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Asymmetric Electrophilic Amination of Chiral Phosphorus-Stabilized Anions

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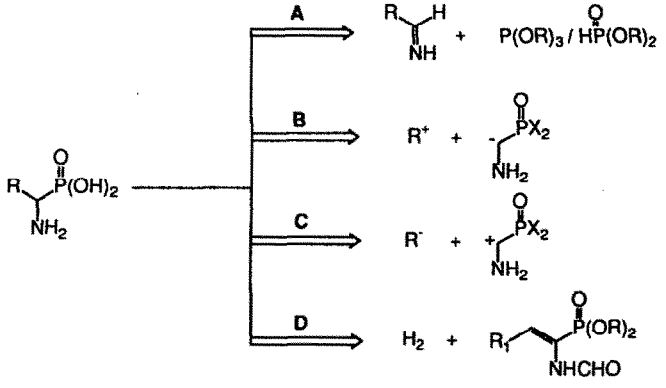
Key Words: Electrophilic Amination; α-Aminophosphonic acid; Chiral Phosphorus-Stabilized Anions.

Abstract: *The asymmetric electrophilic amination of phosphorus-stabilized anions derived from chiral oxazaphosphorinanes and diazaphospholidines is described. Trisyl azide is the reagent of choice for the amination process. The reaction is shown to be dependent on auxiliary structure, nature of the P-alkyl substituent and choice of amination procedure. Using the oxazaphosphorinanes 1a and cis-1e a high level of asymmetric induction can be achieved. Scalemic cis-1e provides the α-aminophosphonic acid 13 with 92% e.e. in the (S) antipode. The implications for anion conformation and effect of auxiliary structure on stereoselectivity are discussed.*

INTRODUCTION

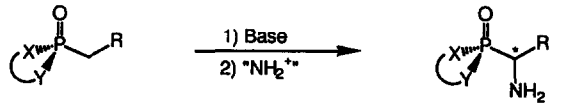
α-Aminophosphonic acids, analogs of α-amino acids,[1] are of interest due to their importance in biological systems where they function as antibiotics,[2] pharmacological agents[3] and enzyme inhibitors.[4] It has been shown that the biological activity of α-aminophosphonic acids is dependent upon absolute configuration[5] which makes the asymmetric synthesis of this class of compounds both interesting and of practical significance. Thus, in recent years, several synthetic methods providing aminophosphonic acids in moderate to good enantiomeric purity have been developed. These may be broadly classified on the basis of the stereodifferentiating event as depicted in Scheme 1.

Scheme 1



Path A involving nucleophilic addition of phosphites to imine and oxoiminum derivatives[6] (either component being chiral) constitutes the majority of asymmetric syntheses of aminophosphonic acids to date. However, these reactions usually exhibit only moderate enantioselectivity. Path B employing anionic[7] and Path C employing cationic[7e,h] phosphonoglycine equivalents have also been successfully employed. A recent synthesis of α-aminophosphonic acids by the alkylation of chiral, bicyclic phosphonamides derived from 1,2-cyclohexanediamine seems most promising in this respect.[7e] This process is however limited by the S_N2 reactivity of the alkylating agent. A report on the asymmetric hydrogenation of dehydroaminophosphonic acid derivatives[8] constitutes the sole example of Path D. Surprisingly, electrophilic amination of chiral, phosphorus-stabilized anions (Scheme 2), which would provide the most efficient and general approach to α-aminophosphonic acids, remains unexplored to date. The analogous electrophilic amination of chiral enolates has been studied in detail and constitutes a general synthesis of α-amino acids.[9] The major limitation of the alkylation procedure, namely reactivity of the alkylating reagent, is not an issue in the amination process.

Scheme 2

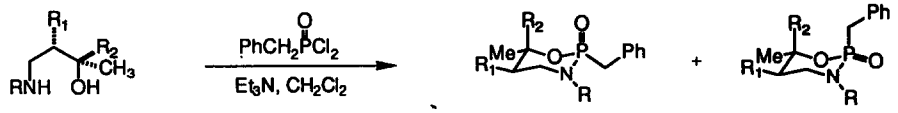


As part of an ongoing program on the development of stereoselective reations of chiral, phosphorus-stabilized anions,[10] an investigation of the feasibility of stereoselective electrophilic amination of such anions was undertaken. Previous studies had indicated that alkylations of anions derived from chiral oxazaphosphorinanes of the type **1** proceed with high diastereoselectivity.[10a] Several oxazaphosphorinanes and oxazaphospholidines were synthesized and examined as substrates for the amination process. The overall objective was to develop an auxiliary that would: 1) be readily available, 2) impose a strong conformational preference and asymmetric environment on the anion, 3) promote a stereoselective reaction and 4) be readily removed and recovered. This report will describe the scope and utility of the electrophilic amination of a variety of chiral phosphorus-stabilized anions.

RESULTS

A. Preparation of Oxazaphosphorinanes and Oxazaphospholidines. Most of the oxazaphosphorinanes and oxazaphospholidines employed in this study were readily prepared by combining benzylphosphosphonic dichloride[11] with the appropriate amino alcohols **2a-e**, **3**, **5a** and **5b**[12] (Table 1 and Scheme 3). In each case the products were obtained as a mixture of stereoisomers at phosphorus. For oxazaphosphorinanes **1d**, **1e** and **1f** the isomer with the *P*-benzyl group *cis* to the C(6) methyl is denoted as the *cis* isomer. *Cis*-**1d** has the benzyl group *cis* to the C(4) methyl group. Likewise, in *cis*-**4** and *cis*-**6a**, **6b** the benzyl group is *cis* to the bicycloheptane bridge. The stereoisomers could be readily differentiated on the basis of the downfield shift of the hydrogen (**1d, 1e, 1f, 6a**) or methyl group (**6b**) on the oxygen bearing carbon, presumably due to anisotropic deshielding by the P=O double bond, in the *cis* isomers. A similar trend was also observed in the ^{31}P spectra (δ ^{31}P *cis* > δ ^{31}P *trans*). The assignments for **1d** are tentative. A summary of the diagnostic NMR data is provided in Table 2. With the exception of **1a** (which is a racemate) these stereoisomers were separated and examined individually in the electrophilic amination reactions.

Table 1. Preparation of Oxazaphosphorinanes.



R	R_1	R_2	amino alcohol			yield, %
t-Bu	H	CH_3	**2a**	**1a**		55%
(S)-1-phenylethyl	H	CH_3	**2b**	**1b**	**1b**	45%
isobornyl	H	CH_3	**2c**	**1c**	**1c**	29%
t-Bu	CH_3	CH_3	**2d**	*trans*-**1d**	*cis*-**1d**	69%
t-Bu	H	H	**2e**	*cis*-**1e**	*trans*-**1e**	49%
$C(Et)_3$	H	H	**2f**			

Scheme 3

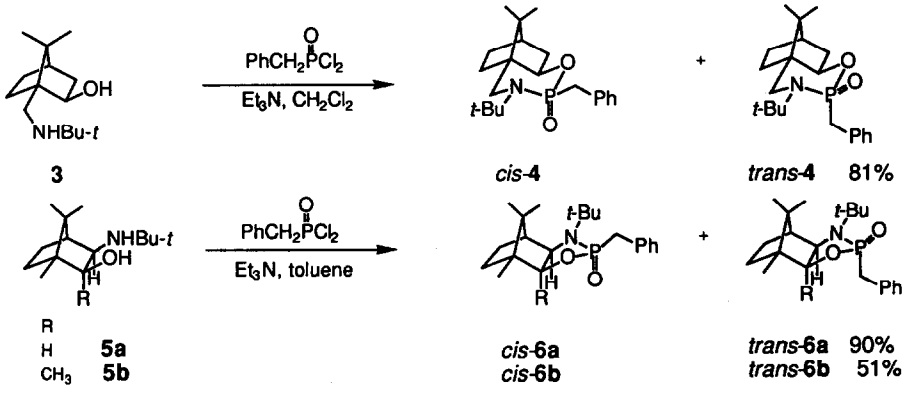


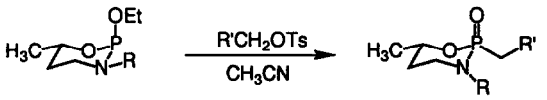
Table 2. Selected Spectroscopic Data.

Substrate	^{1}H NMR (ppm) HC-O[a] or H_3CC-O[b]	^{31}P NMR (ppm)
cis-**1e**	4.42	25.50
trans-**1e**	4.15	21.34
cis-**1f**	4.65-4.57	26.65
trans-**1f**	4.35-4.24	21.97
cis-**4**	4.25	27.90
trans- **4**	3.98	19.80
cis-**6a**	4.31	45.91
trans-**6a**	2.80-2.90	41.30
cis-**6b**	1.52	44.69
trans- **6b**	1.41	37.63

[a] For compounds **1e**, **1f**, **4** and **6a**. [b] For compound **6b**.

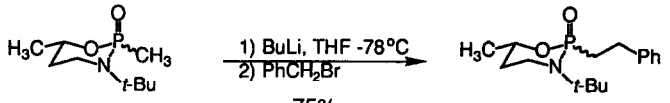
An alternative synthesis leading predominantly to the *cis P*-alkyl oxazaphosphorinanes involved conversion of the amino alcohol to the cyclic ethyl phosphite ($EtOPCl_2$, Et_3N, CH_2Cl_2) followed by subsequent Arbuzov reaction[13] with an appropriate alkyl tosylate (Scheme 4).

Scheme 4



Thus **1e**, **8e**, and **1f** were obtained in a ratio of 8/1, 5/1 and 11/1 with the *cis* isomer predominating (yields 54%, 78% and 78% respectively). The *P*-hydrocinnamyl oxazaphosphorinane *cis/trans*-**10e** was prepared by alkylation of the corresponding *P*-methyl compound *cis/trans*-**9e**, obtained as a 1/1 *cis/trans* mixture by condensation of **2e** and commercially available methylphosphonic dichloride (Scheme 5)

Scheme 5



cis/trans-**9e** *cis/trans*-**10e**

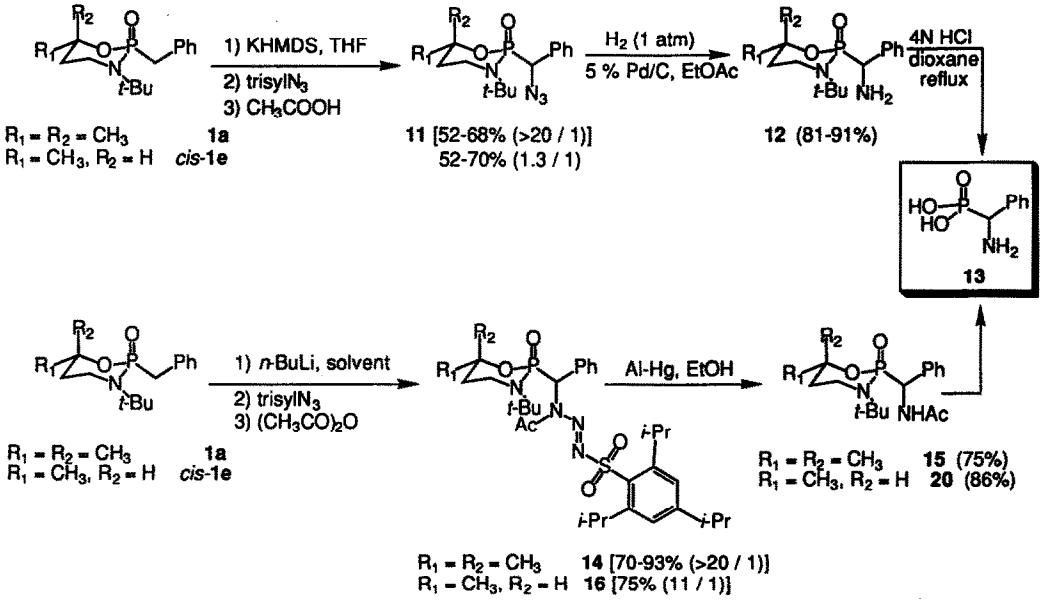
B. Electrophilic Amination of Oxazaphosphorinanes and Oxazaphospholidines. Initial experiments were conducted with the racemic oxazaphosphorinane **1a** (Scheme 6). After a brief survey of aminating reagents[14], trisyl azide was chosen as the ideal candidate due to its stability and chemoselectivity in asymmetric azide transfer to enolates.[9] Two general methods for amination were established after extensive optimization. Method A (Scheme 6, similar to the Evans' procedure[9] for the preparation of α-azido carboxylic acids), involved the deprotonation with KHMDS followed by the addition of trisyl azide and then acetic acid to decompose the triazine. This protocol afforded the α-azido phosphonamidate **11** in good yield (52-68%) with excellent diastereoselectivity. The minor isomer could not be detected by NMR spectroscopy or HPLC. In most of these reactions, unreacted starting material (23-41%) was also recovered. Reaction could not be driven to completion by the use of an excess of base or longer reaction times. Common additives (DMPU, HMPA) significantly increased the amount of recovered starting material suggesting that the reaction may be reversible .

To overcome the problem of incomplete conversion in the azide transfer step a modification was developed (Method B). Since it was suspected that the azide transfer might be reversible, various trapping agents were examined. In the optimized protocol, **1a** was deprotonated with *n*-BuLi, treated with trisyl azide and the intermediate lithiosulfonyltriazine was captured with acetic anhydride to afford a single acetyltriazine (**14**) in excellent yield (70-93%). Again, the minor diastereomer could not be detected by NMR or HPLC.

For the preparation of α-aminophosphonic acids a method for the transformation of the intermediate products was required. This reduction was easily accomplished for **11** by hydrogenation (1 atm, Pd / C) to give the α-aminophosphophonamidate **12**. A small amount of the minor diastereomer could be isolated at this stage and indicated that the selectivity in azide transfer was at least 50 / 1. The free, racemic α-aminophosphonic acid **13** could be obtained in good yield by acidic hydrolysis of **12**. Although the N-N bond in the acetyltriazine **14**

was resistant to hydrogenation (1 atm→100 psi, Pd / C or RaNi) it was readily cleaved by treatment with aluminum amalgam[15] to provide the α-acetamido phosphoramidate **15**. Again, acidic hydrolysis (4N HCl) of **15** gave the free α–aminophosphonic acid 13[1a] in good yield (75%).

Scheme 6



With the protocol for electrophilic amination thus established, the next step was choice of a suitable chiral, auxiliary to obtain scalemic α-aminophosphonic acids. Our success with *cis*-**1e** in stereoselective alkylations[10a] made it the obvious candidate. Thus, subjection of *cis*-**1e** to the electrophilic amination procedure (method A, Scheme 6) furnished the corresponding α-azido compound in good yield (52-70%), but to our amazement, with almost no selectivity (1.3 / 1). Fortunately, amination using method B (THF solvent) furnished the corresponding *N*-acetyltriazine **16** in good yield (56-79%, Scheme 6). Surprisingly, there was an erosion of diastereoselectivity (11 / 1 ratio by HPLC). Although *trans*-**1e** provided the corresponding α-azido compound (method A) with good selectivity (> 20 / 1), the yield was low. These results clearly indicated that the presence of the geminal dimethyl group at C(6) in **1a** was essential for stereoselectivity in the amination step. Apparently, subtle ring conformational effects strongly influence the accessibility of the anionic carbon.

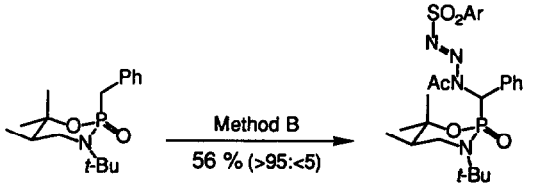
The best results for amination in the scalemic series were obtained with the oxazaphosphorinane *cis*-**1e** using method B and diethyl ether as the solvent. Thus, **16** could be produced in 75% yield as a 13 / 1 ratio of diastereomers (Scheme 6). We therefore attempted to generalize this reaction using substrates *cis*-**8e** (*P*-ethyl) and *cis*-**10e** (*P*-(2)-phenylethyl). Using method B only (in diethyl ether) these gave poor results (4 / 1 and 2 / 1 selectivity for **10e** and **12e** respectively, see Table 3). Interestingly, change of the *N*-alkyl group to triethyl carbinyl (*cis*-**1f**) had no significant effect on the selectivity (method B, 3 / 1).

The stereochemical course of electrophilic amination of *cis*-**1e** was established by cleavage of a 16 / 1 mixture (after chromatography) of acetytriazine diastereomers **16**, with aluminum amalgam followed by acidic hydrolysis of the α-acetamidophosphoramidate **20** (Scheme 6). The resulting phosphonophenyl glycine hydrochloride (98% yield) was neutralized with propylene oxide to furnish 13[16] that was 92% e.e. in the (*S*)-

antipode by HPLC analysis of the derived 3,5-dinitrobenzamide and polarimetry.[16] The auxiliary **2e** was recovered in 86% yield (hydrochloride salt) and > 97% e.e.

The continued search for a chiral auxiliary capable of stereoselection at the level of **1a** focused on maintaining the geminal dimethyl group in the ring. The most obvious solution, resolution of **1a** was clearly not practical. Therefore, we hoped to maintain the high diastereoselectivity inherent in **1a**, while modifying the amino alcohol auxiliary at positions other than C(6). We thus prepared *cis/trans*-**1d** from racemic **2d** and separated the isomers by chromatography. Using method B, *cis*-**1d** provided acetyltriazine **17** in modest yield (50%) and good selectivity (> 20 / 1, Scheme 7). However, this route was abandoned because *cis* **1d** was obtained as the minor component (in a mixture with *trans*-**1d**) after tedious separation and *trans*-**1d** does not react when subjected to the conditions of method B.

Scheme 7

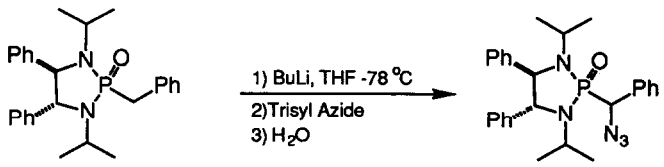


cis-**1d** **17**

An alternative approach involving modification of *N*-alkyl group was therefore investigated. Thus, we prepared *cis/trans*-**1b** and *cis/trans*-**1c** (Scheme 3) by incorporation of (-)-1-(phenyl)ethyl amine and (-)-bornylamine into the amino alcohol (alcohols **2b** and **2c**, Scheme 3). The diastereomeric (*cis/trans*) oxazaphosphorinanes could be readily separated but the configuration at phosphorus was not established. Unfortunately, and somewhat surprisingly, the amine group had a significant effect on the reaction giving complex mixtures of products in low selectivities in most cases. Similarly, the oxazaphosphorinanes *cis/trans*-**4** derived from ketopinic acid were also disappointing. The *cis* diastereomer of **4** reacted with high selectivity using method A (> 20 / 1) but in low yield (30%). The camphor derived oxazaphospholidines *cis/trans*-**6a** and *cis/trans*-**6b** were also investigated. The *cis* isomers gave disappointing results. The corresponding *trans* isomers were not available in sufficient quantity for testing.

We next examined a C_2 symmetric diamine as an auxiliary in a diazaphospholidine. The (*d,l*)-*N,N'*-diisopropyldiphenylethanediamine-derived **18** gave **19** in a 2:1 ratio (quantitative yield of crude product, Scheme 8). However, the reactions of **18** and several other chiral diazaphospholidines were more capricious than in the oxazaphosphorinane series and were not investigated further. A summary of the yields and diastereomeric ratios for all the substrates examined is provided in Table 3.

Scheme 8



(±) **18** **19**

Table 3. Electrophilic Amination of Phosphorus-Stabilized Anions.

entry	substrate	method	yield, %[a]	ratio[b]
1	**1a**	A	52-68	> 20 / 1
2	**1a**	B	70-93	> 20 / 1
3	**1b**	A	70	2 / 1
4	**1b**	B	52	> 20 / 1
5	*cis*-**1c** / *trans*-**1c**	B	74	5.3 / 1
6	(±) *cis*-**1d**	B	56	> 20 / 1
7	*cis*-**1e**	A	52-70	1.3 / 1
8	*cis*-**1e**	B[c]	75	13 / 1
9	*trans*-**1e**	A	34-53	> 20 / 1
10	*trans*-**1e**	B	47-60	3 / 1
11	*cis*-**6a**	B	70	6 / 1
12	*cis*-**6b**	B	85	9 / 1
13	*cis*-**4**	A	30	> 20 / 1
14	*cis*-**4**	B	62	2.5 / 1
15	*trans*-**4**	B	81	4.3 / 1
16	*cis*-**8e**	B	72	4 / 1
17	*cis*-**1f**	B	79	3 / 1
18	*cis*-**10e**	B	63	2 / 1
19	**18**	A	d	2 / 1

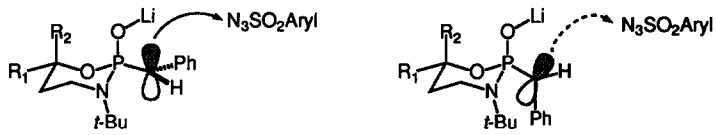
[a] Yield of isolated, purified product. [b] Ratio determined by HPLC or ^{1}H NMR or ^{31}P NMR analysis on crude product. [c] Diethyl ether used as solvent.
[d] Quantitative yield of crude product.

DISCUSSION

The observed selectivity in the electrophilic amination of *cis*-**1e** suggested a preferred reactive conformation for the benzylic carbanion which is dictated by the local chirality of the anion (i.e. phosphorus configuration). The sense of asymmetric induction (*S* configuration of the product α-aminophosphonic acid) implied that the *re* face of the anion underwent attack, the same stereochemical outcome as was observed in alkylation.[10a] Solution NMR studies of anions derived from **1a** and *cis*-**1e** indicate that these exist as a rapidly interconverting mixture of conformers of the oxazaphosphorinane ring.[17] This, combined with the low rotational barrier for the P-C bond in anions of this type[18] complicates a prediction of the reactive conformer in solution. However, two limiting conformations may be considered (Chart I): (**i**) an orthogonal anion in which the phenyl ring is oriented away from the *t*-butyl group and (**ii**) a parallel anion in which the phenyl ring is anti to the P-O bond to avoid interactions with the solvated lithium cluster. Approach of the electrophile 'syn' to the P-O bond in (**i**) and away from the *t*-butyl group in (**ii**) would lead to the observed stereochemistry of amination. The reasons for the drop in selectivity by removal of a single methyl group from C(6) in **1a** (from 50 / 1 in **1a** to 13 / 1 in **1e**) are most likely related to a change in the conformation of the ring and exposure of the anionic carbon in an unshielded environment. Based on the fact that anions of this type are planar[17,18,19] the observed trend in selectivity upon variation of the *P*-alkyl group (**1e** > *cis*-**10e**, *cis*-**8e**) is also consistent with either an

orthogonal or a parallel anion in which reduced interactions between the *P*-alkyl substituent and the *N*-alkyl group or solvated lithium cluster lead to a loss of conformational preference in the anion.

Chart 1



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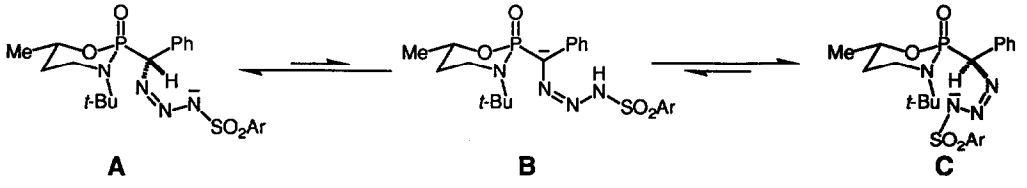
An interesting feature of the amination process is the dependence of diastereoselectivity on the choice of amination method (Table 3). Thus *cis* **1e** provides a 13 / 1 ratio of the acetyl triazine **16** (Scheme 6, method B) but only a 1.3 / 1 of the corresponding azide (method A). The same is true for **1b** (method A: 2 / 1, method B: 20 / 1). However, **4** furnished the azide with > 20 / 1 selectivity but method B proceeded with a selectivity of only 2.5 / 1. While an explanation of these results is not readily apparent, the erosion in selectivity for amination compared to alkylation[10a] may be accounted for either by the suspected reversibility of amination or by an intramolecular proton abstraction process.

Under kinetic control the stereodifferentiating event in either method A or B is addition of the carbanion to trisyl azide. The breakdown of triazine to the azide is, in principle, irrelevant to the stereochemical outcome of the process. However, if the addition were reversible, the more stable adduct would accumulate. This would certainly be dependent on solvent and counterion. Alternatively, equilibration may occur at the level of the triazene anion. Addition of the carbanion to the sulfonyl azide should produce the stereoelectronically favored *(Z)*-triazenyl anion **A**.[9,20] which is poised for an intramolecular proton abstraction leading to loss of stereochemical integrity. Some of the observed product ratios might then arise from a thermodynamic rather than a kinetic process. This may also explain why in some cases (*trans*-**1e**, **4**) azidation is more selective by method A (quench with acetic acid)than by method B (quench with acetic anhydride). Rapid protonation of **A** or **C** would avoid equilibration whereas acylation, which is expected to be slower, would allow the formation of **B** (Scheme 9). Although such a process is obviously inoperative in the electrophilic amination of enolates[9], it may be argued that steric crowding in **A** (due to the tetrahedral phosphorus) favors some process of equilibration.[21] The intrinsic selectivity for amination of the chiral anion may thus remain unexpressed. Such an analysis indicates a strong dependence of stereoselectivity on the acidity of the α-hydrogen in **A** or **C** (which is ultimately dictated by the nature of the substituents on phosphorus), and the reaction conditions (Scheme 9).

Scheme 9



In summary, the scope of electrophilic amination of phosphorus stabilized carbanions in a series of chiral oxazaphosphorinanes and oxazaphosphiolidines has been investigated. It has been demonstrated that the

stereoselectivity of the amination process is dependent on the *P*-alkyl substituent and in some cases a high level of asymmetric induction can be achieved. Current efforts focus on 1) investigation of other electrophilic aminating reagents and 2) the development of C_2-symmetric diamine auxiliaries for phosphorus.

EXPERIMENTAL

General Methods. ^1H NMR and ^{13}C NMR spectra were recorded on General Electric QE-300 (300 MHz for ^1H, 75.5 MHz for ^{13}C) or GN 500 (500 MHz for ^1H and 125.7 MHz for ^{13}C) spectrometer in deuterochloroform with tetramethylsilane (TMS) or chloroform as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration, and interpretation. ^{31}P NMR spectra were recorded on a General Electric GE 300 (121.4 MHz) spectometer in deuterochloroform with 85% phosphoric acid as an external standard. Infrared spectra (IR) were obtained on a IBM FTIR-32 spectrophotometer. Peaks are reported in units of cm^{-1} with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Varian MAT CH-5 spectrometer with ionization voltages of 70 eV. High resolution EI mass spectra were obtained on a Varian MAT-731. Data are reported in the form m/e (intensity relative to base=100) and interpretation. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Analytical thin-layer chromatography (TLC) was performed on Merk silica gel plates with QF-254 indicator. Visualization was accomplished with UV light, iodine, vanillin, and/or *p*-anisaldehyde solution. Silica gel column chromatography was performed by the method of Still[22] with 32-63 μm silica gel (Woelm). Medium pressure liquid chromatography (MPLC) was performed using Merck Lobar columns. Analytical high pressure liquid chromatography (HPLC) was performed on a Hewlett Packard 1090 Liquid Chromatograph with a Perkin-Elmer LC-75 Spectrophotometric Detector. The columns used were a Supelco LC-Si 5μ column and a Pirkle Covalent L-Naphthylalanine 5μ column; the detector wavelength = 254 nm, the flow rate = 1 mL/min, and solvent systems were as denoted. Retention times (t_R) and integrated ratios were obtained from a Hewlett Packard 3390A integrator. Optical rotations were obtained on a Jasco DIP-360 Digital Polarimeter and reported as follows: $[\alpha]^{temperature}_{wavelength}$ (concentration (c = g/100 mL), solvent). Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Bulb-to-bulb distillations were done on a Buchi GKR-50 Kugelrohr; boiling points (bp) refer to air bath temperatures and are uncorrected.

Amino alcohols 2b and 2c: These were prepared by modification of the literature procedure[10c] for the preparation of **2a** using *(S)*-1-(phenyl)ethylamine and *(S)*-bornylamine respectively.

4-[*N*-(*S*)-phenylethyl]amino-2-methyl-2-butanol (2b) Data for **2b**: bp 120-130 °C (0.4 Torr); ^1H NMR (300 MHz) 7.36-7.22 (m, 5 H, Ph), 6.1 (br, 1 H, NH), 3.70 (q, *J* = 6.6, 1H, CHN), 2.79-2.65 (m, 2 H, CH_2N), 1.67-1.40 (m, 2 H, CH_2), 1.36 (d, *J* = 6.6, 3 H, CH_3), 1.21 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 144.37 (Ph), 128.29 (Ph), 126.96 (Ph), 126.39 (Ph), 70.77 (CO), 58.34 (*C*HN), 43.82 (CH_2N), 40.58 (CH_2), 29.90 (CH_3), 28.93 (CH_3), 23.89 (CH_3); IR (neat) 3287 (s), 3061 (s), 3028 (s), 2971 (s), 2924 (s), 1493 (s), 1451 (s), 1362 (s), 1310 (m), 1269 (m), 1246 (m), 1206 (m), 1161 (s), 1119 (s), 1076 (m), 1042 (w), 1028 (m), 980 (m), 957 (m), 889 (m); MS (70 eV) 207 (1, M^+), 192 (55), 174 (20), 145 (24), 134 (14), 118 (15), 106 (20), 105 (100), 91 (15), 79 (12), 77 (14); high resolution MS calcd for $C_{13}H_{21}NO$ (M^+) 207.1623, found 207.1629.

2-Methyl-4-[(1'*R*, exo)-*N*-1',7',7'-trimethylbicyclo[2.2.1]hept-2'-yl]amino-2-butanol (2c) Data for **2c**: bp 120-130 °C (0.4 Torr); ^1H NMR (300 MHz) 2.95-2.87 (m, 1 H), 2.73-2.66 (m, 1 H), 2.46 (t, *J* = 6.4, 1 H), 1.70-1.42 (m), 1.23 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 70.62 (CO), 67.07 (C(2')), 48.07, 46.46, 45.01 (CH_2N), 44.82, 40.60, 38.24, 36.78, 29.89 (CH_3), 29.06 (CH_3), 27.03, 20.32 (CH_3), 12.00 (CH_3); IR (neat) 3314 (m), 2952 (s), 2874 (s), 1476 (m), 1453 (m), 1422 (m), 1364 (m), 1308 (m), 1269 (m), 1248 (w), 1152 (s), 1117 (m), 1098 (w), 1080 (w), 1017 (w), 970 (w), 939 (w), 909 (w), 891 (w); MS (70 eV) 239 (30, M^+), 224 (11), 168 (60), 166 (19), 150 (13), 137 (15), 130 (12), 116 (22), 112 (11), 98 (21), 96 (18), 95 (100), 93 (11), 82 (17), 81 (25), 69 (19), 67 (19), 56 (33), 55 (24), 44 (14), 43 (16), 42 (11), 41 (38); high resolution MS calcd for $C_{15}H_{29}NO$ (M^+) 239.2249, found 239.2251.

(1*R*, exo)-1-(*t*-Butylaminomethyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-ol (3). Data for **3**: mp 66-67 °C; ^{1}H NMR (300 MHz) 5.9 (br, 1 H), 3.91 (dd, J = 8.0, 3.7, 1 H, HC(2)), 2.85 (d, J = 11.7, 1 H, CH_2N), 2.79 (dd, J = 11.7, 1 H, CH_2N), 1.85-1.71 (m, 1 H), 1.71-1.62 (m, 3 H), 1.42-1.32 (m, 1 H), 1.22 (s, 3 H, CH_3), 1.10 (s, 9 H, *t*-Bu), 0.98-1.10 (m, 2 H), 0.87 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 79.12 (C(2)), 50.49 (CH_2N), 50.31 (CN), 46.38 (C(1)), 46.08 (C(4)), 42.59 (C(7)), 39.53, 31.91, 28.70 (*t*-Bu), 27.10, 21.69 (CH_3), 20.63 (CH_3); IR (CCl_4) 3387 (m), 3312 (m), 3169 (m), 2955 (s), 1476 (s), 1453 (s), 1389 (s), 1360 (s), 1294 (w), 1285 (m), 1229 (s), 1183 (s), 1144 (m), 1123 (s), 1103 (s), 1073 (s), 1055 (m), 1003 (s), 939 (s), 855 (s); MS (70 eV) 225 (6, M^+), 211 (15), 210 (100), 192 (65), 135 (19), 107 (17), 93 (13), 79 (10), 58 (62), 57 (12), 41 (21). Anal. Calcd for $C_{14}H_{27}NO$ (225.37): C, 74.61; H, 12.08; N, 6.21. Found: C, 74.58; H, 12.17; N, 6.23.

(1*R*)-3-*t*-Butylimino-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (21, precusor to 5a). To a solution of camphorquinone (996 mg, 6.0 mmol), and *t*-butylamine (3.6 mL, 3.6 mmol), in anhydrous toluene (30 mL) at 0 °C was added a solution of $TiCl_4$ (320 μL, 3.0 mmol) in anhydrous toluene (6 mL). The cooling bath was removed and the reaction mixture was stirred at room temperature overnight (23 h). The mixture was diluted with anhydrous Et_2O and the organic layer was poured into cooled saturated aqueous $NaHCO_3$ slowly. The aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give a yellow solid, which was purified by silica gel column chromatography (hexane/Et_2O, 3/1) to give two fractions. The early fraction (199 mg) was a 10:1 mixture of imine and quinone. The later fraction was pure imine (929 mg, 70 %) as a white solid. Data for **21** mp 96-97 °C (decomp); ^{1}H NMR (300 MHz) 3.05 (d, J = 4.9, 1 H, HC(4)), 2.13-2.03 (m, 1 H), 1.84-1.73 (m, 1 H), 1.59-1.48 (m, 2 H), 1.35 (s, 9 H, *t*-Bu), 1.05 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 206.86 (C(2)), 168.31 (C(3)), 56.52, 56.49, 52.22 (C(4)), 43.87 (C(7)), 29.98 (*t*-Bu), 29.88, 23.95, 20.84 (CH_3), 17.61 (CH_3), 9.04 (CH_3); IR: (CCl_4) 2965 (s), 2874 (m), 1755 (s), 1674 (m), 1555 (w), 1474 (m), 1453 (m), 1390 (m), 1374 (m), 1362 (m), 1323 (w), 1285 (w), 1256 (m), 1233 (m), 1210 (m), 1163 (w), 1107 (w), 1055 (m), 1032 (w), 1017 (m), 990 (w), 922 (w); MS (70 eV) 221 (0, M^+), 193 (16), 122 (21), 110 (21), 109 (27), 96 (10), 85 (26), 69 (16), 57 (100), 55 (12), 54 (22), 41 (36); Anal. Calcd for $C_{14}H_{23}NO$ (221.34): C, 75.97; H, 10.47; N, 6.33. Found: C, 75.98; H, 10.37; N, 6.37; TLC R_f 0.14 (hexane/Et_2O, 3/1)

(1*R*, exo, exo)-3-(*t*-Butylamino)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (5a). To a solution of $NaBH_4$ (151 mg, 4.0 mmol) in anhydrous EtOH (15 mL) was added a solution of the above imine (774 mg, 3.5 mmol) in anhydrous EtOH (5 mL) and the mixture was stirred at room temperature for 3 h. After evaporation of EtOH, saturated aqueous NH_4Cl and Et_2O were added to the residue. The aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH, 9/1) to give amino alcohol **5** (643 mg, 82 %) as a white solid. Data for **5a**: mp:73-74 °C; ^{1}H NMR: (300 MHz) 3.28 (d, J = 7.3, 1 H, HC(2)), 2.83 (d, J = 7.3, 1 H, HC(4)), 1.77-1.68 (m, 1 H), 1.51-1.38 (m, 2 H), 1.10 (s, 9 H, *t*-Bu), 1.00 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), other peaks (2 H) superimposed on 1.10-1.00 ppm; ^{13}C NMR (75.5 MHz) 78.48 (C(2)), 59.03 (C(3)), 52.96 (C(4)), 51.49, 48.48, 46.74, 32.83, 29.00 (t-Bu), 27.32, 21.82 (CH_3), 21.27 (CH_3), 11.34 (CH_3); IR:(CCl_4) 3258 (m), 2959 (s), 2876 (s), 1543 (w), 1474 (m), 1460 (m), 1431 (m), 1391 (m), 1366 (m), 1293 (w), 1231 (m), 1210 (m), 1142 (w), 1113 (m), 1096 (m), 1065 (m), 1017 (w), 965 (w), 916 (w), 893 (w); MS (70 eV) 225 (6, M^+), 210 (65), 196 (47), 154 (29), 140 (81), 127 (10), 109 (10), 99 (11), 98 (53), 96 (13), 95 (25), 86 (10), 84 (100), 70 (10), 67 (11), 58 (32), 57 (46), 56 (46), 55 (20). Anal. Calcd for $C_{14}H_{27}NO$ (225.37): C, 74.61; H, 12.08; N, 6.21.Found: C, 74.67; H, 12.12; N, 6.27.

(1*R*, exo)-2-hydroxy-1,2,7,7-tetramethylbicyclo[2.2.1]heptan-3-one *t*-butylimine (22, Precursor to 5b) To a solution of **21** (443 mg, 2.0 mmol) in anhydrous THF at 0 °C was added a solution of MeLi in ether (3.5 mL, 5.0 mmol) by syringe. The ice bath was removed and the reaction mixture was stirred at room temperature overnight (12 h). Ether and saturated aqueous NH_4Cl were added and the organic layer was separated. The aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give yellow oil, which was purified by silica gel column chromatography (Et_2O/CH_2Cl_2, 1/1) to give pure imino alcohol (297 mg, 63 %) as a colorless oil. Data for the **22**: ^{1}H NMR (300 MHz) 2.74 (d, J = 5.3, 1 H, HC(4)), 2.30 (s, 1 H, OH), 1.84-1.77 (m, 1 H), 1.54 (t, J = 7.4, 2 H), 1.26 (s, 10 H, *t*-Bu, and 1 H), 1.17 (s, 3 H, CH_3), 1.04 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.93

(s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 181.26 (C(3)), 78.46 (C(2)), 54.33 (CN), 53.00 (C(4)), 50.42, 47.64, 30.91, 30.43 (*t*-Bu), 25.01, 22.79, 22.63, 19.62, 9.57; IR (neat) 3418 (m), 2971 (s), 1734 (w), 1686 (s), 1493 (m), 1458 (s), 1391 (s), 1364 (s), 1291 (m), 1235 (s), 1211 (s), 1192 (m), 1117 (s), 1082 (s), 995 (m), 941 (m), 920 (m), 833 (w), 816 (m); MS: (70 eV) 237 (20, M^+), 181 (17), 180 (35), 166 (10), 154 (15), 138 (47), 137 (27), 122 (14), 110 (12), 99 (11), 98 (24), 97 (14), 96 (14), 95 (32), 85 (75), 82 (14), 70 (41), 69 (15), 67 (10), 59 (56), 57 (100), 55 (21), 43 (64), 41 (64); high resolution MS calcd for $C_{15}H_{27}NO$ (M^+) 237.2093; found, 237.2096.

(1*R*, exo, exo)-3-(*t*-Butylamino)-1,2,7,7-tetramethylbicyclo[2.2.1]-heptan-2-ol (5b). To a suspension of $LiAlH_4$ (152 mg, 4.0 mmol) in anhydrous THF (10 mL) was added a solution of the above imino alcohol (474 mg, 2.09 mmol) in anhydrous THF (5 mL) and the mixture was refluxed for 12 h. After cooling to room temparature, saturated aqueous NH_4Cl was added slowly. The organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel column chromatography (CH_2Cl_2/CH_3OH, 9/1) gave amino alcohol **7** (280 mg) as a colorless oil. Data for **7**: ^1H NMR: (300 MHz) 5.1 (br, 1 H, NH), 2.42 (s, 1 H, OH), 1.79-1.69 (m, 1 H), 1.42-1.20 (m, 3H), 1.16 (s, 3 H, CH_3), 1.08 (s, 9 H, *t*-Bu), 0.89 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3), (1H) superimposed on 1.08 ppm (*t*-Bu).

6,6-Dimethyl-*N*-[(*S*)-(1)-phenylethyl]-2-oxo-1,3,2-oxazaphosphorinane (*cis*/*trans*-1b). This compound was obtained from amino alcohol **2b** (621 mg, 3.0 mmol) and benzylphosphonic dichloride by adaptation of the procedure described for *cis*/*trans*-**1d** Purification by silica gel column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) gave pure diastereomers of **1b** 252 mg (24%) and 214 mg (21%). Analytical samples were obtained by recrystallization from pentane. Data for **1b** (higher R_f): mp 79-80 °C (pentane); ^1H NMR: (300 MHz, $CDCl_3$) 7.57 (d, J = 7.5, 2 H, Ph), 7.33-7.19 (m, 8 H, Ph), 5.17-5.09 (m, 1 H, CHN), 3.25 (dd, J = 26.6, 14.7, 1 H, CH_2Ph), 3.19 (dd, J = 24.3, 14.7, 1 H, CH_2Ph), 2.73-2.64 (m, 1 H, HC(4)), 2.51-2.39 (m, 1 H, HC(4)), 1.50 (d, J = 7.2, 3 H, CH_3), 1.24-1.17 (m, 1 H, HC(5)), 1.12 (s, 6 H, CH_3C(6)), 0.87-0.77 (m, 1 H, HC(5)); ^{13}C NMR (75.5 MHz) 140.38 (Ph), 133.72 (J = 9.8, Ph), 129.94 (Ph), 128.18 (Ph), 128.13 (Ph), 127.90 (Ph), 127.09 (Ph), 126.38 (Ph), 80.73 (C(6)), 51.76 (J = 3.3, CN), 38.55 (J = 130, CH_2Ph), 37.69 (C(4)), 35.20 (J = 5.0, C(5)), 29.76 (J = 5.8, CH_3C(6)), 26.47 (CH_3C(6)); ^{31}P NMR (121.4 MHz) 21.82; IR: (neat) 3029 (m), 2977 (s), 2934 (s), 2878 (m), 1495 (s), 1453 (s), 1399 (s), 1387 (s), 1372 (s), 1283 (s), 1248 (s), 1188 (s), 1144 (s), 1105 (s), 1076 (s), 1015 (s), 980 (s), 925 (s), 885 (s), 837 (s); MS (70 eV) 343 (16, M^+), 328 (21), 274 (15), 252 (19), 184 (34), 148 (54), 106 (13), 105 (100), 91 (64), 79 (18), 77 (17), 69 (14), 65 (12), 41 (22); TLC R_f 0.37 (hexane/EtOAc/*i*-PrOH, 35/62/3) R_f 0.21 (hexane/EtOAc/*i*-PrOH, 68/30/2). Anal. Calcd for $C_{20}H_{26}NO_2P$ (343.41): C, 69.95; H, 7.63; N, 4.08; P: 9,02. Found: C, 70.05; H, 7.43; N, 4.09; P: 8.69. Data for **1b** (lower R_f) mp 100-101 °C (pentane); ^1H NMR (300 MHz) 7.40-6.95 (m, 10 H, Ph), 4.97-4.91 (m, 1 H, CHN), 3.24 (dd, J = 36.8, 14.9, 1 H, CH_2Ph), 3.19 (dd, J = 19.0, 14.9, 1 H, CH_2Ph), 3.11-3.04 (m, 1 H, HC(4)), 2.53-2.47 (m, 1 H, HC(4)), 1.69 (d, J = 7.0, 3 H, CH_3), 1.44 (s, 3 H, CH_3C(6)), 1.16 (s, 3 H, CH_3C(6)), 0.76-0.81 (m, 1 H, HC(5)); ^{13}C NMR (75.5 MHz) 141.28 (J = 5.4, Ph), 133.61 (J = 8.8, Ph), 129.86 (J = 4.4, Ph), 128.35 (Ph), 128.07 (Ph), 127.69 (Ph), 127.41 (Ph), 126.30 (J = 4.1, Ph), 80.64 (C(6)), 54.89 (J = 3.9, CN), 38.12 (J = 130, CH_2Ph), 37.71 (C(4)), 35.55 (J = 4.9, C(5)), 29.96 (J = 6.8, CH_3C(6)), 26.65 (CH_3C(6)), 18.12 (CH_3); ^{31}P NMR (121.4 MHz) 22.29; IR: (neat) 3065 (m), 3033 (s), 2980 (s), 2934 (s), 1559 (w), 1495 (m), 1455 (m), 1402 (w), 1387 (m), 1372 (m), 1287 (m), 1256 (s), 1221 (s), 1188 (s), 1142 (w), 1102 (w), 1076 (m), 988 (s), 922 (m); MS: (70 eV) 343 (15, M^+), 328 (28), 274 (20), 252 (19), 184 (41), 148 (43), 145 (12), 106 (14), 105 (100), 91 (71), 79 (17), 77 (18), 71 (15), 69 (18), 65 (12), 57 (54), 56 (29), 55 (11), 43 (30), 42 (11), 41 (42); TLC R_f 0.20 (hexane/EtOAc/*i*-PrOH 35/62/3). Anal. Calcd for $C_{20}H_{26}NO_2P$ (343.41): C, 69.95; H, 7.6; N, 4.08; P, 9.02. Found: C, 69.96; H, 7.65; N, 4.06; P: 9.04.

2-Benzyl-*N*-*t*-butyl-5,6,6-trimethyl-2-oxo-1,3,2-oxazaphosphorinane (*cis*/*trans*-1d). Triethylamine (2.1 mL, 15 mol) was dissolved in anhydrous CH_2Cl_2 (10 mL) in a 50-mL three-necked round-bottomed flask and the solution was heated at reflux. Amino alcohol **2d** (516 mg, 3.0 mmol) was dissolved in anhydrous CH_2Cl_2 (9 mL) as was benzylphosphonic dichloride (630 mg, 3.0 mmol). These solutions were introduced to two 10-mL gas tight syringes, and added dropwise by syringe pump to the refluxing Et_3N solution in CH_2Cl_2 over 1 h to give a pale yellow solution which was stirred at reflux for 4 h. After cooling to room temperature, water was added and the organic layer was separated. The aqueous layer was extracted three times

with CH_2Cl_2. The combined organic layers were dried over K_2CO_3, filtered, and concentrated. Purification of the residue by silica gel column chromatography (EtOAc/*i*-PrOH, 95/5) to give a mixture of oxazaphosphorinane **1d** and **1d'** (636 mg, 69 %) as a white solid. The ratio of two epimers was determined to be 68:32 by HPLC. The isomers were separated by MPLC (silica gel, EtOAc/*i*-PrOH, 95/5). Data for *trans*-**1d** (major isomer): mp 133-134 °C (pentane); ^{1}H NMR (300 MHz) 7.27-7.18 (m, 5 H, Ph), 3.30 (dd, J = 22.8, 15.0, 1 H, CH_2Ph), 3.07 (dd, J = 16.8, 15.0, 1 H, CH_2Ph), 2.69-2.58 (m, 1 H, HC(4)), 2.37-2.29 (m, 1 H HC(4)), 2.17-2.10 (m, 1 H, HC(5)), 1.50 (s, 3 H, CH_3C(6)), 1.33 (s, 9 H, *t*-Bu), 0.96 (s, 3 H, CH_3C(6)), 0.74 (d, J = 7.0, 1 H, CH_3(5)); ^{13}C NMR (75.7 MHz) 134.52 (J = 10, Ph), 129.72 (J = 6.3, Ph), 127.86 (J = 2.6, Ph), 126.09 (J = 3.4, Ph), 83.75 (J = 9.7, C(6)), 54.85 (J = 4.0, CN), 46.17 (C(4)), 44.30 (J = 9.7, C(5)), 39.58 (J = 130, CH_2Ph), 29.97 (CH_3C(6)), 29.07 (J = 2.3, *t*-Bu), 22.78 (J = 6.5, CH_3C(6)), 14.29 (CH_3C(5)); ^{31}P NMR (121.4 MHz, $CDCl_3$) 23.76; IR (CCl_4) 2979 (s), 1653 (m), 1541 (m0, 1497 (w), 1472 (w), 1455 (w), 1393 (m), 1372 (m), 1314 (w), 1256 (s), 1219 (s), 1184 (m), 1159 (m), 1109 (m), 1078 (m), 1034 (m), 1001 (s), 911 (m); MS (70 eV) 309 (2, M^+), 295 (19), 294 (100), 236 (22), 224 (83), 212 (17), 184 (68), 162 (67), 148 (11), 91 (85), 70 (39), 65 (12), 58 (18), 57 (64), 56 (11), 55 (31), 41 (14); TLC R_f 0.16 (hexane/EtOAc/*i*-PrOH 35/62/3); HPLC t_R 9.76 (Supelco LC-Si, EtOAc/*i*-PrOH 96/4). Anal. Calcd for $C_{17}H_{28}NO_2P$ (309.39): C, 66.00; H, 9.12; N, 4.53; P, 10.01. Found: C, 66.14; H, 9.20; N, 4.71; P, 10.32. Data for *cis*-**1d** (minor isomer): mp 102-103 °C (pentane); ^{1}H NMR (300 MHz) 7.31-7.19 (m, 5 H, Ph), 3.25 (dd, J = 22.4, 14.8, 1 H, CH_2Ph), 3.13 (dd, J = 18.1, 14.8, 1 H, CH_2Ph), 2.67-2.60 (m, 2 H, HC(4)), 1.49 (s, 9 H, *t*-Bu), 1.28 (s, 3 H, CH_3C(6)), 1.13 (d, J = 2.3, CH_3(5)), 0.68-0.62 (m, 1 H, HC(5)), 0.61 (s, 3 H, CH_3C(6)); ^{13}C NMR (75.5 MHz); 134.59 (J = 9.8, Ph), 129.99 (J = 4.7, Ph), 127.91 (Ph), 126.23 (Ph), 82.19 (J = 10.1, C(6)), 55.37 (J = 4.5, CN), 47.12 (C(4)), 40.29 (J = 130, CH_2Ph), 38.33 (J = 3.6, C(5)), 29.06 (*t*-Bu), 28.19 (J = 6.1, CH_3), 20.73 (CH_3), 14.33 (CH_3); ^{31}P NMR (121.4 MHz) 21.78; IR (CCl_4) 2979s, 2876m, 1559w, 1495m, 1483m, 1455m, 1387m, 1374m, 1364m, 1279s, 1256s, 1221s, 1186s, 1161s, 1082m, 1066m, 1053m, 1028s, 999s, 941w; MS (70 eV) 309 (5, M^+), 295 (17), 294 (99), 224 (72), 212 (15), 184 (56), 162 (100), 148 (16), 91 (70), 85 (33), 83 (51), 70 (38), 65 (11), 58 (19), 57 (68), 55 (27), 47 (16), 42 (11), 41 (41); TLC R_f 0.16 (hexane/EtOAc/*i*-PrOH 35/62/3); HPLC t_R 8.59 (Supelco LC-Si, EtOAc/*i*-PrOH 96/4). Anal. Calcd for $C_{17}H_{28}NO_2P$ (309.39): C, 66.00; H, 9.12; N, 4.53; P, 10.01. Found: C, 66.04; H, 9.08; N, 4.53; P, 9.96.

(2*R*,4a*S*,8a*R*)-2-Phenylmethyl-3-(2,2-dimethylethyl)-9,9-dimethyldecahydro-4a,7-methano-1H-1,3,2-oxazaisophosphinoline-2-oxide (*cis*-4) and (2*S*,4a*S*,8a*R*)-2-phenylmethyl-3-(2,2-dimethylethyl)-9,9-dimethyldecahydro-4a,7-methano-1H-1,3,2-oxazaisophosphinoline-2-oxide (*trans*-4). To a solution of amino alcohol **3** (319 mg, 1.4 mmol) and benzylphosphonic dichloride (293 mg, 1.4 mmol) in anhydrous CH_2Cl_2 (28 mL) was added Et_3N (0.78 mL, 5.6 mmol) in one portion at room temperature. The mixture was heated to reflux and stirred for 5 h. After cooling to room temperature, saturated aqueous NH_4Cl was added and the organic layer was separated. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel column chromatographyl (hexane/EtOAc/*i*-PrOH, 35/62/3) gave a mixture of *cis*-**4** and *trans*-**4** (407 mg, 81 %) in a ratio of 46:54. The isomers were separated by rechromatography. Analytical samples were obtained by recrystallization from hexane. Data for *trans*-**4**: mp 164-165 °C (hexane); ^{1}H NMR (300 MHz) 7.37-7.22 (m, 5 H, Ph), 3.98 (dd, J = 7.6, 2.3, 1 H, HC(8a)), 3.30-3.17 (m, 3 H, CH_2Ph, CH_2N), 2.96 (dd, J = 13.5, 2.0, CH_2N), 2.08-2.03 (m, 1 H), 1.73-1.60 (m, 2 H), 1.51-1.40 (m, 1 H), 1.36 (s, 9 H, *t*-Bu), 1.30 (s, 3 H, CH_3), 0.99-0.90 (m, 1 H), 0.93 (s, 3 H, CH_3), 0.86-0.81 (m, 1 H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 133.00 (Ph), 129.82 (J = 4.9, Ph), 128.45 (Ph), 126.4 (Ph), 83.93 (J = 9.7, C(8a)), 55.94 (CN), 47.83 (J = 4.7, C(4a)), 46.63, 45.53 (C(7)), 44.20, 38.67 (J=11.7), 34.74 (J = 12, CH_2Ph), 30.99, 29.73 (*t*-Bu), 26.17, 22.02 (CH_3), 20.11 (CH_3); ^{31}P NMR (121.4 MHz, $CDCl_3$) 19.80; IR (CCl_4) 3063 (w), 3029 (m), 2957 (s), 1495 (m), 1478 (m), 1455 (s), 1399 (m), 1391 (m), 1368 (s), 1262 (s), 1198 (s), 1179 (s), 1121 (s), 1063 (s), 1034 (s), 1021 (s), 999 (s), 951 (m), 914 (s), 828 (s); MS (70 eV) 361 (3, M^+), 347 (21), 346 (100), 270 (12), 214 (54), 212 (14), 192 (12), 107 (12), 93 (14), 91 (72), 79 (15), 67 (11), 58 (12), 57 (34), 55 (11), 41 (32); TLC R_f 0.32 (hexane/EtOAc/*i*-PrOH 35/62/3); HPLC: t_R 5.07 (Supelco LC-Si, EtOAc/*i*-PrOH 98:2). Anal. Calcd for $C_{21}H_{32}NO_2P$ (361.46): C, 69.78; H, 8.92; N, 3.87; P, 8.57. Found: C, 69.72; H, 8.90; N, 3.88; P, 8.48. Data for *cis*-**4**: mp 172-173 °C (hexane); ^{1}H NMR (300 MHz) 7.32-7.19 (m, 5 H, Ph), 4.31-4.25 (m, 1 H, HC(8a)), 3.19 (ABq, J = 19.8, 1.6 2H, CH_2Ph), 2.93 (dd, J = 21.4, 14.4, 1 H, CH_2N), 2.66 (dd, J = 14.4, 2.3, 1 H, CH_2N), 1.94-2.13 (m, 1 H), 1.68-1.77 (m, 1 H), 1.40-1.56 (m, 1 H), 1.31 (s, 9 H, *t*-Bu), 1.11-1.02 (m, 1 H), 0.85 (s, 3 H, CH_3),

0.78 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 132.77 (Ph), 129.96 (J = 4.7, Ph), 128.24 (Ph), 126.39 (Ph), 79.12 (J =.6, C(8a)), 54.64 (CN), 53.27 (CH_2N), 46.64, 44.91 (C(7)), 42.72, 37.34 (J = 7.0), 35.80 (J = 121, CH_2Ph), 30.66, 30.25 (t-Bu), 26.46, 20.18 (CH_3), 19.99 (CH_3); ^{31}P NMR (121.4 MHz) 27.90; IR (CCl_4) 3061 (w), 3029 (m), 2950 (s), 2876 (m), 1493 (m), 1480 (m), 1453 (m), 1364 (m), 1291 (m), 1258 (s), 1204 (s), 1078 (s), 1067 (s), 1046 (m), 1013 (s), 994 (w), 932 (s), 914 (s), 862 (s), 823 (s); MS (70 eV) 361 (9, M^+), 348 (13), 347 (99), 346 (100), 238 (11), 224 (14), 214 (20), 212 (80), 192 (70), 184 (19), 172 (19), 150 (14), 135 (38), 134 (12), 133 (15), 119 (11), 95 (12), 94 (17), 93 (45), 92 (31), 91 (100), 84 (12), 82 (12), 81 (20), 80 (13), 79 (53), 77 (27), 70 (30), 69 (21), 68 (11), 67 (34), 65 (27), 58 (44), 57 (83), 56 (14), 55 (36), 53 (15), 41 (98); TLC R_f 0.27 (hexane/EtOAc/*i*-PrOH, 35/62/3); HPLC t_R 6.72 (Supelco LC-Si, EtOAc/*i*-PrOH 98/2). Anal. Calcd for $C_{21}H_{32}NO_2P$(361.46): C, 69.78; H, 8.92; N, 3.87; P, 8.57. Found: C, 69.75; H, 8.97; N, 3.94; P, 8.60

(2*R*,3a*R*,4*R*,7a*S*)-2-phenylmethyl-3-(2,2-dimethylethyl)-7,8,8-trimethyloctahydro-4,7-methano-1H-1,3,2-benzoxazaphosphole-2-oxide (*cis*-6a) and (2*S*,3a*R*,4*R*,7a*S*)-2-phenylmethyl-3-(2,2-dimethylethyl)-7,8,8-trimethyloctahydro-4,7-methano-1H-1,3,2-benzoxazaphosphole-2-oxide (*trans*-6a). To a cold (-40 °C) solution of the amino alcohol **5** (223 mg, 1.0 mmol), and benzylphosphonic dichloride (229 mg, 1.0 mmol) in anhydrous toluene (3 mL) was added Et_3N in one portion. The reaction mixture was stirred at -40°C for 1 h and then at room temperature for 12 h. To the reaction mixture were added CH_2Cl_2 and saturated aqueous NH_4Cl and the organic layer was separated. The aqueous layer was extracted three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel column chromatography (hexane/EtOAc/*i*-PrOH, 68/30/2) gave a 9:1 mixture of oxazaphospholidine *cis*/*trans*-**6a** (326 mg, 90 %). The isomers were separated by MPLC. Data for *cis*-**6a**: ^1H NMR (300 MHz) 7.35-7.19 (m, 5 H, Ph), 4.31 (d, J = 7.3, 1 H, HC(7a)), 3.56 (d, J = 7.3, 1 H, HC(3a)), 3.41 (dd, J = 19.0, 14.3, 1 H, CH_2Ph), 3.22 (dd, J = 18.1, 14.3, 1 H, CH_2Ph), 1.93 (d, J = 4.3, 1 H, HC(4)), 1.74-1.62 (m, 1 H), 1.56-1.47 (m, 1 H), 1.42 (s, 9 H, t-Bu), 1.25 (s, 3 H, CH_3), 1.05-0.95 (m, 2 H), 0.93 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz) 132.82 (J = 9.7, Ph), 129.92 (J = 4.9, Ph), 128.36 (Ph), 126.58 (J = 4.1, Ph), 86.38 (C(7a)), 64.90 (J = 5.0), 53.81, 50.86, 47.87 (J = 7.3), 46.21, 38.96 (J = 122, CH_2Ph), 32.01, 29.71 (t-Bu), 25.63, 23.11, 19.78, 10.75; ^{31}P NMR (121.4 MHz) 45.91; IR (CCl_4) 2963 (s), 2886 (m), 1495 (m), 1482 (m), 1455 (m), 1395 (m), 1364 (m), 1283 (w), 1254 (s), 1237 (s), 1204 (s), 1125 (m), 1090 (m), 1048 (s), 1036 (s), 999 (s), 974 (s), 928 (w), 916 (m); MS(70 eV) 361 (19, M^+), 347 (23), 346 (100), 306 (10), 305 (54), 290 (10), 248 (13), 236 (10), 235 (15), 212 (19), 192 (21), 172 (13), 150 (11), 134 (13), 95 (12), 93 (10), 92 (12), 91 (98), 82 (21), 67 (11), 57 (28), 55 (13), 41 (41); high resolution MS calcd for $C_{21}H_{32}NO_2P$ 361.2171, found 361.2170; TLC R_f 0.25 (hexane/EtOAc/*i*-PrOH, 68/30/2); HPLC t_R 5.63 (Supelco LC-Si, EtOAc/*i*-PrOH 98/2). Data for *trans*-**6a**: ^1H NMR (300 MHz) 7.34-7.23 (m, 5 H, Ph), 3.44 (dd, J = 22.1, 15.0, 1 H, CH_2Ph), 3.30 (dd, J = 17.0, 15.0, 1 H, CH_2Ph), 2.90-2.80 (m, 2 H, HC(7a), HC(3a)), 2.09 (d, J = 4.4, 1 H, HC(4)), 1.52 (s, 9 H, t-Bu), 1.39-1.30 (m, 1 H), 1.30 (s, 3 H), 0.89 (s, 3 H), 0.77 (s, 3 H), 0.70-0.61 (m, 1 H), 0.56-0.51 (m, 1 H), (1H) superimposed on 1.52 (t-Bu); ^{13}C NMR (75.5 MHz) 132.95 (J = 9.6, Ph), 129.73 (J = 6.4, Ph), 128.35 (Ph), 126.61 (J = 3.7, Ph), 86.59 (C(2)), 65.70 (J = 14.9, C(3a)), 52.57 (CN), 48.12 (C(4)), 47.72, 46.36, 38.86 (J=117, CH_2Ph), 31.48, 30.59 (t-Bu), 25.59, 23.28 (CH_3), 20.38 (CH_3), 10.75 (CH_3); ^{31}P NMR (121.4 MHz) 41.30; IR (CCl_4) 2971 (m), 1553 (w), 1495 (w), 1480 (w), 1455 (w), 1395 (m), 1366 (m), 1316 (w), 1287 (m), 1266 (s), 1210 (m), 1188 (m), 1142 (w), 1090 (m), 1078 (m), 1040 (s), 1017 (m), 974 (m), 912 (w); MS (70 eV) 361 (15, M^+), 347 (22), 346 (100), 305 (44), 235 (11), 214 (19), 212 (13), 192 (14), 172 (12), 150 (10), 134 (13), 95 (12), 92 (11), 91 (91), 82 (22), 67 (11), 57 (27), 55 (12), 41 (39); high resolution MS calcd for $C_{21}H_{32}NO_2P$ 361.2171 found 361.2163; TLC R_f 0.25 (hexane/EtOAc/*i*-PrOH, 68/30/2); HPLC t_R 4.68 (Supelco LC-Si, EtOAc/*i*-PrOH 98/2).

(2*R*,3a*R*,4*R*,7a*S*)-2-phenylmethyl-3-(2,2-dimethylethyl)-7a,7,8,8 tetramethyloctahydro-4,7-methano-1H-1,3,2-benzoxazaphosphole-2-oxide (*cis*-6b) and (2*S*,3a*R*,4*R*,7a*S*)-2-phenylmethyl-3-(2,2-dimethylethyl)-3a,4,8,8-tetramethyloctahydro-4,7-methano-1H-1,3,2-benzoxazaphosphole-2-oxide (*trans*-6b). To a cold (-40 °C) solution of the amino alcohol **7** (239 mg, 1.0 mmol), and benzylphosphonic dichloride (229 mg, 1.0 mmol) in anhydrous toluene (3 mL) was added triethylamine (0.56 mL, 4.0 mmol) in one portion. The mixture was stirred at -40 °C for 1h, at room temperature for 15 h (overnight), and then at 60 °C for 5 h. After cooling to room temperature, Et_2O and saturated aqueous NH_4Cl were added and the organic layer was separated. The aqueous layer was extracted

three times with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give pale yellow oil, which was purified by silica gel column chromatography (hexane/EtOAc/*i*-PrOH 68/30/2) to give a 71:29 mixture of oxazaphospholidine *cis*- and *trans*-**6b** (190 mg, 51 %) as a colorless oil. The isomers were separated by MPLC (silica gel, hexane/EtOAc/*i*-PrOH, 60/39/1). Data for *cis*-**6b** (major isomer): ^{1}H NMR (300 MHz) 7.20-7.34 (m, 5 H, Ph), 3.36 (dd, J =19.2, 14.4, 1 H, CH_2Ph), 3.24 (dd, J = 18.3, 14.4, 1 H, CH_2Ph), 3.18 (s, 1 H, HC(3a)), 1.84 (d, J = 4.8, HC(4)), 1.75-1.69 (m, 1 H), 1.52 (s, 3 H, CH_3), 1.40 (s, 9 H, *t*-Bu), 1.32 (s, 3 H, CH_3), 1.01-0.95 (m, 1 H), 0.90 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), (2H) superimposed on 1.40 ppm; ^{13}C NMR (75.5 MHz) 133.01 (J = 8.4, Ph), 129.85 (J = 5.1, Ph), 128.14 (Ph), 126.29 (Ph), 91.81 (C(7a)), 72.08 (C(3a)), 53.48 (J = 4.9), 51.30 (J = 7.5), 50.68 (J = 7.2, C(4)), 48.11, 39.25 (J = 123, CH_2Ph), 29.42 (J = 3.9, *t*-Bu), 25.66, 24.12 (CH_3), 23.40 (CH_3), 20.75 (CH_3), 9.25 (CH_3); ^{31}P NMR (121.4 MHz) 44.69; IR (neat) 2971 (s), 1603 (w), 1495 (s), 1455 (s), 1381 (m), 1364 (m), 1258 (s), 1229 (s), 1142 (s), 1103 (m), 1084 (s), 1059 (s), 1042 (s), 1003 (s), 959 (s), 934 (s), 884 (s), 857 (m), 828 (s); MS (70 eV) 375 (3, M^+), 361 (24), 360 (100), 212 (22), 206 (31), 107 (15), 96 (22), 95 (22), 91 (94), 86 (32), 84 (49), 81 (10), 69 (12), 67 (16), 58 (11), 57 (39), 56 (10), 55 (17), 49 (11), 47 (16), 43 (10), 41 (44); high resolution MS calcd for $C_{22}H_{34}NO_2P$ 375.2327, found 375.2324; TLC R_f 0.27 (hexane/EtOAc/*i*-PrOH, 68/30/2). Data for *trans*-**6b** (minor isomer): ^{1}H NMR (300 MHz) 7.36-7.17 (m, 5 H, Ph), 3.46 (dd, J = 19.2, 14.5, 1 H, CH_2Ph), 3.46 (dd, J = 19.2, 14.5, 1 H, CH_2Ph), 3.15 (d, J = 8.6, 1 H, HC(3a)), 3.05 (dd, J = 15.1, 14.8, 1 H, CH_2Ph), 2.15 (d, J = 5.0, 1 H, HC(4)), 1.79-1.70 (m, 1 H), 1.47 (s, 9 H, *t*-Bu), 1.41 (s, 6 H, CH_3), 1.38-1.26 (m, 1 H), 0.96-0.90 (m, 1 H), 0.88 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) 133.40 (J = 9.6, Ph), 129.79 (J = 6.1, Ph), 128.32 (Ph), 126.25 (Ph), 90.34 (C(7a)), 72.28 (J = 11.9, C(3a)), 52.44 (J = 6.6), 51.89 (J = 5.5), 48.91 (C(4)), 48.52, 41.47 (J = 117, CH_2Ph), 30.69 (*t*-Bu), 30.28, 25.72, 24.53 (CH_3), 23.45 (CH_3), 20.97 (CH_3), 9.39 (CH_3); ^{31}P NMR (121.4 MHz) 37.63; IR (CCl_4) 2975 (s), 1559 (w) , 1495 (m), 1456 (m), 1397 (m), 1366 (m), 1267 (s), 1239 (s), 1210 (s), 1142 (m), 1109 (m), 1090 (s), 1071 (m), 1055 (m), 1015 (m), 963 (m), 941 (s), 878 (m), 851 (m), 826 (m); MS (70 eV) 375 (7, M^+), 361 (23), 360 (100), 284 (20), 250 (11), 228 (49), 212 (16), 209 (12), 206 (16), 149 (16), 148 (13), 147 (10), 107 (11), 96 (20), 95 (12), 91 (60), 57 (26), 55 (12), 41 (31); high resolution MS calcd for $C_{22}H_{34}NO_2P$ 375.2327, found 375.2324; TLC R_f 0.27 (hexane/EtOAc/*i*-PrOH, 68/30/2).

(2*S*,6*S*)-2-Ethoxy-6-methyl-2-oxo-1,3,2-oxazaphosphorinane (7e). To a solution of ethyl dichlorophosphite (280 μL, 1.8 mmol) in anhydrous CH_2Cl_2 (15 mL), was added Et_3N (0.50 mL, 3.6 mmol) and the mixture was heated to reflux. A solution of amino alcohol **2e** (261 mg, 1.8 mmol) in anhydrous CH_2Cl_2 (5 mL) was added by syringe and the reaction mixture was heated to reflux for 1 h. After cooling to room temperature, anhydrous hexane (60 mL) was added to precipitate Et_3N·HCl, which was filtered through a Schlenk tube. The filtrate was evaporated in vacuo and the residue was purified by Kugelrohr distillation to give pure phosphite **7e** (291 mg, 74 %) as a colorless oil. The diastereomeric ratio was determined to be 20:1 (axial/equatorial P-OEt group) on the basis of ^{31}P NMR analysis. Data for **7e**: bp 100-110 °C (0.3 Torr); ^{1}H NMR (300 MHz) 4.39-4.31 (m, 1 H, HC(6)), 3.82-3.67 (m, 2 H, CH_2O), 3.42-3.32 (m, 1 H, HC(4)), 2.93-2.84 (m, 1 H, HC(4)), 1.74-1.61 (m, 2 H, HC(5)), 1.27 (t, J = 7.0, 3 H, CH_3), 1.24 (d, J = 2.5, 9 H, *t*-Bu), 1.19 (d, J = 6.3, 3 H, CH_3C(6)); ^{13}C NMR (75.5 MHz); 64.77 (C(6)), 58.80 (J = 19.1, CH_2O), 54.15 (J = 14.2, CN), 37.12 (C(4)), 35.67 (C(5)), 29.57 (J = 14.1, *t*-Bu), 22.93 (J = 4.3, CH_3), 17.19 (J = 6.2, CH_3); ^{31}P NMR (121.4 MHz, $CDCl_3$) 132.63 (major), 135.26 (minor); IR (neat) 2973 (s), 1472 (m), 1456 (m), 1381 (m), 1362 (m), 1273 (m), 1205 (m), 1119 (s), 1096 (m), 1048 (s), 999 (m), 949 (m), 936 (s), 909 (m), 882 (s), 837 (m); MS (70 eV) 219 (18, M^+), 204 (48), 174 (13), 122 (14), 118 (22), 112 (100), 94 (11), 76 (13), 70 (42), 65 (11), 58 (19), 57 (33), 55 (22), 42 (13), 41 (28); Anal. Calcd for $C_{10}H_{22}NO_2P$ (219.26): C, 54.78; H, 10.11; N, 6.39; P, 14.13. Found: C, 54.76; H, 10.14; N, 6.41; P, 14.09.

2-(1'-Azidophenylmethyl)-*N*-*t*-butyl-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane (11). To a cold (-78 °C), magnetically stirred solution of 2-benzyl-*N*-*t*-butyl-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane (**1a**, 740 mg, 2.5 mmol) in anhydrous THF (75 mL) was added a solution of KHMDS (1.06 *M* in THF, 2.60 mL, 2.75 mmol). The mixture was stirred at -78 °C for 30 min. To the resulting yellow solution was added a solution of trisyl azide (850 mg, 2.75 mmol) in anhydrous THF (50 mL), which was cooled in a dry ice bath prior to addition, via cannula. The reaction mixture was stirred at -78 °C for 3 h. Acetic acid (0.73 mL, 12.5 mmol) was added in one portion and the cooling bath was removed. The mixture was warmed to room temperature and allowed to stir at room temperature for 5 h. Ethyl acetate and saturated aqueous NH_4Cl were added, and the aqueous layer was extracted three times with EtOAc. The combined

organic layers were dried over Na_2SO_4, filtered, and concentrated to give a pale yellow oil. Purification of the residue by silica gel column chromatography (hexane/EtOAc/*i*-PrOH, 35/62/3) gave **11** as a white solid. An analytical sample was obtained by recrystallization from pentane. Data for **11**: mp 105-106°C (pentane); ^{1}H NMR (300 MHz) 7.44-7.26 (m, 5 H, Ph), 4.76 (d, J = 13.4, 1 H, CHN_3), 3.06-2.95 (m, 1 H, HC(4)), 2.73-2.63 (m, 1 H, HC(4)), 1.60-1.51 (m, 1 H, HC(5)), 1.47 (s, 3 H, $CH_3C(6)$), 1.37 (s, 9H, *t*-Bu), 1.17 (s, 3 H, $CH_3C(6)$), 1.05-0.98 (m, 1 H, HC(5)); ^{13}C NMR (75.5 MHz) 134.57 (J = 4.1, Ph), 127.95 (Ph), 127.83 (Ph), 127.76 (Ph), 80.76 (J = 9.7, C(6)), 65.68 (J = 146, CN_3), 55.90 (CN), 39.91 (C(4)), 37.68 (J = 5.4, C(5)), 29.37 (J = 7.3, $CH_3C(6)$), 29.22 (*t*-Bu), 28.22 ($CH_3C(6)$); IR (CCl_4) 2980 (m), 2361 (w), 2105 (s), 1653 (w), 1576 (w), 1559 (m), 1293 (m), 1258 (s), 1198 (m), 1001 (s); MS (70 eV) 336 (0, M^+), 293 (19), 237 (12), 204 (27), 148 (100), 104 (16), 77 (18), 70 (21), 69 (36), 57 (12), 56 (61); TLC R_f 0.20 (hexane/EtOAc/*i*-PrOH 68/30/2); HPLC t_R 7.47 min (Supelco LC-Si, hexane/EtOAc/*i*-PrOH, 62/35/3). Anal. Calcd for $C_{16}H_{25}N_4O_2P$ (336.37): C, 57.13; H, 7.49; N, 16.66; P, 9.21. Found: C, 57.17; H, 7.58; N, 16.59; P, 9.16

2-(1'-Aminophenylmethyl)-*N*-*t*-butyl-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane (12). To a solution of the azide **11** (168 mg, 0.5 mmol) in EtOAc (20 mL) was added 5% Pd/C (20 mg). The flask was charged with H_2 (1 atm) and the solution was stirred at room temperature. After 2 h the catalyst was filtered off and the solvent was removed in vacuo. Purification of the residue by silica gel column chromatography (EtOAc/*i*-PrOH, 7/3) gave amine **12** (141 mg, 91 %) as a colorless oil. An analytical sample was obtained by Kugelrohr distillation. Data for **12**: bp 170-180 °C (0.05 Torr); ^{1}H NMR (300 MHz) 7.41-7.25 (m, 5 H, Ph), 4.27 (d, J = 12.9, 1 H, CHN_3), 2.96-2.91 (m, 1 H, HC(4)), 2.54-2.48 (m, 1 H, HC(4)), 2.00 (br, 2 H, NH_2), 1.44 (s, 9 H, *t*-Bu), 1.51-1.39 (m, 1 H, HC(5)), 1.09 (d, J = 1.7, 3 H, $CH_3C(6)$), 0.82-0.75 (m, 1 H, HC(5)), $CH_3C(6)$ superimposed on 1.44 ppm (*t*-Bu); ^{13}C NMR (75.5 MHz, $CDCl_3$) 139.26 (J = 3.8, Ph), 127.74 (Ph), 127.27 (Ph), 127.09 (Ph), 79.64 (J = 12, C(6)), 58.68 (J = 138, CHNH), 55.58 (CN), 39.77 (C(4)), 37.59 (J = 5.8, C(5)), 29.41 (J = 11, $CH_3C(6)$), 29.34 (*t*-Bu), 28.04 ($CH_3C(6)$); IR (neat) 3345 (s), 3048 (s), 3017 (s), 2950 (s), 1707 (w), 1562 (m), 1485 (m), 1458 (s), 1424 (m), 1393 (s), 1366 (s), 1267 (s), 1242 (s), 1206 (s), 1152 (s), 1113 (m), 1088 (m), 1049 (s), 1036 (s), 949 (s), 905 (s), 791 (s), 752 (s), 720 (s), 677 (s); MS (70 eV) 310 (18, M^+), 239 (10), 190 (40), 148 (11), 126 (17), 106 (100), 104 (14), 94 (11), 79 (14), 70 (12), 57 (16); high resolution MS calcd for $C_{16}H_{27}N_2O_2P$ 310.1825, found 310.1824; TLC R_f 0.18 (EtOAc/*i*-PrOH, 7/3).

***(S)*1-Amino-1-phenylmethylphosphonic acid (13).**[16] A solution of **20** (120 mg, 0.36 mmol) in dioxane (3mL) and 4N HCl (9 mL) was heated to reflux for 4 h after which solvents were removed in vacuo to give an oil. This was dissolved in minimum water and the solution was applied to an ion exchange column (8 cm x 2 cm, AG 50x8, H^+ form). Elution with 0.5 N HCl furnished 78 mg (98%) of **13** as its hydrochloride. Further elution with 2N and 6N HCl gave 78 mg (86%) of the hydrochloride of **2e**. A solution of the hydrochloride of **13** (55mg, 0.25 mmol) in methanol (0.6 mL) was treated with propylene oxide (50 µL, 0.71 mmol) and stored at -20 °C overnight. The precipitated free aminophosphonic acid **13** (22mg) was filtered off. The filtrate was concentrated and the residue triturated with cold methanol to give additional 14 mg of **13** (total 34 mg, 78%). Data for **13**: ^{1}H NMR (D_2O, 300 MHz) 7.44 (s, 5 H, ArH), 4.41 (d, 1 H, J = 16, HC(1)); $[\alpha]_{578}^{20}$ = -18 (c 1, 1N NaOH); reported $[\alpha]_{578}^{20}$ = -20 (c 1, 1N NaOH).[16] HPLC analysis of the derived 3,5 dinitrobenzamide dimethyl ester: *S* enantiomer (major) t_R 11.46, *R* enantiomer (minor) t_R 34.62 (Pirkle Covalent L-Naphthylalanine 5µ column, hexane/EtOAc 65/35), *S*/*R* = 96/4.

2-[1'-[1"-Acetyl-3"-(triisopropylphenylsulfonyl)]triazylphenylmethyl]-*N*-*t*-butyl-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane (14). To a cold (-78 °C), magnetically stirred solution of **1a** (296 mg, 1.0 mmol) in anhydous THF (30 mL) was added a solution of *n*-BuLi (1.52 *M* in hexane, 0.72 mL, 1.1 mmol). The mixture stirred at -78 °C for 30 min. To the mixture was added a cold solution of trisyl azide (340 mg, 1.1 mmol) in anhydrous THF (20 mL) by cannula. The reaction mixture was stirred at -78 °C for 5 h. Acetic anhydride (0.42 mL, 5.0 mmol) was added in one portion and the reaction mixture was allowed to stir at room temperature for 8 h. Ethyl acetate and saturated aqueous NH_4Cl were added and the aqueous layer was extracted with EtOAc (3 x mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel column chromatography (hexane/EtOAc/i-PrOH, 68/30/2 35/62/3) gave analytically pure acetyl triazine **14** as a white solid (598 mg, 93%). Data for **14**: mp 65 °C (decomp); ^{1}H NMR (300 MHz) 7.51 (m, 2 H, Ph), 7.30-7.24 (m, 3 H, Ar), 7.13 (s, 2 H, Ar), 6.31 (brd, J =

19.1, C*H*Ph), 3.80-3.73 (m, 2 H, C*H*Me_2), 2.93 (m, 1 H, HC(4)), 2.91-2.83 (m, 1 H, C*H*Me_2), 2.77-2.68 (m, 1 H, HC(4)), 2.02-1.97 (m, 1 H, HC(5)), 2.02 (s, 3 H, CH_3CO), 1.45 (s, 9 H, *t*-Bu), 1.22-0.97 (m, 25 H, $CH_3C(6)$, $CH(CH_3)_2$, HC(5)); ^{13}C NMR (75.5 MHz) 172.75 (CO), 154.46 (Ar), 151.79 (J = 0.8, Ar), 133.73 (J = 1.7, Ar), 130.78 (J = 1.0, Ar), 129.33 (Ar), 128.24 (J = 1.5, Ar), 123.58 (Ar), 81.03 (J = 10.4, C(6)), 59.88 (J = 149, *C*HNAc), 56.37 (J = 1.3, CN), 40.02 (J = 2.1, C(4)), 37.50 (J = 5.3, C(5)), 34.19 (*C*HCH_3), 30.13, 29.35 (J = 2.5), 29.16, 27.80, 24.63, 24.36, 23.43 (J = 1.2), 21.92 (CH_3); ^{31}P NMR (121.4 MHz,) 10.88; IR (CCl_4) 2965 (s), 2361 (w), 2330 (w), 2074 (w), 1448 (m), 1599 (w), 1559 (m), 1456 (m), 1372 (m), 1339 (m), 1292 (m), 1256 (m), 1181 (m), 1146 (m), 1102 (s), 1059 (m), 1034 (m), 1009 (m), 963 (w), 936 (w), 903 (w); MS (70 eV) 646 (0, M^+), 470 (6), 395 (25), 310 (42), 292 (37), 204 (30), 187 (35), 148 (42), 131 (39), 126 (54), 91 (36), 83 (35), 69 (26), 42 (100); TLC R_f 0.24 (hexane/EtOAc/*i*-PrOH, 68/30/2); HPLC t_R 6.81 (Supelco LC-Si, hexane/EtOAc/*i*-PrOH, 62/35/3). Anal. Calcd for $C_{33}H_{51}N_4O_5PS$ (646.83): C, 61.28; H, 7.95; N, 8.66; P, 4.79; S, 4.96, Found: C, 61.24; H, 8.03; N, 8.64; P, 4.75;,S, 4.89.

2-(1'-Acetylaminophenylmethyl)-*N*-*t*-butyl-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane (15). To a suspension of freshly prepared Al-Hg (made from Al foil (140 mg)) in EtOH (25 mL) and a buffer solution (pH 7, 6 mL), was added acetyl triazine **14** (323 mg, 0.5 mmol). The reaction mixture was stirred at room temparature for 2.5 h.and the solvent was removed in vacuo. To the residue were added EtOAc and water and the organic layer was separated. The aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel column chromatography (EtOAc/*i*-PrOH, 8/2) gave **15** (185 mg) as a white solid. An anlytical sample was obtained by rechromatography followed by recrystallization from acetone. Data for **15**: mp 216-217 °C (acetone); ^1H NMR (300 MHz) 7.38-7.21 (m, 5 H, Ph), 6.93 (brt, J = 7.0, 1 H, NH), 5.26 (dd, J = 17.8, 7.7, 1 H, C*H*NAc), 3.10-3.00 (1 H, HC(4)), 2.82-2.72 (m, 1 H, HC(4)), 2.02 (s, 3 H, CH_3CO), 1.65-1.53 (m, 1 H, HC(5)), 1.45 (t, 9 H, *t*-Bu), 1.40 (s, 3 H, $CH_3C(6)$), 1.21-1.09 (m, 1 H, HC(5)), 1.04 (s, 3 H, $CH_3C(6)$); ^{13}C NMR (75.5 MHz) 169.61 (J = 9.8, CO), 137.85 (J = 4.4, Ph), 127.88 (Ph), 127.80 (Ph), 127.11 (Ph), 80.79 (J = 9.8, C(6)), 56.02 (CN), 55.27 (J = 142, *C*HNAc), 39.60 (C(4)), 37.73 (J = 6.4, C(5)), 29.37 (*t*-Bu), 29.19 (CH_3), 29.11 (CH_3), 23.19 (CH_3); ^{31}P NMR (121.4 MHz) 18.25; IR (CCl_4) 3266 (s), 3202 (m), 3054 (w), 2982 (m), 1671 (s), 1541 (s), 1497 (m), 1476 (w), 1456 (m), 1370 (m), 1292 (m), 1269 (w), 1250 (m), 1227 (m), 1177 (s), 1161 (s), 1142 (w), 1119 (w), 1061 (w), 1003 (s); MS (70 eV) 352 (2, M^+), 190 (21), 148 (18), 131 (100), 130 (13), 126 (14), 106 (29), 79 (7), 57 (23); TLC R_f 0.30 (EtOAc/*i*-PrOH, 8/2). Anal. Calcd for $C_{18}H_{29}N_2O_3P$ (352.41) C, 61.35; H, 8.29; N, 7.95; P, 8.79. Found: C, 61.28; H, 8.32; N, 7.93; P, 8.81.

(2*S*,6*S*)-2-[1'-[1"-Acetyl-3"-(triisopropylphenylsulfonyl)]triazylphenylmethyl]-N-*t*-butyl-6-methyl-2-oxo-1,3,2-oxazaphosphorinane (16) This was prepared by adaptation of the procedure described for **14** from *cis*-**1e** (352 mg, 1.25 mmol), BuLi (0.96 ml, 1.31 M solution, 1.25 mmol), trisylazide (425 mg, 1.38 mmol) and acetic anhydride (0.59 ml, 6.25 mmol) in ether (62 ml).to give 651 mg of crude product (13:1 diastereomeric ratio by HPLC). Purification by silica gel column chromatography (hexane/EtOAc/*i*-PrOH, 55/42/3) gave 595 mg (75%) of analytically pure **16** as a foam (~16 / 1 diastereomeric ratio by HPLC). Data for **16**: mp 63-64 °C; ^1H NMR (500 MHz) Mixture of rotamers 7.53 (br s, 2H, ArH), 7.29-7.31 (m, 3H, ArH), 7.12 (s, 2H, ArH), 6.33 (br d, J = 23.6, 1H, HC(1')), 4.84 (br d, J = 13.8, HC(1'), minor rotamer), 4.43 (br s, 1H, HC(6)), 3.76 (br m, 2H, $H_2C(4)$), 2.98 (m, 1H, $HC(CH_3)_2$), 2.88 (m, 1H, $HC(CH_3)_2$), 2.74 (m, 1H, $HC(CH_3)_2$), 2.02 (s, 3H, $COCH_3$), 1.44 (s, 9H, $C(CH_3)_3$), 1.21 (d, J = 6.9, 6H, ortho $C(CH_3)_2$), 1.17 (d, J = 6.3, 6H, ortho $C(CH_3)_2$), 0.95 (d, J = 6.1, 6H, para $C(CH_3)_2$), 0.55 (br m, 1H, HC(5)); ^{13}C NMR 172.65 (CO), 154.50 (Ar), 151.80 (Ar), 131.06 (Ar), 131.04 (Ar), 128.43 (Ar), 128.31 (Ar), 123.61 (Ar), 73.23 (d, J = 8.3, C(6)), 65.15 d, J = 144.3, C(1')), 59.81 ($CH_3(CO)$), 58.65 ($C(CH_3)_3$), 56.38 (C(4)), 34.22 (C(5)), 30.17 ($C(CH_3)_2$), 29.61 ($C(CH_3)_2$), 29.59 ($C(CH_3)_2$), 24.67 (CH_3), 24.31 (CH_3), 21.93 (CH_3), 23.46 (CH_3), 21.79 (d, J = 8.5, $H_3C(6)$), Minor rotamer (partial spectrum) 133.48, 131.86, 131.80, 129.40, 128.12, 128.02, 127.97, 123.69, 41.64, 32.78, 14.01; ^{31}P NMR (121.6 MHz) 13.06; IR (CCl_4) 2967 (w), 1549 (s), 1462 (w), 1372 (w), 1345 (w), 1256 (m), 1148 (m), 1009 (m), 816 (s); MS (CI, CH_4) 633.5 (MH^+, 0.5), 605 (1.5), 563 (1.5), 372 (5.6), 323 (12), 295 (19), 284 (40), 280 (27), 267 (25), 239 (24), 224 (20), 192 (23), 190 (26), 174 (21), 148 (16), 134 (16), 110 (16), 107 (25), 106 (39), 104 (27), 98 (11), 94 (9), 91 (8), 79 (10), 64 (15), 61 (100), 60 (10), 57 (33), 55 (13); TLC R_f 0.35 (hexane/EtOAc/*i*-PrOH, 35/62/3); HPLC t_R 9.27 (major), 7.87 (minor) (Supelco LC Si hexane/EtOAc/*i*-PrOH

62/35/3). Anal. Calcd for $C_{32}H_{49}N_4OPS$ (632.80): C, 60.74; H, 7.81; N, 8.85; P, 4.89; S, 5.07. Found: C, 60.68; H, 7.84; N, 8.74; P, 5.07; S, 5.09.

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