of the quantum yields for the O-methyl and S-methyl compounds suggests that the photochemical processes are similar.[17] Product differences are determined in subsequent free-radical reactions.

In conclusion, these observations demonstrate an extremely rapid and efficient capture of an aryl radical by a neighboring sulfide group. The chemical consequence of this capture is an apparent displacement reaction at sulfur.

(17) This line of reasoning is not rigorous and would be incorrect if both compounds were photolyzed with quantum yields of unity. The S-methyl and O-methyl compounds, however, yield iodine with a quantum yield of ca. one-half that of ethyl iodide under comparable conditions. Although several values have been reported for the quantum yield for ethyl iodide in solution, the number is certainly less than one.[18] A quantum yield of 0.08 has been reported for the formation of iodine from 4-iodobiphenyl.[18]

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Displacement Reactions on 2-Acetyl-3,4-dimethylthiazolium Iodide

Sir:

2-Acetyl-3,4-dimethylthiazolium iodide (I) serves as a model for 2-acetylthiamine, an intermediate in the phosphoketolase and α-keto oxidase reactions for which thiamine pyrophosphate is a cofactor.[1] Compound I has been prepared and noted to be unstable in aqueous or alcoholic solution[2] and to undergo reaction with water, hydroxylamine, and mercaptide ions to yield acetic acid, acethydroxamic acid, and thiolacetates, respectively.[3] Also, 2-benzoyl-3-methylthiazolium salts readily undergo solvolysis in methanol to give a 68% yield of methyl benzoate.[4] Aside from these few observations no one has carried out a general study of the susceptibility of I to nucleophilic attack nor have any kinetic studies of the displacement of the acyl group from I been reported. In the present communication we describe studies on the hydrolysis and hydroxylaminolysis of I; these studies provide an understanding of the nature of the acyl group of 2-acetylthiamine.

The hydrolysis of I was studied at 30° in water at an ionic strength of 1.0 (with KCl) by observing its conversion to 3,4-dimethylthiazolium ion at 292 mμ with the aid of a Gilford Model 2000 spectrophotometer or a stopped-flow spectrophotometer.[5] At each pH the observed pseudo-first-order rate constant (k_{obsd}, min^{-1}) was determined at ten buffer concentrations. Since the buffers did not influence the value of k_{obsd}, the value of the first-order solvolysis constant (k_1, min^{-1}) at each pH was taken as the average of the ten k_{obsd} constants. Buffers employed were: acetate (pH 4.07–5.18), succinate (pH 5.68), imidazole (pH 6.40–7.72), and Tris (pH 8.35–8.95). In Figure 1 are plotted the values
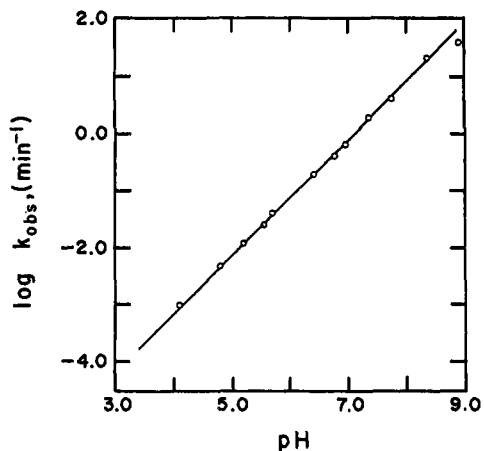
(1) For a review of the literature see: T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. II, W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter 8.
(2) R. Breslow and E. McNelis, *J. Am. Chem. Soc.*, **82**, 2394 (1960).
(3) K. Daigo and L. J. Reed, *ibid.*, **84**, 659 (1962).
(4) F. G. White and L. L. Ingraham, *ibid.*, **82**, 4114 (1960); **84**, 3109 (1962).
(5) T. C. French, S. J. Benkovic, and T. C. Bruice, *Rev. Sci. Instr.*, **36**, 860 (1965).

Figure 1.

of log k_1 vs. pH. It should be noted that the experimental points provide a precise fit to the theoretical line of slope 1.00 anticipated for a specific base catalyzed reaction and that the specific base rate law holds over 10^5 in hydrogen ion activity (a_H).

From the knowledge that specific base catalysis predominates to pH 3 (and presumably to even lower pH values since the rate of hydrolysis of I is quite slow at pH values more acidic than 3) and that the nucleophilic species of the buffers employed do not enhance the rate of disappearance of I from solution, we conclude that the mechanism of hydrolysis of I is that shown in Scheme
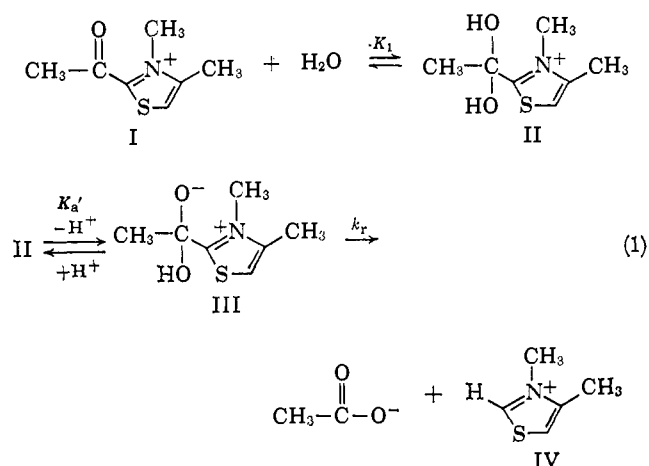
Scheme I

I. For Scheme I in the pH range below pK_a'

$$-\frac{d[I]}{dt} = \left[\frac{k_r K_1 K_a'}{K_w(K_1 + 1)}\right][OH^-]([I] + [II]) \quad (2)$$

where K_w is the autoprotolysis constant for water at 30°. Comparison of (2) to the experimental rate law (3) establishes the second-order rate constant for alkaline

$$-\frac{d[I]}{dt} = k_{OH}[OH^-]([I] + [II]) \quad (3)$$

hydrolysis (k_{OH}) to be

$$k_{OH} = \frac{k_r K_1 K_a'}{K_w(K_1 + 1)} = 5.64 \times 10^{+6} \text{ l. mole}^{-1} \text{ min}^{-1} \quad (4)$$

That k_{OH} could not represent the second-order rate constant for direct nucleophilic attack of [OH$^-$] on the

acyl carbonyl carbon, as in simple ester hydrolysis, is supported by the fact that if the acyl carbonyl were greatly susceptible to nucleophilic attack then the basic species of the buffers (particularly imidazole and Tris) would be anticipated to be nucleophiles as in the case of p-nitrophenyl acetate.[6,7] That hydration of the ketone could not be rate determining is also supported by the lack of effect of the buffer anions as general bases since ketone hydration is known to be quite susceptible to general base catalysis (for a compilation of references see ref 9). Carbonyl compounds whose hydrolysis follow the scheme of (1) are the electron-deficient ketones[8,9] in whose class I most logically falls.

In hydroxylamine buffers at constant pH the rate of disappearance of I from solution decreases with increase in concentration of NH_2OH (but is independent of NH_3^+-OH), reaching a constant minimum value. A reaction scheme in accord with this result is that of

$$I + OH^- \xrightarrow{k_{OH}} CH_3COO^- + IV$$

$$I + NH_2OH \xrightarrow{k_N} CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-NHOH + IV$$
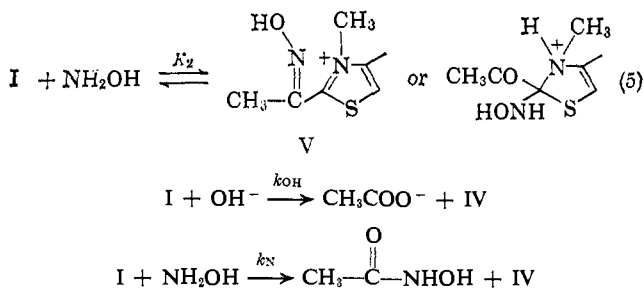
for which

$$\frac{-d[I]}{dt} = \left[\frac{k_{OH}[OH^-] + k_N[NH_2OH]}{1 + K_2[NH_2OH]}\right][T] \quad (6)$$

where $[T] = [I] + [II] + [V]$ (i.e., the amount of [I] added to the solution at t_0). From the best fit of (6) to the experimental data (1620 IBM computer) the value of $k_N = 1.117$ l. mole^{-1} min^{-1} and $K_2 = 100$ mole^{-1}. A comparison of determined values of k_{obsd} (pH 6.04) for the disappearance of I in the presence of hydroxylamine to the values of k_{obsd} calculated from (6) are provided in Table I. Evidence for the ability of hydroxylamine to react at the 2 position of 2-

Table I. Comparison of Calculated (Eq 6) and Determined Values of the Pseudo-First-Order Rate Constants for the Disappearance of I[a]

N_T, M	$k_{obsd} \times 10^2$, min^{-1}	
	Calcd	Found
0.00	8.80	8.90
0.01	6.24	6.22
0.02	4.96	5.03
0.03	4.19	4.19
0.04	3.68	3.70
0.05	3.31	3.36
0.06	3.04	2.98
0.07	2.82	2.90
0.08	2.65	2.60
0.09	2.51	2.44
0.10	2.40	2.33

[a] As a function of $N_T = (NH_2OH + NH_3^+OH)$ concentration (pH 6.04; $\mu = 1.0$ with KCl, solvent water; $T = 30°$).

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(7) M. L. Bender and B. W. Turnquest, ibid., 79, 1656 (1957).
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acylthiazolium compounds has been found in biochemical studies.[10]

The reactions 5 are again those anticipated of an electron-deficient ketone. The ability of NH_2OH to act as a nucleophile toward the carbonyl carbon of I to yield a hydroxamate and an oxime or addition compound to the thiazole ring compared to the inability of the similarly basic imidazole to act as a nucleophile may be easily rationalized on the basis that bases exhibiting the α effect[11] are better nucleophiles than anticipated from their pK_a' values and provide kinetically more favorable and thermodynamically more stable derivatives (as V).[12] It should be concluded that the "high energy" 2-acetylthiamine shares with the also biologically important thioesters[13] the formation of kinetically important tetrahedral intermediates. This feature must be taken into account in the formulation of enzymic mechanisms for acyl transfer reactions involving 2-acetylthiamine. Further work on the mechanism of reactions of I is in progress.

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(12) T. C. Bruice and L. R. Fedor, ibid., 86, 4886 (1964).
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Structure of the Initial Ozone–Olefin Adduct

Sir:

Evidence that initial ozonides (ozone–olefin adducts)[1] actually exist has recently been obtained by Criegee and Schröder[2] and Greenwood[3] for certain *trans* olefins. There has been no proof offered, however, as to whether the structures of these substances are of type IV or V.
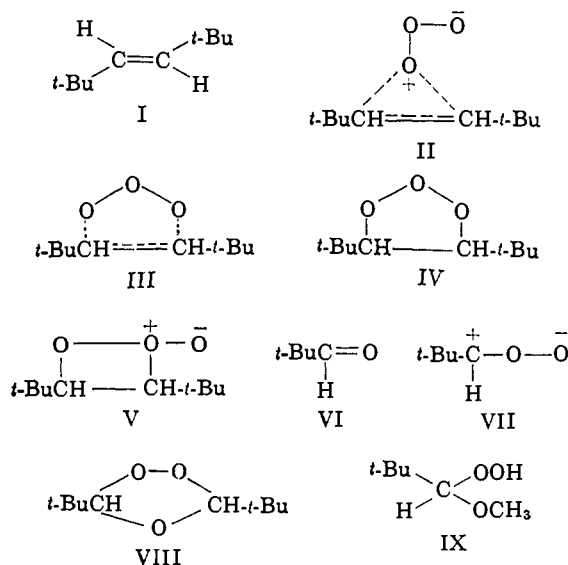
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