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Acid-Catalyzed Hydrolysis of 3-Isopropyloxatriazole

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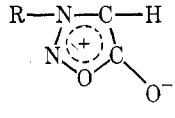
The mechanisms of the acid-catalyzed ring opening of mesoionic 3-aryl- and 3-alkylsydnones (**1**, R = alkyl or aryl) have been studied in some detail.[1,2] In contrast very little is known about the acid-catalyzed decomposition of the analogous (isosteric) oxatriazole system **2**. Boyer and Hernandez observed that cyclohexyloxatriazole (**2a**, R = C_6H_{11}) was re-



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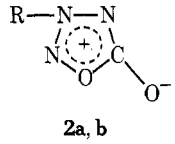


2a, b

sistant to dilute sulfuric acid but decomposed in strong acid to form cyclohexanol, carbon dioxide, and hydrogen azide,[3] whereas the products of hydrolysis of phenyloxatriazole have been reported to be phenyl azide and carbon dioxide.[4] The absence of cyclohexyl azide in the products of decomposition of **2a** reflects the instability of alkyl azides in strong acid.[5] The behavior of oxatriazoles in strong acid seems to be in sharp contrast to that of the sydnones which are converted to the corresponding alkyl and aryl hydrazines. We now report the first kinetic study of the acid-catalyzed ring opening of mesoionic oxatriazoles on 3-isopropyloxatriazole (**2b**, R = *i*-Pr).

The hydrolysis of **2b** only occurs at an appreciable rate at high acidity and high temperature. The first-order rate constants, k_ψ, for the hydrolysis of **2b** in aqueous solutions of mineral acids are shown in Table I.

In spite of the limited range of acidity over which the hydrolysis of **2b** could be studied, a plot of log k_ψ vs. $-H_0$ gives a slope of 1.3.[6] Analysis of the kinetic data in terms of Bunnett's approach[7] leads to a value of w (−0.74) which is in the range associated with reactions in which water does not participate in the rate-determining step. The value of ϕ (−0.30) obtained from the correlation of log k_ψ + H_0 with H_0 + log $[H^+]$[8] leads to a similar conclusion. The value of the entropy

Table I. Hydrolysis Rate, 10^3 k_ψ (min^{-1}), of 2b in Aqueous Mineral Acids

$HClO_4$ Concn, M, at 60 °C						
7.00	7.50	8.00	8.50	9.00	9.50	
1.84	4.69	12.7	38.2	106	460	
H_2SO_4 Concn, M, at 60 °C						
7.00	7.50	8.00	8.50	9.00	9.50	10.0
0.82	1.98	2.87	4.59	7.84	16.2	35.7
HCl Concn, M, at 60 °C						
	8.50	9.00	9.50	10.00		
	0.41	1.53	2.91	6.22		
$HClO_4$ (9.00 M) at Various Temp, °C						
	40.2	45.0	50.0	55.0	60.0	
	10.1	20.0	34.6	65.7	113	

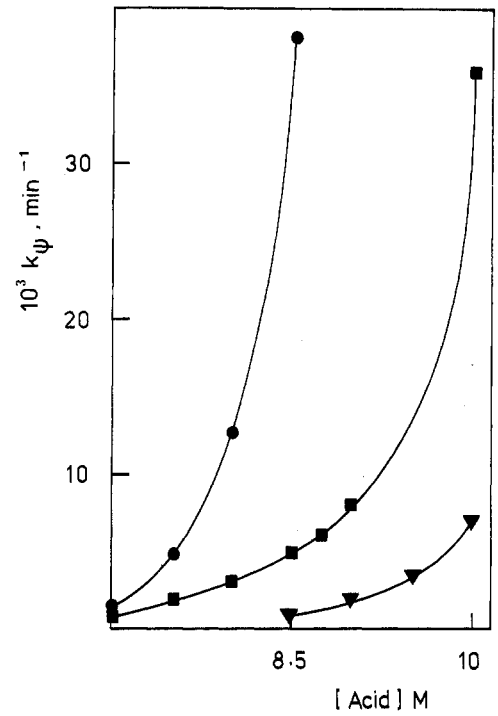
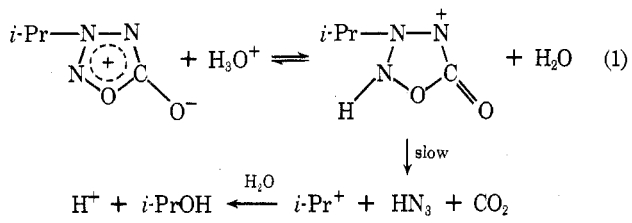


Figure 1. Hydrolysis of **2b** in water at 60 °C: ●, $HClO_4$; ■, H_2SO_4; ▼, HCl.

of activation calculated for 9 M $HClO_4$ ($\Delta S^\ddagger$ = +2.5 eu) is also consistent with an A-1 reaction.[9] The value obtained for the deuterium kinetic solvent isotope effect $[k_\psi(D_2O)/k_\psi(H_2O)$ = 1.42] for the perchloric acid catalyzed hydrolysis of **2b** is characteristic of reactions which proceed via specific hydrogen ion catalysis (although it is perhaps somewhat lower than usually observed for A-1 reactions[10]) and suggests that proton transfer occurs in a preequilibrium step.

The most striking feature of the effect of different acids on the hydrolysis of **2b** (Figure 1) is the order of effectiveness of the acids, viz., $HClO_4 > H_2SO_4 > HCl$. Bunton and his coworkers have suggested that such an order of reactivity is characteristic of A-1 reactions and that the transition states of such reactions are preferentially stabilized by anions of low charge density.[11] All the evidence presently available therefore suggests that the acid-catalyzed hydrolysis of isopropyloxatriazole follows an A-1 mechanism which can be represented as in eq 1. In the absence of any definitive evidence, protonation is assumed to occur on N-2 as has been assumed in the acid-catalyzed hydrolyses of 3-alkylsydnones.[12] Consistent with the proposed mechanism, the major products of hy-



drolysis in the presence of hydrochloric acid were found to be isopropyl chloride and hydrazoic acid.

Experimental Section

The isopropyloxatriazole **2b** prepared by the method of Boyer and Canter[13] had bp 63 °C (0.5 mm) [lit.[13] bp 60–61.5 °C (0.45–0.50 mm)]. Kinetics were followed spectrophotometrically at 255 nm in a Unicam Model S.P. 800 spectrometer using a constant temperature cell thermostated to ±0.1 °C.

Registry No.—**2b**, 7724-83-6; $HClO_4$, 7601-90-3; H_2SO_4, 7664-93-9; HCl, 7647-01-0.

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Reactions of Carbamylimidazoles with Nucleophiles—an Example of an Intramolecular Acyl Transfer Reaction

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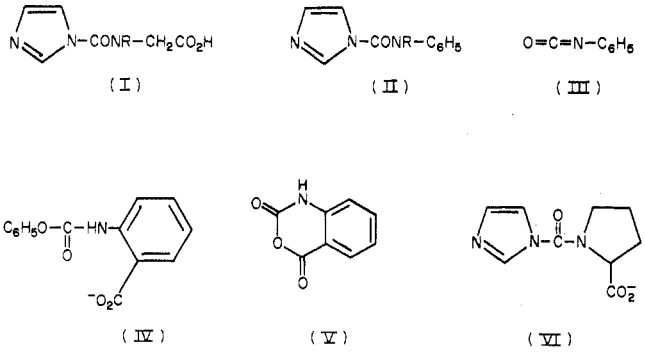
Glycine in an aqueous imidazole buffer has been shown[1] to react with carbonyldiimidazole to yield initially *N*-[imidazolyl-(1)-carbonyl]glycine (I), R = H. This intermediate



slowly polymerizes to yield oligoglycines. The suggested route for this polymerization is via a *N*-carboxyanhydride. The present report presents evidence that the cyclization of I proceeds via an addition–elimination, intramolecular acyl transfer reaction[2] involving a carbamylimidazole.[3,4] In general 1-substituted carbamylimidazoles react with nucleophiles via

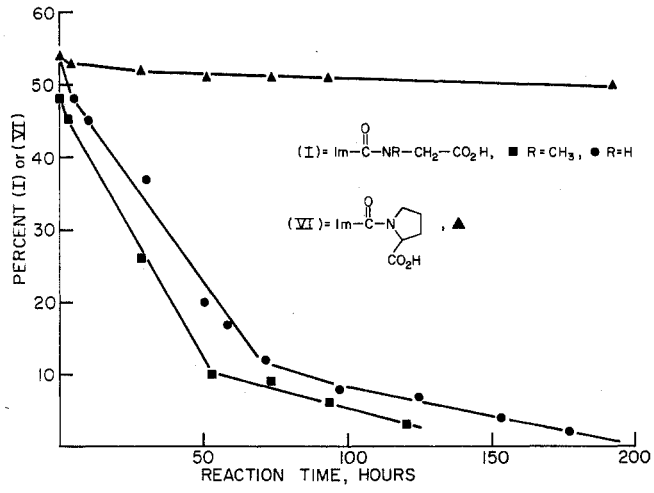


Figure 1. Plot of survival of I and VI as a function of time.

an intermolecular elimination–addition mechanism. Staab and Benz,[5] for example, showed that II, R = H, reacts with amines, while II, R = CH_3, does not. They concluded from this that II, R = H, reacts via its isocyanate (III). Kinetic evidence has been presented[3,4] to show that the hydrolysis of II, R = H, also proceeds via an intermolecular elimination–addition acyl transfer mechanism involving an isocyanate. In this case, II, R = CH_3, hydrolyzes much slower than II, R = H. *N*-Aryl carbamates, like the carbamylimidazoles, undergo hydrolysis[6] via the elimination–addition route. However, phenyl *N*-(*o*-carboxyphenyl)carbamate (IV) follows an addition–elimination route[7] via isatoic anhydride (V). This reaction is analogous to the one which we have discovered.

Carbonyldiimidazole (0.4 M) was added to 0.1 M [α-^{14}C]-glycine, [α-^{14}C]sarcosine, and [α-^{14}C]proline (specific activity in each case, 0.05 mCi/mmol) in imidazole buffer (0.5 M) at pH 7.0 and 0 °C. The carbamylimidazole intermediates I, R = H, I, R = CH_3, and VI were obtained in 84, 48, and 98% yield, respectively, from the three amino acids. The intermediates were identified by their electrophoretic behavior in systems II and III (unit negative charge[1,4,8]) and by their positive reaction with a sulfanilamide reagent.[1,9] As shown in Figure 1, the lifetime of I, R = CH_3, is strikingly similar to that of I, R = H, when the two are formed in approximately the same initial yield. By contrast, VI is extremely long lived.

To determine the rate of appearance of the sarcosine peptides, the origins of the system II electrophoreses papers were cut out, eluted with deionized water, and rerun in system I. The sarcosine peptides, which have almost the same mobility value as sarcosylglycine (see below), appeared at a rate similar to that found for glycine (see Figure 2). To further confirm this the previous experiment was modified as follows. Unlabeled amino acids were used to generate the initial intermediates, I and VI. Immediately after the dissolution of the carbonyldiimidazole at 0 °C, pH 7.0, [α-^{14}C]glycine (0.2 M glycine, 0.5 M imidazole, pH 6.85, specific activity 0.05 mCi/mmol) was added to each of the reaction mixtures in twofold molar excess. The appearance of aminoacylglycine with time is shown in Figure 3. Again, sarcosine behaves like glycine whereas proline is much less reactive. Cochromatography in solvent system IV and coelectrophoresis in solvent system I with authentic samples of sarcosylglycine and prolyglycine were used to establish the nature of the peptides generated in the above experiments.

There are three reasonable mechanisms for the formation of a *N*-carboxyanhydride from VII, R = H. By analogy with the behavior[7] of compound IV the addition–elimination route (2) involving direct closure of VII to the *N*-carboxyanhydride