Formation of Diastereoisomerically Pure Oxazaphospholes and Their Reaction to Chiral Phosphane-Borane Adducts

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Starting with achiral phosphines and (1*S*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol ((+)-pseudoephedrine) or (1*R*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol ((−)-ephedrine), as chiral auxiliaries, diastereoisomerically pure oxazaphospholes were prepared (*Scheme 1*). The configuration at the P-atom is controlled by the configuration at the Ph-substituted C(1) of (+)-pseudoephedrine or (−)-ephedrine, respectively. This was confirmed by X-ray crystal-structure analyses of two intermediate compounds in the synthesis route to the chiral triarylborane-phosphane adducts.

1. Introduction. – Optically active bis[phosphines] [1] such as diop [2], binap [3], biphemp [4], chiraphos [5], bppfa [6], duphos [7], dipamp [8], or a similar, new C_2-symmetric chiral P-ligand [9] and new P^N-ligands [10] are useful for asymmetric catalysis of bulk and laboratory-scale reactions [11]. Only dipamp and some of the new P^P- or P^N-ligands (*cf.* [9] [10c]) have the P-atom as the center of chirality, whereas all the other ligands possess an inherently chiral backbone. In transition-metal catalysis with various kinds of substrates, atropisomeric bis[phosphanes] with additional centers of chirality at the P-atoms, where different steric and electronic properties are tunable, can be crucial for the attainment of high degrees of stereoselectivity. For the best matching and selective recognition of the catalytically active transition-metal complex, bis[phosphanes] with a chiral backbone and equipped with additional centers of chirality at the P-atoms are of great interest. However, not many compounds of this class have been reported so far [8] [9] [12]. Therefore, it is important to further develop accessibility to asymmetrically substituted phosphines. Since phosphanes, due to their oxophilicity, exhibit a strong tendency in air to form the corresponding phosphane oxides, and because of their lability in the presence of aryl- or alkyl halides, it is necessary to perform their synthesis with protective groups. In recent years, there has been a rebirth in the use of BH_3 as a protective group for phosphines [13], even though the extraordinary stability and inertness of the P−B bond has long been known [14]. Using (−)- and (+)-ephedrine as chiral auxiliaries, *Jugé et al.* developed an elegant and flexible synthesis for enantiomerically pure phosphines [15]. However, to the best of our knowledge, the use of the commercially available (+)-pseudoephedrine, with the (1*S*,2*S*)-configuration, which is a diastereoisomer of (−)-ephedrine (opposite configuration at C(1)), has not been reported so far. In this work, we show that the control of the formation of the diastereoisomerically pure oxazaphospholes from the two β-amino alcohols is controlled by the Ph-substituted C(1) atom of both stereoisomers.

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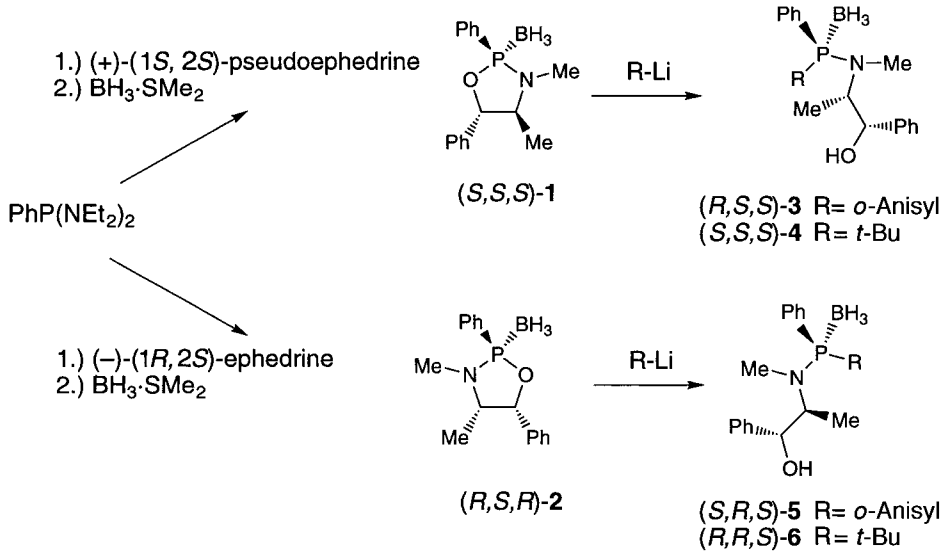
[1]) Part of the Ph. D. thesis of *A.J.R.*, University of Zurich.

2. Results and Discussion. – The reaction of *N*,*N*,*N*′,*N*′-tetraethyl-*P*-phenylphosphinediamine, (+)-pseudoephedrine or (−)-ephedrine, and the dimethylsulfide-borane complex in toluene yielded the corresponding crystalline and diastereoisomerically pure heterocycles (2*S*,4*S*,5*S*)-2,3,4,5-tetrahydro-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphosphole–*P*-borane (1/1) ((*S*,*S*,*S*)-**1**; up to 95% isolated yield) and (2*R*,4*S*,5*R*)-2,3,4,5-tetrahydro-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphosphole–*P*-borane (1/1) ((*R*,*S*,*R*)-**2**; 82%), respectively (*cf. Scheme 1*) [15].

Scheme 1



The two diastereoisomers (*S*,*S*,*S*)-**1** and (*R*,*S*,*R*)-**2** were not distinguishable on the basis of their ^{1}H-NMR spectra, but the chemical shifts and coupling constants in the ^{31}P- and ^{11}B-NMR spectra were distinctly different (see *Table 1*). Also, the opposite sign of the $[\alpha]_D^{25}$ values in $CHCl_3$ for (*S*,*S*,*S*)-**1** (−10.0) and ((*R*,*S*,*R*)-**2** (+4.5) confirmed that they were diastereoisomers. An X-ray crystal-structure analysis has been published for (*R*,*S*,*R*)-**2** [16]. It revealed the *trans*-relationship between the two Ph groups at P(2) and C(5) and led to the conclusion that the sense of chirality at the P-atom is (*R*). As a consequence, a *trans*-relationship between the Ph substituents in its diastereoisomer, (*S*,*S*,*S*)-**1**, would require the (*S*)-configuration at P(2).

Unfortunately, no suitable crystals of (*S*,*S*,*S*)-**1** could be obtained for an X-ray crystal-structure analysis. However, the configuration at P(2) could be deduced from the X-ray crystal-structure analyses of compounds that were derived from (*S*,*S*,*S*)-**1**, because it is known that, in chiral phosphane-borane compounds, the P–O linkage can be cleaved with retention of the configuration at the P-atom [13] by using aryl- or alkyllithium reagents (*cf. Scheme 1*). Thus, (*S*,*S*,*S*)-**1** and (*R*,*S*,*R*)-**2** reacted with either *o*-anisyllithium or *t*-BuLi to give the corresponding *o*-anisyl (=2-methoxyphenyl) derivatives (*R*,*S*,*S*)-**3** and (*S*,*R*,*S*)-**5**, respectively, or their *tert*-butyl analogues (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**6**, respectively, in high yields (93–97%; *Scheme 1*).

Table 1. *Chemical Shifts and Coupling Constants in the $^{31}P\{H\}$- and $^{11}B\{H\}$-NMR Spectra of Compounds* **1**–**8**

Compound	$\delta(^{31}P)$[a]) [ppm]	$^1J(^{31}P, ^{11}B)$[b]) [Hz]	$\delta(^{11}B)$[c]) [ppm]	$^1J(^{31}P, ^{11}B)$[d]) [Hz]
(*S*,*S*,*S*)-**1**	139.9	75.8	– 41.1	75.2
(*R*,*S*,*R*)-**2**	133.0	74.0	– 40.3	74.0
(*R*,*S*,*S*)-**3**	71.5	55.2	– 36.9	56.5
(*S*,*S*,*S*)-**4**	85.5	68.0	– 39.4	69.5
(*S*,*R*,*S*)-**5**	71.1	59.0	– 36.8	58.7
(*R*,*R*,*S*)-**6**	86.5	67.0	– 20.1	68.0
(*R*)-**7**/(*S*)-**7**	107.0	64.5	– 39.8	65.0
(*R*)-**8**/(*S*)-**8**	18.4	54.0	– 37.1	55.3

[a]) ^{31}P-NMR Chemical shifts relative to H_3PO_4 as external standard.
[b]) The signals for the P-atom are *q*.
[c]) ^{11}B-NMR Chemical shifts relative to $BF_3 \cdot OEt_2$ as external standard.
[d]) The signals for the B-atom are *d*.

The ^{1}H-NMR spectra of these compounds clearly showed their diastereoisomeric relationship (*e.g.*, (*R*,*S*,*S*)-**3** and (*S*,*R*,*S*)-**5** on one hand and (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**6** on the other hand). As an example, the *singlet* of Me–C(2) in the compounds derived from (+)-pseudoephedrine appears at 0.8 ppm, whereas it is found at 1.2 ppm for the compounds derived from (–)-ephedrine (*cf. Exper. Part*). In contrast to their precursors, (*S*,*S*,*S*)-**1** and (*R*,*S*,*R*)-**2**, the pairwise diastereoisomeric relationship of the new products **3**–**6** is not obvious from their ^{31}P- and ^{11}B-NMR data (see *Table 1*).

It was possible to grow suitable crystals of (*R*,*S*,*S*)-**3** for an X-ray crystal-structure analysis (*Fig. 1*, and *Tables 2* and *3*). This experiment independently confirmed the absolute configuration of the molecule and revealed that the configuration at the P-atom was indeed *R* (see *Fig. 1*). In turn, this finding requires the (*S*)-configuration at P(2) in (*S*,*S*,*S*)-**1**, since the described substitution reactions occur with retention of configuration at the P-atom[2]).

The observed bond lengths between the P-atom and its ligands in (*R*,*S*,*S*)-**3** are in good agreement with other structures of a similar type (*cf.* [15b][16]). There is a high rotational barrier around the P–B bond (*cf.* [14]) due to hyperconjugation of the B–H orbitals with the d-orbitals of the P-atom. This effect should cause a high dipole moment in such compounds. Indeed, they possess high boiling and melting points compared with their phosphane and borane analogues [14c].

The molecular structure of (*R*,*S*,*S*)-**3** revealed two intramolecular H-bonds. The H-atom of the OH group of the (+)-pseudoephedrine moiety interacts with the N-atom and the O-atom of the anisyl moiety (*cf. Fig. 1*). These H-bonds are part of an anellated five- and six-membered ring system with the H···N bond common to both rings. Because of this H-bonding, the H-atoms at C(1) and C(2) are in an *anti*-periplanar arrangement to each other (for numbering, see *Fig. 1*). Their dihedral angle is 171(2)° in the crystal structure. The ^{1}H-NMR spectrum ($CDCl_3$) of (*R*,*S*,*S*)-**3** discloses a vicinal coupling constant of 9.1 Hz between these two H-atoms, which leads to a dihedral angle of 170° according to the *Karplus-Conroy* equation [17], in excellent agreement with the solid-state structure. As expected, (*S*,*R*,*S*)-**5** shows $^3J(1,2) = 5.5$ Hz, which

[2]) Note that the priority rules of the *CIP* notation of absolute configurations lead in our cases to a formal change of the sense of chirality at the P-atom.

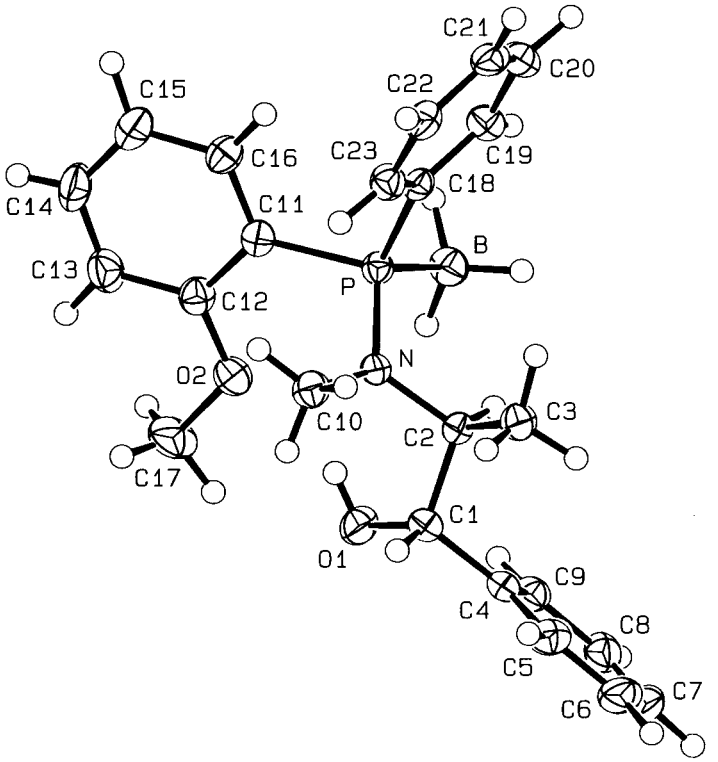


Fig. 1. *Molecular structure of (*R,S,S*)*-**3**. Arbitrary numbering of the atoms; 50% probability ellipsoids.

Table 2. *Bond Lengths* [pm] *and Angles* [°] *around the P-Atom of* (R,S,S)-**3**[a])

P–B	192.3 (2)	N–P–B	112.9(1)
P–N	167.0 (2)	N–P–C(11)	105.20(9)
P–C(11)	182.1 (2)	N–P–C(18)	109.24(8)
P–C(18)	182.4 (2)	C(11)–P–B	113.4(1)
		C(18)–P–B	111.6(1)
		C(11)–P–C(18)	103.96(8)

[a]) E.s.d. in parentheses.

Table 3. *Interatomic Distances* [pm] *and Angles* [°] *at the H-Bonded OH Group of (*R,S,S*)*-**3**[a])

O(1)H···O(2)	218 (3)	O(1)–H···O(2)	152(2)
O(1)H···N	217 (2)	O(1)–H···N	123(2)
O(1)···O(2)	296.0 (3)	O(2)···H···N	85.6(9)
O(1)···N	273.2 (2)	O(1)H···N–P	110.8(7)
		O(1)H···O(2)–C(12)	137.3(6)
		O(1)H···N–C(2)	76.2(7)

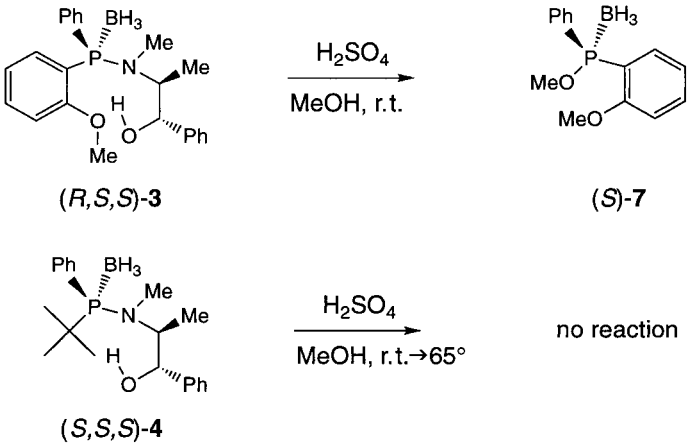
[a]) E.s.d. in parentheses.

would correspond with a dihedral angle for H–C(1)–C(2)–H of 40°. Molecular models demonstrate that this dihedral angle, which is controlled by the (*R*)-configuration at C(1), will also allow intramolecular H-bonding between the OH group at C(1) and N–C(2) as well as MeO of the *o*-anisyl moiety.

Evidence for H-bonding was also found for (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**6**. The dihedral angles of H–C(1)–C(2)–H, calculated from $^3J(1,2)$ of their ^{1}H-NMR spectra, are 180° for (*S*,*S*,*S*)-**4** ($^3J = 9.6$ Hz) and 50° for (*R*,*R*,*S*)-**6** ($^3J = 3.4$ Hz). In these compounds, only the five-membered ring with N–C(2) can be formed upon H-bonding.

By acid-catalyzed methanolysis at room temperature, the P–N bond could easily be cleaved in (*R*,*S*,*S*)-**3** and (*S*,*R*,*S*)-**5** to form (*S*)-**7** and (*R*)-**7**, respectively, in excellent yields (97%). By contrast, (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**6** showed no reaction at all, even after prolonged times under reflux conditions. The starting materials could be isolated without any evidence of decomposition. With a *t*-Bu substituent at the P-atom, it is inert to further substitution reactions ('neopentyl rule') (see *Scheme 2*; (*R*,*S*,*S*)-**3** *vs.* (*R*,*S*,*S*)-**4**). It is noteworthy that the reaction of (*R*,*S*,*S*)-**3** and (*S*,*R*,*S*)-**5** with MeOH in acidic media restores the chiral auxiliaries (+)-pseudoephedrine and (−)-ephedrine, which can be recycled. The methanolysis proceeds with inversion of the configuration at the P-atom. Very characteristic for (*S*)-**7** and (*R*)-**7** is the observed ^3J(H,P) value (between the H-atoms of the MeO group and the P-atom) of 12.1 Hz. The antipodal character and enantiomeric purity of (*S*)-**7** and (*R*)-**7** are obvious from their $[\alpha]_D^{25}$ values.

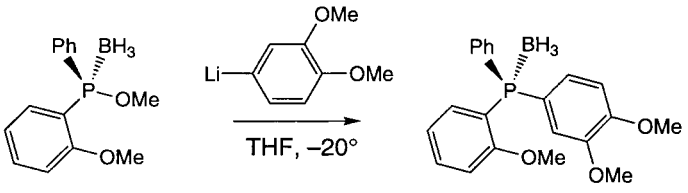
Scheme 2



The newly formed P–O bond in (*S*)-**7** and (*R*)-**7** can be transformed stereospecifically into P–C bonds by using aryl- or alkyllithium reagents, again with retention of the configuration at the P-atom. For example, (3,4-dimethoxyphenyl)lithium reacted with (*S*)-**7** or (*R*)-**7** to give (*R*)-**8** or (*S*)-**8**, respectively, in yields up to 80% (*Scheme 3*)[2]).

The new phosphane-borane adducts with three C-substituents at the P-atom are characterized by their $\delta(^{31}P)$ value of *ca.* 20 ppm. In cases where P–X bonds are involved, *e.g.*, X = N or O, $\delta(^{31}P)$ values are above 100 ppm (*cf. Table 1*). However, remarkable chemical-shift differences are not found in the ^{11}B-NMR spectra of our compounds. They all exhibit $\delta(^{11}B)$ values of *ca.* −38 ppm (see *Table 1*).

Scheme 3



(*R*)-**7** (*S*)-**8**

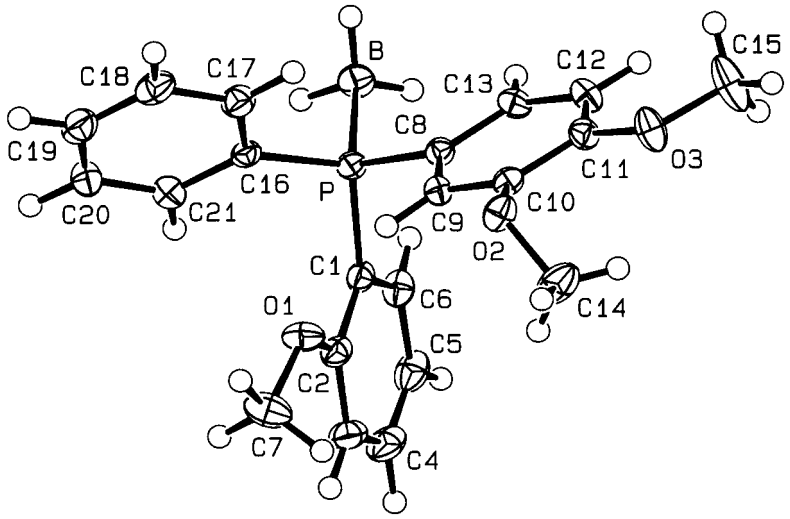


Fig. 2. *Molecular structure of* (S)-**8**. Arbitrary numbering of the atoms; 50% probability ellipsoids.

Compound (*S*)-**8** crystallized well from hexane/AcOEt solution so that it could be subjected to an X-ray crystal-structure determination (*Fig. 2* and *Table 4*). The geometric parameters of (*S*)-**8** are in good agreement with those of other phosphane-borane adducts [16], as well as with those of (*R*,*S*,*S*)-**3**. Remarkable is that all MeO groups are pointing away from the borane group. This crystal effect may provide evidence for the fact that a BH_3 moiety bound to the phosphane carries a high proportion of the electron density of the B–P bond. The absolute configuration of (*S*)-**8** could be confirmed by the X-ray analysis, which also ascertained the stereochemical outcome of the whole reaction sequence starting with (*R*,*S*,*S*)-**2**, where the chiral auxiliary has been (–)-ephedrine.

3. Conclusion. – It has been shown that (+)-pseudoephedrine can be used as a chiral auxiliary to form enantiomerically pure phosphane-borane adducts with different substitution patterns. The opposite configuration at the P-atom can be obtained with (–)-ephedrine as the chiral auxiliary [15]. With (+)-pseudoephedrine as a chiral

Table 4. *Bond Lengths* [pm] *and Angles* [°] *at the P-Atom of* (S)-**8**[a])

P–B	193.3 (2)	C(1)–P–B	112.06(8)
P–C(1)	181.8 (2)	C(1)–P–C(8)	106.03(7)
P–C(8)	181.0 (1)	C(1)–P–C(16)	108.50(7)
P–C(16)	181.1 (2)	C(8)–P–B	113.18(8)
		C(8)–P–C(16)	107.70(7)
		C(16)–P–B	109.17(8)

[a]) E.s.d. in parentheses.

auxiliary, an improvement in the isolated yield (95% *vs.* 82% with (−)-ephedrine) of the diastereoisomerically and enantiomerically pure oxazaphospholes was achieved. Furthermore, it was found that a *trans*-relationship of the Ph substituents in the diastereoisomerically pure oxazaphospholes is crucial for control of the stereoselection. The smaller groups at other positions have no significant influence on the creation of a single configuration at the P-atom by the chiral auxiliaries that have been used.

If a *t*-Bu substituent in an enantiomerically pure phosphane is required, and (+)-pseudoephedrine or (−)-ephedrine are to be used as the chiral auxiliaries, they have to be introduced in the final step. Both enantiomers of such phosphanes are only accessible when both configurations at the P-atom in the five-membered ring of the oxazaphospholes (see (*S*,*S*,*S*)-**1** and (*R*,*S*,*R*)-**2** in *Scheme 1*) are synthetically available. In other cases, where a reversal of the sequence of the substitution reactions at the P-atom is possible, working in the one or the other diastereoisomeric series would be sufficient.

We thank Prof. *W. von Philipsborn* and his former co-workers for ^{11}B- and ^{31}P-NMR spectra, Prof. *M. Hesse* and his co-workers for mass spectra, and the late *H. Frohofer* for elemental analyses. The financial support of this work by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

1. *General.* All reactions were performed under N_2. *N*,*N*,*N*′,*N*′-Tetraethyl-*P*-phenylphosphinediamine was synthesized from *P*,*P*-dichlorophenylphosphine (*Fluka*, *pract.*) and Et_2NH (*Fluka*, *purum*) in Et_2O. THF (*Fluka*, *puriss. p.a.*) was purified over Al_2O_3 (Act. I). Toluene, AcOEt, hexane, i-PrOH, and Et_2O were distilled prior to use. (−)-Ephedrine (=(1*R*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol; *Fluka*, *purum*), (+)-pseudoephedrine (=(1*S*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol; *Fluka*, *purum*), $BH_3 \cdot SMe_2$ (*Fluka*), *t*-BuLi (*Fluka*, *pract. ca.* 1.4M in pentane), 2-bromoanisole (=1-bromo-2-methoxybenzene; *Fluka*, *purum*), Li sand (*Alfa*, in oil; washed with hexane prior to use), and 4-bromoveratrole (=4-bromo-1,2-dimethoxybenzene; *Fluka*, *purum*) were used without further purification. Flash-column chromatography (FC): silica gel (230–400 mesh, ASTM). M.p.: *Büchi* apparatus (model *FP5*); uncorrected. $[\alpha]_D$: *Perkin Elmer 241 MC* polarimeter. NMR Spectra: *Bruker AC 300* (^{1}H), *ARX 300* (^{1}H), and *AM 400* spectrometers (^{11}B, ^{31}P) (^{11}B: 128 MHz, ^{31}P: 161 MHz). δ(H) values relative to internal Me_4Si, δ(B) and δ(P) values relative to $BF_3 \cdot OEt_2$ and H_3PO_4, resp., as external standards; *J* in Hz; f.s.: fine structure. MS: *Finnigan* instrument model *MAT SSQ 700*; EI at 70 eV; ions in *m*/*z* (rel. %).

2. *Crystal-Structure Determinations of* (R,S,S)-**3** *and* (S)-**8**[3]). The data collection and refinement parameters are summarized in *Table 5*. All measurements were conducted on a *Rigaku AFC5R* diffractometer fitted with a 12-kW rotating anode generator. The intensities were collected during $\omega/2\theta$ scans, and three

[3]) 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-134227 and CCDC-134228 for (*R*,*S*,*S*)-**3** and (*S*)-**8**, resp. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033, e-mail: deposit@ccdc.cam.ac.uk).

Table 5. *Crystallographic Data of (*R,S,S*)*-**3** *and (*S*)*-**8**

	(*R*,*S*,*S*)-**3**	(*S*)-**8**
Crystallized from	$CHCl_3$	hexane/AcOEt
Empirical formula	$C_{23}H_{29}BNO_2P$	$C_{21}H_{24}BO_3P$
Formula weight	393.27	366.20
Crystal color, habit	colorless, prism	colorless, prism
Crystal dimensions [mm]	$0.20 \times 0.30 \times 0.33$	$0.20 \times 0.23 \times 0.50$
Temp. [K]	173 (1)	173 (1)
Radiation, wavelength [Å]	MoK_α, 0.71069	MoK_α, 0.71069
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
Z	4	4
Reflections for cell determination	24	23
2θ Range for cell determination [°]	24–40	32–36
Unit cell parameters: a [Å]	14.658(5)	12.984(2)
b [Å]	16.715(8)	14.2447(9)
c [Å]	8.713(5)	10.780(1)
V [Å^3]	2135(1)	1993.8(3)
D_x [g cm^{-3}]	1.224	1.220
μ [mm^{-1}]	0.141	0.149
$2\theta_{(max)}$ [°]	55	60
Total reflections measured	5913	6263
Symmetry-independent reflections	4466	4929
Reflections used ($I > 3\sigma(I)$)	3616	4346
Parameters refined	369	331
R	0.0313	0.0306
wR	0.0268	0.0298
Goodness of fit	1.297	1.575
Final Δ_{max}/σ	0.0007	0.01
$\Delta\rho$ (max; min) [e Å^{-3}]	0.15; −0.19	0.23; −0.19

standard reflections measured after every 150 reflections showed negligible variation in intensity. Each data collection included the measurement of the *Friedel* opposites of all unique reflections with $2\theta < 50°$. The intensities were corrected for *Lorentz* and polarization effects, but not for absorption and equivalent reflections, other than *Friedel* pairs, were merged. Each structure was solved by direct methods with SHELXS86 [18], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The H-atoms were located in difference-electron-density maps, and their positions were refined together with individual isotropic displacement parameters. Corrections for secondary extinction were not applied. All refinements were carried out on F with full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$, where $1/w = [\sigma^2(F_o) + (0.005F_o)^2]$. Neutral-atom scattering factors for non-H-atoms were taken from [19a] and the scattering factors for H-atoms from [20]. Anomalous dispersion effects were included in F_c [21]; the values for f' and f'' were taken from [19b]. All calculations were performed using the TEXSAN [22] crystallographic software package, and the figures were produced with ORTEPII [23].

For each structure, the absolute configuration was determined by refinement [24] of the completed model together with the absolute structure parameter [25], which refined to values of 0.02(8) and 0.09(7) for (*R*,*S*,*S*)-**3** and (*S*)-**8**, resp., and thereby confirmed that the refined coordinates for each structure represent the true enantiomorph.

3. *Syntheses.* 3.1. *(2*S*,4*S*,5*S*)-2,3,4,5-Tetrahydro-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphosphole–*P*-borane (1/1)* ((*S*,*S*,*S*)-**1**). In a three-neck round bottle, a mixture of (+)-pseudoephedrine (10.0 g, 60.5 mmol) and *N,N,N′,N′*-tetraethyl-*P*-phenylphosphinediamine (15.5 ml, 60.5 mmol) in toluene (300 ml) was refluxed overnight. The reaction was monitored by measuring the pH, corresponding to the evolution of Et_2NH. After 16 h, no further Et_2NH could be detected. The slightly yellow soln. was cooled to r.t., and $BH_3 \cdot SMe_2$ (5.8 ml, 60.5 mmol) in toluene (25 ml) was added dropwise. Then, stirring was continued for further 5 h. The solvent was evaporated, and the yellowish, oily residue was crystallized from hexane/i-PrOH, to give (*S*,*S*,*S*)-**1** (16.4 g, 95%).

Colorless crystals. M.p. 103.9–104.7° (hexane/i-PrOH). $[\alpha]_D^{25} = -10.0$ ($c = 0.2$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.30–7.85 (*m*, 10 arom. H); 5.60 (*dd*, $^3J(4,5) = 9.1$, $^3J(5,P) = 2.9$, H–C(5)); 3.68 (*sext.* with f.s., $^3J(4,5) = 9.1$, $^3J(4,Me–C(4)) = 6.5$, $^3J(4,P) = 4.2$, $^4J(4,Me–N) = 11.0$, H–C(4)); 2.68 (*d*, $^4J(4,Me–N) = 11.0$, MeN); 1.7–0.2 (br. *q*, BH_3); 0.83 (*d*, $^3J(4,Me–C(4)) = 6.5$, Me–C(4)). ^{1}H-NOE (400 MHz, $CDCl_3$): 5.60 (*dd*, H–C(5)) → 3.68 (*s*, H–C(4)); 2.68 (MeN) → 3.68 (*m*, H–C(4)); 0.83 (Me–C(4)) → 5.60 (*m*, H–C(5)), 3.68 (*s*, H–C(4)). ^{11}B-NMR ($CDCl_3$): −41.1 (*d*, $^1J(B,P) = 75.2$, BH_3). ^{31}P-NMR: 139.9 (*d*, $^1J(B,P) = 75.8$, P(2)).

3.2. *(2*R*,4*S*,5*R*)-2,3,4,5-Tetrahydro-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphosphole–*P*-borane (1/1)* ((*R*,*S*,*R*)-**2** (*cf.* [15]). As described in *3.1*, with (−)-ephedrine (12.73 g, 78 mmol), *N*,*N*,*N*′,*N*′-tetraethyl-*P*-phenylphosphinediamine (19.5 ml, 78 mmol) in toluene (500 ml), and $BH_3 \cdot SMe_2$ (7.4 ml, 78 mmol) in toluene (32 ml). Crystallization from hexane/i-PrOH gave (*R*,*S*,*R*)-**2** (18.24 g, 82%). White, microcrystalline compound. M.p. 104.7–105.7° (hexane/i-PrOH). $[\alpha]_D^{25} = +4.5$ ($c = 0.1$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.30–7.85 (*m*, 10 arom. H); 5.60 (*dd*, $^3J(4,5) = 9.1$, $^3J(5,P) = 2.9$, H–C(5)); 3.68 (*sext.* with f.s., $^3J(4,5) = 9.1$, $^3J(4,Me–C(4)) = 6.5$, $^3J(4,P) = 4.2$, $^4J(4,Me–N) = 11.0$, H–C(4)); 2.67 (*d*, $^4J(4,Me–N) = 11.0$, MeN); 1.7–0.2 (br. *q*, BH_3); 0.82 (*d*, $^3J(4,Me–C(4)) = 6.5$, Me–C(4)). ^{1}H-NOE (400 MHz, $CDCl_3$): 5.60 (*dd*, H–C(5)) → 3.68 (*s*, H–C(4)); 2.67 (MeN) → 3.68 (*m*, H–C(4)); 0.82 (Me–C(4)) → 5.60 (*m*, H–C(5)), 3.68 (*s*, H–C(4)). ^{11}B-NMR ($CDCl_3$): −40.3 (*d*, $^1J(B,P) = 74$, BH_3). ^{31}P-NMR: 133.0 (*d*, $^1J(B,P) = 74$, P(2)).

3.3. *(1*S*,2*S*)-2-{[(*R*)-(2-Methoxyphenyl)phenylphosphanyl]methylamino}-1-phenylpropan-1-ol–*P*-borane (1/1)* ((*R*,*S*,*S*)-**3**) (*cf.* [15]). To a soln. of (*S*,*S*,*S*)-**1** (1.424 g, 5 mmol) in THF (20 ml) at −78°, 2-methoxyphenyllithium (from 2-bromoanisole (0.62 ml, 5 mmol) and Li sand (35 mg, 5 mmol)) in THF (5 ml) were added dropwise during 10 min. The mixture was stirred for 30 min at −78°, then cooling was stopped. As soon as the mixture reached r.t., the reaction was quenched by addition of H_2O (1 ml). After extraction with Et_2O (3 × 20 ml), the org. phase was dried ($MgSO_4$), and the solvent was removed, and the residue was purified by FC (toluene/AcOEt 10:1). Upon standing, the clear soln. solidified to a white mass: (*R*,*S*,*S*)-**3** (1.91 g, 97%). From $CHCl_3$, colorless crystals were obtained. M.p. 148.6–149.1° ($CHCl_3$). R_f (toluene/AcOEt 10:1): 0.40. $[\alpha]_D^{25} = +16$ ($c = 0.1$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.68–7.00 (*m*, 14 arom. H); 5.15 (*d*, $^3J(1,HO) = 3.6$, OH); 4.52 (*dd*, $^3J(1,2) = 8.3$, $^3J(1,OH) = 3.5$, H–C(1)); 4.08 (*m*, H–C(2)); 3.48 (*s*, MeO); 2.42 (*d*, $^4J(2,MeN) = 8.05$, MeN); 1.7–0.2 (br. *q*, BH_3); 0.86 (*d*, $^3J(2,Me–C(2)) = 6.7$, Me–C(2)). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.80–6.95 (*m*, 14 arom. H); 4.45 (*d*, $^3J(1,2) = 9.6$, H–C(1)); 4.22 (*m*, H–C(2)); 3.93 (*s*, MeO); 2.64 (*d*, $^4J(2,MeN) = 7.6$, MeN); 2.16 (br. *s*, OH); 1.7–0.2 (br. *q*, BH_3); 0.81 (*d*, $^3J(2,Me–C(2)) = 6.7$, Me–C(2)). ^{11}B-NMR ($CDCl_3$): −36.9 (*d*, $^1J(B,P) = 56.5$, BH_3). ^{31}P-NMR: 71.5 (*d*, $^1J(B,P) = 55.2$). CI-MS (NH_3): 394.2 (100, $[M+1]^+$). Anal. calc. for $C_{23}H_{29}BNOP$ (393.28): C 70.24, H 7.43, N 3.56; found: C 70.35, H 7.55, N 3.61.

3.4. *(1*S*,2*S*)-{[(*S*)-(tert-Butyl)phenylphosphanyl]methylamino}-1-phenylpropan-1-ol–P-borane (1/1)* ((*S*,*S*,*S*)-**4**). According to *3.3*, with (*S*,*S*,*S*)-**1** (1.424 g, 5 mmol) in THF (20 ml) and *t*-BuLi (3.7 ml, 5 mmol of a 1.4M soln.). The clear oil solidified upon standing: (*S*,*S*,*S*)-**4** (1.65 g, 94%). M.p. 136.8–138.3°. R_f (toluene/AcOEt 10:1): 0.50. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.84–7.24 (*m*, 10 arom. H); 5.31 (*d*, $^1J(1,OH) = 3.5$, OH); 4.51 (*dd*, $^3J(1,2) = 8.8$, $^3J(1,OH) = 3.5$, H–C(1)); 3.94 (*m*, H–C(2)); 2.58 (*d*, $^4J(2,MeN) = 6.87$, MeN); 1.29 (*d*, $^3J(Me_3C,P) = 14.0$, Me_3C); 1.7–0.2 (br. *q*, BH_3); 0.82 (*d*, $^3J(2,Me–C(2)) = 6.6$, Me–C(2)). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.90–7.23 (*m*, 10 arom. H); 4.46 (*d*, $^3J(1,2) = 9.6$, H–C(1)); 4.10 (*m*, H–C(2)); 2.95 (br. *s*, OH); 2.78 (*d*, $^4J(2,MeN) = 7.5$, MeN); 1.7–0.2 (br. *q*, BH_3); 1.38 (*d*, $^3J(Me_3C,P) = 14.2$, Me_3C); 0.86 (*d*, $^3J(2,Me–C(2)) = 6.6$, Me–C(2)). ^{11}B-NMR ($CDCl_3$): −39.4 (*d*, $^1J(B,P) = 69.5$, BH_3). ^{31}P-NMR: 85.5 (*d*, $^1J(B,P) = 68.0$).

3.5. *(1*R*,2*S*)-2-{[(*S*)-(2-Methoxyphenyl)phenylphosphanyl]methylamino}-1-phenylpropan-1-ol–P-borane (1/1)* ((*S*,*R*,*S*)-**5**) (*cf.* [10c][15]). According to *3.3*. The clear oil solidified: (*S*,*R*,*S*)-**5** (0.366 g, 93%). M.p. 139.6–140.2°. R_f(toluene/AcOEt 10:1): 0.42. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.60–6.80 (*m*, 14 arom. H); 4.89 (*d*, $^3J(1,2) = 5.5$, H–C(1)); 4.32 (*m*, H–C(2)); 3.56 (*s*, MeO); 2.53 (*d*, $^4J(2,MeN) = 8.1$, MeN); 2.10 (br. *s*, OH); 1.7–0.2 (br. *q*, BH_3); 1.21 (*d*, $^3J(2,Me–C(2)) = 6.8$, Me–C(2)). ^{11}B-NMR ($CDCl_3$): −36.8 (*d*, $^1J(B,P) = 58.7$, BH_3). ^{31}P-NMR: 71.1 (*d*, $^1J(B,P) = 59.0$).

3.6. *(1*R*,2*S*)-2-{[(*R*)-(tert-Butyl)phenylphosphanyl]methylamino}-1-phenylpropan-1-ol–P-borane (1/1)* ((*R*,*R*,*S*)-**6**). According to *3.3*, with (*R*,*S*,*R*)-**2** (0.285 g, 1 mmol) in THF (5 ml), and *t*-BuLi (7.2 ml; 1.4M in pentane): (*R*,*R*,*S*)-**6** (0.315 g, 93%). M.p. 139.5–140.5°. R_f (toluene/AcOEt 10:1) 0.51. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.20–7.70 (*m*, 10 arom. H); 5.18 (*d*, $^3J(1,2) = 3.4$, H–C(1)); 4.14 (*m*, H–C(2)); 2.88 (*d*, $^4J(2,MeN) = 6.36$, MeN); 2.08 (br. *s*, OH); 1.32 (*d*, $^3J(Me_3C,P) = 13.8$, Me_3C); 1.7–0.2 (br. *q*, BH_3); 1.16 (*d*, $^3J(2,Me–C(2)) = 7.0$, Me–C(2)). ^{11}B-NMR ($CDCl_3$): −20.1 (*d*, $^1J(B,P) = 68.0$, BH_3). ^{31}P-NMR: 86.5 (*d*, $^1J(B,P) = 67.0$).

3.7. *(*R*)- or (*S*)-Methoxy(2-methoxyphenyl)phenylphosphane–borane (1/1)* ((*R*)- or (*S*)-**7**) (*cf.* [10c][15]). In a two-neck flask (25 ml), (*R*,*S*,*S*)-**3** (0.64 g, 1.63 mmol) or (*S*,*R*,*S*)-**5** (0.64 g, 1.63 mmol) was dissolved in

MeOH (15 ml). To this soln., conc. H_2SO_4 was added (0.16 g, 1.63 mmol), and the mixture was stirred at r.t. for 16 h. At the beginning of the reaction, a white precipitate appeared, which dissolved during the reaction. The mixture was extracted with CH_2Cl_2 (30 ml) and H_2O (with 1 ml of 20% H_2SO_4). The aq. phase was extracted with CH_2Cl_2 (2×30 ml). The combined org. phase was washed with $NaHCO_3$ (2×20 ml). The org. phase was dried ($MgSO_4$), and the solvent was removed to yield (*R*)-**7** or (*S*)-**7** (0.411 g, 97%). Colorless oils. R_f (hexane/AcOEt 3:1) 0.35. $[\alpha]_D^{25} = -25.8$ ($c = 0.1$, $CHCl_3$) for (*R*)-**7**; $[\alpha]_D^{25} = +26.1$ ($c = 0.1$, $CHCl_3$) for (*S*)-**7**. ^{1}H-NMR (300 MHz, $CDCl_3$) 7.93–6.85 (*m*, 9 arom. H); 3.73 (*d*, ^3J(MeO,P) = 12.1, MeOP); 3.62 (*s*, MeO); 1.7–0.6 (br. *q*, BH_3). ^{11}B-NMR ($CDCl_3$): −39.8 (*d*, ^1J(B,P) = 65.0, BH_3). ^{31}P-NMR: 107.0 (*q*, ^1J(B,P) = 64.5).

3.8. *(*R*)- or (*S*)-(3,4-Dimethoxyphenyl)(2-methoxyphenyl)phenylphosphane–borane (1/1)* ((*R*)-**7** or (*S*)-**8**). In a two-neck flask BuLi (1.4 ml, 2.2 mmol; 1.6M in hexane) was added dropwise to a soln. of 4-bromo-1,2-dimethoxybenzene (0.28 ml, 2.25 mmol) in THF (2 ml) at −78°. The mixture was stirred for 1 h at −78°. Then, (*R*)-**8** or (*S*)-**8** (0.48 g, 1.85 mmol) was added dropwise. The mixture was allowed to warm to 0° and kept at this temp. for 2 h. Then, the reaction was quenched by addition of H_2O (1 ml). After extraction with Et_2O (3×30 ml) and H_2O, the org. phase was dried ($MgSO_4$). The solvent was removed, and the residue was purified by FC (hexane/AcOEt 3:1): (*R*)-**8** or (*S*)-**8** (0.49 g, 80%). Colorless crystals. (*S*)-**8** was crystallized from hexane/AcOEt. M.p. 140.8–141.6° ($CHCl_3$). R_f (hexane/AcOEt 3:1) 0.12. $[\alpha]_D^{25} = +43.5$ ($c = 0.5$, $CHCl_3$) for (*S*)-**8**; $[\alpha]_D^{25} = -43.4$ ($c = 0.5$, $CHCl_3$) for (*R*)-**8**. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.60–6.84 (*m*, 12 arom. H); 3.90, 3.81, 3.57 (3*s*, MeO); 1.7–0.5 (br. *q*, BH_3). ^{11}B-NMR ($CDCl_3$): −37.1 (*d*, ^1J(B,P) = 55.3, BH_3). ^{31}P-NMR: 18.4 (*q*, ^1J(B,P) = 54.0). EI-MS: 365.0 (7, $M^{+\cdot}$), 352.0 (100, $[M - BH_3]^{+\cdot}$). Anal. calc. for $C_{18}H_{24}BO_3P$ (329.97): C 65.52, H 7.33; found: C 65.43, H 7.29.

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