

PENTACOVALENT PHOSPHORANES AS INTERMEDIATES IN SUBSTITUTIONS AT PHOSPHORUS

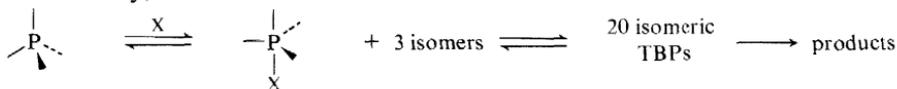
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ABSTRACT

Five-coordinate phosphoranes are intermediates in substitution reactions at phosphorus. The relative stabilities of phosphoranes are discussed in terms of the relative apicophilicities of groups, steric factors and ring strain, and experiments are described which give quantitative data on these. The application of the results to discussion of the course of substitutions at phosphorus is briefly described.

In order to discuss mechanism in organophosphorus chemistry several assumptions have to be made, and it is important that these should be fully spelled out. Among them are (a) that substitutions at tetrahedral phosphorus proceed via five-coordinate intermediates; (b) that these intermediates are trigonal-bipyramidal; (c) that they are formed by apical attack and decompose by apical loss; and (d) that if sufficiently long-lived they may undergo isomerization—that is, the ligands may alter their relative dispositions round the phosphorus, before going on to products or back to reactants. In summary,



Assuming that the course of a given substitution is dictated primarily by thermodynamic considerations, in order to understand the course of that substitution one needs to know how to assess the relative stabilities of the four isomeric TBP's that can be formed initially and of the others that could be formed by subsequent isomerization, the barriers to those isomerizations and the relative rates of the various product-forming steps. We chose to concentrate on the first of these factors, and what follows describes our attempts to provide the necessary data.

The energy difference between two isomeric TBP's can be analysed in terms of changes in the relative apicophilicities¹ of the groups occupying apical positions, changes in ring-strain as small-membered rings move between apical-equatorial and diequatorial positions and changes in steric strain. I shall consider each of these in turn.

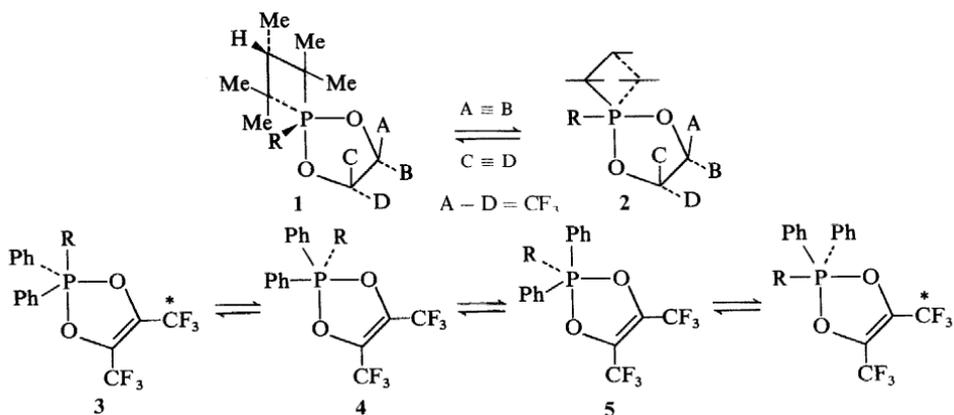
RELATIVE APICOPHILICITIES

The relative apicophilicity of two groups is the change in energy when

these groups exchange apical and equatorial positions in a TBP. Calculations by several groups^{1,2} suggest that apicophilicity should be a function of (a) electronegativity, increase favouring occupation of an apical position; (b) the presence on the atom bonded to phosphorus of a lone-pair of electrons, this favouring occupation of an equatorial position; and (c) the presence on the atom or group of a vacant low-lying orbital, this favouring occupation of an apical position. With three factors to balance it is not surprising that most experimental data can be satisfactorily rationalized. However, what is not clear *a priori* is how far the relative apicophilicity of two groups will vary with the nature of the other groups attached to phosphorus. A wide variation could lead to data which would be extremely difficult to correlate.

Most of our information on relative apicophilicities has been obtained from dynamic n.m.r. studies on stable pentacovalent phosphoranes, the results being interpreted in terms of isomerizations that involve switching the two apical substituents for any two of the equatorial substituents, a condition imposed by the famous Whitesides and Mitchell experiment³. Whether these be Berry pseudorotations or turnstile rotations^{1,4} is not important; out of habit I shall refer to them as pseudorotations. It will, however, be noted that multiple turnstile processes are not invoked.

Typical of the systems studied are the phosphetan-hexafluoroacetone adducts **1** and the perfluorobiacetyl adducts **3**. In the former case⁵ the pseudorotations that are or can be slowed on the n.m.r. time-scale are those that involve placing the four-membered ring diequatorial as in **2**. The free



energy of activation for this process varies with the apicophilicity of R and, if anything, would be expected to underestimate slightly these changes in apicophilicity. *Table 1* gives some results for this system. Later work suggests that the difference in apicophilicity between methyl and phenyl is exaggerated, perhaps because of a change in the geometry of **1** with poorly apicophilic substituents. We recently showed⁶ that adduct **1** ($\text{R} = p\text{-BrC}_6\text{H}_4$) is essentially square-pyramidal.

When R is more apicophilic than phenyl, the most stable conformation of the perfluorobiacetyl is **3**, and equilibration of the CF_3 groups is achieved via the high-energy topomers **4** and **5**. The energy required for this equilibra-

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 Table 1. Free energies of activation for the pseudorotations $1 \rightleftharpoons 2$

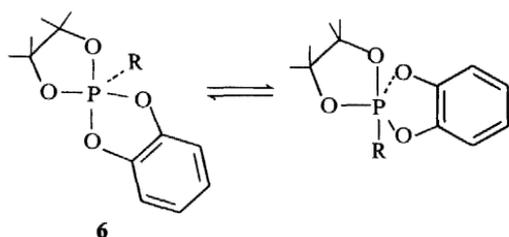
R	Ph	CH:CMe ₂	Pr ⁱ	Me	Me ₂ N	(CH ₂) ₄ N	PhO	H
ΔG^* (kcal mol ⁻¹)	>22	19.1	17.8	16.9	16.2	16.2	9	<8

tion varies as the apicophilicity of R relative to phenyl. Table 2 gives some results for this system. The free energy of activation for a particular R group will overestimate the difference in apicophilicity between R and phenyl. However, pseudorotations between TBPs of identical energies are thought to be very low-energy processes⁸ and high-energy TBPs are usually regarded as transition states rather than intermediates. The overestimate in this and similar systems will therefore probably be small.

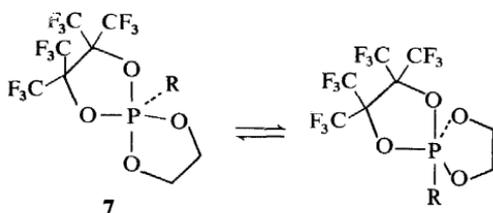
 Table 2. Free energies of activation for the pseudorotations $3 \rightleftharpoons 4$

R	COMe	CN	OC ₆ F ₅	Br	SC ₆ F ₅	OPh	Cl		OMe	NR ₂
ΔG^* (kcal mol ⁻¹)	13.9	13.6	13.2	12.8	12.7	12.6	12.0	9.9	9.8	<8

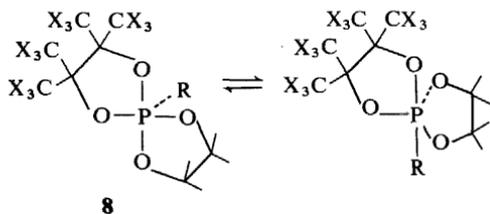
The essential features of the relative apicophilicities implicit in Tables 1 and 2 have been supported by n.m.r. data from many different types of stable pentacovalent phosphoranes. The comparable apicophilicities of ArO and ArS, of considerable interest in view of the unusual stereochemistry often associated with displacement of alkylthio groups⁹, is shown in the phosphoranes **6** and **7**¹⁰; the high apicophilicities of hydrogen and carbonyl are shown in the phosphoranes **8**¹⁰, and the large difference in apicophilicity between PhO and R₂N is shown in the adducts **9**¹¹. An unexpected feature in



R	ΔG^* (kcal mol ⁻¹)
PhO	20.5
PhS	20.7

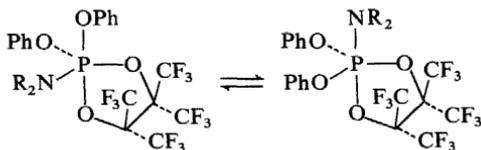


R	ΔG^* (kcal mol ⁻¹)
PhO	17.4
PhS	17.3



8

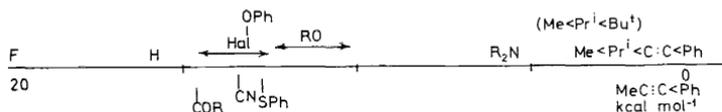
X	R	ΔG^* (kcal mol ⁻¹)
H	H	18.4
H	COPh	21.5
F	H	18.8
F	PhS	22.4



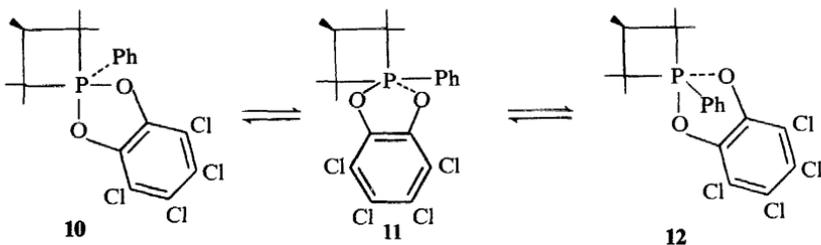
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R	Me ₂	Pr ₂ ⁱ	PhMe	Ph ₂
ΔG^* (kcal mol ⁻¹)	10.5	10.4	10.7	10.6

the last case is the lack of any effect from changing the substituents on nitrogen. Accumulation of data such as these leads to a tentative and approximate scale of apicophilicity such as the following. It must be taken *cum grano salis*!



Some evidence can be obtained from classical kinetic experiments. The geometrical isomers **10** and **12** are stable at room temperature and their interconversion via the high-energy **11** can be followed conveniently in the temperature range 100–140°C¹⁰. The found ΔG^* of 34.0 kcal mol⁻¹ compares favourably with that expected from the known barrier of 20 kcal mol⁻¹ to pseudorotations of the type **13** \rightleftharpoons **14** (see below) plus the difference in apicophilicity between phenyl and phenoxy from the above scale. As expected, ΔS^* for equilibration of **10** and **12** is within experimental error of zero.

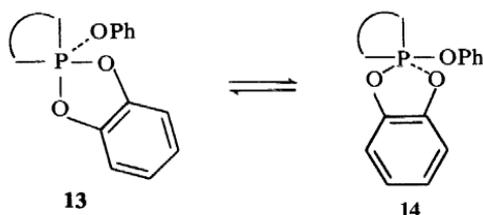


10

11

12

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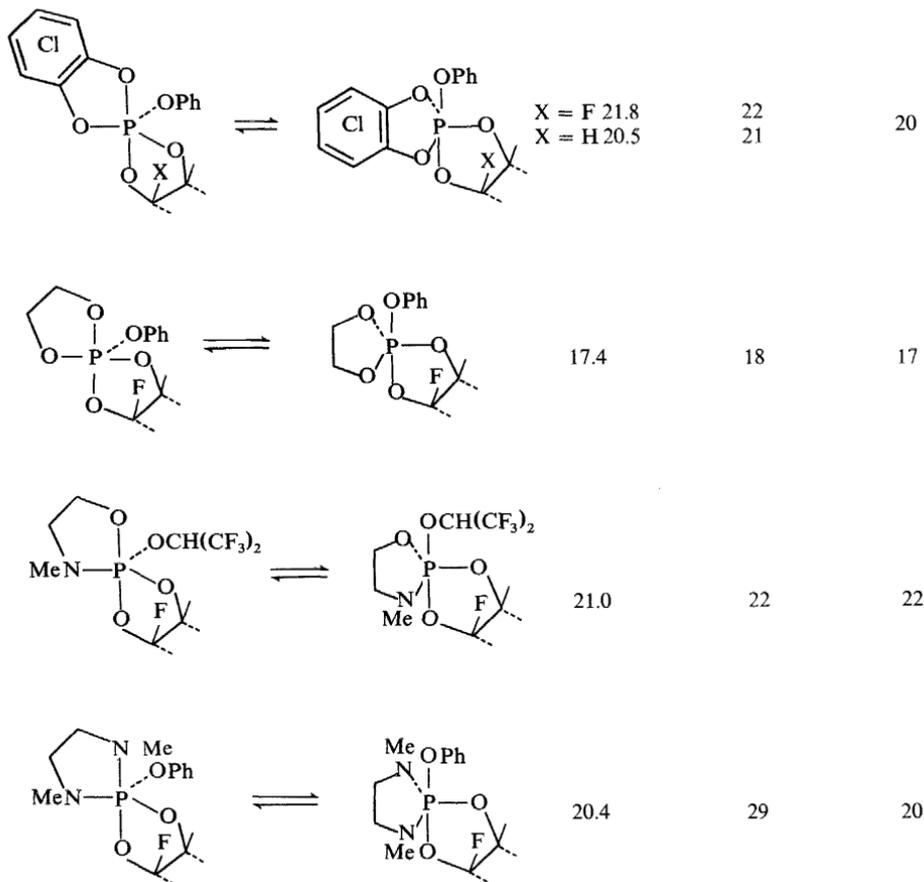


RING STRAIN

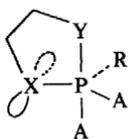
It is generally accepted that small-membered rings prefer to occupy apical-equatorial (*ae*) rather than diequatorial (*ee*) positions in trigonal-bipyramidal pentacovalent phosphoranes but no quantitative data on these preferences have been reported. From the dynamic n.m.r. spectra of a range of stable phosphoranes we have obtained data on the energies required to move various five-membered rings from *ae* to *ee* positions. Table 3 shows a selection of the relevant pseudorotations that can be slowed on the n.m.r. time-scale and gives the free energies of activation for these processes.

Table 3

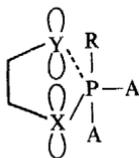
Pseudorotation	ΔG^*	$\Delta G^* - \Delta A$ (kcal mol ⁻¹)	ΔG^* (calc.)
	8.9	8	9
	14.1	15	14
	21.2	21	20



When a ring moves from an *ae* to an *ee* position (e.g. **15** \rightarrow **16**), of necessity some other group moves from an *e* to an *a* position. This may involve a change in apicophilicity of the apical substituents. Even if one allows for this, as in the penultimate column of *Table 3*, two facts are apparent: (1) the energy required to move five-membered rings containing heteroatoms bonded to phosphorus to an *ee* position is considerably greater than is needed in the case of a phospholan ring and (2) the energy required depends not only on the nature of the heteroatom which moves from an *a* to an *e* position but also on the nature of the atom which remains equatorial.



15



16

It is possible to rationalize these data by taking into account the preferred orientation of lone-pairs on equatorially bonded heteroatoms. This preference, for the equatorial plane, is well established both by calculation² and by experiment in the case of PN^{12} and PS^{13} (but not¹⁴ PO) bonds, and leads to a barrier to rotation round these bonds of 5–12 kcal mol⁻¹. The point to note in particular is that in a small-membered *ee* ring the lone-pairs occupying p orbitals on equatorial heteroatoms are in the unfavourable apical plane.

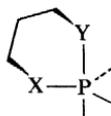
The total energy difference between **15** and **16** is therefore composed of three basic terms: (1) an angle-strain factor due to increase in the bond angle at phosphorus, (2) the energy required to rotate the lone-pair on X from the *e* to the *a* plane and (3) the difference in apicophilicity between R and Y, when the lone-pair on equatorial Y is constrained to the apical plane. The last is equivalent to the 'normal' difference in apicophilicity between A and Y, as shown in acyclic systems in which the lone-pair on Y is free to take up the preferred equatorial orientation, plus the energy required to rotate the lone-pair on Y from the *e* to the *a* plane, i.e.

$$E^{16} - E^{15} = S + R^X + \Delta A(Y - R) + R^Y$$

The data in the last column of *Table 3* were calculated on the following basis:

$$S^{\text{phospholan}} = 8; S^{\text{phospholen}} = 10; \Delta A(\text{PhO-AlkO}) = 1; R^N = 10; \\ R^O = 5 \text{ kcal mol}^{-1}$$

The strain factor for the phospholan ring is consistent with data on the pseudorotation of $(\text{CH}_2)_4\text{PF}_3^{15}$. The only experimental evidence relating to R^O is¹⁴ that it must be less than about 8 kcal mol⁻¹. More information is required on this point, but the general approach appears to be sound provided that steric effects are avoided.

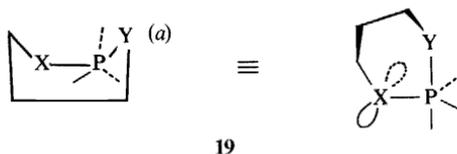


17



18

The application of these ideas to six-membered rings is much more difficult. Models suggest that with strain-free chair conformations occupying either apical-equatorial **17** or diequatorial **18** positions the lone pairs on equatorial heteroatoms are in p orbitals nearer to the apical than to the favourable equatorial plane. However, with an apical-equatorial *boat* conformation **19** the lone-pair on the equatorial substituent X can be in the equatorial plane. The boat lacks some of the destabilizing features of a boat cyclohexane; there is no 'bowsprit-flagpole' interaction and eclipsing occurs on only one side of the ring. Certainly¹⁰ there are considerably greater barriers to placing six-membered heterorings diequatorial (see *Table 4*) than would be expected if these rings were most stable in the chair conformations **17**, and once again the nature of the heteroatom that remains



equatorial significantly affects the height of the barrier. An x-ray analysis on one of these compounds would be most interesting.

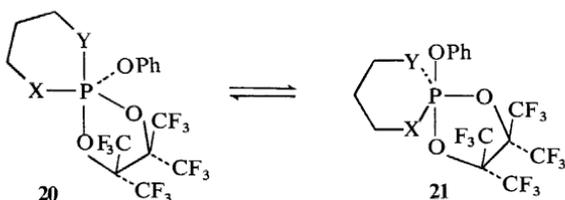


Table 4. Free energies of activation for the pseudorotations $20 \rightleftharpoons 21$

X	O	N	N
Y	O	O	N
ΔG^* (kcal mol ⁻¹)	6.1	9.5	< 6

STERIC FACTORS

It is often assumed that in a trigonal-bipyramidal phosphorane the apical position is the more hindered, for the apical substituent has three nearest neighbours, while the equatorial substituent has only two. However, there is no clear experimental evidence on this point. We have looked for steric effects in the perfluorobiacyl adducts **22** of phenyl phosphinites, where the pseudorotation that can be slowed on the n.m.r. time-scale is $22 \rightleftharpoons 23$, where R^1 is less apicophilic than R^2 . The results are in Table 5¹⁰.

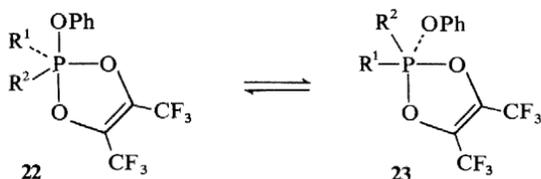
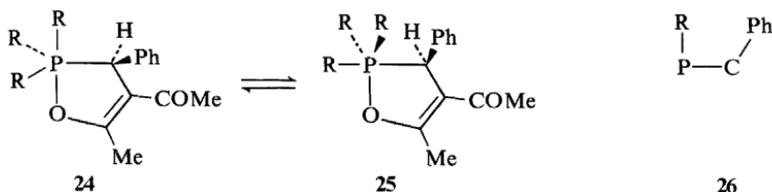


Table 5. Free energies of activation for the pseudorotations $22 \rightleftharpoons 23$

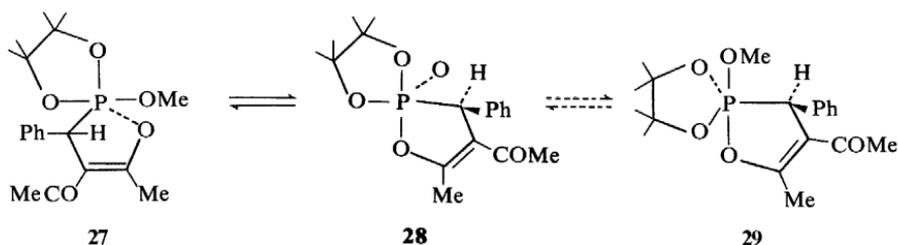
R^1	Me	Et	Pr ⁱ	Bu ⁱ	Ph	Bu ⁱ	Ph
R^2	Me	Et	Pr ⁱ	Bu ⁱ	Ph	Me	Me
ΔG^* (kcal mol ⁻¹)	10.0	10.9	12.9	14.6	12.6	11.1	10.2

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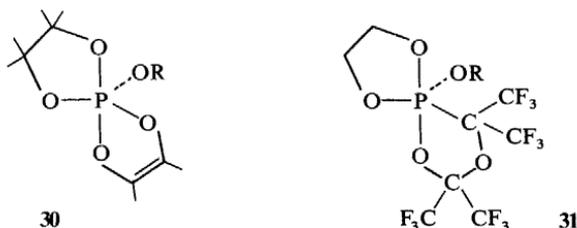
The steadily increasing barrier to pseudorotation as both R^1 and R^2 change from Me to Bu^t is probably due only in minor part to a change in the stereo-electronic component of apicophilicity, as shown by the low barrier in the case of the *t*-butylmethylphosphinite adduct, and is consistent with increasing relative steric compression at the apical position as the alkyl groups remaining equatorial increase in size.



Another form of steric hindrance to pseudorotation is found in small-ring phosphoranes when there are substituents on an α carbon in the ring. A classical example, noted by Gorenstein¹⁶, occurs in benzylideneacetylacetonate adducts **24**, where the barriers to pseudorotation are considerably higher than in the corresponding methyleneacetylacetonate adducts. Note that when the carbon of the oxaphospholen ring is apical, as in **25**, there is complete eclipsing of the type shown in **26**, of the substituents on that carbon and two equatorial substituents. Even in these adducts, however, the effect of the nature of the atom that remains equatorial when a ring takes up a diequatorial position is clearly shown. Thus in the spirophosphorane **28** the barrier to placing the oxaphospholen ring diequatorial as in **27** is 17.6 kcal mol⁻¹, while the pseudorotation of **28** \rightleftharpoons **29** is slow on the n.m.r. time-scale at 170°, i.e. $\Delta G^* > 23$ kcal mol⁻¹ 10,17.

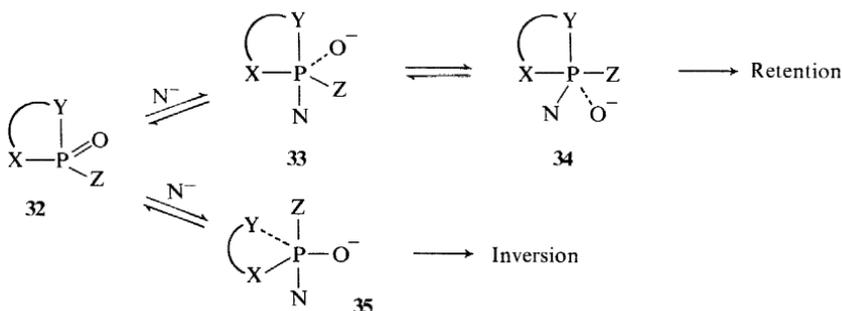


Such steric effects seem to be able to reverse small differences in apicophilicity. Thus, in general, and in, for example, the spirophosphoranes **30**, methoxy is more apicophilic than *t*-butoxy¹⁰. However, in adducts analogous to **28**, and in the 1,3,4-dioxaphospholans **31**, the reverse is the case¹⁰.

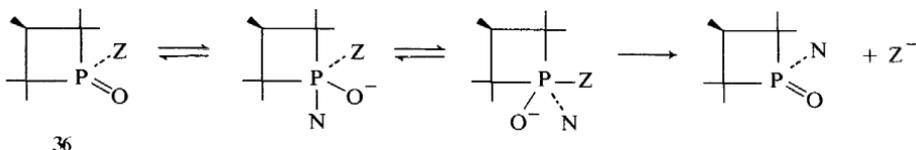


APPLICATIONS

We find the accumulated data on relative apicophilicities and strain factors of considerable help in thinking about reactions at phosphorus, particularly when this atom is part of a ring. In general, nucleophilic substitution at a cyclic phosphoryl centre **32** can proceed via **33** and **34** with retention of configuration at phosphorus or via **35** with inversion. The probable course can be assessed by comparing the energy of **35** with that of



33 or **34**, whichever is the higher. The large energy required to place a five-membered heteroring diequatorial dictates that substitutions in these compounds will involve retention at phosphorus, but in similar six-membered rings the two competing paths could be more evenly balanced. As the apicophilicity of the nucleophile increases, there is obviously the possibility that **34** will be of higher energy than **33**, and a greater probability that the reaction will proceed with inversion at phosphorus.



Phosphetane chemistry is particularly simple in these terms. The 17–18 kcal mol⁻¹ required to place the four-membered ring diequatorial⁵ is too large to be overcome by apicophilicity factors, and substitutions in **36** must involve retention at phosphorus as shown¹⁸.

However, such simple considerations do not always lead to predictions consistent with experiment. There are many unanswered questions in a field in which little is known with certainty and almost all is conjecture.

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