Tetrahedron Letters,Vol.25,No.41,pp 4627-4630,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

STEREOELECTRONIC CONTROL IN THE BASE CATALYZED HYDROLYSIS OF FIVE-MEMBERED RING CYCLIC PHOSPHONAMIDATES

Ji-Charng Yang and David G. Gorenstein*

Department of Chemistry
University of Illinois at Chicago
Chicago, Illinois 60680

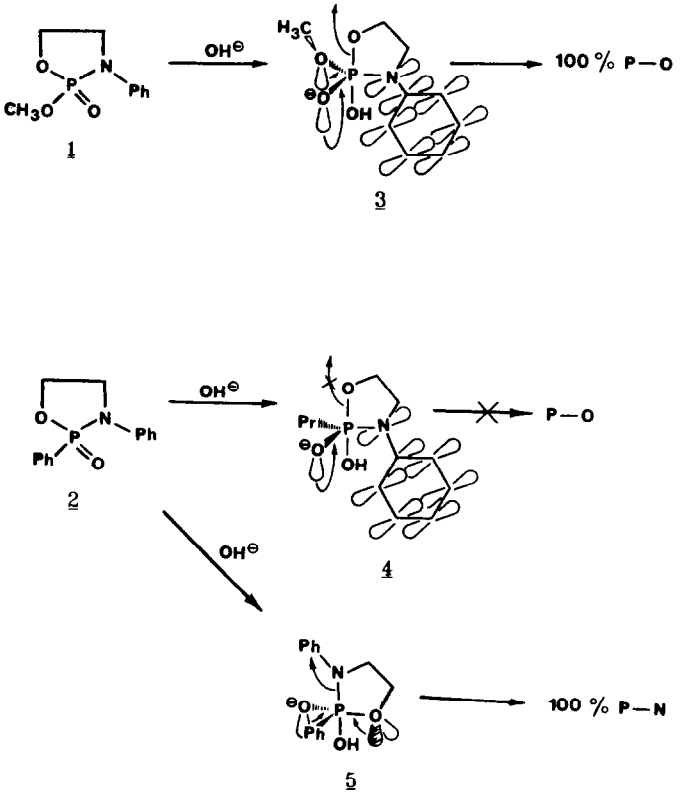
Abstract: The base catalyzed hydrolysis of 2-phenyl-2-oxo-3-(2,6-dimethylphenyl)-1,3,2-oxazaphospholidine, 6, and 2-phenyl-2-oxo-3-(2,6-diisopropylphenyl)-1,3,2-oxazaphospholidine, 7, yields ring opened products involving 95% and 100% P-O cleavage, respectively.

The basic hydrolysis of 5-membered ring cyclic 2-methoxyl-2-oxo-3-phenyl-1,3,2-oxazaphospholidine 1 has been reported by Hudson[1] to give exclusively the P-O bond cleavage product (Scheme I). In surprizing contrast the cyclic 2-phenyl-2-oxo-3-phenyl-1,3,2-oxazaphospholidine 2 yielded exclusively the P-N bond cleavage product.

We have earlier suggested that the dramatic difference in P-O and P-N bond cleavage in 1 and 2 could arise from a stereoelectronic effect.[2] This stereoelectronic effect involves the selective cleavage or formation of bonds which are trans, antiperiplanar (app) to lone electron pairs on directly bonded oxygen and nitrogen atoms. This stereoelectronic effect[2,3] has been theoretically justified and recently experimentally supported for reactions at both carbon[3,4] and phosphorus.[5-7]

As shown in Scheme I the phosphorane 3 formed by hydroxide attack opposite to the ring oxygen in 1 has two lone electron pairs on the basal oxygens app to the apical ester bond which facilitate ring P-O bond cleavage. The phosphorane 4 formed by hydroxide attack

SCHEME I



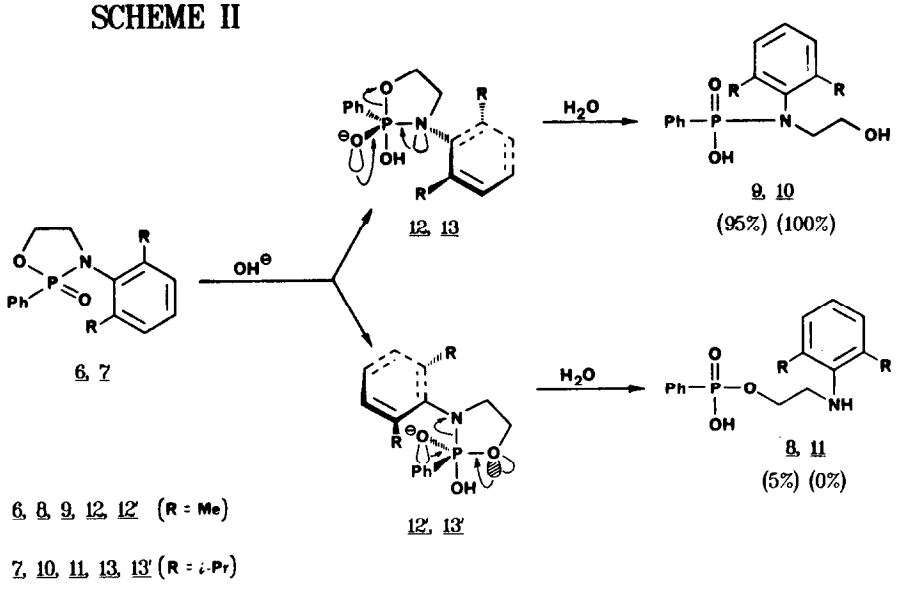
opposite to the ring oxygen in 2 has only one lone electron pair app to the apical ring oxygen (the lone pair on the sp^2-hybridized nitrogen in 3 and 4 will lie in the basal plane because of conjugation with the aromatic ring and the favored orbital orientation of a nitrogen lone pair in a phosphorane[8]). P-O bond cleavage will thus be stereoelectronically more favorable in 3 than in 4. However, $^{-}$OH attack opposite the nitrogen atom would yield a phosphorane 5 in which the apical nitrogen is app to two oxygen lone pairs,[6,7] and thus P-N cleavage would be stereoelectronically favored in the hydrolysis of 2.[9]

In contrast to these results, we wish to report that the basic hydrolysis of N-aryl substituted cyclic 1,3,2-oxazaphospholidines 6 and 7 give almost quantitatively P-O bond cleavage products. The results provide strong support for stereoelectronic control of the bond cleavage step.

Cyclic phosphonamidates 6 and 7 were synthesized by adding the appropriate amino alcohols to a solution of phenyl phosphonic dichloridate in excess dry pyridine at 0-5°C under nitrogen. After column chromatography and recrystallization 6 and 7 were obtained as white crystals, m.p. 135-136° and 158-160°C, respectively. Elemental analysis, ^{1}H NMR, ^{31}P NMR, ^{13}C NMR and mass spectra all confirmed the structures of 6 and 7.

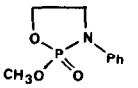
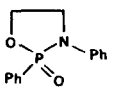
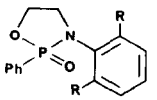
The hydrolysis of 6 and 7 in 0.01-0.30M NaOH, 50% aqueous dioxane was monitored by ^{31}P NMR. 6 and 7 were completely hydrolyzed within 20 min. and as shown in scheme II 6 gave ca. 5% P-N bond cleavage product 8, in addition to 95% of the P-O bond cleavage product 9. 7

SCHEME II



gave exclusively 100% P-O bond cleavage product 10. The product identification was made by addition of an independently synthesized P-N bond cleavage sample to the hydrolysis product and demonstrating that their ^{31}P signals were superimposable. In addition, both ^{13}C NMR spectra of the hydrolysis product 10 and an independently synthesized 11 were recorded and shown to have coupling constants for P-NCH_2 and P-OCH_2, of 7.3 Hz and 4.9 Hz, respectively. Table I presents a comparison of Boudreau et al.'s results[1] and our own.

Table I. Comparison of Base Catalyzed Hydrolysis of Phosphonamides 2, 6, 7

Compound		%P-N cleavage	%P-O cleavage
1		0[a]	100[a]
2		100[a]	0
6 (R = Me)		5[b]	95
7 (R = i-Pr)		0[b]	100

[a]ref. (1) [b]This work.

When the 2,6-positions of the aromatic ring are substituted by alkyl groups (6 R=Me and 7 R=i-Pr), the hybridization of the nitrogen can no longer be sp^2 since the conjugation with the aromatic ring will be destroyed by severe steric interactions between the alkyl substituents on the aromatic ring and the cyclic five-membered ring. Indeed, the proton and carbon NMR spectra of 7 show that the four methyl groups on the isopropyl groups are magnetically distinguishable, indicating restricted rotation about the N-aromatic bond. Phosphoranes 12 and 13 formed by hydroxide attack opposite the ring oxygen will now have two lone pairs app to the scissile apical bond oxygen, one from oxygen and the other at least partially from the sp^3-hybridized nitrogen. As in 4 and 5 the two lone pairs app to the apical bond will facilitate ring cleavage. Apparently in 6 the magnitude of the steric effects, the resulting change in hybridization on nitrogen, and the importance of the stereoelectronic effect are finely balanced so that both P-O and P-N cleavage is observed.

Steric effect considerations alone would suggest that P-N cleavage should be favored in these N-phenyl substituted, sterically crowded pentacovalent transition states. Relief of this steric strain would best be achieved by actually placing the bulky nitrogen leaving

group in the long[5] apical scissile bond. As raised by a reviewer, another factor which may be considered is the possibility of steric hindrance towards solvation of the amine leaving group. Thus, as shown by Deslongchamps and co-workers,[10] N-2,6-dimethylphenyl-N-methyl formamide undergoes carbonyl-oxygen exchange in base, but cleavage of the C-N bond does not occur. In contrast, N-methyl-N-phenylformamide hydrolyzes readily with no carbonyl-oxygen exchange. The two methyl groups on the phenyl ring in the tetrahedral intermediate formed in the hydroxide addition to N-2,6-dimethylphenyl-N-methyl formamide are suggested to prevent hydrogen bonding to the leaving group nitrogen and hence prevent hydrolysis. Similar steric effects may well operate in the hydrolysis of 6 and 7, although stereoelectronic effects rather than hydrogen bonding effects could also explain the formamide hydrolysis results.

Acknowledgement. Support by NSF (Chem 83K0098) is greatly appreciated. Purchase of an IBM WP 200 SY NMR spectrometer was assisted by an NSF Departmental Equipment Grant

References

(1) Boudreau, J. A.; Brown, C.; Hudson, R. F. J. Chem. Soc. Chem. Commun. 1975, 679.

(2) Gorenstein, D.G.; Rowell, R.; Taira, K. ACS Symposium No. 171, Phosphorus Chemistry 1981, 69.

(3) Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry," Pergamon Press, Oxford (1983); Kirby, A. J. "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen," Springer-Verlag, Berlin, pp. 1-149 (1983).

(4) Lehn, J. M.; Wipff, G. J. Am. Chem. Soc. 1974, 96, 4048; Gorenstein, D. G.; Taira, K. submitted.

(5) Lehn, J. M.; Wipff, G. J. Chem. Soc., Chem. Commun., 1975, 800; Gorenstein, D. G.; Findlay, J. B.; Luxon, B. A.; Kar, D. J. Am. Chem. 1977, 99, 3473.; Gorenstein, D. G.; Luxon, B. A.; Findlay, J. B.; Momii, R. ibid. 1977, 99, 4170.; Gorenstein, D. G.; Luxon, B. A.; Findlay, J. B. ibid. 1977, 99, 8048.; Gorenstein, D. G.; Luxon, B. A.; Goldfield, E. M. ibid. 1980 102, 1757.

(6) Taira, K.; Gorenstein, D. G. submitted.

(7) Gorenstein, D. G.; Rowell, R.; Findlay, J. J. Am. Chem. Soc. 1980, 102, 5077; Gorenstein, D. G.; Taira, K. ibid. 1982, 104, 6130; Rowell, R.; Gorenstein, D. G. ibid., 1981, 103, 5894; Taira, K.; Fanni, T.; Gorenstein, D. G., ibid. 1984, 106, 0000; Taira, K.; Mock, W.; Gorenstein, D. G., ibid, 1984, 106, 0000.

(8) Howell, J. M. Chem. Phys. Lett. 1974, 25, 51; Peake, S.C.; Schmutzler, R. J. Chem. Soc., Chem. Commun. 1968, 1662.

(9) Hall, C. R.; Inch, T. D. J. Chem. Soc., Perkin Trans 1 1979, 1104. They have observed exclusive P-N bond cleavage with inversion of configuration in the alkoxide addition to 1,3,2-oxazaphospholidines.

(10) Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry," Pergamon Press, Oxford, pp. 112-114 (1983); Deslongchamps, P.; Gerval, P.; Cheriyan, U. O.; Guida, A.; Taillefer, R. J. Nouv. J. Chim. 1978, 2, 631.

(Received in USA 23 April 1984)