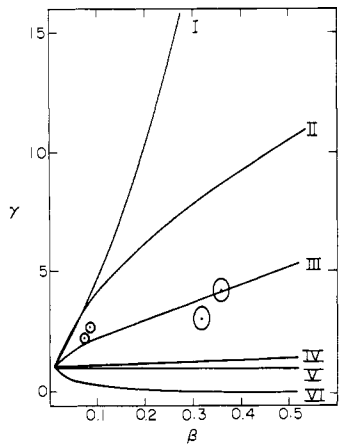

Figure 1. Relations between product isotopic abundance ratios β and γ (see text). The six curves are for all possible combinations of isotopically labeled sites (S) and leaving groups (L); S = 1, 2, and 3 and L = 1, 2, and 3 for CF_3, CF, and CF_2, respectively. There are many possible ways to generate each curve: typical examples are (I) $S = 1$, $L = 2$; (II) $S = 1 + 2$, $L = 1$ or 3; (III) $S = 1$, $L = 1$, 2, or 3; (IV) $S = 1$, $L = 1$ or 3; (V) $S = 1$, $L = 1 + 2 + 3$; (VI) $S = 1$, $L = 1$. The data points were obtained for 0.5-torr perfluoropropene following irradiation at 1004 cm^{-1} (small circles) and 995 cm^{-1} (large circles).

used to determine both the ratio of carbon-13 to carbon-12 in the products [$\beta = (2I^{83} + I^{82})/(2I^{81} + I^{82})$] and a suitably defined peak height distribution factor [$\gamma = (I^{82})^2/(4I^{81}I^{83})$].

The factors γ and β may be related through an intimate description of the reaction mechanism. In the present case this description is complicated as no normal coordinate analysis has been performed upon perfluoropropene,[9] and we are therefore unable to state unequivocally which specific site or sites are isotopically labeled. However, we shall see below that an analysis of the kinetics is not precluded by this lack of information. It would have been considerably simplified though if the assignment of the vibration had been made. We have proceeded by melding all possible combinations of selectively labeled site or sites with all possible combinations of leaving group or groups. There are then six possible relationships between γ and β for any value of the primary selectivity (we are able to vary this selectivity by making small changes to the irradiation frequency). These have been calculated and are displayed in Figure 1. To give a trivial example of this procedure: curve V corresponds to the unlikely mechanism $C_3F_6 \rightarrow 3CF_2$; in this case $\gamma = 1$, independent of labeled site and β. Fortunately, the experimental data points are consistent with only one of the six curves. This curve (III) is pertinent to either of two scenarios: either (i) all three carbon atoms have equivalent isotope shifts or (ii) all three carbon atoms are equally likely to provide the leaving group. We consider the first possibility to be unlikely, and the only reasonable transition state to support the second finding is the cyclic intermediate:

$$C_3F_6 \xrightarrow{nh\nu} [CF_3CFCF_2^* \rightleftharpoons [c\text{-}C_3F_6]] \rightarrow CF_2 + C_2F_4$$

We have demonstrated that isotopically selective laser-driven dissociation of natural abundance material can yield significant topological information. In the present case this information was gleaned in the absence of a precise normal coordinate description of the vibration excited, although such description would have further simplified the data analysis. Wide exploitation of this technique should be possible.

Supplementary Material Available: A full description of the reaction mechanisms considered and a detailed derivation of one of the curves in the figure (7 pages). Ordering information is given on any current masthead page.

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Hydroxide Ion as a Catalyst for Nucleophilic Substitution of Thiamin Analogues by Thiolate Ions. A Rival for Sulfite Ion

John A. Zoltewicz* and Georg Uray

Department of Chemistry, University of Florida Gainesville, Florida 32611

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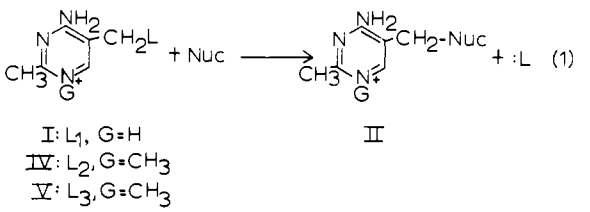
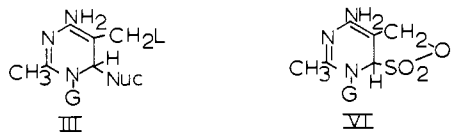
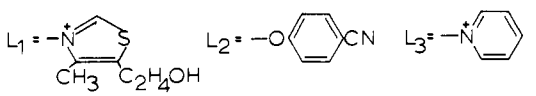
Nucleophilic substitution of thiamin (I, vitamin B_1) by sulfite ion to give sulfonate II (Nuc = SO_3^-) and a thiazole leaving group (L_1) (eq 1) is a characteristic reaction of the vitamin and is often regarded as unique. Only recently has a mechanism been established for this old reaction:[1] sulfite ion adds to protonated substrate to give one or more intermediates such as III (Nuc = SO_3^-, G = H) which then react with a second sulfite ion to lead to product.[2] Kinetic data show under special conditions the required second-order dependence on sulfite ion for thiamin[3] and also for a thiamin analogue.[4]







We now report that hydroxide ion behaves much like sulfite ion when reacting with thiamin analogues. Both nucleophiles react by a similar mechanism.

Thiamin analogues IV and V contain *p*-cyanophenoxide ion and pyridine leaving groups, respectively. Both have a pyrimidine ring made electrophilic by quaternization.[5] In alkaline solution they undergo hydrolysis (eq 1). Spectrophotometrically obtained pseudo-first-order rate constants show a first-order dependence on hydroxide ion; there is no significant buffer catalysis (Table I). Thiamin under comparable conditions undergoes hydrolytic opening of its thiazolium ring[6-8] rather than substitution.

Hydrolysis products were established by using ^1H NMR. Leaving groups are easily identified. Comparison of chemical shifts with those for authentic II (Nuc = OH[9]) identifies the pyrimidine ring. The nature of the nucleophile attached to II is most interesting. When either substrate is hydrolyzed in a PO_4^{3-} buffer, a phosphate ester is formed (Nuc = OPO_3^{2-}), easily characterized by its 6.5-Hz coupling (δ 4.7) between the methylene

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(3) Doerge, D. R.; Ingraham, L. L. *J. Am. Chem. Soc.* **1980**, *102*, 4828.
(4) Zoltewicz, J. A.; Uray, G.; Kauffman, G. A. *J. Am. Chem. Soc.* **1980**, *102*, 3653.
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Table I. Conditions and Results of the Hydrolysis of Thiamin Analogues at 25.0 °C and 1.0 M Ionic Strength[a] in the Presence and Absence of *p*-Nitrobenzenethiolate Ion[b]

[substrate]$_0$, M[c]	pH	[buffer base], M	[$^-SC_6H_5$-NO_2]$_0$, M	k_2, M^{-1} s^{-1}	sulfide[d,e] product, %
IV					
	9.65	0.010 CO_3^{2-}		0.298	
	11.04	0.02 PO_4^{3-}		0.307	
2.48×10^{-3}	11.48	pH-stat		0.317	
	12.54	satd $Ca(OH)_2$		0.316	
4.78×10^{-6}	11.04	0.02 PO_4^{3-}	1.1×10^{-5}	0.286	55
2.39×10^{-5}	11.04	0.02 PO_4^{3-}	5.6×10^{-5}	0.277	80
2.39×10^{-5}	12.54	satd $Ca(OH)_2$	5.2×10^{-5}		35
V					
	9.30	0.010 CO_3^{2-}		2.66	
	10.34	0.050 CO_3^{2-}		2.59	
	10.75	0.24 CO_3^{2-}		2.33	
4.70×10^{-5}	9.89	0.005 CO_3^{2-}	5.5×10^{-5}	2.83	>90
1.59×10^{-4}	10.34	0.050 CO_3^{2-}	1.9×10^{-4}	3.05	>90
7.3×10^{-4}	11.04	0.02 PO_4^{3-}	7.3×10^{-4}		>90
4.7×10^{-5}	11.04	0.02 PO_4^{3-}	7.2×10^{-5}		75
9.4×10^{-6}	11.04	0.02 PO_4^{3-}	1.4×10^{-5}		45

[a] Maintained with KCl. [b] Wavelengths for kinetic studies: 273 for IV and 255 or 310 nm for V. Second-order rate constant is given by $k_\Psi/[OH^-]$; $pK_w = 14.00$. [c] Between 2 and 9×10^{-5} M unless indicated otherwise. [d] The change in the thiolate anion concentration at 406 nm (ϵ 14 800) measures the amount of sulfide formed. [e] For rate constant ratios in keeping with values suggested here see: Cho, M. J.; Pitman, I. H. *J. Am. Chem. Soc.* 1974, *96*, 1843.

group and phosphorus.[10] Significantly, although there is no kinetic dependence on PO_4^{3-}, it is present in the product. In carbonate buffer II is an alcohol, resulting indirectly from decarboxylation of a carbonate monoester or directly from reaction with solvent.[11]

Competition experiments with *p*-nitrobenzenethiolate ion are most revealing. When this nucleophile is present to about the same extent as either substrate, a new product forms; II has this nucleophile bonded to its methylene group as a sulfide. Most significantly, although sulfide may be produced as a major product, second-order rate constants for hydrolysis are unaffected (Table I). Moreover, the amount of sulfide formed shows no significant dependence on the leaving group in spite of a 9-fold variation in hydrolysis rate constants between substrates. Thus, hydroxide ion catalyzes the formation of sulfide substitution product.

Identification of the sulfide product is based on its ultraviolet spectrum and its subsequent reactivity toward sulfite ion. Sulfide product produced at pH 11 in a reaction with V was diluted with sulfite ion and its reactivity measured. The rate constant for substitution by sulfite ion (eq 1) is essentially the same as that ($0.0162\ M^{-1}\ s^{-1}$, 25.0 °C, 340 nm) found for authentic sulfide in a separate experiment.

Preparative experiments also provide evidence for a sulfide product. Both substrates (100 mg) when added to a small excess of *p*-methoxybenzenethiolate ion in 0.1 M hydroxide ion give product II (Nuc = $SC_6H_4OCH_3$-*p*) in 90% isolated yield.[12]

Our results clearly eliminate a single step S_N2 mechanism of substitution. Instead, one or more intermediates must be present which are trapped by thiolate ion or PO_4^{3-} *after* the rate-limiting step. Hydroxide ion reacts with starting material before or during the rate-limiting step to initiate the process.

It seems likely that sulfite and hydroxide ions both add to the pyrimidine ring to give similar intermediate III. While some may have wished to attribute "unique" properties to sulfite ion because of its ability to form sultone intermediate VI from III, this view is untenable because hydroxide ion cannot form such a structure. Yet reactivities of the two ions are quite similar toward a substrate with a common leaving group. This is revealed by a comparison of second-order rate constants for the hydrolysis of V and the sulfite ion substitution of a derivative of V having G = H.[2] Because yields of thiolate ion trapped products do not depend significantly on the identities of the two leaving groups, it seems probable that the leaving group has departed before the second nucleophile attacks, i.e., III eliminates its leaving group before reacting with a second nucleophile. Hence, the likely mechanism is one in which nucleophile adds to pyrimidine ring present in its cationic form, then follows loss of the leaving group, addition of the nucleophile which appears in the product, and rearomatization.

The multistep pathway of substitution found for thiamin and its analogues with sulfite and now with hydroxide ion suggests this mechanism is a general one. Our observations raise the question of whether thiaminase II, thiamin hydrolase,[13] reacts similarly.

Acknowledgment. Our work was kindly supported by Grant AM-17442 from the National Institute of Arthritis, Metabolism and Digestive Diseases.

(10) Gaydou, E. M.; Llinas, J. R. *Org. Magn. Reson.* **1974**, *6*, 23.

(11) Carbonium ions react with water by a general base-catalyzed process. See Ritchie, C. D., Wright, D. J., Huang, D-S., Kamego, A. A. *J. Am. Chem. Soc.* **1975**, *97*, 1163 and references given therein.

(12) Nitrothiolate ion was selected for kinetic studies because of its favorable ultraviolet spectrum, while the methoxy ion gives a highly water-insoluble product.

(13) Evans, W. C. *Vitam. Horm. (N.Y.)* **1975**, *33*, 467.

Identification of a Biradical as the Reactive Form of the 2-Isopropylidenecyclopentane-1,3-diyl Singlet Species

Mark R. Mazur and Jerome A. Berson*

Department of Chemistry, Yale University
New Haven, Connecticut 06511

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The chemistry of 2-isopropylidenecyclopentane-1,3-diyl (**1**) can be dissected into reactions of two molecular spin states, a singlet and a triplet.[1-3] Although the triplet (**1**-T) is clearly a biradical, a subtle and vexatious uncertainty has veiled the true nature of the singlet species, which might be formulated as a biradical, **1**-S, or as its bicyclic valency tautomer, 5-isopropylidenebicyclo-[2.1.0]pentane (**2**). The recent synthesis of the hydrocarbon **2**,

1 2 3

a thermally labile but observable substance,[4] now makes possible a kinetically based identification of the biradical **1** rather than the bicyclic hydrocarbon **2** as the reactive entity in the cycloadditions of the singlet with olefins.

Thermal decomposition of hydrocarbon **2**, prepared[4] by photolysis of a degassed acetone solution of diazene **3** in the absence of a trapping olefin, can be followed by nuclear magnetic resonance (NMR) spectroscopy at 270 MHz. The reaction occurs with clean first-order kinetics and gives the previously reported[1] dimers of **1**. The temperature dependence of the first-order rate constant, measured at eight points from −58 to −26 °C, gives the Arrhenius parameters E_a = 13.7 kcal/mol and log A = 9.6 (A in s^{-1}). These

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