Asymmetric Synthesis of α-Amino Phosphonic Acids by Diastereoselective Addition of Trimethyl Phosphite onto Chiral Oxazolidines[1]

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A simple and general asymmetric synthesis of α-amino phosphonic acids is described. The method involves the highly selective addition of trialkyl phosphite onto various chiral oxazolidines. Oxazaphosphorinanes thus obtained with an excellent diastereoselectivity furnish the corresponding (*S*)-α-substituted amino phosphonic acids in good overall yields and high ee (77→97%) after simple deprotection.

Introduction

The α-amino phosphonic acids **1** (Scheme 1) are attractive substitutes for amino carboxylic acids in biological systems such as peptides, giving rise to interesting new properties. These amino phosphonic acids have found applications as potent active compounds with a large range of biological activities: antibiotics, enzyme inhibitors, herbicides,[2] .... Such an impressive array of applications has stimulated considerable effort toward their synthesis and, more recently, their preparation in nonracemic form.[3] Among the asymmetric syntheses recently reported, very few are both efficient and general, so novel procedures are still needed to enlarge the organic chemist's synthetic potential.

We recently reported a general method[4] involving a diastereoselective alkylation of the anion of a chiral *N*-(phosphonomethyl)oxazolidine **3** derived from (*R*)-(−)-phenylglycinol (**2**) (Scheme 1, route a). In spite of its efficiency, this method furnished α-amino phosphonic acids in only moderate ee. In order to improve this result, we first envisioned the preparation of **6**, a rigid analogue of **3**, and the study of its alkylation (Scheme 1, route c). On the other hand, we decided to develop a new methodology using as the key step the nucleophilic addition of trialkyl phosphite onto chiral alkylated oxazolidines **4** as illustrated in Scheme 1 (route b).

Results

We first investigated the preparation of oxazaphosphorinane **6**[5] and its alkylation (Scheme 2). A number of routes toward **6** were studied. One of these consisted of the opening of the oxazolidine ring of the previously described *N*-(phosphonomethyl)oxazolidine **3**[4] by an organometallic reagent, followed by an intramolecular transesterification of the phosphonate moiety. Indeed, treatment of **3** (prepared from (*R*)-(−)-phenylglycinol and dimethyl phosphite[4] or trimethyl phosphite as reported in this paper) with phenylmagnesium chloride and in the presence of $TiCl_4$ gave directly the expected oxazaphosphorinane **6** but in a low yield (Scheme 2).

It was eventually found that such oxazaphosphorinanes could be obtained more efficiently by including as a key step the nucleophilic attack of the oxazolidine ring by a trialkyl phosphite. As NH oxazolidines are known to be unstable and frequently found in equilibrium with the imine form,[6] we focused on the preparation of N-alkylated oxazolidines, and among them the *N*-benzyloxazolidines were chosen in order to facilitate N-deprotection at the end of the synthesis.

The overall synthesis of **6** starting from (*R*)-(−)-phenylglycinol (**2**) is described in Scheme 3. The *N*-benzylphenylglycinol (**7**) was prepared from **2** by benzoylation followed by $LiAlH_4$ reduction and was then condensed with formaldehyde to afford the oxazolidine **8** in 86% overall yield.

Treatment of **8** with trimethyl phosphite in the presence of 1 equiv of $SnCl_4$ gave the expected oxazaphos-

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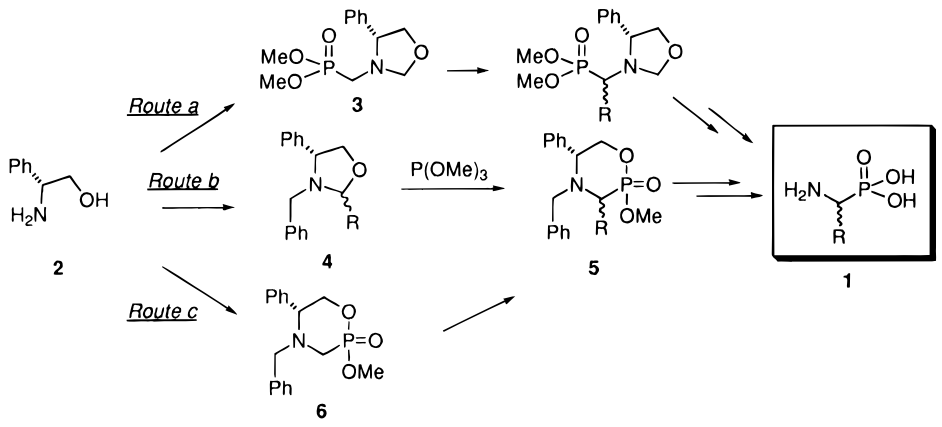
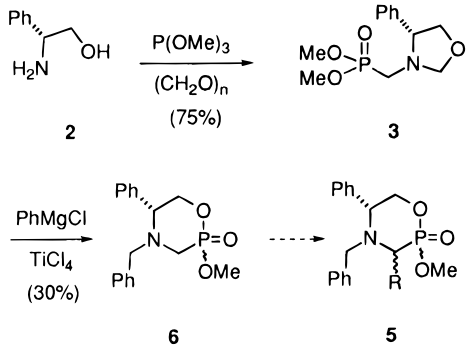
S0022-3263(96)00020-5 CCC: $12.00

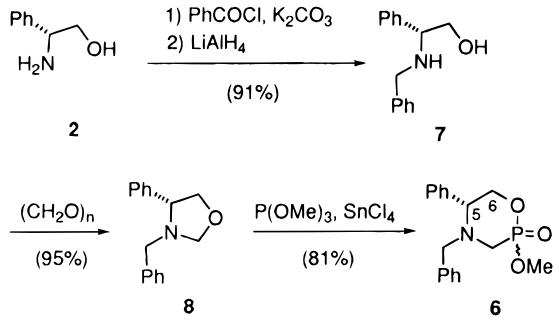
Scheme 1



Scheme 2



Scheme 3



phorinane **6** in 81% yield. This transformation involved a Lewis acid-mediated opening of the oxazolidine ring, followed by an Arbusov-type reaction and an intramolecular transesterification. Compound **6** consisted of a mixture of two diastereomers in a 4:1 ratio and was fully analyzed. Assignment of structure **6a** for the major component and **6b** for the minor one was made on the basis of the ^{1}H NMR and IR spectra data reported in Table 1. Compared to its epimer, the major compound **6a**, with an equatorial P=O bond, has smaller $^3J_{P/H\text{-}6ax}$ and larger $^3J_{P/H\text{-}6eq}$ coupling constants, more shielded protons at C-6 in the ^{1}H NMR spectrum, and a higher P=O bond IR frequency.[7,8] On the other hand, in the ^{13}C NMR spectra the C-5 chemical shift was only slightly affected by epimerization at the phosphorus center.

We were not able to find conditions which could deprotonate oxazaphophorinane **6**, and we thus tried to generalize the above synthetic route for the synthesis of alkylated oxazaphophorinanes **5** using alkylated oxazolidines **4** and studied the stereochemistry of this reaction in order to get a new asymmetric access to α-amino phosphonic acids. The overall synthesis is outline in Scheme 4.

Oxazolidines **4a**−**e** were easily prepared in high yields and diastereomeric excesses[9] (see Table 2) from *N*-benzylphenylglycinol (**7**) and then converted into oxazaphosphorinanes **5a**−**e** by treatment with trimethyl phosphite in the presence of $SnCl_4$ for 12−16 h.

Oxazaphosphorinanes were obtained in good to excellent yield and consisted of a mixture of diastereomers. Two new chiral centers at C-3 and at phosphorus were created in the reaction, and the ratios of diastereomers as determined by ^{1}H, ^{13}C, and ^{31}P NMR spectra are reported in Table 2. Four isomers were found to be formed for R = Me and $(CH_2)_3CO_2Me$ (**5a** and **5e**) and only two for R = Et, Pr, and Bn (**5b, 5c, 5d**).

The different data found in the NMR and IR spectra of these mixtures suggested, by analogy with the above-described study of **6**, that the two major (or the two exclusive) compounds were epimers at the phosphorus center. In other words, formation of the phosphorus−carbon bond is highly to totally diastereoselective. This assertion had to be carefully checked, so we transformed oxazaphosphorinane esters **5** into acids **9,** in which the phosphorus atom was no longer chiral, by treatment with trimethylsilyl bromide (Scheme 5).

HPLC and ^{31}P NMR analysis of oxazaphosphorinanes **9** confirmed our hypothesis showing the presence of only one isomer for **9b**−**d** and two isomers in the case of **9a** and **9e**. Furthermore, the diastereomeric ratios for **9a** and **9e** were in full agreement with those of **5a** and **5e** (see Table 2). Thus, the addition of trialkyl phosphite onto chiral oxazolidines is a highly to totally diastereoselective process leading to the formation of a major *S* configuration at C-3 (*vide infra*) with a de varying from 72% up to 95%.

The α-amino phosphonic acids **1a**−**e** were finally obtained in two steps from oxazaphosphorinanes **5a**−**e** (Scheme 4). The hydrogenolysis of **5a**−**e** at 60 psi and

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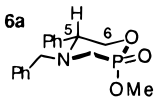
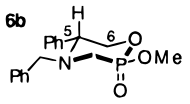
Table 1. Spectroscopic Data for the Mixture of Oxazaphosphorinanes 6

Isomers			**6a** 	**6b** 
IR *(cm^{-1})*		P=O	1258	1239
^{1}H NMR	*δ*	*H-6 ax*	4.25	4.53
		H-6 eq	4.09	4.30
	J (Hz)	*P/H-6 ax*	2.8	7.9
		P/H-6 eq	22.0	16.6
^{13}C NMR	*δ (ppm)*	*C-5*	66.6	65.0

Scheme 4

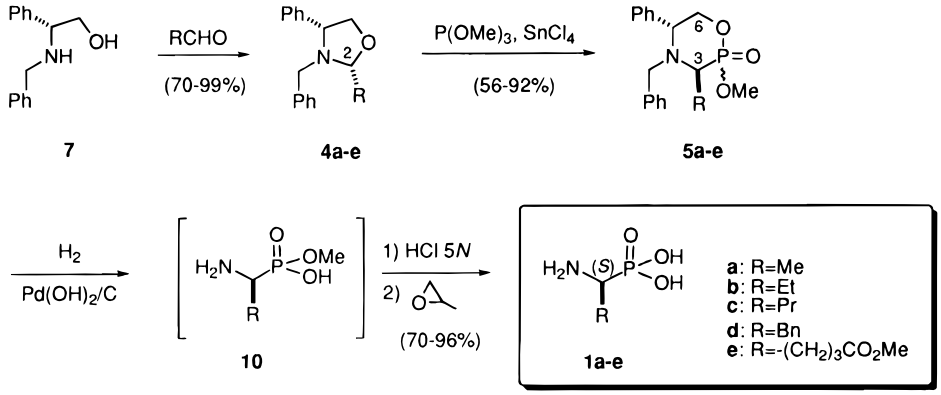
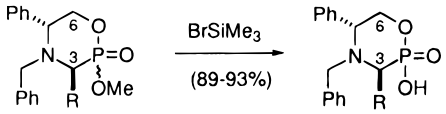


Table 2. Preparation and Diastereoselectivity of Oxazolidines 4 and Oxazaphosphorinanes 5 and 9

	oxazolidines **4**		oxazaphosphorinanes **5**		comp **9**		
R	yield (%)	dr[a] (%)	yield (%)	dr[a] (%)	3*S*/3*R*	yield (%)	3*S*/3*R*[c]
a: Me	92	>98:2	64	64:21:8:7	85:15	91	86:14
b: Et	92	92:8	92	80:20:0:0	100:0	93	100:0
c: Pr	99	>98:2	72	79:21:0:0	100:0	92	100:0
d: Bn	86	>98:2	56	60:40:0:0	100:0	89	100:0
e: $(CH_2)_3CO_2Me$	70	90:10	77	60:33:6:1	93:7	91	90:10

[a] Ratios determined by ^{1}H and ^{13}C NMR. [b] Ratios determined by ^{1}H, ^{13}C, and ^{31}P NMR. [c] Ratios determined by HPLC and ^{31}P NMR.

Scheme 5



in the presence of Pearlman's catalyst gave amino phosphonates **10a**−**e** in high yield. This reaction allowed the complete N-debenzylation and monohydrolysis of the phosphonate. The second ester function was finally cleaved in acidic medium (5 N HCl) and led to the free amino acids **1a**−**e** in good overall yield after treatment with propylene oxide.

All the α-amino phosphonic acids we have prepared had been already described in the literature,[10] which allowed us to determine their absolute configuration as *S*. Enantiomeric excesses of these acids would be the same as the diastereomeric excesses of oxazaphosphorinanes **5** if we suppose complete absence of racemization in the last two steps. Our attempts to determine the enantiomeric excesses of **1** without any further chemical modification[11] —which could also introduce possible racemization—were not successful. Comparison of optical rotations with those of the literature gave ee values in very good agreement with the de values found for **5** (and **9**) in the case of **1a**, **1b**, and **1d** (Table 3). Amazingly, the values reported in the literature for **1c** and **1e** were very different from those we determined. The coherence of the optical rotations we have found in this series, together with the good chemical purity of these amino acids (microanalyses, see the Experimental Section) and high diastereomeric purity of oxazaphosphorinanes **5**, gave credence to the authenticity of our findings.

Discussion

The key step of this α-amino phosphonic acid asymmetric synthesis was the insertion of a phosphorus atom into the C−O linkage of the oxazolidine. This process gave rise to a new chiral carbon center in a highly diastereoselective fashion. The absolute configuration of the target molecules indicates that the phosphorus insertion occurred with invertion of configuration at C-2 suggesting a S_N2 mechanism. Although this mechanism could not be ruled out, it appears to be rather improbable

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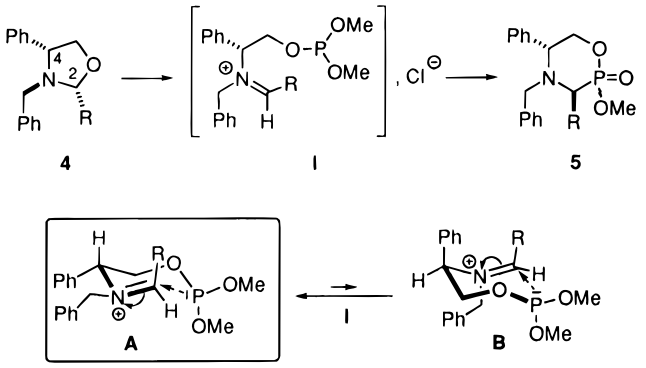
(11) Huber, R.; Vasella, A. *Helv. Chim. Acta* **1987**, *70*, 1461−1476.

Table 3. Formation and Characterization of α-Amino Phosphonic Acids 1a−e

R	yield (%)	$[\alpha]_{578}$ (c = 1, 1 N NaOH)	lit.[10] $[\alpha]_{578}$ (c = 1, 1 N NaOH)	config	ee **1** (%)	de **5** (%)
a: Me	96	+13.1	+17.0	*S*	77	70
b: Et	87	+19.3	+21.0	*S*	92	>95
c: Pr	82	+17.1	−8.3	*S*		>95
d: Bn	70	+50.3	+52.0	*S*	97	>95
e: $(CH_2)_3CO_2H$	81	+27.1	+13	*S*		86

Scheme 6



since the de's of oxazaphosphorinanes **5** or **9** are in some cases different from those of the starting oxazolidines **4**. This is illustrated in the case of **4b**, which exhibited a 84% de and gave **5b** in 92% chemical yield and with a de > 99% (Table 2).

Furthermore, the use of a Lewis acid in this reaction is compatible with a prior opening of the oxazolidine ring to generate a much more reactive iminium salt.

We tried to rationalize our results using a working model depicted in Scheme 6 and established the following. We propose the formation of (*Z*)-iminium salt **I** resulting from the simultaneous transesterification of trimethyl phosphite[12] and opening of the oxazolidine.

The geometry of the double bond of this intermediate depends upon the configuration of the starting oxazolidine. The major oxazolidine possesses a *N*-benzyl group *trans* relative to both phenyl and alkyl substituents at C-2 and C-4. The formation of the iminium salt occurred through a *trans*-antiperiplanar process to give (*Z*)-**I**. In the minor component, the nitrogen lone-pair exchanged rapidly, and both geometries of the iminium could be *a priori* formed. Diastereofacial selectivity to give the major *S* isomer of **5** could be explained by a less constrained transition state **A** compared to **B** with all substituents in axial position.

Experimental Section

General Methods. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium/benzophenone ketyl immediately prior to use. Diisopropylamine was distilled from and stored over KOH. Final solutions before rotary evaporation were dried over Na_2SO_4, and flash chromatography was carried out using 230−400 mesh silica gel. Melting points are uncorrected. Optical rotations were recorded at 20 °C in a 1 dm cell. Microanalyses were carried out at the Service de Microanalyse at the Institut de Chimie des Substances Naturelles.

(4*R*)-(4-Phenyloxazolidin-3-yl)methylphosphonic Acid Dimethyl Ester (3). In a dry round-bottomed flask equipped with a Dean−Stark apparatus was refluxed a mixture of (*R*)-(−)-phenylglycinol (**2**) (commercially available or prepared according to the literature procedure) (137 mg, 1 mmol), trimethyl phosphite (1.2 mmol), and freshly distilled toluene (10 mL). Paraformaldehyde 95% (3.2 mmol) was added in small portions. After 2 h of refluxing, the solvent was evaporated under vacuum and the crude oil purified by flash chromatography on silica gel (ether/ethyl acetate 1:1) to leave to the desired *N*-(phosphonomethyl)oxazolidine **3** in 75% yield.

White crystalline solid: mp 79 °C (Et_2O); IR (cm^{-1}) 1272 (P=O st), 1033 (POC st); ^{1}H NMR: 7.40−7.25 (m, 5H), 4.94 (d, 1H, J = 3.6 Hz), 4.31 (d, 1H, J = 3.6 Hz), 4.25 (t, 1H, J = 7.5 Hz), 3.86 (t, 1H, J = 7.5 Hz), 3.72 and 3.64 (2 × d, 6H, $^3J_{P-H}$ = 10.7 Hz), 3.69 (t, 1H, J = 7.5 Hz), 3.09 (dd, 1H, J = 15.2, $^2J_{P-H}$ = 17.0 Hz), 2.80 (dd, 1H, J = 15.2, $^2J_{P-H}$ = 7.0 Hz); ^{13}C NMR: 138.4, 128.7, 128.0, 127.6, 87.8, 73.0, 69.1 (d, $^3J_{P-C}$ = 16 Hz), 53.1 and 52.6 (2 × d, $^2J_{P-C}$ = 7 Hz), 46.8 (d, $^1J_{P-C}$ = 164 Hz); MS (EI) m/z 271 (11) 162 (100), 161 (54), 148 (100), 132 (38), 104 (100), 103 (37), 91 (63); $[\alpha]^{25}_D$ = −118.7 (c = 1, $CHCl_3$). Anal. Calcd for $C_{12}H_{18}NO_4P$: C, 53.13; H, 6.69; N, 5.16. Found: C, 52.94; H, 6.43; N, 5.21%.

(*R*)-2-(Benzylamino)-2-phenylethanol (7). (*R*)-(−)-Phenylglycinol (1.37 g, 10 mmol) was dissolved in water (5 mL) in the presence of potassium carbonate (1.93 g, 14 mmol). Dichloromethane (20 mL) was introduced, and the mixture was vigorously stirred at room temperature. Benzoyl chloride was then added dropwise. After 5 h, the white solid was filtered off, washed with water and CH_2Cl_2, and dried under vacuum (0.2 mmHg) at 50 °C and in the presence of P_2O_5 for 1 night. The amide was isolated in quantitative yield (2.41 g) and used without further purification.

To a mixture of dry THF (10 mL) and LAH (0.75 g, 19.7 mmol) heated at 65 °C, was carefully added a solution of benzamide (2.05 g, 8.5 mmol) in dry THF. After complete addition (30−45 min), the mixture was refluxed for 24 h. The reaction was quenched at 0 °C by careful, dropwise addition of 0.8 mL of water, followed by 0.8 mL of aqueous 15% NaOH solution, and finally 1.6 mL of water. The thick mixture was then filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. The crude mixture was purified by crystallization from ether to give 1.75 g (91%) of the pure *N*-benzylamino alcohol.

White needles: mp 88 °C (Et_2O); IR (cm^{-1}) 3445 and 3433 (NH and OH st); ^{1}H NMR 7.45−7.20 (m, 10H), 3.80 (dd, 1H, J = 4.2, 8.7 Hz), 3.70 (d, 1H, J = 13.0 Hz), 3.66 (dd, 1H, J = 4.2, 11.0 Hz), 3.55 (d, 1H, J = 13.0 Hz), 3.53 (dd, 1H, J = 8.7, 11.0 Hz), 2.75 (bs, 2H); ^{13}C NMR 140.5, 140.0, 128.7−127.1, 66.8, 63.9, 51.2; MS (CI-isobutane) m/z 228 (100); $[\alpha]^{25}_D$ = −82.5 (c = 1, $CHCl_3$). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.36; H, 7.59; N, 6.04.

(4*R*)-3-Benzyl-4-phenyloxazolidine (8). In a dry round-bottomed flask equipped with a Dean−Stark apparatus, a solution of amino alcohol **7** (1 mmol) and paraformaldehyde (5 mmol) in toluene (2.5 mL) was refluxed for 16 h. The solvent was removed under vacuum, and the crude oil was purified by flash chromatography on silica gel (ether/heptane 2:8) to afford the oxazolidine **8** in 95% yield.

Oil: ^{1}H NMR 7.45−7.20 (m, 10H), 4.56 (d, 1H, J = 3.4 Hz), 4.24 (t, 1H, J = 7.5 Hz), 4.16 (d, 1H, J = 3.4 Hz), 3.88 (d, 1H, J = 13.4 Hz), 3.85 (t, 1H, J = 7.5 Hz), 3.70 (t, 1H, J = 7.5 Hz), 3.41 (d, 1H, J = 13.4 Hz); ^{13}C NMR 139.7, 138.7, 128.6−127.2, 86.9, 73.5, 67.2, 56.4; MS (EI) m/z 239 (51), 209 (42), 208 (26), 162 (16), 148 (52), 118 (99), 104 (34), 103 (19), 91 (100), 77 (23).

Typical Experimental Procedures for the Condensation of Aldehydes with an *N*-Monoprotected Amino

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Alcohol. Procedure A. Freshly distilled aldehyde (3 mmol) was added dropwise, with stirring and under an argon atmosphere, to a refluxing solution of *N*-benzylamino alcohol (1 mmol) in dry CH_2Cl_2 (3 mL) and in the presence of molecular sieves (4 Å). The mixture was refluxed for 8-16 h. After being cooled to room temperature and filtered, the mixture was concentrated under reduced pressure to afford the desired oxazolidine as a viscous colorless oil which was purified by flash chromatography on silica gel (ether/heptane 9:1).

Procedure B. To a stirred solution of *N*-benzylamino alcohol (1 mmol) in dry THF (3 mL) was added anhydrous magnesium sulfate (≈650 mg) under an argon atmosphere, followed by freshly distilled aldehyde (5 mmol). The mixture was stirred at room temperature for 24 h. The magnesium sulfate was filtered off, and the filtrate was concentrated under reduced pressure to afford the desired oxazolidine as a viscous colorless oil which was then purified by flash chromatography on silica gel (ether/heptane 9:1).

(2*R*,4*R*)-3-Benzyl-2-methyl-4-phenyloxazolidine (4a): yield 92%; oil; dr >98:2. Data for the major product: ^{1}H NMR 7.45−7.20 (m, 10H), 4.40 (q, 1H, J = 7.0 Hz), 4.15 (t, 1H, J = 7.5 Hz), 3.90 (t, 1H, J = 7.5 Hz), 3.82 (d, 1H, J = 14.0 Hz), 3.72 (t, 1H, J = 7.5 Hz), 3.50 (d, 1H, J = 14.0 Hz), 1.14 (d, 3H, J = 7.5 Hz); ^{13}C NMR 140.5, 138.3, 129.1−127.1, 93.5, 73.0, 68.3 (C_4), 54.8, 21.4; MS (EI) *m*/*z* 253 (9), 252 (4), 238 (100), 91 (70).

(2*R*,4*R*)-3-Benzyl-2-ethyl-4-phenyloxazolidine (4b): yield 92%; oil; dr 92:8. Data for the major product: ^{1}H NMR 7.50−7.20 (m, 10H), 4.31 (dd, 1H, J = 3.7, 6.6 Hz), 4.13 (t, 1H, J = 7.5 Hz), 3.90 (t, 1H, J = 7.5 Hz), 3.85 (d, 1H, J = 13.8 Hz), 3.69 (t, 1H, J = 7.5 Hz), 3.52 (d, 1H, J = 13.8 Hz), 1.40 (m, 2H), 0.90 (t, 3H, J = 7.3 Hz); ^{13}C NMR 140.1, 138.3, 129.1-126.9, 97.7, 73.3, 68.2, 55.4, 27.7, 21.4; MS (EI) *m*/*z* 267 (1), 239 (43), 238 (100), 210 (4), 104 (15), 91 (100).

(2*R*,4*R*)-3-Benzyl-4-phenyl-3-propyloxazolidine (4c): yield 99%; oil; dr >98:2. Data for the major product: ^{1}H NMR 7.50−7.20 (m, 10H), 4.35 (dd, 1H, J = 2.8, 5.6 Hz), 4.12 (t, 1H, J = 7.5 Hz), 3.89 (t, 1H, J = 7.5 Hz), 3.85 (d, 1H, J = 13.8 Hz), 3.68 (t, 1H, J = 7.5 Hz), 3.53 (d, 1H, J = 13.8 Hz), 1.62 (m, 2H), 1.40 (m, 2H, $CH_2CH_2CH_3$), 0.92 (t, 3H, J = 7.3 Hz); ^{13}C NMR 139.5, 139.9, 138.0, 129.0−126.7, 96.5, 73.0, 67.9, 55.2, 36.9, 17.4, 13.8; MS (CI-isobutane) *m*/*z* 282 (100).

(2*R*,4*R*)-2,3-Dibenzyl-4-phenyloxazolidine (4d): yield 86%; oil; dr >98:2. Data for the major product: ^{1}H NMR 7.40−7.15 (m, 15H), 4.60 (t, 1H, J = 4.8 Hz), 4.08 (t, 1H, J = 7.7 Hz), 3.93 (t, 1H, J = 7.7 Hz), 3.91 (d, 1H, J = 13.3 Hz), 3.60 (t, 1H, J = 7.7 Hz), 3.59 (d, 1H, J = 13.3 Hz), 2.67 (d, 2H, J = 4.8 Hz); ^{13}C NMR 139.5, 139.2, 137.7, 129.9−126.0, 97.1, 72.6, 67.7, 55.6, 41.8; MS (CI-isobutane) *m*/*z* 330 (100).

4-[3-Benzyl-4-phenyloxazolidin-2-yl]butyric acid methyl ester (4e): yield 70%; oil; dr 90:10. Data for the major product: ^{1}H NMR 7.50−7.30 (m, 10H), 4.36 (dd, 1H, J = 2.8 Hz, 5.8 Hz), 4.13 (t, 1H, J = 7.5 Hz), 3.90 (t, 1H, J = 7.5 Hz), 3.86 (d, 1H, J = 14.0 Hz), 3.68 (t, 1H, J = 7.5 Hz), 3.63 (s, 3H), 3.50 (d, 1H, J = 14.0 Hz), 2.20 (t, 2H, J = 7.5 Hz), 1.75 (m, 2H), 1.40 (m, 2H); ^{13}C NMR 173.5, 139.5, 137.7, 128.8−126.6, 95.9, 72.8, 67.8, 54.9, 50.9, 33.6, 19.3; MS (CI-isobutane) *m*/*z* 340 (100).

(5*R*)-4-Benzyl-2-methoxy-5-phenyl-1,4,2-oxazaphosphinane 2-Oxide (6). Procedure A. To a solution of *N*-(phosphonomethyl)oxazolidine **3** (1.36 g, 5 mmol) in freshly distilled CH_2Cl_2 (20 mL) was added a 1 M solution of $TiCl_4$ (5 ml, 5 mmol) in CH_2Cl_2 dropwise under an argon atmosphere and at room temperature. After 1 h, the reaction mixture was diluted into ether (80 ml), and a 2 M solution of PhMgCl (2.5 mL, 5 mmol) in THF was added. After an additional 2 h, the mixture was poured into a NH_4Cl-saturated solution, and organic compounds were extracted with ether (4 × 25 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated by evaporation under reduced pressure to lead to the desired oxazaphosphorinane **6** after purification by flash chromatography on silica gel (ether/ethyl acetate 1:1). This heterocycle was obtained as a white solid (480 mg, 30% yield) and a mixture of 2 diastereomers in a ratio of 2:1.

Procedure B. See the typical experimental procedure described below (yield 81%).

White crystalline solid: mp 156 °C (Et_2O); dr 80:20; IR (cm^{-1}) 1258 (P═O *eq* st), 1239 (P═O *ax* st), 1035 and 1011 (POC st); ^{1}H NMR data for the (2*R*)-isomer (80%) 7.50−7.20 (m, 10H), 4.25 (ddd, 1H, J = 10.5, 11.5 Hz, $^3J_{P-H}$ = 2.8 Hz), 4.09 (ddd, 1H, J = 3.1, 11.5 Hz, $^3J_{P-H}$ = 22.0 Hz), 3.83 (dd, 1H, J = 13.3 Hz, $^4J_{P-H}$ = 7.5 Hz), 3.77 (d, 3H, $^3J_{P-H}$ = 10.7 Hz), 3.68 (dd, 1H, J = 3.1, 10.5 Hz), 3.19 (dd, 1H, J = 14.8 Hz, $^2J_{P-H}$ = 19.2 Hz), 2.95 (d, 1H, J = 13.3 Hz), 2.50 (dd, 1H, J = 14.8 Hz, $^2J_{P-H}$ = 9.0 Hz); data for the (2*S*)-isomer (20%) 7.50−7.25 (m, 10H), 4.53 (ddd, 1H, J = 7.9, 11.6 Hz, $^3J_{P-H}$ = 7.8 Hz), 4.30 (ddd, 1H, J = 3.1, 11.6 Hz, $^3J_{P-H}$ = 16.6 Hz), 3.80 (d, 3H, $^3J_{P-H}$ = 10.8 Hz), 3.77 (dd, 1H, J = 13.3 Hz, $^4J_{P-H}$ = 7.0 Hz), 3.71 (dd, 1H, J = 3.1, 7.9 Hz), 3.22 (d, 1H, J = 13.3 Hz), 3.13 (dd, 1H, J = 14.0 Hz, $^2J_{P-H}$ = 15.0 Hz), 2.57 (dd, 1H, J = 14.0 Hz, $^2J_{P-H}$ = 11.4 Hz; ^{13}C NMR data for the (2*R*)-isomer (80%) 136.8, 129.1−127.5, 73.0 (d, $^2J_{P-C}$ = 6 Hz), 66.6, 60.6 (d, $^3J_{P-C}$ = 18 Hz), 51.9 (d, $^2J_{P-C}$ = 6 Hz), 46.9 (d, $^1J_{P-C}$ = 143 Hz); data for the (2*S*)-isomer (20%) 136.4, 129.1−127.0, 71.9 (d, $^2J_{P-C}$ = 5 Hz), 65.0, 60.3 (d, $^3J_{P-C}$ = 17 Hz), 52.6 (d, $^2J_{P-C}$ = 6 Hz), 46.4 (d, $^1J_{P-C}$ = 143 Hz); MS (CI-isobutane) *m*/*z* 318 (100).

Typical Experimental Procedure for the Addition of Trimethylphosphorus Compounds to Oxazolidines. Distilled trimethyl phosphite (0.5 mL, 4.5 mmol) was added under an argon atmosphere to a solution of oxazolidine (1 mmol) in dry CH_2Cl_2 (10 mL). A 1 M solution of $SnCl_4$ (1 mL, 1 mmol) in CH_2Cl_2 was then added dropwise with stirring. The mixture was stirred at room temperature and monitored by TLC. After completion of the reaction (12−16 h) , the solvent was evaporated under *vacuum* to leave a viscous oil which was purified by chromatography on silica gel (ether) to afford the desired compound as a colorless oil.

Cyclic phosphorus compounds were obtained as mixtures of two or four diastereomers.

(5*R*)-4-Benzyl-2-methoxy-3-methyl-5-phenyl-1,4,2-oxazaphosphinane 2-oxide (5a): yield 64%; oil; dr 64:21:8:7; ^{1}H NMR data for the (2*R*,3*S*)-isomer (64%) 7.45−7.20 (m, 10H), 4.40−4.05 (m, 3H), 3.80 (m, 5H), 3.35 (m, 1H), 1.40 (dd, 3H, J = 7.2 Hz, $^3J_{P-H}$ = 14.0 Hz); data for the (2*S*,3*S*)-isomer (21%) 7.45−7.20 (m, 10H), 4.70-4.40 (m, 3H), 3.80 (m, 5H), 3.20 (m, 1H), 1.35 (dd, 3H, J = 7.2 Hz, $^3J_{P-H}$ = 14.0 Hz); ^{13}C NMR data for the (2*R*,3*S*)-isomer (64%) 137.1, 136.5, 128.3−126.6, 72.2 (d, $^2J_{P-C}$ = 8 Hz), 58.2 (d, $^3J_{P-C}$ = 4 Hz), 51.4 , 51.0, 45.6 (d, $^1J_{P-C}$ = 142 Hz), 5.0; data for the (2*S*,3*S*)-isomer (21%) 137.8, 136.7, 128.3−126.6, 69.3 (d, $^2J_{P-C}$ = 8 Hz), 57.6 (d, $^3J_{P-C}$ = 4 Hz), 52.2), 51.0, 47.7 (d, $^1J_{P-H}$ = 138 Hz), 8.9. It has to be noted that for (2*S*,3*R*) and (2*R*,3*R*) diastereomers only the carbon C_6 could be detected: data for the (2*S*,3*R*)-isomer (8%) 70.3 (d, $^2J_{P-C}$ = 4 Hz); data for the (2*R*,3*R*)-isomer (7%) 71.2 (d, $^2J_{P-C}$ = 5 Hz); ^{31}P NMR data for the (2*R*,3*S*)-isomer (64%) 22.3; data for the (2*S*,3*S*)-isomer (21%) 20.9; data for the (2*S*,3*R*)-isomer (8%) 21.6; data for the (2*R*,3*R*)-isomer (7%) 25.4; MS (CI-isobutane) *m*/*z* 332 (100). Anal. Calcd for $C_{18}H_{22}NO_3P$ + 0.25 H_2O: C, 64.37; H, 6.75; N, 4.17. Found: C, 64.51; H, 6.91; N, 4.19.

(5*R*)-4-Benzyl-3-ethyl-2-methoxy-5-phenyl-1,4,2-oxazaphosphinane 2-oxide (5b): yield 92%; oil; dr 80:20; IR (cm^{-1}) 1258 (P═O *eq* st), 1230 (P═O *ax* st), 1040 and 1012 (POC st); ^{1}H NMR data for the (2*R*,3*S*)-isomer (80%) 7.50−7.20 (m, 10H), 4.60 (m, 2H), 4.20 (m, 1H), 3.85−3,65 (m, 2H), 3.80 (d, 3H, $^3J_{P-H}$ = 10.7 Hz), 2.90 (td, 1H, J = 7.2 Hz, $^2J_{P-H}$ = 16.5 Hz), 1.90 (m, 2H), 1.00 (t, 3H, J = 7.4 Hz); data for the (2*S*,3*S*)-isomer (20%) 7.50-7.20 (m, 10H), 4.80 (m, 2H), 4.20 (m, 1H), 3.85-3,65 (m, 2H), 3.78 (d, 3H, $^3J_{P-H}$ = 11.0 Hz), 3.15 (m, 1H), 1.90 (m, 2H), 1.00 (t, 3H, J = 7.4 Hz); ^{13}C NMR data for the (2*R*,3*S*)-isomer (80%) 137.8, 137.1, 128.4−127.0, 70.0 (d, $^2J_{P-C}$ = 7 Hz), 57.4, 53.0 (d, $^1J_{P-C}$ = 131 Hz), 51.5 (d, $^2J_{P-C}$ = 6 Hz), 51.1 (d, $^3J_{P-C}$ = 5 Hz), 18.6, 11.4 (d, $^3J_{P-C}$ = 7 Hz); data for the (2*S*,3*S*)-isomer (20%) 138.3, 137.4, 128.4−127.0, 66.7, 56.0, 54.2 (d, $^1J_{P-C}$ = 128 Hz), 51.5 (d, $^2J_{P-C}$ = 6 Hz), 50.1, 17.2, 10.6 (d, $^3J_{P-C}$ = 12 Hz); MS (EI) *m*/*z* 345 (11), 330 (7), 316 (32), 220 (61), 205 (93), 149 (94), 110 (100), 109 (52), 104 (61), 91 (94). Anal. Calcd for $C_{19}H_{24}NO_3P$ + 0.25H_2O: C, 65.22; H, 7.05; N, 4.00. Found: C, 65.48; H, 7.21; N, 3.74.

(5*R*)-4-Benzyl-2-methoxy-5-phenyl-3-propyl-1,4,2-oxazaphosphinane 2-oxide (5c): yield 72%; oil; dr 79:21 ; IR (cm^{-1}) 1265 (P═O *eq* st), 1246 (P═O *ax* st), 1035 and 1010 (POC st); ^{1}H NMR data for the (2*R*,3*S*)-isomer (79%) 7.50−7.10 (m, 10H), 4.60 (m, 2H), 4.20 (m, 1H), 3.80 (dd, 1H), 3.77 (d, 3H, $^3J_{P-H}$ = 10.8 Hz), 3.59 (d, 1H), 3.00 (td, 1H, J = 7.2 Hz, $^2J_{P-H}$ = 16.5 Hz), 1.90 (m, 2H), 1.40 (m, 2H), 0.80 (t, 3H, J = 7.4 Hz); data for the (2*S*,3*S*)-isomer (21%) 7.50−7.10 (m, 10H), 4.80 (m, 2H), 4.00−3.70 (m, 6H), 3.25 (m, 1H), 1.90 (m, 2H), 1.40 (m, 2H), 0.80 (t, 3H, J = 7.4 Hz); ^{13}C NMR data for the (2*R*,3*S*)-isomer (79%) 138.2, 137.3, 128.8−127.3, 70.2 (d, $^2J_{P-C}$ = 7 Hz), 57.6 (d, $^3J_{P-C}$ = 5 Hz), 51.8 (d, $^2J_{P-C}$ = 5 Hz), 51.7, 51.3 (d, $^1J_{P-C}$ = 131 Hz), 26.4, 19.9 (d, $^3J_{P-C}$ = 8 Hz), 13.6; data for the (2*S*,3*S*)-isomer (21%) 138.6, 137.7, 128.8−127.3, 66.8 (d, $^2J_{P-C}$ = 8 Hz), 56.2 (d, $^3J_{P-C}$ = 5 Hz), 52.3 (d, $^1J_{P-C}$ = 127 Hz), 51.3 (d, $^2J_{P-C}$ = 5 Hz), 50.4, 27.5, 18.9 (d, $^3J_{P-C}$ = 12 Hz), 13.4; ^{31}P NMR: data for the (2*R*,3*S*)-isomer (79%) 22.2; data for the (2*S*,3*S*)-isomer (21%) 21.0; MS (CI-isobutane) *m*/*z* 360 (100).

(5*R*)-3,4-Dibenzyl-2-methoxy-5-phenyl-1,4,2-oxazaphosphinane 2-oxide (5d): yield 56%; oil; dr 60:40; IR (cm^{-1}) 1266 (P═O *eq* st), 1241 (P═O *ax* st), 1040 and 1011 (POC st); ^{1}H NMR data for the (2*R*,3*S*)-isomer (60%) 7.35−7.05 (m, 15H), 4.72 (m, 2H), 4.36 (dd, 1H, J = 4.5, 7.0 Hz), 3.86 (dd, 1H, J = 13.8 Hz, $^4J_{P-H}$ = 4.5 Hz), 3.78 (d, 3H, $^3J_{P-H}$ = 10.7 Hz), 3.68 (d, 1H, J = 13.8 Hz), 3.41 (dd, 1H, J = 6.7, 8.1 Hz), 3.25 (m, 2H); data for the (2*S*,3*S*)-isomer (21%) 7.35−7.05 (m, 15H), 4.84 (ddd, 1H, J = 3.5, 5.0, 7.3 Hz), 3.90−3.60 (m, 4H), 3.80 (d, 3H, $^3J_{P-H}$ = 10.5 Hz), 3.40 (m, 1H), 3.25 (m, 2H); ^{13}C NMR data for the (2*R*,3*S*)-isomer (60%) 138.0, 137.7, 137.1, 129.2−126.3, 69.5 (d, $^2J_{P-C}$ = 7 Hz), 56.7 (d, $^3J_{P-C}$ = 5 Hz), 53.0 (d, $^1J_{P-C}$ = 129 Hz), 51.9 (d, $^2J_{P-C}$ = 7 Hz), 51.0 (d, $^3J_{P-C}$ = 3 Hz), 31.5 (d, $^2J_{P-C}$ = 5 Hz); data for the (2*S*,3*S*)-isomer (40%) 138.0, 137.8, 137.2, 128.4−127.0, 67.3 (d, $^2J_{P-C}$ = 8 Hz), 56.0 (d, $^3J_{P-C}$ = 4 Hz), 51.2 (d, $^1J_{P-C}$ = 100 Hz), 51.9 (d, $^2J_{P-C}$ = 6 Hz), 50.7, 31.0 (d, $^2J_{P-C}$ = 5 Hz); MS (CI-isobutane) *m*/*z* 408 (100). Anal. Calcd for $C_{24}H_{26}NO_3P + 0.75H_2O$: C, 68.47; H, 6.58; N, 3.32. Found: C, 68.72; H, 6.54; N, 3.21.

4-(4-Benzyl-2-methoxy-2-oxo-5-phenyl-2λ^5-1,4,2-oxazaphosphinan-3-yl)butyric acid methyl ester (5e): yield 77%; oil; dr 60:33:6:1; IR (cm^{-1}) 1735 (C═O st), 1250 (b, P═O *eq* and P═O *ax* st), 1040 and 1010 (POC st); ^{1}H NMR data for the (2*R*,3*S*)-isomer (60%) 7.50−7.20 (m, 10H), 4.90−4.50 (m, 2H), 4.30−4.15 (m, 1H), 4.05−3.75 (m, 2H), 3.85 (d, 3H, $^3J_{P-H}$ = 11.0 Hz), 3.67 (s, 3H), 2.95 (td, 1H, J = 6.9 Hz, $^2J_{P-H}$ = 16.7 Hz), 2.20−1.50 (m, 6H); data for the (2*S*,3*S*)-isomer (33%) 7.50−7.20 (m, 10H), 4.90-4.50 (m, 2H), 4.30−4.15 (m, 1H), 4.05−3.75 (m, 2H), 3.65 (d, 3H, $^3J_{P-H}$ = 10.6 Hz), 3.65 (s, 3H), 3.20 (td, 1H, J = 4.4 Hz, $^2J_{P-H}$ = 9.3 Hz), 2.20−1.50 (m, 6H); ^{13}C NMR: data for the (2*R*,3*S*)-isomer (60%) 173.2, 137.8, 136.9, 129.6−127.1, 70.1 (d, $^2J_{P-C}$ = 8 Hz), 57.2 (d, $^3J_{P-C}$ = 5 Hz), 51.6 (d, $^2J_{P-C}$ = 7 Hz), 51.1, 50.9 (d, $^1J_{P-C}$ = 132 Hz), 50.9, 32.8, 23.4 (d, $^3J_{P-C}$ = 4 Hz), 21.6; data for the (2*S*,3*S*)-isomer (33%) 173.1, 137.1, 136.9, 129.6−127.1, 66.8 (d, $^2J_{P-C}$ = 8 Hz), 55.9 (d, $^3J_{P-C}$ = 5 Hz), 53.9 (d, $^2J_{P-C}$ = 6 Hz), 51.4 (d, $^1J_{P-C}$ = 132 Hz), 51.0, 50.1, 32.7, 24.6 (d, $^3J_{P-C}$ = 4 Hz), 21.5; ^{31}P NMR data for the (2*R*,3*S*)-isomer (60%) 21.5; data for the (2*S*,3*S*)-isomer (33%) 20.1; data for the (2*S*,3*R*)-isomer (6%) 19.0; data for the (2*R*,3*R*)-isomer (1%) 25.2; MS (CI-isobutane) *m*/*z* 418 (100).

Typical Experimental Procedure for the Monohydrolysis of the Phosphonate Group. To a solution of oxazaphosphorinane (1 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added $BrSiMe_3$ (2.4 mmol) dropwise under an argon atmosphere. After being stirred at room temperature for 2 h, the solvent was removed under reduced pressure. The solid was dissolved in methanol, and the solvent was evaporated to give a phoshonic acid monoester.

(3*S*,5*R*)-4-Benzyl-3-methyl-2-oxo-5-phenyl-2λ^5-1,4,2-oxazaphosphinan-2-ol (9a): yield 91%; white solid; dr 86:14; ^{1}H NMR (CD_3OD) data for the major product (3*S*)-isomer (86%) 7.80−7.40 (m, 10H), 4.50−4.20 (m, 5H), 3.40 (m, 1H), 1.70 (dd, 1H, J = 7.0 Hz, $^3J_{P-H}$ = 14.0 Hz); ^{13}C NMR (CD_3OD) data for the (3*S*)-isomer (86%) 132.1−130.0, 67.5, 64.2, 56.4, 53.5 (d, $^1J_{P-C}$ = 135 Hz), 9.8; ^{31}P NMR (CD_3OD) data for the (3*S*)-isomer (86%) 9.0; data for the (3*R*)-isomer (14%) 10.0; HPLC 86.05%−13.95%; MS (CI-isobutane) *m*/*z* 318 (100). Anal. Calcd for $C_{17}H_{20}NO_3P + 0.9HBr$: C, 52.34; H, 5.40; N, 3.59. Found: C, 52.25; H, 5.92; N, 3.45.

(3*S*,5*R*)-4-Benzyl-3-ethyl-2-oxo-5-phenyl-2λ^5-1,4,2-oxazaphosphinan-2-ol (9b): yield 93%; white solid; dr 100:0; ^{1}H NMR (CD_3OD) 7.80−7.40 (m, 10H), 5.20 (m, 1H), 4.70 (m, 1H), 4.40 (m, 2H), 4.05 (d, J = 12.5 Hz), 3.25 (m, 1H), 2.30 (m, 2H), 0.90 (t, 1H, J = 7.0 Hz); ^{13}C NMR (CD_3OD) 132.2−129.9, 67.7 (d, $^3J_{P-C}$ = 4 Hz), 65.4, 59.1 (d, $^1J_{P-C}$ = 131 Hz), 56.6 (d, $^3J_{P-C}$ = 5 Hz), 18.5, 12.4; ^{31}P NMR (CD_3OD) 9.5; HPLC 100%; MS (CI-isobutane) *m*/*z* 332 (100). Anal. Calcd for $C_{18}H_{22}NO_3P + HBr$: C, 52.44; H, 5.62; N, 3.39. Found: C, 52.61; H, 5.90; N, 3.29.

(3*S*,5*R*)-4-Benzyl-2-oxo-5-phenyl-3-propyl-2λ^5-1,4,2-oxazaphosphinan-2-ol (9c): yield 92%; white solid; dr 100:0; ^{1}H NMR (CD_3OD) 7.70−7.30 (m, 10H), 4.95 (m, 1H), 4.75 (m, 1H), 4.42 (ddd, 1H, J = 3, 13.0 Hz, $^3J_{P-H}$ = 18.5 Hz), 4.25 (m, 2H), 3.07 (m, 1H), 2.05 (m, 2H), 1.7 (m, 2H), 0.96 (t, 3H, J = 7.5 Hz); ^{13}C NMR (CD_3OD) 140.2, 139.2, 132.2−129.9, 67.5, 65.1, 57.8 (d, $^1J_{P-C}$ = 132 Hz), 56.4, 27.5, 22.0, 14.2; ^{31}P NMR (CD_3OD) 9.5; MS (FAB) *m*/*z* 346 (100).

(3*S*,5*R*)-3,4-Dibenzyl-2-oxo-5-phenyl-2λ^5-1,4,2-oxazaphosphinan-2-ol (9d): yield 89%; white solid; dr 100:0; ^{1}H NMR (CD_3OD) 7.40−6.90 (m, 15H), 4.80 (m, 2H), 4.20 (m, 1H), 4.00 (dd, 1H, J = 15.0 Hz, $^4J_{P-H}$ = 4.0 Hz), 3.77 (d, J = 15.0 Hz), 3.55 (m, 1H), 3.25 (m, 2H); ^{13}C NMR (CD_3OD) 140.9, 140.8, 140.6, 130.4−126.8, 66.8 (d, $^2J_{P-C}$ = 5 Hz), 58.1, 56.0 (d, $^1J_{P-C}$ = 131 Hz), 51.6, 32.9; ^{31}P NMR (CD_3OD) 15.9; HPLC 100%; MS (CI-isobutane) *m*/*z* 394 (100). Anal. Calcd for $C_{23}H_{24}NO_3P + 0.25H_2O$: C, 69.42; H, 6.20; N, 3.52. Found: C, 69.63; H, 6.96; N, 3.13.

4-(4-Benzyl-2-hydroxy-2-oxo-5-phenyl-2λ^5-1,4,2-oxazaphosphinan-3-yl)butyric acid (9e): yield 91%; white solid; dr 90:10; ^{1}H NMR (NaOH/D_2O): 7.45−7.15 (m, 10H), 4.45 (m, 2H), 3.90 (m, 2H), 3.64 (d, 1H, J = 14 Hz), 2.80 (td, 1H, J = 7.6 Hz, $^2J_{P-H}$ = 15.0 Hz), 2.08 (t, 2H, J = 6.7 Hz), 1.75 (m, 2H), 1.60 (m, 2H); ^{13}C NMR (D_2O/NaOH) 188.4, 139.7, 138.9, 128.8−127.1, 67.5, 57.7, 55.0, 50.1 (d, $^1J_{P-C}$ = 143 Hz), 37.3, 25.5, 23.4; ^{31}P NMR (NaOD + CD_3OD) data for the (3*S*)-isomer (90%) 16.2; data for the (3*R*)-isomer (10%) 17.2; MS (FAB) *m*/*z* 456 (100).

Typical Experimental Procedure for the Obtention of (1-Aminoalkyl)phosphonic Acids from Oxazaphosphorinane Derivatives. The heterocyclic compound (1 mmol) was dissolved in methanol, and $Pd(OH)_2$ on charcoal (20%) (0.2 mmol) was added. The mixture was stirred under hydrogen (60 psi) at room temperature until the reaction was complete (5 h). The reaction mixture was filtered through a Celite pad, and the methanol was removed at reduced pressure. No attempt was made to characterize the (1-aminoalkyl)phosphonic acid monomethyl ester which was formed.

A 5 N hydrochloric acid solution (20 mmol) was added to the crude product, and the resultant solution was heated with stirring under reflux for 3 h. The solvent was then evaporated under *vacuum* to lead to the aminophosphonic acid as a semisolid. This material was dissolved in refluxing ethanol and treated with propylene oxide at 70−80 °C to precipate the aminophosphonic acid as a white crystalline powder. The product was filtered off, washed with diisopropyl ether, and thoroughly dried at 50 °C under reduced pressure and in the presence of a dehydrating agent (P_2O_5).

(*S*)-(1-Aminoethyl)phosphonic acid (1a): yield 96%; white powder, mp 257 °C (EtOH); ^{1}H NMR (D_2O) 4.78 (s, 4H), 3.31 (qd, 1H, J = 7.2 Hz, $^2J_{P-H}$ = 14.5 Hz), 1.42 (dd, 3H, J = 7.2 Hz, $^3J_{P-H}$ = 14.8 Hz); MS (FAB) *m*/*z* 126 (100); $[\alpha]^{25}_{578}$ = +13.1 (*c* = 1, 1 N NaOH). Anal. Calcd for $C_2H_8NO_3P$: C, 19.21; H, 6.45; N, 11.20. Found: C, 19.29; H, 6.35; N, 10.99.

(*S*)-(1-Aminopropyl)phosphonic acid (1b): yield 87%; white powder, mp 271 °C (EtOH); ^{1}H NMR (D_2O) 3.20 (m, 1H), 1.95 (m, 1H), 1.75 (m, 1H), 1.10 (t, 3H, J = 8 Hz); MS (FAB) *m*/*z* 140 (100); $[\alpha]^{25}_{578}$ = +19.3 (*c* = 1, 1 N NaOH). Anal. Calcd for $C_3H_{10}NO_3P$: C, 25.91; H, 7.25; N, 10.07. Found: C, 25.32; H, 6.79; N, 9.23.

(*S*)-(1-Aminobutyl)phosphonic acid (1c): yield 82%; white powder mp 268 °C (EtOH); ^{1}H NMR (NaOH/D_2O) 3.15

(m, 1H), 1.85−1.35 (m, 4H, m, 1H), 0.85 (t, 3H, J = 7.5 Hz); MS (FAB) m/z 154 (100); $[\alpha]^{25}_{578}$ = +17.1 (c = 1, 1 N NaOH). Anal. Calcd for $C_4H_{12}NO_3P$: C, 31.37; H, 7.89; N, 9.14. Found: C, 30.92; H, 7.21; N, 8.68.

(*S*)-(1-Amino-2-phenylethyl)phosphonic acid (1d): yield 70%; white powder, mp 265 °C (EtOH); ^{1}H NMR (NaOH/D_2O) 7.20 (m, 5H), 3.08 (ddd, 1H, J = 2.0, 13.0 Hz, $^3J_{P-H}$ = 2.5 Hz), 2.73 (ddd, 1H, J = 2.0, 11.0 Hz, $^2J_{P-H}$ = 12.0 Hz), 2.35 (ddd, 1H, J = 11.0 , 13.0 Hz, $^3J_{P-H}$ = 6.0 Hz); MS (FAB) m/z 202 (100); $[\alpha]^{25}_{578}$ = +50.3 (c = 1, 1 N NaOH). Anal. Calcd for $C_8H_{12}NO_3P$: C, 47.77; H, 6.01; N, 6.96. Found: C, 47.56; H, 5.80; N, 7.20.

(S)-5-Amino-5-phosphonopentanoic acid (1e): yield 81%; white powder, mp 160 °C (EtOH); ^{1}H NMR (NaOH/D_2O) 3.20 (m, 1H), 2.20 (t, 2H, J = 7.3 Hz), 1.85−1.55 (m, 4H); MS (FAB) m/z 234 (100); $[\alpha]^{25}_{578}$ = +27.1 (c = 1, 1 N NaOH). Anal. Calcd for $C_5H_{12}NO_5P + 0.5\ C_2H_5OH$: C, 32.73; H, 6.86; N, 6.36. Found: C, 32.87; H, 6.35; N, 6.06.

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