Totally Stereoselective P – O to P – C Migration Rearrangement: Application to the Synthesis of New Chiral *o*-Hydroxyaryl Phosphine Oxides

Olivier Legrand, Jean Michel Brunel, Thierry Constantieux, and Gérard Buono*

Abstract: The synthesis of a novel class of chiral *o*-hydroxyaryl phosphine oxides by the rearrangement of a P – O to a P – C bond is described. This reaction proceeds with excellent yields (75 – 95 %) and total retention of the configuration on the phosphorus atom. In the case of the treatment of an equimolar mixture of the diastereomers *anti*-**2e** and *syn*-**2f**, the resulting compounds *anti*-**3e** and *syn*-**3f**, obtained in a 1:1 molar ratio, were separated and characterized by X-ray diffraction. On the basis of the experimental results, we suggest that the migration mechanism is addition – pseudorotation – elimination; this explains the total stereoselectivity observed at the phosphorus atom.

Keywords: asymmetric synthesis · chirality · phosphane oxides · reaction mechanisms · rearrangements

Introduction

In the last 30 years, considerable developments have been achieved for asymmetric transition metal catalyzed systems[1] with chiral ligands such as phosphines and, more recently, phosphorus/nitrogen bidentate donor compounds.[2, 3] In this area, phosphorus analogues of salicylic aldehyde derivatives, such as *o*-hydroxyphenyldialkylphosphine oxides or phosphonic acids, may exhibit similar properties.[4] Nevertheless, few methods for the synthesis of such compounds have been proposed. In 1981, Melvin reported the synthesis of *o*-hydroxyarylphosphonates by the rearrangement of arylphosphates induced by a strong base, such as lithium diisopropylamide (LDA) or *n*-butyllithium.[5] Although the usefulness of this synthetic method has been extensively developed,[6] few mechanistic studies have been performed and the rearrangement was considered to take place via an *ortho*-stabilized carbanion. The formation of the *ortho*-lithiated species was corroborated by Watanabe et al.[7] and Casteel and Peri,[8] who were able to trap the lithiated intermediate at $-105\,^{\circ}C$. When the reaction temperature was allowed to rise to $-78\,^{\circ}C$, the rearrangement proceeded rapidly to afford quantitative yields of the *o*-hydroxyaryl phosphine oxide compound. Moreover, only Welch et al. probed the synthesis of such chiral compounds from (−)-ephedrine.[9] Nevertheless, due to the nature of the amino alcohol under consideration, an epimerization at the C4 methyl group occurred and an elimination product was formed. Thus, these results show that a general retention of the configuration on the phosphorus cannot be unambiguously postulated for the P – O to P – C rearrangement. In this paper, we report a new general procedure for the preparation of various chiral *o*-hydroxyaryl diazaphospholidine oxides, *o*-hydroxyaryl oxazaphospholidine oxides, or *o*-hydroxyarylphosphonates which feature a basic (P=O) and an acid site (OH) and involve a stereoselective P – O to P – C rearrangement. We have investigated the unambiguous stereoselectivity of this reaction at the phosphorus atom in various cases, and we propose a mechanistic pathway based on detailed experiments.

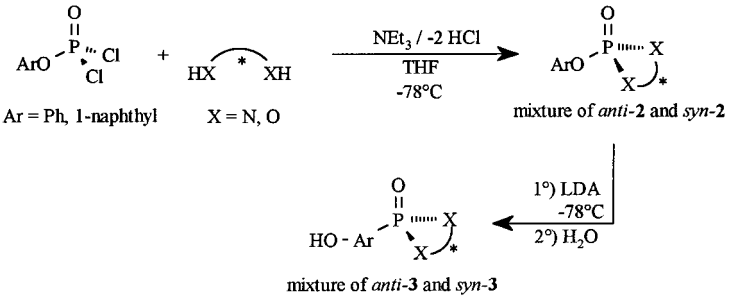
[*] Prof. G. Buono, Dr. J. M. Brunel, Dr. T. Constantieux, O. Legrand
Ecole Nationale Supérieure de Synthèse, de Procédés et d'Ingénierie Chimiques d'Aix Marseille
UMR CNRS 6516, Faculté de St Jérôme
Av. Escadrille Normandie Niemen, 13397 Marseille, Cedex 20 (France)
Fax: (+33) 4-91-02-77-76
E-mail: buono@spi.chim.u-3mrs.fr

Results and Discussion

Already well-known in the synthesis of organoalkoxysilylphenols, the direct metalation of *o*-halogenoaryloxy derivatives of tin and phosphorus seems to be a general method for the preparation of hydroxyaryl tin or phosphorus derivatives.[1, 10, 11] This reaction proceeds via an unstable metalated intermediate which undergoes a fast 1,3-rearrangement with formation of an element – carbon bond. Thus, by the use of a modified procedure, the synthesis of chiral hydroxyaryl phosphine oxides **3** may be achieved in a two-step reaction (Scheme 1).

Precursors **2** were readily available from exchange reactions between an aryl phosphorodichloridate and various chiral substrates, such as amino alcohols, diamines, or diols with high yields ranging from 76 to 95 % (Table 1). Only one

  0947-6539/98/0406-1061 $ 17.50+.25/0



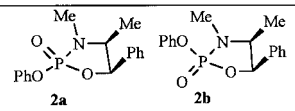
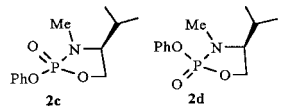
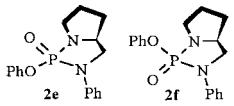
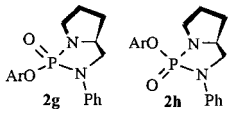
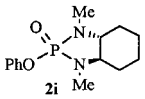
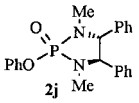
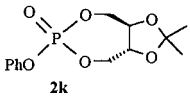
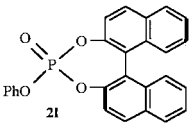
Scheme 1. General procedure for the synthesis of *o*-hydroxyaryl phosphine oxides.

diastereomer is obtained when the chiral auxiliary is of C_2 symmetry (entries 5–8). In the other cases, the formation of the two expected diastereomers was observed in a diastereomeric ratio ranging from 75:25 (entry 2) to 50:50 (entry 3), depending on the nature of the chiral moiety.[12] Moreover, all attempts to separate the diastereomers failed, except for entry 2 where diasteromers *anti*-**2c** and *syn*-**2d** were cleanly separated by column chromatography and then fully characterized by NMR spectroscopic analysis.[13]

A subsequent P–O to P–C rearrangement on treatment of a mixture of the two diastereomers, *anti*-**2** and *syn*-**2** in a 1:1 molar ratio, with LDA in THF at $-78\,^{\circ}C$ led to a 50:50 mixture of diastereomers *anti*-**3** and *syn*-**3** (Table 2). In most cases, these diastereomers were successfully separated by column chromatography in yields ranging from 80 to 95% for each diastereomer. Thus, in contrast to the reported procedures, this method allows the synthesis of the two diastereomers *anti*-**3** and *syn*-**3**.[15] In the case of entry 4, the structures of diastereomer *anti*-**3e** and *syn*-**3f** have been clearly established by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy and X-ray analysis (Figures 1 and 2).[16]

In order to demonstrate the stereoselectivity of the mechanism involved in this reaction, a pure sample of compound *anti*-**3e** was prepared by oxidation of the corresponding chiral phosphine **4**. Subsequent treatment with LDA at $-78\,^{\circ}C$ resulted in the migration of the phosphinyl group from oxygen to carbon to produce *anti*-**3e** stereoselectively in 89% yield (Scheme 2). Thus, the results observed from diastereomerically pure *anti*-**2c**, *syn*-**2d**, and *anti*-**2g** clearly show that the *rearrangement proceeds by a totally stereoselective reaction at the phosphorus atom*.[17]

Table 1. Synthesis of precursors **2**.

Entry	Product	Diastereomeric Ratio (%)[a]	Yield (%)[b]
1	 **2a** **2b**	80 / 20	69[c]
2	 **2c** **2d**	75 / 25	78[c]
3	 **2e** **2f**	50 / 50	91[d]
4	 **2g** **2h** Ar = 1-naphthyl	60 / 40	76[d]
5	 **2i**	-	85
6	 **2j**	-	80
7	 **2k**	-	25
8	 **2l**	-	90

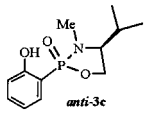
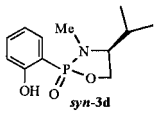
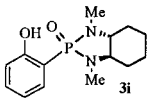
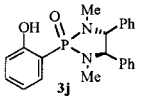
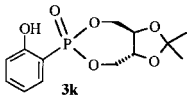
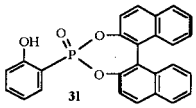
[a] Diastereomeric ratio determined by ^{31}P NMR spectroscopy. [b] Isolated yield after column chromatography. [c] Pure diastereomers separated by column chromatography (see the Experimental Section). [d] Inseparable mixture of diastereomers.

Since it was established that the stereochemistry of the 1,3-phosphorus migration operates with retention of configuration at the phosphorus atom, a mechanism proceeding via a trigonal bipyramidal intermediate (TBP) can be postulated (Scheme 3).[18] This retention of configuration may be explained by an apical addition followed by an equatorial elimination (intermediates **6a** and **6b**) or the opposite pathway suggesting an equatorial addition followed by an apical elimination (intermediates **7a** and **7b**). However, Mislow et al.[19] suggest that if the bond-making or -breaking step is rate-determining, then apical addition and elimination will be more favorable than either equatorial addition and apical elimination or the opposite pathway. Thus, for associative processes with strong nucleophiles, it is generally assumed that the nucleophile approaches a trigonal face of the tetrahedral phosphorus center to form a pentacoordinate intermediate with the entering nucleophile in apical position

Abstract in French: *La synthèse d'une nouvelle classe d'oxyde d'o-hydroxyaryl phosphines chirales via le réarrangement d'une liaison P–O en liaison P–C est décrite. Cette réaction s'effectue avec d'excellents rendements chimiques (75 à 95%) et une totale rétention de configuration au niveau de l'atome de phosphore. Dans le cas de la transposition d'un mélange équimolaire des deux diastéréomères anti-2e et syn-2f, les composés résultants anti-3e et syn-3f obtenus dans un rapport molaire 1:1 ont pu être séparés et caractérisés par diffraction des rayons X. Sur la base de nombreux résultats expérimentaux, le passage par un mécanisme de type addition–pseudorotation–élimination a pu être proposé et permet ainsi de justifier de la totale stéréosélectivité observée au niveau de l'atome de phosphore.*

0947-6539/98/0406-1062 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 6

Table 2. Preparation of compounds **3** by a stereoselective P–O to P–C rearrangement of precursors **2**.

Entry	Substrate (molar ratio)	Product	Yield (%)[a]
1	***anti*-2a / *syn*-2b**	***anti*-3a**	0[b]
	80/20	***syn*-3b**	86
2	***anti*-2c**	 *anti*-3c	89 (100)[c]
3	***syn*-2d**	 *syn*-3d	92 (100)[c]
4	***anti*-2e / *syn*-2f**	***anti*-3e**	94 (100)[d]
	50/50	***syn*-3f**	88
5	***anti*-2g / *syn*-2h**	***anti*-3g**	93 (100)[d]
	60/40	***syn*-3h**	92
6	**2i**	 **3i**	93
7	**2j**	 **3j**	91
8	**2k**	 **3k**	95
9	**2l**	 **3l**	0[c]

[a] Isolated yield based on the proportion of each diastereomer in the starting material mixture. [b] See ref. [14]. [c] The rearrangement proceeds with a totally stereoselective reaction at the phosphorus atom. [d] Rearrangement of pure precursor *anti*-**2** led stereoselectively to pure compound *anti*-**3**. [e] A mixture of various nonidentified products was obtained.

of the TBP (apical attack).[20] *Ortho*-phenyl anion attack at one of the adjacent faces of the tetrahedron of **5**, in line with one of the nitrogen atoms of the diazaphospholane ring, leads to TBP intermediates **6a** or **6b** in which the four-membered oxaphosphetane ring and the five-membered diazaphospholane ring adopt an axial–equatorial position[21–24] and the electron-donating oxygen anion ligand an equatorial position.[25–27] For these TBP intermediates it is possible to consider a low-energy Berry pseudorotation[28] **6a** $\rightleftharpoons$ **7a** and **6b** $\rightleftharpoons$ **7b** spanning the more apicophilic oxygen atom of the oxaphosphetane ring in an apical position. The extracyclic oxygen anion group tends to remain equatorial throughout the pseudorotation process by serving as a pivot. These pseudorotational processes permit overall apical introduction of the *ortho*-stabilized carbanion and apical departure of the

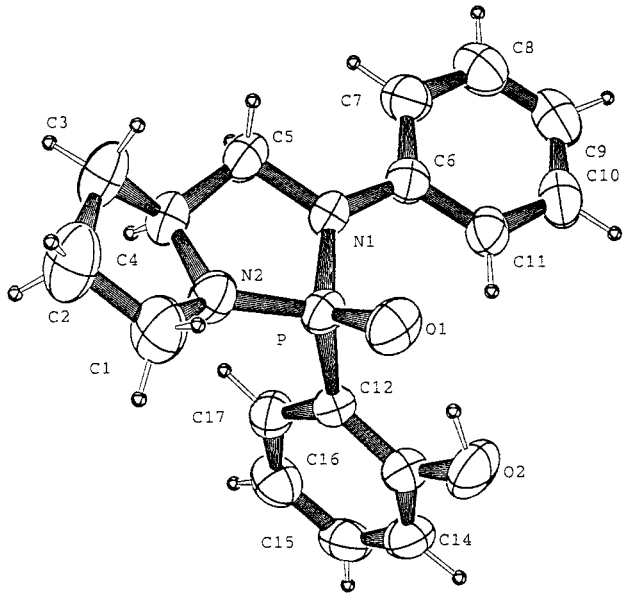


Figure 1. Structure of *anti*-**3e**, showing the labeling scheme. Selected bond lengths [Å] and angles [°]: P–O1 1.485(2), P–N1 1.667(2), P–N2 1.622(2), P–C12 1.790(2), O2–C13 1.356(3); O1-P-N1 117.87(9), O1-P-N2 117.64(9), O1-P-C12 107.89(9), N1-P-N2 94.29(9), N1-P-C12 107.71(9), N2-P-C12 110.7(1), P-N1-C5 114.4(1), P-N1-C6 125.4(1), C5-N1-C6 119.8(2), P-N2-C1 128.4(2), P-N2-C4 115.3(1).

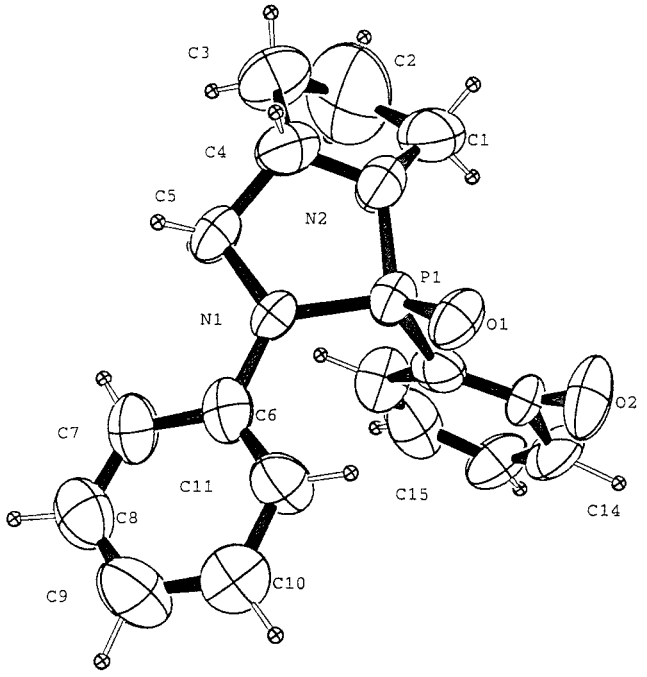
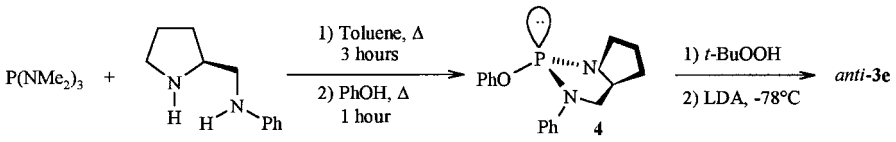
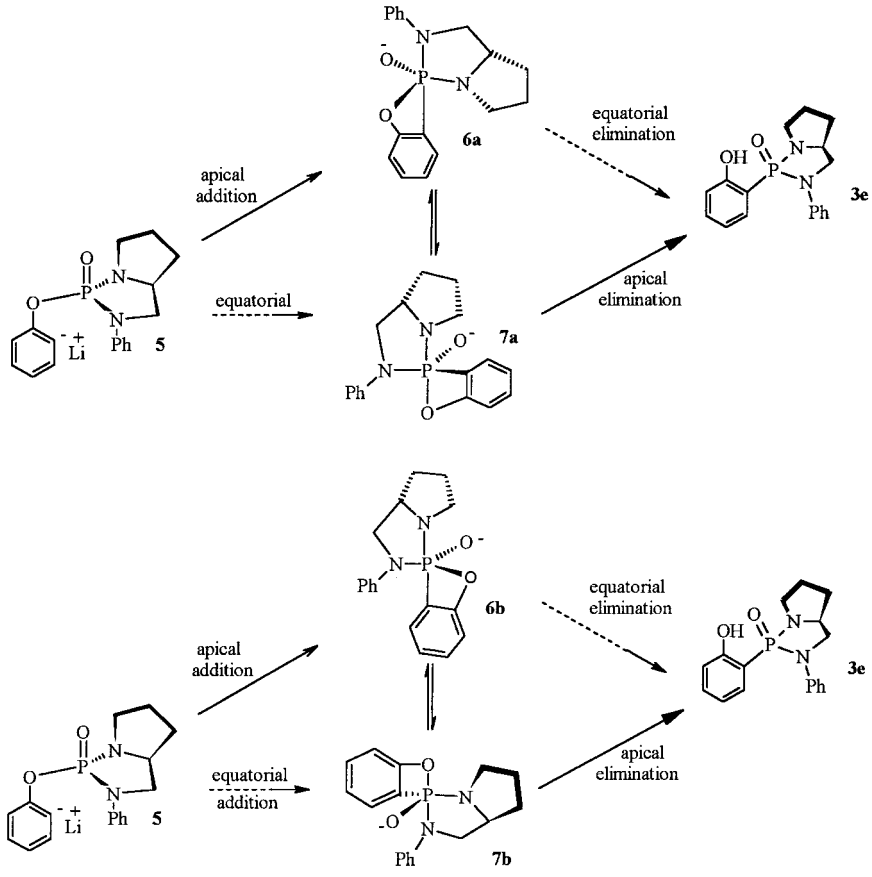


Figure 2. Structure of *syn*-**3f** showing the labeling scheme. Selected bond lengths [Å] and bond angles [°]: P–O1 1.474(8), P–C12 1.82(1), P–N1 1.66(1), P–N2 1.64(1), O2–C13 1.34(2); O1-P-N1 116.9(5), O1-P-N2 115.9(5), O1-P-C12 106.7(5), N1-P-N2 93.3(5), N1-P-C12 111.3(5), N2-P-C12 112.5(6), P-N1-C5 114.4(8), P-N1-C6 124.1(8), C5-N1-C6 120.(1), P-N2-C1 127.8(9), P-N2-C4 113.9(9).

leaving group in agreement with the principle of microscopic reversibility.[20, 29, 30] Moreover, by considering an associative process, the inversion of the configuration at the phosphorus atom is energetically unfavorable since it involves the epimerization of the phosphorus P^V atom in the TBP

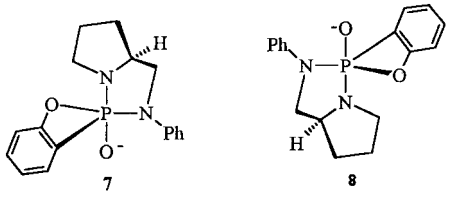


Scheme 2. Synthesis of pure *anti*-**3e**.



Scheme 3. Possible mechanism for the stereoselective P–O to P–C migration rearrangement.

intermediates. Such an epimerization implies high-energy intermediates **7** and **8** in which either the oxaphosphetane or diazaphospholane rings are forced to adopt a constrained diequatorial position with the oxygen anion group in an apical position[31, 32] (Scheme 4).



Scheme 4. High-energy intermediates **7** and **8**.

Conclusion

We have described the first synthesis of various new chiral *o*-hydroxyaryl phosphine oxides by means of a totally stereoselective migration–rearrangement procedure. A mechanistic rationale involving an addition–pseudorotation–elimination pathway has been proposed in agreement with the experimentally observed retention of configuration at the phosphorus atom. Additional studies concerning the use of such compounds as catalysts in various asymmetric catalyzed reactions as well as potential biological activities are currently under investigation.[33]

Experimental Section

Materials and methods: ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectra were recorded on Bruker AC100 and AC200 spectrometers in $CDCl_3$. The chemical shifts (ppm) were determined relative to Me_4Si (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Toluene, tetrahydrofuran (THF), and diethyl ether were distilled from sodium/benzophenone ketyl immediately prior to use. Ethyl acetate and petroleum ether (35–60 °C) were purchased from SDS and used without any further purification. Column chromatography was performed on Merck silica gel (70–230 mesh).

General procedure for the preparation of compounds 2a–l: phenyldichlorophosphate (1.64 mL, 11 mmol) was added dropwise at 0 °C to a solution of the corresponding chiral amino alcohol, diamine, or diol (10 mmol) and freshly distilled NEt_3 (3.8 mL, 30 mmol) in dry THF (25 mL). The mixture was stirred under N_2 at RT overnight, then filtered to remove Et_3NHCl. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on a silica gel column to give the pure compound.

(2*S*,4*R*,5*S*)-3,4-Dimethyl-2-phenoxy-5-phenyl-1,3-,2-oxazaphospholidine 2-oxide (**2a**) and **(2*R*,4*R*,5*S*)-3,4-dimethyl-2-phenoxy-5-phenyl-1,3-,2-oxazaphospholidine 2-oxide** (**2b**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 90:10) afforded **2a** as a white solid in 57% yield and **2b** as a white solid in 12% yield.

2a: M.p. 94 °C; $[\alpha]_D^{25} = -102.0$ ($c = 1$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 13.5$; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.66$ (d, $J = 6.7$ Hz, 3H), 2.88 (d, $J = 10.0$ Hz, 3H), 3.75 (m, 1H), 5.78 (d, $J = 6.2$ Hz, 1H), 7.30 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.2$ (s), 29.5 (d, $J = 5.6$ Hz), 60.0 (d, $J = 13.6$ Hz), 80.9 (d, $J = 2.5$ Hz), 120.7 (d, $J = 4.3$ Hz, 2C), 124.9 (s), 125.6 (s, 2C), 128.2 (s), 128.4 (s, 2C), 129.6 (s, 2C), 135.5 (d, $J = 8.7$ Hz), 151.2 (d, $J = 8.8$ Hz); $C_{16}H_{18}NO_3P$ (303.29): calcd. C 63.4, H 6.0, N 4.6, P 10.2; found C 63.7, H 5.9, N 4.8, P 10.5.

2b: M.p. 122 °C; $[\alpha]_D^{25} = -34.0$ ($c = 1$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 13.5$; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.5$ Hz, 3H), 2.81 (d, $J = 10.3$ Hz, 3H), 3.60 (m, 1H), 5.38 (dd, $J = 6.4$ Hz, $J = 3.9$ Hz, 1H), 7.30 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.2$ (d, $J = 3.6$ Hz), 28.6 (d, $J = 4.4$ Hz), 58.8 (d, $J = 12.8$ Hz), 81.0 (s), 120.5 (d, $J = 4.3$ Hz, 2C), 124.8 (s), 125.9 (s, 2C), 128.3 (s, 3C), 129.6 (s, 2C), 135.4 (d, $J = 7.2$ Hz), 151.1 (d, $J = 8.7$ Hz); $C_{16}H_{18}NO_3P$ (303.29): calcd. C 63.4, H 6.0, N 4.6, P 10.2; found C 63.6, H 6.1, N 4.9, P 10.3.

(2*S*,4*S*)-4-Isopropyl-2-phenoxy-3-methyl-1,3,2-oxazaphospholidine 2-oxide (**2c**) and **(2*R*,4*S*)-4-isopropyl-2-phenoxy-3-methyl-1,3,2-oxazaphospholidine 2-oxide** (**2d**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 80:20).

2c: Pale yellow syrup; yield: 58%; $[\alpha]_D^{25} = +71.4$ ($c = 1.05$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 16.4$; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.9$ Hz, 3H), 2.07 (m, 1H), 2.74 (d, $J = 10.2$ Hz, 3H), 3.19 (m, 1H), 4.07 (m, 2H), 7.17 (m, 3H), 7.34 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.3$ (s), 17.6 (s), 27.4 (d, $J = 5.6$ Hz), 28.9 (d, $J = 5.5$ Hz), 62.3 (d, $J = 13.6$ Hz), 65 (s), 120.3 (d, $J = 5.0$ Hz, 2C), 124.75 (s),

0947-6539/98/0406-1064 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 6

129.5 (s, 2C), 150.2 (d, $J = 7.5$ Hz); $C_{12}H_{18}NO_3P$ (255.25): calcd. C 56.5, H 7.1, N 5.5, P 12.1; found C 57.1, H 7.1, N 5.4, P 12.5.

2d: Pale yellow syrup, yield: 20%; $[\alpha]_D^{25} = -65.5$ ($c = 1.1$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 18.7$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.63$ (d, $J = 6.9$ Hz, 3H), 0.80 (d, $J = 7.0$ Hz, 3H), 1.83 (m, 1H), 2.72 (d, $J = 10.4$ Hz, 3H), 3.35 (m, 1H), 3.80 (m, 1H), 4.22 (m, 1H), 7.14 (m, 3H), 7.34 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.5$ (s), 17.4 (s), 28.1 (d, $J = 6.2$ Hz), 30.5 (d, $J = 5.5$ Hz), 63.4 (d, $J = 13.8$ Hz), 65.4 (s), 120.7 (d, $J = 4.2$ Hz, 2C), 124.8 (s), 129.4 (s, 2C), 150.8 (d, $J = 8.3$ Hz); $C_{12}H_{18}NO_3P$ (255.25): calcd. C 56.5, H 7.1, N 5.5, P 12.1; found C 57.3, H 7.2, N 5.6, P 11.9.

(2*S*,5*S*)-2-Phenoxy-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide (**2e**) and **(2*R*,5*S*)-2-phenoxy-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide** (**2f**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 80:20) afforded an equimolar, inseparable mixture of the two diastereomers **2e** and **2f** as a white solid in 91% yield. ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 16.9$, 10.9; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.05$ (m, 4H), 3.50 (m, 5H), 7.20 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26$ (d, $J = 3.7$ Hz), 27.1 (d, $J = 5.2$ Hz), 31.3 (d, $J = 2.8$ Hz), 32.3 (d, $J = 2.9$ Hz), 44.5 (d, $J = 2.7$ Hz), 46.5 (d, $J = 2.7$ Hz), 49.7 (d, $J = 19.2$ Hz), 51.4 (d, $J = 16.3$ Hz), 56.9 (d, $J = 10.6$ Hz), 57.7 (d, $J = 11.6$ Hz), 116.0 (d, $J = 3.7$ Hz), 117.0 (d, $J = 5.2$ Hz), 120.8 (d, $J = 3.7$ Hz), 121.0 (d, $J = 5.2$ Hz), 121.4 (d, $J = 3.7$ Hz), 121.8 (d, $J = 5.2$ Hz), 124.5 (d, $J = 3.7$ Hz), 124.7 (d, $J = 5.2$ Hz), 129.2 (d, $J = 4.5$ Hz), 129.3 (s), 129.7 (s), 141.4 (s), 141.6 (s), 151.2 (s), 151.9 (s); $C_{17}H_{19}N_2O_2P$ (314.32): calcd. C 65.0, H 6.1, N 8.9, P 9.9; found: C 65.6, H 6.2, N 9.0, P 9.8.

(2*S*,5*S*)-2-Naphthoxy-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide (**2g**) and **(2*R*,5*S*)-2-naphthoxy-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide** (**2h**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 75:25) afforded an inseparable mixture (60:40) of the two diastereomers **2g** and **2h** as a white solid in 76% yield. ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 16.7$ (major), 11.4 (minor); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.85$ (m, 4H), 3.50 (m, 5H), 6.90 (m, 1H), 7.15 (m, 8H), 7.50 (m, 1H), 7.80 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.0$ (d, $J = 4$ Hz), 27.2 (d, $J = 5.3$ Hz); 31.4 (d, $J = 2.6$ Hz), 32.3 (s), 44.8 (d, $J = 2.7$ Hz), 46.5 (d, $J = 2.8$ Hz), 49.7 (d, $J = 18.6$ Hz), 51.7 (d, $J = 16.4$ Hz), 57.0 (d, $J = 10.2$ Hz), 58.0 (d, $J = 11.5$ Hz), 115.5 (d, $J = 3.2$ Hz), 116.4 (d, $J = 4.5$ Hz), 117.2 (d, $J = 4.5$ Hz), 121.4 (s), 121.7 (s), 122 (s), 122.1 (s), 124.3 (s), 124.6 (s), 125.5 (s), 125.9 (s), 126.3 (s), 126.6 (s), 127.2 (s), 127.6 (s), 129.2 (s), 129.4 (s), 134.7 (s), 141.3 (s), 141.6 (s), 147.2 (s), 148 (s); $C_{21}H_{21}N_2O_2P$ (364.38): calcd. C 69.2, H 5.8, N 7.7, P 8.5; found C 68.9, H 5.7, N 7.9, P 8.7.

(1*S*,6*S*)-7,9-Dimethyl-8-phenoxy-7,9-diaza-8-phosphabicyclo[4.3.0]nonane 8-oxide (**2i**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 80:20) afforded **2i** as a pale yellow syrup in 85% yield. $[\alpha]_D^{25} = -56.0$ ($c = 0.925$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 23.8$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.25$ (m, 4H), 1.80 (m, 2H), 2.05 (m, 2H), 2.60 (m, 2H), 2.60 (d, $J = 2.0$ Hz, 3H), 2.65 (d, $J = 2.1$ Hz, 3H), 7.25 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 23.8$ (s, 2C), 27.6 (s), 27.8 (s), 28.1 (d, $J = 10.6$ Hz), 29.7 (d, $J = 2.4$ Hz), 62.5 (d, $J = 10.0$ Hz), 64.5 (d, $J = 9.9$ Hz), 120.7 (d, $J = 3.9$ Hz, 2C), 124.0 (s), 129.2 (s, 2C), 151.4 (d, $J = 9.0$ Hz); $C_{14}H_{21}N_2O_2P$ (280.30): calcd. C 60.0, H 7.5, N 10.0, P 11.0; found C 60.6, H 7.7, N 9.9, P 11.2.

(4*S*,5*S*)-1,3-Dimethyl-4,5-diphenyl-2-phenoxy-1,3,2-diazaphospholidine 2-oxide (**2j**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 80:20) afforded **2j** as a pale yellow syrup in 80% yield. M.p. 108 °C; $[\alpha]_D^{25} = +22.5$ ($c = 1$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 20.3$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.56$ (d, $J = 2.5$ Hz, 3H), 2.61 (d, $J = 6$ Hz, 3H), 3.97 (dd, $J = 21.3$ Hz, $J = 8.5$ Hz, 2H), 6.90 (m, 2H), 7.30 (m, 13H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 29.8$ (d, $J = 3.8$ Hz), 30.8 (d, $J = 2.4$ Hz), 70.3 (d, $J = 11.7$ Hz), 71.5 (d, $J = 12.5$ Hz), 121.0 (s), 121.1 (s), 124.5 (s), 127.6 (s, 2C), 127.9 (s), 128.2 (s), 128.5 (d, $J = 6.7$ Hz, 2C),129.0 (s, 2C), 129.7 (s), 137.0 (d, $J = 10.1$ Hz), 137.9 (d, $J = 7.3$ Hz), 152.4 (d, $J = 8.6$ Hz); $C_{22}H_{23}N_2O_2P$ (378.41): calcd. C 69.8, H 6.1, N 7.4, P 8.2; found C 70.2, H 6.0, N 7.2, P 8.3.

(1*R*,7*R*)-9,9-Dimethyl-4-phenoxy-3,5,8,10-tetraoxa-4-phosphabicyclo-[5.3.0]decane 4-oxide (**2k**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 50:50) afforded **2k** as a colorless syrup in 25% yield. $[\alpha]_D^{25} = +50.9$ ($c = 1.1$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = -8.1$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.47$ (s, 6H), 4.20 (m, 2H), 4. 50 (m, 4H), 7.30 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.6$ (s), 26.7 (s), 66.3 (d, $J = 5.5$ Hz), 67.1 (d, $J = 5.8$ Hz), 77.6 (s), 78.0 (s), 111.4 (s), 119.9 (d, $J = 4.4$ Hz, 2C), 125.5 (s), 129.8 (s, 2C), 169.7 (s); $C_{13}H_{17}O_6P$ (300.24): calcd. C 52.0, H 5.7, P 10.5; found C 52.6, H 5.8, P 10.1.

(*R*,*R*)-1,1′-Binaphthalene-2,2′-diylphenylphosphate (**2l**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 20:80) afforded **2l** as a white solid in 90% yield. $[\alpha]_D^{25} = -276.0$ ($c = 0.5$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = -4.3$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.40$ (m, 12H), 7.71 (d, $J = 8.9$ Hz, 1H), 8.04 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 117.8$ (s), 119.9 (s), 120.0 (s), 120.1 (s), 120.6 (d, $J = 2.7$ Hz), 121.2 (s), 121.6 (s), 123.8 (s), 124.3 (s), 125.6 (s), 125.9 (s, 2C), 126.9 (s, 2C), 127.0 (s), 127.2 (s), 128.6 (d, $J = 4.0$ Hz), 129.9 (s, 2C), 131.2 (s), 131.7 (s), 132.0 (s), 132.3 (s), 146.0 (d, $J = 10.2$ Hz), 147.3 (d, $J = 12.4$ Hz), 150.3 (d, $J = 7.9$ Hz); $C_{26}H_{17}O_4P$ (424.39): calcd. C 73.6, H 4, P 7.3; found: C 73.4, H 4.2, P 7.2.

General procedure for the preparation of compounds 3b–k: To a stirred solution of the corresponding compounds (**2a–k**) (2.5 mmol) in dry THF (25 mL) under N_2 was slowly added at −78 °C a solution of LDA (2M in THF, 5.5 mmol). The mixture was allowed to warm to RT and was then quenched by addition of a saturated solution of NH_4Cl (20 mL). The product was extracted with ethyl acetate (2 × 30 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography on a silica gel column.

(2*S*,4*R*,5*S*)-3,4-Dimethyl-2-(2-hydroxyphenyl)-5-phenyl-1,3,2-oxazaphospholidine 2-oxide (**3b**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 33:67) afforded **3b** as a white solid in 86% yield. M.p. 109 °C; $[\alpha]_D^{25} = -4.4$ ($c = 0.45$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 38.6$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 6.5$ Hz, 3H), 2.68 (d, $J = 10.3$ Hz, 3H), 3.90 (m, 1H), 5.76 (dd, $J = 6.7$ Hz, $J = 4.4$ Hz, 1H), 7.00 (m, 2H); 7.40 (m, 7H); 10.80 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.8$ (s), 28.5 (d, $J = 6.1$ Hz), 59.4 (d, $J = 11.2$ Hz), 83.4 (s), 109.2 (d, $J = 168.5$ Hz), 117.9 (d, $J = 11.1$ Hz), 119.4 (d, $J = 14.4$ Hz), 126.1 (s, 2C), 128.4 (d, $J = 4.2$ Hz, 2C), 131.3 (s), 131.4 (s), 135.2 (s), 135.7 (d, $J = 4.6$ Hz), 163.4 (d, $J = 7.2$ Hz); $C_{16}H_{18}NO_3P$ (303.29): calcd. C 63.4, H 6.0, N 4.6, P 10.2; found C 63.5, H 6.1, N 4.7, P 10.1.

(2*S*,4*S*)-4-Isopropyl-2-(2-hydroxyphenyl)-3-methyl-1,3,2-oxazaphospholidine 2-oxide (**3c**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 25:75) afforded **3c** as a pale yellow solid in 89% yield. M.p. 88 °C; $[\alpha]_D^{25} = +62.0$ ($c = 0.55$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 40.8$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.01$ (d, $J = 7.0$ Hz, 3H), 1.07 (d, $J = 6.8$ Hz, 3H), 2.18 (m, 1H), 2.56 (d, $J = 9.9$ Hz, 3H), 3.58 (m, 1H), 4.35 (m, 2H), 6.92 (m, 2H), 7.17 (m, 1H)), 7.46 (m, 1H), 10.8 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.5$ (s), 18.2 (s), 27.6 (d, $J = 3.7$ Hz), 28.7 (d, $J = 8.7$ Hz), 64.3 (d, $J = 11.5$ Hz), 66.8 (s), 109.4 (d, $J = 164.5$ Hz), 117.9 (d, $J = 11.2$ Hz), 119.3 (d, $J = 14.5$ Hz), 130.8 (d, $J = 8.7$ Hz), 135.0 (s), 163.2 (d, $J = 6.7$ Hz); $C_{12}H_{18}NO_3P$ (255.25): calcd. C 56.5, H 7.1, N 5.5, P 12.1; found C 56.7, H 7.2, N 5.6, P 12.3.

(2*R*,4*S*)-4-Isopropyl-2-(2-hydroxyphenyl)-3-methyl-1,3,2-oxazaphospholidine 2-oxide (**3d**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 25:75) afforded **3d** as a pale yellow solid in 92% yield. M.p. 106 °C; $[\alpha]_D^{25} = -15.0$ ($c = 0.6$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 44.0$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.98$ (d, $J = 7.0$ Hz, 3H), 1.00 (d, $J = 6.9$ Hz, 3H), 2.13 (m, 1H), 2.61 (d, $J = 11.0$ Hz, 3H), 3.55 (m, 1H), 4.15 (m, 1H), 4.45 (m, 1H), 6.90 (m, 2H), 7.30 (m, 2H), 10.8 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 15.1$ (s), 18.1 (s), 28.1 (d, $J = 7.4$ Hz), 29.4 (d, $J = 5.7$ Hz), 62.7 (d, $J = 9.9$ Hz), 67.9 (d, $J = 2.2$ Hz), 109.1 (d, $J = 174.5$ Hz), 117.9 (d, $J = 12.2$ Hz), 119.3 (d, $J = 14.2$ Hz), 132.1 (d, $J = 7.2$ Hz), 135.3 (d, $J = 2.7$ Hz), 163.7 (d, $J = 4.4$ Hz); $C_{12}H_{18}NO_3P$ (255.25): calcd. C 56.5, H 7.1, N 5.5, P 12.1; found C 56.9, H 7.1, N 5.4, P 12.2.

(2*S*,5*S*)-2-(2-hydroxyphenyl)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]-octane 2-oxide (**3e**) and **(2*R*,5*S*)-2-(2-hydroxyphenyl)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide** (**3f**): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 50:50) afforded **3e** as a white solid in 47% yield and **3f** as a white solid in 44% yield.

3e: M.p. 158 °C; $[\alpha]_D^{25} = +51.4$ ($c = 0.7$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 33.2$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.95$ (m, 4H), 2.97 (m, 1H), 3.57 (m, 1H), 3.76 (m, 1H), 3.99 (m, 2H), 6.78 (m, 1H), 6.97 (m, 4H), 7.19 (m, 4H), 11.15 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.7$ (s), 32.3 (s), 44.5 (s), 49.7 (d, $J = 14.6$ Hz), 60.0 (d, $J = 5.9$ Hz), 112.8 (d, $J = 164.3$ Hz), 116.5 (d, $J = 5.8$ Hz, 2C), 117.6 (d, $J = 11.7$ Hz), 119.5 (d, $J = 13.2$ Hz), 121.9 (s), 129.3 (s, 2C), 131.4 (d, $J = 7.4$ Hz), 134.3 (d, $J = 3.0$ Hz),

141.2 (d, $J = 7.0$ Hz), 162.9 (d, $J = 7.0$ Hz); $C_{17}H_{19}N_2O_2P$ (314.32): calcd. C 65.0, H 6.1, N 8.9, P 9.9; found C 65.6, H 6.0, N 8.7, P 10.0.

3f: M.p. 158 °C; $[\alpha]_D^{25} = +11.4$ ($c = 0.7$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 27.9$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.70$ (m, 1H), 2.10 (q, $J = 6.8$ Hz, 2H), 2.25 (m, 1H), 3.10 (m, 2H), 3.60 (td, $J = 8.7$ Hz, $J = 1.9$ Hz, 1H), 4.10 (m, 1H), 4.30 (m, 1H), 6.90 (m, 4H), 7.30 (m, 5H), 11.40 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 27.4$ (d, $J = 5.9$ Hz), 31.9 (d, $J = 4.4$ Hz), 44.1 (d, $J = 7.2$ Hz), 45.4 (d, $J = 10.4$ Hz), 58.1 (d, $J = 10.3$ Hz), 108.4 (d, $J = 146.8$ Hz), 116.1 (d, $J = 5.6$ Hz, 2C), 118.2 (d, $J = 11.3$ Hz), 119.5 (d, $J = 14.4$ Hz), 121.6 (s), 129.3 (s, 2C), 130.5 (d, $J = 9.1$ Hz), 134.8 (d, $J = 2.5$ Hz), 141.8 (d, $J = 7.4$ Hz), 164.8 (d, $J = 6.2$ Hz); $C_{17}H_{19}N_2O_2P$ (314.32): calcd. C 65.0, H 6.1, N 8.9, P 9.9; found C 65.7, H 6.2, N 8.8, P 9.7.

(2*S*,5*S*)-2-(1-Hydroxy-2-naphthyl)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide (3g) and **(2*R*,5*S*)-2-(1-hydroxy-2-naphthyl)-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane 2-oxide (3h)**: Purification by column chromatography (silica gel; dichloromethane) afforded **3g** as a white solid in 56% yield and **3h** as a white solid in 37% yield.

3g: M.p. 233 °C; $[\alpha]_D^{25} = +161.6$ ($c = 0.625$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 34.2$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.10$ (m, 4H), 3.10 (m, 1H), 4.00 (m, 4H), 7.00 (m, 1H), 7.30 (m, 6H), 7.70 (m, 2H), 7.85 (m, 1H), 8.57 (m, 1H), 12.29 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.7$ (s), 32.3 (s), 44.4 (s), 49.7 (d, $J = 14.0$ Hz), 60.0 (d, $J = 5.3$ Hz), 104.4 (d, $J = 167$ Hz), 116.5 (d, $J = 5.3$ Hz, 2C), 119.0 (d, $J = 14.2$ Hz), 121.8 (d, $J = 3.2$ Hz), 123.5 (d, $J = 4.5$ Hz), 125.0 (d, $J = 4.5$ Hz), 125.6 (s, 2C), 125.7 (s), 127.3 (s), 128.7 (s), 129.2 (s), 136.6 (s), 141.1 (s), 161.5 (d, $J = 7.7$ Hz); $C_{21}H_{21}N_2O_2P$ (364.38): calcd. C 69.2, H 5.8, N 7.7, P 8.5; found C 69.1, H 5.7, N 8.1, P 8.6.

3h: M.p. 197 °C; $[\alpha]_D^{25} = -23.0$ ($c = 0.4$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 29.2$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.80$ (m, 1H), 2.06 (q, $J = 6.8$ Hz, 2H), 2.30 (m, 1H), 3.10 (m, 2H), 3.70 (td, $J = 2.1$ Hz, $J = 8.7$ Hz, 1H), 4.10 (m, 1H), 4.35 (m, 1H), 6.87 (m, 2H), 7.20 (m, 5H), 7.60 (m, 3H), 8.47 (d, $J = 8$ Hz, 1H), 12.44 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 27.4$ (d, $J = 6.6$ Hz), 32.0 (d, $J = 4.2$ Hz), 44.2 (d, $J = 7.0$ Hz), 54.5 (d, $J = 10.2$ Hz), 58.1 (d, $J = 10.4$ Hz), 99.9 (d, $J = 149.7$ Hz), 116.1 (d, $J = 4.5$ Hz, 2C), 119.2 (d, $J = 14.3$ Hz), 121.5 (s), 123.7 (s), 124.7 (d, $J = 9.2$ Hz), 125.5 (d, $J = 10$ Hz), 125.9 (s), 127.3 (s), 129.0 (s), 129.3 (s, 2C), 136.8 (s), 141.9 (d, $J = 7.2$ Hz), 164.0 (d, $J = 7.0$ Hz); $C_{21}H_{21}N_2O_2P$ (364.38): calcd. C 69.2, H 5.8, N 7.7, P 8.5; found C 69.3, H 5.9, N 7.9, P 8.5.

(1*S*,6*S*)-7,9-Dimethyl-8-(2-hydroxyphenyl)-7,9-diaza-8-phosphabicyclo[4.3.0]nonane 8-oxide (3i): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 33:67) afforded **3i** as a white solid in 93% yield. M.p. 112 °C; $[\alpha]_D^{25} = +15.8$ ($c = 0.95$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 39.2$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.19$ (m, 4H), 1.97 (m, 4H), 2.27 (d, $J = 12.0$ Hz, 3H), 2.47 (d, $J = 12.0$ Hz, 3H), 2.64 (m, 1H), 2.85 (m, 1H), 6.82 (m, 2H), 7.06 (m, 1H), 7.30 (m, 1H), 11.17 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 24.1$ (s), 24.2 (s), 28.1 (s, 2C), 28.3 (d, $J = 2.1$ Hz), 28.5 (d, $J = 6.0$ Hz), 63.3 (d, $J = 6.0$ Hz), 66.0 (d, $J = 7.0$ Hz), 110.1 (d, $J = 149.0$ Hz), 117.5 (d, $J = 11.0$ Hz), 119.0 (d, $J = 13.0$ Hz), 131.5 (d, $J = 8.0$ Hz), 134.3 (d, $J = 2.0$ Hz), 163.7 (d, $J = 6.0$ Hz); $C_{14}H_{21}N_2O_2P$ (280.30): calcd. C 60.0, H 7.5, N 10.0, P 11.0; found C 60.3, H 7.6, N 10.1, P 11.1.

(4*S*,5*S*)-1,3-Dimethyl-4,5-diphenyl-2-(2-hydroxyphenyl)-1,3,2-diazaphospholidine 2-oxide (3j): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 25:75) afforded **3j** as a pale yellow solid in 91% yield. M.p. 168 °C; $[\alpha]_D^{25} = -49.0$ ($c = 0.525$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 38.8$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.31$ (d, $J = 10.2$ Hz, 3H), 2.50 (d, $J = 10.6$ Hz, 3H), 4.26 (dd, $J = 22.9$ Hz, $J = 8.7$ Hz, 2H), 7.25 (m, 14H), 11.47 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.7$ (d, $J = 6.5$ Hz), 29.8 (d, $J = 4.2$ Hz), 71.6 (d, $J = 7.7$ Hz), 73.6 (d, $J = 8.7$ Hz), 110.2 (d, $J = 155.5$ Hz), 115.5 (s), 118.0 (d, $J = 10.2$ Hz), 119.4 (d, $J = 14.0$ Hz), 120.0 (s), 127.5 (s, 2C), 127.9 (s, 2C), 128.4 (s, 2C), 128.7 (s, 2C), 131.5 (d, $J = 7.9$ Hz), 134.6 (d, $J = 2.3$ Hz), 136.9 (d, $J = 5.8$ Hz), 137.4 (d, $J = 8.9$ Hz), 164.0 (d, $J = 7.2$ Hz); $C_{22}H_{23}N_2O_2P$ (378.41): calcd. C 69.8, H 6.1, N 7.4, P 8.2; found C 70.1, H 6.1, N 7.3, P 8.1.

(1*R*,7*R*)-9,9-Dimethyl-4-(2-hydroxyphenyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[3.5.0]decane 8-oxide (3k): Purification by column chromatography (silica gel; ethyl acetate/petroleum ether 25:75) afforded **3k** as a white solid in 95% yield. M.p. 117 °C; $[\alpha]_D^{25} = +56.0$ ($c = 0.45$, CH_2Cl_2); ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 23.7$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.40$ (s, 3H), 1.41 (s, 3H), 4.04 (m, 2H), 4.25 (m, 1H), 4.34 (m, 1H), 4.51 (m, 2H), 6.86 (m, 2H), 7.35 (m, 2H), 9.00 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.7$ (s), 26.8 (s), 64.4 (d, $J = 7.3$ Hz), 67.4 (d, $J = 8.6$ Hz), 77.9 (d, $J = 2.8$ Hz), 78.8 (s), 111.5 (d, $J = 151.0$ Hz), 112.1 (s), 117.8 (d, $J = 12.8$ Hz), 119.6 (d, $J = 13.6$ Hz), 131.7 (d, $J = 5.5$ Hz), 135.7 (s), 161.2 (s); $C_{13}H_{17}O_6P$ (300.24): calcd. C 52.0, H 5.7, P 10.5; found C 52.4, H 5.9, P 10.2.

Acknowledgments: We thank Dr. Michel Giorgi for his kind assistance with X-ray analysis of compounds **3e** and **3f** and Dr. Frédéric Fotiadu for fruitful discussions. We are grateful to CNRS for its financial support.

Received: November 17, 1997 [F893]

[1] a) I. Ojima, *Catalytic Asymmetric Synthesis*, VCH, Weinheim, **1993**; b) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1993**.

[2] H. Brunner, W. Zeittlmeir, *Handbook of Enantioselective Catalysis: Vol. I*, *Products and Catalysts*, and *Vol II*, *Ligands, References*, VCH, Weinheim, **1993**.

[3] a) A. Togni, L. M. Venanzi, *Angew. Chem.* **1994**, *106*, 517; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497; b) J. M. J. Williams, *Synlett* **1996**, 705.

[4] These compounds may be regarded as analogues of 1,3-diketone-type ligands of various transition metals. They may form complexes with metal ions and have been used in the preparation of ligands capable of extracting ammonium compounds from aqueous to organic phases. See: A. H. Alberts, K. Timmer, J. G. Noltes, A. L. Spek, *J. Am. Chem. Soc.* **1979**, *101*, 3375.

[5] L. S. Melvin, *Tetrahedron Lett.* **1981**, *22*, 3375.

[6] a) B. Dhawan, D. Redmore, *J. Org. Chem.* **1984**, *49*, 4018; b) B. Dhawan, D. Redmore, *J. Org. Chem.* **1986**, *51*, 179; c) B. Dhawan, D. Redmore, *ibid.* **1991**, *56*, 833; d) B. Dhawan, D. Redmore, *Synth. Commun.* **1985**, *15*, 411; e) B. Dhawan, D. Redmore, *ibid.* **1987**, *17*, 465; f) B. Dhawan, D. Redmore, *J. Chem. Res.* **1988**, 222; g) T. Calogeropoulou, G. B. Hammond, D. F. Wiemer, *J. Org. Chem.* **1987**, *52*, 4185; h) S. Li, G. Wang, *Phosphorus Sulfur Silicon Relat. Elem.* **1991**, *61*, 119; i) D. Hellwinkel, R. Lenz, *Chem. Ber.* **1985**, *118*, 66 and references therein.

[7] M. Watanabe, M. Date, K. Kawanishi, T. Hori, S. Furukawa, *Chem. Pharm. Bull.* **1990**, *38*, 2637.

[8] D. A. Casteel, S. P. Peri, *Synthesis* **1991**, 691.

[9] S. C. Welch, J. A. Levine, I. Bernal, J. Cetrullo, *J. Org. Chem.* **1990**, *55*, 5991.

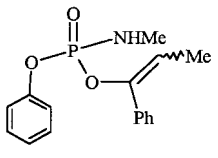
[10] a) T. S. Lobana in *The Chemistry of Organophosphorus Compounds*, *Vol. 2* (Ed.: F. R. Hartley), Wiley, New York, **1992**, pp. 409–566; b) T. S. Lobana, *Prog. Inorg. Chem.* **1989**, *37*, 495; c) H. B. Kagan, M. Sasaki in *The Chemistry of Organophosphorus Compounds*, (Ed.: F. R. Hartley), John Wiley, New York, **1990**, pp. 51–102.

[11] N. Auner, J. Weis, *Organosilicon Chemistry. From Molecules to Materials*, VCH, Weinheim, **1994**, pp. 61–63.

[12] The definitions of the *syn* and *anti* isomers are according to the relative positions of substituents C_4 and C_3 in the five-membered ring with respect to the extracyclic aryl group. If they are on the same side of the five-membered phosphorus-containing ring, we call it a *syn* isomer, otherwise it is an *anti* isomer.

[13] The structure of the major diastereomer has been established by comparison with the results obtained by Inch et al. in the stereospecific synthesis of optically active 1,3,2-oxazaphospholidine-2-one derived from (−)-ephedrine and the fact that these corresponding acid chlorides undergo substitution with phenoxide anions with retention of configuration at the phosphorus atom. See: D. B. Cooper, C. R. Hall, J. M. Harrison, T. D. Inch, *J. Chem. Soc. Perkin Trans. I* **1977**, 1969.

[14] Base-induced rearrangement of diastereomer *syn*-**2b** affords a very labile, nonrearranged eliminative ring-open compound in 60% yield. Its structure has been clearly established by NMR spectroscopic analysis; however, the absolute configuration at the phosphorus atom has not been precisely determined. ^{31}P NMR (40.5 MHz, $CDCl_3$): $\delta = 0.12$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.8$ (dd, $J = 7.4$ Hz, $J = 2.7$ Hz, 3H), 2.6 (dd, $J = 12.7$ Hz, $J = 5.8$ Hz, 3H), 3.34 (m, 1H),



0947-6539/98/0406-1066 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 6

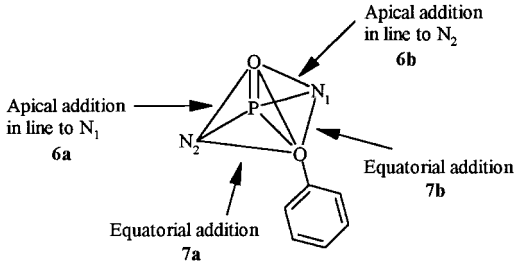
5.89 (dd, $J = 7.3$ Hz, $J = 2.8$ Hz, 1H), 6.9 (m, 1H), 7.30 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 12.9$ (s), 27.5 (s), 111.9 (d, $J = 4.6$ Hz), 115.4 (s), 119.3 (s), 120.1 (d, $J = 4.4$ Hz), 124.6 (s), 128.0 (d, $J = 8.7$ Hz, 2C), 128.3 (d, $J = 4.8$ Hz, 2C), 129.3 (d, $J = 14.3$ Hz, 2C), 134.1 (d, $J = 4.3$ Hz), 146.1 (d, $J = 9.4$ Hz), 150.7 (d, $J = 7.1$ Hz).

[15] Hitherto, the only reported method for the preparation of such compounds consisted of an exchange reaction between bis(dimethylamino)*o*-anisyl phosphine and a chiral auxiliary, followed by oxidation with *t*BuOOH. Subsequent demethylation led exclusively to diastereomer *anti*-**3e** with retention of the configuration on the phosphorus. The *syn* diastereomer could not be obtained owing to the highly unstable intermediate compound which totally epimerizes at the phosphorus atom to produce the thermodynamic *anti* diastereomer. See: a) P. Cros, G. Buono, G. Peiffer, D. Denis, A. Mortreux, F. Petit, *New. J. Chem*. **1987**, *11*, 573; b) H. Arzoumanian, G. Buono, M'B. Choukrad, J. F. Petrignani, *Organometallics* **1988**, *7*, 59; c) J. M. Brunel, O. Chiodi, B. Faure, F. Fotiadu, G. Buono, *J. Organomet. Chem.* **1997**, *529*, 285.

[16] a) **X-ray analysis of *anti*-3g**: A white plate-like single crystal of $C_{17}H_{19}N_2O_2P$, obtained by recrystallization in toluene, with approximate dimensions $0.4 \times 0.3 \times 0.3$ mm, was mounted on a glass capillary. All the measurements were made on a Rigaku diffractometer with $Mo_{K\alpha}$ radiation. Cell constants and the orientation matrix for data collection were obtained from a least-square refinement with setting angles of 30 reflections in the range $80 < 2\theta < 100^\circ$, which corresponded to an orthorhombic cell with dimensions: $a = 8.085(3)$, $b = 10.282(3)$, $c = 19.156(9)$ Å. For $Z = 4$ and $M = 314.33$, $\rho_{calcd} = 1.31$ g cm^{-3}. The space group was determined to be $P2_12_12_1$ from the systematic absences. A total of 3068 reflections were collected at $T = 294$ K. The standards were measured after every 120 reflections. Among the first 200 pairs of reflections, the signs of the corresponding calculated differences established that the molecule is described with the correct absolute configuration *R*. b) **X-ray analysis of *syn*-3f**: A white plate-like single crystal of $C_{17}H_{19}N_2O_2P$, obtained by recrystallization in ethyl acetate, with approximate dimensions $0.7 \times 0.4 \times 0.2$ mm, was mounted on a glass capillary. All the measurements were made on a Rigaku diffractometer with $Mo_{K\alpha}$ radiation. Cell constants and the orientation matrix for data collection were obtained from a least-square refinement with setting angles of 30 reflections in the range $80 < 2\theta < 100^\circ$, which corresponded to an orthorhombic cell with dimensions: $a = 9.035(5)$, $b = 10.660(4)$, $c = 32.77(1)$ Å. For $Z = 8$ and $M = 314.33$, $\rho_{calcd} = 1.32$ g cm^{-3}. The space group was determined to be $P2_12_12_1$ from the systemic absences. A total of 3540 reflections were collected at $T = 294$ K. The standards were measured after every 120 reflections. Among the first 200 pairs of reflections, the signs of the corresponding calculated differences established that the molecule is described with the correct absolute configuration *S*. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101 014. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit§ccdc.cam.ac.uk).

[17] Such retention of configuration has already been described for oxirane formation reaction of pentacoordinate 1,2λ^6-oxathietanes. See: T. Kawashima, F. Ohno, R. Okazaki, H. Ikeda, S. Inagaki, *J. Am. Chem. Soc.* **1996**, *118*, 12 455.

[18] As a result of the stability of some pentacoordinate square pyramidal (SP) phosphorus species, it is also possible to consider mechanistic pathways proceeding via SP intermediates with the four-membered oxaphosphetane ring and the five-membered diazaphospholane ring in basal positions and the oxygen anion group in an axial position. The stereochemistry of the migration derives from a *cis* basal interaction of the entering/leaving group. See also: G. R. J. Thatcher, R. Kluger in *Mechanism and Catalysis of Nucleophilic Substitution in Phosphate Esters* in *Advances in Physical Organic Chemistry*, *Vol. 25* (Ed.: D. Betheil), Academic Press, New York, **1989**, pp. 99–265.



[19] K. Mislow, *Acc. Chem. Res.* **1970**, *3*, 321.

[20] F. Westheimer, *Acc. Chem. Res.* **1968**, *1*, 70.

[21] Such phosphetane intermediates have played an important role in the elucidation of the factors that influence the stereochemistry of the Wittig reaction. See: a) B. E. Maryanoff, A. B. Reitz, *Chem. Rev.* **1989**, *89*, 863; b) E. Vedejs, C. F. Marth, R. Ruggieri, *J. Am. Chem. Soc.* **1988**, *110*, 3940; c) B. E. Maryanoff, A. B. Reitz, *Phosphorus Sulfur Relat. Elem.* **1986**, *27*, 167; d) B. E. Maryanoff, A. B. Reitz, M. S. Mutter, R. R. Inners, H. R. Almond, Jr., R. R. Whittle, R. A. Olofson, *J. Am. Chem. Soc.* **1986**, *108*, 7664; e) A. B. Reitz, S. O. Nortey, A. D. Jordan, Jr., M. S. Mutter, B. E. Maryanoff, *J. Org. Chem.* **1986**, *51*, 3302; f) H. J. Bestmann, K. Roth, E. Wilhelm, R. Böhme, H. Burzlaff, *Angew. Chem.* **1979**, *91*, 945; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 876; g) D. Hellwinkel, W. Krapp, *ibid.* **1974**, *86*, 524 and **1974**, *13*, 540.

[22] Recently, the synthesis of isolable 1,2-oxaphosphetanes has been achieved and X-ray crystallographic analysis have been performed to determine the structure of such compounds. See: a) T. Kawashima, K. Kato, R. Okazaki, *Angew. Chem.* **1993**, *105*, 941; *Angew. Chem. Int. Ed. Engl*. **1993**, *32*, 869; b) T. Kawashima, K. Kato, R. Okazaki, *J. Am. Chem. Soc.* **1992**, *114*, 4008.

[23] E. Vedejs, T. J. Fleck, *J. Am. Chem. Soc.* **1989**, *111*, 5861.

[24] For oxaphosphetane pseudorotation see: E. Vedejs, C. F. Marth, *J. Am. Chem. Soc.* **1989**, *111*, 1519.

[25] R. R. Holmes, *Pentacoordinated Phosphorus, Vol. 2*, ACS Monograph 176, American Chemical Society, **1980**, Washington, D.C.

[26] S. McDowell, A. Streitwieser, *J. Am. Chem. Soc.* **1985**, *107*, 5849.

[27] S. J. Tripett, *Pure Appl. Chem.* **1974**, *40*, 585.

[28] R. S. Berry, *J. Chem. Phys.* **1960**, *32*, 933. Nevertheless, in any case turnstile rotation must be taken into consideration as a mechanistic alternative. See: a) P. Gillespie, P. Hoffmann, H. Klusacek, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis, I. Ugi, *Angew. Chem*. **1971**, *83*, 691; *Angew. Chem. Int. Ed. Engl*. **1971**, *10*, 687; b) F. Ramirez, *Bull. Soc. Chim. Fr.* **1970**, 3491.

[29] K. Mislow, *Acc. Chem. Res.* **1968**, *1*, 70.

[30] R. Luckenbach, *Dynamic Stereochemistry of Pentacoordinated Phosphorus and Related Elements*, Thieme, Stuttgart, **1973**, pp. 99–107.

[31] Previous investigations have been carried out on the sterochemical behavior of the four-membered oxyphosphoranes (1,2-oxaphosphetanes) which have three P–C bonds. See: a) F. Ramirez, J. F. Pilot, O. P. Madan, C. P. Smith, *J. Am. Chem. Soc.* **1968**, *90*, 1275; b) F. Ramirez, C. P. Smith, J. F. Pilot, *ibid.* **1968**, *90*, 6726; c) D. B. Denney, D. Z. Denney, C. D. Hall, K. L. Marsi, *ibid.* **1972**, *94*, 245; d) See also ref. [23] for a recent and pertinent study of the *spiro*-oxaphosphetane pseudorotation.

[32] According to Holmes' model for destabilized TBP intermediates **7** and **8**, the estimated steric interaction energies between the four-membered oxaphosphetane ring or the five-membered diazaphospholane ring and the oxygen anion group are 28 and 26 kcal mol^{-1}, respectively (the relative values of oxaphosphetane ring strain for use in estimating isomer energies in TBP are ax–eq = 2 kcal mol^{-1} and eq–eq = 26 kcal mol^{-1}). See: a) R. R. Holmes, *J. Am. Chem. Soc.* **1978**, *100*, 433; b) ref. [24], Table 1.7–1.9, pp. 35–89.

[33] Recently, analogous chiral compounds, such as phosphoramides[34] as well as oxazaphospholidine oxides,[35] phosphoramidates, and thiophosphinamides[36] have been shown to be efficient chiral catalysts in various enantioselective reactions.

[34] For recent examples see: a) S. E. Denmark, S. B. D. Winter, X. Su, K. Wong, *J. Am. Chem. Soc.* **1996**, *118*, 7404; b) K. Iseki, Y. Kuroki, M. Takahashi, Y. Kobayashi, *Tetrahedron Lett*. **1996**, *37*, 5149.

[35] O. Chiodi, F. Fotiadu, M. Sylvestre, G. Buono, *Tetrahedron Lett*. **1996**, *37*, 39.

[36] a) R. Hulst, H. Heres, N. Peper, R. M. Kellog, *Tetrahedron Asymmetry* **1996**, *7*, 1373; b) K. Soai, Y. Hirose, Y. Ohno, *ibid.* **1993**, *4*, 1473; c) K. Soai, Y. Ohno, Y. Inoue, T. Tsuruoka, T. Hirose, *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 145.