminium salt **14b**, in water, in a process corresponding to k_1 in the kinetics scheme. Subsequent addition of water to the iminium salt is slow enough to allow the observation of **12** and **14** in the NMR spectra. The product of this addition is the protonated lactam hemiacetal **19**, which suffers rapid fission of the C–N bond to give lactam hemiacetal **20** and the protonated form of acetaldehyde. A rapid proton transfer generates **21** as well as one of the observed products, acetaldehyde. Intermediate **20** and its protonated analogue **21** are clearly labile species which lose water reversibly and are susceptible to C–N bond fission to give **22** and the other isolated product ethyl 4-aminobutyrate, **2**, via rapid proton transfer.



23



24a, X = Cl
b, X = BF_4

The lability of intermediate **21** clearly precludes its isolation, but we were able to demonstrate its possible existence by an indirect method. We prepared 2-ethoxypyrroline, **23**, by treatment of 2-pyrrolidinone with diethyl sulfate.[16] Protonation of **23** was accomplished in ether with dry hydrogen chloride or with tetrafluoroboric acid etherate to give 2-ethoxypyrrolidiniminium chloride, **24a**, or tetrafluoroborate, **24b**. Addition of water to the acyclic iminium salt analogues of **24** is well-known.[12] Similar addition of water to **24** would give **21**, providing an indirect and independent entry to the proposed intermediate. When **24a** or **24b** was dissolved in water, **2** was formed and indicates the viability of **21** as an intermediate in the hydrolysis mechanism.

A mechanistic rationale for methanolysis of **1** is shown in Scheme II. By analogy to reaction 3,[6] initial addition of methanol to give **16** and loss of a proton giving **17** are fast processes and **1** is not observed in the NMR spectrum. As shown by our NMR study, conversion of **17** to the iminium salt does not occur in neat methanol, in observable concentrations. Rather, addition of methanol directly to the enamine vinyl group in **17b** or to **15** in a very fast reaction generates **18**. Jimenez has established that alcohols add across the double bond of enamines in a facile manner, albeit reversibly, to give the 2-alkoxyamine.[17] It is also possible that a fast conversion of **17** to **15** is followed by a fast reaction to give **18**, such that **15** is not observed in the NMR. The observation of **14a** during hydrolysis, however, suggests the former explanation to be more reasonable. Each of these pathways are shown in Scheme II.

In methanol, lactam acetal **18** should exhibit facile loss of ethoxy to give **7**, in an equilibrium process. Rather, as previously discussed, we isolate a mixture of **7** and **8** although a slow conversion to **7** was observed. One possible explanation is proton transfer to give **25**. The equilibrium mixture of **18** and **25**, with a large preponderance of **25**, could account for the slow conversion to **7**. One assumes a small concentration of **18** with an equilibrium established between **18** ⇌ **7** and **18** ⇌ **8**. A more attractive explanation, however, argues against a moiety such as **25** and for an equilibrium **7** ⇌ **26** ⇌ **18** ⇌ **27** ⇌ **8**. In the absence of protons, **18** is favored since proton transfer is required to initiate the observed equilibrium. The initial 3:1 mixture of **7**:**8** is clearly the result of such an equilibrium with a slow shift to **7** in methanol. It is interesting to note that lactam acetal **18** was not isolated in any experiment although such *N*-alkyl lactam acetals are known to be stable, isolable compounds.[18] Loss of a species such as MeO^+-

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(H)=$CHCH_3$ from **18** via C—N bond cleavage is less facile than loss of CH_3CHO^+H from **19** and accounts for the absence of C–N cleavage products and the isolation of **7** and/or **8**. Therefore, acetaldehyde was not observed in the methanolysis of **1** although **7** does appear to hydrolyze to **2** very slowly. We believe that the mechanism presented in Scheme II best accounts for our observations for the methanolysis of **1** and is taken to be the general mechanism of alcoholysis.

Experimental Section

The ^1H NMR spectra and rate studies were accomplished by using a Varian Associates EM-360 NMR spectrometer at 60 MHz, in ppm, downfield from tetramethylsilane. The infrared spectra were recorded on a Perkin-Elmer IR-283 instrument. The melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

All glassware was oven-dried overnight and flamed immediately prior to use. All reactions were performed under an argon atmosphere. The ether, obtained from Mallinckrodt, was distilled from $LiAlH_4$ and the CH_2Cl_2, obtained from Baker, was distilled from barium oxide, each under argon, prior to use. The methanol and ethanol, obtained from Baker in anhydrous form, were distilled from magnesium/iodine, under argon, prior to use. The 2-pyrrolidinone, *N*-vinylpyrrolidinone, diethyl sulfate, epichlorohydrin, boron trifluoride etherate, methanol-d_4, D_2O, acetone-d_6, 2,4-dinitrophenylhydrazine, and tetrafluoroboric acid etherate were obtained from Aldrich. The buffers were pHydroin buffers obtained from Micro Essential Laboratory, Brooklyn, NY. Each was dissolved in D_2O to specifications. The buffers consisted of pH 3, potassium phthalate and tartaric acid; pH 4, potassium acid phthalate; pH 6, sodium and potassium phosphate; pH 7, disodium and potassium phosphate; pH 8, sodium and potassium phosphate; pH 9, potassium phosphate and sodium borate; pH 10, sodium borate and sodium carbonate. In D_2O, the pD of each solution was taken to be 1.6, 2.6, 3.6, 5.6, 6.6, 7.6, 8.6 and 9.6, by using the formula, pD = pH – 0.4.[14] The triethyloxonium tetrafluoroborate was prepared from ether, epichlorohydrin, and boron trifluoride etherate by the method of Meerwein.[7a] The elemental analyses were performed by MicAnal, Tucson, AZ.

***N*-Vinyl-2-ethoxypyrrolidiniminium Tetrafluoroborate, 1.** A solution of 50.0 g (263.2 mmol) of triethyloxonium tetrafluoroborate in 0.15 L of CH_2Cl_2 was cooled to 0 °C (ice) under argon, and a solution of 28.42 g (255.7 mmol) of *N*-vinylpyrrolidinone, **4**, in 25 mL of CH_2Cl_2 was added over a period of 5 min. The solution was stirred at 0 °C for 24 h and triturated with pentane. Crystallization at –20 °C followed by filtration (argon atmosphere) afforded 41.79 g (184.1 mmol) of **1** (72%): mp 102.0–102.5 °C; IR (KBr) 2970, 1615, 1490, 1457, 1392, 1320, 1245, 1040, 912, 870, 520 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (3 H, t, J = 6.8 Hz), 2.08–2.62 (2 H, m), 3.25 (2 H, t), 3.90 (2 H, t), 4.52 (2 H, q, J = 6.8 Hz), 4.82–5.24 (2 H, m), 6.40–6.98 (1 H, dd, J = 8.0, 16.0 Hz). Anal. Calcd for $C_8H_{14}NOBF_4$: C, 42.33; H, 6.22; N, 6.17. Found: C, 42.03; H, 6.27; N, 6.22.

Ethyl 4-Aminobutyrate, 2, and Acetaldehyde. (a) From 1 and HOH. A solution of 1.273 g (5.60 mmol) of **1** and 10.1 mL (556.2 mmol) of water was stirred at 25 °C for 10 h. The water was removed at 0.1 mmHg, leaving 1.044 g (4.77 mmol) of a colorless oil which was identified as **2** (85%):[19] ^1H NMR (D_2O) δ 1.35 (3 H, t, J = 6.0 Hz), 1.7–2.3 (2 H, m), 2.55 (2 H, distorted t), 3.11 (2 H, distorted t), 4.15 (2 H, q, J = 6.0 Hz).

The water which was removed from the reaction mixture was trapped at –78 °C (CO_2/acetone) and 0.1 mmHg. Upon return to ambient pressure, the solution was warmed to 25 °C and treated with 30 mL of a solution of 2,4-dinitrophenylhydrazine (3 g of 2,4-dinitrophenylhydrazine in 15 mL of concentrated sulfuric acid added to 20 mL of water and 70 mL of 95% ethanol). Upon cooling in ice, yellow crystals were deposited and filtration afforded 0.34 g (1.52 mmol) of acetaldehyde 2,4-dinitrophenylhydrazone (27%): mp 150–151 °C (lit.[20] mp 147 °C or 168 °C); ^1H NMR ($CDCl_3$) δ 2.02 (3 H, d, J = 5.2 Hz), 7.0–8.2 (3 H, complex m), 8.72 (1 H, d, J = 2.0 Hz).

(b) From 1 and DOD. A solution of 1.066 g (4.7 mmol) of **1** in 9.0 mL (446.5 mmol) of D_2O was stirred at 25 °C for 10 h. The D_2O was removed at 0.1 mmHg and trapped at –78 °C (CO_2/acetone). Upon return to ambient pressure, the solution was warmed to 25 °C and treated with 30 mL of the 2,4-dinitrophenylhydrazine solution prepared in (**a**). Upon cooling, yellow crystals were deposited and filtration afforded 0.22 g (0.98 mmol) of 2-deuterioacetaldehyde 2,4-dinitrophenylhydrazone (21%): mp 149.0–150.5 °C; ^1H NMR ($CDCl_3$) δ 2.02 (2 H, m), 7.0–8.2 (3 H, complex m), 8.72 (1 H, d, J = 2.0 Hz).

***N*-(1-Ethoxyethyl)-2-ethoxypyrrolidiniminium Tetrafluoroborate, 9.** A solution of 3.32 g (14.62 mmol) of **1** in 85.4 mL (1.46 mol) of anhydrous ethanol was stirred for 48 h at 25 °C under argon. The ethanol was removed at 0.1 mmHg, and the resulting solid was crystallized from a minimum amount of fresh ethanol at –20 °C to give 3.429 g (12.56 mmol) of **9** (86%) as white crystals: mp 66.5–67 °C; IR (KBr) 3000, 1660, 1510, 1422, 1395, 1320, 1235, 1180, 1060, 948, 930, 875, 635, 525 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (3 H, t, J = 6.8 Hz), 1.28 (3 H, d, J = 6.0 Hz), 1.45 (3 H, t, J = 6 .4 Hz), 2.02–2.55 (2 H, m), 3.0–3.92 (6 H, m), 4.48 (2 H, q, J = 6.4 Hz), 5.15 (1 H, q, J = 6.0 Hz). Anal. Calcd. for $C_{10}H_{20}NO_2BF_4$: C, 43.98; H, 7.38; N, 5.13. Found: C, 43.69; H, 7.59; N, 5.14.

***N*-(1-Methoxyethyl)-2-methoxypyrrolidiniminium Tetrafluoroborate, 7.** A solution of 0.577 g (2.54 mmol) of **1** in 10.3 mL (254 mmol) of anhydrous methanol was stirred for 48 h under argon. The methanol was removed at 0.1 mmHg and the resulting solid was crystallized from a minimum amount of fresh methanol at –20 °C to give 0.510 g (2.08 mmol) of **7** (82%) as white crystals: mp 151.5–152.0 °C; IR (KBr) 2930, 1670, 1410, 1380, 1280, 1060, 943, 930, 845, 631, 535, 520 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.27 (3 H, t, J = 6.0 Hz), 1.82–2.46 (2 H, m), 2.88–3.40 (2 H, m), 3.17 (3 H, s), 3.40–3.85 (2 H, br t), 4.11 (3 H, s), 5.09 (1 H, q, J = 6.0 Hz). Anal. Calcd for $C_8H_{16}NO_2BF_4$: C, 39.22; H, 6.58; N, 5.72. Found: C, 39.20; H, 6.67; N, 5.64.

Similar treatment of 0.512 g (2.25 mmol) of **1** in 9.1 mL (225 mmol) of methanol for 5 h gave a solid product upon removal of all solvents consisting of 59% of **7** and 41% of **8**, as determined by ^1H NMR. The relative amounts of **7** and **8** were determined via comparison of the signals at 5.08 ppm (q, 2 H) for **7** and at 4.47 ppm (q, 2 H) for **8**. In like manner the reaction of **1** with increasing amounts of methanol and/or for increasing time periods gave mixtures of **7** and **8** and, after a reaction time of 50 h, exclusively **7**.

2-Ethoxypyrroline, 23. Treatment of 54.57 g (354.6 mmol) of diethyl sulfate with 36.00 g (423.0 mmol) of 2-pyrrolidinone over a period of 30 min was followed by heating, at reflux, for 24 h. The brown solution was poured into a mixture of 200 g of ice and 0.15 L of saturated K_2CO_3 and stirred for 15 min. The aqueous phase was extracted with 3 × 0.2 L of ether and then 3 × 0.2 L of CH_2Cl_2 and dried (Na_2SO_4) and the solvents were removed under reduced pressure. Distillation of the resultant oil afforded 26.80 g (236.9 mmol) of **23** (56%):[21] ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, J = 7.0 Hz), 1.6–2.2 (2 H, m), 2.15–2.56 (2 H, m), 3.53 (2 H, distorted t), 4.08 (2 H, q, J = 7.0 Hz).

2-Ethoxypyrrolidiniminium Chloride, 24a. A solution of 0.983 g (8.69 mmol) of **23** in 5 mL of ether was treated with dry HCl gas for 5 min. The white solid was filtered and washed with dry ether to give 1.25 g (8.34 mmol) of **24a** (96%): ^1H NMR ($CDCl_3$) δ 1.45 (3 H, t, J = 7.0 Hz), 2.03–2.54 (2 H, m), 2.63–3.10 (2 H, m), 3.83 (2 H, br t), 4.61 (2 H, q, J = 7.0 Hz), 12.4 (1 H, br s).

2-Ethoxypyrrolidiniminium Tetrafluoroborate, 24b. A solution of 4.22 g (37.3 mmol) of **23** in 25 mL of CH_2Cl_2 was treated with a solution of 6.05 g (37.3 mmol) of HBF_4 etherate in 10 mL of CH_2Cl_2 and stirred at 25 °C for 1 h. Solvents were removed under reduced pressure to give 7.36 g (36.6 mmol) of **24b** (98%):

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(20) "Dictionary of Organic Compounds", Oxford University Press: New York, 1965; Vol. 1, pp 7.

(21) (a) Pilotti, A.; Rueterhall, A.; Torssel, K.; Lindbled, C. G. *Acta Chem. Scand.* **1969**, *23*, 818. (b) Etienne, A.; Correia, Y. *Bull. Soc. Chim. Fr.* **1969**, 3704. (c) Etienne, A.; Correia, Y. *C. R. Hebd. Seances Acad. Sci.* **1964**, *259*, 2660.

^{1}H NMR ($CDCl_3$) δ 1.44 (3 H, t, J = 7.0 Hz), 2.05–2.62 (2 H, m), 2.6–3.15 (2 H, m), 3.76 (2 H, br t), 4.32 (2 H, q, J = 7.0 Hz), 8.6 (1 H, br s).

Hydrolysis of 24. (a) 24a. Reaction of 0.783 g (5.23 mmol) of **24a** with 25 mL of water for 10 h gave, after removal of the water at 0.1 mmHg, 0.772 g (4.61 mmol) of **2** (88%).

(b) 24b. Reaction of 0.56 g (2.79 mmol) of **24b** with 25 mL of water for 10 h gave, after removal of the water at 0.1 mmHg, 0.531 g (2.42 mmol) of **2** (87%).

NMR Study of the Reaction Kinetics of 1. (a) Deuterolysis. In a typical experiment, 0.15 g (0.66 mmol) of 1 was placed in a 5-mm NMR tube. At time = 0 s, 0.5 mL of D_2O was added, via syringe, and the tube was shaken to dissolve 1. The signals at 6.82–7.32, 8.39, and 9.5 ppm were integrated every 60 s and utilized for the determination of the relative amounts of **12**, **14** and CH_3CHO.

(b) d_4 Methanolysis. In a typical experiment, 0.15 g (0.66 mmol) of 1 was placed in a 5-mm NMR tube. At time = 0 s, 0.5 mL of methanol-d_4 was added, via syringe, and the tube was shaken to dissolve 1. The signals at 6.82–7.32 and 5.2–5.7 ppm were integrated every 60 s and utilized for the determination of the relative ratios of **17** and **7**/**8**.

(c) In Acetone-d_6. In a typical experiment, 0.15 g (0.66 mmol) of 1 was dissolved in 0.5 mL of acetone-d_6. At time = 0 s, 0.2 mL of D_2O or methanol-d_4 was added, via syringe, and the tube was shaken. The signals at 6.82–7.3, 8.4, and 9.5 ppm were scanned every 300 s for the first hour and at odd intervals thereafter until the reaction was deemed complete.

Rate of Deuterolysis of 1 as a Function of pD. A total of 0.05 g (0.22 mmol) of 1 was weighed into a 5-mm NMR tube. At time = 0 s, 0.5 mL of a solution of the appropriate buffer, dissolved in D_2O, was added via syringe and the tube was shaken to dissolve 1. The signals at 6.8–7.3, 8.4, and 9.5 ppm were integrated every 30 s until the reaction was complete or had stopped. In this manner, the rate of deuterolysis of 1 as examined at pD = 1.6, 2.6, 3.6, 5.6, 6.6, 7.6, 8.6, and 9.6.

Registry No. 1, 86905-60-4; 2, 86905-61-5; 4, 88-12-0; 7, 86905-65-9; 8, 86905-67-1; 9, 86905-63-7; 23, 931-46-4; 24a, 90670-73-8; 24b, 24419-40-7; 2-deuterioacetaldehyde 2,4-dinitrophenylhydrazone, 90670-74-9; triethyloxonium tetrafluoroborate, 368-39-8; 2-pyrrolidinone, 616-45-5.

2,2,6,6-Tetramethyl-4-phosphorinanol: Synthesis and Conformational Analysis

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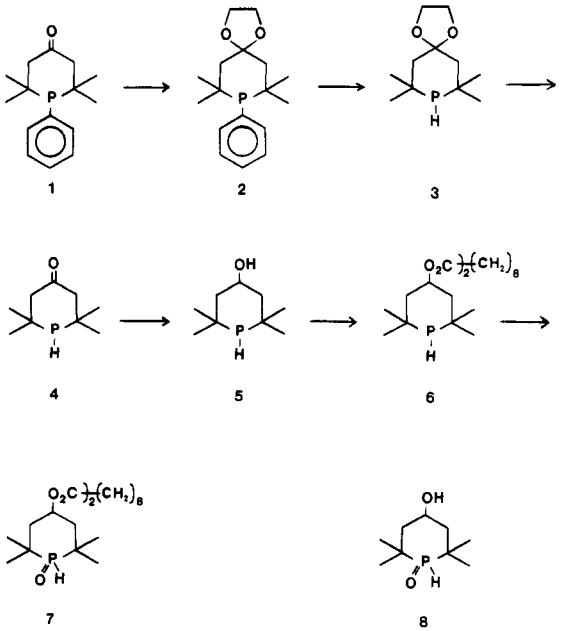
The synthesis and characterization of 2,2,6,6-tetramethyl-4-phosphorinanol (**5**) and its derivatives are described. The protection of the carbonyl group of 2,2,6,6-tetramethyl-1-phenylphosphorinan-4-one as the ethylene ketal, reductive removal of the 1-phenyl substituent with lithium metal in THF, and subsequent removal of the protecting group followed by hydride reduction gave **5**. A mild two-phase procedure for the oxidation of 1*H*-phosphorinanes to 1-oxo-1*H*-phosphorinanes is described. The ^{1}H NMR spectrum of **5** suggests that the ring has a biased conformation in solution where the proton on phosphorus assumes an axial ring position.

The chemistry of phosphorinanes continues to be an active area of research.[1] Quite recently, Berlin and coworkers reported the conformational analysis of C-alkylated phosphorinane derivatives.[2-4] Conformational studies on C-alkylated 1*H*-phosphorinanes would certainly be of interest in light of the high preferance for an axial P–H bond in the parent 1*H*-phosphorinane at room temperature.[5] Unfortunately, methodology previously did not exist for the preparation of alkyl-substituted 1*H*-phosphorinanes. We report herein the synthesis and characterization of the previously unreported 2,2,6,6-tetramethyl-4-phosphorinanol (**5**) and its corresponding derivatives.

Results and Discussion

Synthesis. Following the procedure of Welcher and Day,[6] the phosphorinane **1** was prepared by the condensation of phorone with phenylphosphine in a yield of 55% (distilled). The carbonyl group was protected by the acid-catalyzed condensation of **1** with ethylene glycol to give the ketal **2**.



Grim and Molenda have reported the preparation of lithium dialkylphosphides by the reduction of dialkyl-

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