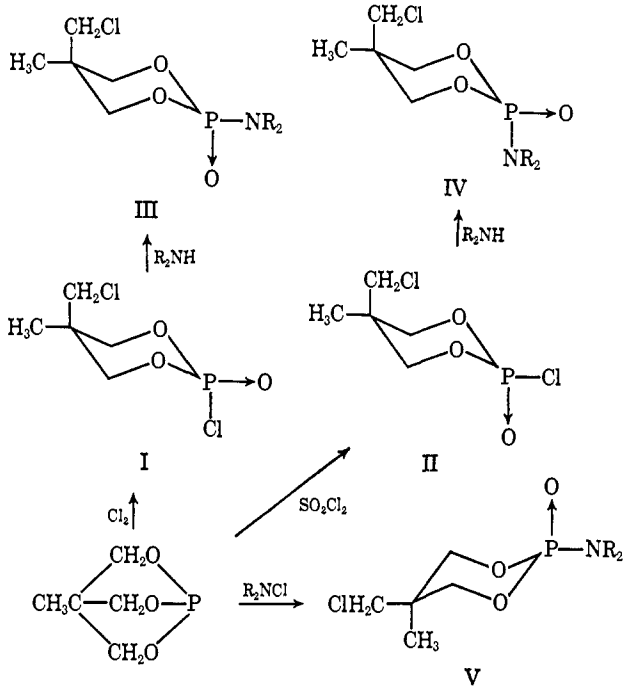
Nucleophilic Displacements at Phosphorus. Evidence for an SN1 (P) Mechanism

Sir:

We wish to report a system which may shed new light on the chemistry of nucleophilic substitutions at phosphorus(V) esters and their derivatives. In a prior publication[1] we showed that two different phosphoramidates were obtained from a bicyclic phosphite depending upon their mode of preparation. We have extended our original work in an attempt to elucidate the structure of the products and transition states which result upon substitution at phosphorus.

Treatment of methyl bicyclic phosphite with chlorine gas at low temperatures gave a cyclic phosphorochloridate, I, mp 59–60°, which lacked stability as witnessed by its slow decomposition to resinous material on standing. A more stable phosphorochloridate, II, mp 69–70°, was obtained by adding the phosphite to a solution of sulfuryl chloride. We assume that the phosphorochloridate I is stereochemically analogous to 2-bromo-5-bromomethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan prepared by adding bromine to the phosphite. The structure of the latter has been confirmed by X-ray analysis.[2] The two phosphorochloridates when treated with piperidine gave phosphoroamidates having different physical properties. Due to the steric requirements of the six-membered rings, the substitutions probably proceed normally *via* trigonal bipyramidal transition states[3] without pseudorotation[4] leading to inversion of configuration about the phosphorus atom. As outlined previously,[1] a third phosphoramidate, V, was obtained by treating the methyl bicyclic phosphite with N-chloropiperidine.



The conformation of the cyclic phosphoramides is based on nmr analysis, a method described by Edmundson.[5] The hydrogens in the chloromethyl group in V are upfield with respect to those in III and IV whereas the methyl hydrogens in V are downfield with respect to the methyl hydrogens in the other two, Table I. Conversion of the phosphorochloridates

Table I. Nuclear Magnetic Resonance Data for 5-Methyl-5-chloromethyl-1,3,2-dioxaphosphorinans

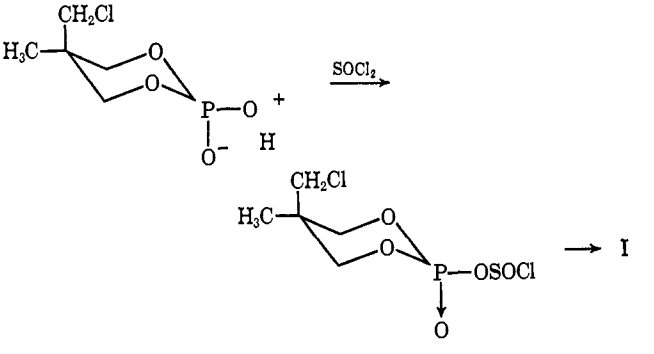
Compd[b]	Mp, °C	CH_3[a]	CH_2Cl
I	59–60	1.10	3.92
II	69–70	1.10	3.90
III	136–137	0.98	3.83
IV	152–153	0.98	3.83
V	182–183	1.28	3.60
VI	144–145	1.03	3.80

[a] Parts per million (δ values) downfield from internal TMS. Recorded on a Varian A60A spectrometer, deuteriochloroform as solvent. [b] All compounds gave satisfactory elemental analysis.

I and II to the amidates did not cause a change in the conformation of the five position. Compounds I and V must have a *cis* configuration (the terms *cis* and *trans* refer to the configurational relationship between the phosphoryl and halomethyl groups[6]), due to their mode of formation. Although the exact conformations of phosphorus in III and IV are not known with absolute certainty, the phosphoramidates must have the interrelationships shown for they have different physical properties including X-ray powder patterns.

The three phosphoramidates are thermodynamically stable for there are no signs of interconversion even at temperatures up to 250°. The energy barrier between IV and V must be unusually high in order for their respective conformations to be retained under these conditions. The stability of V can be rationalized on steric grounds for in the transition state for conversion to IV, 1–3 steric repulsions must be large if similarities with cyclohexane can be inferred. The stability of IV may be due to intramolecular dipole interactions between the chloromethyl group and the ring oxygens.

Both cyclic phosphorochloridates gave the identical acid upon hydrolysis. The acid upon treatment with thionyl chloride in refluxing chloroform gave the least stable phosphorochloridate, I, as evidenced by its physical properties and conversion to the phosphoramidate, III. The nmr of the acid indicated its chloro-



(1) W. S. Wadsworth, Jr., *J. Org. Chem.*, **32**, 1603 (1967).
(2) T. A. Beineke, *Chem. Commun.*, 860 (1966).
(3) M. J. Gallagher and I. D. Jenkins, *Top. Stereochem.*, **3**, 31–38, 82–85 (1968).
(4) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968).
(5) R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc., C*, 3033 (1968).
(6) W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **84**, 610 (1962).

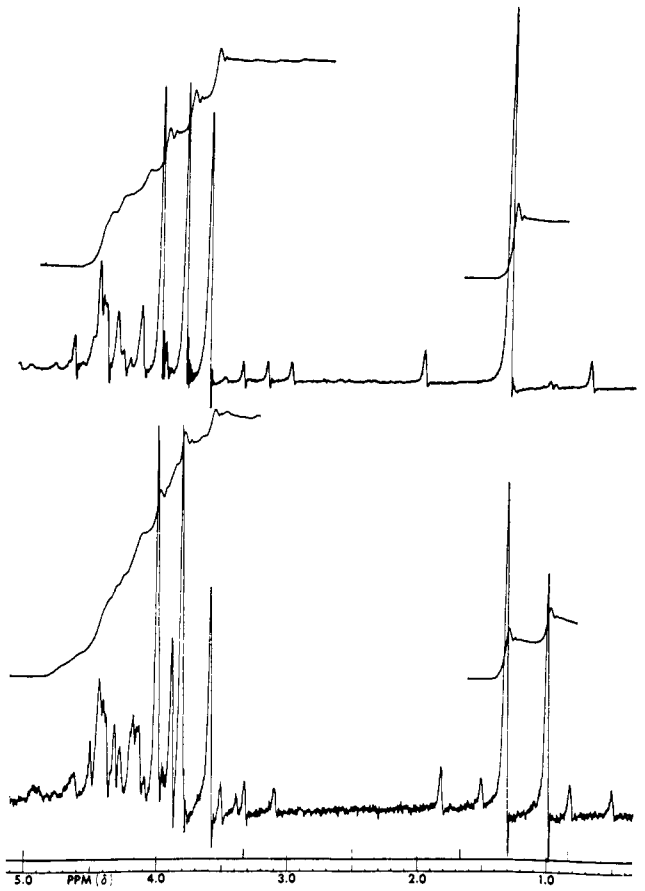
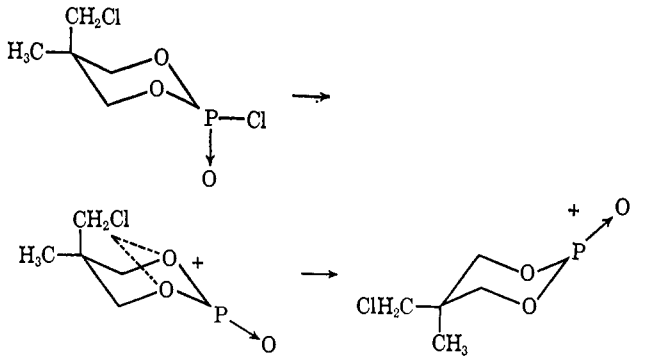


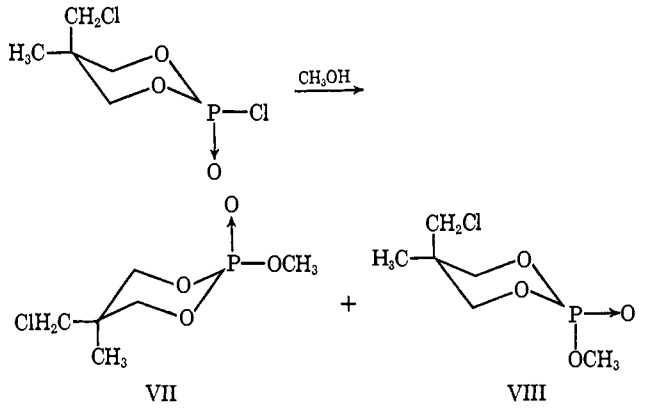
Figure 1. Lower spectrum: product resulting from methanolysis of phosphorochloridate II. Upper spectrum: product resulting from methanolysis of II carried out in the presence of 1 equiv of silver nitrate. Both spectra run in deuteriochloroform on a Varian A-60A spectrometer with TMS as an internal standard.

methyl group to be axial. The thionyl chloride may attack the oxygen at the least hindered equatorial position giving an adduct which, as indicated elsewhere,[7] decomposes with inversion of configuration.

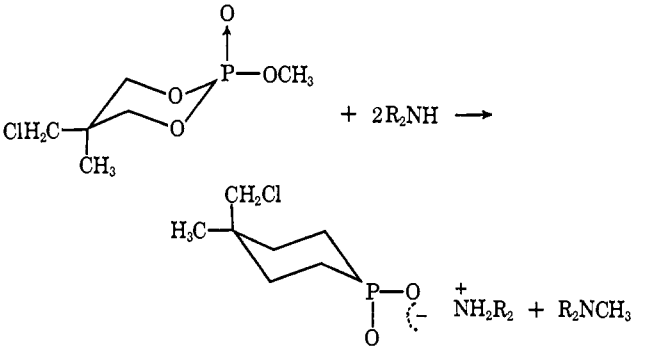
In contrast to the lack of conformational change upon treatment of the phosphorochloridate with an amine, methanolysis does produce a change. A pair of noninterconvertible isomeric esters is obtained upon removal of excess solvent from a methanolic solution which has stood for 24 hr. The nmr of the product, Figure 1, which does not change upon distillation indicates the isomers to be in a ratio of 2:1 with that isomer which has undergone conformational change predominating. The change in conformation is not due merely to a solvent effect for neither a methanolic solution of either isomer nor a methanolic solution of any of the previously described phosphoramidates showed change on standing. The ester VIII may result from direct SN2 (P) substitution with inversion at phosphorus. Evidence points to the fact that the formation of isomer VII with a change in conformation may proceed *via* an SN1 (P) mechanism in which a positive phosphorus ion is an intermediate. The developing positive charge would decrease the dipole



interaction, thus allowing conformational mobility at the five position. Our evidence for an SN1 (P) mechanism and indeed for assuming that VIII occurs by SN2 (P) substitution is strengthened by the discovery that the methanolysis when carried out in the presence of silver ion yields only that ester with a changed conformation, VII, and none of VIII. One would expect that in the presence of a strong electrophile the rate of formation of the positively charged species would be accelerated. The change in conformation can be followed very conveniently *via* nmr using CD_3OD as solvent. In this manner a first-order rate constant of 4×10^4 sec was obtained. Interestingly, for the uncatalyzed reaction only one ester of VII was obtained as evidenced by a single doublet for the methyl ester hydrogens. Methanol must attack the intermediate positive species from only one side. Although direct evidence is lacking we believe the methoxy group to be equatorial in VII for this would represent attack from the least hindered side and for steric reasons would aid in the conformation stability of the molecule. Indeed, when the methyl group is removed, as it is upon treatment of VII with piperdine, the conformation reverts to that of the original phosphorochloridate, the product being the amine salt of the acid.



VII VIII



(7) H. S. Aaron, R. T. Uyeda, H. F. Frack, and J. I. Miller, *J. Amer. Chem. Soc.*, **84**, 617 (1962).

Other reactions using the cyclic system described will be reported in a full paper.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation (Grant No. GP-10959).

(8) To whom inquiries should be sent.

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Dynamic Nuclear Magnetic Resonance Studies on Complex Spin Systems. Degenerate Valence Isomerization of a 3,4-Diazanorcaradiene

Sir:

Dynamic nmr spectroscopy (dnmr) has been a standard and often indispensable tool for many years, but applications to chemical rate processes have frequently been suffering from a notorious unreliability.[1] Arrhenius parameters and enthalpies and entropies of activation obtained by this technique are particularly prone to be in error[1,2] and many workers therefore restrict themselves to reporting only free energies of activation. On theoretical grounds we recently concluded[3,4] that certain inherent shortcomings of nmr line-shape analyses could sometimes be alleviated by deliberately choosing to study more complicated spectra. We now wish to report experimental evidence in support of our claim.[5]

At $-25.1°$[6] the cyclopropyl protons of 2,5-dicarbomethoxy-3,4-diazanorcaradiene (**1**) (15% solution in $CDCl_3$), obtained from 3,6-dicarbomethoxy-1,2,4,5-tetrazine[7] and cyclopropene, give rise to an A_2BC nmr spectrum[8] (Figure 1, top), whose least-squares analysis (Figure 2, top) yields the chemical shifts (at 60 MHz downfield from internal TMS) $\nu_A = 183.07 \pm 0.06$ Hz, $\nu_B = 136.60 \pm 0.06$ Hz, $\nu_C = -1.62 \pm 0.06$ Hz, and coupling constants $J_{AB} = 8.92 \pm 0.07$ Hz, $J_{AC} = 4.75 \pm 0.07$ Hz, $J_{BC} = -3.85 \pm 0.08$ Hz. At higher temperatures the rate of an $A_2BC \rightleftharpoons A_2CB$ mutual-exchange process becomes commensurate with the nmr time scale (Figure 1). Using linear least-squares functions for the temperature dependence of the static parameters (Figure 3), extrapolated to the broadened region,[9] rates were calculated (Figure 2) by the com-

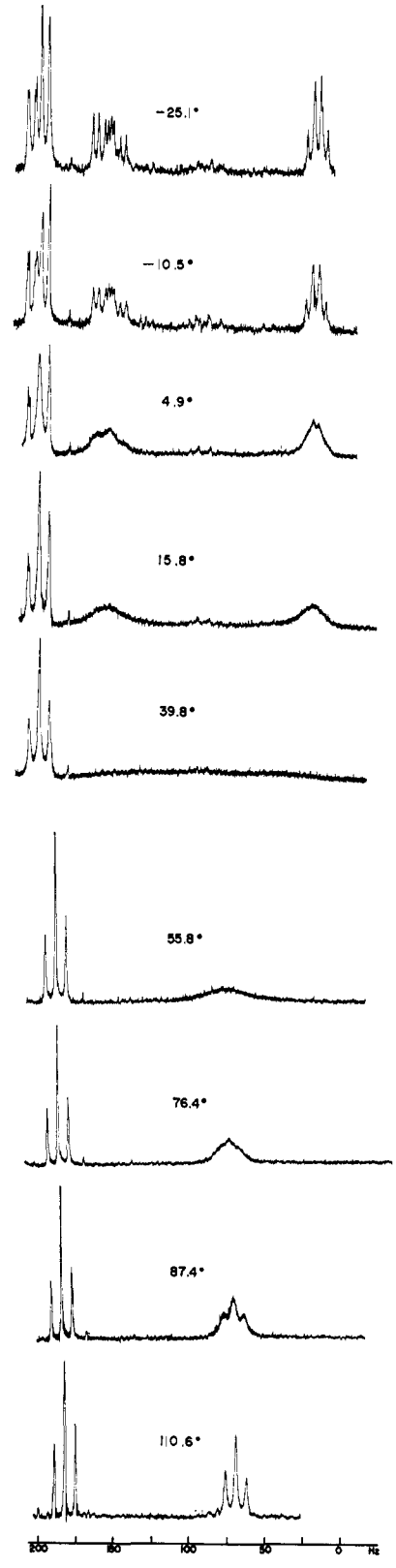
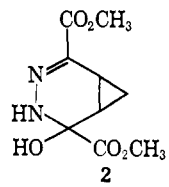


Figure 1. Experimental dnmr spectra of **1**.

(1) For a recent review see G. Binsch, *Top. Stereochem.*, **3**, 97 (1968).
(2) A. Allerhand, H. S. Gutowsky, J. Jonáš, and R. A. Meinzer, *J. Amer. Chem. Soc.*, **88**, 3185 (1966).
(3) G. Binsch, *ibid.*, **91**, 1304 (1969).
(4) D. A. Kleier and G. Binsch, *J. Mag. Resonance*, in press.
(5) Dr. K. I. Dahlqvist and Professor S. Forsén (Lund Institute of Technology, Sweden) have kindly informed us of experiments that lead to similar conclusions.
(6) Temperatures were calculated from the chemical shift difference between the methylene and hydroxyl resonances of an equimolar mixture of ethylene glycol and methyl-d_3 alcohol plus 0.03% of concentrated hydrochloric acid,[5] contained in a sealed capillary within the sample. The standard deviation of the temperature measurements was $\pm 0.3°$.
(7) M. Avram, I. G. Dinulescu, E. Marica, and C. D. Nenitzescu, *Chem. Ber.*, **95**, 2248 (1962); J. Sauer and G. Heinrichs, *Tetrahedron Lett.*, 4984 (1966); G. Heinrichs, H. Krapf, B. Schröder, A. Steigel, T. Troll, and J. Sauer, *ibid.*, in press.
(8) Compound **1** is accompanied by *ca.* 3% of the hydrate **2**, which could not be removed by recrystallizations.



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(9) This extrapolation predicts the time-averaged chemical shift of protons B and C at $+125°$ to within 0.3 Hz of the measured value.