HYDROLYSIS OF CYCLIC 2-ALKOXYIMINIUM SALTS[1a]

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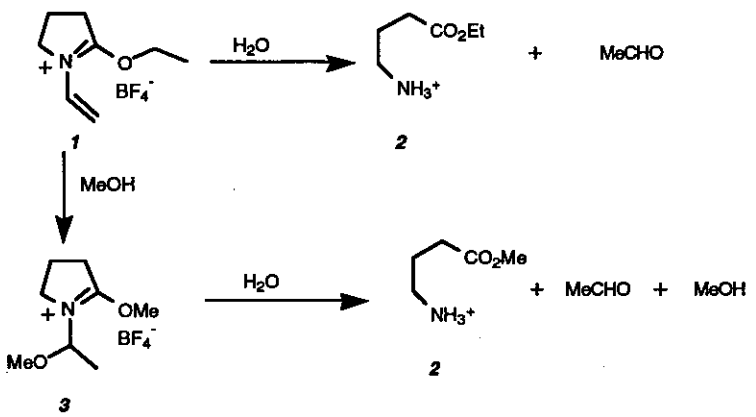
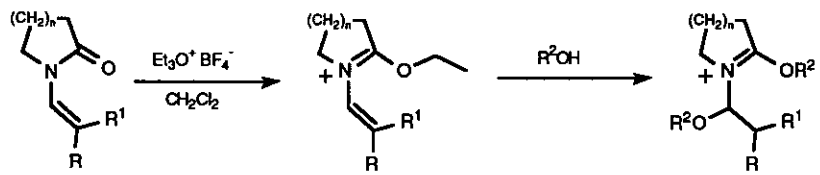
Abstract - *N*-Alkenyl- and *N*-alkoxymethyllactams are readily prepared from the corresponding lactam, and reaction with triethyloxonium tetrafluoroborate generates an 2-ethoxyiminium salt. Hydrolysis in neutral water gives the ethyl ester of 4-amino-butanoic acid (GABA) (or another ω-amino ester), an aldehyde and, in the case of the alkoxymethyl derivatives, an alcohol. The hydrolysis step requires participation of an enamine or *N*-alkoxymethyl moiety in a proton exchange reaction prior to fragmentation of the ring. The reaction shows a steric effect at the 'enamine' or *N*-alkoxymethyl terminus and some dependence on the size of the ring. The alkoxymethyl derivatives hydrolyze much slower than the alkenyllactam derivatives.

We previously showed that *N*-vinyl-2-ethoxypyrrolidiniminium tetrafluoroborate (***1***) was easily prepared from *N*-vinyl-2-pyrrolidinone and triethyloxonium tetrafluoroborate[2] and reacted with water (at neutral pH, $t_{1/2}$ = 8 min) to give ethyl 4-aminobutanoate (ethyl-GABA, ***2***).[2] GABA is a neural transmitting drug important in mammalian brain chemistry.[3] Iminium salt (***1***) also reacted with alcohols to give the corresponding *N*-(1-alkoxyalkyl)pyrrolidiniminium salts (***3***). Hydrolysis in neutral water also gave (***2***), but with a significantly slower rate. Iminium salt (***3***), for example, was formed by reaction of (***1***) with methanol, and hydrolyzed to the methyl ester of (***2***) (in water, neutral pH, $t_{1/2}$ = 9 h), acetaldehyde and methanol. We wanted to study this reaction in greater detail, but this required additional examples of this class of compounds, which are derived from *N*-alkenyl-lactams. We previously showed that *E*-*N*-alkenyllactams (***4-6***) were easily prepared[4] by direct reaction of an enolizable aldehyde and a lactam. The methods previously described in the



literature were of limited scope.[5-8] Using our method, a variety of aldehydes react with lactams [in refluxing benzene (or toluene) and a catalytic amount of *p*-TsOH and a Dean-Stark trap] to produce *N*-alkenyllactams (***4-6***), in good yield.[4] The corresponding iminium salts (***7-9***) required for this study were prepared by reaction of (***4-6***) with triethyloxonium tetrafluoroborate.



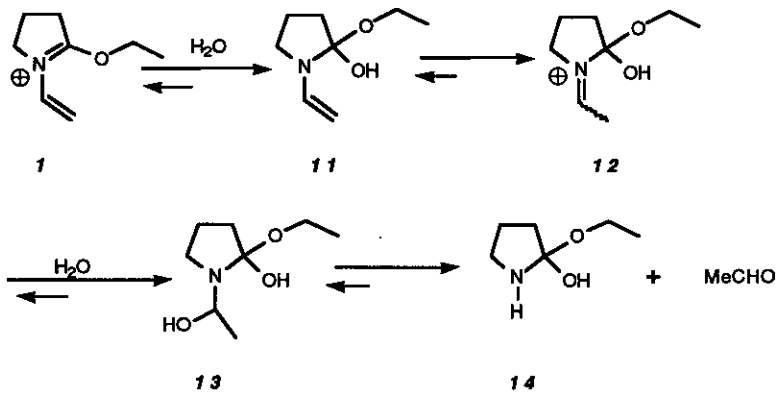
4 n = 1
5 n = 2
6 n = 3

7 n = 1
8 n = 2
9 n = 3

10 n = 1

Our initial study[2] described the mechanism of this hydrolysis in general terms. This paper will focus on the hydrolysis of iminium salts from *N*-alkenyl- and *N*-alkoxymethyllactams to the corresponding amino ester derivatives. The mechanism of hydrolysis will be shown to be essentially identical to the mechanism proposed by Schmir for the hydrolysis of *N*-substituted acetimidate esters.[9] In the course of our investigation, we observed that alkoxymethyliminium salts such as (***10***) hydrolyze with loss of the alcohol and aldehyde moieties and with formation of ethyl GABA. We also studied this reaction since the rate of hydrolysis for iminium salts such as (***10***) was significantly slower than the *N*-alkenyl derivatives. Of particular interest was the clear participation of the alkenyl group in (***7-9***) or alkoxymethyl group in (***10***) in the hydrolysis mechanism. The double bond in the first case or the alkoxy oxygen in the second facilitated proton transfers that led to ring opening.

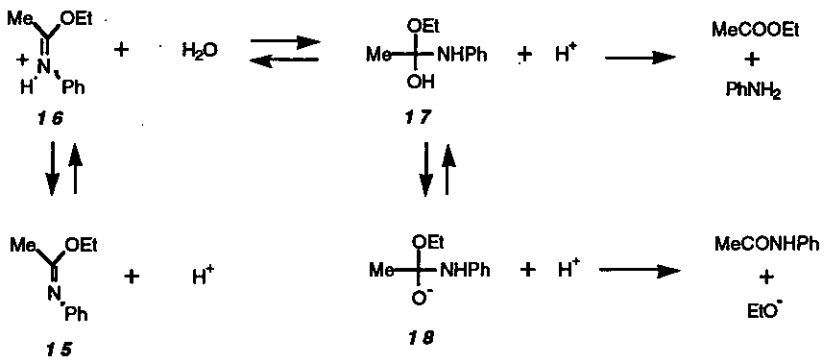
In our previous work we found evidence that (*1*) reacted with water under neutral conditions to give



1 *11* *12*

13 *14*

the corresponding lactam hemi-orthoamide (*11*),[2] which behaved as an enamine in subsequent steps. Intermediate (*11*) was formed at a rate too fast to observe by the ^{1}H nmr technique we used to follow the reaction. An equilibrium was established in a slow step, favoring (*12*) as a transient intermediate which was observed in low concentrations in the nmr spectrum. Addition of a second equivalent of water to (*12*) gave (*13*) in a fast step and α-cleavage gave a mixture of acetaldehyde



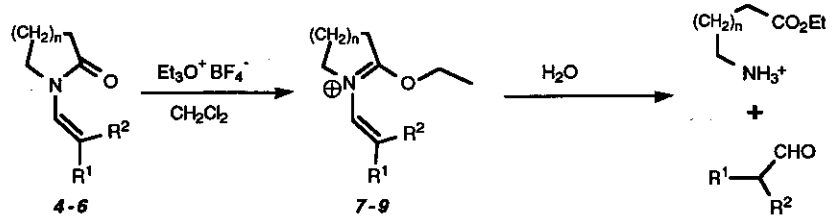
16 *17*

15 *18*

and (*14*). Amino alcohol (*13*) opened under the aqueous conditions with the equilibrium favoring the ring opened product (*2*, ethyl GABA). Hemi-orthoamide (*14*) was not isolated nor observed. Its existence was inferred by preparation of the hydrochloride salt of 2-ethoxypyrroline, which opened to ethyl GABA at a rate too fast to observe in the ^{1}H nmr.[2a] An intermediate such as (*14*) was the only reasonable intermediate for this latter reaction. The reaction proceeded with a half-life of eight

min.[2] This rationale is taken from Schmir's mechanism proposed for the hydrolysis of acetimidate esters such as (***15***).[9] Initial reaction of (***15***) with a proton formed (***16***), an analog of ***1***, ***7***, ***8*** and (***9***). Fast, reversible addition of water generated (***17***) [analogous to (***11-14***)]. Schmir showed that

Table 1. Conversion of Alkenyl Lactams to 2-Ethoxyiminium Salts and Aqueous Hydrolysis to Ethyl GABA and Aldehydes.



4-6 ***7-9***

n	R^1	R^2	Lactam	% (*7-9*)	% Amino Ester
1	H	H	[c]	72[a] (***1***)	--
	Et	H	***4a***	88[a] (***7a***)	89 (***2***)
	C_5H_{11}	H	***4b***	77[a] (***7b***)	90 (***2***)
	Me	Me	***4c***	80[a] (***7c***)	86 (***2***)
	Ph	H	***4d***	81[a] (***7d***)	94 (***2***)
	$-CH_2CH_2CH_2CH_2CH_2-$		***4e***	78[a] (***7e***)	86 (***2***)
2	Et	H	***5a***	87[a] (***8a***)	90 (***26***)
	C_5H_{11}	H	***5b***	74[a] (***8b***)	88 (***26***)
	Me	Me	***5c***	82[a] (***8c***)	83 (***26***)
	Ph	H	***5d***	89[a] (***8d***)	92 (***26***)
3	Et	H	***6a***	>98[b] (***9a***)	92 (***27***)
	C_5H_{11}	H	***6b***	>98[b] (***9b***)	95 (***27***)
	Me	Me	***6c***	>98[b] (***9c***)	85 (***27***)
	Ph	H	***6d***	>98[b] (***9d***)	91 (***27***)

[a] isolated yield. Quantitative by ^1H nmr. Product loss due to partial hydrolysis
[b] Quantitative by ^1H nmr - product an oil, no by-products detectable by nmr.
[c] *N*-vinyl-2-pyrrolidinone

cleavage to the ester and an amine was much faster than cleavage to the amide. The major difference in the hydrolysis of ***1*** and the hydrolysis of ***16*** was the participation of the 'enamine' moiety, which was present in ***11***. This allowed addition of a second equivalent of water to ***12***, followed by cleavage to the amino ester (***2***) and acetaldehyde.

We prepared the parent compound (***1***) *via* reaction of *N*-vinylpyrrolidinone with triethyloxonium tetrafluoroborate.[2] Other pyrrolidiniminium salts (***7***) were prepared in an identical manner, as shown in Table 1. The initial rate of hydrolysis for each reaction was measured for a pseudo first-

order reaction by monitoring loss of the alkenyl signals of (***7-9***) in the proton nmr. These hydrolysis data are shown in Table 2, which also includes hydrolysis data for several *N*- methoxyalkyl derivatives (***24***). Both *N*-alkyl-2-piperidone [3,4,5,6-tetrahydropyridin-2-one, (***5***)] and *N*-alkylcaprolactam

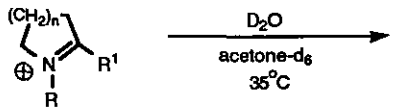
[2H-hexahydroazepin-2-one, (***6***)] derivatives were converted to the corresponding iminium salt [(***8***) and (***9***)] in excellent yields. Iminium salts (***7-9***)and (***24***) were obtained as oils. Hydrolysis of the iminium salts (***7-9***) liberated well known amino ester products (methyl 4-aminobutanoate,[10] methyl 5-aminopentanoate[11] and methyl 6-aminohexanoate).[11b] Hydrolysis of the iminium salts with water led to ring opening and that open-chain product was characterized a slight downfield shift of 0.92-0.95 ppm for the alkene proton adjacent to the nitrogen in the ^{1}H nmr (relative to the cyclic iminium salt). These downfield shifts were 5.03 → 5.87-6.03 ppm for (***4a*** → ***7a***), 4.99-5.17 → 5.98 ppm for (***5a*** → ***8a***) and 4.99-5.12 → 6.01 ppm for (***6a*** → ***9a***). The ω-methylene protons in the lactam ring [C_5 in (***4***), C_6 in (***5***) and C_7 in)***6***)] also shifted downfield by 0.3 - 0.6 ppm upon conversion to the acyclic iminium salt [3.50 → 4.13 ppm for (***4a*** → ***7a***), 3.38 → 3.70 ppm for (***5a*** → ***8a***), 3.57 → 4.10 ppm for (***6a*** → (***9a***)]. Ir analysis showed a shift to shorter wave-numbers [1690 → 1660 cm^{-1} for (***1***)] indicating conversion of the lactam carbonyl to an iminium species.

Several of the substituted iminium salts were poorly soluble in water and the kinetic data was obtained by dissolution of about 100 mg of salt in a 2:3 mixture of D_2O and acetone-d_6. Using ^{1}H nmr , we scanned the 3.0-4.0 ppm (-N-CH_2) region as well as the 5.0-6.0 ppm (-N-CH=CH-) region. A 0.5-0.8 ppm upfield shift was observed for the C_5 methylene of the lactam ring as it opened to the ω-ammonium salt.[2a,7] We observed a gradual loss of the alkenyl signal at 5-6 ppm. In our previous study evidence pointed to this signal being the hydrated product [(***11***)rather than (***1***)].[2a] This was confirmed in only one iminium salt, derived from 2*H*-hexahydroazepin-2-one (***9b***), in which we saw a minor upfield shift (0.1-0.2 ppm) of the signals in the vinyl region (5.0-6.0 ppm) of the nmr over a period of about 90 seconds after dissolution. We attribute this change in signal to the conversion ***9b*** to the hydrated form (***20***) [R = C_5H_{11}], and this transformation is taken as the first reaction of all iminium salts examined.

We observed a small transient signal at 8.4 ppm during the course of each reaction. This was attributed to conversion of the 'enamine' (***11***) to iminium salt (***12***). In our initial study we found that this conversion was independent of the pH of the solution between pH 1-7, and we suspected the 'enamine' moiety in (***11***) reacted with a proton from one of the protonated species in solution,

identically to the *N*-substituted acetimidates[10] and other iminium salts, which showed the same pH profile.[12] During the course of the hydrolysis the proton signal of the aldehyde by-product from (***1***) or (***7-9***) was clearly discernible at 9.0-9.5 ppm and intensified as the signal for the starting material vanished. As mentioned, the kinetic data for the iminium salts are shown in Table 2 and are presented as the initial rate for a pseudo first order process. Excluding (***1***) and (***24***), the slowest hydrolysis rate was observed for (***8c***), with (***7a***) being the fastest. We note that pentyl derivative (***7b***) was poorly soluble in the D_2O-acetone-d_6 medium, leading to unreliable kinetic data. The

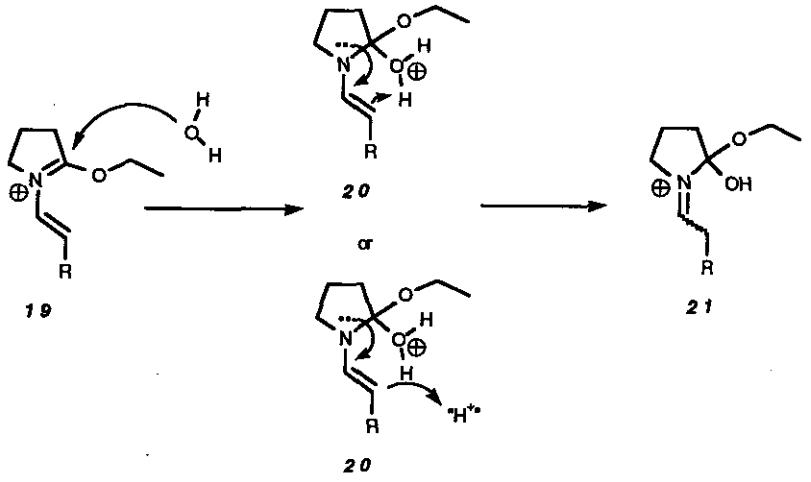
Table 2. Relative Rate of Hydrolysis of Lactam Based Iminium Salts



n	Lactam	R	R^1	k (x 10^{-5})
1	***1***	$CH=CH_2$	OEt	128.4
	7a	CH=CHEt	OEt	39.8
	7b	$CH=CHC_5H_{11}$	OEt	--[a]--
	7c	$CH=CMe_2$	OEt	1.93
	7d	CH=CHPh	OEt	2.11
	7e	CH=C-$(CH_2)_5$-	OEt	3.87
2	***8a***	CH=CHEt	OEt	3.09
	8b	$CH=CHC_5H_{11}$	OEt	9.46
	8c	$CH=CMe_2$	OEt	1.11
	8d	CH=CHPh	OEt	37.7
3	***9a***	CH=CHEt	OEt	16.1
	9b	$CH=CHC_5H_{11}$	OEt	6.15
	9c	$CH=CMe_2$	OEt	3.26
	9d	CH=CHPh	OEt	27.2
1	***25***	CH(OEt)Me	OEt	2.01
	3	CH(OMe)Me	OMe	14.1
	24a	CH_2OMe	OEt	0.43
	24b	CH_2OEt	OEt	0.70
	24c	CH_2OiPr	OEt	0.39
	24d	CH_2Ot-Bu	OEt	3.06
	24e	CH_2OPh	OEt	32.9

[a] Inconclusive kinetic data due to poor solubility in the hydrolysis medium.

analogous larger ring derivatives [(*8b*) and (*9b*)], however, were very soluble and gave excellent results. A steric effect is apparent as the R group on the 'enamine' portion of (*7*), (*8*) or (*9*)increases in size [(*7a*) > (*7d*) > (*7c*), (*8d*) > (*8b*) > (*8a*)> (*8c*), (*9d*) > (*9a*) > (*9b*) > (*9c*)]. This is consistent with intermolecular proton (or deuterium) transfer from a D_3O^+ or D_2OH^+ species in D_2O (or H_3O^+ in H_2O) to the nucleophilic enamine carbon of (*11*). Alternatively, an intramolecular transfer can occur between the 'enamine' moiety and a proton on the H_2O^+ (HOD) or $EtHO^+$ ($EtOD^+$) moieties at C_2. As shown in Table 2, alkyl substitution on the alkenyl moiety decreased the rate of hydrolysis relative to (*1*). The butenyl derivative (*7a*) showed only a three-fold decrease in rate. Both (*7c*) and (*7e*) were significantly slower. The phenyl derivative (*7d*) hydrolyzed at a rate comparable to (*7c*) or (*7e*). These data suggested that increasing the steric hindrance on the enamine inhibits conversion to an iminium salt, consistent with attack by the terminal carbon of the enamine. We were unable to examine the steric effect at the carbon attached to nitrogen (-*N*-C<u>H</u>R'=CHR^1) in alkoxyalkyl derivatives since ketones did not undergo the condensation reaction with lactams under a variety of conditions.



A rationale for these results is suggested by Schmir's studies of iminium salts such as (*16*).[10] Initial addition of water to (*19*) will generate hydrated derivative (*20*), which behaves as an enamine. This enamine reacts with an acidic proton to generate the transient iminium salt (*21*). The nature of this hydrogen transfer remains unknown other than the requirement that the enamine moiety be involved. At this time, we can not determine the specific process for this proton transfer and our aim

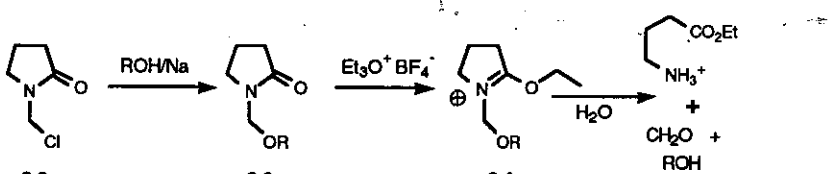
is, therefore, the same as that stated by Schmir: "Our primary aim is to suggest the nature of the ionic species of catalyst and intermediates which may be involved in the overall process of product formation. It may very well be that diffusion-controlled proton transport reactions are kinetically important in these reactions."[13]

The greatly reduced reactivity of (*20*) relative to (*1*) can be explained by a steric effect in which the more bulky carbon is less accessible to the acidic species. The electron releasing effect of alkyl groups, towards nitrogen also decreases the nucleophilicity of the enamine carbon. There was no clear trend of reactivity from the initial rate of hydrolysis data obtained in our experiments. The overall order, taken from Table 2, was (*7a*) > (*8d*) > (*9d*) > (*9a*) > (*8b*) > (*9b*) > (*7e*) > *9c* > (*8a*) > (*7c*) > (*8c*). For specific substituents: (*7a*) > (*9a*) > (*8a*), (*9c*) > (*7c*) > (*8c*), (*8d*) > (*9d*) > (*7d*). The results for the phenyl derivatives are difficult to rationalize since they show generally faster rates than the alkyl derivatives, although there is no trend with regards to ring size. As shown in Table 2, both (*8d*) and (*9d*) react significantly faster than their alkyl analogs. Iminium salt (*7d*), however, showed an initial rate comparable to the alkyl derivatives. The coplanarity of the phenyl moiety and the alkenyl group may lead to a non-bonded interaction of the *ortho*-hydrogens and the ethoxy/hydroxy group, a steric effect that hinders reaction of the enamine carbon and the proton source. The increased flexibility of the six and seven-membered rings may diminish this interaction, allowing facile approach to the acidic proton.

In our initial study we found that iminium salt (*1*) reacted with alcohols to form the corresponding alkoxyalkyliminium salt (*3*) in good yield.[2] When (*1*) reacted with alcohols, only the alkoxy product (*3*) was isolated, in 82 % yield.[2] Similar reaction of (*1*) with ethanol gave (*25*). We found that (*3*) also hydrolyzed in neutral water to give (*2*), but with a half-life of 4.4 h. Reaction of (*1*) was facile with methanol, ethanol, 1-propanol, 2-propanol, 1-butanol and 2,2-dimethylethanol (*t*-butanol) although the iminium salt products were viscous oils. In our previous study, we discovered that reaction of (*1*) with phenol failed to give the phenoxy analog of (*3*) or (*25*), even at temperatures up to 100°C. We found an attractive alternative for the preparation of these compounds in Böhme's work, where *N*-chloromethyl-2-pyrrolidinone (*22*) was prepared from 2-pyrrolidinone by reaction with formaldehyde and treatment with thionyl chloride.[14] It had been shown that (*22*) reacted with alcohols, alkoxides and phenolic compounds to give the corresponding alkoxy (or phenoxy)-methyl 2-pyrrolidinone derivative[8] [as in the conversion of (*22*) to (*23*)].[9] We prepared several derivatives by this method (shown in Table 3) and reaction of each with triethyloxonium

tetrafluoroborate (Meerwein's reagent)[15] generated the expected ethoxyiminium salt (***24***) in good yield. Subsequent dissolution in water gave the ethyl ester of GABA (***2***) as well as the alcohol used to form the ether and formaldehyde [for (***24a-d***)] or acetaldehyde [for (***3***) and (***25***)]. The initial rate data we collected by our ^{1}H nmr experiments is shown in Table 2 and the hydrolysis rates of (***3***), (***25***) or (***24***) were, in all cases, significantly slower than ***1***. One possible reaction pathway for the hydrolysis would involve protonation of the alkoxy oxygen and nucleophilic displacement by water at the methyl carbon. This mechanism would demand that relatively minor increases in steric bulk at the alkoxy alkyl carbon must have major effects on the rate of hydrolysis. It is apparent from Table 2 that there is virtually no steric effect with increasing bulk at the ether oxygen. The kinetic data pointed to a pseudo-first order reaction for the hydrolysis of (***24***) and the most likely mechanism of hydrolysis is also analogous to the hydrolysis of iminium salts such as (***16***).[10] Hydrolysis begins with initial addition of water to (***24***), generating (***26***). The nucleophilic oxygen of (***26***) can react with an acidic proton (from the medium) to generate an oxonium species (***27***), that could be displaced by the nitrogen to give (***28***). Reaction of (***28***) with water gives (***29***), which loses formaldehyde to give (***18***). Ring opening, as with the *N*-alkenyliminium salts, leads to the amino ester. There is a pronounced increase in rate with the phenoxy derivative, possibly due to an

Table 3. Preparation of *N*-Alkoxymethyl-2-pyrrolidinones, Conversion to *N*-Alkoxymethyl-2-ethoxypyrrolidiniminium Salts and Aqueous Hydrolysis.

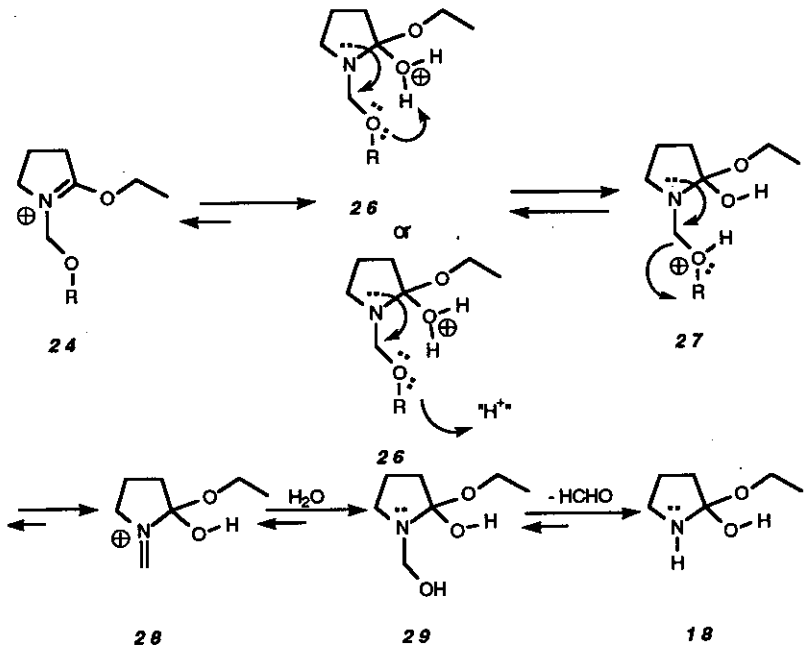


22 ***23*** ***24***

R	% (***23***)	% (***24***)	% (***2***)
OMe	43 (***23a***)	85 (***24a***)	83
OEt	69 (***23b***)	81 (***24b***)	87
OiPr	85 (***23c***)	79 (***24c***)	88
Ot-Bu	67 (***23d***)	73 (***24d***)	82
OPh	54 (***23e***)	68 (***24e***)	93

electron withdrawing effect which enhances displacement of the alkoxy moiety by the nitrogen, forming the iminium salt or by generating phenol as a leaving group. The presence of an α-methyl substituent in ***3*** led to an increase in rate relative to (***24***), possibly due to the electron releasing

effect of the methyl substituent. The rate diminished with the ethoxy derivative (***25***), however. In all cases except phenoxy, the rate of hydrolysis for these salts was significantly slower than the alkenyl derivatives [compare with (***9a***), (***10a***) or (***11a***)], consistent with the reduced nucleophilicity of the alkoxy derivative relative to the enamine intermediate. It is also possible that protonation of the nitrogen significantly slows the rate. Once the alcohol moiety is lost, addition of a second equivalent of water leads to loss of formaldehyde or acetaldehyde and generation of the GABA ester, as with the alkenyl derivatives.



CONCLUSIONS

The reaction of alkenyllactams with triethyloxonium tetrafluoroborate delivers *N*-alkenyl imidates in good to excellent yields. The hydrolysis of these materials follows pseudo first order kinetics and showed dramatic decreases in the initial rate measured by nmr when compared with (***1***). *N*-(1-Methoxyalkyl)-2-methoxypyrrolidiniminium salts were formed in good yield via reaction of *N*-pyrrolidiniminium salts with methanol or by reaction of Meerwein's reagent with (***23***). The rates of hydrolysis appear to be significantly slower than the parent methoxy imidate (***3***).

Table 4. Nmr Data for *N*-Alkyliminium Salts (*7-9*).

	^{1}H Nmr (CDCl$_3$): δ (ppm)	^{13}C Nmr (CDCl$_3$): δ (ppm)
7a	1.05 (3H, t, J = 6.8 Hz), 1.26 (3H, t, J = 7.5 Hz), 2.21-2.09 (2H, m), 2.47-2.30 (2H, m), 3.36 (2H, t, J = 7.5 Hz), 4.13 (2H, t, J = 7.5 Hz), 4.56 (2H, q, J = 6.8 Hz), 5.87-6.07 (1H, m), 6.85 (1H, d, J =13.9 Hz)	12.77 (q), 13.80 (q), 16.59 (t), 23.02 (t), 29.42 (t), 50.82 (t), 74.12 (t), 120.12 (d), 128.64 (d), 184.07 (s)
7b	0.89 (3H, t, J = 7.0 Hz), 1.29 (3H, t, J = 7.8 Hz), 1.53-1.32 (10H, m), 2.49 (2H, t, J = 7.5 Hz), 4.05 (2H, t), 4.69 (2H, q, J = 7.0 Hz), 5.85-5.60 (1H, m), 6.69 (1H, d, J=14.4 Hz)	12.85 (q), 13.27 (q), 16.28 (t), 21.64 (t), 28.05 (t), 29.12 (t), 29.18 (t), 30.49 (t), 50.54(t), 73.64 (t), 120.61 (d), 126.74 (d), 178.19 (s)
7c	*1.47 (3H, t, J = 7.0 Hz). 1.70 (3H, s), 1.80 (3H,* s), 2.46-2.37 (2H, m), 3.31 (2H, t, J = 7.9 Hz), 3.97 (2H, t), 4.66 (2H, q, J = 7.0 Hz), 5.78 (1H, s)	*14.35(q),17.57 (q), 18.18(q), 22.49(t), 29.01* (t) 54.63 (t), 73.82(t), 116.05(d), 139.56(s), 180.21 (s)
7d	1.19 (3H, t, J = 6.9 Hz);2.08-1.95 (2H, m), 2.45 (2H, t, J = 8.3 Hz), 4.29 (2H, t, J = 7.7 Hz), 4.83 (2H, q, J = 6.9 Hz), 6.89 (1H, d, J=14.7 Hz), 7.60-7.36 (6H, m)	13.43(q).14.27(t),29.79(t), 64.91(t), 74.28(t), 119.51(d), 124.51(d) 126.79(d), 128.58(d), 128.58(d), 133.43(s), 178.98 (s)
7e	1.18 (3H, t, J = 6.8 Hz). 1.90-1.75 (8H, m), 2.45-2.30 (2H, m), 3.75 (2H, t, J = 8.3 Hz), 4.11 (2H, t, J = 8.2 Hz),4.56 (2H, q, J = 6.9 Hz), 5.82 (1H, s)	12.82(q).13.45(t), 17.06(t), 24.73(t), 25.25(t), 26.43(t), 27.34(t), 32.38(t), 54.65(t), 73.25(t), 112.60(d), 145.98(s), 180.25 (s)
8a	1.10 (3H, t, J = 6.6 Hz), 1.52 (3H, t, J = 7.3 Hz), 1.70-2.47 (4H, br s), 2.77-3.20 (2H, br s), 3.54 -3.98 (2H, br s), 4.62 (4H, q, J = 6.6 Hz), 5.98 (1H, dt, J = 4 Hz, 7 Hz) 6.88 (1H, d, J = 7 Hz)	12.86 (q), 13.77 (q), 17.44 (t), 19.86 (t), 23.11 (t), 25.46 (t), 48.94 (t), 69.85 (t, OCH_2), 125.15 (d), 128.52 (d), 174.05 (s)
8b	0.98 (3H, dist t), 1.14-2.45 (15H, br m), 2.87-3.23 (2H, br s), 3.60-4.00 (2H, br s), 4.68 (2H, q, J = 7.1 Hz), 5.91 (1H, dt, J = 4 Hz, 7.5 Hz), 6.86 (1H, d, J = 7.5 Hz)	13.83 (q), 14.02 (q), 17.63 (t), 20.13 (t), 22.26 (t), 25.75 (t), 28.36 (t), 30.00 (t), 31.09 (t), 49.31 (t), 70.15 (t), 124.90 (d), 127.72 (d), 174.31 (s)
8c	1.40 (3H, t, J = 7.0 Hz), 1.69 (3H, s), 1.81 (3H, *s), 1.80-2.21 (4H, br s), 2.75-3.10 (2H, br s),* 3.41-3.75 (2H, br s), 4.50 (2H, q, J = 7.0 Hz), 5.84 (1H, br s, C=CH)	14.00 (q), 17.54 (q), 17.89 (q), 20.20 (t), *21.77 (t), 25.22 (t),* 52.17 (t), 69.41 (t), 120.78 (d), 137.47 (s), 176.44 (s)
8d	1.72 (3H, t, J = 7.0 Hz), 2.08-2.42 (4H, br s), 3.10-3.38 (2H, br s), 3.94-4.30 (2H, br s), 4.82 (2H, q, J = 7.0 Hz), 6.98 (2H, d), 7.32-7.90 (5H, br s)	
9a	1.11(3H, t, J = 7.1 Hz), 1.52(3H, t, J = 8.1 Hz), 1.85(6H, m), 2.24(2H, m), 3.19(2H, t, J = 7.8 Hz), 4.10(2H, t, J = 7.8 Hz), 4.73 (2H, q, J = 7.1 Hz), 6.01(1H, m), 7.77 (1H, d, J = 13.6 Hz)	14.10(q), 15.67(q), 23.16(t), 24.74(t), 28.42(t), 39.05(t), 52.37(t), 53.68(t), 72.89(t), 114.92(d), 130.27(d), 181.73(s)
9b	0.89 (3H, t, J = 7.1 Hz), 1.32(3H, t, J = 6.6 Hz), 1.51 (4H, m), 1.87 (6H, m), 2.16 (4H, m), 3.18 (2H, t, J = 8.1 Hz), 4.08 (2H, t, J = 8.0 Hz), 4.68 (2H, q, J = 7.1 Hz), 5.90 (1H, m), 6.64 (1H, m)	14.33(q), 14.86(q),21.12(t), 22.21(t),24.82(t), 27.66(t) 28.22(t), 29.82(t), 31.07(t), 52.41(t), 53.56(t), 72.12(t), 125.54(d), 128.76(d), 179.06(s)
9c	1.45(3H, t, J = 7.0 Hz), 1.61(6H, s), 1.68(2H, m), 1.85, (4H, m), 3.16(2H, t, J = 8.2 Hz), 3.92(2H, t), 4.63 (2H, q, J = 7.0 Hz), 6.01(1H, s)	15.05(q), 18.20(q), 21.93(q), 24.94(t), 27.63 (t), 28.95(t), 32.71(t), 55.89(t), 71.78(t), 122.18 (d), 136.68(s), 181.60(s)
9d	1.53(3H, t, J = 6.9 Hz), 1.85(8H, m), 4.69(2H, q, *J = 6.9 Hz) 7.27 (7H, m)*	4.03(q), 21.05(t), 21.53(t), 27.86(t), 28.28(t), *53.16(t), 72.64(t), 126.08(d),* 127.15(d), 128.80(d), 128.96(d), 129.25 (d), 133.42(s), 179.73(s)

EXPERIMENTAL SECTION

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are uncorrected. ^{1}H and ^{13}C nmr spectra were determined with an IBM WP-200SY spectrometer at 200.13 MHz and 50.3 MHz respectively as solutions in deuteriochloroform. Ir data were recorded with a Perkin-Elmer model 283. High resolution mass spectra were measured on an AEI MS-902 mass spectrometer and are accurate to ±5 ppm. Tlc of neutral materials was accomplished on silica gel 60F-254 sheets from E. Merck. Reverse phase tlc (C_{18}) from E. Merck was used as a criterion of purity for all iminium salts (a single spot using aqueous methanol or aqueous THF or aqueous acetonitrile. Column chromatography was performed with silica gel 60 (70-230 mesh) from E. Merck. All lactams and aldehydes were obtained from Aldrich and were used without further purification. The triethyloxonium tetrafluoroborate was prepared from ether (obtained from Baker), epichlorohydrin and boron trifluoride etherate[16] (obtained from Aldrich). All alkenyllactams used in this study were synthesized by our previously reported procedure from the parent lactam and aldehyde.[2]

General Procedure For The Preparation of *N*-Alkenyl pyrrolidiniminium tetrafluoroborate Salts:

A dry 25 ml round bottom flask was charged with 5-10 mmol of freshly prepared triethyloxonium tetrafluoroborate.[16] The flask was sealed with a rubber septum and 10 ml of dry dichloromethane (P_2O_5) was added with a syringe. Approximately 5-10 mmol of the desired alkenyllactam in 5 ml of dichloromethane was added. The solution was allowed to stir under argon for 12 to 24 h. The solvent was removed *in vacuo* and the residual oil was purified by Kugelrohr distillation. The iminium salt was dissolved in 25 ml of water, stirred for 20 h. Filtration and evaporation of the water, *in vacuo*, allowed isolation of the amino ester.

Reaction of 1.85 g (9.74 mmol) of triethyloxonium tetrafluoroborate with 1.35 g (9.74 mmol) of (***4a***) gave an oil that yielded 2.09 g (8.55 mmol, 88%) of 2-ethoxy-*N*-(E-1-butenyl)pyrrolidiniminium tetrafluoroborate (***7a***). Hydrolysis of 0.50 g of (***7a***)gave 0.38 g (89%) of ethyl 4-aminobutanoate•HBF_4 (***2***).[2a,11] ^{1}H Nmr (D_2O): δ 1.25 (3H, t, J = 6.0 Hz), 1.80-2.10 (2H, br t), 2.25-2.55 (2H, br t), 2.80-3.15 (2H, br t) and 4.05 ppm (2H, q, J = 6.0 Hz). Treatment of an ether solution with 2,4-dinitrophenylhydrazine in HCl and gave the 2,4-DNP of butanal: mp 119-121°C (lit.,[16] 122°C).

Reaction of 0.664 g (3.49 mmol) of triethyloxonium tetrafluoroborate and 0.633 g (3.49 mmol) of (***4b***) gave an oil that yielded 0.796 g (77%) of 2-ethoxy-*N*-(E-1-heptenyl)pyrrolidiniminium

tetrafluoro-borate (***7b***). *Hydrolysis of 0.50 g of (**7b**) gave 0.33 g (90%) of (**2**). Treatment with* 2,4-dinitro-phenylhydrazine in HCl and gave the 2,4-DNP of heptanal: mp 106-107°C (lit., mp,[11,17] 108°C).

Reaction of 1.28 g (6.74 mmol) of triethyloxonium tetrafluoroborate with 0.936 g (6.74 mmol) of (***4c***) gave an oil that yielded 1.23 g (80%) of 2-ethoxy-*N*-(E-2-methyl-1-propenyl)pyrrolidiniminium tetrafluoroborate, (***7c***). Hydrolysis of 0.50 g of (***7c***) gave 0.37 g (86%) of (***2***). Treatment with 2,4-dinitrophenylhydrazine in HCl gave the 2,4-DNP of 2-methyl-1-propanal: mp 178-179°C (lit.,[11,17] mp 182°C).

Reaction of 1.84 g (9.64 mmol) of triethyloxonium tetrafluoroborate with 1.81 g (9.64 mmol) of (***4d***) gave a solid that yielded 2.36 g (7.81 mmol, 81%) of 2-ethoxy-*N*-(E-2-phenyl-1-ethenyl)-pyrrolidin-*iminium tetrafluoroborate (**7d**). mp 129-130°C. Hydrolysis of 0.50 g of (**7d**) gave* 0.34 g (94%) of (***2***). Treatment with 2,4-dinitrophenylhydrazine gave the 2,4-DNP of phenylacetaldehyde: mp 119-120°C (lit.,[17] mp 121°C).

Reaction of 1.88 g (9.84 mmol) of triethyloxonium tetrafluoroborate with 1.77 g (9.84 mmol) of (***4e***) gave an oil that yielded 2.28 g (78%) of 2-ethoxy-*N*-(E-2-cyclohexylidene-1-ethenyl)-pyrrolidin-iminium tetrafluoroborate, (***7e***). Hydrolysis of 0.50 g of (***7d***) gave 0.32 g (86%) of (***2***). Treatment with 2,4-dinitrophenylhydrazine gave the 2,4-DNP of cyclohexane carboxaldehyde: mp 168-169°C (lit.,[17] mp 173-173.8°C).

A solution of 1.001 g (6.53 mmol) of *N*-(*E*-1-butenyl)-3,4,5,6-tetrahydropyridin-2-one (***5a***) in 10 ml of dry CH_2Cl_2 was treated with 1.372 g (7.22 mmol) of triethyloxonium tetrafluoroborate to give 1.530 g *(87%) of 2-ethoxy-N-(E-1-butenyl)-3,4,5,6-tetrahydropyridiniminium tetrafluoroborate (**8a**).* Hydrolysis of 0.50 g of (***8a***) gave 0.39 g (90%) of ethyl 5-aminopentanoate•HBF_4 (***26***).[12] ^{1}H Nmr (D_2O): δ 1.25 (3H, t, J = 7.5 Hz), 1.50-1.85 (4H, m), 2.25-2.55 (2H, br t), 2.85-3.15 (2H, br t) and 4.10 ppm (q, 2H, J = 4.5 Hz); ^{13}C nmr (D_2O): δ 13.26 (q), 21.06 (t); 26.05 (t), 33.20 (t), 39.11 (t), 61.65 (t) and 176.19 (s); ir (Nugol): 1720 cm^{-1}.

A solution of 1.011 g (5.21 mmol) of *N*-(*E*-1-heptenyl-3,4,5,6-tetrahydropyridin-2-one (***5b***) in 10 ml of dry CH_2Cl_2 was treated with 1.064 g (5.60 mmol) of triethyloxonium tetrafluoroborate to give 1.199 g (74%) of 2-ethoxy-*N*-(E-1-heptenyl)-3,4,5,6-tetrahydropyridiniminium tetrafluoroborate (***8b***). Hydrolysis of 0.50 g of (***8b***) gave 0.33 g (88%) of ethyl 5-aminopentanoate•HBF_4 (***26***).

A solution of 1.003 g (6.55 mmol) of *N*-(2-methyl-1-propenyl)-3,4,5,6-tetrahydropyridin-2-one (***5c***)

in 10 ml of dry CH_2Cl_2 was treated with 1.371 g (7.22 mmol) of triethyloxonium tetrafluoroborate to give 1.4448 g (82%) of 2-ethoxy-*N*-(2-methyl-1-propenyl)-3,4,5,6-tetrahydropyridiniminium tetrafluoroborate, (***8c***). Hydrolysis of 0.50 g of (***8c***) gave 0.36 g (83%) of ethyl 5-aminopentanoate•HBF_4 (***26***).

A solution of 1.001 g (4.97 mmol) of *N*-(*E*-1-heptenyl-3,4,5,6-tetrahydropyridin-2-one (***7d***) in 10 ml of dry CH_2Cl_2 was treated with 1.026 g (5.40 mmol) of triethyloxonium tetrafluoroborate to give 1.404 g (89%) of 2-ethoxy-(E-2-phenyl-1-ethenyl)-3,4,5,6-tetrahydropyridiniminium tetrafluoroborate (***8d***).: Hydrolysis of 0.50 g of (***8d***) gave 0.34 g (92%) of ethyl 5-aminopentanoate•HBF_4 (***26***).

Triethyloxonium tetrafluoroborate (1.252 g, 6.59 mmol) was added to a solution of 1.001 g of *N*-(1-butenyl)hexahydroazepin-2-one (***6a***) [5.99 mmol] in 5 ml of anhydrous CH_2Cl_2 to give a quantitative yield of *N*-(E-1-butenyl) 2H-hexahydroazepiniminium tetrafluoroborate (***9a***). Hydrolysis of 0.50 g of (***9a***) gave 0.40 g (92%) of ethyl 6-amino-hexanoate•HBF_4 (***27***).[12b] ^1H Nmr (D_2O): δ 1.25 (3H, t, J = 4.6 Hz); 1.35-1.85 (6H, m), 2.20-2.50 (2H, br t), 2.80-3.15 (2H, br t) and 4.10 ppm (2H, q, J = 4.6 Hz); ^{13}C nmr (D_2O): δ 13.29 (q), 23.61 (t), 24.97 (t), 26.29 (t), 33.36 (t), 39.37 (t), 61.47 (t) and 178.32 ppm (s); ir (Nugol): 1720 cm^{-1}.

Triethyloxonium tetrafluoroborate (0.999 g, 5.26 mmol) was added to a solution of 0.999 g of *N*-(1-hexenyl)hexahydroazepin-2-one (***6b***) (4.78 mmol) in 5 ml of anhydrous CH_2Cl_2 at room temperature to give a quantitative yield of *N*-(E-1-heptenyl) 2H-hexahydroazepiniminium tetrafluoroborate (***9b***). Hydrolysis of 0.50 g of (***9b***) gave 0.36 g (95%) of ethyl 6-amino-hexanoate•HBF_4 (***27***).

Triethyloxonium tetrafluoroborate (1.250 g, 6.58 mmol) was added to a solution of 1.000 g of *N*-(1-isobutenyl) hexahydroazepin-2-one (***6c***) (5.98 mmol) in 5 ml of anhydrous CH_2Cl_2 to give a quantitative yield of *N*-(2-methyl-1-propenyl) 2H-hexahydroazepiniminium tetrafluoroborate (***9c***). Hydrolysis of 0.50 g of (***9c***) gave 0.37 g (85%) of ethyl 6-amino-hexanoate•HBF_4 (***27***).

Triethyloxonium tetrafluoroborate (0.973 g, 5.12 mmol) was added to a solution of 1.000 g of *N*-(2-phenylethenyl) hexahydroazepin-2-one (***6d***) (5.12 mmol) in 5 ml of anhydrous CH_2Cl_2 at room temperature to give a quantitative yield of *N*-(2-phenyl-1-ethenyl) 2H-hexahydroazepiniminium tetrafluoroborate (***9d***). Hydrolysis of 0.50 g of (***9d***) gave 0.34 g (91%) of ethyl 6-aminohexanoate•HBF_4 (***27***).

Preparation of *N*-Chloromethyl-2-pyrrolidinone, (*22*). A mixture of 74.3 g (873 mmol) of 2-pyrrolidinone and 26.2 g of paraformaldehyde was heated to reflux in an oil bath for 3 h. The slurry

was cooled in an ice bath and 103.9 g (873 mol) of thionyl chloride was added, dropwise, over a period of 30 min. The resultant solution was stirred at ambient temperature for 1 h. Distillation, *in vacuo*, gave 60.64 g (52%) of (***22***): bp 102-103°C/2 mm Hg (lit.,[15] bp 97-97.5°C/4 mmHg).

General Procedure For The Preparation of *N*-Alkoxymethyl-2-pyrrolidinones:[15,17] A solution of the appropriate alcohol (4-30 mmol) was treated with one equivalent of NaH or sodium metal and stirred at ambient temperature for 1 h. The alcoholate was cooled to 0°C (ice bath) and a THF solution of *N*-chloromethyl-2-pyrrolidinone (4-30 mmol) (***22***) was added dropwise. Following stirring for 24 h, the slurry was filtered and the solvents removed under reduced pressure. The lactam was distilled (Kugelrohr, reduced pressure) and isolated by silica gel chromatography (98:2 CH_2Cl_2:MeOH).

Reaction of 0.876 g (3.76 mmol) of Na in dry methanol (distilled from Mg/I_2) was followed by addition of 0.502 g (3.76 mmol) of (***22***). Kugelrohr distillation (85°C/0.1 mm Hg) followed by chromatography (R_f, 0.4) gave 0.290 g (43 %) of *N*-methoxymethyl-2-pyrrolidinone (***23a***). (lit.,[18a] bp 74-77°C/ 3 mmHg).

Reaction of 0.187 g (8.12 mmol) of Na in absolute ethanol was followed by addition of 1.0831 g (8.11 mmol) of (***22***). Kugelrohr distillation (83-85°C/0.1 mm Hg) followed by chromatography gave 0.802 g (69%) of *N*-ethoxymethyl-2-pyrrolidinone (***23b***) (lit.,[15,18a] bp 60°C/0.1 mmHg).

Reaction of 0.760 g (33.06 mmol) of Na in 2 ml of dry isopropanol (Mg/I_2) was followed by addition of 4.398 g (32.92 mmol) of (***22***). Kugelrohr distillation (102-103°C/0.2 mm Hg) followed by chromatography gave 4.404 g (85%) of *N*-(1-methylethoxy)methyl-2-pyrrolidinone (***23c***).

Reaction of 1.710 g (15.24 mmol) of potassium *t*-butoxide in 25 ml of dry THF (from Na/benzophenone) was followed by addition of 2.003 g (15.00 mmol) of (***22***). Kugelrohr distillation (105-107°C/0.2 mm Hg) followed by chromatography gave 1.746 g (67%) of *N*-(1,1-dimethylethoxy) methyl-2-pyrrolidinone (***23d***).

A solution of 1.439 g (15.30 mmol) of phenol in 2 ml of dry THF was treated with 0.3540 g (15.4 mmol) of Na and then 2.004 g (15.00 mmol) of (***22***) was added. The solution was washed with 2 x 50 ml of 5% NaOH to remove the phenol and Kugelrohr distillation (158-160°C/0.3 mm Hg) followed by chromatography gave 1.551 g (54%) of *N*-phenoxymethyl-2-pyrrolidinone (***23e***).

General Procedure For The Preparation of *N*-Alkoxymethyl-2-pyrrolidiniminium Salts, (*24*). A solution of *N*-alkoxymethyl-2-pyrrolidinone (2-6 mmol) (***23***) in about 10 ml of

dichloromethane was treated with 1.1 equivalents of triethyloxonium tetrafluoroborate at 0°C. The reaction mixture was stirred for 1 h at 0°C and stored overnight in a freezer at -5°C. The reaction mixture was filtered and the dichloromethane solution was washed with 2 x 50 ml of water, dried (Na_2SO_4) and the solvents were removed under reduced pressure to give the 2-ethoxyiminium salt, (***24***). In all cases the iminium salt was free of lactam and pure by ^1H nmr and tlc analysis.

A mixture of 0.293 g (2.27 mmol) of *N*-methoxymethyl-2-pyrrolidinone (***23a***) and 0.474 g (2.50 mmol) of triethyloxonium tetrafluoroborate in 12 ml of CH_2Cl_2 gave 0.47 g (85%) of 2-ethoxy-*N*-methoxymethyl-2-pyrrolidiniminium tetrafluoroborate (***24a***). Reaction of 0.50 g of (***24a***) in 25 ml of water and stirring for 20 h was followed by filtration and evaporation of solvents to give 0.70 g (83%) of (***2***).

A mixture of 0.778 g (5.43 mmol) of *N*-ethoxymethyl-2-pyrrolidinone (***23b***) and 1.1361 g (5.98 mmol) of triethyloxonium tetrafluoroborate gave 1.136 g (81%) of 2-ethoxy-*N*-ethoxymethyl-2-pyrrolidiniminium tetrafluoroborate (***24b***). Reaction of 0.50 g of (***24b***) in 25 ml of water and stirring for 20 h as above gave 0.66 g (87%) of (***2***).

A mixture of 0.769 g (4.89 mmol) of *N*-(1-methylethoxy)methyl-2-pyrrolidinone (***23c***) and 0.901 g (4.74 mmol) of triethyloxonium tetrafluoroborate in 10 ml of CH_2Cl_2 gave 1.020 g (79%) of 2-ethoxy-*N*-(1-methylethoxy)methyl-2-pyrrolidiniminium tetrafluoroborate (***24c***). Reaction of 0.50 g of (***24c***) in 25 ml of water and stirring for 20 h as above gave 0.61 g (88%) of (***2***).

A mixture of 0.690 g (4.03 mmol) of *N*-(1,1,-dimethylethoxy)methyl-2-pyrrolidinone (***23d***) and 0.844 g (4.44 mmol) of triethyloxonium tetrafluoroborate, in 10 ml of CH_2Cl_2 gave 0.840 g (73%) of 2-ethoxy-*N*-(1,1,-dimethylethoxy)methyl-2-pyrrolidiniminium tetrafluoroborate (***24d***) Hydrolysis of 0.50 g of (***24d***) in 25 ml of water and stirring for 20 h as above gave 0.52 g (82%) of (***2***).

A mixture of 0.460 g (2.41 mmol) of *N*-phenyoxymethyl-2-pyrrolidinone (***23e***) and 0.502 g (2.64 mmol) of triethyloxonium tetrafluoroborate in 8 ml of CH_2Cl_2 gave 0.503 g (68 %) of 2-ethoxy-*N*-phenoxymethyl-2-pyrrolidiniminium tetrafluoroborate (***24e***). Reaction of 0.50 g of (***24e***) in 25 ml of water and stirring for 20 h as above gave 0.53 g (93%) of (***2***).

General Procedure For Pseudo First Order Kinetic Determinations: To an nmr tube was added 50-100 mg of imidate salt. A solution was prepared that yielded 4 ml of acetone-d_6, 6 ml of D_2O and 5 mmol of dimethylformamide added as an internal standard. The nmr reaction tube that yielded the imidate salt was charged with 0.5 ml of this solution, quickly dissolved and the

spectra was recorded immediately. The signals between 4.5-7.0 ppm were scanned every 60 sec for the first h, every h for the first 10 h and approximately even 10-12 h thereafter. A plot of concentration vs. time revealed a pseudo first order relationship. When ln (conc) vs time was plotted via linear least squares analysis, all plots had correlation coefficients of > 0.98 over at least three half-lives.

Table 5. Nmr Data for Lactams (*22*) and (*23a-e*) and Iminium Salts (*24a-e*).

	^{1}H Nmr ($CDCl_3$): δ (ppm)	^{13}C Nmr ($CDCl_3$): δ (ppm)
22	2.10 (2H, m), 2.42 (2H, t, J = 7.7 Hz), 3.56 (2H, t, J = 7.0 Hz) 5.24 (2H, s)	17.54 (d), 30.63 (d), 45.60 (d), 53.58 (d) 175.68 (s)
23a	2.15 (2H, m), 2.40 (2H, t, J = 7.5 Hz), 3.29 (3H, s), 3.49 (2H, t, J = 7.2 Hz) 4.69 (2H, s)	17.86 (t), 20.99 (t), 45.79 (t), 55.80 (q), 73.84 (t), 175.92 (s)
23b	1.22 (3H, br t), 2.09 (4H, m), 2.42 (2H, br t), 3.49 (2H, q, J = 7.3 Hz) 4.75 (2H, s)	14.84 (q), 17.81 (t), 31.00 (t), 45.80 (t), 63.65 (t), 72.30 (t), 175.67
23c	1.02 (6H, d, J = 7.2 Hz), 1.90 (2H, m), 2.25 (2H, t, J = 8.2 Hz), 3.35 (2H, t, J = 7.9 Hz), 3.53 (1H, m) 4.60 (2H, s)	17.37 (q), 22.02 (t), 31.05 (t), 45.26 (t), 69.53 (d), 70.42 (t), 175.11 (s)
23d	1.18 (9H, s), 1.80-2.54 (4H, m), 3.47 (2H, t, J = 7.8 Hz) 4.79 (2H, s)	17.74 (t), 27.81 (q), 31.32 (t), 45.55 (t), 66.69 (t), 76.51 (s) 174.63 (s)
23e	2.01 (2H, m), 2.45 (2H, t, J = 7.7 Hz), 3.51 (2H, t, J = 7.7 Hz), 5.31 (2H, s), 7.04 (3H, m) 7.25 (2H, m)	17.6 (t), 30.7 (t), 45.6 (t), 70.33 (t), 115.34 (d), 115.41 (d), 121.57 (d), 129.42 (d), 156.30 (s) 175.3 (s)
24a	1.49 (3H, t, J = 8.1 Hz), 2.08-2.64 (2H, m), 3.10-4.10 (4H, m), 3.42 (3H, s), 4.62 (2H, q, J = 8.0 Hz) 4.83 (2H, s)	13.74 (q), 17.26 (t), 29.37 (t), 50.05 (t), 53.53 (t),m 57.79 (q), 76.53 (t), 182.05 (s)
24b	1.21 (3H, t, J = 7.6 Hz), 1.52 (3H, t, J = 7.9 Hz), 2.08-2.68 (2H, m), 3.08-4.10 (4H, m), 3.60 (2H, q, J = 7.9 Hz), 4.66 (2H, q, J = 7.9 Hz) 4.91 (2H, s)	13.87 (q), 14.29 (q), 16.99 (t), 29.46 (t), 50.41 (t), 53.32 (t), 65.84 (t, OCH_2), 75.06 (t), 181.55 (s)
24c	1.18 (6H, d, J = 8.1 Hz), 1.47 (3H, t, J = 7.8 Hz), 2.10-2.60 (2H, m), 3.10-4.10 (4H, m), 4.60 (2H, q, J = 8.1 Hz) 4.86 (2H, s)	14.14 (q), 17.21 (q), 21.61 (q), 23.58 (t), 29.71 (t), 50.50 (t), 56.26 (t), 72.05 (d, -$OCHMe_2$), 74.12 (t) 181.58 (s)
24d	1.26 (9H, s), 1.48 (3H, t, J = 8.30 Hz), 2.05-2.60 (2H, m), 3.13-4.18 (4H, m), 4.72 (2H, q, J = 8.1 Hz) 5.00 (2H, s)	13.78 (q), 17.33 (t), 27.01 (q), 29.49 (t), 49.99 (t), 50.53 (t), 74.12 (t), 76.07 (s) 180.89 (s)
24e	1.40 (3H, t, J = 7.7 Hz), 2.10-2.50 (2H, m), 2.95-4.05 (4H, m), 4.55 (2H, q, J = 7.9 Hz), 5.37 (2H, s,) 6.60-7.30 (5H, m)	13.99 (q), 17.26 (t), 29.49 (t), 51.03 (t), 53.54 (t), 74.91 (t), 115.22 (d), 116.24 (d), 123.54 (d), 129.43 (d), 129.97 (d), 155.93 (s), 182.24 (s)

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