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4-Ferrocenyl-1,3-oxazoline derivatives as ligands for catalytic asymmetric allylation reactions

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Abstract

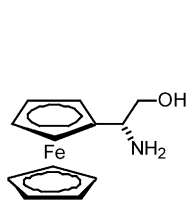
Bis(oxazolines) and 2-(2-phosphinoaryl)oxazolines derived from highly enantiopure 2-amino-2-ferrocenylethanol have been tested as ligands in the asymmetric Pd(0)-catalysed allylic alkylation reaction. Essentially complete enantioselectivity (99.8:0.2 er) has been achieved in the nucleophilic substitution of 1,3-diphenyl-2-propenyl acetate by dimethyl malonate anion. The absolute configuration of the ligands has been unambiguously established by chiroptical methods.

Keywords: Asymmetric synthesis; Ferrocenes; Induced circular dichroism; Oxazolines

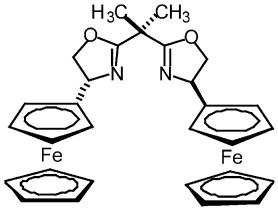
1. Introduction

The use of chiral ferrocene derivatives as ligands for asymmetric catalysis has been receiving an increasing attention in the last decade [1]. While planar chiral 1,1′-disubstituted or 1,2-disubstituted ferrocenes have been extensively studied, much less attention has been paid to central chiral derivatives such as α,β-disubstituted ferrocenes [2]. We have recently described in this Journal [3] the highly enantioselective synthesis of 2-amino-2-ferrocenyl ethanol (**1**) in both enantiomeric forms, as well as its conversion into the oxazoline-based ligands **2** and **3**.

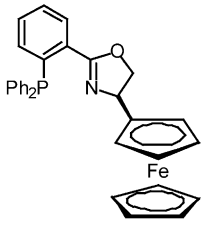
Subsequently to the acceptance of our article, Patti et al. [4] have reported an alternative preparation of amino alcohol (−)-**1** and of phosphinooxazoline (+)-**3**, together with a single example of the application of **3** to asymmetric catalysis. Prompted by the publication of this paper, we wish now to disclose our own results on the use of ligands **2** and **3** in the Pd(0)-catalysed allylic alkylation reaction. In particular, we present for the first time conclusive evidence for the assignation of an (*S*) absolute configuration to amino alcohol (+)-**1**, and we show that the use of an allyl palladium complex derived from **3** as a catalyst in asymmetric allylic alkylations gives rise to extraordinarily high selectivities (up to 99.8:0.2 enantiomer ratio (er)).



(+)-(*S*)-**1**



(-)-(*S,S*)-**2**



(-)-(*S*)-**3**

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2. Results and discussion

2.1. Absolute configuration of ferrocene-based ligands 2 and 3

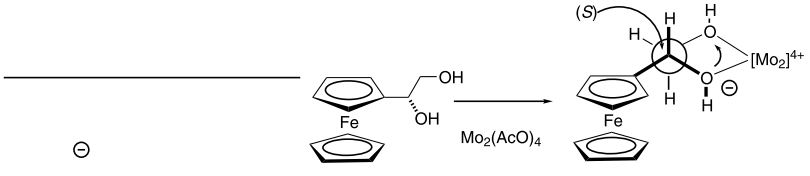
Bis(oxazoline) (−)-**2** and phosphinooxazoline (−)-**3** were prepared in high enantiomeric purity (≥99:1 er), through the intermediacy of amino alcohol (+)-**1**, from (+)-1-ferrocenylethane-1,2-diol (**4**) [5] by the procedures reported in our previous article [3]. It is worth noting, however, that the assignation of an (*S*) configuration to diol (+)-**4** (and, therefore, to the derived compounds (+)-**1**, (−)-**2** and (−)-**3**) ultimately relied on the application of the 'mnemonic device' for the osmium-catalysed asymmetric dihydroxylation of alkenes [6]. Since several exceptions to this rule have been reported in the literature [7], we felt that it was necessary to confirm this assignation by an alternative procedure. Recently, Salvadori et al. [8] have shown that the absolute configuration of chiral acyclic 1,2-diols can be reliably ascertained by analysis of the induced circular dichroism spectrum of their complexes with dimolybdenum tetraacetate in DMSO solution, according to the method initially developed by Snatzke [9]. By application of the empirical rule developed by Salvadori, for which no exceptions are known [10], we should expect an intense negative Cotton effect at ca. 305–310 nm (band IV according to Snatzke's nomenclature) in the induced circular dichroism spectrum of the (*S*) enantiomer of diol **4**. We were pleased to observe that the stationary state induced circular dichroism spectrum of a 4:3 mixture of dimolybdenum tetraacetate and diol (+)-**4** in DMSO solution exhibited a strong negative Cotton effect ($\Delta\varepsilon' = -2.15$) at $\lambda = 315$ nm, a zone in which the circular dichroism spectrum of the uncomplexed diol showed no significant absorption. This negative Cotton effect is indicative of a negative sign for the O–C–C–O dihedral angle in the Cottonogenic derivative of (+)-**4** (Fig. 1), therefore, confirming the assignment of an (*S*) configuration to the stereogenic centers of compounds **1**–**4**, and establishing that the Sharpless' 'mnemonic rule' for asymmetric dihydroxylations can be safely applied to 1-ferrocenyl alkenes [5].

Further evidence for the (*S*) absolute configuration of amino alcohol (+)-**1** was obtained by conversion of the derived oxazolidinone **5** [3] into the *N*-acylated compound **6** (Scheme 1). Treatment of a THF solution of **6** with sodium hexamethyldisilazane at −78 °C, followed by addition of excess methyl iodide afforded the *N*-(3-phenyl-2-methylpropanoyl)oxazolidinone **7** with excellent diastereoselectivity (94:6 diastereomer ratio (dr), measured by HPLC). When this compound was reacted with lithium benzyloxide in the conditions described by Evans the levorotatory ester **8**, of known (2*R*) configuration [11], was obtained. This is the expected product from the attack of the alkyl halide to the less hindered face of the chelated sodium (*Z*)-enolate, assuming an (*S*) configuration for oxazolidinone **5**. Methylation of the sodium enolate derived from (*R*)-4-phenyl-*N*-(3-phenylpropanoyl)oxazolidinone (**10**) took place, as expected, in a completely parallel way (predominant formation of the (2*R*) isomer) but with substantially lower diastereoselectivity (70:30 dr), showing that the ferrocenyl group exerts a higher stereodiscriminating effect than the phenyl one.

2.2. Catalytic asymmetric allylation reactions

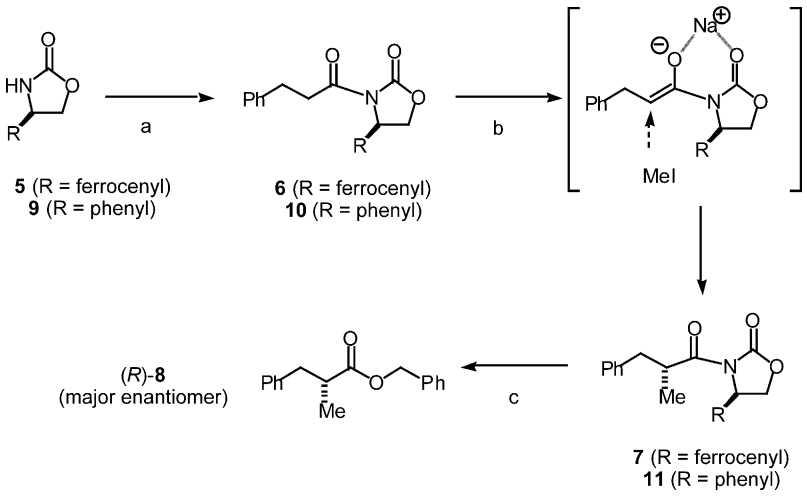
With compounds **2** and **3** in hand, and having firmly established their absolute configuration, we set out to study their applicability in asymmetric catalysis. Ligands **2** and **3** were initially tested in the Pd(0)-catalysed asymmetric allylic alkylation [12] of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate **12** using dimethyl malonate as the nucleophile, a benchmark reaction that has been traditionally used to assess the efficiency of new ligands [13] (Scheme 2).

The results of this study are summarised in Table 1. The required catalysts were either generated in situ (conditions A and B in Table 1) or in a previous step (conditions C and D). Allylpalladium complexes **14** and **15** were readily prepared by reacting allylpalladium chloride dimer with one equivalent of ligands **2** and **3**, respectively, based on palladium, and were isolated as the hexafluorophosphate salts [14].

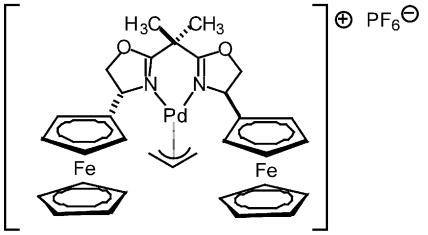


(+)-**4**

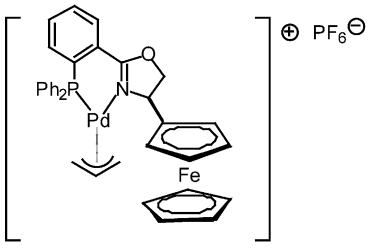
Fig. 1. Induced circular dichroism spectrum at stationary conditions of compound (+)-**4** in solution of dimolybdenum tetraacetate in DMSO, and relation between the absolute configuration of the substrate and the sign of the O–C–C–O dihedral in the Cottonogenic derivative.



Scheme 1. Reagents and conditions: (a) 1.1 equivalents *n*-BuLi, THF, 0 °C; 1.1 equivalents 3-phenylpropanoyl chloride, 0 °C to room temperature (b) 1.5 equivalents sodium bis(trimethylsilyl)amide, THF, −78 °C, 30 min; five equivalents methyl iodide, −78 °C, 3–7 h. (c) 1.5 equivalents lithium benzyloxide, THF, 0 °C, 23 h.



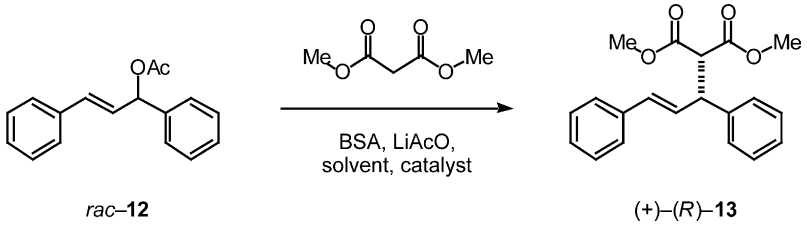
(-)-(*S,S*)-**14**



(-)-(*S*)-**15**

Some reactivity trends are readily apparent from the data gathered in Table 1. First of all, it can be seen that the catalytic activity of the bis(oxazoline) ligand **2** is relatively low, since even after prolonged reaction times the allylic malonate (*R*)-**13** was isolated in minor amounts (9–20% yield), albeit with good optical purity (upto 96:4 er using dichloromethane as the solvent, see entry 2). Not unexpectedly [12b], better results were obtained with the phosphinooxazoline ligand **3**. In this case, both good yields and enantioselectivities (entry 4) were achieved in dichloromethane solution, although tetrahydrofuran also appears to be a suitable solvent (entry 6). The preformed catalyst **15**, both in dichloromethane and in tetrahydrofuran, afforded extraordinarily high enantioselectivities (entries 8 and 9, respectively), but was less reactive that the catalyst prepared in situ. Interestingly enough, when the reaction was performed at 70 °C in tetrahydrofuran solution, the results obtained with the allylpalladium complex **15** (entry 10) were essentially equivalent to those achieved with the catalyst generated in situ in dichloromethane at room temperature. The use of toluene as a solvent (entry 11) led to a significant decrease of the enantioselectivity of the process. In all instances, the major enantiomer of product **13** was the (*R*) one, an stereochemical outcome that can be explained by assuming a nucleophilic attack of the malonate anion to the more sterically crowded terminus of the diphenylallyl moiety in the *exo*-diastereomer of the allylpalladium intermediate (Fig. 2) [12].

We have also briefly examined the behaviour of catalyst **15** in the allylic substitution of *rac*-1,3-dimethylallyl acetate (**16**) (Scheme 3) and of *rac*-2-cyclohexenyl acetate (**18**) (Scheme 4) by dimethyl malonate. In both



Scheme 2. Asymmetric allylic alkylation reaction of diphenylpropenyl acetate **12** using catalysts derived from ligands (*S*,*S*)-**2** and (*S*)-**3**. See Table 1 for the reaction conditions.

Table 1
Asymmetric Pd(0)-catalysed allylic alkylation reactions with 4-ferrocenyl-1,3-oxazoline ligands

Entry	Catalyst [a]	Solvent	Temperature	Time	Yield of **13** (%) [b]	Er of **13** [c]
1	A	Et_2O	Room temperature	26 h	9	94:6
2	A	CH_2Cl_2	Room temperature	26 h	15	96:4
3	B	CH_2Cl_2	Room temperature	92 h	20	94:6
4	C	CH_2Cl_2	Room temperature	17 h	80	94:6
5	C [d]	CH_2Cl_2	Room temperature	18 h	59	95:5
6	C	THF	Room temperature	16 h	72	97:3
7	C	Toluene	Room temperature	19 h	74	94:6
8	D [e]	CH_2Cl_2	Room temperature	7 days	63	99.8:0.2
9	D [e]	THF	Room temperature	7 days	48	98.4:1.6
10	D	THF	70 °C	20 h	78	94:6
11	D	toluene	Room temperature	4 days	48	86:14

[a] A (2% $[Pd(C_3H_5)Cl]_2$, 6% **2**); B (2% **14**); C (2% $[Pd(C_3H_5)Cl]_2$, 6% **3**); D (2% **15**).
[b] Yield of isolated product after chromatographic purification.
[c] Measured by HPLC (Chiralcel-ODH column).
[d] KAcO was used instead of LiAcO.
[e] A 5% of **15** was used in this case.

cases, when the reaction was run in dichloromethane solution at room temperature, conversion was extremely low even after several days. The process was much faster in tetrahydrofuran at 70 °C, and complete conversions were achieved after a few hours. Under these conditions, the (*R*)-enantiomer of the allyl malonate **17** was produced with moderate enantioselectivity (72:28 er), while (*S*)-(2-cyclohexenyl) malonate (**18**) was obtained with very low enantioselectivity. These results are similar to those obtained in general with phosphinooxazoline ligands [12].

In summary, we have shown that 4-ferrocenyl-1,3-oxazolines can give rise to highly enantioselective ligands for asymmetric allylic alkylations, although some structural variation of the 4-ferrocenyl-1,3-oxazoline moiety appears to be necessary in order to improve the applicability scope of the derived catalysts. Work along these lines is underway in our laboratory.

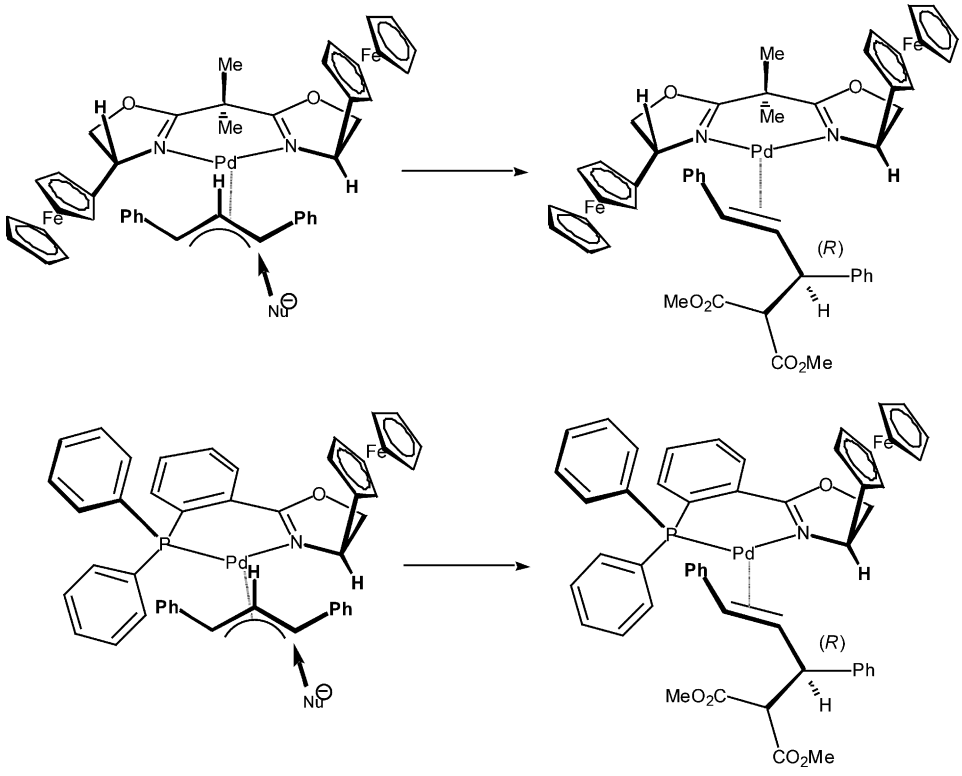
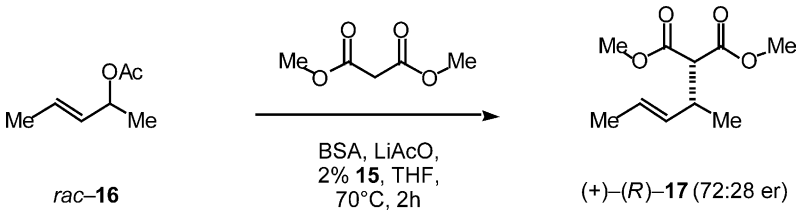
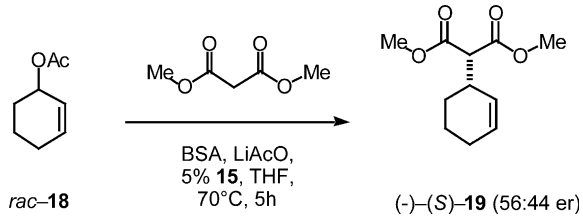


Fig. 2. Rationalisation of the stereochemical outcome of the allylic alkylation reactions mediated by ligands **2** and **3**.



Scheme 3. Asymmetric allylic alkylation reaction of dimethylpropenyl acetate (**16**) using catalyst **15**.



Scheme 4. Asymmetric allylic alkylation reaction of 2-cyclohexenyl acetate (**18**) using catalyst **15**.

3. Experimental

3.1. General and analytical methods

Melting points were determined in an open capillary tube and are uncorrected. Optical rotations were measured at room temperature (r.t.) (23 °C) on a Perkin–Elmer 241 MC polarimeter. Concentrations are given in g 100 ml^{-1}. CD spectra were recorded using a JASCO 720 spectropolarimeter, with a 0.1 cm cell in DMSO and at r.t. Infrared spectra were recorded in a Fourier transform mode, using NaCl film or KBr pellet techniques. The ^{1}H-NMR spectra were recorded at 200 or at 300 MHz (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), and the ^{13}C-NMR spectra were recorded at 50.3 or at 75.4 MHz. ^{31}P-NMR spectra were recorded at 121 MHz. Chemical shifts are given in ppm and referenced to Me_4Si (^{1}H), $CHCl_3$ (^{13}C) or H_3PO_4 (^{31}P). *J* values are given in Hz. Carbon multiplicities were established by DEPT experiments. Mass spectra (MS) were run on a Hewlett–Packard HP-5988 A spectrometer, using CI, EI or FAB ionisation techniques. Exact mass measurements (HRMS) were performed by the 'Unidade de Espectrometria de Masas de la Universidade de Santiago de Compostela'. All reactions were run in flame or oven-dried glassware under a N_2 atmosphere. Reaction progress was followed by TLC (Merck DC-Alufolien KIESELGEL 60 F254). Silica gel (70–230 mesh) was used for column chromatography. Compounds **1**–**5** were prepared as previously described by us [3]. Compounds **9** [15], **12** [16], **16** [17] and **18** [17] were obtained according to published procedures.

3.2. Induced circular dichroism spectrum of (+)-4

To a 1.52 mM DMSO solution of $Mo_2(AcO)_4$ (0.038 mmol in 25 ml), (+)-1-ferrocenylethane-1,2-diol (**4**) (7.0 mg, 0.029 mmol) was added in one portion. The CD spectrum of the mixture was recorded every 10 min, and the stationary state was reached after 1 h at r.t. ICD bands according to Snatzke's nomenclature [9]: λ (nm), $\Delta\varepsilon'$: V, 277, +1.19; IV, 315, −2.15.

3.3. (S)-4-Ferrocenyl-N-(3′-phenylpropanoyl)-1,3-oxazolidin-2-one, (6)

To a cold (0 °C), stirred solution of (*S*)-4-ferrocenyl-1,3-oxazolidin-2-one (**5**) (0.100 g, 0.37 mmol) in anhydrous THF (5 ml), 0.32 ml (0.41 mmol) of a 1.3 M solution of *n*-butyl lithium in hexanes were added with a calibrated syringe, and stirring was maintained for 0.5 h at the same temperature. At this point, 92 μl (0.41 mmol) of 3-phenylpropanoyl chloride was added in one portion. The reaction mixture was then slowly warmed to r.t., and after 1 h TLC analysis showed that no starting material remained. The reaction was quenched by the addition of aqueous saturated ammonium chloride solution (2 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic layers were washed with 1 M aqueous NaOH (2 × 10 ml) and with brine (10 ml), dried over $MgSO_4$ and evaporated at reduced pressure to afford a crude product that upon chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) yielded 0.118 g (79%) of pure (*S*)-4-ferrocenyl-*N*-(3-phenylpropanoyl)-1,3-oxazolidin-2-one (**6**) as a yellow solid.

M.p. 150.5–152.5 °C. $[\alpha]_{\mathbf{D}} = -162.5$ ($c = 0.57$, CH_2Cl_2). IR (KBr): $\nu = 3089$, 2927, 1777, 1702, 1379, 1331, 1248, 1190, 1057, 821 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.91 (m, 2H, 3′-CH_2), 3.16 (m, 2H, 2′-CH_2), 4.21 (m, 8H, Fc), 4.43 (m, 1H, Fc), 4.64 (m, 2H, 5-CH_2), 5.33 (m, 1H, 4-C**H**), 7.20 (m, 5H, Ph). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 30.2 (3′-CH_2), 37.1 (2′-CH_2), 53.4 (4-CH), 65.4 (Fc-CH), 68.5 (Fc-CH), 68.3 (5-CH_2), 68.8 (Fc-CH), 68.9 (Fc-CH), 70.7 (Fc-CH), 84.7 (Fc-Cq), 120.6 (Ph-CH), 128.3 (Ph-CH), 128.4 (Ph-CH), 140.3 (Ph-Cq), 158.0 (1′-Cq), 171.8 (2-Cq). MS (CI, NH_3) $m/e = 404$ [M+1$^+$, 11%], 421 [M+18$^+$, 100%]. HRMS (CI) Calcd. for $C_{22}H_{22}FeNO_3$: 404.0935. Found: 404.0949.

3.4. (*R*)-4-Phenyl-*N*-(3′phenylpropanoyl)-1,3-oxazolidin-2-one (**10**)

To a cold (0 °C), stirred solution of (*R*)-4-phenyl-1,3-oxazolidin-2-one (**9**) (0.500 g, 3.1 mmol) in anhydrous THF (10 ml), 2.0 ml (3.4 mmol) of a 1.6 M solution of *n*-butyl lithium in hexanes were added with a calibrated syringe, and stirring was maintained for 0.5 h at the same temperature. At this point, 0.78 ml (5.6 mmol) of 3-phenylpropanoyl chloride were added in one portion, and the reaction mixture was slowly warmed to r.t. When TLC analysis showed that no starting material remained, the reaction was quenched by the addition of aqueous saturated ammonium chloride solution (5 ml), and extracted with CH_2Cl_2 (3 × 20 ml). The combined organic layers were dried over $MgSO_4$ and evaporated at reduced pressure to afford a crude product that upon chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) yielded 0.859 g (93%) of the desired (*R*)-4-phenyl-*N*-(3-phenylpropanoyl)-1,3-oxazolidin-2-one (**10**) as a colourless solid.

M.p. 122.9–123.8 °C. $[\alpha]_{\mathbf{D}} = -61.0$ ($c = 1.08$, CH_2Cl_2). IR (KBr): $\nu = 2923$, 1779, 1701, 1653, 1559, 1456, 1383, 1259, 1200, 1055, 801 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.93 (m, 2H, 3′-CH_2), 3.27 (m, 2H, 2′-CH_2), 4.27 (dd, $J_{gem(5\text{-}CHH)} = 8.8$ Hz, $J'_{vic(5\text{-}CH,\ 4\text{-}CH)} = 3.8$ Hz, 1H, 5-C**H**H), 4.67 (t, $J_{gem(5\text{-}CHH)} = J'_{vic(5\text{-}CH,\ 4\text{-}CH)} = 8.8$ Hz, 1H, 5-CH**H**), 5.42 (dd, $J_{vic(4\text{-}CH,\ 5\text{-}CH)} = 8.5$ Hz, $J'_{vic(4\text{-}CH,\ 5\text{-}CH')} = 3.8$ Hz, 1H, 4-CH), 7.2–7.3 (m, 10H, Ph). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 30.1 (3′-CH_2), 37.1 (2′-CH_2), 57.5 (4-CH), 69.9 (5-CH_2), 125.8 (Ph-CH), 126.1 (Ph-CH), 128.3 (Ph-CH), 129.1 (Ph-CH), 138.9 (Ph-Cq), 140.2 (Ph-Cq), 154.0 (1′-Cq), 171.7 (2-Cq). MS (CI, NH_3) $m/e = 295$ [M^+, 7%], 296 [$M+1^+$, 100%]. HRMS (CI) Calcd. for $C_{18}H_{18}NO_3$: 296.1287. Found: 296.1290.

3.5. (*S*)-4-Ferrocenyl-*N*-(3′-phenyl-(*R*)-2′-methylpropanoyl)-1,3-oxazolidin-2-one (7)

To a cold (−78 °C) solution of Na[$(Me_3Si)_2N$] (50 mg, 0.25 mmol) in anhydrous THF (5 ml), a solution of the *N*-acyloxazolidinone (**6**) (70 mg, 0.17 mmol) was added slowly via syringe. After stirring for 30 min at the same temperature, a solution of CH_3I (53 μl, 0.85 mmol) in anhydrous THF (5 ml) was added via syringe. The mixture was stirred at −78 °C for 7 h, the reaction was quenched by addition of aqueous saturated ammonium chloride solution (5 ml), and extracted with EtOAc (3 × 15 ml). The combined organic phases were dried over $MgSO_4$ and evaporated at reduced pressure to afford a crude product (94:6 dr) that upon chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) gave 17 mg (24%) of the title compound **7** as a yellow solid. Conditions for the HPLC determination of the diastereomeric purity of **7**: Chiralcel-OD column, 95% C_6H_{14}—5% isopropyl alcohol, $\Phi = 0.5$ ml min^{-1}, $T = 25$ °C, $\lambda = 254$ nm, $t_{R(2'S,4S)} = 65.6$ min, $t_{R\ (2'R,4S)} = 84.3$ min.

M.p. 109.5–111.0 °C. $[\alpha]_{\mathbf{D}} = -186.5$ ($c = 0.50$, CH_2Cl_2). IR (KBr): $\nu = 2925$, 1775, 1701, 1379, 1329, 1231, 1186, 1105, 1030, 957, 820 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.05 (d, $J_{vic(CH3,2'\text{-}CH)} = 6.6$ Hz, 3H, CH_3), 2.64 (dd, $J_{gem(3'\text{-}CHH)} = 13.4$ Hz, $J'_{vic(3'\text{-}CH,2'\text{-}CH)} = 7.2$ Hz, 1H, 3′-C**H**H), 2.98 (dd, $J_{gem(3'\text{-}CHH)} = 13.4$ Hz, $J'_{vic(3'\text{-}CH',2'\text{-}CH)} = 7.8$ Hz, 1H, 3′-CH**H**), 3.9–4.2 (m, 9H, Fc+2′-CH), 4.3–4.4 (m, 2H, Fc+5-C**H**H), 4.61 (dd, $J_{gem(5\text{-}CHH)} = 8.6$ Hz, $J'_{vic(5\text{-}CH,4\text{-}CH)} = 2.6$ Hz, 1H, 5-CH**H**), 5.21 (dd, $J_{vic(4\text{-}CH,5\text{-}CH)} = 8.0$ Hz, $J'_{vic(4\text{-}CH,5\text{-}CH')} = 2.4$ Hz, 1H, 4-CH), 7.25 (m, 5H, Ph). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 16.9 (CH_3), 39.2 (2′-CH), 39.6 (3′-CH_2), 53.5 (4-CH), 65.2 (Fc-CH), 68.3 (5-CH_2), 68.5 (Fc-CH), 68.6 (Fc-CH), 68.7 (Fc-CH), 70.2 (Fc-CH), 84.9 (Fc-Cq), 126.2 (Ph-CH), 128.2 (Ph-CH), 129.1 (Ph-CH), 139.2 (Ph-Cq), 152.7 (1′-Cq), 175.8 (2-Cq). MS (CI, NH3) $m/e = 417$ [M^+, 72%], 418 [$M+1^+$, 100%]. HRMS (CI) Calcd. for $C_{23}H_{24}FeNO_3$: 418.1105. Found: 418.1089.

3.6. (*R*)-4-Phenyl-*N*-(3′-phenyl-(*R*)-2′-methylpropanoyl)-1,3-oxazolidin-2-one (**11**)

To a cold (−78 °C) solution of Na[$(Me_3Si)_2N$] (0.579 g, 3.18 mmol) in anhydrous THF (10 ml), a solution of the *N*-acyloxazolidinone (**10**) (0.627 g, 2.12 mmol) was added slowly via syringe. After stirring for 30 min at the same temperature, a solution of CH_3I (0.62 ml, 10 mmol) in anhydrous THF (5 ml) was added via syringe. The mixture was stirred at −78 °C for 3 h, the reaction was quenched by addition of aqueous saturated ammonium chloride solution (5 ml), and extracted with EtOAc (3 × 20 ml). The combined organic phases were dried over $MgSO_4$ and evaporated at reduced pressure to afford a crude product (dr 70:30, according to ^{1}H-NMR spectroscopy), that upon chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) gave 0.284 g (43%) of the title compound **11** as a colourless solid.

M.p. 88.9–90.0 °C. $[\alpha]_{\mathbf{D}} = -122.5$ ($c = 1.00$, CH2Cl2). IR (KBr): $\nu = 2923$, 1779, 1703, 1603, 1454, 1383, 1236, 1198, 1041, 953 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.14 (m, 3H, CH_3), 2.64 (m, 1H, 3′-C**H**H), 3.01 (m, 1H, 3′-CH**H**), 4.18 (m, 2H, 2′-CH+5-C**H**H), 4.48 (t, $J_{gem(5\text{-}CHH)} = J'_{vic(5\text{-}CH,4\text{-}CH)} = 8.8$ Hz, 1H, 5-CH**H**), 5.29 (dd, $J_{vic(4\text{-}CH,5\text{-}CH)} = 8.8$ Hz, $J'_{vic(4\text{-}CH,5\text{-}CH')} = 3.6$ Hz, 1H, 4-CH), 7.19–7.35 (m, 10H, Ph). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 17.1 (CH_3), 39.4 (3′-CH_2), 39.6 (2′-CH), 57.6 (4-CH), 69.7 (5-CH_2), 125.6 (Ph-CH), 128.2 (Ph-CH), 129.1 (Ph-CH), 139.0 (Ph-Cq), 139.2 (Ph-Cq), 153.2 (1′-Cq), 175.9 (2-Cq). MS (EI) $m/e = 91$ (100%), 118 (83%), 309

[M^+, 12%]. HRMS (EI) Calcd. for $C_{19}H_{19}NO_3$: 309.1365. Found: 309.1374.

3.7. [(S,S)-4-Ferrocenyl-2-(1-methyl-1-(ferrocenyl(1,3-oxazolin-2-yl)ethyl)-1,3-oxazole]-[π-allyl]palladium(II) hexafluorophosphate (**14**)

To a stirred suspension of di-μ-chloro-bis(π-allyl)palladium (28 mg, 0.074 mmol) in absolute EtOH (2 ml), a solution of bis(oxazoline) 2 (78 mg, 0.140 mmol) in absolute EtOH (2 ml) was added via cannula at r.t. The resulting mixture was stirred for 1 h at r.t., at which point an homogeneous orange-coloured solution was obtained. Solid ammonium hexafluorophosphate (25 mg, 0.142 mmol) was added in one portion, and the mixture was left in the refrigerator (4 °C) for 24 h. The precipitate was isolated by filtration, washed with cold (0 °C) absolute EtOH and dried in vacuo to afford 39 mg (33%) of the title compound **14** as a yellow crystalline solid.

M.p. 155.0–156.0 °C. $[\alpha]_{\mathbf{D}} = -269$ ($c = 0.63$, EtOH). IR (KBr): $\nu = 2925$, 1736, 1699, 1684, 1651, 1559, 1474, 1460, 1136, 839, 665 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 1.69 (br s, 6H, $2 \times CH_3$), 2.61 (d, $J_{trans} = 12.3$ Hz, 1H, allyl-C**H**H), 2.64 (d, $J_{trans} = 12.6$ Hz, 1H, allyl-CH**H**), 3.26 (d, $J_{cis} = 6.0$ Hz, 1H, allyl-C′**H**H), 3.85 (dd, $J_{cis} = 6.6$ Hz, $J'_{allyl} = 1.5$ Hz, 1H, allyl-C′H**H**), 4.18 (br s, 14H, Fc), 4.25 (br s, 2H, Fc), 4.31 (br s, 2H, Fc), 4.85 (br, 2H, C**H**HO), 4.99 (br, 4H, CH**H**O + CHN), 5.24 (tt, $J_{trans} = 12.6$ Hz, $J'_{cis} = 6.9$ Hz, 1H, allyl-CH). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 23.5 (CH_3), 27.1 (CH_3), 40.5 (Cq, $C(CH_3)_2$), 61.5 (allyl-CH_2), 61.7 (allyl-C′H_2), 66.3 (CHN), 67.8 (Fc-CH), 68.3 (Fc-CH), 68.8 (Fc-CH), 69.7 (Fc-CH), 75.8 (CH_2O), 87.0 (Fc-Cq), 115.7 (allyl-CH), 172.1 (oxazoline-Cq). HRMS (FAB) Calcd. for $C_{32}H_{35}FeN_2O_2Pd+$: 697.0427. Found: 696.9149.

3.8. [(S)-Diphenyl-(2′-(4-ferrocenyl(1,3-oxazolin-2-yl)phenyl))phosphine]-[π-allyl]palladium(II) hexafluorophosphate (**15**)

To a stirred suspension of di-μ-chloro-bis(π-allyl)palladium (19 mg, 0.051 mmol) in absolute EtOH (2 ml), a solution of phosphinooxazoline **3** (50 mg, 0.097 mmol) in absolute EtOH (2 ml) was added via cannula at r.t. The resulting mixture was stirred for 1 h at r. t., at which point a homogeneous orange-coloured solution was obtained. Solid ammonium hexafluorophosphate (17 mg, 0.089 mmol) was added in one portion, and the mixture was left in the refrigerator (4 °C) for 48 h. The precipitate was isolated by filtration, washed with cold (0 °C) absolute EtOH and dried in vacuo to afford 36 mg (46%) of the title compound **15** as an orange crystalline solid.

M.p. 132.0–135.2 °C. $[\alpha]_{\mathbf{D}} = -284$ ($c = 0.33$, EtOH). IR (KBr): $\nu = 2923$, 1734, 1699, 1653, 1620, 1554, 1541, 1506, 1437, 1119, 837 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 2.8–3.3 (br, 2H, allyl-CH_2), 3.38 (br s, 1H, Fc), 3.71 (m, 1H, allyl-C**H**H), 4.00 (br s, 1H, Fc), 4.12 (s, 5H, Fc), 4.24 (br s, 1H, Fc), 4.28 (br s, 1H, Fc), 4.79 (t, $J_{gem(5\text{-}CHH)} = J'_{vic(5\text{-}CH,4\text{-}CH)} = 9.9$ Hz, 1H, 5-C**H**H), 4.99 (br, 1H, allyl-CH**H**), 5.14 (t, $J_{gem(5\text{-}CHH)} = J'_{vic(5\text{-}CH,4\text{-}CH)} = 9.9$ Hz, 1H, 5-CH**H**), 5.31 (dd, $J_{vic(4\text{-}CH,5\text{-}CH)} = 10.0$ Hz, $J'_{vic(4\text{-}CH,5\text{-}CH')} = 6.9$ Hz, 1H, 4-CH), 5.64 (br, 1H, allyl-CH), 7.03 (m, 2H, Ar-CH), 7.20 (m, 2H, Ar-CH), 7.37 (m, 2H, Ar-CH), 7.4–7.5 (m, 5H, Ar-CH), 7.67 (m, 2H, Ar-CH), 8.20 (dd, J_{vic} (3′-CH,4′-CH) = 7.5 Hz, $4J'_{C\text{-}P} = 4.2$ Hz, 1H, 3′-CH). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 56.0 (br, allyl-CH_2), 65.3 (4-CH), 68.5 (Fc-CH), 68.9 (Fc-CH), 69.2 (Fc-CH), 69.9 (Fc-CH), 74.6 (5-CH_2), 81.0 (br, allyl-CH_2), 87.0 (Fc-Cq), 121.5 (allyl-CH), 127.3 (Ar-Cq), 127.9 (Ar-Cq), 129.4 (Ar-CH), 133.0 (Ar-CH), 133.6 (Ar-CH), 133.7 (Ar-Cq), 133.9 (Ar-CH), 134.1 (Ar-CH), 163.4 (2-Cq). ^{31}P-NMR (121 MHz, $CDCl_3$): δ (ppm) 20.0 (s). HRMS (FAB) Calcd. for $C_{34}H_{31}FeNOPPd$: 662.0517. Found: 661.8481.

3.9. Pd-catalysed allylic substitution of (E)-1,3-diphenyl-2-propenyl acetate (**12**)

3.9.1. With ligand **3** in THF

Phosphinooxazoline **3** (15 mg, 0.03 mmol), di-μ-chloro-bis(π-allyl)palladium (4 mg, 0.01 mmol) and LiOAc (0.6 mg, 0.01 mmol) were dissolved in anhydrous THF (1 ml). After 30 min of stirring at r.t., a solution of the allyl acetate **12** (123 mg, 0.49 mmol) in anhydrous THF (1 ml) was added and stirring was maintained for 1 h. BSA (0.36 ml, 1.46 mmol) and dimethyl malonate (0.17 ml, 1.46 mmol) were added with the aid of a calibrated syringe and the solution was stirred at r.t. for 16 h. At this point, TLC showed that only a trace of the starting acetate was present in the reaction mixture, that was diluted with CH_2Cl_2 (5 ml) and washed with water (3×2 ml). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity). Compound (+)-**13** was isolated as a colourless oil (115 mg, 72% yield, 97:3 er).

3.9.2. With preformed catalyst **15** in CH_2Cl_2

To a stirred solution of complex 15 (11.3 mg, 0.014 mmol) and LiOAc (0.4 mg, 0.006 mmol) in anhydrous CH_2Cl_2 (1 ml) a solution of the allyl acetate 12 (70 mg, 0.28 mmol) in anhydrous CH_2Cl_2 (1 ml) was added and stirring was maintained for 30 min at r. t.. BSA (0.21 ml, 0.83 mmol) and dimethyl malonate (96 μl, 0.83 mmol) were added with the aid of a calibrated syringe and the solution was stirred at r.t. for 7 days. The reaction mixture was diluted with CH_2Cl_2 (5 ml) and washed

with water (3 × 2 ml). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity). Compound (+)-**13** was isolated as a colourless oil (57 mg, 63% yield, 99.8:0.2 er). The absolute configuration of (+)-**13** was assigned by comparison of the optical rotation value ($[\alpha]_D = +18.0$ ($c = 1.1$, EtOH)). with literature data [14]a, [18]. Conditions for the HPLC determination of the enantiomeric purity of **13**: Chiralcel-ODH column, 99% C_6H_{14}–1% isopropyl alcohol, $\Phi = 0.3$ ml min^{-1}, $T = 25$ °C, $\lambda = 254$ nm, $t_{R(R)} = 39.7$ min, $t_{R(S)} = 42.7$ min.

3.10. Pd-catalysed allylic substitution of (*E*)-3-pentenyl acetate (*16*)

To a stirred solution of complex **15** (17.6 mg, 0.022 mmol) and LiOAc (1.4 mg, 0.02 mmol) in anhydrous THF (1 ml) a solution of the allyl acetate **16** (140 mg, 1.09 mmol) in anhydrous THF (1 ml) was added and stirring was maintained for 1 h at r.t. BSA (0.80 ml, 3.27 mmol) and dimethyl malonate (0.38 ml, 3.27 mmol) were added with the aid of a calibrated syringe and the solution was heated and stirred at 70 °C until TLC showed that the starting acetate **16** had disappeared (2 h). After cooling to r.t., the reaction mixture was diluted with CH_2Cl_2 (5 ml) and washed with water (3 × 2 ml). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity). Compound (+)-**17** was isolated as a colourless oil (94 mg, 43% yield, 72:28 er). The absolute configuration of (+)-**17** was assigned by comparison of the optical rotation value ($[\alpha]_D = +7.9$ ($c = 0.10$, $CHCl_3$)). with literature data [18]. Conditions for the GC determination of the enantiomeric purity of **17**: β-DEX column, $T = 80$ °C, $t_{R(S)} = 136.8$ min, $t_{R(R)} = 139.7$ min.

3.11. Pd-catalysed allylic substitution of 2-cyclohexenyl acetate (*18*)

To a stirred solution of complex **15** (19.4 mg, 0.024 mmol) and LiOAc (0.7 mg, 0.01 mmol) in anhydrous THF (1 ml) a solution of the cyclohexenyl acetate **18** (68 mg, 0.48 mmol) in anhydrous THF (1 ml) was added and stirring was maintained for 1 h at r.t. BSA (0.36 ml, 1.44 mmol) and dimethyl malonate (0.17 ml, 1.44 mmol) were added with the aid of a calibrated syringe and the solution was heated and stirred at 70 °C until TLC showed that the starting acetate **18** had disappeared (5 h). After cooling to r.t., the reaction mixture was diluted with CH_2Cl_2 (5 ml) and washed with water (3 × 2 ml). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity). Compound (−)-**19** was isolated as a colourless oil (93 mg, 100% yield, 56:44 er). The absolute configuration of (−)-**19** was assigned by comparison of the optical rotation value ($[\alpha]_D = -3.6$ ($c = 1.66$, $CHCl_3$)). with literature data [19]. Conditions for the GC determination of the enantiomeric purity of **19**: β-DEX column, $T = 120$ °C, $t_{R(S)} = 96.6$ min, $t_{R(R)} = 98.0$ min.

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References

[1] (a) A. Togni, T. Hayashi (Eds.), Ferrocenes, VCH, Weinheim, 1995;
(b) C.J. Richards, A. Locke, Tetrahedron Asymmetry 9 (1998) 2377;
(c) A. Togni, R.L. Halterman (Eds.), Metallocenes, Wiley-VCH, Weinheim, 1998;
(d) A. Togni, N. Bieler, U. Burckhardt, C. Köllner, G. Pioda, R. Schneider, A. Schnyder, Pure Appl. Chem. 71 (1999) 1531.
[2] (a) M. Watanabe, S. Araki, Y. Butsugan, M. Uemura, Chem. Express 5 (1990) 661;
(b) J.A.S. Howell, K. Humphries, P. McArdle, D. Cunningham, G. Nicolosi, A. Patti, M.A. Walsh, Tetrahedron Asymmetry 8 (1997) 1027;
(c) A. Patti, G. Nicolosi, J.A.S. Howell, K. Humphries, Tetrahedron Asymmetry 9 (1998) 4381;
(d) S. Bastin, N. Delebecque, F. Agbossou, J. Brocard, L. Pélinski, Tetrahedron Asymmetry 10 (1999) 1647;
(e) M.R. Paleo, I. Cabeza, F.J. Sardina, J. Org. Chem. 65 (2000) 2108;
(f) S. Bastin, J. Brocard, L. Pélinski, Tetrahedron Lett. 41 (2000) 7303;
(g) N. Taniguchi, M. Uemura, J. Am. Chem. Soc. 122 (2000) 8301.
[3] M. Catasús, A. Bueno, A. Moyano, M.A. Maestro, J. Mahía, J. Organomet. Chem. 642 (2002) 212.
[4] A. Patti, M. Lotz, P. Knochel, Tetrahedron Asymmetry 12 (2001) 3375.
[5] W.G. Jary, J. Baumgartner, Tetrahedron Asymmetry 9 (1998) 2081.
[6] (a) K.B. Sharpless, W. Amberg, Y.L. Bennani, G.A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu, X.-L. Zhang, J. Org. Chem. 57 (1992) 2768;
(b) H.C. Kolb, P.G. Andersson, K.B. Sharpless, J. Am. Chem. Soc. 116 (1994) 1278;
(c) I.E. Markó, J.S. Svendsen, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, vol. 2, Springer-Verlag, Berlin, 1999, p. 713.
[7] See among others: (a) D.L. Boger, J.A. McKie, T. Nishi, T. Ogiku, J. Am. Chem. Soc. 119 (1997) 311;

(b) K.P.M. Vanhessche, K.B. Sharpless, J. Org. Chem. 61 (1996) 7078;
(c) E.M. Carreira, J. Du Bois, J. Am. Chem. Soc. 116 (1994) 10825;
(d) K.J. Hale, S. Manaviazar, S.A. Peak, Tetrahedron Lett. 35 (1994) 425
(e) P. Salvadori, S. Superchi, F. Minutolo, J. Org. Chem. 61 (1996) 4190.

[8] L. Di Bari, G. Pescitelli, C. Pratelli, D. Pini, P. Salvadori, J. Org. Chem. 66 (2001) 4819.

[9] G. Snatzke, U. Wagner, H.P. Wolff, Tetrahedron 37 (1981) 349.

[10] The dibenzoate exciton approach of Harada and Nakanishi is often inappropriate for acyclic 1,2-diols. See: (a) W.T. Wiesler, K. Nakanishi, J. Am. Chem. Soc. 112 (1990) 5574;
(b) K. Nakanishi, N. Berova, in: K. Nakanishi, N. Berova, R.W. Woody (Eds.), Circular Dichroism: Principles and Applications, Wiley-VCH, New York, 2000, Chapter 12.

[11] D.A. Evans, K.T. Chapman, J. Bisaha, J. Am. Chem. Soc. 104 (1982) 1737.

[12] For reviews, see: (a) A. Pfaltz, M. Lautens, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, vol. 2, Springer-Verlag, Berlin, 1999, p. 833;
(b) G. Helmchen, A. Pfaltz, Acc. Chem. Res. 33 (2000) 336. (c) B.M. Trost, D.L. Van Vranken, Chem. Rev. 96 (1996) 395.

[13] Recent examples with ferrocene-based catalysts: (a) T. Fukuda, A. Takehara, M. Iwao, Tetrahedron Asymmetry 12 (2001) 2793;
(b) S.-L. You, X.-L. Hou, L.-X. Dai, J. Organomet. Chem. 637–639 (2001) 762;
(c) W.-P. Deng, S.-L. You, X.-L. Hou, L.-X. Dai, Y.-H- Yu, W. Xiu, J. Sun, J. Am. Chem. Soc. 123 (2001) 6508;
(d) T. Mino, T. Ogawa, M. Yamashita, Heterocycles 55 (2001) 453;
(e) J. Kang, J.H. Lee, J.S. Choi, Tetrahedron Asymmetry 12 (2001) 33.

[14] For the use of preformed allylpalladium complexes as catalysts in asymmetric allylic alkylations, see: (a) J.M. Brown, D.I. Hulmes, P.J. Guiry, Tetrahedron 50 (1994) 4493;
(b) P. Von Matt, G.C. Lloyd-Jones, A.B.E. Mindis, A. Pfaltz, L. Macko, M. Neuburger, M. Zehnder, H. Rüegger, P.S. Pregosin, Helv. Chim. Acta 36 (1995) 265.

[15] J.R. Gage, D.A. Evans, Org. Synth. 68 (1989) 77.

[16] B. Horvath, H.P. Klein, J.P. Schaefer, J. Org. Chem. 33 (1968) 2647.

[17] I. Fleming, D. Higgins, N.J. Lawrence, A.P. Thomas, J. Chem. Soc. Perkin Trans. 1 (1992) 3331.

[18] J. Kang, W.O. Cho, H.G. Cho, Tetrahedron Asymmetry 5 (1994) 1347.

[19] A. Saitoh, M. Misawa, T. Morimoto, Tetrahedron Asymmetry 10 (1999) 1025.