Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 7, pp. 1297-1320, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $7.00+0.00

0957-4166(94)00180-4

Efficient Synthesis of (*R*)- and (*S*)-(6,6'-Difluorobiphenyl-2,2'-diyl) bis(diphenylphosphine); *Electron-Poor* Biphenyl-Type Ligands for Transition Metal Catalysts.

Heiner Jendralla ,* Chang Hua Li , Erich Paulus [1]

Hoechst AG, Allgemeine Pharma Forschung, Postfach 800320, D-65926 Frankfurt / M. 80, Germany

Abstract: *Racemic title compound (RS)-***5** *is synthesized (Scheme 1 , 100g scale) in four simple steps (49% overall yield) from meta-fluorobromobenzene* **1** *. (RS)-***5** *is efficiently resolved (Scheme 2) utilizing commercial (S)-(+)-dipalladium complex* **9** *to give homochiral (S)-(+)-***5** *and (R)-(-)-***5** *in 75 and 95% of theoretical yield , respectively. Enantiomerically pure diphosphines (S)-***5** *and (R)-***5** *do not racemize in organic solutions, even when heated to 207°C. Homochiral palladium(II) dichloride complexes (-)-***11** *and (+)-***11** *are prepared in quantitative yield. In situ rhodium(I)-complex of homochiral* **5** *is an efficient catalyst for alkene - hydroboration by catecholborane and requires high hydrogen pressure to catalyze hydrogenation.*

*Interesting anomalies of the specific rotation are observed for homochiral diphosphines (S)-(+)-***5** *and (R)-(-)-***5** *. The specific rotation* $[\alpha]_D^{25}$ *of (S)-(+)-***5** *measured in similar aromatic hydrocarbons (toluene , o-xylene, mesitylene, tetralin) varies from +114.9 (c 0.99 , toluene) to - 73.9 (c 0.46 , tetralin).*

Homochiral mono- and di-phosphines have gained considerable interest as ligands of transition metal ions in catalytic enantioselective reactions [2,3] , notably in rhodium(I)- [3,4] , ruthenium(II)- [4,5] and iridium(I)- [6] catalyzed asymmetric hydrogenations of prochiral alkenes [3,4], ketones [4,5,6], and imines [7] , in palladium-catalyzed nucleophilic allylic substitutions [8] and Heck-coupling reactions [9], in rhodium(I)-catalyzed hydrosilylations [10], hydroborations [11] and hydroformylations [12] of prochiral alkenes and hydrosilylations of ketones [13] and imines [14], as well as in rhodium(I)-catalyzed asymmetric isomerizations of allylamines to the corresponding enamines [15].

It is striking, that in all of these applications of homochiral phosphines in catalytic asymmetric synthesis [2-15] and in compilations of about two hundred different homochiral phosphines, phosphinites and amidophosphines that have been tested in asymmetric synthesis [2,3], all the phosphines are ***electron-rich***. Chiral dialkylmonoaryl-phosphines (*e.g.* bichep **A** [16] or duphos **B** [17]) or monoalkyldiaryl-phosphines (*e.g.* diop **C** [18]) are of course particurlarly electron-rich. In the phosphorus-chiral dipamp **D** [19] and in less electron-rich triarylphosphines of axial chirality (*e.g.* binap **E** [5] , diphemp **F** [20] or MeO-biphep **G** [21]) the electron-density has been raised by annulated phenyl rings , inductively or conjugatively donating aryl-substituents or a combination of both types of substituents [22]. Therefore , as a rule , chiral phosphines currently used in asymmetric catalysis,

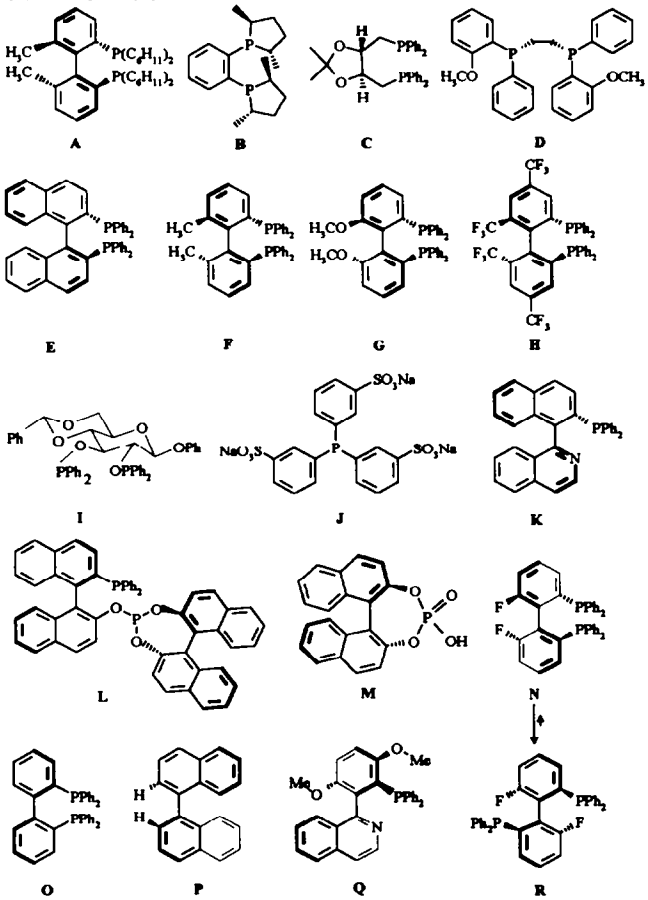
are ***more electron-rich than triphenylphosphine***. Bifup **H** [23] seems to be the only exception to this rule due to strong +I effects of its four trifluoromethyl groups. Ru^{II}-(*S*)-bifup complex was reported to catalyze the asymmetric hydrogenation of methyl-3-oxobutanoate [substrate to catalyst molar ratio (S/C) 1000] with high enantioselectivity (95% ee), however only low catalytic activity [23]. Other applications of bifup have not yet been reported. Excellent results obtained with electron-rich phosphines **A** - **G** attest to the usefulness of this class of ligands in asymmetric catalyses [2-22]. However, there is no indication that high electron-density of the chiral phosphine is prerequisite for good catalytic activity and (or) enantioselectivity of its transition metal complexes [24]. (*R*)-(-)-Phenyl-β-glup **I** [25], a bis(phosphinite), has a drastically reduced basicity of its phosphorus atoms, its rhodium(I)-complex was however successfully employed for the industrial production of *L*-Dopa *via* catalytic asymmetric hydrogenation [26]. There are a few reports which might indicate improvement of catalyst performance by tuning down the basicity of phosphine ligands (reducing their electron density):

Water-soluble rhodium(I)-complex of (achiral) tppts **J**, a triphenylphosphine containing three electron-withdrawing sulfonate substituents in meta positions, is used in the Ruhrchemie / Rhone - Poulenc process for the annual production of 300000 tons of n-butyraldehyde by hydroformylation of propene [27]. A very recent review comes to the conclusion that "all the phosphane ligands tested so far are more active and selective in their water-soluble sulfonated forms, often by a very large margin" [27]. Asymmetric hydroboration (catecholborane) / oxidation (H_2O_2, NaOH) of indene , catalyzed by 1 mol-% of homochiral rhodium(I)-complexes of diop **C** , dipamp **D** or binap **E** in the temperature interval -5°C to +25°C gives 1-indanol with 58% ee [28], 7% ee [29], and 13% ee [30], respectively. Enantioselectivity is significantly improved at lower reaction temperature [28,29], and record optical induction with these electron-rich diphosphines is realized with diop in toluene at -30°C to give 1-indanol of 74% ee with a required reaction time of three days [28,29]. Rhodium(I)-complex (1 mol-%) of less electron-rich [31] ligand **K** leads at 20°C in THF to 1-indanol with 91% ee [32]. Similarly, *p*-methoxystyrene is transformed to 1-(*p*-methoxyphenyl)ethanol of 95% ee employing the rhodium(I) catalyst of ligand **K** in THF at 20°C [32]. The performance of the electron-richer [31] ligand binap **E** is worse even at much lower temperature (85% ee at -30°C in THF [30]), and diop **C** gives only 4% ee with the substrate styrene (THF, 25°C) [30]. Likewise, the performance of the electron-rich ligands **C**, **D**, **E** at temperatures of +5 to +25°C with the substrate norbornene is poor. Product 2-*exo*-norborneol is obtained with 31% ee [29], 0% ee [29], and 15-43% ee [29,30], respectively. Electron-poorer [31] ligand **K** leads to a product of 52% ee at 20°C in THF [32]. Rhodium(I)-complex of (*R,S*)-binaphos **L** induces the highly catalytic (S/C up to 2000) and enantioselective (ee up to 95%) hydroformylation of terminal alkenes and is far superior to the corresponding complex of binap **E** [12]. Likewise a complex formed from $PdCl_2$, $CuCl_2$ and bnppa **M** catalyzes highly enantioselective (up to 91% ee) hydrocarboxylation of prochiral alkenes under exceptionally mild conditions, whereas the much more electron-rich binap **E** or 1,1-bi-2-naphthol are of little use, since they afford acids of less than 10% optical yield under a variety of conditions [33]. However, the advantages of notably ligand **L** in catalytic hydroformylation could also be due to a more favourable natural bite angle [34] rather than to the reduced basicity of its phosphorus atoms.

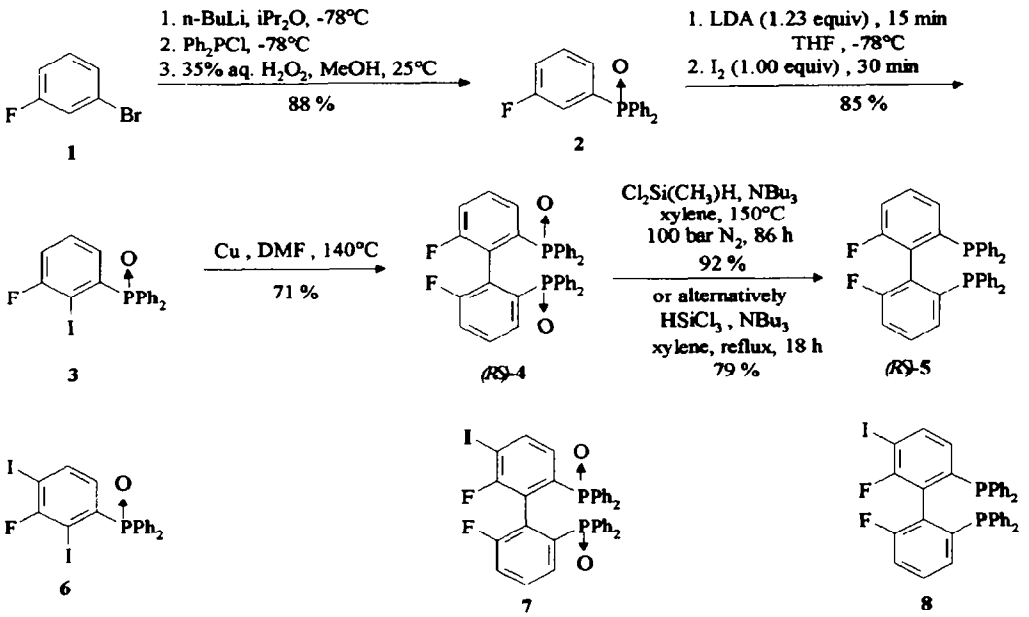
This discussion is in full accord with the correlation of electron donor-acceptor properties of seventy different phosphine ligands ($PX_1X_2X_3$) with the sharp carbonyl stretching frequency ν_{CO} (A_1) of their nickel tricarbonyl complexes $Ni(CO)_3(PX_1X_2X_3)$ in dichloromethane solution : Tolman found that monoalkyldiaryl-phosphines and notably dialkylmonoaryl-phosphines produce lower CO stretching frequencies than triphenylphosphine [35]. *m*-Methoxy, *m*-methyl- and notably *o*-methoxy-groups at the phenyl substituent decrease

and *m*-fluoro-groups increase the CO stretching frequency as compared to triphenylphosphine[35]. In phosphinites and notably phosphites ν_{CO} (A_1) is strongly increased[35]. Tolman attributed the reduced electron density on nickel to a reduced σ donation or an enhanced π-acceptor behaviour of phosphines with electron-withdrawing substituents [35]. Importantly, he also demonstrated that electronic effects of phosphine ligands play only a secondary role compared to steric effects in determining the stability of their metal complexes, sterically undemanding phosphines leading to much more stable complexes than bulky phosphines [36]. Title diphosphine **N** is the smallest conceivable axially chiral *bis*-diphenylphosphine.

If electron-poor homochiral diphosphines were useful ligands in asymmetric catalysis, they would be expected to have additional handling advantages. Monoalkyldiarylphosphines and especially dialkylmonoarylphosphines (like **A** - **D**) are easily oxidized by air to their corresponding mono- and bis-phosphinoxides, notably in organic solution [37]. Triphenylphosphine is air stable in the crystalline state as well as in solution [37]. The more electron-rich binap **E** is already less inert to oxygen: crystalline **E** is air-stable , but in organic solution it is oxidized, unless the solvent is carefully deoxygenated [38]. Similarly, diphemp **F** has been described to be air-stable as a solid, slightly sensitive towards oxidation by air in solution and very air-sensitive during chromatography [20]. Under the perspectives discussed, the synthesis of the unknown (6,6'-difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine) **N** appears to be most attractive.



Homochiral compound **N** is a challenge also in another respect: The configurational stability of known chiral biphenyls and 1,1'-binaphthyls depends on the presence of at least three (usually four) reasonably bulky substituents in the ortho-positions to the biphenyl axis [39]. Whereas **A**, **F**, **G**, and **H** are optically stable at ambient temperature, bpbp **O** containing two ortho-hydrogens is not. Therefore free ligand **O** exists just in its racemic form, although its cationic rhodium(I) complex can be resolved into enantiomers [40]. Likewise , **E** and **K** are enantiomerically stable, but **P** and **Q** are not. 1,1'-binaphthyl **P** racemizes at ambient temperature *via* the *anti*-pathway [41] with an activation energy of 22.5 kcal/mol [42]. Compound **Q** racemizes with an estimated half-life of ca. 1 h at ambient temperature [43]. Since the Van der Waal's radius of fluorine (1.35 Å[44], 1.47 Å[39]) is the smallest next to hydrogen (1.2 Å[44]), steric hindrance of racemization of **N** should only be moderately increased as compared to bpbp **O**. Additionally, each meta-fluorophenyl-diphenylphosphine moiety of **N** would be expected to be polarized, with the fluorine atoms carrying negative and the phosphorus atoms carrying positive charge. Due to intramolecular dipole-dipole interaction and the high affinity of phosphorus for fluorine, conformation **R** should be highly preferred to **N** in solution. The attractive forces between fluorine and phosphorus should tend to pull **R** as much into planarity as sterically feasible. Formation of catalytically active homochiral transition metal chelates would require to overcome the fluorine - phosphorus attraction and to rotate to conformation **N** without passing through planarity (with retention of configuration). It could thus neither be reliably predicted [39], if the chiral diphosphine **R** would be enantiomerically stable [45], nor if it would form transition metal chelates.



Scheme 1. Preparation of racemic diphosphine (*RS*)-**5**.

The preparation of racemic 6,6'-difluorobiphenyl-2,2'-diyl-bis(diphenylphosphine) (*RS*)-**5** is summarized in Scheme 1:

Bromine-metal exchange of 1-bromo-3-fluorobenzene **1** with *n*-butyllithium at -78°C, followed by a quench of the intermediate *meta*-fluorophenyllithium by chlorodiphenylphosphine gives in a very clean reaction (3-fluorophenyl)diphenylphosphine in quantitative yield. Immediate oxidation with aqueous hydrogen peroxide in methanol at 25°C provides the corresponding phosphine oxide **2** in 88% yield after purification by trituration. If THF or diethylether is used instead of diisopropylether bromine-lithium exchange / phosphinylation is unclean, and subsequent oxidation leads to **2** that contains considerable amounts of by-products difficult to remove. They were isolated chromatographically and identified (^{1}H-NMR, MS) as (bromofluorophenyl) diphenyl-phosphine oxide and bis(diphenylphosphinoxido)-fluorobenzene. The constitutions of these by-products indicate, that in THF and diethylether directed metalation is competing with the desired bromine-metal exchange.

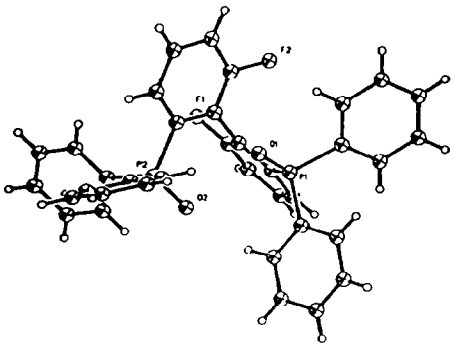
The feasibility of easy metalation *ortho* to fluorine [46], successfully prevented in step one by employment of solvent diisopropylether, is utilized in steps two and three for efficient assembly [47] of the difluorobiphenyl-bis(phosphine oxide) (*RS*)-**4**:

2 is *ortho*-metalated with 1.2 equiv of LDA in THF and the intermediate (3-fluoro-2-lithiophenyl)diphenyl- phosphine oxide is quenched with 1.0 equiv of iodine. The reaction furnishes *ortho*-monoiodide **3** (purity 97.8%) in 85% isolated yield, when the LDA solution is prepared under scrupulously water-free conditions. The presence of as little as 0.2% of water in commercial diisopropylamine is found to give inferior results and leads to 10-15% each of unreacted **2** and diiodide **6**. Ullmann coupling [48] of monoiodide **3**, mediated by activated copper powder in hot DMF, furnishes a crude product consisting of 92% of the bis(phosphine oxide) (*RS*)-**4** and 8% **2**. Trituration with sonication of the crude product in dichloromethane provides (*RS*)-**4** of high purity (>99.5%) in 71% isolated yield.

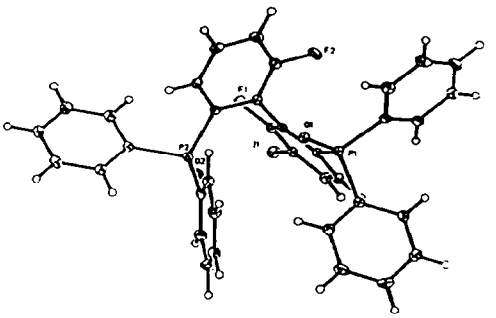
Reduction of the bis(phosphine oxide) (*RS*)-**4** to the racemic diphosphine (*RS*)-**5** proceeds best with dichloromethylsilane / tri-*n*-butylamine in xylene at 150°C. To avoid evaporation losses of the silane we have conducted this reaction in the glass insert of an autoclave under 100 bar of nitrogen to obtain pure *(RS)*-**5** in 92% isolated yield. If an autoclave is not available, trichlorosilane in refluxing xylene can alternatively be employed to provide (*RS*)-**5** of >99% purity in 79% isolated yield.

If monoiodide **3**, containing 10-15% each of **2** and diiodide **6** (*vide supra*) is subjected to Ullmann coupling conditions, the product (*RS*)-**4** contains 7-10% of the difluoro-monoiodo-biphenyl-bis(phosphine oxide) **7**. Removal of **7** by recrystallization or other techniques is tedious and could , in our hands, only be reasonably achieved by RP18-silica gel column chromatography. The 2,2'-positions of the (phosphine oxide) - moieties in **4** and **7** are corroborated by single-crystal X-ray analyses (Figure 1). As expected from X-ray analyses of other 2,2',6,6'-substituted biphenyls [20] the planes of the two phenyl rings of the biphenyl system are virtually orthogonal in both compounds (θ = 86.4° in **4**, 84.3° in **7**), although their specific conformations are distinctly different. The large iodine atom in **7** forces one of the two phenyl rings of P2 to be parallel to one of the phenyl rings of the biphenyl. The dihedral angles P1Ph2 and P2Ph2 are quite different in both compounds: 56.8 and 71.3° in **4**, 62.2 and 91.8° in **7**. This characteristic of the crystalline bis(phosphine oxides) is not reflected in the (solution) NMR spectra. The two phosphorus atoms of **4** are **isochronic** (^{31}P-NMR). The two phenyl substituents of each phosphorus are diastereotopic as expected , due to the axis of chirality in the difluorobiphenyl - moiety, but there are only two (not four) sets of diastereotopic C- and H- resonances for the

Ph_2PO - groups in the ^{13}C- and ^1H-NMR of **4** (*cf.* Experimental). The two Ph_2PO - groups of **4** are equivalent in solution.



(*RS*)-**4**



(*RS*)-**7**

Figure 1. Single-crystal X-ray structures of (*RS*)-**4** and (*RS*)-**7**.

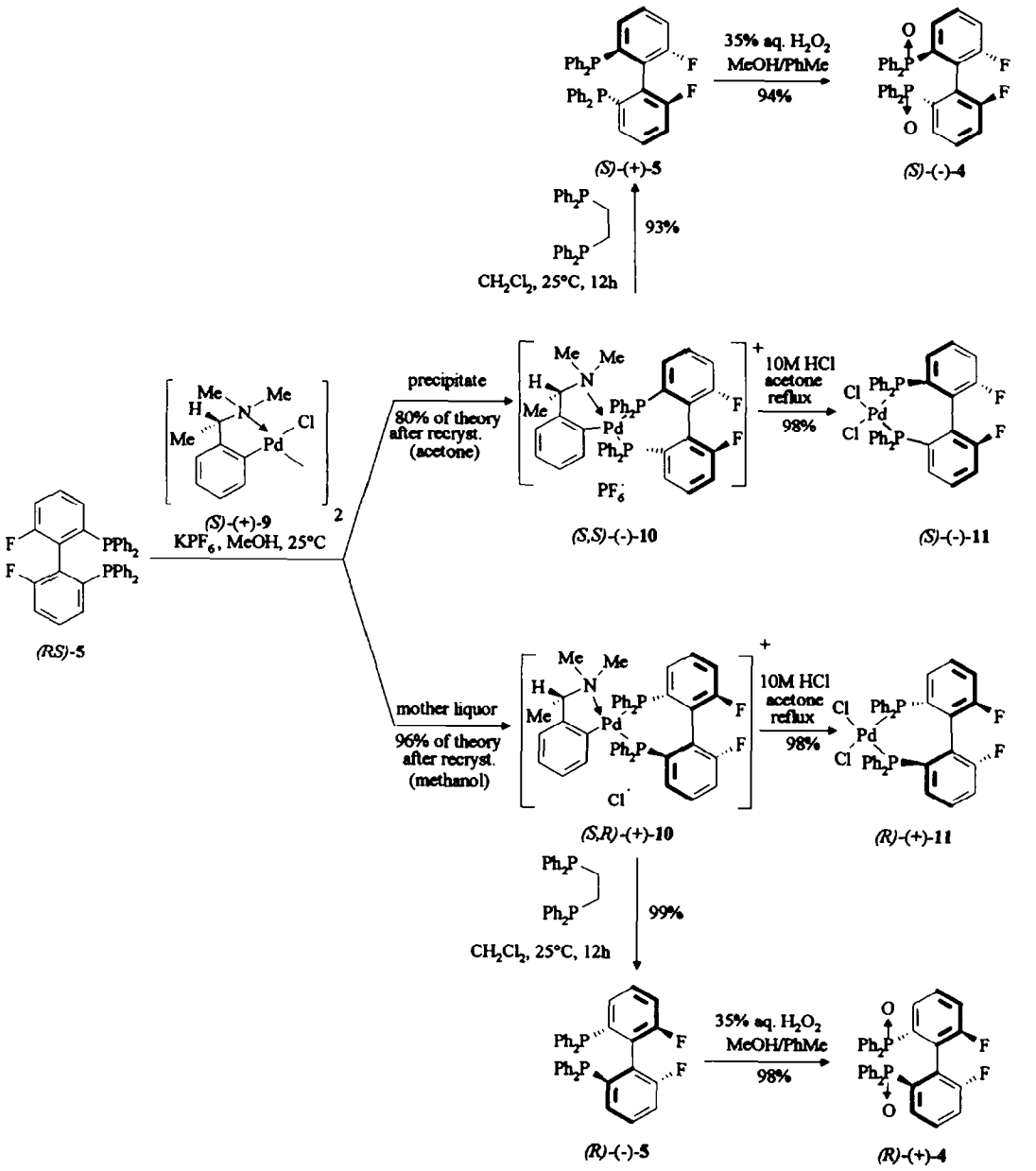
When **7** is submitted to reduction by dichloromethylsilane under the conditions described, deiodination occurs simultaneously to the reduction of the phosphine oxide groups. (*RS*)-**5** is obtained in 100% crude yield and with 91% yield (> 99% purity) after purification by trituration / sonication. There is no indication of any trace of monoiododiphosphine **8**. Similarly, when (*RS*)-**4** containing 7-10% of **7** (or pure **7**) is subjected to reduction by trichlorosilane under the conditions described, reduction of **7** has not progressed beyond the monophosphine oxide within 24 h , whereas reduction of (*RS*)-**4** to diphosphine (*RS*)-**5** is largely concluded in this time. Di- and mono- (phosphine oxides) are much more polar than diphosphine (*RS*)-**5** ,and simple filtration through a pad of silica gel removes all iodine-containing products, providing pure (*RS*)-**5** in good yield in the filtrate.

Since fluoro-monoiodo-phosphine oxide **3** and fluoro-diiodophosphine oxide **6** lead, after all, to the same pure diphosphine (*RS*)-**5** , it is not imperative to exclude traces of water in the *ortho*-metalation / iodination **2** → **3**.

Solutions of (*RS*)-**5** are insensitive to air oxidation at ambient temperature. Di(phosphine oxide) **4** and corresponding monooxide could be detected only in traces in a dichloromethane solution of (*RS*)-**5** that had been allowed to stand unprotected to air for two weeks at ambient temperature. Oxidation by air however occurs at elevated temperature. About 30% of phosphine oxides were detected in a mesitylene solution of diphosphine **5** that had been refluxed (164°C) for 30 min without protection. Difluoro-biphenyl-diphosphine **5** is thus considerably less sensitive to air oxidation in solution than binap **E**. We ascribe this property to a lower electron density at the phosphorus atoms of **5**.

In summary, the racemic diphosphine (*RS*)-**5** is prepared in four steps from commercial **1** with 49% overall yield. The synthesis does not require any chromatography and not even recrystallizations. All

intermediates are purified by simple triturations. The convergence of monoiodophosphine oxide **3** and diiodophosphine oxide **6** to the same pure diphosphine (*RS*)-**5** and its insensitivity to oxygen further contribute to the practicability of the synthesis.



Scheme 2. Resolution of chiral diphosphine **5** and preparation of enantiomerically pure Pd(II)-complex **11**.

Usually, the most convenient and inexpensive method for the resolution of racemic bis(phosphine oxides) is the highly stereoselective precipitation of one of the two diastereomeric adducts with (-)-(2*R*,3*R*)-di-O-benzoyl-tartaric acid, or its enantiomer, respectively [49]. In this way, the bis(phosphine oxides) of bichep **A** [16,50], binap **E** [5,51] and MeO-biphep **G** [21] have been efficiently resolved. Our attempts to resolve (*RS*)-**4** under the conditions described for the former compounds [21,49-51] did not meet with success. We had to take recourse to the formation of diastereomeric complexes with di-μ-chlorobis-{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-*C*,*N*}dipalladium (**9**) (Scheme 2). This method, principally discovered by Cope *et al* [52] and adapted to phosphines and diphosphines by Otsuka [53] , Wild [54] *et al* has been used for the resolution of diphemp **F** [20], MeO-biphep **G** [21] and, employing the analogous naphthyl-dipalladium complex **12**, for the resolution of ligand **K** [32,55]. A suspension of dinuclear palladium complex (*S*)-(+)-**9** and two mols of racemic diphosphine (*RS*)-**5** in methanol is stirred at 25°C to give a clear solution. Addition of an aqueous solution of one mol of potassium hexafluorophosphate leads to the highly diastereoselective precipitation of the hexafluorophosphate (*S*,*S*)-(-)-**10**. The crude complex is obtained in 94% yield. It contains traces of its diastereomer (*S*,*R*)-(+)-**10** according to TLC, but this impurity is too little to be detected by routine ^{1}H-NMR. The diastereoselectivity of the precipitation is estimated to be > 98 : 2. Single recrystallization of the crude precipitate from acetone / diethylether gives pure (*S*,*S*)-(-)-**10** , $[\alpha]_D^{25}$ -203.2 (c 0.98, acetone) in 80% yield based on the (*S*)-**5** content of (*RS*)-**5**. The mother liquor of the precipitation of hexafluorophosphate (*S*,*S*)-(-)-**10** contains the diastereomeric chloride (*S*,*R*)-(+)-**10**. (*S*,*S*)-**10** cannot be detected in the mother liquor , neither by TLC nor by ^{1}H-NMR (diastereoselectivity >> 99 : 1). Single recrystallization from methanol / water gives pure (*S*,*R*)-(+)-**10**, $[\alpha]_D^{25}$ + 208.0 (c 1.01, methanol) in 96% yield based on the (*R*)-**5** content of (*RS*)-**5**. The ^{1}H-NMR spectra of the diastereomeric palladium complexes show characteristic differences as regards their three methyl groups and the tertiary proton at the chiral centre. In (*S*,*S*)-**10** the tertiary proton resonates as a quartet (*J* 6.5 Hz) at δ 5.54 ppm, in (*S*,*R*)-**10** however as a quintet (*J* 6.3 Hz) at δ 3.58 ppm. The strong deshielding in (*S*,*S*)-**10** (Δδ 1.96 ppm) as well as the additional coupling to phosphorus in (*S*,*R*)-**10** should indicate, that this proton is axial in (*S*,*S*)-**10** and equatorial in (*S*,*R*)-**10**. This conclusion is reinforced by the chemicals shifts of the neighbouring methyl group. The equatorial methyl of (*S*,*S*)-**10** is shielded (Δδ 0.91 ppm) relative to the axial methyl in (*S*,*R*)-**10**. The geminal methyl groups bound to nitrogen are only slightly anisochronic in (*S*,*R*)-**10** (Δδ 0.12 ppm), whereas their shift difference Δδ is 1.00 ppm in (*S*,*S*)-**10**. Similar ^{1}H-NMR effects have been described for the corresponding palladium complexes of diphemp **F** [20] and MeO-biphep **G** [21] , and from the internal consistency of data the assignment of the absolute configuration of the biphenyl - moiety in (*S*,*S*)-**10** and (*S*,*R*)-**10** would be regarded as reliable. However, x-ray analyses [32] of the palladium complexes , formed from the **(*R*)-naphthyl**-dipalladium complex analogous to **9** and ligand **K**, have established that the methyl group bound directly to the chiral centre is **axial** in **both** the (*S*,*R*)- **and** the (*R*,*R*)-diastereomer [32]. Figure 2 shows the molecular structure derived from a single-crystal X-ray analysis of (*S*,*S*)-(-)-**10**. The absolute configuration of the diphosphine moiety , as well as the ψ-equatorial conformation of the methyl group at the chiral centre are corroborated. The inner coordination geometry around the palladium atom is strongly distorted square-planar. The palladium atom deviates by 0.195 A from the plane of the three ligands P1, P2, and C01. The fourth ligand N1 is 1.00 A outside of this plane. The Pd-P bond *trans* to the amino group (Pd1-P2 : 2.27 A) is shorter than the *cis*-Pd-P bond (Pd1-P1 : 2.40 A). This is reflected in a chemical shift difference Δδ of 23.8 ppm in the ^{31}P-NMR of (*S*,*S*)-**10**. The interplanar angle θ of the biphenyl system is 67.6°, the Ph-P-Ph dihedral angles of the PPh_2-groups *cis* and *trans* to the amine ligand are 71.4° and 65.1°, respectively.

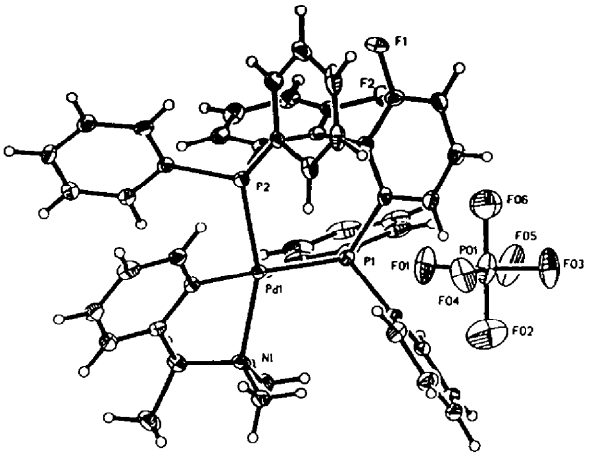


Figure 2. Single-crystal X-ray structure of (*S,S*)-(-)-**10**.

Reflux of the hexafluorophosphate (*S,S*)-(-)-**10** with aqueous hydrochloric acid in acetone cleaves the chiral amine from the palladium and provides the diphosphine-palladium dichloride complex (*S*)-(-)-**11**, $[\alpha]_D^{25}$ -311.9 (c 0.50, dichloromethane) in quantitative yield. The same treatment of the chloride (*S,R*)-(+)-**10** gives the enantiomeric palladium dichloride complex (*R*)-(+)-**11**, $[\alpha]_D^{25}$ + 311.5 (c 0.50, dichloromethane) in quantitative yield. C_2-symmetry is indicated by the appearance of only one resonance (δ 26.72 ppm, d , $^4J_{P,F}$ 6.0 Hz) in the $^{31}P\{^1H\}$-NMR and only one resonance (δ -108.5 ppm) in the ^{19}F-NMR. The mononuclear nature of **11** (as opposed to the dinuclear nature of palladium chloride complex **9**) is deduced from the elemental analysis and corroborated by FAB-MS, that shows M - Cl and M - 2 Cl fragment ions as the peaks of highest mass with the expected isotope distribution. The enantiomers of **11** (mp 310 - 312°C) are thermally and chemically very stable. (*S*)-(-)-**11** is recovered unchanged after stirring 16 h at 25°C in a solution of excess potassium cyanide in water / methanol / dichloromethane. TLC does not indicate any cleavage to the free diphosphine (*S*)-(+)-**5** and potassium tetracyanopalladate. This contrasts with palladium dichloride complexes of other chiral diphosphines, that are cleanly cleaved under these conditions [54].

The optically pure diphosphines (*S*)-**5**, $[\alpha]_D^{25}$ +114.9 (c 0.99, toluene) and (*R*)-**5**, $[\alpha]_D^{25}$ -114.8 (c 1.03, toluene) are obtained by transcomplexation of the hexafluorophosphate (*S,S*)-(-)-**10** and the chloride (*S,R*)-(+)-**10**, respectively, with diphos at ambient temperature (Scheme 2). Their optical purity is easily established by oxidation to the corresponding bis(phosphine oxides). (*S*)-(-)-**4** and (*R*)-(+)-**4** give only one peak on chiral phase HPLC analysis under conditions, where racemic (*RS*)-**4** gives baseline separation of two peaks in the ratio 1 : 1 (*cf.* experimental part). Whereas the optically pure bis(phosphine oxides) (*S*)-(-)-**4** and (*R*)-(+)-**4** melt at the same temperature (282-283°C) as the racemic compound (*RS*)-**4** (283-284°C) , the optically pure diphosphines (*S*)-(+)-**5** and (*R*)-(-)-**5** have a considerably lower melting point (164-165°C) than the racemic diphosphine (*RS*)-**5** (222-223°C). It should therefore not be possible to raise the enantiomeric excess of optically enriched diphosphine by recrystallization. Optically pure diphosphine **5** is very resistent to thermally induced racemization. When a solution of (*S*)-(+)-**5** in tetralin is refluxed (bp 207°C) for 2.5 h in an argon atmosphere , its specific rotation is unchanged and chiral phase HPLC of the corresponding bis(phosphine oxide) still indicates 100% ee.

The specific rotation $[\alpha]_D^{25}$ of optically pure diphosphine (*S*)-(+)-**5** varies dramatically in different solvents (Table 1). Notably, the direction of rotation is reversed from +114.9 to -73.9 , when the solvent toluene is replaced by tetralin. Solutions of (*S*)-(+)-**5** in other alkyl-substituted benzenes like mesitylene (1,3,5-trimethylbenzene) and *o*-xylene (1,2-dimethylbenzene) give specific rotations $[\alpha]_D^{25}$, that are between those in toluene and tetralin. Solutions of (*S*)-(+)-**5** in ethers (THF , dioxane) show high specific rotations ; in chloroform it is much lower than in dichloromethane.

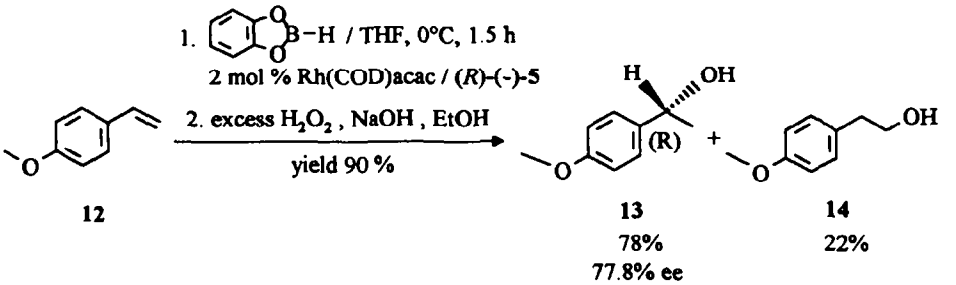
Table 1: Specific rotations $[\alpha]_D^{25}$ of (*S*)-(+)-**5** , measured in different solvents.

$[\alpha]_D^{25}$, (*S*)-(+)-**5**	c	solvent
+ 153.3	1.02	THF
+ 145.3	0.47	dioxane
+ 123.7	1.03	dichloromethane
+ 114.9	0.99	toluene
+ 95.5	0.73	mesitylene
+ 46.7	1.04	chloroform
+ 21.4	0.64	*o*-xylene
- 73.9	0.46	tetralin

In principal, the dependence of specific rotation from solvent is known, and strong effects have been observed when compounds capable of forming hydrogen bonds were measured in solvents of very different polarities (like methanol *vs* hexane). However, a reversal of the direction of specific rotation while going from a solution in one hydrocarbon to a solution in another hydrocarbon has, to the best of our knowledge, not been reported before. The order of specific rotations as depicted in Table 1 does neither correlate with the dielectric constants of the respective solvents, nor with their estimated π-basicity (π–donor ability). Therefore, we do not believe, that it reflects varying degrees of supramolecular structures [*e.g.* dimeric or polymeric aggregates of (*S*)-**5**] or varying degrees of charge transfer complexation between (*S*)-**5** and the solvent. Likewise, a formation of host-guest complexes with solvent molecules does not occur, since crystals , obtained by recrystallization of (*RS*)-**5** from hot toluene and hot tetralin, respectively, do not contain any toluene and only traces of tetralin, after drying at 50 mbar (^{1}H-NMR). To gain some insight into the origin of this effect, we are planning to record full CD spectra of (*S*)-(+)-**5** in different solvents.

We have just begun to apply homochiral diphosphine **5** in asymmetric catalysis. The few reactions conducted do already indicate, that the rhodium(I) complex of (*R*)-(-)-**5** has high catalytic activity in the hydroboration with catecholborane in THF and requires high hydrogen pressure for hydrogenation. Hydroboration of *p*-methoxystyrene **12** with 2 equiv of catecholborane in THF at 0°C in the presence of 2 mol% of an *in situ* - catalyst from (1,5-cyclooctadiene)(2,4-pentadionato)-rhodium(I) and (*R*)-(-)-**5** is quantitative within 1.5 h. Oxidation with excess hydrogen peroxide at 25°C gives 78% of 1-(4-methoxyphenyl)ethanol **13** [77.8% ee of the (*R*)-configuration] and 22% of 4-methoxyphenethyl alcohol **14** (Scheme 3). 2-Benzylidenesuccinic acid 4-[(4-BOC-amino]-1-piperidide] [56] is not hydrogenated at 25°C under 1 bar of hydrogen in the presence of 1 mol% of an *in situ* - catalyst from di-μ-chloro-bis-[(cycloocta-1c,5c-

diene)-rhodium(I) and (*R*)-(-)-**5**. Quantitative hydrogenation is obtained, when the hydrogen pressure is raised to 150 bar, in analogy to the behaviour [23] of bifup **H**.



Scheme 3. Asymmetric hydroboration / oxidation of *p*-methoxystyrene catalyzed by Rh(COD)acac / (*R*)-(-)-**5**

In summary, we have reported a simple, efficient synthesis of electron-poor, homochiral diphosphines (*S*)-(+)-**5** and (*R*)-(-)-**5**. The overall yields (37% and 46%, respectively, based on 1-bromo-3-fluorobenzene **1**) are superior to those reported for other diphosphines (**A**, **E**, **F**, **G**, **H**) and phosphinamines (**K**, **Q**) of axial chirality. The industrial application of this ligand in asymmetric catalysis is however limited yet by the fact, that resolution could only be achieved by the relatively expensive reagent **9**. Optically pure diphosphines **5** do not racemize in organic solution, even when heated to 207°C. Their palladium dichloride complexes (*S*)-(-)-**11** and (*R*)-(+)-**11** are thermally and chemically very stable. Their rhodium(I) complex catalyzes the asymmetric hydroboration of *p*-methoxystyrene with catecholborane and catalyzes asymmetric hydrogenation under high hydrogen pressure. The specific rotation of optically pure diphosphine **5** varies dramatically in different solvents. The direction of rotation is reversed, when the solvent toluene is replaced by tetralin. Single-crystal X-ray structures of (*RS*)-**4**, (*RS*)-**7** and (*S,S*)-**10** have been reported.

EXPERIMENTAL SECTION

Reagents, instrumentation and general methods : Acetone (99.5%, Riedel-de Haen), 1,2-bis(diphenyl phosphino)ethane (99%, Aldrich) , 1-bromo-3-fluorobenzene (>99%, Aldrich) , n-butyllithium (15% solution in hexanes, 1.6 M, Chemetall Gesellschaft), (-)-(2*R*,3*R*)-2,3-O,O'-dibenzoyltartaric acid and its (+)-(2*S*,3*S*)-enantiomer (>99%, Fluka) , catecholborane (1.0 M solution in THF, Aldrich) , (1,5-cyclooctadiene)(2,4-pentadionato)-rhodium(I) (99%, Aldrich), di-μ-chloro-bis[(cycloocta-1*c*,5*c*-diene)-rhodium(I)], (*S*)-(+)-di-μ-chloro-bis{2-[1-(dimethyl- amino)ethyl]phenyl-C,N}dipalladium (**9**) (98%, Aldrich) , dichloromethane (99.8%, Riedel-de Haen) , dichloromethylsilane $Cl_2Si(CH_3)H$ (97% , Janssen), diethylether (>99%, Hoechst) , hydrogen peroxide (35% aqueous solution, Riedel-de Haen), iodine (99.8%, Riedel-de Haen) , mesitylene (99%, Fluka) , methanol (99.5%, 0.2% H_2O, Riedel-de Haen) , potassium hexafluorophosphate (>98%, Fluka) , tetralin (99%, Aldrich) , toluene (>99%, < 0.03% H_2O , Aldrich) , tri-n-butylamine (98% , Merck-Schuchardt), trichlorosilane (99%, Aldrich) , *o*-xylene (99.5% , Riedel-de Haen) were used as purchased.

Chlorodiphenylphosphine $ClPPh_2$ (techn. grade, 95%, Aldrich) (bp 98-100°C / 0.2 Torr) and *p*-methoxy styrene (97%, Aldrich) (bp 41-42°C / 0.5 Torr) were distilled *in vacuo* immediately before use. Diisopropyl amine (99%, Aldrich) and diisopropylether (>99% , Hoechst) were distilled from calcium hydride in an argon

atmosphere immediately before use (Karl Fischer titration indicated < 0.01% H_2O in iPr_2O and ≤ 0.05% H_2O in iPr_2NH). N,N-Dimethylformamide (DMF) was allowed to stand several days in a stoppered flask over activated 4A molecular sieves and then distilled *in vacuo*. Tetrahydrofuran (THF) was dried by passing through ICN alumina B , activity 1 , 1g / 3 mL THF) immediately before use (Karl Fischer titration indicated < 0.01% H_2O).

Copper powder (99.8%, Riedel-de Haen) was activated according to the following procedure:
260 g of copper powder was added to a solution of 52 g of iodine in 2.6 L of acetone, and the mixture was stirred for 10 min. The copper was filtered on a Buchner funnel and stirred 10 min in a solution of 650 mL of concentrated hydrochloric acid in 650 mL of acetone. The copper powder was filtered ,washed with 3 x 200 mL of acetone and dried *in vacuo* in a desiccator.

All reactions were run in dry-glass apparatus under an argon atmosphere.

Melting points (mp) were determined on a Büchi capillary melting point apparatus (according to Dr. Tottoli) and are uncorrected. HPLC : Kontron 420 Pump with Kontron 425 Gradient Former , Kontron 360 Autosampler (20 µL injection loop), Kontron 432 HPLC UV-Detector and Kontron 450-MT2 Data System or alternatively Spectra Physics SP 4200 Pump / 8750 Organizer (10 µL injection loop) with SP 8700 Solvent Delivery System , Spectra 100 UV-Vis Detector and SP 4100 Computing Integrator. TLC : 5 x 10 cm glass plates pre-coated with silicagel 60 F-254 (E.Merck) ; spot visualization with Universal UV Lampe Camag (254 nm). Ultrasonic cleaning bath: Elma Transsonic TS540.

^{1}H-NMR (internal standard TMS): Varian Gemini 200 (200 MHz), Bruker AM 400 (400 MHz) and Bruker ARX 500 (500 MHz). ^{13}C-NMR (internal standard TMS) : Bruker AM 270 (67.93 MHz) and Bruker ARX 500 (125.77 MHz). ^{19}F-NMR (internal standard fluorotrichloromethane): Bruker AC 100 (94.2 MHz), Varian Gemini 200 (188.14 MHz), Bruker AM 400 (376.50 MHz) and Bruker ARX 500 (470.59 MHz). ^{31}P-NMR (external standard 80 aq. phosphoric acid): Bruker AM 270 (109.35 MHz), Bruker AM 360 (145.79 MHz) and Bruker ARX 500 (202.46 MHz) . δ- and J-values given for all compounds except (*RS*)-**4**, (*S*)-(-)-**4** and (*R*)-(+)-**4** correspond to the common "first order analysis" of the spectra. All NMR-spectra of (*RS*)-**4** , (*S*)-(-)-**4** and (*R*)-(+)-**4** were fully analyzed applying decoupling-techniques and ^{1}H- ^{13}C-NMR-correlation (hsqc). IR : Perkin Elmer 683 spectrometer. MS : a) "fast atom bombardment" positive ionization (+FAB): VG ZAB SEQ ; NBA denotes p-nitrobenzylalcohol. b) "dissociation chemical ionization" (DCI): Kratos MS 80. c) "positive electrospray ionization" (+ESI): VG BIO-Q ; acetonitrile / water (1:1) + 0.5% formic acid . Optical rotations were determined on a Perkin-Elmer 241 polarimeter utilizing a 10cm length micro-cuvette.

X-ray structures were determined from single crystals sealed in Lindemann-glass capillaries, utilizing a four circle computer controlled diffractometer (R3m/V, Siemens). 25 Reflections with $\vartheta > 4°$ (for **4** and *S,S*-**10**) or $\vartheta > 8°$ (for **7**), respectively, served to determine the cell dimensions. The phase problem was solved by direct methods [57] , minimization of $\Sigma w(Fo^2 - Fc^2)^2$ [58] , weighting scheme w according to the counting statistics.

***(3-Fluorophenyl)diphenylphosphine Oxide* (2)**

To a solution of 1-bromo-3-fluoro-benzene (**1**) (298.7 g, 1.7 mol) in diisopropylether (4.0 L) was added at - 78°C within 30 min *via* a Flex-needle a 1.6 M solution of n-butyllithium in hexanes (1060 mL, 1.7 mol). The yellow suspension was stirred for an additional hr at -78°C. Chlorodiphenylphosphine (394 g, 1.78 mol) was added dropwise at -78°C - -60°C within 20 min . The yellow solution was allowed to warm up to 0°C within 2 h , changing gradually to a white suspension. A saturated aqueous solution of ammonium chloride (1.0 L) was added dropwise. The organic layer was separated, washed with brine (2 x 700 mL) , dried with $MgSO_4$,

then filtered. The solvent was evaporated in vacuo and the oily residue was dried in high vacuum until crystallization occurred to give a pale yellow semi-solid (479 g , 1.71 mol, 100% yield). This crude product was oxidized to the phosphinoxide without purification. An analytical sample was obtained by washing the crude product with methanol to give colourless crystals of (3-fluorophenyl)diphenylphosphine , mp 59-61°C , R_f 0.26 (cyclohexane) [R_f of **1**: 0.73] , ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.84-7.17 (m, 3H), 7.20-7.60 (m, 11H) ; MS (DCI, CH_3OH): m/e (rel. int.) 281 (M+H, 100), 280 (M, 83), 203 (M-C_6H_5, 24) ; IR (KBr): 3070 , 1602, 1580, 1475, 1437, 1415, 1216, 876, 791, 742, 694, 685 cm^{-1}.

To a suspension of the phosphine (476.5 g , 1.7 mol) in methanol (2.1 L) was added dropwise at < 40°C 35% aqueous hydrogen peroxide (183 mL, 2.1 mol). After the resulting clear yellow solution was stirred 10 min at 20°C , TLC indicated quantitative reaction (ethylacetate / isopropanol 20:1; R_f **2** :0.44; phosphine : 0.75). A saturated aqueous solution of sodium sulfite (640 mL) and 1 N hydrochloric acid (300 mL) was added, and the mixture was stirred until a test with iodine / starch - paper indicated complete reduction of the excess hydrogen peroxide. Methanol was evaporated in vacuo and dichloromethane (4.0 L) was added with stirring. The organic layer was separated , washed with 2 x 1 L saturated sodium bicarbonate solution and with 2 x 1 L water. The organic phase was dried ($MgSO_4$) and the solvent was evaporated *in vacuo* to give a white powder (475 g). It was triturated with diisopropylether (900 mL) in an ultrasonic cleaning bath, filtered, washed again with diisopropylether (300 mL) and dried *in vacuo*: 441 g (1.49 mol, 88% yield based on **1**), mp 143-145°C. HPLC [250 x 4.6 mm Lichrosorb RP18 7µm , 1 mL/min (630 mL CH_3CN + 370 mL H_2O + 0.1% NH_4OAc), det.: 254 nm, t_{ret} 8.50 min) indicates 98.1% purity. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.18-7.80 (m) ; MS (DCI , CH_3OH): m/e (rel. int.) 297 (M+H, 100) , 296 (M, 11), 295 (M-H, 13) ; IR (KBr): 3055 , 1583, 1440, 1228, 1188, 1122, 1110, 725, 708, 700, 690, 542, 511 cm^{-1}.

(3-Fluoro-2-iodophenyl)diphenylphosphine Oxide (3)

Note: It is crucial to use scrupulously dried glassware , THF and diisopropylamine and to avoid an excess of iodine in this step. The presence of as little as 0.2% H_2O contained in commercial diisopropylamine was seen to give inferior results (10-15% each of unreacted **2** *and diiodide* **6**).

To a solution of diisopropylamine (176 mL , 1.24 mol) in THF (1.0 L) was added at -70°C a 1.6 M solution of n-butyllithium in hexanes (769 mL , 1.23 mol). The solution was allowed to warm up to -20°C and was then recooled to -70°C. This clear pale yellow LDA - solution was transferred at -70°C within 25 min via a Flex needle into a cold (-78°C) suspension of **2** (296.3 g, 1.0 mol) in THF (2.0 L). The mixture is allowed to stir for 15 min at -78°C , giving an orange-red suspension. A solution of iodine (254 g, 1.0 mol) in THF (1.0 L) was added dropwise at ≤ -70°C during 30 min , leading to a yellow-orange thick suspension. It was allowed to warm up to 0°C within 1.5 h . A solution of sodium thiosulfate (74 g) in water (600 mL) was added , followed by the addition of brine (1.2 L). The organic phase was separated, washed with 3 x 1.2 L of brine. It was dried ($MgSO_4$) and the solvent was evaporated in vacuo. The residue was triturated with diisopropylether (1.0 L) in an ultrasonic cleaning bath (~ 1 min) . The solid was filtered and dried *in vacuo* to give a colourless powder (358g , 848 mmol , 85% yield) , m.p. 155-157°C. HPLC [250 x 4.6 mm Lichrosorb RP18 7µm , 1.5 mL/min (630 mL CH_3CN + 370 mL H_2O + 0.1% NH_4OAc) , det.: 220 nm] indicated 0.6% **2** (t_{ret} 4.41 min) , 97.8% **3** (t_{ret} 4.71 min), 1.6% **6** (t_{ret} 7.47 min). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.97 (ddd, $^3J_{H,P}$ = 13 Hz, $^3J_{H,H}$ = 7 Hz, $^4J_{H,H}$ = 1 Hz, 1H), 7.15-7.38 (m, 2H), 7.40-7.80 (m, 10H); ^{19}F{^{1}H}-NMR (94.2 MHz, $CDCl_3$): δ -87.3 (d, $^4J_{F,P}$

= 6.8 Hz) ; ^{19}F-NMR (94.2 MHz, $CDCl_3$): δ -87.3 (td, $^4J_{F,P} \sim {}^3J_{F,H} \sim 7.0$ Hz, $^4J_{F,H} = 5.2$ Hz) ; MS (DCI): m/e (rel. int.) 423 (M+H, 100) ; IR (KBr): 2920(w), 1437, 1400, 1244, 1182, 1117, 791, 718, 697, 542, 520 cm^{-1}.

In the products of test reactions that [due to traces of water in the reagents and an excess of iodine (1.13 equiv)] contained up to 15% of diiodide **6** , its characteristic spectral signals were observed : ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.68 (dd, $^3J_{H,P} = 12.5$ Hz, $^3J_{H,H} = 9$ Hz) ; ^{19}F{^{1}H}-NMR (94.2 MHz, $CDCl_3$): δ -65.8 (d, $^4J_{F,P} = 5.9$ Hz); ^{19}F-NMR (94.2 MHz, $CDCl_3$): δ -65.8 (~t, $^4J_{F,P} = 5.9$ Hz, $^4J_{F,H} = 5.7$ Hz); MS (+ESI) : m/e 549 (M+H).

(RS)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine Oxide) **((*RS*)-4)**

A mixture of **3** (350 g, 829 mmol) , activated copper powder (163 g , 2.56 mol, *cf. reagents and instrumentation*) and DMF (1.7 L) was stirred at 140°C (oil-bath temp.) for 1.5 h. The mixture was cooled to room temperature and the solvent was evaporated to dryness *in vacuo* at 70°C. The residue was extracted by repeated stirring with hot dichloromethane (4 x 2 L). The combined, filtered extracts were evaporated to dryness and the residue was dried in high vacuum to give a solid (223 g, 91% yield) that according to HPLC [conditions as described for **3**] consisted of 92% **4** (t_{rel} 7.25 min) and 8% **2** (<0.1% **3**). Sonication in dichloromethane (1.3 L) for 1 min provided a colourless solid (173 g , 71% yield) , mp 280-282°C , >99.5% **4**. An analytical sample was obtained by recrystallization from refluxing dichloromethane / ethylacetate (3:1) to give crystals, mp 283-284°C. NMR-spectra were identical to those of the optically pure compounds **(*S*)-(-)-4** and **(*R*)-(+)-4** (*vide infra*). MS (+FAB, MeOH/NBA): m/e (rel. int.) : 591 (M+H, 100), 513 (M-Ph, 7), 389 (M-Ph_2PO, 17), 201 (Ph_2PO, 27) ; IR (KBr): 3058 (w), 1436, 1422, 1240, 1206, 1192, 1117, 742, 695, 566, 532 cm^{-1}.

Crystals suitable for X-ray analysis were obtained by recrystallization from boiling toluene. Crystal of 0.31 x 0.18 x 0.17 mm^3 ; cell dimensions: a = 26.570 (4), b = 12.840 (4), c = 20.296 (3) A , β = 120.04 (1)° ; C2/c, Z = 8, D_x = 1.309 Mg/m^3; λ (Mo K_α) = 0.7107 A, ϑ_{max} = 25.06°, 5107 unique reflections, 3117 with (Fo) > 4σ; 379 parameters, wR2 = 0.154 (all reflections), R1 = 0.046 (3117 reflections), S = 0.92, maximum and minimum in the difference Fourier synthesis: 0.46, -0.39 e/A^3.

(RS)-(6,6'-Difluoro-5-iodo-biphenyl-2,2'-diyl)bis(diphenylphosphine Oxide) **(7)**

Reaction of monoiodide **3** containing 14% diiodide **6** under the same Ullmann coupling conditions gave a product consisting of 89% **4** ,10% **7** and 1% of an unidentified component. 31.5 g of this mixture was chromatographed over 3 kg RP18-silica gel (eluent methanol / water 1:1) to give after recrystallization from hot dichloromethane / ethylacetate (3:1) 2.7 g **7**, colourless needles, mp 272-274°C , HPLC (conditions as described for **3**, t_{rel} 11.69 min): >99% . ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.78 (dd, $^3J_{H,P} = 13.0$ Hz, $^3J_{H,H} = 8.4$ Hz, 1H), 7.06 (ddd, $^3J_{H,P} = 13.0$ Hz, $^3J_{H,H} = 8.0$ Hz, $^4J_{H,H} = 1.2$ Hz, 1H), 7.12 (br t, $^3J_{H,F} \sim {}^3J_{H,H} \sim 8.5$ Hz, 1H), 7.30-7.36 (m, 5H), 7.40-7.48 (m, 6H), 7.50-7.56 (m, 2H), 7.58-7.68 (m, 8H), 7.70 (ddd, 1H) ; ^{19}F{^{1}H}-NMR (94.2 MHz, $CDCl_3$): δ -89.6 (dt, $^4J_{F,P} = 6.3$ Hz, $^5J_{F,P} = 0.9$ Hz, $^5J_{F,F} = 0.9$ Hz), -110.3 (dt, $^4J_{F,P} = 6.9$ Hz, $^5J_{F,P} = 0.8$ Hz, $^5J_{F,F} = 0.9$ Hz); ^{19}F-NMR (94.2 MHz, $CDCl_3$): δ -89.6 (br t, $^4J_{F,P} = {}^4J_{F,H} = 6.3$ Hz), -110.3 (br qua , $^4J_{F,P} \sim {}^3J_{F,H} \sim {}^4J_{F,H} \sim 7.0$ Hz); ^{31}P{^{1}H}-NMR (109.35 MHz, $CDCl_3$): δ +28.47 (d, $^4J_{P,F} = 6.3$ Hz), +28.58 (d, $^4J_{P,F} = 6.9$ Hz); MS (DCI , MeOH): m/e (rel. int.) 717 (M+H, 85), 515 (M - Ph_2PO) ; IR (KBr): 3057 (w), 1438, 1393, 1203, 1118, 705, 695, 533 cm^{-1}. Baseline separation of the enantiomers of **7** [t_{rel} 20.34 (+)-isomer

and 22.14 min (-)-isomer] was achieved on a 250 x 4.6 mm column DNBPG-Bakerbond with the eluent n-heptane / ethanol 15:1.

Crystals suitable for x-ray analysis were obtained by recrystallization from boiling dichloromethane. Crystal 0.45 x 0.45 x 0.3 mm^3 ; cell dimensions: a = 10.462 (1), b = 14.579 (1), c = 20.467 (2) A ; $P2_12_12_1$, Z = 4 , D_x = 1.524 Mg/m^3 ; λ (Mo K_α) = 0.7107 A, ϑ_{max} = 28.06° , 7569 unique reflections, 7063 with (Fo) > 4σ ; 488 parameters, wR2 = 0.065 (all reflections), R1 = 0.023 (7063 reflections), S = 0.67 , maximum and minimum in the difference Fourier synthesis: 0.53, -0.26 e/A^3.

Attempted Resolution of (R,S)-4 with (-)-(2R,3R)-2,3-O,O'-dibenzoyltartaric Acid

a) The solution of (2R,3R)-(-)-di-O-benzoyl-tartaric acid (951 mg, 2.53 mmol) in ethylacetate (6 mL) was added to the solution of (*RS*)-**4** (815 mg, 1.38 mmol) in boiling dichloromethane (15 mL). The solution was refluxed for 3 h. No precipitate formed. The solution was allowed to stand at 20°C overnight. No precipitate formed.

b) (2S,3S)-(+)-Di-O-benzoyl-tartaric acid monohydrate (1.70 g, 4.50 mmol) and (*RS*)-**4** (2.00 g, 3.35 mmol) were dissolved in dichloromethane (30 mL). n-Heptane (13 mL) was added dropwise with stirring. The cloudy mixture was allowed to stand 30 min, giving two layers. The layers were separated , and both were washed separately with 2 N sodium hydroxide (2 x 15 mL) and with water (2 x 15 mL). The organic solutions were dried ($MgSO_4$), and the solvents were evaporated *in vacuo*. From the upper layer: colourless solid (0.98 g), (*RS*)-**4** (< 1% ee) according to optical rotation (365 nm, c = 0.56, CH_3OH) and chiral-phase HPLC. From the lower layer: colourless solid (0.75 g), (*RS*)-**4** (< 1% ee) according to optical rotation and chiral-phase HPLC.

(RS)(6,6-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine) **((*RS*)-5)**

a) *by reduction of (RS)-4 with trichlorosilane :* To a suspension of (*RS*)-**4** (64.3 g , 109 mmol) in deoxygenated xylene (900 mL) was added tri-n-butylamine (150 mL , 638 mmol) and trichlorosilane (43 mL, 426 mmol). The suspension was heated to reflux (138°C) and became a clear solution. It was kept at gentle reflux for 18 h. After a reaction time of 9 h additional tri-n-butylamine (150 mL , 638 mmol) and trichlorosilane (10 mL , 99 mmol) was added. TLC (EtOAc / MeOH 19:1) indicated quantitative transformation of **4** (R_f 0.30) to **5** (R_f 0.86) and a small amount of monooxide (R_f 0.77). The reaction mixture was cooled to 0°C. Deoxygenated 30% aq. sodium hydroxide (400 mL) and dichloromethane (500 mL) were added and the mixture was stirred at 60°C until the organic and aqueous layers became clear (30 min). The aqueous layer was removed *via* cannula and the organic layer was washed with deoxygenated 30% aq. sodium hydroxide (400 mL) , water (3 x 400 mL) and brine (400 mL), dried ($MgSO_4$) , filtered, and evaporated *in vacuo*. The residue was dried in high vacuum , then dissolved in dichloromethane (1.1 L) , and cyclohexane (1.1 L) was added. The solution was filtered through a pad (30 cm height) of silica gel (35-70 µm, 850 g) , and the pad was washed with dichloromethane / cyclohexane (1:1, 3.0 L). The filtrates were evaporated *in vacuo* to give a colourless solid (48.0 g, 86.0 mmol, 79% yield) , mp 215-217°C , HPLC (250 x 4.6 mm Nucleosil 120 C8 7µm , 1 mL / min 85% acetonitrile / 15% water , det. 254 nm, injection of 10 µl of a solution prepared from 1.0 mg **5** and 5 mL CH_3CN with sonication, t_{ret} 14.50 min) indicated >99% purity. An analytical sample was obtained by recrystallization from boiling toluene / ethanol (4:5) : mp 222-223°C ; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 6.83-6.98 (m, 4H), 7.10-7.40 (m, 22H).; ^{19}F-NMR (188.14 MHz, $CDCl_3$): δ -112.6 (m) ; ^{31}P{^{1}H}-NMR (109.35 MHz, $CDCl_3$): δ -12.70 (t, $^4J_{P,F}$

~ $^5J_{P,F}$ ~ 9.3 Hz) ; MS (DCI, $CHCl_3$) m/e (rel. int.) 559 (M+H, 53) , 373 (M-PPh_2, 100); IR (KBr): 3053 (w), 1562, 1446, 1432, 1417, 1234, 790, 742, 693 cm^{-1}.

b) *by reduction of (RS)-4 with dichloro-methylsilane :* In a cylindrical glass insert for a steel autoclave (*RS*)-**4** (13.47 g , 22.8 mmol) was suspended in *o*-xylene (150 mL). Argon was bubbled through the suspension for 10 min. Dichloromethylsilane (11.9 mL, 13.1 g, 114 mmol) was added, followed by tri-n-butylamine (28.4 mL, 22.2 g, 121 mmol). The argon-filled glass insert was introduced into the autoclave. Nitrogen (5 bar) was pressed in, and the pressure was released very slowly. Nitrogen (100 bar) was pressed in , and the autoclave was heated to 150°C inner temperature for 86 h. The autoclave was allowed to cool to ambient temperature. The nitrogen pressure was then released and the glass insert was taken out. TLC of an aliquote of the dark-brown reaction mixture , diluted with dichloromethane, indicated clean formation of **5**, with residual **4** and monooxide being close to the detection limit. All volatile components were evaporated (bath 60°C / < 20 mbar). Methanol (100 mL) was added to the dark-brown residue , and the suspension was sonicated (ultrasonic cleaning bath) for 5 min. The solid was filtered, washed with methanol (20 mL) and dried *in vacuo* to yield the off-white crude product (12.8 g , 100.5% yield) , mp 213-220°C. Isopropanol (30 mL) was added ,and the suspension was sonicated for 1 min. The solid was filtered and dried *in vacuo*: colourless powder (11.7 g, 21.0 mmol, 92% yield) , mp 221-223°C ; spectra identical to those described under **a)**.

c) *by reduction of (RS)-7 with dichloro-methylsilane :* Reaction of (*RS*)-**7** (1.14g , 1.60 mmol) , dichloromethylsilane (918 mg, 7.98 mmol) and tri-n-butylamine (1.55 g, 8.46 mmol) in *o*-xylene (15 mL) under the same conditions as described in **b)** provided after the same work-up and ultrasonic irradiation in methanol (10 mL) the crude product (908 mg, 102% yield) as an off-white solid , mp 213 - 219°C. Ultrasonic irradiation in isopropanol (2 mL) gave a colourless powder (808 mg, 1.45 mmol, 91% yield), mp 221-223°C ; spectra identical to those described under **a)**.

Resolution of (RS)-5 via Palladium Complexes 10

{(S)-2-[1-(Dimethylamino)ethyl]-phenyl-C,N}[(S)-(6,6'-difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine)] palladium(II) Hexafluorophosphate **(S,S)-(-)-10**

A suspension of (*RS*)-**5** (4.36 g, 7.38 mmol) and (*S*)-(+)-di-μ-chlorobis{2-[1-(dimethylamino)ethyl] phenyl-*C,N*}dipalladium (**9**) (2.19 g , 3.69 mmol) in deoxygenated methanol (430 mL) was stirred 2 h at 25°C to give a virtually clear, pale-yellow solution. A very small amount of undissolved material was removed by filtration. A solution of potassium hexafluorophosphate (680 mg , 3.69 mmol) in deoxygenated water (430 mL) was added dropwise . A pale-yellow solid precipitated and the suspension was stirred for 4 h. Reaction progress could be monitored by TLC (100% isopropanol ; R_f (*RS*)-**5**: 0.72, (*S,S*)-**10**: 0.57, (*S,R*)-**10**: 0.37, **9**: 0.00). The precipitates were collected by filtration , washed with 50% deoxygenated aq. methanol (300 mL) and then with diethylether (150 mL). [While these washings were discarded, the original filtrate was preserved for the isolation of (*S,R*)-(+)-**10** (*cf.* next paragraph)]. The pale-yellow solid was dried in vacuo to give crude (*S,S*)-**10** (3.33 g, 3.48 mmol, yield 94% of theory); mp 218-220°C (dec.) ; $[\alpha]_D^{25}$ -198.6 (c 0.967, acetone). ^{1}H-NMR signals of its diastereomer (*S,R*)-**10** could not be detected , but traces were detected by TLC (diastereoselectivity > 98:2). The crude complex was dissolved in deoxygenated acetone (40 mL) and diethylether (40 mL) was added slowly. The mixture was allowed to stand 8 h in a stoppered flask. The precipitate was collected by filtration and dried *in vacuo* : 2.83 g (2.95 mmol, yield 80% of theory) pale-yellow solid , mp 223-225°C (dec.), $[\alpha]_D^{25}$ -203.2 (c 0.98, acetone) ; ^{1}H-NMR (200 MHz, acetone-d_6) δ 1.36 (d, J =

6.5 Hz, 3H, NCHCH_3), 1.68 (d, J = 2.5 Hz, 3H, NCH_3), 2.68 (m, approx. t, J = 3.7 Hz, 3H, NCH_3), 5.54 (qua, J = 6.5 Hz, 1H, NCHCH$_3$), 6.32 (~t, J = 7.0 Hz , 1H) , 6.58 (~qua d, J = 8.0 and 1.0 Hz, 1H), 6.68-6.86 (m, 4H), 7.06-8.26 (m, 24H) ; ^{31}P{^{1}H}-NMR (145.79 MHz, acetone-d$_6$) δ -143.7 (sept, $^1J_{P,F}$ = 707 Hz, PF_6^-), +11.5 (dd, $^2J_{P,P}$ = 45 Hz, $^4J_{P,F}$ = 8 Hz), +35.3 (dd, $^2J_{P,P}$ = 45 Hz, $^4J_{P,F}$ = 7 Hz) ; ^{19}F{^{1}H}-NMR (376.50 MHz, acetone-d$_6$, the left line of the PF_6-doublett was set to -70.0 ppm in accordance with lit. data for $NaPF_6$) δ -70.9 (d, $^1J_{F,P}$ = 707 Hz, 6F, PF_6^-), -106.2 (ddd, $^4J_{F,P}$ = 7.3 Hz, $^5J_{F,F}$ = 5.9 Hz, $^5J_{F,P?}$ = 1.7 Hz) , -106.4 (ddd, $^4J_{F,P}$ = 7.7 Hz, $^5J_{F,F}$ = 5.9 Hz, $^5J_{F,P?}$ = 1.7 Hz) ; MS (+FAB , MeOH/NBA): m/e (rel. int.) 817 (16), 816 (32), 815 (30), 814 (71), 813 (43), 812 (100), 811 (67) , 810 (27), 809 (2), 808 (3) [the peaks m/e = 816, 814, 812, 811, 810, 808 correspond to the cation $C_{46}H_{40}F_2NP_2Pd$ of the salt with the palladium isotopes (natural abundance) ^{110}Pd (43.2), ^{108}Pd (97.7), ^{106}Pd (100), ^{105}Pd (81.3), ^{104}Pd (40.1), ^{102}Pd (3.5) , respectively] ; IR (KBr): 3060 (w), 1450, 1442, 1418, 841, 746, 697, 556, 502 cm^{-1}.

Crystal: 0.3 x 0.2 x 0.15 mm^3 ; cell dimensions: a = 12.091 (1), b = 18.612 (4), c = 18.958 (2) A; $P2_12_12_1$, Z = 4, D_x = 1.391 Mg/m^3; λ (Mo K_α) = 0.7107 A, ϑ_{max} = 25.0°, 8124 unique reflections , 4722 with (Fo) > 4σ ; 533 parameters, wR2 = 0.076 (all reflections), R1 = 0.047 (4722 reflections), S = 0.83, maximum and minimum in the difference Fourier synthesis: 0.88, -0.61 e/A^3.

{(S)-2-[1-(Dimethylamino)ethyl]-phenyl-C,N}[(R)-(6,6'-difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine)] palladium(II) Chloride **(S,R)-(+)-10**

The original filtrate from the preparation of (S,S)-(-)-**10** (*vide supra*) was evaporated in vacuo to give a pale-yellow solid (3.25 g , 3.83 mmol, yield 104% of theory); mp 162-165° (dec) ; $[\alpha]_D^{25}$ + 184.3 (c 1.02 , methanol). ^{1}H-NMR signals of its diastereomer (S,S)-**10** could not be detected and no traces were detected by TLC (diastereoselectivity >>99 : 1). The crude complex was dissolved in deoxygenated methanol (40 mL) and refluxed for 2 min. Deoxygenated water (150 mL) was added and the mixture was allowed to stand in the stoppered flask for 8 h. The precipitate was collected by filtration, washed with deoxygenated methanol / water (1 : 8, 15 mL) , water (30 mL) , and dried *in vacuo* : pale-yellow crystals (3.00 g , 3.54 mmol, 96% yield) , mp 164-166°C (dec.), $[\alpha]_D^{25}$ +208.0 (c 1.01, methanol) ; ^{1}H-NMR (200 MHz, CD_3OD): δ 2.05 (d, J = 1.9 Hz, 3H, NCH_3), 2.17 (m, approx. t, J ~ 3.3 Hz, 3H, NCH_3), 2.27 (d, J = 6.3 Hz, 3H, NCHCH_3), 3.58 (qui, J = 6.3 Hz, 1H, NCHCH$_3$), 6.26 (tdt, J = 7.5 , 2.5 and 1.3 Hz, 1H), 6.44 (qua d , J = 7.5 and 0.8 Hz), 6.66-6.85 (m, 4H), 6.96-7.76 (m, 24H) ; ^{31}P{^{1}H}-NMR (145.79 MHz, CD_3OD) δ +10.72 (dd, $^2J_{P,P}$ = 44 Hz, $^4J_{P,F}$ = 7.6 Hz) , 33.21 (dd, $^2J_{P,P}$ = 44 Hz, $^4J_{P,F}$ = 7.5 Hz) ; ^{19}F{^{1}H}-NMR (376.50 MHz, CD_3OD): δ -103.37 (qua, $^4J_{F,P}$ ~ $^5J_{F,F}$ ~ 6 8 Hz), -104 46 (~ qua d, $^4J_{F,P}$ ~ $^5J_{F,F}$ ~ 6.8 Hz, $^5J_{F,P?}$ ~ 2 Hz) ; MS (+FAB, MeOH/NBA): identical with MS of (*S,S*)-**10**.

[(S)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine)]palladium(II) Dichloride **(S)-(-)-11**

Deoxygenated 10 M hydrochloric acid (12 mL) was added to the refluxing solution of (*S,S*)-(-)-**10** (1.12 g, 1.17 mmol) in deoxygenated acetone (20 mL) . A yellow precipitate formed after a few minutes. The mixture was refluxed for 2 h and then concentrated *in vacuo* to 10 mL. Deoxygenated water (100 mL) was added and nitrogen was bubbled through the suspension (25°C, 10 min). The solid was collected by filtration and stirred with isopropanol / water (1:1 , 20 mL) for 5 min. The solid was filtered , washed with isopropanol / water (1:1, 5 mL) and dried *in vacuo* to give bright-yellow crystals (846 mg , 1.15 mmol , 98% yield), mp 310-312°C (dec.) , $[\alpha]_D^{25}$ -311.9 (c 0.495, dichloromethane) ; the specific rotation was unchanged after allowing the

solution to stand 8 d at ambient temperature ; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.66-6.86 (m, 4H), 6.90-7.08 (m, 2H), 7.27-7.56 (m, 12H), 7.70 (ddd, J = 12.5, 8.0 , 2.0 Hz, 4H), 7.94 (dd, J = 12.5 and 8.0 Hz) ; ^{31}P{^{1}H}-NMR (145.79 MHz, $CDCl_3$): δ 26.72 (br d, $^4J_{P,F}$ = 6.0 Hz) ; ^{19}F-NMR (188.14 MHz, $CDCl_3$): δ -108.5 (m) ; MS (+FAB, MeOH/NBA): m/e (rel. int.) [705 (14), 704 (20) , 703 (53), 702 (37), 701 (93), 700 (49), 699 (100), 698 (60), 697 (30) M-Cl for different isotopes of Pd and Cl] , [668 (7), 667 (11), 666 (14), 665 (10), 664 (23), 663 (16), 662 (10) M-2Cl for different isotopes of Pd] ; IR (KBr): 3060 (w), 1450, 1437, 1420, 747, 696, 507, 499, 487 cm^{-1} , elemental analysis (found / calc. for $C_{36}H_{26}Cl_2F_2P_2Pd$): C 58.9 / 58.76 , H 3.8 / 3.56 , Cl 9.6 / 9.64 , F 4.7 / 5.16.

[(R)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine)]palladium(II) Dichloride **(R)-(+)-11**

Deoxygenated 10 M hydrochloric acid (22 mL) was added to the refluxing solution of (*S,R*)-(+)-**10** (408 mg, 0.48 mmol) in deoxygenated acetone (20 mL). A yellow precipitate formed after a few minutes. The mixture was refluxed for 2 h . Work-up as described for (*S*)-**11** gave bright-yellow crystals (346 mg, 0.47 mmol, 98% yield), mp 310-311°C (dec.) , $[\alpha]_D^{25}$ +311.5 (c 0.495, dichloromethane); spectra were superimposable to those of (*S*)-**11**.

(S)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine) **(S)-(+)-5**

1,2-Bis(diphenylphosphino)ethane dppe (508 mg , 1.27 mmol, 0.8 equiv.) was added to a solution of (*S,S*)-**10** (1.53 g , 1.59 mmol) in deoxygenated dichloromethane (20 mL). The resulting clear solution was stirred 16 h at 20-25°C. Reaction progress could be monitored by TLC [100% toluene, R_f : (*S,S*)-**10** (0.00) , dppe (0.61), **5** (0.80)], which indicated quantitative reaction of dppe, the presence of **5** and a baseline spot (palladium complexes). Deoxygenated cyclohexane (20 mL) was added, and the mixture was filtered through a frit containing a bed of silicagel (35-70 µm , 13.5 g). The silica bed was washed with deoxygenated dichloromethane / cyclohexane (1:1 , 4 x 20 mL). The combined filtrates were evaporated *in vacuo*. Methanol (3 mL) was added to the residue and the solvent was evaporated *in vacuo* to obtain a colourless solid (657 mg , 1.18 mmol , 93% yield) , mp 161-163°C . An analytical sample was obtained by recrystallization (0°C, 12 h) from boiling toluene / ethanol (4:5), mp 164-165°C, $[\alpha]_D^{25}$ +114.9 (c 0.99, toluene), *cf* Table 1. NMR-spectra were superimposable to those of (*RS*)-**5**. TLC and HPLC [*cf.* (*RS*)-**5**] indicated 100% chemical purity. Oxidation to the bis(phosphine oxide) (*S*)-**4** , followed by chiral-phase HPLC analysis indicated 100% ee (*vide infra*). When (*S,S*)-**10** was reacted , under the same conditions with 1.0 equiv. dppe, considerable amounts of dppe remained unreacted (TLC) and were difficult to remove from the reaction product.

Configurational Stability of (S)-5 on Heating in Solution

A solution of optically pure (*S*)-**5** (44.2 mg) in tetralin (10 mL , bp 207°C) was refluxed 2.5 h in an argon atmosphere. The specific rotation of the solution remained constant and a sample, after oxidation to bis(phosphine oxide) (*S*)-**4** was found to have 100% ee by chiral-phase HPLC analysis.

Configurational stability was also observed , when a solution of (*S*)-**5** in toluene was allowed to stand under argon for 12 d , when this solution was heated to 100°C for 8 h , and when a solution of (*S*)-**5** in mesitylene (bp 164°C) was refluxed for 3 h.

Attempted Preparation of (S)-5 by Reaction of Palladium Dichloride Complex (S)-11 with Potassium Cyanide

To a solution of (*S*)-**11** (87 mg, 0.12 mmol) in dichloromethane (10 mL) was added potassium cyanide (30 mg , 0.46 mmol), water (5 mL) and methanol (10 mL) (all solvents deoxygenated). The clear solution was stirred 2 h. TLC did not indicate the formation of **5**. Potassium cyanide (250 mg) was added, and the solution was allowed to stir 16 h : no reaction.

(R)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine) **(R)-(-)-5**

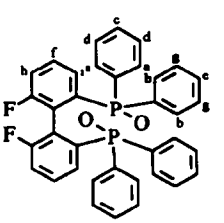
In a procedure analogous to that described for (*S*)-(+)-**5**, reaction of the chloride (*S,R*)-**10** (748 mg, 0.88 mmol) with dppe (282 mg, 0.71 mmol, 0.8 equiv.) in dichloromethane (20 mL) gave the title compound (390 mg, 0.70 mmol, 99% yield), mp 164-165°C, $[\alpha]_D^{25}$ -114.8 (c 1.03, toluene), NMR-spectra superimposable to those of (*RS*)-**5** and (*S*)-**5**. TLC and HPLC indicated 100% chemical purity. Oxidation to the bis(phosphine oxide) (*R*)-**4**, followed by chiral-phase HPLC analysis indicated 100% ee (*vide infra*).

(S)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine Oxide) **(S)-(-)-4**

Methanol (5 mL) , then 35% aq. hydrogen peroxide (1 mL, 11.6 mmol) was added to the solution of (*S*)-**5** (101 mg, 0.18 mmol) in toluene (2 mL). The mixture was stirred 4 h. TLC [*cf.* (*RS*)-**5**] indicated the title compound and traces of residual **5** and monooxide. Hydrogen peroxide (1 mL) was added and stirring was continued for 1 h. TLC now indicated quantitative oxidation. The solution was washed with saturated aq. sodium sulfite solution (3 x 3 mL) and 1 N hydrochloric acid (2 x 2 mL). The solvent was evaporated in vacuo. The residue was extracted with chloroform (3 x 15 mL). The combined extracts were washed with sat. aq. sodium bicarbonate solution (2 x 10 mL) , with water (2 x 10 mL) , and dried over magnesium sulfate. The solvent was evaporated in vacuo to give a colourless solid (100 mg, 0.17 mmol, 94% yield), mp 275-277°C, $[\alpha]_D^{20}$ -11.8 (c 0.92, chloroform). ^{1}H-NMR (*Table 2*) ; ^{13}C-NMR (*Table 3*); ^{19}F{^{1}H}-NMR (470.59 MHz, $CDCl_3$): δ −110.21 ($J_{F,P}$ = 6.6 Hz); ^{31}P{^{1}H}-NMR (202.46 MHz, $CDCl_3$): δ 28.89 ($J_{P,F}$ 6.6 Hz).

Table 2: ^{1}H-NMR [500 MHz, 10 mg (*S*)-(-)-**4** / mL $CDCl_3$]

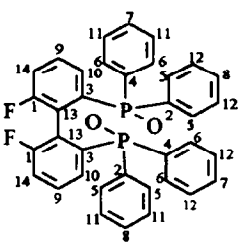
signal	intensity	δ (ppm)	(n) $J_{H,H}$ (Hz) coupl.-partner	(n) $J_{H,F}$	(n) $J_{H,P}$	$^1J_{C,H}$
a	4H	7.527	(3) 7.6 (d) (4) 7.6 (c') (5) 0.7 (d')	-	(3) 12.0	6
b	4H	7.518	(3) 7.6 (g) (4) 7.6 (e) (5) ~0.7 (g')	-	(3) 12.3	5
c	2H	7.427	(3) 7.6 (d,d') (4) 1.5 (b,b')	-	(5) 1.3	7
d	4H	7.338	(3) 7.6 (a) (3) 7.6 (c') (5) ~0.7 (a')	-	(4) 3.3	11



e	2H	7.318	(3) 7.2 (g,g') (4) 1.4 (b,b')	-	(5) 1.4	8
f	2H	7.230	(3) 7.7 (i) (3) 8.1 (h)	(4) 5.1	(4) 3.2	9
g	4H	7.214	(3) 7.6 (b) (3) 7.2 (e) (5) ~0.7 (b')	-	(4) 3.1	12
h	2H	7.039	(3) 8.1 (f) (4) 1.2 (i)	(3) 8.9	(5) 1.5 (6) ~0.9	14
i	2H	6.966	(4) 1.2 (h) (3) 7.7 (f)	(5) -- (6) --	(3) 13.1	10

Table 3: $^{13}C\{^1H\}$-NMR [125.76 MHz, 50 mg (*S*)-(-)-**4** / mL $CDCl_3$]

signal	intensity	δ (ppm)	m ^1H	m ^{19}F	m ^{31}P
1	2C	160.64	s	d; $^1J_{C,F}$=246.8Hz	d; $^3J_{C,P}$= 14.8Hz
2	2C	133.81	s	s	d; $^1J_{C,P}$=105.9Hz
3	2C	133.75	s	t; $^3J_{C,F}$< 0.7Hz	d; $^1J_{C,P}$=101.2Hz
4	2C	133.62	s	s	d; $^1J_{C,P}$=103.8Hz
5	4CH	132.76	d	s	d; $^2J_{C,P}$= 10.2Hz
6	4CH	132.28	d	s	d; $^2J_{C,P}$= 9.6Hz
7	2CH	131.67	d	s	d; $^4J_{C,P}$= 2.8Hz
8	2CH	131.62	d	s	d; $^4J_{C,P}$= 2.8Hz
9	2CH	129.36	d	d; $^3J_{C,F}$ = 8.2Hz	d; $^3J_{C,P}$= 15.0Hz
10	2CH	129.01	d	d; $^4J_{C,F}$ = 3.5Hz	d; $^2J_{C,P}$= 11.7Hz
11	4CH	128.33	d	s	d; $^3J_{C,P}$= 12.1Hz
12	4CH	128.31	d	s	d; $^3J_{C,P}$= 12.4Hz
13	2C	126.59	s	dd; $^3J_{C,F}$= 3.9Hz $^2J_{C,F}$=19.0Hz	d; $^2J_{C,P}$= 7.1Hz $^3J_{C,P}$≤ 0.5Hz
14	2CH	118.26	d	d; $^2J_{C,F}$= 23.2Hz	d; $^4J_{C,P}$= 2.4Hz



Chiral phase HPLC (250 x 4.6 mm DNBPG-Bakerbond, 1.0 mL / min n-hexane + ethanol (20 + 1) , det. 254 nm) in comparison with the racemic reference sample (*RS*)-**4** indicated 100% (*S*)-**4** (t_{ret} 25.50 min) and 0% (*R*)-**4** (t_{ret} 23.63 min). An analytical sample was obtained by recrystallization (0°C, 12 h) from boiling dichloromethane / ethylacetate (3:1), mp 282-283°C , $[\alpha]_D^{20}$ -11.3 (c 0.96, chloroform) ; $[\alpha]_{365}^{20}$ +57.0 (c 0.59, methanol)

(R)-(6,6'-Difluorobiphenyl-2,2'-diyl)bis(diphenylphosphine Oxide) **(R)-(+)-4**

Analogously, oxidation of (*R*)-**5** gave a colourless solid , mp 282-283°C, $[\alpha]_D^{20}$ +11.3 (c 0.83 , chloroform) ; $[\alpha]_{365}^{20}$ -56.5 (c 0.57, methanol). ^{1}H- , ^{13}C{^{1}H}-, ^{19}F{^{1}H}-, ^{31}P{^{1}H}-NMR spectra in $CDCl_3$ were superimposable with those of (*S*)-**4** and (*R/S*)-**4**. Chiral phase HPLC indicated 100% (*R*)-**4**.

Rhodium(I)-(R)-(-)-5 - Catalyzed Asymmetric Hydroboration / Oxidation of p-Methoxystyrene

The solution of *p*-methoxystyrene (**12**) (671 mg, 5.0 mmol), (1,5-cyclooctadiene)(2,4-pentadionato)-rhodium(I) (31.0 mg, 0.10 mmol) and (*R*)-(-)-**5** (61.4 mg, 0.11 mmol) in deoxygenated, dry THF (6 mL) is refluxed 90 min under argon. The solution is then cooled and a 1 M solution of catecholborane in THF (10.0 mL, 10.0 mmol) , that has been purged with argon (10 min) before, is added dropwise within 5 min at 0°C. The solution is stirred 90 min at 0°C under argon . TLC (cyclohexane / ethylacetate 1:1 ; R_f **12**: 0.66 , **13**: 0.41, **14**: 0.30) indicates quantitative reaction of **12**. The solution is cooled to -20°C and ethanol (10 mL), 4 N aqueous sodium hydroxide (5 mL) and 36% aqueous hydrogen peroxide (10 mL) are added successively at ≤ 5°C. The mixture is stirred at ambient temperature overnight, then extracted with diethylether (3 x 50 mL). The combined extracts are washed with 1 N sodium hydroxide (4 x 25 mL), with water (20 mL), brine (20 mL), dried over sodium sulfate and the solvent is evaporated. The residue (780 mg pale-brown oil) is subjected to molecular distillation (bath 60 - 80°C / ~10^{-3} Torr) to give a colourless oil (682 mg, 4.48 mmol, 90% yield) and a brown residue that crystallizes (98 mg). TLC and ^{1}H-NMR indicate that the distillate consists of **13** and **14** (ratio 78:22). $[\alpha]_D^{20}$ +27.7 (c 1.17, chloroform). Correction for 22% achiral **14** gives $[\alpha]_{D\ corr}^{20}$ +35.5 (c 0.91, chloroform). Comparison with lit.[30] indicates that **13** has ~67% ee of the (*R*)-configuration. Chiral phase HPLC analysis [250 mm length, 4.6mm i.d. column Chiralcel OD 10μ (Daicel); 0.5 mL / min n-hexane / ethanol (100 + 0.8), 40°C, det. 254 nm] indicates 68.3% (*R*)-(+)-**13** (t_{rel} 62.80 min), 8.5% of (*S*)-(-)-**13** (79.40 min) and 23.2% **14** (66.14 min). This corresponds to 77 8% ee of the (*R*)-(+)-isomer of **13**.

***Hydrogenation of 2-Benzylidenesuccinic Acid 4-[(4-BOC-amino]-1-piperidide Catalyzed by Neutral Rhodium(I)-(R)-(-)-5* Complex**

(*R*)-(-)-**5** (30.1 mg, 0.054 mmol) is added to the suspension of di-μ-chloro-bis[(cycloocta-1*c*,5*c*-diene)-rhodium(I)] (12.3 mg, 0.025 mmol) in deoxygenated methanol / benzene (3:1) (20 mL) and stirred under argon to give a clear solution within 15 min. In a hydrogenation flask, 2-benzylidenesuccinic acid-4-[(4-BOC-amino)-1-piperidide [56] (1.94 g, 5.0 mmol) is dissolved in deoxygenated methanol / benzene (3:1) (20 mL). The clear catalyst solution is added under argon and the reaction mixture is shaken under 1 bar of hydrogen supplied by a hydrostatic hydrogenation apparatus [56]: no uptake of hydrogen occurs within 6 h. The hydrogenation flask is inserted under argon into a shaking autoclave [56] and 150 bar of hydogen is applied for 2 d. The solvent is evaporated *in vacuo* and the solid residue is dissolved in *tert*-butyl-methylether (40 mL). The cold (0°C) solution is washed with 0.5 N hydrochloric acid (10 mL), with water (10 mL), and dried ($MgSO_4$). The solvent is evaporated to give a solid (1.80 g, 4.61 mmol, 92% crude yield). HPLC [56] indicates quantitative hydrogenation. Chiral phase HPLC [56] indicates 22% ee of the (*R*)-(+)-configuration.

Acknowledgements. We are indebted to Dr. H. Kogler for recording numerous NMR spectra and for the full analyses of the NMR-spectra of **4** , to Dr. H.-W. Fehlhaber for recording the mass spectra, to Dr. V. Teetz for chiral phase HPLC (ee-determinations) and to Mr. H.Leffringhausen for elemental analyses.

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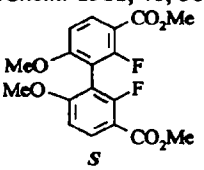

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(*Received in UK* 11 *April* 1994; *accepted* 13 *May* 1994)