Rowland, Colin MacKay and Michael Henchman for stimulating and helpful discussions.

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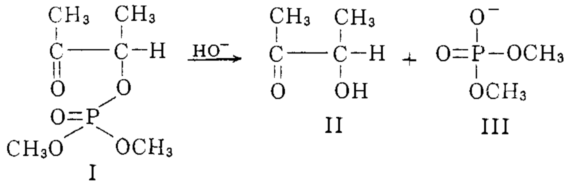
KINETICS AND MECHANISMS OF THE RAPID ALKALINE HYDROLYSIS OF DIMETHYL PHOSPHOACETOIN[1]

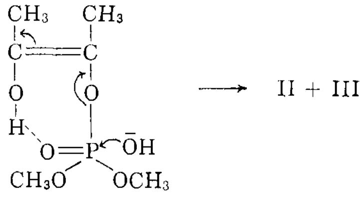
Sir:

The hydrolysis of dimethyl phosphoacetoin[2] (I) in the pH-range 7.7–8.3 gives acetoin (II) and dimethylhydrogen phosphate (III), identified as its barium salt. The reaction is first order with respect to the phosphotriester, I, and first order with respect to hydroxide ion. The second-order rate constant in this pH-range is $k_2 = 360 \pm 20$ liters-mole^{-1}-sec.$^{-1}$ at 25°. The rate was determined in 0.07 *M* $KClO_4$ by titration with 0.02 *M* NaOH in the pH-stat[3] already described. The initial concentration was 4×10^{-4} *M*.

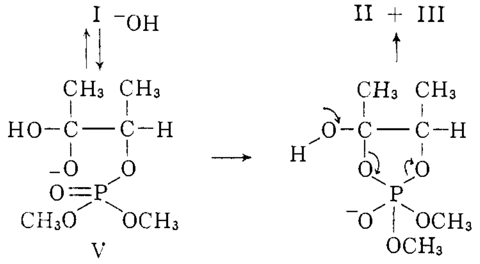

I II III

Measurements of the rate of hydrolysis of a 0.05 *M* solution of trimethyl phosphate in 0.02 *M* $KClO_4$ with 0.05 *M* NaOH gave 1.4×10^{-4} liters-mole^{-1}-sec.$^{-1}$ at 25°. The hydroxide ion-catalyzed hydrolysis of the simple α-ketol phosphotriester, I, is at least 2×10^6 times faster than that of trimethyl phosphate.

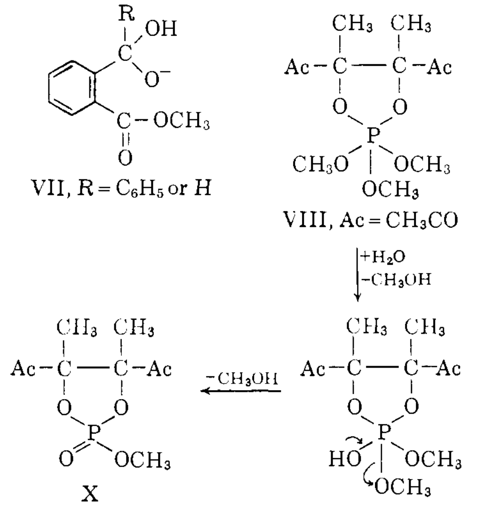
This enormous acceleration could be explained in two ways: (1) A substitution at phosphorus on the enediol-phosphate, IV, in which the rate enhancement would be due to the unsaturated nature of the leaving group and to hydrogen-bonding assistance. This picture is being considered further. (2) Carbonyl participation, (V), and oxyphosphorane formation, (VI), in the hydrolysis.


IV

Newman and Hishida[4] have suggested that the increased rate of alkaline hydrolysis of certain methyl *o*-benzoylbenzoates is a consequence of steric factors which promote a mechanism involving attack of hydroxide ion on the ketonic carbonyl (VII, $R = C_6H_5$) followed by an intramolecular expulsion of a methoxide ion. Subsequently, Bender and Silver[5] explained the fast rate of the hydroxide ion-catalyzed hydrolysis of methyl *o*-formylbenzoate in terms of aldehyde participation (VII, R = H).


V VI

We have interpreted the extremely rapid hydrolysis of the crystalline cyclic saturated oxyphosphorane,[6a] VIII, to the cyclic phosphotriester, X, in benzene or ether solution, as involving the oxyphosphorane intermediate,[6b] IX.


VII, $R = C_6H_5$ or H

VIII, $Ac = CH_3CO$

X

IX

Formulas VI and IX bring out the structural features which could account for the difference in the direction of the hydrolytic cleavage of the ketol phosphate (I) and of the oxyphosphorane (VIII). In the former, the ring is not preserved due to facile C–O bond fission.

These observations may have a bearing on the chemistry of naturally occurring α-ketol phosphomonoesters such as certain sugar phosphates, and, as pointed out by Bender[5] for carboxylic esters, on enzymic processes of phosphate esters in general.

NOTE ADDED IN PROOF.—C. A. Vernon gives $k_2 = 1.3 \times 10^{-4}$ liters-mole^{-1}-sec.$^{-1}$ at 25° for the alkaline hydrolysis of trimethyl phosphate in water; *cf.* "Phosphoric Esters and Related Compounds," The Chemical Society, London, Special Publication No. 8, 1957, p. 30.

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[2] F. Ramirez and N. B. Desai, *J. Am. Chem. Soc.*, **82**, 2652 (1960).

[3] L. Larsson and B. Hansen, *Svensk Kem. Tidskr.*, **68**, 521 (1956).

[4] M. S. Newman and S. Hishida, *J. Am. Chem. Soc.*, **84**, 3582 (1962).

[5] M. L. Bender and M. S. Silver, *ibid.*, **84**, 4589 (1962).

[6] (a) F. Ramirez, N. Ramanathan and N. B. Desai, *ibid.*, **84**, 1317 (1962); (b) in press.

[7] Alfred P. Sloan Fellow 1961–1962. The authors appreciate the opportunity of examining the manuscripts of Newman and Hishida[4] and of Bender and Silver[5] before publication.

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