Enantioselective Catalysis, XIII[◇]

Preparative and Structural Chemistry of Chiral 3-(Diphenylphosphanyl)-pyrrolidines and Their Palladium(II) Complexes

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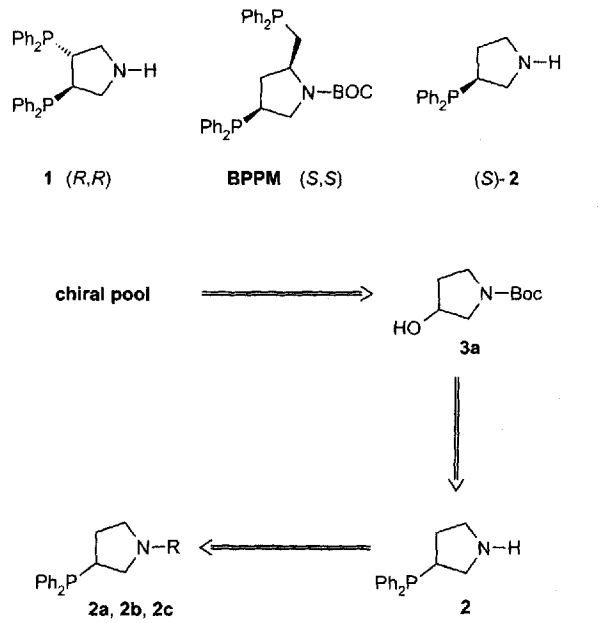
The preparation of both enantiomers of 3-diphenylphosphanylpyrrolidine (**2**) and several *N*-substituted derivatives together with two Pd^{II} complexes of this ligand is reported. From L-malic acid and L-hydroxyproline both enantiomers of 3-hydroxypyrrolidine are prepared without any problems due to epimerization. $KPPh_2$ in the presence of LiCl is shown to be the most effective reagent for the synthesis of **2**. The reported X-ray structure determinations of PdI_2 complexes show a rather rigid bicyclic hetero-norbornane skeleton. The flexibility of the other parts of the molecules is obvious in several polymorphs revealed by this method. This polymorphism is additionally investigated by a ^{31}P-CP-MAS study. From solution ^1H-, ^{13}C- and ^{31}P-NMR studies it is concluded that the bicyclic hetero-norbornane skeleton is retained in solution.

Over the past two decades we have used rhodium complexes with ligands of the (3*R*,4*R*)-3,4-bis(diphenylphosphanyl)pyrrolidine (**1**) family[1] (shown in Scheme 1) as very efficient catalysts in the enantioselective hydrogenation of α-acetylaminocinnamic acid. The nitrogen atom in the backbone has been used for the synthesis of water-soluble[2] or polymer-attached[3] ligands. In all of these investigations we never found any strong influence of this nitrogen atom on the enantioselectivity achieved in hydrogenation. A second family of pyrrolidinebisphosphanes e.g. **BPPM** has been used by Achiwa[4]. In this paper, we report on the synthesis of a third, structurally related family of chiral pyrrolidinephosphanes, which are derivatives of 3-diphenylphosphanylpyrrolidine (**2**). Our synthetic strategy is shown in Scheme 1. The synthesis of enantiomerically pure **2** should facilitate an easy access to many *N*-substituted derivatives (e.g. **2a**–**c**). Furthermore, the synthesis of both enantiomers of **2** was required for further extension of this chemistry.

The application of derivatives of **2** in enantioselective catalysis is of great interest because of the bridged β-aminoalkylphospane skeleton. Kumada and Hayashi showed that nickel complexes of monophosphanes with an amino group in the β-position are clearly superior to 1,2-bisphosphanes (e.g. **1**) in the enantioselective cross-coupling reaction[5].

We were further interested in the structural chemistry of *N*-alkylated derivatives of **2** and their PdI_2 complexes. A recent paper by Pregosin and co-workers[6] clearly proved a different solution structure of the $PdCl_2$ complex of a "Hayashi-type" P,N ligand compared to the structure obtained by X-ray crystallography. We report here our results.

Scheme 1. Relation of the new phosphane **2** to pyrrolidinephosphanes known in the literature and the synthetic strategy for the synthesis of **2** derivatives: **2a**: R = Bzl; **2b**: R = 2-methoxybenzyl; **2c**: R = Et



Synthesis of the Ligands and PdI_2 Complexes

The synthesis of the (*R*)-**3a** enantiomer is known in the literature[7]. Therefore, it is only necessary to mention the modifications made to the well-known synthesis shown in Scheme 2. The crude (*R*)-3-hydroxypyrrolidine, obtained by 2-cyclohexen-1-one catalyzed decarboxylation of L-hydroxyproline was extracted with aqueous acetic acid. Block-

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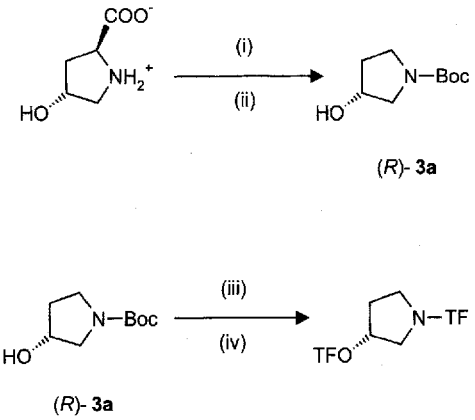
ing the pyrrolidine nitrogen atom with the *tert*-butoxycarbonyl group was achieved by adding di-*tert*-butyl dicarbonate (Boc_2O) in dioxane[8] to the aqueous solution made alkaline by addition of K_2CO_3. The crude (*R*)-**3a** was purified by flash chromatography on silica gel using ethyl acetate as eluent.

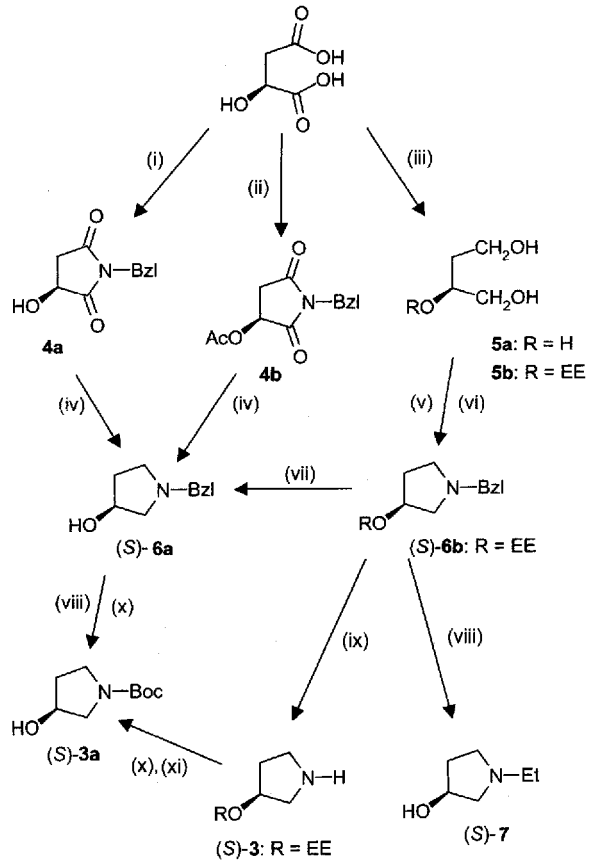
Scheme 2. Preparation of (*R*)-**3a** and the *N*,*O*-bis(trifluoroacetyl) derivative of (*R*)-**3a**; reactions and conditions used: (i) 2-cyclohexen-1-one in boiling cyclohexanol; (ii) K_2CO_3/Boc_2O in dioxane; (iii) trifluoroacetic acid (TFA); (iv) TF_2O and pyridine in dichloromethane



In cooperation with G. Nicholson, Tübingen, we developed a GC separation[9] of the *N*,*O*-bis(trifluoroacetyl) derivative of **3a** on a 25-m L-Chirasil-Val® column. The preparation of this derivative is shown in Scheme 2, experimental details and conditions used for the GC separation are given in the Experimental Section. Starting with racemic **3a** a separation with a net retention time t_2 = 7.11 min and a separation factor $\alpha = t_2/t_1 = 1.035$ was obtained. The order of elution is *S* before *R*. We determined the enantiomeric composition of an (*R*)-**3a** sample. We did not find any epimerization at the chiral center in the 3-position of (*R*)-**3a** during the synthetic transformations [found: 99 ± 1% *ee* of (*R*)-**3a**].

L-Malic acid[10] was used for the synthesis of the enantiomeric product (*S*)-**3a**. The main problem we had to solve was to prevent epimerization at the chiral center in the 2-position (next to the hydroxy group) of L-malic acid during the synthetic transformations. The conversions carried out are outlined in Scheme 3. Initially we synthesized **4a** by heating benzylamine with L-malic acid in boiling xylene. On the basis of m.p. and specific rotation measurements the solid obtained corresponds to the enantiomerically pure compound **4a**[11]. M. Jouillé and co-workers also prepared **4a** from benzylamine and L-malic acid[12]. The reported m.p. and specific rotation data show that in their preparation some epimerization occurred. Unfortunately, all efforts to prevent epimerization in the subsequent reduction yielding (*S*)-**6a** using $LiAlH_4$ or B_2H_6/diglyme or BH_3/THF in variable amounts failed. The enantiomeric purity of an (*S*)-**3a** sample prepared from (*S*)-**6a** by hydrogenolysis of the benzyl group (see discussion below) and derivatization to the *N*,*O*-bis(trifluoroacetyl) derivative was found to be 92% *ee* (GC separation described above). In 1994, a new approach involving the reaction of benzylamine with L-malic acid activated with acetyl chloride was published[13]. Compound **4b** thus obtained could be reduced without epimerization to (*S*)-**6a**.

Scheme 3. Synthesis of (*S*)-**3a** and (*S*)-**7** from L-malic acid; reactions and conditions used: (i) benzylamine in boiling xylene; (ii) ref.[13]; (iii) ref.[14], 74% overall yield, EE = 1′-(ethoxyethyl); (iv) $LiAlH_4$ in THF; (v) TsCl, pyridine in dichloromethane; (vi) benzylamine in dioxane, 80–95°C; (vii) H_3PO_4 then KOH; (viii) Pd/C, H_2 in acidic methanol; (ix) Pd/C, H_2 in methanol; (x) K_2CO_3/Boc_2O in dioxane; (xi) AcOH in methanol



We investigated another approach based on compound **5b**. The high-yielding synthesis of this compound, consisting of three steps, was developed by Seebach and coworkers and reported in 1980[14]. The 2-hydroxy group of (*S*)-diethyl malate is blocked as a 1′-(ethoxyethyl) acetal (EE) group. This compound can be reduced with $LiAlH_4$ to give the blocked derivative **5b**. Van Leusen and Wynberg[15] cleaved the acetal group and obtained **5a**. They compared the specific rotations measured with a sample of **5a** obtained by the reduction of (*S*)-diethyl malate with a sample obtained by the three-step procedure described above. They reached the conclusion that the chiral carbon atom attached to an unprotected hydroxy group is epimerized during the $LiAlH_4$ reduction. This result parallels our finding that epimerization takes place during $LiAlH_4$ reduction of **4a** to (*S*)-**6a**. Compound **4b** has a protected hydroxy group and can be reduced and deprotected in one step without epimerization to yield (*S*)-**6a**.

Following the procedure published by Seebach[14] both free hydroxy groups of **5b** were tosylated in high yield. The crude product was then introduced into a hot solution of excess benzylamine in dioxane. (*S*)-**6b** was separated from excess benzylamine by repeated saturation of a diethyl ether solution with CO_2. The filtrate was then concentrated and the residue was distilled to give pure (*S*)-**6b** in 85% overall yield.

The deprotection of the acetal group was easily accomplished by stirring an ethereal solution of (*S*)-**6b** with excess aqueous H_3PO_4 solution. Pure (*S*)-**6a** was extracted with diethyl ether after the aqueous solution was made alkaline. Subsequent palladium-catalyzed hydrogenolysis of the benzyl group in acidic (acetic acid) methanol solution and blocking the pyrrolidine with the *tert*-butoxycarbonyl group afforded (*S*)-**3a** in 88% yield [calculated for the transformation (*S*)-**6b** ⇒ (*S*)-**3a**]. A quantitative conversion in the hydrogenolytic step was achieved using 10 mmol of palladium on charcoal per mol of (*S*)-**6a** at 40 °C and 30 bar H_2. At hydrogen pressures below 5 bar, only a conversion of 90% was possible.

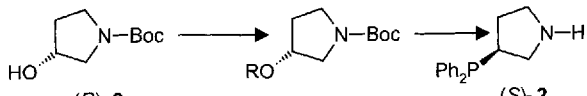
We, however, preferred to carry out a hydrogenolysis of (*S*)-**6b**. The secondary amine (*S*)-**3** could be obtained in quantitative yield. The conditions used were the same as in the previous case, except that no acetic acid was added. (*S*)-**3** is a versatile starting material for many transformations because the blocked hydroxy group suppresses both epimerization and side reactions. When excess acid was added to the reaction mixture of (*S*)-**6b** and Pd/C in methanol, twice the amount of hydrogen was consumed. A 95% yield of pure (*S*)-**7** was isolated from the reaction mixture. In this case, the product formed by hydrogenolysis of the benzyl group reacted with several acetaldehyde acetals [either (*S*)-**3** or (*S*)-**6b** or the dimethyl, diethyl, or mixed ethyl methyl acetals formed by transacetalization from (*S*)-**3** or (*S*)-**6b**], forming the *N*-vinyl derivative of (*S*)-**3**. This was reduced to (*S*)-**7**, consuming a second mol of hydrogen.

To continue with the synthesis of (*S*)-**3a** the secondary amine moiety in (*S*)-**3** was again blocked with the *tert*-butoxycarbonyl group. The acetal was cleaved without any cleavage of the *tert*-butoxycarbonyl group by heating a methanolic solution containing acetic acid for four days, and then evaporating the solvent. This last step removed the dimethyl, diethyl, or mixed ethyl methyl acetals formed by transacetalization. For complete cleavage of the acetal this procedure had to be repeated once more. Following this second route for the transformation (*S*)-**6b** ⇒ (*S*)-**3a**, an 89% yield was obtained. The enantiomeric purities of (*S*)-**3a** samples thus obtained [as *N,O*-bis(trifluoroacetyl) derivatives using the GC separation described above] were found to be 99 ± 1%. Epimerization at the chiral center in the 3-position of (*S*)-**3a** during the synthetic transformations was efficiently suppressed.

The next task was the synthesis of a suitable sulfonic ester derivative of **3a** which could be converted to **2** with clean inversion of the stereogenic center (S_N2 mechanism).

The known synthesis[7] of methanesulfonate ester (*R*)-**3c** by the reaction of (*R*)-**3a** with excess methanesulfonyl chloride in the presence of triethylamine yielded an oily compound of 99% purity (estimated by GC analysis). For use in phosphane synthesis (*R*)-**3c** or *p*-toluenesulfonate ester (*R*)-**3d** of (*R*)-**3a** must contain no excess sulfonyl chloride, because one mol of sulfonyl chloride consumes two mols of phosphide anion. This was shown by a titration of a solution of $LiPPh_2$ in THF at −78 °C with methanesulfonyl chloride. The orange color of the solution disappeared completely after the addition of half an equivalent of methanesulfonyl chloride. A $^{31}P\{^1H\}$-NMR spectrum of this solution showed that all the $LiPPh_2$ had been consumed. We tried to obtain (*R*)-**3c** or (*R*)-**3d** free from any excess sulfonyl chloride by using a small excess of (*R*)-**3a**. This change was shown to reduce yields but again the sulfonyl chloride was not consumed completely. The crude product of a reaction of (*R*)-**3a** with *p*-toluenesulfonyl chloride was purified by flash chromatography on silica gel with 85% ethyl acetate/15% dichloromethane followed by crystallization from petroleum ether. Pure crystalline (*R*)-**3d** {m.p. 68 °C (dec.). − $[\alpha]_D^{20}$ = −27.2 (*c* = 2.83, diethyl ether). − $C_{16}H_{23}O_5NS$ (341.4): calcd. C 56.29, H 6.79, N 4.10; found C 56.71, H 6.85, N 4.11} was obtained in low yield.

Scheme 4. Synthetic scheme for the phosphane synthesis; Ms = methylsulfonyl, Ts = *p*-tolylsulfonyl



(*R*)-**3a** (*R*)-**3c**: R = Ms (*R*)-**3d**: R = Ts (*S*)-**2**

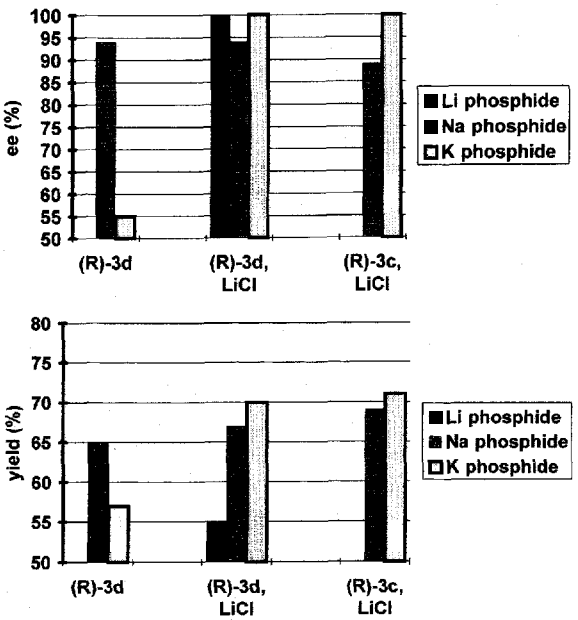
In a new approach we treated a solution of (*R*)-**3a** in THF with one equivalent *n*-butyllithium at −78 °C[16]. To the lithium alkoxide solution thus obtained, methanesulfonyl or *p*-toluenesulfonyl chloride was added slowly at −78 °C. This process was monitored by ^1H NMR, which indicated that a small excess of lithium alkoxide was required for quantitative consumption of the sulfonyl chloride. The solution obtained can be stored in a refrigerator without decomposition for several days.

The synthesis of *N,N*-dimethyl-2-(diphenylphosphanyl) ethylamine[17], published by Issleib and Rieschel in 1965, was the first investigation dealing with the synthesis of β-aminoalkylphosphanes by a substitution mechanism. They showed that the use of the potassium salt of diphenylphosphane gave good yields. Disappointing results were obtained with the lithium salt. Only the products of a redox reaction, tetraphenyldiphosphane and α,ω-bis(dimethylamino)butane, were isolated. The high-yielding synthesis of chiral phosphanes **1** and **BPPM** by an S_N2 mechanism, in order to prevent racemization of chiral centers, required the use of the sodium salt of diphenylphosphane in THF (DMF is a better solvent for **1**)[18,19]. To ensure complete diastereomeric and enantiomeric purity, **1** and **BPPM** were recrystallized.

(*S*)-**2** was obtained by the addition of (*R*)-**3c** or (*R*)-**3d** in THF to a solution of potassium diphenylphosphide in THF at −38 °C. The crude product was isolated and dissolved in TFA to cleave the *tert*-butoxycarbonyl group. Excess TFA

was evaporated and (*S*)-**2** was crystallized as its hydrochloride from diethyl ether. This work-up yielded a very pure product. The use of crystalline (*R*)-**3d** in this synthesis gave a 57% yield of (*S*)-**2**, compared to the 70% yield which was obtained with (*R*)-**3d** prepared by the *n*-butyllithium/*p*-toluenesulfonyl chloride method. The enantiomeric purity of both (*S*)-**2** samples was determined by polarimetry. The sample prepared in 57% yield had $[\alpha]_D^{20} = -8.94$ ($c = 0.585$, diethyl ether), indicating a reduced enantiomeric purity of this sample compared to the second sample prepared in 70% yield {$[\alpha]_D^{20} = -16.15$ ($c = 1.844$, diethyl ether)}. This surprising result prompted us to investigate the salt effects[20] in this reaction. We compared the specific rotations of the pure samples taking $[\alpha]_D^{20} = -16.15$ ($c \approx 1.8$, diethyl ether) as the value for an (*S*)-**2** sample with 100% *ee*. This assumption was subsequently proved to be correct by NMR investigations of diastereomeric derivatives formed by the reaction of (*S*)-**2** with enantiomerically pure carboxylic acids[21]. The results of this investigation together with the yields obtained are collected in Figure 1.

Figure 1. (top) Enantiomeric purity (ee in %) of the (*S*)-**2** samples obtained from *p*-toluenesulfonate ester (*R*)-**3d**; *p*-toluenesulfonate ester (*R*)-**3d**, **LiCl**; methanesulfonate ester (*R*)-**3c**, **LiCl**; (*R*)-**3d**, **LiCl** indicates that 1 mol of LiCl is present per mol (*R*)-**3d** (see text); (bottom) yields (in %) of the pure (*S*)-**2** samples obtained from *p*-toluenesulfonate ester (*R*)-**3d**; *p*-toluenesulfonate ester (*R*)-**3d**, **LiCl**; methanesulfonate ester (*R*)-**3c**, **LiCl**; (*R*)-**3d**, **LiCl** indicates that 1 mol of LiCl is present per mol (*R*)-**3d** (see text)



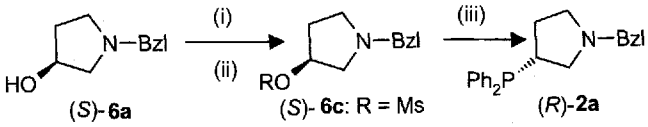
Several interesting conclusions can be drawn. First of all, it is apparent that only the presence of LiCl makes the reaction with clean inversion possible. The use of $KPPh_2$ together with (*R*)-**3c** or (*R*)-**3d** containing one mol of LiCl, formed during the synthesis of the sulfonate ester, yields optically pure (*S*)-**2**. Lower yields of optically pure (*S*)-**2** are obtained when $KPPh_2$ is replaced by $LiPPh_2$. Both chemical and optical yields are reduced when the reaction is carried out using $KPPh_2$ and (*R*)-**3d** containing no LiCl. A comparison of the $^{31}P\{^1H\}$-NMR spectra of the crude product mixture extracted with diethyl ether from the hydrolyzed reaction mixture revealed that the $KPPh_2$/LiCl reagent effectively suppressed the formation of tetraphenyldiphosphane. This by-product is extensively formed when only $KPPh_2$ is used.

With $NaPPh_2$ chemical yields are nearly as high (compared with the $KPPh_2$/LiCl result) or even higher (compared with the $LiPPh_2$ and $KPPh_2$ result). The optical purity of (*S*)-**2** obtained is rather high and is only slightly influenced by added LiCl or the sulfonyl ester derivative used. Both the high chemical and optical yields obtained are responsible for the fact that $NaPPh_2$ was found to be most effective in the synthesis of **1** and **BPPM**. The use of a $KPPh_2$ reagent with added LiCl instead of $LiPPh_2$ should be tested in the synthesis of several chiral phosphanes known in the literature[22].

To summarize our results, the synthesis of (*S*)-**2** is best performed with (*R*)-**3c**, **LiCl** and $KPPh_2$ [71% calculated from (*S*)-**3a**].

Following this new procedure we investigated the synthesis of (*R*)-**2a** from readily available (*S*)-**6a** (Scheme 5).

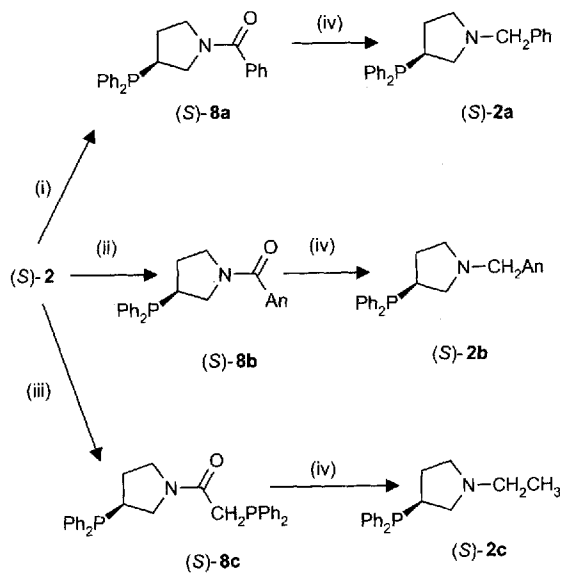
Scheme 5. Synthesis of (*R*)-**2a**, Ms = methylsulfonyl; reactions and conditions used: (i) *n*-butyllithium, −78 °C. − (ii) MsCl, −78 °C. − (iii) $KPPh_2$ in THF



To suppress any problems connected with anchimeric assistance of the nitrogen atom in the tertiary amine (*S*)-**6a** we made the modification of adding (*S*)-**6c** to $KPPh_2$ immediately after its synthesis from (*S*)-**6a** with *n*-butyllithium and methanesulfonyl chloride. The crude (*R*)-**2a** was again crystallized as its hydrochloride from diethyl ether. We obtained a 75% yield of a white solid. The specific optical rotation was compared with a sample prepared from (*R*)-**2** (vide infra), indicating an optical purity of 98 ± 2%.

(*S*)-**8a** and (*S*)-**8b** were obtained by acylation of (*S*)-**2** in diethyl ether with benzoyl chloride or 2-methoxybenzoyl chloride in the presence NEt_3, and could be crystallized as white solids from petroleum ether. 2-(Diphenylphosphanyl)-acetic acid[23] could be activated with 1,1′-carbonyldiimidazole (CDI) in THF at 0 °C. Coupling of the resulting acyl imidazolide with (*S*)-**2** afforded (*S*)-**8c** and imidazole. The advantage of this method is that the imidazole formed during the synthesis can be easily removed with dilute acid. The amide products were reduced with $LiAlH_4$. The green-blue suspension in THF thus obtained was hydrolyzed by adding it to a 30% aqueous KOH solution. The crude phosphanes were purified by making use of their solubility as hydrochlorides in dilute HCl. $LiAlH_4$-induced cleavage of the $P-C_{(alkyl)}$ bond occurred to a small extent in all reductions. The diphenylphosphanyl group bound to the primary carbon atom in (*S*)-**8c** was, however, completely cleaved. We obtained pure (*S*)-**2c** instead of the intended tridentate PNP ligand.

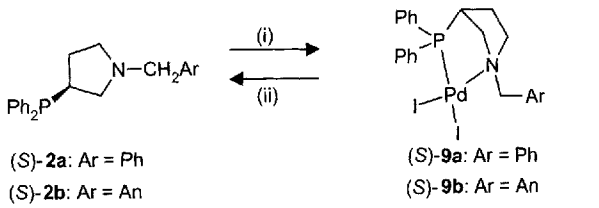
Scheme 6. Synthesis of *N*-alkylated derivatives (*S*)-**2a**, (*S*)-**2b** and (*S*)-**2c** from (*S*)-**2**; reactions and conditions used: (i) BzCl, NEt_3 in diethyl ether, 0°C. – (ii) 2-methoxybenzoyl chloride, NEt_3 in diethyl ether, 0°C (An = 2'-methoxyphenyl). – (iii) 1,1'-carbonyldiimidazole (= CDI), 2-(diphenylphosphanyl)acetic acid in THF. – (iv) $LiAlH_4$ in THF



The synthesis of (*S*)-**8b** and (*S*)-**8c** was carried out with (*S*)-**2** having 94% *ee* (established by a comparison of specific rotation data). Since none of the synthetic transformations involved reaction at the chiral center, one might assume that this degree of *ee* is retained and that all physical data for (*S*)-**8b**, (*S*)-**2b**, (*S*)-**9b** and (*S*)-**8c**, (*S*)-**2c** and (*S*)-**9c** given in the Experimental Section can be assigned to products having 94% *ee*. However, such assumptions are rarely valid. It has been found in recent years that when mixtures of enantiomers are subjected to crystallizations, distillations or chromatography on achiral phases, the enantiomeric composition of the product fraction can be changed[24]. This is possible if one fraction with an enantiomeric composition different from the starting material is withdrawn during the process. The second fraction (product) then has an enantiomeric composition different from that of the starting material. The physical reason for these effects are diastereomeric interactions between the enantiomers during the separation process. The enantiomeric composition of the product is dependent on both the physical data of the diastereomeric aggregates formed during the separation process and the amount of the first fraction that is withdrawn. Nothing is known about these two parameters for each of our new compounds. We would need either specific rotation data of enantiomerically pure compounds or another physical method that is able to show the enantiomeric composition in order to obtain a more reliable estimate of the enantiomeric purity of our products.

(*S*)-**2a** and (*S*)-**2b** were converted to the PdI_2 complexes (Scheme 7). This could be achieved using a stoichiometric amount of Na_2PdCl_4 and excess NaI in acetone. The crude complexes were purified by flash chromatography on silica

Scheme 7. Synthesis and cleavage of the PdI_2 complexes (*S*)-**9a** and (*S*)-**9b** (An = 2'-methoxyphenyl); reactions and conditions used: (i) Na_2PdCl_4, NaI in acetone. – (ii) KCN in dichloromethane, water



gel with dichloromethane/ethyl acetate and toluene/acetone. The pure complexes were crystallized by evaporation of dichloromethane solutions. Air-stable, dark-red crystals were obtained, which could be stored for two years without any chemical decomposition. The ligands could be recovered with KCN and used in catalysis.

Solid-State Structures of (*R*)-**9a**, (*S*)-**9a** *and* (*S*)-**9b**: Although there are two reports of X-ray structures of related $PdCl_2$ complexes of chiral ligands with (β-aminoalkyl)diphenylphosphane skeletons in the literature[25], our X-ray structure determinations show several new features. The crystals used were all obtained by evaporation of dichloromethane solutions. The structure of (*R*)-**9a** was determined twice. We obtained two polymorphs (*R*)-**9a-I** and (*R*)-**9a-II**. (*R*)-**9a-II** crystallizes with one molecule of CH_2Cl_2 in the asymmetric unit. The structure determination of the enantiomeric (*S*)-**9a** complex revealed that there is a third possible conformation of this complex, even in the solid state. The correct absolute structure could always be assigned by means of the Flack parameter[26]. The three related structures of the **9a** enantiomers and the structure of (*S*)-**9b** are shown in Figure 2; bond lengths and angles are collected in Table 1.

In all four structures the ligands are clearly coordinated via P and N, forming a hetero-norbornane skeleton. The atomic numbering scheme for PdI_2 complexes is selected to emphasize this close relation to a 1-azanorbornane structure. It is therefore different from the numbering scheme in the ligands. The pyrrolidine backbone has bond lengths and angles expected for a 1-azanorbornane structure, except that the N–C(7)–C(4) angle is increased from 93 to 101°. The main distortion from this 1-azanorbornane structure is due to the N,Pd,P part of the structure. We apply here the *exo*/*endo* nomenclature of norbornane stereochemistry in order to distinguish between the two phenyl groups of the PPh_2 subunit. For a comparison of the three related structures of the **9a** enantiomers, we define several angles (values are given in Table 1). α_1 is the dihedral angle between the N,Pd,P and the I(1),Pd,I(2) planes. α_{21} is the angle between the P–C(21) bond (*endo*-phenyl group) and the Pd,P,C(4) plane; α_{31} the analogous angle between the P–C(31) bond (*exo*-phenyl group) and again the Pd,P,C(4) plane. The α_{21} and α_{31} values for the (*R*)-**9a-II** polymorph are the same as the values obtained for the analogous angles of CH_2 groups in norbornane. This undistorted orientation of the phenyl groups, however, is combined with the largest α_1 value, indi-

Figure 2. Molecular structure drawings of (*R*)-**9a** polymorphs and (*S*)-**9a**, (*S*)-**9b**; the numbering scheme for the hetero-norbornane skeleton and *ipso*-carbon atoms of phenyl groups is consistent throughout

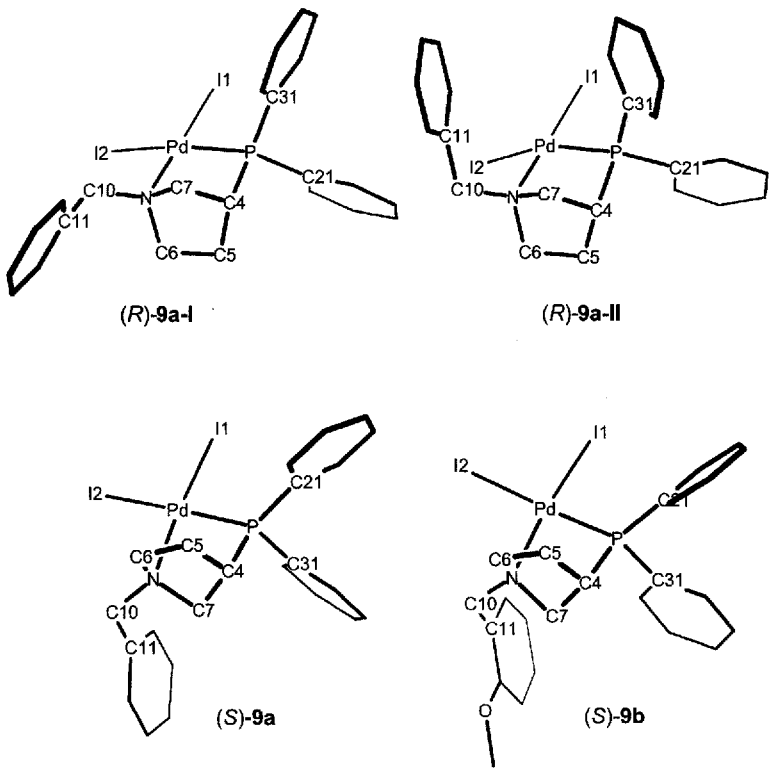


Table 1. Selected bond lengths [Å] and angles [°] of (*R*)-**9a** polymorphs and (*S*)-**9a**, (*S*)-**9b**; α_1, α_{21}, α_{31}, d_{PdC} and ω_1 given as absolute values are defined in the text

	(*R*)-**9a-I**	(*R*)-**9a-II**	(*S*)-**9a**	(*S*)-**9b**
Pd-I(1)	2.583(2)	2.5882(11)	2.542(2)	2.5649(4)
Pd-I(2)	2.649(2)	2.6896(12)	2.6395(13)	2.6997(4)
Pd-N	2.203(6)	2.159(9)	2.172(6)	2.168(3)
Pd-P	2.246(2)	2.230(3)	2.221(2)	2.2386(9)
N-C(6)	1.465(10)	1.505(14)	1.492(8)	1.501(4)
N-C(7)	1.473(9)	1.516(13)	1.462(10)	1.491(4)
N-C(10)	1.506(9)	1.498(14)	1.483(9)	1.492(4)
P-C(4)	1.830(7)	1.841(10)	1.820(8)	1.842(4)
C(4)-C(7)	1.508(10)	1.53(2)	1.498(10)	1.515(5)
C(4)-C(5)	1.553(11)	1.552(14)	1.524(11)	1.556(5)
C(5)-C(6)	1.562(11)	1.54(2)	1.536(10)	1.538(5)
I(1)-Pd-I(2)	90.75(6)	94.08(4)	91.87(5)	91.385(12)
N-Pd-P	84.4(2)	84.2(3)	83.8(2)	83.60(8)
C(4)-P-Pd	97.8(2)	97.2(3)	96.4(3)	96.61(11)
P-Pd-I(1)	91.06(8)	91.44(8)	89.02(6)	90.61(2)
N-Pd-I(2)	94.6(2)	92.5(3)	95.4(2)	94.72(7)
P-C(4)-C(5)	109.3(5)	111.0(7)	111.4(6)	110.9(2)
P-C(4)-C(7)	105.2(5)	102.7(7)	103.1(5)	102.8(2)
C(5)-C(4)-C(7)	102.0(6)	103.0(8)	103.1(6)	102.1(3)
Pd-N-C(6)	108.3(4)	106.3(6)	101.7(4)	103.3(2)
Pd-N-C(7)	105.6(4)	106.3(6)	108.5(4)	110.5(2)
C(7)-N-C(6)	101.9(6)	99.4(8)	103.3(5)	100.6(2)
N-C(7)-C(4)	102.7(6)	100.0(8)	101.4(6)	101.0(3)
N-C(6)-C(5)	105.2(6)	104.6(9)	103.2(6)	103.8(3)
C(6)-C(5)-C(4)	103.5(6)	103.8(9)	105.1(6)	104.5(3)
α_1	10.3	18.9	3.3	11.2
α_{21}	52.75	53.97	42.69	45.09
α_{31}	51.72	55.49	60.59	57.44
d_{PdC}	5.322	3.293	3.628	3.400
ω_1	92.7	92.9	90.7	92.1

cating the largest distortion from square-planar geometry at the palladium center. The (*S*)-**9a** structure, representing the other extreme, has an almost ideal square-planar geometry at the palladium center, combined with a distortion at the PPh_2 group. In this case, α_{21} and α_{31} are very different from the α_{21} and α_{31} set in norbornane and in (*R*)-**9a-II**.

Another interesting feature of these structures is the position of the benzyl groups. A short distance between an *ortho*-phenyl carbon atom and the palladium center might be taken as an indication of possible *ortho*-metalation, which is often found in palladium chemistry. However, this distance designated d_{PdC} in Table 1 clearly indicates a nonbonded situation. We did not find any evidence of *ortho*-metalation in our complexes. The final parameter given in Table 1 is the dihedral angle ω_1 of the [P−C(4)−C(5)−C(6)] bond invoked later in the NMR discussion.

A $^{31}P\{^1H\}$ solid-state CP-MAS NMR measurement with a 10-kHz rotation frequency of an (*S*)-**9a** sample gave a rather broad [half width (gauss fit) = 3 ppm] singlet resonance at δ = 48.4. The big shift difference Δ between the solution and solid-state resonance (Δ = 5.2 ppm) is remarkable, but not unprecedented in the literature[6]. Since polymorphs can have different chemical shifts[27], we hypothesized that the broad resonance contained several almost coincident resonances. We tried to prove this with an X-ray powder diffraction measurement. The powder pattern of this sample could be fitted very well with a powder pattern calculated with the crystal data of the (*S*)-**9a** structure. A small amount of crystals with (*R*)-**9a-II** crystal data, however, cannot be excluded, because the most intense peaks of

(*R*)-**9a-II** in the powder pattern coincide with those of (*S*)-**9a**. Therefore the X-ray powder diffraction measurement cannot prove or disprove the existence of several polymorphs in the (*S*)-**9a** sample.

Viewing all the X-ray results together, we can conclude that the investigated PdI_2 P,N complexes with a bicyclic hetero-norbornane structure are less flexible compared to known examples[25]. Nevertheless, we find that several stable conformations are adopted, even in the solid state. An investigation of the structure in solution is of great interest and will be presented now.

NMR Spectroscopy of the Phosphane Derivatives of **2** *and* **8** *and of the Complexes* **9**: The ^{1}H-NMR spectrum of **2** is very complex. We could, however, achieve a complete assignment of chemical shifts of protons bound to the pyrrolidine ring in **2** · **HCl** by ^{1}H^{1}H-COSY and ^{13}C^{1}H-COSY measurements[28]. From a 2D-*J*-resolved measurement performed with an (*R*)-**2a** sample, a ^{1}H-NMR spectrum showing heteronuclear ^{31}P^{1}H couplings, but not homonuclear ^{1}H^{1}H couplings could be obtained[29]. From this spectrum all chemical shifts for the protons of the pyrrolidine ring together with additional J_{PH} values (given in the Experimental Section) could be determined. The assignment of J_{HH} values was, however, impossible because of additional peaks due to strong ^{1}H^{1}H coupling[30]. The diastereotopic benzylic protons give an AB pattern with J_{AB} = 16 Hz. With this knowledge, an assignment of chemical shifts for the protons of the pyrrolidine ring in the ^{1}H-NMR spectra of other *N*-alkyl and *N*-acyl derivatives of **2** was possible. Upon coordination to form (*R*)-**9a**, the resonances of 3-H (4-H in the X-ray numbering scheme) and one of the benzylic protons are shifted more than 1 ppm downfield. The resonances of the aromatic *endo* protons of the PPh_2 group are shifted to a different extent compared to the protons of the *exo*-phenyl group. A pattern quite similar to that reported by Pregosin and co-workers is obtained[6]. Both the large difference in the chemical shifts of the diastereotopic benzylic protons and the pattern of the PPh_2 protons help to show that (*R*)-**2a** is *P,N*-coordinated to Pd, even in solution.

Further insight in the solution structure is gained from ^{13}C{^{1}H}-NMR studies. By the ^{13}C^{1}H-COSY measurements of **2** · **HCl** mentioned earlier and additional DEPT-135[28] spectra of e.g. **2a** samples, the ^{13}C resonances of the pyrrolidine skeleton can be unambiguously assigned (Table 2). The resonances are doublets due to J_{PC} couplings. Note the large $^2J_{PC}$ constants, which suggest small dihedral angles ω_2 [EP−P−C(3)−C(2)] and ω_3 [EP−P−C(3)−C(4)] (EP is an abbreviation for the free electron pair on the phosphorus atom)[31]. Several geometry optimizations of **2** derivatives with the Hyperchem™[32] program package invariably gave a lowest energy conformation quite similar to the published structure of **1** shown in Figure 3[18]. For comparison we analyzed a ^{13}C{^{1}H}-NMR spectrum of **1**. The CH_2 multiplet (X part of an AA'X pattern, $|^2J_{PC} + {}^3J_{P'C}|$ = 14.8 Hz[33]) can best fitted with $J_{PP'}$ = 10 Hz, $^2J_{PC}$ = 12.8 Hz and $^3J_{P'C}$ = 2 Hz. This $^3J_{P'C}$ value was estimated from the dihedral angle ω_4 [P'−C(4)−C(3)−C(2)] = 87°[34] obtained from an X-ray structure determination. The calculated lowest energy conformations of **2** do not show such a pronounced axial position of the PPh_2 group because the second group is missing. This is responsible for the difference

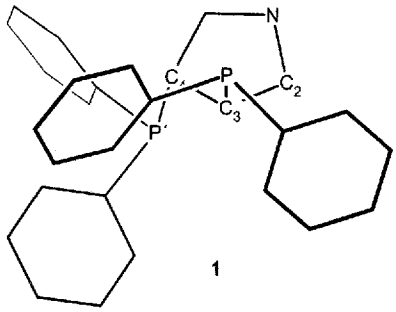
Table 2. Selected ^{13}C{^{1}H}-NMR results

	2	**2a**	**8a**	**8b**	**9a**	**9b**
C-4, (C-5 X-ray)	31.6 (d)	29.6 (d)	29.1 (d), 31.0 (d)	28.8 (d), 30.3 (d)	24.8 (d)	24.4 (d)
$^2J_{CP}$ =	19 Hz	18 Hz	16 Hz, 19 Hz	16 Hz, 18 Hz	4 Hz	2 Hz
C-3, (C-4 X-ray)	36.5 (d)	34.3 (d)	35.3 (d), 37.3 (d)	35.2 (d), 36.4 (d)	35.2 (d)	35.2 (d)
$^1J_{CP}$ =	9 Hz	7 Hz	10 Hz, 10 Hz	8 Hz, 11 Hz	27 Hz,	28 Hz
C-5, (C-6 X-ray)	48.1 (d)	54.6 (d)	46.5 (s), 49.7 (s)	45.7 (d), 47.7 (d)	56.9 (s)	55.5 (s)
$^3J_{CP}$ =	6 Hz	4 Hz		8 Hz, 8 Hz		
C-2, (C-7 X-ray)	52.1 (d)	59.0 (d)	50.2 (d), 53.4 (d)	49.4 (d), 51.1 (d)	60.5 (d)	59.9 (d)
$^2J_{CP}$ =	23 Hz	23 Hz	24 Hz, 27 Hz	26 Hz, 29 Hz	7 Hz	7 Hz
*C*H$_2$Ar		69.8 (s)			64.4 (s)	57.6 (s)
OCH$_3$				55.4 (s), 55.5 (s)		54.6 (s)
CH (*meta* Ph)	128.6 (d), 128.7(d)	128.8 (d), 128.9 (d)	128.8 (m), 128.9 (m)	128.8 (m),	127.6 (d), 128.2 (d)	127.6 (d), 128.2 (d)
$^3J_{CP}$ =	6 Hz	7 Hz			11 Hz	11 Hz
CH (*para* Ph)	128.9 (d)	129.1 (d)	129.3 (m), 129.4 (m)	129.4 (m)	131.3 (d), 131.5 (d)	131.3 (s), 131.5 (s)
$^4J_{CP}$ =	5 Hz	5 Hz			3 Hz	
CH (*ortho* Ph)	132.5 (d), 133.7 (d)	133.4 (d), 133.7 (d)	133.0 (d), 133.3 (d), 133.4 (d), 133.6 (d)	133.0 (d), 133.3(d), 133.4 (d), 133.6 (d)	134.1 (d), 134.2 (d)	134.1 (d), 134.2 (d)
$^2J_{CP}$ =	18 Hz	18 Hz, 19 Hz	20 Hz (all)	20 Hz (all)	9 Hz, 12 Hz	6 Hz, 7 Hz
C (*ipso* Ph)	138.6 (d), 138.7 (d)	138.7 (2 d),	137 (m)	137 (m)	[a]	[a]
$^1J_{CP}$ =	14 Hz, 13 Hz	14 Hz, 15 Hz				
CH$_2$*Ar* or CO*Ar*		126.5, 128.8, 137.5 (4 s)	127.3, 128.5, 130.1, 136.5 (4 s)	111.1, 120.8, 128.4, 130.7, 136.4, 155.2 (6 m)	127.9 (s), 129.9 (s)	110.1, 119.6 129.4, 131.9 (4 s)
*C*OAr			169.7 (s)	167.4 (s)		

[a] Not determined because a DEPT-135 measurement was made.

between the sets of $^3J_{PC}$ and $^2J_{PC}$ constants found for **2** and **1**.

Figure 3. Conformation of **1** in the X-ray structure



1

In **8a** and **8b** the NMR spectra are further complicated due to restricted rotation about the amide bond. A $^{31}P\{^1H\}$-dynamic-NMR (DNMR) study (32.4 MHz) of **8a** gave $\Delta G^{\neq} = 62$ kJ/mol ($T = 298$ K) as an estimate of the rotational barrier. This is clearly in the range expected from literature data[35]. A single restricted rotation about the amide bond in amides bearing two different alkyl substituents on the nitrogen atom yields a rotamer that differs in ground-state energy from the starting rotamer. This interconversion of rotamers with different ground-state energies is associated with two different barriers to rotation. In the DNMR spectra, equilibrium constants K = [major rotamer]/[minor rotamer] smaller than two are found. This gives a $\Delta\Delta G^{\neq}$ value smaller than 1.7 kJ/mol. This in turn is smaller than the absolute error in $\Delta G^{\neq}$. From the $^{13}C\{^1H\}$-NMR data (106 MHz, room temperature) in Table 2, the existence of two rotamers with different J_{PC} values can be proved. A $^{31}P\{^1H\}$-NMR spectrum of **8b** measured at 199 K shows four singlets. A subsequent $^{31}P\{^1H\}$-DNMR study (32.4 MHz) showed a pairwise coalescence of resonances at 233 K and 253 K. The resulting two resonances did not coalesce even at 323 K. In **8b** there is a second restricted rotation about the CO–(2'-methoxyphenyl) bond, discussed as atropisomerism in the literature[36]. The crude estimates of the rotational barriers associated with this atropisomerism are again in accord with published values. The $^{13}C\{^1H\}$-NMR data (106 MHz, room temperature) in Table 2 clearly indicate two rotamers with different chemical shifts and J_{PC} values. A second $^{13}C\{^1H\}$-NMR measurement of a sample of **8b**, with additional decoupling of ^{31}P resonances, further confirmed the assignment of the ^{13}C resonances. Resonances in the range of $\delta = 120-140$ (aromatic carbon atoms) were broader than other resonances. This indicates that coalescence phenomena are present.

The $^{13}C\{^1H\}$-NMR spectra of the palladium complexes **9a** and **9b** were measured with the DEPT-135 technique. Therefore, resonances due to quaternary carbon atoms are not seen[28]. Again (cf. ^1H-NMR discussion) the resonances of the aromatic *endo* carbon atoms of the PPh_2 group are shifted to a different extent compared to the carbon atoms of the *exo*-phenyl group. The small $^2J_{PC}$ values and the large $^1J_{PC}$ value clearly show that the PPh_2 group is coordinated. The very small $^3J_{PC}$ value is consistent with the dihedral angle ω_1 [P–C(4)–C(5)–C(6)] = 92° given in Table 1[31]. Considering all of our solution NMR results, only a small difference between the solution structure and the solid-state structure of our complexes is possible. A completely different solution structure obtained by Pregosin and co-workers for an analogous (β-aminoalkyl)diphenylphosphane complex[6] is prevented in this case by the hetero-norbornane skeleton. This reduced flexibility of a chiral complex is one of the most important requirements for an efficient use in enantioselective catalysis. We have used Ni complexes of our new phosphanes in the Grignard cross-coupling reaction yielding 3-phenyl-1-butene. A comparison of our catalytic results with the results obtained in nickel catalysis with the most effective "Hayashi-type", P,N ligands[5] shows that similar enantioselectivities are obtained[37].

We thank *G. Nicholson*, Tübingen (enantioselective GC separations) and Dr. *W. Weber* (powder diffraction) for measurements and helpful discussions. Na_2PdCl_4 was a generous gift from *Degussa AG*. We are grateful to the *Volkswagen Stiftung* and the *Deutsche Forschungsgemeinschaft* for financial support.

Experimental Section

Element analysis of C, H, N: Carlo Erba, Model 1106 with IBM-PC and Software Eager 1.1. – Polarimetry: Knauer Chiral Detector A 1000. – Mass spectra: Finnigan MAT TSQ 70 (nitrobenzyl alcohol, 70 eV, 50 °C, FAB), Finnigan MAT TSQ 70 (70 eV, 200 °C, EI). – IR: Bruker IFS 48 with Aspekt 1000 computer. – ^1H NMR spectra at 297 K: Bruker AC 250 and DRX 250 and Bruker WM 400 (250.13 and 400.13 MHz), chemical shifts are referenced to the residual ^1H resonances of solvents versus TMS[38]. – $^{13}C\{^1H\}$-NMR spectra at 297 K: Bruker AC 250 and DRX 250 and Bruker WM 400 (62.90 and 100.62 MHz), chemical shifts are referenced to ^{13}C resonances of deuterated solvents versus TMS[38]. – $^{31}P\{^1H\}$-NMR spectra at 297 K: Bruker DRX 250 (101.26 MHz), chemical shifts are referenced to external 85% H_3PO_4; the chemical shift of PPh_3 with $\delta = -5.6$ was taken as second standard for Bruker WP 80 and Bruker AC 80 (32.39 MHz, 32.44 MHz). – $^{31}P\{^1H\}$ solid-state NMR spectra: Bruker ASX 300, wide-bore magnet (7.05 T), magic-angle spinning (MAS) at a rotational frequency of 10 kHz at 297 K; frequencies and standards: 121.49 MHz (85% H_3PO_4, $NH_4H_2PO_4$ $\delta = 0.8$ as second standard). – X-ray powder diffraction: Siemens D 5000 (reflection, Cu-K_α) with Braun OED 50M detector, powder patterns were compared with Powder Cell 1.8 program[39]. – GC: Chrompack, model CP 9000, FID (250 °C), L-Chirasil Val® (25 m, 0.25 mm i.d., NOVA) 65 °C isotherm, 0.48 bar H_2 pressure, split injector 250 °C, integration software Chrompack Mosaic System (PC).

All solvents were dried by standard methods, purified by distillation and kept under argon. The petroleum ether used had a boiling range of 30–50 °C. All manipulations involving phosphanes (standard Schlenk technique) and moisture-sensitive compounds were conducted under dry argon. Hydrogenolysis was performed in a stainless steel reactor with ultra high purity grade hydrogen (Messer Griesheim), the reaction was monitored by the hard- and software used for enantioselective hydrogenations.

L-Malic acid (Fluka), L-hydroxyproline (Merck-Schuchardt) and all other commercial starting materials were purchased from Fluka, Merck-Schuchardt or Aldrich. Diphenylphosphane was prepared from PPh_3 and Li[40] with subsequent hydrolysis and distillation.

(3R)-1-(tert-Butoxycarbonyl)-3-hydroxypyrrolidine [(*R*)-**3a**]: L-Hydroxyproline (10 g, 0.076 mol), suspended in cyclohexanol (100 ml) and 2-cyclohexen-1-one (1 ml, 1 mmol), was heated under reflux at 155°C for 3 h until all the solid had dissolved. The clear, red solution was cooled to 25°C and aqueous acetic acid (100 ml, 20%) and toluene (50 ml) were added. The aqueous layer was separated and extracted twice with toluene (50 ml). The aqueous layer was neutralized with K_2CO_3 and a further 22.2 g (0.13 mol) K_2CO_3 and dioxane (100 ml) were added. At 0°C, di-*tert*-butyl dicarbonate (17.5 g, 0.08 mol) was slowly added and the mixture was stirred for 20 h at 20°C. The aqueous layer was separated and extracted twice with diethyl ether (70 ml). The combined dioxane and diethyl ether solutions were evaporated under reduced pressure and the crude product was redissolved in ethanol. The solution was heated under reflux for 20 h. A chromatographic column [prepared from a suspension of 150 ml dry silica gel (230–400 mesh) in ethyl acetate] was charged with the oily residue obtained by evaporation of the ethanol under reduced pressure. With ethyl acetate as eluent, 1 l of eluate was collected. Ethyl acetate was evaporated under reduced pressure to give pure (*R*)-**3a** as an oil which slowly crystallized; yield 10.8 g (90%); m.p., spectroscopic and optical rotation data matched those of the compound described in ref.[7] in all respects.

(3S,1'RS)-1-Benzyl-3-(1'-ethoxyethyloxy)pyrrolidine [(*S*)-**6b**]: A solution of *p*-toluenesulfonyl chloride (157 g, 0.83 mol) in 400 ml dichloromethane was slowly added at −20°C to a stirred solution of (2*S*,1'*RS*)-2-(1'-ethoxyethyloxy)-1,4-butanediol (**5b**) (55 g, 0.31 mol) in a mixture of dry pyridine (190 ml, 2.36 mol) and 400 ml of dichloromethane. The mixture was allowed to warm to room temperature and stirring was continued for 20 h. Then, a mixture of water (55 ml) and dichloromethane (830 ml) was added very slowly at 0°C. The resulting mixture was poured onto 280 g of crushed ice and HCl (102 ml, 1.2 mol). The aqueous layer was separated and extracted with 400 ml dichloromethane. The combined extracts were washed sequentially with saturated $NaHCO_3$ solution and water and dried (Na_2SO_4, with an added trace of Na_2CO_3). Evaporation of the solvent at room temperature gave (2*S*,1'*RS*)-2-(1'-ethoxyethyloxy)-1,4-butanediyl bis(*p*-toluenesulfonate) (135 g, 90% yield) as a viscous, yellow liquid which was immediately used without further purification.

To a hot solution of benzylamine (114 ml, 1.1 mol) in 300 ml of dioxane at 80°C was added 135 g of the crude bis(*p*-toluenesulfonate) in 200 ml of dioxane over a period of 3 h, raising the reaction temperature slowly to 95°C. The mixture was stirred at 95°C for 18 h, then cooled to room temperature. Stirring was continued for a further 2 d. The resulting mixture was cooled to 0°C and 30% KOH solution (280 ml) and diethyl ether (300 ml) were added. The aqueous layer was separated and extracted further with diethyl ether (3 × 300 ml). The combined extracts were concentrated and the residue was dried in vacuo. The residue was then extracted repeatedly with diethyl ether. The collected ethereal extracts (1 l) were saturated with carbon dioxide and the salt formed was filtered off by suction filtration and washed thoroughly with diethyl ether. This procedure was repeated until no more precipitate was formed. Then the solvent was evaporated and the residue was distilled; yield 64.0 g (84%); b.p. 103°C/0.2 mbar. – MS (70 eV); *m/z* (%): 245 (5) [M^+], 220 (5) [M^+ − Et], 204 (10) [M^+ − OEt], 176 (65) [M^+ − 1'-(ethoxyethyl)], 159 (95) [M^+ − Bzl]. – IR (film): $\tilde{\nu}$ = 3086, 3062, 3028, 2976, 2932, 2790 cm^{-1} (C−H), 1495 (C=C, C−N), 1454, 1378, 1338, 1131, 1099, 1081 (C−O, C−N, C−C), 743, 669 (Ar). – ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.09 (m, 3H, CH_2CH_3), 1.19, 1.21 (2 s, 3H, $CHCH_3$), 1.72, 2.07 (2 m, 2H, 4-H), 2.39, 2.75 (2 m, 2H, 2-H), 2.46, 2.57 (2 m, 2H, 5-H), 3.38, 3.52 (2 m, 2H, CH_2CH_3), 3.52 (m, 2H, CH_2Ph), 4.24 (m, 1H, 3-H), 4.60 (m, 1H, $CHCH_3$), 7.25 (m, 5H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 106.32 MHz): δ = 15.2, 20.43, 20.49 (3 s, CH_2CH_3, $CHCH_3$), 32.0, 32.7 (2 s, C-4), 52.5, 52.7 (2 s, C-5), 60.5 (s, CH_2Ph), 60.1, 60.3, 60.5, 60.9 (4 s, C-2, CH_2CH_3), 73.7, 74.1 (2 s, C-3), 98.8, 98.9 (2 s, $CHCH_3$), 126.9, 128.1, 128.8, 138.8 (4 s, Ar). – $[\alpha]_D^{20}$ = −7.8 (*c* = 5.175, ethanol). – $C_{15}H_{23}O_2N$ (249.4): calcd. C 72.25, H 9.30, N 5.62; found C 72.36, H 9.44, N 6.08.

(3S)-1-(tert-Butoxycarbonyl)-3-hydroxypyrrolidine [(*S*)-**3a**]: Freshly distilled (*S*)-**6b** (12.5 g, 0.05 mol) was dissolved in ethanol (50 ml) and the solution was transferred to a 75-ml stainless steel reactor. After addition of 10% Pd/C (535 mg, 0.5 mmol Pd), the autoclave was closed and evacuated. It was then placed in a water bath at 40°C and pressurized to 30 bar with hydrogen, while the mixture was stirred magnetically. Pressure and temperature data were continuously collected, indicating complete conversion in 15 h. The work-up consisted of filtration through Celite and evaporation of the solvent. The oily residue was dissolved in dioxane and a solution of 7.25 g (0.053 mol) K_2CO_3 in 100 ml water was added. At 0°C, di-*tert*-butyl dicarbonate (11.4 g, 0.052 mol) was slowly added and the mixture was stirred for 20 h at 20°C. The aqueous layer was separated and extracted twice with diethyl ether (70 ml). The combined dioxane and diethyl ether solutions were evaporated under reduced pressure and the residue was dissolved in methanol (200 ml). Acetic acid (4 ml, 0.07 mol) was added to the solution and the mixture was heated under reflux for 4 d. It was then concentrated in vacuo, the residue was redissolved in methanol/acetic acid, and the solution was heated under reflux for 4 d. The crude (*S*)-**3a** obtained by evaporation of the solvent was purified by the same chromatographic procedure as described for (*R*)-**3a**; yield 8.4 g (89%). M.p. and spectroscopic data corresponded in all respects with those of (*R*)-**3a**; as expected the specific optical rotation had opposite sign.

(3S)-1-Benzyl-3-hydroxypyrrolidine [(*S*)-**6a**]: A solution of (*S*)-**6b** (20.9 g, 0.08 mol) in 50 ml diethyl ether was stirred for 3 h with a solution of H_3PO_4 (27.4 ml of 85% acid) in 50 ml of water. The aqueous layer was separated and extracted further with diethyl ether (2 × 100 ml). The combined organic phases were evaporated and the residue dried in vacuo. The residue and the aqueous phase were combined and treated with excess 30% KOH solution (150 ml). The aqueous layer was extracted with diethyl ether (3 × 100 ml) and the combined extracts were evaporated. The residue was distilled twice; yield 12.7 g (90%); b.p. 85°C/0.2 mbar (ref.[41] 89°C/1.3 mbar). – $[\alpha]_D^{20}$ = −3.25 (*c* = 3.685, $CHCl_3$) {ref.[41] $[\alpha]_D^{20}$ = −3.145 (*c* = 1.2, $CHCl_3$)}. – The spectroscopic data are in accord with those reported in ref.[42].

(3S)-1-Ethyl-3-hydroxypyrrolidine [(*S*)-**7**]: A mixture of freshly distilled (*S*)-**6b** (2.75 g, 0.011 mol), dissolved in ethanol (50 ml) containing H_3PO_4 (5 ml of 85% acid) and 10% Pd/C (119 mg, 0.11 mmol Pd), was hydrogenated following the procedure described in the synthesis of (*S*)-**3**. Pd/C was filtered off, the ethanol was evaporated and the residue was treated with excess 30% KOH solution (30 ml). The aqueous layer was extracted with diethyl ether (3 × 30 ml) and the combined extracts were evaporated. The residue was distilled; yield 1.2 g (95%); b.p. 107°C/40 mbar (ref.[43] 109°C/35 Torr). – MS (70 eV); *m/z* (%): 115.1 (40) [M^+], 100.1 (100) [M^+ − CH_3], 86.0 (20) [M^+ − C_2H_5]. – IR (film): $\tilde{\nu}$ = 3382 cm^{-1} (O−H), 2976, 2943, 2787 (C−H), 1488 (C−N), 1433, 1386, 1347, 1183, 1158, 1104 (C−O, C−N, C−C). – ^1H NMR (CD_3OD, protic solvent, 250 MHz): δ = 1.09 (m, 3H, CH_2CH_3), 1.80, 2.11 (2 m, 2H, 4-H), 2.85, 3.27 (2 d, J_{HH} = 12 Hz, 2H, CH_2CH_3), 3.05, 3.48 (2 m, 4H, 2-H and 5-H), 4.31 (m, 1H, 3-H). – $^{13}C\{^1H\}$ NMR (CD_3OD, protic solvent, 62.90 MHz): δ = 11.9, 12.1 (2 s,

CH_2CH_3), 34.2, 35.3 (2 s, C-4), 52.3, 53.7, 53.8, 54.2 (4 s, C-5, CH_2CH_3), 62.4, 62.90 (2 s, C-2), 70.8, 70.9 (2 s, C-3). – $C_6H_{13}ON$ (115.3): calcd. C 62.57, H 11.38, N 6.38; found C 62.46, H 11.44, N 6.68.

Derivatization of **3a** *as N,O-Bis(trifluoroacetyl) Derivative:* **3a** (1.5 g, 8 mmol) was dissolved in 10 ml of trifluoroacetic acid (TFA) at 0°C. The TFA was evaporated and a solution of 15 ml of pyridine in 10 ml of dichloromethane was added to the residue. At 0°C, trifluoroacetic anhydride (2.4 ml, 17 mmol) was added and the solution was stirred for 20 h. The mixture was quenched with 60 ml 2 N HCl at 0°C and the *N,O*-bis(trifluoroacetyl) derivative was extracted with dichloromethane (3 × 10 ml). After evaporation of the solvent, the crude product was redissolved in diethyl ether (50 ml), the solution was filtered and an aliquot was removed for GC analysis. The solvent was evaporated from this aliquot and the residue was again trifluoroacetylated using a published method[9] immediately before the analysis was carried out.

(3R)-3-(Diphenylphosphanyl)pyrrolidine [(*R*)-**2**]: To a suspension of KH (4.1 g, 0.1 mol) in 150 ml of THF, diphenylphosphane (12 ml, 68.9 mmol) was added slowly via a syringe and the mixture was stirred at room temperature for 4 h. The red solution was then filtered through Celite and the filter cake was washed twice with additional 30-ml portions of THF. The potassium phosphide solution was concentrated to 150 ml. At −38°C, a solution of (*S*)-**3c** (cf. below) in 50 ml of THF was added and the mixture was stirred for 20 h at −20°C followed by 2 d at room temperature.

(*S*)-**3c** was prepared by adding *n*-butyllithium (31.25 ml, 50 mmol) via a syringe to a solution of (*S*)-**3a** (9.36 g, 50 mmol) in 75 ml of THF at −78°C. When the solution had reached room temperature it was stirred for a further 10 min and then cooled once more to −78°C, whereupon methanesulfonyl chloride (3.8 ml, 49.1 mmol) was added dropwise over a period of 20 min. The solution was allowed to stir for 20 h at room temperature and then concentrated to yield the 50 ml of THF solution used above. (This solution could be stored in a refrigerator for several days without decomposition.)

To continue with the synthesis of (*R*)-**2**, the THF was evaporated and the solid residue dried and dissolved in a mixture of 100 ml H_2O and 100 ml diethyl ether. The diethyl ether phase was separated and the aqueous layer was further extracted with two 100-ml portions of diethyl ether. The ethereal extracts were collected, filtered through Celite and the solvent was evaporated.

The crude product was dissolved in 70 ml of TFA at 0°C and stirred for 1 h. The TFA was evaporated and the remaining oil was dissolved in a mixture of aqueous KOH (100 ml, 30%) and 100 ml of diethyl ether. The aqueous phase was separated and extracted twice with 100 ml of diethyl ether. The combined ethereal extracts were stirred with excess 2 N HCl (200 ml, 0.4 mol) and the diethyl ether was separated. The aqueous phase was extracted with dichloromethane (three portions of 100 ml). The collected dichloromethane extracts were filtered through Celite and evaporated to yield 20 ml of a concentrated solution of (*R*)-**2** hydrochloride.

This solution was added to 300 ml of diethyl ether with vigorous stirring. The suspension was concentrated to 250 ml and stirred overnight. The white solid was collected by suction filtration, washed with three 50-ml portions of diethyl ether and dried in vacuo. It was then dissolved in a mixture of aqueous KOH (100 ml, 30%) and 100 ml of diethyl ether. The aqueous phase was separated and extracted twice with further diethyl ether (100 ml). The combined ethereal extracts were dried (solid KOH) and evaporated to yield a white solid; yield 9.1 g [71% based on (*S*)-**3a**]. – M.p. 74°C (diethyl ether). – MS (70 eV); *m/z* (%): 255.2 (5) [M^+], 186.8 (80) [Ph_2PH], 69.1 (100) [$M^+ - Ph_2PH$]. – IR (KBr): $\tilde{\nu}$ = 3234 cm^{-1} (N–H), 3067, 3049, 3027, 3000, 2948, 2922, 2863 (C–H), 1480 (C=C, C–N), 1436, 1305, 1089, 1067 (C–P, C–N, C–C), 739, 697 (Ph). – ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 1.59 (s, 1H, NH), 1.54, 1.85 (2 m, 2H, 4-H), 2.66, 2.96 (2 m, 2H, 2-H), 2.73, 2.88 (2 m, 2H, 5-H), 2.81 (m, 1H, 3-H), 7.19, 7.35 (2 m, 10H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.62 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 101.26 MHz): δ = −4.6. – $[\alpha]_D^{20}$ = +16.15 (*c* = 2.95, diethyl ether). – $C_{16}H_{18}NP$ (255.2): calcd. C 75.27, H 7.11, N 5.49; found C 74.78, H 7.00, N 5.47.

(3R)-1-Benzyl-3-(diphenylphosphanyl)pyrrolidine [(*R*)-**2a**]: To a solution of (*S*)-**6a** (12.7 g, 72 mmol) in 150 ml of THF at −78°C, was added *n*-butyllithium (45 ml, 72 mmol) via a syringe. When the slightly red solution had reached room temperature, it was stirred for an additional 10 min, and cooled once more to −78°C, whereupon methanesulfonyl chloride (5.47 ml, 70.7 mmol) was added dropwise over a period of 30 min. The solution was allowed to stir for 15 min at room temperature, then cooled again to −78°C. It was immediately added to a stirred solution of $KPPh_2$ in 250 ml THF at −40°C. This solution was prepared from KH (9.1 g, 0.222 mol) in 250 ml of THF and diphenylphosphane (26.6 ml, 152.9 mmol), as described in the synthesis of (*R*)-**2**. The solution was stirred for 2 h at −40°C, 20 h at −25°C and 2 d at room temperature. The solvent was then evaporated and the dried solid residue was dissolved in a mixture of aqueous KOH (120 ml, 10%) and 100 ml of diethyl ether. The diethyl ether was separated and filtered through Celite and the aqueous layer was extracted with two further 100-ml portions of diethyl ether. The combined ethereal extracts were filtered through Celite, stirred with excess 2 N HCl solution (200 ml, 0.4 mol) and the diethyl ether was separated. The aqueous phase was extracted with dichloromethane (three portions of 100 ml). The collected dichloromethane extracts were filtered through Celite and evaporated to yield 20 ml of a concentrated solution of (*R*)-**2a** hydrochloride. This could be crystallized and converted to (*R*)-**2a** using the same procedure as described in the synthesis of (*R*)-**2**; yield 19.2 g [75% based on (*S*)-**6a**]. – M.p. 59°C (diethyl ether). – MS (70 eV); *m/z* (%): 345.0 (5) [M^+], 254.1 (25) [M^+ – Bzl], 186.8 (30) [Ph_2PH], 159.0 (100) [$M^+ - Ph_2PH$], 91.1 (50) [Bzl]. – IR (KBr): $\tilde{\nu}$ = 3054, 3027, 3001, 2955, 2914, 2866, 2791, 2733 cm^{-1} (C–H), 1494, 1480 (C=C, C–N), 1444, 1274, 1250, 1148, 1030 (C–P, C–N, C–C), 750, 738, 700, 697 (Ph). – ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 1.76 (m, 1H, $^3J_{HP}$ = 17 Hz, 4-H^1), 2.04 (m, 1H, $^3J_{HP}$ = 11 Hz, 4-H^2), 2.40 (m, 1H, $^3J_{HP}$ = 15 Hz, 2-H^1), 2.95 (m, 1H, $^3J_{HP}$ = 8 Hz, 2-H^2), 2.42 (m, 1H, $^4J_{HP} \leq$ 1 Hz, 5-H^1), 2.75 (m, 1H, $^4J_{HP} \leq$ 1 Hz, 5-H^2), 2.86 (m, 1H, $^2J_{HP}$ = 9 Hz, 3-H^1), 3.54, 3.66 (2 d, 2H, $^2J_{HH}$ = 16 Hz, CH_2Ph), 7.25, 7.41 (2 m, 15H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.62 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 101.26 MHz): δ = −4.0. – $[\alpha]_D^{20}$ = +8.95 (*c* = 1.88, dichloromethane). – $C_{23}H_{24}NP$ (345.4): calcd. C 79.98, H 7.00, N 4.05; found C 79.93, H 7.36, N 4.37.

(3S)-1-Benzoyl-3-diphenylphosphanylpyrrolidine [(*S*)-**8a**]: To a stirred solution of (*S*)-**2** (3.83 g, 15 mmol) in 100 ml diethyl ether was added triethylamine (5.11 ml, 30 mmol). At 0°C, benzoyl chloride (1.7 ml, 14.8 mmol) was slowly added via a syringe. The mixture was stirred for an additional 4 h and then hydrolyzed by the addition of 20 ml of aqueous NaOH solution (1.2 g NaOH, 30 mmol). The diethyl ether phase was separated, washed with 70 ml of saturated aqueous citric acid solution and filtered through Celite covered with $MgSO_4$. The diethyl ether was evaporated and the crude product was dried in vacuo. A saturated diethyl ether solution of the product was then added to 50 ml of petroleum ether. The white precipitate formed was filtered, washed with petroleum ether and dried; yield 5.12 g of (*S*)-**8a** (95%). – M.p. 85°C (petroleum ether). – MS (70 eV); *m/z* (%): 360.2 (15) [M^+], 254.1 (30)

[M^+ – Bz], 183.0 (30) [Ph_2PH], 158.2 (80) [M^+ – Bz – Ph_2PH], 104.8 (100) [Bz]. – IR (KBr). $\tilde{\nu}$ = 3069, 2961, 2887 cm^{-1} (C–H), 1628 (CO), 1481 (C=C, C–N), 1444, 1433, 1415, 1349, 1268, 1251, 1216 (C–P, C–N, C–C), 759, 749, 742, 699 (Ph). – ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 1.80 (m, 1H, 4-H^1), 1.94 (m, 1H, 4-H^2), 2.88 (m, 1H, 3-H), 3.38, 3.49, 3.75, 3.84 (4 m, 4H, 2-H, 5-H), 7.20, 7.27, 7.40 (3 m, 15H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.62 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 263 K, 32.39 MHz): δ = –8.1, –9.0. – $[\alpha]_D^{20}$ = –116.2 (*c* = 1.19, diethyl ether). – $C_{23}H_{22}NOP$ (359.4): calcd. C 76.86, H 6.17, N 3.90; found C 77.63, H 6.31, N 3.69.

(3S)-3-(Diphenylphosphanyl)-1-(2'-methoxybenzoyl)pyrrolidine [(*S*)-**8b**]: Starting with a 94% *ee* (*S*)-**2** sample (3.83 g, 15 mmol) and 2-methoxybenzoyl chloride[44] (2.2 ml, 14.8 mmol), an (*S*)-**8b**/NEt_3 mixture was obtained as a diethyl ether solution and separated from aqueous NaOH as described for (*S*)-**8a**. The diethyl ether was evaporated and the residue was dissolved in 100 ml of ethanol containing KOH (20 g, 0.35 mol). The mixture was allowed to stir overnight before the solvent was evaporated and water (50 ml) was added. The product was extracted with three 50-ml portions of diethyl ether, the combined extracts were washed twice with saturated citric acid solution (70 ml), and then filtered through Celite covered with $MgSO_4$. The crude product obtained by evaporation of the diethyl ether was crystallized as described for (*S*)-**8a**; yield 5.37 g (*S*)-**8b** (92%). – M.p. 93°C (petroleum ether). – MS (70 eV); *m/z* (%): 389.4 (20) [M^+], 254.1 (70) [M^+ – COAn, An = 2-methoxyphenyl], 183.0 (90) [Ph_2PH], 135.0 (100) [COAn]. – IR (KBr): $\tilde{\nu}$ = 3066, 3052, 2971, 2934, 2872 cm^{-1} (C–H), 1627 (CO), 1491, 1477, 1463 (C=C, C–N), 1457, 1432, 1297, 1282, 1249, 1183 (C–P, C–N, C–C), 764, 753, 740, 700 (Ph). – ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 1.80 (m, 1H, 4-H^1), 1.92 (m, 1H, 4-H^2), 2.87 (m, 1H, 3-H), 3.20, 3.30, 3.51, 3.86 (4 m, 4H, 2-H, 5-H), 3.7, 3.75 (2 s, 3H, OCH_3), 6.82 (m, 2H, Ar), 7.20, 7.27, 7.40 (3 m, 11H, Ph, Ar), 7.35 (m, 1H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.62 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR (THF, 233 K, 32.39 MHz): δ = –8.2, –9.1, –9.9, –11.7. – $[\alpha]_D^{20}$ = –71.1 (*c* = 1.515, diethyl ether). – $C_{24}H_{24}NO_2P$ (389.4): calcd. C 74.02, H 6.21, N 3.60; found C 72.53, H 6.93, N 3.15.

(3S)-3-(Diphenylphosphanyl)-1-(2'-diphenylphosphanylacetyl)-pyrrolidine [(*S*)-**8c**]: To a solution of 2-(diphenylphosphanyl)acetic acid[23] (4.52 g, 18.5 mmol) in 50 ml of THF at 0°C, was added 1,1'-carbonyldiimidazole (3 g, 18.5 mmol) in small portions. The mixture was stirred for 1 h and then a solution of 94% *ee* (*S*)-**2** (4.1 g, 16 mmol) in 50 ml of THF was added and the mixture was stirred overnight. THF was evaporated and the oily residue was dissolved in ethanol (50 ml) containing 4 g (72 mmol) of KOH and stirred for 6 h. The solvent was evaporated, the residue was dried in vacuo, and then dissolved in 50 ml of water. The product was extracted with three 50-ml portions of diethyl ether, the combined extracts were washed sequentially with 2 N HCl (100 ml, stirring overnight) and twice with water (100 ml), and filtered through Celite covered with $MgSO_4$. The oily product obtained by evaporation of the solvent was dried in vacuo; yield 6.86 g (89%). – MS (70 eV); *m/z* (%): 481.5 (10) [M^+], 254.1 (70) [M^+ – $COCH_2PPh_2$], 227.4 (30) [$COCH_2PPh_2$], 183.0 (90) [Ph_2PH]. – IR (KBr): $\tilde{\nu}$ = 1694 cm^{-1} (CO). – ^1H NMR ($CDCl_3$, 250.13 MHz): δ = 1.70, 1.76 [2 s, (Ph_2PCH_2)], 1.90 (m, 2H, 4-H), 2.88 (m, 1H, 3-H), 3.11, 3.27, 3.51, 3.56 (4 m, 4H, 2-H, 5-H), 7.20, 7.40 (2 m, 20H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 62.89 MHz): δ = 29.3, 30.7 (2 d, $^2J_{CP}$ = 19 Hz, C-4), 36.2, 36.5 (2 s, CH_2PPh_2), 35.3, 36.9 (2 d, $^1J_{CP}$ = 9 Hz, C-3), 46.1, 47.7 (2 d, $^3J_{CP}$ = 9 Hz, C-5), 49.7, 51.4 (2 d, $^2J_{CP}$ = 25 Hz, C-2), 128.3 [m, CH (Ph)], 128.6 [m, CH (Ph)], 133.0 [m, CH (Ph)], 137 [m, C-*ipso* (Ph)], 168.5 (s, CO). – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 101.26 MHz): δ = –8.3, –8.6 ($Ph_2PC_4H_7N$), –16.8, –17.7 (Ph_2PCH_2). – No specific rotation measurement was made. – $C_{30}H_{29}NOP_2$ (481.5): calcd. C 74.85, H 6.07, N 2.91; found C 74.93, H 6.13, N 2.99.

(3S)-1-Benzyl-3-(diphenylphosphanyl)pyrrolidine [(*S*)-**2a**], *(3S)-3-(Diphenylphosphanyl)-1-(2'-methoxybenzyl)pyrrolidine* [(*S*)-**2b**], *(3S)-3-(Diphenylphosphanyl)-1-ethylpyrrolidine* [(*S*)-**2c**] *by $LiAlH_4$ Reduction:* To a solution of 0.77 g (20 mmol) $LiAlH_4$ in 50 ml of THF, a solution of (*S*)-**8a** (15 mmol, 5.4 g) or (*S*)-**8b** (15 mmol, 5.84 g) or (*S*)-**8c** (14.2 mmol, 6.86 g) in 50 ml of THF was slowly added at 0°C. After stirring overnight, the mixture was very cautiously added to a vigorously stirred solution of 30 g of KOH in 100 ml of water. The clear THF phase was separated and the aqueous phase was extracted twice with 50 ml of diethyl ether. The collected organic phases were concentrated in vacuo and the residue was stirred with a mixture of 100 ml of 2 N HCl and 20 ml of diethyl ether for 2 h. The organic phase was separated and the aqueous phase was further extracted with 50 ml of diethyl ether. Then, 50 ml of aqueous KOH (15 g of KOH) solution was slowly added and the resulting solution was extracted with three 50-ml portions of diethyl ether. The combined extracts were dried with solid KOH, filtered through Celite and concentrated. The product was dried in vacuo. The physical data given for (*S*)-**2a**, (*S*)-**2b** were obtained with samples that were cleaved from pure (*S*)-**9a**, (*S*)-**9b** with KCN.

(3S)-1-Benzyl-3-(diphenylphosphanyl)pyrrolidine [(*S*)-**2a**]: Yield 4.86 g (94%); on the basis of m.p., spectroscopic and optical rotation data (except sign) the substance corresponds in all respects with (*R*)-**2a**.

(3S)-3-(Diphenylphosphanyl)-1-(2'-methoxybenzyl)pyrrolidine [(*S*)-**2b**]: Yield 4.80 g (86%). – MS (70 eV); *m/z* (%): 375.1 (5) [M^+], 254.1 (5) [M^+ – CH_2An, An = 2-methoxyphenyl], 188.3 (50) [M^+ – Ph_2PH], 186.8 (50) [Ph_2PH], 121.0 (50) [CH_2An]. – IR (KBr): $\tilde{\nu}$ = 3062, 3052, 3001, 2954, 2922, 2863, 2834, 2790 cm^{-1} (C–H), 1601, 1585 (Ar), 1491, 1480 (C=C, C–N), 1463, 1434, 1283, 1242, 1156, 1100, 1049, 1028 (C–P, C–N, C–C), 750, 697 (Ph). – ^1H NMR ($CDCl_3$, 250.13 MHz): δ = 1.78 (m, 1H, 4-H^1), 2.05 (m, 1H, 4-H^2), 2.48 (m, 2H, 2-H^1, 5-H^1), 2.92 (m, 3H, 2-H^2, 5-H^2, 3-H), 3.74 (s, 3H, OCH_3), 3.61, 3.69 (2 d, 2H, $^2J_{HH}$ = 13 Hz, CH_2Ar), 6.85 (m, 2H, Ar), 7.16, 7.27, 7.44 (3 m, 12H, Ph, Ar). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 62.90 MHz): δ = 29.7 (d, $^2J_{CP}$ = 18 Hz, C-4), 34.3 (d, $^1J_{CP}$ = 6 Hz, C-3), 54.7 (d, $^3J_{CP}$ = 3 Hz, C-5), 59.0 (d, $^2J_{CP}$ = 23 Hz, C-2), 54.0 (s, CH_2An), 55.8 (s, OCH_3), 128.8 [d, $^3J_{CP}$ = 7 Hz, CH(Ph)], 129.1 [d, $^4J_{CP}$ = 6 Hz, CH(Ph)], 133.5 [d, $^2J_{CP}$ = 19 Hz, CH(Ph)], 138.7 [2 d, $^1J_{CP}$ = 14 Hz, $^1J_{CP}$ = 15 Hz, C-*ipso*(Ph)], 110.7, 120.7, 128.4, 130.7, 137.1, 155.2 (6 s, CH_2Ar). – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 101.26 MHz): δ = –4.4. – $[\alpha]_D^{20}$ = –8.7 [*c* = 0.49, dichloromethane, with (*S*)-**2** having 94% *ee*]. – $C_{24}H_{26}NOP \cdot 0.5\ CH_2Cl_2$ (375.5): calcd. C 70.41, H 6.51, N 3.35; found C 70.51, H 7.01, N 3.52.

(3S)-3-(Diphenylphosphanyl)-1-ethylpyrrolidine [(*S*)-**2c**]: Yield 3.8 g (90%). – MS (70 eV); *m/z* (%): 284.0 (100) [M^+], 182.9 (70) [Ph_2PH], 96.8 (100) [M^+ – Ph_2PH]. – IR (KBr): $\tilde{\nu}$ = 3070, 3052, 3029, 2966, 2933, 2873, 2787 cm^{-1} (C–H), 1480 (C=C, C–N), 1447, 1433, 1298, 1278, 1250, 1158, 1027 (C–P, C–N, C–C), 741, 696 (Ph). – ^1H NMR ($CDCl_3$, 250.13 MHz): δ = 0.96 (t, 3H, CH_2CH_3), 1.70 (m, 1H, 4-H^1), 1.93 (m, 1H, 4-H^2), 2.29 (m, 4H, 2-H^1, 5-H^1, CH_2CH_3), 2.83 (m, 3H, 2-H^2, 5-H^2, 3-H), 7.16, 7.35 (2 m, 10H, Ph). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 62.90 MHz): δ = 14.5 (s, CH_2CH_3), 29.6 (d, $^2J_{CP}$ = 18 Hz, C-4), 34.2 (d, $^1J_{CP}$ = 6 Hz, C-3), 54.4 (d, $^3J_{CP}$ = 4 Hz, C-5), 58.6 (d, $^2J_{CP}$ = 23 Hz, C-2), 50.4 (s, CH_2CH_3), 128.8 [d, $^3J_{CP}$ = 7 Hz, CH(Ph)], 129.1 [d, $^4J_{CP}$ = 5

Table 3. Crystal data, description of data collection, structural analysis and refinement and CSD numbers, file IDs and formulae

Compound	(*R*)-**9a-I**	(*R*)-**9a-II**	(*S*)-**9a**	(*S*)-**9b**
Empirical formula	$C_{23}H_{24}I_2NPPd$	$C_{23}H_{24}I_2NPPd{\cdot}CH_2Cl_2$	$C_{23}H_{24}I_2NPPd$	$C_{24}H_{26}I_2NOPPd$
Mol. mass [g mol^{-1}]	705.60	790.50	705.60	735.63
$d_{calcd.}$ [g cm^{-3}]	1.974	1.926	2.098	1.955
Crystal dimensions [mm]	0.35, 0.18, 0.05	0.50, 0.15, 0.10	0.40, 0.25, 0.15	0.30, 0.20, 0.10
Space group	$P2_1$ (No. 4)	$P2_12_12_1$ (No. 19)	$P2_1$ (No. 4)	$P2_12_12_1$ (No. 19)
a, *b*, *c* [Å]	8.501(5), 10.569(6), 13.29(1)	8.717(3), 15.145(5), 20.649(7)	8.953(5), 13.67(1), 9.906(6)	8.035(1), 15.124(2), 20.564(2)
α, β, γ [°]	90, 94.56(2), 90	90, 90, 90	90, 112.88(4), 90	90, 90, 90
V [nm^3], *Z*	1.190(2), 2	2.726(2), 4	1.117(1), 2	2.4990(5), 4
2Θ range [°]	4–50 (±*h*, ±*k*, ±*l*)	4–50 (+*h*, +*k*, ±*l*)	4–50 (±*h*, ±*k*, ±*l*)	4–50 (±*h*, ±*k*, ±*l*)
Scan method	Wyckoff	Wyckoff	ω	ω
Reflections (measured, unique, obs. [$I > 2\sigma(I)$])	8302, 4160, 3676	5325, 4804, 4072	7874, 3945, 3716	17429, 4410, 3929
μ [mm^{-1}]	3.46	3.21	3.68	3.29
Absorption correction: transmission min, max	0.139, 0.187	0.597, 0.743	0.144, 0.245	0.185, 0.212
Parameters	254	276	249	272
F_o/parameter[a]	14.5	14.75	14.92	14.44
R, *wR*2	0.0312, 0.0742	0.0415, 0.0938	0.0286, 0.0751	0.0159, 0.0317
GooF, absol. struct.[b]	1.521, –0.03(3)	2.006, 0.09(5)	1.931, –0.03(3)	1.415, –0.02(2)
CSD No., file ID	405893, R_9a_I	405894, R_9a_II	405895, S_9a	405896, S_9b
Formula	$C_{23}H_{24}I_2NPPd$	$C_{24}H_{26}Cl_2I_2NPPd$	$C_{23}H_{24}I_2NPPd$	$C_{24}H_{26}I_2NOPPd$

[a] All non-hydrogen atoms were refined with anisotropic thermal parameters; hydrogen atoms were included in calculated positions (riding model). – [b] The parameter according to Flack[26] is given.

Hz, CH(Ph)], 133.5, 133.6 [2 d, $^2J_{CP}$ = 19 Hz, CH(Ph)], 138.8 [2 d, $^1J_{CP}$ = 14 Hz, $^1J_{CP}$ = 15 Hz, C-*ipso*(Ph)]. – $^{31}P\{^1H\}$ NMR ($CDCl_3$, 101.26 MHz): δ = −4.6. – $[\alpha]_D^{20}$ = −24.2 [*c* = 0.16, dichloromethane, with (*S*)-**2** having 94% *ee*]. – $C_{18}H_{22}NP \cdot 0.25\ CH_2Cl_2$ (283.4): calcd. C 72.97, H 7.45, N 4.6; found C 72.3, H 7.61, N 4.03.

[(3S)-1-Benzyl-3-(diphenylphosphanyl)pyrrolidine-P,N]diiodopalladium [(*S*)-**9a**] *or [(3S)-3-(Diphenylphosphanyl)-1-(2'-methoxybenzyl)pyrrolidine-P,N]diiodopalladium* [(*S*)-**9b**]: To (*S*)-**2a** (3.45 g, 10 mmol) or (*S*)-**2b** (3.75 g, 10 mmol) was added NaI (15 g, 100 mmol) and the mixture was dissolved in 100 ml acetone. To this mixture was added 1 ml of water and Na_2PdCl_4 (3.11 g, 10.5 mmol) in a single portion. After 2 d, the acetone was evaporated and the dried residue was purified using flash chromatography with ethyl acetate (gradient raised to 50%)/dichloromethane on silica gel. The crude product obtained was purified using flash chromatography with acetone (7.5%)/toluene followed by crystallization from saturated dichloromethane solution.

[(3S)-1-Benzyl-3-(diphenylphosphanyl)pyrrolidine-P,N]diiodopalladium [(*S*)-**9a**]: MS (FAB); *m/z* (%): 705.6 (5) [M^+], 577.8 (25) [M^+ − I], 450.0 (5) [M^+ − 2 I], 255.2 [M^+ − PdI_2]. – IR (KBr): $\tilde{\nu}$ = 2962, 2926 cm^{-1} (C−H), 1456, 1448, 1261, 1024 (C−P, C−N, C−C), 755, 747, 699, 695 (Ph). – ^1H NMR (CD_2Cl_2, 250.13 MHz): δ = 1.97, 2.30, 2.65 (3 m, 6H, 2-H, 4-H, 5-H), 4.21 (m, 1H, 3-H), 3.87, 5.63 (2 d, 2H, $^2J_{HH}$ = 13 Hz, CH_2Ph), 7.27 (m, 8H, Ph), 7.39 (m, 4H, Ph), 7.83 (m, 3H, PPh). – $^{13}C\{^1H\}$ NMR (CD_2Cl_2, DEPT-135, 62.90 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 101.26 MHz): δ = 43.2. – $[\alpha]_D^{26}$ = +204.5 (*c* = 0.058, dichloromethane). – $C_{23}H_{24}I_2NPPd$ (705.6): calcd. C 39.15, H 3.43, N 1.98; found C 39.15, H 3.76, N 1.99.

[(3S)-3-(Diphenylphosphanyl)-1-(2'-methoxybenzyl)pyrrolidine-P,N]diiodopalladium [(*S*)-**9b**]: MS (FAB); *m/z* (%): 735.8 (5) [M^+], 607.9 (100) [M^+ − I], 480.0 (15) [M^+ − 2 I], 376.1 (30) [M^+ − PdI_2]. – IR (KBr): $\tilde{\nu}$ = 2946, 2918, 2883, 2824 cm^{-1} (C−H), 1597, 1490, 1481 (C=C, C−N), 1461, 1433, 1367, 1287, 1244, 1158, 1099, 1074, 1050, 1025 (C−P, C−N, C−C), 764, 754, 712 (Ph). – ^1H NMR (CD_2Cl_2, 250.13 MHz): δ = 2.17, 2.67 (2 m, 6H, 2-H, 4-H, 5-H), 3.64 (s, 3H, OCH_3), 4.0 (m, 1H, 3-H), 4.67, 5.02 (2 d, 2H, $^2J_{HH}$ = 13 Hz, CH_2Ar), 6.75 (m, 1H, Ar), 6.80 (m, 1H, Ar), 7.33 (m, 7H, Ph), 7.83 (m, 5H, PPh, PAr). – $^{13}C\{^1H\}$ NMR (CD_2Cl_2, DEPT-135, 62.90 MHz): See Table 2. – $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 101.26 MHz): δ = 42.4. – $[\alpha]_D^{26}$ = +189.0 [*c* = 0.09, dichloromethane, obtained from (*S*)-**2b**]. – $C_{24}H_{26}I_2NOPPd$ (735.7): calcd. 39.18, H 3.56, N 1.90; found C 39.32, H 3.68, N 1.91.

Cleavage of Ligands from PdI_2 Complexes: A mixture of 1 mmol of PdI_2 complex and 10 mmol of KCN was taken up in a mixture of 20 ml of dichloromethane and 20 ml of water. The red color faded immediately and stirring was continued overnight. The complete cleavage of the phosphane was verified by means of $^{31}P\{^1H\}$ NMR. The dichloromethane was separated and the aqueous layer was extracted twice with further dichloromethane (2 × 20 ml). The combined dichloromethane solutions were concentrated and the oily residue was redissolved in 20 ml of diethyl ether and 20 ml of saturated citric acid solution. The diethyl ether layer was separated and the aqueous phase treated with 30 ml of KOH solution (containing 9 g of KOH). The product was extracted with several portions of diethyl ether. The combined ethereal extracts were washed with saturated aqueous K_2CO_3 solution, filtered through Celite covered with $MgSO_4$ and concentrated. The products obtained were dried in vacuo.

X-ray Structure Determination: Data Collection: Siemens P4 diffractometer, Mo-K_α (λ = 71.073 pm), graphite monochromator, measuring temp. *T* = 173 K, absorption correction with ψ scan (ellipsoid model). – Structure Analysis and Refinement: Program

SHELXTL V5.03[45], solution with Patterson method, full-matrix least-squares refinement. Details including CSD numbers, file IDs and formulae are displayed in Table 3. Further details of the crystal-structure investigations are available on request from the Fachinformationszentrum Karlsruhe, D-76344 Leopoldshafen-Eggenstein, Germany, on quoting the depository numbers.

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