alkylborane derived from 1-hexene gave rise exclusively to ethyl octanoate; no product corresponding to reaction of the 2-hexyl groups was observed.[7] Reactions with hindered organoboranes require a reflux period in order to complete the nitrogen evolution. The results are summarized in Table II.

Table II. Conversion of Olefins into Ethyl Esters by Treatment of the Corresponding Trialkylboranes with Ethyl Diazoacetate

Olefin	Product[a,4]	Yield,[b] %
1-Hexene	Ethyl octanoate	83
1-Octene	Ethyl decanoate	78
Cyclopentene[c]	Ethyl cyclopentylacetate	58
2-Methyl-1-pentene[d]	Ethyl 4-methylheptanoate	40

[a] Structures were proven by direct comparison or satisfactory elemental analyses. [b] By glpc analysis. Yield based on the consumption of one alkyl group of R_3B using a 1:1 molar ratio of ethyl diazoacetate to R_3B. [c] An additional 30-min reflux period was required for complete nitrogen evolution. [d] An additional 2-hr reflux period was necessary to liberate nitrogen completely.

The procedure for the functionalization of 1-hexene into ethyl octanoate is representative. A solution of ethyl diazoacetate (20 mmol) in 15 ml of tetrahydrofuran was added, over a period of 20 min, to an ice-cooled, magnetically stirred solution of trihexylborane[3] (20 mmol) in tetrahydrofuran. The solution was kept at ice-bath temperatures for an additional 30 min, then stirred at room temperature for 2 hr. The ice bath was replaced, and water (5 ml) was added dropwise (exothermic). The reaction mixture was refluxed for 1 hr. Glpc analysis indicated an 83% yield of ethyl octanoate. The solution was concentrated, then poured into water and extracted with pentane. Distillation of the dried (Drierite) organic extract yielded 2.40 g (70%) of ethyl octanoate, identical in all respects with an authentic sample.

The reactions of organoboranes with functionally substituted diazoalkanes thus appear to possess very broad synthetic potential, and we are continuing to pursue these possibilities.

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(7) We could have detected <1% ethyl 3-methylheptanoate under our analytical conditions.

(8) Postdoctoral Research Fellow, 1967–1968.

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Catalysis of Hydrolysis of N-Benzyl-3-cyanopyridinium Bromide. A Model for the Nitrilase Reaction[1]

Sir:

A substantial variety of plant and bacterial species are known to possess enzymes, nitrilases, capable of catalyzing the hydrolysis of a variety of organic nitriles to the corresponding carboxylic acids.[2,3] In each case, reactions catalyzed by these enzymes are susceptible to inhibition by reagents which react with thiol groups of the enzymes. This behavior has led to the suggestion that thiol groups of the enzymes may function as nucleophilic catalysts in these reactions.[2] Among the various nitriles acted upon by these enzymes is 3-cyanopyridine.[2b] An investigation of the catalysis of hydrolysis of a related nitrile, N-benzyl-3-cyanopyridinium ion, by a simple thiol, mercaptoethanol, reveals a substantial number of parallels between the mercaptoethanol-promoted reaction and the enzyme-promoted reactions. Since the nonenzymatic reaction mechanism may shed substantial light on that of the enzymatic reactions, we are prompted to report our findings at this time.

Catalysis of hydrolysis of N-benzyl-3-cyanopyridinium bromide by mercaptoethanol is characterized by the following. First, under neutral or slightly acidic conditions, the predominant reaction product is the corresponding amide. Under conditions more acidic than pH 3 appreciable amounts of the corresponding acid are formed as well. Second, first-order rate constants for disappearance of the nitrile at fixed concentrations of mercaptoethanol exhibit a rate maximum near pH 7. Third, between pH 3.6 and pH 8.9 first-order rate constants for disappearance of the nitrile exhibit saturation with respect to mercaptoethanol concentration. This point and that developed just above are illustrated by the collection of rate constants for this reaction in Table I. Fourth, at the values of pH near 10 excess mercaptoethanol causes inhibition of the reaction.

Table I. First-Order Rate Constants for the Disappearance of N-Benzyl-3-cyanopyridinum Bromide in the Presence of Mercaptoethanol in Aqueous Solution at 25° and Ionic Strength 0.60[a]

	Mercaptoethanol concentration, *M*		
pH	0.04	0.08	0.15
3.63			0.061
3.88			0.112
4.28	0.075	0.154	0.277
4.90	0.25	0.56	1.03
5.45	1.05	2.09	4.04
6.26	3.77	6.28	8.63
6.54	3.50	6.90	9.20
7.00	4.76	7.15	8.20
7.31	4.95	5.96	5.8
7.88	4.29	5.32	5.6
7.46	4.66	6.33	7.6
7.64	3.84	5.45	6.55
7.66	3.02	3.83	
7.85	2.65	3.90	4.57
8.25	2.63	3.52	4.10
8.55	2.43	3.23	4.06
8.89	2.06	2.58	

[a] Rate constants in units of min^{-1}, multiplied by 10^2. The reaction was followed spectrophotometrically at 332 mμ by the periodic withdrawal of aliquots of the reaction mixtures and addition of these to a 0.1 *M* solution of mercaptoethanol, at pH 10.3 ± 0.1. Under these conditions, only the nitrile adds mercaptoethanol to form a 332-mμ chromophore.

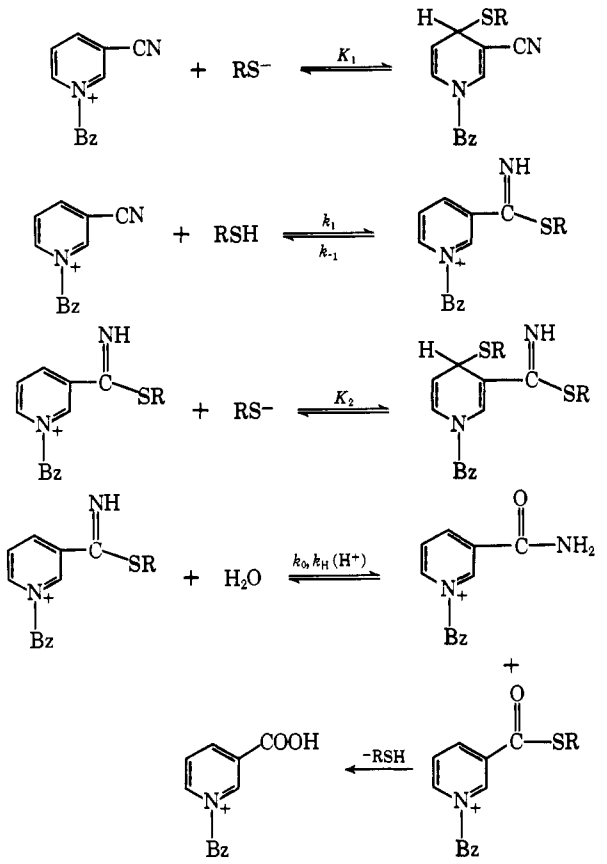
(1) Supported by Grant GE 3277 from the National Science Foundation and by Grant AM08232-05 from the National Institutes of Health. Publication No. 1626 from the Department of Chemistry, Indiana University.

(2) (a) K. V. Thimann and S. Mahadevan, *Arch. Biochem. Biophys.*, 105, 133 (1964); (b) S. Mahadevan and K. V. Thimann, *ibid.*, 107, 62 (1964).

(3) R. H. Hook and W. C. Robinson, *J. Biol. Chem.*, 239, 4263, 4257 (1964).

We believe that the data pertinent to this catalytic process are best understood in terms of the sequence of processes outlined in Scheme I. In terms of this scheme

Scheme I



the saturation kinetics can be understood on the basis of the addition of the anion of mercaptoethanol to the substrate to form a 1,4 adduct, which may be detected directly spectrophotometrically and which is unreactive toward attack of the nucleophilic reagent on the nitrile function. Furthermore, the inhibition of the reaction under basic conditions by excess mercaptoethanol may be understood in terms of the addition of this nucleophilic reagent to the thioimidate intermediate yielding a second nonproductive complex. The pH–rate maximum is interpreted as reflecting rate-determining formation of the thioimidate intermediate under acidic conditions and rate-determining hydrolysis of this intermediate, through both pH-independent and acid-catalyzed reaction pathways, under basic conditions. Relative amounts of amide and acid as product depend on the mode of partitioning of the tetrahedral intermediate formed from addition of water to the thioimidate intermediate. The observations that amide is the predominant product under neutral conditions but that acid is formed in increasing amounts as the reaction medium becomes more acidic are entirely consistent with the results of Schmir and his coworkers who have specifically investigated the mode of decomposition of such tetrahedral intermediates.[4]

That the suggested reaction scheme is in fact correct is supported by studies of the course of this reaction in water employing infrared spectroscopy. On the alkaline side of the pH–rate maximum, in which decomposition of the thioimidate is thought to be rate determining, one observes the immediate appearance of a new band at 1662 cm^{-1} which then continues to increase in intensity with time. Presumably this band reflects absorption due both to the thioimidate intermediate and to the amide product. In addition, one observes the immediate appearance of a new band at 1578 cm^{-1} whose intensity decreases with time. Presumably this band is due to the thioimidate intermediate only. In contrast, on the acid side of the pH–rate maximum one observes only the gradual development of a band near 1667 cm^{-1} which presumably reflects the appearance of amide. Clearly, these observations provide support for the transition in rate-determining step outlined above. Finally, the indicated reaction scheme is consistent with the transient appearance of a material, presumably the thiol ester, which is reactive toward neutral hydroxylamine.

There exists a number of parallels between the mercaptoethanol-mediated nitrile hydrolysis and the enzyme-mediated nitrile hydrolysis. In the first place, mercaptoethanol is an effective catalyst and increases the rate of nitrile hydrolysis at pH 7 from 10,000- to 100,000-fold.[5] In the second place, both reactions exhibit pH–rate maxima, and these occur at similar values of pH. Finally, both reactions depend on thiol groups. The results of this study support previous suggestions of participation of the thiol groups of nitrilases as nucleophilic reagents toward the nitrile function and suggest, furthermore, that thioimidate intermediates bound covalently to the enzymes exist. Furthermore, if the pH–rate maximum for the enzymatic processes derives from the same considerations as that observed in this case, it suggests that decomposition of this intermediate ought to be the rate-determining step on the basic side of the pH maximum and, therefore, that this intermediate ought to be isolable and capable of characterization by the usual methods.

(4) R. K. Chaturvedi, A. E. MacMahon, and G. L. Schmir, *J. Am. Chem. Soc.*, **89**, 6984 (1967).

(5) C. Zervos and E. H. Cordes, unpublished observations.

(6) Career Development Awardee of the National Institutes of Health, Grant K3 GM 10-248-02. Research Fellow of the Alfred P. Sloan Foundation.

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trans-Bicyclo[5.1.0]octanes[1]

Sir:

The last 5 years have witnessed a dramatic insurgence of interest in the chemistry of strained-ring compounds. Bicyclo[1.1.0]butane, bicyclo[2.1.0]pentane, bicyclo[1.1.0]pentane, and numerous tri- and tetracyclic small-ring compounds have been prepared and studied. Of special interest in relation to these compounds has been the nature of the strained carbon–carbon σ bonds, not only in connection with their remarkable chemical activity but also from a theoretical point of view.[2] We

(1) The Chemistry of "Bent" σ Bonds. IX. For the previous paper in this series see P. G. Gassman and G. D. Richmond, *J. Am. Chem. Soc.*, 90, 5637 (1968).

(2) W. Weltner, Jr., *ibid.*, 75, 4224 (1953); M. Randić and Z. Maksić, *Theor. Chim. Acta*, 3, 59 (1965); Z. Maksić, L. Klasinc, and M. Randić,