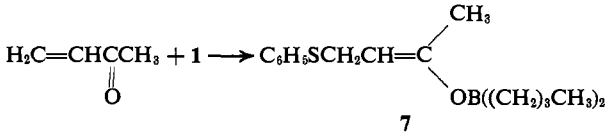
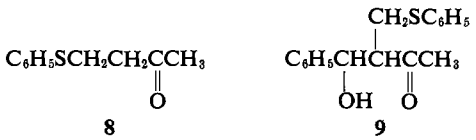
amount of **1** in ether at room temperature for 30 min to give the 1,4-addition product (**7**, pmr ($CCl_4$) $\delta$ 1.78 (s, 3 H), 3.36 (d, $J$ = 8 Hz, 2 H), 4.77 (t, $J$ = 8 Hz, 1 H)), which was hydrolyzed with aqueous methanol to 4-phenylthiobutan-2-one (**8**) in 86% yield.



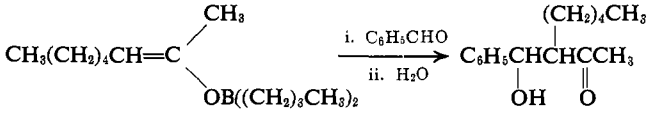
**7**



**8** **9**

The treatment of the above new vinyloxyborane-type intermediate (**7**) with benzaldehyde in ether at room temperature, followed by hydrolysis, afforded the corresponding $\beta$-hydroxy ketone (**9**, 92.5%, oil, ir 3440, 1700 $cm^{-1}$; pmr ($CCl_4$) $\delta$ 1.97 (s, 3 H), 3.20 (d, 2 H), 2.9–3.4 (m, 2 H), 4.80–4.95 (m, 1 H), 7.1–7.4 (m, 10 H)).

Similarly, it was found that the vinyloxyborane (**10**), prepared from tri-*n*-butylborane[3] and vinyl methyl ketone according to the method of Brown and Suzuki, *et al.*,[4] reacted with benzaldehyde to give diastereomeric $\beta$-hydroxy ketones **11a**, **11b** (3:1, separated with preparative tlc) in 91% yield (**11a**, oil, ir 3420, 1695 $cm^{-1}$; pmr ($CCl_4$) $\delta$ 0.6–1.8 (m, 11 H), 1.83 (s, 3 H), 2.70 (m, 1 H), 3.15 (s, 1 H), 4.70 (d, 1 H), 7.23 (s, 5 H); **11b**, oil, ir 3420, 1700 $cm^{-1}$; pmr ($CCl_4$) $\delta$ 0.6–1.8 (m, 11 H), 2.06 (s, 3 H), 2.73 (m, 1 H), 3.32 (s, 1 H), 4.56 (d, 1 H), 7.23 (s, 5 H)).



**10** **11a, b**

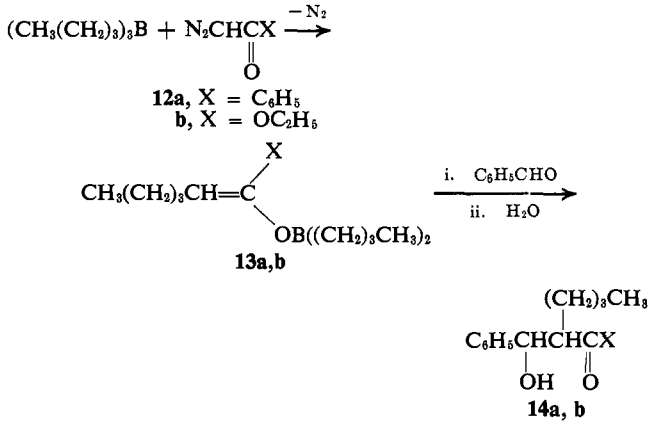
Vinyloxyboranes can also be produced by an alternative pathway from trialkylborane and diazo ketone (**12a**) or ester (**12b**). This reaction was developed by Hooz and his coworkers[5] and the structure of the intermediate, vinyloxyborane, was confirmed by Pasto and Wojtkowski by means of nmr and uv spectra.[6] The vinyloxyboranes (**13a,b**) thus obtained were further treated with benzaldehyde in THF at room temperature for 10 min followed by hydrolysis to afford the expected products, $\beta$-hydroxy ketone (**14a**, 98%, oil, ir 3440, 1660 $cm^{-1}$; pmr ($CCl_4$) $\delta$ 0.3–2.0 (m, 9 H), 3.4–3.9 (m, 2 H), 4.6–4.9 (m, 1 H), 6.8–7.4 (m, 8 H), 7.5–8.0 (m, 2 H)) and $\beta$-hydroxy ester (**14b**, 75%, oil, ir 3450, 1710 $cm^{-1}$; pmr ($CDCl_3$) $\delta$ 0.6–1.6 (m, 9 H), 1.18 (t, 3 H), 2.5–2.9 (m, 1 H), 3.05 (broad s, 1 H), 4.15 (q, 2 H), 4.75 (d, 1 H), 7.25 (s, 5 H)).

(3) Prepared from *n*-butylmagnesium bromide and boron trifluoride methyl etherate in ether.

(4) (a) A. Suzuki, A. Arase, H. Matsumoto, M. Itoh, H. C. Brown, M. M. Rogić, and M. W. Rathke, *J. Amer. Chem. Soc.*, **89**, 5708 (1967); (b) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **89**, 5709 (1967); (c) G. W. Kabalka, H. C. Brown, A. Suzuki, S. Honma, A. Arase, and M. Itoh, *ibid.*, **92**, 710 (1970); (d) H. C. Brown and G. W. Kabalka, *ibid.*, **92**, 712, 714 (1970).

(5) (a) J. Hooz and S. Linke, *ibid.*, **90**, 5936 (1968); (b) *ibid.*, 90, 6891 (1968); (c) J. Hooz and D. M. Dunn, *Chem. Commun.*, 139 (1969); (d) *Tetrahedron Lett.*, 3455 (1969); (e) *J. Amer. Chem. Soc.*, **91**, 6195 (1969).

(6) D. J. Pasto and P. W. Wojtkowski, *Tetrahedron Lett.*, 215 (1970).



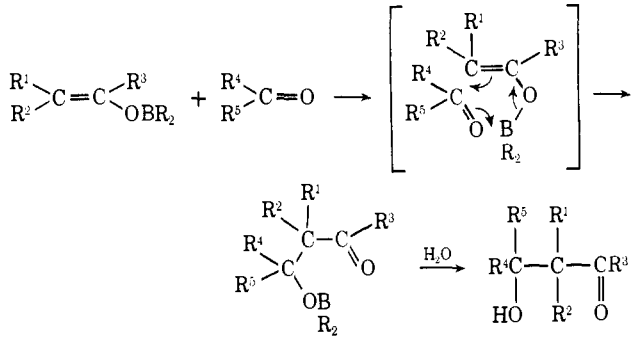
**12a**, X = $C_6H_5$
**b**, X = $OC_2H_5$

**13a,b**

**14a, b**

From the above findings, we considered that vinyloxyboranes reacted with carbonyl compounds according to Scheme I. Vinyloxyboranes should be very useful intermediates in organic synthesis because of their high reactivity with carbonyl compounds[7] and the ease of their preparation in many ways.[6,8,9] Further work is in progress to explore the full synthetic potential of this new reaction.

**Scheme I**



(7) We found that other aldehydes and ketones reacted with vinyloxyboranes in the same way (to be submitted for publication elsewhere).

(8) J. J. Tufariello, L. T. C. Lee, and P. W. Wojtkowski, *J. Amer. Chem. Soc.*, **89**, 6804 (1967).

(9) R. Köster and W. Fenzl, *Angew. Chem.*, **80**, 756 (1968).

**Teruaki Mukaiyama,* Katsuhiko Inomata, Masayoshi Muraki**
*Laboratory of Organic Chemistry, Tokyo Institute of Technology Ookayama, Meguro-ku, Tokyo, Japan*
*Received August 1, 1972*

## One-Proton Catalysis in the Deacetylation of Acetyl-$\alpha$-chymotrypsin

*Sir:*

The rate of deacetylation of acetyl-$\alpha$-chymotrypsin decreases linearly with the atom fraction of deuterium ($n$) in mixtures of protium and deuterium oxides (Table I, Figure 1) which shows that *one proton in the catalytic transition state* produces the solvent isotope effect $k_{H_2O}/k_{D_2O}$ = 2.4. Mechanisms involving multiple proton switches are thus excluded and any suspicion is removed that the moderate solvent isotope effects[1] in these reactions might arise only from changes in protein or substrate hydration or other sources involving small alterations in the binding states of many protons.

(1) M. L. Bender and G. A. Hamilton, *J. Amer. Chem. Soc.*, **84**, 2570 (1962); M. L. Bender, G. R. Schonbaum, G. A. Hamilton, and B. Zerner, *ibid.*, **83**, 1255 (1961).

**Table I.** Zero-Order Rate Constants for Deacetylation of Acetyl-α-chymotrypsin[a] at pH 7.5 and Equivalent[b] in Mixtures of Protium Oxide and Deuterium Oxide (Atom Fraction Deuterium $n$) at 25.00 ± 0.05°

| $n$ | $10^{11}v_n$,[c] $M$ sec$^{-1}$ |
|---|---|
| 0.000 | 2649 ± 3 |
| 0.175 | 2425 ± 11 |
| 0.261 | 2239 ± 4 |
| 0.398 | 2126 ± 11 |
| 0.485 | 1878 ± 7 |
| 0.497 | 2064 ± 32 |
| 0.583 | 1791 ± 14 |
| 0.745 | 1479 ± 13 |
| 0.765 | 1459 ± 10 |
| 0.995 | 1102 ± 24 |

[a] Generated by excess $p$-nitrophenyl acetate from α-chymotrypsin (Sigma 3× crystallized) at 0.2 mg/ml. [b] All solutions contained 0.7571 g/l. of Trizma Base and 3.7319 g/l. of Trizma-HCl buffer components. Because the pH–rate inflections for α-chymotrypsin respond normally to $D_2O$ ($\Delta pK \sim 0.6$),[1] this will maintain the pH(D) of all solutions at the same relative point on the pH(D)–rate profile. [c] Averages of two–five determinations (spectrophotometric appearance of $p$-nitrophenol at 400 nm), calculated from an extinction coefficient of 18,000 $M^{-1}$ cm$^{-1}$ for $p$-nitrophenoxide. Error limits are average deviations from the mean.

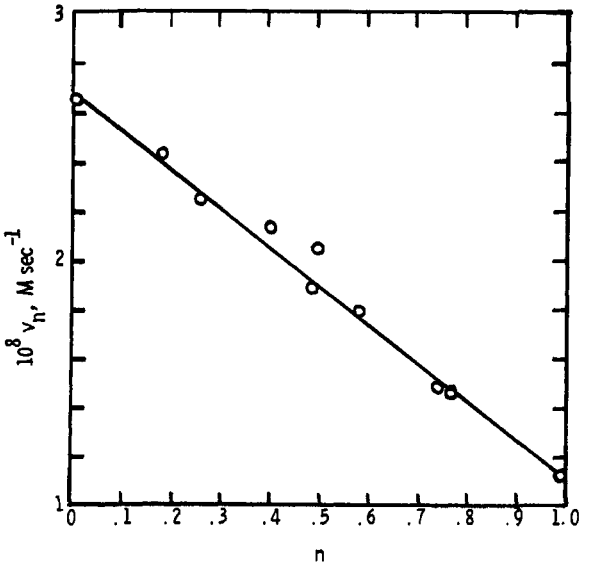



Figure 1. Velocities of deacetylation of acetyl-α-chymotrypsin *vs.* the atom fraction of deuterium in the solvent. The data are from Table I. The dependence is linear, indicating one-proton catalysis.

The linear fall-off in rate with increasing $n$ demonstrates one-proton catalysis because the rate $v_n$ in the mixed isotopic solvent is then just the weighted average of the rates in pure isotopic solvents ($v_0$ in pure $H_2O$ and $v_1$ in pure $D_2O$) as shown in eq 1, where $\phi^*$ is also known as an isotopic fractionation factor.[2]

$$v_n = nv_1 + (1 - n)v_0 = v_0(1 - n + nv_1/v_0) = v_0(1 - n + n\phi^*) \quad (1)$$

This is true only when each increment of deuterium produces a *proportional* increment in rate, which in turn is true only when a single transition-state hydrogenic site is "titrated" by deuterium. In a more general case, the rate is described[2] by eq 2, where $\phi_i^R$ and $\phi_i^T$ are isotopic fractionation factors for the $i$th exchangeable hydrogenic site in reactant and transition states, respectively. Equation 2 shows that any reasonable circumstance other than one-proton catalysis will necessitate a higher order polynomial fit of $v_n(n)$. For example, two-proton catalysis would yield a linear relation only if there were a highly fortuitous cancellation of $n$ dependences between the second-proton factor and the reactant-state contribution (denominator of eq 2).

$$v_n = v_0\prod_i(1 - n + n\phi_i^T)/(1 - n + n\phi_i^R) \quad (2)$$

This result is consistent with enzymic activated complexes[3] involving motion of a proton between the imidazole function of His-57 and the oxygen of a water molecule or the acyl or ether oxygens of acetylated Ser-195 as long as other protons are not substantially altered in binding state. It is also consistent with a rate-determining conformation change of the acyl enzyme[4] if a single-proton alteration accompanies this process. It is not consistent with the "charge-relay" mechanism[5] in which proton transfer between Asp-102 and His-57 is supposed to cooperate with general catalysis by the latter. This would constitute at least two-proton catalysis.

**Acknowledgment.** This research was supported by the National Science Foundation and the National Institutes of Health.

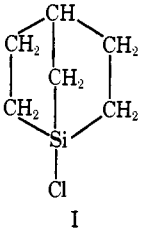
(2) A. J. Kresge, *Pure Appl. Chem.*, 8, 243 (1964); V. Gold, *Advan. Phys. Org. Chem.*, 7, 259 (1969).
(3) G. P. Hess in "The Enzymes," P. D. Boyer, Ed., Vol. III, 3rd ed, Academic Press, New York, N. Y., 1971, pp 217–234.
(4) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 310–312.
(5) D. M. Blow, J. J. Birktoft, and B. S. Hartley, *Nature (London)*, **221**, 337 (1969).
(6) (a) National Science Foundation Undergraduate Research Participant; Sterling College, Sterling, Kan.; (b) Graduate Honors Fellow; (c) holder of a Research Career Development Award of the National Institute of General Medical Sciences.

**Elizabeth Pollock,[6a] John L. Hogg,[6b] Richard L. Schowen*[6c]**
*Department of Chemistry, University of Kansas*
*Lawrence, Kansas 66044*
*Received September 12, 1972*

## Dramatic Stereochemistry Crossover to Retention of Configuration with Angle-Strained Asymmetric Silicon

*Sir:*

More than a decade has passed since we reported that the bridgehead chloride, 1-chloro-1-silabicyclo-[2.2.1]heptane (I), in sharp contrast to its carbon analog,




I

hydrolyzes rapidly in moist air, undergoes quantitative rapid titration of its Si–Cl bond with 0.1 $N$ alkali, and also is rapidly reduced by lithium aluminum hydride giving the Si–H compound.[1] The above very rapid reactions of I occur without destruction of the bridge-

(1) L. H. Sommer and O. F. Bennett, *J. Amer. Chem. Soc.*, **79**, 1008 (1957).