

Topological Representation of the Stereochemistry of Displacement Reactions at Phosphorus in Phosphonium Salts and Cognate Systems¹

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Abstract: Nucleophilic displacement on phosphorus in cyclic phosphonium salts by external nucleophiles is believed to proceed through intermediate phosphoranes, and similar intermediates are involved in internal nucleophilic displacements at phosphorus in acyclic phosphonium salts. The stereochemical consequences (retention or inversion) of such substitution reactions may be systematically and conveniently discussed with the aid of a modification of Balaban's 20-vertex graph, which has the appearance of the carbon skeleton of hexaasterane. Eighteen vertices represent the eighteen stereoisomers of intermediate phosphoranes containing five different ligands, two of which are termini of a ring system incapable of spanning the two apical positions. Twenty-four edges represent the alternative pathways for interconversion of the isomers by pseudorotation. In an idealized (D_{6h}) representation, three planes intersect at the sixfold axis. Each plane divides the graph into two subsets of nine vertices. Each subset represents the nine phosphoranes resulting from external nucleophilic attack on the phosphorus atom of a given enantiomer of a cyclic phosphonium salt. The stereochemical outcome of the displacement is thus given by the positions of intermediate phosphoranes within sectors defined by two intersecting planes. Two additional, scalloped surfaces, whose threefold axis is coincident on the sixfold axis of the idealized figure, divide the graph into two subsets of nine vertices. Each subset contains all the phosphoranes which result from internal nucleophilic attack on the phosphorus atom of a given enantiomer of an acyclic phosphonium salt. A novel topological overview is thus provided of the multiplicity of accessible pathways in such displacement reactions, and of the stereochemistry of these displacements. The scheme is a general one, and is readily extended to any displacement reaction on a tetra-coordinate atom which involves the intermediacy of a trigonal-bipyramidal pentacoordinate species of moderate lifetime. The application of such extensions to cognate systems is indicated.

Nucleophilic displacement reactions which take place by attack on the phosphorus atom in phosphonium salts have different stereochemical consequences, depending on whether or not the phosphorus atom is incorporated in a small (*e.g.*, four- or five-membered) ring system: in the acyclic system, displacement results in *inversion*, whereas in the cyclic system, *retention* of configuration at phosphorus has been observed. Thus, reduction of phosphetane 1-oxides with trichlorosilane in the presence of triethylamine³ or with hexachlorodisilane⁴ affords phosphetanes with retention of configuration, in contrast to the stereochemical direction of the corresponding reductions of acyclic systems.^{5,6} As a further example, base-catalyzed hydrolysis of 1-ethoxyphosphetanium salts affords phosphetane 1-oxides with retention of configuration,⁴ in contrast to the inversion pathway observed in acyclic systems.⁷ Similarly, base-catalyzed hydrolysis of 1-benzylphospholanium salts proceeds with retention of configuration at phosphorus,⁸ whereas the corresponding reaction in acyclic analogs proceeds with inversion.^{9,10}

Just as attack by an external nucleophile on phosphorus in a phosphetane or phospholane system leads to retention of configuration, attack by an internal nucleophile on phosphorus in an acyclic system also leads to predominant retention of configuration whenever a four- or five-membered phosphorus-containing ring system is formed in the intermediate stage of the reaction. For example, in the Wittig reaction of benzaldehyde with ylides derived from benzylphosphonium salts,¹¹ and in related rearrangements,¹² a phosphorane intermediate, in which the four-membered ring spans the apical-equatorial positions,⁹ 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 which accompanies reaction of styrene oxide with ylides derived from benzylphosphonium salts.^{13,14}

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-B.

(2) U. S. Public Health Service Postdoctoral Fellow, 1967-1969, supported by the National Cancer Institute.

(3) S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967).

(4) K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Am. Chem. Soc.*, **91**, 7027 (1969).

(5) L. Horner and W. D. Balzer, *Tetrahedron Lett.*, 1157 (1965).

(6) K. Naumann, G. Zon, and K. Mislow, *J. Am. Chem. Soc.*, **91**, 7012 (1969).

(7) G. Zon, K. E. DeBruin, K. Naumann, and K. Mislow, *ibid.*, **91**, 7023 (1969).

(8) K. L. Marsi, *Chem. Commun.*, 846 (1968); K. L. Marsi, *J. Am. Chem. Soc.*, **91**, 4724 (1969). More recently, and after the present work was completed, it was shown that base-catalyzed hydrolysis of a 1-benzylphosphetanium salt also proceeds with retention of configuration (J. R. Corfield, J. R. Shutt, and S. Trippett, *Chem. Commun.*, 789 (1969)).

(9) W. E. McEwen, K. F. Kumli, A. Bladé-Font, M. Zanger, and C. A. VanderWerf, *J. Am. Chem. Soc.*, **86**, 2378 (1964).

(10) W. E. McEwen in "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, New York, N. Y., 1965, Chapter 1.

(11) A. Bladé-Font, C. A. VanderWerf, and W. E. McEwen, *J. Am. Chem. Soc.*, **82**, 2396 (1960).

(12) L. Horner and H. Winkler, *Tetrahedron Lett.*, 3265 (1964).

(13) A. Bladé-Font, W. E. McEwen, and C. A. VanderWerf, *J. Am. 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).

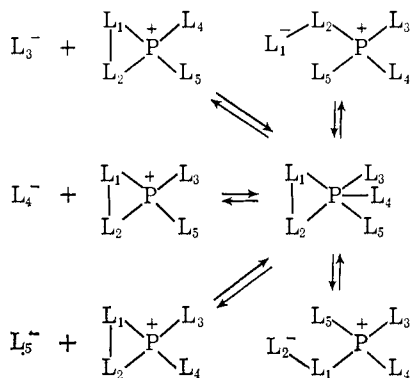
(14) Benzylethylmethylphenylphosphonium iodide yields ethylmethylphenylphosphine oxide of the same sign of rotation, with *ca.* 50% racemization.¹³ From other work reported by the same authors,^{9,11,16} it must be concluded that the net stereochemical course in this reaction is *retention*, even though it has been reported as net "*inversion*" in the original papers.¹³ Reviews which have dealt with this work^{10,16} have perpetuated this error.

(15) K. F. Kumli, W. E. McEwen, and C. A. VanderWerf, *J. Am. Chem. Soc.*, **81**, 3805 (1959).

(16) R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, **2**, 11 (1963); R. F. Hudson, "Structure and Mechanism in Organo-

As indicated above, these nucleophilic displacements are best described as addition-elimination reactions proceeding by way of an intermediate phosphorane. When the phosphorus atom in the phosphorane is part of a ring system, the intermediate is common to both types of displacement discussed above. As shown in Chart I, attack by external nucleophiles L_3 , L_4 , or L_5 on the

Chart I



appropriately substituted cyclic phosphonium ion, in which ligands L_1 and L_2 are the termini of the ring system, leads to the same phosphorane as does internal attack by one of the two termini, L_1 or L_2 , on the phosphorus atom in an acyclic phosphonium ion.

In discussing the stereochemistry of these and related reactions, account must be taken of the possibility that the intermediate phosphorane undergoes stereomutation by pseudorotation,^{17,18} an internal vibration in which pairwise exchange of apical and equatorial ligands in the trigonal-bipyramidal molecule (D_{3h}) takes place by way of a tetragonal-pyramidal (C_{4v}) transition state.^{19,20} Pseudorotation in P(V) compounds assumes an important role in a number of recent studies.^{18,19,21,22} However, in stereochemical studies such as those described in the present paper, the multiplicity of allowable pathways renders the analysis of alternatives awkward in the absence of a generalized scheme. Such a scheme would have to provide a convenient and systematic analysis of the relationship between the configurations of the starting materials and products (*i.e.*, the P(IV) compounds such as the phosphonium salts) and the various conformations²³ of the intermediate and

Phosphorus Chemistry," Academic Press, New York, N. Y., 1965, p 240; A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier Publishing Co., New York, N. Y., 1967, p 198.

(17) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).

(18) M. J. Gallagher and I. D. Jenkins in "Topics in Stereochemistry," Vol. 3, N. L. Allinger and E. L. Eliel, Ed., John Wiley & Sons, Inc., New York, N. Y., 1968, Chapter I.

(19) E. L. Muetterties and R. A. Schunn, *Quart. Rev. (London)*, **20**, 245 (1966); R. R. Holmes and R. M. Deiters, *J. Am. Chem. Soc.*, **90**, 5021 (1968); R. R. Holmes and R. M. Deiters, *Inorg. Chem.*, **7**, 2229 (1968).

(20) Alternative mechanisms are conceivable; *cf.* E. L. Muetterties, *J. Am. Chem. Soc.*, **91**, 4115 (1969); however, see G. M. Whitesides and H. L. Mitchell, *ibid.*, **91**, 5384 (1969).

(21) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968), and references cited therein.

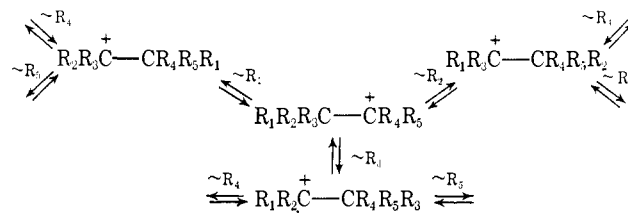
(22) F. Ramirez, *ibid.*, **1**, 168 (1968); G. Wittig, *Bull. Soc. Chim. Fr.*, 1162 (1966); D. Hellwinkel, *Chem. Ber.*, **99**, 3628, 3660, (1966); T. J. Katz, C. R. Nicholson, and C. A. Reilly, *J. Am. Chem. Soc.*, **88**, 3832 (1966); G. M. Whitesides and W. M. Bunting, *ibid.*, **89**, 6801 (1967).

(23) For convenience, we adopt the broad definition of "conformation" given by S. I. Miller in "Advances in Physical Organic Chemistry," Vol. 6, V. Gold, Ed., Academic Press, New York, N. Y., 1968, p 313 ("Excluding normal molecular vibrations, relative atomic motion that breaks no bonds within a molecular framework generates conformations"), a definition that explicitly includes pseudorotation.

stereochemically nonrigid phosphoranes, and it would also have to take fully into account the interconversional pathways linking all these species. In the present paper we present a scheme which meets the stated need by use of an appropriate topological representation. Although, in the general case, representation of polytopal rearrangements²⁴ by stereochemical matrices is preferred over topological representations, it happens that the geometrical representation described below is well suited to the purpose stated above, and, as will be illustrated with a variety of examples, has the advantage of convenience in usage.

Topological Representations. We assume that the phosphorane intermediate has trigonal-bipyramidal symmetry; with five different ligands, there will be 20 ($= 5!/6$)²⁴ chiral stereoisomers, consisting of ten *dl* pairs. Each pseudorotation exchanges a pair of equatorial (*e*) and apical (*a*) ligands.²⁵ Since there are three possible combinations of pairs of *e* ligands, three routes lead, by a single step, from any given stereoisomer to three others, *i.e.*, the connectivity (δ)²⁴ is 3. A single operation connects two isomers, and the total number of interconnecting pseudorotations therefore equals $(20)(3)/2 = 30$.

The first problem is to display the set of 20 interconverting isomers and the network of 30 interconnecting operations in the form of a graph,²⁶ in which the elements of the set (isomers) are represented by vertices and the operations (pseudorotations) by edges. Such a finite and undirected graph cannot be planar and must be presented, in three dimensions, as an interpenetrating figure. Because of the equivalence of all vertices, and the invariance of δ , the graph is regular and of degree 3.²⁷ A centric graph which admirably fulfills these requirements has been presented by Balaban, *et al.*,²⁸ who were concerned with the family of 1,2 shifts in carbonium ions as given in the following partial representation.



The formal relationships developed by Balaban, *et al.*,²⁸ which have been found useful in the discussion of rearranging carbonium ions,²⁹ are applicable *in toto* to the problem at hand. Denoting specific isomers by the apical substituents,²⁴ the family of pseudorotations under discussion is given by the following partial representation of interconversions which are strictly analogous to the 1,2 shifts shown above; the numbers over

(24) E. L. Muetterties, *J. Am. Chem. Soc.*, **91**, 1636 (1969).

(25) In each pseudorotation, the *e* ligand which remains *e* is called the "pivot," about which pseudorotation is said to take place.

(26) O. Ore, "Theory of Graphs," American Mathematical Society, Providence, R. I., 1962, whence definitions used in the text are taken.

(27) Let v = the number of elements in the vertex set and g = the number of edges connecting the vertices. Then in a regular graph of degree δ , $g = \frac{1}{2}v\delta$.²⁶

(28) A. T. Balaban, D. Fărcasiu, and R. Banićă, *Rev. Roum. Chim.*, **11**, 1205 (1966).

(29) H. W. Whitlock, Jr., and M. W. Siefken, *J. Am. Chem. Soc.*, **90**, 4929 (1968). We are grateful to Professor Paul von R. Schleyer for bringing this matter to our attention.

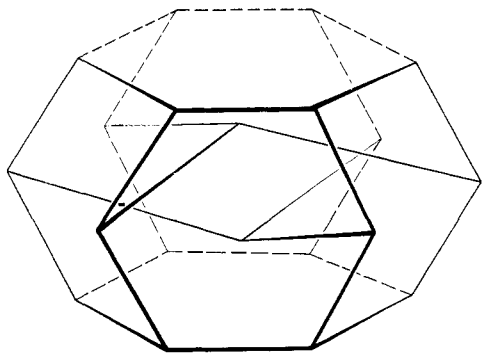
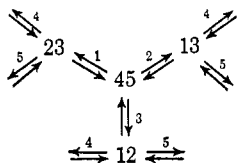


Figure 1.

the arrows now represent the indices of the pivot ligands.²⁵



Balaban's 20-vertex graph is adequate in every respect as a representation of pseudorotational interconversions. As pointed out by Balaban, *et al.*,²⁸ (1) the smallest circuit is a subcycle²⁴ which contains six edges (*i.e.*, interconversion steps) sequentially connecting six vertices or "elements" (*i.e.*, isomers); (2) the shortest arc, or chain,²⁴ connecting an element to its "antipode" contains five edges, and there are 12 such arcs for each element. Two geometric figures, or images, of the 20-vertex graph were presented by Balaban, *et al.*,²⁸ but since isomorphic graphs³⁰ have the same graph properties, it is immaterial which image of the graph is used.³¹ It should be noted that removal of the distinction between antipodes halves the number of vertices and edges. The resulting ten-vertex graph is regular and of degree 3, and the order of the smallest circuit in the ten-vertex graph equals the order of the shortest arc connecting an element to its antipode in the corresponding 20-vertex graph, *i.e.*, 5.³³ The representations of ten-vertex Petersen graphs,³⁴ depicted by Balaban, *et al.*,²⁸ in connection with the interconversion of carboronium ions, have also recently been presented in conjunction with an analysis of pseudorotational interconversions.³⁵

Hexaasterane Graph. Vertices and Edges. Our own variant of Balaban's 20-vertex graph is shown in Figure 1; the idealized image has D_{3d} symmetry. A projection is shown in Figure 2, along with the numbering convention which is explained below. We believe

(30) Two graphs are isomorphic when there is a one-to-one correspondence between vertex sets such that corresponding vertices are joined by edges in one of them only if they are also joined in the other.²⁶

(31) Thus, the 20-vertex graph recently discussed by Lauterbur and Ramirez³² in connection with an analysis of pseudorotational interconversion, though differing in appearance from Balaban's graphs, is an isomorphic representation thereof.

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

(33) As pointed out by Balaban, *et al.*,²⁸ this is a general property relating graphs with sets of equivalent elements to the corresponding graphs with antipodal elements.

(34) J. Petersen, *Acta Math.*, **15**, 193 (1891).

(35) J. D. Dunitz and V. Prelog, *Angew. Chem. Intern. Ed. Engl.*, **7**, 725 (1968).

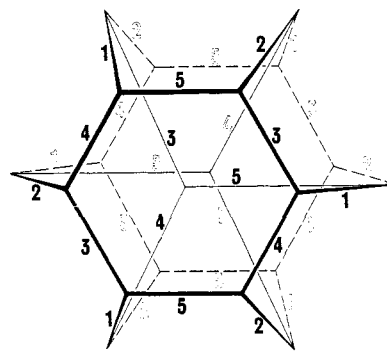


Figure 2.

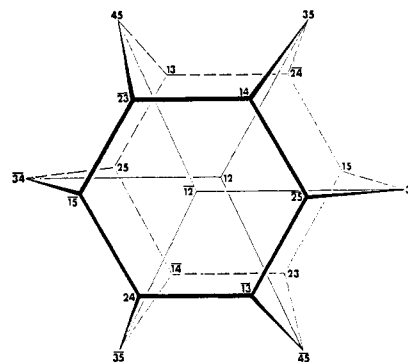


Figure 3.

that this representation carries with it the desired qualities³² of clarity and esthetic appeal.^{35a}

Pseudorotations are represented by the numerical indices over the edges which are related through the center of symmetry. Each such numeral *ipso facto* denotes the index of the pivot²⁵ ligand. Consequently, the identity of each isomer, represented by a vertex, is automatically defined, except for chirality. For example, the vertex at the junction of 2, 3, and 5 represents either 14 or its enantiomer, $\bar{14}$. Chirality may be denoted, arbitrarily, by the ascending numerical order of *e* ligand indices for each isomer: if clockwise when viewed from the *a* ligand with the lower numerical index, the isomer is unbarred; if counterclockwise, barred. The isomer designations thus generated are given in Figure 3.³⁶ As in other representations,^{28,32} enantiomers are related by the center of symmetry. The pattern of the indices is straightforward and easily memorized: 1 and 2 alternate around the top and bottom edges of the points of the star, and the six edges corresponding to each of the other three numerals, 3, 4, and 5, are all parallel. *This simple scheme permits identification of all 30 edges and (except for chirality) of all 20 vertices by designation of only five edges.*

Since our purpose is specifically to formulate a generalized topological representation of the transformations in Chart I, we introduce the following constraint and convention.

Constraint. The phosphorus-containing ring system in the intermediate phosphorane (Chart I) is in-

(35a) NOTE ADDED IN PROOF. This representation is also preferred by M. Gielen and J. Nasielski, *Bull. Soc. Chim. Belges.*, **78**, 339 (1969).

(36) A similar sequence rule has been previously proposed.³² The chirality designation for the 12 isomers corresponding to the vertices in the top and bottom hexagons in Figure 3 are correlated to the order of the pivot ligand indices in Figure 2 when viewed from the outside.

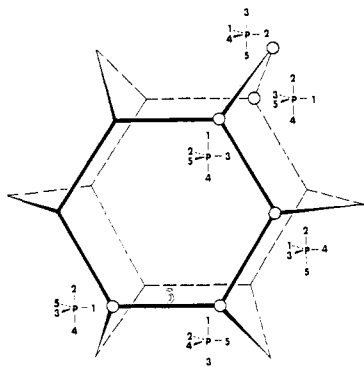


Figure 4.

capable of spanning the two apical positions, *i.e.*, the L_1PL_2 bond angle cannot be close to 180° . This constraint applies to all but the very largest ring systems and is one of the constraints dealt with by Lauterbur and Ramirez³² in their discussion of the 20-vertex graph.

Convention. The index numerals 1 and 2 are assigned to the termini of the phosphorus-containing ring. The remaining index numerals are assigned arbitrarily.

The effect of the constraint coupled with the convention is to remove isomers 12 and $\bar{12}$, and thus to reduce the vertices to 18 in number. At the same time, the six pseudorotations leading to the forbidden *dl* pair are removed, and the edges are thus reduced to 24 in number. The resulting graph is shown in Figure 4 and represents our basic working model. The hollow numerals suffice to identify all 18 vertices and 24 edges, as explained above. In appearance, the graph resembles the carbon skeleton of hexaasterane, a member of the asterane series of hydrocarbons,³⁷ and will for the sake of convenience be referred to by that term.

The 12 vertices on the top and bottom hexagons all represent isomers in which the ring spans the apical and equatorial positions (*ae* ring); the connectivity in each case is 3. The six vertices at the points of the star all represent isomers in which the ring spans the equatorial positions (*ee* ring); the connectivity in each case is 2, since pseudorotation about the "missing pivot" (whose index numeral is deduced from that of any parallel edge) would lead to one of the forbidden isomers, 12 or $\bar{12}$. To the extent that the L_1PL_2 bond angle deviates from 90° and 120° , ring strain is introduced in the *ae* and *ee* ring isomers, respectively, a factor which may have stereochemical consequences. For example, with reference to Figures 3 and 4, the arc traversed from 14 to 24 (*via* $\bar{25}$ and $\bar{13}$) differs from that traversed from 14 to the enantiomer, $\bar{24}$ (*via* 35), in one important respect: 35 has an *ee* ring which, if four membered, would render this path an energetically costly one. Other things being equal, the longer route to 24 would therefore be the preferred pathway. The ambiguity which attends the conversion of a given diastereomer, say 14, to one or another of two enantiomers of the target diastereomer, say 24 and $\bar{24}$, is readily resolved without recourse to the "physical" act of pseudorotation:¹⁷⁻²² since each act of pseudorotation is equivalent to *three* permutations of ligands, the parity of pseudorotations equals the parity of permutations of ligands. In the example

(37) U. Biethan, U. v. Gizycki, and H. Musso, *Tetrahedron Lett.*, 1477 (1965).

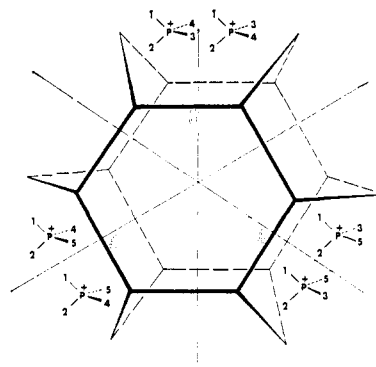


Figure 5.

given, 14 is converted to 24 by the exchange of L_1 and L_2 , *i.e.*, by a single permutation. The number of pseudorotations leading from 14 to 24 must therefore also be odd (the shortest arc has three edges). On the other hand, 14 is converted to $\bar{24}$ by two permutations, and the number of pseudorotations leading from 14 to $\bar{24}$ must therefore also be even (the shortest arc has two edges). Note in that connection that enantiomers are interconverted by a minimum of one permutation and five consecutive pseudorotations, both odd.

Hexaasterane Graph. Planes and Other Surfaces.

The hexaasterane graph is a simplified figure by virtue of an imposed constraint (see above). In consequence, its usefulness as a geometric representation of stereochemical changes extends significantly beyond that of merely reflecting pseudorotational interconversions, a capability which it also shares with earlier models.^{28, 32, 35} A unique feature of the hexaasterane representation, and one which is vital to the stated goal of formulating a generalized topological representation of the transformations in Chart I, is the presence of three planes and two other surfaces which group the phosphoranes represented by the vertices of the graph into subsets whose members are generically related to phosphonium ions of given configurations.

As indicated in Figure 5, three planes intersect at the sixfold axis and, for convenience, will be referred to as σ_n , where the subscript denotes the index of the edges bisected by the plane.³³ Each plane divides the set of 18 vertices into two subsets of nine. The phosphoranes in one subset are enantiomeric to those in the other. Each subset represents the nine chiral phosphoranes which are the initial products of attack by an external nucleophile and ligand-to-be, L_n , on a given enantiomer of a phosphonium ion. Conversely, each member of the same subset of nine chiral phosphoranes reverts to the identical phosphonium ion upon P- L_n bond cleavage. In each subset, four phosphoranes arise from face (*a*) attack and the other five from edge (*e*) attack; the mode of attack on the edge formed by L_1 and L_2 leads to the forbidden isomers.³⁹

(38) In this and the following discussion, the symmetry of the hexaasterane representation will be idealized to D_{6h} . A graph more faithful to the transformations it represents would have a center of symmetry as its only symmetry element: the edges might be depicted as varying in length to indicate variations in rate constants of pseudorotation. Note that in the general case, the planes (σ_n) are not symmetry planes.

(39) The terms "face" and "edge" describe the locus of nucleophilic attack on the tetrahedron which is formed by joining the four atoms bonded to phosphorus in the P(IV) compound. In the absence of constraints and degeneracies, there would thus initially be obtained ten isomers, four from face and six from edge attacks. However, with the adopted ring constraint, one of the modes of attack leads to the for-

As an illustration, σ_5 divides the 18-vertex graph into two subsets of vertices/phosphoranes: one (western sector) resulting from attack by L_5 on (*S*)- $P^+(L_1L_2L_3L_4)$,⁴⁰ and the other (eastern sector) from attack on the *R* isomer. For the *S* isomer, *a* attack affords $\overline{15}$, 25, $\overline{35}$, and 45, and *e* attack 13, $\overline{14}$, $\overline{23}$, 24, and $\overline{34}$; for attack on the *R* isomer, the enantiomeric phosphoranes are formed. Conversely, loss of L_5 from $\overline{15}$, 25, and the other members of the same subset results in formation of the (*S*)-phosphonium ion. Interconversion between enantiomeric subsets of phosphoranes, and therefore interconversion between enantiomeric phosphonium ions, can be effected only by way of pseudorotation around L_5 , *i.e.*, only by an east-west interchange through pathways $13 \rightleftharpoons \overline{24}$, $\overline{13} \rightleftharpoons 24$, $14 \rightleftharpoons \overline{23}$, and $\overline{14} \rightleftharpoons 23$. In this connection, it must be emphasized that there is an important distinction in the racemization pathways available for the interconversion of enantiomeric phosphoranes and enantiomeric phosphonium ions. As has been noted before,³² phosphoranes containing small ring systems are resistant to racemization because any path traversed from a given isomer of $P(L_1L_2L_3L_4L_5)$ to its enantiomer must lead through a high-energy intermediate in which the ring termini L_1 and L_2 span the *ee* position. However, such intermediates, which are represented by the six star point vertices in the hexaasterane graph, may be avoided in the racemization of phosphonium ions. The initial phosphorane formed by attack of, say, L_3 on (*S*)- $P^+(L_1L_2L_3L_4)$ can, by pseudorotation across σ_5 , convert into a phosphorane belonging to the enantiomeric subset. Loss of L_5 from the ultimate phosphorane gives (*R*)- $P^+(L_1L_2L_3L_4)$. Note that the initial and ultimate phosphoranes, though belonging to enantiomeric subsets, cannot themselves be enantiomers of each other if arcs across the star point vertices are avoided. It follows that, in contradistinction to phosphoranes, phosphonium ions and other tetracoordinate phosphorus compounds are capable of racemization (by way of intermediate phosphoranes) even when L_1 and L_2 are termini of small ring systems.

The diagram in Figure 5 provides, at a glance, a map of the stereochemical consequences of displacement reactions on phosphorus in cyclic phosphonium salts which are initiated by external nucleophilic attack. As an illustration, consider nucleophilic displacements of L_4 or L_3 in (*S*)- $P^+(L_1L_2L_3L_4)$ by L_5 . The initial product will be one or several of the phosphoranes in the subset west of σ_5 . Retention and inversion of configuration in the displacement of L_4 give enantiomers of $P^+(L_1L_2L_3L_5)$ for which the corresponding subsets are represented by the vertices southwest and northeast of σ_4 , respectively. The stereochemistry of the displacement therefore depends entirely on whether loss of L_4 occurs from a phosphorane which is in the southwest (retention) or northeast (inversion) sector formed by σ_4 . Similarly, the stereochemistry of the displacement of L_3 depends entirely on whether loss of L_3 occurs from a phosphorane

which is in the northwest (retention) or southeast (inversion) sector formed by σ_3 .

Two other surfaces exist which bisect the edges indexed 1 and 2, *i.e.*, the edges which, by the chosen convention, represent pseudorotations about a ring terminus ligand. According to our representation, these surfaces are *not* planes but are scalloped and of idealized D_{3d} symmetry³⁸ (consistent with the basic image depicted in Figure 1), with the threefold axis coincident on the sixfold axis of the hexaasterane.³⁸ These surfaces, designated σ_1' or σ_2' , depending on which edge is bisected, divide the set of 18 vertices into two subsets of nine. The properties of the subsets are those described above for σ_n , with the difference that the phosphoranes are now products of *intramolecular* nucleophilic attack. In each subset, three phosphoranes arise from *a* attack and the other six from *e* attack.^{39,41}

As an illustration, σ_2' divides the 18-vertex graph into two subsets of vertices/phosphoranes resulting from attack by L_2 on the enantiomers of $P^+(L_1L_3L_4L_5)$. For the *S* isomer,⁴⁰ *a* attack initially affords $\overline{23}$, 24, and $\overline{25}$, and *e* attack $\overline{13}$, 14, $\overline{15}$, 34, $\overline{35}$, and 45. Each of these phosphoranes reverts to the (*S*)-phosphonium salt upon $P-L_2$ bond cleavage. Attack of L_2 on the *R* isomer results in the enantiomeric set. By reference to Figure 3, it is immediately seen that the phosphoranes initially resulting from attack of L_2 on (*S*)- $P^+(L_1L_3L_4L_5)$ occupy the six positions on the top hexagon and, in alternating order, three points of the star. The phosphoranes initially resulting from attack of L_2 on the *R* isomer therefore occupy the six positions on the bottom hexagon and the three remaining star points. It remains to be noted that the phosphoranes in the subsets resulting from division of the graph by σ_1' also occupy the six positions on the top hexagon when L_1 attacks (*S*)- $P^+(L_2L_3L_4L_5)$ and the six positions on the bottom hexagon when the *R* isomer is attacked; only the positions of the star points are reversed (*i.e.*, 34, $\overline{35}$, and 45 are products of attack on the *R* isomer).

In combination, the hexaasterane graph with its 18 vertices, 24 edges, and 5 surfaces provides the first general and systematic topological representation of the stereochemistry of external and internal nucleophilic displacement reactions at phosphorus in which a monocyclic phosphorane is the intermediate, as in the scheme of Chart I.

Applications to Chemical Systems. Attack by External Nucleophiles. Base-catalyzed hydrolysis of *cis*- and *trans*-1-ethoxy-1-phenyl-2,2,3,4,4-pentamethylphosphetanium hexachloroantimonates (**1**) affords *cis*- and *trans*-1-phenyl-2,2,3,4,4-pentamethylphosphetane 1-oxides (**2**) by P-O cleavage, with complete retention of configuration at phosphorus.⁴ Similarly, reduction of *cis*- and *trans*-**2** with hexachlorodisilane affords *cis*- and *trans*-1-phenyl-2,2,3,4,4-pentamethylphosphetanes (**3**) with complete or nearly complete retention of configuration at phosphorus.⁴ The first step in the reduction is presumed to be formation of a trichlorosiloxyphosphetanium ion (**4**), which in a subsequent step suffers attack at phosphorus by trichlorosilyl anion.^{4,6}

In order to refer to the hexaasterane graph, the ligands on phosphorus in **1** and **4** are labeled as follows:⁴² phenyl $\equiv L_3$, the leaving groups (ethoxy in **1** and trichloro-

bidden isomers, 12 and $\overline{12}$, and the allowable isomer number in each subset is therefore reduced to nine. Since face and edge attacks place the nucleophile into apical and equatorial positions, respectively, the terms *a* attack and *e* attack will be used as synonyms.

(40) In the present context, and for convenience in discussion, the chirality rule of R. S. Cahn, C. Ingold, and V. Prelog [*Angew. Chem. Intern. Ed. Engl.*, **5**, 385 (1966)] is applied directly to the index numerals of the phosphonium ions depicted in Figure 5. The points of the compass refer to the same diagram, with north at the top of the figure.

(41) Attack by L_1 or L_2 on the face formed by L_3 , L_4 , and L_5 leads to the forbidden isomers.

(42) These designations are entirely arbitrary and any other distribution of index numerals 3-5 would be equally acceptable.

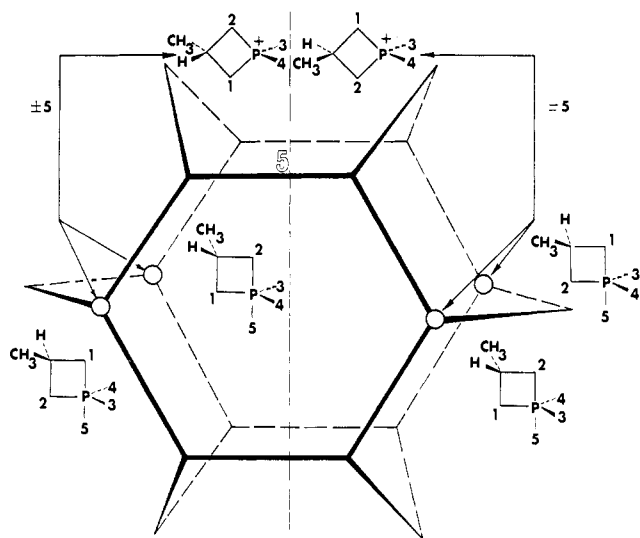
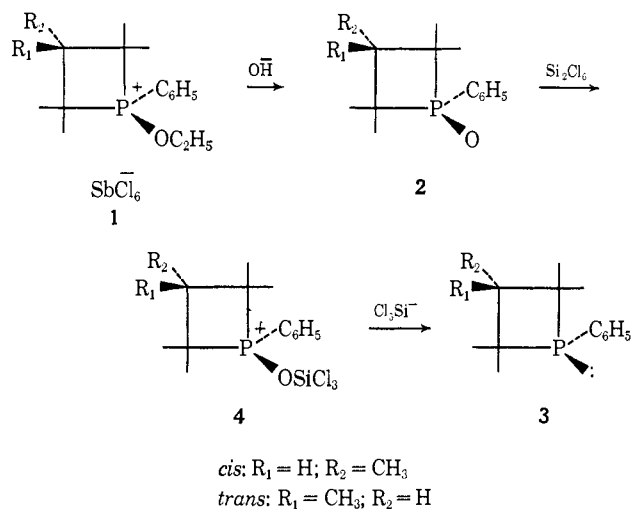


Figure 6.

siloxo in **4**) \equiv L_4 , and the attacking nucleophile (hydroxide in the reaction with **1** and trichlorosilyl anion in the reaction with **4**) \equiv L_5 . By our adopted convention, ring termini are labeled L_1 and L_2 . Since the



$C(CH_3)_2$ branches are enantiotopic with respect to the prochiral phosphorus atom, they are distinguishable and therefore properly assigned different labels. The presence of the prochiral carbon atom (C-3) in the ring provides a marker which confers distinguishability on the enantiotopic branches even under achiral conditions.⁴³ If, arbitrarily, the *pro-R_C* branch⁴⁴ is indexed as L_1 and the *pro-S_C* branch⁴⁴ as L_2 , it follows that *cis-1* and *cis-4* are represented by the phosphonium ion west of σ_5 (Figure 6), corresponding to the *S* isomer⁴⁰ of P^+ ($L_1L_2L_3L_4$) in Figure 5, whereas *trans-1* and *trans-4* are represented by the phosphonium ion to the east of σ_5 , corresponding to the *R* isomer. Attack of L_5 (OH^- or

(43) Under achiral conditions, the enantiotopic branches in *unsubstituted* ring systems, e.g., 1-ethoxy-1-phenylphosphetanium ion, are operationally indistinguishable; therefore $L_1 \equiv L_2$. This degeneracy simplifies the hexastereane graph into a triasterane³⁷ of idealized D_{3h} symmetry. Enantiomers in the three *dl* pairs are related by a plane of symmetry perpendicular to the threefold axis, and the three achiral (C_s) conformers occupy the vertices at the points of the star which are located on that plane.

(44) This nomenclature (K. R. Hanson, *J. Am. Chem. Soc.*, **88**, 2731 (1966)) in the present context refers to the carbon atom as the prochiral center.

Cl_3Si^-) on the *S* isomer yields the subset of phosphoranes west of σ_5 . If the assumption is made that *a* attack is the preferred mode for addition,^{21,45} only phosphoranes $\bar{15}$, 25, $\bar{35}$, and 45 (from *cis-1* or 4) and 15, $\bar{25}$, 35, and $\bar{45}$ (from *trans-1* or 4) remain as candidates for the initial products of addition of L_5 . The isomer number is further reduced by the ring strain (corresponding to a formal L_1PL_2 bond angle deformation of $\Delta\theta$ ca. 30°) produced when a four-membered ring is required to span the *ee* positions, in contrast to the negligible strain ($\Delta\theta$ ca. 0°) when the same ring spans the *ae* positions. As summarized in Figure 6, this leaves only two candidates for the phosphoranes derived from each of the two isomeric phosphonium ions: $\bar{15}$ and 25, enantiomers derived from attack of L_5 on the enantiotopic faces ($L_1L_3L_4$ and $L_2L_3L_4$) of the *cis* isomer of **1** or **4**, and 15 and $\bar{25}$, enantiomers similarly derived from the *trans* isomer.⁴⁶

Retention or inversion depends on the sector in which the ultimate phosphorane is located: starting with *cis-1* or *-4*, retention occurs when the ultimate phosphorane, *i.e.*, the phosphorane which loses L_4 ($C_2H_5O^-$ or Cl_3SiO^-) to form *cis-2* or *-3*, is located in the sector southwest of σ_4 , whereas inversion, and formation of *trans-2* and *-3*, occurs when the ultimate phosphorane is located in the northeast sector. The isomer number in each sector formed by σ_4 is reduced from nine to four by application of the principle of microscopic reversibility,²¹ which states in effect that the stereochemistry (*a* vs. *e*) of entry and departure must be the same. Accordingly, only $\bar{14}$ and 24 remain as candidates for retention, and 14 and $\bar{24}$ for inversion, since ring strain effectively limits access to the *meso* isomers (34, $\bar{34}$, 45, and $\bar{45}$). The ultimate phosphoranes, derived from $\bar{15}/25$, are thus identified as $24/\bar{14}$ for retention and $14/\bar{24}$ for inversion. The ultimate phosphoranes are the same but the stereochemical direction is reversed when the starting phosphorane is $15/\bar{25}$, derived from *trans-1* or *-4*. To simplify the following discussion, differences between enantiomers will be ignored and only the pathways on the top hexagon, representing one set of enantiomers,⁴⁶ will be considered.⁴⁷

Starting from $\bar{15}$, two retention pathways exist: clockwise ($\bar{15} \rightarrow \bar{23} \rightarrow 14 \rightarrow \bar{25} \rightarrow \bar{13} \rightarrow 24$), and counterclockwise ($\bar{15} \rightarrow 24$). The shorter pathway is not necessarily the path of lower energy, but the ambiguity

(45) In nucleophilic substitutions, apical entry and departure are preferred over the equatorial counterparts (S. I. Miller in "Advances in Physical Organic Chemistry," Vol. 6, V. Gold, Ed., Academic Press, New York, N. Y., 1968, p 253).

(46) It is a remarkable property of the systems under discussion that a symmetry plane, perpendicular to the sixfold axis of the graph and passing through the center of inversion, neatly divides the 18 vertices/isomers into three subsets of six. The set corresponding to the vertices on the top hexagon contains six chiral diastereomers which are related to their respective mirror images, arrayed at the vertices on the bottom hexagon, by reflection through the plane. Thus, $\bar{15}$ and 25 are enantiomers, as are $13/\bar{23}$, $14/\bar{24}$, $15/\bar{25}$, $\bar{13}/23$, and $\bar{14}/24$. The remaining six isomers, corresponding to the vertices located on the symmetry plane, *i.e.*, at the points of the star, are *meso* compounds (C_s). In other words, the symmetry properties of the idealized graph are related to the symmetry properties of the molecules represented by its vertices. However, the centric nature of the basic graph (Figures 1-4) remains, and, with respect to the chirality of the phosphorus atom, chiral centers are related through the center of inversion of the graph.

(47) Any arc leading from the top to the bottom hexagon must traverse a star point vertex, which represents a highly strained *meso* compound. Such a pathway is thereby effectively eliminated from consideration, and the two hexagons are thus insulated from each other by the equatorial belt (in the asterane representation) of vertices/*meso*-phosphoranes.

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*-2 or -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 (Figure 7).

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 last step, the exchange of positions of the electropositive (L_3) *a* ligand and the electronegative (L_4) *e* ligand amounts to a rearrangement from relatively unfavorable placements to favorable ones, since *e* and *a* positions are positions of relative preference for more electropositive and electronegative groups, respectively.^{21,45,48} It is likely, therefore, that the last step is a fast one, and that the first pseudorotation ($\overline{15} \rightarrow \overline{23}$) is the rate-determining step for inversion. In the reaction of *cis*-1, pseudorotation about L_3 (retention) merely exchanges the *a* and *e* positions of the two electronegative (hydroxy and ethoxy) ligands, whereas pseudorotation about L_4 (inversion) places both electronegative groups in the *e* positions and the relatively electropositive (phenyl) group in the *a* position, an energetically unfavorable arrangement.^{21,48} It follows that retention is the preferred pathway. In the reaction of *cis*-4, a similar argument leads to the same conclusion if it is granted that trichlorosiloxy is the most electronegative and phenyl the most electropositive of the three ligands L_3 - L_5 . Likewise, retention of configuration in reactions of *trans*-1 and *trans*-4 is accounted for on the reasonable assumption that the relative rates of pseudorotation are not markedly influenced by the stereochemistry at the prochiral carbon center (C-3 of the phosphetane system). The sector northeast of σ_4 now represents retention and the southwest sector inversion; the counter-clockwise 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.

Since $\overline{15}$ and 25 (as well as 15 and $\overline{25}$) are enantiomers and will suffer the same chemical fate under achiral conditions, the analysis is identical⁴⁶ starting from either enantiomer derived from the same phosphonium ion.

If *e* attack of L_5 is the mode for addition, phosphoranes 13, $\overline{23}$, $\overline{14}$, 24, and $\overline{34}$ from *cis*-1 or -4, and $\overline{13}$, 23, 14, $\overline{24}$, and 34 from *trans*-1 or -4, are candidates for the initial products of addition. Of these, *meso*-phosphoranes $\overline{34}$ and 34 are inaccessible due to ring strain, while 13 and $\overline{23}$, as well as $\overline{13}$ and 23, are eliminated on the basis of electronegativity arguments, as above. Consequently, there remain only two phosphoranes derived from each of the two isomeric phosphonium ions: $\overline{14}$ and 24, enantiomers obtained by attack of L_5 on the enantiotopic edges (L_1L_4 and L_2L_3 , respectively) of *cis*-1 or -4, and 14 and $\overline{24}$, enantiomers similarly obtained from *trans*-1 or -4.

The stereochemistry accompanying loss of L_4 from the ultimate phosphoranes is the same as discussed above for *a* attack: starting from *cis*-1 or -4, the phos-

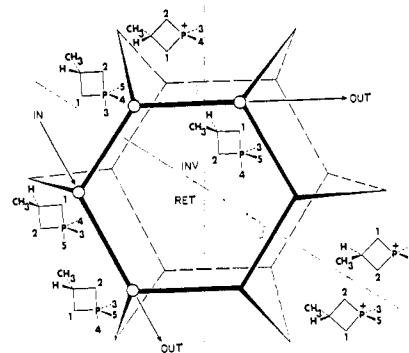
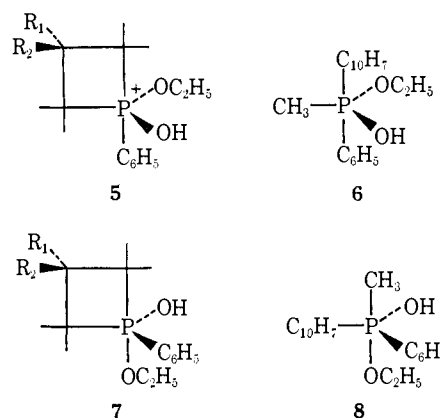


Figure 7.

phoranes in the sector southwest of σ_4 lead to retention while those in the northeast sector result in inversion. Utilizing the arguments outlined above and invoking the principle of microscopic reversibility, the number of ultimate phosphoranes can be reduced to two per sector: $\overline{15}$ and 25 southwest of σ_4 and 15 and $\overline{25}$ northeast of σ_4 . The ultimate phosphoranes derived from $24/\overline{14}$ are thus identified as $\overline{15}/25$ for retention and $\overline{25}/15$ for inversion.

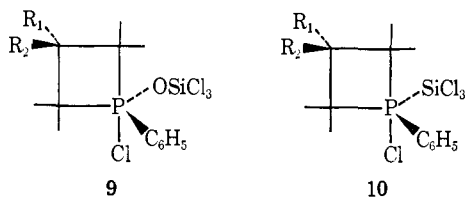
The analysis of the two possible pathways (inversion or retention) for the reaction of either of the two energetically equivalent (under achiral conditions) isomers $\overline{14}/24$ derived from *cis*-1 or -4 is similar to that outlined for *a* attack. Retention is the preferred pathway ($24/\overline{14} \rightarrow \overline{15}/25$) over inversion ($24/\overline{14} \rightarrow \overline{13}/23 \rightarrow \overline{25}/15$), since inversion requires the intermediacy of a phosphorane ($\overline{13}/23$) containing two electronegative groups in *e* positions and a relatively electropositive group in an *a* position. Similarly, the phosphoranes $14/\overline{24}$ derived from *trans*-1 or -4 prefer the retention pathway $14/\overline{24} \rightarrow \overline{25}/15$.

Although, as discussed above, *e* attack and *e* departure involve the same set of intermediate phosphoranes as *a* attack and *a* departure, the following analysis indicates that a nucleophilic displacement pathway *via* the *a* positions is preferred.⁴⁵ Base-catalyzed hydrolysis of **1** and of ethoxymethyl- β -naphthylphenylphosphonium nitrate⁷ by *e* attack should lead to intermediates such as **5** and **6** (inversion pathway) or **7** and **8** (retention pathway), with similar stereochemical results for both systems. The fact that the cyclic and acyclic systems give different stereochemical results is therefore indicative of *a* attack, for it is only thus that the four-membered ring in **1** can play its distinctive role.



(48) P. C. Van Der Voorn and R. S. Drago, *J. Am. Chem. Soc.*, **88**, 3255 (1966); R. Schmutzler in "Halogen Chemistry," Vol. 2, V. Gutmann, Ed., Academic Press, New York, N. Y., 1967, pp 73-113.

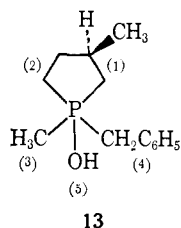
Closely analogous arguments provide an explanation for the epimerizations of **2** and **3** by reaction with silicon tetrachloride.⁴ The first products of reaction are likely to be the adducts formulated as **9** and **10** (and their mirror images), respectively.



The equilibria involving such intermediates are quite complex,⁶ but the *reversibility* of the reactions inevitably leads to thermodynamic (product) control, *i.e.*, to epimerization. Even though the kinetically controlled products have predominantly retained configurations, the inversion pathway is not entirely shut off and a leakage mechanism is thereby provided whereby an equilibrium mixture is eventually obtained.

The mechanism advanced for the silicon tetrachloride catalyzed epimerizations of **2** and **3** is not applicable to the base-catalyzed hydrolysis of *cis*- and *trans*-1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide,⁴⁹ a reaction which, though stereoselective (a predominance of one isomer of **2** is obtained from either isomer of the phosphetanium bromide), is not stereospecific, and which is plainly irreversible. In systems of this kind, clockwise and counterclockwise pathways interconvert *cis*- and *trans*-phosphetanium ions at a rate faster than the rate of loss of L_4 from the ultimate phosphoranes, $\overline{14}/24$ and $14/\overline{24}$.

Retention of configuration observed⁸ in the base-catalyzed hydrolysis of *cis*- and *trans*-1-benzyl-1,3-dimethylphospholanium bromides (**11**) to the phospholane 1-oxide (**12**)⁸ may also be systematically discussed by reference to the hexaasterane graph. Since the chirality of the asymmetric carbon atom in **11** is not affected by pseudorotation, two noninterconverting enantiomeric sets exist, each containing 18 diastereomeric phosphoranes. Members of one set have the *R* configuration and those of the other set the *S* configuration at carbon. Arbitrarily selecting for discussion the set with the *R* configuration at carbon, the set of intermediate phosphoranes (**13**) derived from *cis*-(*R*)_P-**11** is depicted below, along with the indices of the ligands.



Employing the hexaasterane notation developed in the preceding sections, all initially formed isomers of **13** derived from *cis*-(*R*)_P-**11** are members of the subset west of σ_5 . Restricting additions to *a* attack,⁴⁵ and ruling out formation of isomers with *ee* rings,⁵⁰ two diastereo-

(49) S. E. Cremer, R. J. Chorvat, and B. C. Trivedi, *Chem. Commun.*, 769 (1969).

(50) A variety of related studies^{21,22} have demonstrated that considerable strain is introduced when five-membered rings are required to span equatorial positions.

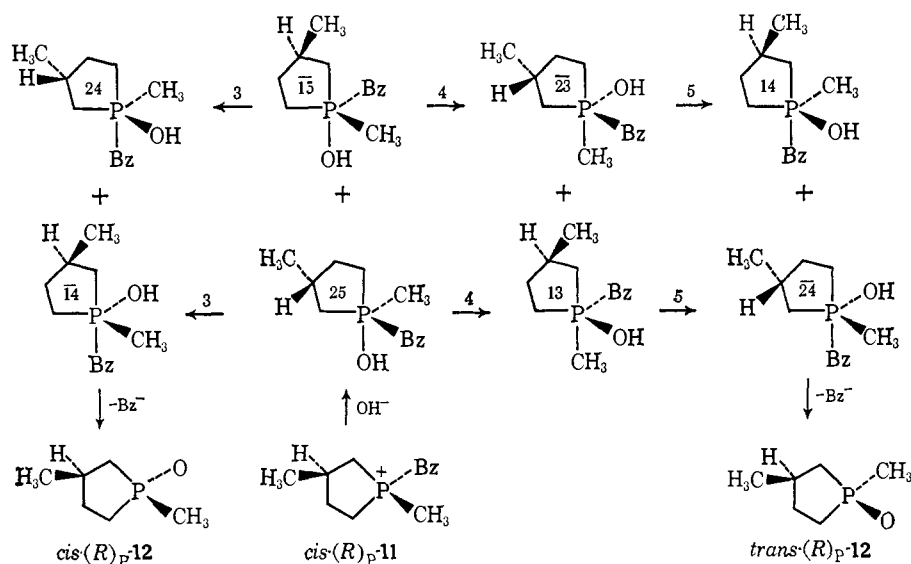
mers of **13** remain as candidates for products of addition, $\overline{15}$ and **25**; these isomers derive from attack of hydroxide (L_5) on the two diastereotopic faces ($L_1L_3L_4$ and $L_2L_3L_4$) of *cis*-(*R*)_P-**11** (Chart II). Granting apical departure of the leaving group,⁴⁵ benzyl (L_4), and assuming that the rate of loss of L_4 is fast compared to the rate of pseudorotation, a clockwise arc leads to **14** and $\overline{24}$, the ultimate phosphoranes for inversion, while a counterclockwise arc leads to $\overline{14}$ and **24**, and retention. There appears to be no obvious reason why any of the four ultimate phosphoranes should differ grossly in energy, since any such differences are due to secondary forces, *i.e.*, to nonbonded interactions. However, the intermediates in the inversion pathway, **13** and $\overline{23}$, exhibit an important distinction from the *a*- L_4 isomers: the electropositive methyl group now occupies the *a* position and the relatively less electropositive benzyl group the *e* position. This unfavorable^{21,48} arrangement raises the energy of **13** and $\overline{23}$ relative to that of $\overline{14}$ and **24**, and renders the retention pathway the preferred exit route (Chart II). Similar considerations lead to the conclusion that *trans*-(*R*)_P-**11** should yield, predominantly, *trans*-(*R*)_P-**12**. Identical reasoning, applied to the enantiomeric set having the *S* configuration at carbon, leads to the same conclusions.

Attack by Internal Nucleophiles. As indicated in Chart I, intramolecular nucleophilic attack on phosphorus in acyclic phosphonium salts may lead to the same phosphoranes which obtain from external nucleophilic attack on cyclic phosphonium salts. It was earlier noted that if L_2 is the attacking nucleophile and ring terminus-to-be, reaction with the two enantiomers of $P^+(L_1L_3L_4L_5)$ affords the two subsets of nine phosphoranes represented by the vertices which result from division of the hexaasterane graph by σ_2' , and that, similarly, attack by L_1 on the enantiomers of $P^+(L_2L_3L_4L_5)$ affords the subsets resulting from division by σ_1' . However, the six star point vertices, representing the six *ee* rings, may be eliminated from consideration in the case of four- or five-membered ring formation, for reasons given above and elsewhere;²¹ accordingly, in such cases, the σ_n' surfaces become, in effect, congruent planes passing through the star point vertices and dividing the graph into top and bottom hexagons, whose vertices represent the two enantiomeric and noninterconverting sets of six diastereomeric phosphoranes derived from the two enantiomeric phosphonium ions.

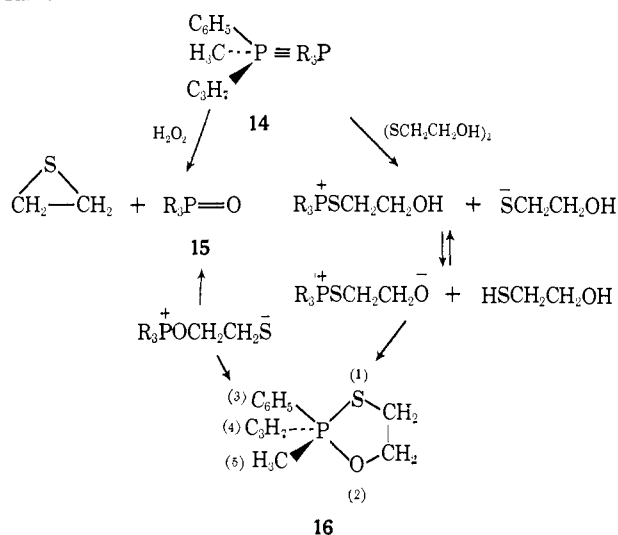
To illustrate the last point, consider the oxidation of phosphines by bis(2-hydroxyethyl) disulfide, a reaction for which an intramolecular displacement mechanism has been proposed.⁵¹ We have found that oxidation of (*R*)-methylphenyl-*n*-propylphosphine (**14**) with this reagent affords the oxide, (-)-(*S*)-**15**, $[\alpha]_D -14^\circ$. Product with $[\alpha]_D -15^\circ$ is obtained upon oxidation of (*R*)-**14** with hydrogen peroxide. The oxidation with bis(2-hydroxyethyl) disulfide therefore proceeds with complete (or nearly complete) stereospecificity, and with retention of configuration at phosphorus.⁵² Denoting phenyl, *n*-propyl, and methyl groups in the intermediate phosphorane **16** (Chart III) as L_3 , L_4 , and L_5 , respectively, and the sulfur and oxygen ring termini as L_1 and L_2 , respectively, *a* attack⁴⁵ of L_2 on the three available faces^{39,41} leads to $\overline{23}$, **24**, and $\overline{25}$ if the starting phos-

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

(52) L. Horner, *Pure Appl. Chem.*, 9, 225 (1964).

Chart II^a

^a The number over the arrows indicates the index of the pivot ligand about which pseudorotation takes place (for numbering, see picture of **13** in text). The stereoisomers of **13** are identified by the numbers inside the ring. Bz = benzyl. The prefixes (*cis*, *trans*) refer to the relationship between the two methyl groups.

Chart III^a

^a Numbers in parentheses denote ligand indices in **16**.

phine has the *R* configuration. Interconversion of these three isomers *via* **13**, **14**, and **15** occurs by pseudorotations in the plane of the top hexagon, as depicted in Figure 8. The six diastereomeric phosphoranes are not converted into their enantiomers, represented by the vertices on the bottom hexagon. Ring opening, by departure of the apically located sulfur (L_1) from any one of the three ultimate phosphoranes (**13**, **14**, and **15**), results in product (**15**) formation with retention of configuration.

The systematic analysis developed above applies with equal force to the retention mechanism in the reaction of phosphonium ylides.¹¹⁻¹⁴

Cognate Systems. Although the above discussions have dealt exclusively with nucleophilic displacement reactions at phosphorus in phosphonium salts which involve the intermediacy of a phosphorane containing a four- or five-membered ring, the generality and scope of our treatment are not impaired when the system under discussion is changed. *The hexaasterane graph 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 the present paper 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

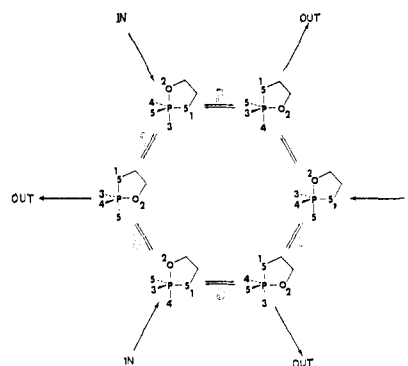


Figure 8.

the elimination of isomers having two strongly electropositive groups simultaneously located in apical positions. Extensions to systems other than phosphonium salts are readily envisaged. For example, hydrolysis of phosphorus esters which involve cyclic phosphoranes^{21,53} may be discussed in analogous fashion. Furthermore, the scheme is not limited to displacements at phosphorus but is in principle applicable to systems in which the central atom is another element, such as silicon,⁵⁴ or sulfur.⁵⁵

Experimental Section

Oxidation of (-)-(*R*)-Methylphenylpropylphosphine (14**) with Bis(2-hydroxyethyl) Disulfide.** A solution of 2-hydroxyethanethiol

(53) D. S. Frank and D. A. Usher, *J. Am. Chem. Soc.*, **89**, 6360 (1967).

(54) K. Tamao, M. Ishikawa, and M. Kumada, *Chem. Commun.*, **73** (1969).

(55) R. Tang and K. Mislow, *J. Am. Chem. Soc.*, **91**, 5644 (1969).

(10 g, 0.13 mol) in water (3 ml) was mixed with potassium hydroxide (ca. 0.5 g) and a catalytic amount of ferric chloride, and air was bubbled through the reaction mixture for 6 hr. Removal of solvent under reduced pressure gave a residue from which the product, bis(2-hydroxyethyl) disulfide, was obtained (ca. 4 g) by rapid distillation (kugelrohr) at reduced pressure, bp ca. 110° (0.01 mm), mp 22–26° (lit.⁵⁶ mp 25–26°).

A sample of (–)-(R)-methylphenylpropylphosphine (14), which was prepared by the hexachlorodisilane reduction⁶ of (+)-(R)-methylphenylpropylphosphine oxide (15),⁵⁷ was reoxidized⁶ with hydrogen peroxide to give (–)-(S)-15, $[\alpha]_D -15.0^\circ$ (methanol), optical purity⁵⁸ 75%.

(56) E. J. Gasson, H. McCombie, A. H. Williams, and F. N. Woodward, *J. Chem. Soc.*, 44 (1948).

A solution of this same sample of (–)-(R)-methylphenylpropylphosphine (50 mg, 0.3 mmol) in benzene (3.3 ml) was added to bis(2-hydroxyethyl) disulfide (46 mg, 0.3 mmol) and the mixture was stirred at ca. 50° for 10 hr. Removal of solvent under reduced pressure gave the crude product, which was rapidly distilled (kugelrohr) at reduced pressure, bp ca. 110° (0.1 mm). The distillate was chromatographed on silica gel, eluting with ethyl acetate, to give (–)-(S)-15 (39 mg, 71%), $[\alpha]_D -14.1^\circ$ (methanol), optical purity 71%.

(57) O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Am. Chem. Soc.*, 90, 4842 (1968).

(58) J. P. Casey, R. A. Lewis, and K. Mislow, *ibid.*, 91, 2789 (1969).

Stereochemistry of Asymmetric Silicon. XIII. General Demonstration of Stereochemistry Crossover for Reactions Involving Certain Leaving Groups and Alkoxide Reagents^{1,2}

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Abstract: Stereochemistry crossover from retention to inversion of configuration (or *vice versa*) in individual reaction series involving alkoxide reagents is reported for the leaving groups OPh, SMe, and F. The reactant is R_3Si^*X (R_3Si^* is α -naphthylphenylmethylsilyl). Mechanistic implications of this work are discussed and further support for the S_N1-Si and S_N2-Si mechanisms is adduced.

Two previous publications have reported that (a) stereochemistry crossover from *inversion* to *retention* of configuration (or *vice versa*) in coupling reactions is a sensitive function of the nature of the organometallic reagent (RLi or $RMgX$) and the basicity of the leaving group ($X = Cl, F, OMe, \text{ or } H$);³ (b) stereochemical variation (per cent *retention vs.* per cent *inversion*) and stereochemistry crossover in alkoxide-alkoxide exchange reactions are a sensitive function of the alcoholic content of the solvent and the nature of the cation;⁴ (c) the relationships that were revealed in both studies are consistent with earlier conclusions that *inversion* reactions of R_3Si^*X with strong nucleophiles proceed by mechanism S_N2-Si and that *retention* reactions follow a quasicyclic S_N1-Si mechanism.³⁻⁵

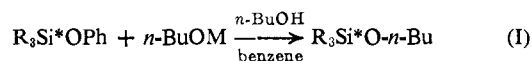
For S_N1-Si , which operates with leaving groups that are usually highly basic and are classed as "poor,"⁵ the only previous extensive and systematic study of solvent and reagent effects on the operation or nonoperation of this mechanism has involved alkoxide leaving groups in alkoxide-alkoxide exchange reactions. We now report additional extensive studies which encompass a variety of leaving groups ($X = OPh, F, \text{ or } SCH_3$) with alkoxide

reagents, for the purpose of extending our detailed knowledge concerning the factors which are critical for operation of the S_N1-Si mechanism.

Stereochemical Studies of the Phenoxide Leaving Group. The phenoxide group in (+) R_3Si^*OPh (R_3Si^* is α -naphthylphenylmethylsilyl) gives replacement with predominant retention of configuration yielding (+) R_3Si^*H when treated with lithium aluminum hydride. Relative configurations for the products of reduction and alkoxide replacement of phenoxide were assigned on the basis of the S_N2-Si stereochemistry rule with particular reference to the inversion path always followed by reactions of R_3Si^*Cl with strong nucleophiles.⁴⁻⁶

The phenoxide group can be classed as a borderline leaving group (poor leaving groups have pK_a of HX larger than ca. 10 and $PhOH$ has $pK_a \sim 10$) and it is, of course, far less basic than an alkoxide group ($MeOH$ has $pK_a \sim 16$). Thus, a comparison of OMe and OPh as leaving groups with alkoxide reagents is of considerable interest. (It may be noted that alkoxide groups are also reduced with lithium aluminum hydride with predominant retention of configuration.)

The first studies concern reaction of R_3Si^*OPh with *n*-butoxide in mixed benzene-butanol solvent and results are presented in Table I. In detail, the reactions studied are



where $M = Li, Na$.

(6) L. H. Sommer, G. A. Parker, N. C. Lloyd, C. L. Frye, and K. W. Michael, *J. Am. Chem. Soc.*, 89, 857 (1967).

(1) For the preceding paper in this series, see L. H. Sommer, J. D. Citron, and G. A. Parker, *J. Am. Chem. Soc.*, 91, 4729 (1969).

(2) We are grateful for vital support of this work by National Science Foundation.

(3) L. H. Sommer and W. D. Korte, *J. Am. Chem. Soc.*, 89, 5802 (1967).

(4) L. H. Sommer and H. Fujimoto, *ibid.*, 90, 982 (1968).

(5) L. H. Sommer, "Stereochemistry, Mechanism, and Silicon," McGraw-Hill Book Co., Inc., New York, N. Y., 1965; see Chapter 11 for a summary.