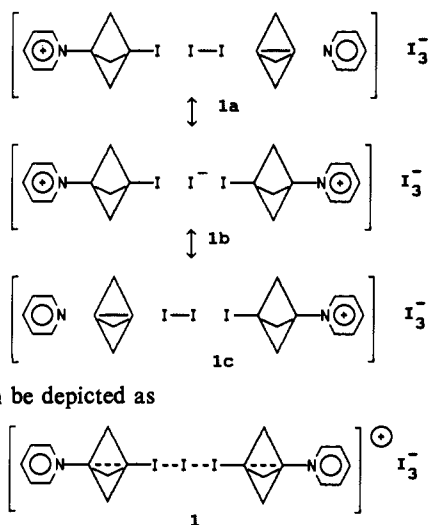
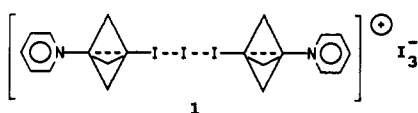


some kind of interaction. Other structural characteristics of this molecule, such as interatomic distances and angles in the pyridine ring<sup>10</sup> and the bicyclo[1.1.1]pentane moiety,<sup>2</sup> are normal.

From all these data it is clear that the real structure of the compound is more complex and may be represented as the resonance hybrid of structures (1a ↔ 1b ↔ 1c):



which can be depicted as



The extremely short nonbonding intercage distance in 1 is then due to contributions from resonance structures 1a and 1c, each of which contains one full ([1.1.1]propellane-type) C<sub>1</sub>-C<sub>3</sub> bond, as well as the short I-I-I distance between the two cage units.

We believe that such substituted azinium salts may well deserve serious attention as possible components for the creation of materials with unusual electronic properties.

**Supplementary Material Available:** Tables of additional X-ray data including coordinates, bond distances, bond angles, and thermal parameters for 1 (8 pages). Ordering information is given on any current masthead page.

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## Kinetic Isotope Effects on the Hydroxide Ion Catalyzed Enolization of Acetone: Relationship between Deuterium and Tritium Isotope Effects

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The hydroxide ion catalyzed enolization of acetone is a prototype ketone ionization reaction, and it is disturbing therefore that deuterium and tritium isotope effects reported for this process<sup>1</sup> give a Swain-Schaad exponent relating the two effects, eq 1, that is anomalously low:  $x = 1.08$ . This value is much less than  $x$

$$(k_H/k_D)^x = k_H/k_T \quad (1)$$

= 1.44 originally predicted by Swain and Schaad on the basis of

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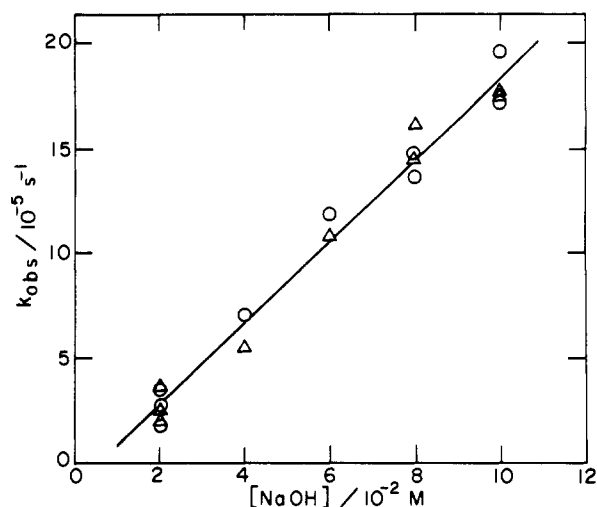


Figure 1. Relationship between sodium hydroxide concentration and observed rate constants for tritium exchange between acetone and water in aqueous solution at 25 °C, ionic strength = 0.10 M (NaCl), measured by monitoring the acetone (O) and water (Δ) tritium NMR signals.

a zero-point energy formulation of isotope effects,<sup>2</sup> and it is well outside the limits,  $x = 1.33-1.58$ , required by more complete theory.<sup>3</sup> Calculations on model systems<sup>4</sup> also indicate that exponents as low as  $x = 1.08$  are quite improbable. This discrepancy in a simple chemical system is especially serious because deviations from the Swain-Schaad relationship have been used lately to diagnose tunneling in enzyme-catalyzed reactions.<sup>5</sup> We have reexamined the acetone system using a new approach to determining the tritium rate constant,  $k_T$ , and also paying particular attention to the efficiency of the bromine scavenging method used to determine the protium rate constant,  $k_H$ . With this reexamination, we now obtain isotope effects that give a Swain-Schaad exponent in complete agreement with theory.

The original tritium isotope effect was based upon rates of detritiation of labeled acetone in aqueous solution determined by a technique that involved a difficult separation of acetone from water.<sup>1</sup> We have chosen to use tritium NMR spectroscopy to monitor the exchange of tritium between acetone and water directly in situ,<sup>6</sup> thus avoiding the troublesome acetone-water separation.

Acetone-*t*<sub>1</sub> (1.2 Ci mmol<sup>-1</sup>) was prepared by base-catalyzed exchange between acetone and tritiated water; the product gave a single tritium NMR signal at  $\delta = 2.1$  ppm. When this substance was dissolved in dilute aqueous sodium hydroxide solution, this signal decayed and another resonance at  $\delta = 4.7$  ppm, attributable to H<sub>2</sub>O-*t*<sub>1</sub>, appeared. Changes in intensity of both signals obeyed the first-order rate law well, and least-squares fitting to exponential functions gave observed rate constants for the rise and the decay which, as Figure 1 shows, agree well with each other. These rate constants increase linearly with sodium hydroxide concentration (Figure 1), and least-squares analysis gives the hydroxide ion catalytic coefficient,  $k_{HO}^T = (1.95 \pm 0.07) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ . This is 20% lower than the value reported before.<sup>1</sup>

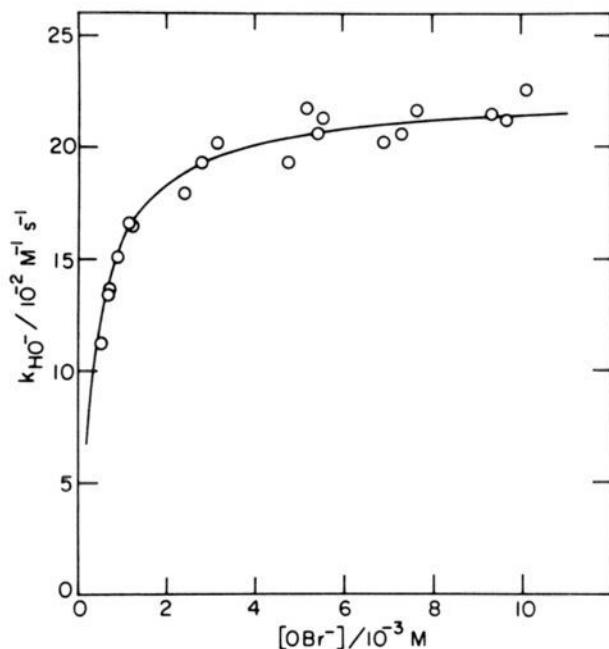
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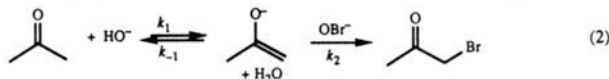
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**Figure 2.** Relationship between  $[OBr^-]$  and apparent rate constants for the enolization of acetone determined by bromine scavenging in aqueous solution at 25 °C, ionic strength = 0.10 M (NaCl).

In the original work,<sup>1</sup> hydroxide ion catalytic coefficients for the protium and deuterium reactions were determined by bromine scavenging of the acetone enolate ion as it formed, eq 2. This



technique requires the scavenging reaction to be sufficiently faster than re-formation of acetone,  $k_2[OBr^-] \gg k_{-1}$ , but it seems likely, now that  $k_{-1}$  is known,<sup>7</sup> that this condition was not fulfilled. We have found that apparent rate constants for the enolization of protioacetone, determined at scavenger concentrations normally used in enolization studies, depend on  $[OBr^-]$  as shown in Figure 2. This is the behavior expected under conditions of inadequate scavenging. Least-squares fitting of the data to the rate law that applies under these conditions, eq 3, gave the true enolization

$$k_{\text{obsd}} = k_1 / (1 + k_{-1}/k_2[OBr^-]) \quad (3)$$

catalytic coefficient  $k_{\text{HO}^-}^{\text{H}} (=k_1) = (2.24 \pm 0.03) \times 10^{-1} \text{ M}^{-1} \text{ s}^{-1}$  and the ratio  $k_{-1}/k_2 = (4.62 \pm 0.20) \times 10^{-4} \text{ M}$ . Combination of this ratio with the known value of  $k_{-1} (=5.0 \times 10^4 \text{ s}^{-1})$ <sup>7</sup> gives  $k_2 = (1.08 \pm 0.06) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ , which is consistent with a previous estimate of this rate constant,  $k = 1.4 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ .<sup>8</sup> Our new catalytic coefficient for the enolization of protioacetone is 40% greater than the value reported before,<sup>1</sup> and we conclude that inadequate scavenging did lead to errors in the previous study. This new catalytic coefficient for the protium reaction, when combined with our rate constant for tritioacetone, gives the isotope effect  $k_{\text{H}}/k_{\text{T}} = 19.2 \pm 0.7$ ; this is nearly twice the previously published result.<sup>1</sup>

There is available a value of the hydroxide ion catalytic coefficient for enolization of deuterioacetone that was obtained from mass spectrometric measurement of deuterium-exchange rates, and this rate constant is consequently not subject to errors introduced by inadequate scavenging.<sup>9</sup> When this result,  $k_{\text{HO}^-}^{\text{D}}$

$= (3.10 \pm 0.08) \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ , is combined with our value of  $k_{\text{HO}^-}^{\text{H}}$ , the isotope effect  $k_{\text{H}}/k_{\text{D}} = 7.24 \pm 0.21$  is obtained. Comparison of this with our newly determined tritium isotope effect gives the Swain-Schaad exponent  $x = 1.49 \pm 0.07$ ; this agrees well with Swain and Schaad's prediction,  $x = 1.44$ , and also falls within the range expected from higher level theory,  $x = 1.33-1.58$ .

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**Registry No.** Acetone, 67-64-1; deuterium, 7782-39-0; tritium, 10028-17-8.

### Cyclodextrin- $B_{12}$ , a Potential Enzyme-Coenzyme Mimic

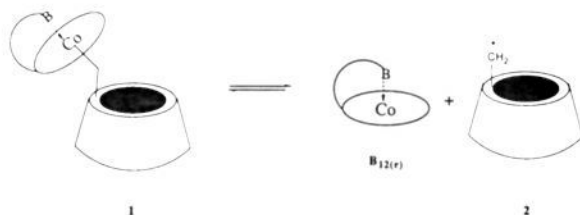
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Since it was suggested<sup>1</sup> that the homolysis of the carbon-cobalt bond of adenosylcobalamin coenzyme (coenzyme  $B_{12}$ ) was the first step in the process that led to product formation in its dependent enzymes, the study of its radical chemistry has been extensive.<sup>2</sup> The standard mechanism for rearrangements catalyzed by this coenzyme is as follows: (a) homolysis to form  $B_{12(r)}$  and the enzyme-bound deoxyadenosyl radical, followed by (b) hydrogen atom transfer from the bound substrate to this radical to form a substrate radical. Then (c) the derived substrate radical rearranges, followed by (d) hydrogen atom transfer back to reform the deoxyadenosyl radical, which then couples with  $B_{12(r)}$  to reform the coenzyme. Although a number of model systems exist that mimic some of the rearrangement steps of such processes,<sup>3</sup> there are not yet examples in which a substrate and  $B_{12}$  or a surrogate are bound together in a receptor site, such that intracomplex atom transfers to the carbon radical can mimic the opening stages of this general mechanism.

It seemed to us that the attachment of cobalamin by a direct cobalt-carbon bond to the primary carbon of  $\beta$ -cyclodextrin should lead to a compound (**1**) with very interesting potential. Homolysis of the carbon-cobalt bond would generate  $B_{12(r)}$  and a primary cyclodextrin radical (**2**) of a glucose unit<sup>4</sup> strongly related to the primary ribose radical formed from the true coenzyme. In water, hydrophobic substrates will bind into the cyclodextrin cavity, so that **2** could perform an intracomplex atom transfer to generate a substrate radical (Figure 1). We have prepared compound **1** and shown that its properties are very promising.



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