Reactions of Chiral Phosphorous Acid Diamides: The Asymmetric Synthesis of Chiral α-Hydroxy Phosphonamides, Phosphonates, and Phosphonic Acids

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Addition of aldehydes to the anions of chiral phosphorous acid diamides in THF solution gave α-hydroxy phosphonamides in good yield. The diastereoselectivity was strongly dependent upon the diamide used and ranged from poor to good. The phosphorous acid diamides **2a** and **2b** ($R^1 = -(CH_2)_4-$, $R^2 = CH_2Ph$ and CH_2CMe_3, respectively) gave the best selectivity, and their reactions with a range of aldehydes were studied. Diamide **2b** consistently gave good selectivities, whereas diamide **2a** was only moderately selective. Aromatic, aliphatic, and unsaturated aldehydes are tolerated under the reaction conditions. The phosphonamides were hydrolyzed with aqueous HCl in dioxane to give α-hydroxy phosphonic acids. While direct methanolysis of the phosphonamides was unsuccessful, methylation of the phosphonic acids with diazomethane gave α-hydroxy dimethylphosphonates.

Introduction

α-Hydroxy phosphoryl compounds (phosphonates and phosphonic acids) are biologically active and have been shown to inhibit the enzymes renin,[1] EPSP synthase,[2] and HIV protease.[3] In addition, α-hydroxy phosphonates are useful intermediates in the synthesis of other α- and γ-substituted phosphonates and phosphonic acids.[4,5] The absolute configuration at the α-position in substituted phosphonic acids has been shown to be important for biological activity.[6] However, in contrast to the more extensively studied α-amino phosphoryl compounds,[7] chiral, nonracemic hydroxy phosphoryl compounds have only recently begun to receive attention.[8] As part of an ongoing program investigating the use of chiral phosphorus compounds as reagents for asymmetric synthesis, we have developed a method for the asymmetric synthesis of α-hydroxy phosphonic acid derivatives involving the addition of a chiral phosphorous acid diamide to aldehydes.[9]

Results

We recently reported the preparation and alkylation[9a,10] of chiral phosphorous acid diamides **2**. These stable and generally crystalline compounds were easily prepared by the addition of N,N'-disubstituted C_2 diamines **1** to PCl_3, followed by the addition of water to the resulting chlorophosphine diamide. Treatment of the diamides **2** in THF solution with strong base resulted in the formation of the acid anion. The lithium salts were prepared using *n*-BuLi, LDA, or $LiN(SiMe_3)_2$ as base. However, varying amounts of an impurity are formed with *n*-BuLi, probably resulting from addition of butyl anion to the phosphoryl group. $NaN(SiMe_3)_2$ and MeMgBr were also effective bases, but $KN(SiMe_3)_2$ resulted in extensive decomposition. Once formed, the anions were stable in solution up to room temperature.[11]

Addition of cinnamaldehyde to the anion solutions (Scheme 1) gave 1-hydroxy phosphonamides **3** in generally good yields, with variable diastereoselectivity (Table 1). The diastereoisomeric pair **3** were easily distinguishable from each other by ^{31}P NMR spectroscopy, thereby

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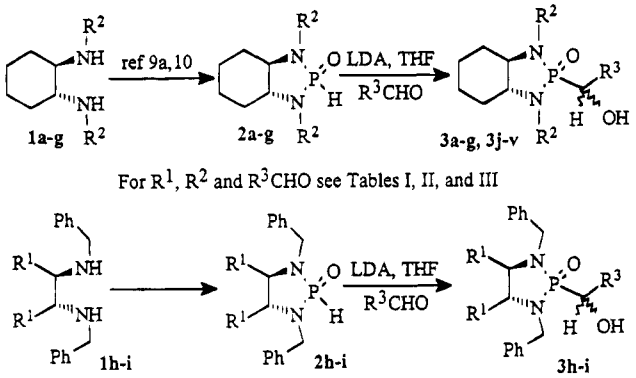
Table 1. Reaction of Phosphorous Acid Diamides 2 with Cinnamaldehyde[a]

	phosphorous acid		yield[b]		isomeric	^{31}P,[d] ppm
	R^1	R^2	(%)	product	ratio[c]	major/minor
2a	$-(CH_2)_4-$	$PhCH_2$	94	**3a**	4.0:1	37.7/36.4
2b	$-(CH_2)_4-$	$(Me)_3CCH_2$	68	**3b**	7.9:1	39.7/39.1
2c	$-(CH_2)_4-$	$(Me)_2CH$	56	**3c**	1:1	36.0/35.1
2d	$-(CH_2)_4-$	$(Me)_2CH(CH_2)_2$	57	**3d**	1.2:1	37.8/36.1
2e	$-(CH_2)_4-$	mesityl-CH_2	25	**3e**	1.1:1	40.2/39.6
2f	$-(CH_2)_4-$	1-Naphth-CH_2	71	**3f**	1.5:1	38.4/39.6
2g	$-(CH_2)_4-$	*o*-tolyl-CH_2	68	**3g**	1:1	39.1/37.9
2h	Me	$PhCH_2$	33	**3h**	2.0:1	33.9/35.3
2i	Ph	$PhCH_2$	74	**3i**	1.5:1	33.8/35.1

[a] The reactions were performed on a 1.2 mmol scale in THF with *n*-Buli, LiHMDS, or LDA as base. [b] Yields are given after purification by recrystallization (1×) or column chromatography. [c] The diastereoisomeric ratios were determined by integration of the ^{31}P NMR spectra of the crude products. [d] NMR spectra were recorded in $CDCl_3$.

Scheme 1



providing a suitable method for the determination of isomeric ratios.[12] The stereoselectivity was found to be strongly dependent upon the diamide employed, and it is clear from the results that the exocyclic substituent (R^2) on nitrogen is the dominant factor in stereocontrol. However, for diamides with an exocyclic benzyl substituent on nitrogen (see Table 1, entries 2a, 2h, and 2i), the bicyclic system **2a** appears to be superior to the monocyclic systems **2h** and **2i**. The phosphorous acid diamides **2a** and **2b** ($R^1 = -(CH_2)_4-$, $R^2 = CH_2Ph$ and CH_2CMe_3, respectively) exhibited the greatest selectivity, and therefore, their reactions with a range of aldehydes were studied. Diamide **2b** (Table 3) consistently gave good selectivities, whereas diamide **2a** (Table 2) was only moderately selective. Aromatic, aliphatic, and unsaturated aldehydes (Table 3) are tolerated under the reaction conditions, and it appears that the larger, sterically bulky aldehydes result in a better selectivity.

In an effort to both improve selectivity and to elucidate a reaction mechanism, we examined the effect of changing several reaction parameters. The addition of diamide **2a** to cinnamaldehyde (Table 2, entry 1) was selected for further study. Increasing the reaction temperature resulted in a decrease in selectivity,[13] with reactions run at room temperature showing no selectivity. However, a practical lower limit was reached at approximately −80 °C due to insolubility of the diamides and their anions in THF solution. Changing the solvent or counterion showed some marginal effects on the selectivity.[14] Surprisingly, the use of ionic metals (Na) or polar cosolvents (12-crown-4 or HMPA) showed selectivities similar to those of the standard lithium experiment. The use of more covalent metals such as Mg and Ti or nonpolar solvents resulted in slight reductions in selectivity. Crossover experiments[15] have determined that the hy-

Table 2. Reaction of the *N,N'*-Dibenzyl-Substituted Phosphorous Acid Diamide 2a with Aldehydes[a]

		yield[b]		isomeric	^{31}P,[d] ppm
entry	aldehyde	(%)	product	ratio[c]	major/minor
1	cinnamaldehyde	94	**3a**	4.0:1	37.7/36.4
2	crotonaldehyde	71	**3j**	5.6:1[d]	36.8/38.5
3	acrolein	54	**3k**	1.4:1	36.1/37.3
4	methacrolein	60	**3l**	1.1:	37.2/35.8
5	benzaldehyde	77	**3m**	1:1	36.9/35.9
6	β-naphthaldehyde	89	**3n**	1:1	36.8/36.0
7	α-naphthaldehyde	93	**3o**	2:1	36.0/35.6
8	heptaldehyde	62	**3p**	2.4:1	39.4/41.4

[a] The reactions were performed on a 1.2 mmol scale in THF with *n*-Buli, LiHMDS, or LDA as base. [b] Yields are given after purification by recrystallization (1×) or column chromatography. [c] The diastereoisomeric ratios were determined by integration of the ^{31}P NMR spectra of the crude products. [d] NMR spectra were recorded in $CDCl_3$. [e] Crystallized to a single diastereoisomer by one or more recrystallizations.

Table 3. Reaction of the *N,N'*-Neopentyl-Substituted Phosphorous Acid Diamide 2b with Aldehydes[a]

		yield[b]		isomeric	^{31}P,[d] ppm
entry	aldehyde	(%)	product	ratio[c]	major/minor
1	cinnamaldehyde	68	**3b**	7.9:1[e]	39.7/39.1
2	crotonaldehyde	91	**3q**	6.9:1[e]	40.4/39.5
3	β-naphthaldehyde	58	**3r**	14:1[e]	39.2/39.1
4	α-naphthaldehyde	91	**3s**	29:1[e]	37.8/37.3
5	benzaldehyde	49	**3t**	25:1[e]	39.0/38.1
6	isovaleraldehyde	82	**3u**	3.4:1	42.6/42.3
7	heptaldehyde	80	**3v**	4:1[e]	42.4/41.8

[a] The reactions were performed on a 1.2 mmol scale in THF with *n*-Buli, LiHMDS, or LDA as base. [b] Yields are given after purification by recrystallization (1×) or column chromatography. [c] The diastereoisomeric ratios were determined by integration of the ^{31}P NMR spectra of the crude products. [d] NMR spectra were recorded in $CDCl_3$. [e] Crystallized to a single diastereoisomer by one or more recrystallizations.

(11) The stability of the anion was examined. A solution of the acid **2a** in THF was deprotonated with *n*-BuLi at −70 °C. Aliquots were removed, quenched and examined by ^{31}P NMR spectroscopy for a period of 2 h. The solution was warmed to 10 °C over 20 min and again examined by ^{31}P NMR spectroscopy. A small amount of an impurity was formed during the initial *n*-BuLi addition, probably due to addition of butyl to the phosphoryl group. However, the impurity did not increase through the course of this study.

(12) The diastereoisomeric ratios were determined by integration of the $^{31}P\{H\}$ NMR spectra of the crude products (2 s delay, standard ^1H decoupling pulse sequence). While integration of ^{31}P NMR spectra are best performed using an inverse-gated pulse sequence (NOE suppressed), a comparison with standard decoupling pulse sequence (NOE enhanced) was made for several samples and no significant difference was observed. Where possible, the results were compared to the ratios determined by integration of suitable signals in the ^1H NMR spectra of the crude products.

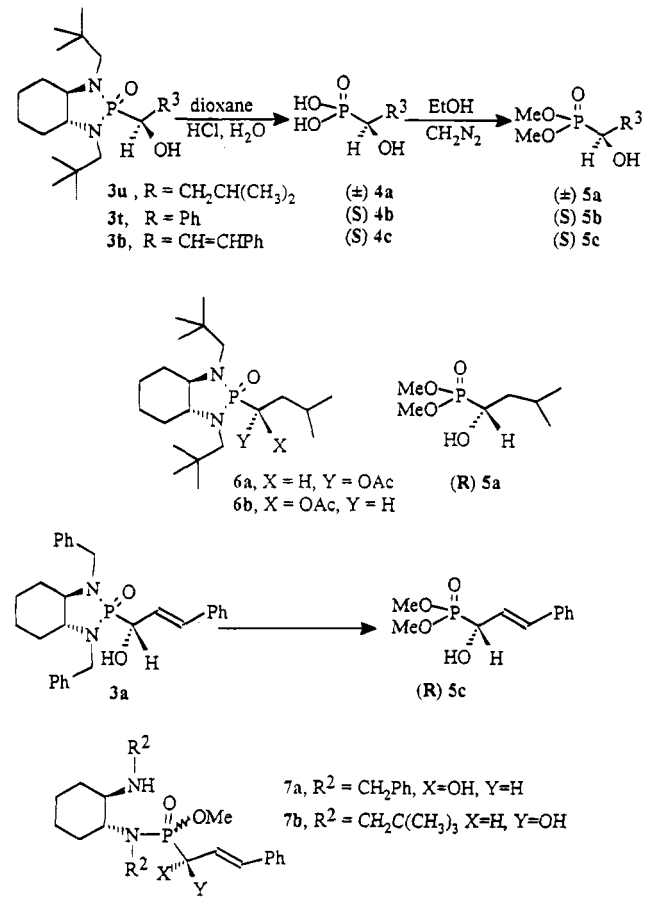
(13) The effect of temperature was studied in the reaction of acid **2a** ($R^1 = -(CH_2)_4-$, $R^2 = PhCH_2$) with cinnamaldehyde. Temperature (ratio): −60 °C (4.2:1), −43 °C (2.3:1), −7 °C (1.8:1), and +6 °C (1.0:1). A practical lower limit is reached at between −70 and −80 °C due to the solubility of the anions in THF.

droxy phosphonamides are stable under the low-temperature reaction conditions. The phosphorous acid diamides **2**, unlike dialkyl phosphites,[16] did not react with aldehydes in the presence of weak bases such as triethylamine and *t*-BuONa in *t*-BuOH.

The relative configuration of C-1′ in two phosphonamides was determined by single crystal X- ray diffraction. A structure determination on hydroxy phosphonamide **3b** (major isomer), formed by reaction of diamide **2b** with cinnamaldehyde (Table 3, entry 1), allowed assignment of the new (C-1') chiral center as *S* resulting from the (*R,R*)-diamide.[17] Whereas the (hydroxyalkyl)-phosphonamide diastereoisomers **3u** were not separable either by crystallization or chromatography, the corresponding acetates **6a** and **6b** were separable by chromatography on silica gel.[18] An X-ray structure determination on the more polar, major acetate diastereoisomer **6b** again allowed assignment of the new chiral center as *S* resulting from an (*R,R*)-diamide.[19]

The conversion of phosphonamides to phosphonic acids and phosphonates was studied with three representative compounds, an alkyl, a benzyl, and an allyl 1-hydroxy phosphonamide (**3u**, **3t**, and **3b** respectively). Related α-amino phosphonamides[20] have been hydrolyzed to amino phosphonic acids with aqueous HCl. The hydroxy phosphonamides were sensitive to treatment with acid at elevated temperature, but were successfully hydrolyzed at room temperature (Scheme 2). (*R,R*)-Phosphonamides **3u** (1.3:1 mixture of isomers), **3t** (14:1 mixture), and **3b** (major isomer) hydrolyzed cleanly at room temperature within 24 h to give the phosphonic acids (±)-**4a**, (*S*)-**4b**, and (*S*)-**4c**, respectively. The phosphonic acids were isolated by ion exchange chromatography (Amberlite IR120+) and characterized as the cyclohexylammonium salts (Table 4). In separate experiments the phosphonic acids were dissolved in ethanol and methylated with etheral diazomethane to give the dimethyl phosphonates (±)-**5a**, (*S*)-**5b**, and (*S*)-**5c**, respectively. The enantiomeric purity of the phosphonates (*S*)-**5b** and (*S*)-**5c** were determined by HPLC[21] as 86% and >99%, respectively, thus the stereochemical integrity of C-1′ remains intact. Phosphonate (*S*)-**5a** showed an $[\alpha]_D$ of

Scheme 2



−38.5, and by comparison with the reported[8e] value indicated that the predominant enantiomer had the *S* configuration (again resulting from the (*R,R*)-diamide). Several attempts at direct methanolysis of phosphonamides with methanolic HCl were unsuccessful. The initial, rapidly formed, product was the result of five-membered ring cleavage and the addition of methanol to the phosphorus atom giving the amide **7b**. Attempts to force the reaction to completion at elevated temperatures resulted in the formation of several products, with the most predominant compound being the monomethyl ester of the hydroxy phosphonic acids.

Since the acetoxy phosphonamides were generally separable by column chromatography, the hydrolysis of the acetate diastereomer **6a** was performed for comparison with the corresponding hydroxy phosphonamide **3u**. Treatment of the minor acetate diastereoisomer (*R,R,R* configuration) **6a** with aqueous HCl in dioxane at room temperature gave mixture of hydroxy and acetoxy phosphonic acids. The mixture was further treated with 1 N aqueous KOH in ethanol to give the hydroxy phosphonic acid potassium salt, which was neutralized (methanolic HCl) and methylated (CH_2N_2 in Et_2O) to give the phosphonate (*R*)-**5a** in 58% isolated yield and >99% ee (HPLC analysis).

(14) A series of reactions were run using acid **2a** and cinnamaldehyde. Solvent or counter ion were varied

solvent	base/counterion	ratio
THF	LDA	4:1
THF	LDA/Ti(O^{i}Pr)$_4$	2:1
THF	LDA/$CeCl_3$	2.8:1
THF	MeMgBr	1.9:1
THF	LiHMDS	4.7:1
THF	NaHMDS	3.8:1
PhMe	NaHMDS	3.7:1
PhMe	LDA	3.7:1
Et_2O	LDA	3.6:1
Hexanes	LDA	1.7:1
THF/HMPA	LDA	3.9:1
THF/12-C-4	LDA	3.6:1

(15) Hydroxy phosphonamide **3b** was added to a solution of the lithium salt of phosphorous acid diamide **2a** in THF. Only **2a** and **3b** were recovered after 4 h and −70 °C. A similar experiment at room temperature resulted in extensive decomposition of materials.

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(18) We have prepared several α-acetoxy phosphonamides, and in most cases we were able to separate the diastereoisomers by chromatography on silica gel.

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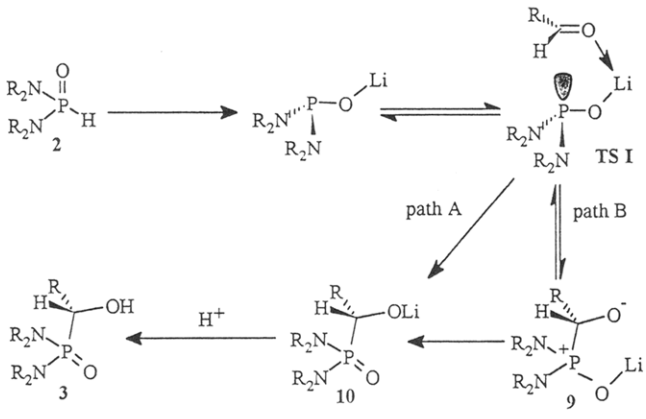
(21) Direct analysis on a ChiralPak AS column: EtOH−hexanes, (9:1 or 2:8), 1 mL/min, detection at 254nm for phosphonates **5b** and **5c**, and using a differential refractometer for phosphonate **5a**. The order of elution was the *R* enantiomer followed by the *S* enantiomer in all three examples. Kozlowski, J. K., Rath, N. P.; Spilling, C. D. *Tetrahedron*, submitted.

Table 4. Hydrolysis of the Phosphonamides

	phosphonamide			phosphonic acid (salt) **4**			dimethyl phosphonate **5**			
	R^2	R^3	ratio	yield	$[\alpha]_D$	no.	yield	$[\alpha]_D$	ee (%)	confign
3u	$(CH_3)_3CCH_2$	$CH_2CH(CH_3)_2$	1.3:1	96		**a**	68			(±)
3t	$(CH_3)_3CCH_2$	Ph	14:1	60	−13.8	**b**	60	−38.5	86%	*S*
3b	$(CH_3)_3CCH_2$	CH=CHPh	>99:1	35	−3.0	**c**	69	−23.6	>99%	*S*
6a	$(CH_3)_3CCH_2$	$CH_2CH(CH_3)_2$	>99:1			**a**	58	−25.0	>99%	*R*
3a	$PhCH_2$	CH=CHPh	>99:1			**c**	69	+19.8	94%[a]	*R*

[a] The ee of recovered diamine was approximately 95%.

Scheme 3



Hydrolysis of the (*R,R*)-*N*-benzylphosphonamide **3a** and methylation of the crude phosphonic acid gave the phosphonate (*R*)-**5c** in 59% yield.[22] Surprisingly, HPLC of (*R*)-**5c** showed that the *R* enantiomer predominated (94% ee), which was the opposite configuration to that observed with the *N*-neopentyl derivatives. Again, attempts to perform direct methanolysis on the phosphonamide **3a** failed, and only the amide **7a** was isolated.

Discussion

The addition of dialkyl phosphite anions to aldehydes (the Pudovik reaction) is well known,[16] and several mechanistic studies under thermodynamic conditions (EtOH, catalytic EtONa) have been carried out.[23] The addition of phosphorous acid diamide anions to aldehydes, while related to the Pudovik reaction, is irreversible[15] and is probably under kinetic control. In considering a possible reaction mechanism for the addition of the diamide anions to aldehydes, it is tempting to postulate a chelated cyclic transition state (TS I, Scheme 3), in which aldehyde and diamide anion are coordinated to lithium ion and react in a concerted manner. ^{1}H NMR and IR spectroscopic studies of the alkali metal salts of dialkyl phosphites suggest that predominant form for the anion is trivalent (P−O−M not M−P=O).[24] The negative charge of the anion is associated with the phosphoryl oxygen, and the lithium (or other metal) cation is strongly chelated by the phosphoryl oxygen. However, several other bonding modes have been described for complexes containing the anions of phosphorous acid diesters (dialkylphosphites)[25] and diamides[26] with transition metals, including coordination through both phosphorus and oxygen. It therefore is not unreasonable to assume that the anion−metal complex would exist in a highly aggregated state. Changing the metal counterion or adding polar cosolvents would be expected to perturb both the aggregation state of the anion and the chelated transition state and thereby change the observed reaction stereoselectivity, whereas such changes had, in most cases, failed to alter the reaction selectivity significantly. As an alternative, the aldehyde can react with the phosphorus without prior coordination to the metal ion to give a polar intermediate **9**. The initial addition step may be reversible with more covalent metals, and the irreversible step is transfer of the metal ion to the new alkoxide oxygen. However, the stereochemical bias of the reaction (described below) suggests that in the transition state the carbonyl oxygen and the phosphoryl oxygen are aligned.

Hanessian *et al.* have examined carbonyl addition and alkylation reactions of several N-substituted chiral bicyclic phosphonamides.[20,27] The bicyclic phosphonamides display high selectivity in many of these C−C bond formations. The selectivity has been rationalized on the basis of the "unique topology" of these bicyclic systems. X-ray crystallography has shown that the geometry of the nitrogen atoms in the bicyclic phosphonamides[10,17,19,28] are midway between tetrahedral and trigonal, whereas the nitrogen geometry in the monocyclic phosphonamides[10,29] is almost trigonal. In the solid state structure of the bicyclic phosphonamides, the exocyclic nitrogen substituents (R^2) are syn to the axial cyclohexyl protons and thus anti to each other, and as a result the nitrogen substituents act to project the chirality of the cyclohexyl carbons closer to the reacting center. Thus, the phosphonamide C-1′ anion has one face blocked and one face accessible to an approaching electrophile (Figure 1). Interestingly, Hanessian has also noted that the *N*-

(22) The rate of hydrolysis of the *N*-benzylphosphonamides is significantly slower than the rate of hydrolysis for the *N*-neopentylphosphonamides.

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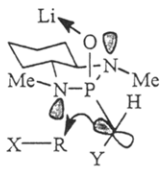

Figure 1.

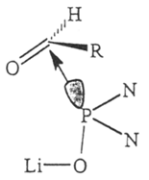

Figure 2.

neopentyl bicyclic phosphonamides give the opposite induced stereochemistry to *N*-methyl, -ethyl, and -benzyl groups. The lack of general selectivity in phosphorous acid diamide additions is at first surprising. However, although it is conceivable that the N-substituents serve the same stereodirecting function in the addition reactions of both the C-1′ anions and phosphorous acid diamide anions, there are several key differences between these reactions. The effective bonding distance of the C−C bond is considerably shorter than the P−C bond. The aldehyde is expected to react with the lone pair of diamide anions, and thus approch from above and slightly in front of the plane of the five-membered ring (Figure 2). These factors require the N-substituents exert their stereodirecting effect at a greater distance and in a different orientation when compared to the C-1′ anions. Only the benzyl and neopentyl substituents are able to achieve this. The ability of the benzyl, and particularly the neopentyl, substituents to direct the approaching aldehyde is a function of their preferred conformation. In the crystal structure,[10,19] the neopentyl group adopts an extended conformation with methyls staggered relative to the CH_2N. This places two methyl groups above the plane of the five-membered ring and two (from the other neopentyl) below the five-membered ring (Figure 3). In this arrangement, *Si* face addition to the aldehyde avoids steric interaction of the aldehyde carbon substituent with the geminal methyls of the neopentyl group in the transition state. In contrast, the phenyl of the benzyl substituent group bisects the CH_2 and continues to bend away from the line of the N−C bond, again placing one phenyl above the ring and one below, but acting to exert an effect in the opposite stereochemical sense to the neopentyl methyls (Figure 4).

In conclusion, we have shown that chiral phosphorous acid diamides are useful reagents for the stereoselective preparation of α-hydroxy phosphonamides, phosphonates, and phosphonic acids. A detailed study of further reactions of chiral phosphorous acid diamides is currently underway in our laboratories and will be reported in due course.

Experimental Section

General Comments. ^1H, ^{31}P, and ^{13}C NMR spectra were recorded in $CDCl_3$ or D_2O solution on a Varian XL-300 spectrometer at 300, 121, and 75 MHz, respectively. The ^1H chemical shifts are reported in ppm downfield from Me_4Si or $Me_3Si(CD_2)_2CO_2Na$ (for D_2O solution). The ^{31}P chemical shifts are reported in ppm downfield from external H_3PO_4. The ^{13}C

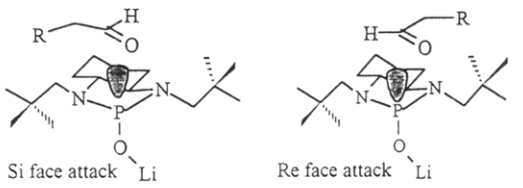

Figure 3.

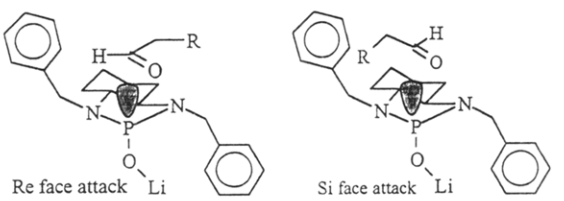

Figure 4.

chemical shifts are reported in ppm relative to the center line of $CDCl_3$ (77.0 ppm) or $Me_3Si(CD_2)_2CO_2Na$ (0.0 ppm). Infrared spectra were recorded on a Perkin-Elmer 1600 series FTIR. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Mass spectra were determined on a Varian Mat 331A spectrometer, and microanalyses were performed by Atlantic Microlab, Inc. Phosphorous acid diamides **2a**−**i** were prepared according to the previously published procedure.[9a,10] The THF was distilled from sodium−benzophenone ketyl, and the reactions were performed under argon. The enantiomeric excess of hydroxy phosphonates **5a**, **5b**, and **5c** was determined by direct analysis on a ChiralPak AS column; EtOH−hexanes (9:1 or 2:8); 1 mL/min, detection at 254 nm or with a differential refractometer.[21]

General Procedure for the Addition of Phosphorous Acid Diamides to Aldehydes. A solution of diisopropylamine (0.182 mL/1.29 mmol) in THF (6 mL) was cooled to −60 °C, and *n*-butyllithium (0.471 mL/1.18 mmol) was added. After 30 min, a fine suspension or solution of phosphorous acid diamide (1.18 mmol) in THF (3 mL) was added via syringe. The resulting solution was maintained at −60 °C for 60 min, and then the aldehyde (1.29 mmol) was added. After an additional 4.5 h at −60 °C, the reaction mixture was quenched with aqueous ammonium chloride (0.5 mL) and diluted with $CHCl_3$ (60 mL). The solution was washed with H_2O (2 × 25 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give the crude product. Crude and isolated yields, physical data, and method of isolation for each compound are given below. Unless otherwise specified, these compounds were characterized as a mixture of isomers.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-di-(2-propyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3c). From racemic diamide **2c**, crude ratio 1.1:1, recrystallization from ethyl acetate, yield 56%, ratio 1:1.6: mp 173.0−173.5 °C; IR (KBr) 3420 (brd), 3195, 2930, 1183cm^{-1}; ^1H NMR δ 7.42−7.20 (m, 5 H), 6.80−6.65 (m, 1 H), 6.61 (dd, J = 3.2 Hz, major), 6.55 (dd, J = 3.2 Hz, major), 6.48 (dd, J = 5.1 Hz, minor), 6.42 (dd, J = 4.9 Hz, minor), 4.82−4.65 (m, 1 H), 3.66−3.44 (m, 2 H), 3.12−2.86 (m, 2 H), 2.50 (t, J = 9.2 Hz), 2.16 (m, 2 H), 1.79 (m, 2 H), 1.46−1.08 (m, 14 H); ^{13}C NMR δ 136.7, 129.9, 129.8, 128.4, 127.3, 127.1, 126.3, 125.1, 71.5 [d, $^1J_{CP}$ = 121.2 Hz, (minor)], 70.0 [d, $^1J_{CP}$ = 119.7 Hz, (major)], 61.3 (major), 60.9 [d, $^2J_{CP}$ = 5.5 Hz, (minor)], 60.0 (minor), 59.7 (major), 45.7 (major), 45.4 (minor), 44.6 (major), 44.2 (minor), 32.2, 31.4, 30.8, 30.4, 24.4, 23.2, 20.7, 20.5, 20.0; ^{31}P NMR δ 36.0 (major), 35.1 (minor); MS (EI/DIP) m/z (rel intensity) 377 (2), 243 (100). Anal. Calcd for $C_{21}H_{33}N_2O_2P$: C, 66.98; H, 8.84; N, 7.44. Found: C, 66.73; H, 8.85; N, 7.36.

2-(1′-Hydroxy-3′-phenyl-(E)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-bis(3-methylbutyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3d). From (*R,R*)-diamide **2d**, reaction temperature −75 °C, crude yield 84%, ratio 1.2:1, column chromatography (SiO_2 eluting with $CHCl_3$), yield 57%, ratio 1.3:1: mp 166.0−169.0 °C (ethyl acetate); IR ($CHCl_3$) 2955,

2870, cm^{-1}; ^1H NMR δ 7.46–7.19 (m, 5 H), 6.78–6.66 (m, 1 H), 6.57–6.39 (m, 1 H), 4.86–4.65 (m, 1 H), 3.20–2.60 (m, 6 H), 2.57–2.45 (m, 1 H), 2.01 (m, 2 H), 1.80 (br s, 2 H), 1.70–1.10 (m, 11 H), 0.75–1.00 (m, 10 H), 0.66 (d, J = 6.1 Hz); ^{13}C NMR δ 136.6 (d, $^4J_{CP}$ = 2.5 Hz), 136.5 (d, $^4J_{CP}$ = 3.0 Hz), 130.3 (d, $^3J_{CP}$ = 11.4 Hz), 129.2 (d, $^3J_{CP}$ = 10.3 Hz), 128.4, 127.3, 126.28, 126.26, 126.0 (d, $^2J_{CP}$ = 3.0 Hz), 125.0 (d, $^2J_{CP}$ = 3.8 Hz), 70.7 (d, $^1J_{CP}$ = 123.7 Hz), 69.4 (d, $^1J_{CP}$ = 121.7 Hz), 63.7 (d, $^2J_{CP}$ = 4.6 Hz), 63.5 (d, $^2J_{CP}$ = 6.2 Hz), 63.1 (d, $^2J_{CP}$ = 5.0 Hz), 62.8 (d, $^2J_{CP}$ = 7.0 Hz), 42.9, 42.2 (d, $^2J_{CP}$ = 1.6 Hz), 40.7 (d, $^2J_{CP}$ = 4.6 Hz), 40.4 (d, $^2J_{CP}$ = 4.5 Hz), 39.7 (d, $^2J_{CP}$ = 4.1 Hz), 38.9, 29.9 (d, $^3J_{CP}$ = 9.8 Hz), 29.6 (d, $^3J_{CP}$ = 9.7 Hz), 29.1 (d, $^3J_{CP}$ = 6.6 Hz), 28.7 (d, $^3J_{CP}$ = 6.6 Hz), 26.5 (d, $^3J_{CP}$ = 2.5 Hz), 26.3 (d, $^3J_{CP}$ = 2.1 Hz), 24.4, 24.2, 22.8, 22.65, 22.59, 22.54, 22.50, 22.42, 22.35, 22.33; ^{31}P NMR δ 37.8 (major), 36.1 (minor); MS (EI/DIP) m/z (rel intensity) 300 (36), 299 (80), 243 (100), 167 (30), 81 (33), 44 (37). Anal. Calcd for $C_{25}H_{41}N_2O_2P$: C, 69.41; H, 9.55; 6.48. Found: C, 69.33; H, 9.53; N, 6.53.

2-(1′-Hydroxy-3′-phenyl-(E)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-bis[(2,4,6-trimethylphenyl)methyl]-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3e). From racemic diamide **2e**, crude yield 111%, ratio 1.3:1, recrystallization from 2-propanol/hexanes, yield 25%, 100% de. Characterized major isomer only: mp 192.0–193.0 °C; IR (KBr) 3415 (brd), 2930, 2860, cm^{-1}; ^1H NMR δ 7.35–7.20 (m, 5 H), 6.78 (s, 2 H), 6.75 (s, 2 H), 6.58–6.50 (m, 1 H), 6.06 (dd, 1 H, J = 4.7 Hz), 6.02 (dd, 1 H, J = 4.7 Hz), 4.40–4.31 (m, 1 H), 4.27–4.18 (m, 2 H), 4.03–3.94 (m, 1 H), 3.91–3.82 (m, 1 H), 2.95–2.85 (m, 2 H), 2.72 (s, 1 H), 2.47 (s, 6 H), 2.32 (s, 6 H), 2.22 (s, 3 H), 2.16 (s, 3 H), 2.10 (m, 1 H), 1.71 (m, 1 H), 1.55 (m, 1 H), 1.39 (m, 1 H), 1.28–1.19 (m, 1 H), 1.18–1.05 (m, 1 H), 0.80–0.70 (m, 1 H); ^{13}C NMR δ 138.0, 137.6, 136.7, 131.5, 131.4, 130.1, 129.7, 129.4, 129.1, 128.5, 127.3, 126.2, 124.1, 71.3 (d, $^1J_{CP}$ = 119.3 Hz), 65.8, 65.2, 42.3, 30.3, 29.2, 24.6, 21.0, 20.6; ^{31}P NMR δ 40.2 (major), 39.6 (minor); MS (EI/DIP) m/z (rel intensity) 409 (19), 134 (15), 133 (100), 132 (47), 117 (15), 91 (17). Anal. Calcd for $C_{35}H_{45}N_2O_2P{\cdot}H_2O$: C, 73.14; H, 8.24; N, 4.87. Found: C, 72.93; H, 7.86; N, 4.98.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-bis(1-naphthylmethyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3f). From (*R,R*)-diamide **2f**, reaction temperature −73 °C, crude ratio 1.9:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 59%, ratio 3.1:1: mp 168.0–171.0 °C (ethyl acetate); IR (KBr) 3445, 2365, 1635, cm^{-1}; ^1H NMR δ 8.25–7.60 (m, 8 H), 7.58–7.20 (m, 6 H), 7.18–6.75 (m, 5 H), 6.53 (dd, J = 15.9, 3.7 Hz, major), 6.38 (dd, J = 15.9, 3.7 Hz, minor), 6.24–6.06 (m, 1 H), 5.11–4.78 (m, 2 H), 4.66–4.32 (m, 2 H), 4.00–3.86 (m, major), 3.72 (br s), 3.38–3.24 (m, 1 H), 3.21–2.90 (m, 2 H), 1.90 (m), 1.78–1.44 (m, 3 H), 1.44–1.31 (m, 2 H), 1.31–1.20 (m, 1 H), 1.20–0.94 (m, 1 H), 0.93–0.80 (m, 1 H); ^{13}C NMR δ 136.2–122.5 (complex multiplet), 71.3 [d, $^1J_{CP}$ = 126.0 Hz, (major)], 71.2 [d, $^1J_{CP}$ = 126.1 Hz, (minor)], 65.8 [d, $^2J_{CP}$ = 4.1 Hz, (minor)], 65.4 (minor), 65.3 [d, $^2J_{CP}$ = 4.1 Hz, (major)], 64.7 [d, $^2J_{CP}$ = 6.1 Hz, (major)], 46.0 (minor), 45.9 [d, $^2J_{CP}$ = 2.1 Hz, (major)], 44.4 (minor), 44.1 [d, $^2J_{CP}$ = 5.2 Hz, (major)], 30.0 [d, $^3J_{CP}$ = 9.6 Hz, (minor)], 29.6 [d, $^3J_{CP}$ = 5.2 Hz, (major)], 29.0 [d, $^3J_{CP}$ = 5.6 Hz, (major)], 24.5 (major), 24.3 (major), 24.2 (minor); ^{31}P NMR δ 38.4 (major), 39.6 (minor); MS (EI/DIP) m/z (rel intensity) 157 (15), 156 (16), 142 (20), 141 (100), 115 (38), 91 (14). Anal. Calcd for $C_{37}H_{37}N_2O_2P{\cdot}2H_2O$: C, 73.01; H, 6.79; N, 4.60. Found: C, 73.23; H, 6.55; N, 4.39.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-bis[(2-methylphenyl)methyl]-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3g). From (*R,R*)-diamide **2g**, reaction temperature −74 °C, crude ratio 1.2:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 68%, recrystallization gave minor isomer in 100% d.e.. Characterized minor isomer only: mp 186.0–187.0 °C (ethyl acetate/hexanes); IR (KBr) 3425 (brd), 3205 (brd), 2935, 2860, cm^{-1}; ^1H NMR δ 7.67–7.55 (m, 2 H), 7.25–7.00 (m, 11 H), 6.58 (ddd, 1 H, J = 16.1, 2.9, 2.0 Hz), 6.28 (ddd, 1 H, J = 16.1, 5.1, 4.4 Hz), 4.50–4.40 (m, 2 H), 4.10–3.95 (m, 2 H), 4.28 (dd, 1 H, J = 5.2, 2.0 Hz), 4.24 (dd, 1 H, J = 5.1, 2.0 Hz), 3.23–3.15 (m, 1 H), 3.04–2.97 (m, 1 H), 2.95–2.70 (m, 1 H), 2.34 (s, 3 H), 2.15 (s, 3 H), 1.88 (m, 1 H), 1.70 (m, 1 H), 1.62 (br s, 1 H), 1.35–1.00 (m, 3 H); ^{13}C NMR δ 137.6, 136.3, 136.1, 135.7, 134.6, 130.2, 129.8, 128.2, 127.2, 126.5, 126.2, 125.9, 125.7, 124.6, 71.2 (d, $^1J_{CP}$ = 126.6 Hz), 65.3, 64.7, 45.6, 43.9, 29.8, 29.1, 24.4, 19.2; ^{31}P NMR δ 39.1 (major), 37.9 (minor); MS (EI/DIP) m/z (rel intensity) 322 (44), 217 (63), 121 (27), 120 (36), 105 (100), 104 (44). Anal. Calcd for $C_{31}H_{37}N_2O_2P$: C, 74.36; H, 7.45; N, 5.60. Found: C, 74.29; H, 7.50; N, 5.54.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-1,3-dibenzyl-4,5-dimethyl-1,3,2-diazaphospholidine 2-Oxide (3h). From racemic diamide **2h**, crude yield 99%, ratio 2.0:1, recrystallization from ethyl acetate, yield 33%, ratio 3.1:1: mp 158.0–159.0 °C; IR (KBr) 3380 (brd), 2965, 2860, cm^{-1}; ^1H NMR δ 7.50–7.18 (m, 15 H), 6.72 (ddd, J = 15.8, 4.8, 1.6 Hz, minor), 6.61 (ddd, J = 16.0, 4.9, 1.5 Hz, major), 6.45 (ddd, J = 16.0, 5.2, 4.3 Hz, minor), 6.32 (ddd, J = 16.0, 6.2, 4.8 Hz, major), 4.76 (ddd, J = 12.2, 5.3, 1.7 Hz, minor), 4.67 (ddd, J = 10.0, 6.2, 1.5 Hz, major), 4.47–4.31 (m, 1 H), 4.27 (dd, J = 7.8, 2.9 Hz, major), 4.18 (dd, J = 16.1, 7.6 Hz, minor), 4.08–3.98 (m, 1 H), 3.05–2.90 (m, 1 H), 2.90–2.80 (m, 1 H), 1.08–0.96 (m, 6 H); ^{13}C NMR δ 138.2, 137.2, 136.5, 131.4, 131.3, 130.5, 128.5, 127.8, 127.5, 127.3, 126.4, 125.4, 71.3 [d, $^1J_{CP}$ = 130.2 Hz, (major)], 70.5 [d, $^1J_{CP}$ = 127.5 Hz, (minor)], 59.6 (minor), 58.3 (major), 57.6 (major), 47.3 (minor), 46.9 (major), 46.1 (minor), 45.6 (major), 18.4 (major), 17.9 (minor); ^{31}P NMR δ 33.8 (major), 35.3 (minor); MS (EI/DIP) m/z (rel intensity) 91 (100), 78 (18), 77 (23), 65 (22), 51 (27), 50 (17). Anal. Calcd for $C_{27}H_{31}N_2O_2P$: C, 72.63; H, 7.00; N, 6.27. Found: C, 72.35; H, 7.04; N, 6.23.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-1,3-dibenzyl-4,5-diphenyl-1,3,2-diazaphospholidine 2-Oxide (3i). From racemic diamide **2i**, crude ratio 1.5:1, recrystallization from ethyl acetate, yield 74%, ratio 2.9:1: mp 180.0–180.5 °C; IR (KBr) 3340 (brd), 3050, 2900, cm^{-1}; ^1H NMR δ 7.40–6.92 (m, 25 H), 6.63–6.52 (m, 1 H), 6.38–6.27 (m, 1 H), 4.97–4.80 (br s, 1 H), 4.50–4.30 (m, 2 H), 4.23 (dd, J = 6.2 Hz, major), 3.98–3.85 (m, 2 H), 3.72–3.52 (m, 2 H); ^{13}C NMR δ 138.8, 137.5, 136.9, 135.9, 131.4, 131.3, 130.9, 130.8, 129.3, 128.5, 128.2, 128.0, 127.7, 127.5, 126.8, 126.4, 125.6, 125.4, 72.6 (minor), 72.3 (d, $^1J_{CP}$ = 117.7 Hz, [major]), 70.6 (minor), 70.1 (minor), 69.0 (major), 67.7 (major), 48.0 (minor), 47.6 (major), 46.4 (minor), 46.3 (major); ^{31}P NMR δ 33.8 (major), 35.1 (minor); MS (EI/DIP) m/z (rel intensity) 347 (26), 196 (18), 152 (12), 92 (11), 91 (100), 65 (15). Anal. Calcd for $C_{37}H_{35}N_2O_2P$: C, 77.87; H, 6.18; N, 4.91. Found: C, 77.60; H, 6.22; N, 4.87.

2-(1′-Hydroxy-3′-phenyl-(E)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3a). From (*R,R*)-diamide, crude ratio 4.0:1, recrystallization from ethyl acetate/hexanes, yield 94%, ratio 14:1. Data listed for major isomer only: mp 180.0–181.0 °C; IR (KBr) 3300 (brd), 2930, 2360, cm^{-1}; ^1H NMR δ 7.50–7.15 (m, 15 H), 6.64 (ddd, 1 H, J = 15.9, 4.7, 1.7 Hz), 6.34 (ddd 1 H, J = 16.1, 5.4, 5.4 Hz), 4.57–4.47 (m, 1 H), 4.55 (dd, 1 H, J = 16.1, 10.0 Hz), 4.39 (dd, 1 H, J = 15.1 Hz), 4.12 (dd, 1 H, J = 15.3, 10.0 Hz), 3.98 (dd, 1 H, J = 16.2, 7.2 Hz), 3.10–3.00 (m, 1 H), 2.90–2.80 (m, 2 H), 1.90–1.83 (m, 1 H), 1.74–1.55 (m, 4 H), 1.10 (br s, 2 H), 1.00–0.90 (m, 1 H); ^{13}C NMR δ 139.8, 138.2, 136.4, 130.8, 130.7, 128.4, 128.1, 127.3, 126.8, 126.3, 124.8, 71.3 (d, $^1J_{CP}$ = 126.1 Hz), 64.5, 63.9, 47.9, 46.5, 29.9, 29.5, 24.3; ^{31}P NMR δ 36.3 (major), 37.6 (minor); MS (CI/GC/CH_4) m/z (rel intensity) 340 (23), 339 (26), 249 (56), 132 (34), 131 (57), 91 (100). Anal. Calcd for $C_{29}H_{33}N_2O_2P{\cdot}0.5H_2O$: C, 72.33; H, 7.12; N, 5.82. Found: C, 72.39; H, 7.12; N, 5.81.

2-(1′-Hydroxy-(*E*)-but-2′-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3j). From (*R,R*)-diamide **2a**, reaction tempertaure −75 °C, crude yield 98%, ratio 5.6:1, recrystallization from ethyl acetate, yield 71%, 100% de. Characterized major isomer only: mp 181.0–182.0 °C; IR (KBr) 3170 (brd), 2935, 2860 cm^{-1}; ^1H NMR δ 7.50–7.20 (m, 10 H), 5.80–5.60 (m, 2 H), 4.57 (dd, 1 H, J = 16.1, 9.5 Hz), 4.43–4.28 (m, 2 H), 4.13–3.91 (m, 3 H), 2.99 (m, 1 H), 2.90–2.78 (m, 2 H), 1.83 (m, 1 H), 1.62 (m, 5 H), 1.10 (m, 3 H), 1.00–0.90 (m, 1 H); ^{13}C NMR δ 140.0, 138.4, 128.6, 128.3, 128.1, 127.2, 126.8, 126.2, 71.2 (d, $^1J_{CP}$ =

127.7 Hz), 64.4, 64.0, 48.0, 46.5, 29.8, 29.5, 24.3, 17.9; ^{31}P NMR δ 36.7 (major), 38.4 (minor); MS (EI/DIP) m/z (rel intensity) 410 (M^+, 17), 340 (32), 339 (54), 91 (100), 71 (16), 65 (22). Anal. Calcd for $C_{24}H_{31}N_2O_2P{\cdot}0.5H_2O$: C, 68.72; H, 7.69; N, 6.68. Found: C, 68.77; H, 7.67; N, 6.63.

2-(1′-Hydroxyprop-2′-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3k). From racemic diamide **2a**, crude yield 108%, ratio 1.4:1, recrystallization from ethyl acetate, yield 54%, ratio 1.4:1: mp 149.5−153.0 °C; IR (KBr) 3265 (brd), 2940 cm^{-1}; ^{1}H NMR δ 7.50−7.20 (m, 10 H), 6.18−6.02 (m, 1 H), 5.40 (m, 1 H), 5.20 (m, 1 H), 4.60 (d, J = 10.4 Hz), 4.55 (d, J = 9.8 Hz), 4.43−4.32 (m, 1 H), 4.15−4.04 (m, 1 H), 4.00−3.90 (m, 1 H), 3.02 (m, 1 H), 2.87 (m, 1 H), 2.75−2.58 (m, 1 H), 1.90−1.54 (m, 5 H), 1.10 (m, 2 H), 1.00−0.84 (m, 1 H); ^{13}C NMR δ 139.9, 138.0, 133.8, 133.7, 128.1, 128.0, 127.9, 127.1, 127.0, 115.4, 115.2, 155.1, 71.6 (major), 71.2 (minor), 70.4 (major), 70.0 (minor), 64.4 (minor), 64.3 (major), 64.1 (minor), 64.0 (major), 48.2 (minor), 48.0 (major), 46.5 (major), 46.4 (minor), 30.0, 29.9, 29.8, 24.1; ^{31}P NMR δ 36.1 (major), 37.3 (minor); MS (EI/DIP) m/z (rel intensity) 396 (M^+, 10), 340 (16), 339 (32), 92 (9), 91 (100), 65 (9). Anal. Calcd for $C_{23}H_{29}N_2O_2P$: C, 69.68; H, 7.37; N, 7.07. Found: C, 69.55; H, 7.41; N, 7.05.

2-(1′-Hydroxy-2′-methylprop-2′-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3l). From racemic diamide **2a**, crude yield 97%, ratio 1.1:1, recrystallization from ethyl acetate, yield 60%, ratio 1.1: 1: mp 150.0−152.0 °C; IR (KBr) 3360 (brd), 2930, 2865 cm^{-1}; ^{1}H NMR δ 7.52−7.15 (m, 10 H), 5.20−5.19 (m, minor), 5.16−5.15 (m, major), 5.02−4.94 (m, 1 H), 4.64−4.52 (m, 1 H), 4.51−4.42 (m, 1 H), 4.31−4.08 (m, 2 H), 3.99−3.82 (m, 1 H), 3.21−3.12 (m, 1 H), 3.07−2.89 (m, 1 H), 2.84−2.73 (m, 1 H), 1.93 (m, 3 H), 1.90−1.70 (m, 1 H), 1.69−1.50 (m, 3 H), 1.19−1.00 (m, 2 H), 0.95−0.78 (m, 1 H); ^{13}C NMR δ 142.3, 142.2, 141.94, 141.88, 140.31, 140.25, 140.12, 140.07, 137.81, 137.76, 137.67, 137.63, 128.6, 128.4, 128.25, 128.21, 128.1, 127.4, 127.3, 127.1, 126.9, 126.8, 112.6, 112.4, 111.6, 111.5, 73.6 [d, $^1J_{CP}$ = 120.7 Hz, (major)], 72.4 [d, $^1J_{CP}$ = 121.6 Hz, (minor)], 64.8, 64.7, 64.6, 63.3, 63.2, 62.72, 62.64, 48.70, 48.67, 47.61, 47.58, 47.0, 46.9, 46.6, 46.5, 29.9, 29.8, 29.7, 29.6, 29.4, 29.2, 24.25 (minor), 24.17 (major), 24.11 (major), 24.0 (minor), 21.3 (major), 20.7 (minor); ^{31}P NMR δ 37.2 (major), 35.8 (minor); MS (EI/DIP) m/z (rel intensity) 340 (28), 339 (61), 249 (26), 106 (25), 92 (27), 91 (100). Anal. Calcd for $C_{24}H_{31}N_2O_2P$: C, 70.22; H, 7.61; N, 6.82. Found: C, 70.06; H, 7.65; N, 6.83.

2-(Phenylhydroxymethyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3m). From racemic diamide **2a**, crude yield 97%, ratio 1.0:1, recrystallization from 2-propanol/hexanes yield 77%, ratio 2.0: 1: mp 169−173 °C; IR (KBr) 3385 (brd), 2930 cm^{-1}; ^{1}H NMR δ 7.54−7.15 (m, 15 H), 5.05 (d, $^2J_{HP}$ = 8.8 Hz, major), 4.90 (d, $^2J_{HP}$ = 7.6 Hz, minor), 4.58 (dd, J = 16.4, 10.7 Hz, major), 4.30 (dd, J = 15.6, 9.8 Hz, minor), 4.18−3.89 (m, 2 H), 3.73 (dd, J = 16.1, 7.1 Hz, minor), 3.57 (dd, J = 16.1, 7.3 Hz, major), 2.73−2.62 (m, 1 H), 2.20 (m, 1 H), 1.85−1.75 (m, 1 H), 1.50−1.60 (m, 1 H), 1.49−1.38 (m, 1 H), 1.35−1.20 (m, 1 H), 1.05−0.90 (m, 2 H), 0.90 (m, 1 H), 0.80−0.64 (m, 1 H); ^{13}C NMR δ 140.3, 137.42, 137.39, 136.8, 128.8, 128.7, 128.4, 128.2, 127.9, 127.8, 127.6, 127.5, 127.48, 127.43, 127.39, 127.34, 126.94, 126.87, 126.43, 126.38, 72.6 [d, $^1J_{CP}$ = 121.1 Hz, (minor)], 72.4 [d, $^1J_{CP}$ = 122.1 Hz, (major)], 64.6 (major), 64.5 (major), 64.4 (minor), 64.3 (minor), 62.8 (major), 62.7 (major), 62.3 (minor), 62.2 (minor), 47.7 (major), 47.4 (minor), 46.6 (minor), 46.53 (minor), 46.48 (major), 46.41 (major), 29.7, 29.6, 29.5, 28.9, 28.8, 24.3 (minor), 24.1 (major), 24.0 (major), 23.9 (minor); ^{31}P NMR δ 35.9 (minor), 36.9 (major); MS (EI/DIP) m/z (rel intensity) 340 (14), 339 (15), 106 (17), 105 (10), 91 (100), 77 (13). Anal. Calcd for $C_{27}H_{31}N_2O_2P$: C, 72.63; H, 7.00; N, 6.27. Found: C, 72.52; H, 7.08; N, 6.22.

2-[(2-Naphthyl)hydroxymethyl]-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3n). From (*R,R*)-diamide **2a**, reaction temperature −73 °C, crude yield 105%, ratio 1:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 89%, ratio 4.2:1. Data listed for major isomer only: mp 174.0−175.0 °C; IR (KBr) 3400 (brd), 3255, 2935, 2855 cm^{-1}; ^{1}H NMR δ 7.95−7.58 (m, 5 H), 7.50−7.12 (m, 12 H), 5.06 (dd, 1 H, J = 8.0, 4.9 Hz), 4.33 (dd, 1 H, J = 15.9, 10.1 Hz), 4.07 (m, 1 H), 3.90 (m, 2 H), 3.73 (dd, 1 H, J = 15.9, 6.8 Hz), 2.70 (s, 2 H), 1.75 (m, 1 H), 1.52 (m, 3 H), 0.97 (m, 2 H), 0.79 (m, 1 H); ^{13}C NMR δ 140.0, 137.2, 135.1, 133.0, 132.7, 128.5, 128.3, 128.1, 127.9, 127.5, 127.3, 126.8, 125.9, 125.7, 125.0, 72.8 (d, $^1J_{CP}$ = 122.0 Hz), 64.4, 62.4, 47.5, 46.6, 29.5, 29.1, 24.1; ^{31}P NMR δ 36.0 (major), 36.8 (minor); MS (FAB) m/z (rel intensity) 497 ([M + 1]$^+$, 100), 479 (48), 415 (36), 371 (50), 323 (81), 283 (54). HRMS (FAB/PEG-300) (M + 1)$^+$ calcd for $C_{31}H_{33}N_2O_2P$ 497.2358, found 497.2338.

2-[(1-Naphthyl)hydroxymethyl]-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3o). From (*R,R*)-diamide **2a**, reaction temperature −75 °C, crude yield 112%, ratio 2.0:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with acetone), yield 93%, ratio 2.0:1: mp 189.0−190.0 °C (chloroform/ethyl acetate); IR (KBr) 3235 (brd), 2935, 2860 cm^{-1}; ^{1}H NMR δ 8.12−7.73 (m, 5 H), 7.60−7.12 (m, 12 H), 5.95 (d, $^2J_{HP}$ = 8.8 Hz, major), 5.71 (d, $^2J_{HP}$ = 8.3 Hz, minor), 4.53 (dd, J = 16.0, 10.4 Hz, minor), 4.44 (dd, J = 16.3, 10.0 Hz, major), 4.14−3.90 (m), 3.81 (dd, J = 16.0, 6.8 Hz, minor), 3.46 (dd, J = 15.2, 8.6 Hz, minor), 3.41 (dd, J = 16.1, 7.4 Hz, major), 3.21 (dd, J = 16.4, 16.4 Hz), 2.80 (m, 1 H), 2.62−2.45 (m, 1 H), 2.13−2.02 (m, 1 H), 1.65−1.45 (m, 2 H), 1.45−1.24 (m, 1 H), 0.90−0.68 (m, 2 H), 0.67−0.45 (m, 1 H); ^{13}C NMR δ 140.2, 136.7, 136.6, 133.9, 133.3, 130.7, 128.8, 128.3, 128.1, 127.2, 126.7, 125.4, 125.1, 124.4, 123.6, 69.3 [d, $^1J_{CP}$ = 122.8 Hz, (major)], 68.6 [d, $^1J_{CP}$ = 120.3 Hz, (minor)], 64.1, 63.8, 61.5, 47.5, 46.7, 46.4, 29.5, 28.3, 24.0; ^{31}P NMR δ 36.0 (major), 35.6 (minor); MS (EI/DIP) m/z (rel intensity) 340 (12), 305 (22), 249 (18), 92 (10), 91 (100), 65 (9). Anal. Calcd for $C_{31}H_{33}N_2O_2P{\cdot}H_2O$: C, 72.35; H, 6.86; N, 5.44. Found: C, 72.68; H, 6.60, N, 5.47.

2-(1′-Hydroxyheptyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3p). From racemic diamide **2a**, crude yield 99%, ratio 2.4:1, recrystallization from ethyl acetate, yield 62%, ratio 2.4:1: mp 114.5−116 °C; IR (KBr) 3385 (brd), 2930, 2860 cm^{-1}; ^{1}H NMR δ 7.47−7.20 (m, 10 H), 4.63−4.32 (m, 2 H), 4.14−3.92 (m, 2 H), 3.90−3.70 (m, 2 H), 3.05−2.95 (m, 1 H), 2.90−2.80 (m, 1 H), 2.60 (s, 1 H), 1.80 (m, 2 H), 1.70−1.50 (m, 5 H), 1.40−1.10 (m, 8 H), 0.95−0.80 (m, 4 H); ^{13}C NMR δ 140.1, 140.0, 138.6, 138.5, 128.7, 128.44, 128.40, 128.3, 128.25, 128.16, 127.8, 127.4, 127.25, 127.22, 126.9, 126.8, 70.2 [d, $^1J_{CP}$ = 128.9 Hz, (major)], 69.4 [d, $^1J_{CP}$ = 127.4 Hz, (minor)], 65.0 (minor), 64.9 (minor), 64.8 (minor), 64.24 (major), 64.15 (major), 64.09 (major), 64.03 (major), 48.4 (minor), 48.0 (major), 46.73 (minor), 46.65 (minor), 46.24 (major), 46.17 (major), 31.8 (minor), 31.6 (major), 31.3 (minor), 31.2 (major), 30.0 (minor), 29.9 (minor), 29.8, 29.7, 29.3, 29.2, 28.9 (major), 26.7 (minor), 26.5 (major), 24.4 (minor), 24.3 (major), 22.5 (major), 14.0 (major); ^{31}P NMR δ 39.4 (major), 41.4 (minor); MS (EI/DIP) m/z (rel intensity) 340 (74), 339 (58), 293 (29), 249 (28), 91 (100), 55 (20). Anal. Calcd for $C_{27}H_{39}N_2O_2P$: C, 71.34; H, 8.65; N, 6.16. Found: C, 71.15; H, 8.64; N, 6.13.

2-(1′-Hydroxy-3′-phenyl-(*E*)-prop-2′-enyl)-2,3,3a,4,5,6,7,-7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3b). From (*R,R*)-diamide **2b**, crude ratio 7.9:1. Recrystallization from 2-propanol (isolated both diastereoisomers with 68% combined yield): mp 182−183 °C (racemic); IR (KBr) 3285 (brd), 2935, 2865, cm^{-1}; Major isomer: mp 182−183 °C (racemic), 175 °C (RRS enantiomer) $[\alpha]^{25}_D$ = −122.4° (c = 0.96, $CHCl_3$); ^{1}H NMR δ 7.40−7.25 (m, 5 H), 6.78 (ddd, 1 H, J = 16.1, 5.1, 2.0 Hz), 6.38 (ddd, 1 H, J = 16.3, 4.9, 4.9 Hz), 5.05−4.95 (m, 1 H), 3.85 (m, 1 H), 3.53−3.30 (m, 2 H), 2.86−2.69 (m, 2 H), 2.46−2.32 (m, 2 H), 2.13−2.03 (m, 1 H), 1.93−1.82 (m, 1 H), 1.73 (br s, 2 H), 1.30−1.16 (m, 2 H), 1.16−1.02 (m, 1 H), 0.97 (s, 9 H,), 0.93 (s, 9 H); ^{13}C NMR δ 136.7, 130.4 (d, $^3J_{CP}$ = 10.8 Hz), 128.6, 127.4, 126.2, 124.7, 72.5 (d, $^1J_{CP}$ = 122.2 Hz), 66.4, 65.4, 57.1, 54.4, 32.6, 31.9, 31.0, 29.0, 28.4, 24.6; ^{31}P NMR δ 39.6; MS (EI/DIP) m/z (rel intensity) 301 (42), 300 (100), 286 (14), 285 (73), 244 (41), 243 (100). Anal. Calcd for $C_{25}H_{41}N_2O_2P$: C, 69.41; H, 9.55; N, 6.48. Found: C, 69.32; H, 9.57; N, 6.51. Minor isomer: mp 174−175 °C; $[\alpha]^{25}_D$ = −7.5° (c = 0.92, $CHCl_3$); ^{1}H NMR δ 7.40−7.20 (m, 5 H), 6.72 (ddd, 1 H, J = 16.1, 4.4, 2.0 Hz), 6.48

(ddd, 1 H, J = 16.1, 5.0, 5.0 Hz), 4.95–4.85 (m, 1 H), 3.35–3.21 (m, 2 H), 3.16–3.04 (m, 1 H), 2.92–2.78 (m, 2 H), 2.55–2.39 (m, 2 H), 2.15–2.05 (m, 1 H), 1.98–1.83 (m, 1 H), 1.83–1.73 (m, 2 H), 1.33–1.07 (m, 4 H), 0.97 (s, 9 H), 0.89 (s, 9 H); ^{13}C NMR δ 136.7, 129.6 (d, $^{3}J_{CP}$ = 11.1 Hz), 128.5, 127.4, 126.5, 126.1, 70.9 (d, $^{1}J_{CP}$ = 121.6 Hz), 65.6, 65.5, 56.6, 54.6, 32.6 (d, $^{3}J_{CP}$ = 1.7 Hz), 31.8, 30.9 (d, $^{3}J_{CP}$ = 8.4 Hz), 30.8 (d, $^{3}J_{CP}$ = 7.1 Hz), 28.9, 28.3, 24.6, 24.5; ^{31}P NMR δ 39.1.

2-(1′-Hydroxy-(*E*)-but-2′-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3q). From (*R,R*)-diamide **2b**, reaction temperature −73 °C, crude yield 103%, ratio 6.9:1, recrystallization from ethyl acetate, yield 91%, ratio 16:1. Data listed for major isomer only: mp 153.5–157.0 °C; IR(KBr) 3240 (brd), 2950, 2865 cm^{-1}; ^{1}H NMR δ 5.90–5.73 (m, 1 H), 5.65–5.55 (m, 1 H), 4.72–4.62 (m, 1 H), 3.41–3.23 (m, 3 H), 2.85–2.65 (m, 2 H), 2.45–2.30 (m, 2 H), 2.05 (m, 1 H), 1.90 (s, 1 H), 1.76 (m, 4 H), 1.35–1.00 (m, 4 H), 0.95–0.87 (m, 18 H); ^{13}C NMR δ 128.1 (d, $^{3}J_{CP}$ = 11.2 Hz), 125.9, 72.1 (d, $^{1}J_{CP}$ = 123.1 Hz), 66.2, 65.5, 56.9, 54.4, 32.5, 31.8, 31.0, 28.9, 28,4, 24.7, 24.6, 18.0; ^{31}P NMR δ 40.4 (major), 39.5 (minor); MS (EI/DIP) m/z (rel intensity) 313 (14), 300 (29), 299 (100), 243 (15), 81 (13), 57 (11). Anal. Calcd for $C_{20}H_{39}N_2O_2P$: C, 64.83; H, 10.61; N, 7.56. Found: C, 64.74; H, 10.67; N, 7.47.

2-[(2-Naphthyl)hydroxymethyl]-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3r). From racemic diamide **2b**, crude yield 100%, ratio 14:1, recrystallization from ethyl acetate, yield 58%, ratio 6.1:1. Data listed for major isomer only: mp 162.0–163.0 °C; IR (KBr) 3185 (brd), 2945, 2865 cm^{-1}; ^{1}H NMR δ 8.08 (s, 1 H), 7.78 (m, 2 H), 7.42 (m, 4 H), 5.47 (d, 1 H, $^{2}J_{HP}$ = 9.6 Hz), 3.60 (m, 1 H), 3.52–3.30 (m, 3 H), 2.75 (m, 1 H), 2.51 (dd, 1 H, J = 14.9, 10.0 Hz), 2.04 (m, 2 H), 1.50 (m, 3 H), 1.26 (m, 1 H), 1.00 (m, 2 H), 1.05 (s, 9 H), 0.88 (s, 9 H), 0.54 (m, 1 H); ^{13}C NMR δ 136.1, 134.5, 132.7, 132.4, 127.6, 127.4, 126.7, 125.8, 125.4, 125.1, 125.0, 72.8 (d, $^{1}J_{CP}$ = 120.2 Hz), 65.8, 64.3, 57.0, 54.2, 32.8, 31.6, 30.5, 29.6, 28.9, 28.2, 24.2; ^{31}P NMR δ 39.3 (major), 38.2 (minor); MS (EI/DIP) m/z (rel intensity) 299 (37), 243 (100), 156 (32), 155 (26), 127 (30), 81 (22). Anal. Calcd for $C_{27}H_{41}N_2O_2P$: C, 71.02; H, 9.05; N, 6.14. Found: C, 71.02; H, 9.01; N, 6.13.

2-[(1-Naphthyl)hydroxymethyl]-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3s). From (*R,R*)-diamide **2b**, reaction temperature −73 °C, crude yield 115%, ratio 29:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 91%, ratio 29:1. Data listed for major isomer only: mp 168.5–170.0 °C; IR (KBr) 3325, 2955 cm^{-1}; ^{1}H NMR δ 8.09 (m, 1 H), 7.86 (m, 3 H), 7.50 (m, 3 H), 5.95 (d, 1 H, $^{2}J_{HP}$ = 8.7 Hz), 3.93 (m, 1 H), 2.97 (m, 2 H), 2.70 (m, 2 H), 2.05 (m, 1 H), 1.77 (m, 1 H), 1.43 (m, 2 H), 1.30 (m, 2 H), 1.02 (s, 9 H), 1.02–0.75 (m, 1 H), 0.85 (s, 9 H), 0.50 (m, 1 H), 0.08 (m, 1 H); ^{13}C NMR δ 133.52, 133.46, 133.3, 133.2, 131.0, 130.9, 128.5, 127.7, 127.6, 125.4, 125.3, 125.15, 125.10, 125.02, 124.95, 124.3, 69.7 (d, $^{1}J_{CP}$ = 115.7 Hz), 63.6, 63.24, 63.16, 62.9, 54.7, 53.7, 33.4, 31.7, 30.1, 29.1, 28.3, 27.9, 25.2, 24.5, 24.1; ^{31}P NMR δ 37.8 (major), 39.2 (minor); MS (EI/DIP) m/z (rel intensity) 300 (45), 299 (71), 243 (100), 128 (45), 81 (42), 57 (48). Anal. Calcd for $C_{27}H_{41}N_2O_2P$: C, 71.02; H, 9.05; N, 6.14. Found: C, 70.76; H, 8.98; N, 6.12.

2-(Phenylhydroxymethyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3t). From (*R,R*)-diamide **2b**, reaction temperature −72 °C, crude yield 90%, ratio 25:1, recrystallized from ethyl acetate, yield 49%, ratio 31:1. Data listed for major isomer only: mp 186.5–187.5 °C; IR (KBr) 3230 (brd), 2950, 2865 cm^{-1}; ^{1}H NMR δ 7.60–7.52 (m, 2 H), 7.40–7.21 (m, 3 H), 5.30 (d, 1 H, $^{2}J_{HP}$ = 9.2 Hz), 3.80 (m, 1 H), 3.37–3.25 (m, 2 H), 2.74 (dd, 1 H, J = 11.9 Hz), 2.45 (dd, 1 H, J = 14.9, 10.0 Hz), 2.11 (dd, 1 H, J = 14.7 Hz), 1.99 (d, 1 H, J = 4.1 Hz), 1.70–1.49 (m, 4 H), 1.30–1.00 (m, 2 H), 1.01 (s, 9 H), 0.88 (s, 9 H), 0.81 (m, 1 H); ^{13}C NMR δ 136.5, 127.6, 127.1, 126.6, 73.0 (d, d, $^{1}J_{CP}$ = 118.2 Hz), 65.6, 64.3, 56.7, 54.2, 33.0, 31.7, 30.6, 29.5, 29.0, 28.3, 24.4; ^{31}P NMR δ 39.0 (major), 38.1 (minor); MS (EI/DIP) m/z (rel intensity) 300 (48), 299 (100), 243 (33), 185 (11), 79 (14), 57 (14). Anal. Calcd for $C_{23}H_{39}N_2O_2P$: C, 67.95; H, 9.67; N, 6.89. Found: C, 67.84; H, 9.74; N, 6.82.

2-(1′-Hydroxy-3′-methyl-butyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3u). From (*R,R*)-diamide **2b**, reaction temperature −72 °C, crude ratio 3.4:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 82%, ratio 1.5:1: mp 190.0–191.5 °C; IR (KBr) 3240 (brd), 2950, 2865 cm^{-1}; ^{1}H NMR δ 4.27–4.15 (m, 2 H), 3.57–3.17 (m, 3 H), 3.03–2.80 (m, 2 H), 2.79–2.69 (m, 1 H), 2.60–2.27 (m, 2 H), 2.13–1.90 (m, 3 H), 1.85–1.75 (m, 2 H), 1.75–1.40 (m, 2 H), 1.32–1.10 (m, 4 H), 1.01–0.95 (m, 4 H), 0.94 (s, 9 H), 0.92 (s, 9 H); ^{13}C NMR δ 69.6 (d, $^{1}J_{CP}$ = 126 Hz), 67.9 (d, $^{1}J_{CP}$ = 125 Hz), 66.7, 66.6, 65.7, 65.6, 65.22, 65.17, 65.12, 57.4 (major), 56.3 (minor), 54.8 [d, $^{2}J_{CP}$ = 2.7 Hz, (major)], 54.5 [d, $^{2}J_{CP}$ = 2.9 Hz, (minor)], 41.0 (minor), 38.7 (major), 32.78, 32.76, 32.25, 32.22, 32.00, 31.96, 31.4, 31.3, 31.2, 31.1, 30.8, 30.72, 30.68, 30.6, 29.0 (minor), 28.9 (major), 28.5 (minor), 28.4 (major), 25.3, 25.2, 24.8, 24.7, 24.6, 24.5, 24.0 (major), 23.8 (minor), 21.3 (minor), 21.2 (major); ^{31}P NMR δ 42.6 (major), 42.3, (minor); MS (EI/DIP) m/z (rel intensity) 329 (61), 243 (100), 81 (67), 44 (62), 43 (100), 41 (87). Anal. Calcd for $C_{21}H_{43}N_2O_2P$: C, 65.25; H, 11.21; N, 7.25. Found: C, 65.35; H, 11.26; N, 7.28.

2-(1′-Hydroxyheptyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (3v). From (*S,S*)-diamide **2b**, reaction temperature −70 °C, crude ratio 4.0:1, column chromatography (SiO_2 eluting with $CHCl_3$ for unreacted aldehyde and then with ethyl acetate), yield 80%, 100% de. Characterized major isomer only: mp 127.0–129.5 °C; IR (KBr) 3425 (brd), 3250 (brd), 2950, 2860 cm^{-1}; ^{1}H NMR δ 4.10 (m, 1 H), 3.68 (m, 1 H), 3.53 (dd, 1 H, J = 14.4, 10.3 Hz), 3.35 (dd, 1 H, J = 15.2 Hz), 2.75 (m, 2 H), 2.43 (dd, 1 H, J = 15.1 Hz), 2.31 (dd, 1 H, J = 14.9, 9.8 Hz), 2.05 (m, 1 H), 1.96 (m, 1 H), 1.80 (m, 3 H), 1.70–1.50 (m, 2 H), 1.30 (br s, 8 H), 1.25 (m, 4 H), 0.93 (s, 9 H), 0.91 (s, 9 H), 0.89 (m, 2 H); ^{13}C NMR δ 71.5 (d, $^{1}J_{CP}$ = 126.1 Hz), 66.5 (d, $^{2}J_{CP}$ = 5.0 Hz), 65.2 (d, $^{2}J_{CP}$ = 7.8 Hz), 57.3, 54.8 (d, $^{2}J_{CP}$ = 2.7 Hz), 32.2 (d, $^{3}J_{CP}$ = 2.2 Hz), 31.9, 31.8, 31.4 (d, $^{3}J_{CP}$ = 9.5 Hz), 31.2 (d, $^{3}J_{CP}$ = 7.6 Hz), 30.1, 29.1, 28.9, 28.4, 26.9, 26.7, 24.6, 22.7, 14.1; ^{31}P NMR δ 42.4 (major), 41.8 (minor); MS (EI/DIP) m/z (rel intensity) 358 (24), 357 (100), 299 (17), 243 (50), 81 (17), 43 (19). Anal. Calcd for $C_{23}H_{47}N_2O_2P$: C, 66.63; H, 11.43; N, 6.76. Found: C, 66.45; H, 11.40; N, 6.67.

(±)-(1-Hydroxy-3-methylbutyl)phosphonic Acid ((±)-4a). To a solution of the hydroxy phosphonamide **3u** (1:1.3 mixture of diastereoisomers) (0.31 g, 0.78 mmol) in dioxane (2 mL) was added aqueous 4 N HCl (1 mL). After 2 h the suspension had completely dissolved. The solution was stirred at room temperature, and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete (approximately 12 h). The solvent was concentrated *in vacuo*, and the residue was passed through an ion exchange column (Amberlite IR-120+) eluting with water. The first 50 mL fraction was evaporated to yield the racemic hydroxy phosphonic acid **4a** (lit.[30]): ^{1}H NMR (D_2O) δ 3.82 (m, 1H), 1.73 (m, 1H), 1.55 (m, 1H), 1.40 (m, 1H), 0.89 (d, 3H, J = 6.6 Hz), 0.85 (d, 3H, J = 6.6 Hz); ^{13}C NMR δ 68.45 (d, CH, $^{1}J_{CP}$ = 159.7 Hz), 42.2 (CH), 26.6 (d, CH_2 $^{2}J_{CP}$ = 14 Hz), 25.6(CH_3), 23.1 (CH_3); ^{31}P NMR (D_2O) δ 25.5 (lit.[30] δ 24.88). The phosphonic acid **4a** was dissolved in ethanol, and cyclohexylamine was added. The solution was cooled to −10 °C for 12 h, and the precipitated salt was collected by filtration (0.276 g, 96% as bis cyclohexylammonium salt). Recrystallization from gave the monocyclohexylammonium salt: mp 230–235 °C dec (MeOH, Et_2O); IR (KBr) 3400 (brd), 2932, 1620, 1447, 1024 cm^{-1}; ^{1}H NMR (D_2O) δ 3.69 (m, 1H), 3.15, (m, 1H), 1.98 (m, 3H), 1.81 (m, 4H), 1.76 (m, 2H), 1.68–1.57 (m, 2H), 1.27–1.18 (m, 2H), 0.95 (d, 3H, J = 6.6 Hz), 0.90 (d, 3H, J = 6.6 Hz); ^{31}P NMR (D_2O) δ 19. Anal. Calcd for $C_5H_{13}O_4P$·($C_6H_{13}N$): C, 49.43; H, 9.80; N, 5.24. Found: C, 48.96; H, 9.85; N, 5.19.

(±)-(1-Hydroxy-3-methylbutyl)phosphonic Acid, Dimethyl Ester ((±)-5a). To a solution of the phosphonic acid (0.138 g, prepared as above) in ethanol (3.5 mL) was added an etheral solution of diazomethane dropwise until a yellow color persisted. The excess diazomethane was quenched with

a few drops of acetic acid, and the solvent was evaporated *in vacuo*. Column chromatography (SiO_2, $CHCl_3$:MeOH, 9:1) yielded the racemic dimethylphosphonate **5a** (0.098g, 68%); mp = 52−54 °C (EtOAc, hexanes); IR (NaCl) 3314, 2956 cm^{-1}; ^1H NMR δ 4.0 (m, 1H), 1.95 (m, 1H), 1.73 (m, 1H), 1.47 (m, 1H), 0.97 (d, 3H, J = 6.6 Hz), 0.92 (d, 3H, J = 6.6 Hz); ^{13}C NMR δ 65.6 (d, CH, $^1J_{CP}$ = 158.5 Hz), 53.25 (d, OCH_3, $^2J_{CP}$ = 5.9 Hz), 53.13 (d, OCH_3, $^2J_{CP}$ = 3.6 Hz), 39.9 (CH), 24.0 (d, CH_2, $^2J_{CP}$ = 13.9 Hz), 23.4 (CH_3), 21.0 (CH_3); ^{31}P NMR δ 28.3. Anal. Calcd for $C_7H_{17}O_4P$; C, 42.86; H, 8.73. Found: C, 42.72, H, 8.79.

(*S*)-(−)-(Phenylhydroxymethyl)phosphonic Acid ((*S*)-4b). To a solution of the phosphonamide **3t** (14:1 mixture of isomers) (0.38 g, 0.93 mmol) in dioxane (2mL) was added aqueous 4 N HCl (1 mL). The solution was stirred at room temperature and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete. The solvent was evaporated *in vacuo*, and the residue was dissolved in water and passed through an ion exchange column (Amberlite IR-120 (+)) eluting with water. The first 50 mL fraction was evaporated to give the phosphonic acid **4b**: ^{31}P NMR (D_2O) δ 20.5, (lit.[30,31] racemic acid). The phosphonic acid was dissolved in ethanol, and cyclohexylamine (0.1 mL) was added. The precipitated salt was collected by filtration (0.189 g, 60%, n = 1.5 salt): mp = 226−228 °C dec (MeOH, Et_2O); $[\alpha]_D$ −13.8 (*c* 0.77, 50% aqueous MeOH); ^1H NMR (D_2O) δ 7.6−7.3 (m, 5H), 4.8 (HOD and C1′-H), 3.15 (m, 1H), 2.0−1.6 (m, 5H), 1.4−1.1 (m, 5H); ^{13}C NMR (D_2O) δ 144.1 (d, $^2J_{CP}$ = 1.9 Hz), 130.7, 129.9, 129.5, 76.82 (d, $^1J_{CP}$ = 140.1 Hz), 53.2, 33.3, 27.3, 26.8; ^{31}P NMR (D_2O) δ 15.9. Anal. Calcd for $C_7H_9O_4P{\cdot}(C_6H_{13}N)_{1.5}$: C, 57.05; H, 8.53; N, 6.24. Found: C, 57.09; H, 8.77; N, 6.59.

(*S*)-(−)-(Phenylhydroxymethyl)phosphonic Acid, Dimethyl Ester ((*S*)-5b). To a solution of the phosphonic acid salt (0.0959 g, 0.355 mmol) in water (5 mL) was added a suspension of acid resin (Amberlite IR120+) in water (1 mL). The suspension was stirred and then filtered. The solvent was evaporated *in vacuo*, and the residue was dissolved ethanol. Ethereal diazomethane was added dropwise until a yellow color persisted. The excess diazomethane was quenched with a few drops of acetic acid. The solvent was evaporated, and the residue was chromatographed (SiO_2, $CHCl_3$:acetone, 10:1) to give the phosphonate **5b** (0.45g, 60%): mp = 96.5−98.5 °C (EtOAc, hexanes) (racemic standard[32,33] 102 °C); $[\alpha]_D$ −38.5 (*c* 0.8, $CHCl_3$) (lit.[8e] *S* enantiomer, −46, *c* 1.0, acetone); 86% ee by HPLC analysis; all solution spectral data were identical with a racemic standard.

(*S*)-(−)-[(1-Hydroxy-3-phenyl-2*E*-propenyl)]phosphonic Acid ((*S*)-4c). To a solution of the hydroxy phosphonamide **3b** (major isomer) (0.31 g, 0.71 mmol) in dioxane (2 mL) was added aqueous 4 N HCl (1 mL). After 1 h the suspension had completely dissolved. The solution was stirred at room temperature, and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete. The solvent was evaporated *in vacuo*, and the residue was dissolved in water and passed through an ion exchange column (Amberlite IR-120 +) eluting with water. The first 50 mL fraction was evaporated to yield the hydroxy phosphonic acid **4c** (lit.[31] racemic acid) ^{31}P NMR (D_2O) δ 20.7. The phosphonic acid was dissolved in ethanol, and cyclohexylamine (0.4 mL) was added. The precipitated salt was collected by filtration. Recrystallization gave the mono cyclohexylammonium salt (0.089g, 34%): mp = 230−231 °C dec (MeOH, Et_2O); $[\alpha]_D$ −3.0 (*c* 0.68, 50% aqueous MeOH); ^1H NMR (D_2O) δ 7.6−7.3 (m, 5H), 6.64 (dd, 1H, J = 16, 3 Hz), 6.57 (ddd, 1H J = 16, 6, 4 Hz), 4.33 (dd, 1H, J = 14, 6 Hz), 3.1 (m, 1H), 1.95, (m, 2H), 1.8 (m, 2H), 1.65 (m, 1H) 1.3 (m, 5H); ^{13}C NMR (D_2O) δ 134.0, 132.2, 131.5, 131.4, 130.1, 129.0, 75.3 (d, CH, $^1J_{CP}$ = 142.3 Hz), 53.1, 33.2, 27.1, 26.6; ^{31}P NMR (D_2O) δ 15.0. Anal. Calcd for $C_9H_{11}O_4P{\cdot}(C_6H_{13}N)$: C, 57.50; H, 7.72; N, 4.47. Found: C, 57.24; H, 7.82; N, 4.47.

(*S*)-(−)-1-Hydroxy-3-phenyl-2(*E*)-propenyl)phosphonic Acid, Dimethyl Ester ((*S*)-5c). To a solution of the hydroxy phosphonamide **3b** (major isomer) (0.45 g, 1.03 mmol) in dioxane (3 mL) was added aqueous 4 N HCl (1.1 mL). After 1 h the suspension had completely dissolved. The solution was stirred at room temperature, and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete. The solution pH was adjusted to 9 with aqueous 4 N KOH and was then extracted with twice with CH_2Cl_2 to recover the diamine. The water was evaporated in vacuo to give the potassium salt. The salt was dissolved in ethanol, and the solution pH was adjusted to 4 with 1.4 N methanolic HCl. The insoluble materials were removed by filtration, and the resulting solution was cooled in an ice bath. Ethereal diazomethane was added until a yellow color persisted and then excess diazomethane was quenched with a few drops acetic acid. The solvents were evaporated *in vacuo*, and the residue was chromatographed (SiO_2, $CHCl_3$:acetone, 9:1, then $CHCl_3$:MeOH, 9:1) to give the dimethyl phosphonate **5c** (0.17 g, 69%): mp = 98.9−99.6 °C (EtOAc, hexanes); (racemic standard[32,33] 101 °C); $[\alpha]_D$ −23.6 (*c* 2.74, $CHCl_3$); >99% ee by HPLC analysis; all solution spectral data were identical with a racemic standard.

2-(1′-Acetoxy-3′-methyl-butyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide (6a and 6b). In separate experiments, solutions of the hydroxy phosphonamide **3u** (approximately 1.3:1 mixture of isomers) in CH_2Cl_2 (0.651g, 1.69 mmol in 10 mL and 0.483 g in 7 mL) were treated with DMAP (0.1 equiv), Et_3N (2 equiv), and Ac_2O (1.5 equiv), and the reactions were monitored by TLC until complete. The solutions were washed with water, 2 M HCl, saturated aqueous $NaHCO_3$, and water, dried, and evaporated *in vacuo*. ^{31}P NMR showed clean conversion to the acetate esters. The combined crude products were chromatographed (SiO_2, $CHCl_3$:acetone, 96:4) to give **6a** (0.229 g), **6b** (0.296 g), and some mixed fractions. The mixed fractions were chromatographed again (SiO_2, $CHCl_3$:acetone, 97:3 then 96:4) to give total yields of **6a** (from minor hydroxy phosphonamide diastereomer) (0.61g) and **6b** (from major hydroxy phosphonamide diastereomer) (0.52 g) (89% combined yield) and some mixed fractions. Acetoxy phosphonamide **6a**: mp 110−111.5 °C; $[\alpha]_D$ −92.4 (c 1.37, $CHCl_3$); IR (KBr) 2950, 1742 cm^{-1}; ^1H NMR δ 5.75 (ddd, 1H, J = 9.9 3.9, 3.9 Hz), 2.24 (dd, 1H, J = 15 and 16 Hz), 3.11 (dd, 1H, J = 15, 11.5 Hz), 2.82 (m, 1H), 2.68 (m, 1H), 2.52 (dd, 1H, J = 16 Hz), 2.39 (dd, 1H, J = 14.4, 10.8 Hz), 2.10 (s, 3H), 2.06−1.75 (m, 6H), 1.66−1.34 (m, 1H), 1.34−1.16 (m, 4H), 0.96 (s, 9H), 0.95 (s, 9H), 0.93 (d, 3H, J = 4.4 Hz), 0.91 (d, 3H, J = 4.4 Hz); ^{13}C NMR δ 169.4, 69.6 (d, $^1J_{CP}$ = 131.8 Hz), 66.1 (d, $^2J_{CP}$ = 7.8 Hz), 65.3 (d, $^2J_{CP}$ = 6.6 Hz), 56.6 (d, $^2J_{CP}$ = 1.7 Hz), 54.7 (d, $^2J_{CP}$ = 2.9 Hz), 41.0, 32.6, 31.9, 31.1, 31.0, 30.8, 28.7, 28.4, 25.5 (d, $^2J_{CP}$ = 11.6 Hz), 24.9, 24.4, 23.4, 21.1, 20.9; ^{31}P NMR δ 38.7. Anal. Calcd for $C_{23}H_{45}N_2O_3P$: C, 64.46; H, 10.58; N, 6.54. Found: C, 64.31; H, 10.61; N, 6.47. Acetoxy phosphonamide **6b**: mp 112.5−113 °C; $[\alpha]_D$ −15.1 (*c* 1.03, $CHCl_3$); ^1H NMR δ 5.67 (m, 1H), 3.27 (dd, 1H, J = 15 Hz), 3.14 (dd, 1H, J = 14.7, 11.4 Hz), 2.89 (m, 1H), 2.71 (m, 1H), 2.47 (dd, 1H, J = 15 Hz), 2.44 (dd, 1H, J = 15, 9.9 Hz), 2.10 (s, 3H), 2.0−1.5 (m, 6H), 1.3−1.0 (m, 4H), 0.97 (s, 9H), 0.94 (t-Bu and Me, 12H), 0.89 (d, 3H, J = 4.4 Hz); ^{13}C NMR δ 175.4, 69.8 (d, $^1J_{CP}$ = 131.2 Hz), 65.4 (d, $^2J_{CP}$ = 6.5 Hz), 65.3 (d, $^2J_{CP}$ = 5.4 Hz), 56.3 (d, $^2J_{CP}$ = 1.5 Hz), 54.5 (d, $^2J_{CP}$ = 3.1 Hz), 38.8, 32.6, 31.9, 31.0, 30.9, 30.7, 30.6, 28.9, 28.4 (d, $^2J_{CP}$ = 12.3 Hz), 24.7, 24.5, 23.7, 21.2, 21.1; ^{31}P NMR δ 37.1. Anal. Calcd for $C_{23}H_{45}N_2O_3P$: C, 64.46; H, 10.58; N, 6.54. Found: C, 64.49; H, 10.57; N, 6.47.

(*R*)-(−)-(1-Hydroxy-3-methylbutyl)phosphonic Acid, Dimethyl Ester ((*R*)-5a). To a solution of the minor acetoxy phosphonamide **6a** (0.39 g, 0.93 mmol) in dioxane (3 mL) was added aqueous 4 N HCl (1.5 mL). The solution was stirred at room temperature, and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete. The solvent was evaporated in vacuo, and the residue was dissolved in water and passed through an ion exchange column (Amberlite IR-120 (+)), eluting with water. The first 50 mL fraction was

(30) Glowacki, Z.; Hoffman, M.; Rachon, J. *Phosphorus, Sulfur Silicon* **1993**, *82*, 39 and references cited therein.

(31) Sekine, M.; Yamamoto, I. Hashizume, A.; Hata, T. *Chem. Lett.* **1977**, 485.

(32) Racemic standards were prepared by addition dimethyl phosphite to the aldehydes (10 mol % Et_3N, neat liquids, or CH_2Cl_2 solution). See: Baraldi, P. G.; Guarneri, M.; Moroder, F.; Pollini, G. P.; Simoni, D. *Synthesis* **1982**, 653.

(33) Texier-Boullet, F.; Foucaud, A. *Synthesis* **1982**, 165.

evaporated. ^{31}P NMR indicated the presence of both the hydroxy phosphonic acid and the acetoxy phosphonic acid. The phosphonic acids were dissolved in ethanol, and 1 N KOH was added until the solution reached pH 14. The resulting solution was placed in the freezer for 48 h. The solution pH was adjusted to 4, and any insoluble material was removed by filtration. The solution was cooled in an ice bath, and ethereal diazomethane was added until a yellow color persisted. Excess diazomethane was quenched with acetic acid, and the solvent was evaporated in vacuo. The residue was chromatographed (SiO_2, EtOAc) to give the phosphonate (0.11g, 58%): $[\alpha]_D$ −25.0 (*c* 0.92, $CHCl_3$); >99% ee HPLC analysis; all solution spectral data were identical with a racemic standard.

(*R*)-(+)-(1-Hydroxy-3-phenyl-2*E*-propenyl)phosphonic Acid, Dimethyl Ester ((*R*)-5c). To a solution of the hydroxy phosphonamide **3a** (major isomer) (0.31 g, 0.71 mmol) in dioxane (2 mL) was added aqueous 4 N HCl (1 mL). After 1 h the suspension had completely dissolved. The solution was stirred at room temperature, and the reaction progress was monitored by ^{31}P NMR spectroscopy until complete. The solution pH was adjusted to 9 with aqueous KOH and was then extracted with twice with CH_2Cl_2 to recover the diamine. The water was evaporated *in vacuo* to give the potassium salt which was dissolved in ethanol. The solution pH was adjusted to 4 with 1.4 N methanolic HCl. The insoluble materials were removed by filtration and the resulting solution was cooled in an ice bath. Etheral diazomethane was added until a yellow color persisted, and then the excess diazomethane was quenched with a few drops of acetic acid. The solvents were evaporated in vacuo. The residue was chromatographed (SiO_2, $CHCl_3$:acetone, 9:1, then $CHCl_3$:MeOH, 9:1) to give the dimethyl phosphonate **5c** (0.17 g, 69%); (racemic standard[32,33]): $[\alpha]_D$ +19.8 (c 0.8, $CHCl_3$); >94% ee by HPLC analysis; all solution spectral data were identical with a racemic standard.

Methanolysis of 2-(1-Hydroxy-3-phenyl-(E)-prop-2-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-dibenzyl-1*H*-1,3,2-benzodiazaphosphole 2-Oxide. The hydroxy phosphonamide **3a** (0.172 g, 0.36 mmol) was dissolved in 1.5 N methanolic HCl (5 mL), and the solution was stirred at room temperature for 6 h. The solvent was evaporated, and the residue was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. The organic layer was separated, dried, and evaporated, and the crude product was chromatographed (SiO_2, $CHCl_3$:acetone, 9:1) to give predominantly one diastereomer **7a** (0.98g, 54%): mp 149−149.5 °C; ^1H NMR ($CDCl_3$) δ 7.5−7.0 (m, 15H), 6.8 (brd dd, 1H), 6.65 (brd dd, 1H), 4.65 (m, 1H), 4.48 (m, 2H), 4.17 (m, 2H), 3.72 (d, 3H, $^3J_{HP}$ = 9 Hz), 3.46, (m, 1H), 3.10 (m, 1H), 2.45 (m, 1H), 2.05 (m, 1H), 1.8−1.5 (m, 4H), 1.4−0.9 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 138.5, 136.8, 129.6 (d, $^3J_{CP}$ = 12 Hz), 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.4, 127.3, 127.2, 126.4, 125.1, 71.8 (d, $^1J_{CP}$ = 146 Hz), 61.8, 57.5, 52.3, 50.4, 44.8, 31.7, 31.1, 25.8, 24.8; ^{31}P NMR ($CDCl_3$) δ 27.0.

Methanolysis of 2-(1-Hydroxy-3-phenyl-(*E*)-prop-2-enyl)-2,3,3a,4,5,6,7,7a-octahydro-1,3-bis(2,2-dimethylpropyl)-1*H*-1,3,2-benzodiazaphosphole 2-Oxide. The hydroxy phosphonamide **3b** (0.22g, 0.51 mmol) was treated as above with 0.92 M methanolic HCl (2.5 mL). Chromatography (SiO_2, $CHCl_3$:MeOH, 95:5) gave a single diastereomer **7b** as an oil. The room temperature NMR spectra showed broadened lines. Data is given for NMR spectra recorded at 50 °C: ^1H NMR ($CDCl_3$) δ 7.41−7.17 (m, 5H), 6.82 (dd, 1H, *J* = 4.8, 16 Hz), 6.48 (ddd, 1H, *J* =16, 4.4, 4.4 Hz), 4.84 (m, 1H), 3.71 (d, 3H, $^3J_{HP}$ = 9.9Hz), 3.05−2.82 (m, 4H), 2.54−2.07 (m, 4H), 1.72−1.66 (m, 3H), 1.25−1.15 (m, 3H), 1.00 (s, 9H), 0.97 (s, 9H); ^{13}C NMR ($CDCl_3$) 137.1, 130.5 (d, $^3J_{CP}$ = 11.5 Hz), 128.3, 127.1, 126.3, 126.2, 126.0 (d, $^2J_{CP}$ = 4.5 Hz), 71.0, 69.0, 59.2, 53.4, 34.0, 32.8, 31.1, 29.1, 27.9, 26.4, 25.1; ^{13}P NMR ($CDCl_3$) 32.1; MS (EI/DIP) *m*/*z* (rel intensity) 464 (M^+) (18), 389 (96), 115 (86), 57 (100), 42 (98).

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