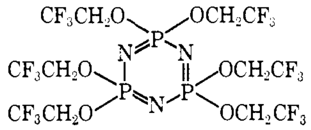
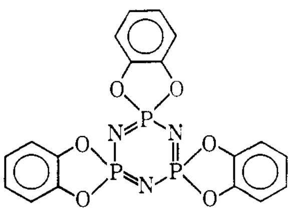
The Base-Catalyzed Hydrolysis of Aryloxy- and Alkoxycyclophosphazenes

Sir:

The hydrolysis reactions of organophosphazenes (organophosphonitriles) in basic media are of considerable importance from the mechanistic, biochemical, and technological points of view. The acidic hydrolysis reactions of phosphazenes have been reported,[1,2] and the alkaline hydrolyses of halophosphazenes have been described.[3,4] However, the alkaline hydrolysis reactions of organophosphazenes have not been investigated in detail, and published reports are confined to brief qualitative observations concerning the stability of specific compounds to base.[5] We now wish to demonstrate that the hydrolytic stability and alkaline hydrolysis mechanisms are markedly dependent on the nature of the side groups attached to the phosphazene ring.

The appreciable differences can be demonstrated by a comparison of the hydrolytic behavior of two cyclotriphosphazenes, hexa(trifluoroethoxy)cyclotriphosphazene (I) and tris(*o*-phenylenedioxy)cyclotriphosphazene (II). These derivatives were prepared by methods reported previously.[5,6] Hydrolysis of I in 50 vol % aqueous methanolic 1 *N* sodium hydroxide solution results in nongeminal, stepwise removal of trifluoroethoxy groups from phosphorus without cleavage of the phosphorus–nitrogen ring. Both III and IV have been isolated and identified by microanalysis, nmr and infrared spectra, and mass spectrometry of the hydroxyphosphazenes formed by acidification. In acidic media these latter derivatives exist in the "phosphazane" form in which the proton resides on nitrogen. It was also found that, although the reaction rates are much slower in aqueous dioxane than in aqueous methanol, the mechanism appears to be similar in both media.


I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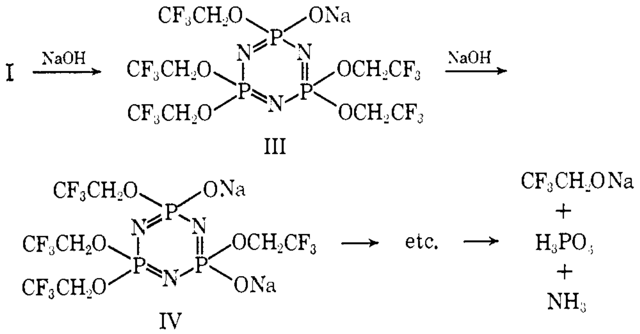
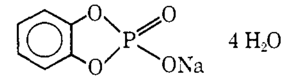

III

IV

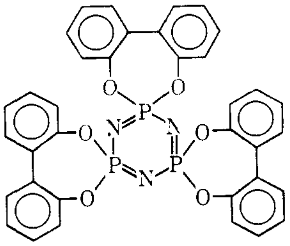
The hydrolysis of II in 1 or 5 vol % water in dioxane containing 4.6×10^{-3} *N* sodium hydroxide proceeds quite differently. The reaction takes place very rapidly, and the first identifiable products formed are ammonia and sodium 1,2-dioxyphenylphosphate (V), isolated as the tetrahydrate. This product was identified by microanalysis, infrared and proton nmr spectra, and comparison with an authentic specimen prepared by an alternative synthetic route.[7] When V was acidified in *organic* media, the corresponding acid ester, $C_6H_4O_2P(O)OH$, was isolated and identified by proton nmr, infrared spectroscopy, boiling point,[7,8] and mass spectrometry, although in acidic *aqueous* media this compound undergoes a ring cleavage to *o*-$HOC_6H_4OP(O)(OH)_2$.


V

Kaiser and Kudo[8] have shown that V itself hydrolyzes very rapidly in 99% water–1% acetonitrile at base concentrations of 1×10^{-2} *N*. However, we have found that the rates of hydrolysis of V in our nonpolar media are considerably less. For example, at 100° with 1×10^{-3} *N* NaOH in a 5% water in dioxane medium, 50% hydrolysis of V occurs in approximately 6 min, and this undoubtedly explains why V can be isolated and identified as a discrete hydrolysis product during degradation of II.

Thus, although we cannot totally exclude the possibility that the initial step in the hydrolysis of II is a rapid, reversible hydroxide attack on phosphorus to cleave a P–O–C bond, the evidence strongly favors the view that phosphorus–nitrogen ring cleavage occurs in preference to side group displacement. The ultimate hydrolysis products are sodium catecholate, quinones, sodium orthophosphate, and ammonia. It should be noted that II is insoluble in methanol, and direct comparison with I in that medium is impossible.

In 5 vol % aqueous dioxane, with 4.25×10^{-3} *N* sodium hydroxide at 100°, the hydrolysis of II proceeds at least 1×10^5 times faster than the hydrolysis of I. In the same medium, hexaphenoxycyclotriphosphazene, $[NP(OC_6H_5)_2]_3$ (VI), and derivative VII underwent no detectable hydrolytic breakdown after 200 hr. In fact, we have so far failed to find conditions under which these two compounds can be cleaved in basic media, even at high base strengths.


VII

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(1) A. Narath, F. H. Lohman, and O. T. Quimby, *J. Am. Chem. Soc.*, **82**, 1099 (1960).

(2) B. W. Fitzsimmons, C. Hewlett, and R. A. Shaw, *J. Chem. Soc.*, 4459 (1964).

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(4) A. J. Bilbo, C. M. Grieve, D. L. Herring, and D. A. Salzbrunn, *Inorg. Chem.*, 7, 2670 (1968).

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(8) E. T. Kaiser, and K. Kudo, *J. Am. Chem. Soc.*, **89**, 6725 (1967).

The enormous rate-enhancing influence of the five-membered ring in II is reminiscent of the behavior of related phosphate esters.[9] Undoubtedly, steric strain in II is an important contributing factor since the O–P–O bond angle in II is known to be 97°,[10] a significant decrease from the preferred angle of 102–104° in most phosphazenes.[11] However, the apparent over-all preference for cleavage of the phosphazene rather than the dioxyphosphole ring of II cannot be readily explained by the phenomenon of pseudorotation of a simple pentacoordinate intermediate, and this provides a contrast to phosphate ester hydrolysis.[9] Thus, in a pentacoordinate transition state, the N–P–N bonds must be equatorial to maintain the preferred 120° phosphazene ring angle,[11] and the O–P–O bonds must occupy axial and equatorial positions to maintain a ~90° benzodioxyphosphole ring angle. Pseudorotation of this structure is sterically inhibited. However, if hydrogen migration to a ring nitrogen occurs to form a phosphazane structure, pseudorotation would be more feasible. Attack by hydroxyl anion on carbon has been ruled out by the absence of $H_2{}^{18}O$ exchange with the ring oxygen atoms of II. Further work is continuing in an attempt to clarify the mechanism.

Acknowledgments. We are indebted to the Public Health Service (P.H.S. Research Grant No. HE 11418-01, National Heart Institute) for the support of this work, and to the National Science Foundation for an Institutional Fellowship to E. J. W.

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[11] H. R. Allcock, "Heteroatom Ring Systems and Polymers," Academic Press, New York, N. Y., 1967, Appendix II and references therein.

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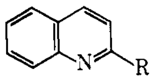
McLafferty Rearrangement and Type II Photocleavage Comparisons in a New System. 2-Substituted Quinolines[1]

Sir:

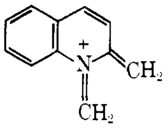
Some correlations of electron-impact fragmentation with photochemical reactivity have recently been reported, nearly all of which deal with molecules containing a carbonyl function. We wish to report some interesting comparisons in a new system.

Irradiation[2] of 2-ethylquinoline (I) for 60 hr resulted in no reaction, and I was recovered quantitatively. Irradiation[2] of 2-*n*-butylquinoline (II) for 58 hr resulted in 45% conversion ($k = 2.5 \times 10^{-6}$ sec^{-1}) to 2-methylquinoline (III) and propylene (trapped as the dibromide). Irradiation[2] of 2-(2-hydroxyethyl)quinoline (IV) for 18 hr resulted in 73% conversion ($k = 2.3 \times 10^{-5}$ sec^{-1}) to III and formaldehyde (trapped as the 2,4-DNP derivative).

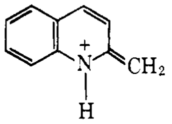


I, R = CH_2CH_3 IV, R = CH_2CH_2OH
II, R = $CH_2CH_2CH_2CH_3$ VII, R = CH_2CH_2OD
III, R = CH_3 IX, R = $CH_2CH_2OCH_3$

The base peak in the mass spectrum[3,4] of 2-ethylquinoline is at *m/e* 156 ($M^+ - 1$) and has been attributed[4] to V. We cannot conceive of a rational photochemical process from I to V, and it is perhaps not surprising that I is stable to light.

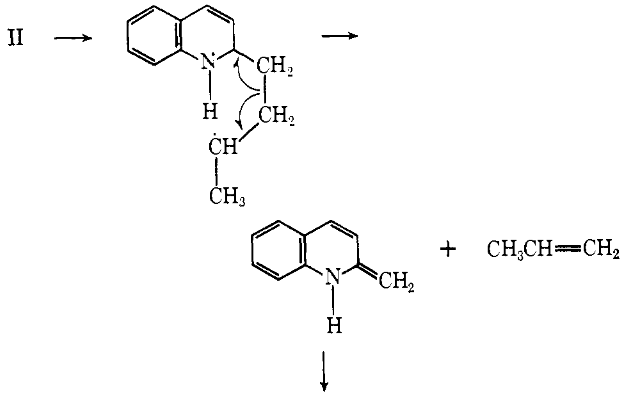


V

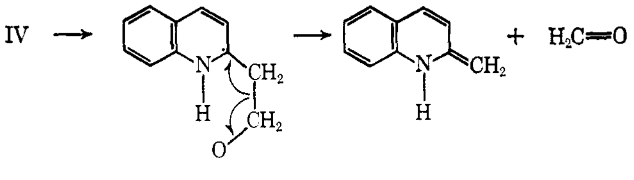


VI

However, the base peak in the mass spectrum[3,4] of II and IV is at *m/e* 143, attributable to VI, and hence, in terms of product formation, a correlation is observed for electron-impact fragmentation and photocleavage. A complete analysis (with deuterium-labeled material) of the mass spectrum of 2-propylquinoline was previously reported,[4] and a McLafferty rearrangement process to VI was proved. Thus, for 2-*n*-butylquinoline photocleavage, it is probably valid to write a process exactly in analogy with ketone "type II" cleavage.



However, for photocleavage of IV abstraction of H from OH must occur if the reaction is to be similarly described. Although this process is unusual, a similar one has been suggested[5] for a 9-substituted isoalloxazine where C═N photoreactivity is also involved. A distinction between the above reaction and abstraction through an unfavored five-membered transition state



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[2] Irradiations were carried out in 10^{-2} *M* benzene solutions (650 ml), under nitrogen, using a Rayonet reactor equipped with 3000-Å lamps. Each of the quinolines had similar absorption spectra with maxima at 273, 302, and 315 nm.

[3] Mass spectra were taken with an AEI MS-12 instrument at 70 eV.

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[5] W. M. Moore and C. Baylor, Jr., *J. Am. Chem. Soc.*, **88**, 5677 (1966), and private communication (1969).