Synthesis of New Chiral Bidentate (Phosphinophenyl)benzoxazine P,N-Ligands

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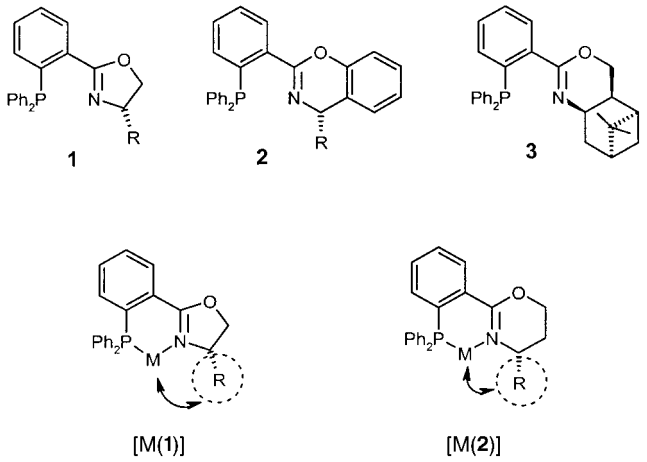
Two new chiral bidentate (phosphinophenyl)benzoxazine P,N-ligands **2a** and **2b** were synthesized from highly enantiomer-enriched 2-(1-aminoalkyl)phenols **4**. Ligand *rac*-**2a** was obtained on refluxing the *t*-Bu-substituted (aminomethyl)phenol **4a** with 2-(diphenylphosphino)benzonitrile in chlorobenzene in the presence of anhydrous $ZnCl_2$ followed by decomplexation (*Scheme 2*). This reaction, when carried out with (+)-(*S*)-**4a**, was accompanied by racemization at the stereogenic center of the alkyl side chain. The enantiomerically pure ligands (+)-(*R*)-**2a** and (−)-(*S*)-**2a** were obtained using a stepwise procedure *via* the amides (−)-(*R*)- and (+)-(*S*)-**5b**, respectively, followed by cyclization to benzoxazines (+)-(*R*)- and (−)-(*S*)-**7b**, respectively, with triflic anhydride and by F-atom substitution by diphenylphosphide (*Schemes 3* and *5*). In the case of the i-Pr analogue **2b**, this last step resulted in racemization (*Scheme 6*). This was overcome by preparing the bromo derivative and introducing the diphenylphosphine group *via* Br/Li exchange and reaction with chlorodiphenylphosphine (*Scheme 7*). The first application of (+)-(*R*)-**2a** in an asymmetric *Heck* reaction showed high enantioselectivity (91%) (*Scheme 8*).

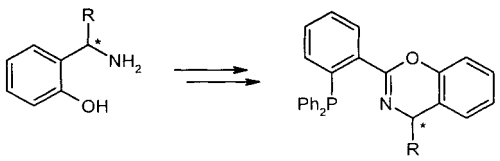
1. Introduction. – Bidentate chiral dihydro(phosphinoaryl)oxazole ligands **1** are readily obtained from 2-aminoalkan-1-ols. They have been applied highly successfully in a number of catalytic reactions including allylic substitution [1], *Heck* reaction [2], hydrogenation [3], hydrosilylation [4], and *Diels-Alder* reaction [5]. Given the success and popularity of ligands **1**, it is surprising that the use of the six-membered analogues is scarce [6]. The prime reason would appear to be the lack of natural sources of the requisite chiral 3-aminoalkan-1-ols, in marked contrast to the abundance of enantiomerically pure 2-aminoalkan-1-ols derived from the chiral pool (amino acids, ephedrins). In this article, we report the synthesis of the chiral ligands **2**, which differ from ligands **1** by having, in place of the five-membered dihydrooxazole ring, a benzo-fused six-membered 4*H*-oxazine ring.

A two-dimensional drawing suggests that the group R at the stereogenic center is closer to the metal in complex [M(**2**)] with the six-membered 5,6-dihydro-4*H*-oxazine ligand than in complex [M(**1**)] with the five-membered dihydrooxazole ligand and that R, therefore, could exert a larger influence on the stereochemical outcome of reactions at the metal center. However, while the dihydrooxazoles are almost flat, the 4*H*-oxazines have chair- and boat-like conformations, and this flexibility may be detrimental to their use as chiral inductors. An efficient way to reduce the number of conformations is ring fusion. This approach has been used successfully by *Evans* and coworkers, who applied the pinene-derived 4*H*-oxazine ligand **3** in Pd-catalyzed asymmetric allylic substitution reactions [6].



We chose fusion of the 4*H*-oxazine ring to an aromatic ring to render the heterocyclic system rigid, and this required chiral enantiomerically pure 2-(1-aminoalkyl)phenols **4** as starting materials (*Scheme 1*). Like the known 1-aminoethyl analogue **4c** [7], the chiral (aminoalkyl)phenols **4a** and **4b** were obtained *via* resolution with mandelic acid (= α-hydroxybenzeneacetic acid) [8]. Alternatively, compounds **4** are accessible by diastereoselective syntheses from chiral imine precursors [8][9].

Scheme 1



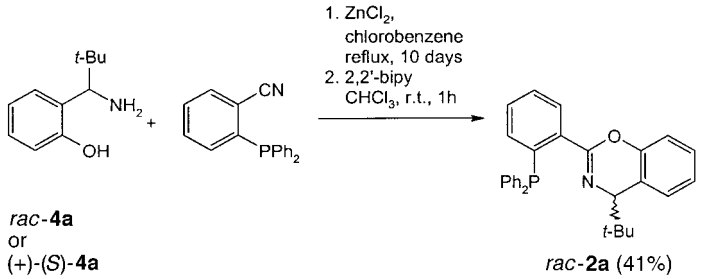
4a R = *t*-Bu
b R = i-Pr
c R = Me

2a,b

In the following, we first describe the synthesis of 4-(*tert*-butyl)-2-[2-(diphenylphosphino)phenyl]-4*H*-1,3-benzoxazine (**2a**) and then that of 2-[2-(diphenylphosphino)phenyl]-4-isopropyl-4*H*-1,3-benzoxazine (**2b**).

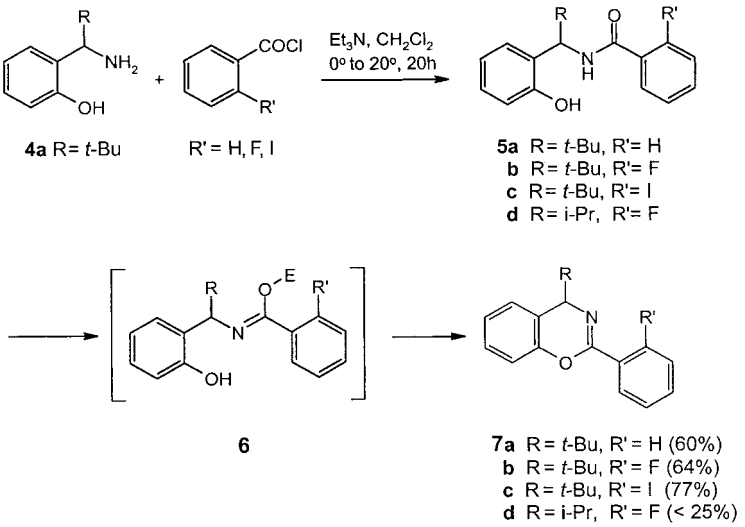
2. Results and Discussion. – According to a literature procedure for the analogous dihydrooxazole ligands **1** [10], racemic (aminoalkyl)phenol *rac*-**4a**, 2-(diphenylphosphino)benzonitrile, and $ZnCl_2$ were refluxed in chlorobenzene. The reaction was very sluggish, and yielded, after 10 days reaction time and ligand exchange at the Zn-center with 2,2′-bipyridine, the expected ligand *rac*-**2a** in 41% yield. The same reaction, when carried out with highly enantiomer-enriched (+)-(*S*)-**4a** (> 96% ee), again yielded **2a** in racemic form (*Scheme 2*).

Scheme 2



Racemization at the stereogenic center of the alkyl side chain had thus occurred under the harsh reaction conditions required for the oxazine-ring synthesis. A sample of enantiomerically pure **2a** was obtained by prep. HPLC with the chiral column *Chiralpak AD*[1]). Preliminary tests of this ligand in the asymmetric *Heck* reaction gave promising results (*vide infra*), and we therefore focused on milder, stepwise synthetic procedures *via* the amides **5**. Compounds **5** were readily obtained in nearly quantitative yields (*Scheme 3*), but their cyclization to the oxazines **7** with thionyl chloride, a procedure commonly used for the synthesis of dihydrooxazoles [11], failed to give satisfactory results (*Table*, *Entry 1*). An alternative procedure, *i.e.*, reaction with $POCl_3$ and pyridine followed by NaOH treatment, gave better results, but was not satisfactory with the 2-fluorobenzamide **5b** (*Entries 2* and *3*). Not surprisingly, the cyclization methods that work well for substrates containing a primary-alcohol group could not be

Scheme 3



[1]) The preparative-scale separation of the enantiomers of *rac*-**2a** was carried out at *Novartis Inc.* (separation laboratories headed by *E. Francotte*).

Table 1. *Synthesis of 2-Aryl-4*H*-1,3-benzoxazines* **7**

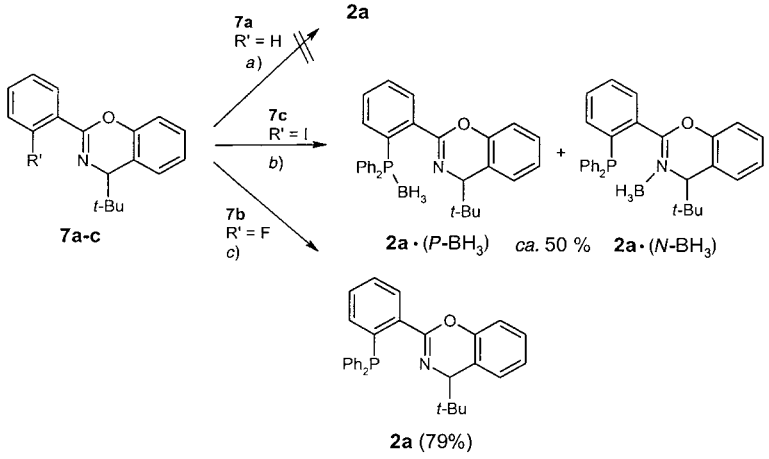
Entry	**5** (Yield [%])	R	R′	Reaction conditions	**7** (Yield [%])
1	**5b**[a]) (99)	*t*-Bu	F	1) $SOCl_2$, CH_2Cl_2, 20°, 1 d; 2) NaOH	**7b** ($\leq$ 10)
2	**5a**[a]) (100)	*t*-Bu	H	1) $POCl_3$, CH_2Cl_2, −40°, 1 h; 2) Py, 20°, 20 h; 3) NaOH	**7a** (60)
3	**5b**[a]) (100)	*t*-Bu	F	1) $POCl_3$, CH_2Cl_2, −40°, 1 h; 2) Py, 20°, 90 h; 3) NaOH	**7b** (32)
4	**5b**[a]) (100)	*t*-Bu	F	1) Tf_2O, CH_2Cl_2, 0°, 0.3 h; 2) Et_3N, 0° → 20°, 1 h	**7b** (64)
5	**5c**[a]) (99)	*t*-Bu	I	1) Tf_2O, CH_2Cl_2, 0°, 0.3 h; 2) Et_3N, 0° → 20°, 1 h	**7c** (77)
6	**5d**[b]) (86)	i-Pr	F	1) Tf_2O, CH_2Cl_2, −78° → 0°; 2) Et_3N, −30° → 0°	**7d** (< 23)

[a]) Prepared from the corresponding chloride. [b]) Prepared from 2-fluoro-*N*-[1-(2-methoxyphenyl)-2-methylpropyl]benzamide, followed by demethylation with BBr_3.

readily applied to the phenol derivatives **5**. Whereas in the former case, hydroxy activation is followed by nucleophilic displacement by the amide O-atom, cyclization of **5** involves the reverse mode of reaction: the phenolate moiety attacks at an imidate intermediate **6** (*Scheme 3*). We, therefore, turned to triflic anhydride (=trifluoromethanesulfonic anhydride), known to efficiently form the imidate triflate **6** (E = Tf) [12]. Indeed, treatment of the racemic amide *rac*-**5b** with triflic anhydride, followed by addition of Et_3N, afforded 2-(2-fluorophenyl)-1*H*-1,3-benzoxazine (*rac*-**7b**) in 64% yield (*Entry 4*). This method was also used to prepare highly enantiomer-enriched (−)-(*S*)- and (+)-(*R*)-**7b** and *rac*-**7c** (*Entry 5*).

Introduction of the PPh_2 group at the phenyl substituent of **7** was first tried by the *ortho*-lithiation procedure applied to **7a**, analogously to the method used for phenyldihydrooxazoles [13] (*Scheme 4*). This approach did not work though in the case at hand, and we note a literature precedent of a similar example with a *t*-Bu substituent at a dihydrooxazole ring [14].

Scheme 4

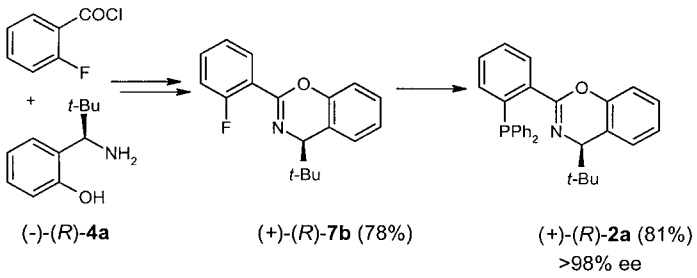


a) 1. BuLi (1.1 equiv.), TMEDA (1.1 equiv.), THF, −78°, 2 h; 2. $ClPPh_2$ (2 equiv.). *b*) $Ph_2HP \cdot BH_3$ (3 equiv.), K_2CO_3 (2 equiv.), $[Pd(PPh_3)_4$ (5 mol-%), MeCN/THF, reflux, 60 h. *c*) *t*-BuOK (1.1 equiv.), $HPPh_2$ (1.1 equiv.), [18]crown-6 (1.3 equiv.), THF, 0° to r.t., 21 h.

Pd(0)-Catalyzed coupling of 4-(*tert*-butyl)-2-(2-iodophenyl)-4*H*-1,3-benzoxazine and $HPPh_2 \cdot BH_3$ [15] gave a moderate yield of the borane complex of **2a**. This route was not further pursued since the product, a mixture of the *N*-borane and the *P*-borane adduct of **2a**, resisted borane removal by Et_2NH or by HBF_4, and because at that stage, another route (see *c* in *Scheme 4*) had been successful.

Nucleophilic aromatic substitution of the F-atom in (2-fluorophenyl)dihydrooxazole by either $LiPPh_2$ or $KPPh_2$ has been reported [16]. Accordingly, *rac*-**7b** was first reacted with $LiPPh_2$; but on finding that this afforded only traces of **2a**, we turned to the more reactive $KPPh_2$. The latter was prepared *in situ* from *t*-BuOK and $HPPh_2$, and its reaction with *rac*-**7b** at room temperature gave *rac*-**2a** in 43% yield. The yield was increased to 71% when 2 equiv. of $KPPh_2$ were used, and to 79% with 1.1 equiv. of $KPPh_2$ in the presence of 1.3 equiv. of [18]crown-6 (*Scheme 4*). This procedure was also applied to enantiomerically enriched (+)-(*R*)-**7b** as shown in *Scheme 5*. HPLC Analysis of the obtained (+)-(*R*)-**2a** confirmed that no racemization had occurred in any of the steps from the starting (aminoalkyl)phenol (−)-(*R*)-**4a**.

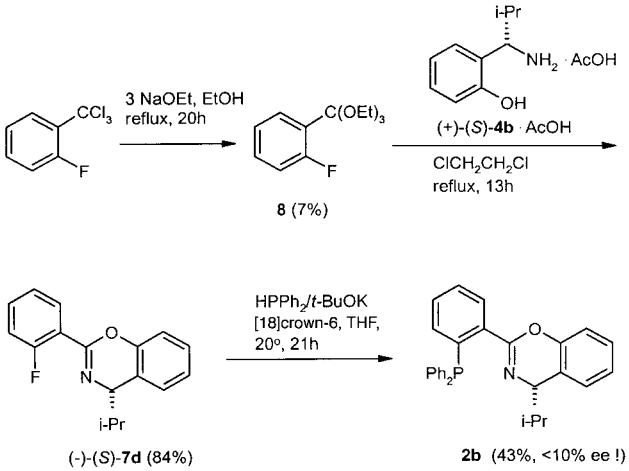
Scheme 5



In extension of the synthesis of ligand **2a**, we undertook the preparation of the i-Pr analogue **2b** by the same methodology. However, cyclization of the i-Pr-substituted amide **5d** to the (2-fluorophenyl)benzoxazine **7d** (*Scheme 3*) with triflic anhydride and Et_3N gave low yields ($\leq 25\%$). This could be overcome by extending a recently reported protocol for dihydrooxazole synthesis to the oxazines [17]. Refluxing 2-fluorobenzoic acid triethyl orthoester **8** and the (aminoalkyl)phenol (+)-(*S*)-**4b** in 1,2-dichloroethane in the presence of AcOH afforded the benzoxazine (−)-(*S*)- **7d** in 84% yield (*Scheme 6*). The drawback here is the synthesis of the triethyl orthoester **8**. Under the same conditions that were reported for the synthesis of benzoic acid triethyl orthoester (71% yield [18]), α,α,α-trichloro-2-fluorotoluene gave a product mixture from which the triethyl orthoester **8** was isolated in only 7% yield. Shorter reaction times led to incomplete Cl-substitution, while F-substitution became a problem at longer reaction times.

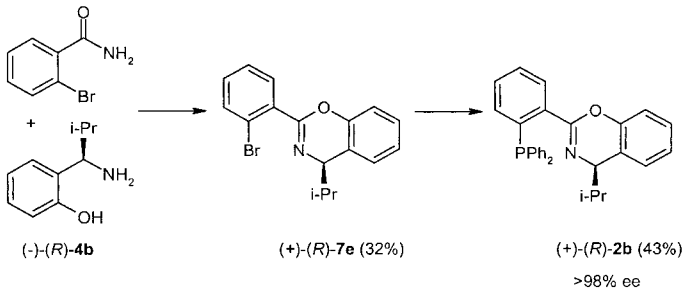
We were dismayed, however, to find that the substitution of the F-atom of (−)-(*S*)-**7d** by diphenylphosphine with potassium diphenylphosphide was accompanied by racemization at the stereogenic center C(4). A number of other attempts to synthesize highly enantiomer-enriched **2b**, *e.g.*, the synthesis of 2-(diphenylphosphino)benzoic acid orthoester, *Stille* coupling of 4-isopropyl-2-(trimethylstannyl)-4*H*-1,3-benzoxazine with 2-(bromodiphenylphosphino)benzene, and nucleophilic substitution of 2-ethoxy-

Scheme 6



4-isopropyl-4*H*-1,3-benzoxazine by 2-(diphenylphosphino)phenyllithium, were all unsuccessful. Finally it was found that Br/Li exchange in (*R*)-2-(2-bromophenyl)-4-isopropylbenzoxazine (+)-(*R*)-**7e**, followed by reaction with chlorodiphenylphosphine, provided a viable route to (*R*)-2-[2-(diphenylphosphino)phenyl]-4-isopropylbenzoxazine (+)-(*R*)-**2b** (*Scheme 7*). No racemization occurred, but reaction conditions have not yet been optimized. The oxazine (+)-(*R*)-**7e** was synthesized from 2-bromobenzamide, *Meerwein*'s salt, and the (aminoalkyl)phenol (−)-(*R*)-**4b** [19].

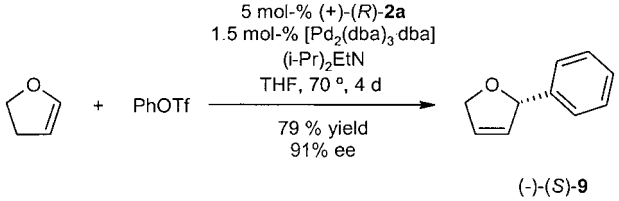
Scheme 7



The first application of (+)-(*R*)-**2a** in the asymmetric *Heck* reaction is promising: 2,3-dihydrofuran and phenyl triflate (= phenyl trifluoromethanesulfonate) reacted in the presence of 5 mol-% of (+)-(*R*)-**2a**, 1.5 mol% of $[Pd_2(dba)_3 \cdot dba]$ (dba = dibenzylidene acetone) and 2 equiv. of $(i\text{-}Pr)_2EtN$ to give (−)-(*S*)-**9** in 79% yield and with an enantiomeric excess of 91% (*Scheme 8*).

3. Conclusions. – Syntheses of the new chiral 4-(*tert*-butyl)- and 4-isopropyl-substituted 2-[2-diphenylphosphino)phenyl]-4*H*-1,3-benzoxazine ligands **2a** and **2b**, respectively, starting with highly enantiomer-enriched (aminoalkyl)phenols **4**, have

Scheme 8



been developed. The first application of the ligand (+)-(*R*)-**2a** in the asymmetric *Heck* reaction of 2,3-dihydrofuran and phenyl triflate led to product (−)-(*S*)-**9** in 79% yield and with 91% ee. Further applications in the areas of *Heck* reactions, Pd-catalyzed allylic substitutions, iridium-catalyzed hydrogenation, hydrosilylation, and in *Lewis*-acid-catalyzed *Diels-Alder* reactions are in progress, in collaboration with Prof. *A. Pfaltz*, Basel.

Experimental Part

1. *General*. Reactions were carried out under purified N_2 with an inert gas/vacuum double manifold and standard *Schlenk* techniques. THF and Et_2O were dried and distilled from Na/benzophenone, and CH_2Cl_2 and chlorobenzene from CaH_2 under N_2 before use. All other chemicals were purchased from *Aldrich* or *Fluka* and were purified following standard literature procedures. All glassware was flame-dried prior to use. TLC: *Merck SIL G/UV$_{254}$*; detection by UV/VIS or 2% $KMnO_4$/4% $NaHCO_3$ soln. Flash column chromatography (FC): silica gel *Merck 60*. HPLC: *Jasco PU-980*; *Chiralpak AD*, 25 cm; detection at 254 nm; t_R in min. GC: *Hewlett-Packard-HP-6890* instrument; *FS-595-*(*t*-Bu)Me_2Si-*β-CD/SE-54* capillary column [20]; t_R in min. Melting points: *Büchi 510*; uncorrected. Optical rotations: *Perkin-Elmer-241* polarimeter; 10-cm cell. UV/VIS: *Uvikon 860*; λ in nm (log ε). CD: *Jasco J-715*; λ in nm ([$\Delta\varepsilon$]). IR: *Perkin-Elmer FT-IR 1650*; $\tilde{\nu}$ in cm^{-1}. NMR: *Varian-XL-200* or *Bruker 400 MHz*, δ in ppm rel. to internal $SiMe_4$ or to the signal of the residual solvent (^{19}F: C_6F_6, external reference; ^{31}P: H_3PO_4, external reference), *J* in Hz. MS: *Varian CH4* or *SM1*; ionizing voltage 70 eV; *m/z* (intensity in %). HR-MS: *VG* anal. *7070E* (data system 11 250, resolution 7000). Elemental analyses were performed by Dr. *H. J. Eder*, Service de Microchimie, Département de Chimie Pharmaceutique, Université de Genève.

2. rac-*4-(*tert-*Butyl)-2-[2-(diphenylphosphino)phenyl]-4*H-*1,3-benzoxazine* (*rac*-**2a**), *using* $ZnCl_2$. (+)-(*S*)-**4a** (707 mg, 3.94 mmol), 2-(diphenylphosphino)benzonitrile (863 mg, 3.00 mmol), and freshly dried $ZnCl_2$ (533 mg, 3.91 mmol) in chlorobenzene (10 ml) were refluxed for 10 d. The mixture was poured directly onto a column (silica gel) and eluted with Et_2O/hexane 1:4 to give, after evaporation, a yellow solid (887 mg). The solid was dissolved in $CHCl_3$ (15 ml), 2,2′-bipyridine (247 mg, 1.58 mmol) added, and the soln. stirred for 1 h at r.t. After filtration through a short column (silica gel, 3 × 4 cm) and washing of the column with $CHCl_3$ (100 ml), the soln. was evaporated and the residue purified by FC (silica gel, AcOEt/hexane 1:2): **2a** (551 mg, 41%). White powder. M.p. 130°. TLC: R_f 0.6 (Et_2O/hexane 1:2). UV (EtOH): 216 (2.80). IR ($CHCl_3$): 3059*w*, 2961*m*, 2384*m*, 1674*m*, 1488*m*, 1215*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.94 (*s*, 9 H); 4.35 (*s*, 1 H); 6.52 (*dd*, *J* = 7.6, 1.6, 1 H); 6.97–7.47 (*m*, 16 H); 7.88–8.02 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.1; 38.2; 64.7; 115.4; 123.8; 127.6; 128.2; 128.3; 128.3; 128.4; 128.5; 129.7 (*d*, *J* = 4.4); 130.2, 133.8 (*d*, *J* = 19.8); 134.0 (*d*, *J* = 20.3); 134.6; 134.7; 137.4 (*d*, *J* = 21.9); 137.9 (*d*, *J* = 11.2); 138.2 (*d*, *J* = 11.3); 149.9; 153.5. ^{31}P-NMR (162 MHz, $CDCl_3$): −7.7 (97%); 29.8 (3%, *P*-oxide of **2a**). MS: 449 (36, M^+), 434 (61), 392 (58), 372 (100), 286 (17), 208 (12), 183 (20), 77 (11), 51 (10). HR-MS: 449.19164 (M^+, $C_{30}H_{28}NO_2P^+$; calc. 449.19086). Anal. calc. for $C_{30}H_{28}NO_2P$: C 80.15, H 6.27, N 3.12; found: C 79.92, H 6.19, N 3.08.

3. rac-N-*[1-(2-Hydroxyphenyl)-2,2-dimethylpropyl]benzamide* (*rac*-**5a**). To *rac*-**4a** (896 mg, 5.0 mmol) in CH_2Cl_2 (15 ml), benzoyl chloride (0.581 ml, 703 mg, 5.0 mmol) was added at 0°. Et_3N (0.760 ml, 555 mg, 5.48 mmol) was added slowly, and the soln. was stirred for 32 h at r.t. The mixture was poured onto a short silica gel column (2 × 7 cm). Elution with AcOEt and evaporation gave *rac*-**5a** (1.40 g, 99%). White solid. M.p. 90–94°. TLC (CH_2Cl_2/AcOEt 10:1): R_f 0.36. IR ($CHCl_3$): 3278*w*, 2968*m*, 1652*s*, 1523*s*, 1487*m*, 1455*w*, 1357*w*, 1246*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 0.90 (*s*, 9 H); 5.46 (*s*, 1 H); 6.74 (*t*, *J* = 7.5, 1 H); 6.79 (*d*, *J* = 8.0, 1 H); 7.03

(*td*, $J = 7.1$, $J = 1.3$, 1 H); 7.38–7.56 (*m*, 4 H); 7.76 (*d*, $J = 7.1$, 2 H); 8.31 (*d*, $J = 8.4$, 1 H); 9.52 (*s*, 1 H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 26.7; 36.1; 53.9; 115.2; 118.3; 127.3; 127.5; 128.2; 129.1; 129.6; 130.9; 135.3; 154.8; 166.1. MS: 283 (7, M^+), 226 (88), 147 (11), 121 (15), 105 (100), 77 (81), 51 (20). HR-MS: 283.1580 (M^+, $C_{18}H_{21}NO_2^+$; calc. 283.1572).

4. rac-*2-Fluoro*-N-*[1-(2-hydroxyphenyl)-2,2-dimethylpropyl]benzamide* (*rac*-**5b**). To *rac*-**4a** (358 mg, 2.0 mmol) in CH_2Cl_2 (3 ml), 2-fluorobenzoyl chloride (0.237 ml, 318 mg, 2.0 mmol) was added at 0°. Et_3N (0.291 ml, 212 mg, 2.1 mmol) was added slowly, and the soln. was stirred for 24 h at r.t. The mixture was poured onto a short silica gel column (2 × 5 cm). Elution with AcOEt and evaporation gave *rac*-**5b** (601 mg, 100%). White foam. M.p. 178–180°. IR ($CHCl_3$): 3301*w*, 2965*m*, 1655*s*, 1528v*s*, 1481*m*, 1455*w*, 1356*w*, 1292*w*, 1235*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.05 (*s*, 9 H); 5.36 (*d*, $J = 7.8$, 1 H); 6.71–7.53 (*m*, 6 H); 8.02–8.17 (*m*, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.1; 36.6; 64.4; 116.5; 116.8; 117.3; 120.5; 125.5; 126.8; 128.9; 133.1; 134.0 (*d*, $J = 9.2$); 155.4; 160.5; 163.0; 164.0 (*d*, $J = 0.4$). ^{19}F-NMR (376 MHz, $CDCl_3$): 49.9. MS: 244 (96, [$M - t$-Bu]$^+$), 226 (11), 123 (100), 95 (23), 57 (17). HR-MS: 301.1472 (M^+, $C_{18}H_{20}FNO_2^+$; calc. 301.1478).

According to the procedure described for *rac*-**5b**, (+)-(*S*)-**4a** (1.793 g, 10.0 mmol), 2-fluorobenzoyl chloride (1.183 ml, 1.59 g, 10.0 mmol), and Et_3N (1.46 ml, 1.07 g, 10.5 mmol) gave (+)-(*S*)-**5b** (3.04 g, 100%). M.p. 187–190°. $[\alpha]_{21}^{D} = +61.6$ ($c = 0.56$, $CHCl_3$).

According to the procedure described for *rac*-**5b**, (−)-(*R*)-**4a** (3.589 g, 20.0 mmol), 2-fluorobenzoyl chloride (2.37 ml, 3.17 g, 20.0 mmol), and Et_3N (2.91 ml, 2.12 g, 21.0 mmol) gave (−)-(*R*)-**5b** (6.01 g, 100%). M.p. 185–192°. $[\alpha]_{21}^{D} = -62.3$ ($c = 0.75$, $CHCl_3$).

5. rac-N-*[1-(2-Hydroxyphenyl)-2,2-dimethylpropyl]-2-iodobenzamide* (*rac*-**5c**). According to the procedure described for *rac*-**5b**, *rac*-**4a** (539 mg, 3.01 mmol), 2-iodobenzoyl chloride (804 mg, 3.02 mmol), and Et_3N (0.437 ml, 319 mg, 3.15 mmol) gave *rac*-**5c** (1.222 g, 99%). M.p. 82–83°. TLC (AcOEt): R_f 0.8. IR ($CHCl_3$): 3282*w*, 3003*w*, 2967*m*, 1742*w*, 1656*s*, 1586*w*, 1509*s*, 1458*m*, 1360*w*, 1290*w*, 1215*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.02 (*s*, 9 H); 5.17 (*d*, $J = 9.7$, 1 H); 6.75–6.87 (*m*, 2 H); 7.00–7.16 (*m*, 3 H); 7.26–7.36 (*m*, 2 H); 7.81 (*d*, $J = 8.0$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 27.3; 36.9; 60.4; 92.4; 116.7; 119.8; 128.1; 128.1; 128.2; 128.3; 131.0; 140.0; 142.5; 154.2; 169.1. MS: 409 (1, M^+), 352 (55), 231 (100), 203 (13), 76 (13). HR-MS: 409.0537 (M^+, $C_{18}H_{20}INO_2^+$; calc. 409.0539).

6. rac-*2-Fluoro*-N-*[1-(2-hydroxyphenyl)-2-methylpropyl]benzamide* (*rac*-**5d**). At 0°, 1-(2-methoxyphenyl)-2,2-dimethylpropylamine (365 mg, 2.04 mmol) and 2-fluorobenzoyl chloride (0.237 ml, 318 mg, 2.00 mmol) were stirred for 5 min. Et_3N (0.291 ml, 212 mg, 2.10 mmol) was added, and the mixture was stirred for 21 h at r.t. and then poured onto a silica gel column. Elution with AcOEt/hexane 1:2 and evaporation gave a colorless oil, which was dissolved in CH_2Cl_2 (5 ml) and treated at −78° with BBr_3 (0.580 ml, 1.51 g, 6.0 mmol). The yellow soln. was allowed to warm to r.t. and then added to 1N NaOH (50 ml) at 0°. Conc. HCl soln. was added until pH 6 was reached. The aq. layer was extracted wtih CH_2Cl_2 (3 × 20 ml) and the combined org. layer dried ($MgSO_4$) and evaporated. *rac*-**5d** (491 mg, 86%). White solid. M.p. 138–140°. IR ($CHCl_3$) 3449*w*, 3180*w*, 3017*s*, 2964*w*, 1637*s*, 1528*s*, 1313*w*, 1281*w*, 1199*m*, 672*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*d*, $J = 6.9$, 3 H); 1.20 (*d*, $J = 6.7$, 3 H); 2.42 (*sept. d*, $J = 10.3$, 6.9, 1 H); 4.93–5.00 (*m*, 1 H); 6.86–6.98 (*m*, 2 H); 7.08–7.28 (*m*, 3 H); 7.38–7.53 (*m*, 2 H); 8.05–8.13 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.2; 20.4; 30.9; 55.7; 115.9; 116.1; 118.2; 120.2; 120.5; 124.9; 127.3; 128.8; 132.3; 133.7; 133.8; 155.2; 159.6; 162.0; 164.2. ^{19}F-NMR (376 MHz, $CDCl_3$): 50.4. MS: 287 (2, M^+), 244 (40), 123 (100), 95 (16). HR-MS: 287.1329 (M^+, $C_{17}H_{18}FNO_2^+$, calc. 287.1322). Anal. calc. for $C_{17}H_{18}FNO_2$: C 71.06, H 6.31, N 4.87; found: C 70.47, H 6.39, N 4.66.

7. rac-*4-(*tert-*Butyl)-2-phenyl-4*H-*1,3-benzoxazine* (*rac*-**7a**). To a soln. of *rac*-**5a** (284 mg, 1.00 mmol) in CH_2Cl_2 (10 ml) at −40°, $POCl_3$ (0.091 ml, 153 mg, 1.0 mmol) was added and the mixture stirred for 30 min. Pyridine (0.480 ml, 470 mg, 6.0 mmol) was added next, and stirring was continued for 15 min at −40° and for 20 h at r.t. Then, 1N NaOH (20 ml) was added, the yellow mixture stirred for 15 min and extracted with Et_2O (3 × 10 ml), and the combined org. phase dried ($MgSO_4$) and evaporated. FC (AcOEt/hexane 1:20) yielded *rac*-**7a** (160 mg, 60%). Colorless oil. IR ($CHCl_3$): 2964*s*, 2873*w*, 1666*s*, 1584*w*, 1486*m*, 1457*w*, 1352*w*, 1245*m*, 1193*m*, 1094*m*, 1068*w*, 1025*w*, 909*w*, 697*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.01 (*s*, 9 H); 4.49 (*s*, 1 H); 7.08–7.18 (*m*, 3 H); 7.26–7.33 (*m*, 1 H); 7.43–7.54 (*m*, 3 H); 8.14 (*d*, $J = 1.7$, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.0, 38.7; 64.5; 115.4; 121.4; 123.9; 127.7; 127.7; 127.9; 128.3; 128.3; 128.5; 131.1; 132.0; 150.2; 152.5. MS: 265 (0.4, M^+), 208 (100), 105 (16), 77 (30), 51 (27). HR-MS: 208.0758 ([$M - t$-Bu]$^+$, $C_{14}H_{10}NO^+$; calc. 208.0762).

8. rac-*4-(*tert-*Butyl)-2-(2-fluorophenyl)-4*H-*1,3-benzoxazine* (*rac*-**7b**). *rac*-**5b** (452 mg, 1.5 mmol) was dissolved in CH_2Cl_2 (15 ml) at 0°. Triflic anhydride (0.271 ml, 466 mg, 1.65 mmol) was added slowly, and the soln. was stirred for 20 min at 0°. Et_3N (0.48 ml, 350 mg, 3.5 mmol) was added, and the soln. was stirred for 1 h at r.t. Evaporation followed by FC (Et_2O/pentane 1:10) gave *rac*-**7b** (274 mg, 64%). Colorless oil. TLC (Et_2O/hexane 1:20): R_f 0.20. IR ($CHCl_3$): 3018*m*, 2961*s*, 1672*s*, 1613*w*, 1488*m*, 1456*m*, 1352*w*, 1216*s*, 1115*w*. ^{1}H-NMR

(200 MHz, $CDCl_3$): 1.02 (*s*, 9 H); 4.48 (*s*, 1 H); 6.99–7.50 (*m*, 7 H); 7.80–7.90 (*m*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 26.0; 38.6; 65.0; 115.4; 116.7 (*d*, *J* = 21.7); 121.1; 123.9 (*d*, *J* = 3.9); 124.1; 128.0; 128.5; 130.8 (*d*, *J* = 1.7); 132.3 (*d*, *J* = 8.5); 150.2; 163.7. ^{19}F-NMR (376 MHz, $CDCl_3$): 51.6. MS: 284 (6, $[M+H]^+$), 226 (98), 123 (36), 105 (40), 95 (13), 91 (13), 77 (93), 57 (27), 51 (100). HR-MS: 283.1370 (M^+, $C_{18}H_{18}FNO^+$; calc. 283.1372).

According to the procedure described for *rac*-**7b**, (+)-(*S*)-**5b** (2.968 g, 9.85 mmol), triflic anhydride (1.78 ml, 3.06 g, 10.8 mmol), and Et_3N (3.14 ml, 2.29 g, 22.7 mmol) gave (−)-(*S*)-**7b** (2.15 g, 77%). $[\alpha]_{21}^{D} = -41.6$ (*c* = 1.53, $CHCl_3$).

According to the procedure described for *rac*-**7b**, (−)-(*R*)-**5b** (6.012 g, 20.0 mmol), triflic anhydride (3.43 ml, 5.90 g, 20.9 mmol), and Et_3N (6.07 ml, 4.43 g, 43.8 mmol) gave (+-(*R*)-**7b** (4.45 g, 78%). $[\alpha]_{21}^{D} = +45.9$ (*c* = 1.09, $CHCl_3$).

9. rac-*4-(*tert-*Butyl)-2-(2-iodophenyl)-4*H-*1,3-benzoxazine* (*rac*-**7c**). According to the procedure described for *rac*-**7b**, *rac*-**5c** (613 mg, 1.50 mmol), triflic anhydride (0.260 ml, 450 mg, 1.58 mmol), and Et_3N (0.440 ml, 321 mg, 3.17 mmol) gave *rac*-**7c** (454 mg, 77%). M.p. 97–99°. TLC (Et_2O/pentane 1:5): R_f 0.23. IR ($CHCl_3$): 2967*m*, 1677*m*, 1486*w*, 1351*w*, 1294*w*, 1214*s*, 1190*m*, 1097*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.08 (*s*, 9 H); 4.55 (*s*, 1 H); 7.12–7.24 (*m*, 4 H); 7.29–7.36 (*m*, 1 H); 7.47 (*t*, *J* = 7.4, 1 H); 7.70 (*d*, *J* = 7.4, 1 H); 7.94 (*d*, *J* = 7.9, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.2; 38.7; 64.7; 94.2; 116.0; 121.0; 125.1; 128.4; 128.8; 132.1; 132.3; 133.9; 134.5; 139.8; 140.6; 150.2. MS: 391 (1, M^+), 334 (100), 77 (11), 51 (15). HR-MS: 391.0404 (M^+, $C_{18}H_{18}INO^+$; calc. 391.0433). Anal. calc. for $C_{18}H_{18}INO$: C 55.26, H 4.64, N 3.58; found: C 55.32, H 4.65, N 3.44.

10. rac-*4-(*tert-*Butyl)-2-[2-(diphenylphosphino)phenyl]-4*H-*1,3-benzoxazine* (*rac*-**2a**) *from* rac-**7b**. To a soln. of *t*-BuOK (120 mg, 1.07 mmol) and [18]crown-6 (332 mg, 1.26 mmol) in THF (6 ml) at 0°, diphenylphosphine (0.183 ml, 198 mg, 1.06 mmol) was added, and the resulting orange soln. was stirred for 1 h at 0°. A soln. of *rac*-**7b** (274 mg, 0.967 mmol) in THF (1 ml) was added slowly, and the mixture was stirred for 20 h at r.t. After evaporation, MeOH (2 ml) was added, the resulting suspension stirred for 5 min and the evaporated, and the residue purified by FC (CH_2Cl_2): *rac*-**2a** (342 mg, 79%). White solid. HPLC (*Chiralpak AD*; 25 cm; hexane/i-PrOH 95:5, 0.5 ml min^{-1}; detection at 254 nm): t_R 9.2 (*S*) and 12.4 (*R*).

According to the procedure described for *rac*-**2a**, *t*-BuOK (920 mg, 8.20 mmol), [18]crown-6 (2.563 g, 9.70 mmol), diphenylphosphine (1.41 ml, 1.52 g, 8.18 mmol), and (−)-(*S*)-**7b** (2.10 g, 7.41 mmol) gave (−)-(*S*)-**2a** (2.22 g, 67%). M.p. 61–63°. $[\alpha]_{21}^{D} = -111$ (*c* = 0.78, $CHCl_3$; >98% ee by HPLC). CD (89.0 μM, EtOH): 226 (+15.40, max.), 245 (−2.39, min.), 287 (−2.74, min.). HPLC (hexane/i-PrOH 95:5, 0.5 ml min^{-1}): 9.3 (*S*) and 12.5 (*R*).

According to the procedure described for *rac*-**2a**, *t*-BuOK (1.93 mg, 17.2 mmol), [18]crown-6 (5.39 g, 20.4 mmol), diphenylphosphine (2.98 ml, 3.22 g, 17.3 mmol), and (+)-(*R*)-**7b** (4.45 g, 15.7 mmol) gave (+)-(*R*)-**2a** (5.74 g, 81%). M.p. 60–62°. $[\alpha]_{21}^{D} = +110$ (*c* = 0.87, $CHCl_3$; >99% ee by HPLC). CD (91.2 μM, EtOH): 225 (−13.38, min.), 245 (+1.57, max.), 289 (+1.89, max.). HPLC (hexane/i-PrOH 95:5, 0.5 ml min^{-1}): 12.7 (*R*); the other enantiomer was not detected.

11. *2-Fluorobenzoic Acid Triethyl Orthoester* (= *1-Fluoro-2-(triethoxymethyl)benzene)* (**8**). Small pieces of Na (3.82 g, 166 mmol) were added to dry EtOH (40 ml). When all the Na had reacted, α,α,α-trichloro-2-fluorotoluene (7.4 ml, 11 g, 50 mmol) was added, and the resulting soln. was heated to reflux for 20 h. The soln. was allowed to cool to r.t. and filtered over *Celite*. The solvent was evaporated and the residue distilled twice to afford **8** (854 mg, 7%). Colorless liquid. B.p. 65–75°/0.3 mbar. IR ($CHCl_3$): 3019*w*, 2981*w*, 2933*w*, 2896*w*, 1615*w*, 1586*w*, 1485*w*, 1451*m*, 1392*w*, 1281*m*, 1241*m*, 1087*s*, 1060*s*. ^{1}H-NMR (200 MHz, C_6D_6): 1.14 (*t*, *J* = 7.2, 9 H); 3.51 (*q*, *J* = 7.2, 6 H); 6.82–7.00 (*m*, 3 H); 7.86 (*td*, *J* = 7.0, 2.0, 1 H). ^{13}C-NMR (50 MHz, C_6D_6): 15.1; 57.9; 113.1; 116.5 (*d*, *J* = 22.1); 123.4 (*d*, *J* = 3.8); 130.7 (*d*, *J* = 6.7); 131.1 (*d*, *J* = 3.1); 160.8 (*d*, *J* = 253.0). ^{19}F-NMR (376 MHz, C_6D_6): 51.8. MS: 242 (0.5, M^+), 197 (92), 169 (309), 141 (100), 123 (62), 95 (16). HR-MS: 197.0978 ($[M-OEt]^+$, $C_{11}H_{14}FO_2^+$; calc. 197.0987).

12. *(−)-(*S*)-2-(2-Fluorophenyl)-4-isopropyl-4*H-*1,3-benzoxazine* ((−)-(*S*)-**7d**). (*S*)-**4b**·AcOH (454 mg, 2.02 mmol) and **8** (602 mg, 2.5 mmol) were heated under reflux for 22 h in 1,2-dichloroethane (10 ml). Sat. $NaHCO_3$ soln. (20 ml) was added at r.t. The aq. phase was extracted with CH_2Cl_2 (3 × 15 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (AcOEt/hexane 1:10): (−)-(*S*)-**7d** (451 mg, 84%). Colorless oil. $[\alpha]_{21}^{D} = -68.1$ (*c* = 0.42, $CHCl_3$). TLC (AcOEt/hexane 1:10): R_f 0.49. IR ($CHCl_3$): 3450*w*, 3018*s*, 2965*s*, 2875*w*, 1672*s*, 1615*m*, 1586*w*, 1525*m*, 1489*s*, 1456*s*, 1419*w*, 1359*m*, 1304*m*, 1232*s*, 1193*s*, 1110*m*, 1061*m*, 908*m*, 783*w*, 729*m*, 666*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.91 (*d*, *J* = 6.8, 3 H); 1.09 (*d*, *J* = 6.8, 3 H); 2.15 (*sept. d*, *J* = 6.8, 4.0, 1 H); 4.71 (*d*, *J* = 4.0, 1 H); 6.97–7.18 (*m*, 7 H); 7.76 (*td*, *J* = 7.4, 1.5, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.0; 18.6; 36.3; 60.2; 115.3; 116.7 (*d*, *J* = 5); 121.8; 123.9; 123.9; 124.8; 126.6; 128.0; 130.7; 149.6; 159.7; 162.3; 163.1 (*d*, *J* = 257). ^{19}F-NMR (376 MHz, $CDCl_3$): 51.7. MS: 269

(1, M^+), 226 (87), 121 (100), 105 (12), 94 (36), 84 (27), 57 (18). HR-MS: 269.1201 (M^+, $C_{17}H_{16}FNO^+$; calc. 269.1216).

13. rac-*2-(2-Bromophenyl)-4-isopropyl-4*H-*1,3-benzoxazine* (*rac*-**7e**). At r.t., 1.0M triethyloxonium tetrafluoroborate in CH_2Cl_2 (1.0 ml) was added to a soln. of 2-bromobenzamide (201 mg, 1.0 mmol) in 1,2-dichloroethane (10 ml), and the soln. was stirred for 14 h. After addition of *rac*-**4b** (154 mg, 0.93 mmol) in CH_2Cl_2 (2 ml), the soln. was refluxed for 48 h. Sat. $NaHCO_3$ soln. (20 ml) was added at r.t., the aq. layer extracted with CH_2Cl_2 (2 × 20 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (Et_2O/pentane 1:5): *rac*-**7e** (68 mg, 21%). Pale yellow oil. TLC (Et_2O/hexane 1:5): R_f 0.4. IR ($CHCl_3$): 2965*m*, 1682*m*, 1589*w*, 1487*m*, 1462*m*, 1360*w*, 1298*m*, 1226*m*, 1192*m*, 1104*m*, 1033*w*, 909*w*, 762*s*, 730*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.96 (*d*, *J* = 6.9, 3 H); 1.11 (*d*, *J* = 6.9, 3 H); 2.18 (*sept. d*, *J* = 6.9, 4.0, 1 H); 4.70 (*d*, *J* = 4.0, 1 H); 6.95–7.48 (*m*, 6 H); 7.60–7.69 (*m*, 2 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 17.2; 18.8; 36.3; 60.6; 115.3; 121.4; 122.0; 124.8; 126.6; 127.2; 128.0; 131.1; 131.2; 133.5; 149.8. MS: 330 (1, M^+), 288 (100), 286 (100), 148 (23), 133 (53), 105 (26), 77 (27), 51 (28). HR-MS: 287.9847 ([M − i-Pr]$^+$, $C_{14}H_9BrNO^+$; calc. 287.9846).

According to the procedure described for *rac*-**7e**, 2-bromobenzamide (600 mg, 3.0 mmol), triethyloxonium tetrafluoroborate (3.0 ml, 3.0 mmol), and (*R*)-**4b** (497 mg, 3.0 mmol) gave (+)-(*R*)-**7e** (320 mg, 32%). $[\alpha]_{21}^{D} = +136$ (*c* = 1.18, $CHCl_3$).

14. rac-*2-[2-(Diphenylphosphino)phenyl]-4-isopropyl-4*H-*1,3-benzoxazine* (*rac*-**2b**). At −78°, 1.6M BuLi in hexane (0.12 ml, 0.19 mmol) was added to *rac*-**7e** (62 mg, 0.19 mmol) in Et_2O (5 ml). The resulting red soln. was stirred for 15 min at −78°, then $ClPPh_2$ (60 mg, 0.27 mmol) was added dropwise. The yellowish soln. was stirred for 1 h at −78° and then allowed to warm up to r.t. within 14 h. Sat. $NaHCO_3$ soln. (20 ml) was added, the aq. layer extracted with CH_2Cl_2 (3 × 20 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (CH_2Cl_2): *rac*-**2b** (36 mg, 44%). White solid. M.p. 118–120°. TLC (CH_2Cl_2): R_f 0.6. HPLC (hexane/i-PrOH 9:1, 1.0 ml min^{-1}): t_R 23.0 (*S*) and 29.9 (*R*). IR ($CHCl_3$): 3060*w*, 2967*s*, 2873*w*, 1677*m*, 1587*w*, 1485*m*, 1462*m*, 1435*w*, 1363*m*, 1227*s*, 1203*s*, 1102*m*. ^{1}H-NMR (400 MHz, C_6D_6): 0.90 (*d*, *J* = 6.9, 3 H); 0.94 (*d*, *J* = 6.9, 3 H); 1.98 (*sept. d*, *J* = 6.9, 3.4, 1 H); 4.56 (*d*, *J* = 3.4, 1 H); 6.68 (*td*, *J* = 8.0, 1.5, 2 H); 6.77–7.40 (*m*, 15 H); 8.16–8.21 (*m*, 1 H). ^{13}C-NMR (100 MHz, C_6D_6): 17.1; 19.2; 36.3; 60.3; 115.5; 122.5; 124.5; 126.7; 127.9; 128.3; 128.3; 128.4; 128.5; 129.3 (*d*, *J* = 3.0); 130.3; 134.0 (*d*, *J* = 19.7); 134.6 (*d*, *J* = 20.5); 135.4; 138.1 (*d*, *J* = 21.2); 138.8 (*d*, *J* = 25.0); 139.9 (*d*, *J* = 2.3); 140.0 (*d*, *J* = 4.5); 150.3; 151.9. ^{31}P-NMR (162 MHz, C_6D_6): −6.7. MS: 435 (48, M^+), 420 (66), 292 (29), 358 (199), 287 (32), 208 (14), 196 (12), 183 (25). HR-MS: 435.1739 (M^+, $C_{29}H_{26}NOP^+$; calc. 435.1752). Anal. calc. for $C_{29}H_{26}NOP$: C 79.98, H 6.02, N 3.22; found: C 79.51, H 6.25, N 3.06.

According to the procedure described for *rac*-**2b**, 1.6M BuLi in hexane (0.55 ml, 0.89 mmol) (+)-(*R*)-**7e** (289 mg, 0.875 mmol), and $ClPPh_2$ (232 mg, 1.05 mmol) gave (+)-(*R*)-**2b** (165 mg, 43%). M.p. 42–45°. $[\alpha]_{21}^{D} = +80$ (*c* = 0.37, $CHCl_3$; >99% ee by HPLC). HPLC (hexane/i-PrOH 9:1, 1.0 ml min^{-1}): t_R 29.8 (*R*); the other enantiomer was not detected.

15. *(−)-(*S*)-2,5-Dihydro-2-phenylfuran*. ((−)-(*S*)-**9**). [Pd_2(dba)$_3$·dba] (17.5 mg, 15.2 μmol, 1.5 mol-%) and (+)-(*R*)-**2a** (22.8 mg, 50.7 μmol, 5.2 mol-%) were placed under Ar in a *Carius* tube equipped with a magnetic stirring bar and a *Young* tap. THF (5 ml) was added and the resulting red soln. stirred for 20 min. Tridecane (56.9 mg, 0.309 mmol) as internal GC standard, *N*,*N*-diisopropylethylamine (0.35 ml, 266 mg, 2.06 mmol), 2,3-dihydrofuran (0.23 ml, 214 mg, 3.05 mmol), and phenyl triflate (222 mg, 0.982 mmol) were added, and the soln. was stirred at 70° for 90 h. At r.t., pentane (8 ml) was added and the mixture filtered over silica gel. Evaporation and FC (*t*-BuOMe/pentane 1:20) afforded (−)-(*S*)-**9** (114 mg, 79%). Colorless oil. $[\alpha]_{21}^{D} = -265$ (*c* = 0.925, $CHCl_3$; 91% ee by GC). GC (*FS-595-*(*t*-Bu)Me_2Si-*β-CD/SE-54* capillary column [20], 25 m; 80°, 1.5° min^{-1}, 130°, 15° min^{-1}, 160°; 90 kPa): t_R 17.3 ((*S*)-**9**, 95.3%) and 18.8 ((*R*)-**9**, 4.7%). TLC (*t*-BuOMe/pentane 1:20). R_f 0.30. IR ($CHCl_3$): 3371*w*, 3062*m*, 3031*m*, 2954*w*, 2852*s*, 1600*w*, 1492*m*, 1452*s*, 1354*m*, 1264*m*, 1227*m*, 1081*s*, 1063*s*, 1028*s*, 841*m*, 760*s*, 700*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.77 (*dddd*, *J* = 12.6, 4.2, 2.4, 1.5, 1 H); 4.85 (*dddd*, *J* = 12.6, 6.0, 2.4, 1.5, 1 H); 5.76–5.82 (*dtd*, *J* = 6.0, 2.4, 1.5, 1 H); 6.03 (*dtd*, *J* = 6.0, 2.4, 1.5, 1 H); 7.23–7.39 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 76.2; 88.3; 126.3; 126.5; 127.7; 128.4; 129.9; 142.0. MS: 146 (50, M^+), 127 (12), 115 (64), 105 (100), 91 (24), 77 (40), 69 (14), 63 (10), 51 (18).

We thank *E. Francotte*, *Novartis-Pharma Inc.* for his help with the preparative HPLC (chiral phase) separation of *rac*-**2a** and *A. Pfaltz* for welcoming *P.M.* in his group for one month. We are indebted to *A. Pinto* and *J. P. Saulnier*, Université Genève, for obtaining the NMR spectra. Financial support by the *Swiss National Science Foundation* (Chiral 2, project 2027-048319.96) is gratefully acknowledged.

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Received May 20, 1999