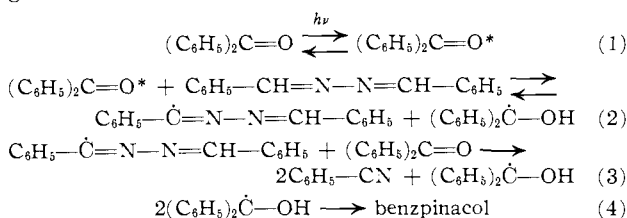


TABLE I^a
YIELD OF SUBSTITUTED NITRILES FROM
THE CORRESPONDING AZINES

Solvent	Azine	Nitrile yield, %	Benz-pinacol yield, %
Cyclohexane	Benzal	85	82
Cyclohexane	<i>o</i> -Chlorobenzal	88	84
Benzene	<i>p</i> -Chlorobenzal	82	80
Benzene	<i>p</i> -Methoxybenzal	82	79
Dioxane	<i>p</i> -Nitrobenzal	95	93
Benzene	<i>p</i> -Dimethylaminobenzal	80	78

^a The yields are based on 1-5-g. experiments, repeated thrice, and averaged. The products were isolated in pure state by distillation or crystallization and the yields were checked with extraction procedures and gas chromatography. The last three entries of Table I required longer irradiation times to obtain the stated yields. The best procedure is to irradiate the solutions until the yellow golden color of the azines disappears or becomes very faint.

tization⁴ but an example of triplet or diradical hydrogen transfer.⁵ The mechanism can be outlined as



The synthetic usefulness of the reaction is somewhat clouded because aldehydes are normally employed to synthesize the azine derivatives. Synthesis of the azines⁶ is, however, exceedingly simple and the yields are quantitative. Possible extension of this reaction to the aliphatic series is being investigated.

Acknowledgment.—This work was supported by a grant (P-058) from the Robert A. Welch Foundation.

(4) G. S. Hammond, N. F. Turro, and P. A. Leermakers, *J. Phys. Chem.* **66**, 1144 (1962).

(5) See W. M. Moore, G. S. Hammond, and R. P. Foss, *J. Am. Chem. Soc.*, **83**, 2789 (1961), and ref. cited; S. G. Cohen, S. Orman, and D. A. Lanfer, *ibid.*, **84**, 3905 (1962); S. G. Cohen and W. V. Sherman, *ibid.*, **85**, 1642 (1963).

(6) H. H. Hatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y. 1943, p. 395.

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RECEIVED JUNE 27, 1963

Elimination Mechanisms. Position of Proton in E2 Transition States¹

Sir:

We have found that the isotope effects for DO⁻ in D₂O vs. HO⁻ in H₂O as attacking bases in the E2 elimination reactions of two β-phenylethyl derivatives at 80° are $k_1/k_H = 1.79$ for C₆H₅CH₂CH₂N⁺(CH₃)₃Br⁻ and 1.57 for C₆H₅CH₂CH₂S⁺(CH₃)₂Br⁻ salts.²

The effect for the sulfonium salt is complicated by exchange of D for H on the carbon atoms adjacent to the sulfur atom. Any isotope effect from this source should be small, however, because the sulfur isotope

(1) Supported in part by the United States Atomic Energy Commission, to which royalty-free right of reproduction is hereby granted. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

(2) Our rate constant for HO⁻ with the sulfonium salt agrees well with that in the literature.³ Rate constants were measured by titration; for the ammonium compound, the amine was removed under reduced pressure before titration of each aliquot.

(3) W. H. Saunders, Jr., and D. H. Edison, *J. Am. Chem. Soc.*, **82**, 138 (1960).

effect for the reaction is exceedingly small, indicating very little C-S bond-breaking at the transition state.⁴ These effects are so strong that we must conclude that the proton positions in the transition states for these reactions are product-like, *i.e.*, have a larger H-O than C-H stretching force constant. DO⁻ in D₂O is a stronger base than HO⁻ in H₂O by a factor of *ca.* 1.6 at 80°.⁵ Thus, even allowing for a substantial solvent isotope effect (say 20%) superimposed upon the secondary isotope effect due to the attacking base, we still conclude that the proton must be considerably detached from the carbon atom in the transition state.

It is very probable that the secondary isotope effect k_D/k_H for attack of DO⁻ vs. HO⁻ must be considerably larger for the ammonium compound than for the sulfonium compound even after correction for possible solvent isotope effects caused by the fact that the DO⁻ reaction is carried out in D₂O while the HO⁻ reaction is carried out in H₂O. The solvent isotope effects should be weak and also should be similar for both compounds because in both cases a positively charged organic ion reacts with base.

Coupled with the primary isotope effects for eliminations under similar conditions, our results provide even stronger evidence. For C₆H₅CD₂CH₂S⁺(CH₃)₂Br⁻ vs. the corresponding completely nondeuterated compound $k_H/k_D = 4.14$ in H₂O with HO⁻ at 80°,³ 5.05 in H₂O at 50°, 5.93 in H₂O at 30°, and 5.07 in ethanol with ethoxide at 30°. The effect for the compound with trimethylamine as leaving group in place of dimethyl sulfide is 2.98 in ethanol with ethoxide ion at 50° and 3.02 in 50% ethanol-water at 50°. These relatively small isotope effects indicate that the respective transition states have either a considerably larger H-O than C-H stretching force constant or a considerably larger C-H than H-O stretching force constant. For equal C-H and H-O stretching force constants, a maximal isotope effect is expected⁶ (assuming that effects due to bending vibrations are small relative to those due to stretching vibrations and/or are nearly constant for transition states with different degrees of proton transfer). For example, a large isotope effect, $k_H/k_D = 7.11$ in ethanol with ethoxide at 30°, is observed for C₆H₅CD₂CH₂Br,³ indicating the proton is approximately equally tightly bound by C and O in the transition state.

The relative values of the secondary isotope effects show that the proton is more tightly attached to the oxygen atom in the ammonium transition state than in the sulfonium transition state. Then the only way the ammonium compound can have a smaller primary isotope effect than the sulfonium compound is if the proton is more strongly bonded to oxygen than to carbon in the ammonium transition state. This evidence is based only on the relative magnitudes of the secondary and

(4) W. H. Saunders, Jr., and S. Ašperger, *ibid.*, **79**, 1612 (1957).

(5) Calculated from data given by C. G. Swain and R. F. W. Bader, *Tetrahedron*, **10**, 197 (1960). It is the square root of their equilibrium constant for eq. 9, *i.e.*, 1.79 at 25°, and, from the temperature dependence of equilibria 7 and 8, 1.6 at 80°. A recent estimate of *ca.* 1.25, probably too low, is given by A. J. Kresge and A. L. Allred, *J. Am. Chem. Soc.*, **85**, 1541 (1963). This low value does not seem consistent with their value for the relative acidities of D₃O⁺ and the self-ionization constants of D₂O and H₂O. Using the two values of the isotope effect on the self-ionization of water, the DO⁻-HO⁻ effect is either 1.79 or 2.27 at 25° (W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **32**, 1397 (1936); R. W. Kingerly and V. K. La Mer, *J. Am. Chem. Soc.*, **63**, 3256 (1941); it is not clear why the discrepancy exists). However, for reactions which appear to proceed *via* a prior equilibrium which converts hydroxide to water, the kinetic isotope effects seem too small to be consistent with a value as high as 2.27. For example, the cyclization of ethylene chlorohydrin is faster with DO⁻ in D₂O by a factor of 1.54 (C. G. Swain, A. D. Ketley, and R. F. W. Bader, *ibid.*, **81**, 2353 (1959); P. Ballinger and F. A. Long, *ibid.*, **81**, 2347 (1959)).

(6) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

primary isotope effects and is, therefore, separate from the evidence based on the absolute magnitudes of the secondary isotope effects.

From these two pieces of evidence, we conclude that the proton is almost completely transferred to oxygen in the transition state for E2 elimination by HO⁻ in H₂O on C₆H₅CH₂CH₂N⁺(CH₃)₂. For the corresponding sulfonium ion, the proton is less completely transferred, and for the bromide, the proton is still less completely transferred. This work demonstrates how primary and secondary isotope effects in the same reaction can complement one another.

The rates of elimination of β-phenylethyl compounds substituted in the ring lead to good Hammett ρσ correlations. The chloride, bromide, iodide, tosylate, and dimethylsulfonium leaving groups all give ρ values between 2 and 3 with sodium ethoxide in ethanol at 30°, these large values indicating considerable carbanion character in the transition states.⁷ Although large ρ values could conceivably be due to other factors than carbanion character, e.g., to the incipient double bond conjugated with the ring in the transition state, our results show that the proton is substantially transferred in these transition states.

We plan to extend this method to other systems because it should help to explain the Hofmann-Saytzeff orientation effects which are currently ascribed to steric influences⁸ by some investigators and to electrical influences by other investigators.⁹

(7) W. H. Saunders, Jr., and R. A. Williams, *J. Am. Chem. Soc.*, **79**, 3712 (1957); W. H. Saunders, Jr., C. B. Gibbons, and R. A. Williams, *ibid.*, **80**, 4099 (1958); C. H. DePuy and D. H. Fromsdorf, *ibid.*, **79**, 3710 (1957); C. H. DePuy and C. A. Bishop, *ibid.*, **82**, 2532, 2535 (1960). The ρ value for trimethylammonium under the same conditions is even larger, 3.77 (W. H. Saunders, Jr., and D. G. Bushman, unpublished).

(8) H. C. Brown, in "The Transition State," Special Publication No. 16, The Chemical Society, London, 1962, pp. 143-144.

(9) D. V. Bantrophe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 4054 (1960).

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The Hydrolysis of Five-Membered Cyclic Phosphotriesters to Cyclic Phosphodiester¹

Sir:

The alkaline hydrolysis of methyl ethylene phosphate is much faster than that of trimethyl phosphate and occurs with P-O fission and *ring opening*.² The heat of saponification of methyl ethylene phosphate exceeds that of dimethyl 2-hydroxyethyl phosphate by about 5.5 kcal./mole.^{2c} Several hypotheses have been advanced to explain these kinetic and thermodynamic observations.^{2,3}

Recently, Covitz and Westheimer³ found that the hydrolysis of methyl ethylene phosphate in acid solution gave predominantly methyl 2-hydroxyethyl hydrogen phosphate, and, in addition, some ethylene hydrogen phosphate (from 5 to 30%). There was, therefore, some preservation of the five-membered ring.

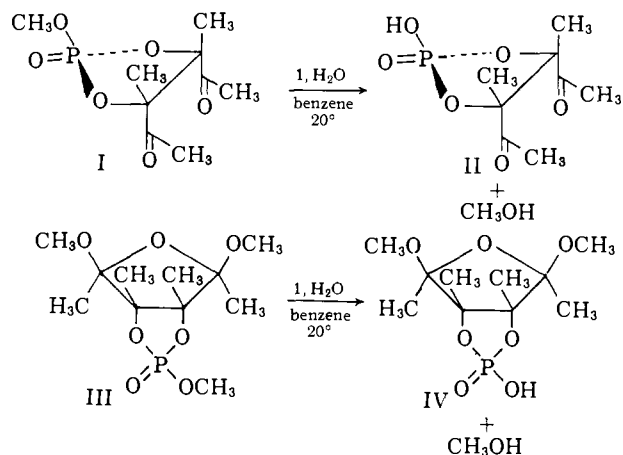
We have observed that certain five-membered cyclic phosphotriesters (I, III) react very rapidly with one mole equivalent of water in aprotic solvents at 20°, yielding *cyclic phosphodiester* II and IV almost ex-

(1) We gratefully acknowledge the support of the Cancer Institute of the National Institutes of Health (CY-4769), the National Science Foundation (G 19509), and the Petroleum Research Fund of the American Chemical Society (286-A).

(2) (a) P. Haake and F. H. Westheimer, *J. Am. Chem. Soc.*, **83**, 1102 (1961), and references therein; (b) R. E. Wall, Thesis, Harvard University, 1960; (c) E. T. Kaiser, M. Panar, and F. H. Westheimer, *J. Am. Chem. Soc.*, **85**, 602 (1963).

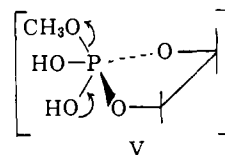
(3) F. Covitz and F. H. Westheimer, *ibid.*, **85**, 1773 (1963).

clusively. The cyclic diesters were readily isolated in crystalline form; they were converted into the original triesters by diazomethane and were characterized also as cyclohexylammonium and piperidinium salts.

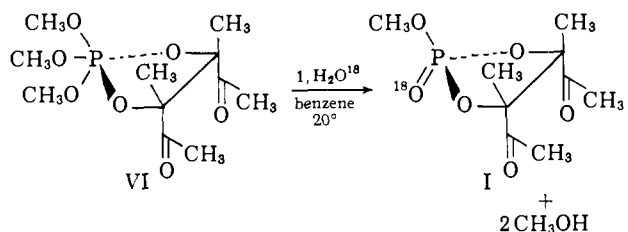


Trimethyl phosphate and dimethyl phosphoacetoin⁴ were not affected by water in benzene solution under comparable conditions.

It seems possible that the formation of cyclic phosphodiester from cyclic phosphotriester, at least in aprotic solvents, may proceed by way of an oxyphosphorane intermediate V. In other words, it may be possible under certain conditions to hydrate the phosphoryl group of a cyclic phosphate ester.



If an oxyphosphorane V is indeed an intermediate in the hydrolysis of a cyclic triester to a cyclic diester, the collapse of the oxyphosphorane must occur with preservation of the five-membered ring, since an open-chain diester should not cyclize under the experimental conditions. Some information on the mode of collapse of cyclic oxyphosphoranes analogous to V can be obtained from a study of the hydrolysis of the crystalline pentaalkoxyphosphorane VI in aprotic solvents, using water enriched with O¹⁸. We had previously shown,⁵ using unlabeled water, that this hydrolysis is extremely fast and gives rise to the cyclic phosphotriester I.



The experiments with labeled water have shown that the oxygen atom of the water becomes attached to the phosphorus of the phosphate ester, presumably as a phosphoryl group, PO. Precisely how this happens remains a problem on the mechanism of substitution at quintuply-connected phosphorus; however, the results suggest the participation of an oxyphosphorane VII in the hydrolysis of the pentaalkoxyphosphorane VI. Evidently, VII tends to collapse with preservation of the five-membered ring, since the product is a cyclic phosphate I. Therefore, the oxyphosphorane V,

(4) F. Ramirez, B. Hansen, and N. B. Desai, *ibid.*, **84**, 4588 (1962).

(5) F. Ramirez, N. B. Desai, and N. Ramanathan, *ibid.*, **85**, 1874 (1963)