Diastereoselective alkylations of chiral, phosphorus-stabilized carbanions: *N*-alkyl substituent effects in *P*-alkyl-1,3,2-diazaphosphorinane 2-oxides

Scott E. Denmark and Jung-Ho Kim

Abstract: A systematic study of the diastereoselective alkylation of anions derived from racemic *N*-substituted *P*-alkyl 1,3,2-diazaphosphorinane 2-oxides was carried out with variation of the *N*-substituent. High diastereoselectivity for the methylation of a *P*-benzyl anion has been achieved with *N*-neopentyl derivative **5d**. Similarly, a *P*-ethyl anion derived from *N*-neopentyl derivative **6d** showed high diastereoselectivity upon benzylation. The observed difference in alkylation diastereoselectivity between *P*-ethyl and *P*-benzyl anions for various *N*-alkyl substituents is discussed.

Key words: phosphonamide-stabilized carbanions, alkylation, asymmetric, stereoselective, organolitihium.

Résumé : On a réalisé une étude systématique de l'alkylation diastéréosélective d'anions dérivés de 2-oxydes de *P*-alkyl-1,3,2-diazaphosphorinanes *N*-substitués racémiques portant divers substituants sur l'azote. Avec l'anion **5d** qui porte des groupes *P*-benzyle et *N*-néopentyle, la méthylation se fait avec une diastéréosélectivité élevée. Il en est de même lors de la réaction de benzylation de l'anion **6d** qui porte des groupes *P*-éthyle et *N*-néopentyle. On discute des différences observées dans la diastéréosélectivité des anions *P*-éthyle et *P*-benzyle portant divers substituants *N*-alkyles.

Mots clés : carbanions phosphonamides stabilisés, alkylation, asymétrique, stéréosélective, organolithium.

[Traduit par la Rédaction]

Introduction and background

In recent years there has been considerable interest in carbon–carbon single-bond forming reactions involving heteroatom-stabilized carbanions (for reviews see ref. (1)). Among them, phosphorus-based reagents have great potential for auxiliary-based chiral modification (2). As part of an ongoing program on the chemistry of chiral, phosphorus-stabilized carbanions (3) we have been interested in developing general auxiliaries which give rise to highly selective transformations at the anionic carbon. The design criteria we formulated require that the auxiliary be capable of biasing the rotameric population about the C—P bond and also shield one of the anion faces to achieve a highly selective approach of the electrophilic reagents. In addition, other practical considerations were: (*i*) ease of synthesis in enantiomerically pure form, (*ii*) chemical stability under the attachment and recovery conditions, and (*iii*) structural simplicity while providing high stereochemical bias. Auxiliaries (4, 5) and controller groups (6) of C_2-symmetry have been utilized a great deal in asymmetric synthesis. In the chemistry of phosphorus-stabilized anions as well, Hanessian has pioneered the use of the 1,2-cyclohexanediamine based auxiliary for controlling the environment in a phosphonamide (7). Cyclic phosphonamides derived from C_2-symmetric diamines exist as a single pair of enantiomers because phosphorus is not a stereogenic center. Therefore, these auxiliaries can eliminate problems associated with amino alcohol auxiliaries in which the P-atom is stereogenic and contains a strong P—O bond (3*f*). As part of our examination of the relationship of anion structure and reaction stereoselectivity, we were interested in evaluating the various aspects of ring size, polycyclic structure, and nitrogen substituent in the design of phosphorus-based auxiliaries and the investigation of the anions derived therefrom. With this in mind we have chosen a collection of candidates in the C_2-diamine family to survey (Chart 1).

Our previously reported X-ray crystal structural analysis (8) of the lithio 2-benzyl-1,3-dimethyl-1,3,2-diazaphosphorinane 2-oxide showed that the anion is intrinsically chiral as the nitrogens are pyramidal and the *N*-methyl groups are oriented in equatorial and axial positions (Fig. 1). Furthermore, the key features of this structure are: (*i*) there is no C-Li contact, (*ii*) the carbanion is almost planar, and (*iii*) the phenyl group is oriented *anti* to the P=O bond (O–P–C–C dihedral angle = 168.9°). Further studies on the dynamic, solution behavior (8*a*, 9) of this and related anions and computational studies (10) have shown that the rotational

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Dedicated to Professor Stephen Hanessian in recognition of his significant contributions to the art of organic synthesis

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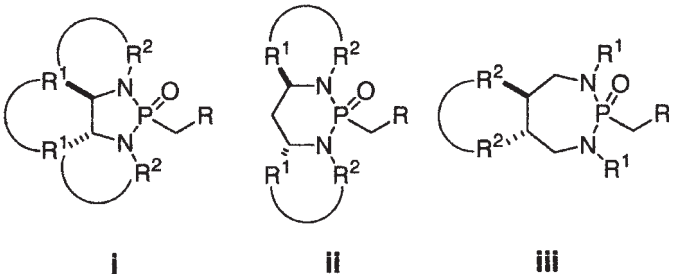
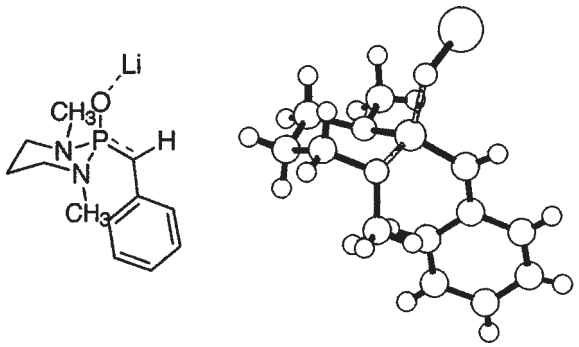
Chart 1.



barrier around the C—P bond in the benzyl anion is extremely low (ca. 6–8 kcal/mol). On the basis of the observations in the simple six-membered ring system, the chirally modified diazaphosphorinane **ii** was selected to investigate alkylation behavior of the derived *P*-alkyl anions. By comparison to five- and seven-membered analogs **i** and **iii**, system **ii** has the advantage of having the *N*-alkyl group closest to the anionic center due to ring angles[2].

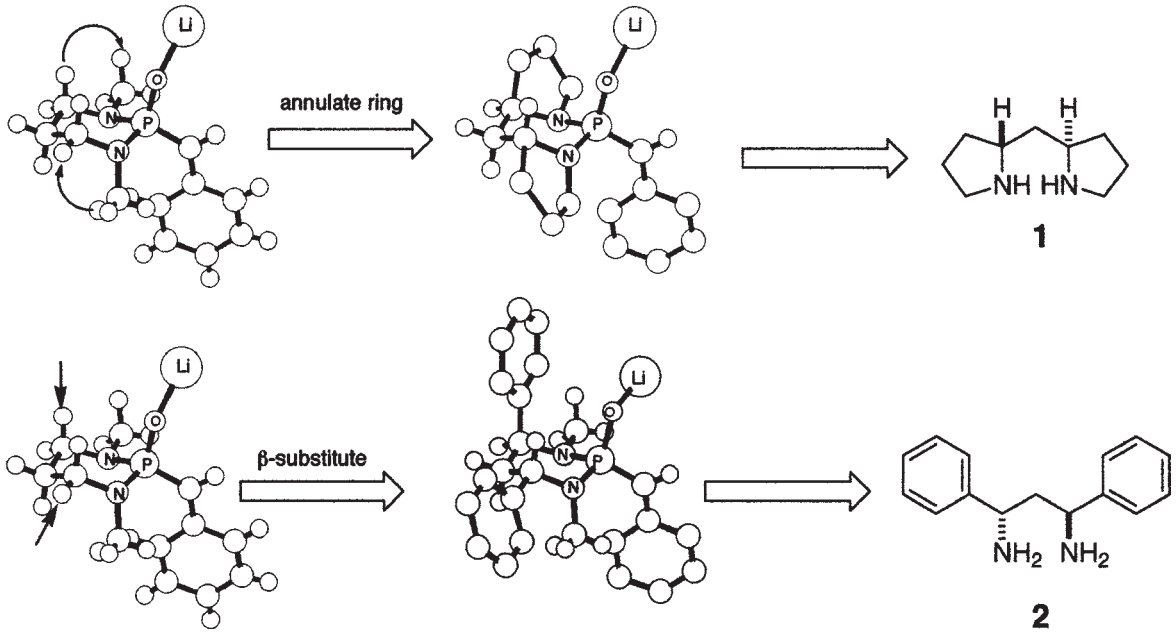
The key controlling attribute to obtaining high selectivity in alkylation was expected to be the ability to preordain the disposition of the N-substituents which in turn provide the chiral environment necessary for asymmetric reaction. On the basis of the assumption that chirally modified system **ii** would maintain the basic features of the parent system as elucidated in the X-ray crystal structure (8), diamines **1** and **2** were chosen as specific models to be investigated (Fig. 2). As shown in Fig. 2, the two proposed mechanisms for controlling the disposition of the N-substituents are: (*i*) annulating two five-membered rings to the central 1,3,2-diazaphospholidine ring thus leading to the dipyrrolidinomethane **1**, and (*ii*) placing substituents at the C(4) and C(6) positions to influence the hybridization of the nitrogen through torsional interactions. The *P*-alkyl anions derived from **1** and **2** provide six-membered ring phosphorus heterocycles which are expected to maintain a chair conformation, though the distortions due to the axially oriented phenyl group were not a priori obvious. Additionally, the *P*-benzyl-1,3,2-diazaphosphorinane 2-oxide anions generated from diamines **1** and **2** should adopt a conformation similar to the model in which the nitrogens are pyramidal. Thus, the disposition of the *N*-alkyl groups or the two *N*-methylenes of the fused rings distinguish the faces in the anions.

Fig. 1. Chem-3D presentation of lithio 2-benzyl-1,3-dimethyl-1,3,2-diazaphosphorinane 2-oxide (8).



In a preliminary study we prepared the tricyclic *P*-benzyl diazaphosphorinane **3** derived from **1** by simple condensation with benzylphosphonic dichloride[3] (11). The methylation diastereoselectivity of the lithio anion derived from **3**

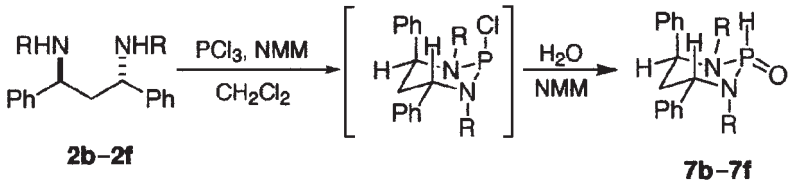
Fig. 2. Chiral 1,3-diamine design to control nitrogen substituent pyramidality.



[2] In the five-membered-ring analog **i**, the N-substituents are pulled away from the anion due to the external bond angles. In the seven-membered analog **iii**, the ring is considerably more flexible allowing the N-substituents to avoid the anionic center.

[3] The diamine **3** was prepared in enantiomerically enriched form (96% ee) from L-proline in nine steps and convertd to **3** using benzylphosphonic dichloride.

Table 1. Preparation of the cyclic phosphoramides **7b**–**7f**.

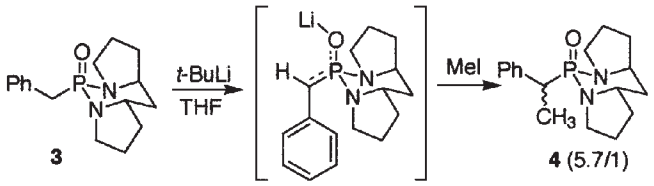


Entry	Diamine	R	Phosphite	Yield (%)[a]
1	**2b**	Et	**7b**	63[b]
2	**2c**	*i*-Pr	**7c**	82
3	**2d**	*t*-BuCH_2	**7d**	96
4	**2e**	PhCH_2	**7e**	92
5	**2f**	2,4,6-$(CH_3)_3C_6H_2CH_2$	**7f**	82[b]

[a]Yields are for isolated products after chromatography.

[b]Triethylamine was used.

Scheme 1.



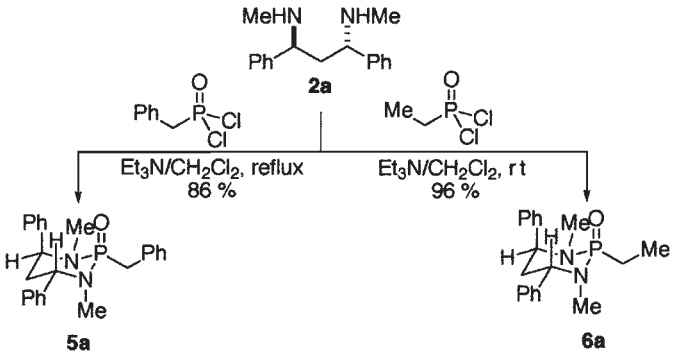
was 5.7/1 (Scheme 1). Since perhydropyrimidines normally exist in chair conformations (12), we expected the tricyclic system **3** to adopt a *cis*/*anti*/*cis* chair conformation thereby forcing the two different methylene units to orient in equatorial and axial positions. Thus, electrophiles approach away from the axial *N*-methylene unit. Unfortunately, the steric bulk of the methylene unit does not provide a sufficiently strong π-facial discrimination. Further variation was considered to be impractical since placing additional substituents in the five-membered rings would be synthetically challenging. Consequently, we chose to pursue the opportunities provided by the acyclic 1,3-diamine **2** which is much more amenable to variation in the size of the N-substituent. We describe herein a systematic examination of the effect of steric bulk of the N-substituent in the alkylation selectivity of anions derived from diamine **2**.

Results

Preparation of *P*-alkyl-1,3,2-diazaphosphorinanes

For the systematic study of the steric effect of *N*-alkyl substituents, six different *P*-benzyl-1,3,2-diazaphosphorinanes (*N*-methyl (**5a**), *N*-ethyl (**5b**), *N*-isopropyl (**5c**), *N*-neopentyl (**5d**), *N*-benzyl (**5e**), and *N*-mesitylmethyl (**5f**)) and three different *P*-ethyl-1,3,2-diazaphosphorinanes (*N*-methyl (**6a**), *N*-isopropyl (**6c**), and *N*-neopentyl (**6d**)) were chosen. All six requisite diamines (**2a**–**f)** were prepared by our previously reported procedures (13). Generally, the preparation of *P*-alkyl-1,3,2-diazaphosphorinanes was accomplished in a straightforward manner by combining the appropriate alkylphosphonic dichlorides (14) with the requisite diamines in the presence of triethylamine (2, 15). Sterically less demanding *N*,*N*′-dimethyl-1,3-diphenyl-1,3-propanediamine (**2a**) was amenable to these reaction conditions, providing *P*-benzyl- and *P*-ethyl diazaphosphorinane **5a** and **6a** in 86% and 96% yield, respectively (Scheme 2). Unfortunately, other higher alkyl diamines (**2b**–**f**) did not provide products in reasonable yield presumably due to the steric bulk of the diamines.

Scheme 2.

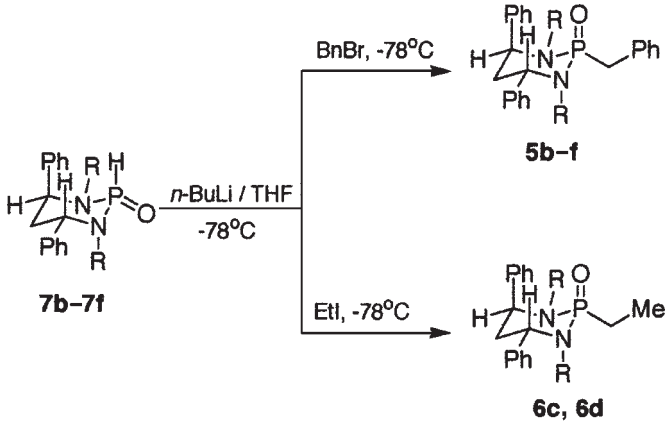


Fortunately, diamines **2b**–**f** did react with phosphorus trichloride (PCl_3) in the presence of *N*-methylmorpholine (NMM) or triethylamine (Et_3N) to afford *P*-chlorodiazaphosphorinanes which upon hydrolysis produced cyclic hydrogen phosphites **7b**–**f** in good yield (63–96%) (Table 1). Phosphites **7b**–**f** were unexpectedly stable and could be purified by silica gel column chromatography. It is important to note the buttressing effect of the 4 and 6-phenyl groups toward *N*-alkyl groups which will make the phosphorus center more sterically hindered and thus less sensitive to oxidation. The characteristic structural feature of phosphites **7b**–**f** is strong tautomeric preference for cyclic hydrogen phosphondiamide structure as evidenced by a strong infrared stretching band for the P=O group (1217–1246 cm^{-1}) and a diagnostic stretching band for the P—H unit (2211–2384 cm^{-1}) (16). The magnitude of the P—H coupling constant (J_{PH} = 595–629 Hz) is strongly suggestive of an axial P—H bond (17) The characteristic NMR spectral data are summarized in Table 2. Unlike trivalent trialkyl phosphites in which the phosphorus resonance appears in the neighborhood of 140 ppm (17), all resonances of the hydrogen phosphonamides **7b**–**f** appeared at –0.86–12.69 ppm.

Table 2. ^{31}P NMR data of phosphites **7b–f** and phosphorinanes **5a–f** and **6a**, **6c**, **6d**.

Entry	R	Phosphite, **7**, δ (ppm)	R′	Phosphorinane, **5**/**6**, δ (ppm)
1	Me		CH_2Ph	**5a**, 27.67
2	Me		Et	**6a**, 31.73
3	Et	**7b**, 3.61	CH_2Ph	**5b**, 24.96
4	*i*-Pr	**7c**, –0.86	CH_2Ph	**5c**, 21.64
5	*i*-Pr		Et	**6c**, 27.51
6	*t*-$BuCH_2$	**7d**, 12.69	CH_2Ph	**5d**, 24.45
7	*t*-$BuCH_2$		Et	**6d**, 30.99
8	$PhCH_2$	**7e**, 5.81	CH_2Ph	**5e**, 24.84
9	$(CH_3)_3C_6H_2CH_2$	**7f**, 3.09	CH_2Ph	**5f**, 26.87

Table 3. Preparation of *P*-alkyl 1,3,2-diazaphosphorinane 2-oxides.



Entry	Phosphite	R	Phosphonamide	Yield (%)[a]
1	**7b**	Et	**5b**	93
2	**7c**	*i*-Pr	**5c**	61
3	**7c**	*i*-Pr	**6c**	97
4	**7d**	*t*-$BuCH_2$	**5d**	81
5	**7d**	*t*-$BuCH_2$	**6d**	62
6	**7e**	$PhCH_2$	**5e**	83
7	**7f**	2,4,6-$(CH_3)_3C_6H_2CH_2$	**5f**	61

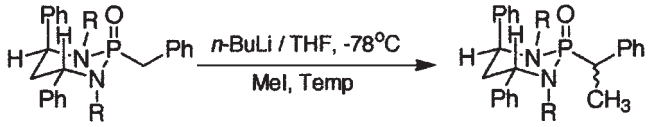
[a]Yields are for isolated products after chromatography.

Though less acidic than the corresponding dioxa analogs,[4] the hydrogen phosphonamides **7b–f** are sufficiently acidic to be deprotonated by *n*-BuLi at low temperature (–78°C). Importantly, no nucleophilic addition products to the phosphorus center were observed in the diaza analogs, presumably due to a combination of steric hindrance coupled with electronic deactivation of phosphonamides versus phosphonates. The use of triethylamine led to a sluggish reaction even at elevated temperatures and hydride bases such as NaH and KH were not suitable, affording unidentified side products. However, treatment of hydrogen phosphites **7b–f** with *n*-BuLi followed by alkylation with ethyl iodide and benzyl bromide afforded *P*-alkyl-1,3,2-diazaphosphorinane 2-oxides **5b–f, 6c,** and **6d**, in reasonable yields (61–97%) (Table 3).

The structures of the *P*-alkyl-1,3,2-diazaphosphorinanes **5a–f** and **6a**, **6c**, **6d**, and were secured by spectroscopic methods. First, in the ^{13}C NMR spectra, the α-methylene carbons displayed resonances at 38.55–43.40 ppm ($^1J_{CP}$ = 102.7–121.6 Hz) for *P*-benzyl-1,3,2-diazaphosphorinane 2-oxides **5a–f** and 25.43–29.35 ppm ($^1J_{CP}$ = 121.8–129.7 Hz) for *P*-ethyl-1,3,2-diazaphosphorinanes **6a**, **6c**, and **6d**. Second, diagnostic α-methylene protons showed phosphorus-coupled eight-line patterns at 3.35–3.69 ppm for *P*-benzyl-1,3,2-diazaphosphorinanes **5a–f** and 1.88–2.38 ppm for *P*-ethyl-1,3,2-diazaphosphorinanes **6a**, **6c**, and **6d**. Finally, the observation of a strong, characteristic P=O stretch (1208–1271 cm^{-1}) obviously eliminated the possibility of the formation of regioisomeric *O*-alkylated products. It is noteworthy that the reaction of the lithiated phosphite with silylating agents provided *O*-silylated phosphite exclusively (18). Additional characteristic features were noted in the ^{31}P NMR as all *P*-alkyl 1,3,2-diazaphosphorinane 2-oxides displayed resonances in the region shifted downfield (21.64–31.73 ppm)

[4]Diethyl hydrogenphosphonate is easily deprotonated at 0°C using NaH or Et_3N.

Table 4. Methylations of *P*-benzyl-1,3,2-diazaphosphorinane 2-oxides **5a**–**f**.

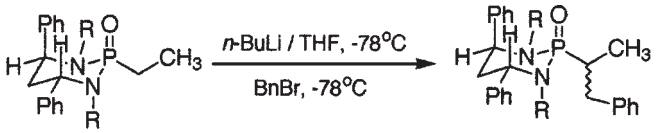


5a–5f **8a–8f**

Entry	5	R	Time (h)	Temp (°C)	d.s.	Yield (%)[a]
1	**5a**	Me	2.5	–78	7.7:1[b]	**8a**, 91
2	**5b**	Et	3.0	–78 to –60	1.6:1[b]	**8b**, 78[d]
3	**5c**	*i*-Pr	3.0	–78 to –60	1.4:1[c]	**8c**, 87
4	**5d**	*t*-BuCH_2	3.0	–78 to –60	11.5:1[c]	**8d**, 82[e]
5	**5e**	PhCH_2	2.0	–78	3.0:1[c]	**8e**, 96
6	**5f**	$(CH_3)_3C_6H_2CH_2$	2.0	–78	2.9:1[c]	**8f**, 94

[a]Yields are for isolated products after chromatography.
[b]Ratio determined by HPLC.
[c]Ratio determined by ^{31}P NMR.
[d]15% of **5b** recovered.
[e]11% of **5d** recovered.

Table 5. Diastereoselective benzylations of *P*-ethyl-1,3,2-diazaphosphorinane 2-oxide **6a**, **6c**, and **6d**.



6a, 6c, 6d **9a, 9c, 9d**

Entry	6	R	d.s.	Yield (%)[a]
1	**6a**	Me	1.3:1[b]	**9a**, 83
2	**6c**	*i*-Pr	3.6:1[c]	**9c**, 96
3	**6d**	*t*-BuCH_2	11.5:1[c]	**9d**, 98

[a]Yields are for isolated products after chromatography.
[b]Ratio determined by ^{31}P NMR.
[c]Ratio determined by HPLC.

compared to those of hydrogen phosphoramides **7b**–**f** (Table 2). The ring conformation is believed to adopt an axial P=O unit on the basis of X-ray crystallographic evidence (19) and the large difference in ^{1}H NMR resonances for HC(4) and HC(6) in **5** and **6** compared to **7**.

Diastereoselective methylation of *P*-benzyl-1,3,2-diazaphosphorinane 2-oxides 5a–f

The methylation of benzylic carbanions derived from **5a**–**f** was examined first. The sterically least demanding *N*-methyl analog **5a** and *N*-benzylic derivatives **5e**, and **5f** reacted rapidly and were completely methylated at –78°C within 2 to 2.5 h. However, in the case of sterically demanding substrates **5b**, **5c**, and **5d**, the reaction was sluggish at –78°C but proceeded at –60°C within 3 h. Clearly, the steric bulk of the *N*-alkyl group controlled the facility of the approach of the electrophile to the anionic center. *N*-Benzylic derivatives **5e** and **5f**, which are somewhat bulkier than methyl groups, may also benefit from contributions of the aromatic ring. As shown in Table 4, the methylation of the *P*-stabilized benzylic carbanions Li^+**5a**–**f**$^-$ proceeded with moderate to high diastereoselectivity. Interestingly, diastereoselectivity was not merely a function of the steric bulk of the alkyl group on the nitrogen as the *N*-methyl analog **5a** afforded remarkably high diastereoselectivity compared to the corresponding *N*-ethyl (**5b**) and *N*-isopropyl (**5c**) analogs. The most sterically demanding *N*-neopentyl analog **5d** showed the highest selectivity (entry 4). Moderate selectivities were found in the case of benzyl and mesityl analogs **5e** and **5f**.

Diastereoselective benzylations of *P*-ethyl-1,3,2-diazaphosphorinanes 6a, 6c, and 6d

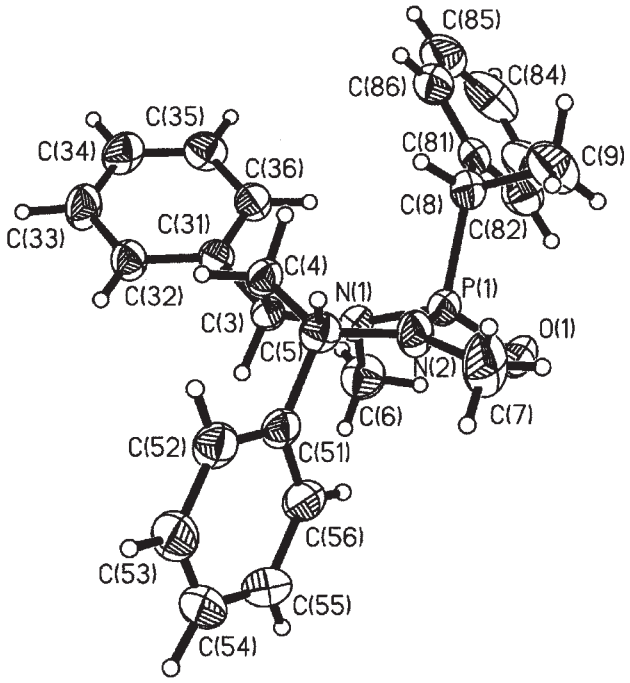
P-Ethyl anions were much more reactive than the corresponding *P*-benzyl anions as evidenced by the consumption of educt which was complete at –78°C within 30 min. Moreover, in contrast to the alkylation behavior of the *P*-benzyl anions, the benzylation of the *P*-ethyl anions from **6a**, **6c**, and **6d** showed a qualitative linear dependency of diastereoselectivity as a function of steric bulk of the *N*-alkyl groups (Table 5). The most sterically demanding *N*-neopentyl

Table 6. Data for the methylation products **8a**–**8f**.

N-Substituent	**8**	ratio	^{31}P NMR (δ, ppm)		HPLC (t_R, min)[a]	
			major	minor	major	minor
Me	**8a**	7.7:1	31.80	29.82		
Et	**8b**	1.6:1	29.34	28.76	8.37	7.25
i-Pr	**8c**	1.4:1	29.16	28.13	8.57	7.30
t-BuCH_2	**8d**	11.5:1	28.47	29.55	8.30	9.62
PhCH_2	**8e**	3.4:1	29.54	29.54	19.15	16.39
$(CH_3)_3C_6H_2CH_2$	**8f**	2.4:1	30.42	32.15		

[a]Column: Supelco LC-NH_2.

Fig. 3. ORTEP (35% thermal ellipsoids) representation of (*S**,*S**,*S**)-**8a**.



analog **6d** gave the highest selectivity (entry 3) whereas the sterically least demanding *N*-methyl analog **6a** afforded the lowest selectivity (entry 1). The disparate behavior of the *P*-benzyl and *P*-ethyl series may ultimately relate to the differences in conformational composition and rotational barriers (vide infra). The discrepancy between *N*-isopropyl analogs **5c** and **6c** might also be explained by the size difference of the electrophiles (benzyl vs. methyl). An electrophile dependence in the alkylation of related *P*-benzyl 1,3,2-oxazaphosphorinane 2-oxides has been previously noted, however in this case, methylation proceeds with higher selectivity than benzylation (3*c*)[5].

Stereochemical course of the reaction

In the course of the routine characterization of the alkylation products we noticed an interesting trend which suggested that the sense of asymmetric induction may not be the same for all of the substrates **5a–5f.** The two diagnostic features are the ^{31}P NMR chemical shifts and the HPLC elution orders for the two diastereomeric methylation products (Table 6). For the *N*-methyl (**8a**), *N*-ethyl (**8b**), and *N*-isopropyl (**8c**) alklyation products, the major diastereomer displays a lower field ^{31}P NMR chemical shift and is more strongly retained on the HPLC (aminopropyl silica). The *N*-benzyl alkylation products (**8e**) display a single ^{31}P resonance, but have a similar behavior on HPLC. Curiously, the *N*-neopentyl (**8d**) and *N*-mesityl (**8f**) analogs exhibit the reverse trend, i.e., the major diastereomer appears at *higher field* and is *less retained* on the HPLC. We thus suspected that the sense of relative asymmetric induction for **5a–5c** and **5e** might be different from that for **5d** and **5f**. This is an intriguing hypothesis which would require a complex conformational/mechanistic analysis to explain the reversal. It would however, help clarify the "non-linear" dependence of alkylation selectivity on N-substituent. Thus, to verify this hypothesis we elected to independently establish the configurations of the major alkylation products from the most selective representatives in the series, **8a** and **8d**.

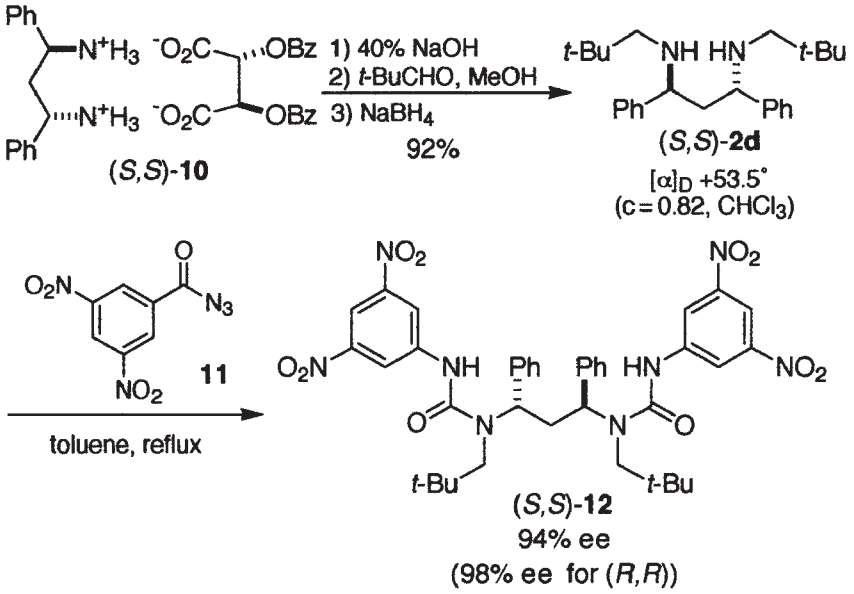
The sense of asymmetric induction in the major alkylation product **8a** was established by a single crystal X-ray analysis of the racemic compound. The ORTEP image is shown in Fig. 3. Simple inspection of the structure provides the answer that the (*S*,*S*)-diazaphosphorinane induced the *S* configuration at the newly created stereogenic center in the alkylation. Other implications of the structure and an interpretation of the origin of stereoselection are provided in the discussion section.

To establish the stereochemical course for the alkylation reaction of **5d**, diamine **2** was resolved with dibenzoyl-D-tartaric acid according to the literature procedure (20). The enantiomeric purity of the diamine was determined for the *N*,*N*-dineopentyldiamine derivative **2d** by analyzing the Pirkle derivative by chiral HPLC on an *N*-naphthyl-L-alanine column (21). The enantiomeric excesses were 94% for the (*S*,*S*)-enantiomer and 98% for (*R*,*R*)-enantiomer (Scheme 3).

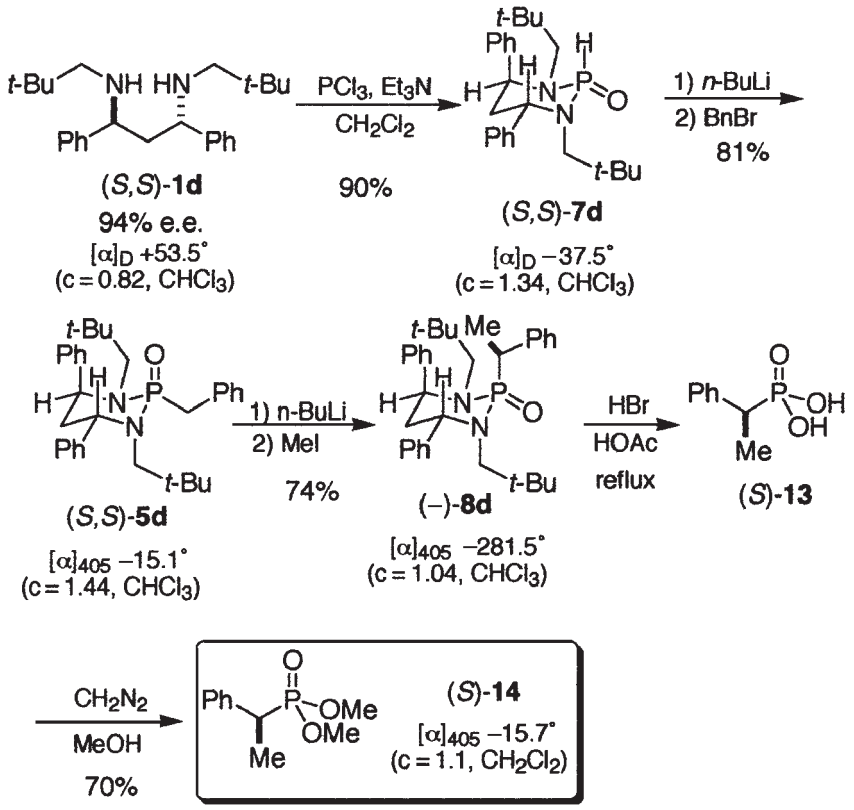
Preparation of enantiomerically enriched (*S*,*S*)-**5d** was carried out following the procedure for the racemic material described previously (Scheme 4). Thus, treatment of diamine (*S*,*S*)-**2d** with PCl_3 and Et_3N followed by hydrolytic workup gave phosphite (*S*,*S*)-**7d** in 90% yield. Subsequent transformation of (*S*,*S*)-**7d** to (*S*,*S*)-**5d** was performed in 81% yield. The asymmetric methylation of (*S*,*S*)-**5d** was accomplished by treatment with *n*-BuLi followed by addition of an excess of methyl iodide to give a 15.7:1 ratio of mixture of diastereomers of (–)-**8d** and 21% of unreacted (*S*,*S*)-**5d**. The

[5] Attempted benzylation of Li^+**5d**$^-$ at –60°C was unsuccessful. Warming to –20°C resulted in a diastereomeric mixture (2:1) of benzylated products.

Scheme 3.

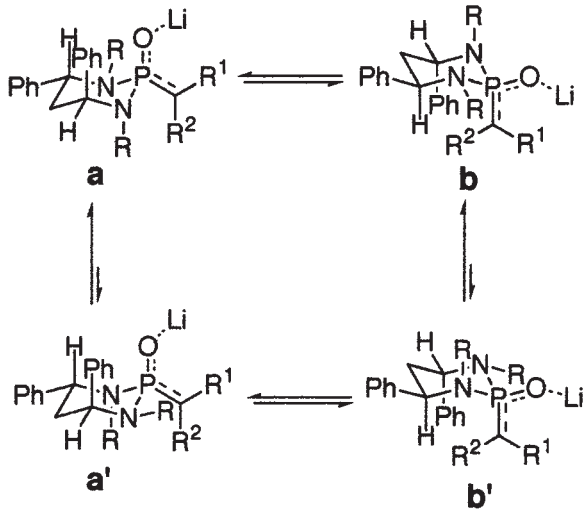


Scheme 4.



mixture of diastereomers was subjected to conventional hydrolysis conditions to give the phosphonic acid: 1 N HCl in THF, 6 N or 12 N HCl in dioxane. However, the very sterically hindered alkylation product (–)-**8d** was unaffected by these conditions. Eventually, (–)-**8d** was cleanly hydrolyzed with aqueous 48% HBr in refluxing acetic acid to give phosphonic acid (–)-**13**. The phosphonic acid (–)-**13** was purified by ion-exchange column chromatography and then was converted to the dimethyl phosphonate ester (–)-**14** by treatment with diazomethane (70% yield) followed by further purification by silica gel column chromatography. The absolute configuration of the dimethyl phosphonate (–)-**14** was confirmed to be *S* by comparison of its specific rotation with the literature value (3*c*, 3*f*). Therefore, net result of the

Fig. 4. Limiting chair-like conformations of the anions.



reaction is stereochemical conversion of 2-benzyl-1,3,2-diazaphosphorinane 2-oxide ((*S*,*S*)-**5d**) to dimethyl phosphonate (*S*)-**14**. *This fact then establishes unambiguously that the stereochemical course of alkylation of* ***5a*** *and* ***5d*** *proceeded in the same relative sense.*

Discussion

The central issue in all of our studies of phosphorus-stabilized anions is to create a structural model of reactivity which provides an understanding and ultimately a prediction of the stereochemical course of the reactions at the anionic centers. For the molecules examined in this study, the key question is the way in which the chirality of the 1,3,2-diazaphosphorinane skeleton (due to the phenyl substituents) is manifest in the dissymetry of the two faces of the benzylic anion.

To begin the analysis, we make recourse to the X-ray crystal structures of the achiral, unsubstituted lithio 1,3,2-oxazaphosphorinane 2- oxides, e.g., Fig. 1. The first point of consideration is the aggregation state of the anions. Even though the model anion crystallized as a dimer (8), the more sterically demanding 3,5-diphenyl substituted chiral anions might exist as *monomeric species*. Moreover, the aggregation state of these anions has been shown to be dependent on the nature of the substituents on nitrogen. For example, the anion derived from highly sterically demanding 1,3-bis(*tert*-butyl)-2-isopropyl-1,3,2-diazaphosphorinane has shown characteristic dynamic solution behavior of a monomer (10)[6]. That notwithstanding, Denmark et al. (8) have previously shown that aggregation effects for the oxaza-analog did not influence diastereoselectivity (21). Indeed, the anion derived from enantiomerically enriched (94% ee) diazaphosphorinane (*S*,*S*)-**5d** produced a diastereomeric mixture in a similar ratio compared to the anion derived from (±)-**5d**. Addition of the highly coordinating triamine, pentamethyldiethylentriamine, to the reaction in THF did not change the reaction selectivity. This implied that either the aggregate structure (homochiral vs. heterochiral dimers) is not responsible for the different alkylation selectivities or the reactive species are monomeric.

Fig. 5. Rationale for the diastereoselective methylation of *P*-benzyl-1,3,2-diazaphosphorinanes (**5**).

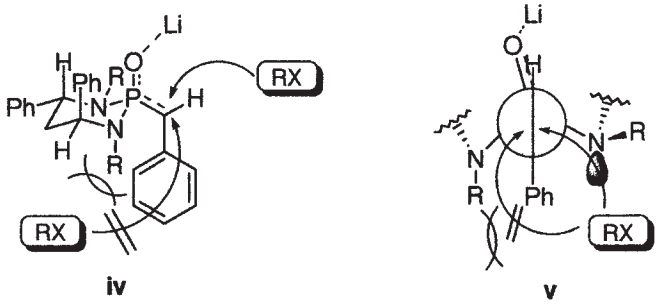
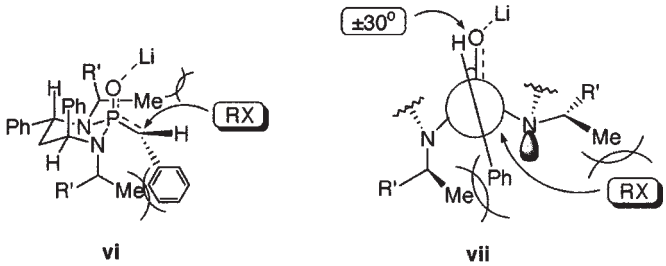


Fig. 6. Proposed skewed conformation of the anions.



The second critical issue is the conformation of the anion. Without direct spectroscopic information, we can only speculate about the ring conformation on the basis of the X-ray structures of unsubstituted anions and the neutral alkylation product (*S**,*S**,*S**)-**8a**. Close inspection of this structure reveals a surprising, albeit understandable deviation from the ideal chair conformation usually seen for these structures. The ring in (*S**,*S**,*S**)-**8a** is a flattened boat. The reason for this conformation most likely originates in a second unusual feature namely the axial positioning of the 1-phenylethyl group which itself results from an avoidance of non-bonding interactions of this phosphorus substituent with the neighboring *N*-methyl groups. Thus, to avert severe 1,3-diaxial interactions with one of the phenyl groups, the ring distorts to a boat. The flattening of the ring is due to the near planarity of the nitrogen atoms. It is however noteworthy that N(1) is slightly pyramidalized (Σangles = 356.3°) compared to N(2) (Σangles = 359.9°). Finally, the locations of the peripheral *N*-alkyl groups are determined by a combination of the ring conformation, gauche interactions with the phenyl groups at C(3) and C(5) and the hybridization of the nitrogen atoms.

Clearly, the proximal *N*-alkyl groups of the anions served as the chiral controlling elements during the course of the alkylation reaction. If we assume that the anion takes up a chair-like conformation, the limiting structures to consider at depicted in Fig. 4. We propose that the preferred anion is represented by structures **a**/**a′** in which the phosphonyl oxygen (and attendant lithium counterion with solvent) is in an axial position and the phenyl group is antiperiplanar to the P—O bond (R^1 = H, R^2 = Ph). The **a**/**a′** equilibrium relates

[6] P.C. Miller. Unpublished results from these laboratories.

to the alternative invertomers at the nitrogen atoms assuming, as is the case in all 1,3,2-diazaphosphorinane 2-oxide anions, that one substituent is axial and one is equatorial. Examination of the non-bonding interactions of the substituents around the ring shows that vicinally located pair of *N*-alkyl *C*-phenyl groups prefer invertomer **a** due to the elimination of one gauche interaction.

The high diastereoselectivity obtained from *N*-neopentyl analog **5d** results from a strong stereochemical bias between two π-faces of the derived planar anion Li^+**5d**$^-$ in which the phenyl ring might similarly orient anti to the P=O bond as shown in the model. The simplified structure of the antiperiplanar anion is depicted as **iv** and Newman projection **v** in Fig. 5. The electrophile would approach from the side away from the axially disposed *N*-alkyl group to avoid van der Waals interactions. For the neopentyl derivatives, the differentially disposed *N*-*tert*-butyl groups tethered by a methylene chain locate differently with respect to the anionic center.

The low diastereoselectivity observed from the *P*-benzyl anions derived from *N*-ethyl and *N*-isopropyl derivatives is believed to arise from a change in location of the phenyl ring. The phenyl group of the anion is believed to exist in a skew form and thus reside anticlinal (±150°) to the P=O bond to avoid non-bonding interaction with the substituent on the axially disposed *N*-alkyl group. The reactive conformation of this anion (**vi**) along with its Newman (**vii**) are shown in Fig. 6. Approach of the electrophile to either face of this anion experiences similar interactions with either of the N-substituents thus affording little bias in the alkylation event.

The direct relationship of the diastereoselectivity to steric bulkiness of the *N*-alkyl groups in the case of benzylation of the *P*-ethyl anion is explained by invoking the antiperiplanar anionic conformer **vii**. Since the α-methyl group of the anion is comparably small, the interaction with axially disposed *N*-alkyl group is insufficient to force the anion to be skewed. Thus, the diastereoselectivity directly reflects the steric bulkiness of *N*-alkyl groups. The erosion of selectivity for *P*-ethyl anions is mostly due to the low rotation barrier of the P—C bond and the lesser bias toward the antiperplanar vs. the synplanar conformation.[7]

It should also be recognized that the anions may exist in flattened boat-like conformations with an axially standing *P*-benzyl group. Here, the shielding of the anion faces is much less predictable. Moreover, the anion ring conformation may in fact be dependent on the ring substituents, making a consistent analysis impossible.

In summary, the methylation of Li^+**5a**$^-$–Li^+**5h**$^-$ proceeds with moderate to high diastereoselectivity and was highly conformation dependent due to the *N*-alkyl substituents. The benzylation selectivity of Li^+**6a**$^-$, Li^+**6c**$^-$, and Li^+**6d**$^-$ showed linear dependency on the *N*-alkyl steric bulk. *N*-Neopentyl analogs **5d** and **6d** afforded the highest selectivities (92:8) in both cases. From a systematic study of *N*-alkyl substituents and a comprehensive understanding of the structure of the anions, new C_2-symmetric diamine-based auxiliaries and their utilities in the reaction of the phosphorus-based alkyl anions can be developed in the future.

Experimental section

General Methods

See supporting information.[8]

Starting materials

The diamines **2a**–**f** were prepared in these laboratories and the procedures have been reported elsewhere (14). Ethylphosphonic dichloride is commercially available. Benzylphosphonic dichloride was prepared by a literature procedure and used after recrystallization from pentane (15).

*(*RS*)-(4*l*,6*l*)-2-Benzyl-1,3-dimethyl-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**5a**)*: In a 25-mL, three-necked round bottom flask equipped with a reflux condenser, a N_2 inlet tube, a rubber septum, and a magnetic stirring bar was placed with 0.57 mL (4.13 mmol) of Et_3N in 5 mL of CH_2Cl_2. This solution was heated to reflux and then 420 mg (1.65 mmol) of diamine **2a** in 6 mL of CH_2Cl_2 and 362 mg (1.73 mmol) of benzylphosphonic dichloride in CH_2Cl_2 (6 mL) were simultaneously added over 1 h by syringe pump. After heating to reflux for 10 h, the oil bath was removed. The cooled reaction mixture was poured into water (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The extracts were dried (Na_2SO_4), filtered, and concentrated to give 700 mg of yellow orange oil, which was purified by SiO_2 column chromatography (EtOAc/*i*-PrOH, 19:1) to give 552 mg (86%) of diazaphosphorinane **5a** as a colorless solid. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 147–148°C. IR (CCl_4): 3065 w, 1271 s. TLC: R_f 0.35 (EtOAc/*i*-PrOH, 19:1). ^{1}H NMR (300 MHz): 7.45–7.29 (m, 11 H), 7.18 (t, J = 3.0, 2 H), 6.79 (dd, J = 6.0, 3.0, 2 H), 4.23 (dt, J = 13.7, 3.8, 1 H), 3.75 (dd, J = 11.5, 3.5, 2 H), 3.51 (dd, J = 19.4, 4.8, 1 H), 3.36 (dd, J = 18.5, 4.8, 1 H), 2.66 (d, J = 8.2, 3 H), 2.48 (d, J = 9.0, 3 H), 1.80 (m, 2 H, 2 H). ^{13}C NMR (75.5 MHz): 142.38 (J_{CP} = 6.5), 140.15, 134.76 (J_{CP} = 8.9), 129.82, 129.74, 128.67, 128.34, 128.29, 128.24, 127.36, 127.15, 126.84, 126.48, 126.41, 62.65, 58.58, 41.43 (J_{CP} = 3.5), 38.55 (J_{CP} = 121.6), 34.07 (J_{CP} = 4.6), 32.28 (J_{CP} = 3.0). ^{31}P NMR (121.6 MHz): 27.67. MS (70 eV): 390 (M^+ < 0.1), 299 (100). Anal. calcd. for $C_{24}H_{27}N_2OP$ (390.46): C 73.83, H 6.97, N 7.17, P 7.93; found: C 73.79, H 6.98, N 7.11, P 7.84.

*(*RS*)-(4*l*,6*l*)-1,3-Dimethyl-4,6-diphenyl-2-ethyl-1,3,2-diazaphosphorinane 2-oxide (**6a**)*: In a 50-mL, three-necked round bottom flask equipped with a N_2 inlet tube, a septum and a magnetic stirring bar was placed 370 mg (1.45 mmol) of diamine **2a** and 0.51 mL (3.63 mmol) of Et_3N in 15 mL of CH_2Cl_2. Ethylphosphonic dichloride (170 μL, 1.60 mmol) was then added by a syringe over a time period of 5 min.

[7] S.E. Denmark, K.A. Swiss, R.L. Dorow, P.C. Miller, and S.R. Wilson. In a detailed NMR study, no decoalescence of the achiral parent of **6a** was detected down to –117°C (500 MHz, ^{1}H NMR observation). Manuscript in preparation.

[8] General experimental methods along with full spectroscopic data and assignments for **5a-f**, **6a**, **6c**, **6d**, **7b-f**, **8a-f**, **9a**, **9c**, **9d**, and **14** (15 pages). Copies of material on deposit may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council of Canada, Ottawa, ON, K1A OS2, CANADA.

After stirring for 22 h at rt, the reaction mixture was concentrated under reduced pressure. The residue was treated with EtOAc (15 mL), filtered, and the filter cake was washed with EtOAc (2 × 10 mL). The combined filtrates were washed with brine (15 mL) and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated to give a colorless oil, which was purified by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3, then EtOAc/*i*-PrOH (9:1) to afford 457 mg (96%) of diazaphosphorinane **6a** as a foam. An analytical sample was obtained by recrystallization from pentane/TBME: mp 66–68°C. TLC: R_f 0.30 (EtOAc/*i*-PrOH, 9:1). IR (CCl_4): 3030 w, 1267 s. ^{1}H NMR (300 MHz): 7.50–7.11 (m, 10 H), 4.33 (dt, J = 13.4, 3.8, 1 H), 3.78 (dd, J = 10.1, 1.7, 1 H), 2.70 (d, J = 8.1, 3 H), 2.54 (d, J = 8.8, 3 H), 2.40 (ddd, J = 14.2, 12.4, 4.6, 1 H), 2.20–1.88 (m, 3 H), 1.31 (dt, J = 19.3, 7.5, 3 H). ^{13}C NMR (75.5 MHz): 142.01 (J_{CP} = 5.0), 140.06, 128.44, 128.33, 127.13, 126.93, 126.29, 126.11, 62.33, 59.42, 41.90 (J_{CP} = 5.2), 33.52 (J_{CP} = 4.7), 32.66 (J_{CP} = 3.1), 25.43 (J_{CP} = 129.7), 7.68 (J_{CP} = 6.3). ^{31}P NMR (121.6 MHz) 31.73. MS (70 eV): 329 (M^+ + 1, 22), 328 (M^+, 98), 299 (100). Anal. calcd. for $C_{19}H_{25}N_2OP$ (328.39): C 69.49, H 7.67, N 8.53, P 9.43; found: C 69.49, H 7.69, N 8.51, P 9.40.

*Representative procedure for the preparation of cyclic hydrogen phosphites **7b-f***

The detailed procedure for the preparation of **7b** is given. For all of the other phosphites only the amounts of reagents and methods of purification are provided along with the analytical data.

*(*RS*)-(4*l*,6*l*)-1,3-Diethyl-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**7b**)*: In a 25-mL, three-necked, round bottom flask, equipped with a reflux condenser, a rubber septum, a N_2 inlet tube and a magnetic stirring bar was placed 109 μL (1.25 mmol) of PCl_3, and a solution of 0.35 mL (2.51 mmol) of Et_3N in 5 mL of CH_2Cl_2. The mixture was heated to reflux and a solution of 335 mg (1.19 mmol) of diamine **2b** in CH_2Cl_2 (5 mL) was added via syringe over a time period of 5 min. After heating to reflux for an additional 1.5 h, 0.18 mL (1.25 mmol) of Et_3N was added. The oil bath was removed and the reaction mixture was poured into 20 mL of water and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried (Na_2SO_4) and concentrated to give a yellow oil which was purified by SiO_2 column chromatography eluting with EtOAc/*i*-PrOH (19:1) to give 247 mg (63%) of cyclic phosphite **7b** as a colorless oil which solidified at –20°C. An analytical sample was obtained by recrystallization from Et_2O: mp 111–112°C. IR (CCl_4): 3031 w, 1240 s. TLC: R_f 0.34 (EtOAc/*i*-PrOH, 19:1). ^{1}H NMR (300 MHz): 7.74 (d, J = 599.4, 1 H), 7.45–7.23 (m, 10 H), 4.27–4.14 (m, 2 H), 3.37–3.16 (m, 2 H), 2.91–2.81 (m, 2 H), 2.36 (m, 2 H), 1.03 (t, J = 7.1, 3 H), 0.97 (t, J = 7.1, 3 H). ^{13}C NMR (75.5 MHz): 141.39, 140.72, 128.49, 128.41, 127.30, 127.35, 126.72, 126.28, 57.67, 57.47, 42.42 (J_{CP} = 9.6), 40.45 (J_{CP} = 5.6), 40.25 (J_{CP} = 8.1), 14.08, 13.44. ^{31}P NMR (121.6 MHz): 3.61. MS (70 eV): 328 (M^+, 29), 134 (100). Anal. calcd. for $C_{19}H_{25}N_2OP$ (328.39): C 69.49, H 7.67, N 8.53, P 9.43; found: C 69.50, H 7.67, N 8.50, P 9.37.

*(*RS*)-(4*l*,6*l*)-1,3-Bis-(1-methylethyl)-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**7c**)*: From 315 mg (1.02 mmol) of diamine **2c**, 95 μL (1.09 mmol) of PCl_3 and 0.36 mL (3.27 mmol) of *N*-methylmorpholine followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3) was obtained 288 mg (79%) of **7c** as a colorless solid. A lager scale reaction gave 82% of **7c**. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 126–127°C. IR (CCl_4): 3067 w, 1275 s. TLC: R_f 0.32 (hexane/EtOAc/*i*-PrOH, 35:62:3). ^{1}H NMR (300 MHz): 7.83 (d, J = 595.4, 1 H), 7.51 (d, J = 7.2, 2 H), 7.41–7.27 (m, 8 H), 4.24 (m, 1 H), 4.11 (ddd, J = 13.2, 8.5, 5.1, 1 H), 3.58 (heptet, J = 6.8, 1 H), 3.38 (heptet, J = 6.8, 1 H), 2.40 (m, 2 H), 1.32 (d, J = 6.8, 3 H), 1.22 (d, J = 6.8, 3 H), 1.08 (d, J = 6.8, 3 H), 0.96 (d, J = 6.8, 3 H). ^{13}C NMR (75.5 MHz): 142.58, 128.28, 127.01, 126.69, 126.15, 55.56, 55.37, 49.73 (J_{CP} = 5.1), 48.16 (J_{CP} = 8.2), 43.67 (J_{CP} = 10.6), 22.00 (J_{CP} = 2.8), 21.68, 21.05 (J_{CP} = 4.1), 20.86. ^{31}P NMR (121.6 MHz): –0.86. MS (70 eV): 356 (M^+, 16), 176 (100). Anal. calcd. for $C_{21}H_{29}N_2OP$ (356.45): C 70.76, H 8.20, N 7.86, P 8.69; found: C 70.91, H 8.20, N 7.83, P 8.53.

*(*RS*)-(4*l*,6*l*)-1,3-Bis(2,2-dimethylpropyl)-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**7d**)*: From 410 mg (1.12 mmol) of diamine **2d**, 107 μL (1.23 mmol) of PCl_3, and 0.41 mL (3.73 mmol) of *N*-methylmorpholine followed by purification by SiO_2 column chromatography (hexane/EtOAc, 4:1) was obtained 379 mg (82%) of **7d** as a sticky oil. A larger scale reaction gave 96% yield of **7d**. A sample of (*S*,*S*)-**7d** was also prepared from (*S*,*S*)-**2d** (94% ee) in 90% yield. For (*S*,*S*)-**7d**: $[\alpha]_D$ –37.5 (c = 1.34, $CHCl_3$). IR (CCl_4): 3065 w, 1246 s. TLC: R_f 0.33 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz): 7.77 (d, J = 608.9, 1 H), 7.42–7.20 (m, 10 H), 4.33 (ddd, J = 17.1, 7.6, 5.2, 1 H), 4.18 (quintet, J = 5.8, 1 H), 3.05 (dd, J = 15.2, 12.8, 1 H), 2.98 (dd, J = 14.8, 12.3, 1 H), 2.74 (dd, J = 14.8, 9.1, 1 H), 2.39 (m, 2 H), 2.34 (dd, J = 15.2, 12.8, 1 H), 0.76 (s, 9 H), 0.72 (s, 9 H). ^{13}C NMR (75.5 MHz): 141.35, 140.66, 128.55, 128.52, 127.18, 126.61, 62.09, 60.97, 58.89 (J_{CP} = 3.7), 56.95 (J_{CP} = 4.3), 42.10 (J_{CP} = 12.6), 34.26 (J_{CP} = 1.5), 33.62 (J_{CP} = 1.9), 28.14, 28.08. ^{31}P NMR (121.6 MHz): 12.69. MS (70 eV): 412 (M^+), 355 (100). Anal. calcd. for $C_{25}H_{37}N_2OP$ (412.55): C 72.78, H 9.04, N 6.79, P 7.51; found: C 72.56, H 9.01, N 6.65, P 7.42.

*(*RS*)-(4*l*,6*l*)-1,3-Dibenzyl-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**7e**)*: From 84 μL (0.97 mmol) of PCl_3, 358 mg (0.88 mmol) of **2e**, and 0.39 mL (2.77 mmol) of *N*-methylmorpholine followed by purification by SiO_2 column chromatography (hexane/EtOAc, 2:1) was obtained 366 mg (92%) of **7e** as a colorless oil which solidified on standing at –20°C. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 59–60°C. IR (CCl_4): 3065 w, 1227 s. TLC: R_f 0.41 (hexane/EtOAc, 1:1). ^{1}H NMR (300 MHz): 8.14 (d, J = 628.9, 1 H), 7.36–7.11 (m, 20 H), 4.73 (dd, J = 14.6, 9.9), 4.66 (dd, J = 15.6, 10.9, 1 H), 4.12 (quintet, J = 5.5, 1 H), 3.93 (m, 1 H), 3.70 (dd, J = 15.6, 9.8, 1 H), 3.62 (dd, J = 14.6, 11.3, 1 H), 2.30 (ddd, J = 14.5, 9.3, 4.7, 1 H), 2.13 (ddd, J = 14.5, 6.0, 4.8, 1 H). ^{13}C NMR (75.5 MHz): 140.57 (J_{CP} = 1.4) 139.43, 136.89 (J_{CP} = 2.8), 136.74, 129.42, 128.67, 128.46, 128.40, 128.16, 128.08,

127.46, 127.36, 127.33, 127.27, 126.80, 126.59, 57.45, 56.50, 48.51 (J_{CP} = 6.9), 48.29 (J_{CP} = 5.6), 41.58 (J_{CP} = 12.6). ^{31}P NMR (121.6 MHz): 5.81. MS (70 eV): 452 (M^+, 3), 91 (100). Anal. calcd. for $C_{29}H_{29}N_2OP$ (452.53): C 76.97, H 6.46, N 6.19, P 6.84; found: C 76.94, H 6.48, N 6.18, P 6.82.

*(*RS*)-(4*l*,6*l*)-1,3-Bis-(2,4,6-trimethylphenylmethyl)-4,6-diphenyl-1,3,2-diaza-phosphorinane 2-oxide (**7f**)*: From 127 μL (1.45 mmol) of PCl_3, 0.62 mL (4.46 mmol) of NEt_3, and 680 mg (1.39 mmol) of **2f** followed by purification by SiO_2 column chromatography (hexane/EtOAc, 2:1) was obtained 612 mg (82%) of **7f** as a gummy solid. An analytical sample was obtained by recrystallization from pentane/TBME: mp 178–190°C. IR (CCl_4): 3029 w, 1217 s. TLC: R_f 0.36 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz): 7.48–7.09 (m, 10 H), 7.22 (d, J = 616.0, 1 H), 6.78 (s, 2 H), 6.67 (s, 2 H), 4.36 (dd, J = 13.5, 3.3, 1 H), 4.27 (dd, J = 13.5, 7.2, 1 H), 4.06 (dd, J = 12.7, 5.1, 1 H), 4.01–3.92 (m, 2 H), 3.68 (t, J = 12.7, 1 H), 2.34 (m, 2 H), 2.24 (s, 3 H), 2.16 (s, 3 H), 2.13 (s, 6 H), 2.08 (s, 6 H). ^{13}C NMR (75.5 MHz): 141.46, 140.89, 138.34 (J_{CP} = 4.3), 137.33, 136.81, 128.93, 128.83, 128.60, 128.21, 127.98, 127.91, 127.24, 126.78, 125.82, 59.29, 55.88, 48.59 (J_{CP} = 6.9), 44.99 (J_{CP} = 6.6), 42.12 (J_{CP} = 9.0), 20.76, 20.60, 19.86, 19.61. ^{31}P NMR(121.6 MHz): 3.09. MS (70 eV): 536 (M^+, 2), 133 (100). Anal. calcd. for $C_{35}H_{41}N_2OP$ (412.55): C 78.33, H 7.70, N 5.22, P 5.77; found: C 78.31, H 7.79, N 5.14, P 5.56.

Representative procedure for the preparation of 2-alkyl-1,3,2-diaza-phosphorinane 2-oxides

The detailed procedure for the preparation of **5b** is given. For all of the other diazaphosphorinanes only the amounts of reagents and methods of purification are provided along with the analytical data.

*(*RS*)-(4*l*,6*l*)-2-Benzyl-1,3-diethyl-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**5b**)*: To a flame-dried, 25-mL, three-necked, round bottom flask equipped with a thermometer, a rubber septum, a N_2 inlet, and a magnetic stirring bar was added a solution of 180 mg (0.55 mmol) of phosphite **7b** in THF (10 mL). The mixture was cooled to –78°C and 0.34 mL (0.58 mmol) of *n*-BuLi (1.71 M) was slowly added to give a yellow-orange solution which was stirred at –78°C for 15 min. Benzyl bromide (71 μL, 0.60 mmol) was then added via syringe and the color dissipated immediately. After being stirred for 1 h at –78°C, the reaction mixture was warmed to rt, poured into water (20 mL), extracted with EtOAc (3 × 15 mL), washed with brine (10 mL), and dried (Na_2SO_4). Filtration followed by concentration gave a yellow oil which was purified by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3) to afford 140 mg (61%) of diazaphosphorinane **5b** as a foam. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 98–99°C. IR (CCl_4): 3031 w, 1239 s. TLC: R_f 0.22 (hexane/EtOAc/*i*-PrOH, 34:63:3). ^{1}H NMR (300 MHz): 7.52–7.16 (m, 13 H), 6.77 (m, 2 H), 4.49 (dt, J = 15.4, 3.7, 1 H), 3.93 (dd, J = 12.0, 3.0, 1 H), 3.45 (d, J = 18.9, 2 H), 3.51–3.35 (m, 1 H), 3.24 (heptet, J = 7.3, 1 H), 2.90 (heptet, J = 7.3, 1 H), 2.53–2.36 (m, 1 H), 2.07 (ddd, J = 14.0, 12.3, 4.3, 1 H), 1.91 (dt, J = 14.0, 3.2, 1 H), 1.01 (t, J = 7.1, 3 H), 0.96 (t, J = 6.9, 3 H). ^{13}C NMR (75.5 MHz): 141.35 (J_{CP} = 5.0), 140.55, 134.90 (J_{CP} = 8.4), 129.97, 129.89, 128.45, 128.34, 128.31, 128.21, 127.30, 127.12, 126.94, 126.78, 126.35, 126.31, 58.14, 54.58, 41.66 (J_{CP} = 4.7), 40.54 (J_{CP} = 121.3), 39.87 (J_{CP} = 4.6), 38.87 (J_{CP} = 3.6), 13.52 (J_{CP} = 2.4), 13.36. ^{31}P NMR (121.6 MHz): 24.96. MS (70 eV): 328 (M^+ + 1 – $PhCH_2$, 22), 327 (M^+ – $PhCH_2$, 100). Anal. calcd. for $C_{26}H_{31}N_2OP$ (418.52): C 74.62, H 7.47, N 6.69, P 7.40; found: C 74.49, H 7.57, N 6.63, P 7.25.

*(*RS*)-(4*l*,6*l*)-2-Benzyl-1,3-bis-(1-methylethyl)-4,6-diphenyl-1,3,2-diaza-phosphorinane 2-oxide (**5c**)*: From 195 mg (0.55 mmol) of diamine **7c**, 0.33 mL (0.61 mmol) of *n*-BuLi (1.84 M), and 78 μL (0.66 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 45:52:3) was obtained 198 mg (81%) of **5c** as a colorless solid. An analytical sample was obtained by recrystallization from Et_2O: mp 144–145°C. IR (CCl_4): 3065 w, 1240 s. TLC: R_f 0.54 (hexane/EtOAc/*i*-PrOH, 45:52:3). ^{1}H NMR (300 MHz): 7.63–7.07 (m, 15 H), 4.56 (dt, J = 14.9, 3.7, 1 H), 3.91–3.82 (m, 2 H, HC(4)), 3.59 (dd, J = 18.6, 14.6, 1 H), 3.50–3.33 (m, 1 H), 3.38 (dd, J = 17.6, 14.6, 1 H), 2.28 (ddd, J = 15.2, 14.3, 3.9, 1 H), 2.12 (dt, J = 14.2, 4.1, 1 H), 1.12 (d, J = 6.6, 3 H), 1.03 (d, J = 7.0, 3 H), 0.87 (d, J = 6.7, 3 H), 0.76 (d, J = 6.7, 3 H). ^{13}C NMR (75.5 MHz): 144.35 (J_{CP} = 3.0), 142.82, 134.80 (J_{CP} = 7.8), 130.28, 130.19, 128.25, 128.15, 128.13, 128.02, 127.11, 126.93, 126.60, 126.28, 126.25, 58.34, 53.40, 49.64 (J_{CP} = 2.7), 46.22 (J_{CP} = 5.4), 43.60 (J_{CP} = 7.2), 43.40 (J_{CP} = 117.6), 23.51, 22.23, 21.30, 20.13 (J_{CP} = 2.5). ^{31}P NMR (121.6 MHz) 21.64. MS (70 eV): 446 (M^+), 355 (100). Anal. calcd. for $C_{28}H_{35}N_2OP$ (446.57): C 75.31, H 7.90, N 6.27, P 6.94; found: C 75.26, H 7.94, N 6.24, P 6.86.

*(*RS*)-(4*l*,6*l*)-2-Benzyl-1,3-bis-(2,2-dimethylpropyl)-4,6-diphenyl-1,3,2-diaza-phosphorinane 2-oxide (**5d**)*: From 150 mg (0.36 mmol) of **7d**, 0.27 mL (0.40 mmol) of *n*-BuLi (1.48 M), and 87 μL (0.73 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 4:1) was obtained 123 mg (67%) of **5d** as a viscous oil. A sample of (*S*,*S*)-**5d** was also prepared from (*S*,*S*)-**7d** in 81% yield. For (*S*,*S*)-**5d**: [α] = –2.1 (c = 1.44, $CHCl_3$), [α] = – 15.1 (c = 1.44, $CHCl_3$). IR (CCl_4): 3065 w, 1235 s. TLC: R_f 0.44 (hexane/EtOAc, 4:1). ^{1}H NMR (300 MHz): 7.65–7.05 (m, 15 H), 4.62 (dt, J = 15.3, 4.0, 1 H), 4.13 (ddd, J = 11.5, 7.2, 4.2, 1 H), 3.69 (dd, J = 18.4, 14.8, 1 H), 3.48 (dd, J = 17.4, 14.8, 1 H), 3.13 (dd, J = 14.8, 8.9, 1 H), 2.84 (dd, J = 14.9, 8.6, 1 H), 2.75 (dd, J = 14.9, 7.8, 1 H), 2.50 (ddd, J = 15.1, 12.0, 3.9, 1 H), 2.42 (dd, J = 14.8, 11.2, 1 H), 2.15 (dt, J = 13.9, 4.1, 1 H), 0.78 (s, 9 H), 0.72 (s, 9 H). ^{13}C NMR (75.5 MHz): 141.62, 140.46, 134.98 (J_{CP} = 7.4), 130.23, 130.14 128.35, 128.30, 128.12, 127.33, 127.31, 127.17, 127.03, 126.27, 126.24, 61.98, 59.32, 58.33 (J_{CP} = 2.3), 55.91 (J_{CP} = 2.8), 43.23 (J_{CP} = 115.2), 42.88 (J_{CP} = 9.3), 33.66, 33.02 (J_{CP} = 3.4), 28.98, 28.83. ^{31}P NMR (121.6 MHz): 24.45. MS (70 eV): 446 (M^+ + 1 – $(CH_3)_3C$, 16), 445 (M^+ – $(CH_3)_3C$, 51), 91 (100). Anal. calcd. for $C_{32}H_{43}N_2OP$ (502.68): C 76.46, H 8.62, N 5.57, P 6.16; found: C 76.32, H 8.62, N 5.53, P 6.20.

*(*RS*)-(4*l*,6*l*)-1,2,3-Tribenzyl-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**5e**)*: From 288 mg (0.64 mmol) of **7e**, 0.45 mL (0.77 mmol) of *n*-BuLi (1.70 M), and 83 μL (0.70 mmol) of

benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 2:1) afforded 285 mg (83%) of **5e** as a colorless solid. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 137–138°C. IR (CCl_4): 3065 w, 1219 s. TLC: R_f 0.35 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz): 7.54–7.14 (m, 23 H) and 6.85–6.82 (m, 2 H), 4.76 (dd, *J* = 15.7, 8.6, 1 H), 4.48 (dd, *J* = 14.5, 8.6, 1 H), 4.35 (dt, *J* = 15.0, 3.7, 1 H), 3.85 (dd, *J* = 15.7, 5.8, 1 H), 3.68 (dd, *J* = 19.8, 14.6, 1 H), 3.70–3.62 (m, 1 H), 3.51 (dd, *J* = 17.9, 14.6, 1 H), 3.18 (t, *J* = 13.8, 1 H), 2.30 (ddd, *J* = 14.1, 12.6, 4.4, 1 H), 1.88 (dt, *J* = 14.4, 3.2, 1 H). ^{13}C NMR (75.5 MHz): 141.14 (J_{CP} = 4.4), 139.06, 137.26 (J_{CP} = 4.2), 136.63, 134.33 (J_{CP} = 8.3), 130.10, 130.05, 128.61, 128.40, 128.37, 127.67, 127.45, 127.30, 127.09, 127.06, 126.93, 126.53, 126.49, 58.53, 55.41, 48.88 (J_{CP} = 4.6), 47.85 (J_{CP} = 3.2), 42.90 (J_{CP} = 121.6), 41.82 (J_{CP} = 5.2). ^{31}P NMR (121.6 MHz): 24.84. MS (70 eV): 91 (100). Anal. calcd. for $C_{36}H_{35}N_2OP$ (542.66): C 79.68. H 6.50, N 5.16, P 5.71; found: C 79.62, H 6.53, N 5.07, P 5.65.

*(*RS*)-(4*l*,6*l*)-2-Benzyl-1,3-bis-(2,4,6-trimethylphenylmethyl)-4,6-diphenyl-1,3,2-diazaphosphorinane 2-oxide (**5f**)*: From 570 mg (1.06 mmol) of phosphite **7f**, 0.65 mL (1.11 mmol) of *n*-BuLi (1.71 M), and 138 μL (1.17 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 4:1–2:1) afforded 402 mg (61%) of diazaphosphorinane **5f** as a foam. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 149–150°C. IR (CCl_4): 3063 w, 1223 s. TLC: R_f 0.54 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz): 7.63 (d, *J* = 7.5, 1 H), 7.40–7.22 (m, 9 H), 6.99 (dd, *J* = 5.1, 1.6, 2 H), 6.74 (dd, *J* = 7.5, 3.7, 2 H), 6.64 (s, 2 H), 6.32 (s, 2 H), 4.33–4.24 (m, 4 H), 4.10 (dd, *J* = 13.5, 9.1, 1 H), 3.36 (quintet, *J* = 5.6), 3.48 (dd, *J* = 19.7, 14.4, 1 H), 3.35 (dd, *J* = 17.4, 14.4, 1 H), 2.46 (m, 1 H), 2.10 (m, 1 H), 2.19 (s, 6 H), 2.14 (s, 3 H), 2.00 (s, 3 H), 1.68 (s, 6 H, 2 X). ^{13}C NMR (75.5 MHz): 142.97 (J_{CP} = 2.7), 141.01, 138.21 (J_{CP} = 7.8), 136.72, 136.15, 134.26 (J_{CP} = 7.3), 130.25, 130.16, 129.60, 129.46 (J_{CP} = 5.5), 128.83, 128.19, 128.11, 127.38, 126.61, 126.39, 126.32, 126.29, 126.10, 125.67, 59.92, 57.14, 45.96 (J_{CP} = 2.4), 44.81 (J_{CP} = 2.0), 43.41 (J_{CP} = 6.4), 42.57 (J_{CP} = 102.7), 20.60, 20.40, 20.09, 19.55. ^{31}P NMR (121.6 MHz): 26.87. MS (70 eV): 626 (M^+, 1), 133 (100). Anal. calcd. for $C_{42}H_{47}N_2OP$ (626.82): C 80.48, H 7.56, N 4.47, P 4.94; found: C 80.60, H 7.62, N 4.40, P 4.86.

*(*RS*)-(4*l*,6*l*)-1,3-Bis-(1-methylethyl)-4,6-diphenyl-2-ethyl-1,3,2-diaza-phosphorinane 2-oxide (**6c**)*: From 310 mg (0.87 mmol) of phosphite **7c**, 0.56 mL (0.96 mmol) of *n*-BuLi, and 104 μL (1.31 mmol) of ethyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3) afforded 310 mg (93%) of diazaphosphorinane **6c** as a colorless solid. An analytical sample was obtained by recrystallization from Et_2O/pentane: mp 141–142°C. IR (CCl_4): 3063 w, 1246 s. MS (70 eV): 384 (M^+, 22), 355 (100). TLC: R_f 0.31 (hexane/EtOAc/*i*-PrOH, 35:62:3). ^{1}H NMR (300 MHz): 7.60 (d, *J* = 7.4, 2 H), 7.38 (t, *J* = 7.5, 2 H), 7.30–7.17 (m, 4 H), 7.16 (d, *J* = 6.8, 2 H), 4.51 (dt, *J* = 10.9, 3.7, 1 H), 3.98 (dheptet, *J* = 15.9, 6.9, 1 H), 3.85 (dt, *J* = 11.4, 4.7, 1 H), 3.68 (dheptet, *J* = 15.9, 6.9, 1 H), 2.30–2.12 (m, 3 H), 1.96 (octet, *J* = 7.5, 1 H), 1.39 (dt, *J* = 19.1, 7.6), 1.19 (d, *J* = 6.5, 3 H), 1.17 (d, *J* = 6.8, 3 H), 0.93 (d, *J* = 7.2, 3 H), 0.90 (d, *J* = 7.2, 3 H). ^{13}C NMR (75.5 MHz): 144.76 (J_{CP} = 3.2), 142.67, 128.21, 127.79, 126.91, 126.71, 126.63, 126.24, 55.73, 52.90, 48.69 (J_{CP} = 3.2), 45.61 (J_{CP} = 6.0), 43.54 (J_{CP} = 7.3), 27.88 (J_{CP} = 123.7), 23.01 (J_{CP} = 2.5), 22.72, 21.19, 19.92, 8.31 (J_{CP} = 6.3). ^{31}P NMR (121.6 MHz): 27.51. Anal. calcd. for $C_{23}H_{33}N_2OP$ (384.50): C 71.85, H 8.65, N 7.29, P 8.06; found: C 71.93, H 8.64, N 7.30, P 8.08.

*(*RS*)-(4*l*,6*l*)-1,3-Bis-(2,2-dimethylpropyl)-4,6-diphenyl-2-ethyl-1,3,2-diaza-phosphorinane 2-oxide (**6d**)*: From 670 mg (1.52 mmol) of phosphite **7d**, 1.05 mL (1.79 mmol) of *n*-BuLi (1.70 M), and 195 μL (2.44 mmol) of ethyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 3:1–2:1) afforded 697 mg (97%) of diazaphosphorinane **6d** as a foam. An analytical sample was obtained by recrystallization from pentane: mp 124–125°C. IR (CCl_4): 3031 w, 1246 m. TLC: R_f 0.34 (hexane/EtOAc, 2:1). ^{1}H NMR (300 MHz): 7.55 (d, *J* = 7.4, 2 H), 7.41 (t, *J* = 7.5, 2 H), 7.33–7.24 (m, 4 H), 7.12 (d, *J* = 7.1, 2 H), 4.62 (dt, *J* = 15.0, 4.0, 1 H), 4.10 (ddd, *J* = 11.8, 7.4, 4.5, 1 H), 3.30 (dd, *J* = 14.8, 9.2, 1 H), 3.05 (dd, *J* = 14.7, 8.0, 1 H), 2.70 (dd, *J* = 14.8, 9.2, 1 H), 2.64 (dd, *J* = 14.7, 10.9, 1 H), 2.52–2.28 (m, 2 H), 2.18–1.97 (m, 2 H), 1.38 (dt, *J* = 18.5, 7.6, 3 H), 0.88 (s, 9 H), 0.79 (s, 9 H). ^{13}C NMR (75.5 MHz): 142.03, 140.17, 128.41, 128.18, 127.26, 127.12, 127.09, 126.92, 61.44, 59.55, 57.35 (J_{CP} = 3.0), 56.50 (J_{CP} = 2.5), 42.29 (J_{CP} = 9.4), 33.79, 33.23 (J_{CP} = 2.9), 29.35 (J_{CP} = 121.8), 28.89, 28.85, 8.60 (J_{CP} = 6.0). ^{31}P NMR (121.6 MHz): 30.99. MS (70 eV): 425 ($M^+ - CH_3$, 2.7), 383 (100). Anal. calcd. for $C_{27}H_{41}N_2OP$ (440.61): C 73.60, H 9.38, N 6.36, P 7.03; found: C 73.65, H 9.42, N 6.34, P 6.98.

Representative procedure for the alkylation of 1,3,2-diazaphosphorinane 2-oxides

The detailed procedure for the methylation of **5a** to afford **8a** is given. For all of the other alkylations, only the amounts of reagents, methods of analysis of diastereomeric mixtures and purification of the products are provided, along with the analytical data.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Dimethyl-4,6-diphenyl-2-(1-phenylethyl)-1,3,2-diaza-phosphorinane 2-oxide (**8a**)*: A flame-dried, 25-mL, three-necked, round-bottomed flask was charged with 105 mg (0.27 mmol) of diazaphosphorinane **5a** and 4 mL of THF. The flask was cooled to –78°C using a dry ice-acetone bath. *n*-BuLi (0.16 mL, 0.27 mmol, 1.71 M) was added to give a pale-yellow solution which was stirred for 30 min. Methyl iodide (65 μL, 1.04 mmol) was added by a syringe and the color dissipated slowly. After stirring for 1.1 h at –78°C, the reaction mixture was quenched with water (0.2 mL), then poured into water (10 mL), extracted with EtOAc (3 × 10 mL), and dried (Na_2SO_4). Filtration followed by concentration gave a pale yellow oil, which was assayed by HPLC (Supelco LC-NH_2) and found to be a mixture of diastereomers (87:13). Purification by column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3) gave 19 mg (17.5%) of minor **8a′** and 79.8 mg (73.3%) of major **8a** as a colorless solids. Data for **8a**: mp 141–142°C (pentane/Et_2O). IR (CCl_4): 3065 w, 1267 s. TLC: R_f = 0.3 (hexane/EtOAc/*i*-PrOH, 35:62:3). ^{1}H NMR (300 MHz): 7.48–7.17 (m, 13 H),

6.91 (m, 2 H), 4.08 (ddd, *J* = 11.7, 4.7, 2.6, 1 H), 3.69 (dd, *J* = 11.9,3.1, 1 H), 3.51 (dq, *J* = 20.3, 7.3, 1 H), 2.78 (d, *J* = 7.8, 3 H), 2.45(d, *J* = 8.9, 1 H), 1.77 (dd, *J* = 17.1, 7.4, 3 H), 1.59 (m, 1 H), 1.47 (ddd, *J* = 14.3, 12.0, 4.8, 1 H). ^{13}C NMR (75.5 MHz): 141.56 (J_{CP} = 6.5), 140.43 (J_{CP} = 6.7), 140.35, 128.77, 128.69, 128.62, 128.12, 128.08, 128.04, 127.22, 127.14, 126.91, 126.64, 126.59, 126.53, 61.16, 59.12, 44.16 (J_{CP} = 121.3), 40.86 (J_{CP} = 3.3), 34.45 (J_{CP} = 4.4), 33.99 (J_{CP} = 1.7), 15.80 (J_{CP} = 4.2). ^{31}P NMR (121.6 MHz): 31.80. MS (70 eV): 300 (M^+ +1 – PhC_2H_4, 20), 626 (M^+ – PhC_2H_4, 100). Anal. calcd. for $C_{25}H_{29}N_2OP$ (404.49): C 74.24, H 7.23, N 6.93, P 7.66; found: C 74.31, H 7.26, N 6.94, P 7.76. Data for **8a′**: TLC: R_f = 0.42 (hexane/EtOAc/*i*-PrOH, 35:62:3). ^{1}H NMR (300 MHz): 7.51–7.09 (m, 15 H), 4.26 (dt, *J* = 11.3, 3.5, 1 H), 3.77 (dd, *J* = 12.2, 1.5, 1 H), 3.35 (dq, *J* = 17.8, 7.2, 1 H), 2.59 (d, *J* = 8.4, 3 H), 2.45 (m, 1 H), 2.07 (d, *J* = 7.4, 3 H), 2.03 (m, 1 H), 1.77 (dd, *J* = 117.6, 7.2, 3 H). ^{31}P NMR (121.6 MHz): 29.82. MS (70 eV): 313 (14), 300 (M^+ + 1 – PhC_2H_4, 20), 626 (M^+ – PhC_2H_4, 100).

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Diethyl-4,6-diphenyl-2-(1-phenylethyl)-1,3,2-diaza-phosphorinane 2-oxide (**8b**)*: From 98 mg (0.23 mmol) of **5b**, 138 µL (0.23 mmol) of *n*-BuLi (1.70 M), and 44 µL (0.71 mmol) of methyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 31:62:7) was obtained 80 mg (78%) of a 61:39 (HPLC) diastereomeric mixture of **8b** as a sticky oil and 14.3 mg (13%) of recovered **5b**. An analytical sample was obtained by recrystallization from pentane/Et_2O at –78°C: mp 49–53°C. IR (CCl_4): 3029 w, 1239 s. TLC: R_f 0.44 (minor), 0.34 (major) (hexane/EtOAc/*i*-PrOH, 31:62:7). HPLC: t_R = 7.25 min (39%), 8.37 min (61%), (Supelco LC-NH_2, (hexane/EtOAc, 30:70), flow rate = 1.0 mL/min). ^{1}H NMR (300 MHz): 7.57–7.08 (m, 15 H), 4.50–4.45 (m, 1H), 4.02–3.95 (m, 1 H), 3.53–3.19 (m, 2.6 H), 3.04–2.90 (m, 1 H), 2.64–2.52 (m, 1 H), 2.42 (ddd, *J* = 14.0, 10.2, 4.1, 0.4 H), 2.31 (dheptet, *J* = 9.2, 6.9, 0.4 H), 2.07 (dt, *J* = 14.6, 3.1, 0.4 H), 1.95 (ddd, *J* = 16.8, 14.2, 4.3, 0.6 H), 1.83–1.78 (m, 0.6 H), 1.77 (dd, *J* = 9.6, 7.4, 1.8 H), 1.74 (dd, *J* = 10.0, 7.3, 1.2 H), 1.08 (t, *J* = 7.1, 1.8 H), 1.03 (t, *J* = 7.0, 1.2 H), 0.96 (t, *J* = 6.9, 1.8 H), 0.44 (t, *J* = 7.1, 1.2 H). ^{13}C NMR (75.5 MHz): 142.20 (J_{CP} = 4.8), 141.38 (J_{CP} = 5.3), 140.94 (J_{CP} = 5.7), 140.81 (J_{CP} = 6.2), 140.31, 140.05, 129.03, 128.99, 128.59, 128.44, 128.39, 128.29, 128.12, 128.06, 127.42, 127.38, 127.22, 127.20, 127.10, 126.99, 126.92, 126.67, 126.60, 126.58, 126.46, 57.87, 57.41, 55.05, 54.18, 48.46 (J_{CP} = 121.7), 45.86 (J_{CP} = 122.0), 41.61 (J_{CP} = 5.8), 41.27 (J_{CP} = 4.2), 39.93 (J_{CP} = 2.9), 39.85, 39.81, 39.64, 17.63 (J_{CP} = 3.2), 17.26 (J_{CP} = 3.7), 13.59, 13.33 (J_{CP} = 3.7), 13.28, 12.20 (J_{CP} = 3.6). ^{31}P NMR (121.6 MHz): 29.34 (major), 28.76 (minor). MS (70 eV): 328 (M^+ +1 – PhC_2H_4, 22), 327 (M^+ – PhC_2H_4, 100). Anal. calcd. for $C_{27}H_{33}N_2OP$ (432.54): C 74.97, H 7.69, N 6.48, P 7.16; found: C 74.88, H 7.87, N 6.36, P 6.94.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Bis(1-methylethyl)-4,6-diphenyl-2-(1-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**8c**)*: From 170 mg (0.38 mmol) of **5c**, 224 µL (0.38 mmol) of *n*-BuLi (1.70 M), and 71 µL (1.14 mmol) of methyl iodide followed by purification by column chromatography (hexane/EtOAc/*i*-PrOH, 35:60:5) was obtained 153 mg (87%) of a 58:42 (^{31}P NMR) diastereomeric mixture of **8c** as a foam. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 114–117°C. IR (CCl_4): 2904 s, 1252 s. TLC: R_f 0.41 (hexane/EtOAc/*i*-PrOH, 35:60:5). HPLC: t_R = 7.30 min (42%), 8.57 min (58%), Supelco LC-NH_2, (hexane/EtOAc, 3:2), flow rate = 1.0 mL/min). ^{1}H NMR ($CDCl_3$, 300 MHz): 7.48–7.17 (m, 15 H), 4.55 (dt, *J* = 13.1, 3.7, 0.4 H), 4.46 (dt, *J* = 9.9, 3.8, 0.6 H), 4.14 (dt, *J* = 12.4, 3.0, 0.6 H), 4.04–3.77 (m, 1 H), 3.69–3.26 (m, 1.4 H), 2.62–2.52 (m, 0.6 H), 2.33–2.23 (m, 0.4 H), 1.98–1.80 (m, 1 H), 1.82 (dd, *J* = 17.5, 7.2, 1.8 H), 1.74 (dd, *J* = 17.4, 7.3, 1.2 H), 1.29 (d, *J* = 6.8, 1.8 H) 1.22 (d, *J* = 6.7, 1.2 H), 1.16 (d, *J* = 6.9, 1.2 H), 0.96 (d, *J* = 6.8 1.8 H), 0.86 (d, *J* = 6.6, 1.2 H), 0.72 (d, *J* = 6.7, 1.8 H), 0.54 (d, *J* = 6.8, 1.2 H), 0.48 (d, *J* = 6.7, 1.8 H). ^{13}C NMR (75.5 MHz): 145.30 (J_{CP} = 3.8), 144.33 (J_{CP} = 4.7), 143.47, 143.43, 141.50 (J_{CP} = 5.2), 141.12 (J_{CP} = 4.8), 129.25, 129.17, 129.06, 128.98, 128.42, 128.21, 128.19, 128.00, 127.97, 127.93, 127.91, 127.83, 127.26, 127.11, 127.07, 127.03, 126.95, 126.84, 126.49, 126.45, 126.30, 126.28, 55.20, 54.97, 54.47 (J_{CP} = 1.9), 54.25, 49.35, 48.57 (J_{CP} = 117.6), 47.54 (J_{CP} = 3.4), 47.01 (J_{CP} = 4.3), 46.85 (J_{CP} = 119.6), 43.10 (J_{CP} = 6.2), 43.00, 25.15, 24.74, 23.12 (J_{CP} = 3.3), 21.91 (J_{CP} = 2.6), 21.89, 21.36, 20.22 (J_{CP} = 4.2), 18.71 (J_{CP} = 3.4), 18.27 (J_{CP} = 4.1), 18.06 (J_{CP} = 3.4). ^{31}P NMR (121.6 MHz): 29.16 (major), 28.13 (minor). MS (70 eV): 445 (M^+ – CH_3), 355 (100). Anal. calcd. for $C_{29}H_{37}N_2OP$ (460.60): C 75.62, H 8.10, N 6.08, P 6.72; found: C 75.42, H 8.17, N, 5.99, P 6.74.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Bis-(2,2-dimethylpropyl)-4,6-diphenyl-2-(1-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**8d**)*: From 180 mg (0.36 mmol) of **5d**, 211 µL (0.36 mmol) of *n*-BuLi (1.70 M), and 67 µL (1.07 mmol) of methyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 2:1) was obtained 152 mg (82%) of a 92:8 (^{31}P NMR) diastereomeric mixture of **8d** as a foam and 19.5 mg (11%) of recovered **5d**. An analytical sample was obtained by recrystallization from TBME. Enantiomerically enriched (–)-**8d** was also prepared from (*S*,*S*)-**5d** in 74% yield with 94:6 ratio of diastereomers: mp 150–152°C. For (–)-**8d**: [α] = – 98.4 (c = 1.04, $CHCl_3$), [α] = – 281.5 (c = 1.04, $CHCl_3$). IR (CCl_4): 3065 w, 1244 s. TLC: R_f 0.54 (hexane/EtOAc, 2:1). HPLC: t_R = 8.30 min (92%), 9.62 min (8%), (Supelco LC-NH_2, (hexane/EtOAc, 85:15), flow rate = 1.0 mL/min). ^{1}H NMR (300 MHz): 7.60–7.14 (m, 15 H), 4.65–4.58 (m, 0.08 H), 4.39–4.33 (m, 1.84 H), 4.24–4.17 (m, 0.08 H), 3.46 (dq, *J* = 14.3, 7.3, 1 H), 3.29 (dd, *J* = 14.6, 8.0, 0.92 H), 3.22 (dd, *J* = 14.8, 8.4, 0.08 H), 3.12 (dd, *J* = 14.8, 5.9, 0.08 H), 2.96 (dd, *J* = 15.2, 8.5, 0.08 H), 2.73 (ddd, *J* = 16.5, 12.9, 4.2, 0.92 H), 2.55–2.44 (m, 1.92 H), 2.34–2.21 (m, 0.08 H), 2.15–1.93 (m, 2 H), 1.77 (dd, *J* = 17.6, 7.2, 0.24 H), 1.75 (dd, *J* = 16.8, 7.2, 2.76 H). ^{13}C NMR (75.5 MHz): 142.07, 141.86 (J_{CP} = 5.5), 141.67, 129.38, 129.29, 129.06, 128.99, 128.66, 128.28, 128.03, 127.62, 127.41, 127.33, 127.19, 127.10, 127.01, 126.85, 126.57, 126.54, 126.42, 63.44, 61.36 (J_{CP} = 1.7), 60.89, 58.75, 57.98, 57.70 (J_{CP} = 2.7), 56.11 (J_{CP} = 1.9), 55.19 (J_{CP} = 2.2), 49.64 (J_{CP} = 109.5), 47.11 (J_{CP} = 110.0), 42.78 (J_{CP} = 9.5), 42.49 (J_{CP} = 7.2), 34.27, 33.52, 32.46 (J_{CP} = 3.7), 31.68 (J_{CP} = 3.2), 29.34, 29.23, 29.09, 28.27, 20.19 (J_{CP} = 4.9), 18.66 (J_{CP} = 4.2). ^{31}P NMR (121.6 MHz): 29.55 (minor), 28.47 (major). MS (70 eV): 501 (M^+ – CH_3, 2.2), 411

(100). Anal. calcd. for $C_{29}H_{37}N_2OP$ (516.71): C 76.71, H 8.78, N 5.42, P 5.99; found: C 76.64, H 8.79, N 5.40, P 5.97.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Dibenzyl-4,6-diphenyl-2-(1-phenylethyl)-1,3,2-diaza-phosphorinane 2-oxide (**8e**)*: From 192 mg (0.35 mmol) of **5e**, 0.21 mL (0.35 mL) of *n*-BuLi (1.70 M), and 66 mL (1.06 mmol) of methyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 4:1–2:1) was obtained 189 mg (96%) of a 75:25 (HPLC) diastereomeric mixture of **8e** as a colorless solid. An analytical sample was obtained by recrystallization from pentane/Et_2O: mp 175–179°C. IR (CCl_4): 3065 w, 1210 s. MS (70 eV): 451 (100). TLC: R_f 0.47 (hexane/EtOAc, 4:1). HPLC: t_R = 16.39 min (25%), 19.15 min (75%), (Supelco LC-NH_2, (hexane/EtOAc, 85:15), flow rate = 1.0 mL/min). ^{1}H NMR (300 MHz): 7.70–6.49 (m, 25 H), 4.90 (dd, *J* = 16.5, 8.1, 0.75 H), 4.86 (dd, *J* = 14.0, 7.0, 0.25 H), 4.40 (dd, *J* = 14.8, 7.8, 0.75 H), 4.36 (dt, *J* = 15.4, 3.5, 0.75 H), 4.11 (dt, *J* = 12.7, 3.6, 0.25 H), 4.03 (dd, *J* = 16.5, 4.0, 0.75 H), 3.88 (dd, *J* = 14.7, 7.3, 0.25 H), 3.79–3.75 (m, 0.25 H), 3.67 (dd, *J* = 14.7, 3.4, 0.25 H), 3.60–3.40 (m, 2 H), 2.89 (t, *J* = 14.2), 2.57–2.47 (m, 0.25 H), 2.29–2.19 (m, 0.75 H), 1.87 (dd, *J* = 17.9, 7.3, 0.75 H), 1.76 (dd, *J* = 17.4, 7.2, 2.25 H), 1.76 (dd, *J* = 17.4, 7.2, 2.25 H), 1.87–1.64 (m, 1 H). ^{13}C NMR (75.5 MHz): 141.81 (J_{CP} = 3.7), 141.04 (J_{CP} = 6.1), 140.61 (J_{CP} = 4.7), 138.88, 138.67, 137.32 (J_{CP} = 4.8), 136.73 (J_{CP} = 4.9), 136.60 (J_{CP} = 7.3), 130.52, 130.26, 129.15, 129.06, 128.98, 128.71, 128.47, 128.45, 128.32, 128.20, 128.18, 128.12, 128.06, 127.77, 127.51, 127.56, 127.43, 127.29, 127.18, 126.98, 126.89, 126.82, 126.61, 126.53, 59.30, 58.77, 55.34, 55.14, 50.48 (J_{CP} = 3.3), 49.43 (J_{CP} = 3.9), 48.98 (J_{CP} = 120.7), 48.72 (J_{CP} = 123.7), 48.39 (J_{CP} = 2.7), 48.08 (J_{CP} = 2.1), 41.61 (J_{CP} = 5.1), 18.76 (J_{CP} = 4.3), 18.06 (J_{CP} = 3.8). ^{31}P NMR (121.6 MHz): 29.54 (as a mixture). Anal calcd. for $C_{29}H_{37}N_2OP$ (556.69): C 75.62, H 8.10, N 6.08, P 6.72; found: C 75.42, H 8.17, N 5.99, P 6.74.

*(*RS*)-(4*l*,6*l*,1′*x*)-4,6-Diphenyl-1,3-bis-(2,4,6-trimethylphenylmethyl)-2-(1-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**8f**)*: From 250 mg (0.40 mmol) of **5f**, 0.24 mL (0.40 mmol) of *n*-BuLi (1.70 M), and 75 μL (1.05 mmol) of methyl iodide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 4:1) was obtained 240 mg (94%) of a 74:26 (^{31}P NMR) diastereomeric mixture of **8f** as a colorless solid. An analytical sample was obtained by recrystallization from Et_2O: mp 208–209°C. IR (CCl_4) 3063 m, 1229 s. TLC: R_f 0.42 (hexane/EtOAc, 4:1). ^{1}H NMR (300 MHz): 7.63 (d, *J* = 7.4, 2 H), 7.38 (t, *J* = 7.3, 2 H), 7.27–6.80 (m, 11.26 H), 6.85 (m, 1.48 H), 6.57 (s, 0.74 H), 6.53 (s, 0.26 H), 6.43 (d, *J* = 7.6, 0.26 H), 6.40 (s, 0.26 H), 6.27 (s, 0.74 H), 4.90 (dd, *J* = 13.8, 6.3, 0.76 H), 4.68 (dd, *J* = 13.4, 7.7, 0.26 H), 4.51 (dd, *J* = 13.8, 8.1, 0.26 H), 4.42 (dd, *J* = 13.8, 4.4, 0.76 H), 4.41–4.34 (m, 0.26 H), 4.12 (m, 0.74 H), 3.98 (dd, *J* = 13.5, 6.0, 0.74 H), 3.91–3.84 (m, 1.52 H), 3.71–3.65 (m, 0.26 H), 3.59 (dq, *J* = 14.1, 7.1, 0.74 H), 3.41 (dq, *J* = 16.3, 7.4, 0.26 H), 2.85–2.74 (m, 0.74 H), 2.62 (d, *J* = 13.5, 0.78 H), 2.49–2.38 (m, 0.26 H), 2.34 (s, 0.78 H), 2.13–1.79 (m, 20.44 H). ^{13}C NMR (75.5 MHz): 142.53 (J_{CP} = 4.5), 142.22 (J_{CP} = 2.1), 142.07 (J_{CP} = 1.7), 141.40 (J_{CP} = 5.1), 140.78 (J_{CP} = 5.4), 138.78, 138.01, 137.73, 136.62, 136.45, 136.18, 129.74, 129.67, 129.63, 129.55, 129.39, 129.31, 128.96, 128.88, 128.74, 128.66, 128.27, 128.20, 127.40, 126.96, 126.93, 126.81, 126.71, 126.64, 126.52, 126.41, 126.12, 126.07, 125.99, 125.60, 125.43, 60.87, 60.44, 56.61, 56.43, 49.40, 47.57 (J_{CP} = 113.4), 46.93 (J_{CP} = 2.9), 45.57, 44.41 (J_{CP} = 2.0), 43.31, 42.98 (J_{CP} = 10.6), 22.22, 20.87, 20.59, 20.51, 20.36, 20.07, 19.71, 19.43 (J_{CP} = 3.5), 17.60 (J_{CP} = 4.8), 14.08, 13.96. ^{31}P NMR (121.6 MHz): 32.15 (minor), 30.42 (major). MS (70 eV): 640 (M^+, 0.7), 133 (100). Anal. calcd. for $C_{43}H_{49}N_2OP$ (640.85): C 80.59, H 7.71, N 4.37, P 4.83; found: C 80.64, H 7.71, N 4.35, P 4.79.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Dimethyl-4,6-diphenyl-2-(1-methyl-2-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**9a**)*: From 230 mg (0.70 mmol) of **6a**, 0.45 mL (0.70 mmol) of *n*-BuLi (1.55 M), and 125 μL (1.05 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:60:5) was obtained 243 mg (83%) of a 65:35 (^{31}P NMR) diastereomeric mixture of **9a** as a viscose oil. IR (CCl_4): 3067 w, 1267 s. TLC: R_f 0.51 (hexane/EtOAc/*i*-PrOH, 35:60:5). ^{1}H NMR (300 MHz): 7.47–7.12 (m, 15 H), 4.43–4.35 (m, 1 H), 3.82–3.79 (m, 1 H), 3.48 (ddd, *J* = 112.1, 8.1, 2.9, 0.35 H), 3.38 (ddd, *J* = 12.5, 9.0, 2.4, 0.65 H), 2.75 (d, *J* = 7.6, 3 H), 2.64 (d, *J* = 8.2, 1.95 H), 2.61 (d, *J* = 7.8, 1.05 H), 2.71–2.46 (m, 2 H), 2.43–2.24 (m, 1 H), 2.13–2.04 (m, 1 H), 1.22 (dd, *J* = 17.8, 7.3, 1.95 H), 1.19 (dd, *J* = 17.5, 7.2, 1.05 H). ^{13}C NMR (75.5 MHz): 142.00 (J_{CP} = 5.1), 140.17, 140.06, 139.93, 139.87, 139.84, 128.72, 128.67, 128.55, 128.40, 128.17, 128.13, 127.23, 127.09, 126.46, 126.33, 126.18, 126.00, 125.89, 125.85, 62.32, 62.20, 59.87, 59.80, 42.43 (J_{CP} = 126.6), 41.64 (J_{CP} = 4.4), 41.49 (J_{CP} = 5.3), 40.40 (J_{CP} = 126.9), 37.02, 36.59, 34.31, 34.26, 34.18, 33.59, 13.54 (J_{CP} = 3.7), 12.99 (J_{CP} = 3.3). ^{31}P NMR (121.6 MHz): 33.82 (minor), 33.76 (major). MS (70 eV): 418 (M^+, 5), 91 (100). Anal. calcd. for $C_{36}H_{31}N_2OP$ (418.52): C 74.62, H 7.47, N 6.69, P 7.40; found: C 74.47, H 7.53, N 6.62, P 7.28.

*(*RS*)-(4*l*,6*l*,1′*x*)-1,3-Bis-(1-methylethyl)-4,6-diphenyl-2-(1-methyl-2-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**9c**)*: From 240 mg (0.62 mmol) of **6c**, 0.40 mL (0.62 mmol) of *n*-BuLi (1.56 M), and 111 μL (0.93 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc/*i*-PrOH, 35:62:3) was obtained 286 mg (96%) of a 78:22 (HPLC) diastereomeric mixture of **9c** as a colorless solid. An analytical sample was obtained by recrystallization from pentane/TBME: mp 138–142°C. IR (CCl_4): 3029 w, 1231 s. TLC: R_f 0.56 (hexane/EtOAc/*i*-PrOH, 35:60:5). HPLC: t_R = 19.08 min (78%), 23.20 min (22%), (Supelco LC-NH_2, (hexane/EtOAc, 4:1), flow rate = 1.0 mL/min). ^{1}H NMR (300 MHz): 7.67–7.19 (m, 15 H), 4.59 (dt, *J* = 14.6, 3.6, 1 H), 4.08–3.95 (m, 2 H), 3.84–3.59 (m, 2 H), 2.65 (ddd, *J* = 12.9, 12.6, 3.9, 1 H), 2.63–2.33 (m, 2 H), 2.02 (dt, *J* = 14.3, 3.6, 1 H), 1.40–1.19 (m, 4 H), 1.38 (d, *J* = 6.8), 1.27 (d, *J* = 6.7), 0.98 (d, *J* = 6.8), 0.94 (d, *J* = 6.8, 12 H), 0.91 (d, *J* = 6.9), 0.87 (d, *J* = 6.9). ^{13}C NMR (75.5 MHz): 144.53 (J_{CP} = 4.7), 143.03, 140.71 (J_{CP} = 17.3), 128.75, 128.67, 128.19, 128.17, 127.78, 126.94, 126.80, 126.65, 126.42, 125.84, 125.79, 55.24, 54.74, 53.64, 53.58, 49.39 (J_{CP} = 1.9), 48.83 (J_{CP} = 2.8), 46.49 (J_{CP} = 7.4), 46.41 (J_{CP} = 5.3), 43.54 (J_{CP} = 7.4), 43.46 (J_{CP} = 5.7), 39.98 (J_{CP} = 124.1),

38.72 (J_{CP} = 125.4), 38.49, 37.52, 24.21, 23.89, 22.91 (J_{CP} = 3.2), 22.54 (J_{CP} = 2.2), 21.48, 21.39, 20.13 (J_{CP} = 4.0), 19.96 (J_{CP} = 3.5), 15.01 (J_{CP} = 3.6), 13.75 (J_{CP} = 2.8). ^{31}P NMR (121.6 MHz): 31.58 (minor), 31.23 (major). MS (70 eV): 355 (100). Anal. calcd for $C_{30}H_{39}N_2OP$ (474.62): C 75.92, H 8.28, N 5.90, P 6.53; found: C 75.86, H 8.34, N 5.85, P 6.42.

*(*RS*)-(4*l,6*l,*1′*x)-1,3-Bis-(2,2-dimethylpropyl)-4,6-diphenyl-2-(1-methyl-2-phenylethyl)-1,3,2-diazaphosphorinane 2-oxide (**9d**)*: From 265 mg (0.60 mmol) of **6d**, 0.38 mL (0.60 mmol) of *n*-BuLi, and 107 μL (0.90 mmol) of benzyl bromide followed by purification by SiO_2 column chromatography (hexane/EtOAc, 2:1) was obtained 314 mg (98%) of a 92:8 (HPLC) diastereomeric mixture of **9d** as a foam. An analytical sample was obtained by recrystallization from Et_2O: mp 208–209°C. IR (CCl_4): 3065 w, 1200 s. TLC: R_f 0.48 (hexane/EtOAc, 2:1). HPLC: t_R = 46.13 min (8%), 49.36 min (92%), (LC-Prep-Si (hexane/EtOAc/*i*-PrOH, 79.8:20:0.2), flow rate = 1.2 mL/min). ^{1}H NMR (300 MHz): 7.61–7.13 (m, 15 H), 4.70 (dt, *J* = 15.1, 3.6, 0.92 H), 4.69 (dt, *J* = 14.4, 3.6, 0.08 H), 4.36–4.20 (m, 1 H), 3.72–3.66 (m, 0.92 H), 3.56–3.47 (m, 0.08 H), 3.39–3.22 (m, 2 H), 3.04 (dd, *J* = 14.8, 6.1, 0.08 H), 2.93 (dd, *J* = 14.9, 5.6, 0.92 H), 2.81–2.43 (m, 4 H), 2.12 (dt, *J* = 14.5, 3.8, 1 H), 1.36 (dd, *J* = 17.3, 6.9, 0.06 H), 1.22 (dd, *J* = 18.0, 7.0, 2.7 H), 0.87 (s, 9 H), 0.85 (s, 9 H). ^{13}C NMR (75.5 MHz): 141.51, 140.68, 140.45, 139.80, 128.92, 128.79, 128.43, 128.30, 128.27, 127.50, 127.24, 127.16, 127.07, 126.06, 125.96, 61.42, 61.05, 58.35 (J_{CP} = 2.6), 58.28 (J_{CP} = 1.8), 58.04, 57.46, 55.98(J_{CP} = 1.7), 55.77 (J_{CP} = 1.9), 42.77 (J_{CP} = 7.0, 42.62 (J_{CP} = 2.9), 41.35 (J_{CP} = 120.6), 38.00, 37.77, 33.99, 33.04, 32.91 (J_{CP} = 3.9), 32.77 (J_{CP} = 3.6), 29.51, 29.38, 29.18, 29.11, 14.66 (J_{CP} = 2.0), 14.31 (J_{CP} = 3.1). ^{31}P NMR (121.6 MHz): 33.18 (as a mixture). MS (70 eV): 515 ($M^+ - CH_3$, 2.7), 473 (100). Anal. calcd. for $C_{34}H_{47}N_2OP$ (530.73): C 76.95, H 8.93, N 5.28, P 5.84; found: C 76.90, H 9.03, N 5.26, P 5.82.

*(*S*)-Dimethyl-1-phenylethylphosphonate (**14**)*: In a 25-mL, round-bottomed flask equipped with a reflux condenser was placed a solution of (–)-**8d** in 4 mL of HOAc acid and 48% HBr solution. The reaction mixture was heated to reflux for 15 h, then was concentrated under reduced pressure to give a yellow orange oil. The oil was passed through ion-exchange resin column (AG® 50W-X8) using water as eluent. The major fraction was collected and concentrated to give a white solid. The solid was dissolved in water and basified with 1 N NaOH solution (pH ~ 13), reacidified, concentrated, and the acidic residue dissolved in methanol. The methanolic solution of **13** was treated with excess etheneal diazomethane diluted with water (10mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give a yellow oil. The oil was purified by SiO_2 column chromatography (EtOAc/*i*-PrOH, 99:1) to give 53 mg (70%) of (*S*)-**14** as a colorless oil. An analytical sample was obtained by Kugelrohr distillation: bp 115°C (0.3 Torr (1 Torr = 133.322 Pa)). $[\alpha]_{405}$ –15.7 c = 1.1, CH_2Cl_2) ((*S*)-configuration, 87% ee). TLC: R_f 0.23 (EtOAc/*i*-PrOH, 99:1). ^{1}H NMR (300 MHz): 7.37–7.24 (m, 5 H), 3.69 (d, *J* = 10.0, 3 H), 3.53 (d, *J* = 10.0, 3 H), 3.21 (dq, *J* = 22.7, 7.7, 1 H), 1.58 (dd, *J* = 18.5, 7.5, 3 H). ^{31}P NMR (121.6 MHz): 32.75.

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