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Experimental Determination of the $n_N \rightarrow \sigma^*_{P-O}$ Interaction Energy of O-Equatorial C-Apical Phosphoranes Bearing a Primary Amino Group

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The reaction of a chlorophosphorane (**9-Cl**) with primary amines produced anti-apicophilic spirophosphoranes (**5**, O-equatorial phosphoranes), which violate the apicophilicity concept, having an apical carbon-equatorial oxygen configuration, along with the ordinarily expected O-apical stereoisomers (**6**) with the apical oxygen-equatorial carbon configuration. Although the amino group is electronegative in nature, the O-equatorial phosphoranes were found to be stable at room temperature and could still be converted to their more stable O-apical pseudorotamers (**6**) when they were heated in solution. X-ray analysis implied that this remarkable stability of the O-equatorial isomers could be attributed to the orbital interaction between the lone-pair electrons of the nitrogen atom (n_N) and the antibonding σ^*_{P-O} orbital in the equatorial plane. A kinetic study of the isomerization of **5** to **6** and that between diastereomeric O-apical phosphoranes **13b-exo** and **13b-endo** revealed that **5b** bearing an *n*-propylamino substituent at the central phosphorus atom was found to be less stable than the corresponding isomeric **6b** by ca. 7.5 kcal mol^{-1}. This value was smaller than the difference in energy (11.9 kcal mol^{-1}) between the O-equatorial (**1b**) and the O-apical *n*-butylphosphorane (**2b**) by 4.4 kcal mol^{-1}. This value of 4.4 kcal mol^{-1} can be regarded as the stabilization energy induced by the $n_N \rightarrow \sigma^*_{P-O}$ interaction. The experimentally determined value was in excellent agreement with that derived from density functional theory (DFT) calculations at the B3PW91 level (4.0 kcal mol^{-1}) between the nonsubstituted aminophosphoranes (**5g** is less stable than **6g** by 10.1 kcal mol^{-1}) and their P-methyl-substituted counterparts (**1a** is less stable than **2a** by 14.1 kcal mol^{-1}).

Introduction

Pentacoordinate organophosphorus compounds (phosphoranes) play important roles in biological systems in processes such as phosphoryl transfer,[1] as well as in synthetic chemistry in transformations such as the Wittig reaction.[2] To establish an understanding of the chemistry of phosphoranes, where there are two distinct types of bonds, "equatorial" and "apical" bonds, in the trigonal bipyramidal (TBP) structure,[3] the relationship between the structure of the isomers and the reactivity of each isomer must be clarified. However, these studies had previously been hampered by the fast stereomutation process (Berry pseudorotation (BPR))[4]

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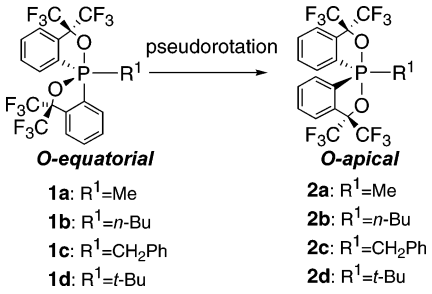
Scheme 1. Isolated O-equatorial Alkylphosphoranes and Their Isomerization



and the electronic preference for an electronegative substituent to occupy the apical position (apicophilicity).[5,6]

Recently, we reported the synthesis of spirophosphoranes with a monodentate alkyl substituent bearing an apical carbon-equatorial oxygen array (**1**, O-equatorial) using the Martin ligand via dehydrogenative cyclization of monocyclic P−H(apical) phosphoranes.[7a,c] Also, further investigations provided an improved synthetic method for O-equatorial phosphoranes (i.e., oxidative cyclization of dianionic phosphoranes by I_2).[7b,d] This represented the first examples of 10-P-5 phosphorane pseudorotamers which violate the apicophilicity concept and could still be converted to their more stable pseudorotamers with an apical oxygen-equatorial carbon configuration (**2**, O-apical) (Scheme 1).[8] This provided the first opportunity, of which we are aware, to investigate the difference in the reactivity and stability between isomeric phosphoranes differing only in stereochemistry upon the pentacoordinate phosphorus atom.

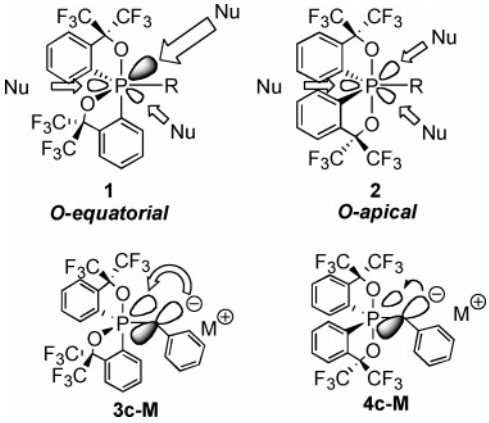


Figure 1. Enhanced electrophilicity of **1** and the increased stability of the carbanion (**3c**) based on the lower-lying σ^*_{P-O} orbital of the O-equatorial phosphorane in comparison with the corresponding higher-lying σ^*_{P-C} orbital of the O-apical phosphorane.

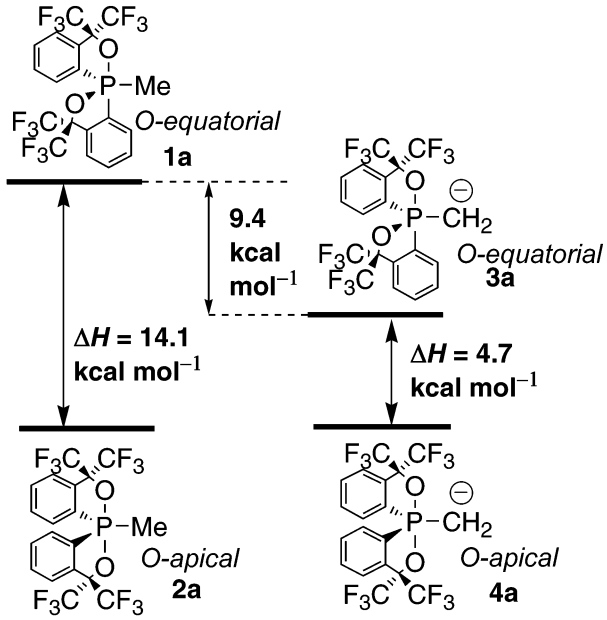


Figure 2. Calculated energy differences of **1a** and **2a** and their conjugate bases (**3a** and **4a**).

The novel spirophosphoranes (**1**, O-equatorial) showed significantly enhanced reactivity toward nucleophiles, such as *n*-$Bu_4N^+F^-$ (TBAF) and MeLi, in comparison with their O-apical counterparts (**2**). The enhanced reactivity of the

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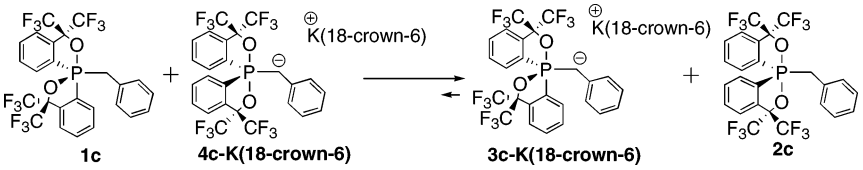
Scheme 2. Relative Stability of **3c−k (18-crown-6)** and **4c−k (18-crown-6)**



O-equatorial isomers could be explained by the presence of a low-lying σ^*_{P-O}(equatorial) orbital in the equatorial plane, whereas the corresponding orbital is a higher-lying σ^*_{P-C}(equatorial) orbital in the O-apical isomer (Figure 1). DFT calculations on the actual compounds provided theoretical support for this assumption.[9a] In addition, we found that the benzylic anion α to the phosphorus atom in the O-equatorial benzyl phosphorane is much more stable than that generated from the corresponding O-apical compound. These results could also be explained by the $n_C \rightarrow \sigma^*_{P-O}$ interaction in the O-equatorial anionic species (Figure 1). The stabilization energy by the $n_C \rightarrow \sigma^*_{P-O}$ interaction in the anion (**3a**) was estimated from the theoretically calculated energy difference between **1a** and **2a** (14.1 kcal mol^{-1}) and between **3a** and **4a** (4.7 kcal mol^{-1}) (Figure 2). The difference of 9.4 kcal mol^{-1} could be considered to be the stabilizing energy of the $n_C \rightarrow \sigma^*_{P-O}$ interaction in the anion (**3a**) with the assumption that the stabilization by the $n_C \rightarrow \sigma^*_{P-C}$ interaction in **4a** was negligible.[9a] The calculation was apparently supported by the equilibration reaction between **1c** and **4c**, which gave a mixture consisting only of **2c** and **3c**, implying some stability of **3c** (Scheme 2). A quantitative experimental evaluation of the stabilizing $n_C \rightarrow \sigma^*_{P-O}$ interaction energy was not possible because the anion (**3a**) could not be isolated and also because the above system shows the relative stability between the systems of **1c** and **4c** and **2c** and **3c**.

We now report the first isolation of O-equatorial spirophosphoranes bearing a monodentate primary amino substituent (**5**) (Figure 3), which were surprisingly stable, taking into account the fact that equatorial substituents more

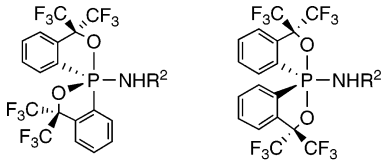


Figure 3. Isolated aminophosphoranes.

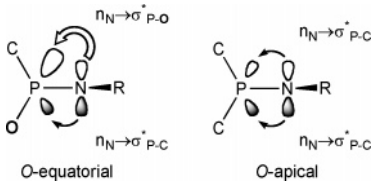
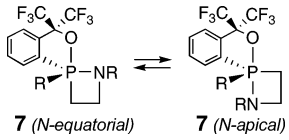


Figure 4. Schematic representation of the $n_N \rightarrow \sigma^*_{P-X}$ interaction.

Scheme 3. Reported Pseudorotamers of 1,2-Azaphosphetidines in Equilibrium



electronegative than carbon are ordinarily expected to facilitate pseudorotation and hamper the isolation of such phosphoranes. As with **1**, **5b−5e** could be isolated at room temperature, and they completely isomerized to their more stable O-apical pseudorotamers (**6**) when heated in solution. The main reason for this remarkable stabilization could be attributed to the favorable interaction between the σ^*_{P-O} orbital in the equatorial plane and the lone pair electrons of the nitrogen atom (n_N) (Figure 4). On the basis of the experimentally determined energy barrier for the isomerization of **5** to **6**, a quantitative evaluation of the $n_N \rightarrow \sigma^*_{P-O}$ interaction energy was possible for the first time, assuming that the $n_N \rightarrow \sigma^*_{P-C}$ interaction is negligible. The experimentally determined $n_N \rightarrow \sigma^*_{P-O}$ stabilizing interaction energy (ca. 4.4 kcal mol^{-1}) in **5** was highly consistent with a calculated value (R^2═H, 4.0 kcal mol^{-1}).

Although the $n_N \rightarrow \sigma^*_{P-O}$ stabilizing interaction has been proposed as a reason for the relatively low apicophilicity of the NMe_2 group, which has been found to be less apicophilic than the H or the OMe group,[5a,h,i] on the basis of kinetic analyses, and although the N-equatorial C-apical isomer (**7**) has been observed in an equilibrium mixture with the N-apical C-equatorial isomer for 1,2-azaphosphetidines (Scheme 3),[10] compounds suitable for the evaluation of the stabilizing $n_N \rightarrow \sigma^*_{P-O}$ interaction energy have not been discovered. This study has confirmed, on a quantitative basis, what has previously only been assumed, thus providing new experimental insight which may lead to a clearer detailed understanding of the biologically important pentacoordinate phosphorus compounds.

Results and Discussion

Synthesis. The aminophosphoranes **5** (O-equatorial) and **6** (O-apical) were obtained from the reaction of chlorophosphorane **9-Cl**, which was generated in-situ from the P−H spirophosphorane (**8**),[11] with the corresponding amine (Scheme 4): the bulkier the substituent of the primary amine (R^2),

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(11) Ross, M. R.; Martin, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 1234−1235.

Scheme 4. Synthesis of O-equatorial (**5**) and O-apical Phosphoranes (**6**)

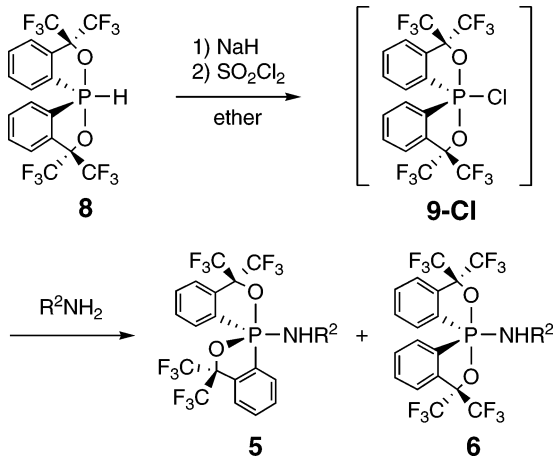


Table 1. Yields and Ratios of Aminophosphoranes

			ratio of isomer	^{31}P NMR ($CDCl_3$, δ)	
	R^2NH	yield (%)	**5**/**6**	**5**	**6**
a	MeNH	48	<2/>98		−31.4
b	*n*-PrNH	64	36/64	−28.2	−31.4
c	$PhCH_2NH$	56	62/38	−28.8	−31.3
d	*i*-PrNH	82	80/20	−29.6	−32.9
e	*t*-BuNH	92	>98/<2	−25.8	−26.5
f	PhNH	74	<2/ >98		−35.3

the higher the ratio of **5** (O-equatorial) (Table 1). However, the reaction of **9-Cl** with secondary amines (dimethylamine, diethylamine, or benzylmethylamine) exclusively gave the corresponding O-apical phosphoranes. In addition, neither methylamine nor aniline produced the corresponding O-equatorial isomer. Isomers **5** and **6** were easily separated by conventional chromatographic techniques in all cases. All isolated compounds were characterized by NMR and elemental analyses. A general trend in the ^{31}P NMR was that the chemical shifts of **5** were shifted downfield compared with those of the corresponding **6** isomers, showing a similarity with alkylphosphoranes, albeit to a smaller degree. Although the O-equatorial phosphoranes **5** were stable in solution at room temperature, they quantitatively converted into their corresponding **6** isomers upon heating in solution, indicating that the **5** phosphoranes are kinetic products, as in the case of O-equatorial alkylphosphoranes.[7a,9a]

Crystal Structure. The structures of **5c** and **5e** were unambiguously determined to be in the O-equatorial configuration by single-crystal X-ray analyses. Figure 5 shows the ORTEP drawings for **5c**, **5e**, and **6e** with the amino proton (H1) which could be located by differential Fourier synthesis. For the benzylamino derivative (**5c**), the geometry around the phosphorus atom is a slightly distorted trigonal bipyramid (TBP). As expected, the equatorial bond distances [P1—C1 = 1.824(2) Å, P1—O2 = 1.6645(15) Å] were shorter than the corresponding apical distances [P1—C10 = 1.857(2) Å, P1—O1 = 1.7381(16) Å]. The geometry of the nitrogen atom (N1) is almost planar, and the nitrogen plane is nearly perpendicular to the equatorial plane (O2—P1—N1—C19 = −94.4(2)°). This implies that the lone-pair electrons of the nitrogen atom are in an alignment favorable for interaction with the equatorial σ^*_{P-O} orbital at the phosphorus atom, and this interaction could contribute to the unusual stability of the O-equatorial phosphoranes **5** (vide infra). The structure of **5e** was crystallographically determined to be basically similar to that of **5c**. However, in the case of **5e**, the steric bulkiness of the *tert*-butyl group was shown to affect the bond angles around the phosphorus and the nitrogen atoms as shown in Figures 6 and 7. The C1—P1—N1 and P1—N1—C19 bond angles of **5e** are greater than those of **5c** by ca. 8° and 7°, respectively, whereas O2—P1—N1 is smaller by 4° (Figure 6), and the *tert*-butyl group of **5e** is somewhat tilted toward the equatorial oxygen (O2) to avoid steric repulsion (dihedral angle = O2—P1—N1—C19 = −76.7-(4)°) (Figure 7), indicating that the structural strain around the phosphorus atom of **5e** is greater than that of **5c**. These structural factors would make the $n_N \rightarrow \sigma^*_{P-O}$ interaction of **5e** less efficient than the other O-equatorial aminophosphoranes, such as **5c**, and thus affect the relative stability of **5e**. This turned out to be true as discussed in a kinetic study (vide infra). For the O-apical phosphorane **6e**, on the other hand, the geometry around the phosphorus atom is nearly an ideal TBP (Figure 5) and is very similar to that of a previously reported dimethylaminophosphorane.[5a]

Possible Mechanism for the Formation of O-Equatorial Aminophosphoranes. The ratio of the stereoisomers (**5** and **6**) in the preparation was highly dependent on the bulkiness of the amine, as already described (Table 1). In addition, we examined the fluoro-, bromo-, and iodophosphoranes as the reacting intermediate and found that the product ratio was also affected by the halogen atom of the intermediate **9-X** (Scheme 5). When the fluorophosphorane (**9-F**) was treated with isopropylamine, the highest [**5d**]/[**6d**] ratio of 91/9 was obtained (Table 2). These stereochemical results can be rationalized with the mechanism shown in Scheme 6. Since it is reasonable to assume that the attack of nucleophiles occurs within the equatorial plane, an amine can attack the phosphorus atom in two ways: one is anti to the halogen (rear attack, **Atk-a**) and the other is syn to the halogen atom (front attack, **Atk-b**). Rear attack (**Atk-a**) is the electronically preferred route,[12] since the nucleophile would be in line with the electronegative halogen atom and the halogen atom can readily be released from the hexacoordinate intermediate (**Int-a**) to give the O-apical phosphorane (**6**). As for front-side attack, the reaction would inevitably be anti to a carbon atom, and since carbon cannot function as a leaving group in the present reaction, the initially formed hexacoordinate intermediate, **Int-b1**, is expected to be relatively long-lived. This would allow the highly electronegative oxygen atom of the Martin ligand to become the nucleofuge and give intermediate **Int-b2**. Intermediate **Int-b2** would isomerize to its more stable stereoisomer **Int-b3** by a one step pseudorotation. Attack of the oxide anion in **Int-b3** then occurs probably syn to the halogen atom residing in the equatorial

(12) Kojima, S.; Nakamoto, M.; Yamazaki, K.; Akiba, K.-y. *Tetrahedron Lett.* **1997**, *38*, 4107−4110. In this communication, a stereochemical study in the nucleophilic substitution reaction toward sterically rigid phosphoranes was reported, in which it was found that nucleophilic attack predominantly occurs anti to the electronegative substituent.

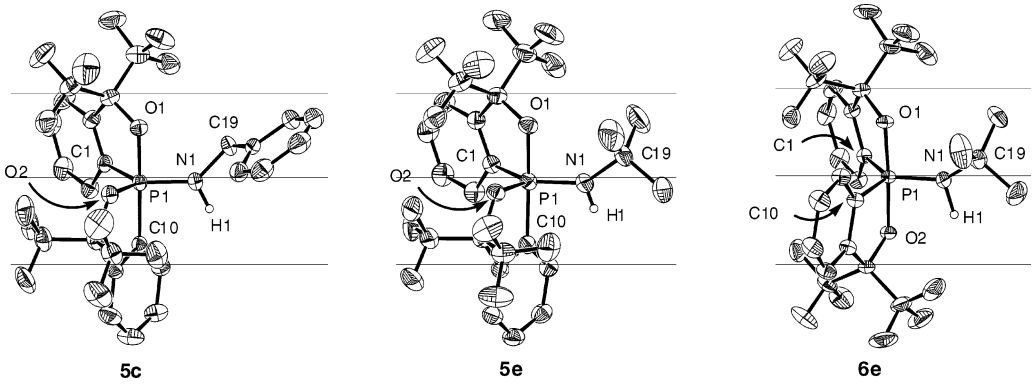


Figure 5. ORTEP drawings for **5c**, **5e**, and **6e** showing the thermal ellipsoids at the 30% probability level. The hydrogen atoms other than H1 are omitted for clarity. Selected bond distances (Å): **5c** (R^2 = CH_2Ph) P1—O1 = 1.7381(16), P1—O2 = 1.6645(15), P1—C1 = 1.824(2), P1—C10 = 1.857(2), P1—N1 = 1.6394(19); **5e** (R^2 = *t*-Bu) P1—O1 = 1.729(2), P1—O2 = 1.6653(19), P1—C1 = 1.839(3), P1—C10 = 1.871(3), P1—N1 = 1.641(3); **6e** (R^2 = *t*-Bu) P1—O1 = 1.7694(19), P1—O2 = 1.7378(19), P1—C1 = 1.825(3), P1—C10 = 1.821(3), P1—N1 = 1.648(3). Selected bond angles (deg): **5c** (R^2 = CH_2Ph) O1—P1—O2 = 85.09(7), O1—P1—C1 = 87.46(9), O1—P1—C10 = 172.89(9), O1—P1—N1 = 89.83(9), O2—P1—C1 = 113.02(9), O2—P1—C10 = 88.39(9), O2—P1—N1 = 122.11(9), C1—P1—C10 = 97.72(10), C1—P1—N1 = 124.33(10), C10—P1—N1 = 91.24(10), P1—N1—C19 = 133.60(18); **5e** (R^2 = *t*-Bu) O1—P1—O2 = 87.67(10), O1—P1—C1 = 87.10(11), O1—P1—C10 = 176.28(11), O1—P1—N1 = 90.32(13), O2—P1—C1 = 109.40(11), O2—P1—C10 = 88.71(10), O2—P1—N1 = 118.36(12), C1—P1—C10 = 94.93(12), C1—P1—N1 = 132.01(13), C10—P1—N1 = 90.63(13), P1—N1—C19 = 140.6(3); **6e** (R^2 = *t*-Bu) O1—P1—O2 = 175.74(10), O1—P1—C1 = 87.23(11), O1—P1—C10 = 88.57(11), O1—P1—N1 = 89.07(11), O2—P1—C1 = 93.19(11), O2—P1—C10 = 87.69(11), O2—P1—N1 = 94.54(12), C1—P1—C10 = 124.29(13), C1—P1—N1 = 116.26(15), C10—P1—N1 = 119.18(14), P1—N1—C19 = 136.3(3). Selected dihedral angles (deg): **5c** (R^2 = CH_2Ph) O1—P1—N1—C19 = −10.3(2), O2—P1—N1—C19 = −94.4(2), C1—P1—N1—C19 = 76.5(2), C10—P1—N1—C19 = 176.7(2); **5e** (R^2 = *t*-Bu) O1—P1—N1—C19 = 10.8(4), O2—P1—N1—C19 = −76.7(4), C1—P1—N1—C19 = 97.2(4), C10—P1—N1—C19 = −165.6(4); **6e** (R^2 = *t*-Bu) O1—P1—N1—C19 = −153.3(4), O2—P1—N1—C19 = 28.9(4), C1—P1—N1—C19 = −66.9(4), C10—P1—N1—C19 = 118.8(4).

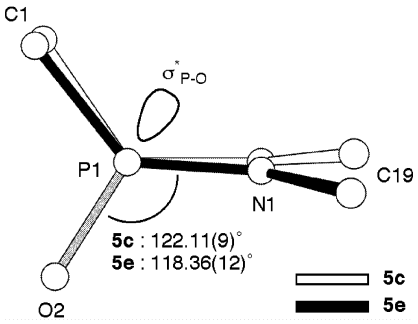


Figure 6. Top views of **5c** and **5e**.

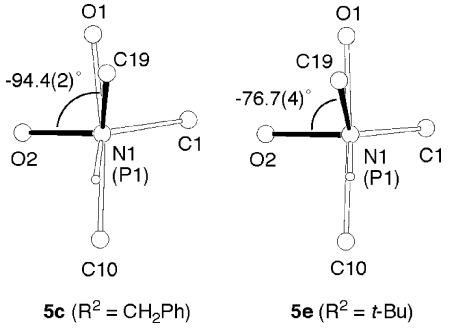
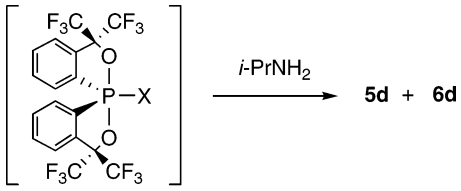


Figure 7. Front views of **5c** and **5e**.

plane, where it is less congested, to produce the O-equatorial phosphorane (**5**). This mechanism is in good agreement with the fact that bulkier amine nucleophiles (when the halogen is fixed) and smaller halogens (when the amine is fixed) result in higher ratios of **5**, which are products of front attack. This mechanism is quite similar to what we have proposed for the formation of O-equatorial alkylphosphoranes (**1**).[7b] Dissociative pathways for the formation of O-equatorial aminophosphoranes are highly unlikely because of the instability of the phosphonium cation bearing two Martin ligands.[13]

Scheme 5. Reaction of Halophosphoranes with Isopropylamine



9-X

X = F, Cl, Br or I

Table 2. Effect of Halogen Atom in **9-X** on the Product (**5d** and **6d**) Ratio

X	yield (%)	**5d**/**6d**	^{31}P NMR (ether, δ)
F	81	91/9	−3.0 ($^1J_{P-F}$ = 977 Hz)
Cl	82	80/20	−7.6
Br	73	34/66	−30.6
I	55	11/89	−21.8

O-Equatorial phosphoranes were not observed in the reaction of **9-Cl** with the secondary amines. The X-ray structures of **5c** and **5e** suggest the reason. The alkyl substituent on the nitrogen atom is directed toward the apical oxygen (O1) of the Martin ligand (Figure 5). This is an indication that the lower (apical-carbon, C10) side of the O-equatorial phosphorane is sterically hindered by the ortho hydrogen atom of the Martin ligand bearing the apical carbon atom. In addition, the P1—N1—C19 bond angles for **5c** (133.6°) and **5e** (140.6°) are much larger than that for an ordinary planar nitrogen atom (120°), implying that bond angles involving the hydrogen atom on the lower side of the nitrogen

(13) Granoth, I.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 4618−4622.

Scheme 6. Possible Mechanism for the Formation of the O-equatorial Aminophosphorane (**5**)

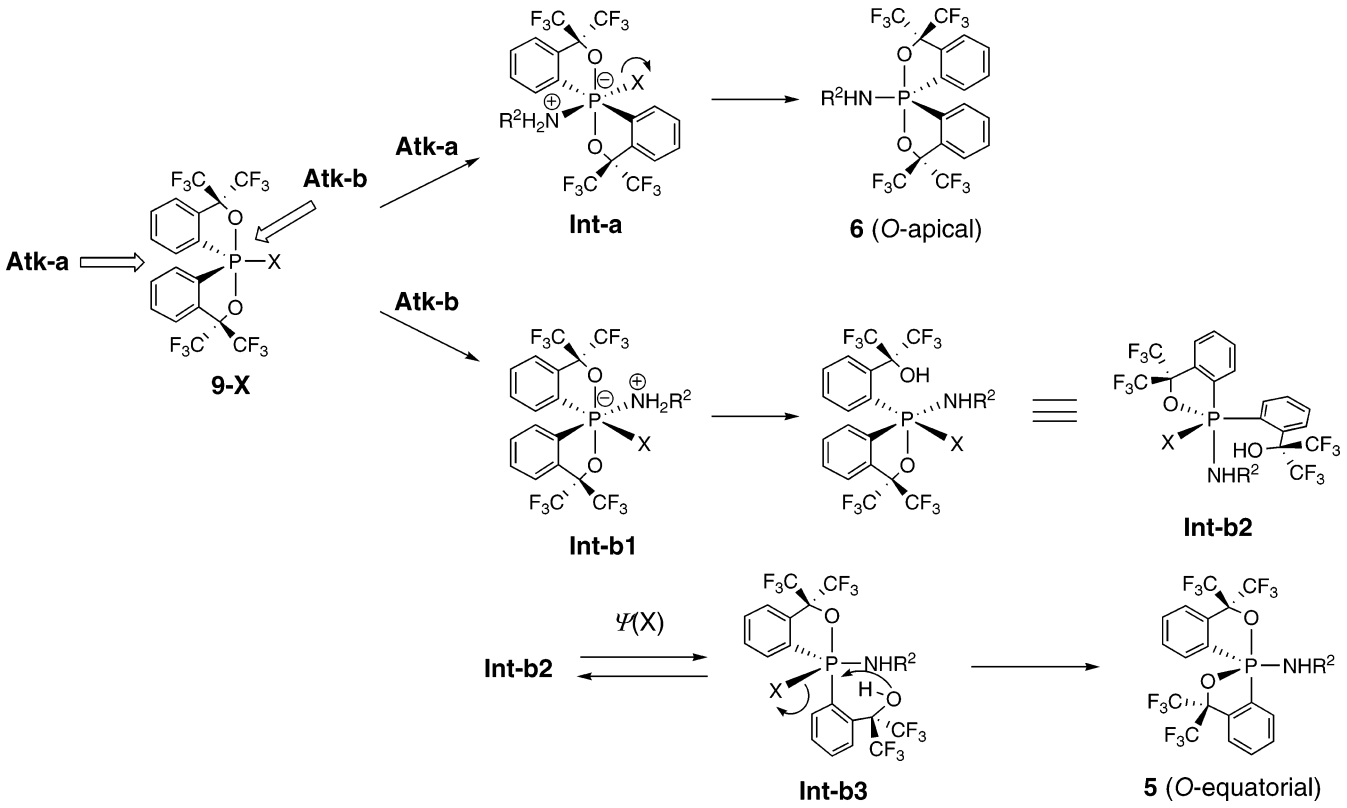
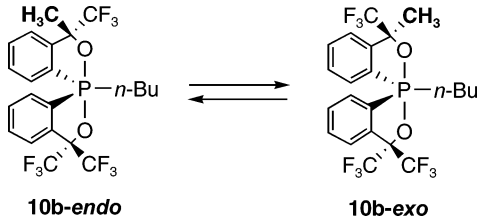


Table 3. Activation Parameters for Pseudorotation of **5** to **6** and **1** to **2**

	substituent on P	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)	$\Delta G^{\ddagger}_{298}$ (kcal mol^{-1})	ref
5b → **6b**	*n*-PrNH	24.4 ± 0.4	−6.8 ± 1.2	26.4	this work
5c → **6c**	$PhCH_2NH$	23.7 ± 0.6	−7.8 ± 1.8	26.0	this work
5d → **6d**	*i*-PrNH	23.4 ± 0.9	−13.4 ± 2.6	27.4	this work
5e → **6e**	*t*-BuNH	22.1 ± 0.7	−12.3 ± 1.9	25.8	this work
1a → **2a**	Me	19.3 ± 0.4	−10.8 ± 1.5	22.5	this work
1b → **2b**	*n*-Bu	21.8 ± 0.4	−9.0 ± 1.2	24.5	7a, 7c
1d → **2d**	*t*-Bu	27.2 ± 0.8	−13.1 ± 1.8	31.1	7c

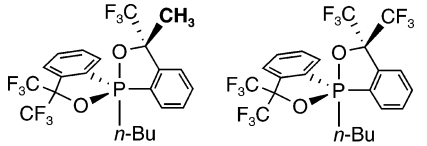
Scheme 7. Isomerization between Diastereomeric *n*-Butylphosphoranes (**10b**)



atom are rather acute, an environment unsuitable for substituents larger than hydrogen. Therefore, even if the O-equatorial phosphorane with a secondary amino group were to form, it would be quite unstable because it would be difficult for the amino plane to remain parallel with the apical axis because of the steric repulsion and, thus, the stabilization by $n_N \rightarrow \sigma^*_{P-O}$ interaction would be insufficient.

Kinetic Study. Kinetic measurements of the irreversible isomerization of **5** to **6** were performed in *p*-xylene as the solvent. The isomerization process followed first-order kinetics, and the Eyring plots of the rates showed high correlations. Activation parameters were calculated from these plots (see Supporting Information). The activation entropy values ($\Delta S^{\ddagger}$) were typical for the Berry pseudorotation process (Table 3), suggesting that the mechanism does not include a bond-dissociation process. Since the activation energy of pseudorotation in bicyclic systems are dependent on the apicophilicity of the monodentate ligand, it is reasonable that, for the alkyl series (Table 3), the sterically bulky and less apicophilic *t*-Bu has a much larger barrier than the other alkylphosphoranes.[7c] However, the activation enthalpies ($\Delta H^{\ddagger}$) for **5b**−**5e** were only slightly dependent on the steric bulkiness of the monodentate ligand, and moreover, it is noteworthy that the $\Delta H^{\ddagger}$ value for **5e** (*t*-BuNH, $\Delta H^{\ddagger} = 22.1 \pm 0.7$ kcal mol^{-1}), which has the bulkiest substituent on the nitrogen atom, was somewhat smaller than that for the other aminophosphoranes ($\Delta H^{\ddagger} = 23.4-24.4$ kcal mol^{-1}). Since the $n_N \rightarrow \sigma^*_{P-O}$ interaction can be assumed to be less efficient in **5e** as already discussed, it could be that the activation energy for the isomerization of **5** is highly dependent on the degree of stabilization by the $n_N \rightarrow \sigma^*_{P-O}$ interaction.

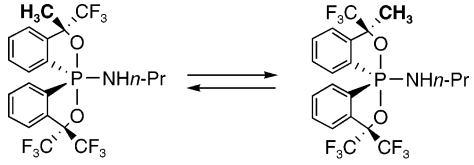
On the basis of the reasonable assumption that the pseudorotation of O-equatorial isomer **1b** to O-apical phosphorane **2b** and that between enantiomers of **2b** involve common processes and thus the same transition state, we previously estimated the O-apical phosphorane **2b** to be more stable than the O-equatorial isomer **1b** by ca. 12 kcal mol^{-1} by the activation parameters deduced from kinetic measurements on the interconversion process between the diastereomeric derivatives **10b-endo** and **10b-exo** (Scheme 7).[7a,c] That is,



11 **12**

Figure 8. Possible highest-energy structures in the isomerization.

Scheme 8. Isomerization of Diastereomeric *n*-Propylaminophosphoranes (**13b**)



13b-*endo* **13b-*exo***

the $\Delta H^{\ddagger}$ value of the isomerization between **10b-endo** and **10b-exo** was measured to be ca. 33.7 kcal mol^{-1} (from endo to exo = 33.5 ± 0.9 kcal mol^{-1}; from exo to endo = 33.8 ± 0.9 kcal mol^{-1}), and the $\Delta H^{\ddagger}$ of the isomerization of **1b** to **2b** was 21.8 kcal mol^{-1} (Table 3), giving a value of 12 (33.7 − 21.8) kcal mol^{-1}. Since species **11** and **12** (Figure 8), which can be regarded as the highest-energy structures (because of the severe ring strain in the equatorial bidentate) on their respective multistep pseudorotation processes, are expected to be very similar in energy, this rationalization should be valid.

An analogous analysis would give the energy difference between **5** and **6**, and a comparison of this difference with that between **1b** and **2b** would provide a value for the $n_N \rightarrow \sigma^*_{P-O}$ stabilizing interaction energy in **5**, since such an interaction is absent in **1b**. The *n*-propylamino derivatives (**5b** and **6b**) were chosen for the kinetic measurements because the steric bulkiness of these compounds is similar to that of the *n*-Bu derivatives (**1b** and **2b**).

Because the epimerization barrier for **6b** was too high for the coalescence method in NMR, the diastereomers **13b-endo** and **13b-exo** (Scheme 8), bearing a methyl group in the place of one of the trifluoromethyl groups, were chosen for the kinetic examination, as in the case of the *n*-butylphosphorane examination, and they were synthesized from a mixture of diastereomeric P−H phosphoranes according to a previously described procedure.[5a,7c] In this case, however, the O-equatorial isomers were not observed (see page S12 in Supporting Information). Although complete separation of the diastereomers was unsuccessful by chromatography, a **13b-endo**-enriched mixture (**endo**/**exo** = 10:1) could be obtained by repeated recrystallization, and this sample was used for the kinetic measurements. The relative stereochemistry of these diastereomers was determined by ^{1}H NMR NOE experiments. The interconversion of the isomers of **13b** followed reversible first-order kinetics. The activation parameters are shown in Table 4. The averaged activation enthalpy for the stereomutation between **13b-endo** and **13b-exo** was 31.9 ± 0.4 kcal mol^{-1}. This value is consistent with that for the dimethylaminophosphorane (average of 32.1 ± 0.6 kcal mol^{-1}), which has already been reported by us.[5a]

Table 4. Activation Parameters for Stereomutation between **13b-endo** and **13b-exo**

	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)	$\Delta G^{\ddagger}_{298}$ (kcal mol^{-1})
13b-endo → 13b-exo	32.0 ± 0.4	−6.8 ± 0.9	32.5
13b-exo → 13b-endo	31.9 ± 0.4	−7.5 ± 0.8	32.4

Quantitative Evaluation of the $n_N \rightarrow \sigma^*_{P-O}$ Interaction. With the activation enthalpy ($\Delta H^{\ddagger}$) for the isomerization of **5b** to **6b** and that between **13b-endo** and **13b-exo** in hand, an energy diagram of pseudorotation of the O-equatorial isomer to the O-apical isomer for the *n*-propylaminophosphorane could be formulated and compared with that for the *n*-butylphosphorane (Scheme 9). Although the $\Delta H^{\ddagger}$ value for the isomerization between isomers of **13b** (31.9 ± 0.4 kcal mol^{-1}) was slightly smaller than that between isomers of *n*-butylphosphorane (**10b**) (33.7 ± 0.9 kcal mol^{-1}) by 1.8 kcal mol^{-1}, the $\Delta H^{\ddagger}$ value for **5b** → **6b** (24.4 ± 0.4 kcal mol^{-1}) was clearly larger than that for the *n*-butylphosphorane (**1b** → **2b**) (21.8 ± 0.4 kcal mol^{-1}) by 2.6 kcal mol^{-1}. Thus, the energy difference between **5b** and **6b** (ΔE_1) can be considered to be ca. 7.5 (31.9 − 24.4) kcal mol^{-1}, which is smaller than that between **1b** and **2b** (ΔE_2) (ca. 11.9 kcal mol^{-1}) by 4.4 kcal mol^{-1} ($\Delta E_2 - \Delta E_1$). This difference can be rationalized as being the result of the stabilization of **5b** by the $n_N \rightarrow \sigma^*_{P-O}$ interaction, which is not available in **1b**. Since the σ^*_{P-O} orbital has been calculated to be lower-lying than the σ^*_{P-C} orbital in **1a** by 18.7 kcal mol^{-1},[9a] the stabilizing effect of the σ^*_{P-C} orbital can be considered to be negligible. There could be error in the calculated values because the monomethyl-substituted compounds (**10b** and **13b**) were used in place of the tetra-trifluoromethyl-substituted compounds (**2b** and **6b**) for some kinetic examinations. However, since we are doing a subtraction here, this effect should cancel out, and the elucidated value of 4.4 kcal mol^{-1} for the $n_N \rightarrow \sigma^*_{P-O}$ interaction in the equatorial plane should be reasonable.

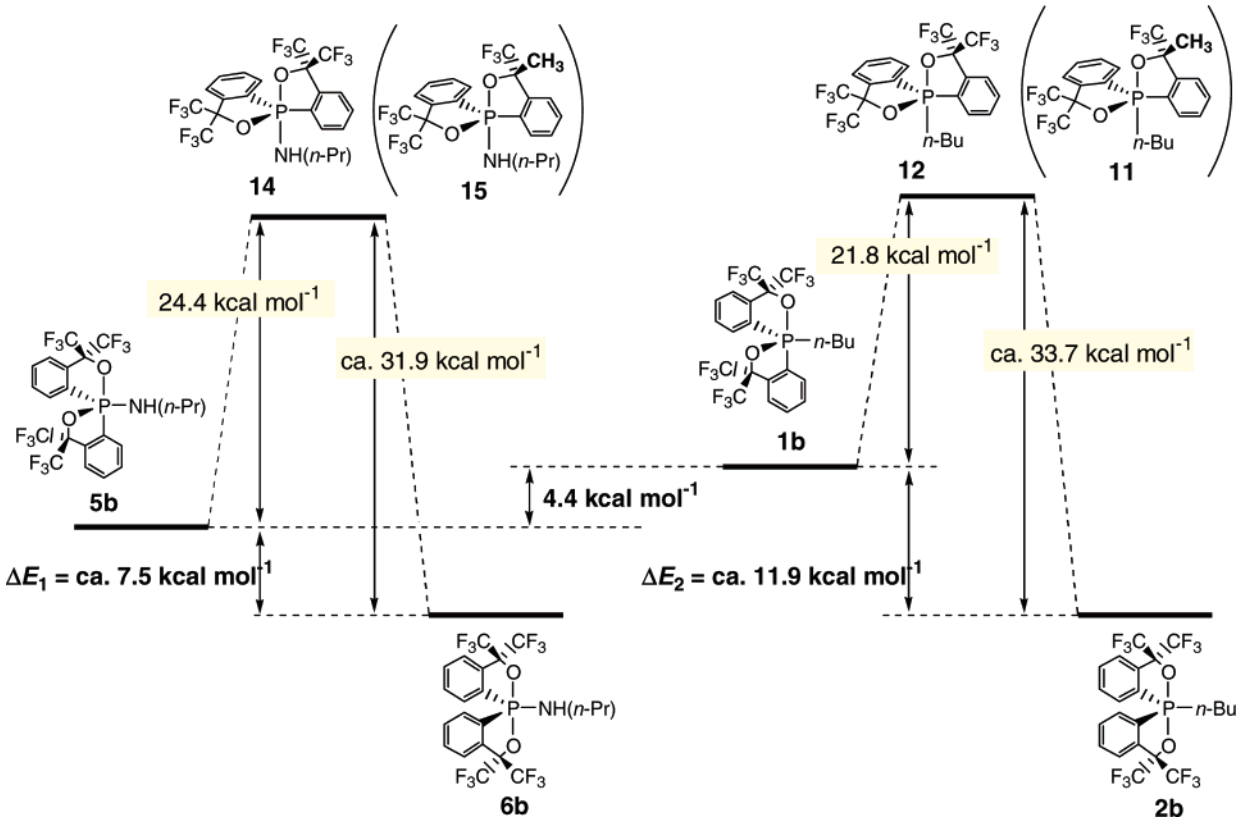
Theoretical Estimation of the $n_N \rightarrow \sigma^*_{P-O}$ Interaction for the O-Equatorial Phosphorane. The structures of the model compounds (**5g** and **6g**), which have an amino (−NH_2) group as a monodentate ligand, were optimized with density functional theory (DFT) calculations at the hybrid B3PW91 level[14] using the Gaussian98 program.[15] The basis sets employed were 6-31G(d)[16] for C, H, N, O, and F, and

(14) (a) Becke, A. D. *Phys. Rev.* **1988**, *A38*, 3098−3100. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Perdew, J. P.; Wang, Y. *Phys. Rev.* **1992**, *B45*, 13244−13249.

(15) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.5; Gaussian, Inc.: Pittsburgh, PA, 1998.

(16) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654−3665.

Scheme 9. Energy Diagrams of Pseudorotation of the O-equatorial Isomer to the O-apical Isomer for *n*-Propylaminophosphorane (left) and *n*-Butylphosphorane (right) from Kinetic Measurements



6-311G(2d)[17] for P. The calculated bond lengths around the phosphorus atom are in good agreement with those obtained from X-ray analysis (Table 5 in Supporting Information). Before the calculations on the aminophosphoranes, we checked the reliability of the calculation method by applying it to **1a** (the energy difference between **1a** and **2a** was calculated to be 14.1 kcal mol^{-1}).[9a] This was quite consistent with the experimental value of ca. 14.2 kcal mol^{-1} derived from kinetic measurements.[18] Aminophosphorane **5g** was calculated to be less stable than **6g** by 10.1 kcal mol^{-1}. Thus, the energy difference between **5g** and **6g** is smaller than that between the methylphosphorane isomers **1a** and **2a** (14.1 kcal mol^{-1}) by 4.0 kcal mol^{-1}. This is in excellent agreement with the experimentally derived value of 4.4 kcal mol^{-1} for **5b**, as already described.

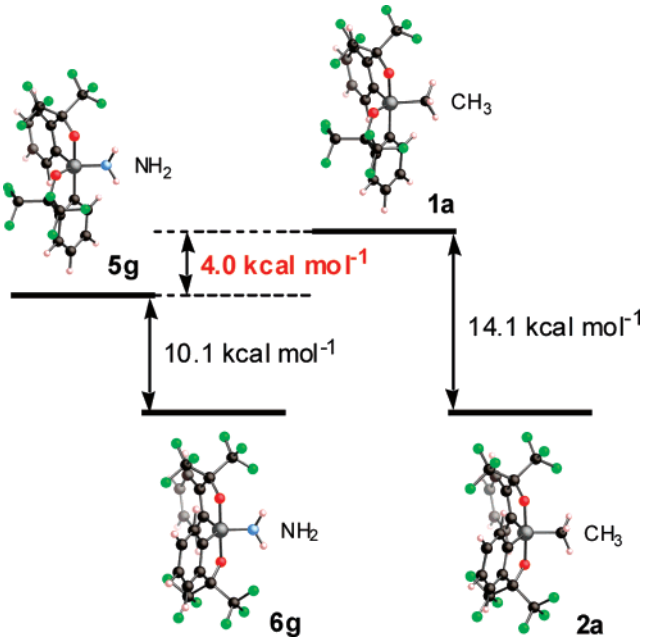


Figure 9. Calculated energies for amino- (**5g** and **6g**) and methylphosphoranes (**1a** and **2a**).

Conclusion

In summary, we have described the isolation, structural analysis, and kinetic investigations of the O-equatorial thermodynamically unstable spirophosphoranes (**5**) bearing a primary amino group. The X-ray analysis revealed that the nitrogen plane was located nearly parallel to the apical axis, suggesting that the stabilizing $n_N \rightarrow \sigma^*_{P-O}$ interaction in the equatorial plane was the primary reason for the unusual stability of **5**. Kinetic and theoretical studies provided support for this rationalization, and the $n_N \rightarrow \sigma^*_{P-O}$ interaction energy was quantitatively estimated to be ca. 4 kcal mol^{-1}. This shows a very general example of stereoelectronic effects in

(17) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639−5648.

(18) $\Delta H^{\ddagger}$ for the stereomutation of **1a** to **2a** was measured to be 19.3 kcal mol^{-1} (Table 4), and that between **10a-endo** and **10a-exo** was ca. 33.5 kcal mol^{-1} (see ref 5a). Therefore, **2a** is estimated to be more stable than **1a** by ca. 14.2 kcal mol^{-1} (33.5−19.3).

phosphoranes and should be helpful for rationalization of the stereochemistry of the reactions of the biologically important pentacoordinate phosphorus compounds.

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Supporting Information Available: Table 5, experimental methods, and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

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