Asymmetric Catalysis

Oxazoline-Mediated Interannular Cyclopalladation of Ferrocene: Chiral Palladium(II) Catalysts for the Enantioselective Aza-Claisen Rearrangement**

Albert Moyano, Malgorzata Rosol, Rosa M. Moreno, Concepción López, and Miguel A. Maestro*

Cyclopalladated complexes derived from organic molecules bearing N-donor groups were first described by Cope et al. almost forty years ago.[1] Since then, the study of these complexes has become a fundamental area of research in organometallic chemistry.[2] Cyclopalladated ferrocene derivatives are particularly interesting,[3] as they are planar chiral compounds with increasing applications in materials chemistry, asymmetric synthesis, and catalysis.[4–6] Up until now, the cyclopalladation of ferrocene compounds with nitrogen-containing substituents, such as amines, imines, and oximes, has invariably led to the formation of *ortho*-palladated derivatives,[7] although very few of these chiral complexes have been obtained in the optically active form.[8] On the other hand, the direct cyclopalladation of 2-ferrocenyl-1,3-oxazolines, which are compounds of special relevance in asymmetric synthesis,[3,9,10] is not successful because of concurrent oxidation of the ferrocene ligand by Pd^{II} salts, and for this reason the corresponding *ortho*-palladated derivatives either have been obtained by indirect methods or have been replaced in some applications by cobaltocene complexes.[11] 4-Ferrocenyl-1,3-oxazoline derivatives form a new class of chiral ferrocene compounds that are easily available in both enantiomeric forms and with excellent optical purities. We report herein the cyclopalladation of several 4-ferrocenyl-1,3-oxazoline derivatives that takes place in good yield to furnish a hitherto unknown type of metalated ferrocenes in which the carbon–palladium bond is formed by using a carbon atom in the unsubstituted cyclopentadiene ring (we have coined the term "interannular cyclometalation" for this reaction).[12]

[*] Prof. A. Moyano, M. Rosol, R. M. Moreno
Departament de Química Orgànica
Universitat de Barcelona, Facultat de Química
C. Martí i Franquès, 1–11, 08028-Barcelona (Spain)
Fax: (+34) 93-339-78-78
E-mail: amoyano@ub.edu
Prof. C. López
Departament de Química Inorgànica
Universitat de Barcelona, Facultat de Química
C. Martí i Franquès, 1–11, 08028-Barcelona (Spain)
Prof. M. A. Maestro
Área de Química Orgánica
Departamento de Química Fundamental, Facultade de Ciencias
Universidade da Coruña, 15071 A Coruña (Spain)

[**] The authors thank the DGI (grant BQU2003-03426) and the Generalitat de Catalunya (DURSI) (grant 2001SGR50) for financial support. M.R. and R.M.M. are grateful to the DURSI for predoctoral fellowships.

 DOI: 10.1002/ange.200462434

The initial impetus for this research came from the reasoning that in 4-ferrocenyl-1,3-oxazoline compounds, in contrast to what happens in the regioisomeric 2-ferrocenyl-1,3-oxazolines, the conformation in which the carbon–nitrogen heterocyclic bond would be coplanar with the cyclopentadiene ring is strongly destabilized by steric hindrance between the C5 oxazoline carbon atom and the ferrocenyl moiety. Therefore, the most stable conformer would be that in which the C4–H bond is coplanar with the upper cyclopentadiene ring, thus directing the nitrogen atom towards the lower one. Simple quantum-mechanical calculations[13] support this hypothesis by showing that 2-(*tert*-butyl)-4-ferrocenyl-1,3-oxazoline had only one stable conformer (Figure 1).

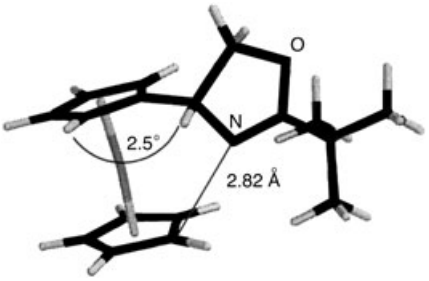
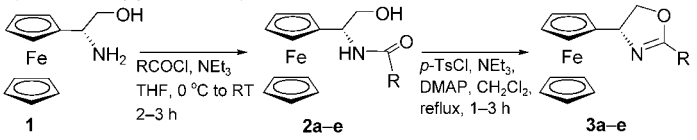


Figure 1. Energy-minimized geometry of (*R*)-2-(*tert*-butyl)-4-ferrocenyl-1,3-oxazoline, as determined by PM3 calculations.

This observation prompted us to synthesize a series of 4-ferrocenyl-1,3-oxazolines with different C2 substituents and study their cyclopalladation. Highly enantiopure (98% *ee*) (*S*)-2-amino-2-ferrocenylethanol (**1**)[14] was readily converted into the target oxazolines **3a–e** by standard procedures (Table 1).

Table 1: Preparation of (*S*)-4-ferrocenyl-1,3-oxazolines.[a]



Entry	R	Yield of **2** [%][b]	Yield of **3** [%][b]
1	*tert*-butyl	71 (**2a**)	77 (**3a**)
2	1-adamantyl	77 (**2b**)	68 (**3b**)
3	phenyl	78 (**2c**)	80 (**3c**)
4	isopropyl	78 (**2d**)	60 (**3d**)
5	ethyl	81 (**2e**)	64 (**3e**)

[a] Ts = *para*-toluenesulfonyl, DMAP = 4-dimethylaminopyridine. [b] Yield of product isolated after purification by chromatography.

We were pleased to find that after the oxazoline **3a** and 1.5 equivalents of $Pd(OAc)_2$ had been stirred together overnight at room temperature in benzene a palladated derivative **4a** was obtained in 78% yield after recrystallisation. Both the ^1H and ^{13}C NMR spectra indicated that the unsubstituted cyclopentadiene ring of **3a** had been palladated, which was in agreement with our hypothesis. Moreover, both the NMR spectroscopic and the mass-spectrometric analysis clearly showed the presence of two ferrocenyloxazoline units, three palladium atoms, and four acetate bridges in this compound. Finally, the unprecedented structure of **4a** was unequivocally established by X-ray diffraction analysis (Figure 2).

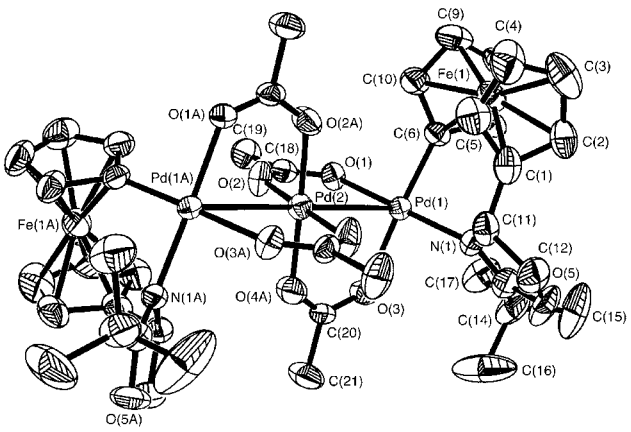
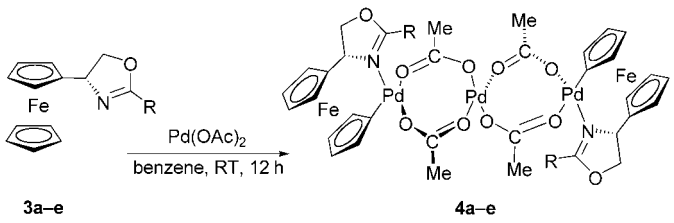


Figure 2. ORTEP representation of the crystal structure of **4a**. Hydrogen atoms have been omitted for clarity.

Several structural features of **4a** deserve some comment: The three palladium atoms show a very small departure (less than 1.1°) from linearity. Although the formation of linear trinuclear cyclopalladated complexes has been reported in a few cases starting from $C(sp^3)$ donors,[15] **4a** represents the first example of this type of complex with $C(sp^2)$–Pd bonds and also the only one whose geometry has been determined by X-ray diffraction analysis. The Pd–Pd bond of 3.0457(5) Å is somewhat shorter than that observed in the palladium diacetate trimer (ca. 3.15 Å),[16] but clearly beyond the upper value (ca. 2.87 Å) reported for neutral bimetallic complexes with weak bonding interactions between the two palladium atoms.[17] The Pd–C distance at 1.961(7) Å is appreciably longer than that reported for dimeric cyclopalladated ferrocenylimines with acetate bridges, but the Pd–N bond length at 2.021(6) Å falls in the range observed in these compounds.[8f]

We submitted the other 4-ferrocenyl-1,3-oxazolines **3b–e** to the same reaction conditions used for **3a** (Scheme 1) to study the scope of this new cyclopalladation reaction. Both the spectral and analytical data of the cyclopalladated complexes **4b** and **4c** revealed that they were structurally analogous to **4a**. It is worth noting that cyclopalladation did not take place at the phenyl ring in the case of **3c**, which is in accordance with the preferences observed in the *ortho* palladation of imine derivatives of benzoyl ferrocene.[7d] On the other hand, the cyclopalladation of both **3d** and **3e** led to complex mixtures of unidentified products. Clearly, the presence of C–H bonds in the α position of the oxazoline substituent at C2 has a deleterious effect in this reaction.

Electrochemical studies of **3a** and **4a** were performed[18] to elucidate the effect of interannular palladation upon the



Scheme 1. Interannular cyclopalladation of ferrocenyloxazoline derivatives **3**. Yields: **4a** 78%, **4b** 78%, **4c** 64%, **4d** <2%, **4e** 0%. R = *tert*-butyl (**4a**), 1-adamantyl (**4b**), phenyl (**4c**), isopropyl (**4d**), ethyl (**4e**).

proclivity of the iron(II) center towards oxidation. The cyclic voltammogram (CV) of **3a** exhibits an anodic signal with a directly associated cathodic signal in the reverse scan (Figure 3). The value of the half-wave potential ($E_{1/2}$) for **3a**

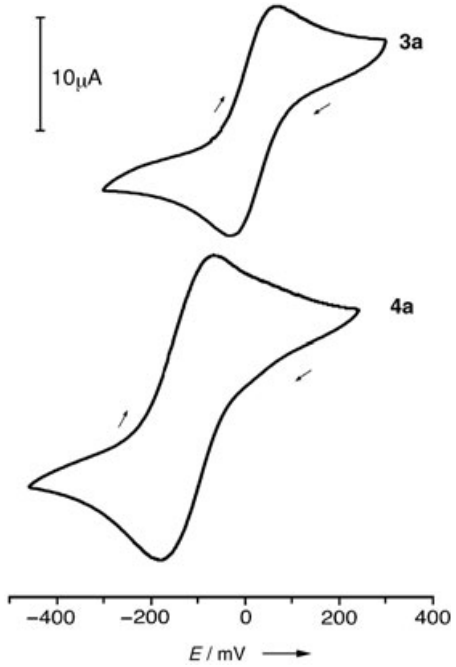
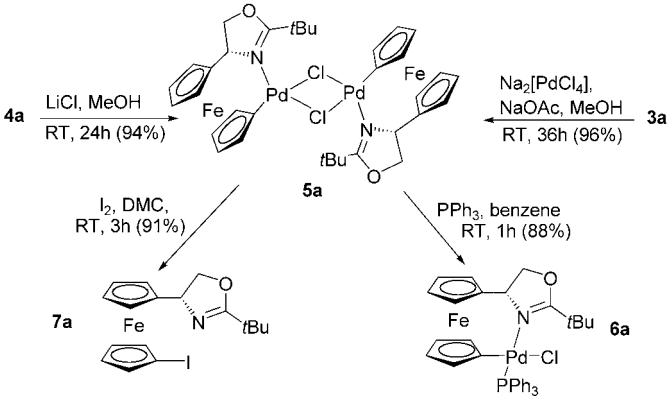


Figure 3. Cyclic voltammograms of 10^{-3} M solutions of **3a** or **4a** in CH_3CN at 20°C and at a scan speed of $\upsilon = 100$ mV s^{-1} (electrochemical data: anodic (E_{pa}), cathodic (E_{pc}), and half-wave potentials ($E_{1/2}$) potentials (in mV) referred to ferrocene $E_{pa} = 54$ (for **3a**) and −52 (for **4a**), $E_{pc} = -33$ (for **3a**) and −184 (for **4a**), and $E_{1/2} = 10$ and −123 for **3a** and **4a**, respectively).

is smaller than those reported for [(η^5-C_5H_5)Fe{(η^5-C_5H_4)-$C(R^1)$=N-R^2}] (in the range of 85–200 mV) but greater than those of the ferrocenylamines [(η^5-C_5H_5)Fe{(η^5-C_5H_4)-$(CH_2)_n$-NH_2}] ($n = 1$ or 2) and the Schiff bases [(η^5-C_5H_5)Fe-{(η^5-C_5H_4)-CH_2-N=$CH(R^3)$}] with $E_{1/2}$ values varying from −30 to −5 mV.[19] These findings suggest that the electron-withdrawing character of the 4′-oxazoline moiety is between those of the −"-CH_2-N=$CH(R^3)$" and the −"-$C(R^1)$H=N-R^2" substituents.[20] Only one wave was observed for **4a** and the intensity of the signal was double than that of **3a**, thus indicating that the two ferrocene moieties in **4a** do not interact electronically with each other. Moreover, the wave was shifted to a more cathodic potential (Figure 3). This finding agrees with the results reported for the ferrocenylimines [(η^5-C_5H_5)Fe{(η^5-C_5H_4)-$C(R^1)$=N-R^2}] and their cyclopalladated derivatives where a σ(Pd–C(sp^2)) bond is held in the adjacent position to the functional >C=N group.[19] However, the magnitude of the shift was greater (ca. 130 mV) for **4a** than for the previously reported systems (in the range of 40–80 mV).

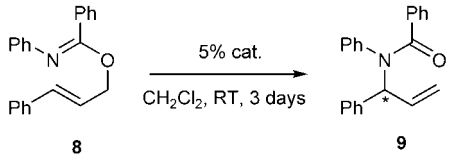
The chemical behavior of these novel complexes appears to be similar to that of previously known *ortho*-palladated ferrocene derivatives (Scheme 2). Thus, the treatment of **4a**



Scheme 2. Preparation and reactivity of the di-μ-chloro complex **5a**. DMC = dimethylaminoethyl chloride hydrochloride.

with lithium chloride produces a di-μ-chloro complex **5a**. The same compound is obtained when **3a** is treated with Na_2-$[PdCl_4]$ in the presence of NaOAc. In turn, **5a** is readily converted into the mononuclear complex **6a** by cleavage with triphenylphosphine. Finally, iodination of **5a** affords (*S*)-2-(*tert*-butyl)-4-(1′-iodoferrocenyl)-1,3-oxazoline (**7a**) in high yield and provides conclusive evidence of the high reactivity of the σ(Pd–C(sp^2)) bond in **5a**. This reaction paves the way for the preparation of 1,1′-disubstituted ferrocenes.

These new chiral cyclopalladated complexes hold significant promise as catalysts for asymmetric transformations and are far from being a mere chemical curiosity. In particular, preliminary results show that the trinuclear complexes **4a–c** and the di-μ-chloro complex **5a** are able to catalyze the enantioselective rearrangement of allylic imidates to allylic amides. This Pd^{II}-catalyzed aza-Claisen reaction offers convenient access to various allylic amides from the corresponding allylic alcohols. Some *ortho*-palladated complexes derived from ferrocene and which combine both central and planar chirality have also been shown to give high yields and enantioselectivities in the rearrangement of imidates derived from alkyl-substituted allylic alcohols.[6,21] The reaction of imidates derived from aryl-substituted allylic alcohols is, however, much less stereoselective. In the light of these precedents, we investigated the performance of our 1′-palladated complexes in the [3,3]-sigmatropic rearrangement of (*E*)-3-phenylallyl (*N*-phenyl)benzimidate (**8**) (Scheme 3).[22]



8 9

cat. = **5a**: 45% yield, 32% ee ((+)-**9**)
cat. = **4a**: 30% yield, 72% ee ((−)-**9**)
cat. = **4c**: 49% yield, 90% ee ((−)-**9**)

Scheme 3. Asymmetric catalysis of the aza-Claisen rearrangement by complexes **4a**, **4c**, and **5a**.

The di-μ-chloro complex **5a** afforded the dextrorotatory allylic amide (+)-**9** in 45% yield and with low, but significant, optical purity (32% *ee* according to HPLC analysis) whereas the mononuclear complex **6a** did not show any catalytic activity in this reaction. We found that the opposite levorotatory enantiomer of **9** became the major rearranged product (with a 72% *ee*) when the trinuclear cyclopalladated complex **4a** was used. This unexpected change in enantioselectivity is certainly surprising when it is considered that the only chirality element present in **4a** and in **5a** is the C4 oxazoline stereogenic carbon atom (which is of *S* absolute configuration). Finally, the use of the (*S*)-2-phenyl-4-ferrocenyloxazoline-derived trinuclear complex **4c** gave (−)-**9** in 49% yield and with an unprecedented high optical purity (90% *ee*).[23] These reactions constitute the first examples of an asymmetric transformation catalyzed by a cyclopalladated ferrocene derivative that exhibites only central chirality.

In summary, the rational design of a ferrocenyloxazoline ligand that allows a direct interannular cyclopalladation of ferrocene derivatives[24] for the first time has led to a new structural type of chiral palladium-bridged heteropolynuclear complexes of potential interest in several fields of chemistry.

Experimental Section

3a: M.p. 50–51 °C; $[\alpha]_D^{20} = -85$ ($c = 0.47$, CH_2Cl_2). IR (KBr): $\tilde{\nu} = 3080$, 2980, 1650, 1489, 1120, 1020, 810 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.26$ (s, 3H, $3 \times CH_3$), 4.15 (m, 9H, Fc), 4.36 (m, 1H, C*H*OH), 4.50 (m, 1H, CHO*H*), 4.86 ppm (dd, $^1J = 9.6$ Hz, $^2J = 7.4$ Hz, 1H, CHN); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 27.9$ ($3 \times CH_3$), 35.2 (*t*Bu-Cq (quaternary carbon center)), 64.7 (CH-N), 66.2 (CH-Fc), 67.2 (CH-Fc), 67.8 (CH-Fc), 7.9 (CH-Fc), 68.3 (CH-Fc), 73.4 (CH_2-O), 90.8 (Cq-Fc), 172.8 ppm (C=O); HRMS (CI, NH_3): *m*/*z* calcd for $C_{17}H_{21}FeNO$: 312.1006, found: 312.1001.

4a: A solution of **3a** (0.15 g, 0.48 mmol) and $Pd(OAc)_2$ (1.5 equiv) in dry benzene (7 mL) was stirred overnight at room temperature. The resulting dark brown solution was filtered through a small pad of celite with $CHCl_3$ and evaporated. The resulting dark residue was dissolved in a minimal amount of CH_2Cl_2 and hexane was added. The solution was filtered to remove impurities that had precipitated after heating. Recrystallization from dichloromethane/hexane afforded the red–brown pentametallic complex **4a** as a crystalline solid (0.22 g, 78% yield). M.p. 160 °C (decomp); $[\alpha]_D^{20} = +463$ ($c = 0.26$, CH_2Cl_2); IR (KBr): $\tilde{\nu} = 3100$, 2971, 1626, 1578, 1408, 1342, 1167, 1024, 1034, 804 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.80$ (s, 6H, $2 \times CH_3$ bridge), 1.92 (s, 18H, $6 \times CH_3$), 2.01 (s, 6H, $2 \times CH_3$ bridge), 3.97 (m, 1H, CH-Fc), 3.99 (m, 1H, CH-Fc), 4.01 (m, 1H, CH-Fc), 4.03 (m, 1H, CH-Fc), 4.10 (m, 1H, CH-Fc), 4.30 (m, 1H, CH-Fc), 4.44 (m, 1H, CH-Fc), 4.47 (m, 2H, CH_2-O), 4.80 (m, 1H, CH-Fc), 6.18 ppm (dd, $^1J = 4.6$ Hz, $^2J = 2.2$ Hz, 1H, CH-N); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 23.7$ (CH_3 bridge), 23.8 (CH_3 bridge), 28.7 ($3 \times CH_3$), 34.3 (*t*Bu-Cq), 64.7 (CH-Fc), 65.8 (CH-N), 66.2 (CH-Fc), 66.7 (CH-Fc), 67.3 (CH-Fc), 69.0 (CH-Fc), 72.6 (CH-Fc), 72.7 (CH-Fc), 73.4 (CH-Fc), 73.4 (CH_2-O), 84.7 (Cq-Fc-Pd), 87.9 (Cq-Fc-ox), 175.3 (C=N), 181.7 (C=O), 184.4 ppm (C=O); MS (FAB+): *m*/*z* (%) 1176.0 (9.9) [M^+], 475.1 (100). HRMS: *m*/*z* calcd for $C_{19}H_{23}FeNO_3Pd$: 474.0078; found: 474.0072.**5a**: **3a** (85 mg, 0.27 mmol) was added to a solution of $Na_2[PdCl_4]$ (81 mg, 0.27 mmol) and NaOAc (23 mg, 0.27 mmol) in dry methanol (2 mL) at room temperature and stirring was maintained for 36 h. The resulting dark brown solution was filtered through a sintered glass frit and washed with methanol. The filtrate was concentrated and the crude product was purified by dissolving in a minimal amount of CH_2Cl_2 followed by the addition of hexane. The solution was filtered to remove impurities that had precipitated after heating and the tetrametallic complex **5a** was obtained as an orange solid (118 mg, 96%). M.p. 156 °C (decomp); $[\alpha]_D^{20} = +436$ ($c = 0.15$, CH_2Cl_2); IR (KBr): $\tilde{\nu} = 3100$, 2927, 1624, 1578, 1458, 1400, 1362, 1169, 1032, 806, 733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.72$ (s, 18H, $6 \times CH_3$), 3.85 (m, 1H, CH-Fc), 3.93 (m, 1H, CH-Fc), 3.99 (m, 1H, CH-Fc), 4.02 (m, 1H, CH-Fc), 4.08 (m, 1H, CH-Fc), 4.35 (m, 1H, CH-Fc), 4.39 (m, 1H, CH-Fc), 4.46 (m, 2H, CH_2-O), 4.47 (m, 1H, CH-Fc), 5.04 ppm (m, 1H, CH-N); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 28.8$ ($6 \times CH_3$), 34.3 (*t*Bu-Cq), 64.9 (CH-Fc), 66.0 (CH-Fc), 66.3 (CH-Fc), 67.0 (CH-N) 67.8 (CH-Fc), 69.5 (CH-Fc), 71.7 (CH-Fc), 72.1 (CH-Fc), 73.2 (CH-Fc), 73.2 (CH_2-O), 87.9 (Cq-Fc-Pd), 88.9 (Cq-Fc-ox), 175.3 ppm (C=N); MS (MALDI-TOF) *m*/*z* (%): 903.5 (100) [$M+1$]$^+$; HRMS: *m*/*z* calcd for $C_{34}H_{40}Cl_2Fe_2N_2O_2Pd_2$: 901.9241; found: 901.9230.

General experimental procedure for the aza-Claisen rearrangement of **8**: A solution of (*E*)-3-phenylallyl (*N*-phenyl)benzimidate (**8**) (45 mg, 0.14 mmol) and the cyclopalladated complex (**4a**, **4c**, or **5a**; 0.007 mmol) in anhydrous CH_2Cl_2 (1 mL) was stirred at room temperature under nitrogen for 3 days. The solution was concentrated and the residue was purified by column chromatography on silica gel with ethyl acetate/hexanes (4:96) as the eluant to afforded the optically active **9** (30–49% yield). Conditions for the HPLC determination of the enantiomeric purity of **9**: chiralpak AS column, hexane/isopropyl alcohol (96:4), $\Phi = 0.5$ mL min^{-1}, $\lambda = 254$ nm, $t_R(+) = 28.1$ min, $t_R(-) = 34.1$ min.

Received: October 26, 2004
Published online: February 18, 2005

Keywords: allylic compounds · asymmetric catalysis · metalation · metallocenes · palladium

[1] a) A. C. Cope, R. W. Siekman, *J. Am. Chem. Soc.* **1965**, *87*, 3272–3273; b) A. C. Cope, E. C. Friedrich, *J. Am. Chem. Soc.* **1968**, *90*, 909–913.

[2] Reviews: a) J. Dupont, M. Pfeffer, J. Spencer, *Eur. J. Inorg. Chem.* **2001**, 1917–1927; b) S. B. Wild, *Coord. Chem. Rev.* **1997**, *166*, 291–311; c) G. R. Newkome, W. E. Puckett, V. K. Gupta, G. E. Fiefer, *Chem. Rev.* **1986**, *86*, 451–489; d) D. W. Evans, G. R. Baker, G. R. Newkome, *Coord. Chem. Rev.* **1989**, *93*, 155–183; e) A. D. Ryabov, *Chem. Rev.* **1990**, *90*, 403–489.

[3] a) *Ferrocenes. Homogeneous Catalysis, Organic Synthesis and Materials Sciences* (Eds.: A. Togni, T. Hayashi), VCH, Weinheim, **1995**; b) I. R. Whittall, A. M. Mc Donagh, M. C. Humphrey, M. Samoc, *Advances in Organometallic Chemistry*, *Vol. 42*, Academic Press, San Diego, **1998**, p. 291.

[4] Heck reactions: a) S. Iyer, A. Jayanthi, *Tetrahedron Lett.* **2001**, *42*, 7877–7878; b) F. Yang, Y. Zhang, R. Zheng, J. Tang, M. He, *J. Organomet. Chem.* **2002**, *651*, 146–148.

[5] Suzuki–Miyaura couplings: D. A. Alonso, C. Nájera, M. C. Pacheco, *J. Org. Chem.* **2002**, *67*, 5588–5594.

[6] Asymmetric aza-Claisen rearrangements of allylic imidates and related reactions: a) F. Cohen, L. E. Overman, *Tetrahedron: Asymmetry* **1998**, *9*, 3213 – 3222; b) T. K. Hollis, L. E. Overman, *J. Organomet. Chem.* **1999**, *576*, 290 – 299; c) Y. Donde, L. E. Overman, *J. Am. Chem. Soc.* **1999**, *121*, 2933 – 2934; d) J. Kang, K. H. Yew, T. H. Kim, D. H. Choi, *Tetrahedron Lett.* **2002**, *43*, 9509 – 9512; e) L. E. Overman, T. P. Remarchuk, *J. Am. Chem. Soc.* **2002**, *124*, 12 – 13.

[7] For some leading references, see: a) M. Pfeffer, M. A. Rotteveel, J. Pascal, A. De Cian, J. Fischer, *J. Organomet. Chem.* **1989**, *371*, C21 – 5; b) W. Tao, L. J. Silverberg, A. L. Rheingold, R. F. Heck, *Organometallics* **1989**, *8*, 2550 – 2559; c) M. Nonoyama, K. Hamamura, *J. Organomet. Chem.* **1991**, *407*, 271 – 277; d) R. Bosque, C. López, J. Sales, X. Solans, *J. Organomet. Chem.* **1994**, *483*, 61 – 71; e) C. López, A. Caubet, X. Solans, M. Font-Bardia, *J. Organomet. Chem.* **2000**, *598*, 87 – 102; f) S. Pérez, C. López, A. Caubet, R. Bosque, X. Solans, M. Font-Bardía, A. Roig, E. Molins, *Organometallics*, **2004**, *23*, 224 – 236.

[8] a) K. Takao. M. Nonoyama, J. Fujita, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 186 – 189; b) L. L. Troitskaya, N. S. Khruschova, V. I. Sokolov, O. A. Reutov, *Zh. Obshch. Khim.* **1982**, 2606 – 2608; c) G. Zhao, F. Xue, Z.-Y. Zhang, T. C. W. Mak, *Organometallics* **1997**, *16*, 4023 – 4026; d) Z. Gang, Q.-C. Yang, T. C. W. Mak, *Organometallics* **1999**, *18*, 3623 – 3636; e) C. López, R. Bosque, X. Solans, M. Font-Bardía, *Tetrahedron: Asymmetry* **1996**, *7*, 2527 – 2530.

[9] Reviews: a) C. J. Richards, A. Locke, *Tetrahedron: Asymmetry* **1998**, *9*, 2377 – 2407; b) L.-X. Dai, T. Tu, S.-L. You, W.-P. Deng, K. L. Hou, *Acc. Chem. Res.* **2003**, *36*, 659 – 667; c) P. J. Guiry, C. P. Saunders, *Adv. Synth. Catal.* **2004**, *346*, 497 – 537.

[10] Recent references: a) C. Bolm, N. Hermanns, A. Classen, K. Muñiz, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1795 – 1798; b) T. Tu, X.-L. Hou, L.-X. Dai, *Org. Lett.* **2003**, *5*, 3651 – 3653; c) Y. Nishibayashi, A. Yamauchi, G. Onodera, S. Uemura, *J. Org. Chem.* **2003**, *68*, 5875 – 5880.

[11] a) L. E. Overman, C. E. Owen, M. M. Parvan, C. J. Richards, *Org. Lett.* **2003**, *5*, 1809 – 1812; b) C. E. Anderson, L. E. Overman, *J. Am. Chem. Soc.* **2003**, *125*, 12412 – 12413; c) J. Kang, T. H. Kim, H. Y. Kyoung, W. K. Lee, *Tetrahedron: Asymmetry* **2003**, *14*, 415 – 418; d) S. F. Kirsch, L. E. Overman, M. P. Watson, *J. Org. Chem.* **2004**, *69*, 8101 – 8104.

[12] A few examples of interannular lithiation of ferrocenes can be found in the literature, see: a) G. Iftime, C. Moreau-Bossuet, E. Manoury, G. G. A. Balavoine, *Chem. Commun.* **1996**, 527 – 528; b) G. Iftime, J.-C. Daran, E. Manoury, G. G. A. Balavoine, *Organometallics* **1996**, *15*, 4808 – 4815; c) M. Tsukazaki, M. Tinkl, A. Roglans, B. J. Chapell, N, J. Taylor, V. Snieckus, *J. Am. Chem. Soc.* **1996**, *118*, 685 – 686.

[13] Optimization of the geometry was performed with the semi-empirical PM3(tm) procedure, as implemented in the SPARTAN package of programs.

[14] Obtained as described in: a) M. Catasús, A. Bueno, A. Moyano, M. A. Maestro, J. Mahía, *J. Organomet. Chem.* **2002**, *642*, 212 – 226. (*R*)-**1** is also obtained in high enantiomeric purity by the same method or by the alternative procedure of: b) A. Patti, M. Lotz, P. Knochel, *Tetrahedron: Asymmetry* **2001**, *12*, 3375 – 3380.

[15] a) Y. Fuchita, K. Hisaki, T. Uchiyama, *J. Organomet. Chem.* **1985**, *280*, C51-C54; b) M. Pfeffer, E. Wehman, G. van Koten, *J. Organomet. Chem.* **1985**, *282*, 127 – 131; c) G. G. A. Balavoine, J. C. Clinet, *J. Organomet. Chem.* **1990**, *390*, C84 – C88; d) M. T. Alonso, O. Juanes, J. de Mendoza, J. Rodríguez-Ubis, *J. Organomet. Chem.* **1992**, *430*, 349 – 356.

[16] A. C. Skapshi, M. L. Smart, *Chem. Commun.* **1970**, 658 – 659.

[17] T. Murahashi, H. Kurosawa, *Coord. Chem. Rev.* **2002**, *231*, 207 – 228.

[18] Electrochemical data for **3a** and **4a** were obtained by cyclic-voltammetric analysis under nitrogen gas at approximately 20 °C using HPLC-grade acetonitrile as the solvent, tetrabutylammonium hexafluorophosphate (0.1 M) as the supporting electrolyte, and a potentiostat from EG&G instruments. The half-wave potentials $E_{1/2}$ were referenced to an $Ag/AgNO_3$ (0.1 M in acetonitrile) electrode separated from the solution by a medium-porosity fritted disk. A platinum-wire auxiliary electrode was used in conjunction with a platinum disk working TACUSSEL-EDI rotatory electrode (3.14 mm^2). Cyclic voltammograms of ferrocene were recorded before and after each sample to ensure the reproducibility of the results, in particular to test and monitor the stability of the $Ag/AgNO_3$ electrode (for the Fc/Fc^+ couple $E_{1/2} = 50 \pm 2$ mV). Three consecutive scans of freshly prepared solutions (10^{-3} M) of the samples in acetonitrile were run and the average $E_{1/2}$ values measured were then referred to the Fc/Fc^+ couple ($E_{1/2}$(Fc)) which was used as the internal reference. No additional waves were observed up to 2 V. The standard error of the measured potentials was ± 5 mV in these experimental conditions and the cyclic voltammograms were registered using scan speeds varying from $\upsilon = 10$ to 100 $mV\,s^{-1}$ in all experiments.

[19] a) R. Bosque, C. López, J. Sales, *Inorg. Chim. Acta* **1996**, *244*, 141 – 145; b) C. López, R. Bosque, X. Solans, M. Font-Bardía, D. Tramuns, G. Fern, J. Silver, *J. Chem. Soc. Dalton Trans.* **1994**, 3039 – 3046.

[20] a) P. Zanello, A. Cinquantini, S. Mangani, G. Opromolla, L. Pardi, C. Janiak, M. D. rausch, *J. Organomet. Chem.* **1994**, *471*, 171 – 177; b) P. Zanello, G. Opromolla, L. Pardi, K. H. Panell, K. H. Sharma, *J. Organomet. Chem.* **1993**, *450*, 193 – 196; c) W. F. Little, C. N. Reilley, J. D. Johnson, A. P. Sanders, *J. Am. Chem. Soc.* **1964**, *86*, 1382 – 1386; d) G. L. Hoh, W. E. McEwen, J. Kleinberg, *J. Am. Chem. Soc.* **196**1, 83, 3949 – 3953.

[21] a) M. Calter, T. K. Hollis, L. E. Overman, J. Ziller, G. G. Zipp, *J. Org. Chem.* **1997**, *62*, 1449 – 1445; b) Y. Jiang, J. M. Langmire, X. Zhang, *Tetrahedron Lett.* **1999**, *40*, 1449 – 1450.

[22] Prepared from (*E*)-cinnamyl alcohol in 84 % yield according to the literature procedure: L. Engman, *J. Org. Chem.* **1993**, *58*, 2394 – 2401.

[23] The asymmetric rearrangement of **8** to (−)-**9** catalyzed by a dimeric (di-μ-trifluoroacetate)palladium complex derived from (*R*)-*N*,*N*-dimethyl-2(-ferrocenyl)ethylamine occurred in 47 % yield with 47 % *ee*; see: T. K. Hollis, L. E. Overman, *Tetrahedron Lett.* **1997**, *38*, 8837 – 8840.

[24] The low-yield, multistep-formation of metallaferrocenophanes by insertion of Pd^0 and Pt^0 complexes into silicon- or phosphido-bridged ferrocenophanes has been described; see: T. Mizuta, M. Onishi, T. Nakazono, H. Nakazawa, K. Miyoshi, *Organometallics* **2002**, *21*, 717 – 726.

