X-ray and ^1H NMR Studies of the Conformational Equilibria of 2-Z-3-Phenyl-1,3,2-oxazaphosphorinanes. Steric and Stereoelectronic Influences on the Unexpected Axial Preferences of Me_2N and MeNH Substituents on Three-Coordinate Phosphorus

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Received July 20, 1993®

A series of 2-Z-3-phenyl-1,3,2-oxazaphosphorinanes **7–14** (Z = MeO, $(CF_3)_2CHO$, Ph, MeNH, and Me_2N) containing three-coordinate phosphorus was prepared. The conformations of the six-membered rings were investigated by ^1H and ^{31}P NMR spectroscopy and X-ray crystallography. The rings with substituents MeO, $(CF_3)_2CHO$, Ph, and MeNH on phosphorus can be unambiguously assigned in solution to a single chair conformation with the substituent of phosphorus axial. An X-ray crystal structure of 5,5-dimethyl-2,3-diphenyl-1,3,2-oxazaphosphorinane, **11**, reveals a chair form ring with the phenyl group attached axially to phosphorus. For **13** and **14** with a Me_2N substituent on phosphorus, a chair–chair equilibrium (**20** ⇄ **21**) is found in solution that features an 80–90% population (ΔG° = 0.9–1.1 kcal/mol) of the Me_2N axial conformation (**20**). This finding contrasts sharply with the known 1 kcal/mol preference for the Me_2N to be equatorial in the corresponding 2-(dimethylamino)-1,3,2-dioxaphosphorinanes. The ability of the 1,3,2-oxazaphosphorinane ring to accommodate the Me_2N substituent axially is also seen in the X-ray crystal of 5,5-dimethyl-3-phenyl-2-(dimethylamino)-1,3,2-oxazaphosphorinane, **13**, which features a chair conformation ring that is considerably distorted compared to that of **11**, quite evidently to allow the Me_2N to be in the observed axial orientation, conformation **20**. It is argued that the axial orientation of the Me_2N in **13** and **14** is at least partly in response to steric repulsions in the alternative chair conformation **21** between the *equatorial* Me_2N and the phenyl substituent at N(3). This effect is *in direct contrast* to the repulsive interactions between the N(3)Ph and *axial* Me_2N on phosphorus previously demonstrated for *four-coordinate*, 2-oxo-1,3,2-oxazaphosphorinanes. The increased bond lengths within the 1,3,2-oxazaphosphorinane ring over its 1,3,2-dioxaphosphorinane counterpart (C–N vs C–O) and increased ring flexibility, along with potential $n \rightarrow \sigma^*$ stereoelectronic factors of the type operative in the anomeric effect, are also proposed as potential contributors to the preferred axial orientation of Me_2N in **13** and **14**. The diastereomeric molecules *cis*- and *trans*-5-*tert*-butyl-3-phenyl-2-(dimethylamino)-1,3,2-oxazaphosphorinane, **17**, also were prepared. At thermodynamic equilibrium at room temperature, *cis*-**17** (2-Me_2N and 5-*t*-Bu groups cis) is favored (cis/trans = 80/20). *cis*-**17** displays a conformational equilibrium (Scheme 1) involving a chair conformer (≈60%) with the *t*-Bu equatorial and Me_2N axial, *cis*-**17a**, and a single twist or boat form with both substituents pseudoequatorial, *cis*-**17d** (≈40%). *trans*-**17** exists in solution in three conformations in approximately equal populations: a chair form with both *t*-Bu and Me_2N equatorial (*trans*-**17a**) and two boat/twist forms (*trans*-**17b** and *trans*-**17c**) with the *t*-Bu pseudoequatorial and the Me_2N pseudoaxial. The distributions of chair and boat/twist conformations can be reasonably understood in terms of the same 1,3-*syn* axial and vicinal PhN(3)/Me_2N(eq) steric repulsions invoked to explain the chair–chair equilibria noted for the unsubstituted and 5,5-dimethyl-2-(dimethylamino)-3-phenyl-1,3,2-oxazaphosphorinanes **13** and **14**. The free energy difference between chair and boat/twist forms evidently is very small.

Introduction

The conformational properties of heterocyclic six-membered rings containing O, N, S, and P atoms have been the subject of considerable study.[1] Most thoroughly investigated have been the conformations of both three- and four-coordinate 1,3,2-dioxaphosphorinanes. Substituents on three-coordinate phosphorus show a preference for the axial position in the order ArO > RO > Ph > Me > *i*-Pr. The dimethylamino group and the sterically large *t*-Bu prefer the equatorial orientation.[1] MeNH displays an intermediate, more nearly neutral, axial–equatorial preference.[1]

The conformations of four-coordinate 2-oxo-1,3,2-oxazaphosphorinanes, which include the important antitumor drugs cyclophosphamide, **1**, and its congeners trofosphamide, **2**, and isofosphamide, **3**, also have been examined.[2] The nature of the substituent on N(3) has been found to be of great importance in determining the orientations of more bulky groups such as Me_2N on phosphorus. A major effect of ring heteroatoms is the lowering of the free energy differences between chair and twist conformations as is observed for both 1,3,2-dioxa- and 1,3,2-oxazaphosphorinanes.[3] Thus, the conformational energies of six-membered rings containing heteroatoms are strongly influenced by steric interactions and by stereoelectronic effects.[2]

Surprisingly, the conformations of three-coordinate 1,3,2-oxazaphosphorinanes have received little attention. Although a series of such compounds was prepared by Nifant'ev et al.,[4] a detailed conformational analysis was

® Abstract published in *Advance ACS Abstracts*, October 1, 1993.

(1) Reviews may be found in: (a) Bentrude, W. G.; Setzer, W. N. In *Phosphorus-31 Spectroscopy in Stereochemical Analysis;* Verkade, G., Quin, L.D., Eds.; VCH Publishers: Deerfield Beach, FL, 1987; pp 365–389. (b) Maryanoff, B. E.; Hutchins, R. O.; Maryanoff, C. A. *Top. Stereochem.* **1979**, *11*, 187–317.

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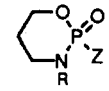
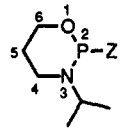


1 R = H, Z = $N(CH_2CH_2Cl)_2$
2 R = CH_2CH_2Cl, Z = $N(CH_2CH_2Cl)_2$
3 R = CH_2CH_2Cl, Z = $NHCH_2CH_2Cl$

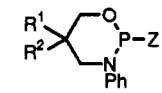
not attempted. However, on the basis of ^1H and ^{13}C NMR data, Nifant'ev et al. concluded that 2-(dimethylamino)-3-isopropyl-1,3,2-oxazaphosphorinane (4), 2-phenyl-3-isopropyl-1,3,2-oxazaphosphorinane (5), and 2-ethoxy-3-isopropyl-1,3,2-oxazaphosphorinane (6) all exist in chair conformations with substituents on phosphorus axial (20).[4a] In fact, as we will show, 1,3,2-oxazaphosphorinane 4 is 75–80% in this conformation. This 0.7 kcal/mol axial propensity of the 2-Me_2N group is surprising, since the Me_2N group displays a 1 kcal/mol preference for equatorial attachment to phosphorus in three-coordinate 2-(dimethylamino)-1,3,2-dioxaphosphorinanes.[5]



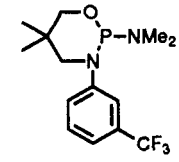
4 Z = NMe_2
5 Z = Ph
6 Z = OEt

We reported preliminary results of the conformational study of a series of 3-phenyl-1,3,2-oxazaphosphorinanes.[6] The more highly populated conformer for 13 in that series was the chair form with the 2-Me_2N axial (20, $H_Y = H_X = CH_3$). In the present paper, we examine the chair–chair equilibria, corresponding to 20 ⇄ 21 of three-coordinate 3-phenyl-1,3,2-oxazaphosphorinanes 7–16 in detail. Like the corresponding three-coordinate 1,3,2-dioxaphosphorinanes, 7–11 are in a single chair conformation, 20 (or the 5,5-dimethyl analog).

Thus, MeO, $(CF_3)_2CHO$, and Ph substituents on phosphorus display a strong axial preference. However, *unlike the three-coordinate dioxaphosphorinanes*, 12–16 also are very largely in chair conformations with the MeNH or Me_2N group axial in agreement with Nifant'ev's finding



7 $R^1 = R^2$ = Me, Z = OMe
8 $R^1 = R^2$ = Me, Z = $OCH(CF_3)_2$
9 $R^1 = R^2$ = H, Z = OMe
10 $R^1 = R^2$ = H, Z = $OCH(CF_3)_2$
11 $R^1 = R^2$ = Me, Z = Ph
12 $R^1 = R^2$ = Me, Z = NHMe
13 $R^1 = R^2$ = Me, Z = NMe_2
14 $R^1 = R^2$ = H, Z = NMe_2



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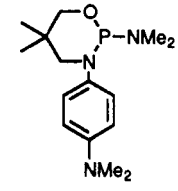

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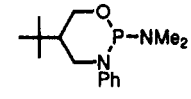


17

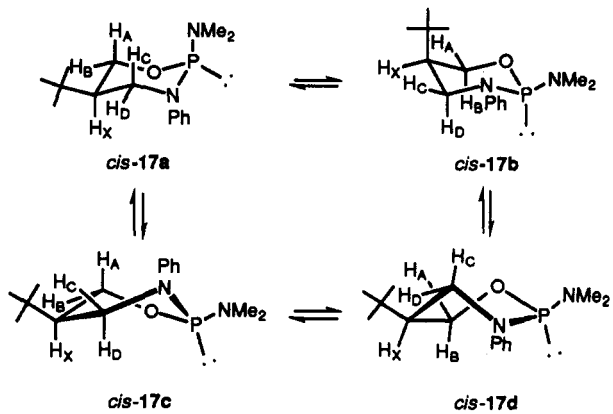
for 4. Furthermore, the chair–chair equilibrium for three-coordinate oxazaphosphorinanes 13–16 is seen to be not significantly influenced by solvent change or placement of either electron-withdrawing or -donating groups on the phenyl substituent at N(3). Lastly, we report a study of the chair–twist equilibria for previously unreported *cis*- and *trans*-17 (Schemes I and II) which also demonstrates the propensity of the 2-Me_2N to be axial and shows the free energy difference between chair and twist conformations to be very small.

We assign the axial preference of the Me_2N in 13 and 14 in part to repulsive interactions between *equatorial* Me_2N and the phenyl substituent at N(3) in conformation 21, as proposed by Nifantiev[4] for 4. This effect is in *direct contrast* to the repulsions assigned previously to these two substituents in their four-coordinate, 2-oxo-1,3,2-oxazaphosphorinane counterparts in the conformation analogous to 20 in which the Me_2N is *axial*.[2a-e] These findings demonstrate the variety of steric and stereoelectronic interactions operative in the conformational equilibria of 1,3,2-oxazaphosphorinanes and *the surprising differences in the conformational properties of this ring system when it contains three- rather than four-coordinate phosphorus.*

Results

Preparation. 1,3,2-Oxazaphosphorinanes 7–10 resulted in 81–91% yields from the reaction of the appropriate

Scheme I



cis-17a *cis*-17b *cis*-17c *cis*-17d

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(3) See, for example: Nelson, K. A.; Bentrude, W. G.; Setzer, W. N.; Hutchinson, J. P. *J. Am. Chem. Soc.* **1987**, *109*, 4058–4064 and references cited therein.

(4) (a) Nifant'ev, E. E.; Borisenko, A. B.; Sorokina, S. F.; Grachev, M. K.; Zavalishina, A. I. *Zh. Obshch. Khim.* **1977**, *47*, 2474–2480 and references cited therein. (b) Milliaresi, E. E.; Kharshan, M. A.; Preobrazhenskaya, E. A.; Nifant'ev, E. E. *Zh. Obshch. Khim.* **1984**, *54*, 1049–1051 and references cited therein.

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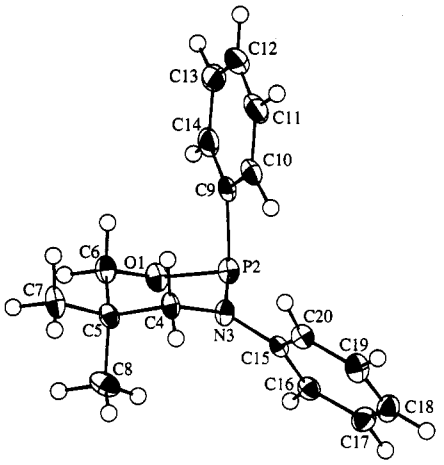


Figure 1. ORTEP plot for 11.

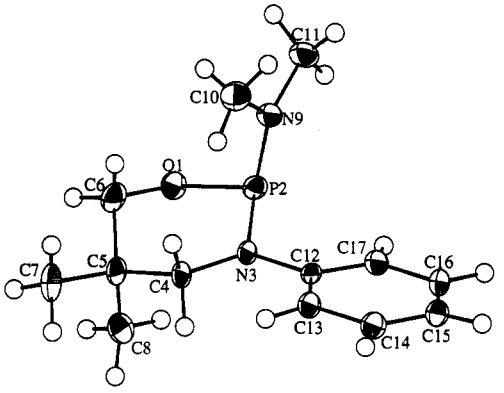
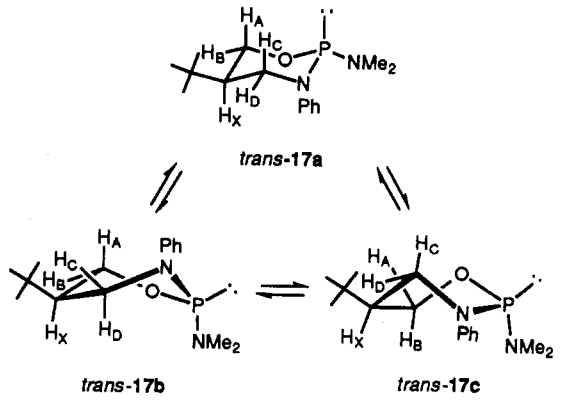


Figure 2. ORTEP plot for 13.

Scheme II



2-chloro-3-phenyl-1,3,2-oxazaphosphorinane with ROH in the presence of Et_3N. Compound 11 was prepared by the reaction of bis(*N*,*N*-diethylamino) phenylphosphine with the amino alcohol in 67% yield. Compounds 13–16 were synthesized in 47–73% yield by the reaction of the amino alcohol with hexamethylphosphorous triamide. The reaction of the 2-chloro-1,3,2-oxazaphosphorinane with methylamine and dimethylamine afforded 12 and 17. Compound 17 was formed as a mixture of cis and trans diastereomers. The ^1H NMR parameters of 17 were obtained from spectra on materials with cis/trans ratios of 18/82 (freshly made) which changed to 64/36 on distillation. The latter mixture was further equilibrated on standing in C_6D_6 at room temperature to an 80/20 (cis/trans) ratio (taken to be the equilibrium ratio) for determination of the parameters for *cis*-17.

Table I. Crystal Data for 11 and 13 at −125 °C

compd	11	13
mol formula	$C_{17}H_{20}NOP$	$C_{13}H_{21}N_2OP$
mol wt	285.329	252.299
space grp	$P2_1/n$ (No. 14)	$P2_1/n$ (No. 14)
cryst system	monoclinic	monoclinic
cell dimens		
a, Å	15.207(1)	13.581(2)
b, Å	5.942(1)	6.024(1)
c, Å	18.098(1)	16.315(2)
α, deg		
β, deg	113.35(1)	90.70(1)
γ, deg		
v, Å^3	1501.40	1334.73
Z	4.0	4.0
D_{calcd}, g/cm^3	1.262	1.255
radiation, Å	λ (Cu) 1.54180	λ (Cu) 1.54180
2θ range, deg	4.00–130.00	4.00–130.00
scan technique	$\theta/2\theta$	$\theta/2\theta$
scan width, deg	0.8000 + 0.1400 tan θ	0.8000 + 0.1400 tan θ
no. of reflns used	2128	2505
absorption coeff, cm^{-1}	15.659	17.105
data to param ratio	9.195	9.166
shift to error ratio	0.000	0.004
R	0.0453	0.0498
R_w	0.0495	0.0547

Table II. Selected Bond Lengths (Å), Bond Angles (deg), and Torsion Angles (deg) for 11 and 13

	compd	
atoms	11	13
P(2)–O(1)	1.633(2)	1.631(2)
P(2)–N(3)	1.689(2)	1.727(3)
P(2)–N(9)		1.667(3)
P(2)–C(9)	1.844(3)	
O(1)–C(6)	1.451(3)	1.441(5)
N(3)–C(4)	1.474(3)	1.464(4)
O(1)–P(2)–N(3)	101.1(1)	99.3(1)
P(2)–O(1)–C(6)	118.8(2)	123.4(2)
P(2)–N(3)–C(4)	119.9(2)	125.8(2)
P(2)–N(3)–C(12)		116.4(2)
C(4)–N(3)–C(12)		115.7(3)
P(2)–N(3)–C(15)	119.4(2)	
C(4)–N(3)–C(15)	119.7(2)	
P(2)–N(9)–C(10)		127.2(2)
P(2)–N(9)–C(11)		116.5(3)
C(10)–N(9)–C(11)		114.0(3)
O(1)–C(6)–C(5)	112.5(2)	110.5(3)
N(3)–C(4)–C(5)	110.6(2)	113.6(3)
C(4)–C(5)–C(6)	109.1(2)	108.2(3)
P(2)–O(1)–C(6)–H(3)	−63.01(2.53)	−52.38(2.90)
P(2)–O(1)–C(6)–H(4)	179.24(2.27)	174.70(3.10)
P(2)–N(3)–C(4)–H(1)	65.95(2.56)	92.18(2.78)
P(2)–N(3)–C(4)–H(2)	−175.72(2.64)	−153.43(3.17)
N(3)–P(2)–N(9)–C(10)		40.41(0.30)
N(3)–P(2)–N(9)–C(11)		−158.26(0.22)
O(1)–P(2)–N(9)–C(10)		−63.64(0.30)
O(1)–P(2)–N(9)–C(11)		97.68(0.24)

Single-Crystal X-ray Structures of 11 and 13. ORTEP perspective views of 11 and 13 are given in Figures 1 and 2. Crystal data for 11 and 13 are compiled in Table I. Selected bond distances, bond angles, and torsion angles are shown in Table II.

The ORTEP structures of 11 and 13 show that they are in the chair conformation in the solid state. The six-membered ring of 13 is somewhat more distorted from a perfect chair geometry (see below) than is that of 11. The sums of the bond angles around N(3) and N(9) of 13 are 357.9° and 357.7°, respectively. This indicates that the nitrogen atoms approach sp^2 hybridization. (The sum of the bond angles for approximately sp^3-hybridized NH_3 is 321.9°.[7]) However, one of the bond angles about N(3) and N(9) is larger than 120° while the others are less (∠P(2)N(3)C(4) = 125.8 (2)°, ∠P(2)N(3)C(12) = 116.4 (2)°,

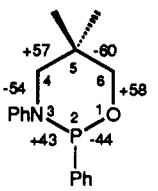
Table III. Selected ^{1}H NMR Coupling Constants (Hz) for 7–17[a]

compd	solvent	$^3J_{AP}$	$^3J_{BP}$	$^3J_{CP}$	$^3J_{DP}$	$^4J_{BD}$	$^3J_{AX}$	$^3J_{BX}$	$^3J_{CX}$	$^3J_{DX}$	$^3J_{AY}$	$^3J_{BY}$	$^3J_{CY}$	$^3J_{DY}$
4	C_6D_6	7.7	9.2	3.7	*b*	−0.9	9.9	4.4	10.1	4.4	3.3	4.6	3.7	4.7
4	CD_3CN	7.2	9.3	3.8	5.2	−0.8	10.3	4.5	10.3	4.5	3.3	4.3	3.5	4.4
7	C_6D_6	3.7	12.6	1.8	5.5	−2.1								
7	CD_3CN	3.1	12.6	1.1	5.4	−2.2								
8	C_6D_6	3.7	13.5	2.9	6.4	−2.2								
8	CD_3CN	3.8	13.2	2.9	6.3	−2.2								
9[c]	C_6D_6	3.5	11.9	1.8	5.2	−1.5	12.0	4.4	12.0	4.5	2.8	2.8	2.9	3.3
10[c]	C^6D_6	3.6	12.4	2.9	5.9	−1.4	11.5	4.5	11.6	4.4	2.9	3.1	2.9	4.3
11[d]	C_6D_6	3.4	11.8	<0.5	2.9	−2.2								
11	CD_3CN	3.4	11.8	<0.5	3.3	−2.1								
12	C_6D_6	4.9	12.0	1.3	5.3	−2.1								
13	C_6D_6	7.4	10.6	2.1	4.6	−1.8								
13	CD_3CN	7.0	10.8	1.5	4.9	−1.8								
14[c]	C_6D_6	8.0	9.7	1.8	4.5	−0.9	9.8	4.8	10.7	4.6	3.7	4.6	3.6	4.5
15[d]	C_6D_6	8.7	10.5	2.3	4.3	−1.6								
15	CD_3CN	7.7	10.8	1.4	4.7	−1.8								
16[d]	C_6D_6	8.6	10.3	3.9	4.5	−1.5								
16	CD_3CN	7.7	10.5	3.3	5.0	−1.8								
cis-17[e]	C_6D_6	11.9	8.9	1.2	5.0	−1.2	8.7	5.7	11.4	4.8				
trans-17[e]	C_6D_6	7.0	12.9	2.5	7.2	−0.7	9.0	6.6	9.3	5.2				

[a] At 300 MHz, ambient temperature, unless otherwise noted. [b] Overlapped with Me_2N signal. [c] Iteratively refined with LAOCN5 program: rms error, 0.136 Hz (**9**), 0.099 Hz (**10**), 0.072 Hz (**14**); probable error, 0.012–0.018 Hz (**9**), 0.009 Hz (**10**), 0.006–0.010 Hz (**14**); *J* 0.017–0.039 Hz (**9**), 0.013–0.019 Hz (**10**), 0.009–0.017 Hz (**10**). [d] Simulated by use of LAOCN5. [e] At 500 MHz.

∠C(4)N(3)C(12) = 115.7 (3)°; ∠P(2)N(9)C(10) = 127.2 (2)°, ∠P(2)N(9)C(11) = 116.5 (3)°, ∠C(10)N(9)C(11) = 114.0 (3)°). Further distortion is seen in torsion angles P(2)O(1)C(6)H_A and P(2)O(1)C(6)H_B, −52.4° and 174.7°, respectively. On the other hand, the sum of the bond angles around N(3) of **11** is 359.0°, and each bond angle is almost the same indicating that the nitrogen atom is truly sp^2 hybridized and that *the six-membered ring of 11 is less distorted than that of 13.* For **11**, the torsion angles of P(2)O(1)C(6)H_A and P(2)O(1)C(6)H_B are −63.0° and 179.2°, respectively, close to those for an idealized, undistorted, cyclohexane geometry, −60° and 180°, respectively.

The ring torsion angles for **11** and **13** are given in structures **18** and **19**, respectively. Angles O(1)P(2)N(3)C(4) and P(2)N(3)C(4)C(5) of **13** are about 20° less than those of **11**. The N(3)P(2)O(1)C(6) angle of **13** is reduced by 10°. This indicates that the distortion of the ring of **13** is best characterized as *flattening at the N(3)–P(2) end.*



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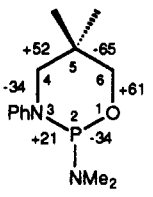

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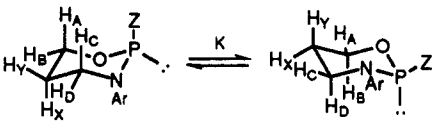
^{1}H NMR Parameters and Conformations of 7–16. In Tables III and IV are listed the pertinent ^{1}H NMR coupling constants and chemical shifts for **7–16**. Protons on the six-membered ring are designated H_A, H_B, H_C, H_D, H_X, and H_Y, as shown in **20** and **21**. For 5,5-dimethyl compounds **7**, **8**, and **11–13**, **15**, and **16**, H_X and H_Y are replaced by methyl groups. As the values of $^3J_{PNCH}$ have not been found to be useful in conformational analyses of three-coordinate phosphorus containing heterocyclic six-membered rings,[8] only the values of $^3J_{POCH}$ and $^3J_{HH}$ are used to determine the conformations of these six-membered rings.

Table IV. Selected ^{1}H NMR Chemical Shifts (ppm) for 7–17[a]

compd	solvent	A	B	C	D	X	Y
4	C_6D_6	4.07	3.63	3.04	2.52	1.60	1.23
4	CD_3CN	4.09	3.65	3.21	2.83	1.78	1.56
7	C_6D_6	3.98	3.18	3.50	2.66		
7	CD_3CN	4.00	3.33	3.55	2.92		
8	C_6D_6	3.97	3.17	3.41	2.48		
8	CD_3CN	4.05	3.50	3.62	2.96		
9	C_6D_6	4.07	3.50	3.57	2.88	1.90	1.15
10	C_6D_6	4.00	3.45	3.38	2.69	1.68	1.08
11	C_6D_6	3.61	3.28	3.19	3.06		
11	CD_3CN	3.62	3.45	3.28	3.38		
12	C_6D_6	3.64	3.16	2.98	2.80		
13	C_6D_6	3.80	3.25	3.29	2.92		
13	CD_3CN	3.87	3.35	3.48	3.15		
14	C_6D_6	3.87	3.56	3.39	3.12	1.69	1.24
15	C_6D_6	3.65	3.22	3.12	2.82		
15	CD_3CN	3.87	3.41	3.47	3.21		
16	C_6D_6	3.85	3.36	3.38	2.98		
16	CD_3CN	3.81	3.35	3.43	3.01		
cis-17[b]	C_6D_6	3.90	3.77	3.52	3.44	1.72	
trans-17[b]	C_6D_6	3.73	3.96	3.26	3.50	1.93	

[a] At 300 MHz, ambient temperature, unless otherwise noted. [b] At 500 MHz.



20 21

The small $^3J_{AP}$ (3.1–3.8 Hz) and large $^3J_{BP}$ (11.8–13.5 Hz) recorded for **7–11** (Table III) are similar to those seen for the corresponding three-coordinate 1,3,2-dioxaphosphorinanes with Z = MeO, $(CF_3)_2CHO$, and Ph[1] and allow **7–11** to be assigned to a single chair conformation (**20**). In addition, the large $^3J_{AX}$ and $^3J_{CX}$ (11.5, 12.0 Hz for diaxial protons) and small $^3J_{BX}$ and $^3J_{DX}$ (4.4, 4.5 Hz for gauche protons) for **9** and **10** are typical values for vicinal couplings of chair-form rings. Furthermore, relatively large long-range W-configuration couplings, $^4J_{BD}$ (−1.4 to −2.2 Hz), are observed for **7–11**, as expected for **20**. 1,3,2-Oxazaphosphorinane **12** also largely populates a single chair with the NHMe group axial on phosphorus, as evidenced by

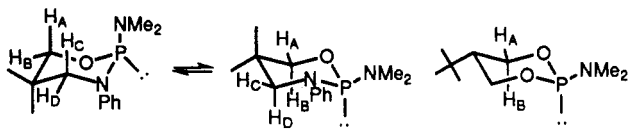
(7) Wade, L. G. *Organic Chemistry*, Prentice-Hall, Inc.: New York, 1987; pp 55.

(8) Hutchins, R. O.; Maryanoff, B. E.; Albrand, J. P.; Cogne, A.; Gagnaire, D.; Robert, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 9151–9158.

$^3J_{AP}$ (4.9 Hz) and $^3J_{BP}$ (12.0 Hz). However, for **13–16** $^3J_{AP}$ (7.0–8.7 Hz) is increased by about 4 Hz compared to $^3J_{AP}$ for **7–11**. Likewise, $^3J_{BP}$ (9.7–10.8 Hz) is decreased by approximately 2 Hz. The values of $^3J_{AX}$ and $^3J_{CX}$ for **14** (9.8 and 10.7 Hz, respectively) also are reduced and $^3J_{BY}$ (4.6 Hz) and J_{DY} (4.5 Hz) are appropriately increased. Thus, although **20** remains the major conformer populated, *both conformers* of the chair-chair equilibrium **20** ⇄ **21** are present in solution for **13-16** (Z = Me_2N). Clearly, the values of $^3J_{CP}$ and $^3J_{DP}$ show no trends useful in discerning the population of **20** vs **21**.

For **15** and **16**, two different substituents are attached to the *N*-phenyl group, the electron-withdrawing *m*-CF_3, and the electron-donating *p*-NMe_2. However, there is a near- constancy of the $^3J_{AP}$ and $^3J_{BP}$ values for both compounds, which indicates a lack of either an electronic substituent or solvent effect on the equilibrium **20** ⇄ **21** (Table III).

Chair–Chair Equilibrium Constants for 13–16. The equilibrium constants (*K*, **20** ⇄ **21**) can be estimated for **13–16** on the basis of the observed coupling constants $^3J_{AP}$ and $^3J_{BP}$. The mole fraction of **13a** (*N*(**13a**)) can be readily estimated.



Thus, it is clear that

$$N(\mathbf{13a})^3J_{AP}(\mathbf{13a}) + N(\mathbf{13b})^3J_{AP}(\mathbf{13b}) = {}^3J_{AP}(\text{obsd}) \quad (1)$$

$$N(\mathbf{13a}) = 1 - N(\mathbf{13b}) \quad (2)$$

therefore,

$$N(\mathbf{13a}) = ({}^3J_{AP}(\text{obsd}) - {}^3J_{AP}(\mathbf{13b}))/({}^3J_{AP}(\mathbf{13a}) - {}^3J_{AP}(\mathbf{13b})) \quad (3)$$

Similarly, for $^3J_{BP}$

$$N(\mathbf{13a}) = ({}^3J_{BP}(\text{obsd}) - {}^3J_{BP}(\mathbf{13b}))/({}^3J_{BP}(\mathbf{13a}) - {}^3J_{BP}(\mathbf{13b})) \quad (4)$$

The values of $^3J_{AP}$(**13b**) and $^3J_{BP}$(**13b**) in eqs 3 and 4 are for the specific conformation **13b** and can be assumed to be those for **22**[9] (19.6 and 3.8 Hz, respectively), which is known to be in the chair conformation shown. (The axial lone-pair orientation greatly enhances $^3J_{AP}$). However, $^3J_{AP}$(**13a**) and $^3J_{BP}$(**13a**) for conformation **13a** cannot be assumed from model compounds because of the ring distortion present in **13a** (Figure 2). However, they could be calculated from Karplus eq 5 were the constants *A* and *B* known.

$$^3J_{POCH} = A\cos^2\phi_{HP} + B\cos\phi_{HP} \quad (5)$$

To determine *A* and *B*, we chose **11** as the model compound. As noted above, the six-membered ring of **11** is relatively undistorted in the solid phase (Figure 1) with the phenyl group attached axially to phosphorus atom. It can be assumed, based on its J_{HP} values, that **11** in solution is essentially 100% in the same chair conformation. Thus, constants *A* and *B* in eq 5 can be determined from the observed $^3J_{AP}$ and $^3J_{BP}$ values of **11** (3.4 and 11.8 Hz, respectively) and the measured torsion angles, ϕ_{AP} = 63°, ϕ_{BP} = 179°, from the crystal structure of **11**. They were found to be 13.3 (*A*) and 1.47 (*B*). The reliability of this approach was checked by plotting $^3J_{POCH}$ vs dihedral angle (Figure 3) from the Karplus curve (□) generated from eq 5 (*A* = 13.3 and *B* = 1.47) along with experimental data from the literature (◆).[10] There is a reasonably good agreement between the curve calculated by eq 5 (50° ≤ ϕ_{PH} ≤ 180°) and the limited number of experimental values available. This equation assumes $^3J_{HP}$ is zero at 90° which may not be true. However, near the angles measured for **13** it is considered to be adequate, since the experimental points fall reasonably near the curve in the critical area of about 60–70°, just above the 52° angle for ϕ_{AP} of **13**. The value for J_{BP} of **13a** in fact could have been assumed from that for **11** (11.8 Hz), since the angles ϕ_{AP} for **11** and **13a** are very close (175°, 179°), and a Karplus curve will not be steep in the region 175-180°.

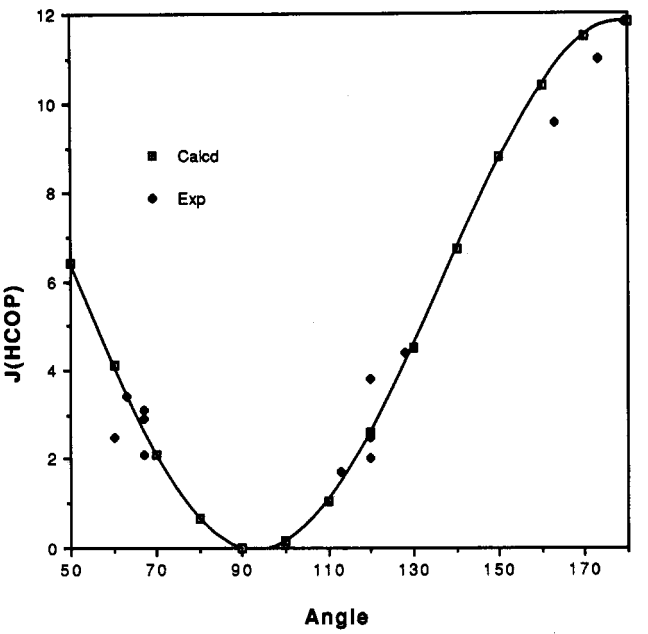


Figure 3. Dihedral angle dependence of $^3J_{HP}$ for three-coordinate 1,3,2-dioxaphosphorinanes. □ are points calculated from eq 5 with *A* = 13.3, *B* = 1.47. ◆ are experimental data from ref 10.

The values of $^3J_{AP}$ (5.8 Hz) and $^3J_{BP}$ (11.7 Hz) for **13a** were calculated from eq 5 and torsion angles ϕ_{AP} (52°) and ϕ_{BP} (175°) taken from the crystal structure of **13**. (Note that the major effect of ring distortion is on $^3J_{AP}$.) The mole fraction of **13a** was calculated to be 88% from eq 3 ($^3J_{AP}$) and 86% from eq 4 ($^3J_{BP}$), in excellent internal agreement. Similarly, for **14–16** the chair-chair equilibrium constants (*K*) were calculated on the assumption that the six-membered rings of conformer **20** are distorted to the same degree as those for **13a**. The assumed coupling constants were as follows: $^3J_{AP}$(**20**) = 5.8 Hz, $^3J_{BP}$(**20**) = 11.7 Hz, $^3J_{AP}$(**21**) = 19.6 Hz, $^3J_{BP}$(**21**) = 3.8 Hz. The calculated results are recorded in Table V.

Chair–Twist Equilibria for *cis*- and *trans*-17. ^{1}H NMR coupling constants for *cis*- and *trans*-**17** are quite different from those for **7–16** (Table III). The values of

(9) Bentrude, W. G.; Tan, H.-W. *J. Am. Chem. Soc.* **1973**, *95*, 4666–4675. Values of J_{HP} of 19.5–21.5 Hz have been found for J_{AP} of the *t*-BuP analog of **22** (ref 13a) and for other three-coordinate 1,3,2-oxazaphosphorinanes with R_2N on phosphorus that are clearly in a single chair conformation like **13b** (Huang, Y., Mullah, N. Unpublished results).

(10) White, D. W.; Verkade, J. G. *J. Magn. Reson.* **1970**, *3*, 111–116 and references cited therein.

Table V. Estimated Equilibrium Constants (K = 21/20) at 25 °C

compd	% 20 based on obsd[a] J_{AP}	% 20 based on obsd[a] J_{BP}	avg	K	$\Delta G°$ (kcal/mol)
13	88	86	87	0.15	1.1
14	84	75	80	0.25	0.82
15	79	85	82	0.22	0.90
16	80	82	81	0.23	0.87
4[b]	86	68	77	0.30	0.71
26[c]	31	28	30	2.3	−0.50

[a] See text for assumed $^3J_{AP}$ and $^3J_{BP}$ for 20 and 21. [b] Based on coupling constants measured at 300 MHz in C_6D_6. [c] Reference 16.

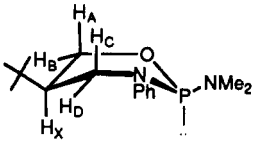
$^3J_{HP}$ and $^3J_{HH}$ show that *cis*- and *trans*-17 populate *nonchair conformations*, at least in part. A similar approach, using assumed $^3J_{HP}$ or $^3J_{HH}$ values for various conformers, allows estimates of conformer populations for *cis*-17 and *trans*-17 to be made.

For the nonchair (twist/boat) forms depicted in Schemes I and II, one side of the ring remains in a geometry about the C4–C5 or C5–C6 bond that is the same as the chair conformation from which it is formed. The protons attached to C4 or C6 remain axial or equatorial as in the chair. They also move into positions synclinal and antiperiplanar, respectively, with respect to phosphorus and become fully pseudoaxial and pseudoequatorial if the degree of twisting of the ring moves the conformation fully into a boat form on the boat–twist–boat pseudorotational cycle. These geometrical considerations apply, for example, to the oxygen side (H_A and H_B) of the ring in *cis*-**17c** and *trans*-**17b** and the nitrogen side (H_C and H_D) of *cis*-**17d** and *trans*-**17c**. At the same time the methylene protons on the opposite side of the ring move from axial and equatorial toward pseudoequatorial and pseudoaxial positions, respectively. Simultaneously, the lone pair on phosphorus moves from equatorial in *cis*-**17a** toward the pseudoaxial position in its twist/boat forms and vice versa for the lone pair of *trans*-**17a**. The degree of twist, for example, in *cis*-**17c** and *cis*-**17d**, determines the extent to which the methylene protons and lone pair fully assume their new positions. In true boat conformations, certain of the H–C–C–H and H–C–O–P torsion angles are of the order 60° or 180° as in a chair, and values of $^3J_{HP}$ and $^3J_{HH}$ can be assumed from three-coordinate 1,3,2-oxazaphosphorinanes (Table III) or 1,3,2-dioxaphosphorinanes that populate a single chair conformation.

From the inspection of the observed, time-averaged values of $^3J_{HH}$ and $^3J_{HP}$ for *cis*-17 and *trans*-17 (Table III), it is relatively easy to discern *qualitatively* the nature of the conformational equilibria involved. Thus, for *cis*-**17** it is clear that *cis*-**17c** and *cis*-**17b** are not populated or the value of $^3J_{CX}$ would be reduced from the 11.4 Hz value observed which is typical of trans diaxial protons in chair forms similar to *cis*-**17a** (Table III). However, in *cis*-**17d** H_C and H_X remain antiperiplanar and essentially trans diaxial. The increase in $^3J_{AP}$ observed to a time-averaged value (11.9 Hz), much larger than the 5.8 Hz value predicted for *cis*-**17a** by the above Karplus curve analysis of such rings with axial Me_2N, shows unmistakably that *cis*-**17d** *is populated to a significant degree*. This also leads to a reduction in $^3J_{BP}$ (8.9 Hz) from the close to 12 Hz value found in Table III for similar equatorial hydrogens on chair-form rings with axial substituents on phosphorus (**7–12**) and from the 11.7 Hz value estimated for **13** from the above Karplus curve considerations and presumably applicable to *cis*-**17a**.

For *trans*-17 there are only three possible conformers in equilibrium worthy of consideration (Scheme II) because the diaxial-substituted chair form would be too high in energy. The observed reductions in $^3J_{AX}$ and $^3J_{CX}$ mean that *trans*-**17a** is depopulated. The near-equal values of $^3J_{AX}$ (9.0 Hz) and $^3J_{CX}$ (9.3 Hz) indicate that *trans*-**17b** and *trans*-**17c** are approximately equally populated, if the degree of twist is about equal in each; i.e., $^3J_{CX}$ for *trans*-**17b** is equal to $^3J_{AX}$ for *trans*-**17c**. The accompanying increase in $^3J_{BX}$ (6.6 Hz) from the 4–5 Hz value for an equatorial hydrogen of the chair form ring of **9**, **10**, or **14** (Table III) is fully expected if the ring of *trans*-**17c** is twisted far enough for H_B and H_X to become nearly eclipsed, and $^3J_{BX}$ for *trans*-**17c** is therefore large. The increase in $^3J_{DX}$, though smaller, is similarly explained by *trans*-**17b**.

Estimation of actual conformer populations for the above equilibria must be done with caution and care, because the coupling constants to hydrogen and phosphorus for pseudoaxial and pseudoequatorial protons depend in a Karplus equation dependent fashion on the degree of twisting, as noted above. It appears from Dreiding models that the estimation of conformer populations from measured $^3J_{HP}$ values is likely to be more accurate than if observed $^3J_{HH}$ values are used. This results first from the greater validity of assumed $^3J_{HP}$ values. Thus, a rotation of about 60° about the C–O and C–N bonds of *cis*-**17e** is required to convert it to one of the boat



cis-**17e**

conformations (*cis*-**17c** or *cis*-**17d**) on either side of it on the pseudorotational pathway. In so doing the protons at C4 and C6 assume fully pseudoaxial or pseudoequatorial positions for which assumed $^3J_{HP}$ values can be taken from those of axial and equatorial protons of model chair-form molecules. Further rotation does not change the HCOP (the angle of prime interest) or HCNP torsion angle. By contrast the HCCH torsion angles related to C4–C5 and C5–C6 bond rotation continue to change on the way to the next true boat conformation (beyond *cis*-**17c** or *cis*-**17d**). Secondly, the differences between $^3J_{HP}$(obsd) and the values expected for the chair forms *cis*-**17a** and *trans*-**17a** (i.e., the changes in $^3J_{HP}$ (obsd)) are considerably greater than those seen when considering $^3J_{HH}$ values (Table III) which leads to more accurate calculations. (As for **7–16** variations in $^3J_{CP}$ and $^3J_{DP}$ show no useful trends). Therefore, in the estimates of equilibria made below, we rely first on the measured $^3J_{HP}$ values and then check those numbers against those obtained from observed $^3J_{HH}$.

For the equilibrium *cis*-**17a** ⇄ *cis*-**17d**, one may reasonably assume the values for *cis*-**17a** estimated by the Karplus relation for **13** (rounded off to the nearest Hz: $^3J_{AP}$ = 6 Hz; $^3J_{BP}$ = 12 Hz). For *cis*-**17d** those for **22** (similarly rounded off) are reasonable if *cis*-**17d** is sufficiently twisted so that H_A and H_B are essentially pseudoequatorial and pseudoaxial, respectively: $^3J_{AP}$ = 20 Hz; $^3J_{BP}$ = 4 Hz. It is readily shown, by the algebra used to obtain eqs 3 and 4, that

$$N(\mathbf{17a}) = (^3J_{AP}(\text{obsd}) - {}^3J_{AP}(\mathbf{17d}))/(^3J_{AP}(\mathbf{17a}) - {}^3J_{AP}(\mathbf{17d})) \quad (6)$$

where the terms are as defined for eqs 1–4 and *refer only*

to the conformers of Scheme I representing cis-17. A similar equation can be written for $^3J_{BP}$. From eq 6 and its $^3J_{BP}$ equivalent, N(**17a**) values of 0.58 and 0.61 are calculated based on observed $^3J_{AP}$ and $^3J_{BP}$, respectively. This is very good agreement and says that about 60% of *cis*-**17** remains in the chair form, *cis*-**17a**, with the remaining 40% in boat/twist form **17d**. If $^3J_{AX}$ for *cis*-**17a** is 11.5 Hz, as in **22**, and has a value of 4.5 Hz in *cis*-**17d**, $^3J_{AX}$(obsd) is calculated for a 60/40 ratio of *cis*-**17a**/*cis*-**17d** to be 8.7 Hz, the experimentally observed value. We have no good model compound from which to assume $^3J_{AX}$ for *cis*-**17d**, as its H_A–C6–C5–H_X torsion angle is approximately 120° if *cis*-**17d** is a boat form as required for the assumed values of $^3J_{HP}$ to be reasonably correct. However, even if the value of $^3J_{AX}$ for *cis*-**17d** is only 3.7 Hz, the calculated $^3J_{AX}$ would still be 8.4 Hz, nearly within the experimental error of the observed 8.7 Hz value.

The three-conformer equilibrium of Scheme II can be treated rather simply algebraically if it is assumed that N(*trans*-**17b**) = N(*trans*-**17c**) as proposed above. This means that

$$N(\textit{trans}\text{-}\mathbf{17a}) + (2N(\textit{trans}\text{-}\mathbf{17b})) = 1$$

Since for J_{AP}

$$N(\mathbf{17a})J_{AP}(\mathbf{17a}) + N(\mathbf{17b})J_{AP}(\mathbf{17b}) + N(\mathbf{17c})J_{AP}(\mathbf{17c}) = J_{AP}(\text{obsd})$$

it is easy to derive expression 7 for *trans*-**17** under conditions that N(**17b**) = N(**17c**):

$$N(\mathbf{17b}) = (J_{AP}(\mathbf{17a}) - J_{AP}(\text{obsd}))/(2J_{AP}(\mathbf{17a}) - J_{AP}(\mathbf{17b}) - J_{AP}(\mathbf{17c})) \quad (7)$$

Assuming that *trans*-**17b** and *trans*-**17c** are twisted such that H_A and H_B are truly pseudoequatorial and pseudoaxial with respect to phosphorus in *trans*-**17b** and vice versa for *trans*-**17c**, then reasonable values for $^3J_{AP}$ (rounded off to the nearest Hz) can be assumed from those of **22** and the rings of Table III that are completely in chair conformations (i.e., **7–12**): J_{AP}(**17a**) = 4 Hz; J_{AP}(**17b**) = 4 Hz; J_{AP}(**17c**) = 12 Hz. These values lead from eq 7 to N(*trans*-**17b**) = N(*trans*-**17c**) = 0.38. The analogous expression for J_{BP} and assumed values: J_{BP}(**17a**) = 20 Hz; J_{BP}(**17b**) = 12 Hz; J_{BP}(**17c**) = 4 Hz gives N(*trans*-**17b**) = N(*trans*-**17c**) = 0.30. The average of these two estimates is 0.34. Thus, one can say that a *roughly equal amount of each conformer of Scheme II is populated by trans-17.* As a cross check, use of the reasonable values for $^3J_{AX}$ for the **17a** and **17b** conformers of *trans*-**17** of 12 Hz, along with the 4.5 Hz $^3J_{AX}$ value assumed for *cis*-**17d**, predicts $^3J_{AX}$ for *trans*-**17** to be 9.5 Hz, compared to the 9.0 Hz experimental value.

One must again state that the estimates made above *are only approximate* because of the errors in assumed couplings. However, the agreements reached using J_{AX} along with J_{AP} and J_{BP} are gratifying. Also, as outlined in the Discussion, the equilibria of Schemes I and II can be reasonably well interpreted in terms of the steric effects on the chair–chair equilibria observed for PhN(3)/Me_2N compounds (Table III). For these interpretations, the assignment of conformer populations need not be precise.

^{31}P Chemical Shifts for 7–17. The ^{31}P NMR chemical shifts of **7–17** are tabulated in Table VI. Individual signals were observed for each diastereomer of **17**. The upfield signal was assigned to the cis diastereomer.[2c] This assignment was confirmed by stereospecific retentive oxidation of **17** to the respective cis and trans isomers of 2-oxo-2-(dimethylamino)-3-phenyl-5-*tert*-butyl-1,3,2-oxazaphosphorinane whose identities were established previously.[2c] The so-called δ substituent effect[11] in ^{31}P NMR spectroscopy is observed for **7–14**. This effect arises from the presence of the equatorial methyl of the gem dimethyl substitution at C(5) and *the axial substituent* on three-coordinate phosphorus and results in an approximately 7.5 ppm upfield chemical shift in three-coordinate 1,3,2-dioxaphosphorinanes.[11] Thus, for **7**, **8**, and **13**, the *gem* dimethyl substitution at C(5) is accompanied by a 6.2–8.2 ppm upfield ^{31}P shift compared to unsubstituted **9**, **10**, and **14**. This is consistent with the postulated predominant axial orientation of the Z substitutent of **7–14**. For *cis*- and *trans*-**17**, the combination of δ substituent effects (5.5 ppm upfield for the equatorial 5-*tert*-butyl substituent[11]) and cis/trans effects (*cis*, P–Z axial upfield of *trans*, P–Z equatorial[1b]) should generate a large difference in chemical shift if they were both in chair conformations. However, only a 2.8 ppm difference between *cis*- and *trans*-**17** was observed. This is further evidence for the chair–twist equilibria proposed for *cis*- and *trans*-**17** in which the Me_2N is moved out of the axial position in *cis*-**17d** but becomes pseudoaxial in *trans*-**17b** and *trans*-**17c**.

Table VI. ^{31}P NMR Chemical Shifts (ppm) for 7–17 in C_6D_6[a]

compd	δ	compd	δ	compd	δ
7	125.5	11	111.9	15	120.8
8	131.1	12	108.6	16	124.3
9	133.7	13	120.7	*cis*-7	124.2
10	138.7	14	126.9	*trans*-17	127.0

[a] Positive chemical shifts are downfield from the external 85% H_3PO_4. At 121 MHz, ambient temperature.

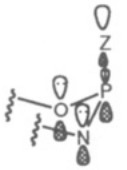
Discussion

The position of the equilibrium **20** ⇄ **21** and, therefore, the orientation of a substituent (Z) on phosphorus are determined by a balance of steric interactions and stereoelectronic factors.[12] The three potentially relevant steric factors are as follows: repulsive 1,3-*syn* axial (Z/H) interactions (destabilizing conformer **20**); repulsions between vicinal diequatorial substituents on N(3) and P (e.g., Ph/Z_{eq}) destabilizing conformer **21**; and repulsions between vicinal axial–equatorial (Ph/Z_{ax}) substituents (destabilizing conformer **20**). Stereoelectronic factors of potential consequence include stabilizing n–σ^* interactions of the type likely involved in the *endo* anomeric effect.[12] Thus, an axial P–Z orientation (**20**) would be stabilized by oxygen (n_O/σ^*_{PZ}) and nitrogen (n_N/σ^*_{PZ}) lone pair overlap with the antibonding P–Z orbital (structure **23**). This stabilization might be further aided by interaction of the equatorial lone pair on phosphorus with endocyclic C–O and C–N antibonding orbitals, a factor not always considered. Back donation of a lone pair on an axial Z, e.g., the nitrogen lone pair on Me_2N, to an endocyclic P–O or P–N antibonding orbital or via pπ–dπ bonding also could stabilize the axial P–Z bond. Because of expected steric restrictions on axial P–Z bond conformations, this sort of

(11) Haemers, M.; Ottinger, R.; Zimmermann, D.; Reisse, J. *Tetrahedron* **1973**, *29*, 3539–3545 and references cited therein.

(12) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: West Berlin, Heidelberg, New York, 1983. Juaristi, E.; Gabriel, C. *Tetrahedron* **1992**, *48*, 5019–5087. For applications to six-membered rings see especially: Juaristi, E. *Introduction to Stereochemistry and Conformational Analysis;* Wiley-Interscience: New York, 1991, Chapters 17 and 18.

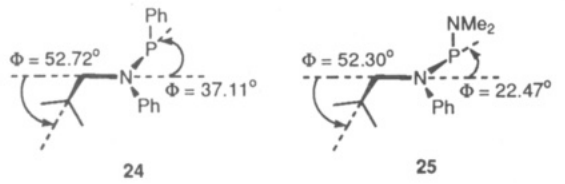
exo anomeric effect[12] is generally less important than the analogous stabilization that is available to an equatorial Z.



23

In three-coordinate 1,3,2-dioxaphosphorinanes, vicinal diequatorial steric interactions are absent. Stereoelectronic effects dominate and orient nearly all substituents preferentially axial (CH_3, CH_3O, PhO, Cl, Ph).[1,9,13] The six-membered ring is in the chair conformation like **20** (NPh = O). With more sterically demanding substituents, e.g., isopropyl and *tert*-butyl, 1,3-*syn* axial interactions increase and shift the equilibrium toward **21** (NPh = O).[9] Substituents NMe_2 and *tert*-butyl strongly prefer the equatorial orientation, the latter for obvious steric reasons. The 1 kcal/mol equatorial preference of Me_2N is believed to result to a large extent from optimal stereoelectronic stabilization in the equatorial orientation that is lost in the axial position, **21**.[9,13] The MeNH substituent (Z) leads to an approximately equal population of **20** and **21**.[13a]

As shown above for **7–16** and by Nifant'ev et al. for **5** and **6**,[4a] substituents (Z) on phosphorus such as OMe, $OCH(CF_3)_2$, and Ph in three-coordinate 1,3,2-oxazaphosphorinanes also strongly favor the axial orientation (**20**).[4a,6] However, by contrast to the findings for 1,3,2-dioxaphosphorinanes containing three-coordinate phosphorus, NHMe and even NMe_2 groups are seen to be *predominantly axial in the three-coordinate 1,3,2-oxazaphosphorinanes* studied. One or more of the relevant steric or stereoelectronic factors mentioned above may be responsible. *Firstly*, a reduction in the magnitude of 1,3-*syn* axial repulsions in **20** can be anticipated from the X-ray structures of **11** and **13**. The P–N and C–N bond lengths (Table II) are longer than those for P–O and C–O, respectively, which increases the distance between axial protons and axial NMe_2. In addition, the N-containing six-membered ring appears to be readily deformable in relief of 1,3-*syn* axial steric repulsions. This is seen in the bond angles P(2)N(3)C(4) (125.8°) and P(2)O(1)C(6) (123.4°) of **13**, which are considerably larger than those of **11** (118.8 and 119.9°, respectively), and in the interplane angles for **11** and **13** depicted in structures **24** and **25**. (Best plane through O1, N(3), C4, C6 used). The angle P(2)N(9)C(10) is enlarged to 127.2 (2)°, perhaps also to decrease 1,3-syn axial repulsions. As a result the axial Me_2N is rotated about its P–N bond so as to move one methyl group over the ring and closer to the axial hydrogen at C4 while maintaining near planarity about the axial nitrogen (sum of angles about nitrogen, 358°), Figure 4. With an assumed van der Waals radius of 2.0 Å for the CH_3[14] group and 1.20 Å for hydrogen,[15] the measured C···H_C internuclear distance (3.6 Å) is considerably beyond the van der Waals sum (3.2 Å). That for C···H_A (3.1 Å) is somewhat shorter.



24 25

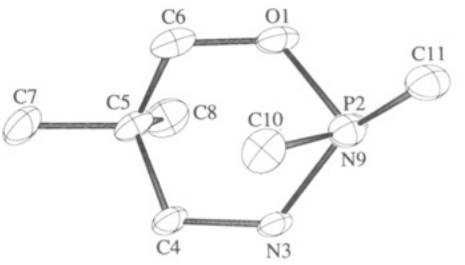


Figure 4. Truncated ORTEP plot for **13** showing conformation about the axial P–N bond.

The *second* steric factor, one which is not present in 1,3,2-dioxaphosphorinanes, involves potential *vicinal* repulsive interactions in **20** or **21** between the substituent Z on phosphorus and the *i*-Pr (**5** and **6**) or Ph (**7–16**) substituent on ring nitrogen (N(3)). Indeed, in the corresponding 2-oxo-1,3,2-oxazaphosphorinanes, such repulsions have been shown to *destabilize conformations with axial Z* corresponding to **20** and *cis*-**17a**.[2a-h] This effect appears not to be a dominant factor in the three-coordinate cases, however. As shown in other work in this laboratory, the details of which will be published separately,[16] replacement of N(3)Ph in **13** or **14** by $N(3)CH_3$ (structure **26**) shifts the equilibrium toward **21** (**26b**) (Table V). By contrast, the same substitution in the 2-oxo series shifts the chair–twist equilibrium for Z = Me_2N[17] in the opposite direction and has the same effect on both chair–chair and chair–twist equilibria for Z = Ph.[2h] The replacement of Ph at N(3) with the much smaller hydrogen has an even greater effect *in the same direction*.[2a-h] These effects have been assigned[2a-h] to dominant vicinal *axial–equatorial repulsions* present between axial Me_2N and Ph on phosphorus and substituents at N(3) decreasing in the order Ph > Me > H. Conversely, we interpret the greater stability of **20** over **21** in **13** and **14** to result *primarily* from steric repulsion accompanying the *equatorial–equatorial* positioning of the Me_2N and PhN(3) in **21**.

We also measured the coupling constants for **4** at 300 MHz (Table III) and found them to be surprisingly close to those determined by Nifant'ev et al. from a less well-dispersed 100-MHz spectrum. The percentage of the Me_2N-axial chair conformer corresponding to **20** was determined for **4** to be 77% (Table V) in the same manner as it was for **7–16** (eqs 3 and 4). Recall the result discussed earlier in which replacement of the *i*-Pr at N(3) or **4** with Me (**26**) was seen to shift the equilibrium strongly toward **21** (**26b**). (Indeed, about 70% of **26b** becomes populated (Table V)). Thus, the N(3) substitutents, Ph and *i*-Pr, *both of which are larger than Me*, destabilize **21** and shift the equilibrium toward Me_2N-axial conformations represented by **20**.

The importance of stereoelectronic effects *not present in 1,3,2-dioxaphosphorinanes*, a possible *third* factor in the enhanced preference of Me_2N and MeNH substituents on phosphorus for the axial position in 1,3,2-oxazaphos-

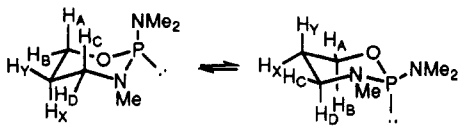
(13) (a)Bentrude, W. G.; Tan, H.-W.; Yee, K. C. *J. Am. Chem. Soc.* **1975**, *97*, 573–582. (b) Mosbo, J. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 4659-4665.

(14) Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960; p 260.

(15) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.

(16) Huang, Y. Results from this laboratory to be published separately.

(17) Chandradrasekaran, S. Unpublished results from this laboratory.



26a 26b

phorinanes, is not so readily assessed. However, the orientation of the Me_2N in **13** (Figures 2 and 4) is such that its nitrogen lone pair can be involved in stabilizing n–σ^* donation to the σ^* orbital of the O(1)–P bond. (The preferred orthogonality of phosphorus and nitrogen lone pairs is well known.[18]) This stabilization would result in a kind of *exo anomeric effect*.[12] In addition, the conventional *endo anomeric effect* may be enhanced in 1,3,2-oxazaphosphorinanes if the N(3) lone pair is higher in energy than that of a lone pair on ring oxygen thus increasing overall n–σ^* stabilization. It had been hoped that the substituents on the phenyl rings of **15** and **16** might perturb the energy of the N(3) lone pair sufficiently to alter the equilibrium of **20** ⇄ **21**. However, no perceptible change occurs. Either the perturbation is too small to be seen or n → σ^* interactions involving the N(3) lone pair and the axial σ_{PZ}^* orbital are not important in these molecules. The latter seems highly unlikely. Perhaps an increase in n → σ^* stabilization involving the equatorial phosphorus lone pair and the endocyclic C–N antibonding orbital results when an electron-withdrawing substitution is placed on the N(3)Ph. This would offset the expected increased n_N/σ_{PZ}^* stabilization when Z is axial.

Chair–Twist Equilibria. That the cis diastereomer of **17** is the more stable one is not surprising in view of the axial preference of the Me_2N in **13** and **14**. Nonetheless, boat/twist forms must be very energetically available for *cis*-**17**. Thus, even more of *cis*-**17d** (Me_2N pseudoequatorial) is populated in equilibrium with *cis*-**17a** (*cis*-**17a**/*cis*-**17d** ≅ 60/40) than is **21** (Me_2N equatorial) in chair–chair equilibrium with **20** for **14** (**20**/**21** = 80/20). Dreiding models show that in boat/twist form *cis*-**17d** the Me_2N and N(3)Ph are moved away from one another (P–N and N–Ph bonds less eclipsed) to *relieve the equatorial–equatorial repulsion* that leads to the destabilization present in *trans*-**17a** (and **21**). This also makes boat/twist form *cis*-**17d** of lower energy than *cis*-**17c** and explains the lack of population of the latter. It is likely the reduced equatorial–equatorial repulsion in *cis*-**17d** that makes it so readily formed from *cis*-**17a**. It is difficult to estimate *quantitatively* the intrinsic resistance of conformation *cis*-**17a** to conversion to twist form *cis*-**17d**. The driving force for the *cis*-**17a** → *cis*-**17d** reorientation of the axial Me_2N cannot be estimated from the equilibrium **20** ⇄ **21** because in *cis*-**17d** there is not present the repulsive equatorial–equatorial N(3)Ph/NR_2 interaction of **21**. Nonetheless, the chair–twist free energy difference must be very small as it is in three-coordinate 1,3,2-dioxaphosphorinanes.[9,19]

For *trans*-**17**, the destabilizing equatorial–equatorial interaction present in **21** is operative in *trans*-**17a** but relieved in formation of *trans*-**17b** and *trans*-**17c**. The near-equal energies of *trans*-**17b** and *trans*-**17c** are reasonable in view of the *pseudoaxial* positions of the Me_2N in both which, therefore, are devoid of the equatorial–equatorial repulsions present in twist form *cis*-**17c** and in chair conformations *trans*-**17a** and **21**. As for *cis*-**17**, twist conformations must be very little higher in energy intrinsically than chair conformations. Here, the equilibria *do* involve, in formation of *cis*-**17b** and *cis*-**17c**, relief of the equatorial/equatorial repulsion felt in *trans*-**17a**. Since equilibrium **20** ⇄ **21** favors the Me_2N axial form by about 0.8–1.1 kcal/mol (**13** and **14** Table V) the resistance to chair to twist interconversion to place the Me_2N pseudoaxial (*trans*-**17b** and *trans*-**17c**) must be a *few tenths of a kcal greater than 0.8–1.1 kcal/mol, as trans-17a is not fully depopulated.*

It also should be noted that the boat/twist conformations formed from *cis*- and *trans*-**17** are not the same. Thus, *trans*-**17b** and -**17c** have the Me_2N pseudoaxial, and those formed from *cis*-**17a** have the Me_2N pseudoequatorial. Notably, boat/twist forms are not populated by **22**,[9] as is consistent with the propensity of its Me_2N to be equatorial.

Low free energy differences for three-coordinate 1,3,2-oxazaphosphorinanes of chair, and the ease of population of boat or twist forms, are not surprising since this also is true for three-[9,19] and four-coordinate 1,3,2-dioxaphosphorinanes[20–22] and four-coordinate 1,3,2-oxazaphosphorinanes.[2c,d,g,h] In these ring systems it is usually presumed that the relatively long endocyclic P–O and P–N bonds and accompanying flattening of the rings about phosphorus reduce not only 1,3-*syn* axial repulsions in chair forms but also cross-ring torsional repulsions in boat/twist conformations. The very long P–N bonds of three-coordinate 1,3,2-oxazaphosphorinanes (Table II) may make boat/twist forms even more accessible.

Conclusion

The series of 1,3,2-oxazaphosphorinanes **7**–**11** with Z = MeO, $(CF_3)_2CHO$, or Ph at phosphorus behaves conformationally much like the well-studied 1,3,2-dioxaphosphorinanes. Each populates a single chair conformation, **20**. This is most likely in response to n → σ^* stereoelectronic interactions related to the anomeric effect that favor axial orientation of Z to the degree that repulsive 1,3-*syn* axial interactions present in **20** are overcome. The ring with Z = MeNH, **12**, also is essentially all in conformer **20** in solution, even though in the 1,3,2-dioxaphosphorinane

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(19) Nelson, K. A.; Sopchik, A. E.; Bentrude, W. G. *J. Am. Chem. Soc.* **1983**, *105*, 7752–7754. Hermans, R. J. M.; Buck, H. M. *J. Org. Chem.* **1987**, *52*, 5150–5157.

(20) For monocyclic systems see: (a) Day, R. O.; Bentrude, W. G.; Yee, K. C.; Setzer, W. N.; Deiters, J. A.; Holmes, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 103–106. (b) Mosbo, J. A. *Org. Magn. Reson.* **1978**, *11*, 281–286. (c) Gerlt, J. A.; Gutterson, N. I.; Drews, R. E.; Sokolow, J. A *J. Am. Chem. Soc.* **1980**, *102*, 1665–1670. (d) Bentrude, W. G.; Yee, K. C. *Chem. Commun.* **1972**, 169–170. (e) Bentrude, W. G.; Hargis, J. H. *J. Chem. Soc., Chem. Commun.* **1969**, 1113–1114.

(21) For trans-fused six/six ring systems see: Taira, K.; Lai, K.; Gorenstein, D.G. *Tetrahedron* **1986**, *42*, 229–238. Rowell, R.; Gorenstein, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 5894–5902. Gorenstein, D. G.; Rowell, R.; Findlay, J. *J. Am. Chem. Soc.* **1980**, *102*, 5077–5081. Gorenstein, D. G.; Rowell, R. *J. Am. Chem. Soc.* **1979**, *101*, 4925–4928. Bouchu, D. *Phosphorus Sulfur Relat. Elem.* **1983**, *15*, 33–49. Bouchu, D.; Dreux, J. *Tetrahedron Lett.* **1980**, *21*, 2513–2516. Yang, J.-C.; Shah, D. O.; Rao, N. U. M.; Freeman, W. A.; Sosnovsky, G.; Gorenstein, D. G. *Tetrahedron* **1988**, *44*, 6305–6314.

(22) For rings of cyclic nucleotides and related five/six fused systems see ref 3 and: Nelson, K. A.; Bentrude, W. G. *Carbohydr. Res.* **1992**, *234*, 141–156. Sopchik, A. E.; J. Beres, J. Tomasz, Bentrude, W. G. *J. Org. Chem.* **1991**, *56*, 5911–5918. Hermans, R. J. M.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 82–88. Bottka, S.; Radics, L.; Tomasz, J. *Nucleosides Nucleotides* **1989**, *8*, 1217–1229.

ring system the MeNH substituent displays a nearly neutral equatorial–axial preference in solution. Moreover, the Me_2N of **13** and **14** is preferentially axial as measured by the 80–90% population of chair conformer **20** by these molecules. Thus, conformer **20** is 0.8–1.1 kcal/mol more stable than is conformer **21** in contrast to the approximate 1 kcal/mol preference of the Me_2N for the equatorial position when attached to phosphorus of the corresponding 1,3,2-dioxaphosphorinane ring. This surprising finding evidently is *partially* rationalized in terms of the reduction in 1,3-*syn* axial repulsions for axial Me_2N in the 1,3,2-oxazaphosphorinane ring. Thus, in addition to the presence of relatively long endocyclic N–P bonds, evidence is seen from the X-ray structures of **11** and **13** that the ring of **13** is distorted somewhat to accommodate the axial Me_2N of **13** which is rotated about the axial P–N bond into a conformation in which it benefits from close to optimal stereoelectronic interactions. However, the previous proposal of Nifant'ev regarding axial orientation of the Me_2N of **4**, which we showed above to be 75–80% in conformation **20**, together with unpublished results from this laboratory concerning the primary population of **21** by **26**, the analog of **14** with Me in place of Ph at N(3), requires an additional, overriding consideration. The dominant influence on the equilibrium **20** $\rightleftarrows$ **21** for **4**, **13**, and **14** appears to be the strong destabilization of **21** by steric repulsions between the relatively large substituents Ph and *i*-Pr at N(3) and the equatorial Me_2N. The dominance of steric repulsions between relatively large substitutents on N(3) and *equatorial* Me_2N on phosphorus is in contrast to the established influence on conformations of the corresponding 2-oxo-1,3,2-oxazaphosphorinanes of repulsions between *axial* Me_2N or Ph on phosphorus and Me or Ph at N(3). The latter interactions were shown to *destabilize the 2-oxo form of 20 in favor of the chair conformation corresponding to 21.*

The essential correctness of the above ideas is further supported by their use to rationalize the conformational (chair–boat/twist) equilibria observed for *cis*- and *trans*-**17**. It also is evident from the studies of *cis*- and *trans*-**17** that the free energy difference between chair and boat/twist conformations of three-coordinate 1,3,2-oxazaphosphorinanes is comparatively small. These studies clearly demonstrate the variety of steric and stereoelectronic interactions that are operative in the conformational equilibria of 1,3,2-oxazaphosphorinanes. One also sees the contrasting conformational features of 1,3,2-dioxa- and 1,3,2-oxazaphosphorinanes that possess three-coordinate phosphorus, and the differences between the conformational properties of 1,3,2-oxazaphosphorinanes containing three-coordinate phosphorus and those of their 2-oxo counterparts.

Experimental Section

Materials. Commercial reagents and solvents were used as received unless otherwise noted. Diethyl ether and tetrahydrofuran (THF) were dried over sodium/benzophenone. Both were freshly distilled before use. Other solvents were OmniSolv grade from EM industries Inc. Zinc chloride was dried under vacuum with occasional heating with a heat gun for 30 min. Anilines were freshly distilled before use. 2,2-Dimethyl-3-hydroxypropionaldehyde, purchased from Aldrich Chemical Co., was purified by Kugelrohr distillation.

Spectral and Physical Data. ^{31}P NMR spectra were taken on Varian XL-300 and Unity-300 spectrometers at 121 MHz with proton-decoupling ($\{^1H\}$). Positive ^{31}P NMR chemical shifts are expressed in ppm downfield from external 85% H_3PO_4. Integrated ^{31}P spectra (**17**) were obtained using a 50-s delay between aquisitions. ^1H NMR spectra were recorded on Varian XL-300, Unity-300, and VXR-500 spectrometers. ^{13}C NMR spectra were determined at 75 MHz on Varian XL-300 and Unity-300 spectrometers. An APT (attached proton test) ^{13}C NMR spectrum was obtained to aid the assignments of the resonances of **17**. ^1H and ^{13}C NMR chemical shifts are expressed in ppm relative to the internal tetramethylsilane (TMS). Detailed NMR parameters not given in Tables III–IV are recorded in this section. For compounds **7–17** only ^1H NMR couplings not given in the tables are recorded below.

Crystals **11** and **13**, both from *n*-pentane, with dimensions of $0.23 \times 0.19 \times 0.15$ mm^3 and $0.28 \times 0.15 \times 0.08$ mm^3, respectively, were glued and sealed in capillary tubes under argon atmosphere and then mounted on the instrument. The data were collected on an Enraf-Nonius CAD4 diffractometer at −125 °C. Cell constants were obtained from 25 reflections within $15° < 2\theta < 25°$. The space groups were determined from subsequent least-squares refinement. Standard reflections showed decay (4% for **11** and 12% for **13**) during data collection, and an anisotropic decay correction was applied. Lorentz and polarization corrections, and an empirical absorption correction, based on a series of ψ scans, were applied to the data. The structures were solved by direct method techniques with a SDP/VAX package. All hydrogen atoms were located and refined with fixed isotropic thermal parameters. Scattering factors[23] and $\Delta f'$ and $\Delta f''$ factors[24] were taken from the literature. A more detailed description of the above procedures has been published.[25,26]

Mass spectra (GC/MS and GC/HRMS) were recorded on a Finnigan MAT 95 instrument operating in the electron ionization mode (EI). Gas chromatographic analyses were performed on a Varian 3300 gas chromatograph equipped with an HP-capillary column (25 m × 0.32 mm) and flame ionization detection. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA, and Galbraith laboratories, Inc., Knoxville, TN. Melting points are uncorrected.

Preparation of *N*-Phenyl-2-(hydroxymethyl)-2-methylpropylamine. Zinc chloride (3.65 g, 26.8 mmol) and sodium cyanoborohydride (3.43 g, 51.9 mmol) were added to 90 mL of methanol. The solution was stirred at room temperature for 1 h and then poured into a solution of 2,2-dimethyl-3-hydroxypropionaldehyde (5.47 g, 53.5 mmol) and aniline (6.86 g, 73.6 mmol) in 140 mL of methanol at room temperature which was then rapidly stirred under argon over a 36-h period. The reaction was quenched with 300 mL of 0.1 N NaOH. After most of the methanol was removed under reduced pressure, the aqueous solution was extracted with 3 × 150 mL of diethyl ether. The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was short-path distilled under vacuum to give 6.33 g of a colorless liquid (35.3 mmol, 66% yield): bp 110–114 °C (0.2 mmHg) (lit.[27] bp 108–110 °C (0.25 mmHg)).

Preparation of *N*-(*m*-(Trifluoromethyl)phenyl)-2-(hydroxymethyl)-2-methylpropylamine. By a procedure directly analogous to the above, reaction of zinc chloride (3.65 g, 26.8 mmol) and sodium cyanoborohydride (3.36 g, 50.9 mmol) in 90 mL of methanol and a solution of 2,2-dimethyl-3-hydroxypropionaldehyde (5.47 g, 53.5 mmol) and *m*-(trifluoromethyl)aniline (12.9 g, 80.3 mmol) in 140 mL of methanol at room temperature gave 7.31 g of product as a colorless liquid (29.6 mmol, 55% yield): bp 112–115 °C (0.25 mmHg) (lit.[27] bp 104–105 °C (0.07 mmHg)).

Preparation of 3-(Phenylamino)-1-propanol. A mixture of 3-chloro-1-propanol (17.4 g, 15.4 mL, 0.181 mol) and aniline (50 mL, 51.1 g, 0.549 mol) was heated at 95–105 °C for 5 h. The reaction mixture was taken up in 100 mL of diethyl ether and washed with 2 × 100 mL of 1 N NaOH. The combined aqueous

(23) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IX, Table 2.2B.

(24) Cromer, D. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England; Vol. IV, Table 2.3.1.

(25) Yu, J. H.; Arif, A. M.; Bentrude, W. G. *J. Am. Chem. Soc.* **1990**, *112*, 7451–7461.

(26) The authors have deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

layers were extracted with diethyl ether (2 × 100 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was short-path distilled to give 19.7 g of a thick yellow-green liquid (0.131 mol, 72% yield): bp 122–126 °C (0.3 mmHg) (lit.[28] bp 172–179 °C (11 mmHg)); ^1H NMR (300 MHz, $CDCl_3$) δ 1.87 (quintet, $^3J_{HH}$ = 6.1 Hz, 2 H, $CH_2CH_2CH_2$), 3.27 (t, 2 H, CH_2NH), 3.80 (t, 2 H, CH_2OH), 6.62–6.79, 7.15–7.21 (m, 5 H, C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$, $\{^1H\}$) δ 31.63 (s, 1 C, $CH_2CH_2CH_2$), 41.55 (s, 1 C, CH_2NH), 61.01 (s, 1 C, CH_2OH), 112.98 (s, 2 C, *o*-Ph), 117.44 (s, 1 C, *p*-Ph), 129.08 (s, 2 C, *m*-Ph), 148.16 (s, 1 C, *ipso*-Ph). Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.63; N, 9.22. Found: C, 71.23; H, 8.64; N, 9.20.

2-(Dimethylamino)-3-isopropyl-1,3,2-oxazaphosphorinane (4) was prepared by the method of Nifant'ev et al.[4a] The requisite 2-chloro-3-isopropyl-1,3,2-oxazaphosphorinane precursor was obtained from PCl_3 and the amino alcohol, prepared by a literature procedure.[29]

Preparation of 2-Methoxy-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (7). A solution of 2-chloro-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane[2g] (3.60 g, 14.8 mmol) in 25 mL of dry diethyl ether was added dropwise to a solution of methanol (0.50 g, 16.3 mmol) and triethylamine (1.70 g, 16.3 mmol) in 55 mL of dry diethyl ether at 0 °C with rapid stirring. The mixture was slowly warmed to room temperature and continuously stirred overnight. The salt was removed by Schlenk techniques, and the solvent was removed by rotary evaporation. The residue was short-path distilled to give 2.90 g of a colorless liquid, 99% pure by GC (12.0 mmol, 81% yield): bp 90–91 °C (0.025 mmHg). Further purification by molecular distillation gave analytically pure product (bp 40–41 °C (0.025 mmHg)): ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 125.5 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.47, 1.09 (two s, 6 H, $C(CH_3)_2$), 2.66 (ddd, 1 H, H_D, $^2J_{CD}$ = −11.8 Hz), 3.18 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.4 Hz), 3.19 (d, $^3J_{PH}$ = 12.1 Hz, 3 H, OCH_3), 3.51 (dd, 1 H, H_C, $^2J_{CD}$ = −11.8 Hz), 3.98 (dd, 1 H, H_A, $^2J_{AB}$ = −10.4 Hz), 6.83–6.89, 7.13–7.15 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6, $\{^1H\}$) δ 23.08, 24.23 (two s, 2 C, $C(CH_3)_2$), 31.85 (s, 1 C, C_5), 50.67 (d, 1 C, OCH_3, $^2J_{PC}$ = 17.7 Hz), 54.30 (d, 1 C, C_4, $^2J_{PC}$ = 2.1 Hz), 68.35 (d, 1 C, C_6, $^2J_{PC}$ = 2.8 Hz), 120.69 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 13.1 Hz), 122.08 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 2.1 Hz), 129.38 (s, 2 C, *m*-Ph), 148.34 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 17.9 Hz). Anal. Calcd for $C_{12}H_{18}NO_2P$: C, 60.24; H, 7.58; N, 5.85. Found: C, 60.18; H, 7.61; N, 5.79.

Preparation of 2-(1,1,1,3,3,3-Hexafluoroisopropoxy)-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (8). By a procedure directly analogous to that for the preparation of 7, the reaction of 1,1,1,3,3,3-hexafluoro-2-propanol (2.50 g, 14.4 mmol) and triethylamine (1.50 g, 14.4 mmol) in 50 mL of dry diethyl ether and 2-chloro-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane[2g] (3.50 g, 14.4 mmol) in 20 mL of dry diethyl ether gave 4.50 g of a colorless liquid (12.0 mmol, 83% yield): bp 82–83 °C (0.025 mmHg); ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 131.1 (septet, $^4J_{PF}$ = 6.2 Hz); ^1H NMR (300 MHz, C_6D_6) δ 0.34, 0.97 (two s, 6 H, $C(CH_3)_2$), 2.48 (ddd, 1 H, H_D, $^2J_{CD}$ = −11.9 Hz), 3.17 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.6 Hz), 3.41 (dd, 1 H, H_C, $^2J_{CD}$ = −11.9 Hz), 3.97 (dd, 1 H, H_A, $^2J_{AB}$ = −10.6 Hz), 4.04 (d of septet, 1 H, $OCH(CF_3)$, $^3J_{PH}$ = 13.6 Hz, $^3J_{FH}$ = 6.0 Hz), 6.87–6.93, 7.00–7.04, 7.08–7.14 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6, $\{^1H\}$) δ 22.67, 23.76 (two s, 2 C, $C(CH_3)_2$), 31.36 (d, 1 C, C_5, $^3J_{PC5}$ = 1.0 Hz), 55.28 (d, 1 C, C_4, $^2J_{PC4}$ = 2.7 Hz), 69.68 (d, 1 C, C_6, $^2J_{PC6}$ = 3.6 Hz), 71.01 (d of septet, 1 C, $OCH(CF_3)_2$, $^2J_{PC}$ = 21.0 Hz, $^1J_{FC}$ = 33.4 Hz), 122.29 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 11.4 Hz), 123.87 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 2.5 Hz), 129.49 (s, 2 C, *m*-Ph), 146.37 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 18.4 Hz). The CF_3 carbon signals were too weak to be observed. Anal. Calcd for $C_{14}H_{16}F_6NO_2P$: C, 44.81; H, 4.30; N, 3.73. Found: C, 44.87; H, 4.31; N, 3.67.

Preparation of 2-Methoxy-3-phenyl-1,3,2-oxazaphosphorinane (9). By a procedure directly analogous to that for the preparation of 7, the reaction of methanol (0.71 g, 0.90 mL, 22.0 mmol) and triethylamine (2.22 g, 22.0 mmol) in 50 mL of dry diethyl ether and 2-chloro-3-phenyl-1,3,2-oxazaphosphorinane[2g] (4.31 g, 20.0 mmol) in 150 mL of dry diethyl ether gave 3.55 g of a colorless liquid (16.8 mmol, 84% yield): bp 90 °C (0.025 mmHg); ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 133.7 (s); ^1H NMR (300 MHz, C_6D_6) δ 1.15 (ddddd, 1 H, H_Y, $^2J_{XY}$ = −13.7 Hz), 1.90 (ddddd, 1 H, H_X, $^2J_{XY}$ = −13.7 Hz), 2.88 (ddddd, 1 H, H_D, $^2J_{CD}$ = −12.0 Hz), 3.19 (d, 3 H, OCH_3, $^3J_{PH}$ = 12.2 Hz), 3.50 (ddddd, 1 H, H_B, $^2J_{AB}$ = −10.7 Hz), 3.57 (dddd, 1 H, H_C, $^2J_{CD}$ = −12.0 Hz), 4.07 (dddd, 1 H, H_A, $^2J_{AB}$ = −10.7 Hz), 6.83–6.90, 7.10–7.17 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6 $\{^1H\}$) δ 27.19 (d, 1 C, C_5, $^3J_{PC5}$ = 1.7 Hz), 42.60 (d, 1 C, C_4, $^2J_{PC4}$ = 2.0 Hz), 50.68 (d, $^2J_{PC}$ = 17.9 Hz, 1 C, OCH_3), 59.06 (d, 1 C, C_6, $^2J_{PC6}$ = 2.7 Hz), 119.98 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 13.3 Hz), 121.85 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 2.5 Hz), 129.33 (s, 2 C, *m*-Ph), 148.06 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 17.9 Hz). Anal. Calcd for $C_{10}H_{14}NO_2P$: C, 56.87; H, 6.68; N, 6.63. Found: C, 56.81; H, 6.69; N, 6.58.

Preparation of 2-(1,1,1,3,3,3-Hexafluoroisopropoxy)-3-phenyl-1,3,2-oxazaphosphorinane (10). By a procedure analogous to that for the preparation of 7, the reaction of 2-chloro-3-phenyl-1,3,2-oxazaphosphorinane[2g] (6.73 g, 31.2 mmol) in 150 mL of diethyl ether with triethylamine (3.47 g, 4.80 mL, 34.3 mmol) and hexafluoro-2-propanol (5.83 g, 3.7 mL, 34.3 mmol) in 50 mL of diethyl ether gave 9.91 g of product (28.5 mmol, 91% yield): bp 97–98 °C (0.25 mmHg); ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 138.7 (septet, $^4J_{PF}$ = 6.2 Hz); ^1H NMR (300 MHz, C_6D_6) δ 1.08 (ddddd, 1 H, H_Y, $^2J_{XY}$ = −14.0 Hz), 1.68 (ddddd, 1 H, H_X, $^2J_{XY}$ = −14.0 Hz), 2.69 (ddddd, 1 H, H_D, $^2J_{CD}$ = −11.7 Hz), 3.38 (dddd, 1 H, H_C, $^2J_{CD}$ = −11.7 Hz), 3.45 (ddddd, 1 H, H_B, $^2J_{AB}$ = −11.0 Hz), 4.00 (dddd, 1 H, H_A, $^2J_{AB}$ = −11.0 Hz), 4.05 (d of septet, 1 H, $OCH(CF_3)_2$, $^3J_{PH}$ = 7.7 Hz, $^3J_{FH}$ = 6.0 Hz), 6.85–6.91, 6.77–7.01, 6.97–7.01, 7.08–7.14 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6 $\{^1H\}$) δ 26.36 (d, 1 C, C_5, $^3J_{PC5}$ = 2.1 Hz), 43.44 (d, 1 C, C_4, $^2J_{PC4}$ = 2.8 Hz), 60.56 (d, 1 C, C_6, $^2J_{PC6}$ = 3.6 Hz), 70.01 (d of septet, 1 C, $OCH(CF_3)_2$, $^2J_{PC}$ = 21.1 Hz, $^2J_{FC}$ = 33.2 Hz), 121.30 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 12.0 Hz), 122.08 (q, 2 C, $CH(CF_3)_2$, $^1J_{FC}$ = 284.2 Hz), 123.54 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 2.6 Hz), 129.43 (s, 2 C, *m*-Ph), 146.18 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 18.2 Hz). Anal. Calcd for $C_{12}H_{12}F_6NO_2P$: C, 41.51; H, 3.48; P, 8.92; N, 4.03. Found: C, 41.48; H, 3.49; P, 8.49; N, 4.04.

Preparation of 2,3-Diphenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (11). A solution of *N*-phenyl-2-(hydroxymethyl)-2-methylpropylamine (2.79 g, 15.6 mmol) and bis(diethylamino)phenylphosphine[30] (3.93 g, 15.6 mmol) in refluxing acetonitrile (250 mL) over a period of 9 days gave 3.00 g of product as an oil (10.5 mmol, 67% yield) which became solid at −20 °C and was recrystallized from *n*-pentane to give white crystals: mp 56.5–57.0 °C; ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 111.9 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.17, 1.08 (two s, 6 H, $C(CH_3)_2$), 3.06 (ddd, 1 H, H_D, $^2J_{CD}$ = −13.6 Hz), 3.19 (d, 1 H, H_C, $^2J_{CD}$ = −13.6 Hz), 3.28 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.7 Hz), 3.61 (dd, 1 H, H_A, $^2J_{AB}$ = −10.7 Hz), 6.84–6.89, 7.05–7.10, 7.13–7.22, 7.46–7.51 (m, 10 H, two phenyl); ^{13}C NMR (75 MHz, $CDCl_3$, $\{^1H\}$) δ 23.13, 23.69 (two s, 2 C, $C(CH_3)_2$), 33.30 (d, 1 C, C_5, $^3J_{PC5}$ = 1.0 Hz), 50.03 (d, 1 C, C_4, $^2J_{PC4}$ = 3.1 Hz), 72.23 (d, 1 C, C_6, $^2J_{PC6}$ = 5.4 Hz), 119.26 (d, 2 C, *o*-PhN, $^3J_{PC}$ = 15.8 Hz), 120.98 (d, 1 C, *p*-PhN, $^5J_{PC}$ = 1.7 Hz), 129.47 (s, 2 C, *m*-PhN), 150.92 (d, 1 C, *ipso*-PhN, $^2J_{PC}$ = 23.8 Hz), 128.83 (d, 1 C, *p*-PhP, $^4J_{PC}$ = 1.7 Hz), 129.21 (d, 2 C, *o*-PhP, $^2J_{PC}$ = 2.0 Hz), 130.23 (d, 2 C, *m*-PhP, $^3J_{PC}$ = 15.6 Hz), 140.74 (d, 1 C, *ipso*-PhP, $^1J_{PC}$ = 30.7 Hz). Anal. Calcd for $C_{17}H_{20}NOP$: C, 71.56; H, 7.07. Found: C, 71.64; H, 7.12.

Preparation of 2-(Methylamino)-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (12). To a rapidly stirred solution of triethylamine (2.51 g, 24.8 mmol) in 150 mL of dry diethyl ether cooled with an ice/salt bath at −15 to −12 °C was added dropwise a solution of 2-chloro-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane[2g] (6.05 g, 24.8 mmol) in 50 mL of dry diethyl ether. Methylamine gas was simultaneously bubbled through the stirred solution. The admission of methylamine gas was continued for another 5 min after the addition was complete. The resulting mixture was slowly warmed to room temperature and continuously stirred overnight. The salt was removed by Schlenk techniques, and the solvent was removed by rotary evaporation to give 4.50 g of product as an oil, >98% pure by GC (18.5 mmol, 75% yield). An attempt to further purify a sample

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by vacuum distillation failed (oil bath 180 °C (0.025 mmHg); sample was decomposed): GC/HRMS calcd for $C_{12}H_{19}N_2OP$ (*m/z*) 238.1235, found 238.1240; ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 108.6 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.53, 1.07 (two s, 6 H, $C(CH_3)_2$), 2.11 (1 H, $NHCH_3$, broad s), 2.33 (dd, 3 H, $NHCH_3$, $^3J_{PH}$ = 12.1 Hz, $^3J_{HH}$ = 5.9 Hz), 2.80 (ddd, 1 H, H_D, $^2J_{CD}$ = −12.3 Hz), 2.98 (dd, 1 H, H_C, $^2J_{CD}$ = −12.3 Hz), 3.16 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.7 Hz), 3.64 (dd, 1 H, H_A, $^2J_{AB}$ = −10.7 Hz), 6.80–6.86, 7.14–7.16 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6, $\{^1H\}$) δ 23.12, 24.20 (two s, 2 C, $C(CH_3)_2$), 28.54 (d, 1 C, $NHCH_3$, $^2J_{PC}$ = 24.7 Hz), 31.96 (s, 1 C, C_5), 54.65 (d, 1 C, C_4, $^2J_{PC4}$ = 2.9 Hz), 67.57 (d, 1 C, C_6, $^2J_{PC6}$ = 3.4 Hz), 119.50 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 14.4 Hz), 120.83 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 2.3 Hz), 129.25 (s, 2 C, *m*-Ph), 149.43 (d,1 C, *ipso*-Ph, $^2J_{PC}$ = 16.9 Hz).

Preparation of 2-(Dimethylamino)-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (13). A solution of *N*-phenyl-2-(hydroxymethyl)-2-methylpropylamine (0.99 g, 5.5 mmol) and hexamethylphosphorous triamide (HMPT) (0.90 g, 1.0 mL, 5.5 mmol) in 20 mL of dry acetonitrile was refluxed under an argon atmosphere over a period of 34 h. GC analysis showed the reaction to be complete. The solvent was removed under reduced pressure, and the residue was short-path distilled to give 0.58 g of product (2.3 mmol, 42% yield): bp 97–98 °C (0.05 mmHg). No attempt was made to optimize the yield. The product became solid at −20 °C and was recrystallized from *n*-pentane to give white crystals: mp 46–47 °C; ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 120.7 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.61, 0.98 (two s, 6 H, $C(CH_3)_2$), 2.36 (d, 6 H, $N(CH_3)_2$, $^3J_{PH}$ = 8.6 Hz), 2.92 (ddd, 1 H, H_D, $^2J_{CD}$ = −12.3 Hz), 3.29 (dd, 1 H, H_C, $^2J_{CD}$ = −12.3 Hz), 3.25 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.6 Hz), 3.80 (dd, 1 H, H_A, $^2J_{AB}$ = −10.6 Hz), 6.82–6.88 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, $CDCl_3$, $\{^1H\}$) δ 23.68, 24.48 (two s, 2 C, $C(CH_3)_2$), 37.28 (d, 2 C, $N(CH_3)_2$, $^2J_{PC}$ = 17.9 Hz), 32.41 (d, 1 C, C_5, $^3J_{PC}$ = 1.0 Hz), 56.13 (d, 1 C, C_4, $^2J_{PC}$ = 0.8 Hz), 70.41 (d, 1 C, C_6, $^2J_{PC}$ = 2.4 Hz), 119.30 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 14.1 Hz), 120.84 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 1.9 Hz), 129.24 (s, 2 C, *m*-Ph), 149.66 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 17.4 Hz). Anal. Calcd for $C_{13}H_{21}N_2OP$: C, 61.89; H, 8.39; P, 12.28. Found: C, 61.77; H, 8.43; P, 12.35.

Preparation of 2-(Dimethylamino)-3-phenyl-1,3,2-oxazaphosphorinane (14). By a procedure directly analogous to that for the preparation of **13**, the reaction of 3-(phenylamino)-1-propanol (9.58 g, 63.4 mmol) and HMPT (10.3 g, 11.5 mL, 63.4 mmol) in ethyl acetate (80 mL) and toluene (80 mL) over a period of 23 h gave 9.39 g of a colorless liquid (41.9 mmol, 66% yield): bp 115–122 °C (0.1 mmHg); ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 126.9 (s); ^1H NMR (300 MHz, C_6D_6) δ 1.24 (ddddd, 1 H, H_Y, $^2J_{XY}$ = −13.4 Hz), 1.69 (ddddd, 1 H, H_X, $^2J_{XY}$ = −13.4 Hz) 2.40 (d, 6 H, $N(CH_3)_2$, $^3J_{PH}$ = 8.6 Hz), 3.12 (ddddd, 1 H, H_D, $^2J_{CD}$ = −12.4 Hz), 3.39 (dddd, 1 H, H_C, $^2J_{CD}$ = −12.4 Hz), 3.56 (ddddd, 1 H, H_B, $^2J_{AB}$ = −10.8 Hz), 3.87 (dddd, 1 H, H_A, $^2J_{AB}$ = −10.8 Hz), 6.83–6.89, 7.09–7.21 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6 $\{^1H\}$) δ 27.10 (d, 1 C, C_5, $^3J_{PC5}$ = 2.3 Hz), 37.08 (d, 2 C, $N(CH_3)_2$, $^2J_{PC}$ = 18.1 Hz), 43.97 (d, 1 C, C_4, $^2J_{PC4}$ = 1.1 Hz), 60.38 (d, 1 C, C_6, $^2J_{PC6}$ = 2.3 Hz), 118.61 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 13.5 Hz), 120.65 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 1.9 Hz), 129.20 (s, 2 C, *m*-Ph), 149.32 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 17.2 Hz). Anal. Calcd for $C_{11}H_{17}N_2OP$: C, 58.92; H, 7.64; N, 12.49. Found: C, 59.01; H, 7.68; N, 12.42.

Preparation of 2-(Dimethylamino)-3-(*m*-(trifluoromethyl)phenyl)-5,5-dimethyl-1,3,2-oxazaphosphorinane (15). A procedure analogous to that for the preparation of **13** was used for the reaction of *N*-(*m*-(trifluoromethyl)phenyl)-2-(hydroxymethyl)-2-methylpropylamine (9.15 g, 37.0 mmol) and HMPT (6.03 g, 6.7 mL, 37.0 mmol) in 60 mL of toluene and 60 mL of ethyl acetate for 2 days to give 8.24 g of a colorless liquid (26.9 mmol, 73% yield): bp 109–114 °C (0.05 mmHg); ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 120.8 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.57, 0.86 (two s, 6 H, $C(CH_3)_2$), 2.30 (d, 6 H, $N(CH_3)_2$, $^3J_{PH}$ = 8.6 Hz), 2.82 (ddd, 1 H, H_D, $^2J_{CD}$ = −12.2 Hz), 3.12 (dd, 1 H, H_C, $^2J_{CD}$ = −12.2 Hz), 3.22 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.5 Hz), 3.65 (dd, 1 H, H_A, $^2J_{AB}$ = −10.5 Hz), 6.95 (t, 1 H, *m*-Ph, $^3J_{HH}$ = 7.8 Hz), 7.04 (d, 1 H, *o*-Ph, $^3J_{HH}$ = 7.8 Hz), 7.19 (dq, 1 H, *p*-Ph, $^3J_{HH}$ = 7.8 Hz, $^4J_{HF}$ = 1.5 Hz), 7.49 (q, 1 H, *o*-Ph, $^4J_{HF}$ = 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $\{^1H\}$) δ 23.7, 24.5 (two s, 2 C, $C(CH_3)_2$), 32.57 (d, 1 C, C_5, $^3J_{PC}$ = 1.1 Hz), 37.10 (d, 2 C, $N(CH_3)_2$, $^2J_{PC}$ = 18.1 Hz), 56.14 (s, 1 C, C_4), 70.94 (d, 1 C, C_6, $^2J_{PC}$ = 1.9 Hz), 114.6 (dq, 1 C, *o*-Ph, $^2J_{PC}$ = 13.4 Hz, $^3J_{FC}$ = 4.0 Hz), 116.6 (dq, 1 C, *p*-Ph, $^5J_{PC}$ = 1.9 Hz, $^3J_{FC}$ = 7.7 Hz), 121.4 (dq, 1 C, *o*-Ph, $^3J_{PC}$ = 15.3 Hz, $^5J_{FC}$ = 1.2 Hz), 124.2 (q, 1 C, CF_3, $^1J_{FC}$ = 272.4 Hz), 129.3 (s, 1 C, *m*-Ph), 131.1 (q, 1 C, *m*-Ph, $^2J_{FC}$ = 32.0 Hz), 149.5 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 16.7 Hz). Anal. Calcd for $C_{14}H_{20}F_3N_2OP$: C, 52.50; H, 6.29; N, 8.75. Found: C, 52.49; H, 6.28; N, 8.67.

Preparation of 2-(Dimethylamino)-3-(*p*-*N*,*N*-dimethylanilino)-5,5-dimethyl-1,3,2-oxazaphosphorinane (16). A solution of N-(*p*-(*N*,*N*-dimethylamino)phenyl)-2-(hydroxymethyl)-2-methylpropylamine[2j] (1.94 g, 8.72 mmol) and HMPT (1.42 g, 8.72 mmol) in 50 mL of acetonitrile was refluxed overnight. The solvent was removed under reduced pressure, and the residue was Kugelrohr distilled to give 1.20 g of a white solid (4.1 mmol, 48% yield): air bath temperature 125–130 °C (0.025 mmHg); mp 54–55 °C; ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ 124.3 (s); ^1H NMR (300 MHz, C_6D_6) δ 0.73, 1.03 (two s, 6 H, $C(CH_3)_2$), 2.48 (d, 6 H, $PN(CH_3)_2$, $^3J_{PH}$ = 8.5 Hz), 2.55 (s, 6 H, $C_6H_4N(CH_3)_2$), 2.98 (ddd, 1 H, H_D, $^2J_{CD}$ = −12.1 Hz), 3.36 (ddd, 1 H, H_B, $^2J_{AB}$ = −10.5 Hz), 3.38 (dd, 1 H, H_C, $^2J_{CD}$ = −12.1 Hz), 3.85 (dd, 1 H, H_A, $^2J_{AB}$ = −10.5 Hz), 6.65, 7.18 (m, 4 H, C_6H_4); ^{13}C NMR (75 MHz, C_6D_6, $\{^1H\}$) δ 23.85, 24.52 (two s, 2 C, $C(CH_3)_2$), 32.58 (d, 1 C, C_5, $^3J_{PC}$ = 1.4 Hz), 37.35 (d, 2 C, $PN(CH_3)_2$, $^2J_{PC}$ = 18.0 Hz), 41.22 (s, 2 C, $C_6H_4N(CH_3)_2$), 58.33 (s, 1 C, C_4), 70.76 (d, 1 C, C_6, $^2J_{PC}$ = 1.5 Hz), 114.46 (s, 2 C, *m*-$C_6H_4N(CH_3)_2$), 122.60 (d, 2 C, *o*-$C_6H_4N(CH_3)_2$, $^3J_{PC}$ = 10.5 Hz), 140.31 (d, 1 C, *ipso*-$C_6H_4N(CH_3)_2$, $^2J_{PC}$ = 17.3 Hz), 146.77 (d, 1 C, *p*-$C_6H_4N(CH_3)_2$, $^5J_{PC}$ = 1.7 Hz). The analytical sample was prepared by molecular distillation and transferred in a glove bag under a nitrogen atmosphere to an ampoule which was flame sealed. Anal. Calcd for $C_{15}H_{26}N_3OP$: C, 60.99; H, 8.87, N, 14.23. Found: C, 60.74; H, 8.81; N, 14.08.

Preparation of 2-(Dimethylamino)-3-phenyl-5-*tert*-butyl-1,3,2-oxazaphosphorinane (17). By a procedure directly analogous to that for the preparation of **12**, the reaction of 2-chloro-3-phenyl-5-*tert*-butyl-1,3,2-oxazaphosphorinane[2c] (7.83 g, 28.9 mmol) and triethylamine (2.93 g, 28.9 mmol) and dimethylamine in 300 mL of dry diethyl ether for 4 h was run. The salt was removed by Schlenk techniques, and the solvent was removed in vacuo at 0 °C to give 7.46 g of a white solid product containing cis/trans diastereomers in an 18/82 (cis/trans) ratio (^{31}P NMR) (26.6 mmol, 92% yield). After distillation the cis/trans ratio changed to 64/36. This ratio slowly changed to a stable value of 80/20 (cis/trans) in C_6D_6 at room temperature: ^{31}P NMR (121 MHz, C_6D_6, $\{^1H\}$) δ *cis*-diastereomer 124.2 (s), *trans*-diastereomer 127.0 (s); ^1H NMR (300 MHz, C_6D_6) *cis*-diastereomer δ 0.690 (s, 9 H, $C(CH_3)_3$), 1.72 (dddd, 1 H, H_X), 2.48 (d, $^3J_{PH}$ = 8.8 Hz, 6 H, $N(CH_3)_2$), 3.44 (dddd, 1 H, H_D, $^2J_{CD}$ = −12.7 Hz), 3.52 (ddd, 1 H, H_C, $^2J_{CD}$ = −12.7 Hz), 3.77 (dddd, 1 H, H_B, $^2J_{AB}$ = −11.2 Hz), 3.90 (ddd, 1 H, H_A, $^2J_{AB}$ = −11.2 Hz), 6.85–6.90, 7.09–7.12, 7.18–7.24 (m, 5 H, phenyl); *trans*-diastereomer δ 0.687 (s, 9 H, $C(CH_3)_3$), 1.93 (dddd, 1 H, H_X), 2.57 (d, $^3J_{PH}$ = 8.3 Hz, 6 H, $N(CH_3)_2$), 3.26 (ddd, 1 H, H_C, $^2J_{CD}$ = −11.9 Hz), 3.50 (dddd, 1 H, H_D, $^2J_{CD}$ = −11.9 Hz), 3.73 (ddd, 1 H, H_A, $^2J_{AB}$ = −11.3 Hz), 3.96 (dddd, 1 H, H_B, $^2J_{AB}$ = −11.3 Hz), 6.85–6.90, 7.09–7.12, 7.18–7.24 (m, 5 H, phenyl); ^{13}C NMR (75 MHz, C_6D_6, $\{^1H\}$) *cis*-diastereomer δ 27.17 (s, 3 C, $C(CH_3)_3$), 31.73 (s, 1 C, $C(CH_3)_3$), 36.92 (d, 2 C, $N(CH_3)_2$, $^2J_{PC}$ = 18.4 Hz), 45.77 (d, 1 C, C_5, $^3J_{PC5}$ = 1.4 Hz), 44.87 (d, 1 C, C_4, $^2J_{PC4}$ = 2.4 Hz), 61.83 (s, 1 C, C_6), 118.22 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 14.0 Hz), 120.43 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 1.7 Hz), 129.33 (s, 2 C, *m*-Ph), 149.28 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 18.1 Hz); *trans*-diastereomer δ 27.29 (s, 3 C, $C(CH_3)_3$), 32.00 (s, 1 C, $C(CH_3)_3$), 36.63 (d, 2 C, $N(CH_3)_2$, $^2J_{PC}$ = 19.2 Hz), 46.84 (d, 1 C, C_5, $^3J_{PC5}$ = 3.8 Hz), 46.60 (d, 1 C, C_4, $^2J_{PC4}$ = 3.6 Hz), 62.88 (s, 1 C, C_6), 119.16 (d, 2 C, *o*-Ph, $^3J_{PC}$ = 10.1 Hz), 120.79 (d, 1 C, *p*-Ph, $^5J_{PC}$ = 1.4 Hz), 129.27 (s, 2 C, *m*-Ph), 149.25 (d, 1 C, *ipso*-Ph, $^2J_{PC}$ = 14.8 Hz). Anal. Calcd for $C_{15}H_{25}N_2OP$: C, 64.26; H, 8.99; N, 9.99. Found: C, 64.10; H, 8.97; N, 9.90.

Acknowledgment. Support of this work by a grant (CA11045) from the National Cancer Institute of the Public Health Service is gratefully acknowledged. We also thank Dr. Alan E. Sopchik for the 500-MHz spectra and help in analyzing those spectra. Funds for the purchase of the Finnigan MAT 95 mass spectrometer were supplied by National Science Foundation Grant CHE-9002690 and the University of Utah Institutional Funds Committee.