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β-Ferrocenyl-β-amino alcohols: a new class of central chiral ferrocene derivatives

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Abstract

An efficient procedure for the enantioselective synthesis of β-ferrocenyl-β-amino alcohols, a new class of central chiral ferrocene derivatives suitable for the elaboration of auxiliaries and ligands for asymmetric synthesis, is described. Key steps of the method are the catalytic asymmetric dihydroxylation of 1-ferrocenyl alkenes and the regio- and stereoselective azide substitution of the hydroxyl group adjacent to the ferrocene moiety. The stereochemistry of the substitution step has been established by X-ray diffraction analysis of a cyclic derivative. The first catalytic enantioselective synthesis of a β-ferrocenyl-β-amino acid derivative is also disclosed.

Keywords: β-Amino acids; β-Amino alcohols; Asymmetric synthesis; Ferrocenes

1. Introduction

The chiral β-amino alcohol moiety is an important structural motif in several bioactive compounds [1], as well as in a great number of useful auxiliaries or ligands used in asymmetric synthesis [2]. Although the most common sources of chiral β-amino alcohols involve the reduction or derivatisation of α-amino acids [3] or of other natural products [4], the search for novel, purely synthetic chiral β-amino alcohols is a subject of unabated interest [5].

With the aim of extending the structural diversity of β-amino alcohols, we envisaged the replacement of the β substituent by a ferrocenyl group. A number of advantages could be expected from this transformation: (i) increasing the steric hindrance at the nitrogenated stereogenic center, due to the three-dimensional nature of the ferrocene nucleus, that might result in improved stereoselectivities [6]; (ii) nucleophilic substitution reactions at positions vicinal to the ferrocene moiety are highly favoured, and they take place with retention of configuration [7]; (iii) the ferrocene nucleus is chemically stable, and its derivatives are in many instances crystalline. In fact, several very useful chiral ligands incorporating a ferrocene moiety have been developed in the last decade [8]. An exhaustive bibliographical search showed however that while some structural types of ferrocene-containing amino alcohols have been described in the literature [9–14], 3-amino-3-ferrocenyl-1,2-propanediol (I) and 2-amino-2-ferrocenylethanol (II) derivatives were still unknown. We report in this paper the first, highly stereoselective, approach to both types of compounds.

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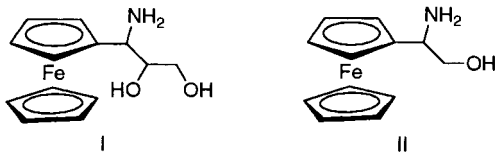


(Structures I and II)

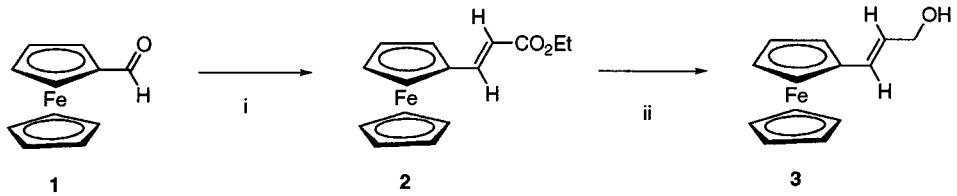
2. Results and discussion

2.1. Synthesis of (2S,3S)- and of (2R,3R)-3-amino-3-ferrocenyl-1,2-propanediol

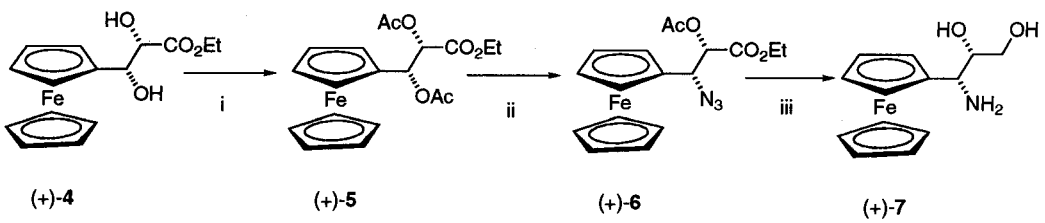
We devoted our first efforts to the preparation of the ferrocenyl-substituted amino alcohols of type I, by an extension of the methodology developed in our laboratory [15] for the enantioselective synthesis of *anti*-3-amino-1,2-alkanediols, that implies the asymmetric Sharpless epoxidation [16] of an (*E*)-allyl alcohol followed by the regio- and stereoselective oxirane ring opening by a nitrogen nucleophile. To that end, we obtained the known [17] (*E*)-3-ferrocenyl-2-propanol (**3**) by the improved procedure shown in Scheme 1, that involves two steps from commercially available ferrocenecarbaldehyde (**1**) and takes place in 84% overall yield.

However, all our efforts to isolate or trap the epoxyalcohol derived from **3**, either in racemic (by reaction with *m*-chloroperbenzoic acid) or in optically active form (by Sharpless epoxidation), were totally unsuccessful, probably due to the highly reactive nature of ferrocenyl-substituted oxiranes [18]. At the light of these results, we decided to explore an alternative route based on the asymmetric dihydroxylation of ferrocenyl acrylate (**2**) [19,20]. After some experimentation, we were able to find suitable conditions for the preparation of the desired diols in high enantiomeric purity (Table 1).

As previously observed by Baumgartner in the dihydroxylation of 1-ferrocenylalkenes [20], ligands based on the pyrimidine nucleus gave better results than those derived from phthalazide (compare entries 1 and 2 in Table 1). Further improvement was attained by changing the non-aqueous solvent from acetonitrile to *tert*-butyl alcohol (entry 3). In these first experiments, we observed that ferrocenecarbaldehyde (**1**) was a minor product of the reaction, and that conversions were never greater than 62%. We discovered that this was due to a concurrent Michael addition-retroaldol sequence on acrylate **3** arising from the basic aqueous reaction medium. We performed some further experiments in order to minimise this unwelcome process. The addition of methanesulfonamide [19] did not improve either the yield or the enantioselectivity of the reaction (entries 4 and 5). Best results were obtained by using the conditions of entry 6, which reproducibly led to highly enantiopure (+)-**4** with satisfactory conversions (73%). Further increasing the amount of the stoichiometric oxidant (entry 7) significantly eroded the yield of the reaction. We were pleased to find that the levorotatory enantiomer of **4** could also be obtained in good enantiomeric excess (94% ee) under the same optimised conditions, but using the pseudoenantiomeric $(DHQ)_2PYR$ ligand (entry 10 of Table 1). Taking into account the generally observed sense of asymmetric induction of Sharpless' dihydroxylation [19], we assigned (2*S*,3*S*) and (2*R*,3*R*) absolute configurations to (+)-**4** and to (−)-**4**, respectively. With both enantiomers of the diol **4** in our hands, we proceeded to their conversion into the target amino alcohols **7** (Scheme 2).

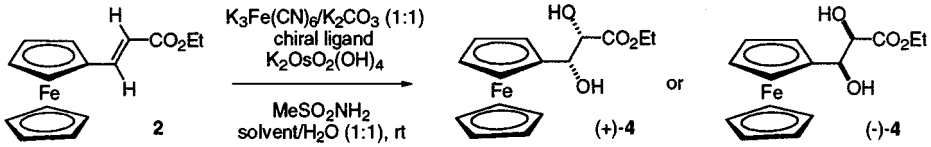


Scheme 1. *Reagents and conditions:* (i) three equivalents $(EtO)_2PO–CH_2–CO_2Et$, two equivalents NaH, benzene, 60 °C, reflux, 20 h, 97%; (ii) 2.4 equivalents DIBAL-H, diethyl ether, −75 °C, 2 h, −20 °C, 1 h, 87%.



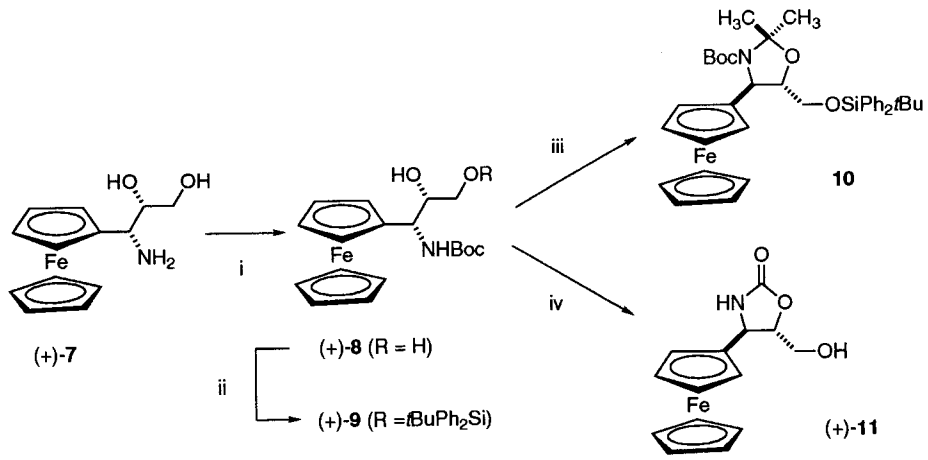
Scheme 2. *Reagents and conditions:* (i) 11 equivalents Ac_2O, pyridine, r.t., 17 h, 98%; (ii) six equivalents NaN_3, MeOH–water (1:3), r.t., 66 h, 77%; (iii) seven equivalents LAH, THF, reflux, 3.5 h, 83%.

Table 1
Asymmetric dihydroxylation of ferrocenylacrylate (**2**)



Entry	Solvent	Ligand (mol. equiv.)	Fe(III) mol. equiv.	Os(VI) mol. equiv.	$MeSO_2NH_2$ mol. equiv.	Reaction time (h)	Conversion (%)	Yield of **1** (%) [a]	Yield of **4** (%) [a]	% ee of **4** (configuration) [b]
1	CH_3CN	$(DHQD)_2PHAL$ (0.10)	3	0.10	0.12	22	37	8	19	57 (2*S*,3*S*)
2	CH_3CN	$(DHQD)_2PYR$ (0.10)	3	0.10	0	110	68	4	30	93 (2*S*,3*S*)
3	^{t}BuOH	$(DHQD)_2PYR$ (0.10)	3	0.10	0	62	61	9	36	98 (2*S*,3*S*)
4	^{t}BuOH	$(DHQD)_2PYR$ (0.10)	3	0.10	0.40	65	61	10	41	98 (2*S*,3*S*)
5	^{t}BuOH	$(DHQD)_2PYR$ (0.10)	3	0.10	1.0	138	54	8	38	99 (2*S*,3*S*)
6	^{t}BuOH	$(DHQD)_2PYR$ (0.20)	6	0.20	0	66	73	20	51	98 (2*S*,3*S*)
7	^{t}BuOH	$(DHQD)_2PYR$ (0.20)	12	0.20	0	70	87	18	9	95 (2*S*,3*S*)
8	CH_3CN	$(DHQ)_2PHAL$ (0.10)	3	0.10	0.12	44	35	n.d. [c]	10	62 (2*R*,3*R*)
9	^{t}BuOH	$(DHQ)_2PYR$ (0.10)	3	0.10	0	66	61	6	32	97 (2*R*,3*R*)
10	^{t}BuOH	$(DHQ)_2PYR$ (0.20)	6	0.20	0	47	84	26	47	94 (2*R*,3*R*)

[a] Yield of isolated product after chromatographic purification.
[b] By HPLC (Chiralcel-ODR column).
[c] Not determined.



Scheme 3. *Reagents and conditions:* (i) 1.2 equivalents Boc_2O, three equivalents $NaHCO_3$, MeOH, ultrasound, r.t., 2 h, 78%; (ii) 2.2 equivalents imidazole, 1.1 equivalents $^tBuPh_2SiCl$, DMF, r.t., 24 h, 89%; (iii) 10 equivalents $(MeO)_2CMe_2$, cat. *p*TsOH, benzene, reflux, 5.5 h, 69%; (iv) 2.5 equivalents NaH, DMF, r.t., 1.5 h; 1 M aq. HCl, r.t., 83%.

Reaction of (+)-**4** with acetic anhydride in pyridine led in essentially quantitative yield to the diacetate (+)-**5**, that was treated with a solution of sodium azide in methanol–water to afford the azido acetate (+)-**6** in 77% yield after chromatographic purification. Spectral analysis of this compound clearly showed that, as anticipated, the substitution had taken place with complete regio- and stereoselectivity (only one diastereomer was detected). Moreover, the enantiomeric purity of (+)-**6** (98% ee) was totally coincident with that of the starting diol. When a tetrahydrofuran solution of (+)-**6** was heated in the presence of lithium aluminum hydride, the reduction of the azido, acetate and ethoxycarbonyl groups took concomitantly place, giving rise to 3-amino-3-ferrocenyl-1,2-propanediol (+)-**7**—to which we assign a (2*S*,3*S*) configuration—in 83% yield. In a totally similar way, (−)-**4** was transformed into (−)-**7**. In order to establish without doubt that the azide substitution step had taken place with retention of configuration, we synthesised some cyclic derivatives of **7** (Scheme 3).

Following protection of the amino and of the primary hydroxyl groups of (+)-**7** as *tert*-butyl carbamate and *tert*-butyldiphenylsilyl ether, respectively, (+)-**9** was converted into the 2,2-dimethyl-1,3-oxazolidine (**10**). In this compound, the coupling constant between the two vicinal protons of the heterocycle was of 6.3 Hz, a value that is compatible with that of a *trans*-4,5-disubstituted-1,3-oxazolidine [21]. On the other hand, when (+)-**9** was treated with sodium hydride in *N*,*N*-dimethylformamide, highly crystalline oxazolidinone (+)-**11** was isolated in 83% yield after acidic hydrolysis of the silyl ether. Again, the 6.4 Hz value of the coupling constant between the two vicinal ring protons was compatible with a *trans* stereochemistry for this compound [22]. Recrystallisation of (+)-**11** from methanol afforded crystals suitable for X-ray diffraction analysis. The resolved structure (Fig. 1 and Table 2) fully confirmed our assumptions on the regio- and stereochemical course of azide substitution in **5**.

No significant deviations were found in the structure of the ferrocene nucleus in **11** relative to those of other monosubstituted ferrocene derivatives [23]. Thus, the iron–cyclopentadienyl carbon bond lengths fall in the 2.03–2.05 Å range. The two cyclopentadienyl rings are oriented in an eclipsed fashion. On the other hand, the oxazolidinone ring is essentially planar, with a small torsion of ca. 8° around the two sp^3 carbons. Interestingly enough, the ferrocenyl moiety adopts a conformation such that the interactions with the hydroxymethyl substituent are minimised, and is disposed away from the heterocycle. This fact results in a substantial steric hindrance on one of the two diastereotopic faces of the planar C(1)–NH–C(2) moiety (the *Si*-face for the (4*S*,5*S*) enantiomer of **11**), a phenomenon that could be very important for the application of auxiliaries or ligands derived from **7** in asymmetric synthesis.

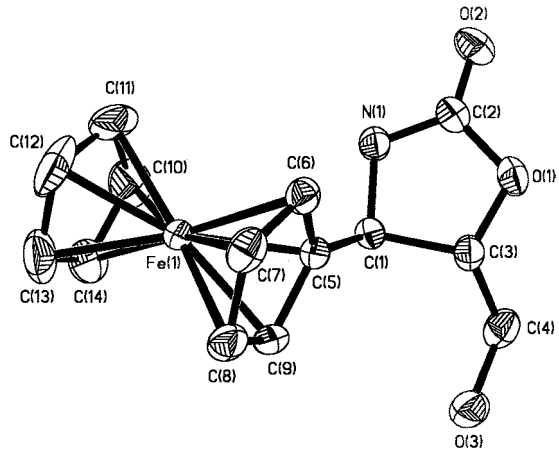


Fig. 1. ORTEP representation of the crystal structure of (+)-**11**. Hydrogen atoms have been omitted for clarity.

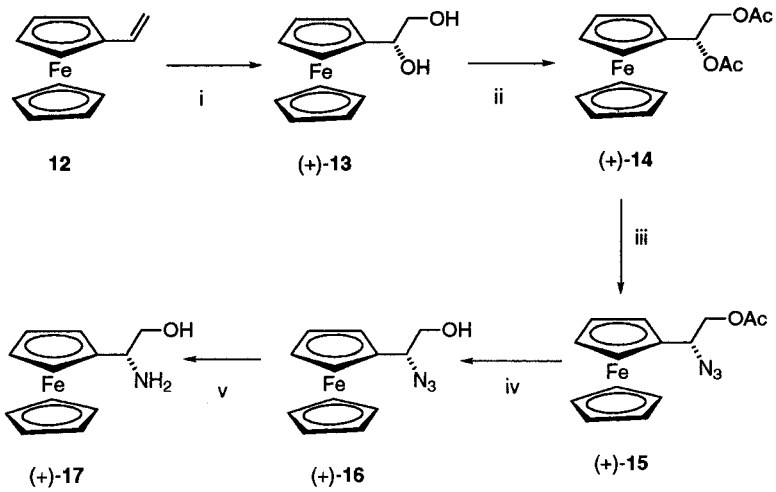
2.2. Synthesis of (2S)- and of (2R)-2-amino-2-ferrocenylethanol

Having established the feasibility of effecting a highly regio- and stereoselective azide substitution of the hydroxyl group adjacent to the ferrocene moiety in 1-ferrocenyl-1,2-alkanediol derivatives, we applied this strategy to the synthesis of 2-amino-2-ferrocenylethanol (Scheme 4).

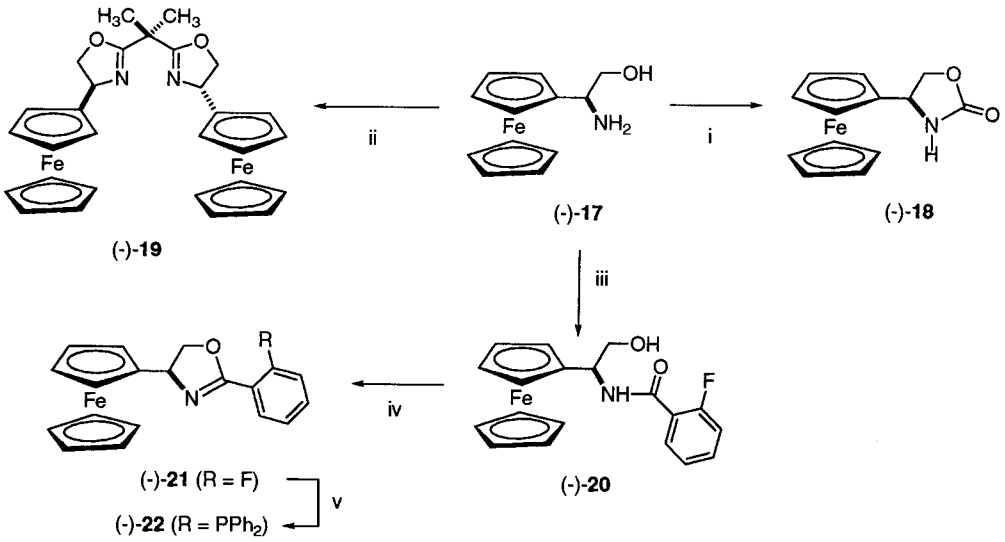
Asymmetric dihydroxylation of vinylferrocene (**12**) using $(DHQD)_2PYR$ as the chiral ligand [20] afforded (+)-**13**—for which a (1*S*) configuration was assumed—in good yield and with excellent optical purity (98% ee). When the corresponding diacetate (+)-**14** was reacted with sodium azide in aqueous methanol, monosubstitution cleanly took place to afford (+)-**15**. The enantiomeric purity, checked by HPLC, of this compound was identical to that of (+)-**13**, establishing that this process is racemisation-free. Although (+)-**15** could be converted into the target 2-amino-2-ferrocenylethanol (**17**) by reaction with lithium aluminum hydride, better results were obtained by means of a two step sequence involving diisobutylaluminum hydride-mediated reduction of the acetate and catalytic hydrogenation, that afforded (+)-**17** in 97% yield. The reactions summarised in Scheme 4 also allowed the transformation of diol (−)-**13** (obtained in 86% yield by asymmetric dihydroxylation of **12** using $(DHQ)_2PYR$ as a ligand) [20] into the amino alcohol (−)-**17**, whose enantiomeric excess (measured by HPLC at the level of azido acetate (−)-**15**) was 87%. In order to illustrate the applicability of these new β-amino alcohols in the preparation of chiral auxiliaries and ligands, we synthesised the oxazolidinone (−)-**18**, the bis(oxazoline) (−)-**19** and the phosphinooxazoline (−)-**22** from (−)-**17** in the way shown in Scheme 5.

Table 2
Selected bond lengths (Å) and angles (°) for 4-(ferrocenyl)oxazolidinone ((+)-**11**)

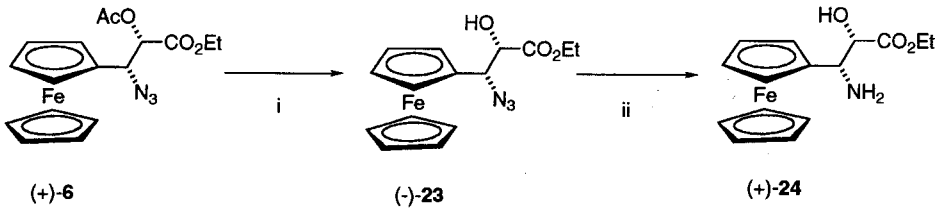
Bond lengths	
N(1)–C(1)	1.456(2)
N(1)–C(2)	1.330(2)
C(1)–C(3)	1.555(2)
C(1)–C(5)	1.496(2)
O(1)–C(2)	1.361(2)
O(2)–C(2)	1.215(2)
Fe(1)–C(10)	2.037(2)
Fe(1)–C(12)	2.0273(19)
Fe(1)–C(14)	2.0391(18)
Fe(1)–C(5)	2.0330(15)
Fe(1)–C(6)	2.0468(14)
Fe(1)–C(8)	2.0329(17)
Bond angles	
C(12)–Fe(1)–C(7)	106.86(9)
C(5)–Fe(1)–C(10)	109.07(8)
Fe(1)–C(5)–C(1)	132.57(11)
C(5)–C(1)–C(3)	110.06(12)
C(1)–C(3)–C(4)	115.49(14)
O(3)–C(4)–C(3)	110.15(14)
O(2)–C(2)–O(1)	121.58(6)
N(1)–C(2)–C(1)	109.84(14)
Torsional angles	
C(5)–C(51)–C(3)–C(4)	109.92(15)
N(1)–C(1)–C(5)–C(9)	155.36(15)
C(2)–N(1)–C(1)–C(3)	7.44(17)
C(1)–N(1)–C(2)–O(1)	176.73(17)
C(10)–Fe(1)–C(5)–C(1)	0.82(17)



Scheme 4. *Reagents and conditions:* (i) three equivalents $K_3[Fe(CN)_6]$, three equivalents K_2CO_3, 0.1 equivalents $(DHQD)_2PYR$, 0.1 equivalents $K_2OsO_2(OH)_4$, CH_3CN–water (1:1), r.t., 12 h, 79% (98% ee); (ii) nine equivalents Ac_2O, pyridine, r.t., 12 h, 97%; (iii) 5.5 equivalents NaN_3, MeOH–water (1:3), r.t., 12 h, 72%; (iv) 2.5 equivalents DIBAL-H, diethyl ether, −78 °C, 1 h, 97%; (v) H_2 (1 atm), cat. 10% Pd/C, ethyl acetate, r.t., 12 h, 100%.



Scheme 5. *Reagents and conditions:* (i) 1.5 equivalents triphosgene, 4.4 equivalents aq. NaOH, DCM, r.t., 1 h, 74%; (ii) one equivalent $Me_2C(CO_2H)_2$, 2.4 equivalents *N*-hydroxysuccinimide, 2.4 equivalents DCCI, THF, r.t., 2.5 + 15 h, 77%; five equivalents NEt_3, 0.1 equivalents DMAP, 1.4 equivalents *p*TsCl, 1,2-dichloroethane, reflux, 2 h, 29%; (iii) 1.9 equivalents NEt_3, one equivalents 2-fluorobenzoyl chloride, THF, 0 °C to r.t., 2 h, 89%; (iv) 4.9 equivalents NEt_3, 0.5 equivalents DMAP, 1.4 equivalents *p*TsCl, DCM, reflux, 1 h, 78%; (v) three equivalents $LiPPh_2$, THF, −20 °C, 2 h, r.t., 12 h, 76%.



Scheme 6. *Reagents and conditions:* (i) one equivalent NaEtO, EtOH, 0 °C, 1.5 h, 85%; (ii) H_2 (1 atm), cat. 10% Pd/C, ethyl acetate, r.t., 18 h, 82%.

2.3. Synthesis of (2S,3S)-3-amino-3-ferrocenyl-2-hydroxypropanoate

The introduction of ferrocene derivatives into bioactive molecules has received much attention in the last years, due to the unique redox and geometrical properties of the ferrocene nucleus [24]. Up to now, however, the incorporation of ferrocenes into peptide or bis(peptide) chains has been effected exclusively in the form of *N*-ferrocenoyl derivatives, since ferrocenyl-α- or β-amino acids are virtually unknown compounds [25]. We envisioned that the strategy that we had developed for the synthesis of **7** could also provide an excellent entry to highly enantiopure β-ferrocenyl-β-amino acid derivatives. This possibility was exemplified by the preparation of the ethyl ester of *syn*-3-amino-3-ferrocenyl-2-hydroxypropanoic acid from the azido acetate intermediate **6** (Scheme 6). Base-catalysed transesterification with ethanol followed by catalytic hydrogenation gave access to (+)-**24** in 70% overall yield from (+)-**6**. This represents the first catalytic asymmetric synthesis of a β-ferrocenyl-β-amino acid derivative. Given the easy availability of (−)-**6**, the levorotatory enantiomer of **24** should be equally accessible by this route.

In summary, we have developed an efficient procedure for the enantioselective synthesis of β-ferrocenyl-β-amino alcohols, a new class of ferrocene-derived chiral scaffolds for the construction of auxiliaries or ligands for asymmetric synthesis. This method, whose key steps are the catalytic asymmetric dihydroxylation of ferrocenyl alkenes and the totally regio- and stereoselective azide substitution of the hydroxyl group adjacent to the ferrocene nucleus, not only allows the preparation of both enantiomeric series of these previously unknown β-amino alcohols, but also constitutes a convenient entry to β-ferrocenyl-β-amino acids. Both the extension of this strategy to the preparation of other β-ferrocenyl-β-amino alcohols and the application of the derived auxiliaries and ligands to asymmetric synthesis are being actively pursued in our laboratories.

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}. 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. Chemical shifts are given in ppm and referenced to Me_4Si or $CHCl_3$. J values are given in Hz. Carbon multiplicities were established by DEPT experiments. Elemental analyses were performed by the 'Servei de Microanàlisi del CSIC de Barcelona' and by the 'Servicios Xerais de Apoio á Investigacion, Universidade da Coruña'. Exact mass measurements (HRMS) were performed by the 'Servicio de Espectroscopía de Masas de la Universidad de Córdoba' or by the 'Unidad de Espectrometría de Masas de la Universidad 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. Vinylferrocene (**12**) was prepared by a literature procedure [26].

3.1.1. (E)-3-Ferrocenyl-2-propenoic acid ethyl ester (2)

To a cold (0 °C), stirred suspension of NaH (2.45 g, 55% in paraffine oil, 56 mmol) in anhydrous C_6H_6 (50 ml), triethyl phosphonoacetate (14 ml, 70 mmol) was added dropwise. When the addition was finished and H_2 evolution subsided, the mixture was stirred 1 h at r.t. A solution of ferrocenecarbaldehyde (**1**) (5.00 g, 23.4 mmol) in dry C_6H_6 (20 ml) was added via cannula and the resulting mixture was heated to reflux for 20 h, after which time TLC analysis showed the complete disappearance of starting product **1**. After cooling to r.t., the reaction mixture was treated with water (70 ml), transferred to a separation funnel and extracted with Et_2O (2 × 100 ml). The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of the solvent afforded a crude product that was purified by column chromatography on silica gel, eluting with C_6H_{14}–EtOAc mixtures of increasing polarity, to give 6.40 g (97%) of pure ester **2** as an orange-coloured solid.

M.p. 69–70 °C (lit: 69.5–70 °C) [27]. IR (KBr): ν = 2975, 1704, 1636, 1316, 1208, 1175, 1044, 980 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.33 (t, J = 7 Hz, 3H), 4.16 (s, 5H), 4.22 (q, J = 7 Hz, 2H), 4.44 (m, 4H), 6.03 (d, J = 15.6 Hz, 1H), 7.57 (d, J = 15.8 Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.4 (CH_3), 60.2 (CH_2), 68.5 (CH), 69.6 (CH), 70.8 (CH), 78.7 (Cq, Cp), 114.8 (CH), 145.5 (CH), 167.1 (Cq, CO).

3.1.2. (E)-3-Ferrocenyl-2-propen-1-ol (3)

To a cold (−75 °C), stirred solution of ferrocenylacrylate (**2**) (0.130 g, 0.46 mmol) in anhydrous Et_2O (2 ml), 1.1 ml (1.1 mmol) of a 1 M solution of diisobutylaluminum hydride in hexanes were added with a calibrated syringe, and stirring was maintained for 2 h at the same temperature and for 1 h at −20 °C. At this point, TLC analysis showed that only a trace of starting material remained; MeOH (1 ml) was added dropwise, the reaction mixture was warmed up to r.t. and stirred until a white precipitate was formed. The solids were filtered off, washed with Et_2O and the filtrates were washed with brine, dried over Na_2SO_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 0.097 g (87%) of pure (*E*)-3-ferrocenyl-2-propen-1-ol (**3**) as a yellow solid.

M.p. 68.5–70 °C (lit: 69–70 °C) [17a]. IR (KBr): ν = 3240, 1656, 1370, 1208, 1106, 1001, 961, 816 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.34 (t, J = 6 Hz, 1H, OH), 4.20 (m, 11H), 5.97 (dt, J = 15.6 Hz, J' = 6 Hz, 1H), 6.36 (d, J = 15.8 Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 64.0 (CH), 66.9 (CH), 68.7 (CH_2), 69.2 (CH), 82.4 (Cq), 125.7 (CH), 129.4 (CH). MS (CI, NH_3) m/e = 225 [$M - OH^+$, 100%], 243 [$M + 1^+$, 4%], 260 [$M + 18^+$, 1%]. Anal. Calc. for $C_{13}H_{14}FeO$: C, 64.50; H, 5.83; O, 6.61. Found: C, 64.65; H, 5.87; O, 6.65%.

3.1.3. (2S,3S)-2,3-Dihydroxy-3-ferrocenylpropionic acid ethyl ester ((+)-4) and (2R,3R)-2,3-dihydroxy-3-ferrocenylpropionic acid ethyl ester ((−)-4)

To a solution of $K_3Fe(CN)_6$ (3.49 g, 10.6 mmol), K_2CO_3 (1.47 g, 10.6 mmol) and $(DHQD)_2PYR$ (0.313 g, 0.35 mmol) in *tert*-butyl alcohol (300 ml) and water (300 ml), solid $K_2OsO_2(OH)_4$ (0.129 g, 0.35 mmol) was added in one portion, and the resulting mixture was vigorously stirred until complete solution of the osmate (2 h). Ethyl (*E*)-3-ferrocenylpropionate (**2**) (0.50 g, 1.8 mmol) was added in 0.10 g portions over 1.5 h, and stirring was maintained for 66 h at r.t. After addition of Na_2SO_3 (2.7 g), the reaction mixture was extracted with EtOAc (3 × 300 ml). The organic extracts were washed with brine and dried over Na_2SO_4. Following evaporation of the solvents at reduced pressure, column chromatography of the crude product (silica gel, C_6H_{14}–EtOAc mixtures as eluent) gave 0.136 g (27% recovery) of **2**, 74 mg (20%) of **1** and 0.287 g (51%) of ethyl (2*S*,3*S*)-2,3-dihydroxy-3-ferrocenylpropanoate ((+)-**4**) (98% ee) as a yellow solid.

M.p. 54–55.5 °C. $[\alpha]_D$ = +35.4° (c = 1.28, $CHCl_3$). IR (KBr): ν = 3448, 2983, 1735, 1412, 1270, 1106, 1025

cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.35 (t, $J = 7$ Hz, 3H), 2.33 (br d, $J = 7$ Hz, 1H, OH), 3.11 (br d, $J = 6.2$ Hz, 1H, OH), 4.28 (m, 12H), 4.75 (br d, $J = 5.2$ Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.2 (CH_3), 62.1 (CH_2), 67.0 (CH), 67.5 (CH), 68.3 (CH), 68.4 (CH), 68.6 (CH), 70.9 (CH), 73.8 (CH), 88.5 (Cq, Cp), 172.8 (Cq, CO). MS (CI, NH_3) $m/e = 301$ [$M - OH^+$, 100%], 319 [$M + 1^+$, 1%], 336 [$M + 18^+$, 60%]. Anal. Calc. for $C_{15}H_{18}FeO_4$: C, 56.63; H, 5.70. Found: C, 56.64; H, 5.82%.

In a similar way, but using $(DHQ)_2PYR$ as a ligand, ferrocenylacrylate (**2**) (0.51 g, 1.8 mmol) gave 82 mg (16% recovery) of **2**, 97 mg (26%) of **1** and 0.261 g (47%) of ethyl (2*R*,3*R*)-2,3-dihydroxy-3-ferrocenylpropanoate ((−)-**4**) (94% ee). Conditions for the HPLC determination of the enantiomeric purity of **4**: Chiralcel-ODR column, 85% 0.5 M aq. $NaClO_4$–15% MeOH, $\Phi = 0.5$ ml min^{-1}, $T = 25$ °C, $\lambda = 220$ nm, $t_{R(2S,3S)} = 11.5$ min, $t_{R(2R,3R)} = 10.7$ min.

3.1.4. Ethyl (2S,3S)-2,3-diacetyloxy-3-ferrocenylpropanoate ((+)-5) and ethyl (2R,3R)-2,3-diacetyloxy-3-ferrocenylpropanoate ((−)-5)

To a solution of diol (+)-**4** (0.242 g, 0.76 mmol) in Py (1.5 ml), Ac_2O (0.76 ml, 8.1 mmol) was added in one portion. The mixture was stirred at r.t. for 17 h, and both Py and excess Ac_2O were removed at reduced pressure to afford 0.300 g (98%) of ethyl (2*S*,3*S*)-2,3-diacetyloxy-3-ferrocenylpropanoate ((+)-**5**) as an orange-coloured oil, that was not further purified.

$[\alpha]_D = +33°$ ($c = 1.22$, $CHCl_3$). IR (NaCl film): $\nu =$ 2985, 1750, 1374, 1219, 1106, 1046 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.28 (t, $J = 7.2$ Hz, 3H), 2.12 (s, 3H), 2.19 (s, 3H), 4.19 (m, 11H), 5.40 (d, $J = 2.6$ Hz, 1H), 6.29 (d, $J = 2.6$ Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.0 (CH_3), 20.6 (CH_3), 20.8 (CH_3), 61.9 (CH_2), 67.3 (CH), 68.2 (CH), 68.3 (CH), 68.4 (CH), 68.9 (CH), 70.3 (CH–O), 74.4 (CH), 83.3 (Cq, Cp), 167.1 (Cq, CO), 169.6 (Cq, CO), 170.1 (Cq, CO). MS (CI, NH_3) $m/e = 343$ [$M - OAc^+$, 100%], 420 [$M + 18^+$, 5%]. HRMS (EI) Calc. for $C_{19}H_{22}FeO_6$: 402.0766. Found: 402.0768.

In an analogous way, 0.254 g (0.80 mmol) of diol (2*R*,3*R*)-**4**, treated with 1.5 ml Py and 0.80 ml (8.47 mmol) of Ac_2O gave 0.311 g (97%) of ethyl (2*R*,3*R*)-2,3-diacetyloxy-3-ferrocenylpropanoate ((−)-**5**) as an orange oil.

3.1.5. Ethyl (2S,3S)-2-acetyloxy-3-azido-3-ferrocenylpropanoate ((+)-6) and ethyl (2R,3R)-2-acetyloxy-3-azido-3-ferrocenylpropanoate ((−)-6)

To a stirred suspension of diacetate (+)-**5** (0.300 g, 0.75 mmol) in 3:1 MeOH–water (21 ml), sodium azide (0.296 g, 4.55 mmol) was added in one portion, and the resulting mixture was stirred for 66 h at r.t. After elimination of MeOH by rotary evaporation at reduced pressure and addition of brine (5.2 ml), the mixture was extracted with methylene chloride (3×25 ml). The organic extracts were dried over Na_2SO_4. Elimination of the solvents followed by chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures as eluents) gave 0.225 g (77% yield, 98% ee) of ethyl (2*S*,3*S*)-2-acetyloxy-3-azido-3-ferrocenylpropanoate ((+)-**6**) as a yellow–orange oil.

$[\alpha]_D = +15.6°$ ($c = 0.77$, $CHCl_3$). IR (NaCl film): $\nu = 2927$, 2109, 1752, 1374, 1221, 1108, 1028 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.30 (t, $J = 7.4$ Hz, 3H), 2.21 (s, 3H), 4.23 (m, 11H), 4.74 (d, $J = 3$ Hz, 1H), 5.43 (d, $J = 3$ Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.1 (CH_3), 20.7 (CH_3), 61.5 (CH_2), 62.1 (CH), 67.2 (CH), 68.1 (CH), 68.59 (CH), 68.63 (CH), 69.1 (CH), 75.4 (CH), 82.8 (Cq, Cp), 167.3 (Cq, CO), 169.8 (Cq, CO). MS (CI, NH_3) $m/e = 343$ ($M - N_3^+$, 69%), 386 [$M + 1^+$, 1%], 403 [$M + 18^+$, 25%]. HRMS (EI) Calc. for $C_{17}H_{19}FeN_3O_4$: 385.0725. Found: 385.0726.

In a similar way, 0.300 g of the (2*R*,3*R*)-diacetate ((−)-**5**) and 0.289 g (4.55 mmol) of NaN_3 afforded 0.186 g (65%) of ethyl (2*S*,3*S*)-2-acetyloxy-3-azido-3-ferrocenylpropanoate ((−)-**6**). Conditions for the HPLC determination of the enantiomeric purity of **6**: Chiralcel-OD column, 99% C_6H_{14}–1% isopropyl alcohol, $\Phi = 0.3$ ml min^{-1}, $T = 25$ °C, $\lambda = 254$ nm, $t_{R(2S,3S)} = 39.6$ min, $t_{R(2R,3R)} = 36.7$ min.

3.1.6. (2S,3S)-3-Amino-3-ferrocenylpropane-1,2-diol ((+)-7) and (2R,3R)-3-amino-3-ferrocenylpropane-1,2-diol ((−)-7)

To a stirred solution of azido acetate (+)-**6** (0.237 g, 0.62 mmol) in anhydrous THF (6 ml) $LiAlH_4$ (0.164 g, 4.31 mmol) was added in one portion, and the resulting mixture was heated to reflux for 2 h. After cooling to r.t., water (0.1 ml), 15% aq. NaOH (0.1 ml) and water (3×0.1 ml) were added sequentially. Stirring was continued for 30 min, until a crystalline white precipitate settled out. Ethyl acetate (10 ml) was added and stirring was maintained for 30 min, after which time the solids were filtered out, the filtrates were dried over Na_2SO_4 and the solvents were eliminated at reduced pressure, to afford 0.141 g (83%) of (2*S*,3*S*)-3-amino-3-ferrocenylpropane-1,2-diol ((+)-**7**) as a yellow solid, that can be further purified by recrystallisation from CH_2Cl_2–C_6H_{14}.

M.p. 91.5–93.0 °C. $[\alpha]_D = +42.5°$ ($c = 1.46$, $CHCl_3$). IR (KBr): $\nu = 3354$, 2923, 1571, 1104, 1040, 812 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.85 (br s, 4H, NH_2, 2OH), 3.63 (m, 4H), 4.17 (m, 9H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 52.9 (CH), 64.7 (CH_2), 65.2 (CH), 67.8 (CH), 67.9 (CH), 68.4 (CH), 68.8 (CH), 74.8 (CH), 91.5 (Cq, Cp). MS (CI, NH_3) $m/e = 199$ [$M - 76^+$, 16%], 214 [$M - 61^+$, 4%], 259 [$M - NH_2^+$, 78%], 276 [$M + 1^+$, 100%]. HRMS (EI) Calc. for $C_{13}H_{17}FeNO_2$: 275.0609. Found: 275.0605.

In a similar way, 0.273 g (0.71 mmol) of (2*R*,3*R*)-azido acetate ((−)-**6**), treated with 0.188 g (4.96 mmol) of $LiAlH_4$ in 7 ml THF, gave 0.124 g (64%) of (2*R*,3*R*)-3-amino-3-ferrocenylpropane-1,2-diol ((−)-**7**).

3.1.7. (2S,3S)-3-(tert-Butoxycarbonylamino)-3-ferrocenylpropane-1,2-diol ((+)-8)

A mixture of 3-amino-3-ferrocenylpropane-1,2-diol ((+)-**7**) (69 mg, 0.25 mmol), di-*tert*-butyl dicarbonate (66 mg, 0.30 mmol) and $NaHCO_3$ (63 mg, 0.75 mmol) in MeOH (1.3 ml) was sonicated in a cleaning bath at r.t. for 2 h. The solids were filtered off and washed with MeOH. Concentration of the filtrate and column chromatography on Et_3N-pretreated silica gel (2.5% v/v), eluting with C_6H_{14}–EtOAc mixtures of increasing polarity, gave 73 mg (78%) of the *N*-Boc amino alcohol (+)-**8** as an orange-coloured semi-solid.

$[\alpha]_D = +17.9°$ ($c = 1.75$, $CHCl_3$). IR (NaCl film): $\nu = 3406$, 3097, 2979, 1686, 1507, 1368, 1250, 1169, 1050 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.26 (t, $J = 4$ Hz, 1H, OH), 1.50 (s, 9H), 2.85 (br, 1H, OH), 3.52 (m, 2H), 3.79 (m, 1H), 4.20 (m, 9H), 4.61 (dd, $J = 8.8$ Hz, $J' = 2.6$ Hz, 1H), 5.19 (br d, $J = 8.8$ Hz, 1H, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 28.4 (CH_3), 51.0 (CH), 63.3 (CH_2), 65.8 (CH), 67.8 (CH), 68.0 (CH), 68.8 (CH), 74.9 (CH), 80.3 (Cq), 87.8 (Cq, Cp), 157.1 (Cq, CO). MS (CI, NH_3) $m/e = 259$ [M − NHBoc$^+$, 16%], 375 [M$^+$, 51%], 376 [M + 1$^+$, 11%], 393 [M + 18$^+$, 2%]. HRMS (EI) Calc. for $C_{18}H_{25}FeNO_4$: 375.1133. Found: 375.1132.

3.1.8. (2S,3S)-1-(tert-Butyldiphenylsilyloxy)-3-(tert-butoxycarbonylamino)-3-ferrocenyl-2-propanol ((+)-9)

A mixture of the *N*-Boc amino alcohol (+)-**8** (0.100 g, 0.27 mmol), DMF (1.3 ml), imidazole (41 mg, 0.59 mmol) and *tert*-butyldiphenilsilylchloride (0.78 ml, 0.30 mmol) was stirred at r.t. for 24 h, diluted with Et_2O (5 ml) and washed with aq. sat. NH_4Cl solution (3 × 5 ml). The aq. phase was washed with Et_2O (3 × 5 ml), and the combined organic phase was dried over Na_2SO_4. Elimination of the solvents, followed by chromatographic purification on Et_3N-pretreated silica gel using C_6H_{14}–EtOAc mixtures of increasing polarity as eluents afforded 0.145 g (89%) of the title compound as an orange–yellow semi-solid.

$[\alpha]_D = +8.3°$ ($c = 1.10$, $CHCl_3$). IR (NaCl film): $\nu =$ 3438, 3074, 2933, 1694, 1505, 1428, 1169, 1113 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.08 (s, 9H), 1.43 (s, 9H), 2.66 (br s, 1H, OH), 3.61 (m, 2H), 3.93 (m, 1H), 4.11 (m, 9H), 4.55 (br d, $J = 7.8$ Hz, 1H), 5.21 (br d, $J = 8.0$ Hz, 1H, NH), 7.41 (m, 6H), 7.64 (m, 4H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 19.3 (Cq), 26.6 (CH_3), 26.9 (CH_3), 28.4 (CH_3), 50.5 (CH), 65.3 (CH_2), 66.6 (CH), 67.3 (CH), 67.7 (CH), 68.7 (CH), 74.5 (CH), 89.1 (Cq, Cp), 127.6*, 127.7 (CH), 129.6*, 129.8 (CH), 133.0 (CH), 134.7*, 135.5 (CH), 155.8 (Cq, CO) (* signal corresponding to a rotamer of the *N*-Boc group). MS (CI, NH_3) $m/e = 497$ [M − NHBoc$^+$, 32%], 556 [M − ^{t}Bu$^+$, 100%], 613 [M$^+$, 55%], 614 [M + 1$^+$, 47%], 393 [M + 18$^+$, 6%]. HRMS (EI) Calc. for $C_{34}H_{43}FeNO_4Si$: 613.2311. Found: 613.2299.

3.1.9. (4S,5S)-N-(tert-Butoxycarbonyl)-2,2-dimethyl-4-ferrocenyl-5-[(tert-butyldiphenylsilyloxy)-methyl]-1,3-oxazolidine (10)

A solution of (+)-**9** (30 mg, 0.05 mmol) and 2,2-dimethoxypropane (65 ml, 0.50 mmol) in C_6H_6 (0.2 ml) was heated to reflux for 5.5 h in the presence of a trace of *p*-toluenesulfonic acid, diluted with EtOAc (10 ml) and washed with aq. sat. $NaHCO_3$ and with brine. After drying over Na_2SO_4, elimination of the solvents followed by chromatographic purification on Et_3N-pretreated silica gel using C_6H_{14}–EtOAc mixtures of increasing polarity as eluents afforded 22 mg (69%) of the oxazolidine **10** as an orange–yellow oil.

IR (NaCl film): $\nu = 3074$, 2933, 2860, 1700, 1378, 1108 cm^{-1}. ^{1}H-NMR (300 MHz, 55 °C, $CDCl_3$): δ (ppm) = 1.10 (m, 12H), 1.46 (m, 9H), 3.77 (d, $J = 6.3$ Hz, 2H), 4.13 (m, 9H), 4.69 (m, 1H, CH), 4.93 (m, 1H, CH), 7.41 (m, 6H), 7.72 (m, 4H). ^{13}C-NMR (75 MHz, 55 °C, $CDCl_3$): δ (ppm) 19.3 (Cq), 26.7 (CH_3), 27.0 (CH_3), 28.6 (CH_3), 58.1 (CH), 65.8 (CH_2), 66.7 (CH), 67.6 (CH), 68.6 (CH), 79.8 (Cq, Cp), 127.7 (CH), 129.6 (CH), 129.8 (CH), 133.3 (CH), 133.4 (CH), 133.4 (CH), 134.9 (CH), 135.7 (CH), 151.8 (Cq, CO). MS (CI, NH_3) $m/e = 654$ [M + 1$^+$, 57%], 671 [M + 18$^+$, 4%]. HRMS (EI) Calc. for $C_{37}H_{47}FeNO_4Si$: 653.2624. Found: 653.2638.

3.1.10. (4S,5S)-4-Ferrocenyl-5-(hidroxymethyl)-1,3-oxazolidin-2-one ((+)-11)

To an stirred suspension of NaH (60% in paraffine oil, 12 mg, 0.30 mmol) in DMF (1 ml), a solution of (+)-**9** (73 mg, 0.12 mmol) in DMF (0.76 ml) was added via cannula. The resulting mixture was stirred at r.t. for 1.5 h, treated with aq. 1 M HCl (1.5 ml) and extracted with CH_2Cl_2 (3 × 5 ml). The organic extracts were washed with brine, dried over Na_2SO_4 and submitted to rotative evaporation to give a crude product that after chromatographic purification (Et_3N-pretreated silica gel, C_6H_{14}–EtOAc mixtures) afforded 30 mg (83%) of the oxazolidinone (+)-**11** as a yellow solid.

M.p. 178 °C (dec.). $[\alpha]_D = +41.8°$ ($c = 0.45$, C_2H_4O). IR (KBr): $\nu = 3365$, 2925, 1729, 1414, 1364, 1106, 1052, 1027 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 3.68 (br s, 1H, OH), 3.75 (m, 1H), 3.90 (m, 1H), 4.20 (m, 9H), 4.38 (m, 1H), 4.60 (d, $J = 6.4$ Hz, 1H), 5.26 (br s, 1H, NH). ^{13}C-NMR (75 MHz, Me_2SO-d_6): δ (ppm) 52.5 (CH), 62.1 (CH_2), 65.9 (CH), 66.3 (CH), 68.1 (CH), 68.4 (CH), 68.8 (CH), 82.9 (CH), 90.0 (Cq, Cp), 158.5 (Cq, CO). MS (CI, NH_3) $m/e = 302$ [M + 1$^+$,

6%], 319 [$M+18^+$, 100%]. HRMS (EI) Calc. for $C_{14}H_{15}FeNO_3$: 301.0401. Found: 301.0402.

3.1.11. X-ray structure determination and refinement of compound (+)-11

A suitable crystal grown from a MeOH solution (block, brown, dimensions $0.35 \times 0.20 \times 0.15$ mm) was used for the structure determination. X-ray data were collected using a Bruker SMART CCD area detector single-crystal diffractometer with graphite monochromatised Mo–K_α radiation ($\lambda = 0.71073$ Å) by the ϕ–ω scan method at r.t. Crystal data: $C_{14}H_{15}FeNO_3$, $M = 301.12$; Orthorhombic; space group $P2_12_12_1$ (No. 19); $a = 7.2281(16)$ Å, $b = 10.6983(17)$ Å, $c = 16.010(5)$ Å; $V = 1238.0(5)$ Å^3; $Z = 4$; $D_{calc} = 1.616$ g cm^{-3}; air-stable crystals, μ(Mo–K_α) = 1.220 mm^{-1}. A total of 1271 frames of intensity data were collected. The first 50 frames were recollected at the end of data collection to monitor for decay. The integration process yielded a total of 8568 reflections in the range $2.3 < \theta < 28.3$, of which 3065 [$R_{int} = 0.0178$] were independent. Absorption corrections were applied using the SADABS [28] program (maximum and minimum transmission coefficients 0.838 and 0.675). The structure was solved using the Bruker SHELXTLC-PC [29] software by direct methods and refined by full-matrix least-squares procedures on F^2. Hydrogen atoms were included in calculated positions and refined in the riding mode. Convergence was reached at a final $R_1 = 0.0225$ [$R_1 = \Sigma \| |F_o| - |F_c| \| / \Sigma |F_o|$] and $wR_2 = 0.0581$ [$wR_2 = \{\Sigma [w(F_o^2 - F_c^2)^2] / \Sigma [w[(F_o^2)^2]\}^{1/2}$], for $I > 2\sigma(I)$; and $R_1 = 0.0244$ and $wR_2 = 0.0590$ [for all data], 275 parameters, with allowance for the thermal anisotropy for all non-hydrogen atoms. The weighting scheme employed was $w = [\sigma^2(F_o^2 + (0.0373P)^2 + 0.0590P]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$ and the goodness-of-fit on F^2 was 1.044 for all observed reflections. Residual electron densities extremes were 0.21 and -0.32 e Å^{-3} (Table 3).

Table 3
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å$^2 \times 10^3$) for (+)-11

Atom	x	y	z	U_{eq} [a]
Fe(1)	8305(1)	10080(1)	4945(1)	23(1)
O(1)	9861(2)	6760(1)	7388(1)	39(1)
O(2)	6844(2)	6368(1)	7615(1)	41(1)
O(3)	13750(2)	8877(1)	7023(1)	43(1)
N(1)	7820(2)	8089(1)	6883(1)	32(1)
C(1)	9554(2)	8689(1)	6651(1)	25(1)
C(2)	8030(2)	7034(2)	7313(1)	30(1)
C(3)	10955(2)	7667(1)	6930(1)	28(1)
C(4)	12508(2)	8115(2)	7485(1)	38(1)
C(5)	9752(2)	8965(1)	5739(1)	24(1)
C(6)	9060(2)	8244(1)	5056(1)	27(1)
C(7)	9783(2)	8763(2)	4308(1)	33(1)
C(8)	10924(2)	9793(2)	4524(1)	35(1)
C(9)	10915(2)	9921(2)	5410(1)	30(1)
C(10)	6249(3)	10953(2)	5591(2)	51(1)
C(11)	5504(2)	10200(2)	4960(2)	61(1)
C(12)	6221(3)	10635(2)	4183(2)	60(1)
C(13)	7404(3)	11653(2)	4355(1)	51(1)
C(14)	7408(3)	11839(2)	5223(1)	45(1)

[a] U_{eq} is defined as one-third of the trace of the orthogonalised U_{ij} tensor.

3.1.12. (S)-1-Ferrocenylethane-1,2-diol ((+)-13) and (R)-1-ferrocenylethane-1,2-diol ((−)-13)

To a stirred solution of $K_3[Fe(CN)_6]$ (0.986 g, 3.0 mmol) and K_2CO_3 (0.415 g, 3.0 mmol) in 1:1 MeCN–water (100 ml), were added $(DHQD)_2PYR$ (88 mg, 0.10 mmol) and $K_2OsO_2(OH)_4$ (37 mg, 0.10 mmol), and stirring was maintained at r.t. until complete dissolution of the osmate. At this point, vinylferrocene (**12**) (0.212 g, 1.0 mmol) was added in one portion. The reaction was monitored by TLC. When no starting vinylferrocene remained (12 h stirring at r.t.), Na_2SO_3 (1.7 g, 13 mmol) was added and stirring maintained for 30 min. The reaction mixture was extracted with EtOAc (3×15 ml); the organic extracts were dried over Na_2SO_4 and the solvents were removed at reduced pressure. Column chromatography of the crude product (silica gel, C_6H_{14}–EtOAC mixtures as eluent) afforded 0.196 g (79%) of (*S*)-1-ferrocenyl-1,2-ethanediol ((+)-**13**) (98% ee) as a yellow solid.

M.p. 98.2–100.2 °C. (lit: 98–100 °C) [20]. $[\alpha]_D = +32.3°$ ($c = 0.38$, CH_2Cl_2). (lit: +23.8) [20]. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.08 (m, 1H, OH), 2.15 (m, 1H, OH), 3.66 (m, 1H), 3.76 (m, 1H), 4.23 (m, 9H), 4.47 (m, 1H).

In a similar way, but using $(DHQ)_2PYR$ as the chiral ligand, vinylferrocene (**12**) (1.0 mmol) afforded 0.211 g (86%) of (*R*)-1-ferrocenyl-1,2-ethanediol ((−)-**13**) (ee > 80%) as a yellow solid. M.p. 95.5–96.7 °C. (lit: 101–103 °C) [20]. $[\alpha]_D = -23.1°$ ($c = 0.38$, CH_2Cl_2). (lit: −23.3) [20]. Conditions for the HPLC determination of the enantiomeric purity of **13**: Chiralcel-OD column, 95% C_6H_{14}–5% isopropyl alcohol, $\Phi = 0.8$ ml min^{-1}, $T = 25$ °C, $\lambda = 220$ nm, $t_{R(S)} = 36.4$ min, $t_{R(R)} = 38.5$ min.

3.1.13. (S)-2-Acetyloxy-1-ferrocenylethyl acetate ((+)-14) and (R)-2-acetyloxy-1-ferrocenylethyl acetate ((−)-14)

A solution of (*S*)-ferrocenylethanediol ((+)-**13**) (1.50 g, 6.1 mmol) in anhydrous Py (12 ml) was treated with Ac_2O (6 ml, 54 mmol) and the resulting mixture was stirred at r.t. for 12 h (when TLC monitoring showed that the reaction was complete). Evaporation of the solvents at reduced pressure afforded the diacetate (+)-**14** (1.942 g, 97%) as a brown–orange dense oil that was used without further purification, since extensive decomposition took place during column chromatogra-

phy (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity).

M.p. 64.8–69.8 °C. $[\alpha]_D = +9.5°$ ($c = 1.03$, $CHCl_3$). IR (NaCl film): $\nu = 1740$, 1371, 1240, 1107, 1045, 820 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.09 (s, 3H), 2.10 (s, 3H), 4.19 (m, 9H), 4.26 (m, 1H), 4.62 (m, 1H), 5.90 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 20.8 (CH_3), 21.1 (CH_3), 65.7 (CH_2), 66.4 (CH), 68.1 (CH), 68.3 (CH), 68.4 (CH), 68.9 (CH), 69.9 (CH), 83.1 (Cq, Cp), 170.4 (Cq, CO), 170.8 (Cq, CO). MS (CI, NH_3) $m/e = 330$ [M^+, 1%], 331 [$M + 1^+$, 1%], 271 [$M - 59^+$, 100%].

In a similar way, diol (−)-**13** afforded diacetate (−)-14, $[\alpha]_D = -9.2°$ ($c = 1.05$, $CHCl_3$).

3.1.14. (S)-2-Azido-2-ferrocenylethyl acetate ((+)-15) and (R)-2-azido-2-ferrocenylethyl acetate ((−)-15)

To a solution of diacetate (+)-**14** (1.20 g, 3.64 mmol) in a 1:3 MeOH–water mixture (100 ml) sodium azide (1.31 g, 20.1 mmol) was added in one portion. The mixture was stirred at r.t. until TLC analysis showed no presence of the starting product (12 h). After eliminating most of the MeOH at reduced pressure, saturated brine solution (25 ml) was added and the mixture was extracted with CH_2Cl_2 (3 × 20 ml). The organic phases were dried over $MgSO_4$, stripped of solvents at reduced pressure and purified by column chromatography (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) to afford 0.82 g (72%) of the azido acetate (+)-**15** (98% ee) as a yellow solid.

M.p. 48.5–50.5 °C. $[\alpha]_D = +21.4°$ ($c = 0.99$, $CHCl_3$). IR (KBr): $\nu = 3096$, 2957, 2105, 1746, 1383, 1225, 1108, 1043, 1003, 822 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.25 (s, 3H), 4.53 (m, 2H), 4.18 (m, 10H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 20.9 (CH_3), 60.4 (CH_2), 66.3 (CH), 66.7 (CH), 67.3 (CH), 68.4 (CH), 68.5 (CH), 69.0 (CH), 84.0 (Cq, Cp), 170.4 (Cq, CO). MS (CI, NH_3) $m/e = 13$ [M^+, 2%], 271 [$M - 42^+$, 90%]. HRMS (EI) Calc. for $C_{14}H_{15}FeN_3O_2$: 313.0514. Found: 313.0514.

In a similar way, diacetate (−)-**14** afforded azido acetate (−)-**15** (87% ee), $[\alpha]_D = -20.7°$ ($c = 1.00$, $CHCl_3$). Conditions for the HPLC determination of the enantiomeric purity of **15**: Chiralcel-OD column, 90% C_6H_{14}–10% isopropyl alcohol, $\Phi = 0.5$ ml min^{-1}, $T =$ 25 °C, $\lambda = 220$ nm, $t_{R(S)} = 17.9$ min, $t_{R(R)} = 16.6$ min.

3.1.15. (S)-2-Azido-2-ferrocenylethanol ((+)-16) and (R)-2-azido-2-ferrocenylethanol ((−)-16)

To a cold (−78 °C), stirred solution of the azido acetate (+)-**15** (0.470 g, 1.5 mmol) in anhydrous Et_2O (4 ml), 3.8 ml (3.8 mmol) of a 1 M solution of diisobutylaluminum hydride in hexanes were added via syringe, and stirring was maintained for 1 h at the same temperature. At this point, TLC analysis showed that no starting material remained; MeOH (5 ml) was added dropwise, the reaction mixture was warmed up to r.t. and stirred until a white precipitate was formed. The solids were filtered out, washed with EtOAc and the filtrates were evaporated at reduced pressure to afford 0.395 g (97%) of pure azido alcohol (+)-**16** as a yellow solid.

M.p. 41–43 °C. $[\alpha]_D = +50.5°$ ($c = 0.49$, $CHCl_3$). IR (KBr): $\nu = 3386$, 2929, 2105,1258, 1107, 1044, 821 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.99 (br, 1H), 3.72 (m, 1H), 3.91 (m, 1H), 4.19 (m, 9H), 4.44 (dd, $J_1 = 8$ Hz, $J_2 = 4$ Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 63.9 (CH), 65.8 (CH_2), 66.3 (CH), 67.2 (CH), 68.3 (CH), 68.5 (CH), 68.9 (CH), 84.0 (Cq). MS (CI, NH_3) $m/e = 271$ [M^+, 2%], 289 [$M + 18^+$, 20%], 229 [$M - 42^+$, 100%]. HRMS (EI) Calc. for $C_{12}H_{13}FeN_3O$: 271.0408. Found: 271.0420.

In a similar way, azido acetate (−)-**15** afforded azido alcohol (−)-**16**, $[\alpha]_D = -42.1°$ ($c = 1.05$, $CHCl_3$).

3.1.16. (S)-2-Amino-2-ferrocenylethanol ((+)-17) and (R)-2-amino-2-ferrocenylethanol ((−)-17)

To a stirred suspension of 10% Pd/C (0.100 g) in EtOAc (15 ml) under a H_2 atmosphere, a solution of (*S*)-2-azido-2-ferrocenylethanol ((+)-**16**) (1.07 g, 3.95 mmol) in EtOAc (15 ml) was added via cannula. The mixture was stirred at r.t. for 12 h under H_2; the mixture was filtered through a Celite® pad and the solvent was removed under vacuum, to afford 0.967 g (100%) of the desired amino alcohol (+)-**17** as a yellow solid.

M.p. 97.8–101.5 °C. $[\alpha]_D = +11.1°$ ($c = 1.03$, MeOH). IR (KBr): $\nu = 3095$, 2925, 1653, 1559, 1458, 1412, 1258, 1105, 1040, 1001, 818, 733 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 2.10 (br s, 3H), 3.46 (m, 1H), 3.75 (m, 2H), 4.18 (m, 9H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 51.9 (CH), 65.7 (CH), 66.4 (CH), 67.2 (CH_2), 67.7 (CH), 67.8 (CH), 68.4 (CH), 90.8 (Cq). MS (CI, NH_3) $m/e = 245$ [M^+, 2%], 246 [$M + 1^+$, 7%], 229 [$M - 16^+$, 100%]. HRMS (EI) Calc. for $C_{12}H_{15}FeNO$: 245.0503. Found: 245.0492.

In a similar way, azido alcohol (−)-**16** afforded amino alcohol (−)-**17**, $[\alpha]_D = -9.7°$ ($c = 1.18$, MeOH).

3.1.17. (S)-4-Ferrocenyl-1,3-oxazolidin-2-one ((+)-18) and (R)-4-ferrocenyl-1,3-oxazolidin-2-one ((−)-18)

To a solution of (*S*)-2-amino-2-ferrocenylethanol ((+)-**17**) (0.100 g, 0.41 mmol) in CH_2Cl_2 (2 ml) was added a 6 M NaOH aq. solution (0.3 ml, 1.8 mmol). The resulting mixture was cooled to 0 °C and triphosgene (60 mg, 0.2 mmol) was added in one portion; stirring was maintained for 1 h at the same temperature and at this point TLC analysis showed that the reaction was complete. The dark-brown mixture was diluted

with water (8 ml) and the aq. phase was extracted with CH_2Cl_2 (3×10 ml). The combined organic extracts were dried over Na_2SO_4 and the solvents were distilled off under vacuum. Chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures of increasing polarity) afforded 82 mg (74%) of the title compound as an orange solid.

M.p. 154.2–155.0 °C. $[\alpha]_D = +24.9°$ ($c = 1.00$, $CHCl_3$). IR (KBr): $\nu = 3250$, 3095, 2910, 1790, 1755, 1415, 1390, 1245, 1110, 1035, 815 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 4.21 (m, 10H), 4.66 (m, 2H), 5.30 (br s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 52.1 (CH), 66.0 (CH), 66.4 (CH), 68.6 (CH), 68.6 (CH), 68.9 (CH), 71.5 (CH_2), 87.0 (Cq, Cp), 159.2 (Cq, CO). MS (CI, NH_3) $m/e = 271$ [M^+, 1%], 289 [$M + 18^+$, 74%], 306 [$M + 35^+$, 100%]. HRMS (EI) Calc. for $C_{13}H_{13}FeNO_2$: 271.0296. Found: 271.0298.

In a similar way, amino alcohol (−)-**17** furnished (*R*)-4-ferrocenyl-1,3-oxazolidin-2-one ((−)-**18**), $[\alpha]_D = -23.7°$ ($c = 1.09$, $CHCl_3$).

3.1.18. (R,R)-4-Ferrocenyl-2-[1-methyl-1-(ferrocenyl-(1,3-oxazolin-2-yl))ethyl]-1,3-oxazoline ((−)-19)

To a stirred solution of dimethylmalonic acid (27 mg, 0.20 mmol) in anhydrous THF (2 ml) were added a solution of *N*-hydroxysuccinimide (57 mg, 0.49 mmol) in anhydrous THF (1.5 ml) and a solution of *N*,*N*′-dicyclohexylcarbodiimide (101 mg, 0.49 mmol) in anhydrous THF (1.5 ml). The resulting mixture was stirred at r.t. for 2.5 h, and a solution of (*R*)-2-amino-2-ferrocenylethanol ((−)-**17**) (100 mg, 0.41 mmol) in anhydrous THF (2 ml) was added with a calibrated syringe. The reaction was monitored by TLC. When no starting amino alcohol remained (15 h), the solvent was removed at reduced pressure, the residue was taken up in EtOAc (15 ml) and washed with brine (3×10 ml). The combined organic extracts were dried over Na_2SO_4. Elimination of the solvent afforded a crude product that was purified by column chromatography on silica gel, eluting with C_6H_{14}–EtOAc mixtures of increasing polarity, to give 92 mg (77%) of the expected bis(hydroxyamide) as a yellow solid.

M.p. 54.2–57.0 °C. IR (KBr): $\nu = 3315$, 3090, 2915, 1730, 1655, 1505, 1185, 1125, 1110, 970, 820, 735 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 1.58 (s, 3H), 1.63 (s, 3H), 3.32 (m, 2H), 3.99 (m, 4H), 4.22 (m, 18H), 4.90 (m, 2H), 6.87 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 23.6 (CH_3), 50.8 (CH), 66.2 (CH), 66.4 (CH), 66.5 (CH), 68.2 (CH_2), 68.8 (CH), 86.0(CH), 86.0 (Cq, Cp), 173.7 (Cq, CO). MS (posit. electrospray) $m/e = 587$ [$M + 1^+$], 569.

To a stirred solution of the above-obtained compound (90 mg, 0.16 mmol) in 1,2-dichloroethane (3 ml), Et_3N (0.22 ml, 1.57 mmol), 4-(*N*,*N*-dimethylamino)pyridine (2 mg, 0.016 mmol) and *p*-toluenesulphonyl chloride (84 mg, 0.44 mmol) were added sequentially. The resulting mixture was heated to reflux for 2 h. Elimination of the solvent under vacuum followed by chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures) afforded 25 mg (29%) of the title compound as a brown semi-solid.

$[\alpha]_D = -45.4°$ ($c = 0.56$, $CHCl_3$). IR (NaCl film): $\nu = 3095$, 2910, 1737, 1655, 1498, 1470, 1245, 1110 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.60 (s, 6H), 4.14 (m, 18H), 4.40 (t, $J = 7.7$ Hz, 2H), 4.57 (dd, $J_1 = 9.8$ Hz, $J_2 = 8.0$ Hz, 2H), 4.93 (dd, $J_1 = 9.8$ Hz, $J_2 = 7.7$ Hz, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 24.5 (CH_3), 38.8 (Cq), 64.8 (CH), 66.4 (CH), 66.9 (CH), 67.86 (CH), 67.94 (CH), 68.4 (CH), 74.1 (CH_2), 90.4 (Cq, Cp), 168.8 (Cq). MS (CI, NH_3) $m/e = 550$ [M^+, 100%], 551 [$M + 1^+$, 37%], 568 [$M + 18^+$, 14%]. HRMS (EI) Calc. for $C_{29}H_{30}Fe_2N_2O_2$: 550.1006. Found: 550.1033.

3.1.19. (R)-N-(1-Ferrocenyl-2-hydroxyethyl)-(2-fluorophenyl)carboxamide ((−)-20)

To a stirred solution of (*R*)-2-amino-2-ferrocenylethanol ((−)-**17**) (0.500 g, 2.04 mmol) in anhydrous THF (3 ml) freshly distilled Et_3N (0.55 ml, 3.95 mmol) was added with a calibrated syringe. The resulting mixture was cooled to 0 °C, a solution of 2-fluorobenzoyl chloride (0.310 g, 1.96 mmol) in anhydrous THF (2.5 ml) was added dropwise, and the mixture was stirred at r.t. for 2 h, at which point TLC analysis showed the complete disappearance of the starting amino alcohol. The solvents were distilled under vacuum, the residue was taken up in CH_2Cl_2 (10 ml) and washed with brine (10 ml). The organic phase was dried over Na_2SO_4 and stripped of solvents at reduced pressure. Chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures) afforded 0.641 g (89%) of hydroxyamide (−)-**20** as a yellow solid.

M.p. 101.5–103.0 °C. $[\alpha]_D = -3.6°$ ($c = 1.00$, CH_2Cl_2). IR (KBr): $\nu = 3037$, 2915, 1727, 1640, 1510, 1473, 1105, 1035, 815, 757 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 3.36 (br s, 1H), 3.86 (dd, $J_1 = 10.8$ Hz, $J_2 = 3.8$ Hz, 1H), 4.00 (dd, $J_1 = 10.8$ Hz, $J_2 = 3.8$ Hz, 1H), 4.12 (dd, $J_1 = 6.0$ Hz, $J_2 = 3.8$ Hz, 1H), 4.23 (s, 9H), 5.10 (br, 1H), 7.1–7.6 (m, 3H), 8.17 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 51.3 (CH), 66.1 (CH), 66.5 (CH), 66.8 (CH_2), 66.9 (CH), 68.1 (CH), 68.6 (CH), 86.4 (Cq, Cp), 116.0 (CH), 120.2 (Cq), 124.8 (CH), 132.1 (CH), 133.5 (CH), 158.1 (Cq), 163.2 (Cq). MS (FAB(+)) $m/e = 367$ [M^+], 349 [$M - 18^+$], 399 [$M + 23^+$]. HRMS (EI) Calc. for $C_{19}H_{18}FFeNO_2$: 367.0671. Found: 367.0679.

3.1.20. (R)-4-Ferrocenyl-2-(2-fluorophenyl)-1,3-oxazoline ((−)-21)

To a solution of the hydroxyamide (−)-**20** (0.560 g, 1.53 mmol) in anhydrous CH_2Cl_2 (4.5 ml), 4-(*N*,*N*-dimethylamino)pyridine (93 mg, 0.76 mmol), freshly

distilled Et_3N (1.05 ml, 7.53 mmol) and *p*-toluenesulphonyl chloride (0.407 g, 2.13 mmol) were added sequentially. The resulting mixture was heated to reflux for 1 h, when TLC analysis showed that the reaction was complete, and cooled to r.t. After the addition of water (0.1 ml), stirring was maintained for 30 min and the reaction mixture was washed with water (3 × 5 ml). The organic phase was extracted with CH_2Cl_2 (5 ml). The combined organic phases were dried over Na_2SO_4 and the solvent was distilled off at reduced pressure. Chromatographic purification (silica gel, C_6H_{14}–EtOAc mixtures) gave 0.415 g (78%) of the desired oxazoline (−)-**21** as an orange solid.

M.p. 175.0–177.4 °C. $[\alpha]_D = -118°$ ($c = 1.02$, CH_2Cl_2). IR (KBr): $\nu = 2362$, 1636, 1560, 1497, 1457, 780 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 4.17 (m, 9H), 4.54 (t, $J = 8$ Hz, 1H), 4.71 (dd, $J_1 = 9.8$ Hz, $J_2 = 8$ Hz, 1H), 5.15 (dd, $J_1 = 10$ Hz, $J_2 = 7.8$ Hz, 1H), 7.20 (m, 2H), 7.46 (m, 1H), 7.93 (m, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 65.5 (CH), 66.3 (CH), 67.3 (CH), 68.0 (CH), 68.2 (CH), 68.5 (CH), 73.3 (CH_2), 89.9 (Cq, Cp), 116.2 (Cq), 116.6 (CH), 123.9 (CH), 131.3 (CH), 132.9 (CH), 160.4 (Cq), 162.9 (Cq). MS (CI, NH_3) $m/e = 349$ [M^+, 100%], 350 [$M + 1^+$, 25%]. HRMS (EI) Calc. for $C_{19}H_{16}FFeNO$: 349.0565. Found: 349.0565.

3.1.21. (R)-Diphenyl[2-(4-ferrocenyl(1,3-oxazolin-2-yl))phenil]phosphine ((−)-22)

To a cold (−78 °C), stirred suspension of (*R*)-4-ferrocenyl-2-(2-fluorophenyl)-1,3-oxazoline ((−)-**21**) (0.100 g, 0.29 mmol) in anhydrous THF (2 ml), under Ar atmosphere, a filtered THF solution of lithium diphenylphosphide (prepared from 13 mg (1.9 mmol) of Li, 0.262 g (1.0 mmol) of triphenylphosphine and 0.110 g (1.12 mmol) of NH_4Br in 4 ml of anhydrous THF) was added via cannula. The resulting mixture was stirred at −20 °C for 2 h and at r.t. for 12 h, and treated with a solution of Na_2SO_4 (0.425 g) in water (0.55 ml). The organic layer was filtered through a short pad of silica gel, that was subsequently washed with EtOAc. Elimination of the solvents under vacuum afforded a crude product that was purified by column chromatography on silica gel, eluting with C_6H_{14}–EtOAc mixtures of increasing polarity, to give 0.112 g (76%) of the title compound as an orange solid.

M.p. 54.5–56.3 °C. $[\alpha]_D = -72.4°$ ($c = 0.76$, CH_2Cl_2). IR (KBr): $\nu = 3069$, 1653, 1476, 1434, 1355, 1090, 1032, 959, 909, 743, 697 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 4.05 (m, 9H), 4.22 (t, $J = 7.9$ Hz, 1H), 4.38 (dd, $J_1 = 9.8$ Hz, $J_2 = 8.1$ Hz, 1H), 4.92 (dd, $J_1 = 9.8$ Hz, $J_2 = 8.1$ Hz, 1H), 6.93 (m, 2H), 7.2–7.5 (m, 10H), 7.95 (m, 2H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 65.4 (CH), 66.5 (CH), 66.9 (CH), 67.6 (CH), 67.9 (CH), 68.4 (CH), 73.1 (CH_2), 90.1 (Cq, Cp), 128.0, 128.2, 128.26, 128.32, 128.37, 128.41, 128.46, 129.2, 129.9, 130.0, 130.4 (CH–Ar), 131.8 (Cq–Ar, $J_{C-P} = 20$ Hz), 133.5, 133.8, 133.9, 134.2 (CH–Ar), 138.0 (Cq–Ar, $J_{C-P} = 10.4$ Hz), 138.1 (Cq–Ar, $J_{C-P} = 11.8$ Hz), 138.7 (Cq–Ar, $J_{C-P} = 25.5$ Hz), 163.2 (Cq). MS (FAB(+)) $m/e = 516$ [M^+], 331 [$M - 185^+$]. HRMS (EI) Calc. for $C_{31}H_{27}FeNOP$ 516.1180. Found: 516.1190.

3.1.22. Ethyl (2S,3S)-3-azido-3-ferrocenyl-2-hydroxypropanoate ((−)-23)

A cold (0 °C) solution of sodium ethoxide, prepared from 12 mg (0.52 mmol) of Na and anhydrous EtOH (12 ml), was added via cannula to azido acetate (+)-**6** (0.197 g, 0.51 mmol), and the resulting mixture was stirred at 0 °C until TLC showed that no starting product remained (1.5 h). A 10% aq. solution of citric acid (12 ml) was added and the mixture was extracted with CH_2Cl_2 (3 × 20 ml). The organic extracts were dried over Na_2SO_4 and the solvents were eliminated at reduced pressure. Column chromatography on silica gel, eluting with C_6H_{14}–EtOAc mixtures of increasing polarity, afforded 0.150 g (85%) of the desired 2-hydroxypropanoate (−)-**23** as a yellow–orange solid.

M.p. 85.5–87.0 °C. $[\alpha]_D = -61.7°$ ($c = 0.9$, $CHCl_3$). IR (KBr): $\nu = 3496$, 3097, 2929, 2109, 1735, 1266, 1108 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.37 (t, $J = 7.4$ Hz, 3H), 3.15 (d, $J = 6$ Hz, 1H, OH), 4.25 (m, 11H), 4.55 (d, $J = 2$ Hz, 1H), 4.61 (dd, $J = 6$ Hz, $J = 2$ Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.3 (CH_3), 62.5 (CH_2), 63.2 (CH), 68.1 (CH), 68.5 (CH), 68.6 (CH), 68.8 (CH), 68.9 (CH), 74.1 (CH), 84.0 (Cq, Cp), 172.1 (Cq, CO). MS (CI, NH_3) $m/e = 301$ [$M - N_3^+$, 100%], 344 [$M + 1^+$, 6%], 361 [$M + 18^+$, 71%]. HRMS (EI) Calc. for $C_{15}H_{17}FeN_3O_3$: 343.0619. Found: 343.0629.

3.1.23. Ethyl (2S,3S)-3-amino-3-ferrocenyl-2-hydroxypropanoate ((+)-24)

A solution of the azido ester (−)-**23** (0.100 g, 0.29 mmol) in EtOAc (1 ml) was stirred under an atmosphere of H_2 at r.t. for 18 h, in the presence of 10% Pd/C (10 mg). The reaction mixture was filtered through a Celite® pad, that was thoroughly washed with EtOAc. Elimination of the solvent at reduced pressure followed by chromatographic purification on Et_3N-pretreated silica gel (2.5% v/v) using C_6H_{14}–EtOAc mixtures of increasing polarity as eluents afforded 75 mg (82%) of ethyl (2*S*,3*S*)-3-amino-3-ferrocenyl-2-hydroxypropanoate ((+)-**24**) as an orange-coloured dense oil.

$[\alpha]_D = +49.5°$ ($c = 0.85$, $CHCl_3$). IR (NaCl film): $\nu =$ IR (KBr): 3380, 2990, 2910, 1715, 1550, 1395, 1248, 1090, 1010 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ (ppm) 1.31 (t, $J = 7.4$ Hz, 3H), 2.35 (br s, 3H, NH_2 + OH), 4.32 (m, 13H). ^{13}C-NMR (50 MHz, $CDCl_3$): δ (ppm) 14.2 (CH_3), 53.4 (CH), 61.7 (CH_2), 66.2 (CH),

67.2 (CH), 67.7 (CH), 67.9 (CH), 68.4 (CH), 74.5 (CH), 91.1 (Cq, Cp), 173.4 (Cq, CO). MS (CI, NH_3) $m/e =$ 301 [$M - NH_2^+$, 100%], 318 [$M + 1^+$, 36%]. HRMS (EI) Calc. for $C_{15}H_{19}FeNO_3$: 317.0714. Found: 317.0705.

4. Supplementary material

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-167245 for compound (+)-**11**. Copies of this data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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