The synthesis of IIa and b, therefore, *unequivocally* establishes the  $\beta$ -configuration for the nucleoside bond in I. This, together with the data of Hanessian and Haskell,<sup>3</sup> establishes the anomeric linkages of amicetin to be as shown in structure I.

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## Kinetic Evidence for the Formation of a Tetrahedral Intermediate in the Aqueous Solvolysis of Ethyl Trifluorothiolacetate<sup>1</sup>

Sir:

A previous study provided kinetic evidence for the existence of tetrahedral intermediates in the reaction of methoxyl- and hydroxylamine with a series of thiol esters and lactones.<sup>1c</sup> In this communication we report kinetic evidence for the formation of a tetrahedral intermediate in the aqueous solvolysis of ethyl trifluorothiolacetate. This represents the first instance of the demonstration of a metastable intermediate in the reaction of a thiol ester with an oxygen nucleophile.

The hydrolysis of ethyl trifluorothiolacetate (temperature  $30^{\circ}$ ,  $\mu = 1 M$  with KCl) in water in the pH range 0-8 is kinetically described by (1). The pH-rate

$$v = [[1/(2.31 + 6.6a_{\rm H})] + (5.25 \times 10^5)a_{\rm OH}][\text{ester}]$$
(1)

profile (Fig. 1) was constructed from eq. 1 and the points were experimentally determined. The  $k_{obsd}$ values in the acid region of Fig. 1 were obtained by following the disappearance of ester at 244 m $\mu$  in dilute hydrochloric acid. The  $k_{obsd}$  values between pH 2.5 and 8.0 in Fig. 1 were obtained by extrapolation of linear plots of pseudo-first-order rate constants vs. total buffer concentration to zero buffer concentration, employing each of the buffers acetate, formate, phosphate, and imidazole at five concentrations at each pH. The relationship between rate and acidity from pH 0 to 6 is given by (2), which correctly predicts

$$v/[\text{ester}] = k_{\text{obsd}} = 1/(2.31 + 6.6a_{\text{H}})$$
 (2)

that a plot of  $1/k_{obsd}$  vs.  $a_{\rm H}$  is linear, with slope 6.6  $M^{-1}$  min. and intercept 2.31 min. Of many possible mechanisms considered,<sup>2</sup> one is consistent with the experimental data. This mechanism involves general-base-catalyzed nucleophilic attack of water at the ester bond and the unsymmetrical partitioning of a tetrahedral intermediate which collapses spontaneously to products and is converted back to ester by hydronium ion via general-acid catalysis (eq. 3).

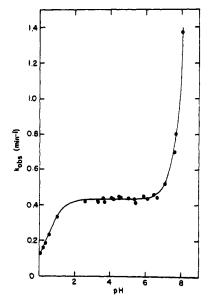


Fig. 1.—pH-rate profile for the solvolysis of ethyl trifluorothiolacetate in H<sub>2</sub>O at zero buffer concentration (30°;  $\mu = 1.0$ *M*). The solid line is constructed from eq. 1 and the points are experimentally determined values.

on whether one assumes steady state in T and TH or pre-equilibrium formation of T and TH, the rate ex-

$$CF_{3}COSC_{2}H_{5} + H_{2}O \xrightarrow[k_{1}, H_{3}O]{} CF_{3} - \stackrel{O}{\underset{k_{2}, H_{3}O^{+}}{\overset{k_{1}}{\longleftarrow}} CF_{3} - \stackrel{O}{\underset{k_{2}, H_{3}O^{+}}{\overset{k_{2}}{\longleftarrow}} CF_{3} - \stackrel{O}{\underset{k_{2}, H_{3}O^{+}}{\overset{k_{3}}{\longrightarrow}} CF_{3} - OH CF_{3}CO_{2}H + C_{2}H_{5}SH + H^{+} \downarrow \uparrow - H^{+} K_{a} OH (3)$$

$$CF_{3} - \stackrel{O}{\underset{OH}{\overset{K_{1}}{\longleftarrow}} CF_{3} - C - SC_{2}H_{5} (TH) OH (3)$$

pressions (4) or (5), respectively, can be derived.

$$v/[\text{ester}][\text{H}_2\text{O}] = k_{\text{obsd}} = \frac{k_1k_3}{k_3 + k_2 [\text{H}_3\text{O}^+]}$$
(4)  
= 1/[1/k\_1 + (k\_2/k\_1k\_3)[\text{H}\_3\text{O}^+]]

 $v/[ester][H_2O] =$ 

$$k_{\rm obsd} = \frac{k_3 k_1 K_a}{k_1 K_a + (k_2 K_a + k_1) [\rm H_3O^+]}$$
(5)  
= 1/[1/k\_3 + (k\_2/k\_1 k\_3 + 1/k\_3 K\_a) [\rm H\_3O^+]]

Either expression has the form of (2).<sup>3</sup> The steadystate derivation leading to (4) is preferred to the assumption of the pre-equilibrium formation of T and TH leading to (5). The preference is based on  $k_{\rm H_2O}/k_{\rm D_2O} = 3.3$  for the neutral water rate which corresponds to  $k_1$  in (4) or  $k_3$  in (5). No deuterium solvent kinetic isotope effect should be associated with the collapse of the tetrahedral intermediate. Also, the Arrhenius activation energy of 11.7 kcal. mole<sup>-1</sup>, determined for  $k_1$  in (4) or  $k_3$  in (5), is more consistent with the general-base-catalyzed attack of a water molecule at

<sup>(1)</sup> A detailed presentation of results will appear as Thiol Esters. IV. For parts I-III see (a) T. C. Bruice, J. J. Bruno, and W. S. Chou, J. Am. Chem. Soc., **85**, 1659 (1963); (b) L. R. Fedor and T. C. Bruice, *ibid.*, **86**, 4117 (1964); (c) T. C. Bruice and L. R. Fedor, *ibid.*, **86**, 738, 739, 4886 (1964).

<sup>(2)</sup> A detailed consideration of possible mechanisms will be given in Thiol Esters IV.

<sup>(3)</sup> A mechanism involving attack of hydroxide ion at the ester bond to form a tetrahedral intermediate which is converted to products by hydronium ion catalysis also gives a steady-state derivation which has the form of (2). However, it can be shown that the second-order rate constant for hydroxide attack would be ca.  $10^{14}$ , a value greater than the rate constant for a diffusion-controlled process.

the ester bond than the collapse of a metastable intermediate. More important is the observation that acetate and formate ions act as general-base catalysts and acetic acid and formic acid act as inhibitors of the neutral water rate. Thus in (3) acetic acid and formic acid can replace hydronium ion as general-acid catalysts and acetate and formate ions can replace water as general-base catalysts. Only a steady-state assumption allows the derivation of an equation consistent with the experimental data obtained in acetate and formate buffers. The value of  $k_{\rm H_2O}/k_{\rm D_2O}$  at  $a_{\rm H} = a_{\rm D}$ for acetate was determined to be 2.1. From (2) and (4)  $k_1 = 0.433$  min.<sup>-1</sup> and  $k_2/k_3$ , the partitioning coefficient, = 2.86. As would be predicted from (3),  $k_2/k_3$  increased in deuterium oxide solution to 4.95.

The reaction of ethyl trifluorothiolacetate with other oxygen nucleophiles as well as with nitrogen nucleophiles has been investigated and will be reported in detail. Whereas in the hydroxylaminolysis and methoxylaminolysis of thiol esters and lactones the partitioning is symmetrical, in both general-base and general-acid catalysis, the reaction discussed herein must involve unsymmetrical partitioning. On the basis of this study it is clear that the requirement of microscopic reversibility should not be confused with any requirement for symmetry.

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(4) Postdoctoral fellow of the Department of Biological Sciences, University of California, Santa Barbara.

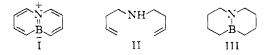
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## Synthesis and Nuclear Magnetic Resonance Spectrum of 10,9-Borazaronaphthalene<sup>1</sup>

Sir:

During the past six years a new series of heteroaromatic compounds has been reported in which boron atoms appear in six-membered aromatic rings.<sup>2</sup> We have now prepared one of the more interesting members of this series, 10,9-borazaronaphthalene (I), a compound isoelectronic with naphthalene but containing no boron-free aromatic rings.



Treatment of 1-chloro-3-butene (200 g.) with liquid ammonia (350 g.) in an autoclave at  $100^{\circ}$  gave a mixture of the known 3-butenylamine (61 g.) together with

di-3-butenylamine (II) (38 g.), b.p. 153-155°.3 Hydroboration of II (25 g.) with trimethylamine borane (15 g.) in boiling toluene gave octahydro-10,9-borazaronaphthalene (III, 2.8 g.), b.p. 73-75° (20 mm.), as a colorless oil which oxidized rapidly in air. Anal. Found: C, 68.6; H, 12.1; N, 10.8. The structure of III was confirmed by its mass spectrum and by its n.m.r. spectrum which showed peaks at  $\tau$  7.1, 8.5, and 9.1 in the ratio 1:2:1; the peak at low field corresponds to a methylene adjacent to nitrogen and that at high field to one adjacent to boron. Dehydrogenation of III (3.6 g.) over palladized charcoal at 300-350° gave, after chromatography on alumina, I (0.1 g), which after sublimation formed colorless plates, m.p. 41-43°. Anal. Found: C, 74.5; H, 6.3; N, 10.6. The high-resolution mass spectrum showed peaks at  $128.0782 \pm 0.0004$  and  $129.0743 \pm$ 0.0006 mµ. (Calcd. for C<sub>8</sub>H<sub>8</sub>NB<sup>10</sup>: 128.0786. Calcd. for C<sub>8</sub>H<sub>8</sub>NB<sup>11</sup>: 129.0750.)

10,9-Borazaronaphthalene forms colorless plates, resembling naphthalene in both appearance and odor. Its chemical and physical properties are consistent with its formulation as a new aromatic system, isomeric with 2,1-borazaronaphthalene,<sup>2</sup> and the proton n.m.r. spectrum is also consistent with this. It consists of a well-defined doublet centered at  $\tau$  2.28, a welldefined quartet at  $\tau$  3.36, and lines in the region  $\tau$ 2.5-2.8 that can be interpreted as a doublet centered at 2.67 and a quartet at 2.53. Evidently a ring current must be present since at least one pair of  $\beta$ protons shows a resonance in the "aromatic" region, and any inductive effects of nitrogen or boron would be small in the  $\beta$ -positions.

The low-field doublet must clearly be assigned to the 1- and 8-protons, adjacent to nitrogen; likewise the high-field quartet must be ascribed to the 2- and 7protons rather than the 3- and 6-protons, since all theories agree in predicting a much higher  $\pi$ -electron density at the 2- and 7-positions of I than at the 3and 6-positions and since no other effect could account for the large difference between the two pairs of  $\beta$ protons. The doublet at  $\tau$  2.67 must then be assigned to the 4- and 5-protons and the quartet at  $\tau$  2.53 to the 3- and 6-protons. The spacings of the multiplets are consistent with this assignment, the coupling constants for pairs of vicinal protons being  $J_{12} = 6.5$ ,  $J_{23} = 6.0$ , and  $J_{34} = 10.0$  c.p.s. Fine structure in the quartet at  $\tau$  3.36 indicates that there are also small long-range couplings.

If these assignments are accepted, some unexpected conclusions follow concerning the  $\pi$ -electron distribution in I. Data for other compounds (e.g., III) indicate that signals for protons  $\alpha$  to boron are shifted upfield relative to those  $\alpha$  to nitrogen by ca.  $\tau$  2, due to the inductive effects of nitrogen and boron; in I the difference ( $\tau$  0.39) between the 1- and 8-protons and the 4- and 5-protons is very much less than this. It seems clear that the  $\pi$ -electron density at the 1- and 8-positions of I must be much greater than at the 4and 5-positions. The position of the quartet at  $\tau$ 3.36 likewise indicates that the  $\pi$ -electron density must be much greater in the 2- and 7-positions than elsewhere, for inductive effects of nitrogen and boron must be small in the  $\beta$ -positions of I, while differential effects

(3) All new substances gave satisfactory analyses.

<sup>(1)</sup> This work was supported by grants from the Robert A. Welch Foundation and the National Institutes of Health, U. S. Public Health Service (Grant No. CA 07172-01).

<sup>(2)</sup> See M. J. S. Dewar in "Boron-Nitrogen Chemistry," R. F. Gould, Ed., Advances in Chemistry Series, No. 42, American Chemical Society, Washington, D. C., 1964.