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Synthesis of chiral (phosphinoaryl)oxazolines, a versatile class of ligands for asymmetric catalysis

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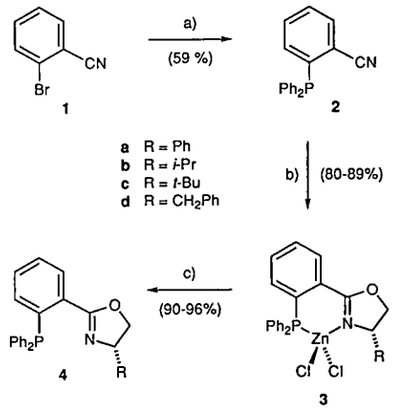
Abstract. Enantiomerically pure 2-[2-(diphenylphosphino)aryl]oxazolines are readily prepared from 2-bromobenzonitrile by transmetalation with BuLi, subsequent reaction with chlorodiphenylphosphine and conversion of the resulting phosphinoaryl nitrile to the oxazoline by treatment with a chiral amino alcohol in the presence of $ZnCl_2$. An alternative synthesis is based on the orthometalation of 2-aryloxazolines followed by reaction with chlorodiphenylphosphine.

Chiral 2-(phosphinoaryl)oxazolines [b] such as **4** (Scheme 1) have proven to be highly effective ligands for enantiocontrol of palladium-catalyzed allylic substitution[1]. More recently, we have found that the same ligands can also induce high enantioselectivities in tungsten-catalyzed allylic alkylations of 2-aryl-2-propenyl phosphates with dimethyl malonate[2] and in Heck-type reactions of alkenyl and aryl triflates with cycloalkenes[3]. Here we report experimental procedures for the synthesis of these versatile ligands which allow the preparation of a variety of differently substituted derivatives.

The first synthesis, which is summarized in Scheme 1, starts from 2-bromobenzonitrile. Metalation with *n*-butyllithium in diethyl ether and subsequent reaction with chlorodiphenylphosphine leads to 2-(diphenylphosphino)-benzonitrile[4] (**2**) in *ca.* 60% yield. Traces of phosphine oxide are easily removed by recrystallization affording analytically pure product in 59% yield. The nitrile is converted to the corresponding oxazoline by treatment with a slight excess of an equimolar mixture of amino alcohol and anhydrous zinc chloride in refluxing chlorobenzene, following the procedure of *Witte* and *Seeliger*[5]. The dichlorozinc complexes of phosphinooxazolines **3a-d** are isolated in excellent yields and high purity after filtration through a short column of silica gel. The structure of one of the complexes, **3b**, was confirmed by X-ray analysis and showed the expected tetrahedral coordination geometry[6]. Reactions with catalytic amounts of zinc dichloride leading directly to **4** gave distinctly lower yields. The crystalline zinc complexes **3a** and **3b** are readily obtained in analytically pure form by a single recrystallization from chloroform/*tert*-butyl-methyl-ether. Treatment with an equimolar amount of 2,2′-bipyridine followed by simple filtration of the reaction mixture through a short column of silica gel affords analytically pure ligands **4a** and **4b**. The zinc complex **3c** did not crystallize; however, after decomplexation with 2,2′-bipyridine, the *tert*-butyl-oxazoline **4c** could be purified by recrystallization from petroleum ether/diethyl ether. By these procedures, ligands **4a-c** were readily prepared in analytically pure form without the need for chromatography in any of the steps shown in Scheme 1. The benzyl derivative **4d**, on the other hand, had to be purified by column chromatography because neither the free ligand nor the corresponding zinc complex **3d** could be crystallized.

Another route to 2-(phosphinoaryl)oxazolines **4** is based on the orthometalation of 2-aryloxazolines developed by *Gschwend* and *Meyers*[7] (Scheme 2). The required oxazolines are readily prepared from the corresponding imidates[8] or nitriles[5] and amino alcohols. 2-Phenyloxazolines **5b** and **5e** react smoothly with *n*-butyllithium in THF at −40°C, and subsequent treatment of the resulting ortholithiated intermediates with chlorodiphenylphosphine in the presence of *N,N,N′,N′*-tetramethylethanediamine (TMEDA)[7c] leads to the 2-(2-phosphinophenyl)oxazolines **4b** and **4e**. It is important to add the TMEDA *after* the reaction with butyllithium because



Scheme 1. (a) 1. BuLi, Et_2O, −78°C; 2. Ph_2PCl. (b) Amino alcohol (1.3 equiv.), $ZnCl_2$ (1.3 equiv.), PhCl, reflux. (c) 2,2′-Bipyridine (0.99 equiv.), $CHCl_3$, RT.

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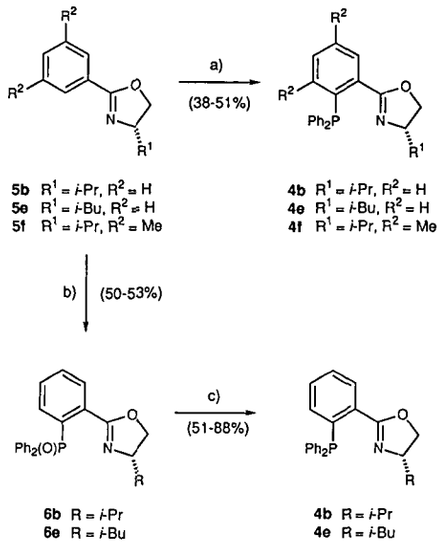
[b] IUPAC name: 4,5-dihydro-2-(2-phosphinoaryl)oxazole.



Scheme 2. (a) 1. BuLi, THF, −40°C; 2. TMEDA, Ph_2PCl, THF, −40°C → RT; or: 1. s-BuLi, TMEDA, THF, −78°C; 2. $ClPPh_2$, THF, −78°C → RT. (b) 1. s-BuLi, TMEDA, THF, −78°C; 2. $ClPPh_2$, THF, −78°C → RT; 3. H_2O_2. (c) $PhSiH_3$, 120°C.

lithiation was found to be inhibited by TMEDA. The yields of 2-(2-phosphinophenyl)oxazolines critically depend on the work-up procedure. The method of choice proved to be addition of silica gel to the reaction mixture, evaporation of the solvent, transfer of the dry silica gel to the top of a silica gel column and subsequent flash chromatography. In this way, the desired products could be isolated in 38–51% yield. Aqueous work-up, on the other hand, led to a complex mixture of products.

The same method, applied to the 3,5-dimethylphenyl derivative **5f**, gave only a 15% yield of the desired product **4f**. The problem was found to be the lithiation step. When *n*-butyllithium was replaced by the more reactive metalating agent *sec*-butyllithium/TMEDA[9], (phosphinoaryl)-oxazoline **4f** was obtained in 51% yield. Quenching experiments with D_2O showed that lithiation is complete after 5 min at −78°C in THF. The analogous 3,5-dimethylphenyl derivative with a *tert*-butyl substituent in the oxazoline ring, however, could not be prepared by this method.

In all these reactions, small amounts of the corresponding phosphine oxides are formed which are removed by column chromatography. The purified compounds, on the other hand, are quite stable and can be handled in air without noticeable oxidation. For longer periods, however, they should be stored under nitrogen. Attempts to improve the yields were unsuccessful, although no side-products were detected in the reaction mixture. In addition to the desired products, 20–30% of starting material could usually be recovered. As an alternative, we also investigated the preparation of ligands **4b** and **4e** via the phosphinoxides **6b** and **6e** (Scheme 2)[10]. The best yields of **6b** and **6e** were obtained by lithiation with *sec*-butyllithium/TMEDA, treatment with chlorodiphenylphosphine, and subsequent oxidation with hydrogen peroxide. The more direct method – lithiation followed by reaction with diphenylphosphinyl chloride – gave somewhat lower yields. The phosphine oxides **6b** and **6e** were converted to the corresponding phosphino-oxazolines **4b** and **4e** by reduction with phenylsilane[11]. The more common reagent trichlorosilane/triethylamine gave less satisfactory results. The detour *via* the phosphine oxides is attractive in cases where partial oxidation to the phosphine oxide is a problem. Another advantage is the easy chromatographic separation of the phosphine oxides **6** from unreacted aryloxazolines **5**, whereas the phosphino-oxazolines **4** often have very similar R_f values on silica gel as the precursors **5**.

Other syntheses of 2-(2-phosphinoaryl)oxazolines of type **4**, developed by the groups of *Helmchen*[1b] and *Williams*[1c,12], start from 2-fluorobenzonitrile or 2-bromobenzoic acid, which are converted to the corresponding oxazolines. The phosphino group is introduced by reaction of the 2-(2-fluorophenyl)oxazoline with potassium diphenylphosphide or by metalation of the 2-(2-bromophenyl)oxazoline with magnesium and subsequent reaction with chlorodiphenylphosphine. The synthesis shown in Scheme 1 affords similar yields as the two-step synthesis from 2-fluorobenzonitrile[12]. Our synthesis has the advantage that the oxazoline ring is introduced in the second step, allowing the preparation of different oxazoline derivatives from the same precursor **2** in high yield. In addition, the zinc complexes **3** can often be obtained in analytically pure form by simple recrystallization without prior chromatographic purification, making this route very attractive for large-scale preparation. The alternative syntheses shown in Scheme 2, which are based on the orthometalation of 2-aryloxazolines, are attractive because a wide variety of 2-(2-phosphinoaryl)oxazolines with different substituents in the aryl ring can be prepared by this route.

Experimental

General remarks

THF (Fluka puriss.) was distilled from Na/benzophenone. *n*-Butyllithium: Aldrich, 1.6M in hexanes. *sec*-Butyllithium: Aldrich, 1.3M in cyclohexane. Chlorobenzene, 1,2-dichloroethane, benzonitrile: Fluka puriss. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA): Fluka puriss., dist. over $LiAlH_4$. *P*-Chlorodiphenylphosphine, oxalyl chloride, 3,5-dimethylbenzoic acid, phenylsilane, triethyloxonium tetrafluoroborate, ethyl benzimidate hydrochloride: Fluka purum. $ZnCl_2$, anhydrous: Siegfried. Amino alcohols were synthesized by reduction of amino acids using literature procedures[13]. Reactions were carried out under argon using dried glassware. Flash column chromatography: silica gel C 560, 0.035–0.070 mm, Chemische Fabrik Uetikon. TLC: silica gel 60 Merck, 0.25 mm, F 254, staining with basic $KMnO_4$ or vanillin in H_2SO_4. Specific rotation: Perkin-Elmer-241 polarimeter; $d = 1$ dm, 23°C, concentration in g/100 ml of solution, estimated error: ±5%. IR: selected bands in cm^{-1}. ^1H-NMR, 300 MHz, ^{13}C-NMR, 75 MHz; ^{31}P-NMR, 121 MHz, triphenyl phosphate as external reference (−18 ppm). MS: selected peaks; *m/z* (%; fragment); matrix for FAB-MS: 3-nitrobenzyl alcohol (NBA).

A. Synthesis of (Phosphino-oxazolines 4a-d from 2-bromobenzonitrile (Scheme 1)

2-(Diphenylphosphino)benzonitrile (2)

To a solution of 40.2 g (221 mmol) of 2-bromobenzonitrile (**1**) in 3.0 l of diethyl ether under argon at −78°C were added dropwise 142 ml (227 mmol) of a 1.6M solution of BuLi in hexanes. After 10 min, a solution of 39 ml (211 mmol) of *P*-chlorodiphenylphosphine in 200 ml of diethyl ether was slowly added at −78°C to the dark brown solution over a period of 45 min. The resulting mixture was stirred for an additional 3 h at −78°C, then slowly allowed to warm to room temperature and stirred overnight under argon. The red brown suspension was treated with 500 ml of water and stirred for 10 min. The aqueous layer was separated from the ether layer and extracted with 500 ml of diethyl ether. The combined ether layers were dried over $MgSO_4$. Concentration *in vacuo* yielded 44.4 g of crude product. The product was dissolved under argon in 350 ml of hot isopropanol saturated with argon. The solution was heated to reflux, treated with 60 ml of isopropanol and charcoal, filtered and slowly cooled to room temperature. Crystallization yielded 41.2 g of 2-(diphenylphosphino)benzonitrile containing 4% of the corresponding phosphinoxide. A second recrystallization from 300 ml of iso-

propanol afforded 37.4 g (59%) of **2** which was free of phosphine oxide. ^{1}H-NMR: δ 7.02–7.06 (m, 1 H, arom. H); 7.25–7.50 (m, 12 H, arom. H); 7.68–7.72 (m, 1 H, arom. H) ppm. ^{31}P NMR: δ −8.8 ppm [2-(diphenylphosphinyl)benzonitrile at δ 26.3 ppm, not detected].

Zn(II) complexes **3a-d**

General procedure. A stirred suspension of 6.28 g (21.9 mmol) of 2-(diphenylphosphino)benzonitrile (**2**), 3.90 g (28.4 mmol) of (+)-(*S*)-2-amino-2-phenylethanol and 3.87 g (28.4 mmol) of $ZnCl_2$ in 70 ml of chlorobenzene was heated to reflux under argon for 144 h. The reaction mixture was transferred directly onto a 7×5 cm silica-gel column and eluted with 400 ml of ethyl acetate. Evaporation of the solvent afforded a pale yellow glassy solid which was crystallized from chloroform/*tert*-butyl-methyl-ether to give 9.76 g (82%) of **3a** as colourless crystals.

(+)-{(4S)-4,5-Dihydro-2-[2'-(diphenylphosphino)phenyl]-4-phenyloxazole}zinc(II) dichloride (**3a**). M.p. > 250°C; $[\alpha]_D$ +88.4 (*c* 0.99, $CHCl_3$). IR ($CHCl_3$): 3062w, 3005s, 1624s, 1456s, 1481m, 1438s, 1369s, 1313w, 1143w, 1115m, 1060m, 947w, 693s. ^{1}H-NMR: δ 4.43 (dd, *J* 9.0 and 6.9 Hz, 1 H, $H_2C(5)$); 4.75 (dd, *J* 10.2 and 9.0 Hz, 1 H, $H_2C(5)$); 5.59 (dd, *J* 10.2 and 6.9 Hz, 1 H, HC(4)); 7.05–7.72 (4 m, 18 H, arom. H); 8.20 (ddd, *J* 7.8, 4.5 and 1.2 Hz, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 68.9 (d, J_{PC} 3 Hz, HC(4)); 75.2 ($H_2C(5)$); 127.0, 128.5, 128.8, 129.4 (d, J_{PC} 11 Hz), 131.4, 131.6 (d, J_{PC} 2 Hz), 131.7, 132.8 (d, J_{PC} 6 Hz), 133.4 (d, J_{PC} 5 Hz), 134.3 (d, J_{PC} 14 Hz), 135.0 (arom. CH); 125.4 (d, J_{PC} 22 Hz), 125.8 (d, J_{PC} 22 Hz) (arom. C); 127.6 (d, J_{PC} 13 Hz, C(1')); 130.6 (d, J_{PC} 24 Hz, C(2')); 138.3 (arom. C); 167.8 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −19.9 ppm. MS (NBA, KCl): 580 (11, $[M+K]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 587–580, calcd. (obsd.): 1.6 (1.3), 5.1 (4.3), 4.2 (3.5), 11.9 (11.1), 5.6 (5.5), 15.3 (15.3), 3.6 (3.4), 11.5 (10.9); 522 (18, $[M+O-Cl]^+$, ^{64}Zn, ^{35}Cl); 506 (93, $[M-Cl]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 515–506, calcd. (obsd.): 0.2 (0.2), 4.3 (4.6), 16.0 (15.9), 19.7 (19.0), 59.3 (55.7), 34.0 (33.4), 87.3 (83.3), 28.7 (32.7), 92.7 (92.7); 302 (100). Anal. calcd. for $C_{27}H_{22}Cl_2NOPZn$ (543.74): C 59.64, H 4.08, O 2.94; found: C 59.42, H 4.10, O 2.71%.

(+)-{(4S)-4,5-Dihydro-2-[2'-(diphenylphosphino)phenyl]-4-isopropyloxazole}zinc(II) dichloride (**3b**). 80% yield (reaction time 84 h): crystallized from tert-butyl-methyl-ether/chloroform; colourless crystals; m.p. 221–223°C; $[\alpha]_D$ +52.3 (*c* 1.52, $CHCl_3$). IR ($CHCl_3$): 3006m, 1632m, 1568w, 1483m, 1438m, 1369m, 1247m, 1206s, 1147w, 1111w, 1056w, 998w, 956w. ^{1}H-NMR: δ 0.55 (d, *J* 6.9 Hz, 3 H, $CH(CH_3)_2$); 0.89 (d, *J* 7.1 Hz, 3 H, $CH(CH_3)_2$); 2.56 (m, 1 H, $CH(CH_3)_2$); 4.29 (dd, $^1J \approx {}^2J$ 9.0 Hz, 1 H, $H_2C(5)$); 4.38 (dd, *J* 9.0 and 6.2 Hz, 1 H, $H_2C(5)$); 4.59 (ddd, *J* 9.0, 6.2 and 3.5 Hz, 1 H, HC(4)); 7.11 (m, 1 H, HC(4')); 7.43–7.66 (m, 12 H, arom. H); 8.08 (m, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 13.9, 18.9 ($CH(CH_3)_2$); 29.7 ($CH(CH_3)_2$); 68.0 ($H_2C(5)$); 70.4 (d, J_{PC} 3 Hz, (HC(4)); 129.5, 129.6 (d, J_{PC} 10 Hz), 130.2, 131.5, 131.9 (d, J_{PC} 2 Hz), 132.7 (d, J_{PC} 6 Hz), 133.2 (d, J_{PC} 5 Hz), 134.4 (d, J_{PC} 17 Hz), 134.5 (d, J_{PC} 17 Hz), 135.1 (arom. CH); 125.6 (d, J_{PC} 35 Hz), 125.8 (d, J_{PC} 35 Hz), 127.0 (d, J_{PC} 13 Hz), 130.2 (d, J_{PC} 25 Hz) (arom. C); 166.8 (d, J_{PC} 4 Hz) ppm. ^{31}P-NMR: δ −20.1 ppm. MS (NBA, KCl): 546 (20, $[M+K]^+$, ^{64}Zn, ^{35}Cl) isotope cluster 555–546 calcd. (obsd.): 15.4 (15.8), 4.3 (3.8), 20.4 (20.4), 6.9 (6.2), 15.7 (14.7), 5.1 (4.1), 6.7 (6.2), 1.9 (0.3), 1.4 (0), 0.3 (0); 488 (23, $[M+O-Cl]^+$, ^{64}Zn, ^{35}Cl) isotope cluster 496–488 calcd. (obsd.): 23.6 (23.6), 6.6 (6.3), 22.1 (20.5), 8.0 (7.2), 14.9 (13.6), 4.5 (4.1), 4.0 (3.2), 1.0 (3.8), 0.2 (2.2); 472 (100, $[M-Cl]^+$, ^{64}Zn, ^{35}Cl) isotope cluster 481–472 calcd. (obsd.): 100 (100), 27.7 (28.7), 93.3 (92.4), 33.6 (33.4), 62.8 (60.0), 19.2 (18.1), 16.6 (15.5), 4.1 (3.4). Anal. calcd. for $C_{24}H_{24}Cl_2NOPZn$ (509.72): C 56.55, H 4.74, N 2.75, O 3.14; found: C 56.76, H 4.78, N 2.71, O 3.29%.

*(+)-{(4S)-4-*tert*-Butyl-4,5-dihydro-2-[2'-(diphenylphosphino)-phenyl]oxazole}zinc(II) dichloride* (**3c**). 88% yield (reaction time 108 h); pale yellow glass; $[\alpha]_D$ +60.9 (*c* 1.13, $CHCl_3$). IR ($CHCl_3$): 3005s, 2968s, 2873w, 1626s, 1483m, 1438s, 1376m, 1367s, 1317m, 1119m, 950m, 693s. ^{1}H-NMR: δ 1.02 (s, 9 H, $C(CH_3)_3$); 4.00 (dd, *J* 9.6 and 9.0 Hz, 1 H, $H_2C(5)$); 4.43 (ddd, *J* 9.6, 4.2 and 0.9 Hz, 1 H, HC(4)); 4.51 (dd, *J* 9.0 and 4.2 Hz, 1 H, $H_2C(5)$); 7.06 (dd, *J* 7.7 and 1.4 Hz, 1 H, HC(4')); 7.39–7.69 (m, 12 H, arom. H); 7.85 (ddd, *J* 7.7, 4.5 and 1.4 Hz, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 25.6 ($C(CH_3)_3$); 34.9 ($C(CH_3)_3$); 70.3 ($H_2C(5)$); 73.7 (d, J_{PC} 2 Hz, HC(4)); 129.4 (d, J_{PC} 10 Hz), 129.5 (d, J_{PC} 10 Hz), 130.9 (d, J_{PC} 7 Hz), 130.2, 131.7 (d, J_{PC} 2 Hz), 131.8 (d, J_{PC} 2 Hz), 132.7 (d, J_{PC} 5 Hz), 134.0, 134.4 (d, J_{PC} 12 Hz), 134.5 (d, J_{PC} 13 Hz) (arom. CH); 124.8 (d, J_{PC} 34 Hz), 126.2 (d, J_{PC} 33 Hz), 129.2 (d, J_{PC} 16 Hz), 129.5 (d, J_{PC} 25 Hz) (arom. C); 168.5 (d, J_{PC} 2 Hz, C(2)) ppm. ^{31}P-NMR: δ −22.1 ppm. MS (NBA, KCl): 560 (7, $[M+K]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 566–560, calcd. (obsd.): 3.5 (2.7), 2.7 (2.2), 8.2 (7.2), 3.7 (4.0), 10.6 (10.6), 2.3 (1.9), 8.0 (7.3); 502 (18, $[M+O-Cl]^+$, ^{64}Zn, ^{35}Cl); 486 (64, $[M-Cl]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 495–486, calcd. (obsd.): 0.1 (4.6), 0.6 (10.3), 2.7 (3.9), 10.8 (12.6), 21.7 (11.9), 40.6 (38.1), 22.2 (21.2), 60.0 (57.6), 18.5 (18.6), 64.1 (64.1); 404 (100).

(+)-{(4S)-4-Benzyl-4,5-dihydro-2-[2'-(diphenylphosphino)phenyl]oxazole}zinc(II) dichloride (**3d**). 84% yield (reaction time 144 h); pale yellow glass; $[\alpha]_D$ +73.8 (*c* 0.94, $CHCl_3$). IR ($CHCl_3$): 3062w, 3005s, 1629s, 1608w, 1480m, 1438m, 1371m, 1117m, 965w, 693s. ^{1}H-NMR: δ 2.42 (dd, *J* 13.5 and 10.2 Hz, 1 H, CH_2Ph); 3.63 (dd, *J* 13.5 and 3.3 Hz, 1 H, CH_2Ph); 4.21 (dd, *J* 9.0 and *ca.* 9.4 Hz, 1 H, $H_2C(5)$); 4.31 (dd, *J* 9.0 and 6.0 Hz, 1 H, $H_2C(5)$); 4.82 (m, 1 H, HC(4)); 7.07–7.16 (m, 1 H, HC(4')); 7.16–7.35 (m, 5 H, arom. H); 7.41–7.66 (m, 12 H, arom. H); 7.95–8.02 (m, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 39.9 (CH_2Ph); 66.6 (d, J_{PC} 3 Hz, HC(4)); 71.5 ($H_2C(5)$); 126.8, 128.6, 129.3, 129.5 (d, J_{PC} 10 Hz), 131.4, 131.8 (d, J_{PC} 2 Hz), 131.9 (d, J_{PC} 2 Hz), 132.6 (d, J_{PC} 6 Hz), 133.2 (d, J_{PC} 6 Hz), 134.29 (d, J_{PC} 14 Hz), 134.34 (d, J_{PC} 15 Hz), 134.9 (arom. CH); 125.4 (d, J_{PC} 34 Hz), 125.5 (d, J_{PC} 35 Hz) (arom. C); 127.8 (d, J_{PC} 12 Hz, C(1')); 130.1 (d, J_{PC} 25 Hz, C(2')); 167.2 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −19.3 ppm. MS (NBA, KCl): 594 (14, $[M+K]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 602–594, calcd. (obsd.): 1.3 (1.0), 14.0 (13.4), 6.8 (8.2), 18.0 (18.0), 4.3 (6.6), 13.5 (13.8); 536 (16, $[M+O-Cl]^+$, ^{64}Zn, ^{35}Cl); 520 (100, $[M-Cl]^+$, ^{64}Zn, ^{35}Cl), isotope cluster 529–520, calcd. (obsd.): 0.2 (0.1), 1.1 (1.7), 4.8 (4.8), 17.5 (17.9), 22.0 (20.4), 64.4 (60.3), 37.8 (37.3), 94.6 (93.7), 32.2 (34.4), 100 (100).

Phosphino-oxazolines **4a-d**

General procedure. To a solution of 9.50 g (17.5 mmol) of **3a** in 130 ml of chloroform under argon was added 2.72 g (17.4 mmol) of 2,2'-bipyridine at room temperature. The resulting suspension was stirred for 1 h. The reaction mixture was transferred directly onto a 6×7 cm silica-gel column and eluted with 800 ml of chloroform. Evaporation of the solvent afforded 6.78 g (95%) of **4a** as a pale yellow glassy solid.

(+)-(4S)-4,5-Dihydro-2-[2'-(diphenylphosphino)phenyl]-4-phenyloxazole (**4a**). $[\alpha]_D$ +30.9 (*c* 1.00, $CHCl_3$). IR ($CHCl_3$): 3060s, 2965m, 2905w, 2360w, 2335w, 1970w, 1955w, 1885w, 1820w, 1645s, 1475m, 1435s, 1355m, 1090m, 1035m, 950m. ^{1}H-NMR: δ 3.93 (dd, *J ca.* 9.0 and ca. 8.3 Hz, 1 H, $H_2C(5)$); 4.55 (dd, *J* 10.1 and 8.3 Hz, 1 H, $H_2C(5)$); 5.22 (dd, *J* ca. 10.1 and ca. 9.0 Hz, 1 H, HC(4)); 7.11 (m, 1 H, arom. H); 6.86–6.96 (m, 3 H, arom. H); 7.14–7.22 (m, 3 H, arom. H); 7.24–7.41 (m, 12 H, arom. H); 8.00 (ddd, *J* 7.5, 3.6 and 1.5 Hz, 1 H, HC(6')) ppm. ^{13}C NMR: δ 70.1 ($H_2C(5)$); 74.3 (HC(4)); 126.6, 127.1, 128.0, 128.36, 128.45 (d, J_{PC} 2 Hz), 128.46, 128.51 (d, J_{PC} 20 Hz), 128.52, 130.3 (d, J_{PC} 3 Hz), 130.6, 133.78, 133.83 (d, J_{PC} 20 Hz), 134.3, (d, J_{PC} 21 Hz) (arom. CH); 131.4 (d, J_{PC} 19 Hz), 137.8 (d, J_{PC} 10 Hz), 138.0 (d, J_{PC} 13 Hz), 139.1 (d, J_{PC} 25 Hz), 141.9 (C arom.); 164.7 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −5.7 ppm. MS (CI, NH_3): 410 (5), 409 (30), 408 (100, $[M+H]^+$), 302(6), 187(5). TLC: R_f 0.27 (hexane/ethyl-acetate 5/1).

(−)-(4S)-4,5-Dihydro-2-[2'-(diphenylphosphino)phenyl]-4-isopropyloxazole (**4b**). 96% yield; colourless solid; $[\alpha]_D$ −44.9 (c 1.40, $CHCl_3$). IR ($CHCl_3$): 3070w, 3060m, 3010m, 2965s, 2905m, 2875m, 1950w, 1885w, 1815w, 1650s, 1585w, 1480m, 1470w, 1435s, 1355m, 1310m, 1245m, 1090s, 1050m, 1030m, 965m. ^{1}H-NMR: δ 0.70 (d, *J* 6.8 Hz, 3 H, $CH(CH_3)_2$); 0.81 (d, *J* 6.8 Hz, 3 H, $CH(CH_3)_2$); 1.43–1.54 (m, 1 H, $CH(CH_3)_2$); 3.80–3.90 (m, 2 H, $H_2C(5)$); 4.09–4.19 (m, 1 H, HC(4)); 6.85–6.89 (m, 1 H, HC(4')); 7.24–7.37 (m, 12 H, arom. H); 7.88–7.92 (m, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 18.3 ($CH(CH_3)_2$); 18.9 ($CH(CH_3)_2$); 32.7 ($CH(CH_3)_2$); 70.0 ($H_2C(5)$); 73.1 (HC(4)); 127.8, 128.05, 128.16, 128.26, 128.27 (d, J_{PC} 15 Hz), 129.6 (d, J_{PC} 3 Hz), 130.1, 133.5 (d, J_{PC} 20 Hz), 133.7, 134.1 (d, J_{PC} 21 Hz) (arom. CH); 131.7 (d, J_{PC} 19 Hz), 137.9 (d, J_{PC} 10 Hz), 138.1 (d, J_{PC} 12 Hz), 138.8 (d, J_{PC} 25 Hz) (arom. C); 162.7 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −5.8 ppm. MS (EI): 372(3, M^+), 358(7), 330(20), 302(100), 282(31), 240(10), 228(8), 183(16). TLC: R_f 0.40 (hexane/ethyl-acetate 6/1). Anal. calcd. for $C_{24}H_{24}NOP$ (373.43): C 77.19, H 6.48, N 3.75; found: C 77.08, H 6.61, N 3.75%.

*(−)-(4S)-4-*tert*-Butyl-4,5-dihydro-2-[2'-(diphenylphosphino)phenyl]-oxazole* (**4c**). The product was recrystallized from petroleum-ether/diethyl-ether to yield 92% of colourless crystals. M.p. 104–105°C. $[\alpha]_D$ −58.3 (*c* 0.92, $CHCl_3$). IR ($CHCl_3$): 3070w, 3055m, 2960s, 2905m, 2865m, 1650s, 1480s, 1435s, 1355m, 1245m, 1095m, 1025m, 965m. ^{1}H-NMR: δ 0.73 (s, 9 H, $C(CH_3)_3$); 3.87 (dd, *J* 10.2 and 8.3 Hz, 1 H, $H_2C(5)$); 4.00 (dd, ^1J, ^2J 8.3 Hz, 1 H, HC(4)); 4.08 (dd, *J* 10.2 and 8.3 Hz, 1 H, $H_2C(5)$); 6.87 (m, 1 H, HC(4')); 7.18–7.41 (m,

12 H, arom. H); 7.94 (ddd, *J* 7.8, 3.6 and 1.5 Hz, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 25.7 (C(CH_3)$_3$); 33.6 (C(CH$_3$)$_3$); 68.2 (H_2C(5)); 76.7 (HC(4)); 128.0, 128.1, 128.2 (d, J_{PC} 2 Hz), 128.3 (d, J_{PC} 20 Hz), 128.4, 129.8 (d, J_{PC} 3 Hz), 130.3, 133.5 (d, J_{PC} 20 Hz), 134.1, 134.3 (d, J_{PC} 21 Hz) (arom. CH); 131.9 (d, J_{PC} 20), 138.2 (d, J_{PC} 10 Hz), 138.5 (d, J_{PC} 12 Hz), 138.8 (d, J_{PC} 25 Hz) (arom. C); 162.7 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −6.3 ppm. MS (CI, NH_3): 389 (28), 388 (100, [M+H]$^+$), 330(6), 302(7). TLC: R_f 0.36 (hexane/ethyl-acetate 6/1). Anal. calcd. for $C_{25}H_{26}NOP$ (587.46): C 77.50, H 6.76, N 3.62; found: C 77.43, H 6.75, N 3.62%.

(+)-(4S)-4-Benzyl-4,5-dihydro-2-[2'-(diphenylphosphino)phenyl]-4-oxazole (**4d**). 95% yield; pale yellow glassy solid; $[\alpha]_D$ +25.8 (*c* 1.10, $CHCl_3$). IR (*film*): *3060m, 2965m, 2360m, 2340m, 1950w, 1885w,* 1820w, 1650s, 1605m, 1585m, 1495m, 1475s, 1455m, 1435s, 1355s, 1245w, 1135w, 1090s, 1055w, 1030m, 965s, 920w. ^{1}H-NMR: δ 2.11 (dd, *J* 13.8 and 9.2 Hz, 1 H, CH_2Ph); 2.92 (dd, *J* 13.8 and 5.0 Hz, 1 H, CH_2Ph); 3.78 (dd, $^1J \approx {}^2J$ *ca.* 8 Hz, 1 H, H_2C(5)); 4.03 (dd, $^1J \approx {}^2J$ ca. 8 Hz, 1 H, H_2C(5)); 4.35 (m, 1 H, HC(4)); 6.86 (ddd, *J* 7.6, 4.4 and 1.4 Hz, 1 H, HC(4')); 7.02–7.12 (m, 2 H, arom. H); 7.14–7.44 (m, 15 H, arom. H); 7.86 (ddd, *J* 7.4, 3.5 and 1.7 Hz, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 41.1 (CH$_2$Ph); 67.9 (HC(4)); 71.4 (H_2C(5)); 126.2, 127.9, 128.3, 128.39 (d, J_{PC} 3 Hz), 128.49, 128.52, 128.55 (d, J_{PC} 21 Hz), 129.0, 129.9 (d, J_{PC} 3 Hz), 130.4, 133.5 (d, J_{PC} 2 Hz), 133.8 (d, J_{PC} 21 Hz), 134.4 (d, J_{PC} 21 Hz) (CH arom.); 131.5 (d, J_{PC} 18 Hz), 137.8 (d, J_{PC} 10 Hz), 138.0 (d, J_{PC} 14 Hz), 138.1, 138.9 (d, J_{PC} 25 Hz) (arom. C); 163.9 (d, J_{PC} 2 Hz, C(2)) ppm. ^{31}P-NMR: δ −5.0 ppm. MS (CI, NH_3): 423 (31), 422 (100, [M+H]$^+$), 330(14), 302(10). TLC: R_f 0.30 (hexane/ethyl-acetate 4/1).

B. Synthesis of phosphino-oxazolines 4b,e,f by orthometallation (Scheme 2)

Oxazolines **5b,e**

Procedure 1. A stirred solution of L-2-amino-3-methylbutan-1-ol (4.55 g, 44.1 mmol), benzonitrile (5.0 ml, 48.7 mmol) and $ZnCl_2$ (179 mg, 1.31 mmol) in 20 ml of chlorobenzene was heated to reflux under nitrogen for 63 h. After concentration and distillation (71°C/0.03 mbar) 6.70 g (81%) of **5b** were obtained as a colourless oil.

Procedure 2. A suspension of 5.39 g (29.0 mmol) of ethyl benzimidate hydrochloride and 3.29 g (31.9 mmol) of L-2-amino-3-methylbutan-1-ol in 70 ml of 1,2-dichloroethane was heated under reflux for 15 h. After cooling to room temperature the reaction mixture was filtered and concentrated *in vacuo*. The residue was dissolved in *tert*-butyl methyl ether, filtered again and concentrated. Kugelrohr distillation afforded 5.13 g (93%) of **5b** as a colourless oil.

(−)-(4S)-4,5-Dihydro-4-isopropyl-2-phenyloxazole (**5b**). $[\alpha]_D$ −85.2 (*c* 1.09, $CHCl_3$). IR ($CHCl_3$): 3062w, 2960s, 2890m, 1739w, 1652s, 1495m, 1450s, 1353s, 1318m, 1251m, 1081s, 1065s, 1026m, 968m. ^{1}H-NMR: δ 0.92 (d, *J* 6.7 Hz, 3 H, CH(CH_3)$_2$); 1.03 (d, *J* 6.9 Hz, 3 H, CH(CH_3)$_2$); 1.82–1.89 (m, 1 H, CH(CH$_3$)$_2$); 4.05–4.15 (m, 2 H, H_2C(5)); 4.35–4.40 (m, 1 H, HC(4)); 7.36–7.45 (m, 3 H, HC(3'), HC(4'), HC(5')); 7.94–7.97 (m, 2 H, HC(2'), HC(6')) ppm. ^{13}C NMR: δ 18.1 (CH(CH_3)$_2$); 18.9 (CH(CH_3)$_2$); 32.8 (CH(CH$_3$)$_2$); 70.0 (H_2C(5)); 72.5 (HC(4)); 127.9 (C(1')); 128.16, 128.19 (HC(3'), HC(4'), HC(5')); 131.1 (HC(2'), HC(6')); 163.3 (C(2)) ppm. MS (EI): 189(2, M$^+$), 146(100), 118(22), 104(12), 91(30), 77(20). TLC: R_f 0.31 (hexane/diethyl-ether 8/1).

(−)-(4S)-4,5-Dihydro-4-isobutyl-2-phenyloxazole (**5e**). 77% yield (*Procedure 1*); 93% yield (*Procedure 2*); b.p. 85°C (0.04 mbar); $[\alpha]_D$ −79.9 (*c* 0.95, $CHCl_3$). IR ($CHCl_3$): 3063w, 2959s, 1651s, 1495m, 1468m, 1450m, 1357m, 1079m, 1063m, 694s. ^{1}H-NMR: δ 0.97 (d, *J* 6.5 Hz, 3 H, CH(CH_3)$_2$); 0.99 (d, *J* 6.4 Hz, 3 H, CH(CH_3)$_2$); 1.38 (ddd, *J* 13.2, 7.8 and 6.6 Hz, 1 H, CH_2CH(CH$_3$)$_2$); 1.74 (ddd, ^1J 13.2 and $^2J \approx {}^3J$ ca. 6.5 Hz, 1 H, CH_2CH(CH$_3$)$_2$); 1.80 (septett, *J* 6.6 Hz, 1 H, CH(CH$_3$)$_2$); 3.87 (dd, $^1J \approx {}^2J$ ca. 7.9 Hz, 1 H, H_2C(5)); 4.27–4.37 (m, 1 H, HC(4)); 4.49 (dd, *J* 9.2 and 8.0 Hz, 1 H, H_2C(5)); 7.36–7.45 (m, 3 H, HC(3'), HC(4'), HC(5')); 7.95 (d, *J* 7.1 Hz, 2 H, HC(2'), HC(6')) ppm. ^{13}C-NMR: δ 22.6 (CH(CH_3)$_2$); 22.8 (CH(CH_3)$_2$); 25.4 (CH(CH$_3$)$_2$); 45.5 (CH$_2$CH(CH$_3$)$_2$); 65.1 (HC(4)); 73.0 (H_2C(5)); 127.9 (C(1')); 128.09, 128.14, 131.0 (arom. CH); 163.1 (C(2)) ppm. MS (EI): 203(5, M$^+$), 188(7), 161(20), 146(100), 130(17), 118(29), 105(81), 91(40), 77(37). TLC: R_f 0.24 (hexane/ethyl-acetate 10/1).

(−)-(4S)-4,5-Dihydro-2-(3',5'-dimethylphenyl)-4-isopropyloxazole[14] (**5f**)

To a solution of 10.0 g (66.6 mmol) of 3,5-dimethylbenzoic acid in 150 ml of dichloromethane were added dropwise 7.5 ml (87 mmol) of oxalyl chloride under argon at 0 °C. The reaction mixture was stirred at room temperature for 16 h. Then 67 ml of a 25% solution of aqueous ammonia was added at 0°C over 30 min. The mixture was then poured into ice-water and extracted three times with tert-butyl methyl ether. The organic layers were washed with saturated aqueous NaCl and dried over Na_2SO_4. Concentration *in vacuo* afforded 9.54 g (96%) of 3,5-dimethylbenzamide as a colourless solid. Recrystallization from diethyl ether gave 8.70 g (88%) of 3,5-dimethylbenzamide as colourless crystals; m.p. 134–135°C. ^{1}H-NMR: δ 2.35 (s, 6 H, CH_3); 6.15–6.35 (br s, 2 H, NH_2); 7.15 (s, 1 H, arom. CH); 7.42 (s, 2 H, arom. H) ppm.
A mixture of 6.41 g (43.0 mmol) of 3,5-dimethylbenzamide and 8.31 g (43.9 mmol) of triethyloxonium tetrafluoroborate in 400 ml of anhydrous 1,2-dichloroethane was stirred under argon at ambient temperature for 20 h. Then 5.2 ml (47 mmol) of L-2-amino-3-methylbutan-1-ol were added and the solution was heated under reflux for 24 h. The mixture was cooled to room temperature, diluted with 500 ml of dichloromethane and washed with saturated aqueous $NaHCO_3$, water, and saturated aqueous NaCl. Drying over $MgSO_4$ and evaporation of the solvent in vacuo, followed by filtration over silica gel (4×3 cm, hexane/ethyl-acetate 6/1), afforded 7.79 g (83%) of (−)-(4*S*)-4,5-dihydro-2-(3',5'-dimethylphenyl)-4-isopropyloxazole (**5f**) as a colourless oil. ^{1}H-NMR: δ 0.92 (d, *J* 6.7 Hz, 3 H, CH(CH_3)$_2$); 1.02 (d, *J* 6.7 Hz, 3 H, CH(CH_3)$_2$); 1.75–1.92 (m, 1 H, CH(CH$_3$)$_2$); 2.33 (s, 6 H, CH_3); 4.03–4.15 (m, 2 H, H_2C(5)); 4.30–4.42 (m, 1 H, HC(4)); 7.08 (s, 1 H, HC(4')); 7.58 (s, 2 H, HC(2'), HC(6')) ppm.

Synthesis of phosphino-oxazolines **4b,e** *from* **5b,e**

General procedure. To 3.92 g (20.7 mmol) of **5b** in 200 ml of THF under argon at −45°C (dry ice/chlorobenzene bath) were added 14.5 ml of a 1.6M solution of BuLi in hexanes (23.2 mmol). The resulting orange solution was stirred for 2½ h. Then 6.2 ml (41 mmol) of TMEDA were added dropwise. After 10 min a solution of 5.7 ml (30.9 mmol) of *p*-chlorodiphenylphosphine in 40 ml of THF was added over a period of 15 min. The reaction mixture was stirred at ambient temperature for 19 h. Under argon 10 g of silica gel were added to the mixture and the solvent was removed *in vacuo*. Purification by flash chromatography (hexane/ethyl acetate 100:6) afforded 2.96 g (38%) of **4b** as a colourless oil (spectroscopic data: see above).

(−)-(4S)-4,5-Dihydro-2-[2'-(diphenylphosphino)phenyl]-4-isobutyl-oxazole (**4e**). 45% yield; m.p. 98°C; $[\alpha]_D$ −27.8 (*c* 0.98, $CHCl_3$). IR (KBr): 3067w, 2955m, 2910m, 1642s, 1456s, 1435s, 1086m, 1048s, 1034s, 977m, 781m, 743s, 696s. ^{1}H-NMR: δ 0.81 (d, *J* 6.9 Hz, 3 H, CH(CH_3)$_2$); 0.84 (d, *J* 6.6 Hz, 3 H, CH(CH_3)$_2$); 0.93 (ddd, *J* 13.5, 7.3 and 7.2 Hz, 1 H, CH_2CH(CH$_3$)$_2$); 1.29 (ddd, *J* 13.6, 6.9 and 6.7 Hz, 1 H, CH_2CH(CH$_3$)$_2$); 1.57 (septett, *J* 6.9, 1 H, CH$_2$CH(CH$_3$)$_2$); 3.48 (dd, *J* 7.9, 7.7, 1 H, H_2C(5)); 4.06–4.12 (m, 1 H, HC(4)); 4.22 (dd *J* 9.3 and 7.7 Hz, 1 H, H_2C(5)); 6.82–6.89 (m, 1 H, HC(4')); 7.24–7.36 (m, 12 H, arom. H); 7.84–7.88 (m, 1 H, HC(6')) ppm. ^{13}C-NMR: δ 22.5 (CH(CH_3)$_2$); 22.9 (CH(CH_3)$_2$); 25.2 (CH(CH$_3$)$_2$); 45.0 (CH$_2$CH(CH$_3$)$_2$); 65.2 (HC(4)); 72.7 (H_2C(5)); 127.8, 128.15, 128.25, 128.28 (d, J_{PC} 3 Hz), 128.4 (d, J_{PC} 19 Hz), 129.7 (d, J_{PC} 3 Hz), 130.2, 133.5 (d, J_{PC} 2 Hz), 133.7 (d, J_{PC} 21 Hz), 134.2 (d, J_{PC} 21 Hz) (arom. CH); 131.8 (d, J_{PC} 18 Hz), 137.9 (d, J_{PC} 10 Hz), 138.0 (d, J_{PC} 12 Hz), 138.7 (d, J_{PC} 25 Hz) (arom. C); 163.1 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ −5.2 ppm. MS (FAB): 404(12), 388(100, M$^+$), 344(44), 331(13), 310(32), 302(71), 296(63), 288(40), 252(8), 240(21), 228(13), 210(20), 183(34), 165(12). TLC: R_f 0.18 (hexane/diethyl-ether 100/6). Anal. calcd. for $C_{25}H_{26}NOP$ (387.51): C 77.50, H 6.76, N 3.62; found: C 77.71, H 6.85, N 3.60%.

(−)-(4S)-4,5-Dihydro-2-[3',5'-dimethyl-2'-(diphenylphosphino)-phenyl]-4-isopropyloxazole (**4f**)

Under argon a mixture of a 1.3M solution of *s*-BuLi in cyclohexane (24 ml, 31.2 mmol) and 100 ml of THF was treated with 4.6 ml (30 mmol) of TMEDA at −78°C. To the resulting bright yellow solution was added dropwise a solution of 6.10 g (28.1 mmol) of **5f** in 14 ml of THF. The dark red reaction mixture was stirred for 2 h at −78°C. A solution of 10.4 ml (56.3 mmol) of *p*-chlorodiphenylphosphine in 28 ml of THF was slowly added with a syringe. After 3 h the mixture was allowed to warm slowly to room temperature and was stirred

overnight under argon. Then 15 g of silica gel were added under argon, the solvent was removed *in vacuo* and the product was eluted by flash chromatography (hexane/*tert*-butyl-methyl-ether 4/1) to give a colourless oil (5.73 g, 51%). Additionally, 1.34 g (22%) of starting material were recovered. **4f**; $[\alpha]_D$ −45.8 (*c* 1.20, $CHCl_3$). IR ($CHCl_3$): 3052w, 2958s, 2924m, 2871m, 1661s, 1600w, 1585w, 1480m, 1434s, 1352m, 1192w, 1134m, 968m, 743s, 697s. ^{1}H NMR: δ 0.89 (d, *J* 5.9 Hz, 3 H, $CH(CH_3)_2$); 0.95 (d, *J* 6.0 Hz, 3 H, $CH(CH_3)_2$); 1.72–1.79 (m, 1 H, $CH(CH_3)_2$); 1.91 (s, 3 H, CH_3); 2.33 (s, 3 H, CH_3); 3.73–3.81 (m, 1 H, HC(4)); 3.90 (dd, *J* 8.2 and 8.1 Hz, 1 H, $H_2C(5)$); 4.06 (dd *J* 9.7 and 8.2 Hz, 1 H, $H_2C(5)$); 7.06 (s, 1 H, HC(4′)); 7.23–7.41 (m, 11 H, arom. H) ppm. ^{13}C-NMR: δ 18.6 ($CH(CH_3)_2$); 19.1 ($CH(CH_3)_2$); 21.0 (arom. CH_3); 22.7 (arom. CH_3); 32.7 ($CH(CH_3)_2$); 70.2 (HC(4)); 76.6 ($H_2C(5)$); 127.4 (d, J_{PC} 5 Hz) (arom. CH); 127.98, 128.02, 128.05, 128.10 (4 lines, 3 arom. CH); 128.3 (d, J_{PC} 7 Hz), 131.8 (d, J_{PC} 18 Hz), 132.0 (d, J_{PC} 19 Hz), 134.0 (arom. CH); 129.7 (d, J_{PC} 21 Hz), 136.3 (d, J_{PC} 14 Hz), 136.4 (d, J_{PC} 12 Hz), 137.5 (d, J_{PC} 30 Hz) (arom. C); 139.7 (C(5′)); 144.7 (d, J_{PC} 5 Hz, C(3′)); 165.3 (d, J_{PC} 4 Hz, C(2)) ppm. ^{31}P-NMR: δ −8.0 ppm. MS (EI): 401(1, M^+), 386(6), 358(23), 330(100), 310(34), 268(10), 256(6), 77(5). TLC: R_f 0.18 (hexane/diethyl-ether 7/2).

Synthesis of phosphine oxides **6b,e**

General procedure. To 4 ml of THF at −78°C under argon were added dropwise 0.98 ml (1.3 mmol) of a 1.3M solution of *s*-BuLi in cyclohexane and 0.19 ml (1.3 mmol) of TMEDA. After 10 min, a solution of 200 mg (1.06 mmol) of **5b** in 1 ml of dry THF was added slowly. The resulting orange solution was stirred at −78°C for 30 min. After dropwise addition of a solution of 0.39 ml (2.11 mmol) of *p*-chlorodiphenylphosphine in 1 ml of THF, the bright yellow reaction mixture was kept at −78°C for 1 h and then allowed to warm slowly to room temperature overnight. The mixture was quenched with 5 ml of a 5% aqueous solution of H_2O_2 and stirred for 15 min. After dilution with 10 ml of ethyl acetate, the layers were separated. The aqueous layer was extracted three times with ethyl acetate, and the combined organic extracts were washed with saturated aqueous Na_2CO_3 and saturated aqueous NaCl. Drying over anhydrous $MgSO_4$ and concentration *in vacuo* gave 550 mg of a yellow oil. Purification by flash chromatography (dichloromethane/methanol 20/1) yielded 220 mg (53%) of (−)-(4*S*)-4,5-dihydro-2-[2′-(diphenylphosphinyl) phenyl]-4-isopropyloxazole (**6b**) as a highly viscous oil; $[\alpha]_D$ −33.1 (*c* 1.03, $CHCl_3$). IR ($CHCl_3$): 3063m, 2967s, 2873m, 1656s, 1591w, 1566w, 1469m, 1438s, 1359m, 1310m, 1178s, 1120s, 1108s, 1062m, 954m, 694s. ^{1}H-NMR: δ 0.76 (d, *J* 6.7 Hz, 3 H, $CH(CH_3)_2$); 0.86 (d, *J* 6.7 Hz, 3 H, $CH(CH_3)_2$); 1.55 (septett, *J* 6.7 Hz, 1 H, $CH(CH_3)_2$); 3.47–3.55 (m, 1 H, HC(4)); 3.66 (dd, $^1J \approx {}^2J$ 8.3 Hz, 1 H, $H_2C(5)$); 3.80 (dd, *J* 8.3 and 9.8 Hz, 1 H, $H_2C(5)$); 7.40–7.77 (m, 13 H, arom. H); 7.87–7.92 (m, 1 H, arom. H) ppm. ^{13}C-NMR: δ 18.5 ($CH(CH_3)_2$); 19.1 ($CH(CH_3)_2$); 32.6 ($CH(CH_3)_2$); 70.7 ($H_2C(5)$); 72.8 (HC(4)); 128.2 (d, J_{PC} 13 Hz, 4 arom. CH), 130.1 (d, J_{PC} 12 Hz), 130.7 (d, J_{PC} 9 Hz), 131.2 (d, J_{PC} 3 Hz), 131.3, 131.4 (d, J_{PC} 10 Hz), 131.70 (d, J_{PC} 10 Hz), 131.72 (d, J_{PC} 2 Hz), 134.8 (d, J_{PC} 11 Hz) (arom. CH); 131.8 (d, J_{PC} 108 Hz), 132.5 (d, J_{PC} 12 Hz), 133.4 (d, J_{PC} 108 Hz), 133.6 (d, J_{PC} 105 Hz) (arom. C); 163.1 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ 29.4 ppm. MS (EI): 389(9, M^+), 346(100), 319(96), 312(45), 306(44), 268(34), 226(12), 199(12), 179(24), 165(13), 152(12), 77(19). TLC: R_f 0.2 (dichloromethane/methanol 20/1).

(−)-(4S)-4,5-Dihydro-2-[2′-(diphenylphosphinyl)phenyl]-4-isobutyl-oxazole (**6e**). 50% yield; $[\alpha]_D$ −50.0 (*c* 1.38, $CHCl_3$). IR ($CHCl_3$): 3062m, 2962s, 2871m, 1654s, 1468m, 1591m, 1565m, 1438s, 1361s, 1312m, 1178s, 1119s, 1061m, 998m, 966m, 948m, 910m, 694s. ^{1}H NMR: δ 0.84 (d, *J* 6.6 Hz, 3 H, $CH(CH_3)_2$); 0.85 (d, *J* 6.6 Hz, 3 H, $CH(CH_3)_2$); 1.00–1.09 (m, 1 H, $CH_2CH(CH_3)_2$); 1.37–1.46 (m, 1 H, $CH_2CH(CH_3)_2$); 1.58 (septett, *J* 6.7 Hz, 1 H, $CH(CH_3)_2$); 3.40–3.46 (m, 1 H, $H_2C(5)$); 3.80–3.91 (m, 1 H, HC(4)); 3.98 (dd, *J* 7.6 and 9.4 Hz, 1 H, $H_2C(5)$); 7.40–7.61 (m, 9 H, arom. H); 7.65–7.77 (m, 4 H, arom. H); 7.86–7.90 (m, 1 H, arom. H) ppm. ^{13}C-NMR: δ 22.4 ($CH(CH_3)_2$); 22.7 ($CH(CH_3)_2$); 25.2 ($CH(CH_3)_2$); 44.6 ($CH_2CH(CH_3)_2$); 64.9 (HC(4)); 73.2 ($H_2C(5)$); 128.3 (d, J_{PC} 13 Hz, 4 arom. CH), 130.1 (d, J_{PC} 12 Hz), 130.8 (d, J_{PC} 9 Hz), 131.26 (d, J_{PC} 3 Hz), 131.34 (d, J_{PC} 3 Hz), 131.5 (d, J_{PC} 10 Hz), 131.6 (d, J_{PC} 10 Hz), 131.8 (d, J_{PC} 3 Hz), 134.8 (d, J_{PC} 11 Hz) (arom. CH); 131.9 (d, J_{PC} 111 Hz), 132.6 (d, J_{PC} 18 Hz), 133.4 (d, J_{PC} 107 Hz), 133.7 (d, J_{PC} 108 Hz) (arom. C); 163.1 (d, J_{PC} 3 Hz, C(2)) ppm. ^{31}P-NMR: δ 29.3 ppm. MS (EI): 403(12, M^+), 346(49), 326(39), 319(100), 305(81), 268(12), 226(12), 179(30), 77(24). TLC: R_f 0.1 (dichloromethane/methanol 40/1).

Reduction of phosphine oxides **6b,e**

General procedure. A mixture of 398 mg (1.02 mmol) of **6b** and 170 ml (1.36 mmol) of phenylsilane was heated at 120°C for 40 h under argon. The reaction was quenched with hot methanol and the resulting slurry was filtered. After washing with hot methanol and concentration in vacuo the residue was filtered through silica gel (3×4 cm, hexane/ethyl-acetate 2/1) to afford 335 mg (88%) of **4b** as a colourless oil. The same procedure gave **4e** in 51% yield (spectroscopic data: see above).

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References and notes

1a *P. von Matt* and *A. Pfaltz*, Angew. Chem. **105**, 614 (1993); Angew. Chem., Int. Ed. Engl. **32**, 566 (1993);
b *J. Sprinz* and *G. Helmchen*, Tetrahedron Lett. **34**, 1769 (1993);
c *G.J. Dawson, C.G. Frost, J.M.J. Williams* and *S.J. Coote*, Tetrahedron Lett. **34**, 3149 (1993);
d *P. von Matt, O. Loiseleur, G. Koch, A. Pfaltz, C. Lefeber, T. Feucht* and *G. Helmchen*, Tetrahedron: Asymmetry **5**, 573 (1994).
2 *G.C. Lloyd-Jones* and *A. Pfaltz*, Angew. Chem., in press.
3 *O. Loiseleur* and *A. Pfaltz*, Chimia **48**, 281 (1994).
4 *B.N. Storhoff, D.P. Harper, I.H. Saval* and *J.H. Worstell*, J. Organomet. Chem. **205**, 161 (1981).
5 *H. Witte* and *W. Seeliger*, Liebigs Ann. Chem. 996 (1974).
6 *L. Macko, M. Neuburger, M. Zehnder*, Institut für Anorganische Chemie, Universität Basel, unpublished results.
7a *H.W. Gschwend* and *A. Hamdan*, J. Org. Chem. **40**, 2009 (1975);
b *A.I. Meyers* and *E.D. Mihelich*, J. Org. Chem. **40**, 3158 (1975);
c *H.W. Gschwend* and *H.R. Rodriguez*, Org. React. **26**, 1 (1979).
8 *D.G. Neilson*, "The chemistry of amidines and imidates", Chapter 9, *S. Patai*, ed., Wiley, London, 1975, p. 389ff and 445ff.
9a *P. Beak* and *R.A. Brown*, J. Org. Chem. **42**, 1823 (1977);
b *P. Beak* and *R.A. Brown*, J. Org. Chem. **47**, 34 (1982).
10 For a similar transformation of (1-phenylalkyl)amines to 1-[2-(diarylphosphino)phenyl]alkylamines, see *L. Horner* and *G. Simons*, Phosphorus Sulfur **19**, 65 (1984).
11 *H. Fritzsche, U. Hasserodt* and *F. Korte*, Chem. Ber. **97**, 1988 (1964).
12a *S.J. Coote, G.J. Dawson, C.G. Frost* and *J.M.J. Williams*, Synlett 509 (1993);
b *J.V. Allen, G.J. Dawson, C.G. Frost, J.M.J. Williams* and *S.J. Coote*, Tetrahedron **50**, 799 (1994).
13a *A. Abiko* and *S. Masamune*, Tetrahedron Lett. **33**, 5517 (1992);
b *M.J. McKennon, A.I. Meyers, K. Drauz* and *M. Schwarm*, J. Org. Chem. **58**, 3568 (1993).
14 Cf. *Q. Zhou* and *A. Pfaltz*, Tetrahedron **50**, 4467 (1994).