Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 19 (2008) 838–846

Chemo-enzymatic synthesis of new ferrocenyl-oxazolidinones and their application as chiral auxiliaries

Bernhard J. Ueberbacher,[a,b,*] Herfried Griengl[a,b] and Hansjörg Weber[a]

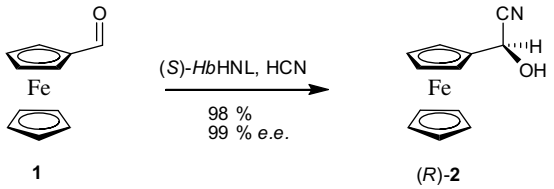
[a]*Institute of Organic Chemistry, Graz University of Technology, Stremayrgasse 16, 8010 Graz, Austria*
[b]*Research Centre Applied Biocatalysis, Petersgasse 14, 8010 Graz, Austria*

Received 31 January 2008; accepted 10 March 2008
Available online 15 April 2008

Abstract—A chemo-enzymatic synthesis of new chiral ferrocenyl-oxazolidinones has been developed. The key step was the addition of HCN to formylferrocene catalysed by the hydroxynitrile lyase from *Hevea brasiliensis*, which yielded an enantiomerically pure ferrocenyl-cyanohydrine in excellent yield and ee. The ferrocenyl-oxazolidinones obtained by this strategy were tested as chiral auxiliaries for asymmetric alkylations and aldol reactions and were shown to be effective in terms of yields, stereoselectivities and cleavage conditions.

1. Introduction

Chiral ferrocene derivatives have been firmly established in asymmetric synthesis as ligands and auxiliaries for the preparation of chiral compounds.[1] Biocatalysis has proven to be a powerful tool for the synthesis of enantiopure ferrocene compounds, giving good yields and enantioselectivities in many cases.[2] Furthermore, the fact that enzymes accept these bulky organometallic compounds, which do not occur in Nature is noteworthy in light of the emerging area of bioinorganic chemistry. Recently we reported the highly enantioselective and high yielding synthesis of (*R*)-ferrocenyl cyanohydrin[1] **2** catalysed by the hydroxynitrile lyase from *Hevea brasiliensis*[3] (Scheme 1).



Scheme 1. Hydroxynitrile lyase-catalysed cyanohydrin synthesis.

Herein, we report the conversion of this useful compound (*R*)-**2** into enantiopure aminoalcohols and the subsequent transformation of the latter into chiral auxiliaries. Chiral auxiliary methodology continues to be an effective method in asymmetric synthesis.[4] In this context, the most widely used chiral auxiliaries are the versatile oxazolidin-2-ones **3a** (Fig. 1) as pioneered by Evans. The *N*-acyl-derivatives of Evans auxiliaries have been utilised in numerous highly diastereoselective reactions, including alkylation, amination, azidation, bromination, hydroxylation, aldol additions, Diels–Alder reactions and conjugate additions.[5] Despite these impressive efforts, there is an ongoing search for auxiliaries with improved efficiency in terms of diastereoselectivity, ease of preparation and auxiliary cleavage. In recent years, research in this area has focused on auxiliaries of the general structure **3b** bearing bulky substituents at the 5-position of the oxazolidin-2-one ring[6] (Fig. 1).

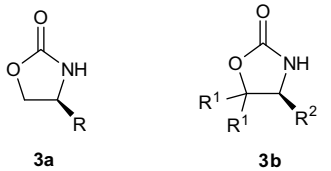
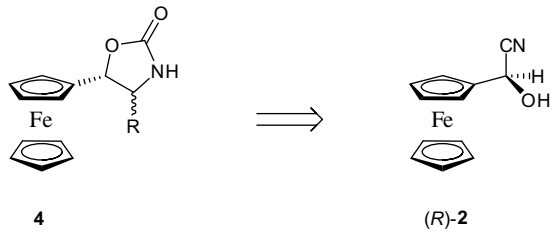


Figure 1. Chiral oxazolidinones as auxiliaries.

Incorporation of the sterically demanding ferrocenyl-functionality into oxazolidinone-auxiliaries has received only a little attention so far.[7] Since the preparation of cyanohydrin **2** can easily be scaled up, we decided to develop a

* Corresponding author. Tel.: +43 316 873 8249; fax: +43 316 873 8740; e-mail: bernhard.ueberbacher@tugraz.at

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.03.009



4 (*R*)-**2**

Scheme 2. Retrosynthetic analysis of 5-ferrocenyl-oxazolidin-2-ones.

synthetic route to new 5-ferrocenyl-oxazolidin-2-ones **4** starting from **2** (Scheme 2), in order to explore the influence of the bulky ferrocenyl-substituent on the performance of these auxiliaries. An important feature of this synthetic plan is the combination of enzymatic and chemical methodologies to obtain chiral auxiliaries from achiral starting material (ferrocenyl aldehyde **1**), while most 'classical' auxiliary-synthesis relies on a 'chiral pool' strategy, starting from amino acids.

2. Results and discussion

2.1. Preparation of chiral ferrocenyl-oxazolidinones

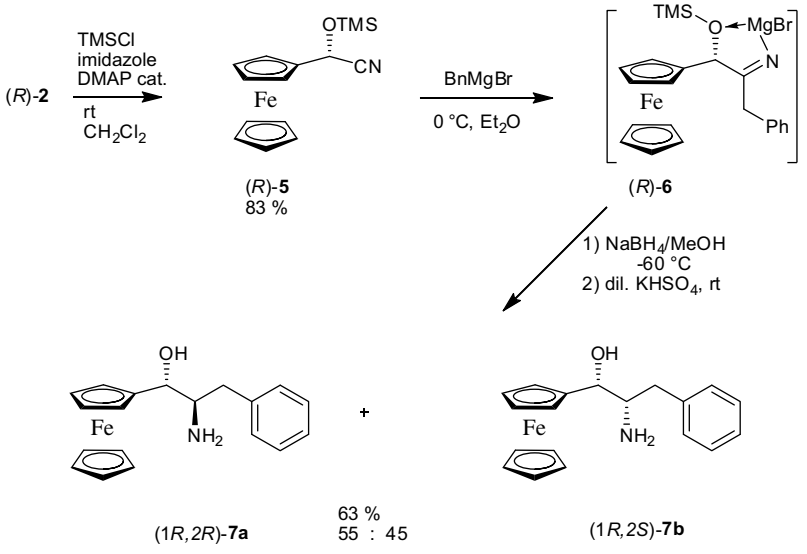
2-Substituted 2-amino-1-ferrocenyl-alcohols can be prepared by the reductive cross-coupling of planar chiral ferrocenecarboxaldehydes with imines[8] or by the addition of ferrocenyllithium to aminoaldehydes.[9] Our new synthetic approach is based on the addition of Grignard-reagents to cyanohydrins, followed by the reduction of the imine-intermediate (Scheme 3). Surprisingly, this methodology, despite its proven usefulness for the preparation of a wide range of aminoalcohols,[10] has never to the best of our knowledge been applied to ferrocenyl-cyanohydrins.

Due to the well-known instability of cyanohydrins under basic conditions, the hydroxy-group has to be protected prior to nucleophilic addition at the nitrile functionality. The TMS-group was chosen because of its good stability under basic conditions and the ease of implementation and removal. The TMS-group was introduced under standard conditions with TMSCl/imidazole in the presence of a catalytic amount of DMAP, affording the TMS-protected cyanohydrin **5** in good yield (83%) and purity (Scheme 3).

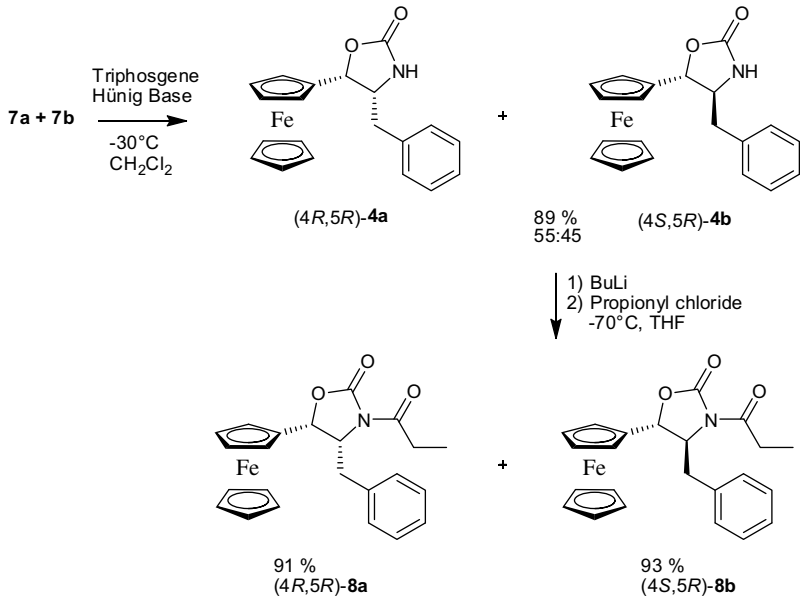
The benzyl-substituted aminoalcohols **7a** and **7b** were subsequently prepared in a three-step/one-pot reaction sequence. Nucleophilic addition of benzylmagnesium-bromide to the nitrile functionality of cyanohydrin **5**, followed by $NaBH_4$-reduction of the resulting imine-intermediate **6** and deprotection of the hydroxy-group during acidic workup afforded aminoalcohols **7a** and **7b** as a 55:45 diastereomeric mixture in 63% overall yield. A surprise was the observed low diastereoselectivity in the $NaBH_4$-reduction step, which is in contrast to the reported *erythro*-selectivity for the reduction of cyanohydrin-derived imines.[10] The diastereomers were not separated but used directly in the subsequent cyclisation reaction. The reaction of aminoalcohols **7a** and **7b** with triphosgene and Hünig-base in dichloromethane provided the corresponding oxazolidine-2-ones **4a** and **4b** in 89% yield. At this stage, the diastereomers could be conveniently separated by column chromatography. N-Acylations of the oxazolidin-2-ones **4a** and **4b** were carried out by deprotonation with *n*-BuLi followed by treatment with propionyl-chloride and afforded the *N*-acyl oxazolidinones **8a** and **8b** in 91% and 93% yields, respectively (Scheme 4).

2.2. Alkylation studies

The N-acylated oxazolidin-2-ones were subsequently subjected to diastereoselective alkylations, to explore their scope and limitations as chiral auxiliaries. Benzylation of the LDA-generated Li-enolates of both **8a** and **8b** turned out to be very slow, and, in addition to the recovered starting material, only the parent auxiliaries **4a** and **4b** were obtained. Compounds **4a** and **4b** were presumably formed via a ketene decomposition pathway of the Li-enolate. This

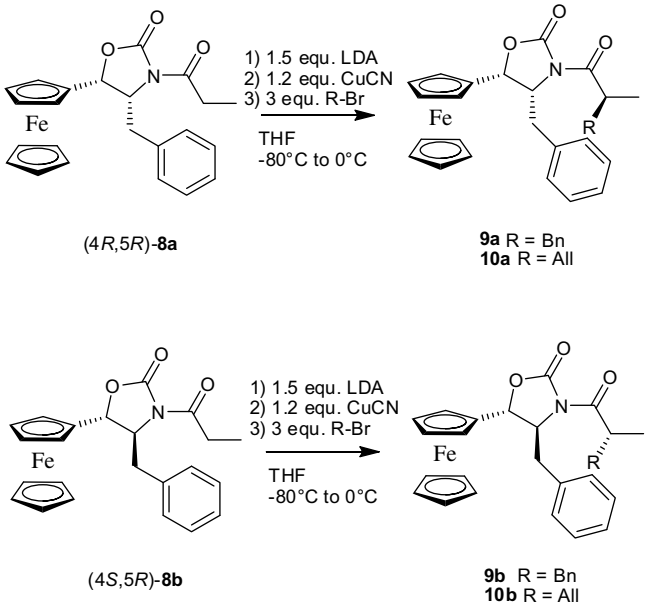


Scheme 3. Synthesis of 2-amino-1-ferrocenyl-alcohols **7a** and **7b**.



Scheme 4. Acylation of the ferrocenyl-oxazolidinones **4a** and **4b**.

behaviour of Li-enolates has also been observed by Davies and Seebach in their alkylation studies of 5,5-diaryloxazolidinones, and seems to be a general behaviour for oxazolidin-2-ones with bulky substituents in the 5-position.[6] Seebach et al.[6] solved this problem by transmetallation to the corresponding Zn-enolate, which showed a better reactivity profile. Due to the great success of organocopper reagents in nucleophilic-substitution chemistry, it seemed reasonable that transmetallation of our Li-enolates to the corresponding copper enolates could also be a solution to this problem. The addition of 1.2 equiv of CuCN, followed by 3 equiv of benzyl bromide afforded the benzylated products **9a** and **9b** in good yields. In an analogous manner, the reaction of copper enolates with allyl bromide afforded allylated products **10a** and **10b** (Scheme 5).



Scheme 5. Diastereoselective alkylations of **8a** and **8b**.

Table 1. Alkylation of oxazolidinon-2-ones **8a** and **8b**

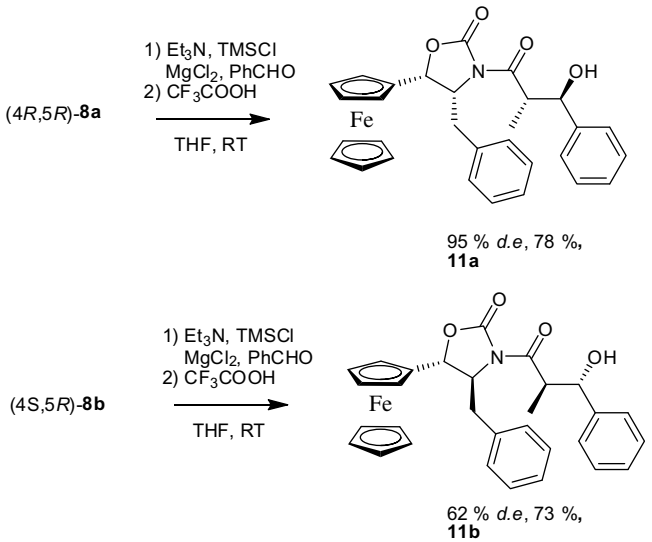
Auxiliary	R	Alkylated product	de[a] (%)	Yield (%)
8a	CH_2-Ph	**9a**	95	78
8a	CH_2–CH=CH_2	**10a**	>95	82
8b	CH_2-Ph	**9b**	70	69
8b	CH_2–CH=CH_2	**10b**	78	72

[a] Determined by NMR-spectroscopic analysis of crude reaction products.

The observed diastereoselectivities turned out to be excellent for auxiliary **8a**, but only moderate for auxiliary **8b** (Table 1). This can be explained by the *matched* stereoinduction from the two stereocentres of **8a**, shielding off the same side of the enolate, compared to the *mismatched* case of **8b**. The absolute configuration of alkylation products **9b** and **10b** showed that the sense of stereoinduction is governed by the configuration at the 4-position, despite the greater steric bulk of the ferrocenyl substituent at the 5-position.

2.3. Aldol reactions

In contrast to the very well developed *syn*-aldol reaction methodology, based on B-, Ti- and Sn-enolates,[11] the corresponding *anti*-aldol reactions pose greater problems. Recently, Evans et al. have developed a promising methodology based on Mg-enolates, providing the corresponding *anti*-aldol products with high yields and selectivities.[12] Since, to the best of our knowledge, only the classical Evans-oxazolidinones and thiazolidinones have been employed for these reactions, we decided to test the performance of the ferrocenyl auxiliaries in this important reaction. When acylated '*cis*'-oxazolidinone **8a** was treated

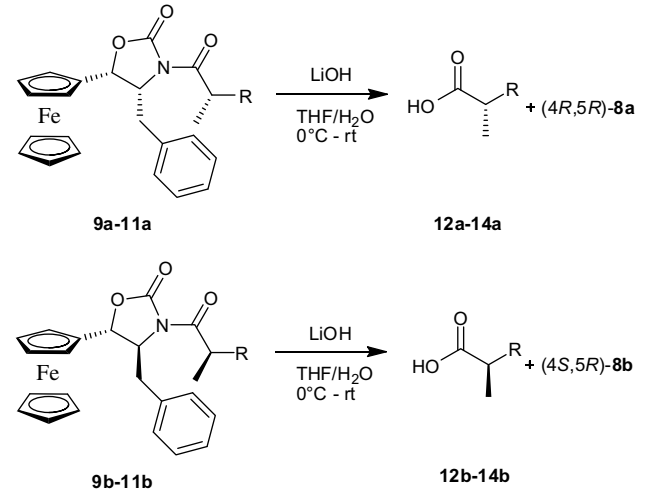


Scheme 6. Diastereoselective aldol reactions of **8a** and **8b**.

with triethylamine, TMSCl, $MgCl_2$ and benzaldehyde in THF, the corresponding *anti*-aldol product **11a** was obtained in high yield and selectivity. Again '*trans*'-auxiliary **8b** showed moderate diastereoselectivity (62% de), leading to the product **11b** with the opposite absolute configuration (Scheme 6).

2.4. Cleavage of the chiral auxiliary

Following a stereoselective reaction of an *N*-acyl-oxazolidin-2-one, the chiral auxiliary has to be removed, separated from the product, and preferably, recycled. One of the drawbacks of the Evans-methodology involves the removal of the auxiliary. If the *N*-acyl group is sterically demanding or α-branched, then the unwanted endocyclic hydrolysis can predominate to yield a ring-opened amide rather than the required exocyclic cleavage to afford the carboxylic acid derivative and the recovered chiral auxiliary. Several groups[6] have shown that auxiliaries possessing bulky substituents at the 5-position do not suffer from the undesired endocyclic cleavage. Therefore, we anticipated that the ferrocenyl substituent should have a beneficial effect in this respect as well.



Scheme 7. Auxiliary cleavage.

As expected, the hydrolyses of both the alkylation and aldol products with LiOH at 0 °C in THF/H_2O resulted in clean exocyclic cleavage and afforded the corresponding carboxylic acids as well as the recovered auxiliaries **8a** and **8b** in high yields without any loss of stereochemical integrity (Scheme 7, Table 2). No products from the endocyclic cleavage pathway were observed. The enantiomeric purity of the cleavage products and their absolute configurations were confirmed by the comparison of their specific rotation with literature data, and, if possible, by chiral HPLC-analysis.

Table 2. Auxiliary cleavage

	R	Cleavage product	ee (%)	Yield cleavage product (%)	Recovered auxiliary (%)
9a	CH_2-Ph	**12a**	95[a]	89	92
10a	CH_2–CH=CH_2	**13a**	95[b]	77	87
11a	CH(OH)-Ph	**14a**	93[b]	84	89
9b	CH_2–Ph	**12b**	70[a]	82	83
10b	CH_2–CH=CH_2	**13b**	78[b]	74	94
11b	CH(OH)-Ph	**14b**	62[b]	73	91

[a] Determined by HPLC-analysis.
[b] Calculated from measured $[\alpha]_D$ in comparison to the literature values.

3. Conclusions

In conclusion, we have developed a new chemo-enzymatic route to enantiomerically pure chiral ferrocenyl-aminoalcohols, starting from the easily available (*R*)-ferrocenyl cyanohydrin **2**.

The 4-benzyl-5-ferrocenyl-oxazolidin-2-ones, prepared from the corresponding aminoalcohols, have been shown to be effective Evans-type auxiliaries for asymmetric aldol and alkylation reactions. Particularly the crystallinity and the mild cleavage conditions of the auxiliaries are superior to the 'classical' Evans-oxazolidinones.

4. Experimental

4.1. General experimental procedures

All reagents and solvents were obtained from commercial sources and appropriately purified, if necessary. Analytical thin layer chromatography was carried out on Merck Silica Gel 60 F_{254} plates. Flash chromatography was performed on Merck Silica Gel 60, 230–400 mesh.

Analytical HPLC was carried out with a Hewlett Packard Series 1100 HPLC using a G1315A diode array detector or MWD detector. ^1H and ^{13}C NMR spectra were recorded on a Varian INOVA 500 (^1H 499.82 MHz, ^{13}C

125.69 MHz) or on a Varian GEMINI 200 (^{1}H 199.98 MHz, ^{13}C 50.29 MHz). Melting points were determined on an Electrothermal MEL-TEMP apparatus and are uncorrected. $[\alpha]_D^{20}$-values were measured on a Perkin Elmer Polarimeter 341.

4.2. HCN formation—Caution

All reaction equipments in which cyanides are used or produced were placed in a well-ventilated hood. Proper gloves were worn when handling dry sodium cyanide. Rubber gloves and splash proof goggles were also applied when substantial amounts of sodium cyanide solution were used. The required amount of HCN was freshly formed by dropping a saturated NaCN solution into sulfuric acid (60%) at 80 °C and trapping HCN at −12 °C in a cooling trap. For continuous warning an electrochemical sensor for HCN detection was used. Waste solutions containing cyanides were treated with sodium hypochlorite which converted them into harmless cyanate. These could be further transformed into ammonia and carbon dioxide by the addition of diluted sulfuric acid to the solution until a pH of 7 was reached.

4.2.1. (*R*)-(Cyanohydroxymethyl)ferrocene 2. Fifty millilitres of (*S*)-*Hb*HNL enzyme solution,[3] which was provided in a concentration of 6.5 kU/mL, was diluted with 50 mL distilled water and the pH value was adjusted to 4.8–5.0 by the addition of a citric acid solution. This mixture was then added to a solution of 7 g (32.8 mmol) of formylferrocene in 350 mL of MTBE, and then cooled to 0 °C. After vigorous stirring for 20 min, a stable emulsion had formed and 6.4 mL (166 mmol) of freshly prepared HCN was added. The reaction mixture was stirred for 3 h at 0 °C. After TLC had indicated that starting material was no longer present, additional MTBE and large amounts of Celite were added. Filtration and washing the Celite plug with MTBE provided an organic phase, which was then dried over Na_2SO_4. Rapid filtration over a pad of silica and removal of the solvent under reduced pressure provided 7.72 g (98%) of **2** as a pale brown solid; mp: 90 °C (lit.[3] 89–90 °C); $[\alpha]_D^{22} = +150$ (*c* 0.30, CH_3CN) (lit.[3] 150); ee: 99% (for determination see below); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.74 (1H, br s; OH), 4.36 (9H, m; Cp-*H*), 5.25 (1H; s, C*H*(OH)CN), ^{13}C NMR (50 MHz, $CDCl_3$): δ 60.7, 66.6, 68.5, 69.3, 69.6, 84.0, 118.7.

4.2.2. Determination of the enantiomeric purity of (*R*)-2. (*R*)-**1** (40 mg, 0.17 mmol) was dissolved in 5 mL of CH_2Cl_2, and acetyl chloride (16 μL, 0.22 mmol) and triethylamine (42 μL, 0.30 mmol) were added at 0 °C. The mixture was stirred at 0 °C for 1 h, then the reaction was quenched by the addition of 10 mL of satd aqueous $NaHCO_3$. The organic phase was washed sequentially with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo to afford 48 mg (99%) of (+)-(*R*)-(acetoxycyanomethyl)ferrocene. The ee of this compound was shown to be 99% by HPLC analysis (ODH-column, mobile phase *n*-heptane/2-propanol = 95:5), $v = 0.50$ mL min^{-1}, 10 °C, UV 238 nm, ($t_R(S) =$ 21.4 min, $t_R(R) = 29.7$ min).

4.2.3. (*R*)-[Cyano(trimethylsilyloxy)methyl]ferrocene 5. (*R*)-Cyanohydrin **2** (6 g, 25 mmol), dissolved in 60 mL of dichloromethane, was added to a stirred solution of TMSCl (6.3 mL, 50 mmol, 2 equiv), imidazole (5.1 g, 75 mmol, 3 equiv) and 4-dimethylaminopyridine (305 mg, 2.5 mmol, 0.1 equiv) in 100 mL of dichloromethane at room temperature. The resulting turbid solution was stirred for 5 h at room temperature, then it was quenched by the addition of satd NH_4Cl solution. The organic phase was washed sequentially with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and filtered quickly through a pad of silica (eluent: CH_2Cl_2). The resulting solution was concentrated in vacuo to afford 6.5 g (83%) of TMS-protected cyanohydrin **2**; mp: 80–82 °C (lit.[3] 80–82 °C); $[\alpha]_D^{22} = +153$ (*c* 0.25, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.17 (9H, s, $(CH_3)_3$), 4.23 (2H, s, Cp-*H*), 4.25 (5H, s, Cp-*H*), 4.28 (1H, s, Cp-*H*), 4.46 (1H, s, Cp-*H*), 5.31 (1H, s, C*H*-OTMS); ^{13}C NMR (125 MHz, $CDCl_3$): δ 0.08, 61.40, 67.53, 68.63, 69.21, 69.46, 69.55, 83.53, 119.15.

4.2.4. 2-Amino-3-phenyl-1-ferrocenyl-propan-1-ol (1*R*,2*R*)-7a and (1*R*,2*S*)-7b. To a solution of 43 mmol benzylmagnesiumbromide in 40 mL of Et_2O [prepared by refluxing benzyl bromide (5.1 mL, 43 mmol) and Mg (1.1 g, 45 mmol) in 40 mL of Et_2O for 3 h], (*R*)-[cyano(trimethylsilyloxy)methyl]ferrocene **5** (4.5 g, 14.4 mmol, dissolved in 50 mL Et_2O) was added at 0 °C. After completion of the addition, the mixture was allowed to warm to room temperature and stirred for another 3 h. Then it was cooled to −80 °C and 20 mL of MeOH abs. was added, followed by $NaBH_4$ (1.1 g, 29 mmol). The mixture was allowed to warm to room temperature over 2 h, stirred for another 12 h and quenched by pouring it on ice. The resulting heterogeneous mixture was stirred vigorously at 0 °C, after which 6 M HCl was added until a pH value of 1 was reached and the phases were separated. The aqueous phase was extracted three times with dichloromethane and the organic phases were discarded. Then the aqueous phase was brought to pH 12 with 2 M NaOH solution and extracted with dichloromethane (3 × 100 mL). The organic phases were washed with brine, dried over Na_2SO_4 and concentrated in vacuo to afford 3.03 g (63%) of aminoalcohols **7a** and **7b** as a mixture of diastereomers (**7a**:**7b** = 55:45), mp: 88 °C; $[\alpha]_D^{22} = -31$; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.38 (1H, dd, $J = 9.8$ and 13.7 Hz, *anti* CH_aH$_b$-Ph), 2.47 (1H, dd, $J = 9.3$ and 13.2 Hz, *syn* CH_aH$_b$-Ph), 2.88 (2H, m, *syn* + *anti* CH_aH$_b$-Ph), 2.99 (1H, m, $J = 4.9$ Hz, *syn* C*H*–N), 3.09 (1H, m, $J = 4.9$ Hz, *anti* C*H*–N), 4.17–4.19 (3H, m, Cp-*H*, C*H*–O), 4.20 (1H,s, Cp-*H*), 4.21 (s, 5H, *syn* Cp-*H*), 4.22 (1H, s, Cp-*H*) 4.24 (s, 5H, *anti* Cp-*H*), 4.26 (1H. s, Cp-*H*) 4.30–4.34 (m, 4H, Cp-*H*, C*H*–O), 7.18–7.23 (6H, m, Ph-*H*), 7.27–7.31 (4H, m, Ph-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.74 (*anti*-*C*H$_2$), 40.45 (*syn*-*C*H$_2$) 57.68 (*anti*-*C*–N), 58.40 (*syn*-*C*–N), 65.24 (*anti*-*C*–O), 65.43 (*syn*-*C*–O), 67.90 (Cp), 67.98 (Cp), 68.07 (2 × Cp), 68.26 (Cp), 68.58 (Cp), 68.63 (Cp), 68.72(Cp), 72.59 (*syn*-Cp), 73.27 (*anti*-Cp), 90.43 (*anti*-Cp), 91.50 (*syn*-Cp), 126.34 (*anti*-Ar), 126.42 (*syn*-Ar), 128.59 (*anti*-Ar), 128.62 (*syn*-Ar), 129.33 (*anti*-Ar), 129.38 (*syn*-Ar), 139.34 (*syn*-Ar), 139.41 (*anti*-Ar).

4.2.5. 4-Benzyl-5-ferrocenyl-oxazolidin-2-ones 4a and 4b. Triphosgene (1.1 g, 3.8 mmol), dissolved in 10 mL of dichloromethane, was added to a solution of 3.2 g (9.6 mmol) of aminoalcohols **7a** and **7b** and 3.44 mL (20 mmol) of diisopropylethylamine in 60 mL dichloromethane at −80 °C under an argon atmosphere. The reaction mixture was allowed to warm to −40 °C and stirred at this temperature, until TLC indicated complete consumption of the starting material. Saturated aqueous $NaHCO_3/NH_4Cl$ (1:1) solution was added and stirring continued for 15 min at room temperature. The organic phase was washed with saturated aqueous $NaHCO_3$ (3 × 40 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated in vacuo. The obtained mixture of diastereomers was separated by column chromatography to afford 1.59 g (46%) of **4a** and 1.48 g (43%) of **4b**.

4.2.6. (4*R*,5*R*)-4-Benzyl-5-ferrocenyl-oxazolidin-2-one 4a. Mp: 200 °C (decomposition); $[\alpha]_D^{22} = -114$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.29 (1H, dd, $J = 11.2$ and 13.8 Hz, CH_aH$_b$-Ph), 2.41 (1H, dd, $J = 3.5$ and 13.8 Hz, CH$_a$$H_b$-Ph), 4.01 (1H, m, C*H*–N), 4.20 (1H, s, Cp-*H*), 4.23 (1H, s, Cp-*H*), 4.28 (5H, s, Cp-*H*), 4.29 (1H, s, Cp-*H*), 4.39 (1H, s, Cp-*H*), 4.97 (1H, s, N–*H*), 5.57 (1H, d, $J = 7.8$ Hz, C*H*–O), 7.04 (2H, d, $J = 7.0$ Hz, Ph-*H*), 7.20–7.29 (3H, m, Ph-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 38.0, 57.92, 65.86, 67.80, 68.54, 68.74, 69.37, 79.34, 81.88, 127.08, 128.99, 129.01, 137.10, 158.67.

4.2.7. (4*S*,5*R*)-4-Benzyl-5-ferrocenyl-oxazolidin-2-one 4b. Mp: 210 °C (decomp.); $[\alpha]_D^{22} = -37.8$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.90 (1H, dd, $J = 8.3$ and 13.7 Hz, CH_aH$_b$-Ph), 2.99 (1H, dd, $J = 5.4$ and 13.7 Hz, CH$_a$$H_b$-Ph), 3,94 (1H, m, $J = 4.9$ Hz, C*H*–N), 4.09 (1H, s, Cp-*H*) 4.18 (7H, s, Cp-*H*), 4.22 (1H, s, Cp-*H*), 5.06 (1H, d, $J = 4.4$ Hz, Cp-C*H*–O), 5.59 (1H, s, N–*H*), 7.22 (2H, d, $J = 6.8$ Hz, Ph-*H*), 7.30 (1H, t, $J = 7.3$ Hz, Ph-*H*), 7.37 (2H, t, $J = 6.8$ Hz, Ph-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 41.82, 60.94, 66.25, 66.73, 68.85, 69.02, 69.10, 80.39, 85.70, 127.49, 129.22, 129.30, 136.16, 158.57. Anal. Calcd for $C_{20}H_{19}NO_2Fe$: C, 66.51; H, 5.30; N, 3.88. Found: C, 66.40; H, 5.33; N, 3.89.

4.3. General procedure for N-acylation of oxazolidin-2-ones

n-BuLi (2.7 mL of a 1.6 M solution in hexane, 4.3 mmol) was added to a stirred suspension of oxazolidin-2-one **4a** or **4b**, respectively (1.3 g, 3.6 mmol), in 30 mL of THF at −80 °C, and the resulting clear solution was stirred at this temperature for 30 min. Propionyl-chloride (0.44 mL, 5 mmol) was added, the reaction mixture was stirred for 30 min at −80 °C, before being warmed to −20 °C and quenched by the addition of satd aqueous $NaHCO_3$. The organic phase was washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, concentrated in vacuo and purified by column chromatography.

4.3.1. (4*R*,5*R*)-4-Benzyl-3-propionyl-5-ferrocenyl-oxazolidin-2-one 8a. Reaction of oxazolidinone **4a** (1.3 g, 3.6 mmol) under the reaction conditions described above, followed by column chromatography on silica gel eluting with cyclohexane–ethylacetate (10:1), gave the title compound **8a** (1.40 g, 91%) as a yellow solid; mp: 128 °C; $[\alpha]_D^{22} = -116$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.15 (3H, t, $J = 7.3$ Hz, CH_3), 2,68 (1H, dd, $J = 13.7$ and 8.8 Hz, CH_aH$_b$-Ph), 2.78 (1H, dd, $J = 13.7$ and 4.0 Hz, CH$_a$$H_b$-Ph), 2.95 (2H, m, $J = 7.3$ Hz, CH_2–CH$_3$), 3.89 (1H, d, $J = 1$ Hz, Cp-*H*), 4.07 (1H, s, Cp-*H*), 4.21 (5H, s, Cp-*H*), 4.29 (1H, s, Cp-*H*), 4.46 (1H, d, $J = 1$ Hz, Cp-*H*), 4,74 (1H, m, $J = 4.4$ and 3.9 Hz, C*H*–N), 5.49 (1H, d, $J = 7.3$ Hz, Cp-C*H*–O), 6.81 (2H, m, Ar-*H*), 7.09 (3H,m, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.45, 29.42, 35.05, 59.89, 66.47, 68.60, 68.78, 68.89, 69.30, 78.31, 79.95, 126.38, 128.03, 129.49, 136.72, 153.42, 173.85. Anal. Calcd for $C_{23}H_{23}NO_3Fe$: C, 66.21; H, 5.55; N, 3.36. Found: C, 66.07; H, 5.56; N, 3.32.

4.3.2. (4*S*,5*R*)-4-Benzyl-3-propionyl-5-ferrocenyl-oxazolidin-2-one 8b. Reaction of oxazolidinone **4a** (1.3 g, 3.6 mmol) under the reaction conditions described above, followed by column chromatography on silica gel eluting with cyclohexane–ethylacetate (10:1), gave the title compound **8a** (1.42 g, 91%) as a yellow solid; mp: 104 °C; $[\alpha]_D^{22} = +42$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23 (3H, t, $J = 7.3$ Hz, CH_3), 2.82 (1H, dd, $J = 13.2$ and 10.3 Hz, CH_aH$_b$-Ph), 2.99 (2H, m, $J = 7.3$ Hz, CH_2–CH$_3$), 3.38 (1H, dd, $J = 13.2$ and 2.9 Hz, CH$_a$$H_b$-Ph), 3.86 (1H, s, Cp-*H*), 3.87 (5H, s, Cp-*H*), 4.04 (1H, s), 4.14 (1H, s, Cp-*H*), 4.17 (1H, s, Cp-*H*), 4.71 (1H, ddd, $J = 10.25$, 2.9, 2.0 Hz, C*H*–N), 5.12 (1H, d, $J = 2.0$ Hz, Cp-C*H*–O), 7.31 (1H, t, $J = 7.3$ Hz, Ar-H), 7.35 (2H, d, $J = 7.3$ Hz, Ar-H), 7.40 (2H, t, $J = 7.3$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.48, 29.37, 38.44, 61.10, 65.55, 67.35, 68.80, 69.16, 69.41, 76.96, 84.17, 127.74, 129.27, 129.76, 135.77, 152.99, 174.27. Anal. Calcd for $C_{23}H_{23}NO_3Fe$: C, 66.21; H, 5.55; N, 3.36. Found: C, 65.84; H, 5.54; N, 3.33.

4.4. Representative procedure for diastereoselective alkylation

n-BuLi (0.45 mL of a 1.6 M solution in hexane, 0.72 mmol) was added to a solution of diisopropylamine (0.10 mL, 0.72 mmol) in THF (5 mL) at −80 °C, the reaction mixture allowed to warm to −40 °C and stirred at this temperature for 30 min. Propionyl-auxiliary **8a** or **8b** (200 mg, 0.48 mmol), dissolved in THF (1 mL), was added at −80 °C and the resulting mixture stirred at this temperature for 30 min. CuCN (53 mg, 0.58 mmol) was added and stirring was continued for another 30 min, before the halide (3 equiv benzyl bromide or allyl bromide, respectively) was added at −80 °C. The reaction mixture was allowed to warm to −20 °C, stirred for 4 h at this temperature and was allowed to warm to 0 °C overnight. Then the reaction was quenched by the addition of satd aqueous NH_4Cl, the mixture extracted with dichloromethane, the organic phases were combined, dried over Na_2SO_4 and concentrated in vacuo.

4.4.1. (4*R*,5*R*)-4-Benzyl-3-((2*S*)-2-methyl-3-phenylpropanoyl)-5-ferrocenyl-oxazolidin-2-one 9a. Benzylation of oxazolidinone **8a** (200 mg, 0.48 mmol) with benzyl bromide (0.17 mL, 1.44 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spec-

troscopy. The benzylated product **9a** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (15:1, respectively) as a yellow solid (190 mg, 78%); mp: 51 °C; $[\alpha]_D^{22} = -62$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.07 (3H, d, $J = 6.4$ Hz, CH_3), 2.43–2.53 (3H, m, CH_2-Ph, CH_a-Ph), 3.03 (1H, q, $J = 6.4$ Hz, CH_b-Ph), 3.77 (1H, m, Cp-*H*), 3.97 (1H, m, Cp-*H*), 3.98 (1H, m, C*H*–CH_3), 4.13 (5H, s, Cp-*H*), 4.20 (1H, dd, $J = 2.4$ and 3.4 Hz, Cp-*H*), 4.32 (1H, t, $J = 1.0$ Hz, Cp-*H*), 4.66 (1H, m, C*H*–N), 5.38 (1H, d, $J = 7.3$ Hz, C*H*–O), 6.68–6.70 (2H, m, Ph-H), 6.98–7.00 (3H, m, Ph-H), 7.20 (6H, m, Ph-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.43, 33.72, 34.49, 39.74, 40.01, 59.92, 66.40, 68.61, 68.77, 68.80, 69.28, 77.98, 79.97, 126.35, 126.48, 128.00, 128.45, 128.55, 128.93, 129.16, 129.44, 129.47, 136.68, 139.28, 153.04, 176.50. Anal. Calcd for $C_{30}H_{29}NO_3Fe$: C, 71.02; H, 5.76; N, 2.76. Found: C, 70.58; H, 5.85; N, 2.66.

4.4.2. (4*R*,5*R*)-4-Benzyl-3-((2*S*)-2-methyl-pent-4-enoyl)-5-ferrocenyl-oxazolidin-2-one 10a. Allylation of oxazolidinone **8a** (200 mg, 0.48 mmol) with allyl bromide (0.12 mL, 1.44 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spectroscopy. The allylated product **10a** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (15:1, respectively) as a yellow solid (180 mg, 82%) mp: 79 °C; $[\alpha]_D^{22} = -104$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.19 (3H, d, $J = 6.8$ Hz, CH_3), 2.17 (1H, pent, $J = 7.1$ Hz, CH_aH$_b$–CH=CH_2), 2.48 (1H, pent, $J = 6.8$ Hz, CH_aH_b–CH=CH_2), 2.67 (1H, dd, $J = 14.2$ and 8.8 Hz, CH_aH$_b$-Ph), 2.76 (1H, dd, $J = 14.2$ and 3.4 Hz, CH_aH_b-Ph), 3.83–3.90 (2H, m, $CH_2CH(CH_3)$-C=ON, Cp-H), 4.06 (1H, s, Cp-H), 4.22 (5H, s, Cp-H), 4.30 (1H, s. Cp-H), 4.47 (1H, s, Cp-H), 4.77 (1H, m, $J = 3.4$, 8.8 and 7.4 Hz, C*H*–N), 5.03 (1H, dd, $J = 10.3$ and 1.0 Hz, CH=CH_aH$_b$), 5.08 (1H, dd, 17.1 and 1.5 Hz, CH=CH_aH_b), 5.48 (1H, d, $J = 7.3$, C*H*–O), 5.77 (1H, m, $J = 6.8$, 10.3 and 17.1 Hz, C*H*=CH_2), 6.81 (2H, m, Ph-H), 7.08 (3H, m, Ph-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.54, 35.14, 37.39, 38.12, 60.07, 66.44, 68.66, 68.81, 68.89, 69.34, 78.02, 80.08, 117.29, 126.36, 128.03, 129.49, 135.45, 136.74, 153.05, 176.45.

4.4.3. (4*S*,5*R*)-4-Benzyl-3-((2*R*)-2-methyl-3-phenylpropanoyl)-5-ferrocenyl-oxazolidin-2-one 9b. Benzylation of oxazolidinone **8b** (200 mg, 0.48 mmol) with benzyl bromide (0.17 mL, 1.44 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spectroscopy. The benzylated product **9b** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (15:1, respectively) as a yellow solid (170 mg, 69%); mp: 108 °C; $[\alpha]_D^{22} = +25$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.12 (3H, d, $J = 6.8$ Hz, CH_3), 2.55 (1H, dd, $J = 10.25$ and 13.18 Hz, CH_aH$_b$-Ph), 2.63 (1H, dd, $J = 7.8$ and 13.2 Hz, CH_aH_b-Ph), 3.04 (1H, d, $J = 13.2$ Hz, CH_aH$_b$-Ph), 3.10 (1H, q, $J = 6.8$ Hz, CH_aH_b-Ph), 3.72 (1H, s, Cp-H), 3.77 (1H, s, Cp-H), 3.80 (5H, s, Cp-H), 3.94 (1H, s, Cp-H), 4.09 (2H, m, $CH_2CH(CH_3)$C=ON, Cp-H), 4.62 (1H, d, $J = 9.3$ Hz, C*H*-N), 4.97 (1H, s, C*H*–O), 7.18–7.31 (10 H, m, Ph-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.96, 38.23, 39.55, 39.88, 61.13, 65.55, 67.37, 68.75, 68.84, 69.24, 69.44, 76.60, 84.25, 126.52, 127.69, 128.47, 129.22, 129.48, 129.74, 135.67, 139.31, 152.53, 176.76.

4.4.4. (4*S*,5*R*)-4-Benzyl-3-((2*R*)-2-methyl-pent-4-enoyl)-5-ferrocenyl-oxazolidin-2-one 10b. Allylation of oxazolidinone **8b** (200 mg, 0.48 mmol) with allyl bromide (0.12 mL, 1.44 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spectroscopy. The allylated product **10b** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (15:1, respectively) as a yellow solid (158 mg, 72%); mp: 96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.19 (3H, d, $J = 6.8$ Hz, CH_3) $J = 2.25$ (1H, pent, $J = 7.2$ Hz, CH_2), 2.54 (1H, pent, $J = 6.8$ Hz, CH_2), 2.77 (1H, dd, $J = 10.4$ and 13.1 Hz, CH_2), 3.33 (1H, dd, $J = 7.0$ and 13.2 Hz, CH_2), 3.83 (1H, d, $J = 1.2$ Hz, Cp-*H*), 3.85 (5H, s, Cp-*H*), 3.91 (1H, m, $J = 6.9$ Hz, O=C–C*H*(CH_3)–CH_2), 4.01 (1H, d, $J = 1.2$ Hz, Cp-*H*), 4.13 (1H, s, Cp-*H*), 4.16 (1H, s, Cp-*H*), 4.71 (1H, m, $J = 10.3$ Hz, C*H*–N), 5.07 (1H, dd, $J = 10.2$ and 1.0 Hz, C=CH_2), 5.10–5.13 (2H, m, C*H*–O and C=CH_2), 5.84 (m, $J = 10.2$ and 7.2 Hz, C*H*=CH_2),7.30 (t, $J = 7.1$ Hz, Ph-H), 7.35–7.41 (4H, m, Ph-H); ^{13}C NMR (125 MHz): δ 16.76, 37.23, 38.01, 38.67, 61.38, 65.50, 67.43, 68.81, 69.21, 69.44, 76.79, 84.16, 117.31, 127.76, 129.26, 129.88, 135.48, 135.86, 152.62, 176.76.

4.5. Representative procedure for Mg-mediated aldol reactions

To a solution of 100 mg (0.24 mmol) of oxazolidinone **8a** or **8b** in 2 mL of THF abs. were added triethylamine (83 μL, 0.60 mmol), $MgCl_2$ (23 mg, 0.24 mmol), benzaldehyde (30 μL, 29 mmol) and trimethylsilylchloride (45 μL, 0.36 mmol) at room temperature. The mixture was stirred for 48 h at room temperature, diluted with 5 mL of Et_2O and filtered though a plug of silica. To the obtained solution 2 mL of methanol was added along with two drops of trifluoroacetic acid. This was stirred for 0.5 h at room temperature and quenched with satd aqueous $NaHCO_3$. The organic phase was washed subsequently with sat. aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. NMR-spectroscopic analysis of the obtained residue gave the isomeric composition of the product. The crude product was subsequently purified by flash chromatography.

4.5.1. (4*R*,5*R*)-4-Benzyl-5-ferrocenyl-3-((2*S*,3*R*)-3-hydroxy-2-methyl-3-phenylpropanoyl)oxazolidin-2-one 11a. Aldol reaction of oxazolidinone **8a** (100 mg, 0.24 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spectroscopy. The aldol product **11a** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (10:1, respectively) as a yellow solid (98 mg, 78%); mp: 79 °C; $[\alpha]_D^{22} = -58$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.09 (3H, d, $J = 6.8$ Hz, CH_3), 2.62 (1H, dd, $J = 8.8$ and 14.2 Hz,

CH_aH$_b$-Ph), 2.72 (1H, dd, $J = 3.4$ and 14.2 Hz, CH$_a$$H_b$-Ph), 2.94 (1H, d, $J = 6.8$ Hz, OH), 3.86 (1H, s, Cp-H), 4.06 (1H, s, Cp-H), 4.21 (5H, s, Cp-H), 4.29 (1H, s, Cp-H), 4.33 (m, 1H, $J = 7.3$ Hz, Ph-CH(OH)CH(CH$_3$)-C=ON), 4.44 (1H, s, Cp-H), 4.72–4.77 (2H, m, CH(OH) and CH–N), 5.48 (1H, d, $J = 7.3$ Hz, Cp-CH–O), 6.79–6.81 (2H, m, Ar-H), 7.08–7.26 (3H, m, Ar-H), 7.30–7.43 (5H, m, Ar-H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 15.01, 34.76, 44.78, 60.41, 66.52, 68.73, 68.82, 68.93, 69.35, 77.52, 78.21, 79.79, 126.34, 126.85, 128.03, 128.17, 128.69, 129.47, 136.84, 141.98, 153.46, 176.52.

4.5.2. (4*S*,5*R*)-4-Benzyl-5-ferrocenyl-3-((2*R*,3*S*)-3-hydroxy-2-methyl-3-phenylpropanoyl)oxazolidin-2-one 11b. Aldol reaction of oxazolidinone **8b** (100 mg, 0.24 mmol) under the reaction conditions described above provided the crude reaction product, the composition of which was determined by ^{1}H NMR spectroscopy. The aldol product **11a** was subsequently isolated by column chromatography on silica gel eluting with cyclohexane–ethylacetate (10:1, respectively) as a yellow solid (92 mg, 73%); mp: 76 °C; $[\alpha]_D^{22} = +53$ (c 1.0, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.12 (3H, d, $J = 6.9$ Hz, CH_3), 2.74 (1H, dd, $J = 10.3$ and 13.2 Hz, CH_aH$_b$-Ph), 3.17 (1H, d, $J = 6.8$ Hz, OH), 3.27 (1H, dd, $J = 2.44$ and 13.7 Hz, CH$_a$$H_b$-Ph), 3.85 (1H, s, Cp-$H$), 3.88 (5H, s, Cp-$H$), 4.04 (1H,s, Cp-$H$), 4.15 (1H, s, Cp-$H$), 4.18 (1H, s, Cp-$H$), 4.40 (1H, pent, $J = 7.3$ Hz, Ph-CH(OH)CH(CH$_3$)C=ON), 4.74 (1H, d, $J = 9.8$ Hz, CH–N), 4.85 (1H, t, $J = 7.3$ Hz, CH(OH)), 5.10 (1H, s, Cp-CH–O), 7.29–7.46 (10H, m, Ar-H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 15.02, 38.17, 44.39, 61.31, 65.55, 67.55, 68.86, 69.33, 69.56, 77.50, 83.88, 126.80, 127.74, 128.19, 128.72, 129.28, 129.79, 135.71, 142.13, 153.01, 176.83.

4.6. General procedure for auxiliary cleavage

LiOH (3 equiv) was added to a solution of alkylation product (100 mg, 1 equiv) in 5 mL of a THF/H$_2$O mixture (3:1) at 0 °C. The mixture was stirred at 0 °C for 1 h and at room temperature for 16 h. Saturated aqueous NaHCO$_3$ was added and the phases were separated. The aqueous phase was washed with dichloromethane (3 × 10 mL), and the organic phases were combined, washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo to give the auxiliary as a yellow, crystalline solid. The spectroscopic data of the recovered auxiliary were identical to those recorded above. To the original aqueous extract was added 1 M HCl until pH 1 was reached. The mixture was extracted with ethylacetate (3 × 10 mL) and the organic extracts were combined, washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo to give the respective carboxylic acid. The crude acids were purified by silica gel column chromatography (eluent CH$_2$Cl$_2$/MeOH 10:1). Absolute configuration and enantiomeric purity were assigned by the comparison of the measured specific rotation with literature values.

4.6.1. Hydrolysis of (4*R*,5*R*)-4-benzyl-3-((2*S*)-2-methyl-3-phenyl-propionyl)-5-ferrocenyl-oxazolidin-2-one 9a. Hydrolysis of **9a** (100 mg, 0.20 mmol) under the above-mentioned conditions gave (4*R*,5*R*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4a** (66 mg, 92%) as a yellow solid, and (*S*)-2-methyl-3-phenylpropionic acid **12a** (28 mg, 89%) as a colourless oil. Compound **12a**: $[\alpha]_D^{22} = +26.3$ (c 1.0, CHCl$_3$) (lit.[6n] +26.5); ee 95% (for determination see below); ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.19 (3H, d, $J = 6.9$ Hz, CH$_3$), 2.70 (1H, dd, $J = 8.0$ and 13.5 Hz, CH$_2$), 2.78 (1H, m, $J = 6.8$ Hz, CH–CH$_3$), 3.10 (1H, dd, $J = 6.5$ and 13.5 Hz, CH$_2$), 7.20–7.33 (5H, m, Ph-H); ^{13}C NMR (125 MHz, CDCl$_3$): δ 16.60, 39.38, 41.36, 126.57, 128.56, 129.14, 139.16, 182.57.

4.6.2. Hydrolysis of (4*R*,5*S*)-4-benzyl-3-((2*R*)-2-methyl-3-phenyl-propionyl)-5-ferrocenyl-oxazolidin-2-one 9b. Hydrolysis of **9b** (100 mg, 0.20 mmol) under the above-mentioned conditions gave (4*R*,5*S*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4b** (60 mg, 83%) as a yellow solid, and (*R*)-2-methyl-3-phenylpropionic acid **12b** (27 mg, 82%) as a colourless oil; **12b**: $[\alpha]_D^{22} = -18$ (c 1.0, CHCl$_3$) (lit.[6i] −26.1); ee 70% (for determination see below).

4.6.2.1. Determination of enantiomeric purity of 12a and 12b. TMSCHN$_2$ (2.0 M in hexane, 1 mL, 2 mmol) was added to a stirred solution of acid **12a** or **12b** (10 mg) in MeOH–THF (1:3.5 mL) at room temperature. The resulting mixture was stirred at room temperature for 30 min and the solution became clear. The solvent was removed under reduced pressure and the ee of the prepared methyl-2-methyl-3-phenylpropanoate was determined by HPLC on a Chiralcel OD column (hexane/*i*-PrOH 99.75:0.25; flow 1 mL/min, detection at 254 nm; t_R of (*R*)-enantiomer: 15 min, of (*S*)-enantiomer: 19 min) to be 95% for (*S*)-**12a** and 70% for (*R*)-**12b**.

4.6.3. Hydrolysis of (4*R*,5*R*)-4-benzyl-3-((2*S*)-2-methyl-pent-4-enoyl)-5-ferrocenyl-oxazolidin-2-one 10a. Hydrolysis of **10a** (100 mg, 0.22 mmol) under the above-mentioned conditions gave (4*R*,5*R*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4a** (69 mg, 87%) as a yellow solid, and (*S*)-2-methyl-pent-4-enoic acid **13a** (19 mg, 77%) as a colourless oil. Compound **13a**: $[\alpha]_D^{22} = +10.1$ (c 1.0, CHCl$_3$), (lit.:[13] 10.1); ee >95%; ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.19 (3H, d, $J = 6.3$ Hz, CH$_3$), 2.20, (1H, m, CH$_2$), 2.43 (1H, m, CH$_2$), 2.55 (1H, s, CH), 5.05–5.11 (2H, m, C=CH_2), 5.77 (1H, m, CH=CH$_2$), 9.2 (1H, br s, COOH); ^{13}C NMR (125 MHz, CDCl$_3$): δ 16.5, 37.62, 39.28, 117.31, 135.29, 182.44.

4.6.4. Hydrolysis of (4*R*,5*S*)-4-benzyl-3-((2*R*)-2-methyl-pent-4-enoyl)-5-ferrocenyl-oxazolidin-2-one 10b. Hydrolysis of **10b** (100 mg, 0.22 mmol) under the above-mentioned conditions gave (4*R*,5*S*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4b** (74 mg, 94%) as a yellow solid, and (*R*)-2-methyl-pent-4-enoic acid **13b** (18 mg, 74%) as a colourless oil. Compound **13b**: $[\alpha]_D^{22} = -8.1$ (c 1.0, CHCl$_3$), (lit.:[14] −10.2); ee 78%; ^{1}H and ^{13}C NMR: identical with **13a**.

4.6.5. Hydrolysis of (4*R*,5*R*)-4-benzyl-3-((2*S*,3*R*)-3-hydroxy-2-methyl-3-phenyl-propionyl)-5-ferrocenyl-oxazolidin-2-one 11a. Hydrolysis of **11a** (100 mg, 0.19 mmol) under the above-mentioned conditions gave (4*R*,5*R*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4a** (0.61 mg, 89%) as a yellow solid, and (2*S*,3*R*)-3-hydroxy-2-methyl-3-

phenyl-propionic acid **14a** (29 mg, 84%) as a colourless oil. Compound **14a**: $[\alpha]_D^{22} = +38$ (c 0.66, $CHCl_3$), lit.:[15] +17.8; ^1H NMR (500 MHz, $CDCl_3$): δ 1.00 (3H, d, $J = 6.8$ Hz), 2.81 (1H, dq, $J = 7.3$ Hz), 4.72 (1H, d, $J = 8.8$ Hz), 7.31–7.37 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.48, 47.16, 76.47, 126.91, 128.48, 128.78, 141.19, 180.91.

4.6.6. Hydrolysis of (4*R*,5*S*)-4-benzyl-3-((2*R*, 3*S*)3-hydroxy-2-methyl-3-phenyl-propionyl)-5-ferrocenyl-oxazolidin-2-one 11b. Hydrolysis of **11b** (100 mg, 0.19 mmol) under the above-mentioned conditions gave (4*R*, 5*S*)-4-benzyl-5-ferrocenyl-oxazolidin-2-one **4b** (63 mg) as a yellow solid, and (2*R*,3*S*)-3-hydroxy-2-methyl-3-phenyl-propionic acid **14b** (25 mg, 73%) as a colourless oil. Compound **14b**: $[\alpha]_D^{22} = -26$ (c 0.66, $CHCl_3$), (lit.:[16] −40.7); ee 72%; ^1H NMR (500 MHz, $CDCl_3$): δ 1.00 (3H, d, $J = 6.8$ Hz), 2.81 (1H, dq, $J = 7.3$ Hz), 4.72 (1H, d, $J = 8.8$ Hz), 7.31–7.37 (5H, m): ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.48, 47.16, 76.47, 126.91, 128.48, 128.78, 141.19, 180.91.

References

1. (a) Richards, C. J.; Locke, A. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2377–2407; (b) Togni, A.; Hayashi, T. *Ferrocenes—Homogeneous Catalysis, Organic Synthesis, Material Science*; VCH: Weinheim, 1995; (c) Togni, A.; Halterman, R. L. In *Metallocenes*; Wiley-VCH: Weinheim, 1998; Vol. 2; (d) Three issues dedicated to ferrocene chemistry in: *J. Organomet. Chem.* **2001**, *637–639*, 1.
2. (a) Yamazaki, Y.; Kobayashi, H. *Tetrahedron: Asymmetry* **1993**, *4*, 1287–1294; (b) Izumi, T.; Aratani, S. J. *J. Chem. Technol. Biotechnol.* **1995**, *63*, 25–32; (c) Morrone, R.; Nicolosi, G.; Patti, A. *Gazz. Chim. Ital.* **1997**, *127*, 5–9; (d) Howell, J. A. S.; Humphries, K.; McAardle, P.; Cunningham, D.; Nicolosi, G.; Patti, A.; Walsh, M. A. *Tetrahedron: Asymmetry* **1997**, *8*, 1027–1030; (e) Patti, A.; Nicolosi, G.; Howell, J. A. S.; Humphries, K. *Tetrahedron: Asymmetry* **1998**, *9*, 4381–4394; (f) Kijima, T.; Yaginuma, Y.; Izumi, T. *J. Chem. Technol. Biotechnol.* **1999**, *74*, 501–508; (g) Veum, L.; Brouard, H.; Meffre, P.; Larcheveque, M.; Buisson, D.; Demousseau, E.; Azerad, R. *Tetrahedron: Asymmetry* **2000**, *11*, 4055–4059; (h) Patti, A.; Nicolosi, G. *Tetrahedron: Asymmetry* **2000**, *11*, 815–822; (i) Patti, A.; Nicolosi, G. *Tetrahedron: Asymmetry* **2000**, *11*, 3687–3692; (j) Lee, H. K.; Ahn, Y. *Bull. Korean Chem. Soc.* **2004**, *25*, 1471–1473; (k) D'Antona, N.; Lambusta, D.; Morrone, R.; Nicolosi, G.; Secundo, F. *Tetrahedron: Asymmetry* **2004**, *15*, 3835–3840; (l) Patti, A.; Pedotti, S. *Tetrahedron: Asymmetry* **2006**, *17*, 778–785.
3. Fröhlich, R. F. G.; Zabelinskaja-Mackova, A. A.; Fechter, M. H.; Griengl, H. *Tetrahedron: Asymmetry* **2003**, *14*, 355–362.
4. (a) Seyden-Penne, J. *Chiral Auxiliaries and Ligands for Asymmetric Synthesis*; Wiley: New York, 1995; (b) Procter, G. *Asymmetric Synthesis*; Oxford University Press: Oxford, 1996.
5. Reviews: (a) Ager, D. J.; Prakash, J.; Schaad, D. R. *Aldrichim. Acta* **1997**, *30*, 3–12; (b) Ager, D. J.; Prakash, J.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835–875.
6. (a) Davies, S. G.; Sanganee, H. J.; Szolcsanyi, P. *Tetrahedron* **1999**, *55*, 3337–3354; (b) Gibson, C. L.; Gillon, K.; Cook, S. *Tetrahedron Lett.* **1998**, *39*, 6733–6736; (c) Brenner, M.; Seebach, D. *Helv. Chim. Acta* **1999**, *82*, 2365–2379; (d) Gaul, C.; Seebach, D. *Org. Lett.* **2000**, *2*, 1501–1504; (e) Fukuzawa, S.-i.; Matsuzawa, H.; Yoshimitsu, H. *J. Org. Chem.* **2000**, *65*, 1702–1706; (f) Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith, A. D. *Tetrahedron: Asymmetry* **2000**, *11*, 3475–3479; (g) Bull, S. D.; Davies, S. G.; Key, M.-S.; Nicholson, R. L.; Savory, E. D. *Chem. Commun.* **2000**, 1721–1722; (h) Yamamoto, H.; Watanabe, S.; Kadotani, K.; Hasegawa, M.; Noguchi, M.; Kanesama, S. *Tetrahedron Lett.* **2000**, *41*, 3131–3136; (i) Alexander, K.; Cook, S.; Gibson, C. L.; Kennedy, A. R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1538–1549; (j) Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith, A. D. *Org. Biomol. Chem.* **2003**, *1*, 2886–2899; (k) Davies, S. G.; Nicholson, R. L.; Smith, A. D. *Org. Biomol. Chem.* **2004**, *2*, 3385–3400; (l) Davies, S. G.; Hunter, I. A.; Nicholson, R. L.; Roberts, P. M.; Savory, E. D.; Smith, A. D. *Tetrahedron* **2004**, *60*, 7553–7577; (m) Bull, S. D.; Davies, S. G.; Garner, A. C.; Kruchinin, D.; Key, M.-S.; Roberts, P. M.; Savory, E. D.; Smith, A. D.; Thomson, J. E. *Org. Biomol. Chem.* **2006**, *4*, 2945–2964; (n) Bull, S. D.; Davies, S. G.; Jones, S.; Sanganee, H. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 387–398.
7. (a) Alonso, F.; Davies, S. G.; Smethurst, C. A. P. *J. Organomet. Chem.* **1998**, *553*, 463–468; (b) Kimura, T.; Shoda, R.; Taniguchi, N.; Kamikawa, K.; Uemura, M. *Inorg. Chim. Acta* **2004**, *357*, 1829–1835; (c) Bueno, A.; Moreno, R. M.; Moyano, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1763–1778.
8. Tanaka, Y.; Taniguchi, N.; Kimura, T.; Uemura, M. J. *J. Org. Chem.* **2002**, *67*, 9227–9237.
9. (a) Bastin, S.; Brocard, J.; Pelinski, L. *Tetrahedron Lett.* **2000**, *41*, 7303–7307; (b) Bastin, S.; Ginj, M.; Brocard, J.; Pelinskia, L.; Novogrocki, G. *Tetrahedron: Asymmetry* **2003**, *14*, 1701–1708.
10. (a) de Vries, E. F. J.; Steenwinkel, P.; Brussee, J.; Kruse, C. G.; van der Gen, A. *J. Org. Chem.* **1993**, *58*, 4315–4325; (b) Tellitu, I.; Badia, D.; Dominguez, E.; Garcia, F. J. *Tetrahedron: Asymmetry* **1994**, *5*, 1567–1578; (c) Pagliarin, R.; Papeo, G.; Sello, G.; Sisti, M. *Tetrahedron* **1996**, *52*, 13783–13794; (d) Jackson, W. R.; Jacobs, H. A.; Matthews, B. R.; Jayatilake, G. S.; Watson, K. G. *Tetrahedron Lett.* **1990**, *31*, 1447–1450; (e) Effenberger, F.; Eichhorn, J. *Tetrahedron: Asymmetry* **1997**, *8*, 469–476; (f) Krepski, L. R.; Jensen, K. M.; Heilmann, S. M.; Rasmussen, J. K. *Synthesis* **1986**, 301–303.
11. (a) Evans, D. A.; Rieger, D. L.; Bilodeau, M. T.; Urpi, F. *J. Am. Chem. Soc.* **1991**, *113*, 1047–1049; (b) Evans, D. A.; Nelson, J. V.; Taber, T. *Top. Stereochem.* **1982**, *13*, 1–115; (c) Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 83–91.
12. (a) Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tedrow, J. S. *Org. Lett.* **2002**, *4*, 1127–1130; (b) Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2002**, *124*, 392–393.
13. Ghosh, A. K.; Cho, H.; Onishi, M. *Tetrahedron: Asymmetry* **1997**, *8*, 821–824.
14. Enholm, E. J.; Gallagher, M. E.; Jiang, S.; Batson, W. A. *Org. Lett.* **2000**, *2*, 3355–3357.
15. van Draanen, N. A.; Arseniyadis, S.; Crimmins, M. T.; Heathcock, C. H. *J. Org. Chem.* **1991**, *56*, 2499–2506.
16. Ghosh, A. K.; Kim, J.-H. *Org. Lett.* **2003**, *5*, 1063–1066.