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New chiral ferrocenyloxazolines: The first planar chiral triferrocenylmethane derivative and its use in asymmetric catalysis

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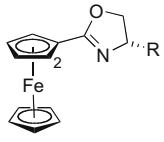
ABSTRACT

New planar chiral enantiopure ferrocenyloxazolines have been prepared including ferrocenyldiphenylmethanol, diferrocenylphenylmethanol and triferrocenylmethanol derivatives (*S*,*pR*)-**10** – (*S*,*pR*)-**12**, the latter being the first chiral triferrocenylmethanol derivative. The ferrocenyldiphenylmethanol derivative (*S*,*pR*)-**10** has been crystallographically characterized. Asymmetric ethylation of some arylaldehydes using diethylzinc in the presence of the planar chiral triferrocenylmethanol derivative (*S*,*pR*)-**12** afforded good yields and *ees*, which were higher than those obtained with related ferrocenyloxazolines.

1. Introduction

Chiral ferrocenyloxazolines **1** give access to valuable catalysts for a variety of enantioseletive reactions [1,2]. This is due to the fact that a large number of chiral ferrocenyloxazolines **1** are readily accessible in enantiomerically pure form from ferrocene carboxylic acid and enantiopure 2-amino alcohols, which are available by reduction of respective α-amino acids thus defining the substituent R. In addition, the oxazoline substituent facilitates a stereoselective metalation at C-2 resulting in planar chiral ferrocenyloxazolines after electrophilic quench with E [3,4]. In this context phosphinoferrocenyloxazolines (**2**, $E = PR'_2$) have gained particular importance as bidendate catalyst ligands [2,5].



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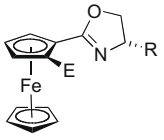

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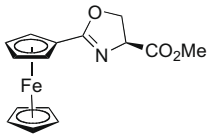
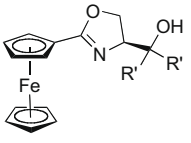
Here, we report on the synthesis of some new complexes of types **1** and **2** including some bearing diphenylhydroxymethyl, ferrocenylphenylhydroxymethyl and diferrocenylhydroxymethyl substituents E. In addition, some catalytic properties of the latter were evaluated.

2. Results and discussion

The coordination of oxazoline moieties at metal atoms is the basis for important *ortho* metalation reactions as well as of transition metal catalyzed asymmetric transformations [2,6,7]. Along with the oxazoline N and O atoms, substituents R and E in **1** and **2** may offer additional possibilities for coordination at metal atoms.



(*S*)-**3**



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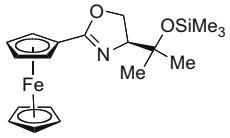
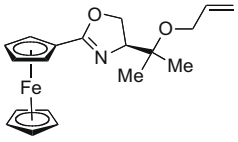
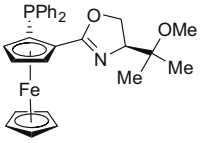
With respect to substituent R this implies the use of amino alcohols bearing additional functionality. Starting from (*S*)-serine, Richards prepared some interesting ferrocenyloxazolines such as methyl ester (*S*)-**3** (*ee* > 95%), from which alcohols **4** (R′ = H, Me, Et, Ph) and the respective methyl ethers were obtained in high yields [8]. In this context we prepared the new ferrocenyloxazolines (*S*)-**5** and (*S*)-**6** from (*S*)-**4** (R′ = Me) by deprotonation followed by treatment with chlorotrimethylsilane or allylbromide in 64% and 48% yield, respectively. (*S*)-**5** and (*S*)-**6** are precursors of 1,2-disubstituted derivatives with a masked functionality at the oxazoline side arm. In addition, (*S*,*pR*)-**7** and (*S*,*pS*)-**8** were prepared in 31% and 63% yield, respectively, from Richard's methyl ether by treatment with BuLi/TMEDA at −78 °C followed by electrophilic quench with chlorodiphenylphosphane or benzophenone. The stereochemical assignments are based on the analogy to published reactions [4,9].



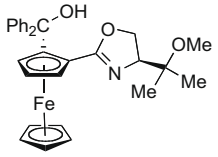
(*S*)-**5**



(*S*)-**6**

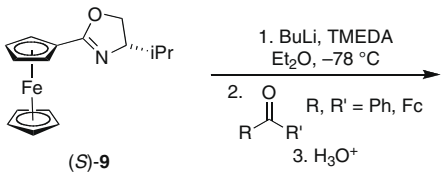


(*S*,*pR*)-**7**

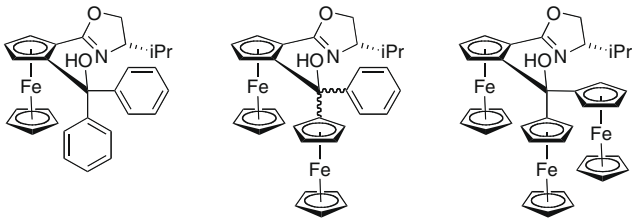


(*S*,*pS*)-**8**

In connection with our interest in triferrocenylmethane derivatives [10,11] we envisaged a combination of this motif with the option of planar chirality resulting from respective ferrocenyloxazolines. Therefore, we prepared (*S*)-**9** [1,5], whose diastereoselective metalation under modified Sammakia conditions followed by quench with benzophenone, benzoylferrocene [12,13] or ferrocenoylferrocene [14,15] afforded complexes (*S*,*pR*)-**10**, **11**, and (*S*,*pR*)-**12** in 96%, 80%, and 61% yield, respectively, with **11** having been formed as a 3:1 diastereomeric mixture. To our knowledge (*S*,*pR*)-**12** is the first known chiral triferrocenylmethanol derivative. All three products were identified spectroscopically with all spectra being in full accord with the assigned formulas. In addition, it was possible to obtain crystals of (*S*,*pR*)-**10** suitable for an X-ray crystal structure analysis (Fig. 1) from *tert*-butyl methyl ether (TBME).

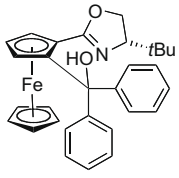


(*S*)-**9**



(*S*,*pR*)-**10** (96 %) (*S*)-**11** (3:1, 80 %) (*S*,*pR*)-**12** (61 %)

The structure shows that the phenyl groups adopt a conformation almost perpendicular to the cyclopentadienyl plane, which is almost coplanar with that of the conjugated oxazoline ring. The hydroxy group shows a H bridge to the oxazoline N atom, a feature, which has also been observed by Bolm in the structure of (*S*,*pR*)-**13** as well as in that of a related tricarbonylrhenium complex [16–18].



(*S*,*pR*)-**13**

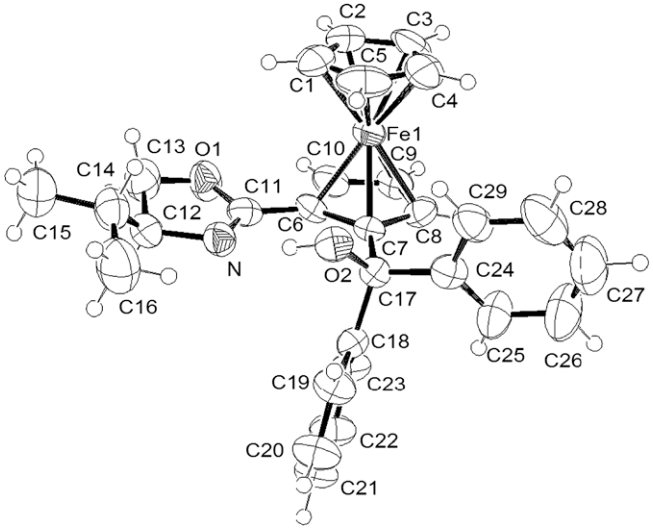
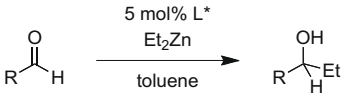


Fig. 1. Structure of (*S*,*pR*)-**10** in the crystal. Selected bond lengths [pm], angles [°] and dihedral angles [°]: C6–C11 146.3(4), C7–C17 154.7(4), C11–N 126.2(4), C11–O1 136.4(3), C17–O2 142.9(3), C17–C18 152.5(4), C17–C24 152.9(4), O2–C17–C7 110.4(3), N–C11–C6 129.0(3), N–C12–C14 112.0(3), C7–C6–C11 128.3(3), N–C11–C6–C7 –6.8, N–C11–C6–C10 176.5, O2–C17–C7–C6 –51.7, C25–C24–C17–C7 –84.6, C23–C18–C17–C7 20.8, C29–C24–C17–C7 91.4.



Ferrocenyloxazolines bearing alkylated or arylated hydroxymethyl substituents have been used as catalysts for the asymmetric alkylation and alkynylation of aldehydes [16,17,19]. Therefore, we became interested in testing complexes (*S*,*pR*)-**10** and (*S*,*pR*)-**12** as catalysts for this reaction. The results of the alkylation of some aryl aldehydes with diethylzinc are summarized in Table 1, and for the purpose of comparison those obtained by using the closely related (*S*,*pR*)-**13** as catalyst are also included [16,17].The data in Table 1 show that catalysis by (*S*,*pR*)-**10** or by (*S*,*pR*)-**12** has the same stereochemical outcome as that with (*S*,*pR*)-**13**, all products show *R* configuration. While the reaction times were somewhat longer than with (*S*,*pR*)-**13** the yields and the *ee*s obtained are in the range of that with (*S*,*pR*)-**13** or even somewhat higher. Particularly the reactions catalyzed by the triferrocenylmethanol derivative (*S*,*pR*)-**12** are successful giving the highest *ee*s in most cases.

With respect to the transition state we believe that the situation described by Bolm et al. [17] is enhanced by the additional steric bulk of the two ferrocenyl substituents in place of the two phenyl groups in (*S*,*pR*)-**13** thereby further stabilizing the transition state leading to the *R* product as compared to that leading to the *S* product (Fig. 2). The proposed transition state shows a delicate combination of the central chirality located at the oxazoline carbon atom and the planar chirality of the disubstituted ferrocene moiety [20]: there is obviously cooperation resulting in an efficient steric shielding of the face of the O–Zn–N seven membered ring, at which the isopropyl group and the unsubstituted cyclopentadienyl ligand of the disubstituted ferrocene moiety are located. The higher steric bulk of the other two ferrocene moieties as compared to phenyl groups will presumably reduce the conformational flexibility of the system and thereby stabilize this transition state.

Attempts to perform asymmetric arylations [21] with (*S*,*pR*)-**10** or with (*S*,*pR*)-**12** carried out in cooperation with the Bolm group gave, however, disappointing results: While the results with (*S*,*pR*)-**10** were similar to those obtained with (*S*,*pR*)-**13** [22], the reactions with (*S*,*pR*)-**12** gave almost no stereoselection [23].

Hou has reported the asymmetric addition of phenylethyne to aldehydes giving the respective propargylic alcohols in high enantiomeric excess with a series of chiral ferrocenyloxazolines bearing a hydroxydiphenylmethyl substituent at the other cyclopentadienyl ligand thereby lacking planar chirality [19]. The aldehydes listed in Table 1 were used for testing this reaction with (*S*,*pR*)-**10** and (*S*,*pR*)-**12** as catalysts. However, while the yields achieved were up to 92%, the enantiomeric excesses remained below 20%.

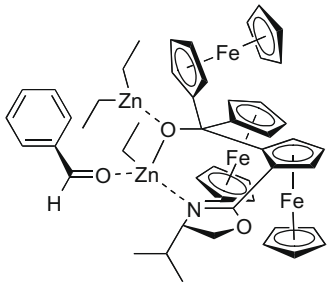


Fig. 2. Proposed transition state for the ethylation of benzaldehyde with Et_2Zn catalyzed by (*S*,*pR*)-**12**.

3. Conclusion

In addition to a number of new enantiopure ferrocenyloxazolines, we have prepared the planar chiral triferrocenylmethanol catalyst (*S*,*pR*)-**12**, which behaves superior to related ones in the ethylation of aryl aldehydes. In the proposed transition state there appears to be a cooperation between the central chirality of the oxazolinyl substituent, the planar chirality of the disubstituted ferrocene moiety and the steric bulk of the two other ferrocenyl substituents, presumably resulting in a reduction the conformational flexibility of the system.

4. Experimental

General: All operations involving air sensitive materials were performed under argon using standard Schlenk techniques. Diethyl ether (EE), THF, and benzene were dried over Na/K – benzophenone; petroleum ether (PE) and *tert*-butyl methyl ether (TBME) were dried over $CaCl_2$. Dibutyl ether and dichloromethane were dried over CaH_2 and distilled under Ar prior to use. Starting materials were either purchased or prepared according to literature procedures. IR: Perkin Elmer 2000, FT 1170 (ATR). – ^{1}H NMR: Bruker AVS 400 (400.1 MHz). Chemical shifts refer to

Table 1
Asymmetric ethylation of arylaldehydes.

Entry	RCHO	L*	Reaction time (h)	Yield[a] (%)	*ee* (%)	Absolute configuration[d]
1	C_6H_5CHO	(*S*,*pR*)-**10**	24	97	83[b]	R
2 [16,17]	C_6H_5CHO	(*S*,*pR*)-**13**	6	83	93	R
3	C_6H_5CHO	(*S*,*pR*)-**12**	24	95	97[b]	R
4	p-ClC_6H_4CHO	(*S*,*pR*)-**10**	24	80	85[b]	R
5 [16,17]	p-ClC_6H_4CHO	(*S*,*pR*)-**13**	6	94	86	R
6	p-ClC_6H_4CHO	(*S*,*pR*)-**12**	24	80	97[b]	R
7	PhCH=CHCHO	(*S*,*pR*)-**10**	24	87	70[b]	R
8 [16,17]	PhCH=CHCHO	(*S*,*pR*)-**13**	6	89	78	R
9	PhCH=CHCHO	(*S*,*pR*)-**12**	24	99	80[b]	R
10	p-$MeOC_6H_4CHO$	(*S*,*pR*)-**10**	24	98	84[b]	R
11 [16,17]	p-$MeOC_6H_4CHO$	(*S*,*pR*)-**13**	9	93	91	R
12	p-$MeOC_6H_4CHO$	(*S*,*pR*)-**12**	24	95	90[b]	R
13	1-Naphtaldehyde	(*S*,*pR*)-**10**	24	94	90[c]	R
14	1-Naphtaldehyde	(*S*,*pR*)-**12**	24	98	97[c]	R

[a] Yield in % based on aldehyde.
[b] Determined by GC.
[c] Determined by ^{1}H NMR.
[d] Configurations were assigned by comparison of the specific rotations with those of known compounds.

δ_{TMS} = 0 ppm or to residual solvent peaks. br: broad, unresolved signal – ^{13}C NMR: Bruker AVS 400 (100 MHz). Chemical shifts refer to δ_{TMS} = 0 ppm or to residual solvent peaks. – MS (EI, ESI-MS): AMD 604 Inectra, Finnigan MAT 112, MAT 312, 70 eV. – HRMS: Finnigan MAT 312, VG Autospect. – Melting points: Electrothermal IA 9200. GC: Hewlett Packard HPGC, SE-54 capillary column, FID detector 19231 D/E.

4.1. (S)-2-Ferrocenyl-4-(1-trimethylsilyloxy-1-methylethyl)oxazoline [(S)-**5**]

A suspension of (*S*)-1-(2-ferrocenyl-4,5-dihydrooxazol-4-yl)-1-methylethanol [3] (0.120 g, 0.4 mmol), imidazol (0.122 g, 1.8 mmol) and Me_3SiCl (0.10 mL, 0.8 mmol) in anhydrous THF (15 mL) was stirred at 25 °C for 24 h. Hydrolysis was performed by addition of a saturated aqueous solution of $NaHCO_3$ (20 mL). The reaction mixture was diluted with TBME (100 mL) and the organic layer was washed with H_2O (3 × 25 mL), dried over $MgSO_4$, and the solvent was removed at reduced pressure. Column chromatography (SiO_2, 25 × 2.5 cm, PE/EE 9:1) gave pure (*S*)-2-ferrocenyl-4-(1-trimethylsilyloxy-methylethyl)oxazoline [(*S*)-**5**] (0.095 g, 0.2 mmol, 64%) as a red liquid.

IR (ATR): $\tilde{\nu}$ = 2963 cm^{-1} (w), 2920 (w), 2851 (w), 1569 (s, C=N), 1261 (s), 1126 (s), 1086 (s), 1019 (s, SiOC), 793 (s, SiOC). ^{1}H NMR (400 MHz, $CDCl_3$):δ 0.12 [s, 9H, Si(CH_3)$_3$], 1.20 (s, 3H, CCH_3), 1.37 (s, 3H, CCH_3), 4.02 (dd, ABX line system, $^3J_{trans}$ = 7.2 Hz, $^3J_{cis}$ = 9.8 Hz, 1H, NCH), 4.19 (s, 5H, CpH), 4.24 (dd, ABX line system, $^2J_{gem}$ = –8.8 Hz, $^3J_{cis}$ = 9.8 Hz, 1H, OCH_2), 4.31 (m, 2H, CpR), 4.38 (dd, ABX line system, $^3J_{trans}$ = 7.3 Hz, $^2J_{gem}$ = –8.7 Hz, 1H, OCH_2), 4.72 (m, 1H, CpR), 4.76 (m, 1H, CpR) ppm. ^{13}C NMR (100 MHz, BB, HMBC, HMQC, $CDCl_3$):δ 2.5 [Si(CH_3)$_3$], 24.3 (CCH_3), 28.8 (CCH_3), 68.7 (OCH_2), 68.9 (*C*H-CpR), 69.0 (*C*H-CpR), 69.4 (*C*H-CpH), 70.10 (*C*H-CpR), 70.12 (*C*H-CpR), 70.5, (*C*R-CpR), 74.9 (NCH*C*OSi), 76.2 (NCH), 167.0 (OC=N) ppm. MS (ESI, ES$^+$): *m/z* = 386 [M+H$^+$]. HRMS (ESI) ($C_{19}H_{28}FeNO_2Si$): Calc.: 386.1239; found: 386.1232 [M+H].

4.2. (S)-2-Ferrocenyl-4-[1-(2-propenoxy)-1-methylethyl]oxazoline [(S)-**6**]

To a suspension of (*S*)-1-(2-ferrocenyl-4,5-dihydrooxazol-4-yl)-1-methylethanol [3] (0.134 g, 0.4 mmol) and NaH (0.400 g, 60% in mineral oil, 10.0 mmol) in anhydrous THF (40 mL) under nitrogen, allyl bromide (0.25 mL, 2.4 mmol) was added and the reaction mixture was heated at reflux for 3 h until no starting material remained (TLC, EE). Hydrolysis was performed by addition of a saturated aqueous solution of $NaHCO_3$ (25 mL). The reaction mixture was diluted with EE (25 mL), and the organic layer was washed with H_2O (3 × 25 mL), dried over $MgSO_4$, and the solvent was removed at reduced pressure. Column chromatography (SiO_2, 25 × 4 cm, PE/EE 7:3) gave pure (*S*)-2-ferrocenyl-4-(1-allyloxy-methylethyl)oxazoline [(*S*)-**6**] (0.073 g, 0.2 mmol, 48%) as a yellow liquid.

$[\alpha]_{20}^{D}$ = +98 (*c* = 0.51, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3098 cm^{-1} (w, =CH), 3062 (w), 2976 (w), 2931 (w), 1646 (s, C=N). ^{1}H NMR (400 MHz, $CDCl_3$):δ 1.15 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 3.9 (m, 2H, OCH_2CH=), 4.16–4.21 (m, 1H, NCH), 4.18 (s, 5H, CpH), 4.27 (ddd, ABMX line system, *J* = 9.9 Hz, 1H, OCH_2), 4.32 (m, 2H, CpR), 4.43 (dd, *J* = 7.1 Hz, *J* = 8.5 Hz, 1H, OCH_2), 4.71 (m, 1H, CpR), 4.76 (m, 1H, CpR), 5.11 (dd, ABX line system, *J* = 1.6 Hz, *J* = 10.4 Hz, 1H, =CH_2), 5.25 (dd, ABX line system, *J* = 1.7 Hz, *J* = 17.2 Hz, 1H, =CH_2), 5.89 (m, 1H, *C*H=CH_2) ppm. ^{13}C NMR (100 MHz, BB, APT, HMBC, HMQC, $CDCl_3$):δ 20.0 (–, CH_3), 23.8 (–, CH_3), 62.9 (+, OCH_2CH=), 68.4 (+, OCH_2CHN), 68.9 (–, *C*H-CpR), 69.0 (–, *C*H-CpR), 69.5 (–, *C*H-CpH), 70.09 (–, *C*H-CpR), 70.13 (–, *C*H-CpR) 70.5 (+, *C*R-CpR), 74.4 (–, NCH), 76.4 [–, NCH*C*(CH_3)$_2$], 115.5 (+, =CH_2), 135.8 (–, *C*H=CH_2), 166.9 (+, OCN) ppm. - MS (ESI, ES$^+$): *m/z* = 354 [M+H$^+$]. HRMS (ESI) ($C_{19}H_{24}FeNO_2$): Calc.: 354.1156; found: 354.1147 [M+H].

4.3. General procedure for the ortho-functionalization of ferrocenyloxazolines (**GP1**)

To a dark orange solution of the ferrocenyloxazoline and TMEDA in anhydrous Et_2O, a solution of BuLi in hexane was added dropwise at –78 °C. After stirring at –78 °C for 4 h the electrophile was added and the solution was allowed to warm to 25 °C over 14 h. H_2O was added and the reaction crude dissolved in EE. The organic layer was washed with water (3 × 20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, giving the pure compound after recrystallization or column chromatography.

4.4. (S,pR)-2-(2-Diphenylphosphanylferrocenyl)-4-(1-methoxy-1-methylethyl)oxazoline [(S,pR)-**7**]

GP1; (*S*)-2-Ferrocenyl-4-(1-methoxy-1-methylethyl)oxazoline [(*S*)-**4**, R′ = Me] [8] (0.309 g, 0.9 mmol), TMEDA (0.2 mL, 1.2 mmol); Et_2O (3.6 mL), BuLi (0.8 mL, 1.6 M in hexane, 1.3 mmol), Ph_2PCl (0.4 mL, 2.2 mmol), column chromatography (SiO_2, 25 × 2 cm, EE followed by EE/Et_3N 20:1) gave pure (*S,pR*)-**7** (0.151 g, 0.3 mmol, 31%, >95% *de*) as a red liquid. The configuration assignment is based on literature precedence [4,9].

$[\alpha]_{20}^{D}$ = −62.5 (*c* = 0.176, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3075 cm^{-1} (w, =CH), 2970 (w), 2925 (w), 2828 (w), 1618 (s, C=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 3H, CCH_3), 1.12 (s, 3H, CCH_3), 3.14 (s, 3H, OCH_3), 3.79 (dd, ABX line system, *J* = *J* = 8.0 Hz, 1H, CH_2), 3.86 (m, 1H, CpR), 3.90 (dd, ABX line system, *J* = *J* = 8.0 Hz, 1H, NCH), 4.15 (dd, ABX line system, *J* = *J* = 9.1 Hz, 1H, CH_2), 4.42 (m, 1H, CpR), 4.46 (s, 5H, CpH), 5.0 (m, 1H, CpR), 7.34–7.44 (m, 6H, Ph), 7.60–7.65 (m, 2H, Ph), 7.80–7.75 (m, 2H, Ph) ppm. ^{13}C NMR (100 MHz, BB, HMQC, HMBC, $CDCl_3$): δ 18.9 (CCH_3), 22.4 (CCH_3), 49.4 (OCH_3), 68.6 (CH_2), 71.16 (CH_{CpH}), 71.3 (CH_{CpR}), 73.7 (CH_{CpR}), 73.8 [C_{Fc}C=N], 74.0 (NCH), 74.2 [d, J_{P-C} = 16.7 Hz, C_{Fc}P], 76.3 ($COCH_3$), 78.4 (d, J_{P-C} = 14.5 Hz, CH_{CpR}), 127.8 (d, J_{P-C} = 7.2 Hz, C_{Ph}), 128.0 (d, J_{P-C} = 6.7 Hz, C_{Ph}), 130.7 (d, J_{P-C} = 2.7 Hz, C_{Ph}), 131.0 (d, J_{P-C} = 2.5 Hz, C_{Ph}), 131.1 (d, J_{P-C} = 9.7 Hz, C_{Ph}), 131.5 (d, J_{P-C} = 9.1 Hz, C_{Ph}), 134.1 (d, J_{P-C} = 11.4 Hz, C_{Ph}), 135.2 (d, J_{P-C} = 16.4 Hz, C_{Ph}), 164.5 (OCN) ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ 27.4 (PPh_2) ppm. MS (ESI, ES$^+$): *m/z* = 528 [M+O+H$^+$], 512 [M+H$^+$], 550 [M+O+Na$^+$]. HRMS (ESI) ($C_{29}H_{31}FeNO_2$): Calc.: 512.1442; found: 512.1453 [M+H].

4.5. (S,pS)-2-(2-Diphenylhydroxymethylferrocenyl)-4-(1-methoxy-1-methylethyl)-oxazoline [(S,pS)-**8**]

GP1; (*S*)-2-Ferrocenyl-4-(1-methoxy-1-methylethyl)oxazoline [(*S*)-**4**, R′ = Me] [8] (0.174 g, 0.5 mmol), TMEDA (0.1 mL, 0.7 mmol), Et_2O (2.0 mL), BuLi (0.4 mL, 1.6 M in hexane, 0.7 mmol), benzophenone (0.206 g, 1.1 mmol), column chromatography (SiO_2 deactivated with a 5% Et_3N solution in PE, 25 × 4 cm, PE/CH_2Cl_2 10:1) gave pure (*S,pS*)-**B** (0.170 g, 0.3 mmol, 63%, >95% *de*) as a yellow-red solid. Recrystallization from hexane gave yellow-red crystals (m.p. 143 °C) of (*S,pS*)-**B.** The configuration assignment is based on literature precedence [4,9].

$[\alpha]_{20}^{D}$ = +328 (*c* = 0.36, $CHCl_3$). IR (ATR): $\tilde{\nu}$ = 3095cm^{-1} (w, OH), 3076 (w, =CH), 2962 (w), 2931 (w), 2828 (w), 1650 (s, C=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (s, 3H, CCH_3), 1.34 (s, 3H, CCH_3), 3.30 (s, 3H, OCH_3), 3.76 (dd, *J* = 1.7 Hz, 1H, CH_{CpR}), 3.88 (dd, ABX line system, *J* = 8.2 Hz, *J* = 9.9 Hz, 1H, NCH), 4.18 (dd, ABX line system, ^3J = ^2J = 9.9 Hz, 1H, CH_2), 4.32 (dd, ^3J = ^4J = 2.5 Hz, 1H, CH_{CpR}), 4.37 (s, 5H, CH_{CpH}), 4.38 (dd, ABX line system, *J* = *J* = 8.5 Hz, 1H, CH_2), 4.82 (dd, ^3J = ^4J = 2.4 Hz, 1H, CH_{CpR}), 7.20 (m, 5H, Ph), 7.31 (m, 1H, Ph), 7.36–7.40 (m, 2H, Ph), 7.57–7.59 (m, 2H, Ph), 9.23 (s,

1H, OH) ppm. ^{13}C NMR (100 MHz, BB, HMQC, HMBC, $CDCl_3$): δ 20.5 (CCH_3), 22.7 (CCH_3), 49.5 (OCH_3), 65.6 (CR_{CpR}), 68.0 (CH_{CpR}), 68.3 (CH_2), 70.4 (CH_{CpR}), 70.6 (CH_{CpH}), 75.0 (CH_{CpR}), 75.4 ($COCH_3$), 73.7 (NCH), 77.3 (COH), 101 (CR_{CpR}), 126.2 (Ph), 126.5 (Ph), 127.0 (Ph), 127.1 (Ph), 127.3 (Ph), 127.8 (Ph), 146.3 (Ph), 149.1 (Ph), 158.4 (OCN) ppm. MS (ESI, ES$^+$): m/z = 492 [M$^+$–OH], 510 [M+H$^+$], 532 [M+Na$^+$]. HRMS (ESI) ($C_{30}H_{32}FeNO_3$): Calc.: 510.1732; found: 510.1732 [M+H]. $C_{30}H_{31}FeNO_3$: Calc.: C, 70.73; H, 6.13; N, 2.75. Found: C, 70.64; H, 6.09; N, 2.69%.

4.6. (S,pR)-**2**-[(2-Diphenylhydroxymethyl)ferrocenyl]-4-isopropyloxazoline [(S,pR)-**10**]

GP1; (*S*)-2-ferrocenyl-4-isopropyloxazoline [(*S*)-**9**, 0.504 g, 1.7 mmol], TMEDA (0.33 mL, 2.2 mmol), Et_2O (6.3 mL), BuLi (1.4 mL, 1.6 M in hexane, 2.2 mmol), benzophenone (0.309 g, 1.7 mmol), column chromatography (SiO_2 deactivated with a 5% Et_3N solution in PE, 25 × 4 cm, PE/CH_2Cl_2 10:1) gave pure (*S,pR*)-**10** (0.777 g, 1.6 mmol, 96%, >95% *de*) as a yellow-red solid. Recrystallization from hexane gave crystals of (*S,pR*)-**10** (0.511 g, 1.1 mmol, 63%, >95% *de*, m.p. 135 °C).

$[\alpha]_{20}^{D} = -366$ (c = 0.12, $CHCl_3$). IR (ATR): $\tilde{\nu} = 3514\ cm^{-1}$ (w, OH), 3056 (w, Cp-H), 2954 (w), 2873 (w), 1650 (s, C=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.05 (d, ^3J = 6.7 Hz, 3H, CH_3), 1.83–1.75 [m, 1H, $CH(CH_3)_2$], 3.67–3.61 (ddd, ABMX line system, ^3J = 6.4 Hz, $^3J_{trans}$ = 8.4 Hz, $^3J_{cis}$ = 9.8 Hz, 1H, NCH), 3.72 (dd, J = 1.6 Hz, J = 2.5 Hz, 1H, CpR), 3.98 (dd, ABX line system, $^3J_{trans} = {}^2J_{gem}$ = 8.3 Hz, 1H, OCH_2), 4.17 (dd, ABX line system, $^2J_{gem}$ = 8.4 Hz, $^3J_{cis}$ = 9.8 Hz, 1H, OCH_2), 4.27 (t, J = 2.5 Hz, 1H, CpR), 4.28 (s, 5H, CpH), 4.76 (dd, J = 1.6 Hz, J = 2.5 Hz, 1H, CpR), 7.14–7.18 (m, 5H, Ph), 7.24–7.36 (m, 3H, Ph), 7.53–7.55 (m, 2H, Ph), 9.3 (s, 1H, OH) ppm. ^{13}C NMR (100 MHz, BB, DEPT, $CDCl_3$): δ 18.6 (CH_3), 18.8 (CH_3), 32.4 [$CH(CH_3)_2$], 66.0 (CpR_2), 67.9 (NCH), 70.0 (CpR_2), 70.4 (CH_2), 70.6 (CpH), 71.5 (CpR_2), 74.9 (CpR_2), 77.2 (CpR_2), 100.5 (CPh_2) 126.2 (Ph), 126.5 (Ph), 127.0 (Ph), 127.1 (Ph), 127.4 (Ph), 127.8 (Ph), 146.4 (Ph), 149.2 (Ph), 167.5 (OCN) ppm. MS (ESI, ES$^+$): m/z = 462 [M$^+$–OH], 480 [M+H$^+$]. HRMS (ESI) ($C_{29}H_{30}FeNO_2$): Calc.: 480.1626; found: 480.1606 [M+H]. $C_{29}H_{29}FeNO_2$: Calc.: C, 72.66; H, 6.10; N, 2.92. Found: C, 72.33; H, 5.95; N, 2.80%.

Crystal Structure Analysis of (*S,pR*)-**10** : $C_{29}H_{29}FeNO_2$, molecular weight, 479.38 g mol^{-1}, temperature 297 K, crystal system tetragonal, space group $P4_12_12$ (No. 92), a = 11.851(3), b = 11.851(3), c = 35.173(15) Å, α = 90°, β = 90°, γ = 90°, V = 4940(3) Å^3, Z = 8, ρ_{calc} = 1.289 g cm^{-3}, F(000) = 2016, Absorption coefficient = 0.636 mm^{-1}, crystal size 0.21 × 0.14 × 0.14 mm, Stoe IPDS area detector diffractometer, θ range = 1.81–24.24°, limiting indices $-13 \leqslant h \leqslant 13$, $-13 \leqslant k \leqslant 13$, $-40 \leqslant l \leqslant 40$, reflections collected/unique 53815/3979 [R_{int} = 0.1239], completeness of data (θ = 24.24): 99.5%, empirical absorption correction (multi-scan), no extinction correction, refinement method full-matrix least-squares on F^2, goodness-of-fit on F^2 = 0.708, R_1 = 0.0302, wR_2 = 0.0338 ($I > 2\sigma(I)$), R-indices [all data]: R_1 = 0.0808, wR_2 = 0.0391, minimal and maximal residual electron density –0.267/0.162 e Å^{-3}.

4.7. (S,pR)-2-[2-(Diferrocenylhydroxymethyl)ferrocenyl]-4-isopropyloxazoline (S,pR)-**12**

GP1; (*S*)-2-ferrocenyl-4-isopropyloxazoline [(*S*)-**9**] 0.503 g, 1.7 mmol], TMEDA (0.33 mL, 2.2 mmol), Et_2O (6.3 mL), BuLi (1.4 mL, 1.6 M in hexane, 2.2 mmol), diferrocenylketone [14,15] (0.678 g, 1.7 mmol) solution in anhydrous THF (20 mL); column chromatography (SiO_2 deactivated with Et_3N 5% in PE, 25 × 4 cm, PE/CH_2Cl_2 10:1) gave (*S,R*$_P$)-**12** (0.718 g, 1.0 mmol, 61%, >95% *de*) as a red liquid. Crystallization from TBME gave pure 1,1-bisferrocenylpentan-1-ol [24] (0.154 g, 0.3 mmol, 24%, characterized crystallographically [25]) as yellow crystals and pure (*S,pR*)-**12** (0.564 g, 0.8 mmol, 48%, >95% *de*) as a yellow foam.

(*S,R*$_P$)-**12**: $[\alpha]_{20}^{D} = +94$ (c = 0.10, $CHCl_3$). IR (ATR): $\tilde{\nu} = 3095 cm^{-1}$ (w, OH), 2958 (w), 1650 (s, C=N), 814 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.15 (d, ^3J = 6.8 Hz, 3H, CH_3), 2.12–1.98 [m, 1H, $CH(CH_3)_2$], 3.88 (s, 5H, CpH), 3.89 (m, 1H, CpR_2), 3.95 (m, 1H, CpR_2), 4.04 (s, 5H, CpH), 4.05 (m, 1H, CpR_2), 4.07 (s, 5H, CpH), 4.09 (m, 2H, 2 × CpR), 4.16 (m, 2H, 2 × CpR), 4.16 (m, ABX line system, 2H, OCH_2), 4.26 (m, 1H, CpR), 4.34 (m, ABX line system, 1H, NCH), 4.63 (m, 1H, CpR), 4.72 (m, 1H, CpR), 4.75 (m, 1H, CpR), 8.95 (s, 1H, OH) ppm. - ^{13}C NMR (100 MHz, BB, HMQC, HMBC, $CDCl_3$): δ 18.0 (CH_3), 19.2 (CH_3), 32.0 [$CH(CH_3)_2$], 64.8 (*C*R-CpR), 65.8 (*C*H-CpR), 65.9 (*C*R-CpR), 66.2 (*C*H-CpR), 66.5 (*C*H-CpR), 66.7 (*C*H-CpR), 67.6 (*C*H-CpR), 67.8 (*C*H-CpR), 68.1 (*C*H-CpR), 68.4 (*C*H-CpR), 68.5 (*C*H-CpH), 69.0 (*C*H-CpH), 69.4 (NCH), 69.9 (*C*H-CpR), 70.8 (*C*H-CpH), 72.0 (C-12), 72.2 (*C*H-CpR), 73.5 (*C*H-CpR), 100.0 (*C*R-CpR), 100.3 (COH), 101.1 (*C*R-CpR), 168.5 (NCO) ppm. MS (ESI, ES$^+$): m/z = 678 [M$^+$–OH], 695 [M$^+$]. HRMS (ESI) ($C_{37}H_{37}Fe_3NO_2$): Calc.: 695.0872; found: 695.0897 [M$^+$]. $C_{37}H_{37}Fe_3NO_2$: Calc.: C, 63.92; H, 5.36; N, 2.01. Found: C, 64.37; H, 5.57; N, 1.92%.

4.8. (S,pR,R)-2-(2-Ferrocenylphenylhydroxymethylferrocenyl)-4-isopropyloxazoline (S,pR,R)-**11** and (S,pR,S)-2-(2-ferrocenylphenyl-hydroxymethylferrocenyl)-4-isopropyl-oxazoline (S,pR,S)-**11**

GP1; (*S*)-2-ferrocenyl-4-isopropyloxazoline [(*S*)-**9**, 0.507 g, 1.7 mmol], TMEDA (0.3 mL, 2.2 mmol), Et_2O (2.5 mL), BuLi (1.4 mL, 1.6 M in hexane, 2.2 mmol), benzoylferrocene [26] (0.493 g, 1.7 mmol) solution in anhydrous THF (20 mL), column chromatography (SiO_2, deactivated with Et_3N 5% in PE, 25 × 4 cm, PE/EE 9:1) gave a 3:1 or 1:3 mixture of diastereoisomers (*S,R*$_P$,*R*)-**11** and (*S,R*$_P$,*S*)-**11** (0.802 g, 1.4 mmol, 80%, >95% *de* R_P) as a red oil. Recrystallization from TBME gave a 2.5:1 mixture of diastereoisomers (0.491 g, 0.8 mmol, 49%, >95% *de* R_P) as yellow crystals. The analytical data did not allow a clear cut assignment of the diastereomers.

(*S,pR,R*)-**11** and (*S,R*$_P$,*S*)-**11**: $[\alpha]_{20}^{D} = -24$ (c = 0.20, $CHCl_3$). IR (ATR): $\tilde{\nu} = 3095\ cm^{-1}$ (w, OH), 2961 (w), 2928 (w), 2871 (w), 1648 (s, C=N). MS (ESI, ES$^+$): m/z: 570 [M$^+$–OH], 588 [M+H$^+$]. HRMS (ESI) ($C_{33}H_{32}Fe_2NO$): Calc.: 570.1183; found: 570.1171 [M–OH]. $C_{33}H_{33}Fe_2NO_2$: Calc.: C, 67.49; H, 5.66; N, 2.38. Found: C, 67.48; H, 5.47; N, 2.13%.

(*S,pR,R*)-**11** or (*S,R*$_P$,*S*)-**11**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.10 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.8–1.9 [m, 1H, $CH(CH_3)_2$], 3.62 (ddd, ABMX line system, J = 6.5 Hz, J = 9.4 Hz, J = 15.9 Hz, 1H, NCH), 3.66 (s, 1H, CpR), 3.88 (m, ABX line system, 1H, OCH_2), 3.90 (m, 1H, CpR), 4.04 (s, 5H, CpH), 4.06 (d, 1H, J = 1.4 Hz, CpR), 4.10 (m, 1H, OCH_2), 4.16 (dd, $J = J$ = 2.6 Hz, 1H, CpR), 4.25 (s, 5H, CpH), 4.27 (m, 1H, CpR), 4.54 (dd, 1H, J = 1.6 Hz, J = 2.4 Hz, CpR), 4.71 (dd, $J = J$ = 1.1 Hz, 1H, CpR), 7.10–7.50 (m, 4H, Ph), 7.78 (d, J = 7.2 Hz, 1H, Ph), 8.71 (s, 1H, OH) ppm. - ^{13}C NMR (100 MHz, BB, $CDCl_3$): δ 18.6 (CH_3), 19.3 (CH_3), 32.4 [$CH(CH_3)_2$], 65.1 [*C*R-CpR (C_{Fc}COH)], 66.9 (*C*H-CpR), 67.0 (*C*H-CpR), 67.1 (*C*H-CpR), 67.3 (*C*H-CpR), 68.4 (*C*H-CpR), 68.8 (*C*H-CpH), 69.77 (*C*H-CpR), 69.84 (OCH_2), 70.6(*C*H-CpH), 71.7 (NCH), 74.12 (*C*H-CpR), 74.3 [*C*R-CpR(C_{Fc}COH)], 96.63 (COH), 102.8 [*C*R-CpR(C_{Fc}CN)], 126.4 (Ph), 126.8 (Ph), 127.7 (Ph), 147.6 (Ph), 170.4 (NCO) ppm.

(*S,pR,R*)-**11** or (*S,R*$_P$,*S*)-**11**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.1 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.2 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.95 [m, 1H, $CH(CH_3)_2$], 3.76 (m, 1H, CpR), 3.86–3.90 (m, 1H, CpR), 4.0–4.2 (m, 3 × 1H, CpR), 4.02 (s, 5H, CpH), 4.03 (s, 5H, CpH), 4.1–4.2 (m, ABX line system, 2H, OCH_2 or NCH), 4.24 (m, 1H, CpR), 4.39 (m,

ABX line system, 1H, OCH_2 or NCH), 4.75 (m, 1H, CpH), 7.1–7.41 (m, 5H, Ph), 9.6 (s, 1H, OH) ppm. ^{13}C NMR (100 MHz, BB, $CDCl_3$): δ 18.9 (CH_3), 19.0 (CH_3), 32.9 [*C*H(CH_3)$_2$], 64.6 [*C*R-CpR(C-18)], 65.5 (*C*H-CpR), 67.3 (*C*H-CpR), 67.9 (OCH_2), 68.3 (*C*H-CpR), 68.8 (*C*H-CpH), 68.9 (*C*H-CpR), 70.4 (NCH), 70.7 (*C*H-CpR), 70.8 (*C*H-CpH), 72.1 (*C*H-CpR), 73.9 (*C*H-CpR), 74.5 [*C*R-CpR(C_{Fc}COH)], 98.4 (COH), 101.7 [*C*R-CpR(C_{Fc}CN)], 126.3 (Ph), 126.5 (Ph), 127.7 (Ph), 148.1 (Ph), 168.2 (COH) ppm.

4.11. General procedure for the catalytic asymmetric addition of diethylzinc to aldehydes (GP2)

To a solution of the ferrocene ligand (0.03 mmol) in anhydrous toluene (1.3 mL), diethylzinc (1.0 ml, 1.0 mmol, 1.0 M in hexane) was added at 25 °C. After 30 min, the reaction mixture was cooled to 0 °C, and the aldehyde (0.5 mmol) was added in an argon atmosphere. After having stirred for the appropriate time, the reaction was quenched by addition of HCl (5 mL, 3.0 M in water). The mixture was extracted with TBME (3×5 mL). The organic layer was washed with brine (2×25 mL), dried over $MgSO_4$, and the solvent was evaporated at reduced pressure to give an oily residue. Purification by column chromatography (SiO_2, 25×2 cm) gave the optically active alcohol. The enantiomeric excess was determined by GC analysis or by ^1H NMR. Configurations were assigned by comparison of the sign of the specific rotation with that of the known compound.

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Appendix A. Supplementary material

CCDC 709580 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

[1] O.B. Sutcliffe, M.R. Bryce, Tetrahedron: Asymmetry 14 (2003) 2297–2325.
[2] H.A. McManus, P.J. Guiry, Chem. Rev. 104 (2004) 4151–4202.
[3] T. Sammakia, H.A. Latham, D.R. Schaad, J. Org. Chem. 60 (1995) 10–11.
[4] T. Sammakia, H.A. Latham, J. Org. Chem. 60 (1995) 6002–6003.
[5] C.J. Richards, A.W. Mulvaney, Tetrahedron: Asymmetry 7 (1996) 1419–1430.
[6] Y. Miyake, Y. Nishibayashi, S. Uemura, Synlett (2008) 1747–1758.
[7] A.I. Meyers, J. Org. Chem. 70 (2005) 6137–6151.
[8] G. Jones, C.J. Richards, Tetrahedron: Asymmetry 15 (2004) 653–664.
[9] C.J. Richards, A.J. Locke, Tetrahedron: Asymmetry 9 (1998) 2377–2407.
[10] J.R. Garabatos Perera, R. Wartchow, H. Butenschön, J. Organomet. Chem. 689 (2004) 3541–3549.
[11] J.R. Garabatos-Perera, H. Butenschön, J. Organomet. Chem. 693 (2008) 357–360.
[12] C.G. Rodriguez-Cendejas, L.S. Liebeskind, E. Pena-Cabrera, ARKIVOC (2005) 250–265.
[13] R. Wang, X. Hong, Z. Shan, Tetrahedron Lett. 49 (2008) 636–639.
[14] D.C. O'Connor Salazar, D.O. Cowan, J. Organomet. Chem. 408 (1991) 219–225.
[15] C. Imrie, L. Cook, D.C. Levendis, J. Organomet. Chem. 266-275 (2001) 637–639.
[16] C. Bolm, K.M. Fernández, A. Seger, G. Raabe, Synlett (1997) 1051–1052.
[17] C. Bolm, K. Muniz-Fernandez, A. Seger, G. Raabe, K. Günther, J. Org. Chem. 63 (1998) 7860–7867.
[18] C. Bolm, M. Kesselgruber, N. Hermanns, J.P. Hildebrand, G. Raabe, Angew. Chem. 113 (2001) 1536–1538; Angew. Chem. Int. Ed. 40 (2001) 1488–1490.
[19] M. Li, X.-Z. Zhu, K. Yuan, B.-X. Cao, X.-L. Hou, Tetrahedron: Asymmetry 15 (2004) 219–222.
[20] K. Muñiz, C. Bolm, Chem. Eur. J. 6 (2000) 2309–2316.
[21] F. Schmidt, R.T. Stemmler, J. Rudolph, C. Bolm, Chem. Soc. Rev. 35 (2006) 454–470.
[22] C. Bolm, K. Muniz, Chem. Commun. (1999) 1295–1296.
[23] We cordially thank Frank Schmidt for performing these experiments at the RWTH Aachen University.
[24] P.L. Pauson, W.E. Watts, J. Org. Chem. 27 (1962) 3880–3886.
[25] J.R. Garabatos-Perera, R. Wartchow, H. Butenschön, in preparation.
[26] M. Rausch, M. Vogel, H. Rosenberg, J. Org. Chem. 22 (1957) 903–906.