Synthesis of silica-supported chiral ferrocenylphosphine ligands and their application in some stereoselective reactions

Battsengel Gotov,[a] Štefan Toma*[a] and Duncan J. Macquarrie[b]

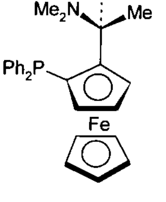
[a] *Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University, 84215 Bratislava, Slovakia*
[b] *Centre for Clean Technology, Department of Chemistry, University of York, Heslington, York, UK YO1 5DD. djm13@york.ac.uk; Fax: +441904 432516*

Received (in Montpellier, France) 5th April 2000, Accepted 30th May 2000
Published on the Web 17th July 2000

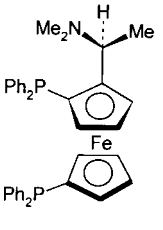
Synthesis of new BPPFA analogues, having exchanged one of the *N*-methyl groups for a long (–$C_{10}H_{20}$–) or short (–C_4H_8–) alkyl chain with a terminal methoxycarbonyl group, and their immobilization on silica are described. Immobilization resulted in considerable lowering of the reaction rates as well as stereoselectivity in hydrogenation reactions. On the other hand, both homogeneous **3a** as well as immobilized ligand **6a** with a longer spacer (–$C_{10}H_{20}$–) have activities and enantioselectivities in allylic nucleophilic substitution comparable to the known BPPFA ligand. This is true also for homogeneous ligand **3b** with a shorter chain (–C_4H_8–), but its immobilization resulted in a big drop of activity as well as selectivity.

Transition-metal catalysed reactions are the most effective route for the preparation of compounds in high enantiopurity. In many cases, homogeneous catalysts have activity and selectivity patterns that cannot be obtained with classical heterogeneous catalysts. On the other hand, the technical use of heterogeneous catalysts is well established. The heterogenisation of effective homogeneous catalysts has been an important aspect of research in enantioselective synthesis during recent years.[1] Transition-metal complexes containing chiral ferrocenylphosphine ligands are amongst the most useful classes of catalysts for asymmetric synthesis, for example in Rh(I) catalysed hydrogenation of α-acetamidocinnamic acid derivatives[2] and allylic substitutions *via* π-allyl Pd complexes.[3] Pugin described the successful anchoring of ferrocenylphosphine ligand Xyliphos on silica and organic polymers and its iridium and rhodium complexes were used as catalysts for the hydrogenation of alkenes and ketimines in quantitative yields and high optical purity (78% ee).[4–6] Cullen and Han used a polymer-supported analogue of the ferrocenylphosphine PPFA ligand **1** for the hydrosilylation of styrene (15% ee).[7] Recently, Thomas and coworkers described the chiral BPPFA (**2**) ligand analogue anchored to the surface of the mesoporous support MCM-41, whose complex with Pd exhibits high regio- and stereoselectivity in the allylic amination of cinnamyl acetate with benzylamine.[8]

The main goal of the work described in this paper was the immobilization of an enantiopure ferrocenylphosphine ligand (*S*,*R*)-(+)-BPPFA *via* a long (–$C_{10}H_{20}$–) or short (–C_4H_8–) flexible spacer onto the surface of silica and to compare the catalytic activity and selectivity of these ligands with the corresponding homogeneous ligands.



1



2

Results and discussion

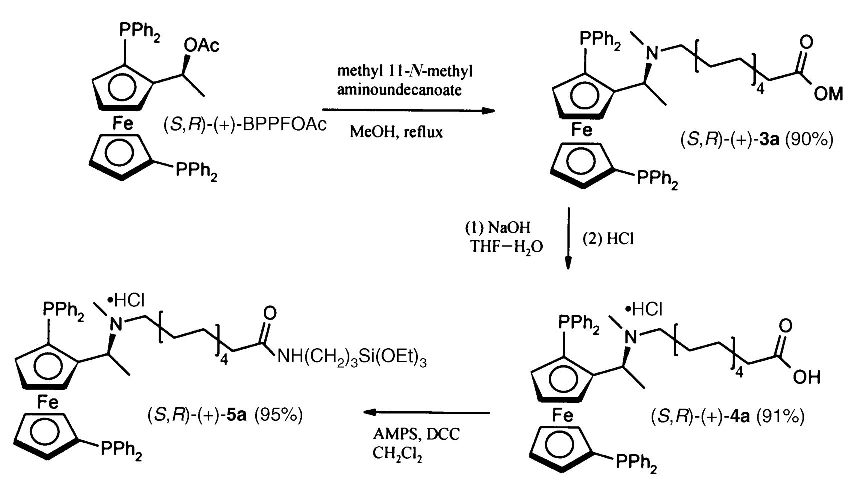
The synthesis of homogeneous homochiral ligands is presented in Schemes 1 and 2.

Ferrocenylphosphine derivative (+)-BPPFOAc was treated with methyl 11-*N*-methylaminoundecanoate to give **3a**, a ferrocenylphosphine derivative with a long (–$C_{10}H_{20}$–) spacer chain and a terminal carboxymethyl group. This compound was obtained in 90% yield. Hydrolysis of **3a** (91%) and condensation of the resulting acid **4a** with 3-triethoxysilylpropylamine (AMPS) in the presence of dicyclohexylcarbodiimide (DCC) afforded 95% of the amide **5a** (Scheme 1). When (+)-BPPFOAc was treated with aqueous methylamine solution the compound (+)-(*S*,*R*)-*N*-methyl-1-(2,1′-bis(diphenylphosphino))ferrocenylethylamine (BPPFNMe) was obtained in 85% yield (Scheme 2). Reaction of this compound with methyl 5-bromovalerate gave the ferrocenylphosphine derivative **3b** with a terminal carboxymethyl group on the shorter (–C_4H_8–) spacer chain. This compound was further treated, as shown in Scheme 2, to give the acid **4b** and finally the amide **5b** in excellent yields.

The anchoring of the ligand unit on the solid was carried out by reaction of the functional silanes with silica in toluene. After anchoring of the silane was complete, the resultant materials were directly treated with hexamethyl disilazane (HMDS) to convert surface SiOH groups to $SiOSiMe_3$ groups. Modified silica **6a** with –$C_{10}H_{20}$– spacer chain and **6b** with –C_4H_8– spacer chain were obtained as yellow powders.

The degree of functionalisation was found to be 0.06 and 0.07 mmol g^{-1} for **6a** and **6b**, respectively, according to AAS (Fe) determination. While these loadings may appear to be low, they are by no means untypical for grafted materials on amorphous silica, especially when the grafted group is large. Our modified silica **6a** was characterised by measuring the ^{13}C CPMAS-NMR and FTIR (DRIFTS) spectra. The ^{13}C CPMAS-NMR spectrum of solid **6a** resembles closely that of the unsupported silane **5a**. The resonances due to the ferrocene carbon atoms are observed at 65–80 ppm and 95–100 ppm; diphenylphosphine carbon atoms resonate at 125–145 ppm. Peaks due to residual ethoxy groups on the silane (or on the silica surface) are also seen at 10–15 ppm and at 55–60

DOI: 10.1039/b002528n



Scheme 1 Synthesis of ferrocenylphosphine ligand **5a**.

ppm. Resonances due to the linker C atoms are evident at 10–15 (SiCH_2), 20–30 (chain carbons) and 35–45 (CH_2N, COCH_2 and NCH_3) ppm. The presence of Me_3Si groups on the surface is demonstrated by a large peak at 0 ppm. The resonance of the carbonyl carbon atom is not observed, probably due to its low sensitivity and high peak width. Apart from the broadness of the peaks (partly due to the range of chemically different environments in which the molecules are located[9]), the spectra of the supported and unsupported silane are very similar. This indicates that the ligand has been attached intact to the surface of the silica. The infrared spectrum clearly indicates the presence of the organic groups bound to the surface, with C–H(str) and amide I and II bands (1527 and 1634 cm^{-1}) being distinct.

The structural characteristics of the materials were determined by nitrogen porosimetry. The parent silica, Merck Kieselgel 60, has a pore size distribution centred around 6 nm, and an isotherm with definite hysteresis, signifying a relatively irregular pore structure. Specific surface area was measured as 458 m^2 g^{-1}. For catalyst **6a**, essentially the same isotherm and pore size distribution were seen, but the surface area had dropped to 286 m^2 g^{-1}. This indicates that no major structural changes have taken place during grafting, the lowering of surface area being typical of the attachment of groups to the pore walls, possibly causing some blockage to the pore system.

Two reactions were chosen to test the activity of our new supported homochiral ferrocenylphosphine ligands: enantioselective catalytic hydrogenation of (*Z*)-α-acetamidocinnamic acid and allylic substitution of *rac*-(*E*)-1,3-diphenyl-3-acetoxy-1-propene with the *C*-nucleophile generated from pentan-2,4-dione, using metal complexes of the homogeneous (**2**, **3a**, and **3b**) and heterogeneous (**6a**, **6b**) ligands (Fig. 1).

Initially, we examined the hydrogenation procedure described by Yamamoto and co-workers:[10] using a mixture of methanol–benzene (3 : 1 v/v) as solvent, at a pressure of 20 atm, 0.5% Rh(I) and a 1 : 1 ratio of Rh to L (method A). Unfortunately, we could not reproduce the results described in the original paper. For example, hydrogenation of (*Z*)-α-acetamidocinnamic acid catalysed by Rh(I)–(*S*,*R*)-(+)-BPPFA complex gave (*S*)-*N*-acetylphenylalanine with an ee of only 42%, whereas the literature described an 86% ee (*S*). The enantioselective hydrogenation of (*Z*)-α-acetamidocinnamic acid catalysed by Rh(I)–chiral ferrocenylphosphine complexes carried out according to the procedure of Hayashi *et al.*[2] (method B) gave higher selectivity. The reaction conditions and results obtained are summarised in Table 1. It was found that in hydrogenations catalysed by Rh(I) complexes of ligands **3a** and **3b** the product was isolated with a lower selectivity than that obtained with the known homogeneous ligand BPPFA. It seems that the change of one of the *N*-methyl groups for a longer chain (–C_4H_8– or –$C_{10}H_{20}$–) has a negative influence on catalytic properties. Hydrogenation with

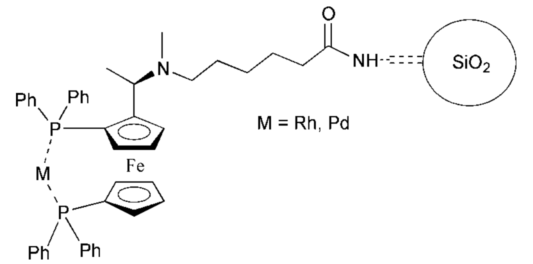
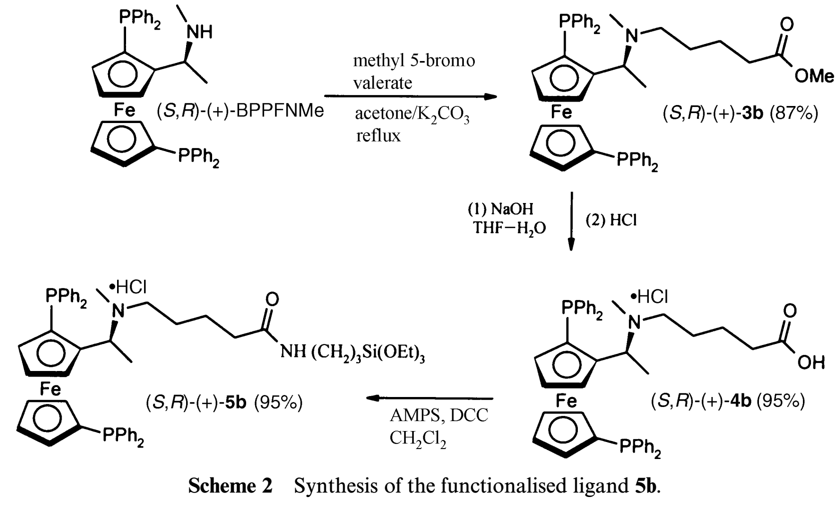
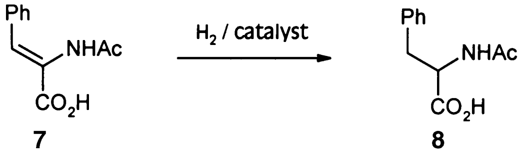


Fig. 1 Structures of chiral ferrocenes PPFA (**1**) and BPPFA (**2**).



Scheme 2 Synthesis of the functionalised ligand **5b**.

Table 1 Enantioselective hydrogenation of (*Z*)-α-acetamidocinnamic acid catalysed by chiral ferrocenylphosphine ligand L–Rh(I) complexes



Ligand L	Method[a]	Time/h	Rh(I) (%)	Yield (%)[b]	ee (%)[c]
(+)-BPPFA (**2**)	A	20	0.5	100	42 (86)[e]
(+)-BPPFA–$C_{10}H_{20}$–COOMe (**3a**)	A	20	0.5	98	28
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)	A	70	0.5	93	14
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)[d]	A	70	0.5	11	12
(+)-BPPFA (**2**)	B	20	0.5	100	88 (93)[c]
(+)-BPPFA–$C_{10}H_{20}$–COOMe (**3a**)	B	20	0.5	100	58
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)	B	20	0.5	17	52
(+)-BPPFA-$C_{10}H_{20}$–[SiO_2] (**6a**)	B	70	0.5	61	52
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)	B	70	1.0	100	46
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)[d]	B	70	1.0	82	36
(+)-BPPFA–C_4H_8–COOMe (**3b**)	B	20	0.5	100	66.5
(+)-BPPFA–C_4H_8–[SiO_2] (**6b**)	B	70	1.0	100	34

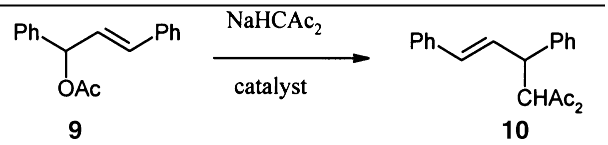
[a] Method A: $p(H_2) = 20$ atm, methanol–benzene (3 : 1 v/v; 10 cm^3), substrate (5 mmol), $[RhCl(C_6H_{10})]_2$ (1.25×10^{-2} mmol, 0.5% Rh), ligand L (2.5×10^{-2} mmol). Method B: $p(H_2) = 50$ atm, methanol (10 cm^3), substrate (5 mmol), $[RhCl(C_6H_{10})]_2$ (1.25×10^{-2} mmol, 0.5% Rh), ligand L (3×10^{-2} mmol, 1.2 equiv.). [b] According to the ^1H NMR spectrum of the reaction mixture after evaporation of the solvent. [c] Determined by CZE (capillary zone electrophoresis) with chiral selector α-CD-NHMe, the configuration of the major enantiomer (*S*) was determined according to the value of the optical rotation. Hayashi and co-workers[2] obtained a 93% ee (*S*) with (*S*, *R*)-(+)-BPPFA. [d] Regenerated catalyst: 0.5% Rh(I)–**6a** complex was reused. [e] Literature result from ref. 10.

immobilized ligand **6a** gave product in comparable yield to its homogeneous analogue **3a**, but with lower selectivity. Similarly, comparable yields and a significant decrease in enantioselectivity was observed for immobilized ligand **6b** in comparison with its homogeneous analogue **3b**. The lower hydrogenation rate for catalytic systems with immobilized ligands could be due to mass transport problems in the amorphous and irregular pore systems of the silicas used. The higher selectivity of hydrogenation using method B rather than method A can be rationalised by the explanation proposed by Eisen and co-workers,[11,12] who claimed that the active site of the catalyst was saturated with hydrogen and the approach of the substrate at higher pressure was therefore restricted and more selective. The immobilized ligand–Rh(I) complex was easily separated from the reaction mixture by filtration. The activity of recovered catalyst was examined and a decrease in both catalytic activity and selectivity was observed. The reason for the decrease of catalyst activity is not yet clear.

Asymmetric allylic substitutions catalyzed by Pd(0)–chiral ferrocenylphosphine ligands were performed according to the procedure of Hayashi *et al.*[3] Results and reaction conditions are given in Table 2. It is interesting that a homogeneous catalyst with **3a** or **3b** as ligand gave product in comparable isolated yield and enantioselectivity as the known BPPFA ligand. The reaction with immobilized ligand **6a** gave a lower yield, but the enantioselectivity was comparable to that obtained with BPPFA. The lower yield could be due to mass transport difficulties. Therefore, we pretreated modified silica **6a** by ultrasound irradiation, but no increase of reaction yield was observed. Ultrasound can help to make irregular porous structures more open, allowing better mass transport. In the reaction with immobilized ligand **6b**, having a shorter spacer chain, a significant decrease of selectivity was observed.

In conclusion, we have proved that exchange of one of the *N*-methyl groups on the BPPFA ligand for a longer alkyl chain with a terminal methoxycarbonyl group does not cause any reduction in catalytic activity for hydrogenation, but the stereoselectivity of the reaction drops by approximately 25%. A method has also been described for the immobilization of these new chiral ferrocenylphosphine ligands on a silica surface. Immobilization resulted in considerable lowering of the reaction rates as well as causing a reduction in stereoselectivity in hydrogenation reactions. On the other hand, both the homogeneous (**3a**) as well as the immobilized (**6a**) new ligands with a longer spacer have activity and selectivity in allylic nucleophilic substitution reactions comparable to the BPPFA ligand. While the homogeneous ligand (**3b**) with a shorter chain has similar activity and selectivity to BPPFA, its immobilization (giving catalyst **6b**) resulted in a significant drop in activity as well as selectivity. Interestingly, the better performance achieved with longer spacer chains in both reaction types contrasts with the results obtained by Thomas and co-workers,[8] who found that a very short linker gave excellent results in their MCM-41 supported system. It may therefore be that the regularity of the pore system and structure is an important determinant of enantioselectivity in such systems, whereas,

Table 2 Allylic substitution of *rac*-(*E*)-1,3-diphenyl-3-acetoxy-1-propene catalysed by chiral ferrocenylphosphine ligand I–Pd(0) complexes[a]



Ligand L	Isolated yield (%)	ee (%)[b]
(+)-BPPFA (**2**)	53	62[c]
(+)-BPPFA–$C_{10}H_{20}$–COOMe (**3a**)	52	54
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)	36	60
(+)-BPPFA–$C_{10}H_{20}$–[SiO_2] (**6a**)[d]	38	60
(+)-BPPFA–C_4H_8–COOMe (**3b**)	48	62
(+)-BPPFA–C_4H_8–[SiO_2] (**6b**)	29	16

[a] Reaction conditions: dry THF (10 ml), NaH (1.2 mmol, 1.2 equiv.), pentane-2,4-dione (1.5 mmol, 1.5 equiv.), substrate (1 mmol), $Pd_2(dba)_3 \cdot CHCl_3$ (0.5×10^{-2} mmol, 1% Pd), ligand L (1.1×10^{-2} mmol, 1.1 equiv.), 24 h, N_2 atm., 40 °C. [b] Determined by ^1H NMR with a chiral shift reagent [$Eu(hfc)_3$], the configuration of the major enantiomer (*R*) was determined according to the value of the optical rotation. [c] Hayashi and co-workers[3] obtained a 62% ee (*S*) with (*R*,*S*)-(−)-BPPFA ligand. [d] Immobilized ligand (+)-BPPFA-$C_{10}H_{20}$-[SiO_2] (**6a**) was pretreated by ultrasound for 1 h.

with amorphous silicas, the irregularity of the walls can only be mitigated by distancing the ligand from the catalyst surface.

Experimental

Methods and materials

NMR (δ) spectra of samples were obtained from $CDCl_3$ solutions at 300 (^1H) and at 75 (^{13}C) MHz with TMS as internal standard. IR and UV-VIS spectra of soluble samples were measured as $CHCl_3$ (Merck, Uvasol) solutions. Optical rotations were measured on a Perkin–Elmer 241 polarimeter instrument. ^{13}C CPMAS-NMR (δ) spectrum of modified silica was obtained on a Bruker 300MSL spectrometer at 75 MHz operating frequency. Diffuse reflectance FTIR (DRIFTS) spectrum of modified silica was measured as a mixture of 5% sample and 95% KBr in an environmental chamber at 150 °C under vacuum on a Bruker Equinox FTIR. Nitrogen porosimetry was carried out using a Coulter SA3100 nitrogen porosimeter. Samples were pretreated by out-gassing at 150 °C for 5 h before nitrogen adsorption. Surface areas were calculated using the BET equation, and pore size distributions calculated from the BJH model. Melting points are uncorrected.

Solvents were purified and dried according to standard published methods. (*S*,*R*)-(+)-BPPFA was prepared and transformed to its derivative (*S*,*R*)-(+)-BPPFOAc according to described methods.[13] 3-Triethoxysilylpropylamine (AMPS, 96%), 11-bromoundecanoic acid (90%), and 5-bromovaleric acid were purchased from Fluka and were used without additional purification. 11-*N*-Methylaminoundecanoic acid was prepared according to the method of Champetier and coworkers[14] and its methyl ester and methyl 5-bromovalerate were prepared by treatment with diazomethane. 1,1,1,3,3,3-Hexamethyldisilazane (HMDS, 97%) and $[RhCl(C_6H_{10})]_2$ were purchased from Aldrich. The complex $Pd_2(dba)_3 \cdot CHCl_3$ was prepared according to the method of Ukai and coworkers.[15] (*Z*)-α-Acetamidocinnamic acid was prepared according to the described procedure.[16] Reduction of chalcone by $NaBH_4$ in the presence of $CeCl_3$ in methanol,[17] followed by the 4-dimethylaminopyridine (DMAP) catalysed acetylation by acetic anhydride in diethyl ether gave *rac*-(*E*)-1, 3-diphenyl-3-acetoxy-1-propene as a colourless clear liquid (bp 180 °C/1 mmHg). Silica (Merck SiO_2 60, particle size 63–200 μm) was used and dried at 150 °C/1 mmHg for 4 h before attachment of the silane.

Syntheses

(+)-(*S*,*R*)-*N*-Methyl-1-(2,1′-bis(diphenylphosphino))ferrocenylethylamine (BPPFNMe). (+)-(*S*,*R*)-BPPFOAc (1.601 g, 2.5 mmol) was dissolved in hot methanol (40 cm^3) and a 35% (w/w) aqueous solution of methylamine (11.5 cm^3) was added. The reaction mixture was refluxed in an oil bath heated to 75–80 °C under N_2 atmosphere for 24 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on an Al_2O_3 column (50 g). Unreacted starting acetate and by-product were eluted by diethyl ether, product was eluted by 5% (v/v) Et_3N in diethyl ether. Compound BPPFNMe was obtained in 85% yield as a dark-orange solid, mp 53–55 °C. For $C_{37}H_{35}FeNP_2$ (611.48) calcd: 61.22% C, 5.77% H, 2.29% N; found: 61.18% C, 5.71% H, 2.16% N. $[\alpha]_D^{20}$ + 273, $[\alpha]_{578}^{20}$ + 292, $[\alpha]_{546}^{20}$ + 369 (0.545, $CHCl_3$). ^1H NMR: δ 1.33 (d, 3H, CH_3), 1.92 (s, 3H, NCH_3), 3.86 (dq, 1H, CH); 3.62, 3.67, 4.09, 4.12, 4.39, 4.42 (m, 7H, ferrocene), 7.20–7.51 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 18.74 (CH_3), 32.59 (NCH_3), 52.27 (d, $^3J_{PC} = 9.4$ Hz, CH), 71.16–76.89 (ferrocene), 98.42 (d, $^2J_{PC} = 23.6$ Hz, C_i), 128.14–140.00 (PPh_2, $P'Ph_2$).

Methyl (*S*,*R*)-(+)-11-{*N*-methyl-*N*-[1-(2,1′-bis(diphenylphosphino))ferrocenylethyl]amino}undecanoate (3a). (*S*,*R*)-(+)-BPPFOAc (1.28 g, 2 mmol) and methyl 11-*N*-methylaminoundecanoate (4.588 g, 20 mmol) were dissolved in methanol (10 cm^3) and the reaction mixture was gently refluxed in an oil bath heated to 70–75 °C under an N_2 atmosphere for 9 h. The solvent was evaporated under reduced pressure and the residue purified by chromatography on an Al_2O_3 column (50 g) using diethyl ether as eluent. Product **3a** was obtained in 90% yield as an orange oil. For $C_{49}H_{57}FeNO_2P_2$ (809.76) calcd: 72.68% C, 7.09% H, 1.73% N; found: 72.73% C, 7.14% H, 1.61% N. $[\alpha]_D^{30}$ + 295.5 (1.0, $CHCl_3$). UV-VIS: λ_{max} nm 260, 432. IR: ν cm^{-1} 1713 (CO). ^1H NMR: δ 0.80–1.65 [m, 16H, $-(CH_2)_8-$], 1.14 (d, $^3J_{HH} = 6.9$ Hz, 3H, CH_3), 1.65 (s, 3H, NCH_3), 2.05 (m, 1H, H_A), 2.11 (m, 1H, H_B), 2.29 (t, 2H, CH_2CO), 3.46, 3.64, 3.92, 4.05, 4.07, 4.36 (m, 7H, ferrocene); 3.65 (s, 3H, OCH_3), 4.16 (dq, 1H, CH), 7.07–7.48 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 15.26 (CH_3), 24.68–29.57 [$-(CH_2)_8-$], 34.03 (CH_2CO), 34.13 (NCH_3), 51.36 (OCH_3), 54.34 (NCH_2), 57.15 (d, $^3J_{PC} = 7.12$ Hz, CH), 65.81–76.92 (ferrocene); 98.32 (d, $^2J_{PC} = 23.25$ Hz, C_i), 126.97–141.17 (PPh_2, $P'Ph_2$), 174.44 (CO).

Methyl (*S*,*R*)-(+)-11-{*N*-methyl-*N*-[1-(2-diphenylphosphino)ferrocenylethyl]amino}valerate (3b). (+)-(*S*,*R*)*N*-Methyl-1-(2,1′-bis(diphenylphosphino))ferrocenylethylamine (1.223 g, 2 mmol) was dissolved in a suspension of K_2CO_3 (0.414 g, 3 mmol) in acetone (3 cm^3), methyl 5-bromovalerate (0.390 g, 2 mmol) was added and the reaction mixture refluxed in an oil bath heated to 55–60 °C. After 24 h, the reaction mixture was cooled, the solvent was evaporated under reduced pressure and residue was purified by chromatography on an Al_2O_3 column (50 g) using diethyl ether as eluent. Product **3b** was obtained in 87% yield as an orange oil. For $C_{43}H_{45}FeNO_2P_2$ (725.63) calcd: 71.17% C, 6.25% H, 1.93% N; found.: 71.12% C, 6.16% H, 1.76% N. $[\alpha]_D^{20}$ + 314 (0.645, $CHCl_3$). UV-VIS: λ_{max} nm 262, 424. IR: ν cm^{-1} 1725 (CO). ^1H NMR: δ 0.81–1.21 [m, 4H, $(CH_2)_2$], 1.14 (d, 3H, CH_3), 1.65 (s, 3H, NCH_3), 2.04 (m, 2H, CH_AH_B), 2.07–2.34 (m, 2H, NCH_AH_B), 3.61 (s, 3H, OCH_3), 3.47, 3.64, 3.91, 4.06, 4.36 (m, 7H, ferrocene), 4.16 (dq, 1H, CH) 7.05–7.50 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 9.13 (CH_3), 22.88, 27.30 ($-CH_2CH_2-$), 34.10 (NCH_3), 34.17 (CH_2CO), 51.47 (OCH_3), 53.86 (NCH_2), 57.43 (d, $^3J_{PC} = 7.2$ Hz, CH), 70.71–77.45 (ferrocene), 98.30 (d, $^2J_{PC} = 23.8$ Hz, C_i), 127.21–141.41 (PPh_2, $P'Ph_2$), 174.331 (CO).

(*S*,*R*)-(+)-11-{*N*-Methyl-*N*-[1-(2,1′-bis(diphenylphosphino))ferrocenylethyl]amino}undecanoic (4a) and valeric acid hydrochloride (4b). Compound **3a** (0.809 g, 1 mmol) was dissolved in a solution of NaOH (0.4 g, 10 mmol) in THF–water (6 : 1, 7 cm^3) and the reaction mixture was stirred for 20 h at room temperature. Solvent was then evaporated under vacuum and the residue was dissolved in water (50 cm^3). The resulting solution was neutralised by addition of 10% HCl and organic material was extracted into dichloromethane. The extracts were washed with water, dried, and solvent was evaporated under reduced pressure. The residue was triturated with diethyl ether and product **4a** was isolated in 91% yield as an orange solid. For $C_{48}H_{55}FeNO_2P_2 \cdot HCl$ (832.23) calcd: 4.26% Cl; found: 4.28% Cl. $[\alpha]_D^{30}$ + 268 (0.84, $CHCl_3$). UV-VIS: λ_{max} nm 267, 439. IR: ν cm^{-1} 1700 (CO). ^1H NMR: δ 0.60–1.60 [m, 16H, $-(CH_2)_8-$], 1.61 (d, $^3J_{HH} = 6.6$ Hz, 3H, CH_3); 2.08 (s, 3H, N^+CH_3), 2.30 (t, 2H, CH_2CO), 2.40 (m, 2H, N^+CH_2), 3.44, 3.58, 4.06, 4.14, 4.35, 4.45, 4.60 (m, 8H, ferrocene, CH), 7.20–7.53 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 19.42 (CH_3), 24.28–29.03 [$-(CH_2)_8-$]; 34.72 (CH_2CO), 35.56 (N^+CH_3), 54.64 (N^+CH_2), 59.56 (d, $^3J_{PC} = 11.84$ Hz, CH), 72.71–78.32 (ferrocene); 89.76 (d, $^2J_{PC} = 29.67$ Hz, C_i), 128.36–138.78 (PPh_2, $P'Ph_2$), 178.19 (CO).

From compound **3b** (0.726 g, 1 mmol) by a similar procedure to that described above, product **4b** was isolated in 95% yield as an orange solid. For $C_{42}H_{43}FeNO_2P_2 \cdot HCl$ (748.07) calcd: 4.74% Cl; found: 4.64% Cl. $[\alpha]_D^{20}$ + 292.5 (0.4, $CHCl_3$). UV-VIS: λ_{max} nm 265, 437. IR: ν cm^{-1} 1705 (CO). ^1H NMR: δ 0.84–1.60 [m, 4H, $-(CH_2)_2-$]; 1.78 (d, 3H, CH_3), 2.08 (t, 2H, CH_2CO), 2.22 (s, 3H, N^+CH_3), 2.42 (m, 2H, N^+CH_2), 3.46, 4.05, 4.30, 4.35, 4.45, 4.48 (m, 7H, ferrocene), 4.72 (dq, 1H, CH), 7.18–7.52 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 20.08 (CH_3), 21.45, 23.57 [$-(CH_2)_2-$]; 33.39 (CH_2CO), 35.56 (N^+CH_3), 54.64 (N^+CH_2), 60.16 (d, CH), 72.84–78.45 (ferrocene), 88.63 (d, $^2J_{PC}$ = 29.85 Hz, C_i), 128.44–138.35 (PPh_2, $P'Ph_2$), 176.33 (CO).

(*S*,*R*)-(+)-11-{*N*-Methyl-*N*-[1-(2,1′-bis(diphenylphosphino))-ferrocenylethyl]amino}undecanoyl (5b) and valeroyl 3-triethoxysilylpropylamide (5b). Compound **4a** (0.832 g, 1 mmol), AMPS (0.221 g, 1 mmol), and dicyclohexyl carbodiimide (DCC, 0.206 g, 1 mmol) were dissolved in dry dichloromethane (4 cm^3). The reaction mixture was stirred for 24 h at room temperature. Diethyl ether (20 cm^3) was added and the insoluble *N*,*N*′-dicyclohexylurea was filtered off. The solution was extracted with 13% aq. NH_3, washed with water, dried, and the solvent was evaporated under reduced pressure. Product **5a** was isolated in 95% yield as an orange oil. For $C_{57}H_{76}FeN_2O_4P_2Si$ (999.13) calcd: 68.52% C, 7.67% H, 2.80% N; found: 68.39% C, 7.52% H, 2.67% N. $[\alpha]_D^{30}$ + 234 (1.14, $CHCl_3$). UV-VIS: λ_{max} nm 262, 429. IR: ν cm^{-1} 1000–1100 (SiOR), 1645 (CO). ^1H NMR: δ 0.63 (t, 2H, CH_2Si), 0.80–1.62 [m, 18H, $-(CH_2)_8-$, CH_2], 1.14 (d, $^3J_{HH}$ = 6.6 Hz, 3H, CH_3), 1.22 (t, 9H, OCH_2CH_3), 1.64 (s, 3H, NCH_3), 2.11 (m, 1H, H_A), 2.15 (t, 2H, CH_2CO), 2.29 (m, 1H, H_B), 3.24 (m, 2H, CH_2NHCO), 3.81 (q, 6H, OCH_2CH_3), 3.46, 3.63, 3.91, 4.05, 4.35 (m, 7H, ferrocene), 4.08 (dq, 1H, CH), 5.70 (br s, 1H, NHCO), 7.07–7.47 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 8.03 (CH_2Si), 15.50 (CH_3), 18.53 (OCH_2CH_3), 23.16–29.84 [$-(CH_2)_8-$, CH_2], 34.25 (NCH_3), 37.18 (CH_2CO), 41.85 (CH_2NHCO), 54.58 (NCH_2), 58.71 (OCH_2CH_3), 57.42 (d, $^3J_{PC}$ = 7.35 Hz, CH), 65.79–76.94 (ferrocene), 98.49 (d, $^2J_{PC}$ = 24.00 Hz, C_i), 127.21–141.35 (PPh_2, $P'Ph_2$), 173.24 (CO).

From compound **4b** (0.749 g, 1 mmol) by a similar procedure to that described above, product **5b** was isolated in 95% yield as an orange oil. For $C_{51}H_{64}FeN_2O_4P_2Si$ (914.96) calcd: 66.95% C, 7.05% H, 3.06% N; found: 66.81% C, 6.92% H, 2.87% N. $[\alpha]_D^{20}$ + 294 (0.45, $CHCl_3$). UV-VIS: λ_{max} nm 264, 425. IR: ν cm^{-1} 1000–1100 (SiOR); 1640 (CO). ^1H NMR: δ 0.63 (t, 2H, CH_2Si); 0.80–1.41 [m, 6H, $-(CH_2)_2-$, CH_2]; 1.13 (d, 3H, CH_3), 1.21 (t, 9H, OCH_2CH_3), 1.65 (s, 3H, NCH_3), 2.11–2.24 (m, 4H, CH_AH_B, CH_2CO), 3.26 (m, 2H, CH_2NHCO), 3.81 (q, 6H, OCH_2CH_3), 3.45, 3.63, 3.91, 4.05, 4.35 (m, 7H, ferrocene), 4.18 (dq, 1H, CH), 5.70 (br s, 1H, NHCO), 7.07–7.47 (m, 20H, PPh_2, $P'Ph_2$). ^{13}C NMR: δ 7.93 (CH_2Si), 9.45 (CH_3), 18.53 (OCH_2CH_3), 22.86, 27.34, 28.12 [$-(CH_2)_2-$, CH_2], 34.15 (NCH_3), 37.18 (CH_2CO), 41.85 (CH_2NHCO), 53.89 (NCH_2), 58.71 (OCH_2CH_3), 57.42 (d, $^3J_{PC}$ = 7.15 Hz, CH), 70.79–77.47 (ferrocene), 98.29 (d, $^2J_{PC}$ = 23.6 Hz, C_i), 127.20–141.42 (PPh_2, $P'Ph_2$), 173.22 (CO).

Modified silica $[SiO_2]-C_{10}H_{20}$–BPPFA (6a) and $[SiO_2]-C_4H_8$–BPPFA (6b). The dried silica (2.5 g) was suspended in dry toluene (15 cm^3) and stirred for 2 h at room temperature under an Ar atmosphere. The compound (*S*,*R*)-(+)-**3** (0.5 mmol) was added in dry dichloromethane (2.5 cm^3) and the reaction mixture was stirred for 24 h under an Ar atmosphere at room temperature. HMDS (2.5 cm^3) was added and the reaction mixture was refluxed for 1 h in an oil bath heated to 120 °C under Ar atmosphere. Then the solid was filtered, washed with toluene, acetone, ethanol, and diethyl ether. The resulting product was purified by Soxhlet extraction with a dichloromethane–diethyl ether (1 : 2) mixture for 6 h and dried at 40 °C *in vacuo*. Modified silicas **6a,b** were obtained as yellowish powders. The loading of ferrocenyl units on the resulting solids was determined by AAS. The loading was found to be 0.06 mmol g^{-1} for **6a** and 0.07 mmol g^{-1} for **6b**. ^{13}C CPMAS-NMR spectrum of **6a**: δ 0 [$Si(CH_3)_3$]; 10–15 OCH_2CH_3, $SiCH_2$, CH_3), 20–30 [$-(CH_2)_8-$, CH_2), 35–45 ($NHCH_2$, NCH_3, $COCH_2$), 55–60 (OCH_2CH_3, CH), 65–80 (ferrocene); 95–100 (C_i); 125–145 (PPh_2, $P'Ph_2$). DRIFTS spectrum of **6a**: ν cm^{-1} 1000–1200, 1446, 1527, 1634, 1875, 2866, 2911, 2964, 3107, 3312, 3661.

General procedure for hydrogenation of (*Z*)-α-acetamidocinnamic acid 7

In a teflon reactor were placed $[RhCl(C_6H_{10})]_2$ (5.5 mg, 1.25 × 10^{-2} mmol, 0.5% Rh), ferrocenylphosphine ligand (3 × 10^{-2} mmol, 1.2 equiv.), and **7** (1.026 g, 5 mmol) under a nitrogen atmosphere. Methanol (10 cm^3), previously degassed, was added to the mixture. The reaction mixture was placed in an autoclave, hydrogen was then introduced after three successive substitutions of nitrogen with hydrogen (50 atm). Reactions were carried out at 50 atm hydrogen pressure with stirring for an appropriate time at room temperature. If a soluble catalyst was used, then the solvent was evaporated and crude product was isolated. Heterogeneous catalyst was filtered off and washed with methanol and diethyl ether before evaporation of solvent. The ratio of product substrate was determined according to the ^1H NMR (d_6-DMSO) spectrum of crude product. Enantiomeric purity was determined by CZE analysis of crude product **8** with chiral selector α-CD-NHMe. ^1H NMR spectrum of substrate **7**: δ 1.98 (s, 3H, $COCH_3$), 7.21 (s, 1H, H), 7.38–7.62 (m, 5H, Ph), 9.47 (s, 1H, NH). ^1H NMR spectrum of product **8**: δ 1.77 (s, 3H, $COCH_3$), 2.83 (dd, $^2J_{AB}$ = 13.8 Hz, $^3J_{HH}$ = 9.6 Hz, 1H, CH_A), 3.04 (dd, $^3J_{HH}$ = 4.8 Hz, 1H, CH_B), 4.40 (m, 1H, C*H); 7.20–7.30 (m, 5H, Ph), 8.18 (d, $^3J_{HH}$ = 8.1 Hz, 1H, NH).

General procedure for allylic substitution reaction of *rac*-*E*-1,3-diphenyl-3-acetoxy-1-propene 9

Sodium hydride (30 mg, 1.2 mmol, 1.2 equiv.) was suspended in freshly dried THF (5 cm^3) under a nitrogen atmosphere. The pentane-2,4-dione **9** (0.15 g, 1.5 mmol, 1.5 equiv.) was added dropwise, the resulting salt suspension was then vigorously stirred at room temperature. The ferrocenylphosphine ligand (1.1 × 10^{-2} mmol, 1.1 equiv.), $Pd_2(dba)_3 \cdot CHCl_3$ (5.2 mg, 0.5 × 10^{-2} mmol, 1% Pd) and substrate (0.252 g, 1 mmol) were mixed in THF (5 cm^3); the resulting red-purple solution was then added to the suspension. The reaction mixture was placed in an oil bath heated to 40 °C (the colour of the reaction mixture changed to lemon-yellow) and was stirred under a nitrogen atmosphere for 24 h. Water (50 cm^3) was added, the organic material was extracted with diethyl ether (50 cm^3), and finally the organic extract was washed with water (50 cm^3), dried and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a SiO_2 column (30 g) using 2-methylpentane–ethyl acetate (7 : 1) as eluent. Product **10** was obtained after evaporation of solvent as a white solid. Enantiomeric purity was determined according to ^1H NMR ($CDCl_3$) spectra of the product with the chiral shift reagent [Eu(hfc)$_3$]. ^1H NMR spectrum of substrate **9**: δ 2.12 (s, 3H, CH_3), 6.34 (dd, $^3J_{12}$ = 15.66 Hz, $^3J_{23}$ = 6.94 Hz, 1H, H_2), 6.45 (d, 1H, H_3), 6.63 (d, 1H, H_1), 7.25–7.40 (m, 10H, Ph, Ph′). ^1H NMR spectrum of product **10**: δ 1.93 (s, 3H, $COCH_3$); 2.25 (s, 3H, $COCH_3$), 4.35 (m, 2H, H_3, H_4), 6.19 (ddd, $^3J_{12}$ = 15.66 Hz, $^3J_{23}$ = 7.96 Hz, $^4J_{24}$ = 2.74 Hz, 1H, H_2), 6.42 (d, 1H, H_1), 7.20–7.40 (m, 10H, Ph, Ph′).

Acknowledgements

Our thanks are due to Dr K. Gaplovská and Dr Solčániová, and their staff, for microanalysis and ^1H, ^{13}C NMR spectra as well as to Dr M. Žemberyová for AAS determinations and to Dr P. Mikuš and Associate Professor D. Kaniansky (all of Comenius University, Bratislava) for CZE analysis. DJM thanks the Royal Society for a University Research Fellowship. This work was supported by VEGA granting agency, grant No 1/4166/97.

References

1 H. U. Blaser and B. Pugin, in *Chiral Reactions in Heterogeneous Catalysis*, eds. G. J. James and V. Dubois, Plenum Press, New York, 1995, p. 33.

2 T. Hayashi, T. Mise, S. Mitachi, K. Yamomoto and M. Kumada, *Tetrahedron Lett.*, 1976, 1133.

3 T. Hayashi, A. Yamomoto, T. Hagihara and Y. Ito, *Tetrahedron Lett.*, 1986, 191.

4 B. Pugin, *Eur. Pat. Appl.* EP 729,969, 1996; *Chem. Abs.*, 1996, **125**, 276188z.

5 B. Pugin, *PCT Int. Appl.* WO 9632,400, 1996; *Chem. Abs.*, 1997, **126**, 8302r.

6 B. Pugin, *PCT Int. Appl.* WO 9702,232, 1997; *Chem. Abs.*, 1997, **126**, 185879e.

7 W. R. Cullen and N. F. Han, *J. Organomet. Chem.*, 1987, **333**, 269.

8 B. F. G. Johnson, S. A. Raynor, D. S. Shephard, T. Mashmeyer, J. M. Thomas, G. Sankar, S. Bromley, R. Oldroyd, L. Gladden and M. Mantle, *Chem. Commun.*, 1999, 1167.

9 S. O'Brien, J. Tudor, S. Barlow, M. J. Drewitt, S. J. Heyes and D. O'Hare, *Chem. Commun.*, 1997, 641.

10 K. Yamamoto, J. Wakatsuki and R. Sugimoto, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1132.

11 M. Eisen, J. Blum, H. Schumann and B. Gorella, *J. Mol. Catal.*, 1989, **56**, 329.

12 M. Eisen, J. Blum, G. Hoehne, H. Schumann and H. Schwarz, *Chem. Ber.*, 1989, **122**, 1599.

13 T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, M. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Kanishi, K. Yamamoto and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1138.

14 G. Champetier, M. Lavalou and J. P. Pied, *Bull. Soc. Chim. Fr.*, 1958, 708.

15 T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet and J. A. Ibers, *J. Organomet. Chem.*, 1974, **65**, 253.

16 R. M. Herbst and D. Shemin, in *Organic Synthesis*, eds. J. S. Buck and W. S. Ide, Wiley, New York, **coll. vol. II**, p. 1.

17 A. L. Gemal and J. L. Luche, *J. Am. Chem. Soc.*, 1981, **103**, 5454.