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Preparation of planar-chiral multidonor phosphanylferrocene carboxamides and their application as ligands for palladium-catalysed asymmetric allylic alkylation

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Amide coupling of (S_p)-2-(diphenylphosphanyl)ferrocene-1-carboxylic acid with appropriate terminal amines mediated by 1-hydroxybenzotriazole and a carbodiimide affords multi-donor amides terminally functionalized with planar-chiral (S_p)-2-(diphenylphosphanyl)ferrocen-1-yl moieties in good to excellent yields. Palladium catalysts based on these ligands efficiently promote asymmetric allylic alkylation of 1,3-diphenylallyl acetate with *in situ* generated dimethyl malonate anion to give the C-alkylated product with ees up to 93% at room temperature. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: ferrocene; phosphanes; carboxamides; PAMAM; palladium; asymmetric allylic alkylation

Introduction

The use of dendrimeric molecules as supporting scaffolds to catalytic systems has recently gained considerable attention largely because it can lead to multifunctional catalysts, which can be recycled while often retaining high activity and selectivity of their corresponding homogeneous, low-molecular weight counterparts. Dendrimers for catalytic applications, mostly with phosphane donor sites, are typically prepared with a single functional moiety in (or close to) the core of the hyperbranched structure, or with several functional units attached at the periphery. The latter approach is particularly attractive as it may result in unique materials showing unusual reactivity due to the formation of specific microcompartments within the highly functionalized structures.[1]

In view of our previous work aimed at the preparation, coordination behaviour and catalytic chemistry of ferrocene-based phosphanylcarboxylic acids[2] and the corresponding carboxamide derivatives,[3] we recently synthesized dendrimer-like assemblies containing *several* covalently bonded terminal 1′-(diphenylphosphanyl)ferrocen-1-yl groups at the exterior.[4] For the synthesis of the latter molecules, we made use of the amidation reaction between 1′-(diphenylphosphanyl)ferrocene-1-carboxylic acid (Hdpf)[5,2a] and the terminal NH_2 groups of first-generation poly(amido-amine) dendrimers (PAMAM).[6,7] Even these relatively simple compounds containing one to four phosphanylferrocenyl moieties exerted a distinct positive dendritic effect on the reaction rate in palladium-catalysed Suzuki–Miyaura and Heck–Mizoroki reactions. This led us to design, prepare and study analogous compounds derived from the planar-*chiral* isomer of Hdpf, viz. (S_p)-2-(diphenylphosphanyl)ferrocene-1-carboxylic acid [(S_p)–**1**].[8]

With this contribution, we report on the preparation of several amides derived from (S_p)–**1** and small PAMAM-like amines or related model compounds (Scheme 1), and on their use as ligands in palladium-catalysed asymmetric allylic alkylation.[9] These newly prepared donors not only widen the scope of the chiral phosphanyl–carboxamide ligands synthesized so far from (S_p)–**1**,[3e,8a,b,10] but also further demonstrate the alternative approach towards the preparation of chiral phosphanylferrocenyl dendrimers.[11]

Results and Discussion

Syntheses and Characterization

The series of phosphanylferrocenyl amides was designed comprising both simple monoferrocenyl derivatives analogous to the compounds studied earlier[3e] and their larger PAMAM-like congeners (Scheme 1). Compounds **2**–**5** were obtained by the reactions of (S_p)-2-(diphenylphosphanyl)ferrocene-1-carboxylic acid [(S_p)–**1**][8] with appropriate terminal amines in the presence of peptide coupling agents[12] (Scheme 1). The starting amines were synthesized as described in the literature (see Experimental) except for the precursor to compound **4**, which was obtained via the coupling of N-Boc protected 1,2-diaminoethane (**8**) and β-alanine (**9**) followed by removal of the protecting groups, and was isolated as dihydrochloride **6** (Scheme 2).

The amidation reactions with small amines proceeded very well and afforded the products in good to excellent isolated

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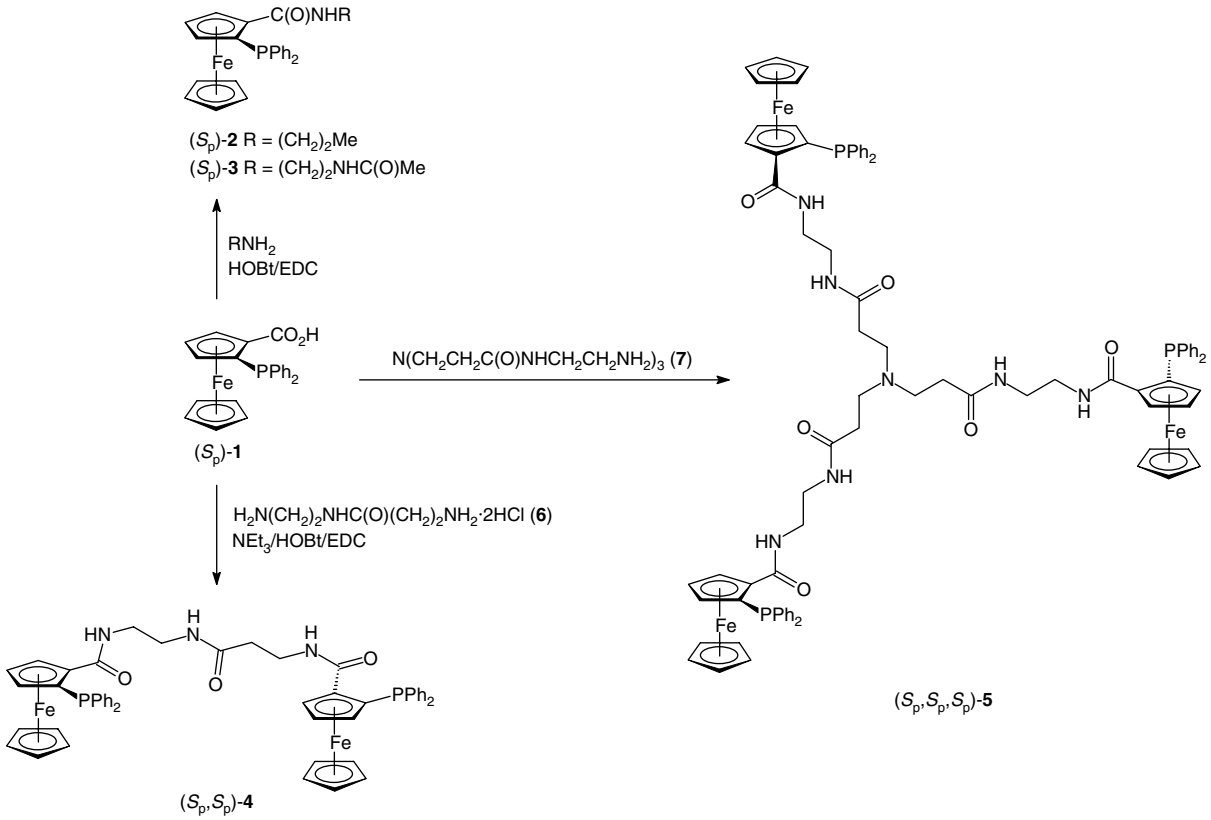
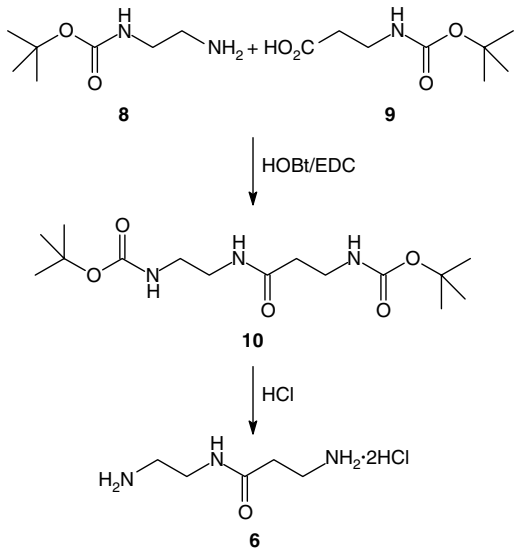


Scheme 1. Preparation of phosphane-amide ligands **2**–**5** (EDC = 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide, HOBt = 1-hydroxybenzotriazole).



Scheme 2. Preparation of the starting amido-diamine dihydrochloride **6** (see legend to Scheme 1).

yields. In the case of larger molecules, however, the isolation was complicated by chemical similarity and overall high polarity of the main and side products, which resulted in relatively lower yields (cf. the synthesis of compound **5**). Finally, an attempted preparation of a penta(amidoferrocenyl) derivative from $\{H_2N(CH_2)_2NHC(O)(CH_2)_2\}_2NCH_2CH_2N\{(CH_2)_2C(O)NH(CH_2)_2NH_2\}CH_2CH_2N\{(CH_2)_2C(O)NH(CH_2)_2NH_2\}_2$ analogously to the synthesis of **5** was unsuccessful due to complications during the isolation step.

Amido-phosphanes **2**–**5** were characterized by multinuclear NMR spectroscopy, electrospray (ESI) mass spectrometry and by optical rotation. In the ^{1}H and ^{13}C NMR spectra, they showed signals typical for 1,2-disubstituted ferrocene moieties and signals due to the amide substituents. The ^{13}C NMR spectra further comprised resonances of the amide C═O groups due to the ferrocenyl-bound amide units (a doublet with $^3J_{PC} = 3$–4 Hz) and the organic linkers (singlets), all in the narrow range δ_C *ca* 170.3–173.2. ^{31}P{^{1}H} NMR spectra of **2, 3** and **5** displayed single resonances at δ_P around −20, whereas the unsymmetric diphosphane **4** expectedly showed two signals. On the other hand, the unsymmetric diphosphane **4** showed two signals at very similar positions (δ_P −19.7 and −19.8). In ESI mass spectra, compounds **2**–**5** gave rise to characteristic pseudomolecular ions ($[M + Z]^+$, Z = H, Na or K; $[M - H]^-$).

Solid-state Structure of (S_p)–2

The solid-state structure of (S_p)–**2** was established by single-crystal X-ray diffraction analysis. A view of the molecular structure is presented in Fig. 1 together with selected geometric data. The structure of (S_p)–**2** is not unexpected and corroborates both the connectivity and chirality at the ferrocene moiety. Besides, the molecular geometry compares well with the structural data reported for (S_p)-1-(*N*-benzylcarbamoyl)-2-(diphenylphosphanyl)ferrocene[3e] and (S_p)-2-(diphenylphosphanoyl)-1-ferrocene-1-carboxylic acid.[8c]

The ferrocene moiety in (S_p)–**2** exerts balanced Fe–Cg distances and negligible tilting [dihedral angle of the mean cyclopentadienyl ring planes being 1.8(1)°]. As indicated by the relatively minor differences in the pairs of adjacent C2/C5–C1–C11

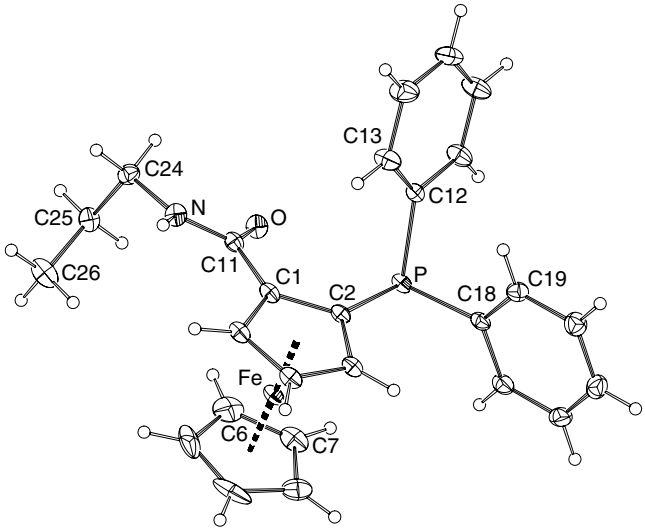


Figure 1. View of the molecular structure of (S_p)–**2** showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. Selected distances and angles: Fe–Cg1 1.6443(7), Fe–Cg2 1.653(1), P–C2 1.826(1), P–C12 1.837(2), P–C18 1.850(2), C1–C11 1.487(2), C11–O 1.240(2), C11–N 1.343(2), N–C24 1.465(2) Å; <Cp1,Cp2 1.8(1), C2–C1–C11 124.7(1), C5–C1–C11 126.9(1), C1–C11–O 121.4(1), C1–C11–N 115.4(1), O–C11–N 123.2(1), C11–N–C24 121.2(1), C1–C2–P 126.9(1), C3–C2–P 126.7(1), C2–P–C12 103.23(6), C2–P–C18 97.60(7), C12–P–C18 99.29(7). The ring planes are defined as follows: Cp1 = C(1–5), Cp2 = C(6–10); Cg1 and Cg2 denote the respective ring centroids.

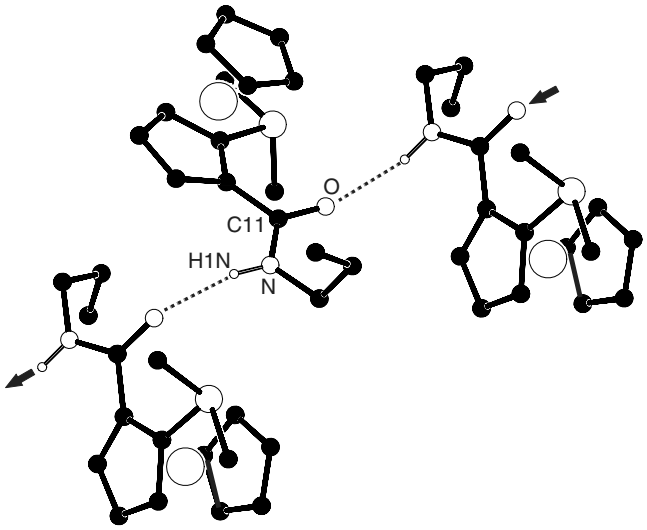


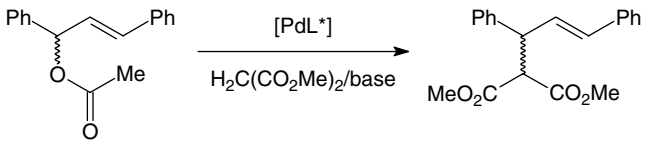
Figure 2. A section of the infinite hydrogen bonded chain in the structure of (S_p)–**2**. Only pivotal phenyl ring carbons and H-bonded hydrogen atoms are shown for clarity. Hydrogen bond parameters, N–H1N···O′: N···O′ = 3.006(2) Å, N–H1N···O′ = 161° (prime-labelled atoms are generated by the (2 − *x*, *y* − 1/2, 1 − *z*) symmetry operation).

and C1/C3–C2–P angles being 2.2 and 0.2°, respectively, and further by the torsion angle C11–C1–C2–P being 0.6(2)°, the substituents bind symmetrically to the ferrocene scaffold without any notable torsional deformation. On the other hand, the carbamoyl group (C11,O,N) is rotated from the plane of its bonding cyclopentadienyl ring by as much as 20.5(2)° with its bulkier $N(CH_2)_2CH_3$ moiety pointing above the ferrocene unit and away from the PPh_2 group. In the crystal, individual molecules of (S_p)–**2** aggregate into infinite chains by means of N–H···O hydrogen bonds between proximal molecules related by crystallographic 2_1 screw axis (Fig. 2). A similar packing arrangement has been noted in the structure of the aforementioned *N*-benzyl amide.

Catalytic Tests

Although asymmetric palladium-catalysed allylic alkylation is both a valuable synthetic tool and a widely used benchmark test,[9] there have been published only a few reports concerning the use of chiral, dendrimer-supported phosphanes as ligands for this reaction.[11d,13] In the present case, we have employed asymmetric allylic alkylation because it allows for a comparison of the newly prepared multidonor phosphanylferrocene carboxamides with the related ligands. For testing, we used the alkylation of the symmetrical substrate 1,3-diphenylprop-2-en-1-yl acetate (**11**) with *in situ* generated malonate anion (Scheme 3).

The results summarized in Table 1 clearly show that there was only relatively minor variation in the ee upon increasing the number of the chiral 2-phosphanylferrocenyl units per ligand molecule, the (*R*)–**12** always being the major product. In terms of enantioselectivity, the reaction outcome was similar to or slightly better than that achieved with simple benzylic amides derived from acid (S_p)–**1**[3e] and considerably better than that reported for analogous, donor-unsymmetric chiral-pocket bisamides.[10a]



11 **12**

Scheme 3. The model asymmetric allyic alkylation reaction.

Table 1. Application of the chiral phosphano-amides **2**–**5** to palladium-catalysed enantioselective allylic alkylation[a]

Entry	Ligand	Additive	Conversion	ee[b]
1	(S_p)–**2**	None	65	82
2	(S_p)–**3**	None	70	91
3	(S_p,S_p)–**4**	None	7	87
4	(S_p,S_p,S_p)–**5**	None	22	88
5	(S_p)–**3**	LiOAc	13	84
6	(S_p)–**3**	NaOAc	45	92
7	(S_p)–**3**	KOAc	33	92
8	(S_p)–**3**	RbOAc	57	93
9	(S_p)–**3**	CsOAc	96	91

[a] The results are an average of two independent runs. For detailed conditions, see Experimental. [b] (*R*)–**12** was the dominating component of the enantiomeric mixture in all cases.

On the other hand, the conversions achieved with ligands **2**–**5** were far from complete after 24 h and varied greatly with the ligand structure, being lower with the larger ligands (Table 1). Fortunately, however, the conversion could be varied significantly upon adding alkali metal acetates a catalytic base additives to *N*, *O*-bis(trimethylsilyl)acetamide. With ligand (S_p)–**3**, which performed best in the series of ligands tested, and caesium acetate as the base additive, the conversion was nearly complete within 24 h

while the degree of asymmetric induction remained unaffected (Table 1).

Conclusions

Oligoamides bearing one to three (S_p)-2-(diphenylphosphanyl) ferrocen-1-yl pendant groups at the periphery are readily available via amide coupling of (S_p)-2-(diphenylphosphanyl)ferrocene-1-carboxylic acid with appropriate terminal amines. When combined with bis[chlorido(η^3-allyl)palladium(II)] as a metal source, these donors give rise to efficient catalysts for asymmetric allylic alkylation of 1,3-diphenylallyl acetate. Whereas the enantioselectivity varies only slightly with the ligand structure (maximum ee being 93%), the reaction rate changes considerably more, being lower with the larger donor molecules. However, the reaction can be improved by adding an appropriate alkali metal acetate as a catalytic base additive.

Experimental

Materials and Methods

All syntheses were performed under an argon atmosphere. Dichloromethane was dried over anhydrous potassium carbonate and distilled under argon. Acetone and methanol were distilled under argon. Acid (S_p)–**1**,[8c] *N*-(2-aminoethyl)acetamide,[14] *tert*-butyl *N*-(2-aminoethyl)carbamate (**8**)[15] and 3-[(*tert*-butoxycarbonyl)amino]propanoic acid (**9**)[16] were prepared according to the literature procedures.

NMR spectra were recorded on a Varian Unity Inova 400 spectrometer at 25 °C (^{1}H, 399.95; ^{13}C, 100.58 and ^{31}P, 161.90 MHz). Chemical shifts (δ/ppm) are given relative to internal tetramethylsilane (^{13}C and ^{1}H) or to external 85% aqueous H_3PO_4 (^{31}P). Low-resolution electrospray (ESI) mass spectra were measured with a Bruker Esquire 3000 spectrometer on methanol solutions whereas the high-resolution data were obtained with a Thermo Fisher Scientific LCQ Fleet spectrometer. Optical rotations were determined with an Autopol III automatic polarimeter (Rudolph Research) at room temperature.

Preparation of simple amides. A general procedure

N-(3-Dimethylaminopropyl)-*N′*-ethylcarbodiimide (EDC) was slowly added to a mixture of acid (S_p)–**1**, 1-hydroxybenzotriazole (HOBt) and dry dichloromethane (10–15 ml) while cooling in an ice bath. The resultant mixture was stirred at 0 °C for 5 min, whereupon the solids dissolved to give a clear orange-red solution. The appropriate amine was introduced (dissolved in a small amount of dichloromethane) and stirring was continued at room temperature for 20 h. Then, the mixture was washed successively with 1 M HCl, saturated aqueous $NaHCO_3$ solution and with brine. The organic phase was separated, dried over $MgSO_4$, and evaporated under vacuum, leaving and orange residue, which was subsequently purified by column chromatography (silica gel, dichloromethane–methanol 20 : 1, v/v) to give the desired amide after evaporation under vacuum.

*(S_p)-2-(Diphenylphosphanyl)-1-(N-n-propylcarbamoyl)ferrocene [(S_p)–**2**]*

Starting with (S_p)–**1** (208 mg, 0.50 mmol), HOBt (76 mg, 0.51 mmol), EDC (0.15 ml, 0.75 mmol) and *n*-propylamine (35 mg, 0.60 mmol), the general procedure afforded amide (S_p)–**2** as an orange oil, which slowly crystallized at +4 °C. Yield: 205 mg (91%).

$[\alpha]_D = -201^\circ$ (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 0.87 (t, $^3J_{HH}$ = 7.5 Hz, 3 H, CH_3), 1.50 (m, 2 H, CH_2), 3.30 (m, 2 H, CH_2), 3.79 (m, 1 H, C_5H_3), 4.11 (s, 5 H, C_5H_5), 4.45 (m, 1 H, C_5H_3), 5.18 (m, 1 H, C_5H_3), 7.12–7.59 (m, 11 H, PPh_2, and N*H*); ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 11.45 (CH_3), 22.91, 41.37 (2 × CH_2), 70.79 (C_5H_5), 71.35 (C_5H_3 *C*H), 73.79 (d, J_{PC} = 2 Hz, C_5H_3 *C*H), 74.25 (d, J_{PC} = 4 Hz, C_5H_3 *C*H), 74.72 (d, J_{PC} = 9 Hz, C_5H_3 C_{ipso}), 81.35 (d, J_{PC} = 20 Hz, C_5H_3 C_{ipso}), 128.36 (d, $^3J_{PC}$ = 7 Hz, PPh_2 CH_m), 128.40 (PPh_2 CH_p) 128.43 (d, $^3J_{PC}$ = 6 Hz, PPh_2 CH_m), 129.75 (PPh_2 CH_p), 132.10 (d, $^2J_{PC}$ = 17 Hz, PPh_2 CH_o), 135.13 (d, $^2J_{PC}$ = 21 Hz, PPh_2 CH_o), 135.92, 137.84 (2× d, $^1J_{PC}$ = 6 Hz, PPh_2 C_{ipso}), 170.04 (d, $^3J_{PC}$ = 4 Hz, CONH); ^{31}P{^{1}H} NMR ($CDCl_3$) = δ −20.1 (s); MS ESI$^+$: m/z = 456 ([M + H]$^+$), 478 ([M + Na]$^+$), 494 ([M + K]$^+$); MS ESI−: m/z = 454 ([M − H]$^-$); HR MS (ESI$^+$) calcd for $C_{26}H_{27}{}^{56}FeNOP$ ([M + H]$^+$) 456.1174, found 456.1172.

*(S_p)-2-(Diphenylphosphanyl)-1-{N-[2-(acetylamino)ethyl]carbamoyl}ferrocene [(S_p)–**3**]*

Following the general procedure, acid (S_p)–**1** (83 mg, 0.20 mmol), HOBt (30 mg, 0.22 mmol), EDC (0.05 ml, 0.30 mmol) and *N*-(2-aminoethyl)acetamide (26 mg, 0.25 mmol) gave amide (S_p)–**3** as an orange solid foam. Yield: 62 mg (62%).

$[\alpha]_D = -147^\circ$ (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 1.84 (s, 3 H, CH_3), 3.25–3.59 (m, 4 H, CH_2), 3.81 (m, 1 H, C_5H_3), 4.12 (s, 5 H, C_5H_5), 4.47 (m, 1 H, C_5H_3), 5.11 (m, 1 H, C_5H_3), 6.02 (br s, 1 H, N*H*COMe), 7.13–7.58 (m, 11 H, PPh_2, and C_5H_3CON*H*); ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 23.21 (CH_3), 39.45, 40.87 (2 × CH_2), 70.91 (C_5H_5), 71.65 (C_5H_3 *C*H), 73.18 (d, J_{PC} = 2 Hz, C_5H_3 *C*H), 74.46 (d, J_{PC} = 4 Hz, C_5H_3 *C*H), 75.42 (d, J_{PC} = 10 Hz, C_5H_3 C_{ipso}), 80.41 (d, J_{PC} = 18 Hz, C_5H_3 C_{ipso}), 128.40–128.55 (m, PPh_2 CH_m and CH_p), 129.83 (PPh_2 CH_p), 131.87 (d, $^2J_{PC}$ = 17 Hz, PPh_2 CH_o), 135.13 (d, $^2J_{PC}$ = 21 Hz, PPh_2 CH_o), 135.82, 138.18 (2× d, $^1J_{PC} \approx$ 6 Hz, PPh_2 C_{ipso}), 170.66 (CH_3*C*ONH), 171.70 (d, $^3J_{PC} \approx$ 3 Hz, C_5H_3*C*ONH); ^{31}P{^{1}H} NMR ($CDCl_3$): δ = −19.8 (s); MS ESI$^+$: m/z = 499 ([M + H]$^+$), 521 ([M + Na]$^+$), 537 ([M + K]$^+$); MS ESI−: m/z = 497 ([M − H]$^-$); HR MS (ESI$^+$) calcd for $C_{27}H_{27}{}^{56}FeN_2O_2P$ (M$^+$) 498.1160, found 498.1156.

*Preparation of 2-[N-(2-aminoethyl)carbamoyl]ethylamine dihydrochloride (**6**)*

A suspension of 3-[(*tert*-butoxycarbonyl)amino]propanoic acid (**9**; 1.89 g, 10.0 mmol) and HOBt (1.50 g, 11.0 mmol) in dichloromethane (100 ml) was cooled in an ice bath. EDC (2.2 ml, 12.0 mmol) was slowly introduced, and the mixture was stirred at 0 °C for 5 min. To the resulting clear solution, a solution of *tert*-butyl (2-aminoethyl)carbamate (**8**; 1.92 g, 12.0 mmol) in dichloromethane (20 ml) was added, and the reaction mixture was stirred at room temperature for 20 h. Then, it was washed with saturated aqueous citric acid and brine (50 ml each). The organic phase was dried over $MgSO_4$ and evaporated under vacuum, leaving a pale yellow viscous oil. Subsequent purification by column chromatography (silica gel, dichloromethane–methanol, 10 : 1 v/v) gave **10** as a colourless solid, yield: 2.96 g (89%).

^{1}H NMR ($CDCl_3$): δ = 1.43, 1.44 (2× s, 9 H, CMe_3), 2.39 (t, ^3J = 5.8 Hz, 2 H, $COCH_2$), 3.20–3.45 (m, 6 H, CH_2), 4.99, 5.21, 6.40 (3× br s, 1 H, N*H*); HR MS (ESI$^+$) calcd for $C_{15}H_{29}N_3NaO_5$ ([M + Na]$^+$) 354.1999, found 354.2001.

In the next step, the Boc-protected derivative **10** (500 mg, 1.51 mmol) was dissolved in acetone (30 ml, in air), and dry HCl

gas was bubbled through the stirred solution for 15 min, causing separation of a fine white precipitate. The mixture was stirred for another 2 h and then evaporated to dryness under vacuum. The resulting colourless solid was identified as pure dihydrochloride **6** and was used directly in the following synthesis without any further purification.

^{1}H NMR (D_2O): δ = 2.73 (t, ^3J = 6.7 Hz, 2 H, CH_2), 3.17 (t, ^3J = 5.8 Hz, 2 H, CH_2), 3.29 (t, ^3J = 6.6 Hz, 2 H, CH_2), 3.54 (t, ^3J = 5.9 Hz, 2 H, CH_2), 4.77 (br s, 6 H, NH_3^+); HR MS (ESI$^+$) calcd for $C_5H_{14}N_3O$ ([**6** − H − 2Cl]$^+$, i.e. monodeprotonated cation) 132.1131, found 132.1130.

*Preparation of compound (S_p,S_p)–**4***

EDC (0.05 ml, 0.30 mmol) was added to a mixture of (S_p)–**1** (83 mg, 0.20 mmol), HOBt (30 mg, 0.22 mmol) and dichloromethane (10 ml) with cooling in an ice bath. After stirring for 5 min, the resulting clear orange-red solution of the pre-formed active ester was added to a suspension of compound **6** (35 mg, 0.15 mmol) in triethylamine (0.1 ml, 0.72 mmol) and dichloromethane (10 ml). The heterogeneous mixture was stirred at room temperature for 22 h and worked up in the same manner as described in the general procedure. Yield: 68 mg (74%) of (S_p,S_p)–**4**; an orange solid foam.

$[\alpha]_D = -153^\circ$ (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 2.25 (m, 2 H, CH_2), 3.15–3.60 (m, 6 H, 3× CH_2), 3.79 (m, 2 H, 2× C_5H_3), 4.11, 4.12 (2× s, 5 H, C_5H_5), 4.42, 4.46, 5.04, 5.11 (4× m, 1 H, C_5H_3), 6.09 (br t, $^3J_{HH}$ = 5.4 Hz, 1 H, $CH_2NHCOCH_2$), 7.11–7.59 (m, 22 H, 2× PPh_2, and 2× C_5H_3CONH); ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 35.51, 36.01, 39.50, 40.52 (4 × CH_2), 70.86, 70.90 (2 × C_5H_5), 71.29, 71.58 (2× C_5H_3 CH), 72.62, 73.13 (2× d, J_{PC} = 2 Hz, C_5H_3 CH), 74.27, 74.40 (2× d, J_{PC} = 4 Hz, C_5H_3 CH), 75.52, 76.34 (2× d, J_{PC} = 11 Hz, C_5H_3 C_{ipso}), 80.50, 80.81 (2× d, J_{PC} = 18 Hz, C_5H_3 C_{ipso}), 128.05–128.52 (m, 2× PPh_2 CH_m and CH_p), 129.45, 129.75 (2× PPh_2 CH_p), 131.85, 132.00 (2× d, $^2J_{PC}$ = 18 Hz, PPh_2 CH_o), 135.13, 135.20 (2× d, $^2J_{PC}$ = 21 Hz, PPh_2 CH_o), 135.94, 136.89, 138.25, 138.75 (4× d, $^1J_{PC} \approx$ 8 Hz, PPh_2 C_{ipso}), 170.29, 171.37 (2× d, $^3J_{PC}$ = 3 Hz, C_5H_3CONH), 171.87 ($CH_2CONHCH_2$); ^{31}P{^{1}H} NMR ($CDCl_3$): δ = −19.8, −19.7 (2× s); MS ESI$^+$: m/z = 924 ([M + H]$^+$), 946 ([M + Na]$^+$), 962 ([M + K]$^+$); MS ESI−: m/z = 922 ([M − H]$^-$), 958 ([M + Cl]$^-$); HR MS (ESI$^+$) calcd for $C_{51}H_{48}{}^{56}Fe_2N_3O_3P_2$ ([M + H]$^+$) 924.1864, found 924.1869.

*Preparation of amino-amide **7***

Compound **7** was obtained by a two-step procedure as reported previously by Tomalia *et al.*[17] Methyl acrylate (14.5 g, 0.168 mol) and excess 1,2-diaminoethane (49.0 g, 0.815 mol) were successively added to a solution of ammonia in methanol (4 ml, 0.028 mol), and the reaction mixture was stirred at room temperature for 72 h. Subsequent removal of the volatiles under vacuum yielded **7** as a colourless oil (10.0 g, 99% based on the ammonia).

*Preparation of compound (S_p,S_p,S_p)–**5***

Acid (S_p)–**1** (230 mg, 0.55 mmol) and HOBt (75 mg, 0.55 mmol) were added to a solution of **7** (64 mg, 0.18 mmol) in dichloromethane (20 ml) while cooling in an ice bath. After stirring at 0 °C for 1 h, a solution of EDC (100 mg, 0.65 mmol) in dichloromethane (5 ml) was introduced slowly. The resulting mixture was stirred at room temperature overnight, washed with aqueous ammonium chloride solution (0.5 M), dried over $MgSO_4$, and evaporated under reduced pressure. The product was isolated by column chromatography on alumina using dichloromethane-ethanol (100 : 1 v/v) as the eluent. Subsequent evaporation afforded amide (S_p,S_p,S_p)–**5** as an orange amorphous solid. Yield: 150 mg (54%).

^{1}H NMR ($CDCl_3$): δ = 2.19 (unresolved t, 2 H), 2.44–2.69 (br m, 2H), 3.18–3.37 (m, 4 H) (4× CH_2); 3.78 (m, 1 H, C_5H_3), 4.13 (s, 5 H, C_5H_5), 4.42 (t, J = 2.6 Hz, 1 H, C_5H_3), 5.08 m, 1 H, C_5H_3), 7.07 (br unresolved t, 1 H, NH), 7.12–7.57 (m, 11 H, PPh_2 + NH); ^{13}C{^{1}H} NMR ($CDCl_3$): δ = 33.86 (br), 39.61, 40.01 and 49.90 (4 × CH_2), 70.96 (C_5H_5), 71.51 (C_5H_3 CH), 72.51 (d, J_{PC} = 2 Hz, C_5H_3 CH), 74.42 (d, J_{PC} = 4 Hz, C_5H_3 CH), 80.37 (d, J_{PC} = 17 Hz, C_5H_3 C_{ipso}), 128.1–128.5 (m, PPh_2, four CH_m + one CH_p), 129.45 (PPh_2 CH_p), 132.04 (d, $^2J_{PC}$ = 18 Hz, PPh_2 CH_o), 135.13 (d, $^2J_{PC}$ = 21 Hz, PPh_2 CH_o), 136.97, 138.98 (2× d, $^1J_{PC}$ = 8 Hz, PPh_2 C_{ipso}), 171.17 (d, $^3J_{PC}$ = 3 Hz, C_5H_3CONH), 173.2 (br, CH_2CONH) (note: the signal due to C_5H_3 C_{ipso} is probably obscured by another resonance); ^{31}P{^{1}H} NMR ($CDCl_3$): δ = −19.6; MS ESI$^+$: m/z = 1548 ([M + H]$^+$), 1570 ([M + Na]$^+$), 1586 ([M + K]$^+$); HR MS (ESI$^+$) calcd for $C_{84}H_{85}{}^{56}Fe_3N_7O_6P_3$ ([M + H]$^+$) 1548.3817, found 1548.3818.

Asymmetric allylic alkylation. A general procedure

Ligand (12.5 µmol), [{Pd(η^3-C_3H_5)Cl}$_2$] (2.3 mg, 6.3 µmol) and alkali metal acetate (25 µmol; if appropriate) were mixed with dry dichloromethane (3 ml), and the mixture was stirred at room temperature for 15 min. Racemic 1,3-diphenylprop-2-en-1-yl acetate (**11**; 63 mg, 0.25 mmol) was introduced next, followed after stirring for another 5 min by *N*,*O*-bis(trimethylsilyl)acetamide (BSA; 0.19 ml, 0.75 mmol) and dimethyl malonate (0.09 ml, 0.75 mmol). The reaction mixture was stirred at room temperature for 24 h and then washed with saturated aqueous NH_4Cl solution (2 × 5 ml). The organic layer was separated, dried over $MgSO_4$, and concentrated under vacuum. Subsequent purification by flash chromatography (silica gel; hexane-ethyl acetate, 3 : 1 v/v) afforded the mixture of the alkylation product and the starting acetate **11**. The conversions were determined by ^{1}H NMR spectroscopy. Enantiomeric excesses were established from ^{1}H NMR spectra recorded in C_6D_6 in the presence of the chiral lanthanide shift reagent tris(3-trifluoroacetyl-*d*-camphorato)europium(III). The configuration of the major component was assigned on the basis of optical rotation of the mixture.[18]

X-ray Crystallography

Single-crystals of (S_p)–**2** suitable for X-ray diffraction analysis were selected directly from the reaction batch (orange-brown block, 0.38 × 0.50 × 0.55 mm^3). Full-set diffraction data ($\pm h$ $\pm k$ $\pm l$; $2\theta \leq 55^\circ$) were collected with a Nonius KappaCCD image plate diffractometer equipped with a Cryostream Cooler (Oxford Cryosystems) at 150(2) K using graphite monochromatized MoK_α radiation (λ = 0.71073 Å) and were analysed with the HKL program package.[19]

The phase problem was solved by direct methods (SIR97[20]) and the structure was refined by full-matrix least squares procedure based on F^2 (SHELXL97[21]). All non-hydrogen atoms were refined with anisotropic displacement parameters. The amide hydrogen atom (H1N) was identified on a difference density map and refined as a riding atom with U_{iso}(H1N) = 1.2 U_{eq}(N). The remaining hydrogen atoms were included in calculated positions and refined as riding atoms with U_{iso}(H) assigned to a multiple of U_{eq}(C) of their bonding carbon atom. Geometric parameters and structural drawings were obtained with a recent version of PLATON program.[22]

Crystallographic data: $C_{26}H_{26}FeNOP$, $M = 455.3$ g mol^{-1}, monoclinic, space group $P2_1$ (no. 4), $a = 9.6809(1)$, $b = 9.6817(2)$, $c = 11.8994(2)$ Å; $\beta = 100.897(1)^\circ$, $V = 1095.19(3)$ Å^3, $Z = 2$, $D = 1.381$ g ml^{-1}, μ(Mo K_α) = 0.779 mm^{-1}; 28 930 diffractions of which 5026 were unique and 4895 observed according to $I_o > 2\sigma(I_o)$ criterion ($R_{int} = 1.65\%$); 272 parameters, R(observed diffractions) = 2.15%, R(all data) = 2.26%, wR(all data) = 5.31%, Flack's enantiomorph parameter: 0.002(9).

The crystallographic data for (S_p)-**2** have been deposited at the Cambridge Crystallographic Centre as supplementary publication CCDC-749434. This data can be obtained free of charge from the Cambridge Crystallographic Centre, via http://www.ccdc.cam.ac.uk/data_request/cif.

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