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Novel Chiral 1-(ferrocenylalkyl)-(*S*)-prolinols and their Application in Enantioselective Synthesis

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Abstract—Diastereomeric ferrocenylphosphine ligands, (−)-(*S*,*R*,*pS*)-BPPF-Pro (**3a**) and (+)-(*S*,*S*,*pR*)-BPPF-Pro (**3b**), containing the (*S*)-prolinol moiety were prepared. A detailed structural elucidation of these ligands was carried out using NMR. The Pd-complexes of these ligands were used for enantioselective catalysis of allylic substitution reactions of *rac*-(*E*)-1,3-diphenyl-3-acetoxyprop-1-ene with C-nucleophiles generated from pentan-2,4-dione and dimethyl malonate. A series of chiral ferrocene aminoalcohols with (*S*)-prolinol moiety (**4a**–**c**) were also prepared. The role of the configuration of stereogenic centers for stereoselectivity in diethylzinc addition to benzaldehyde was studied.

Introduction

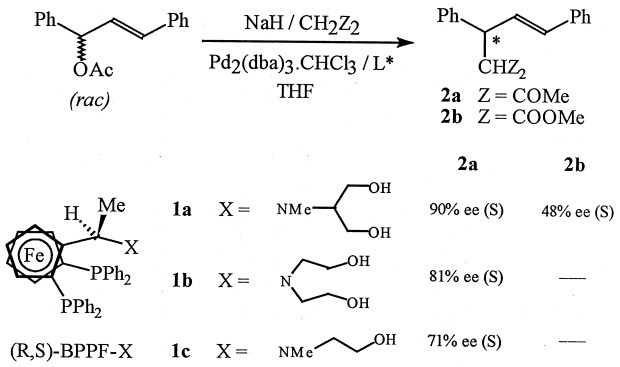
Transition-metal catalyzed reactions are the most effective route to prepare compounds in high enantiomerical purity. Chiral ferrocenyl ligands are very often used for enantioselective hydrogenation, hydrosilylation, palladium-catalyzed allylation of soft nucleophiles, dialkylzinc addition to aldehydes, etc.[1] Chiral ferrocenylphosphines containing the α-(2-hydroxyethylamino) side chain (**1a**–**c**) (Scheme 1) have been demonstrated to be superior to other chiral diphosphines (BPPFA, DIOP and BPPM) for allylic substitutions via π-allyl Pd-complexes.[2] The enantioselectivity increases as the number of hydroxyl groups on the side chain increases. High enantioselectivity was explained by hydrogen bonding interactions of hydroxyl groups with the C-nucleophile. It was found that the distance between the terminal hydroxyl group and the ferrocene moiety is also important, because the derivative with a 3-hydroxypropylamino side chain was found to be less enantioselective than the 2-hydroxyethylamino derivative.[3]

Patti et al.[4] recently described novel hydroxyaminoferrocene catalysts which have a single stereogenic center in the α-position to the ferrocene unit. It was found that these ferrocene aminoalcohols gave 1-phenyl-1-propanol in modest enantioselectivity (41% ee) and reasonable conversion (53–88%).

1-(Ferrocenylmethyl)-*O*-methyl-(*S*)-prolinols having a planar ferrocene stereogenic unit were described by Ganter and Wagner,[5] but their utilization in stereoselective synthesis has not been studied. Ferrocenyloxazoline ligands posessing planar chirality were studied by Bolm and co-workers[6] for enantioselective addition of diethylzinc to benzaldehyde and they found[7] that the stereochemical outcome of the reaction depended on the configuration of that enantiomeric ligand which forms the complex with the lower energy transition state, even in the case when the other enantiomeric ligand is in excess. You and co-workers[8] have used the ferrocenyloxazoline ligands for enantioselective Pd-catalyzed allylic substitution and found no effect of the configuration at the ferrocene planar stereogenic unit on the product configuration.

The main goals of this work were:

1. to prepare diastereomeric ferrocenylphosphine ligands containing a rigid (*S*)-prolinol unit and examine



Scheme 1.

Keywords: enantioselective synthesis; ferrocenylphosphine ligands; prolinol.

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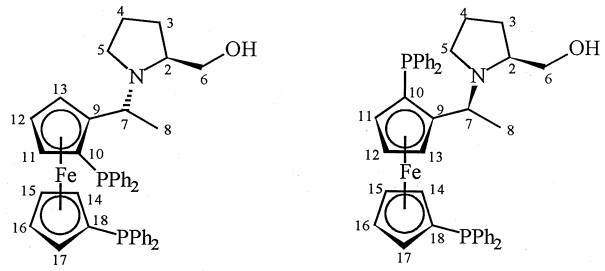


3a (S,R,pS)-BPPF-Pro **3b** (S,S,pR)-BPPF-Pro

Scheme 2.

them as ligands for Pd-catalyzed allylic substitution reactions;

2. to prepare a series of chiral ferrocene aminoalcohols with a (*S*)-prolinol rigid unit with one (central), two (central–central) and three (central–central–planar) stereogenic elements and examine their catalytic properties in the addition of diethylzinc to benzaldehyde.

Results and Discussion

Diastereomeric ferrocenylphosphine ligands **3a**,**b** (Scheme 2) were prepared from enantiopure (*R*,*pS*)-(−)-BPPFOAc and (*S*,*pR*)-(+)-BPPFOAc by replacement of the acetoxy group by (*S*)-(+)-prolinol with retention of configuration on the α-carbon atom analogously to the known procedure.[9] Products were fully characterized by spectroscopic methods: ^{1}H, ^{13}C NMR (see Tables 1 and 2), UV–Vis and IR spectra. The assignment of the ^{1}H chemical shifts was derived from 2D HH-COSY spectra and the appropriate assignment of the ^{13}C chemical shifts from APT and 2D HMQC spectra. The magnetic non-equivalence of protons as well as carbon atoms of the monosubstituted Cp ring was observed; this is caused by their diastereotopicity due to planar chirality.[10] The largest differences of chemical shifts for both diastereomers were observed for protons H-4,4′ and H-5,5′. The very low values of chemical shifts for diastereomer **3a**: 0.45 and 1.60 (H-4,4′) and 2.19 and 1.90 (H-5,5′) as compared with the values for diastereomer **3b**: 1.90 and 2.19 (H-4,4′) and 2.80 and 2.36 (H-5,5′) point to shielding of these protons by the ring current effect of one phenyl ring. This arrangement is possible only for isomer **3a** in which protons H-4,4′ and H-5,5′ are above the plane of the phenyl ring. The ^{13}C NMR spectra showed the doublet of doublet splitting for carbons C-15,16 and C-11 in both diastereomers **3a**,**b**. The additional splitting (1.7, 1.1 and 0.9 Hz) indicated a coupling between the mentioned carbons and the phosphorus on the other cyclopentadienyl ring. A similar coupling $J_{P'C}$=1.5 Hz was also observed for the ferrocene derivative 1′-diphenylphosphinoferrocene carboxylic acid between P and C-3,4 carbons of the other cyclopentadienyl ring.[11]

The evidence that this splitting was caused by P′–C coupling and not by different chemical shifts was obtained by measuring the spectra at a higher temperature (80°C, d_6-DMSO) and using a higher field spectrometer (125 MHz). The results of both measurements confirmed that this additional splitting was caused by the P′–C coupling via the iron atom of the ferrocene. The unambiguous proof of the P′–C coupling was shown by measuring the ^{13}C{^{1}H,^{31}P} decoupled spectrum (Bruker DRX 500) for a similar ferrocene derivative (*S*,*pR*)-(+)-BPPFA. All carbon signals collapsed to singlets. The distance of this coupling was

Table 1. ^{1}H NMR spectra of diastereomeric ferrocenylphosphine ligands **3a** and **3b**

Proton	δ(ppm), mult., (*J*, Hz) for **3a**	δ(ppm), mult., (*J*, Hz) for **3b**
H-2	2.79, m	2.69, m
H-3	1.48, m	1.22 m
H-3′	1.28, m	
H-4	1.60, m	
H-4′	0.45, m	
H-5	2.19, m	2.80, m
H-5′	1.89, m	2.36, m
H-6	3.69, m	3.19, dd, $^{2}J_{6,6'}$=10.6 Hz, $^{3}J_{2,6}$=3.7 Hz
H-6′	3.19, m	2.86, dd, $^{3}J_{2,6'}$=2.2 Hz
H-7	4.47, dq, $^{4}J_{HP}$=1.6 Hz, $^{3}J_{7,8}$=6.6 Hz	4.23, dq, $^{4}J_{HP}$=3.0 Hz, $^{3}J_{7,8}$=6.9 Hz
H-8	1.18, d	1.42, d
H-11	4.41, dd, $^{3}J_{11,12}$=2.2 Hz, $^{4}J_{11,13}$=1.1 Hz	4.36, m
H-12	4.09, pt, $^{3}J_{12,13}$=2.2 Hz	4.16, pt, $^{3}J_{11,12}$=2.5 Hz
H-13	3.73, dd	3.93, m
H-14	3.44, dd, $^{3}J_{14,15}$=2.4 Hz, $^{4}J_{14,16}$=1.1 Hz	3.46, m
H-15	3.90, dd, $^{3}J_{15,16}$=2.4 Hz, $^{4}J_{15,17}$=1.1 Hz	3.77, m
H-16	4.34, m	4.36, m
H-17	4.08, dd, $^{3}J_{16,17}$=2.2 Hz	4.08, m
Ph	7.26–7.47, m	7.25–7.58, m

Table 2. ^{13}C NMR spectra of diastereomeric ferrocenylphosphine ligands **3a** and **3b**

Carbon	δ(ppm), mult., (*J*, Hz) for **3a**	δ(ppm), mult., (*J*, Hz) for **3b**
C-2	59.73, s	57.84, d, $^{5}J_{PC}$=2.6 Hz
C-3	27.41, s	28.70, s
C-4	22.75, s	23.80, s
C-5	45.29, s	50.58, s
C-6	63.91, s	63.60, s
C-7	51.65, d, $^{3}J_{PC}$=5.2 Hz	51.12, d, $^{3}J_{PC}$=9.4 Hz
C-8	8.30, s	17.14, s
C-9	98.16, d, $^{2}J_{PC}$=23.5 Hz	98.16, d, $^{2}J_{PC}$=28.1 Hz
C-10	75.39, d, $^{1}J_{PC}$=4.6 Hz	75.57, d, $^{1}J_{PC}$=10.0 Hz
C-11	71.86, dd, $^{2}J_{PC}$=4.7 Hz, $J_{P'C}$=1.7 Hz	71.29, dd, $^{2}J_{PC}$=4.6 Hz, $J_{P'C}$=1.7 Hz
C-12	70.98, d, $^{3}J_{PC}$=2.0 Hz	71.47, d, $^{3}J_{PC}$=2.6
C-13	73.16, d, $^{3}J_{PC}$=5.0 Hz	72.56, d, $^{3}J_{PC}$=4.9 Hz
C-14	72.99, d, $^{2}J_{PC}$=8.3 Hz	73.19, d, $^{2}J_{PC}$=10.6 Hz
C-15	73.16, d, $^{3}J_{PC}$=2.0 Hz	73.01, dd, $^{3}J_{PC}$=2.8 Hz, $J_{P'C}$=1.1 Hz
C-16	74.42, dd, $^{3}J_{PC}$=5.1 Hz, $J_{P'C}$=1.2 Hz	74.25, dd, $^{3}J_{PC}$=4.6 Hz, $J_{P'C}$=0.9 Hz
C-17	75.95, d, $^{2}J_{PC}$=21.2 Hz	75.57, d, $^{2}J_{PC}$=18.3 Hz
C-18	76.69, d, $^{1}J_{PC}$=7.4 Hz	76.48, d, $^{1}J_{PC}$=7.5 Hz
Ph(*ipso*)	139.64, d, $^{1}J_{PC}$=6.3 Hz; 139.59, d, $^{1}J_{PC}$=7.2 Hz; 138.67, d, $^{1}J_{PC}$=9.5 Hz and 137.49, d, $^{1}J_{PC}$=5.4 Hz	139.95, d, $^{1}J_{PC}$=8.7 Hz; 139.70, d, $^{1}J_{PC}$=9.7 Hz; 139.67, d, $^{1}J_{PC}$=8.0 Hz and 139.34, d, $^{1}J_{PC}$=10.0 Hz
Ph(*o*)	135.31, d, $^{1}J_{PC}$=21.2 Hz; 133.98, d, $^{2}J_{PC}$=19.9 Hz; 133.31, d, $^{2}J_{PC}$=19.0 Hz and 132.31, d, $^{2}J_{PC}$=18.3 Hz	135.27, d, $^{2}J_{PC}$=22.3 Hz; 133.80, d, $^{2}J_{PC}$=20.0 Hz; 133.37, d, $^{2}J_{PC}$=20.5 Hz and 132.80, d, $^{2}J_{PC}$=19.5 Hz
Ph(*m*,*p*)	129.33, 128.87, 128.52, 128.41, 128.36, 128.33, 128.27, 128.17, 128.09 and 128.00	129.27, 128.77, 128.57, 128.35, 128.33, 128.31, 128.27, 128.24, 128.20 and 128.00

Table 3. Allylic substitution of (*rac*)-(*E*)-1,3-diphenyl-3-acetoxyprop-1-ene catalyzed by chiral ferrocenylphosphine ligand/Pd(0) complexes

Ligand (L[a])	Nucleophile	Yield (%)	ee (%) (conf.)[a]
(+)-BPPFA	$NaCH(COMe)_2$	53	62 (*R*)[b]
(−)-BPPF-Pro (**3a**)		20	80 (*S*)
(+)-BPPF-Pro (**3b**)		58	72 (*R*)
(−)-BPPF-Pro (**3a**)[c]		58	73 (*S*)
(+)-BPPFA	$NaCH(COOMe)_2$	62	40 (*R*)
(−)-BPPF-Pro (**3a**)		50	60 (*S*)
(+)-BPPF-Pro (**3b**)		24	34 (*R*)
(−)-BPPF-Pro (**3a**)[c]		66	53 (*S*)

[a] Determined by ^{1}H NMR with chiral shift reagents Eu(hfc)$_3$, the configuration of the major enantiomer was ascribed according to the sense of optical rotation.[2]
[b] Hayashi and co-workers described 62% ee (*S*) with 1 mol% Pd/(*R*,*pS*)-(−)-BPPFA complex.[2]
[c] 5% Pd/L were used.

only possible if the cyclopentadienyl rings have anti-conformation due to steric crowding of substituents on both cyclopentadienyl rings. The coupling was probably due to a through space mechanism rather than through Cp–Fe–Cp bonds.[12]

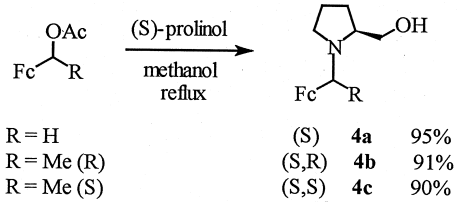
The R_f values of the prepared ferrocenylphosphines **3a**,**b** are different. This can be useful for their synthesis from *rac*-BPPFOAc (*R*,*S*+*S*,*R*) following chromatographic separation of the resulting diastereomers (**3a** *S*,*R*,*S* and **3b** *S*,*S*,*R*).

Enantioselective allylic substitution reactions were carried out according to Hayashi's procedure[2] with several different ferrocenylphosphine ligands, 1 mol% Pd and two compounds with an active methylene group (pentan-2,4-dione and dimethyl malonate). The enantiomeric purity of the products was determined by ^{1}H NMR using chiral shift reagent Eu(hfc)$_3$.

The achieved results (isolated yield of products and their enantiopurity) are given in Table 3. The diastereomer **3a** as ligand gave products in higher selectivity (for **2a**—80% ee and for **2b**—60% ee) than diastereomer **3b** (for **2a**—72% ee and for **2b**—34% ee). The results for **3a** are comparable to the ligands described by Hayashi **1a**–**c**, but the isolated yields of the products are lower.

To increase the yields, reactions with 5% Pd/**3a** were carried out. The products were isolated in higher yields, but decrease of enantioselectivity was observed (for **2a**—73% ee and for **2b**—53% ee).

In conclusion, we demonstrated that the diastereomeric ferrocenylphosphine derivatives **3a**,**b** with (*S*)-prolinol unit in the α-position to the ferrocene moiety can be used as ligands for Pd-catalyzed allylic substitution reactions. We also proved that the introduction of another stereogenic center to the ligand structure offers the possibility for increasing the enantioselectivity of the allylic substitution reaction.



Scheme 3.

New ferrocene aminoalcohols needed for enantioselective diethylzinc addition on benzaldehyde, i.e. (*S*)-(−)-1-(ferrocenylmethyl)prolinol (**4a**), (*S*,*R*)-(−)-1-(ferrocenylethyl)-prolinol (**4b**) and (*S*,*S*)-(+)-1-(ferrocenylethyl)prolinol (**4c**) containing a (*S*)-prolinol moiety were prepared from the appropriate acetoxyalkylferrocene derivatives by nucleophilic replacement of the acetoxy group with (*S*)-prolinol. **4a**–**c** were obtained in high yields (90–95%), as orange solids isolated after 1 h reflux in methanol (Scheme 3). Reactions proceeded with retention of configuration on the α-carbon and from optically pure (*R*)-(−)- or (*S*)-(+)-1-acetoxyethylferrocene were obtained pure diastereomeric aminoalcohols **4b** and **4c**, which was proved by ^{1}H NMR spectra. the isolated products were characterized by ^{1}H and ^{13}C NMR spectra, microanalysis and optical rotation measurements.

The enantioselective addition of diethylzinc to benzaldehyde catalyzed by aminoalcohols (**4a**–**c**), (*S*,*R*,*pS*)-(+)-1-[1-(2,1′-bis(diphenylphosphino)ferrocenylethyl]prolinol (**3a**) and (*S*,*S*,*pR*)-(+)-1-[1-(2,1′-bis(diphenylphosphino)-ferrocenylethyl]prolinol (**3b**) were performed at room temperature according to the procedure described by Patti et al.[4]

The progress of the reaction was monitored by GC-analysis of the reaction mixture and the enantiomeric excess was determined by GC on a chiral column (20% of permethylated β-CD on OV-1 phase). The obtained results (conversion and enantiomeric excess) are summarized in Table 4.

High conversion of benzaldehyde was observed after 1 h, but the reaction times were prolonged to 3 or 6 h to reach nearly complete conversion. Enantioselectivity of the reaction with the catalyst **4a** having just one stereogenic center on the C-2 position of the (*S*)-prolinol moiety was low (19.5% ee) and the major isomer of the product had (*S*) configuration. Using the aminoalcohol **4c** with both stereogenic centers in (*S*,*S*) configuration (C-2 and α-positions) afforded the product in 37% ee, the main isomer again having the (*S*) configuration. Diastereomeric aminoalcohol (*S*,*R*)-**4b** gave the product with 45% ee, and, surprisingly, with (*S*) configuration too. This fact shows that the configuration of the product is determined by the configuration on C-2 of the prolinol unit. Catalyst **3b** with a new element

Table 4. Catalytic properties of ferrocene aminoalcohols in addition of diethylzinc to benzaldehyde

Catalyst	Reaction time (h)	Conversion (%)	ee (%) (conf.)
2a	6	90	9.0 (*R*)
2b	6	95	26.0 (*S*)
4a	3	99	19.5 (*S*)
4b	3	98	45.0 (*S*)
4c	6	94	37.0 (*S*)

of chirality, a diphenylphosphine group in *R* position of the cyclopentadienyl ring, gave (*S*)-1-phenyl-1-propanol in 26% ee. If the configuration of the planar chirality was opposite (**3a**), the product was obtained only in 9% ee (S), but with the opposite configuration (*R*).

Two points may be noted from these observations:

1. Decrease of selectivity due to incorporation of diphenylphosphine group. This fact can be explained by the competition of the N and P ligand centers.
2. The configuration of planar chiral element can also determinate the configuration of the product. This is an interesting observation, in spite of the fact that very low asymmetric induction (9% ee) was observed. No such phenomenon was found in previous studies.[6,8]

In conclusion, we have demonstrated that new (*S*)-1-(1-ferrocenylalkyl)prolinols as catalysts for addition of diethylzinc to benzaldehyde gave products in modest enantioselectivity but higher conversion.

Experimental

^{1}H and ^{13}C NMR (δ, ppm) spectra of samples were obtained for $CDCl_3$ solutions on a Varian Gemini 2000 spectrometer operating at 300 MHz frequency for ^{1}H NMR spectra and at 75 MHz for ^{13}C NMR spectra with tetramethylsilane as internal standard. IR and UV–Vis spectra of soluble samples were determined as $CHCl_3$ (Merck, Uvasol) solutions on a Specord 75IR spectrometer and Perkin–Elmer Lambda 5 UV–Vis spectrophotometer, respectively. Optical rotations were measured on a Perkin–Elmer 241 polarimeter instrument. Melting points were measured on a Koffler hot plate apparatus and are uncorrected. Solvents were purified and dried according to the published methods.

(*R*,*pS*)-(−)-BPPFA and (*S*,*pR*)-(+)-BPPFA were prepared and transformed to their derivatives (*R*,*pS*)-(−)-BPPFOAc and (*S*,*pR*)-(+)-BPPFOAc according to described methods.[9] (*S*)-(+)-Prolinol was prepared by reduction of (*S*)-(+)-proline (Avocado).[13] Reduction of chalcone by $NaBH_4$ in the presence of $CeCl_3$ in methanol,[14] following acetylation by acetic anhydride catalyzed by 4-dimethylamino pyridine (DMAP) in diethyl ether gives (*rac*)-(*E*)-1,3-diphenyl-3-acetoxy-prop-1-ene as a colorless clear liquid (bp 180°C/1 mmHg). A complex $Pd_2(dba)_3{\cdot}CHCl_3$ was prepared according to published method.[15] Acetoxyalkylferrocene derivatives were prepared according to the procedure described by Schmalz and co-workers.[16]

(*S*,*R*,*pS*)-(−)-*N*-[1-(2,1′-Bis(diphenylphosphino)ferrocenyl)ethyl]-prolinol (3a). (*S*)-(+)-Prolinol (0.506 g, 5 mmol) and (*R*,*pS*)-(−)-BPPFOAc (0.320 g, 0.5 mmol) were dissolved in hot methanol (2 mL) and the reaction mixture was gently refluxed in an oil bath heated to 70–75°C under N_2-atmosphere for 5 h. The solvent was evaporated in vacuo and residue was purified by chromatography on Al_2O_3-column (20 g, 33% hexane/Et_2O). The *title compound* **3a** (0.270 g, 79%) was obtained as a yellow solid, mp 77–80°C; [Found: C, 72.34; H, 6.02; N, 1.92. $C_{41}H_{41}FeNOP_2$ (681.58) requires C, 72.25; H, 6.06; N, 2.06%]; R_f (33% hexane/Et_2O, Al_2O_3) 0.69; $[\alpha]_D^{25}$ −363 (c=0.525, $CHCl_3$); λ_{max} 284 nm (ϵ=1.25, c=1.00 mM, 1 cm); ν_{max} ($CHCl_3$) 1090, 1160, 1305, 1369, 1435, 1478, 1585, 1818, 1887, 1954, 2874, 2972, 3005, 3380 cm^{-1}.

(*S*,*S*,*pR*)-(+)-*N*-[1-(2,1′-Bis(diphenylphosphino)-ferrocenyl)ethyl]-prolinol (3b). (*S*)-(+)-Prolinol (0.506 g, 5 mmol) and (*S*,*pR*)-(+)-BPPFOAc (0.320 g, 0.5 mmol) were dissolved in hot methanol (2 mL) and the reaction mixture was gentle refluxed in an oil bath heated to 70–75°C under N_2-atmosphere for 4 h. The solvent was evaporated in vacuo and residue was purified by chromatography on Al_2O_3-column (20 g, 33% hexane/Et_2O). The *title compound* **3b** (0.232 g, 68%) as a yellow solid, mp 62–65°C; [Found: C, 72.13; H, 6.02; N, 1.91. $C_{41}H_{41}FeNOP_2$ (681.58) requires C, 72.25, H, 6.06, N, 2.06%]; R_f (33% hexane/Et_2O, Al_2O_3) 0.40; $[\alpha]_D^{25}$ +360 (c=0.53, $CHCl_3$); λ_{max} 282 nm (ϵ=1.04, c=0.94 mM, 1 cm); ν_{max} ($CHCl_3$) 1090, 1160, 1305, 1369, 1435, 1478, 1586, 1820, 1890, 1959, 2878, 2964, 3006, 3360 cm^{-1}.

General procedure for allylic substitution reaction of (*rac*)-*E*-1,3-diphenyl-3-acetoxyprop-1-ene

Sodium hydride (0.029 g, 1.2 mmol, 1.2 equiv.) was suspended in freshly dried THF (5 mL) under N_2-atmosphere. The compound with active methylene group (1.5 mmol, 1.5 equiv.) was added dropwise and the resulting salt suspension was vigorously stirred at room temperature. The ferrocenylphosphine ligand (**3a** or **3b**) (7.5 mg, 1.1×10^{-2} mmol, 1.1 equiv.), $Pd_2(dba)_3{\cdot}CHCl_3$ (5.2 mg, 0.5×10^{-2} mmol, 1 mol% Pd) and substrate (0.252 g, 1 mmol) were mixed in THF (5 mL), and the resulting red-purple solution was added to the suspension. The reaction mixture was placed in an oil bath heated to 40°C (the color of the reaction mixture was changed to lemon-yellow) and was stirred under N_2-atmosphere for 24 h. Water (100 mL) was added, extracted with diethyl ether (100 mL), the organic layer was washed with water (100 mL), dried, and the solvent was evaporated under reduced pressure. The residue was purified by chromatography on a SiO_2-column (30 g, 12.5% EtOAc/hexane). Product (**2a** or **2b**) was obtained after evaporation of solvent as a white solid. Enantiomeric purity was determined according to the ^{1}H NMR spectra of the product with chiral shift reagent $Eu(hfc)_3$.

^{1}H NMR spectrum of substrate: 2.12 (s, 3H, CH_3); 6.34 (dd, $^3J_{12}$=15.7 Hz, $^3J_{23}$=6.9 Hz, 1H, H_2); 6.45 (d, $^3J_{23}$=6.9 Hz, 1H, H_3); 6.63 (d, $^3J_{12}$=15.7 Hz, 1H, H_1); 7.25–7.40 (m, 10H, Ph, Ph′).

^{1}H NMR spectrum of product **2a**: 1.93 (s, 3H, $COCH_3$); 2.25 (s, 3H, $COCH_3$); 4.35 (m, 2H, H_3, H_4); 6.19 (ddd, $^3J_{12}$=15.7 Hz, $^3J_{23}$=8.0 Hz, $^4J_{24}$=2.7 Hz, 1H, H_2); 6.42 (d, $^3J_{12}$=15.7 Hz, 1H, H_1); 7.20–7.40 (m, 10H, Ph, Ph′).

^{1}H NMR spectrum of product **2b**: 3.52 (s, 3H, $COOCH_3$); 3.71 (s, 3H, $COOCH_3$); 3.96 (d, 1H, $^3J_{34}$=11.0 Hz, H_4); 4.26 (dd, $^3J_{23}$=8.5 Hz, $^3J_{34}$=11.0 Hz, 1H, H_3); 6.33 (dd, $^3J_{12}$=15.7 Hz, $^3J_{23}$=8.5 Hz, 1H, H_2); 6.49 (d, 1H, $^3J_{12}$=15.7 Hz, H_1); 7.20–7.40 (m, 10H, Ph, Ph′).

General procedure for preparation of aminoalcohols (4a–c)

(*S*)-(+)-Prolinol (0.506 g, 5 mmol) and the appropriate acetoxyalkylferrocene derivative (0.5 mmol) were dissolved in hot methanol (2 mL) and the reaction mixture was gentle refluxed in an oil bath heated to 70–75°C under N_2-atmosphere for 1 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on an Al_2O_3-column (20 g, 33% hexane/Et_2O).

From ferrocenylmethyl acetate (0.129 g, 0.5 mmol) product **4a** (0.142 g, 95%) was obtained as a orange solid, mp 92–94°C; [Found: C, 64.14; H, 7.02; N, 4.42. $C_{16}H_{21}FeNO$ (299.20) requires C, 64.23; H, 7.07; N, 4.68%]; $[\alpha]_D^{25}$ −41.9; $[\alpha]_{578}^{25}$ −43.9; $[\alpha]_{546}^{25}$ −49.6 (c=1.035, $CHCl_3$); δ_H 1.61–1.88 (m, 4H, $-CH_2-CH_2-$); 2.63 (m, 1H, H-5); 2.73 (m, 1H, H-5′); 2.98 (m, 1H, H-2); 3.30 (d, $^2J_{77'}$=12.9 Hz, 1H, H-7); 3.36 (bd, $^2J_{66'}$=10.8 Hz, 1H, H-6); 3.61 (dd, $^3J_{26'}$=3.9 Hz, $^2J_{66'}$=10.8 Hz, 1H, H-6′); 3.68 (d, $^2J_{77'}$=12.9 Hz, 1H, H-7′); 4.11–4.16 (m, 9H, Fc); δ_C 23.46 (C-4); 28.08 (C-3); 53.22 (C-5); 54.25 (C-7); 62.09 (C-6); 63.29 (C-2); 68.10; 68.30 (C-α; C-α′); 68.68 (Cp); 69.87; 69.99 (C-β; C-β′); 84.27 (C_i); ν_{max} ($CHCl_3$) 925, 1095, 1315, 1410, 1508, 1610, 3300 cm^{-1}.

From (*R*)-1-ferrocenylethyl acetate (0.136 g, 0.5 mmol) product **4b** (0.143 g, 91%) was obtained as a orange solid, mp 114–116°C; [Found: C, 65.08; H, 7.31; N, 4.31. $C_{17}H_{23}FeNO$ (313.22) requires C, 65.19; H, 7.40; N, 4.47%]; $[\alpha]_D^{25}$ −23.5; $[\alpha]_{578}^{25}$ −26.0; $[\alpha]_{546}^{25}$ −38.8 (c=0.51, $CHCl_3$); δ_H 1.40 (d, $^3J_{78}$=6.6 Hz, 3H, CH_3); 1.57–1.85 (m, 4H, $-CH_2-CH_2-$); 2.58 (m, 1H, H-5); 2.17 (m, 1H, H-5′); 2.96 (m, 1H, H-2); 3.25 (dd, $^2J_{66'}$=10.5 Hz, $^3J_{26}$=2.4 Hz, 1H, H-6); 3.46 (dd, $^3J_{26'}$=4.2 Hz, $^2J_{66'}$=10.5 Hz, 1H, H-6′); 3.82 (q, $^3J_{78}$=6.6 Hz, 1H, H-7); 4.11–4.20 (m, 9H, Fc); δ_C 14.30 (C-8); 24.34 (C-4); 29.29 (C-3); 48.37 (C-5); 53.49 (C-7); 59.66 (C-2); 62.78 (C-6); 66.55; 67.39 (C-α; C-α′); 68.82 (Cp); 67.78; 68.86 (C-β; C-β′); 91.49 (C_i); ν_{max} ($CHCl_3$) 910, 1118, 1328, 1420, 1625, 3400 cm^{-1}.

From (*S*)-1-ferrocenylethyl acetate (0.136 g, 0.5 mmol) product **4c** (0.141 g, 90%) was obtained as an orange solid, mp 93–95°C; [Found: C, 65.04; H, 7.32; N, 4.33. $C_{17}H_{23}FeNO$ (313.22) requires C, 65.19; H, 7.40; N, 4.47%]; $[\alpha]_D^{25}$ +0.8; $[\alpha]_{578}^{25}$ +4.9; $[\alpha]_{546}^{25}$ +26.7 (c=0.51, $CHCl_3$); δ_H 1.45–1.64 (m, 4H, $-CH_2-CH_2-$); 1.54 (d, $^3J_{78}$=7.2 Hz, 3H, CH_3); 2.30 (m, 1H, H-5); 2.81–2.88 (m, 2H, H-5′; H-2); 3.30 (dd, $^2J_{66'}$=10.2 Hz, $^3J_{26}$=2.1 Hz, 1H, H-6); 3.58 (dd, $^3J_{26'}$=3.6 Hz, $^2J_{66'}$=10.2 Hz,1H, H-6′); 3.84 (q, $^3J_{78}$=7.2 Hz, 1H, H-7); 4.08–4.13 (m, 9H, Fc); δ_C 19.81 (C-8); 23.53 (C-4); 28.39 (C-3); 46.82 (C-5); 52.78 (C-7); 59.72 (C-2); 62.09 (C-6); 67.24; 67.56 (C-α; C-α′); 68.83 (Cp); 67.69; 69.15 (C-β; C-β′); 86.97 (C_i); ν_{max} ($CHCl_3$) 905, 1108, 1315, 1410, 1620, 3400 cm^{-1}.

General procedure for enantioselective addition of diethylzinc to benzaldehyde

Freshly destilled benzaldehyde (54 mg, 0.5 mmol) and appropriate catalyst (**3a**,**b**, **4a**–**c**) (0.025 mmol, 5 mol%) were dissolved in dry toluene (1.3 mL) under N_2-atmosphere at room temperature. The 1 M solution of diethylzinc in hexane (1 mL, 1 mmol, 2 equiv.) was added and the reaction mixture was stirred under N_2-atmosphere at room temperature. The progress of reaction was monitored by GC-analysis of the reaction mixture. After completion of the reaction the reaction mixture was diluted by addition of a saturated solution of NH_4Cl (2 mL) and extracted by diethyl ether (10 mL). The organic layer was dried (Na_2SO_4) and the solvent was evaporated. The enantiopurity of 1-phenyl-1-propanol was determined by GC-analysis of the crude product on a chiral column (20% permethylated β-CD dissolved in the OV-1 phase).

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