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Role of Pseudorotation in the Stereochemistry of Nucleophilic Displacement Reactions

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Bimolecular nucleophilic displacements at M, a $(n - 1)$-coordinate reaction center, may proceed either by direct (SN2) substitution or by way of an addition–elimination mechanism. In the former, structure **1** represents a transition state, while in the latter, **1** is an n-coordinate intermediate whose lifetime is sufficient to render it operationally detectable. In eq 1, charges are not specified in order to maintain the generality of the scheme.

$$X + ML_{n-2}Y \rightleftarrows \underset{\mathbf{1}}{ML_{n-2}YX} \rightleftarrows ML_{n-2}X + Y \quad (1)$$

The stereochemical consequences of nucleophilic displacement at a chiral center are described in terms of the familiar concepts of inversion, retention, and racemization. When substitution occurs at a saturated carbon atom ($n = 5$) and at other first row atoms, the above condition of intermediacy is not encountered, and the stereochemistry of the displacement is conventionally described by attribution of inversion to backside attack, retention to front-side attack or to a sequence of an even number of inversion steps, and racemization to the formation of a species in which the carbon center is no longer chiral or to combinations of inversion and retention steps.

In contradistinction, by virtue of the capacity to achieve higher coordination numbers exhibited by the second-row and higher row elements, displacement at such centers by the two-step mechanism becomes a viable alternative to direct substitution, particularly since for such elements the unimolecular route is a relatively less favored pathway.[1] Interpretation of the stereochemical consequences of substitution now becomes significantly more complex. Such is the case for nucleophilic substitution at tetracoordinate phosphorus, where the intermediacy of pentacoordinate compounds of phosphorus (phosphoranes) has long been recognized.[2]

One of the ways in which an intermediate **1** may be recognized is by its stereochemical nonrigidity: the n ligands may suffer a nondissociative intramolecular exchange of sites, provided that the energy barriers to interconversion are low enough, and given a sufficient lifetime for **1** relative to dissociation into the $(n - 1)$-coordinate reaction partners. Intramolecular ligand reorganization has attracted particular attention to the pentacoordinate ($n = 5$) family of phosphorus compounds, in large measure through the pioneering investigations on phosphoranes by Wittig,[3] Hellwinkel,[4] Muetterties, *et al.*,[5] Ramirez,[6] and Westheimer.[7]

Phosphoranes exhibit trigonal-bipyramidal geometry.[5] The phosphorus atom lies within a triangle defined by three of the nearest bonding atoms which form the basal plane of the trigonal bipyramid. Bonds between phosphorus and these three ligands are designated as "equatorial" and, for the regular (D_{3h}) array (*e.g.*, as in PF_5), the equatorial bonds subtend an angle of 120°. The remaining two ligands, situated above and below the basal plane, are designated as "apical." In the D_{3h} array, the apical bonds subtend an angle of 180° with the phosphorus atom, and the axis connecting the three atoms is perpendicular to the basal plane.

Phosphoranes may undergo intramolecular ligand exchange by pseudorotation,[8] a vibrational motion akin in some respects to the pyramidal inversion of ammonia.[9] In pseudorotation by the Berry mechanism,[8]

(1) E. Ciuffarin and A. Fava, *Progr. Phys. Org. Chem.*, **6**, 81 (1968).
(2) W. E. McEwen, *Top. Phosphorus Chem.*, **2**, 1 (1965); M. J. Gallagher and I. D. Jenkins, *Top. Stereochem.*, **3**, 1 (1968).
(3) G. Wittig, *Bull. Soc. Chim. Fr.*, 1162 (1966).
(4) D. Hellwinkel, *Chem. Ber.*, **99**, 3628, 3642, 3660 (1966); *Angew. Chem.*, **78**, 749 (1966); *Chimia*, **22**, 488 (1968); D. Hellwinkel and H. J. Wilfinger, *Tetrahedron Lett.*, 3423 (1969).
(5) E. L. Muetterties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, **2**, 613 (1963); E. L. Muetterties, W. Mahler, K. J. Packer, and R. Schmutzler, *ibid.*, **3**, 1298 (1964); E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, **20**, 245 (1966); R. Schmutzler, *Angew. Chem., Int. Ed. Engl.*, **4**, 496 (1965); R. Schmutzler in "Halogen Chemistry," Vol. 2, V. Gutmann, Ed., Academic Press, New York, N. Y., 1967, p 73 ff.
(6) F. Ramirez, *Trans. N. Y. Acad. Sci.*, **30**, 410 (1968); *Accounts Chem. Res.*, **1**, 168 (1968).
(7) F. H. Westheimer, *ibid.*, **1**, 70 (1968).
(8) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).
(9) R. R. Holmes and R. M. Deiters, *J. Amer. Chem. Soc.*, **90**, 5021 (1968); *Inorg. Chem.*, **7**, 2229 (1968).

pairwise exchange of apical and equatorial ligands in the trigonal-bipyramidal molecule takes place by way of a tetragonal-pyramidal transition state.[10] The "pivot bond," which remains equatorial in the process, occupies the apex of the pyramid in the transition state. This motion is illustrated in Figure 1, where the ligand pairs which undergo exchange are designated by 2,3 and 4,5 and the pivot ligand by 1. Rearrangements such as this have been termed polyhedral or polytopal by Muetterties.[11] It is readily perceived that, if the phosphorus atom in the starting molecule is a chiral or prochiral[12] center, pseudorotation in the intermediate state (**1**) may profoundly affect the stereochemical outcome of the reaction in eq 1.

Recent years have witnessed intense concern on the part of several research groups, including our own, with this effect on the stereochemistry of displacements at phosphorus and other second-row atoms. This Account discusses some of this work, with special emphasis on a topological representation which greatly facilitates orderly and systematic analysis of the complex displacement–rearrangement chemistry.

Topological Representations

As illustrated in Figure 2, a given isomer of a phosphonium ion in which the phosphorus atom is bonded to four distinguishable ligands can undergo attack by a nucleophile, the fifth ligand-to-be, at any one of four different faces or six different edges; face attack and edge attack place the entering substituent in the apical and equatorial positions, respectively. In the general case, when all five ligands are different, and in the absence of special constraints, ten stereoisomeric phosphoranes are thus produced from a given stereoisomer of the starting ion, or a total of 20 phosphoranes from both starting isomers.

Since each pseudorotation exchanges a pair of equatorial and apical ligands, and since each isomer has three equatorial ligands which may serve as pivots, three access routes lead, by a single step, from any given stereoisomer to three others. For 20 isomers, there should thus be a total of 60 pseudorotation steps, but since each pseudorotation connects two isomers, the maximum number of interconnecting steps is reduced to half that number.

The set of 20 interconverting isomers and the network of 30 interconnecting pseudorotations may be depicted in the form of a *Desargues–Levi* graph,[13] with isomers and pseudorotations represented by vertices

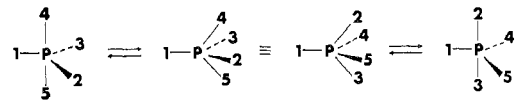


Figure 1. Pseudorotation. At the far left, ligands 4 and 5 are apical, and ligands 1, 2, and 3 are equatorial; at the far right, ligands 2 and 3 are apical, while 1, 4, and 5 are equatorial. Ligand 1 is the pivot.

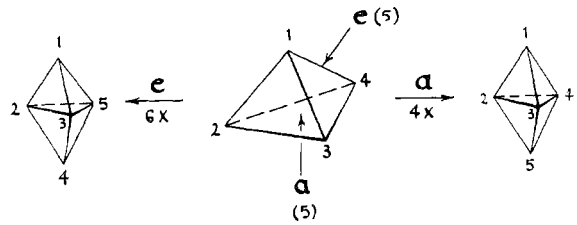


Figure 2. Edge attack by ligand 5 on a four-coordinate, tetrahedral structure (center) introduces the ligand in an equatorial (e) position (at left), while attack at mid-face introduces it in an apical (a) position (at right).

and edges, respectively. Such a graph is regular, since the vertices are all equivalent, but it is impossible to project such a graph in three dimensions without distorting the appearance of equivalence of the 20 vertices. For that reason, all such geometric figures (images) are, in a way, misrepresentations. Nevertheless, with this limitation in mind, the topological representations fulfill an extremely useful function in discussion, for they provide, as will be described below, an overview and map of the multiple interconversion pathways available to the reaction system.

The chief advantage of analysis of these phenomena in terms of the Desargues–Levi graph lies in the convenience and economy of this approach. The same conclusions could ultimately be arrived at by a complete listing of all alternative pathways and interrelationships. In contrast to such a cumbersome procedure, use of the Desargues–Levi graph enables the whole network of displacements and isomerizations to be viewed at a glance. It powerfully aids intellectual analysis, somewhat as algebra facilitates the analysis and solution of problems that could also be dealt with through verbal reasoning and arithmetic.

The first chemical application of the Desargues–Levi graph was reported by Balaban, *et al.*,[14] who were concerned with the family of 1,2 shifts in carbonium ions. More recently, Lauterbur and Ramirez[15] utilized the same graph[16] to describe the interconversion of stereoisomeric phosphoranes by pseudorotation. Our own geometric realization[16,17] of the Desargues–Levi graph has idealized D_{3d} symmetry (Figure 3).[18] Pseu-

(10) Alternative mechanisms are conceivable; *cf.* E. L. Muetterties, *J. Amer. Chem. Soc.*, **91**, 4115 (1969). However, see G. M. Whitesides and H. L. Mitchell, *ibid.*, **91**, 5384 (1969); R. R. Holmes, R. M. Deiters, and J. A. Golen, *Inorg. Chem.*, **8**, 2612 (1969).

(11) E. L. Muetterties, *J. Amer. Chem. Soc.*, **91**, 1636 (1969).

(12) K. R. Hanson, *ibid.*, **88**, 2731 (1966). For purposes of the present discussion, a prochiral center is one in which two of the ligands are enantiotopic, as in CH_2FCl.

(13) This name was suggested by Professor H. S. M. Coxeter (private communication); *cf.* H. S. M. Coxeter, *Bull. Amer. Math. Soc.*, **56**, 413 (1950). For related definitions and terminology, see O. Ore, "Theory of Graphs," American Mathematical Society, Providence, R. I., 1962, or F. Harary, "Graph Theory," Addison-Wesley, Reading, Mass., 1969.

(14) A. T. Balaban, D. Fărcaşiu, and R. Bănică, *Rev. Roum. Chim.*, **11**, 1205 (1966).

(15) P. C. Lauterbur and F. Ramirez, *J. Amer. Chem. Soc.*, **90**, 6722 (1968).

(16) Since isomorphic graphs have the same graph properties, it is merely a matter of taste and convenience which image of the graph is employed.

(17) K. E. DeBruin, K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7031 (1969).

(18) This image is also preferred by M. Gielen and J. Nasielski, *Bull. Soc. Chim. Belges*, **78**, 339 (1969).

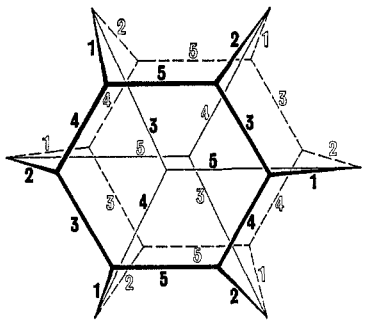


Figure 3. Desargues–Levi graph projected onto a plane. Isomers are represented by vertices and pseudorotations by the lines connecting vertices, the index of the pivot ligand for each pseudorotation being shown alongside the line.

dorotations are designated by the numerals over the edges, related through the center of symmetry, and each such numeral denotes the index of the pivot (necessarily equatorial) ligand. Consequently, the identity of each isomer is automatically defined, except for chirality. For example, the vertex at the junction of 2, 3, and 5 represents the isomer whose equatorial ligands are 2, 3, and 5. The apical ligands are therefore identified as 1 and 4. According to the convention employed, a given isomer is designated by the apical ligands, *i.e.*, 14, or its enantiomer, $\overline{14}$, in the present example. Chirality is denoted, arbitrarily, by the ascending numerical order of equatorial ligand indices for each isomer: if clockwise when viewed from the apical ligand with the lower numerical index, the isomer is unbarred; if counterclockwise, barred.[17] The isomer designations thus generated are given in Figure 4.

Effect of Ring Constraint on the Stereochemistry of Displacement Reactions by External Nucleophilic Attack

Nucleophilic displacement reactions which take place by attack on phosphorus in phosphonium ions have different stereochemical consequences depending on whether or not the phosphorus atom is incorporated in a small (*i.e.*, four- or five-membered) ring system; in the acyclic system, displacement usually results in *inversion*, whereas in the cyclic system, *retention* of configuration at phosphorus is usually observed. This is strikingly illustrated in displacement reactions on tetracoordinate phosphorus incorporated in a four-membered-ring (phosphetane) system, and credit for the first such observation belongs to Cremer and Chorvat,[19a] who found that reduction of phosphetane 1-oxides with $HSiCl_3$–$(C_2H_5)_3N$ affords phosphetanes with retention of configuration, in contrast to the inversion observed in the reduction of analogous acyclic phosphine oxides.[19b] Neither the mechanism of the reduction nor the rationale for the stereochemistry was at that time (1967) recognized. It should be noted in this connection that asymmetric phosphines, $R_1R_2R_3P$,

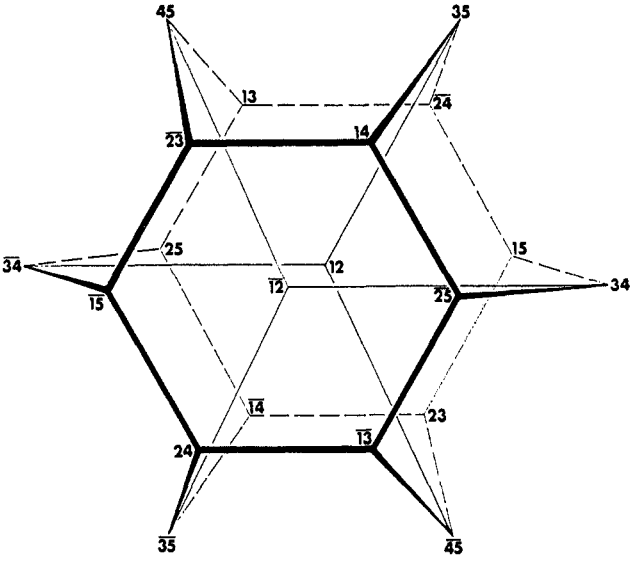
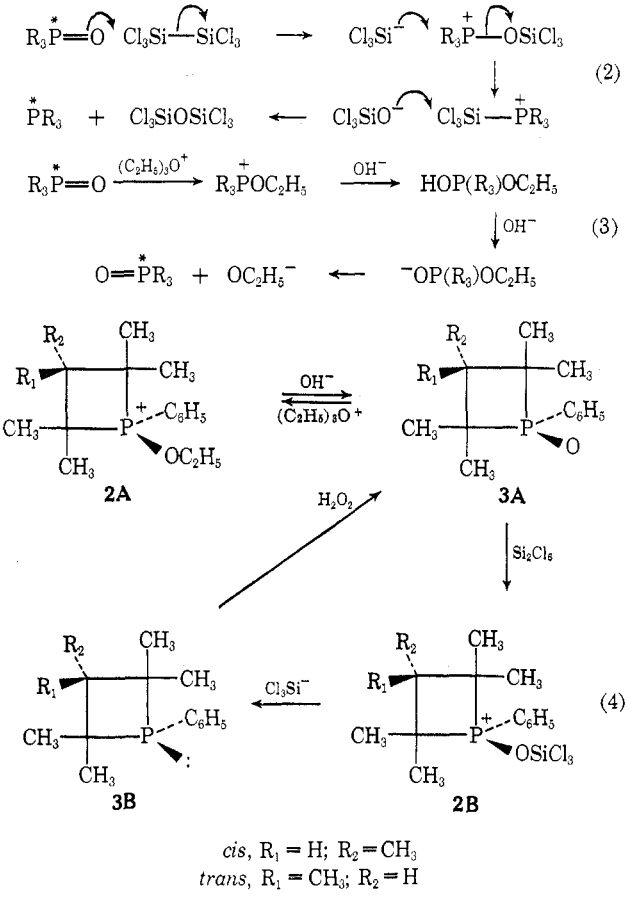


Figure 4. Desargues–Levi graph projection, showing designations of isomers represented by vertices. Each isomer is designated by the indices of its apical ligands; thus, 14 has ligands 1 and 4 apical, and $\overline{14}$ is its mirror image.

are configurationally stable under the conditions of this and other reactions described below; temperatures in excess of 100° are generally required to effect significant pyramidal inversion.[20]

In connection with our studies on optically active

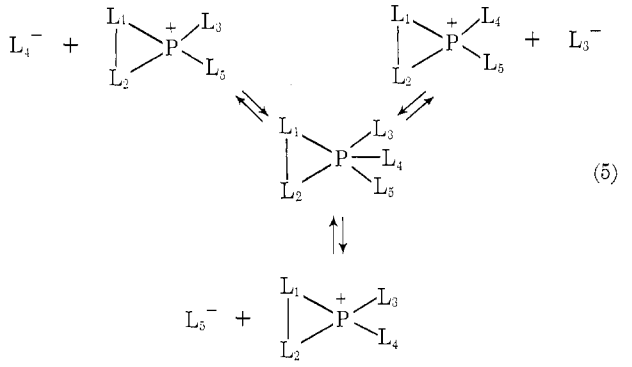


(19) (a) S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967); (b) L. Horner and W. D. Balzer, *Tetrahedron Lett.*, 1157 (1965).

(20) R. D. Baechler and K. Mislow, *J. Amer. Chem. Soc.*, **92**, 3090 (1970), and references cited therein.

phosphine oxides,[21] we had found that deoxygenation of acyclic phosphine oxides with hexachlorodisilane proceeds with overall inversion of configuration[22] (eq 2), that base-catalyzed hydrolysis of ethoxyphosphonium ions derived from acyclic phosphine oxides likewise proceeds with overall inversion of configuration[23] (eq 3), but that the same nucleophilic displacement reactions proceed with overall retention of configuration when the phosphorus atom is constrained in the phosphetane system[24] (eq 4). In order to assess the factors responsible for these contrasting results, a detailed analysis of the stereochemistry at the intermediate phosphorane stage was undertaken.

Displacements such as those in eq 4 may be generalized by eq 5, in which the convention is employed of



(5)

assigning indices 1 and 2 to the ring termini. Bearing in mind that the phosphetane ring is incapable of spanning (and therefore L_1 and L_2 of simultaneously occupying) the apical positions, diastereomer 12,$\overline{12}$ is eliminated, and excision of the corresponding two vertices and six connecting edges from the graph in Figure 4 leaves the 18-vertex graph which is shown in Figure 5 and which resembles the carbon skeleton of hexaasterane, a member of the asterane series of hydrocarbons.[25]

Let us now pass three surfaces through the three-dimensional representation of the 18-vertex graph, so that each surface divides the set of 18 vertices into two subsets of nine. These surfaces, indicated by the dashed lines in Figure 5 as projections of planes, shall be referred to as σ_n, where the subscript denotes the index of the edges bisected by the plane.

Also shown in Figure 5 are the formulas of three pairs of phosphonium ions. The members of each pair differ in chirality at phosphorus. Each pair straddles a dashed line and is operationally associated with the corresponding surface in the following sense: each of the six phosphonium ions may give rise to the

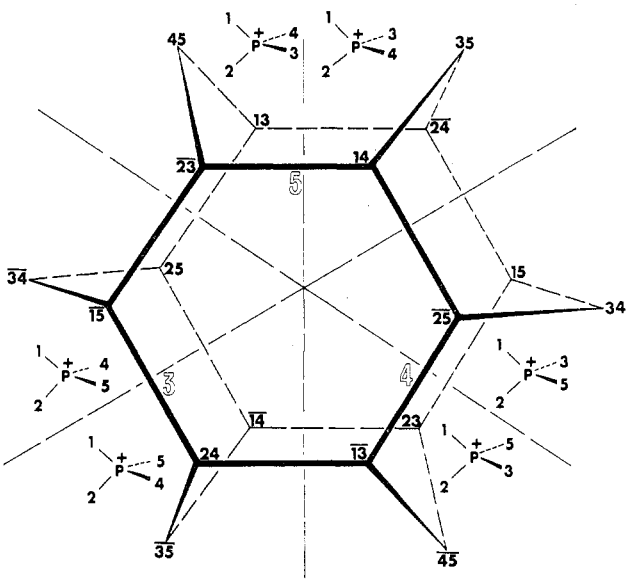


Figure 5. Hexasterane graph for phosphoranes derived from ring compounds such as **2** and **5**. The ring-member ligands are indexed 1 and 2, and isomers 12 and $\overline{12}$ are omitted. The long-dashed lines and the tetrahedral structures shown are explained in the text.

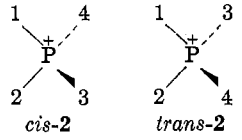
nine phosphoranes on its side of the dashed line by addition of the fifth ligand. For example, 13, $\overline{14}$, $\overline{15}$, $\overline{23}$, 24, 25, $\overline{34}$, $\overline{35}$, and 45 are the members of the western (*i.e.*, west of σ_5) subset of diastereomeric phosphoranes which are initial products of attack by an external nucleophile and ligand-to-be, L_5, on the phosphonium ion shown on the top left of Figure 5. As a second example, $\overline{13}$, $\overline{14}$, 15, 23, 24, $\overline{25}$, 34, $\overline{35}$, and $\overline{45}$, members of the southeastern (*i.e.*, southeast of σ_3) subset, are initial products of attack by L_3 on the phosphonium ion shown in the lower left-hand corner of Figure 5. By microscopic reversibility, each member of the same subset of nine phosphoranes reverts to the identical phosphonium ion upon P–L_n bond cleavage.

Figure 5 thus provides a stereochemical map of the displacement reactions in eq 5.[17] *In applications to chemical systems, it is immaterial whether the phosphorus atom in the phosphonium ion is a chiral or a prochiral center, but it should be noted that the vertex–isomer relationship depends on which type of center is involved.* If P is a *chiral* center, all vertices represent chiral molecules, enantiomers are related through the center of symmetry of Figure 5 (*e.g.*, 15 and $\overline{15}$ are enantiomers), and the phosphoranes in each subset are enantiomers of those in the partner subset related by σ_n. On the other hand, if P is a *prochiral* center, as in **2** ($R_1 \neq R_2$), the vertices on the top hexagon of Figure 5 represent six chiral diastereomers which are related to their respective mirror images, arranged at the vertices on the bottom hexagon, by reflection through a plane containing the points of the star (*e.g.*, $\overline{15}$ and 25 are enantiomers). The six isomers corresponding to the points of the star are meso forms, and the phosphoranes in each subset are diastereomers of those in the partner subset related by σ_n.

The phosphetanium ions **2** in eq 4 may be coded as shown, where L_1 and L_2 are the enantiotopic ring branches, L_3 = C_6H_5, and L_4 = OC_2H_5 (A) or $OSiCl_3$

(21) O. Korpiun and K. Mislow, *J. Amer. Chem. Soc.*, **89**, 4784 (1967); O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *ibid.*, **90**, 4842 (1968); R. A. Lewis and K. Mislow, *ibid.*, **91**, 7009 (1969).
(22) K. Naumann, G. Zon, and K. Mislow, *ibid.*, **91**, 7012 (1969).
(23) G. Zon, K. E. DeBruin, K. Naumann, and K. Mislow, *ibid.*, **91**, 7023 (1969).
(24) K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *ibid.*, **91**, 7027 (1969).
(25) U. Biethan, U. v. Gizycki, and H. Musso, *Tetrahedron Lett.*, 1477 (1965).

(B). It follows that attack by L_5 (OH^- or $SiCl_3^-$) on *cis*- and *trans*-**2** is capable in principle of yielding any



cis-**2** *trans*-**2**

one of the subset of phosphoranes in the sectors west and east of σ_5, respectively. A number of simplifying assumptions may now be made. First, face (apical) attack is preferred over edge (equatorial) attack;[17,26] this eliminates all but $\overline{15}$, 25, $\overline{35}$, and 45 from *cis*-**2**, and 15, $\overline{25}$, 35, and $\overline{45}$ from *trans*-**2**. Second, ring strain (corresponding to a formal L_1PL_2 bond angle deformation of *ca.* 30°), produced when a four-membered ring is required to span the equatorial-equatorial positions, eliminates 35, $\overline{35}$, 45, and $\overline{45}$. This leaves $\overline{15}$ and 25, enantiomers derived from attack on the enantiotopic faces of *cis*-**2**, and $\overline{25}$ and 15, enantiomers similarly derived from *trans*-**2**, as sole candidates for the initially produced phosphoranes.

The effect of the displacement reaction is to substitute L_5 for L_4. Retention or inversion therefore depends upon the sector in which the ultimate phosphorane, *i.e.*, the isomer which loses L_4 to give product, is located: the product will be *cis*- or *trans*-**3** depending upon whether the ultimate phosphorane is located in the southwest or northeast sector defined by σ_4.

The isomer number in each of these sectors is reduced from nine to four by application of an "extended" principle of microscopic reversibility,[7] which states in effect that the stereochemistry (apical *vs.* equatorial) of entry and departure must be the same. This concept has been broadly applied to displacement reactions at tetracoordinate phosphorus,[7,17] and it may be germane to elaborate in further detail on some of the underlying assumptions.

The principle of microscopic reversibility (PMR) merely states that, in mechanistic terms, the pathways of forward and reverse reactions at equilibrium are described by the same energy surface; it decidedly does *not* state that the profile of such a surface must be symmetrical with respect to the reaction path.[28] It would therefore be incorrect to state, without qualifications, that apical attack on phosphorus by nucleophile X (eq 1), followed by equatorial departure of Y (assuming that X = Y), violates the PMR. Only if the energy profile has mirror symmetry does this limitation apply, and in that case the corresponding mechanistic limitation is that equatorial *attack* (as well as departure) is excluded.[26] In the last analysis, the most that can be said on the basis of the PMR is that, assuming bond-making and -breaking processes are rate determining, equatorial departure is rendered unfavorable to the same extent (for symmetry reasons[28]) as apical attack is preferred[26] over equatorial attack. However, if the pseudorotational processes are rate determining, apical entry and equatorial departure (or *vice versa*) can no longer be ruled out as alternatives. To this must be added the further reservation that a symmetric energy profile is no longer possible when $X \neq Y$. The "extended" principle, and therefore any argument based on it, is weakened in proportion to the extent by which X and Y differ in character (nucleophilicity, electronegativity, etc.), *i.e.*, in proportion to the distortion in the symmetry of the energy profile for the displacement reaction which is introduced by this difference. Nevertheless, as a simplifying postulate, apical attack and apical departure will be assumed throughout this discussion, unless otherwise noted.

We shall now return to the elimination of isomers from the possible candidates for ultimate phosphoranes in the transformation of **2** to **3**. The isomer number is further reduced from four to two in each sector since ring strain effectively limits access to the star-points.[29] Accordingly, the ultimate phosphoranes derived from *cis*-**2** *via* $\overline{15}$ and 25 are identified as 24 and $\overline{14}$, respectively, for retention and 14 and $\overline{24}$, respectively, for inversion. The ultimate phosphoranes are the same but the stereochemical direction is reversed when one starts from *trans*-**2** *via* $\overline{25}$ and 15. To simplify the following discusssion, differences between enantiomers will be ignored, for enantiomers suffer the same chemical fate under achiral conditions, and only the pathway on the top hexagon, representing one set of enantiomers,[29] will be considered.

Starting from $\overline{15}$, two retention pathways exist: clockwise ($\overline{15} \rightarrow \overline{23} \rightarrow 14 \rightarrow \overline{25} \rightarrow \overline{13} \rightarrow 24$), and counterclockwise ($\overline{15} \rightarrow 24$). The shorter pathway is not necessarily the path of lower energy, but the ambiguity is resolved by recourse to the postulate that, in the reaction under discussion, the rate of loss of L_4 is fast compared to the rate of pseudorotation. Accordingly, if the rate of conversion of 14 into *trans*-**3** exceeds the rate of pseudorotation of 14 to 24, the clockwise mechanism is ruled out for retention and, by the same token, becomes the pathway for inversion.

(26) That apical attack and apical departure are the preferential modes of bond making and breaking, at least when the ligands in question are relatively electronegative, follows from several independent lines of argument: (a) apical bonds are longer and weaker than equatorial bonds [J. K. Wilmshurst and H. J. Bernstein, *J. Chem. Phys.*, **27**, 661 (1957); M. J. Taylor and L. A. Woodward, *J. Chem. Soc.*, 4670 (1963); M. Rouault, *Ann. Phys. (New York)*, **14**, 78 (1940); K. W. Hansen and L. S. Bartell, *Inorg. Chem.*, **4**, 1775 (1965); W. C. Hamilton, S. J. LaPlaca, F. Ramirez, and C. P. Smith, *J. Amer. Chem. Soc.*, **89**, 2268 (1967); R. D. Spratley, W. C. Hamilton, and J. Ladell, *ibid.*, **89**, 2272 (1967)]; (b) semiempirical (EHMO) calculations indicate that apical bonds are weaker and more ionic than equatorial bonds;[27] other EHMO calculations [D. B. Boyd, *ibid.*, **91**, 1200 (1969)] bear out the essential features of Westheimer's mechanism[7] of the hydrolysis of cyclic phosphate esters, including the preference for apical attack and loss. See also S. I. Miller, *Advan. Phys. Org. Chem.*, **6**, 253 (1968).

(27) P. C. Van Der Voorn and R. S. Drago, *J. Amer. Chem. Soc.*, **88**, 3255 (1966).

(28) R. L. Burwell, Jr., and R. G. Pearson, *J. Phys. Chem.*, **70**, 300 (1966).

(29) In transformations symbolized by the edges in Figure 5, any arc leading from the top to the bottom hexagon or *vice versa* must traverse a star-point vertex. For four- or five-membered ring compounds, this represents a highly strained form since the ring termini are in the equatorial positions. Such a pathway is thereby effectively eliminated from consideration, and the two hexagonal "tracks" are thus insulated from each other by a virtual barrier, the equatorial belt of vertices/phosphoranes.

It is now possible to analyze the distinguishing features of the two competing pathways. Retention ($\overline{15} \rightarrow 24$) requires one pseudorotation about L_3. Inversion ($\overline{15} \rightarrow \overline{23} \rightarrow 14$) requires two pseudorotations, one about L_4, followed by one about L_5. However, in the conversion of $\overline{15}$ to $\overline{23}$, switching the relatively electropositive equatorial ligand (L_3) and the relatively electronegative apical ligand (L_5) into apical and equatorial positions, respectively, amounts to an energetically unfavorable rearrangement,[30] whereas the conversion of $\overline{15}$ to 24 merely exchanges the apical and equatorial positions of the two relatively electronegative ligands, L_4 and L_5. The phosphorane at the crossroads, $\overline{15}$, thus faces three alternatives, *i.e.*, pseudorotation about L_2, L_4, and L_3, leading to $\overline{34}$, $\overline{23}$ (and thence to 14), and 24, respectively. The first pathway is blocked by ring strain,[29] and the second by the unfavorable placement of ligands described above (which for purposes of the present discussion we term "stereoelectronic strain"). This leaves $\overline{15} \rightarrow 24$ as the only viable alternative, and it follows that retention (*cis*-**2** → *cis*-**3**) is the preferred pathway.

Retention of configuration in reactions of *trans*-**2** is likewise accounted for. The sector northeast of σ_4 now represents retention and the southwest sector inversion; the counterclockwise pathway $\overline{25} \rightarrow 14$ (retention) is preferred over the clockwise pathway $\overline{25} \rightarrow \overline{13} \rightarrow 24$ (inversion), for the reasons given above.

It is remarkable that nonempirical LCAO–MO–SCF calculations on a heuristic model system,[33] using a moderately large basis set of Gaussian-type functions, lead to the same conclusions as the arguments advanced above. In this model, the gross features of the phosphoranes under discussion are approximated as follows: (a) L_1, L_2, and L_3 are represented by hydrogen atoms; (b) the relatively more electronegative groups L_4 and L_5 are simulated by hydrogen atoms modified by a 10% increase in nuclear charge; (c) phosphoranes with the ring spanning the apical-equatorial positions are regarded as having suffered no angle distortion from idealized trigonal-bipyramidal geometry;[34] (d) to represent phosphoranes in which the ring spans the equatorial-equatorial positions, one of the equatorial HPH (representing L_1PL_2) angles has been symmetrically contracted to 90°; and (e) the transition state for pseudorotation is given tetragonal-pyramidal symmetry.[35] The salient results of the calculation are depicted in Figure 6 for the displacement of L_4 in *cis*-**2** by L_5. The relative energies, in kilocalories/mole, of the phosphoranes shown are given by the parenthesized numbers adjacent to the circled vertices. The unparenthesized numbers superimposed on the edges of the graph give the calculated minimum energy, in kilocalories/mole, that must be expended in pseudorotation *in the direction indicated by the arrow*. Once again, $\overline{15}$, the initial phosphorane from *cis*-**2**, faces three alternatives, and once again pseudorotation about L_3 (2.5 kcal/mol) is favored over pseudorotation about L_2 (ring strain, 7.1 kcal/mol) or about L_4 (stereoelectronic strain, 8.7 kcal/mol). Hence, configuration is retained. However, the model calculations reveal previously unsuspected features of the reaction system: the four structures (34, $\overline{34}$, 35, and $\overline{35}$) in which ring strain is combined with stereoelectronic strain (L_4 or L_5 in an equatorial position) and those (13, $\overline{13}$, 23, and $\overline{23}$) in which stereoelectronic strain is at a maximum (L_4 and L_5 both in equatorial positions), *i.e.*, the eight structures in which L_3 occupies an apical position, are transition states or saddle points on the reaction surface, rather than stable or metastable intermediates. It follows that if stereoelectronic strain were to be overcome ($\overline{15} \rightarrow \overline{23}$), the subsequent conversion to 45 (followed by loss of L_4 and inversion of configuration) would require *no* additional energy, in contrast to the alternative pseudorotation step ($\overline{23} \rightarrow 14$, 2.4 kcal/mol). The model calculations[33] thus indicate the conditions under which the star-point barrier[29] is penetrable. They further reveal that the relief in stereoelectronic strain afforded when *both* electronegative groups occupy apical positions (as in 45) all but compensates for ring strain, and experiments discussed below appear to vindicate this conjecture.

The preceding stereochemical analysis of the reaction system **2** → **3** may be generalized to account for retention of configuration in other nucleophilic displacement reactions involving intermediate phosphoranes in which two of the ligands have significantly greater electronegativity than the other three, and in which two of the other three are termini of a small-ring system, for example, the alcoholysis and aminolysis of four-membered ring phosphinates and phosphinyl chlorides[36] and the $HSiCl_3$–$(C_2H_5)_3N$ reduction[19a] of **3A**.[37] However, an element of ambiguity enters when the distinction between the electronegativity of the reactive groups (L_4 and L_5 in our example) and that of the stable ligands (L_1, L_2, and L_3) is not clear-cut. This is the case in the base-catalyzed hydrolysis of 1-benzylphosphetanium (**4**)[38] and 1-benzylphospholanium (**5**)[39] ions which, in contrast to the hydrolysis of acyclic analogs,[40] proceeds

(30) Electronegative substituents prefer the apical positions, electropositive substituents the equatorial positions. This generalization may be derived empirically,[5,7] by extension of *ad hoc* valence bond arguments,[31,32] by semiempirical (EHMO) calculations,[27] or by nonempirical LCAO–MO–SCF calculations on model molecules.[33]

(31) A. D. Walsh, *Discuss. Faraday Soc.*, **2**, 18 (1947).

(32) H. A. Bent, *Chem. Rev.*, **61**, 275 (1961).

(33) A. Rauk, unpublished work. We are indebted to Professor L. C. Allen for helpful discussions.

(34) No geometry search was attempted. The assumed bond lengths in the D_{3h} structure of the hypothetical molecule PH_5 ($P–H_a$ = 1.508 Å, $P–H_e$ = 1.402 Å) were chosen by considering the P–H bond length in PH_3 and the relative apical and equatorial bond lengths in PCl_5.

(35) The C_{4v} structure represents the halfway point for conversion of one D_{3h} structure[34] to another (assumed $P–H_{ap}$ = 1.402 Å, $P–H_{bas}$ = 1.455 Å, $H_{ap}PH_{bas}$ = 103° 57′).

(36) W. Hawes and S. Trippett, *J. Chem. Soc. C*, 1465 (1969); S. E. Cremer and B. C. Trivedi, *J. Amer. Chem. Soc.*, **91**, 7200 (1969).

(37) The original observations[19a] are rationalized by an extension of the analysis here presented for **3A** → **3B**, granted that perchloropolysilanes are active intermediates in the deoxygenation.[22]

(38) J. R. Corfield, J. R. Shutt, and S. Trippett, *Chem. Commun.*, 789 (1969).

(39) K. L. Marsi, *ibid.*, 846 (1968); *J. Amer. Chem. Soc.*, **91**, 4724 (1969).

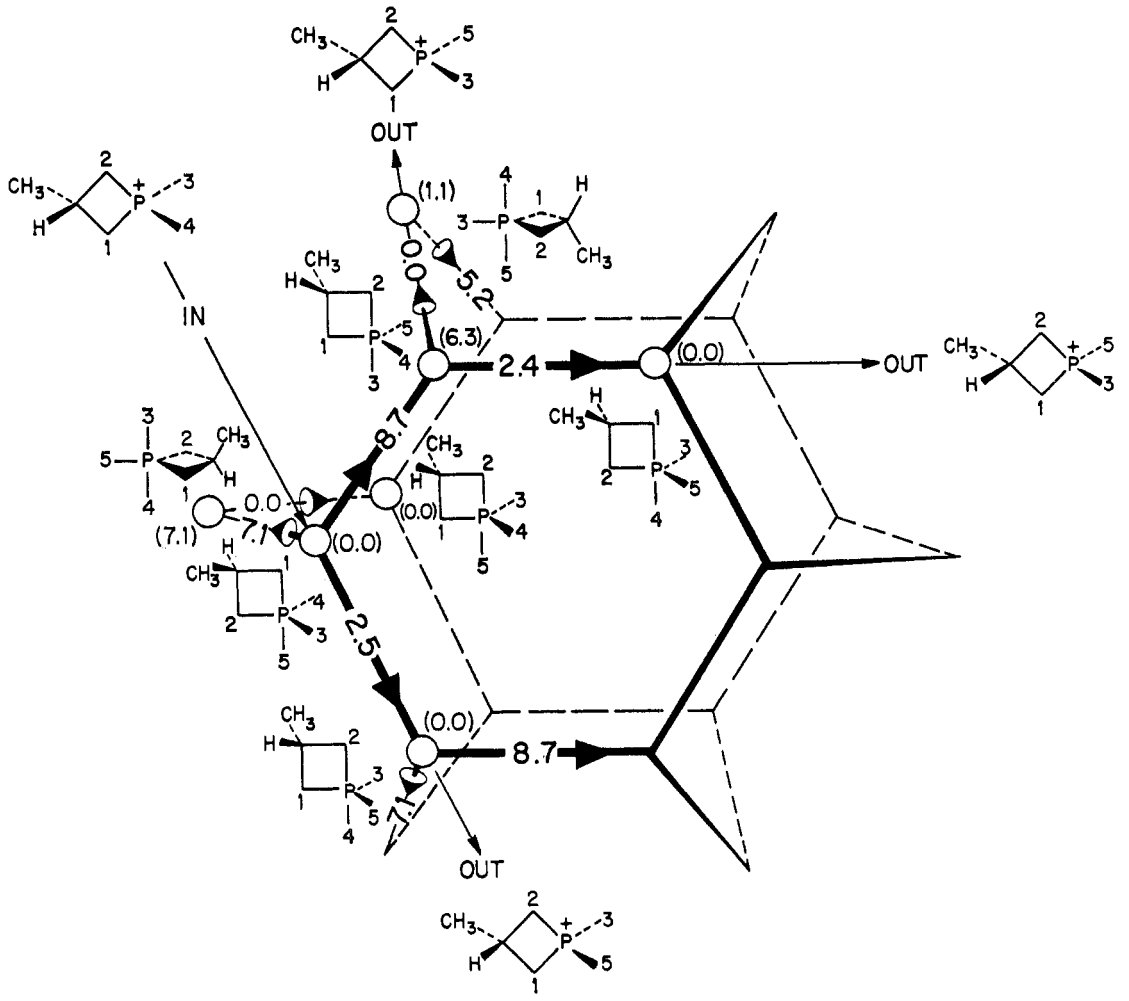


Figure 6. Displacement of L_4 in *cis*-**2** by L_5. Calculated relative energies (kcal/mol; in parentheses) of intermediate isomeric phosphoranes and calculated minimum activation energies (kcal/mol; on edges) for pseudorotation in the direction indicated by the arrows.

with complete retention of configuration. While an analysis along the lines discussed above is still admissible,[17] apical attack by hydroxide ion followed by equatorial departure of benzyl anion is a reasonable alternative, as the difference in electronegativity between benzyl and hydroxyl groups is now substantial and that between benzyl and alkyl or aryl groups correspondingly lessened.[41]

The present discussion bears on the question of the dependence of stereochemistry on ring size. When the displaced group is a poor leaving group and not markedly electronegative, *e.g.*, benzyl, the stereochemical crossover point comes at the six-membered-ring stage: the alkaline hydrolysis of 1-benzylphosphorinanium ions (**6**) proceeds with partial inversion of configuration.[42] However, when the displaced group is a good leaving group, and with an electronegativity comparable to that of the nucleophile, the crossover point is already reached at the five-membered-ring stage: the hexachlorodisilane reduction of phospholane 1-oxides (**7**), a reaction analogous to the transformation in eq 4, proceeds with predominant inversion.[43] This observation dramatically illustrates the relative importance of substituent electronic effects and ring strain in controlling stereochemistry. When the leaving group is benzyl, ring strain controls stereochemistry, and, whatever the mechanism of the displacement,[41] the five-membered ring maintains the apical-equatorial position throughout. By thus avoiding the unfavorable[4,7,39,44] spanning of equatorial-equatorial positions, retention stereochemistry is assured. However, when the attacking nucleophile (trichlorosilyl anion) and the displaced group (trichlorosiloxide) are both significantly more electronegative than alkyl or aryl, the lowest energy pathway leads, by way of apical attack, to an intermediate phosphorane in which entering and

(40) A. Bladé-Font, C. A. VanderWerf, and W. E. McEwen, *J. Amer. Chem. Soc.*, **82**, 2396 (1960); W. E. McEwen, K. F. Kumli, A. Bladé-Font, M. Zanger, and C. A. VanderWerf, *ibid.*, **86**, 2378 (1964).

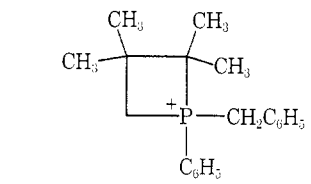
(41) A conceivable pathway is apical attack on **4**–**6** by hydroxide, followed by loss of a proton, pseudorotation (to place the electropositive oxide group in the equatorial position), and departure of benzyl anion from the apical position. This mechanism may also apply to **2A** → **3A** and would equally well account for the observed stereochemistry.

(42) K. L. Marsi and R. T. Clark, *J. Amer. Chem. Soc.*, **92**, 3791 (1970).

(43) W. Egan, G. Chauvière, K. Mislow, R. T. Clark, and K. L. Marsi, *Chem. Commun.*, 733 (1970).

(44) D. A. Usher, E. A. Dennis, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **87**, 2320 (1965); *cf.* also G. M. Whitesides and W. M. Bunting, *ibid.*, **89**, 6801 (1967).

leaving groups occupy apical positions (45 or $\overline{45}$ in Figure 4, using previously adopted conventions): relief of stereoelectronic strain more than compensates for the concomitant ring strain. If departure of the leaving group is faster than pseudorotation, the displacement will thus result in inversion of configuration. One might accordingly anticipate that the hexachlorodisilane reduction of six-membered-ring phosphorinane 1-oxides should proceed with nearly complete inversion of configuration, as in the acyclic analogs.[22,23]



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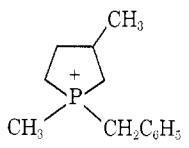

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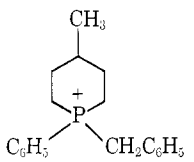

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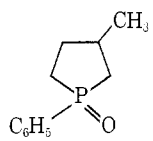

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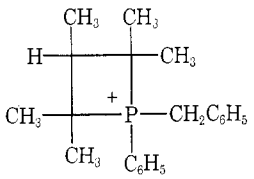


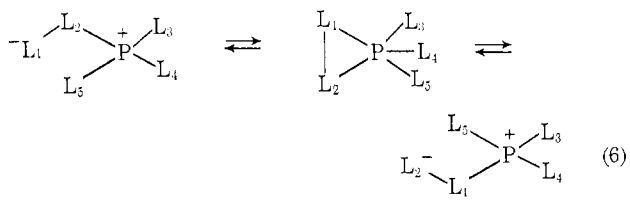
8

The same considerations serve to explain[45] the striking difference in stereochemistry of the alkaline hydrolysis of benzyl- and ethoxy-*tert*-butylmethylphenylphosphonium ions: the former is hydrolyzed with predominant retention,[46] the latter with nearly complete inversion[45] of configuration. In this example, the steric effect of the *tert*-butyl group replaces ring constraint as the key factor controlling conformation.

When X does not displace Y (eq 1) and pseudorotation occurs in the intermediate stage (**1**), stereomutation may be the result of the overall reaction. Examples are known in phosphorus stereochemistry, *e.g.*, hydrogen chloride catalyzed epimerization of 9-phenyl-9-phosphabicyclo[4.2.1]nonatriene,[47] lithium aluminum hydride catalyzed epimerization of **3A** (which is faster than reduction),[48] and base-catalyzed epimerization of **8** (which is faster than hydrolysis).[49] In all three examples, stereomutation may be rationalized by attack of X (formally, Cl^-, H^-, and OH^-, respectively), followed by three pseudorotations and loss of X. This can be readily visualized by reference to Figure 5. For instance, if X = L_5, apical attack on the tetracoordinate phosphonium ion west of σ_5 yields 45, $\overline{15}$, 25, or $\overline{35}$ as the only possible initial phosphoranes; three consecutive pseudorotations convert these to the four possible ultimate phosphoranes 35, $\overline{25}$, 15, or $\overline{45}$, respectively, which yield the inverted product upon loss of L_5. In each case the second pseudorotation, about L_5, crosses the surface, σ_5, which divides the stereoisomeric subsets. It must be emphasized that *inversion of configuration at tetracoordinate phosphorus by the addition–elimination mechanism does not require inversion of configuration of any of the intermediate phosphoranes.* To achieve inversion of configuration of phosphoranes, *five* (rather than three) pseudorotations are required,[50] and in the case of phosphoranes incorporated in small-ring systems, this pathway must lead through a high-energy intermediate,[15] symbolized in the present notation by a star-point.[17,29] This constraint does not apply to the pathway of stereomutation of P(IV) compounds, *e.g.*, (*S*)-$P^+(L_1L_2L_3L_4)$ $\rightleftarrows$ 15 $\rightleftarrows$ $\overline{23}$ $\rightleftarrows$ 14 $\rightleftarrows$ 25 $\rightleftarrows$ (*R*)-$P^+(L_1L_2L_3L_4)$, the sole prerequisite being the maintenance of equilibrium conditions and the further requirement that loss of other groups (*e.g.*, L_4) be slow compared to pseudorotation and addition–elimination of X = L_5.[51] In this connection, note that the initial and ultimate phosphoranes, *e.g.*, $\overline{15}$ and $\overline{25}$, are diastereomers, not enantiomers, in contrast to starting and final P(IV) compounds.

Intramolecular Displacement Reactions Proceeding through Cyclic Phosphorane Intermediates

Attack by an internal nucleophile on phosphorus in an acyclic system also leads to predominant retention of configuration, since the intermediate phosphorane is incorporated in a small-ring system (eq 6). For example, in the Wittig reaction of benzaldehyde with ylides derived from benzylphosphonium salts,[40] and in related rearrangements,[52] a phosphorane intermediate, in which the four-membered ring spans the apical-equatorial positions, is consistent with the observed retention of configuration. Similarly, phosphorane intermediates in which a five-membered ring spans the apical equatorial positions may be invoked to rationalize the predominant retention of configuration[17] which accompanies reaction of styrene oxide with ylides derived from benzylphosphonium salts.[53]



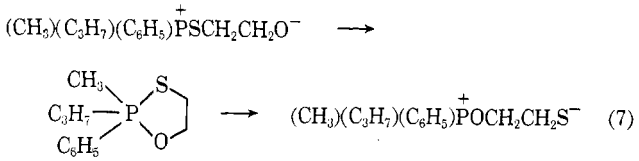
(6)

The transformations in eq 5 and 6 share the same cyclic phosphorane intermediate, and the detailed stereochemical analysis of intramolecular displacements therefore follows the lines described in the preceding section. Division of the hexaasterane graph (Figures 3

(45) R. A. Lewis, K. Naumann, K. E. DeBruin, and K. Mislow, *Chem. Commun.*, 1010 (1969).
(46) N. J. De'Ath and S. Trippett, *ibid.*, 172 (1969).
(47) T. J. Katz, C. R. Nicholson, and C. A. Reilly, *J. Amer. Chem. Soc.*, **88**, 3832 (1966).
(48) P. D. Henson, K. Naumann, and K. Mislow, *ibid.*, **91**, 5645 (1969).
(49) S. E. Cremer, R. J. Chorvat, and B. C. Trivedi, *Chem. Commun.*, 769 (1969).
(50) E. L. Muetterties, *Inorg. Chem.*, **6**, 635 (1967).
(51) For a detailed discussion, see K. E. DeBruin and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7393 (1969).
(52) L. Horner and H. Winkler, *Tetrahedron Lett.*, 3265 (1964).
(53) W. E. McEwen, A. Bladé-Font, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, **84**, 677 (1962); W. E. McEwen, A. P. Wolf, C. A. VanderWerf, A. Bladé-Font, and J. W. Wolfe, *ibid.*, **89**, 6685 (1967).

or 4, minus vertices 12 and $\overline{12}$ and their six connecting edges) by two surfaces which bisect edges indexed 1 and 2 now generates the subsets of phosphoranes which are relevant to *intra*molecular displacements and which derive from attack by L_1 and L_2 on the two enantiomers of starting phosphonium ion. Granted further that the equatorial belt of star-point vertices represents a virtual barrier,[29] the two surfaces in effect fuse into a single plane which divides the graph into top and bottom hexagons, whose vertices represent the two enantiomorphorus and noninterconverting sets of six diastereomeric phosphoranes derived from the two enantiomeric phosphonium ions.

As an illustration, consider the oxidation of acyclic phosphines by bis(2-hydroxyethyl) disulfide,[54] whose stereochemistry has been investigated.[17] The essential portion of the reaction sequence is given in eq 7.



(7)

Denoting phenyl, *n*-propyl, and methyl groups in the intermediate phosphorane as L_3, L_4, and L_5, respectively, and the sulfur and oxygen ring termini as L_1 and L_2, respectively, apical attack of L_2 on the three available faces of the *R* enantiomer leads to $\overline{23}$, 24, and $\overline{25}$. Interconversion of these three isomers *via* $\overline{13}$, 14, and $\overline{15}$ occurs by pseudorotations in the plane of the top hexagon, as depicted in Figure 7. The six diastereomeric phosphoranes are not converted into their enantiomers, represented by the vertices on the bottom hexagon. Ring opening, followed by departure of the apically located sulfur (L_1), may occur from any one of the three ultimate phosphoranes ($\overline{13}$, 14, and $\overline{15}$). The overall reaction thus results in retention of configuration regardless of which are the initial and ultimate phosphoranes, for the six diastereomers are all constrained to one side of the horizontal plane throughout, *i.e.*, they all belong to the same configurational subset.

In this and in the preceding section, we have dealt exclusively with nucleophilic displacement reactions at phosphorus in phosphonium ions which involve the intermediacy of a phosphorane containing a four- or five-membered ring. It should be noted, however, that the generality and scope of our treatment are not impaired when the system under discussion is changed. *The hexaasterane graph (Figure 5) applies to any displacement reaction in which ligand exchange on a tetracoordinate chiral or prochiral center takes place, and in which one of the diastereomers in the pentacoordinate trigonal-bipyramidal intermediate is eliminated.* The isomers ruled out of consideration in this and the preceding section are those in which a ring spans the apical positions, but it is conceivable, for example, that in *acyclic* systems the corresponding constraint might consist in the elimination of isomers having two strongly electropositive groups simultaneously located in apical positions.

(54) M. Grayson and C. E. Farley, *Chem. Commun.*, 831 (1967).

Extensions to Systems Other than Phosphoranes

Polytopal rearrangements are by no means restricted to pentacoordinate structures, and appropriate topological representations have been worked out.[11,55] For $n > 5$, the grouping of vertices, representing *n*-coordinate stereoisomers, into sectors defined by surfaces, and the identification of these subsets with the configuration of the $(n - 1)$-coordinate reaction precursors or products, should in principle follow the precedent set for the $n = 5$ system.[17] Alternatively, the equivalent matrix representation may be employed.[56]

Extensions to elements other than phosphorus are readily envisaged. However, rather than catalog the numerous likely candidates for M and *n*, we shall restrict discussion to two neighbors of phosphorus in the periodic table, sulfur and silicon. Nonempirical LCAO–MO–SCF calculations[33] on SH_5^+, PH_5, and SiH_5^- indicate a remarkable similarity in the barrier to pseudorotation in all three hypothetical molecules (4–5 kcal/mol).

The only known examples of pentacoordinate compounds of sulfur are SOF_4, $R_2NS(O)F_3$, and CF_3NSF_4, unless ligand definition is taken to include a nonbonding electron pair (phantom ligand) residing in a valence orbital, as in SF_4.[5] The molecular geometry of such "pentacoordinate" compounds may be viewed, in the light of the valence shell electron pair repulsion theory,[57] as a slightly distorted trigonal bipyramid, with the effectively electropositive lone pair in an equatorial position[5] and the most electronegative groups disposed apically.[58] The role of pseudorotation in nucleophilic displacement at sulfur is thus subject to a test: if "pentacoordinate" intermediates are produced in the base-catalyzed hydrolysis of *cis*- and *trans*-1-ethoxy-3-methylthietanium ions, and if such intermediates are capable of pseudorotation, arguments strictly analogous to those employed to rationalize the stereochemistry of **2A** → **3A** would lead one to expect overall retention of configuration. However, such is not the case, and the displacement reaction in fact proceeds with complete inversion (eq 8).[59] One is forced to conclude that pseudorotation in this "pentacoordinate" sulfur species, if it occurs at all, is less facile than in the phosphoranes, or, as an alternative likelihood, that the reaction does not proceed through an intermediate of significant lifetime and is better described as a direct SN2 displacement.[59] The same conclusion applies to nucleophilic displacement at phosphorus in chlorophosphetanes, in

(55) See also M. Gielen and J. Topart, *J. Organometal. Chem.*, **18**, 7 (1969).

(56) A. Robson (Princeton), unpublished work.

(57) (a) N. V. Sidgwick and H. M. Powell, *Proc. Roy. Soc., Ser. A*, **176**, 153 (1940); (b) R. J. Gillespie and R. S. Nyholm, *Quart. Rev., Chem. Soc.*, **11**, 339 (1957); R. J. Gillespie, *Angew. Chem., Int. Ed. Engl.*, **6**, 819 (1967).

(58) N. C. Baenziger, R. E. Buckles, R. J. Maner, and T. D. Simpson, *J. Amer. Chem. Soc.*, **91**, 5749 (1969).

(59) R. Tang and K. Mislow, *ibid.*, **91**, 5644 (1969).

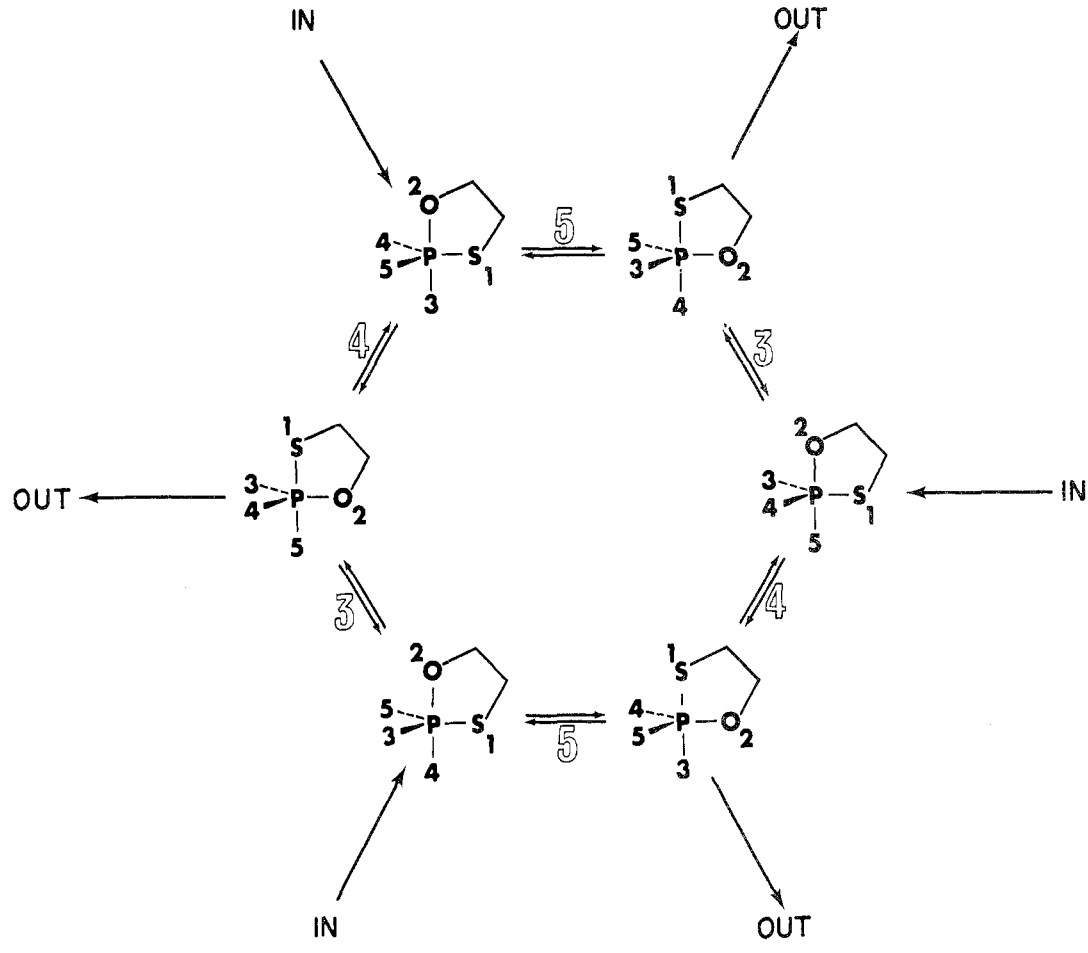
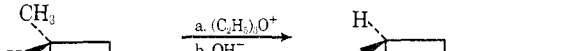


Figure 7. Pseudorotations involved in reaction of eq 7.

which the lone pair on phosphorus acts as a phantom ligand, and which also proceeds with inversion of configuration.[60]

It thus appears at this time that the stereochemistry of displacement reactions involving pentacoordinate intermediates cannot be extrapolated to those cases in which a lone pair of electrons acts as a phantom ligand in the coordination sphere.



(8)

Pentacoordinate compounds of silicon exhibit near-trigonal-bipyramidal geometry,[61] and nmr evidence has been adduced for rapid intramolecular ligand exchange in pentafluorosilicate anion.[62] It is therefore conceivable that in nucleophilic displacement reactions at silicon pentacoordinate intermediates are formed which are capable of pseudorotation. In 1968, Westheimer suggested[7] that pseudorotation of such intermediates "probably provides the correct explanation" for the rapid hydrolysis of strained cyclic and bicyclic silanes,[63] and in the following year pseudorotation was proposed as a possible explanation for the alcohol-induced stereomutation of *cis*- and *trans*-1,2-difluoro-1,2-dimethyl-1,2-disilacyclohexane,[64] for the rearrangement of the cis isomer of trimethylsilylacetylacetonate,[65] for retention of configuration in alkoxide–alkoxide exchange reactions at asymmetric silicon,[66] and for the alcohol-induced racemization of fluorosilanes.[67] Similarly, the crossover in the stereochemistry of organometallic displacements at silicon in cyclic and acyclic silanes[68] may be taken as *prima facie* evidence for pseudorotation of intermediate pentacoordinate species. However, what Sommer has termed SN2*-Si and SN2**-Si mechanisms (*i.e.*, eq 1, M = Si, n = 5) are considered relatively uncommon,[69] and it has been pointed out[66] that the instability of $R_3SiF_2^-$ [62] militates against the pseudorotation route. Consequently, tempting though it is to ascribe retention stereochemistry in nucleophilic

(60) D. J. H. Smith and S. Trippett, *Chem. Commun.*, 855 (1969).
(61) For example, see F. P. Boer, J. J. Flynn, and J. W. Turley, *J. Amer. Chem. Soc.*, **90**, 6973 (1968); R. Rudman, W. C. Hamilton, S. Novick, and T. D. Goldfarb, *ibid.*, **89**, 5157 (1967).
(62) F. Klanberg and E. L. Muetterties, *Inorg. Chem.*, **7**, 155 (1968).
(63) L. H. Sommer, O. F. Bennett, P. G. Campbell, and D. R. Weyenberg, *J. Amer. Chem. Soc.*, **79**, 3295 (1957).
(64) K. Tamao, M. Ishikawa, and M. Kumada, *Chem. Commun.*, 73 (1969).
(65) J. J. Howe and T. J. Pinnavaia, *J. Amer. Chem. Soc.*, **91**, 5378 (1969).
(66) L. H. Sommer and H. Fujimoto, *ibid.*, **91**, 7040 (1969).
(67) L. H. Sommer and D. L. Bauman, *ibid.*, **91**, 7045 (1969).
(68) R. Corriu and J. Masse, *Tetrahedron Lett.*, 5197 (1968); *Chem. Commun.*, 1373 (1968).
(69) L. H. Sommer, "Stereochemistry, Mechanism and Silicon," McGraw-Hill, New York, N. Y., 1965, Chapter 11.

displacement reactions at silicon to pseudorotation of intermediates (**1**), rather than to the operation of the more prosaic conventional mechanisms,[69] there is at present no compelling evidence which would allow a decision between these alternatives.

As the preceding discussion demonstrates, studies dealing with the role of pseudorotation in the stereochemistry of nucleophilic displacement reactions at centers other than phosphorus are still in their infancy, and one may look forward to the exploration of divers systems[70] in coming years.

Finally, it should be emphasized that even though the pseudorotational mechanisms which form the body of this Account are quite conjectural in nature, and the evidence for them circumstantial rather than direct, they have so far yielded a consistent picture of observed stereochemical events. At least as a heuristic model they have proved remarkably successful, whatever their ultimate fate as representations of the underlying physical processes may turn out to be.

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(70) For recent examples, see M. Gielen, M. De Clercq, G. Mayence, J. Nasielski, J. Topart, and H. Vanwuytswinkel, *Recl. Trav. Chim.*, **88**, 1337 (1969); G. J. D. Peddle and G. Redl, *J. Amer. Chem. Soc.*, **92**, 365 (1970); C. A. Udovich and R. J. Clark, *ibid.*, **91**, 526 (1969); J. D. Warren and R. J. Clark, *Inorg. Chem.*, **9**, 373 (1970).

Studies of Internal Molecular Motions and Conformation by Microwave Spectroscopy

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Since its inception shortly after World War II, microwave spectroscopy[1] has proved to be a powerful tool for the study of a wide variety of molecular properties. Although investigators were initially primarily concerned with the accurate determination of molecular structural parameters, research in microwave spectroscopy now encompasses many diverse areas.[2]

One area which has been particularly fruitful is the study of internal molecular motions. Although the main characteristics of a microwave spectrum are normally determined by the molecular geometry and nuclear masses, internal motions affect the spectrum in a number of ways. One way is through the phenomenon of quantum mechanical tunneling. Tunneling can occur when there are two or more equivalent molecular configurations which are interconvertible by some internal motion. Examples are rotation of a methyl group and inversion of amines. Tunneling gives rise to a splitting of some or all of the spectral lines. Since the splittings are quite sensitive to the potential function involved, they provide an accurate way of determining the potential.

Another way in which internal motions affect a spectrum is by shifting the spectral lines. This most commonly occurs through a modification of the moments of inertia. Thus while molecular rotational spectra can in many cases be analyzed as if the molecule were effectively rigid, the moments of inertia obtained always contain vibrational contributions. Although these contributions are often only of the order of 0.1%, they result in frequency shifts which are large compared to the resolution of a microwave measurement. Every vibrational state has a different set of effective moments of inertia and a distinct set of rotational transitions. For some cases, the vibrational perturbations may be sufficiently severe that the effective rigid rotor formulation no longer applies. In such instances very large frequency shifts may result.

Additional information may be obtained from the presence of separate sets of rotational lines for each vibrational state by making intensity measurements. The intensity of a transition is proportional to the number of molecules available to undergo that transition. Thus the intensity of a rotational transition in a given vibrational state is proportional to the population of the vibrational state. Since the population depends on the energy of the state through its Boltzmann factor, intensity measurements can be used to obtain vibrational energies. These energies in turn give information about the potential function governing the vibration.

Through one or more of the vibrational effects mentioned above, microwave studies have been made on internal motions of a number of molecules. The kinds of motion which have been studied so far are internal rotation about single bonds, inversion of amino groups, ring puckering in four-membered rings, and pseudorotation in five-membered rings.

(1) As used here, the term "microwave spectroscopy" means gas-phase rotational spectroscopy and does not include electron magnetic resonance.

(2) For a general review of the information which can be obtained from microwave spectroscopy see (a) E. B. Wilson, *Science*, **162**, 59 (1968); (b) D. R. Lide, *Surv. Progr. Chem.*, **5**, 95 (1969).