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Chiral Phosphinooxazolines with a Pentamethylferrocene Backbone—Synthesis and Use as Ligands in Asymmetric Catalysis

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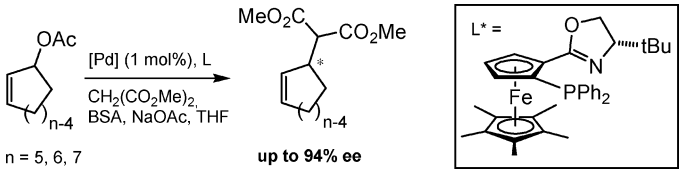

Novel phosphinooxazolines, containing a unit of central and a unit of planar chirality in a matched case combination, have been successfully tested in the Pd-catalyzed asymmetric allylic substitution with cycloalkenyl acetates as substrates.

Introduction

Pd-catalyzed asymmetric allylic substitutions[1] have been successfully applied in organic synthesis.[2] Numerous chiral ligands have been tested, however, only a few have been found that induce an enantiomeric excess of >90% in the reaction with a cyclic substrate.[3] Only a few of these ligands have been applied in syntheses of biologically active compounds. These are the ligands **A** and **B**, developed in our group and Trost's ligand **C**, which is a member of a large class of ligands (Figure 1).[3a−c]

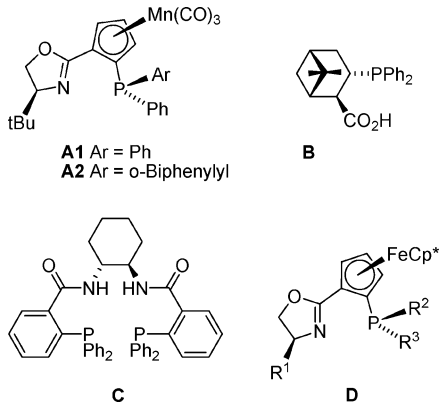

FIGURE 1. Chiral ligands useful in Pd-catalyzed allylic substitutions at cyclic substrates.

The basis of the design of ligands **A** is conformational confinement of the aryl groups at P by the $Mn(CO)_3$ moiety via a steric effect. With ligand **A1**, containing a PPh_2 group, moderate enantioselectivities were achieved; the ligand **A2**,

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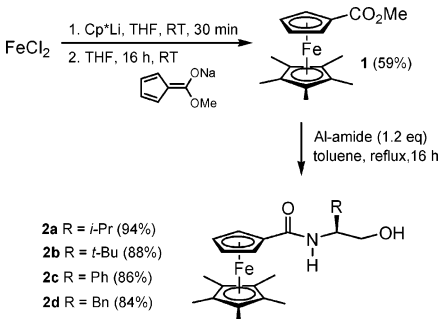
SCHEME 1



containing an *o*-biphenylyl group at P, induced an excellent enantiomeric excess of >90% ee. We wondered whether a similar effect would be obtained upon replacement of the cymantrene by a pentamethylferrocene unit, that is, with ligands of the type **D**. Ligands **D** are generally more electron rich than ligands **A**; it was hoped that the large steric bulk of the pentamethylcyclopentadienyl (Cp*) moiety might give rise to high levels of enantioselection even for ligands **D** with a nonstereogenic phosphino group, for example $PR^2R^3 = PPh_2$. Ligands with a planar-chiral pentamethylferrocene unit have previously been prepared by Fu and co-workers and Togni and co-workers.[4]

Ligands with a planar-chiral ferrocene unit,[5] including phosphinooxazolines with a ferrocene backbone, have been extensively studied, and their synthesis is well-established. The key step in the preparation of the phosphinoxazolines is directed lithiation of a chiral oxazoline.[6] This reaction usually proceeds with a high degree of diastereoselection and was also applied here.

Results and Discussion

At the early stage of the project, pentamethylferrocene carboxylic acid amides **2** (Scheme 1) were prepared from pentamethylferrocene via pentamethylferrocene carboxylic acid, which was prepared according to a procedure of Bildstein et al.[7] The acid was treated with oxalyl chloride to give the acid chloride, and this was reacted with the amino alcohol. The yields were generally poor.[8] As a consequence, a new route was worked out, involving aminolysis of the ester **1** (Scheme 1), that eventually allowed the preparation of amides **2a**−**d** (Scheme 2) from readily available starting materials in satisfactory yields.

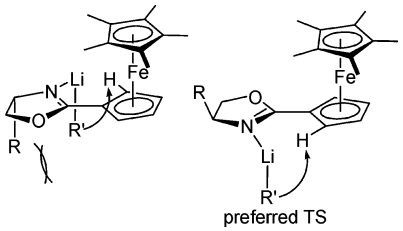
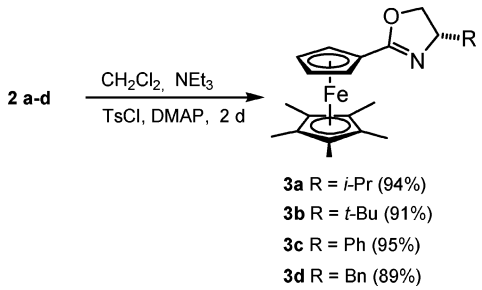


FIGURE 2. Stereoselective directed lithiation.

SCHEME 2



The requisite pentamethylferrocene carboxylic acid methyl ester **1** was prepared by reaction of $FeCl_2$ with 1.1 equiv of lithium pentamethyl cyclopentadienide and 1.0 equiv of sodium methoxycarbonylcyclopentadienide,[9] using a procedure developed for the synthesis of pentasubstituted acylferrocenes[10] (Scheme 1). Decamethylferrocene, produced in small amount as a side product, could be easily removed by filtrative column chromatography. The preparation of **1** has been carried out on a 200 mmol scale.

Reaction of the ester **1** with aluminum amides[11] in refluxing toluene furnished the amides **2a**−**d** in yields of 84−94% (Scheme 1). Lower yields (41−72%) were obtained with lithium or sodium amides or with the use of solvents with a boiling point lower than that of toluene. The amides **2** were transformed into the oxazolines **3** by treatment with *p*-TsCl/triethylamine and a catalytic amount of DMAP (Scheme 2).

As mentioned above, the directed metalation of ferrocenyloxazolines is an established reaction and allows electrophiles to be introduced conveniently.[6] The steric course anticipated for reactions with oxazolines **3a**−**d** is described in Figure 2.

Nevertheless, there was no information available on the metalation of pentamethylferrocenyloxazolines. Accordingly, suitable reaction conditions had to be worked out for compounds **3a**−**d** (Table 1).

Preliminary experiments quickly revealed that *t*-BuLi was not suited as a base because of metalation of the methyl groups of the Cp* moiety. Similarly, reaction with *s*-BuLi/Et_2O followed by quenching with a chlorophosphane gave poor results (Table 1, entry 1). Better results were generally achieved with *s*-BuLi/TMEDA.

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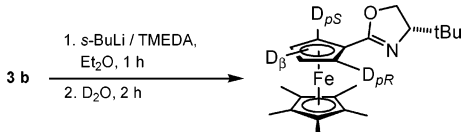
TABLE 1. Synthesis of L1−L5 from Oxazolines 3a−3d, According to Scheme 4

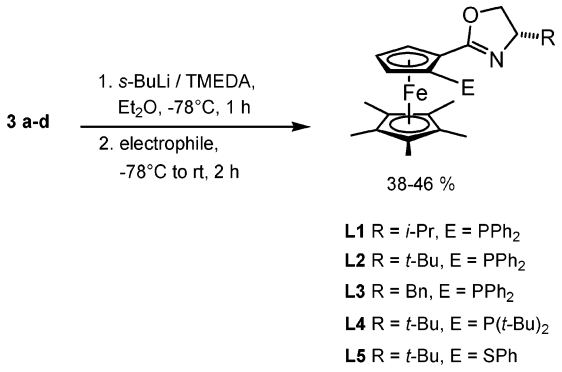
entry	R	equiv of *s*-BuLi	equiv of TMEDA	electrophile	conv.[a] (%)	yield[b] (%)	de[c]
1	*t*-Bu	1.1	0	PPh_2Cl	<5	n.d.	n.d.
2	*t*-Bu	1.1	1.1	PPh_2Cl	31	n.d.	>99
3	*t*-Bu	1.1[d]	1.1	PPh_2Cl	23	n.d.	92
4[e]	Bn	1.2	1.2	PPh_2Cl	42	n.d.	63
5	*i*-Pr	1.1	1.1	PPh_2Cl	38	n.d.	>99
6	Bn	1.3	1.3	PPh_2Cl	n.d.	40	98
7	*i*-Pr	1.3	1.3	PPh_2Cl	n.d.	46	>99
8	*t*-Bu	1.3	1.3	PPh_2Cl	59	38	>99
9	*t*-Bu	1.3	1.3	$P(t\text{-Bu})_2Cl$	n.d.	37	>99
10	*t*-Bu	1.3	1.3	$(PhS)_2$	52	42	>99

[a] Determined by ^{1}H NMR. [b] Determined by column chromatography. [c] Determined by ^{1}H NMR or ^{31}P NMR. [d] Metalation with *n*-BuLi. [e] *n*-Hexane was used as solvent.

SCHEME 3



SCHEME 4



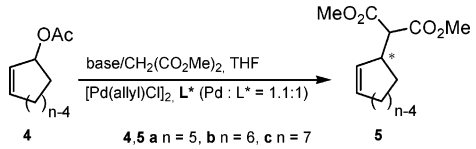
To assess the efficiency of the metalation step, lithiation of the oxazoline **3b** was carried out at −78, −40, and 0 °C with 1.3 equiv of *s*-BuLi/TMEDA, followed by quenching with D_2O after 1 h (Scheme 3). At −78 °C, 74% (*pR*)-monodeuteration occurred. The reaction at −40 °C gave rise to 95% deuterium in the (*pR*) and 14% in the (*pS*) position. After the metalation at 0 °C, 59% of the deuterium was found in the (*pR*), 19% in the (*pS*), and 14% in the β position. Accordingly, the metalation as well as the subsequent reaction with an electrophile have to be carried out at a temperature well below −40 °C.

In the reaction with Ph_2PCl and $(PhS)_2$, significant conversion was only achieved after metalation with *s*-BuLi/TMEDA. The diastereomeric purity of the coupling products was excellent: >99% for the formation of **L1**, **L2**, **L4**, and **L5** (cf. Table 1, entries 2, 5 and 7−10). In the case of oxazoline **3c**, the dihydrooxazolyl group was metalated at the ═N−CH position, according to the ^{1}H NMR spectrum of the crude product. With *n*-hexane as solvent, slightly improved yield but very low diastereoselectivity was obtained (Table 1, entry 4).

The relative configurations of the products **L1**−**L5**, as given in Scheme 4, is assumed to be the same as those of the 2-substituted ferrocenyloxazolines, prepared in the same way by Richards and Sammakia.[6] In the case of **L2**, this assumption was proven correct by the X-ray crystal analyses of two cationic Pd complexes containing diastereomerically pure **L2** (see below).

Ligands **L1**−**L5** were tested in the asymmetric allylic alkylation of cyclic substrates **4** with dimethyl sodiomalonate (see Scheme 5 and Table 2). The latter was generated from dimethyl malonate either by a reaction with NaH or in situ by an addition of *N*,*O*-bistrimethylsilyl acetamide (BSA)/sodium acetate to the reaction mixture. In all reactions, the products with the (*R*) configuration were preferentially formed.[12] This was also found for allylic substitutions promoted by ligands **A1** and **A2** (cf. Figure 1, Table 2, entries 20−22).

SCHEME 5



Substrate **4b** was used for the optimization of reaction conditions and the assessment of ligands (Table 2, entries 1−11) because of the particularly convenient determination of the enantiomeric excess of the substitution product **5b**. The best results were obtained with ligand **L2** in conjunction with the BSA method using THF or dioxane as solvent (Table 2, entries 4 and 9). Similar results were obtained with DMF as solvent; however, reactions were slower than with THF. While results with **L1** and **L3** were acceptable, those with **L4** and **L5** were not. Typical for many Pd-catalyzed allylic substitutions using N,S-chelate ligands,[13] reactions promoted by **L5** displayed low yield because of the precipitation of metallic palladium.

Typical for most Pd-catalyzed allylic substitutions of cyclic substrates,[3] reactions of the seven-membered substrate **4c** displayed the highest level of selectivity (Table 2, entry 12).

Cyclopentenyl acetate **4a**, expectedly,[3] was the most reactive substrate (Table 2, entries 13−19). This allowed the lowering of the reaction temperature to −30 °C; at this temperature, essentially quantitative yield and an enantiomeric excess of 92% was achieved (Table 2, entries 18 and 19).

The results achieved with ligand **L2** are surprisingly good in comparison with those previously obtained with the ligand **A1** (cf. Table 2, entry 20). They are indeed similar to those obtained with the more complicated ligand **A2** containing a stereogenic phosphorus center. The configuration of the products (*R*) are as expected for reactions proceeding via an *exo*-[(π-allyl)-(PHOX)] complex (cf. Figure 5), with a preferred addition of the nucleophile at the allylic C trans to phosphorus.

To shed further light on the intermediary π-allyl complexes, the complexes **K1** and **K2** were prepared (Scheme 6). These were obtained by a reaction of the commercially available complex **6a** and complex **6b**[14] with **L2**, followed by an anion exchange by the addition of $AgSbF_6$. In $CDCl_3$ solution, **K1** consisted of a mixture of two η^3-allyl complexes in a ratio of 77:23, and **K2** consisted of two complexes in a ratio of 99:1 (^{31}P NMR).

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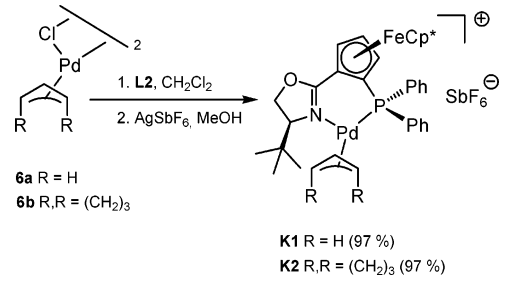
TABLE 2. Allylic Alkylation of Cyclic Substrates 4a−c, According to Scheme 5

entry	*n*	ligand[a]	solvent	base	temp (°C)	time (h)	conv.[b] (%)	yield[c] (%)	ee (%)
1	6	**L1**[d]	THF	NaH	20	1.5	>99	n.d.	73 (*R*)[f]
2	6	**L2**[e]	THF	NaH	20	2	>99	94	81 (*R*)[f]
3	6	**L3**[d]	THF	NaH	20	4	92	n.d.	66 (*R*)[f]
4	6	**L2**[e]	THF	BSA	20	5	98	92	84 (*R*)[f]
5	6	**L2**[e]	DMF	NaH	20	2	99	n.d.	81 (*R*)[f]
6	6	**L2**[e]	DMF	NaH	0	16	>99	n.d.	84 (*R*)[f]
7	6	**L2**[e]	DMF	BSA	20	5	>99	n.d.	80 (*R*)[f]
8	6	**L2**[e]	CH_2Cl_2	BSA	20	4	>99	n.d.	78 (*R*)[f]
9	6	**L2**[e]	dioxane	BSA	20	5	86	n.d.	85 (*R*)[f]
10	6	**L4**[d]	THF	BSA	20	5	97	n.d.	15 (*R*)[f]
11	6	**L5**[e]	THF	BSA	20	16	<5	n.d.	n.d.
12	7	**L2**[d]	THF	BSA	20	3	>99	93	94 (*R*)[g]
13	5	**L2**[e]	THF	NaH	20	<0.1	>99	n.d.	64 (*R*)[h]
14	5	**L2**[e]	DMF	NaH	20	<0.1	>99	95	79 (*R*)[h]
15	5	**L2**[e]	THF	BSA	20	<0.1	>99	n.d.	83 (*R*)[h]
16	5	**L2**[e]	THF	BSA	0	<0.1	>99	96	88 (*R*)[h]
17	5	**L2**[e]	THF	BSA	−20	4	>99	97	91 (*R*)[h]
18	5	**L2**[e]	THF	BSA	−30	16	>99	96	92 (*R*)[h]
19	5	**L2**[e]	DMF	NaH	−30	48	>99	97	92 (*R*)[h]
20[i]	6	**A1**[e]	THF	NaH	20	0.2	n.d.	97	31 (*R*)[f]
21[i]	6	**A2**[e]	THF	NaH	20	0.2	n.d.	95	85 (*R*)[f]
22[i]	6	**A2**[e]	DMF	NaH	20	0.6	n.d.	97	87 (*R*)[f]

[a] Molar ratio of ligand/Pd = 1.1:1. [b] Determined by GC: Chrompack permethyl β-CD (see footnotes f and g below). [c] Isolated yield after column chromatography. [d] 4.4 mol % of ligand. [e] 1.1 mol % of ligand. [f] Determination by GC: Chrompack permethyl β-CD, 110 °C, t_R [(*S*)-**5b**] = 44.5 min, t_R [(*R*)-**5b**] = 45.8 min. [g] Determination by GC: Chrompack permethyl β-CD, 100 °C, t_R [(*R*)-**5c**] = 135.6 min, t_R [(*S*)-**5c**] = 141.4 min. [h] Determined via an iodolactone as the derivative, as described in ref 2g. [i] Data taken from ref 3a.

SCHEME 6



Crystals suitable for X-ray crystal structure determination were grown by slow diffusion (rt) of diethyl ether into the solution of the complex in CH_2Cl_2.[15] In the case of **K1**, the crystal contained two *exo*-complexes in 1:1 ratio that displayed small differences in the positions of the Ph and the Cp* groups. In the case of **K2** only the *exo*-complex was found in the crystal (Figures 3 and 4).

Characteristic structural data is presented in the Supporting Information and Figures 4 and 6. Typical for all (π-allyl)-(PHOX)Pd complexes is the long bond between Pd and the allylic terminus ($C3_a$) in a trans position relative to phosphorus (bond lengths Pd−$C3_a$ = 2.262 Å and Pd−$C1_a$ = 2.128 Å for **K2**), that is, the bond broken in the allylic substitution to give the product configuration that is observed (*R*) (cf. Figure 5).[16]

In the case of **K1**, the conformation of the PHOX ligand relative to the coordination plane [N,Pd,P], mainly determined by the angle χ, the angle between the 'best-fit' plane through the ligand atoms N, C2, C6, C7, and P and the plane [N,Pd,P] (cf. Figure 4), is similar to that of the corresponding Pd complex of **A2**. However, the angle χ of complex **K2** is extremely small, that is, this complex possesses an unusually flat backbone. This is immediately apparent upon inspection of the model displayed in Figure 6. A consequence is stronger shielding of the half space of the coordination plane containing the *tert*-butyl and the Ph_{Re} group. This is in accord with the very pronounced preference of the exo isomer in the case of **K2**. Thus, the structural features support the view that the preferred enantiomer arises by the addition of the nucleophile at the allylic carbon trans to P of the *exo*-π-allyl complex.

In conclusion, sterically highly demanding planar chiral PHOX ligands with a pentamethylferrocene backbone have been synthesized and used as ligands in Pd-catalyzed asymmetric allylic alkylations of cyclic substrates. With the ligand **L2**, excellent yield and enantioselectivity were achieved at a low load of the catalyst.

Experimental Section

Methyl 1′,2′,3′,4′,5′-Pentamethylferrocenecarboxylate (1). A: A suspension of $FeCl_2$ (10.4 g, 82.0 mmol) in THF (800 mL) was vigorously stirred in the dark for 5 h.

B: A mixture of sodium cyclopentadienide (45.0 mL of a 2.0 M solution in THF, 90.0 mmol) and dimethyl carbonate (13.4 mL, 148.8 mmol) in THF (80 mL) was heated at reflux for 4 h.

C: For the preparation of lithium pentamethylcyclopentadienide, *n*-BuLi (56.7 mL of a 1.6 M solution in *n*-hexane, 90.0 mmol) was added dropwise to a cooled (−78 °C) solution of pentamethylcyclopentadiene (14.1 mL, 90.0 mmol) in THF (200 mL), and the resultant mixture was stirred at room temperature for 2 h.

The suspension C was transferred via cannula to the suspension A, and the mixture was stirred at room temperature for 1 h; its color turned to green. Then suspension B was added via cannula,

(15) Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-293068 (**K1**) and CCDC-293069 (**K2**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax, (+44)1223−336−033; e-mail, deposit@ccdc.cam.ac.uk).

(16) For systematic studies on crystal structures of [(η^3-allyl)(PHOX)-Pd] complexes, see: (a) Kollmar, M.; Goldfuss, B.; Reggelin, M.; Rominger, F.; Helmchen, G. *Chem.—Eur. J.* **2001**, *7*, 4913−4927. (b) Kollmar, M.; Steinhagen, H.; Janssen, J. P.; Goldfuss, B.; Malinovskaya, S. A.; Vázquez, J.; Rominger, F.; Helmchen, G. *Chem.—Eur. J.* **2002**, *8*, 3103−3114. (c) Zehnder, M.; Schaffner, S.; Neuburger, M.; Plattner, D. A. *Inorg. Chim. Acta* **2002**, *337*, 287−298 and references therein.

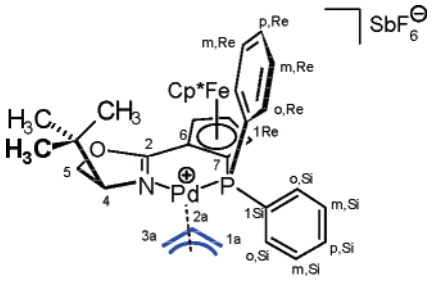


FIGURE 3. Atom numbering for **K1a**.

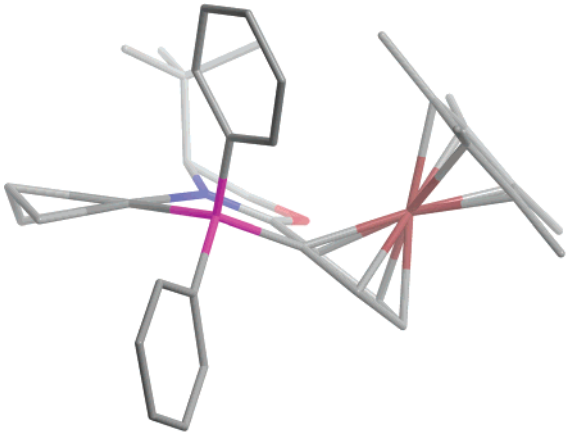


FIGURE 4. X-ray crystal structure of **K1a** (hydrogen atoms and the counteranion are omitted); color coding according to the Chem3D ultra program; selected bond lengths (Å) with estimated standard deviations, Pd−$C1_a$, 2.101(3); Pd−$C2_a$, 2.181(3); Pd−$C3_a$, 2.240(3); selected angle (χ), angle between the "best-fit" plane through the ligand atoms N, C2, C6, C7, and P and the plane [N,Pd,P] = 23.4°.

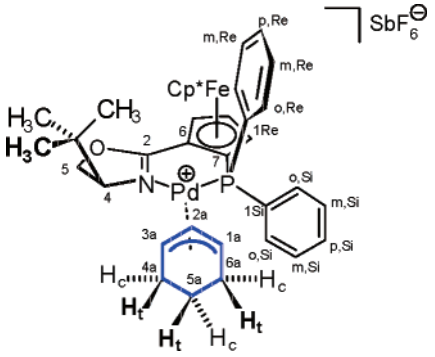


FIGURE 5. Atom numbering for **K2**.

and the resultant mixture was stirred at room temperature for 16 h. The solvents were then removed in vacuo, the residue was dissolved in ether/*n*-pentane 1:1, and the solution was filtered through a short pad of alumina (neutral, 13% H_2O). A ^{1}H NMR spectrum of the crude product showed a mixture of **1** (93%), dimethyl ferrocenedicarboxylate (5%), and ferrocenes (1,2,3,4,5-pentamethylferrocene and decamethylferrocene, 2%). Column chromatography (silica, petroleum ether/diethyl ether, 9:1) afforded 15.25 g (59%) of pure **1** as an orange solid. Mp 96−98 °C. TLC: R_f = 0.34 (petroleum ether/diethyl ether, 9:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 4.26 (t, J = 1.8 Hz, 2H, H_{Fc}), 3.94 (t, J = 1.8 Hz, 2H, H_{Fc}), 3.81 (s, 3H, CO_2CH_3), 1.82 (s, 15H, C_{Fc}—CH_3). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 171.5 (s, CO_2CH_3), 81.8 (5s, C_{Fc}—CH_3), 79.2 (s, C_{Fc}—CO_2CH_3), 75.6 (2d, C_{Fc}—H), 72.9 (2d, C_{Fc}—H), 51.4 (q, CO_2CH_3), 10.8 (5q, C_{Fc}—CH_3). HRMS (FAB) *m*/*z* calcd for

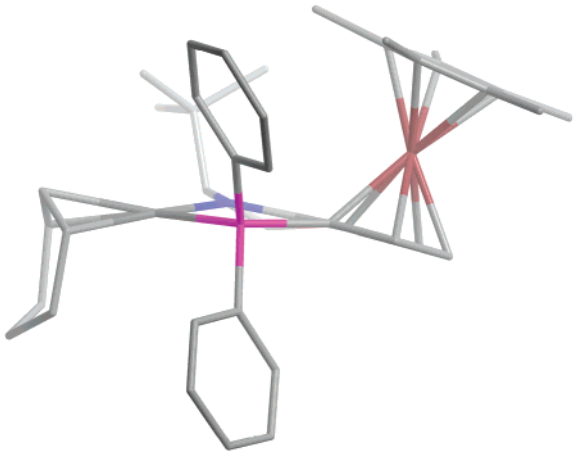


FIGURE 6. X-ray Crystal Structure of **K2** (hydrogen atoms and the counteranion are omitted); color coding according to the Chem3D ultra program; selected bond lengths (Å) with estimated standard deviations, Pd−$C1_a$, 2.128(3); Pd−$C2_a$, 2.149(3); Pd−$C3_a$, 2.262(3); selected angle (χ), angle between the "best-fit" plane through the ligand atoms N, C2, C6, C7, and P and the plane [N,Pd,P] = 7.3°.

$C_{17}H_{22}O_2Fe$ (M^+), 314.0969; found, 314.0984. Anal. Calcd for $C_{17}H_{22}O_2Fe$: C, 64.99; H, 7.06. Found: C, 65.20; H, 6.97.

General Procedure for the Preparation of the Amides 2a−d. A solution of Me_3Al (2.0 M in toluene, 2.28 equiv) was added dropwise to a cold (0 °C) about 0.4 M solution of (*S*)-amino alcohol (1.2 equiv) in toluene. The mixture was allowed to warm to room temperature and was further stirred for 60 min. Then ester **1** was added in one portion. The resulting orange mixture was heated at reflux for 16 h (72 h in the case of **2b**). After cooling to room temperature, a 20% aqueous solution of Seignette's salt was added with care, and the resultant mixture was vigorously stirred for at least 2 h. The organic layer was separated, and the aqueous layer was extracted several times with EtOAc. The organic layers were combined, washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica, petroleum ether/ethyl acetate, 2:1).

(1*S*)-*N*-(1-Hydroxymethyl-2,2-dimethylprop-1-yl)-1′,2′,3′,4′,5′-pentamethylferroceneamide (2b). Following the general procedure, **1** (6.00 g, 19.1 mmol), (*S*)-*tert*-leucinol (2.69 g, 22.9 mmol), and Me_3Al (21.0 mL of a 2.0 M solution in toluene, 42.0 mmol) were reacted in toluene (55 mL) to afford 6.74 g (88%) of **2b** as yellow solid. Mp 126−127 °C. TLC: R_f = 0.17 (petroleum ether/ethyl acetate 2:1). $[\alpha]^{20}_D$ −56.2 (*c* 0.34, EtOH). ^{1}H NMR (300.13 MHz, CD_2Cl_2): δ 5.68 (d, J = 5.8 Hz, 1H, CONH), 4.07 (br s, 1H, H_{Fc}), 4.04 (br s, 1H, H_{Fc}), 3.90 (br s, 2H, H_{Fc}), 3.85 (m, 1H, CH_2OH), 3.77 (dt, J = 7.5, 2.6 Hz, 1H, NHC*H*), 3.59 (dd, J = 10.6, 7.5 Hz, 1H, CH_2OH), 3.55 (br s, 1H, OH), 1.82 (s, 15H, C_{Fc}—CH_3), 1.00 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 171.4 (s, CONH), 81.3 (5s, C_{Fc}—CH_3), 77.5 (s, C_{Fc}—CONH), 74.7 (2d, C_{Fc}—H), 70.6 (2d, C_{Fc}—H), 64.6 (t, CH_2OH), 61.3 (d, NHCH), 33.3 (s, $C(CH_3)_3$), 27.0 (3q, $C(CH_3)_3$), 10.5 (5s, C_{Fc}—CH_3). HRMS (FAB) *m*/*z* calcd for $C_{22}H_{33}NO_2Fe$ (M^+), 399.1861; found, 399.1805. Anal. Calcd for $C_{22}H_{33}NO_2Fe$: C, 66.17; H, 8.33; N, 3.51. Found: C, 65.92; H, 8.45; N, 3.74.

General Procedure for the Preparation of Oxazolines 3a−d. A solution of amide **2** and NEt_3 (5 equiv) in CH_2Cl_2 (6 equiv) was stirred with molecular sieves (4 Å) at room temperature for 1 h. Then TsCl (1.05 equiv) was added, and the reaction mixture was stirred at room temperature for 2 d. It was then treated with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. Drying over anhydrous Na_2SO_4, filtration, and concentration in vacuo gave the crude product, which was purified by column chromatography (silica, petroleum ether/ethyl acetate, 9:1).

1-[4(*S*)-*tert*-Butyl-2-oxazolin-2-yl]-1′,2′,3′,4′,5′-pentamethylferrocene (3b). Following the general procedure, **2b** (0.876 g, 2.19 mmol) was reacted with TsCl (0.423 g, 2.21 mmol) in a mixture of NEt_3 (1.34 mL, 9.6 mmol) and CH_2Cl_2 (0.81 mL, 11.6 mmol) to afford 0.758 g (91%) of **3b** as an orange liquid. TLC: R_f = 0.47 (petroleum ether/ethyl acetate, 9:1). $[\alpha]^{20}_D$ 49.6 (*c* 0.63, $CHCl_3$). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 4.28 (m_c, 1H, H_{Fc}), 4.26 (dd, J = 9.8, 8.4 Hz, 1H, OCH_2), 4.15 (m_c, 1H, H_{Fc}), 4.06 (t, J = 8.4 Hz, 1H, OCH_2), 3.92 (dd, J = 9.8, 8.6 Hz, 1H, C═N−CH), 3.85 (t, J = 1.9 Hz, 2H, H_{Fc}), 1.84 (s, 15 H, C_{Fc}−CH_3), 0.94 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 165.1 (s, OC═N), 81.6 (5s, C_{Fc}−CH_3), 77.6 (d, C═N−*C*H), 74.4 (d, C_{Fc}−H), 74.2 (d, C_{Fc}−H), 72.4 (s, C_{Fc}−C_{ox}), 71.8 (d, C_{Fc}−H), 71.6 (d, C_{Fc}−H), 68.3 (t, OCH_2), 34.0 (s, $C(CH_3)_3$), 26.5 (3q, $C(CH_3)_3$), 11.0 (5q, C_{Fc}−CH_3). HRMS (EI) *m*/*z* calcd for $C_{22}H_{31}NOFe$ (M^+), 381.1755; found, 381.1746. Anal. Calcd for $C_{22}H_{31}NOFe$: C, 69.29; H, 8.19; N, 3.67. Found: C, 69.13; H, 8.25; N, 3.61.

General Procedure for the Preparation of L1−L5. A cold (−78 °C) solution of **3** and TMEDA (1.3 equiv) in Et_2O was treated dropwise with precooled *sec*-butyllithium (1.3 M solution in cyclohexane, 1.3 equiv). The resultant solution was stirred for 1 h, treated with an electrophile (1.3 equiv), and then allowed to warm to room temperature over a period of 2 h. The solvent was removed in vacuo, the resulting slurry was treated with aqueous $NaHCO_3$ solution, and the mixture was then extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (silica, CH_2Cl_2/MeOH, 99:1). In all cases, starting material was recovered.

1-[4(*S*)-*tert*-Butyl-2-oxazolin-2-yl]-2(p*S*)−(diphenylphosphino)-1′,2′,3′,4′,5′-pentamethylferrocene (L2). Following the general procedure, **3b** (3.263 g, 8.56 mmol) was reacted with *sec*-butyllithium (8.56 mL of a 1.3 M solution in cyclohexane, 11.13 mmol), TMEDA (1.65 mL, 11.13 mmol), and PPh_2Cl (2.456 g, 11.13 mmol) in Et_2O (8.5 mL) to afford (after workup) 1.842 g (3.26 mmol, 38%) of **L2** as a yellow solid. Mp 105−108 °C. TLC: R_f = 0.64 (CH_2Cl_2/MeOH, 98:2). $[\alpha]^{20}_D$ 185 (*c* 0.28, EtOH). ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 7.57−7.51 (m, 2H, H_{Ph}), 7.35−7.27 (m, 3H, H_{Ph}), 7.19−7.11 (m, 5H, H_{Ph}), 4.49 (br s, 1H, H_{Fc}), 4.16 (t, J = 9.0 Hz, 1H, OCH_2), 3.94 (t, J = 2.4 Hz, 1H, H_{Fc}), 3.73 (t, J = 9.2 Hz, 1H, C═N−CH), 3.55 (t, J = 8.5 Hz, 1H, OCH_2), 3.27 (br s, 1H, H_{Fc}), 1.82 (s, 15H, C_{Fc}−CH_3), 0.65 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 164.8 (s, OC═N), 140.7 (d, $^1J_{C,P}$ = 14.1 Hz, C_{Ph}−P), 139.0 (d, $^1J_{C,P}$ = 14.1 Hz, C_{Ph}−P), 136.2 (d, C_{Ph}), 136.0 (d, C_{Ph}), 132.7 (d, C_{Ph}), 132.6 (d, C_{Ph}), 129.3 (d, C_{Ph}), 128.4 (d, C_{Ph}), 128.3 (d, C_{Ph}), 128.3 (d, C_{Ph}), 128.2 (d, C_{Ph}), 127.9 (d, C_{Ph}), 81.9 (5s, C_{Fc}−CH_3), 78.9 (d, $^1J_{C,P}$ = 15.2 Hz, C_{Fc}−P), 76.8 (d, C_{Fc}−H), 76.2 (d, C═N−*C*H), 75.7 (d, C_{Fc}−H), 75.5 (d, C_{Fc}−H), 68.4 (t, OCH_2), 33.7 (s, $C(CH_3)_3$), 26.2 (3q, $C(CH_3)_3$), 11.1 (5q, C_{Fc}−CH_3). ^{31}P NMR (202.46 MHz, $CDCl_3$): δ −23.8. HRMS (FAB) *m*/*z* calcd for $C_{34}H_{40}NOPFe$ (M^+), 565.2197; found, 565.2204. Anal. Calcd for $C_{34}H_{40}NOPFe$: C, 72.21; H, 7.13; N, 2.48; P, 5.48. Found: C, 71.92; H, 7.11; N, 2.49; P, 5.61.

General Procedure for the Allylic Alkylation of Cyclic Substrates 4. Dimethyl Sodiomalonate as a Nucleophile: A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (5 μmol) and the ligand (11 μmol) in dry THF (1 mL) was stirred for 10 min at room temperature. Substrate **4** (1.0 mmol) was added, and the resultant orange-red mixture was stirred for 10 min at room temperature. The reaction temperature was adjusted, and a clear solution of dimethyl sodiomalonate, kept at the same temperature, was added. This was prepared from dimethyl malonate (1.5 mmol) and sodium hydride (1.1 mmol) in THF (4 mL). Conversion was monitored by TLC (petroleum ether/ethyl acetate, 4:1, detection of spots with iodine vapor). After the complete reaction, saturated aqueous NH_4Cl solution (10 mL) was added, and the mixture was extracted with ethyl acetate (5 × 20 mL). The organic layer wasdried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to column chromatography (silica, *n*-pentane/diethyl ether, 9:1).

BSA-Method: A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (5 μmol) and the ligand (11 μmol) in dry THF (1 mL) was stirred for 10 min at room temperature. Substrate **4** (1.0 mmol) was added, and the resultant orange-red mixture was stirred for 10 min at room temperature. The reaction temperature was adjusted, and then dimethyl malonate (3.0 mmol) and BSA (3.0 mmol) were added. The reaction was started by the addition of sodium acetate (0.03 mmol), and the conversion was monitored by TLC (petroleum ether/ethyl acetate, 4:1, detection of spots with iodine vapor). After the disappearance of the substrate, saturated aqueous NH_4Cl solution (10 mL) was added, and the mixture was extracted with ethyl acetate (5 ×). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to column chromatography (silica, *n*-pentane/diethyl ether, 9:1).

Complex K1. A mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (18.3 mg, 50.0 μmol), **L2** (56.6 mg, 100.0 μmol), and CH_2Cl_2 (2 mL, degassed) was stirred for 10 min at room temperature to give a clear orange-red solution. Then a solution of $AgSbF_6$ (34.4 mg, 100.0 μmol) in methanol (0.5 mL, degassed) was added, and the resultant dark-red mixture was stirred for 1 h under exclusion of light. Filtration through Celite and evaporation of the solvents yielded 92.9 mg (97%) of **K1** as a red solid. Crystals suitable for X-ray crystal structure determination were grown by slow diffusion of Et_2O into a solution of **K1** in CH_2Cl_2 at room temperature. Structure **a** (77%): ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.94−7.82 (m, 2H, H_{Ph}), 7.80−7.64 (m, 3H, H_{Ph}), 7.36−7.26 (m, 3H, H_{Ph}), 6.93−6.83 (m, 2H, H_{Ph}), 5.62 (m_c, 1H, H_{allyl}), 4.91 (m, 1H, H_{allyl}), 4.76 (m, 1H, H_{Fc}), 4.65 (m, 1H, OCH_2), 4.57 (dd, J = 9.2, 5.5 Hz, 1H, OCH_2), 4.40 (m, 1H, H_{Fc}), 4.33 (m, 1H, H_{Fc}), 4.19 (m, 1H, C═N−CH), 3.84 (dd, J = 14.1, 8.6 Hz, 1H, H_{allyl}), 3.14 (m, 1H, H_{allyl}), 1.46 (s, 15H, C_{Fc}−CH_3), 1.41 (m, 1H, H_{allyl}), 1.13 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 174.9, 136.4 ($J_{C,P}$ = 16.0 Hz), 133.2, 131.2 ($J_{C,P}$ = 13.2 Hz), 130.2, 130.1 ($J_{C,P}$ = 12.2 Hz), 128.8 ($J_{C,P}$ = 12.2 Hz), 121.7, 87.2, 84.3, 81.1, 80.1, 79.2, 70.7, 55.3, 35.0, 27.3, 10.9, quartet of C's missing; ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 16.6. Structure **b** (23%): ^{1}H NMR (500.13 MHz, $CDCl_3$) δ 8.09−7.98 (m, 2H, H_{Ph}), 7.80−7.64 (m, 3H, H_{Ph}), 7.36−7.26 (m, 3H, H_{Ph}), 6.93−6.83 (m, 2H, H_{Ph}), 5.24 (m_c, 1H), 4.81−4.68 (m, 2H), 4.65 (m, 1H), 4.57 (m, 1H), 4.40 (m, 1H), 4.33 (m, 1H), 4.11 (m, 1H), 3.51 (m, 1H), 2.84 (m, 1H), 2.33 (m, 1H), 1.46 (s, 15H, C_{Fc}−CH_3), 1.18 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75.47 MHz, $CDCl_3$) intensities too low for safe assignments; ^{31}P NMR (121.49 MHz, $CDCl_3$) δ 14.7. HRMS (FAB) *m*/*z* calcd for $C_{37}H_{45}NOPFe^{110}Pd^{121}SbF_6$ (M^+), 951.0582; found, 951.0594; *m*/*z* calcd for $C_{37}H_{45}NOPFe^{108}Pd^{121}SbF_6$ (M^+), 949.0569; found, 949.0573; *m*/*z* calcd for $C_{37}H_{45}NOPFe^{106}Pd^{121}SbF_6$ (M^+), 947.0565; found, 947.0557; *m*/*z* calcd for $C_{37}H_{45}NOPFe^{105}Pd^{121}SbF_6$ (M^+), 946.0582; found, 946.0579.

Complex K2. A mixture of $[Pd(\eta^3\text{-}C_6H_9)Cl]_2$ (19.7 mg, 44.2 μmol), **L2** (50.1 mg, 88.6 μmol), and CH_2Cl_2 (2 mL, degassed) was stirred for 10 min at room temperature to give a clear orange-red solution. Then a solution of $AgSbF_6$ (30.4 mg, 88.6 μmol) in methanol (0.5 mL, degassed) was added, and the resultant dark red mixture was stirred for 1 h under exclusion of light. Filtration through Celite and evaporation of the solvents yielded 85.1 mg (86.1 μmol, 97%) of **K2** as a red solid. Crystals suitable for X-ray crystal structure determination were grown by slow diffusion of Et_2O into a solution of **K2** in CH_2Cl_2 at room temperature. ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 7.95−7.79 (m, 2H, H_{Ph}), 7.75−7.60 (m, 3H, H_{Ph}), 7.39−7.29 (m, 3H, H_{Ph}), 7.03−6.86 (m, 2H, H_{Ph}), 5.90 (m_c, 1H, H_{allyl}), 5.61 (t, J = 7.0 Hz, 1H, H_{allyl}), 4.74 (m_c, 1H, H_{Fc}), 4.61 (t, J = 9.4 Hz, 1H, OCH_2), 4.57 (m, 1H, OCH_2), 4.39 (m, 2H, H_{Fc}), 4.22 (dd, J = 9.7, 5.1 Hz, 1H, C═N−CH), 3.95 (m, 1H, H_{allyl}), 1.97 (m, 1H, CH_2), 1.71 (m, 1H, CH_2), 1.44 (s, 15H, C_{Fc}−CH_3), 1.16 (m, 1H, CH_2), 1.14 (s, 9H, $C(CH_3)_3$), 0.91−0.75 (m, 2H, CH_2), −0.34 (m, 1H, CH_2). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 171.6 (s, OC═N), 136.5 (2d, C_{Ph}), 135.1 (d, $^1J_{C,P}$ =

49.0 Hz, C_{Ph}—P), 133.0 (2d, C_{Ph}), 131.8 (2d, C_{Ph}), 131.5 (d, $^1J_{C,P}$ = 48.0 Hz, C_{Ph}—P), 130.0 (2d, C_{Ph}), 128.8 (2d, C_{Ph}), 111.1 (d, C_{allyl}), 103.3 (d, C_{allyl}), 84.2 (5s, C_{Fc}—CH_3), 80.4 (2d, C_{Fc}—H and C═N—*C*H), 80.0 (d, C_{Fc}—H), 78.9 (d, C_{Fc}—H), 74.3 (d, $^2J_{C,P}$ = 23.5 Hz, C_{Fc}—C_{ox}), 72.8 (d, $^1J_{C,P}$ = 37.7 Hz, C_{Fc}—P), 70.5 (t, OCH_2), 68.5 (d, C_{allyl}), 35.2 (s, *C*$(CH_3)_3$), 28.7 (t, CH_2), 27.2 (3q, C(*C*$H_3)_3$), 25.1 (t, CH_2), 20.6 (t, CH_2), 10.9 (5q, C_{Fc}—*C*H_3). ^{31}P NMR (121.49 MHz, $CDCl_3$): δ 18.2 (s, intensity 99%), 14.3 (s, intensity 1%). HRMS (FAB) *m*/*z* calcd for $C_{40}H_{49}NOPFe^{110}Pd^{121}SbF_6$ (M^+), 991.0895; found, 991.0909; *m*/*z* calcd for $C_{40}H_{49}NOPFe^{108}Pd^{121}SbF_6$ (M^+), 989.0883; found, 989.0899; *m*/*z* calcd for $C_{40}H_{49}NOPFe^{104}Pd^{123}SbF_6$ (M^+), 987.0888; found, 987.0899; *m*/*z* calcd for $C_{40}H_{49}NOPFe^{105}Pd^{121}SbF_6$ (M^+), 986.0894; found, 986.0919.

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Supporting Information Available: Syntheses and compound characterization of compounds **2a**, **2c**, **2d**, **3a**, **3c**, **3d**, and **L1**−**L5**. ^{1}H NMR spectra of compounds **1a**−**d**, **2a**−**d**, **3a**−**d**, **5a**−**c**, **L1**−**L5**, **K1**, and **K2**. Tables of crystal data and structure refinement and the full list of bond lengths and angles from the X-ray crystallographic study of **K1** and **K2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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