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Base Catalyzed Nucleophilic Displacement Reactions of Pentacovalent Phosphorus.

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13. ABSTRACT (Maximum 200 words) Pentaoxyphosphoranes are studied as intermediates or activated states in nucleophilic displacement reactions at pentacovalent phosphorus. The work concentrated on the synthesis and structural characterization of cyclic oxyphosphoranes and their role in reaction mechanisms of cyclic AMP with phosphodiesterases and protein kinases. Both experimental and ab-initio calculations support mechanistic schemes for inversion of cAMP by phosphodiesterases which position the ring axial-equatorially in a trigonal bipyramid (TBP) and argue against retention mechanisms for the action of cAMP with protein kinases involving a covalently bound intermediate with the ring located diequatorially. Active site constraints, i.e., hydrogen bonding, electronegativity, steric, and ring strain, were used in synthesizing new oxyphosphorane model intermediates. Rings varying in size from five- to eight-membered prefer apical-equatorial sites of a TBP. Variable temperature NMR and single crystal X-ray diffraction gave energy barriers for ring interchange and solid state molecular structures, respectively. Both the theoretical and experimental work suggest that enhanced reactivity of cyclic phosphorus compounds should be aided by both ring strain relief and factors which remove electron density from the phosphorus reaction center such as hydrogen bonding and the presence of ligands of high electronegativity.

14. SUBJECT TERMS: Nucleophilic displacement reactions, cyclic oxyphosphoranes, reaction intermediates, cyclic AMP, phosphorinane rings, ab-initio calculations, trigonal bipyramidal geometry, protein kinases, phosphodiesterases.

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BASE CATALYZED NUCLEOPHILIC DISPLACEMENT REACTIONS OF
PENTACOVALENT PHOSPHORUS

FINAL REPORT

ROBERT R. HOLMES

SEPTEMBER 30, 1991

U.S. ARMY RESEARCH OFFICE

DAAL03-88-K-0190

UNIVERSITY OF MASSACHUSETTS

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A. STATEMENT OF THE PROBLEM STUDIED

Base catalyzed nucleophilic displacement reactions of phosphate esters, cyclic phosphates, and pentavalent phosphorus in general, proceed via phosphorane intermediates as activated states. Since the time I wrote an ACS Monograph on reaction mechanisms of phosphorus compounds, not a great deal of progress has been made in understanding underlying principles controlling reaction rates, mechanistic course, or the influence of the nucleophilicity of attacking reagents. The theoretical and correlative aspects also have lagged behind.

The aim of the work was to establish principles applicable to a wide variety of nucleophilic substitution reactions of phosphorus and to learn how these are altered with changes in reaction environment by means of a combination of theoretical and complimentary experimental studies. The work was directed to uncover factors leading to greater rate accelerations, particularly in hydrolysis reactions and enzymatic reactions.

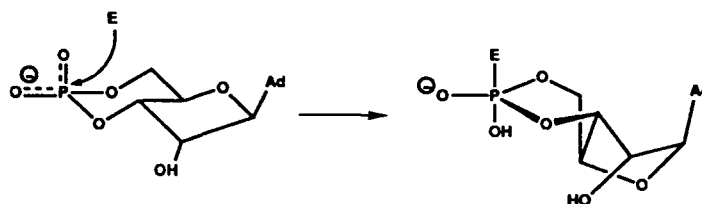
In this phase of the work, effort centered on the synthesis of new cyclic oxyphosphoranes and their characterization in the solid and solution state. Molecular structures were analyzed by X-ray diffraction studies to obtain geometries and bond parameters useful in the theoretical program in modeling reaction pathways. In particular, considerable effort was directed to an understanding of enzymatic reactions of cyclic adenosine monophosphate with phosphodiesterases and protein kinases. The theoretical program employed *ab-initio* calculations executed at the supercomputer level to aid in defining energetics and bonding features critical to a reaction pathway and to extract factors influencing mechanistic changeover produced by alterations in the nucleophiles, leaving groups, and the make-up of the nondeparting groups. The information obtained should be of direct applicability in connection with the Army Research Office's interest in rapid means of breakdown of phosphorus-containing chemical agents.

B. SUMMARY OF THE MOST IMPORTANT RESULTS

Appended are abstracts of eight of the twelve papers completed under this research program which summarize the main features of the work. Publication 12 (in progress) which represents an expansion of an invited paper presented at the symposium on "Phosphorus Chemistry in America - 1991," Fourth Chemical Congress of North America, August 25-30, 1991, summarizes a great deal of the research results directed toward cyclic pentaoxyphosphoranes as reactive intermediates. Superscripts refer to specific publications listed in Section C.

Relative to cyclic adenosine monophosphate (cAMP) action with protein kinases, we have established that a required intermediate with the trans-annulated six-membered ring situated diequatorially in a trigonal bipyramidal geometry lies approximately 6-12 kcal/mol above the trigonal bipyramidal geometry with this ring located in axial-equatorial positions.¹² These results were obtained from variable temperature ¹H and ¹³C NMR data giving activation energies for intramolecular ring rearrangement³⁻⁶ and from *ab-initio* calculations¹² carried out with a Cray supercomputer using the Gaussian system of programs of Pople and coworkers.

The synthesis and X-ray structural characterization of requisite cyclic oxyphosphoranes was carried out on systems in which ring sizes were varied from five- to eight-membered³⁻¹¹ and incorporated heterocyclic sulfur^{2,8} and nitrogen^{7,9} atoms in place of oxygen in some derivatives to assess their influence. Hydrogen bonding^{7,9} and the inclusion of trans-fused⁶ rings were utilized as added constraints in some derivatives to ascertain their influence on ring geometry and conformational preference. The introduction of hydrogen bonding^{7,9} led to stabilization of a chair form for six-membered saturated rings instead of the more conventional boat form found in the absence of hydrogen bonding in oxyphosphoranes. The molecular geometries determined from single crystal X-ray analysis reveal that the six-membered ring derivatives that are saturated have boat structures³⁻⁵ such that maximum pi bonding is present between phosphorus and oxygen located in the equatorial plane of a trigonal bipyramid. These results on pentaoxyphosphoranes change previous conclusions in a number of studies based on NMR data that have supported positioning of six-, seven-, and eight-membered rings in diequatorial sites, e.g., enzyme action on cAMP.¹² We find that the structures established in the



solid state are retained in solution based on variable temperature ^{13}C , ^1H , and ^{31}P NMR spectroscopy.³⁻⁵

Some important synthetic advances have occurred in this work. For example, the first example of a phosphorane structure containing a dithiaphosphorinane ring compound was prepared with the ring sulfur atoms bonded to phosphorus.² It exhibited an apical-equatorial orientation for the sulfur containing ring. The expected structure would place the more electronegative oxygen atoms in apical positions leaving the sulfur ring atoms in equatorial sites with the ring in a chair conformation. Use of electronegative trifluoroethoxy groups led to the synthesis of the first pentacoordinate oxyphosphorane containing an eight-membered ring situated in diequatorial positions of a trigonal bipyramid.¹⁰ A study of ring strain preferences support a lower ring strain for a saturated eight-membered ring in the latter geometry compared to saturated six-membered rings.^{3,4,9,12}

In summary, the results argue against mechanistic proposals in the literature on enzymatic action of c-AMP with protein kinases requiring a preference for diequatorial ring placement in a c-AMP pentacoordinated intermediate. Our work supports a greater relief of ring strain encountered in boat and chair conformations that are invariably found for saturated six-membered rings in axial-equatorial sites of a trigonal bipyramid of pentaoxyphosphoranes compared to that encountered for diequatorial ring placement. In accord, these results support inversion mechanisms of cAMP with phosphodiesterases that proceed in-line to give an oxyphosphorane intermediate resulting in the formation of 5'-AMP.

In a more general sense, both the theoretical and experimental work suggest that enhanced reactivity of cyclic phosphorus compounds should be aided by both ring strain relief and hydrogen bonding of the type revealed here which removes electron density from the phosphorus reaction center. One can expect a large enhancement in reactivity with the proper choice of nucleophile.

C. LIST OF PUBLICATIONS

1. K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day, and R. R. Holmes. "Cyclic Oxyphosphoranes with Six- and Seven-Membered Rings," *Phosphorus, Sulfur and Silicon* **49/50**, 367-372 (1990).
2. K. C. Kumara Swamy, J. M. Holmes, R. O. Day, and R. R. Holmes. "First Structural Study of a Thiophosphorane Containing a Six-Membered Ring. Phosphorus-Sulfur vs. Phosphorus-Oxygen Ligand Preferences," *J. Am. Chem. Soc.* **112**, 6092-6094 (1990).
3. K. C. Kumara Swamy, R. O. Day, J. M. Holmes, and R. R. Holmes. "Conformational Preferences of Spirocyclic Pentaoxyphosphoranes Varying in Ring Size," *J. Am. Chem. Soc.* **112**, 6095-6103 (1990).
4. S. D. Burton, K. C. Kumara Swamy, J. M. Holmes, R. O. Day, and R. R. Holmes. "Conformational Preferences of Monocyclic Pentaoxyphosphoranes Varying in Ring Size," *J. Am. Chem. Soc.* **112**, 6104-6115 (1990).
5. K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day, and R. R. Holmes. "Cyclic Oxyphosphoranes," *Phosphorus, Sulfur and Silicon* **53**, 437-455 (1990).
6. R. R. Holmes, K. C. Kumara Swamy, J. M. Holmes, and R. O. Day. "Conformational Effects of Ring Fusion and Heteroatom Substitution in Six-Membered Rings of Bicyclic Oxyphosphoranes," *Inorg. Chem.* **30**, 1052-1062 (1991).
7. R. O. Day, K. C. Kumara Swamy, L. Fairchild, J. M. Holmes, and R. R. Holmes. "Influence of Hydrogen Bonding on the Formation of Boat and Chair Conformations of Six-Membered Rings in Spirocyclic Tetraoxyphosphoranes," *J. Am. Chem. Soc.* **113**, 1627-1635 (1991).
8. J. Hans, R. O. Day, L. Howe, and R. R. Holmes. "Boat and Chair Forms for Sulfur-Containing Cyclic Oxyphosphoranes," *Inorg. Chem.*, **30**, 3132-3140 (1991).
9. J. Hans, R. O. Day, and R. R. Holmes. "Hydrogen Bonded Chain and Dimer Formations of Spirocyclic Tetraoxyphosphoranes Possessing Phosphorinane Chair Conformations," *Inorg. Chem.* **30**, 0000 (1991).
10. T. K. Prakasha, R. O. Day, and R. R. Holmes. "A New Structural Form for a Pentaoxyphosphorane. Diequatorial Ring Formation in a Trigonal Bipyramid," submitted for publication.
11. J. Hans, R. O. Day, L. Howe, and R. R. Holmes. "Conformational Comparison of a Seven-Membered Ring in Tri- and Pentacoordinated Geometries of Oxygen Containing Phosphorus Compounds. Solution NMR Behavior of Seven- and Eight-Membered Rings in Oxyphosphoranes," submitted for publication.
12. R. R. Holmes, R. O. Day, J. A. Deiters, K. C. Kumara Swamy, J. M. Holmes, J. Hans, S. D. Burton, and T. K. Prakasha, "Cyclic Oxyphosphoranes. Models for Reaction Intermediates," *ACS Symposium Series*, submitted for publication.

D. LIST OF PARTICIPATING SCIENTIFIC PERSONNEL

K. C. Kumara Swamy, Postdoctoral Research Associate

Sarah D. Burton, Graduate Research Assistant

Charles G. Schmid, Graduate Research Assistant

Joan M. Holmes, Staff Research Associate

Lisa Fairchild, Graduate Research Assistant

Johannes Hans, Postdoctoral Research Associate

Channareddy Sreelatha, Postdoctoral Research Associate

Tavarekere Prakasha, Postdoctoral Research Associate

T. Mohan, Postdoctoral Research Associate

Hari Gupta, Postdoctoral Research Associate

Both Sarah D. Burton and Charles G. Schmid received Ph.D. degrees.

E. APPENDIX

Abstracts of publications 1-8 listed in Section C are appended.

CYCLIC OXYPHOSPHORANES WITH SIX- AND SEVEN-MEMBERED RINGS

K. C. KUMARA SWAMY, SARAH D. BURTON, JOAN M. HOLMES,
ROBERTA O. DAY, AND ROBERT R. HOLMES⁺

Abstract X-ray and variable temperature NMR investigations of cyclic pentaoxyphosphoranes reveal a preference of six- and seven-membered rings for apical-equatorial orientations of trigonal bipyramids. Saturated six-membered rings prefer a boat conformation. Apical-equatorial ring pseudorotations are more facile for five-membered rings, whereas ligand exchange via diequatorial ring placement is more facile for the larger rings. Application to enzymatic reactions of cyclic AMP is emphasized.

INTRODUCTION

Although an abundance of structural studies¹ of phosphoranes containing five-membered rings have been performed, little is known about larger rings. In the area of pentaoxyphosphoranes, only one structural study exists. This concerns an X-ray study recently reported by D. Schomburg and coworkers² of a cyclic derivative containing a six-membered ring.

What we report here are X-ray and NMR studies of a series of related cyclic pentaoxyphosphoranes containing ring sizes from five- to seven-membered. The studies were undertaken to determine ring site preferences and solution state exchange processes, the knowledge of which should prove useful in interpreting mechanisms of nucleophilic displacement reactions of cyclic phosphorus compounds.

⁺Author to whom correspondence should be directed.

First Structural Study of a Thiophosphorane Containing a Six-Membered Ring. Phosphorus-Sulfur vs Phosphorus-Oxygen Ligand Preferences^{1,2}

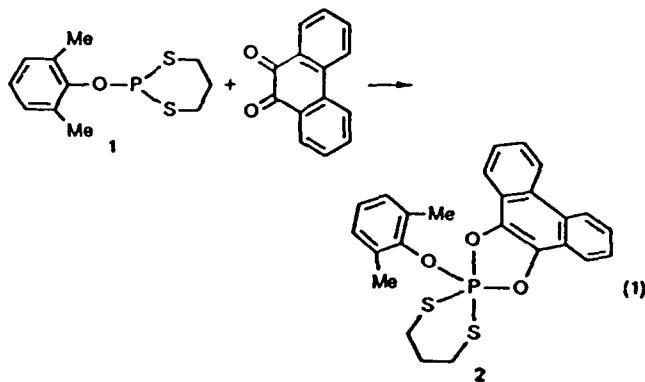
K. C. Kumara Swamy, Joan M. Holmes, Roberta O. Day, and Robert R. Holmes*

Contribution from the Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003. Received September 15, 1989.

Revised Manuscript Received March 31, 1990

Abstract: Oxidative addition of phenanthrenequinone to the newly synthesized dithiaphosphorinane, (Xylyl-O)P-S(CH₂)₃S (1), results in a new thiophosphorane containing a sulfur-bonded six-membered ring. X-ray analysis on separate crystals reveals both a monoclinic and triclinic modification. This represents the first structural study of a six-membered ring containing thiophosphorane. The structure which is a trigonal bipyramid has the ring sulfur atoms located in apical-equatorial sites instead of the expected diequatorial arrangement. As a consequence, the more electronegative xylyloxy oxygen atom is relegated to an equatorial position. A slightly twisted boat conformation exists for the dithiaphosphorinane ring. ¹H NMR spectroscopy is consistent with the retention of the solid-state structure in solution which undergoes rapid intramolecular ligand exchange.

Although an abundance of structural studies indicating conformational preferences for phosphoranes containing five-membered rings has been performed,^{3,4} little is known about corresponding six-membered ring systems.⁵ In the case of analogous thiophosphoranes, no structural information appears to be available.⁶ In this paper we report the first structural study of an unusual thiophosphorane containing a six-membered phosphorinane ring with ring sulfur atoms bonded to phosphorus. It is obtained in both a triclinic form, 2A, and a monoclinic form, 2B, from the oxidative addition reaction of phenanthrenequinone to 1 (eq 1), followed by recrystallization from dichloromethane.



(1) (a) Pentacoordinated Molecules. 80. (b) Part 79: Kumara Swamy, K. C.; Chandrasekhar, V.; Harland, J. J.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* 1990, 112, 2341.

(2) (a) Kumara Swamy, K. C.; Burton, S. D.; Holmes, J. M.; Day, R. O.; Holmes, R. R. Presented in part at the XI International Conference on Phosphorus Chemistry, Tallinn, Estonia, SSR/USSR, July 1989; Abstract 2-22. (b) Burton, S. D.; Kumara Swamy, K. C.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* 1990, 112, third of three papers in this issue.

(3) Holmes, R. R. *Pentacoordinated Phosphorus—Structure and Spectroscopy*; ACS Monograph 175; American Chemical Society: Washington, DC, 1980; Vol. 1 and references cited therein.

(4) Holmes, R. R. *Prog. Inorg. Chem.* 1984, 32, Chapter 2 and references cited therein.

(5) Some X-ray studies of phosphoranes with six-membered rings in a boat or twist-boat conformation involving oxygen and nitrogen ring atoms attached to phosphorus are as follows: (a) Barlow, J. H.; Bone, S. A.; Russell, D. R.; Trippett, S.; Whittle, P. J. *J. Chem. Soc., Chem. Commun.* 1976, 1031. (b) Schomburg, D.; Weferling, N.; Schmutzler, R. *Ibid.* 1981, 810. (c) Pochlauer, P.; Petter, W.; Peringer, P.; Müller, E. P. *Ibid.* 1985, 1760. (d) Schomburg, D.; Hacklin, H.; Röschenhaler, G. V. *Phosphorus Sulfur* 1988, 35, 241. (e) Yu, J. H.; Bentrude, W. G. *J. Am. Chem. Soc.* 1988, 110, 7587 (A report of a non-chair conformation for a six-membered oxygen-nitrogen ring bonded to pentacoordinated phosphorus apically and equatorially based on solution ¹H NMR evidence. More recently, these same workers reported a twist conformation for a model system closely related to cAMP: Yu, J. H.; Bentrude, W. G. *Tetrahedron Lett.* 1989, 30, 2195).

(6) A report of a phosphorane with a six-membered dithianaphthalene ring system is available but no structural information is given: Kimura, Y.; Kokura, T.; Saegusa, T. *J. Org. Chem.* 1983, 48, 3815.

X-ray analysis shows that the two crystalline modifications of 2 possess a trigonal-bipyramid structure with the principal difference between them being in the orientation of the *O*-xylyl group relative to the remainder of the molecule (Figure 1). Moreover, an apical-equatorial orientation for the sulfur-containing ring in both modifications arises in preference to a diequatorial ring placement that would allow the more electronegative oxygen atom of the xylyloxy group access to its preferred apical location. The observed structure is also unexpected on the basis of relative ring strain effects. In the diequatorial position, the six-membered ring suffers little strain, being accommodated with an ideal angle at phosphorus of 120°, whereas the actual structure contains the ring at a trigonal-bipyramidal angle at phosphorus of 90°.

In the monoclinic form, 2B, the intermolecular packing includes stacking interactions between phenanthrene groups of inversion related pairs of molecules (Figure 2). The phenanthrene planes of such pairs, required by symmetry to be parallel, are separated by a distance of 3.524 Å. In the triclinic form, 2A, inversion related pairs are in van der Waals' contact via atoms of the six-membered heterocyclic rings and no stacking interactions are observed. The packing is apparently more efficient in the monoclinic form as evidenced by the densities: 1.405 g/cm³ for 2B versus 1.346 g/cm³ for 2A.

Despite the marked difference in the mode of packing for the two forms, the geometries of the spirocyclic systems are nearly identical and the only important difference in the molecular geometries involves the disposition of the xylyloxy group (Figure 1). This provides fairly compelling evidence that the apical-equatorial placement of the six-membered ring is in no way due to the energetics of packing, but rather reflects energy minimization within the molecule.

A further feature of the two forms of 2 is the presence of the six-membered ring in a near boat (or twist boat) conformation, with the axial sulfur atom, S1, and the opposing carbon atom, C2, at the prow and the stern of the boat (Figure 3). The five-membered ring is essentially planar and coplanar with the fused phenanthrene group (the 17 atom system is coplanar to within ±0.059 Å for 2B and ±0.114 Å for 2A).

The axial-equatorial orientation for the six-membered ring in a near boat conformation is of the type discussed by Trippett^{3a,7} for phosphoranes that allows lone pairs of the equatorial ring atoms bonded to phosphorus to be placed near the equatorial plane for effective back-bonding.⁸ The extent to which this effect might occur for sulfur atoms in a derivative of this type is not known with any certainty.⁹ However, the preferred ring stabilization

(7) (a) Trippett, S. *Pure Appl. Chem.* 1974, 40, 595. (b) Bone, S. A.; Trippett, S.; Whittle, P. J. *J. Chem. Soc. Perkin I* 1977, 80.

(8) Hoffmann, R.; Howell, J. M.; Muetterties, E. L. *J. Am. Chem. Soc.* 1972, 94, 3047.

112,6095-6103

K. C. Kumara Swamy, Roberta O. Day, Joan M. Holmes, and Robert R. Holmes*

(1990)

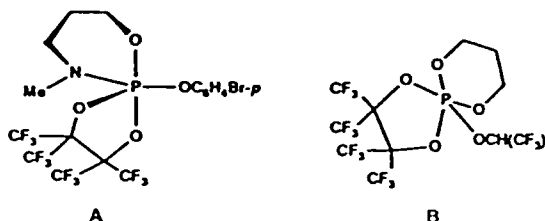
Contribution from the Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003. Received November 6, 1989

Abstract: New bicyclic pentaoxyphosphoranes 1–3 containing ring sizes varying from five to seven membered were synthesized by oxidative addition of a quinone or a diol to a cyclic phosphite. Variable-temperature solution ¹H and ¹³C NMR studies revealed the presence of dynamic intramolecular ligand exchange processes, one in which apical–equatorial ring interchange occurred between trigonal bipyramidal ground states and a higher temperature process supporting an exchange intermediate with the ring located diequatorially in a trigonal bipyramid. Activation energies for the latter process were determined. X-ray analysis supported the interpretation of the solution-state behavior and showed that saturated six-membered rings prefer a boat conformation occupying apical–equatorial positions in trigonal bipyramidal structures. The stability of the six-membered ring in this conformation is supported by the shorter P–O bond lengths found for this ring size compared to that for phosphoranes having five- and seven-membered rings. Phosphorane 1 crystallizes in the monoclinic space group *P2₁/n* with *a* = 10.633 (3), *b* = 17.648 (3), *c* = 13.601 (1) Å, β = 102.47 (1)°, and *Z* = 4. The bicyclic 2 crystallizes in the monoclinic space group *P2₁/n* with *a* = 10.459 (2), *b* = 12.712 (1), *c* = 19.949 (2) Å, β = 95.28 (1)°, and *Z* = 4. Bicyclic 3 crystallizes in the monoclinic space group *P2₁/n* with *a* = 9.655 (4), *b* = 11.662 (4), *c* = 22.720 (6) Å, β = 94.28 (3)°, and *Z* = 4. The bicyclic phosphorane 4 crystallizes in the orthorhombic space group *Pbcn* with *a* = 13.922 (4), *b* = 11.050 (2), *c* = 11.020 (3) Å, and *Z* = 4. The final conventional unweighted residuals are 0.037 (1), 0.093 (2), 0.050 (3), and 0.062 (4).

Introduction

While a great deal of effort has been expended in learning conformational requirements of five-membered rings in oxyphosphoranes,^{3,4} little is known about larger ring systems.^{16,5} Much of the work on oxyphosphoranes with five-membered rings derives from their interest as intermediates or transition states in non-enzymatic and enzymatic processes,⁶ e.g., phosphate ester hydrolysis, an area that has been extensively studied by Westheimer⁷ and Ramirez⁸ and their co-workers. Similar interests exist for phosphorus compounds with six-membered rings^{9–11} particularly with respect to the formation of pentacoordinated intermediates in enzymatic reactions of nucleoside 3',5'-monophosphates such as cAMP.^{12–14} Prior structural studies of phosphoranes containing six-membered rings are few but include a ring containing oxygen and nitrogen bonded to phosphorus, A,¹⁵ and one that is a pentaoxyphosphorane, B.¹⁶ Both derivatives

have these rings in a boat conformation. Solution NMR studies



(1) (a) Pentacoordinated Molecules. 81. (b) Part 80: Kumara Swamy, K. C.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* 1990, 112, first of three papers in this issue.

(2) Kumara Swamy, K. C.; Burton, S. D.; Holmes, J. M.; Day, R. O.; Holmes, R. R. Presented in part at the XI International Conference on Phosphorus Chemistry, Tallinn, Estonia, SSR/USSR, July 1989; Abstract 2-22.

(3) Holmes, R. R. *Pentacoordinated Phosphorus—Structure and Spectroscopy*; ACS Monograph 175; American Chemical Society: Washington, DC, 1980; Vol. 1 and references cited therein.

(4) Holmes, R. R. *Prog. Inorg. Chem.* 1984, 32, Chapter 2 and references cited therein.

(5) Burton, S. D.; Kumara Swamy, K. C.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.*, following paper in this issue and references cited therein.

(6) Holmes, R. R. *Pentacoordinated Phosphorus—Reaction Mechanisms*; ACS Monograph 176; American Chemical Society: Washington, DC, 1980; Vol. II, Chapter 2 and references cited therein.

(7) Westheimer, F. H. *Acc. Chem. Res.* 1968, 1, 70. *Ibid. Pure Appl. Chem.* 1977, 49, 1059.

(8) (a) Ramirez, F.; Ugi, I. *Bull. Soc. Chim. Fr.* 1974, 453. (b) Ramirez, F.; Marecek, J. F.; Ugi, I.; Lemmen, P.; Marquarding, D. *Phosphorus* 1975, 5, 73. (c) Marquarding, D.; Ramirez, F.; Ugi, I.; Gillespie, P. *Angew. Chem.* 1973, 85, 99.

(9) Cherkasov, R. A.; Ovchinnikov, V. V.; Pudovik, M. A.; Pudovik, A. N. *Russ. Chem. Revs.* 1982, 51, 746.

(10) Hall, C. R.; Inch, T. D. *Tetrahedron* 1980, 36, 2059.

(11) Reference 6, pp 149–163.

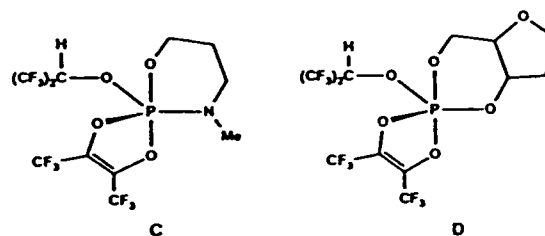
(12) Van Ool, P. J. J. M.; Buck, H. M. *Eur. J. Biochem.* 1982, 121, 329 and references cited therein.

(13) Nelson, K. A.; Bentrude, W. G.; Setzer, W. N.; Hutchinson, J. P. *J. Am. Chem. Soc.* 1987, 109, 4058.

(14) DeWit, J. W.; Hekstra, D.; Jastorff, B.; Stec, W. J.; Baraniak, J.; Van Driel, R. *Eur. J. Biochem.* 1984, 142, 255.

(15) Barlow, J. H.; Bone, S. A.; Russell, D. R.; Trippett, S.; Whittle, P. *J. J. Chem. Soc., Chem. Comm.* 1976, 1031.

support these findings. Detailed ¹H NMR studies by Yu and Bentrude have indicated the presence of the phosphorinane ring in a nonchair (boat and/or twist) conformation for C^{17a} and a twist conformation for D.^{17b} Further, they suggest^{17b} that the normal conformation for dioxo- and oxazaphosphorinanes is a nonchair form located in apical–equatorial sites.



Six-membered rings in trigonal-bipyramidal arrangements are expected to exert less ring strain than five-membered rings.¹⁸ Whereas five-membered rings invariably span apical–equatorial sites, six-membered rings might be expected to be located either apically–equatorially or diequatorially with little energy preference between them. On comparison of ligand exchange energies determined from dynamic NMR studies on cyclic oxyphosphoranes where diequatorial exchange activated states are proposed, it is apparent that six-membered rings provide lower barriers than five-membered ring systems.^{18a,19} For example, the pseudorotational process postulated for equilibration of CF₃ groups in E is accompanied by an exchange barrier of 17.4 kcal/mol compared

(16) Schomburg, D.; Hacklin, H.; Rösenthaller, G.-V. *Phosphorus Sulfur* 1988, 35, 241.

(17) (a) Yu, J. H.; Bentrude, W. G. *J. Am. Chem. Soc.* 1988, 110, 7897.

(b) *Ibid. Tetrahedron Lett.* 1989, 30, 2195.

(18) (a) Trippett, S. *Pure Appl. Chem.* 1974, 40, 595. (b) Bone, S. A.; Trippett, S.; Whittle, P. *J. J. Chem. Soc., Perkin I* 1977, 80.

(19) Chang, B. C.; Conrad, W. E.; Denney, D. B.; Denney, D. Z.; Edelman, R.; Powell, R. L.; White, D. W. *J. Am. Chem. Soc.* 1971, 93, 4004.

4

Conformational Preferences of Monocyclic Pentaoxyphosphoranes Varying in Ring Size^{1,2}

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Contribution from the Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003. Received November 6, 1989

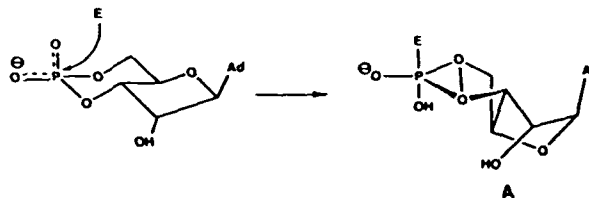
Abstract: New monocyclic pentaoxyphosphoranes 1-4, 6 and the furanosyl derivative, 7, were synthesized from the reaction of tris(2,6-dimethylphenyl) phosphite (5) with a diol or a quinone. The pentacoordinated derivatives 1-4 were studied by X-ray analysis and represent the first structurally characterized monocyclic oxyphosphoranes that have six-, seven-, and eight-membered rings. All possess trigonal-bipyramidal geometries with the rings spanning apical-equatorial positions. Retention of these structures in solution is indicated by ¹H, ¹³C, and ³¹P NMR. Twist-boat, rowboat, and distorted-tub conformations are found for the six- (1), seven- (2), and eight- (4) membered ring derivatives, respectively. Phosphorane 3 has a more planar phosphorinane ring, a consequence of ring unsaturation. Variable-temperature ¹H and ¹³C NMR establish nonrigid behavior supporting a simple Berry pseudorotation in which the rings exchange apical-equatorial positions. It is concluded that six-membered rings of pentaoxyphosphoranes prefer apical-equatorial sites of a TBP. The preferred conformation of saturated six-membered rings is generally that of a boat. Phosphorane 1 crystallizes in the monoclinic space group *C*₂/*c* with *a* = 29.392 (8), *b* = 11.420 (5), *c* = 16.379 (2) Å, β = 92.22 (1)°, and *Z* = 8. Compound 2 crystallizes in the monoclinic space group *P*2₁ with *a* = 12.268 (2), *b* = 9.916 (3), *c* = 12.625 (2) Å, β = 91.79 (1)°, and *Z* = 2. The monocyclic derivative 3 crystallizes in the monoclinic space group *P*2₁/*c* with *a* = 20.114 (6), *b* = 9.554 (2), *c* = 17.178 (3) Å, β = 114.24 (2)°, and *Z* = 4. Phosphorane 4 crystallizes in the triclinic space group *P* $\bar{1}$ with *a* = 9.690 (2), *b* = 15.414 (4), *c* = 21.350 (5) Å, α = 93.07 (2)°, β = 90.17 (2)°, γ = 99.97 (2)°, and *Z* = 4. The final conventional unweighted residuals are 0.056 (1), 0.039 (2), 0.038 (3), and 0.076 (4).

Introduction

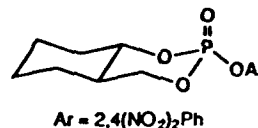
As the preceding paper has shown,^{1b} a series of bicyclic oxyphosphoranes subjected to X-ray analysis exhibited boat conformations for the six-membered rings comprising one of the cyclic components. The same result was found for a bicyclic pentaoxyphosphorane by Schomburg and co-workers⁴ and for a bicyclic oxythiophosphorane containing a six-membered phosphorus-sulfur bonded ring.⁵ The rings in these compounds which varied from five to seven membered were located apically-equatorially in trigonal-bipyramidal geometries. The uniformity in conformation and orientation of the six-membered rings might possibly be associated with the presence of the bicyclic system. However, related structural studies on monocyclic oxyphosphoranes with six-membered rings which could assist in deciding this issue appear nonexistent.

Previous work both of an experimental and theoretical nature indicates conflicting views concerning placement of six-membered rings. For example, on the basis of NMR and molecular model considerations, Ramirez et al.⁶⁻⁸ conclude that diequatorial ring placement in a trigonal bipyramid is lower in energy compared to an apical-equatorial orientation. van Ool and Buck find support for this conclusion from semiempirical molecular orbital calculations^{9,10} (CNDO/2) performed on possible pentacoordinated

intermediates for the hydrolysis of cAMP. The results indicate a lower energy for diequatorial ring placement of the six-membered ring in a trigonal bipyramid, about 28 kcal/mol, compared to an apical-equatorial ring position. In the activation of protein kinases by cAMP,¹¹⁻¹³ these calculations^{9,10} support diequatorial placement of the cyclophosphate ring which is proposed to result from attack by a functional group of the enzyme yielding a covalent complex, A. Also consistent with the above are proposed diequatorial ring



orientations in trigonal-bipyramidal transition states for the hydrolysis of epimeric phosphorinanes,^{14,15} e.g.,



By way of contrast, a low-temperature ¹³C NMR study¹⁶ indicates the occupancy of apical-equatorial sites for the diox-

(1) (a) Pentacoordinated Molecules 82. (b) Part 81: Kumara Swamy, K. C.; Day, R. O.; Holmes, J. M.; Holmes, R. R. *J. Am. Chem. Soc.*, preceding paper in this issue.

(2) Kumara Swamy, K. C.; Burton, S. D.; Holmes, J. M.; Day, R. O.; Holmes, R. R. Presented in part at the XI International Conference on Phosphorus Chemistry, Tallinn, Estonia, SSR/USSR, July 1989; Abstract 2-22.

(3) This work represents in part a portion of the Ph.D. Thesis of Sarah D. Burton, University of Massachusetts, Amherst, MA.

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Review

CYCLIC OXYPHOSPHORANES

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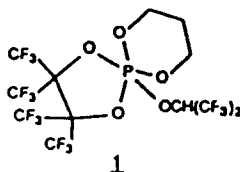
A review on pertinent information on cyclic oxyphosphoranes is presented. Recent X-ray structures and variable temperature ^1H NMR investigations of cyclic pentaoxyphosphoranes reveals a preference for a boat conformation for saturated six-membered rings in apical-equatorial orientations of trigonal bipyramids. These studies include five-, six-, and seven-membered rings and show that the solid state structures are retained in solution. Apical-equatorial ring pseudorotations are more facile for five-membered rings, whereas ligand exchange via diequatorial ring placement is more facile for the larger rings. The importance of the apical-equatorial ring orientation for phosphorinanes appearing as trigonal bipyramidal intermediates in enzymatic reactions of cyclic AMP analogs is emphasized.

Key words: Cyclic oxyphosphorane; trigonal bipyramid; Berry pseudorotation; cyclic AMP.

INTRODUCTION

Pentaoxyphosphoranes are useful models for intermediates in phosphate ester hydrolysis.^{1,2} The inclusion of five-membered cyclic substituents in phosphoranes has aided the interpretation of the great acceleration in hydrolysis of similarly constructed cyclic phosphate esters of importance in biological mechanisms. The latter interpretation has been summarized in the Westheimer model.²

Although an abundance of structural studies³ of phosphoranes containing five-membered rings has been performed, little is known about six-membered rings. In the area of pentaoxyphosphoranes, only one structural study had been reported up until our entrance into this field. This concerns compound **1** whose X-ray structure was recently reported by D. Schomburg.⁴



Six-membered rings in trigonal bipyramidal arrangements are expected to exert less ring strain than five-membered rings. Whereas, five-membered rings invariably span apical-equatorial sites, six-membered rings might be expected to be located either apical-equatorially or diequatorially with little energy preference between them. A greater knowledge of this preference would be of considerable

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nation step. A great amount of heat was given off, causing the THF to reflux during the time the solid isopropyltri-hydroborate was dissolving, so slow addition of THF was necessary.

Cyanation went more quickly and at lower temperatures than for isobutyltri-hydroborate, probably due to a stronger inductive effect of the secondary carbon of the isopropyl group. The method of at first using a deficiency reaction followed by adding the remainder of required $\text{Hg}(\text{CN})_2$ to complete the reaction worked well. Advantage was taken of the apparent order of reactivity of hydroborates with $\text{Hg}(\text{CN})_2$: $\text{RBH}_3^- > \text{BH}_4^- > \text{RBH}_2\text{CN}^- > \text{BH}_3\text{CN}^-$, allowing for complete conversion to the desired isopropylcyanodihydroborate, without either the dicyanation product or uncyanated $i\text{-PrBH}_3^-$ being present. A ^{11}B NMR spectrum taken of the amine-isopropylcyanoborane products (6a and 7a) revealed that neither over- nor undercyanation had occurred on the isopropyltri-hydroborate center and that the tetrahydroborate byproduct had been approximately half-cyanated to give BH_3CN^- .

The pyridine adduct 6a was a liquid that solidified at approximately 10°C . Since a small amount of isopropylboronic acid was present in 6a (as indicated in the ^{11}B NMR spectrum), no elemental analysis was obtained. The carbamoylborane product formed from 6a proved to have a good elemental analysis, showing that pyridine-isopropylcyanoborane had indeed been synthesized as an intermediate.

The other adduct was the quinuclidine-containing product 7a. This proved to be a crystalline solid, and it was the first quinuclidine adduct that was directly isolated without the use of column chromatography. After recrystallization to a sandlike colorless crystalline solid that melted at $132\text{--}134^\circ\text{C}$, a good elemental

analysis indicated successful purification of this derivative. Work on the purification of 7c continues.

Biological Activity. Samples of several of these new compounds have been submitted to Professor Iris Hall (School of Pharmacy, University of North Carolina, Chapel Hill, NC) for biological testing. Preliminary results indicate that these amine-alkylborane derivatives have similar hypolipidemic activity in general to that reported previously for the glycine boron analogues.^{2c,26} Some of the new compounds were found to have antiinflammatory activity that was more effective than indomethacin. Of most significance was the antineoplastic activity of selected compounds in vitro with respect to certain murine and human cell lines. In certain cases the cytotoxicity (ED_{50} $\mu\text{g}/\text{mL}$) values were better than those of 5-fluorouracil. A full report of this pharmacological activity will be published in the near future.

Acknowledgment. This work was supported by the U. S. Army Research Office and The Public Health Service.

Registry No. 1a, 124287-27-0; 1b, 131236-93-6; 1c, 131250-02-7; 2a, 124287-29-2; 2b, 131250-01-6; 2c, 131237-00-8; 3a, 124287-33-8; 3b, 125844-06-6; 3c, 125844-02-2; 4a, 124287-30-5; 4b, 131236-95-8; 4c, 131237-01-9; 5a, 124287-31-6; 5b, 131236-97-0; 5c, 131237-02-0; 6a, 131236-90-3; 6b, 131236-99-2; 6c, 131237-03-1; 7a, 131236-91-4; $i\text{-PrLi}$, 1888-75-1; $\text{Me}_2\text{S-BH}_3$, 13292-87-0; Et_3OBF_4 , 368-39-8; lithium isopropyltri-hydroborate, 84280-38-6; lithium isopropylcyanodihydroborate, 131236-89-0; pyridine hydrochloride, 628-13-7; quinuclidine, 100-76-5.

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Conformational Effects of Ring Fusion and Heteroatom Substitution in Six-Membered Rings of Spirocyclic Oxyphosphoranes^{1,2a}

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Spirocyclic oxyphosphoranes containing six-membered rings 1-5 were synthesized by oxidative addition of cyclic phosphites with phenanthrenequinone. Substituent variations in 1-5 allowed the examination of the conformational stability of the six-membered ring system. This ring in 4 was trans annelated with cyclopentane, established by X-ray analysis. The latter feature has relevance to c-AMP. A cis-fused phosphorinane derivative containing a furanose ligand 7 was also prepared. X-ray structures revealed trigonal-bipyramidal frameworks with the phosphorinane ring occupying apical-equatorial positions. The saturated six-membered ring was uniformly in a boat conformation. Despite considerable electronegativity and ring substituent effects, no diequatorial ring placement was evident. Variable-temperature ^1H NMR data indicated retention of solid-state structures in solution. Rapid pseudorotation is indicated for the various phosphoranes with the thio derivative 2 appearing more fluxional. Analogies with models for cyclic AMP action are discussed. Phosphorane 1 crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 7.769$ (2) \AA , $b = 10.191$ (2) \AA , $c = 29.594$ (5) \AA , and $Z = 4$. The thiophosphorane 2 crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 7.696$ (1) \AA , $b = 10.441$ (2) \AA , $c = 30.130$ (6) \AA , and $Z = 4$. The diaminothiophosphorane 3 crystallizes in the triclinic space group $P\bar{1}$ with $a = 10.078$ (3) \AA , $b = 10.133$ (3) \AA , $c = 12.253$ (3) \AA , $\alpha = 101.60$ (2)°, $\beta = 92.81$ (2)°, $\gamma = 105.00$ (2)°, and $Z = 2$. The fused-ring phosphorane 4 crystallizes in the monoclinic space group $P2_1/c$ with $a = 15.147$ (3) \AA , $b = 9.092$ (2) \AA , $c = 18.089$ (4) \AA , $\beta = 108.92^\circ$, and $Z = 4$. The final conventional unweighted residuals are 0.037 (1), 0.036 (2), 0.040 (3), and 0.040 (4).

Introduction

In recent studies on monocyclic and spirocyclic oxyphosphorane compounds,²⁻⁵ we have found that the structures assumed trigo-

nal-bipyramidal forms with the rings, which varied from five- to eight-membered, spanning apical-equatorial positions. For saturated six-membered rings, the preferred conformation is that of a boat with the axial atom at the prow of the boat and the opposing carbon atom at the stern. The latter observation agrees with model considerations presented earlier by Trippett,⁶ from which he concluded that the boat conformation is the only one that allows the lone pair on the equatorial atom to be in the favored equatorial plane.

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Influence of Hydrogen Bonding on the Formation of Boat and Chair Conformations of Six-Membered Rings in Spirocyclic Tetraoxyphosphoranes¹

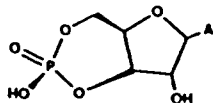
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Abstract: Oxidative addition reactions of the monocyclic phosphite, $(\text{Me}_2\text{C}_2\text{H}_4\text{O}_2\text{P}(\text{O-Xyl}))$, with aminophenol and aminocresol derivatives yielded the new bicyclic tetraoxyphosphoranes containing saturated six-membered rings, $(\text{C}_5\text{H}_{10}\text{O}_2)(\text{Xyl-O})\text{P}(\text{I-O-2-NHC}_6\text{H}_4)$ (1) and $(\text{C}_5\text{H}_{10}\text{O}_2)(\text{Xyl-O})\text{P}(\text{I-O-2-NH-X-MeC}_6\text{H}_3)$ ($\text{X} = 4$ (2), 5 (3)). Hydrogen bonding was introduced via N-H...O intermolecular interactions to ascertain their importance as a structural determinant. X-ray analysis revealed phosphoranes in a trigonal-bipyramidal framework with the rings positioned in axial-equatorial sites. Hydrogen bonding between molecular units gave rise to helical chain form 1 and dimeric forms 2 and 3. The phosphorane rings were present in a twist-chair conformation for 1 and in both twist-chair and twist-boat conformations for 2 and 3. Variable-temperature solution-state ¹H and ¹³C NMR supported retention of the solid-state structures and the presence of hydrogen bonding. Activation energies for intramolecular ligand exchange suggested at least a 10-kcal/mol requirement for reorientation of the six-membered ring in these phosphoranes to diequatorial locations in a TBP. The relevance of these results to pentaoxyphosphorane intermediates in c-AMP enzyme reactions is discussed. 1 crystallizes in the tetragonal space group $P4_1$ with $a = b = 10.772$ (3) Å, $c = 16.917$ (3) Å, and $Z = 4$. 2 crystallizes in the triclinic space group $P\bar{1}$ with $a = 12.529$ (2) Å, $b = 14.638$ (4) Å, $c = 14.842$ (3) Å, $\alpha = 60.78$ (2)°, $\beta = 76.21$ (2)°, $\gamma = 59.25$ (2)°, and $Z = 4$. 3 crystallizes in the monoclinic space group $P2_1/c$ with $a = 21.607$ (5) Å, $b = 14.901$ (4) Å, $c = 13.679$ (3) Å, $\beta = 108.30$ (2)°, and $Z = 8$. The final conventional unweighted residuals are 0.035 (1), 0.041 (2), and 0.049 (3).

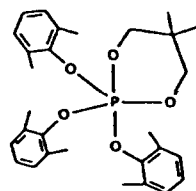
Introduction

Previous work^{1b,3-7} on cyclic pentaoxyphosphoranes which have ring systems varying from five- to eight-membered has revealed the principal structural features attributable to these compounds. Those phosphoranes which contain six-membered rings comprise a class of compounds that serve as models for intermediates or transition states in reactions of the nucleoside cyclic 3',5'-monophosphate, c-AMP.⁸⁻¹⁰ We have examined the molecular

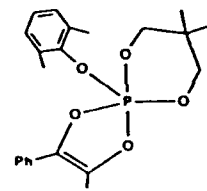


c-AMP

structures of eight^{1b,3-6} such members by X-ray crystallography and find that the rings of both monocyclic³ and spirocyclic^{1b,4} derivatives are positioned at apical-equatorial sites of a trigonal bipyramid. In the case of derivatives with six-membered saturated rings,^{1b,3-7} the rings reside in boat or twist boat conformations with the axial oxygen atoms and carbon atoms opposite them at the prow and the stern of the boat, e.g., A³ and B.⁴

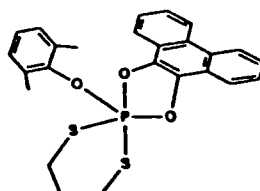


A³

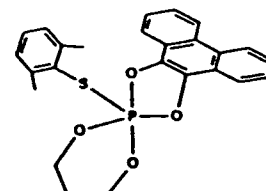


B⁴

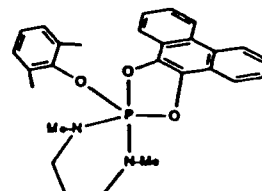
Additional X-ray analyses on members C-F^{1b,11,12} which have sulfur or nitrogen atoms in place of oxygen show that these structural preferences are maintained. Introduction of a



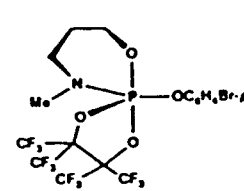
C¹¹



D^{1b}



E^{1b}



F¹²

trans-fused five-membered ring as is present in c-AMP also does not cause any significant structural variation. The first X-ray structures of three such members have recently been reported, G,^{1b,11} H,^{14a} and one that closely resembles H.^{14b}

(1) (a) Pentacoordinated Molecules 85. (b) Part 84: Holmes, R. R.; Kumara Swamy, K. C.; Holmes, J. M.; Day, R. O. *Inorg. Chem.*, in press. (c) Holmes, R. R.; Day, R. O.; Fairchild, L.; Kumara Swamy, K. C.; Holmes, J. M.; Burton, S. D. Presented in part at the 199th National Meeting of the American Chemical Society, Boston, MA, April 1990; INOR 503.

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(5) Burton, S. D.; Kumara Swamy, K. C.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* 1990, 112, 6104.

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the lower silicon-ligand bond strengths⁴² and greater positive charge at silicon⁴³ in the pentacoordinated anionic state compared to that in the tetracoordinate state as factors influencing enhanced reactivity of five-coordinated anionic silicon.

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Supplementary Material Available: Tables of atomic coordinates, thermal parameters, additional bond lengths and angles, and hydrogen atom parameters (Tables S1-S4 for 1 and Tables S5-S8 for 2, respectively) (22 pages); tables of calculated and observed structure factors (20 pages). Ordering information is given on any current masthead page.

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Boat and Chair Forms for Sulfur-Containing Cyclic Oxyphosphoranes^{1,2}

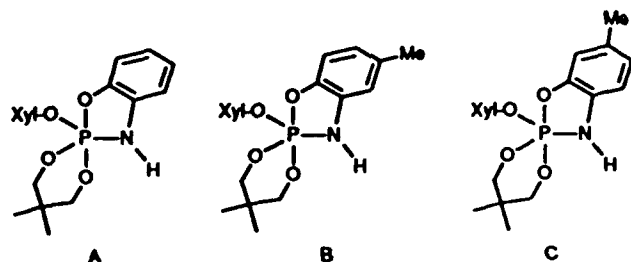
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Oxidative-addition reactions of pentafluorophenol or phenanthrenequinone to cyclic phosphites resulted in the formation of the new cyclic phosphoranes $(Me_2C_3H_4O_2)P(OC_6F_5)_2(S-Xyl)$ (1), $(C_3H_6S_2)P(OC_6F_5)_2(O-Xyl)$ (2), and $(C_3H_6S_2)P(O_2C_4H_8)(O-Xyl)$ (3). The monocyclic derivative 1 is unique in having the phosphorinane ring in a chair conformation at axial-equatorial sites of a trigonal bipyramid (TBP). Previously, boat forms were found at this location unless hydrogen bonding was present. Further, the ring in 1 has equal P-O axial and equatorial bond lengths, representing the first observance of this kind in pentacoordinate phosphorus chemistry. A combination of an electronegativity effect ascribed to the pentafluorophenyl groups and a steric contribution in the molecule is suggested as responsible for the uniqueness of 1. Both 2 and 3 have TBP structures with the thiophosphorinane ring in 2 residing in a twisted-boat conformation and the sulfur-containing five-membered ring of 3 present in an envelope conformation. Both rings are located at axial-equatorial sites. ¹H NMR spectra reveal that 1 undergoes rapid pseudorotation at room temperature involving axial-equatorial ring interchange, which is "stopped" at -65 °C. Most likely 2 is nonrigid similar to 1. The ¹H NMR spectra of 3 are invariant from 20 to -90 °C, showing nonrigid behavior indicating axial-equatorial to diequatorial activation for the phenanthrene ring in a pseudorotational process allowing equivalence of all four methylene protons of the sulfur-containing five-membered saturated ring. The monocyclic derivative 1 crystallizes in the triclinic space group *P* $\bar{1}$ with *a* = 11.239 (11) Å, *b* = 11.288 (5) Å, *c* = 11.934 (8) Å, α = 74.72 (5)°, β = 65.34 (6)°, γ = 74.58 (6)°, and *Z* = 2. The monocyclic derivative 2 crystallizes in the monoclinic space group *P*2₁/*c* with *a* = 14.485 (5) Å, *b* = 10.573 (4) Å, *c* = 16.626 (3) Å, β = 99.85 (2)°, and *Z* = 4. Spirocyclic 3 crystallizes in the monoclinic space group *P*2₁/*c* with *a* = 13.493 (2) Å, *b* = 9.048 (3) Å, *c* = 18.149 (6) Å, β = 96.86 (2)°, and *Z* = 4. The final conventional unweighted residuals are 0.095 (1), 0.036 (2), and 0.044 (3).

Introduction

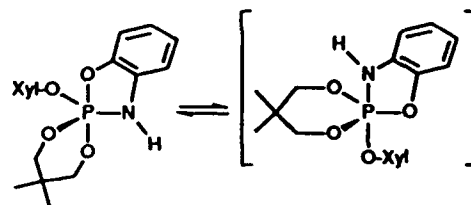
In our work on oxyphosphoranes with saturated six-membered rings, we reported that the normally observed boat conformation, which resides in axial-equatorial sites of a trigonal bipyramid (TBP), resulted in chair conformations when hydrogen bonding was introduced into the framework.⁴ This was found for the spirocyclic tetraoxyaminophosphoranes A-C by X-ray analysis.



For A, the solid-state structure consisted of a spiral arrangement of hydrogen-bonded (N-H...O) chains of trigonal bipyramids with the phosphorinane ring in a twist-chair form. For B and C, dimer formulations were found. In these dimer arrangements, both twist-chair and twist-boat forms were present. The results

indicate that the conformational conversion of boat and chair forms for phosphorinane rings in oxyphosphoranes is within the range of hydrogen-bond energies, i.e., of the order of a few kilocalories per mole.

Variable-temperature solution ¹H NMR data⁴ on A-C indicate intramolecular exchange (pseudorotation) via an intermediate having the phosphorinane ring located diequatorially, e.g., A.



Activation energies suggest that a minimum of about 10 kcal/mol is required to stabilize a six-membered ring of an oxyphosphorane of the type used here in diequatorial positions in preference to the axial-equatorial positions of a TBP when xylyloxy groups are present. However, so far no X-ray analyses of this class of compounds have shown diequatorial ring placement.⁴⁻¹⁰

- (1) (a) Pentacoordinated Molecules. 88. (b) Part 87: Kumara Swamy, K. C.; Sreelatha, C.; Day, R. O.; Holmes, J. M.; Holmes, R. R. *Inorg. Chem.*, preceding paper in this issue.
- (2) Presented in part at the 201st National Meeting of the American Chemical Society, Atlanta, GA, April 1991; INOR 300.
- (3) This work represents in part a portion of the M.S. Thesis of Lori Howe, University of Massachusetts, Amherst, MA, 1990.
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